

PRACA  
DOKTORSKA

INSTYTUT CHEMII ORGANICZNEJ  
POLSKIEJ AKADEMII NAUK



**Synteza nieracemicznych 3,3-dipodstawionych alkoholi  
allilowych oraz ich wykorzystanie w syntezie wysoce  
sfunkcjonalizowanych alliloamin i aminokwasów**

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Monotematyczny cykl publikacji z komentarzem przedstawiony  
Radzie Naukowej Instytutu Chemii Organicznej Polskiej Akademii Nauk  
w celu uzyskania stopnia doktora nauk chemicznych

Promotor: dr hab. Sebastian Stecko

A-21-6

K-p-172

K-c-121

K-c-125

K-c-130

Warszawa 2020

Biblioteka Instytutu Chemii Organicznej PAN

Org.-B.420/20



80000000341666



B. Org. 420/20

**Badania do pracy doktorskiej zostały wykonane w ramach projektów:**



*„Wykorzystanie asymetrycznego sigmatropowego przegrupowania cyjanianów allilowych w syntezie aminokwasów i ich pochodnych posiadających czwartorzędowy atom węgla”*  
**OPUS 8 NCN (2014/15/B/ST5/04398)**



*„Wykorzystanie pochodnych seryn jako prekursorów w syntezie farmakoforów morfolinowych i piperazynowych posiadających czwartorzędowe centrum stereogeniczne”*  
**PRELUDIUM 15 NCN (2018/29/N/ST5/01388)**



*„Synteza chiralnych 3,3-dipodstawionych alkoholi allilowych oraz ich wykorzystanie w syntezie czwartorzędowych alliloamin i aminokwasów”*  
**ETIUDA 6 NCN (2018/28/T/ST5/00267)**



***Pragnę serdecznie podziękować:***

***dr. hab. Sebastianowi Stecko, mojemu Promotorowi, za wskazanie drogi naukowej, poświęcony czas oraz nieocenioną pomoc podczas realizacji niniejszej pracy,***

***prof. Bartłomiejowi Furmanowi za wsparcie, życzliwość oraz umożliwienie rozpoczęcia ścieżki naukowej w Zespole II,***

***dr. Michałowi Pieczykolanowi za przekazaną wiedzę, poświęcony czas oraz ogromną życzliwość na początku mojej pracy,***

***wszystkim Koleżankom i Kolegom z Zespołów II, V oraz XXI za przyjazną atmosferę oraz wszelką pomoc przy realizacji eksperymentów.***



## SPIS TREŚCI

1. CEL BADAŃ.....	13
2. WSTĘP LITERATUROWY .....	17
2.1. Nienaturalne aminokwasy w syntezie organicznej.....	17
2.2. Alliloaminy w syntezie organicznej .....	19
2.3. Przegrupowania typu tlen-do-azotu .....	20
2.4. Alkohole allilowe w syntezie organicznej.....	25
3. BADANIA WŁASNE – PRZEWODNIK PO PUBLIKACJACH .....	39
3.1. Synteza $\beta,\beta$ -dipodstawionych alkoholi allilowych .....	40
3.2. Przegrupowanie cyjanianów allilowych do izocyjanianów – synteza $\alpha,\alpha$ - dipodstawionych alliloamin .....	45
3.3. Funkcjonalizacja izocyjanianów – synteza <i>N</i> -podstawionych alliloamin .....	46
3.4. Funkcjonalizacja wiązania podwójnego w alliloaminach .....	47
3.4.1. Wykorzystanie alliloamin w syntezie $\alpha,\alpha$ -dipodstawionych aminokwasów ...	48
3.4.2. Wykorzystanie alliloamin w syntezie aminoalkoholi, diamin oraz związków heterocyklicznych.....	48
3.5. Synteza alliloamin w skali gramowej.....	50
4. PODSUMOWANIE .....	52
5. BIBLIOGRAFIA .....	54
6. PUBLIKACJE ORIGINALNE.....	58
7. OŚWIADCZENIA WSPÓŁAUTORÓW PUBLIKACJI.....	132





## SPIS PUBLIKACJI WCHODZĄCYCH W SKŁAD ROZPRAWY DOKTORSKIEJ

1. M. Pieczykolan, A. Narczyk, S. Stecko, *The synthesis of chiral  $\beta,\beta$ -diaryl allylic alcohols and their use in the preparation of  $\alpha$ -tertiary allylamines and quaternary  $\alpha$ -amino acids*, *J. Org. Chem.* **2017**, *82*, 5636-5651,
2. A. Narczyk, M. Pieczykolan, S. Stecko, *The synthesis of non-racemic  $\beta$ -alkyl- $\beta$ -aryl-disubstituted allyl alcohols and their transformation into quaternary allylamines and amino acids*, *Org. Biomol. Chem.*, **2018**, *16*, 3921-3946,
3. A. Narczyk, S. Stecko, *The synthesis of unnatural  $\alpha$ -alkyl- and  $\alpha$ -aryl-substituted serine derivatives*, *Org. Biomol. Chem.*, **2020**, *18*, 1204-1213.

Publikacja wystana do redakcji:

4. A. Narczyk, S. Stecko, *An entry to enantiopure  $\beta$ -tertiary- $\beta$ -amino alcohols, building blocks for synthesis of aziridine, piperazine, and morpholine scaffolds.*

Spis publikacji nie wchodzących w skład rozprawy doktorskiej:

5. M. Szewczyk, M. Morawiak, A. Narczyk, Z. Pakulski, Z. Urbanczyk-Lipkowska, *Chlorogenic Acids Mimics - Synthesis, Structure and Antioxidant Activity*, *J. Chem. Biochem.*, **2018**, *6*, 28-37,
6. A. Narczyk, M. Mrozowicz, S. Stecko, *Total synthesis of levetiracetam*, *Org. Biomol. Chem.*, **2019**, *17*, 2770-2775.

## SPIS WYSTĄPIEŃ KONFERENCYJNYCH

1. „5th Symposium on Asymmetric Synthesis”  
12-14.09.2019 Warszawa, Polska (wystąpienie w formie posteru),
2. „3rd International Symposium on Synthesis and Catalysis 2019 (ISySyCat2019)”  
3.09-6.09.2019, Evora, Portugalia (wystąpienie w formie prezentacji ustnej),
3. „21st European Symposium on Organic Chemistry”  
14.07-18.07.2019, Wiedeń, Austria (wystąpienie w formie posteru),
4. „XVI International Congress of Young Chemists – YoungChem2018”  
10.10-14.10.2018, Bydgoszcz, Polska (wystąpienie w formie prezentacji ustnej),
5. IX Sympozjum „Postępy w syntezie związków nieracemicznych”  
17-20.10.2018, Karpacz, Polska (wystąpienie w formie prezentacji ustnej)
6. 10th Biennial International Conference on Organic Synthesis „Balticum Organicum Syntheticum 2018”  
1-4.07.2018, Tallinn, Estonia (wystąpienie w formie posteru),
7. „VI Łódzkie Sympozjum Doktorantów Chemii”  
10-11.05.2018, Łódź, Polska (wystąpienie w formie posteru),
8. „20th JCF-Frühjahrssymposium”  
21-24.03.2018, Konstancja, Niemcy (wystąpienie w formie posteru),
9. 20th International Symposium „Advances in the Chemistry of Heteroorganic Compounds”  
23-24.11.2017, Łódź, Polska (wystąpienie w formie posteru),
10. XV International Congress of „Young Chemists – YoungChem2017”  
11.10-15.10.2017, Lublin, Polska (wystąpienie w formie prezentacji ustnej),
11. XII Warszawskie Seminarium Doktorantów Chemików „ChemSession'17”  
9.06.2017, Warszawa, Polska (wystąpienie w formie posteru),
12. „V Łódzkie Sympozjum Doktorantów Chemii”  
11-12.05.2017, Łódź, Polska (wystąpienie w formie posteru),
13. Ogólnopolskie Studenckie Mikrosympozjum Chemików „Chemia – przyszłość zaczyna się dziś”  
30.03-02.04.2017, Białystok, Polska (wystąpienie w formie prezentacji ustnej),
14. XIX International Symposium „Advances in the Chemistry of Heteroorganic Compounds”  
25.11.2016, Łódź, Polska (wystąpienie w formie posteru),
15. XII Warszawskie Seminarium Doktorantów Chemików „ChemSession'16”  
10.06.2016, Warszawa, Polska (wystąpienie w formie posteru).

## STRESZCZENIE W JĘZYKU POLSKIM

Celem niniejszej rozprawy doktorskiej było wykorzystanie reakcji przegrupowania cyjanianów allilowych do izocyjanianów w syntezie  $\alpha$ -aminokwasów posiadających centrum stereogeniczne zlokalizowane na czteropodstawionym  $\alpha$ -atomie węgla. Cyjaniany allilowe można otrzymać z odpowiednich łatwo dostępnych karbaminianów allilowych. Przekształcenie enancjomerycznie czystych karbaminianów allilowych umożliwia stereospecyficzne tworzenie nowego wiązania C-N, z efektywnym transferem chiralności, poprzez cykliczny stan przejściowy. Realizacja przedstawionego projektu, wymagała także zaproponowania efektywnej metody pozyskiwania  $\beta,\beta$ -dipodstawionych nieracemicznych alkoholi allilowych.

Podczas realizacji niniejszej pracy doktorskiej opracowano: (1) efektywne i komplementarne metody syntezy  $\beta,\beta$ -dipodstawionych alkoholi allilowych o wysokiej czystości optycznej i z wysoką selektywnością *E/Z* a następnie, (2) dogodne i ogóle metody syntetyczne pozwalające na łatwy dostęp do szerokiej gamy: (a)  $\alpha,\alpha$ -diarylowych, (b)  $\alpha$ -alkilowych,  $\alpha$ -arylowych, (c)  $\alpha,\alpha$ -dialkilowych nienaturalnych aminokwasów. Opracowana metoda może stanowić użyteczne narzędzie w przemyśle farmaceutycznym lub chemicznym w syntezie związków o udowodnionej aktywności biologicznej lub farmakologicznej. Warto także nadmienić, że otrzymane aminokwasy są nie tylko atrakcyjnymi związkami biologicznie aktywnymi, ale znajdują także zastosowanie jako chiralne katalizatory lub ligandy w enancjoselektywnych transformacjach.

## ABSTRACT IN ENGLISH

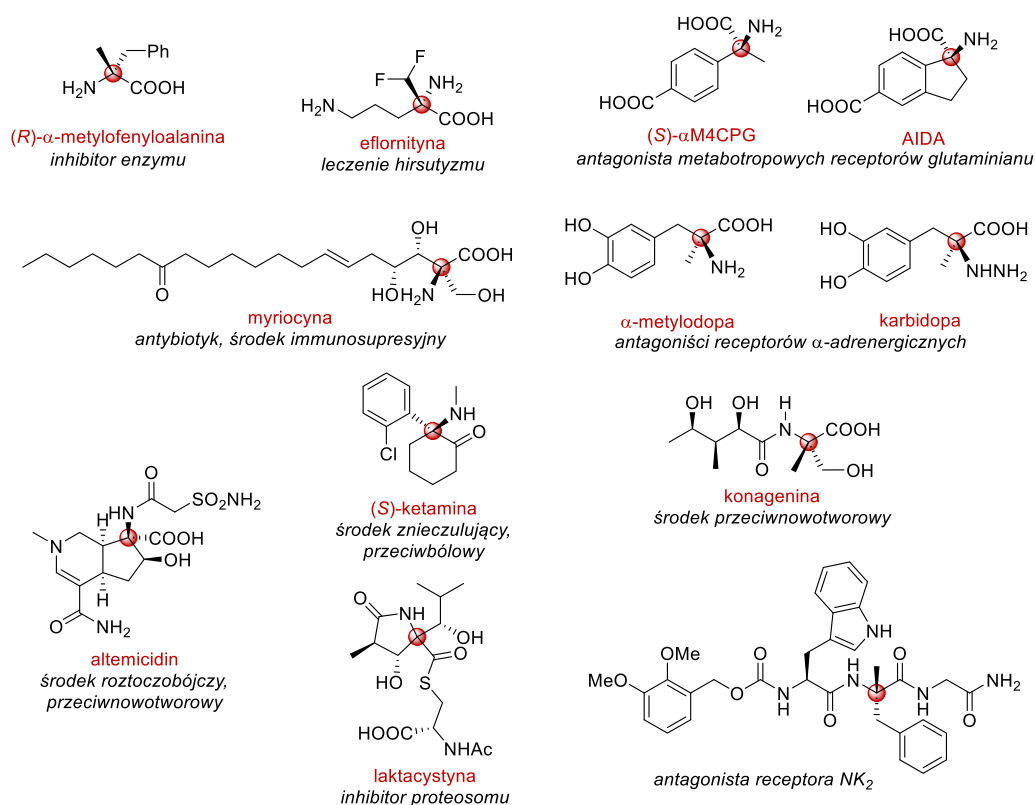
The main aim of this PhD dissertation was to demonstrate that the rearrangement of allyl cyanates can serve as a key step in the preparation of  $\alpha$ -amino acids bearing a tetrasubstituted  $\alpha$ -carbon. Allyl cyanates species can be prepared from the corresponding readily available allyl carbamates. The transformation of enantiomerically pure allyl carbamates enables the stereospecific formation of a new C-N bond with a complete chirality transfer through a cyclic transition state. The implementation of this project also required to propose an effective method of obtaining  $\beta,\beta$ -disubstituted nonracemic allyl alcohols.

During the realization of this PhD dissertation, I developed: (1) effective and complementary methods for the synthesis of  $\beta,\beta$ -disubstituted allyl alcohols with high stereoselectivity and high *E/Z* selectivity, followed by (2) convenient and general synthetic methods allowing easy access to a wide range of: (a)  $\alpha,\alpha$ -diaryl, (b)  $\alpha$ -alkyl, $\alpha$ -aryl, (c)  $\alpha,\alpha$ -dialkyl unnatural amino acids. The developed method can be a useful tool, for the pharmaceutical or chemical industry, in the synthesis of compounds bearing biological or pharmacological activity. It is also worth mentioning, that the obtained amino acids are not only attractive biologically active compounds, but also can be used as chiral catalysts or ligands in enantioselective transformations.

# 1. CEL BADAŃ

Aminokwasy są klasą związków organicznych o kluczowym znaczeniu dla organizmów żywych. Uczestniczą w wielu ważnych procesach życiowych, jak również są podstawowymi elementami budulcowymi między innymi białek, hormonów czy neuroprzekazników. Struktury białek organizmów żywych tworzy 20 podstawowych, tak zwanych kanonicznych, aminokwasów białkowych. Jednakże, oprócz tej dwudziestki znanych jest ponad 500 innych aminokwasów, zwanych niebiałkowymi, które również można znaleźć w strukturze niektórych białek oraz innych produktów pochodzenia naturalnego. Grupę tą poszerzają aminokwasy, które pozyskiwane są w wyniku syntezy organicznej. Wszystkie z nich określane są mianem nienaturalnych aminokwasów.<sup>1</sup>

Nienaturalne aminokwasy i ich pochodne, takie jak alliloaminy czy aminoalkohole, są nie tylko ważnymi blokami budulcowymi w syntezie organicznej, ale stanowią także elementy strukturalne substancji biologicznie czynnych. Niejednokrotnie same nienaturalne aminokwasy lub ich proste pochodne są też substancjami czynnymi leków, stąd ich istotne znaczenie z punktu widzenia chemii medycznej. Wiele z nich można znaleźć zarówno w naturalnych jak i syntetycznych peptydach oraz peptydomimetykach, ponieważ wbudowanie ich w strukturę peptydów znacznie zmienia ich właściwości, niejednokrotnie zwiększając ich bioaktywności i biodostępności. Na skutek zmiany ich konformacji, w porównaniu do natywnych układów, oraz poprzez usztywnienie struktury takie peptydomimetyki wykazują zwiększoną trwałość i stabilność wobec enzymów proteolitycznych. Dzięki temu odgrywają one kluczową rolę w projektowaniu nowych peptydów i peptydomimetyków wykazujących aktywność biologiczną.<sup>1,2</sup>

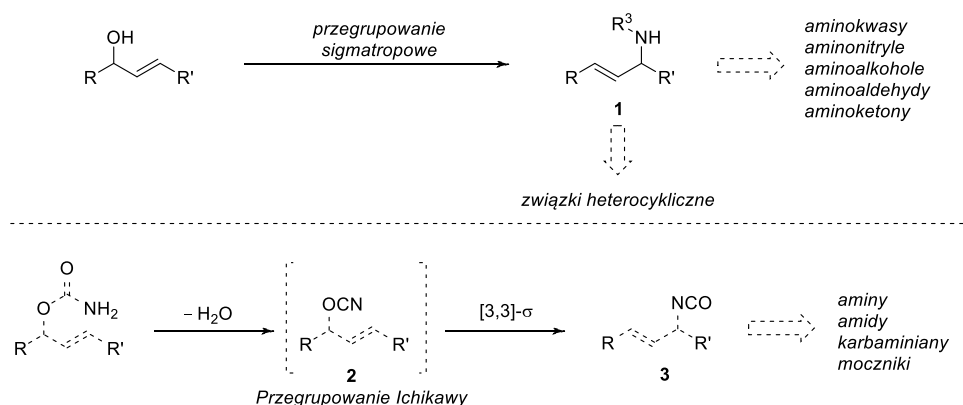


**Rysunek 1.** Wybrane związki biologicznie aktywne posiadające fragment nienaturalnego aminokwasu.

Ważną grupą nienaturalnych aminokwasów są α,α-dipodstawione aminokwasy, zwane też zwyczajowo „czwartorzędowymi” aminokwasami.<sup>3</sup> Aminokwasy te posiadają czteropodstawiony atom węgla w pozycji α, przy którym oprócz grup aminowej i karboksylowej znajdują się dwa

dotatkowe podstawniki. Wybrane przykłady takich aminokwasowych pochodnych wykazujących aktywność biologiczną przedstawiłam na powyższym rysunku. Istotnym czynnikiem limitującym szersze wykorzystanie  $\alpha,\alpha$ -dipodstawionych aminokwasów w medycynie jest ich ograniczona dostępność. Znanych jest kilka strategii syntezy „czwartorzędowych” aminokwasów lub ich prekursorów, jednakże żadna z tych metod nie jest uniwersalna.<sup>4</sup> Opracowane dotychczas strategie charakteryzują się niewystarczającą efektywnością i/lub stereoselektywnością. W wielu przypadkach kluczowym problemem jest zawada steryczna, która uniemożliwia skuteczne łączenie reagentów w procesach międzycząsteczkowych. W rezultacie cały czas poszukiwane są nowe metody pozyskiwania aminokwasów, zwłaszcza tych nienaturalnych.

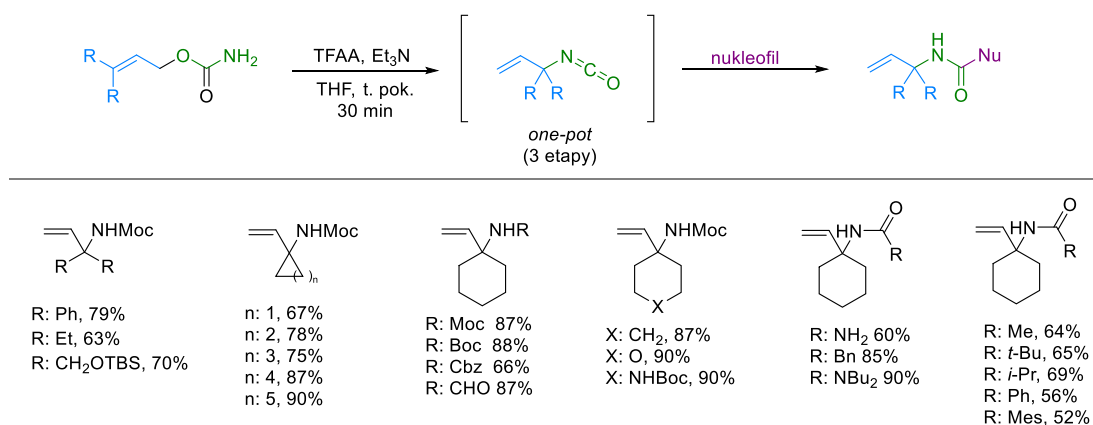
Atrakcyjnymi prekursorami w syntezie sterycznie zatłoczonych aminokwasów mogą być odpowiednie alliloaminy otrzymywane w wyniku reakcji przegrupowań molekularnych, na przykład przegrupowań sigmatropowych.<sup>5,6</sup> W Zespole XXI Instytutu Chemii Organicznej PAN od kilku lat prowadzone są prace nad wykorzystaniem reakcji pericyklicznych w syntezie substancji biologicznie aktywnych, w tym substancji pochodzenia naturalnego jak również syntetycznych związków farmakoaktywnych. W ostatnich latach prace te koncentrują się między innymi nad wykorzystaniem reakcji przegrupowań [3,3]-sigmatropowych w syntezie alliloamin oraz funkcjonalizacji tych ostatnich prowadzącej do nienaturalnych aminokwasów i ich pochodnych<sup>7</sup> oraz peptydowych leków.<sup>8</sup>



**Schemat 1.** Wykorzystanie reakcji przegrupowań [3,3]-sigmatropowych w syntezie alliloamin.

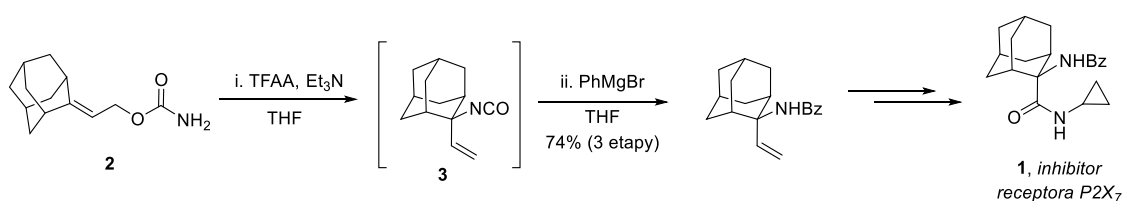
Szczególnie atrakcyjna okazała się reakcja przegrupowania cyjanianów allilowych do odpowiednich izocyjanianów, zwana też reakcją Ichikawy.<sup>5,9</sup> Największą zaletą tego podejścia jest tworzenie się, jako produktu pośredniego, izocyjanianu allilowego, którego dalsza funkcjonalizacja umożliwia syntezę szerokiej gamy strukturalnie zróżnicowanych alliloamin. Takie alliloaminy, jako związki bifunkcyjne, są użytecznymi blokami budulcowymi w syntezie organicznej.<sup>10</sup>

W 2016 roku, w Zespole XXI IChO PAN, wykazano, że ta prosta transformacja łatwo dostępnych karbaminianów allilowych może być użytecznym narzędziem w syntezie  $\alpha,\alpha$ -geminalnie dipodstawionych alliloamin.<sup>11</sup> Metoda okazała się niezwykle efektywna w syntezie zarówno układów acyklicznych, jaki i cyklicznych, w tym układów heterocyklicznych. Co więcej, stosując szeroką gamę odczynników nukleofilowych do bezpośredniej funkcjonalizacji tworzącego się izocyjanianu, możliwe było otrzymanie odpowiednich karbaminianów, pochodnych mocznika lub amidów.



**Schemat 2.** Synteza  $\alpha,\alpha$ -geminalnie dipodstawionych alliloamin.

W pracach tych zademonstrowano także praktyczne wykorzystanie przedstawionej strategii w syntezie substancji bioaktywnych. Jedną z nich była adamantylowa pochodna **1**, będąca inhibitorem receptora P2X<sub>7</sub>. Przykład ten doskonale prezentuje zalety jakie wynikają z wyboru reakcji Ichikawy jako kluczowej dla całej syntezy. Powstający w wyniku odwodnienia karbaminianu **2** (i następczego przegrupowania) izocyjanian allilowy **3**, poddano bezpośrednio reakcji z PhMgBr, co pozwoliło na wprowadzenie fragmentu benzamidowego, który jest obecny w docelowej strukturze **1**.<sup>11</sup>

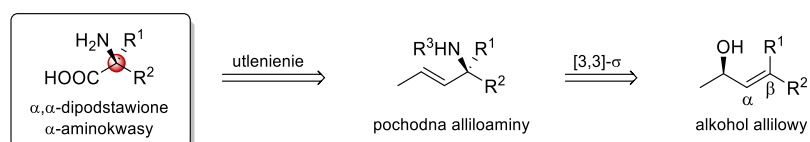


**Schemat 3.** Synteza inhibitora receptora P2X<sub>7</sub>.

Mając na uwadze ogromny potencjał wykorzystania reakcji przegrupowań [3,3]-sigmatropowych, jako narzędzia w syntezie alliloamin oraz ich pochodnych. Postanowiłam sprawdzić czy analogiczne podejście umożliwiłoby syntezę alliloamin posiadających dwa różne podstawniki w pozycji alfa, dając dostęp do chiralnych związków posiadających centrum stereogeniczne zlokalizowane na czteropodstawionym atomie węgla. Takie produkty byłyby bardzo atrakcyjnymi prekursorami aminokwasów, aminoalkoholi lub  $\alpha$ -trzeciorzędowych amin i diamin (Schemat 1). Ponadto można by je wykorzystać jako bloki budulcowe w syntezie związków heterocyklicznych oraz karbocyklicznych amin.

W związku z powyższym, przystępując do prac badawczych, postawiłam sobie za cel opracowanie atrakcyjnej metody otrzymywania  $\alpha,\alpha$ -dipodstawionych aminokwasów w oparciu o dwa kluczowe etapy: (1) reakcję przegrupowania [3,3]-sigmatropowego aktywowanych alkoholi allilowych do alliloamin oraz (2) oksydacyjną funkcjonalizację wiązania podwójnego (Schemat 4). Zaletą takiego podejścia jest wewnątrzcząsteczkowy przebieg reakcji przegrupowania sigmatropowego, umożliwiający tworzenie sterycznie zatłoczonych układów, których synteza w wariacie międzycząsteczkowym jest niejednokrotnie utrudniona lub wręcz niemożliwa. Ponadto, reakcja przegrupowania przebiegająca poprzez cykliczny stan przejściowy z całkowitym [1,3]-transferem chiralności umożliwia efektywne i stereospecyficzne tworzenie nowego centrum stereogenicznego.





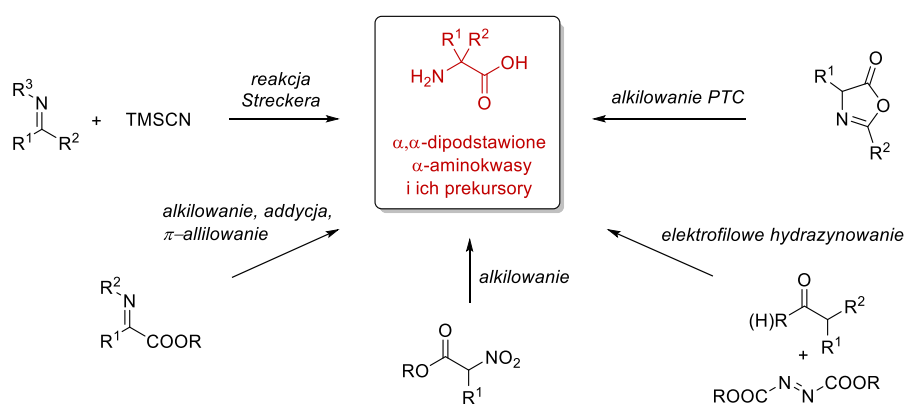
**Schemat 4.** Strategia syntezy nienaturalnych  $\alpha$ -aminokwasów.

Podczas realizacji mojej pracy doktorskiej, postawiłam sobie za zadanie opracowanie dogodnych i ogólnych metod syntetycznych pozwalających na łatwy dostęp do szerokiej gamy: (1)  $\alpha, \alpha$ -diarylowych, (2)  $\alpha$ -alkilowych- $\alpha$ -arylowych, (3)  $\alpha, \alpha$ -dialkilowych „czwartorzędowych” aminokwasów. Z uwagi na ogromne znaczenie wymienionych klas związków jako bloków budulcowych w syntezie organicznej oraz ich znaczenie dla chemii medycznej, opracowane metody syntetyczne mogłyby w przyszłości znaleźć potencjalne zastosowanie w przemyśle farmaceutycznym lub chemicznym w syntezie istotnych związków o aktywności biologicznej lub farmakologicznej.

## 2. WSTĘP LITERATUROWY

### 2.1. Nienaturalne aminokwasy w syntezie organicznej

Chociaż minęły już prawie trzy dekady od opracowania pierwszych asymetrycznych metod syntezy  $\alpha,\alpha$ -dipodstawionych aminokwasów<sup>12</sup> to nadal istnieją poważne wyzwania w otrzymywaniu tej klasy związków. Znanych jest kilka strategii syntezy nienaturalnych aminokwasów lub ich prekursorów. Wśród nich należy wymienić klasyczną reakcję Streckera, nukleofilową addycję do iminoestrów oraz niektóre procesy katalizowane metalami przejściowymi (Schemat 5).<sup>4</sup> Chociaż istnieje wiele interesujących strategii, nadal brak ogólnej metody syntezy omawianej grupy aminokwasów. Przedstawione w literaturze metody mają kilka istotnych wad i ograniczeń, w szczególności gdy docelowo mają prowadzić do produktów enancjomerycznie wzbogaconych.



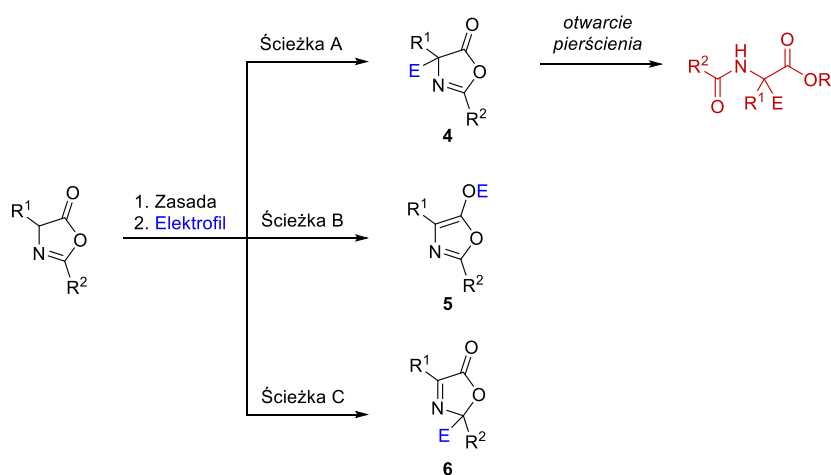
Schemat 5. Podstawowe strategie syntezy nienaturalnych aminokwasów lub ich prekursorów.

W większości przedstawionych powyżej strategii, indukcja asymetryczna jest wynikiem zastosowania strukturalnie złożonych chiralnych kompleksów metali<sup>13</sup> (np. palladu) lub organokatalizatorów<sup>14</sup>, których często koszt jest wysoki, a synteza czasochłonna. Wykorzystuje się też chiralne pomocniki w ilości stechiometrycznej co czyni taką strategię niekorzystną z punktu ekonomii atomowej. W przypadku enancjoselektywnego cyjanowania aldimin (reakcja Streckera) opracowano szereg efektywnych układów katalitycznych oraz pomocników chiralnych. Jednakże analogiczny proces dla sterycznie bardziej rozbudowanych ketimin, jest mniej efektywny za równo pod kątem reaktywności jak i enancjoselektywności,<sup>15</sup> między innymi z powodu konkurencyjnej reakcji izomeryzacji do odpowiedniej enaminy. Co więcej, wysoką enancjoselektywność obserwuje się wyłącznie wtedy, gdy występuje spora różnica w rozmiarze podstawników w ketiminie.<sup>16</sup> Ponadto, reakcjom z udziałem iminoestrów często towarzyszy szereg reakcji ubocznych, takich jak redukcja wiązania C=N w iminie czy addycja do atomu azotu zamiast do atomu węgla.<sup>13a</sup>

Reakcja elektrofilowego hydrazynowania enolanów,<sup>17</sup> wydawałaby się jednym z najprostszych podejść w syntezie  $\alpha$ -aminokwasów, jednakże ogranicza ją dostępność do elektrofilowych źródeł azotu. W przypadku wykorzystania jako substratów imin (reakcja Streckera czy addycja do iminoestrów), nie zawsze istnieje dowolność doboru reagentów tego typu. Często synteza jest ograniczona wyłącznie do aktywowanych substratów, np. *N*-tosylo- lub *N*-nosyloimin. Usunięcie, w kolejnych etapach, takich grup zabezpieczających wymaga często drastycznych warunków, na przykład przy użyciu sodu w amoniaku. Warunki te mogą być niekompatybilne z innymi grupami funkcyjnymi obecnymi w cząsteczce. Co więcej, konieczność

przeprowadzenia dodatkowych reakcji zabezpieczenia grupy aminowej, wydłuża samą syntezę obniżając jej sumaryczną ekonomię. Natomiast, w reakcji Streckera konieczna jest następcza hydroliza grupy CN do kwasu karboksylowego, co także zwiększa ilość etapów prowadzonej syntezy. Podobnie dla reakcji pochodnych  $\alpha$ -nitrokarboksylowych, niezbędna jest ich dalsza funkcjonalizacja otrzymanych produktów, polegająca na redukcji grupy nitrowej.

Dogodnymi prekursorami  $\alpha,\alpha$ -dipodstawionych  $\alpha$ -aminokwasów są azlaktony.<sup>18</sup> Dzięki łagodnym warunkom alkirowania azlaktonów w warunkach katalizy przeniesienia międzyfazowego (PTC) proces ten znalazł szerokie zastosowanie w syntezie prekursorów  $\alpha$ -aminokwasów. W warunkach PTC, azlaktony mogą reagować z różnymi reagentami elektrofilowymi, między innymi nitroalkenami,  $\alpha,\beta$ -nienasyconymi aldehydami/ketonami czy estrami. Istotnym aspektem tych procesów jest ich regioselektywność oraz możliwość jej kontroli co ma istotne znaczenie z syntetycznego punktu widzenia. Reakcja z odczynnikami elektrofilowymi może bowiem zachodzić na trzy różne sposoby. Kluczowe jest żeby proces przebiegał na atomie węgla C-4 (Schemat 6, Ścieżka A), bo tylko wtedy prowadzi do pożądanych produktów **4**, które mogą posłużyć jako prekursorzy w syntezie  $\alpha,\alpha$ -dipodstawionych  $\alpha$ -aminokwasów. Następnie, otwarcie 5-członowego pierścienia azlaktonu **4** prowadzi do pochodnej aminokwasowej. Konkurencyjne ścieżki reakcji przebiegają w udziale tautomerycznych form azlaktonów i mogą prowadzić do produktu sfunkcjonalizowanego na atomie tlenu (Schemat 6, Ścieżka B) oraz na atomie węgla C-2 (Schemat 6, Ścieżka C) z utworzeniem produktów ubocznych **5** oraz **6**.



**Schemat 6.** Azlaktony w syntezie  $\alpha,\alpha$ -dipodstawionych  $\alpha$ -aminokwasów.

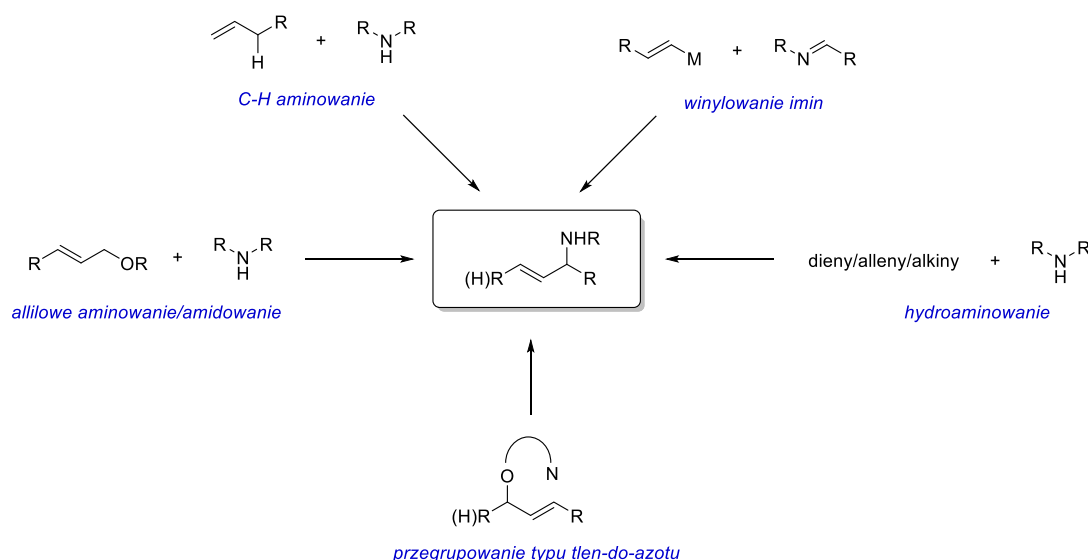
W odniesieniu do syntezy sterycznie zatłoczonych „czwartorzędowych” aminokwasów, omówione powyżej procesy, charakteryzują się nie tylko niską skutecznością, ale także niezadowalającą stereoselektywnością. Co więcej brak im ogólności, wspomniane metodologie często sprawdzają się tylko dla wąskiego zakresu substratów albo gdy występują spore różnice w wielkości podstawników.<sup>13a</sup> Często ogranicza je także dostęp to substratów, takich jak odpowiednie iminy czy hydrazyny. Co więcej, metodom tym towarzyszy szereg reakcji ubocznych, obniżając tym samym wydajność procesu.<sup>13a,18</sup>

Nieskuteczność wspomnianych strategii, w wielu przypadkach spowodowana jest zawadą steryczną, która utrudnia wydajne i selektywne łączenie się reagentów w procesach międzycząsteczkowych. Z tego względu, procesy wewnątrzcząsteczkowe, takie jak reakcje przegrupowań sigmatropowych, wydają się interesującą alternatywą. Szczególnie atrakcyjnymi prekursorami  $\alpha,\alpha$ -dipodstawionych aminokwasów są odpowiednie alliloaminy, otrzymywanie

w wyniku wspomnianych przegrupowań. Chociaż związki te są bardzo ważnymi blokami budulcowymi, ich synteza nie jest prostym zadaniem i to właśnie na tej klasie związków oraz metodom ich syntezy chciałabym się skupić w dalszej części niniejszej rozprawy.

## 2.2. Alliloaminy w syntezie organicznej

Alliloaminy to grupa związków chemicznych, które można znaleźć w strukturze wielu substancji o aktywności biologicznej.<sup>5</sup> Ponadto, są one chętnie używanymi produktami pośrednimi w syntezie bardziej złożonych molekuł.<sup>19</sup> Zarówno grupa aminowa, jak i wiązanie wielokrotne, są grupami które w dosyć łatwy sposób można przekształcić w inne użyteczne pochodne. Z uwagi na tak cenne właściwości, znanych jest szereg metod ich syntezy, także w wariacie stereoselektywnym. Spośród tych metod na szczególną uwagę zasługują strategie przedstawione na Schemacie 7. Pierwszą z nich są reakcje tworzenia wiązania C-N poprzez reakcję bezpośredniego C-H aminowania alkenów w pozycji allilowej.<sup>20</sup> Kolejną grupę stanowią transformacje oparte na reakcjach podstawienia w układzie alkoholu allilowego (lub jego pochodnej) za pomocą reagentów będących nośnikiem grupy aminowej (substytucja S<sub>N</sub>2, allilowe aminowanie/amidowanie).<sup>10a,21,22</sup> Alliloaminy można również utrzymać poprzez reakcje winylowania imin lub hydroaminowanie wiązań podwójnych.<sup>23</sup>



**Schemat 7.** Strategie syntezy alliloamin.

Wszystkie wymienione strategie można zaliczyć do współczesnych metod syntezy alliloamin. Jednak pomimo ich niewątpliwiej atrakcyjności, mają one też szereg wad i ograniczeń. Większość z nich to procesy katalityczne, wymagające złożonych katalizatorów na bazie kompleksów metali przejściowych, zwłaszcza palladu, irydu czy rodu. Reakcje bezpośredniego C-H aminowania oraz hydroaminowania są jednymi z najbardziej pożądanym procesów ze względu na ich ekonomię atomową. Wykazano, że zarówno dla reakcji C-H aminowania,<sup>20</sup> jak i hydroaminowania,<sup>23</sup> układ katalizowany palladem jest najlepszym układem umożliwiającym syntezę alliloamin o wysokiej czystości optycznej. Jednakże niejednokrotnie są to katalizatory drogie oraz strukturalnie skomplikowane. Ponadto, często niezbędny jest precyzyjny dobór reagentów, tak aby aminowanie zachodziło regioselektywnie. W tym celu zwykle stosuje się symetryczne substraty ewentualnie substraty posiadające jedną grupę allilową znacznie bardziej aktywną lub mniej dostępną. Brak kontroli nad regioselektywnością powstawania produktu

liniowego względem rozgałęzionego, stanowi ciągle nierozwiązany problem reakcji C-H aminowania.

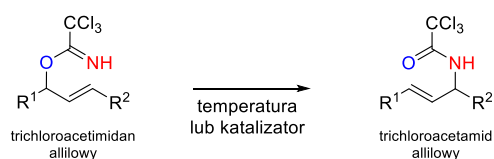
Inną grupą reakcji otrzymywania pochodnych alliloamin są transformacje grupy funkcyjnej znajdującej się uprzednio w pozycji allilowej. Istnieje szeroki wachlarz takich metod, począwszy od reakcji typu  $S_N2$ , a skończywszy na reakcjach opartych na allilowym aminowaniu/amidowaniu typu Tsuji-Trosta wykorzystujących kompleksy palladu, rodu lub irydu.<sup>10a,21,22</sup> Katalizator w tej reakcji determinuje kierunek ataku czynnika nukleofilowego w odpowiednim miejscu cząsteczki oraz faworyzując jedną ze stron fragmentu alilowego zapewniając odpowiednio kontrolę regio- oraz stereoselektywności procesu. W przypadku substratów allilowych z terminalnym wiązaniem podwójnym, w obecności kompleksów palladu tworzą się liniowe alliloaminy. Natomiast tworzenie „rozgałęzionych” alliloamin jest bardziej preferowane, gdy reakcje prowadzi się wobec kompleksów irydu.<sup>24</sup> Pomimo opracowania wielu metod, nadal problematyczną jest kwestia kontroli regioselektywności w przypadku substratów allilowych z wewnętrznym, a nie terminalnym, wiązaniem podwójnym. Co więcej, nie zawsze możliwa jest też eliminacja procesów ubocznych jak choćby w przypadku C-H aminowania, któremu często towarzyszy proces azirydowania.<sup>25</sup>

Do tej grupy metod syntezy alliloamin, szczególnie optycznie czynnych, możemy także zaliczyć różnego rodzaju przegrupowania typu tlen-do-azotu, w wyniku których następuje kontrolowane zerwanie wiązania C-O i utworzenie wiązania C-N. Właśnie na tej grupie przegrupowań chciałabym się skupić w następnym rozdziale.

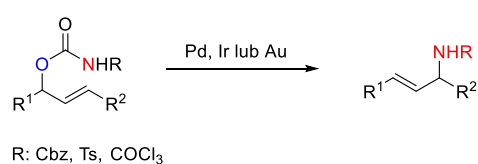
### 2.3. Przegrupowania typu tlen-do-azotu

Jak wspomniałam powyżej, spośród licznych metod syntezy alliloamin na szczególną uwagę zasługują reakcje przegrupowań typu tlenu-do-azotu w obrębie układu allilowego.<sup>6c</sup> Przykładem takiego procesu może być reakcja przegrupowania Overmana (Schemat 8.1) albo reakcja dekarboksylacyjnego allilowego amidowania przedstawiona na Schemacie 8.2. Innym przykładem tego typu transformacji jest przegrupowanie cyjanianów allilowych do izocyjanianów, zwane też reakcją Ichikawy (Schemat 8.3), które to stało się kluczowym przekształceniem w dalszej części mojej rozprawy doktorskiej.

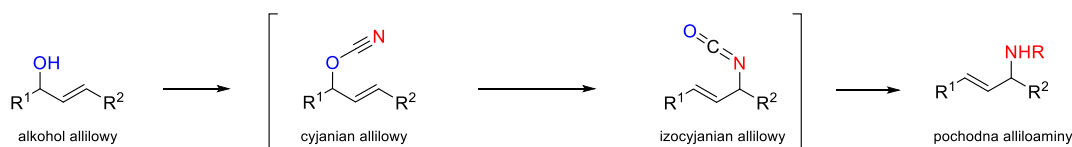
#### 1) Przegrupowanie trichloroacetimidatów (przegrupowanie Overmana)



#### 2) Dekarboksylacyjne allilowe amidowanie



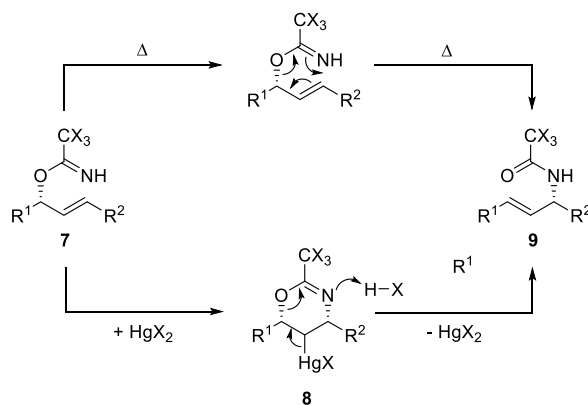
#### 3) Przegrupowanie cyjanianów allilowych (przegrupowanie Ichikawy)



**Schemat 8.** Przykłady reakcji przegrupowań typu tlenu-do-azotu.

Reakcja przegrupowania Overmana (Schemat 8.1), analogicznie jak reakcja przegrupowania Ichikawy, są przykładami reakcji pericyklicznych, w których następuje

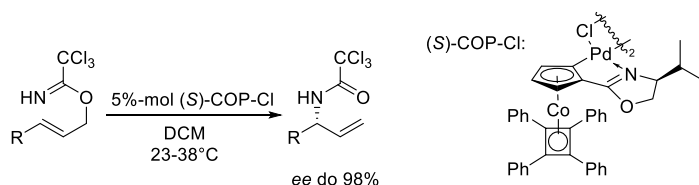
jednoczesne tworzenie i zrywanie wiązań chemicznych, według uzgodnionego mechanizmu przebiegającego przez cykliczny stan przejściowy. Istnieją dwa warianty realizacji przegrupowania Overmana<sup>6b,26</sup> (Schemat 9). Pierwszy, klasyczny wariant termiczny, polega na ogrzewaniu roztworu trichloroacetimidanu **7** w odpowiednim wysoko wrzącym rozpuszczalniku. Reakcję zwykle prowadzi się w temperaturach ok. 100-140 °C w toluenie lub ksylenie. W tych warunkach przegrupowanie jest procesem uzgodnionym biegnącym przez wspomniany sześciocłonowy stan przejściowy, dzięki czemu w przypadku użycia nieracemicznych substratów przebiega ono z pełnym transferem chiralności.<sup>27</sup> Drugi wariant przeprowadzania reakcji Overmana, katalityczny, opiera się na odpowiednim dodatku soli rtęci(II) lub soli palladu(II).



**Schemat 9.** Mechanizm reakcji przegrupowania Overmana.

W przypadku wariantu katalitycznego zakłada się dwuetapowy mechanizm reakcji. W pierwszym etapie następuje aktywacja wiązania podwójnego za pomocą kompleksu metalu oraz atak nukleofilowy prowadzący do produktu cyklicznego **8**. Następnie zachodzi reakcja eliminacji połączona z odejściem kompleksu metalu i zerwaniem wiązania C-O z utworzeniem trichloroacetamidu **9**. Niejednokrotnie wariant katalityczny pozwala na obniżenie temperatury reakcji przy jednoczesnym jej przyspieszeniu. W przypadku wariantu katalitycznego nie ma konieczności użycia chiralnego substratu do reakcji przegrupowania. Zastosowanie chiralnych kompleksów metalu pozwala na otrzymywanie enancjomerycznie wzbogaconych produktów z prochiralnych substratów.<sup>28</sup>

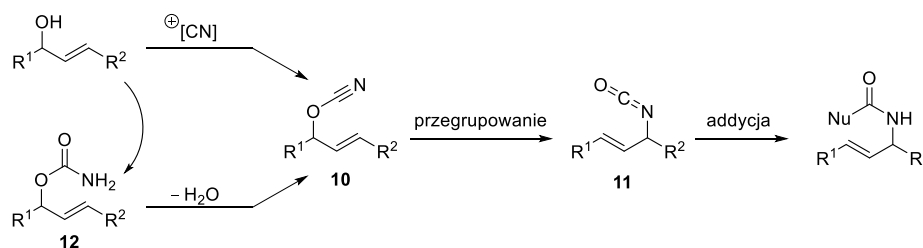
Przegrupowanie Overmana jest jedną z najczęściej wykorzystanych tego typu transformacji w syntezie chiralnych alliloamin, ma ono jednak kilka wad i ograniczeń. Po pierwsze, substraty wykorzystywane w reakcji, trichloroacetimidany **7**, mają ograniczoną trwałość, jak również są wrażliwe na kwaśne zanieczyszczenia. Z tego względu nie przechowuje się większych ich ilości przez dłuższy czas, tylko generuje *in situ* bezpośrednio przed reakcją. Kolejnym przykładem może być wysoka temperatura prowadzenia reakcji, w przypadku wariantu termicznego, co wyklucza możliwość wykorzystania tej reakcji w przypadku termicznie nietrwałych substratów. Ponadto, dla wariantu katalitycznego konieczność stosowania soli metali ciężkich, których używania unika się w przypadku syntezy związków mających być substancjami czynnymi leków. Co najistotniejsze, w literaturze występują nieliczne przykłady przeprowadzenia reakcji Overmana w wariacie enancjoselektywnym, ze względu na konieczność zastosowania złożonych strukturalnie chiralnych katalizatorów, np. (S)-COP-Cl (Schemat 10) o bardzo wysublimowanych właściwościach elektronowych.<sup>28</sup>



**Schemat 10.** Przykład wykorzystania reakcji Overmana w wariacie enancjoselektywnym.

Podobnie jest w przypadku reakcji dekarboksylacyjnego allilowego amidowania<sup>29</sup> przedstawionej na Schemacie 8.2, która wymaga zarówno podwyższonej temperatury jak i katalizatora w postaci soli palladu, irydu lub złota(I). Ponadto, z syntetycznego punktu widzenia, reakcja Overmana jak i reakcja dekarboksylacyjnego allilowego amidowania posiadają jeszcze jedną niedogodność. Powstające jako produkty tych reakcji amidy mają pewne ograniczone zastosowanie i większości przypadków konieczne są dodatkowe transformacje na atomie azotu. W celu przeprowadzenia dalszych przekształceń często niezbędna jest wymiana grupy zabezpieczającej na Boc lub Cbz co jest istotnym mankamentem, ponieważ wymaga przeprowadzenia dwóch dodatkowych reakcji, odbezpieczania i zabezpieczenia, wydłużając tym samym syntezę i obniża jej sumaryczną ekonomię.

W tym świetle, dużo atrakcyjniejszym podejściem wydaje się synteza chiralnych alliloamin poprzez mechanistycznie analogiczny proces przegrupowania cyjanianów allilowych **10** do izocyjanianów **11**, zwany także reakcją Ichikawy<sup>5</sup> (Schemat 11). Uzgodniony mechanizm tej reakcji, przebiegającego poprzez cykliczny stan przejściowy, umożliwia efektywny transfer chiralności od substratu do produktu, z utworzeniem nowego centrum stereogenicznego.



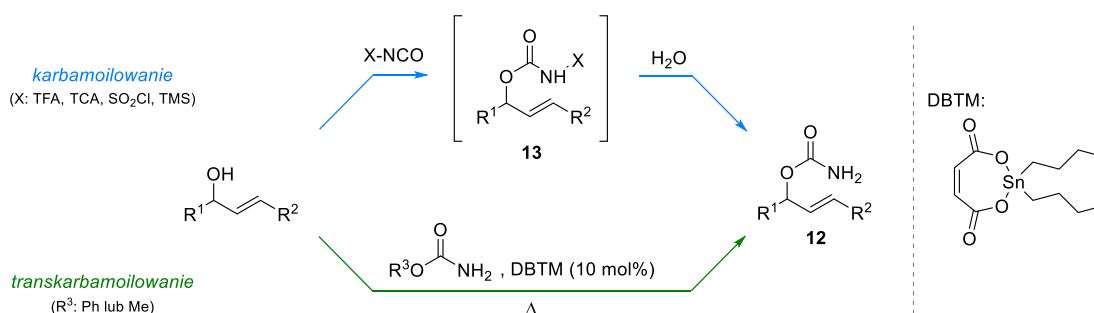
**Schemat 11.** Reakcja przegrupowania cyjanianów allilowych do izocyjanianów.

Uzyskiwane w pierwszym etapie reakcji Ichikawy cyjaniany **10** są związkami dość nietrwałymi przez co najczęściej generuje się je *in situ*. W jednym z pierwszych doniesień literaturowych związki te uzyskiwano w wyniku cheletropowej przemiany tiazoli allilowych.<sup>30</sup> Inną metodą jest reakcja alkoholu allilowego z chloro lub bromocyjanem.<sup>31</sup> Inną metodą może być reakcja alkoholu allilowego z BrCN<sup>32</sup> lub innym nośnikiem elektrofilowej grupy CN.<sup>33</sup> Jednakże z uwagi na toksyczność stosowanych w tych przekształceniach reagentów przedstawione metody mają ograniczoną stosowalność.

Dogodnymi prekursorami cyjanianów allilowych **10** są karbaminiany allilowe **12**, które to wykazują wysoką trwałość i stabilność. Karbaminiany, pod wpływem czynnika odwadniającego, zostają przekształcone w odpowiednie cyjaniany allilowe **10**, które następnie ulegają spontanicznemu [3,3]-sigmatropowemu przegrupowaniu do odpowiednich izocyjanianów **11**, jak to zobrazowano na powyższym schemacie. Ta spontaniczność procesu przegrupowania jest niewątpliwą zaletą reakcji Ichikawy, gdyż nie wymaga termicznej inicjacji lub użycia katalizatora. Co więcej, przegrupowanie przebiega w łagodnych warunkach i w krótkim czasie. Uzyskiwane

w wyniku odwodnienia i przegrupowania izocyjaniiny allilowe **11** można wydzielić, jednakże z uwagi na dużą reaktywność grupy -NCO, dużo korzystniejsze jest ich bezpośrednio poddanie reakcji z czynnikiem nukleofilowym. Warto tu zwrócić uwagę na jeden istotny fakt. Choć przegrupowanie to trzy reakcje, obejmujące odwodnienie/przegrupowanie i addycję, to jednak cała ta sekwencja jest prowadzona w jednym naczyniu reakcyjnym co pozwala na zmaksymalizowanie jej efektywności (wariant „one-pot”).<sup>9</sup>

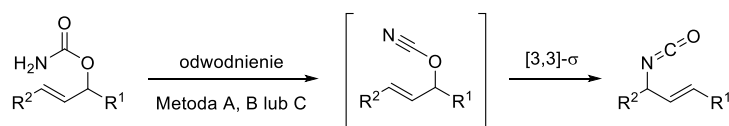
Jak już wcześniej wspomniałam, karbaminiany są związkami o wysokiej trwałości, nieulegającymi istotnej degradacji nawet po wielomiesięcznym przechowywaniu, w przeciwieństwie do imidanów wykorzystywanych w reakcji Overmana. Otrzymuje się je w prosty sposób z odpowiednich alkoholi allilowych w wyniku reakcji karbamoilowania lub transkarbamoilowania (Schemat 12). W pierwszym przypadku alkohol traktuje się izocyjaniem trichloroacetylowym (TCA-NCO),<sup>9</sup> z następczą hydrolizą zasadową pośrednio tworzącego się imidu **13** prowadzą co odpowiedniego karbaminianu **12**. Karbaminiany typu **12** można również wydajnie uzyskiwać stosując izocyjanie chlorosulfonylowe (CSI)<sup>34</sup> oraz izocyjanie trimetylosililowe.<sup>35</sup>



**Schemat 12.** Synteza karbaminianów allilowych.

Druga metoda, reakcja transkarbamoilowania, polega na katalicznym przeniesieniu grupy karbaminowej z karbaminianu fenylu lub metylu, na alkohol allilowy.<sup>36</sup> Katalizatorem w tym przekształceniu jest maleinian dibutylocynku (DBTM), a reakcja prowadzona jest najczęściej w toluenie w podwyższonej temperaturze (90 °C).

Kolejną istotną zaletą przegrupowania Ichikawy są łagodne warunki prowadzenia reakcji. Pierwszy etap, dehydratację karbaminianu, można realizować na kilka sposobów<sup>5,9</sup> jak przedstawiłam na Schemacie 13.



Metoda	Warunki
A	CBr <sub>4</sub> , PPh <sub>3</sub> , Et <sub>3</sub> N, CH <sub>2</sub> Cl <sub>2</sub> , -20 °C
B	Tf <sub>2</sub> O, i-Pr <sub>2</sub> NEt, CH <sub>2</sub> Cl <sub>2</sub> , -78 °C
C	TFAA, Et <sub>3</sub> N, THF, 0 °C

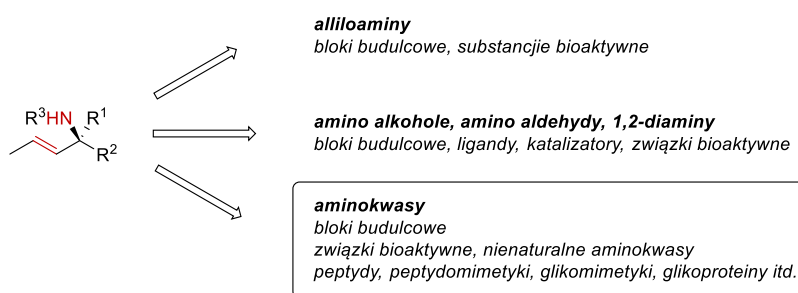
**Schemat 13.** Warunki odwodnienia karbaminianów allilowych.

W swych oryginalnych pracach, Ichikawa<sup>9</sup>, stosował kombinację reagentów: PPh<sub>3</sub>, CBr<sub>4</sub> i Et<sub>3</sub>N jako mieszaninę odwadniającą (Metoda A, Schemat 13). Choć jest to bardzo skuteczna metoda, to jednak niesie ze sobą pewne mankamenty. Przede wszystkim, ze względu na tworzące się w toku reakcji produkty uboczne takie jak bromoform i tlenek fosfiny, których oddzielenie od



powstałego produktu może okazać się problematyczne, szczególnie w przypadku tego ostatniego. Równie skuteczna jest metoda Baldwina (Metoda B, Schemat 13) wykorzystująca w tym celu  $\text{Tf}_2\text{O}$  w obecności diizopropylloaminy. Niestety wspomniany bezwodnik jest niezwykle reaktywnym odczynnikiem (reakcję z jego udziałem należy prowadzić w  $-78\text{ }^\circ\text{C}$ ), jak również drogim. Najkorzystniejszą metodą jest wykorzystanie w tym celu tanich reagentów, takich jak bezwodnik trifluorooctowy (TFAA) w połączeniu z  $\text{Et}_3\text{N}$  (Metoda C, Schemat 13). W tym przypadku odwodnienie prowadzi się w bardzo łagodnych warunkach, początkowo w  $0\text{ }^\circ\text{C}$ , w trakcie dodawania TFAA do mieszaniny reakcyjnej, a następnie w temperaturze pokojowej. Co więcej, proces ten jest szybki, odwodnienie i następcze przegrupowanie przebiega w przeciągu 30-60 min.<sup>5,9</sup> Jak już wcześniej nadmieniałam, wartym podkreślenia jest fakt, że przeciwieństwo do przegrupowania Overmana, sigmatropowe przegrupowanie cyjanianów allilowych nie wymaga stosowania wysokich temperatur ani kompleksów metali przejściowych.

Tworzenie, w wyniku reakcji przegrupowania, izocyjanianu jest kolejną zaletą omawianej reakcji, a to z uwagi na reaktywność tej klasy związków. Uzyskiwane w wyniku odwodnienia i przegrupowania izocyjaniany allilowe można wydzielić, jednak dużo korzystniejszym, ze względu na ich reaktywność, jest bezpośrednio poddanie reakcji z czynnikiem nukleofilowym. Otrzymane w ten sposób alliloaminy stanowią niezwykle cenne bloki budulcowe w syntezie organicznej z uwagi na obecność funkcji aminowej i wiązania podwójnego, które to dają szerokie możliwości dalszej funkcjonalizacji tych struktur (Rysunek 2).<sup>19</sup>

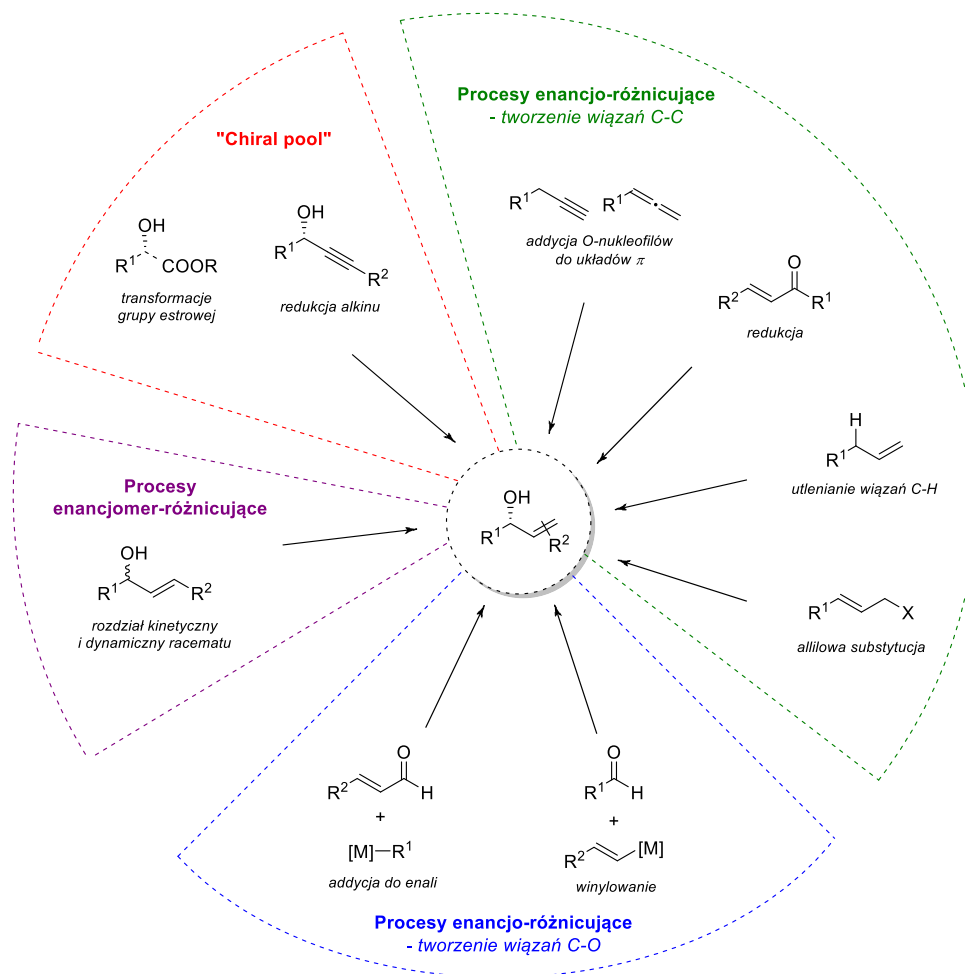


**Rysunek 2.** Zastosowanie alliloamin jako bloków budulcowych.

W kontekście wykorzystania reakcji przegrupowania cyjanianów allilowych do izocyjanianów w syntezie chiralnych  $\alpha$ -trzeciorzędowych alliloamin kluczowe jest posiadanie efektywnej metody pozyskiwania wyjściowych nieracemicznych alkoholi allilowych. Taka metoda syntezy przedstawionych alkoholi powinna spełniać dwa wymagania: (1) musi zapewniać produkt o wysokiej czystości enancjomerycznej oraz (2) musi umożliwiać pełną kontrolę tworzenia geometrii wiązania podwójnego. Niestety, ze względu na spontaniczność reakcji Ichikawy nie możliwe jest zastosowanie zewnętrznego źródła chiralności odpowiedzialnego za indukcję asymetryczną procesu w postaci chiralnego kompleksu metalu. Natomiast rozwiązaniem jest użycie w reakcji przegrupowania nieracemicznego substratu, co pozwala na uzyskanie enancjomerycznie czystej alliloaminy dzięki stereospecyficznemu przebiegowi reakcji z pełnym transferem chiralności. W takiej sytuacji teoretyczna czystość enancjomeryczna produktu będzie taka sama jak wyjściowego karbaminianu. Jednakże, jeżeli substrat będzie zanieczyszczony drugim izomerem geometrycznym (przy założeniu 100% czystości centrum stereogenicznego), wówczas powstający produkt, alliloamina, będzie miała niższą czystość enancjomeryczną. Dlatego też warunkiem możliwości szerokiego wykorzystania tej metody jest dostępność odpowiednich nieracemicznych karbaminianów allilowych, a dokładnie odpowiednich alkoholi allilowych, z których się je otrzymuje.

## 2.4. Alkohole allilowe w syntezie organicznej

Alkohole allilowe, podobnie jak alliloaminy, stanowią niezwykle użyteczną klasę związków chemicznych wykorzystywanych w syntezie organicznej. Wynika to z obecności dwóch kluczowych grup funkcyjnych, wiązania podwójnego oraz grupy hydroksylowej. Szerokie spektrum przemian, którym one ulegają sprawia, że są jednymi z najczęściej wykorzystywanych bifunkcyjnych cząsteczek w syntezie związków pochodzenia naturalnego, syntetycznych substancji bioaktywnych, w tym leków.<sup>37</sup>



**Schemat 14.** Strategie syntezy nieracemicznych alkoholi allilowych.

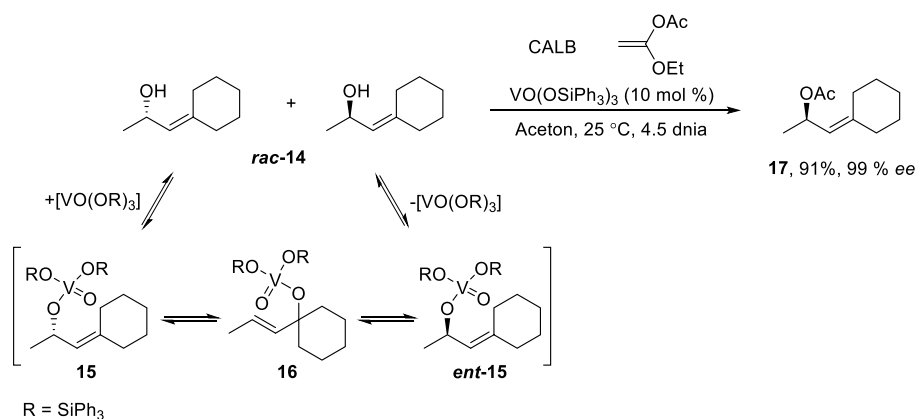
Jednakże synteza alkoholi allilowych, szczególnie w formie enancjomerycznie wzbogaconej, nie jest prostym zadaniem, ponieważ wymaga kontroli tworzenia nie tylko centrum stereogenicznego, ale także geometrii wiązania podwójnego. Chciałabym wyróżnić trzy strategie ich otrzymywania (Schemat 14), obejmują one: (1) **procesy enancjomer-różnicujące** (kinetyczny lub dynamiczny rozdział racematu), (2) procesy enancjo-różnicujące, a więc wszystkie reakcje, w których z prochiralnych substratów tworzymy chiralne produkty. Możemy tutaj wydzielić dwie podgrupy, są to: (2a) **metody enancjoselektywnego tworzenia wiązania C-C**, na drodze nukleofilowej 1,2-addycji do grupy karbonylowej (w tym addycja do enali oraz reakcja winylowania) oraz (2b) **metody enancjoselektywnego tworzenia wiązania C-O**, które można realizować na cztery sposoby poprzez: allilową substytucję, utlenianie wiązań C-H, addycję O-nukleofilów do układów  $\pi$ -elektronowych oraz redukcję enoli. Ostatnia grupa metod

(3) wykorzystuje łatwo dostępne, chiralne bloki budulcowe (**strategia „chiral pool”**). W dalszej części niniejszego rozdziału scharakteryzuję wymienione powyżej metody.

#### 6.4.1. Kinetyczny i dynamiczny rozdział racematu

Szeroko wykorzystywaną metodą pozyskiwania chiralnych alkoholi allilowych jest kinetyczny rozdział racematu. Opracowano wiele procedur dla tej transformacji, w tym rozdziały enzymatyczne i nieenzymatyczne. Przedstawione reakcje są jednoetapowe, względnie proste oraz dają możliwość uzyskania obu enancjomerów. Jednakże ogranicza je maksymalna teoretyczna wydajność wynosząca 50%, co obniża atrakcyjność tego podejścia z punktu widzenia ekonomii atomowej. Rozwiązaniem tego problemu, może być prowadzenie rozdziału w wariacie dynamicznym, kiedy proces rozdziału kinetycznego połączony jest z szybką racemizacją wolniej reagującego enancjomeru substratu. W tym przypadku możliwe jest uzyskanie teoretycznie ilościowej wydajności co czyni tą metodę atrakcyjniejszą w syntezie enancjomerycznie wzbogaconych alkoholi allilowych i ich pochodnych. Niestety nie zawsze łatwo jest dobrać odpowiednio aktywny czynnik racemizujący dla konkretnej grupy substratów. Proces racemizacji może być katalizowany enzymami, kwasami lub zasadami.<sup>38</sup> Racemizatorami mogą być także kompleksy metali przejściowych, na przykład katalizator Shvo.<sup>39</sup> Metody z ich użyciem stanowią najefektywniejsze podejście w syntezie chiralnych alkoholi allilowych. Powszechnie stosuje się dwie strategie racemizacji metalami przejściowymi. Pierwsza, wprowadzona przez grupy badawcze Williamsa<sup>40</sup> oraz Bäckvalla<sup>41</sup>, polega na transferze atomu wodoru przy użyciu (di)wodorków metali i ketonów jako związków pośrednich stosując kompleksy rodu i rutenu. Druga natomiast wykorzystuje kompleksy  $\pi$ -allilometalowe jako związki pośrednie, czego pionierami byli Allen i Williams.<sup>42</sup>

Obok kompleksów rutenu, także kompleksy wanadu znalazły zastosowanie jako efektywne czynniki racemizujące w dynamicznym rozdziale kinetycznym racematu. Na przykład, Akai i Kita,<sup>43</sup> wykorzystali  $\text{VO}(\text{OSiPh}_3)_3$  i lipazę B z *Candida antarctica* (CALB) w dynamicznym rozdziale alkoholu **rac-14**. Racemizacja przebiegała na skutek izomeryzacji substratu **15** poprzez 1,3-transpozycję grupy hydroksylowej i prowadziła do mieszaniny równowagowej dwóch regioizomerycznych pochodnych alkoholi **16** i **ent-15**. W obecności lipazy następował wysoce enancjo- i chemoselektywny rozdział prowadzący do utworzenia z wysoką wydajnością optycznie czystego octanu **17** (Schemat 15).



**Schemat 15.** Dynamiczny rozdział kinetyczny w syntezie alkoholi allilowych.

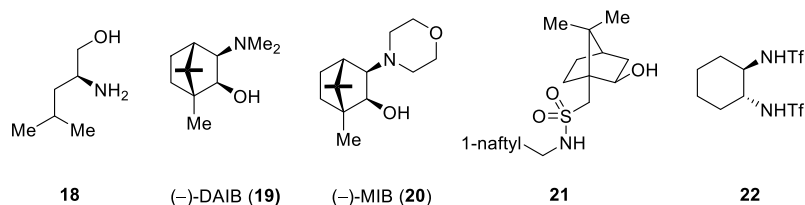
Dynamiczny rozdział kinetyczny racematu jest niewątpliwie efektywną metodą otrzymywania omawianej grupy związków, jednak zakres stosowalności tej reakcji jest ograniczony głównie do substratów acyklicznych. Enancjoróżnicowanie w układach cyklicznych jest mniej efektywne na skutek gorszego ich dopasowania do miejsca aktywnego enzymu.<sup>44</sup> Co więcej, konieczne jest użycie zarówno metalu przejściowego jak i enzymu, a opracowanie optymalnego układu reakcyjnego dla tych dwóch nie zawsze jest proste do wykonania. Główny problem stanowi kompatybilność enzymu i katalizatora metalicznego, ponieważ zazwyczaj pracują one w całkowicie odmiennych warunkach. Poza tym istnieje ryzyko, że katalizator chemiczny będzie interferować z enzymem. Dobór katalizatorów oraz odpowiednich dla nich warunków reakcyjnych jest zatem elementem kluczowym dla dynamicznego rozdziału kinetycznego.<sup>44</sup>

W dalszej części tego rozdziału chciałabym skupić się na metodach syntezy enancjomerycznie wzbogaconych alkoholi allilowych opartych na reakcjach asymetrycznych. W szczególności pragnę skoncentrować się na dwóch najważniejszych transformacjach enancjoselektywnego tworzenia wiązania C-C, a mianowicie 1,2-addycji do grup karbonylowych oraz reakcji podstawienia allilowego z użyciem C-nukleofilu.

#### 6.4.2. Nukleofilowa 1,2 addycja do grup karbonylowych

Enancjoselektywna 1,2-addycja nukleofilu do  $\alpha,\beta$ -nienasyconych związków karbonylowych to jedna z najczęściej stosowanych metod syntezy chiralnych alkoholi allilowych. Reakcja ta od lat jest badana przez chemików organicznych czego rezultatem było opracowanie szeregu procedur syntetycznych.<sup>37</sup> Niemożliwym jest przytoczenie tu wszystkich, z tego względu pragnę skoncentrować się jedynie na wybranych strategiach, ze szczególnym uwzględnieniem tych wykorzystujących odczynniki cynkoorganiczne.

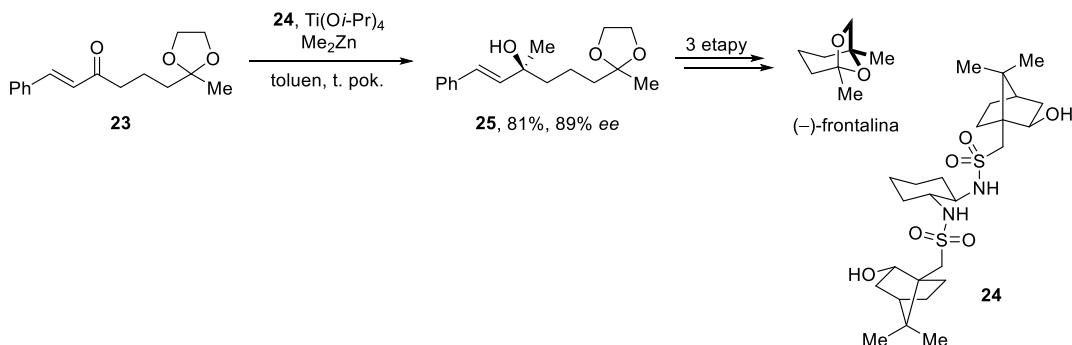
Pierwsze prace w tym temacie pojawiły się w 1984 roku, kiedy to Oguni i Omi wykorzystali (*S*)-leucinol (**18**) jako chiralny ligand w enancjoselektywnej addycji odczynników cynkoorganicznych do aldehydów. Od tego czasu opracowano wiele innych ligandów, takich jak (-)-DAIB (**19**) czy (-)-MIB (**20**), następnie wykorzystanych w syntezie przez Noyoriego<sup>46</sup> i Nugenta.<sup>47</sup> Pierwsze przykłady analogicznej addycji odczynników cynkoorganicznych do ketonów zostały ogłoszone dużo później, bo dopiero w 1998 roku. W tym przypadku za indukcję asymetryczną odpowiedzialne były ligandy typu **19** (grupa Fu<sup>48</sup>) i **21** (grupa Yusa<sup>49</sup>). Omawiając tą grupę reakcji nie można pominąć prac zespołu Knochela,<sup>50</sup> który to zastosował chiralny triflamid **22** oraz nadmiar  $Ti(Oi-Pr)_4$  lub  $Ti(Ot-Bu)_4$  w reakcji addycji odczynników alkilocynkowych do  $\alpha,\beta$ -nienasyconych aldehydów.



**Rysunek 3.** Przykłady chiralnych ligandów wykorzystywanych w 1,2-addycji do enonów.

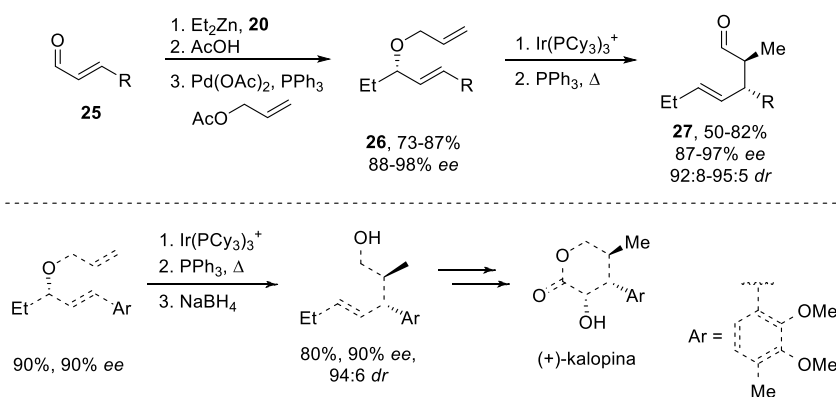
Od tamtej pory pojawił się szereg przykładów wykorzystania wspomnianych metod w syntezie organicznej. Jako przykład niech posłuży opracowana przez Yusa<sup>51</sup> i współpracowników synteza totalna (-)-frontaliny (Schemat 16), będącej substancją wykorzystywaną w systemie komunikacji chemicznej u wielu gatunków owadów. Kluczowym etapem syntezy była

enantjoselektywna addycja  $\text{Me}_2\text{Zn}$  do ketonu **23** prowadzona w obecności  $\text{Ti}(\text{O}i\text{-Pr})_4$  i chiralnego ligandu **24**. Oczekiwany trzeciorzędowy alkohol allilowy **25** uzyskano z dobrą wydajnością i bardzo dobrym nadmiarem enancjomerycznym (81%, 89% ee; Schemat 16). W kolejnych etapach obejmujących ozonolizę, redukcję powstałego aldehydu i cyklizację w warunkach kwaśnych, alkohol **25** przekształcono w docelową (-)-frontalinę.



Schemat 16. Synteza totalna (-)-frontaliny.

Natomiast Nelson i Wang<sup>52</sup> wykorzystali ligand Nugeta (-)-MIB (**20**, Rysunek 3) w enantjoselektywnej addycji  $\text{Et}_2\text{Zn}$  do aldehydów **25**. Reakcja ta w połączeniu z następczym *O*-allilowaniem umożliwiła syntezę enancjomerycznie wzbogaconych eterów diallilowych **26**. Następnie w wyniku izomeryzacji oraz przegrupowania Claisena otrzymano enancjomerycznie wzbogacone związki **27**. Strategia ta znalazła między innymi zastosowanie w syntezie totalnej (+)-kalopiny, będącej metabolitem występującym u grzybów (Schemat 17).

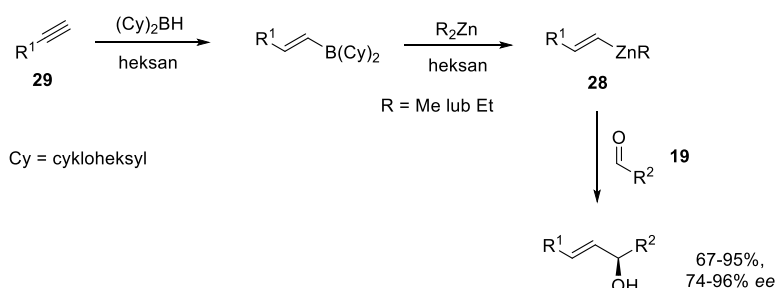


Schemat 17. Enantjoselektywna addycja  $\text{Et}_2\text{Zn}$  do aldehydów.

Ograniczeniem powyżej przedstawionej metody jest dostępność odczynników cynkoorganicznych. W reakcji wykorzystywane są głównie proste alkilowe odczynniki cynkoorganiczne, w szczególności  $\text{Et}_2\text{Zn}$  i  $\text{Me}_2\text{Zn}$ . Przy czym ten ostatni jest niestety bardzo drogim reagentem (np. Merck: 1430 zł/50 mL 1 M roztworu w heptanie). Addycja z udziałem bardziej złożonych odczynników  $\text{R}_2\text{Zn}$  jest zazwyczaj nieefektywna. Co prawda, oprócz związków cynkoorganicznych możliwe jest wykorzystanie, na przykład, odczynników Grignarda, odczynników glikoorganicznych, związków boru, cynoorganicznych czy krzemowych, jednakże są to już znacznie rzadziej stosowane podejścia, niejednokrotnie mniej wydajne zarówno jeśli chodzi o wydajność jak i uzyskiwane nadmiary enancjomeryczne produktów. Brak im też ogólności.<sup>37</sup>

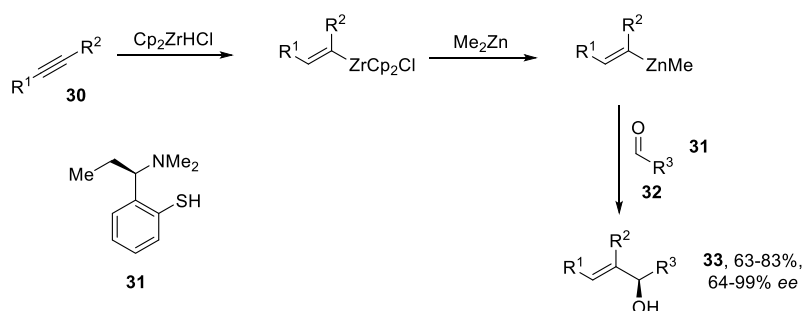
Alternatywną do wcześniejszej strategii syntezy alkoholi allilowych, jest wprowadzanie fragmentu zawierającego wiązanie podwójne poprzez reakcję winylowania aldehydów i ketonów.

Także w tym przypadku, najlepszymi reagentami okazały się odczynniki cynkoorganiczne. Pierwsze przykłady asymetrycznego winylowania aldehydów zostały opisane przez Oppolzera.<sup>53</sup> Odpowiednie reagenty winylcynkowe **28** uzyskiwano z alkinów **29** poprzez ich hydroborowanie i następcze transmetalowanie B-Zn za pomocą Et<sub>2</sub>Zn lub Me<sub>2</sub>Zn (Schemat 18). Wysokie wydajności i nadmiary enancjomeryczne uzyskano w wyniku reakcji addycji odczynników cynkowych do różnych aldehydów w obecności ligandu Noyoriego (–)-DAIB (**19**, Rysunek 3).



**Schemat 18.** Asymetryczne winylowanie aldehydów metodą Oppolzera.

Natomiast w analogicznej strategii asymetrycznego winylowania aldehydów, opisaną przez Wipfa<sup>54</sup> i współpracowników, odpowiednie reagenty cynkoorganiczne otrzymywano poprzez hydrocyrkonowanie alkinów **30** i następczą wymianę Zr-Zn (Schemat 19). Tak uzyskane reagenty, w obecności aminy van Kotensa **31** ulegały addycji do aldehydów **32** dając odpowiednie alkohole allilowe **33** z dobrymi wydajnościami i wysokimi nadmiarami enancjomerycznymi. Proces przebiegał zarówno dla terminalnych jak i wewnętrznych alkinów **30**.



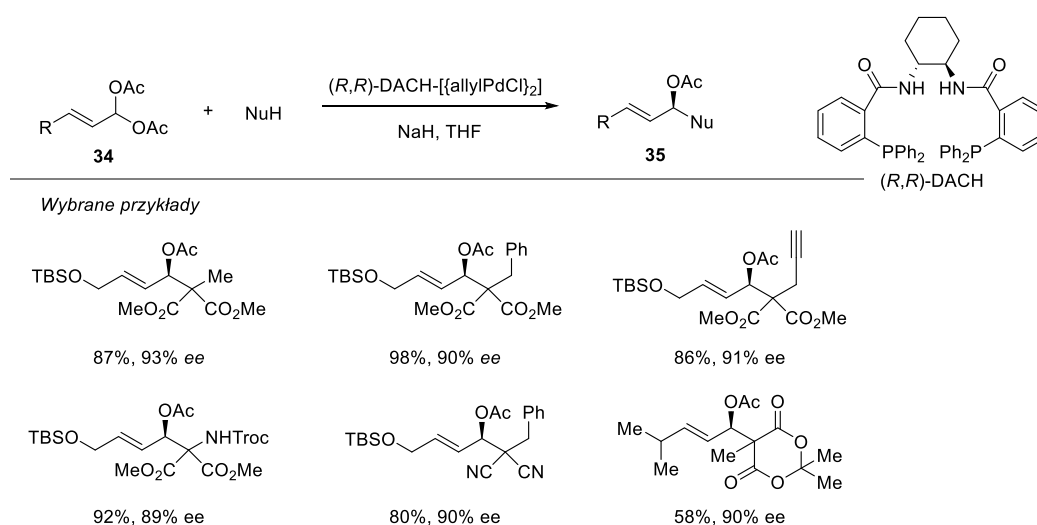
**Schemat 19.** Asymetryczne winylowanie aldehydów metodą Wipfa.

Choć wyżej wymienione podejścia w enancjoselektywnym winylowaniu związków karbonylowych są wysoce skuteczne pod względem enancjoselektywności, to jednak 2-etapowe generowanie *in situ* odczynników metaloorganicznych jest pracochłonne oraz wymaga doświadczenia. Na przykład, odczynniki organoboronowe zazwyczaj otrzymuje się z odpowiednich odczynników litoorganicznych, które z kolei wytwarza się metodą wymiany halogen-metal za pomocą *n*- lub *t*-butylolitu. Co oznacza, że trzy przygotowane wcześniej odczynniki metaloorganiczne są stosowane w ilości stechiometrycznej. Takie podejście produkuje spore ilości produktów ubocznych, co więcej wymaga pracy z odczynnikami wrażliwymi na powietrze i wilgoć. Szczególnie widać to w przypadku stosowania odczynnika Schwartza (Cp<sub>2</sub>ZrHCl), który choć jest niezwykle użyteczny w procesach hydrometalowania, to jednak do tanich nie należy.

### 6.4.3. Allilowa substytucja

Kolejną ważną metodą syntezy alkoholi allilowych jest allilowa substytucja z wykorzystaniem odczynników nukleofilowych.<sup>21,55</sup> Choć opracowano szereg systemów katalitycznych umożliwiających utworzenie wiązania C-C w omawianej reakcji, to jednak procedury prowadzące do produktów enancjomerycznie wzbogaconych są nieliczne.

Warte uwagi są pionierskie prace Trosta,<sup>56</sup> który zastosował chiralny katalizator palladowy (*R,R*)-DACH-[[allylPdCl]<sub>2</sub>] w enancjoselektywnym alkilowaniu geminalnych acetalu **34** za pomocą odczynników C-nukleofilowych (Schemat 20). Powstające w tych warunkach octany allilowe **35** otrzymywano z doskonałymi nadmiarami enancjomerycznym i doskonałą regioselektywnością. Metodę tę z powodzeniem wykorzystano w syntezie totalnej sfingofunginy<sup>57</sup> E i F, związków wyizolowanych z fermentacji *Paecilomyces Variotii*. Sfingofunginy E i F blokują biosyntezę sfingolipidów, co prowadzi do apoptozy zarówno w komórkach drożdży, jak i ssaków.

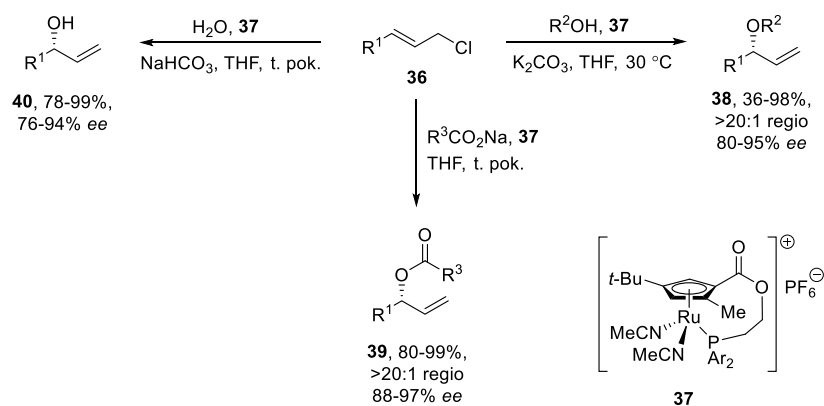


Troc = trichloroetoksykarbonyl

**Schemat 20.** Enancjoselektywne alkilowanie geminalnych dikarboksylianów.

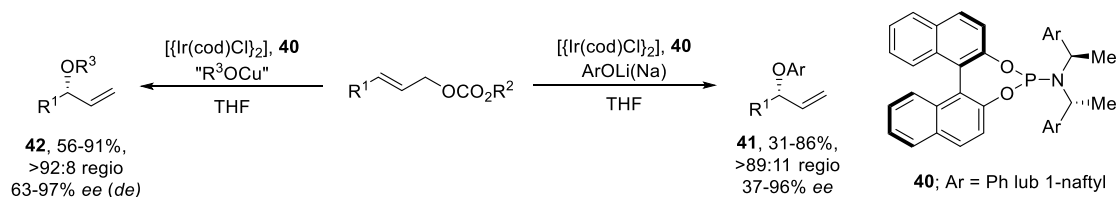
Dużo szerzej stosowanym wariantem allilowej substytucji są reakcje z wykorzystaniem czynników *O*-nukleofilowych, które umożliwiają syntezę różnorodnych pochodnych alkoholi allilowych. Intensywne badania czołowych grup badawczy doprowadziły do opracowania szeregu układów katalitycznych opartych na kompleksach palladu, rutenu, irydu, miedzi i rodu.

Przykładem mogą być prace Onitsuki'ego, który opracował warunki dla enancjoselektywnej substytucji chlorków allilowych **36** wykorzystując chiralny kompleks rutenu **37**. W reakcji tej, jako czynniki nukleofilowe, doskonale sprawdziły się zarówno alkohole<sup>58a</sup> jak i karboksylany<sup>58b</sup> oraz woda<sup>58c</sup>. W opracowanych warunkach możliwa była synteza rozgałęzionych eterów allilowych **38**, estrów **39** oraz alkoholi **40**, z doskonałymi nadmiarami enancjomerycznymi i regioselektywnością.



Schemat 21. Katalizowane rutenem reakcje alilowej substytucji.

Również kompleksy irydu okazały się skutecznymi katalizatorami do syntezy rozgałęzionych alkoholi alilowych i ich pochodnych.<sup>55c</sup> Grupa Hartwiga wykorzystwała w tym celu kompleksy irydu z chiralnym ligandem fosforoamidynowym **40**. Jak przedstawiałam na poniższym schemacie, w reakcji mogą uczestniczyć zarówno alkohole jak i fenole. Sam proces przebiegał z wysoką regioselektywnością dając, w przeciwieństwie do procesów katalizowanych kompleksami palladu, „rozgałęzione” produkty typu **41** oraz **42** z wysokimi wydajnościami oraz wysoką indukcją asymetryczną.<sup>59</sup>



Schemat 22. Katalizowana irydem alilowa substytucja alkoholami.

Katalizowane metalami przejściowymi reakcje  $\pi$ -alilowej substytucji zapewniają prosty i szybki dostęp do liniowych II-rzędowych alkoholi alilowych. Niemniej jednak, pomimo szerokiego zastosowania, nadal pozostaje wiele problemów do rozwiązania. Jednym z nich jest ograniczenie reakcji substytucji do symetrycznie dipodstawionych układów  $\pi$ -alilowych. Istotnym problemem jest niska regioselektywność reakcji z udziałem substratów rozbudowanych sterycznie. Ponadto, tworzenie czteropodstawionych centrów stereogenicznych jest, jak dotąd, niemożliwe przy użyciu tych metod.

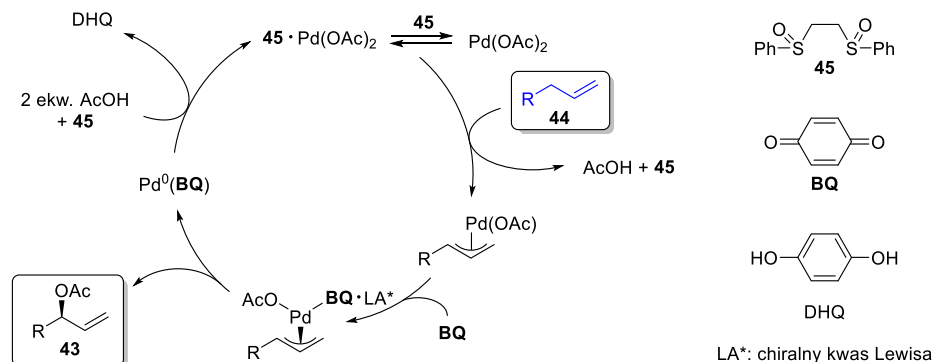
#### 6.4.4. Utlenianie wiązań C-H w pozycji alilowej

Szczególnie atrakcyjnym podejściem w syntezie pochodnych alkoholi alkoholowych jest alilowe utlenianie wiązań C-H. Zaletą tej strategii jest możliwość bezpośredniego przekształcenia alkenów w jednym etapie w cenne elementy budulcowe. W przeciwieństwie do alilowej substytucji, wstępna aktywacja substratu nie jest wymagana, co zmniejsza ilość generowanych odpadów. Obecnie, większość badań w tej dziedzinie koncentruje się na stosowaniu katalizatorów na bazie kompleksów palladu i miedzi. Jednak aby omawiany proces był użyteczny w syntezie złożonych cząsteczek, reakcje te muszą przebiegać z wysoką chemo-, regio- i stereoselektywnością.

Chociaż opracowano kilka strategii katalizowanej palladem estryfikacji wiązań C-H,<sup>60</sup> to jedynie ta opisana przez White<sup>61</sup> i współpracowników daje możliwość selektywnej syntezy

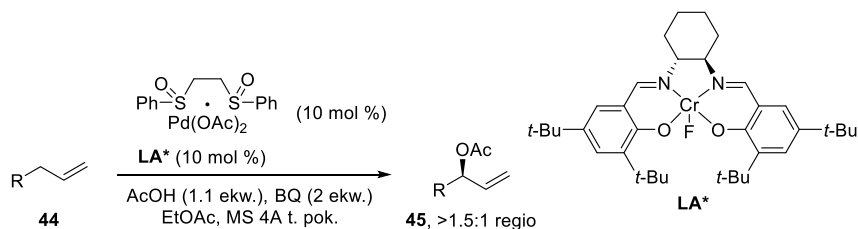


rozgałęzionego izomeru. Enancjomerycznie wzbogacone octany alkoholi allilowych **43** otrzymano w reakcji terminalnych alkenów **44** i kwasu octowego katalizowanej kompleksem palladu z chiralnym kwasem Lewisa ( $LA^*$ ) oraz w obecności dwóch ekwiwaleatów benzochinonu (**BQ**) jako końcowego utleniacza.<sup>62</sup> Autorzy wykazali, że reakcja przebiega przez nowy mechanizm, w którym dwa różne ligandy (tj. sulfotlenek **45** i **BQ**) oddziałują sekwencyjnie z metalem w celu promowania odrębnych etapów cyklu katalicznego (tj. odpowiednio C-H funkcjonalizację i tworzenie wiązania C-O).

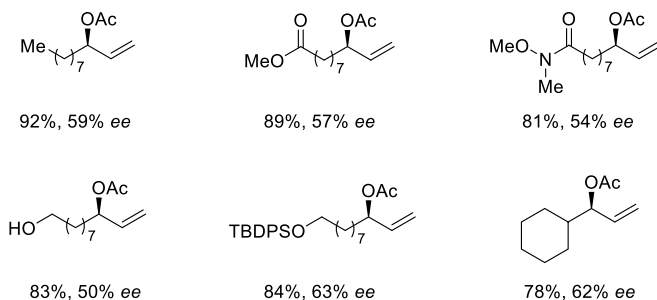


**Schemat 23.** Postulowany mechanizm reakcji allilowego utleniania wiązań C-H.

Opracowane warunki pozwoliły na syntezę szeregu octanów allilowych **45** posiadających różne grupy funkcyjne, takie jak grupa estrowa, amidowa, zabezpieczone grupy hydroksylowe. Niestety regioselektywność oraz uzyskane nadmiary enancjomeryczne były umiarkowane. Co więcej, proces wymagał stechiometrycznych ilości utleniacza, niezbędnego do regeneracji katalizatora co czyni to podejście nieatrakcyjne w odniesieniu do ekonomii atomowej.



Wybrane przykłady

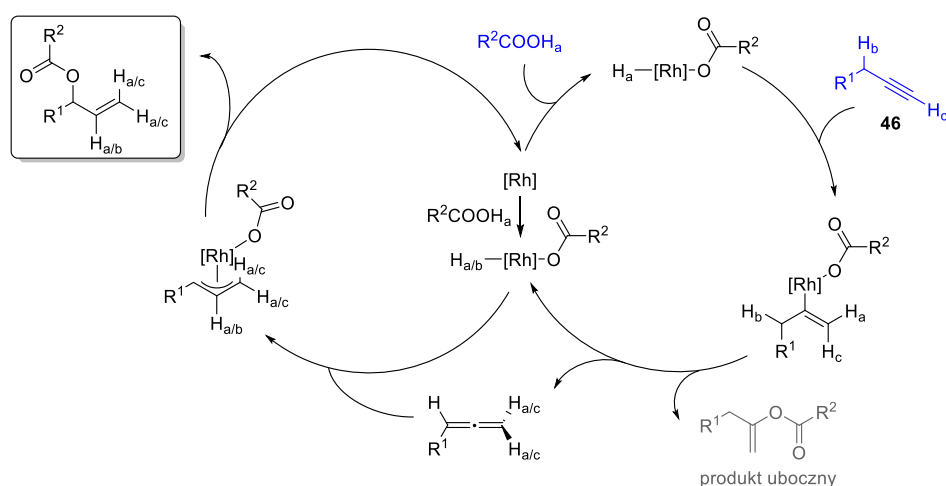


TBDSO = *tert*-butylodifenylsilyl

**Schemat 24.** Enancjoselektywne katalizowane palladem allilowe utlenianie wiązań C-H.

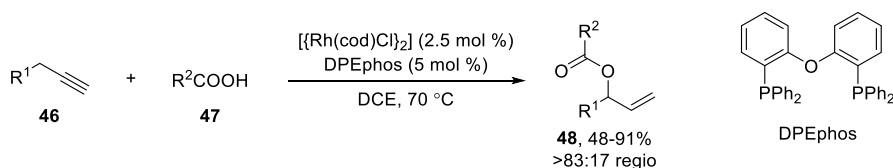
### 6.4.5. Addycja czynników *O*-nukleofilowych do układów $\pi$

Alternatywną do powyżej omówionej metody syntezy alkoholi allilowych jest addycja odczynników *O*-nukleofilowych do wiązań  $\pi$ . Na uwagę zasługują wyniki prac grupy Breita.<sup>63</sup> Autorzy stwierdzili, że zastąpienie alkenowego substratu typu **44** (Schemat 23 i 24) odpowiednim terminalnym alkinem **46** (Schemat 25) prowadzi do wewnętrznego, neutralnego pod względem redoks, utlenienia wiązania C-H (propargilowego) z jednoczesnym przesunięciem wodorku. Tak więc alkin **46**, w omawianym procesie, służy jako wewnętrzny utleniacz, który jednocześnie jest redukowany do alkenu. Uniknięto w ten sposób konieczności zastosowania stechiometrycznej ilości zewnętrznego utleniacza.



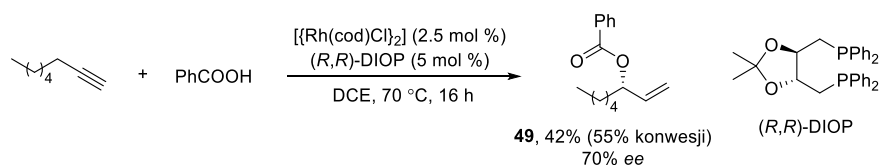
**Schemat 25.** Postulowany mechanizm reakcji sprzęgania alkinów terminalnych z kwasami karboksylowymi.

Alkiny **46** poddano reakcji sprzęgania z kwasami karboksylowymi **47** otrzymując rozgałęzione estry allilowe **48**. Autorzy wykazali, że zastosowanie jako katalizatora kompleksu  $[\{\text{Rh}(\text{cod})\text{Cl}\}_2]/\text{DPEphos}$  umożliwiło syntezę racemicznych pochodnych alkoholi allilowych **48** z wysoką wydajnością i doskonałą selektywnością.



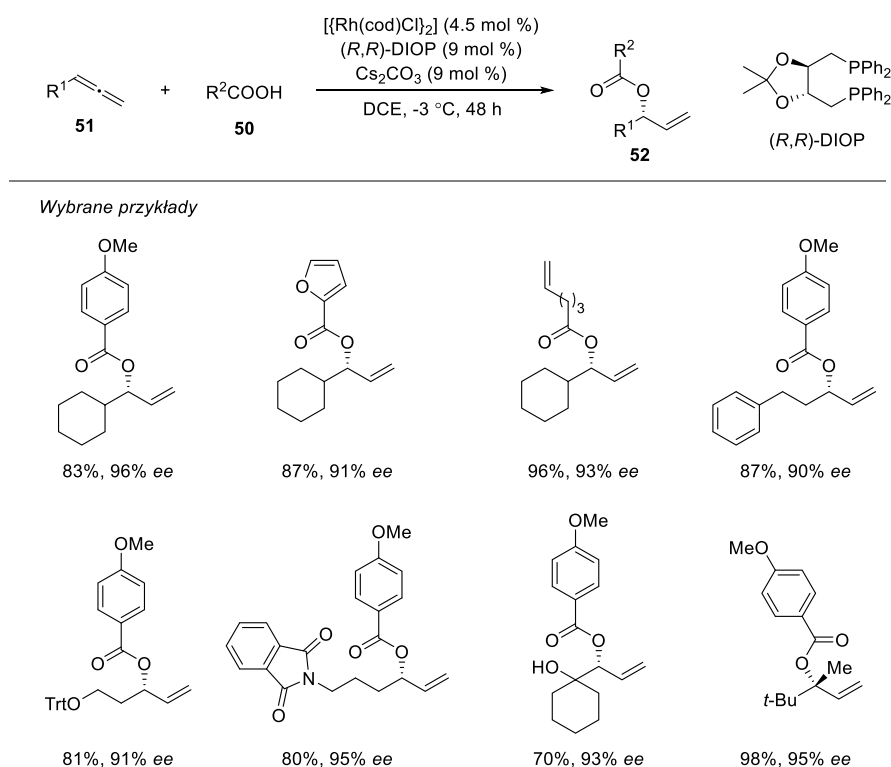
**Schemat 26.** Katalizowane rodem sprzęganie alkinów terminalnych z kwasami karboksylowymi.

Dla modelowej reakcji (Schemat 27), autorzy przedstawili możliwość przeprowadzenia powyższej reakcji w wariacie enancjoselektywnym. W tym przypadku, w reakcji pomiędzy  $\text{PhCOOH}$  a 1-oktynem, zamiast ligandu  $\text{DPEphos}$  użyto chiralny ligand  $(R,R)$ -DIOP. Oczekiwany produkt **49** uzyskano z umiarkowaną wydajnością, ale obiecującą enancjoselektywnością (70% *ee*).



**Schemat 27.** Enancjoselektywne sprzęganie alkinów terminalnych z kwasami karboksylowymi.

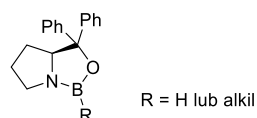
Jak wykazały kolejne prace z zespołu Breita,<sup>64</sup> układ katalityczny Rh(I)/(*R,R*)-DIOP okazał się niezwykle skuteczny w enancjoselektywnym sprzęganiu kwasów karboksylowych **50** z allenami **51** prowadzącym do enancjomerycznie wzbogaconych estrów alkoholi allilowych **52**. W opracowanych warunkach, reakcje sprzęgania zarówno z alifatycznymi jak i aromatycznymi kwasami karboksylowymi przebiegały z doskonałą regioselektywnością, dając z wysokimi wydajnościami produkty o bardzo dobrych nadmiarach enancjomerycznych (Schemat 28). Co więcej, metoda umożliwiła także syntezę trzeciorzędowych alkoholi allilowych wychodząc z 1,1-dipodstawionych allenów. Trudno jednak wyciągnąć wnioski na temat użyteczności opracowanej metodologii, z uwagi na wąski zakres substratowy, który jest ograniczony do prostych pochodnych kwasu benzoowego oraz prostych alifatycznych allenów nie posiadających w strukturze wymagających grup funkcyjnych. Co więcej, autorzy nie pokazali możliwości syntezy układów z wewnętrznym wiązaniem podwójnym.



**Schemat 28.** Enancjoselektywne sprzęganie allenów z kwasami karboksylowymi.

#### 6.4.6. Redukcja nienasyconych związków karbonylowych

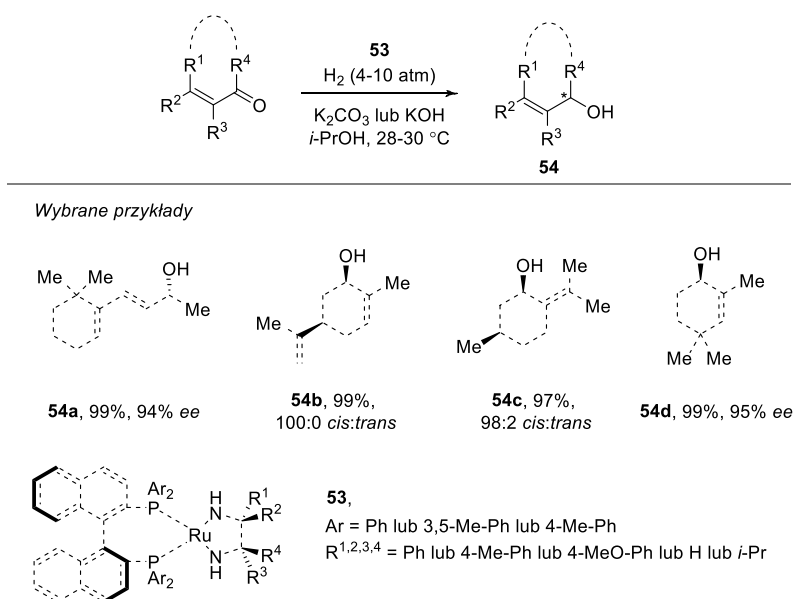
Alternatywnym podejściem do syntezy omawianej grupy związków jest 1,2-redukcja  $\alpha,\beta$ -nienasyconych ketonów. Transformacja ta odbywa się na dwa sposoby albo poprzez transferowe uwodornienie lub przy użyciu generowanych *in situ* wodorków metali. W ostatnich dziesięcioleciach opracowano kilka różnych enancjoselektywnych metod redukcji enonów.<sup>65</sup> Najczęściej wykorzystywana to redukcja Corey-Bakshi-Shibata (CBS) przy użyciu chiralnych oksazaborolidyn jako katalizatorów i boranów jako czynników redukujących.<sup>66</sup>



**Rysunek 4.** Przykłady chiralnych oksazaborolidyn wykorzystywanych do redukcji CBS.

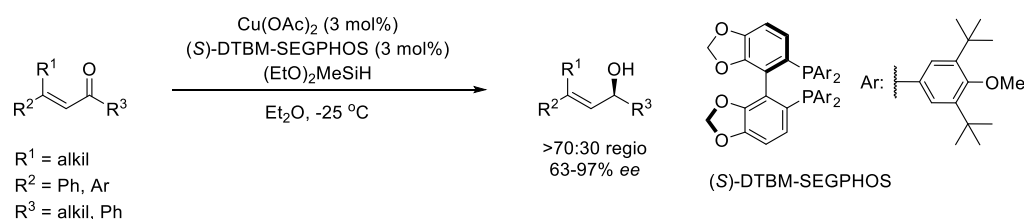
Użyteczność tej metody została wykazana przez liczne zastosowania w syntezie totalnej produktów naturalnych, takich jak atraktyligenina,<sup>67</sup> brevetoksyna-B<sup>68</sup> czy (-)-frondosina-B.<sup>69</sup> Z uwagi na mnogość tych doniesień omawianie przekracza możliwości tej pracy. Na uwagę jednak zasługuje fakt, iż o ile redukcja CBS dobrze się sprawdza dla liniowych enonów, to jest mało skuteczna w przypadku cyklicznych układów, na przykład cykloheksenonu.<sup>70</sup> Cykliczna struktura substratu sprawia, że enancjoróżnicowanie przez chiralny czynnik redukujący jest słabe, co prowadzi do niskiej enancjoselektywności procesu. W takim przypadku często w pozycję  $\alpha$  wiązania podwójnego wprowadza się brom lub jod.<sup>70</sup> Redukcja takich halo pochodnych, metodą CBS, przebiega już z wysoką enancjoselektywnością. Niestety po przeprowadzeniu redukcji konieczny jest dodatkowy etap mający na celu usunięcie atomu halogenu.<sup>71</sup>

Alternatywną metodą enancjoselektywnej redukcji enonów są reakcje katalitycznego enancjoselektywnego uwodornienia z zastosowaniem kompleksów Ru(II)-difosfino-1,2-diamin typu **53** opracowane przez Noyoriego,<sup>72</sup> a następnie rozwijane przez inne zespoły.<sup>73</sup> Metody te pozwalają na syntezę pożądaných alkoholi z bardzo dobrymi wydajnościami i świetnymi nadmiarami enancjomerycznymi. Co więcej, synteza chiralnych alkoholi allilowych **54a-d** podkreśla użyteczność opisanej strategii (Schemat 29). Związki te stanowią niezwykle ważne półprodukty w przemyśle aromatów i substancji zapachowych.



**Schemat 29.** Asymetryczne uwodornienie enonów z wykorzystaniem katalizatora Noyori.

W 2012 roku, Lipshutz<sup>74</sup> opracował warunki katalizowanej kompleksami Cu(II)/(*S*)-DTBM-SEGPPOS regio- i enancjoselektywnej redukcji  $\beta,\beta$ -dipodstawionych enonów. Jako reduktor wykorzystano dietoksymetylosilan. Alkohole uzyskano z umiarkowanym do doskonałego nadmiarem enancjomerycznym i dobrą 1,2-regioselektywnością (Schemat 30).



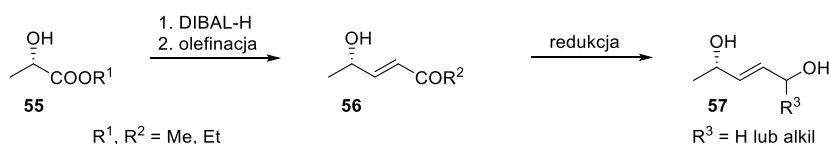
**Schemat 30.** Katalizowana miedzią 1,2-redukcja  $\beta,\beta$ -dipodstawionych enonów.

Pomimo opracowania szerokiej gamy warunków dla redukcji  $\alpha,\beta$ -nienasyconych ketonów to warto pamiętać, że redukcje te z wysoką enancjoselektywnością przebiegają zwykle wtedy, gdy dwie grupy przy węglu karbonylowym ketonu znacząco różnią się wielkością. Co więcej, nadal problematyczne jest wyeliminowanie ubocznego procesu 1,4-addycji albo uwodorniania wiązania podwójnego w enonach. Przedstawione metody bazują na stosowaniu katalizatorów metali przejściowych, co wymaga inertnych warunków prowadzenia procesu pod względem zawartości tlenu i wilgoci. Warto też podkreślić fakt, że większość przedstawionych metod redukcji wymaga stosowania stechiometrycznych ilości reduktorów co nie jest ani ekonomiczne atomowo, ani przyjazne dla środowiska szczególnie w zastosowaniach na dużą skalę.

#### 6.4.7. Synteza alkoholi allilowych z wykorzystaniem chiralnych bloków budulcowych

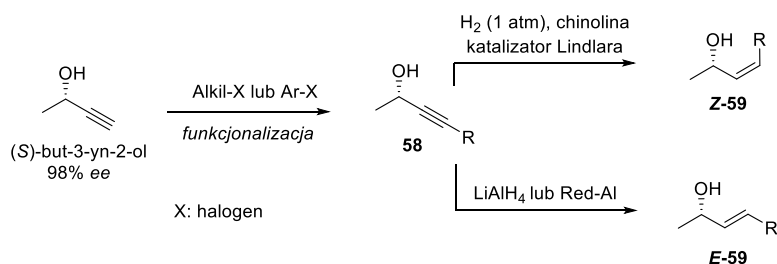
Ostatnią strategią, o której chciałabym wspomnieć, jest podejście wykorzystujące łatwo dostępne, chiralne bloki budulcowe (strategia „chiral pool”). Jednymi z powszechnie wykorzystywanych, chiralnych substratów pochodzenia naturalnego, w syntezie organicznej, w tym w syntezie enancjomerycznie wzbogaconych alkoholi allilowych, są estry kwasu L-mlekowego. Równie użytecznymi blokami budulcowymi są ich pochodne, na przykład alkohol propargilowy (*S*)-3-butyn-2-ol.

Prosta redukcja esteru **55** do aldehydu, a następnie olefinacja, prowadzi do produktu **56** (Schemat 31). Kolejna reakcja redukcji prowadzi do dioli typu **57**.<sup>8,75,76</sup> Tak otrzymane alkohole allilowe typu **56** i **57** znalazły szereg zastosowań w syntezie złożonych struktur organicznych<sup>75</sup> oraz w syntezach totalnych związków naturalnych.<sup>8,76</sup> Diole **57** same w sobie są cennymi blokami budulcowymi ze względu na obecność pierwszorzędowego alkoholu ( $R^3=H$ ), który to można wykorzystać w dalszych przekształceniach np. poddać bezpośrednio sprzęganiu z kwasami aryloboronowymi<sup>7b</sup> lub halogenkami aryłowymi,<sup>77</sup> ale też grupę hydroksylową można wymienić na brom<sup>78</sup> czy chlor.<sup>79</sup>



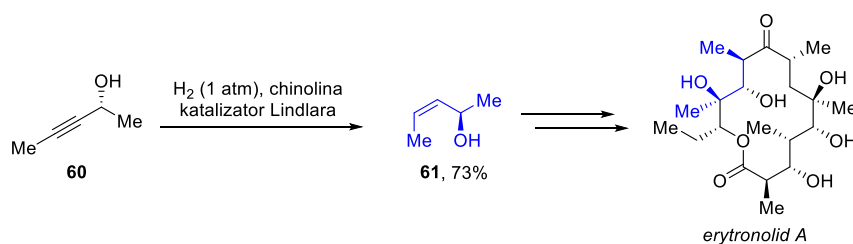
**Schemat 31.** Synteza alkoholi allilowych z pochodnych kwasu mlekowego.

Jak już wcześniej wspomniałam, w syntezie omawianej grupy związków wykorzystywane są też chiralne alkohole propargilowe.<sup>80</sup> Użycie (*S*)-but-3-yn-2-olu daje możliwość funkcjonalizacji terminalnego alkinu w wyniku reakcji alkilowania np. z halogenkami alkilowymi albo reakcji sprzęgania np. Sonogashiry z wykorzystaniem halogenków arylowych. Następnie, w zależności od warunków redukcji wiązania potrójnego w chiralnych alkoholach propargilowych **58** możliwe jest otrzymywanie szerokiej gamy (*E*)- lub (*Z*)-alkoholi allilowych **59**.<sup>80</sup>



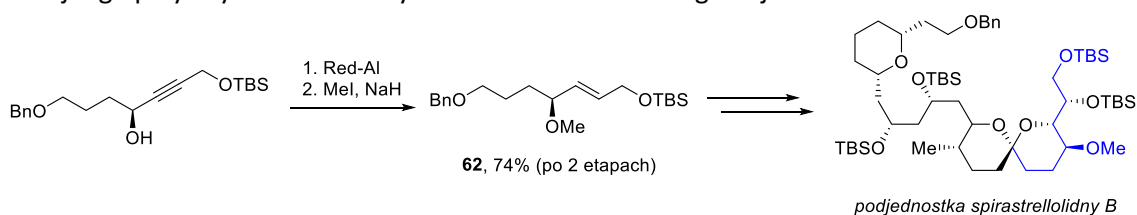
**Schemat 32.** Synteza *Z*- i *E*-alkoholi allilowych z chiralnego alkoholu propargilowego.

Wiązanie potrójne, w związkach typu **58**, można podać reakcji redukcji, na przykład w obecności katalizatora Lindlara, co daje możliwość syntezy alkenów o konfiguracji *Z*. Użyteczność tego przekształcenia została potwierdzona w syntezie totalnej erythronolidu A, opracowanej przez grupę Carreiry (Schemat 33).<sup>81</sup> Wiązanie potrójne w alkoholu **60**, zostało zredukowane do *Z*-alkenu **61** z wysoką wydajnością, a następnie w wyniku dalszych przekształceń umożliwił syntezę erythronolidu A, który jest aglikonem jednego z najbardziej znanych antybiotyków makrolidowych, erytromycyny A. Oprócz katalizatora Lindlara, efektywne w powyżej opisanym przekształceniu okazały się:  $Ti(Oi-Pr)_4$ , rodowe oraz rutenowe katalizatory.<sup>37</sup>



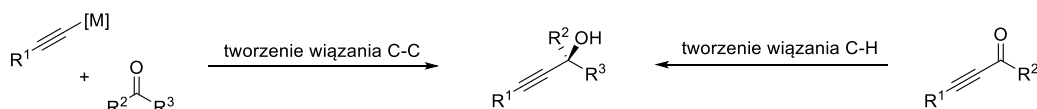
**Schemat 33.** Synteza totalna erythronolidu A.

Natomiast redukcja potrójnego wiązania w alkoholach propargilowych za pomocą  $LiAlH_4$  lub Red-Al prowadzi do (*E*)-alkenów (Schemat 34). Keaton i Phillips<sup>82</sup> pokazali efektywne wykorzystanie tej transformacji w syntezie podjednostki spirastrellolidny B, która została po raz pierwszy wyizolowana, w 2003 roku, przez Andersona<sup>83</sup> i współpracowników z morskiej gąbki *Spirastrella coccinea*. Wykazano, że spirastrellolidna B ma potencjalne właściwości względem hamowania fosfataz białkowych. Jednym z etapów przytoczonej syntezy była redukcja wiązania potrójnego przy użyciu Red-Al w syntezie alkenu **62** o konfiguracji *E*.



**Schemat 34.** Synteza totalna podjednostki spirastrellolidny B.

Warto zaznaczyć, że takie chiralne alkohole propargilowe można otrzymać także w wyniku enancjoselektywnej syntezy. Możliwe są dwa sposoby realizacji takiego procesu: albo poprzez enancjoselektywne alkynyłowanie związków karbonylowych albo poprzez asymetryczną redukcję ynonów<sup>37</sup> (Schemat 35).



**Schemat 35.** Synteza chiralnych alkoholi propargilowych.

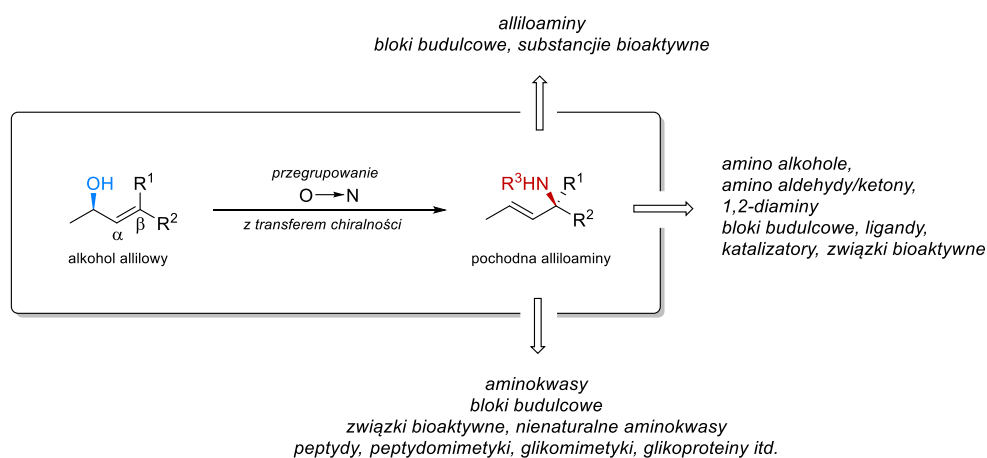
Przedstawione powyżej procesy dotyczą najprostszego wariantu zaprezentowanego na schematach **31** oraz **32**. Jednakże sytuacja komplikuje się, gdy wzrasta stopień podstawienia wiązania podwójnego oraz gdy te podstawniki mają złożoną strukturę lub też zawierają różne wrażliwe grupy funkcyjne. Co więcej, tworzenie wiązania podwójnego w takich układach nie zawsze pozwala na syntezę jednego czystego izomeru geometrycznego. Często otrzymuje się mieszaninę izomerów *E* i *Z*, których rozdzielenie klasycznymi metodami takimi jak chromatografia jest niemożliwe.

#### 6.4.8. Podsumowanie

Podsumowując tę część, w ciągu ostatnich dziesiątek lat opracowano szereg wysoce skutecznych metod otrzymywania omawianej grupy alkoholi. Spośród powyżej przedstawionych strategii do najczęściej wykorzystywanych należą: dynamiczny rozdział kinetyczny racematu, enancjoselektywne winylowanie związków karbonylowych oraz reakcje typu Tsiji-Trosta. Strategie te umożliwiają syntezę zróżnicowanych strukturalnie alkoholi allilowych, których użyteczność potwierdzono poprzez wykorzystanie ich w syntezie związków naturalnych i środków terapeutycznych. Niemniej jednak nadal istnieje zapotrzebowanie na alternatywne, ogólne, wydajne, chemoselektywne metody syntezy tej klasy związków o wysokiej czystości enancjomerycznej. Dotychczasowe strategie, choć dobre, mają wciąż istotne ograniczenia, do których należy zaliczyć złożoną strukturę i wysoką cenę stosowanych układów katalitycznych, jak na przykład kompleksy Noyori'ego czy układy na bazie irydu lub rodu. Kolejnym problemem jest niska ekonomia atomowa niektórych z omawianych procesów. Konieczność zastosowania stechiometrycznych ilości reaktywnych odczynników metaloorganicznych lub aktywowanych elektrofilowych czynników allilowych stanowi kolejne ograniczenie, zawężając w ten sposób pulę substratów oraz ograniczając chemoselektywność. W ciągu ostatniej dekady coraz większym zainteresowaniem cieszą się reakcje utleniania wiązań C-H, które pozwalają na syntezę alkoholi allilowych bezpośrednio z alkenów lub alkinów. Wstępne publikacje w tym obszarze wykazują potencjał takiego podejścia. Niestety prace te nadal koncentrują się na transformacjach prostych modelowych substratów, natomiast w przypadku bardziej złożonych układów konieczne są dalsze starania nad poprawą regio- i stereoselektywności.

### 3. BADANIA WŁASNE – PRZEWODNIK PO PUBLIKACJACH

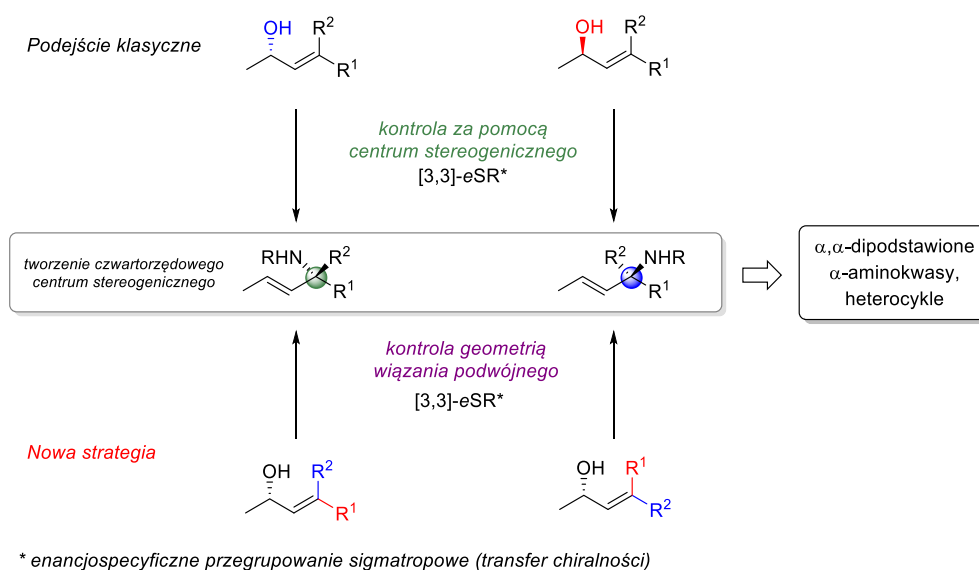
Dołączając do zespołu XXI IChO PAN, rozpoczęłam prace w projekcie, którego celem było wykorzystanie reakcji przegrupowania cyjanianów allilowych do izocyjanianów w syntezie  $\alpha$ -aminokwasów posiadających centrum stereogeniczne zlokalizowane na czteropodstawionym atomie węgla. Przystępując do realizacji badań przyjąłm cztery kluczowe zadania: (1) opracowanie efektywnej metody syntezy  $\beta,\beta$ -dipodstawionych alkoholi allilowych o wysokiej czystości optycznej i ściśle określonej geometrii wiązania  $E/Z$ , (2) przekształcenie wspomnianych alkoholi w odpowiednie karbaminiany allilowe, (3) wykorzystanie przegrupowania Ichikawy w syntezie  $\alpha$ -trzeciorzędowych alliloamin, a następnie, tak zwanych „czwartorzędowych” aminokwasów, (4) określenie zakresu stosowności opracowanych transformacji. Zaproponowaną strategię zamierzam wykorzystać w syntezie trzech grup związków:  $\alpha,\alpha$ -diarylo-,  $\alpha$ -alkilo- $\alpha$ -arylo- oraz  $\alpha,\alpha$ -dialkilopodstawionych aminokwasów.



**Schemat 36.** Założenia realizowanego projektu.

Realizowany przeze mnie projekt miał także na celu weryfikację dwóch strategii wykorzystania zaprezentowanego przegrupowania. Reakcja Ichikawy jest procesem uzgodnionym, przebiegającym przez cykliczny stan przejściowy. Rezultatem tego jest stereospecyficzny przebieg przegrupowania, w przypadku użycia nieracemicznego substratu, któremu towarzyszy całkowity transfer chiralności. Pierwsze podejście, klasyczne, zakłada kontrolę stereochemicznego przebiegu reakcji za pomocą konfiguracji absolutnej centrum stereogenicznego obecnego w substracie. Natomiast drugie, rzadziej wykorzystywane podejście, zakłada kontrolę stereochemicznego przebiegu reakcji za pomocą geometrii wiązania podwójnego, przy założeniu niezmienności konfiguracji absolutnej centrum stereogenicznego (Schemat 37). Drugie podejście było szczególnie istotne w przypadku syntezy omawianych alkoholi allilowych z łatwo dostępnych chiralnych prekursorów. W badaniach prowadzonych w Zespole XXI IChO PAN takimi blokami budulcowymi były pochodne kwasu L-mlekowego. Kwas L-mlekowy jest tanim, łatwo dostępnym, chiralnym odczynnikiem. Niestety jego nienaturalny enancjomer jest wielokrotnie droższy, przez co możliwość jego wykorzystania w syntezie organicznej jest dużo mniej atrakcyjna i bardzo kosztowna.



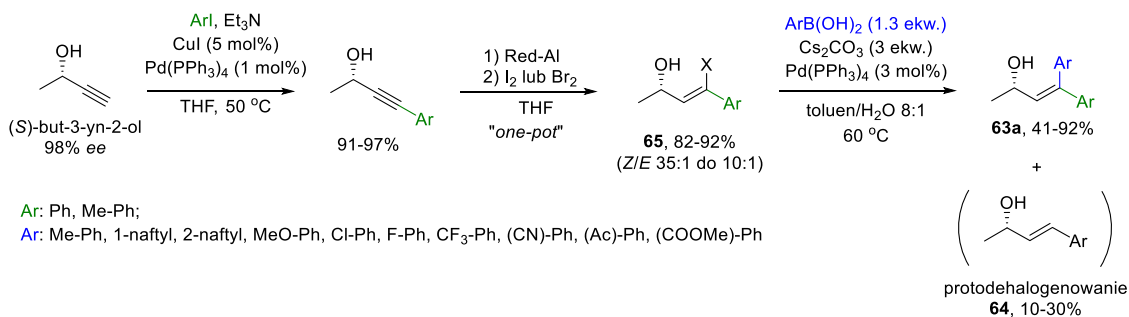


**Schemat 37.** Strategie kontroli stereochemicznego przebiegu reakcji przegrupowania.

### 3.1. Synteza $\beta,\beta$ -dipodstawionych alkoholi allilowych

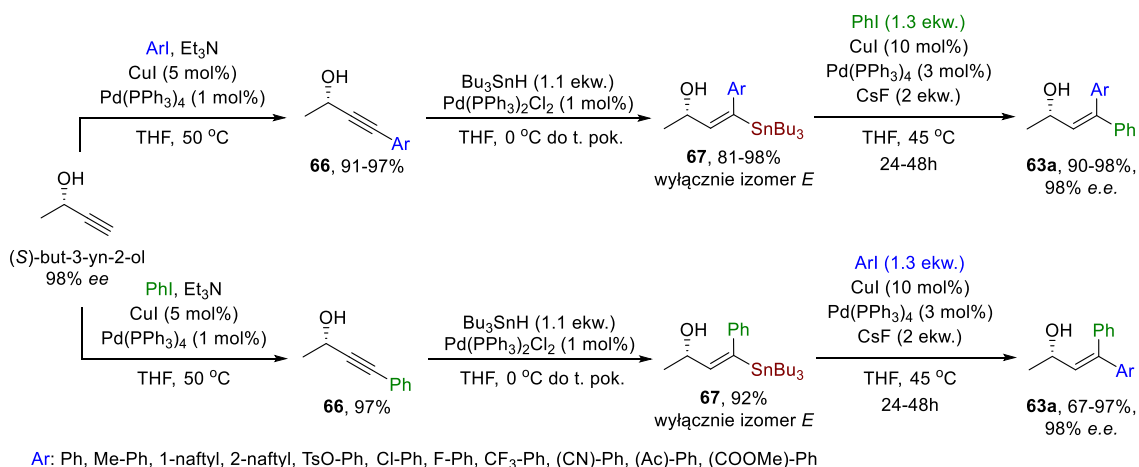
Jak już nadmieniałam, możliwość wykorzystania w reakcji przegrupowań sigmatropowych  $\beta,\beta$ -dipodstawionych alkoholi allilowych wiąże się z koniecznością opracowania efektywnej metody ich syntezy z wysoką czystością optyczną i wysoką selektywnością *E/Z*. Włączając się aktywnie w prace prowadzone w zespole XXI IChO PAN postanowiłam opracować ogólną metodę otrzymywania tej grupy alkoholi allilowych posiadających zarówno podstawniki alkilowe jak i aryłowe w pozycji  $\beta$  wiązania podwójnego. Rozważałam dwa podejścia realizacji wspomnianej syntezy. Pierwsze zakładało syntezę alkoholi allilowych na drodze syntezy asymetrycznej, na przykład poprzez enancjoselektywną redukcję enonów. Natomiast w drugim podejściu planowałam wykorzystać proste, łatwo dostępne związki nieracemiczne („chiral pool”) i przekształcić je w pożądane alkohole allilowe.

Pracę rozpocząłam wspólnie z dr. Pieczykolanem od syntezy  $\beta,\beta$ -diarylowych alkoholi allilowych. W pierwszej kolejności skupiliśmy się na syntezie nieracemicznych (*E*)- oraz (*Z*)- $\beta,\beta$ -diarylowych alkoholi allilowych przedstawionych na Schemacie 38. Synteza tych związków klasyczną metodą poprzez asymetryczną redukcję odpowiednich enonów okazała się mało selektywna. Ponadto synteza samych enonów jest też kłopotliwa z uwagi na tworzenie zwykle równomolowej mieszaniny izomerów *E* i *Z*. W związku z powyższym, zaproponowaliśmy dwa alternatywne podejścia oparte o sekwencyjne sprzężenie z udziałem nieracemicznego alkoholu propargilowego – (*S*)-3-butyn-2-olu. Pierwsza to połączenie reakcji sprzężenia Sonogashiry i Suzukiego. W przedstawionych warunkach otrzymaliśmy serię alkoholi allilowych **63a** z dobrymi wydajnościami. Niestety w reakcji powstawała także niewielka ilość związku **64** (10-30%), co prawdopodobnie wynikało z ubocznego procesu protodehalogenowania. Mimo prób dalszej optymalizacji warunków reakcji nie udało się wyeliminować tworzenia związku **64**. Co więcej, po dokładnym przeanalizowaniu widm NMR bromków winylowych **65** stwierdziliśmy obecność niewielkich ilości ich izomerów geometrycznych. Stosunek *Z/E* był w zakresie od 35:1 do 10:1. Niestety nie można było efektywnie usunąć ubocznie tworzących się izomerów *E* bromków winylowych. Także próby rozdzielania izomerów geometrycznych po przeprowadzeniu reakcji sprzężenia Suzukiego nie zakończyły się sukcesem.



**Schemat 38.** Synteza  $\beta,\beta$ -diarylowych alkoholi allilowych.

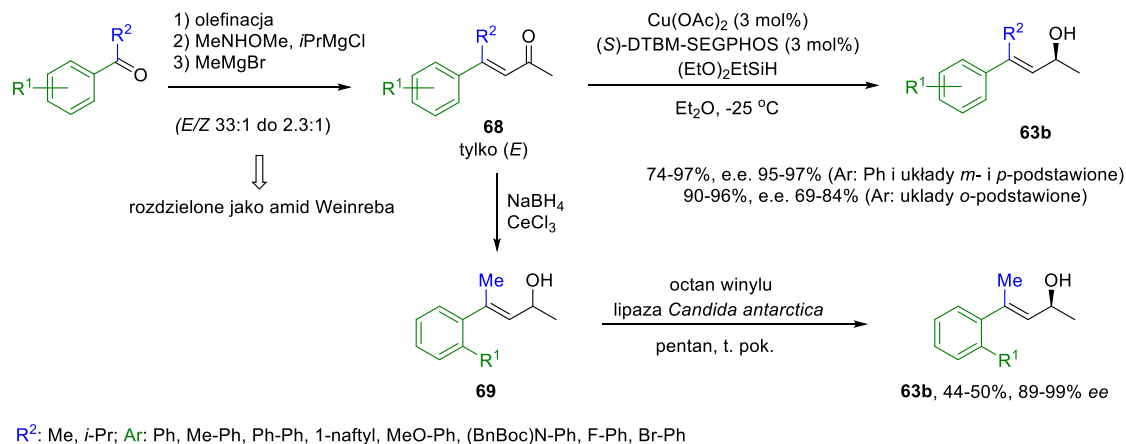
Kontynuując rozpoczęte prace, zaproponowałam drugie podejście do syntezy tej grupy alkoholi allilowych, obejmujące sekwencję reakcji sprzęgania Sonogashiry/Stille'a. Omawiana strategia okazała się atrakcyjniejsza, niż ta przedstawiona powyżej, ze względu na wyższą selektywność *E/Z* procesu hydrocynowania, co jest szczególnie istotne z punktu widzenia stereokontroli opisanego dalej etapu przegrupowania sigmatropowego, oraz brak ubocznego procesu protodehalogenowania jaki towarzyszył reakcji Suzukiego. Handlowo dostępny (*S*)-3-butyn-2-ol poddałam reakcji sprzęgania Sonogashiry z szeregiem jodków arylowych w obecności katalizatora palladowego. Następnie, przeprowadziłam addycję  $\text{Bu}_3\text{SnH}$  do alkoholi propargilowych **66**, a uzyskane związki cynoorganiczne **67** zostały poddane sprzęganiu Stille'a. Reakcje dla jodków arylowych posiadających podstawniki w pozycjach *meta* i *para* przebiegały bez problemów i z dobrymi wydajnościami. Natomiast w przypadku *orto*-podstawionych jodków arylowych, reakcje przebiegały wolniej i wymagały wydłużenia czasu, ale nadal z bardzo dobrymi wydajnościami. Przedstawione podejście umożliwiło mi także otrzymanie serii izomerycznych alkoholi **63a**, poprzez zmianę kolejności wprowadzania podstawników arylowych, co obrazuje druga ścieżka reakcji przedstawiona na Schemacie 39.



**Schemat 39.** Synteza  $\beta,\beta$ -diarylowych alkoholi allilowych.

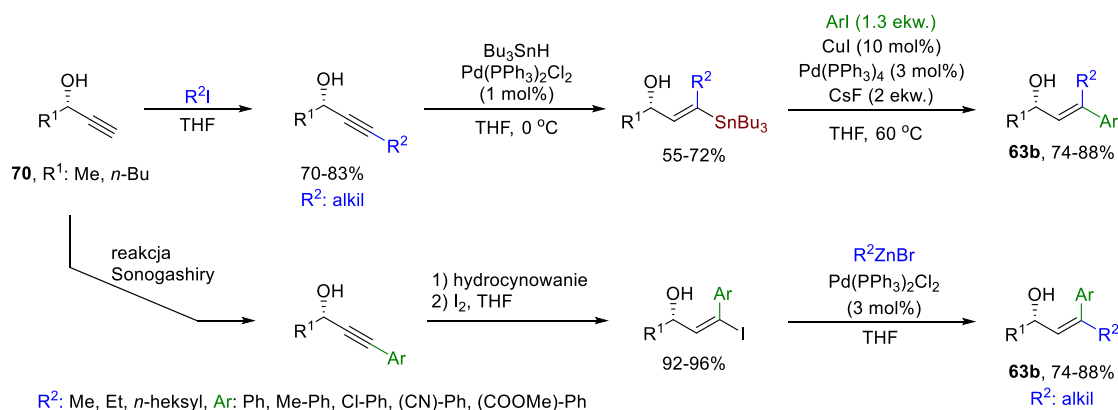
W kolejnym kroku skupiłam się na syntezie chiralnych  $\beta$ -alkilo- $\beta$ -arylo-dipodstawionych alkoholi allilowych. W przeciwieństwie do wcześniej omawianych układów diarylowych, w tym przypadku możliwe było wykorzystanie, aż trzech strategii syntezy docelowych alkoholi. Pierwsza z nich polegała na asymetrycznej redukcji enonów **68** prowadzonej za pomocą silanu w obecności chiralnego kompleksu  $\text{Cu(II)}$ . Wykorzystałam przy tym warunki reakcyjne opracowane przez Lipshutza i współpracowników.<sup>74</sup> Odpowiednie alkohole **63b** tworzyły się z wysokimi

wydajnościami (>74%) i wysoką enancjoselektywnością (95-97% *ee*) w przypadku, gdy grupą arylową był *para*- lub *meta*-podstawiony pierścień fenyłowy lub sam fenyl (Schemat 40). Natomiast w przypadku układów *orto*-podstawionych nadmiary były niższe, w zakresie 69-84%. Dla tych układów lepsze nadmiary enancjomeryczne (89-99%) uzyskałam na drodze enzymatycznego rozdziału kinetycznego racemicznych alkoholi **69** (Schemat 40).



**Schemat 40.** Synteza  $\beta$ -alkilo- $\beta$ -arylowych alkoholi allilowych.

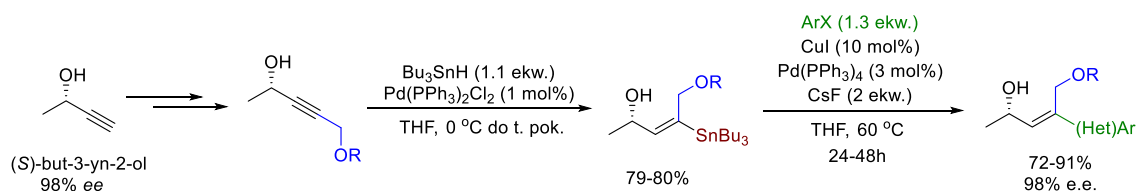
Równoległe opracowałam także warunki syntezy  $\beta$ -alkilo- $\beta$ -arylo-dipodstawionych alkoholi allilowych wychodząc z chiralnych alkoholi propargilowych **70** poddając je kolejno reakcji alkilowania, hydrocynowania i reakcji Stille'a. Docelowe alkohole **63b** uzyskałam z wysokimi wydajnościami, bez utraty czystości optycznej, oraz wyłącznie jako izomery (*E*) lub (*Z*). Reakcja sprzęgania Stille'a przebiegała efektywnie w 60 °C dla szerokiej gamy jodków arylowych posiadających zarówno podstawniki elektronodonorowe oraz elektronoakceptorowe. Podobnie jak wcześniej, reakcje z udziałem *orto*-podstawionych jodków arylowych wymagały wydłużenia czasu reakcji z 24 do 48 godzin. Druga badana przeze mnie strategia oparta na sekwencji reakcji sprzęgania Sonogashiry, hydrocynowaniu/wymianie na Sn-halogen oraz reakcji sprzęgania Negishiego okazała się znacznie mniej efektywna. Na etapie reakcji Negishiego możliwe było wykorzystanie wyłącznie prostych, liniowych odczynników cynkoorganicznych. W przypadku bardziej rozgałęzionych układów takich jak *i*-Pr czy *t*-Bu obserwowałam głównie produkt protodehalogenowania.



**Schemat 41.** Synteza  $\beta$ -alkilo- $\beta$ -arylowych alkoholi allilowych.

Zaproponowana przeze mnie strategia okazała się także atrakcyjna w syntezie  $\beta$ -arylowych alkoholi allilowych posiadających dodatkowe ugrupowanie hydroksymetylowe

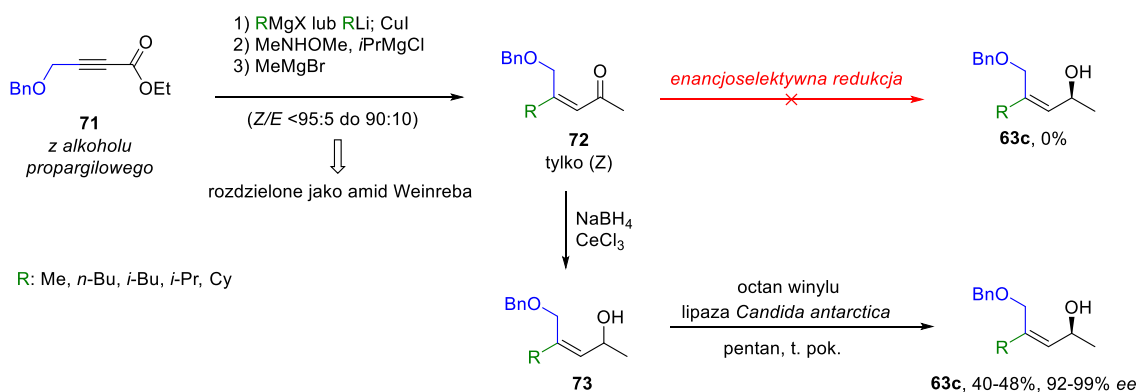
(Schemat 42). Tą grupę alkoholi miałam zamiar wykorzystać w syntezie hydroksy-alliloamin, a następnie arylowych pochodnych seryny. Warty podkreślenia jest fakt, że możliwa była także wydajna synteza heteroaromatycznych alkoholi allilowych tj. pochodnych pirydyny, chinoliny, tiofenu i benzofuranu.



R: MOM, Bn; Ar: Ph, Me-Ph, 1-naftyl, MeO-Ph, (BnBoc)N-Ph, CF<sub>3</sub>-Ph, F-Ph, Cl-Ph, Br-Ph, (CN)-Ph, (COOMe)-Ph, Het

**Schemat 42.** Synteza  $\beta$ -hydroksymetylowych,  $\beta$ -arylowych alkoholi allilowych.

Następnie, skupiłam się na syntezie nieracemicznych  $\beta$ -alkilowych alkoholi allilowych posiadających dodatkowe ugrupowanie hydroksymetylowe (Schemat 43). Realizację tej części projektu rozpocząłam wykorzystując katalizowaną CuI reakcję 1,4-addycji do alkinów **71** w syntezie  $\alpha,\beta$ -nienasyconych estrów. Następnie, po kilku przekształceniach, otrzymałam odpowiednie enony **72**, które planowałam poddać reakcji asymetrycznej redukcji w oparciu o uprzednio stosowane przeze mnie metody. Niestety żadna z tych strategii nie pozwoliła na uzyskanie enancjomerycznie wzbogaconych alkoholi allilowych typu **63c**. W większości przypadków reakcje w ogóle nie przebiegały. W związku z tym, przygotowałam serię racemicznych alkoholi typu **73**, które następnie poddałam enzymatycznemu rozdziałowi kinetycznemu, co umożliwiło mi otrzymanie enancjomerycznie czystych alkoholi **63c** (Schemat 3). Tak uzyskane alkohole allilowe planowałam wykorzystać w syntezie hydroksy-alliloamin, a następnie alkilowych pochodnych seryny.

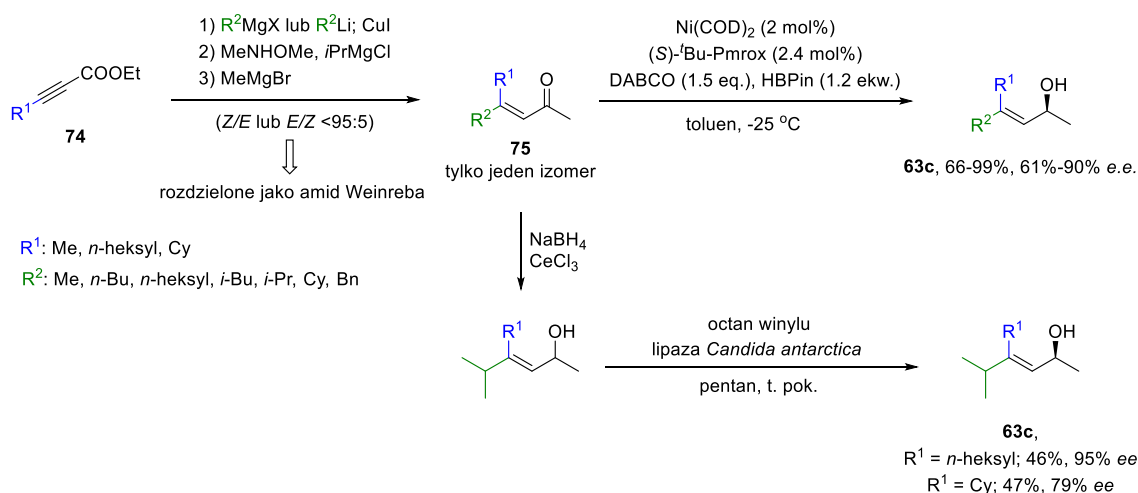


**Schemat 43.** Synteza  $\beta$ -hydroksymetylowych,  $\beta$ -alkilowych alkoholi allilowych.

Opisana powyżej metoda stereoselektywnej syntezy  $\beta$ -hydroksymetylo- $\beta$ -alkilowych alkoholi allilowych stanowi wstęp do realizacji ostatniej części mojej rozprawy doktorskiej – kontrolowanej syntezy  $\beta,\beta$ -dialkilowych alkoholi allilowych (Schemat 44). Niestety wymogi formalne związane z czasem trwania studiów doktoranckich oraz sztywne ramy czasowe stypendium Etiuda, obligują mnie do złożenia rozprawy doktorskiej w ściśle wyznaczonym czasie. Zrealizowane przeze mnie badania syntezy alkoholi  $\beta,\beta$ -dialkilowych zostały przygotowane w formie publikacji naukowej i wysłane do redakcji. Niestety proces oceny przez niezależnych recenzentów wyznaczonych przez Edytora periodyku okazał się dość długi. Natomiast ze względu na ich wartość dopełniającą moje badania zdecydowałam się przedstawić je w niniejszym

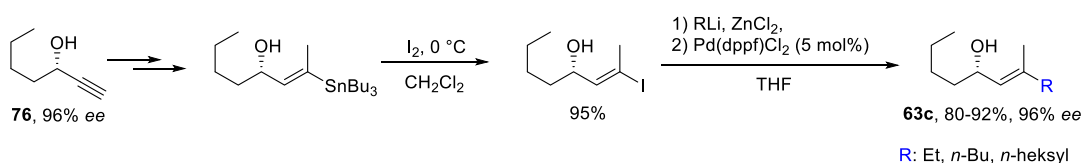
przewodniku (Schemat 44). Poniższe wyniki są aktualnie recenzowane w czasopiśmie *Org. Biomol. Chem.*, a potwierdzenie z datą wpłynięcia do wydawnictwa załączam w niniejszym przewodniku.

Jak już nadmieniałam, ostatnim etapem tej części badań była synteza  $\beta,\beta$ -dialkilowych alkoholi allilowych. Realizację projektu rozpoczęłam, analogicznie do syntezy alkoholi allilowych typu **63c** przedstawionej na Schemacie 43, od wykorzystania katalizowanej CuI reakcji 1,4-addycji do alkinu **74** otrzymując serię  $\alpha,\beta$ -nienasyconych estrów (Schemat 44). Uzyskałam produkty zanieczyszczone tylko niewielką ilością (<5%) izomeru geometrycznego (*E*) lub (*Z*).  $\alpha,\beta$ -Nienasycone estry przekształciłam, w dwóch etapach, w odpowiednie enony **75**, które poddałam asymetrycznej redukcji w obecności chiralnego kompleksu niklu oraz HBPIn jako źródła wodorku. Alkohole **63c**, posiadające proste liniowe podstawniki, takie jak Me, *n*-Bu, *n*-heksyl, *i*-Bu, Bn, uzyskałam z bardzo dobrymi wydajnościami (85-99%) i bardzo dobrymi nadmiarami enancjomerycznymi (92-98% *ee*). Redukcja enonów zawierających jedną sterycznie zatłoczoną grupę alkilową, taką jak *i*-Pr czy cykloheksyl, przebiegały nadal skutecznie (70-98%), jednak czas reakcji musiał zostać wydłużony do 48 z 24 godzin. W przypadku tych ostatnich alkoholi uzyskiwane nadmiary enancjomeryczne były niższe (82-88% *ee*). Wprowadzenie do cząsteczki enonu **75** dwóch rozbudowanych podstawników jednocześnie, powodowało znaczny spadek efektywności redukcji (66%, 71%) oraz enancjoselektywności (70%, 61% *ee*) prowadzonego procesu. Dla takiej grupy alkoholi allilowych najlepszą metodą syntezy okazał się enzymatyczny rozdział kinetyczny.



Schemat 44. Synteza  $\beta,\beta$ -dialkilowych alkoholi allilowych.

Równoległe opracowałam także warunki syntezy dialkilowych alkoholi typu **63c** wychodząc z chiralnego alkoholu propargilowego **76**, który poddałam kolejno alkilowaniu, hydrocynowaniu i sprzęganiu Negishiego. Wykorzystanie w tym przekształceniu katalizatora Pd(dppf)Cl<sub>2</sub> pozwoliło na wydajną syntezę alkoholi allilowych **63c**, bez śladu ubocznego produktu protodehalogenowania. Niestety proces ten był ograniczony do wprowadzenia wyłącznie prostych, liniowych grup alkilowych, takich jak Et lub *n*-Bu, *n*-heksyl.

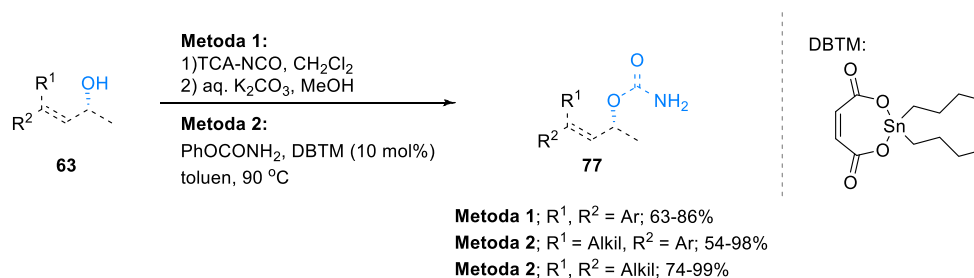


Schemat 45. Synteza  $\beta,\beta$ -dialkilowych alkoholi allilowych.

### 3.2. Przegrupowanie cyjanianów allilowych do izocyjanianów – synteza $\alpha,\alpha$ -dipodstawionych alliloamin

Mając w ręku szeroką gamę chiralnych  $\beta,\beta$ -dipodstawionych alkoholi allilowych, w kolejnym kroku rozpoczęłam badania nad ich transformacją w odpowiednie alliloaminy w procesie przegrupowania [3,3]-sigmatropowego typu tlenu-do-azotu. Kontynuując prace zespołu XXI IChO PAN postanowiłam wykorzystać reakcję przegrupowania cyjanianów allilowych do izocyjanianów zwaną też reakcją Ichikawy. Jest to szybka i prosta metoda transformacji alkoholi allilowych w odpowiednie alliloaminy. Jak już wcześniej wspomniałam, reakcja przebiegała w łagodnych warunkach i bez użycia jakichkolwiek katalizatorów metalicznych. Uzgodniony mechanizm tej reakcji gwarantuje efektywny [1,3]-transfer chiralności do nowo utworzonego centrum stereogenicznego. Ponadto powstający w reakcji Ichikawy izocyjanian jako związek pośredni daje możliwość bezpośredniej funkcjonalizacji z różnymi czynnikiemami nukleofilami co umożliwia tworzenie szerokiej gamy pochodnych alliloaminy, takich jak amidy, karbaminiany lub moczniki.

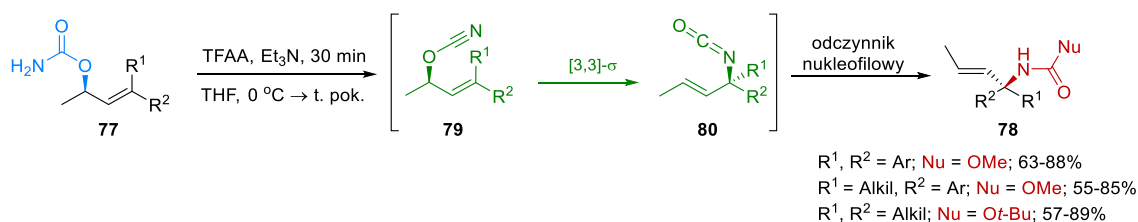
W tym celu, uzyskane alkohole **63** przekształcałam w odpowiednie karbaminiany allilowe **77** (Schemat 46). Początkowo dla układów posiadających dwa podstawniki arylowe w pozycji  $\beta$  wiązania podwójnego wykorzystywałam reakcję karbamoilowania za pomocą izocyjanianu trichloroacetylowego z następczą hydrolizą zasadową (Metoda 1, Schemat 46). Reakcja przebiegała efektywnie dla szerokiej gamy alkoholi allilowych niezależnie od charakteru podstawników przy pierścieniu aromatycznym. Następnie, skupiłam się na syntezie  $\beta$ -alkilo- $\beta$ -arylowych karbaminianów allilowych. Nieoczekiwanie, opisana powyżej metoda, wielokrotnie wykorzystywana w naszym zespole dała słabe efekty. Pożądane karbaminiany otrzymałam z wydajnościami nie przekraczającymi 60%. Ponadto zaobserwowałam częściowy rozkład substratów w warunkach reakcji. W związku z tym, uzyskane wcześniej alkohole allilowe, przekształcałam w odpowiednie karbaminiany w reakcji transkarbamoilowania za pomocą karbaminianu fenylu wobec katalizatora na bazie cyny (Metoda 2, Schemat 46).<sup>36</sup> Zmiana warunków reakcji wyeliminowała reakcje uboczne i umożliwiła syntezę pożądanych produktów z wysokimi wydajnościami. Metoda ta została także z powodzeniem wykorzystana przeze mnie w syntezie  $\beta,\beta$ -dialkilowych karbaminianów allilowych.



**Schemat 46.** Synteza  $\beta,\beta$ -dipodstawionych karbaminianów allilowych.

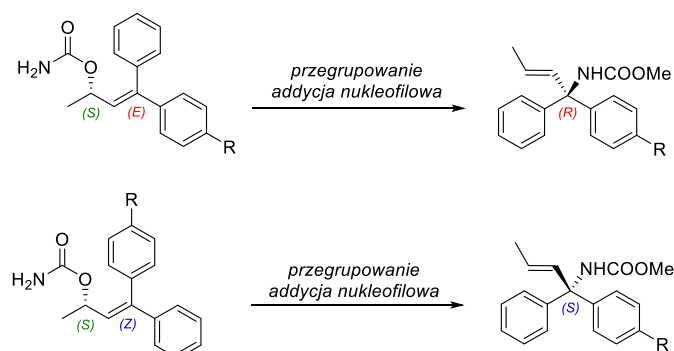
Otrzymane w ten sposób karbaminiany **77** poddałam reakcji przegrupowania uzyskując  $\alpha$ -trzeciorzędowe alliloaminy **78** posiadające w pozycji  $\alpha$  zarówno podstawniki alkilowe jak i arylowe (Schemat 47). Odwodnienie karbaminianów do cyjanianów **79** prowadziłam przy użyciu TFAA w obecności Et<sub>3</sub>N. Odwodnienie i następcze przegrupowanie do izocyjanianów **80** przebiega w łagodnych warunkach (0 °C) i w krótkim czasie (30 min). Powstałych izocyjanianów allilowych **80** nie wydzielalam tylko traktowałam bezpośrednio odczynnikami nukleofilowym (np. MeOLi lub

*t*-BuOLi) otrzymując w ten sposób pożądane produkty przegrupowania **78** z dobrymi wydajnościami po 3 etapach. Choć przegrupowanie obejmuje sekwencje trzech reakcji to wszystkie z nich realizowałam w jednym naczyniu, poprzez dodawanie kolejnych odczynników (wariant „one-pot”). Mając na celu określenie zakresu stosowalności omówionej metody wykorzystywałam strukturalnie zróżnicowane karbaminiany posiadające zarówno alkilowe jak i arylove podstawniki oraz dodatkowe grupy funkcyjne. Przeprowadzone eksperymenty wykazały, że badane reakcje przebiegają z wysokimi wydajnościami, na które w niewielkim stopniu wpływa struktura substratu. Co ważne, reakcja przegrupowania przebiegała z całkowitym transferem chiralności od substratu do produktu generując nowe centrum stereogeniczne.



**Schemat 47.** Synteza  $\alpha,\alpha$ -dipodstawionych alliloamin.

Zgodnie z oczekiwaniami, przegrupowanie alkoholi o konfiguracji (*S,E*) prowadziło do (*R*)-alliloamin, natomiast (*S,Z*)-izomery umożliwiły syntezę alliloamin o konfiguracji (*S*) (Schemat 48). Wynik ten jednoznacznie pokazuje możliwość kontroli stereochemicznego przebiegu reakcji przegrupowania także za pomocą geometrii wiązania podwójnego przy założeniu niezmienności konfiguracji absolutnej centrum stereogenicznego.

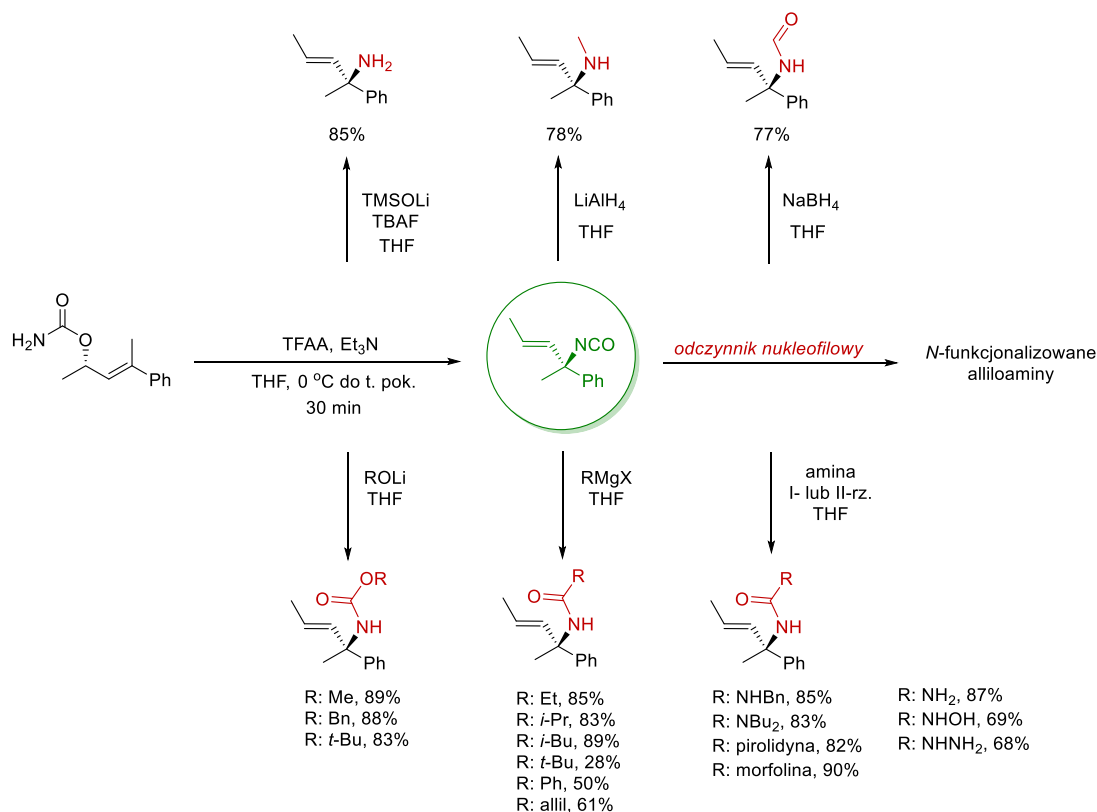


**Schemat 48.** Reakcja przegrupowania kontrolowana geometrią wiązania podwójnego.

### 3.3. Funkcjonalizacja izocyjanianów – synteza *N*-podstawionych alliloamin

Tworzenie jako produktu reakcji Ichikawy izocyjanianu jest niewątpliwą zaletą tego przegrupowania. Powstający izocyjanian można wydzielić, choć wymaga to ostrożnego postępowania z uwagi na wysoką reaktywność tej klasy związków. Dużo korzystniejszym i praktyczniejszym rozwiązaniem jest poddanie uzyskanego w wyniku przegrupowania izocyjanianu bezpośrednio reakcji z odczynnikami nukleofilowymi. Dzięki zastosowaniu różnych reagentów nukleofilowych możliwe jest uzyskanie szerokiej gamy *N*-funkcjonalizowanych alliloamin, które stanowią niezwykle cenne bloki budulcowe w chemii organicznej. Zaproponowana przeze mnie metodologia syntezy alliloamin, poprzez reakcję Ichikawy, jest kompatybilna z różnymi odczynnikami nukleofilowymi, w tym alkoholami, aminami i ich pochodnymi, odczynnikami litoorganicznymi i odczynnikami Grignarda lub odczynnikami wodorkowymi. Wszystkie te

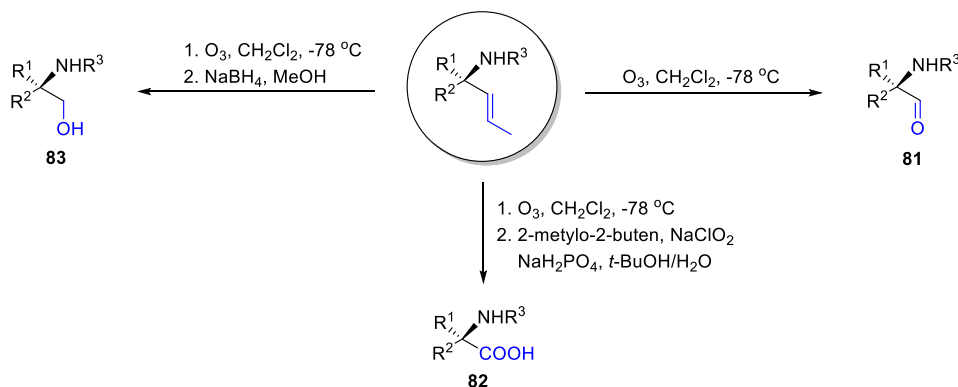
reagenty pozwalają na syntezę *N*-podstawionych alliloamin takich jak: aminoestrów, amidów, pochodnych mocznika, formamidów, *N*-metyloamin czy wolnych amin (Schemat 49).



Schemat 49. Synteza *N*-funkcjonalizowanych alliloamin.

### 3.4. Funkcjonalizacja wiązania podwójnego w alliloaminach

Alliloaminy są niezwykle cennymi blokami budulcowymi w syntezie organicznej ze względu na obecność grupy aminowej oraz podwójnego wiązania, które dają możliwość dalszej funkcjonalizacji tych struktur. Otrzymane alliloaminy mogą ulegać szerokiej gamie transformacji wiązania podwójnego, z czego kilka przykładów przedstawiłam na poniższym schemacie. Zwróciłam uwagę na reakcję ozonolizy prowadzącą do aldehydu **81**. Powstający w ten sposób aminoaldehyd **81** można utlenić do aminokwasu **82**, albo zredukować do aminoalkoholu **83**. Takie przekształcenia będą szczególnie atrakcyjne z punktu widzenia niniejszej pracy (Schemat 50).

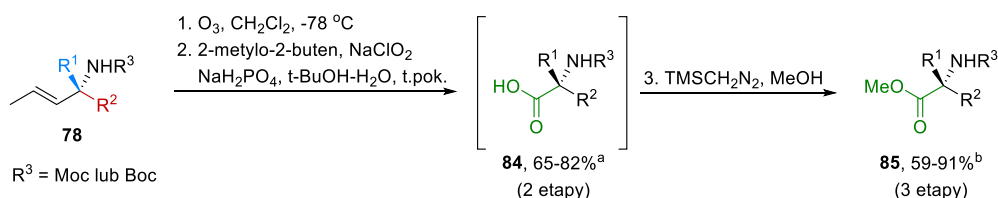


Schemat 50. Funkcjonalizacja wiązania podwójnego w alliloaminach.



### 3.4.1. Wykorzystanie alliloamin w syntezie $\alpha,\alpha$ -dipodstawionych aminokwasów

Ukoronowaniem prowadzonych przeze mnie badań była transformacja otrzymanych wcześniej alliloamin **78** do  $\alpha,\alpha$ -dipodstawionych aminokwasów. W tym celu, alliloaminy **78** poddałam reakcji ozonolizy połączonej z następczą reakcją utleniania Pinnicka-Lindgrena (i ewentualnego diazowania). Odpowiednie aminokwasy i ich pochodne wydzieliłam albo w postaci wolnych kwasów **84** albo estrów metylowych **85** w celu ułatwienia oczyszczania pożądaných produktów.



<sup>a</sup> wydajność dla wolnego kwasu

<sup>b</sup> wydajność dla estru metylowego, po 3 etapach, bez wydzielenia wolnego kwasu

**Schemat 51.** Synteza  $\alpha,\alpha$ -dipodstawionych aminokwasów.

Warto zaznaczyć, że powyżej przedstawiona transformacja nie powiodła się dla układów zawierających ugrupowania heteroarylowe (tj. pochodne pirydyny, chinoliny, tiofenu i benzofuranu). W przedstawionych warunkach obserwowałam wyłącznie rozkład substratów.

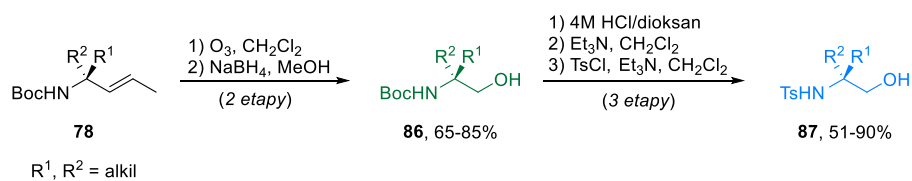
### 3.4.2. Wykorzystanie alliloamin w syntezie aminoalkoholi, diamin oraz związków heterocyklicznych

Wyniki uzyskane w niniejszym rozdziale są przedmiotem publikacji będącej obecnie w recenzji, w czasopiśmie *Org. Biomol. Chem.* Dotyczą one wykorzystania  $\alpha,\alpha$ -dialkylowych alliloamin, otrzymanych z odpowiednich  $\beta,\beta$ -dialkylowych alkoholi allilowych (Schemat 44 oraz 45, str. 44), w syntezie wybranych układów heterocyklicznych. Chcąc pokazać potencjał alliloamin jako bloków budulcowych w otrzymywaniu ważnych w kontekście syntezy organicznej i chemii medycznej związków, zdecydowałam się przedstawić poniższe wyniki w tym przewodniku.

Realizując postawione cele, postanowiłam przekształcić otrzymane  $\alpha,\alpha$ -dialkylowe alliloaminy typu **78** w odpowiednie aminoalkohole **86** oraz **87** (Schemat 52). Chiralne 1,2-aminoalkohole są klasą związków organicznych, której poświęcono wiele uwagi w dziedzinie syntezy organicznej. Są one związkami pośrednimi w wytwarzaniu biologicznie aktywnych substancji, a także wykorzystywane w przemyśle farmaceutycznym. Ponadto,  $\beta$ -aminoalkohole również odgrywają ważną rolę jako chiralne ligandy i chiralne substancje pomocnicze w asymetrycznej katalizie.<sup>84</sup>

Kontynuując prace w tym temacie, alliloaminy **78** poddałam reakcji ozonolizy, a następnie redukcji za pomocą  $NaBH_4$  prowadzącej do odpowiednich *N*-Boc zabezpieczonych aminoalkoholi **86** z bardzo dobrymi wydajnościami po 2 etapach. Ponadto,  $\beta$ -aminoalkohole **86** można łatwo przekształcić w ich *N*-Ts zabezpieczone pochodne **87**, poprzez potraktowanie ich 4M roztworem HCl w dioksanie, z następczym *N*-tosylowaniem za pomocą TsCl w obecności  $Et_3N$  (Schemat 52).

Obie te grupy są niezwykle cennymi związkami w chemii organicznej,<sup>84</sup> które można wykorzystać w dalszych przekształceniach.

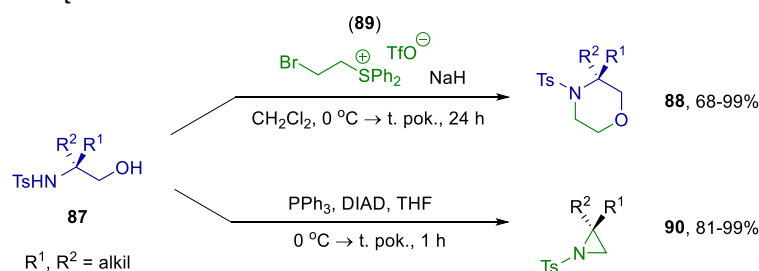


Schemat 52. Synteza  $\beta$ -aminoalkoholi.

Tak otrzymane  $\beta$ -aminoalkohole **86/87** postanowiłam wykorzystać w syntezie wybranych układów heterocyklicznych. Heterocykle, zawierające atom azotu, takie jak morfoliny,<sup>85</sup> piperazyny<sup>85d-g,86</sup> oraz azirydyny<sup>87</sup> są ważnymi farmakoforami w chemii medycznej. Chociaż znany jest szereg strategii syntezy wspomnianych układów heterocyklicznych, to tylko nieliczne metody nadają się do syntezy układów posiadających centrum stereogeniczne na czteropodstawionym atomie węgla. Niewątpliwie jest to spowodowane ograniczonym dostępem do odpowiednich substratów oraz wydajnych, wysoce stereoselektywnych metod ich syntezy. Zatem, aby zademonstrować użyteczność opisanej przeze mnie strategii otrzymywania nieracemicznych  $\beta$ -aminoalkoholi **86/87**, postanowiłam przeprowadzić ich transformację do wspomnianych związków heterocyklicznych.

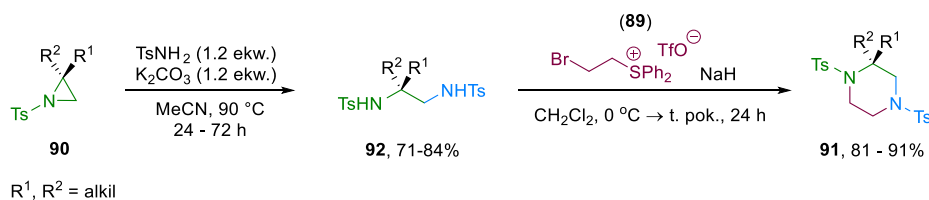
Pracę w tym temacie rozpoczęłam od syntezy odpowiednich *gem*-podstawionych morfolin **88**. Cyklizację 1,2-aminoalkoholi **87** prowadziłam przy użyciu soli bromoetylosulfoniowej (**89**)<sup>88</sup> w obecności NaH jako zasady, jak przedstawiałam na Schemacie 53. Otrzymałam pożądane morfoliny **88** z bardzo dobrymi wydajnościami.

Następnie, skupiałam się na transformacji  $\beta$ -aminoalkoholi **87** w odpowiednie azirydyny **90**. Postanowiłam przeprowadzić cyklizację w warunkach reakcji Mitsunobu, wykorzystując w tym celu PPh<sub>3</sub> i DIAD w THF. Synteza azirydyn **90** przebiegała efektywnie, w krótkim czasie i z niemal ilościową wydajnością.



Schemat 53. Synteza morfolin i azirydyn.

Ostatnim przykładem wykorzystania  $\beta$ -aminoalkoholi **86/87** w syntezie ważnych z punktu widzenia chemii medycznej heterocykli, było przekształcenie wybranych związków **90** w odpowiednie piperazyny **91**. Kontynuując pracę w tym temacie, azirydyny **90** poddałam reakcji otwarcia pierścienia za pomocą TsNH<sub>2</sub> w obecności K<sub>2</sub>CO<sub>3</sub> jako zasady. Uzyskane pochodne diamionowe **92** (Schemat 54) poddałam następnie cyklizacji w obecności soli sulfoniowej **89**<sup>88</sup> i zasady (NaH) uzyskując odpowiednie chiralne piperazyny **91** z bardzo dobrymi wydajnościami.

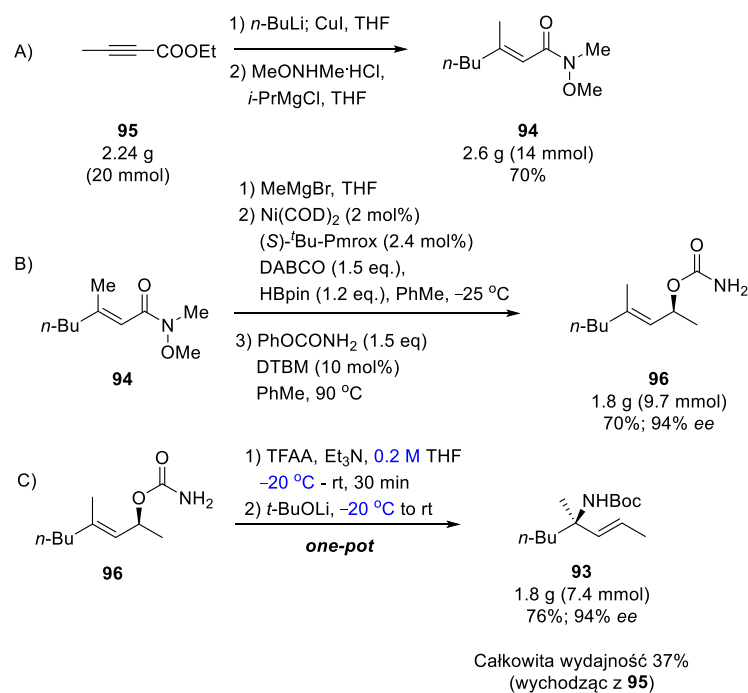


**Schemat 54.** Synteza diamin i piperazyn.

### 3.5. Synteza alliloamin w skali gramowej

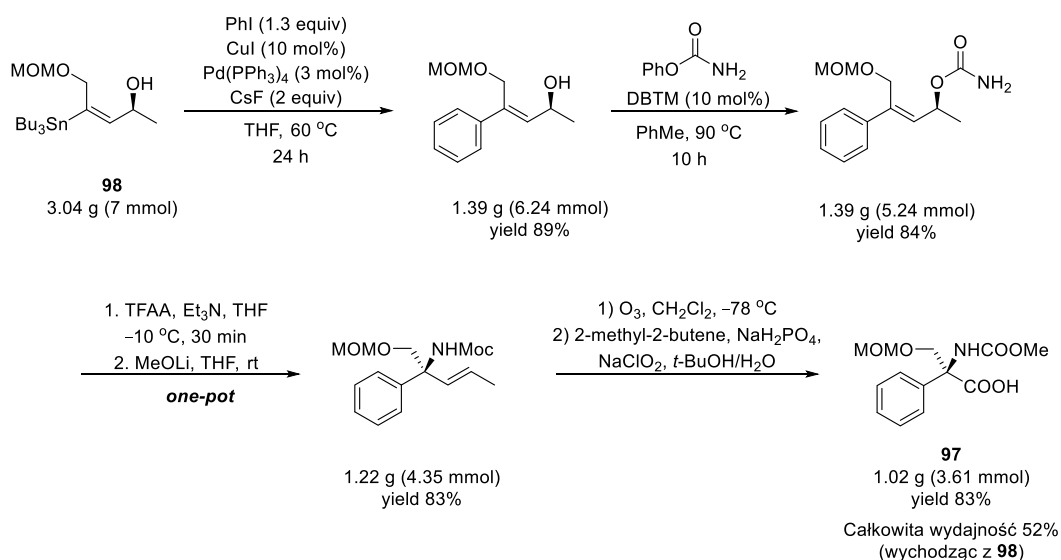
Przedstawione we wcześniejszych rozdziałach transformacje prowadzące do nieracemicznych alliloamin oraz aminokwasów prowadziłam zazwyczaj w skali poniżej 1 mmol. Chcąc zademonstrować użyteczność zaproponowanych przeze mnie przekształceń postanowiłam sprawdzić skalowalność opracowanych metod syntetycznych. Zilustrowałam to na przykładzie syntezy alliloaminy **93** (Schemat 55). W celu zmaksymalizowania wydajności procesu i zminimalizowania strat podczas oczyszczania związków pośrednich, postanowiłam poszczególne etapy syntezy połączyć w trzy bloki (A, B i C), tak aby izolację/oczyszczanie związków pośrednich ograniczyć do prostych ekstrakcji.

Pierwszy blok transformacji obejmował syntezę amidu Weinreba **94** z prostego, handlowo dostępnego alkinu **95** (Blok A, Schemat 55). Następny blok reakcji to addycja odczynnika Grignarda do amidu **94**, enancjoselektywna redukcja do alkoholu oraz transkarbamioilowanie tego ostatniego prowadzące do karbaminianu **96** (Blok B, Schemat 55). Związki pośrednie, keton i alkohol allilowy, wydzieliłam poprzez ekstrakcję, a następnie bez dalszego oczyszczania wykorzystałam w kolejnych etapach syntezy (Blok B, Schemat 55). Ostatni blok reakcji obejmował transformację karbaminianu **96** do alliloaminy **93** w oparciu o sekwencje reakcji odwodnienia, przegrupowania sigmatropowego i addycji odczynnika nukleofilowego (Blok C, Schemat 55). W rezultacie, przedstawiona na poniższym schemacie, 7-etapowa synteza, wymagała tylko trzech operacji oczyszczania metodą chromatografii kolumnowej, kolejno, na etapie: (1) amidu **94** (w celu wyeliminowania zanieczyszczenia niewielką ilością izomeru *Z*), (2) karbaminianu **96**, (gdyż niewielkie zanieczyszczenia mogą wpływać na wydajność reakcji przegrupowania) oraz (3) oraz finalnej aminy **93**. Pozostałe kroki wymagały jedynie prostej ekstrakcji. Prowadzenie reakcji Ichiikawy było również skuteczne w większej skali, jednakże wymagało niewielkich modyfikacji procedur. Na etapie reakcji przegrupowania korzystne było obniżenie temperatury mieszaniny do  $-20\text{ }^{\circ}\text{C}$ , w trakcie dodawania TFAA do roztworu karbaminianu **96** i  $\text{Et}_3\text{N}$ , aby uniknąć przegrzania. Ponadto, w przypadku syntezy w dużej skali, zwiększyłam stężenie mieszaniny reakcyjnej, liczone względem substratu, z 0.05 M (dla skali  $<1\text{ mmol}$ ) do 0.2 M. Umożliwiło to zmniejszenie ilości stosowanego rozpuszczalnika, a w rezultacie ilości generowanych odpadów. Podsumowując, wychodząc z 20 mmoli (2.24 g) alkinu **95**, otrzymałam 1.8 g (7.4 mmola) produktu **93** z ogólną wydajnością równą 37% (Schemat 55).



**Schemat 55.** Synteza allilobaminy **93** w skali gramowej.

W analogiczny sposób sprawdziłam możliwość syntezy pochodnej seryny **97** w skali gramowej. Seryna i jej pochodne są niezwykle cennymi blokami budulcowymi w syntezie organicznej, ponieważ posiadają trzy różne grupy funkcyjne (hydroksylową, aminową oraz karboksylową), które dają możliwość szerokiej gamy potencjalnych transformacji. Syntezę  $\alpha$ -fenyloseryny **97** rozpocząłam z 3 g (7 mmol) związku cynoorganicznego **98**. Kolejne przekształcenia doprowadziły do otrzymania 1 g produktu **97** z całkowitą wydajnością 52% (Schemat **56**). Warto zaznaczyć, że aminokwas **97** wyizolowałam wyłącznie przez ekstrakcję i żadne dodatkowe metody oczyszczania nie były potrzebne.

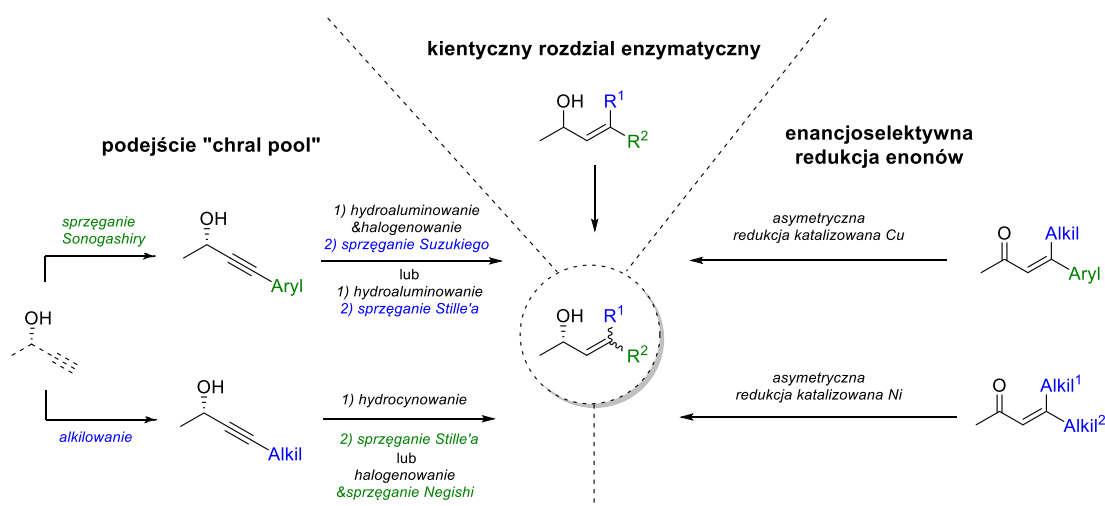


**Schemat 56.** Synteza aminokwasu **97** w skali gramowej.

## 4. PODSUMOWANIE

Celem niniejszej rozprawy doktorskiej było opracowanie ogólnej i efektywnej metody syntezy strukturalnie zróżnicowanych, enancjomerycznie wzbogaconych  $\alpha,\alpha$ -dipodstawionych  $\alpha$ -aminokwasów, w oparciu o reakcję przegrupowania [3,3]-sigmatropowego aktywowanych alkoholi allilowych do alliloamin.

Rozwiązanie problemu dostępności syntetycznej nienaturalnych aminokwasów, wymagało ode mnie zaproponowania efektywnej metody pozyskiwania  $\beta,\beta$ -dipodstawionych nieracemicznych alkoholi allilowych. W toku prowadzonych badań opracowałam trzy metody pozyskiwania wspomnianych alkoholi, posiadających zarówno podstawniki alkilowe jak i aryłowe, z wysoką czystością optyczną i wysoką selektywnością *E/Z* (Schemat 58). Pierwsza polegała na wykorzystaniu łatwo dostępnych chiralnych bloków budulcowych (**podejście „chiral pool”**) głównie nieracemicznego alkoholu propargilowego – (*S*)-3-butyn-2-olu, który poddawałam sekwencji reakcji sprzęgania. Omawiana metoda okazała się szczególnie atrakcyjna w przypadku syntezy alkoholi posiadających dwa różne podstawniki aryłowe oraz alkoholi posiadających podstawnik aryłowy i alkilowy. Drugie badane przeze mnie podejście opierało się na **enancjoselektywnej redukcji enonów** w obecności chiralnych kompleksów Cu(II) lub Ni(II). Wspomniana strategia okazała się wysoce efektywna w syntezie  $\beta$ -alkilo, $\beta$ -aryłowych oraz  $\beta,\beta$ -dialkilowych układów. W przypadku  $\beta,\beta$ -diaryłowych alkoholi allilowych synteza samych enonów w postaci czystego izomeru (*E*) lub (*Z*) była nieskuteczna. Warto podkreślić przy tym komplementarność obu powyższych podejść. Trzecia strategia to **kinetyczny rozdział enzymatyczny** racemicznego alkoholu. Reakcja ta przebiegała z wysoką stereoselektywnością i okazała się niezwykle skuteczna w przypadku syntezy sterycznie rozbudowanych alkoholi allilowych. Wspomniana metoda okazała się skutecznym rozwiązaniem zwłaszcza w przypadku syntezy alkoholi, których synteza, na przykład poprzez redukcję odpowiednich enonów, przebiegała z niską enancjoselektywnością.

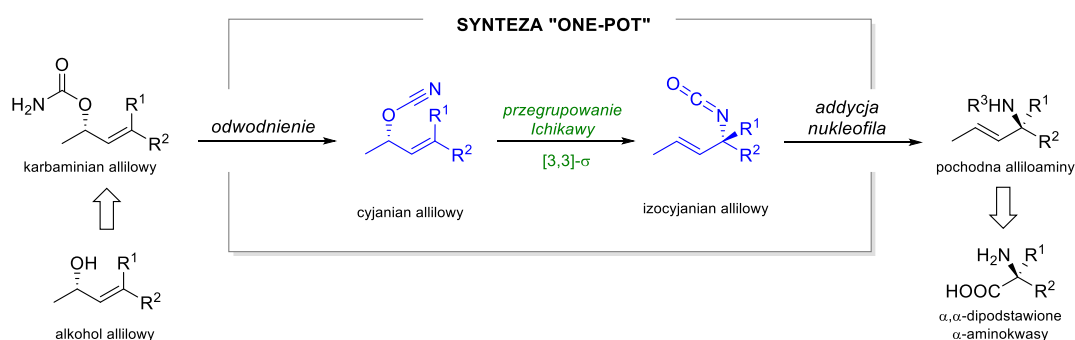


Schemat 58. Synteza  $\beta,\beta$ -dipodstawionych nieracemicznych alkoholi allilowych.

W drugiej części pracy, poszukując metody pozyskiwania alliloamin, które zamierzałam wykorzystać w syntezie aminokwasów, zdecydowałam się na reakcję [3,3]-sigmatropowego przegrupowania cyjanianów allilowych do izocyjanianów, zwaną także reakcją Ichikawy (Schemat 59). Otrzymane alkohole allilowe przekształcałam w odpowiednie nieracemiczne karbaminiany allilowe, które następnie poddałam sekwencji reakcji odwodnienia/przegrupowania/addycji

nukleofila. Badane przeze mnie transformacje przebiegały bardzo wydajnie, umożliwiając syntezę szerokiej gamy strukturalnie zróżnicowanych  $\alpha$ -trzeciorzędowych alliloamin. Produkty uzyskiwałam z pełnym transferem chiralności od substratu do produktu z utworzeniem nowego centrum stereogenicznego. Ponadto wykazałam, że dzięki enancjosepcyficznosci procesu przegrupowania, stereochemią produktu można sterować nie tylko poprzez zmianę konfiguracji absolutnej centrum stereogenicznego, ale również poprzez geometrię wiązania podwójnego. Jest to szczególnie istotne w przypadku strategii „chiral pool”, kiedy tylko jeden z enancjomerycznych substratów jest tani i łatwo dostępny.

W ostatnim etapie, uzyskane alliloaminy przekształcałam w pożądane pochodne  $\alpha,\alpha$ -dipodstawionych  $\alpha$ -aminokwasów. Skuteczność opracowanych metodologii otrzymywania nienaturalnych aminokwasów, potwierdziłam poprzez przeprowadzenie wybranych reakcji w skali gramowej.



Za swoje największe osiągnięcie uważam: (1) opracowanie efektywnych i komplementarnych metod syntezy  $\beta,\beta$ -dipodstawionych alkoholi allilowych o wysokiej czystości optycznej i z wysoką selektywnością  $E/Z$  a następnie, (2) opracowanie dogodnych i ogólnych metod syntetycznych pozwalających na łatwy dostęp do szerokiej gamy: (a)  $\alpha,\alpha$ -diarylowych, (b)  $\alpha$ -alkilowych,  $\alpha$ -arylowych, (c)  $\alpha,\alpha$ -dialkilowych nienaturalnych aminokwasów. Opracowana przeze mnie metodologia może stanowić użyteczne narzędzie w przemyśle farmaceutycznym lub chemicznym w syntezie związków o udowodnionej aktywności biologicznej lub farmakologicznej. Warto także nadmienić, że otrzymane przeze mnie aminokwasy są nie tylko atrakcyjnymi związkami biologicznie aktywnymi, ale znajdują także zastosowanie jako chiralne katalizatory lub ligandy w enancjoselektywnych transformacjach.

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## **6. PUBLIKACJE ORIGINALNE**

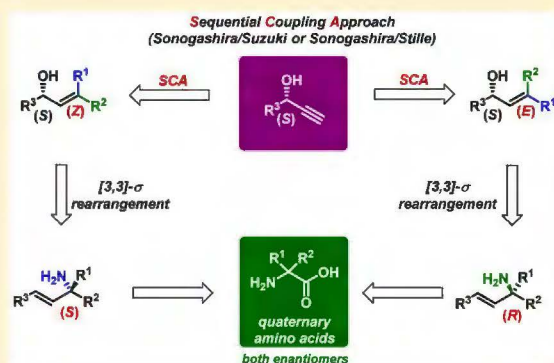
# The Synthesis of Chiral $\beta,\beta$ -Diaryl Allylic Alcohols and Their Use in the Preparation of $\alpha$ -Tertiary Allylamines and Quaternary $\alpha$ -Amino Acids

Michał Pieczykolan, Aleksandra Narczyk, and Sebastian Stecko\*<sup>✉</sup>

Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland

**S** Supporting Information

**ABSTRACT:** An approach to nonracemic  $\beta,\beta$ -diarylsubstituted allyl alcohols is described. Their synthesis starts from L-lactic acid-derived propargyl alcohol, which is submitted to sequential Sonogashira/Suzuki or Sonogashira/Stille coupling reactions. Both approaches enable the synthesis of either (*Z*)- or (*E*)-allylic alcohols regarding the order of introducing coupling agents. The obtained allyl alcohols were applied in the synthesis of nonracemic  $\alpha$ -tertiary allyl amines via stereocontrolled cyanate-to-isocyanate sigmatropic rearrangement reactions of the corresponding allyl carbamates. The stereoselectivity of the process is controlled by the geometry of the double bond of the starting allyl derivative. As demonstrated, a rearrangement of (*S,Z*)-allyl carbamates provides (*S*)-tertiary allyl amines, whereas the transformation (*S,E*)-isomers leads to (*R*)-allyl amines.



Received: February 28, 2017

Published: May 11, 2017



































# The synthesis of chiral $\beta,\beta$ -diaryl allylic alcohols and their use in the preparation of $\alpha$ -tertiary allylamines and quaternary $\alpha$ -amino acids

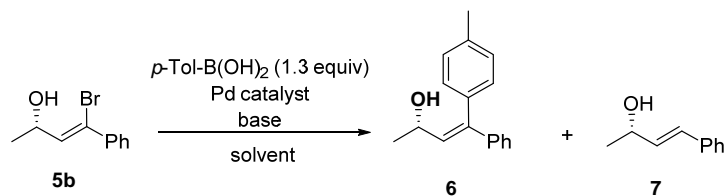
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## SUPPLEMENTARY MATERIALS

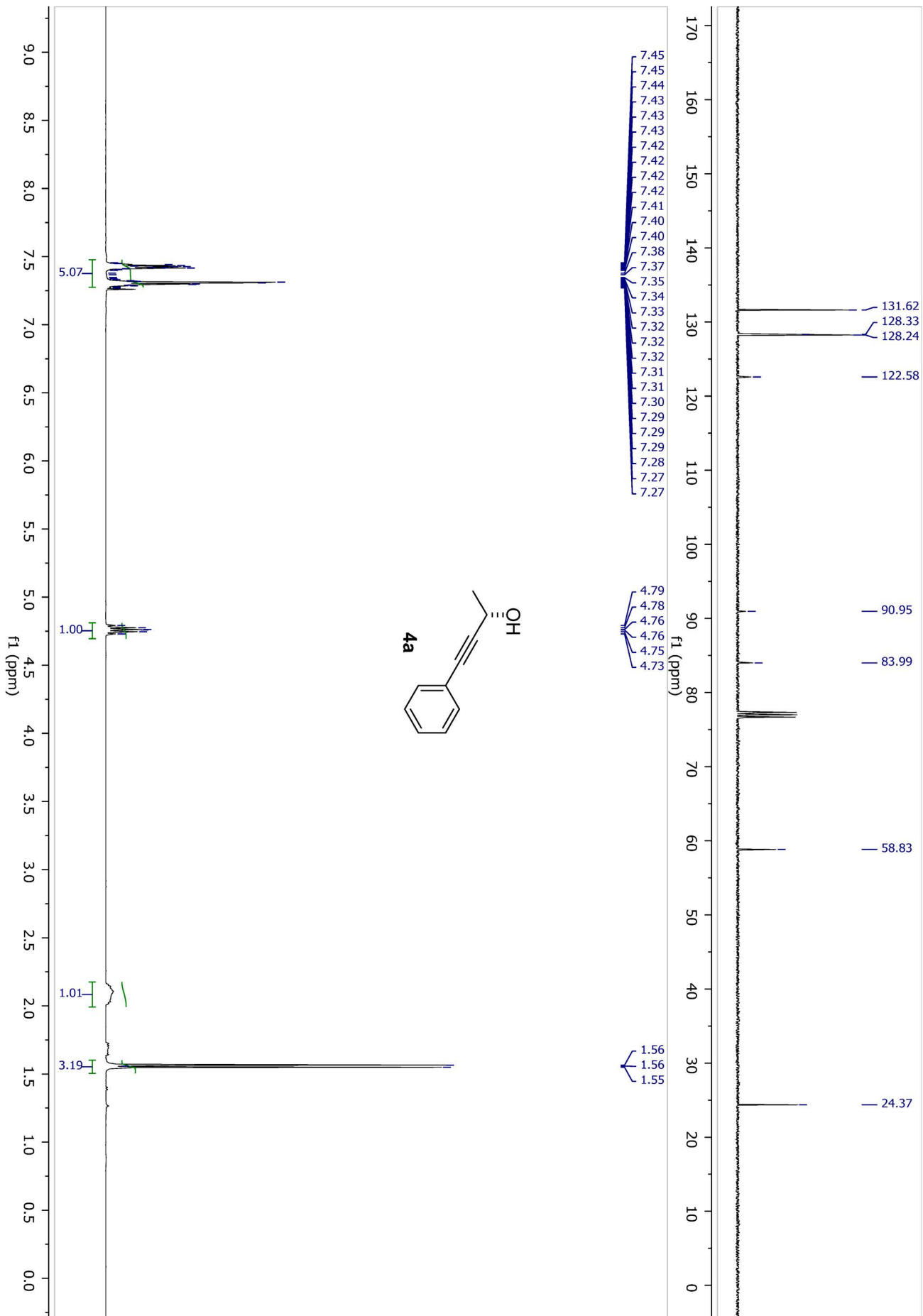
1. Optimization of Suzuki coupling reaction of vinyl bromide 5b with 4-tolylboronic acid.....S2
2.  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  NMR spectra and HPLC data.....S3

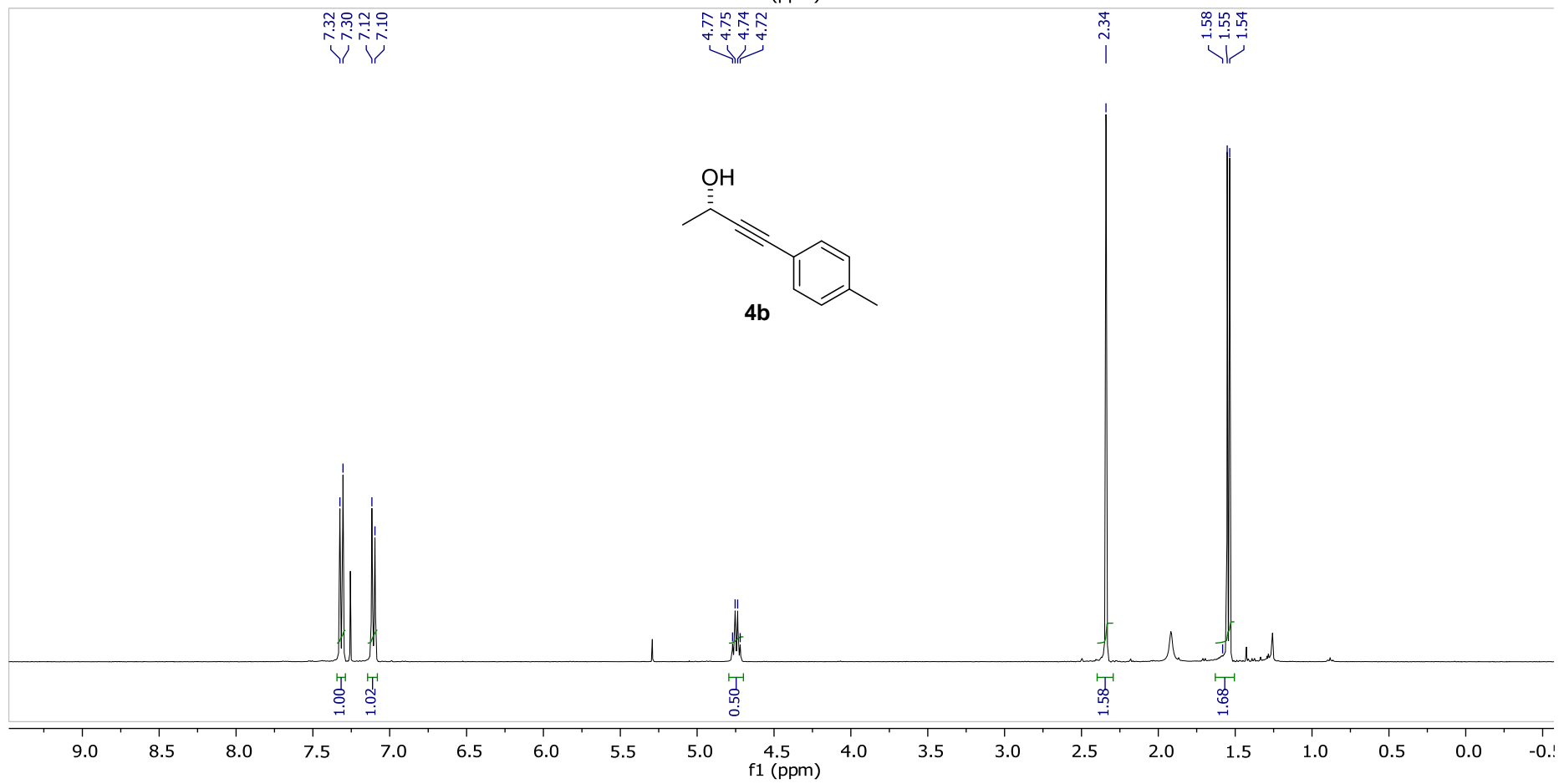
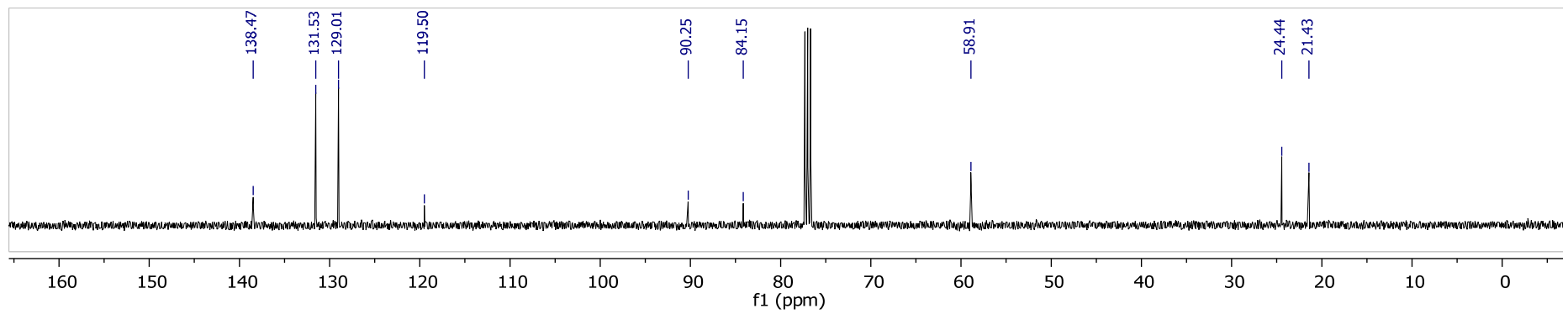
## 1. Optimization of Suzuki coupling reaction of vinyl bromide 5b with 4-tolylboronic acid

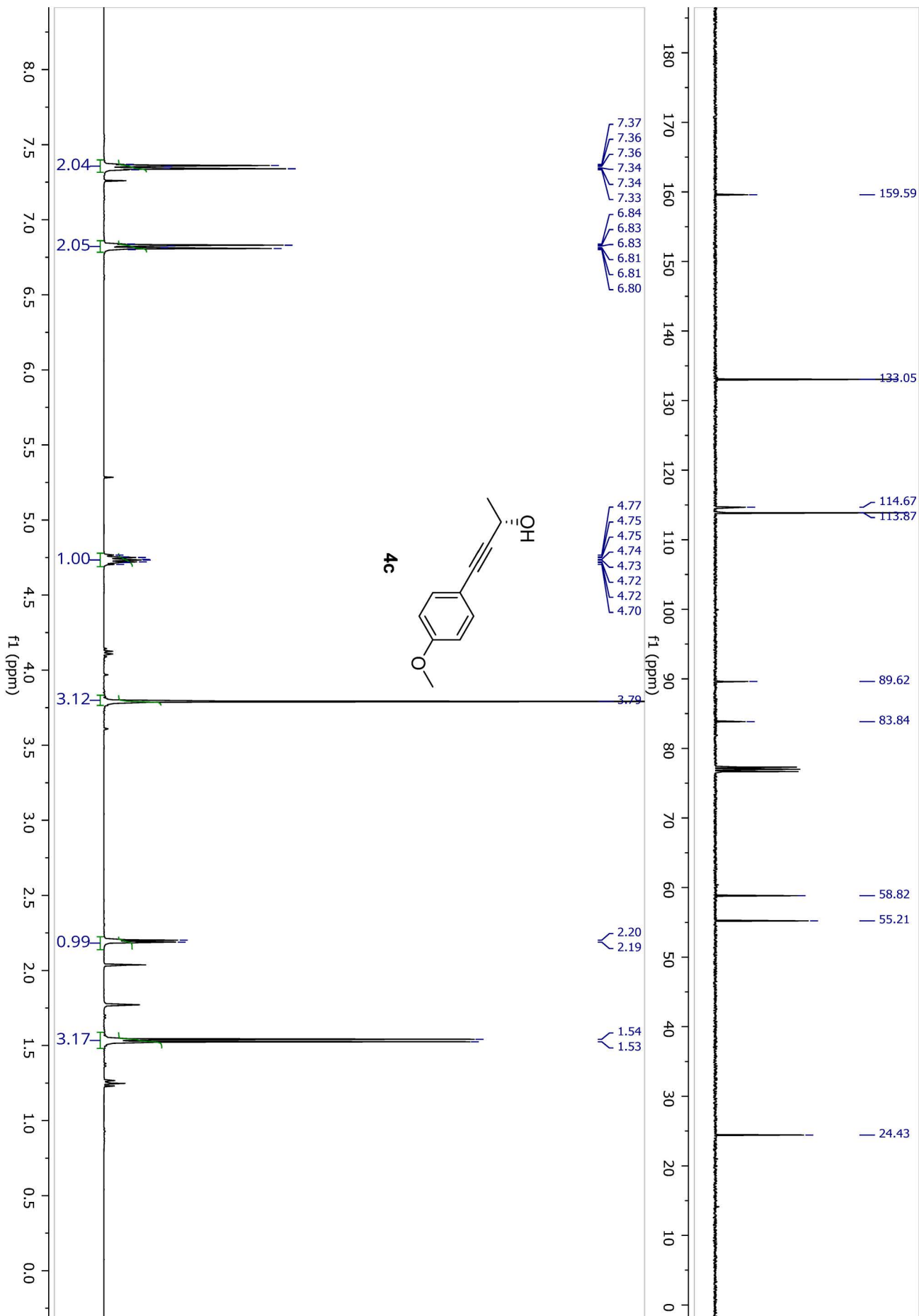


Ent.	Catalyst	Base (equiv)	Solvent	Temp. [°C]	Time [h]	Yield <b>6(7)</b> [%]
1	Pd <sub>2</sub> dba <sub>3</sub> /P(2-furyl) <sub>3</sub> (5 mol%)	Na <sub>2</sub> CO <sub>3</sub> (2)	1,4-dioxane/H <sub>2</sub> O (9:1)	70	24	60 (10)
2	PdCl <sub>2</sub> (dppf) (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	DMF/H <sub>2</sub> O (9:1)	100	24	55 (20)
3	PdCl <sub>2</sub> (dppe) (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	DMF/H <sub>2</sub> O (9:1)	100	24	37 (40)
4	Pd <sub>2</sub> dba <sub>3</sub> /P( <i>o</i> -tol) <sub>3</sub> (5 mol%)	K <sub>2</sub> CO <sub>3</sub> (3)	THF/H <sub>2</sub> O (5:1)	60	34	53 (35)
5	Pd <sub>2</sub> dba <sub>3</sub> /PPh <sub>3</sub> (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	PhMe/H <sub>2</sub> O (9:1)	70	24	70 (10)
6	Pd(Ph <sub>3</sub> P) <sub>4</sub> (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	PhMe/H <sub>2</sub> O (8:1)	60	18	72 (10)
7	Pd(Ph <sub>3</sub> P) <sub>4</sub> (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	DMF/H <sub>2</sub> O (8:1)	60	20	70 (12)
8	Pd(Ph <sub>3</sub> P) <sub>4</sub> (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	THF/H <sub>2</sub> O (8:1)	60	25	57 (20)
<b>9</b>	<b>Pd(Ph<sub>3</sub>P)<sub>4</sub> (3 mol%)</b>	<b>Cs<sub>2</sub>CO<sub>3</sub> (3)</b>	<b>PhMe/H<sub>2</sub>O (8:1)</b>	<b>60</b>	<b>18</b>	<b>71 (11)</b>
10	Pd(Ph <sub>3</sub> P) <sub>4</sub> (5 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	1,4-dioxane/H <sub>2</sub> O (9:1)	75	24	69 (12)
11	Pd(Ph <sub>3</sub> P) <sub>4</sub> (5 mol%)	K <sub>2</sub> PO <sub>4</sub> (3)	PhMe/H <sub>2</sub> O (9:1)	100	30	60 (14)
12 <sup>a</sup>	Pd(Ph <sub>3</sub> P) <sub>4</sub> (3 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	PhMe/H <sub>2</sub> O (8:1)	60	18	70 (11)
13 <sup>b</sup>	Pd(Ph <sub>3</sub> P) <sub>4</sub> (3 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	PhMe/H <sub>2</sub> O (8:1)	60	18	69 (11)
14	Pd(Ph <sub>3</sub> P) <sub>4</sub> (3 mol%)	Cs <sub>2</sub> CO <sub>3</sub> (3)	PhMe/H <sub>2</sub> O (8:1)	40	30	50 (25)

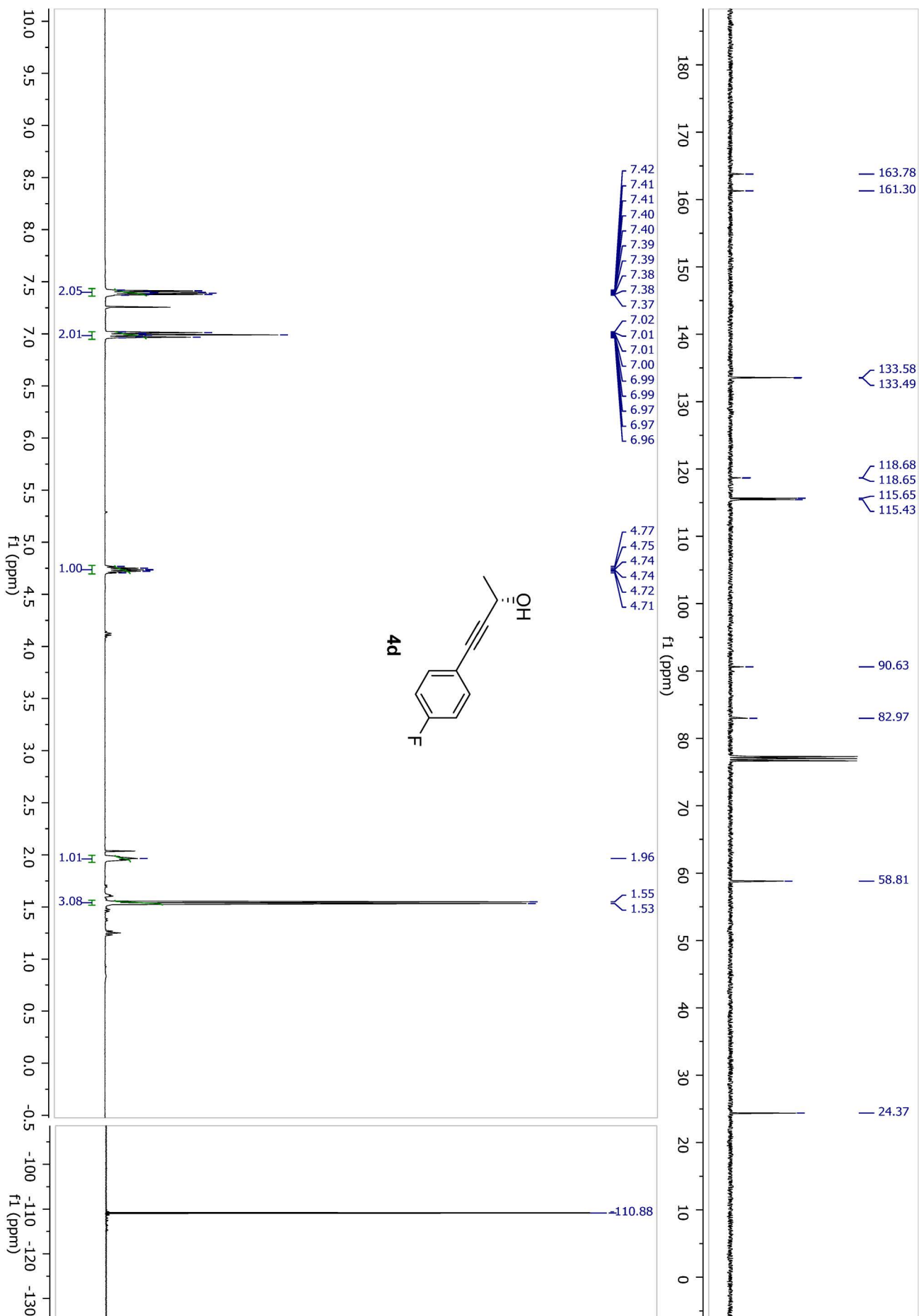
<sup>a</sup> 1.5 equiv of *p*-Tol-B(OH)<sub>2</sub>; <sup>b</sup> 3 equiv of *p*-Tol-B(OH)<sub>2</sub>;

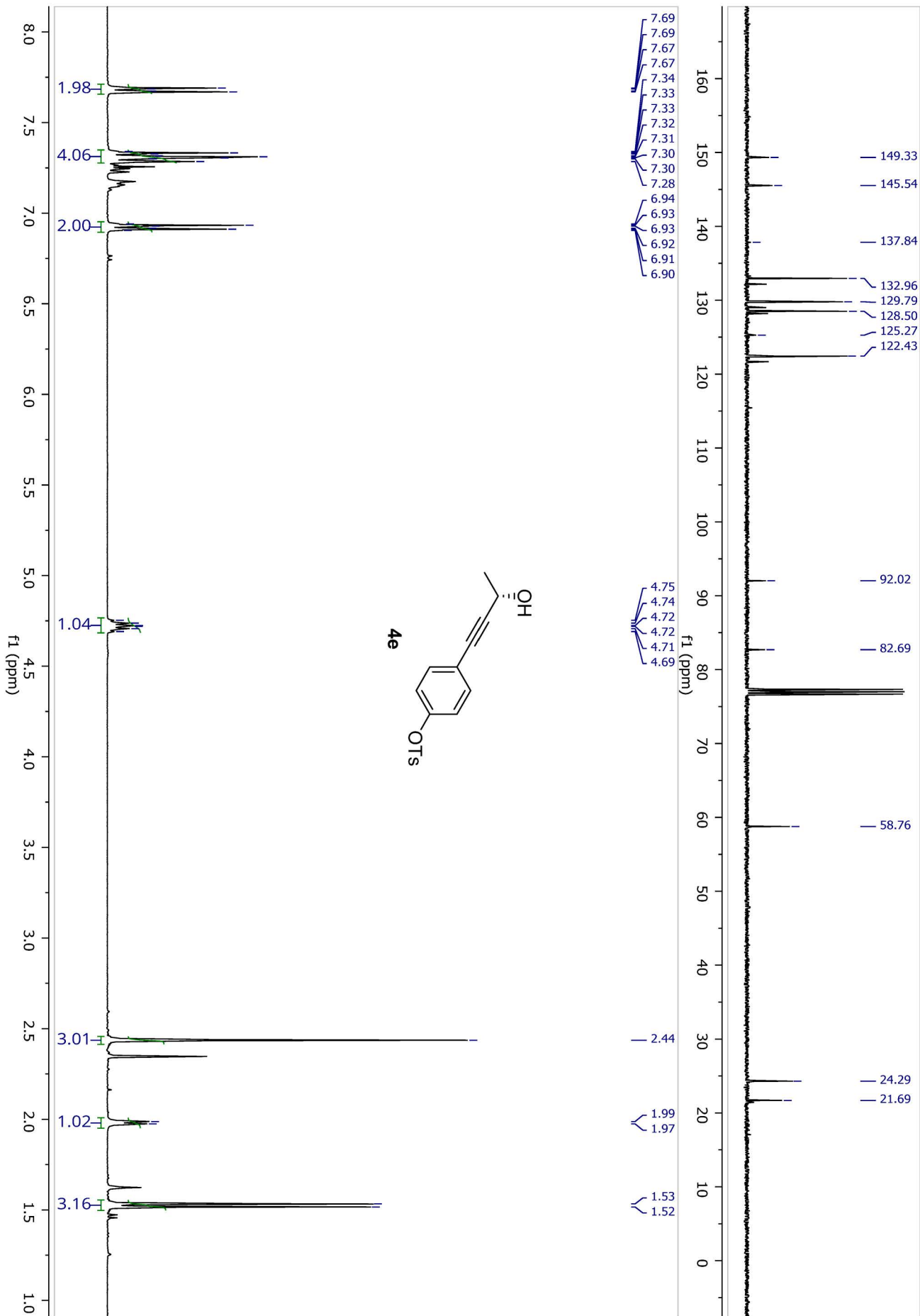


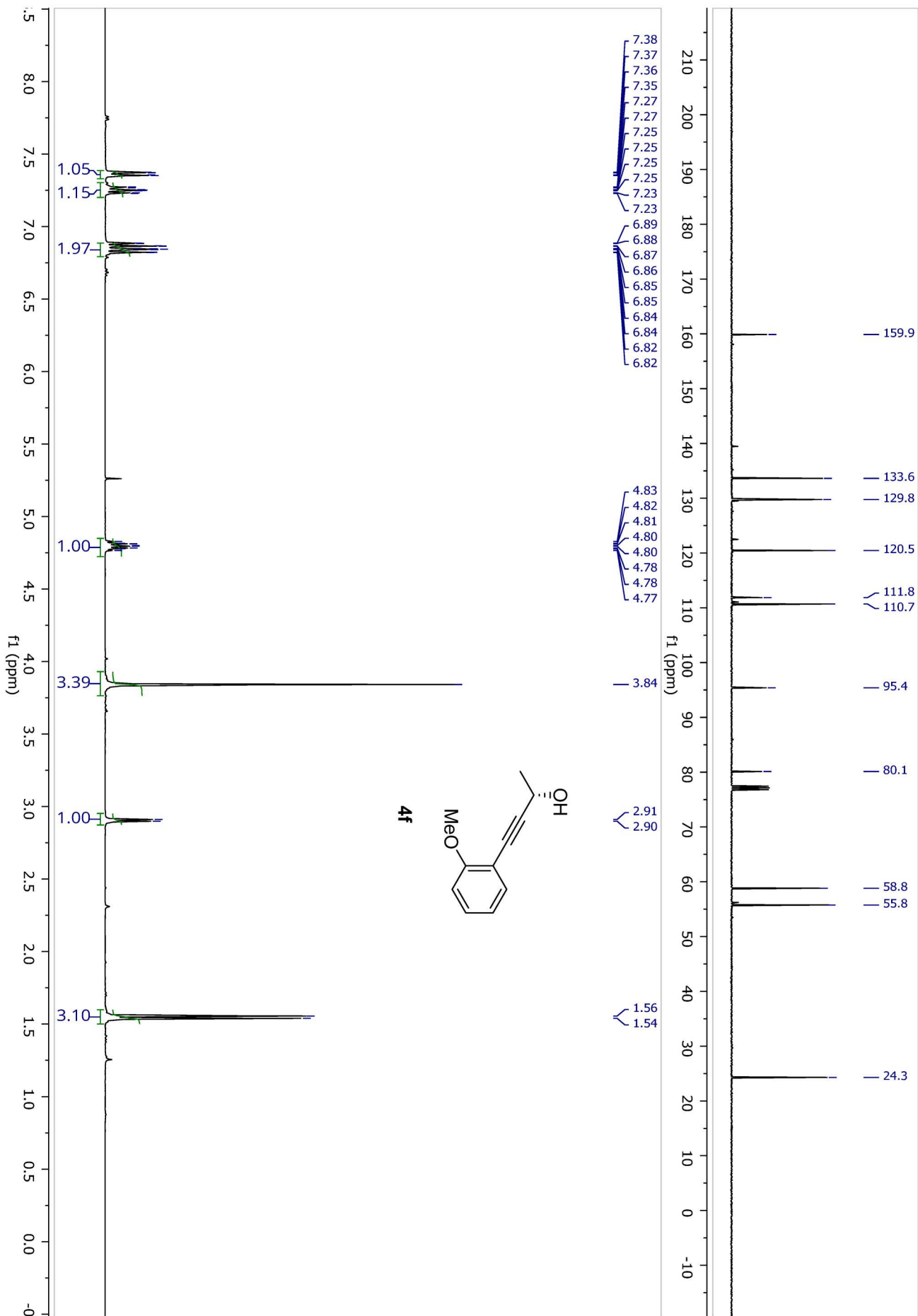


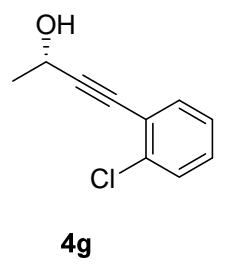
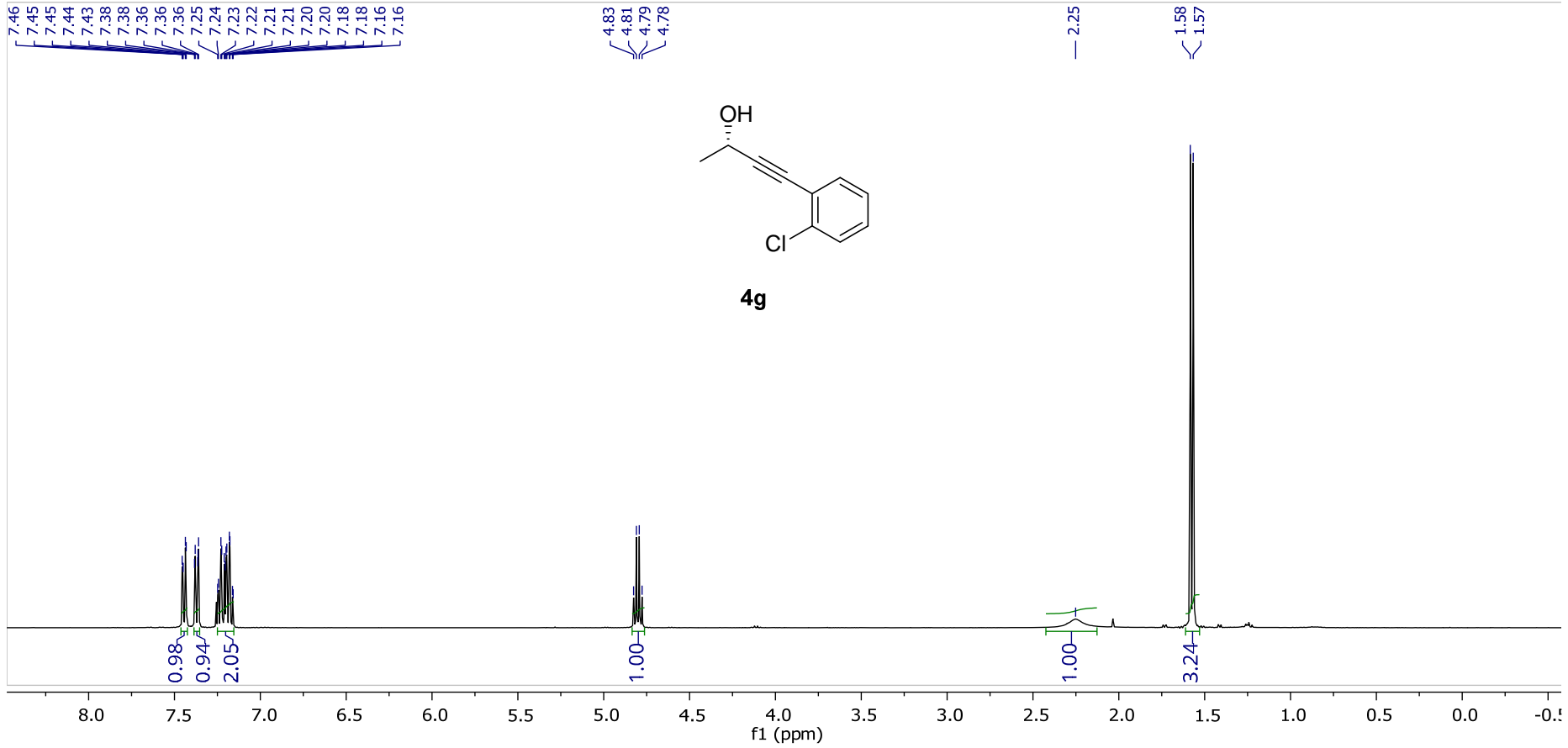
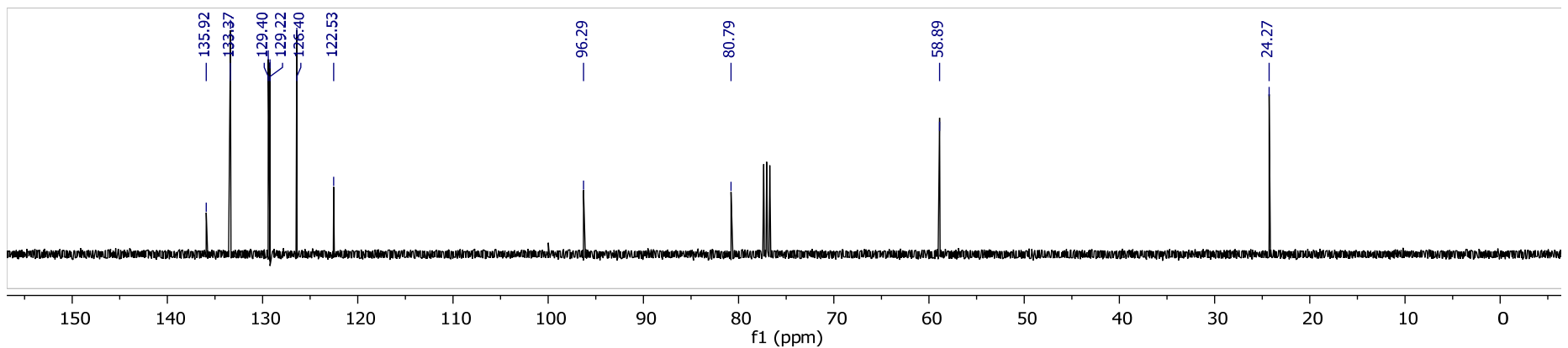


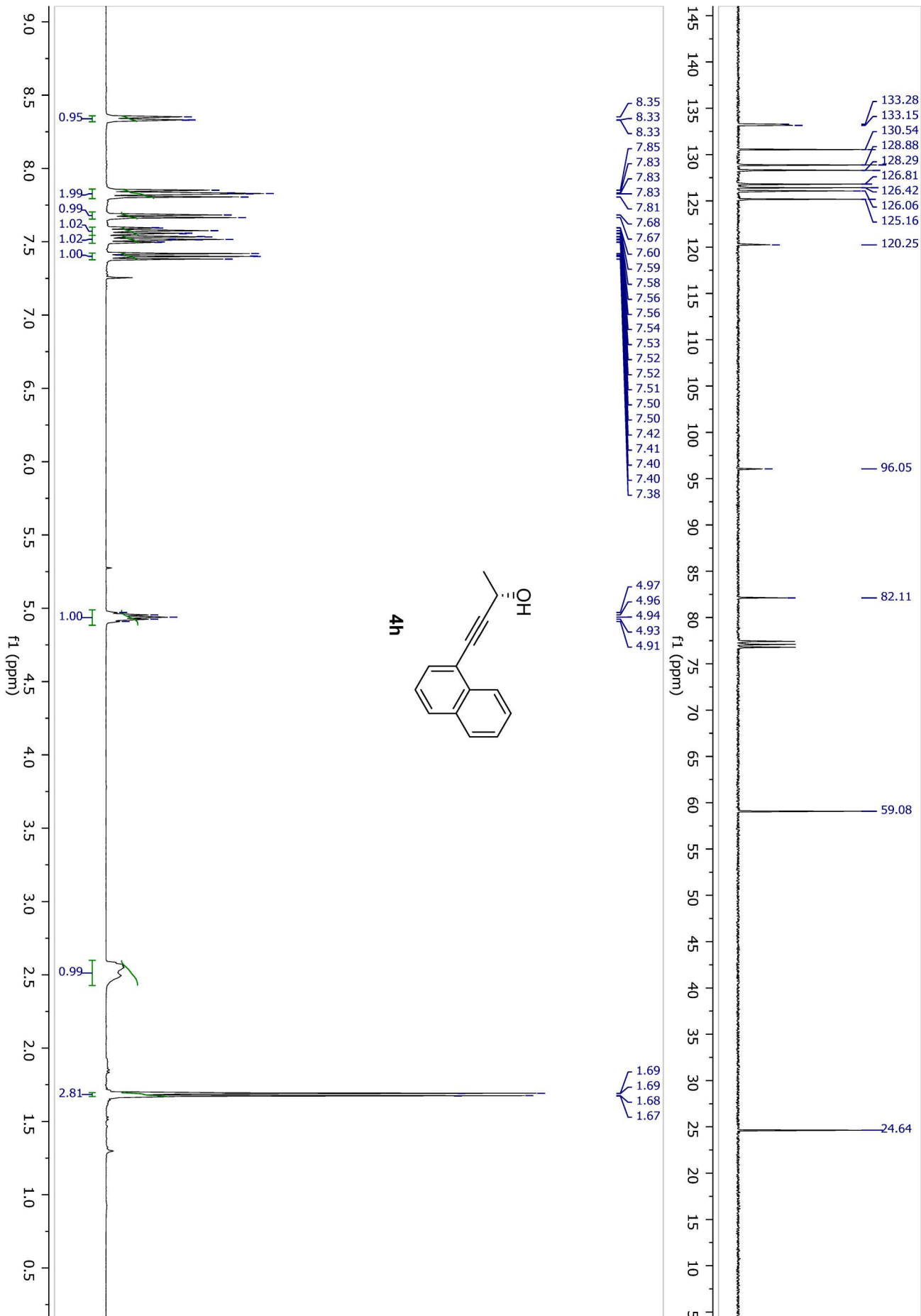


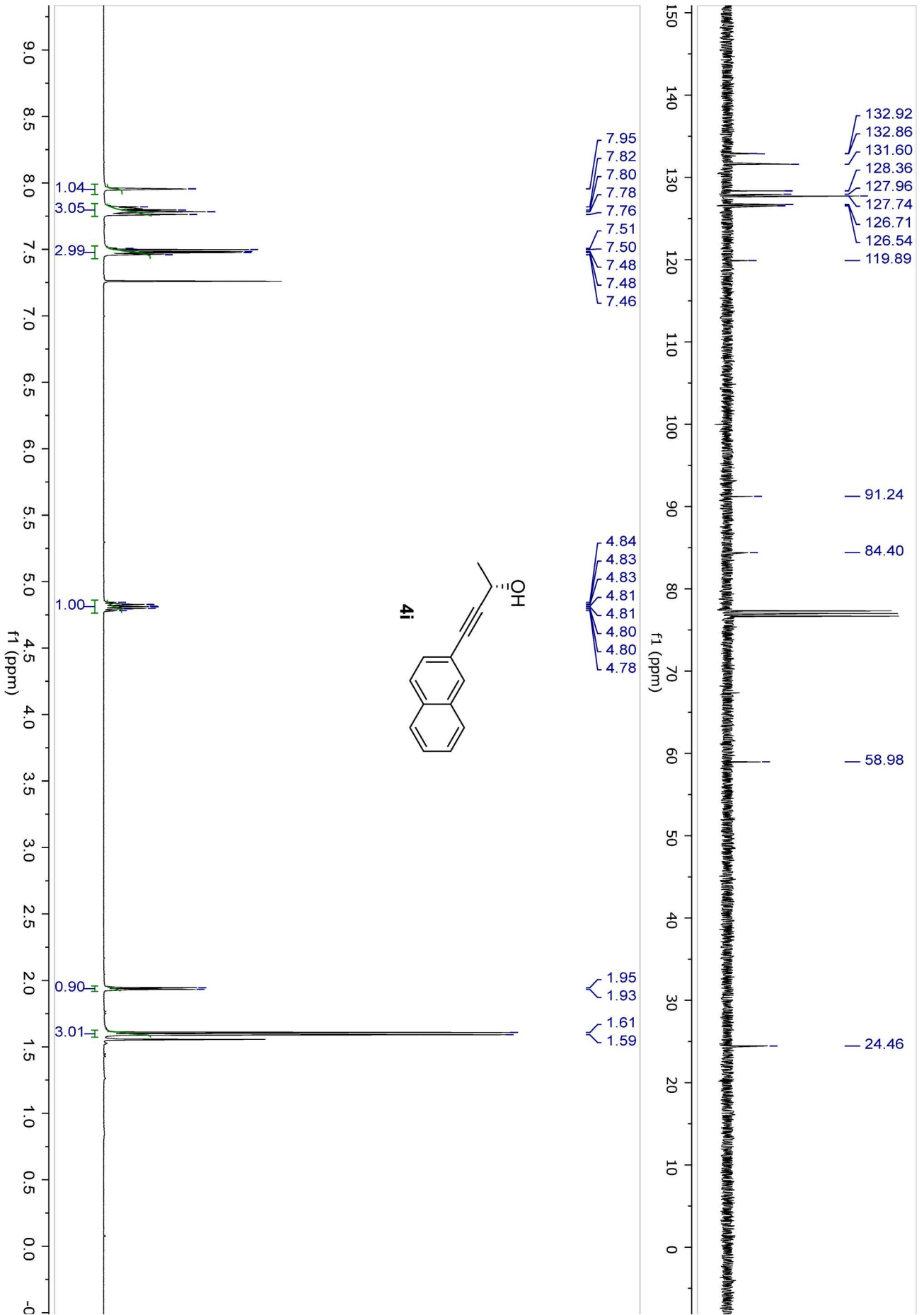
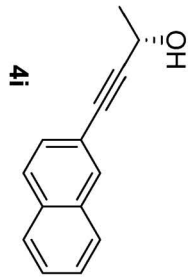


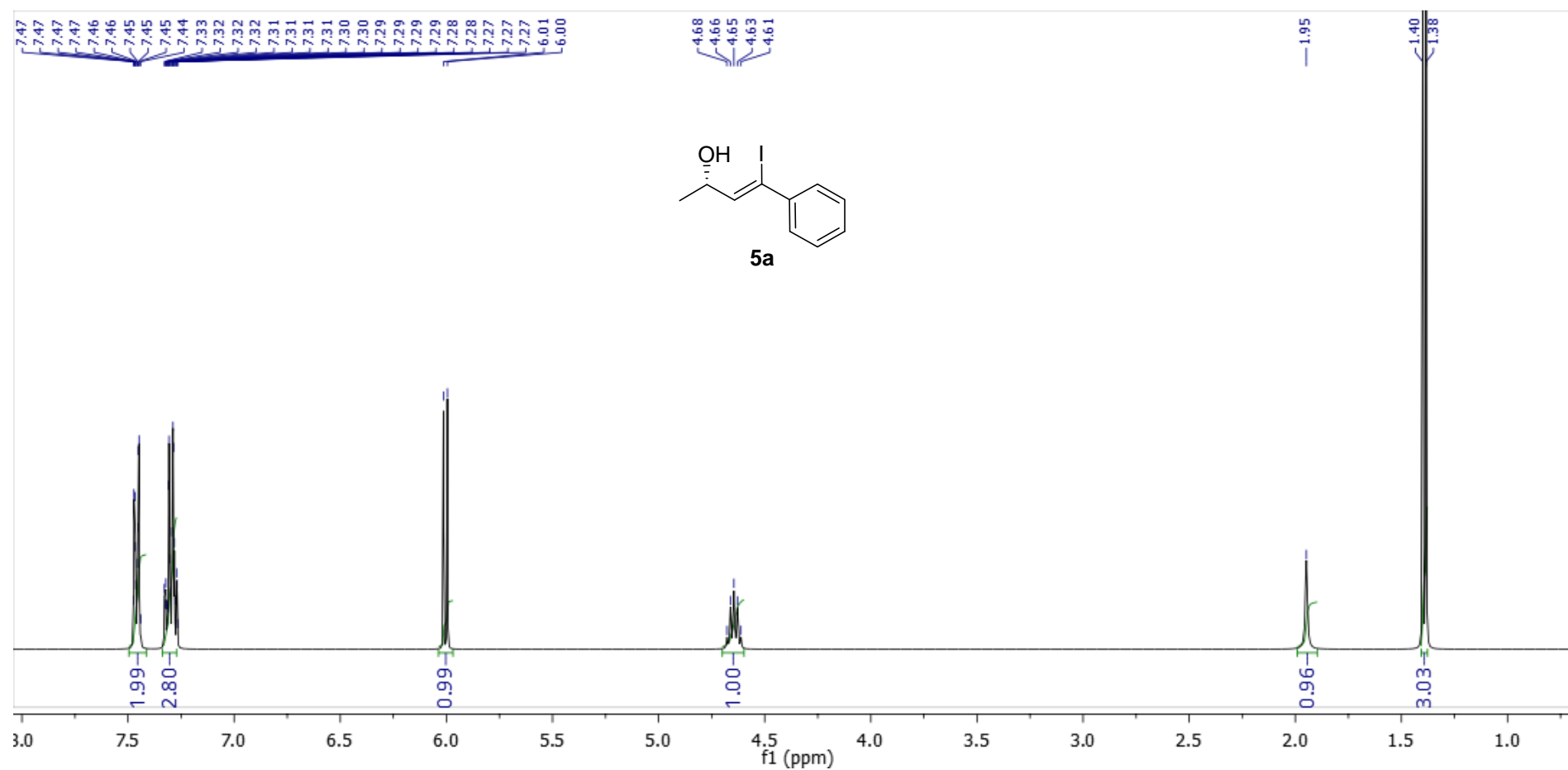
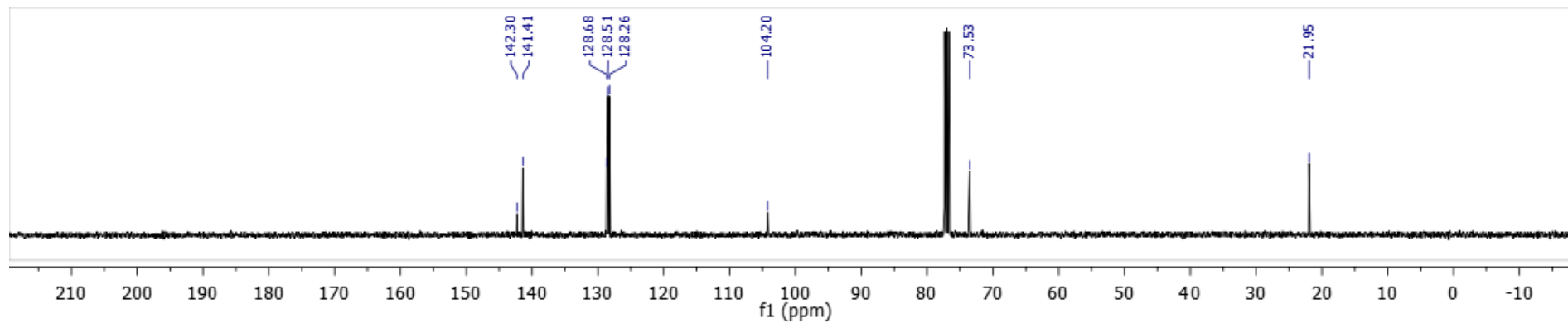


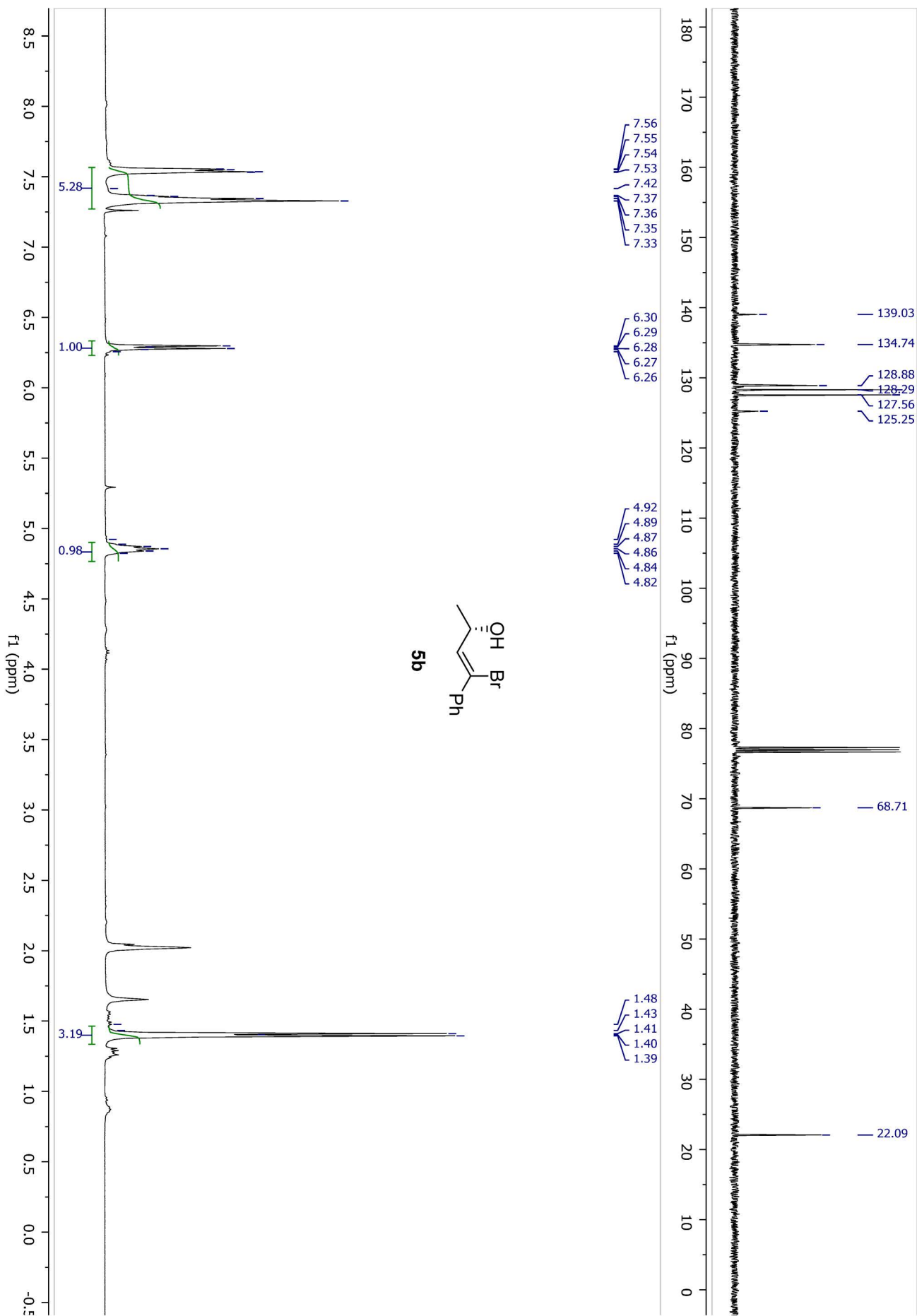




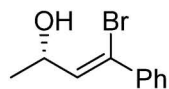




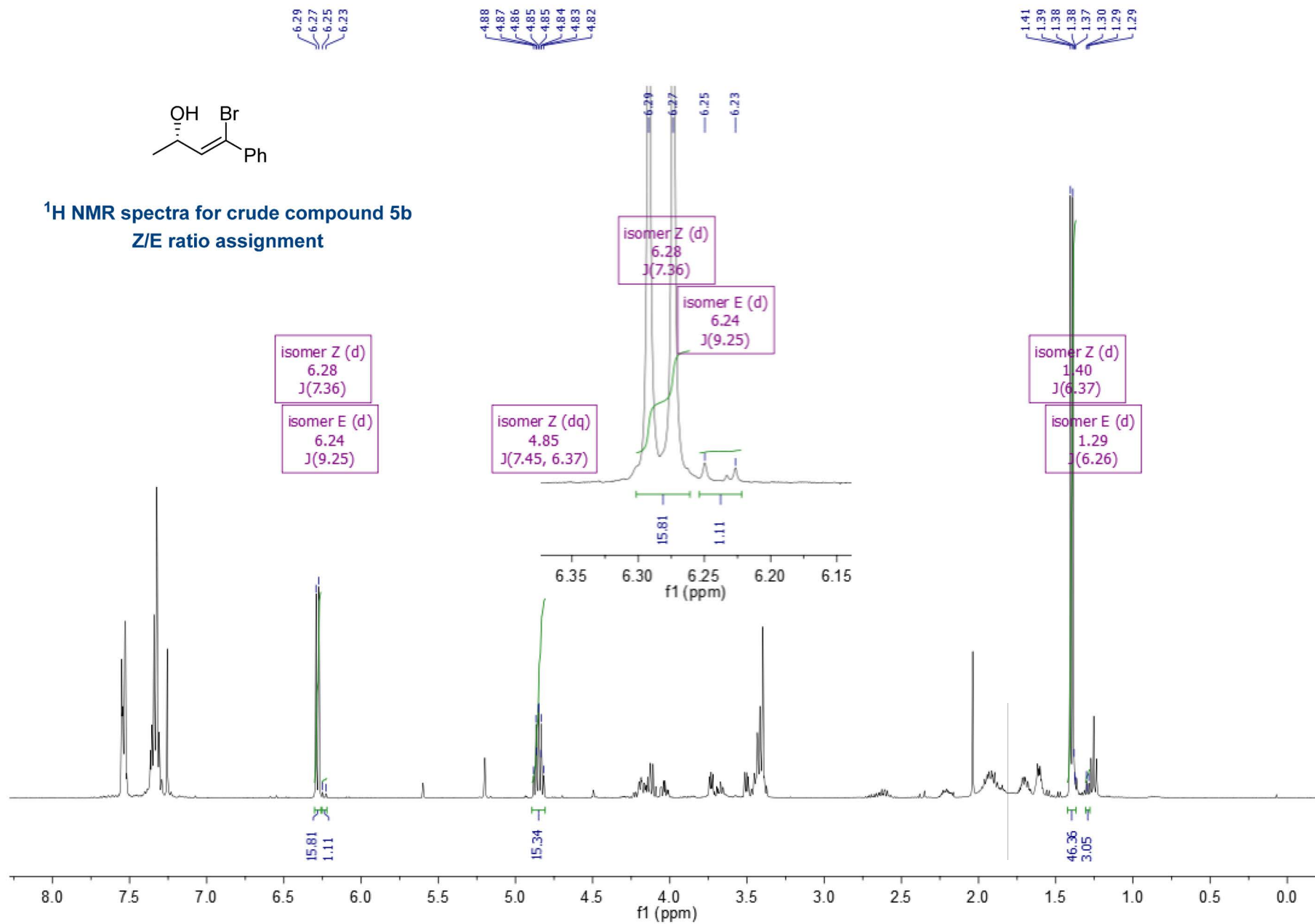


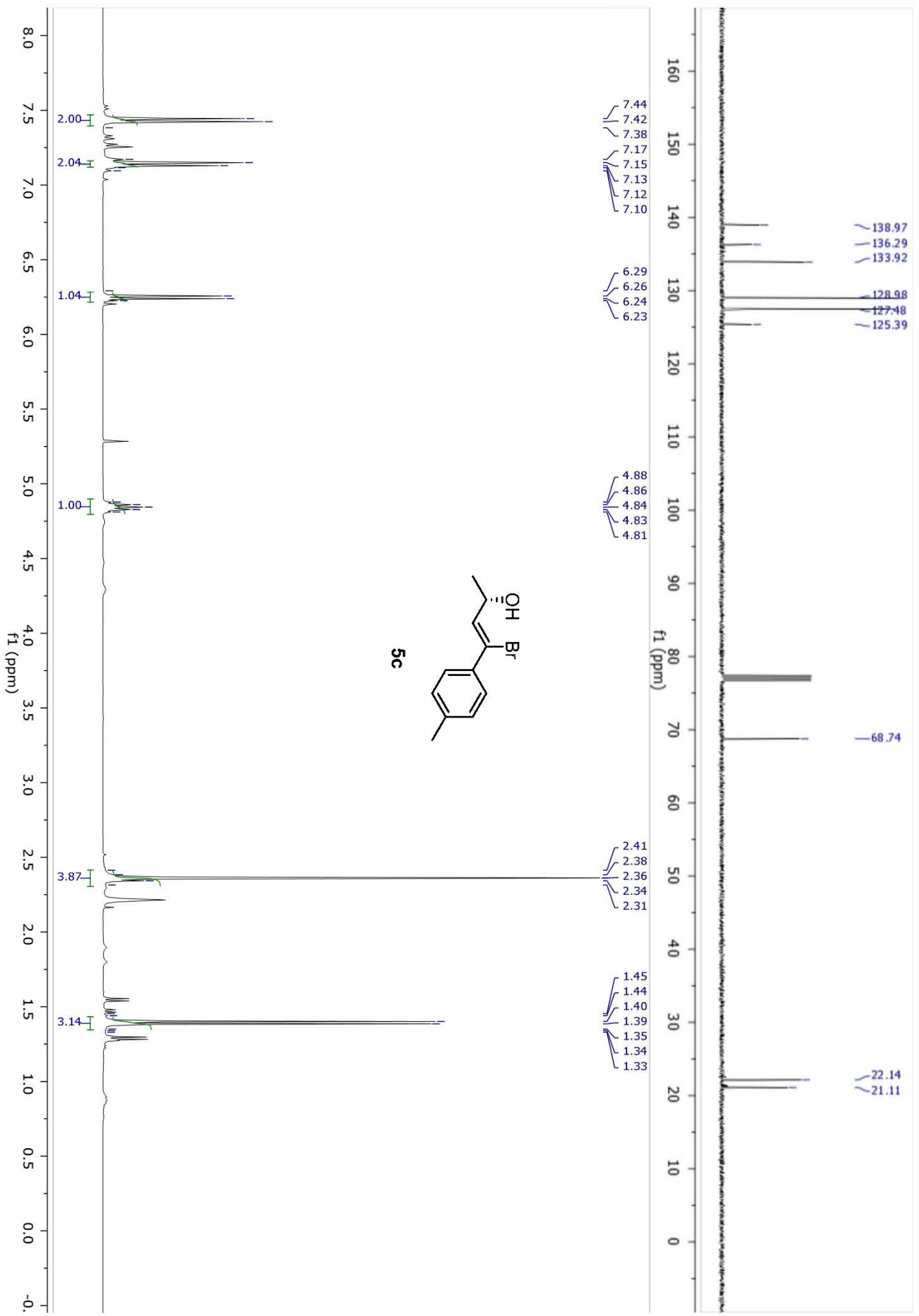


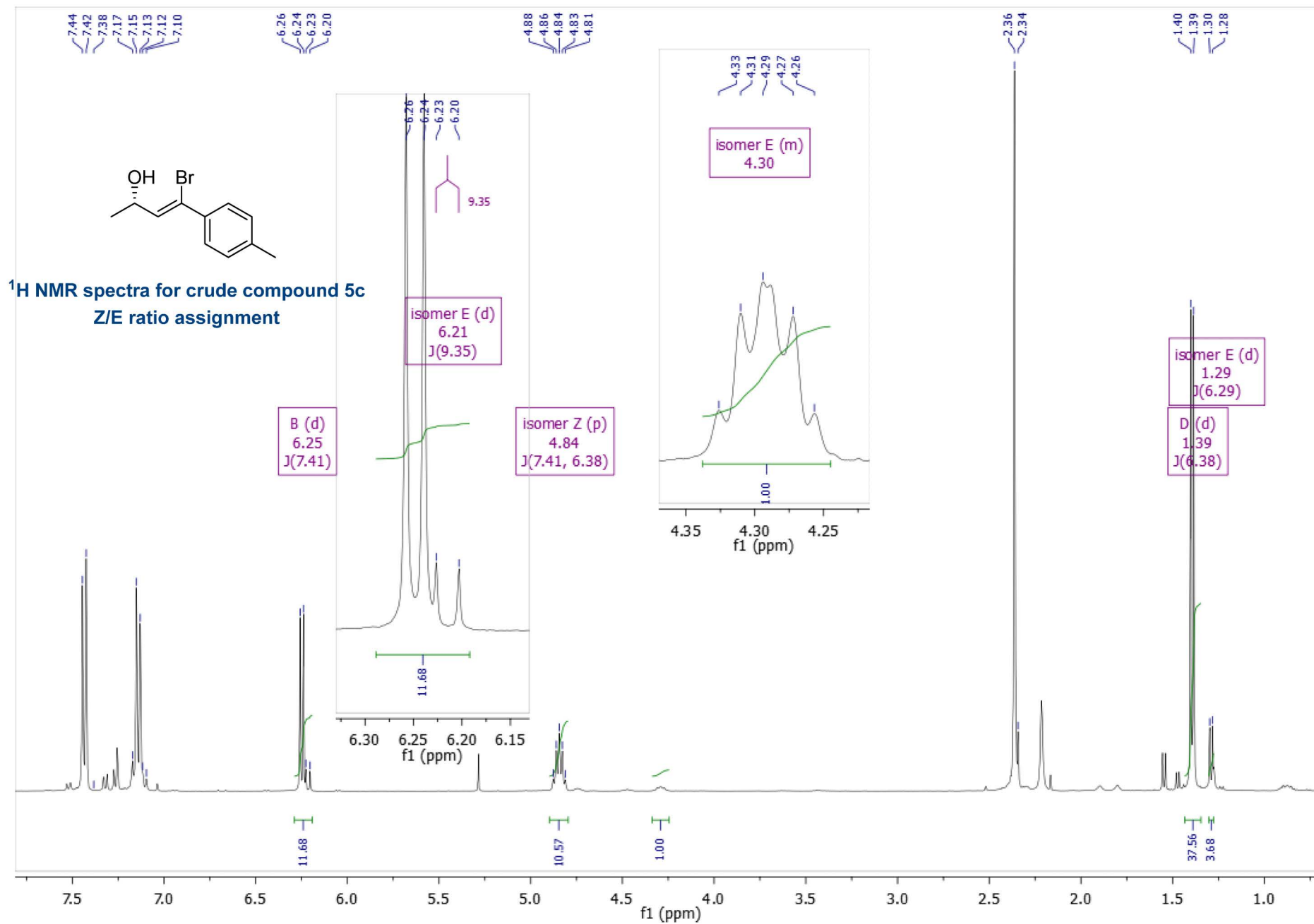


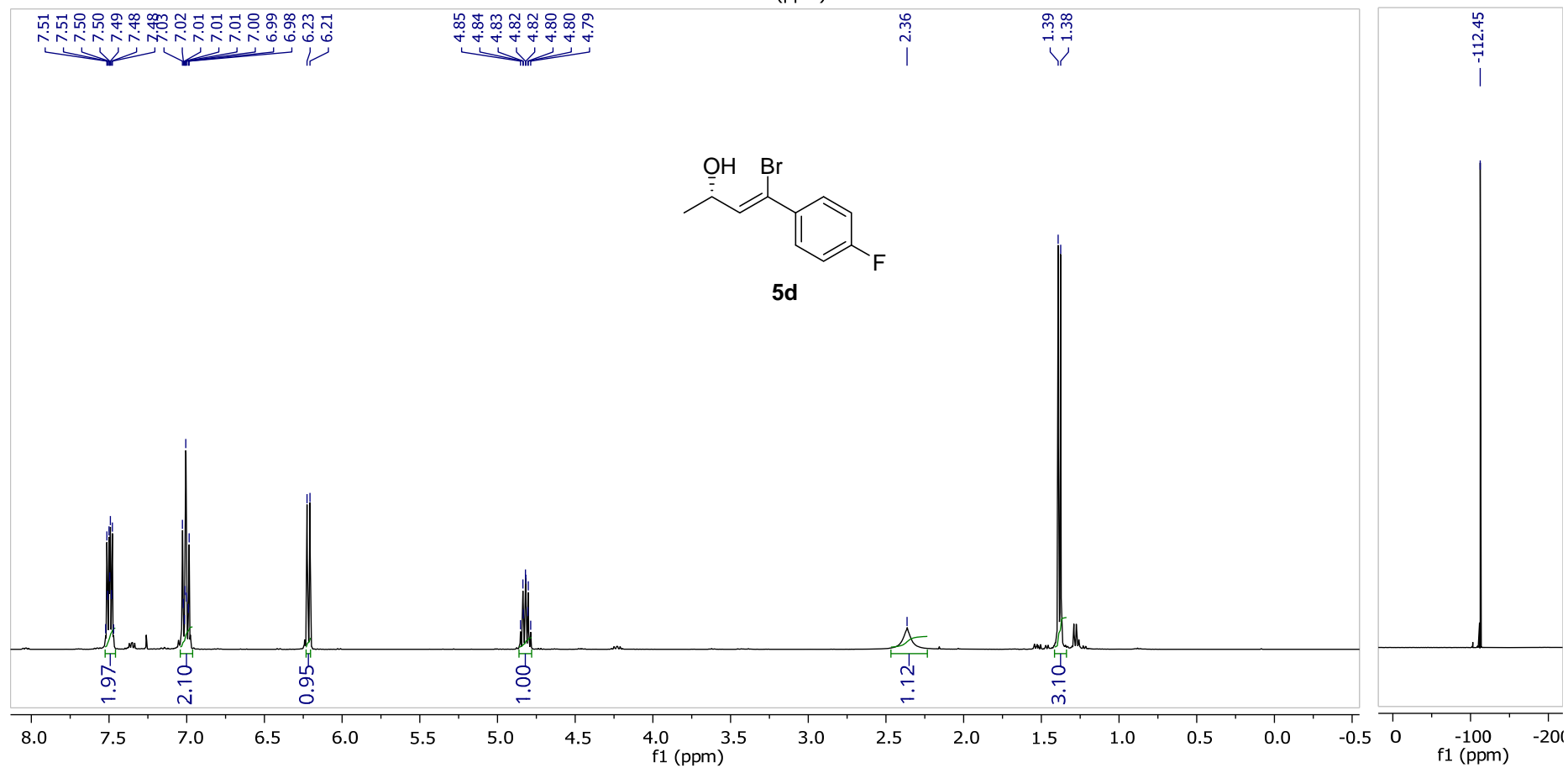
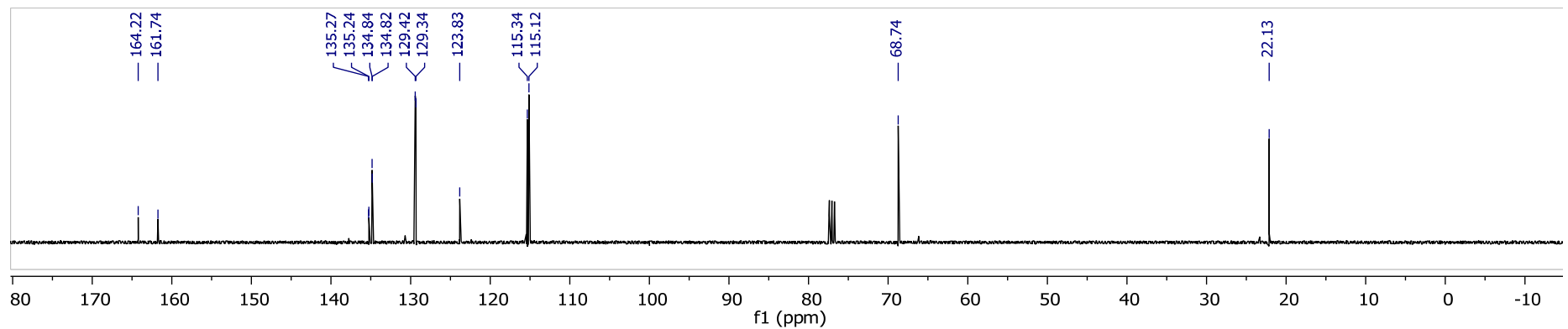


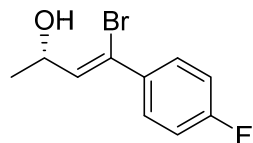
<sup>1</sup>H NMR spectra for crude compound 5b  
Z/E ratio assignment



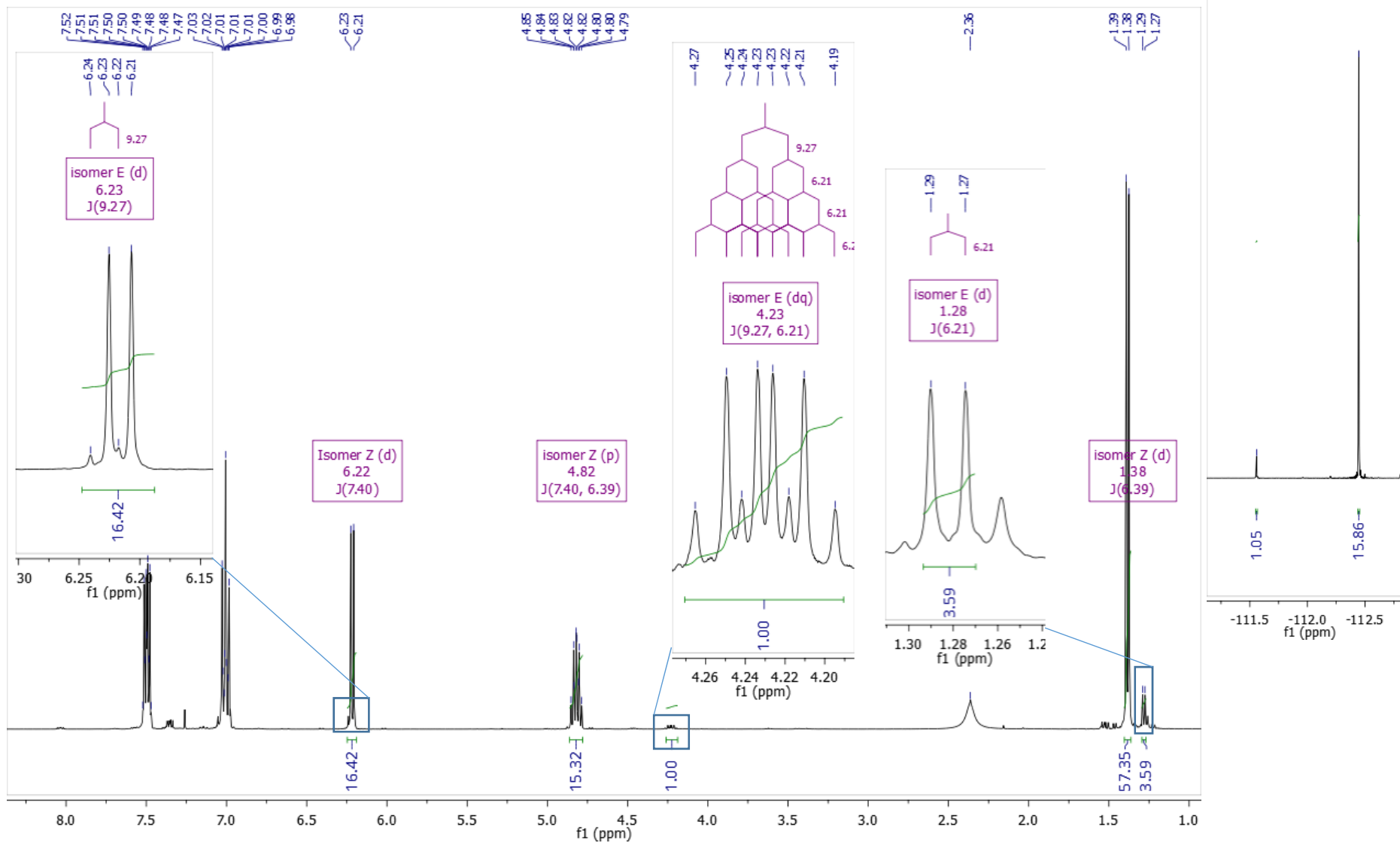


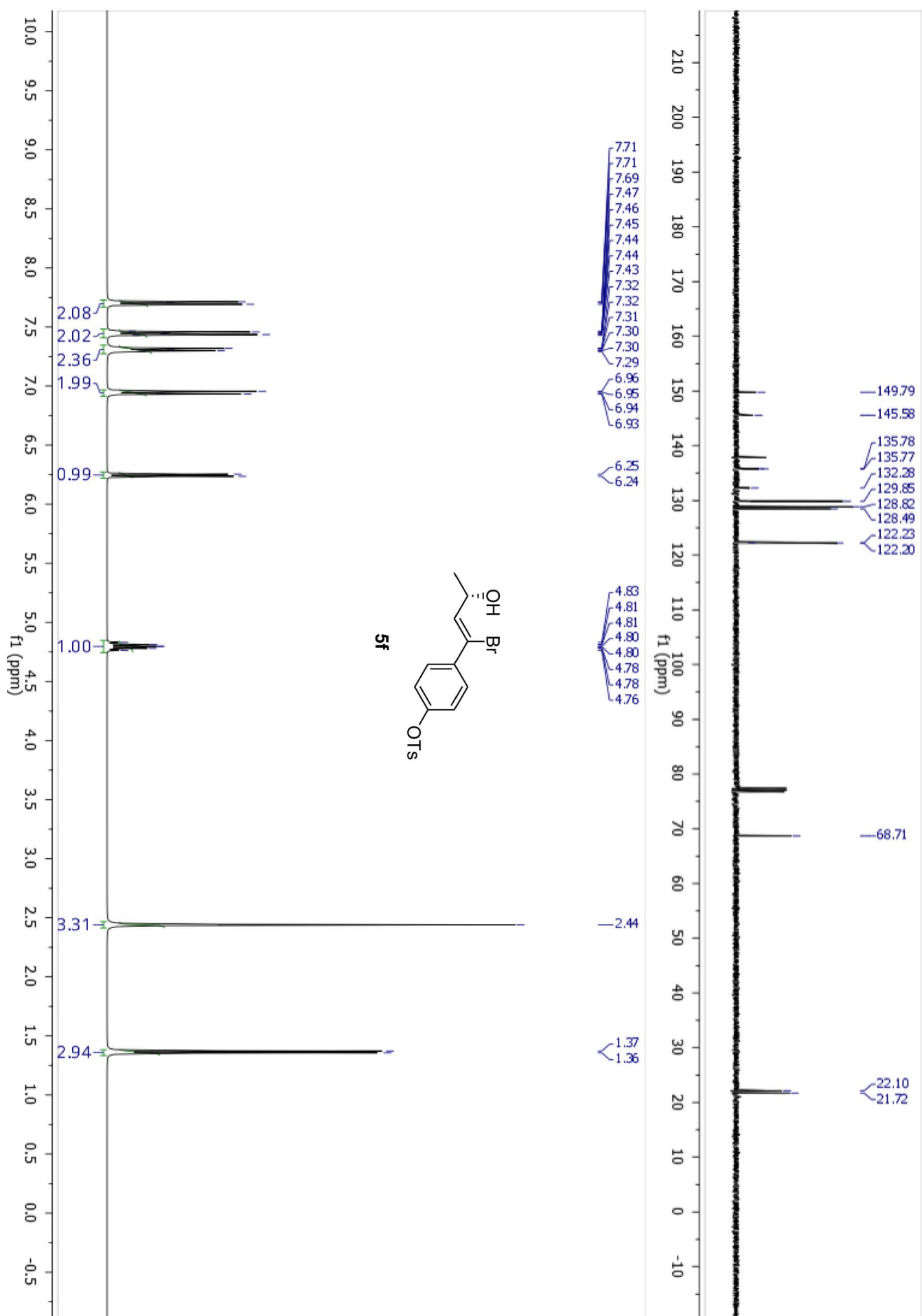


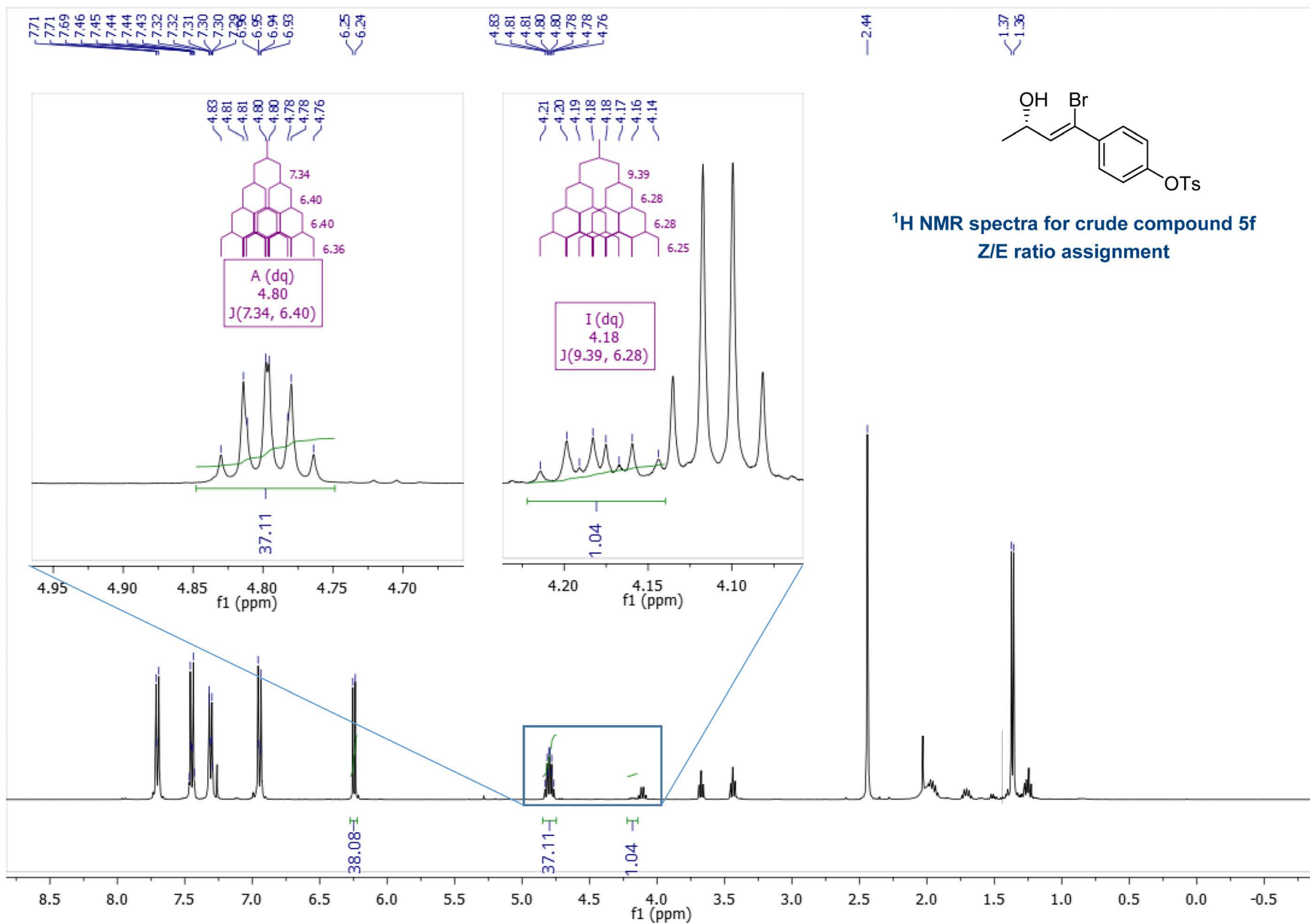


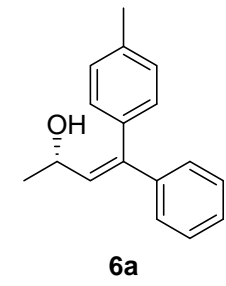
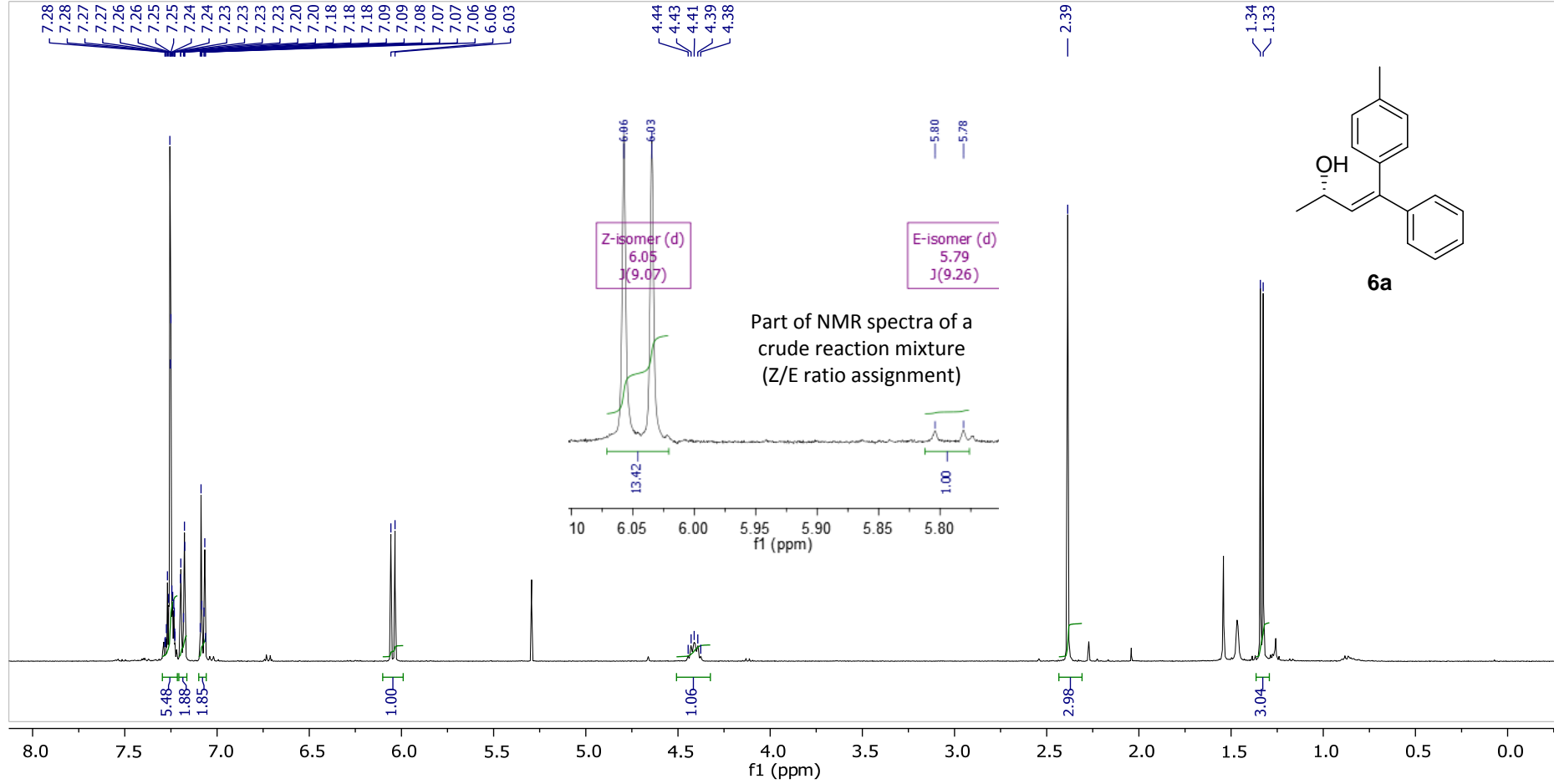
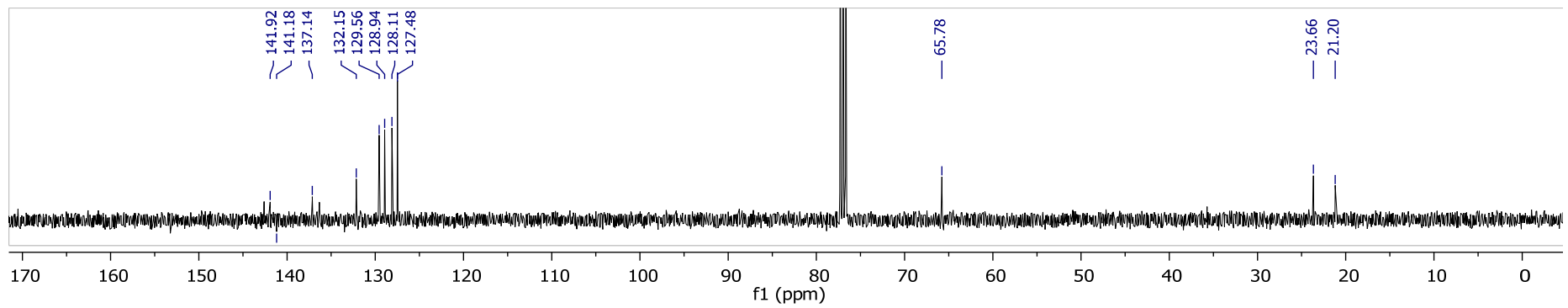


**<sup>1</sup>H and <sup>19</sup>F NMR spectra for crude compound 5d**  
**Z/E ratio assignment**

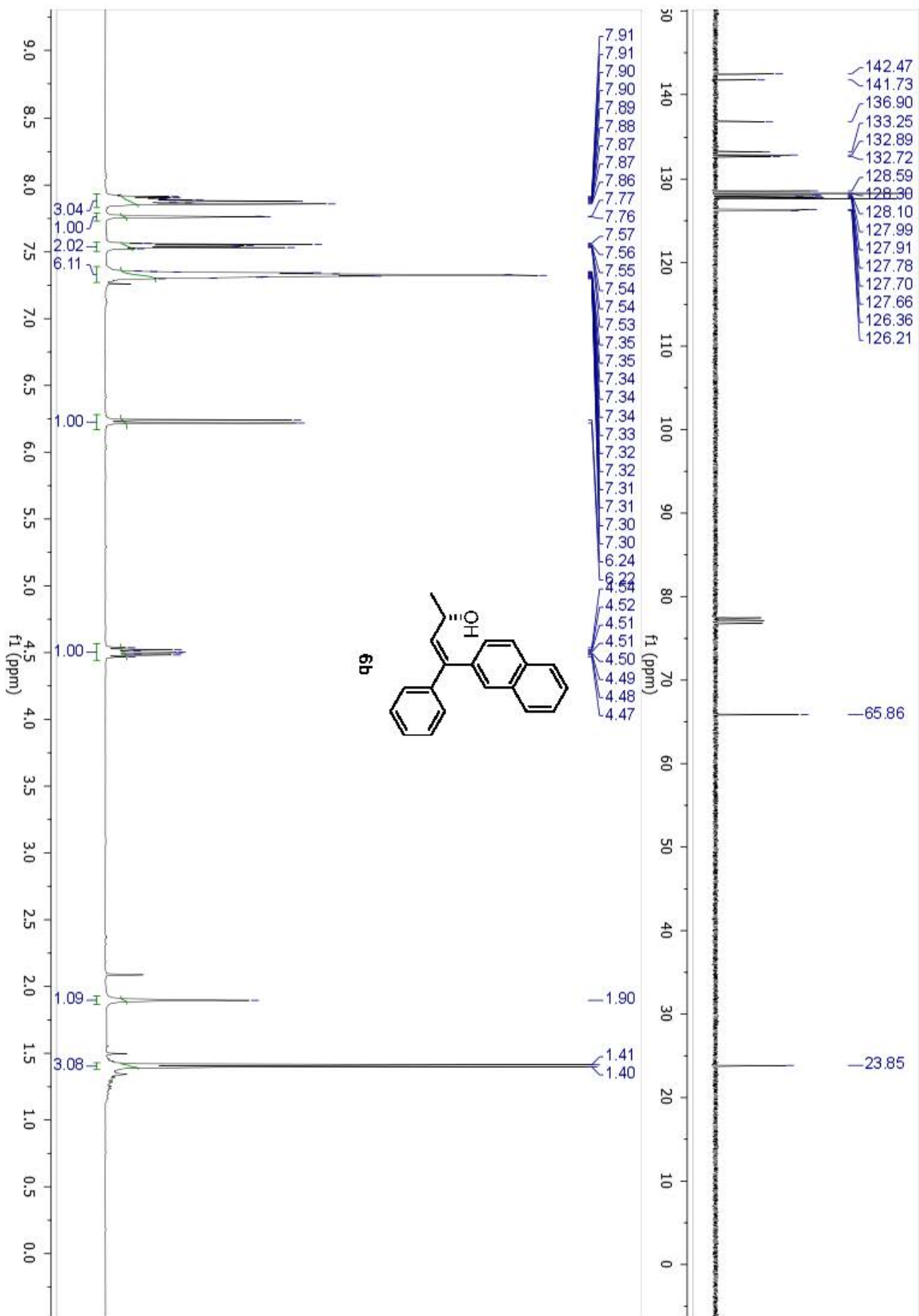


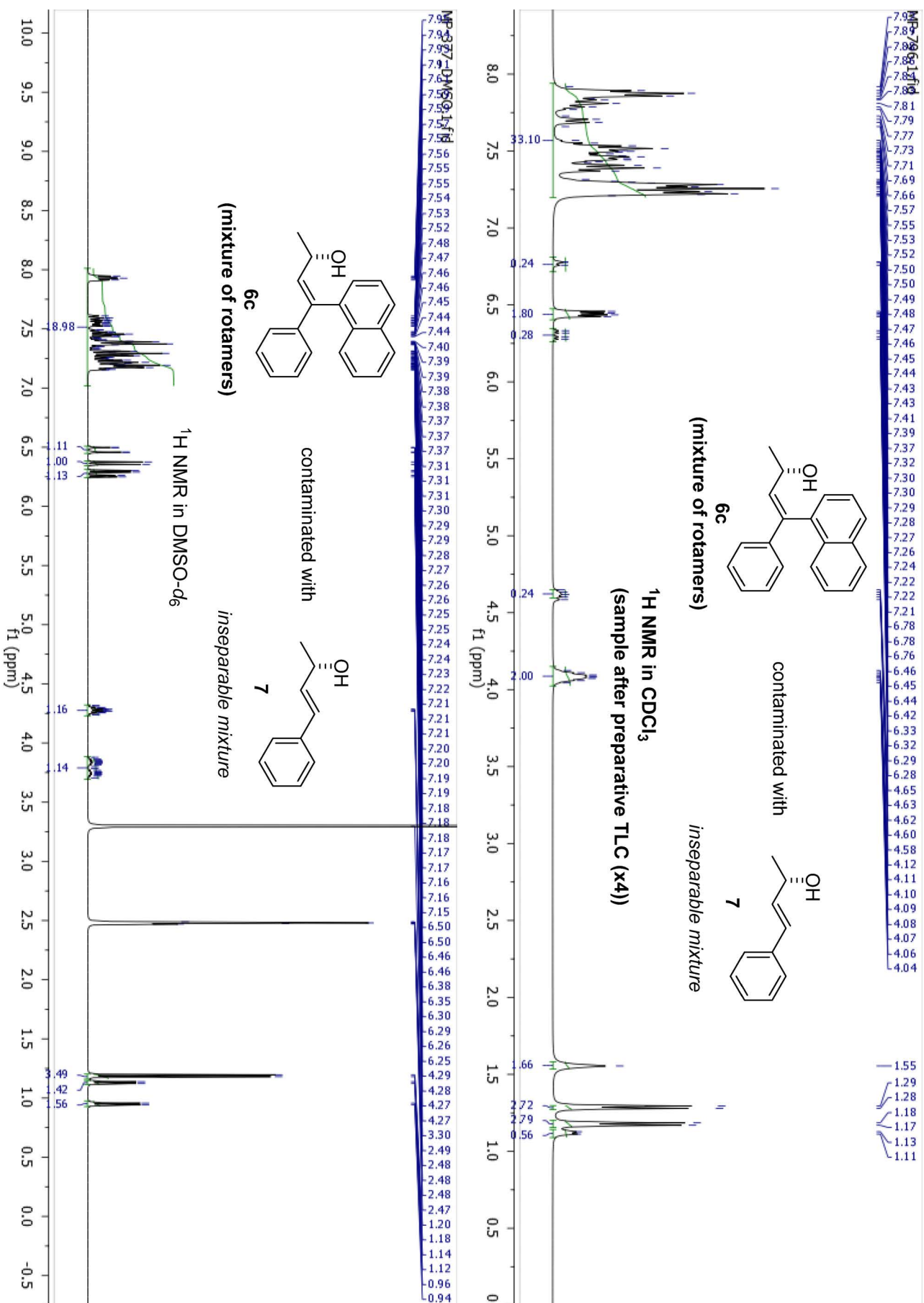


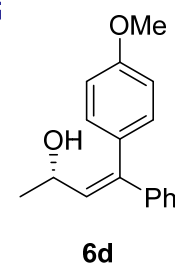
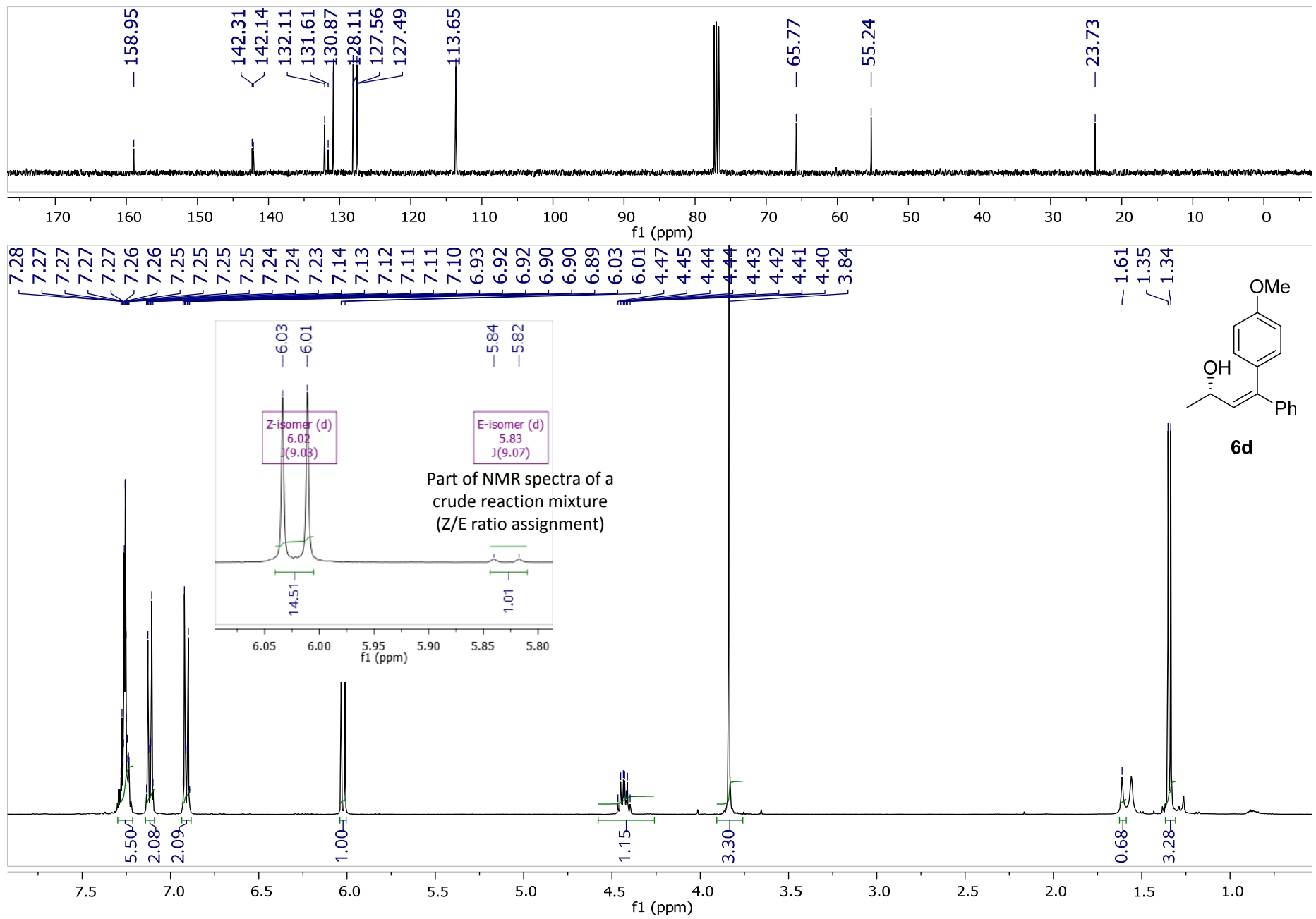


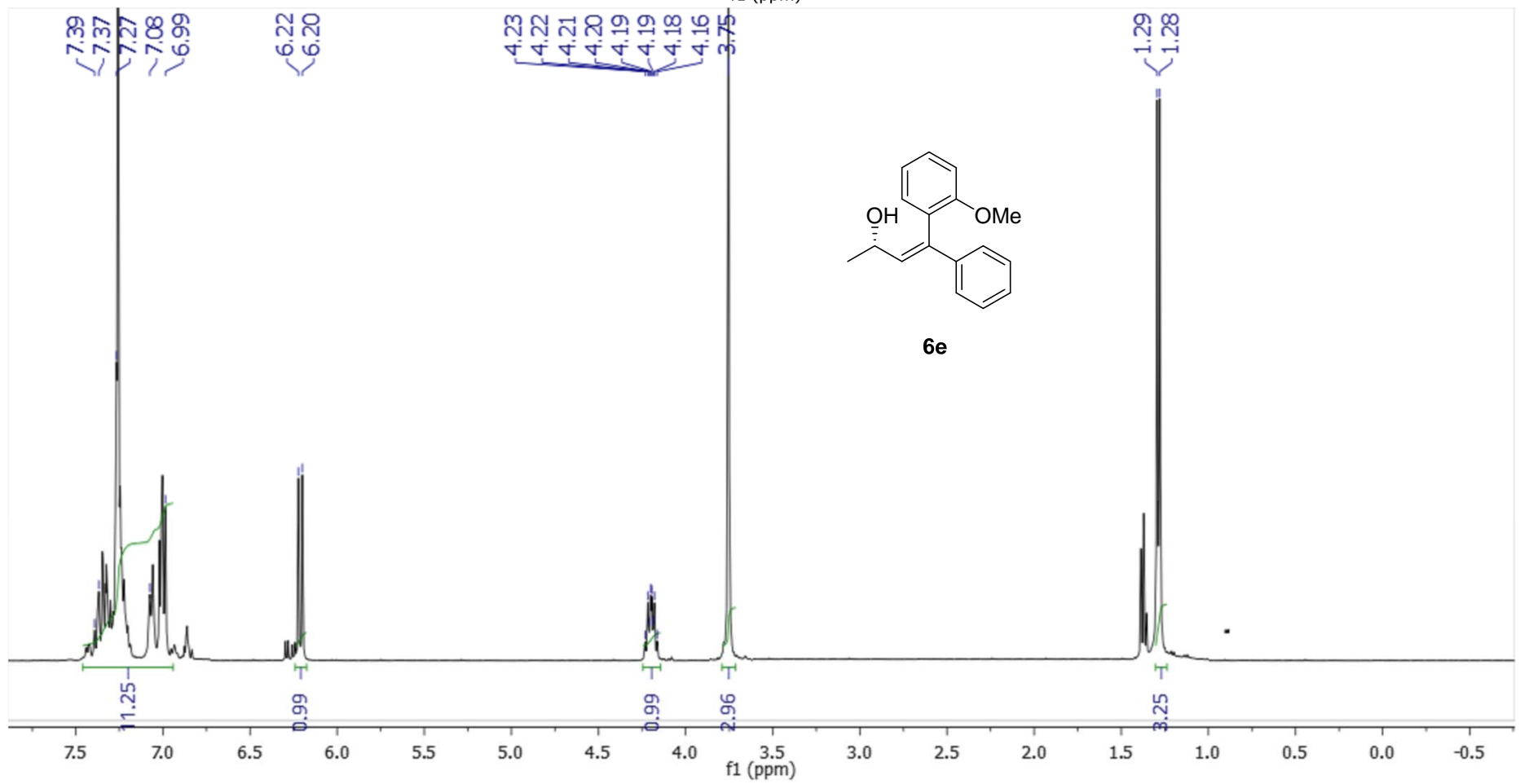
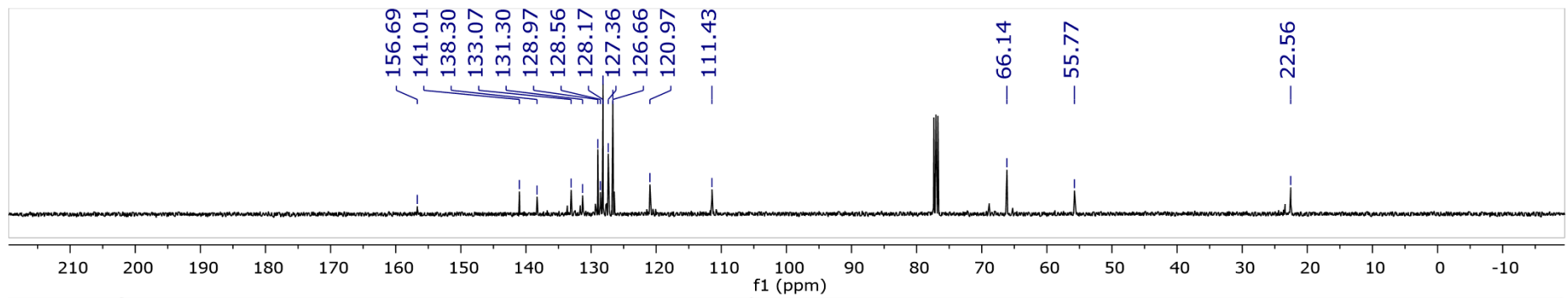


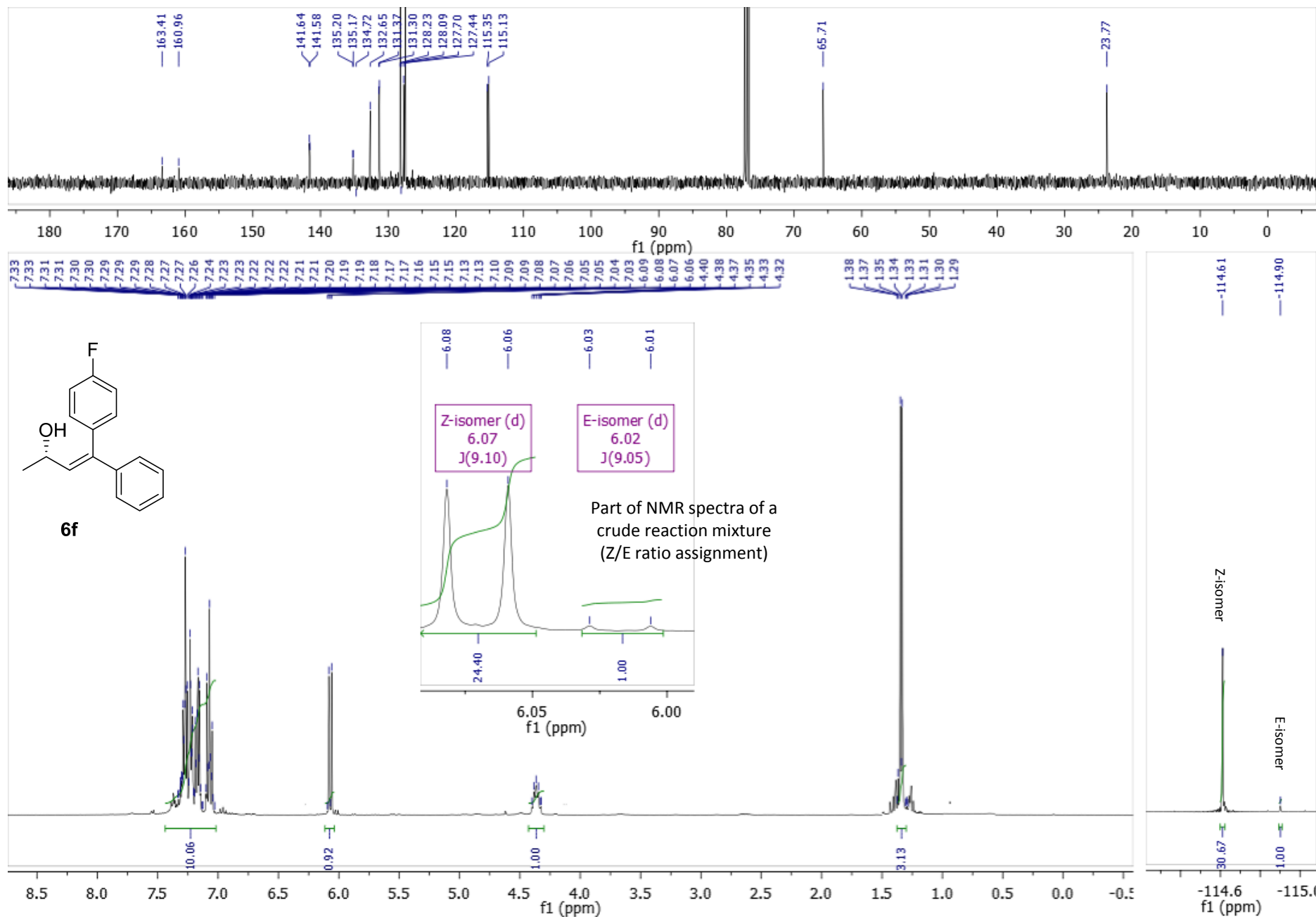


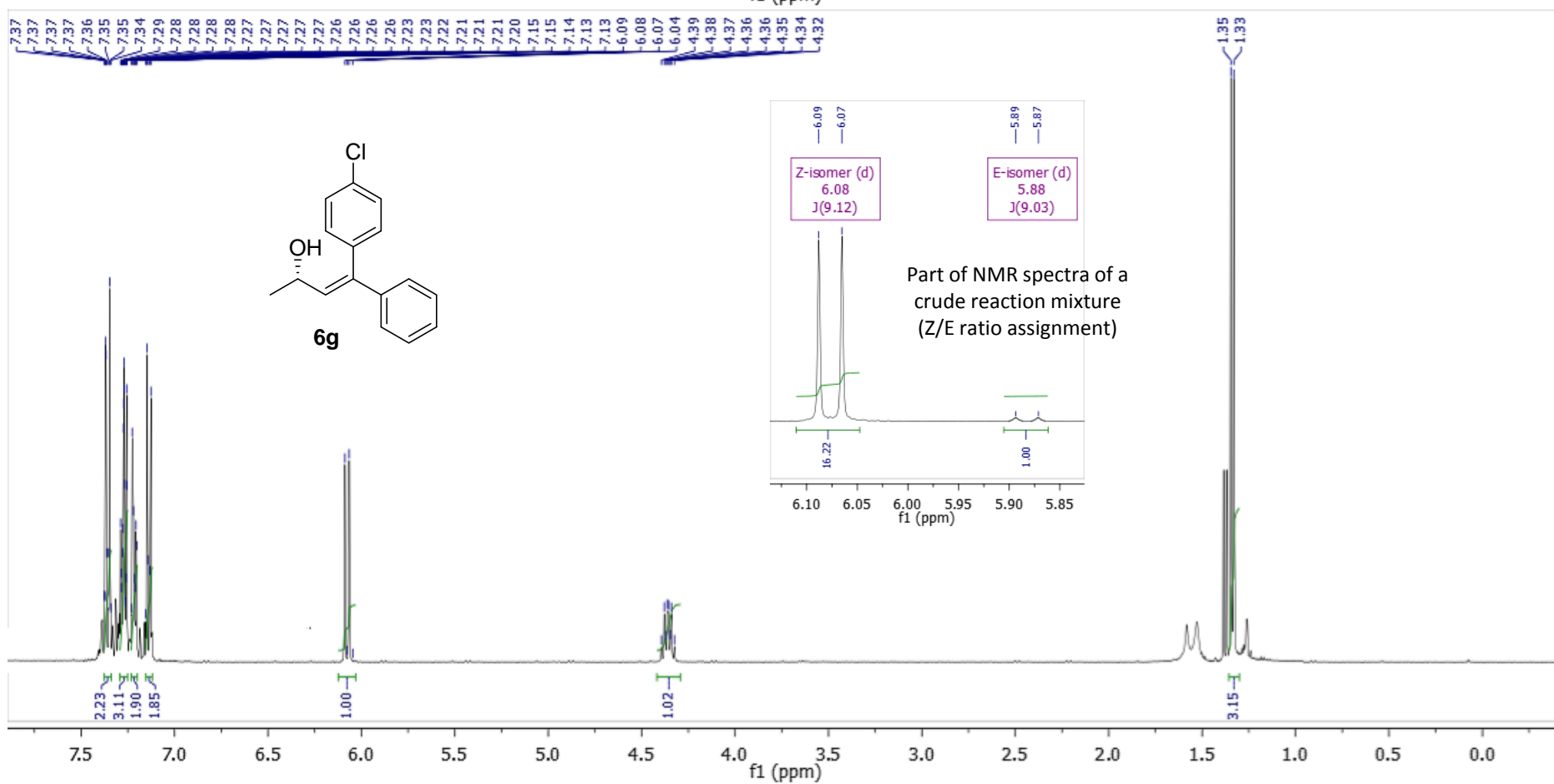
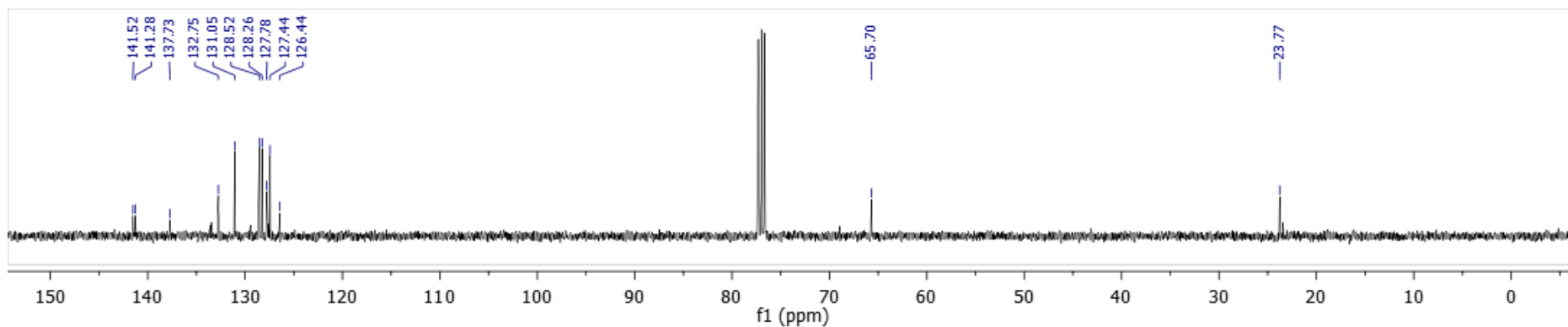


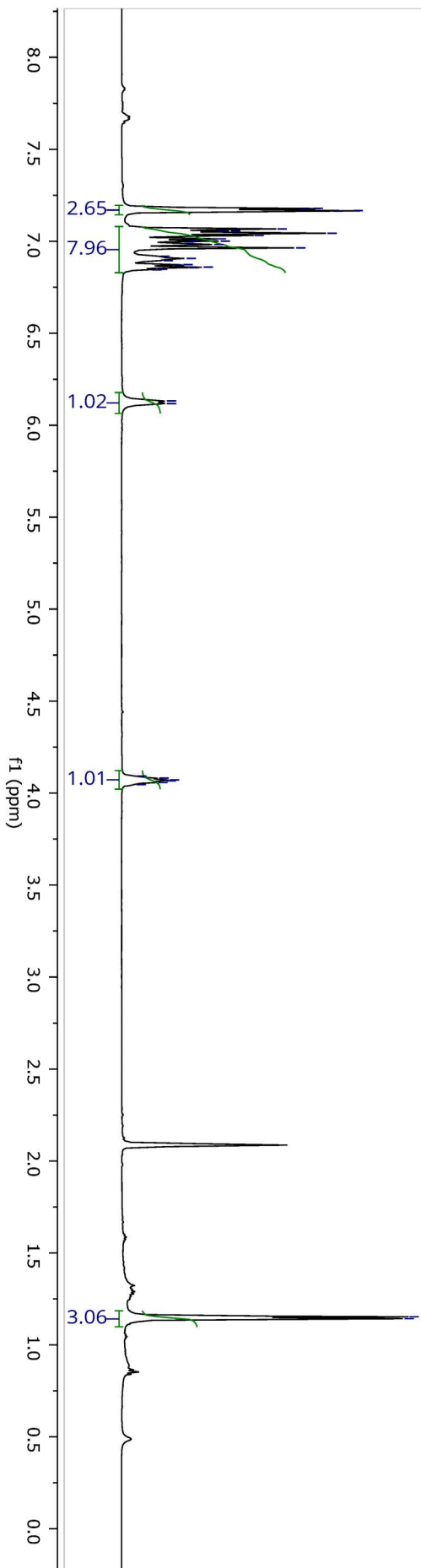
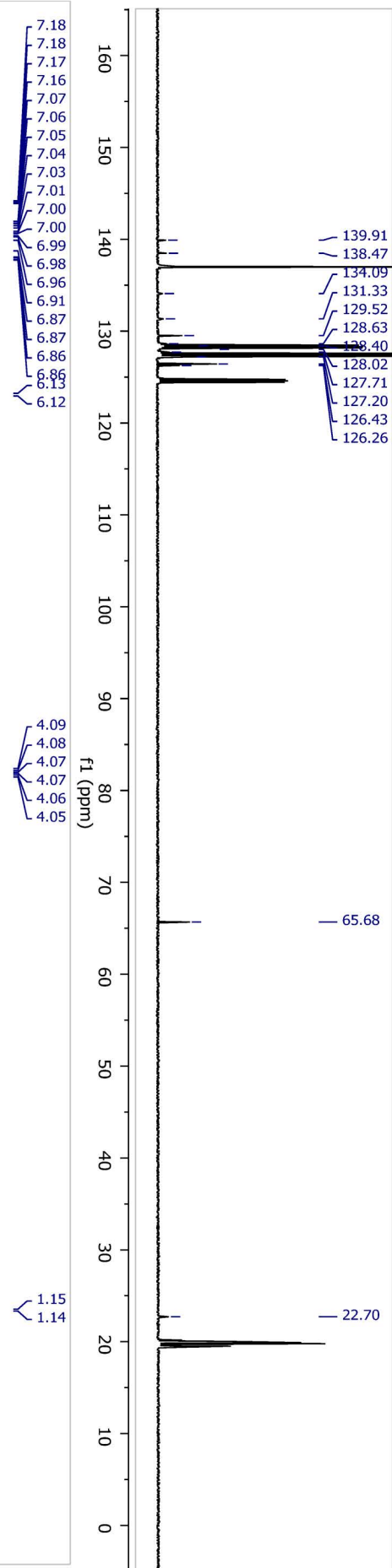
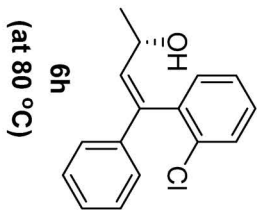


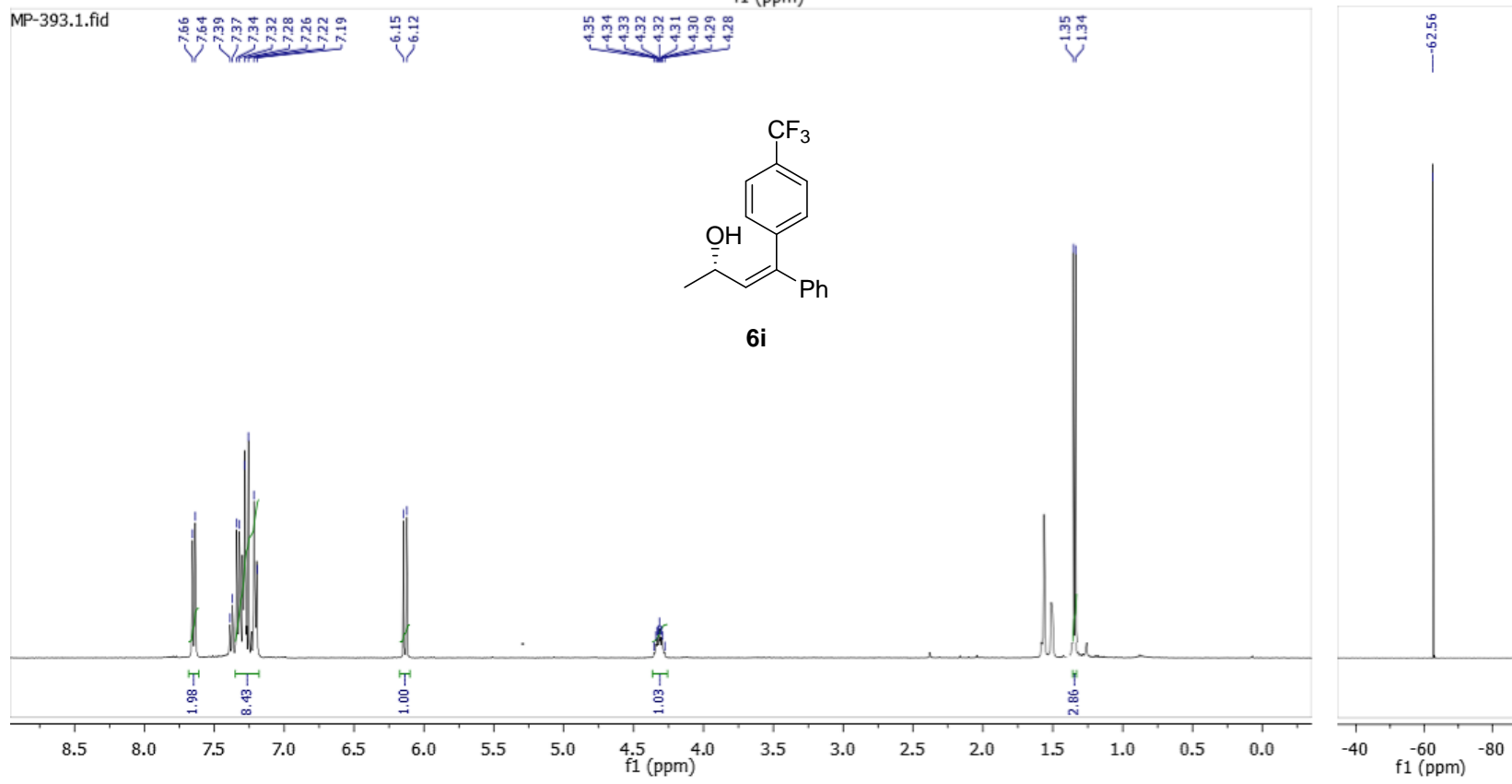
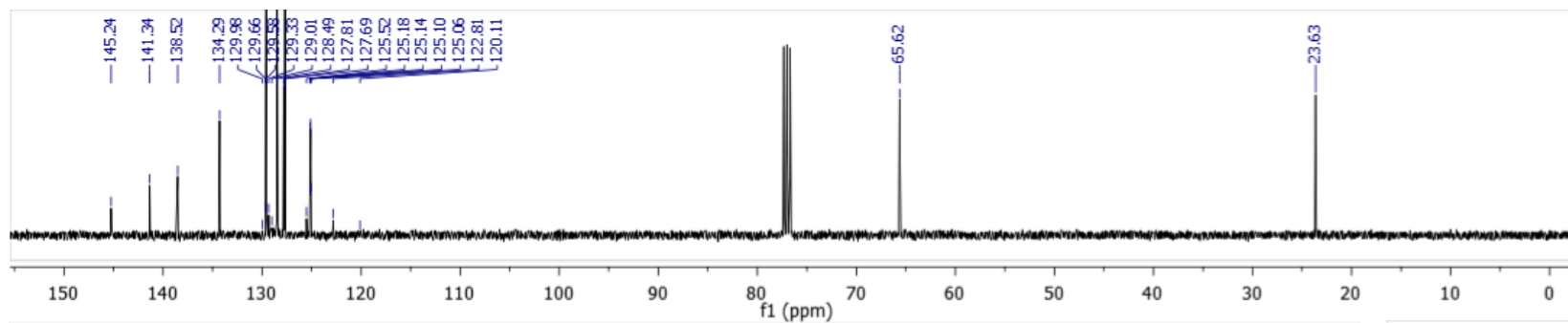




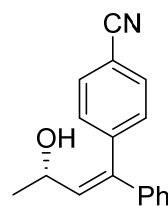
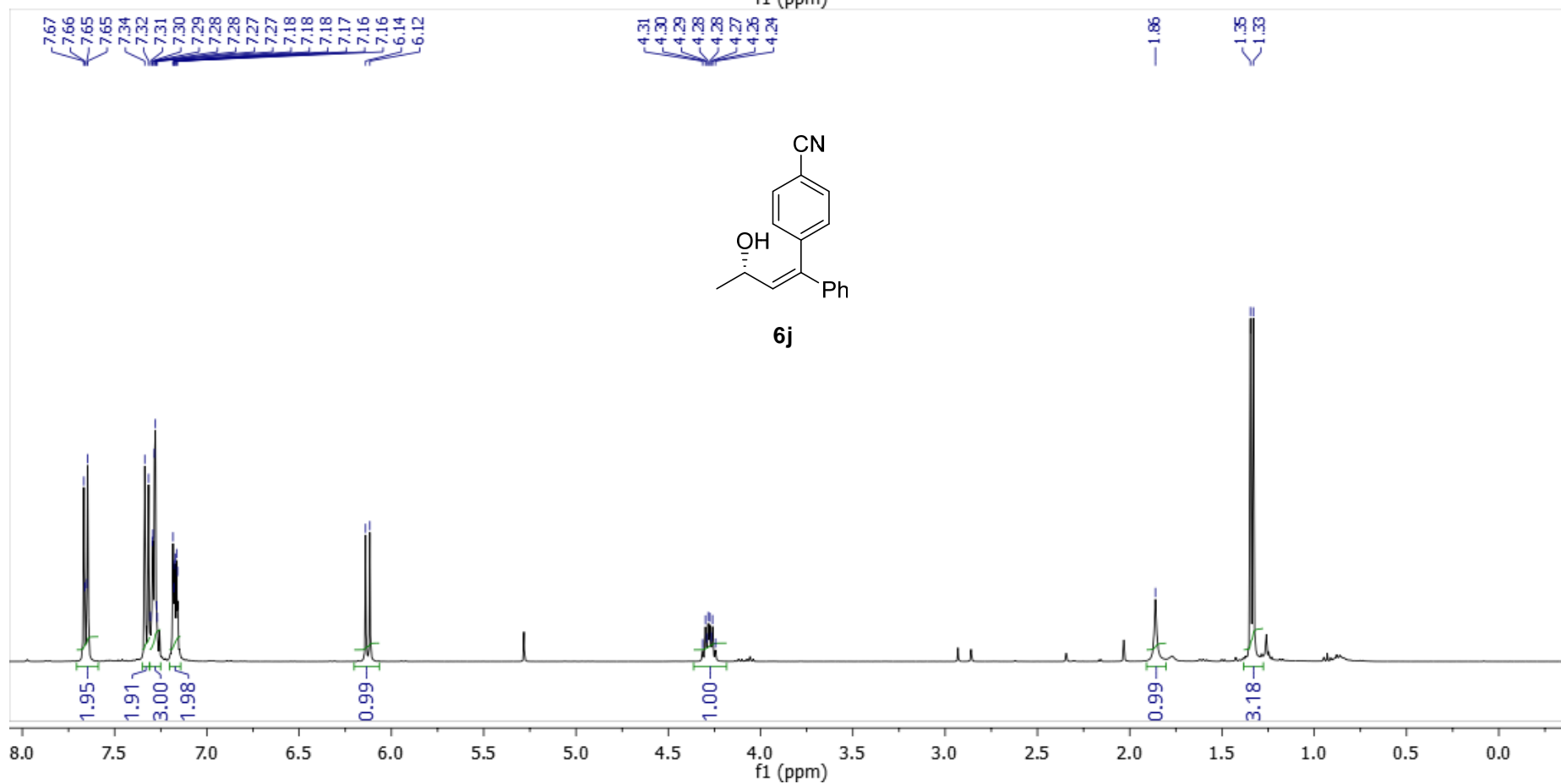
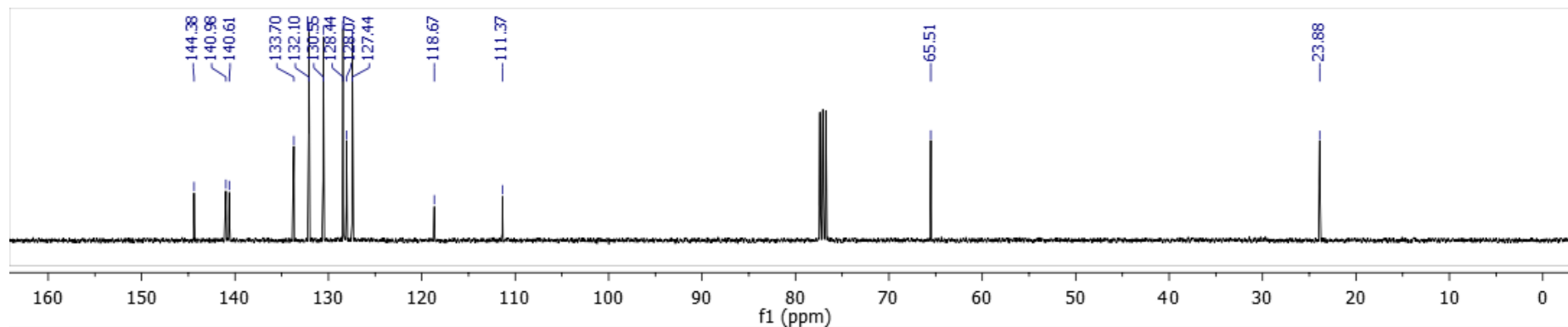




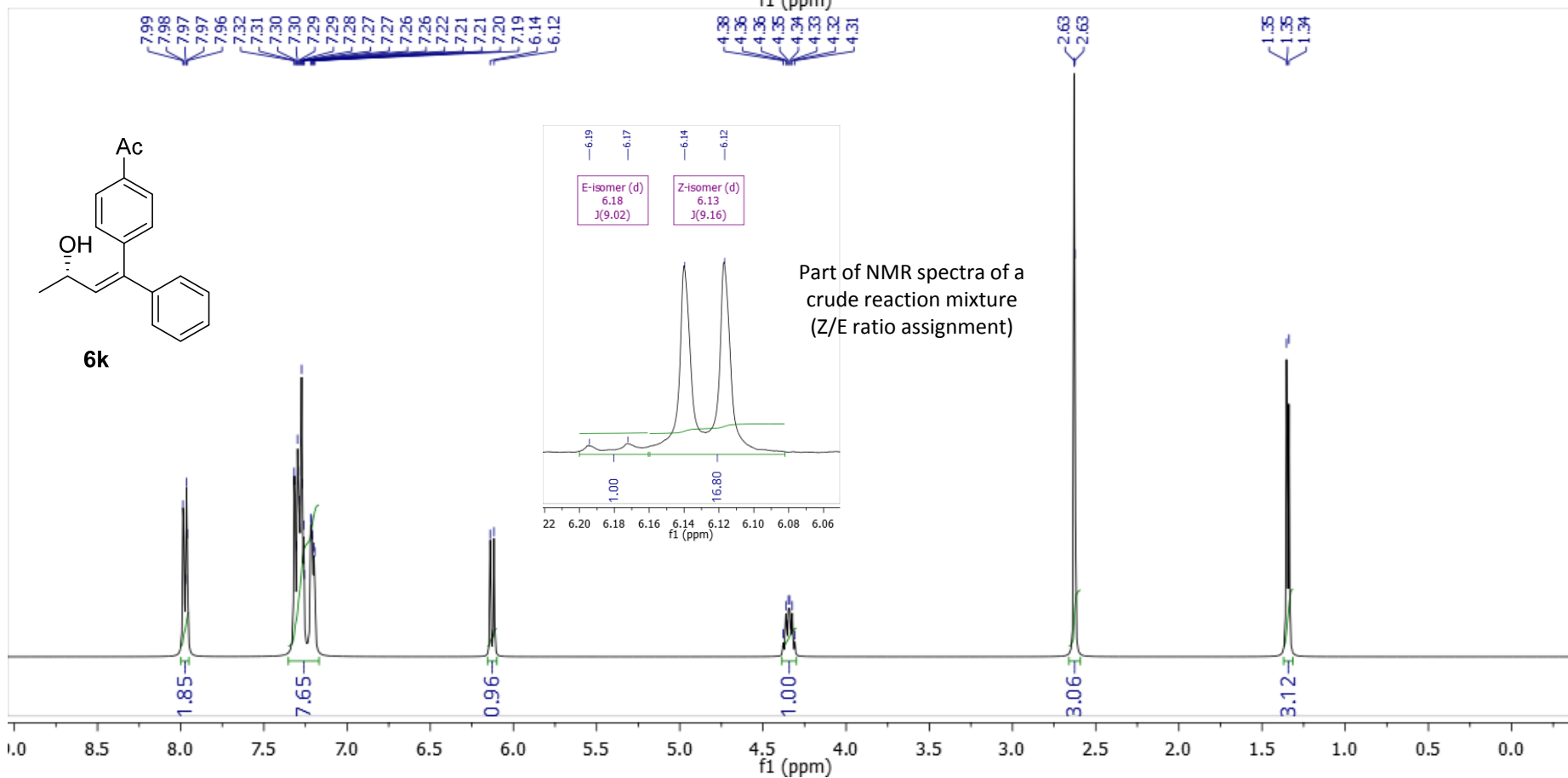
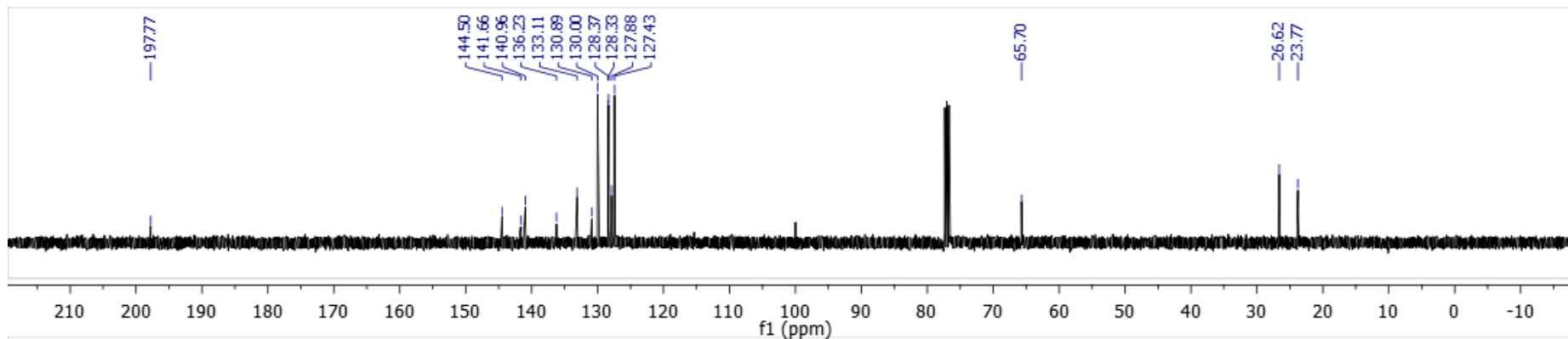


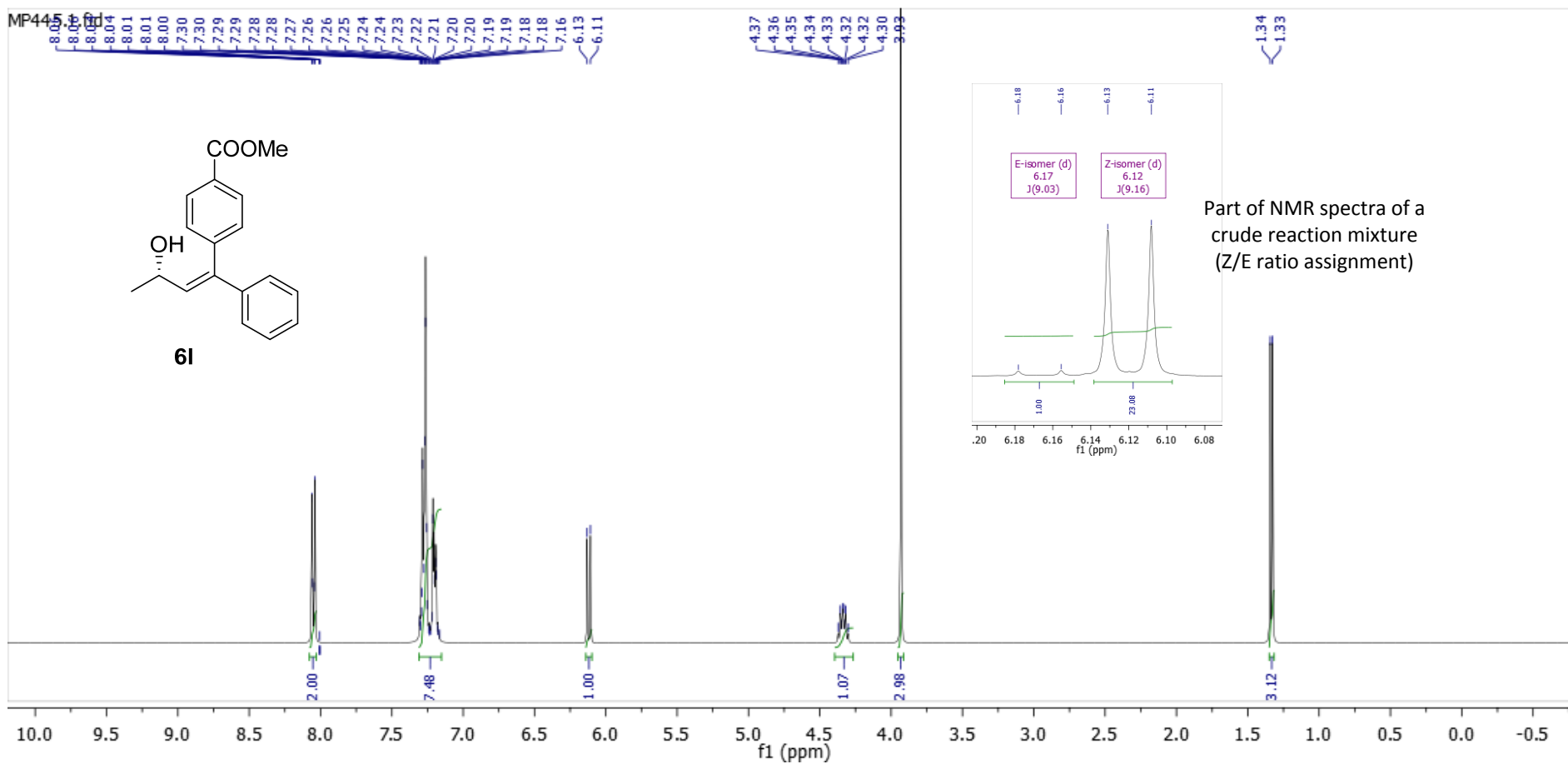
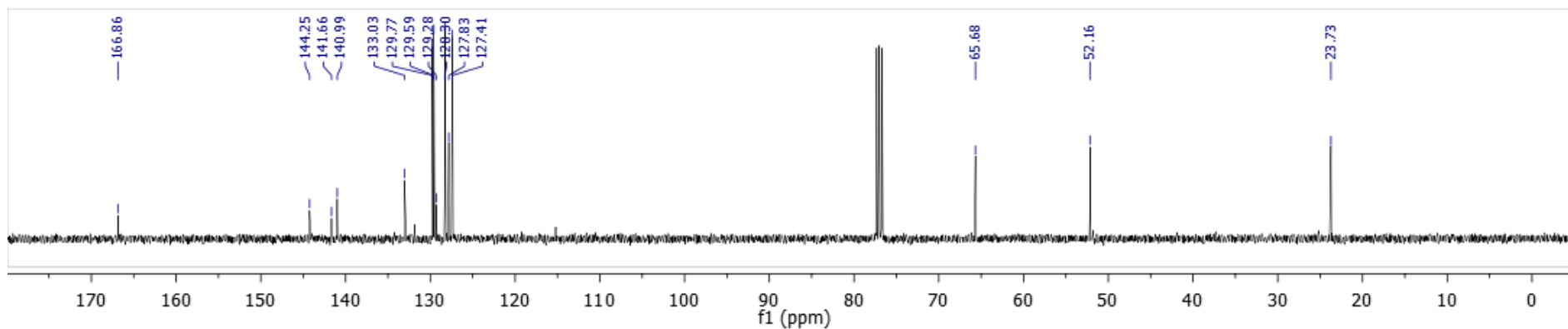


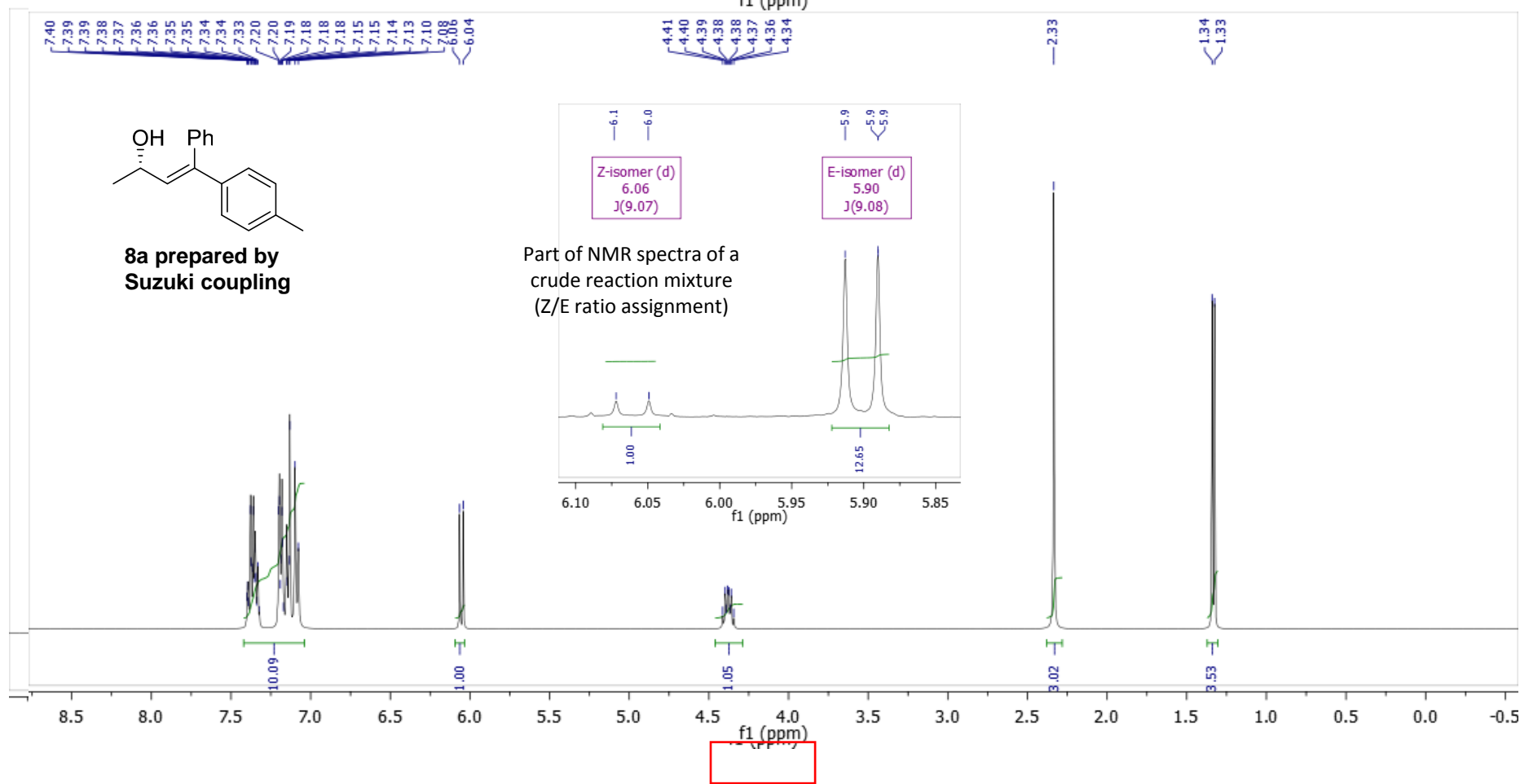
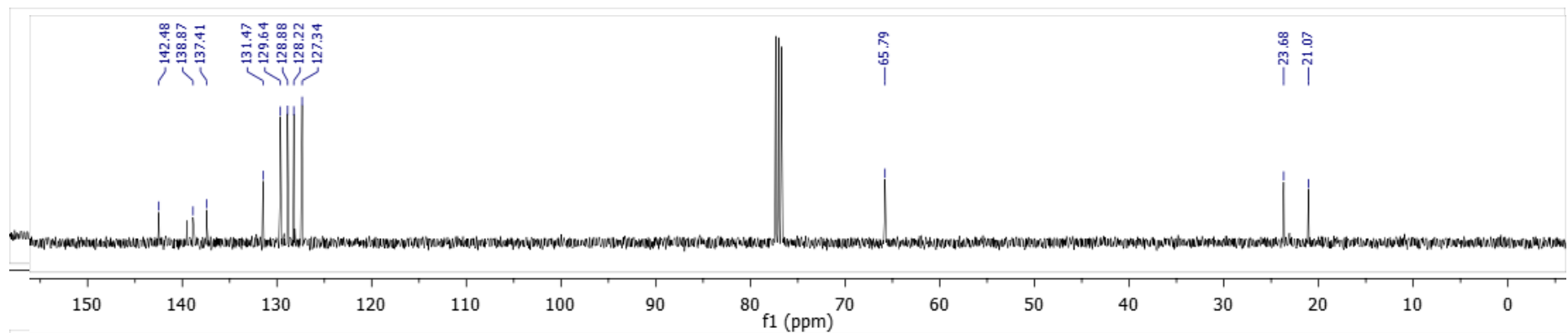


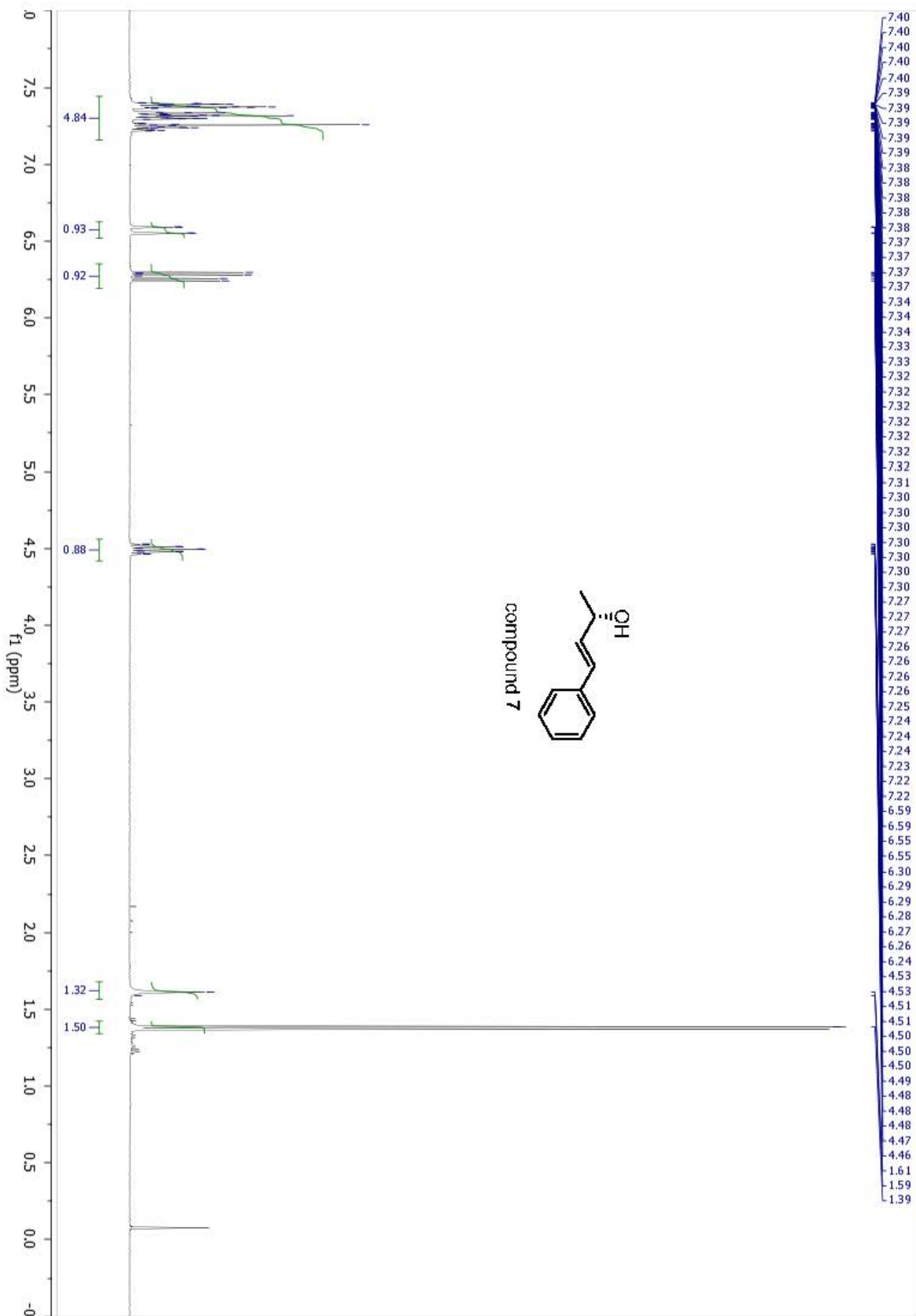


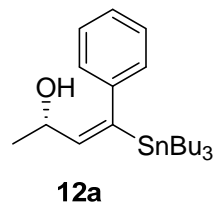
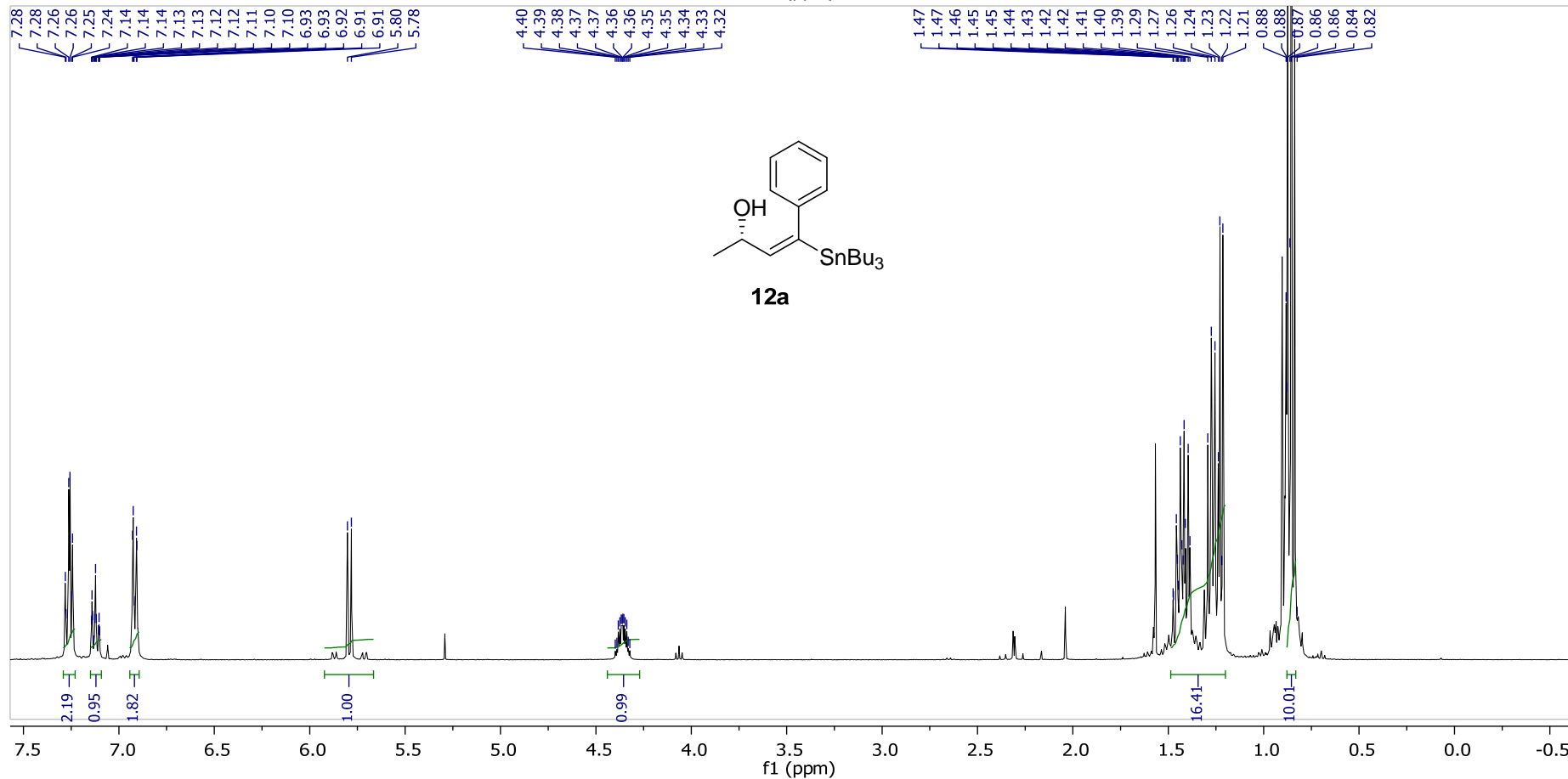
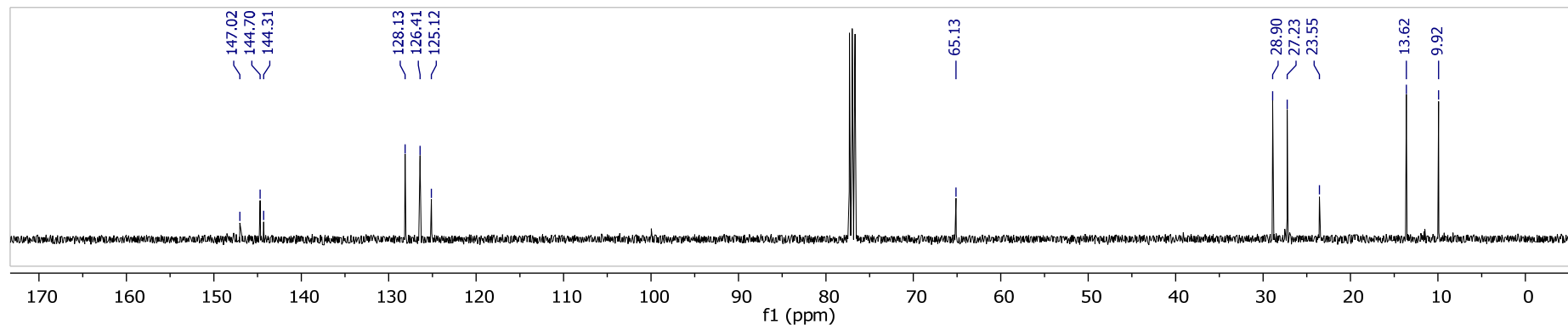
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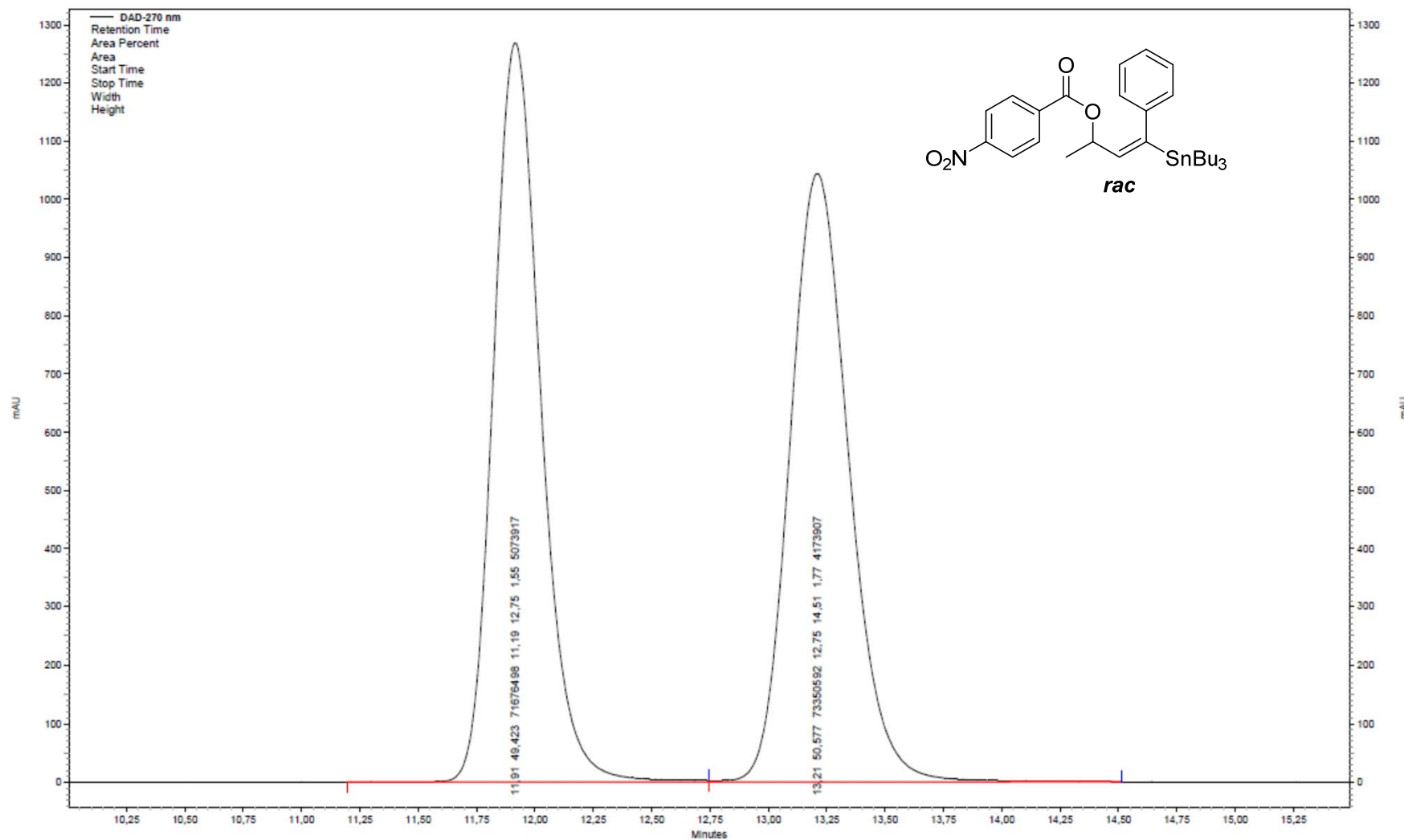




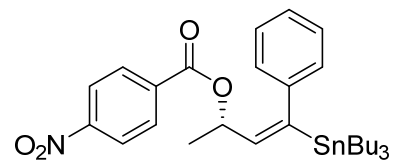


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Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5 mL/min  
Detection: UV, 270 nm

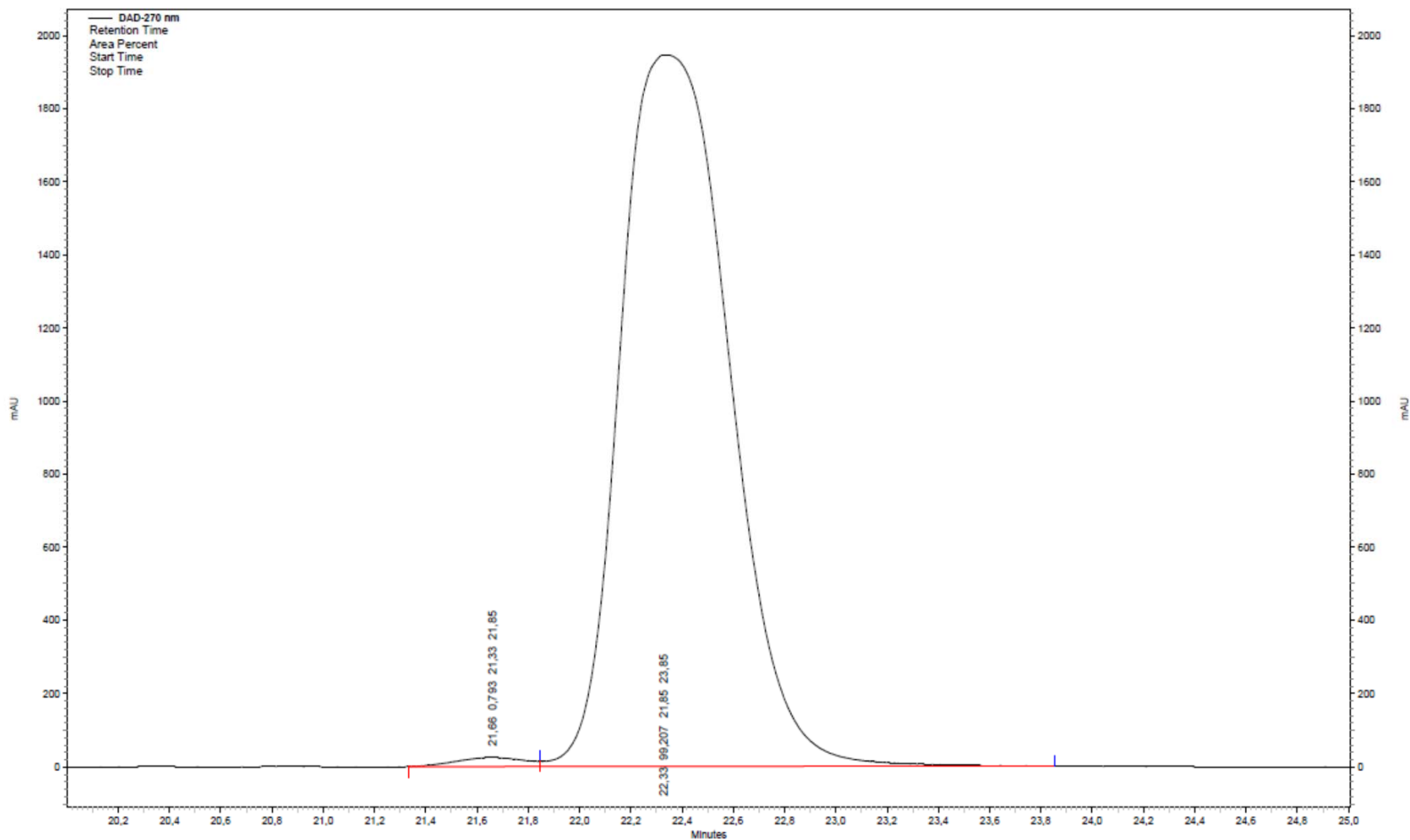
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2	13.21	12.75	14.51	73350592	4173907	50.577	1.77



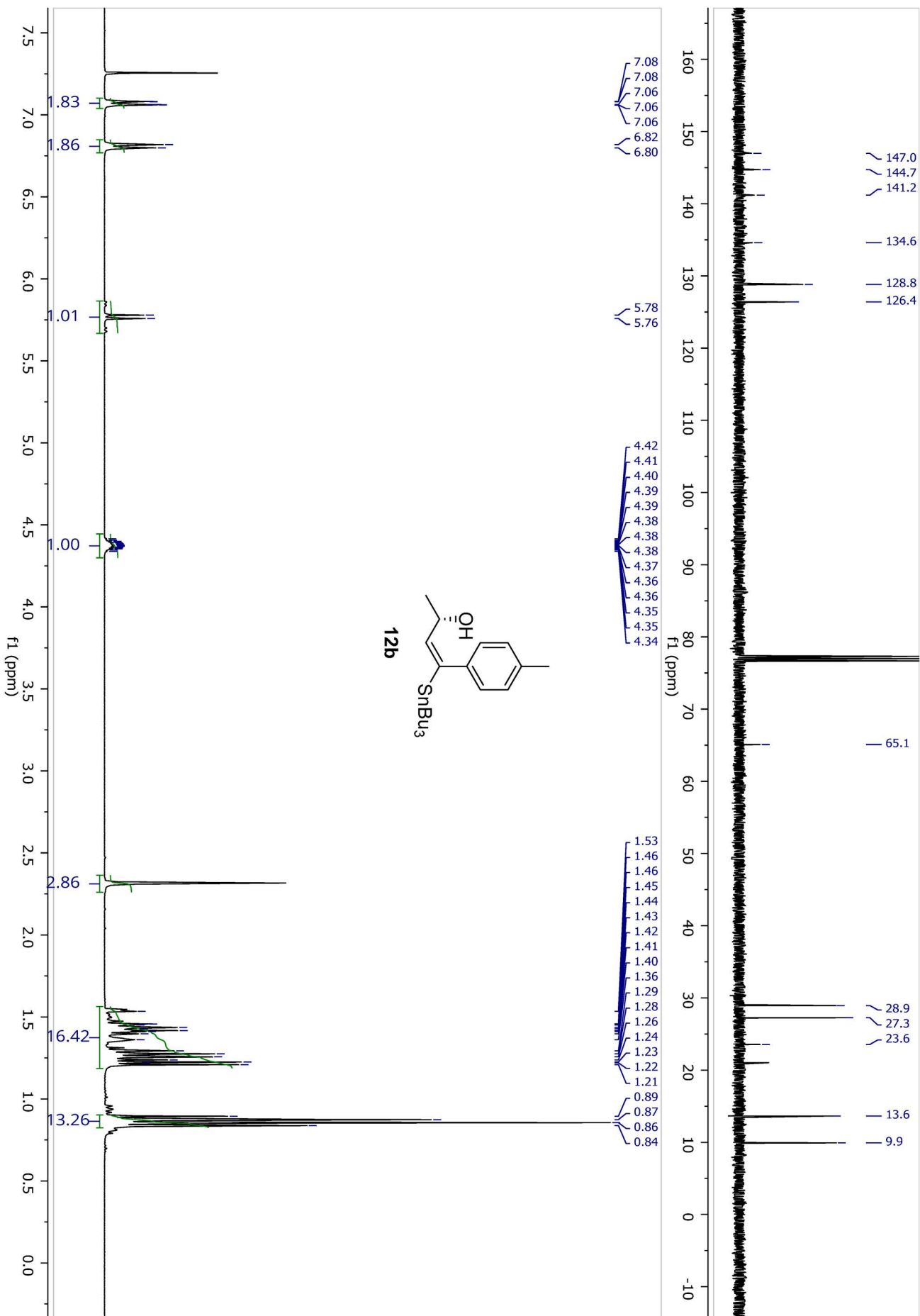
Column: Chiralpak IB  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5 mL/min  
Detection: UV, 270 nm



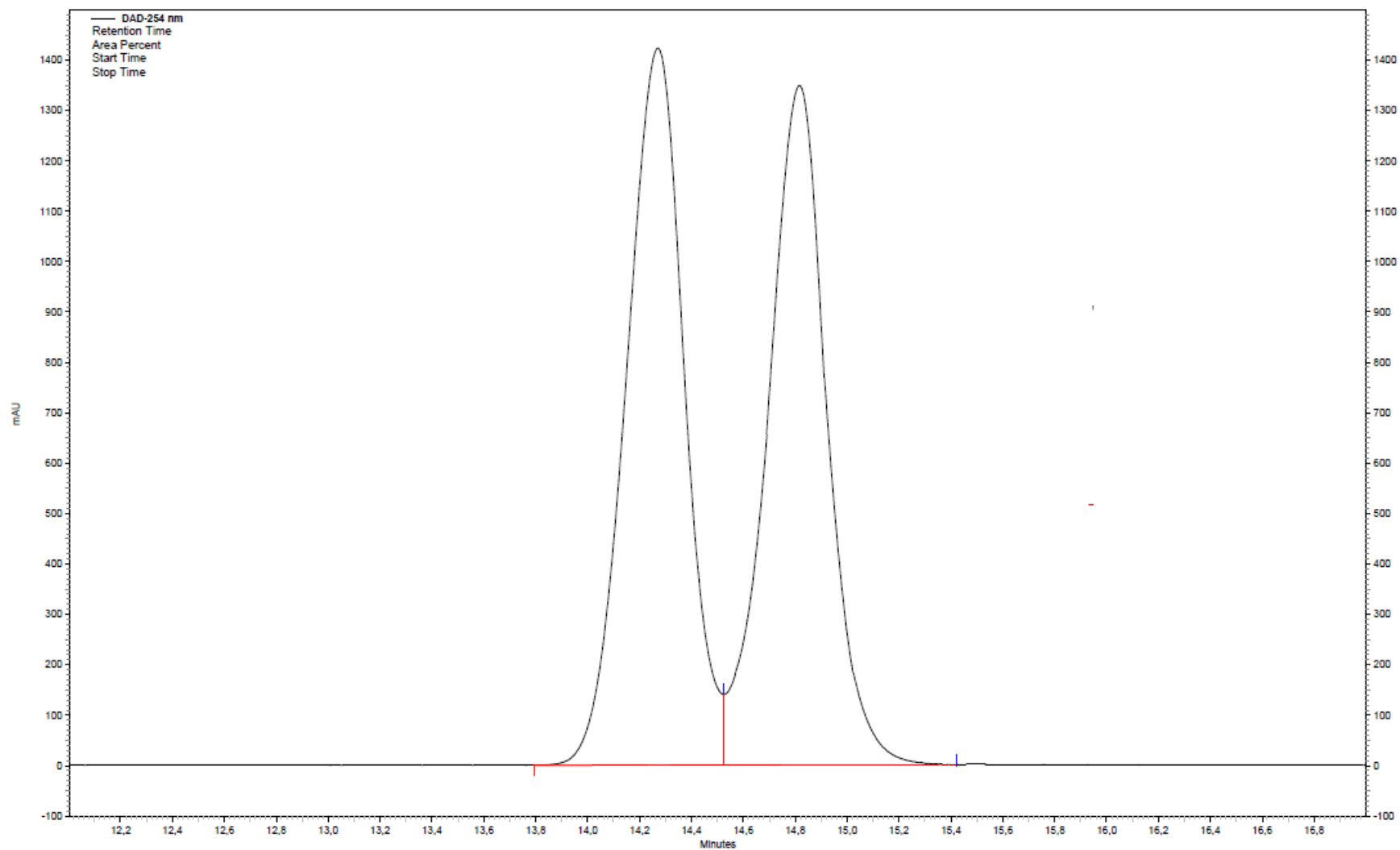
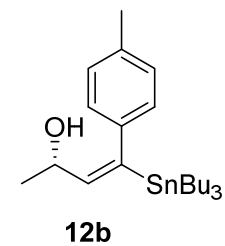
4-nitrobenzoate of **12a**



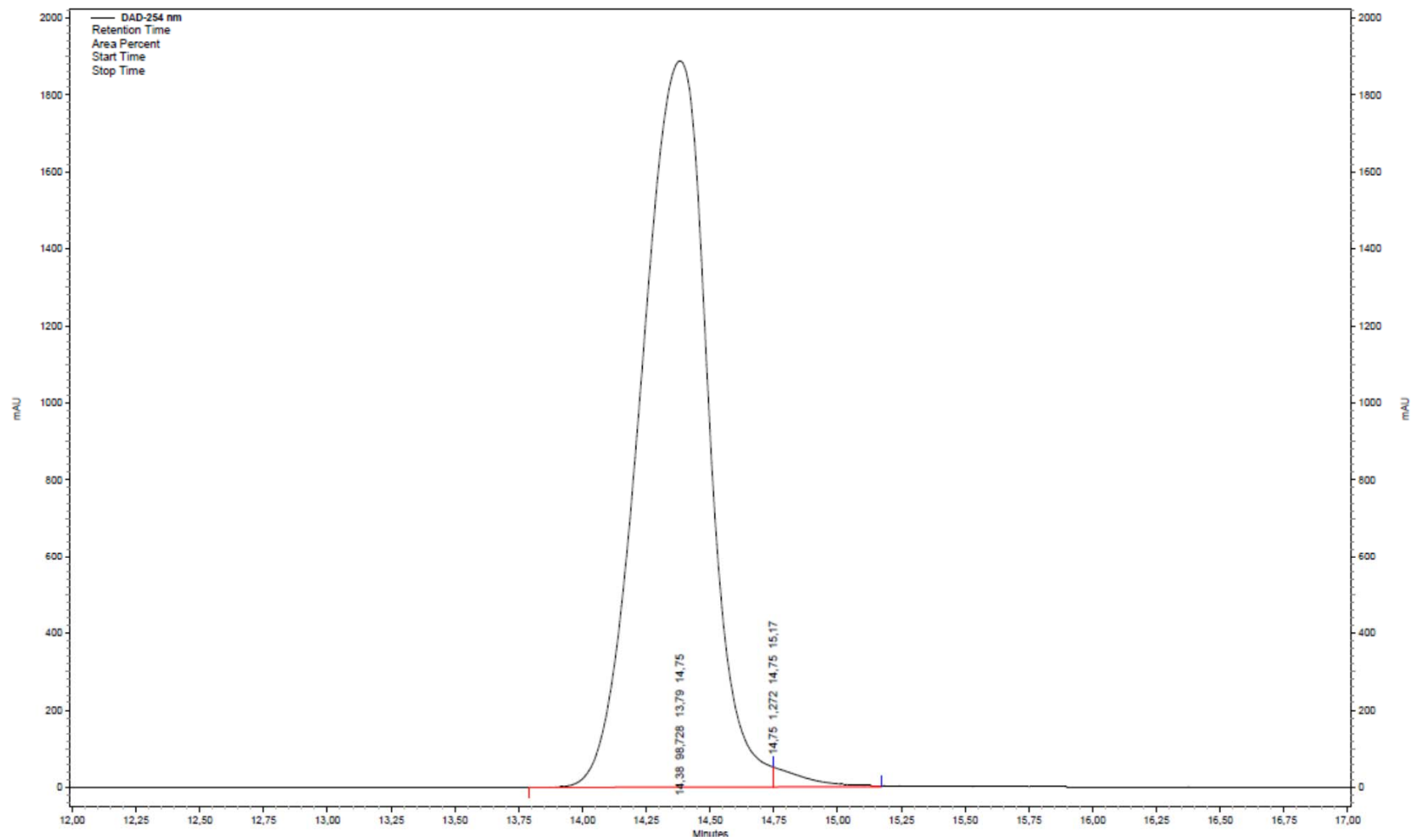
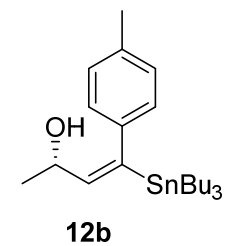


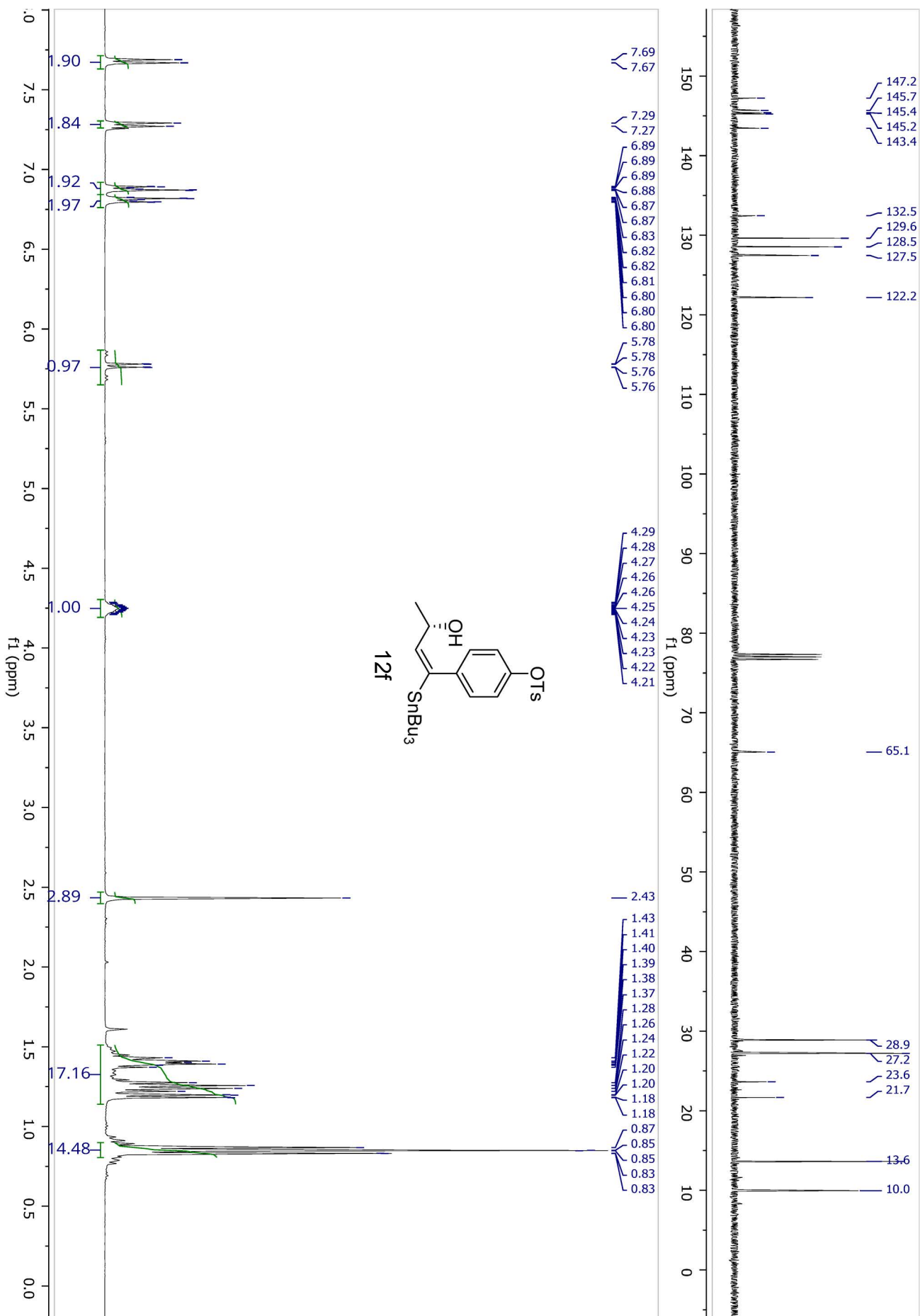


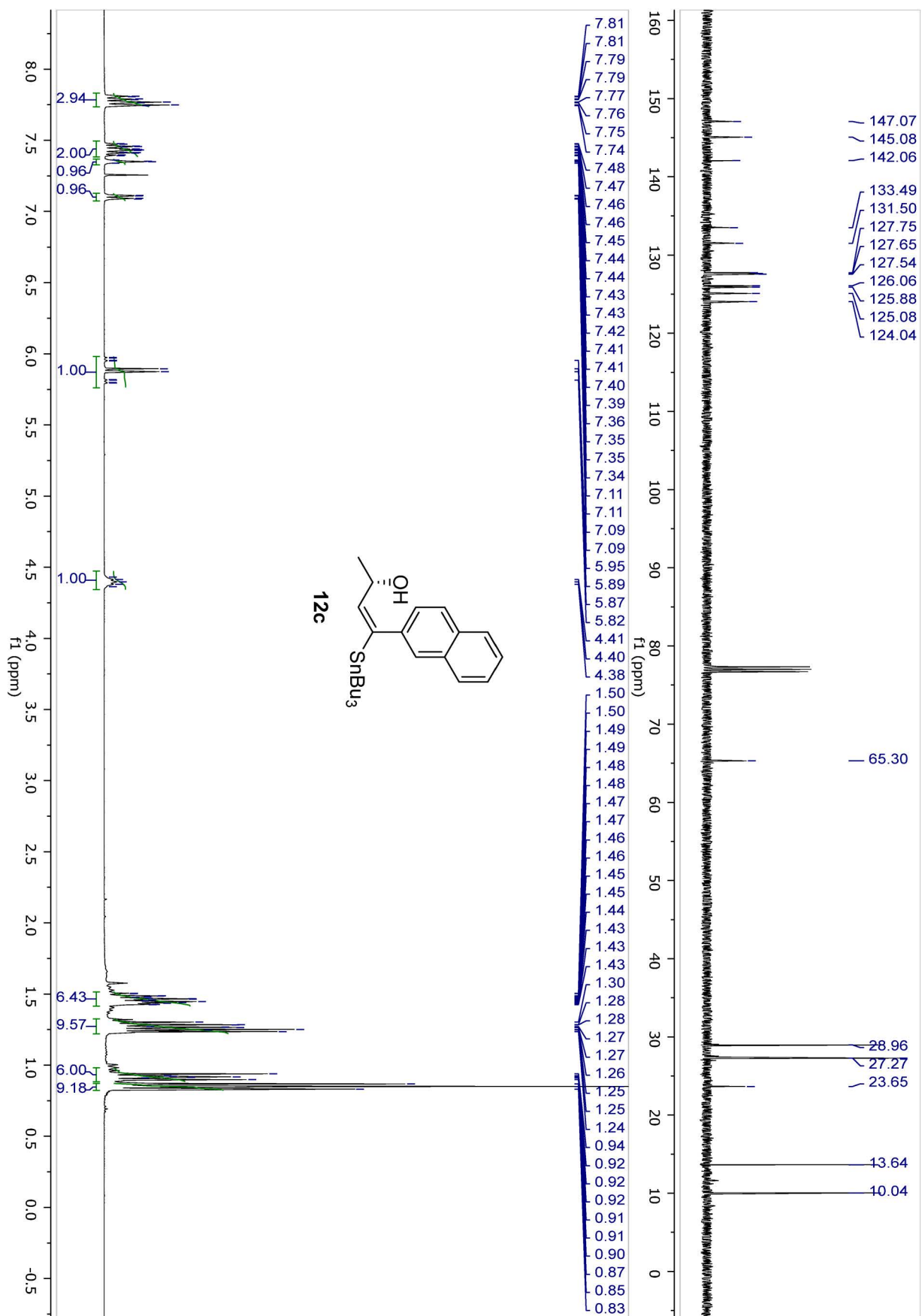
Column: Chiralpak IB  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5 mL/min  
Detection: UV, 254 nm

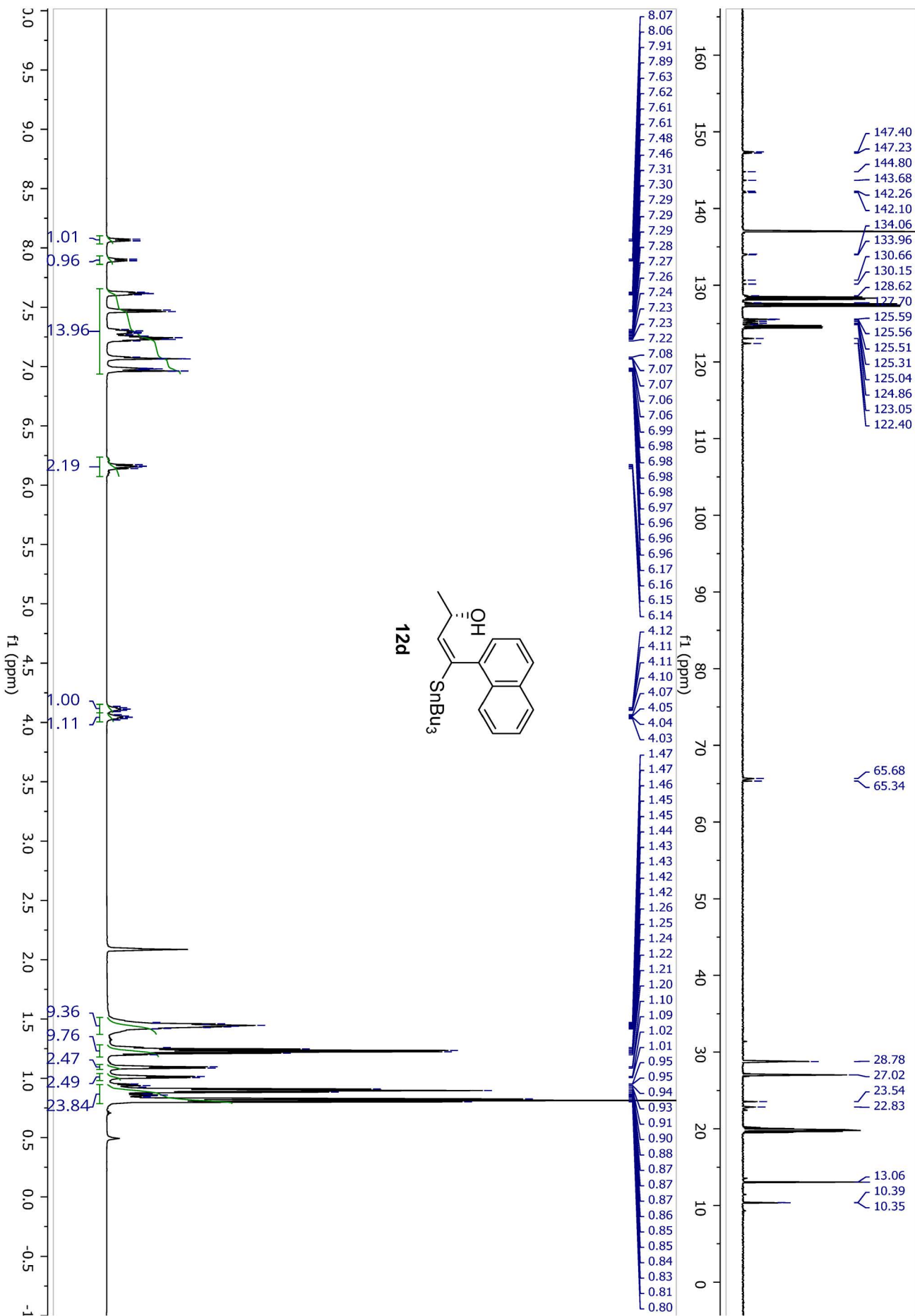


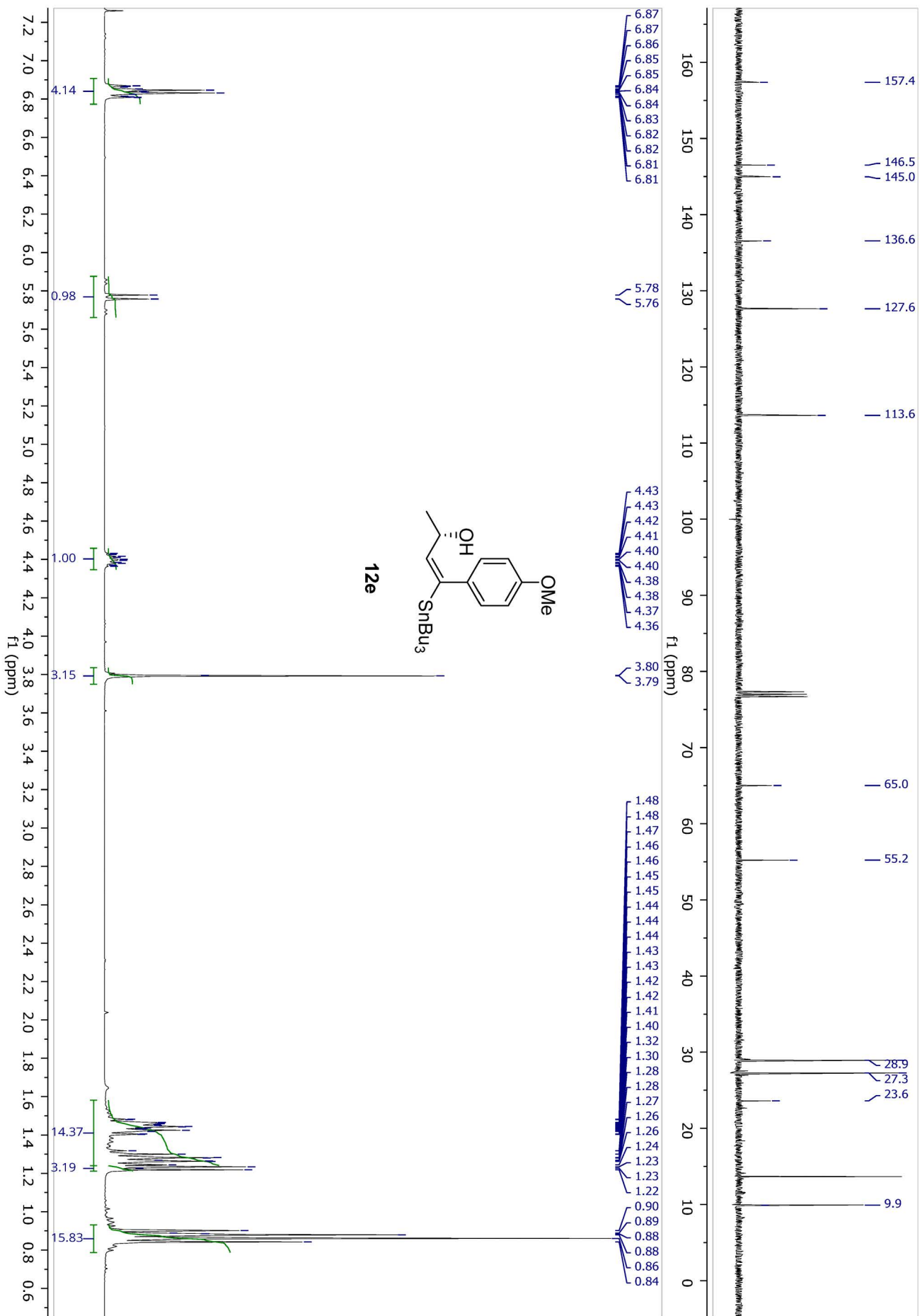
Column: Chiralpak IB  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5 mL/min  
Detection: UV, 254 nm



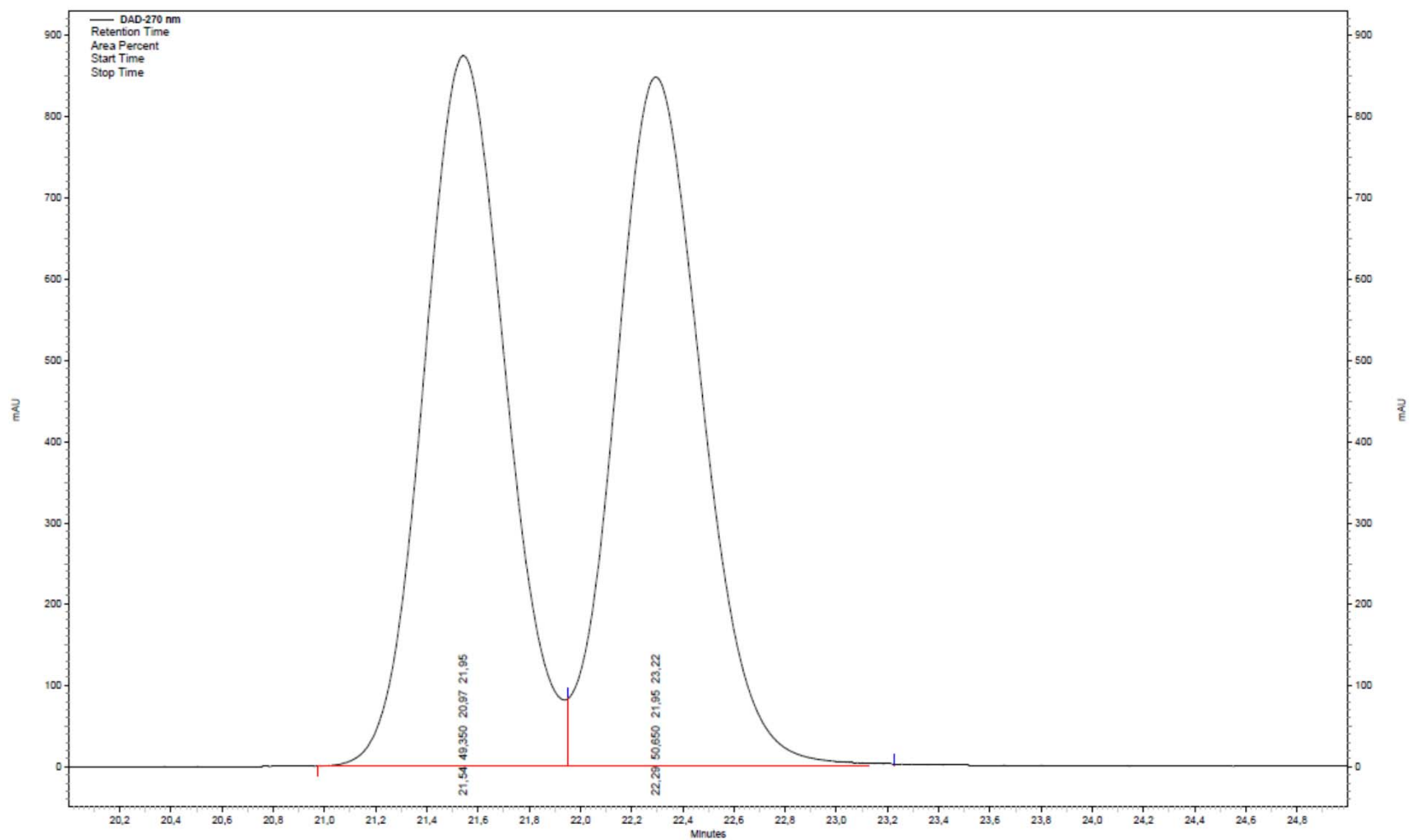
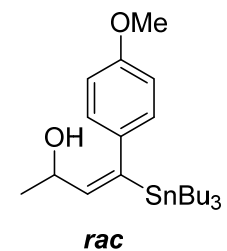






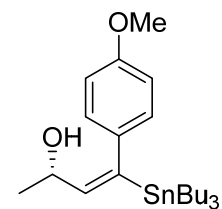


Column: Chiralpak IB  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5 mL/min  
Detection: UV, 270 nm

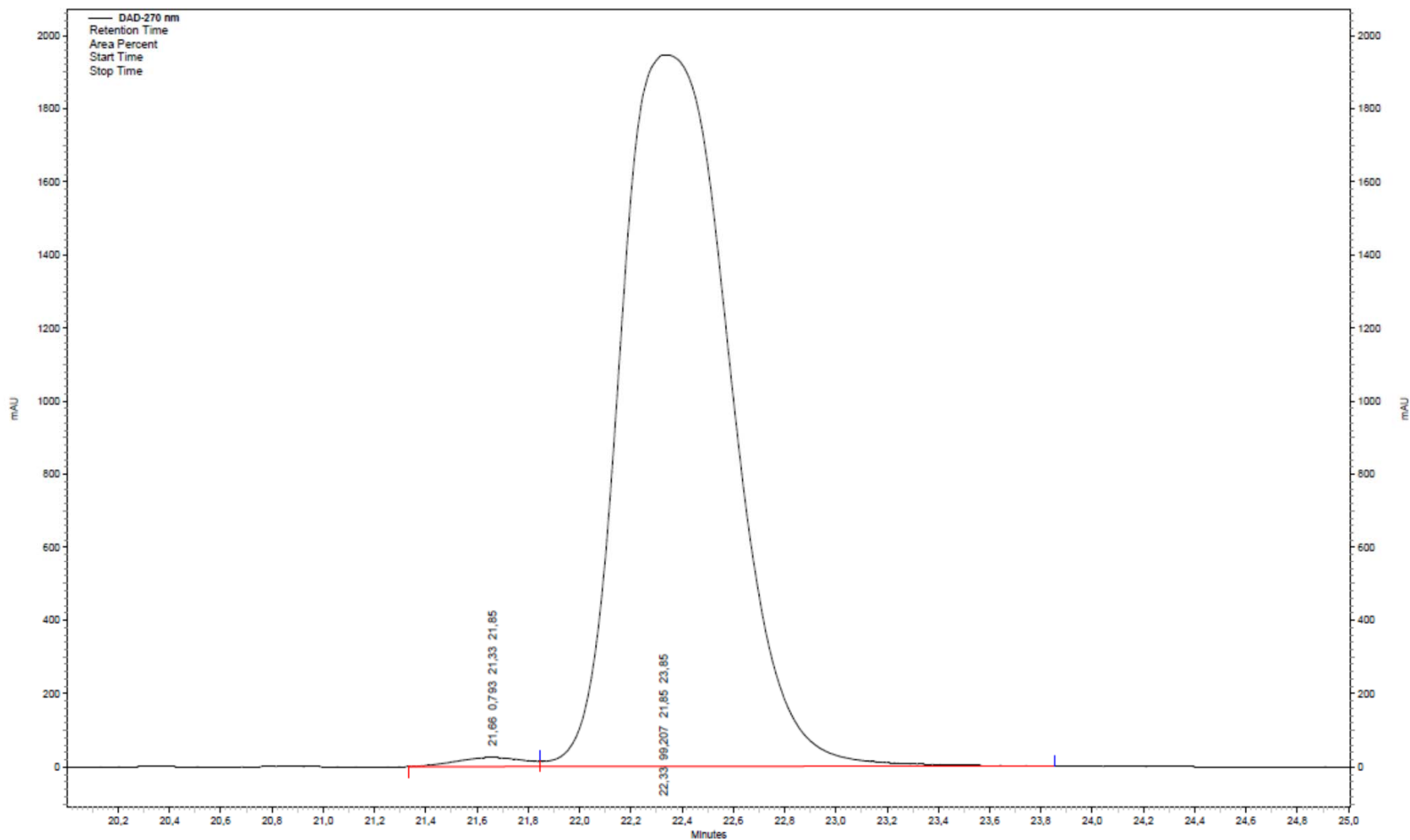


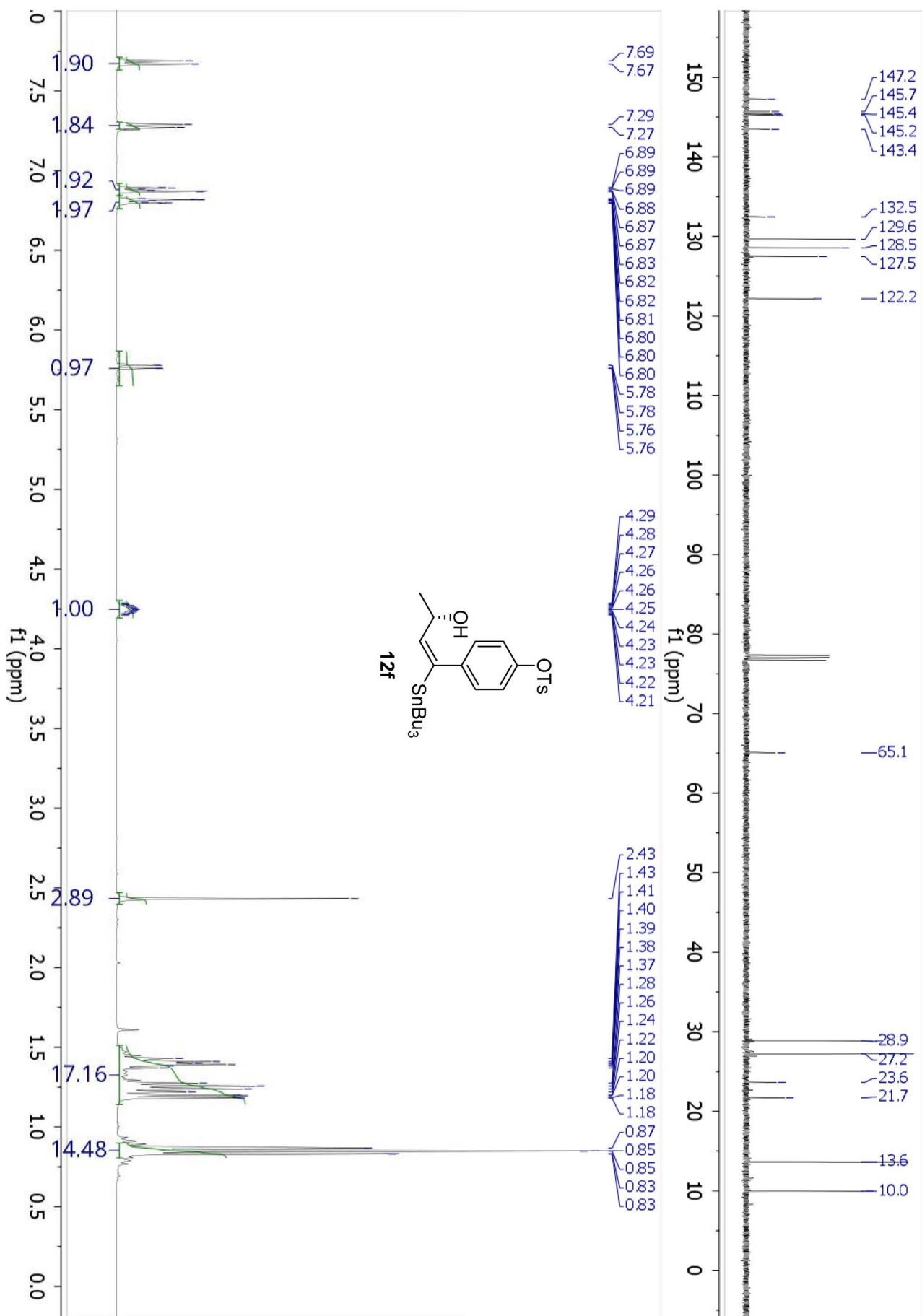


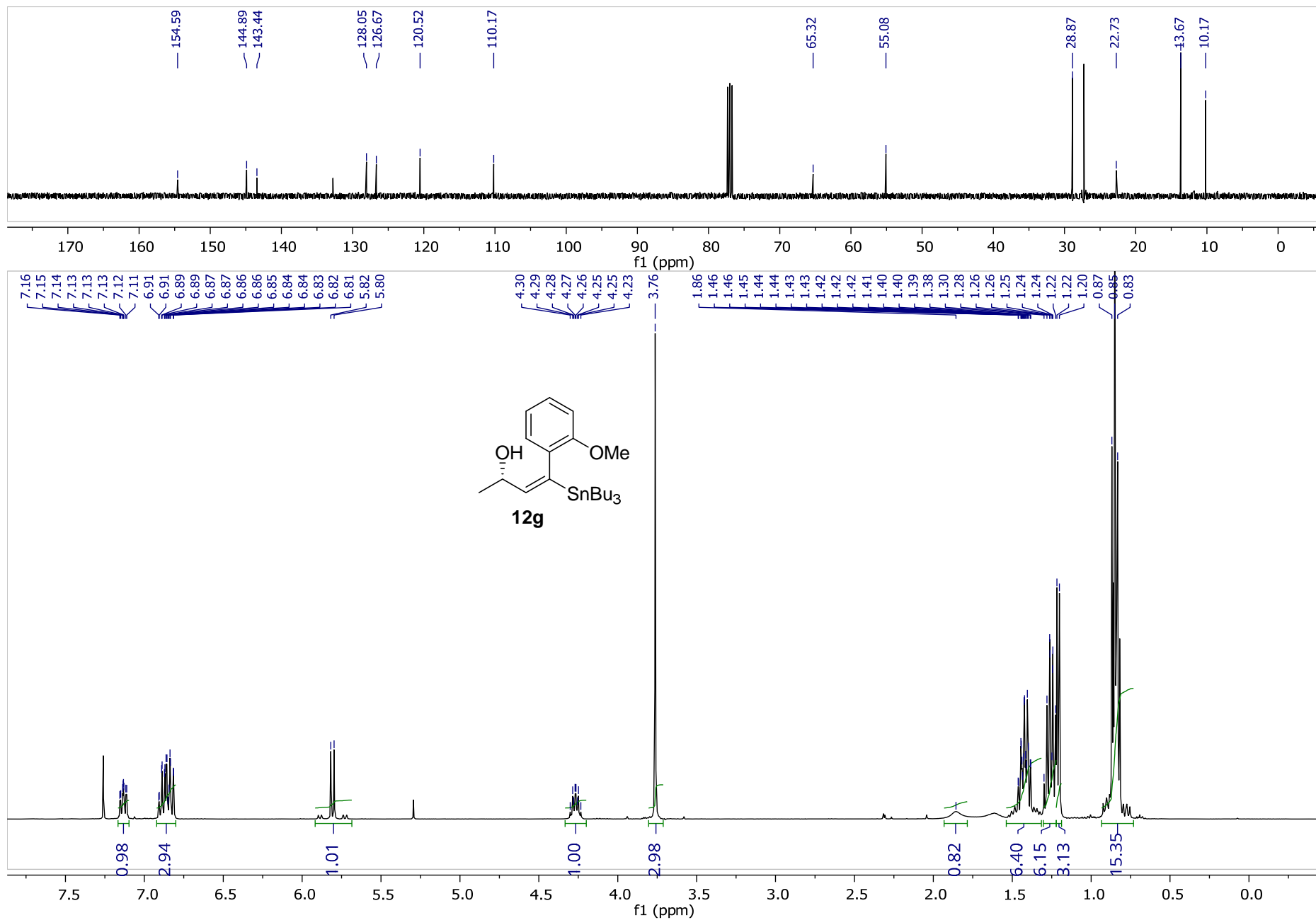
Column: Chiralpak IB  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5 mL/min  
Detection: UV, 270 nm

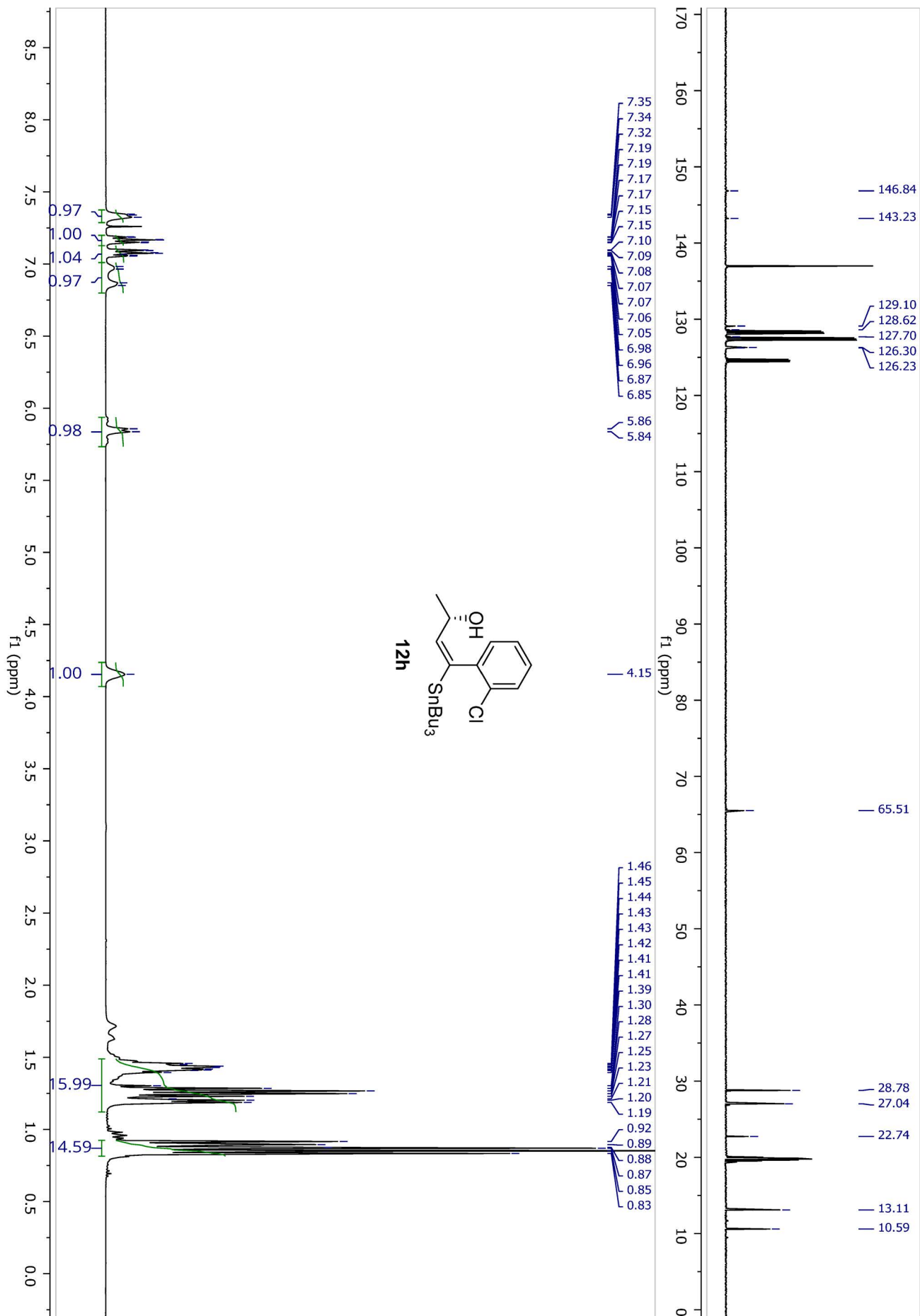


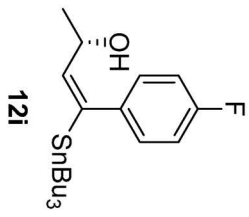
**12e**



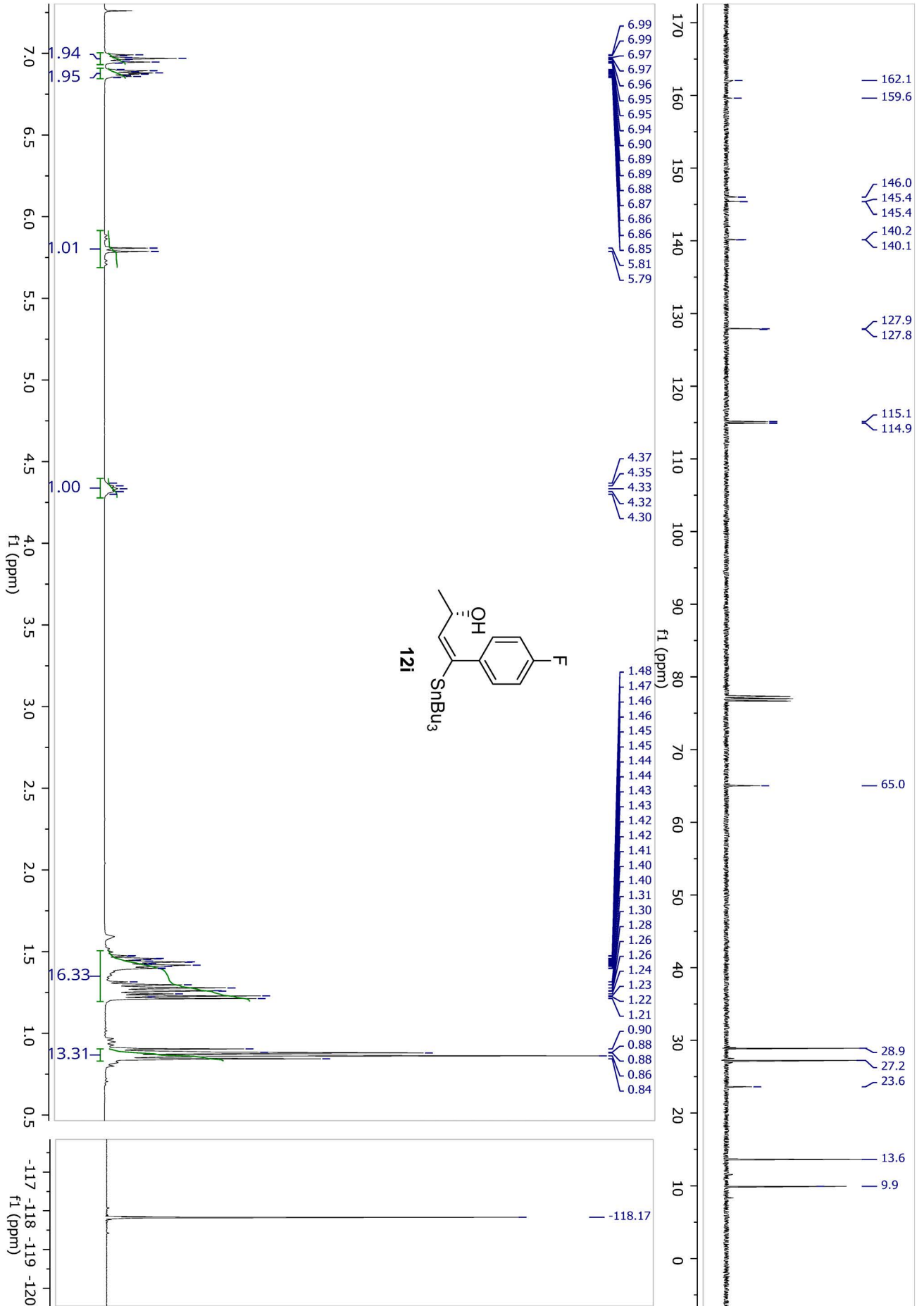


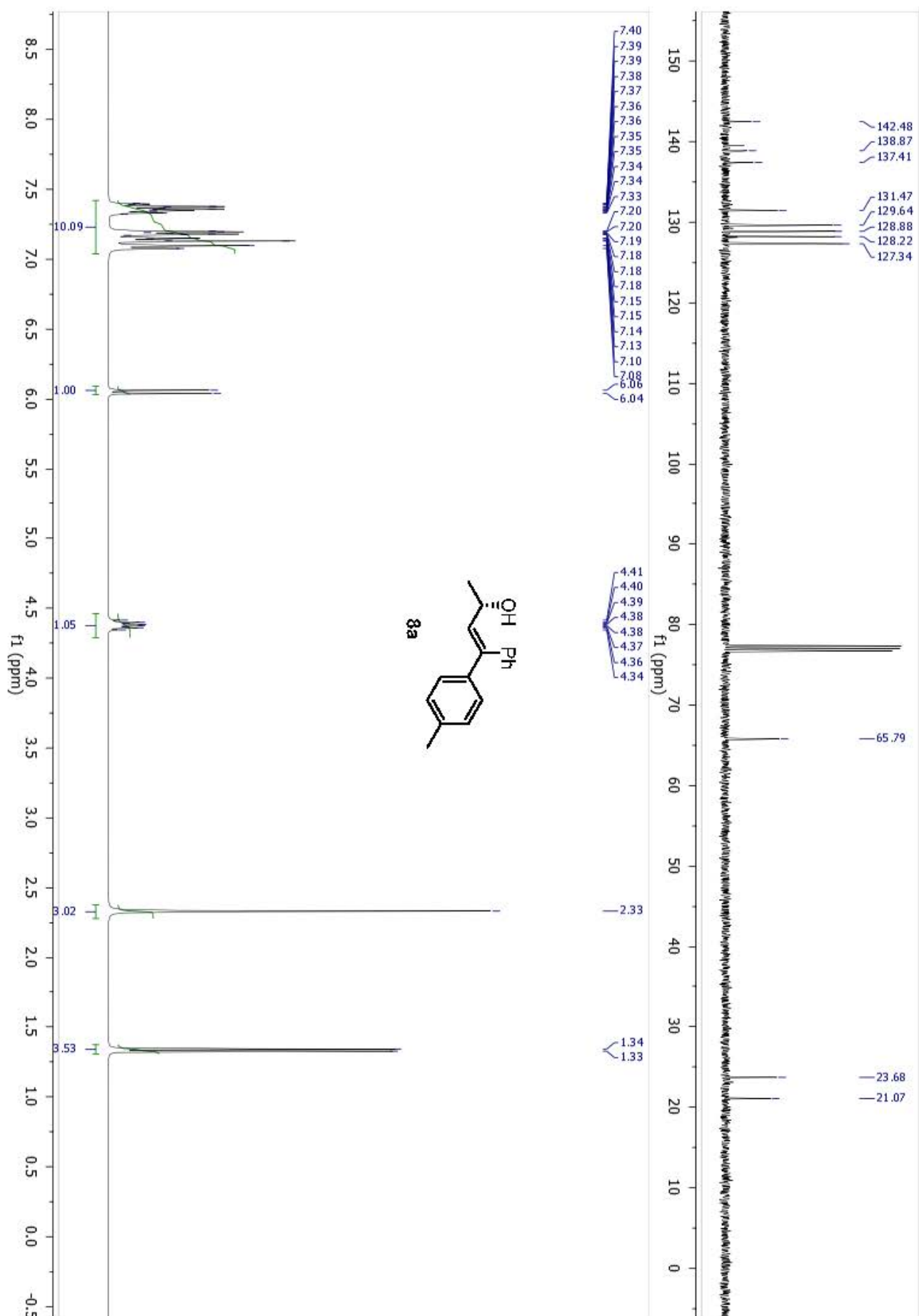


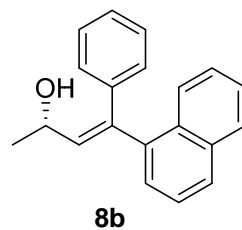
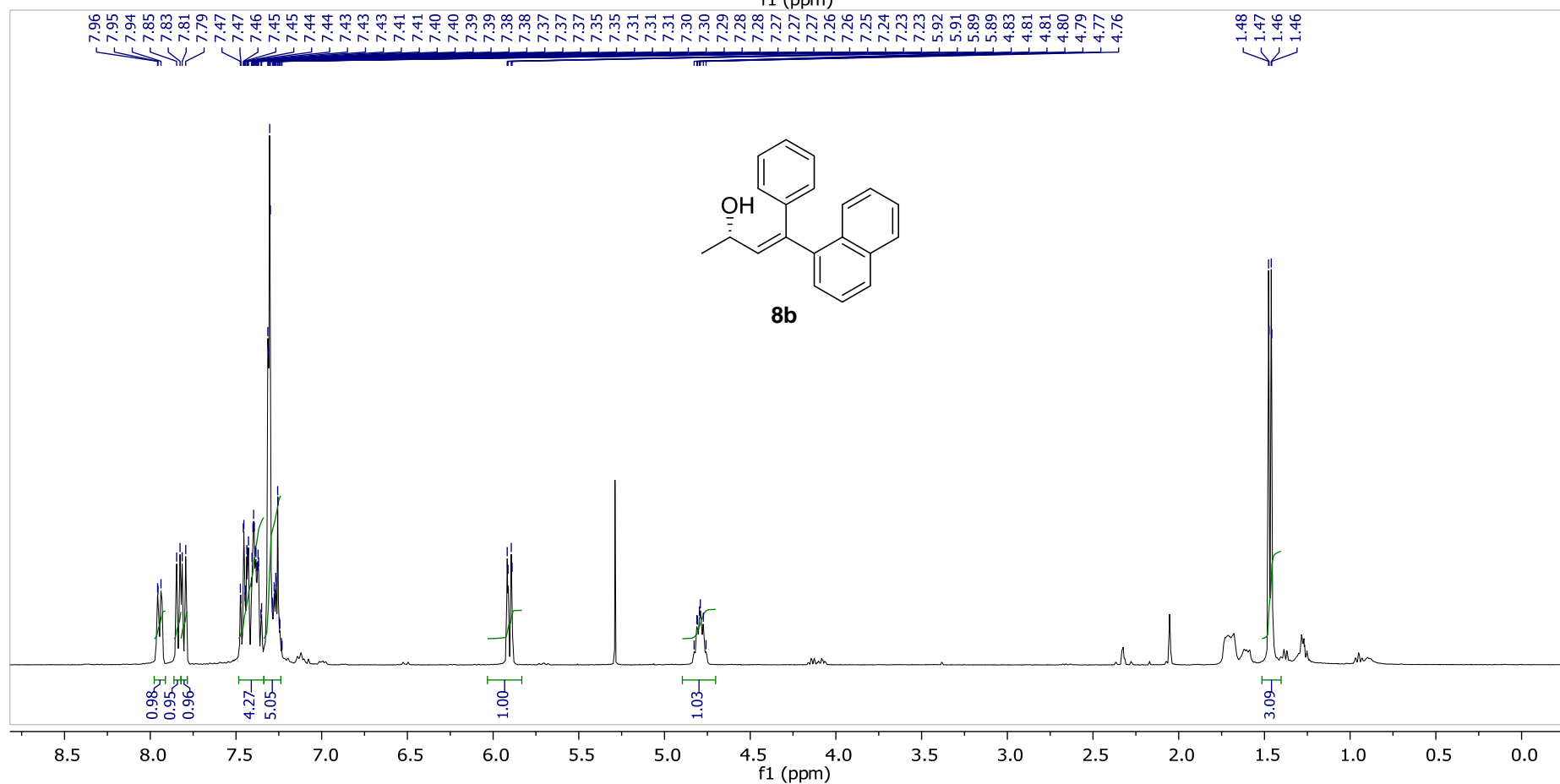
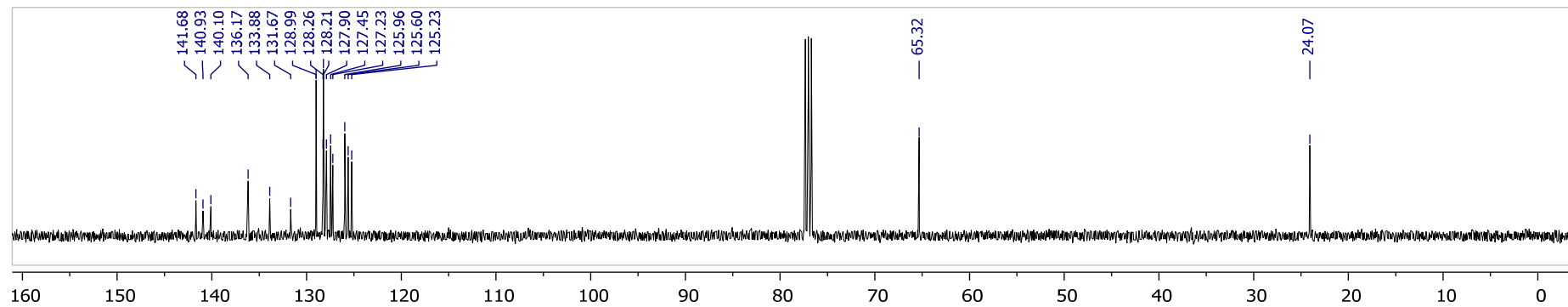


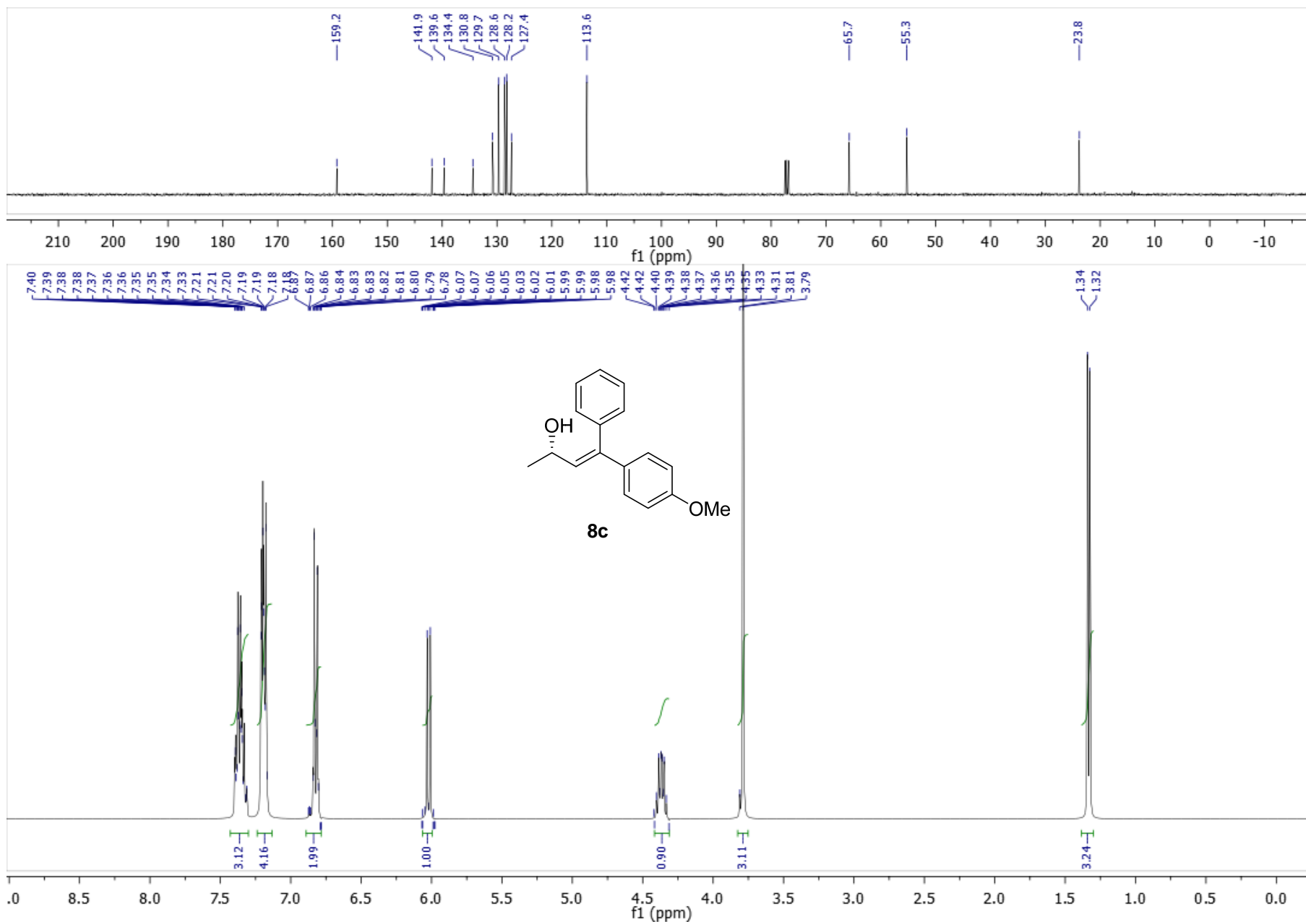


121

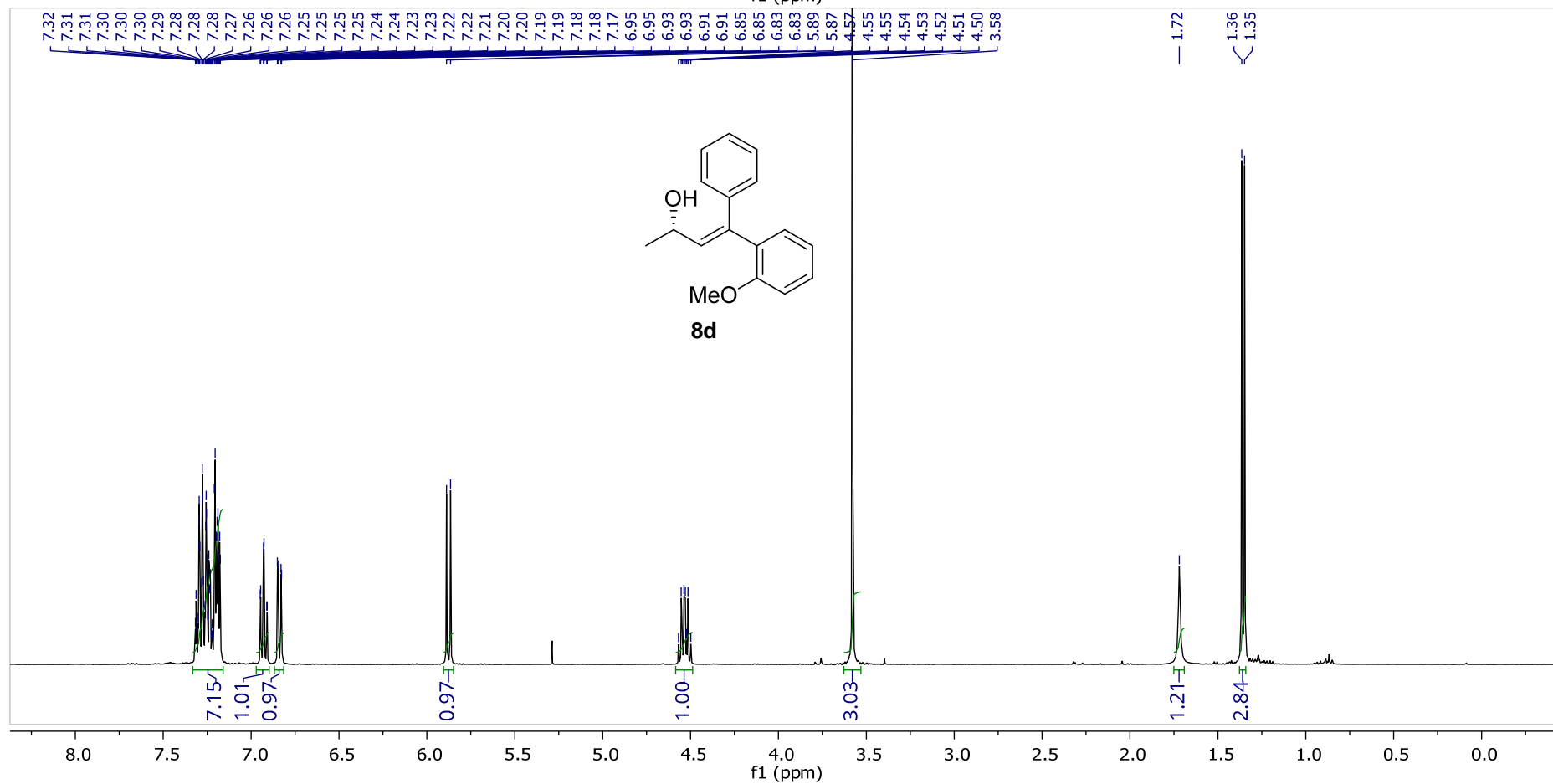
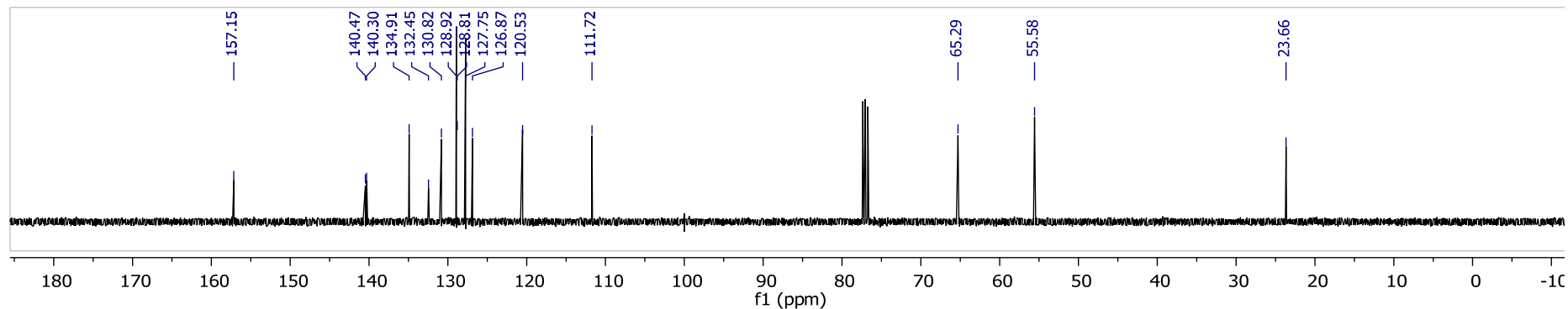


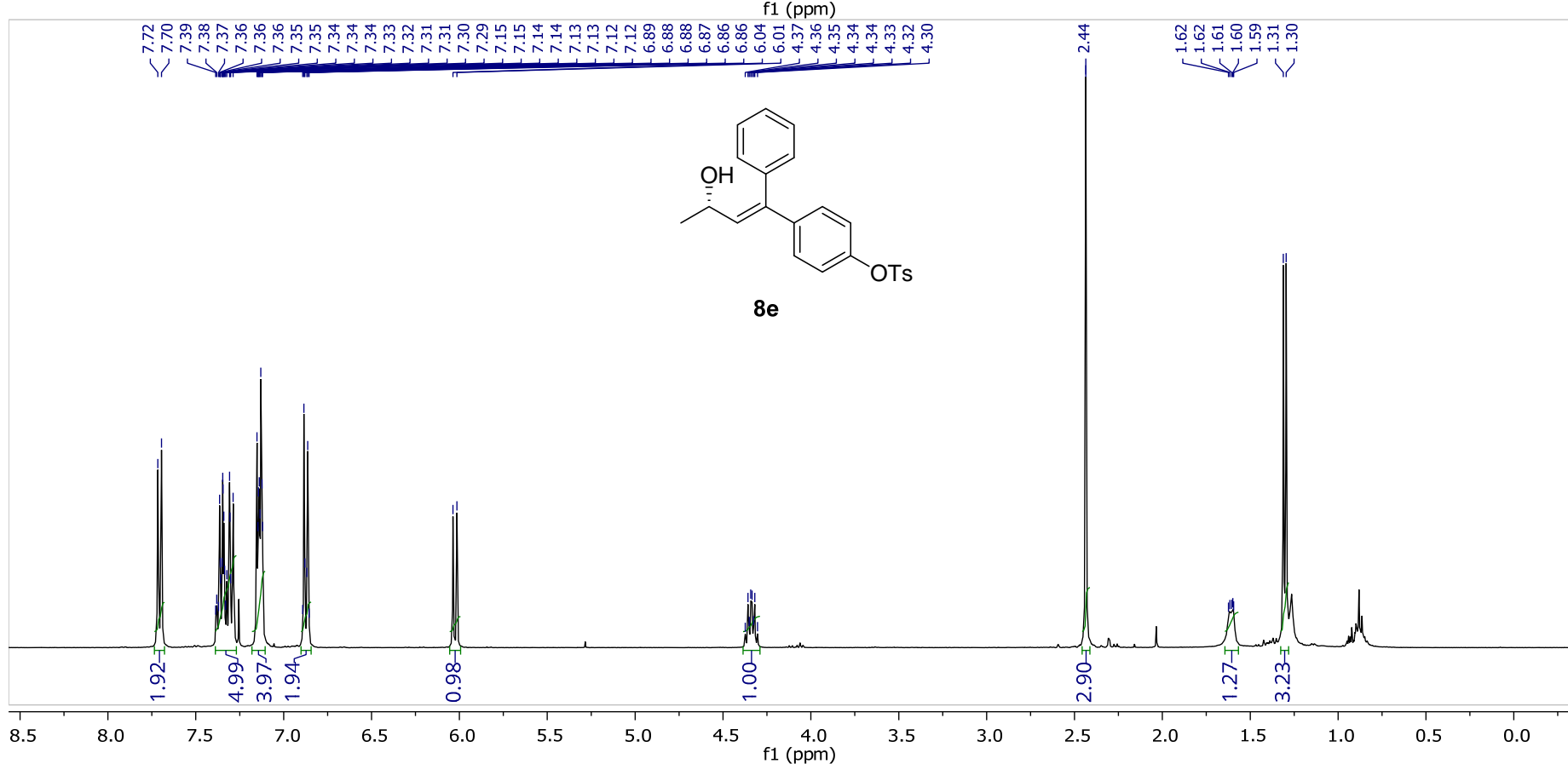
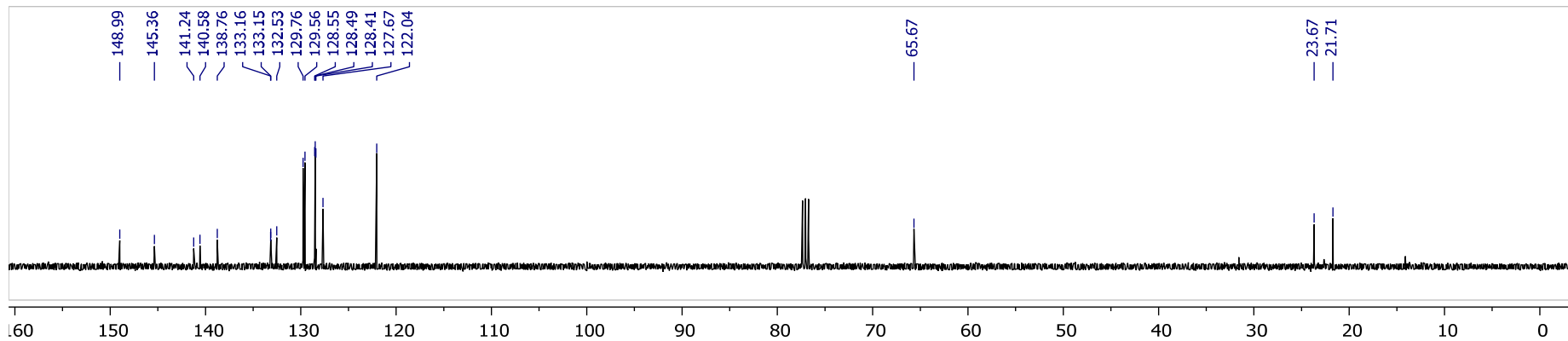


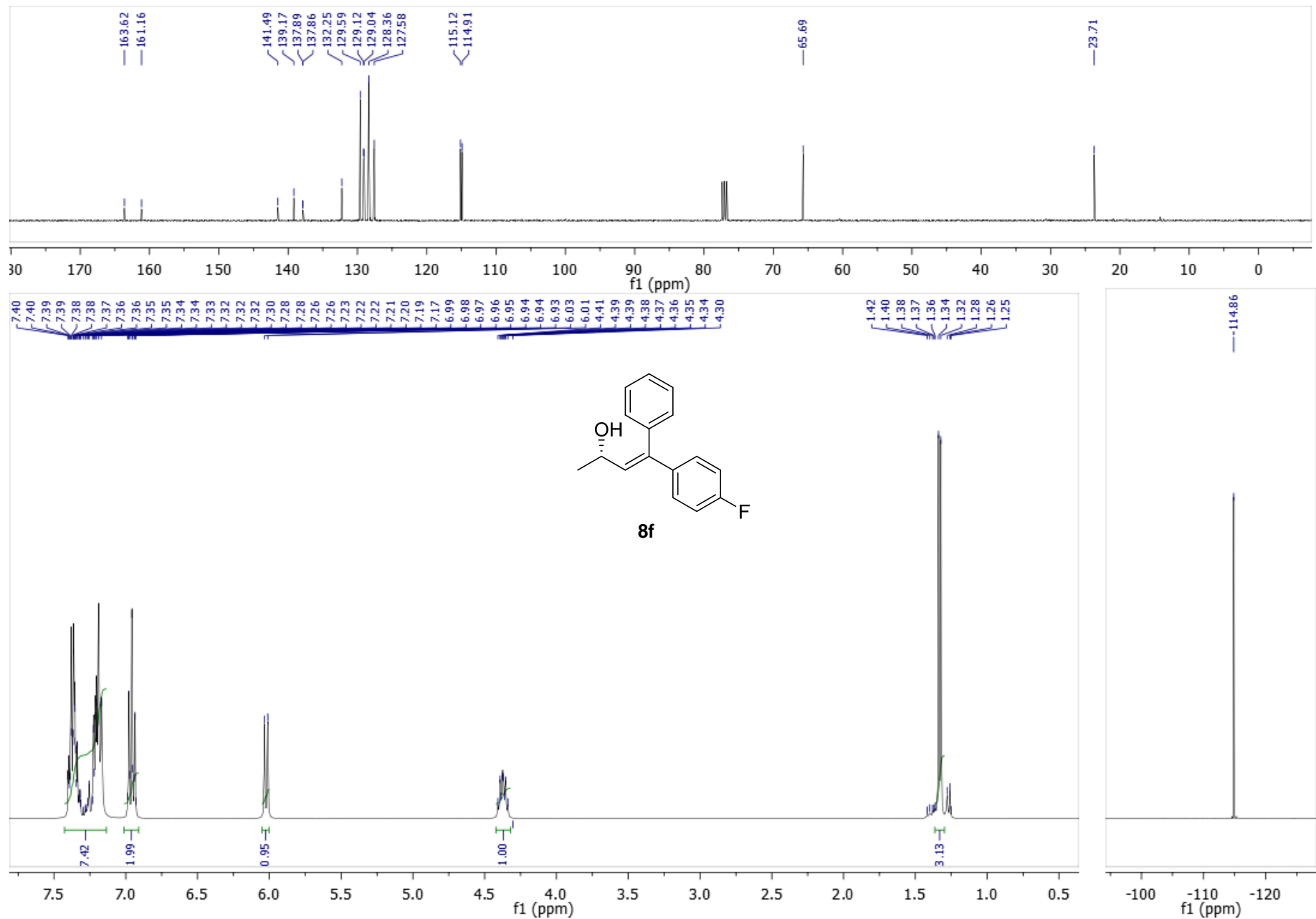


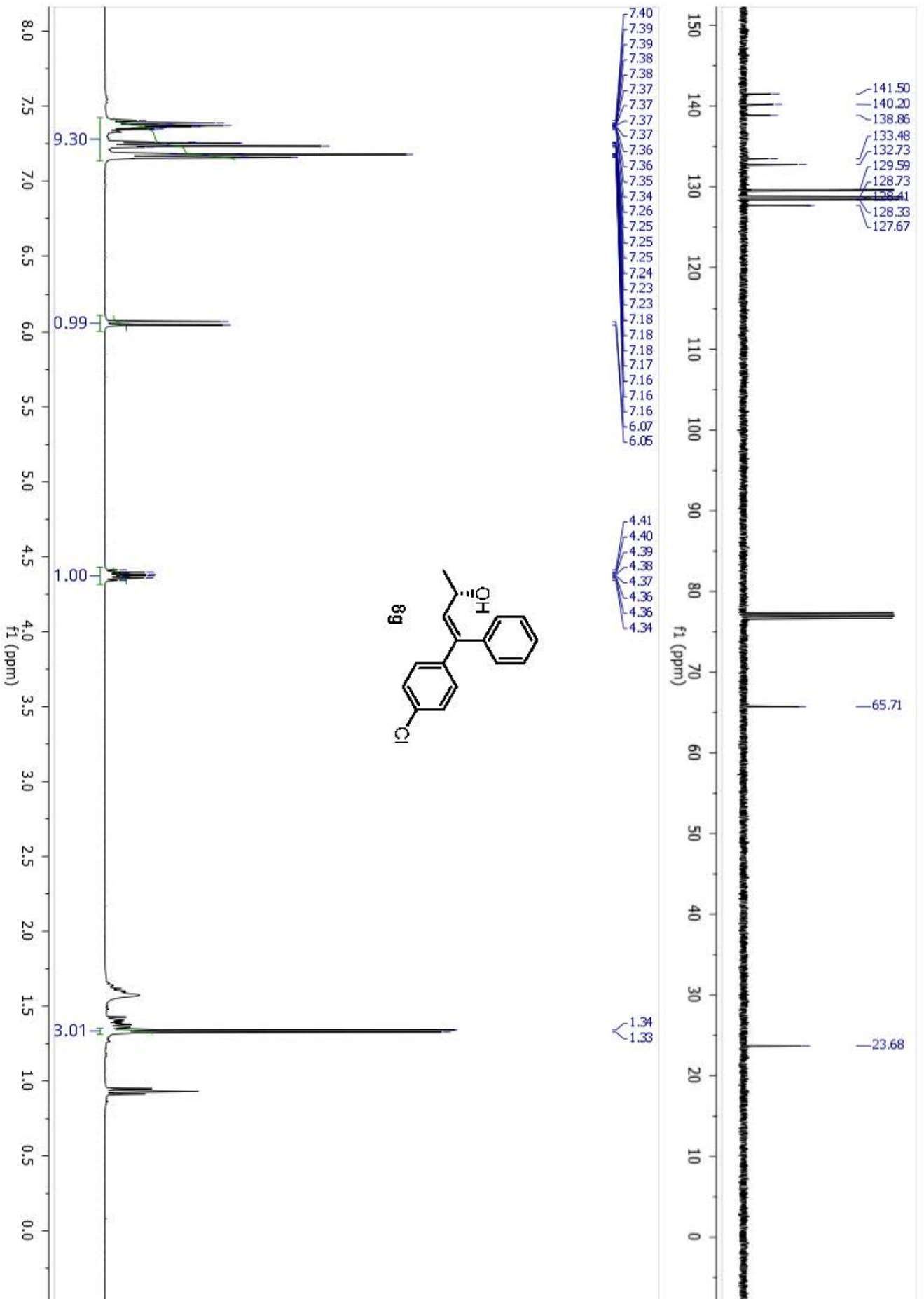


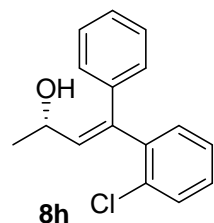
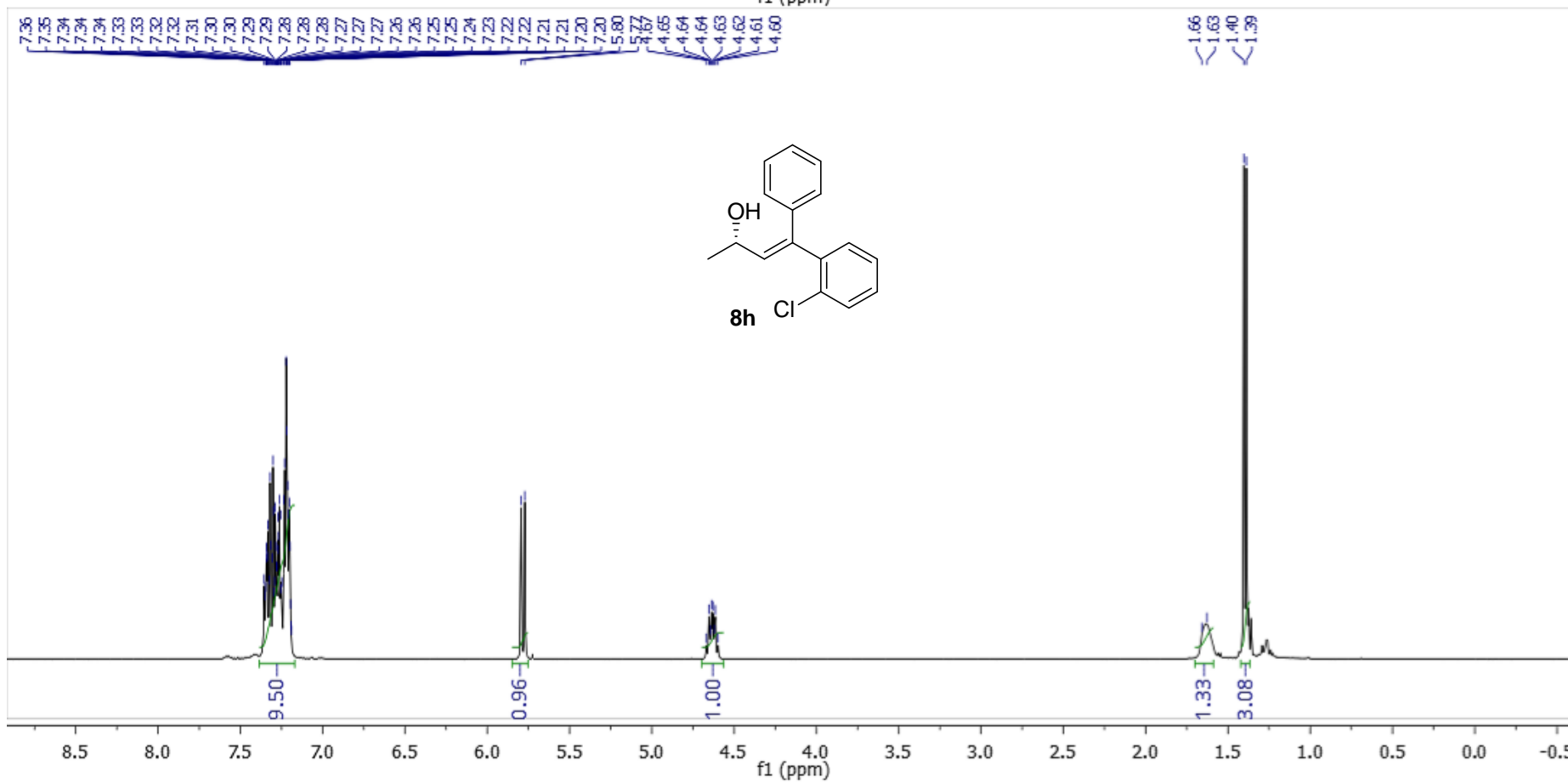
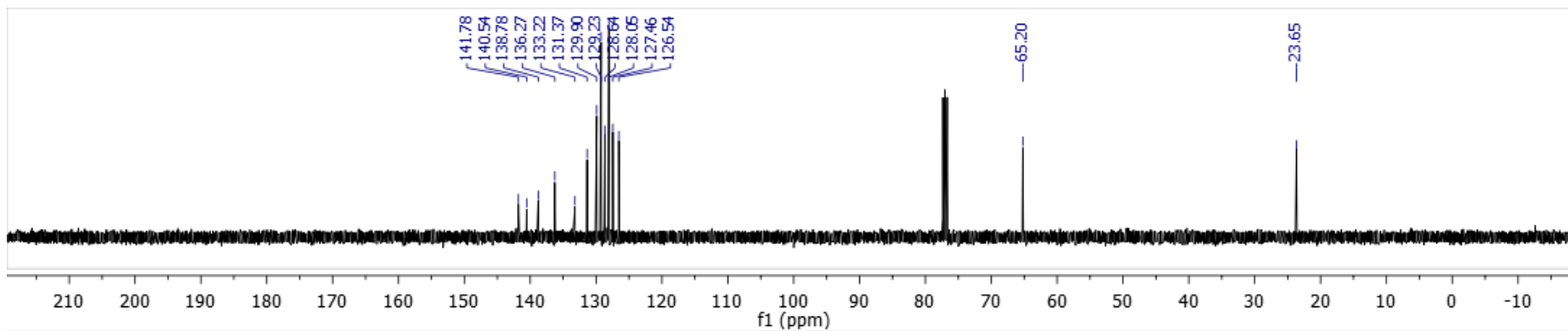


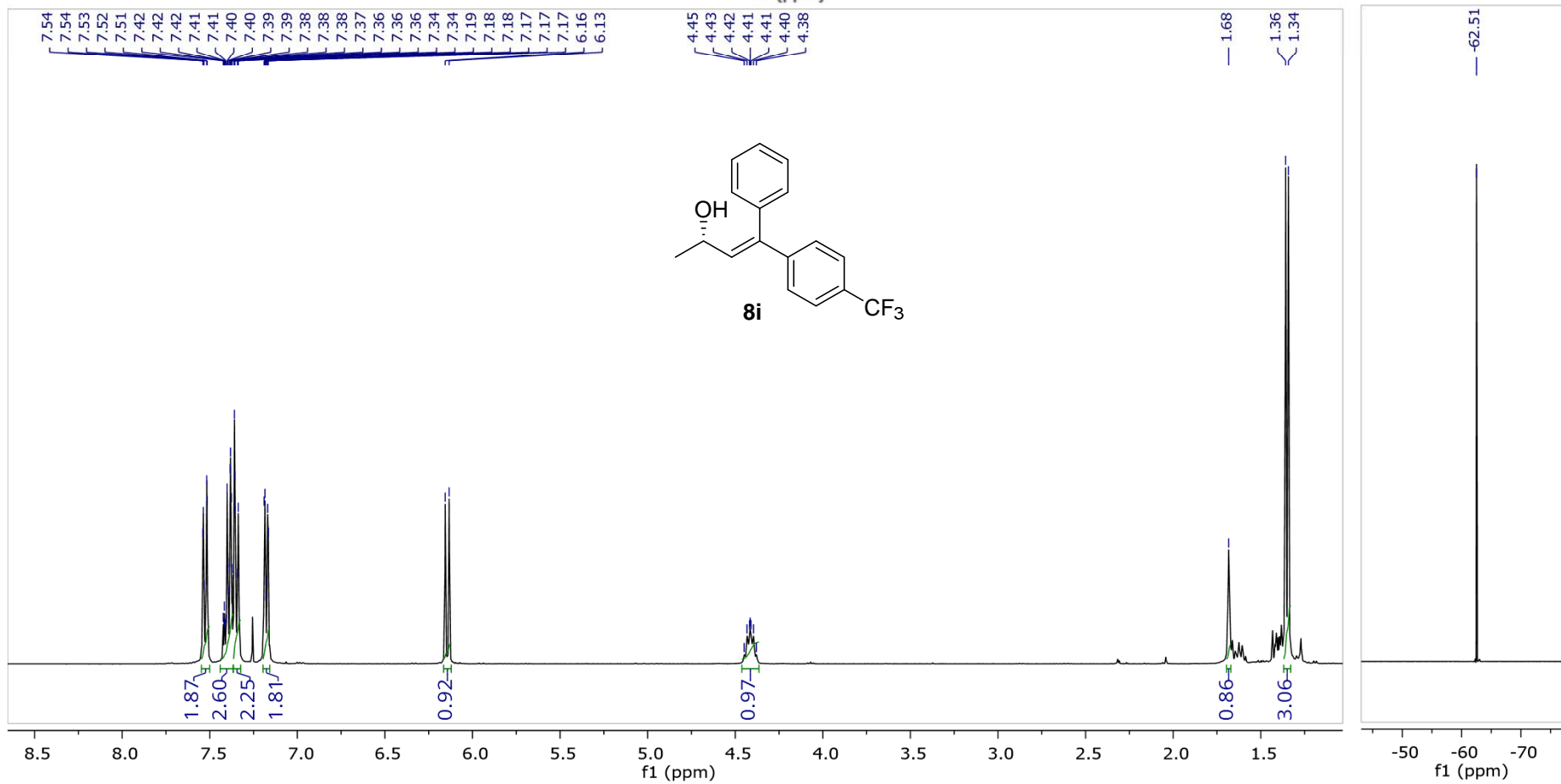
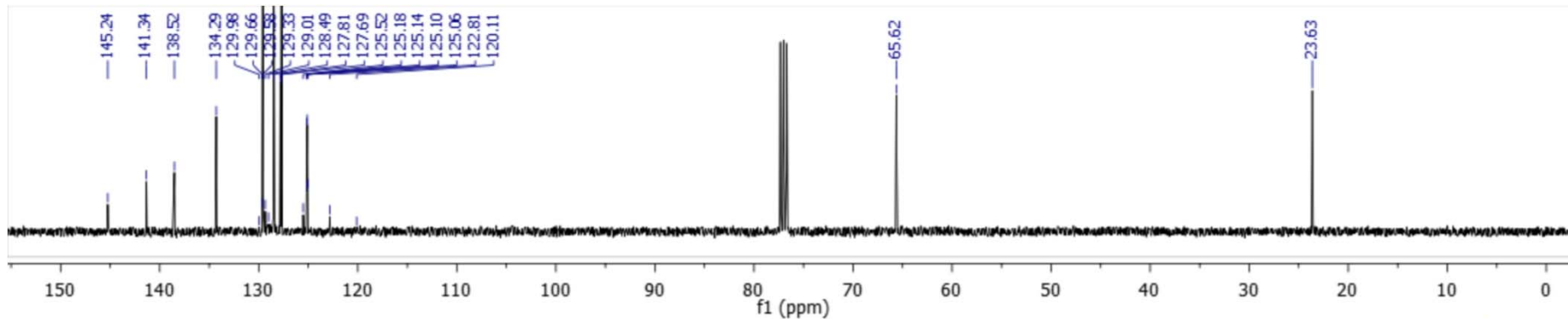


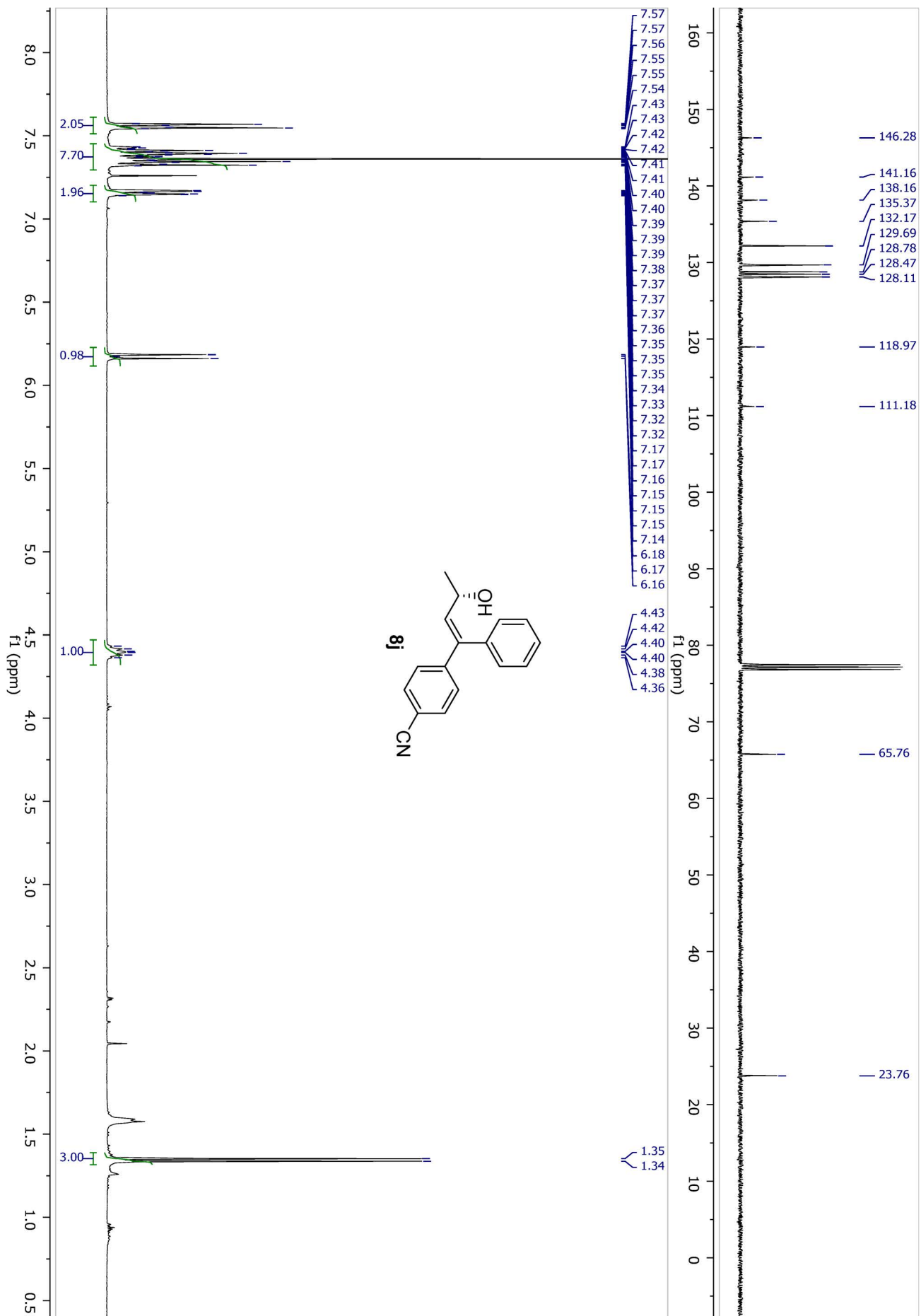


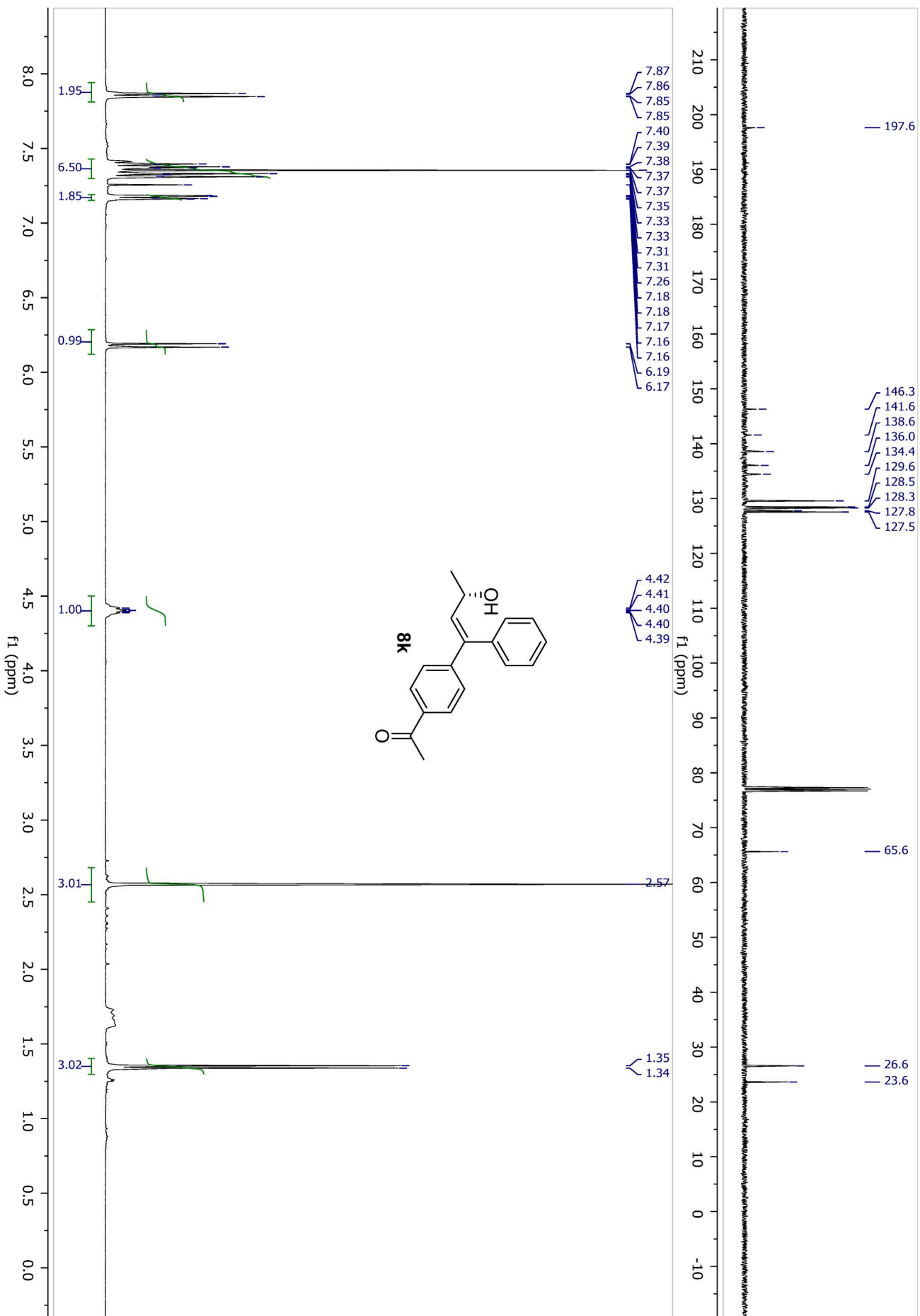




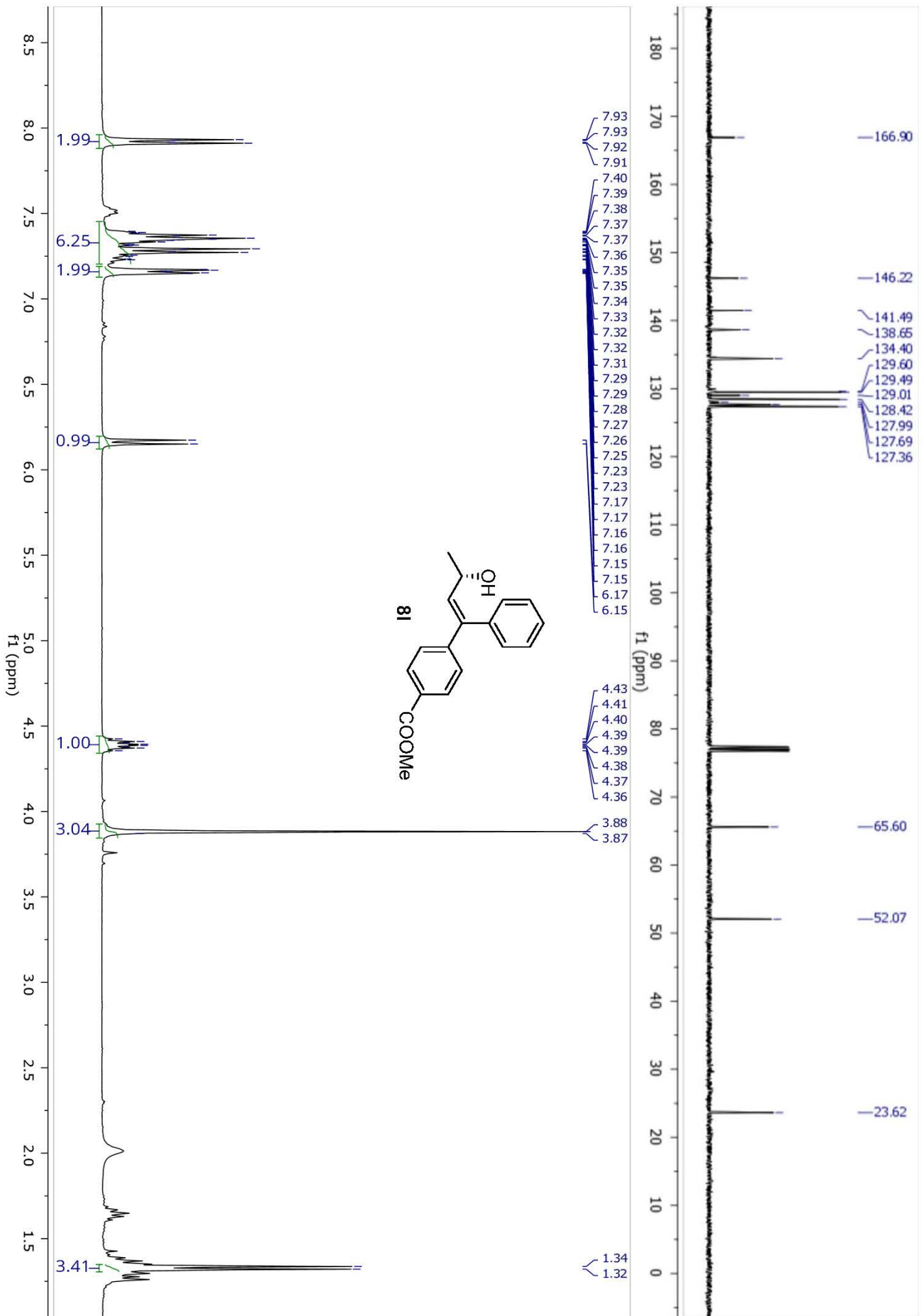


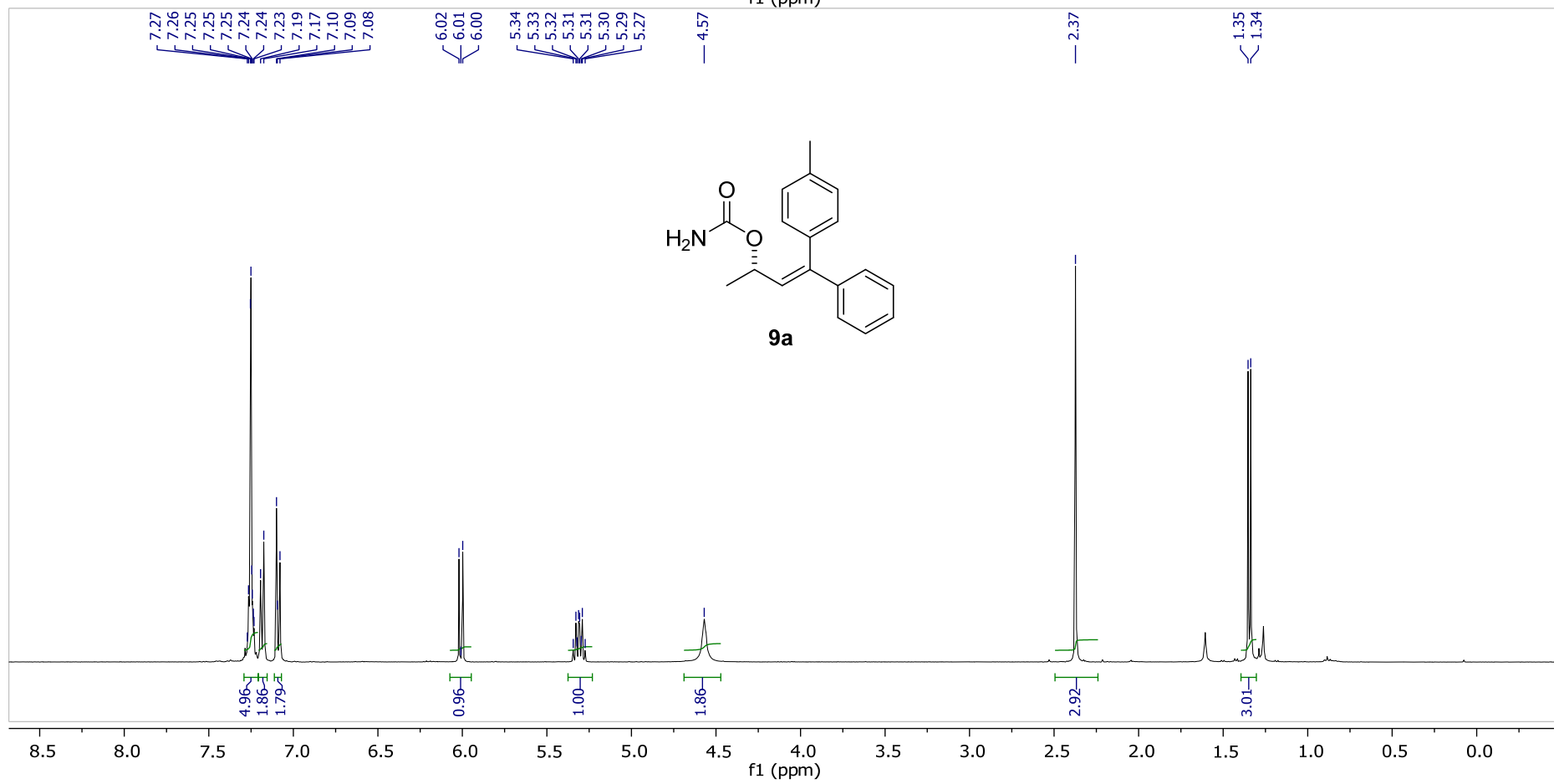
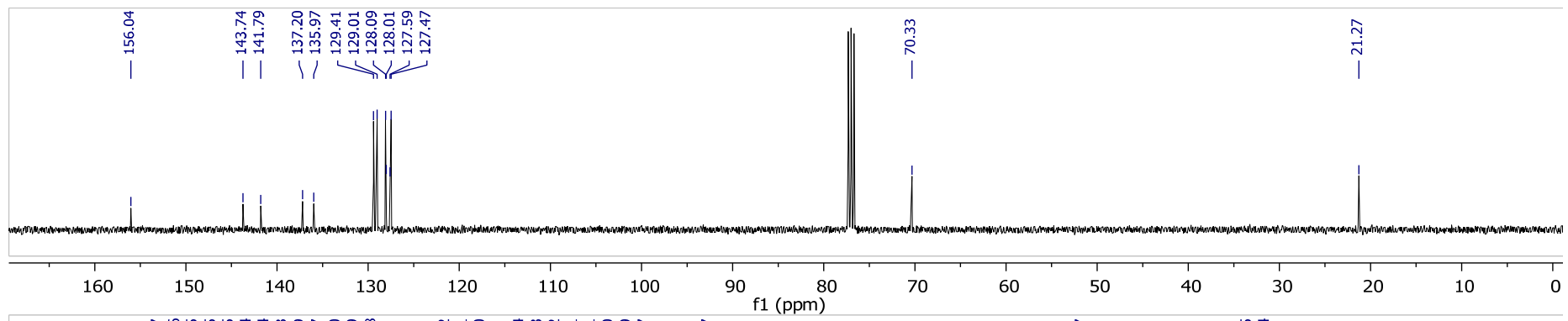


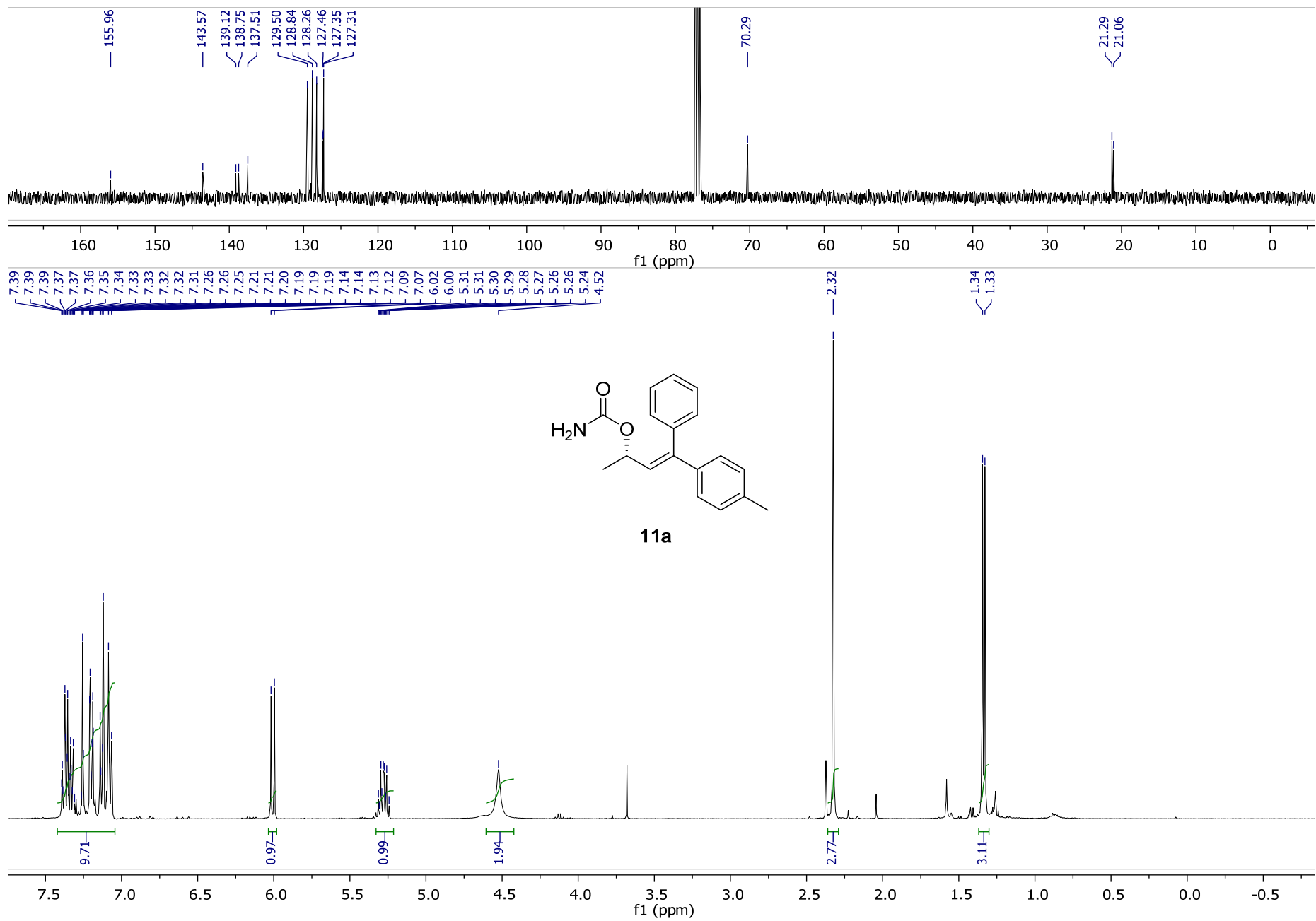


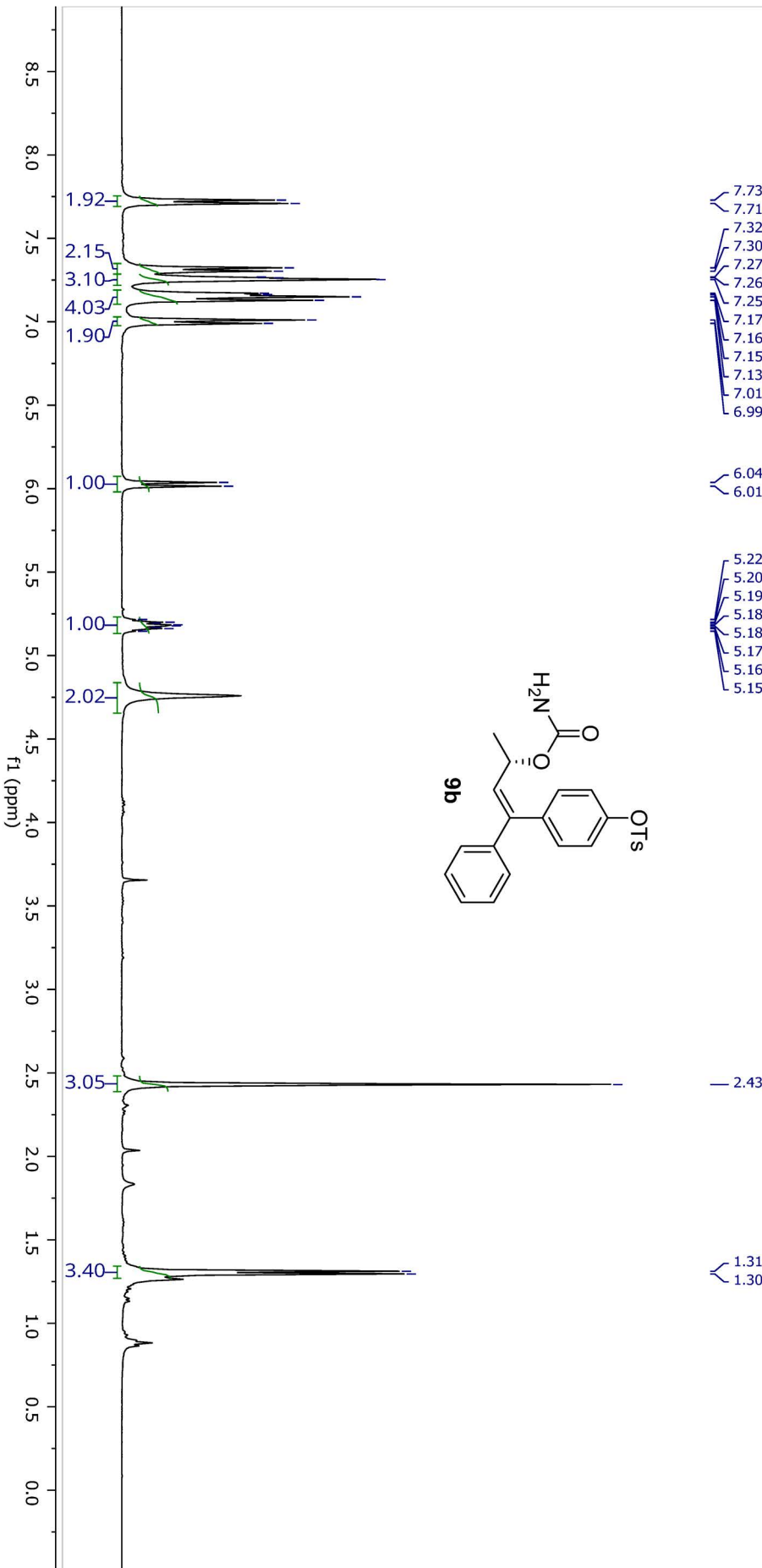
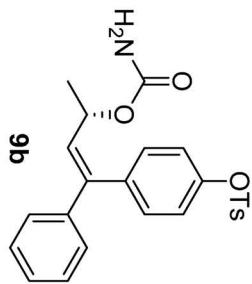
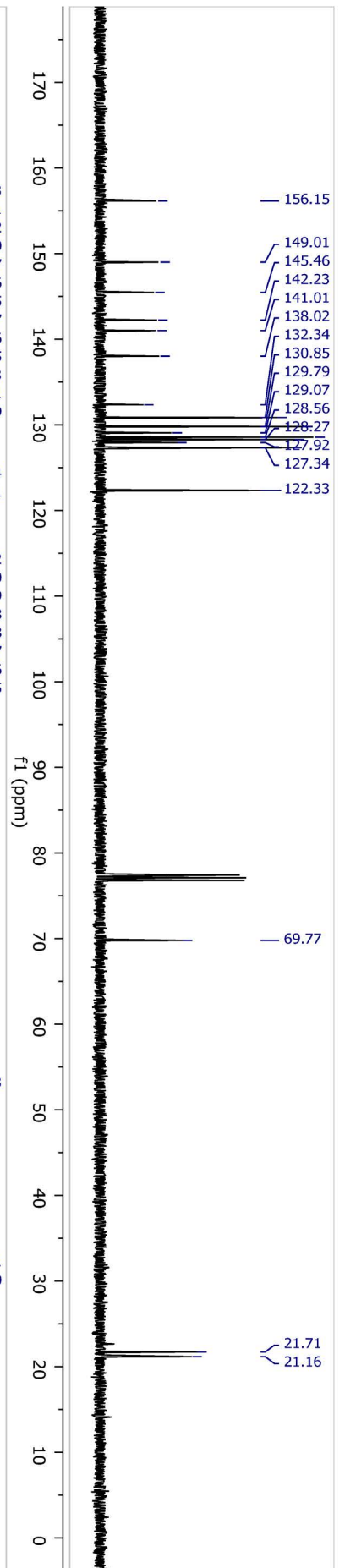


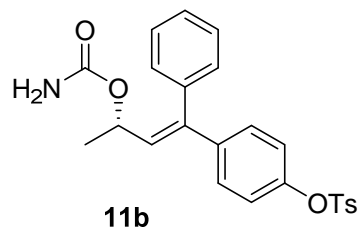
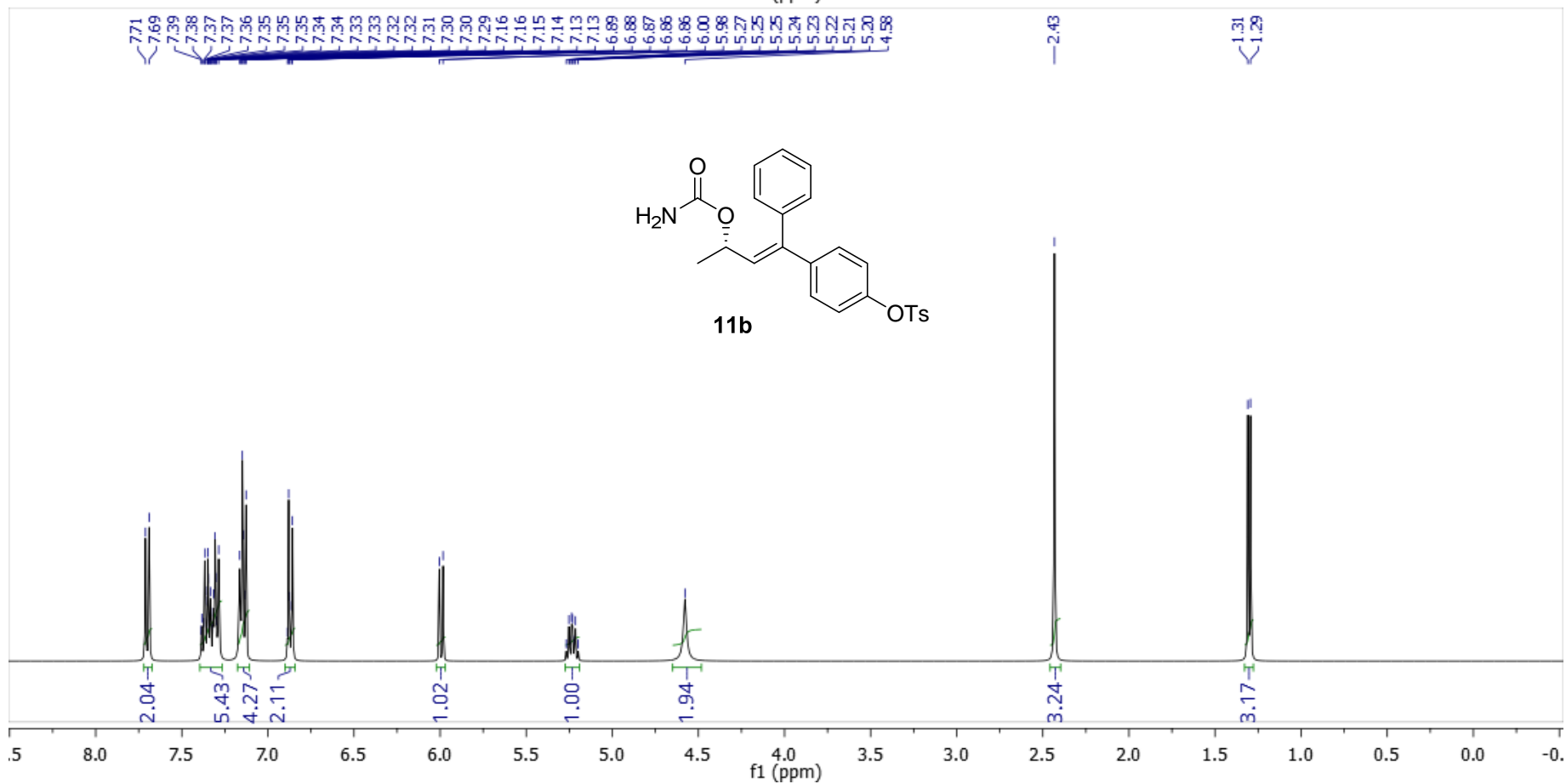
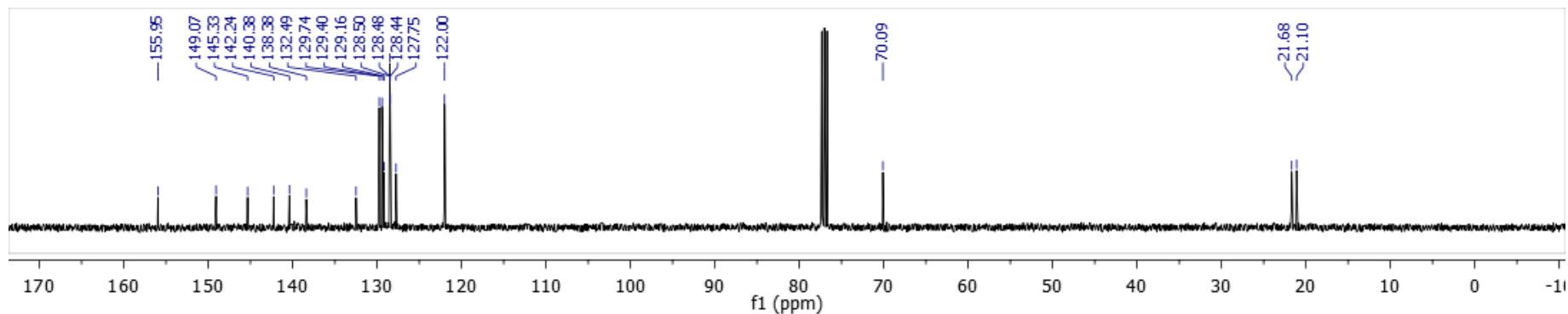


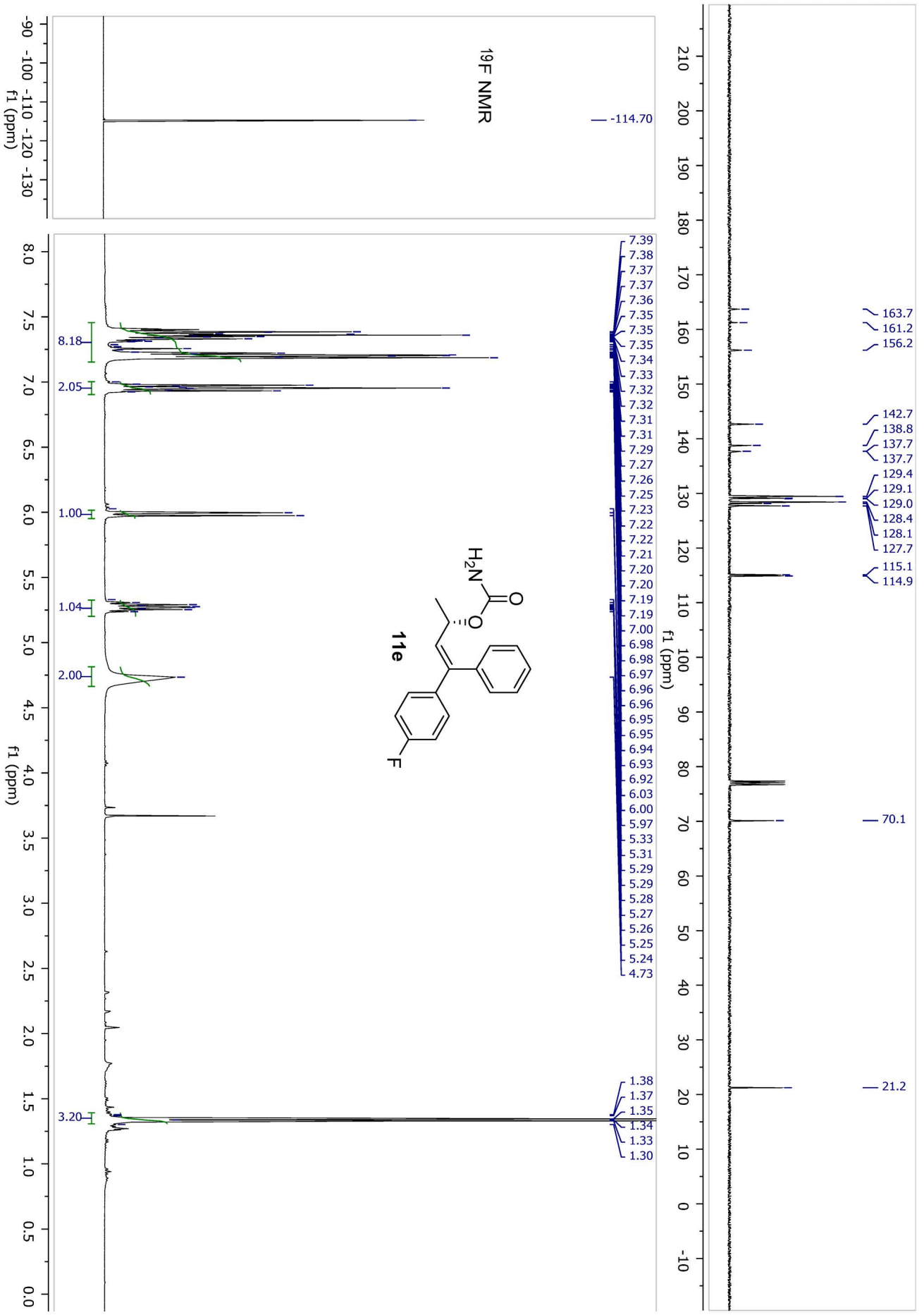


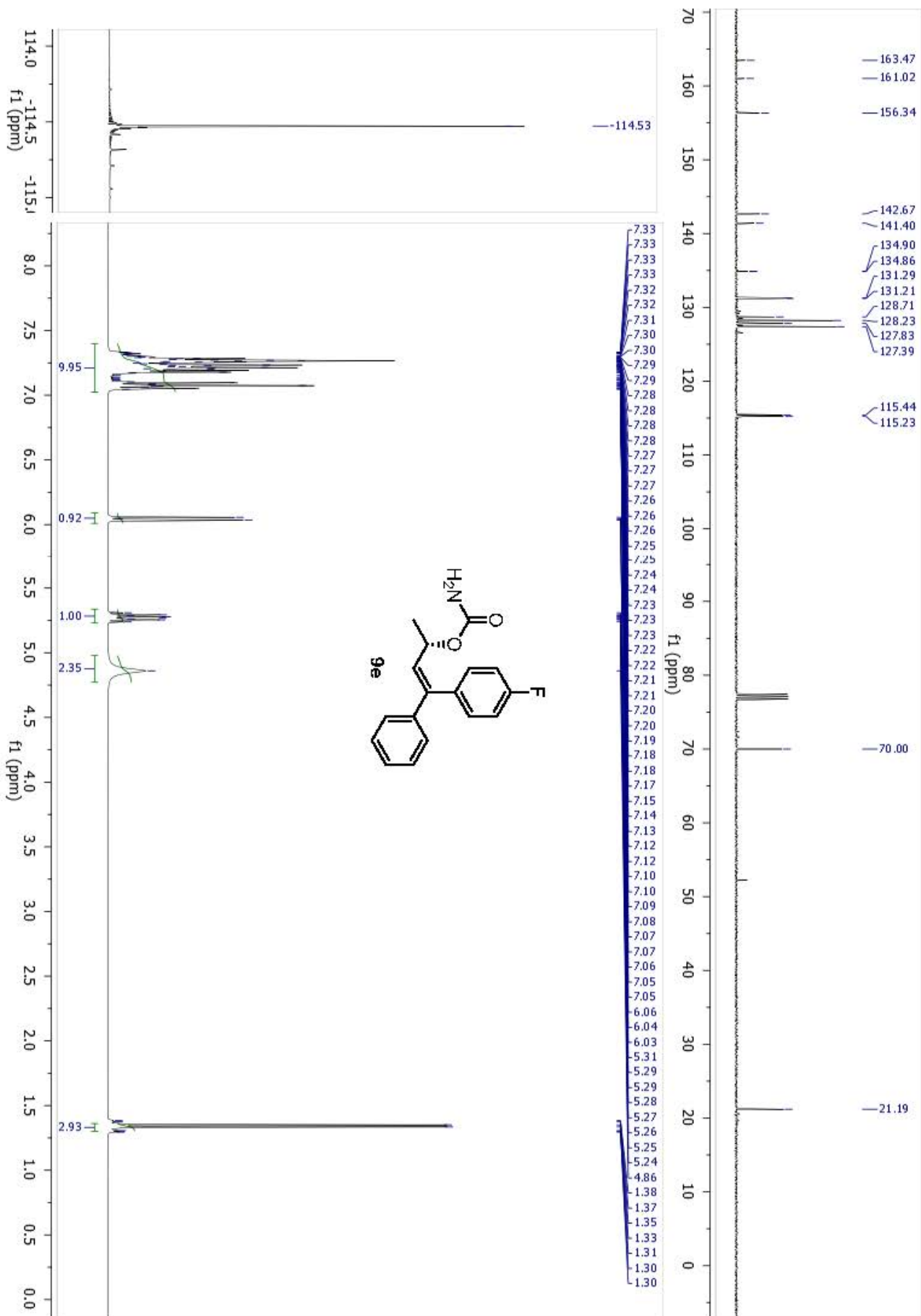


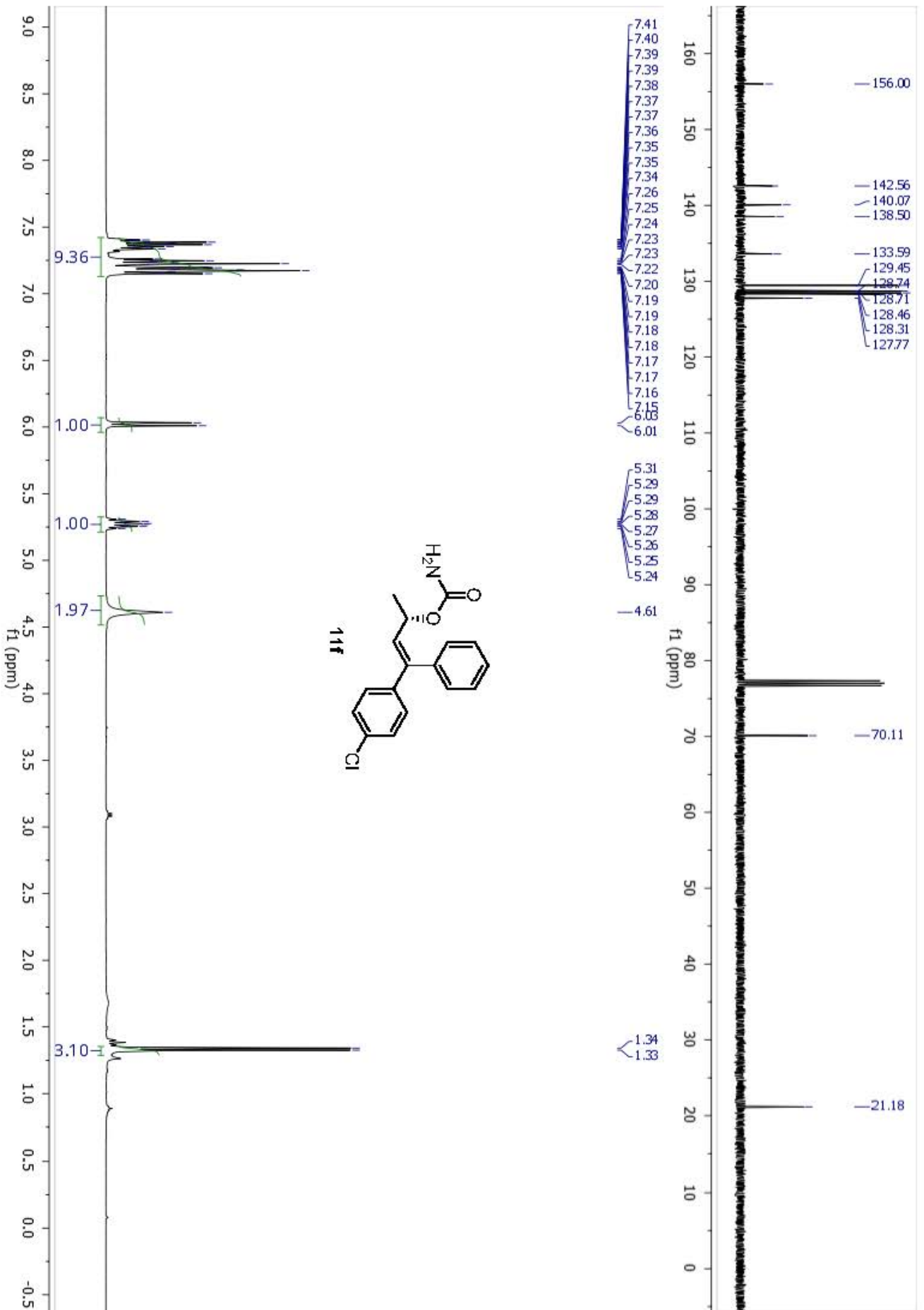




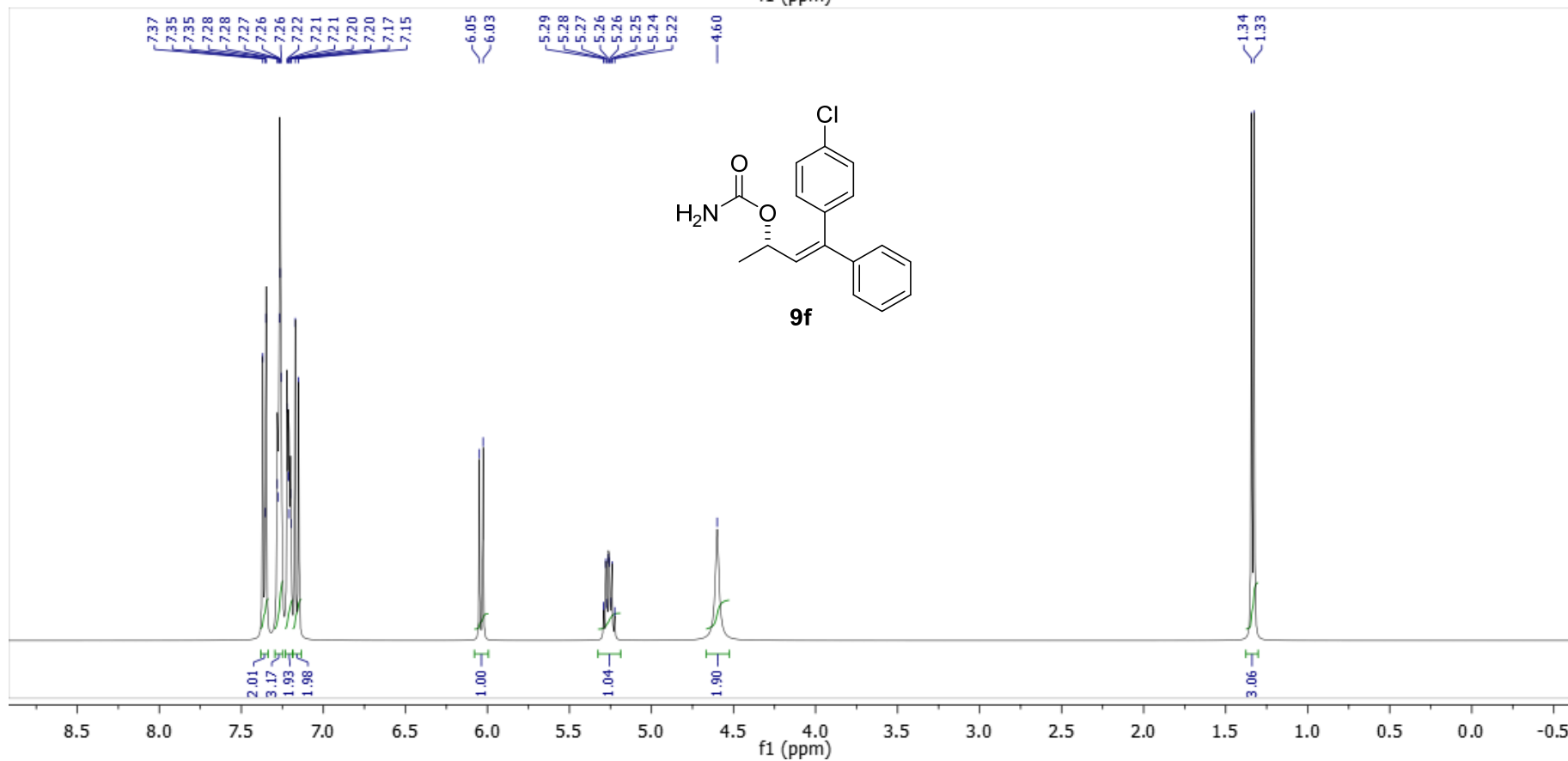
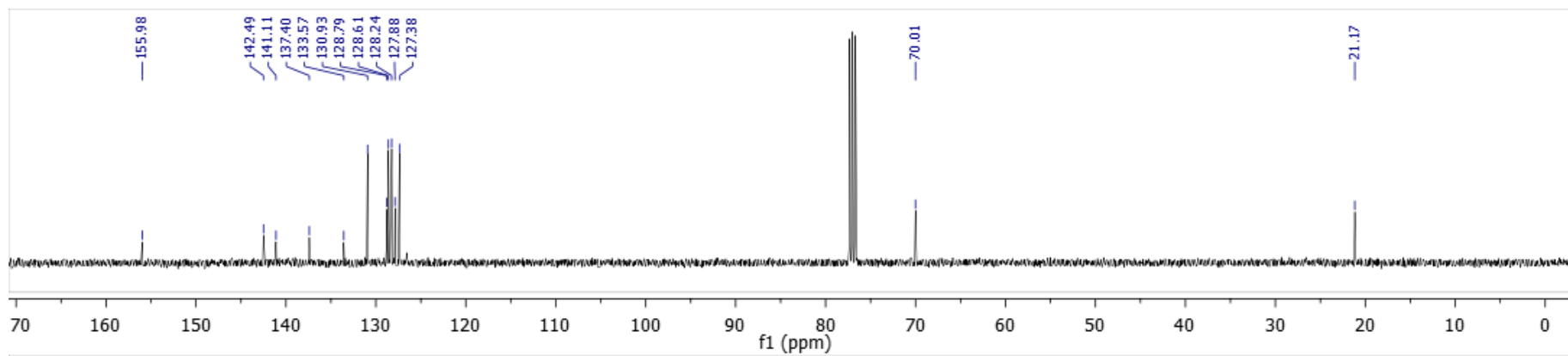


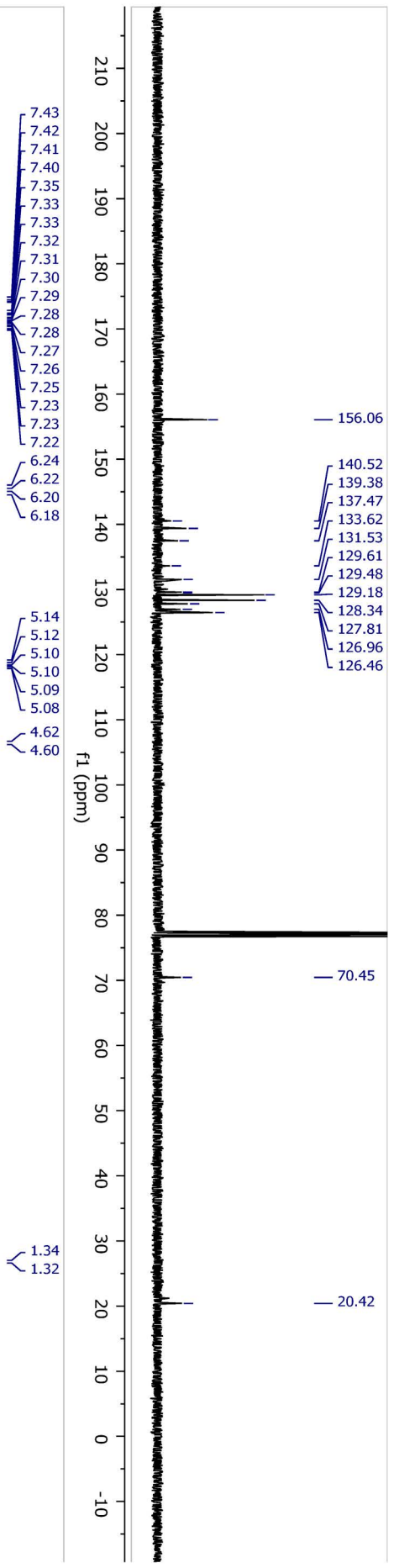
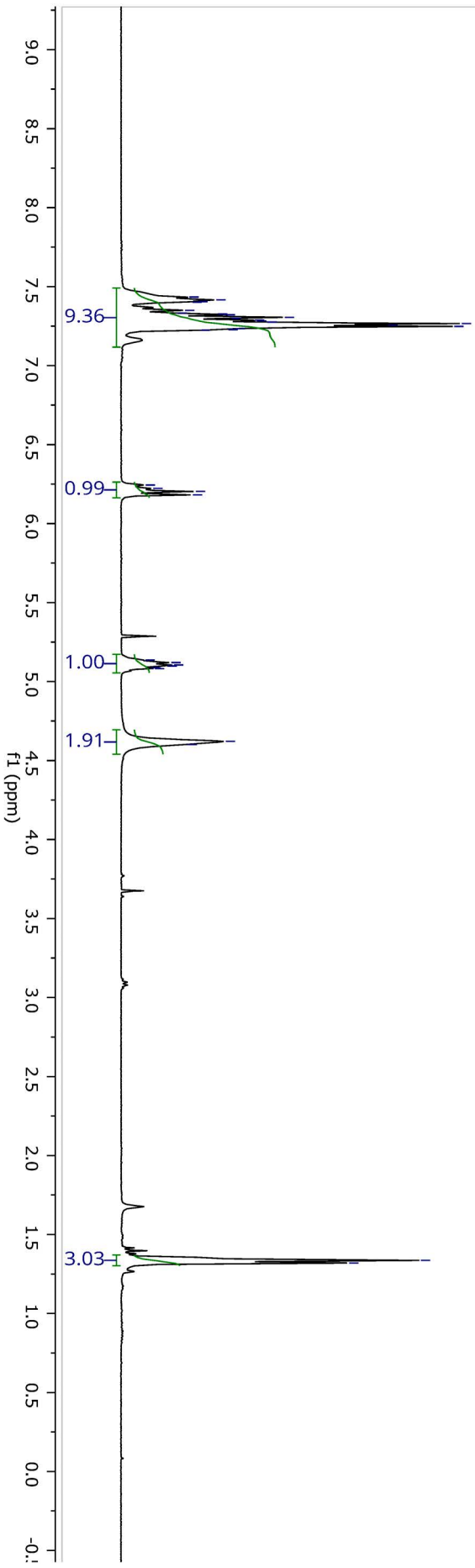
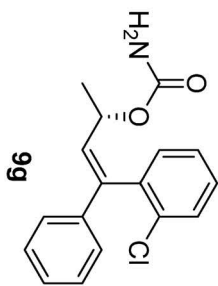


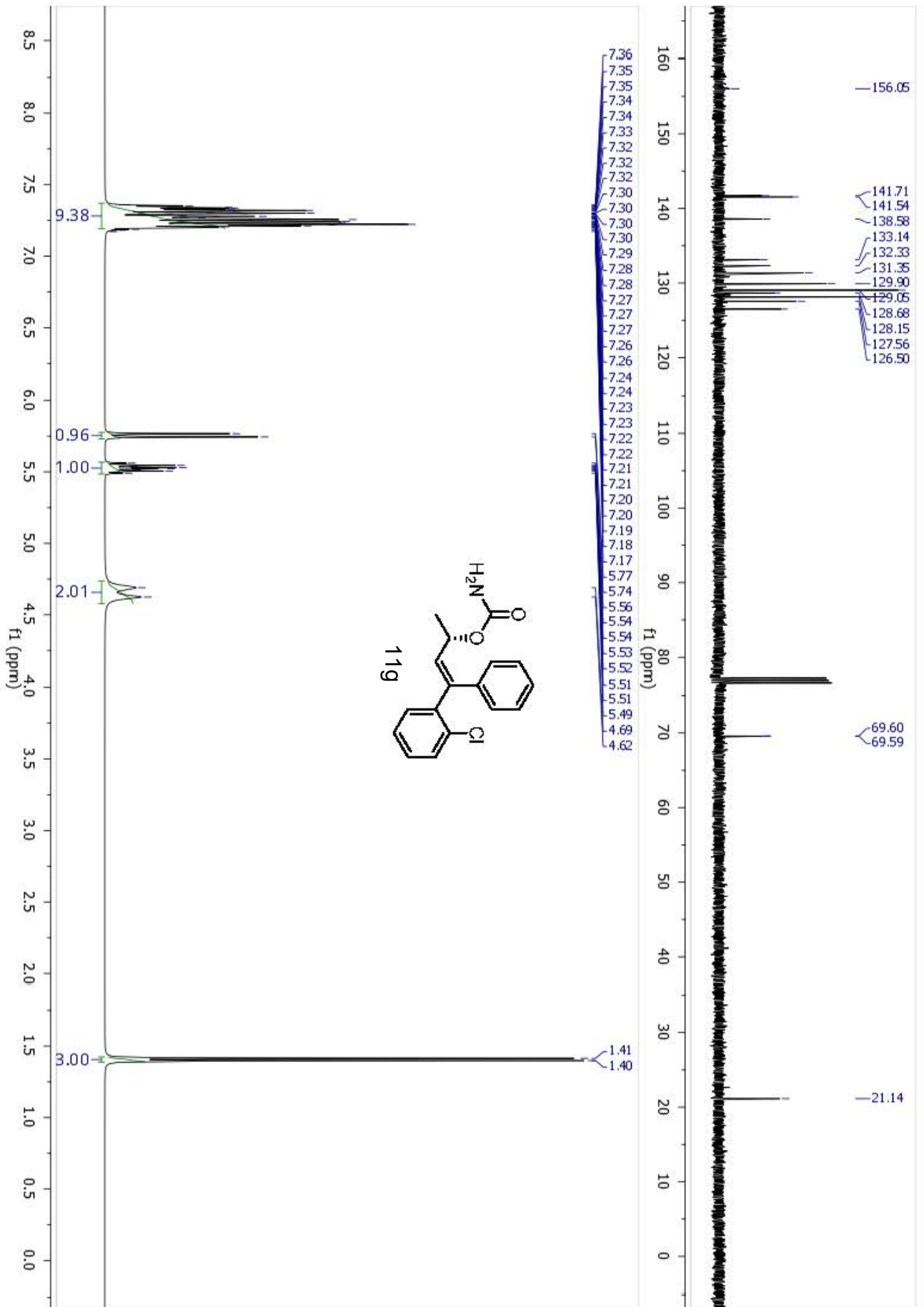


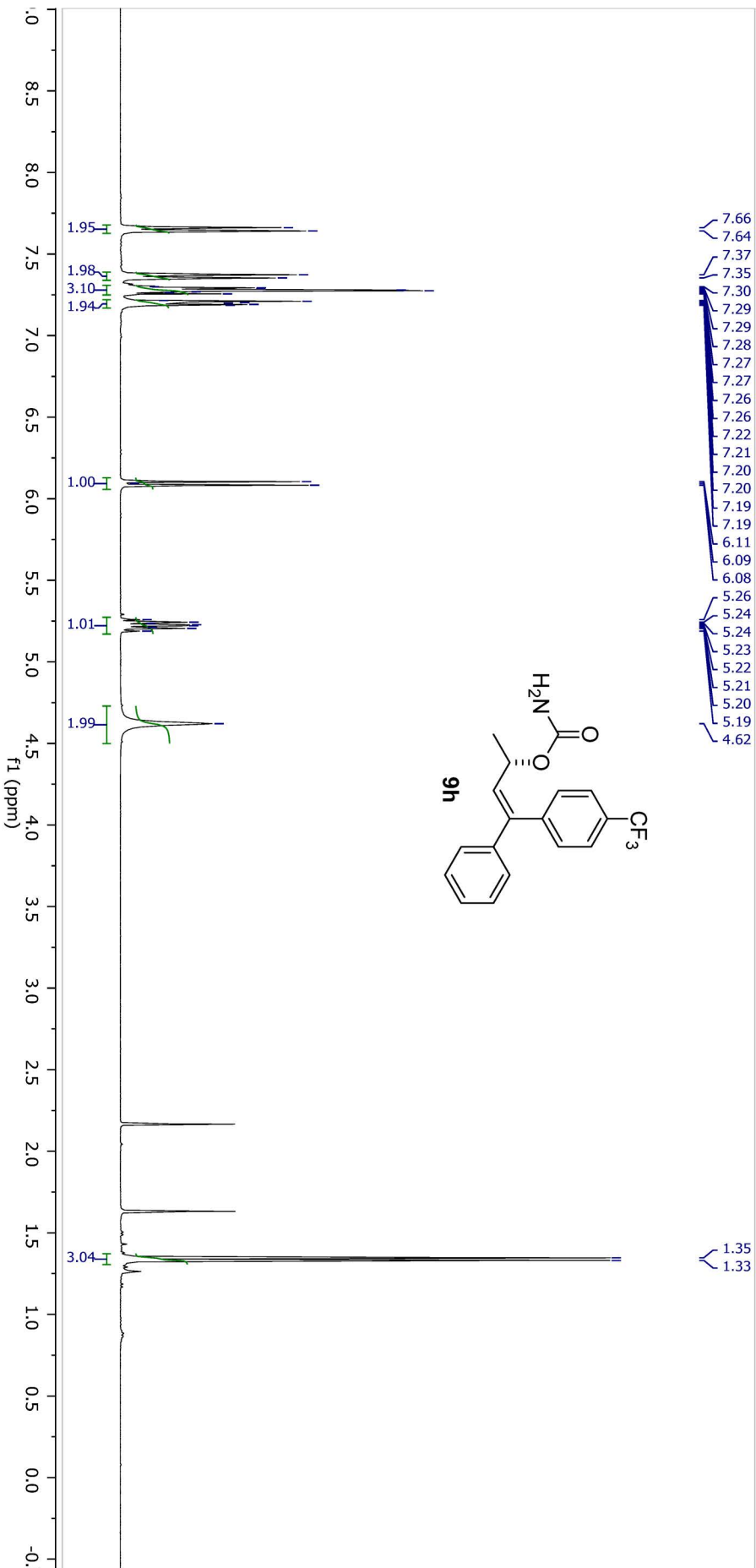
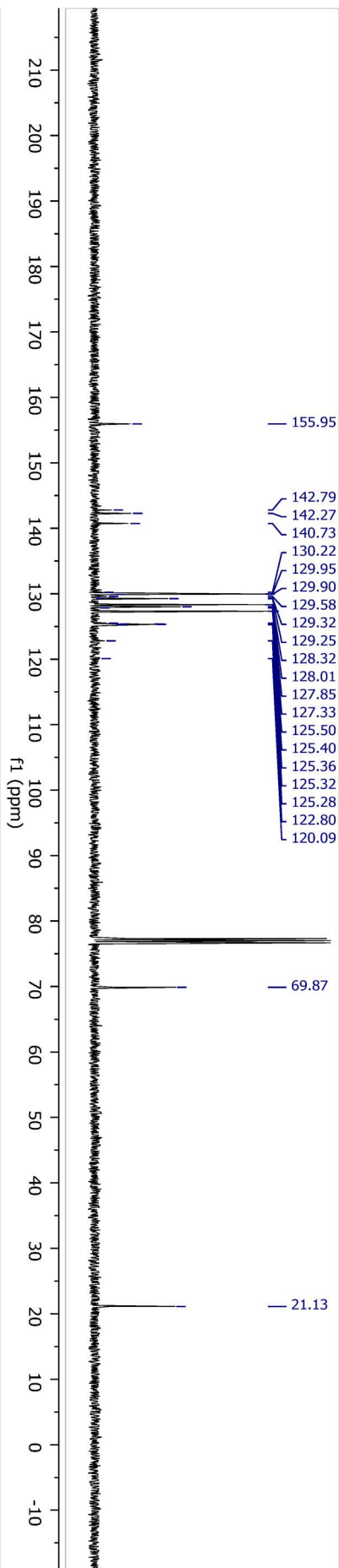
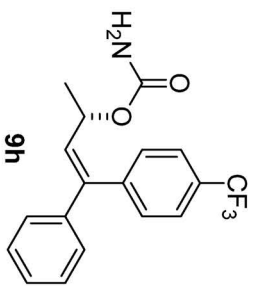


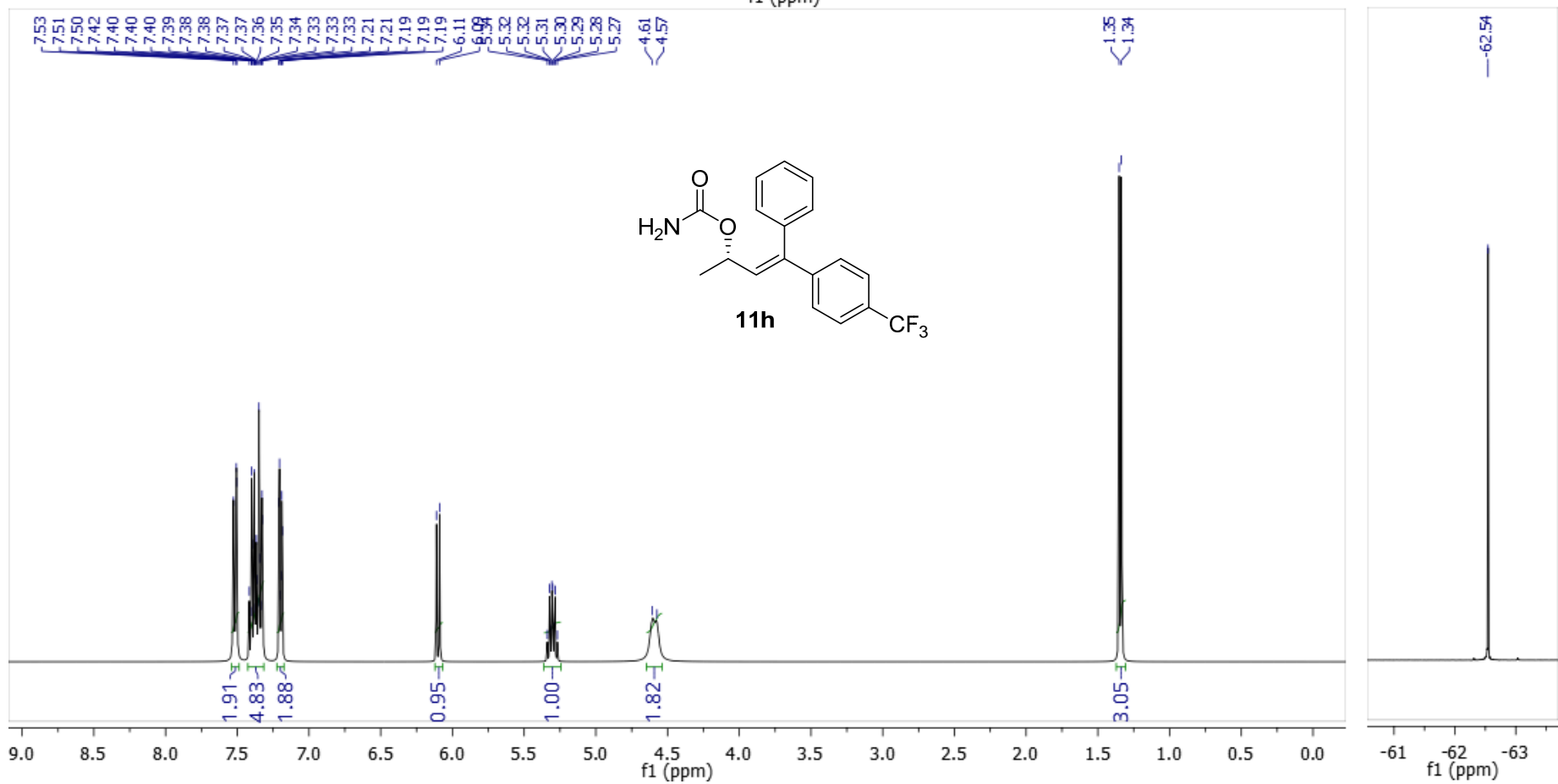
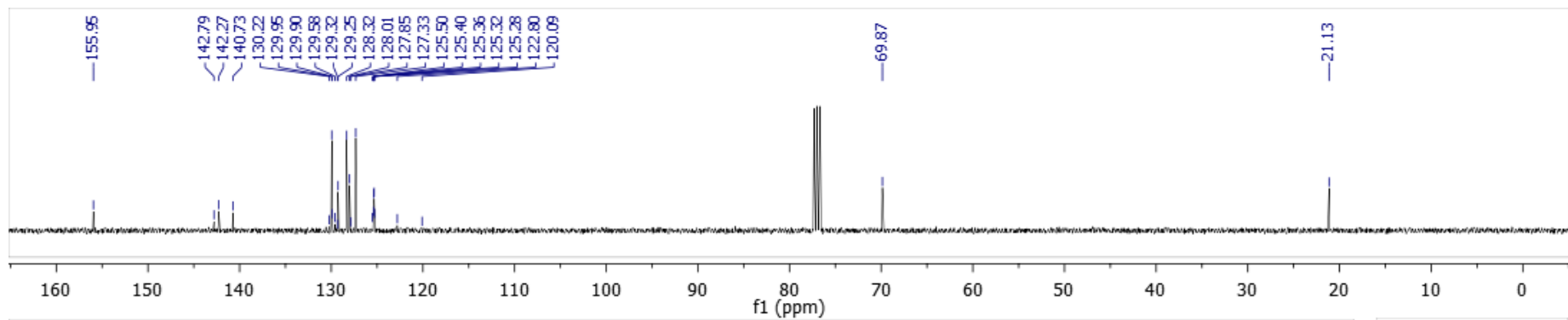


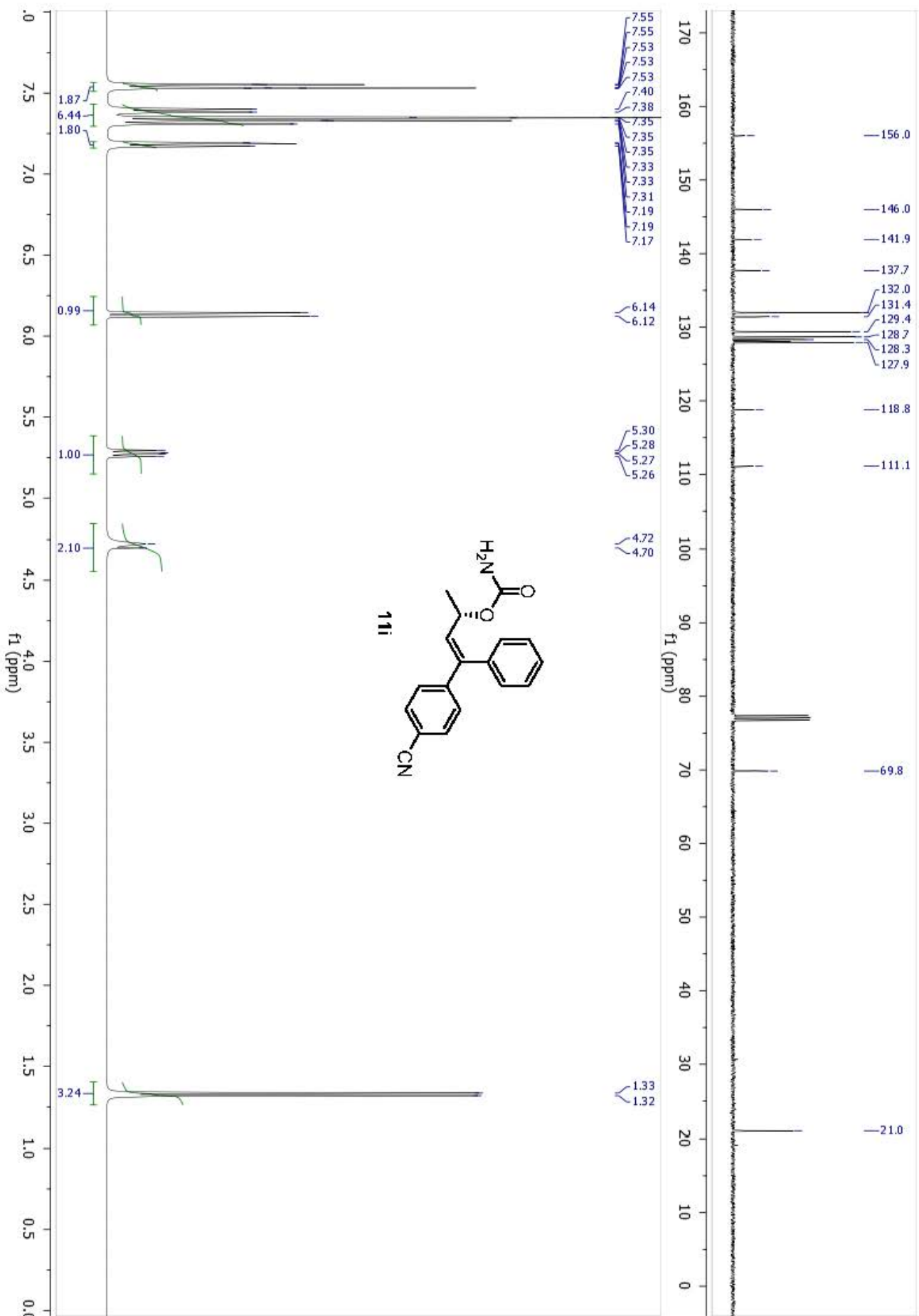


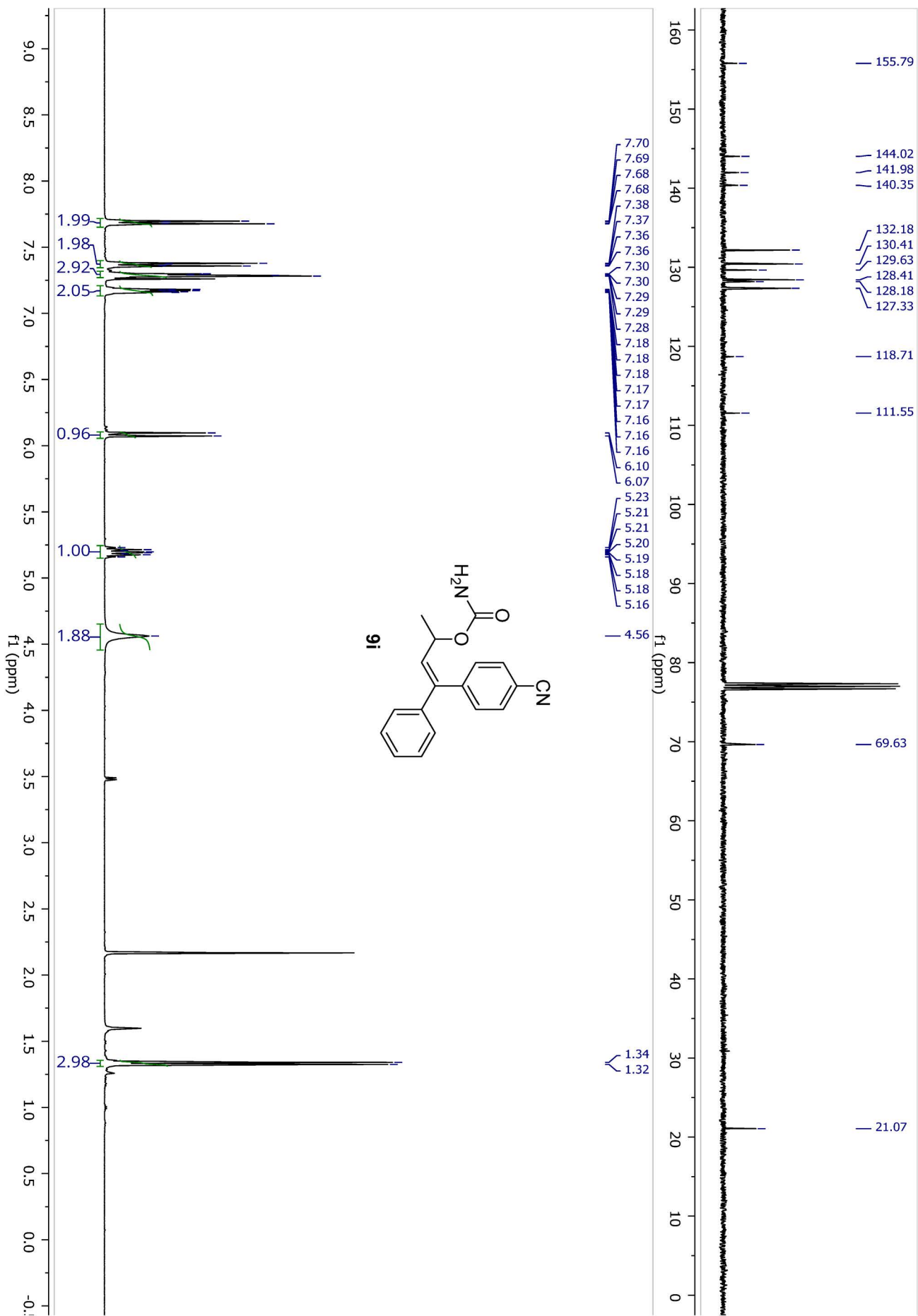


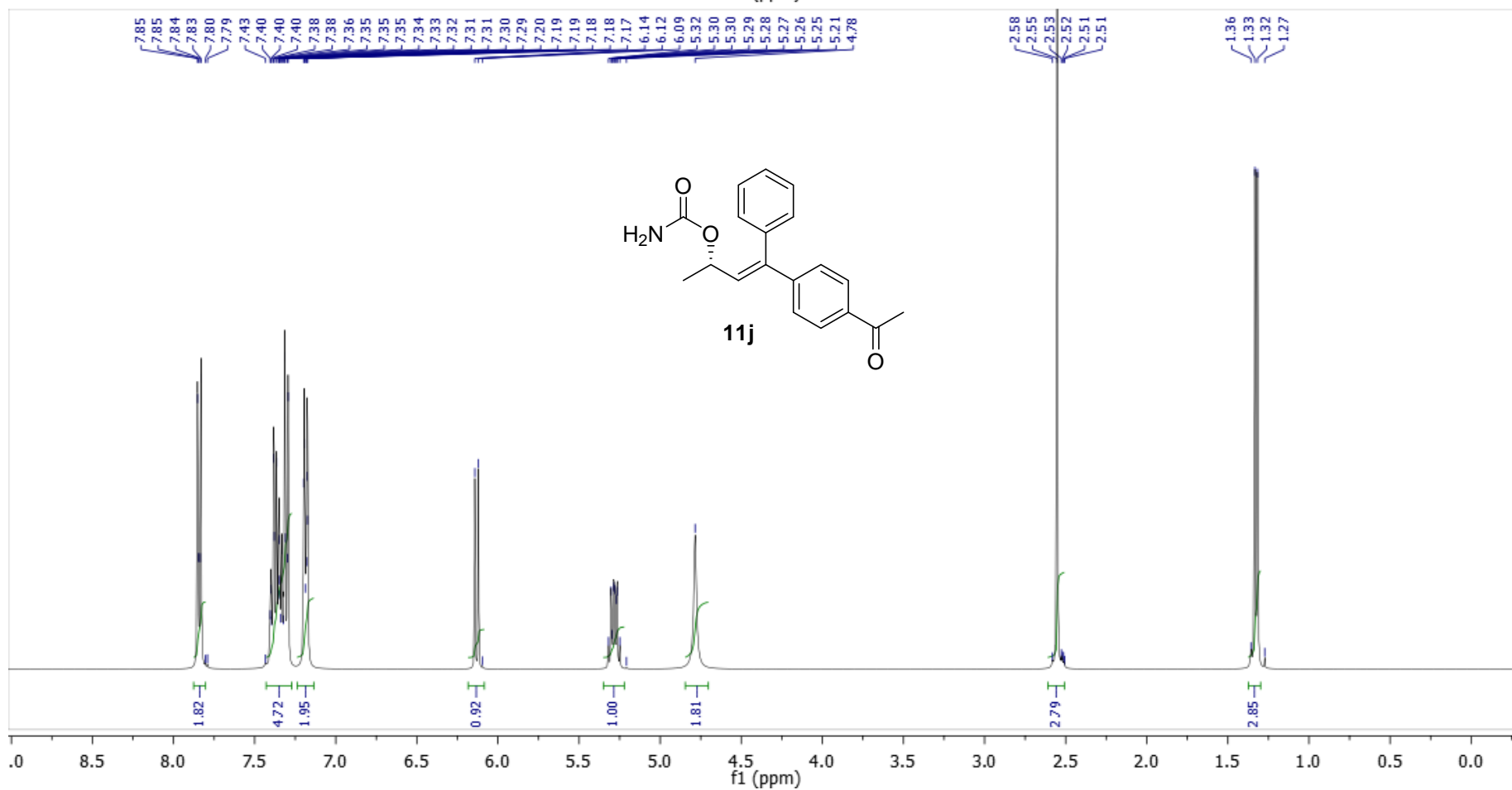
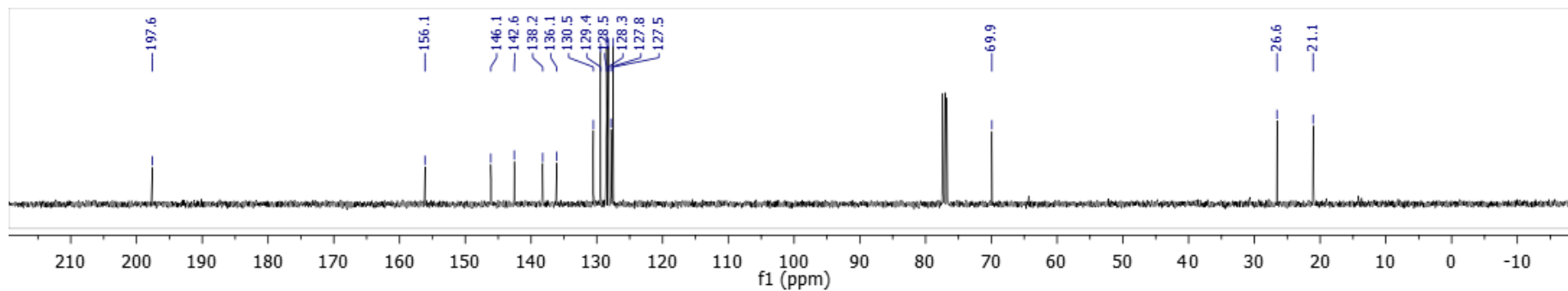




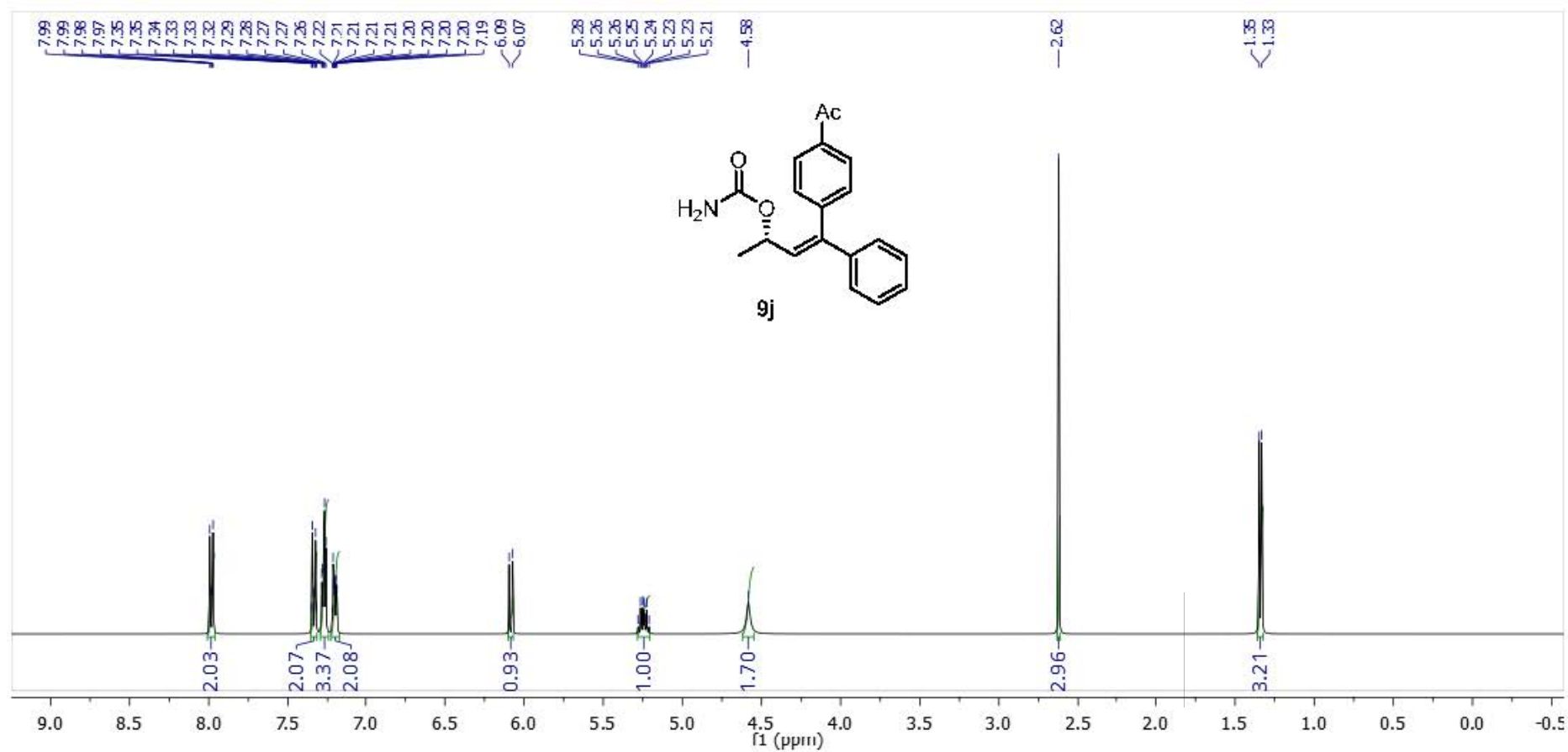
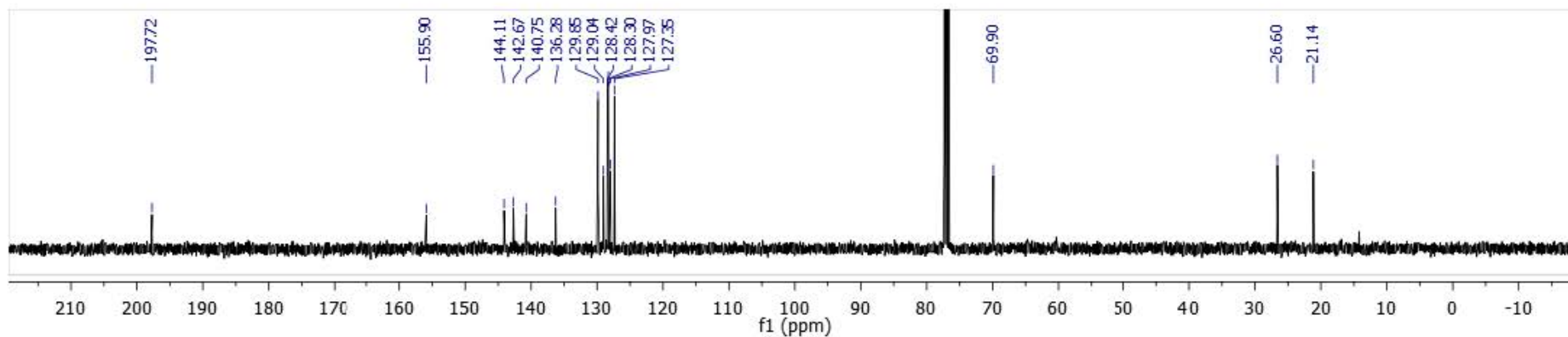


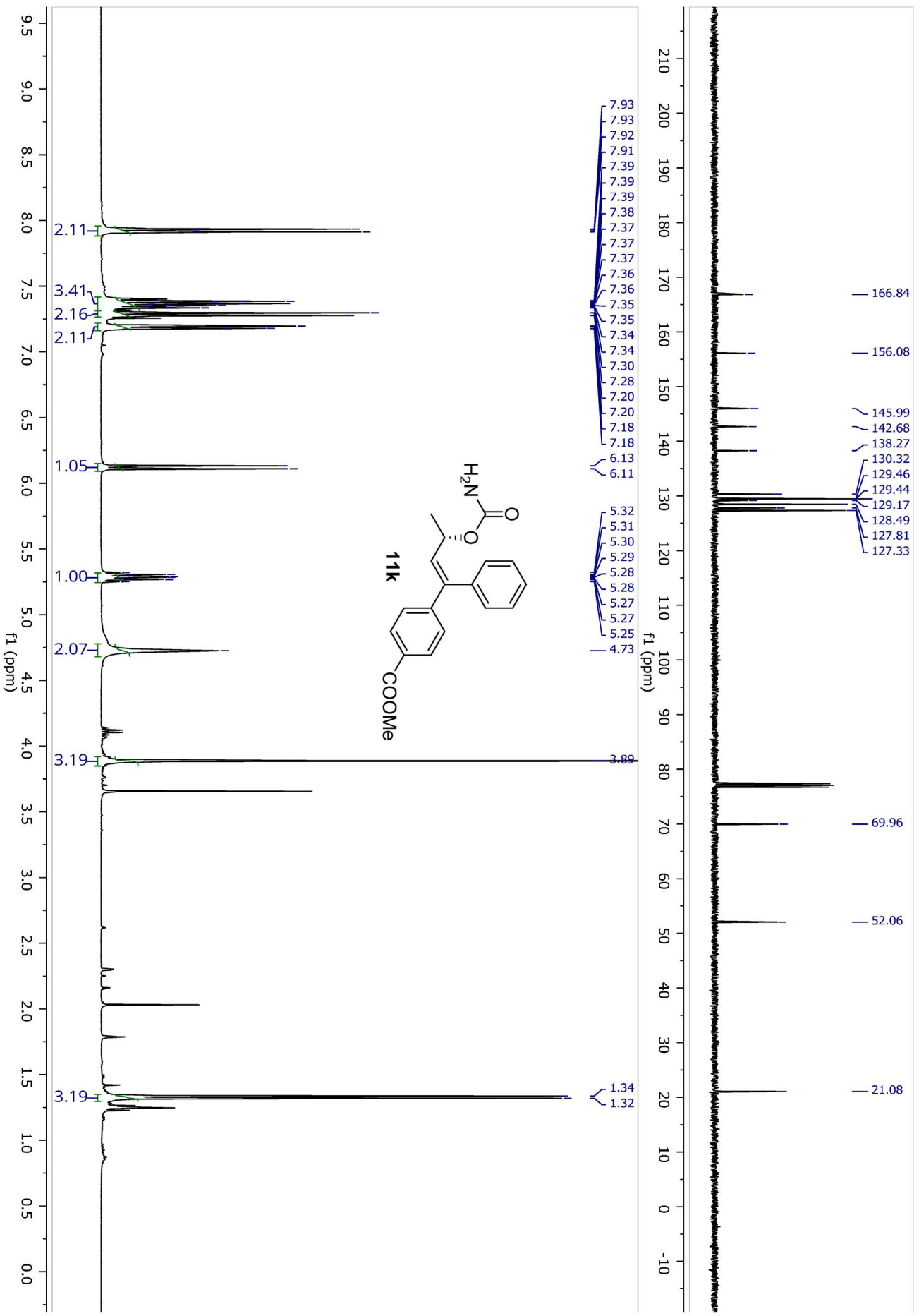


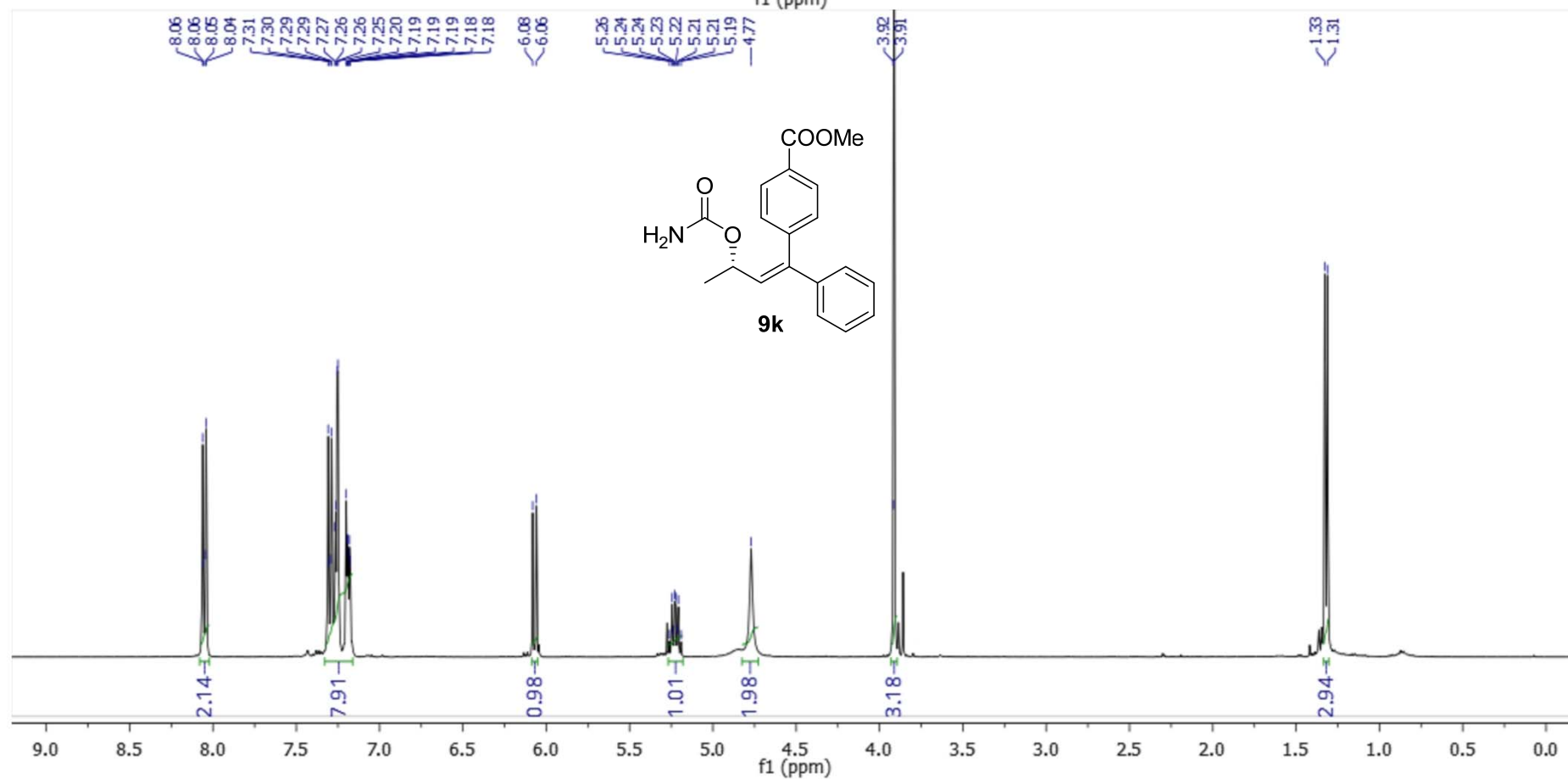
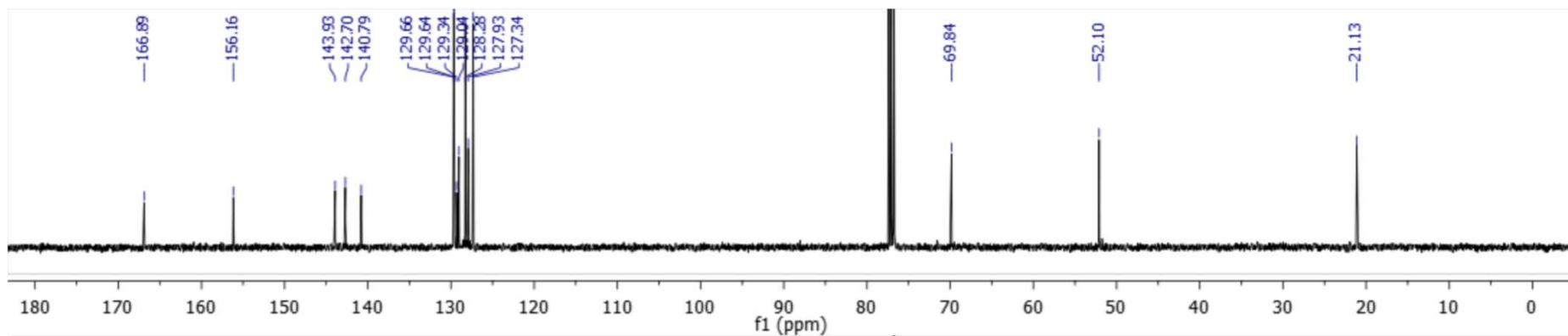


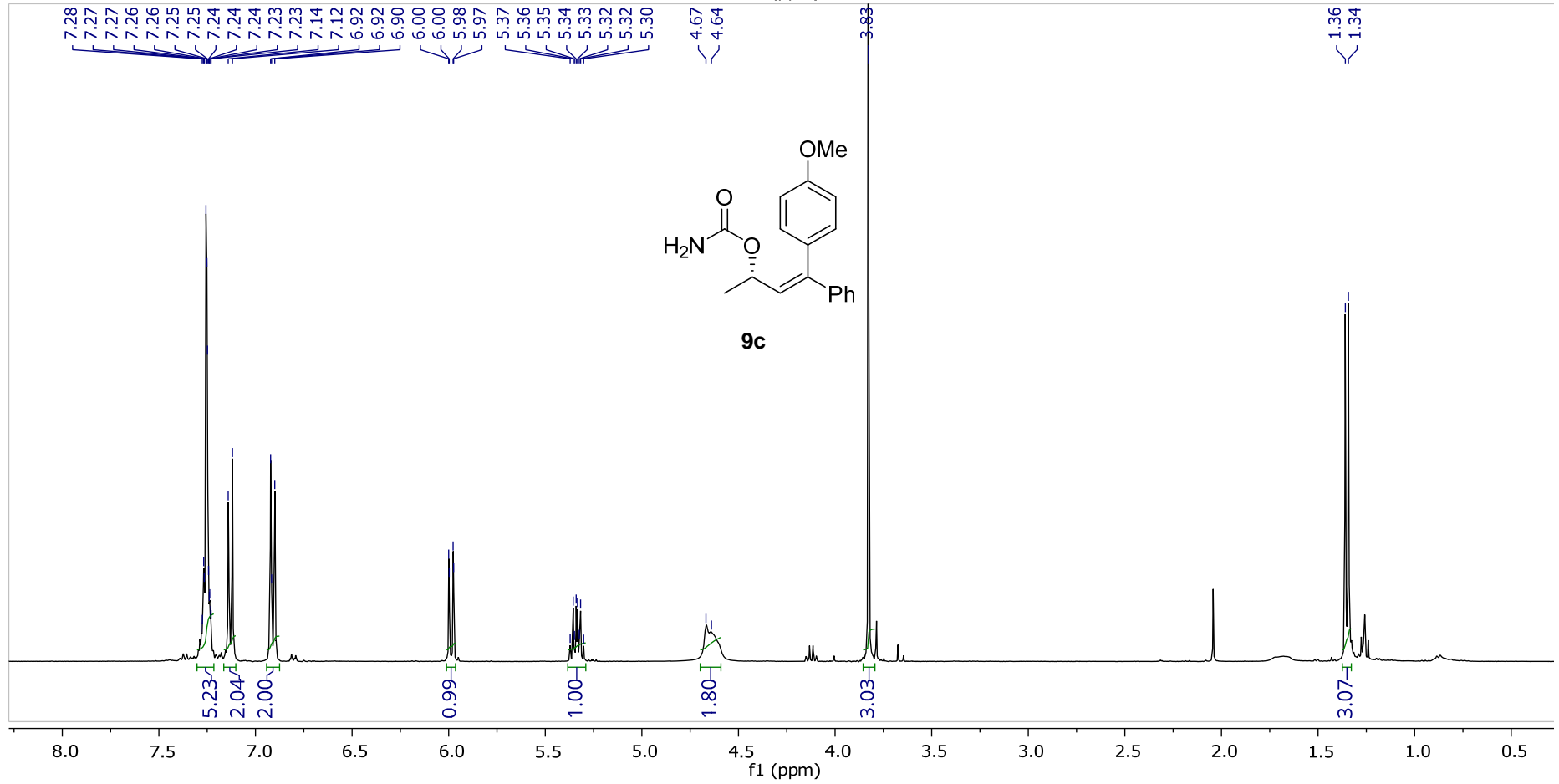
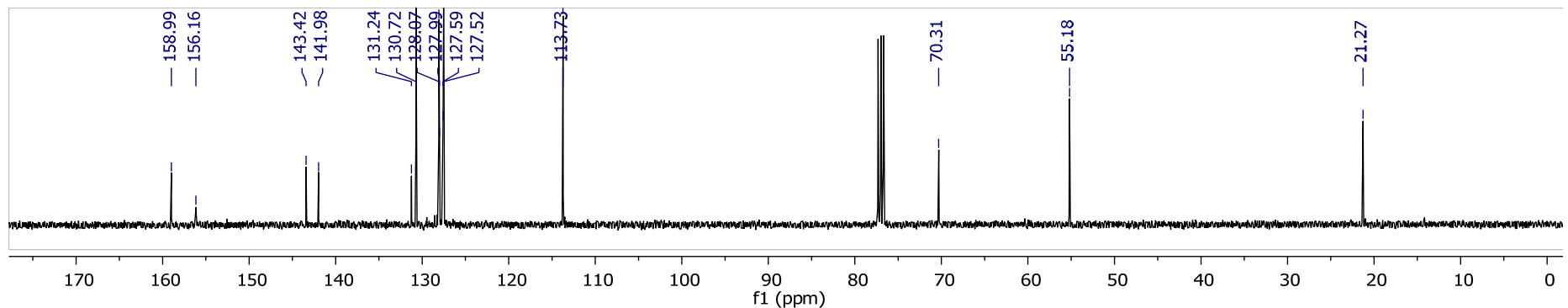


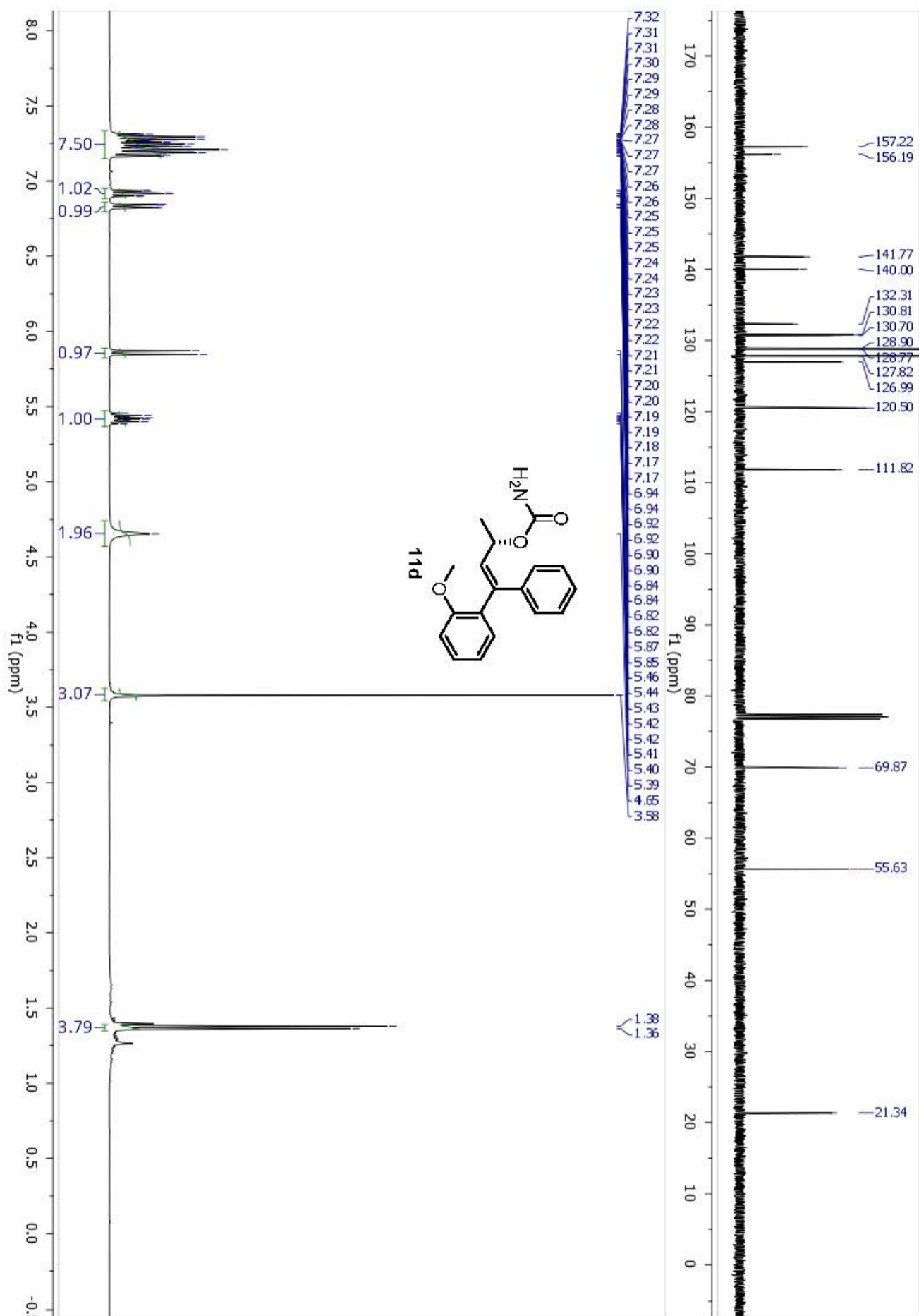


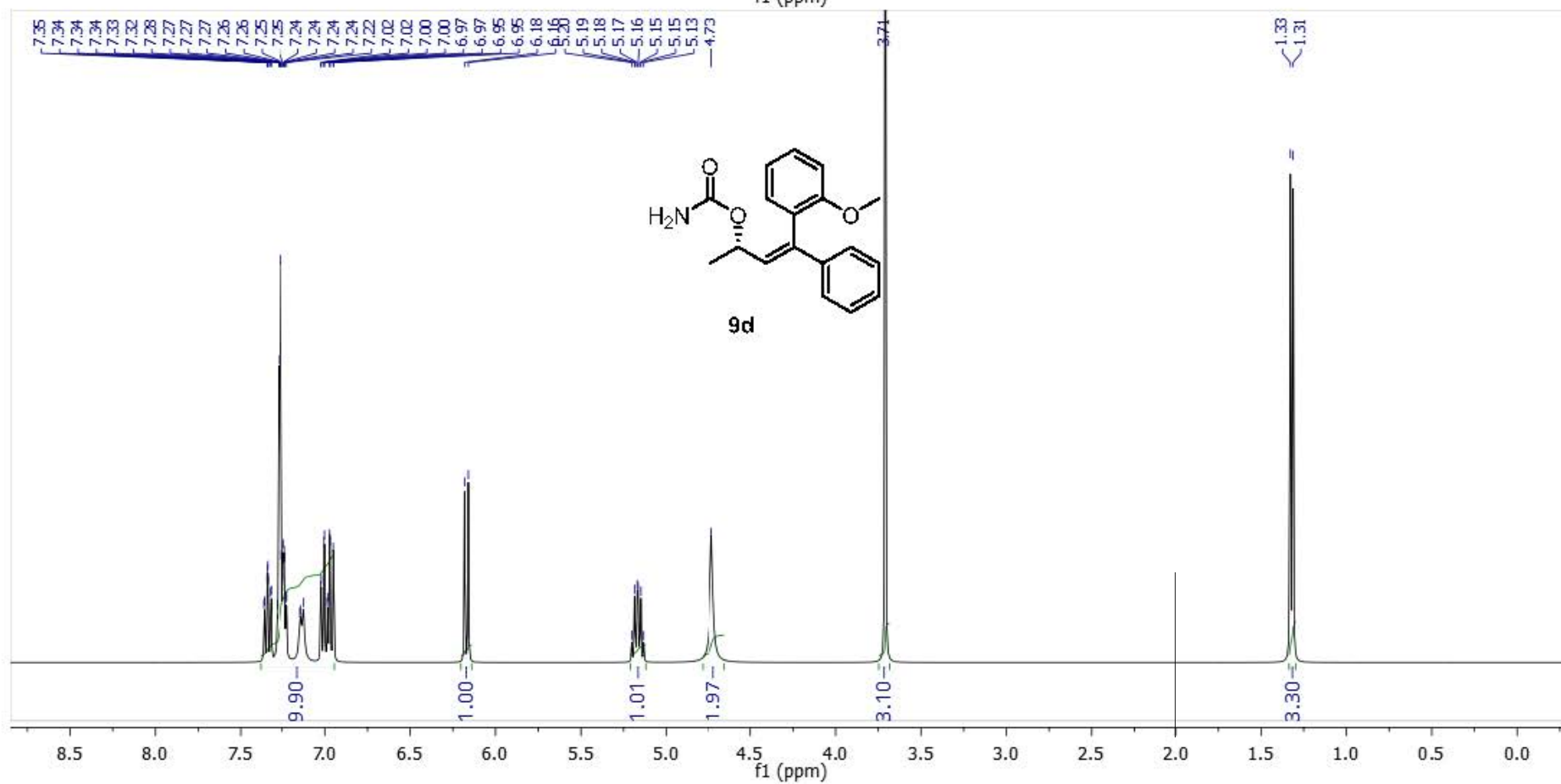
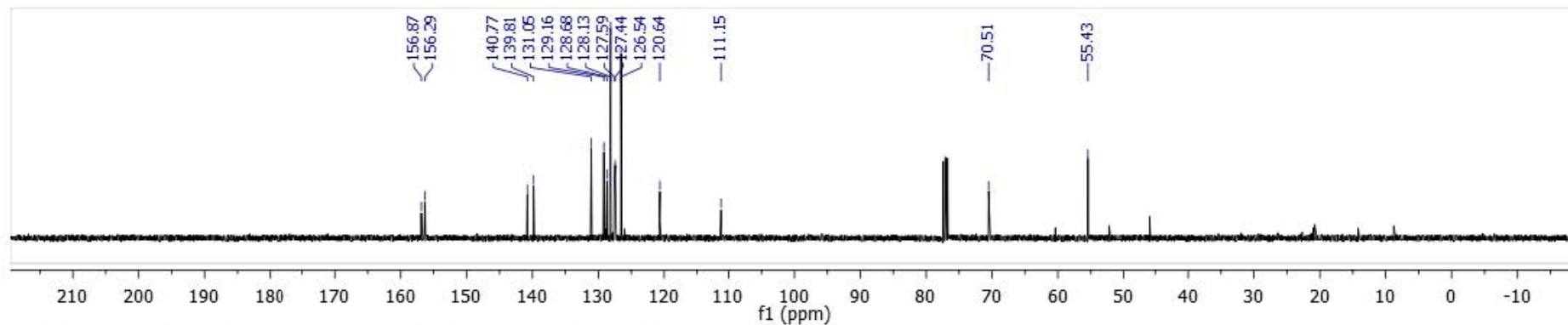


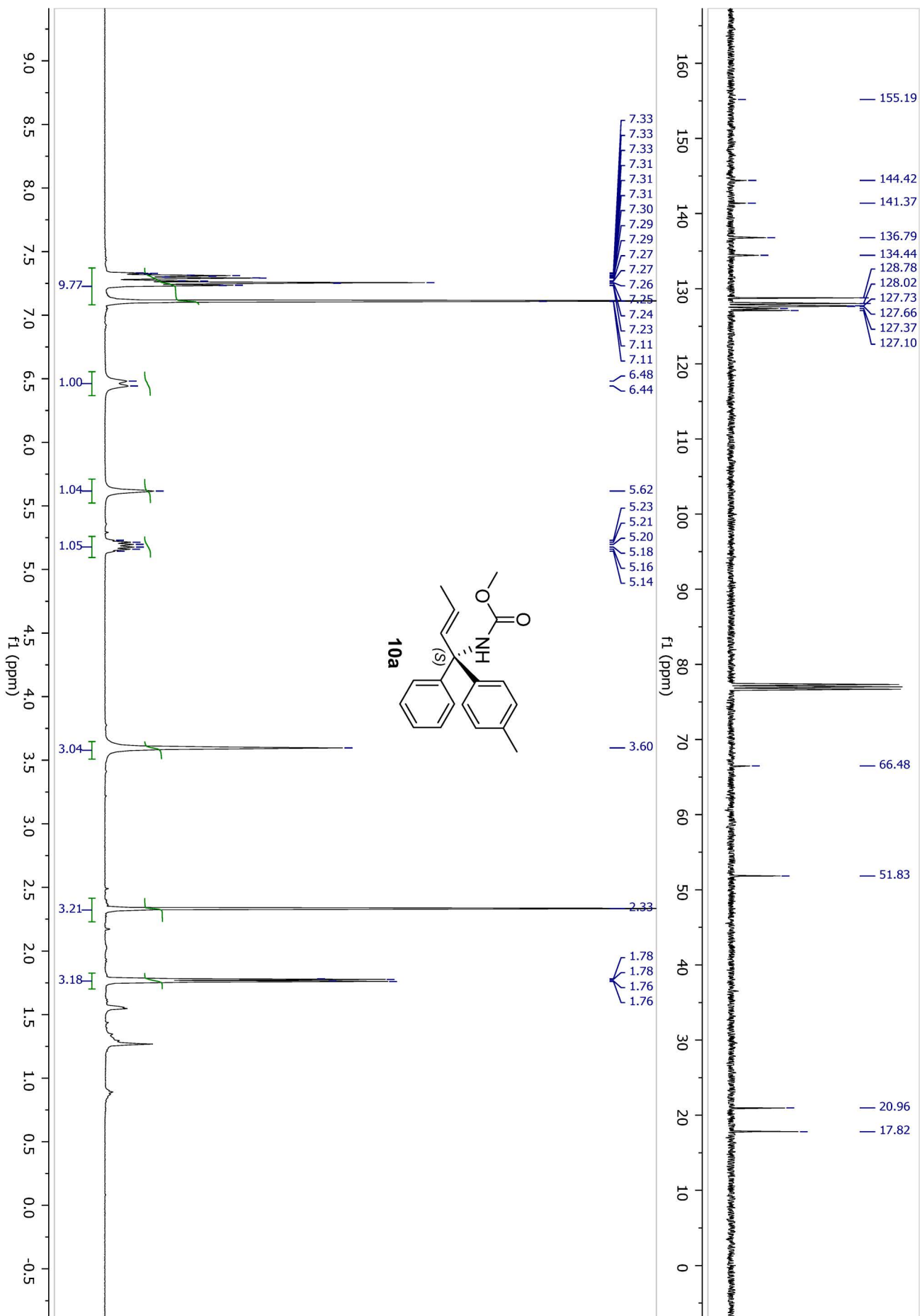


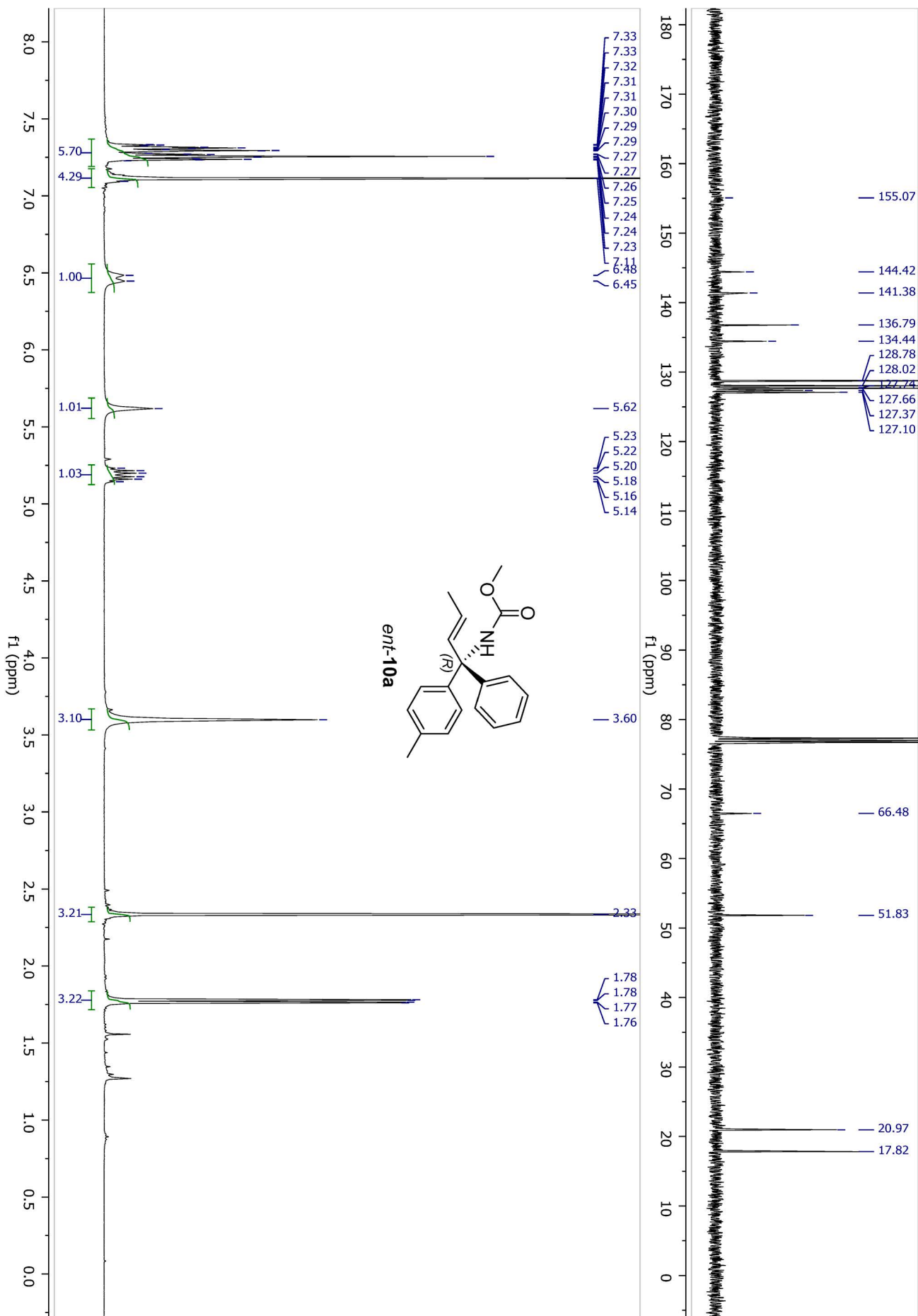








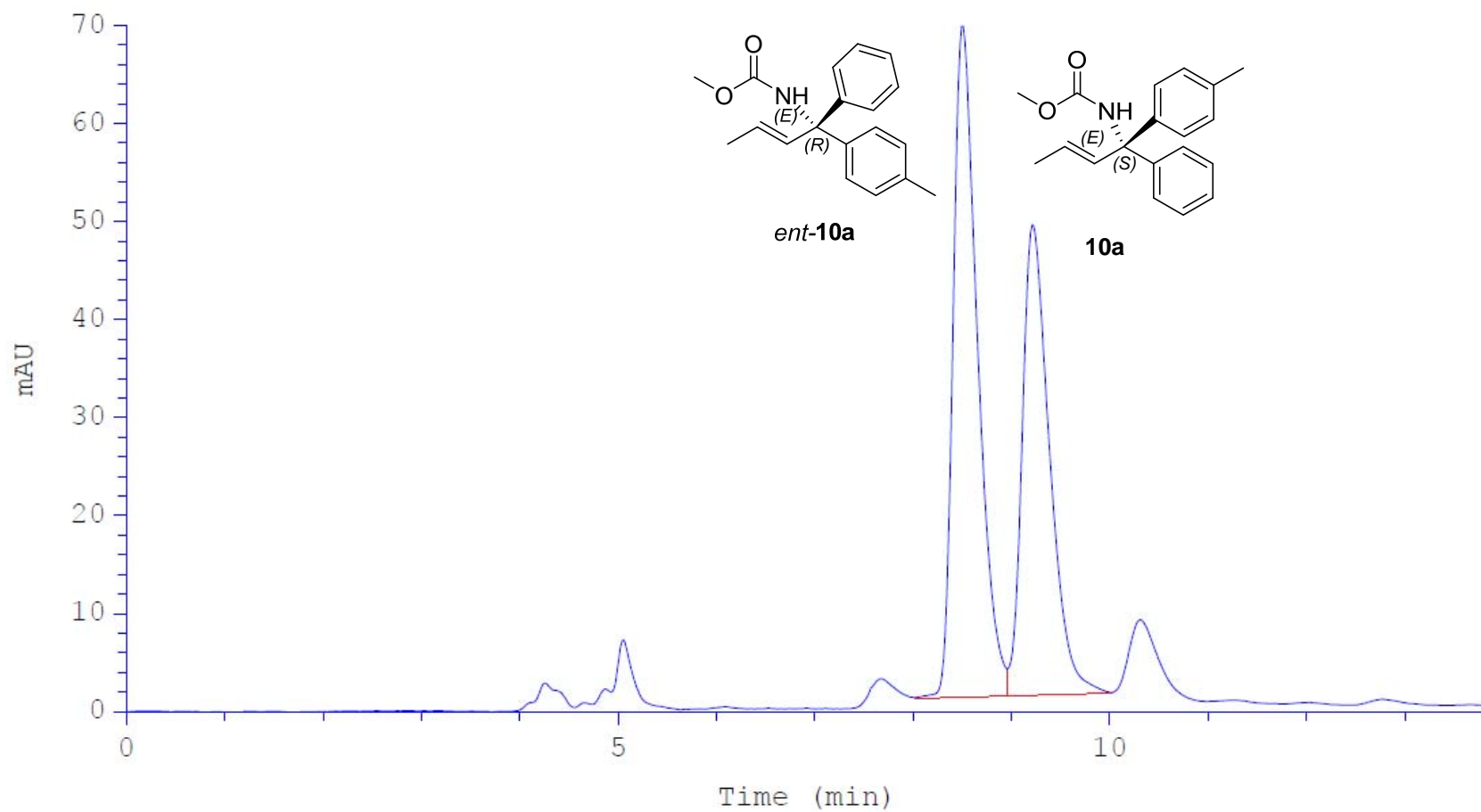






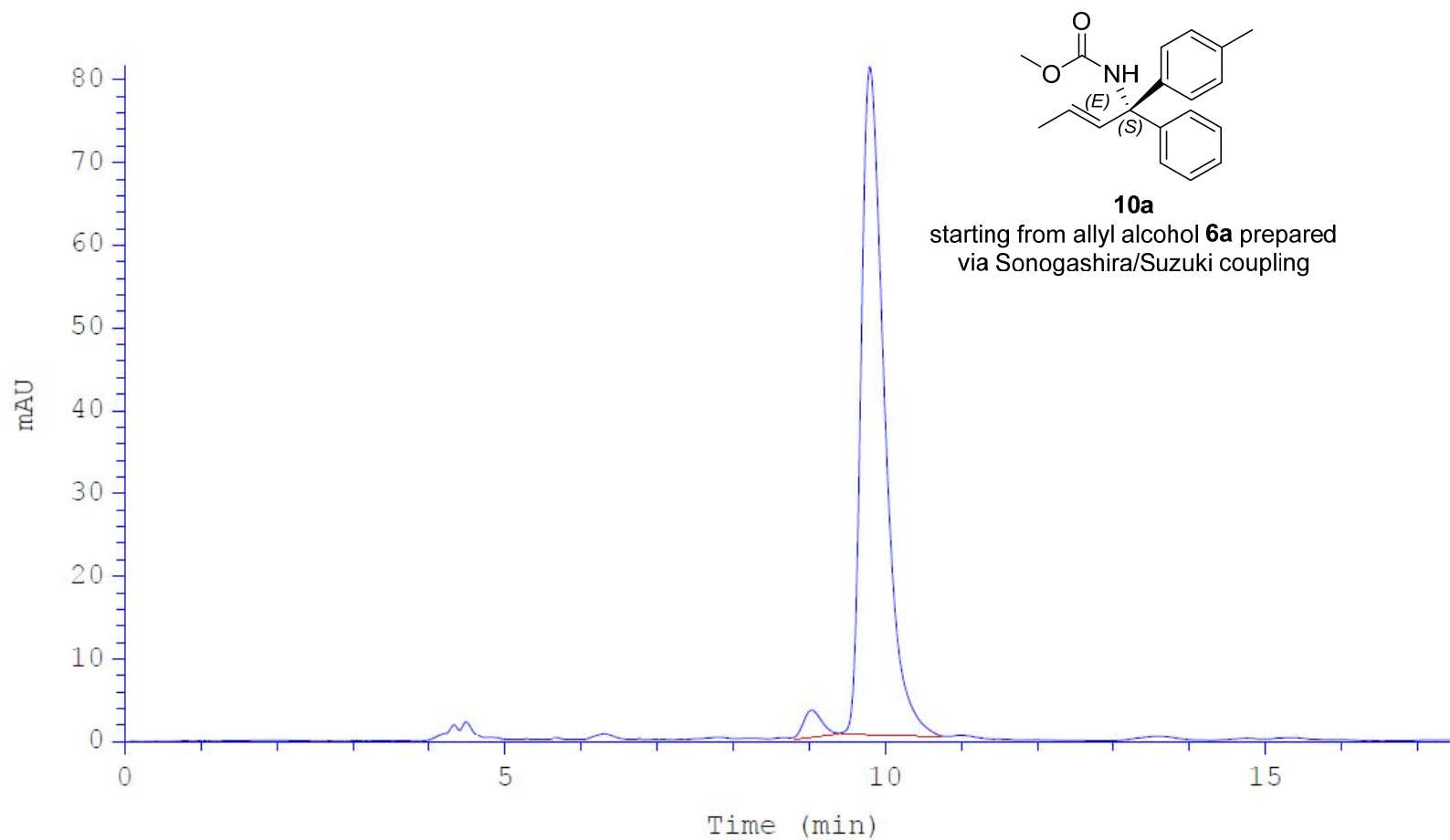
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area mAU*min	Height [mAU]	% Area	Width [min]
1	8.509	8.18	8.94	18.5220	67.0365	57.0392	0.258
2	9.209	8.94	9.90	13.9504	45.8221	42.9608	0.286



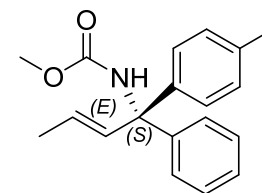
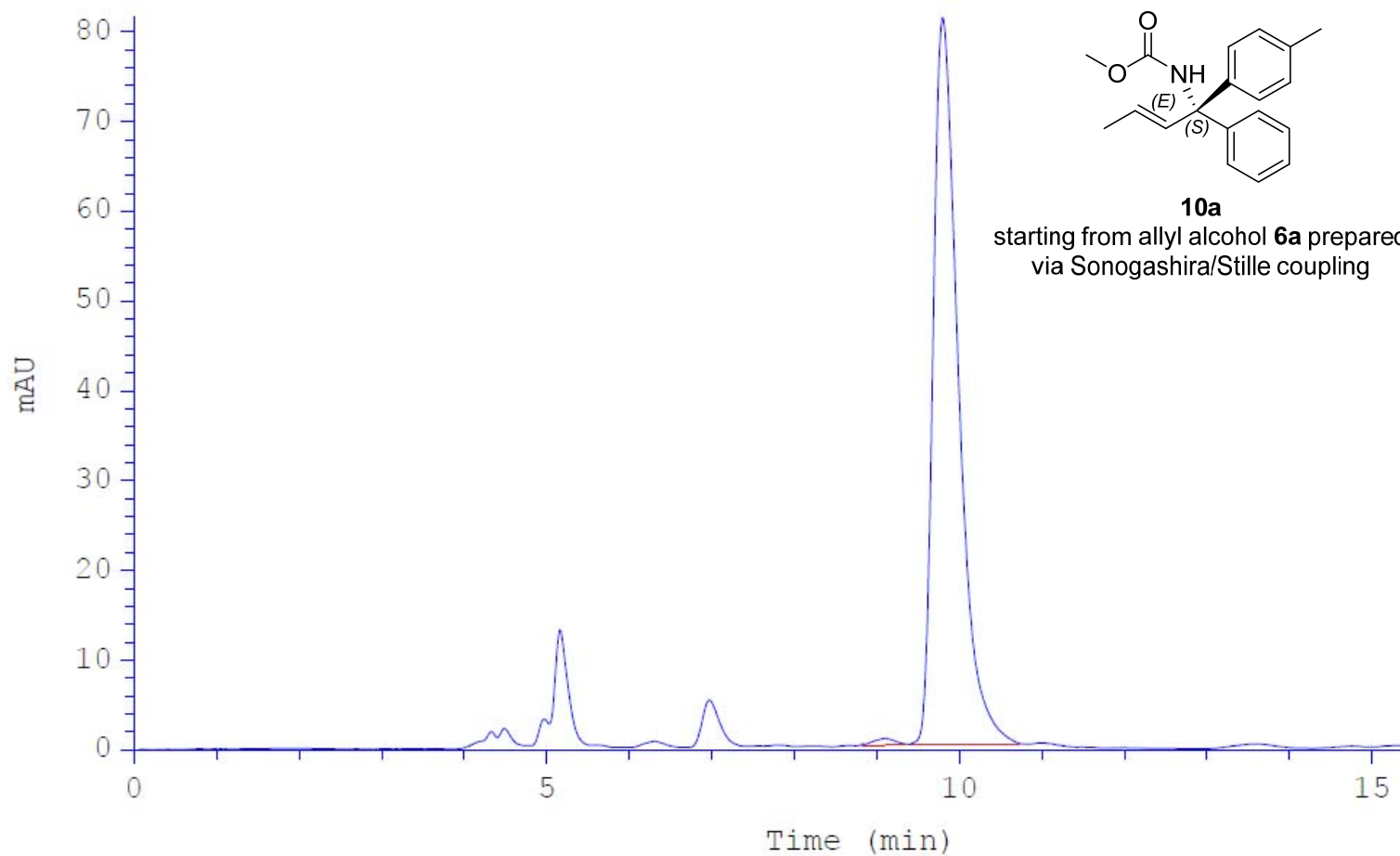
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area mAU*min	Height [mAU]	% Area	Width [min]
1	9.040	8.81	9.40	0.0705	0.0654	2.7655	0.25
2	9.791	9.40	10.96	28.3756	80.5828	97.2345	0.319



Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area
1	9.035	8.76	9.3	0.8071	1.5245	0.7854
2	9.782	9.39	10.94	28.3756	80.5284	99.2146

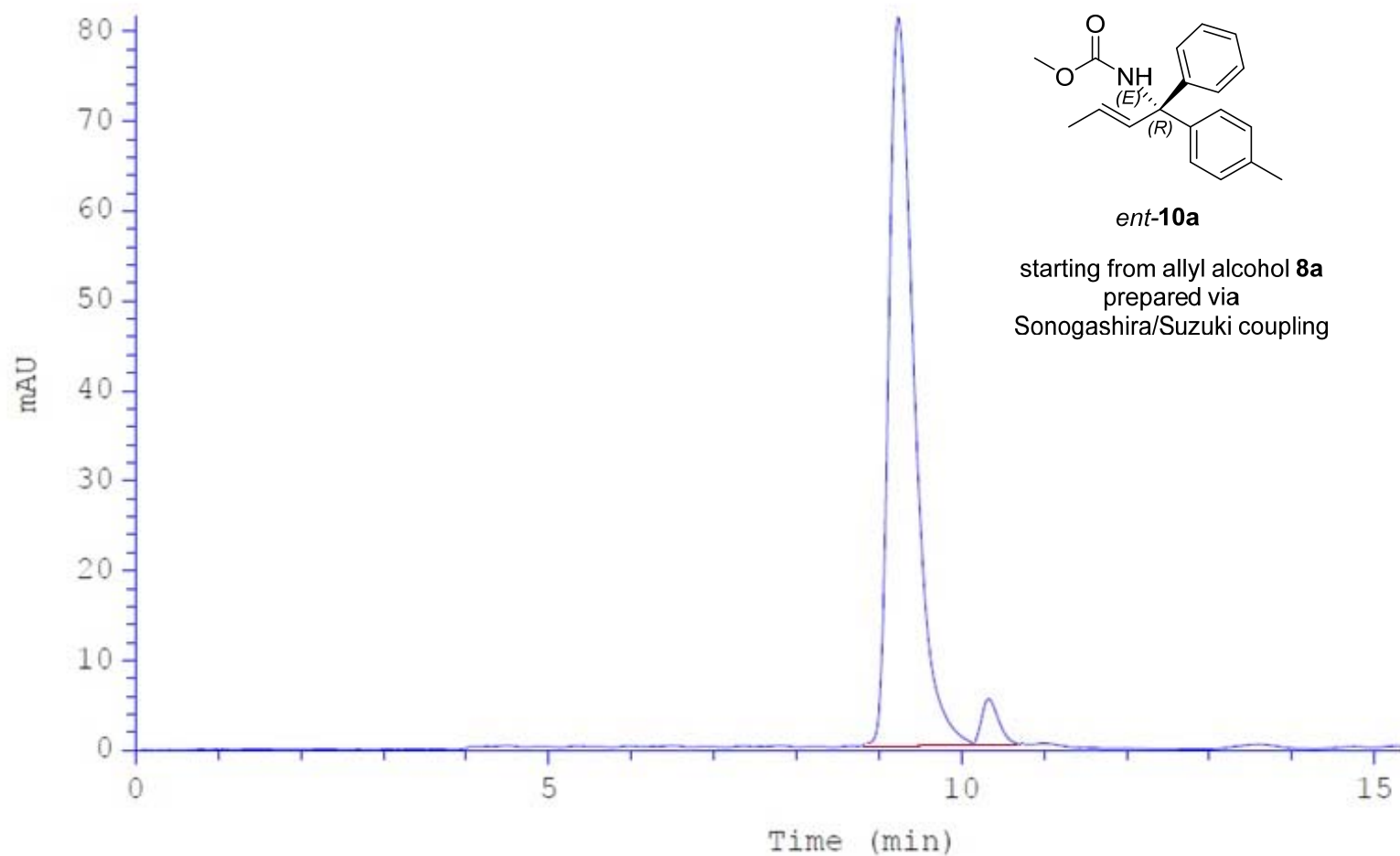


**10a**

starting from allyl alcohol **6a** prepared  
via Sonogashira/Stille coupling

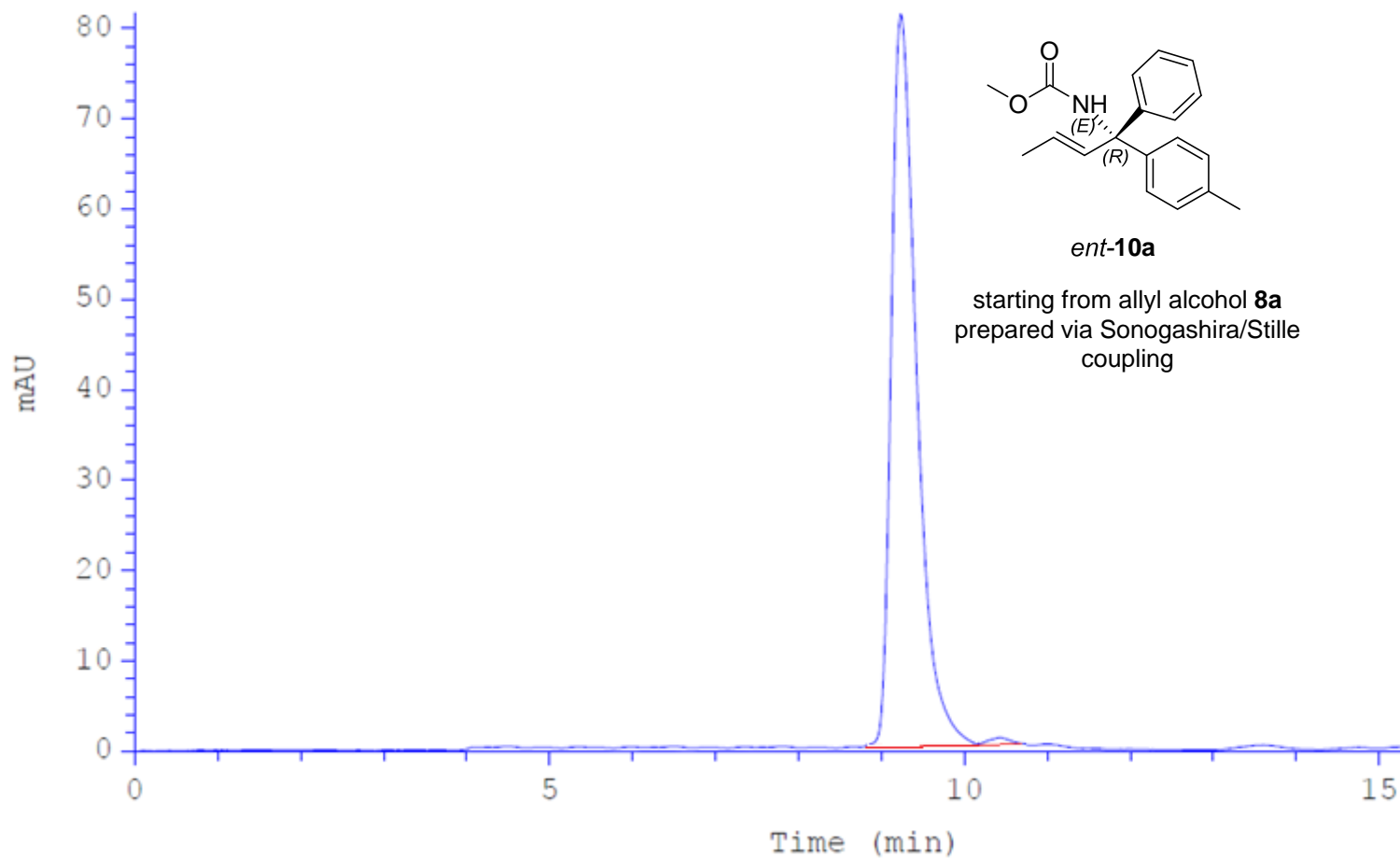
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

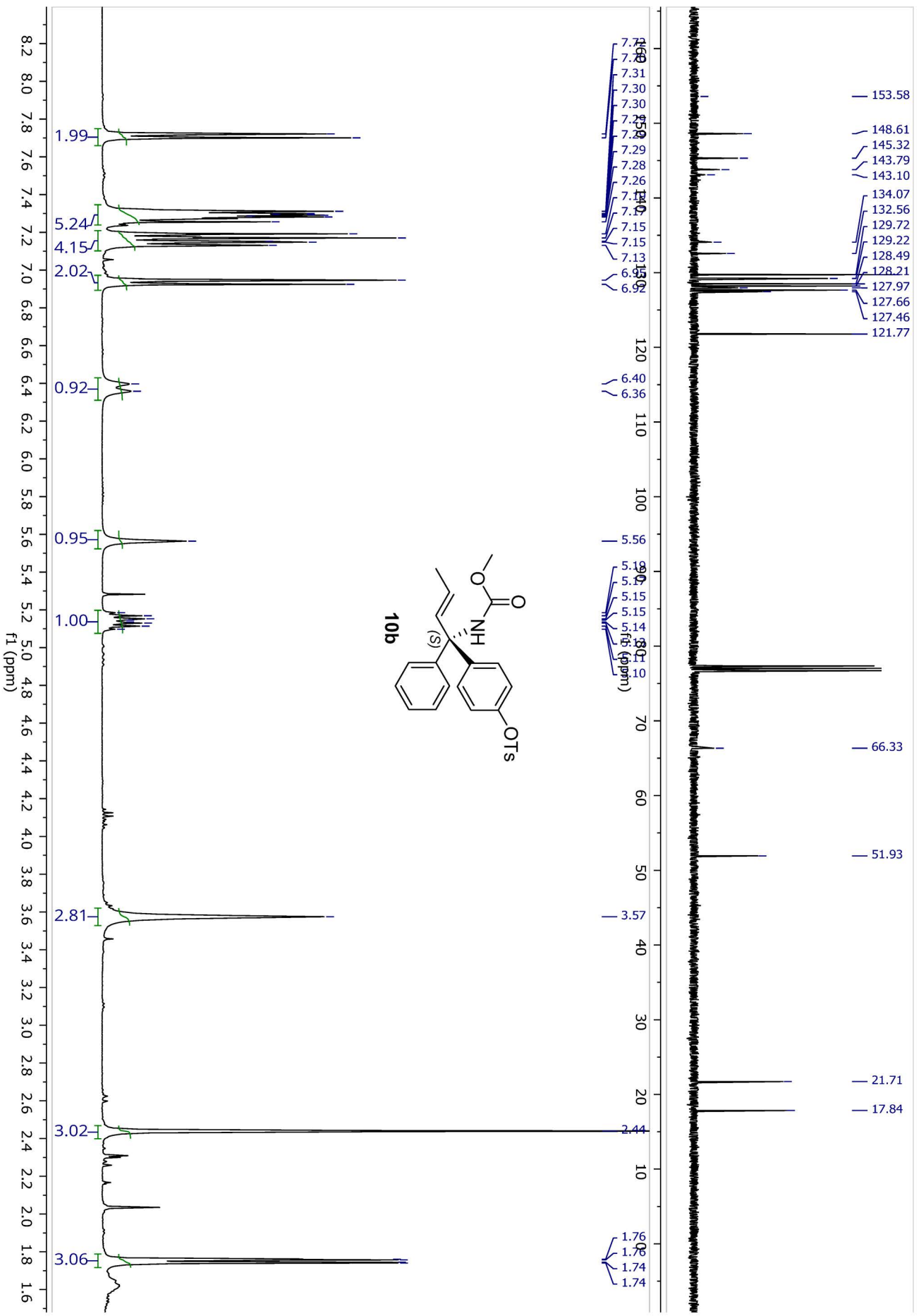
	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.27	8.9	10.16	80.3975	5073917	96.5621	1.54
2	10.32	10.16	10.69	2.8624	3.8314	3.4379	1.45

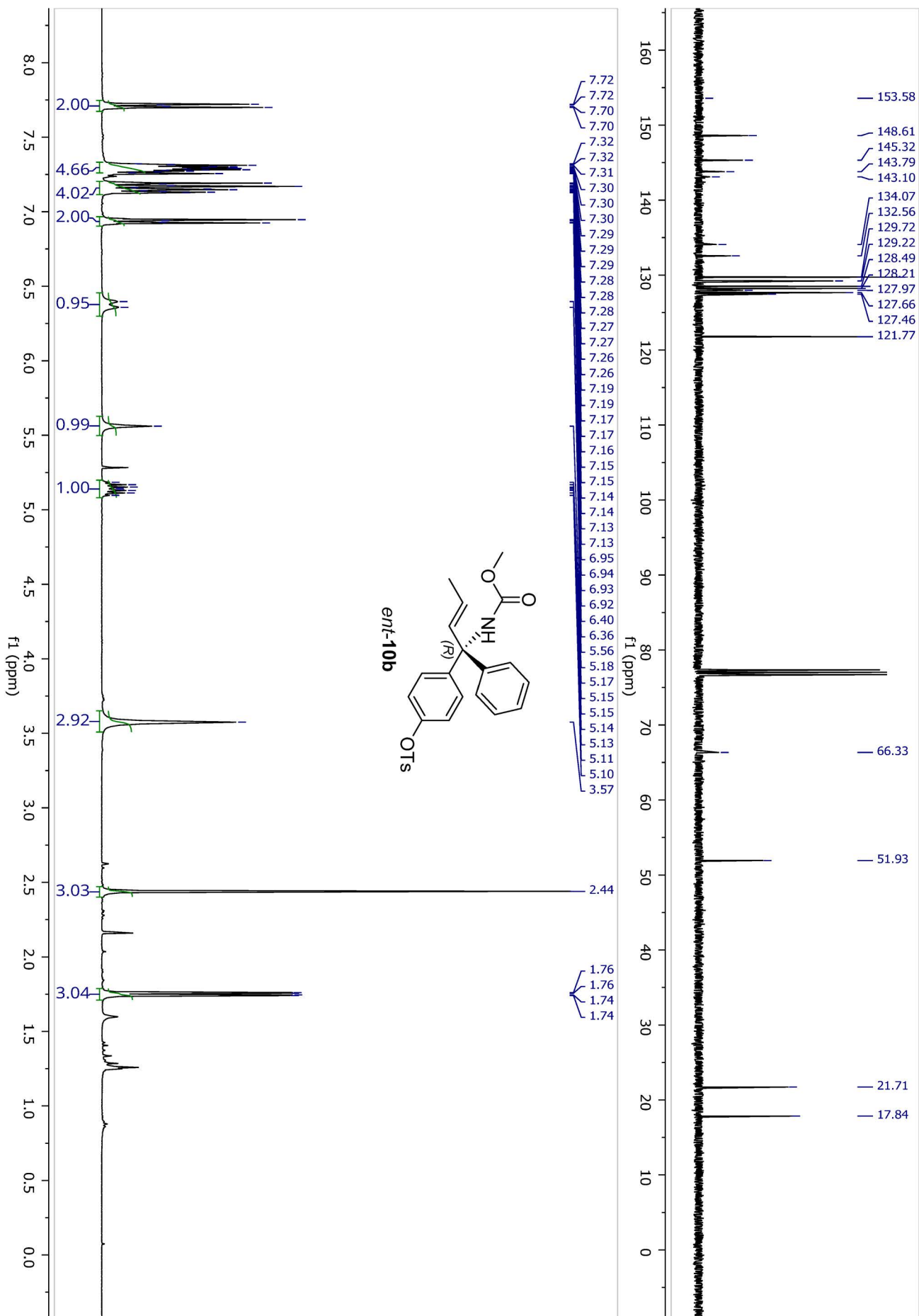


Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.21	8.92	10.12	80.2975	5073917	98.8037	1.54
2	10.39	10.12	10.72	0.97227	1.5314	1.1963	1.75







**HPLC conditions:**

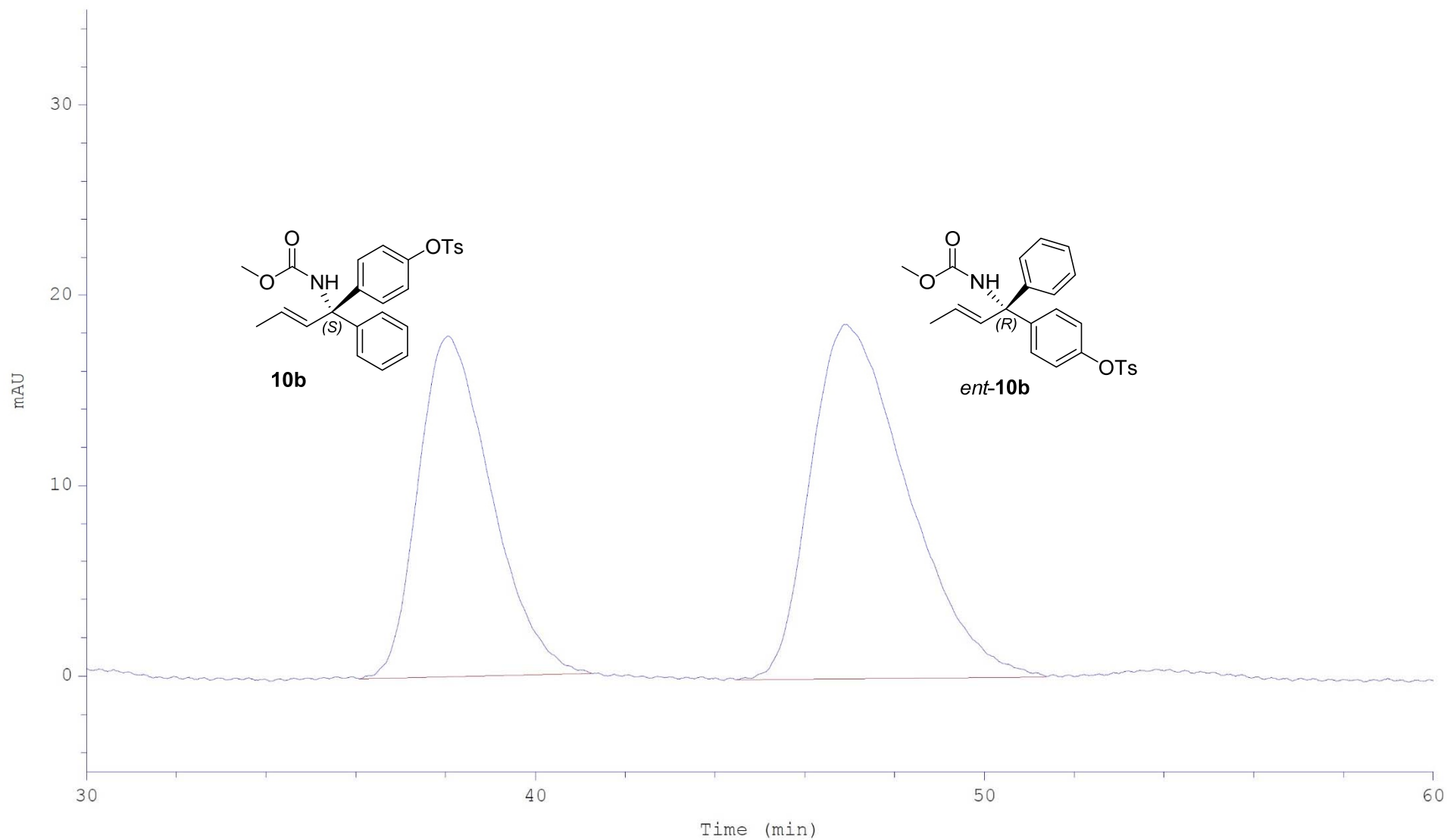
Column: Chiralpak AS-H

Eluent: 10% i-PrOH/hexanes

Flow: 1mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	38.053	35.84	42.23	34.0788	17.9074	42.2768	1.771
2	46.887	44.11	52.01	46.5299	18.5876	57.7232	2.328





**HPLC conditions:**

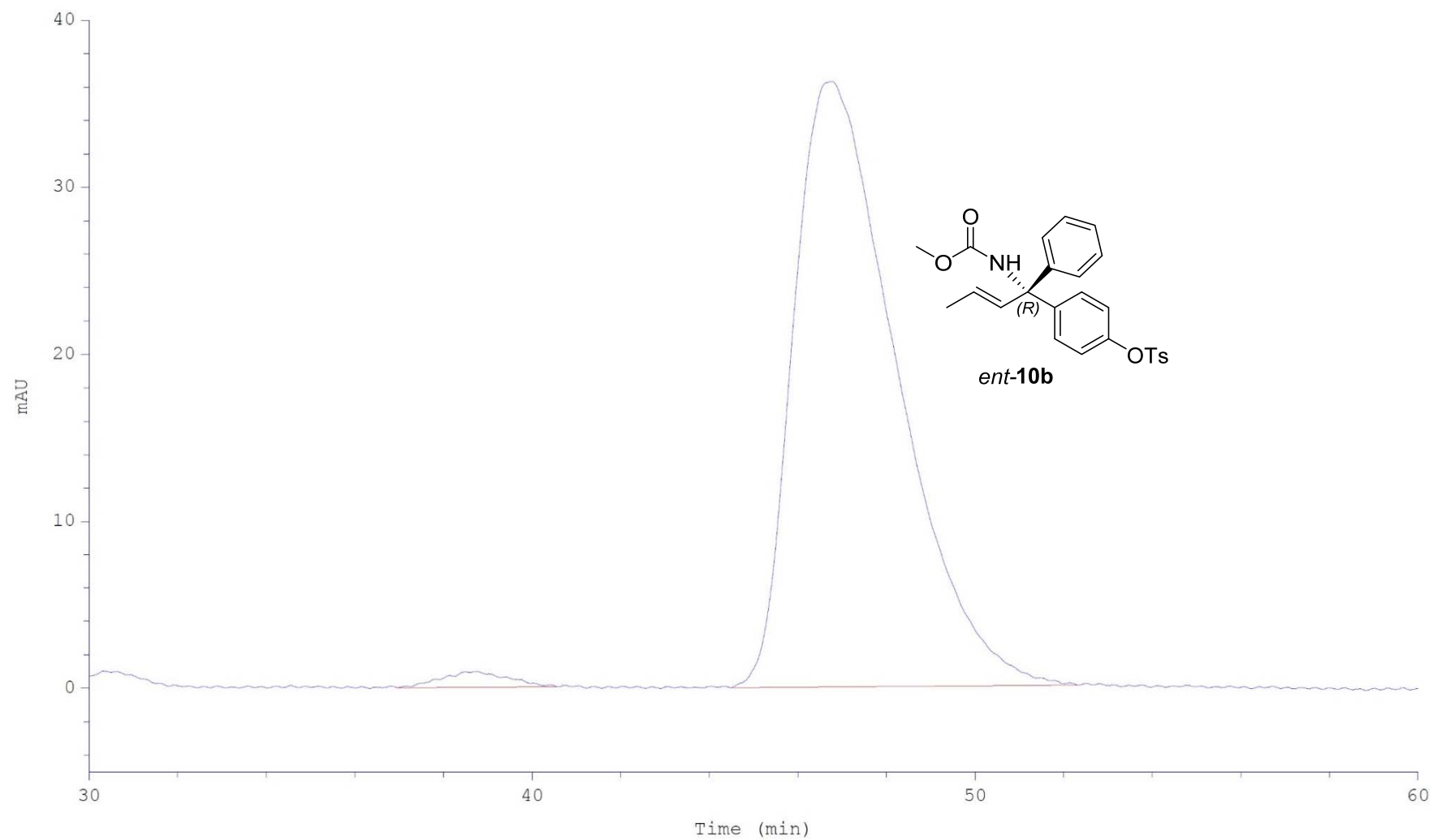
Column: Chiralpak AS-H

Eluent: 10% i-PrOH/hexanes

Flow: 1mL/min

Detection: UV, 254 nm

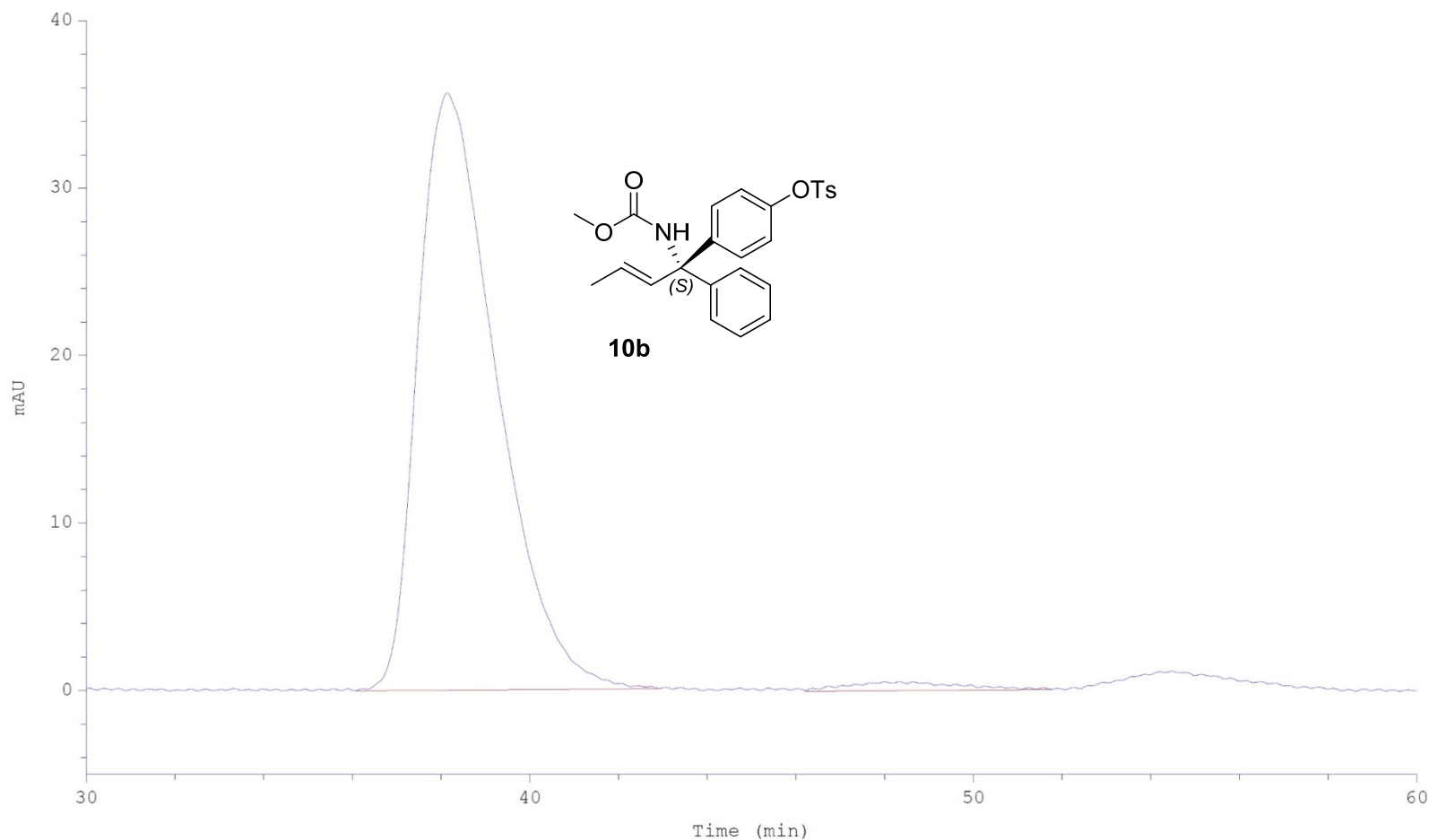
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	38.770	36.34	41.48	1.88918	0.993042	1.8931	1.805
2	46.737	43.98	53.39	97.9033	36.2198	98.1069	2.523

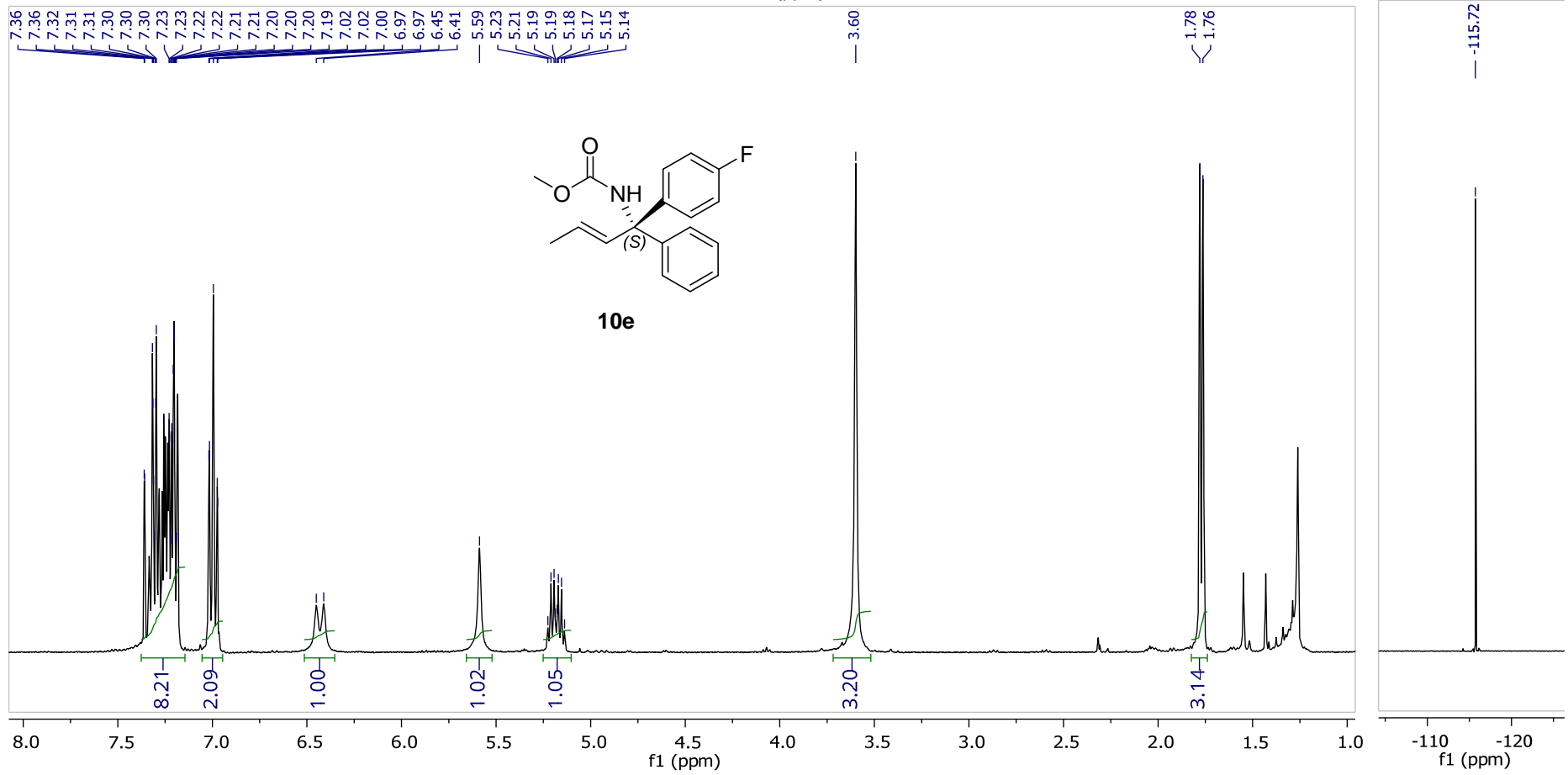
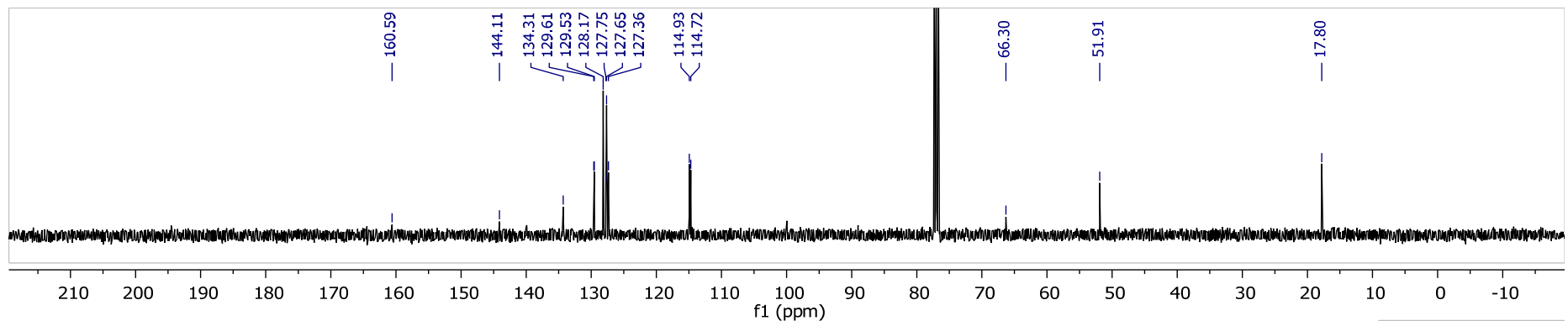


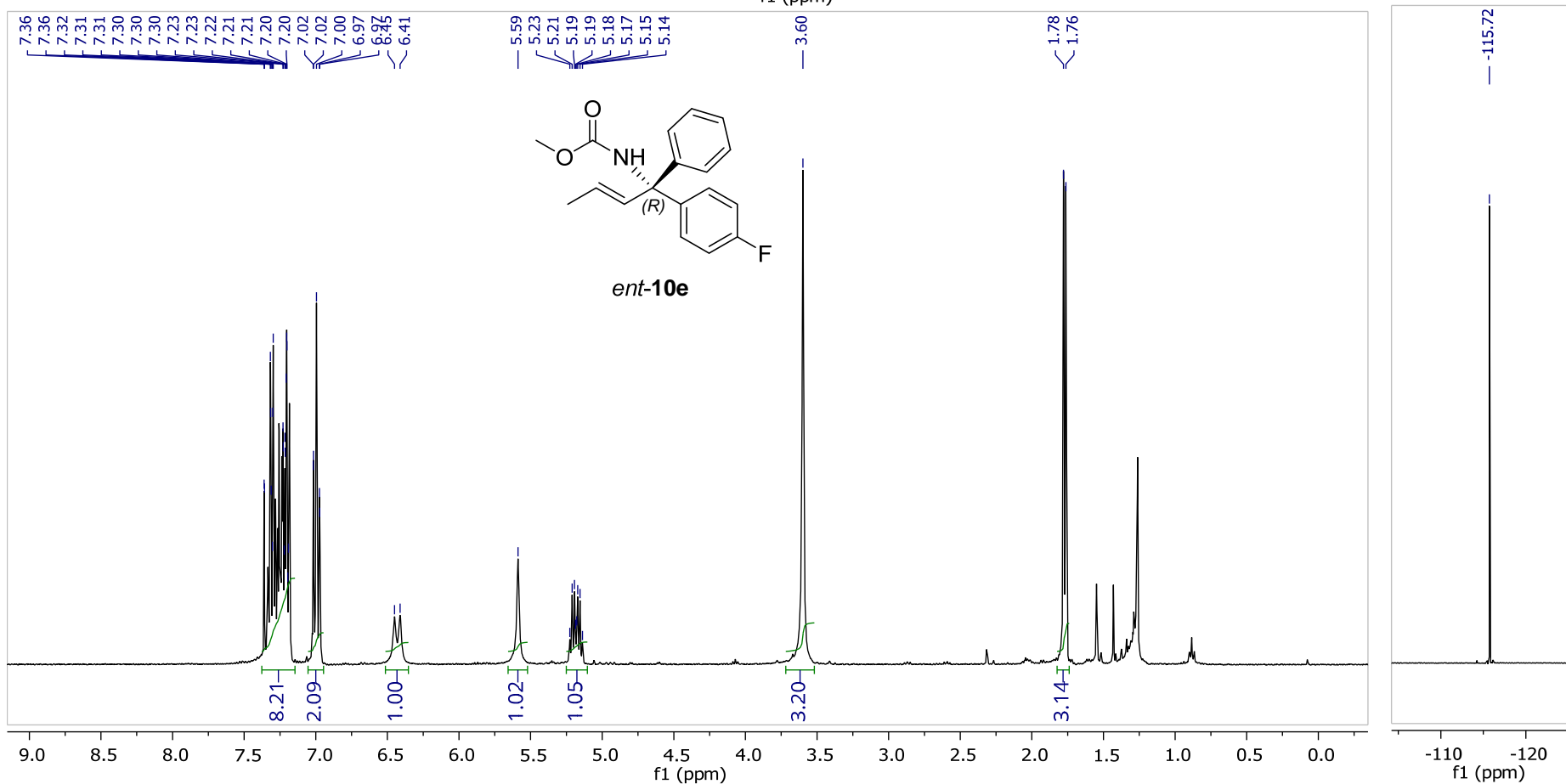
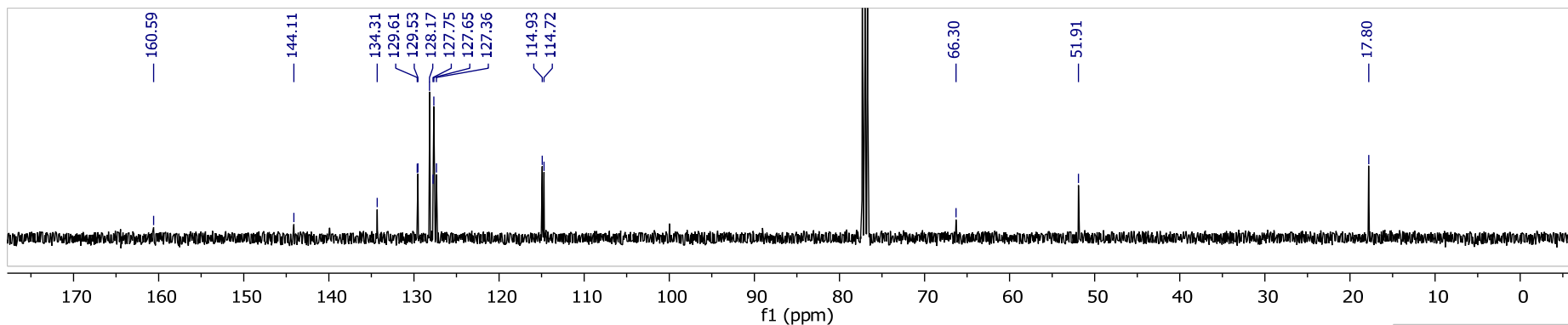
**HPLC conditions:**

Column: Chiralpak AS-H  
Eluent: 10% i-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	38.135	35.58	43.48	72.7409	35.5734	98.9320	1.894
2	47.986	45.74	51.26	0.785282	0.405583	1.0680	1.806



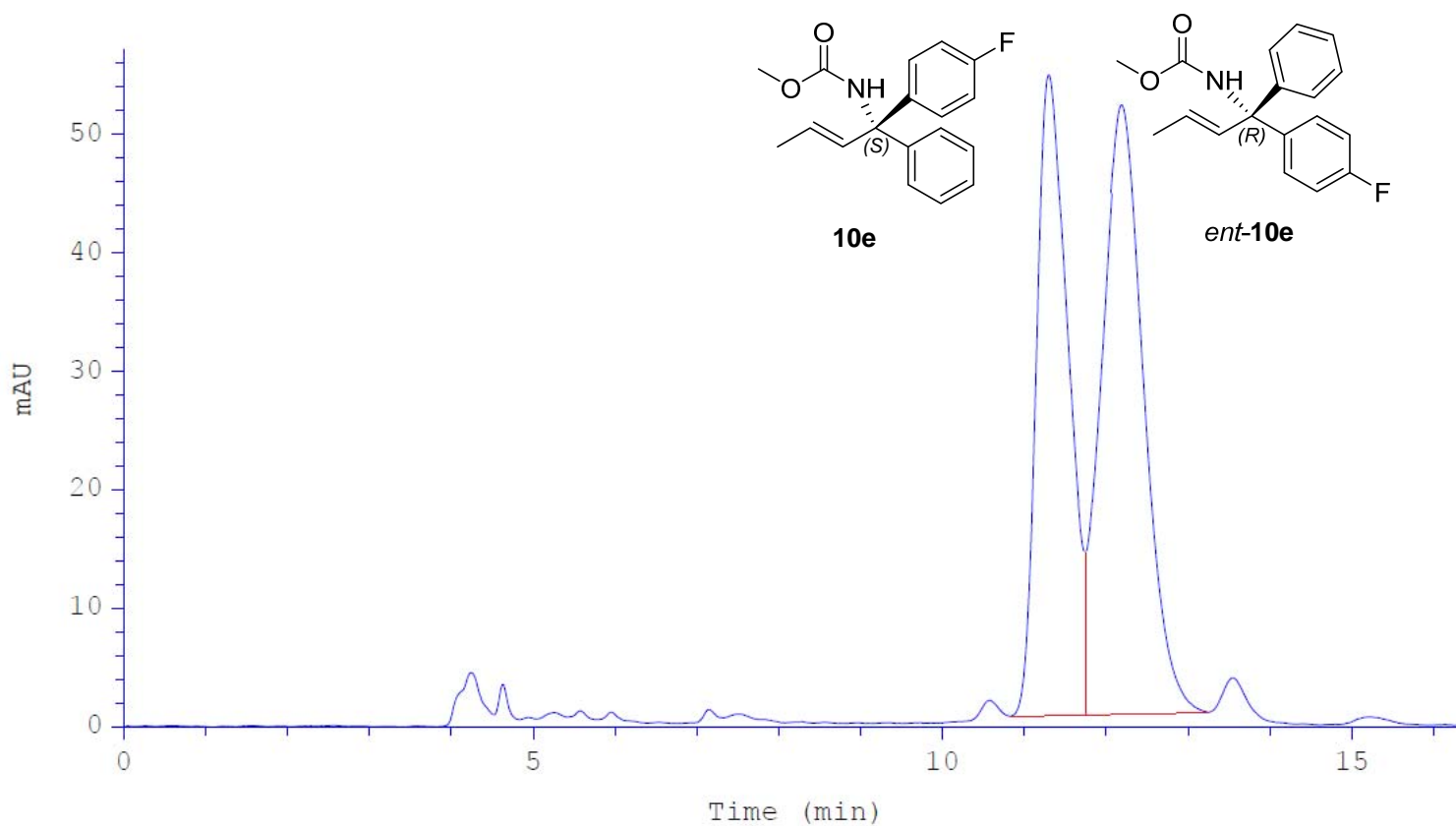




**HPLC conditions:**

Column: Chiralpak AS-H  
Eluent: 5% i-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

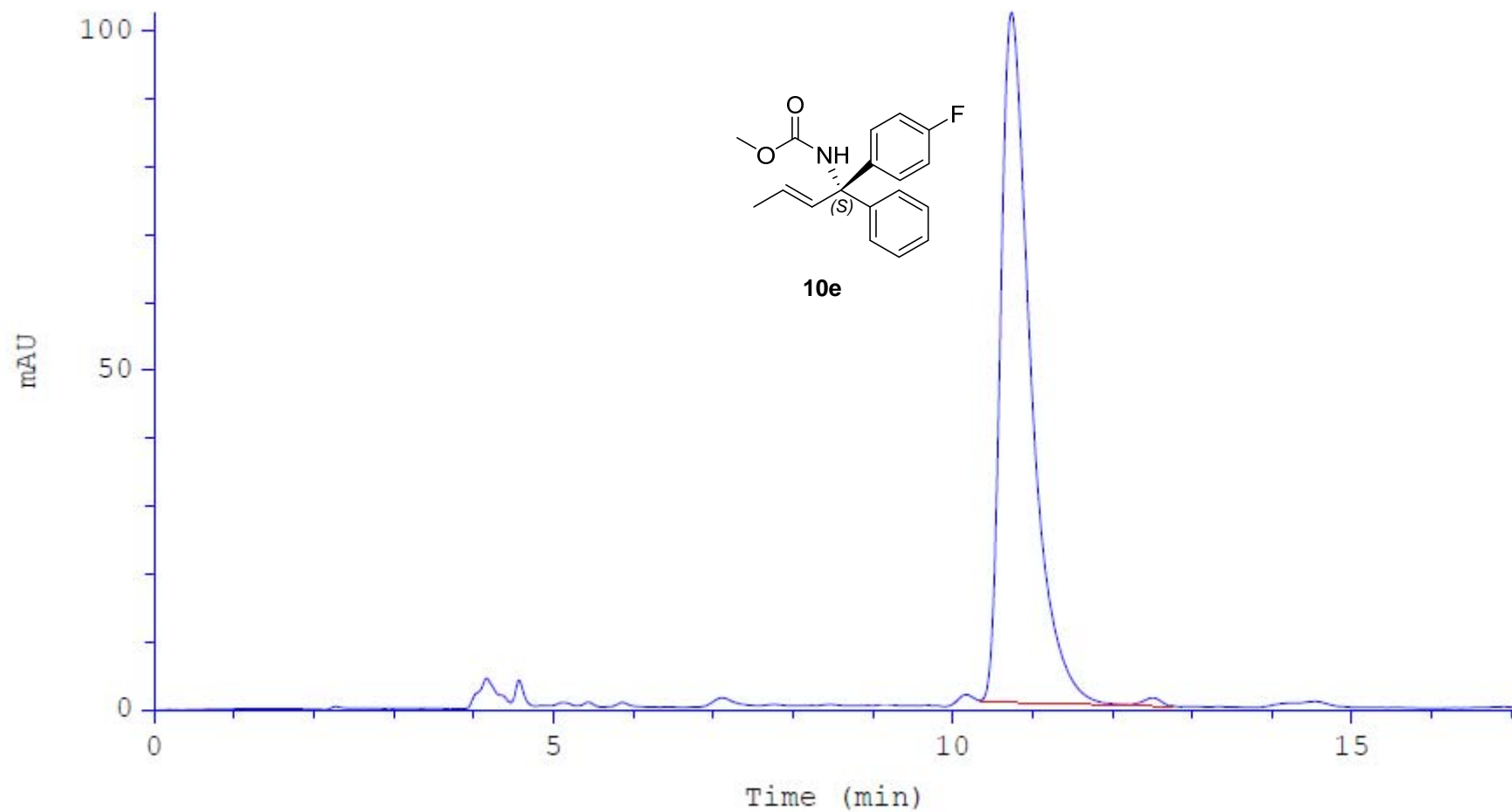
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	11.726	11.29	11.96	19.8442	54.4755	43.3982	0.276
2	12.193	11.96	13.24	25.8816	50.274	56.6018	0.402



**HPLC conditions:**

Column: Chiralpak AS-H  
Eluent: 5% i-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.72	10.34	12.10	44.1239	101.419	98.484	0.383
2	12.56	12.14	13.16	0.6792	3.13483	1.516	0.314



**HPLC conditions:**

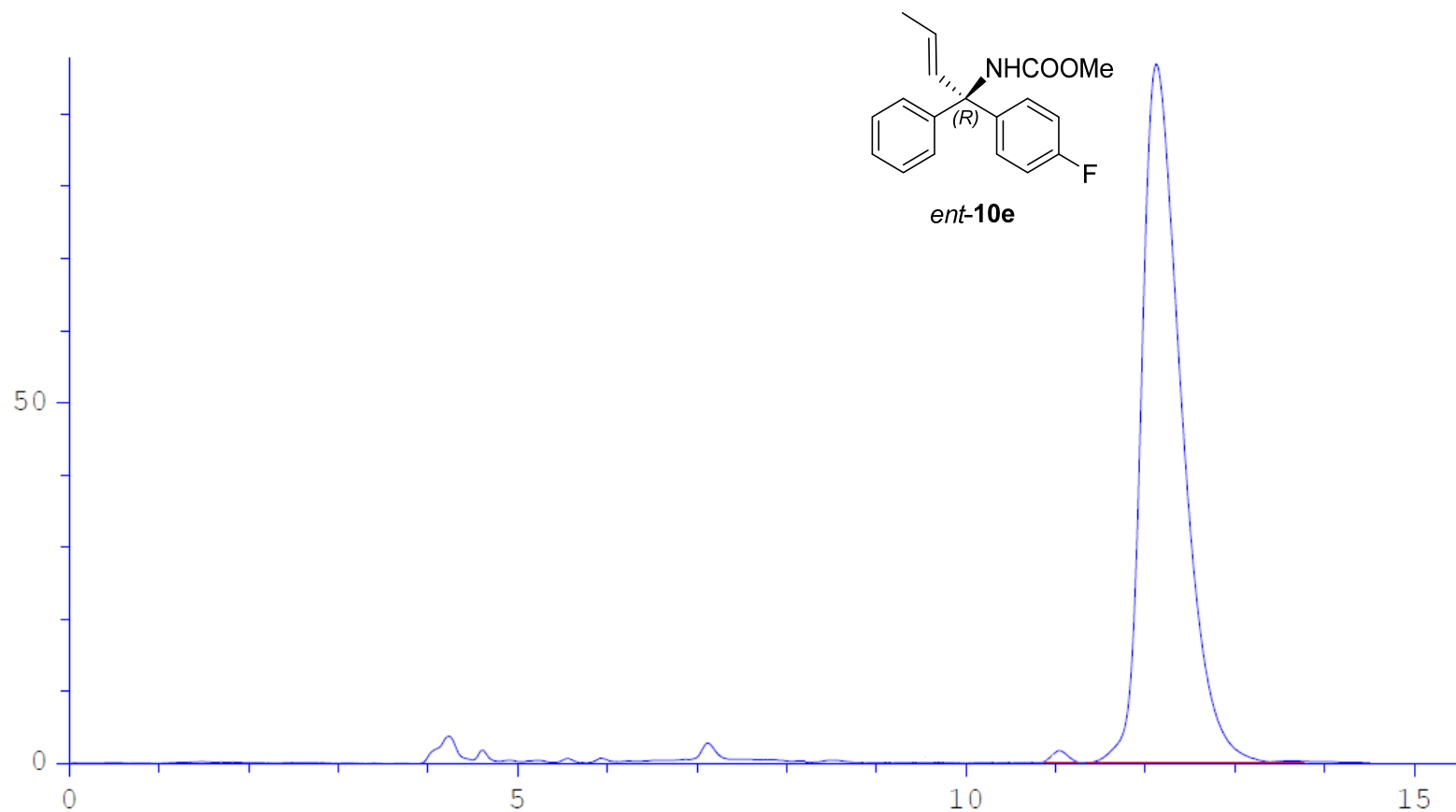
Column: Chiralpak AS-H

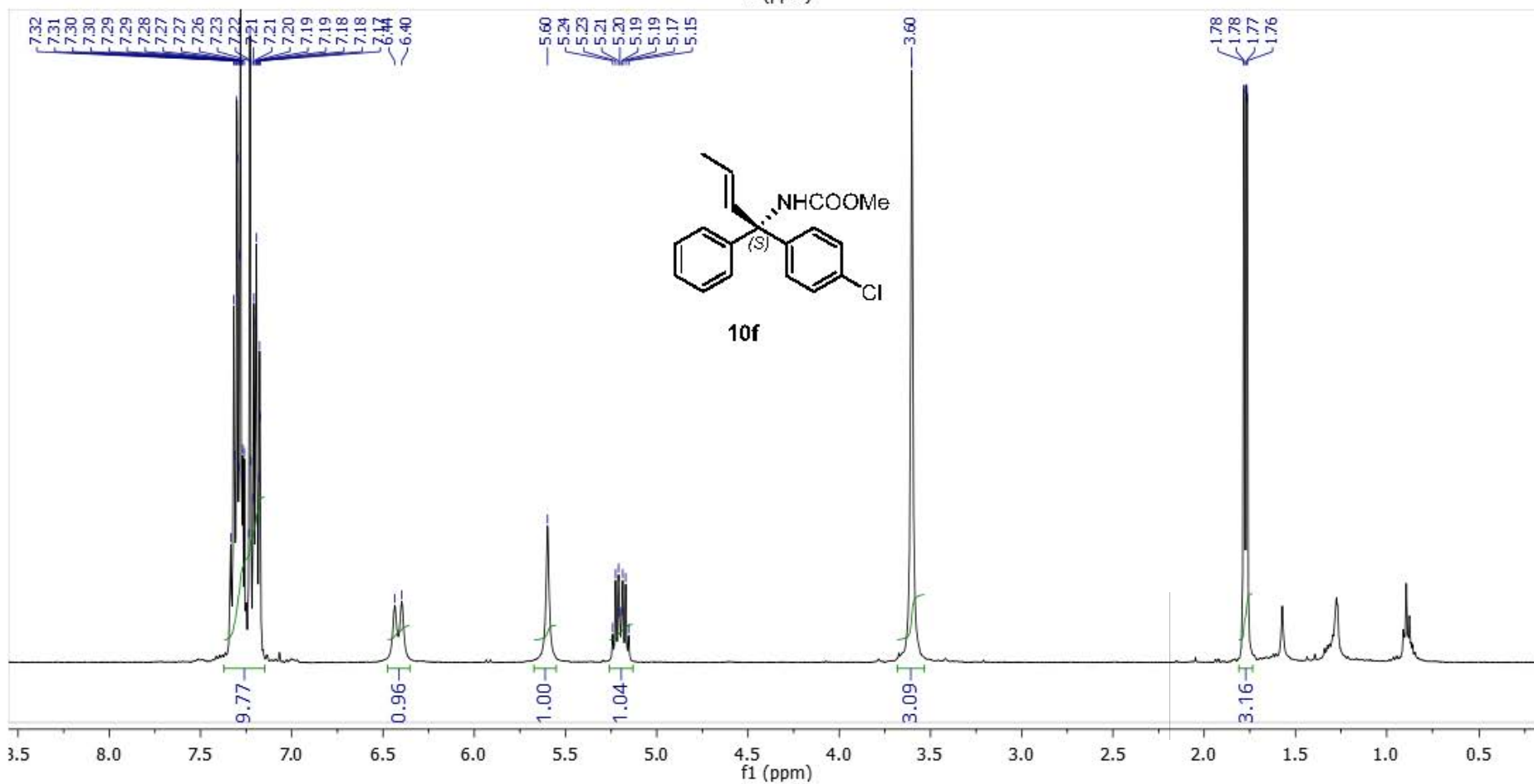
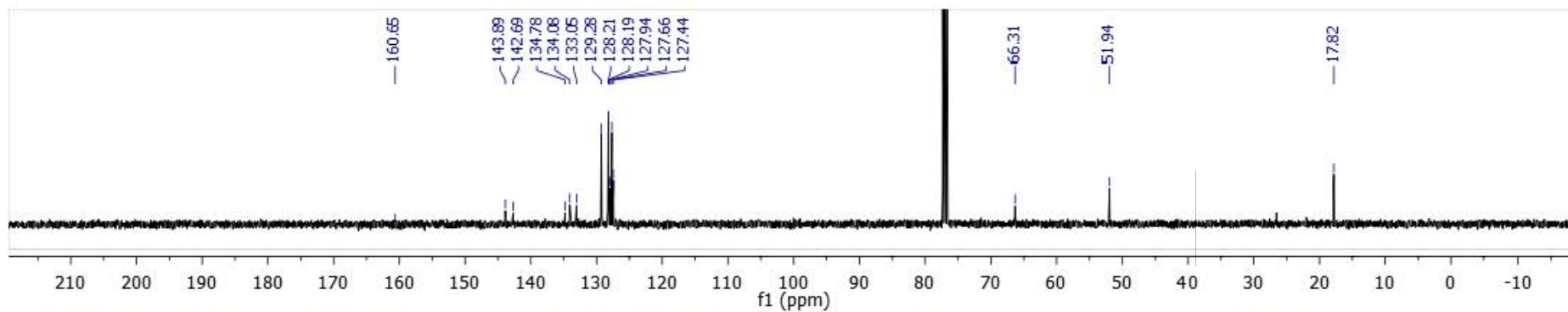
Eluent: 5% i-PrOH/hexanes

Flow: 1 mL/min

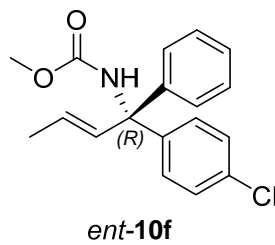
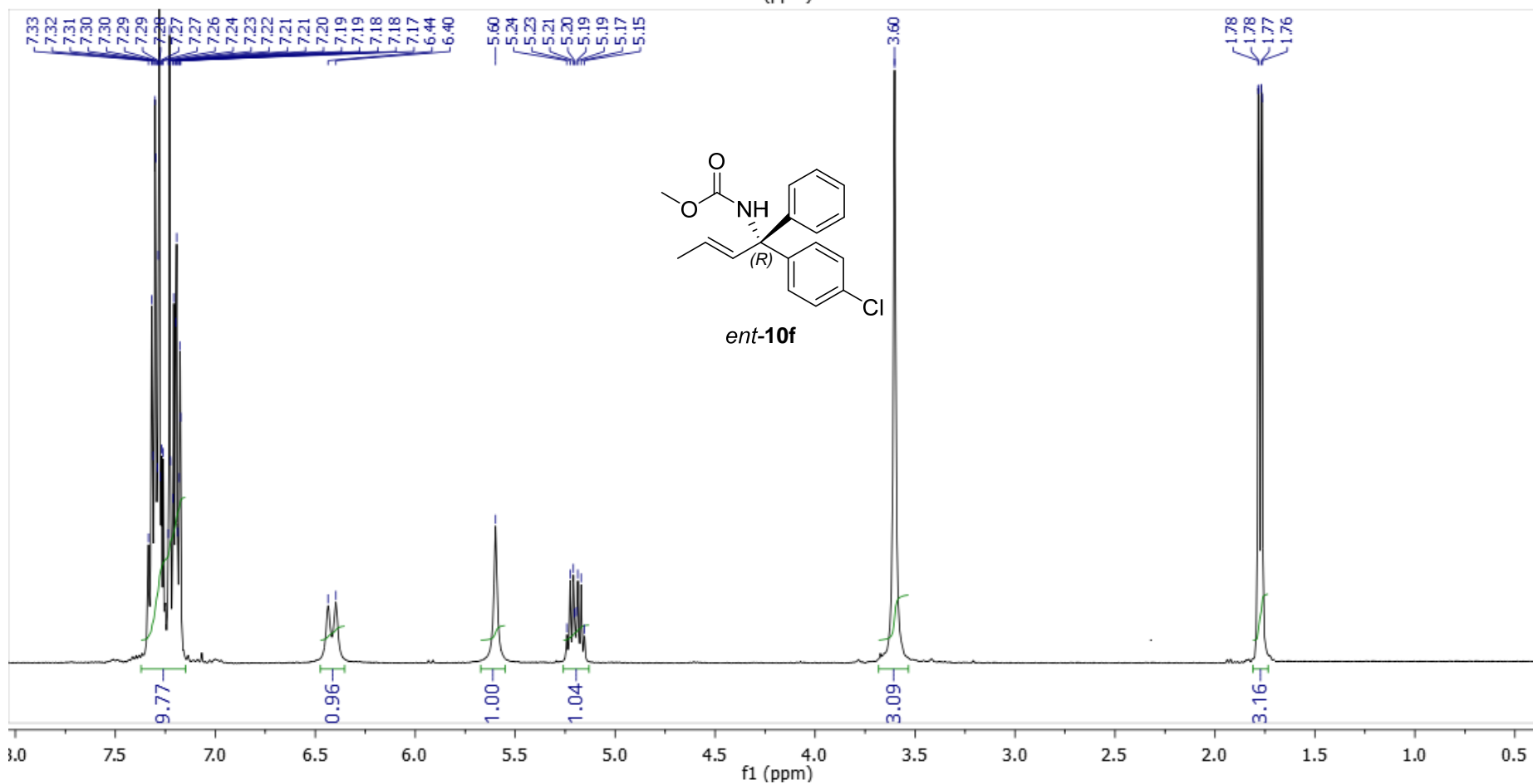
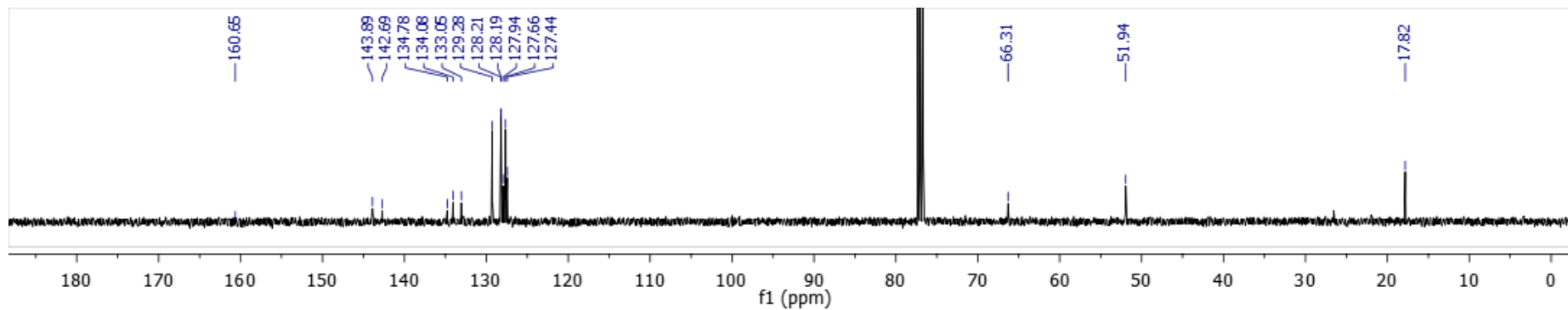
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	11.043	10.77	11.39	0.275721	1.07004	0.5511	0.259
2	12.061	11.41	13.66	49.7587	96.763	99.4489	0.464









### HPLC conditions:

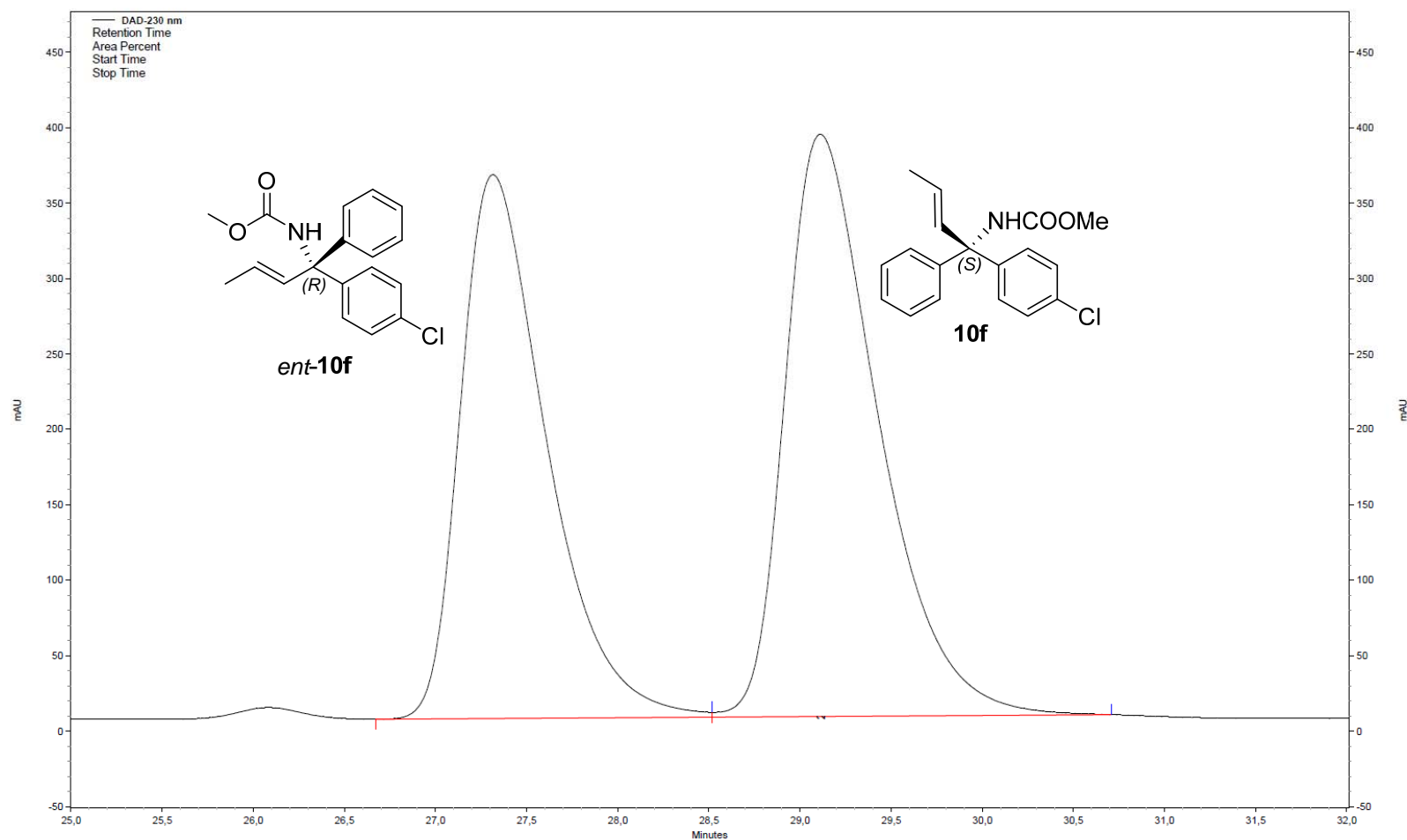
Column: Chiralpak IB

Eluent: 1% *i*-PrOH/hexanes

Flow: 0.5 mL/min

Detection: UV, 230 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	27.31	26.67	28.52	73567543	2576585	46.377	1.54
2	29.11	28.52	30.71	81602522	2726837	53.623	1.67



**HPLC conditions:**

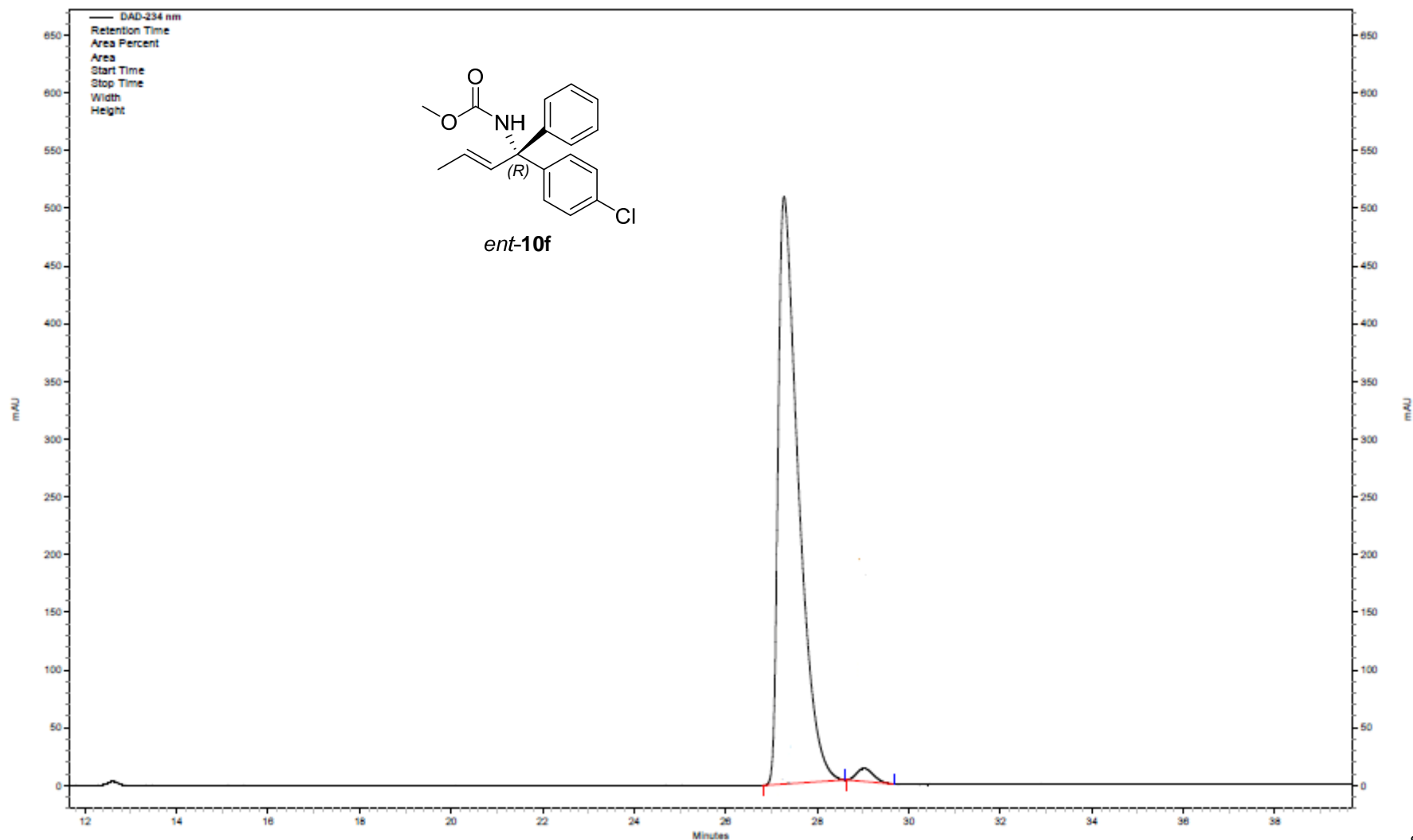
Column: Chiralpak IB

Eluent: 1% *i*-PrOH/hexanes

Flow: 0.5 mL/min

Detection: UV, 230 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	27.2	26.7	28.8	62722306	2035676	98.2	1.79
2	29.1	28.8	29.7	1181091	45924	1.8	1.05



**HPLC conditions:**

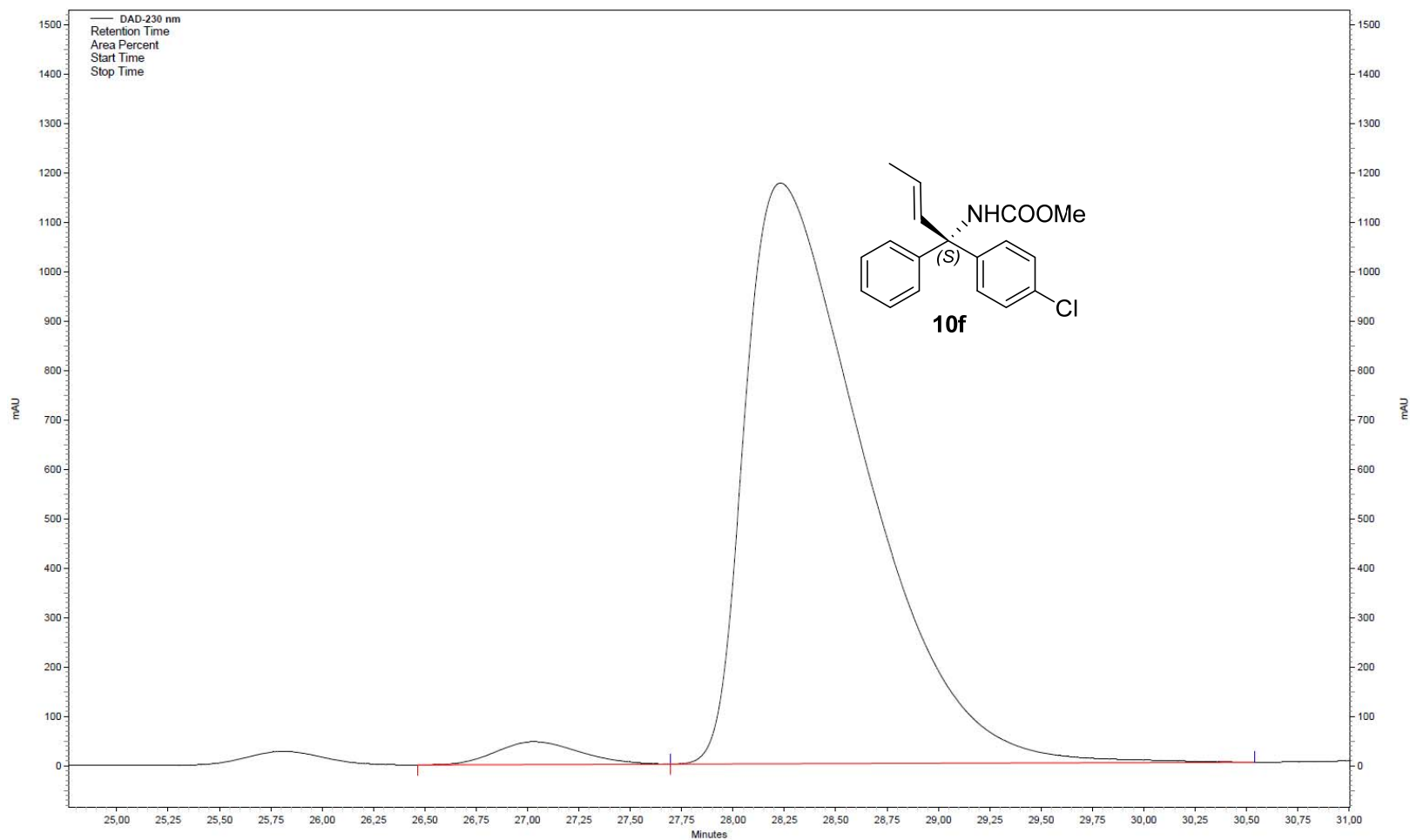
Column: Chiralpak IB

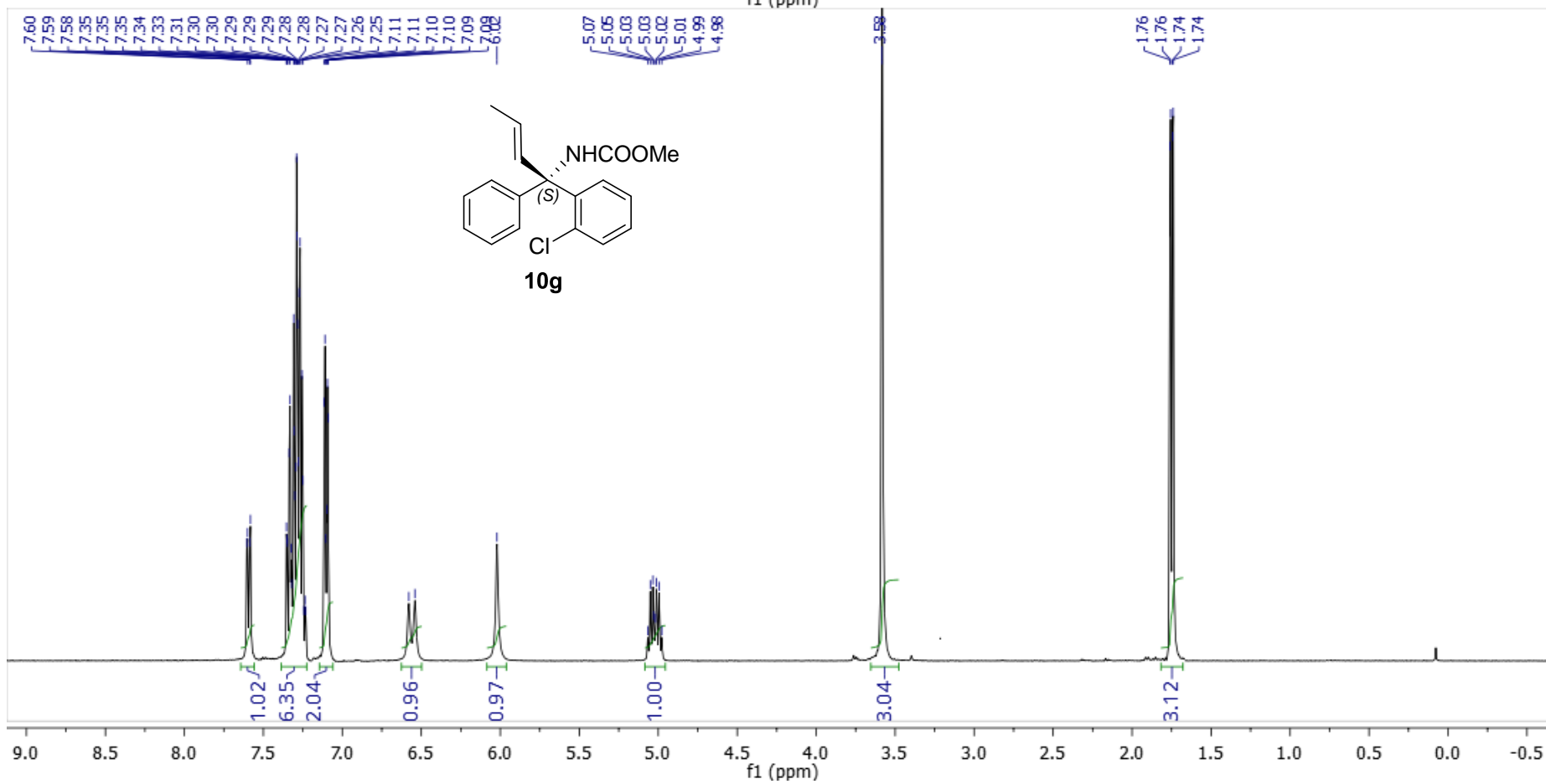
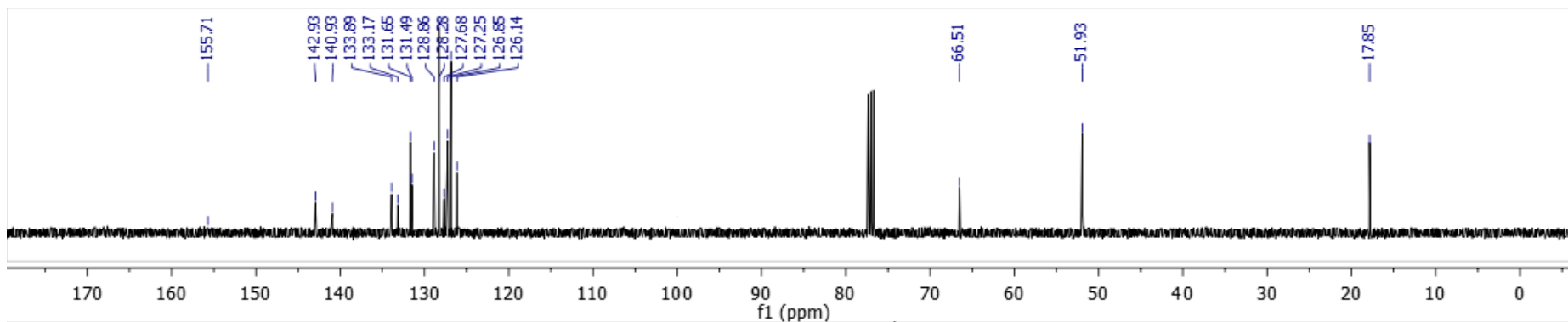
Eluent: 1% *i*-PrOH/hexanes

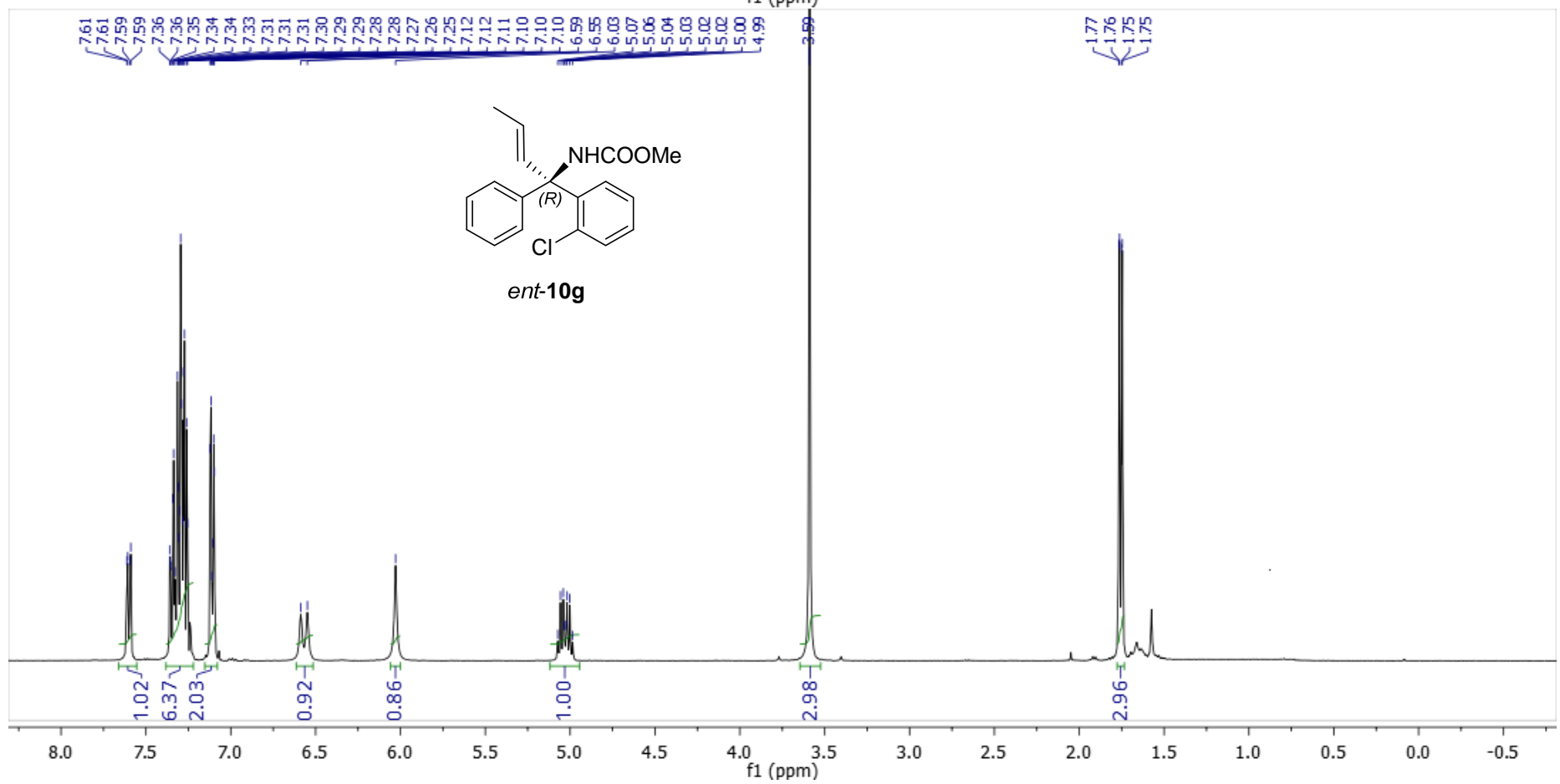
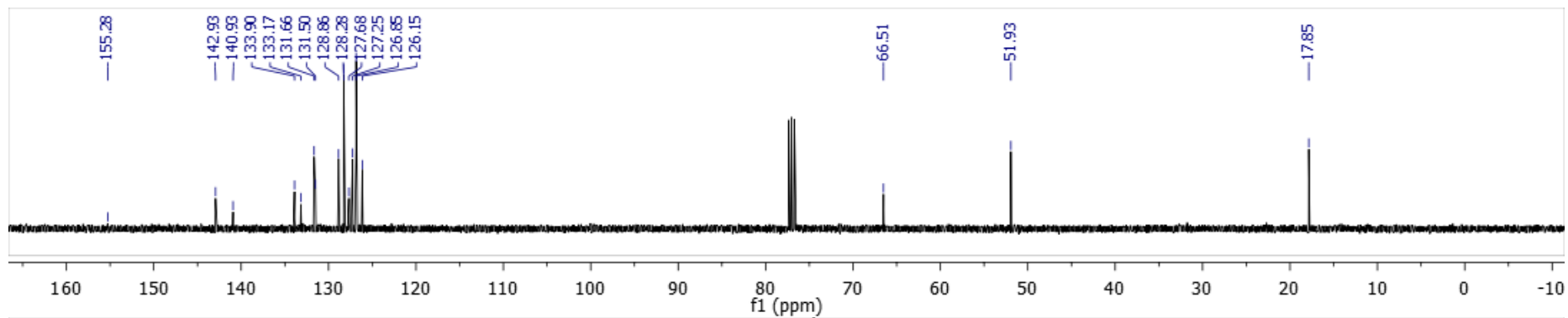
Flow: 0.5 mL/min

Detection: UV, 230 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	27.03	26.47	27.69	4335299	152735	1.689	1.57
2	28.23	27.69	30.54	159556506	3975131	98.311	1.68







**HPLC conditions:**

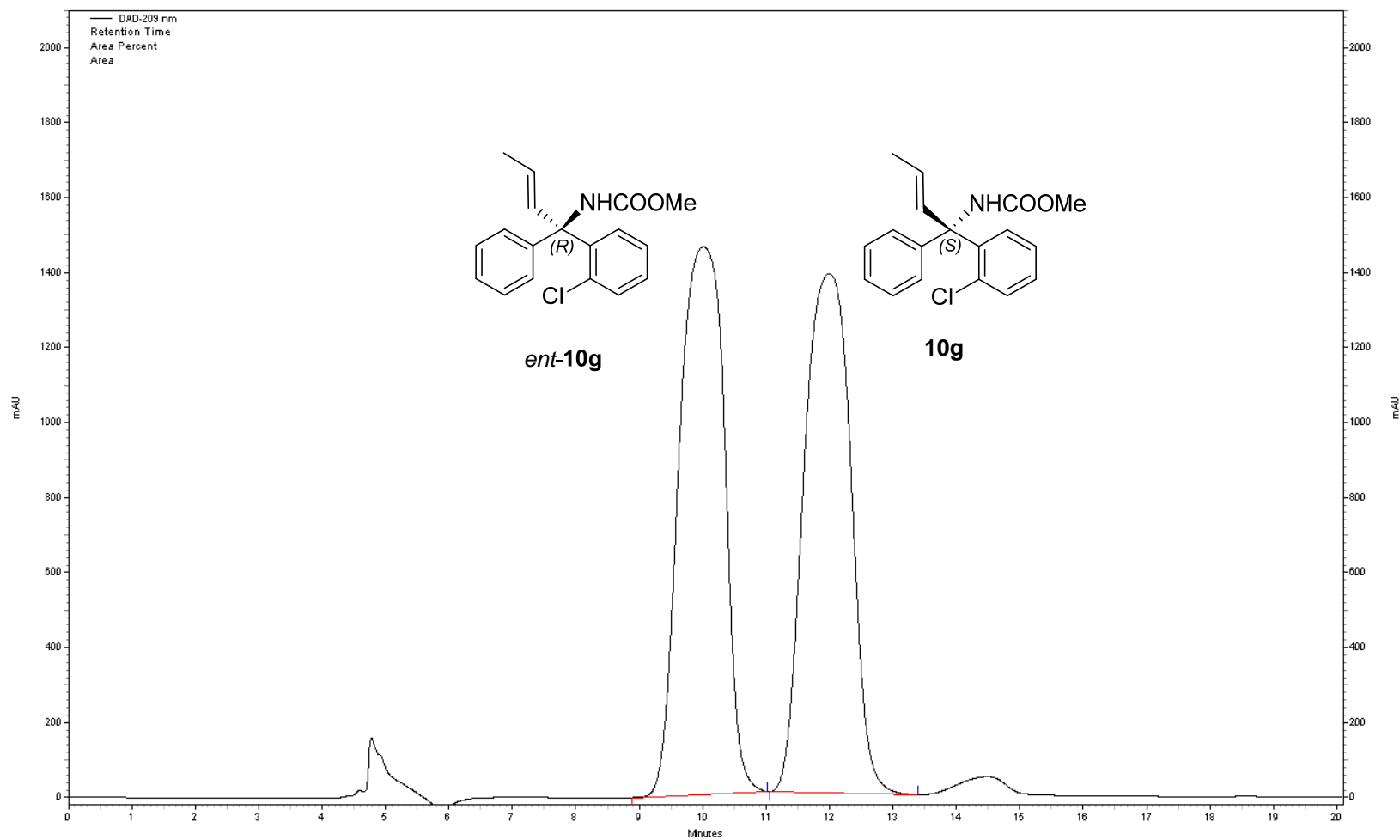
Column: Chiralpak IB

Eluent: 1% i-PrOH/hexanes

Flow: 1mL/min

Detection: UV, 210 nm

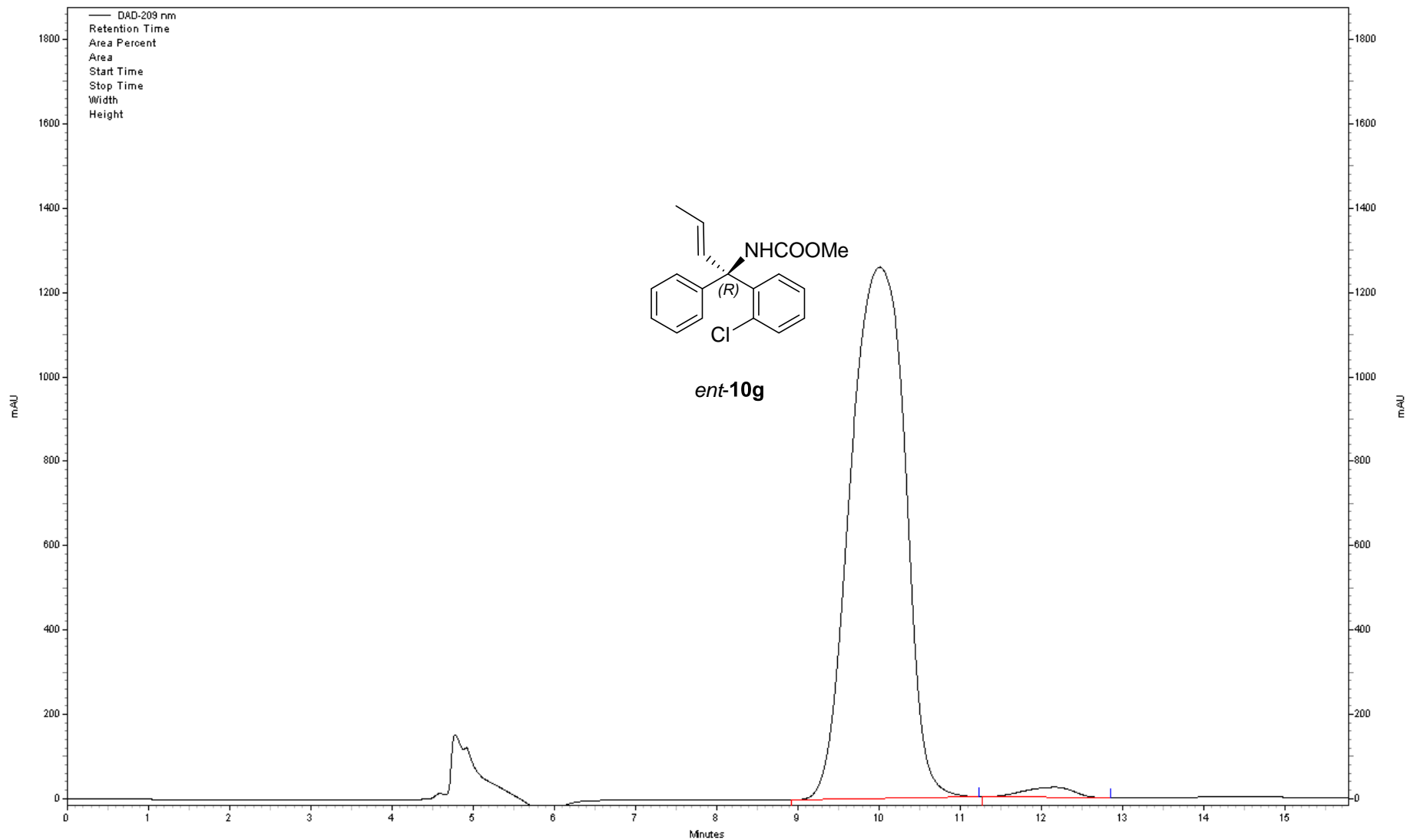
	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.02	8.89	11.05	288913947	5844559	50.5	2.16
2	12.00	11.07	13.32	283569942	5541710	49.5	2.25



**HPLC conditions:**

Column: Chiralpak IB  
Eluent: 1% i-PrOH/hexanes  
Flow: 1mL/min  
Detection: UV, 210 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.01	8.92	11.23	236087759	50400089	98.3	2.31
2	12.17	11.28	12.85	4193200	97939	1.7	1.57





**HPLC conditions:**

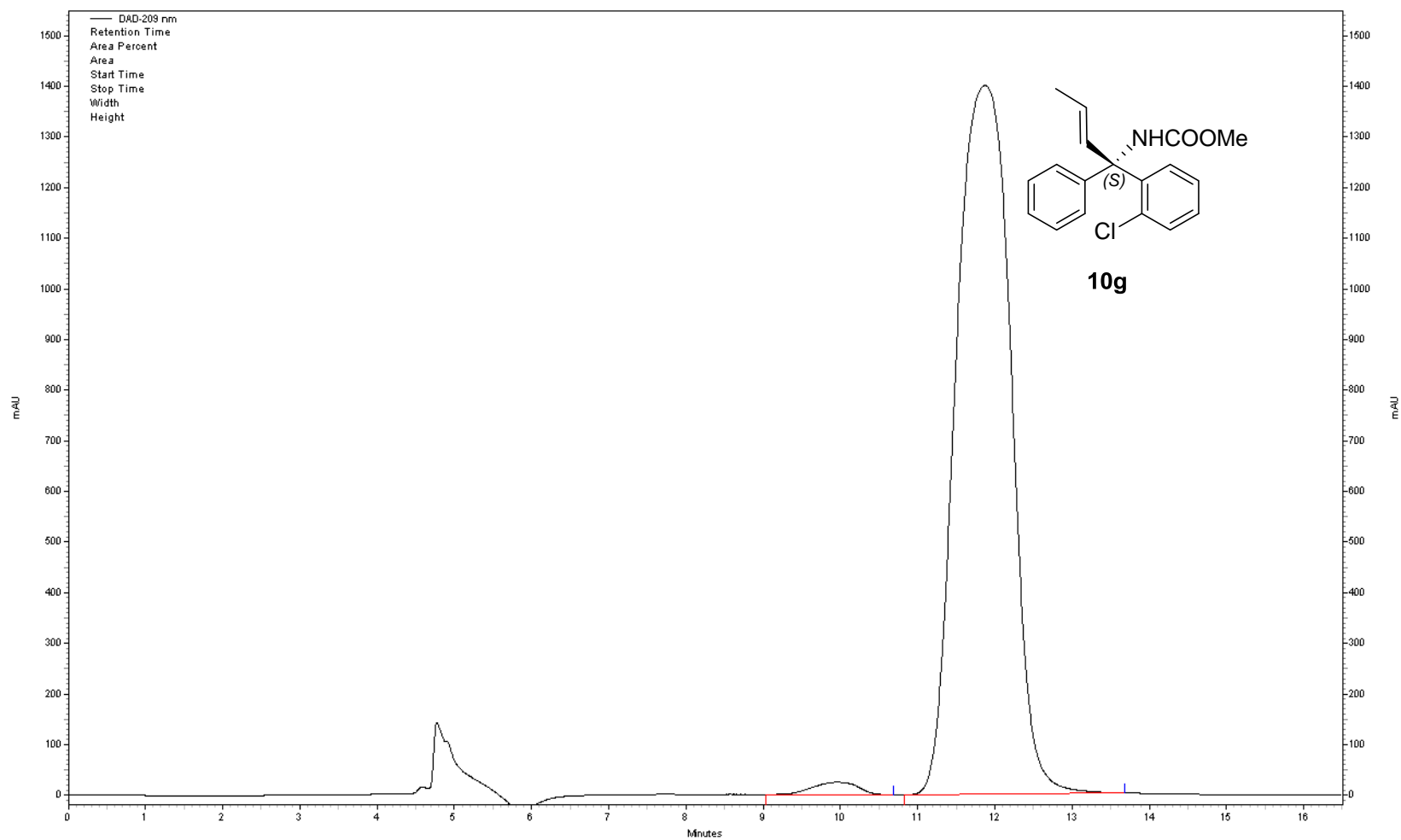
Column: Chiralpak IB

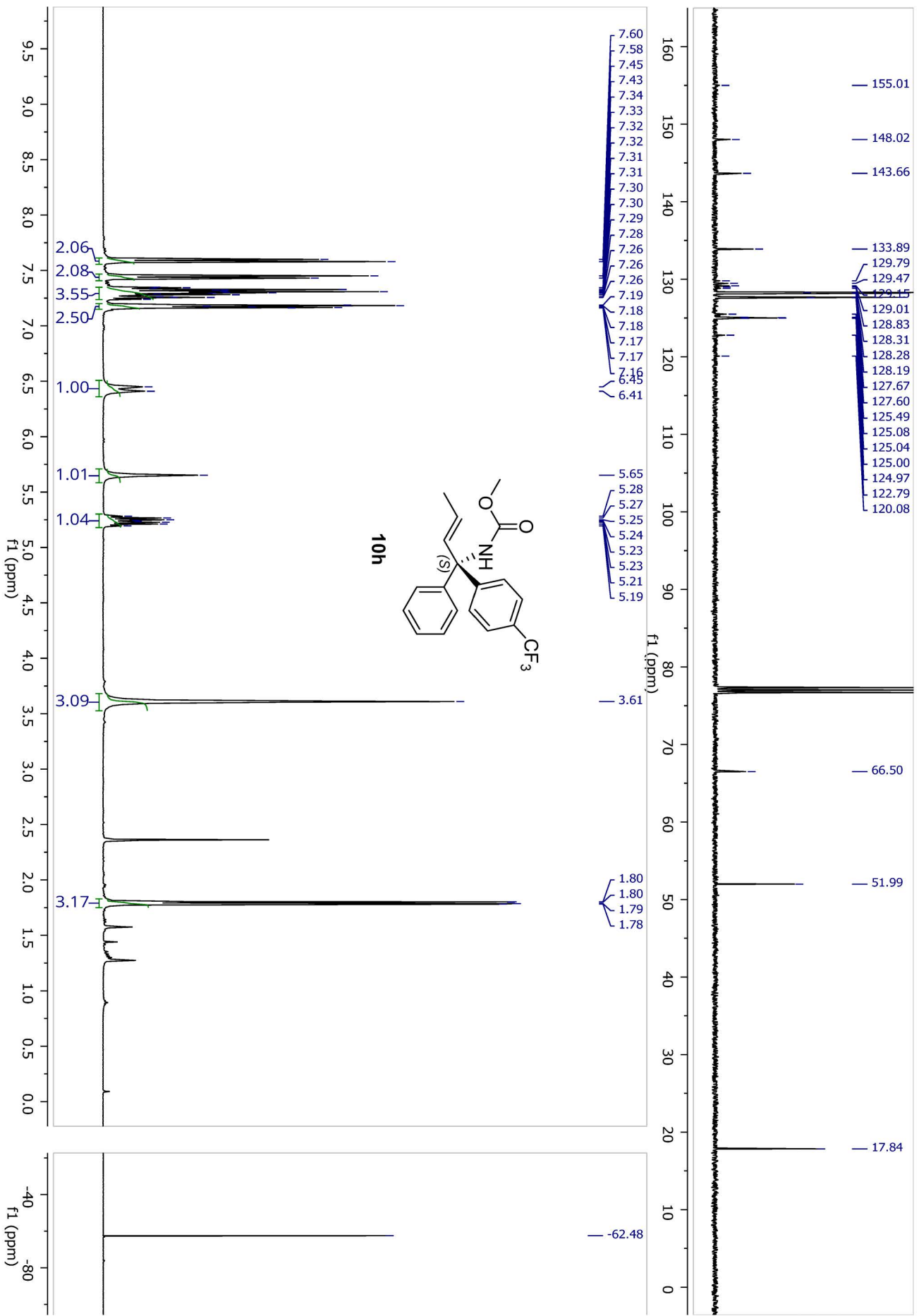
Eluent: 1% i-PrOH/hexanes

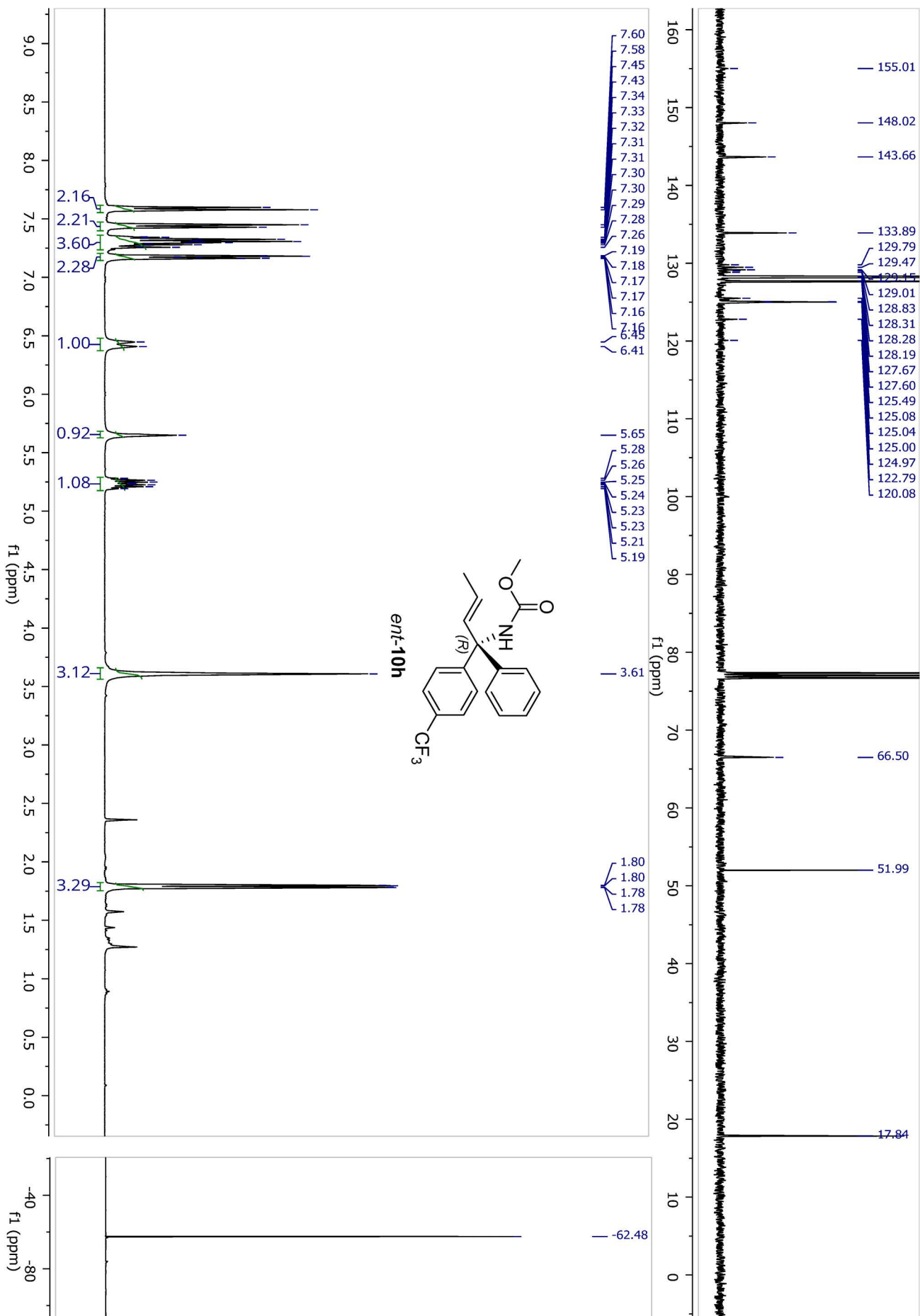
Flow: 1mL/min

Detection: UV, 210 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.96	9.04	10.68	3979644	97914	1.4	1.64
2	11.87	10.83	13.68	274830313	5598206	98.6	2.85







**HPLC conditions:**

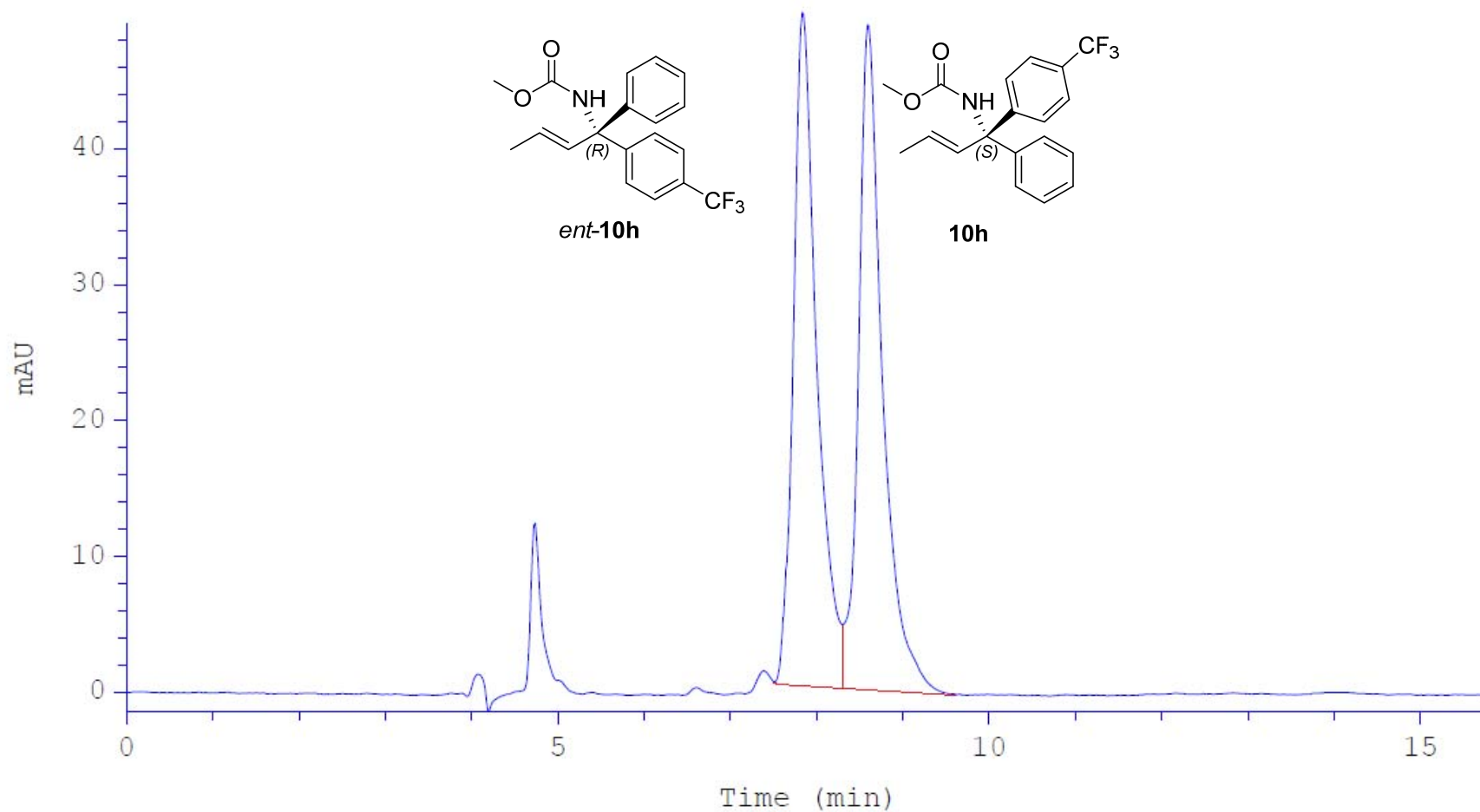
Column: OD-H

Eluent: 5% i-PrOH/hexanes

Flow: 1mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.96	7.70	8.31	13.8258	46.0125	51.60	0.255
2	8.59	8.31	9.42	12.9634	45.3904	48.39	0.257



**HPLC conditions:**

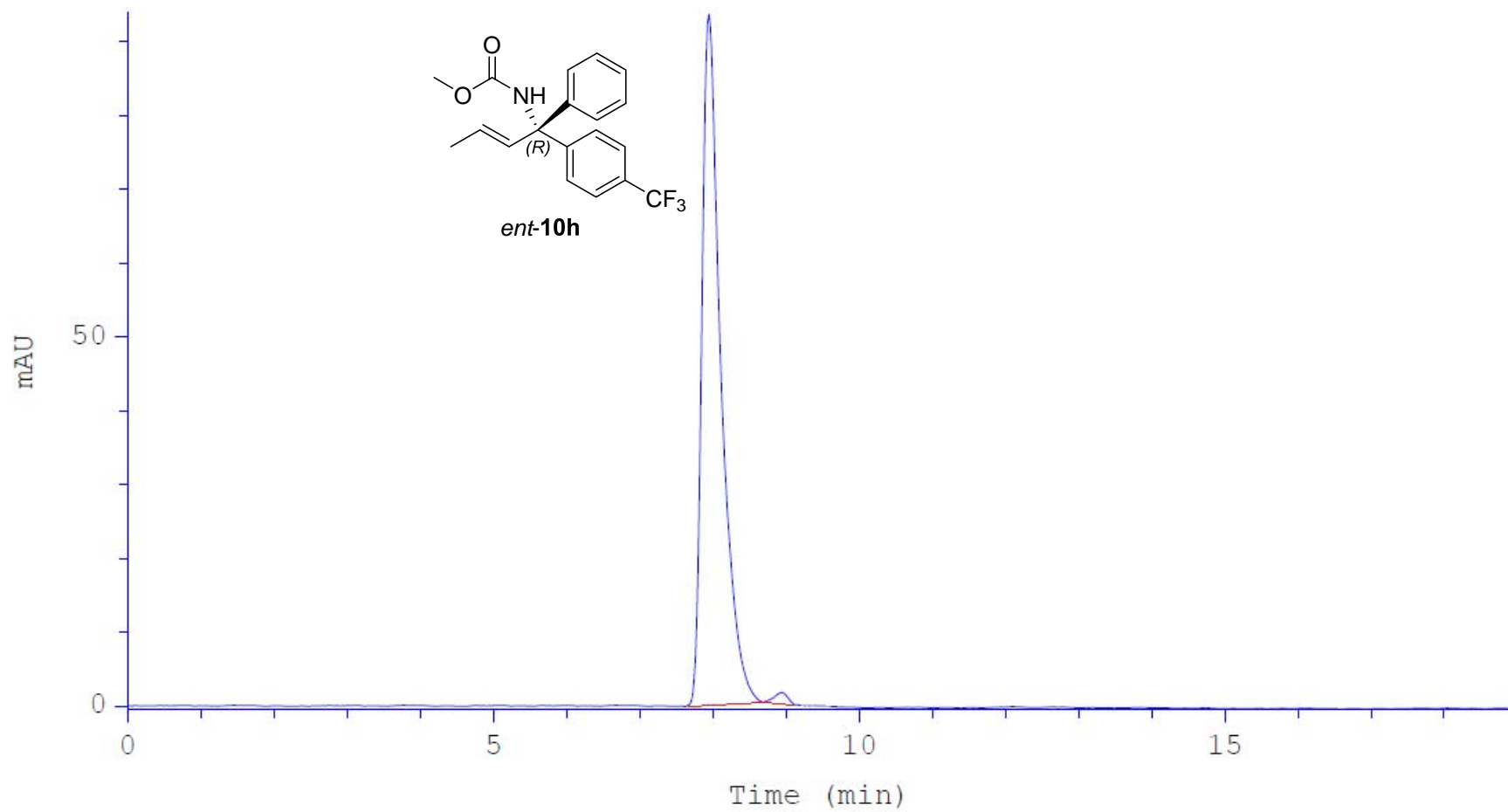
Column: OD-H

Eluent: 5% i-PrOH/hexanes

Flow: 1 mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.12	8.01	8.86	18.7010	46.0125	98.87	0.235
2	8.98	8.88	9.17	0.2137	2.2897	1.13	0.257



**HPLC conditions:**

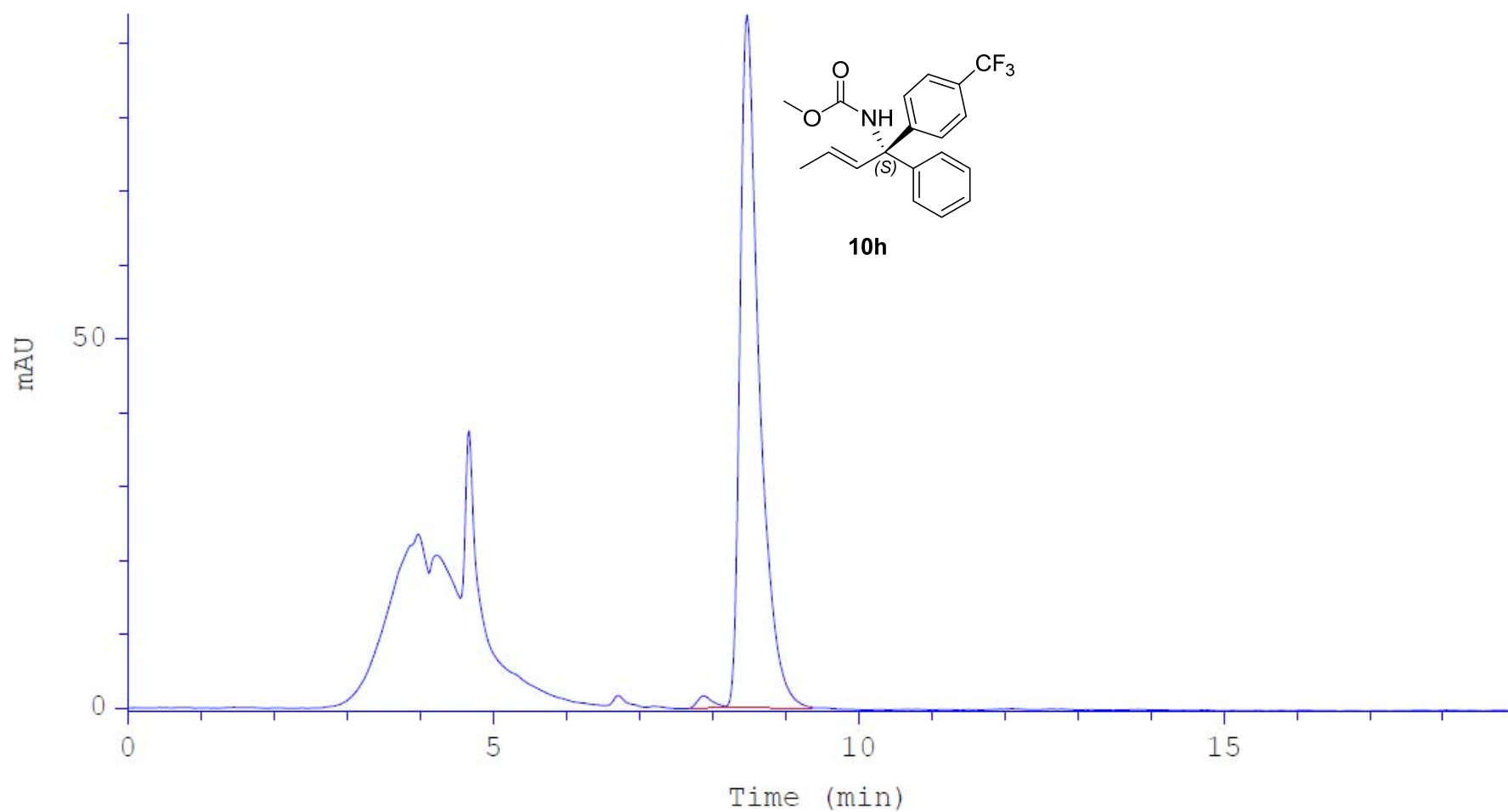
Column: OD-H

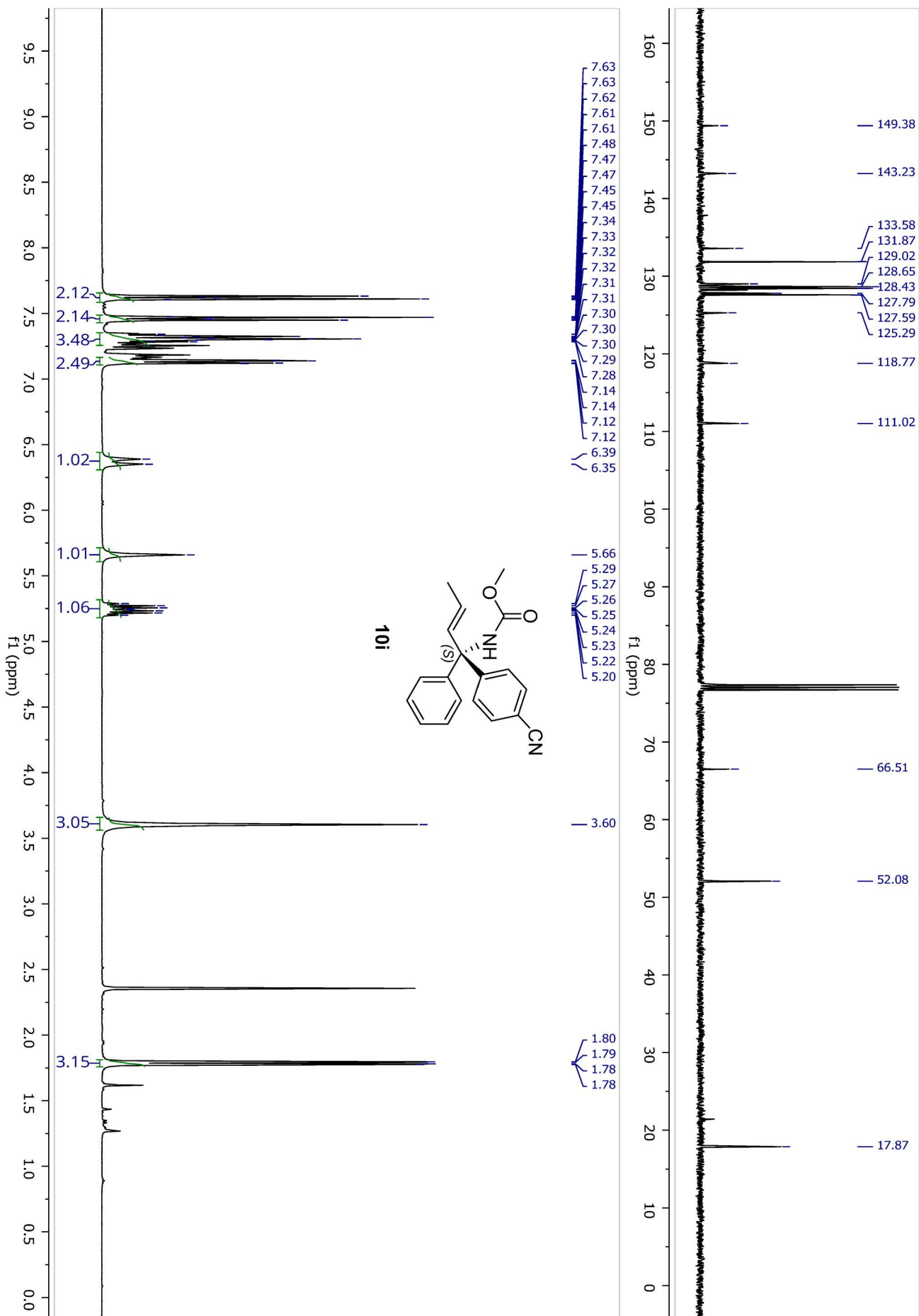
Eluent: 5% i-PrOH/hexanes

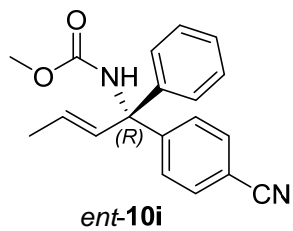
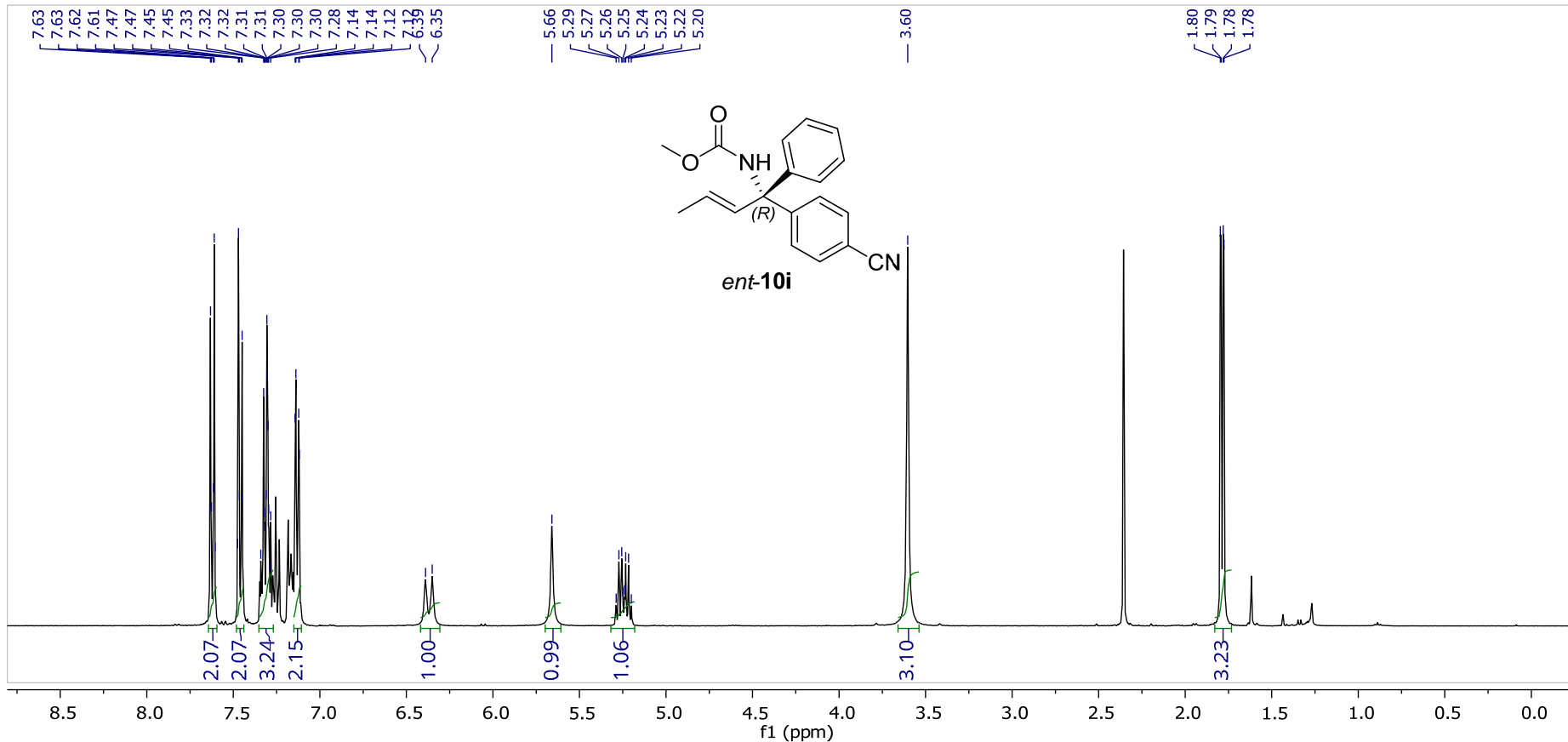
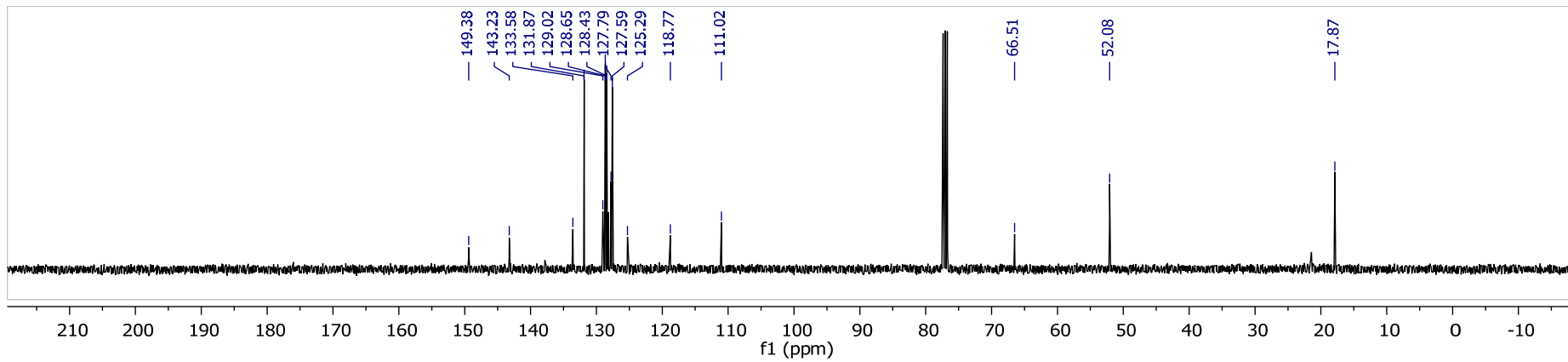
Flow: 1mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.87	7.66	8.19	0.35999	1.59723	1.2945	1.57
2	8.47	8.19	9.41	28.6392	93.6668	98.7055	1.68









**HPLC conditions:**

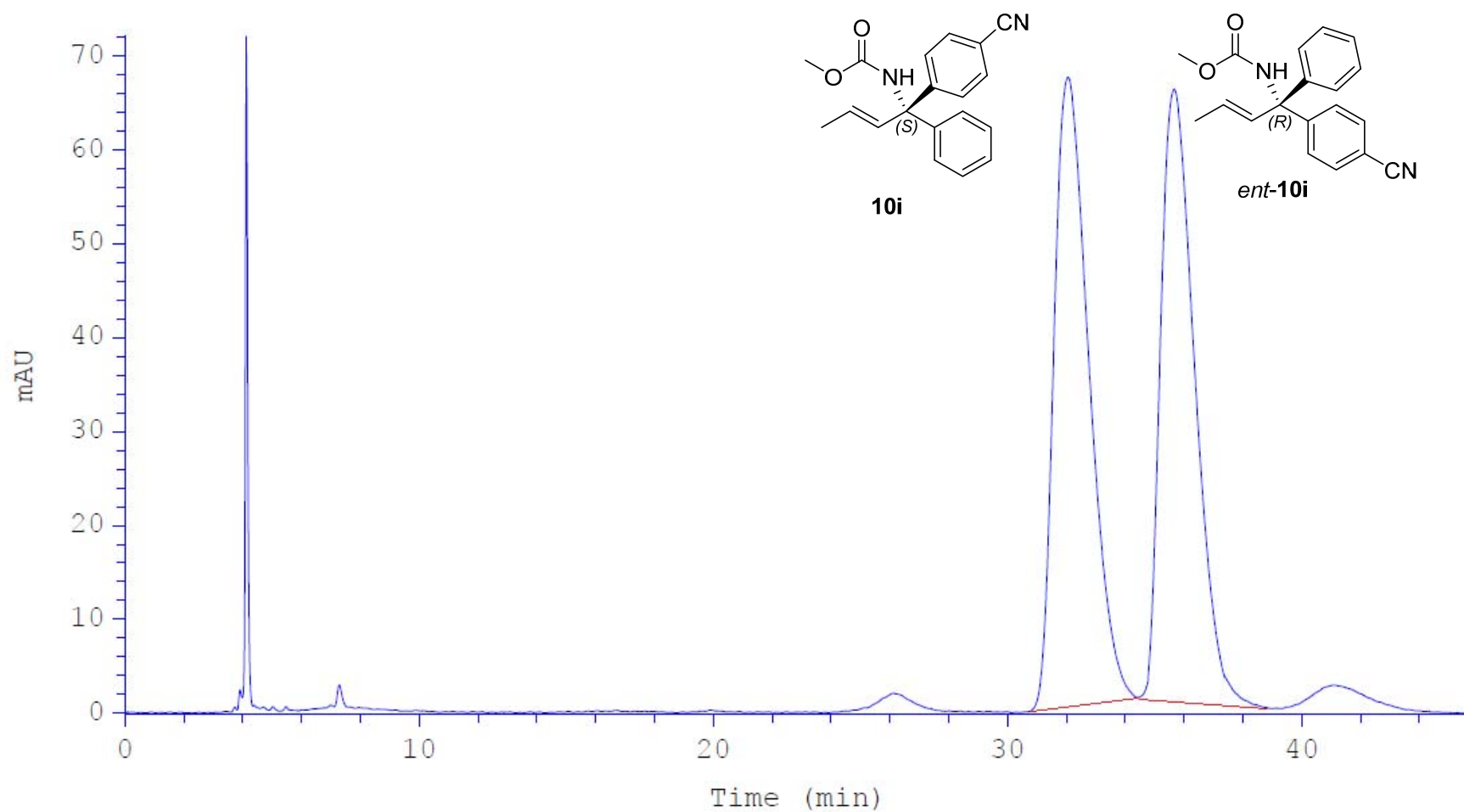
Column: AS-H

Eluent: 5% *i*-PrOH/hexanes

Flow: 1 mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	32.056	30.56	34.48	91.9194	67.0434	50.203	1.92
2	35.806	34.48	39.54	91.1763	66.9472	49.797	1.90



**HPLC conditions:**

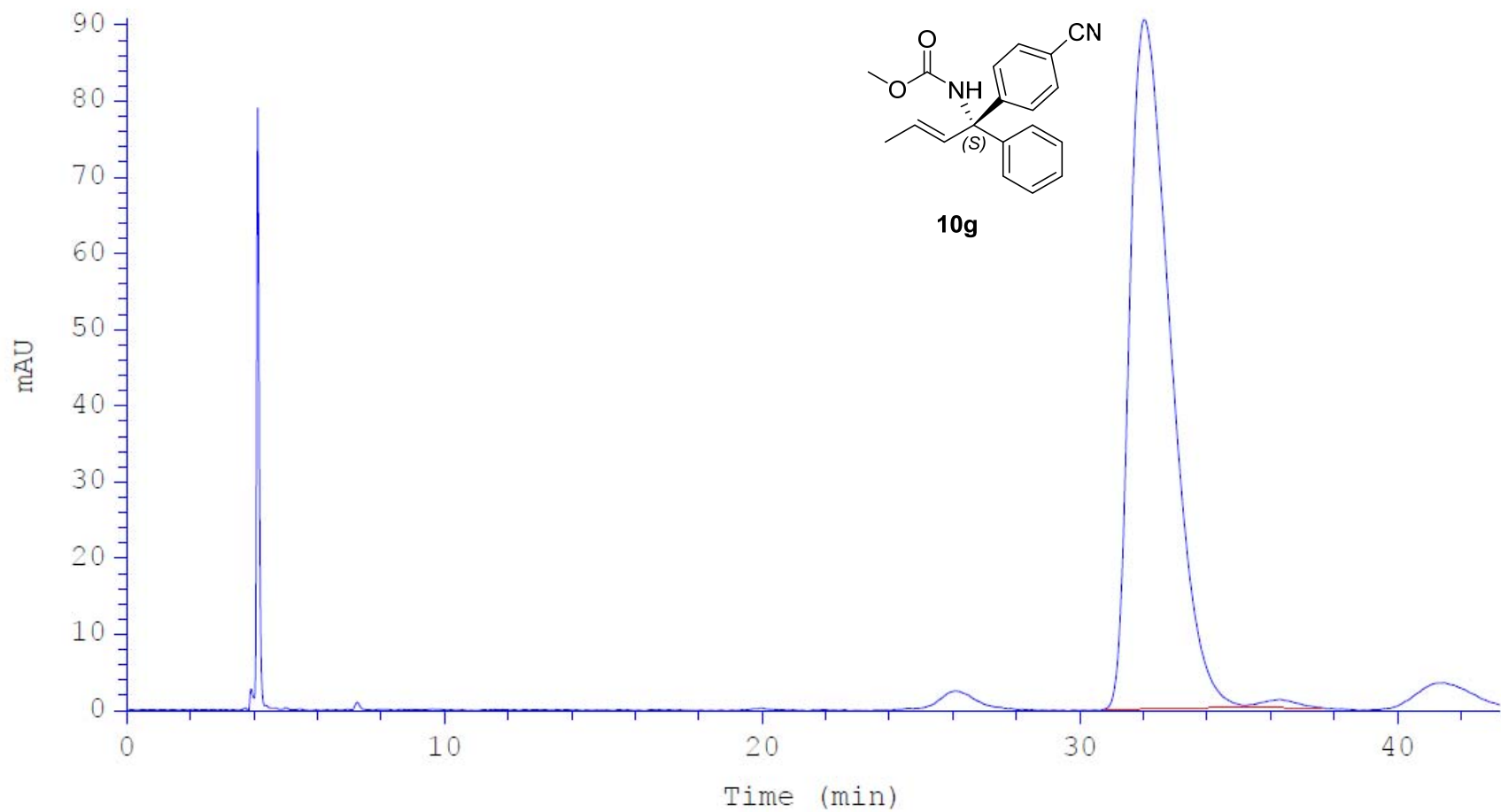
Column: AS-H

Eluent: 5% *i*-PrOH/hexanes

Flow: 1 mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	32.023	30.59	35.21	133.967	90.4768	99.0891	1.389
2	36.291	35.21	37.78	1.23155	0.98613	0.9109	1.247



**HPLC conditions:**

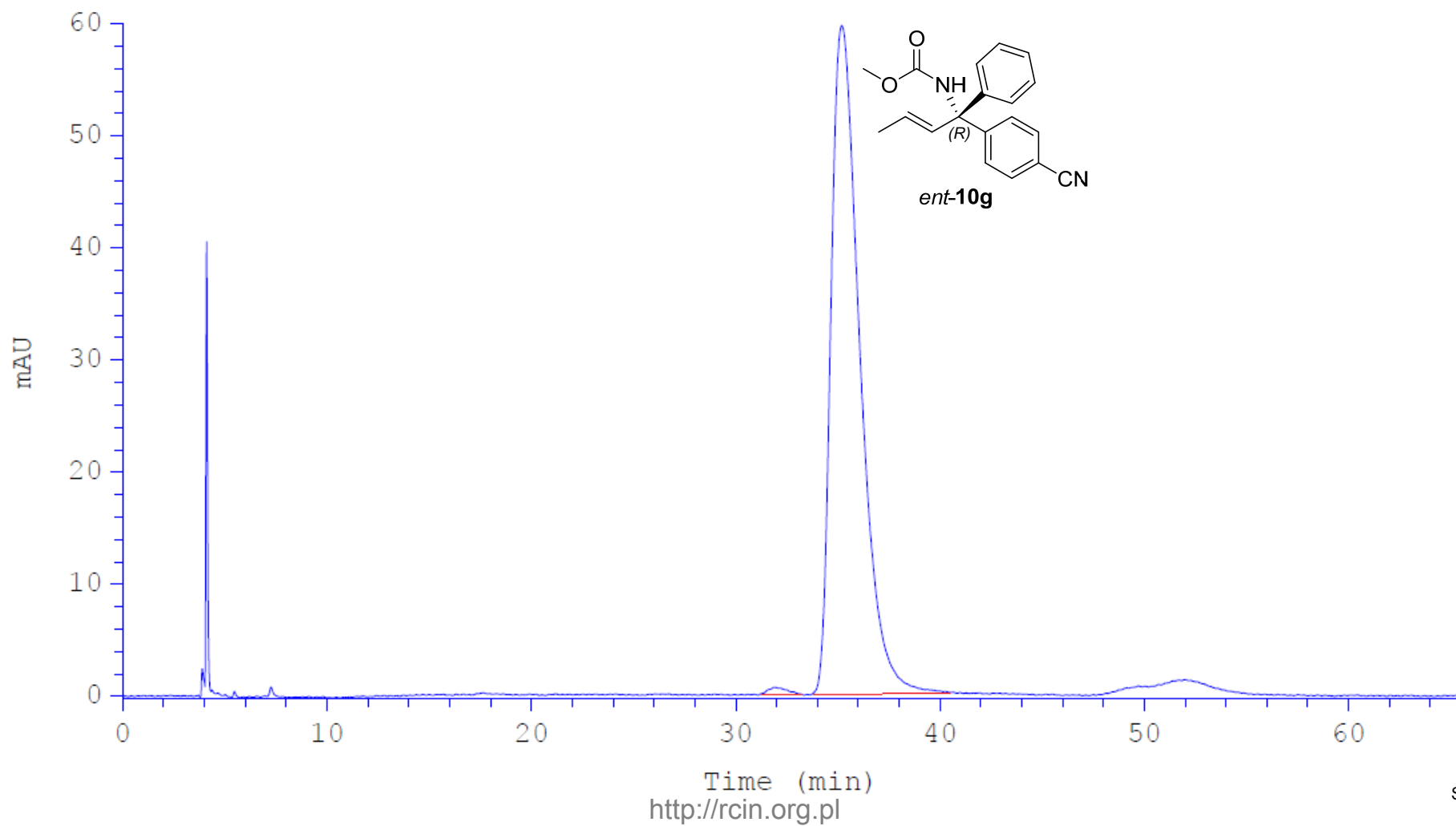
Column: AS-H

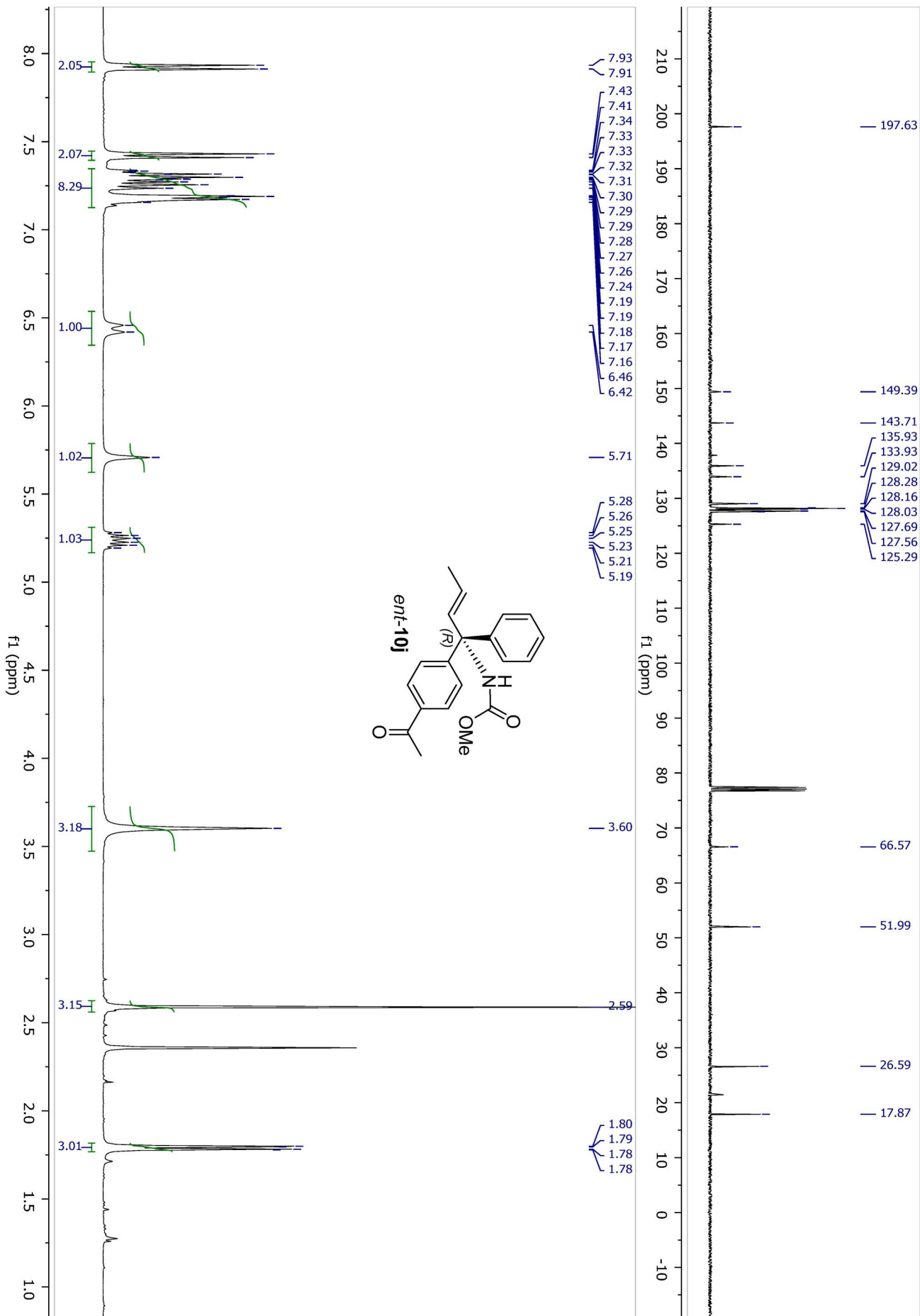
Eluent: 5% *i*-PrOH/hexanes

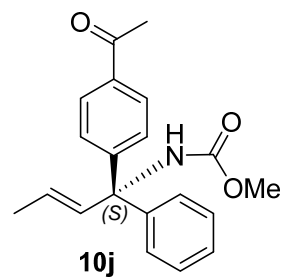
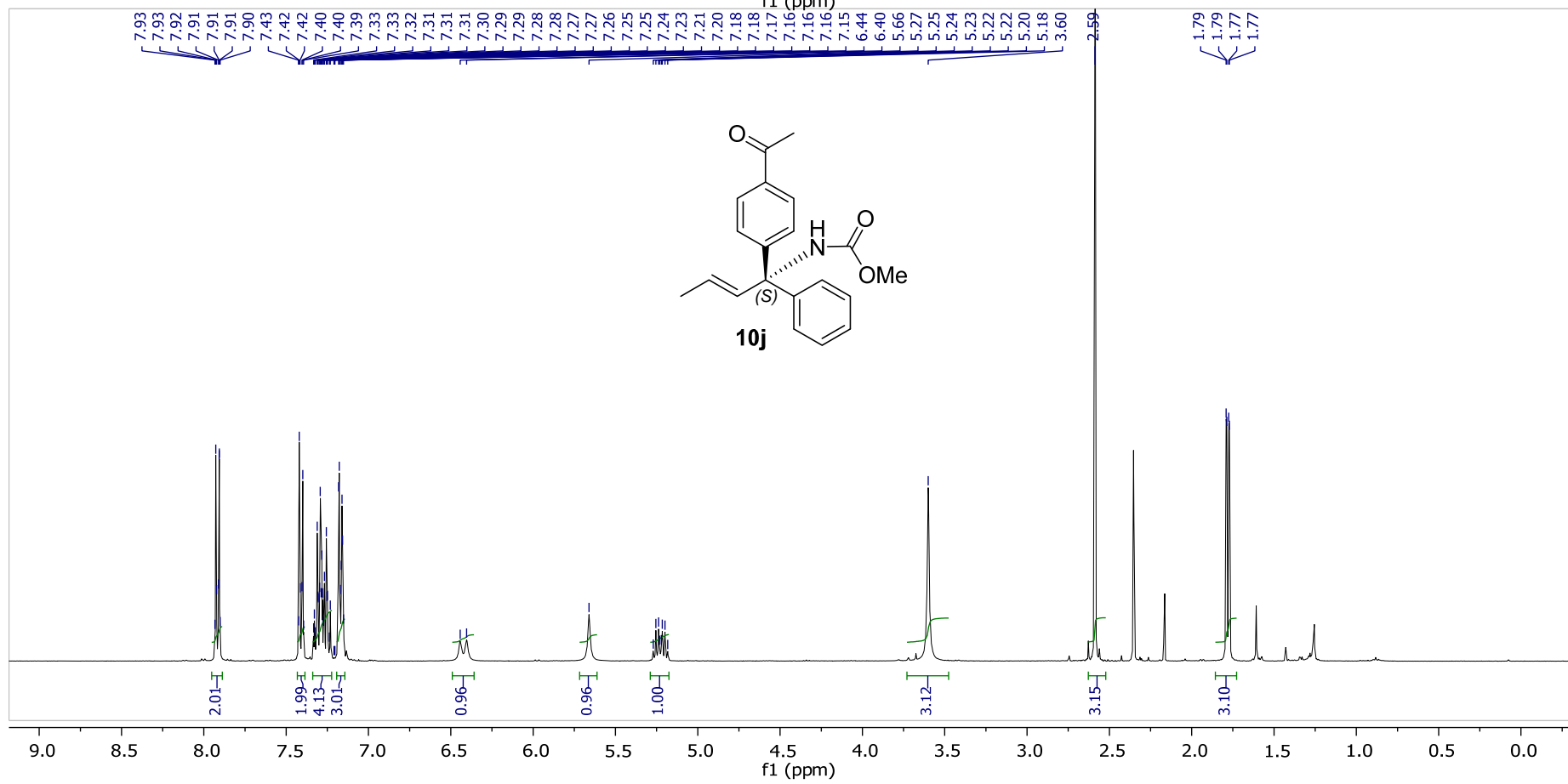
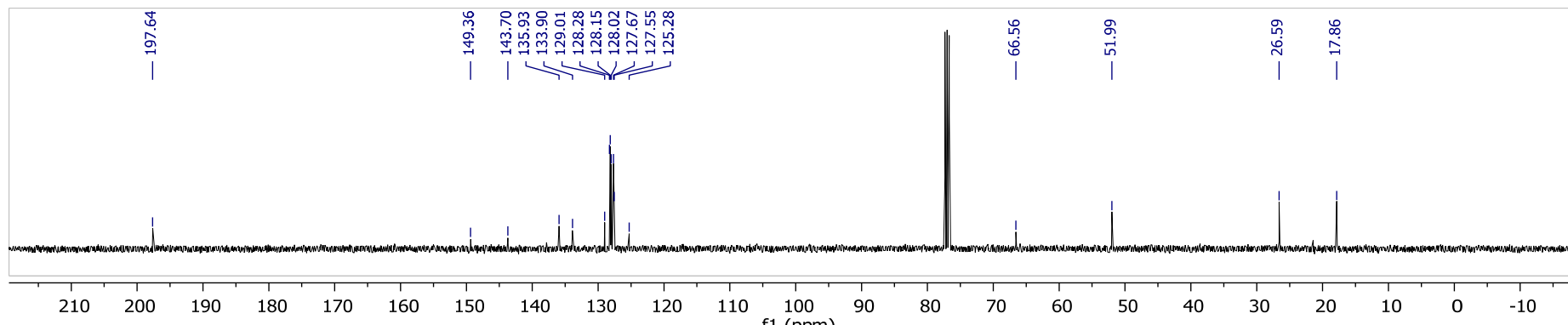
Flow: 1 mL/min

Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	31.952	30.91	33.12	0.609036	0.609957	0.6265	1.070
2	35.186	33.49	39.27	96.6095	59.5216	99.3735	1.486



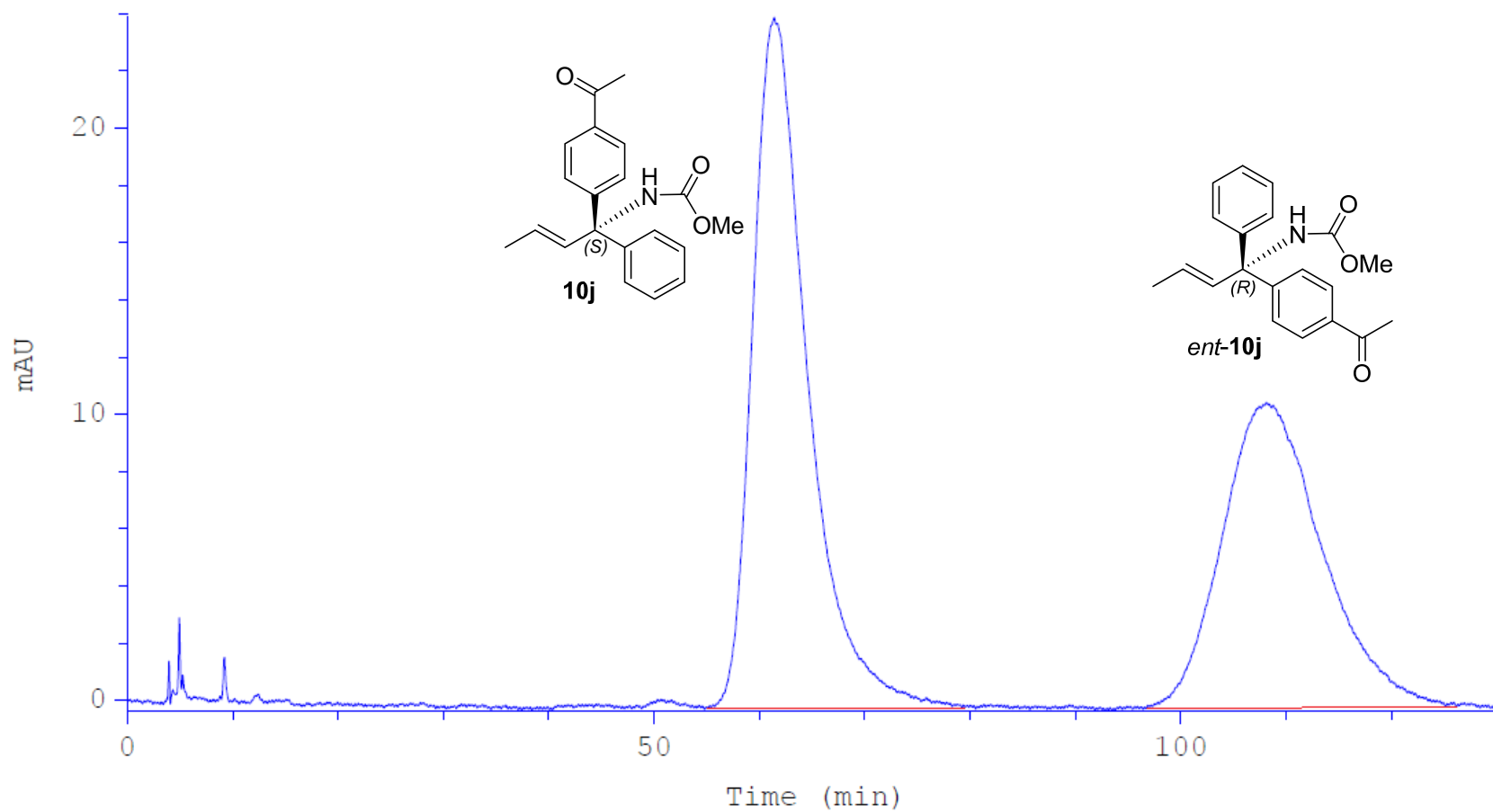




**HPLC conditions:**

Column: Chiralcel OJ-H  
Eluent: 3% *i*-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	61.403	54.28	79.36	144.235	24.051	55.4812	5.279
2	108.105	94.96	128.95	115.736	10.6262	44.5188	9.972



**HPLC conditions:**

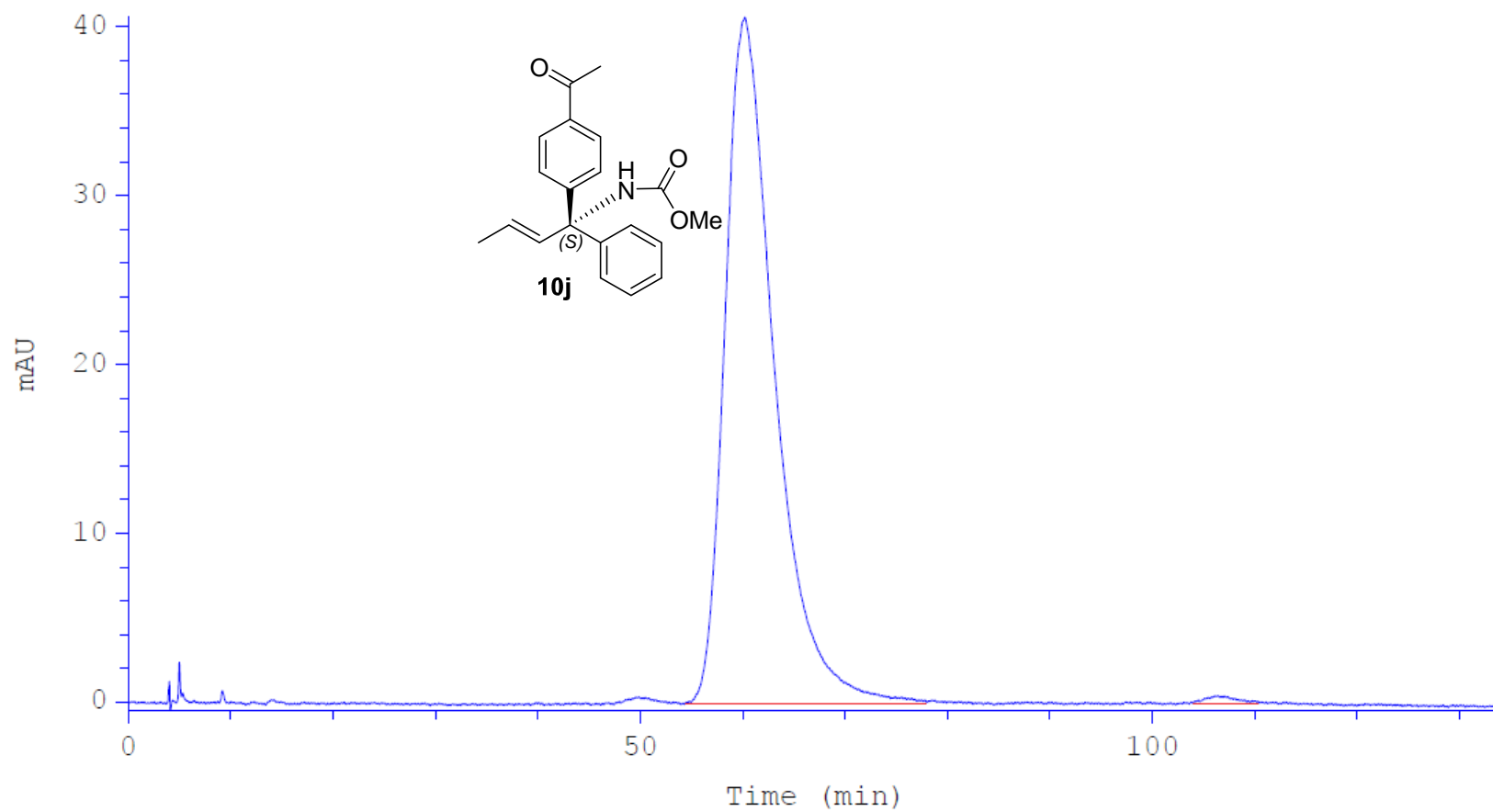
Column: Chiralcel OJ-H

Eluent: 3% *i*-PrOH/hexanes

Flow: 1 mL/min

Detection: UV, 254 nm

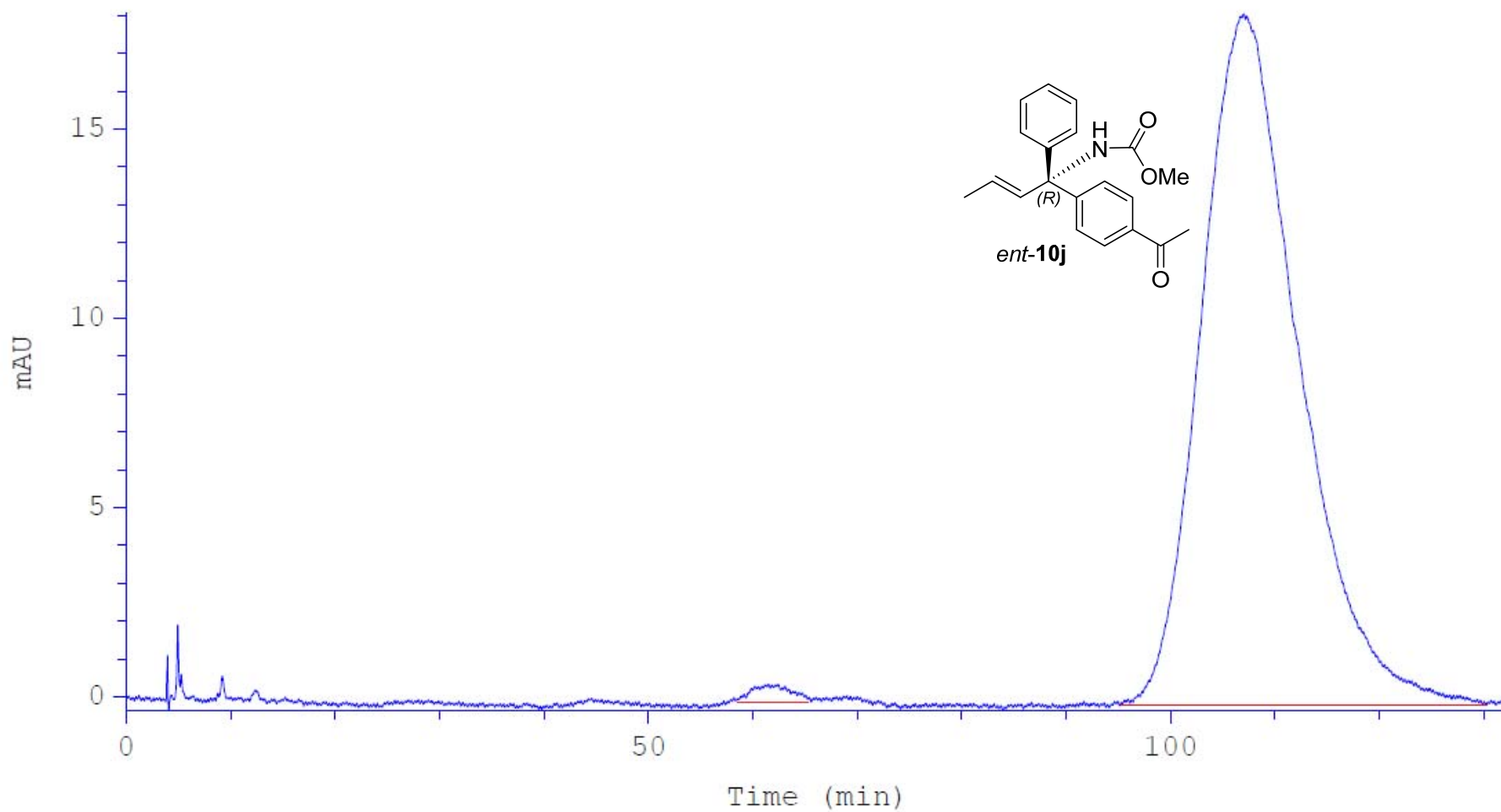
	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	60.202	53.73	81.80	227.008	40.5592	98.992	4.921
2	107.154	105.12	108.19	1.55765	0.448958	1.008	2.256



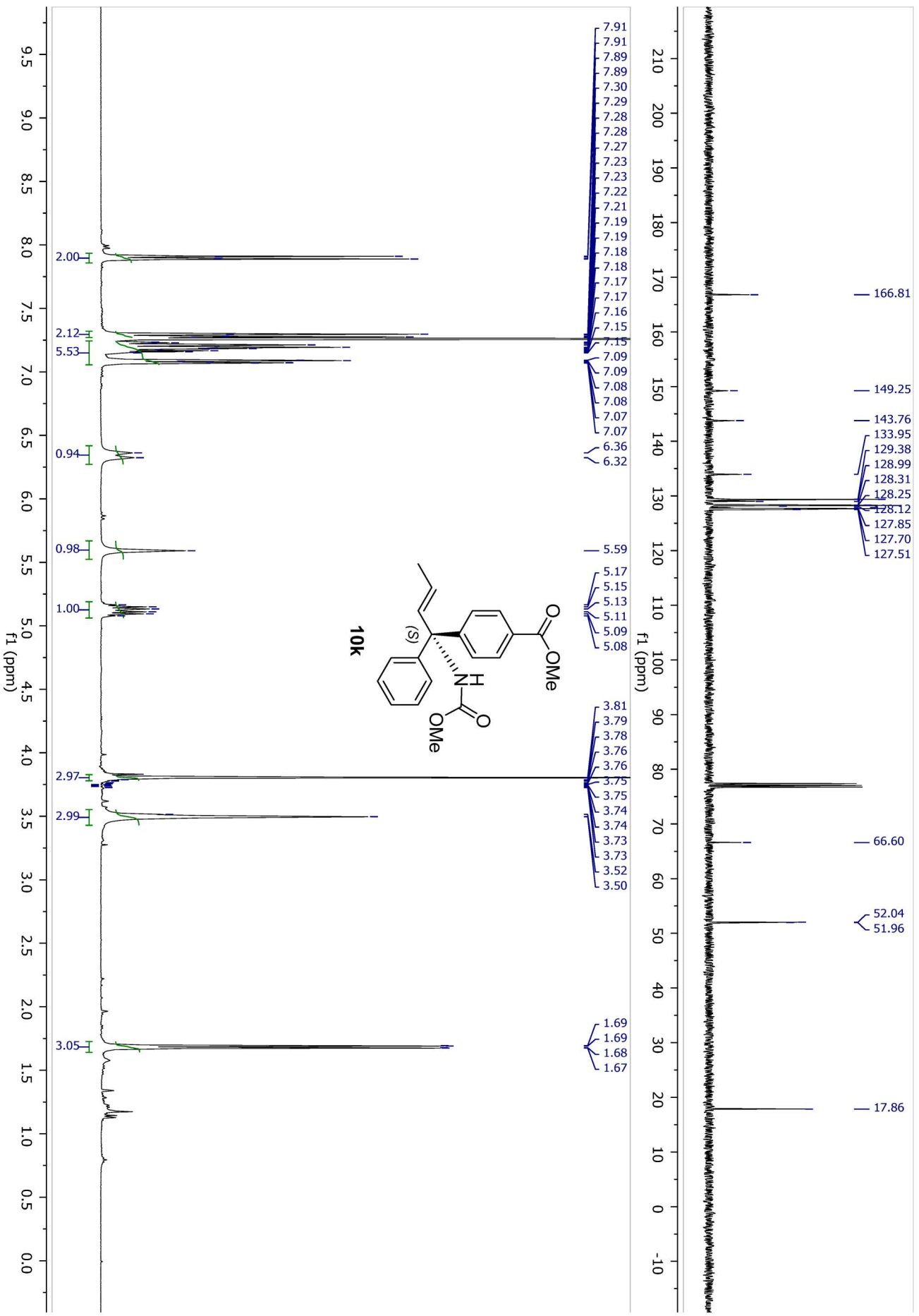
**HPLC conditions:**

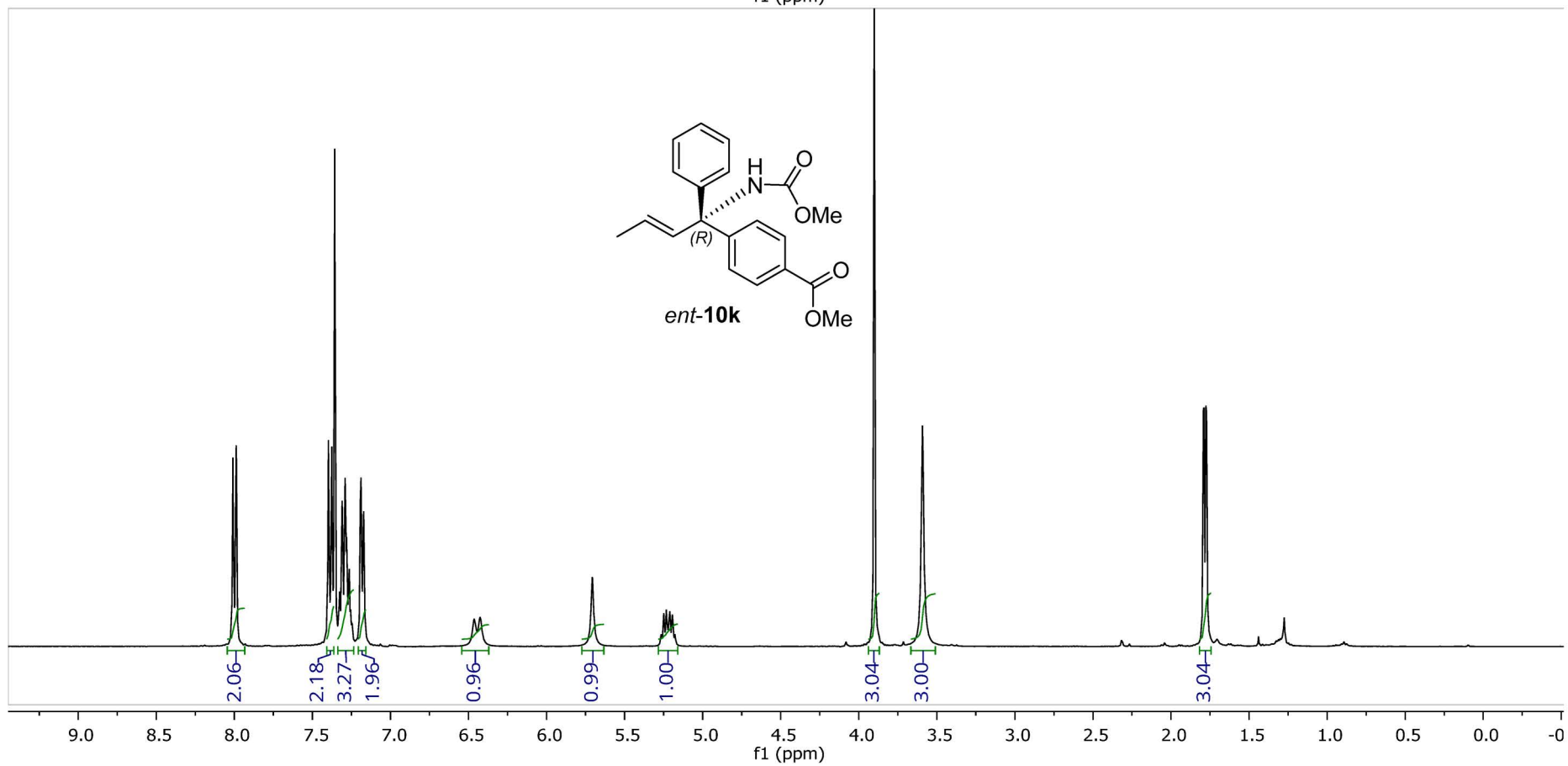
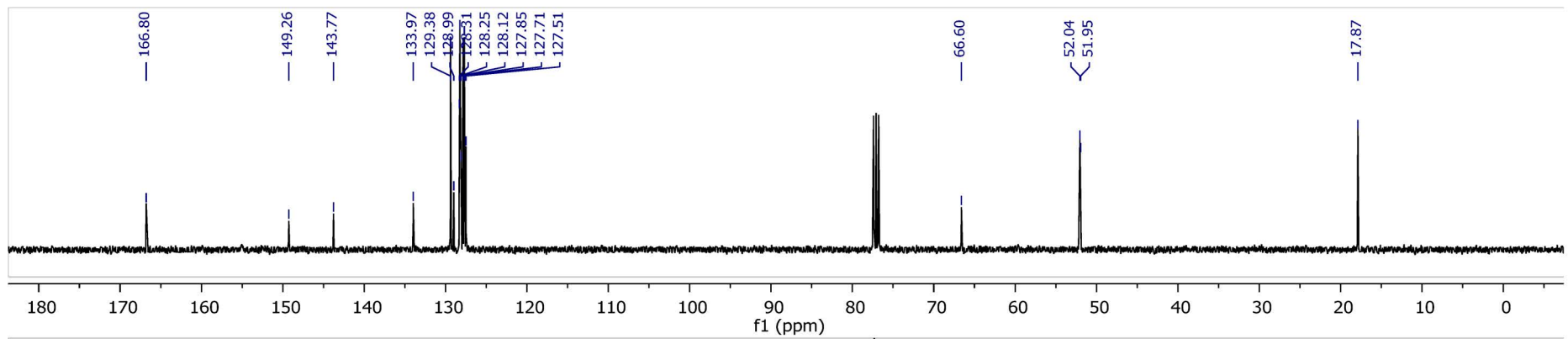
Column: Chiralcel OJ-H  
Eluent: 3% *i*-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	61.503	54.29	68.34	1.53764	0.438958	0.7811	4.087
2	106.988	92.43	130.91	195.306	18.2188	99.2188	9.793





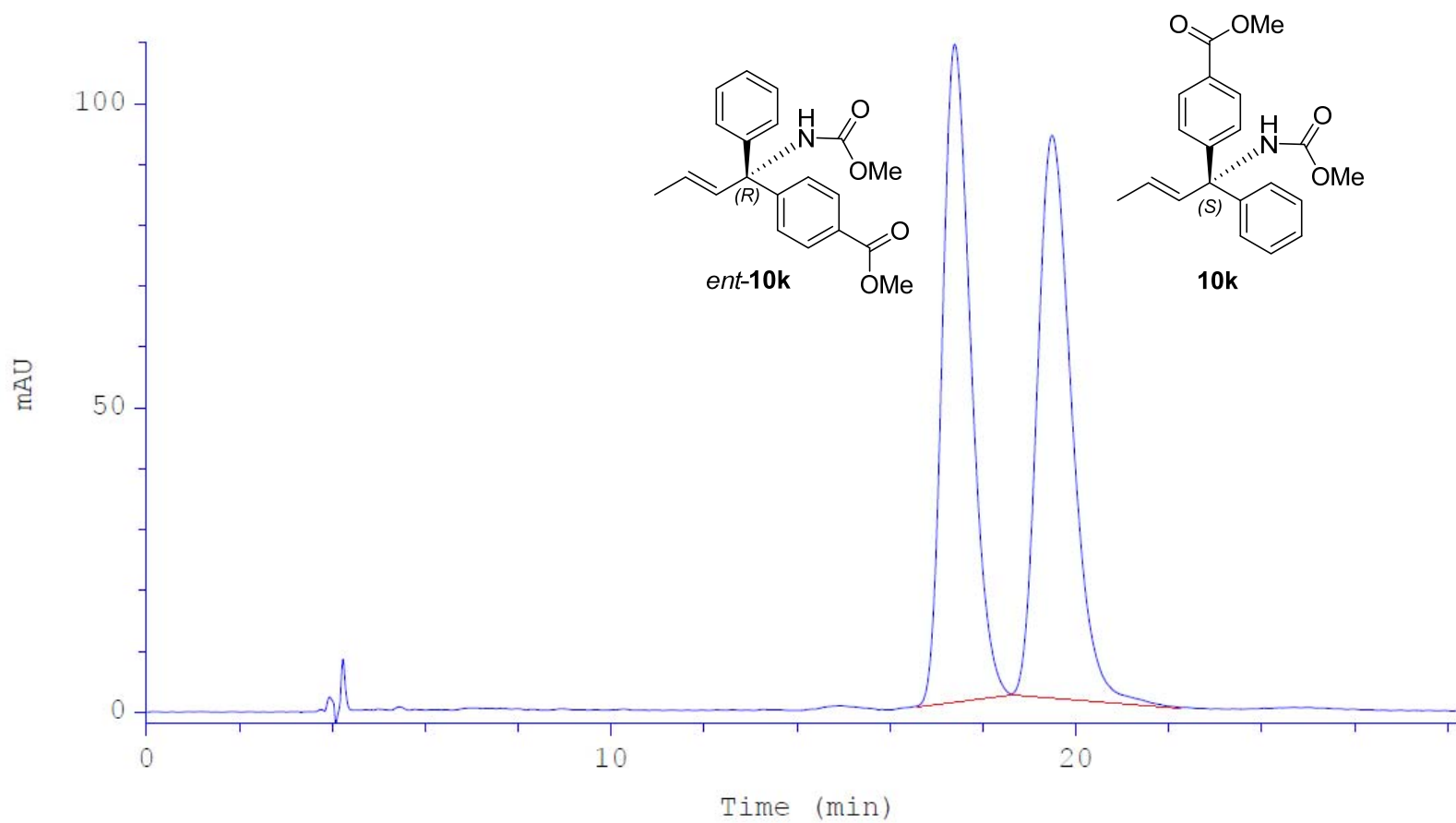




**HPLC conditions:**

Column: Chiralpak AS-H  
Eluent: 5% *i*-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	17.392	16.17	18.64	76.1263	107.935	49.1892	0.656
2	19.493	18.65	22.01	78.636	92.2564	50.8108	0.783



**HPLC conditions:**

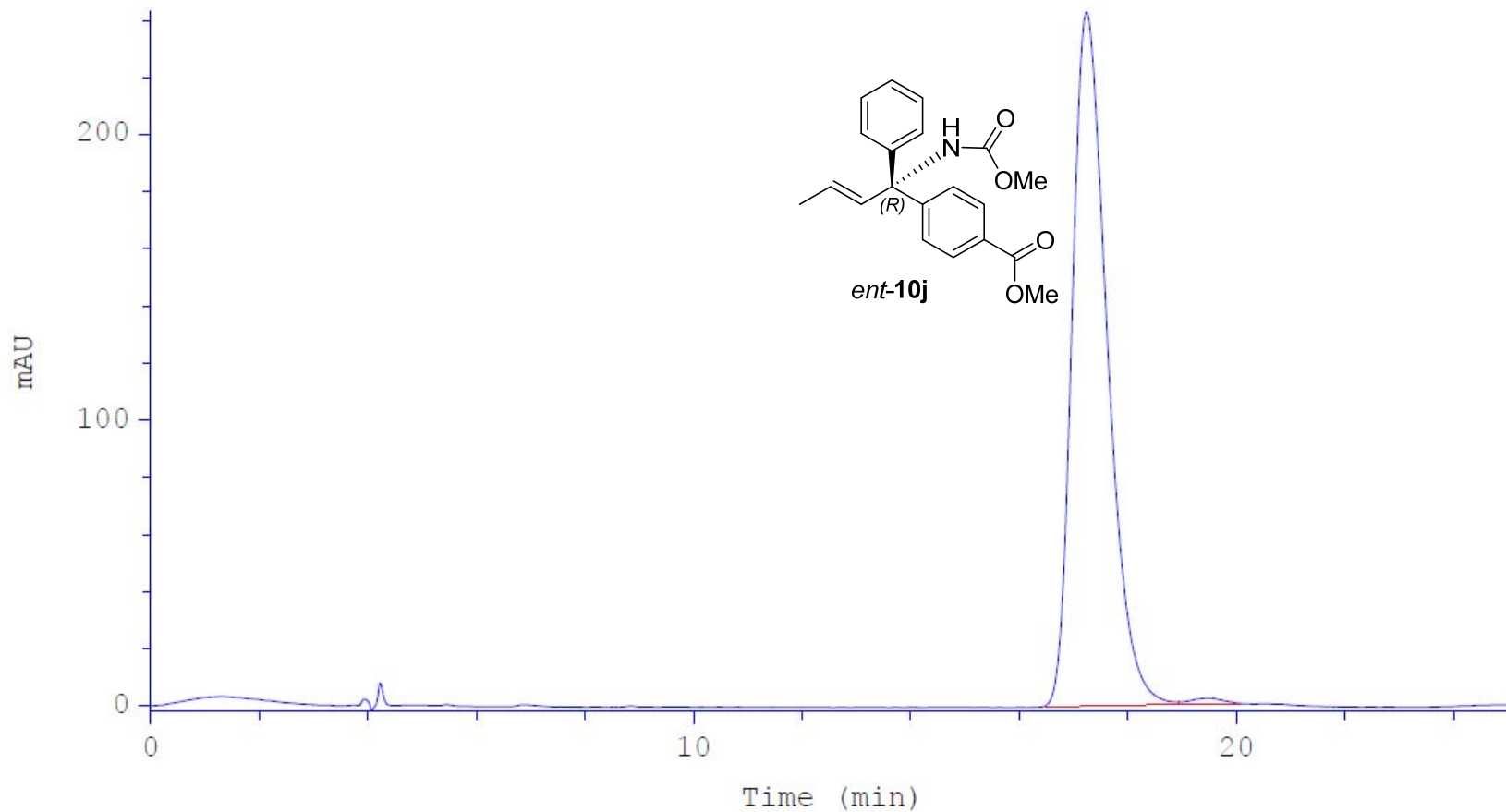
Column: Chiralpak AS-H

Eluent: 5% *i*-PrOH/hexanes

Flow: 1 mL/min

Detection: UV, 254 nm

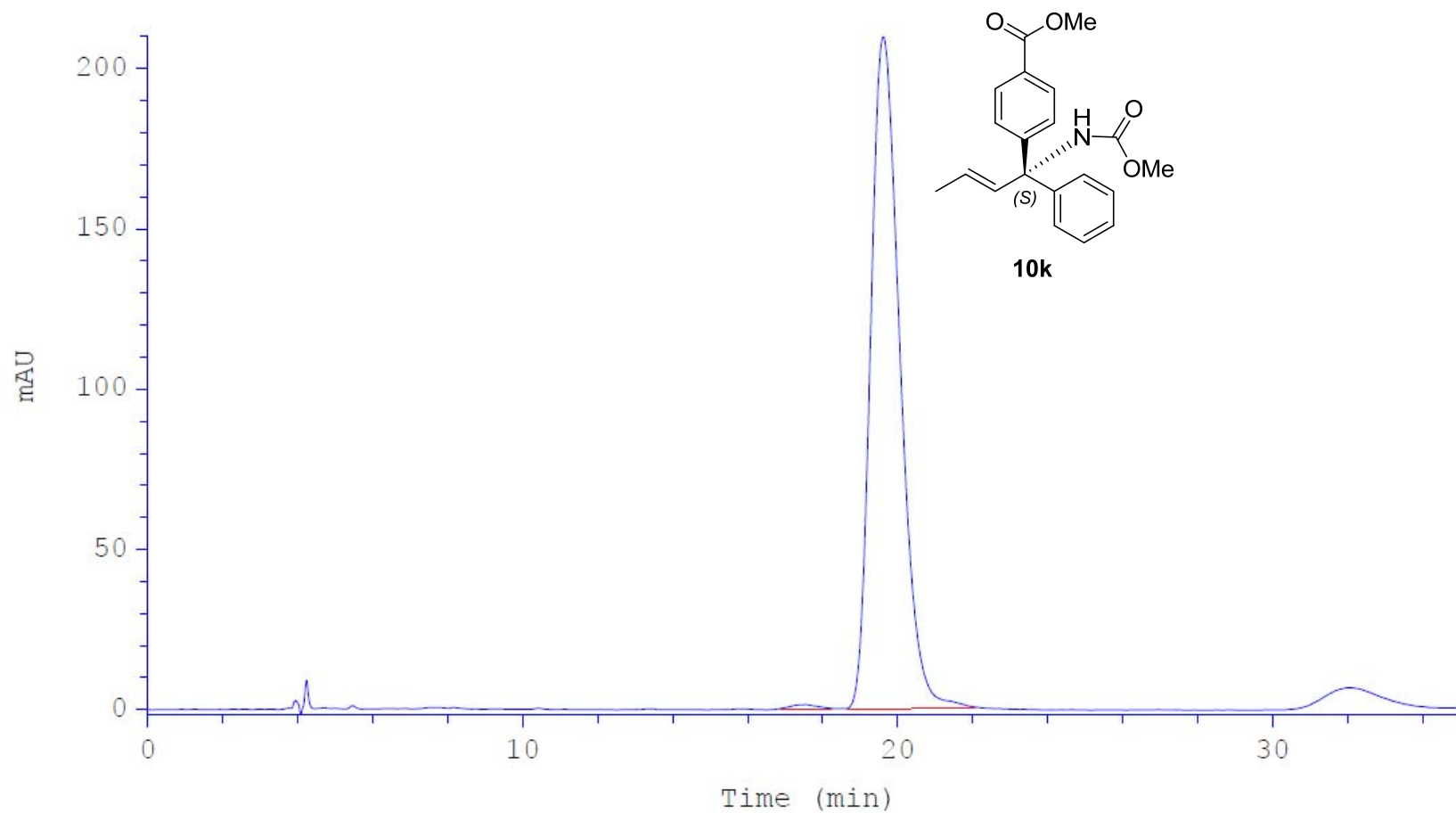
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	17.243	16.26	18.92	181.204	242.757	99.4880	0.690
2	19.478	18.92	20.07	0.932464	1.6041	0.5120	0.583

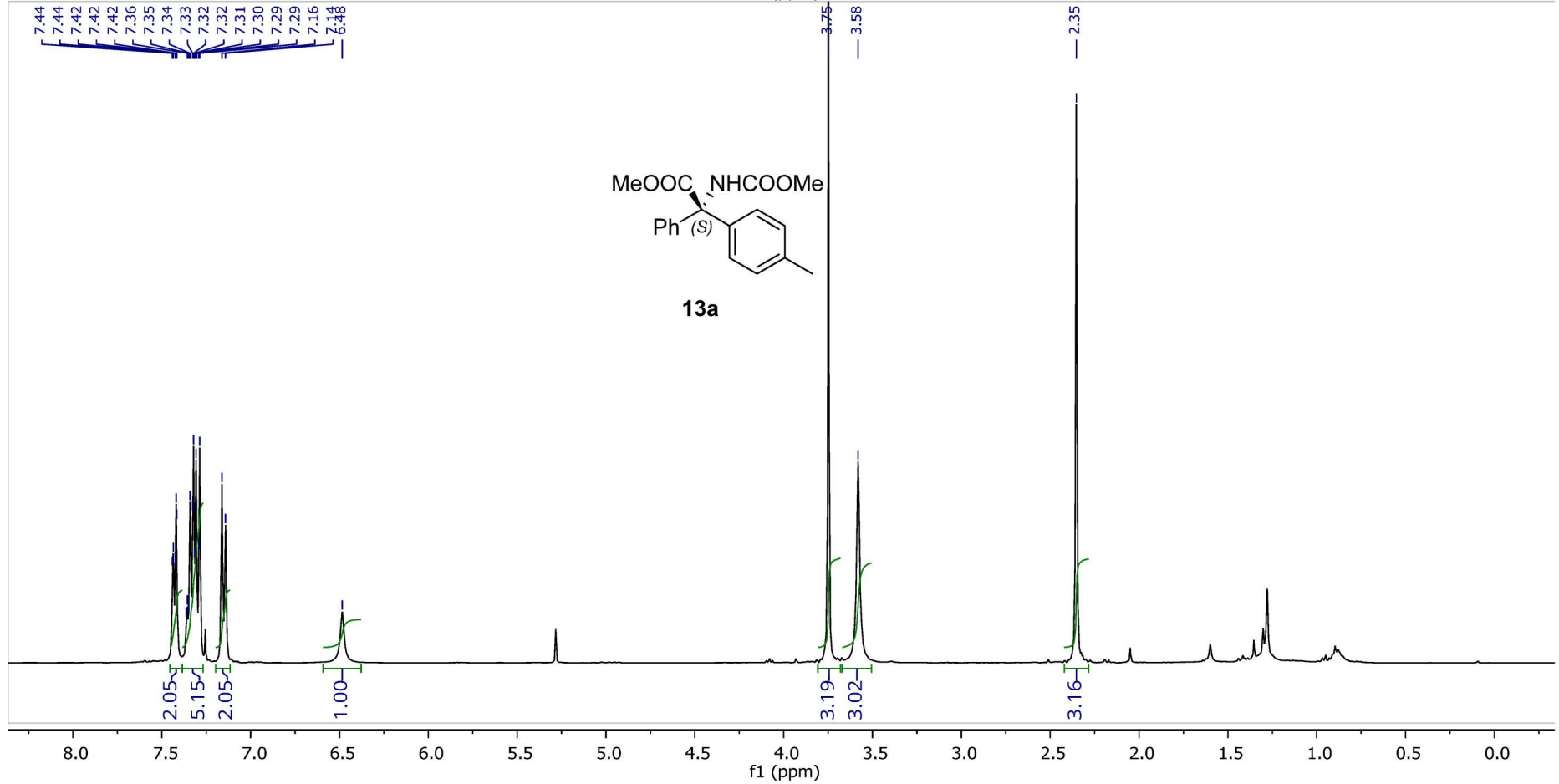
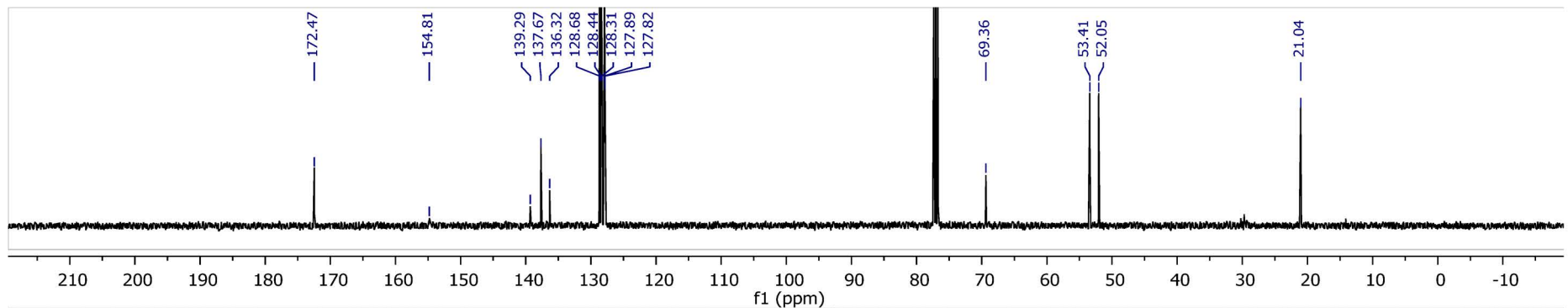


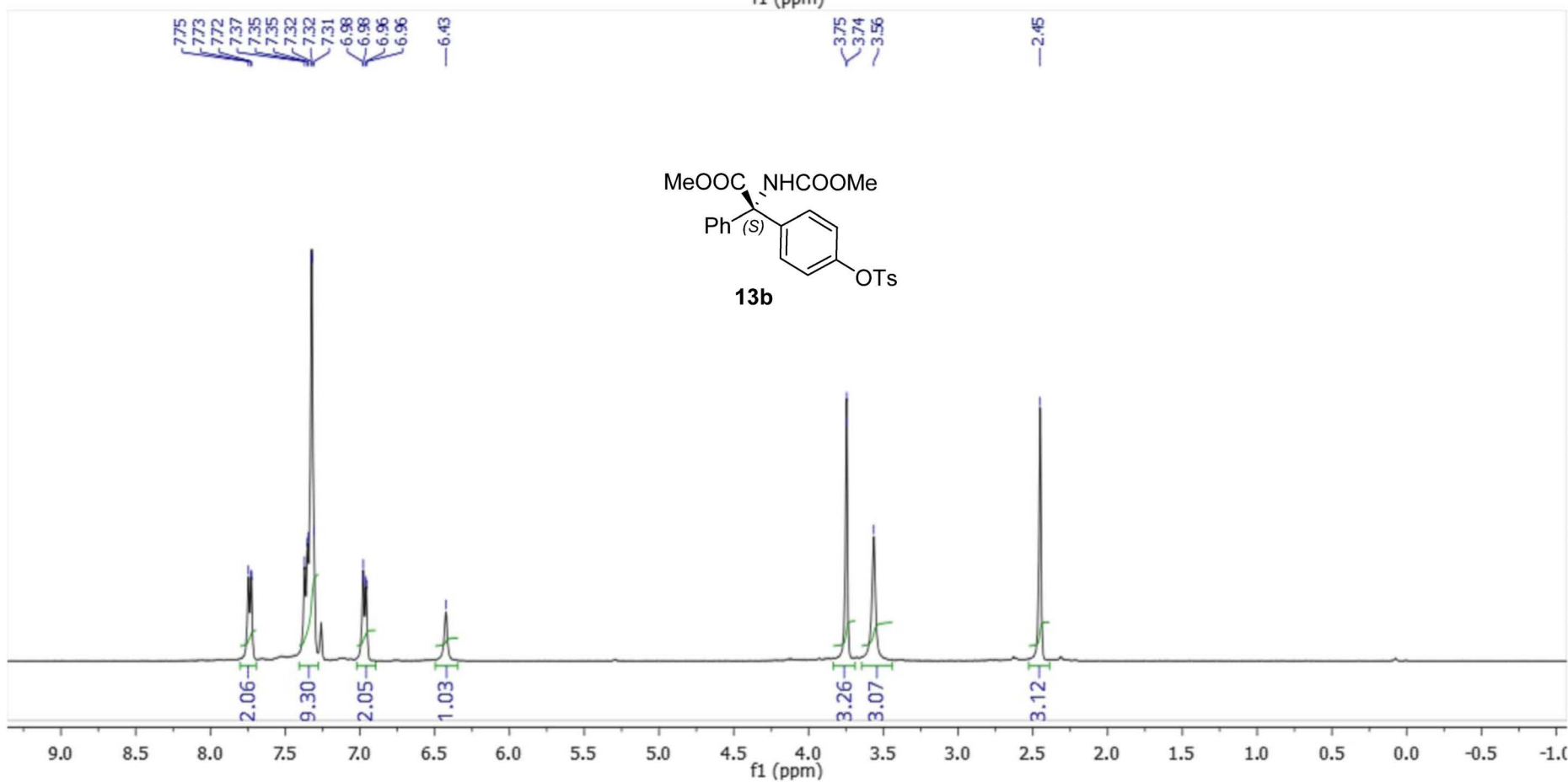
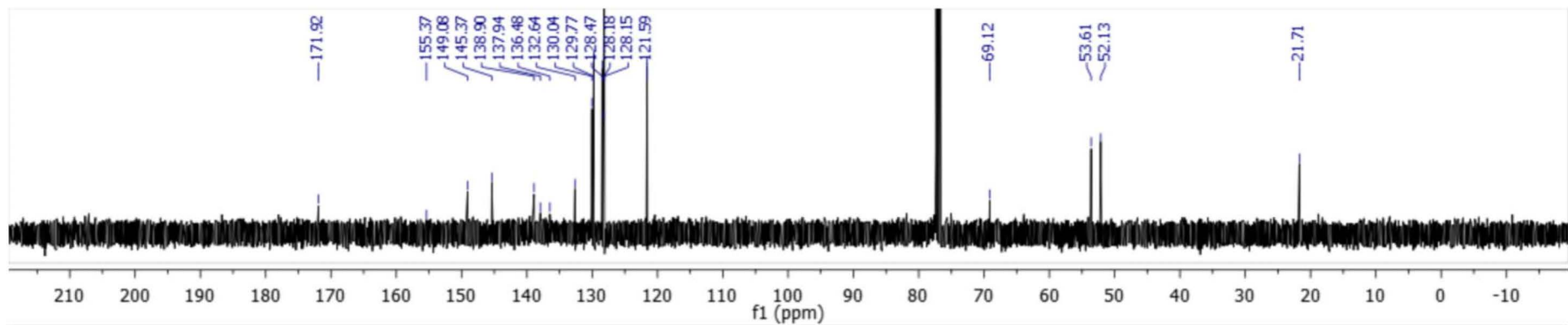
**HPLC conditions:**

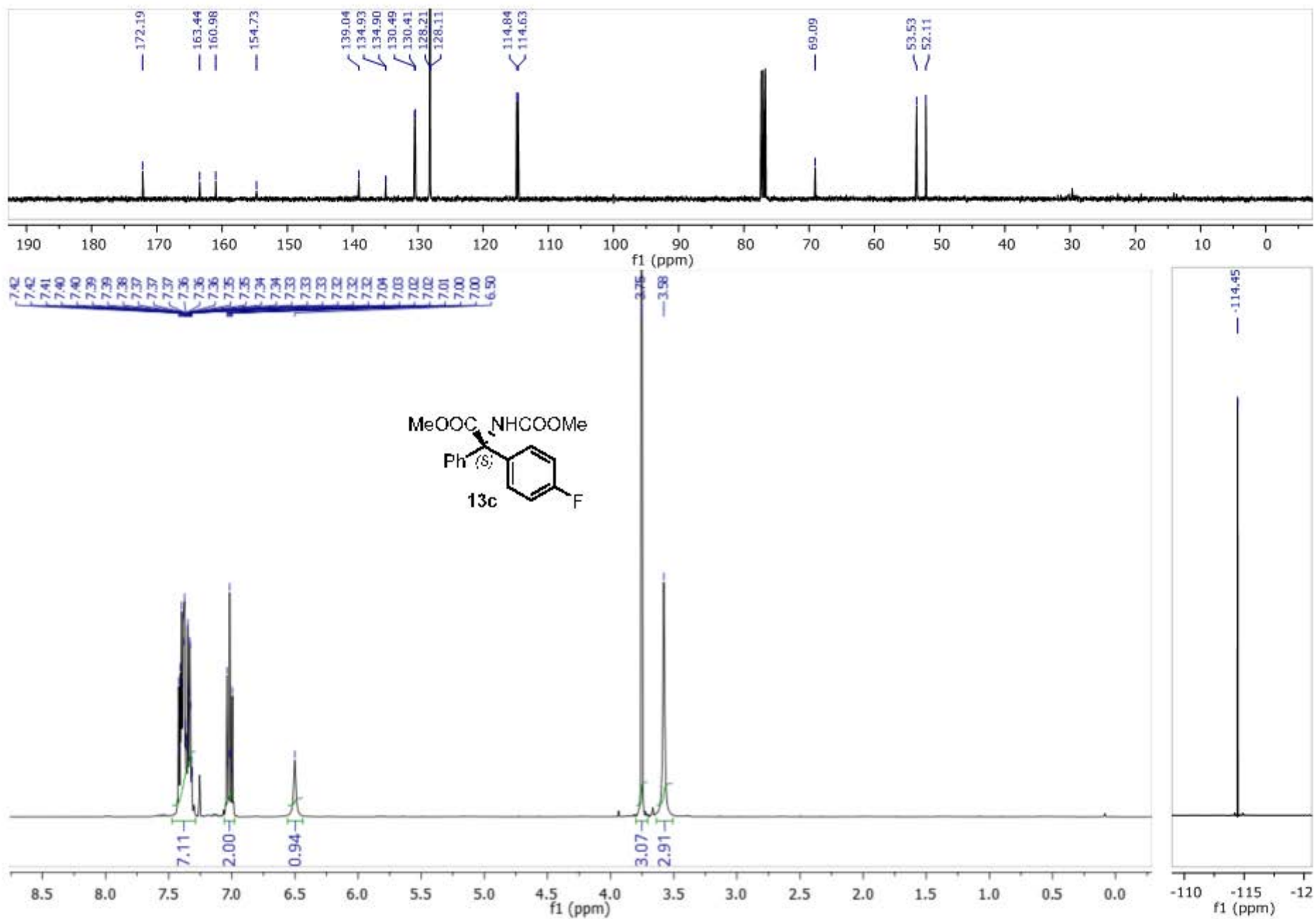
Column: Chiralpak AS-H  
Eluent: 5% *i*-PrOH/hexanes  
Flow: 1 mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	END [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	17.56	16.94	18.47	1.6146	1.521	0.8478	0.92
2	19.62	18.51	22.10	188.82	209.409	99.1522	0.835

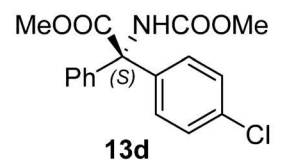
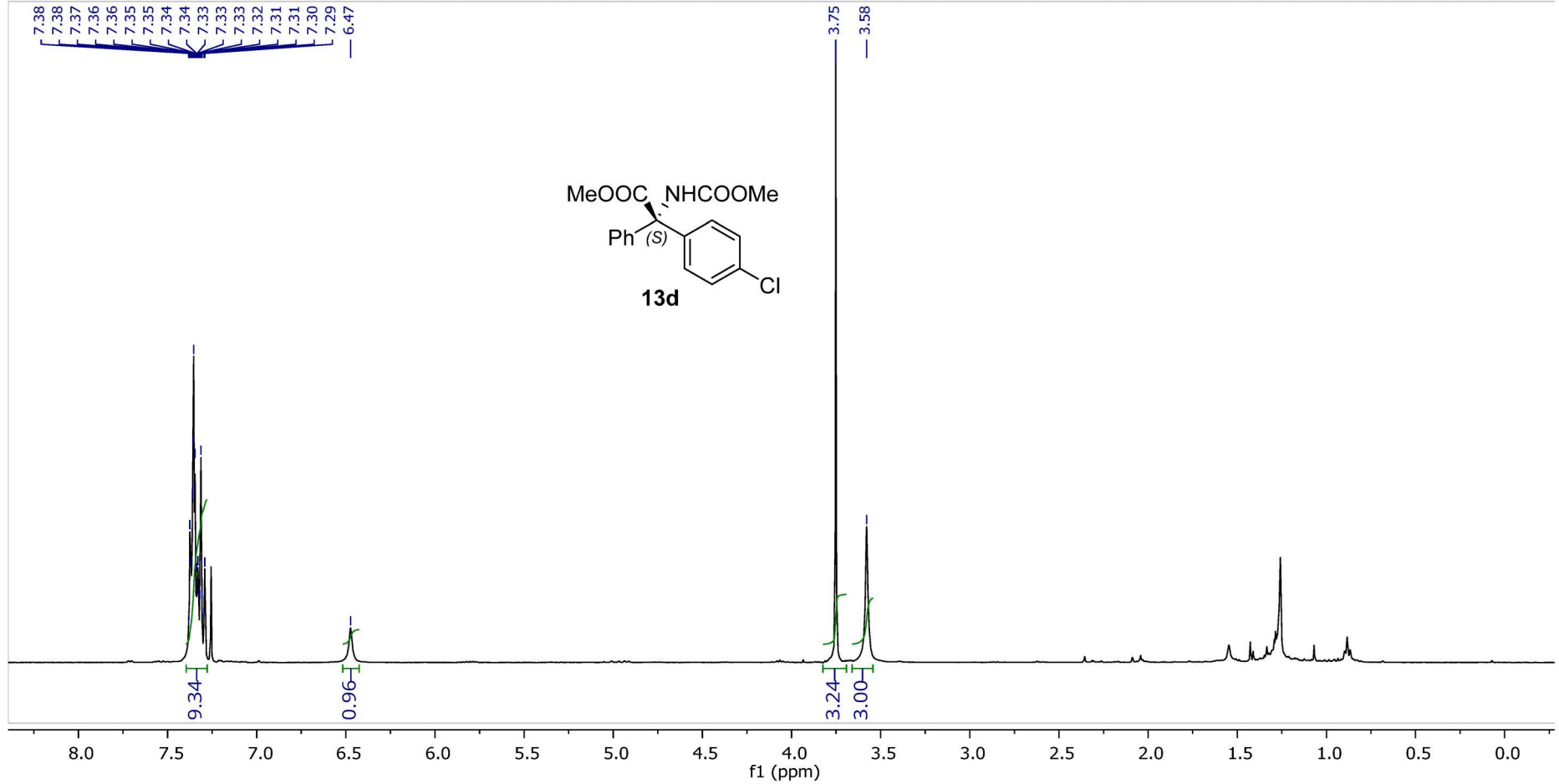
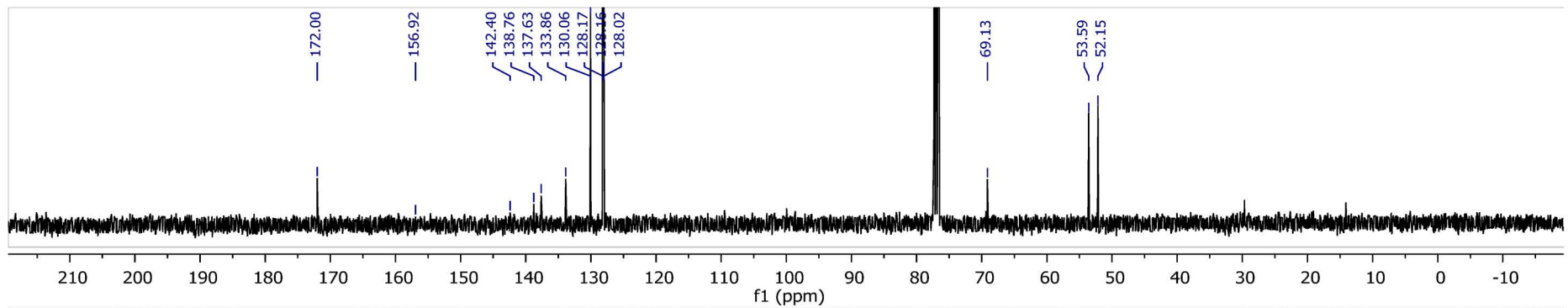


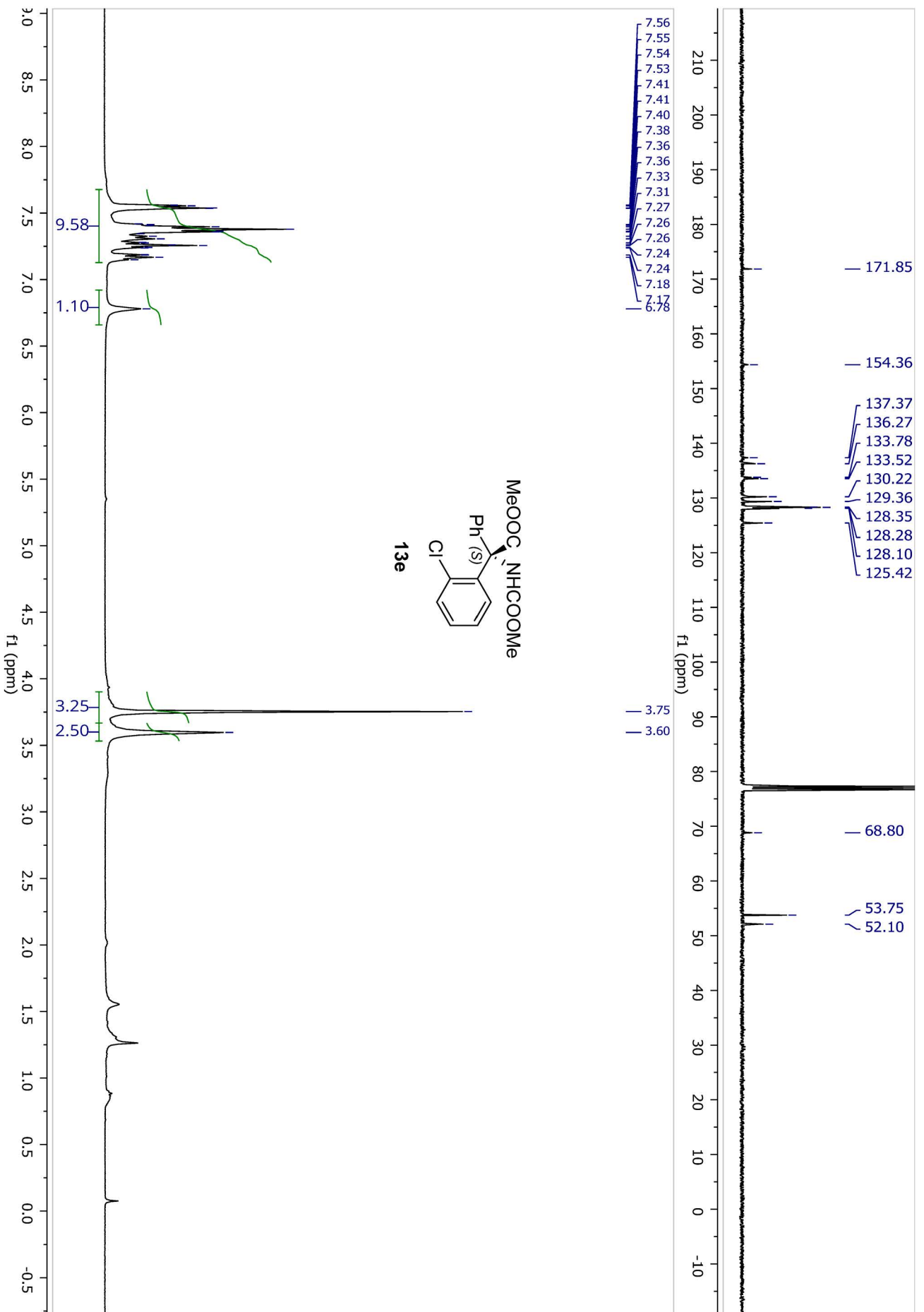


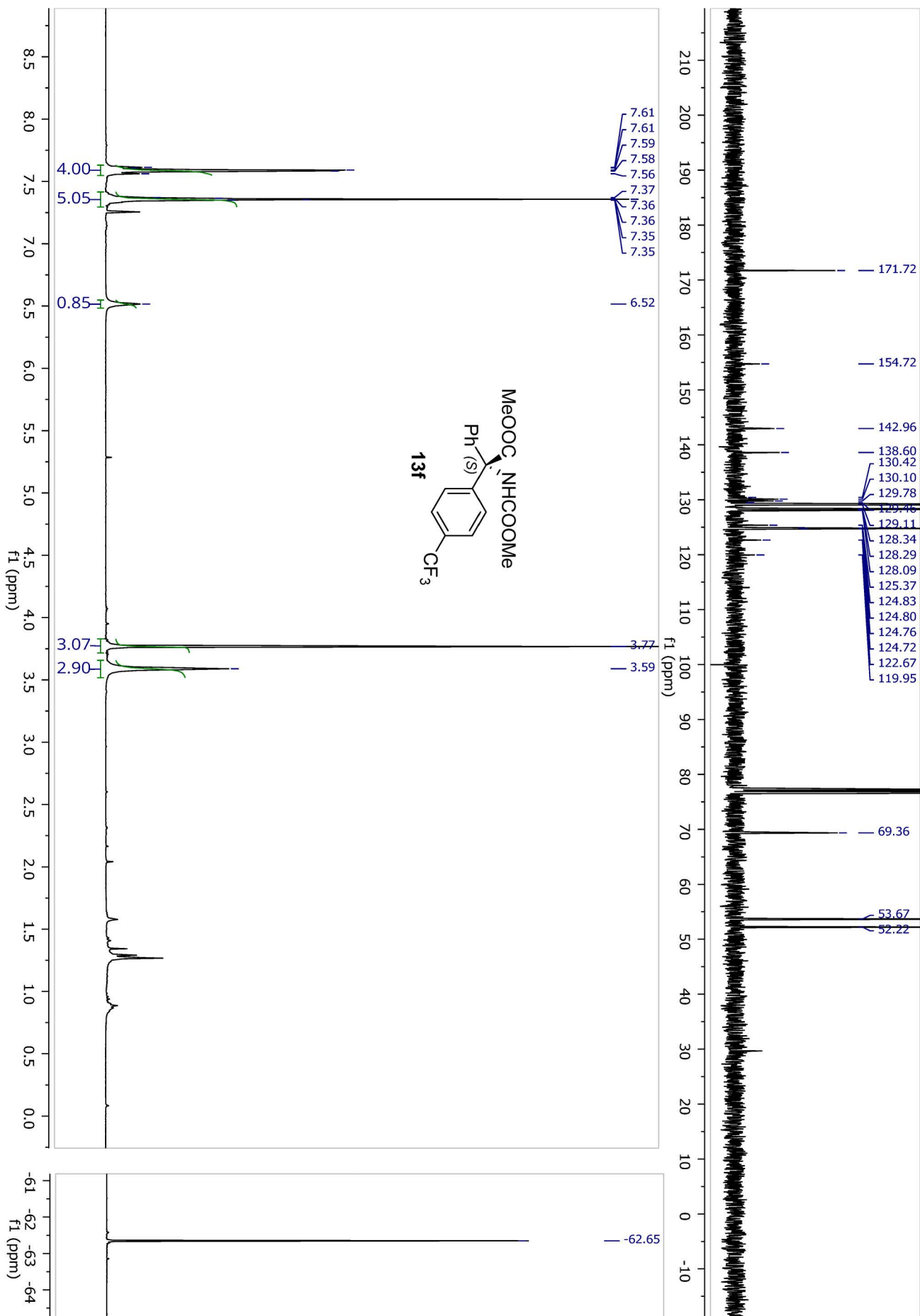


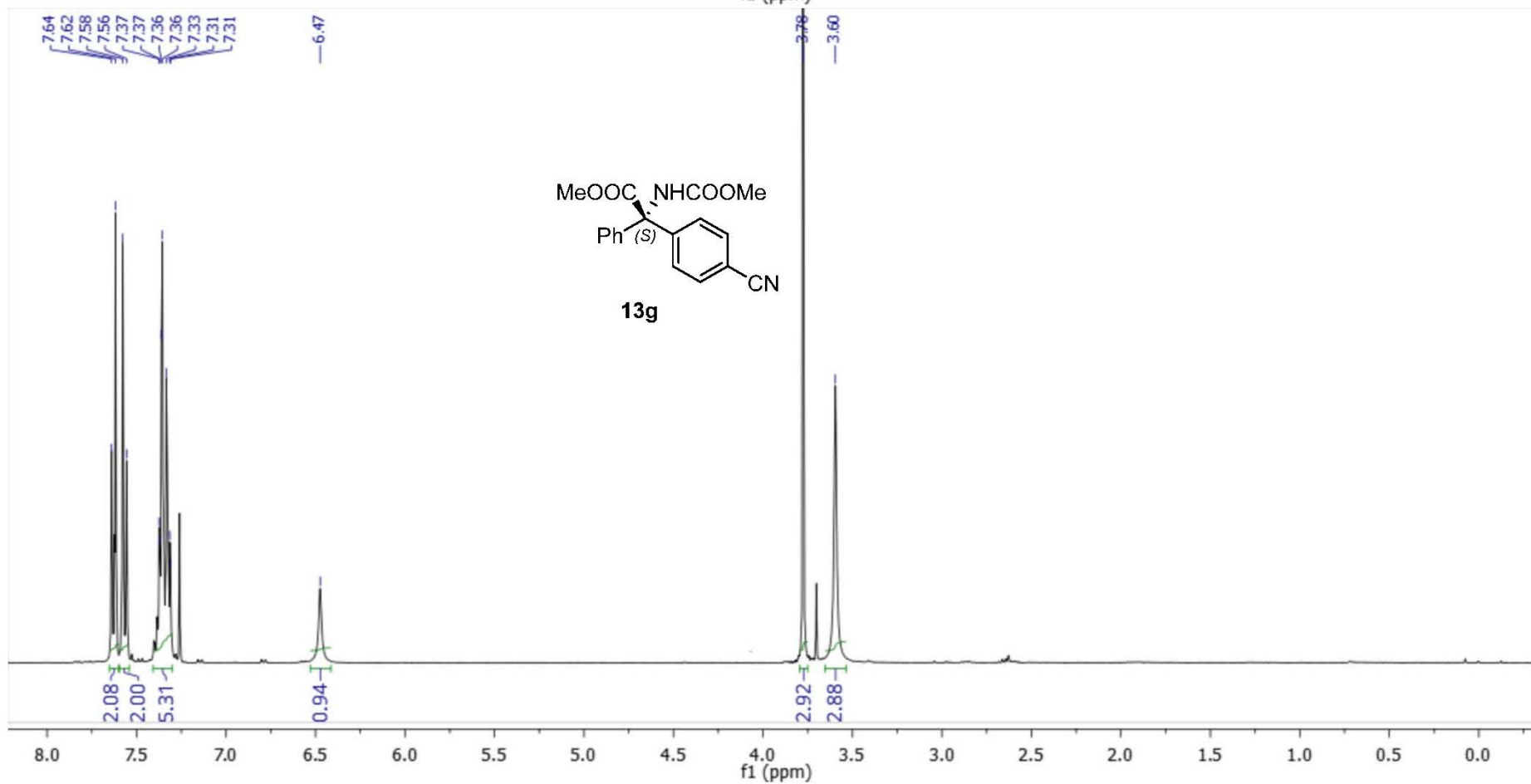
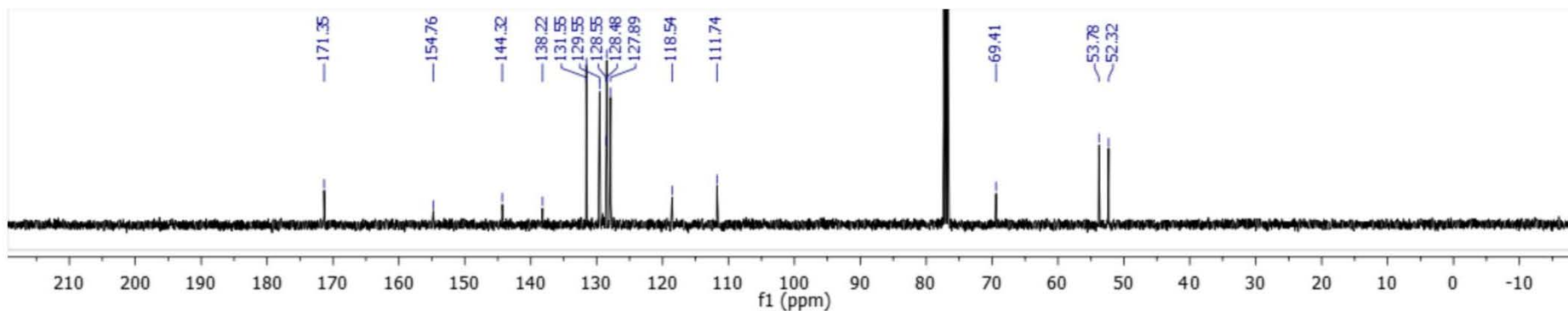


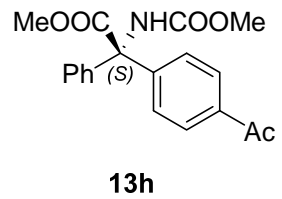
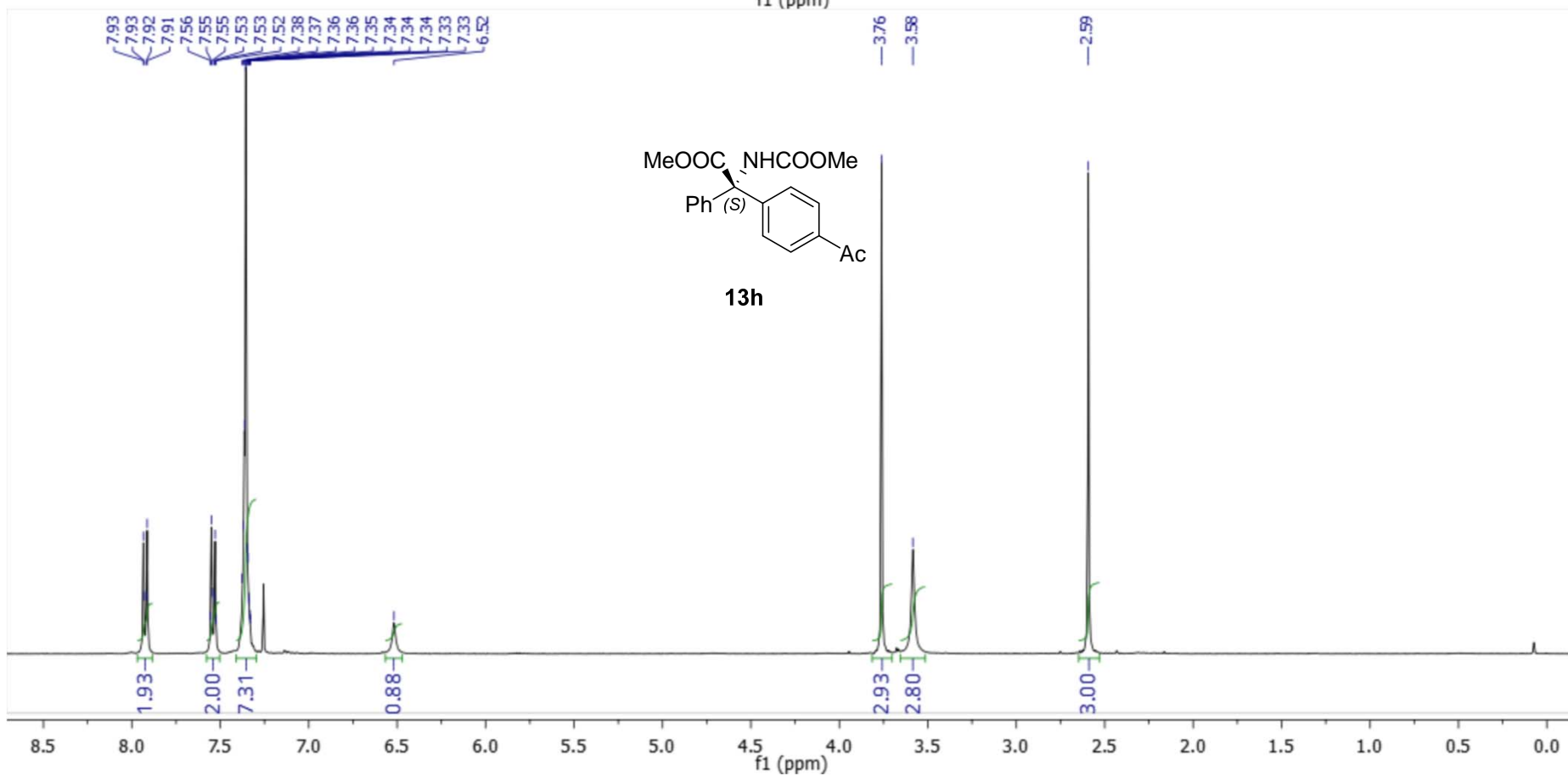
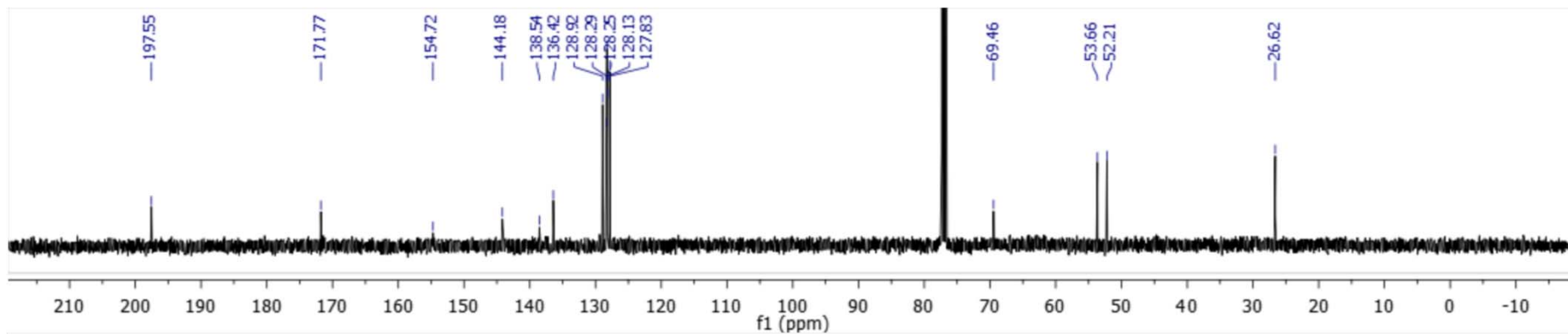


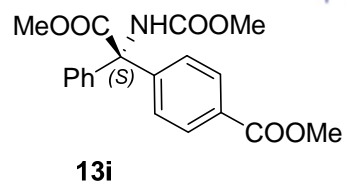
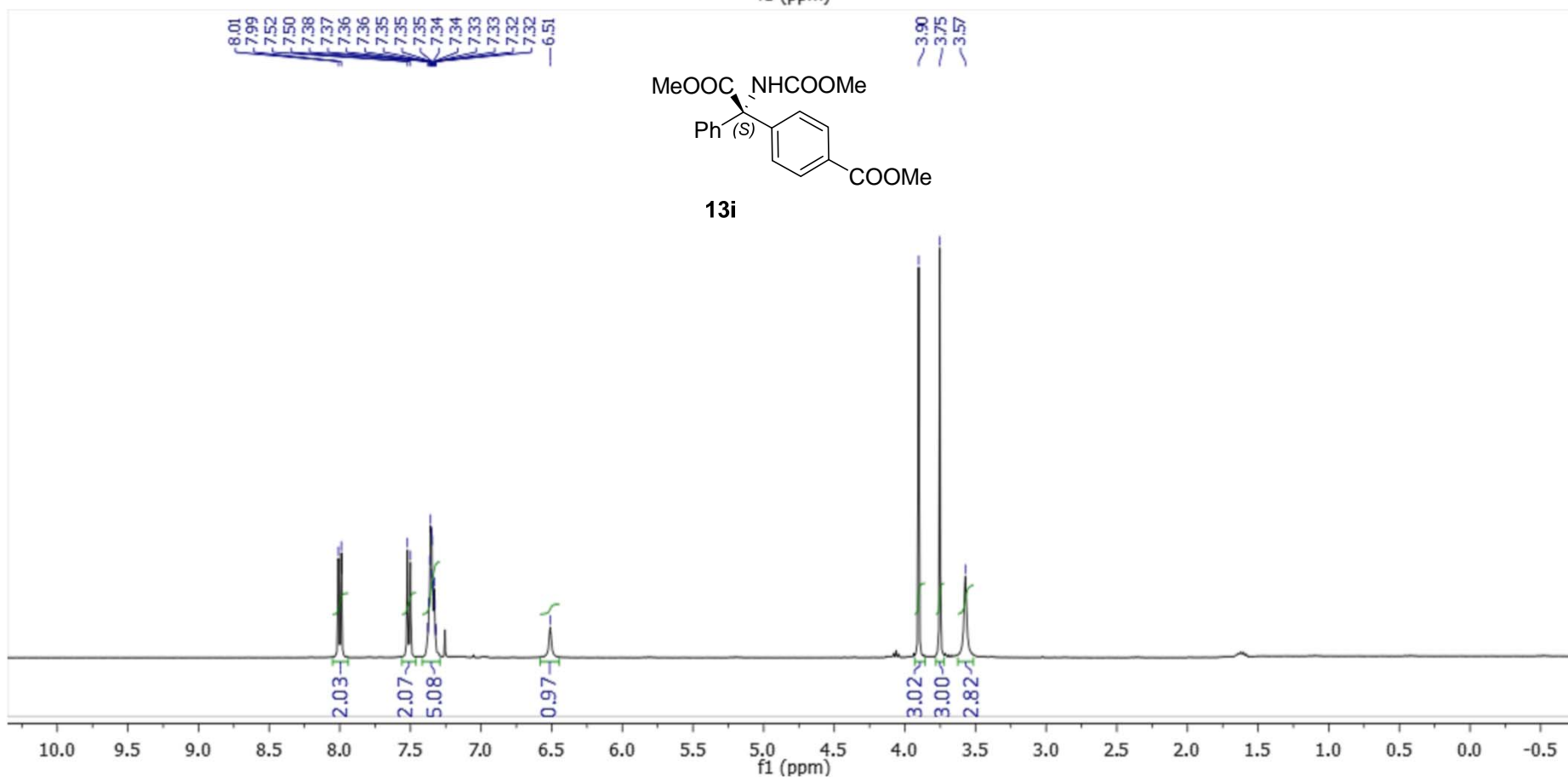
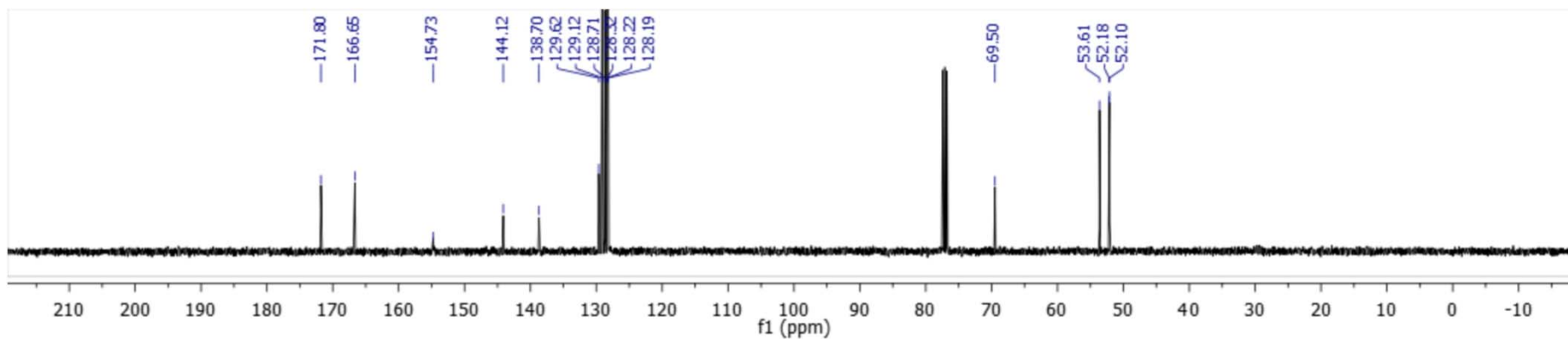














Cite this: *Org. Biomol. Chem.*, 2018, **16**, 3921

## The synthesis of non-racemic $\beta$ -alkyl- $\beta$ -aryl-disubstituted allyl alcohols and their transformation into allylamines and amino acids bearing a quaternary stereocenter†

Aleksandra Narczyk, Michał Pieczykolan and Sebastian Stecko \*

A synthesis of non-racemic  $\beta$ -alkyl- $\beta$ -aryl allyl alcohols and their transformation into allylamines bearing a quaternary stereogenic center is reported. The allyl alcohols were prepared either by Cu-catalyzed enantioselective reduction of enones or by sequential alkylation/hydrostannylation/Stille coupling of non-racemic propargyl alcohols. The prepared  $\beta$ -alkyl- $\beta$ -aryl allyl alcohols were converted (after carbamoylation) to the corresponding allylamine derivatives through cyanate-to-isocyanate rearrangement/nucleophilic addition with complete chirality transfer. Varying the nucleophilic agents allowed the preparation of various allylamine derivatives, including carbamates, amides, formamides, ureas, and free amines. The ozonolysis/oxidation of the resulting allylamines provided non-racemic quaternary  $\alpha$ -amino acids.

Received 27th March 2018,  
Accepted 28th April 2018

DOI: 10.1039/c8ob00731d

rsc.li/obc



























































# The synthesis of non-racemic $\beta$ -alkyl- $\beta$ -aryl-disubstituted allyl alcohols and their transformation into allylamines and amino acids bearing a quaternary stereocenter

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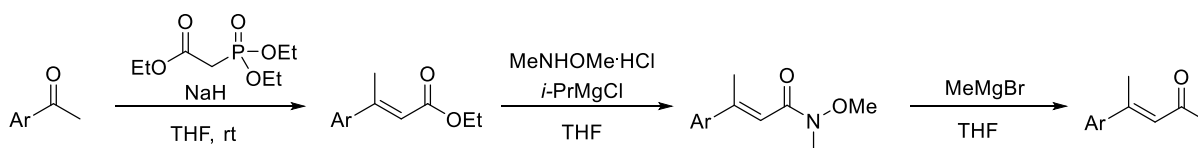
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## SUPPLEMENTARY MATERIALS

1. Synthesis of starting materials.....1
2. The copies of  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$  NMR spectra and HPLC data.....32

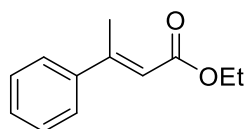
### The synthesis of enones 1. Step 1 - olefination:<sup>1</sup>



To a suspension of sodium hydride (60% dispersion in oil, 1.3 equiv) in dry THF (c 0.2-0.3 M), triethyl phosphonoacetate (1.3 equiv) was added dropwise at room temperature under argon atmosphere. The mixture was stirred for 0.5 h and then cooled to 0 °C. Ketone (1 equiv) was added dropwise and the resulting mixture

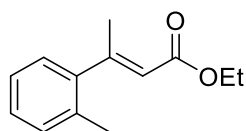
was warmed slowly to room temperature. The progress of the reaction was followed by TLC. When the reaction was completed, a saturated aq.  $\text{NaHCO}_3$  solution was added to the mixture. The aqueous phase was extracted with AcOEt and the combined organic phase was washed with brine, and dried over  $\text{Na}_2\text{SO}_4$ . After the removal of solvents, the residue was purified by column chromatography on silica gel. *E*-Isomer was a dominant. The minor *Z*-isomer was removed by column chromatography of the corresponding Weinreb amides.

**Ethyl (*E*)-3-phenylbut-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 2-5% AcOEt in hexanes. Yield: 3.06 g (overall 80%; *E/Z* ratio 33:1,  $^1\text{H}$  NMR) starting from 5.83 g of acetophenone; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51–7.44 (m, 2H), 7.40 – 7.33 (m, 3H), 6.14 (q,  $J = 1.4$  Hz, 1H), 4.22 (q,  $J = 7.1$  Hz, 2H), 2.59 (d,  $J = 1.4$  Hz, 3H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.8, 155.4, 142.3, 128.9, 128.5, 126.3, 117.2, 59.8, 17.9, 14.3.

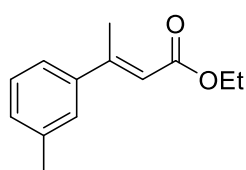
**Ethyl (*E*)-3-(*o*-tolyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 3% AcOEt in hexanes. Yield: 3.71 g (overall 91%; *E/Z*

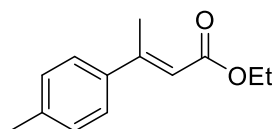
ratio 3.7:1,  $^1\text{H}$  NMR) starting from 2.68 g of methyl *o*-tolyl ketone; yellow liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23–7.14 (m, 3H), 7.10 – 7.04 (m, 1H), 5.77 (q,  $J = 1.5$  Hz, 1H), 4.22 (q,  $J = 7.1$  Hz, 2H), 2.46 (d,  $J = 1.5$  Hz, 3H), 2.30 (s, 4H), 1.32 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.6, 158.2, 143.9, 133.8, 130.4, 127.6, 127.1, 125.7, 119.4, 59.8, 20.8, 19.7, 14.3.

**Ethyl (*E*)-3-(*m*-tolyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 3% AcOEt in hexanes. Yield: 3.06 g (overall 75%; *E/Z* ratio 10:1,  $^1\text{H}$  NMR) starting from 2.68 g of methyl *m*-tolyl ketone; yellow liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31–7.23 (m, 3H), 7.19 – 7.15 (m, 1H), 6.14 (q,  $J = 1.0$  Hz, 1H), 4.23 (q,  $J = 7.1$  Hz, 2H), 2.58 (d,  $J = 1.0$  Hz, 3H), 2.38 (s, 3H), 1.33 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.8, 155.7, 142.3, 138.0, 129.7, 128.4, 127.0, 123.4, 117.0, 59.7, 21.4, 17.9, 14.3.

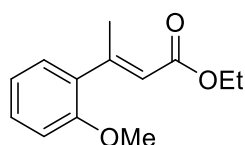
**Ethyl (*E*)-3-(*p*-tolyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 48 h. Column chromatography: silica gel, 3% AcOEt in hexanes. Yield: 4.06 g (overall 99%; *E/Z* ratio 6.7:1, NMR) starting from 2.68 g methyl *p*-tolyl ketone; yellow liquid;  $^1\text{H}$  NMR

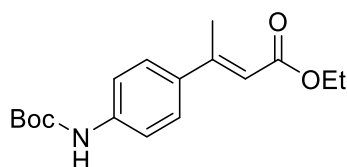
(400 MHz, CDCl<sub>3</sub>) δ 7.42–7.36 (m, 2H), 7.21–7.14 (m, 2H), 6.15 (q, *J* = 1.2 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 2.59 (d, *J* = 1.2 Hz, 3H), 2.37 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.9, 155.3, 139.3, 139.0, 129.2, 126.2, 116.3, 59.7, 21.1, 17.7, 14.4.

**Ethyl (*E*)-3-(2-methoxyphenyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 3% AcOEt in hexanes. Yield: 4.12 g (overall 94%; *E/Z* ratio 25:1, <sup>1</sup>H NMR) starting from 3.00 g of *o*-methoxyacetophenone; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.32–7.24 (m, 1H), 7.14 (d, *J* = 7.5 Hz, 1H), 6.95 – 6.92 (m, 1H), 6.91 – 6.87 (m, 1H), 5.90 (q, *J* = 1.4 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 2.50 (d, *J* = 1.4 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.7, 156.5, 156.3, 133.1, 129.4, 128.8, 120.5, 119.3, 111.0, 59.7, 55.4, 19.8, 14.3.

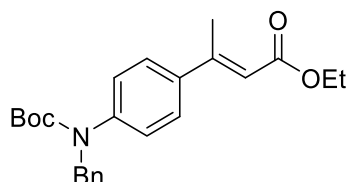
**Ethyl (*E*)-3-(4-((tert-butoxycarbonyl)amino)phenyl)but-2-enoate:**



The reaction mixture was stirred for 4 days at rt, and additionally for 3 days at 50 °C. Column chromatography: silica gel, 5% AcOEt in hexanes. Yield: 1.02 g (overall 96%; *E/Z* ratio 2.9:1, <sup>1</sup>H NMR) starting from 826 mg of *t*-butyl (4-acetylphenyl)carbamate; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.47–7.30 (m,

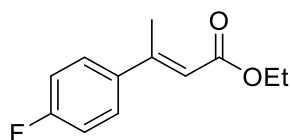
4H), 6.69 (br s, 1H), 6.14–6.07 (m, 1H), 4.20 (q,  $J = 7.1$  Hz, 2H), 2.54 (t,  $J = 1.0$  Hz, 3H), 1.51 (s, 9H), 1.30 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.0, 154.7, 152.5, 139.3, 136.4, 127.0, 118.1, 115.8, 80.8, 59.7, 28.3, 17.6, 14.3.

**Ethyl (*E*)-3-(4-(benzyl(*tert*-butoxycarbonyl)amino)phenyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 48 h. Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 310 mg (overall 76%; *E/Z* ratio 4:1,  $^1\text{H}$  NMR) starting from 335 mg of *t*-butyl (4-acetylphenyl)(benzyl)carbamate; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43–7.35 (m, 2H), 7.34–7.27 (m, 2H), 7.27–7.21 (m, 3H), 7.21–7.15 (m, 2H), 6.10 (q,  $J = 1.3$  Hz, 1H), 4.85 (s, 2H), 4.20 (q,  $J = 7.1$  Hz, 2H), 2.53 (d,  $J = 1.3$  Hz, 3H), 1.43 (s, 9H), 1.30 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.8, 154.6, 154.5, 143.6, 139.2, 138.5, 128.4, 127.2, 127.1, 126.6, 126.0, 116.8, 80.9, 59.8, 53.7, 28.2, 17.7, 14.3.

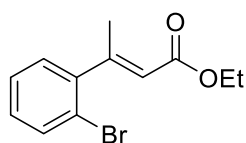
**Ethyl (*E*)-3-(4-fluorophenyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 3% AcOEt in hexanes. Yield: 3.40 g (overall 82%; *E/Z* ratio 11:1,  $^1\text{H}$  NMR) starting from 2.76 g of *p*-fluoroacetophenone; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47–7.39 (m, 2H), 7.07–6.99 (m, 2H), 6.07 (q,  $J = 1.4$  Hz,

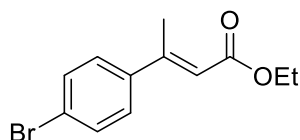
1H), 4.20 (q,  $J = 7.1$  Hz, 2H), 2.54 (d,  $J = 1.4$  Hz, 3H), 1.30 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.6, 163.2 (d,  $J = 248.9$  Hz), 154.1, 138.2 (d,  $J_{\text{C-F}} = 3.0$  Hz), 128.1 (d,  $J_{\text{C-F}} = 8.2$  Hz), 117.1 (d,  $J_{\text{C-F}} = 1.0$  Hz), 115.4 (d,  $J_{\text{C-F}} = 21.6$  Hz), 59.8, 17.8, 14.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -112.6.

**Ethyl (*E*)-3-(2-bromophenyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 3-10% AcOEt in hexanes. Yield: 4.84 g (overall 90%, *E/Z* ratio 2.3:1,  $^1\text{H}$  NMR) starting from 3.98 g of *o*-bromoacetophenone; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.57–7.53 (m, 1H), 7.30–7.24 (m, 1H), 7.17–7.11 (m, 2H), 5.80 (q,  $J = 1.5$  Hz, 1H), 4.22 (q,  $J = 7.1$  Hz, 2H), 2.48 (d,  $J = 1.5$  Hz, 3H), 1.30 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.3, 156.9, 144.7, 133.0, 129.1, 128.8, 127.3, 120.7, 120.5, 59.9, 20.3, 14.3.

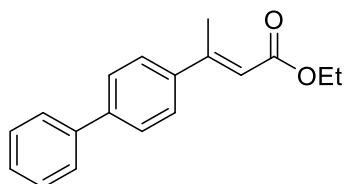
**Ethyl (*E*)-3-(4-bromophenyl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 3-10% AcOEt in hexanes. Yield: 4.07 g (overall 76%; *E/Z* ratio 6.3:1,  $^1\text{H}$  NMR) starting from 3.98 g *p*-bromoacetophenone; colourless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51–7.45 (m, 2H), 7.36–7.29 (m, 2H), 6.12–6.07 (m, 1H),

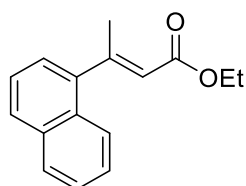
4.21 (q,  $J = 7.2$  Hz, 2H), 2.53 (s, 3H), 1.30 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.5, 154.0, 141.0, 131.6, 127.9, 123.2, 117.6, 59.9, 17.7, 14.3.

**Ethyl (*E*)-3-([1,1'-biphenyl]-4-yl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 48 h. Column chromatography: silica gel, 3% AcOEt in hexanes. Yield: 4.53 g (overall 85%, *E/Z* ratio 3.5:1,  $^1\text{H}$  NMR) starting from 3.93 g of *p*-phenylacetophenone; waxy solid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.66–7.54 (m, 6H), 7.51–7.43 (m, 2H), 7.41–7.34 (m, 1H), 6.23 (q,  $J = 1.3$  Hz, 1H), 4.25 (q,  $J = 7.1$  Hz, 2H), 2.64 (d,  $J = 1.3$  Hz, 3H), 1.35 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 154.8, 141.8, 141.0, 140.3, 128.9, 127.6, 127.1, 127.0, 126.8, 117.0, 59.9, 17.8, 14.4.

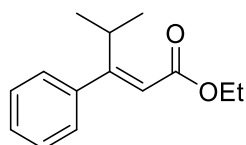
**Ethyl (*E*)-3-(naphthalen-1-yl)but-2-enoate:**



The reaction mixture was stirred at room temperature for 24 h. Column chromatography: silica gel, 2-7% AcOEt in hexanes. Yield: 4.26 g (overall 89%; *E/Z* ratio 4.5:1,  $^1\text{H}$  NMR) starting from 3.40 g of 1-acetonaphthone; yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.96–7.85 (m, 2H), 7.81 (d,  $J = 8.3$  Hz, 1H), 7.54–7.47 (m, 2H), 7.47–7.41 (m, 1H), 7.30 (d,  $J = 7.1$  Hz, 1H), 6.02 (q,  $J = 1.4$  Hz, 1H), 4.29 (q,  $J = 7.1$  Hz,

2H), 2.65 (d,  $J = 1.4$  Hz, 3H), 1.36 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.6, 157.0, 142.1, 133.7, 130.1, 128.5, 128.1, 126.3, 126.0, 125.3, 125.2, 124.2, 120.6, 59.9, 21.7, 14.4.

**Ethyl (*E*)-4-methyl-3-phenylpent-2-enoate:**

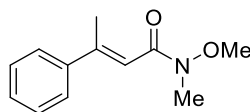


To a 1M solution of LiHMDS in THF (6.5 mL, 6.5 mmol), triethyl phosphonoacetate (6.5 mmol) was added dropwise at room temperature under argon atmosphere. The mixture was stirred for 0.5 h and then cooled to 0 °C, and phenyl *i*-propyl ketone (5 mmol) was added dropwise. The resulting mixture was warmed slowly to room temperature. After stirring for 24 h, an additional portion of HWE reagent (6.5 mmol) was added. The progress of the reaction was followed by TLC. The starting material was consumed after 4 days. Next, sat.  $\text{NH}_4\text{Cl}$  solution was added and the aqueous phase was extracted with AcOEt. The combined organic layers were washed with brine, and dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude residue was purified by column chromatography on silica gel (2% AcOEt in hexanes) to obtain 1.03 g of product as an inseparable mixture of *E/Z* isomers in 1.5:1 ratio (overall yield 94%). Colourless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , selected signals for major *E*- isomer)  $\delta$  7.34–7.29 (m, 3H), 7.22–7.16 (m, 2H), 5.70 (s, 1H), 4.20 (q,  $J = 7.1$  Hz, 2H), 4.11 (sept,  $J = 7.0$  Hz, 1H), 1.30 (t,  $J = 7.1$  Hz, 3H), 1.09 (d,  $J = 7.0$  Hz, 6H);



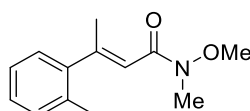
**Step 2 - synthesis of Weinreb Amides:**<sup>1</sup> Suspension of  $\alpha,\beta$ -unsaturated ester (1 equiv) and *N,O*-dimethylhydroxylamine hydrochloride (2 equiv) in dry THF (c 0.2-0.3 M) was cooled to  $-5\text{ }^{\circ}\text{C}$  under argon atmosphere, and 2M soln. of *i*-PrMgCl in THF (4 equiv) was added dropwise. The progress of the reaction was followed by TLC. After stirring at  $-5\text{ }^{\circ}\text{C}$  for 0.5-1 h, the reaction was quenched by the addition of sat.  $\text{NH}_4\text{Cl}$ . The aqueous phase was extracted with ethyl acetate and the combined organic phase was washed with brine, and dried over sodium sulfate. After the removal of the solvent, the crude residue was purified by column chromatography on silica gel to provide pure *E* isomer.

**(*E*)-*N*-Methoxy-*N*-methyl-3-phenylbut-2-enamide:**



Column chromatography: silica gel, 10-20% AcOEt in hexanes. Yield: 799 mg (86%) starting from 866 mg of ethyl (*E*)-3-phenylbut-2-enoate; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49–7.44 (m, 2H), 7.39–7.30 (m, 3H), 6.56 (s, 1H), 3.68 (s, 3H), 3.25 (s, 3H), 2.52 (d,  $J = 1.3\text{ Hz}$ , 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 152.2, 143.0, 128.5, 128.4, 126.3, 116.0, 61.5, 32.4, 18.0.

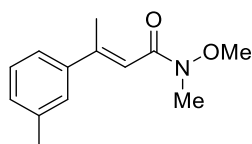
**(*E*)-*N*-Methoxy-*N*-methyl-3-(*o*-tolyl)but-2-enamide:**



Column chromatography: silica gel, 10-20% AcOEt in hexanes. Yield: 2.60 g (85%) starting from 2.85 g of ethyl (*E*)-3-(*o*-tolyl)but-2-enoate; yellowish oil;  $^1\text{H}$  NMR (400

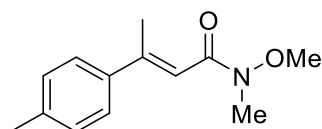
MHz, CDCl<sub>3</sub>) δ 7.24–7.14 (m, 3H), 7.14–7.06 (m, 1H), 6.21 (s, 1H), 3.66 (s, 3H), 3.25 (s, 3H), 2.42 (d, *J* = 1.6 Hz, 3H), 2.31 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 167.7, 154.9, 144.6, 134.0, 130.3, 127.4, 127.3, 125.7, 117.8, 61.5, 32.2, 20.6, 19.7.

**(*E*)-*N*-Methoxy-*N*-methyl-3-(*m*-tolyl)but-2-enamide:**



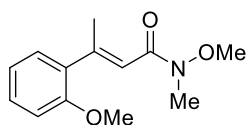
Column chromatography: silica gel, 10-20% AcOEt in hexanes. Yield: 2.97 g (89%) starting from 2.80 g of ethyl (*E*)-3-(*m*-tolyl)but-2-enoate; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.31–7.22 (m, 3H), 7.18–7.11 (m, 1H), 6.55 (s, 1H), 3.70 (s, 3H), 3.26 (s, 3H), 2.52 (d, *J* = 1.4 Hz, 3H), 2.37 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.0, 152.4, 143.0, 138.0, 129.3, 128.3, 127.0, 123.4, 115.8, 61.5, 32.4, 21.5, 18.1.

**(*E*)-*N*-Methoxy-*N*-methyl-3-(*p*-tolyl)but-2-enamide:**



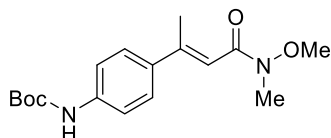
Column chromatography: silica gel, 10-20% AcOEt in hexanes. Yield: 2.93 g (82%) starting from 3.33 g of ethyl (*E*)-3-(*p*-tolyl)but-2-enoate; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40–7.33 (m, 2H), 7.14 (d, *J* = 8.0 Hz, 2H), 6.56 (s, 1H), 3.66 (s, 3H), 3.23 (s, 3H), 2.51 (s, 3H), 2.33 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.0, 152.1, 140.0, 138.5, 129.1, 126.1, 115.2, 61.5, 32.3, 21.1, 17.8.

**(*E*)-*N*-Methoxy-3-(2-methoxyphenyl)-*N*-methylbut-2-enamide:**



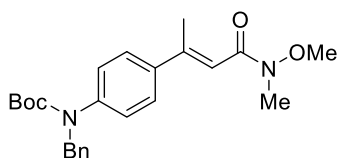
Column chromatography: silica gel, 30% AcOEt in hexanes. Yield: 3.65 g (95%) starting from 3.59 g of ethyl (*E*)-3-(2-methoxyphenyl)but-2-enoate; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33–7.20 (m, 1H), 7.15 (d,  $J = 7.5$  Hz, 1H), 6.99–6.80 (m, 2H), 6.32 (s, 1H), 3.79 (s, 3H), 3.66 (s, 3H), 3.23 (s, 3H), 2.44 (d,  $J = 1.5$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 156.5, 152.8, 133.7, 129.1, 128.9, 120.5, 117.9, 111.1, 61.4, 55.4, 32.3, 19.7.

***tert*-Butyl (*E*)-(4-(4-(methoxy(methyl)amino)-4-oxobut-2-en-2-yl)phenyl)carbamate:**



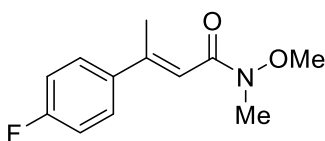
Column chromatography: silica gel, 40% AcOEt in hexanes. Yield: 335 g (86%) starting from 371 mg of ethyl (*E*)-3-(4-((*tert*-butoxycarbonyl)amino)phenyl)but-2-enoate; yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44–7.32 (m, 4H), 7.03 (br s, 1H), 6.52 (s, 1H), 3.66 (s, 3H), 3.22 (s, 3H), 2.47 (d,  $J = 1.4$  Hz, 3H), 1.48 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.1, 152.7, 151.6, 139.2, 137.0, 126.9, 118.3, 114.6, 80.5, 61.5, 32.4, 28.3, 17.7.

***tert*-Butyl (*E*)-benzyl(4-(4-(methoxy(methyl)amino)-4-oxobut-2-en-2-yl)phenyl)carbamate:**



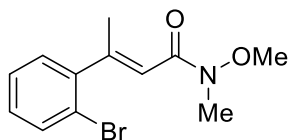
Column chromatography: silica gel, 20-40% AcOEt in hexanes. Yield: 86 mg (70%) starting from 120 mg of ethyl (*E*)-3-(4-(benzyl(*tert*-butoxycarbonyl)-amino)phenyl)but-2-enoate; yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43–7.34 (m, 2H), 7.34–7.14 (m, 7H), 6.53 (s, 1H), 4.85 (s, 2H), 3.68 (s, 3H), 3.24 (s, 3H), 2.48 (d,  $J$  = 1.3 Hz, 3H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.9, 154.6, 151.4, 143.2, 140.0, 138.6, 128.4, 127.1, 127.1, 126.5, 125.9, 115.7, 80.8, 61.5, 53.8, 32.4, 28.3, 17.8.

**(*E*)-3-(4-Fluorophenyl)-*N*-methoxy-*N*-methylbut-2-enamide:**



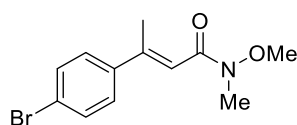
Column chromatography: silica gel, 30% AcOEt in hexanes. Yield: 1.35 g (81%) starting from 1.56 g of (*E*)-3-(4-fluorophenyl)but-2-enoate; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46–7.39 (m, 2H), 7.07–6.99 (m, 2H), 6.51 (s, 1H), 3.69 (s, 3H), 3.24 (s, 3H), 2.48 (d,  $J$  = 1.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.8, 162.9 (d,  $J_{\text{C-F}}$  = 248.1 Hz), 151.0, 138.9 (d,  $J_{\text{C-F}}$  = 2.6 Hz), 128.0 (d,  $J_{\text{C-F}}$  = 8.1 Hz), 115.9, 115.3 (d,  $J_{\text{C-F}}$  = 21.5 Hz), 61.5, 32.3, 18.0;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -113.29.

**(*E*)-3-(2-Bromophenyl)-*N*-methoxy-*N*-methylbut-2-enamide:**



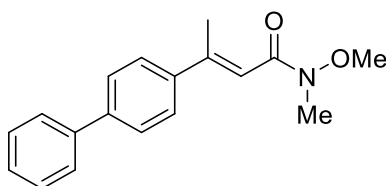
Column chromatography: silica gel, 30% AcOEt in hexanes. Yield: 1.22 g (98%) starting from 1.19 g of (*E*)-3-(2-bromophenyl)but-2-enoate; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.58–7.54 (m, 1H), 7.31–7.25 (m, 1H), 7.20–7.11 (m, 2H), 6.23 (s, 1H), 3.71–3.65 (m, 3H), 3.28–3.22 (m, 3H), 2.42 (d, *J* = 1.6 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 167.2, 153.4, 145.2, 132.9, 129.0, 128.9, 127.4, 120.9, 119.1, 61.8, 32.2, 20.1.

**(*E*)-3-(4-Bromophenyl)-*N*-methoxy-*N*-methylbut-2-enamide:**



Column chromatography: silica gel, 15% AcOEt in hexanes. Yield: 2.81 g (76%) starting from 3.50 g of (*E*)-3-(4-bromophenyl)but-2-enoate; yellowish solid; m.p. 38–40 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.50–7.45 (m, 2H), 7.35–7.30 (m, 2H), 6.53 (s, 1H), 3.69 (s, 3H), 3.25 (s, 3H), 2.48 (d, *J* = 1.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 167.6, 150.8, 141.8, 131.6, 127.9, 122.7, 116.5, 61.6, 32.3, 17.8.

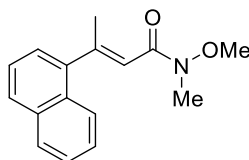
**(*E*)-3-([1,1'-Biphenyl]-4-yl)-*N*-methoxy-*N*-methylbut-2-enamide:**



Column chromatography: silica gel, 15–25% AcOEt in hexanes. Yield: 3.14 g (77%) starting from 3.86 g of (*E*)-3-(4-phenylphenyl)but-2-enoate; white solid; m.p. 123–124 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.64–7.55 (m, 6H), 7.48–7.43 (m, 2H), 7.39–7.34 (m, 1H), 6.65 (s, 1H), 3.73 (s, 3H), 3.29 (s, 3H), 2.58 (d, *J* = 1.3 Hz, 3H); <sup>13</sup>C NMR

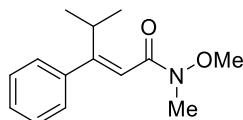
(101 MHz, CDCl<sub>3</sub>)  $\delta$  168.0, 151.7, 141.8, 141.5, 140.4, 128.8, 127.5, 127.1, 127.0, 126.7, 115.9, 61.6, 32.4, 17.9.

**(E)-N-Methoxy-N-methyl-3-(naphthalen-1-yl)but-2-enamide:**



Column chromatography: silica gel, 20% AcOEt in hexanes. Yield: 719 mg (85%) starting from 800 mg of (E)-3-(1-naphthyl)but-2-enoate; yellow oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.99–7.94 (m, 1H), 7.90–7.84 (m, 1H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.52–7.43 (m, 3H), 7.34–7.30 (m, 1H), 6.42 (s, 1H), 3.67 (s, 3H), 3.30 (s, 3H), 2.61 (d, *J* = 1.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  167.7, 153.7, 142.8, 133.8, 130.4, 128.5, 127.9, 126.2, 125.9, 125.4, 125.3, 124.3, 119.2, 61.6, 32.3, 21.5.

**(E)-N-Methoxy-N,4-dimethyl-3-phenylpent-2-enamide:**

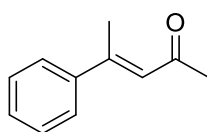


Column chromatography: silica gel, 15% AcOEt in hexanes. Yield: 941 mg (77%) starting from 725 mg of ethyl (E)-4-methyl-3-phenylpent-2-enoate; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.35–7.24 (m, 3H), 7.24–7.15 (m, 2H), 6.08 (s, 1H), 4.02–3.81 (m, 1H), 3.64 (s, 3H), 3.22 (s, 3H), 1.07 (d, *J* = 7.1 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  167.5, 162.8, 141.4, 127.9, 127.7, 127.3, 117.6, 61.4, 32.3, 30.0, 21.5.

**Step 3 - synthesis of enones 1:**<sup>1</sup> A 3 M soln. of MeMgBr in THF (1.3 equiv) was slowly added to a solution of Weinreb amide (1 equiv) in THF (c 0.2-0.3 M) cooled

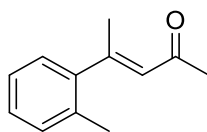
to  $-30\text{ }^{\circ}\text{C}$ . After addition, the mixture was slowly warmed to  $-5\text{ }^{\circ}\text{C}$  and stirred for 0.5 h. The progress of the reaction was followed by TLC. Next, sat.  $\text{NH}_4\text{Cl}$  was added and the resulting mixture was extracted with AcOEt. The combined organic layers were washed with brine, and dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the residue was purified by column chromatography on silica gel.

**(E)-4-Phenylpent-3-en-2-one:**



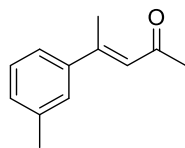
Column chromatography: silica gel, 5% AcOEt in hexanes. Yield: 595 mg (96%) starting from 793 mg of (*E*)-*N*-methoxy-*N*-methyl-3-phenylbut-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50–7.45 (m, 2H), 7.40–7.34 (m, 3H), 6.50 (q,  $J = 1.3$  Hz, 1H), 2.53 (d,  $J = 1.3$  Hz, 3H), 2.28 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 153.8, 142.5, 129.1, 128.5, 126.4, 124.5, 32.2, 18.3.

**(E)-4-(*o*-Tolyl)pent-3-en-2-one:**



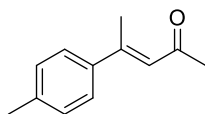
Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 1.45 g (96%) starting from 1.90 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*o*-tolyl)but-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.23–7.14 (m, 3H), 7.09–7.04 (m, 1H), 6.15 (q,  $J = 1.5$  Hz, 1H), 2.42 (d,  $J = 1.5$  Hz, 3H), 2.29 (s, 3H), 2.25 (s, 4H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 156.5, 144.1, 133.9, 130.4, 127.7, 127.1, 126.6, 125.7, 32.0, 21.2, 19.7.

**(E)-4-(*m*-Tolyl)pent-3-en-2-one:**



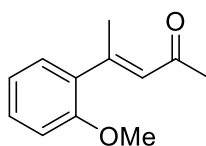
Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 2.10 g (89%) starting from 2.97 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*m*-tolyl)but-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30–7.23 (m, 3H), 7.20–7.15 (m, 1H), 6.52–6.47 (m, 1H), 2.53 (d,  $J = 1.4$  Hz, 3H), 2.38 (s, 3H), 2.28 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 154.0, 142.5, 138.1, 129.8, 128.4, 127.1, 124.3, 123.6, 32.2, 21.4, 18.3.

**(E)-4-(*p*-Tolyl)pent-3-en-2-one:**



Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 2.15 g (92%) starting from 2.93 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*p*-tolyl)but-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40–7.36 (m, 2H), 7.19–7.14 (m, 2H), 6.50 (q,  $J = 1.4$  Hz, 1H), 2.52 (d,  $J = 1.4$  Hz, 3H), 2.35 (s, 3H), 2.26 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 153.7, 139.5, 139.2, 129.2, 126.4, 123.7, 32.1, 21.2, 18.1.

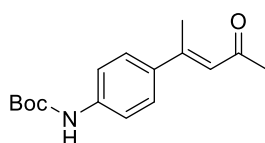
**(E)-4-(2-Methoxyphenyl)pent-3-en-2-one:**





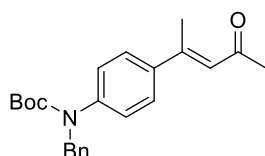
Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 2.92 g (96%) starting from 3.65 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*o*-methoxyphenyl)but-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.31–7.25 (m, 1H), 7.14–7.11 (m, 1H), 6.95–6.92 (m, 1H), 6.92–6.87 (m, 1H), 6.27 (q,  $J = 1.5$  Hz, 1H), 3.81 (s, 3H), 2.45 (d,  $J = 1.5$  Hz, 3H), 2.24 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 156.5, 154.9, 133.2, 129.5, 128.7, 126.6, 120.5, 111.1, 55.4, 32.0, 20.3.

***tert*-Butyl (*E*)-(4-(4-oxopent-2-en-2-yl)phenyl)carbamate:**



Column chromatography: silica gel, 25% AcOEt in hexanes. Yield: 263 mg (91%) starting from 331 mg of *tert*-butyl (*E*)-(4-(4-(methoxy(methyl)amino)-4-oxobut-2-en-2-yl)phenyl)carbamate; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45–7.36 (m, 4H), 6.94 (br s, 1H), 6.48 (d,  $J = 1.4$  Hz, 1H), 2.49 (d,  $J = 1.4$  Hz, 3H), 2.26 (s, 3H), 1.50 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.9, 153.2, 152.6, 139.7, 136.4, 127.2, 123.1, 118.2, 80.7, 32.2, 28.3, 18.0.

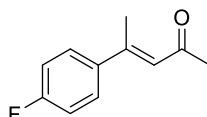
***tert*-Butyl (*E*)-benzyl(4-(4-oxopent-2-en-2-yl)phenyl)carbamate:**



Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 70 mg (91%) starting from 86 mg of *tert*-butyl (*E*)-benzyl(4-(4-(methoxy(methyl)amino)-4-oxobut-2-en-2-yl)phenyl)carbamate; yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45–

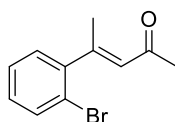
7.35 (m, 2H), 7.34–7.15 (m, 7H), 6.47 (s, 1H), 4.85 (s, 2H), 2.49 (d,  $J = 1.3$  Hz, 3H), 2.26 (s, 3H), 1.43 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 154.5, 152.9, 143.7, 139.4, 138.5, 128.4, 127.1, 127.1, 126.8, 126.0, 124.1, 80.9, 53.7, 32.2, 28.3, 18.1.

**(E)-4-(4-Fluorophenyl)pent-3-en-2-one:**



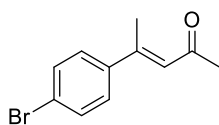
Column chromatography: silica gel, 5% AcOEt in hexanes. Yield: 961 mg (89%) starting from 1.35 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*p*-fluorophenyl)but-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48–7.42 (m, 2H), 7.08–7.01 (m, 2H), 6.45 (q,  $J = 1.3$  Hz, 1H), 2.49 (d,  $J = 1.3$  Hz, 3H), 2.27 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.6, 163.3 (d,  $J = 249.1$  Hz), 152.5, 138.5 (d,  $J = 3.3$  Hz), 128.3 (d,  $J = 8.4$  Hz), 124.4 (d,  $J = 1.1$  Hz), 115.5 (d,  $J = 21.6$  Hz), 32.2, 18.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -112.3.

**(E)-4-(2-Bromophenyl)pent-3-en-2-one:**



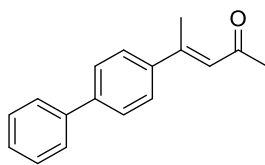
Column chromatography: silica gel, 2-5% AcOEt in hexanes. Yield: 852 mg (90%) starting from 1.13 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*o*-bromophenyl)but-2-enamide; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.58–7.54 (m, 1H), 7.31–7.25 (m, 1H), 7.18–7.11 (m, 2H), 6.16 (q,  $J = 1.5$  Hz, 1H), 2.42 (d,  $J = 1.5$  Hz, 3H), 2.26 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 154.9, 144.8, 133.0, 129.1, 128.8, 127.5, 127.3, 120.7, 32.0, 20.7.

**(E)-4-(4-Bromophenyl)pent-3-en-2-one:**



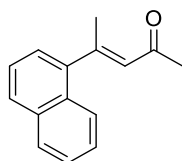
Column chromatography: silica gel, 5-20% AcOEt in hexanes. Yield: 2.21 g (93%) starting from 2.81 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*p*-bromophenyl)but-2-enamide; yellowish solid; ; m.p. 54-56 °C [lit.<sup>2</sup> 49-51 °C]; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.51–7.46 (m, 2H), 7.35–7.31 (m, 2H), 6.47 (q, *J* = 1.3 Hz, 1H), 2.48 (d, *J* = 1.3 Hz, 3H), 2.27 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.6, 152.3, 141.3, 131.7, 128.0, 124.7, 123.3, 32.2, 18.1.

**(*E*)-4-([1,1'-Biphenyl]-4-yl)pent-3-en-2-one:**



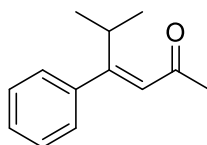
Column chromatography: silica gel, 30-50% AcOEt in hexanes. Yield: 2.10 g (97%) starting from 2.58 g of (*E*)-*N*-methoxy-*N*-methyl-3-(*p*-phenylphenyl)but-2-enamide; yellowish solid; m.p. 136-138 °C [Lit.<sup>3</sup> 120-121 °C]; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.65–7.56 (m, 6H), 7.49–7.43 (m, 2H), 7.41–7.36 (m, 1H), 6.59 (q, *J* = 1.4 Hz, 1H), 2.60 (d, *J* = 1.4 Hz, 3H), 2.32 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.7, 153.2, 142.0, 141.2, 140.2, 128.9, 127.7, 127.2, 127.0, 127.0, 124.3, 32.3, 18.2.

**(*E*)-4-(Naphthalen-1-yl)pent-3-en-2-one:**



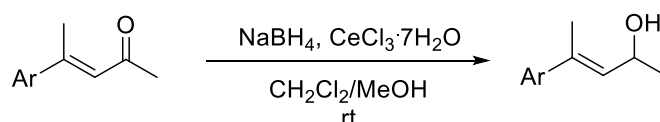
Column chromatography: silica gel, 5-20% AcOEt in hexanes. Yield: 2.08 g (96%) starting from 2.64 g of (*E*)-*N*-methoxy-*N*-methyl-3-(naphthalen-1-yl)but-2-enamide; yellow oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.93–7.85 (m, 2H), 7.81 (d, *J* = 8.3 Hz, 1H), 7.53–7.48 (m, 2H), 7.48–7.42 (m, 1H), 7.29 (d, *J* = 7.1 Hz, 1H), 6.38 (q, *J* = 1.4 Hz, 1H), 2.63 (d, *J* = 1.4 Hz, 3H), 2.30 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.8, 155.3, 142.3, 133.8, 130.1, 128.5, 128.2, 127.8, 126.3, 126.0, 125.3, 125.2, 124.2, 32.1, 22.1.

### **(*E*)-5-Methyl-4-phenylhex-3-en-2-one:**



Column chromatography: silica gel, 5% AcOEt in hexanes. Yield: 562 mg (87%) starting from 802 mg of (*E*)-*N*-methoxy-*N*,4-dimethyl-3-phenylpent-2-enamide; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.36–7.27 (m, 3H), 7.24–7.15 (m, 2H), 6.06 (s, 1H), 4.03 (sept, *J* = 7.0 Hz, 1H), 2.23 (s, 3H), 1.06 (d, *J* = 7.0 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.7, 165.4, 140.9, 127.8, 127.6, 127.6, 126.0, 32.2, 29.5, 21.3.

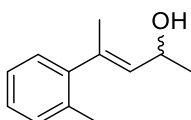
### **Synthesis of racemic allylic alcohols 3:**



To a suspension of enone **1** (3 mmol) and CeCl<sub>3</sub>·7H<sub>2</sub>O (3.6 mmol) in CH<sub>2</sub>Cl<sub>2</sub>/MeOH (4:1 v/v, 50 mL), NaBH<sub>4</sub> (3.6 mmol) was added portionwise. After stirring at ambient temperature for 2 h, the reaction mixture was partitioned between CH<sub>2</sub>Cl<sub>2</sub> and

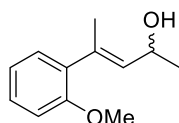
H<sub>2</sub>O. The organic layer was separated, and the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic solutions were dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (20% AcOEt in hexanes) to afford mixture of alcohols **3**.

**(E)-4-(*o*-Tolyl)pent-3-en-2-ol (3b):**



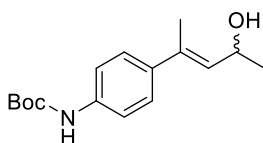
Yield: 246 mg (98%) starting from 248 mg enone **1b**; yellowish oil; spectral data in agreement with **2b**.

**(E)-4-(2-Methoxyphenyl)pent-3-en-2-ol (3e):**



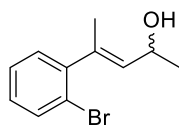
Yield: 168 mg (83%) starting from 200 mg enone **1e**; yellowish oil; spectral data in agreement with **2e**.

***t*-Butyl (E)-(4-(4-hydroxypent-2-en-2-yl)phenyl)carbamate (3f):**



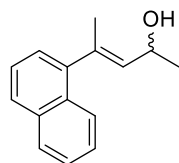
Yield: 221 mg (93%) starting from 235 mg enone **1f**; yellow oil; spectral data in agreement with **2f**.

**(E)-4-(2-Bromophenyl)pent-3-en-2-ol (3i):**



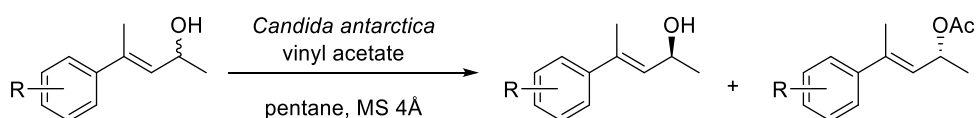
Yield: 167 mg (83%) starting from 200 mg enone **1i**; yellowish oil; spectral data in agreement with **2i**.

**(E)-4-(Naphthalen-1-yl)pent-3-en-2-ol (3l):**



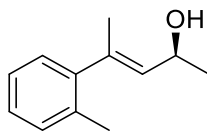
Yield: 188 mg (93%) starting from 200 mg enone **1i**; yellowish oil; spectral data in agreement with **2l**.

**Enzymatic kinetic resolution of racemic  $\beta,\beta$ -disubstituted allyl alcohols **3**.<sup>4</sup>**



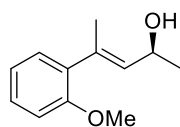
A suspension of racemic alcohols **3** (2.5 mmol), Novozyme 435 (18 mg), 4 Å molecular sieves (100 mg), and vinyl acetate (25 mmol, 2.2 g, 2.3 mL) in pentane (7 mL) was stirred in room temperature. The progress of the reaction was followed by <sup>1</sup>H NMR. The reaction mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (15% AcOEt in hexanes).

**(S,E)-4-(o-Tolyl)pent-3-en-2-ol (2b):**



The reaction mixture was stirred for 48 h. Yield: 109 mg (44%) starting from 247 mg racemic alcohol **3b**; yellowish oil;  $[\alpha]_D^{23} -14.3$  (c 1.06,  $\text{CHCl}_3$ ), *e.e.* 93%; (HPLC:  $R_t$  9.9 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.21–7.12 (m, 3H), 7.12–7.06 (m, 1H), 5.38 (dq,  $J = 8.5, 1.6$  Hz, 1H), 4.75 (dq,  $J = 8.5, 6.3$  Hz, 1H), 2.30 (s, 3H), 2.00 (d,  $J = 1.6$  Hz, 3H), 1.36 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.6, 137.6, 134.5, 133.6, 130.1, 128.0, 126.8, 125.6, 64.9, 23.5, 19.7, 18.3; FTIR (film)  $\nu$ : 3347, 2969, 2925, 1487, 1450, 1374, 1271, 1120, 1060, 759, 727  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{16}\text{O}$  [M] 176.1201; found 176.1198; HPLC (racemate) column Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm; 7.3 min (*R*-enantiomer) and  $R_t$  9.7 min (*S*-enantiomer).

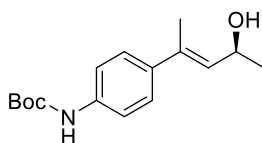
**(*S,E*)-4-(2-Methoxyphenyl)pent-3-en-2-ol (2e):**



The reaction mixture was stirred for 4 days. Yield: 107 mg (46%) starting from 233 mg racemic alcohol **3e**; yellowish oil;  $[\alpha]_D^{22} -21.7$  (c 1.32,  $\text{CHCl}_3$ ), *e.e.* 96%; (HPLC:  $R_t$  13.8 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.26–7.20 (m, 1H), 7.14–7.10 (m, 1H), 6.94–6.88 (m, 1H), 6.88–6.84 (m, 1H), 5.50 (dq,  $J = 8.4, 1.5$  Hz, 1H), 4.73 (dq,  $J = 8.4, 6.3$  Hz, 1H), 3.81 (s, 3H), 2.04 (d,  $J = 1.5$  Hz, 4H), 1.86 (br s, 1H), 1.33 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 136.6, 133.9, 133.7, 129.5, 128.3, 120.6, 110.8, 64.8, 55.4, 23.3, 17.3; FTIR (film)  $\nu$ : 3367, 2967, 2927, 1489, 1463, 1435, 1248, 1227, 1121,

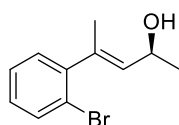
1054, 1028, 753  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{16}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  215.1048; found 215.1043; HPLC (racemate) column Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm; 9.1 min (*R*-enantiomer) and  $R_t$  13.8 min (*S*-enantiomer).

***tert*-Butyl (*S,E*)-(4-(4-hydroxypent-2-en-2-yl)phenyl)carbamate (2f):**



The reaction mixture was stirred for 24 h. Column chromatography: silica gel was deactivated by addition of TEA. Yield: 89 mg (46%) starting from 191 mg racemic alcohol **3f**; white solid; m.p. 102-103 °C  $[\alpha]_D^{22}$  -36.5 (*c* 1.08,  $\text{CHCl}_3$ ), *e.e.* 89%; (HPLC:  $R_t$  23.9 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 (s, 4H), 6.69 (br s, 1H), 5.75 (dq, *J* = 8.3, 1.4 Hz, 1H), 4.72 (dq, *J* = 8.3, 6.3 Hz, 1H), 2.04 (d, *J* = 1.4 Hz, 3H), 1.90 (br s, 1H), 1.51 (s, 9H), 1.32 (d, *J* = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  152.8, 137.5, 137.5, 135.4, 130.9, 126.3, 118.3, 80.5, 65.2, 28.3, 23.6, 15.9; FTIR (film)  $\nu$ : 3324, 2976, 2928, 1702, 1592, 1524, 1409, 1367, 1318, 1240, 1162, 1058, 830  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  300.1576; found 300.1571; HPLC (racemate) column Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm; 7.4 min (*R*-enantiomer) and  $R_t$  9.9 min (*S*-enantiomer).

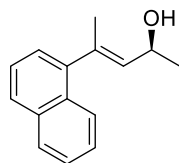
**(*S,E*)-4-(2-Bromophenyl)pent-3-en-2-ol (2i):**





The reaction mixture was stirred for 48 h. Yield: 69 mg (50%) starting from 138 mg racemic alcohol **3i**; yellowish oil;  $[\alpha]_D^{22} -10.7$  (c 2.31, CHCl<sub>3</sub>), *e.e.* 91%; (HPLC:  $R_t$  10.1 min); spectral data in agreement with literature:<sup>2</sup> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.55–7.51 (m, 1H), 7.28–7.22 (m, 1H), 7.18–7.13 (m, 1H), 7.13–7.07 (m, 1H), 5.41 (dq,  $J = 8.5, 1.5$  Hz, 1H), 4.73 (dq,  $J = 8.5, 6.3$  Hz, 1H), 2.02 (d,  $J = 1.5$  Hz, 3H), 1.61 (br s, 1H), 1.34 (d,  $J = 6.3$  Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  145.3, 137.6, 134.6, 132.7, 129.7, 128.3, 127.3, 122.0, 64.9, 23.2, 17.9; LRMS [EI]  $m/z$  240.0; HPLC (racemate) column Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm; 7.4 min (*R*-enantiomer) and  $R_t$  9.9 min (*S*-enantiomer).

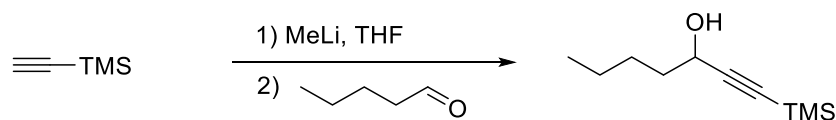
**(*S,E*)-4-(Naphthalen-1-yl)pent-3-en-2-ol (2l):**



The reaction mixture was stirred for 24 h. Yield: 101 mg (50%) starting from 201 mg racemic alcohol **3i**; yellowish oil;  $[\alpha]_D^{23} -15.1$  (c 1.37, CHCl<sub>3</sub>), *e.e.* 99%; (HPLC:  $R_t$  19.7 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.05–7.94 (m, 1H), 7.93–7.84 (m, 1H), 7.78 (d,  $J = 8.2$  Hz, 1H), 7.55–7.40 (m, 3H), 7.30 (d,  $J = 7.1$  Hz, 1H), 5.62 (dq,  $J = 8.4, 1.6$  Hz, 1H), 4.89 (dq,  $J = 8.5, 6.3$  Hz, 1H), 2.20 (d,  $J = 1.6$  Hz, 3H), 1.45 (d,  $J = 6.3$  Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  142.8, 136.7, 134.8, 133.8, 130.9, 128.4, 127.2, 125.8, 125.6, 125.5, 125.4, 124.8, 65.1, 23.7, 19.3; FTIR (film)  $\nu$ : 3341, 2967, 1444, 1395, 1373, 1120, 1056, 800, 777 cm<sup>-1</sup>; HRMS (EI)  $m/z$  calcd for C<sub>15</sub>H<sub>16</sub>O [M] 212.1201; found 212.1205; HPLC (racemate) column Chiralcel OD-H, 10% *i*-PrOH in hexanes,

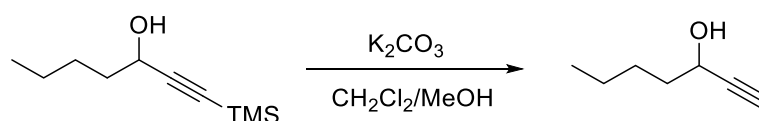
flow 1 mL/min, det. 254 nm; 16.2 min (*R*-enantiomer) and  $R_t$  19.4 min (*S*-enantiomer).

### 1-(Trimethylsilyl)hept-1-yn-3-ol:



Ethynyltrimethylsilane (74.8 mmol, 7.4 g, 10.7 mL) was dissolved in THF (300 mL) and cooled to  $-78$  °C under argon atmosphere. Then, a solution of MeLi (1.6 M in Et<sub>2</sub>O, 81.6 mmol, 51 mL) was added dropwise. The mixture was stirred for 1.5 h at  $-78$  °C. Next, pentanal (68.0 mmol, 5.8 g, 7.2 mL) was added dropwise. The mixture was slowly warmed to room temperature and stirred for another 1.5 h. The progress of the reaction was followed by NMR. When the reaction was complete, a saturated aqueous ammonium chloride solution was added to the mixture. The aqueous phase was extracted with Et<sub>2</sub>O and the combined organic phase was dried over sodium sulfate. After the removal of the solvent, the crude residue was purified by column chromatography on silica gel (5% AcOEt in hexanes). Yield: 11.23 g (90%); colourless oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.33 (td,  $J = 6.6, 5.4$  Hz, 1H), 1.97 (br s, 1H), 1.76–1.59 (m, 2H), 1.53–1.21 (m, 4H), 0.90 (t,  $J = 7.1$  Hz, 3H), 0.15 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  107.0, 89.2, 62.8, 37.4, 27.3, 22.3, 13.9,  $-0.2$ .

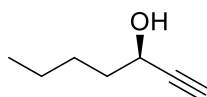
### Hept-1-yn-3-ol:



A suspension of 1-(trimethylsilyl)hept-1-yn-3-ol (60.7 mmol, 11.2 g),  $K_2CO_3$  (121.4 mmol, 16 g), MeOH (30 mL) and  $CH_2Cl_2$  (100 mL) was stirred overnight at room temperature. When the reaction was complete, water was added to the mixture. The aqueous phase was extracted with  $CH_2Cl_2$  and the combined organic phase was dried over sodium sulfate. After the removal of the solvent, the crude residue was purified by column chromatography on silica gel (10-50%  $Et_2O$  in pentanes). Yield: 6.21 g (91%); colourless liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  4.32 (tdd,  $J = 6.7, 5.3, 2.1$  Hz, 1H), 2.59 (br s, 1H), 2.42 (d,  $J = 2.1$  Hz, 1H), 1.76–1.59 (m, 2H), 1.48–1.25 (m, 4H), 0.88 (t,  $J = 7.2$  Hz, 3H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  85.1, 72.7, 62.1, 37.3, 27.1, 22.3, 13.9.

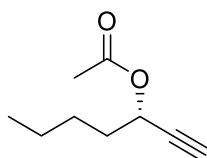
**Kinetic resolution of hept-1-yn-3-ol:** A suspension of racemic hept-1-yn-3-ol (52.7 mmol), Novozyme 435 (392 mg), 4 Å molecular sieves (1.8 g), and vinyl acetate (263.6 mmol) in pentane (73 mL) was stirred at room temperature. The progress of the reaction was followed by  $^1H$  NMR. The reaction mixture was stirred for 5 h, and filtered through Celite. The solvent was carefully removed under reduced pressure (500-600 mBar). The residue was chromatographed on silica gel (0-50%  $Et_2O$  in pentanes). The purified product was analyzed by chiral GC for the determination of *e.e.* Yield: 3.96 g (49%) of (*S*)-hept-1-yn-3-yl acetate and 2.87 g (48%; *e.e.* 90%) of (*R*)-hept-1-yn-3-ol. In order to achieve enriched enantiopurity of the (*R*)-allyl alcohol, enzymatic resolution was performed again. Yield: 2.00 g (70%) of (*R*)-hept-1-yn-3-ol.

**(R)-Hept-1-yn-3-ol:**



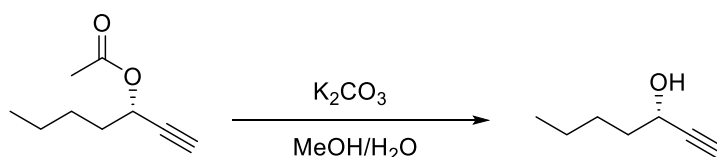
Yield: 2.00 g (34%, after 2 steps); colourless liquid;  $[\alpha]_D^{20} +11.3$  (c 1.07,  $\text{CHCl}_3$ ), *e.e.* 99%; (GC:  $R_t$  15.4 min) [lit.<sup>5</sup>  $[\alpha]_D^{20} +9.3$  (c 1.05,  $\text{CHCl}_3$ ) for *e.e.* 97%]; spectral data in agreement with literature:<sup>5</sup>  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.32 (tdd,  $J = 6.7, 5.3, 2.1$  Hz, 1H), 2.59 (br s, 1H), 2.42 (d,  $J = 2.1$  Hz, 1H), 1.76–1.59 (m, 2H), 1.48 – 1.25 (m, 4H), 0.88 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  85.1, 72.7, 62.1, 37.3, 27.1, 22.3, 13.9; LRMS [EI]  $m/z$  112.1; GC (racemate) column Agilent Cyclosil-B (30m x 0.25 mm x 0.25  $\mu\text{m}$ ), Injection temp.: 150 °C, Detection temp.: 270 °C, Oven temp: 90 °C (30 min), 5°C/min to 150°, hold for 5.00 min; 14.2 min (*S*-enantiomer) and  $R_t$  15.5 min (*R*-enantiomer).

**(S)-Hept-1-yn-3-yl acetate:**



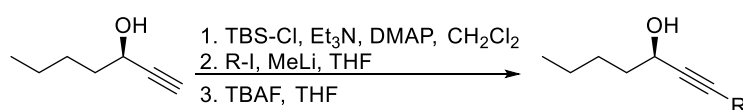
Yield: 3.96 g (49%); yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.34 (td,  $J = 6.7, 2.2$  Hz, 1H), 2.43 (d,  $J = 2.2$  Hz, 1H), 2.08 (s, 3H), 1.86–1.70 (m, 2H), 1.49–1.27 (m, 4H), 0.91 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  169.8, 81.3, 73.3, 63.8, 34.3, 27.0, 22.2, 20.9, 13.8.

**(S)-Hept-1-yn-3-ol:**



A suspension of (*S*)-hept-1-yn-3-yl acetate (25.4 mmol, 3.9 g), K<sub>2</sub>CO<sub>3</sub> (50.8 mmol, 7.0 g), MeOH (50 mL) and H<sub>2</sub>O (20 mL) was stirred for 15 minutes at room temperature. When the reaction was complete, water was added to the mixture. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> and the combined organic phase was dried over sodium sulfate. After the removal of the solvent, the crude product (NMR spectrum was clean) was used in the next step without further purification. Yield: 2.82 g (99%, *e.e.* 86%) of (*S*)-hept-1-yn-3-ol. Because of the low enantiomeric excess of (*S*)-hept-1-yn-3-ol (25.4 mmol, *e.e.* 86%), enzymatic resolution was performed again to enrich enantiopurity as in case of (*R*)-enantiomer (yield: 3.05 g, 78%). Hydrolysis was performed again, according to the procedure described above. Yield: 2.20 g (37%, after 4 steps) of (*S*)-hept-1-yn-3-ol; colorless oil; [α]<sub>D</sub><sup>19</sup> – 5.2 (c 1.07, CHCl<sub>3</sub>), *e.e.* 97%; (GC: *R*<sub>t</sub> 13.8 min) [lit.<sup>29</sup> [α]<sub>D</sub><sup>20</sup> – 9.7 (c 1.03, CHCl<sub>3</sub>) for *e.e.* >99.9%]; spectral data were identical with those for *R*-enantiomer; LRMS [EI] *m/z* 112.1; GC (racemate) column Agilent Cyclosil-B (30m x 0.25 mm x 0.25 μm), Injection temp.: 150 °C, Detection temp.: 270 °C, Oven temp: 90 °C (30 min), 5°C/min to 150°, hold for 5.00 min; 14.2 min (*S*-enantiomer) and *R*<sub>t</sub> 15.5 min (*R*-enantiomer).

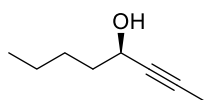
### Synthesis of alkynes 13:



A solution of TBSCl (3.7 mmol, 558 mg) dissolved in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) was added dropwise to a solution of (*R*)-hept-1-yn-3-ol (3.7 mmol, 415 mg), Et<sub>3</sub>N (7.4 mmol,

749 mg, 1 mL), DMAP (0.37 mmol, 45 mg) and CH<sub>2</sub>Cl<sub>2</sub> (8 mL) at 0 °C. After stirring overnight, sat. NH<sub>4</sub>Cl was added and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the crude residue was filtered through a short pad of silica gel and rinsed with pentanes. O-Silylated alcohol was dissolved in THF (18 mL), cooled to -78 °C, and a 1.6 M soln. of MeLi in Et<sub>2</sub>O (4.1 mmol, 2.8 mL) was added dropwise. After stirring for 1 h at -78 °C, alkyl iodide (4.1 mmol) was added, and the mixture was allowed to warm slowly to rt and left to stand overnight. Next, aq. NH<sub>4</sub>Cl was added, the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic layers was dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the crude residue was dissolved in THF (10 mL), cooled to 0 °C, and TBAF (1M in THF, 5.6 mmol, 5.6 mL) was added dropwise. The mixture was allowed to warm slowly to rt and left overnight. Next, water was added, the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of solvents, the crude product was purified by column chromatography on silica gel. If necessary, the silyl by-products were removed by bulb-to-bulb distillation prior to chromatography.

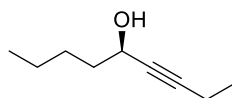
**(R)-Oct-2-yn-4-ol (13a):**



Column chromatography: silica gel, 10-50% Et<sub>2</sub>O in pentanes. Bulb-to-bulb distillation (Kugelrohr) at 50-60 °C under 5 Torr to remove silyl by-products. Yield: 348 mg (75%, after 3

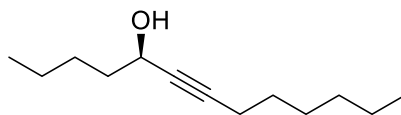
steps) starting from 412 mg (*R*)-hept-1-yn-3-ol; yellowish liquid;  $[\alpha]_D^{17} +3.6$  (c 0.98, CHCl<sub>3</sub>), *e.e.* 99%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.41 – 4.22 (m, 1H), 1.84 (d, *J* = 2.2 Hz, 3H), 1.71 (d, *J* = 5.5 Hz, 1H), 1.70 – 1.60 (m, 2H), 1.47 – 1.27 (m, 4H), 0.91 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 80.7, 80.6, 62.7, 37.8, 27.3, 22.4, 13.9, 3.4; LRMS [EI] *m/z* 126.1.

**(*R*)-Non-3-yn-5-ol (13b):**



Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 85 mg (83%, after 3 steps) starting from 82 mg (*R*)-hept-1-yn-3-ol; yellowish liquid;  $[\alpha]_D^{24} +2.9$  (c 1.00, CHCl<sub>3</sub>), *e.e.* 99%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.46–4.17 (m, 1H), 2.21 (qd, *J* = 7.5, 2.0 Hz, 2H), 1.76–1.56 (m, 3H), 1.49–1.23 (m, 4H), 1.13 (t, *J* = 7.5 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 86.6, 80.8, 62.6, 37.8, 27.3, 22.3, 13.9, 13.8, 12.3; LRMS [EI] *m/z* 140.1.

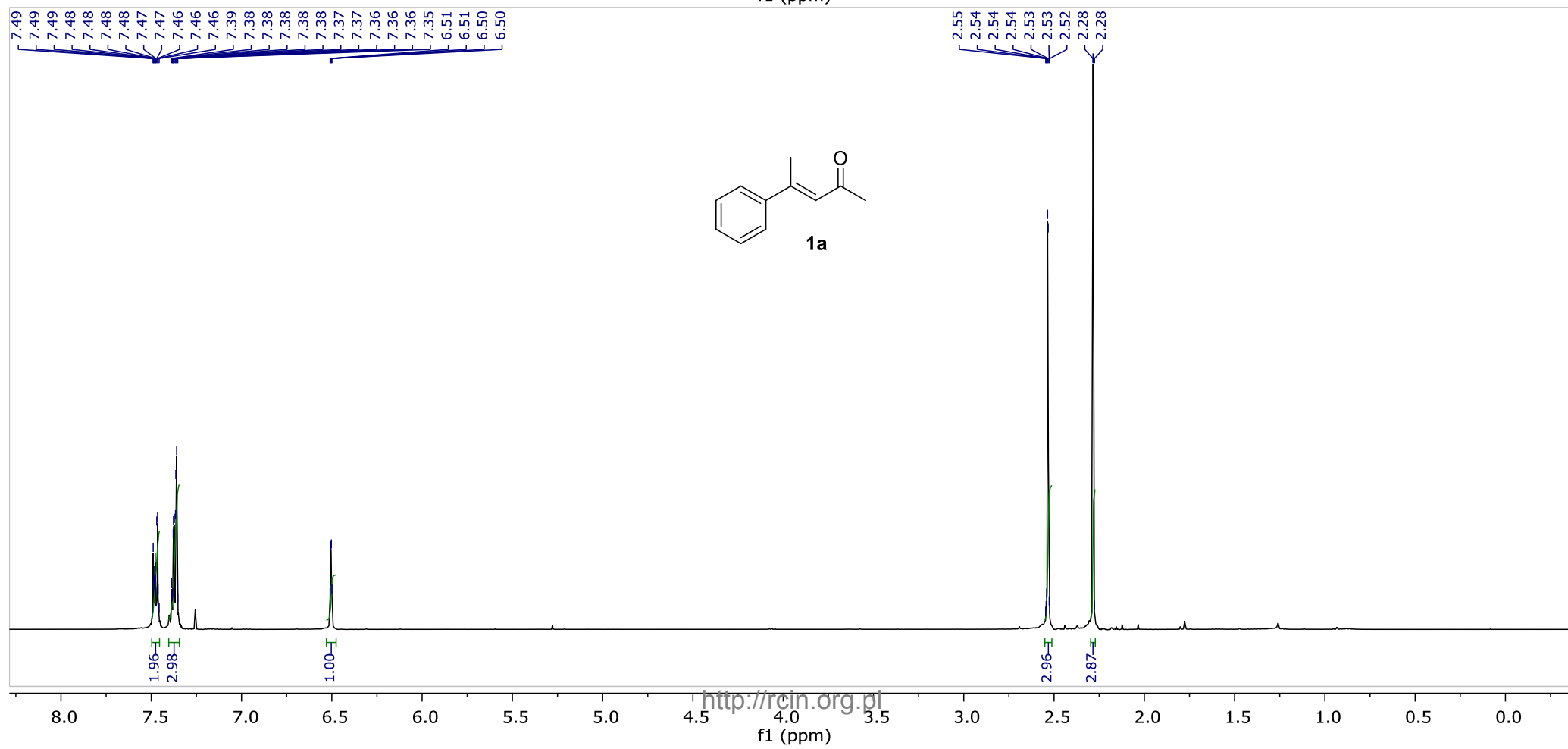
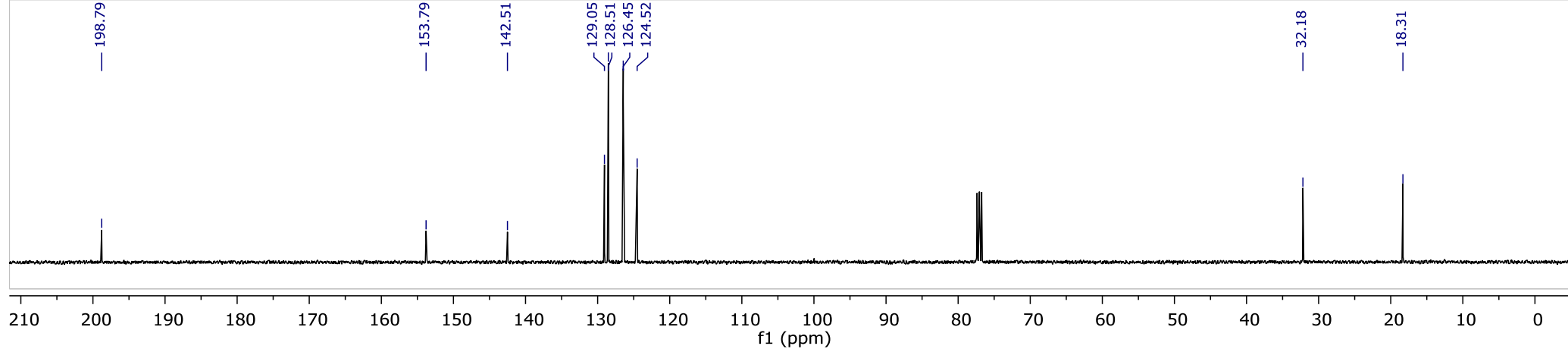
**(*R*)-Tridec-6-yn-5-ol (13c):**



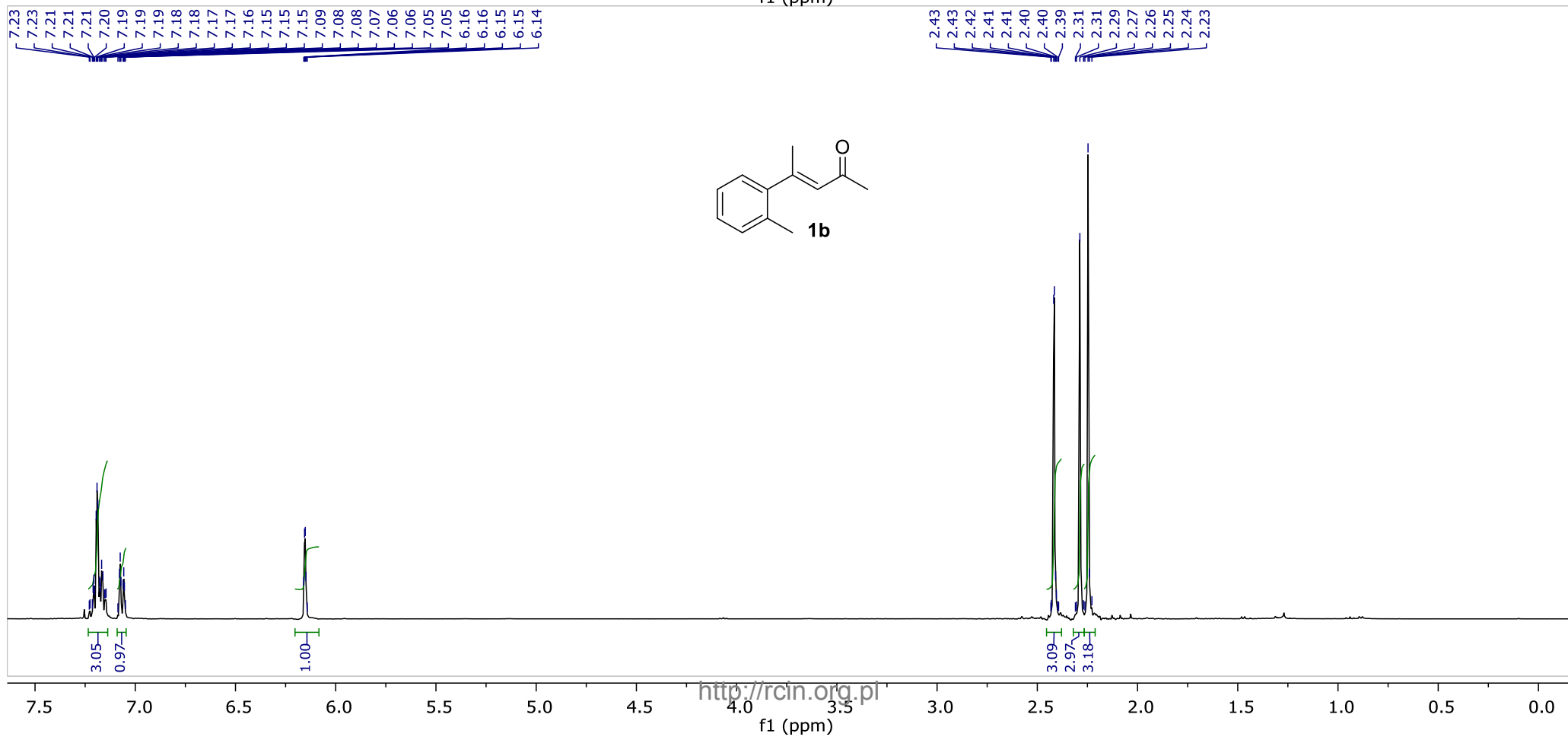
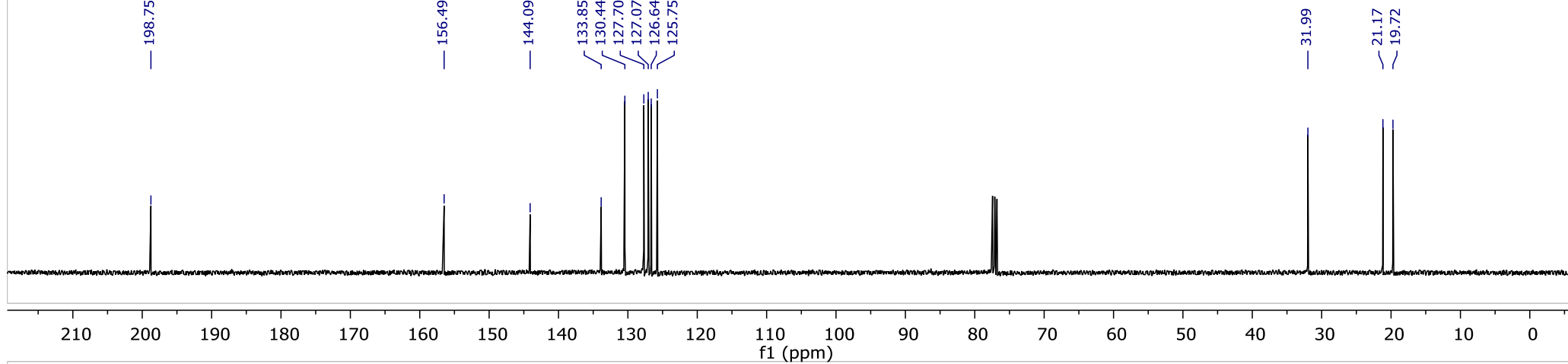
Column chromatography: silica gel, 5-10% AcOEt in hexanes. Yield: 95 mg (70%, after 3 steps) starting from 77 mg (*R*)-hept-1-yn-3-ol; yellowish liquid;  $[\alpha]_D^{17} +6.7$  (c 0.99, CHCl<sub>3</sub>), *e.e.* 99%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.31 (tt, *J* = 6.6, 2.0 Hz, 1H), 2.17 (td, *J* = 7.1, 2.0 Hz, 2H), 2.03 (br s, 1H), 1.73–1.55 (m, 2H), 1.54–1.17 (m, 12H), 0.99–0.76 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 85.3, 81.4, 62.6, 37.9, 31.3, 28.6, 28.5, 27.4, 22.5, 22.4, 18.6, 13.9; LRMS [EI] *m/z* 196.2.

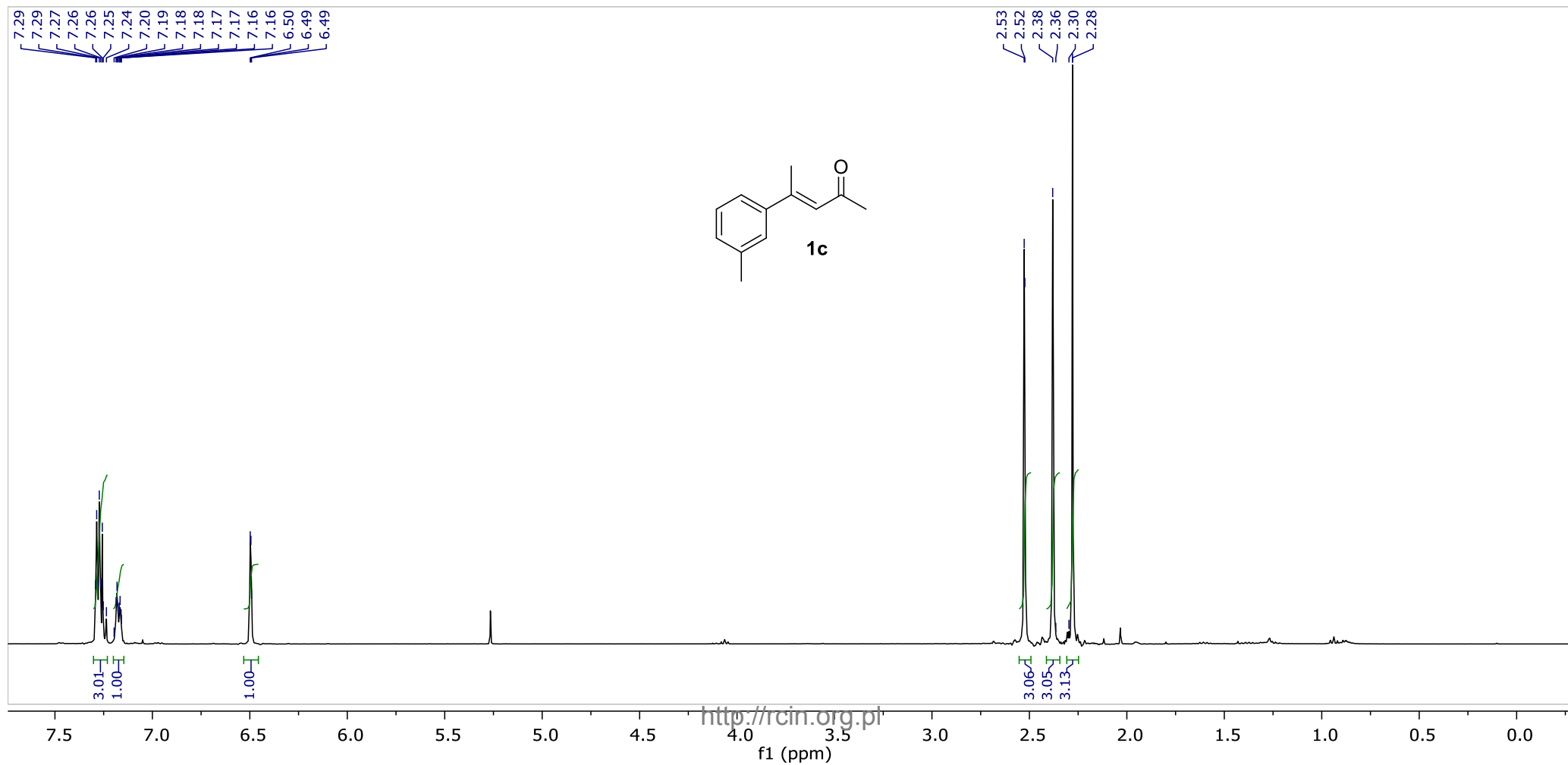
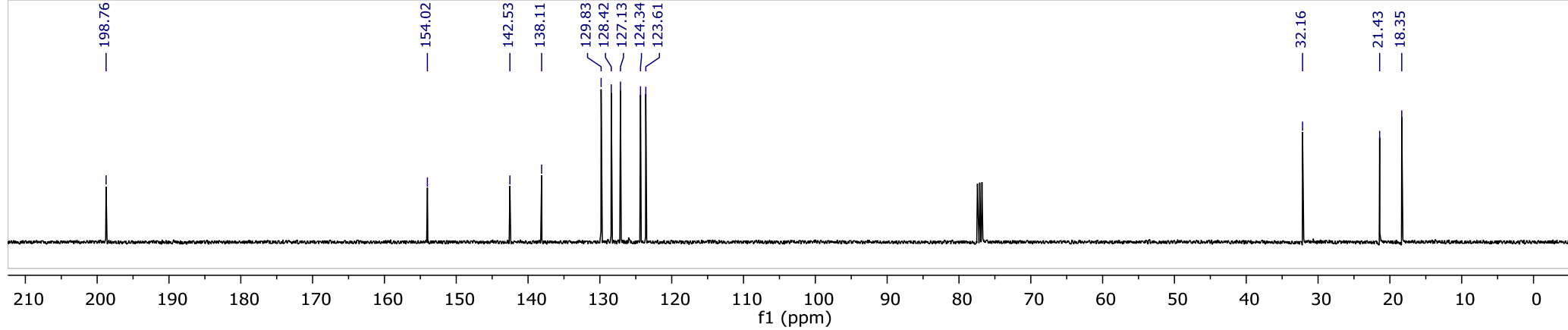
**References:**

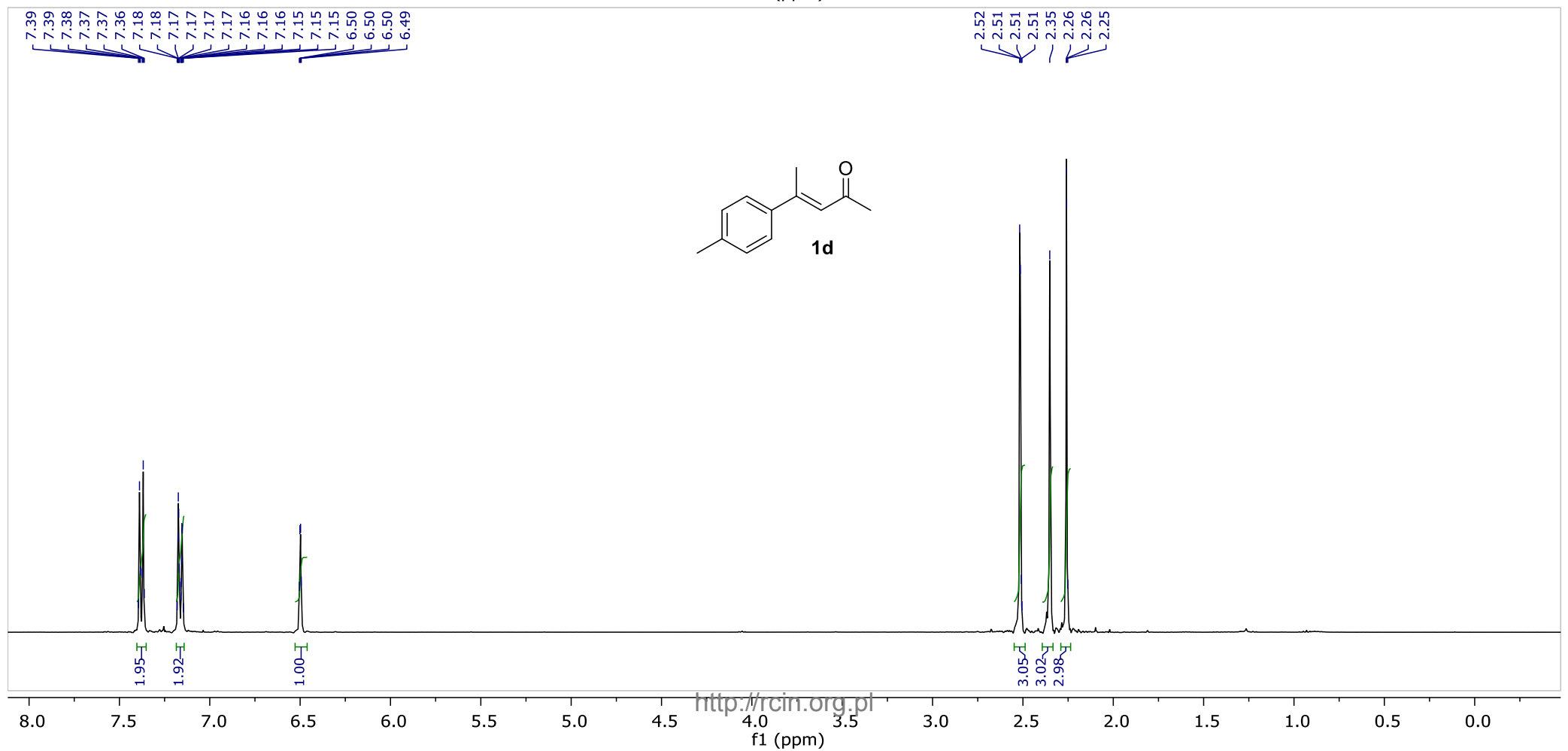
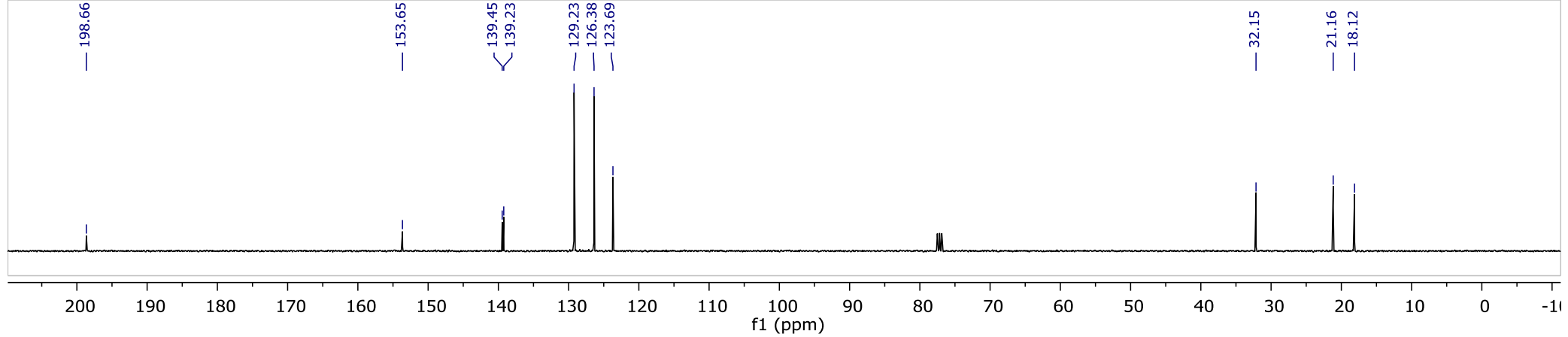
1. Chen, X.; Zhou, H.; Zhang, K.; Li, J.; Huang, H., *Org. Lett.* **2014**, *16*, 3912-3915.
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3. Bethi, V.; Fernandes, R. A., *J. Org. Chem.* **2016**, *81*, 8577-8584.
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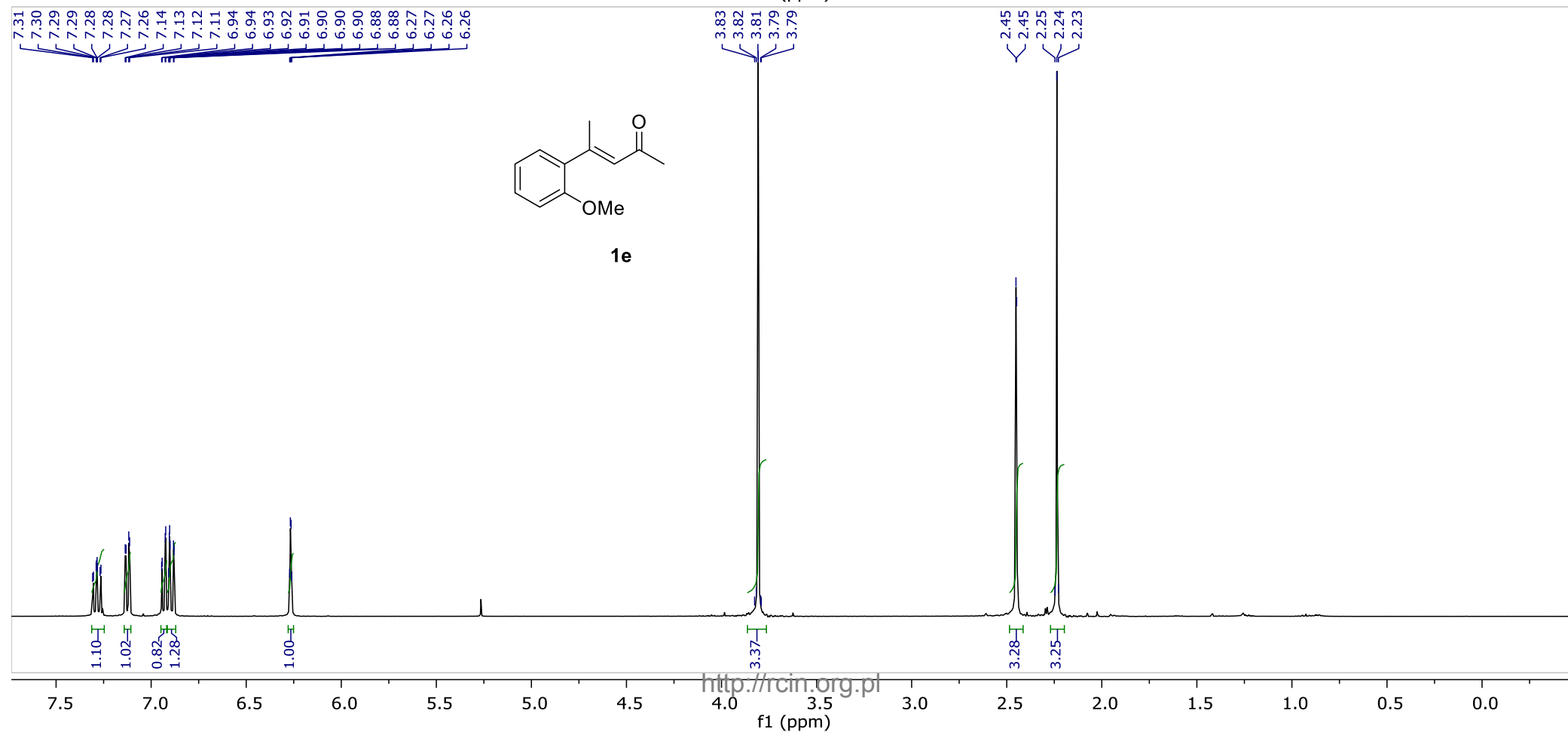
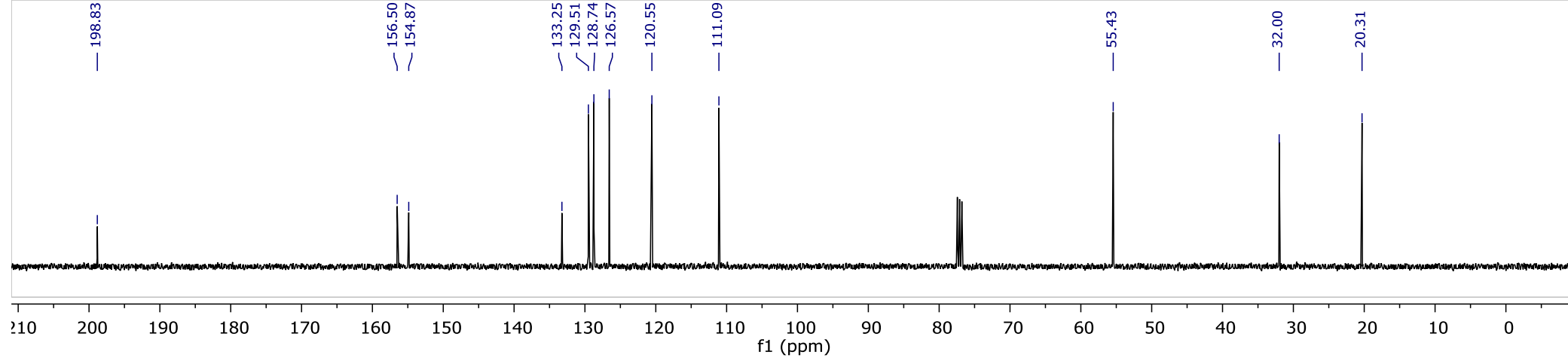


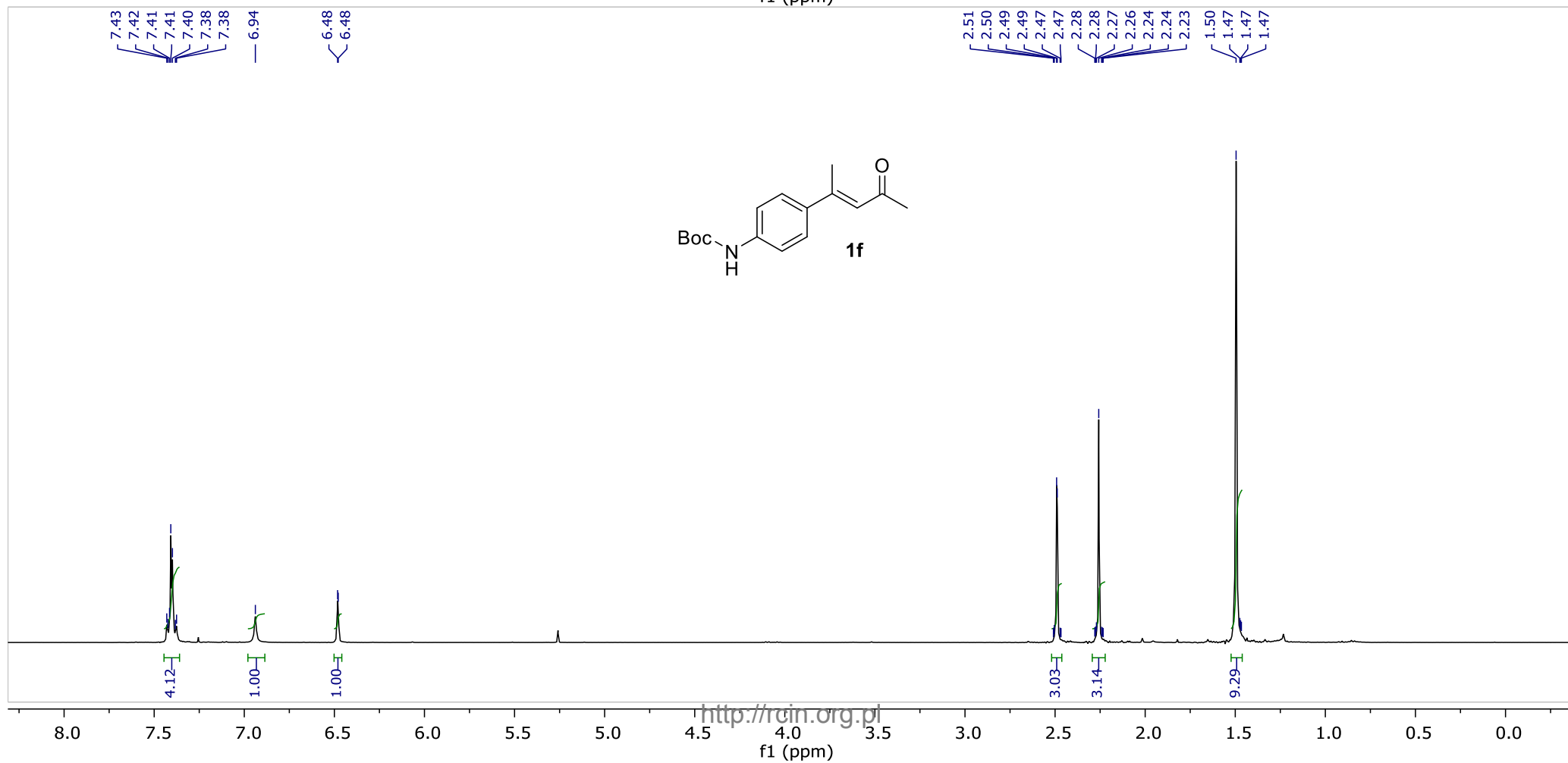
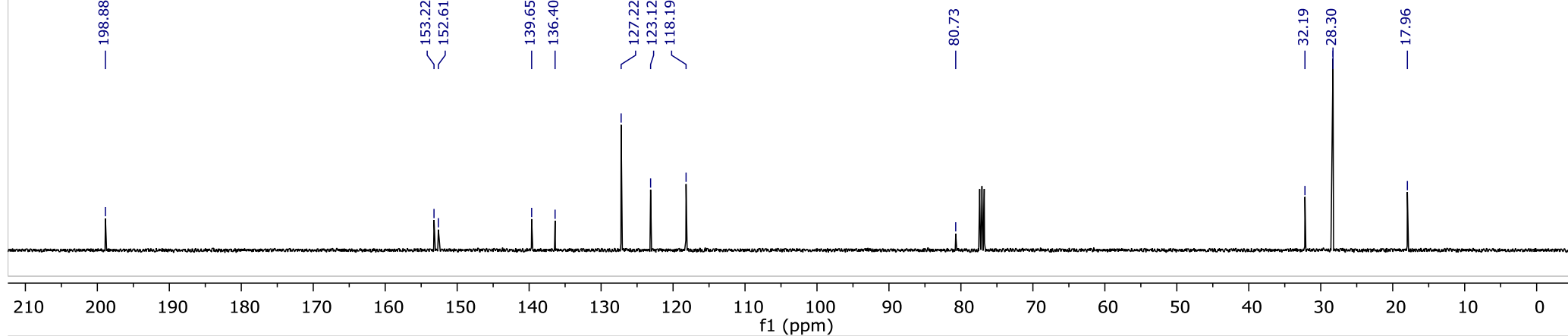


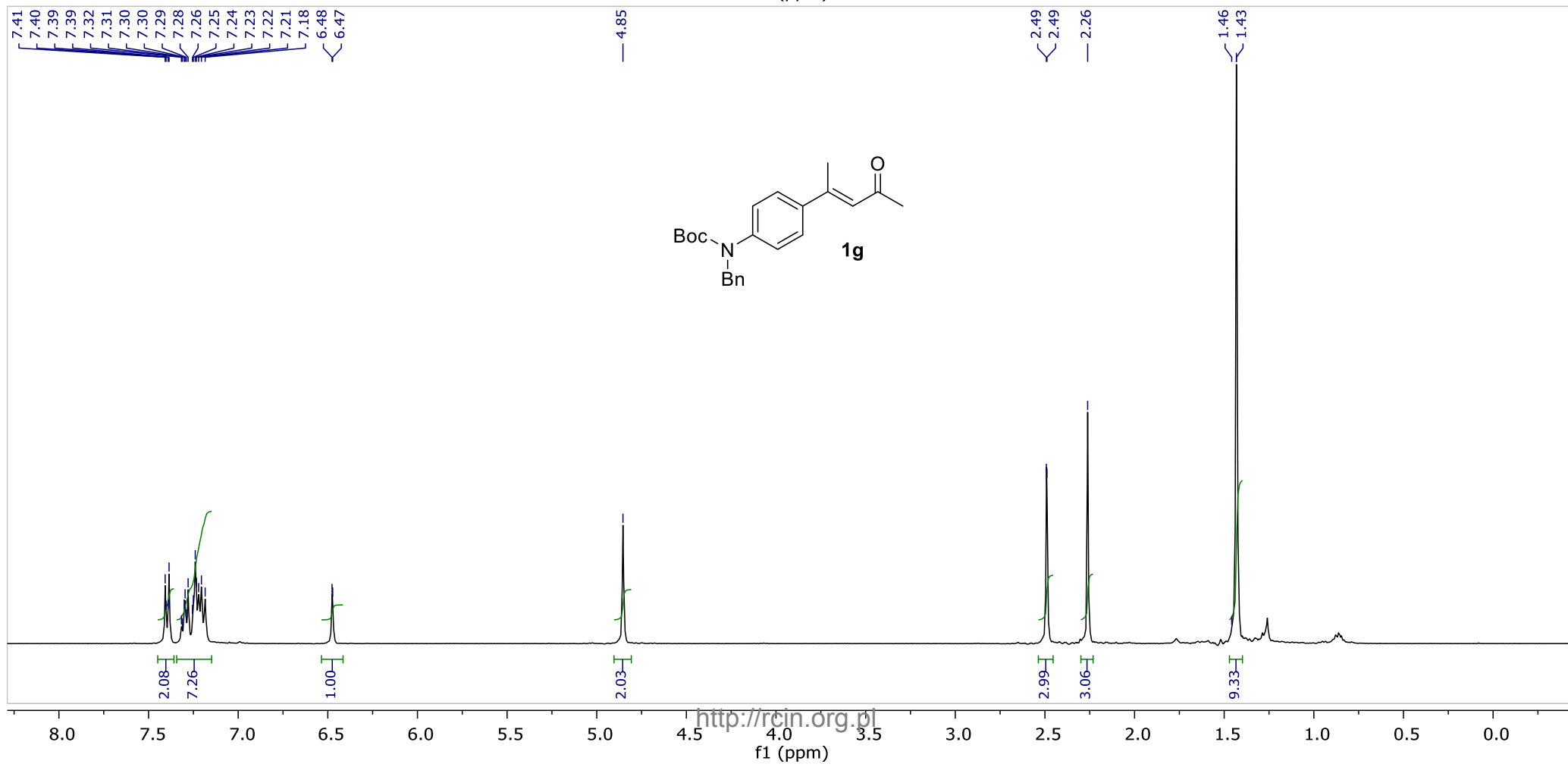
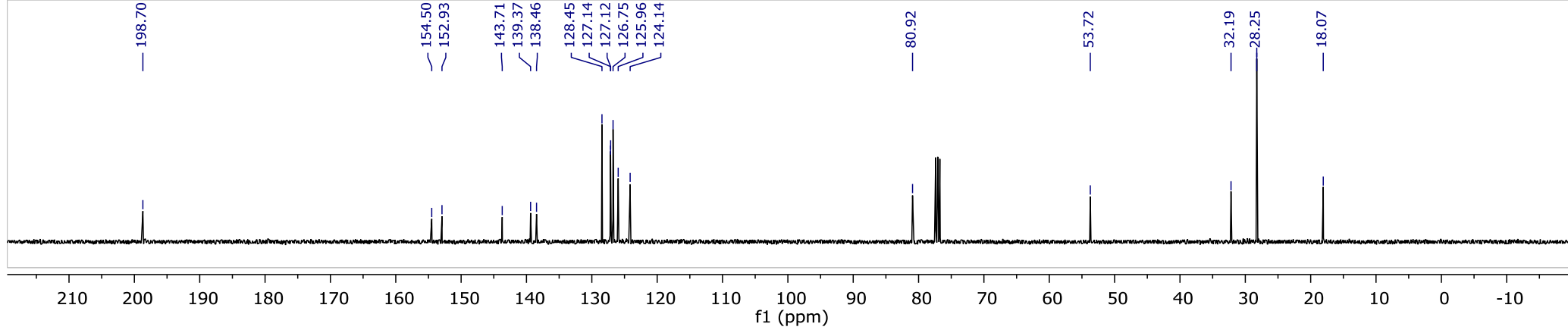


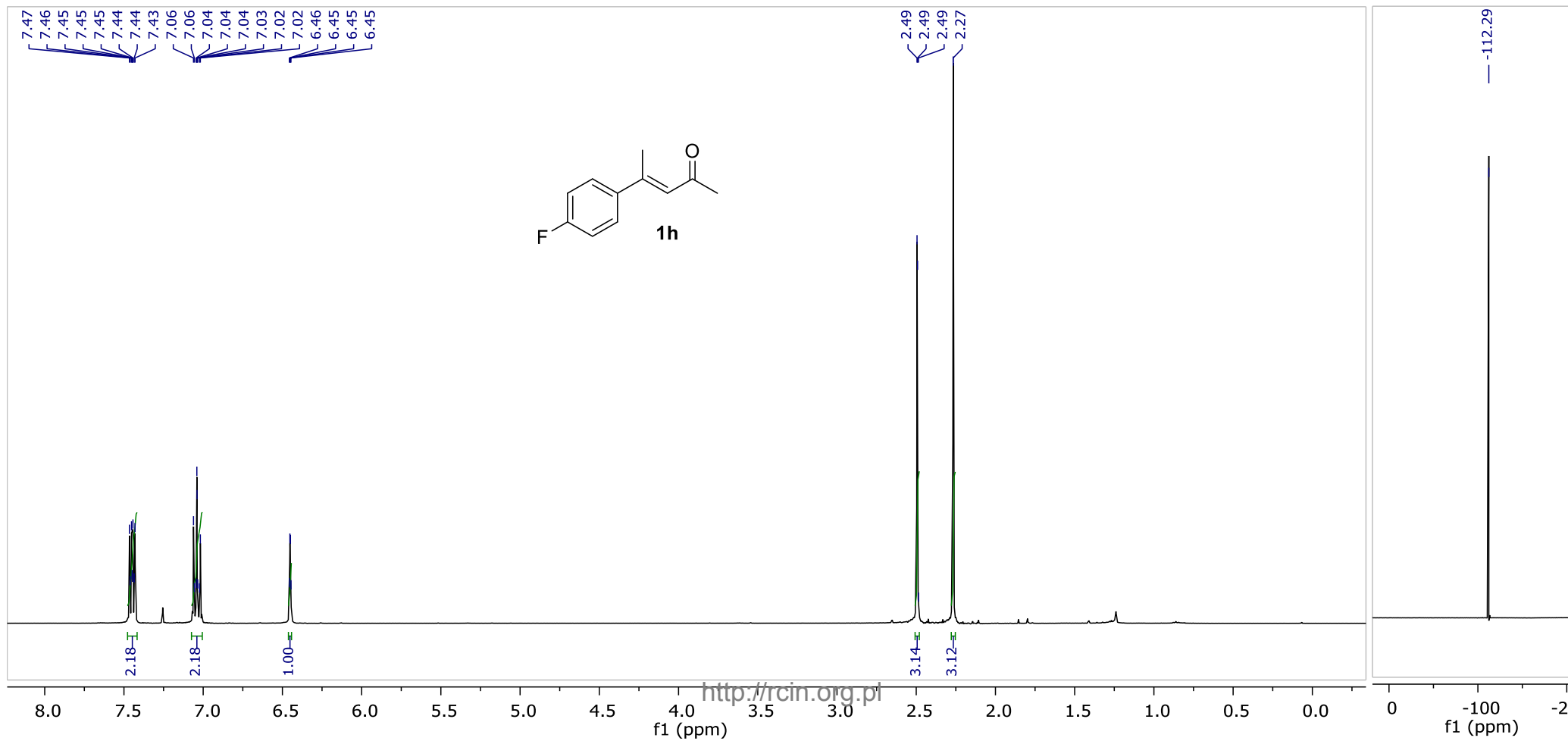
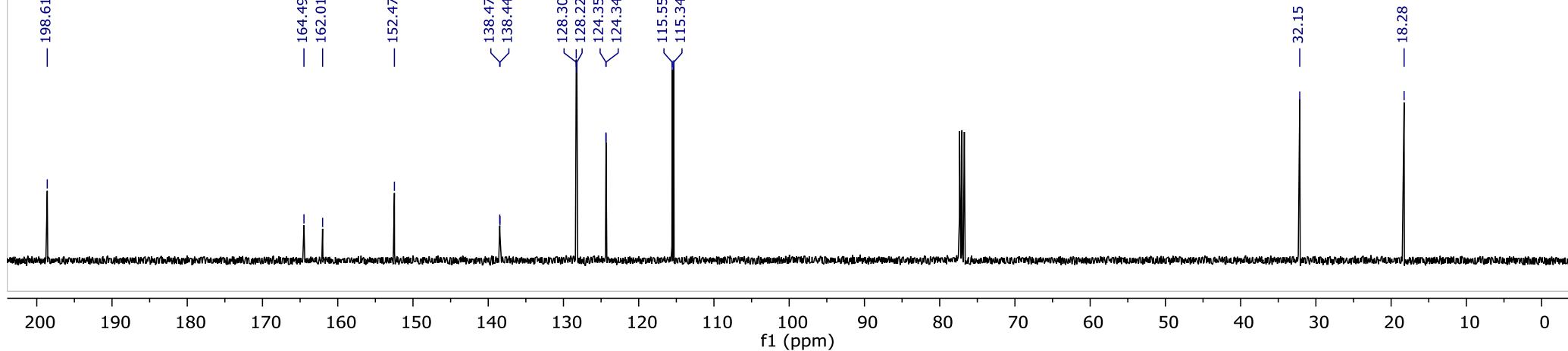


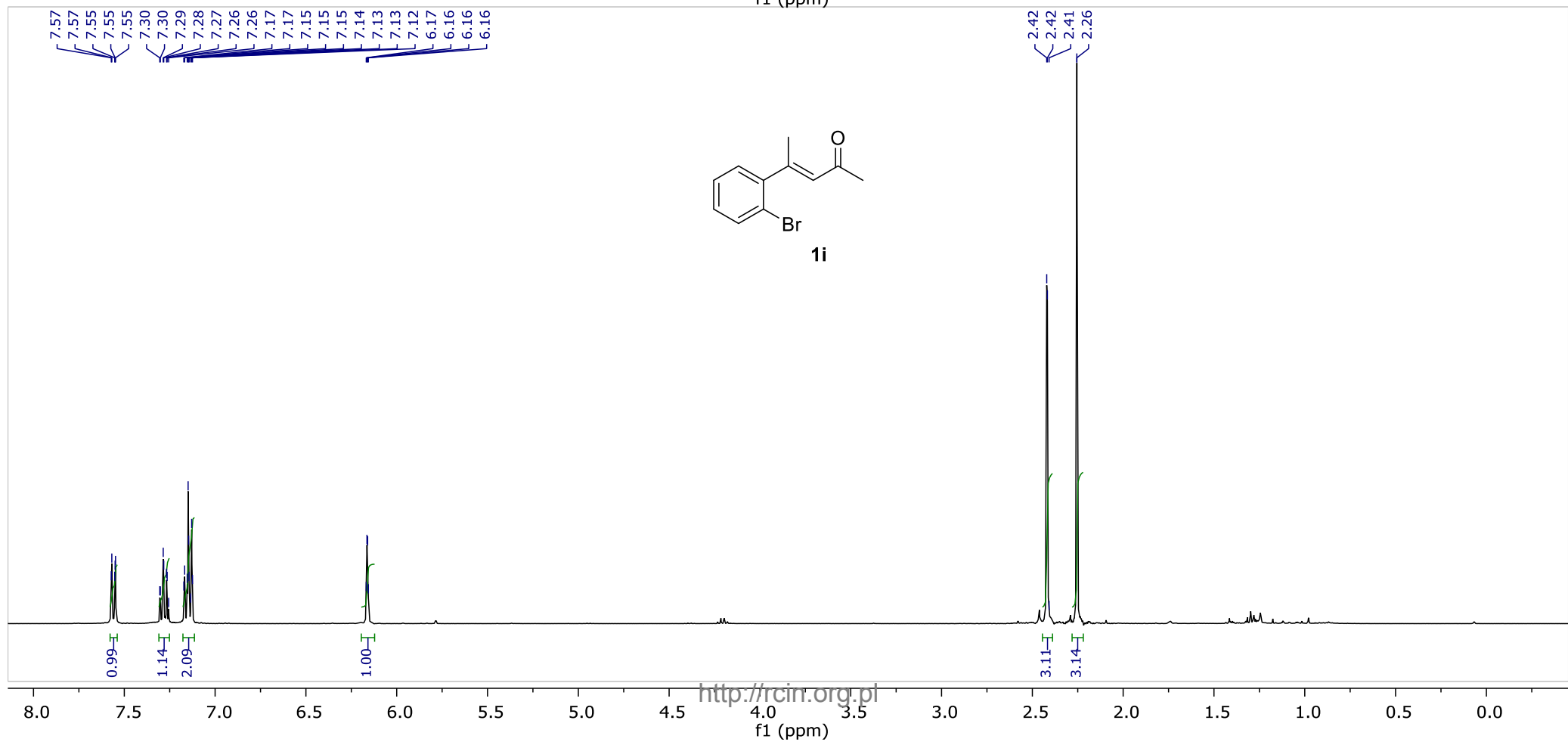
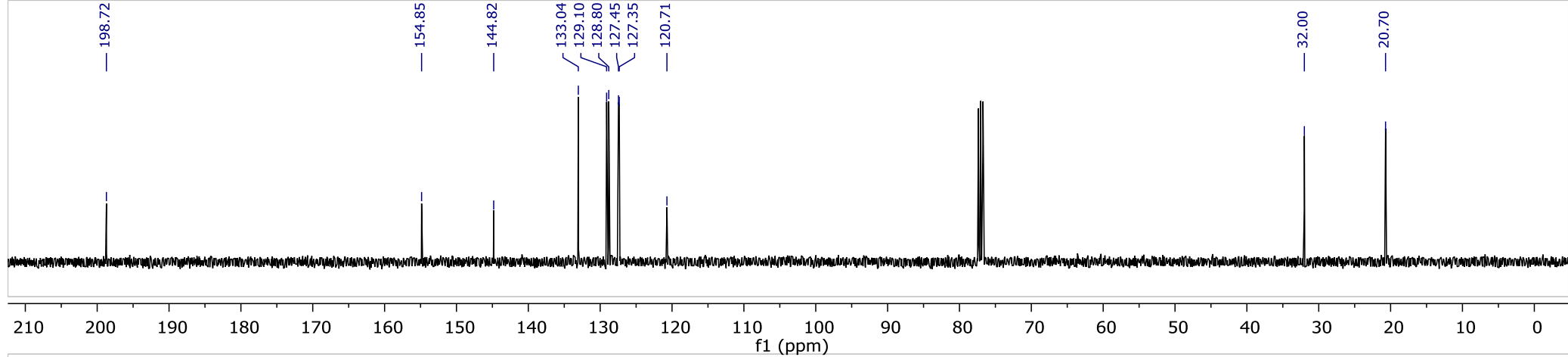




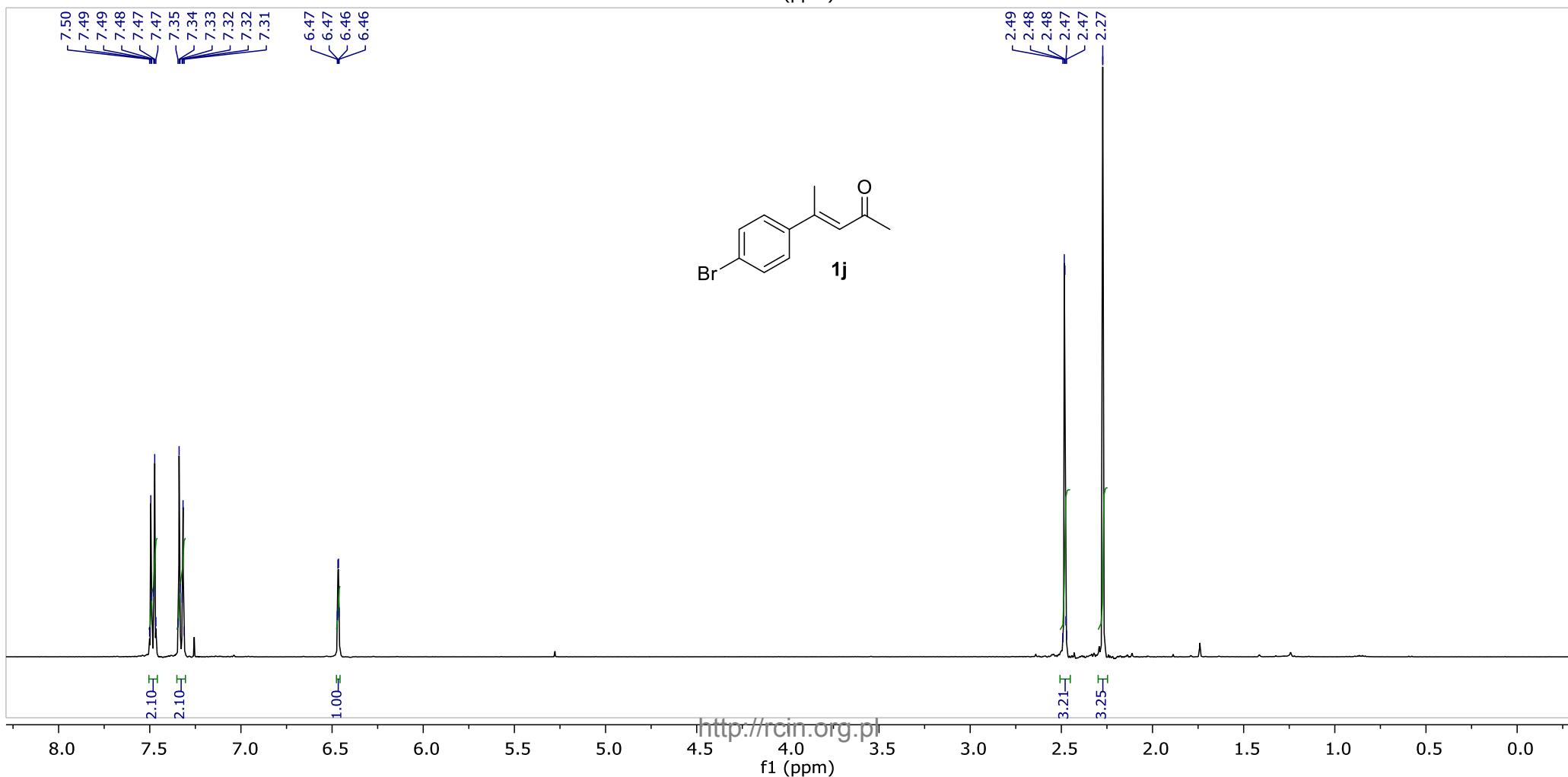
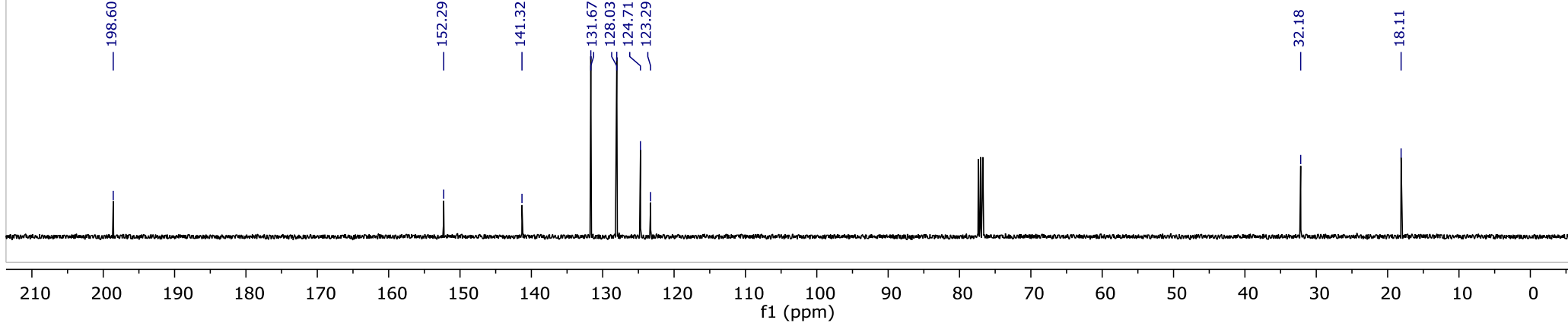


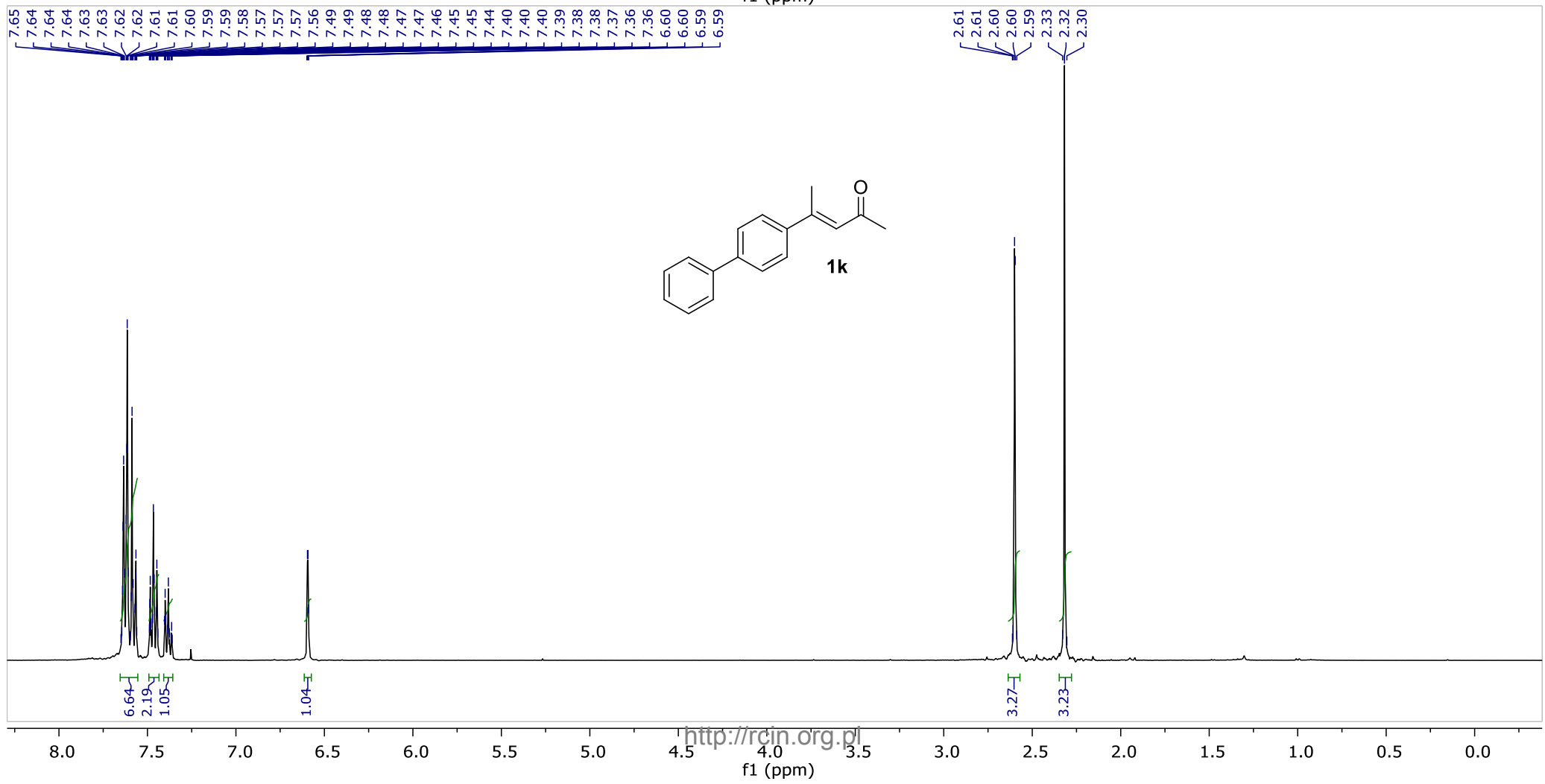
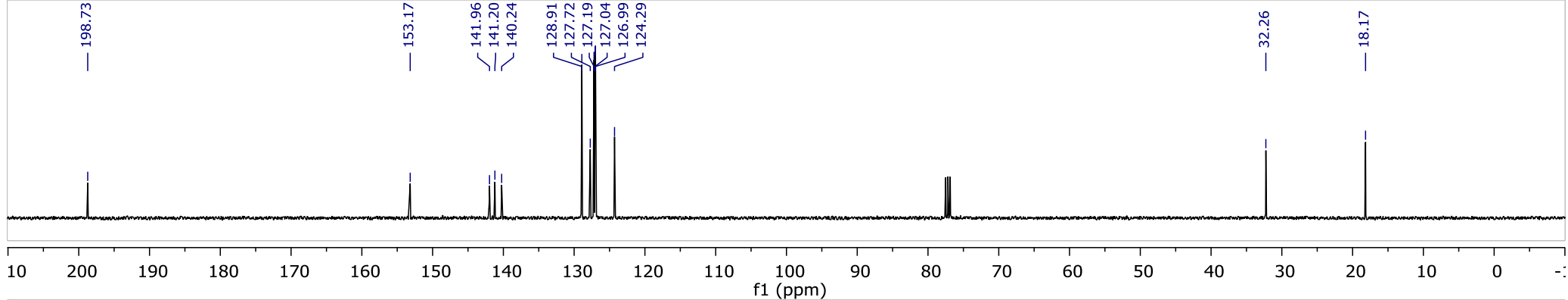


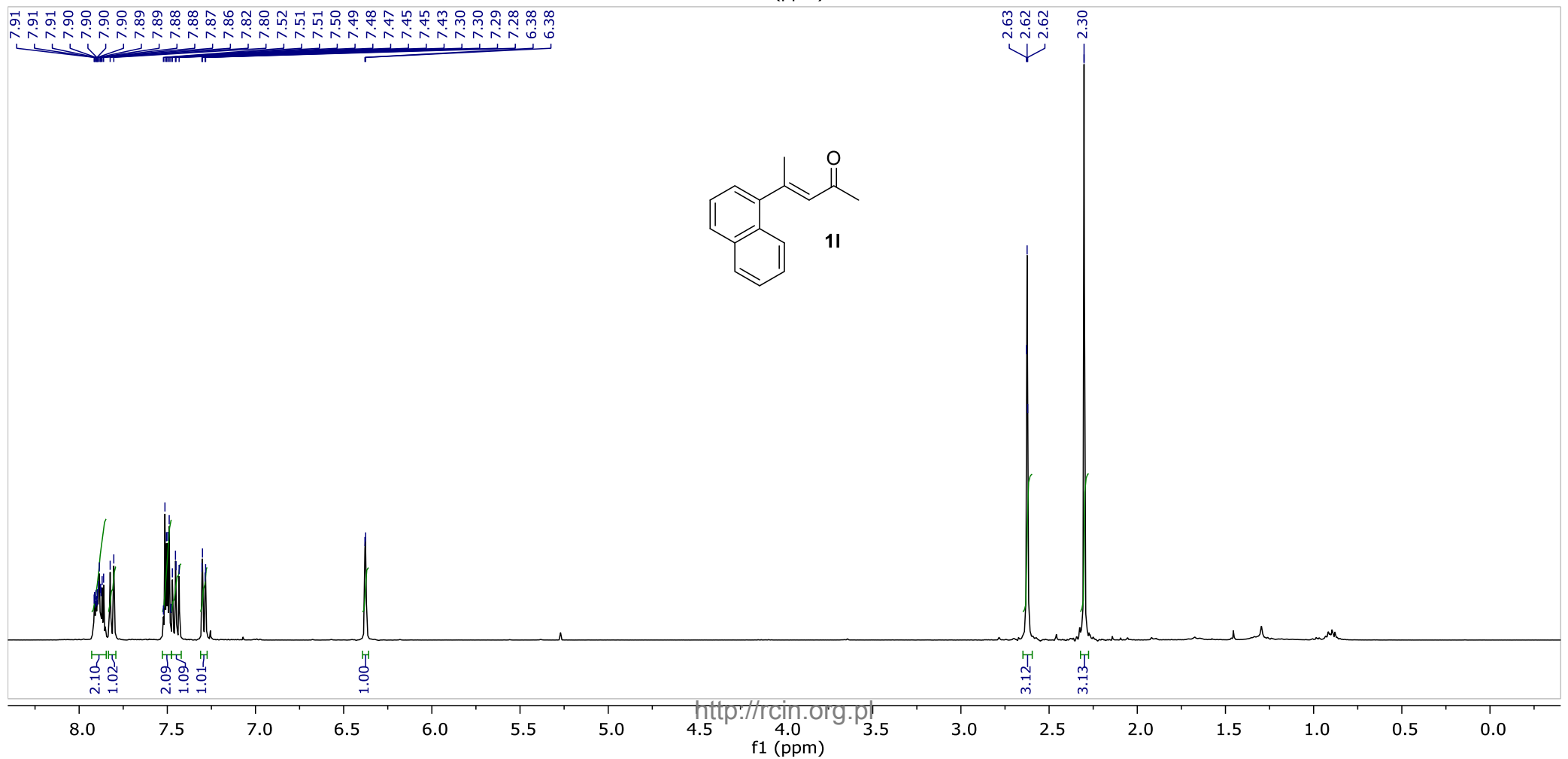
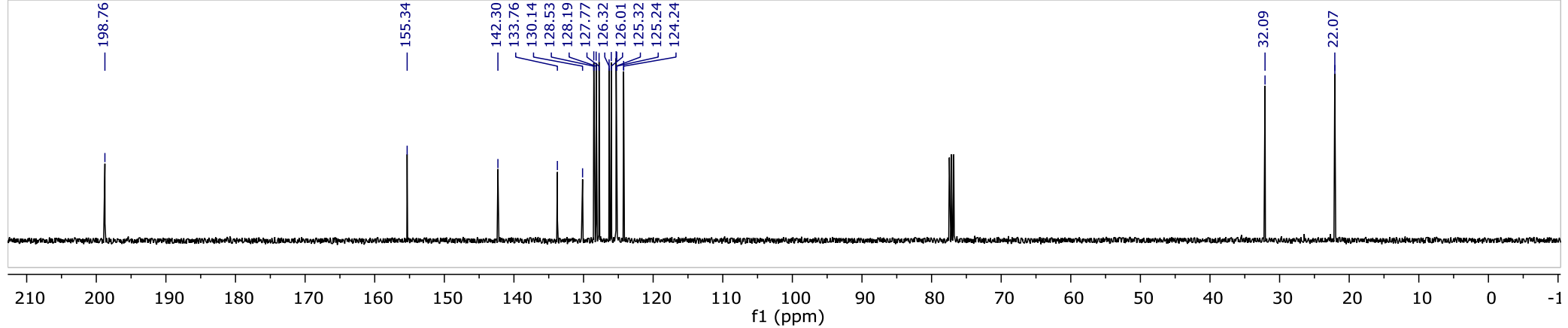


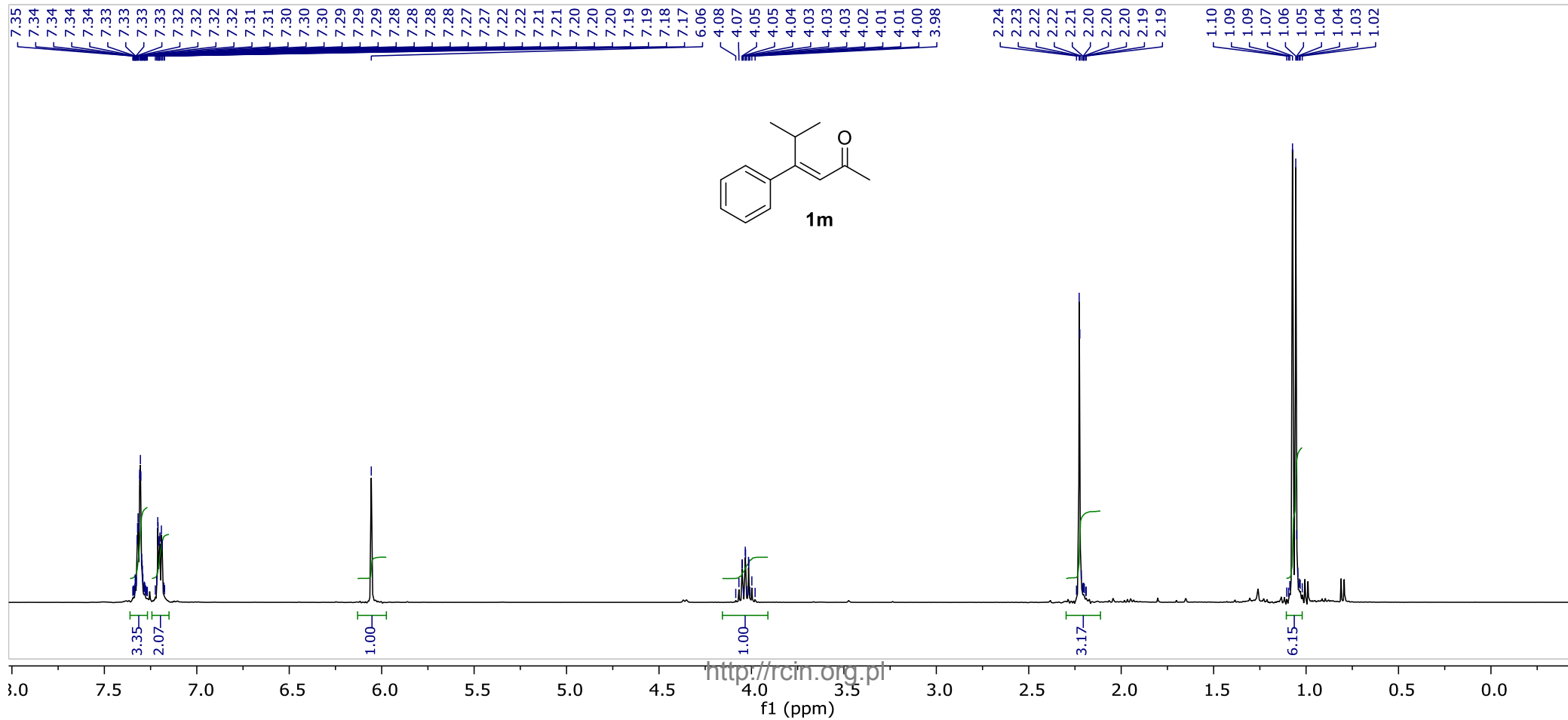
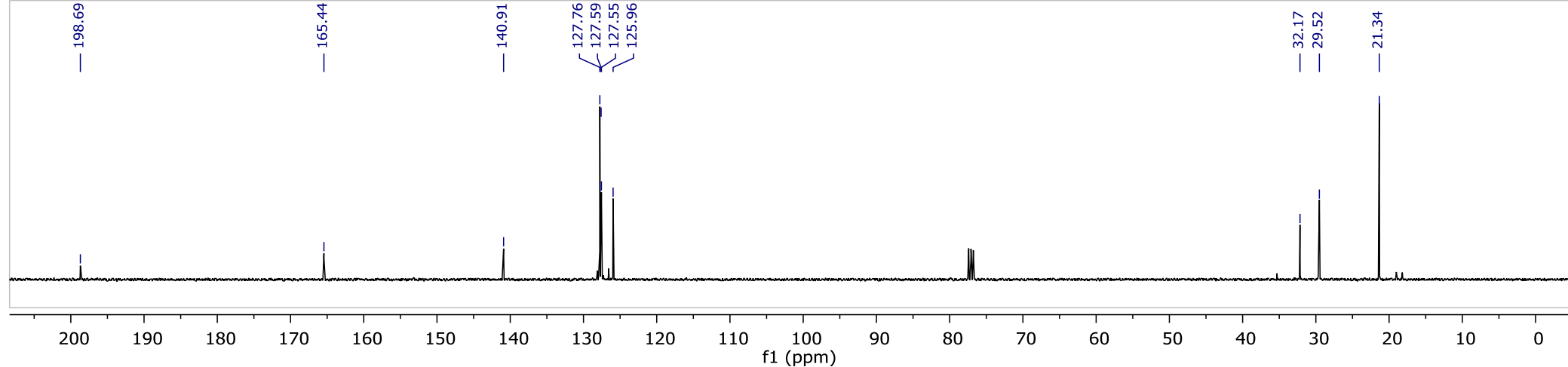


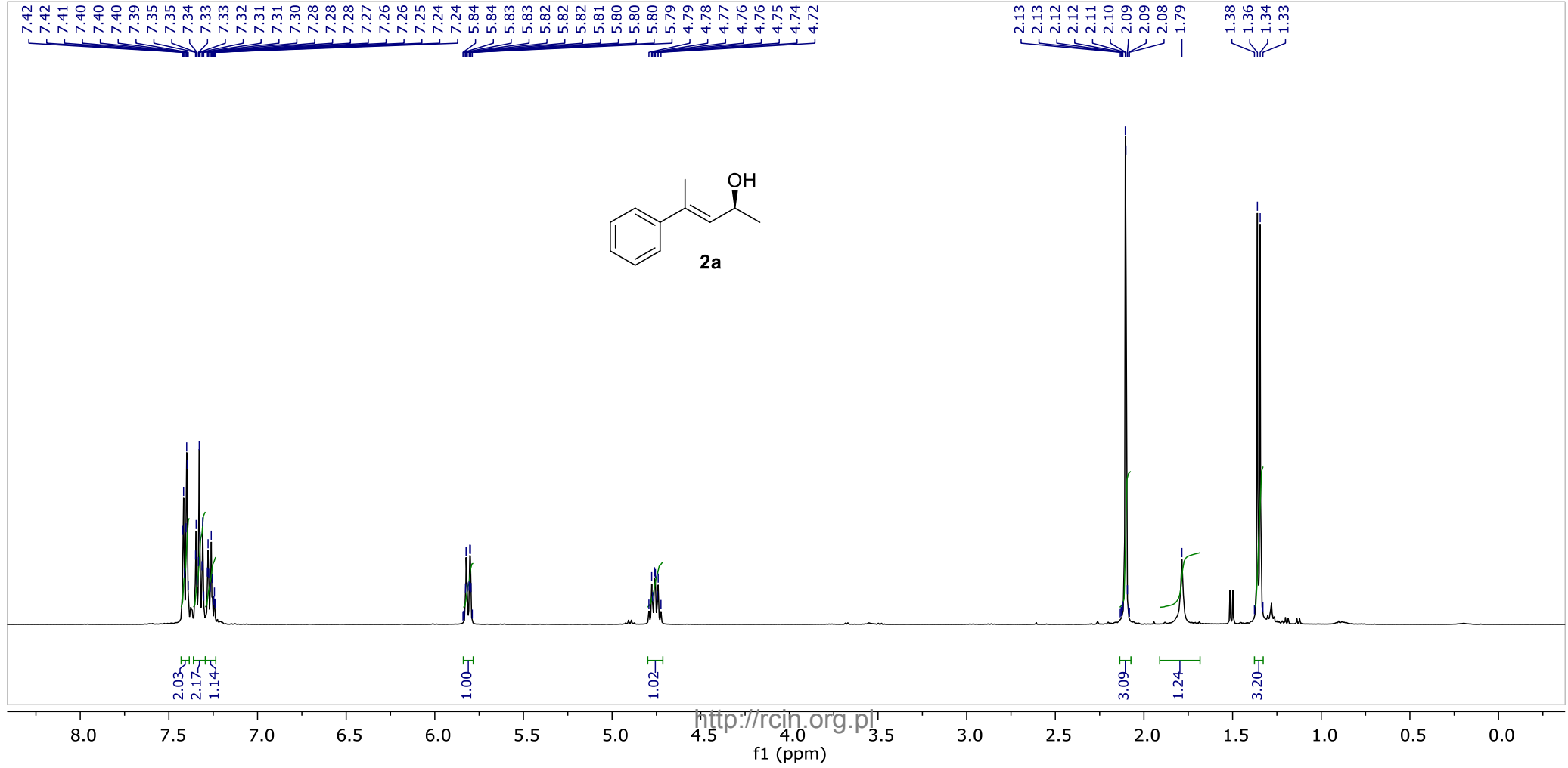
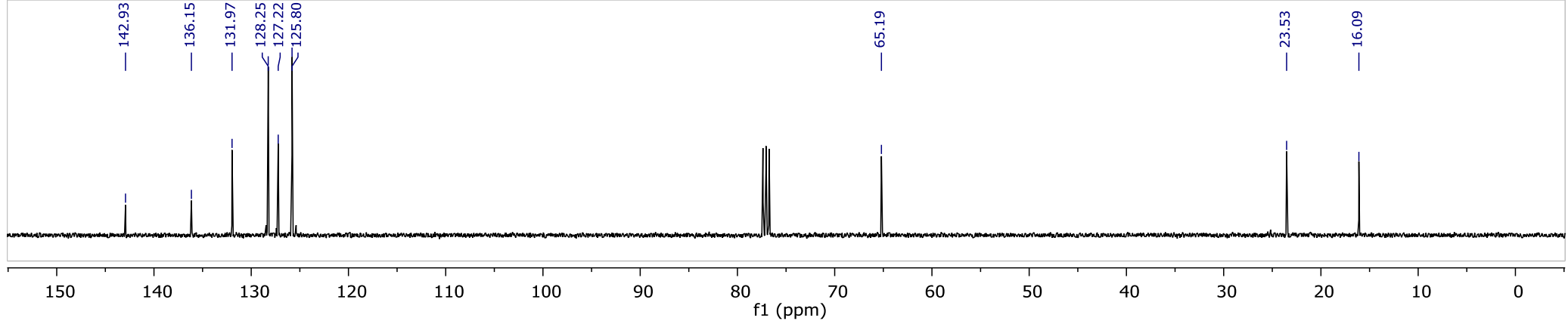






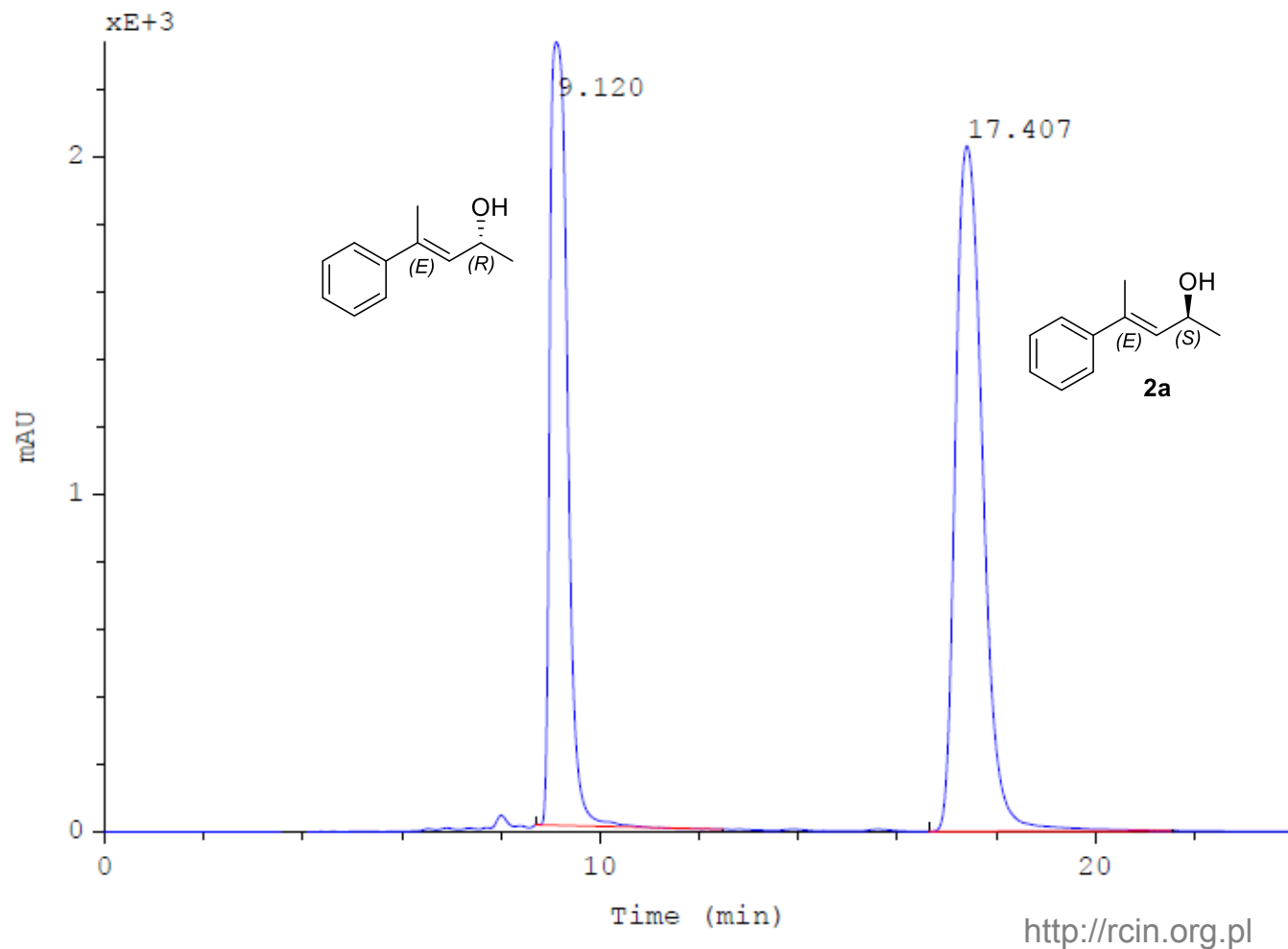






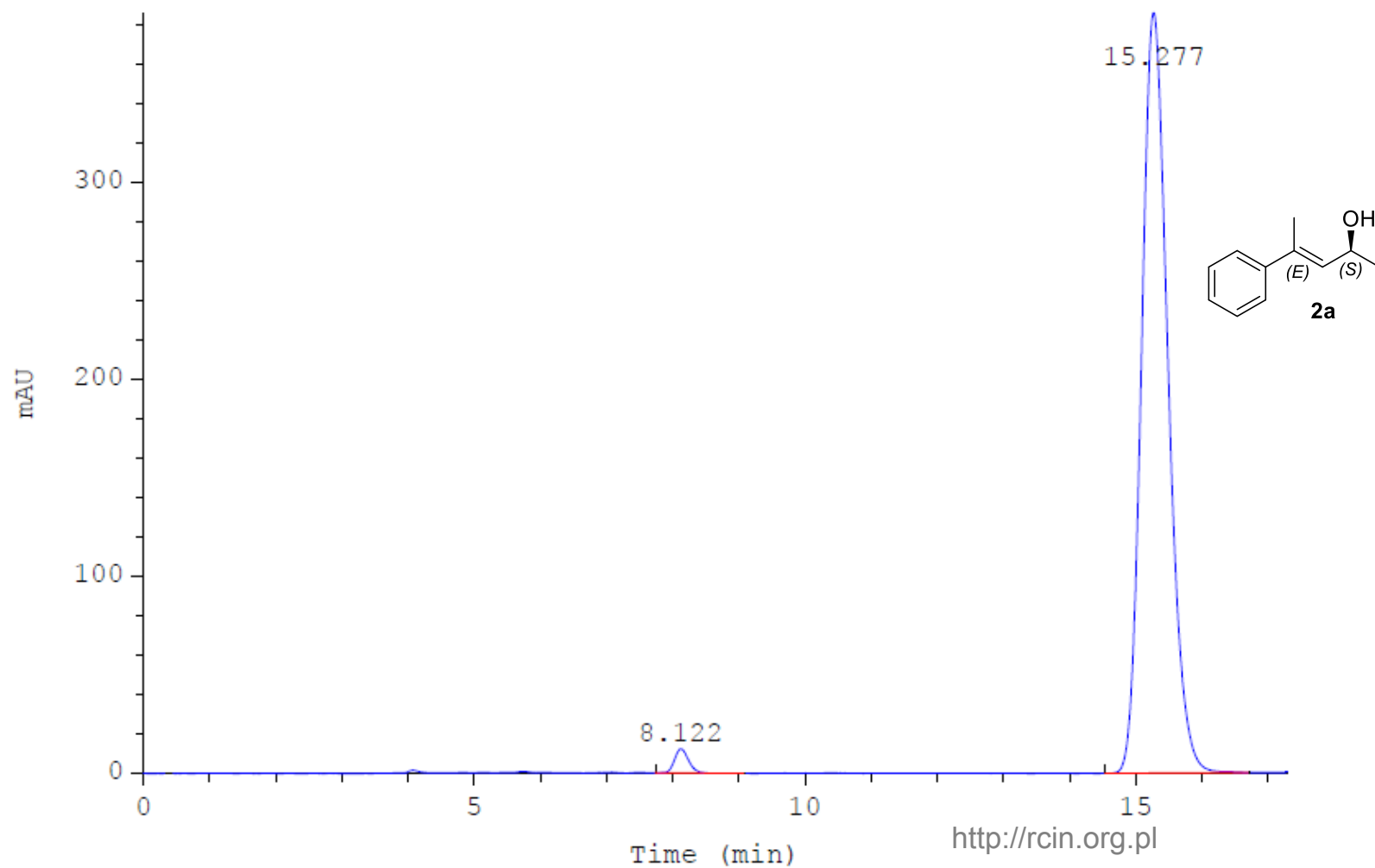
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Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

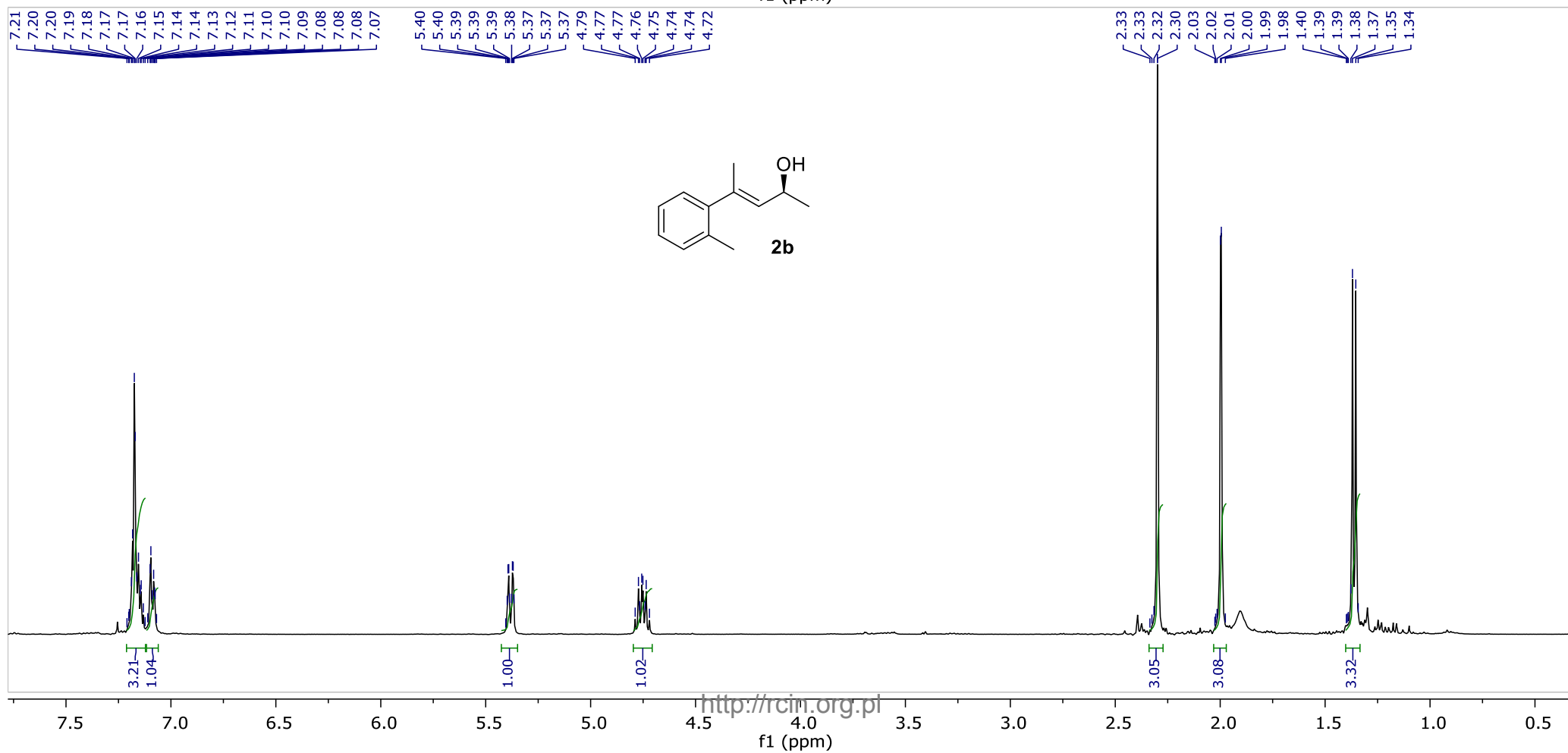
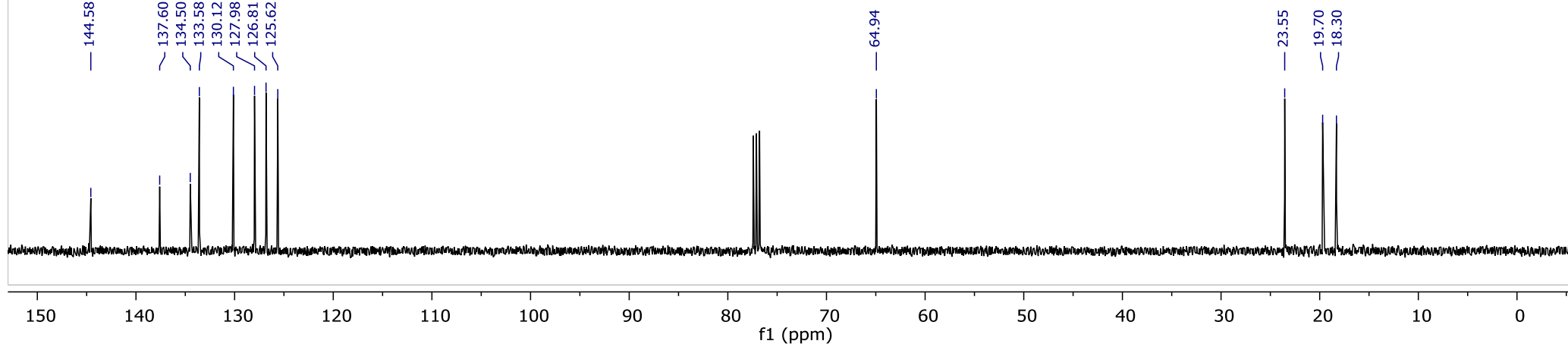
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2	17.407	16.66	21.56	1296.06	2031.35	57.6347	0.589



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
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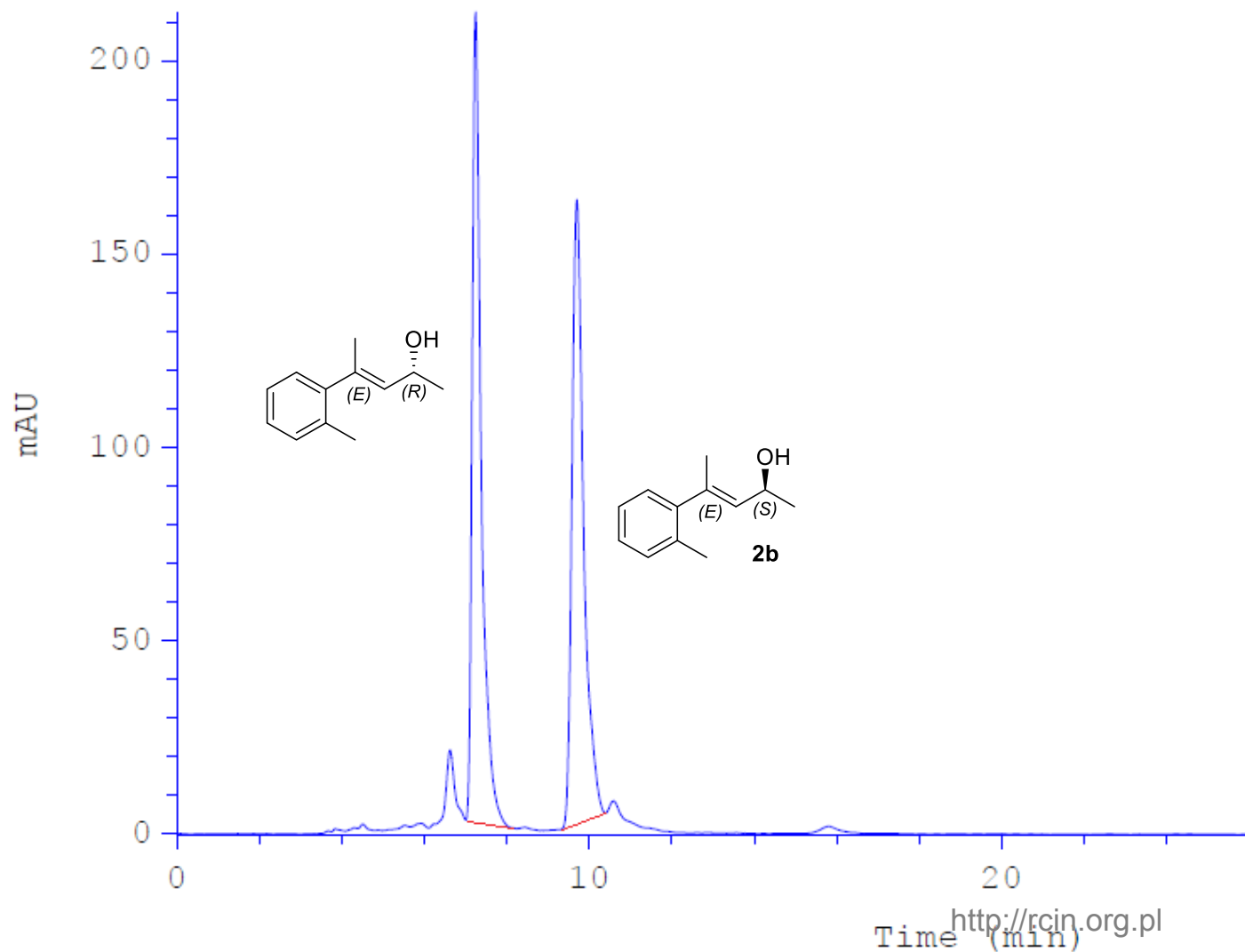






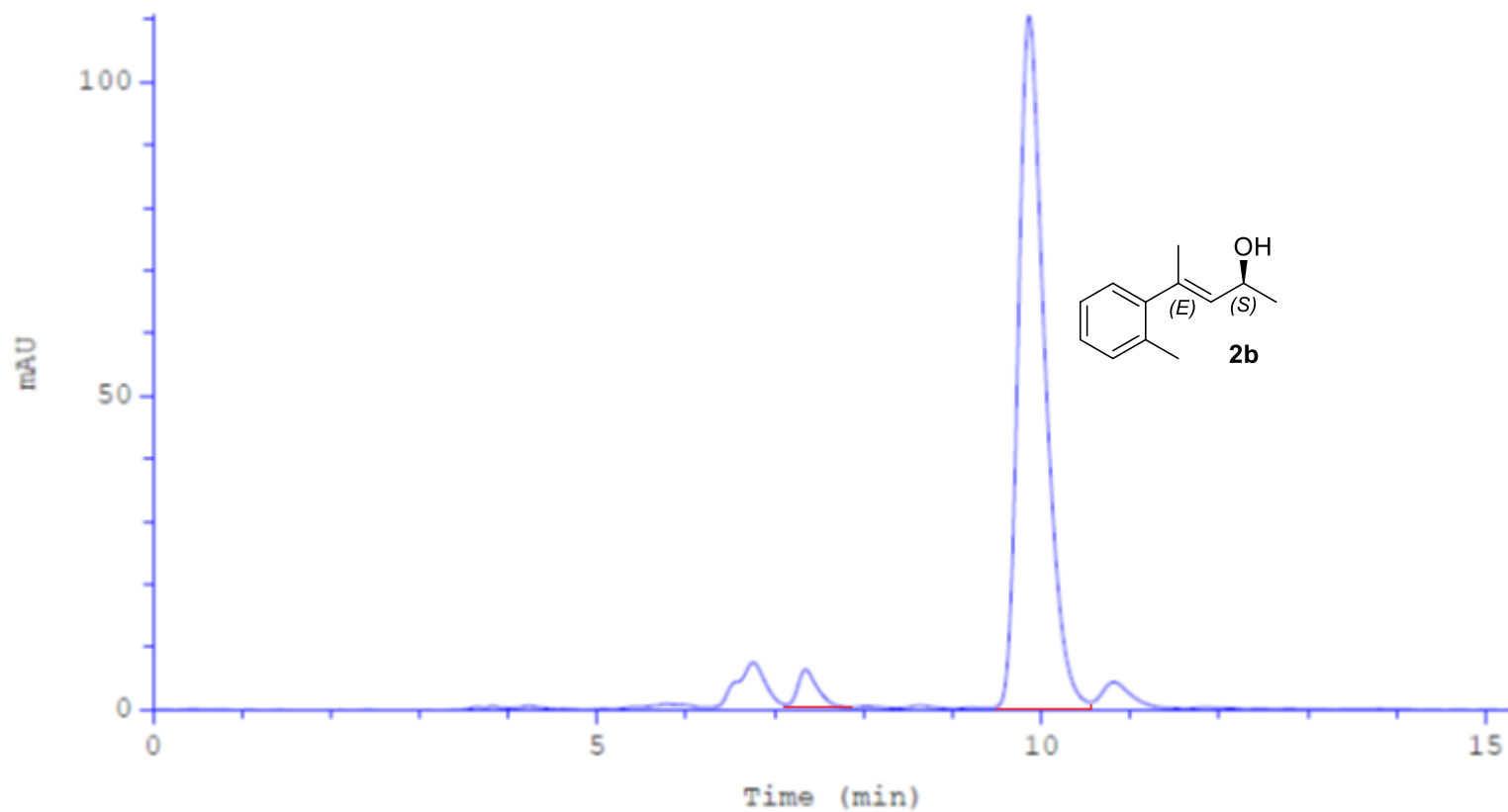
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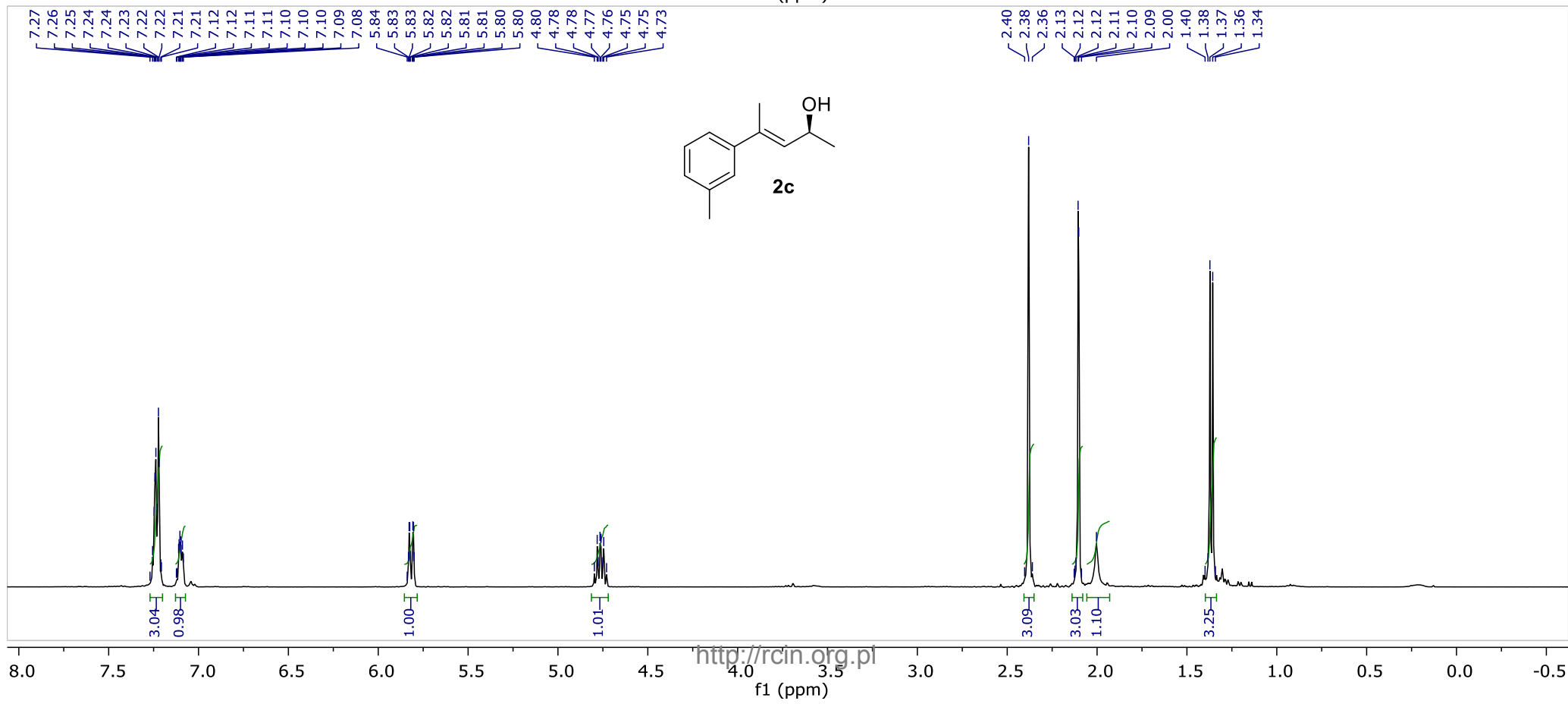
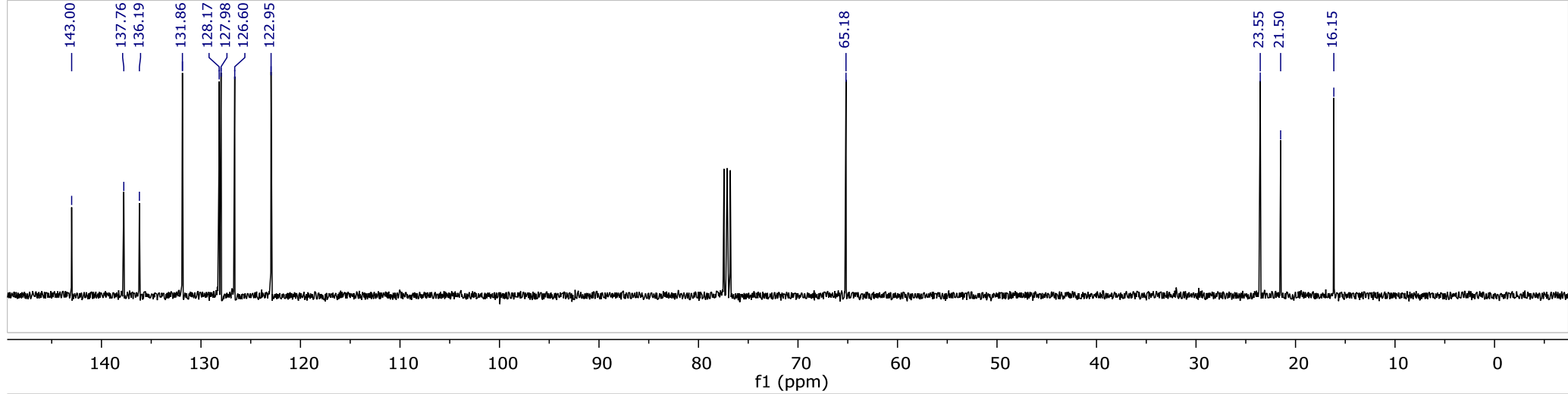
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Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

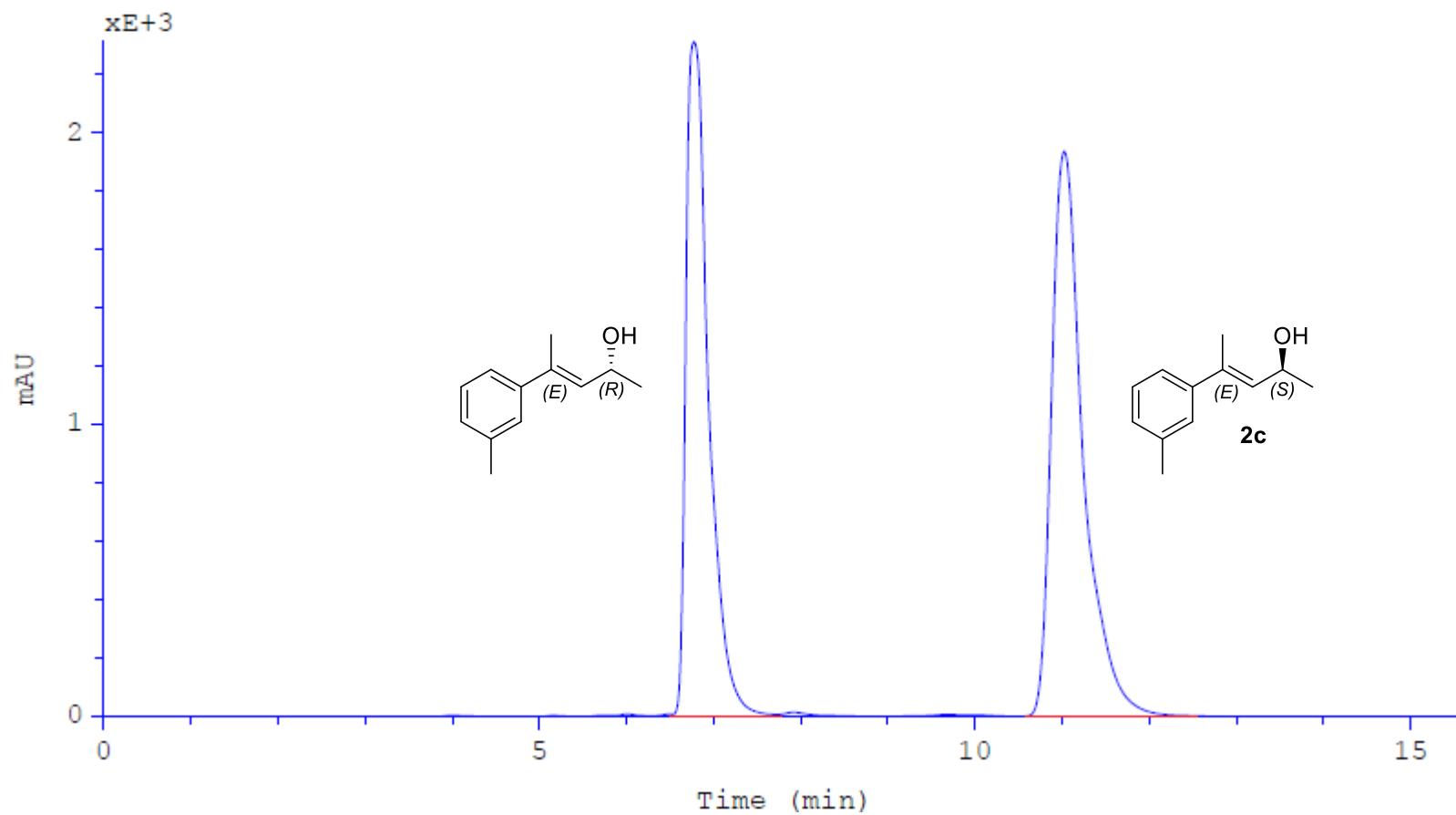
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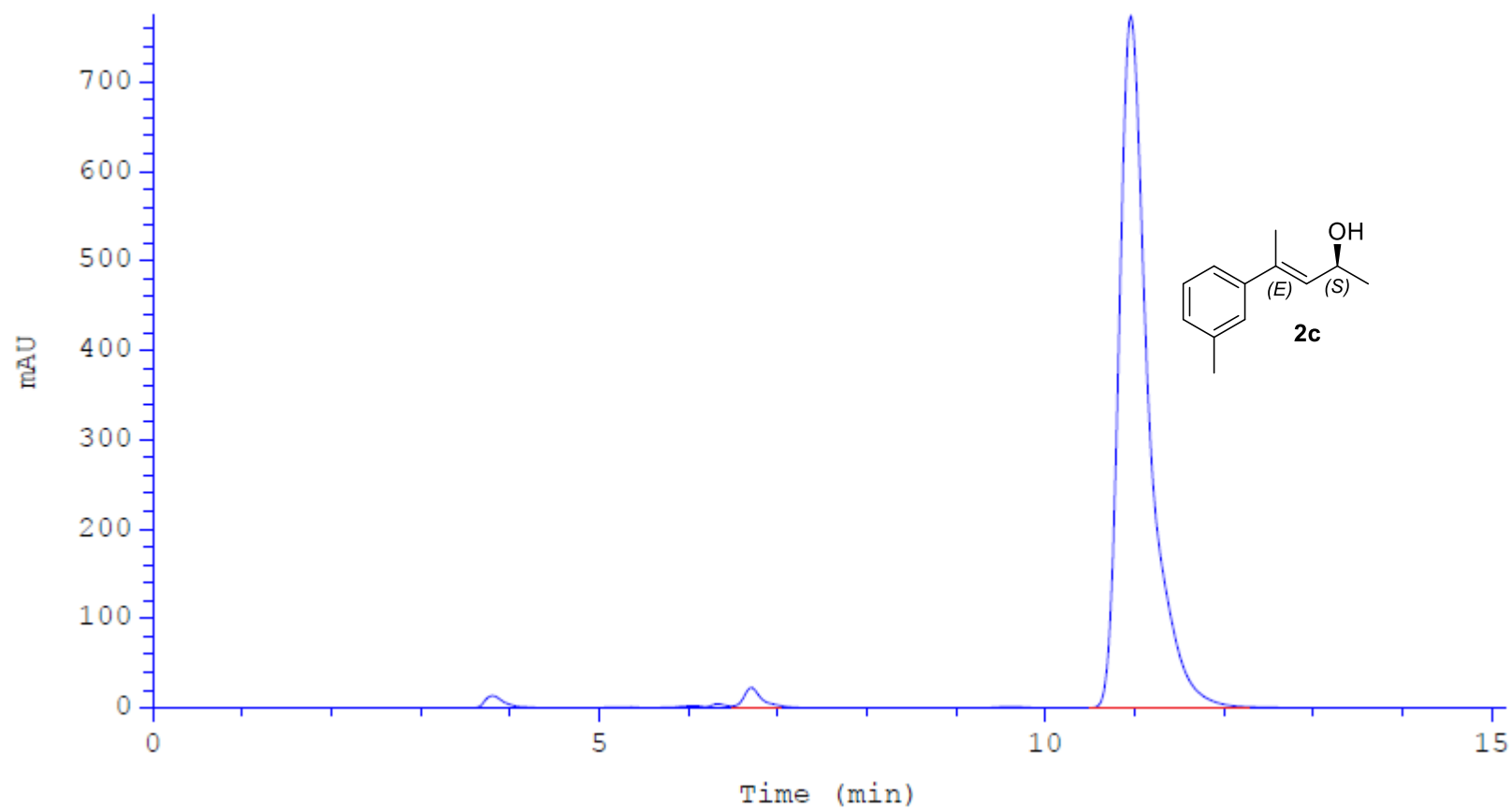
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Flow: 1mL/min  
Detection: UV, 254 nm

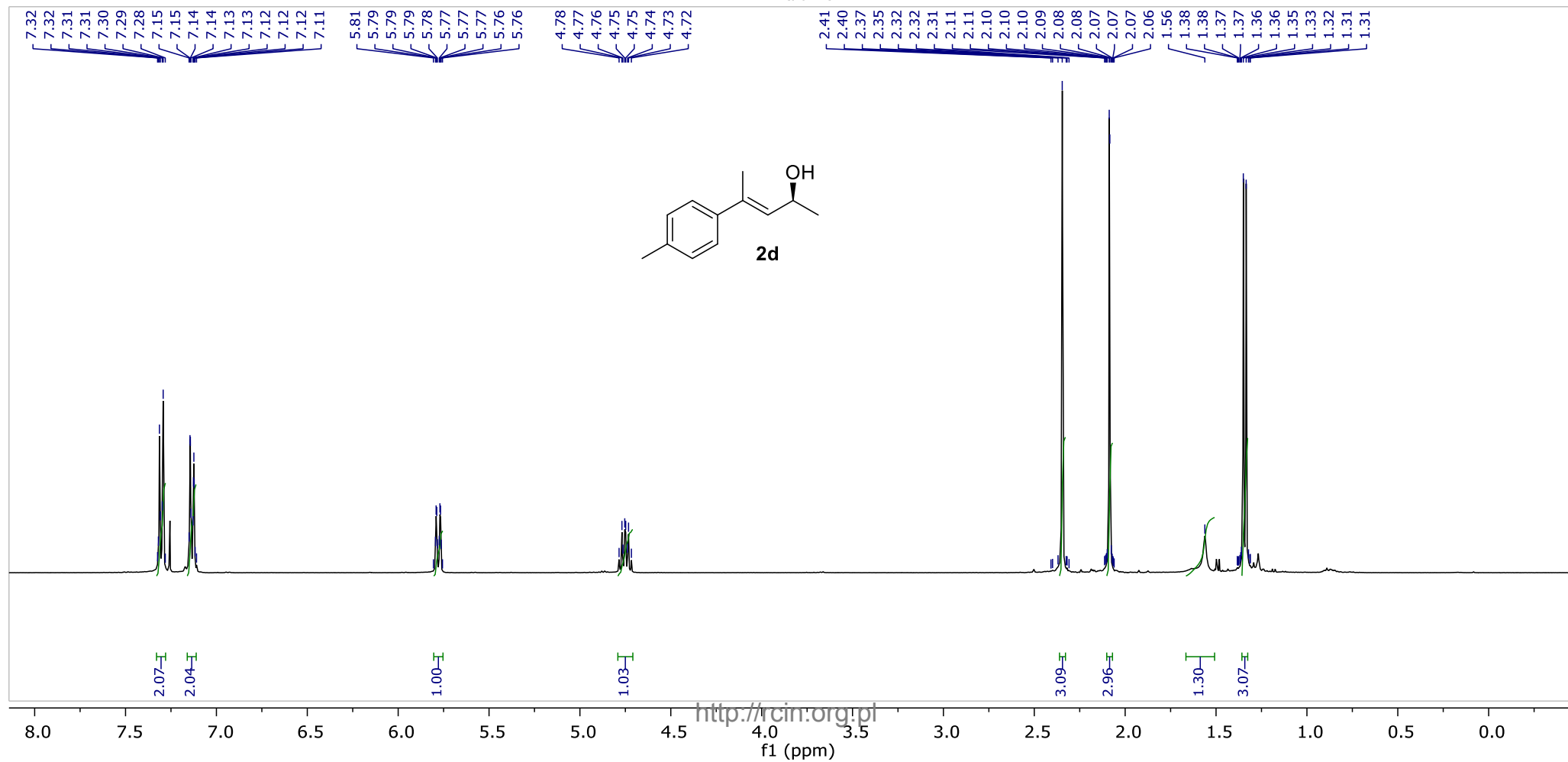
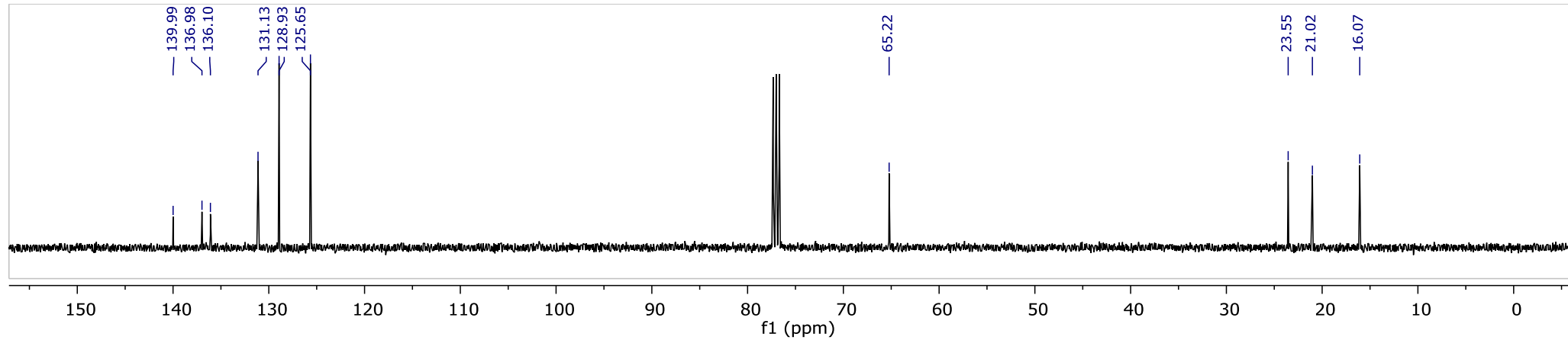
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.772	6.52	7.58	688.581	2304.35	45.8604	0.259
2	11.025	10.62	12.47	812.891	1935.07	54.1396	0.356



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

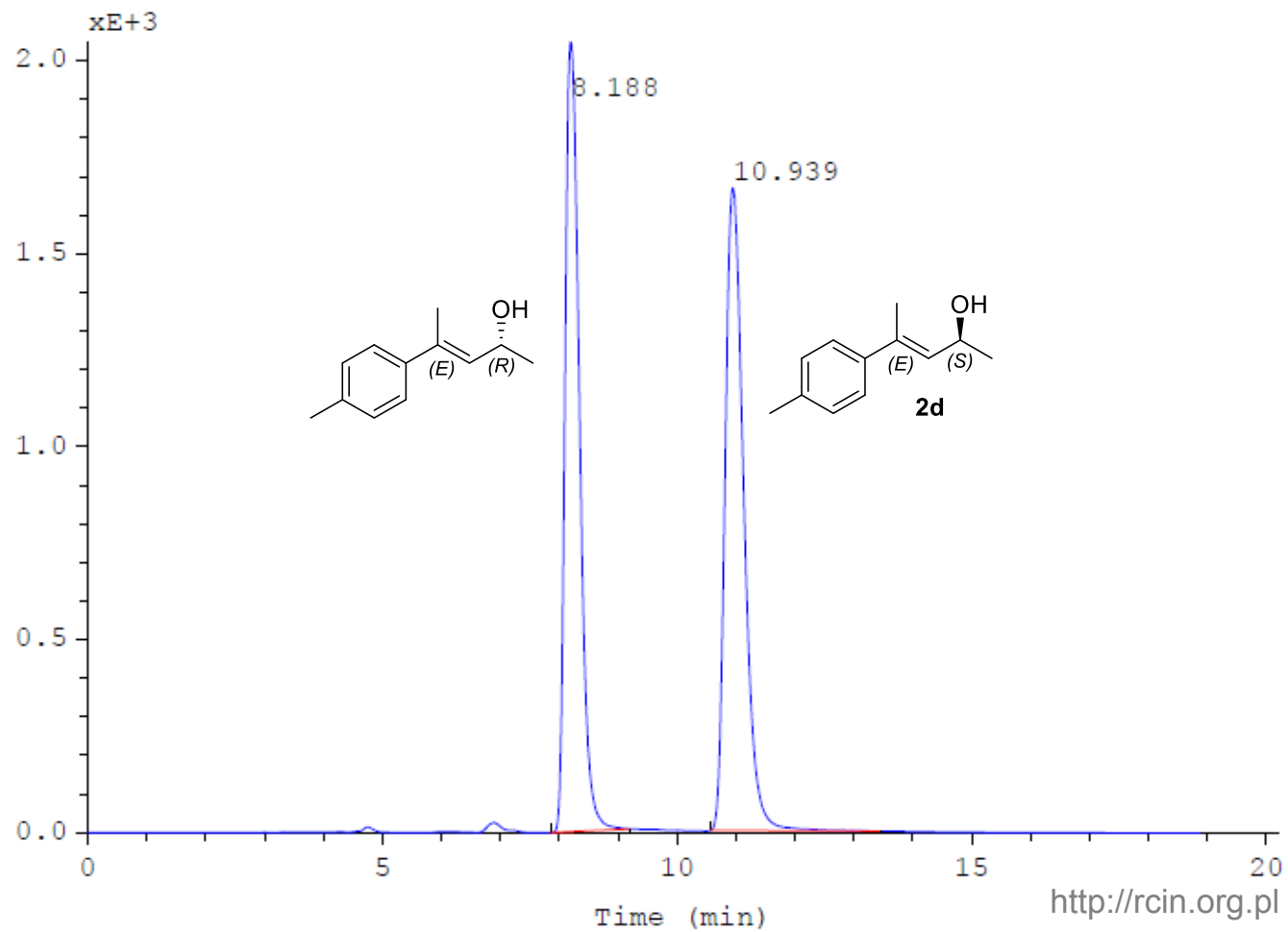
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.706	6.56	7.08	3.84529	19.5029	1.2935	0.174
2	10.959	10.55	12.20	293.425	773.467	98.7065	0.316





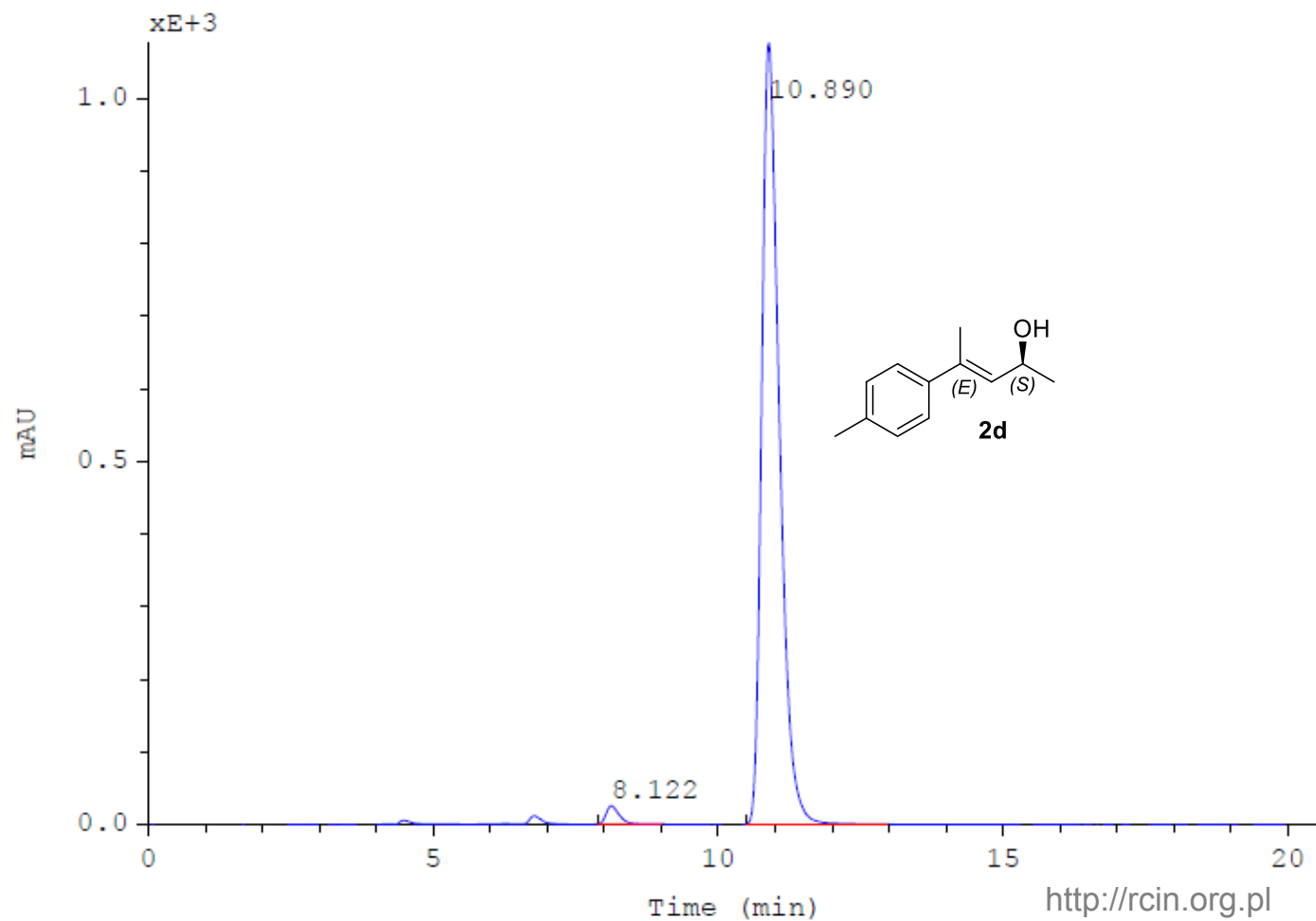
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.188	7.88	9.19	580.425	2046.28	48.7404	0.262
2	10.939	10.58	13.46	610.425	1665.72	51.2596	0.336

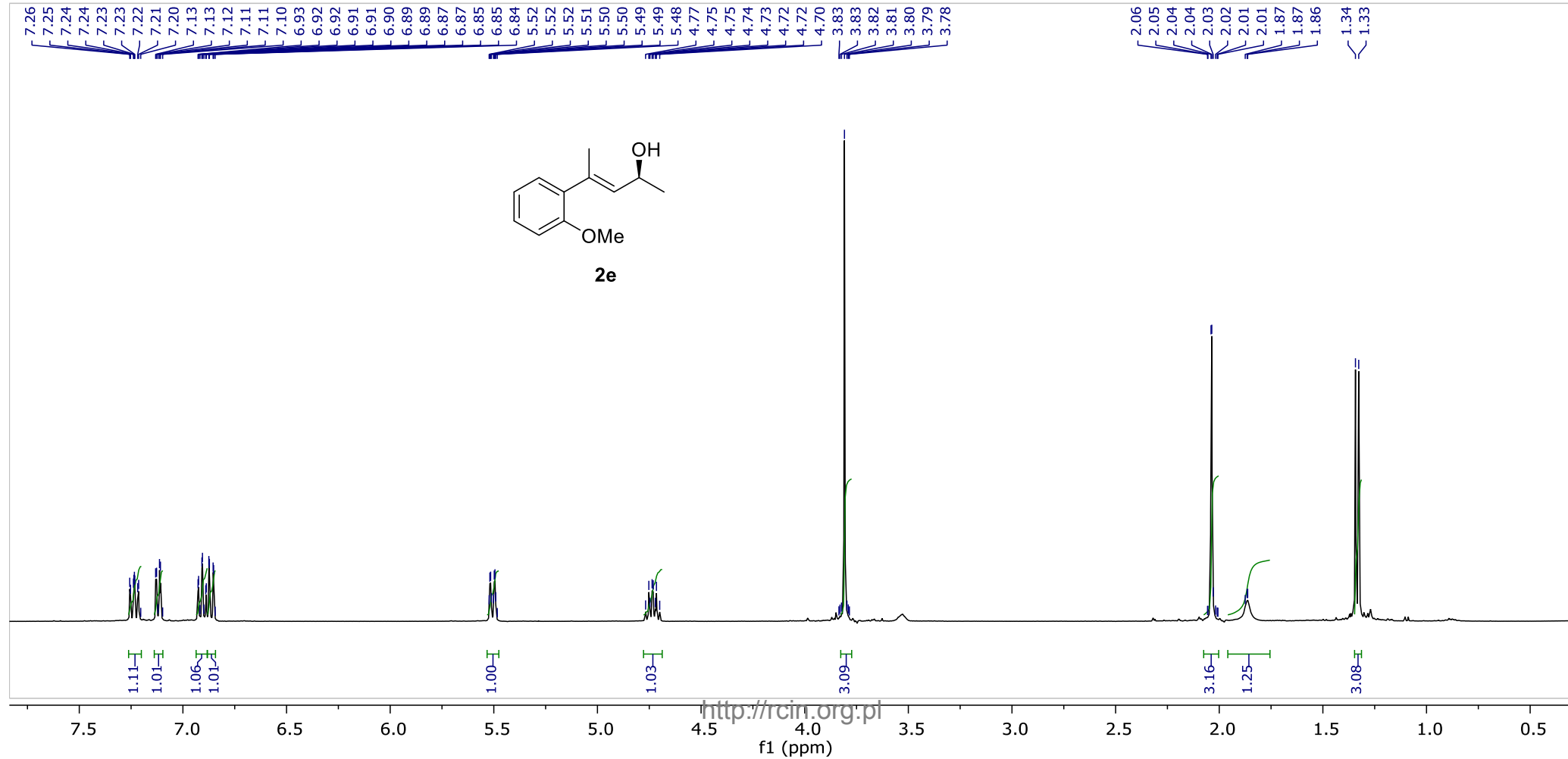
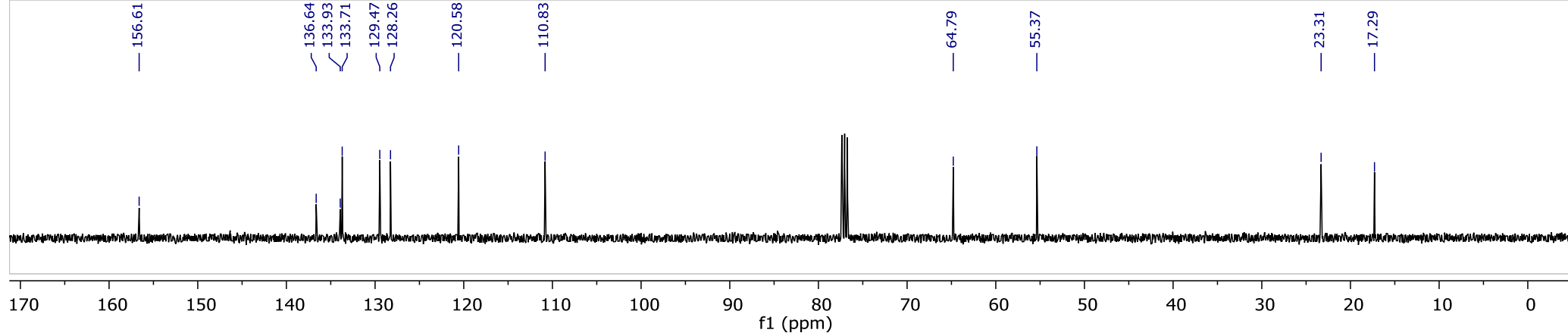


Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.122	7.90	9.03	6.5009	24.9986	1.6570	0.238
2	10.890	10.49	12.99	385.818	1076.24	98.3430	0.326

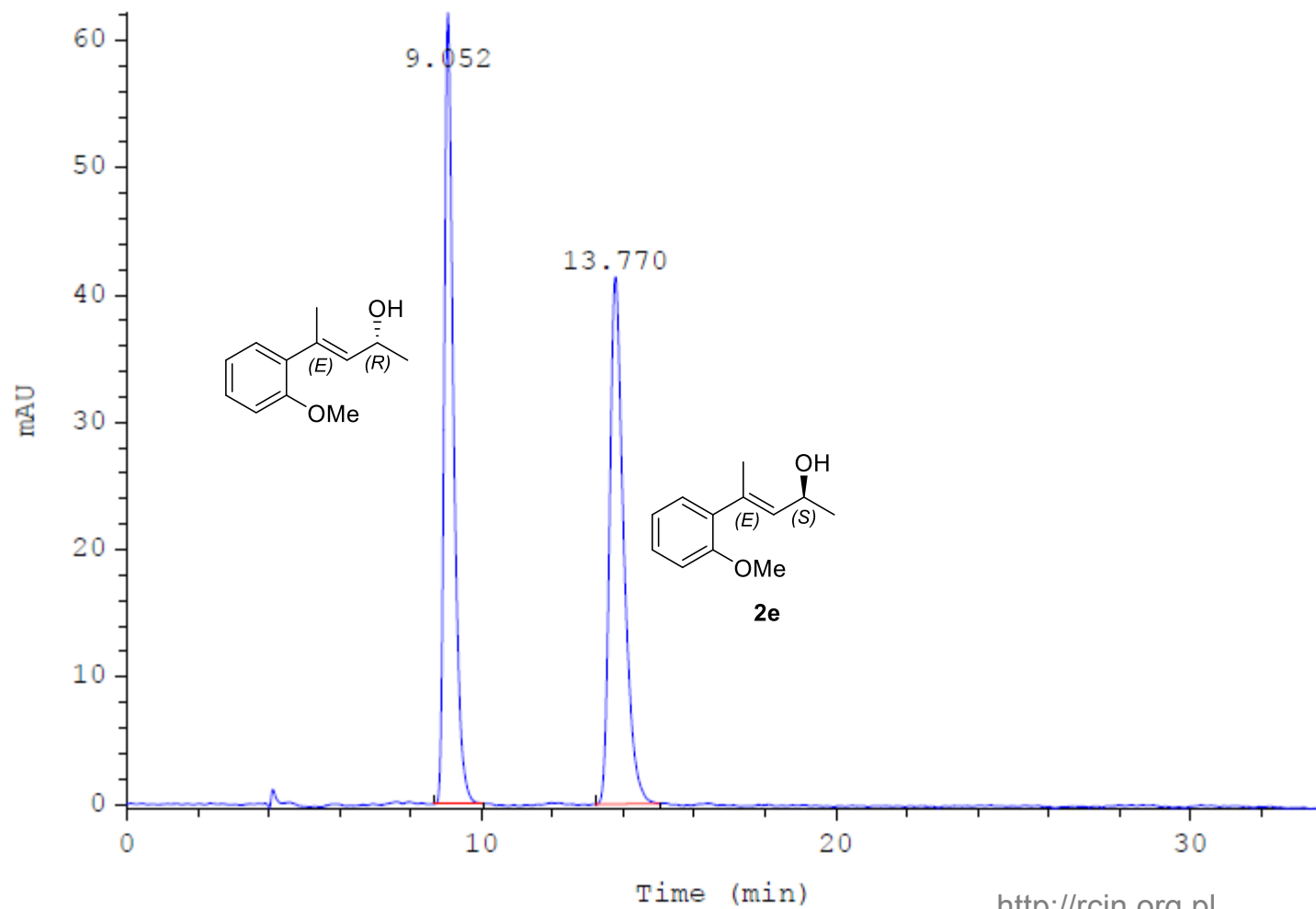






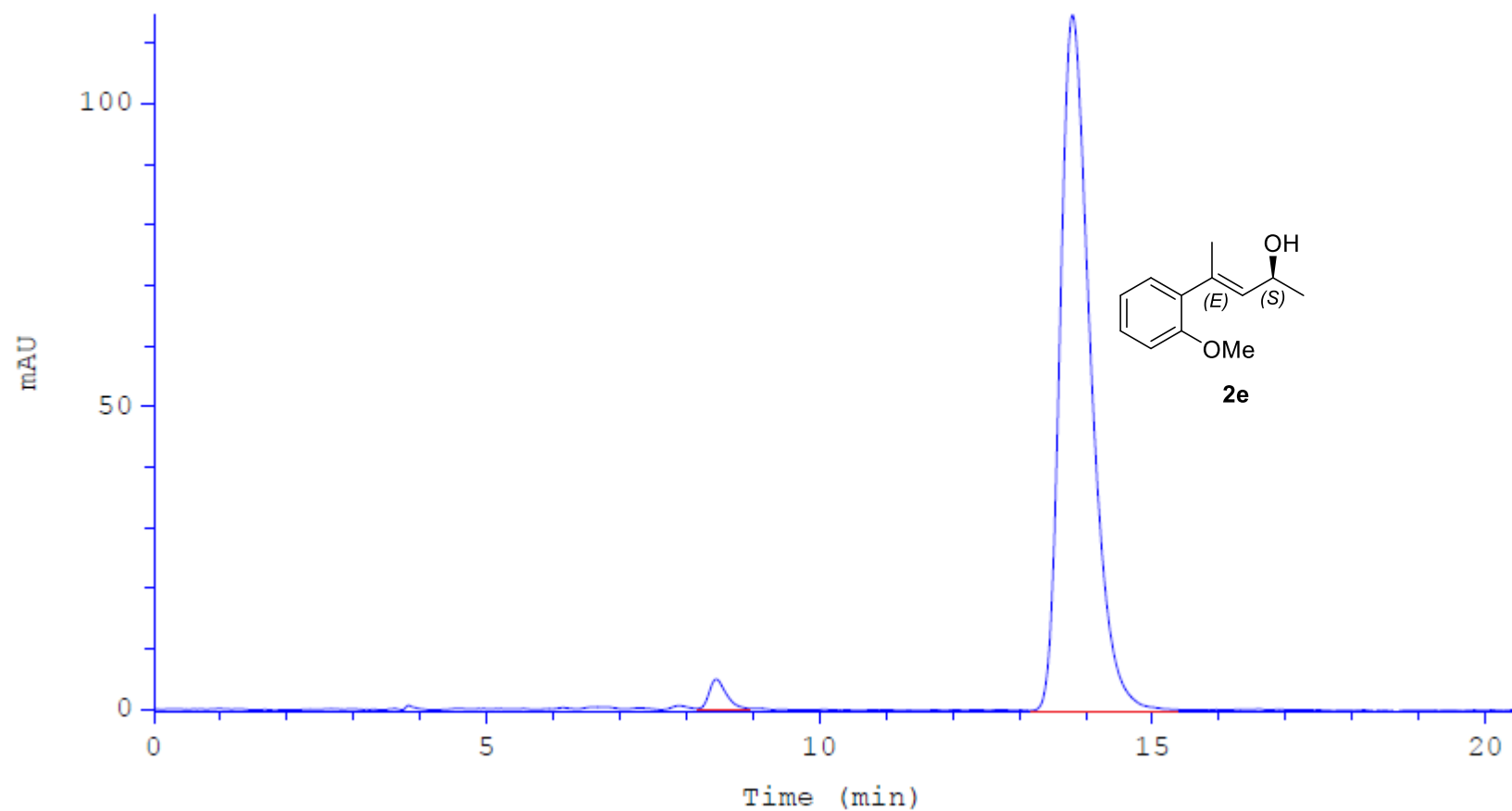
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

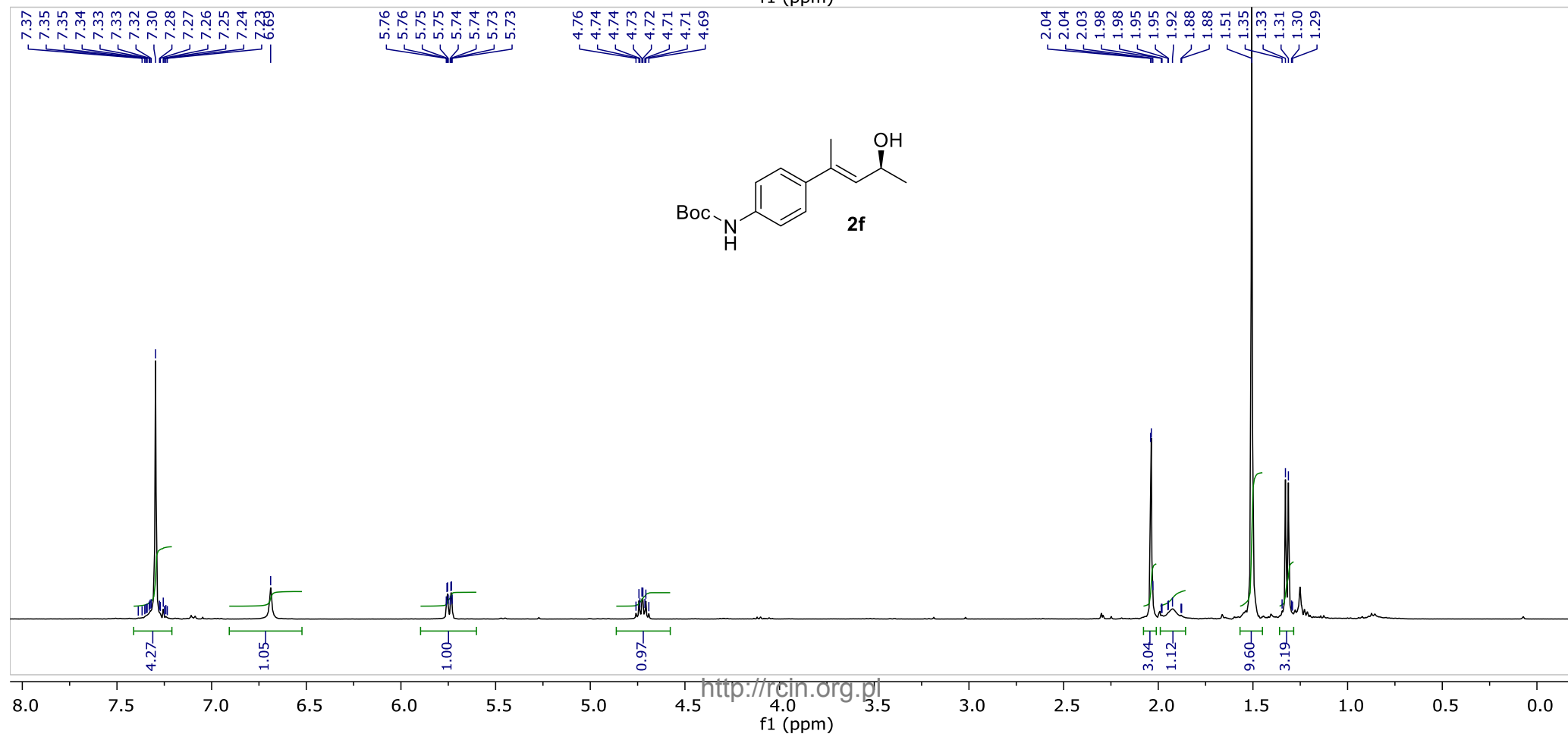
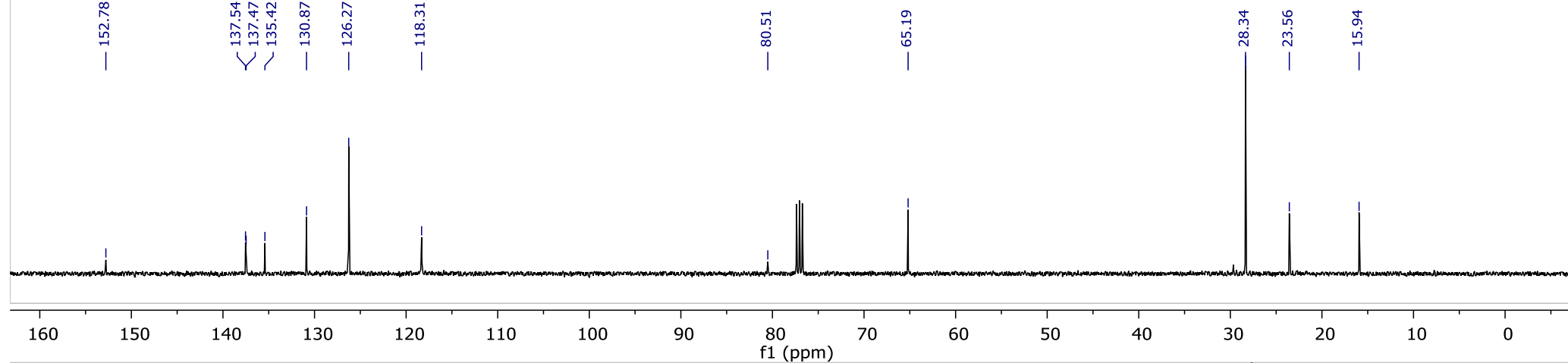
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.052	8.67	10.07	19.0154	62.1575	49.8933	0.270
2	13.770	13.22	15.02	19.0967	41.4038	50.1067	0.410



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

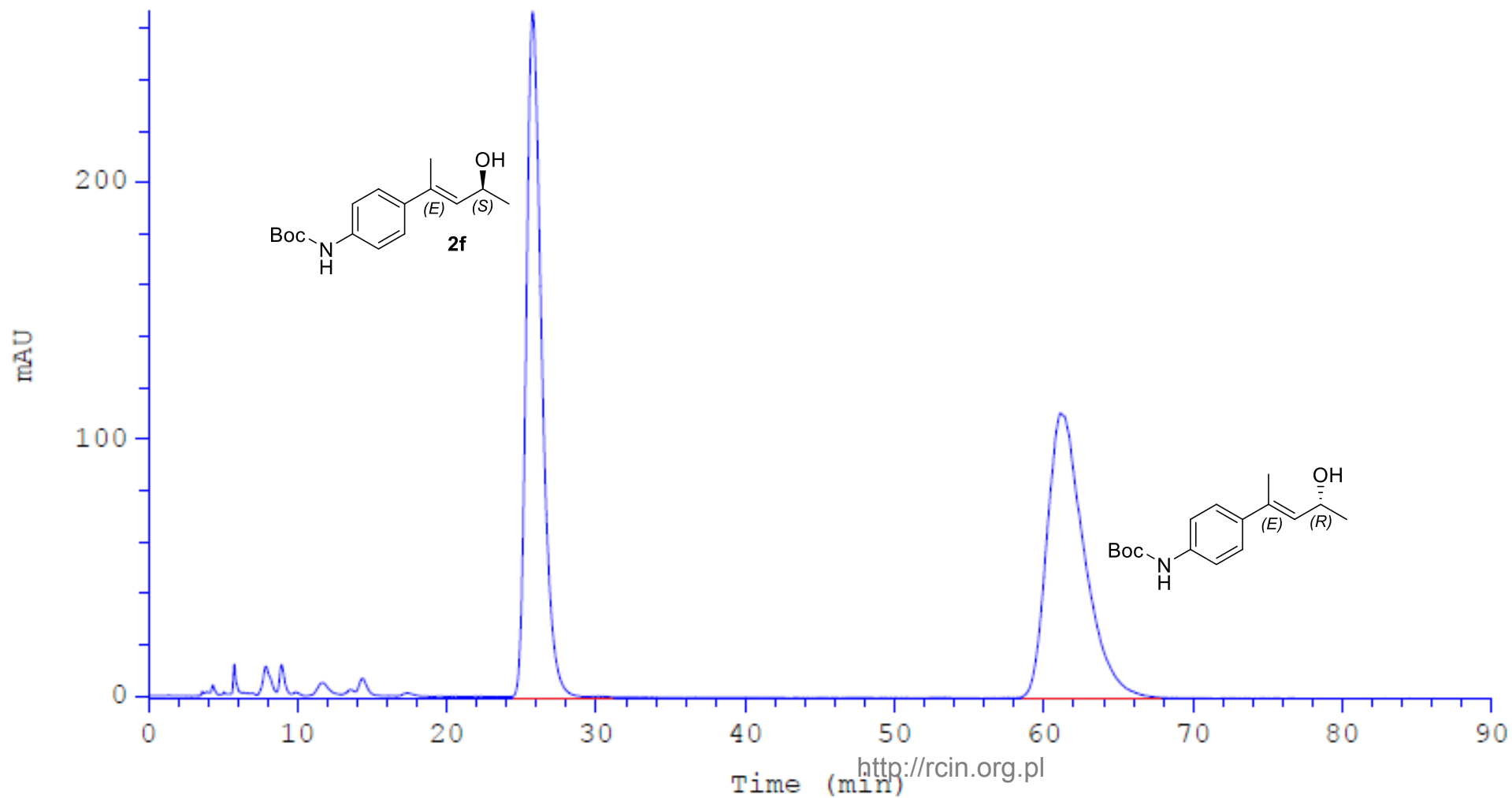
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.455	8.21	8.80	1.24973	4.65458	2.0256	0.253
2	13.791	13.23	15.32	60.4457	114.758	97.9744	0.478





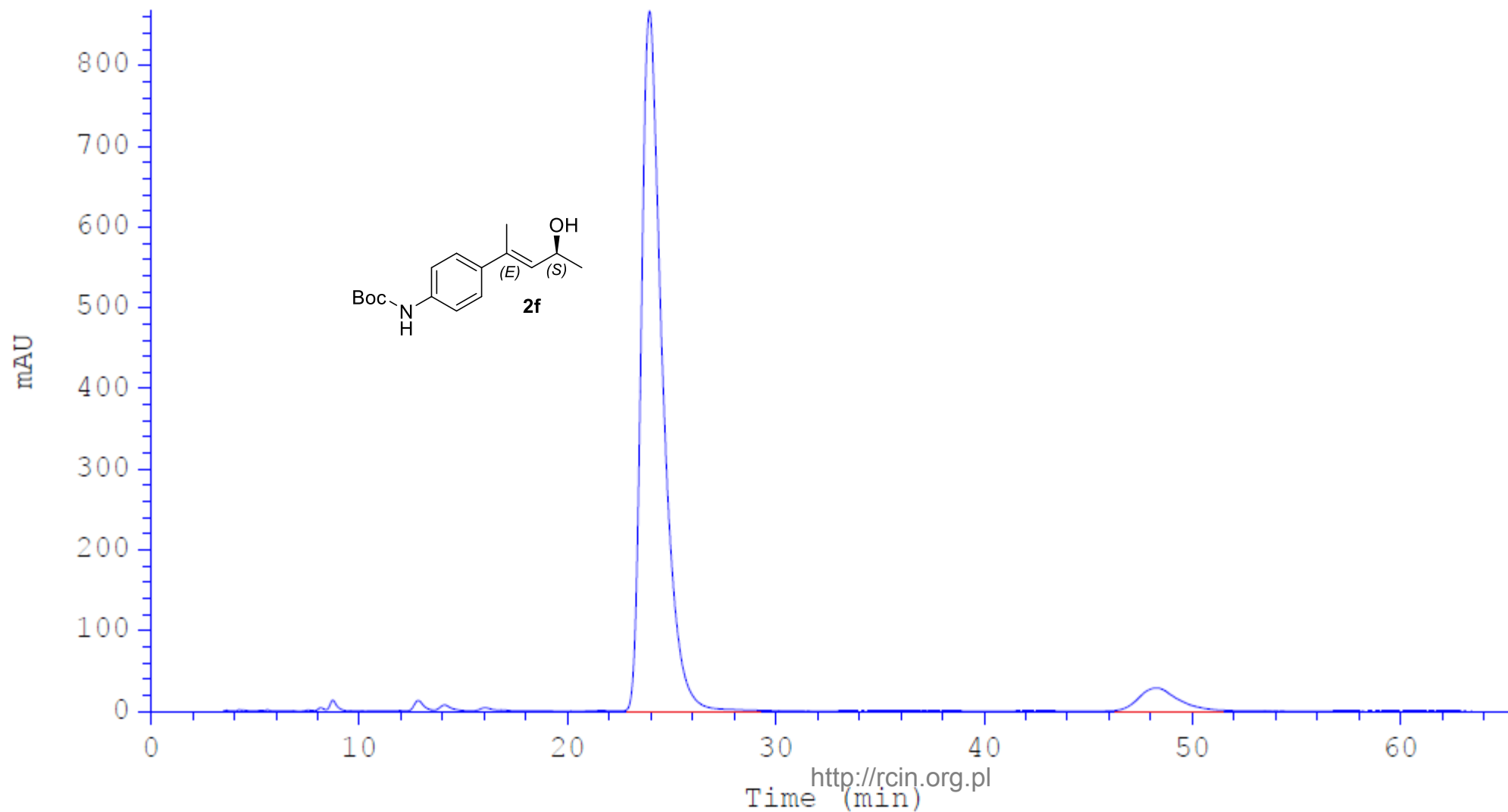
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

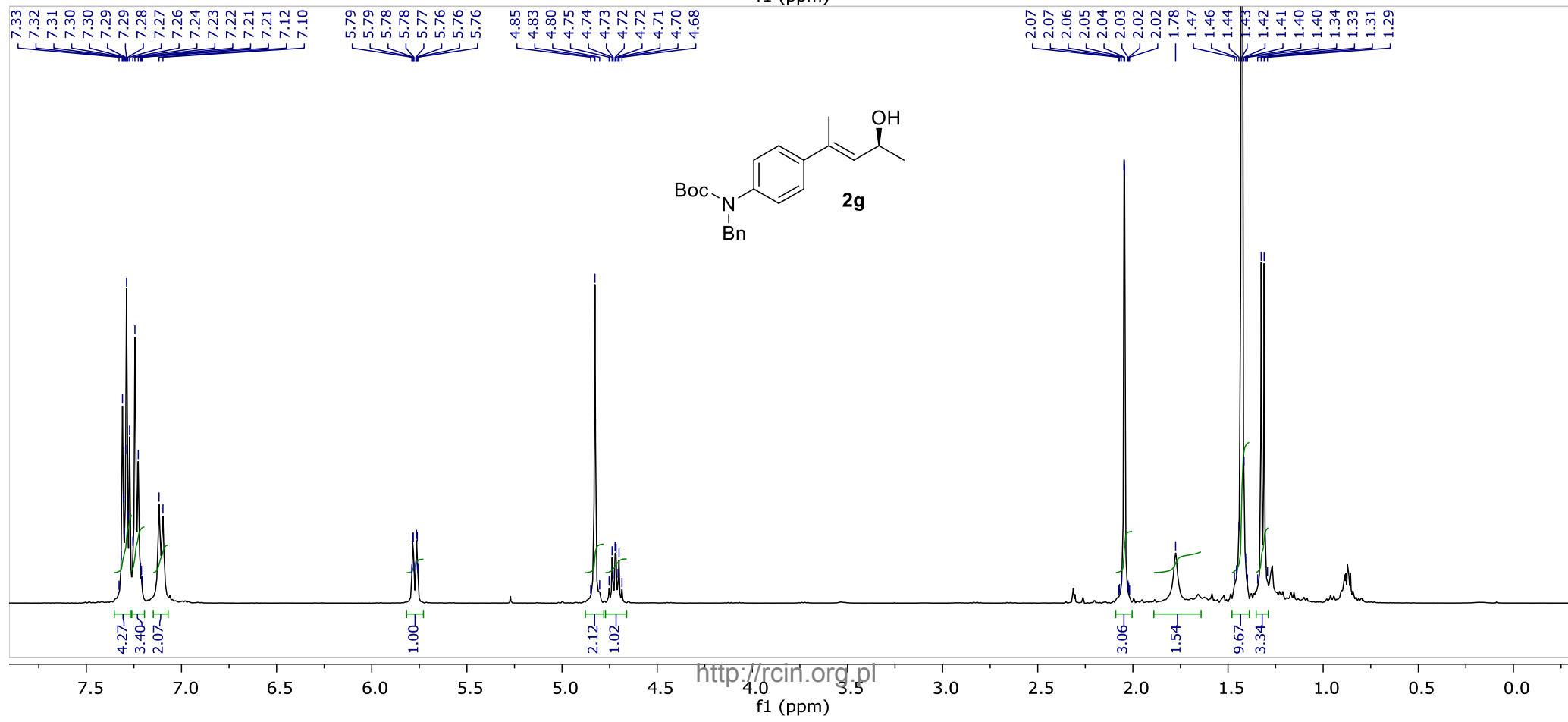
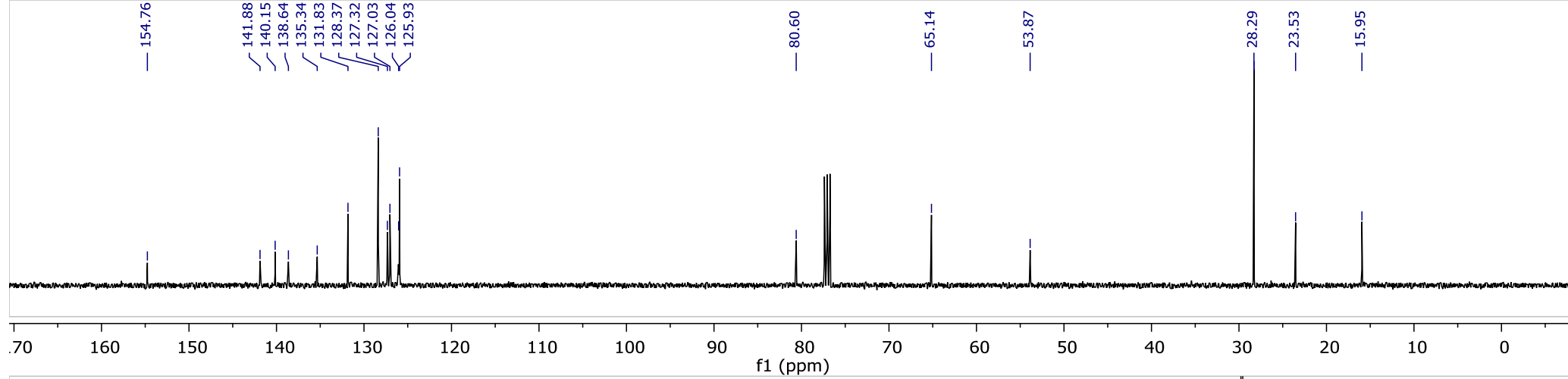
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	25.750	24.30	30.95	319.273	266.812	50.0495	1.082
2	61.100	58.40	67.56	318.641	110.728	49.9505	2.638



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

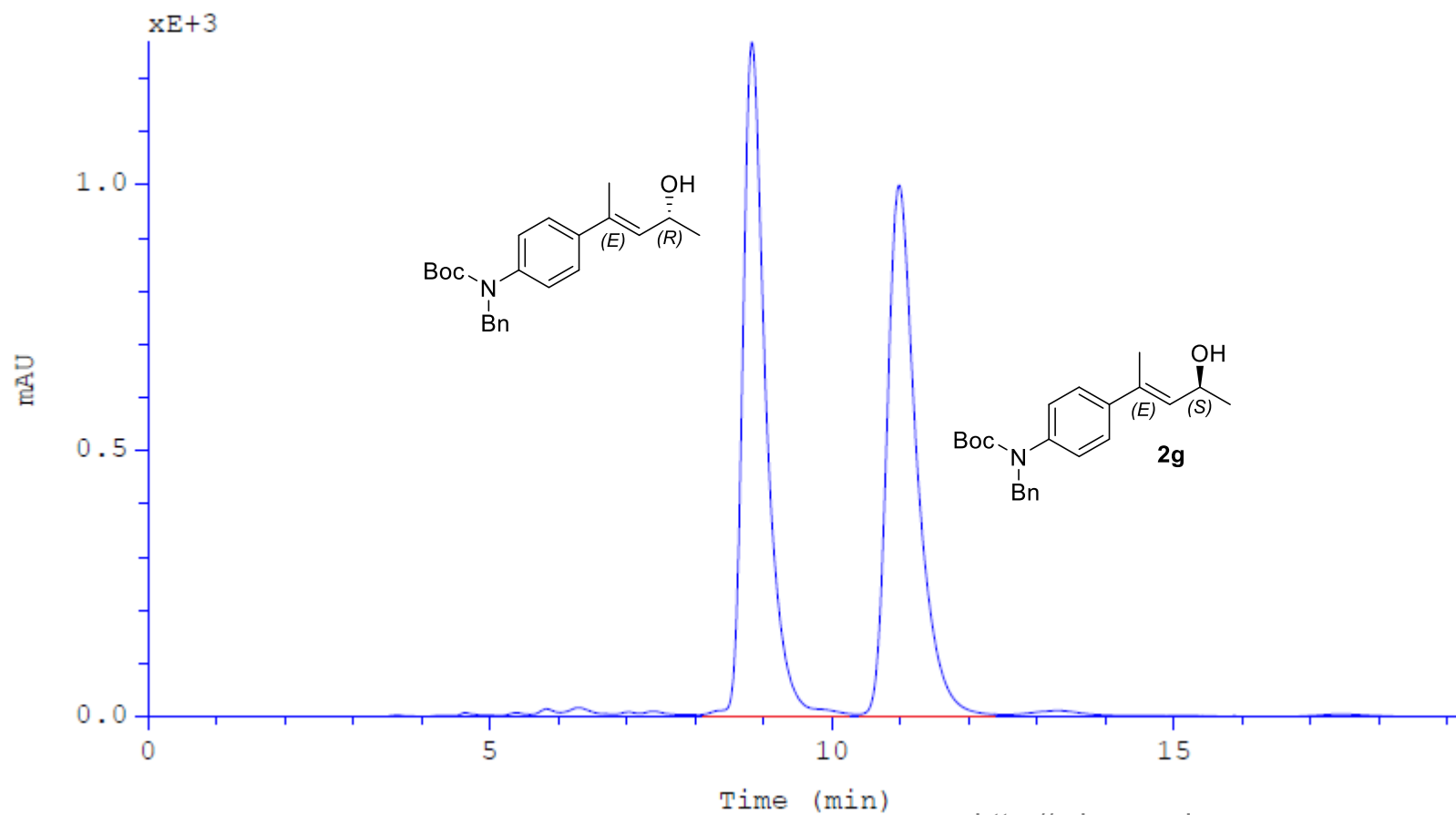
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	23.935	22.71	29.23	1012.84	866.758	94.5190	1.035
2	48.337	46.34	51.60	58.7327	27.7086	5.4810	1.938





Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

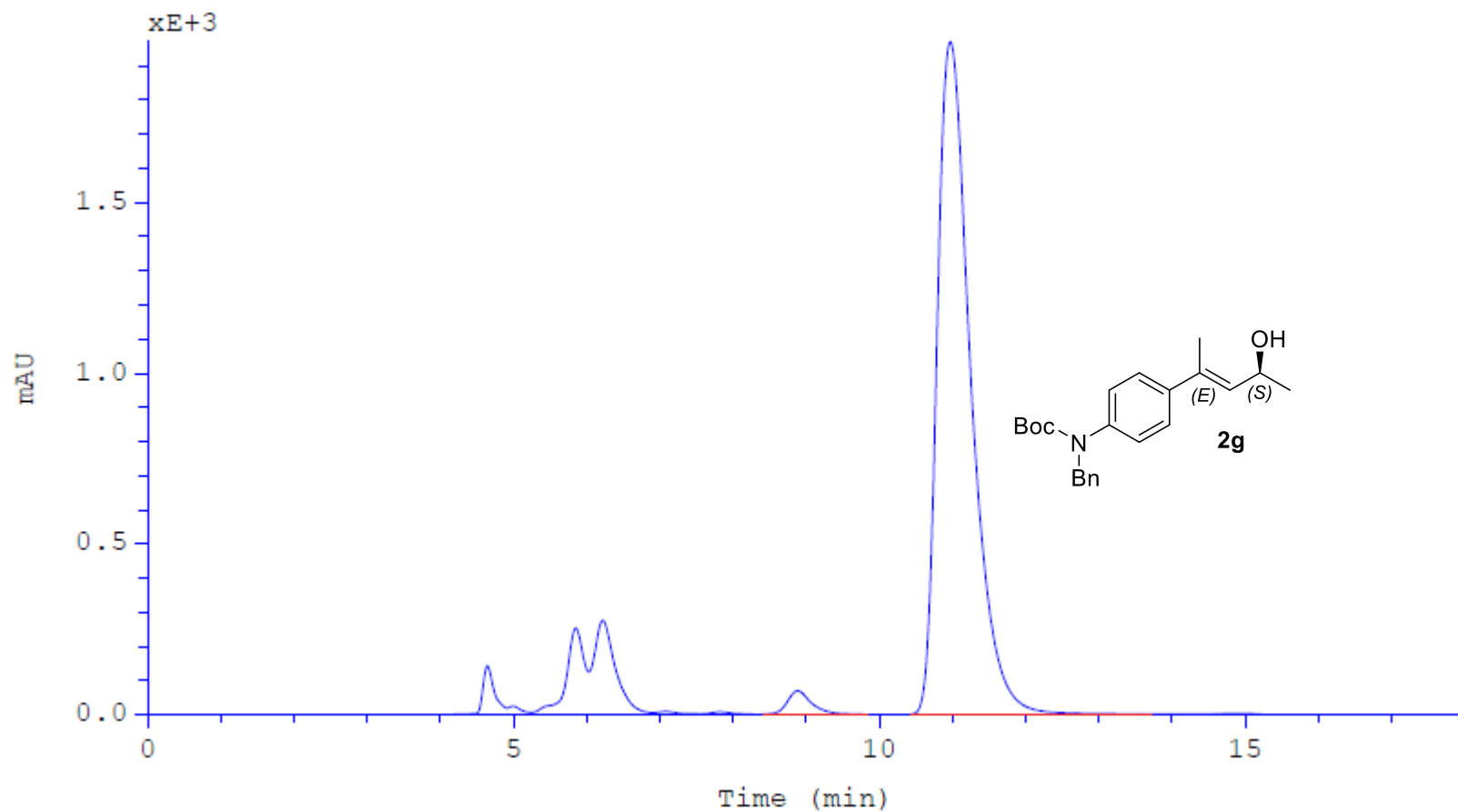
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.823	8.17	10.19	488.435	1261.15	49.8067	0.336
2	10.974	10.42	12.22	492.226	993.055	50.1933	0.440

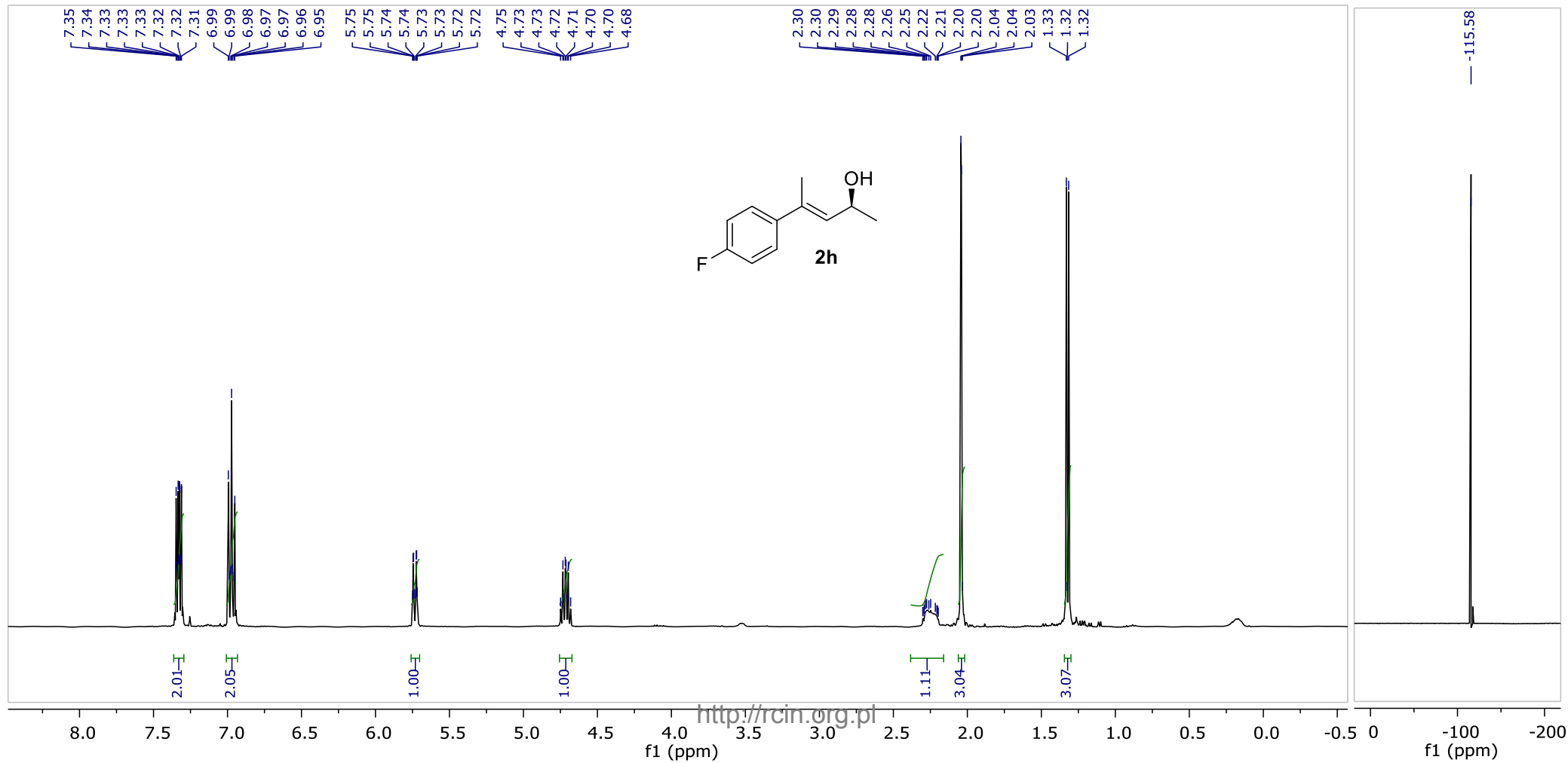
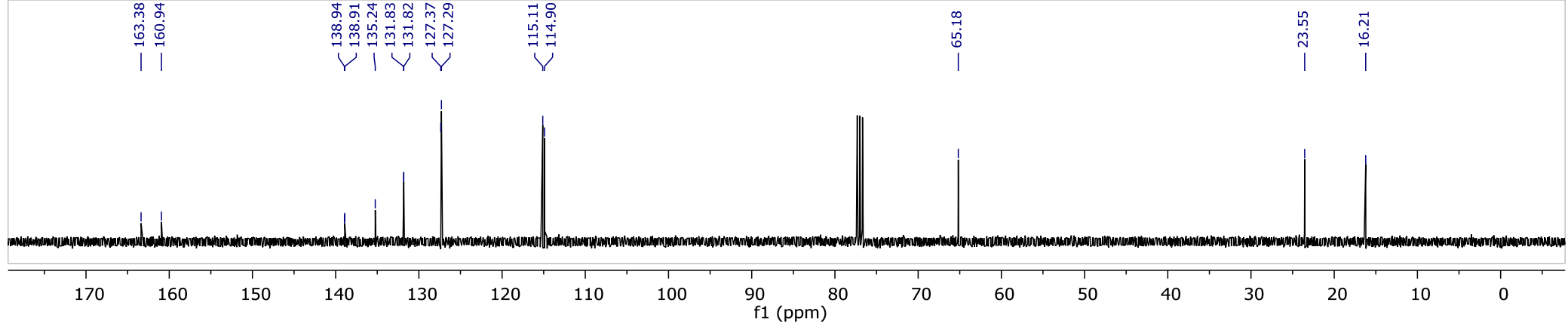




Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

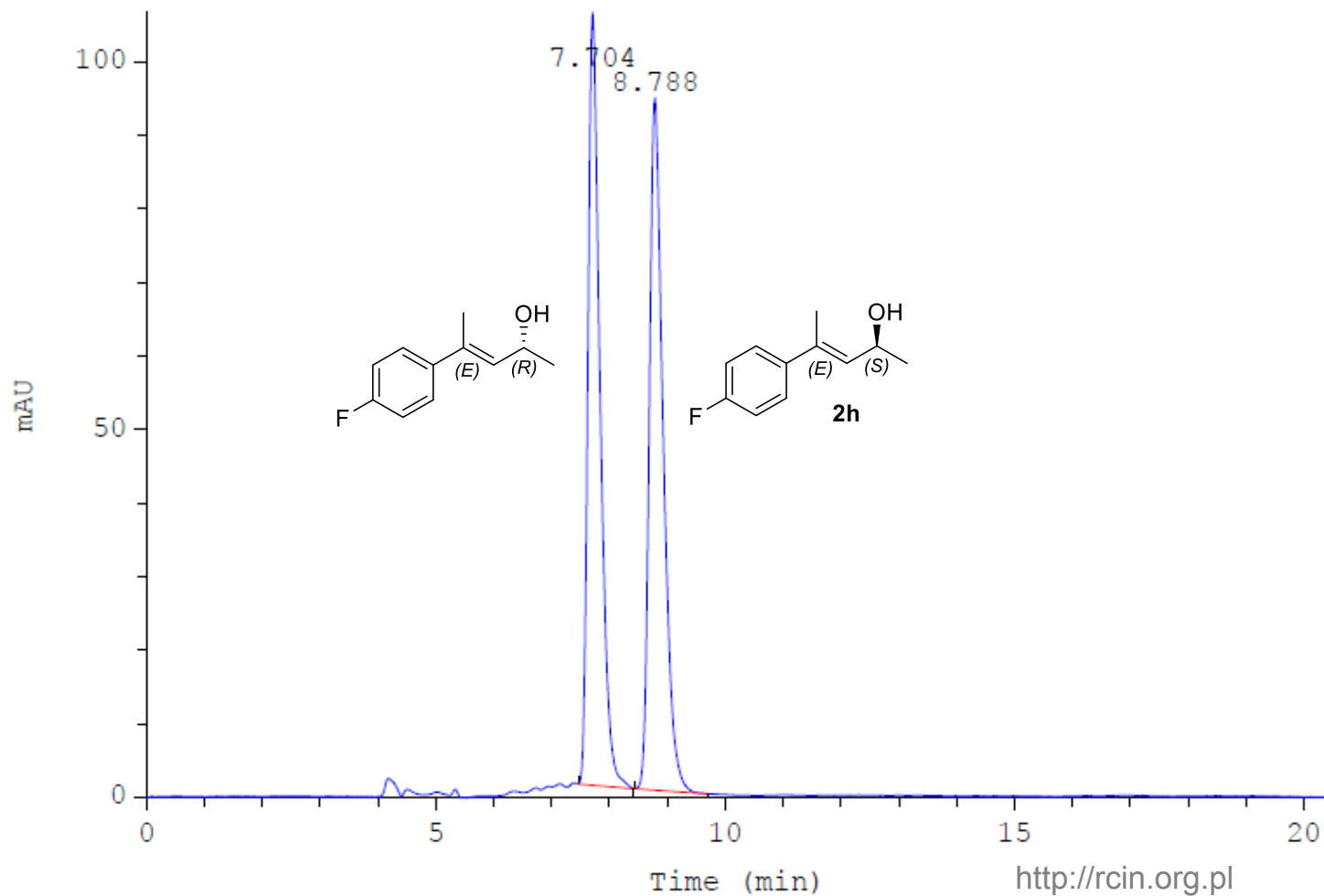
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.890	8.46	9.71	25.6102	68.1521	2.3848	0.331
2	10.975	10.42	13.89	1048.3	1969.63	97.6152	0.476





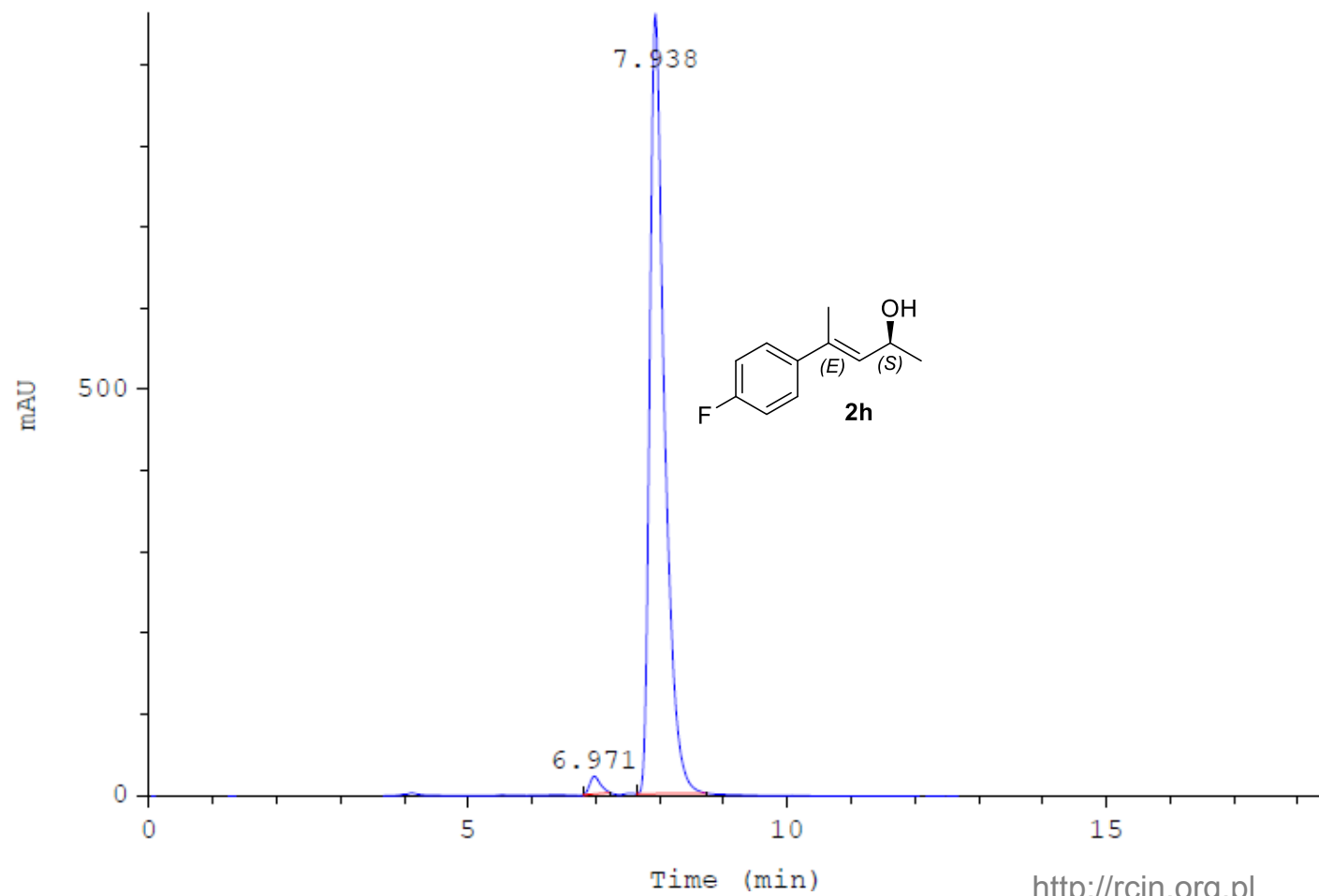
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

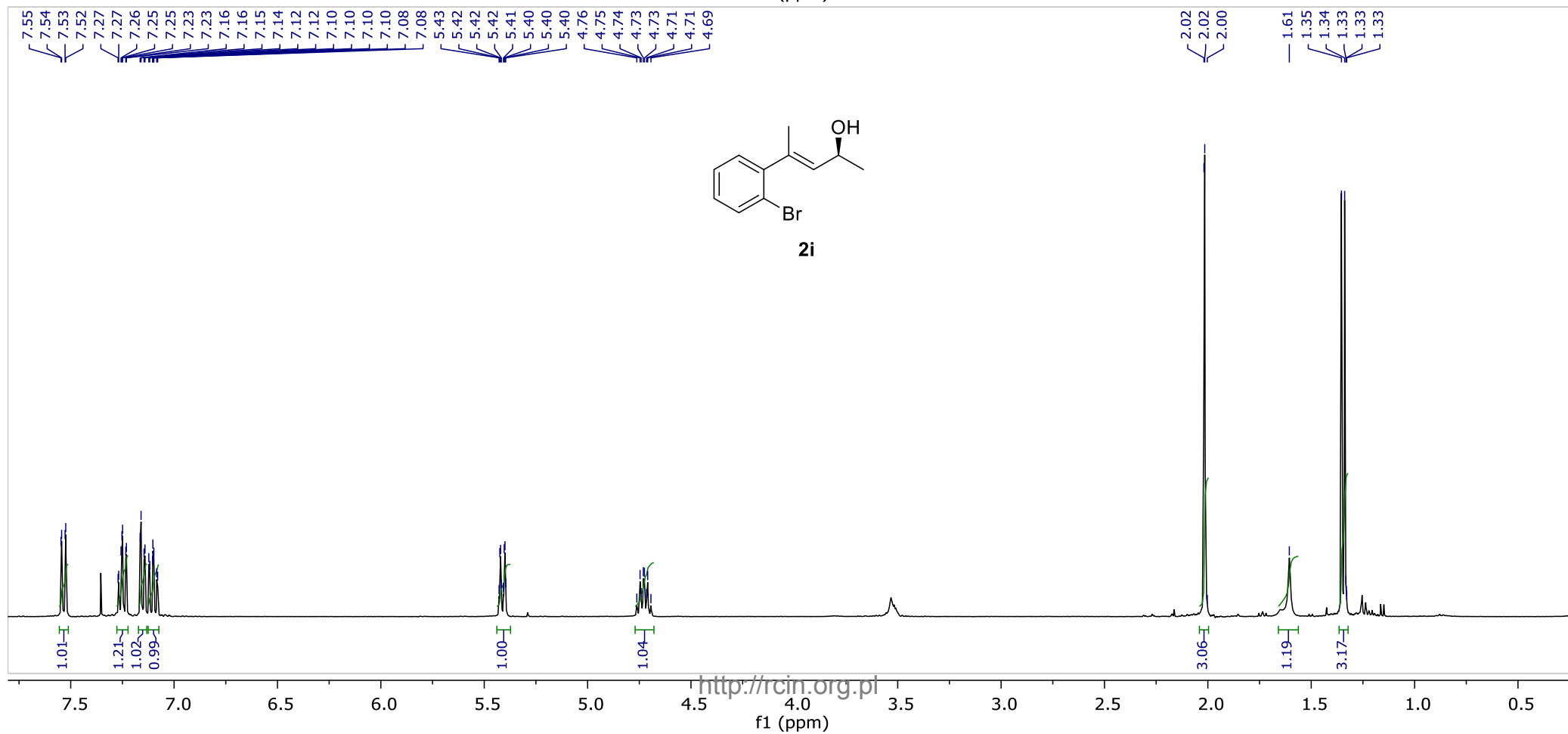
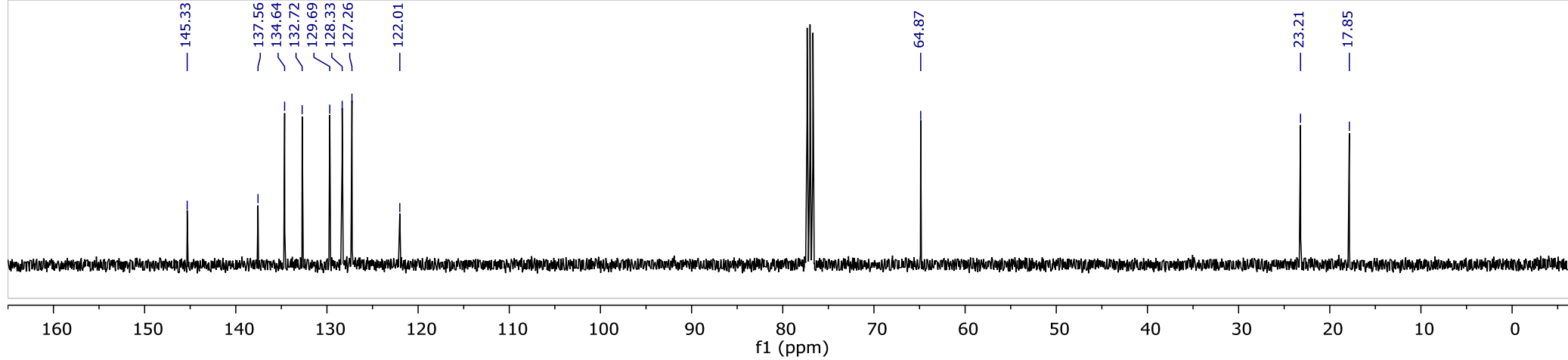
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.704	7.47	8.42	25.4682	105.096	49.4413	0.220
2	8.788	8.44	9.71	26.0438	94.106	50.5587	0.251



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

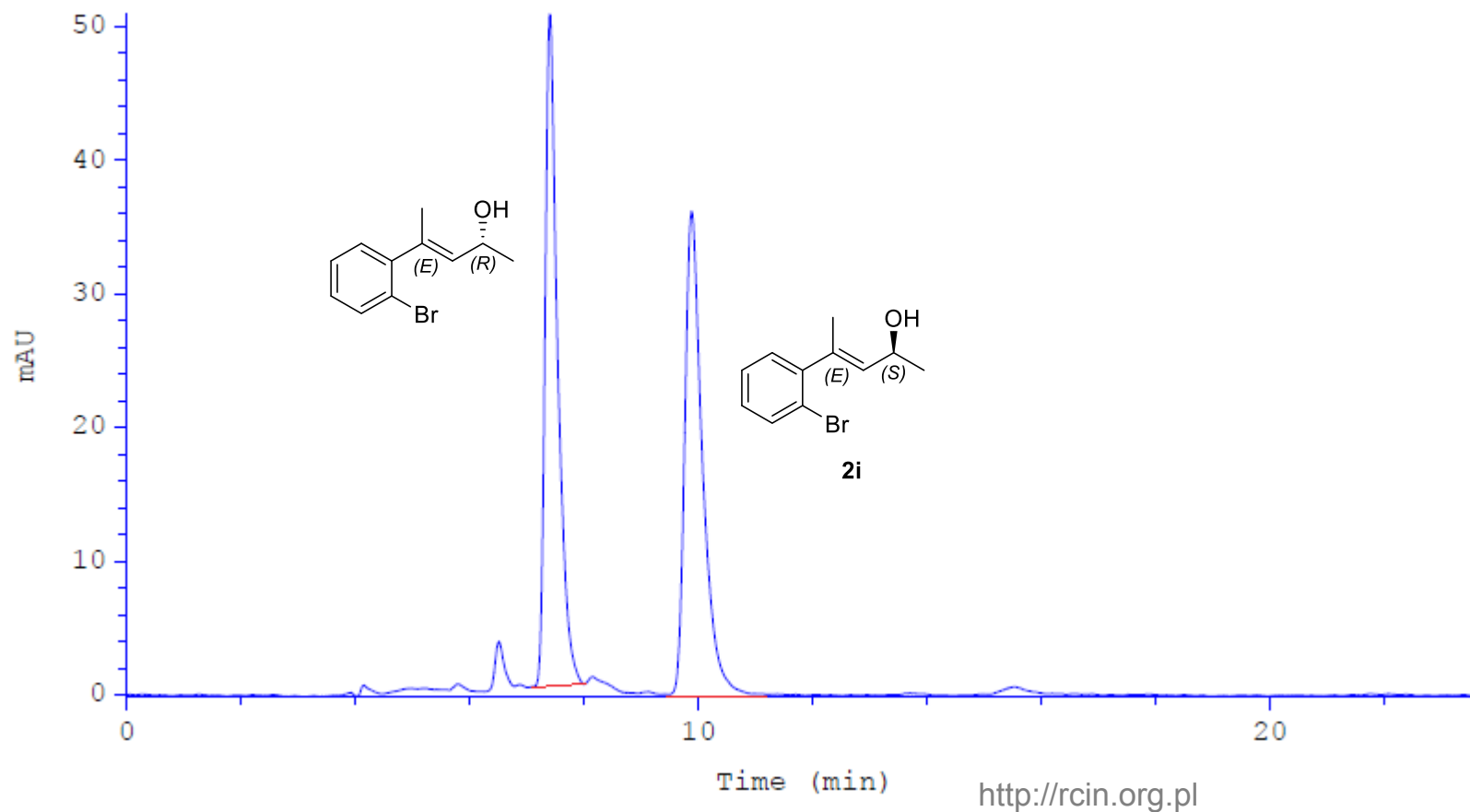
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.971	6.81	7.23	4.1632	21.7962	1.5959	0.177
2	7.938	7.64	8.75	256.71	960.368	98.4041	0.233





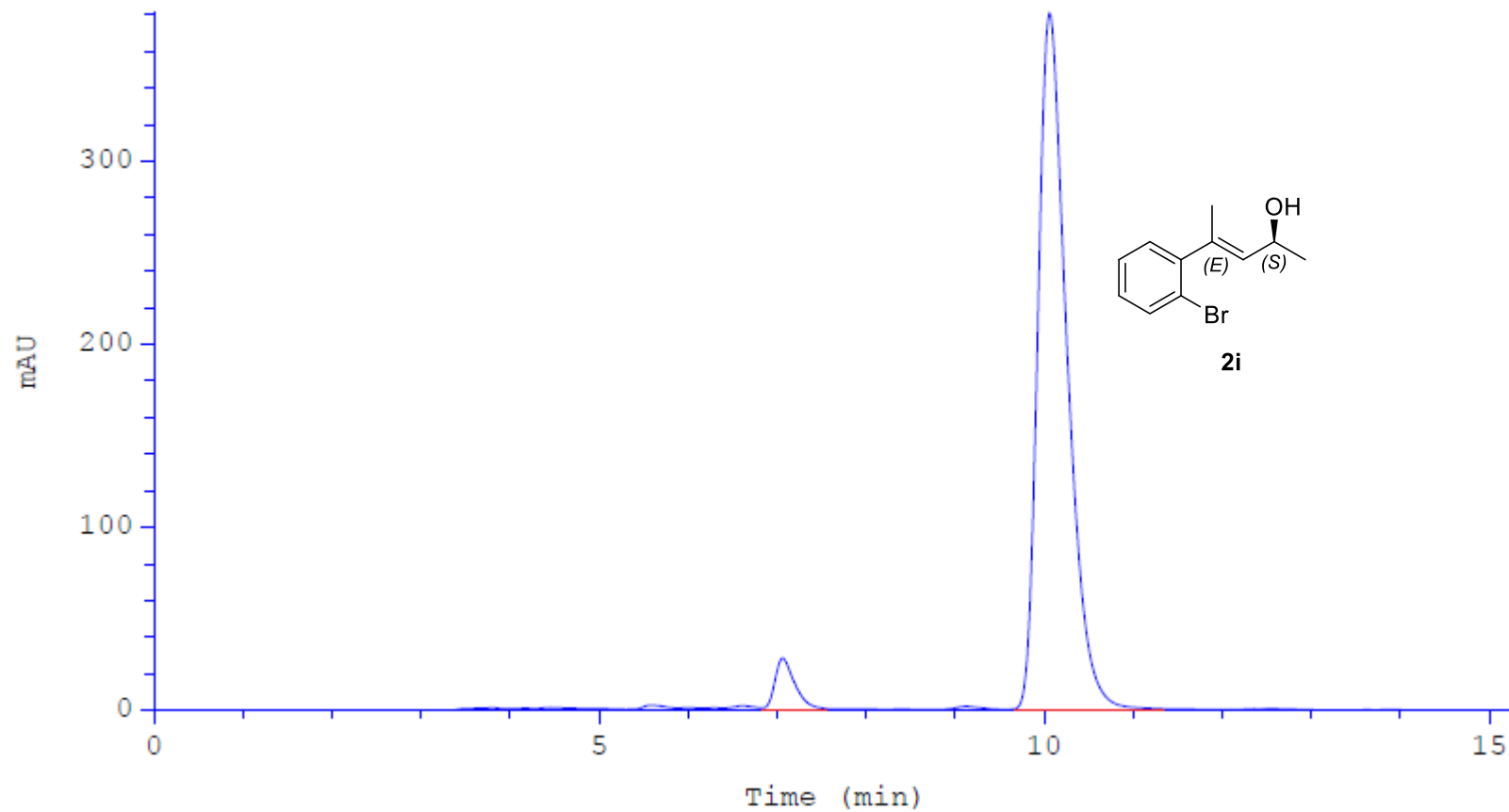
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

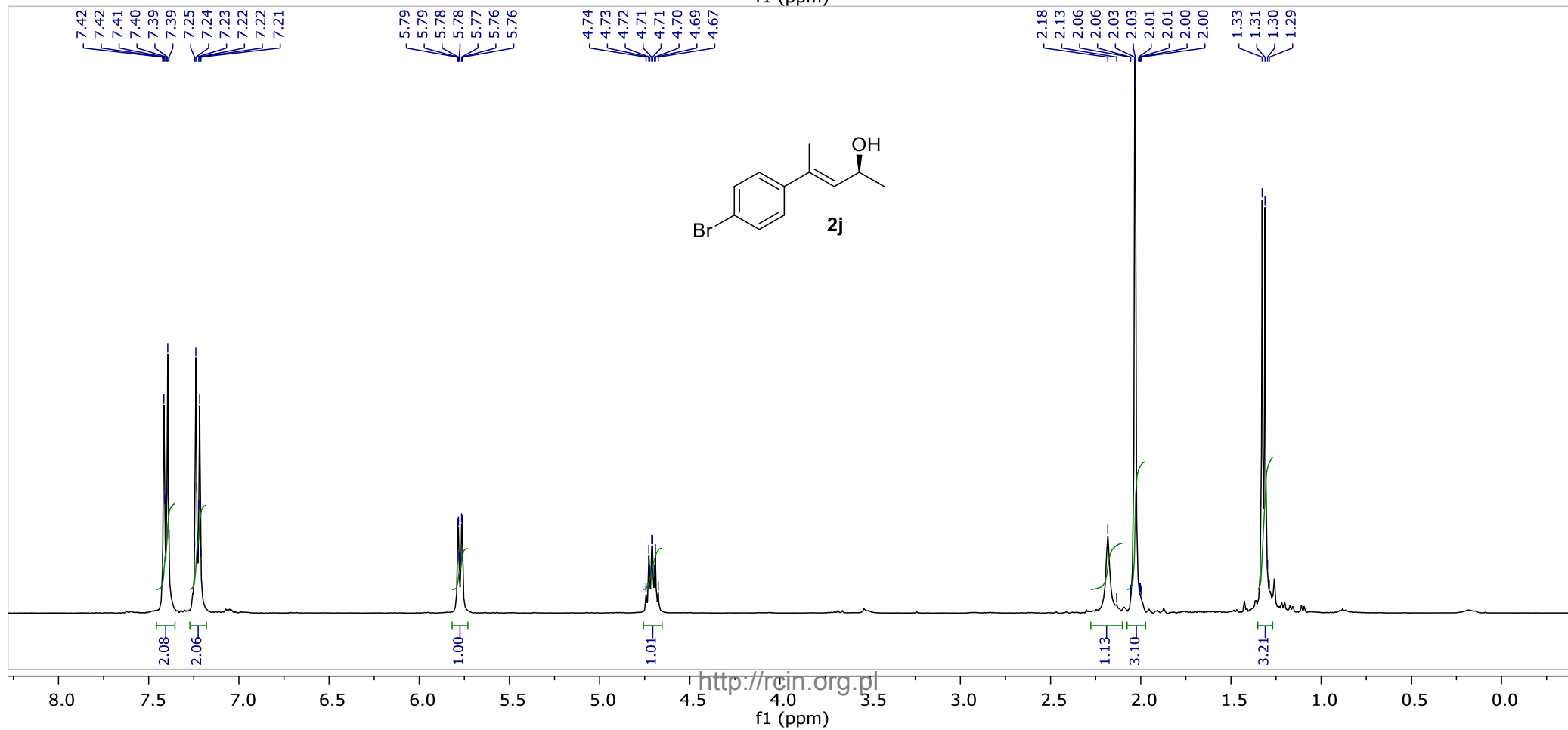
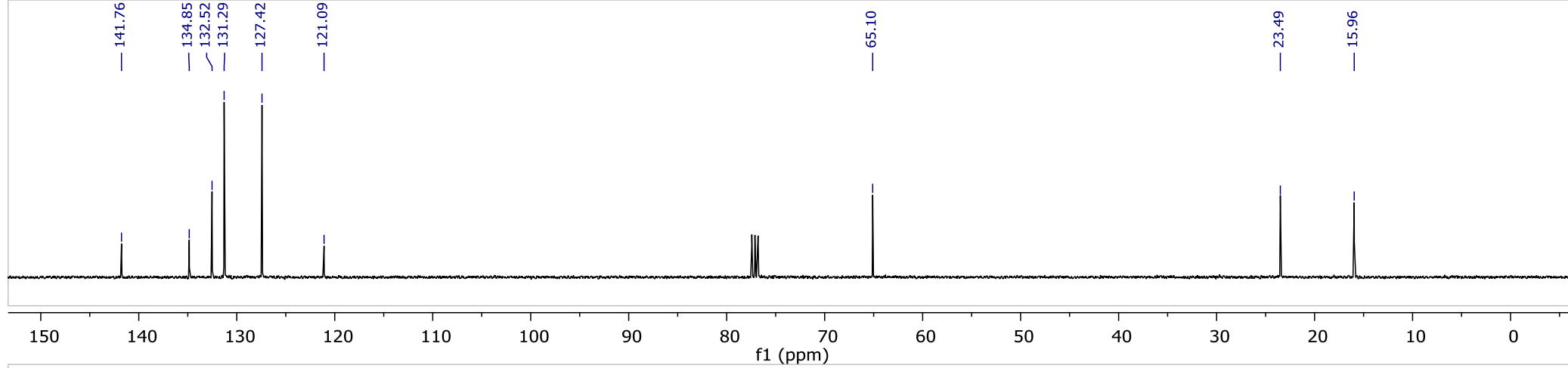
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.386	7.12	7.98	12.7896	50.2308	50.0287	0.223
2	9.871	9.50	10.88	12.7749	36.1299	49.9713	0.310



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.056	6.87	7.50	6.54871	26.8452	4.3799	0.225
2	10.058	9.69	11.18	142.967	379.783	95.6201	0.345

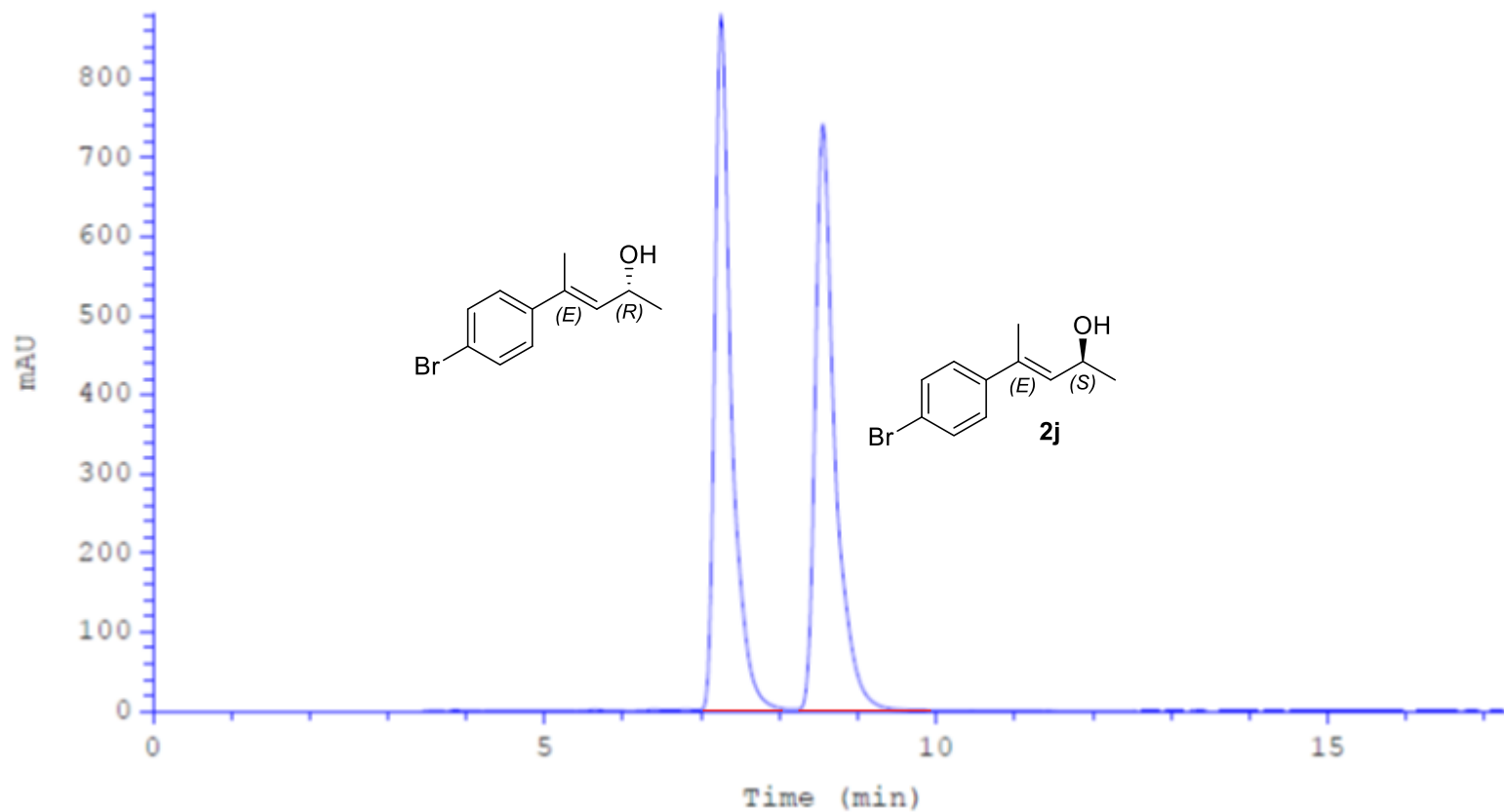






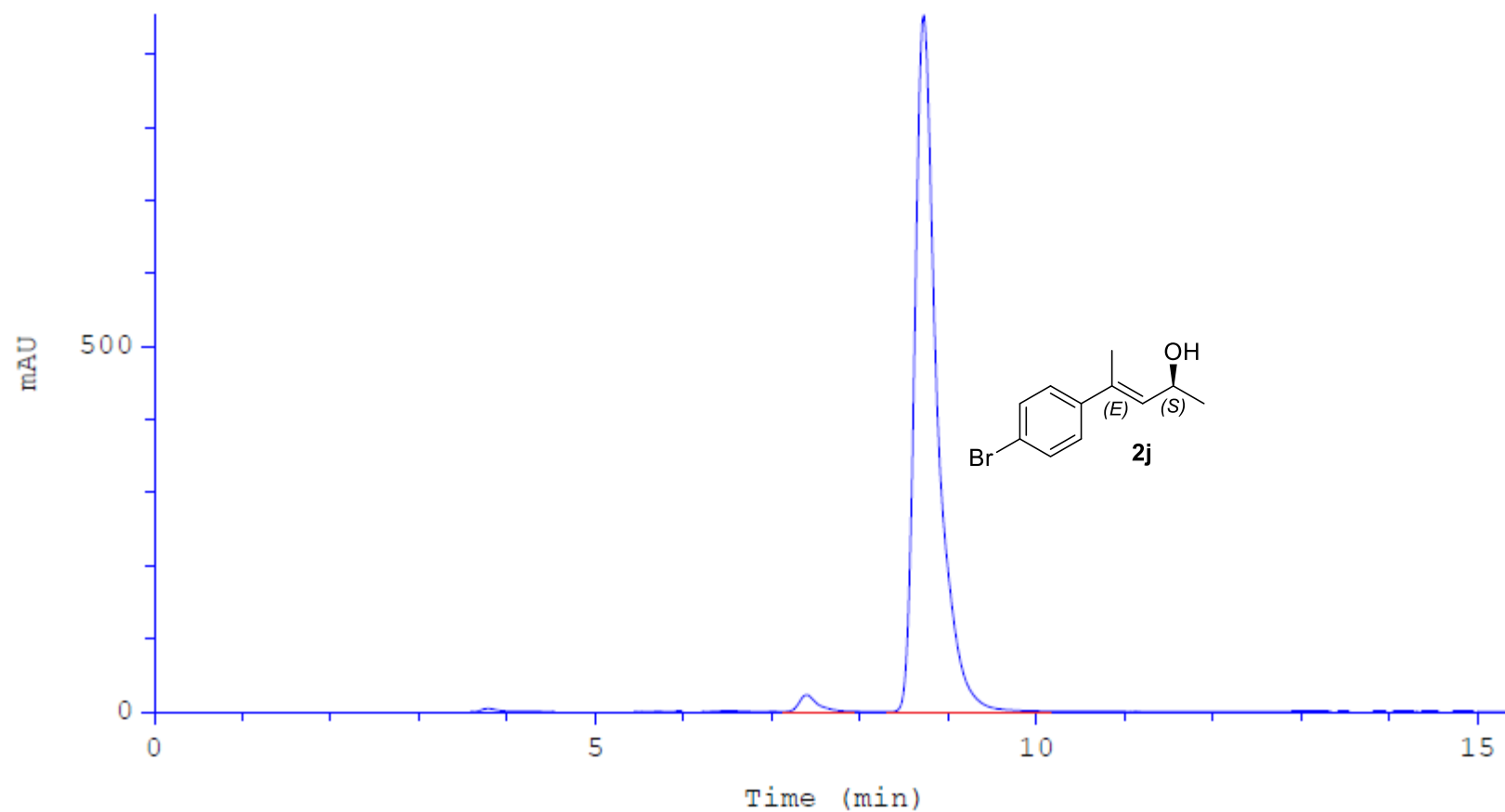
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

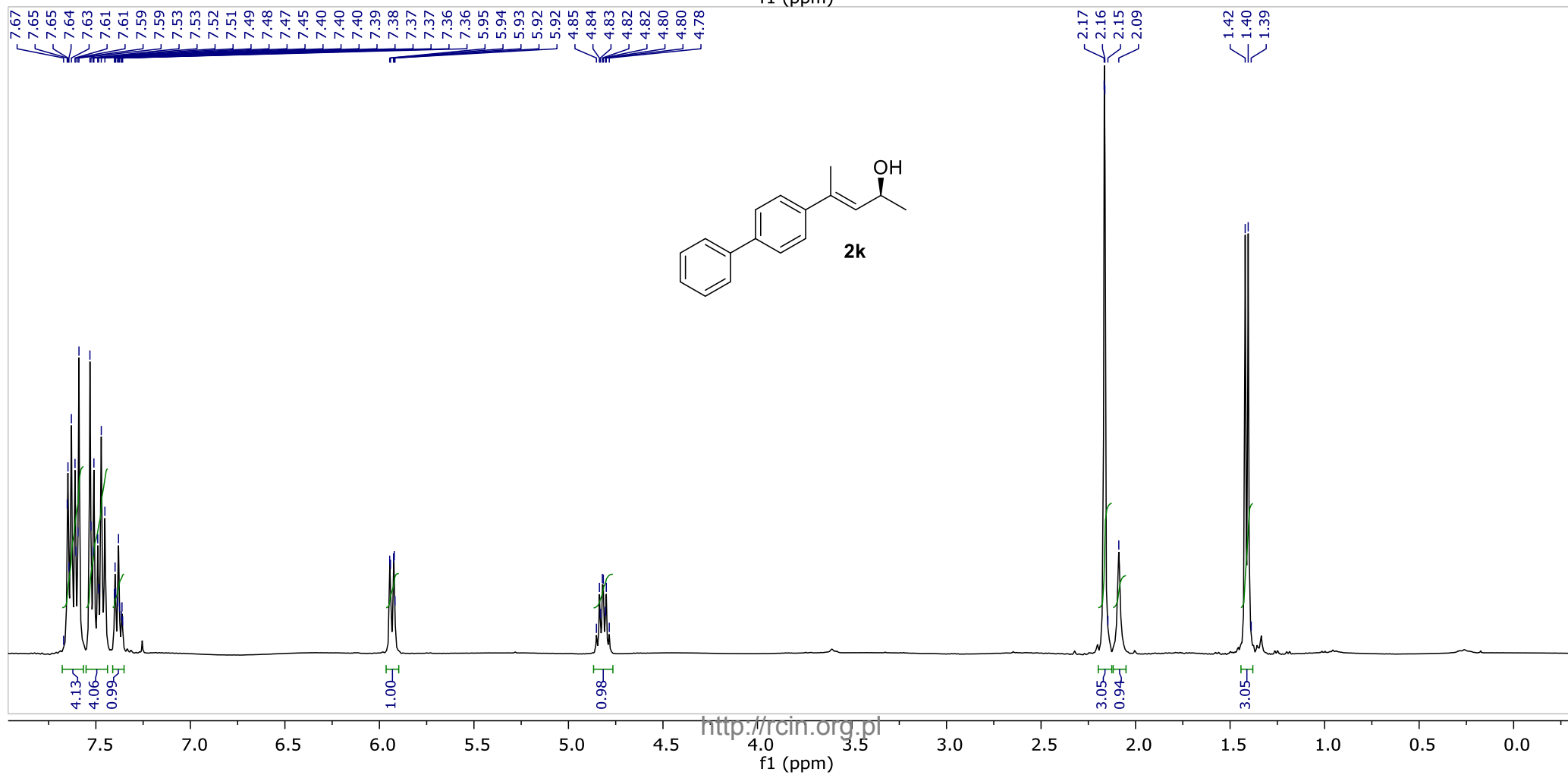
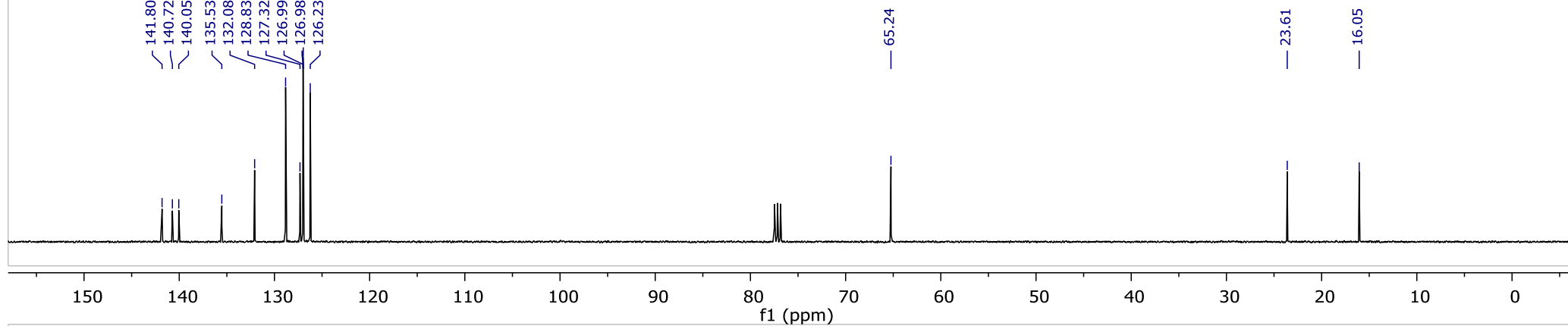
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.255	7.00	8.04	213.109	879.447	49.9770	0.201
2	8.556	8.27	9.96	213.306	739.344	50.0230	0.241



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

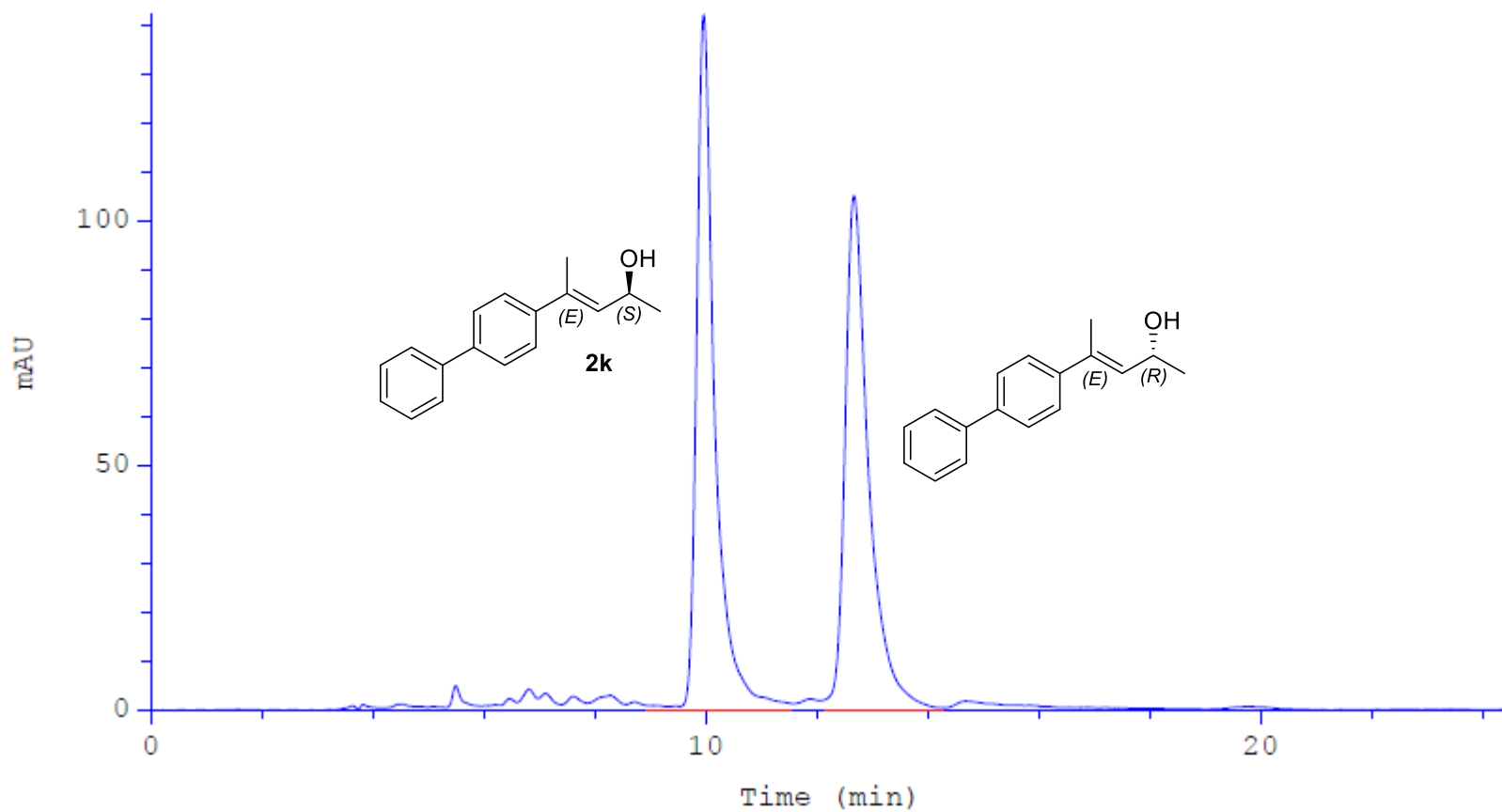
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.389	7.16	7.85	5.34146	22.7371	1.8779	0.200
2	8.724	8.38	10.15	279.098	953.007	98.1221	0.244





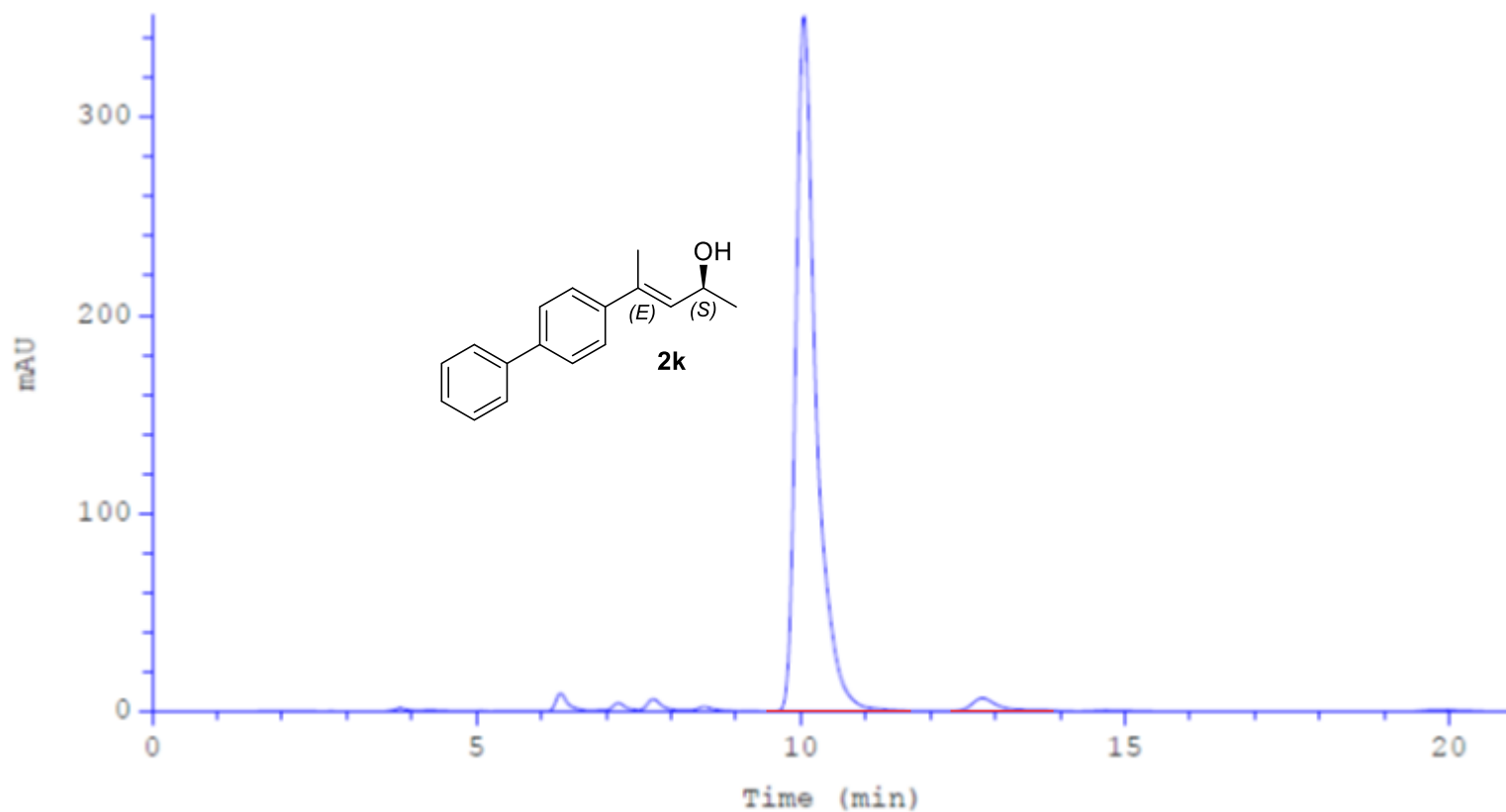
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

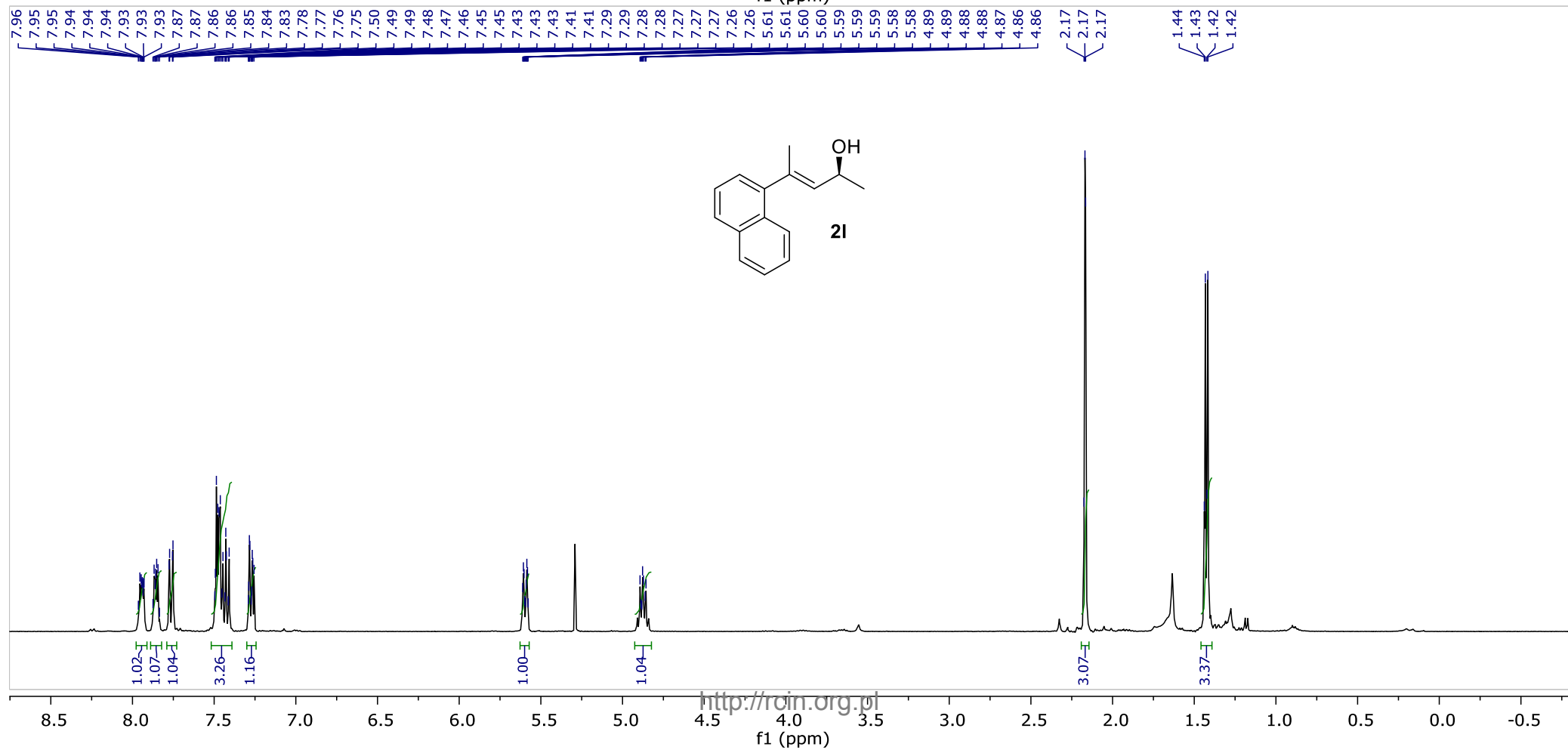
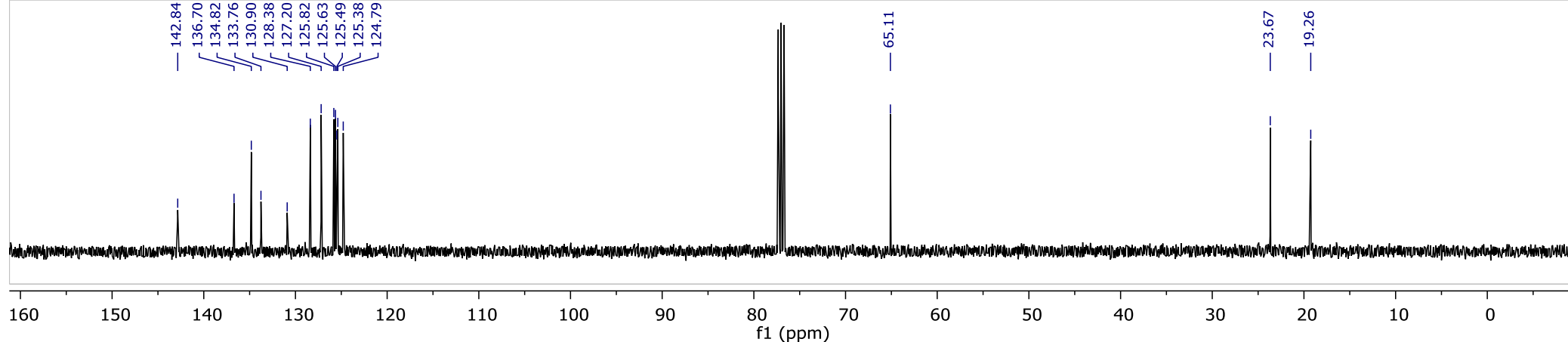
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.971	9.54	11.60	52.4511	141.21	51.2552	0.304
2	12.672	12.07	14.21	49.8821	103.646	48.7448	0.410



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

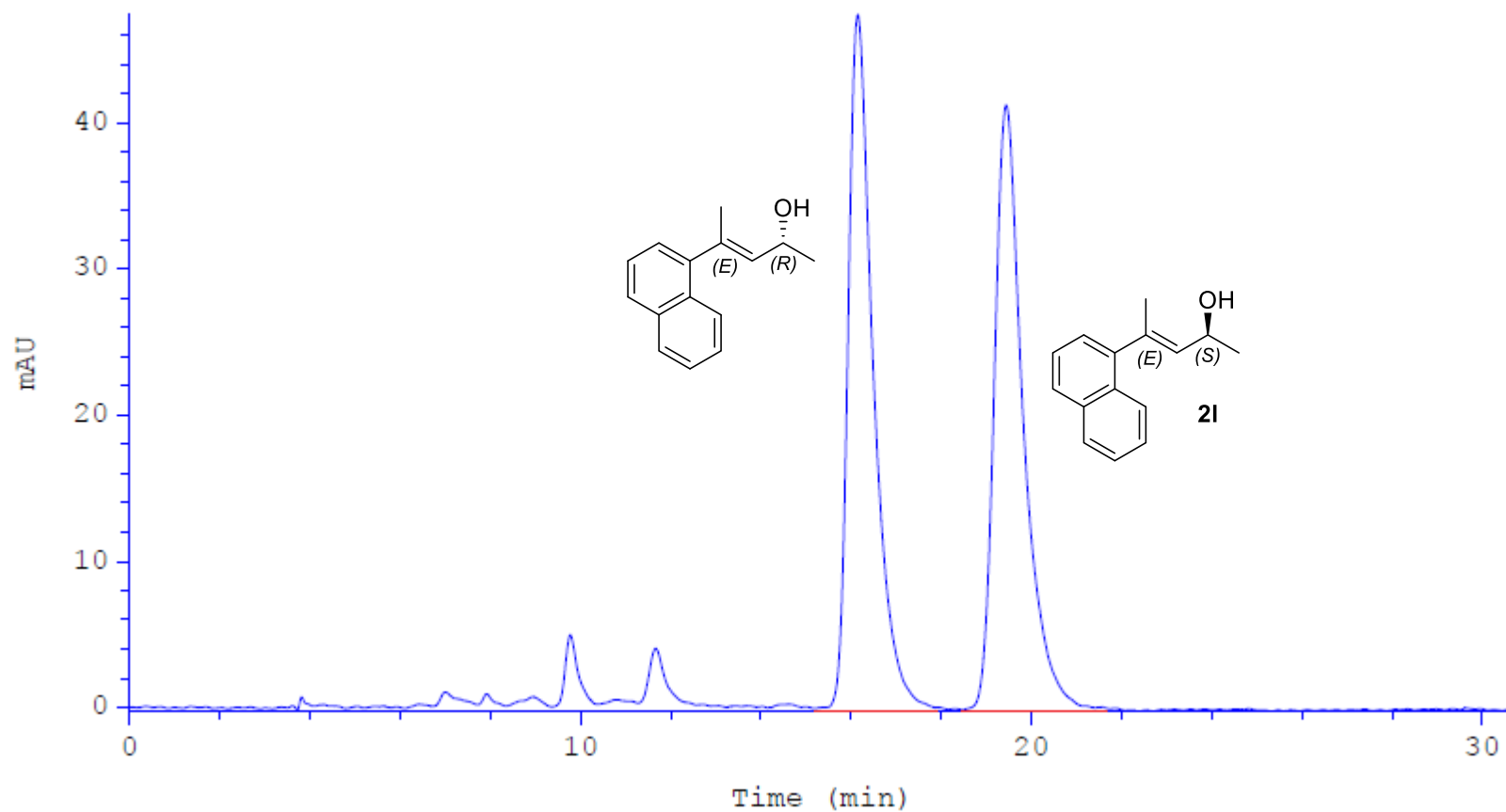
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.055	9.64	11.61	125.813	350.911	97.8268	0.300
2	12.807	12.42	13.90	2.79492	6.30792	2.1732	0.377





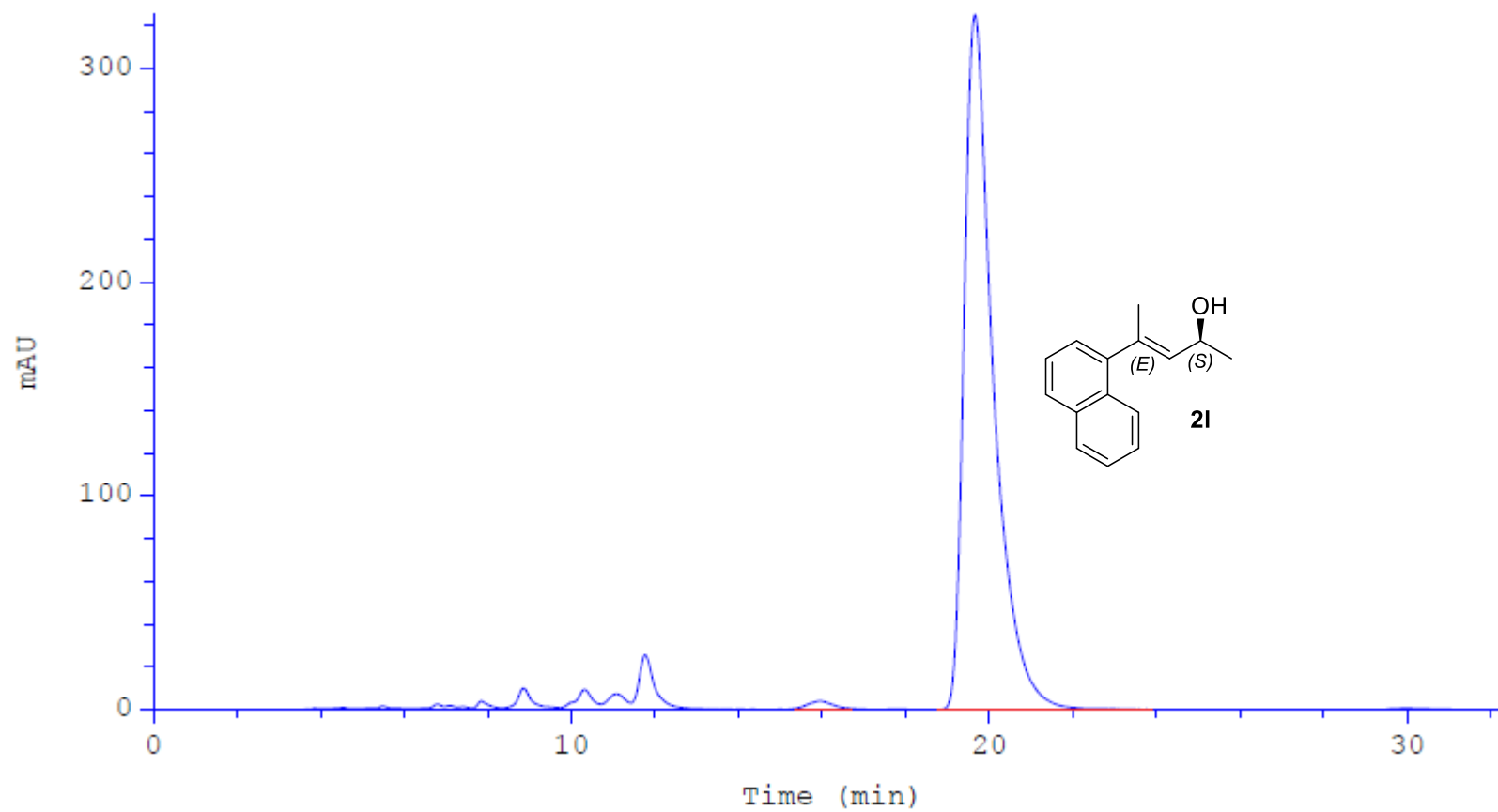
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	16.154	15.37	17.96	30.3979	47.4034	49.9883	0.565
2	19.438	18.67	21.43	30.4121	41.2347	50.0117	0.641

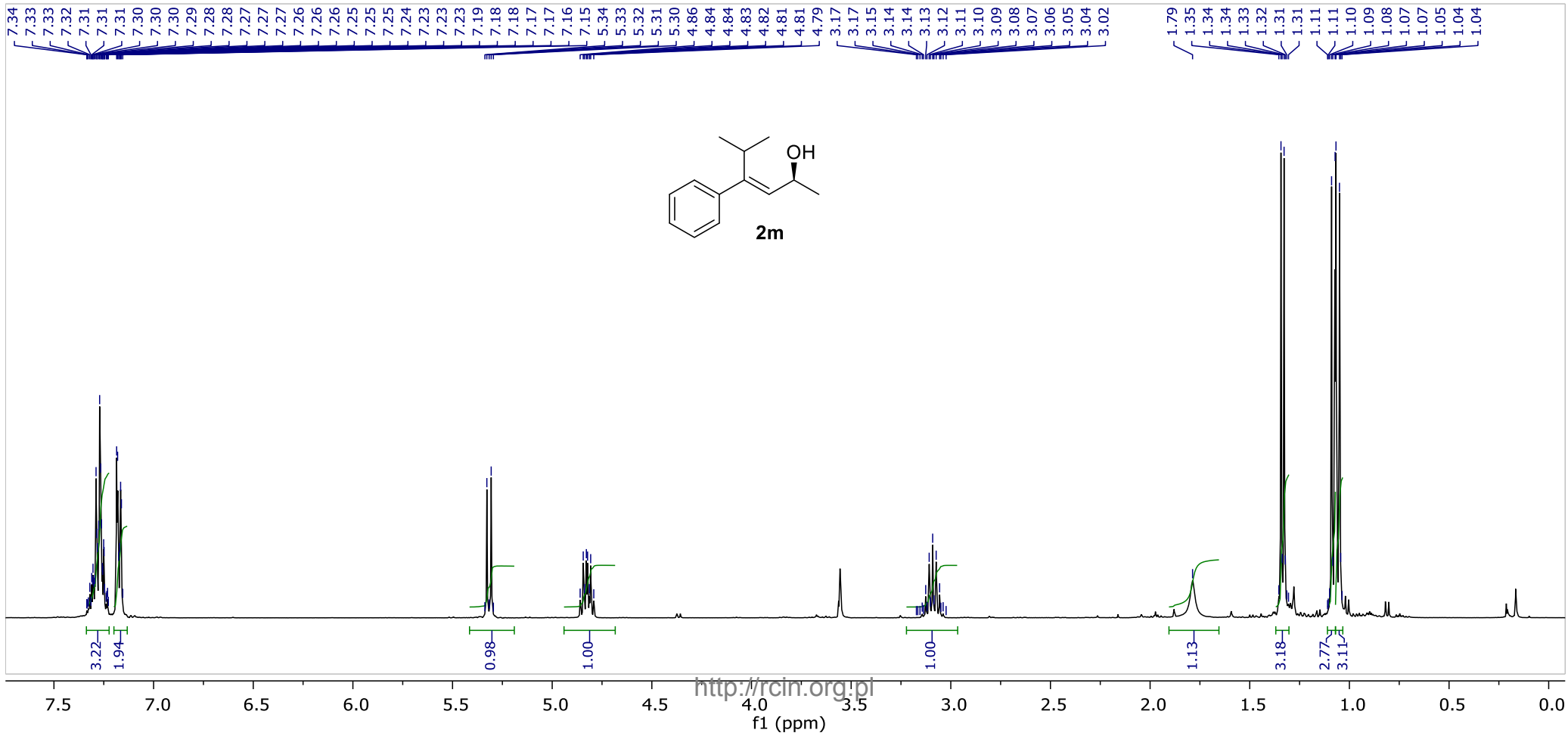
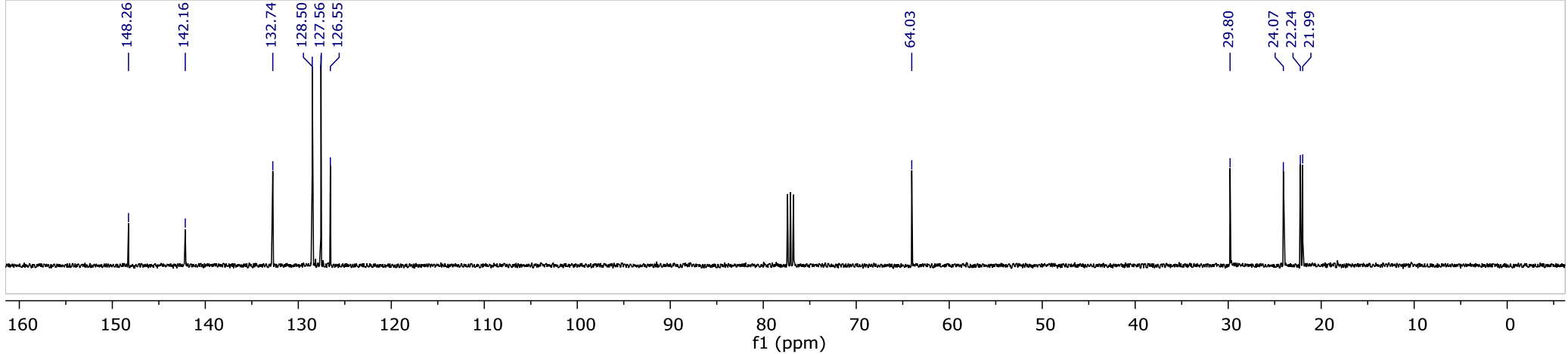


Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.970	15.46	16.43	1.62042	2.93634	0.6170	0.552
2	19.655	18.80	21.94	260.994	324.84	99.3830	0.697

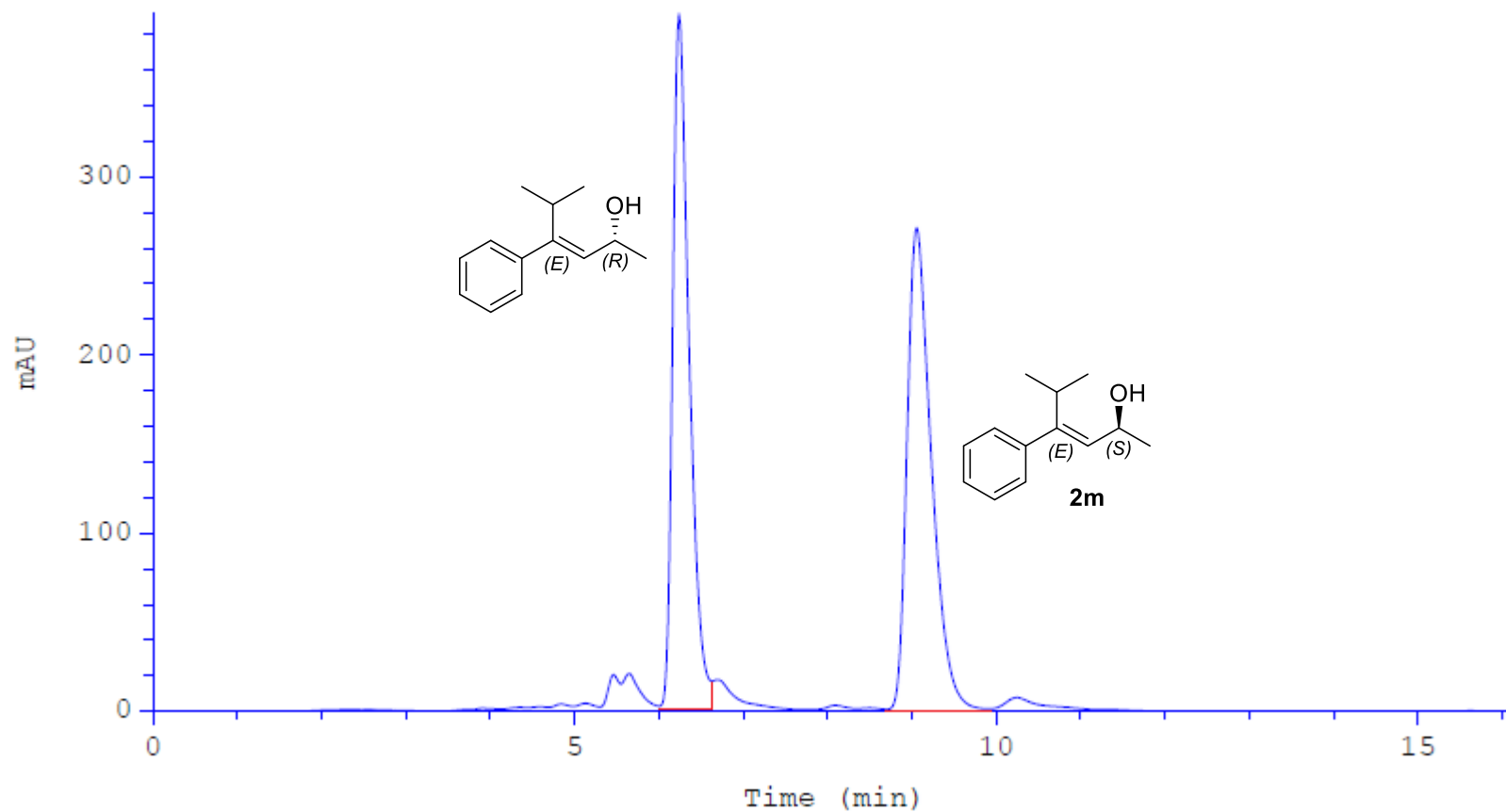






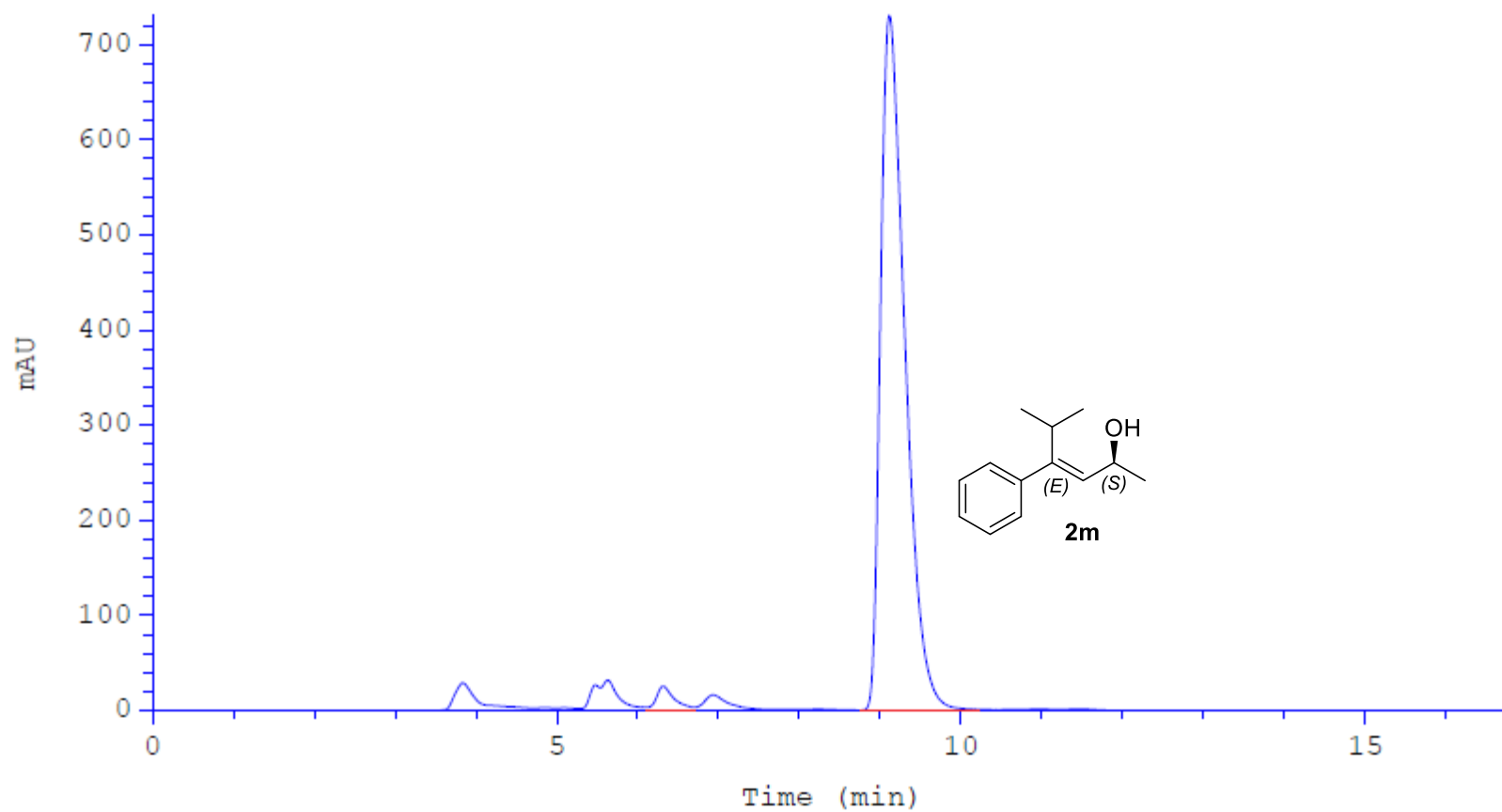
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

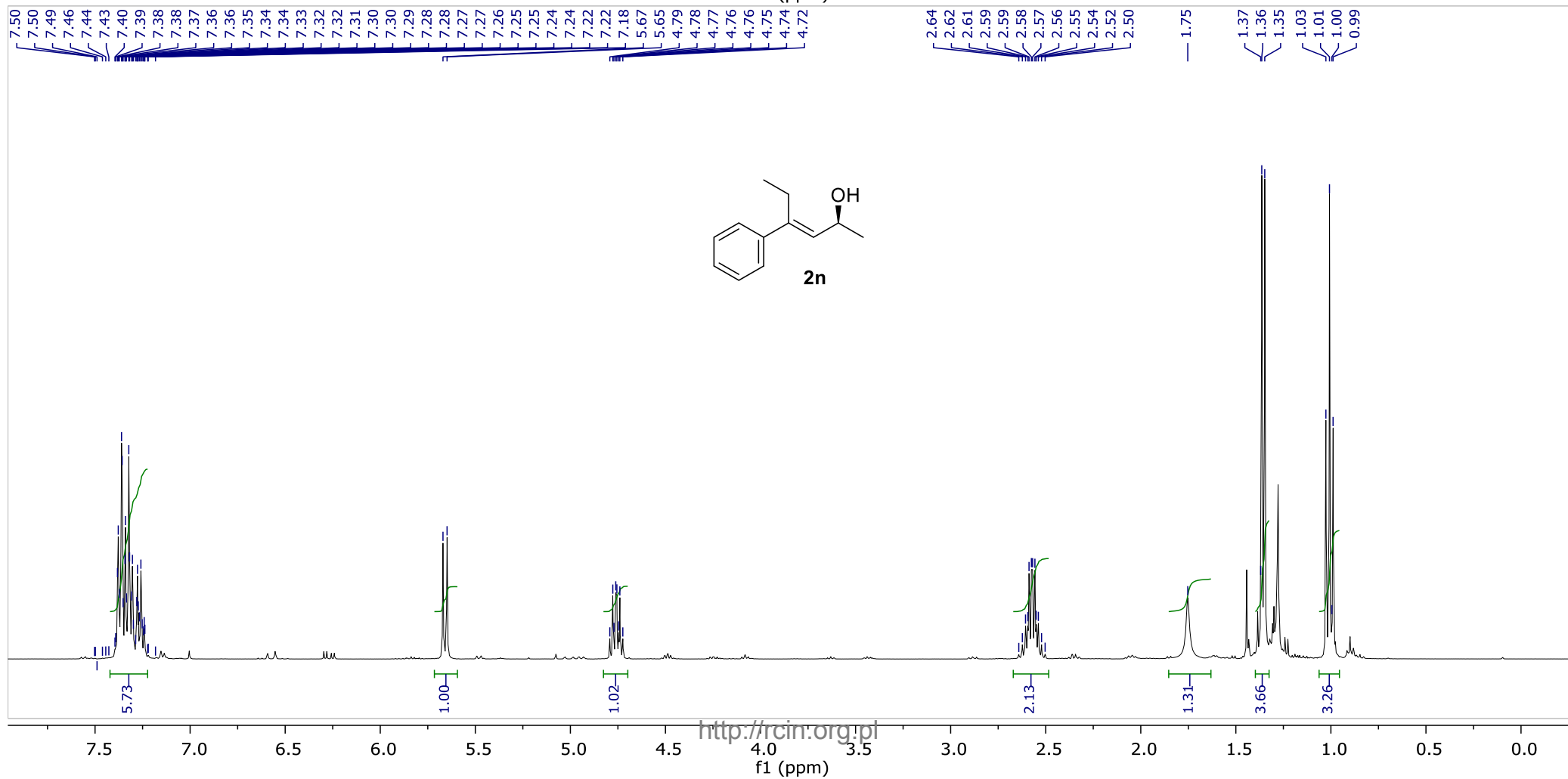
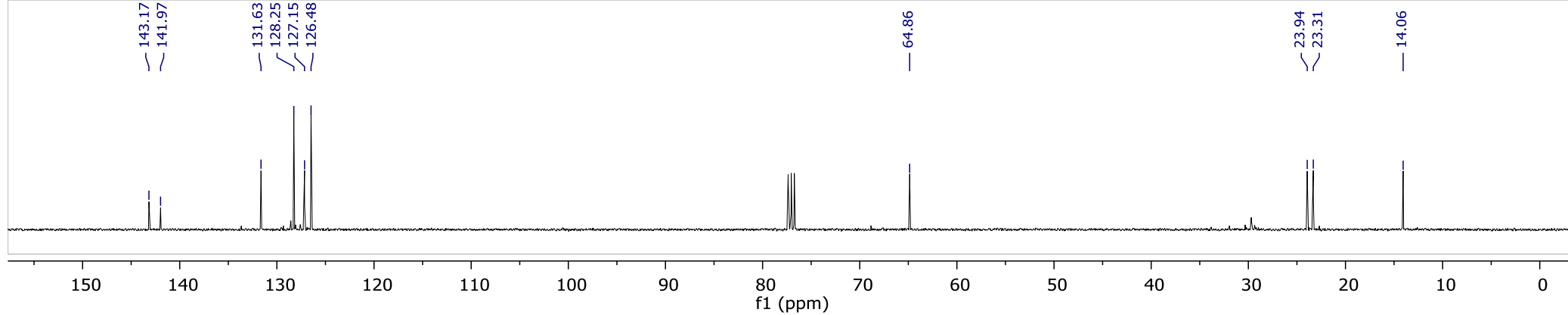
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.238	5.97	6.64	83.0466	382.912	48.3411	0.202
2	9.057	8.75	9.78	88.7463	269.615	51.6589	0.303

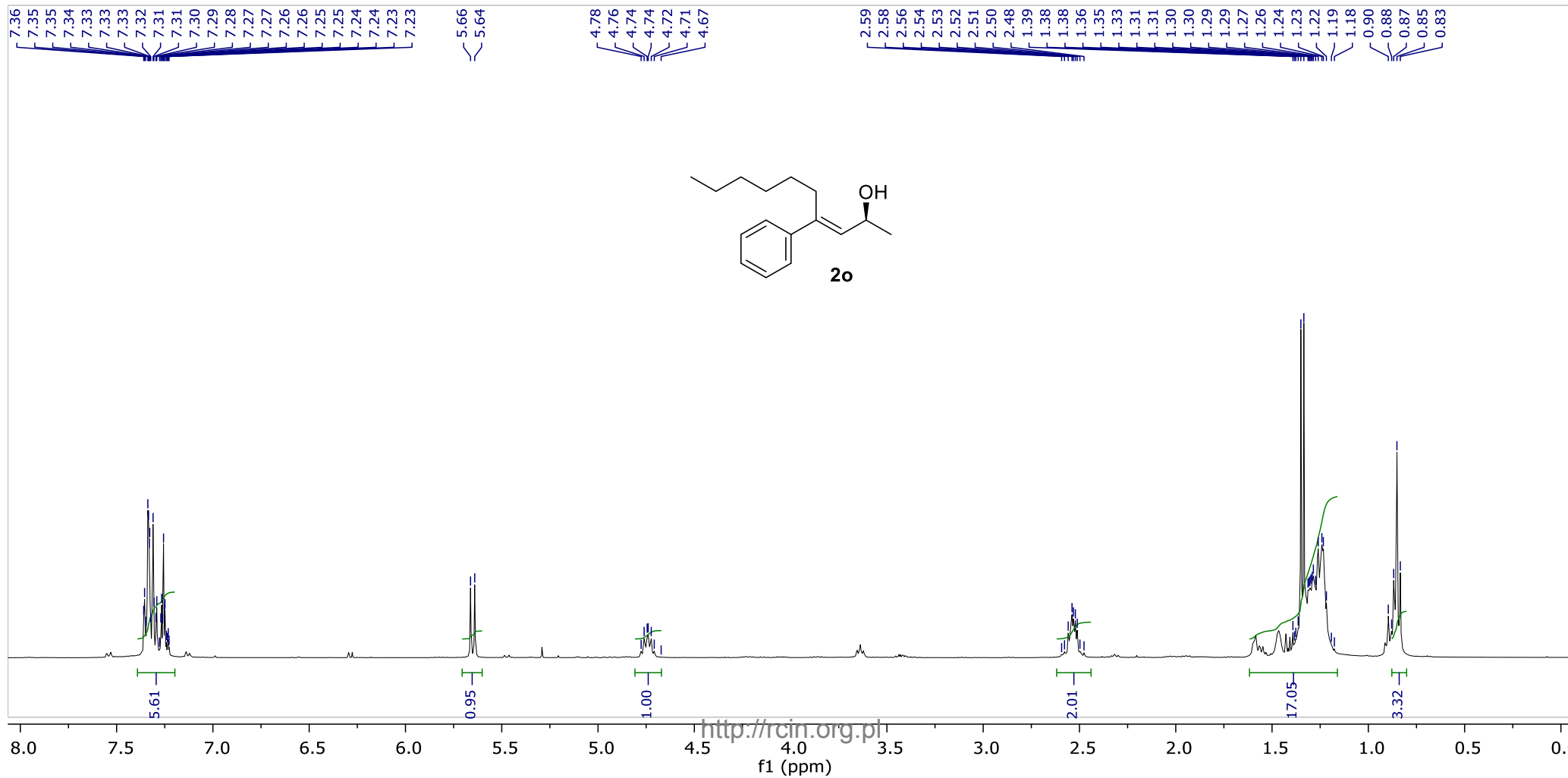
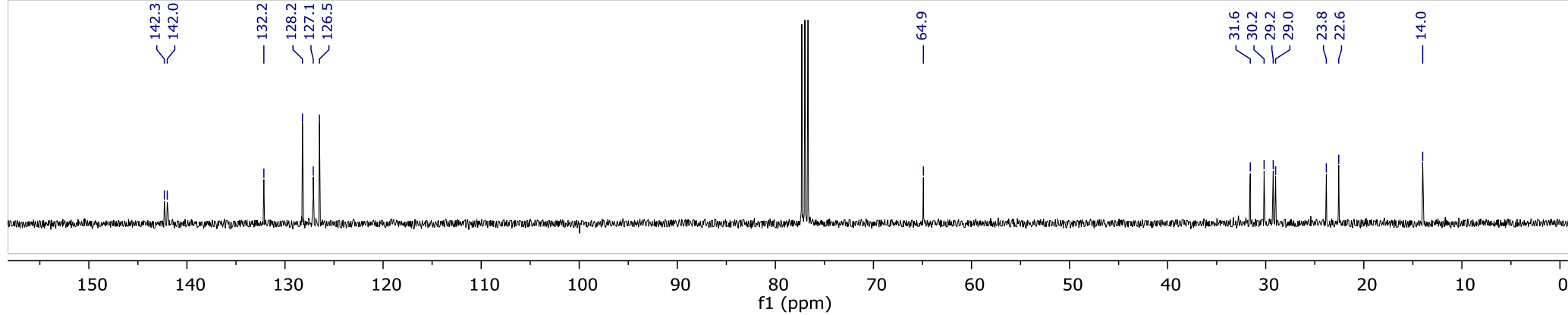


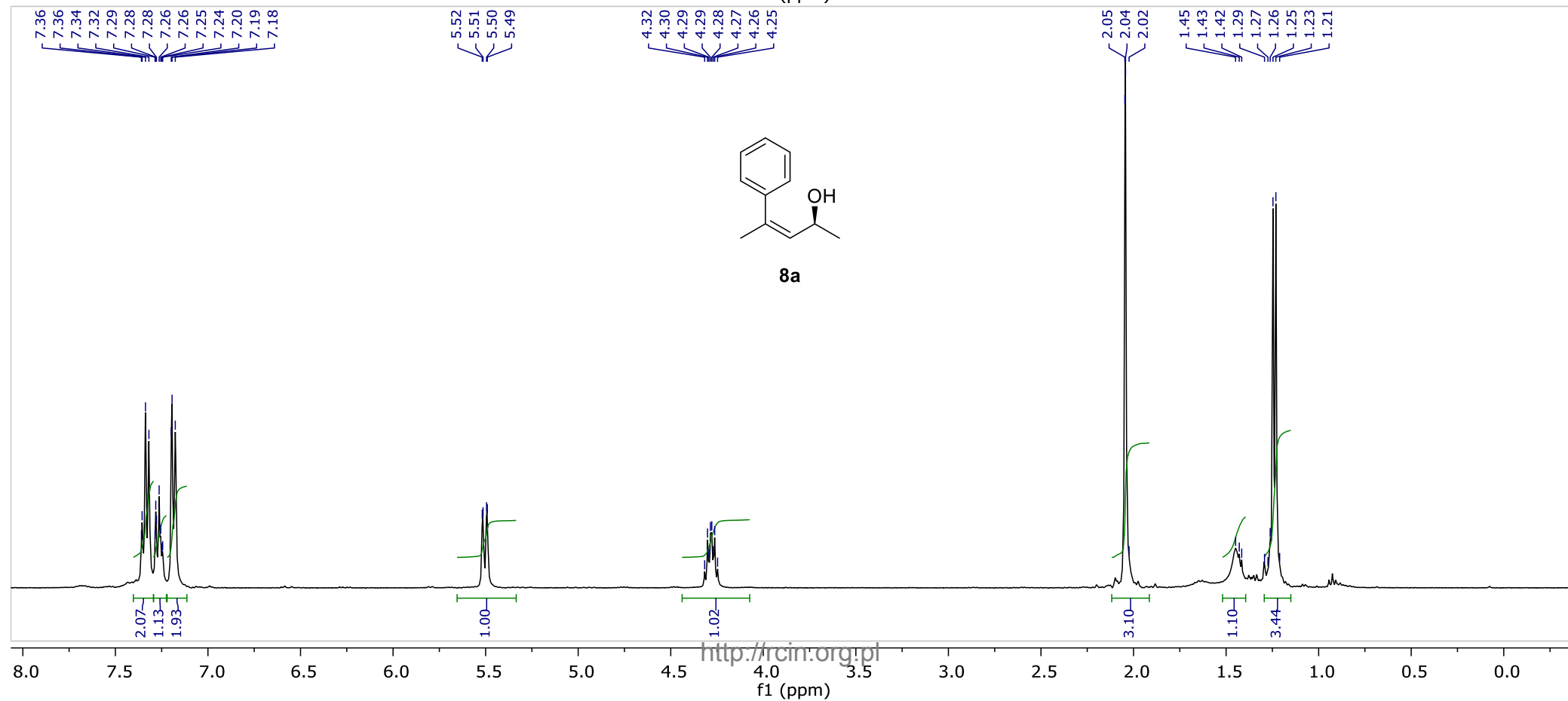
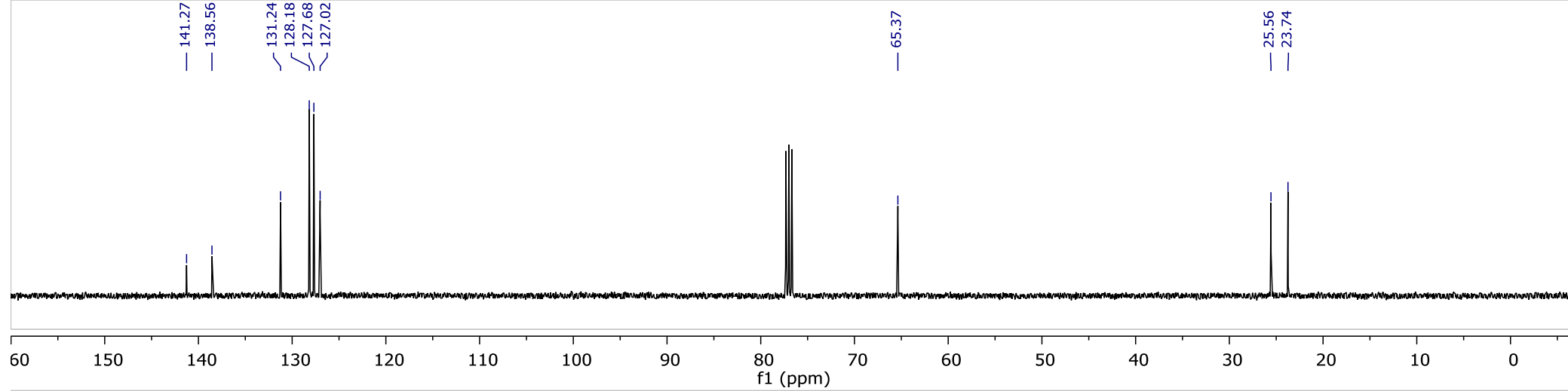
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

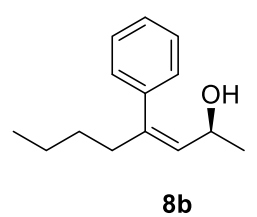
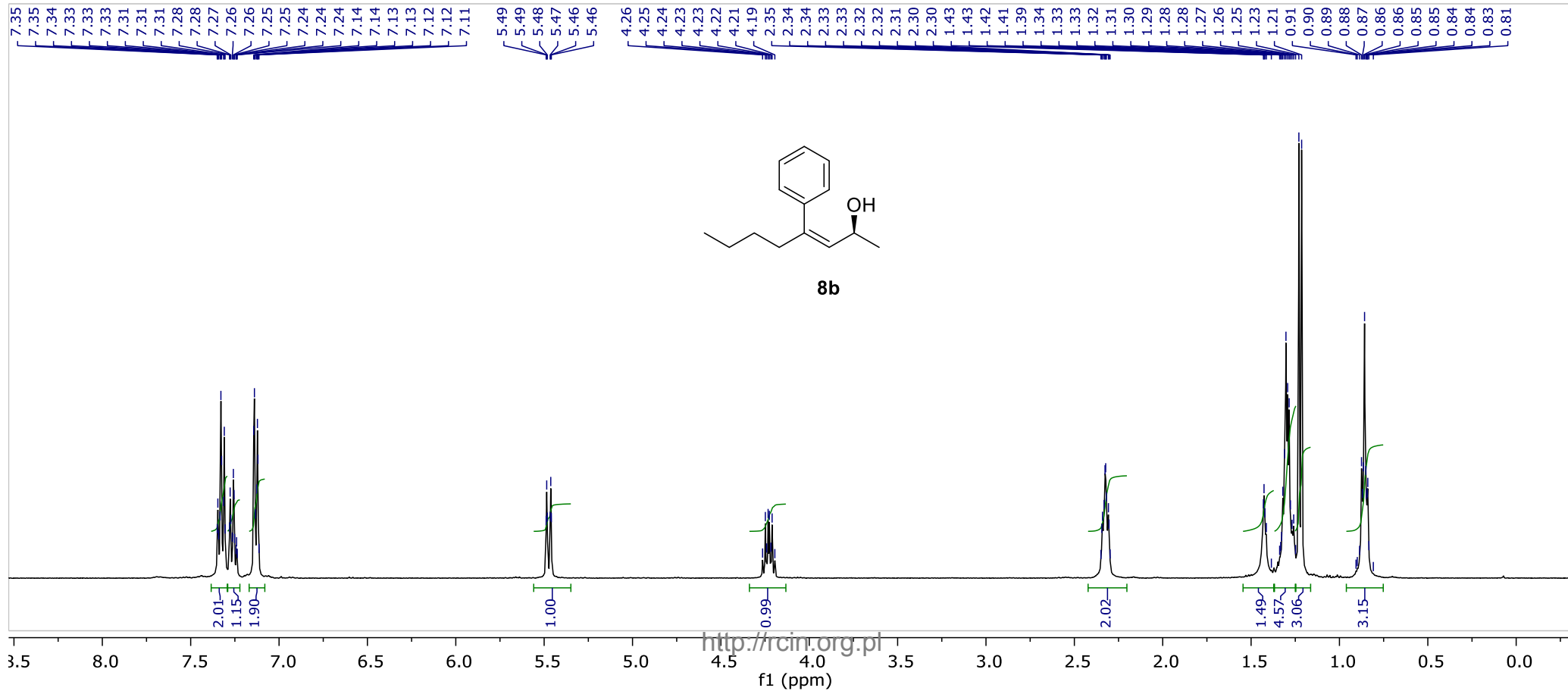
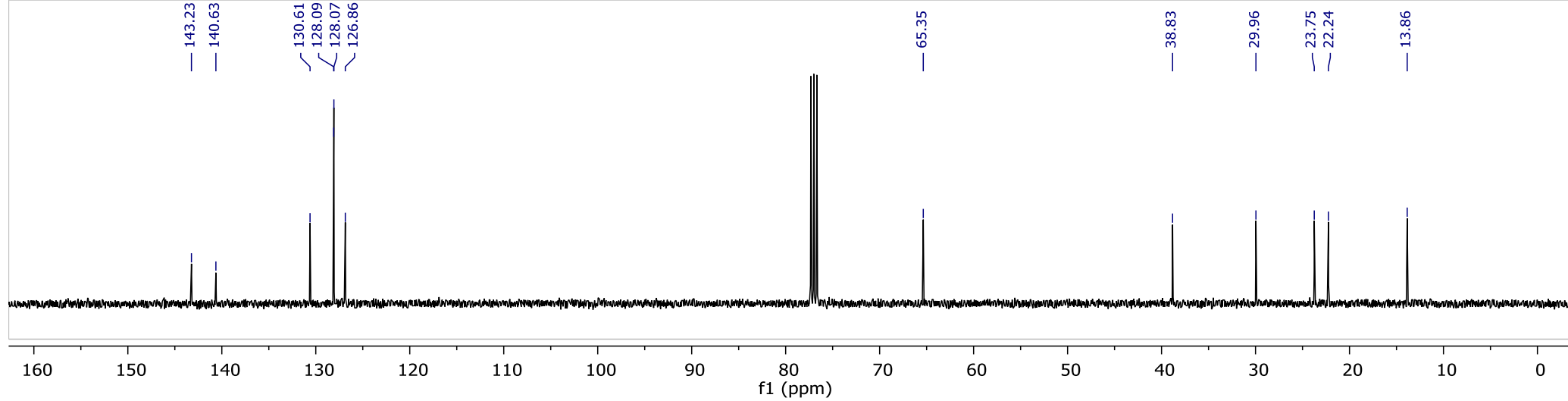
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.321	6.12	6.68	4.82593	22.0849	1.8503	0.195
2	9.106	8.79	10.13	255.998	729.49	98.1497	0.326

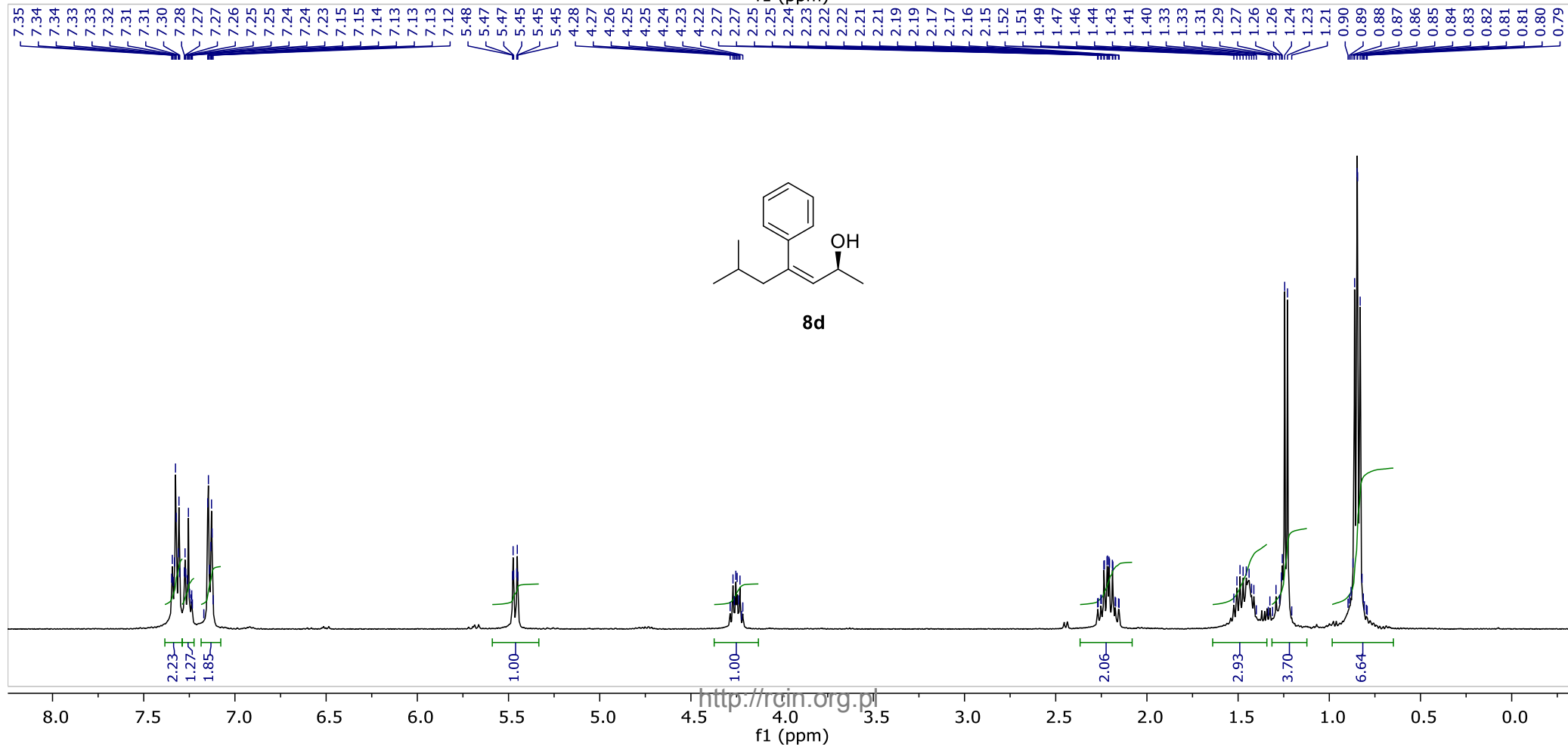
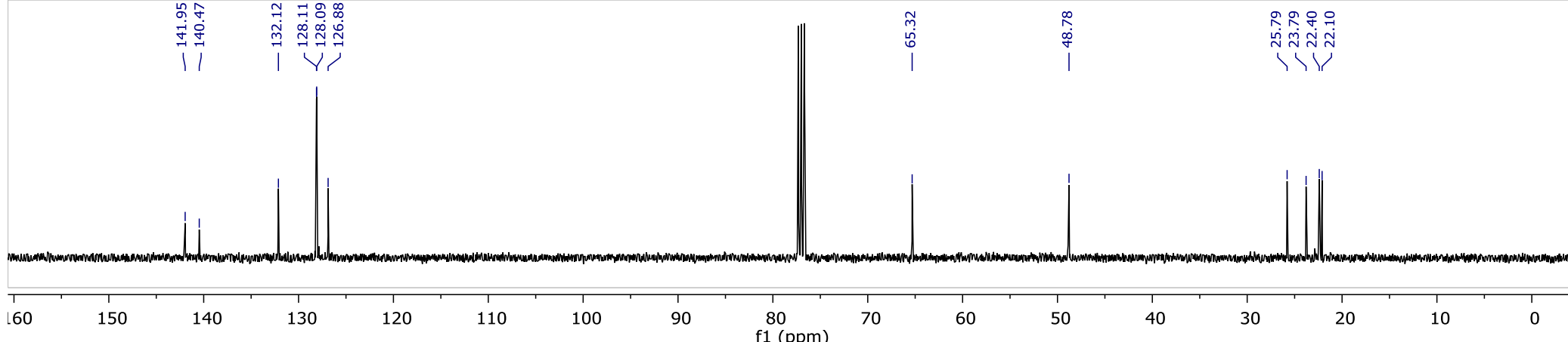




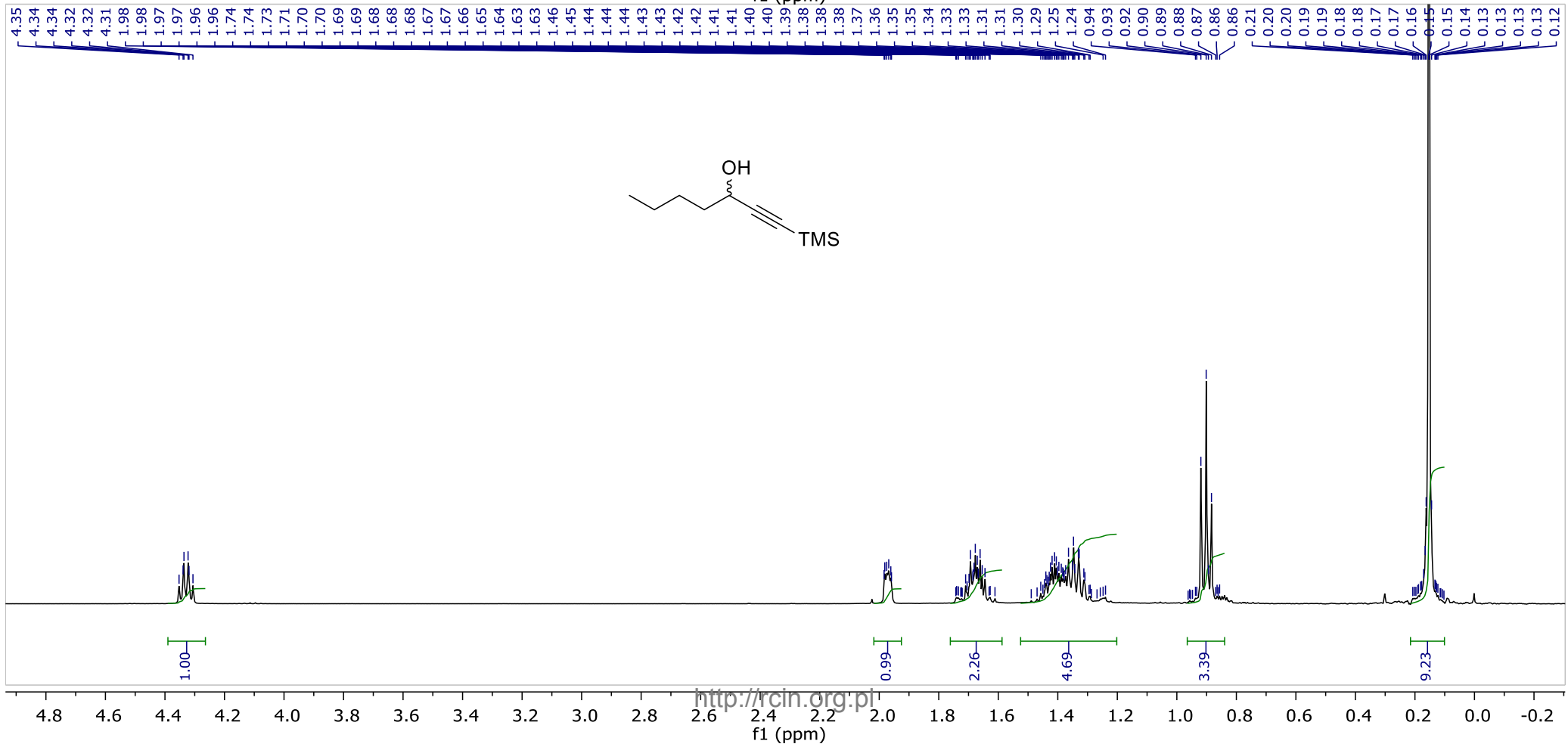
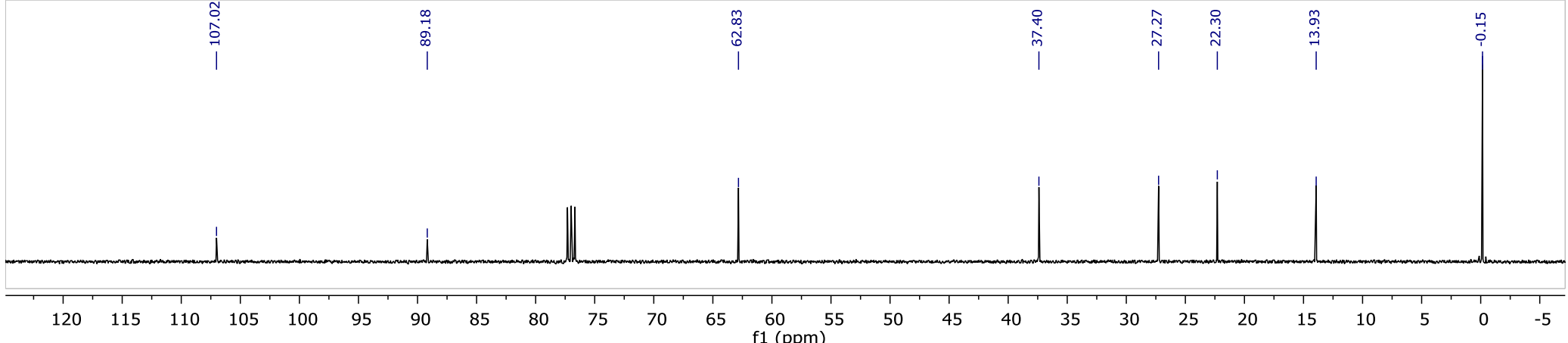


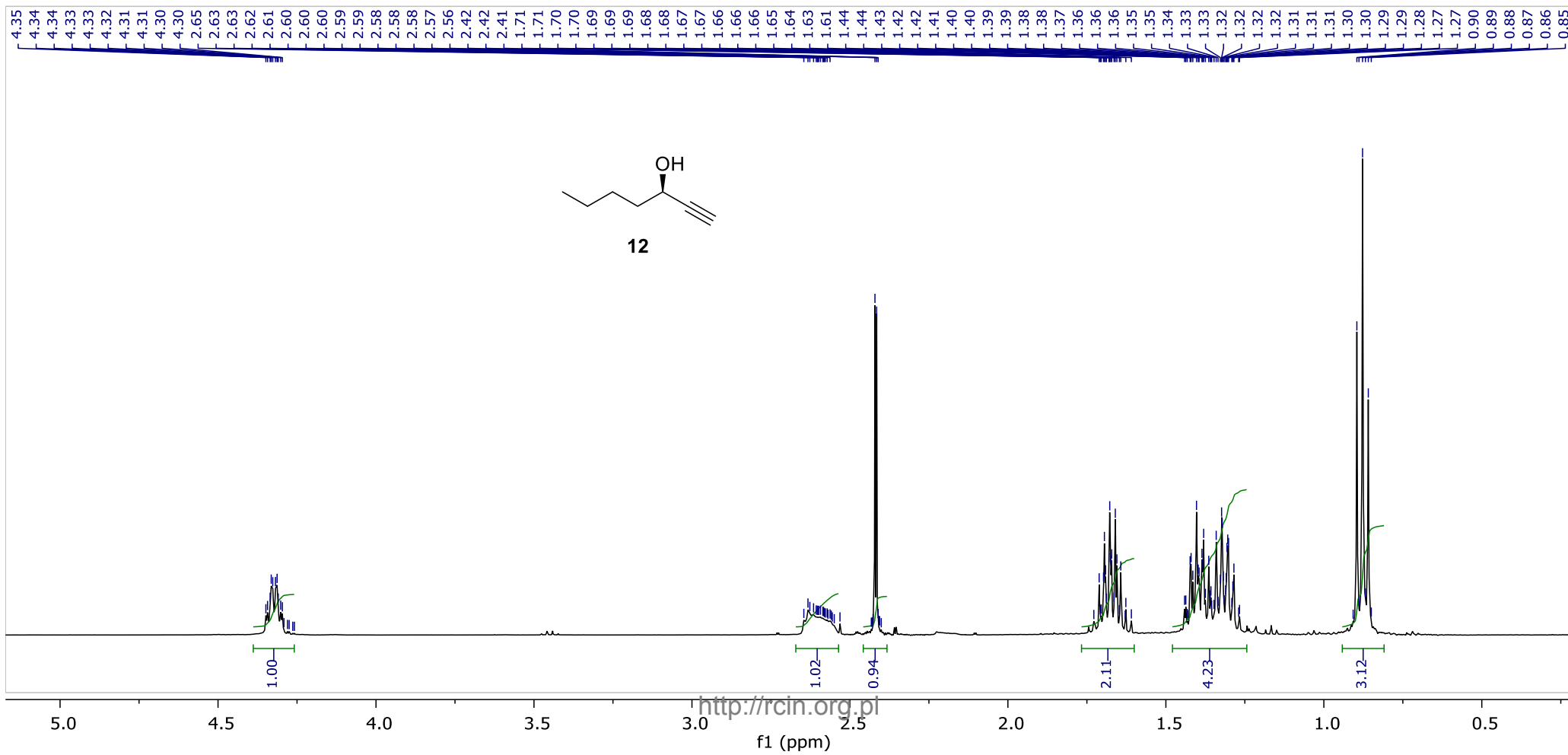
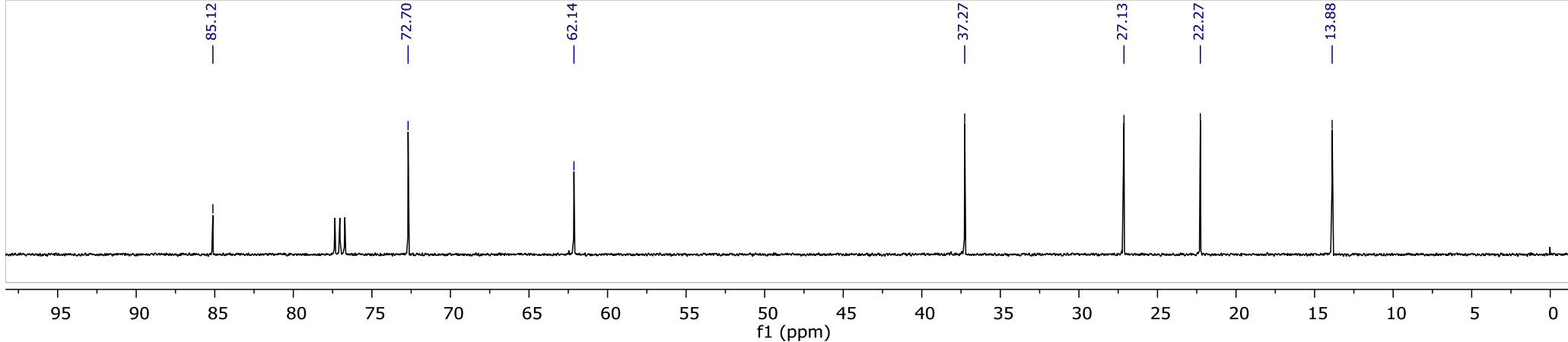






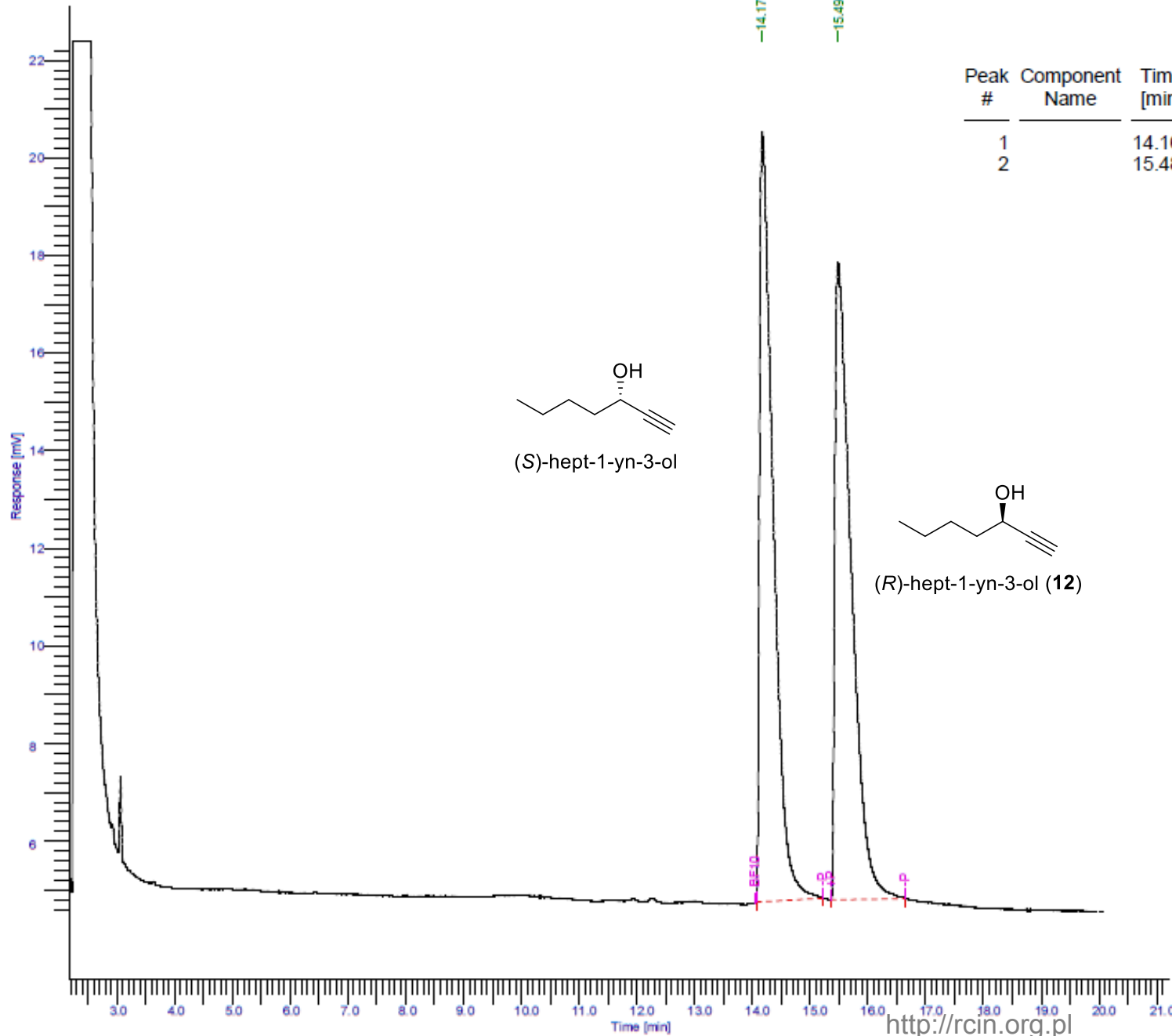






# DEFAULT REPORT

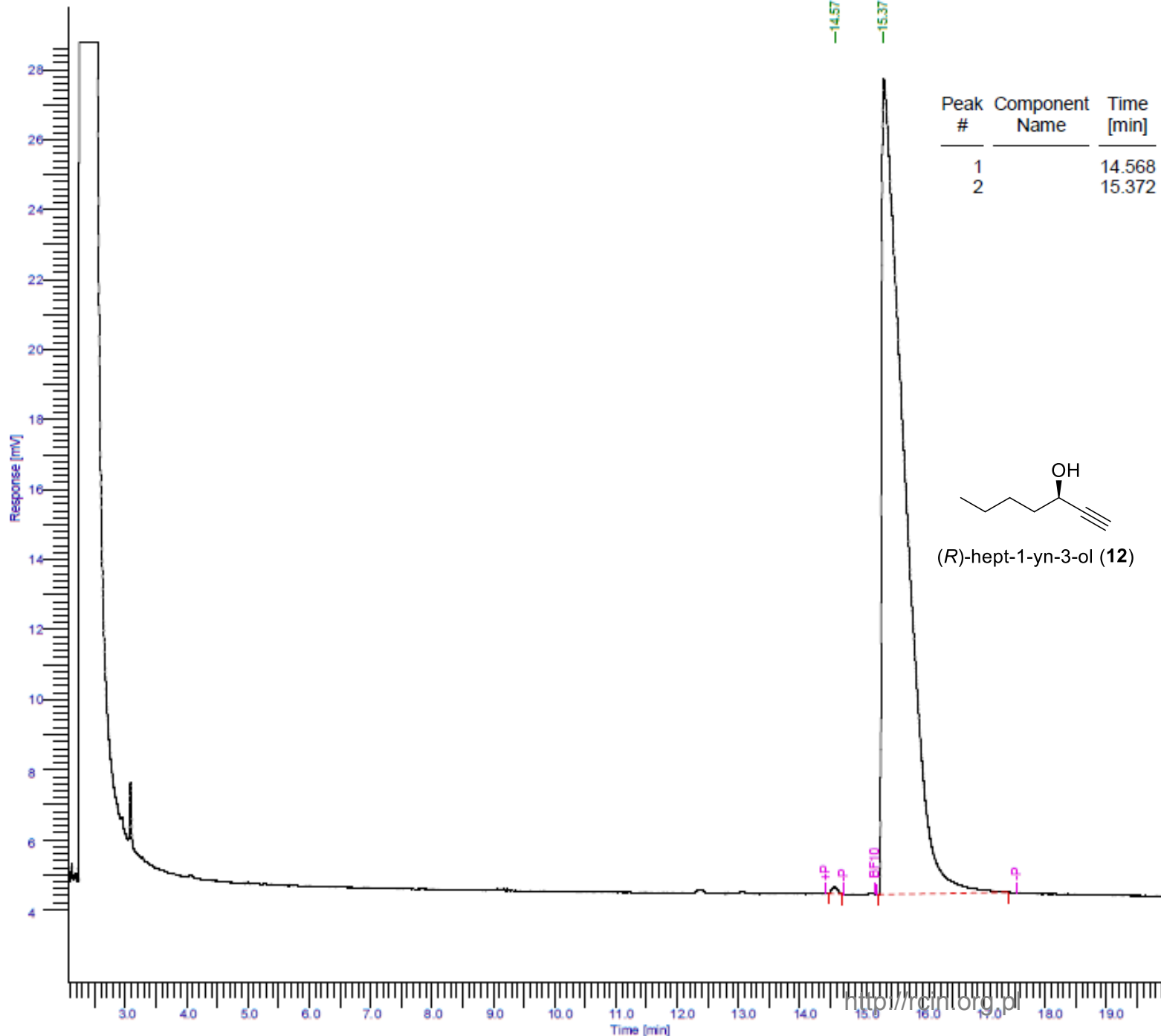
Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount	Adjusted Amount
1		14.169	258124.99	15779.42	50.06	50.06			+ *BB	-----	-----
2		15.486	257557.62	13051.53	49.94	49.94			*BB	0.2576	0.2576
			515682.61	28830.95	100.00	100.00				0.2576	0.2576



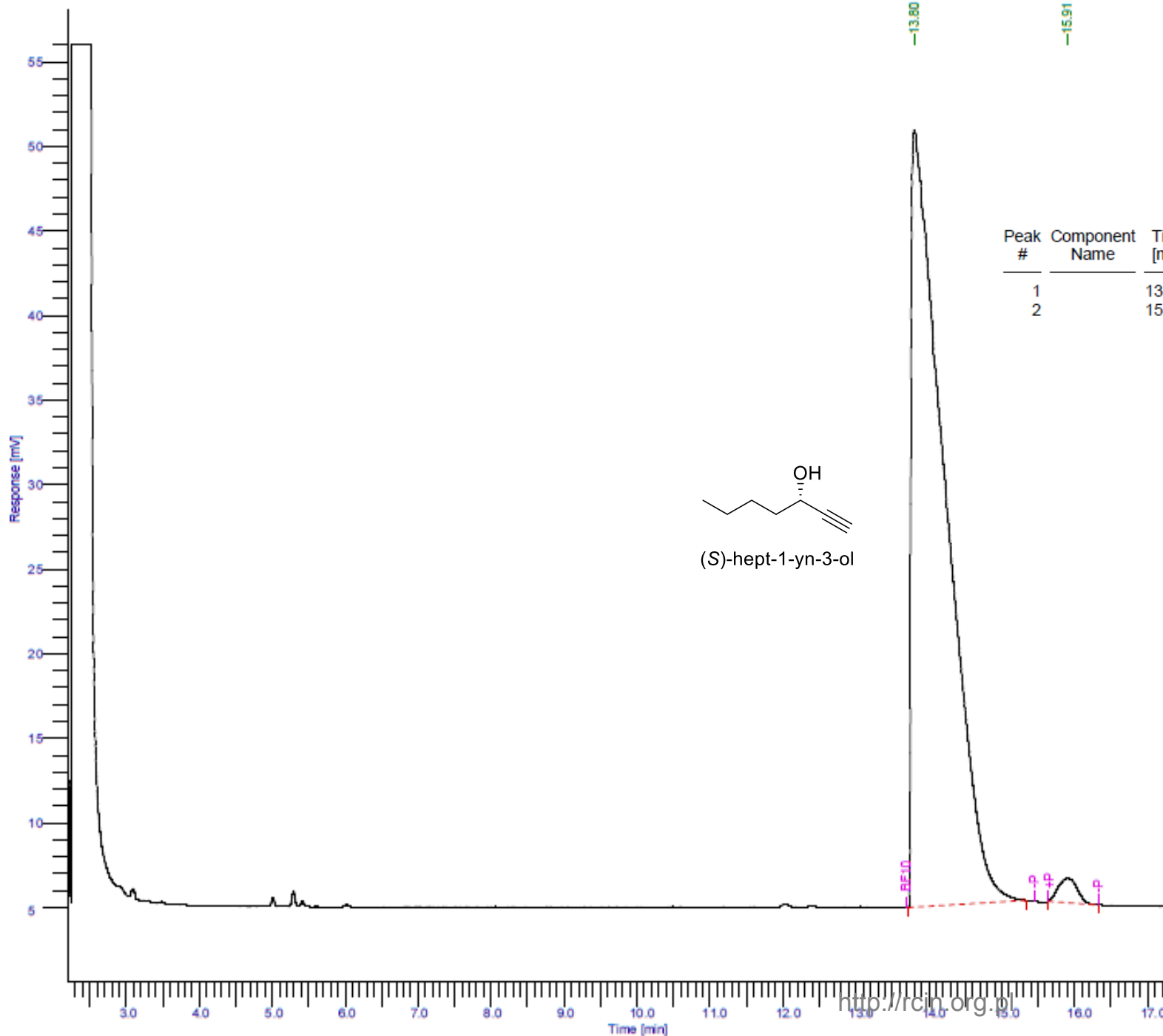
Column: Agilent Cyclosil-B  
(30m x 0.25 mm x 0.25  $\mu$ m)  
Injection temp.: 150  $^{\circ}$ C  
Detection temp.: 270  $^{\circ}$ C  
Oven temp: 90  $^{\circ}$ C (30 min),  
5 $^{\circ}$ C/min to 150 $^{\circ}$ , hold for 5.00 min

# DEFAULT REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount	Adjusted Amount
1		14.568	1201.46	186.97	0.20	0.20				BB 0.0012	0.0012
2		15.372	596664.39	23303.66	99.80	99.80				*BB 0.5967	0.5967
			597865.85	23490.62	100.00	100.00				0.5979	0.5979



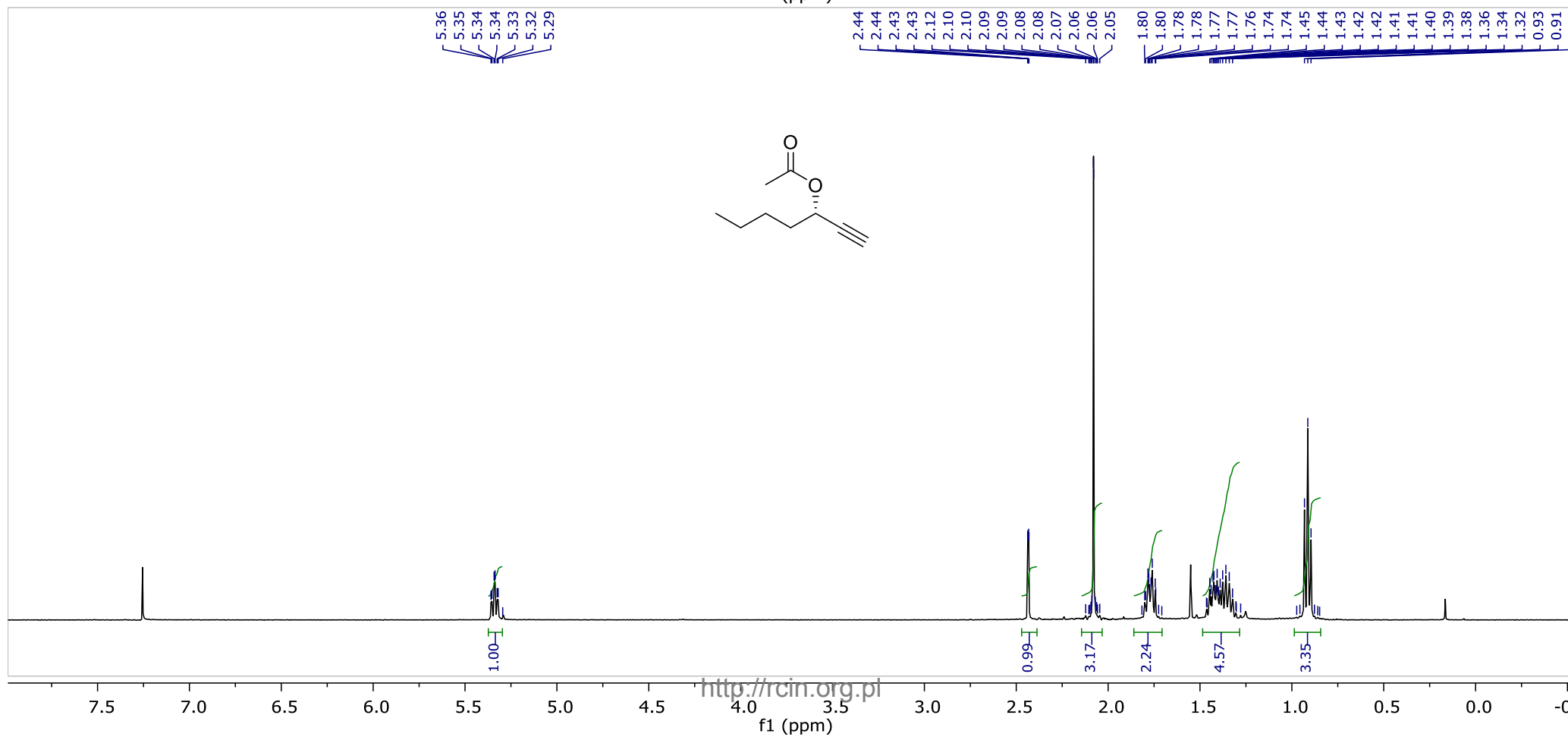
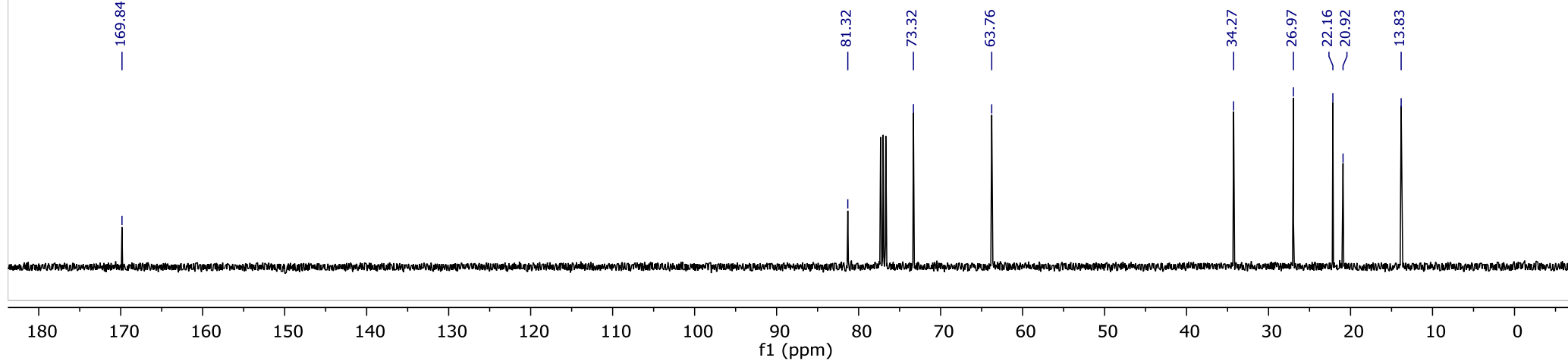
Column: Agilent Cyclosil-B  
(30m x 0.25 mm x 0.25  $\mu$ m)  
Injection temp.: 150 °C  
Detection temp.: 270 °C  
Oven temp: 90 °C (30 min),  
5°C/min to 150°, hold for 5.00 min

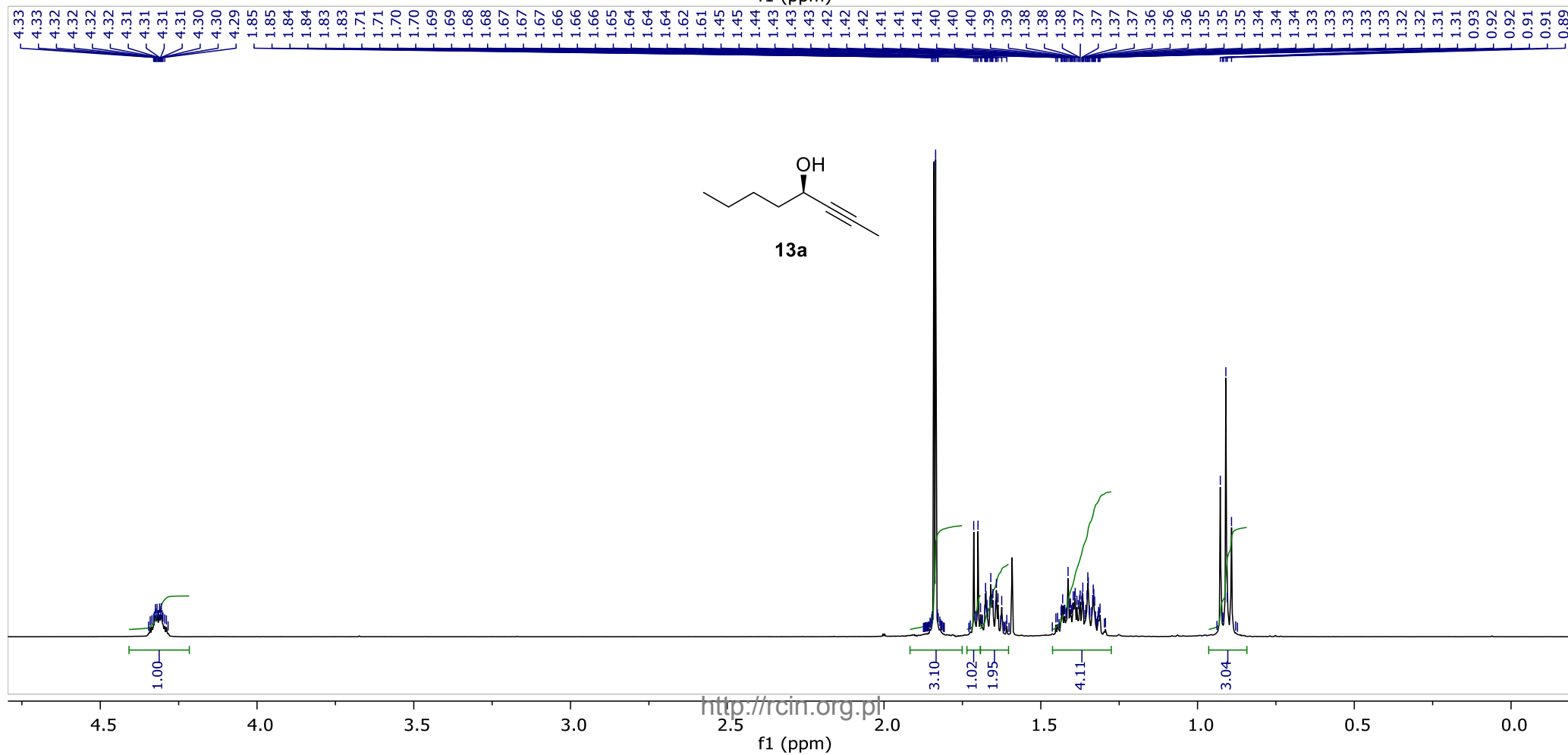
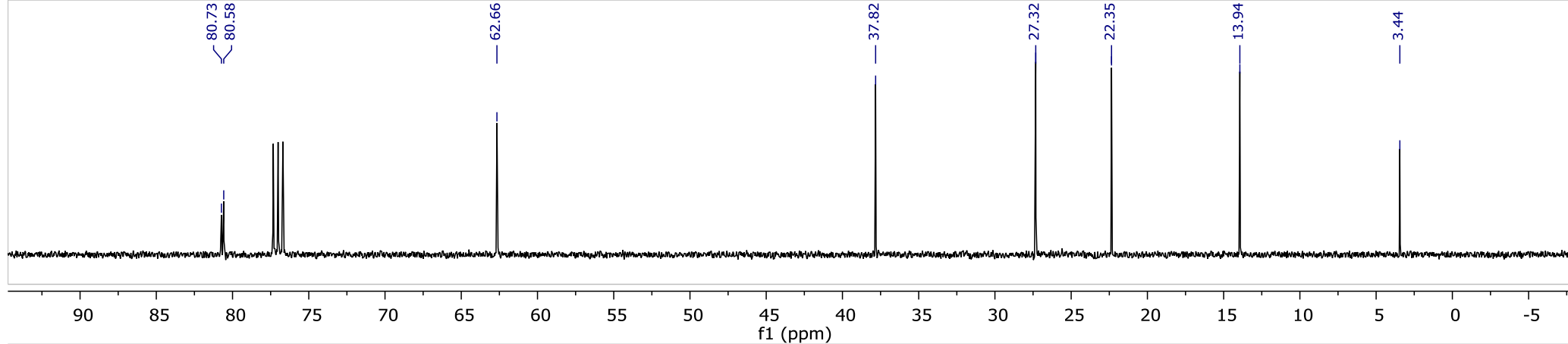


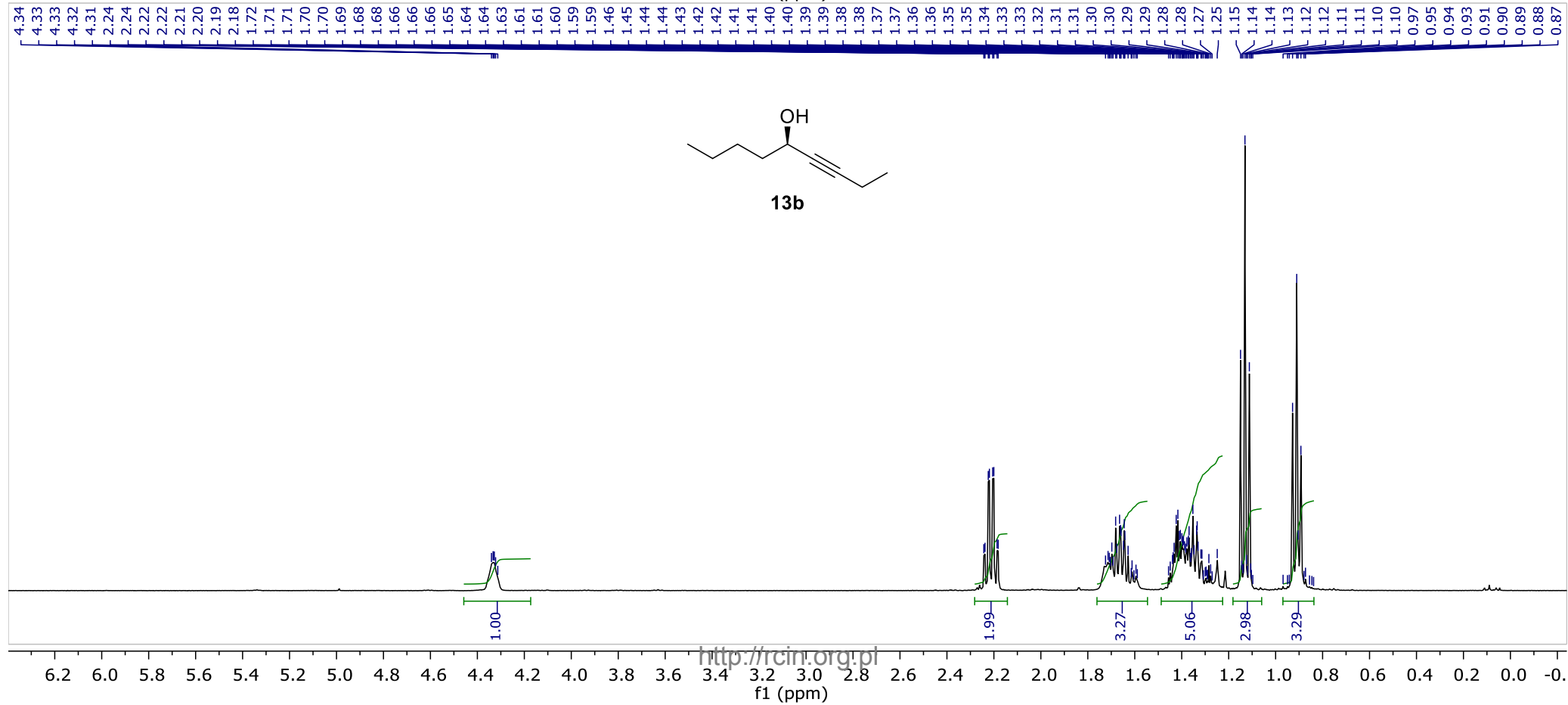
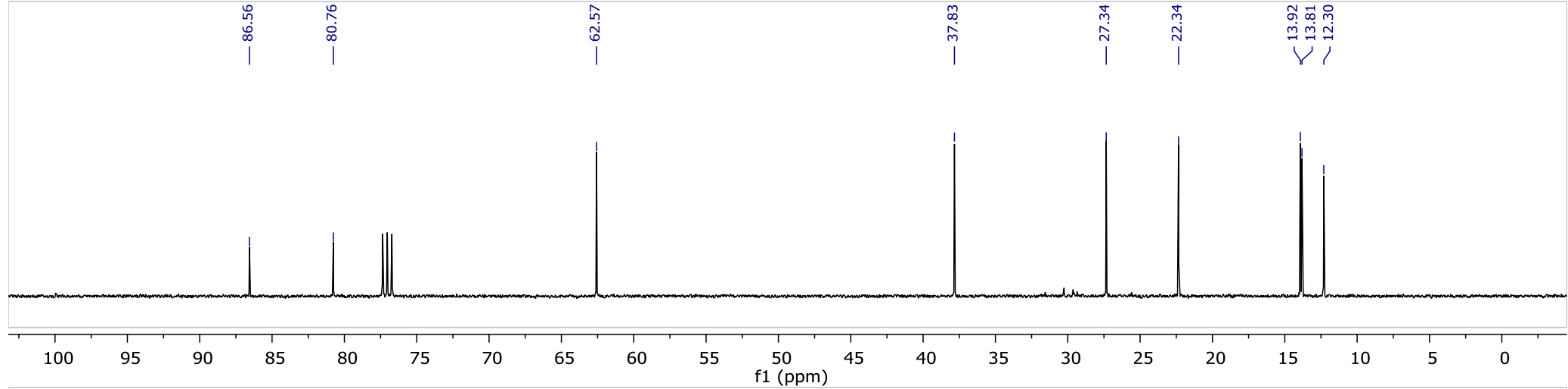
## DEFAULT REPORT

Peak #	Component Name	Time [min]	Area [uV*sec]	Height [uV]	Area [%]	Norm. Area [%]	Cal. Range	Volt Range	BL	Raw Amount	Adjusted Amount
1		13.802	1465400.63	45968.97	98.25	98.25			*BB	1.4654	1.4654
2		15.908	26135.29	1449.19	1.75	1.75			*BB	0.0261	0.0261
			1491535.92	47418.16	100.00	100.00				1.4915	1.4915

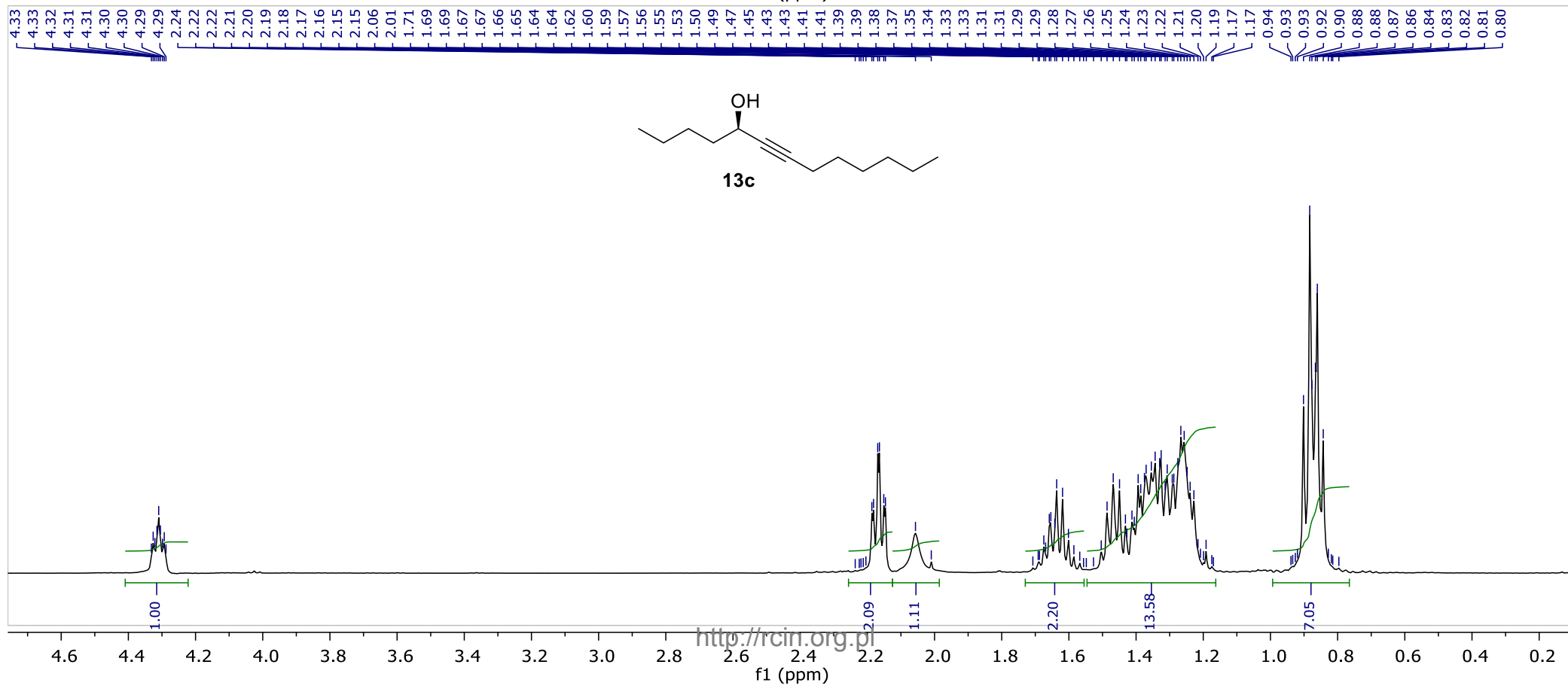
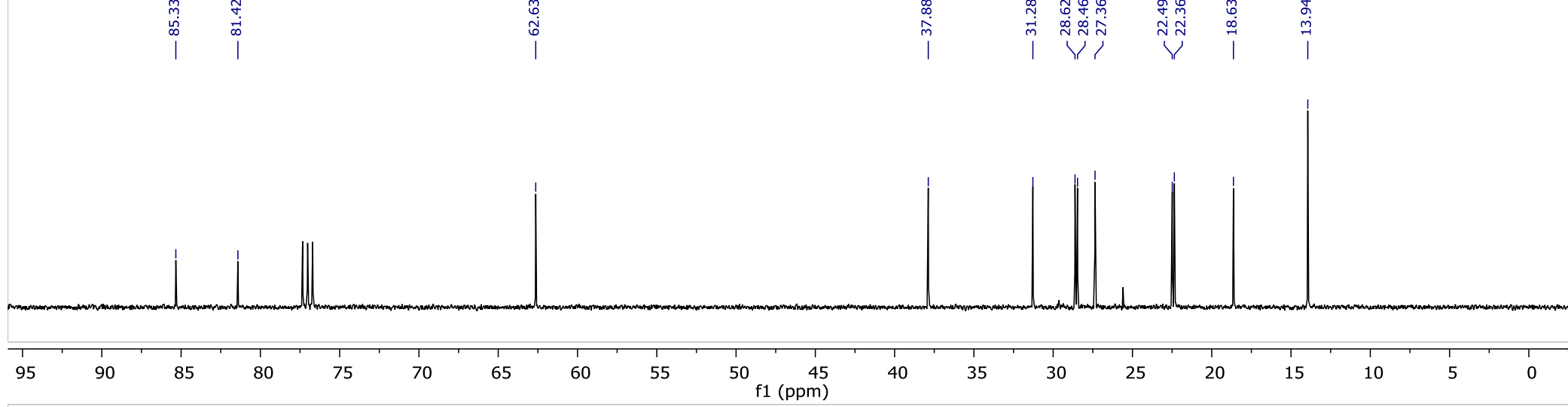
Column: Agilent Cyclosil-B  
 (30m x 0.25 mm x 0.25  $\mu$ m)  
 Injection temp.: 150 °C  
 Detection temp.: 270 °C  
 Oven temp: 90 °C (30 min),  
 5°C/min to 150°, hold for 5.00 min

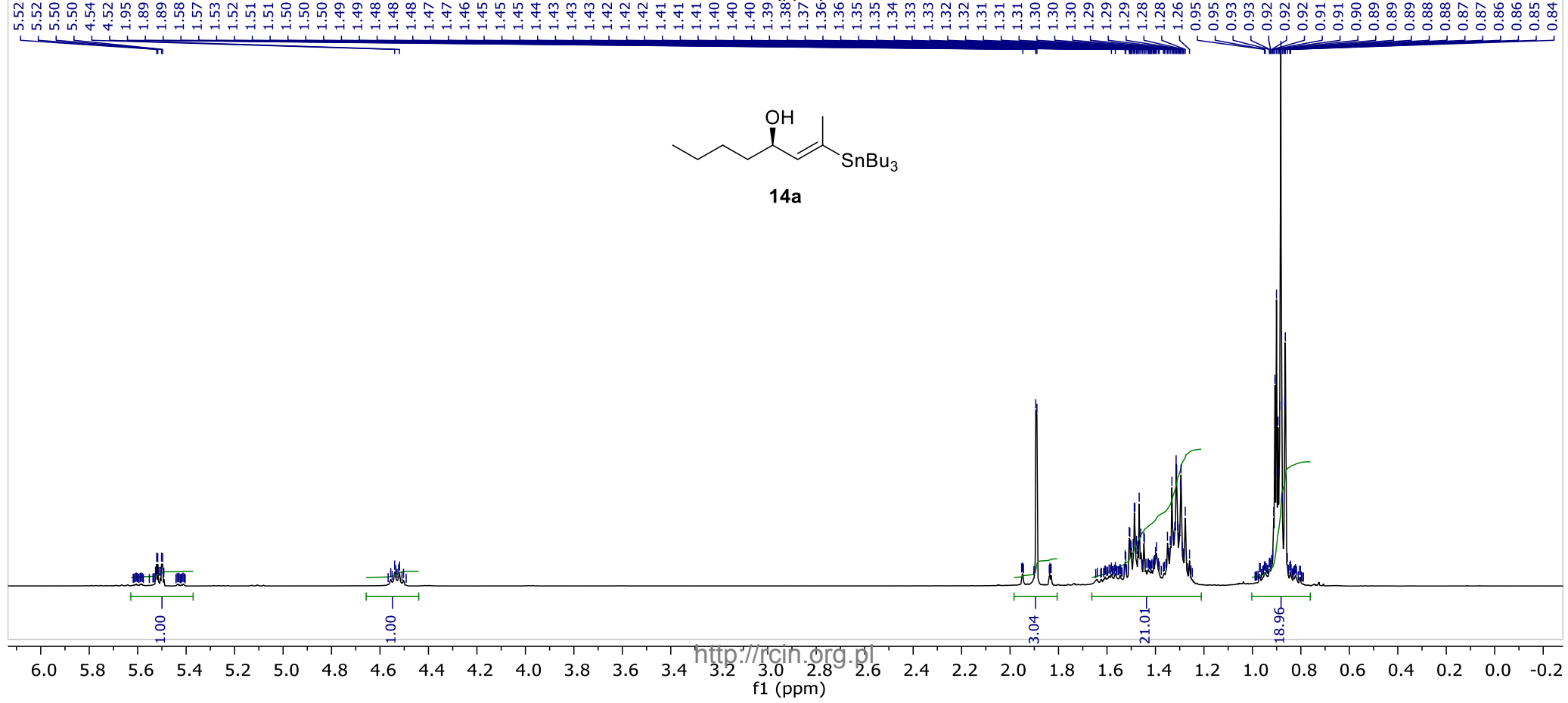
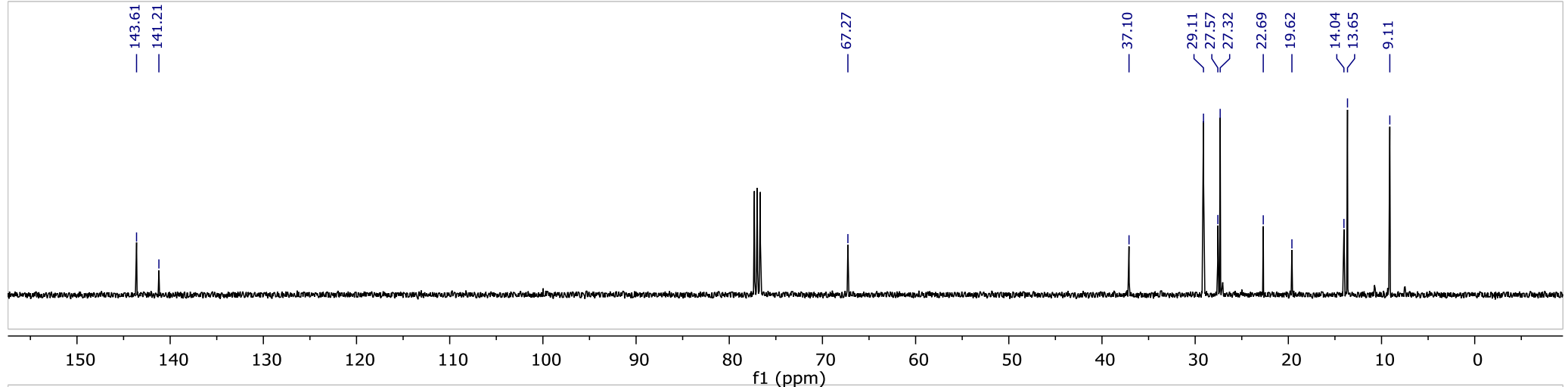


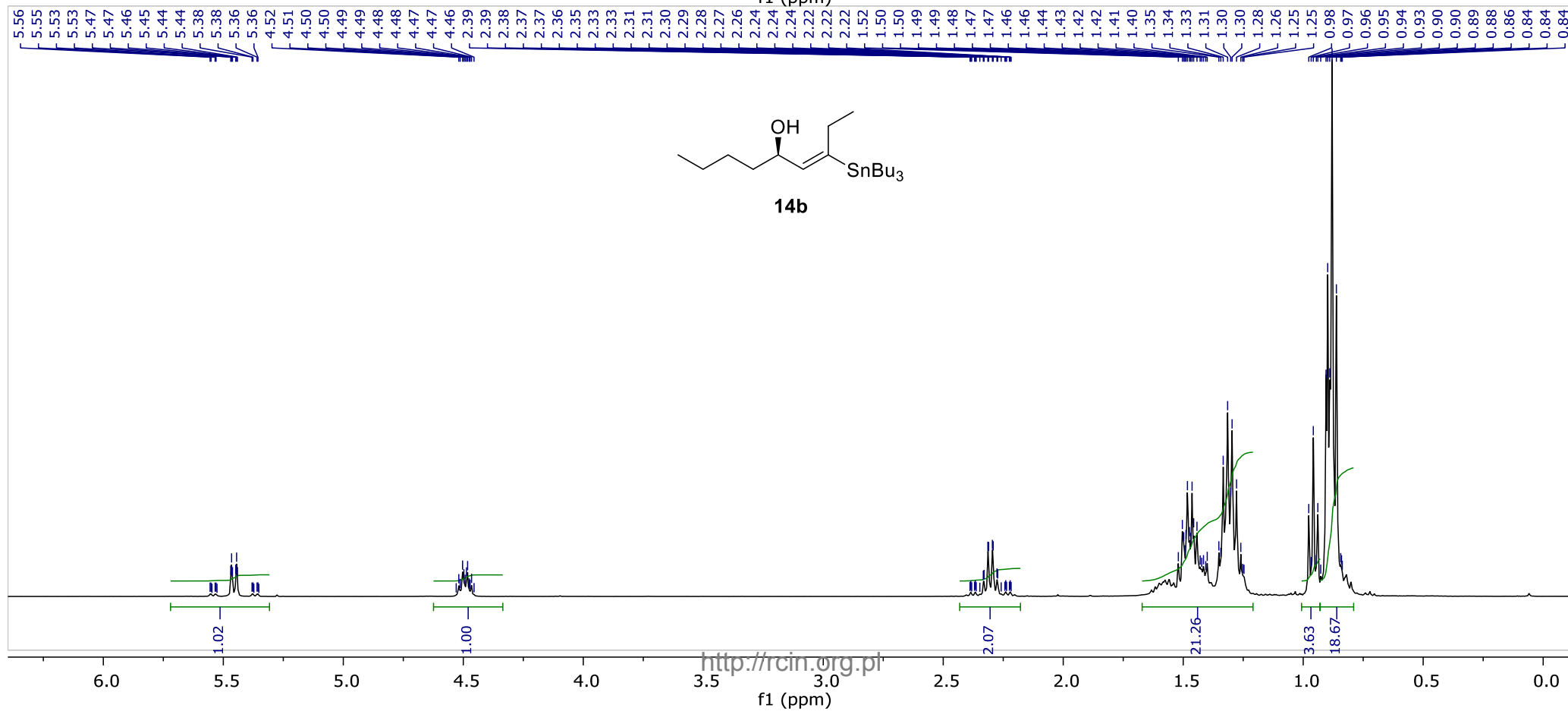
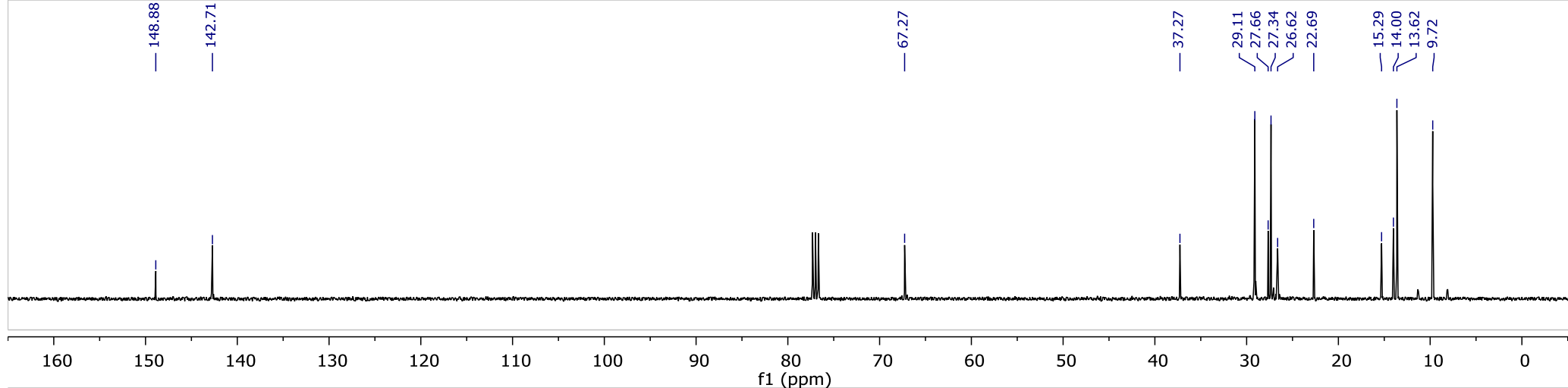


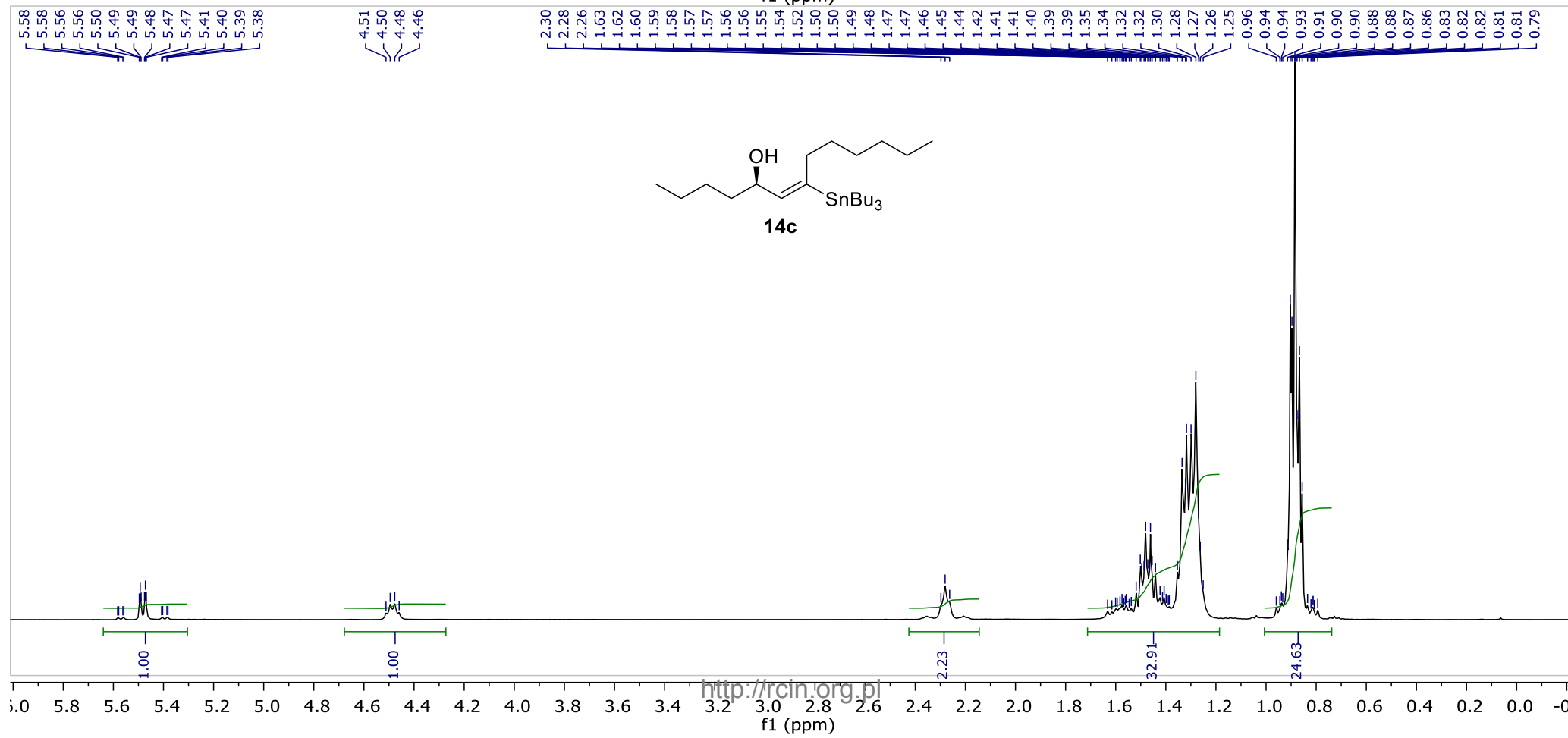
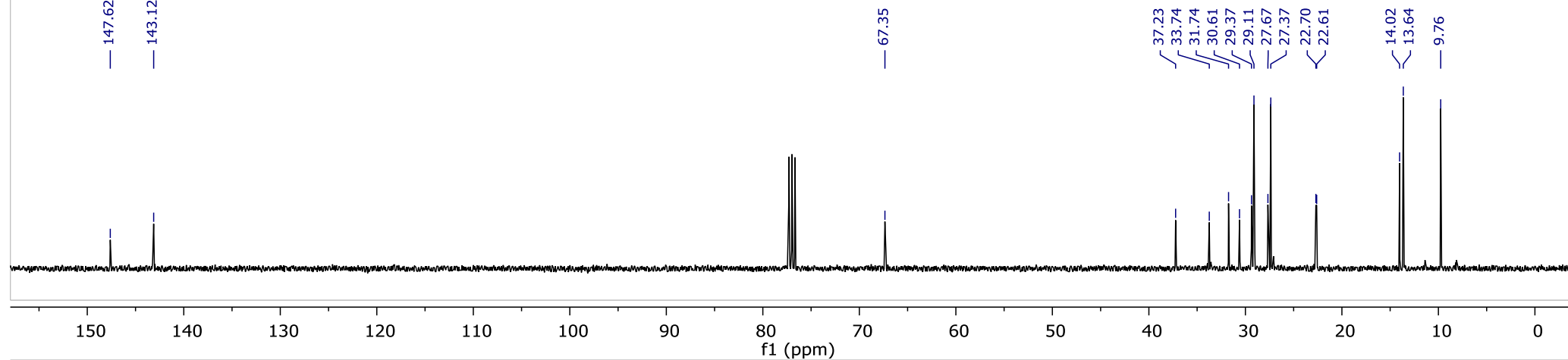


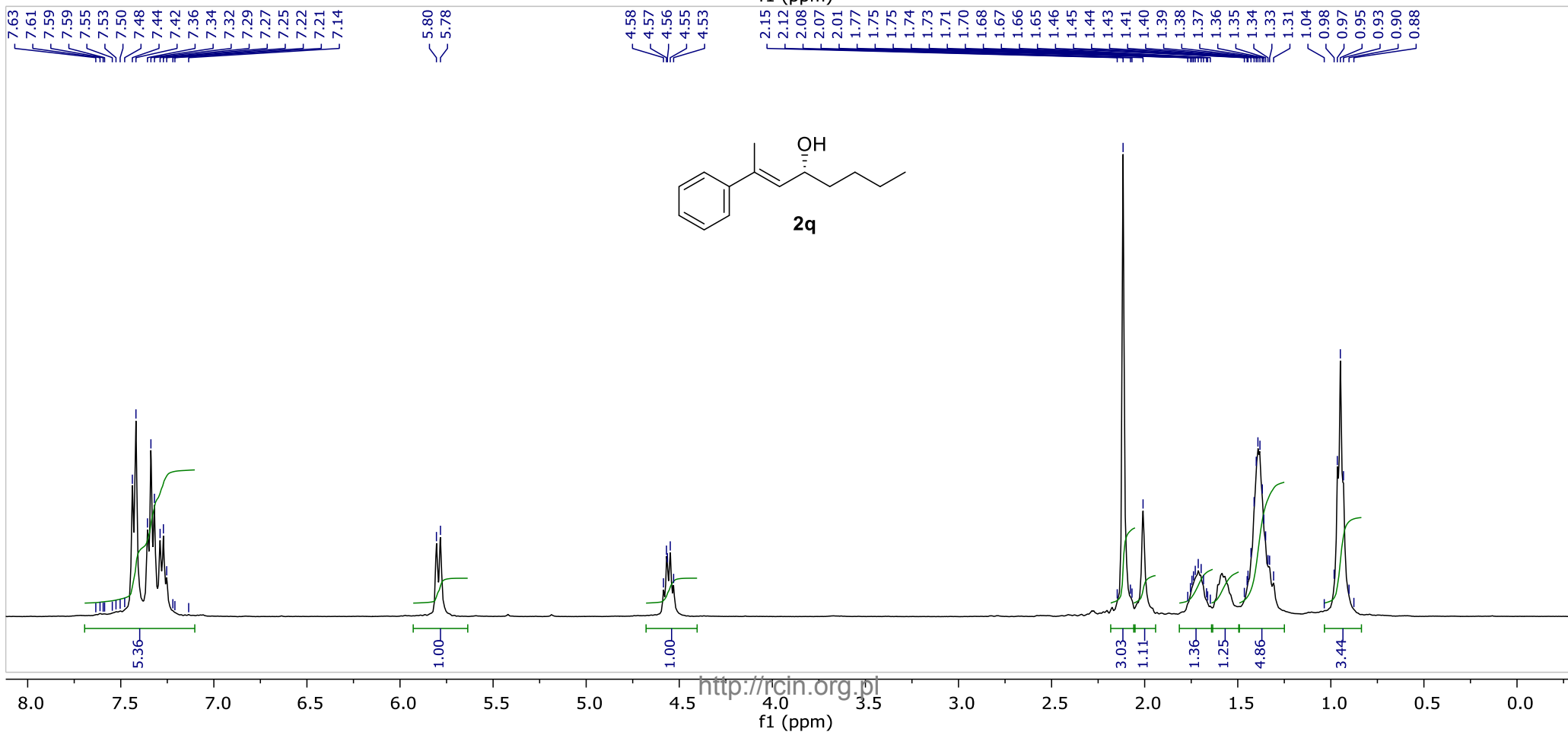
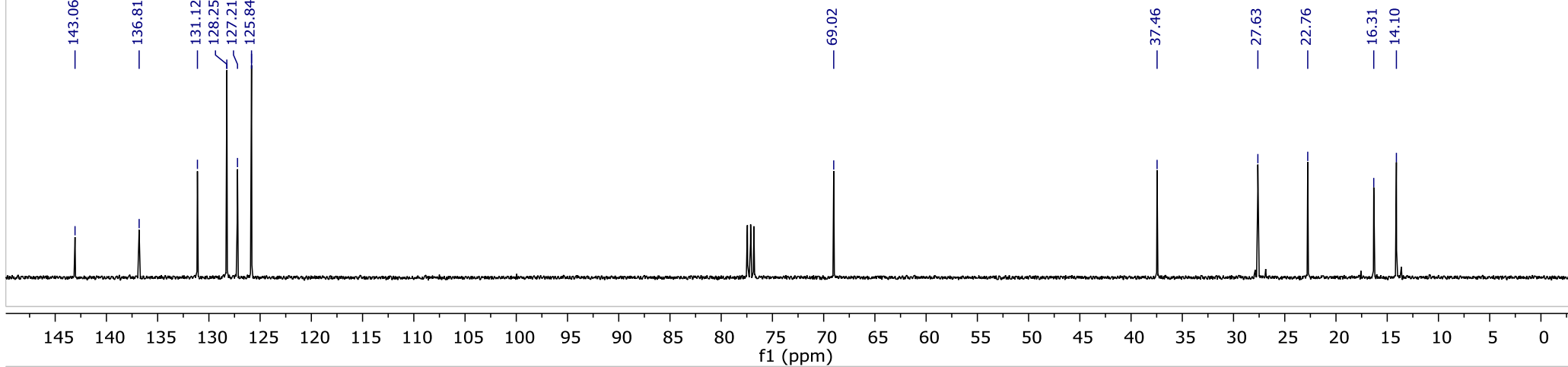






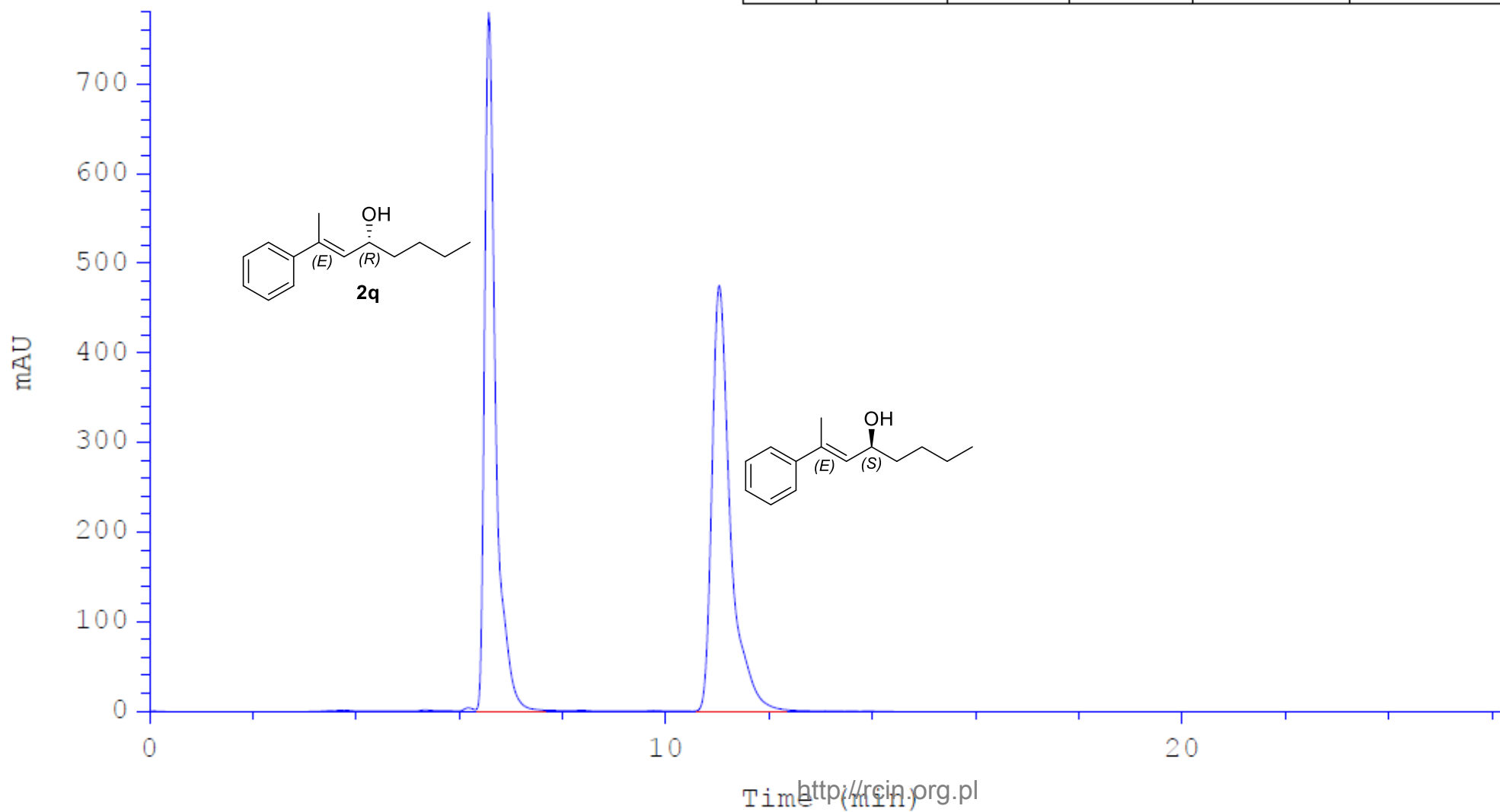






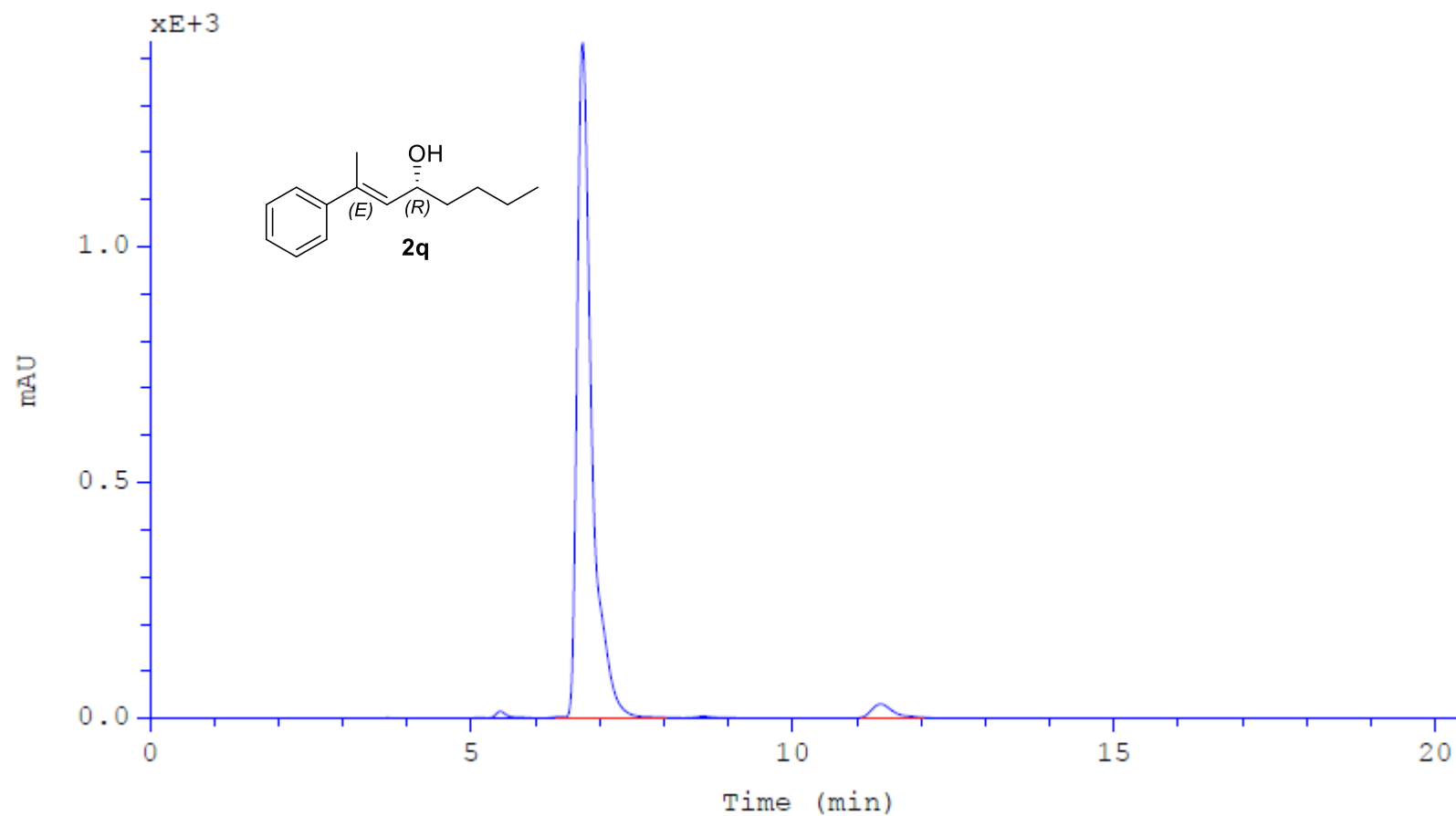
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

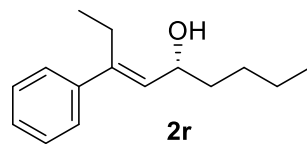
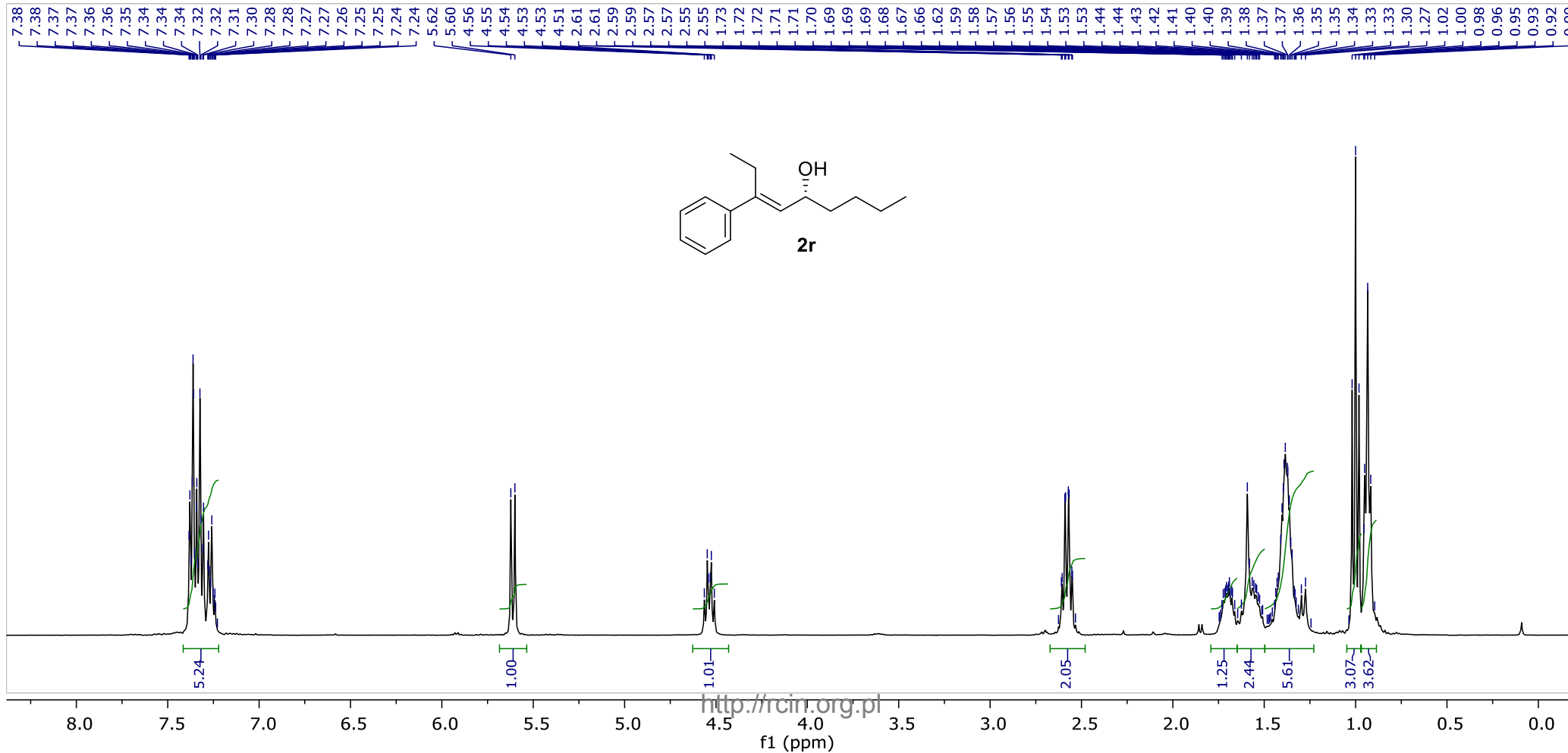
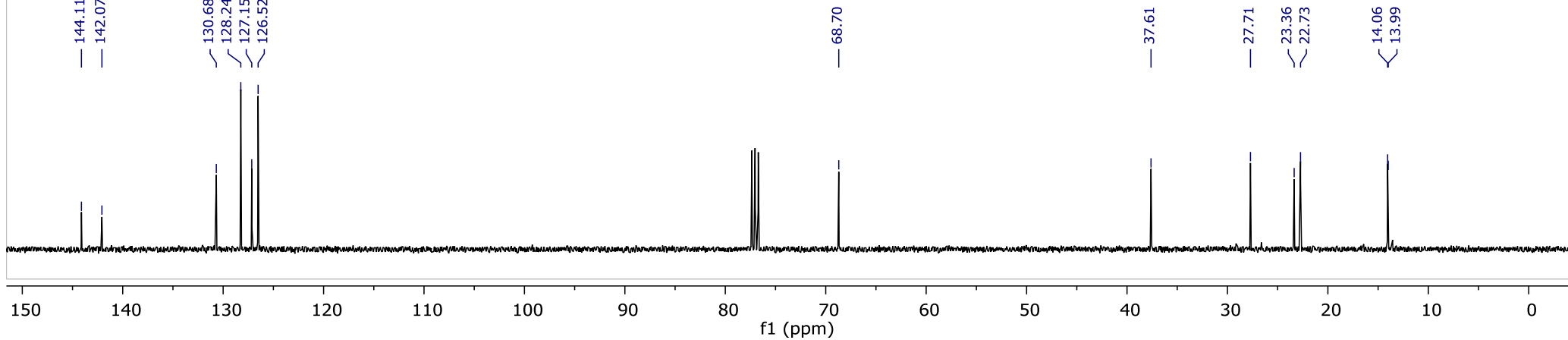
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.569	6.32	7.52	191.925	777.776	49.6627	0.205
2	11.037	10.58	12.28	194.532	474.402	50.3373	0.343



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.737	6.24	8.08	376.616	1431.04	97.0847	0.217
2	11.373	11.03	12.09	11.309	29.3863	2.9153	0.337

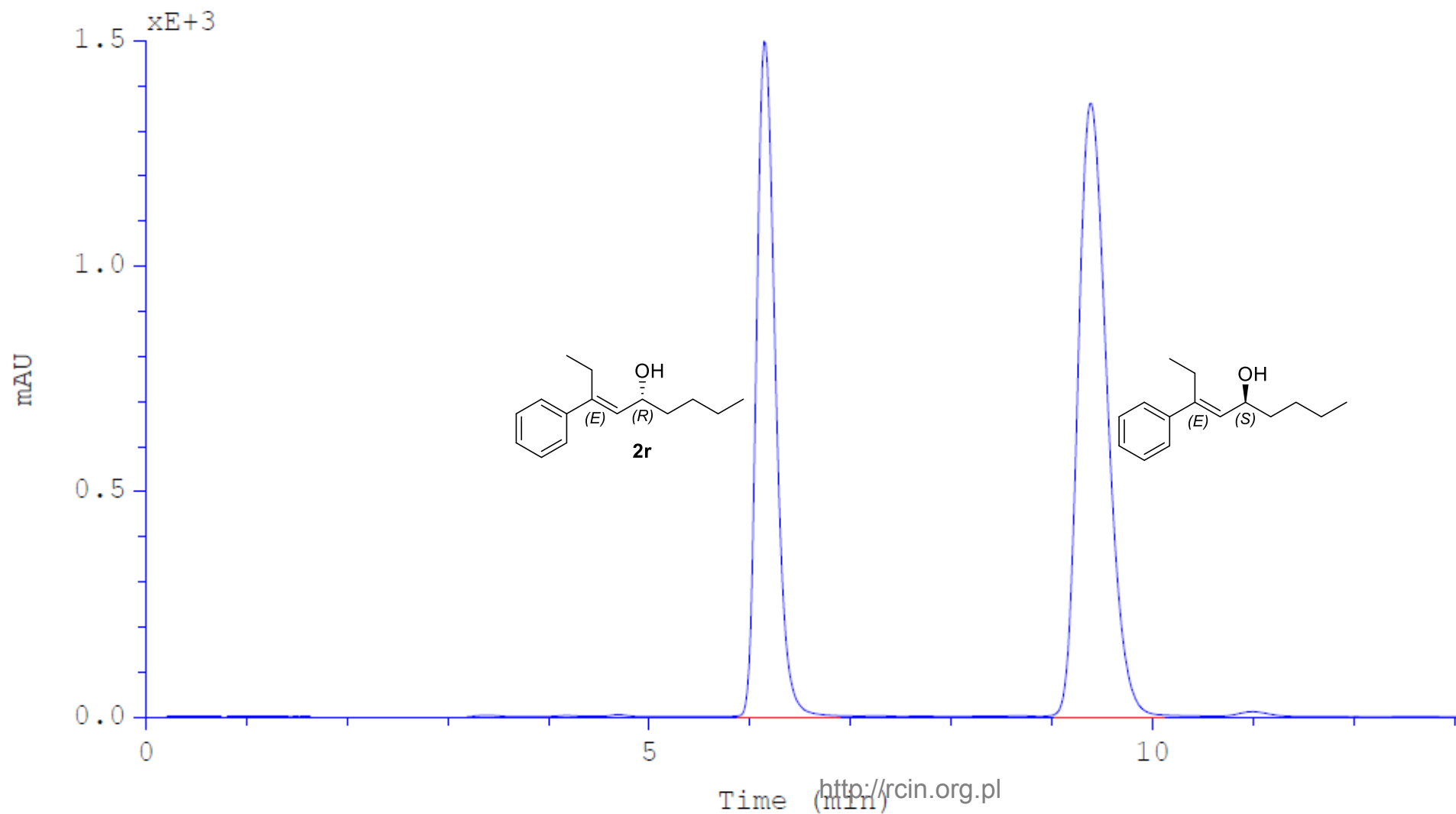






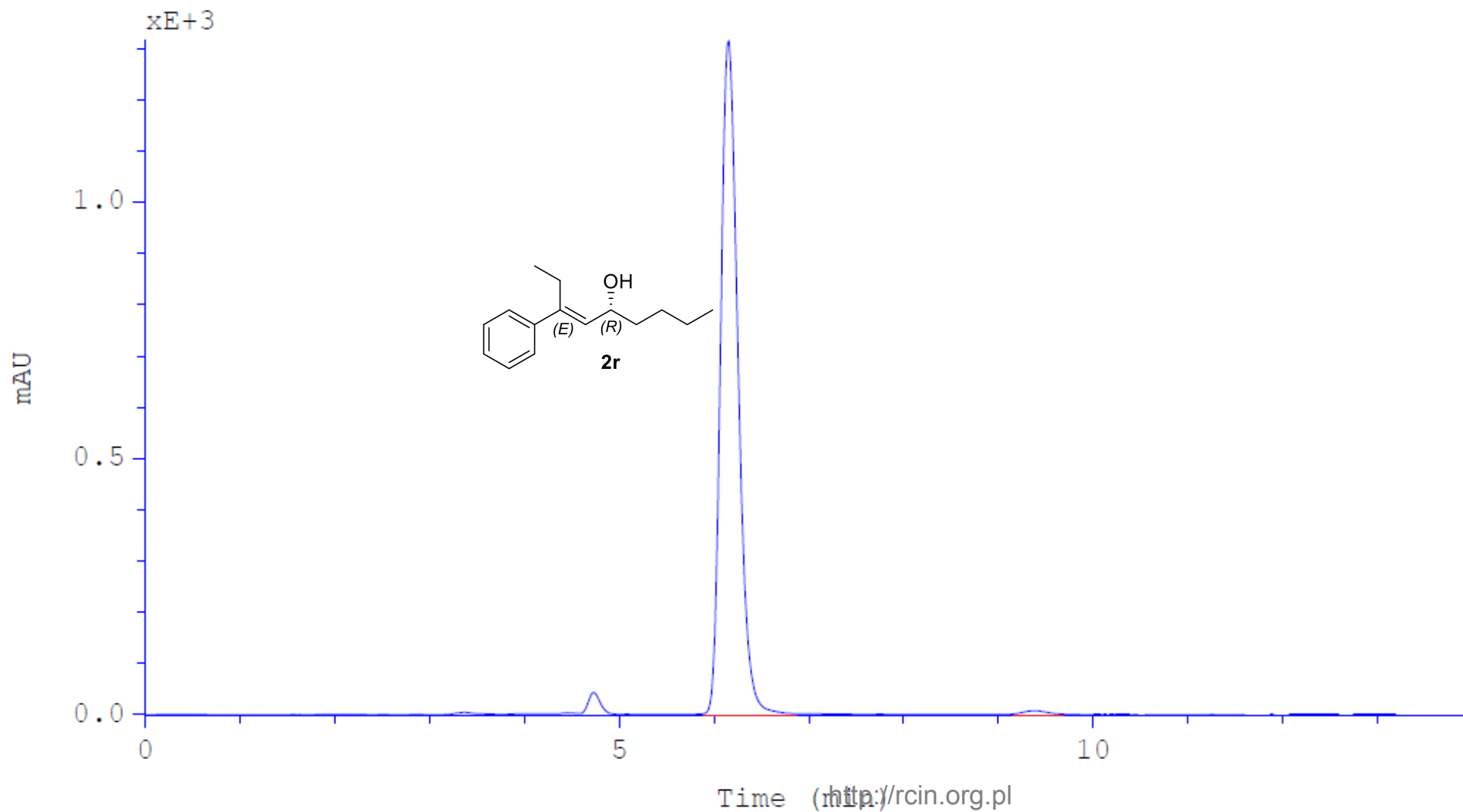
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

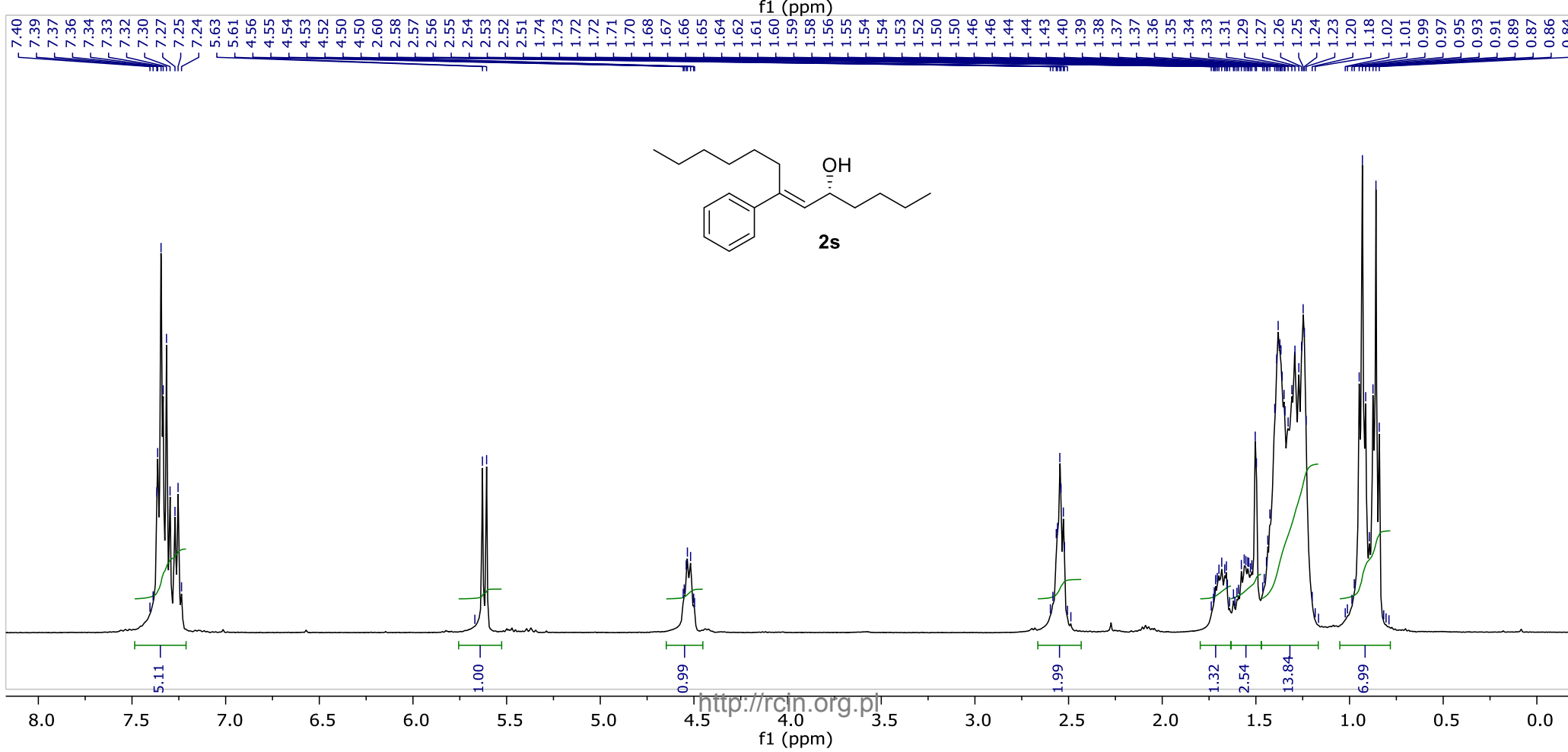
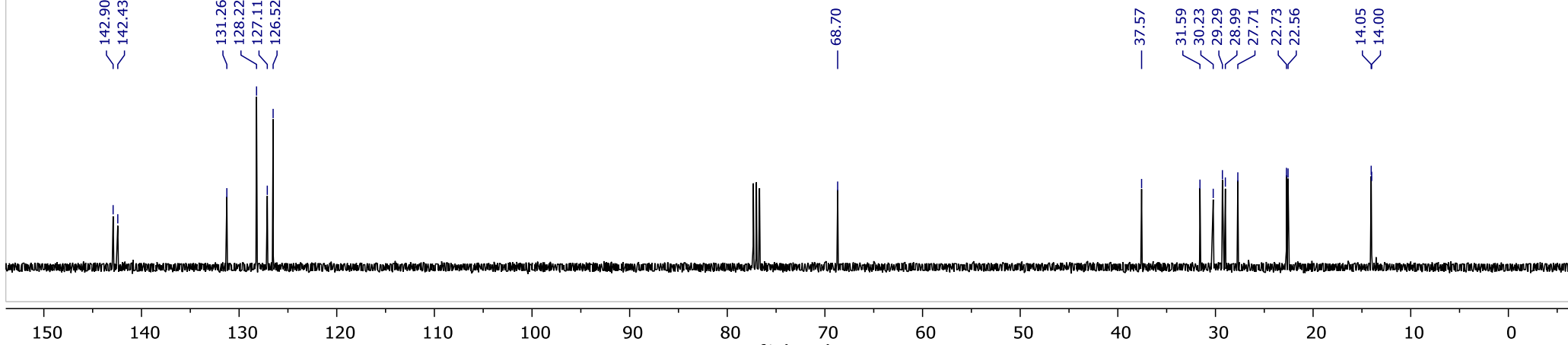
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.140	5.90	6.72	321.278	1494.72	41.6499	0.199
2	9.394	9.02	10.07	450.1	1357.15	58.3501	0.309



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

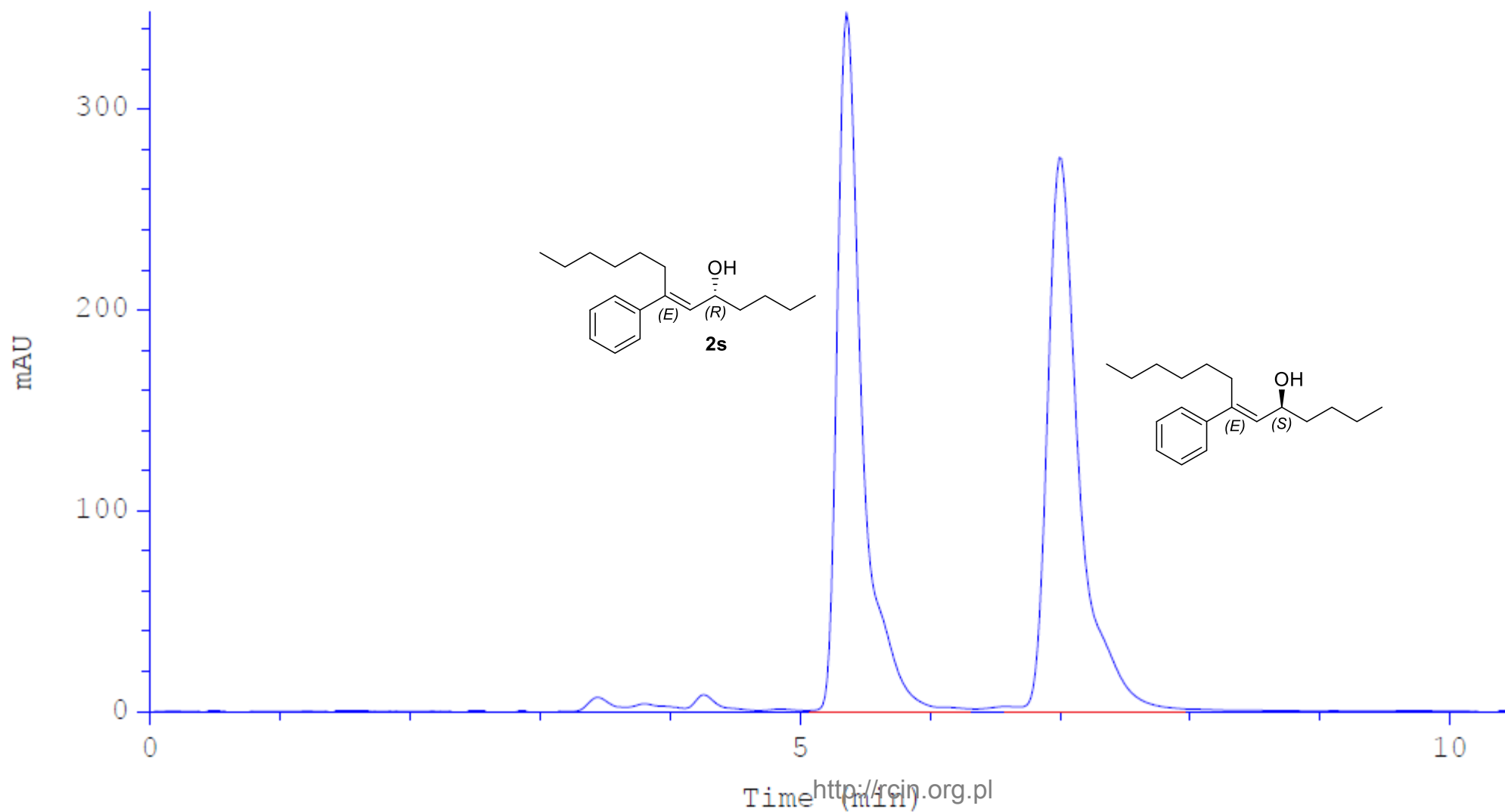
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.156	5.88	6.75	276.973	1313.17	99.6549	0.195
2	9.376	9.23	9.58	0.959164	4.65585	0.3451	0.200





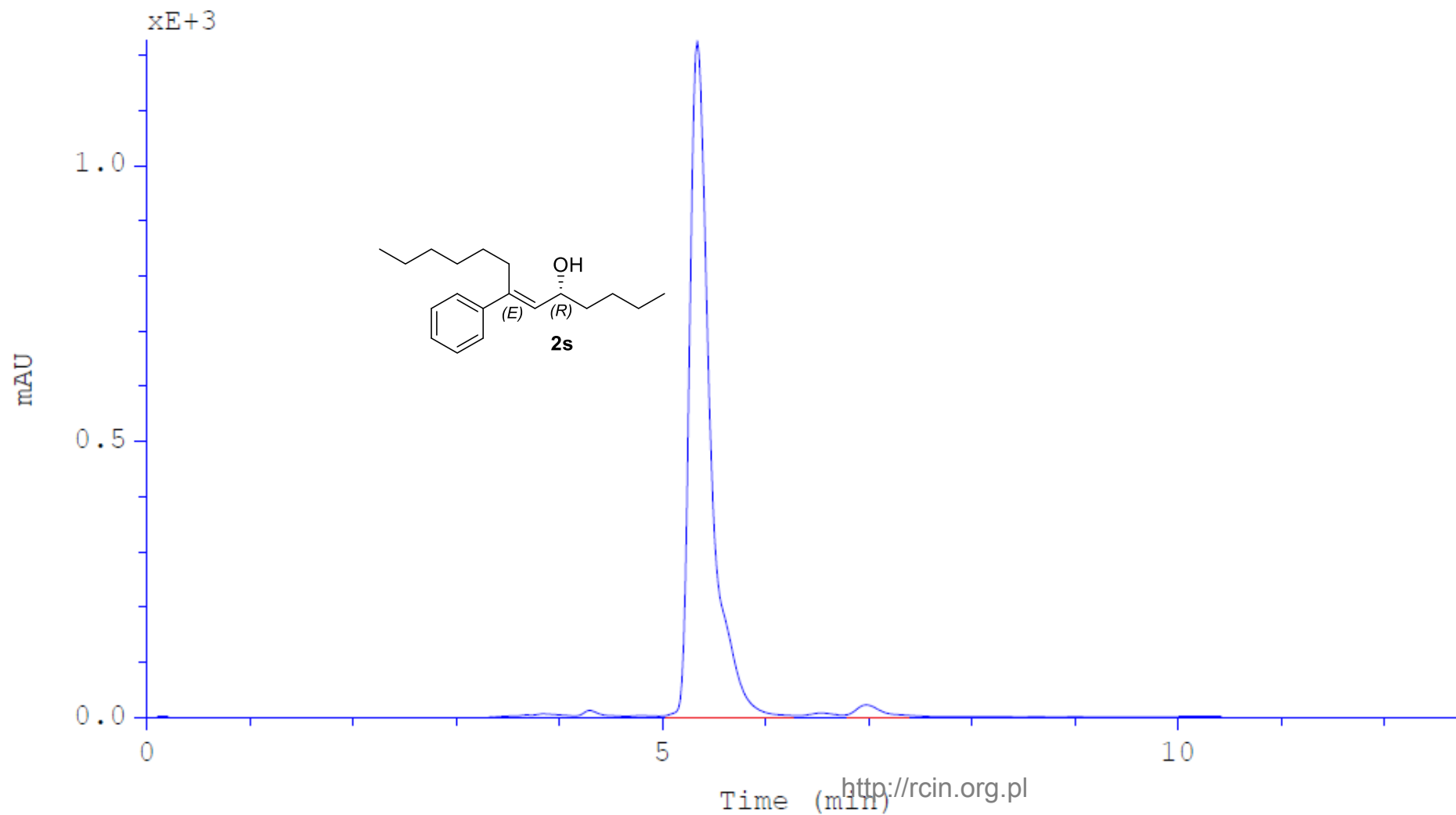
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

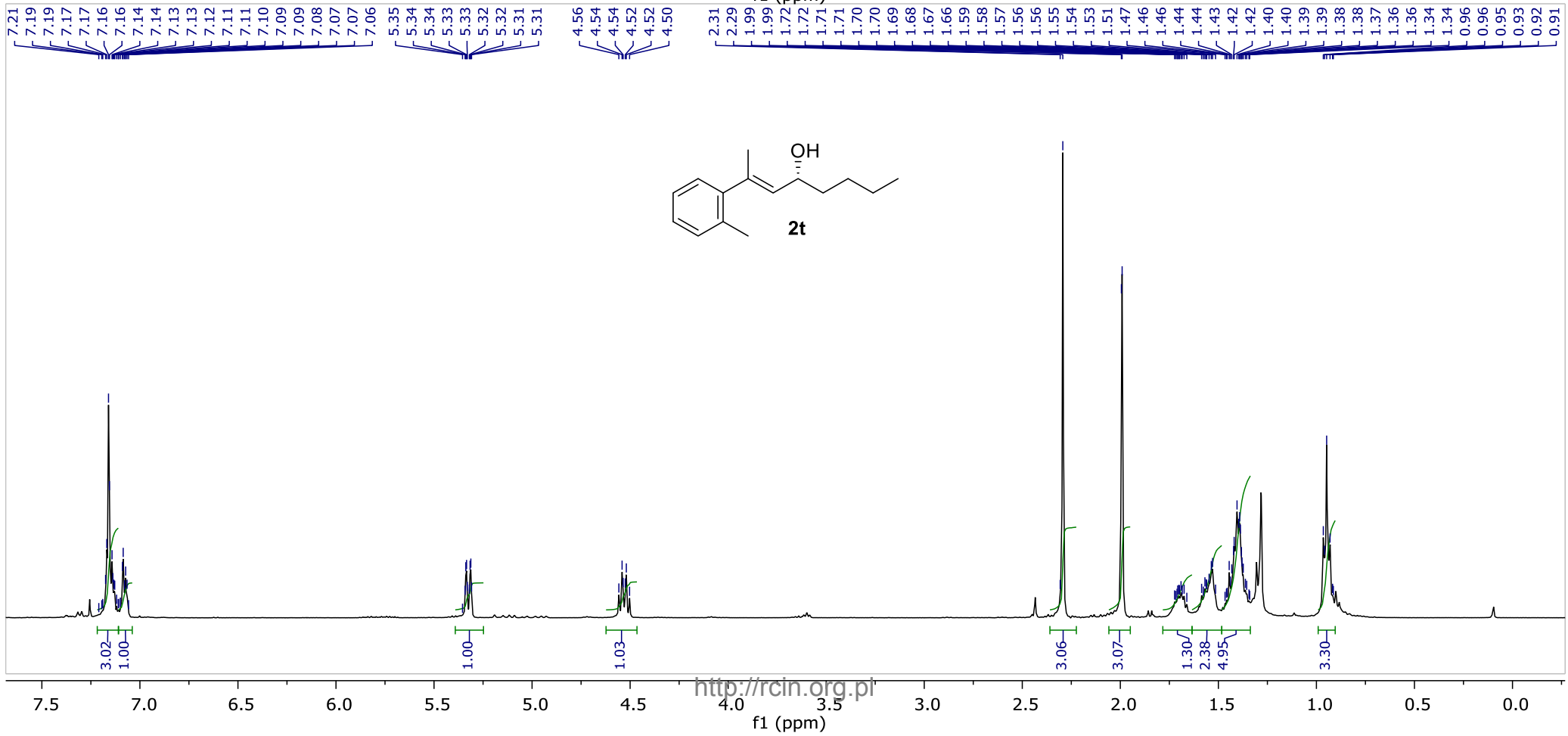
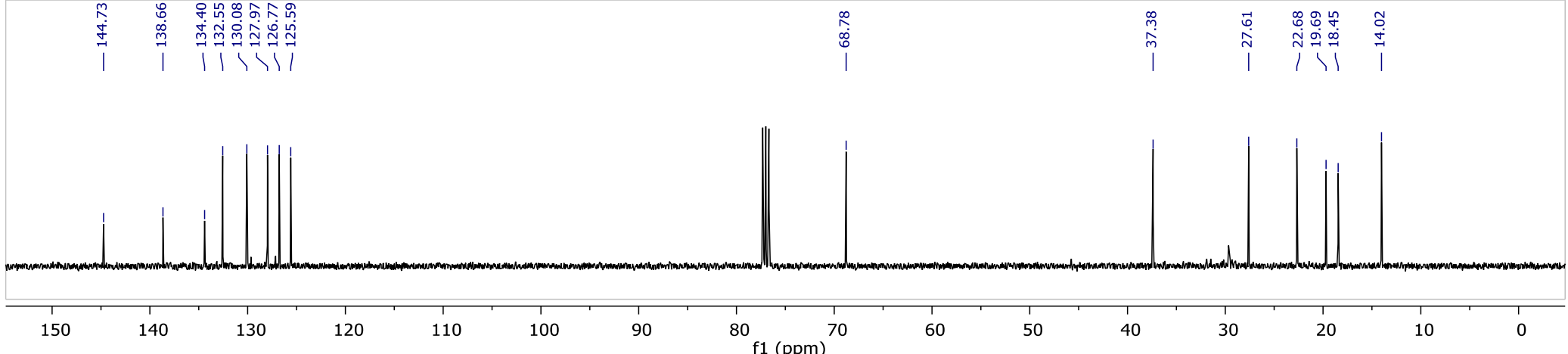
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.357	5.12	6.28	76.3848	347.354	49.9300	0.180
2	6.993	6.42	7.94	76.599	274.639	50.0700	0.232



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

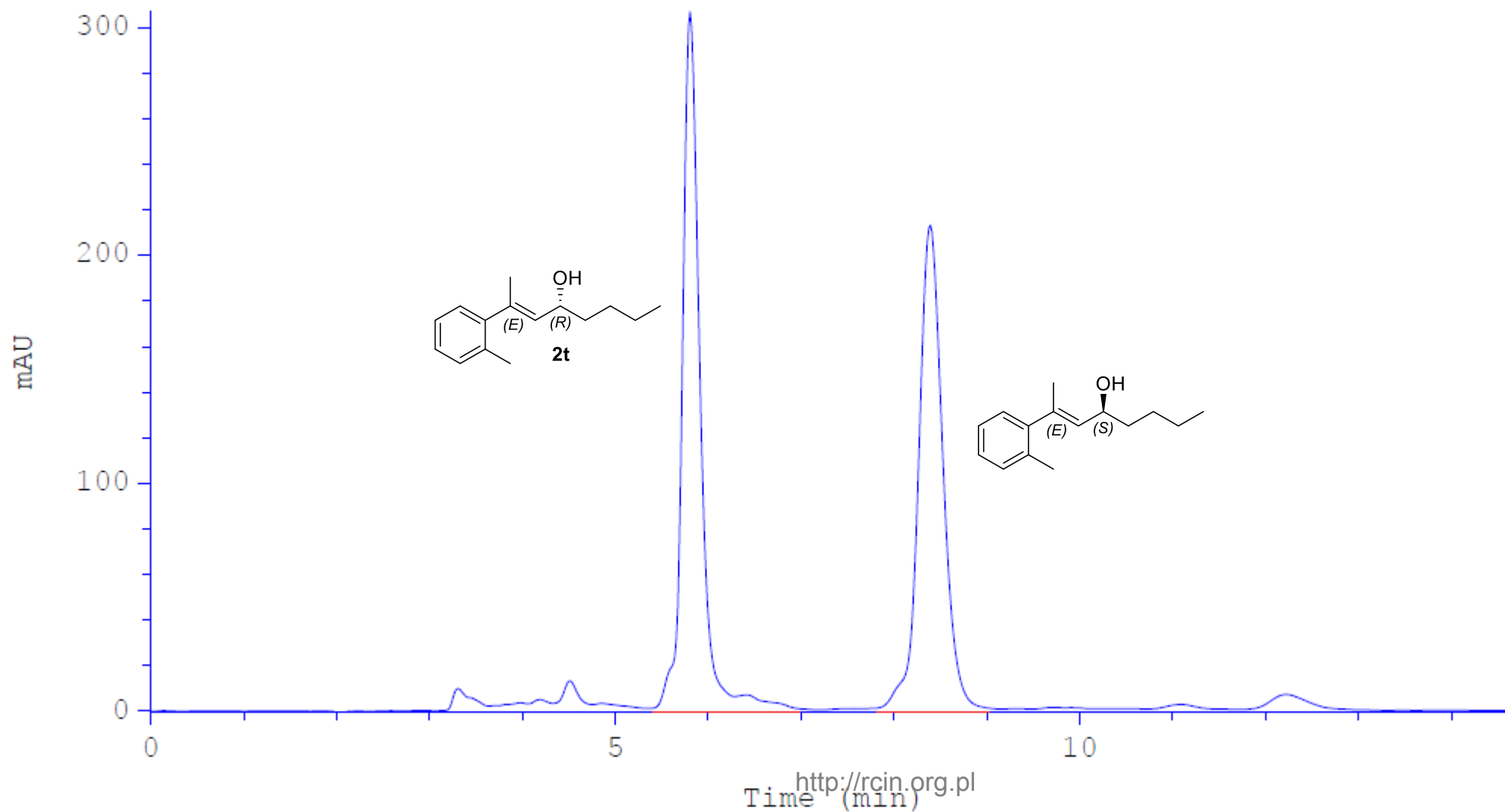
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.339	5.05	6.22	281.65	1222.52	98.5749	0.192
2	6.974	6.80	7.37	4.07188	17.7057	1.4251	0.220





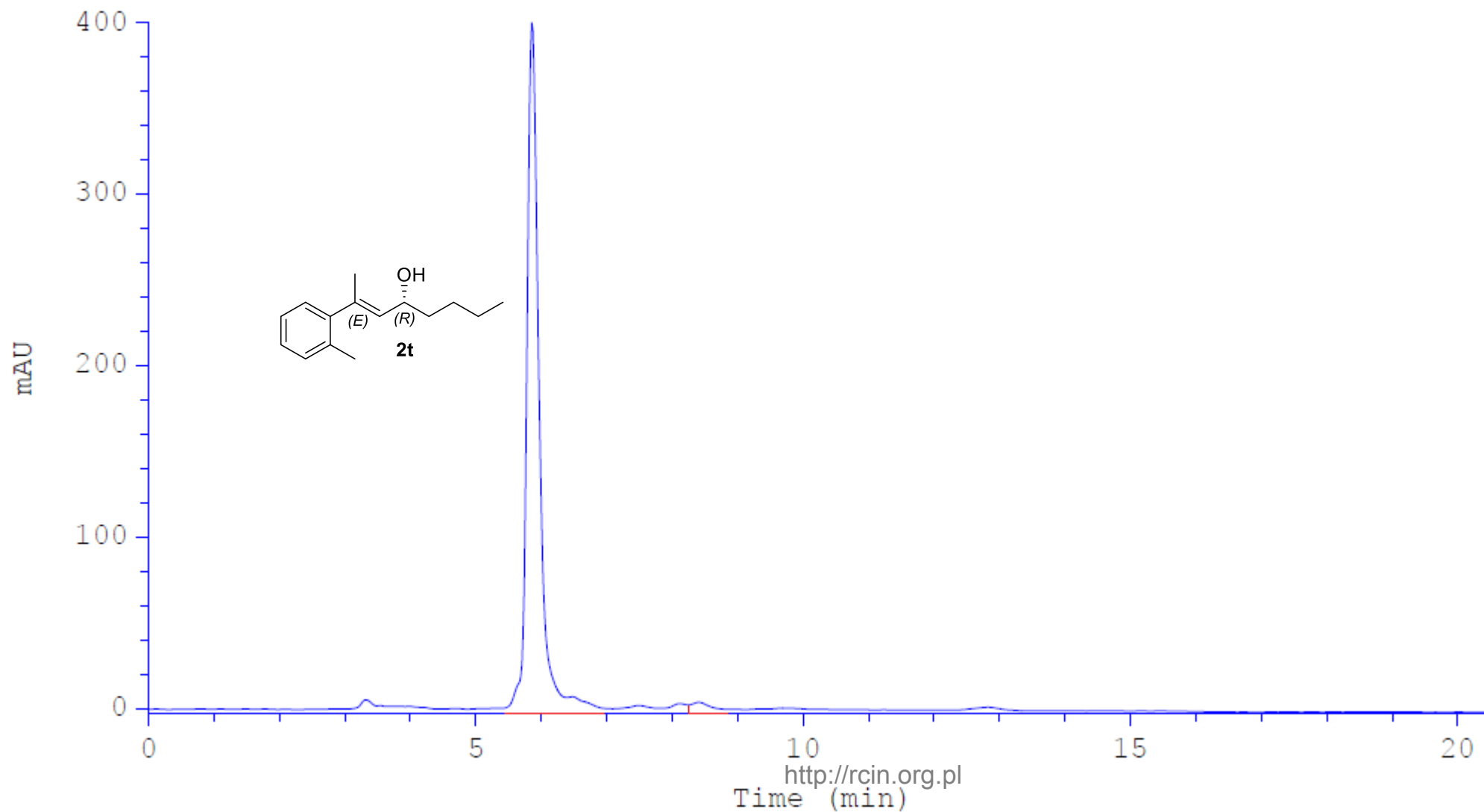
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.806	5.43	6.93	66.6667	305.35	51.2678	0.185
2	8.391	7.80	9.02	63.3695	212.105	48.7322	0.267

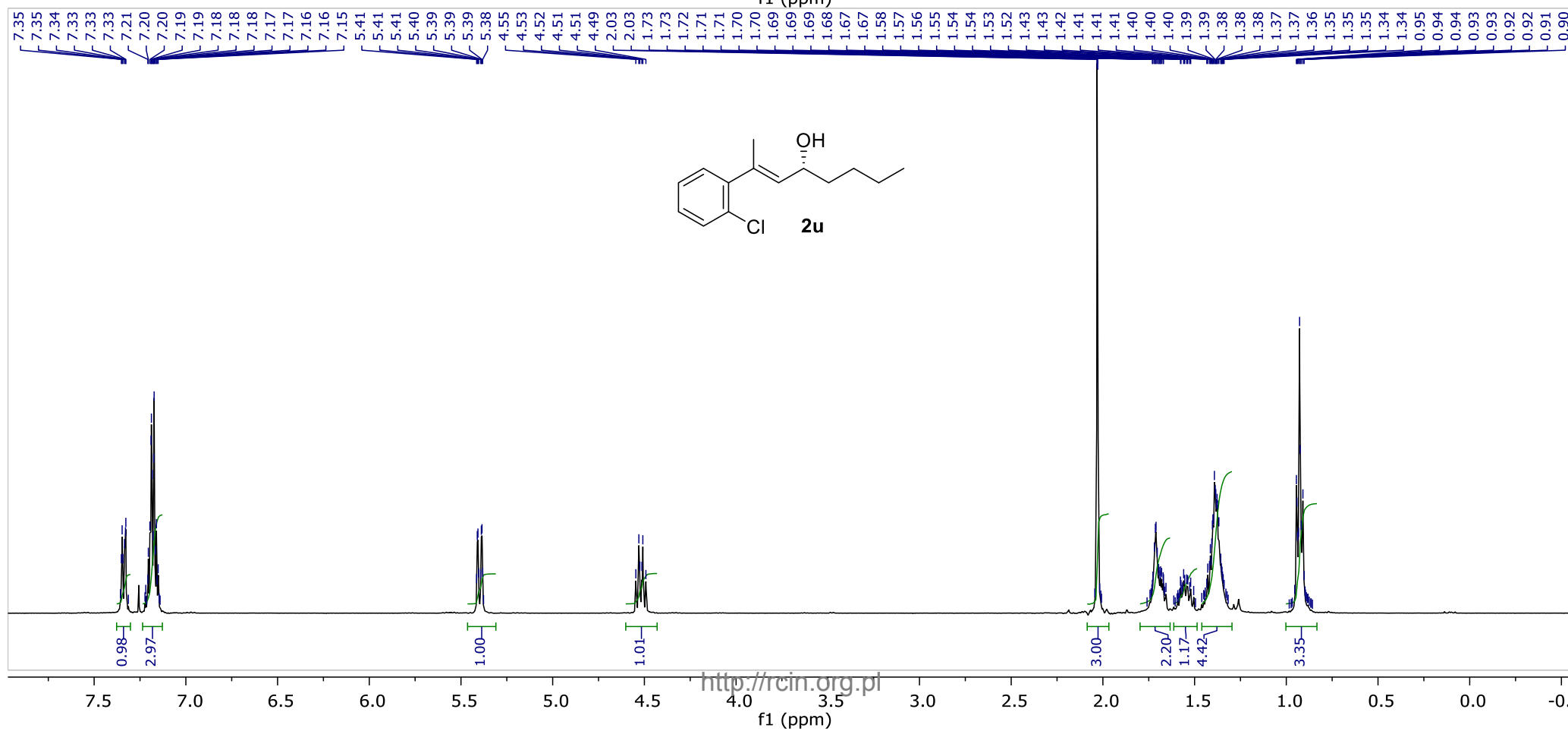
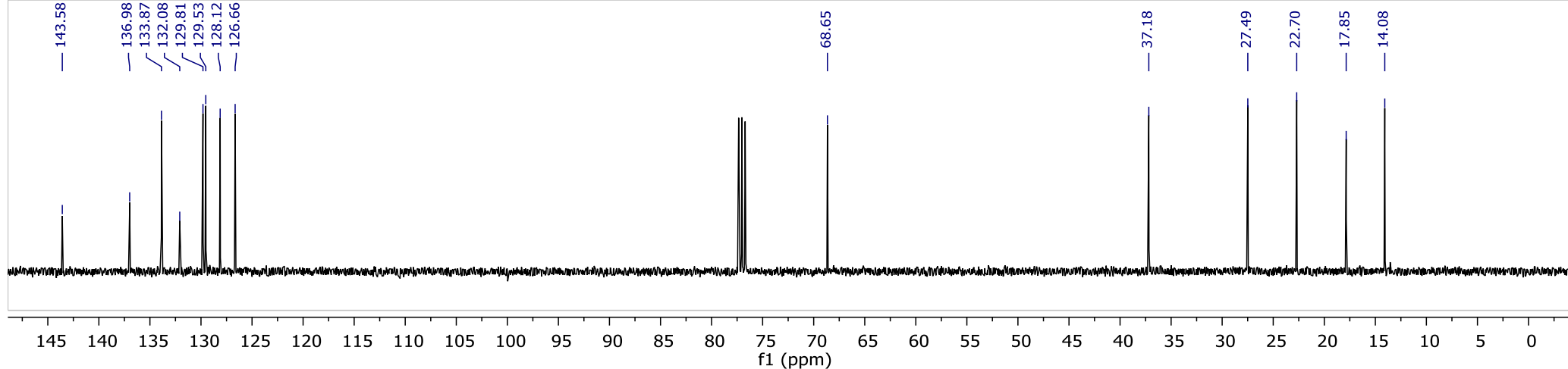


Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.854	5.48	6.88	84.8736	398.87	99.4449	0.182
2	8.405	8.22	8.82	0.473728	2.27438	0.5551	0.227

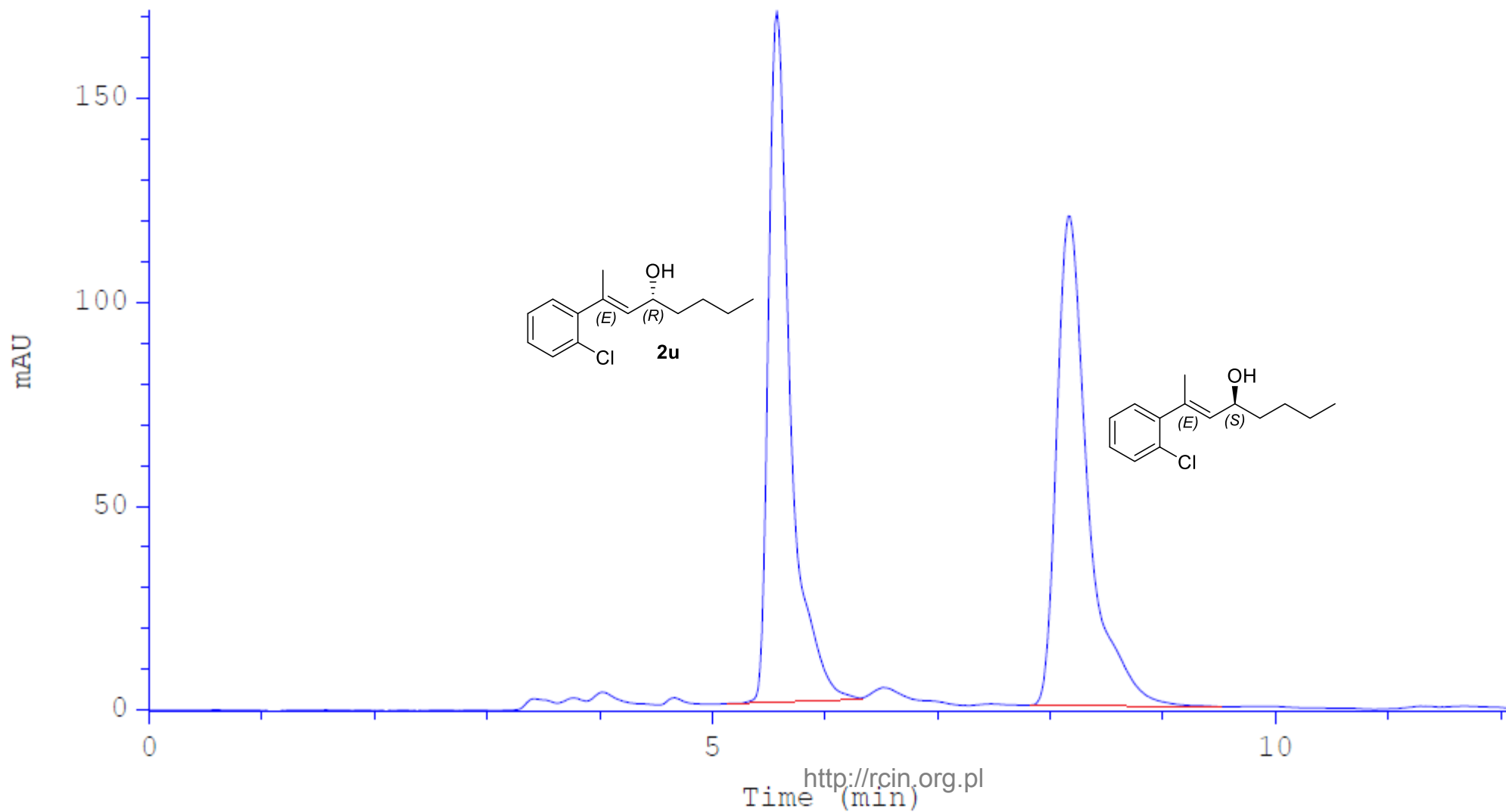






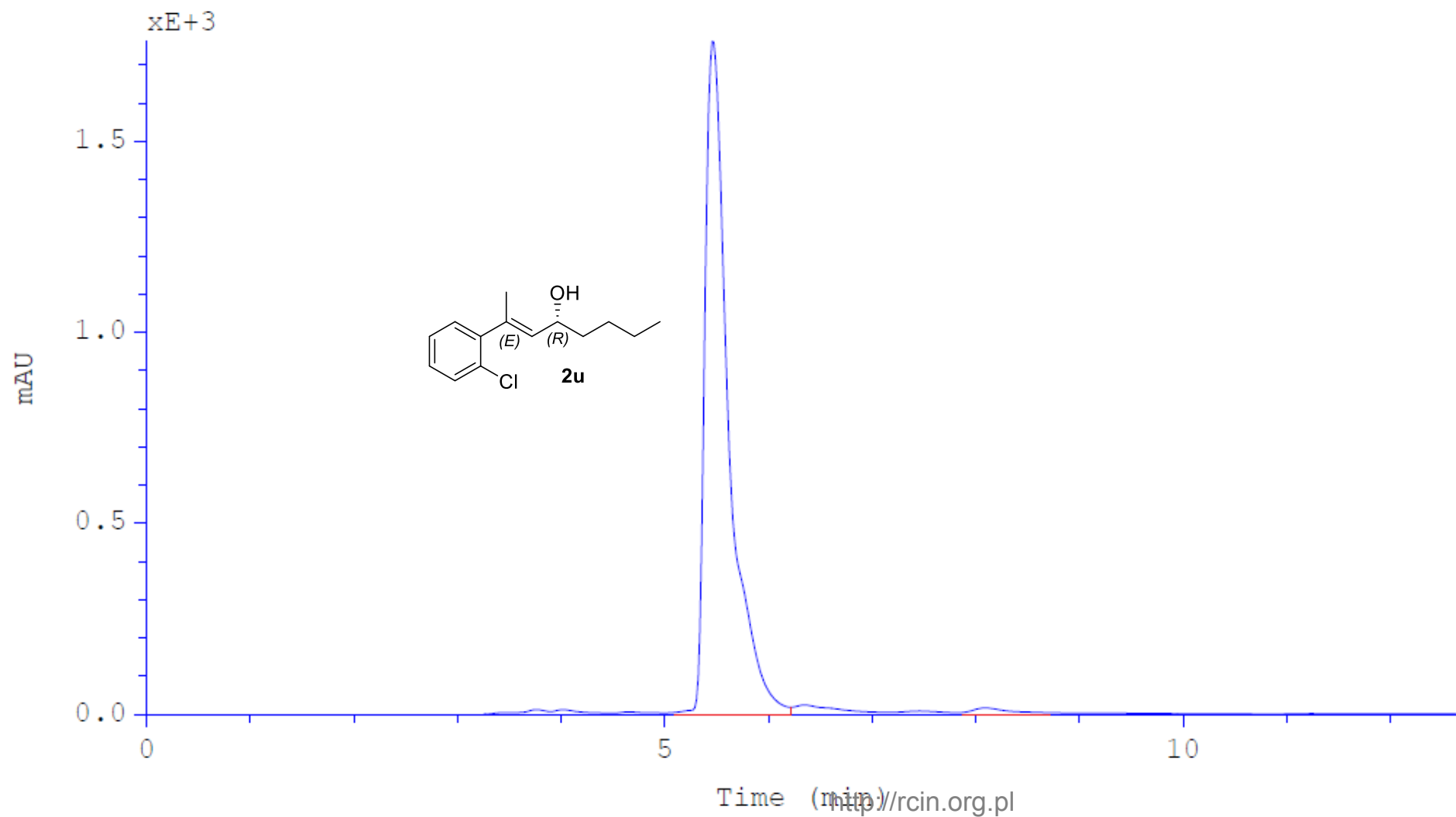
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

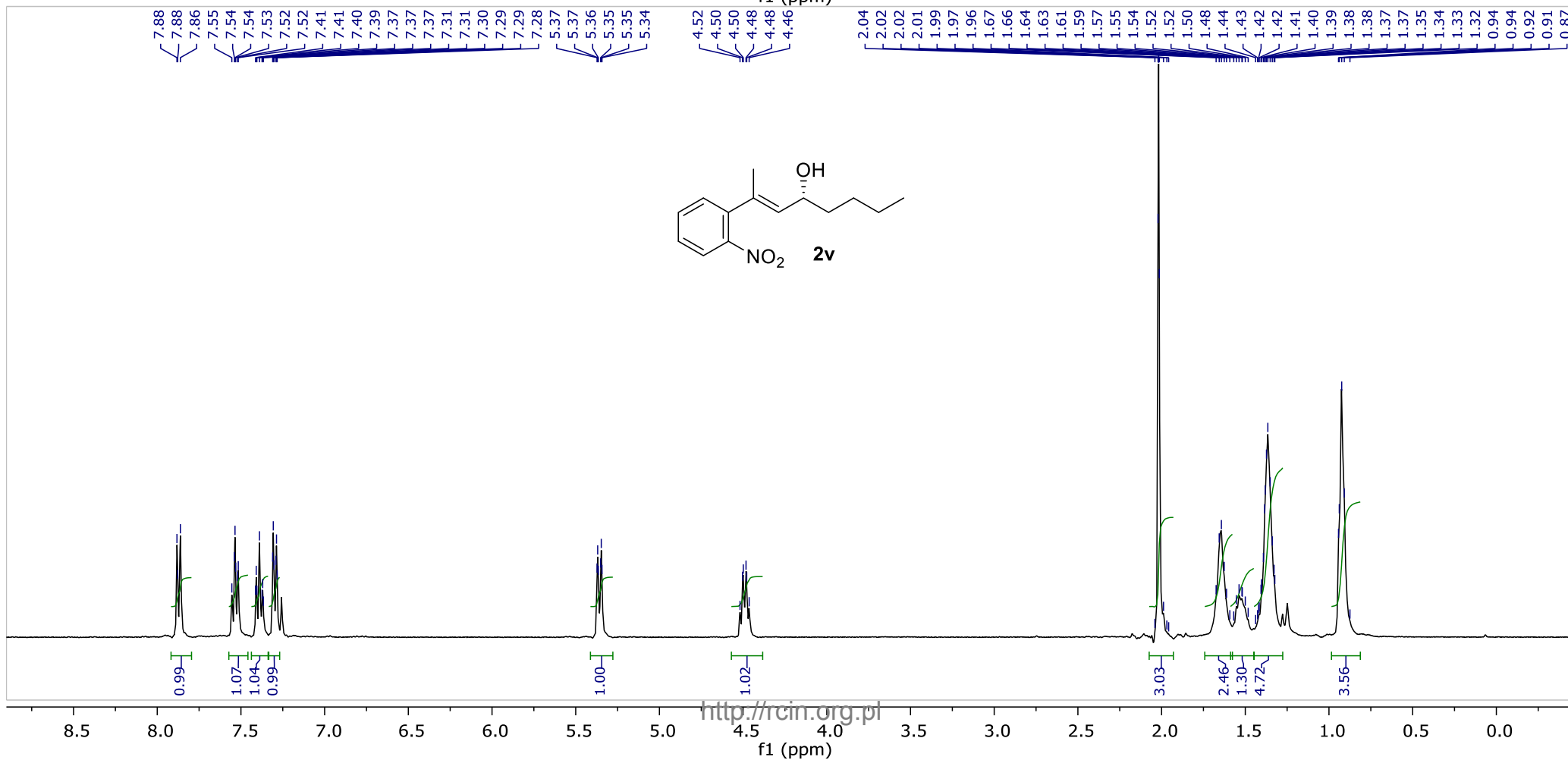
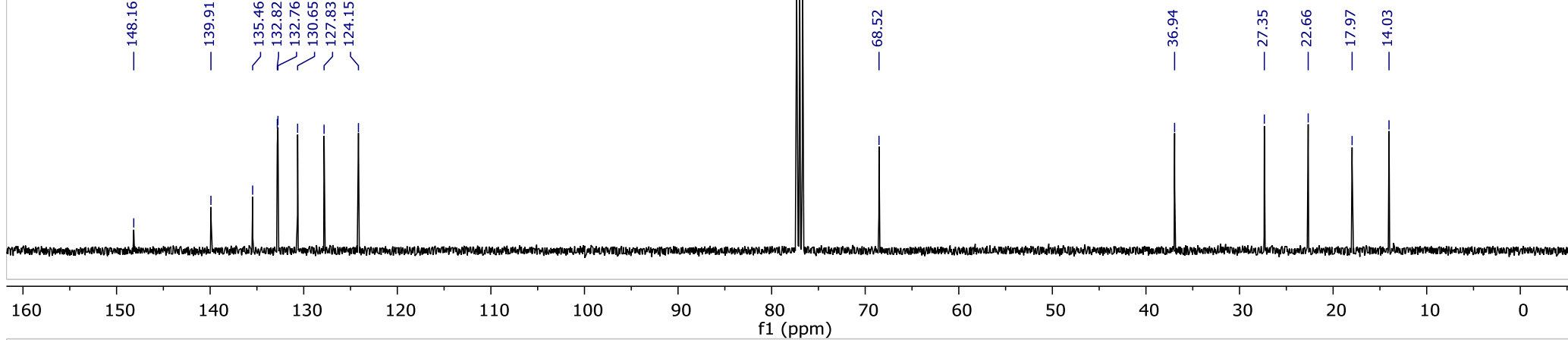
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.573	5.11	6.33	37.9536	169.363	49.5321	0.187
2	8.160	7.84	9.44	38.6707	120.028	50.4679	0.269



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

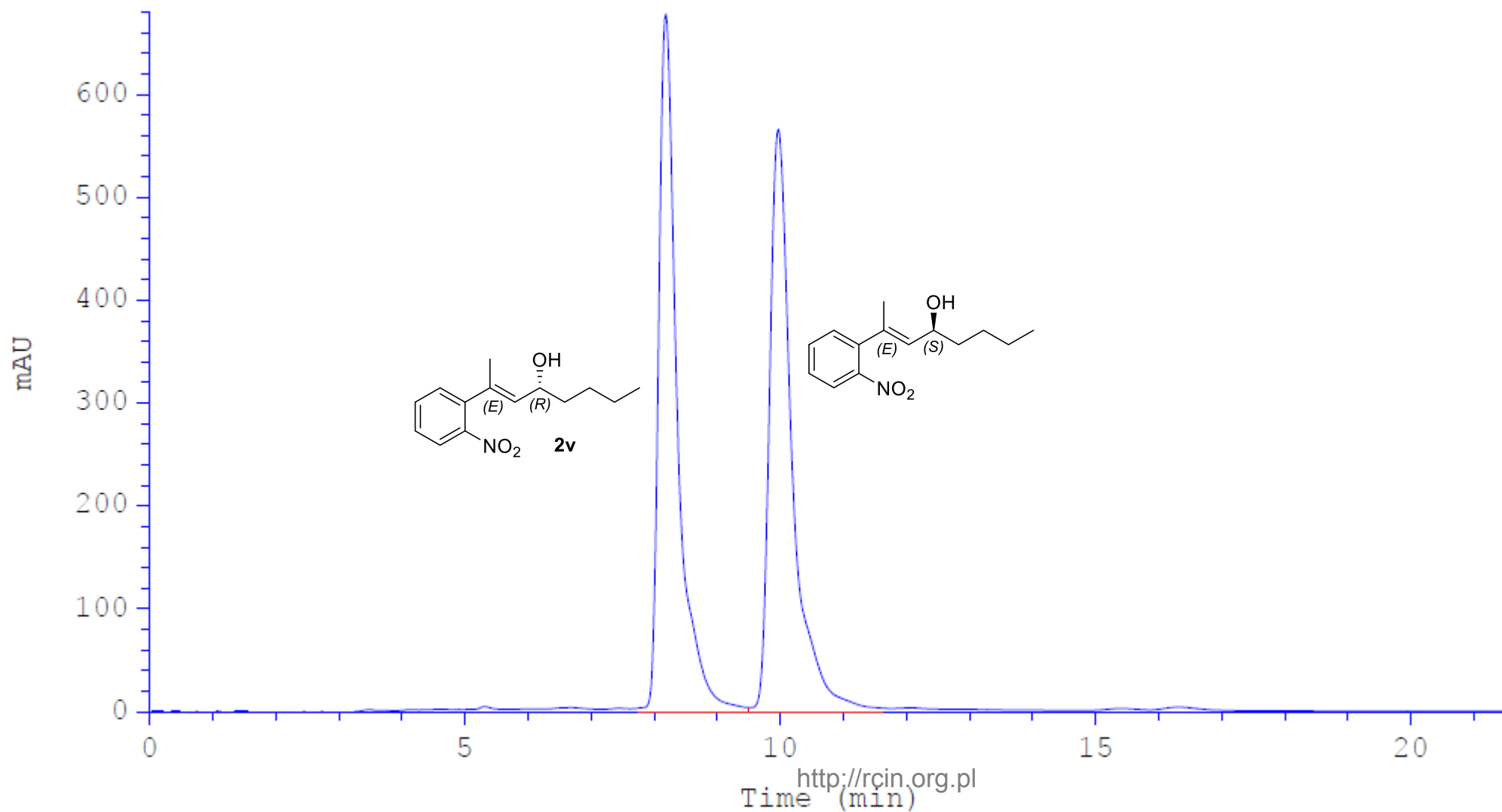
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.456	5.05	6.23	456.631	1751.89	99.4594	0.217
2	8.092	7.94	8.72	2.48212	9.54315	0.5406	0.259





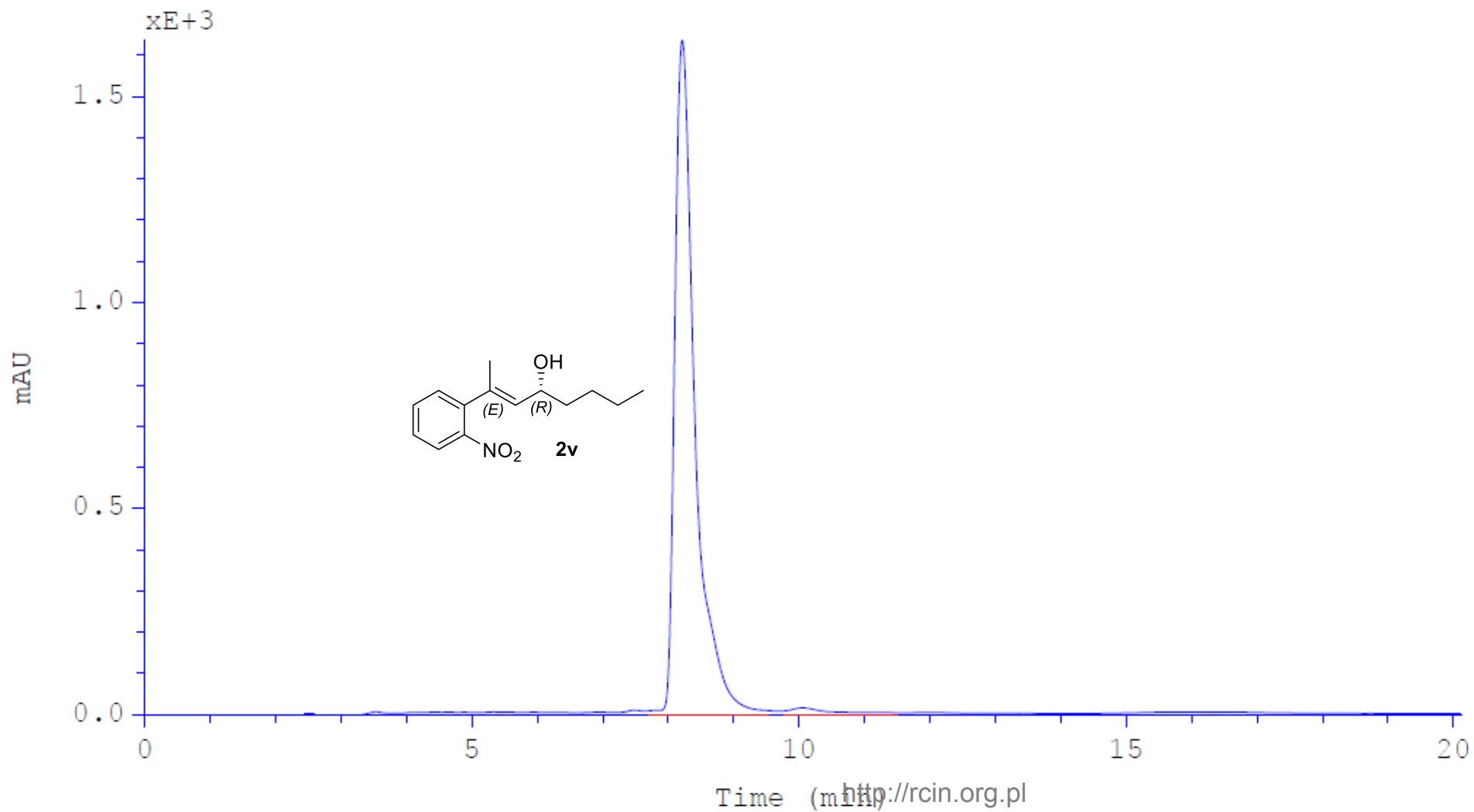
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

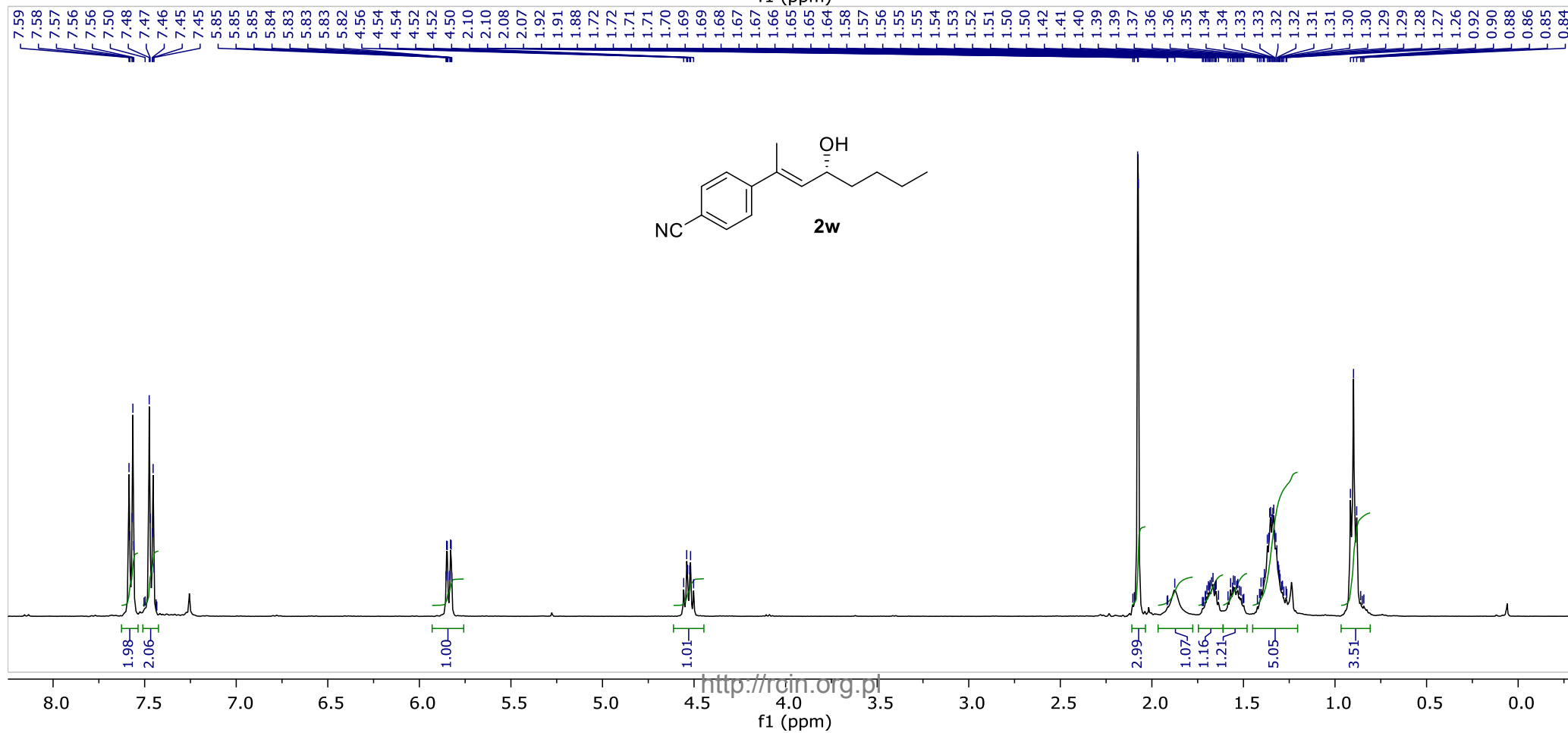
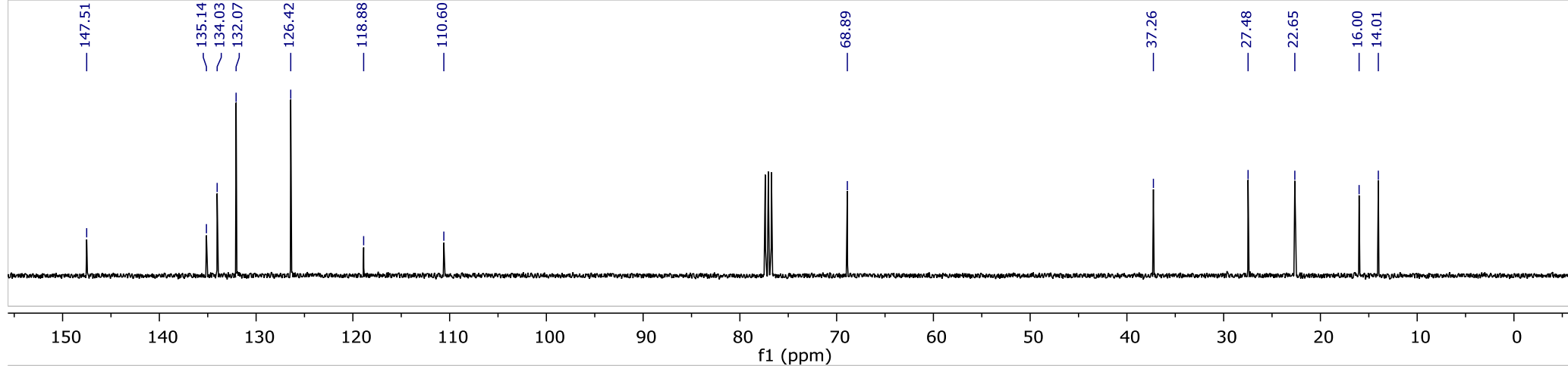
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.188	7.80	9.50	226.488	674.353	49.7288	0.281
2	9.973	9.52	11.53	228.958	562.191	50.2712	0.340



Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

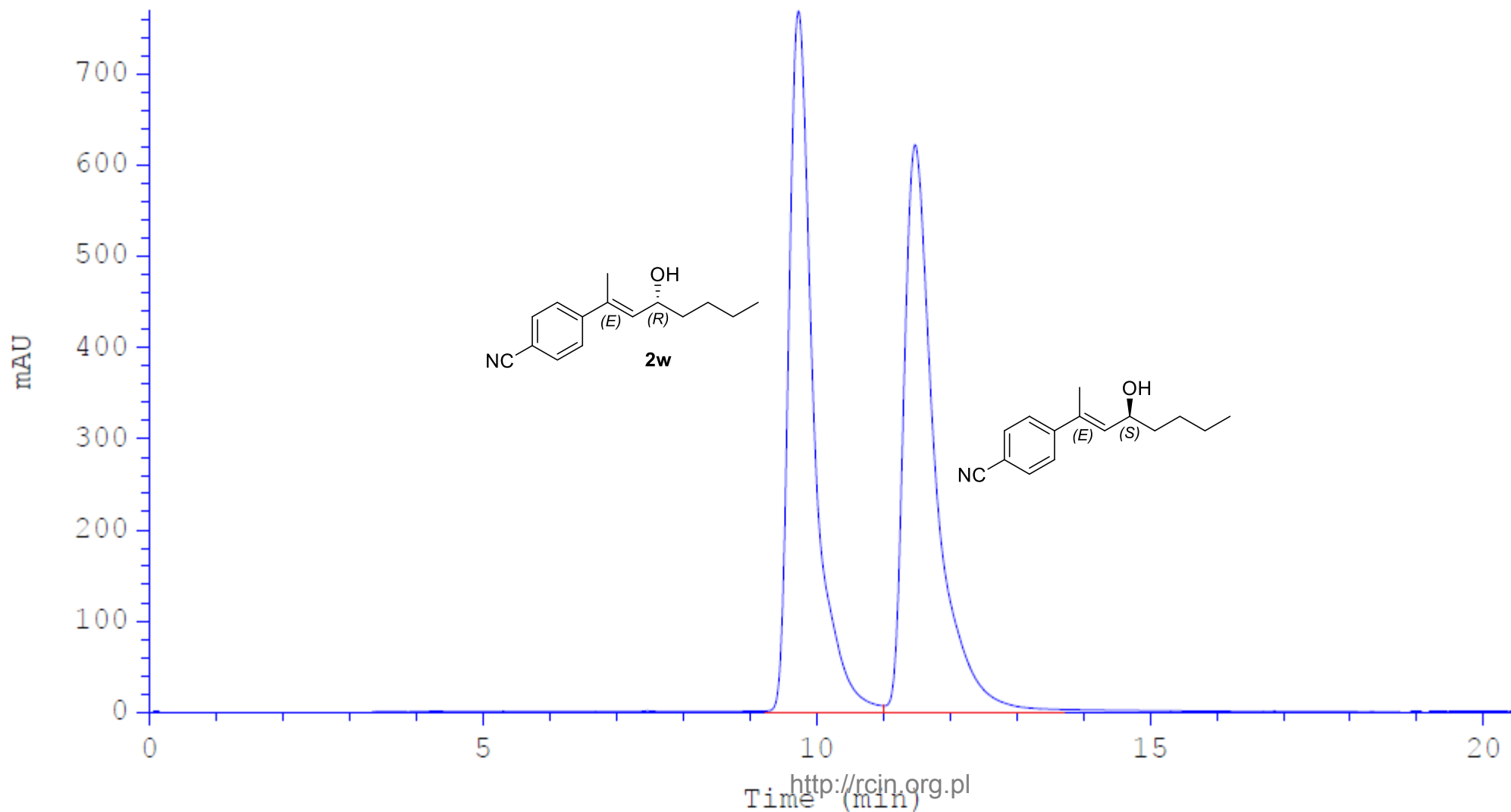
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.222	7.71	9.52	572.109	1626.55	99.6857	0.296
2	10.056	9.80	11.45	1.80382	7.71316	0.3143	0.368





Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

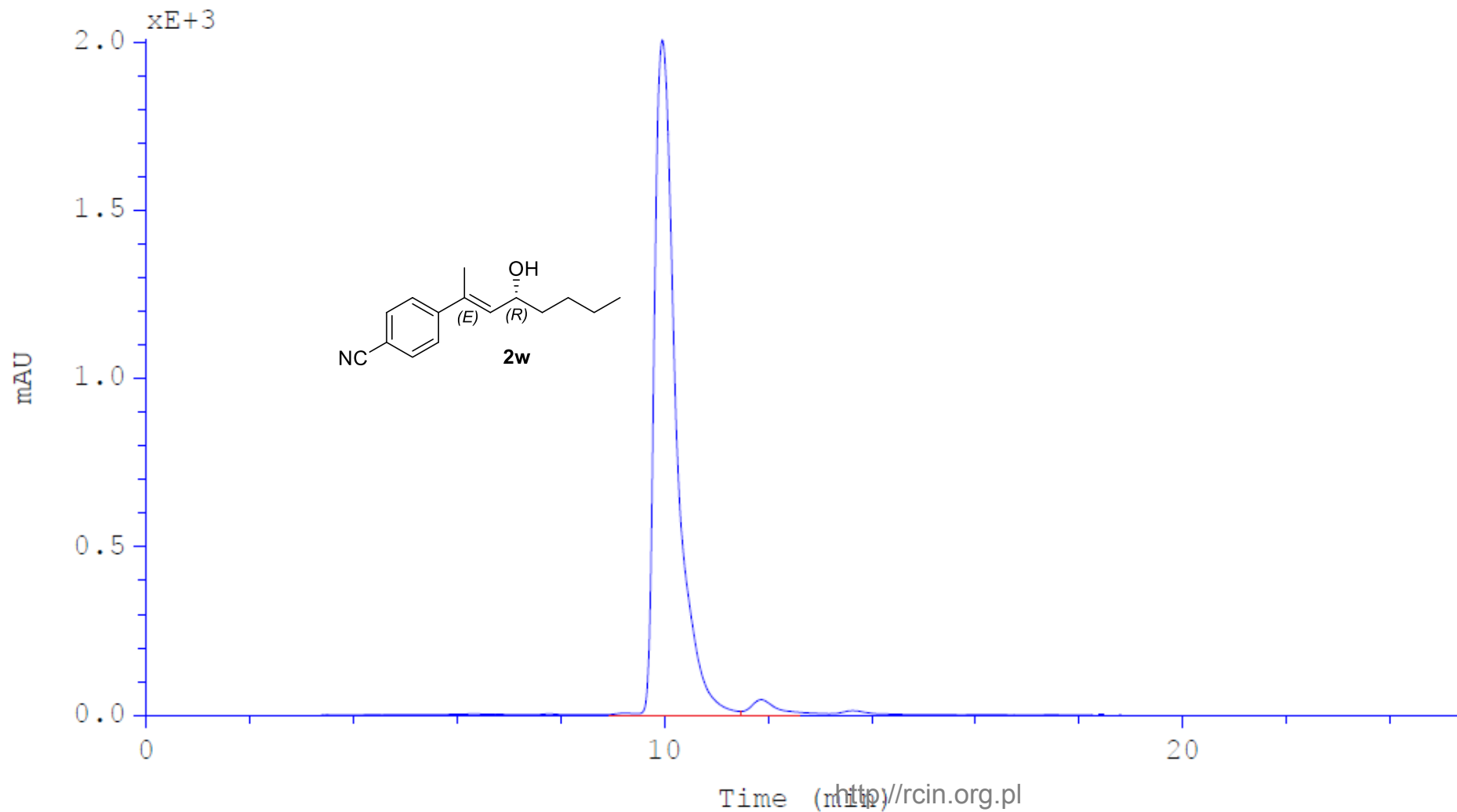
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.723	9.28	10.87	321.075	766.611	49.7003	0.355
2	11.474	11.01	13.57	324.947	617.235	50.2997	0.444

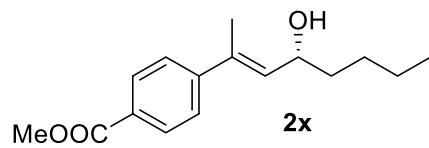
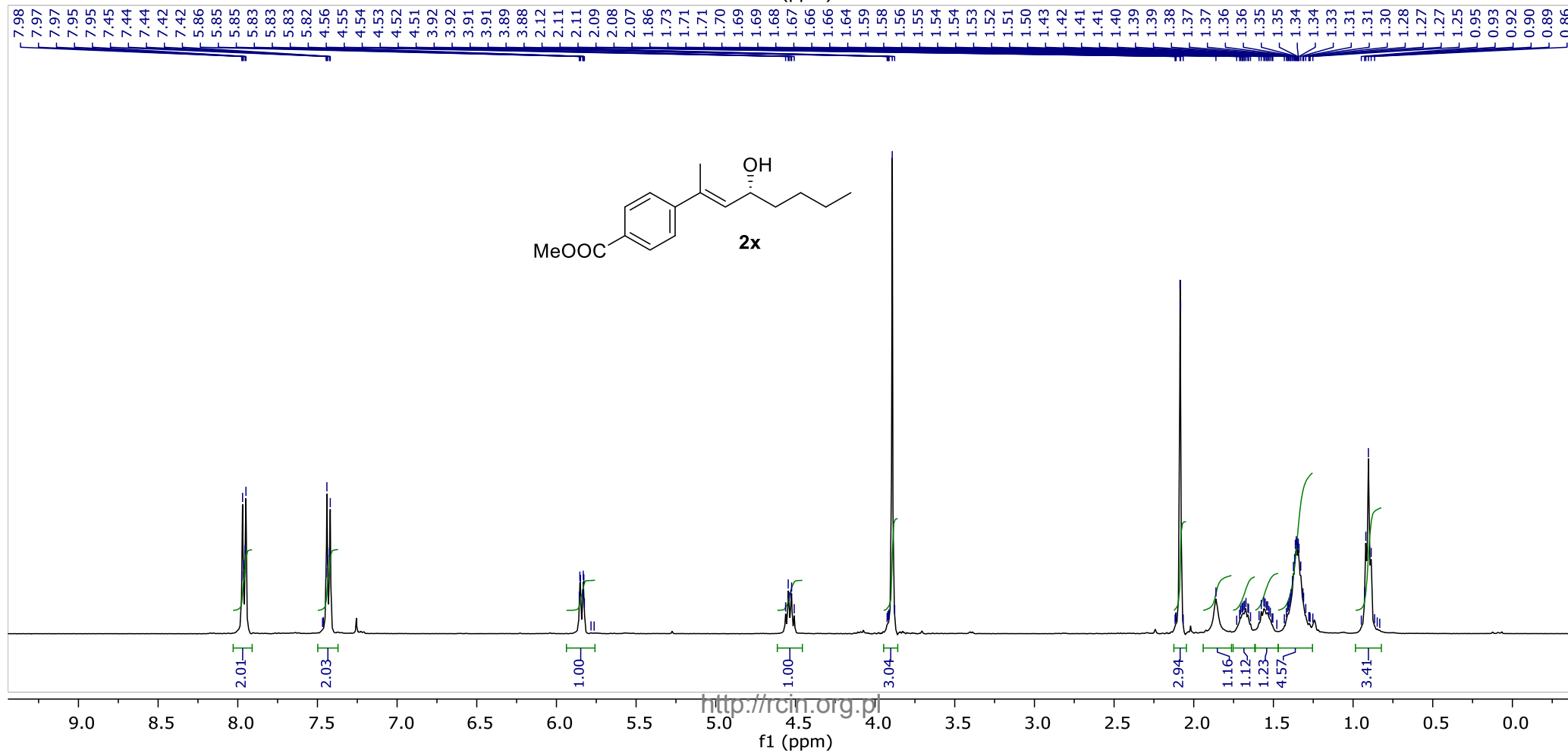
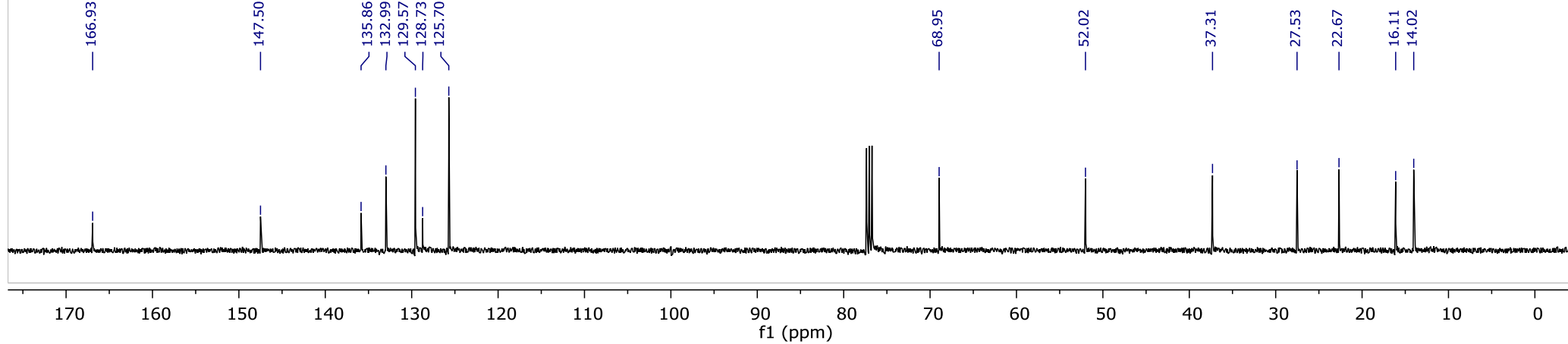




Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

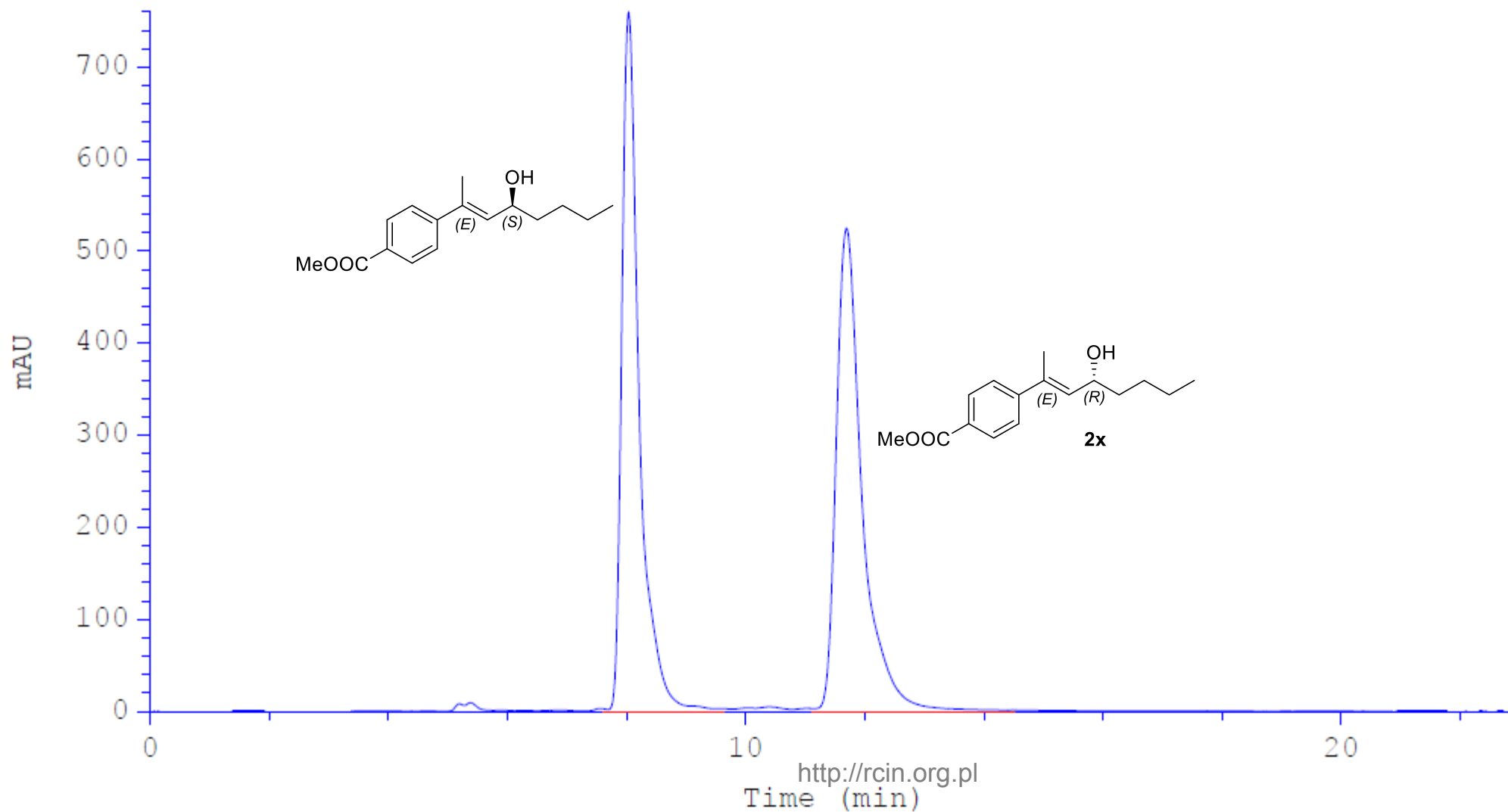
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.955	9.53	11.27	949.379	1998.86	98.6300	0.406
2	11.872	11.57	12.50	13.1876	33.1776	1.3700	0.378





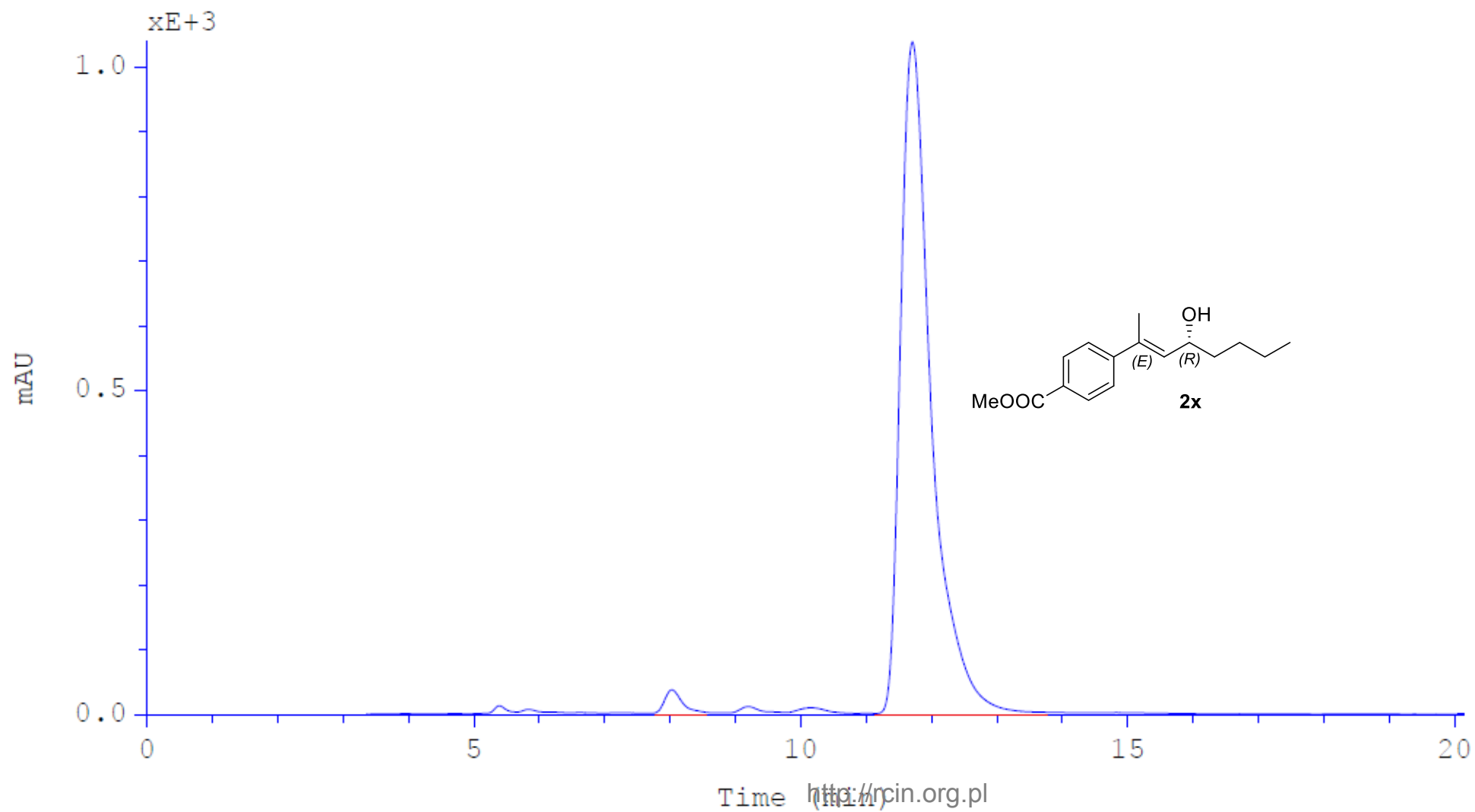
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

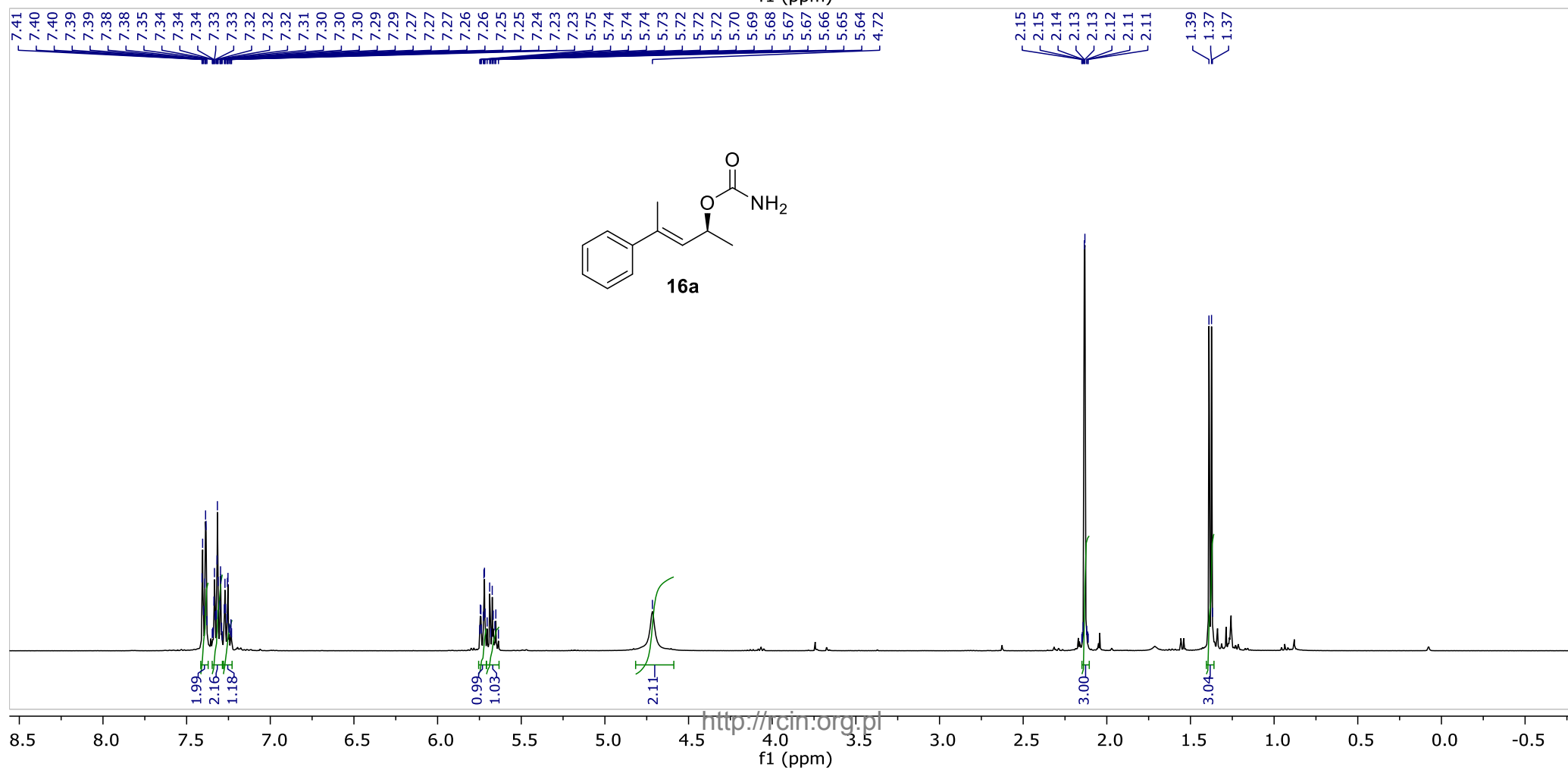
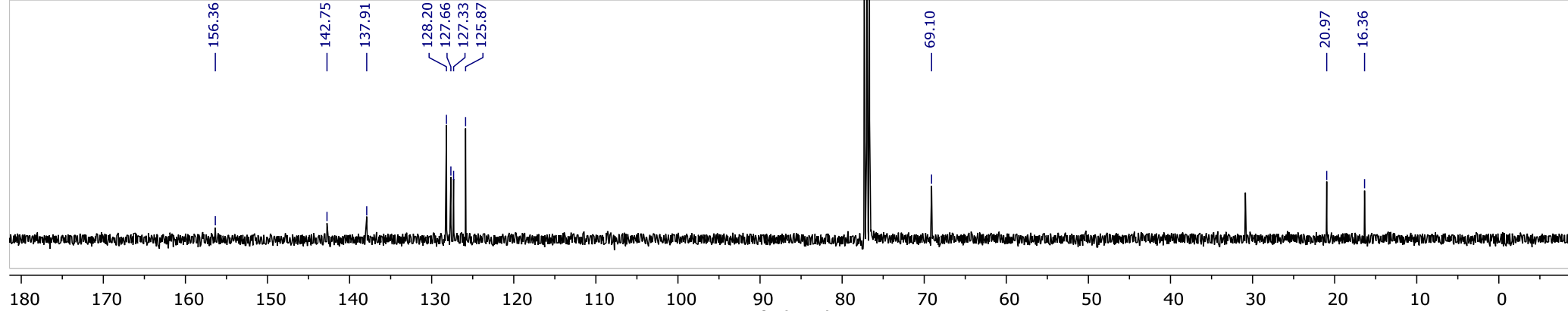
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.038	7.69	9.47	254.114	757.81	49.6862	0.281
2	11.690	11.20	13.41	257.324	521.955	50.3138	0.417

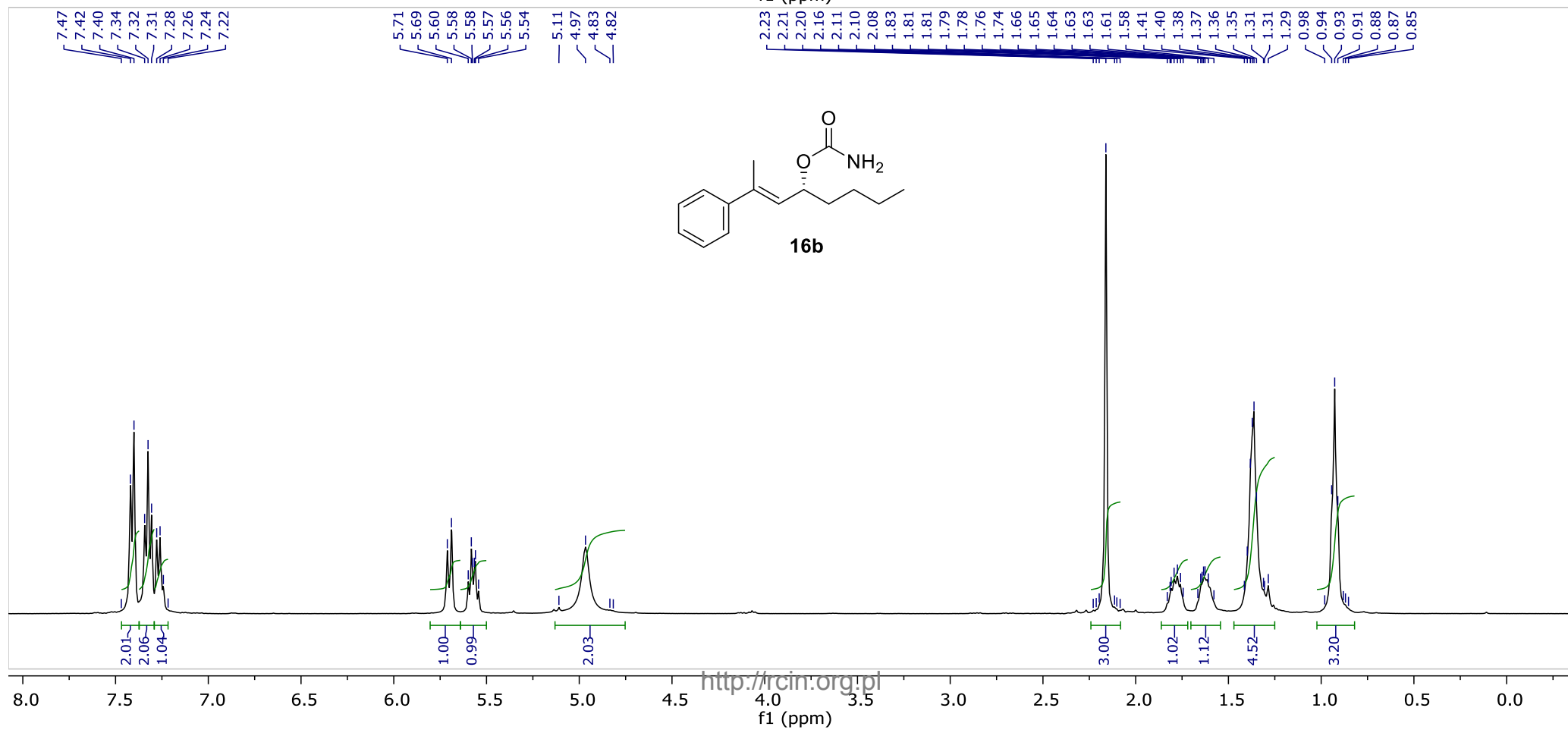
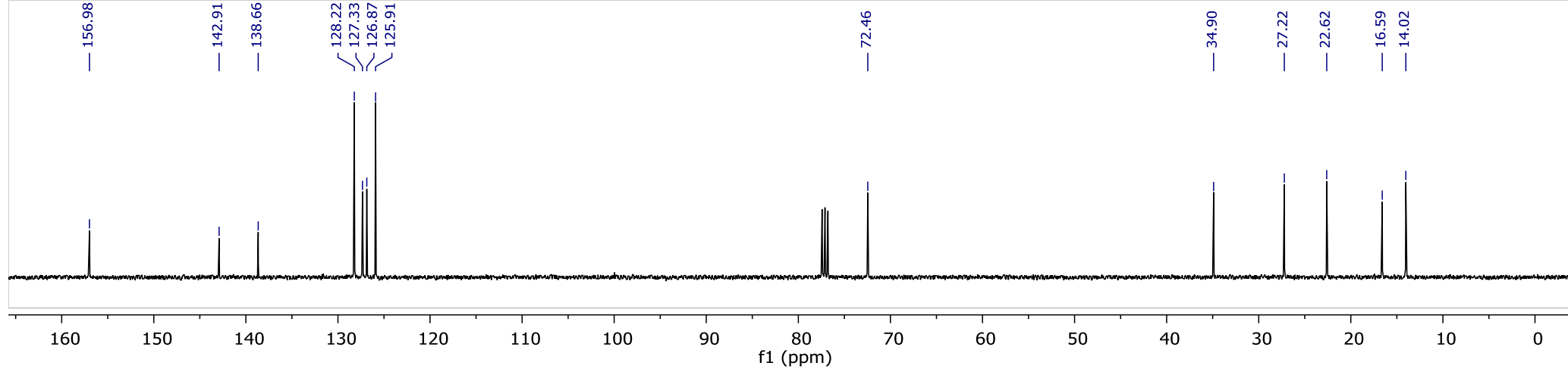


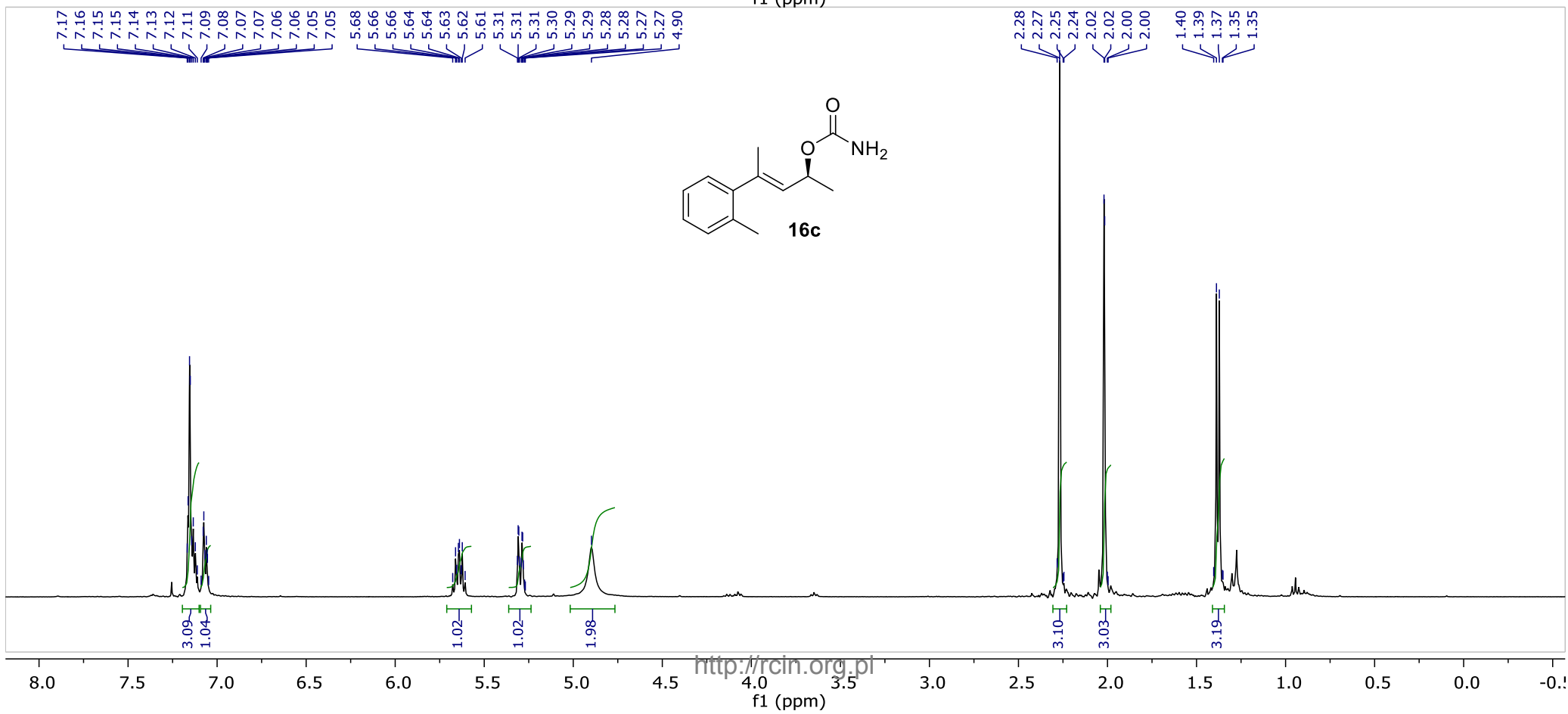
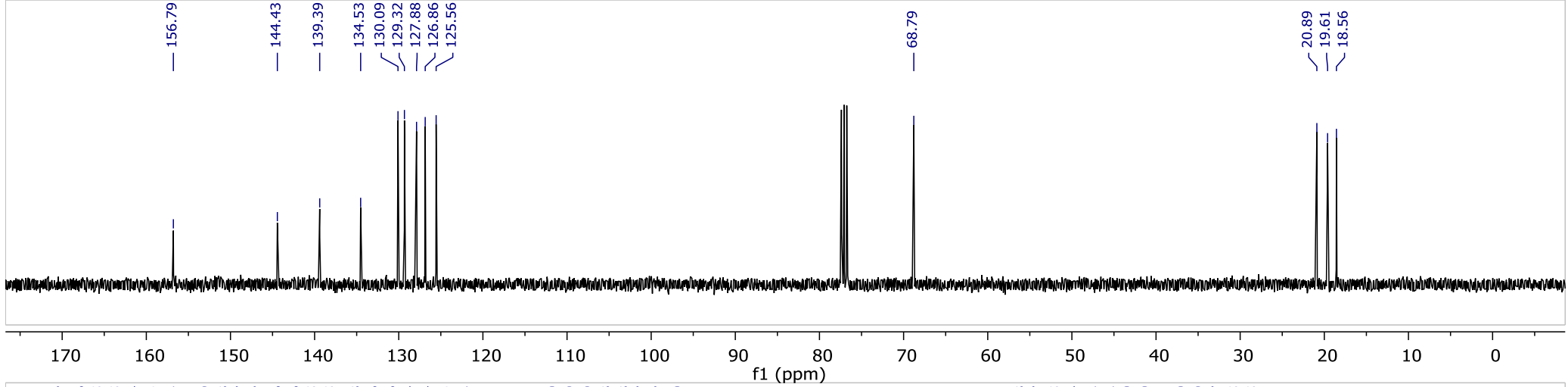
Column: Chiralcel OD-H  
Eluent: 10% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 254 nm

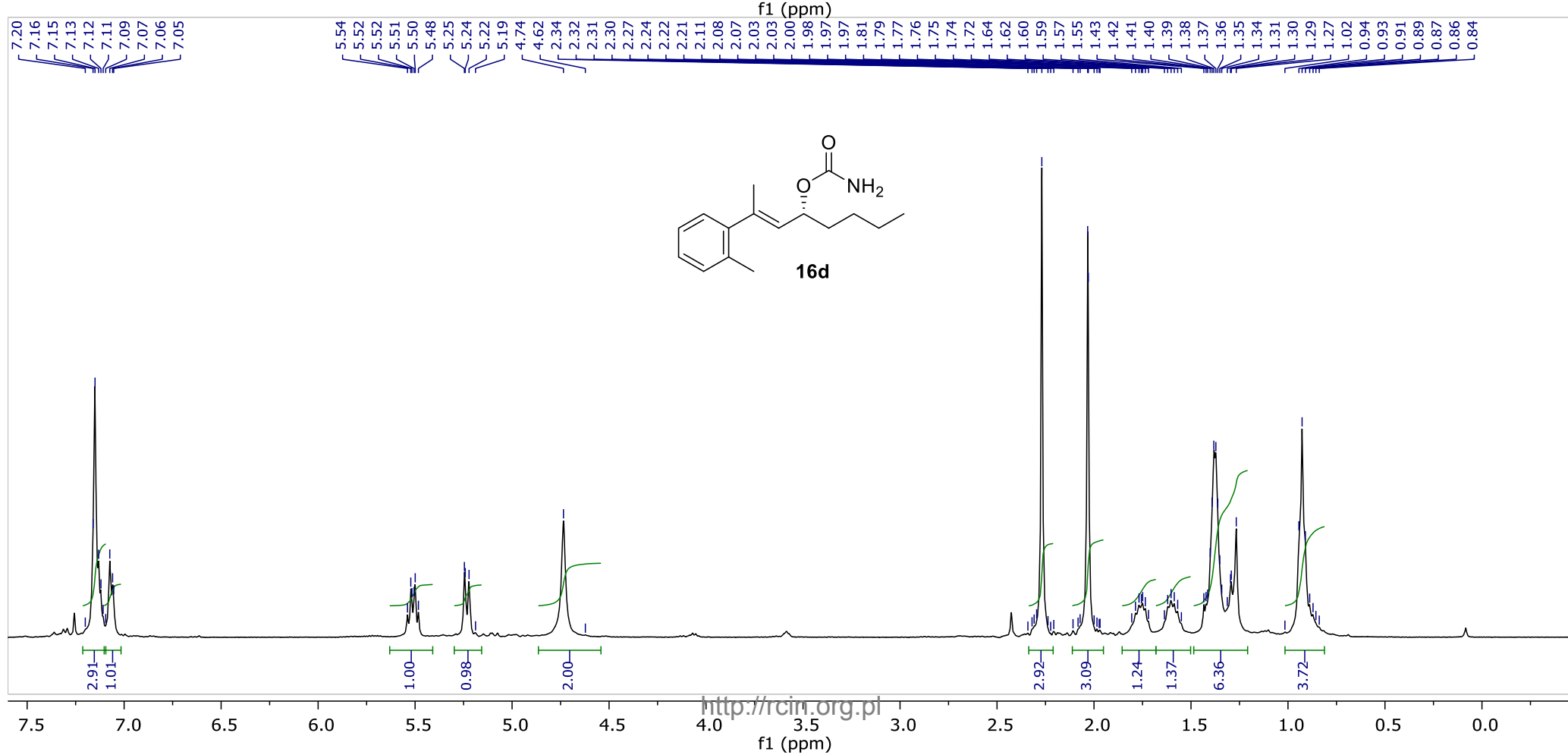
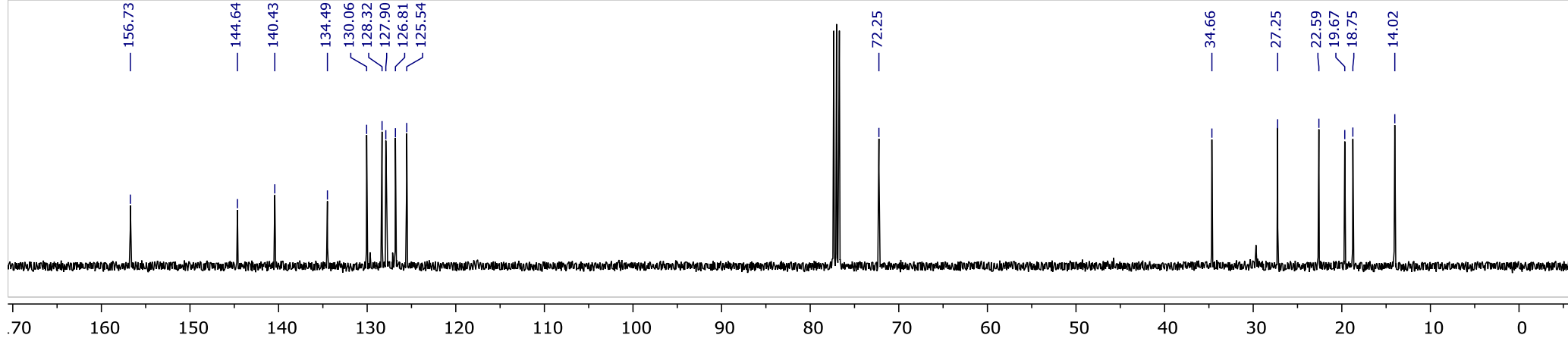
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.022	7.79	8.55	10.2689	35.0787	1.7944	0.262
2	11.708	11.20	13.68	562.019	1037.73	98.2056	0.462



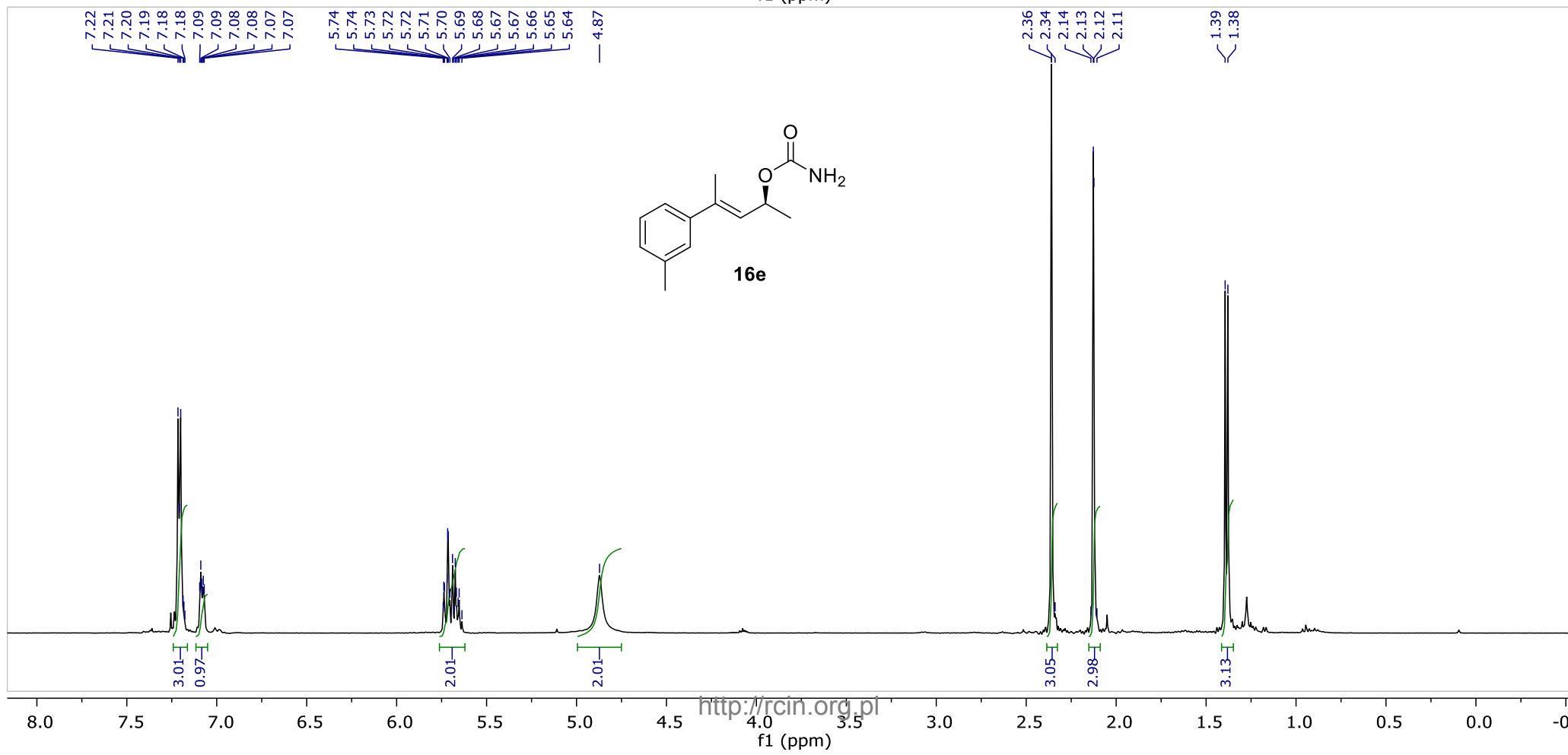
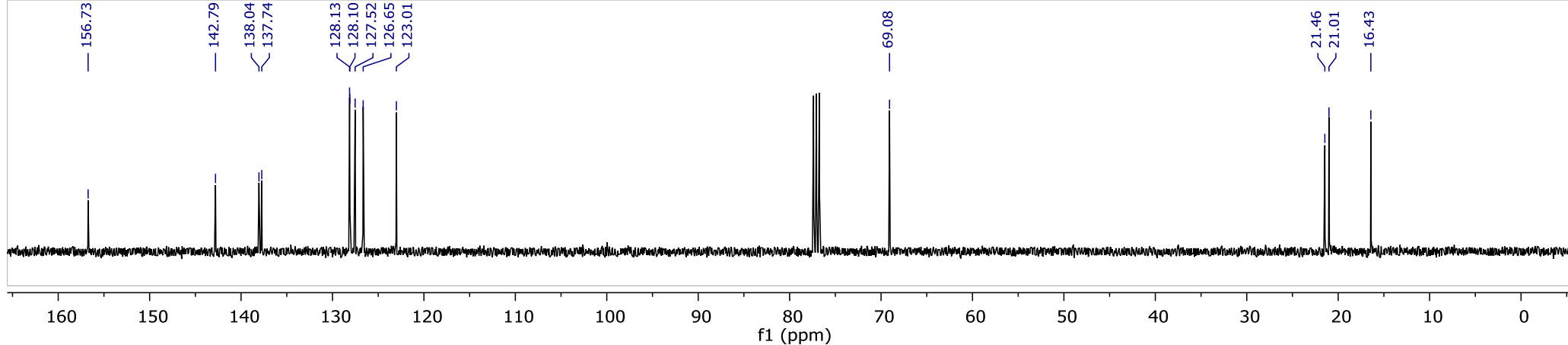


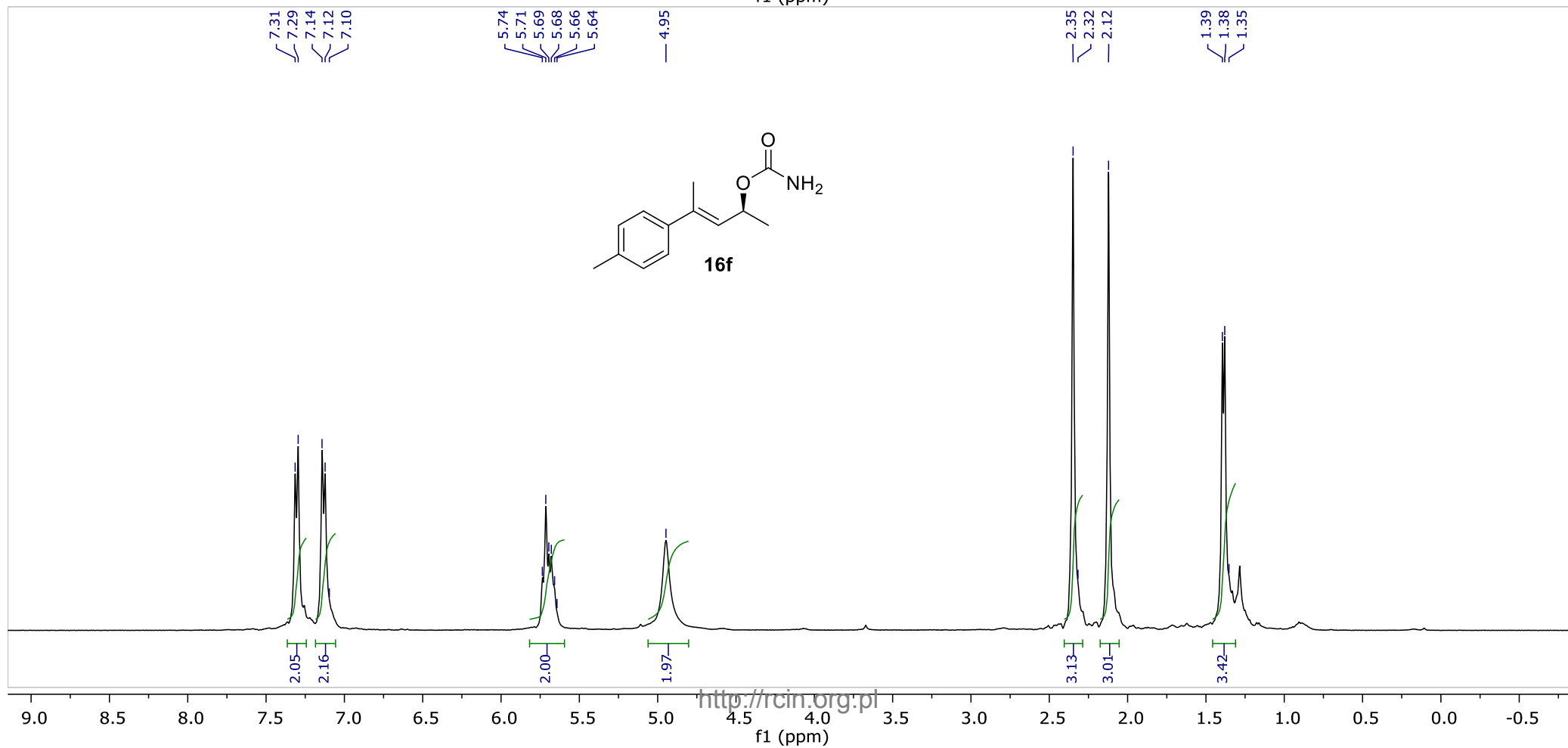
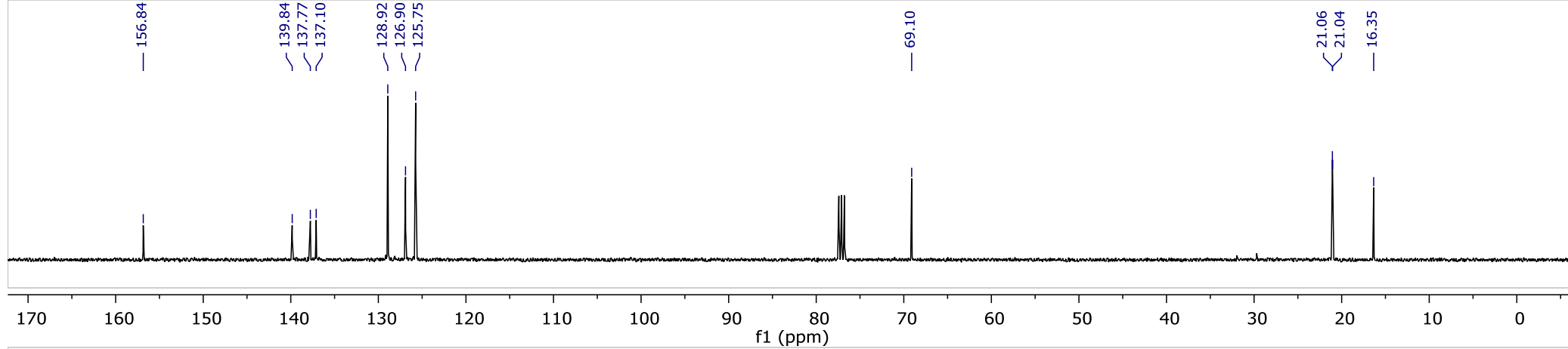


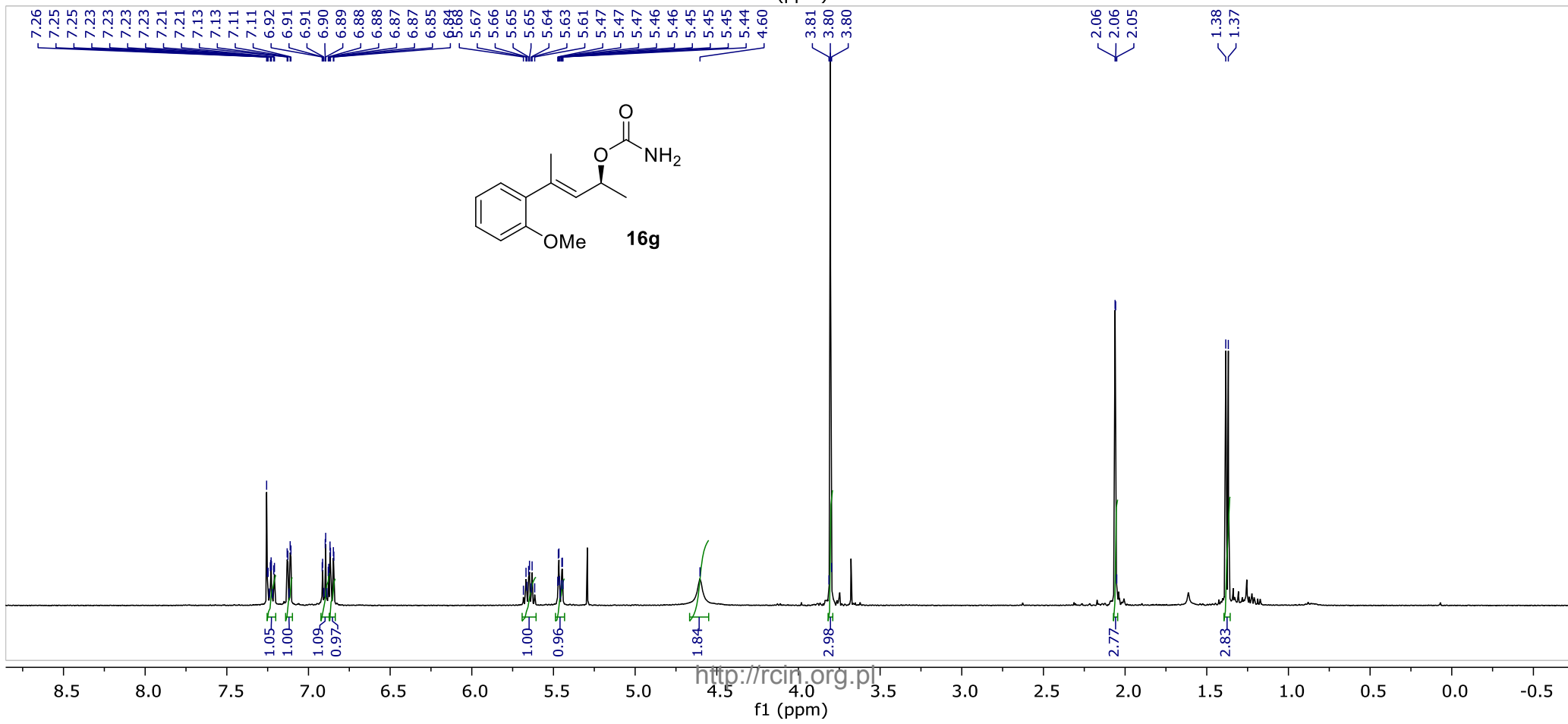
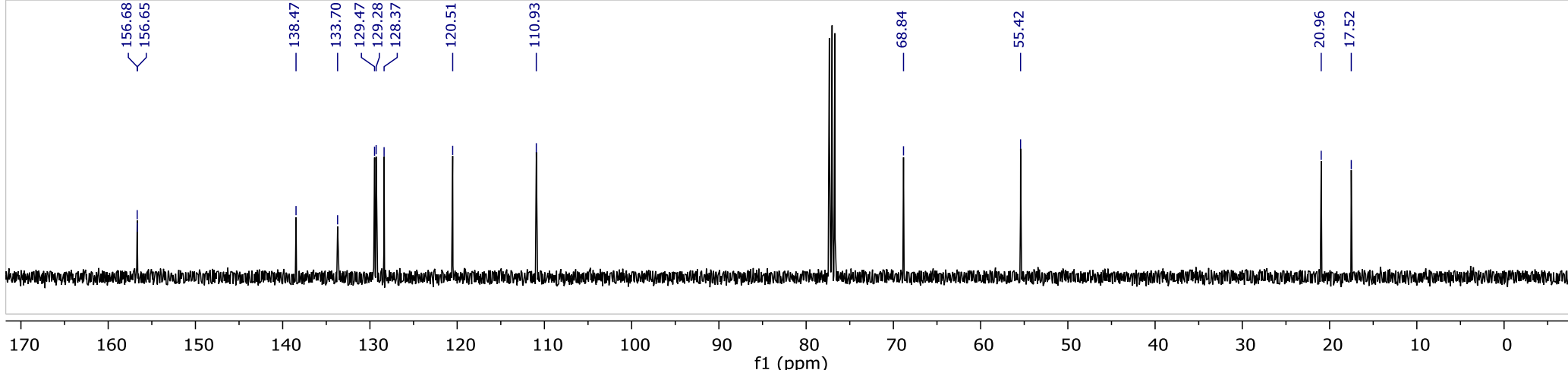


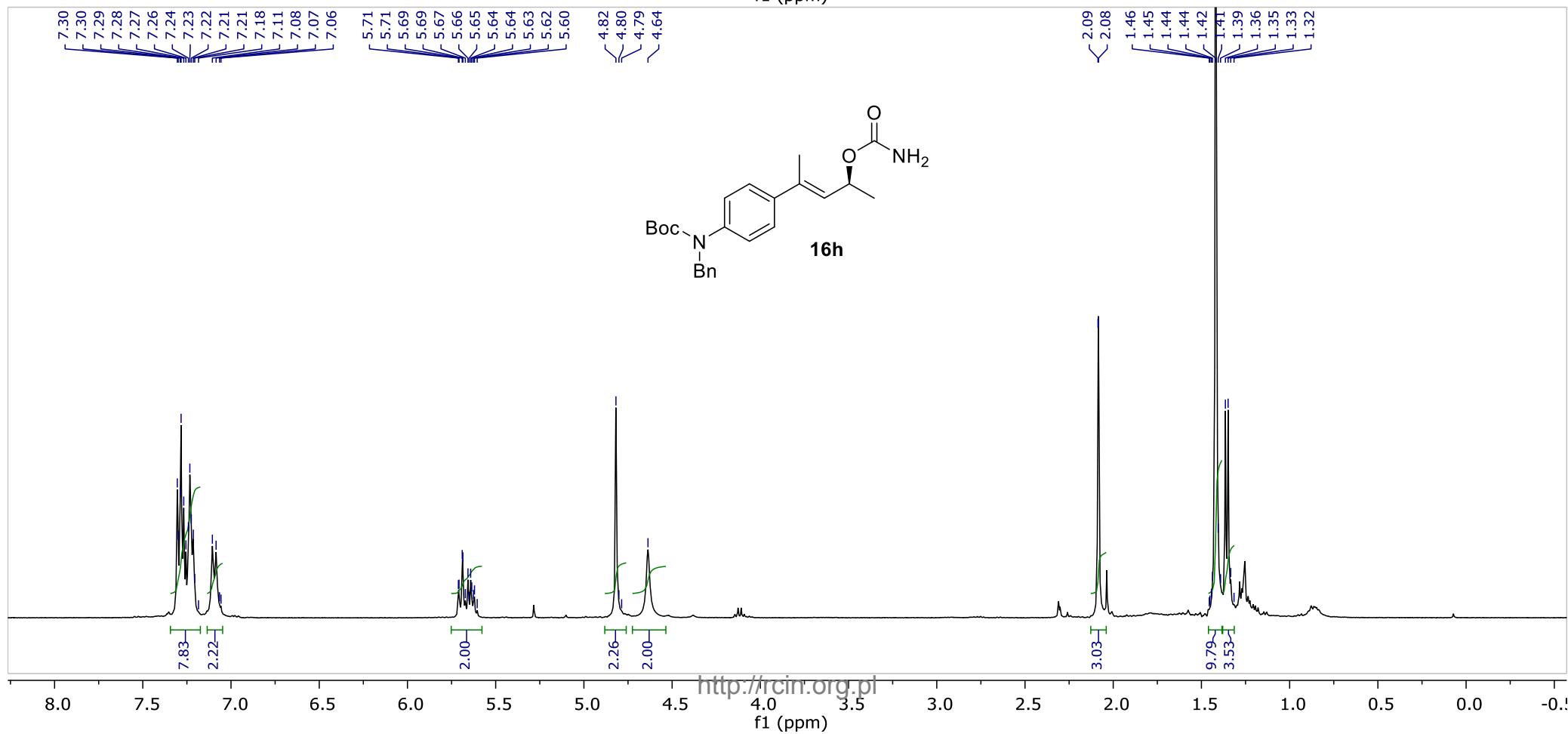
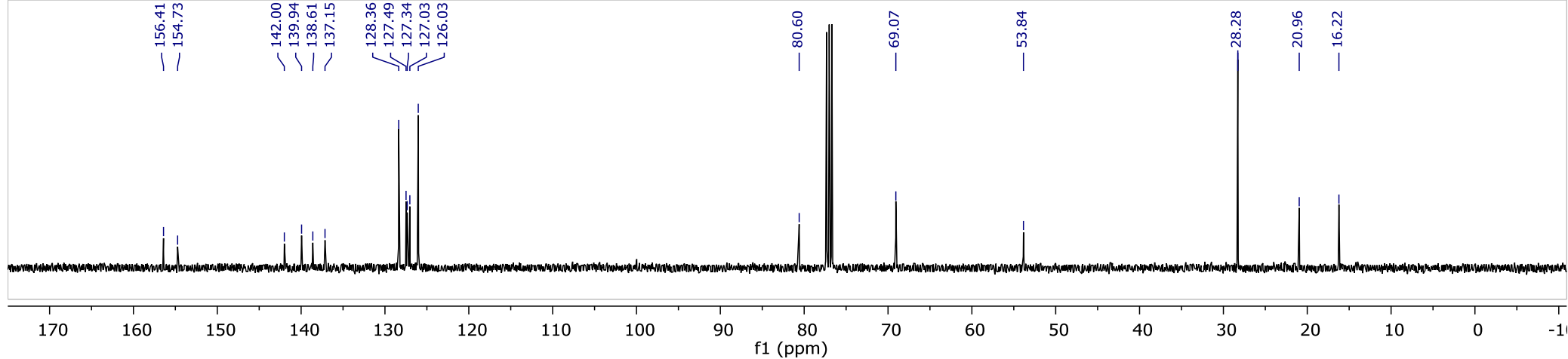


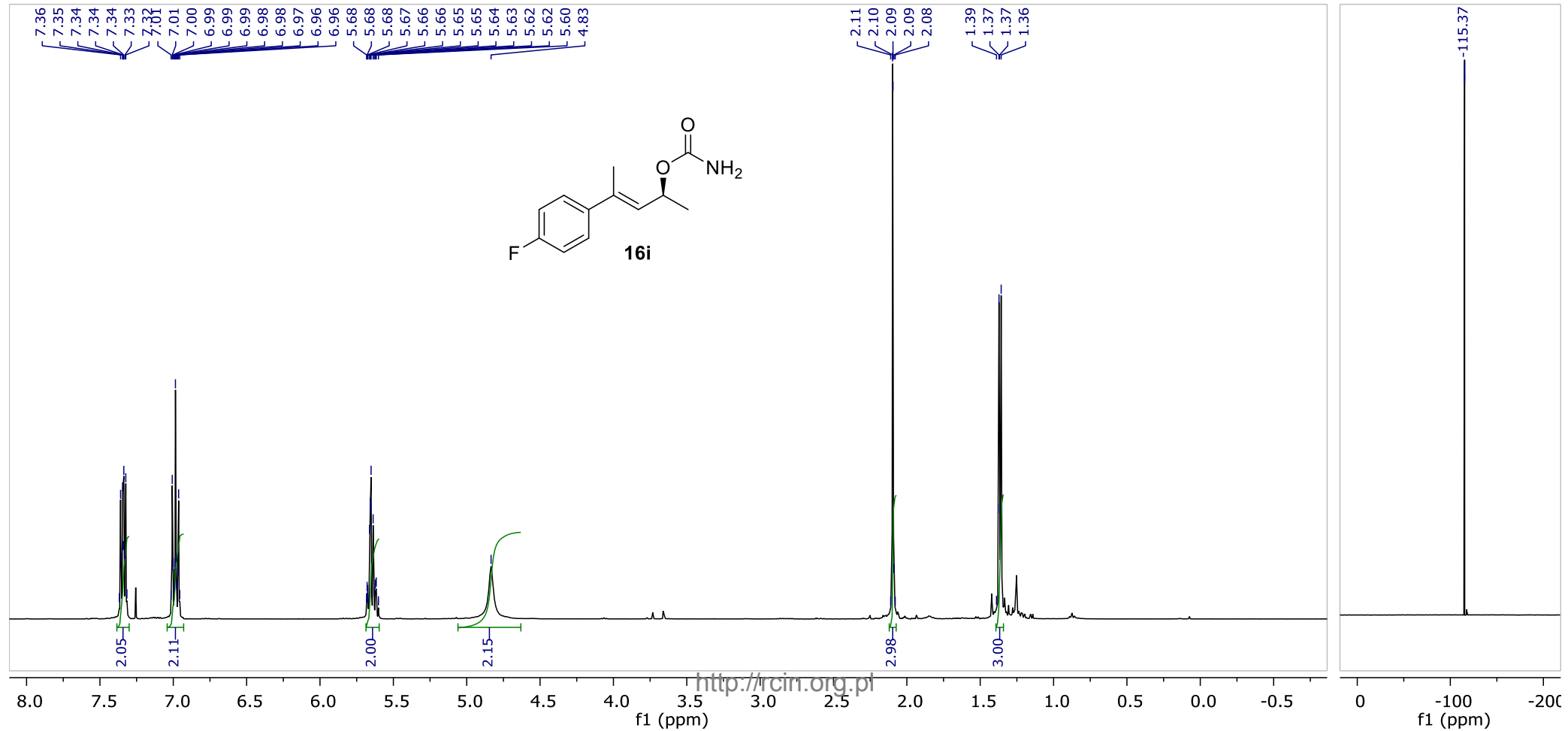
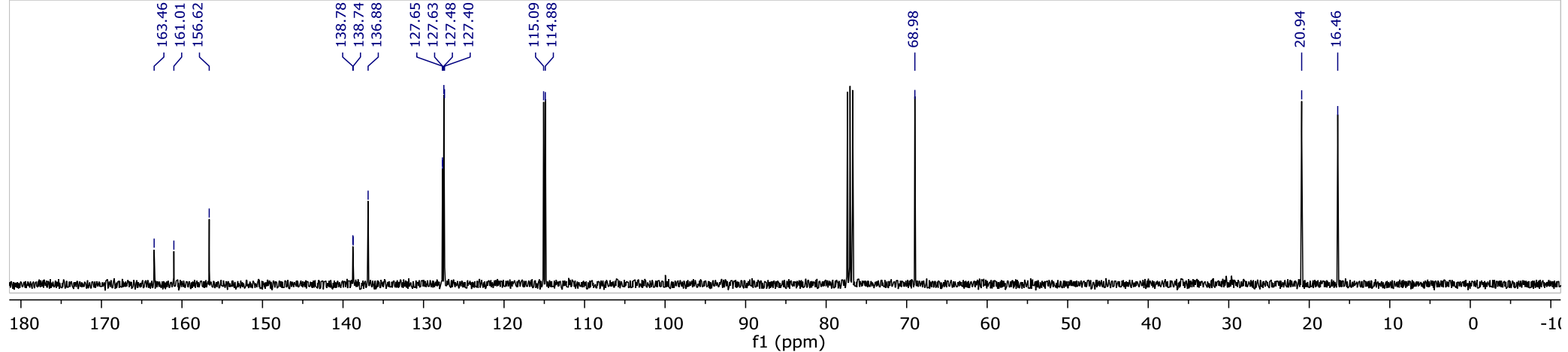


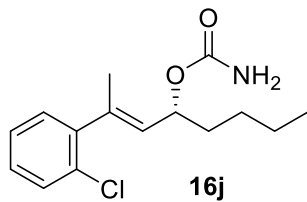
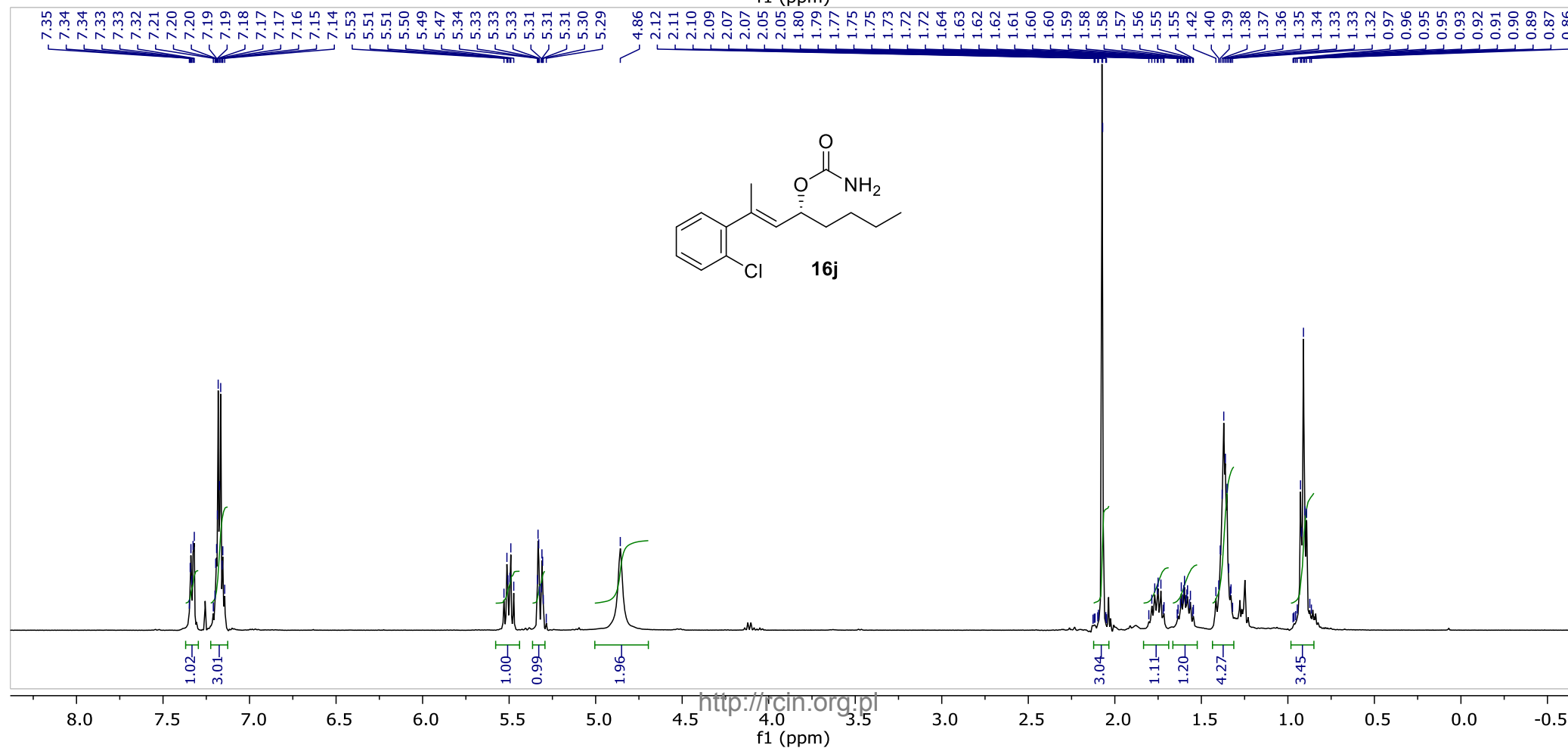
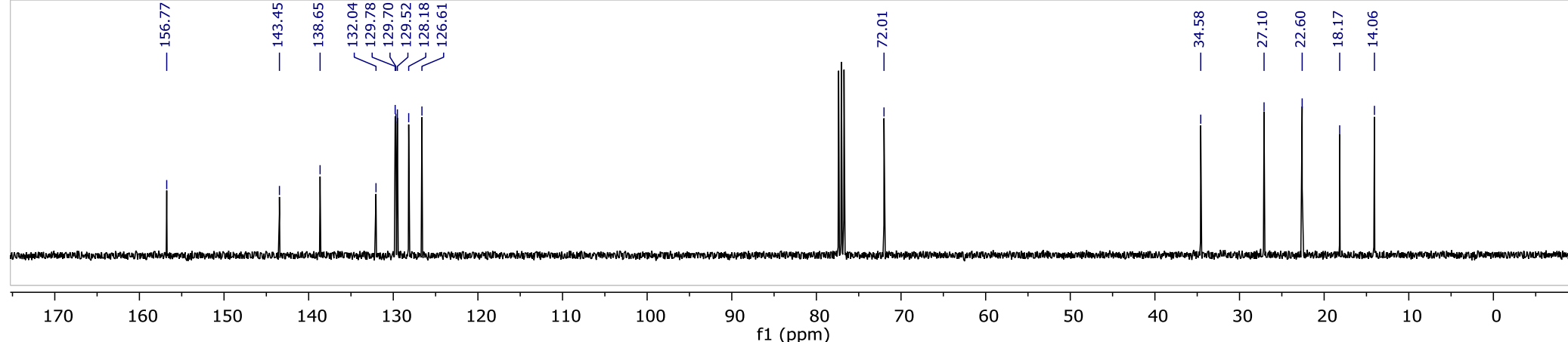


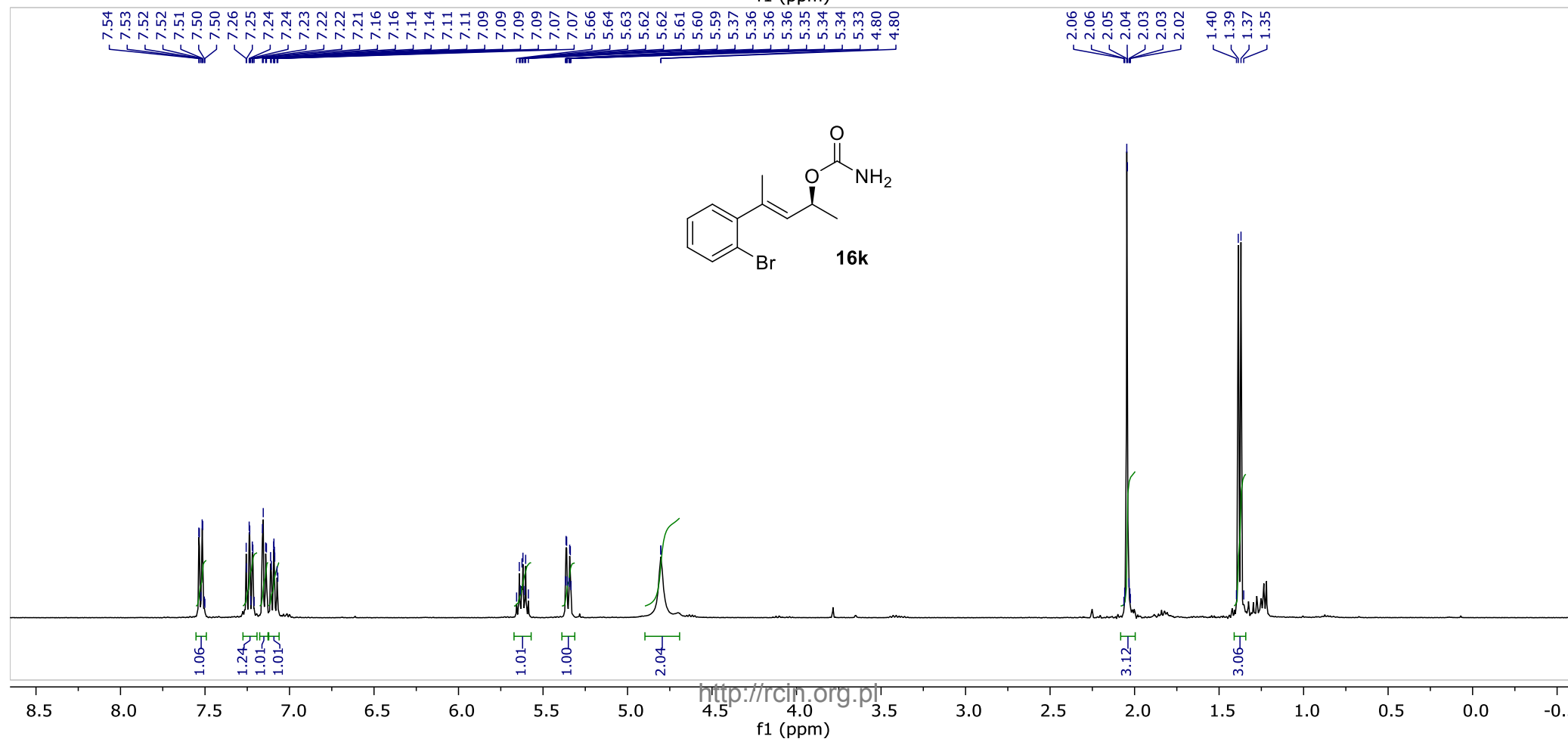
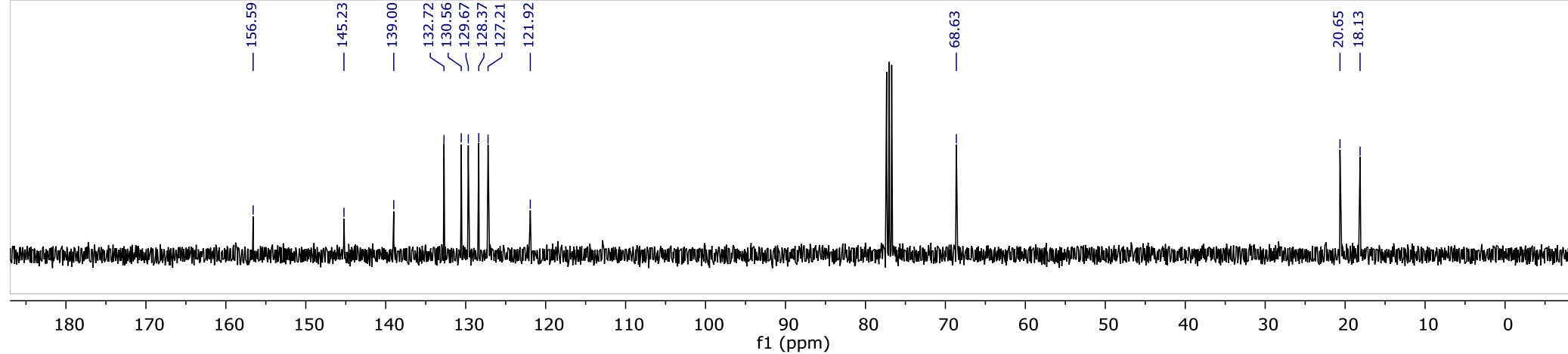


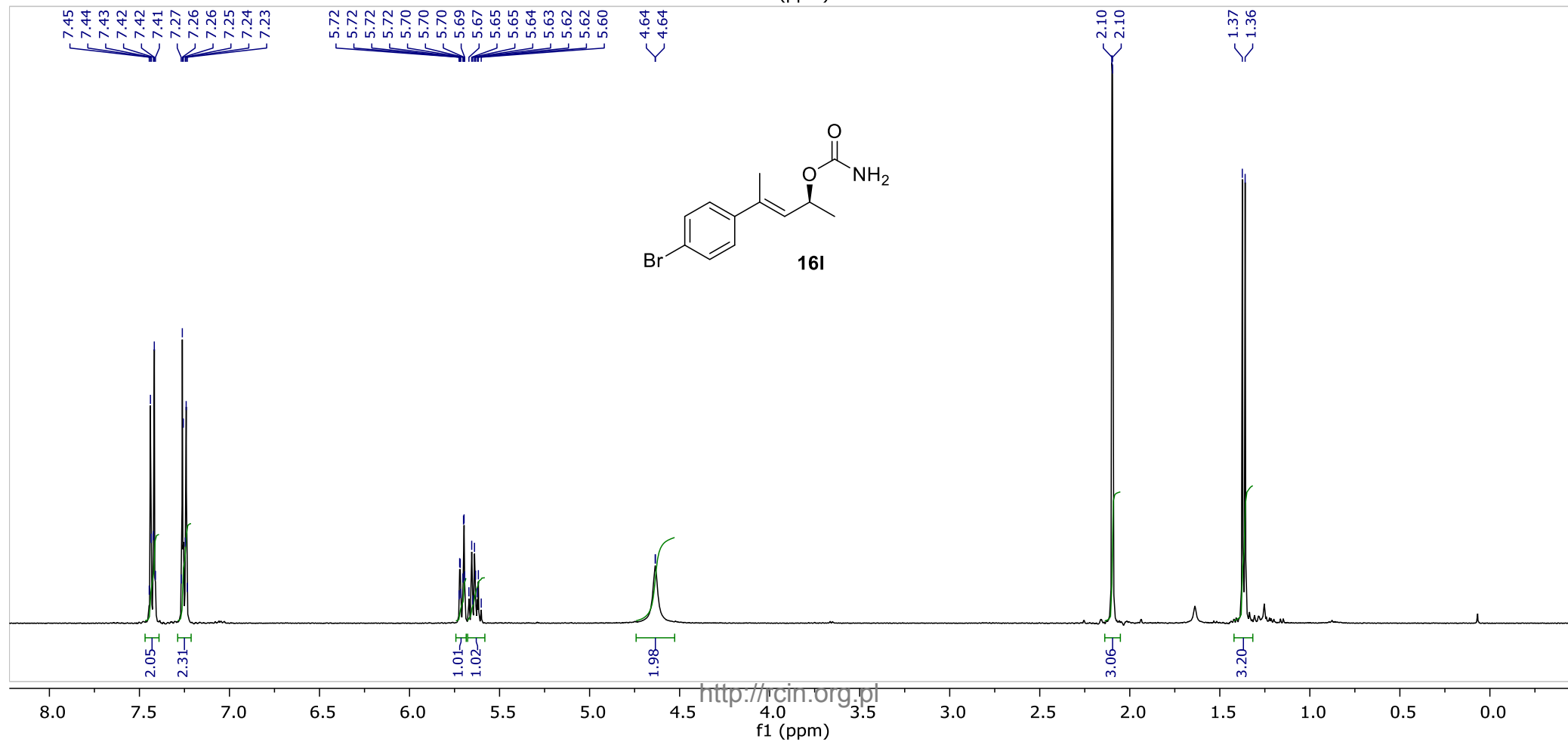
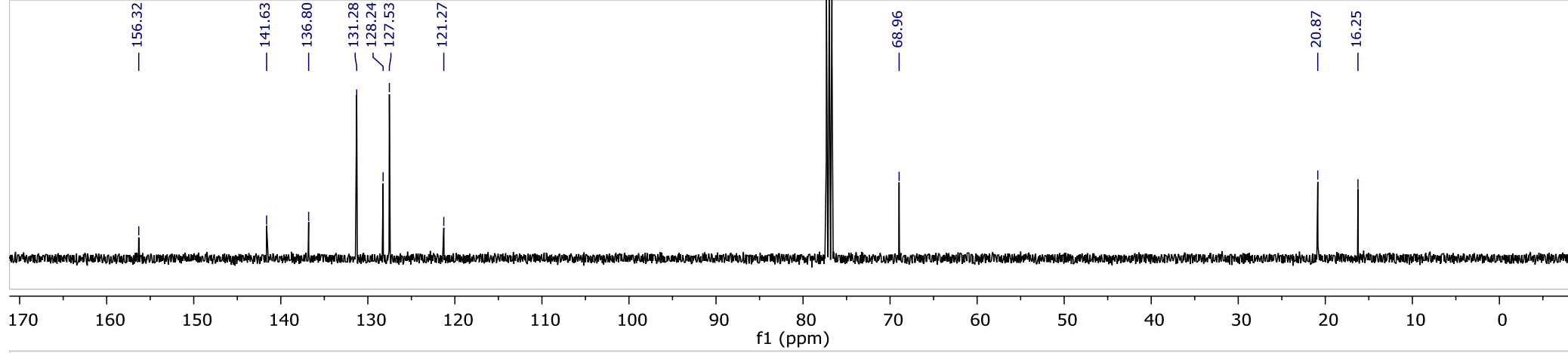




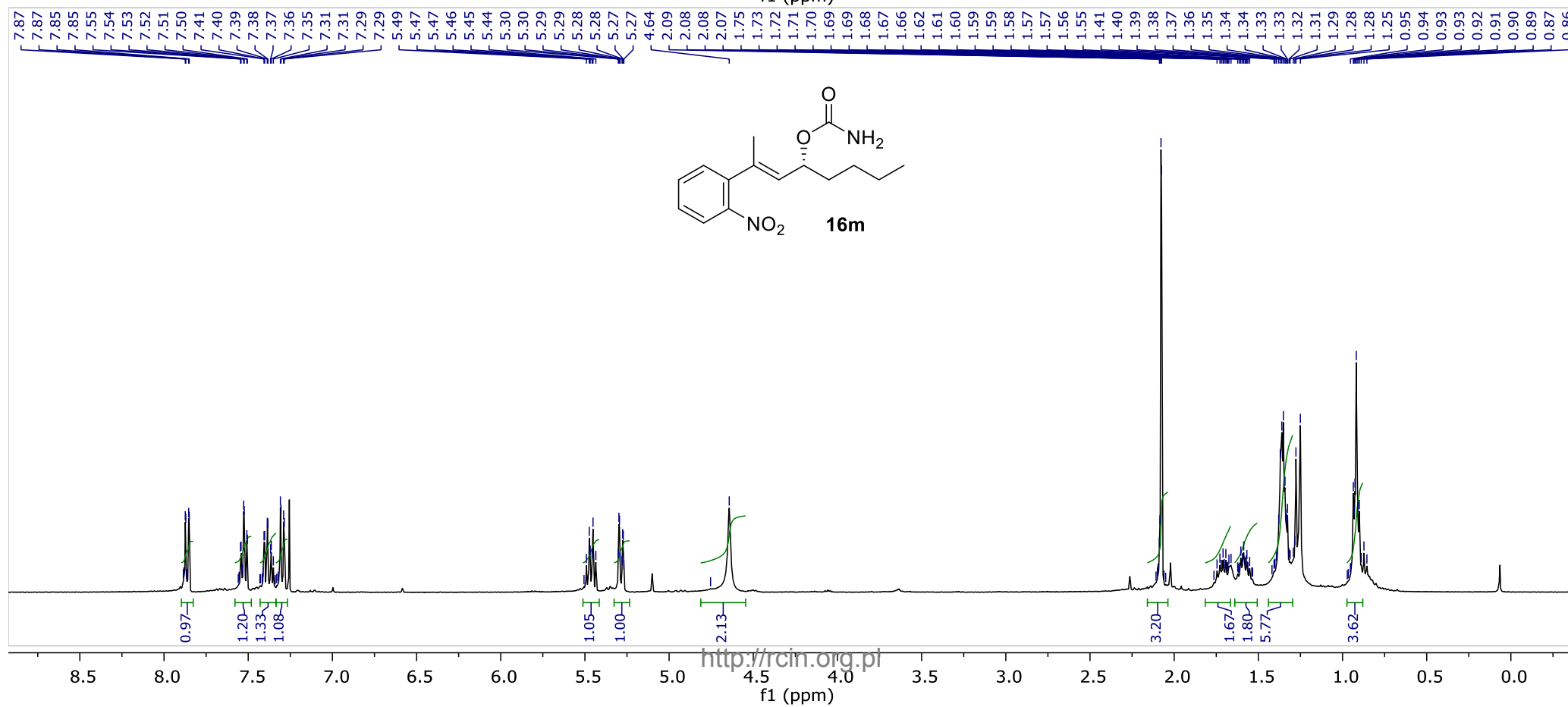
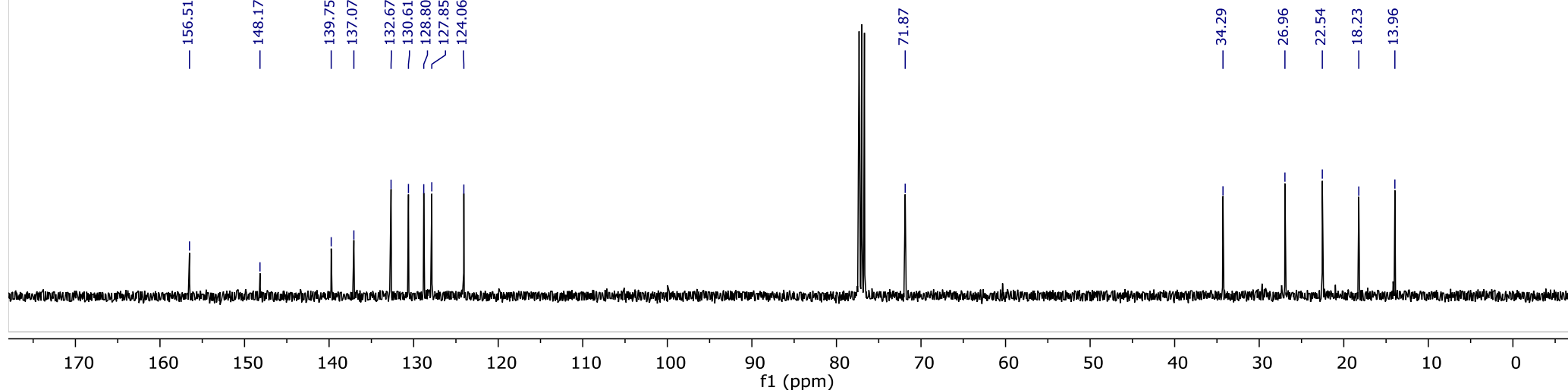


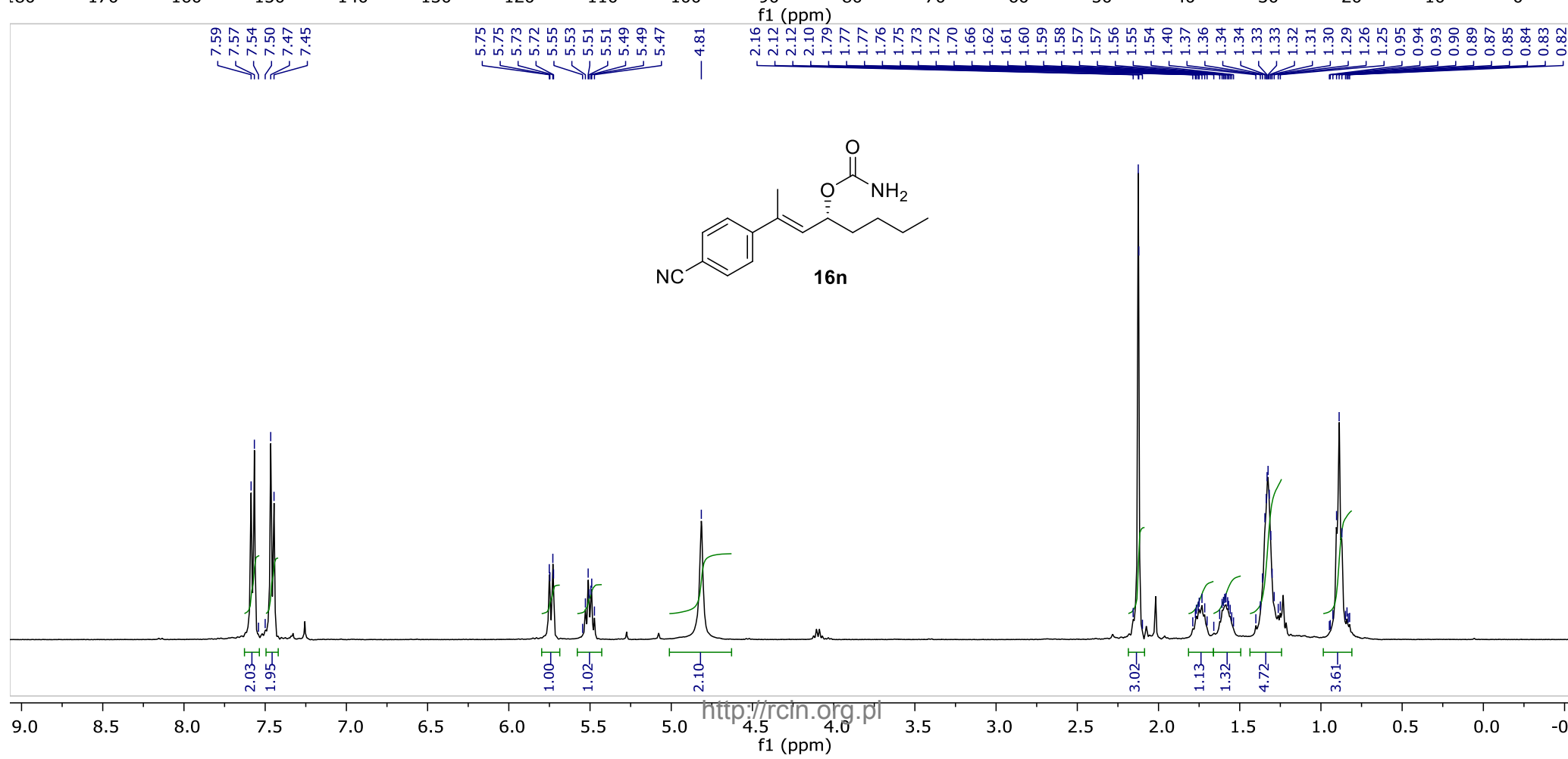
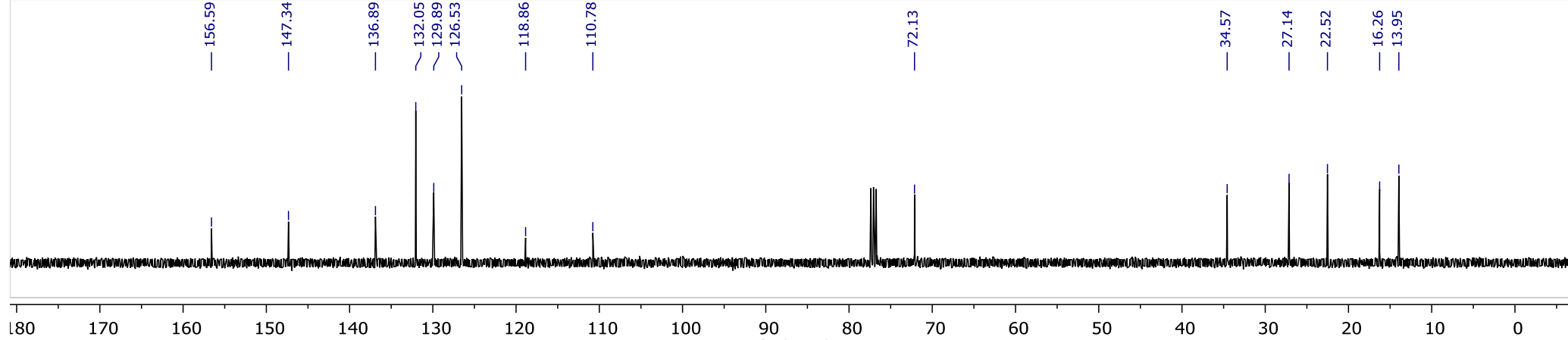


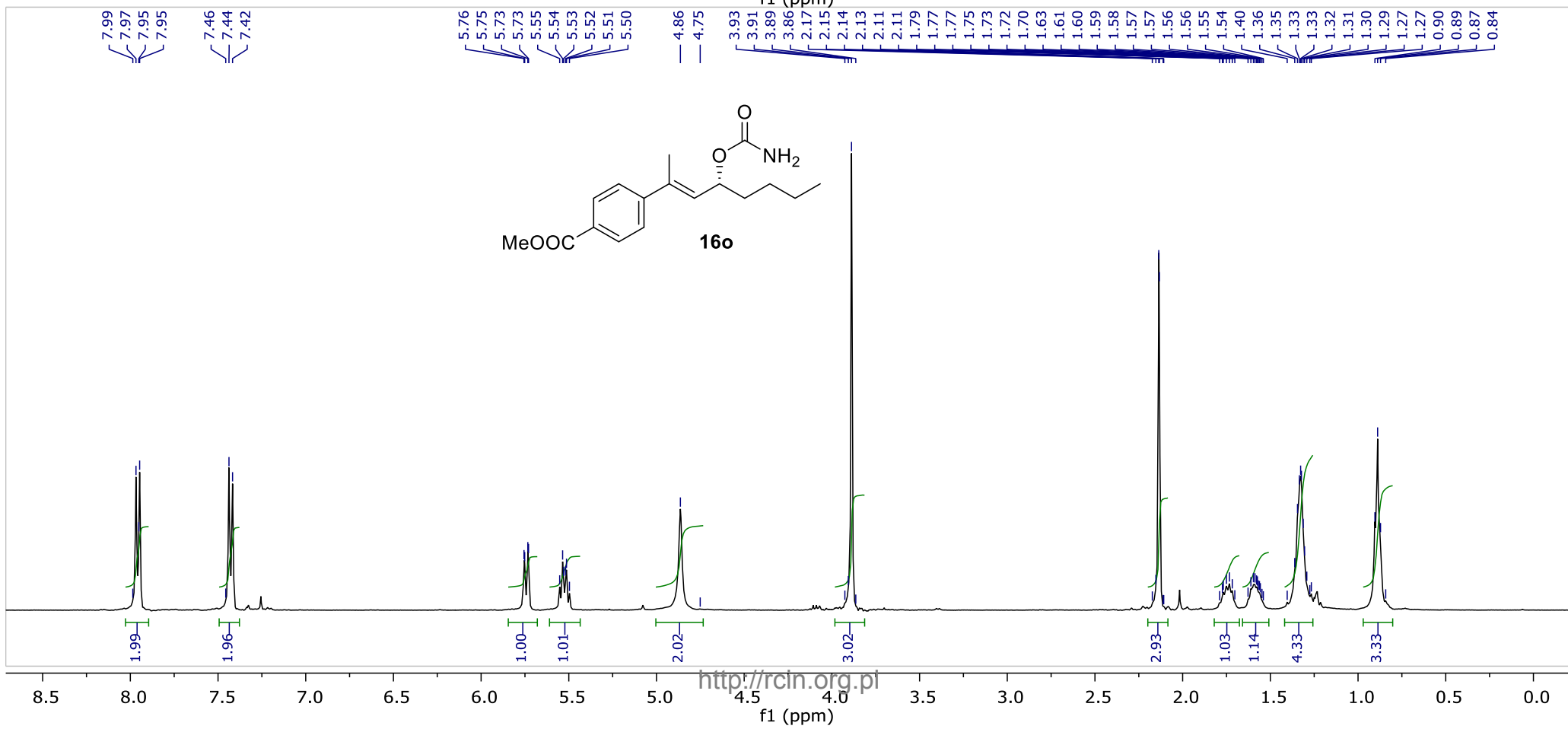
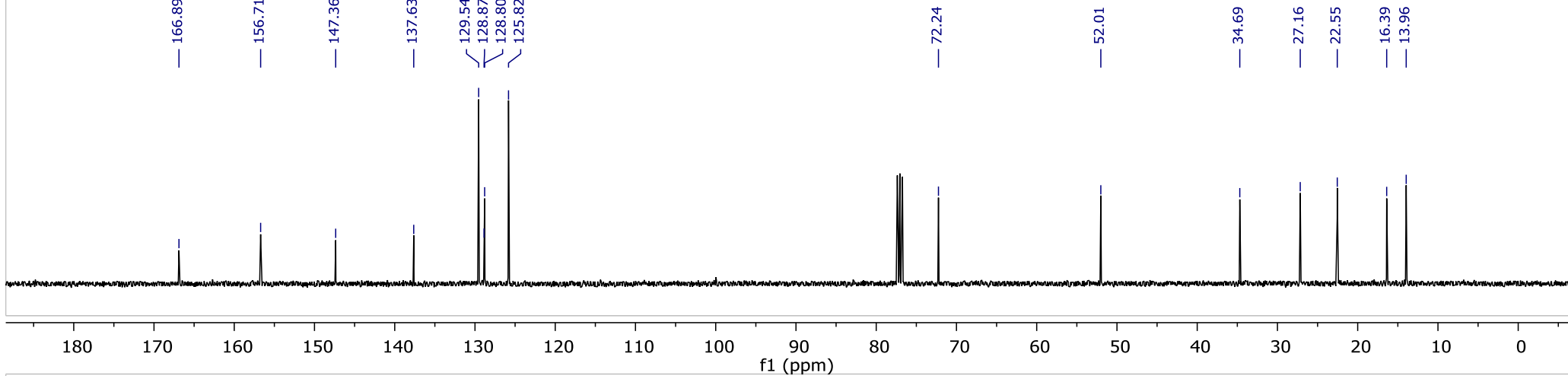


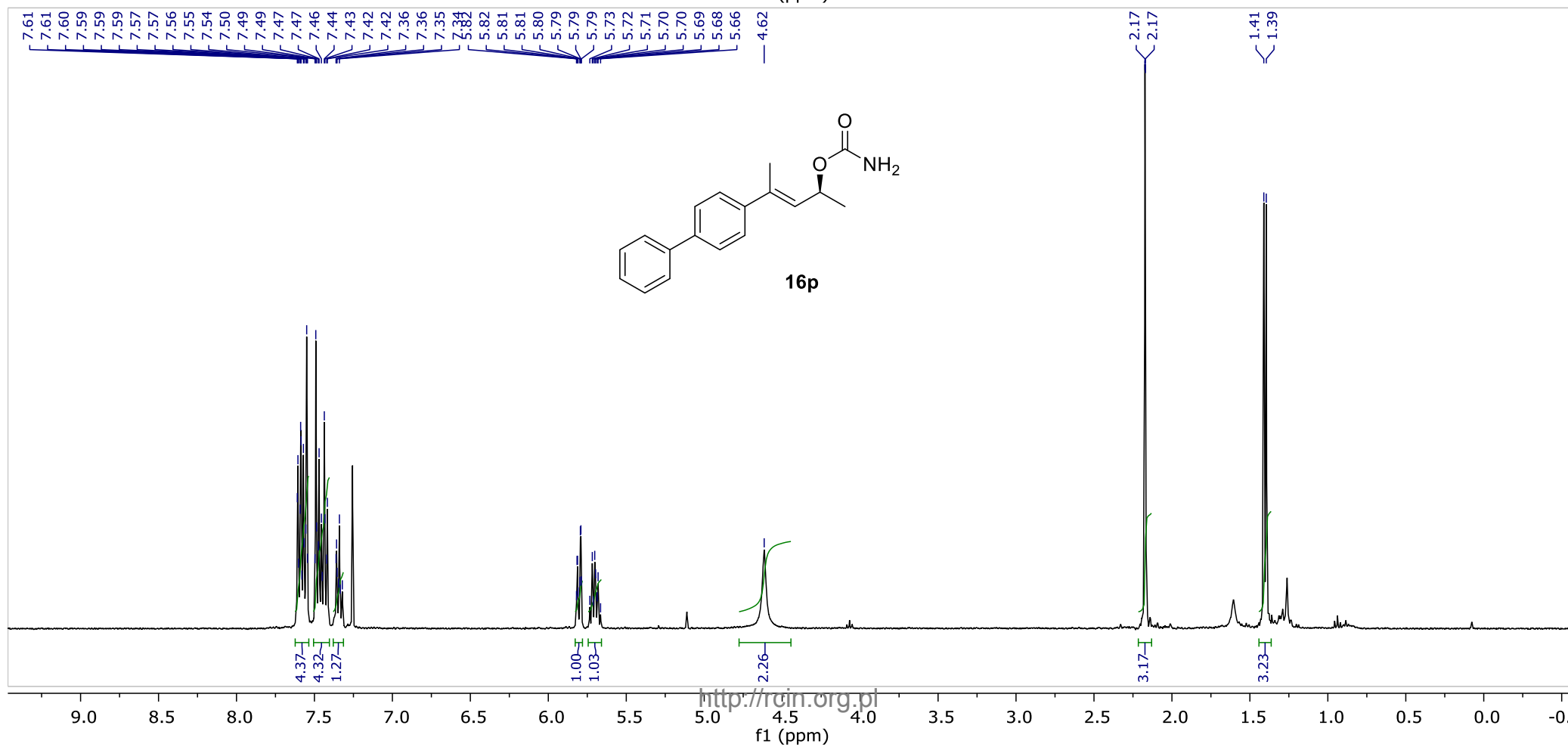
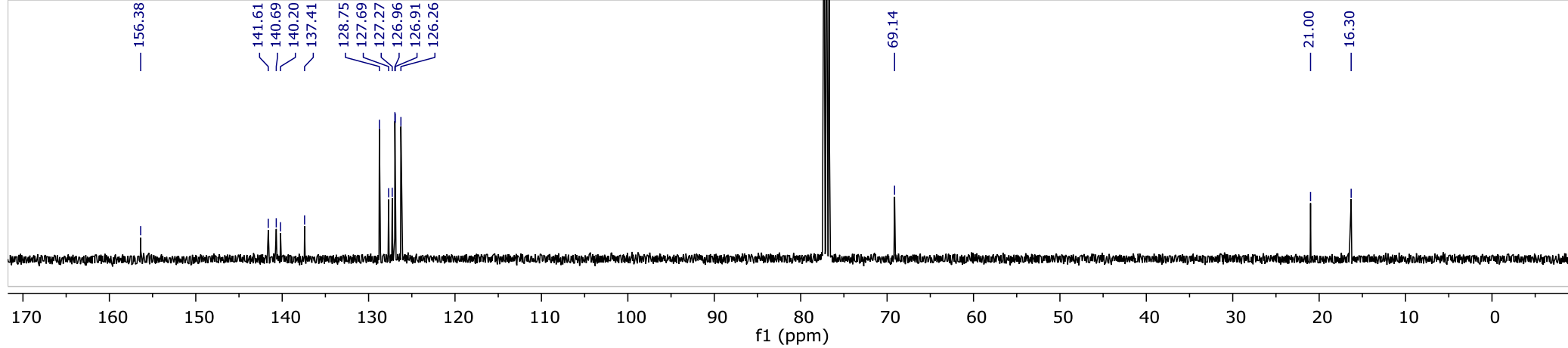


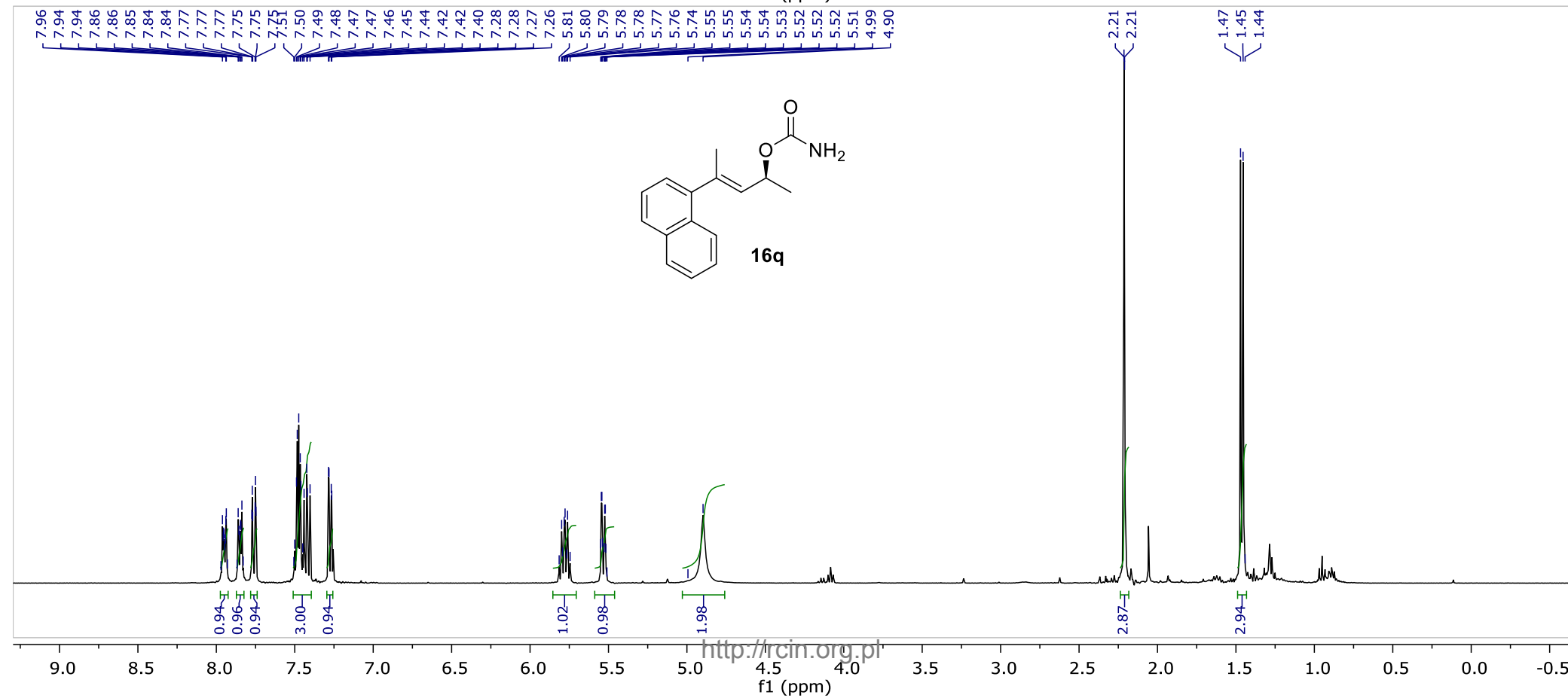
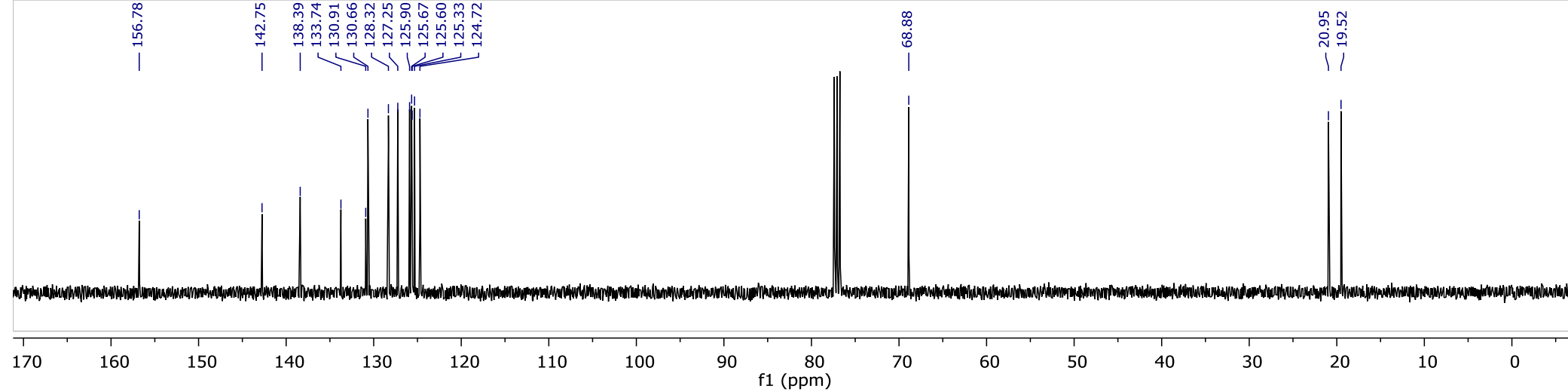


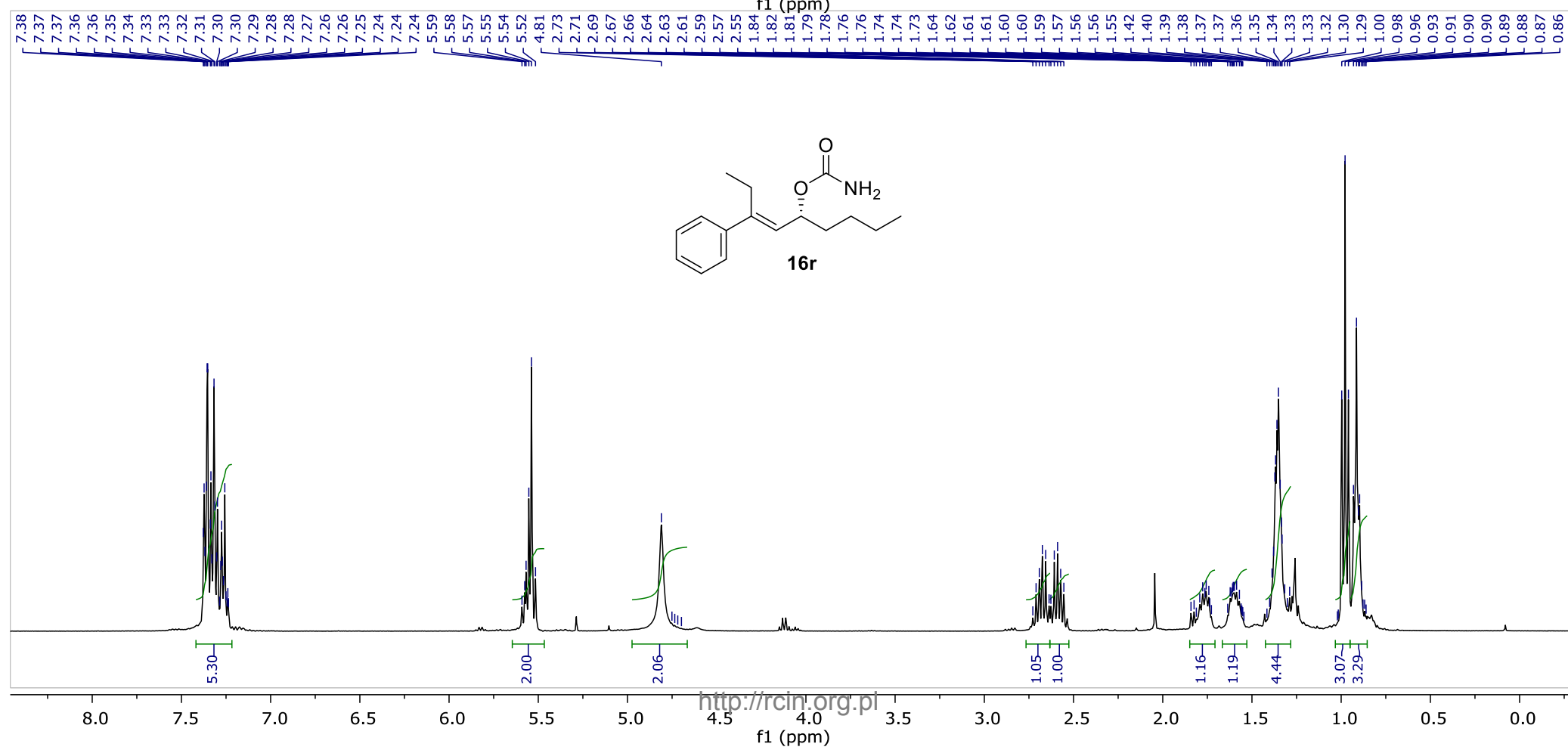
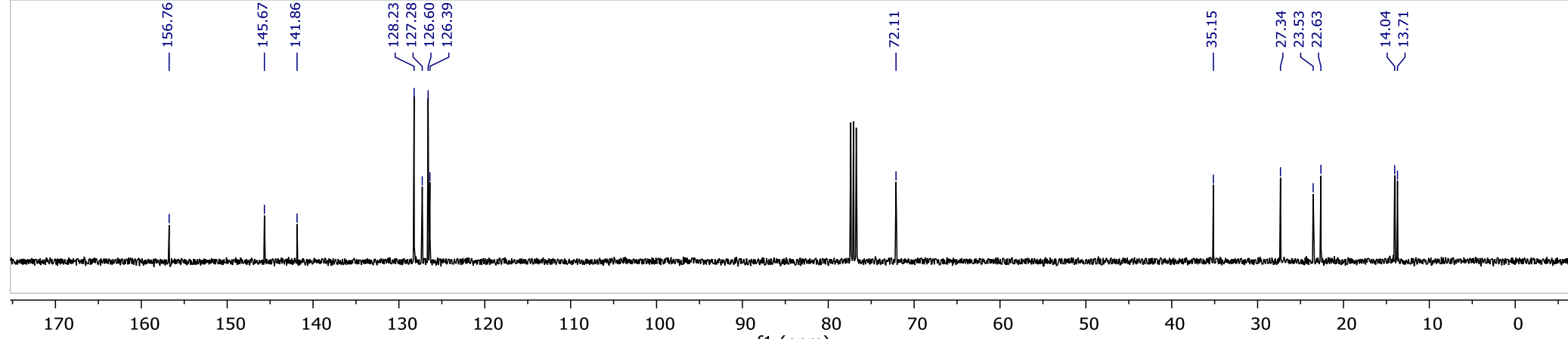


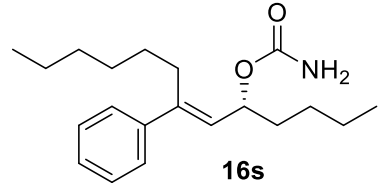
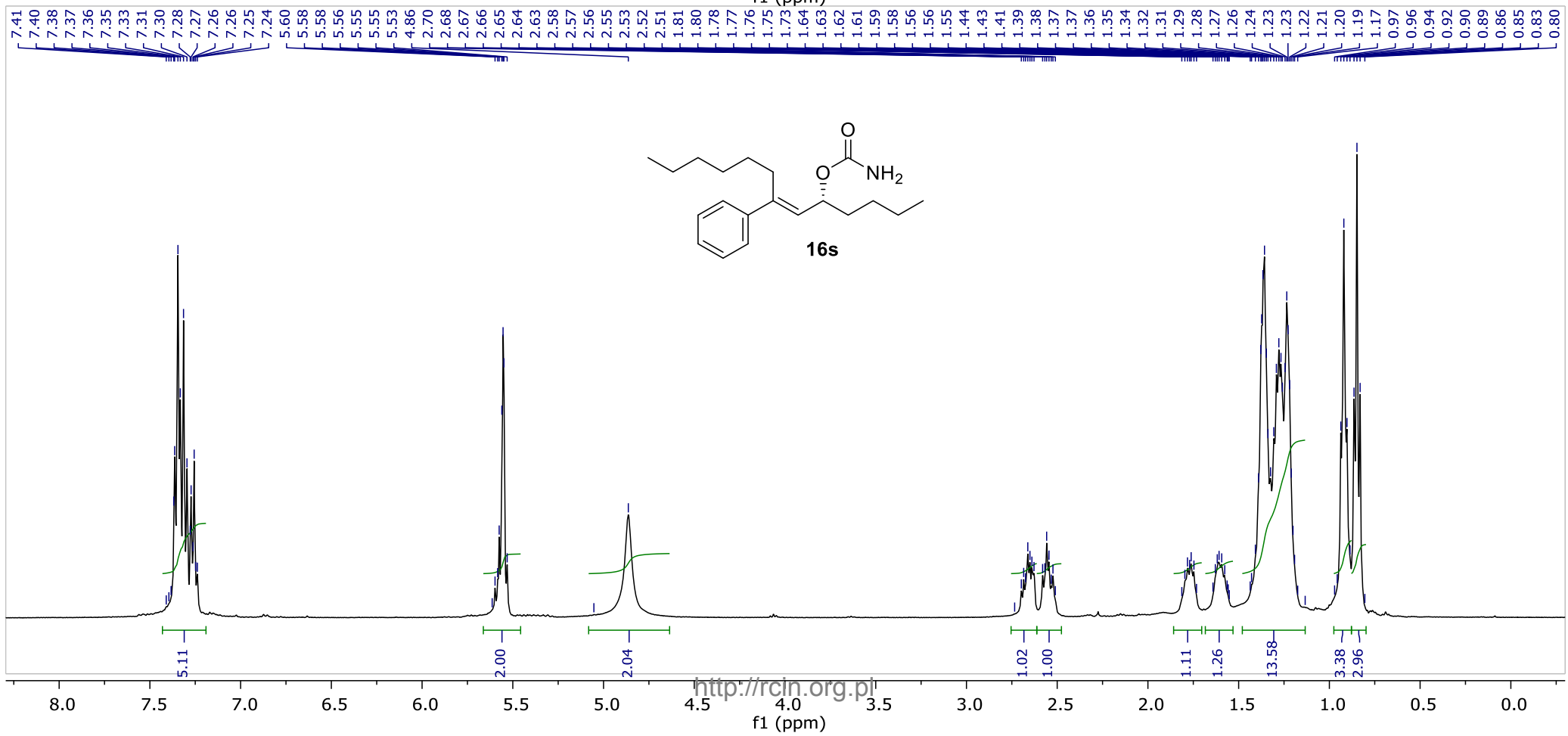
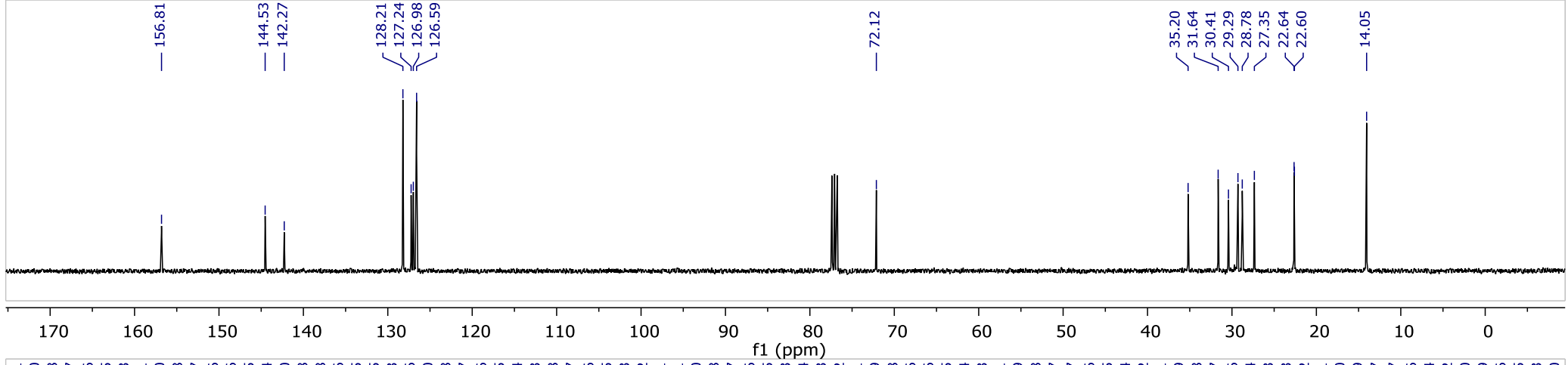


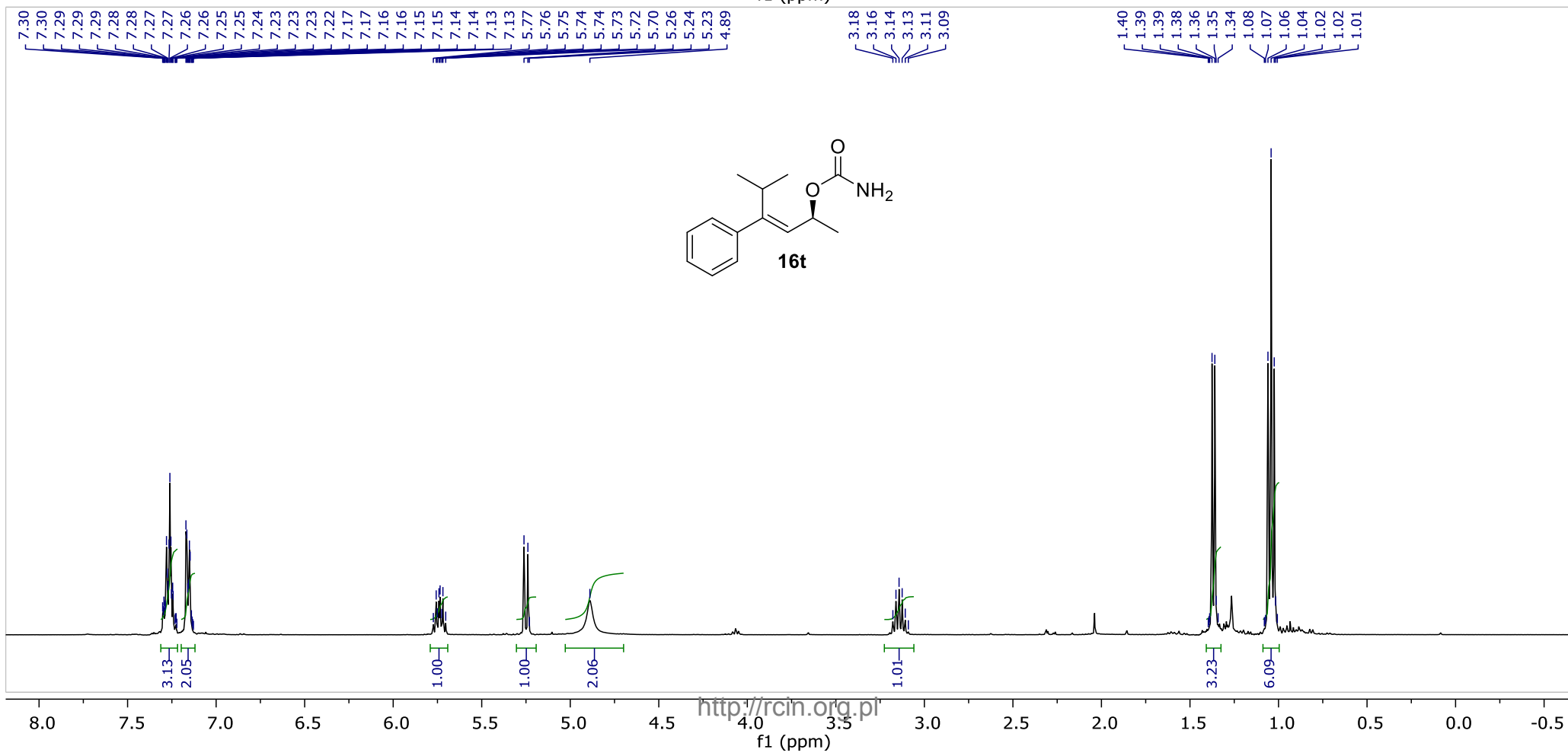
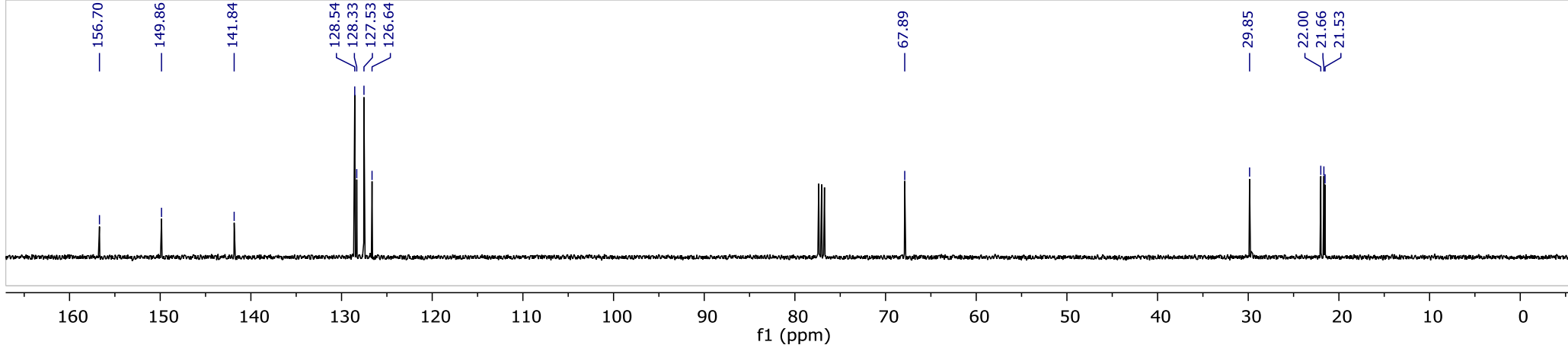




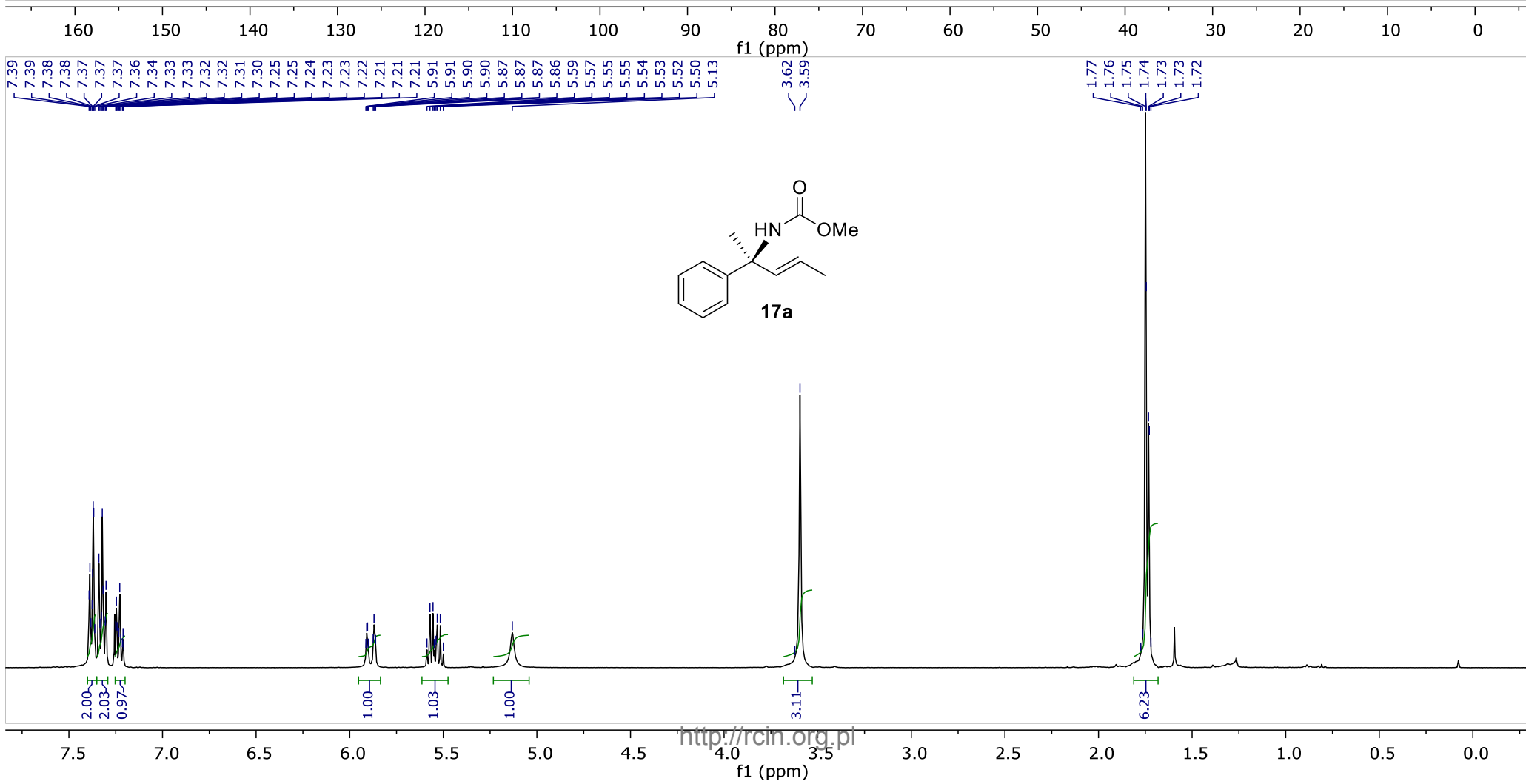
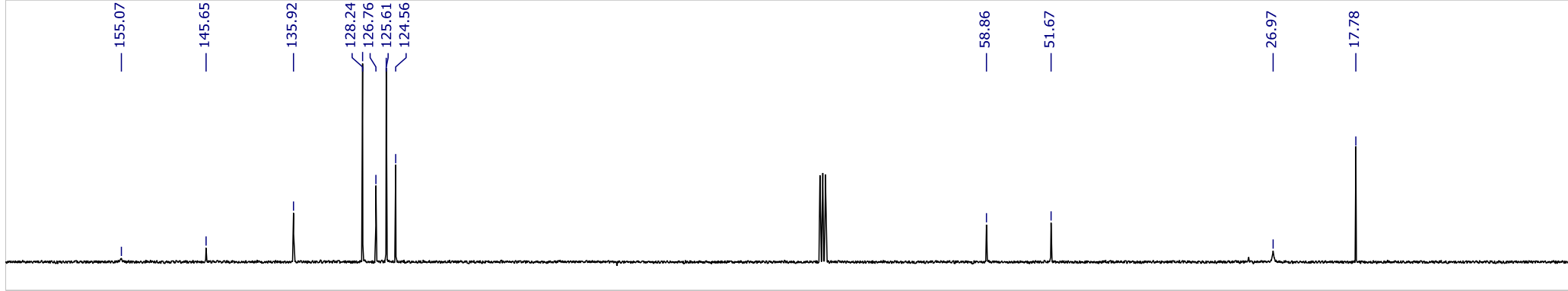


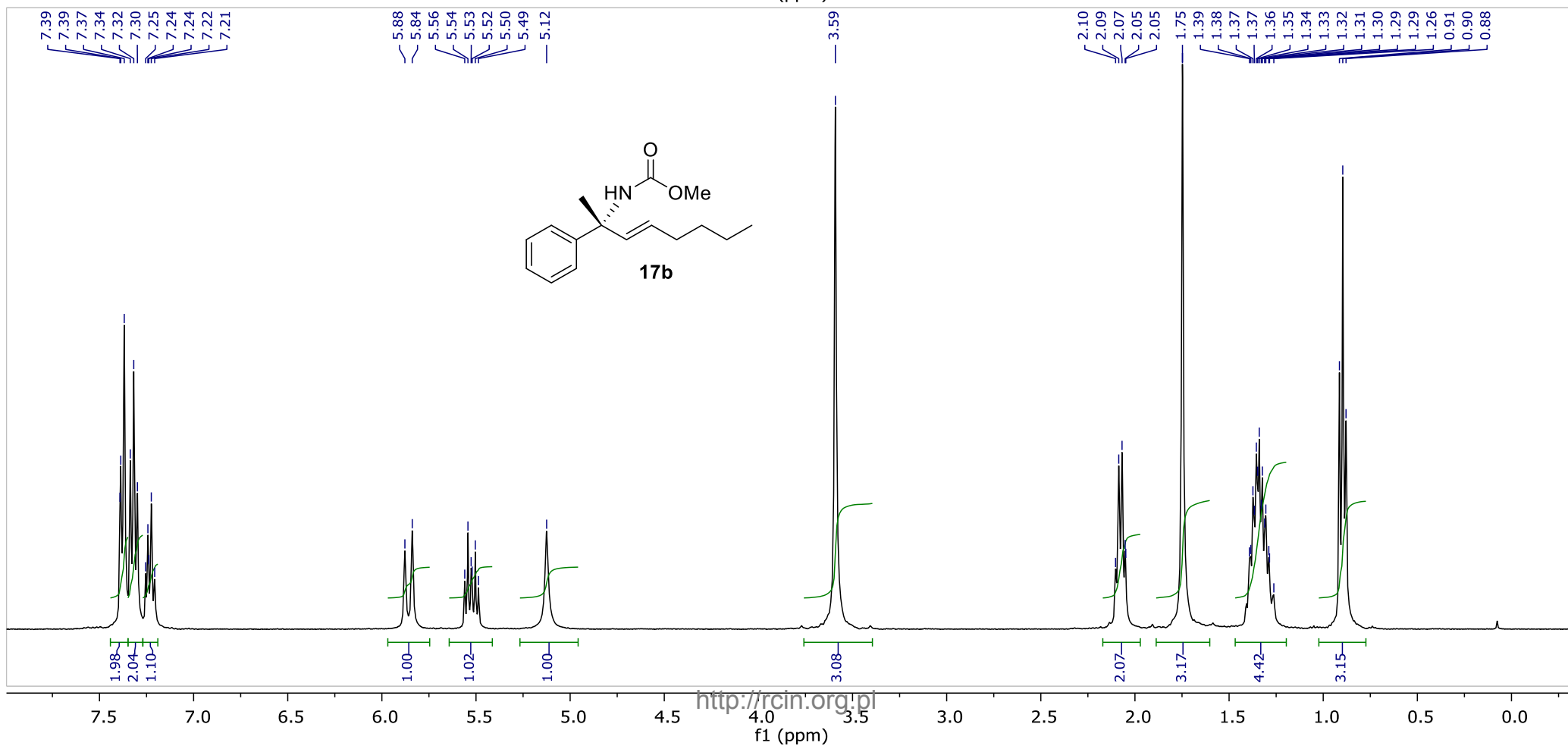
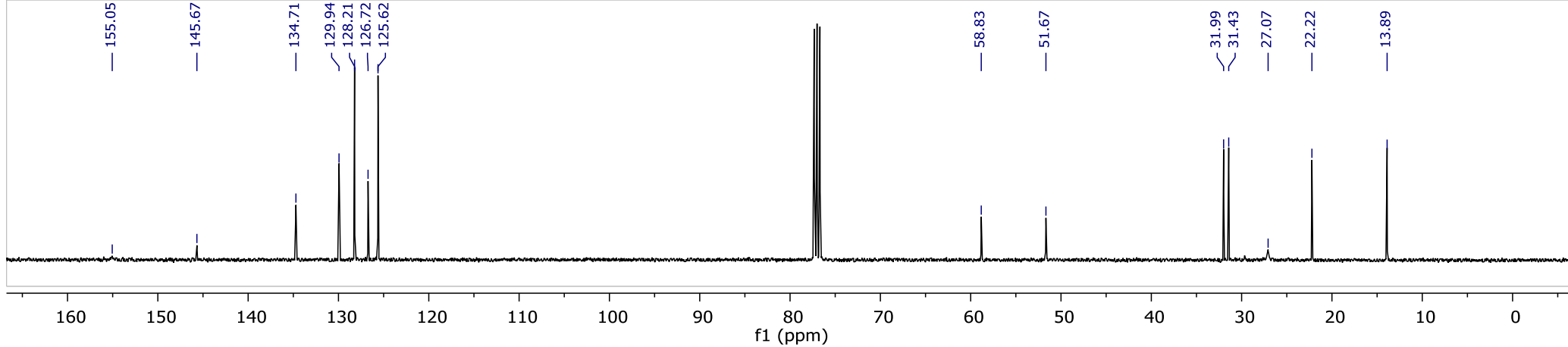






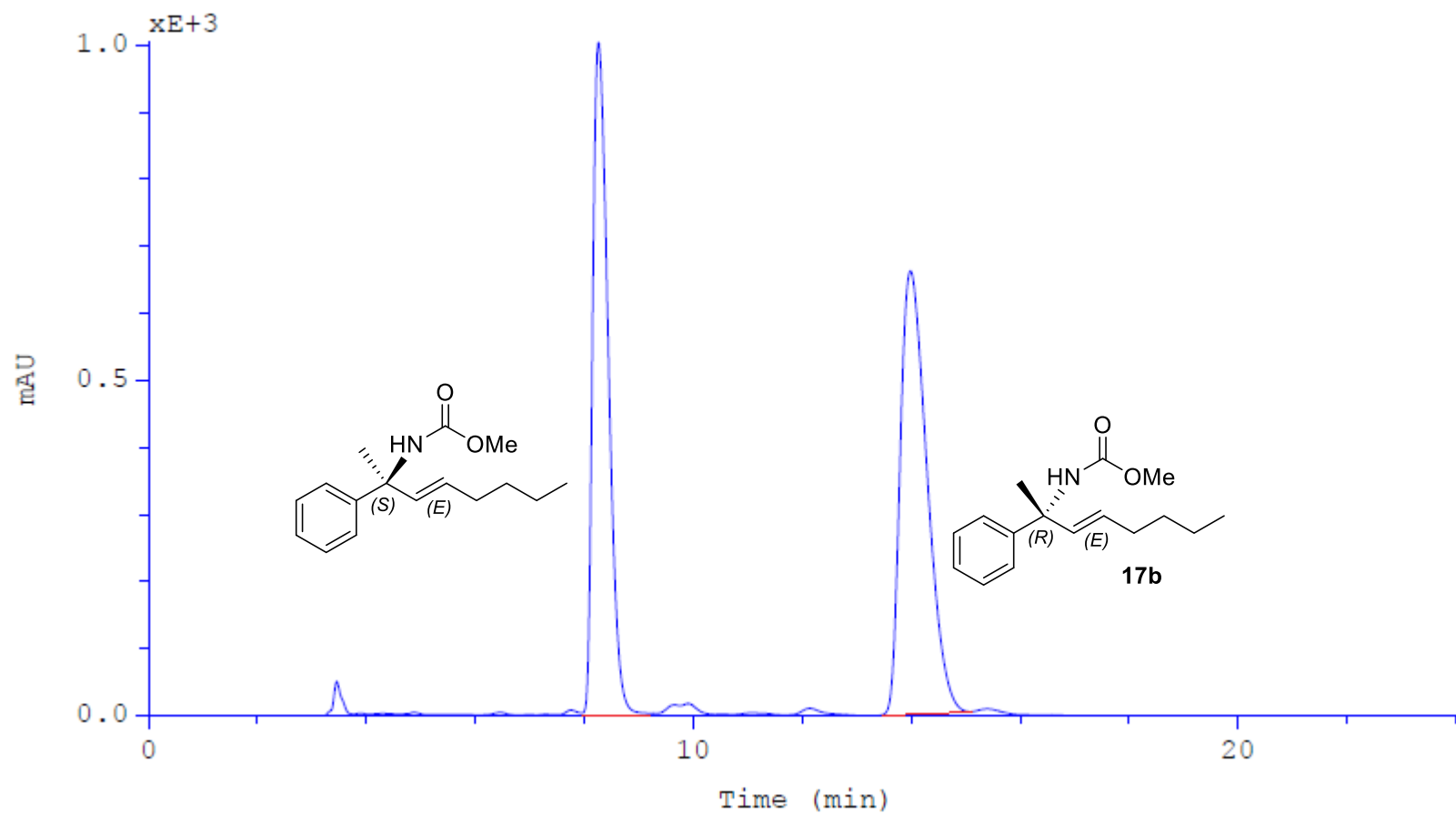






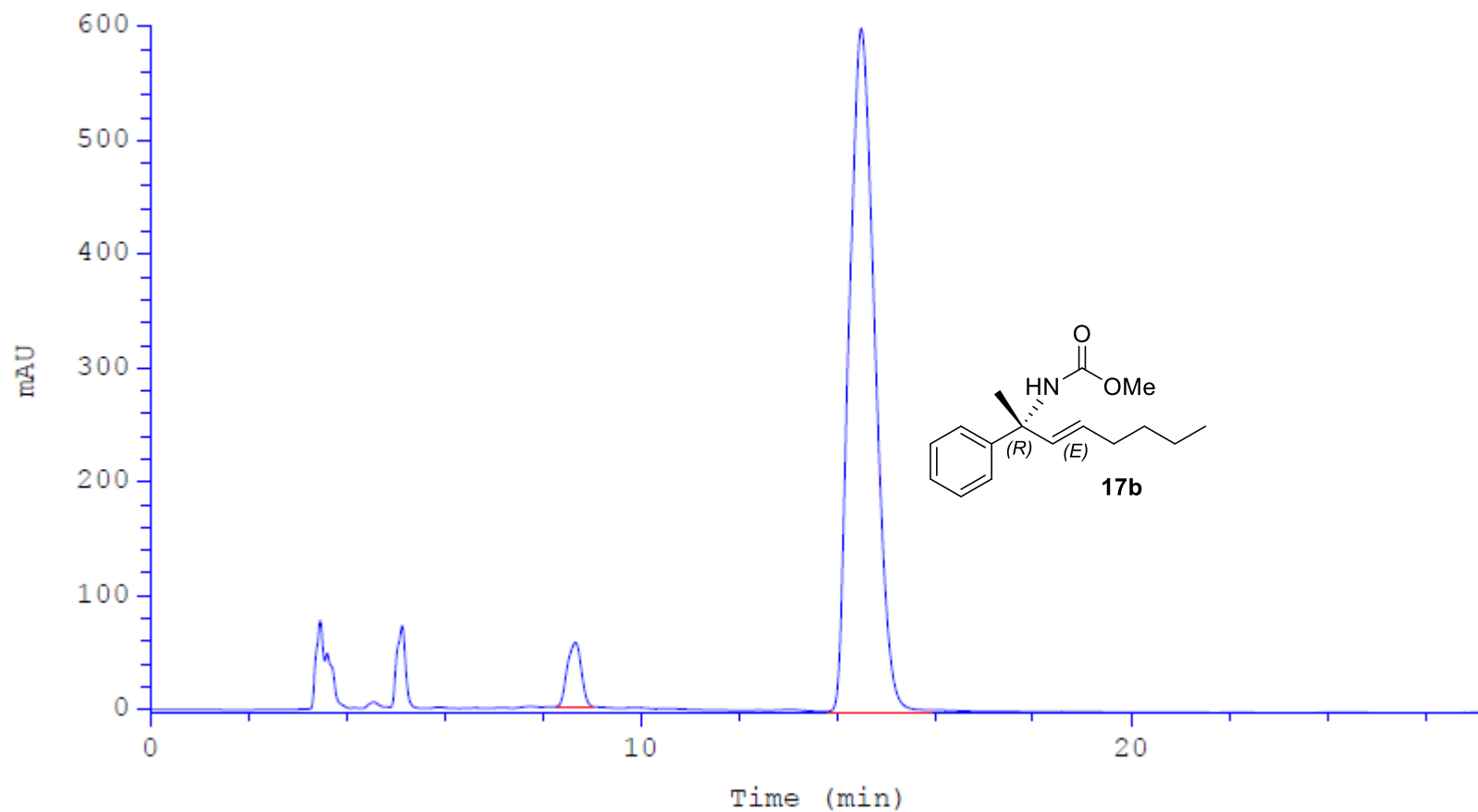
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

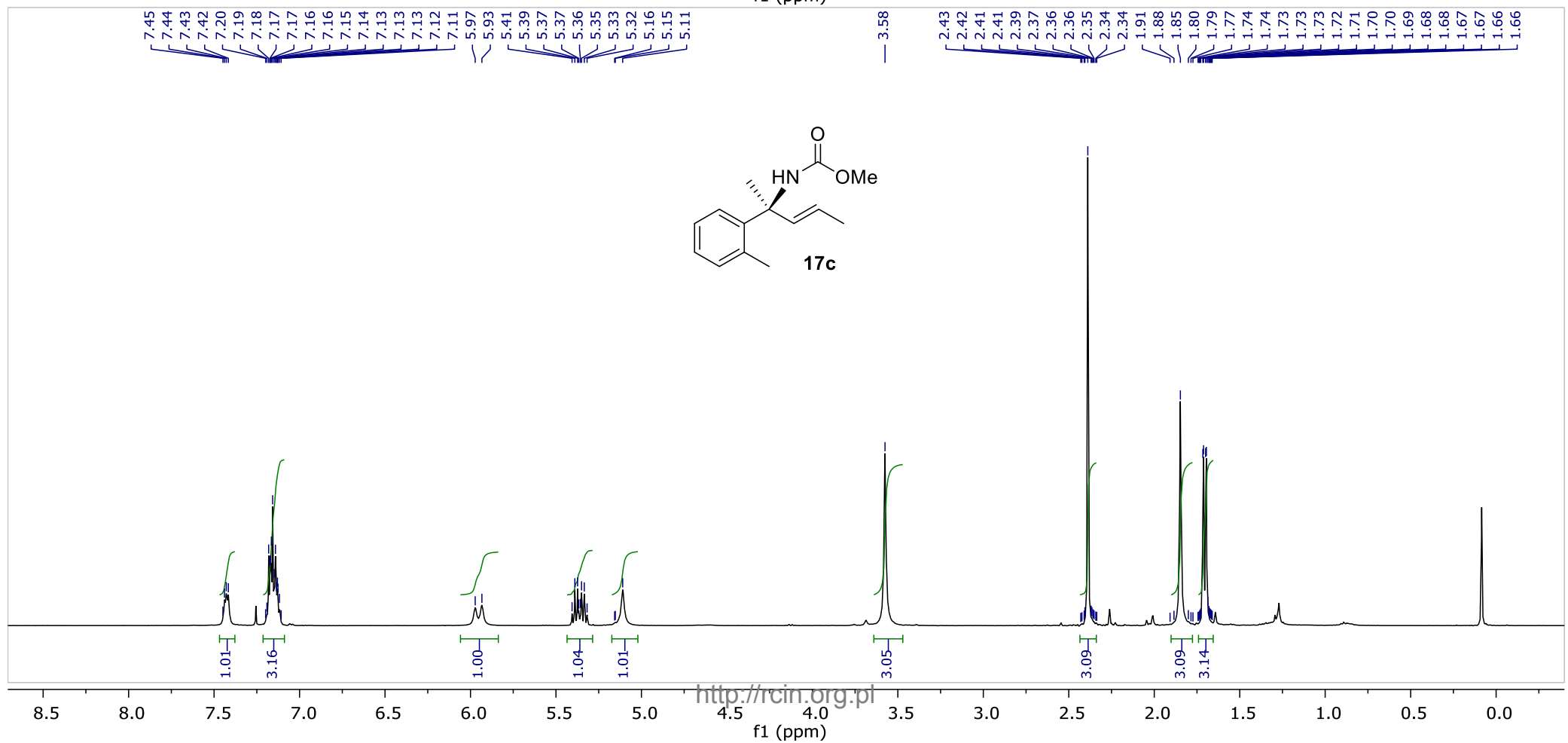
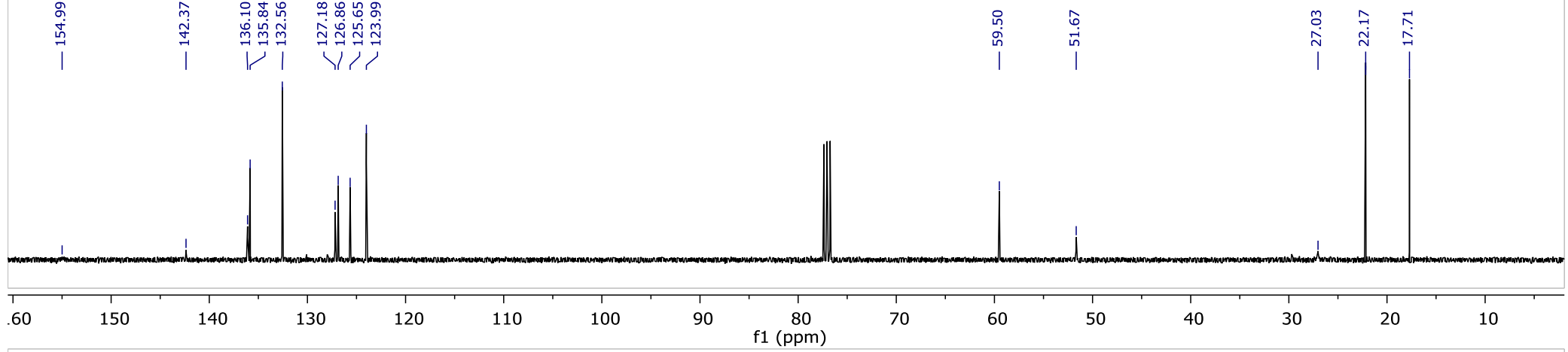
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.253	7.96	9.11	328.771	999.66	46.9562	0.312
2	13.989	13.48	14.93	371.394	659.341	53.0438	0.536

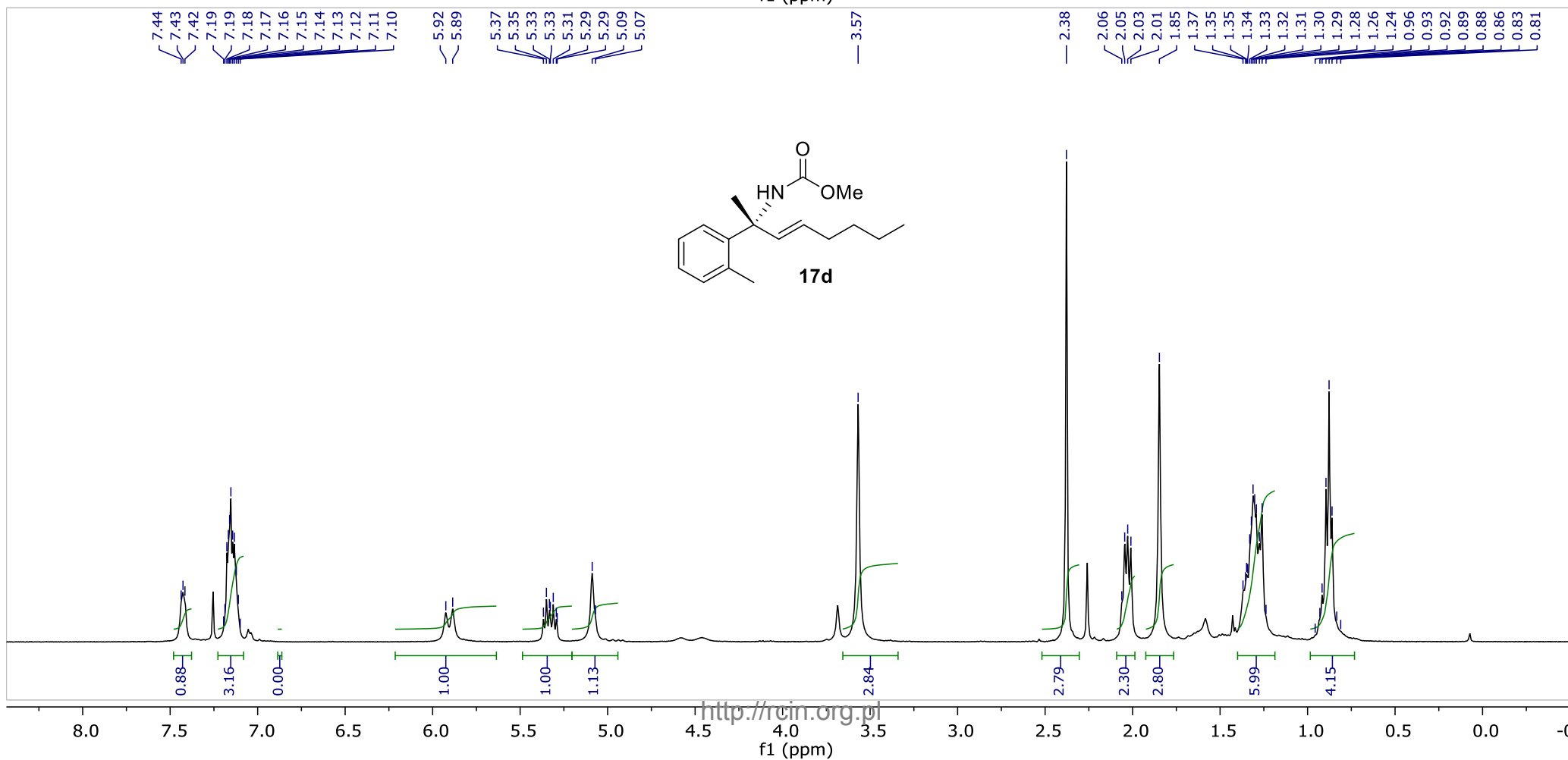
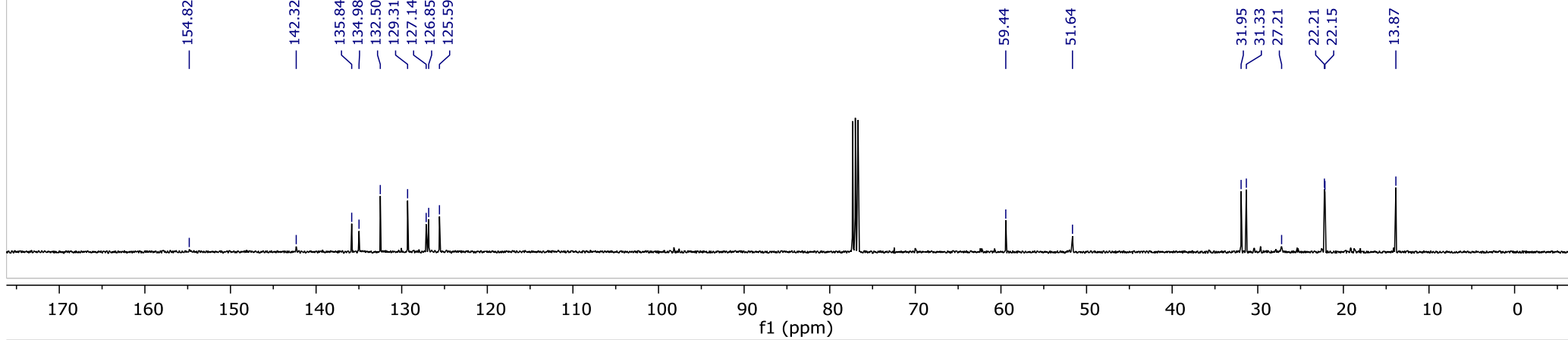


Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.670	8.38	8.99	16.4914	53.2211	4.4119	0.316
2	14.505	13.84	15.93	357.3	599.355	95.5881	0.582

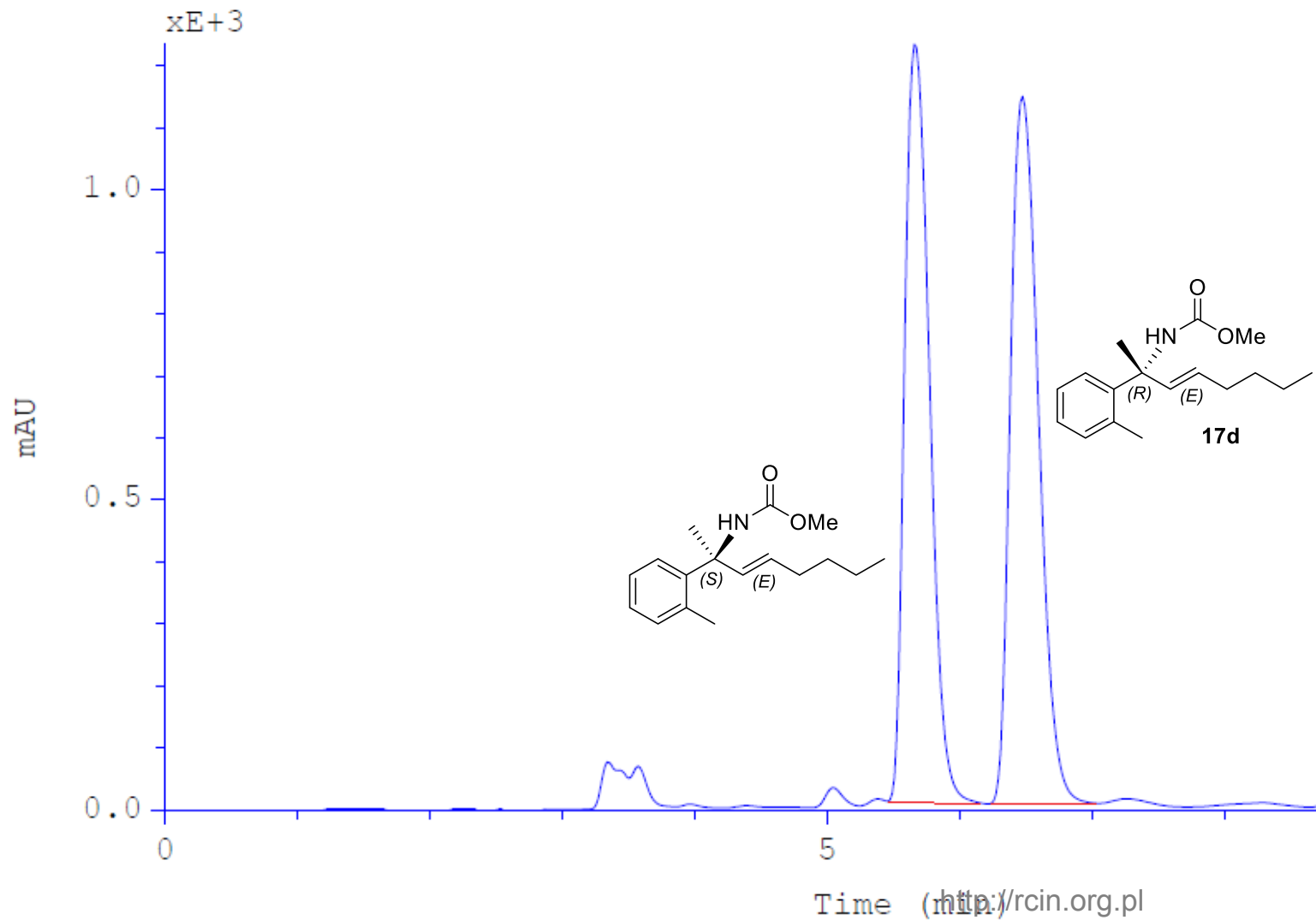






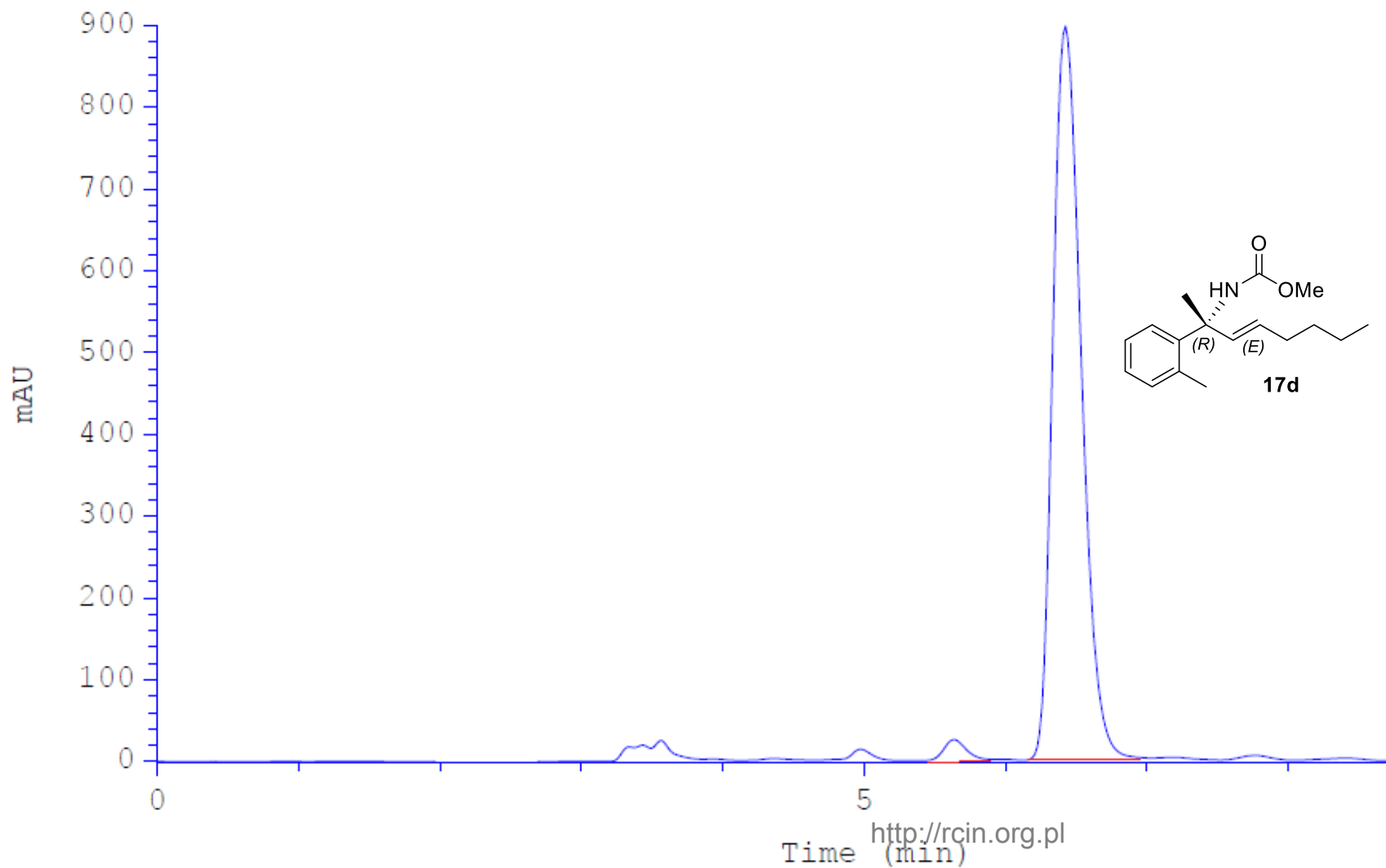
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.657	5.46	6.16	265.642	1221.88	48.6358	0.208
2	6.474	6.24	7.01	280.544	1140.44	51.3642	0.234

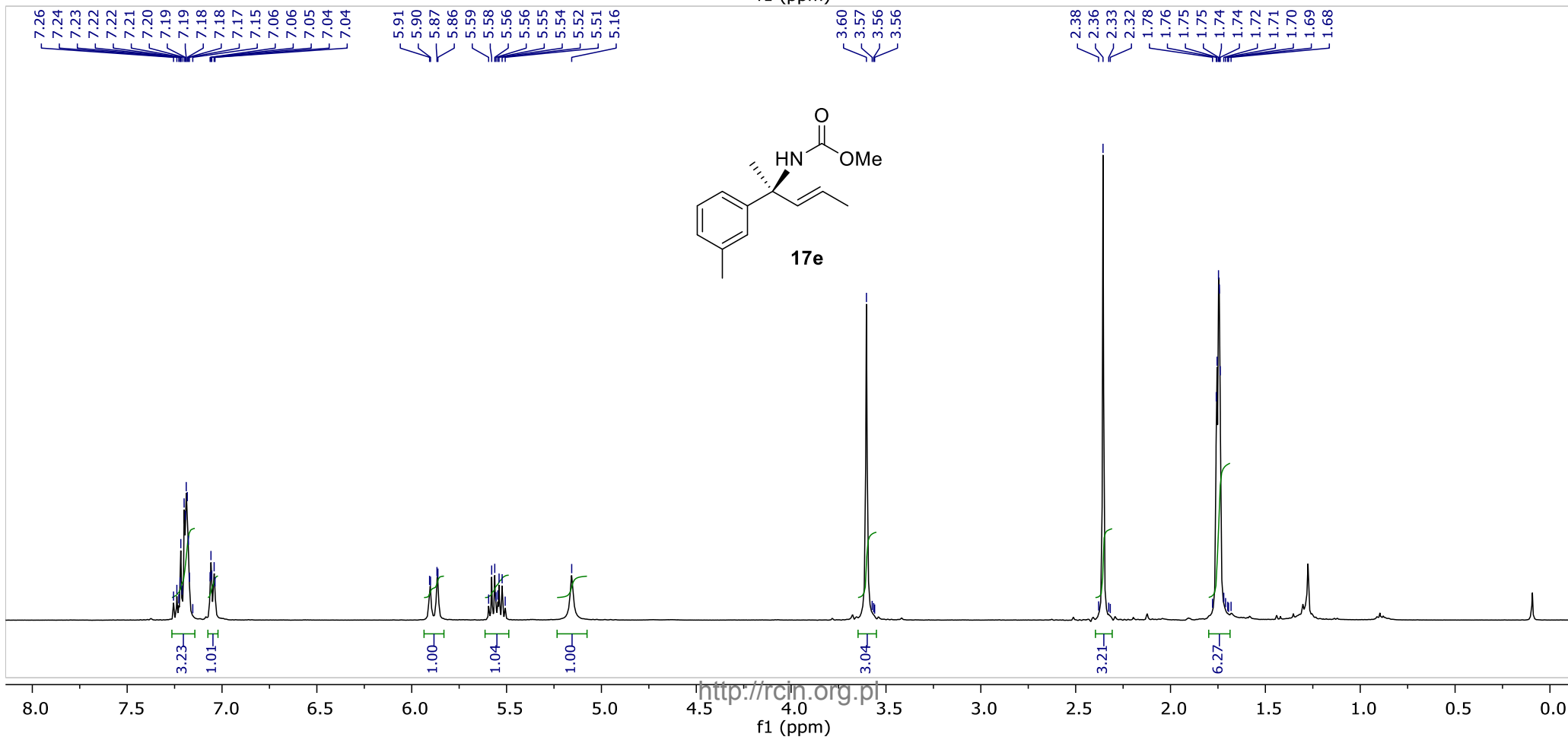
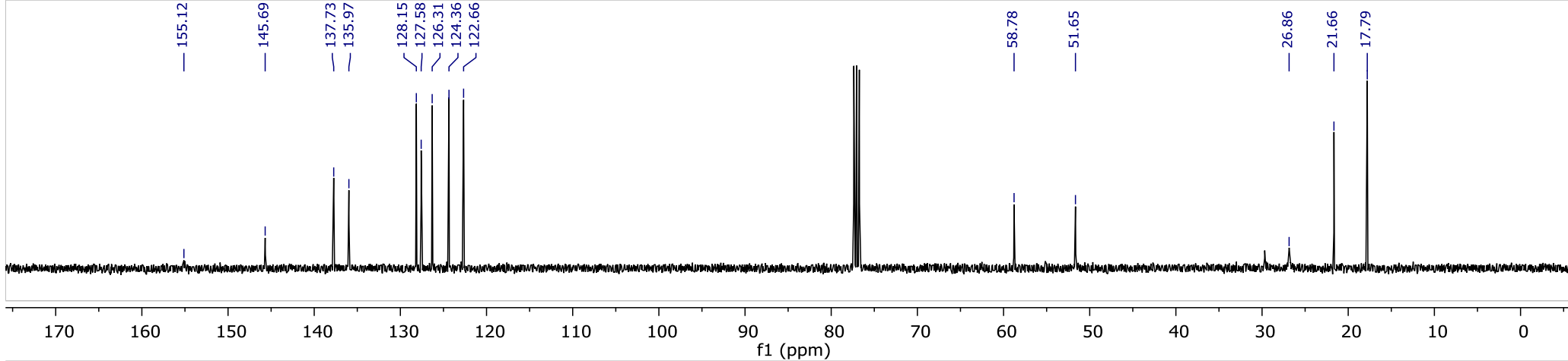


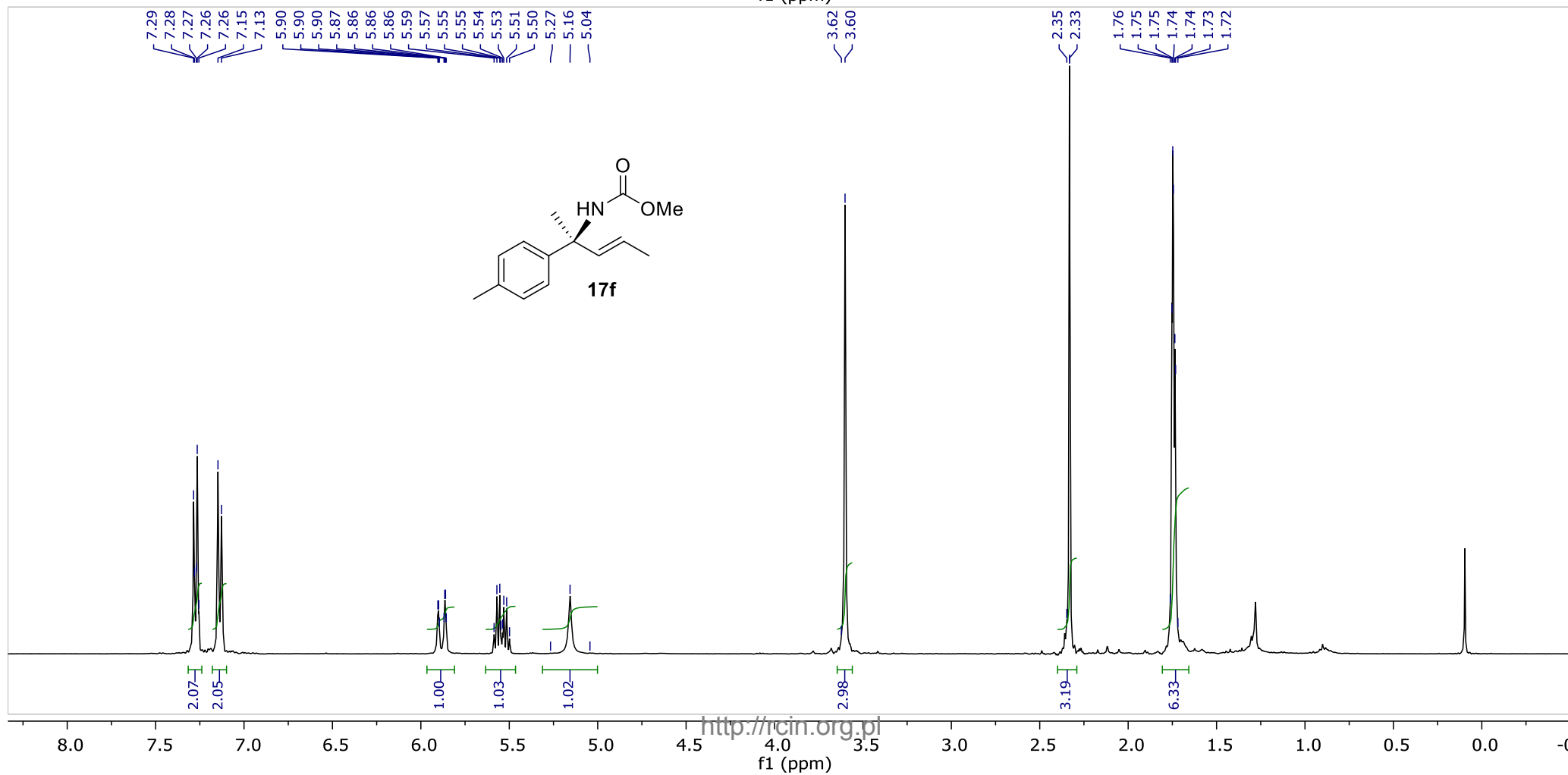
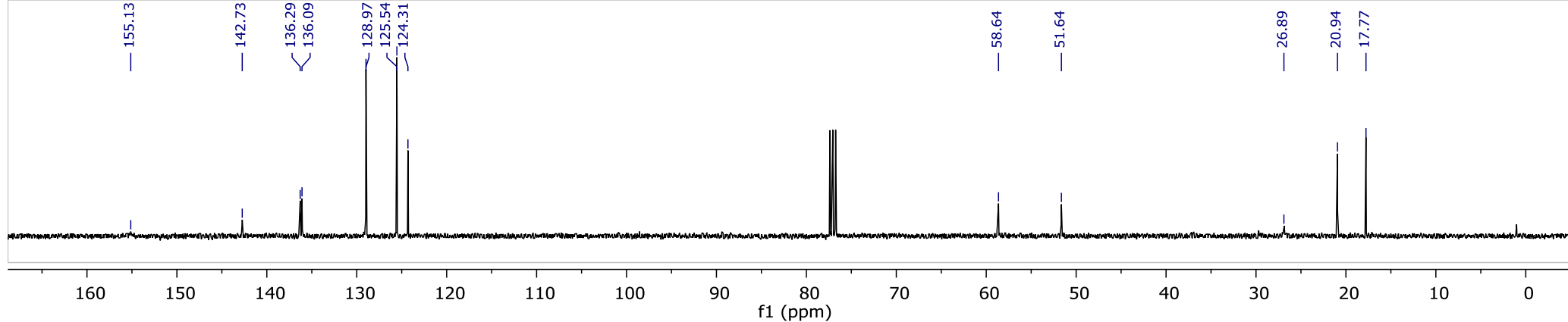
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

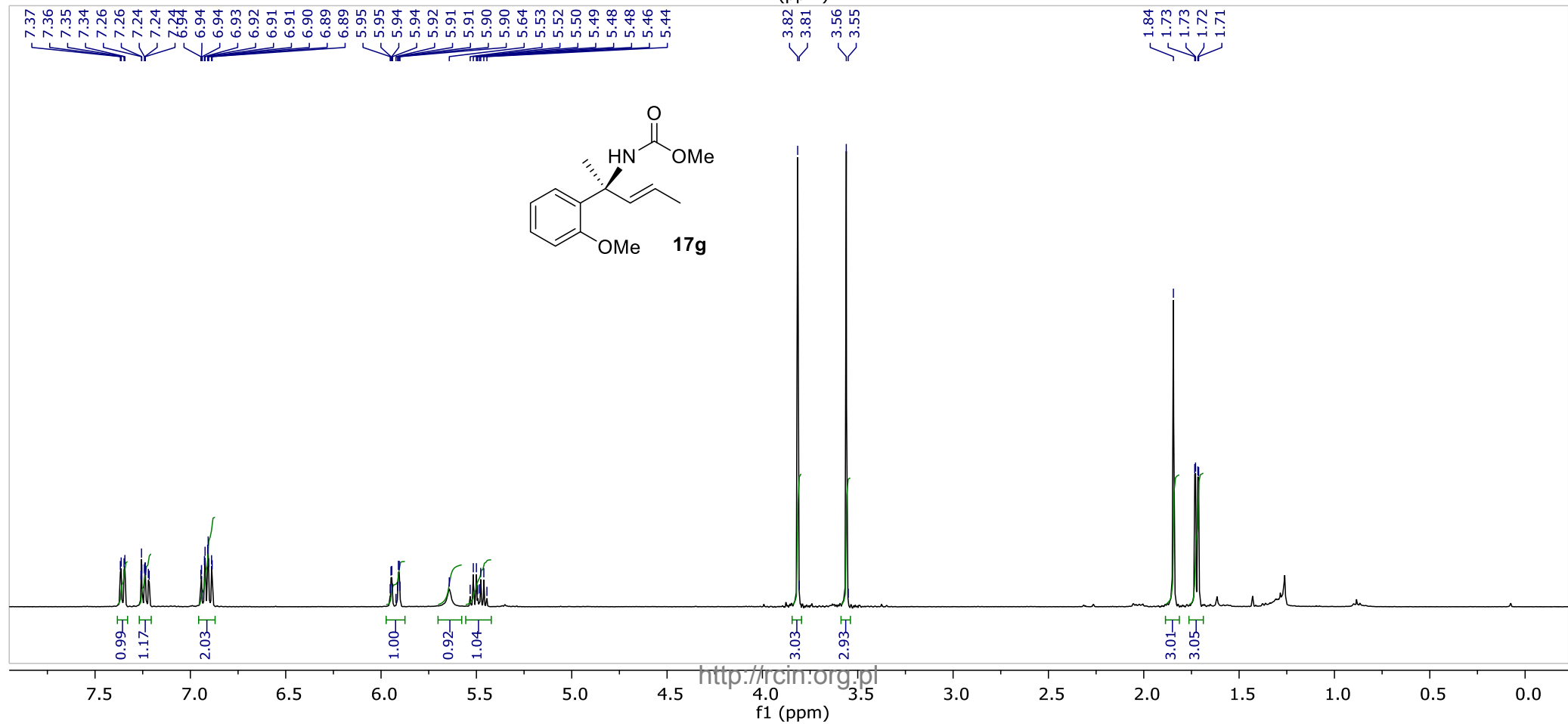
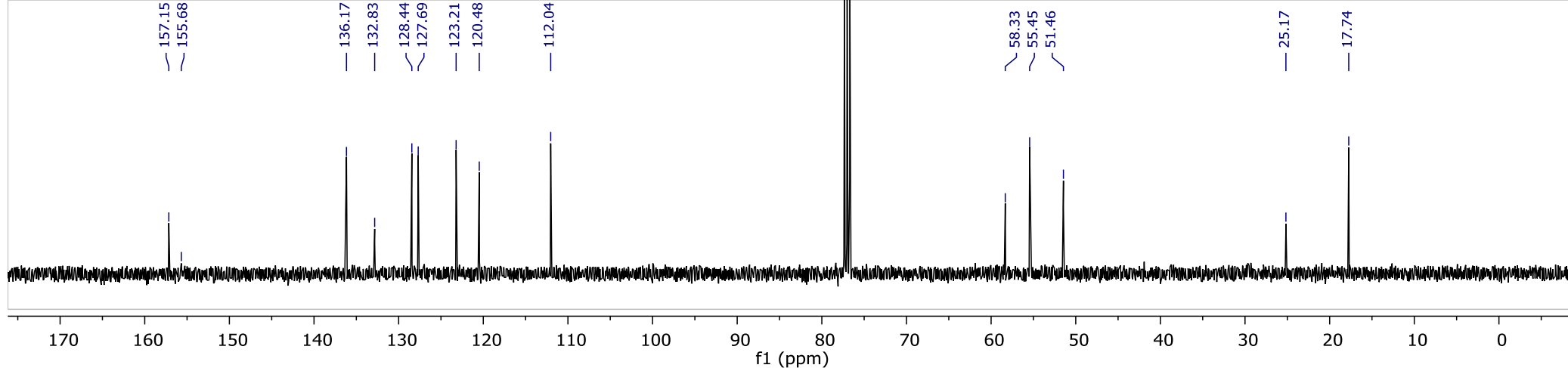
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.641	5.49	5.86	3.97294	23.7872	1.8836	0.159
2	6.425	6.16	6.88	206.949	895.261	98.1164	0.218

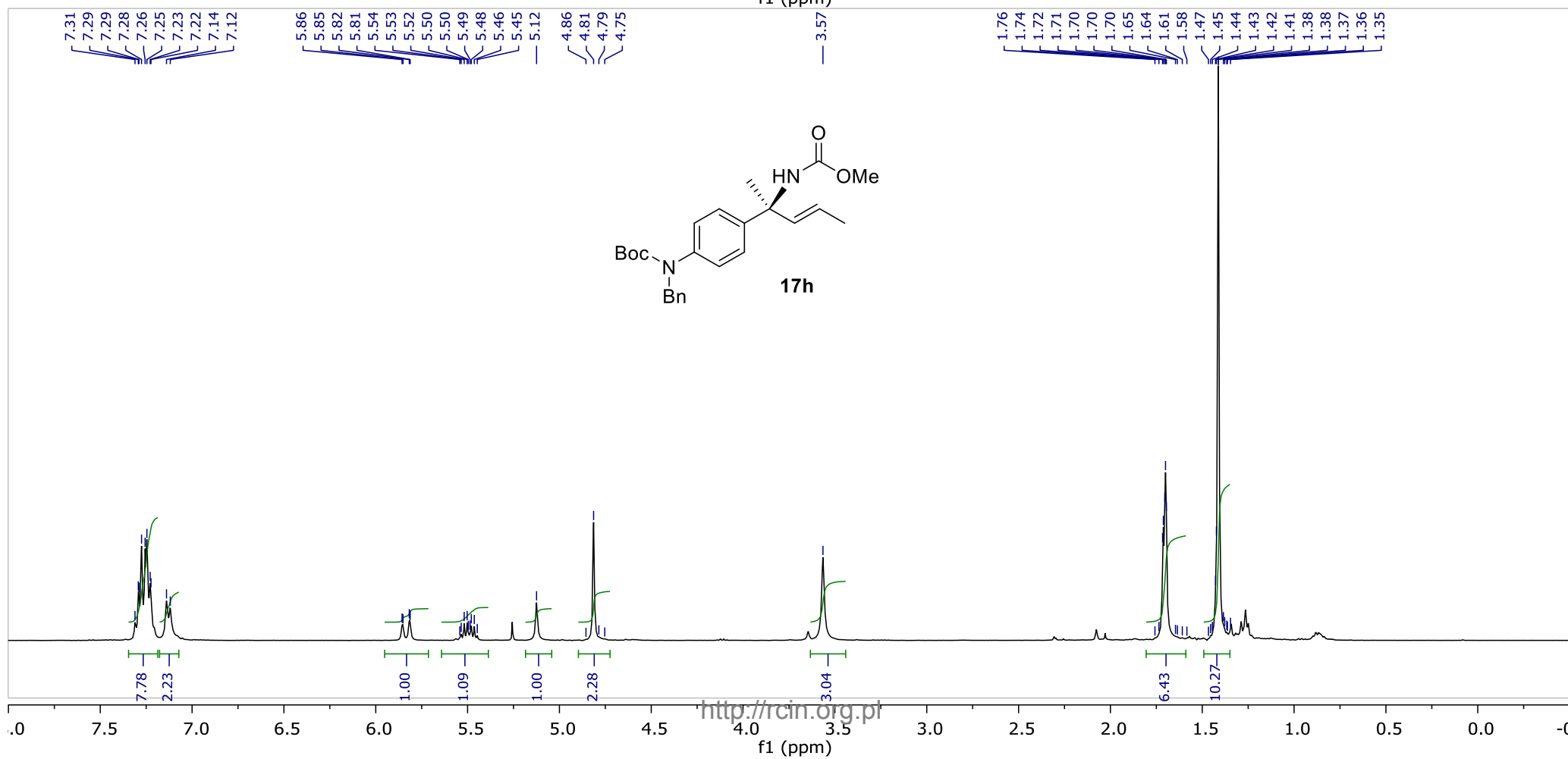
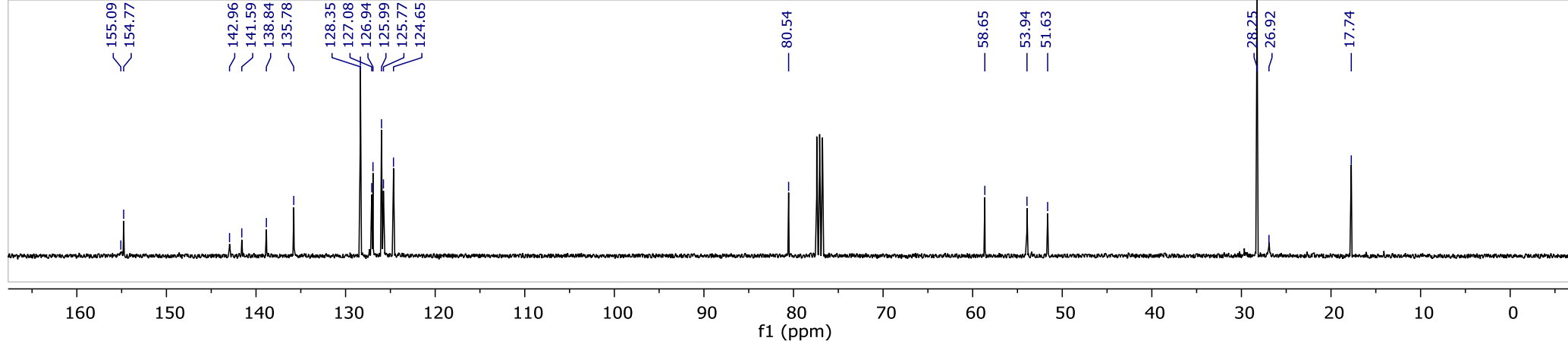


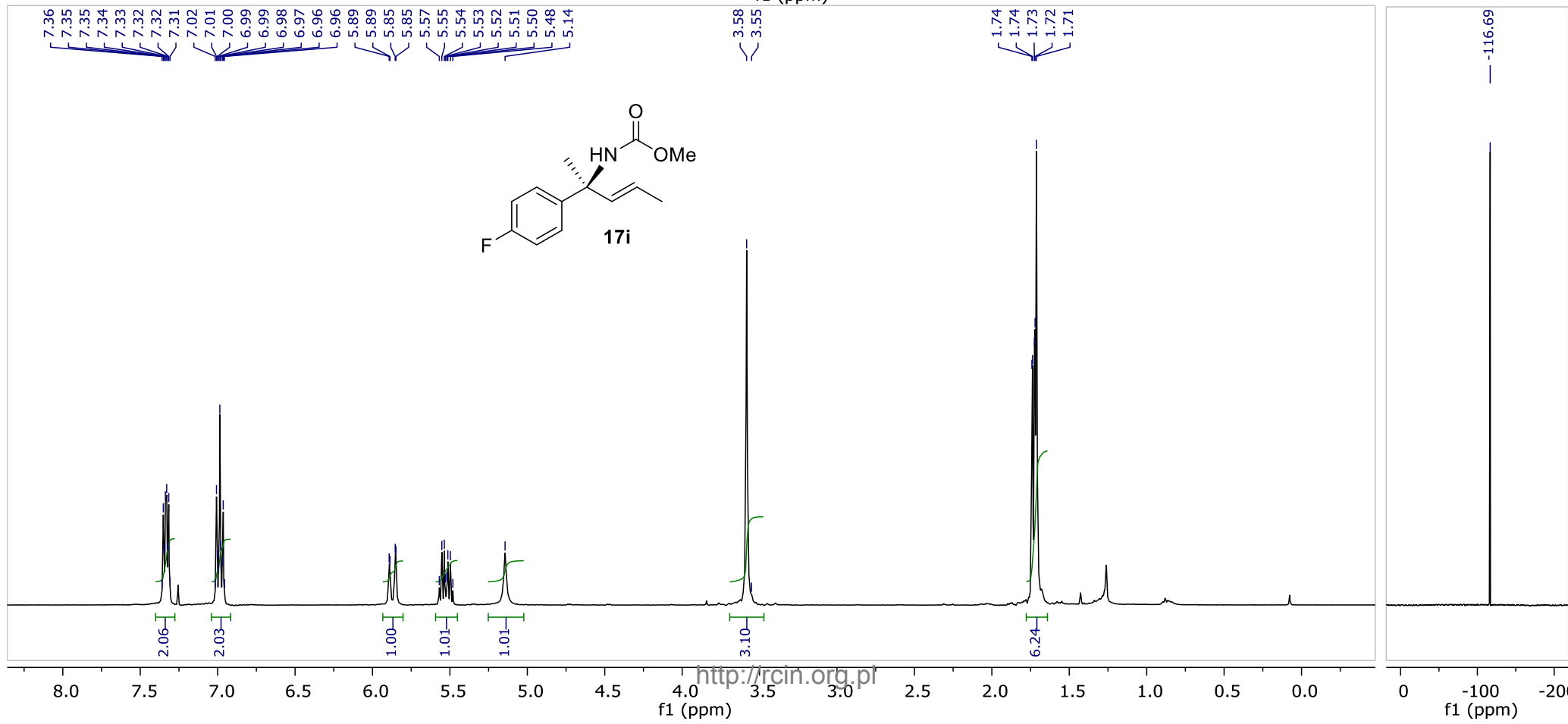
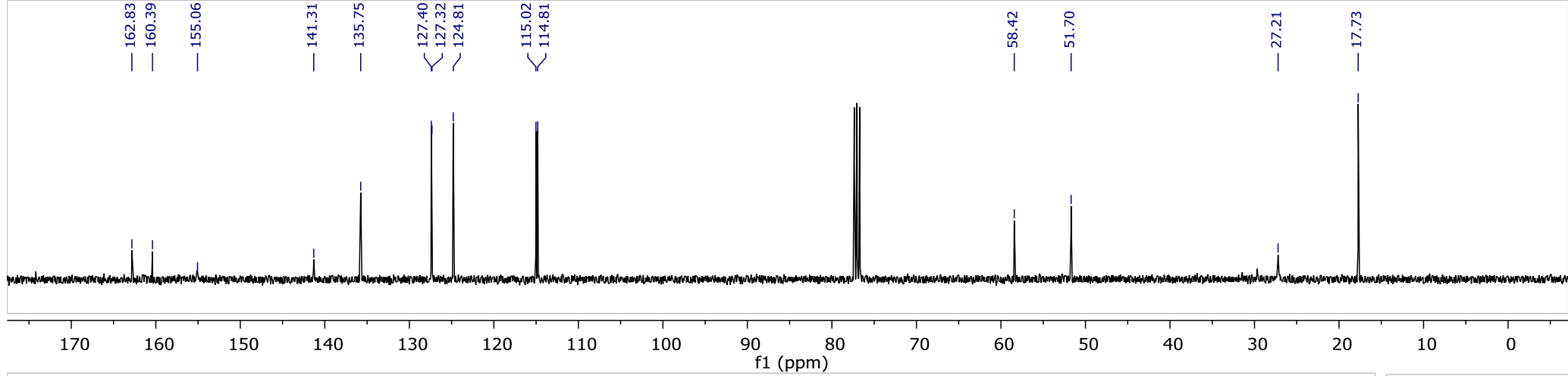


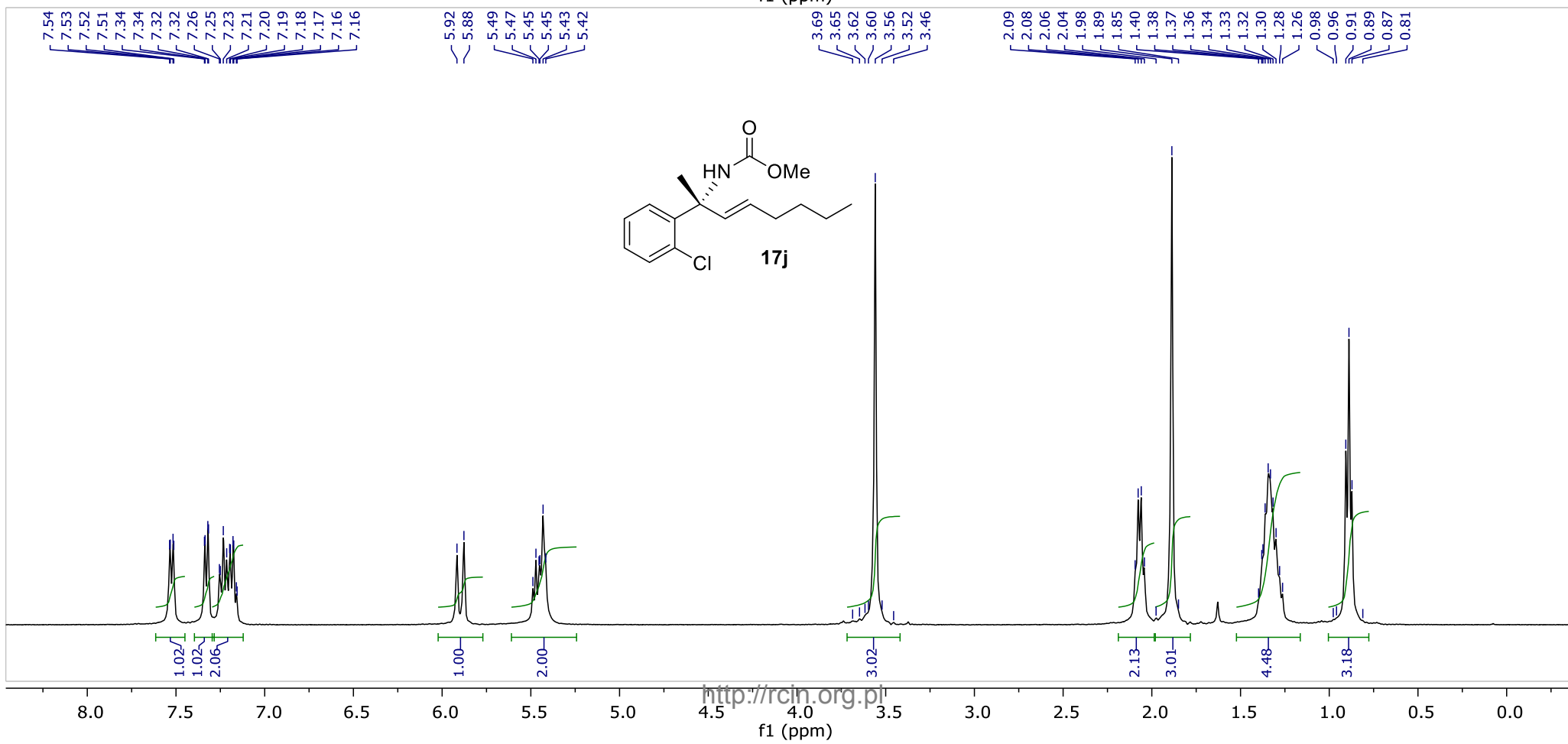
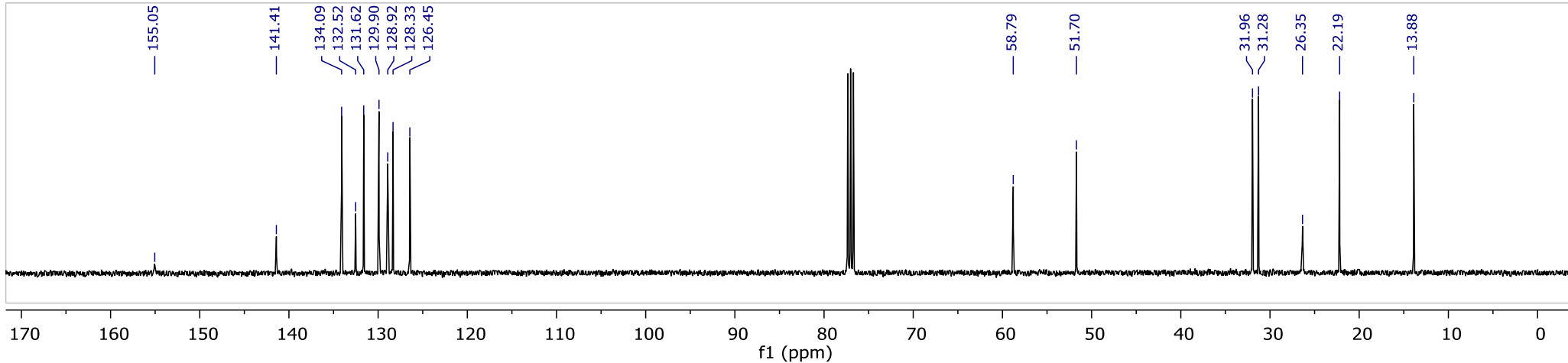






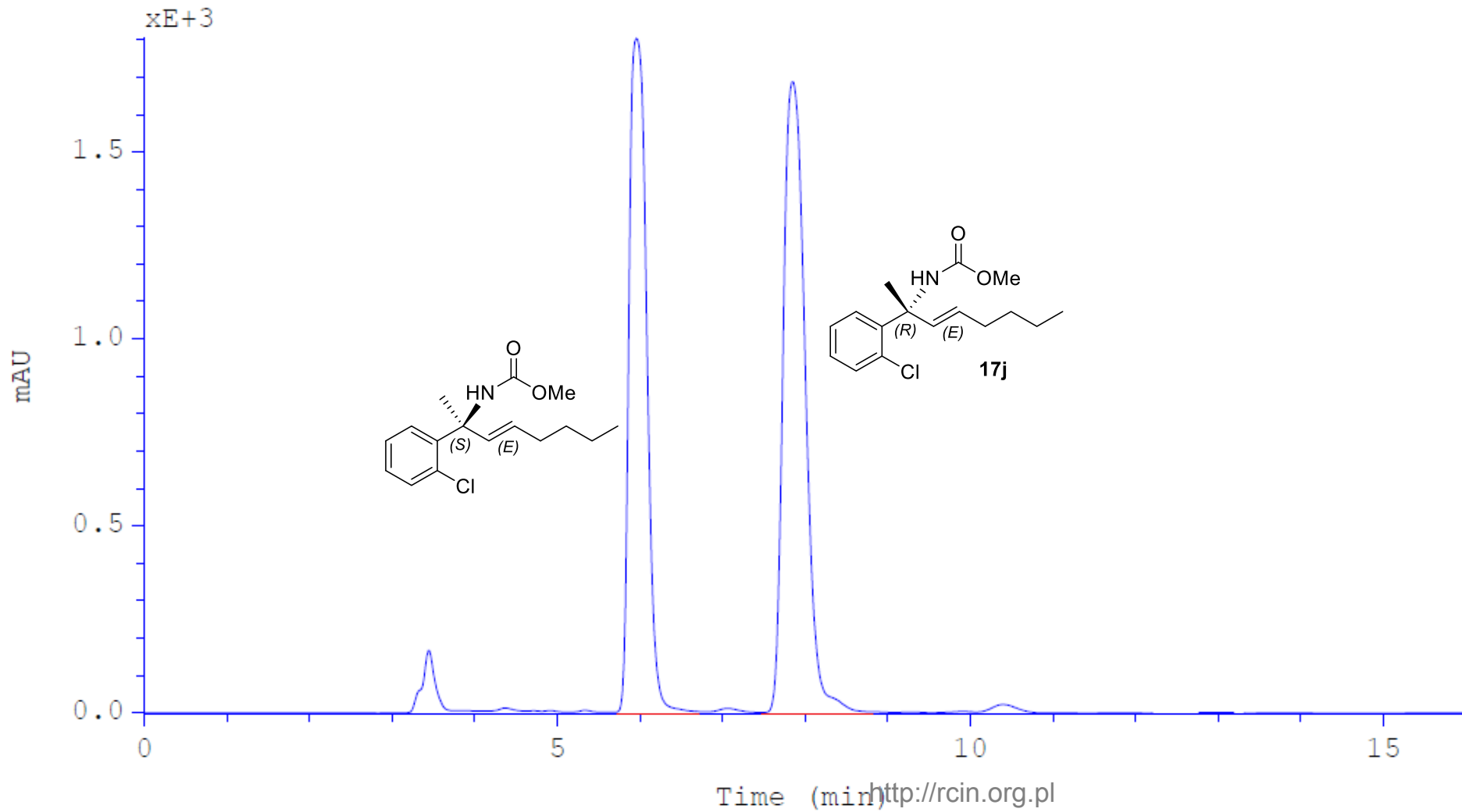






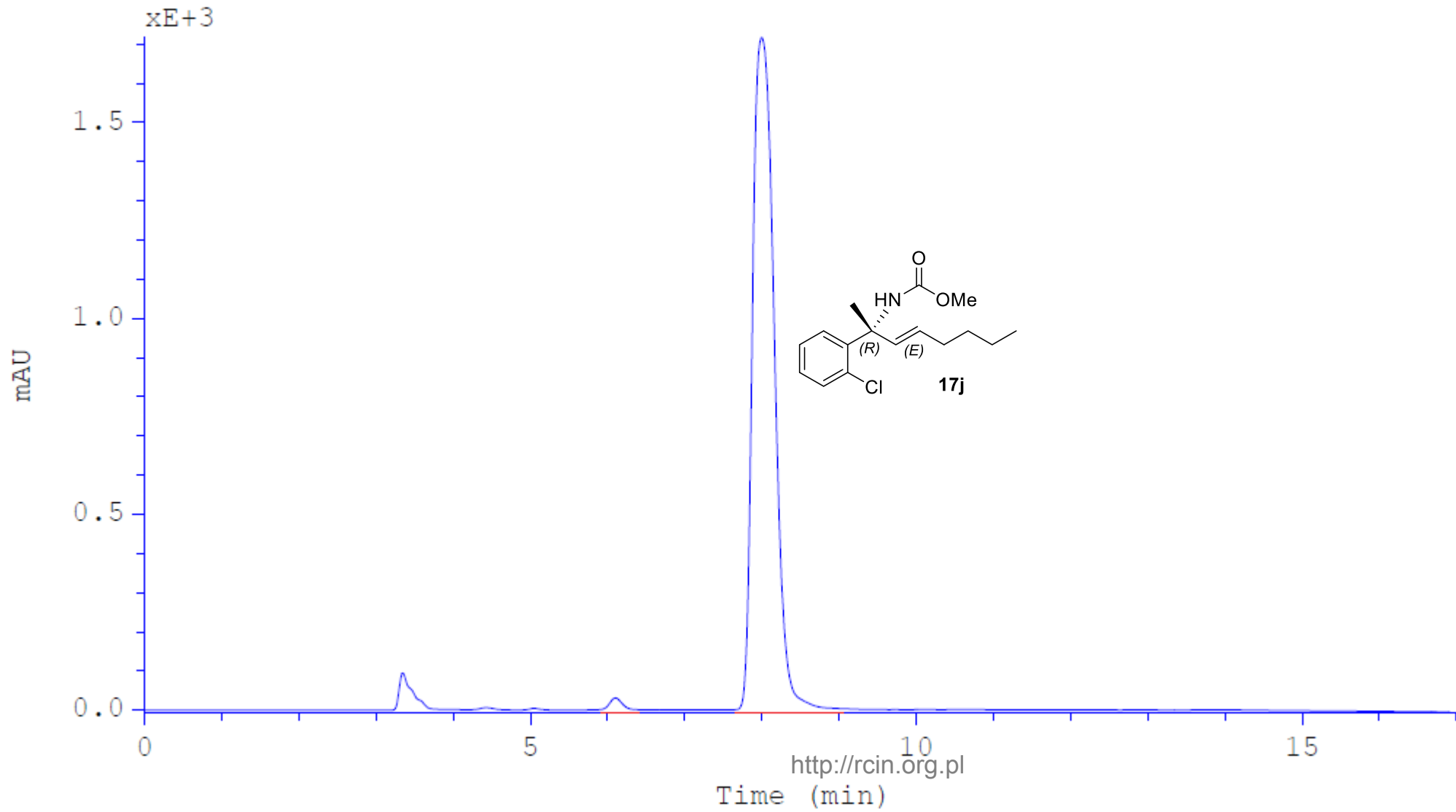
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	5.955	5.72	6.66	443.727	1801.01	46.1824	0.235
2	7.839	7.54	8.71	517.088	1684.65	53.8176	0.287

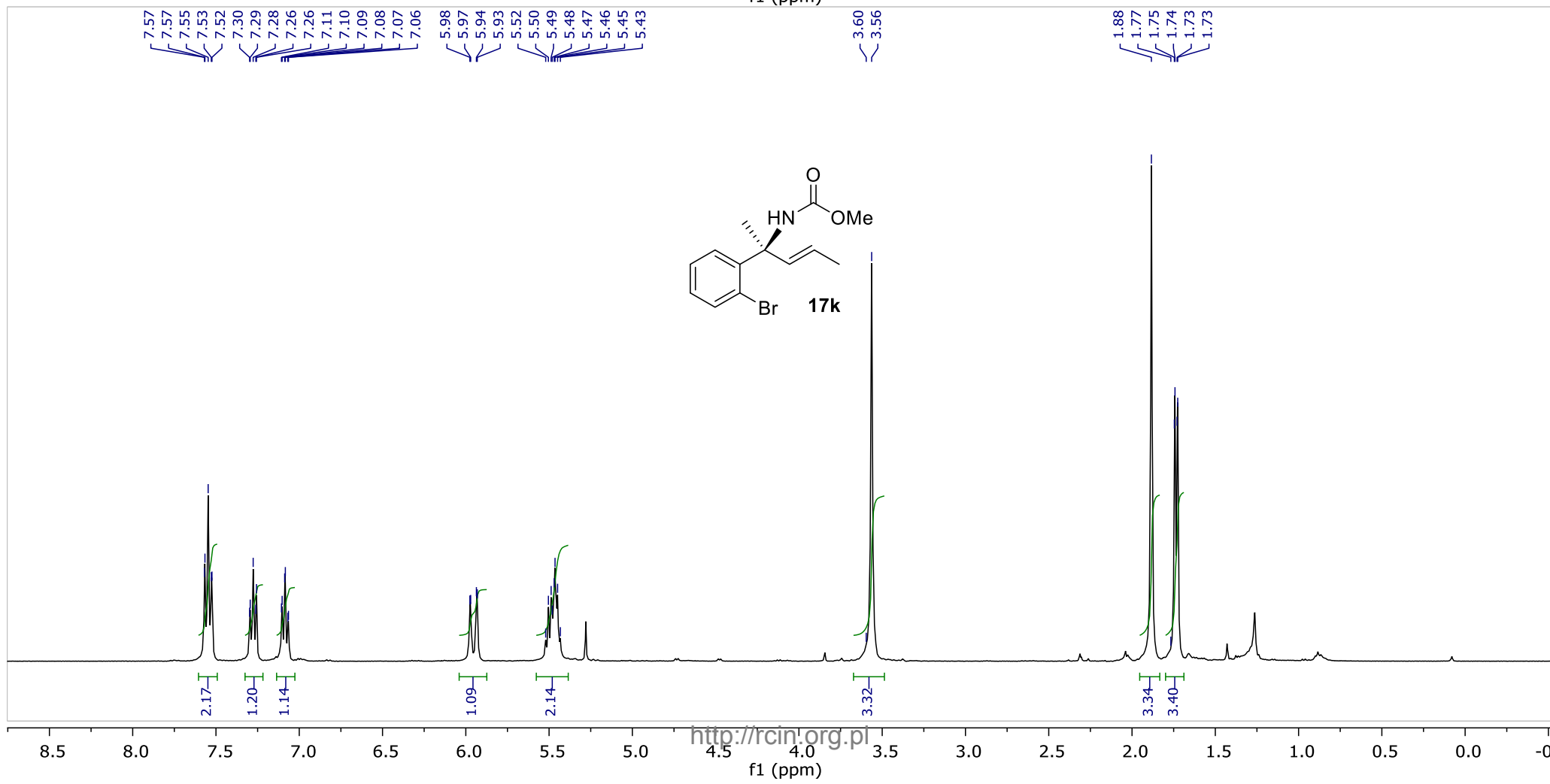
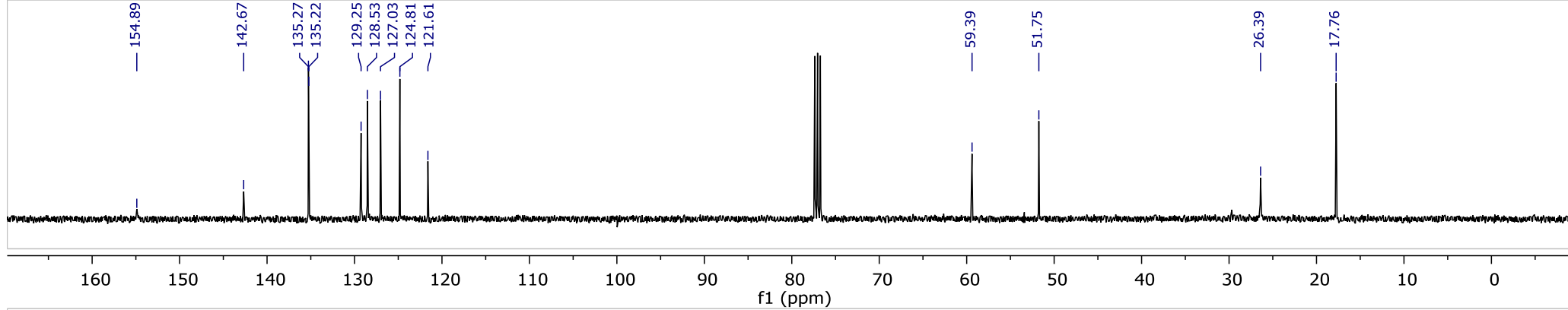


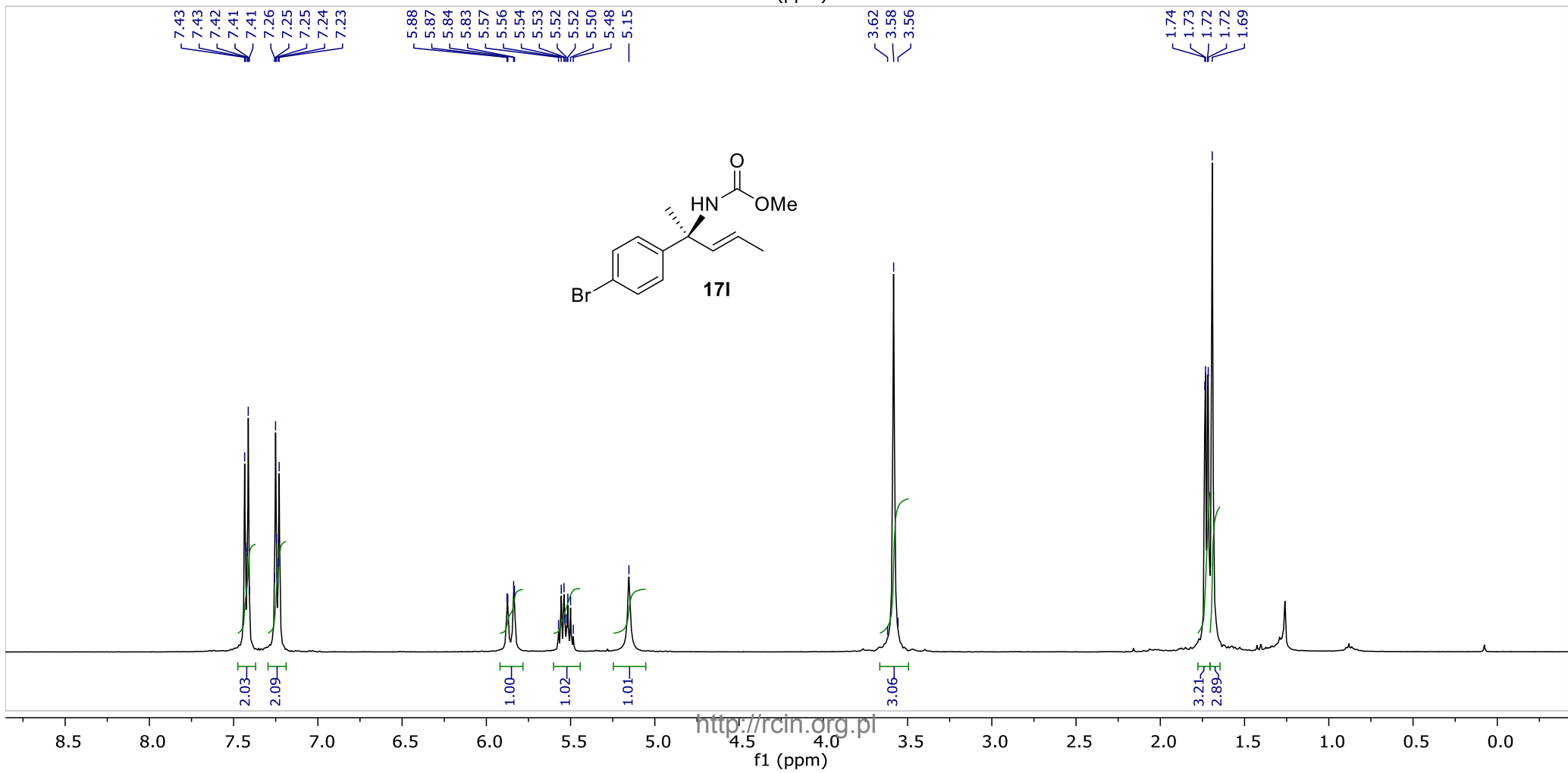
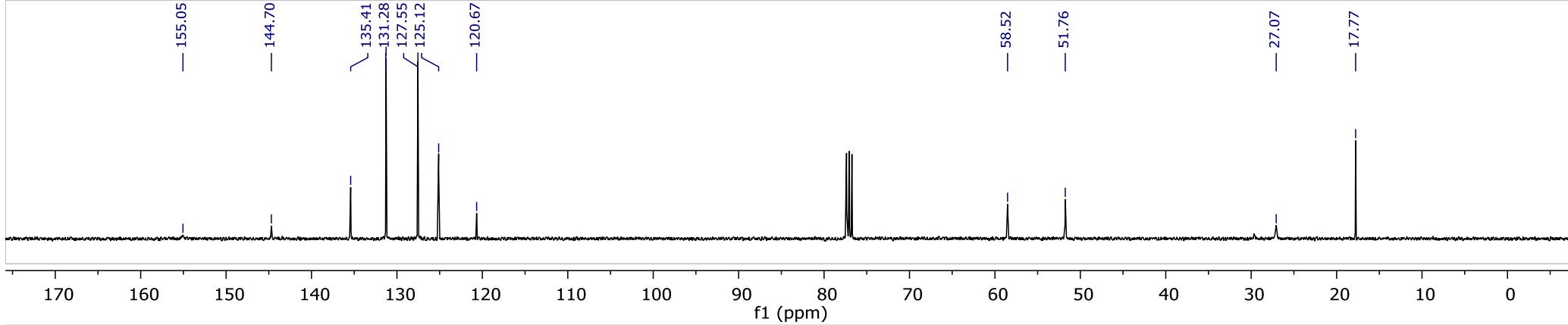
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

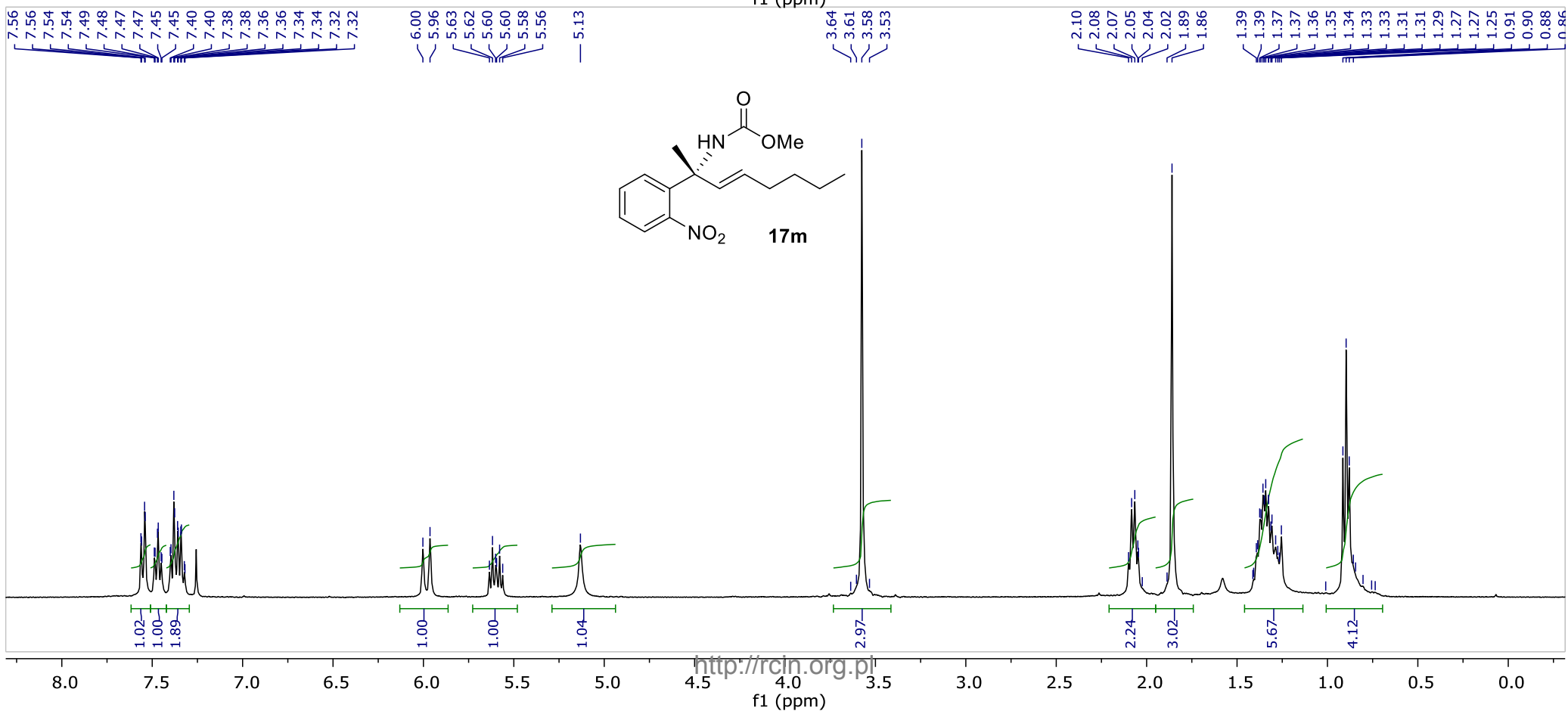
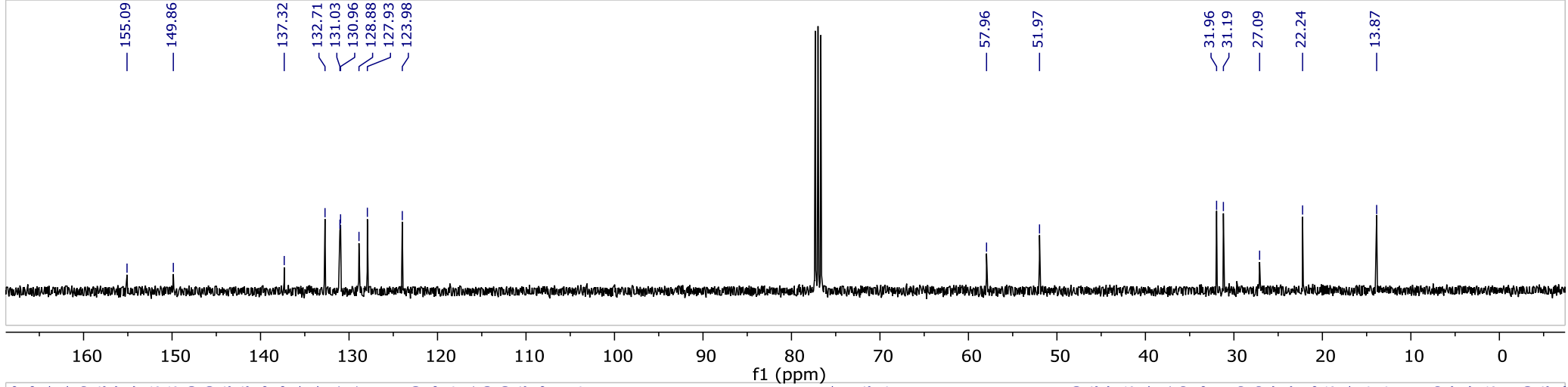
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.104	5.95	6.31	4.68586	28.0389	0.8392	0.162
2	7.989	7.69	9.07	553.678	1713.9	99.1608	0.306





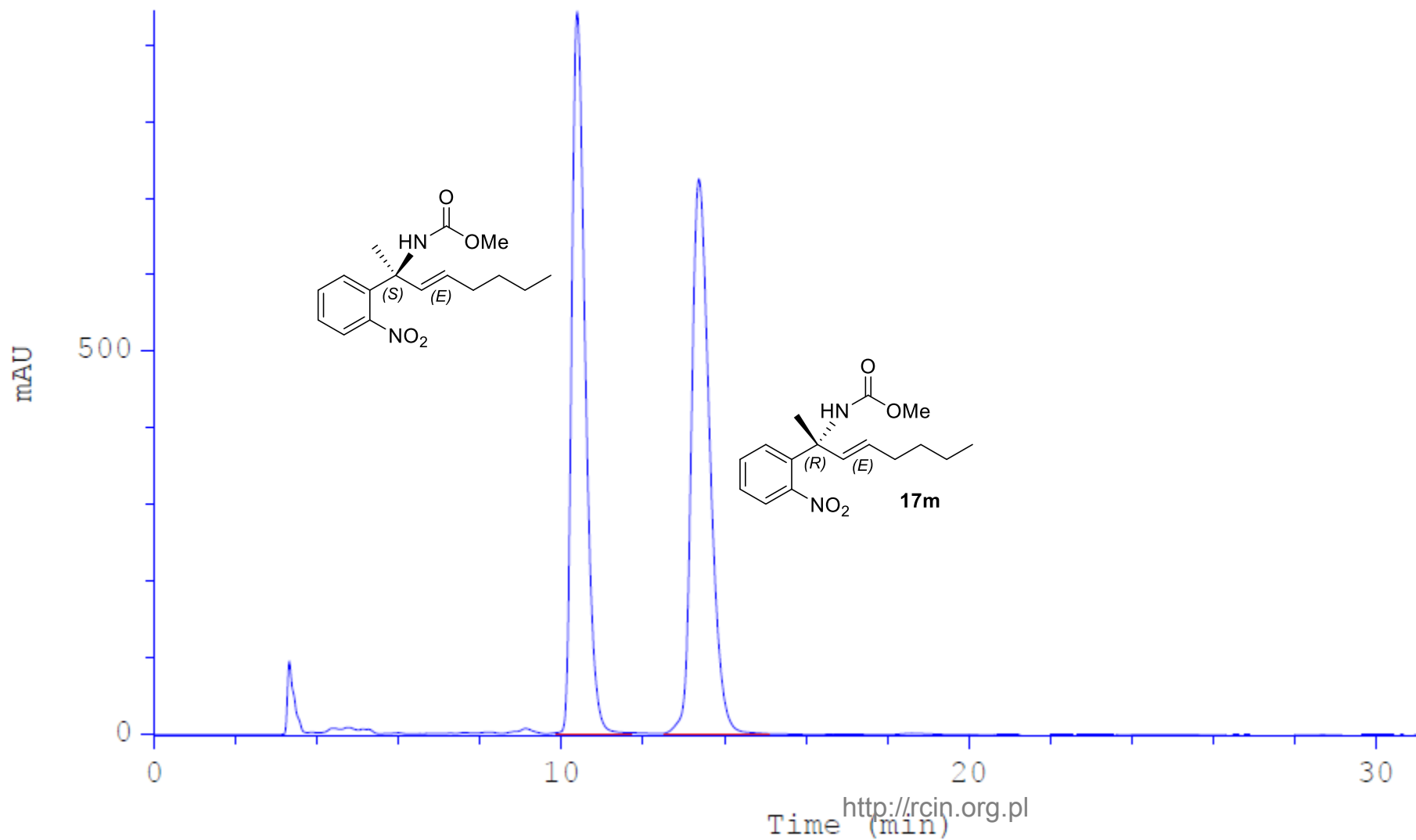






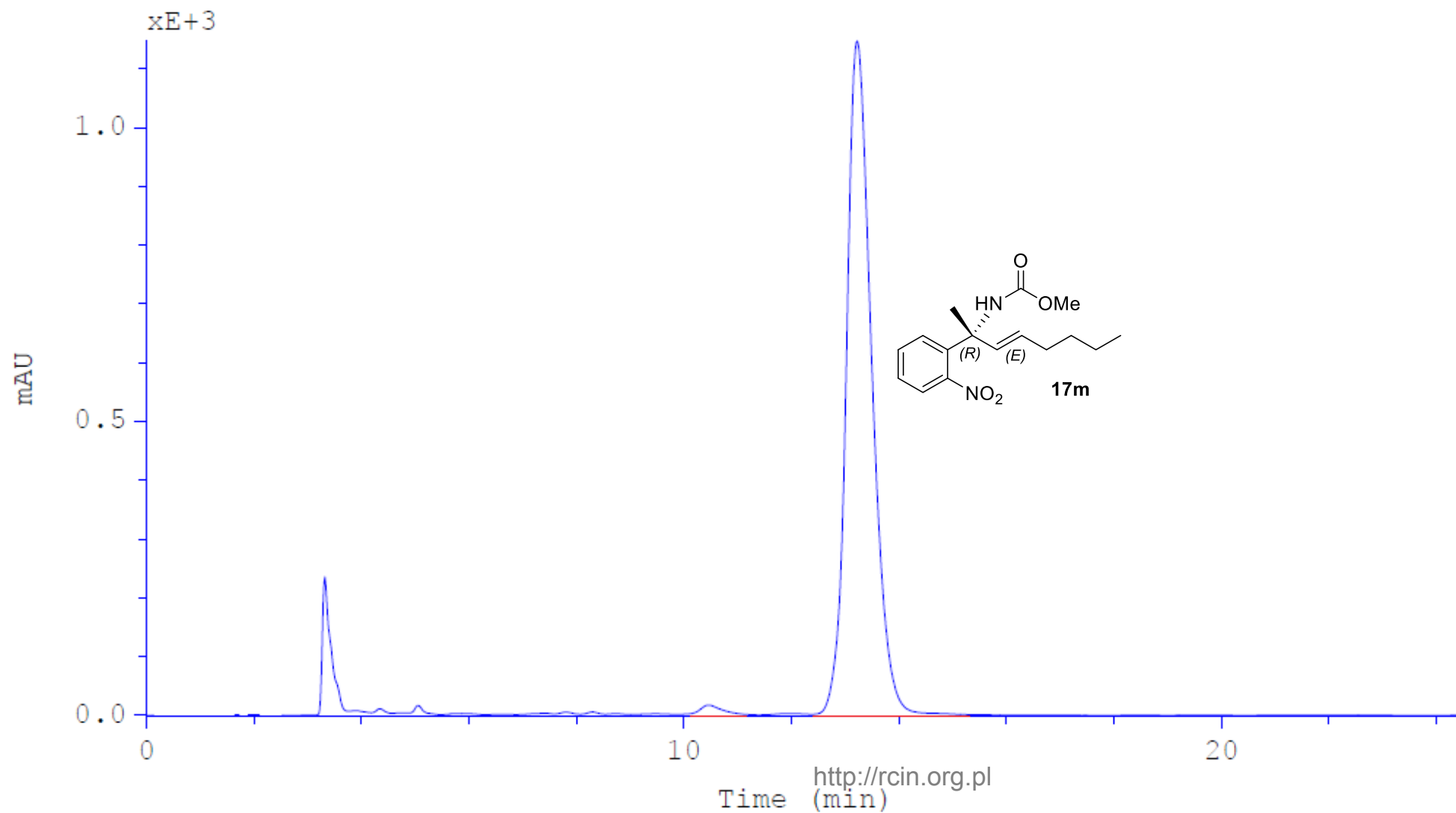
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

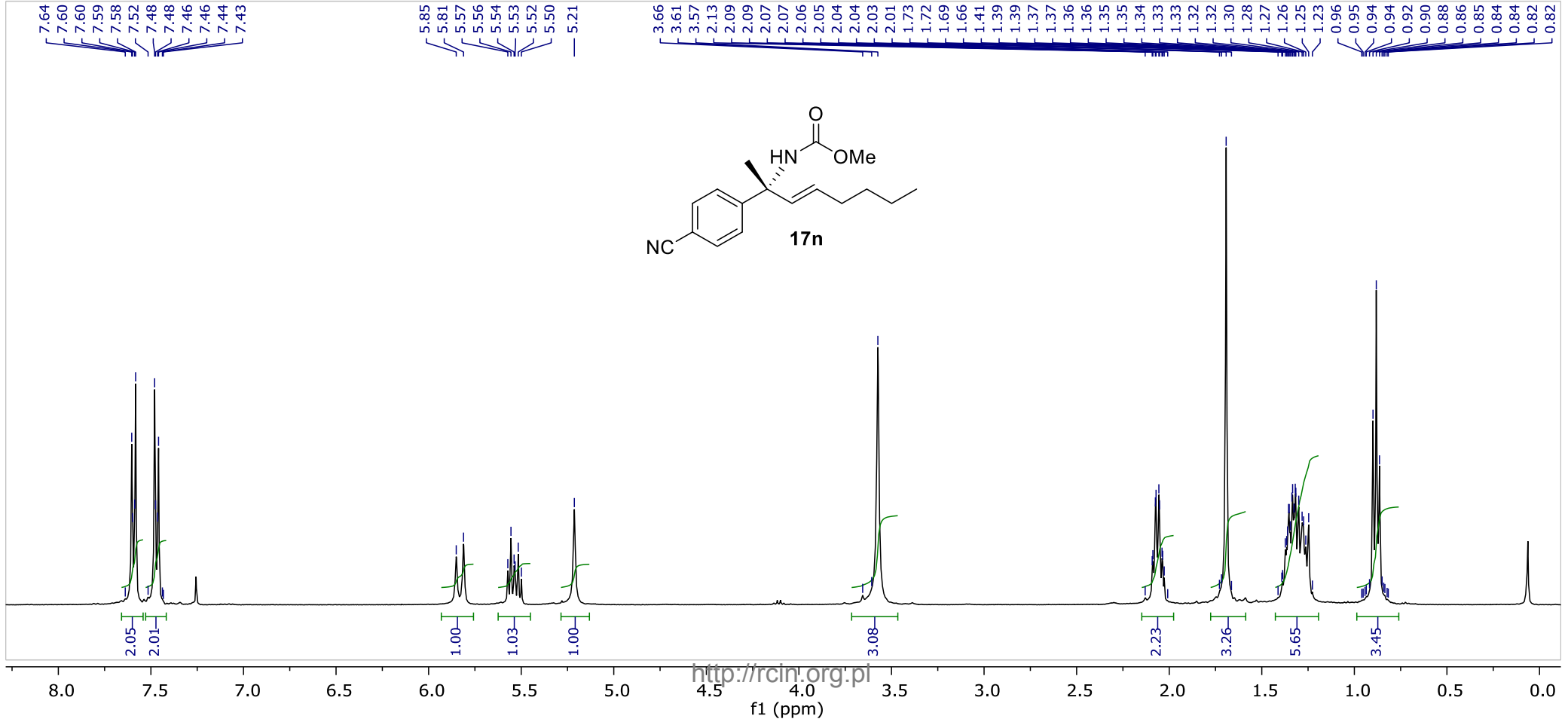
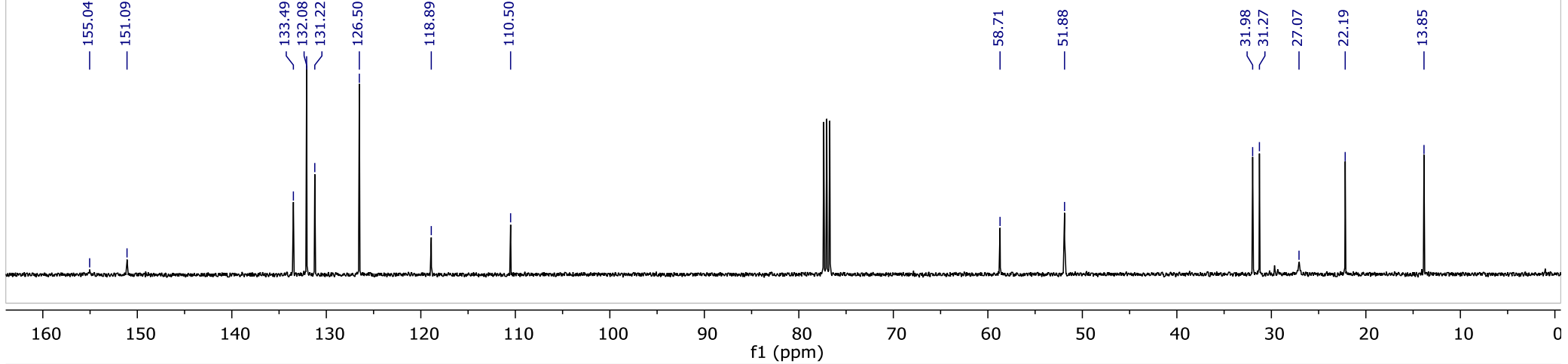
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.385	9.97	11.42	359.999	940.537	49.0925	0.354
2	13.369	12.59	14.54	373.307	722.36	50.9075	0.475



Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

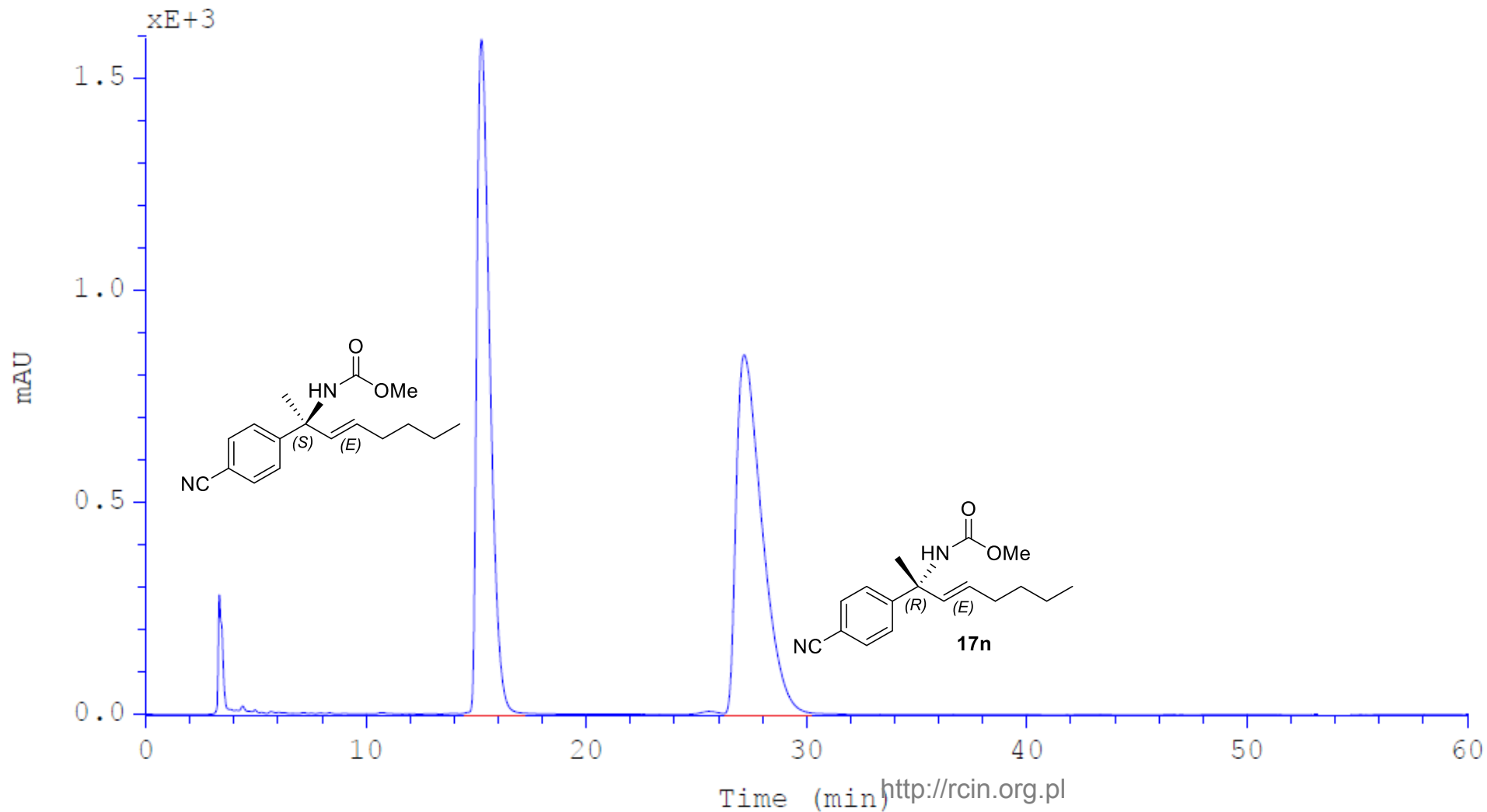
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.454	10.14	11.00	5.7683	14.4982	0.9207	0.371
2	13.222	12.45	14.82	620.728	1144.54	99.0793	0.491





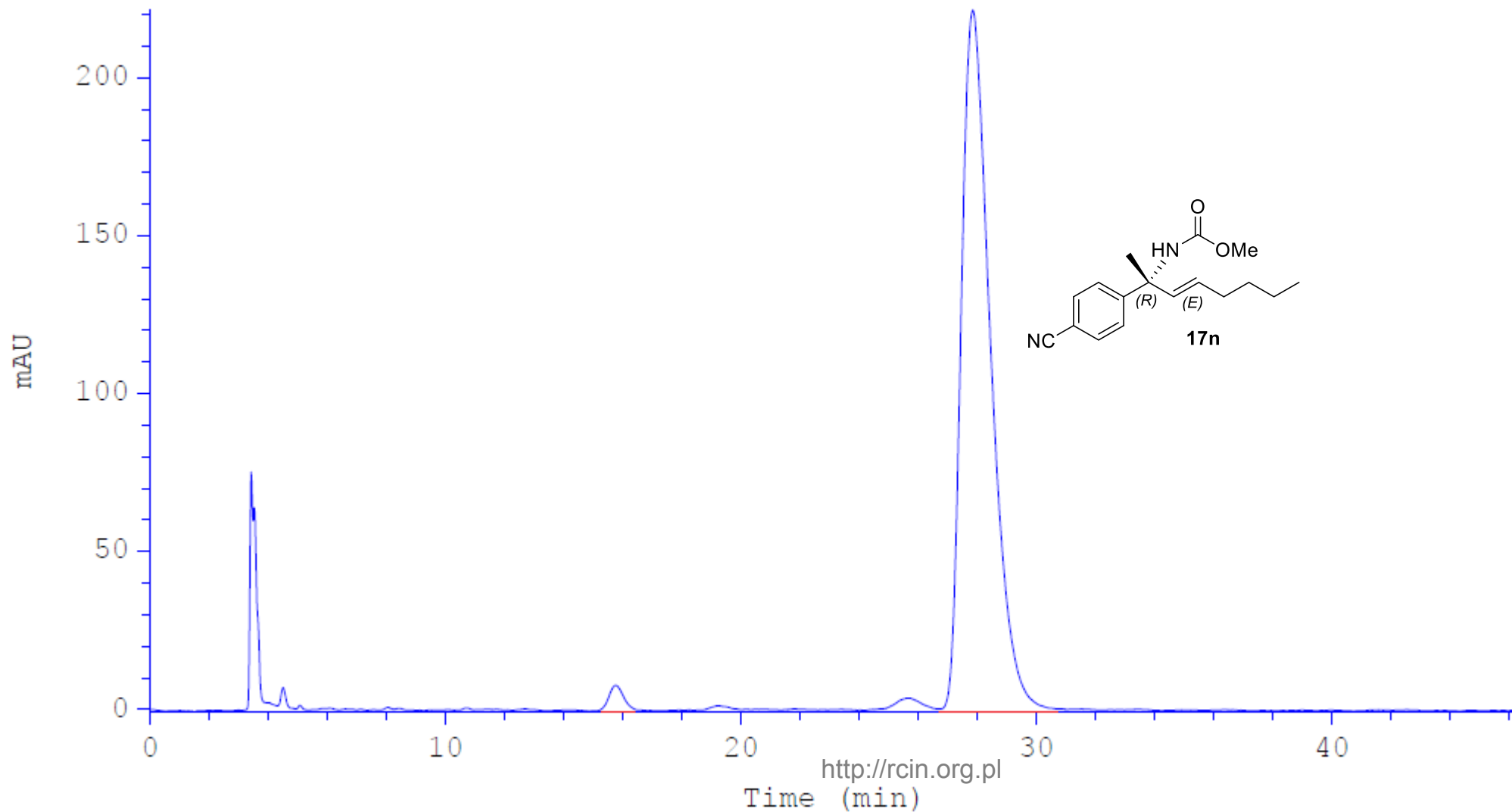
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.233	14.53	16.99	1082.47	1587.74	48.7383	0.638
2	27.167	26.18	30.14	1138.51	845.353	51.2617	1.256

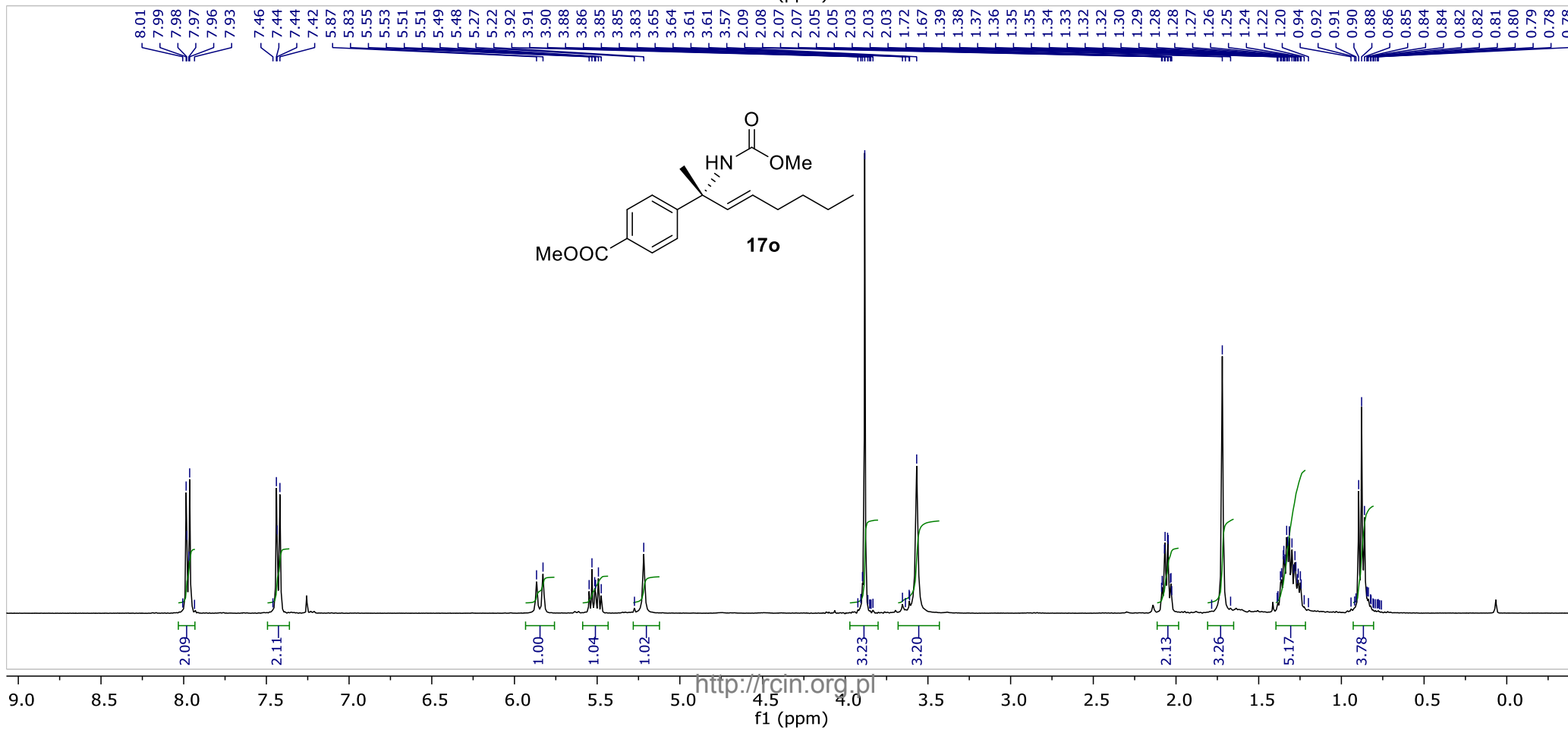
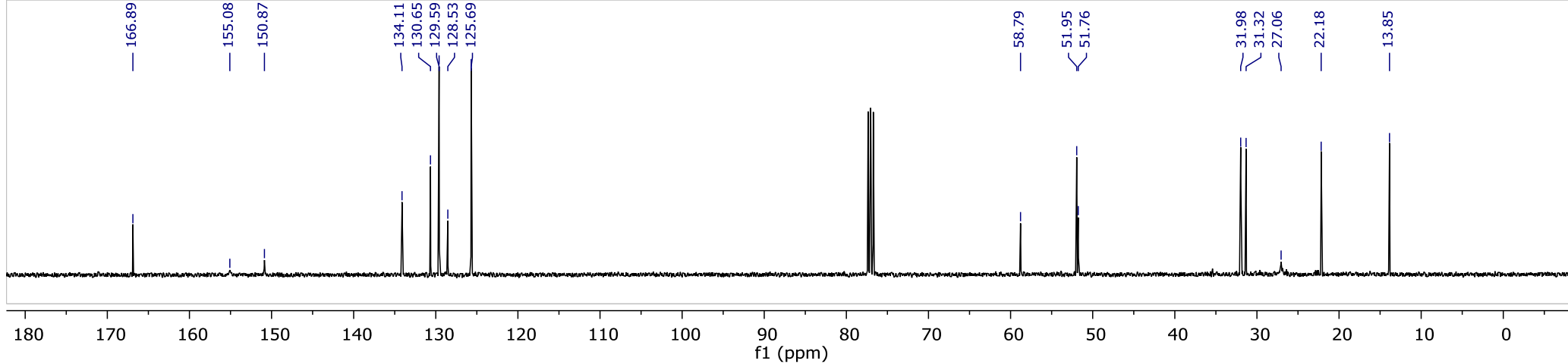


Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.768	15.09	16.37	4.23921	7.70122	1.6528	0.524
2	27.836	26.74	30.53	252.241	221.07	98.3472	1.054

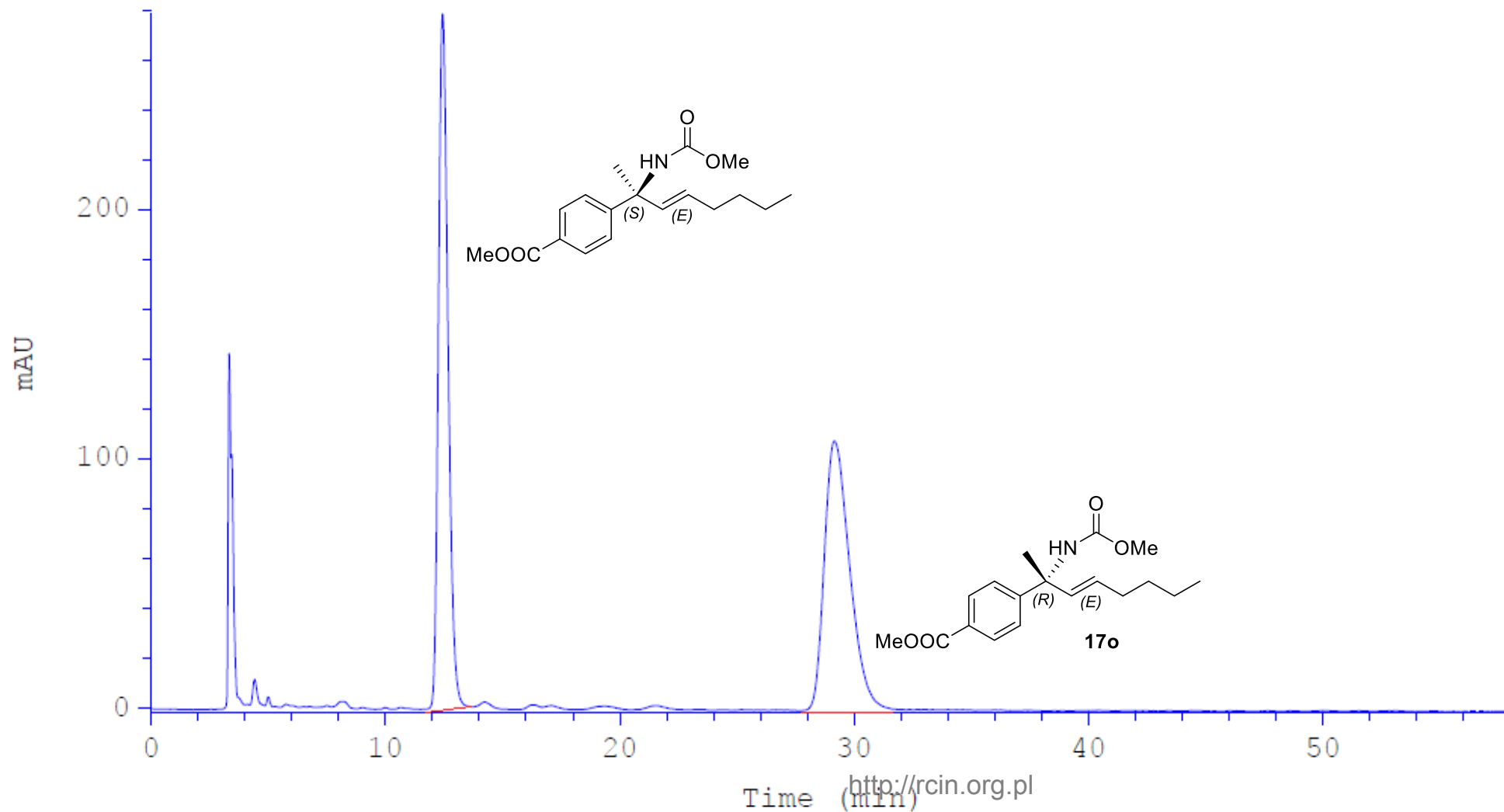






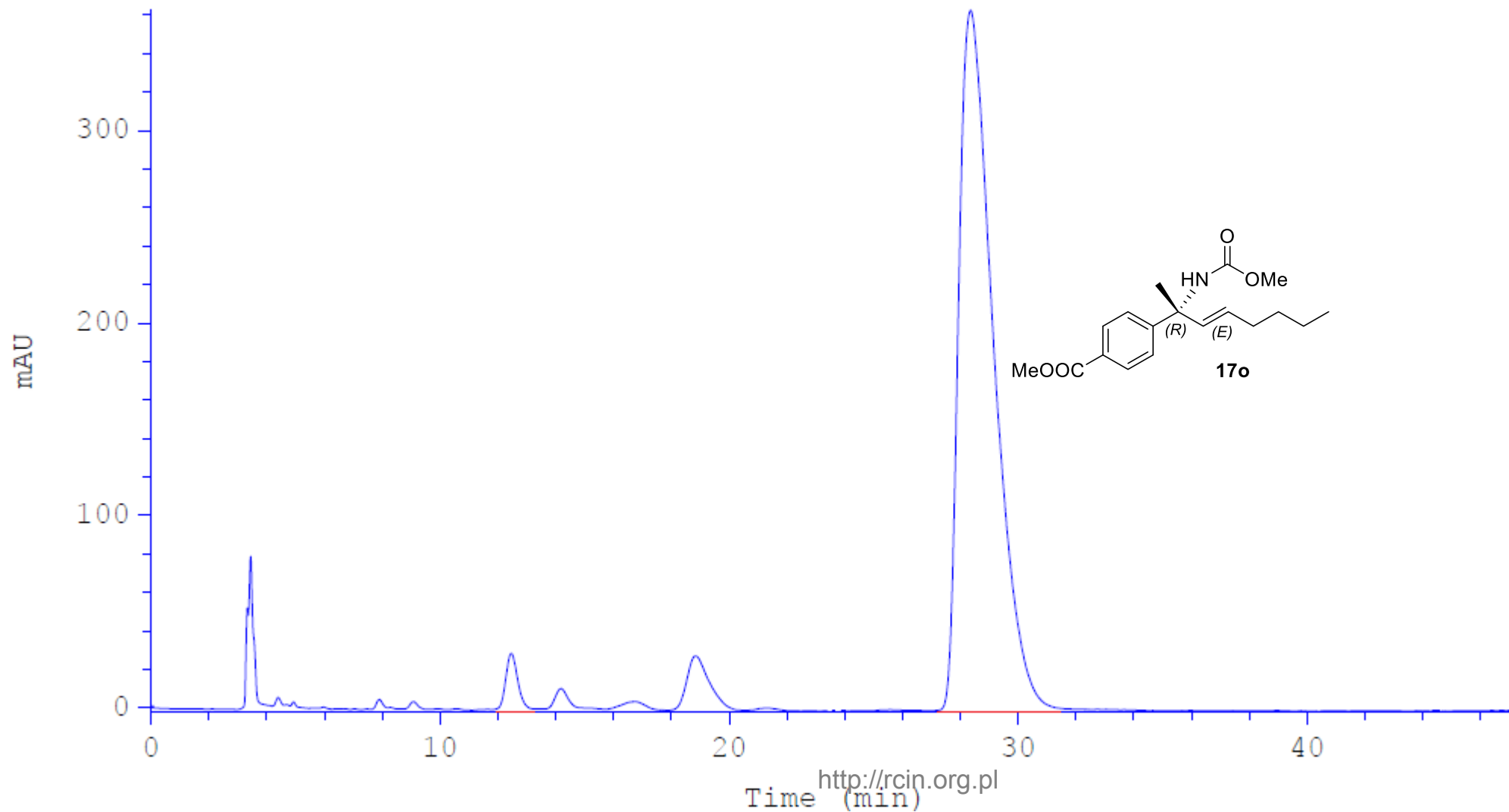
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

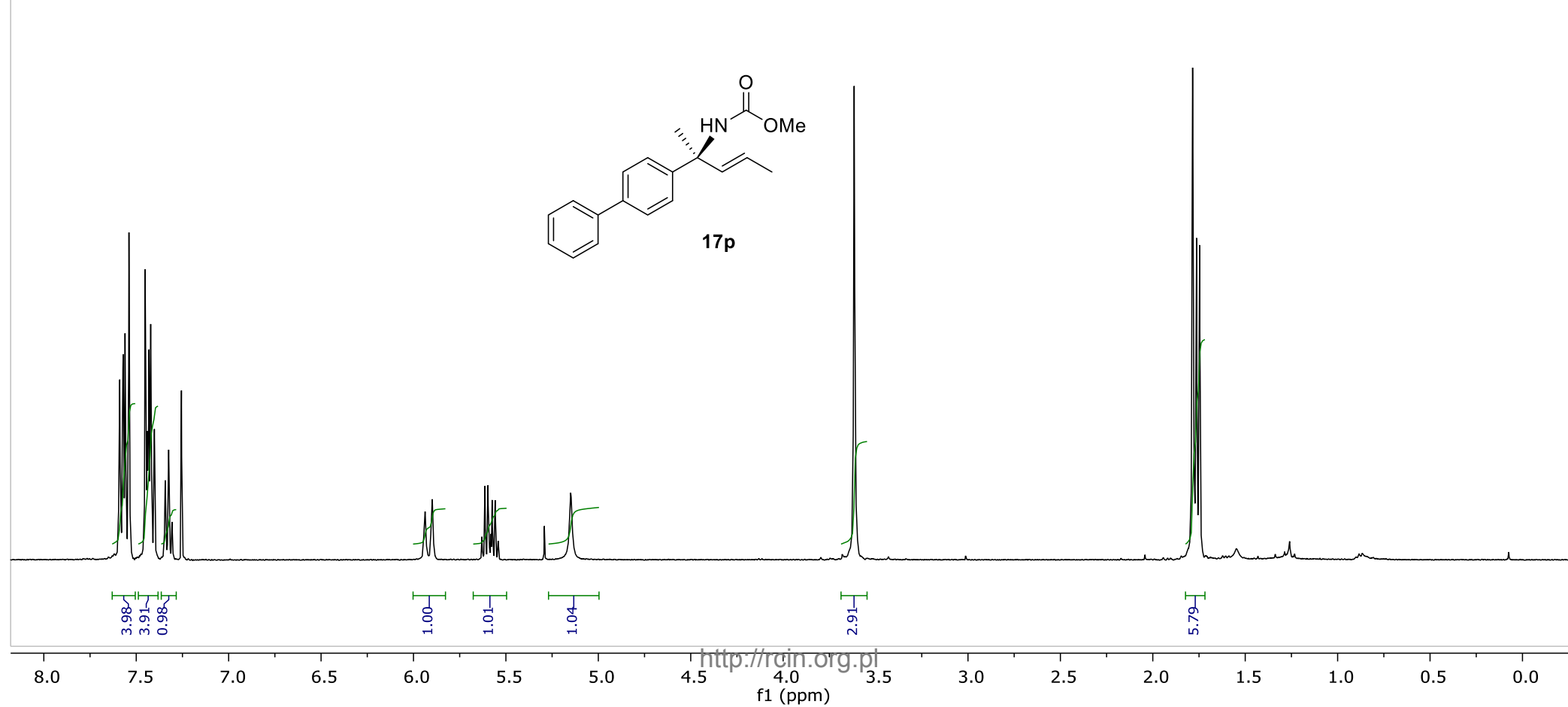
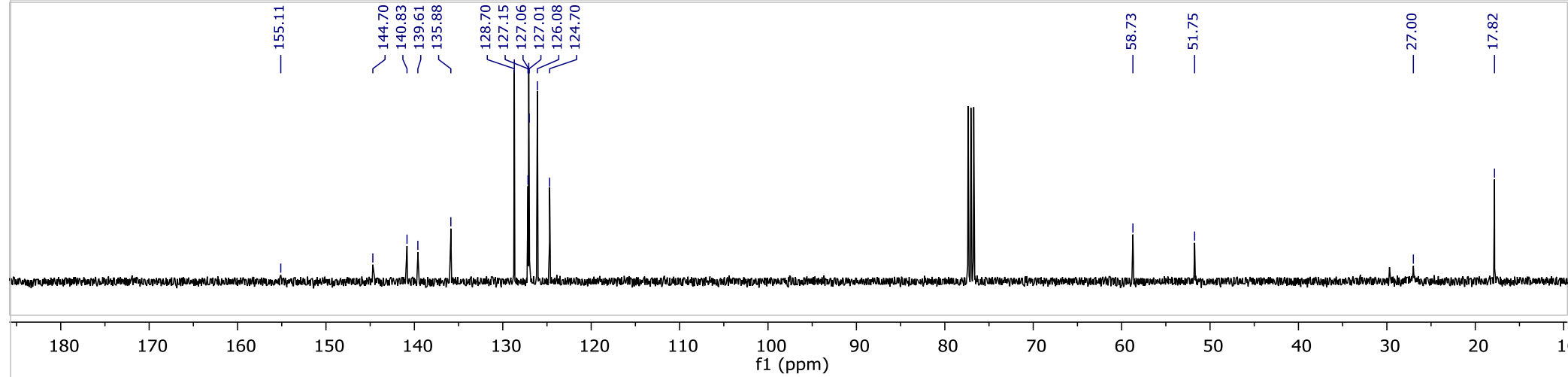
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	12.433	11.86	13.53	132.055	278.176	49.7354	0.440
2	29.150	27.74	31.42	133.46	107.694	50.2646	1.157

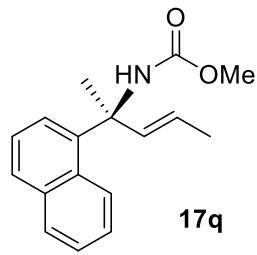
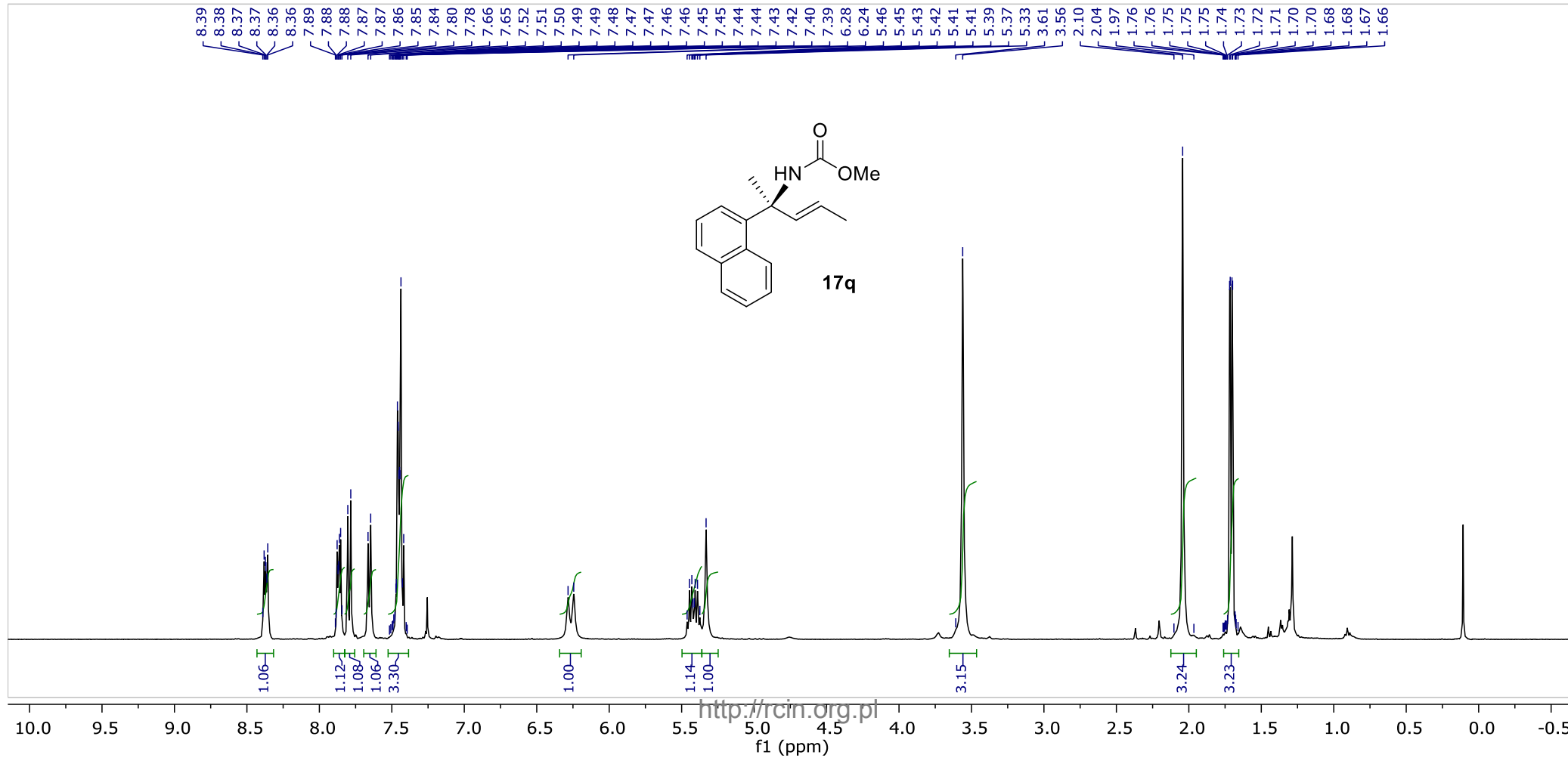
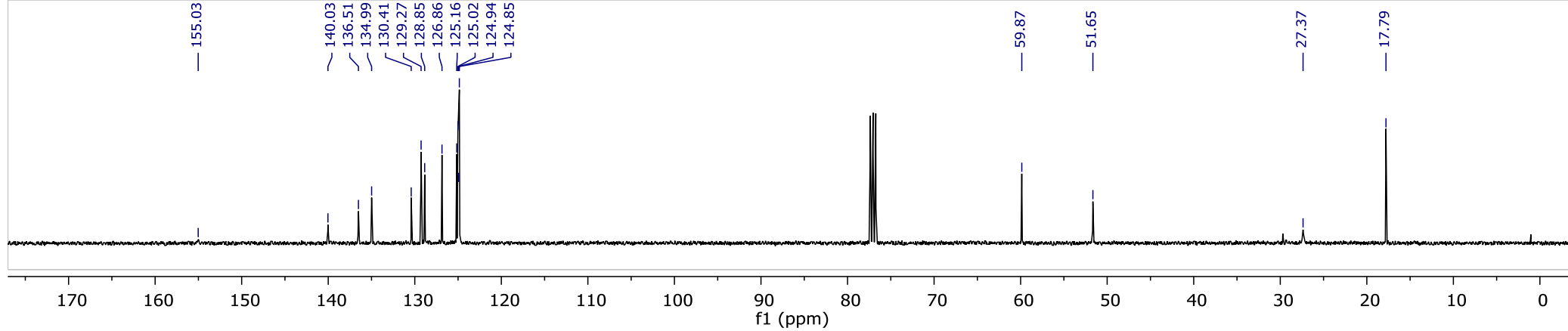


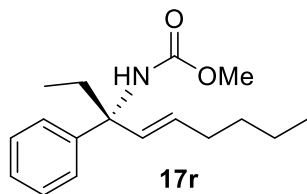
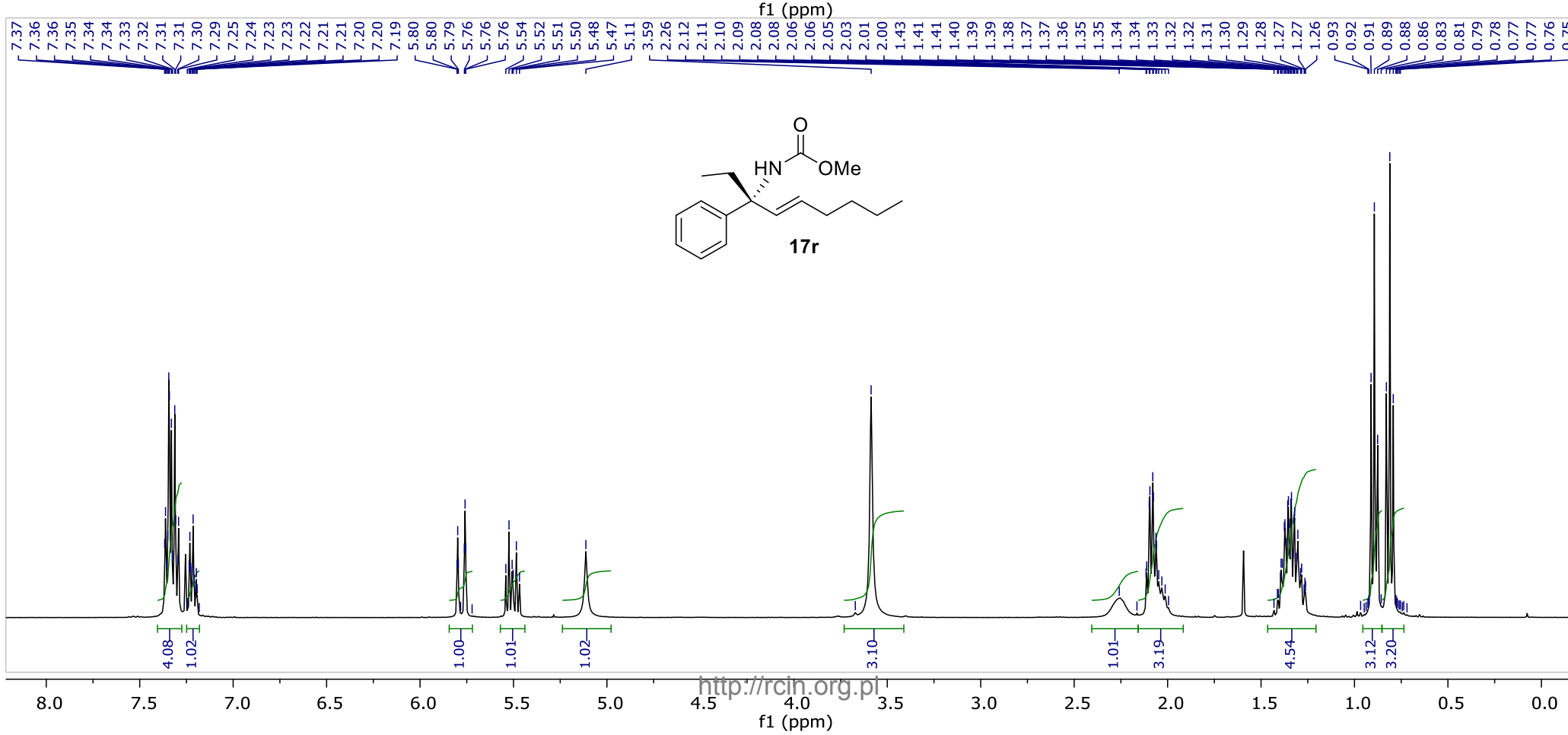
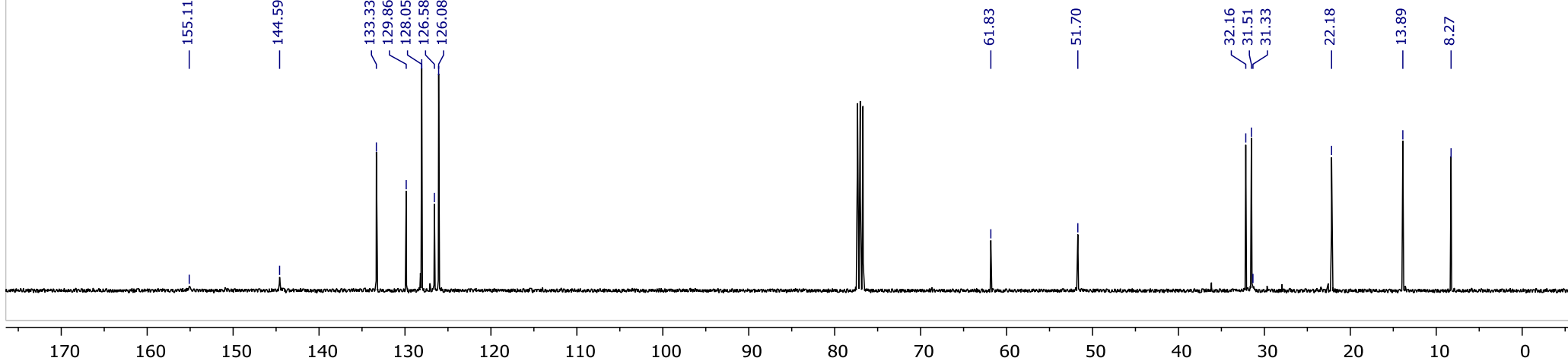
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	12.468	11.97	13.14	13.2338	28.6651	2.5545	0.433
2	28.352	27.24	31.59	504.819	363.456	97.4455	1.288



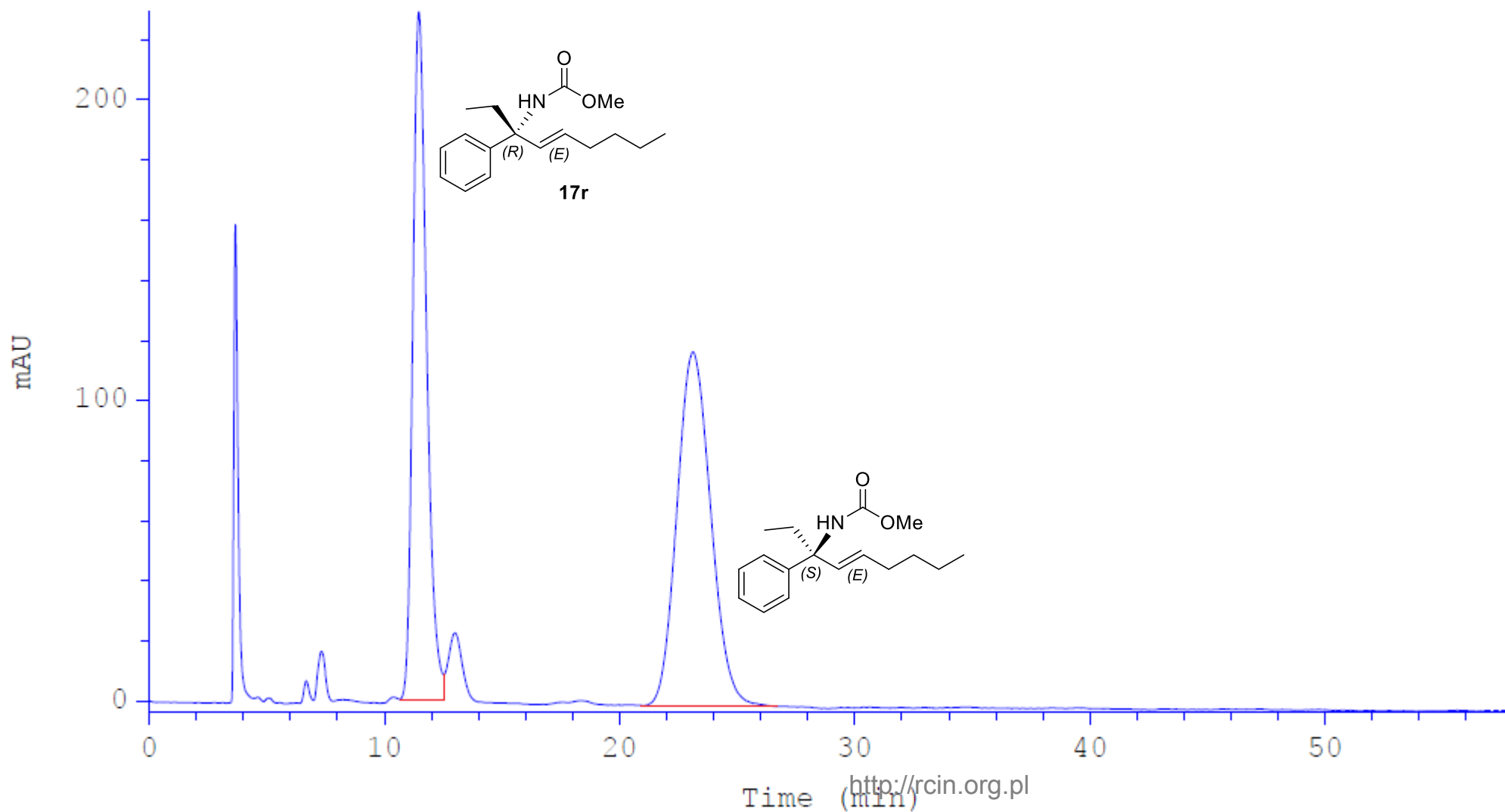






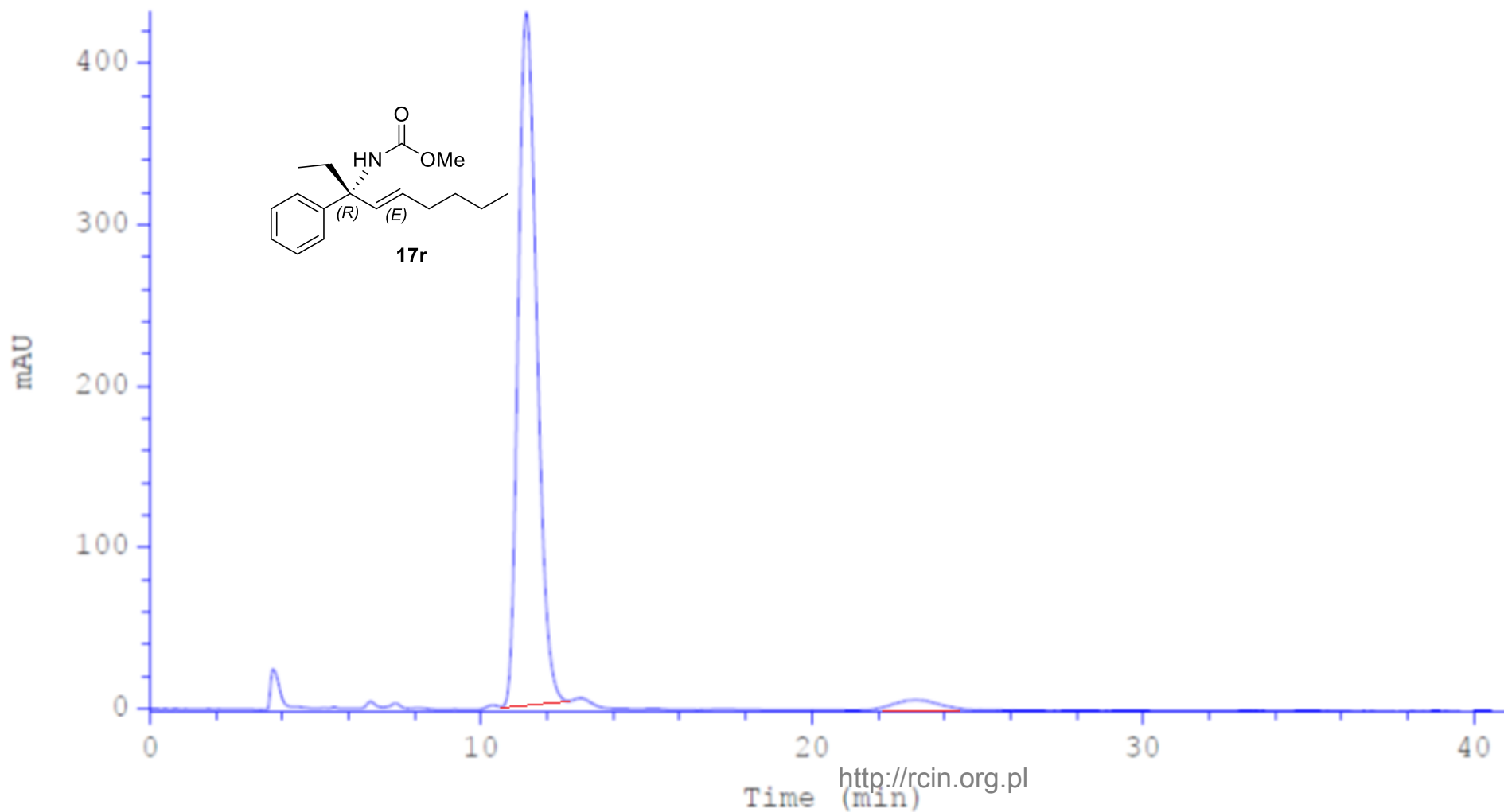
Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	11.467	10.15	12.57	146.813	224.144	42.8863	0.615
2	23.117	21.14	26.45	195.518	117.534	57.1137	1.560

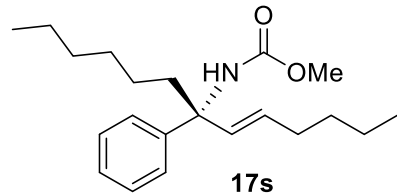
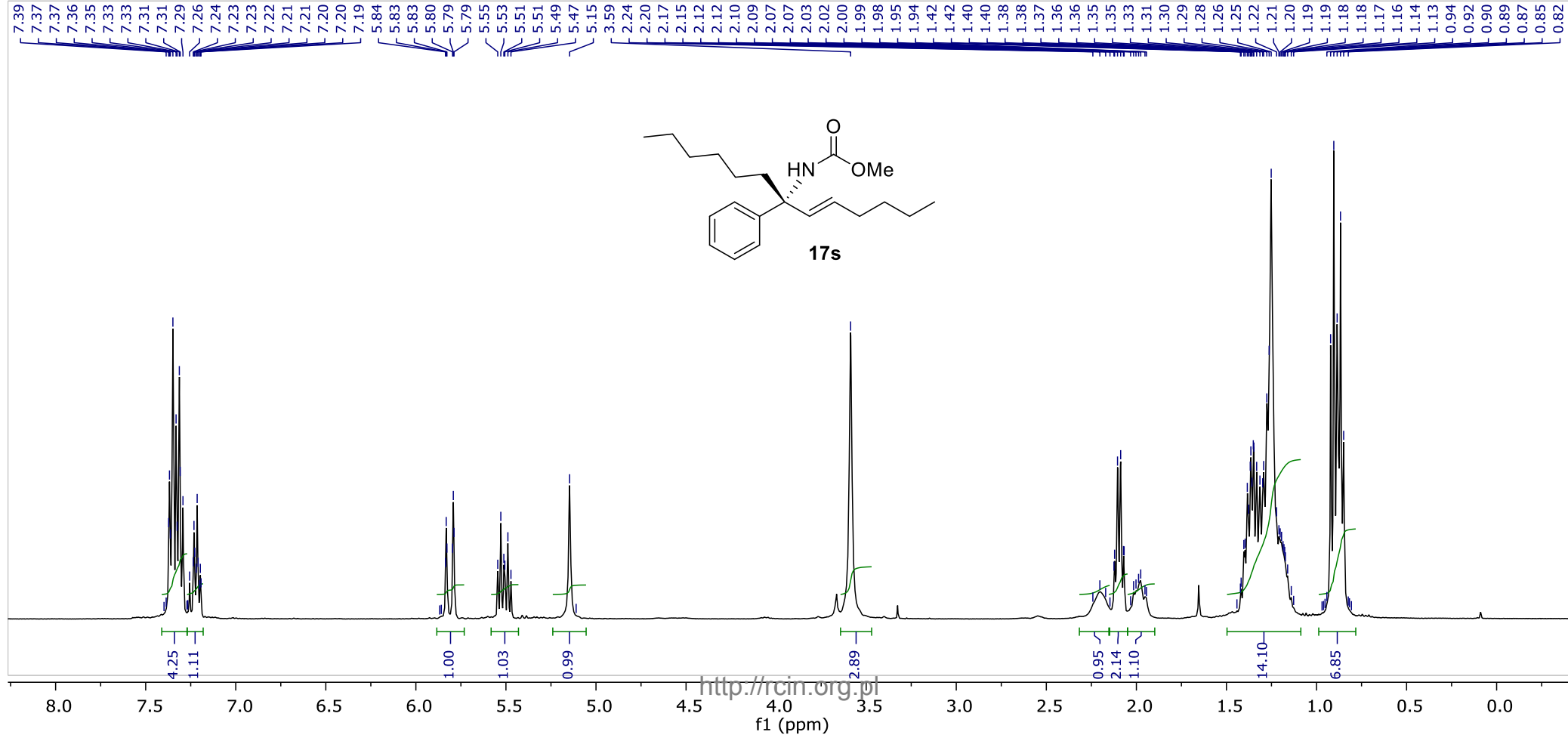
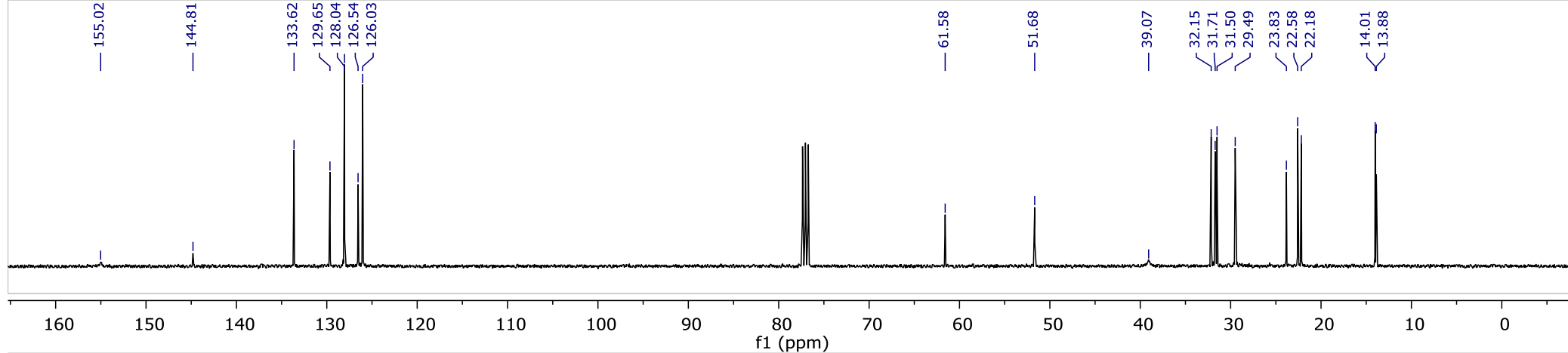


Column: Chiralcel OD-H  
Eluent: 5% *i*-PrOH in hexanes  
Flow: 1mL/min  
Detection: UV, 215 nm

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	11.368	10.57	12.79	278.879	429.014	97.6656	0.610
2	23.153	22.04	24.36	6.66588	5.05244	2.3344	1.338

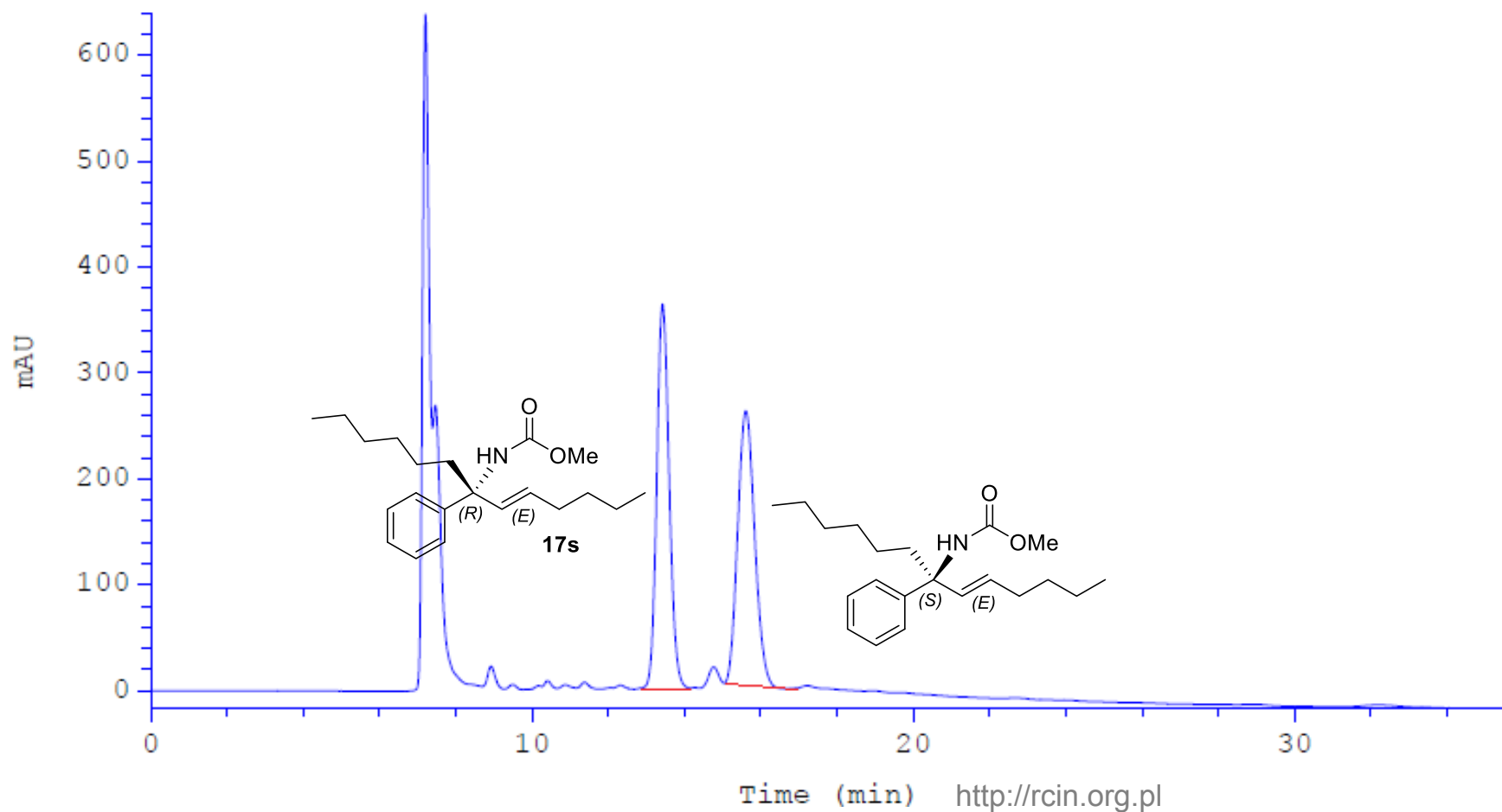






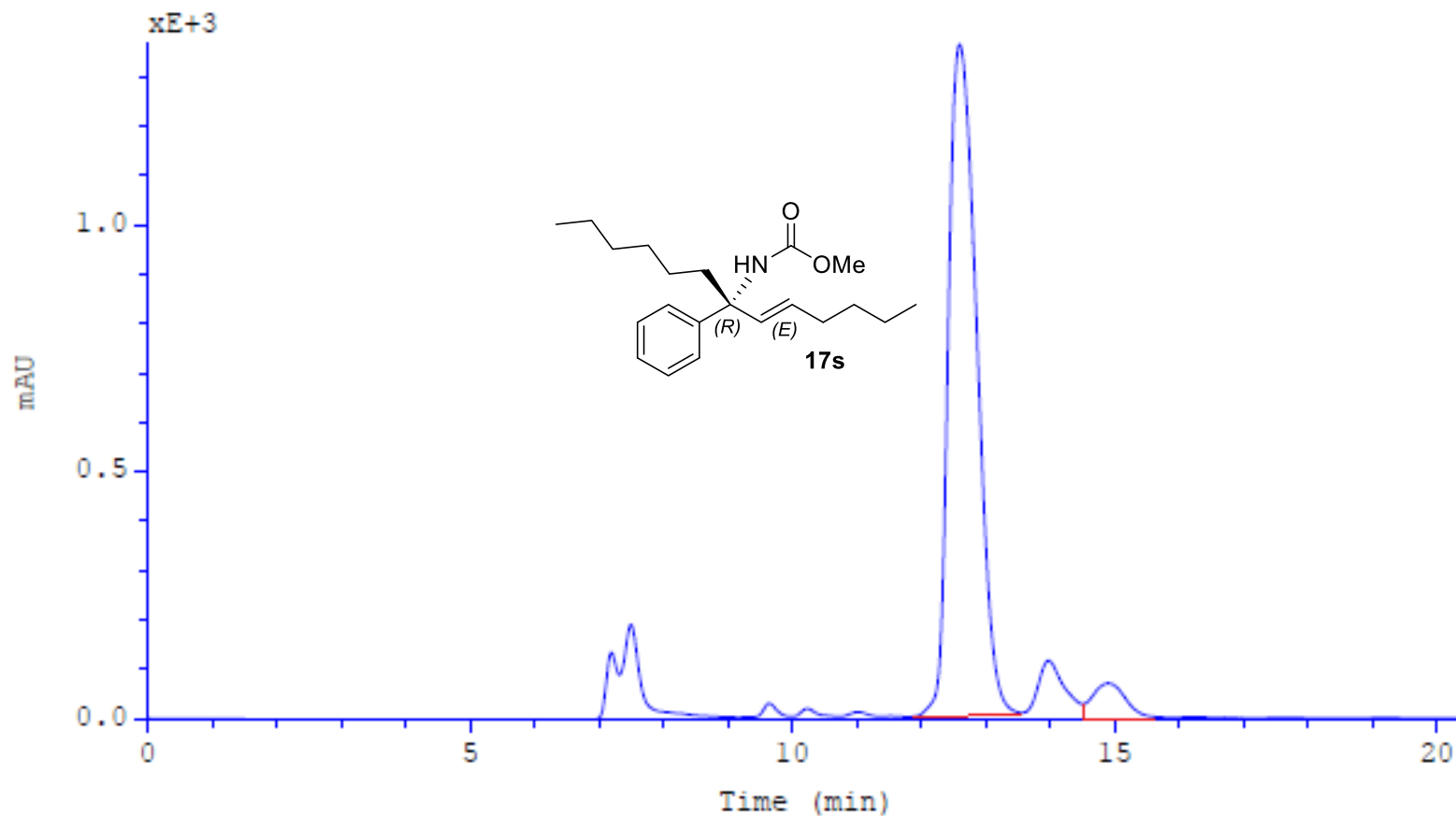
Column: Chiralpak AS-H  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5mL/min  
Detection: UV, 215 nm

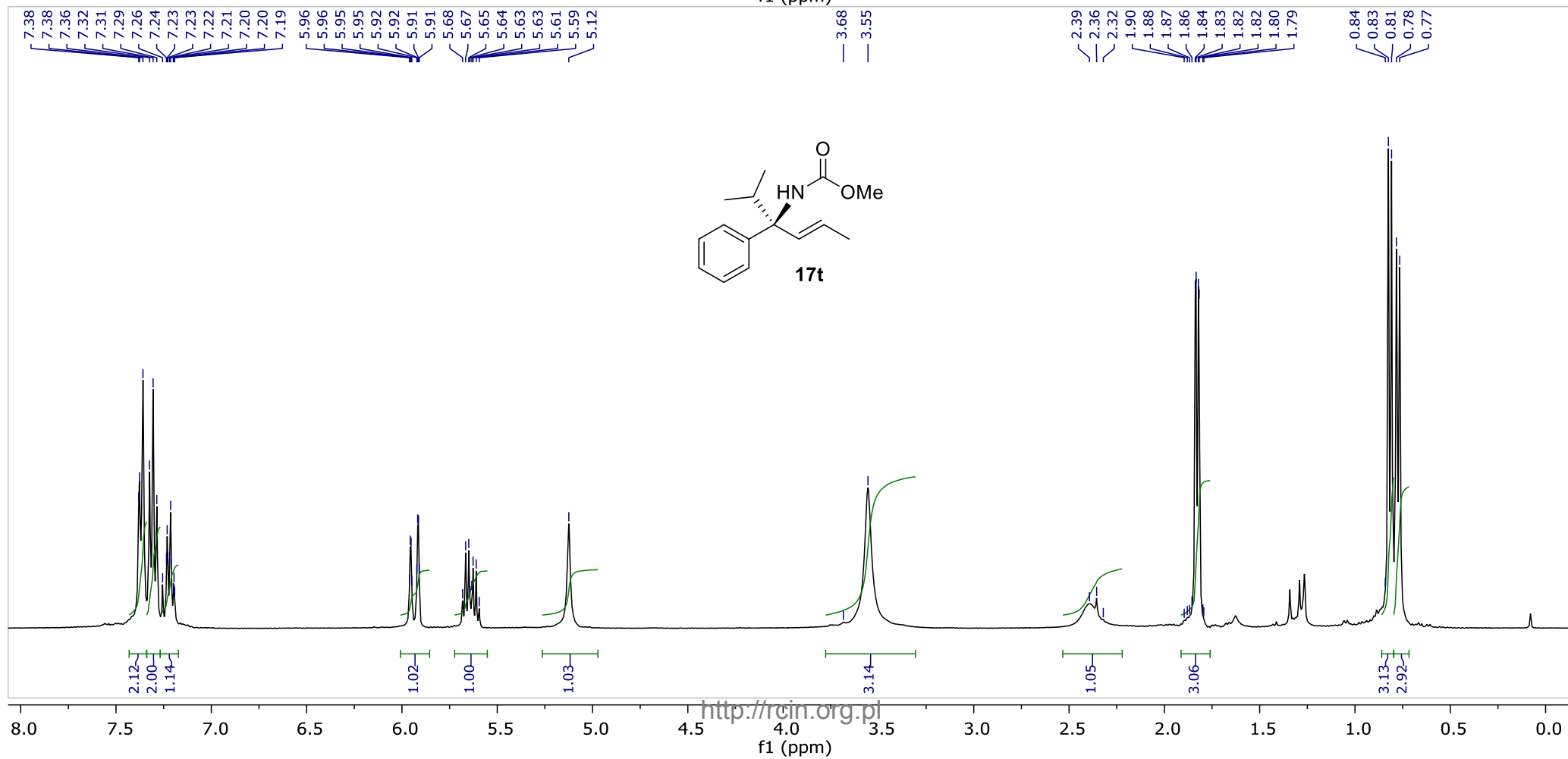
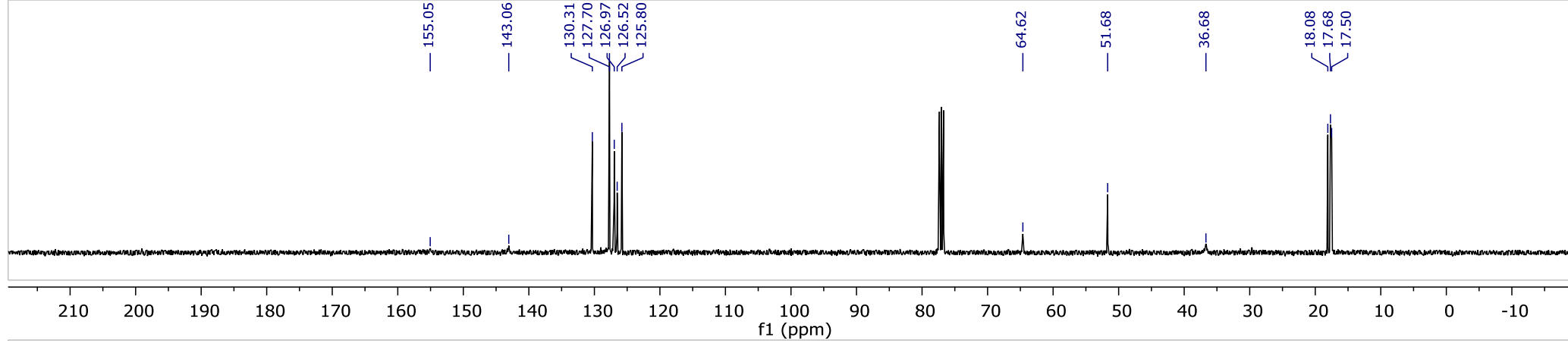
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	13.419	12.86	14.13	136.465	362.278	50.5122	0.351
2	15.603	15.03	16.44	133.697	258.986	49.4878	0.487

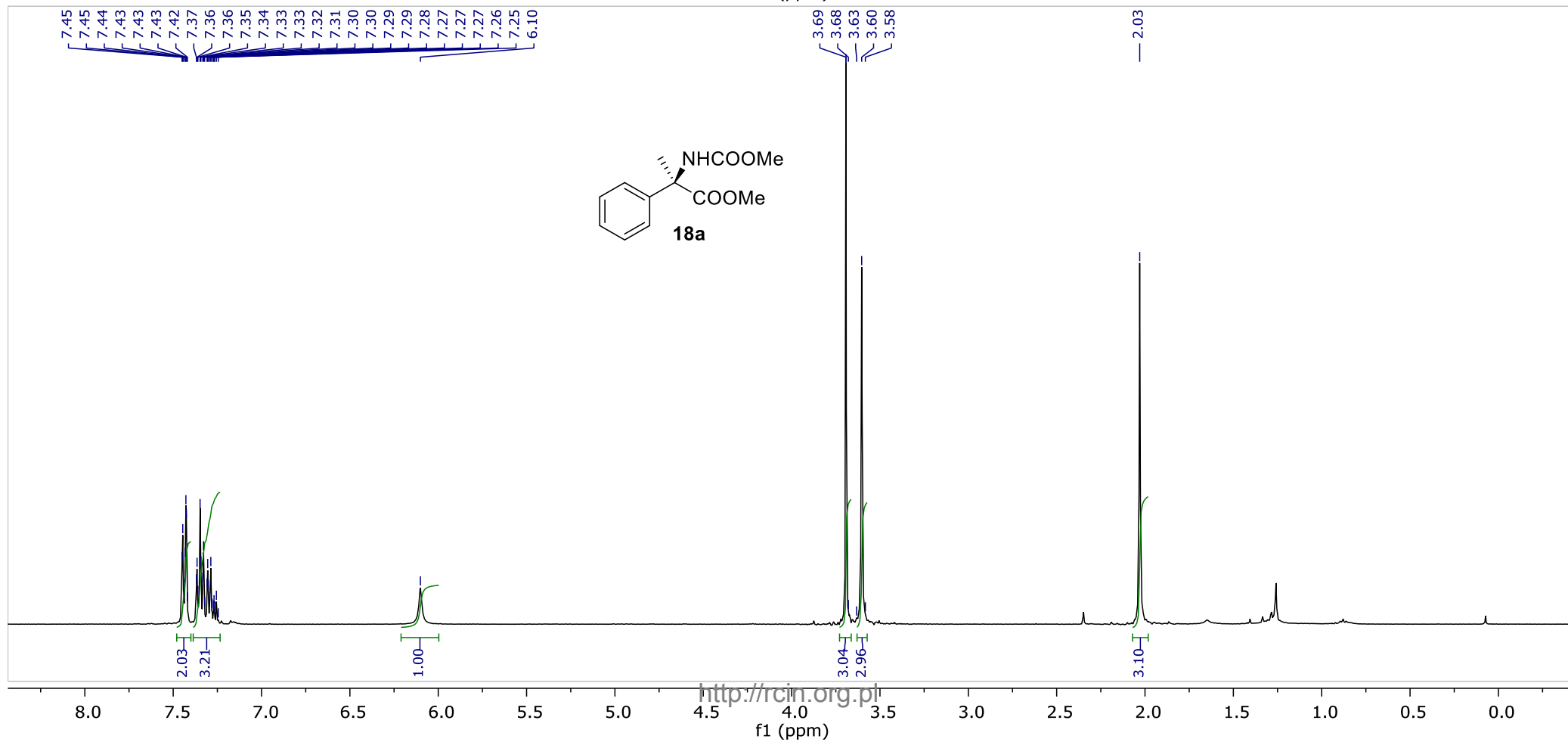
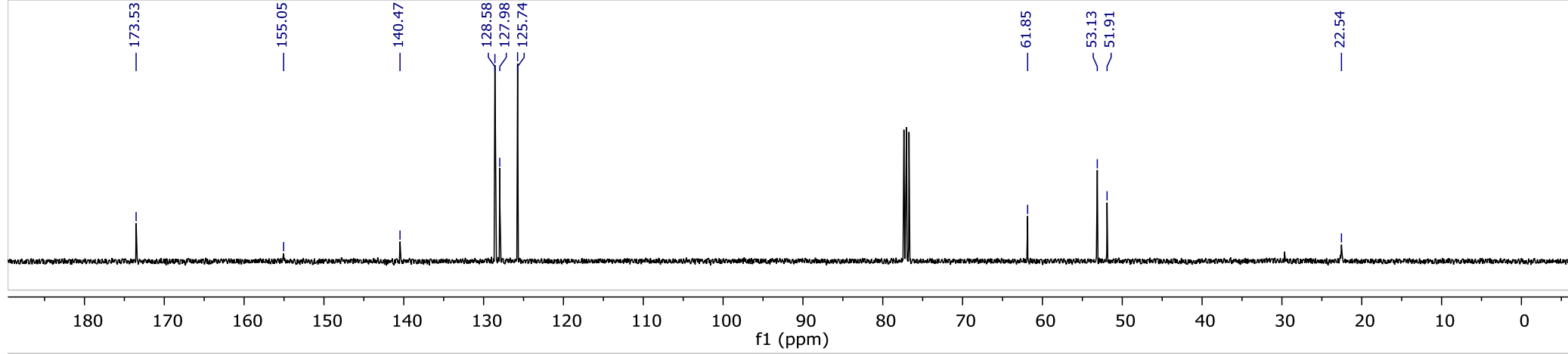


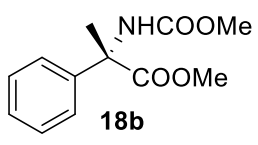
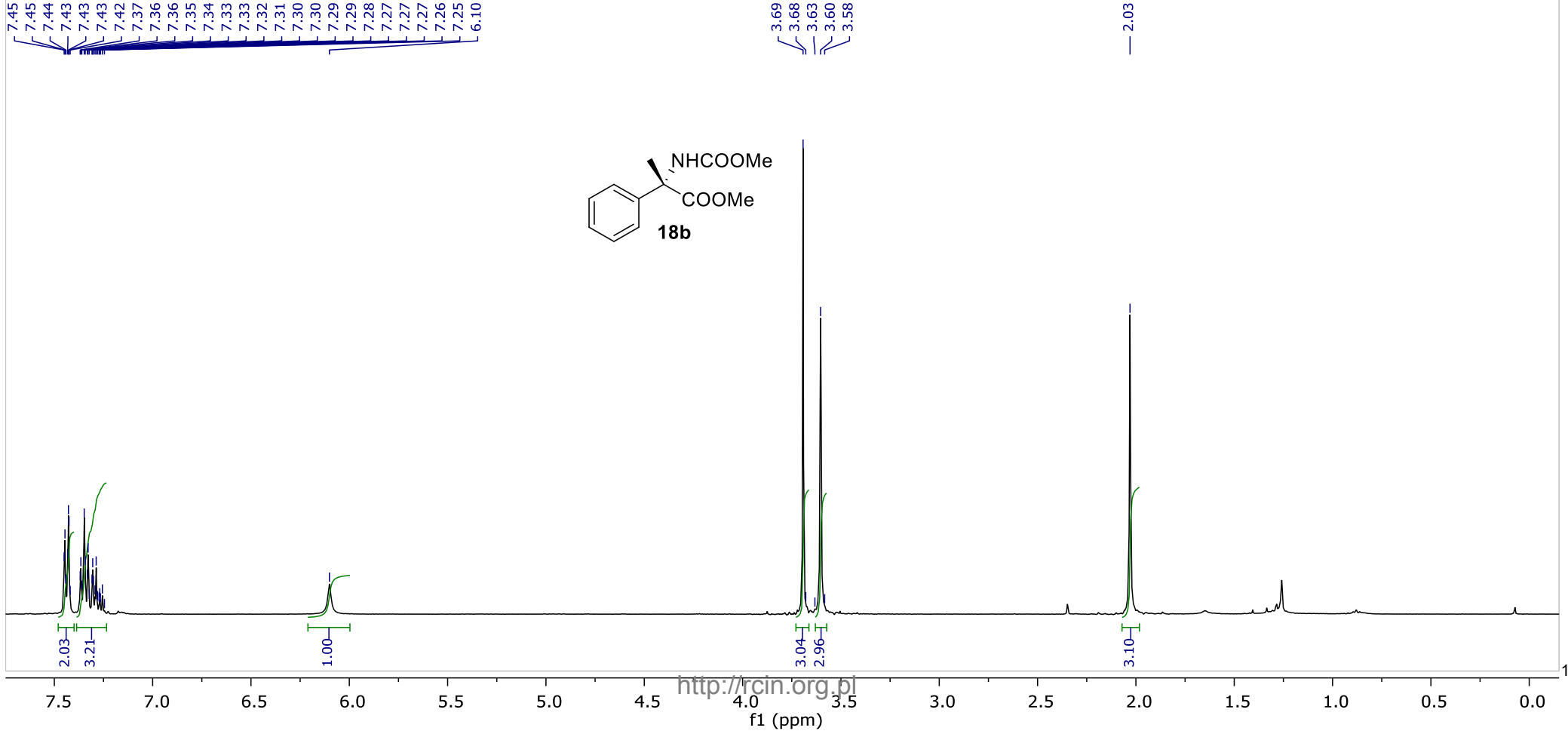
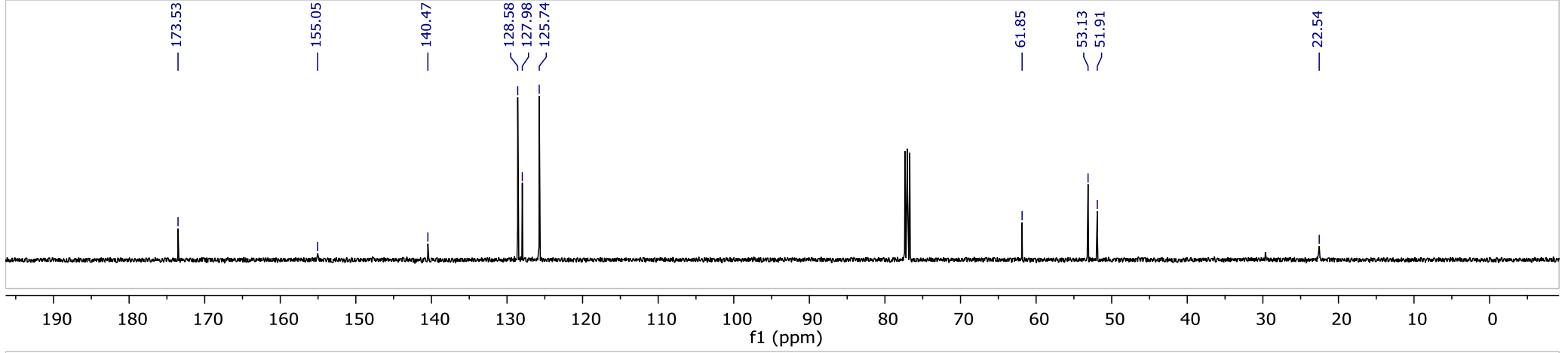
Column: Chiralpak AS-H  
Eluent: 1% *i*-PrOH in hexanes  
Flow: 0.5mL/min  
Detection: UV, 215 nm

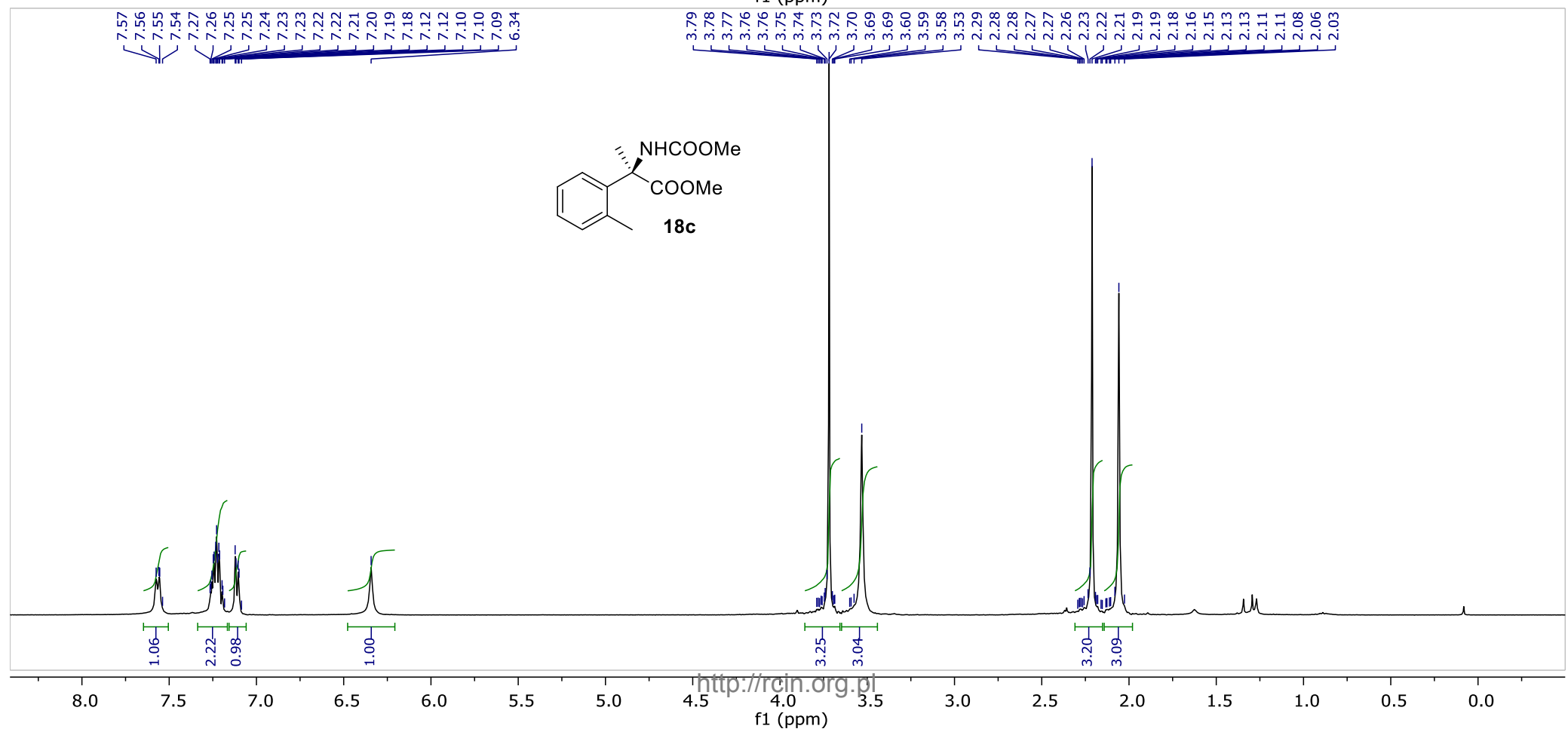
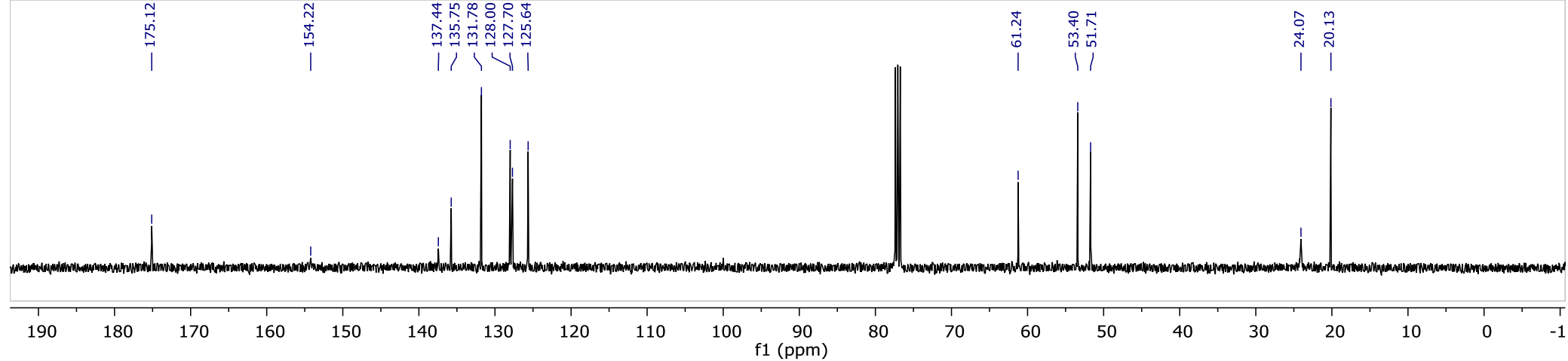
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	12.590	11.86	13.48	687.027	1357.58	96.4789	0.488
2	14.908	14.51	15.63	25.074	51.1382	3.5211	0.503

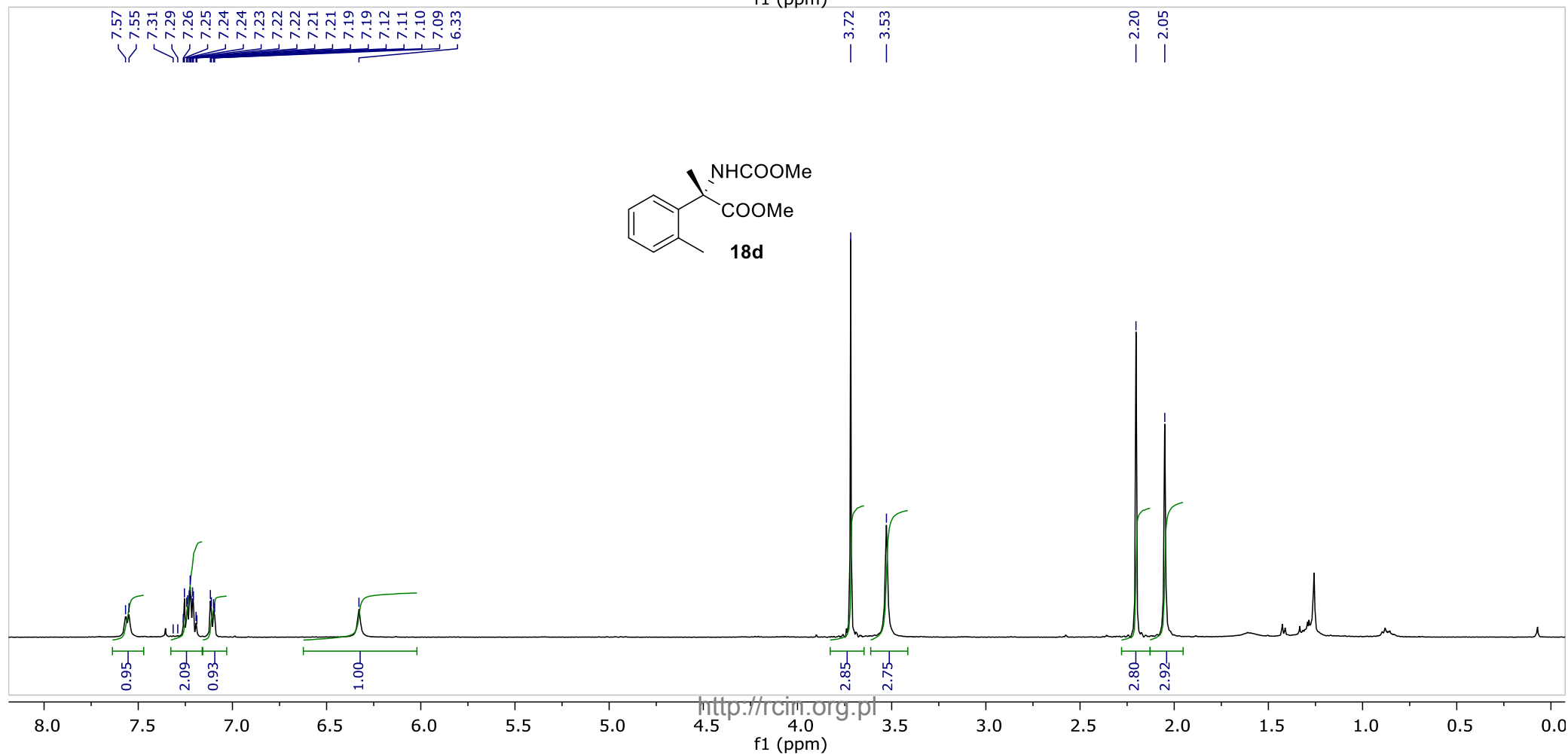
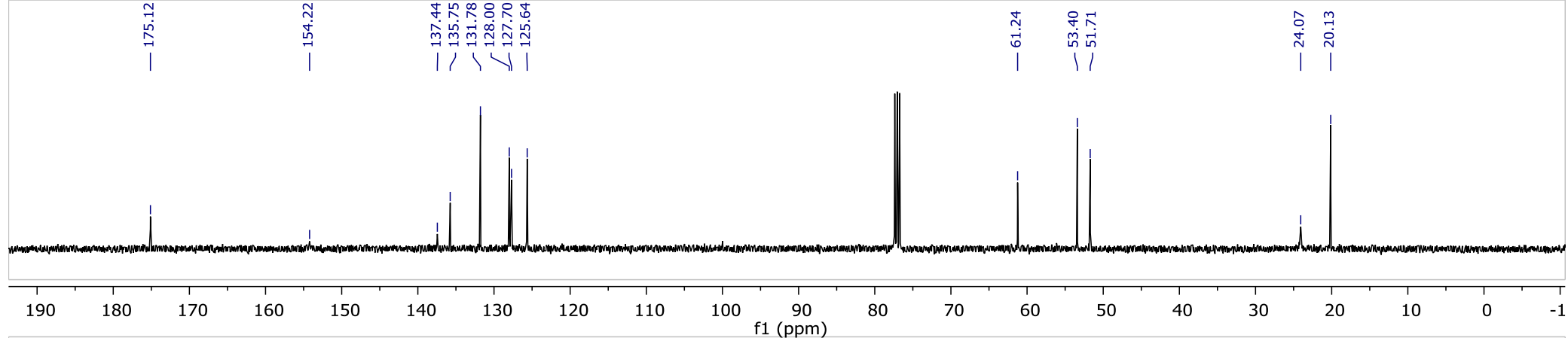




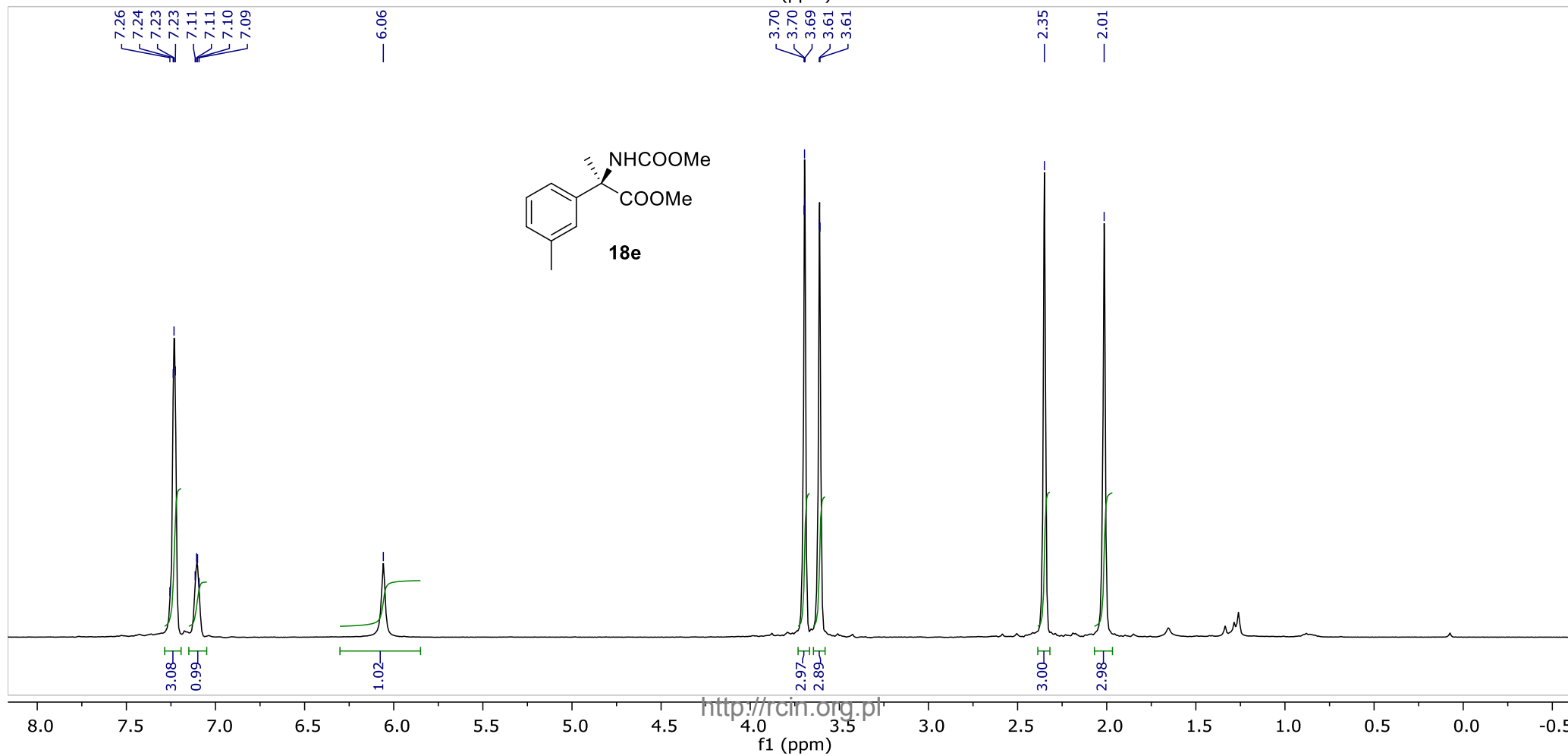
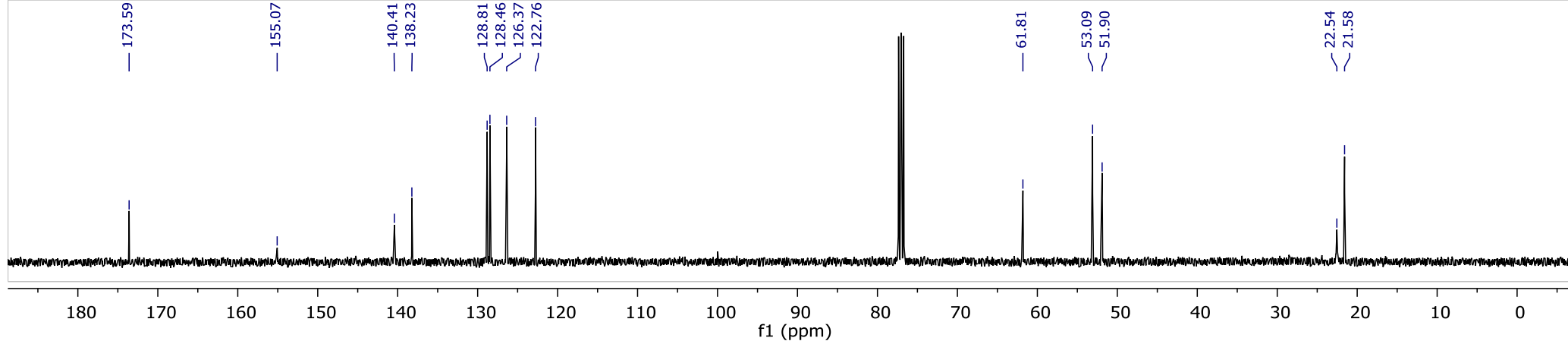


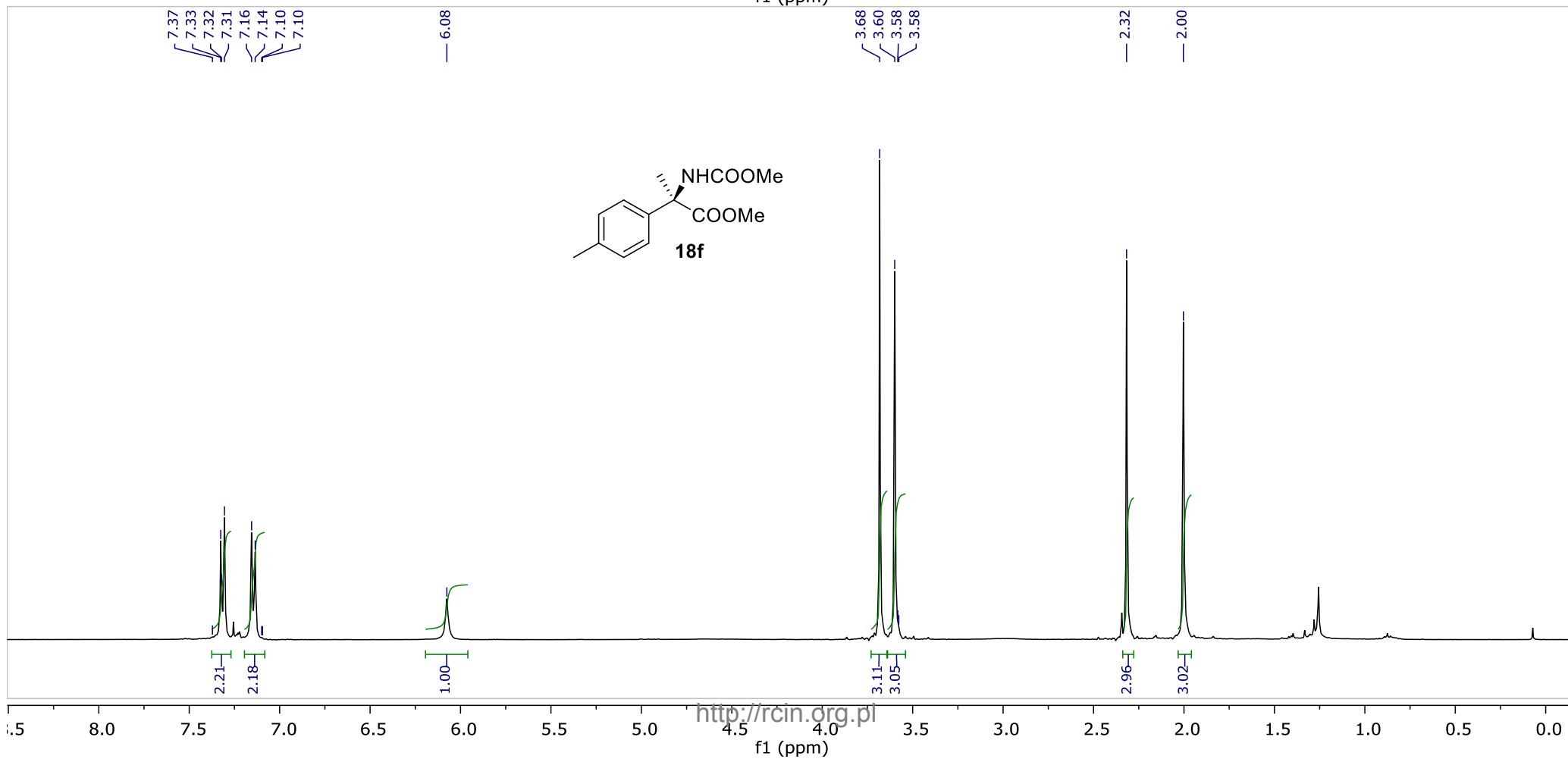
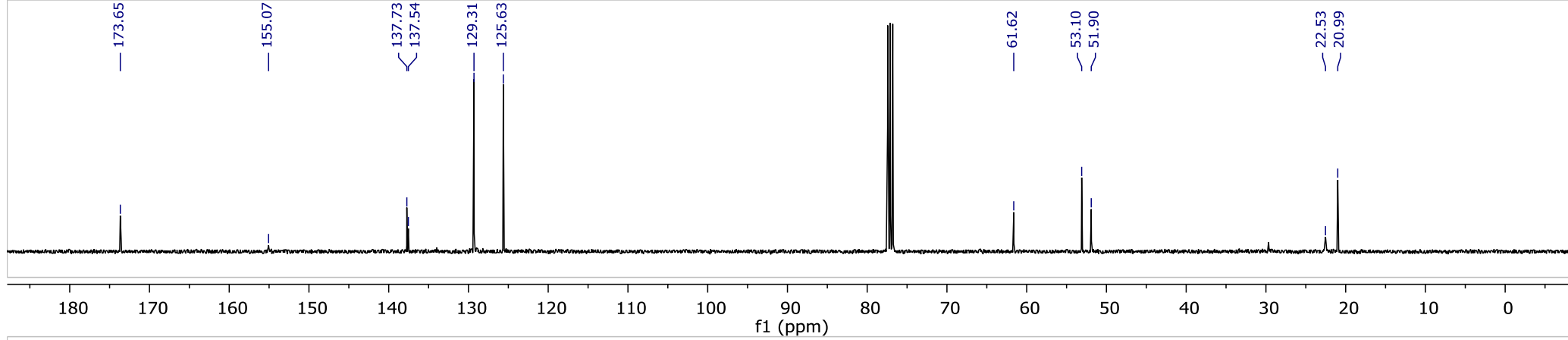


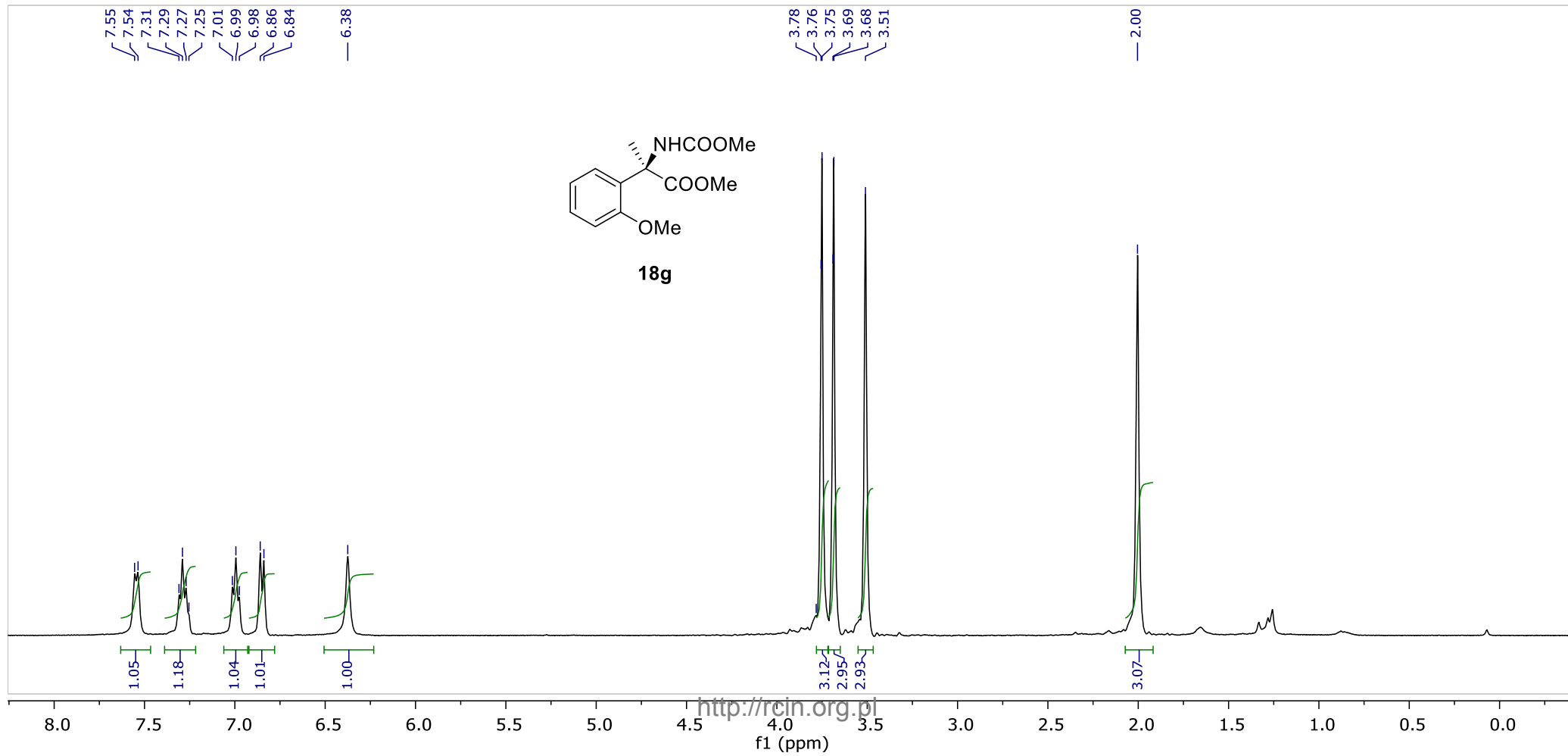
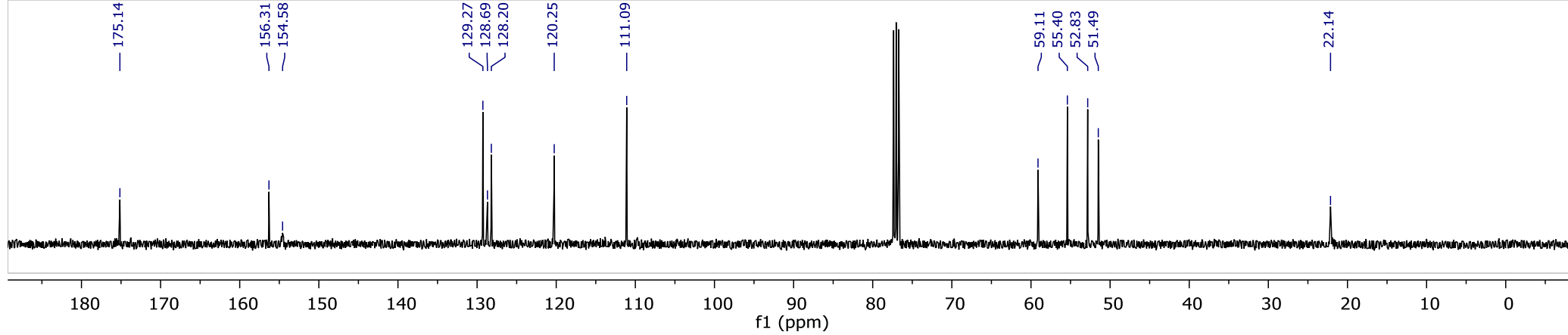


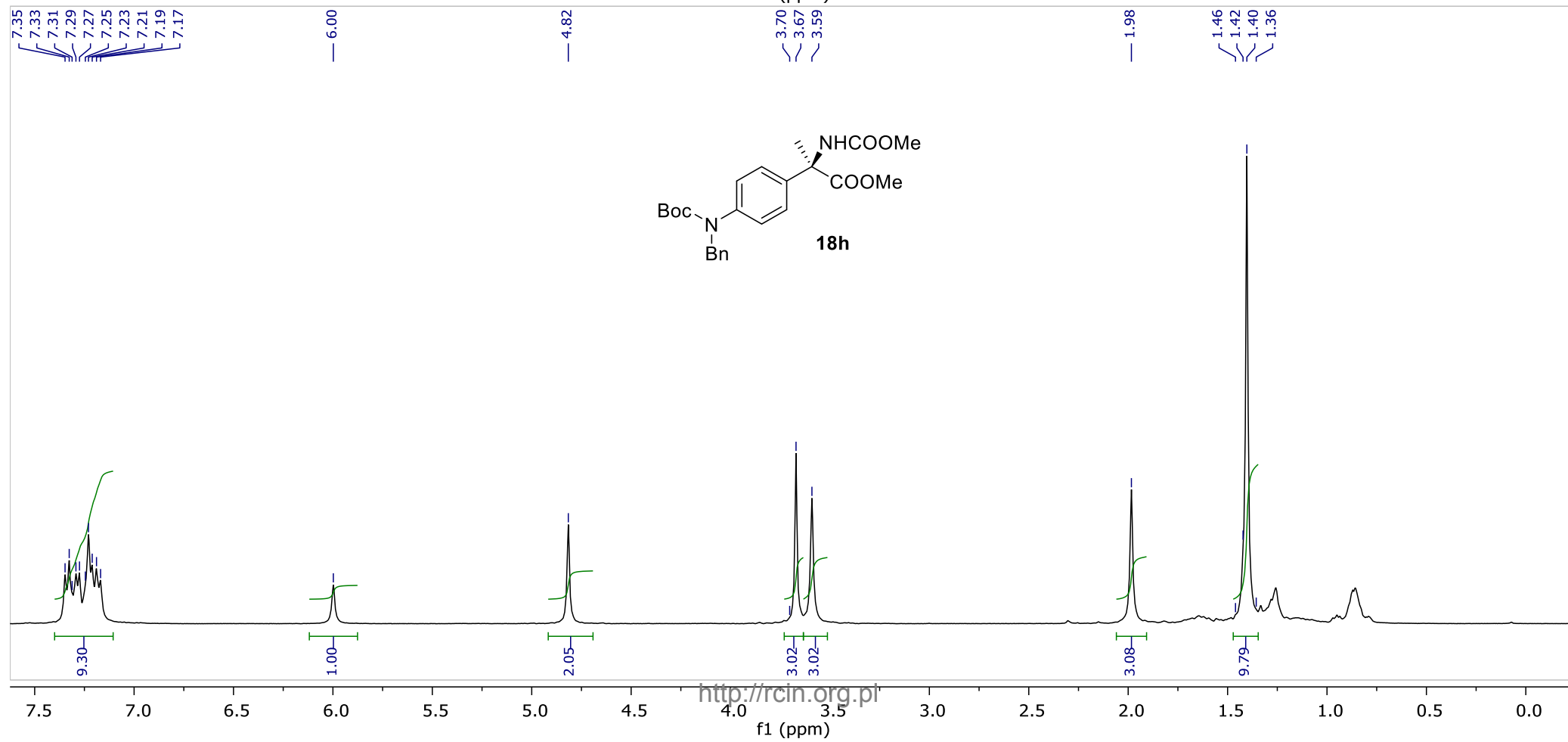
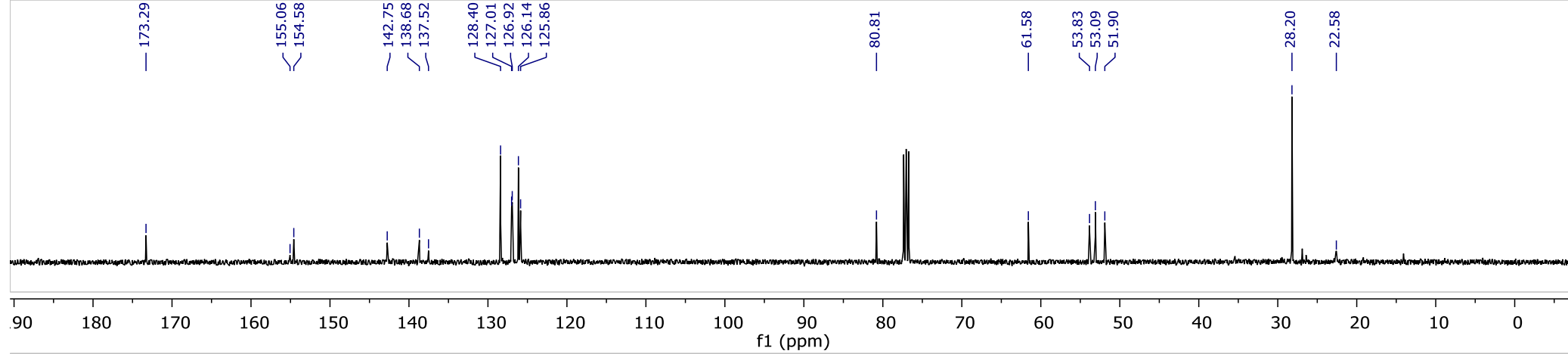


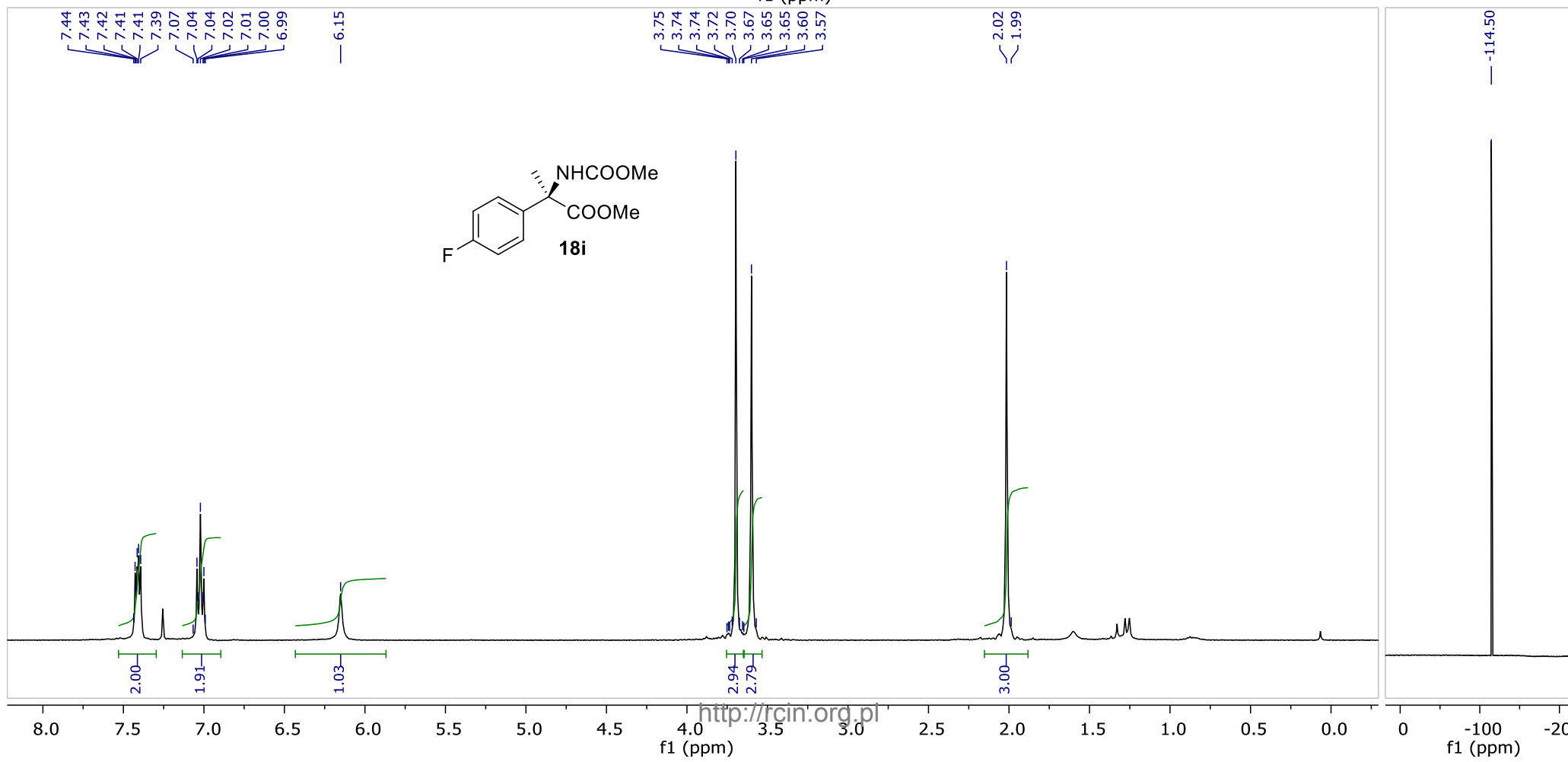
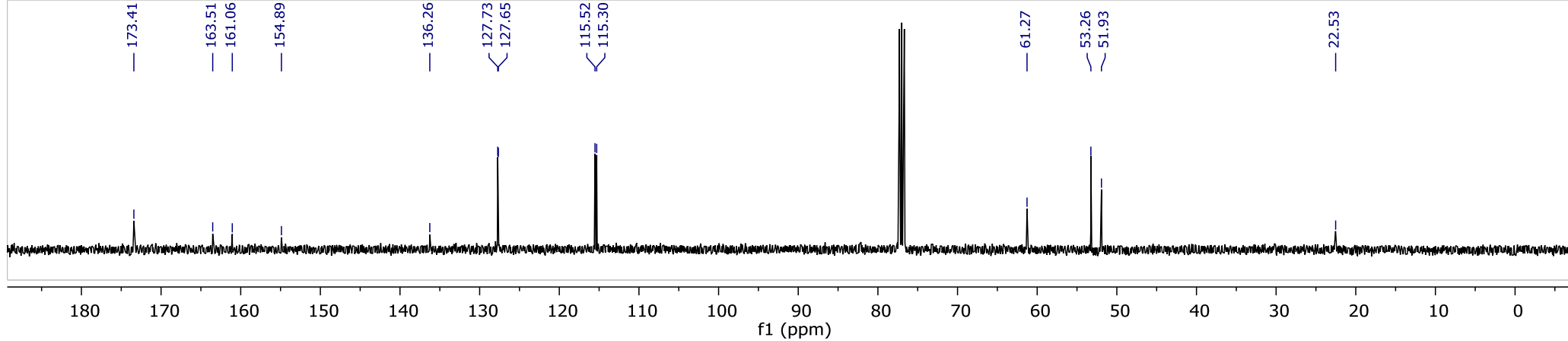


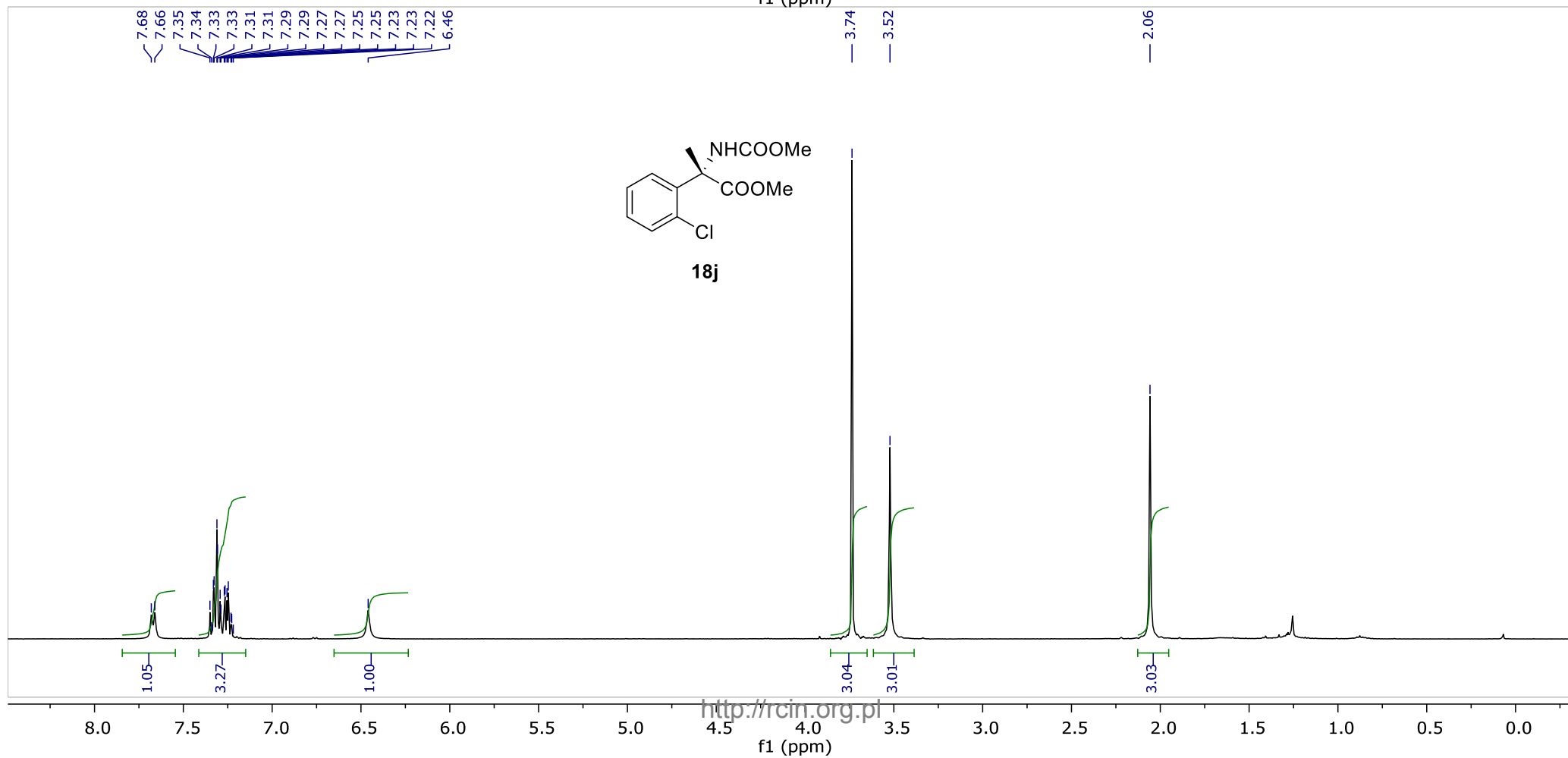
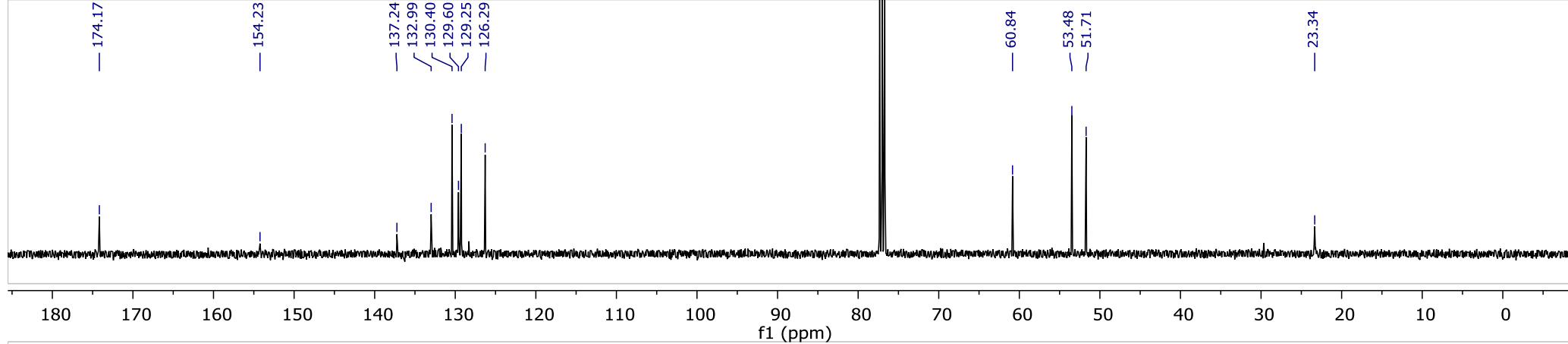


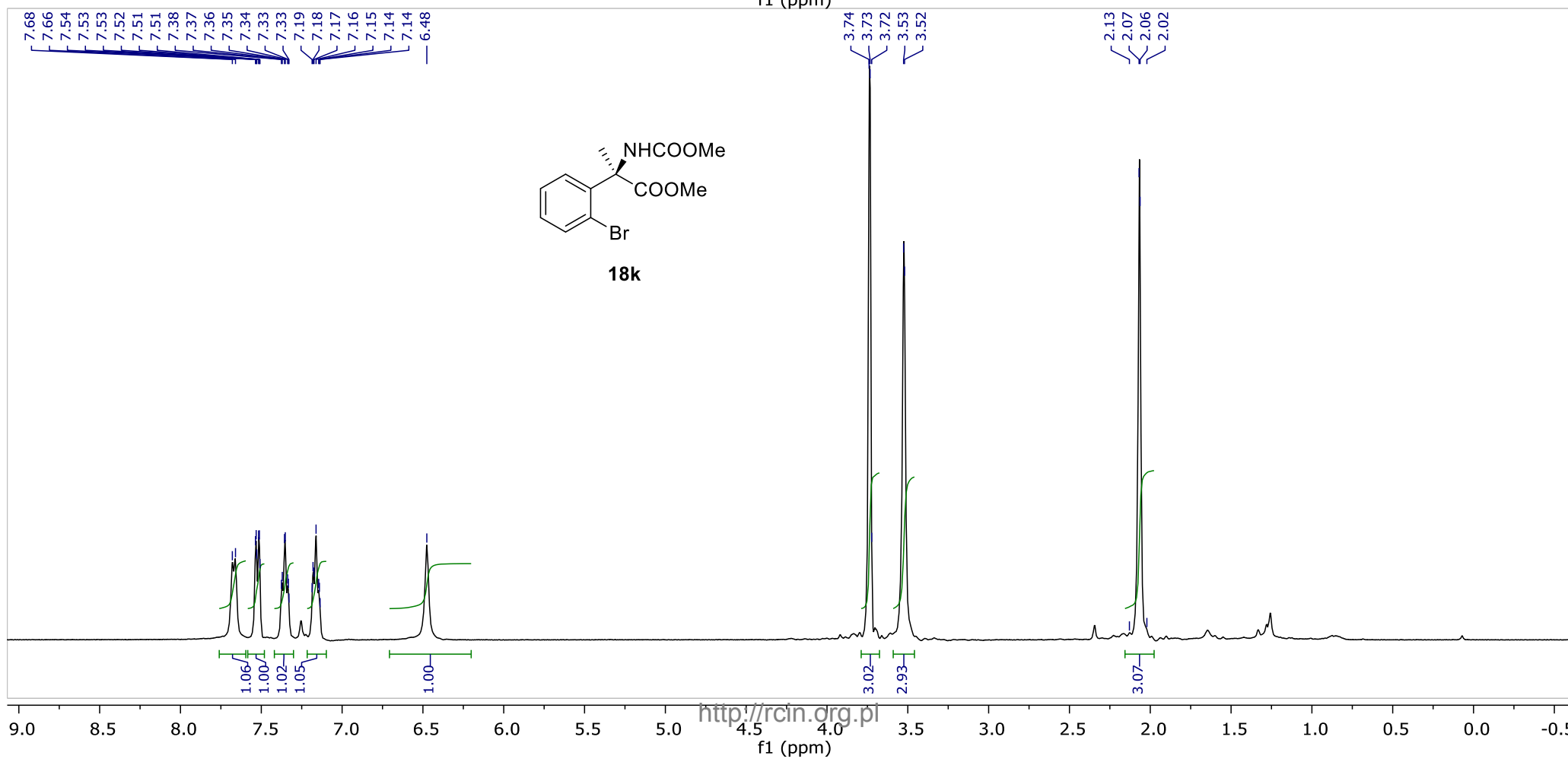
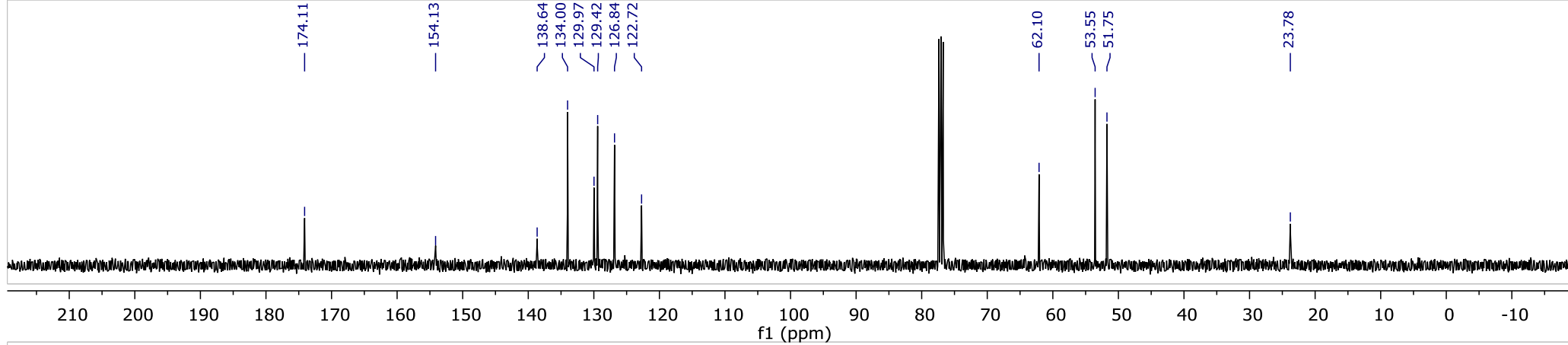


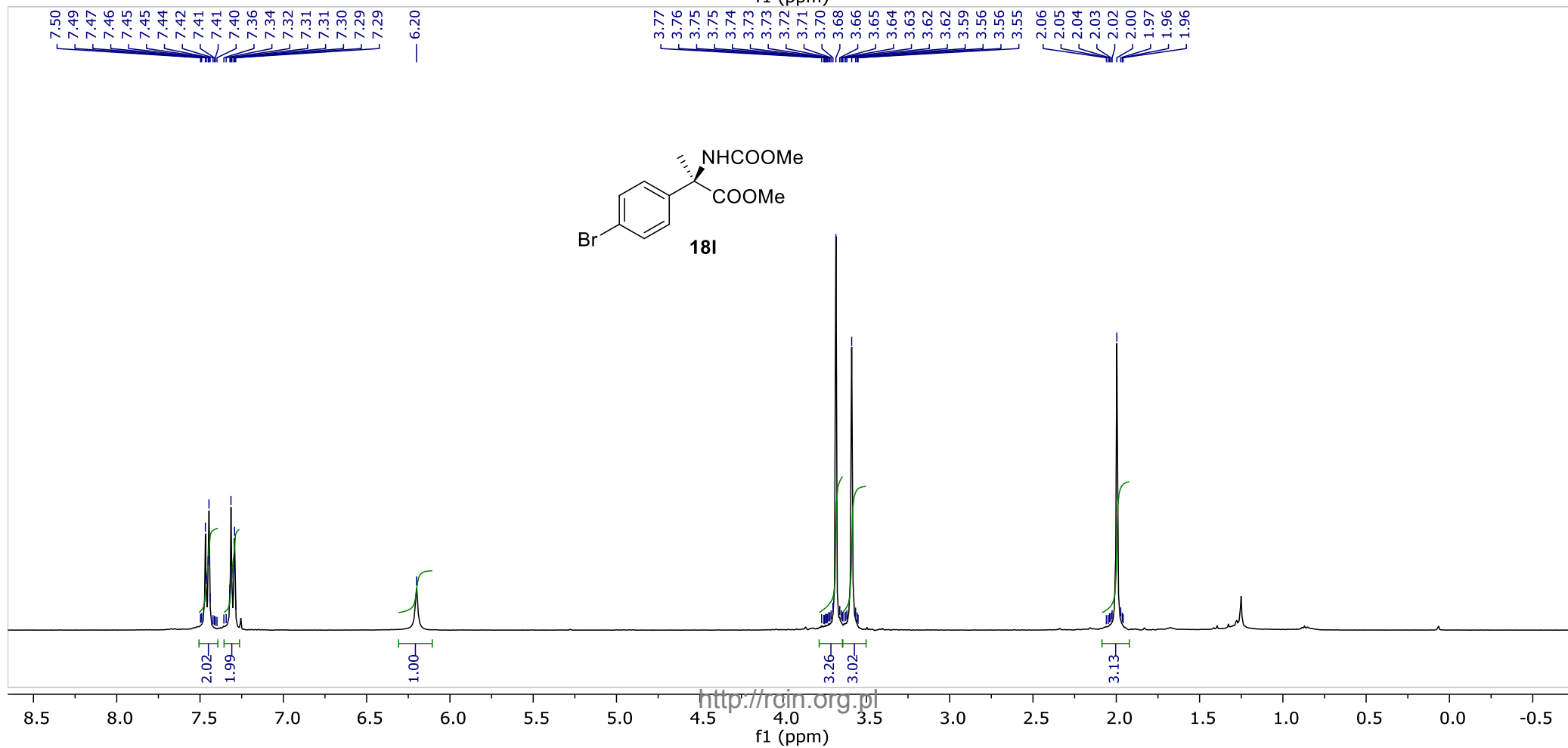
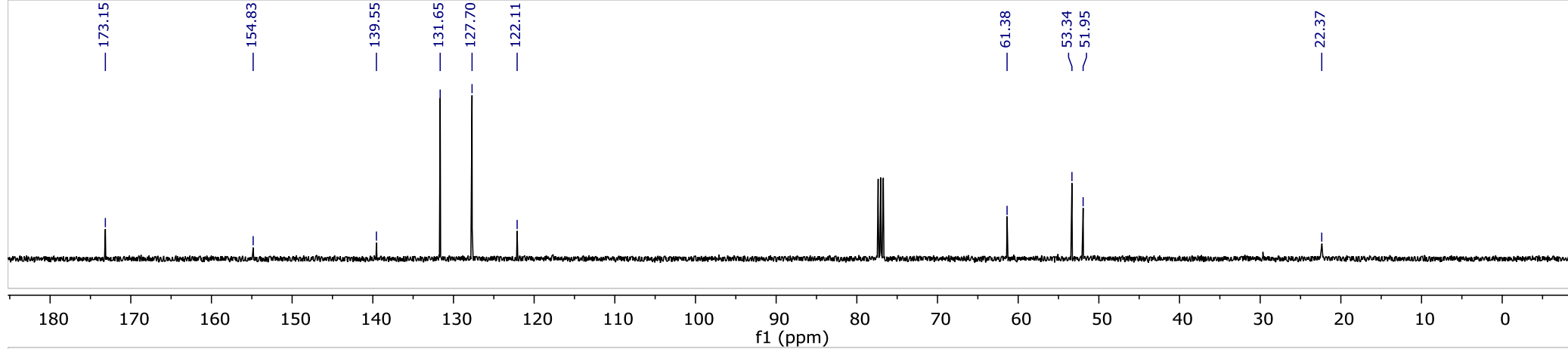




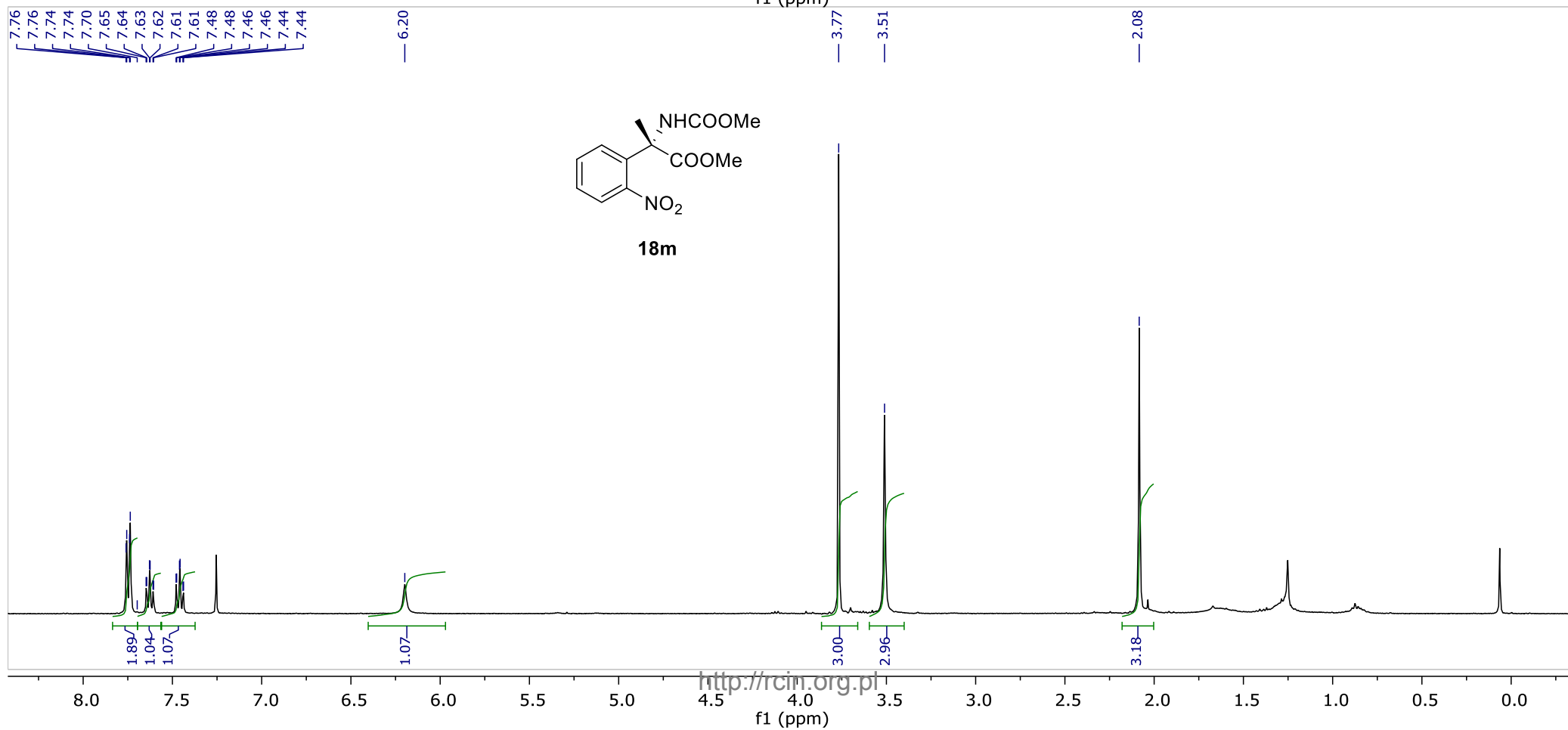
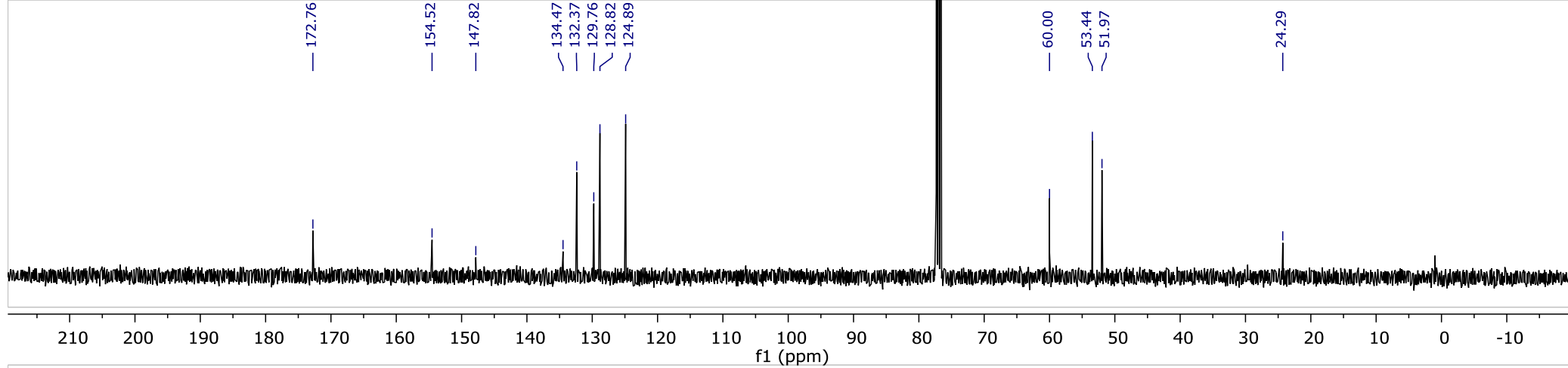


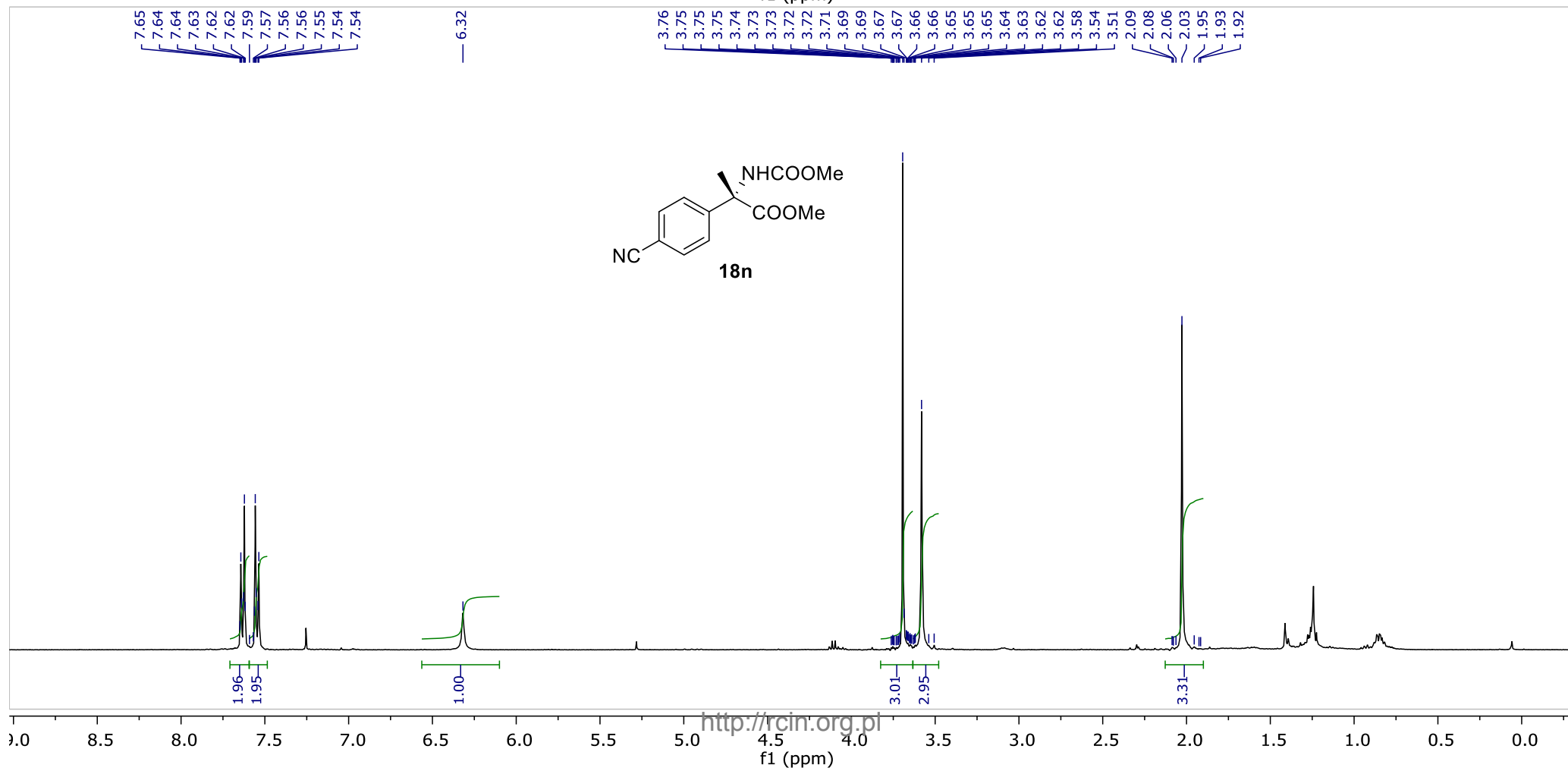
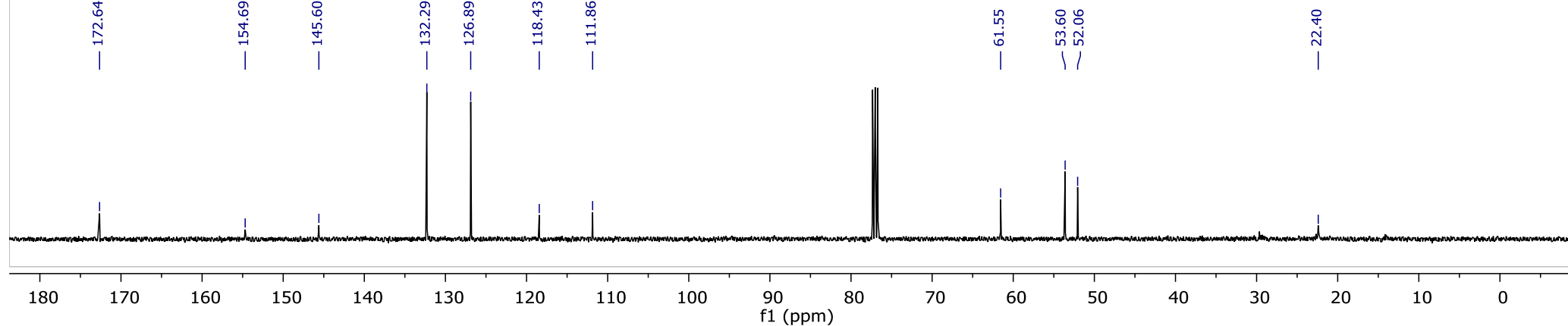


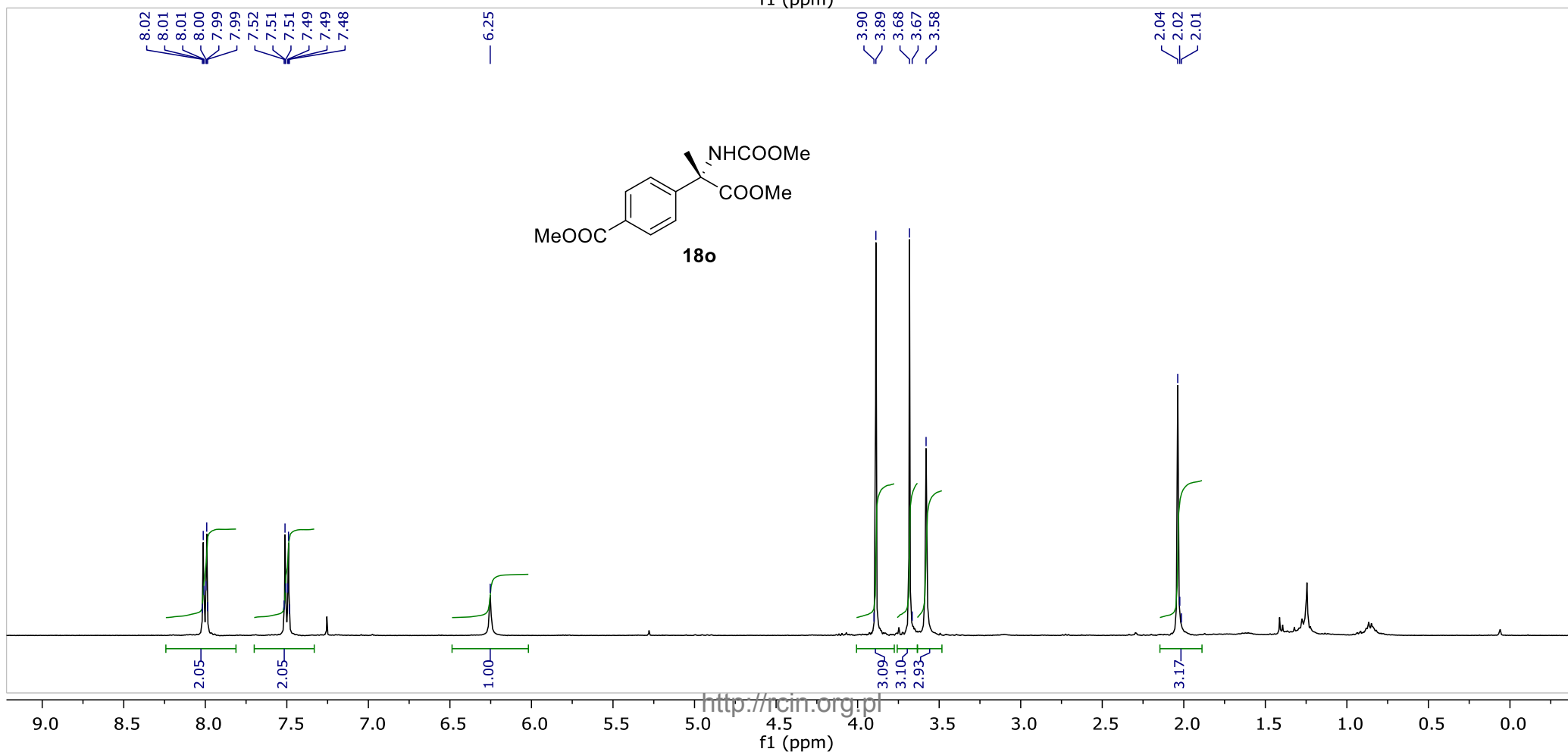
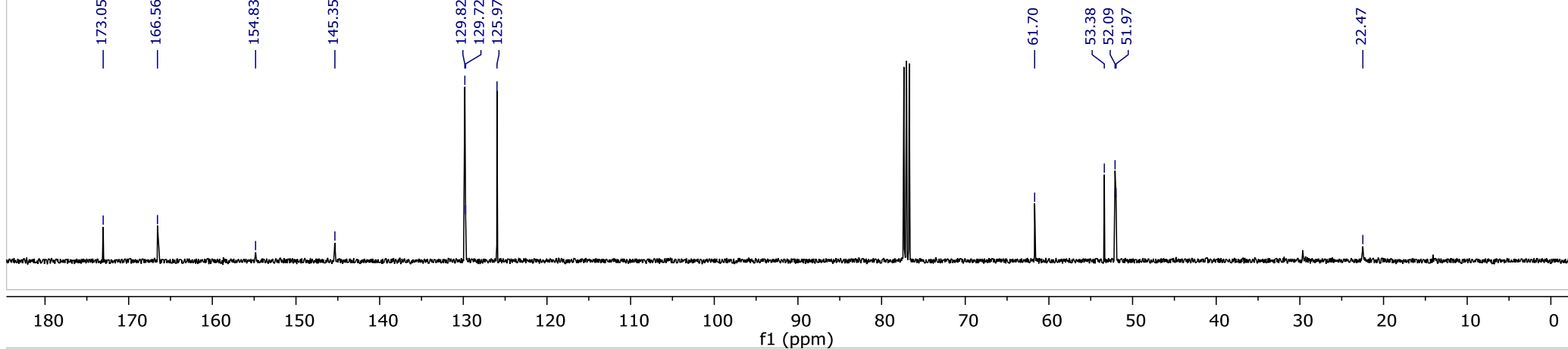


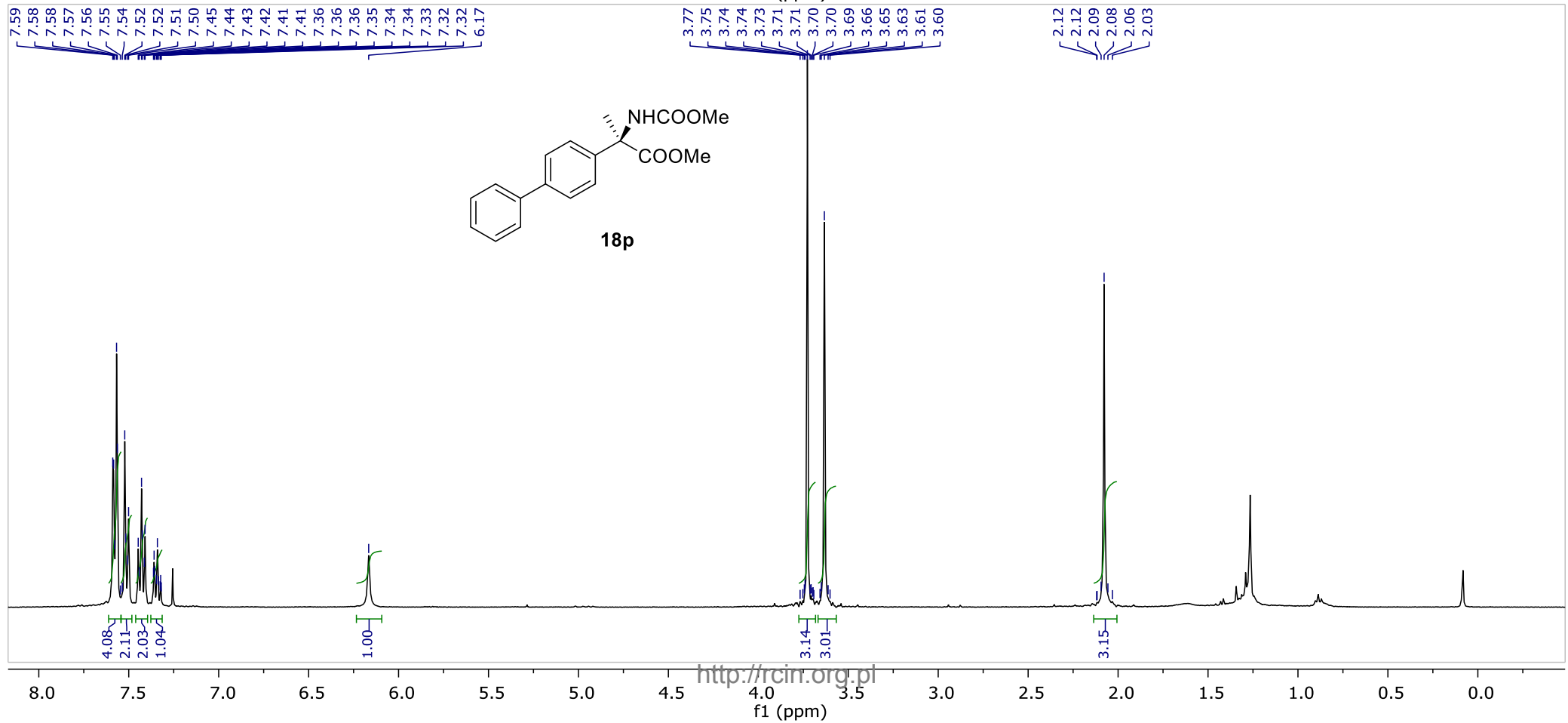
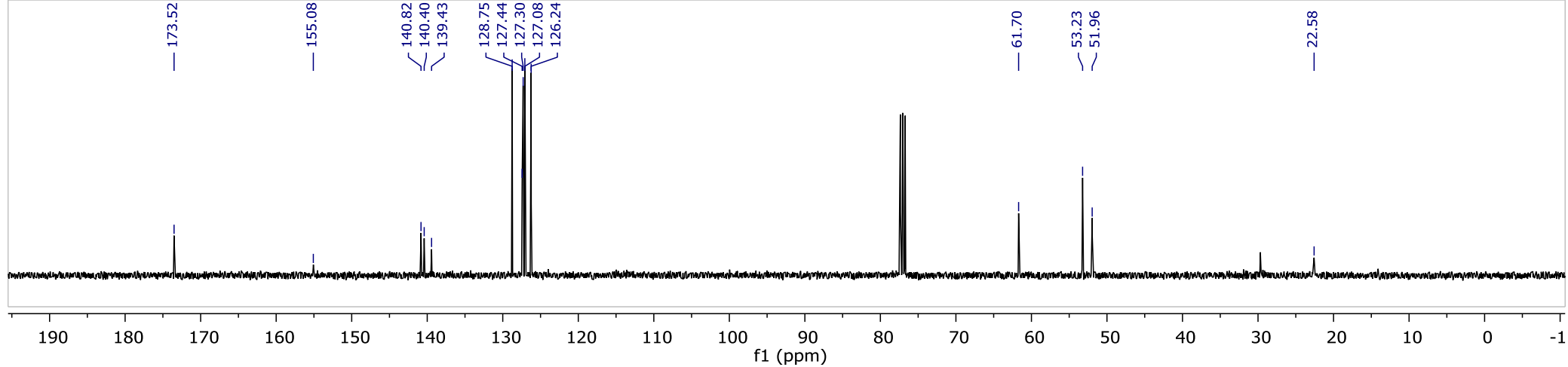


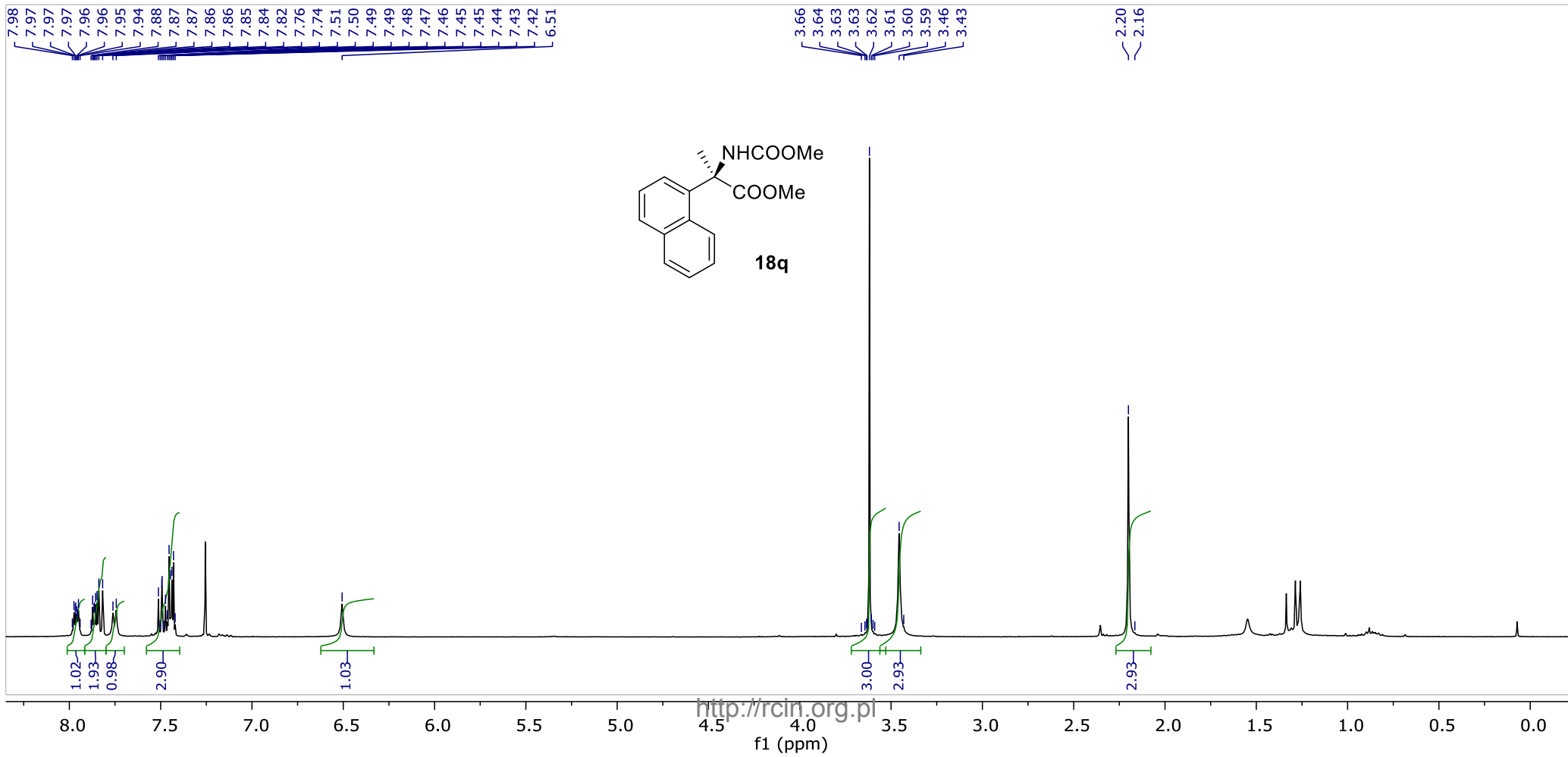
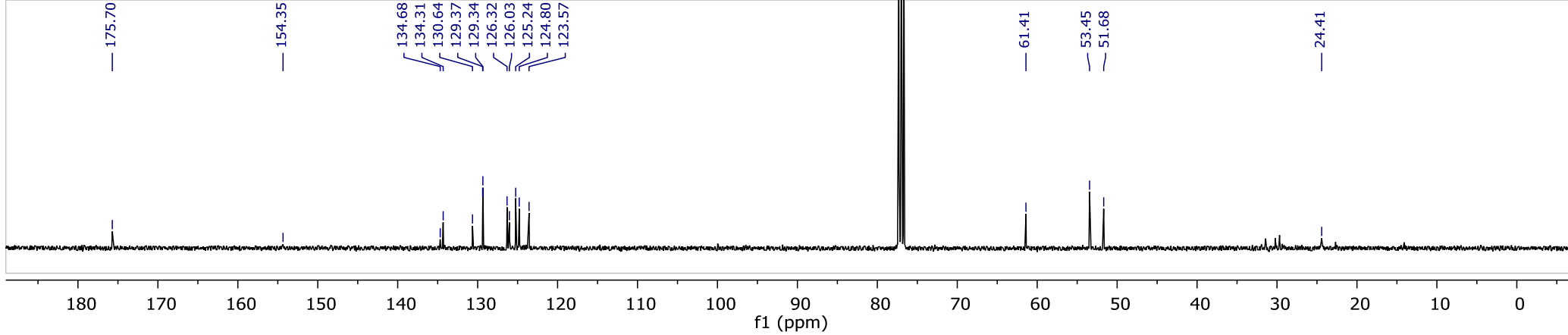


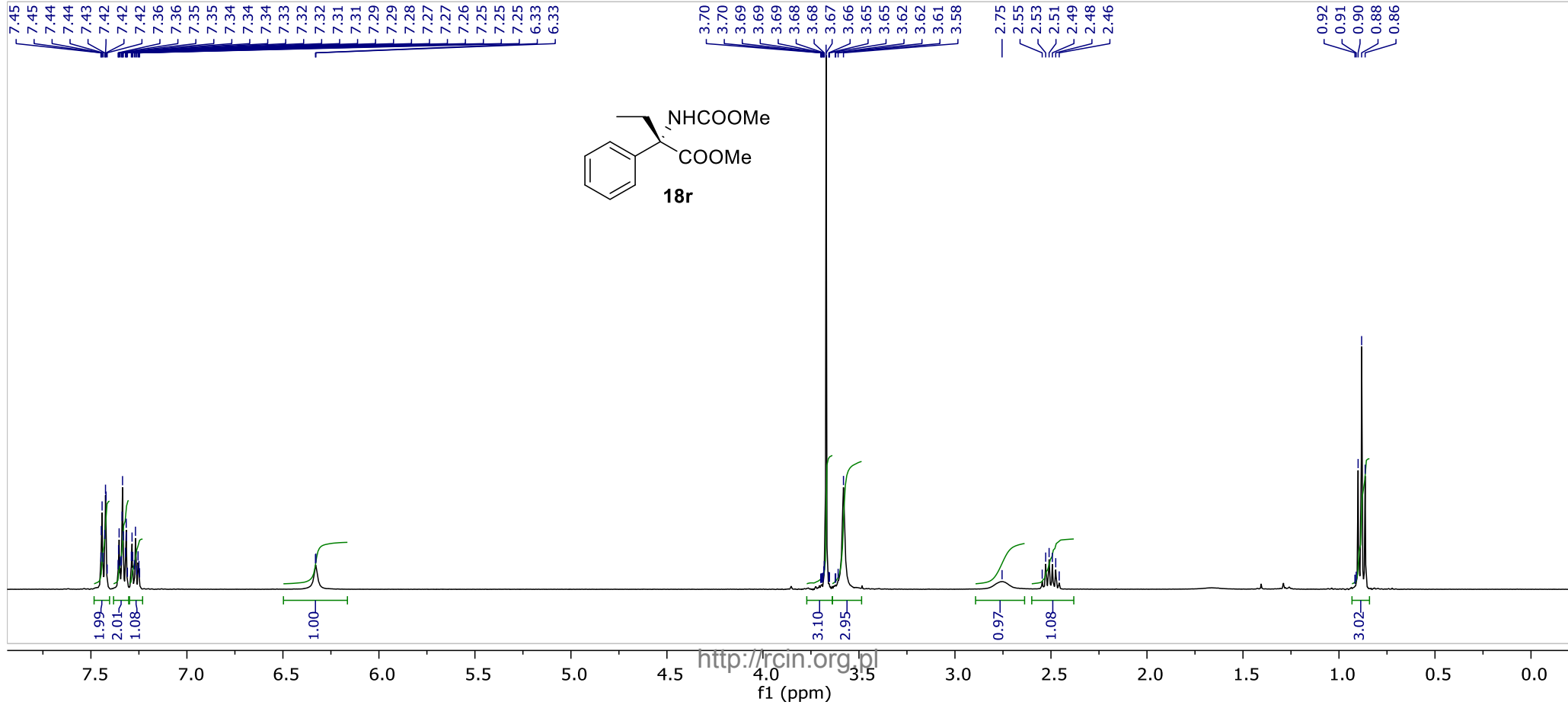
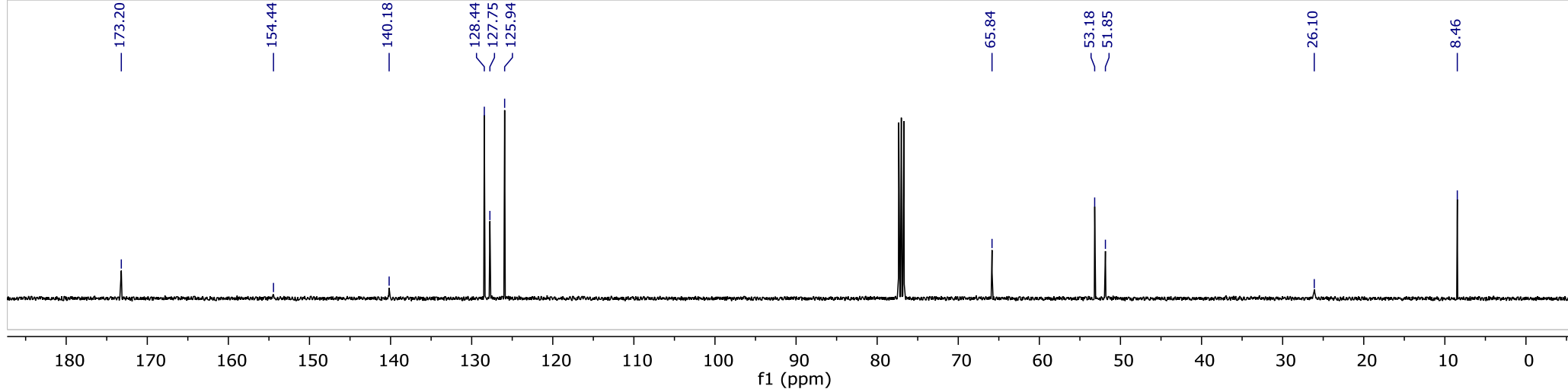


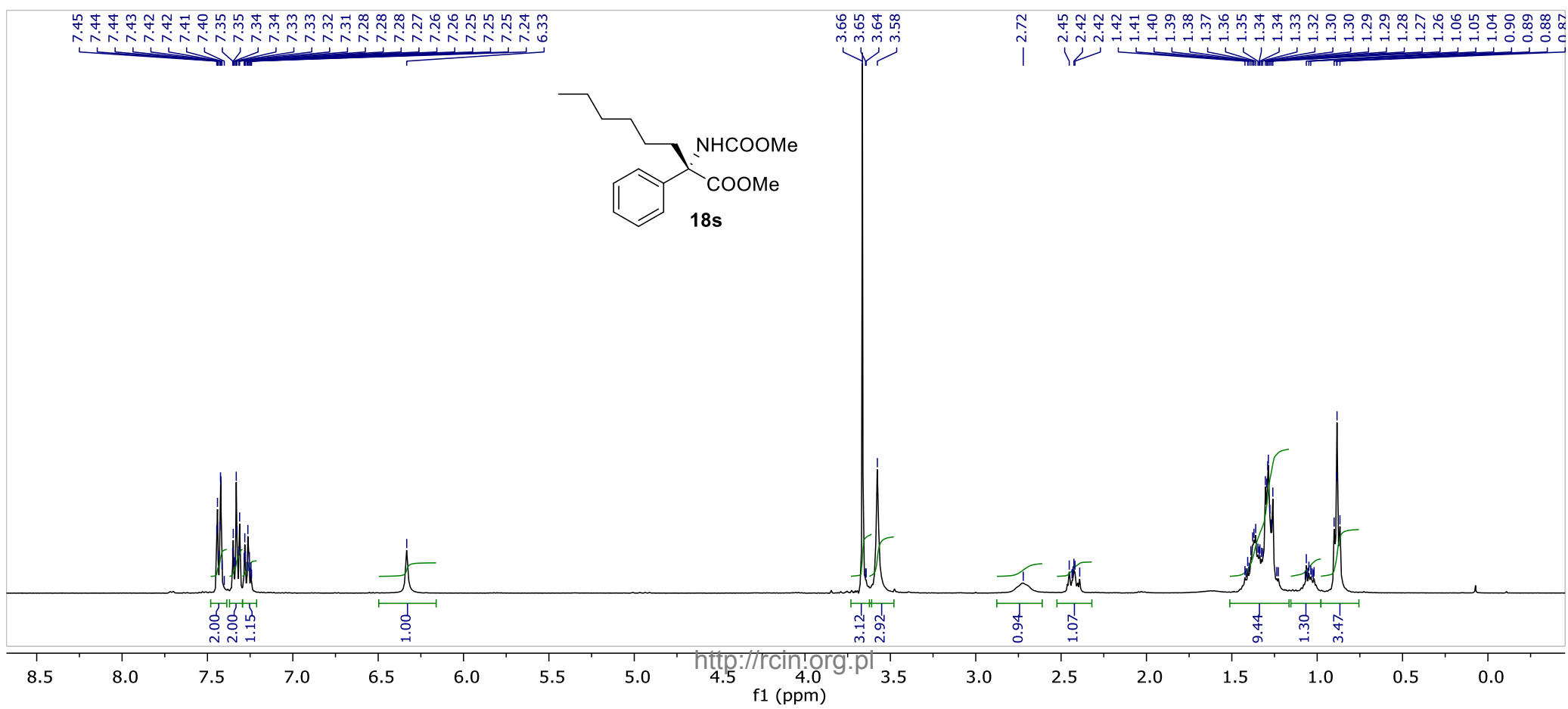
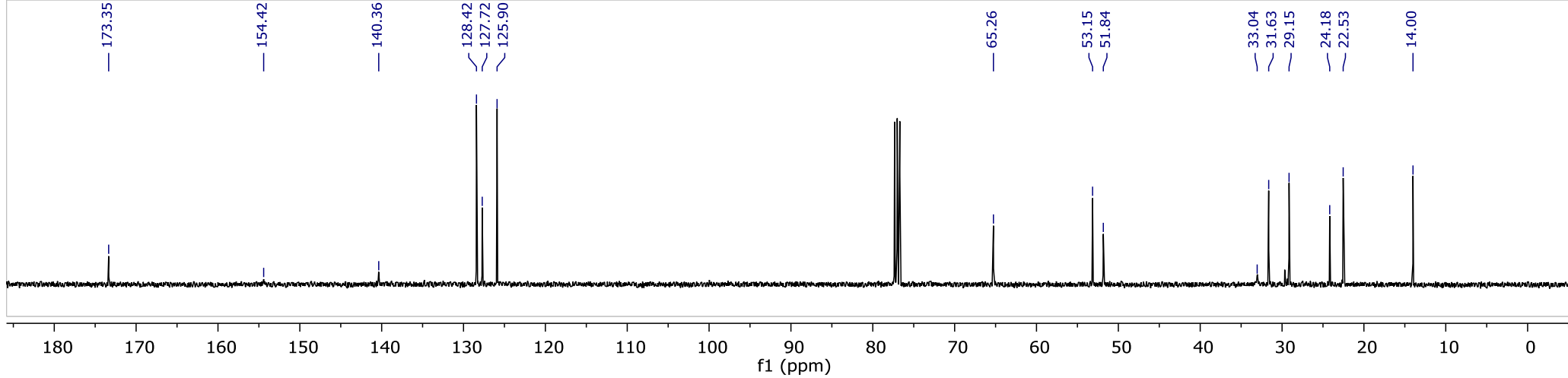


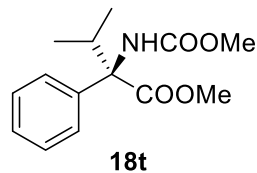
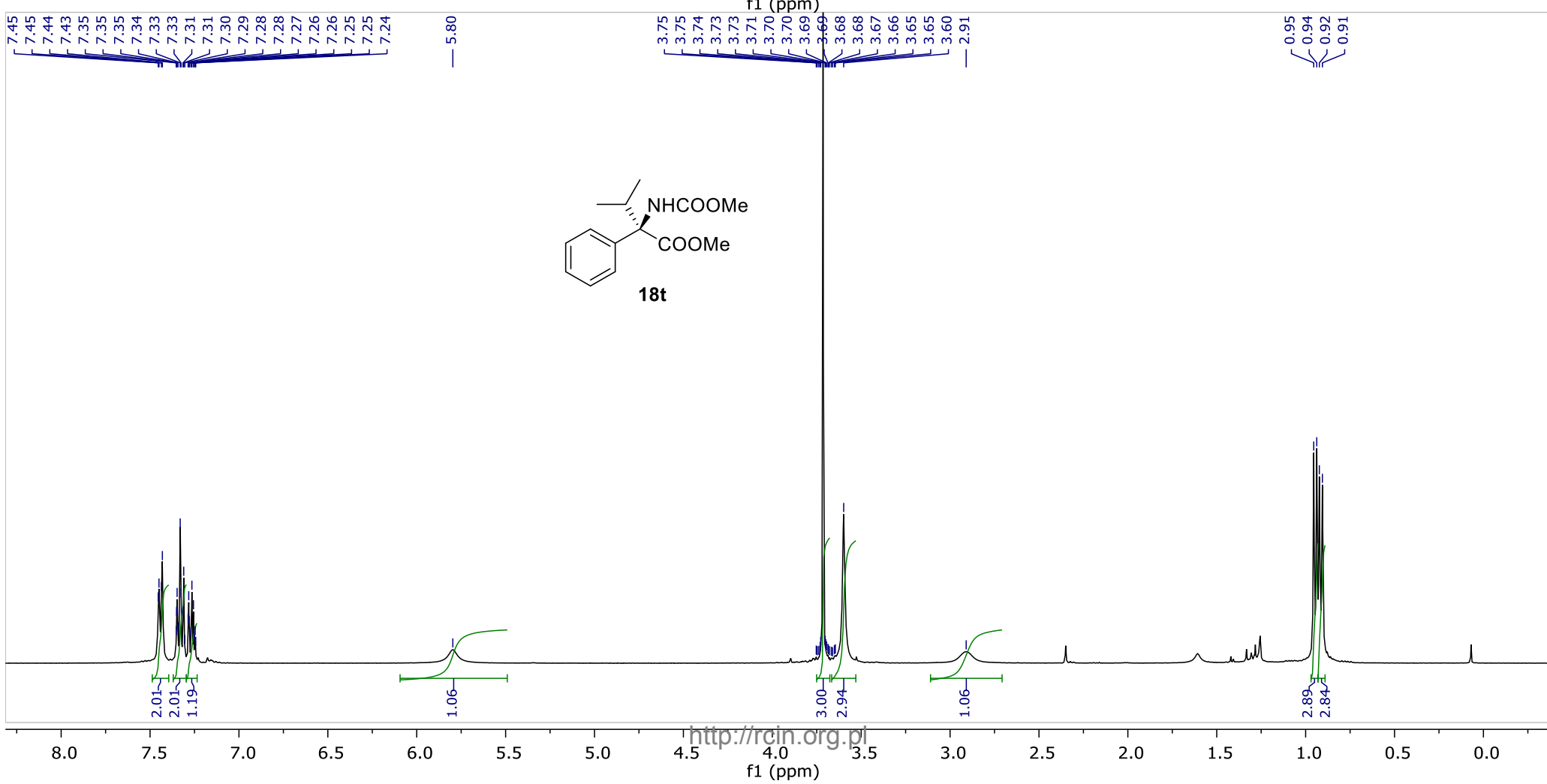
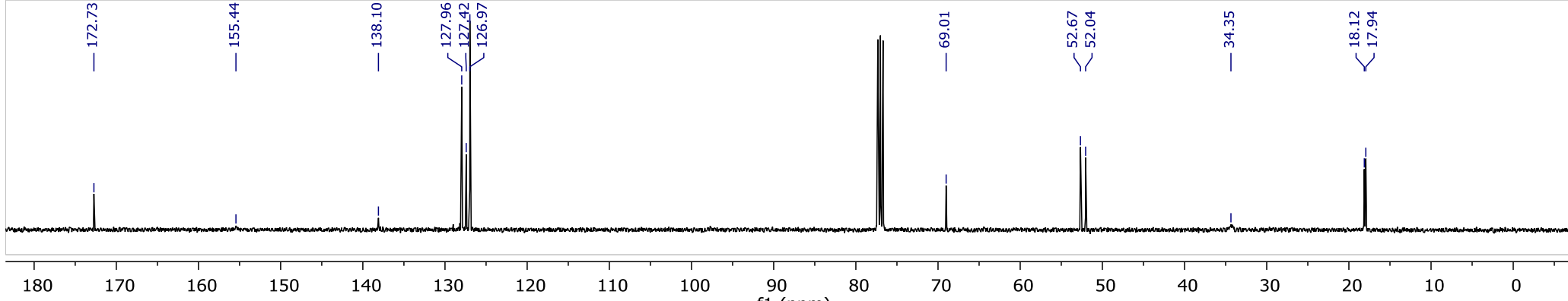




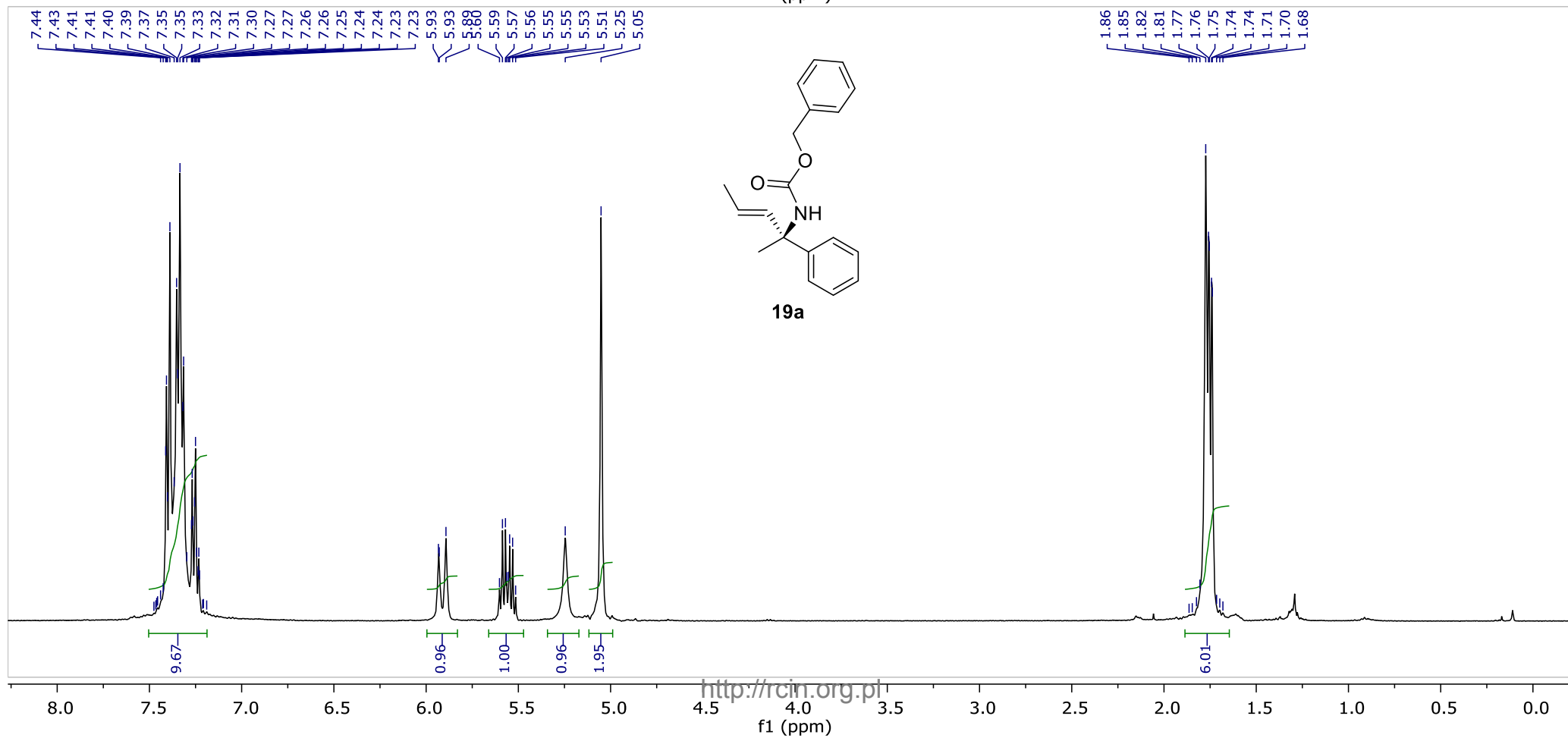
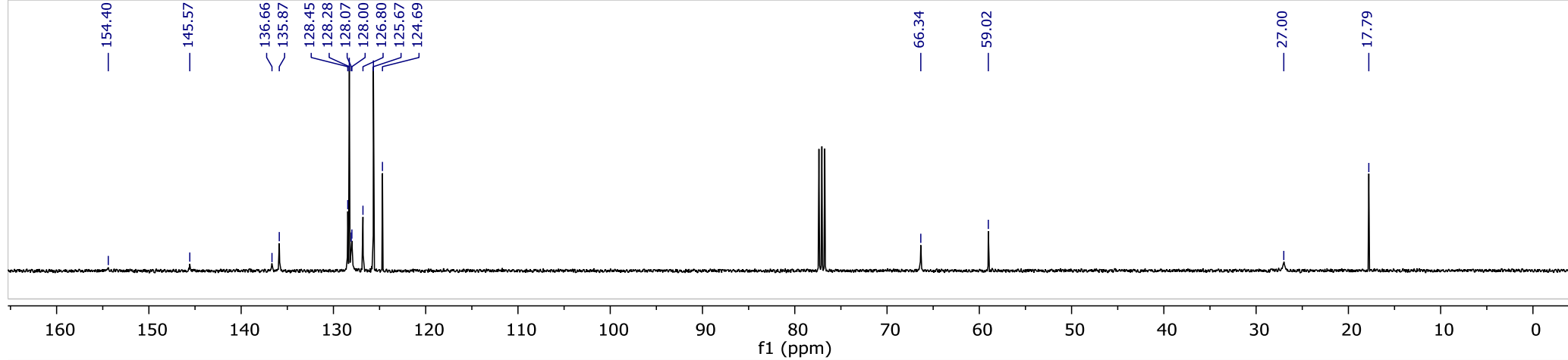


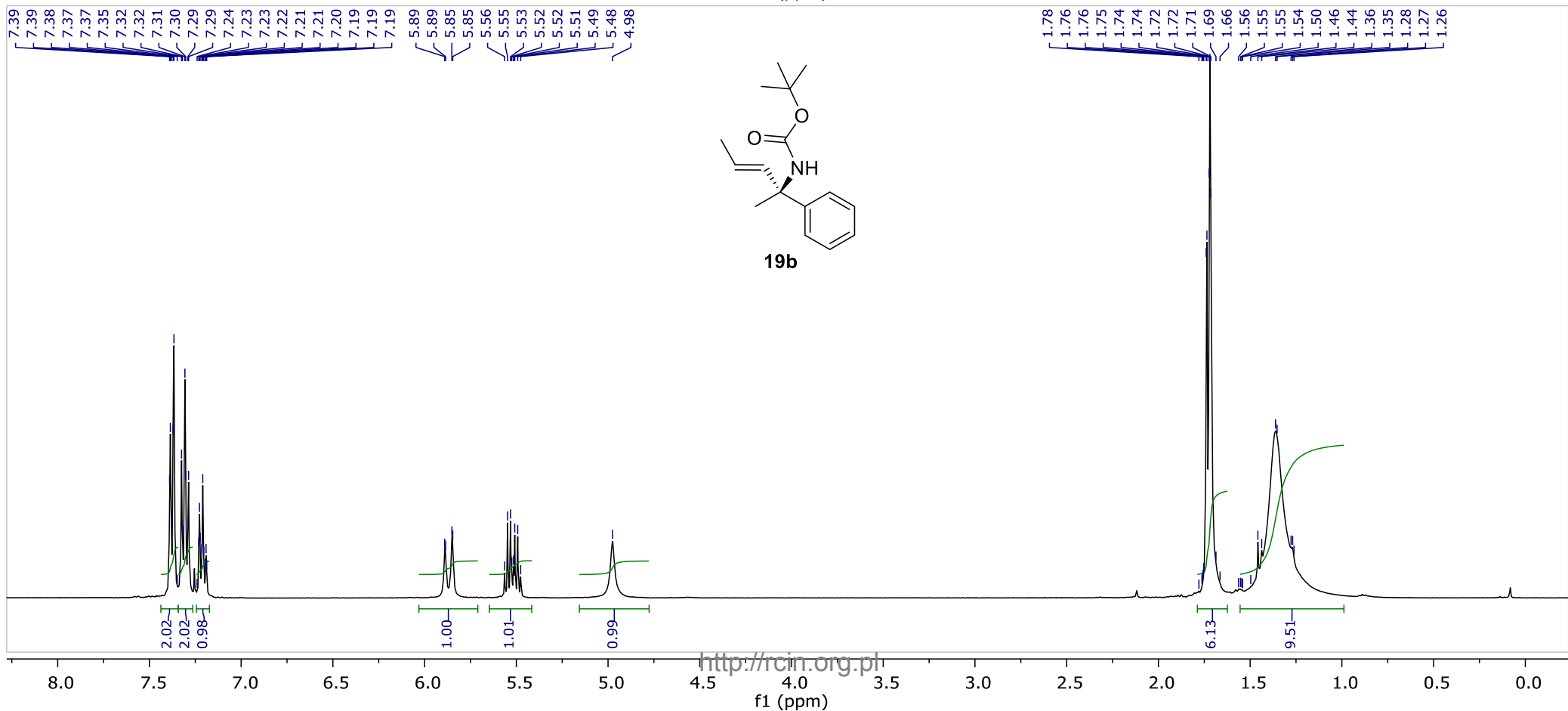
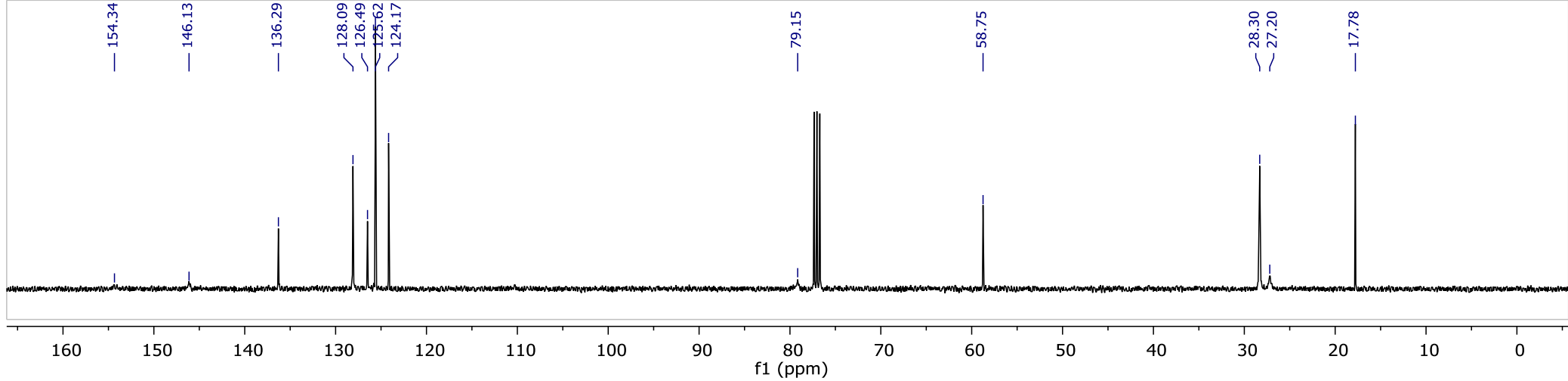


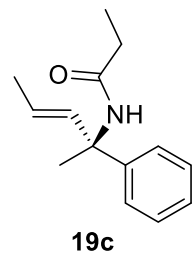
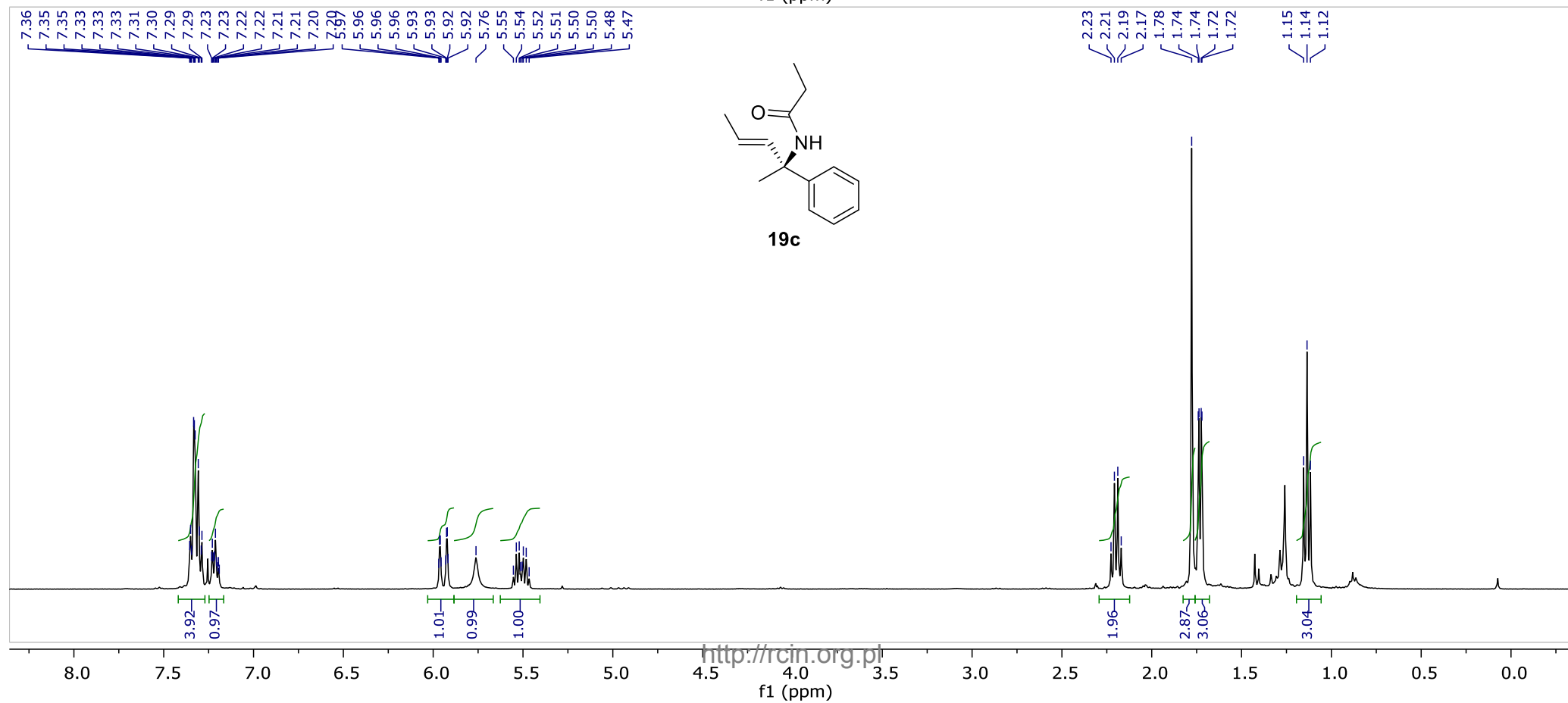
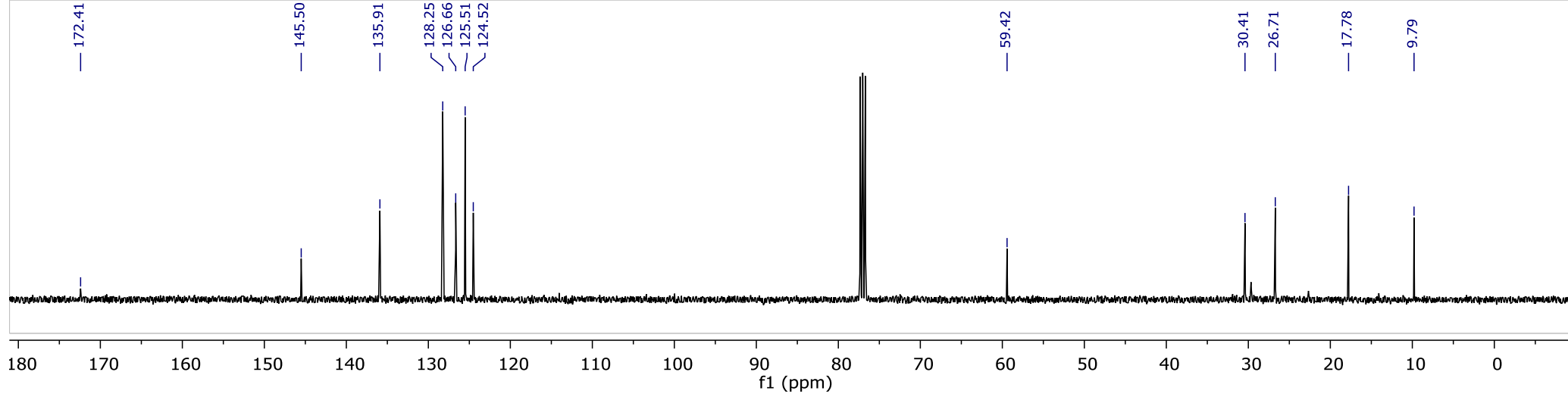


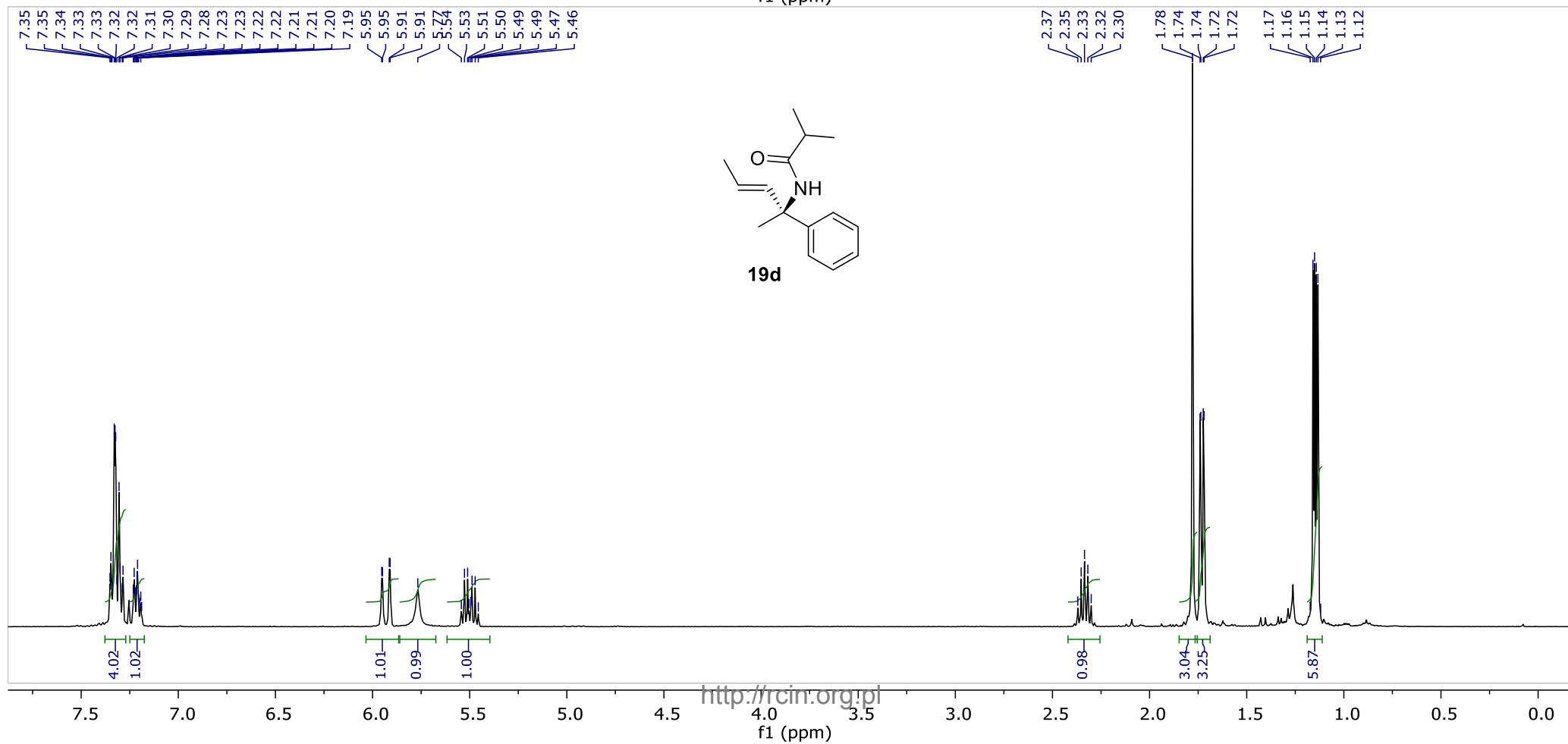
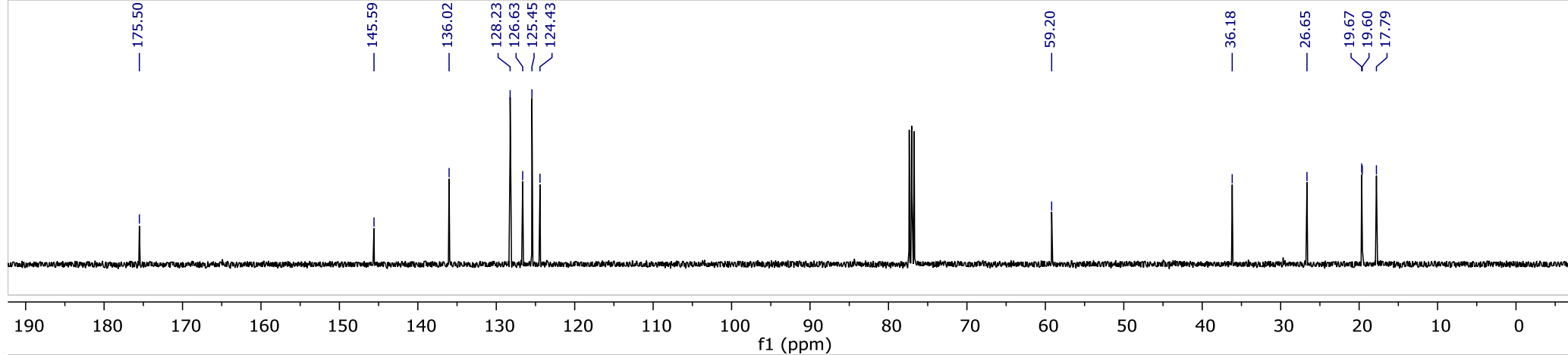


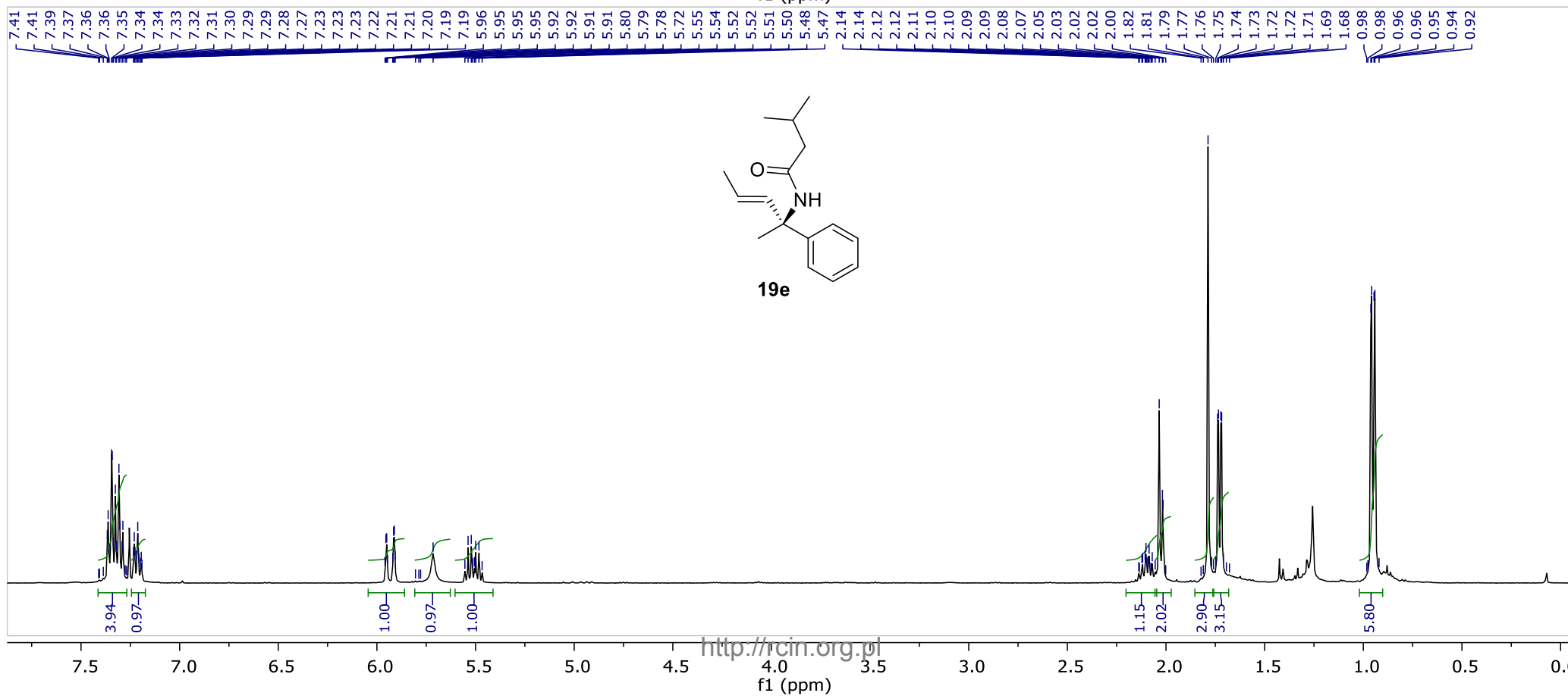
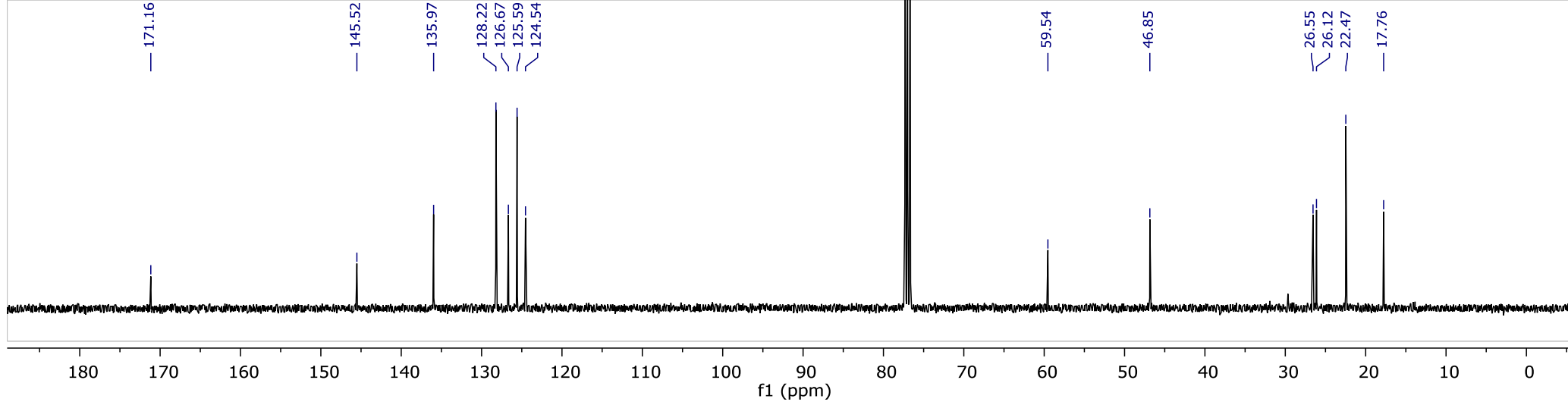


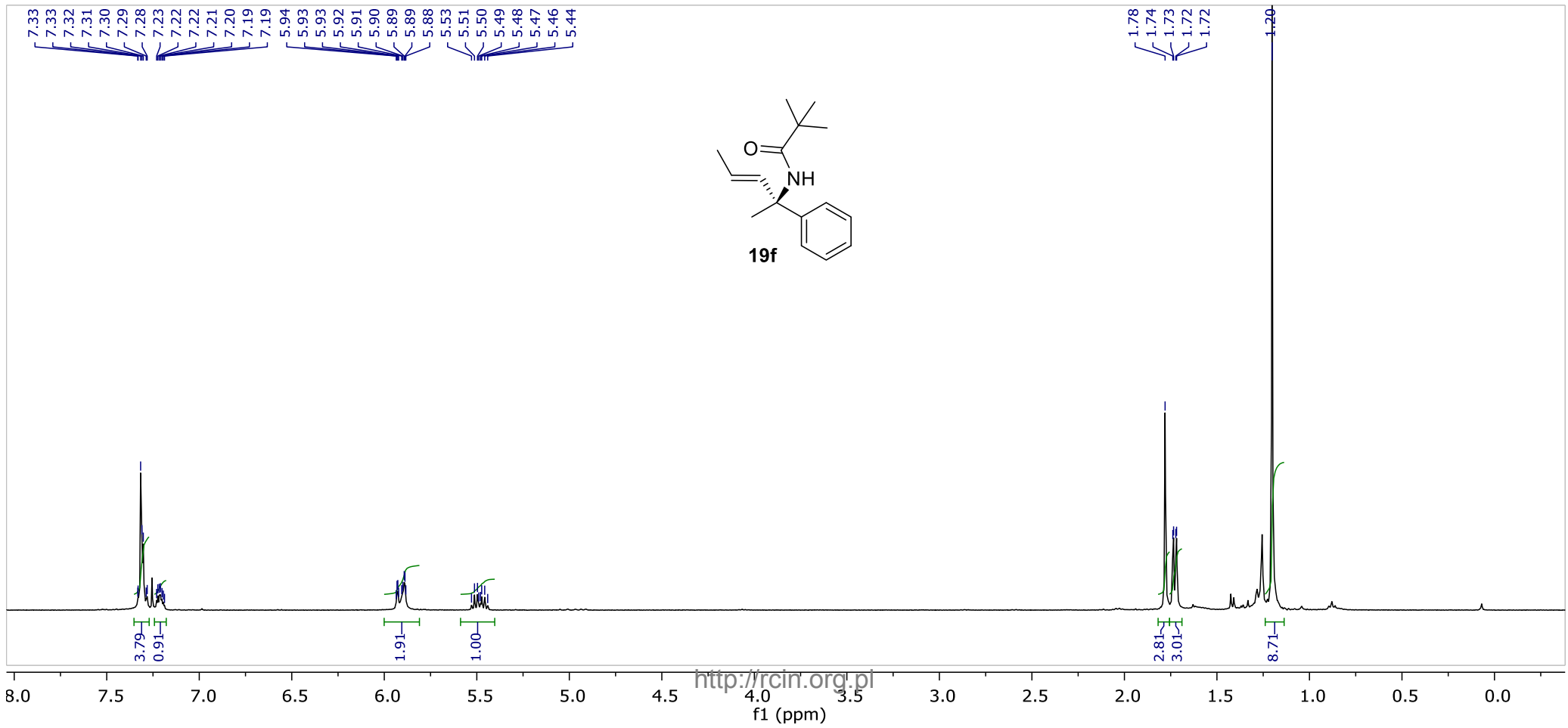
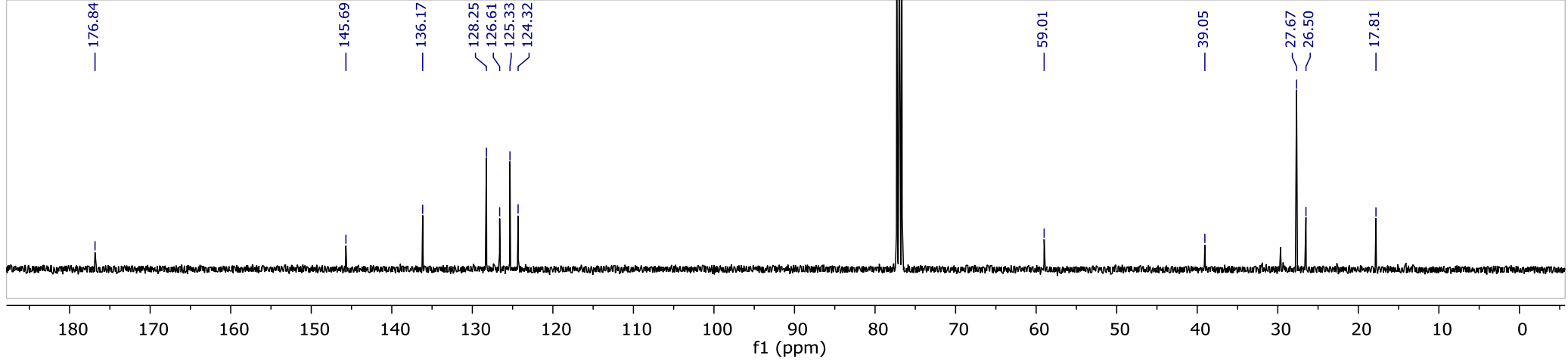


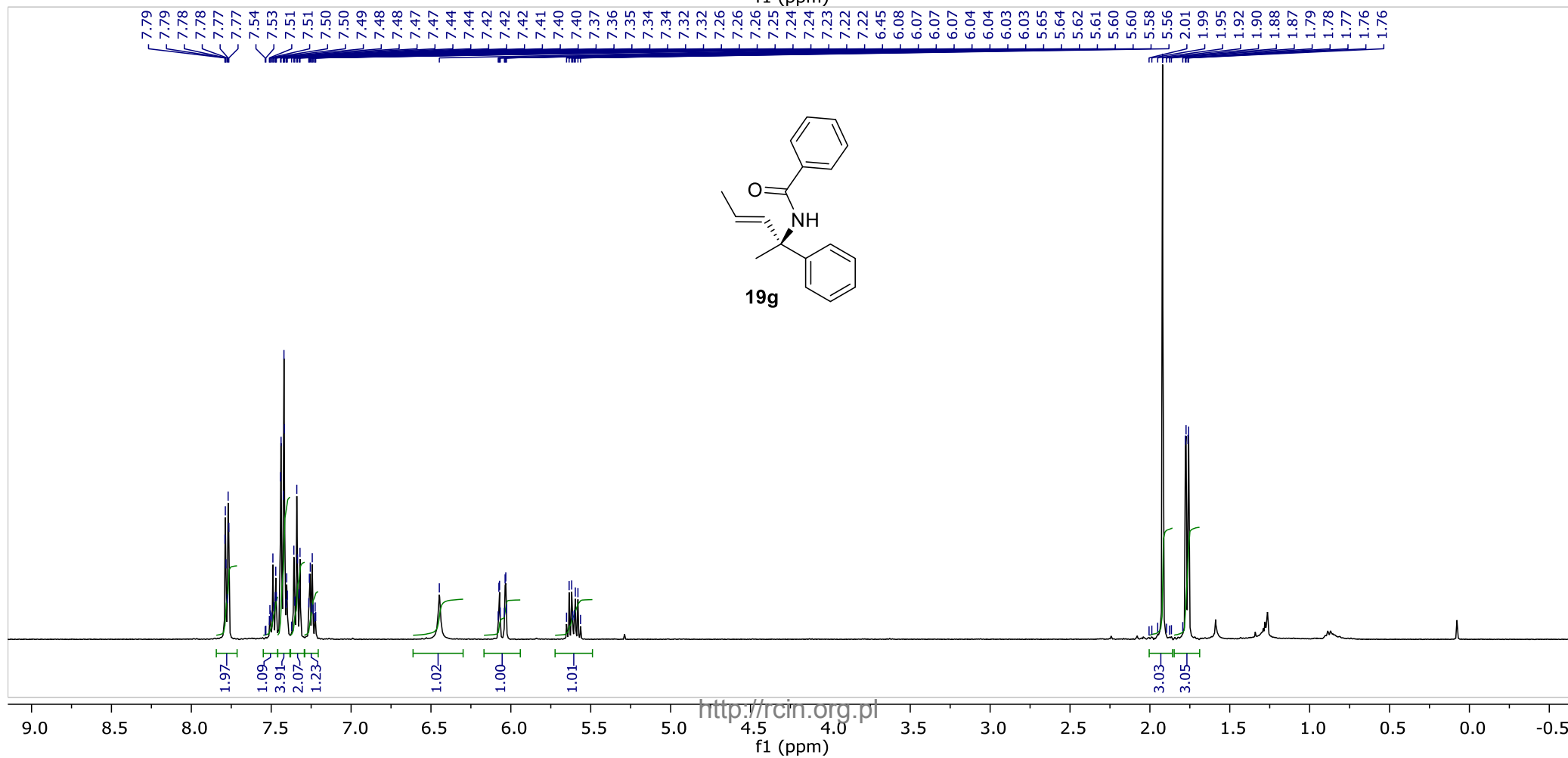
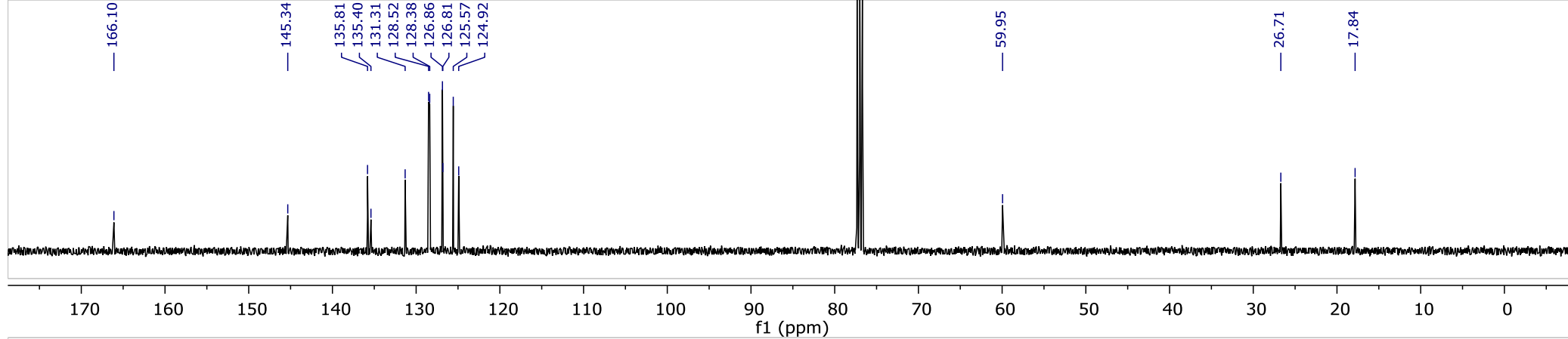


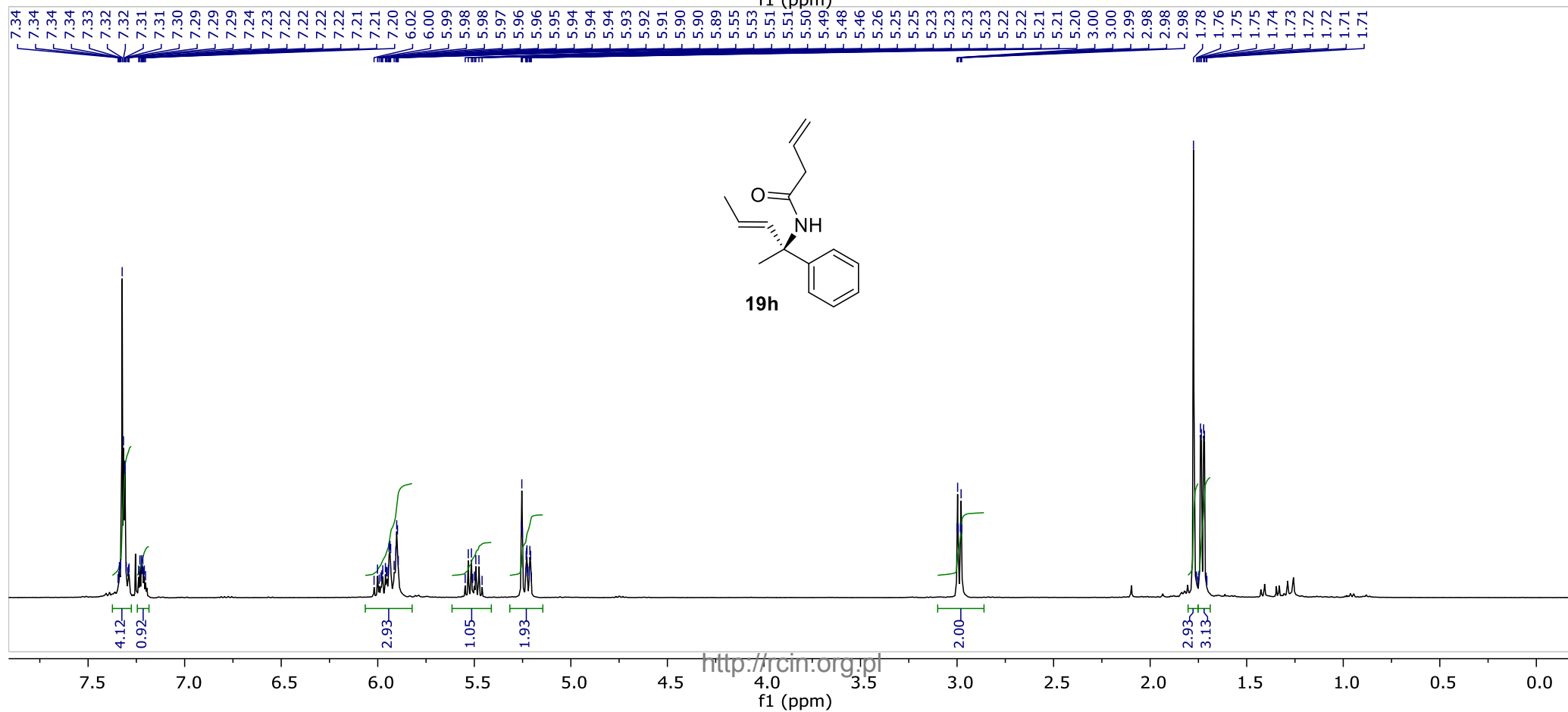
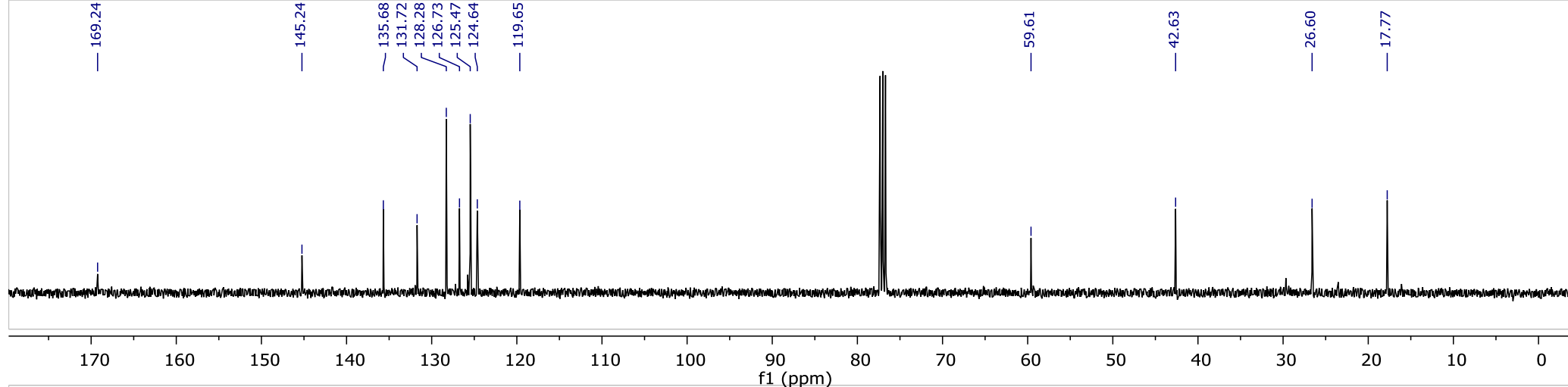




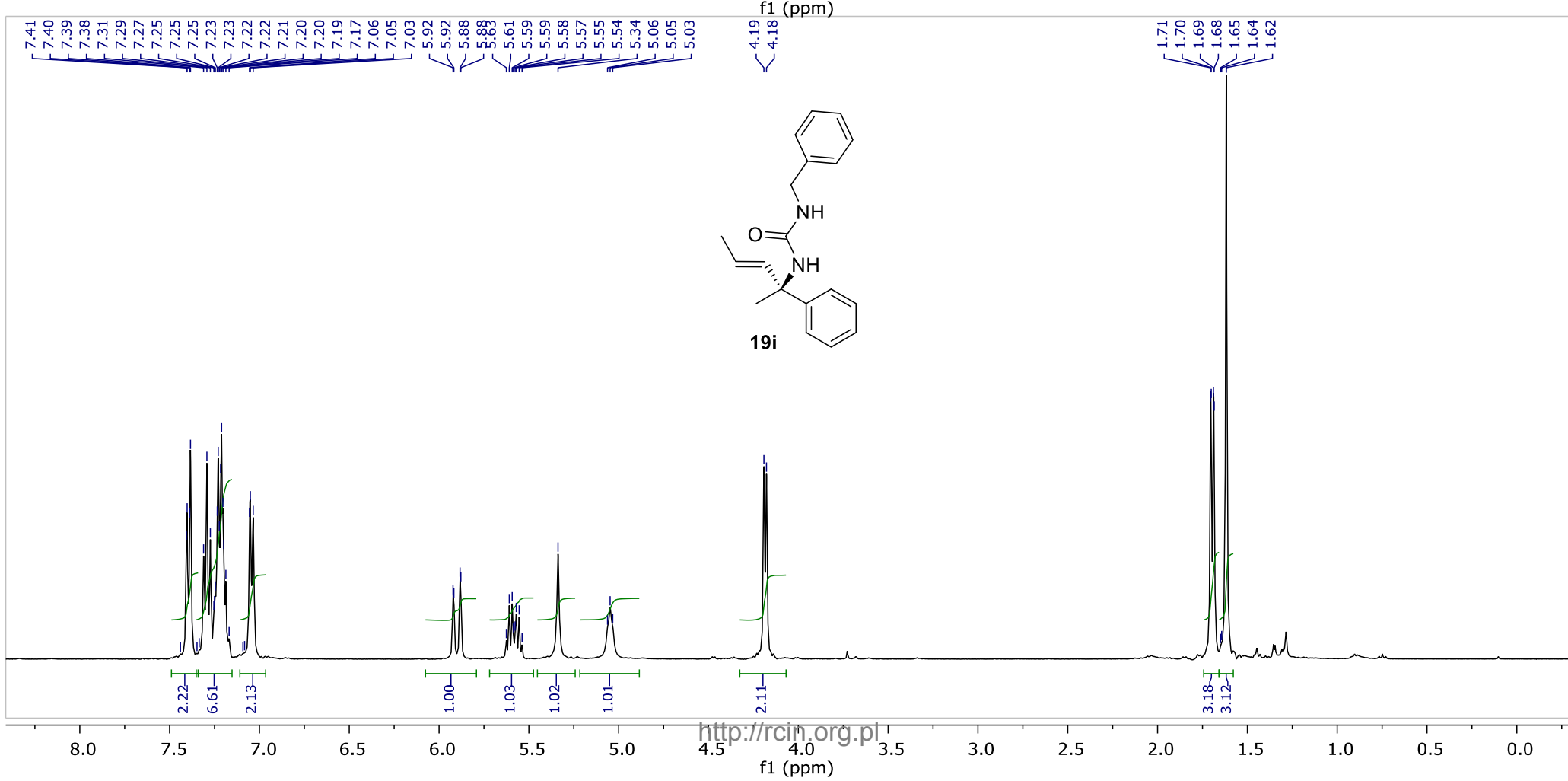
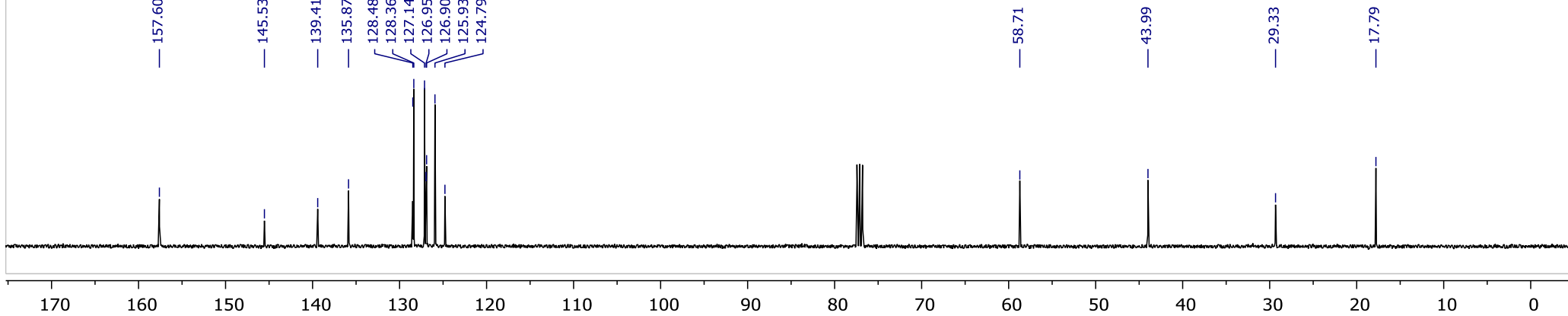


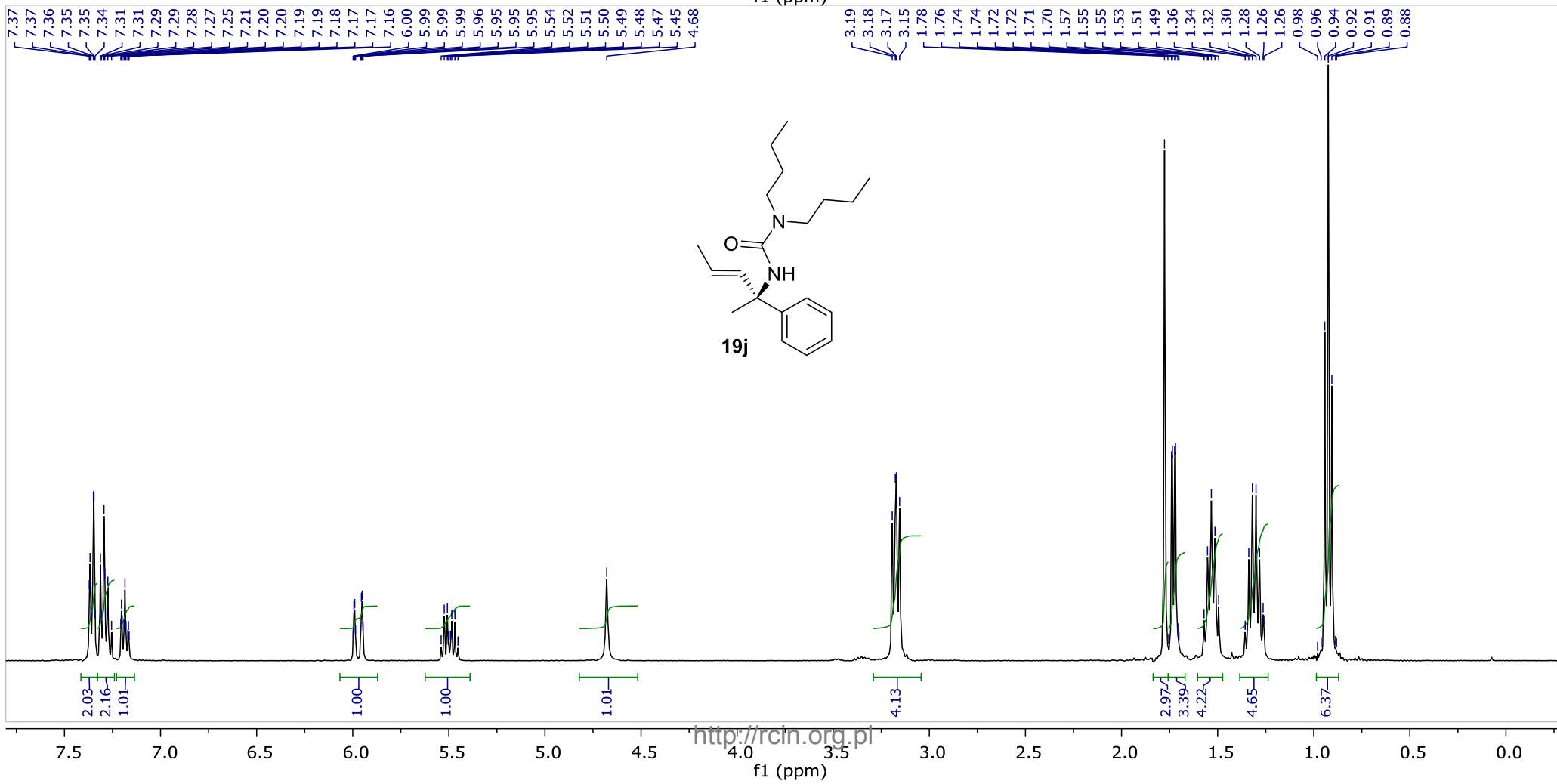
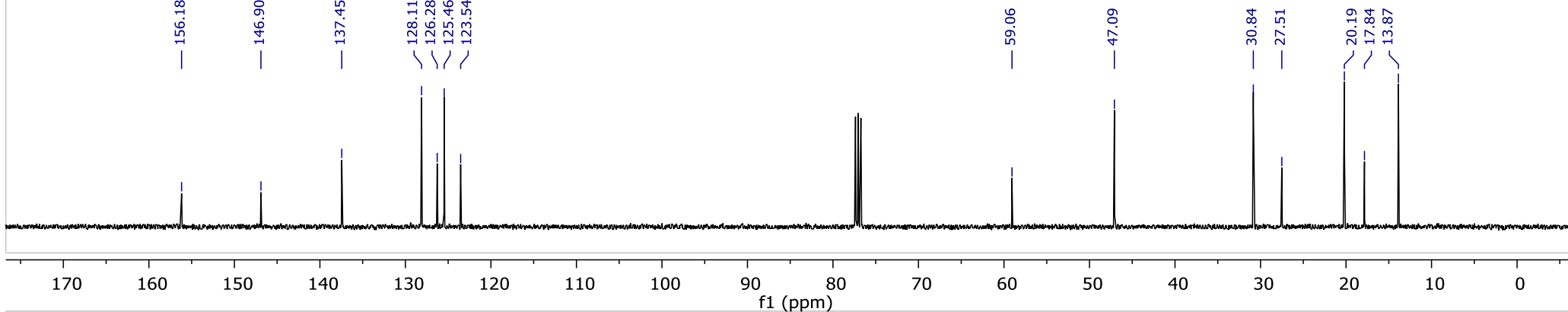


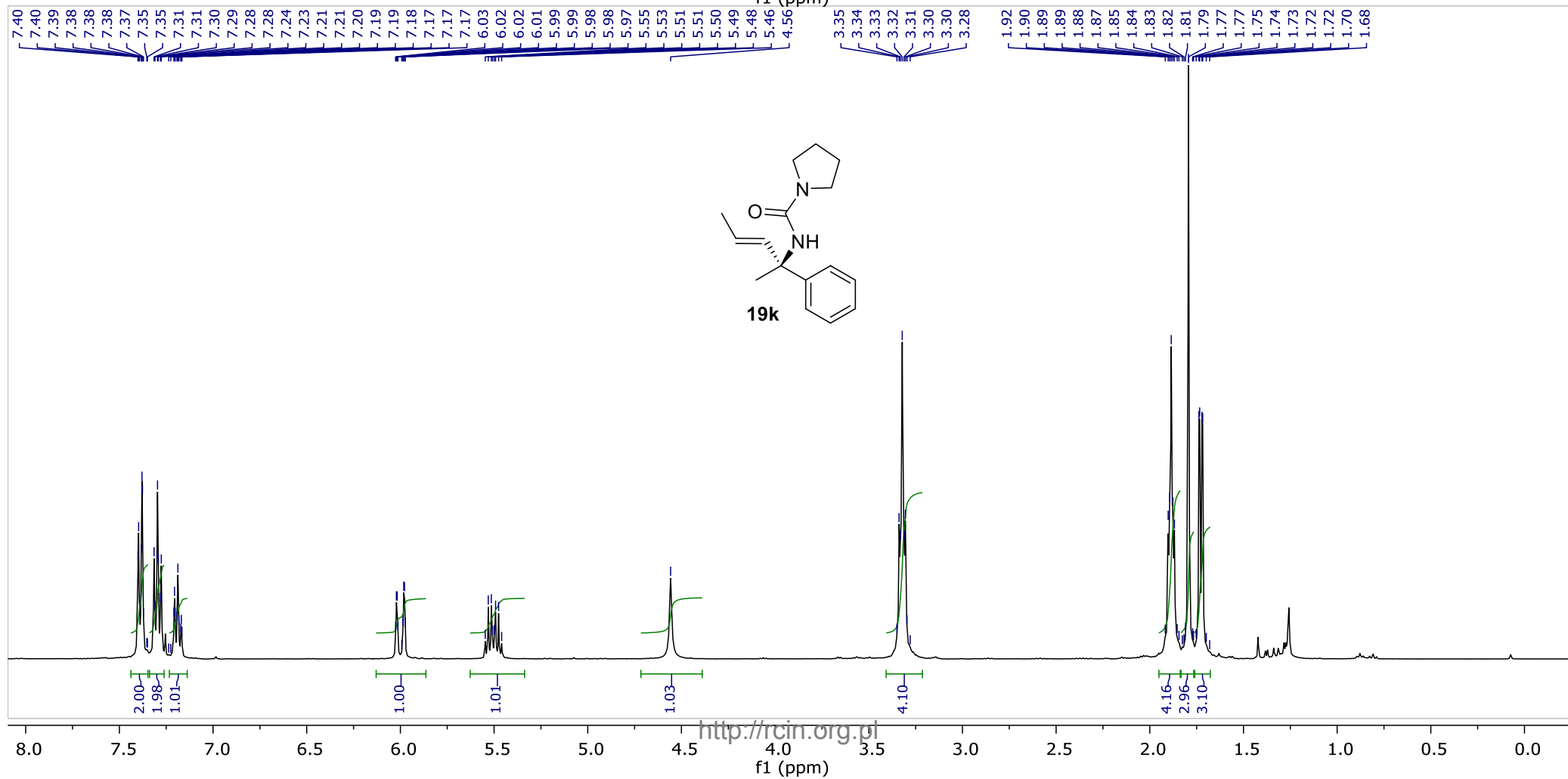
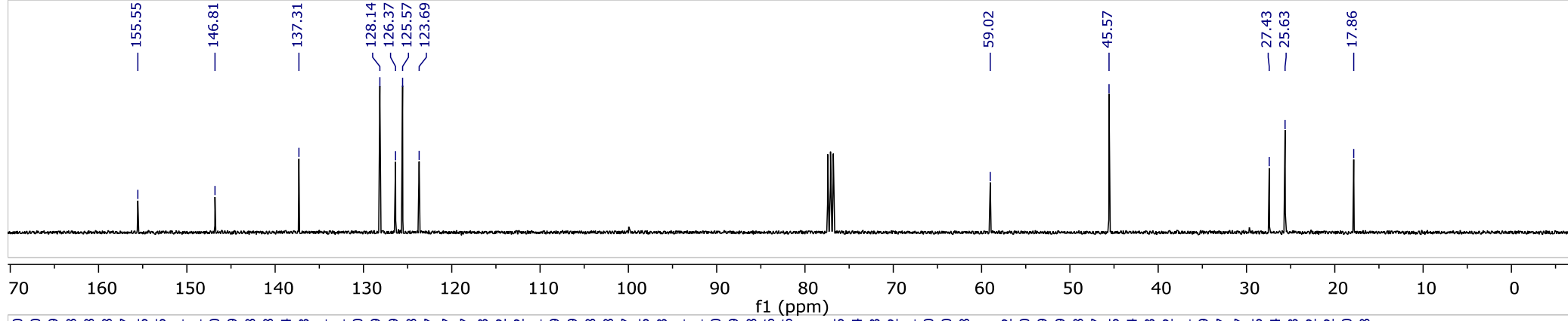


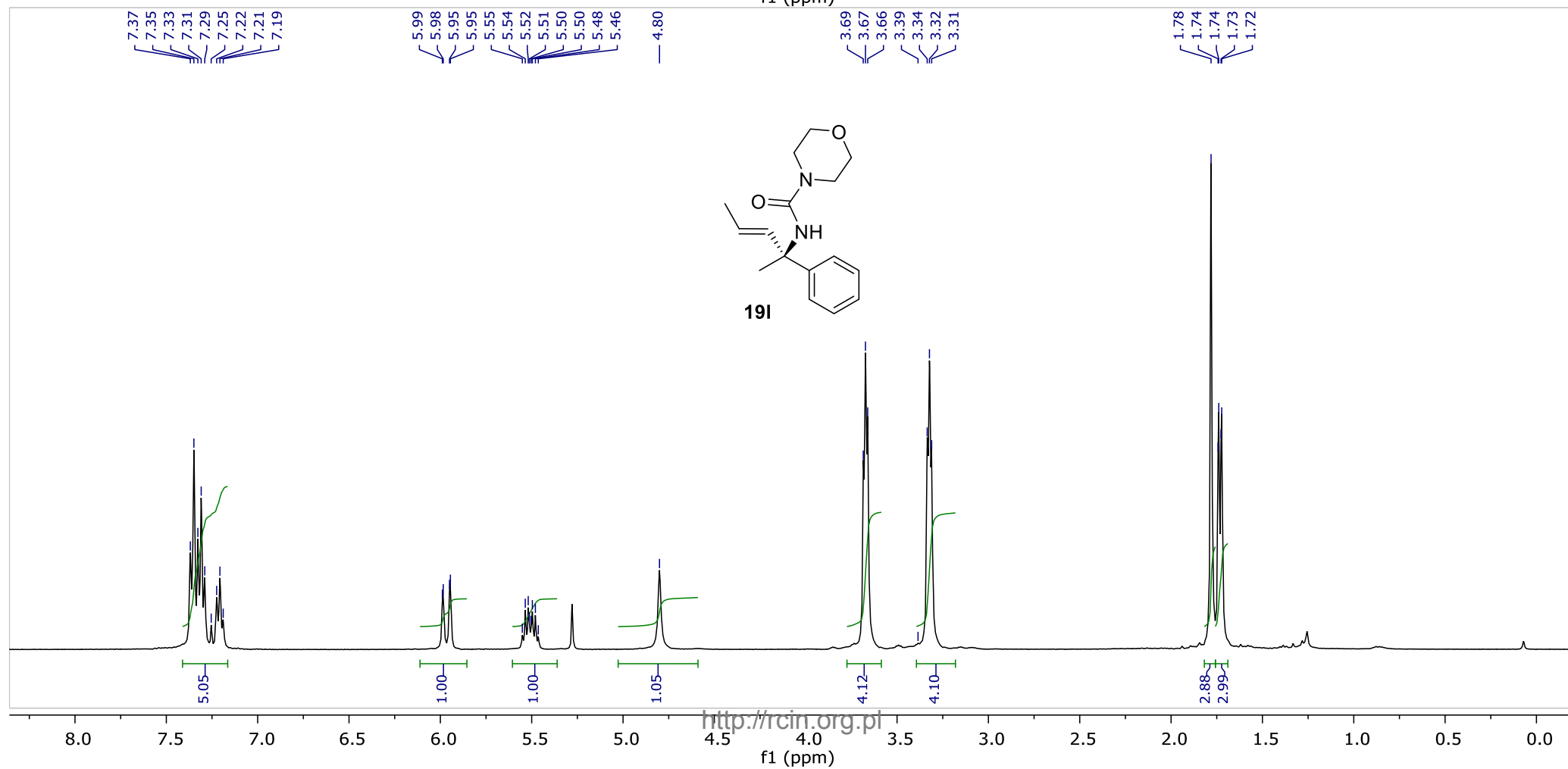
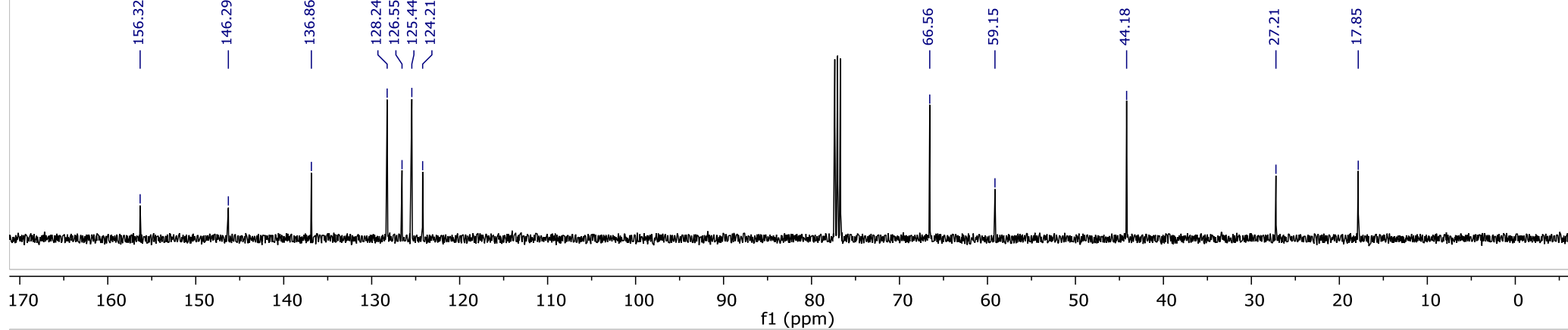


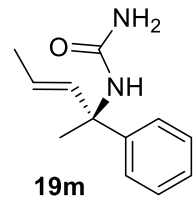
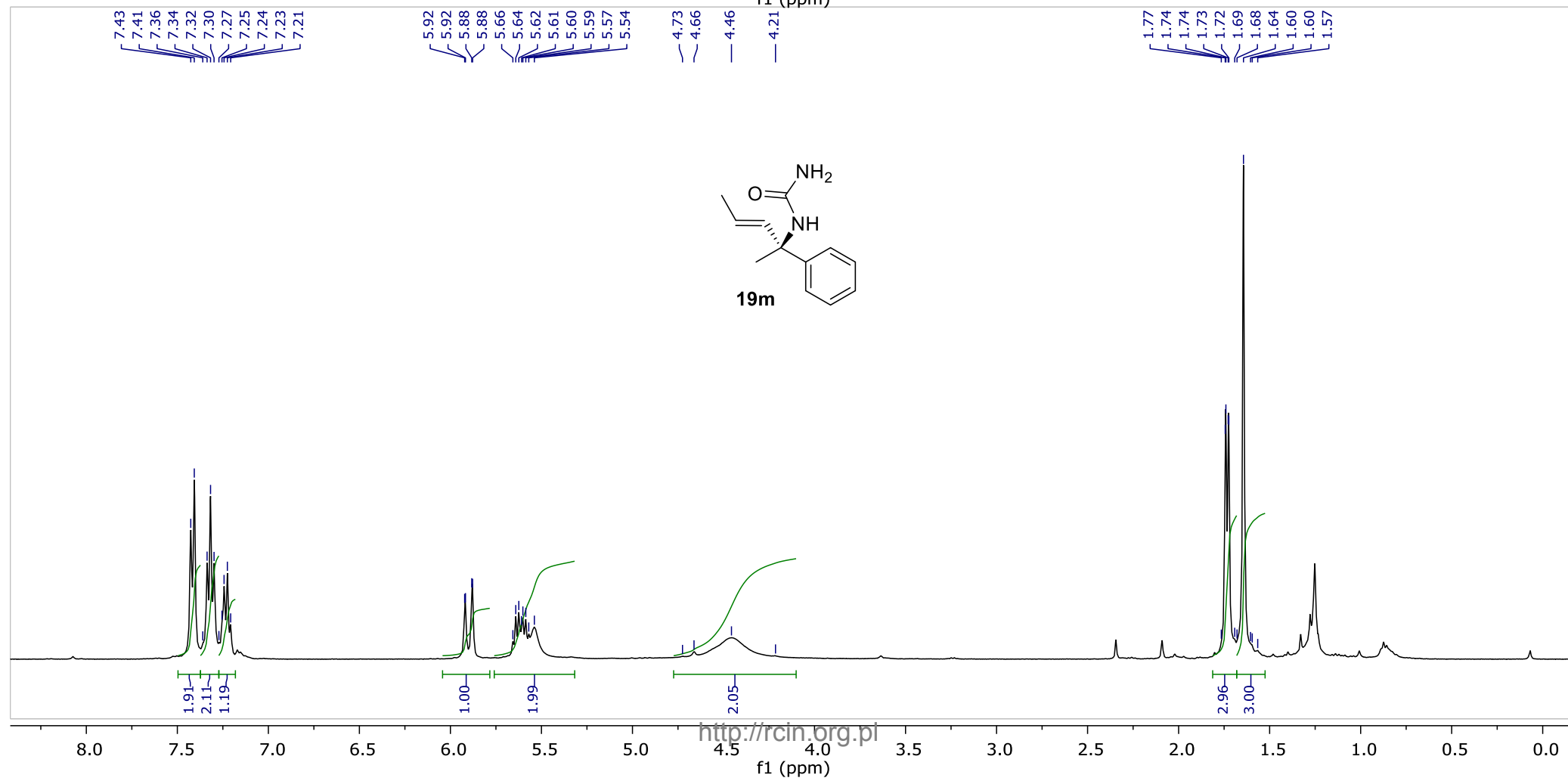
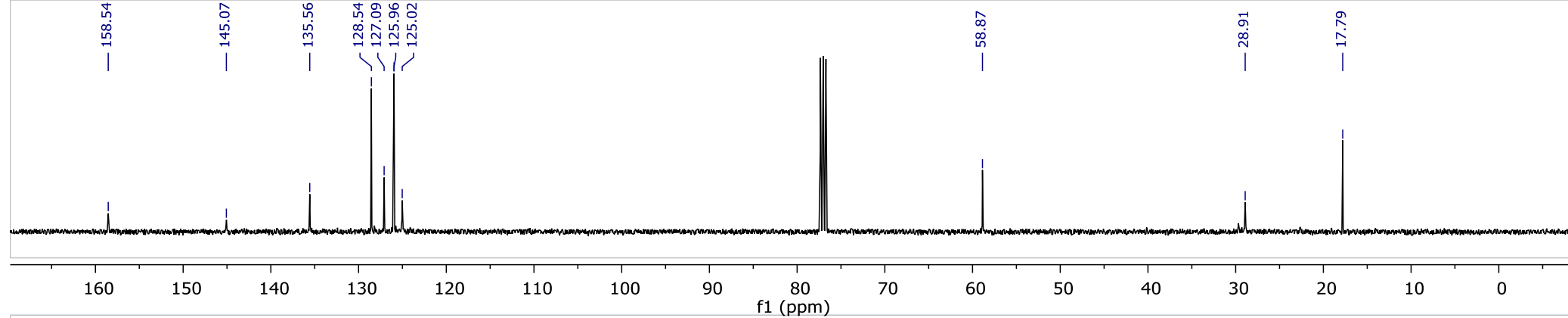


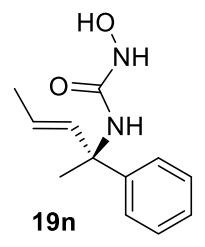
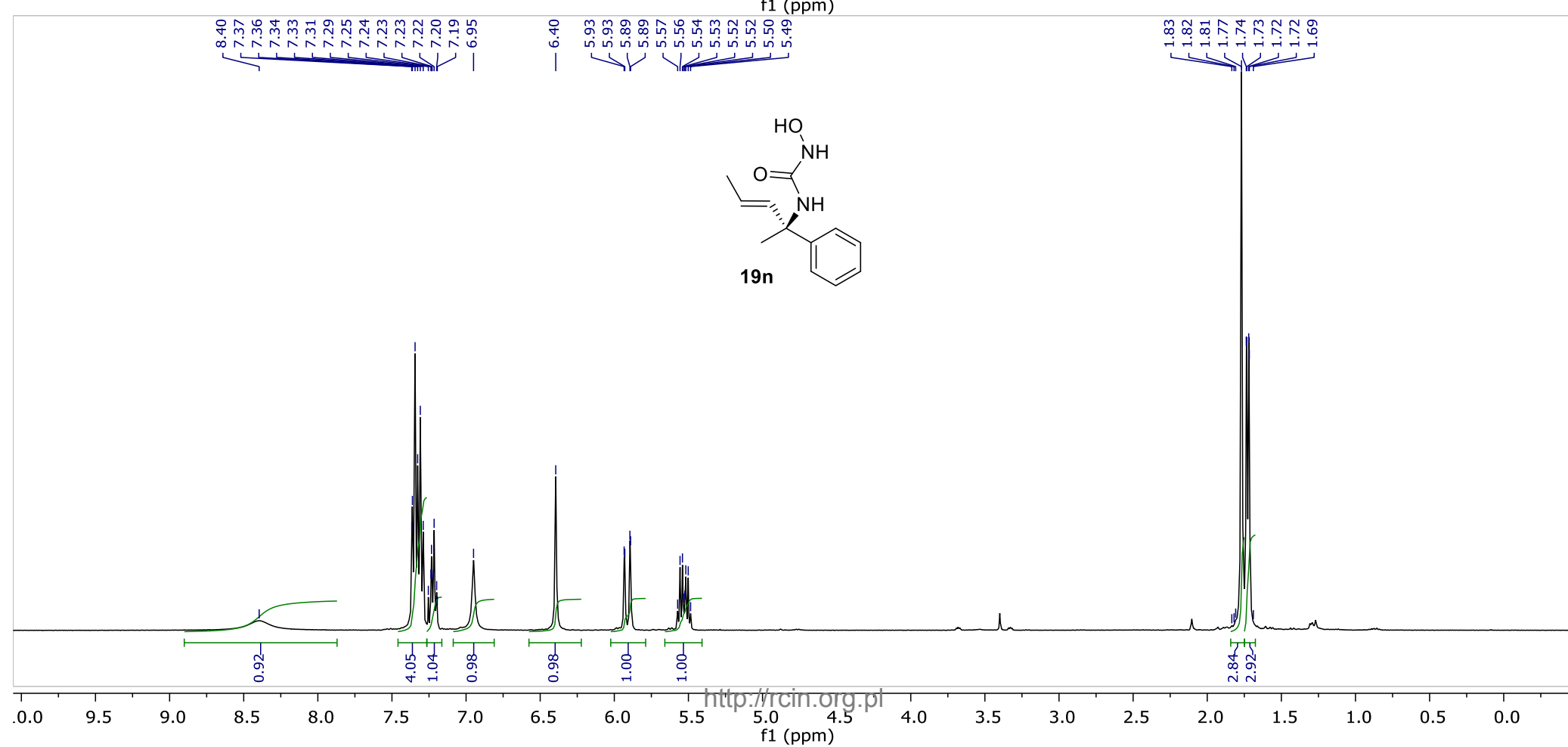
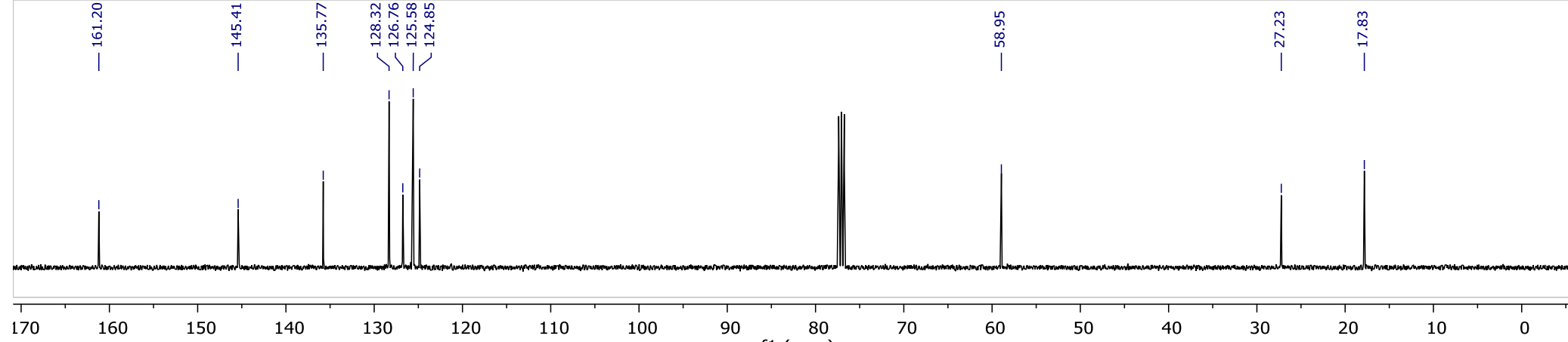


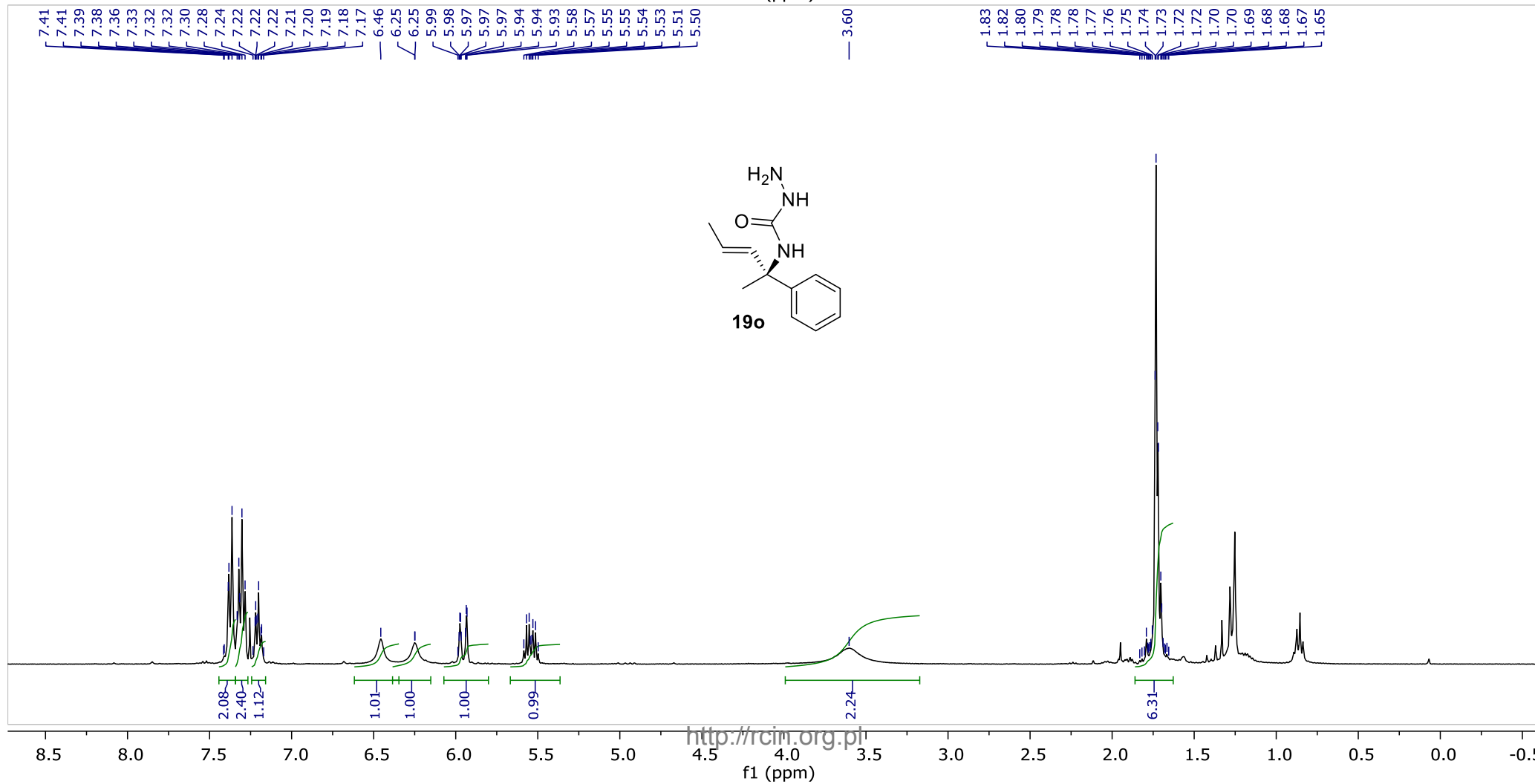
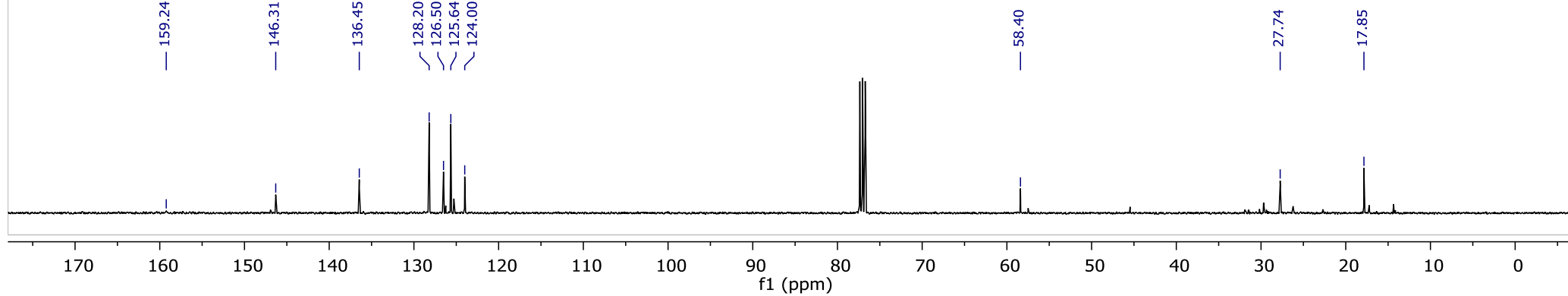


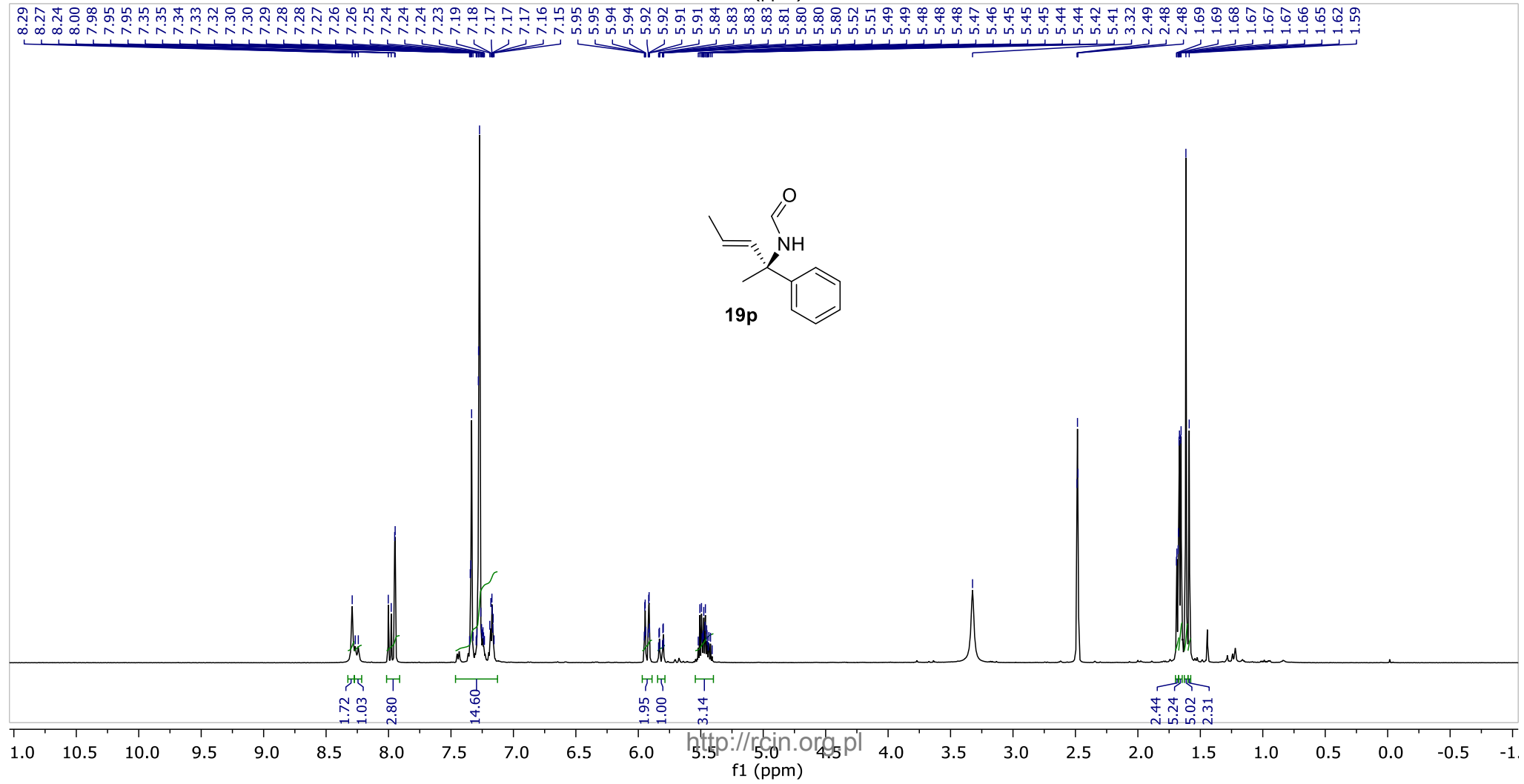
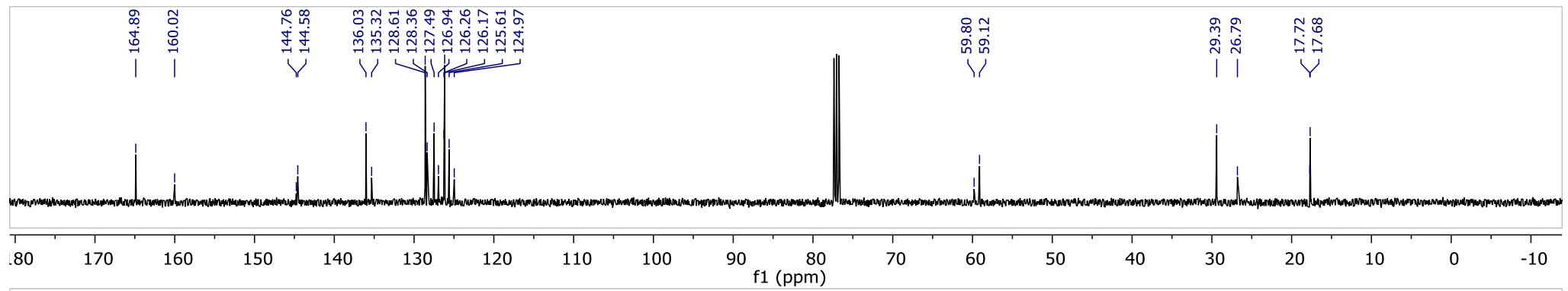




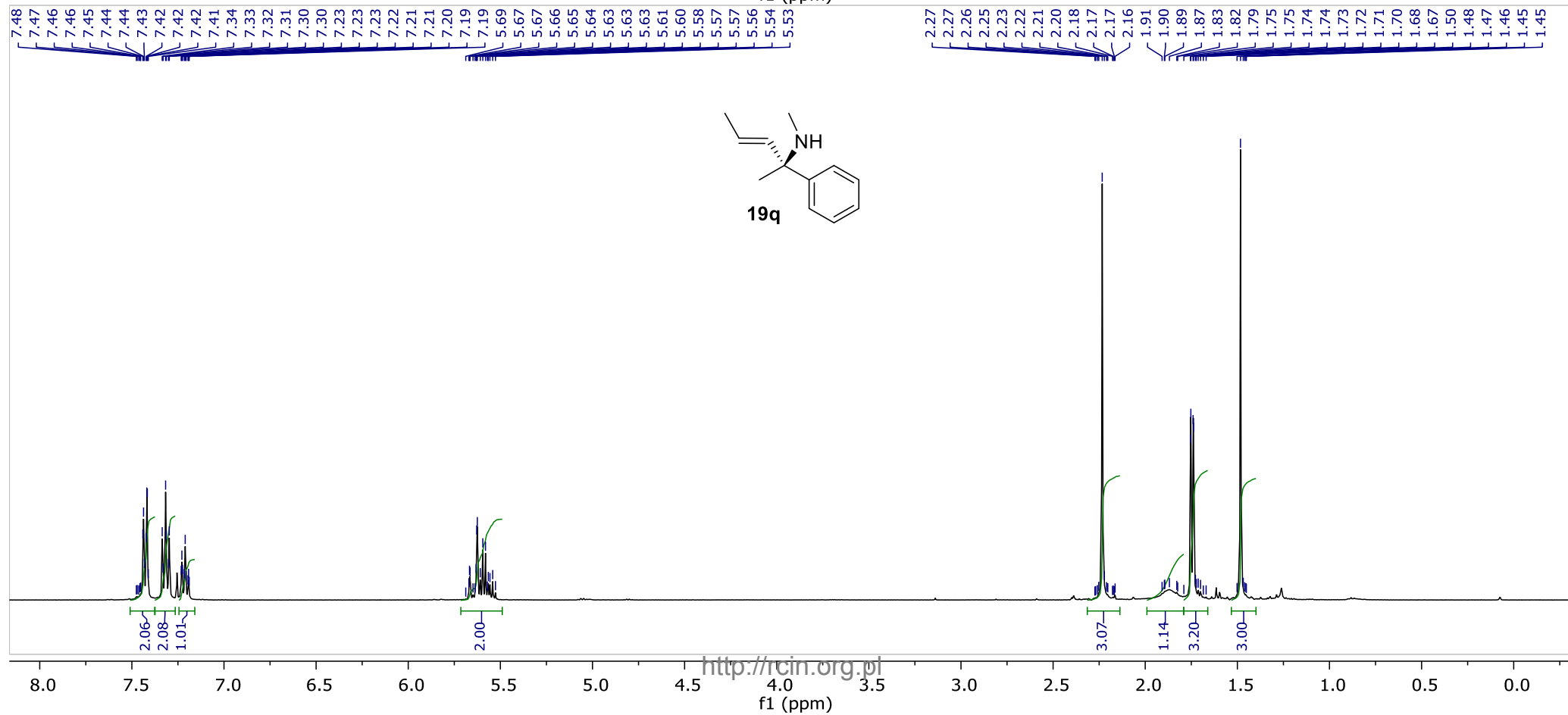
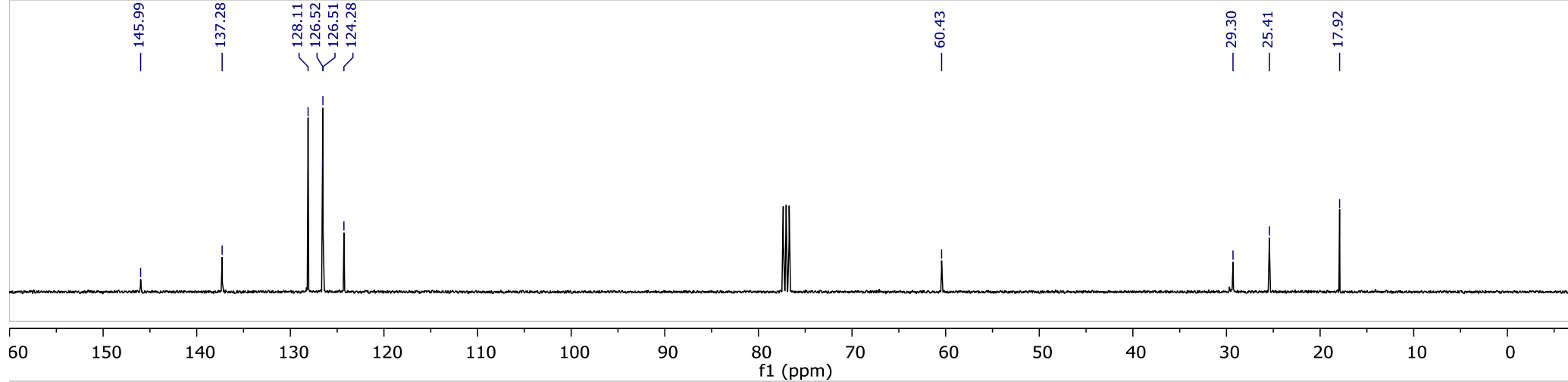


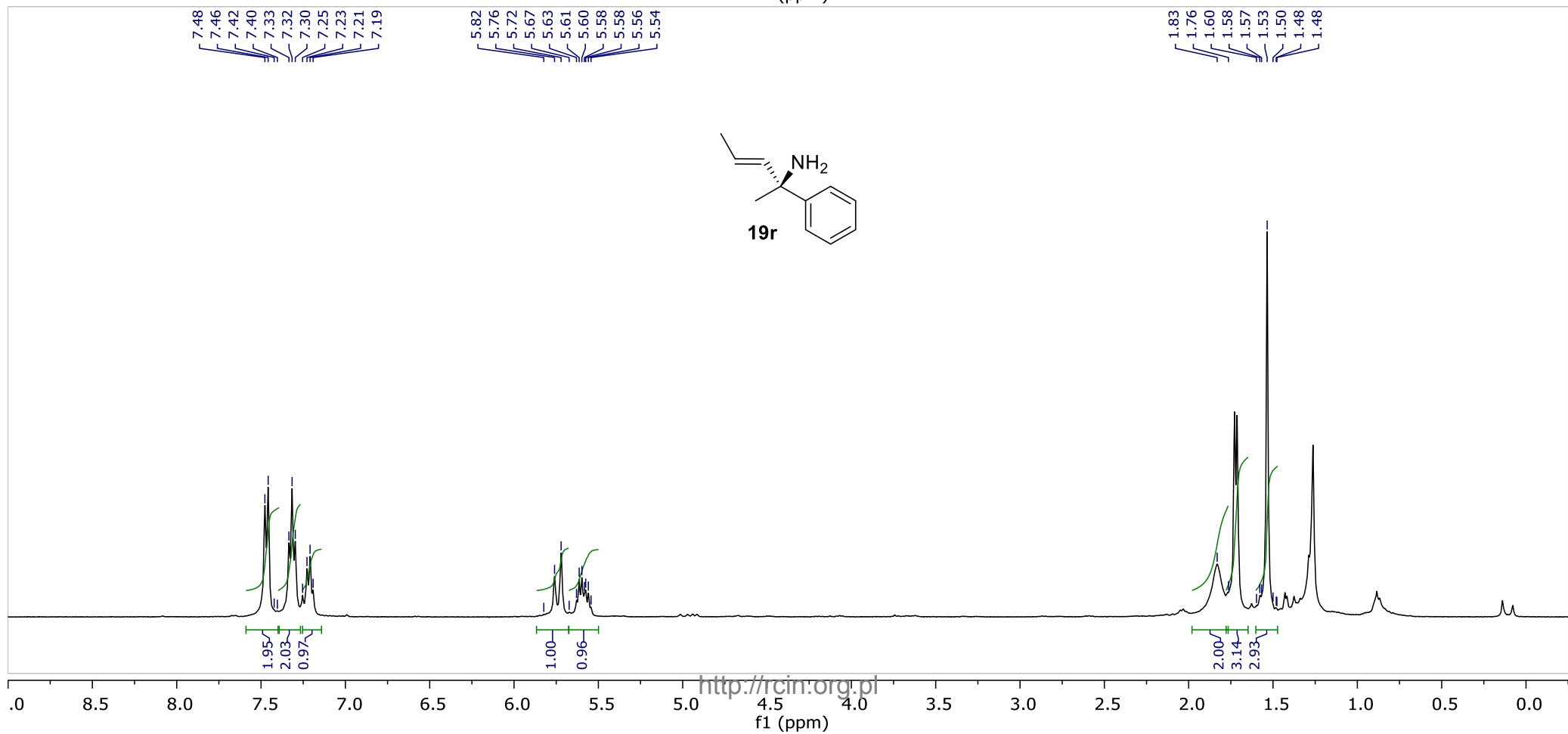
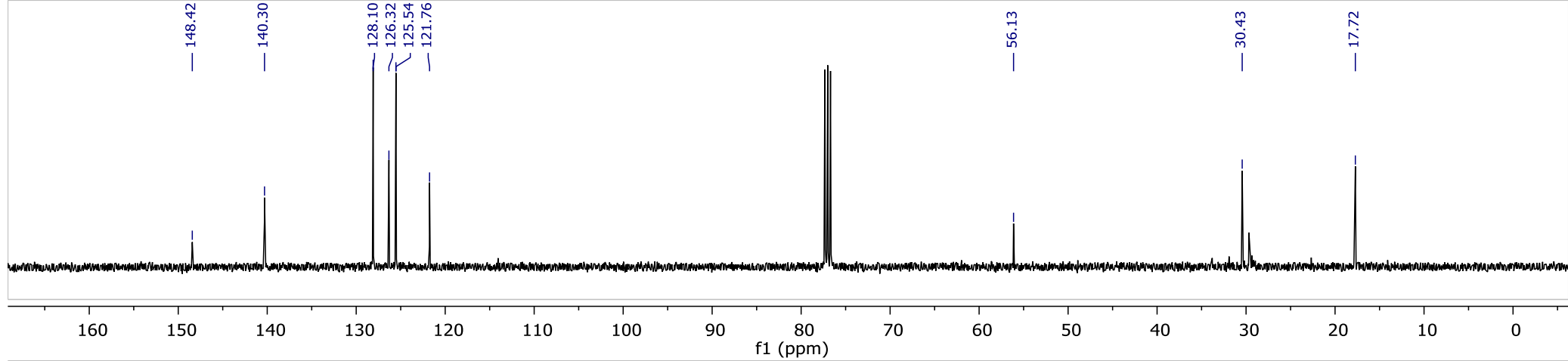


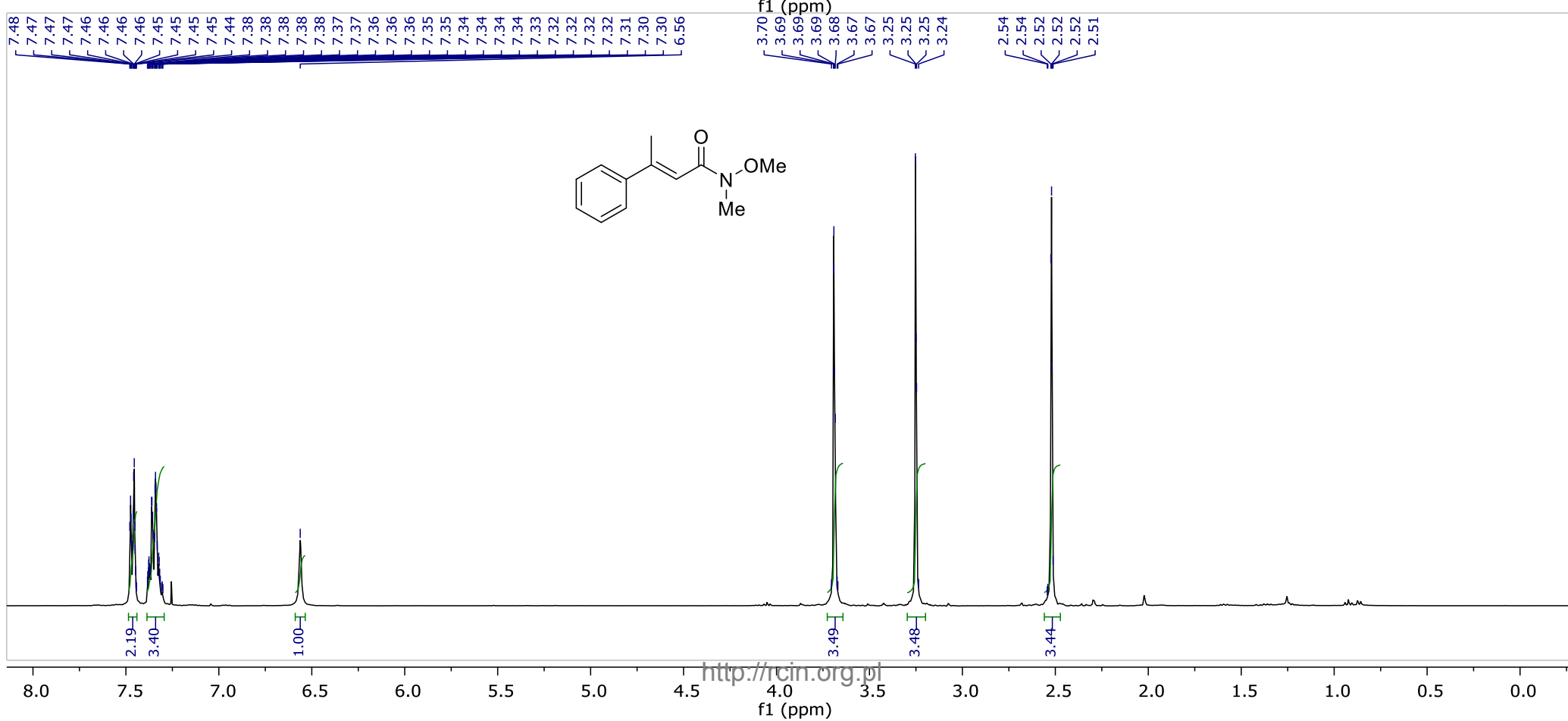
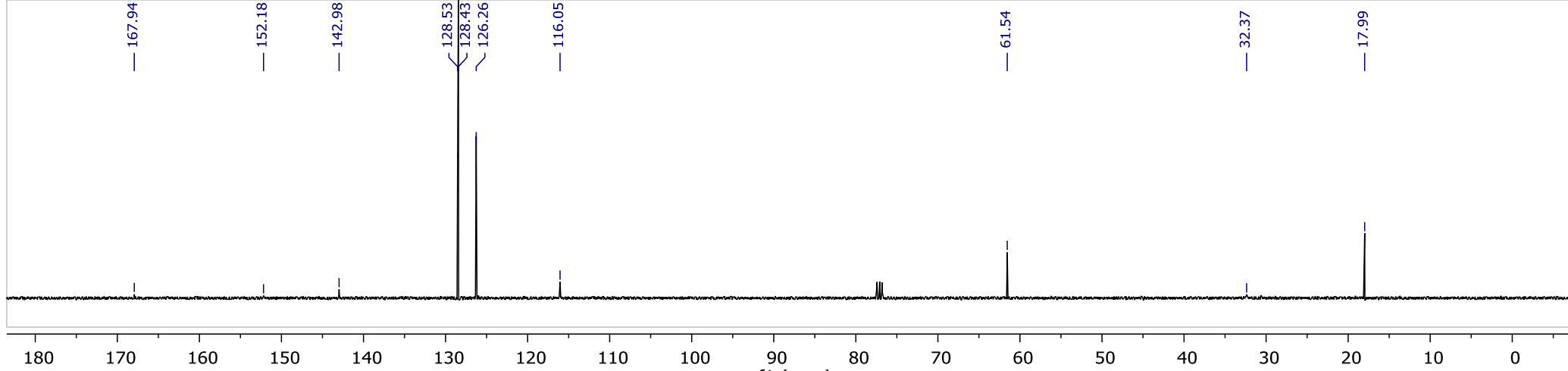


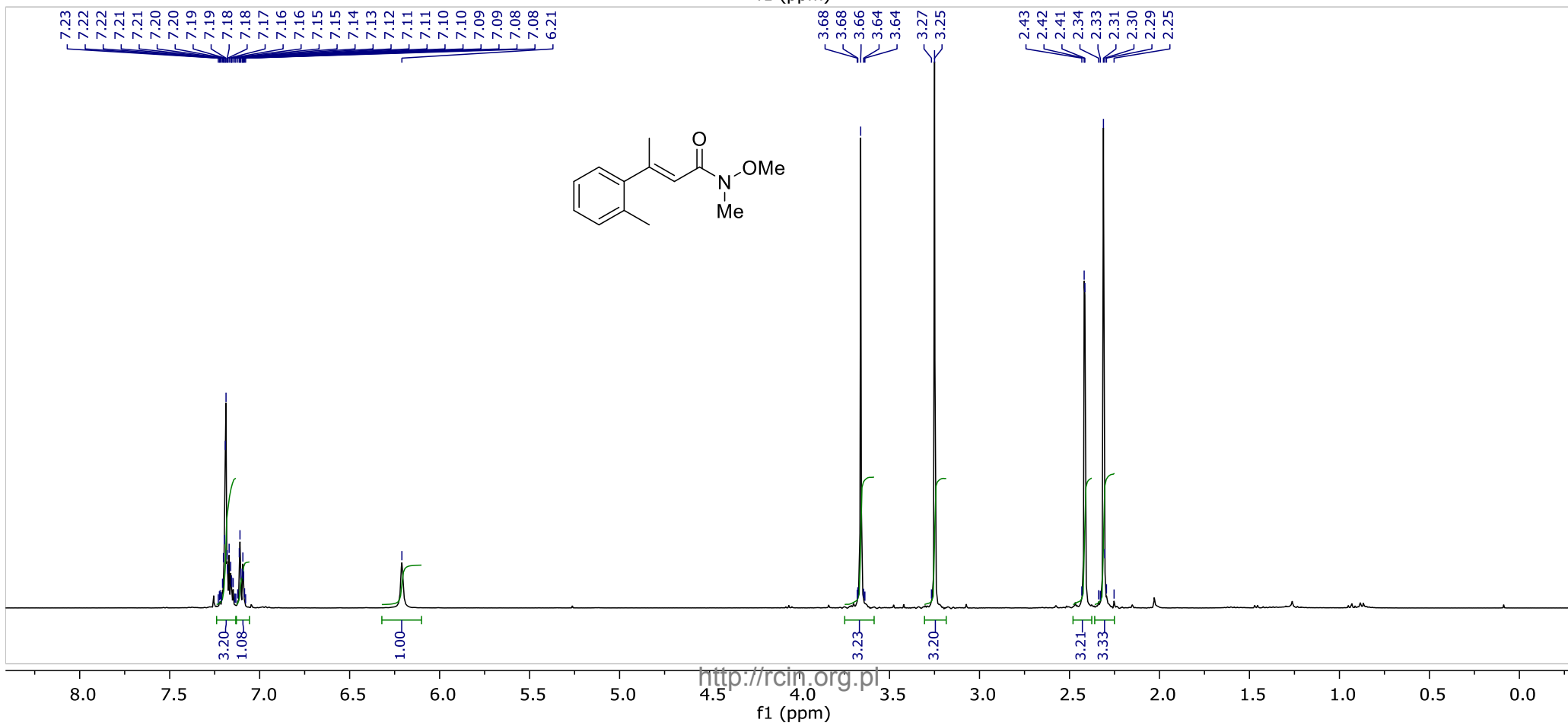
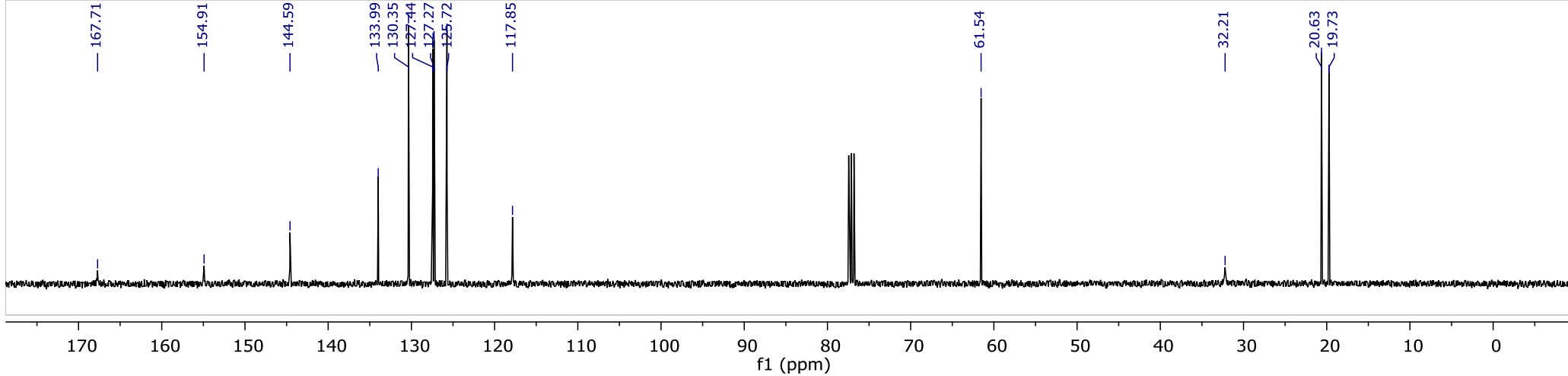


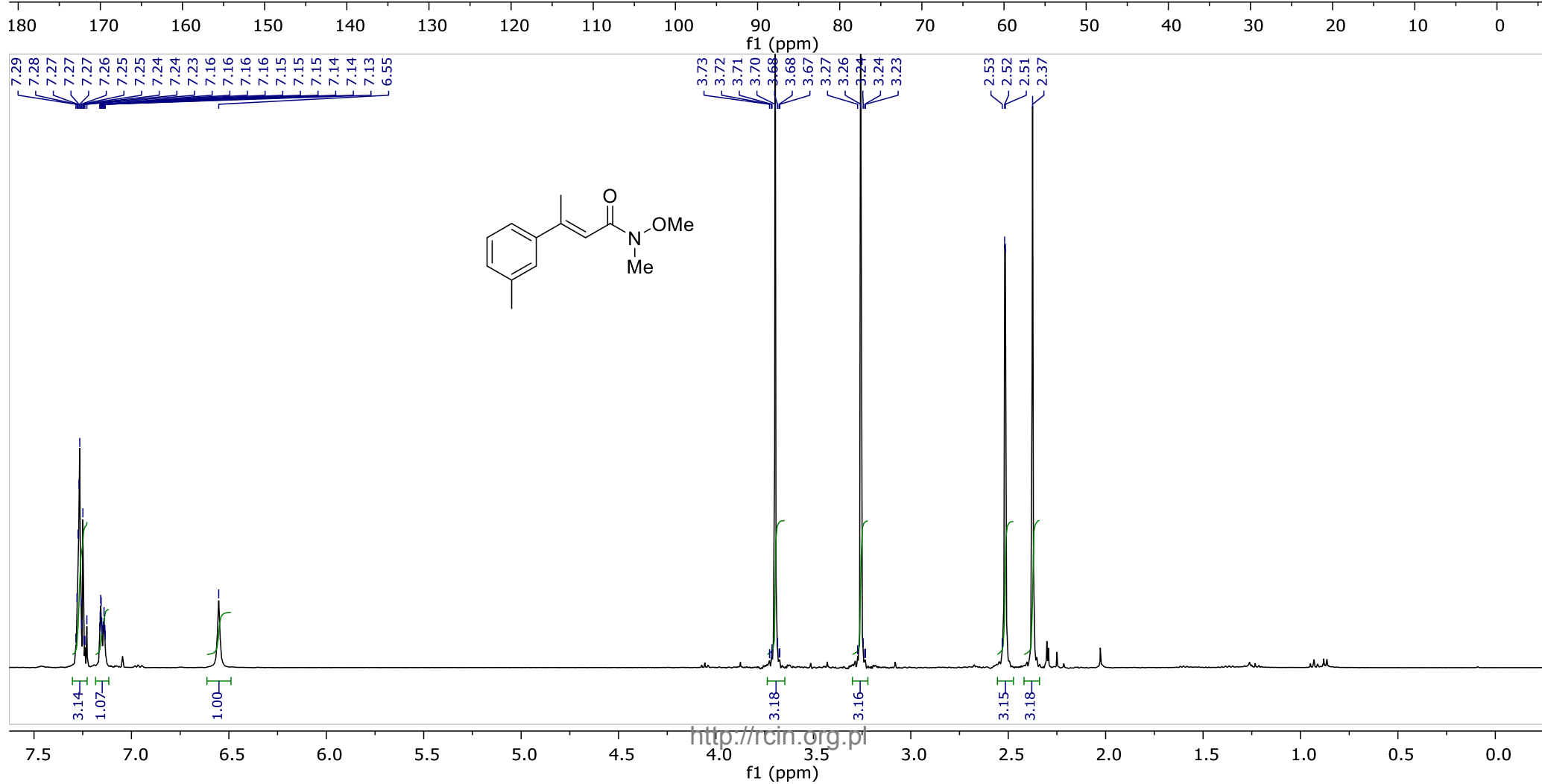
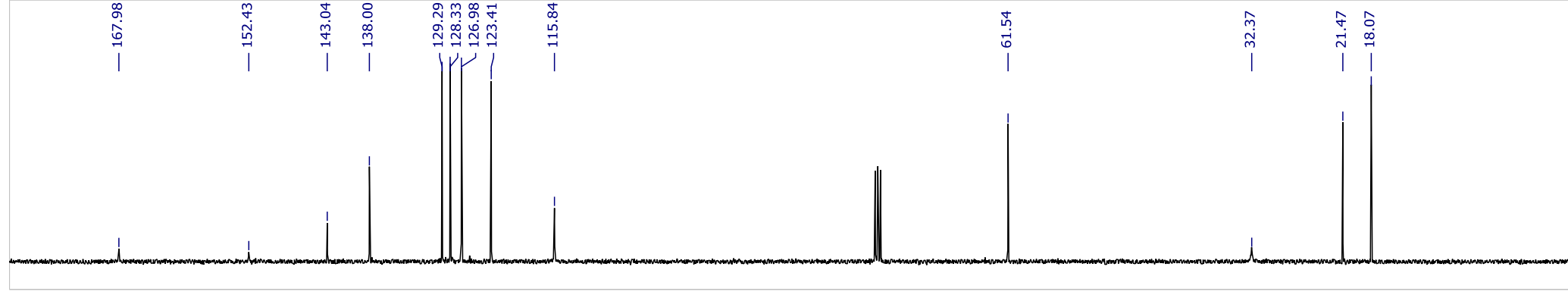


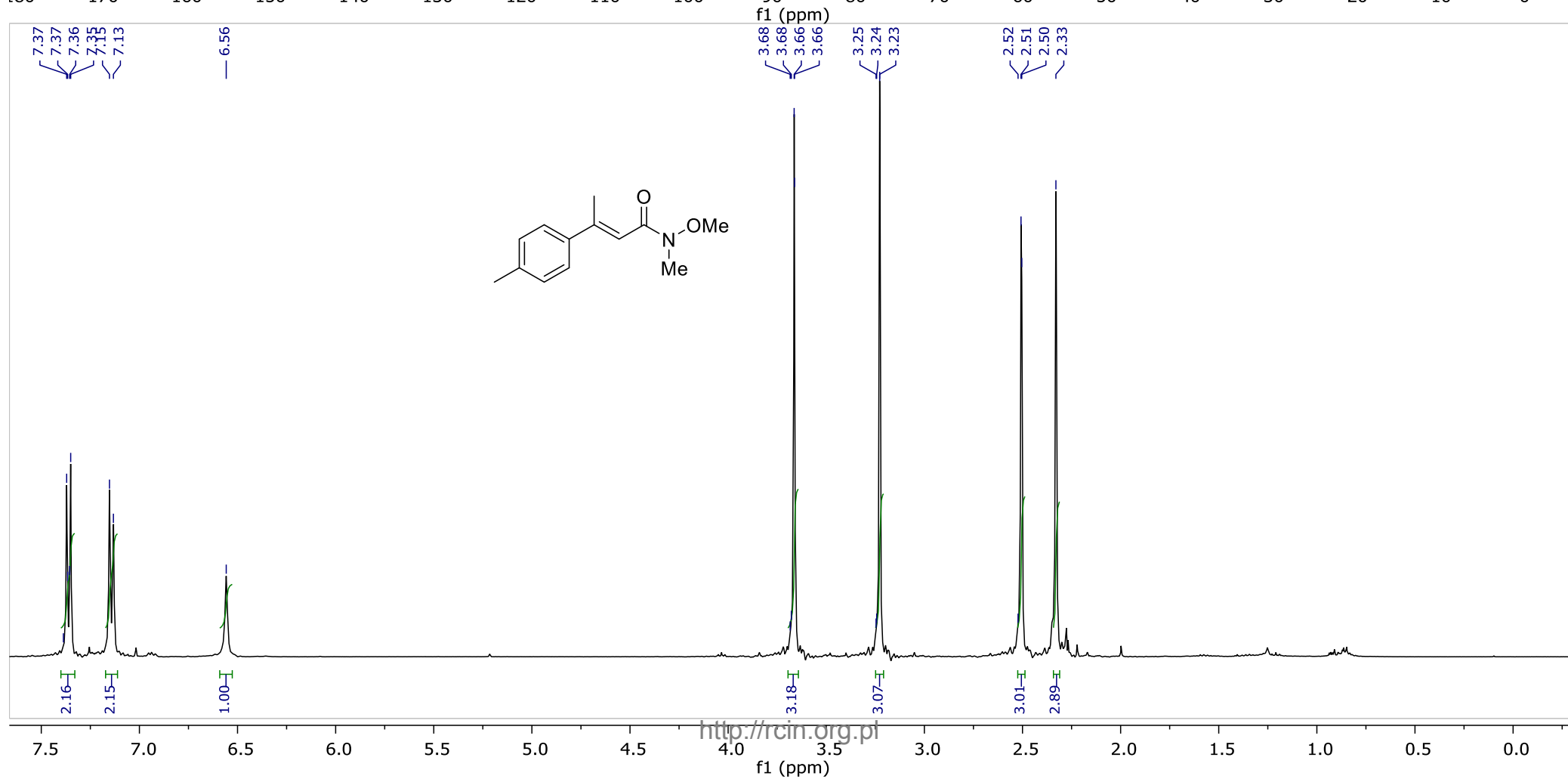
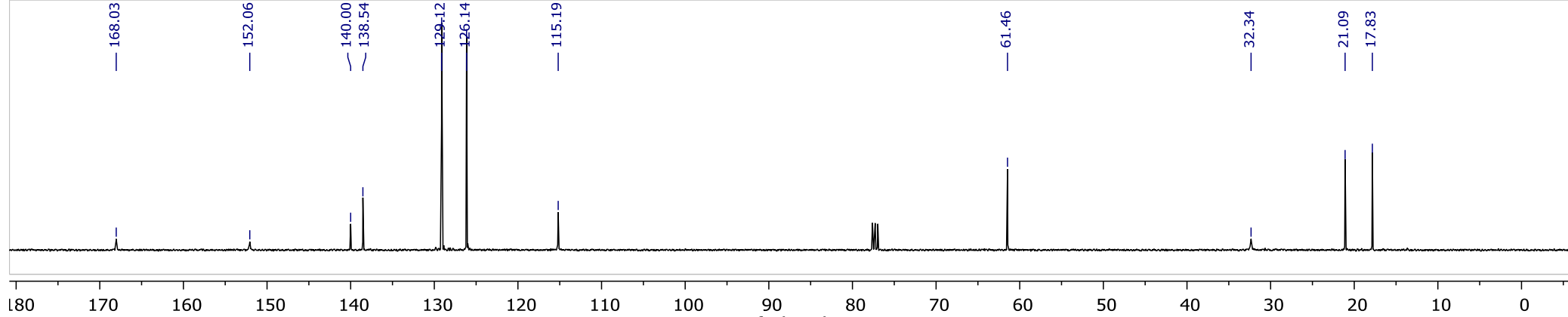


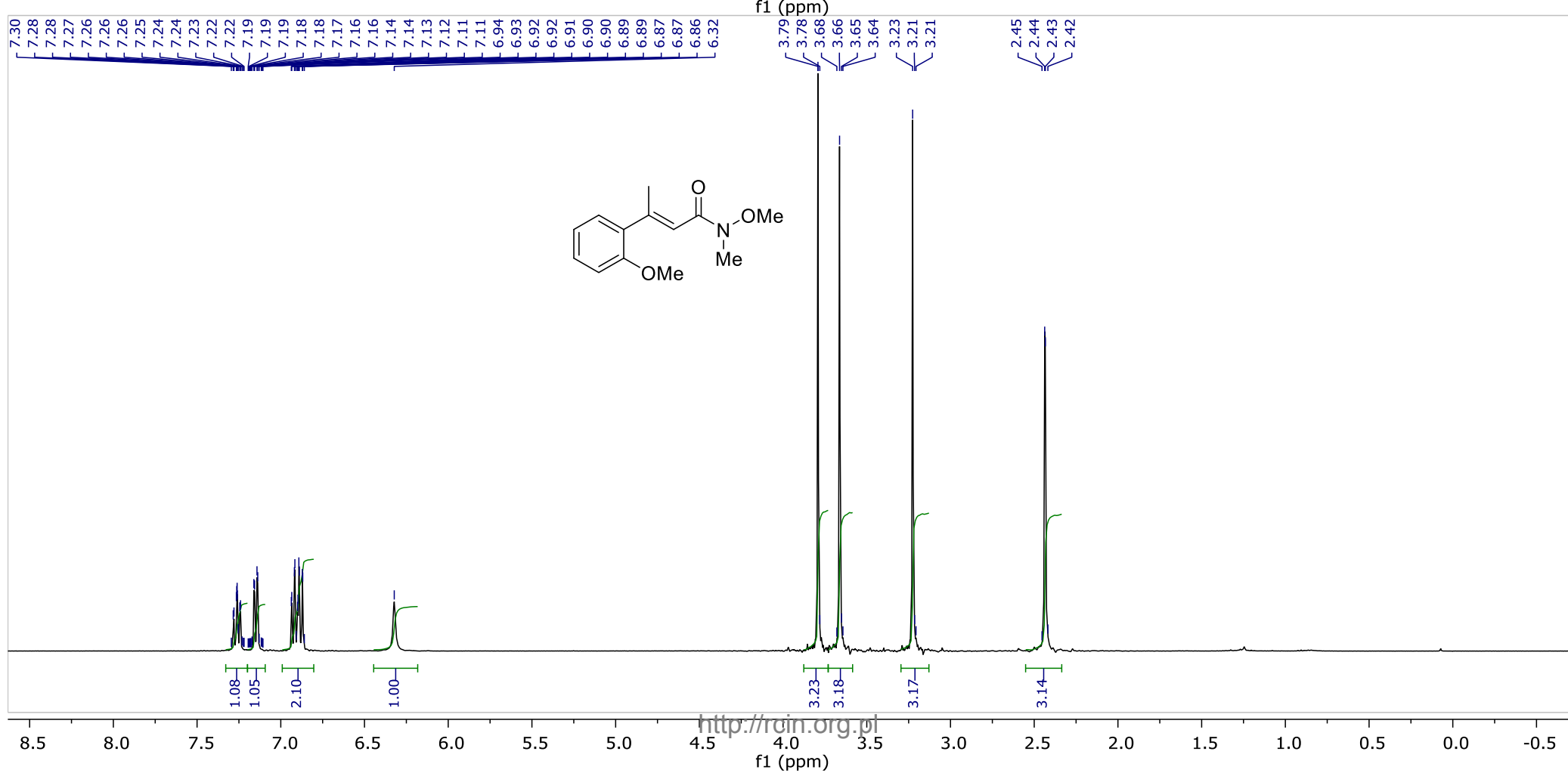
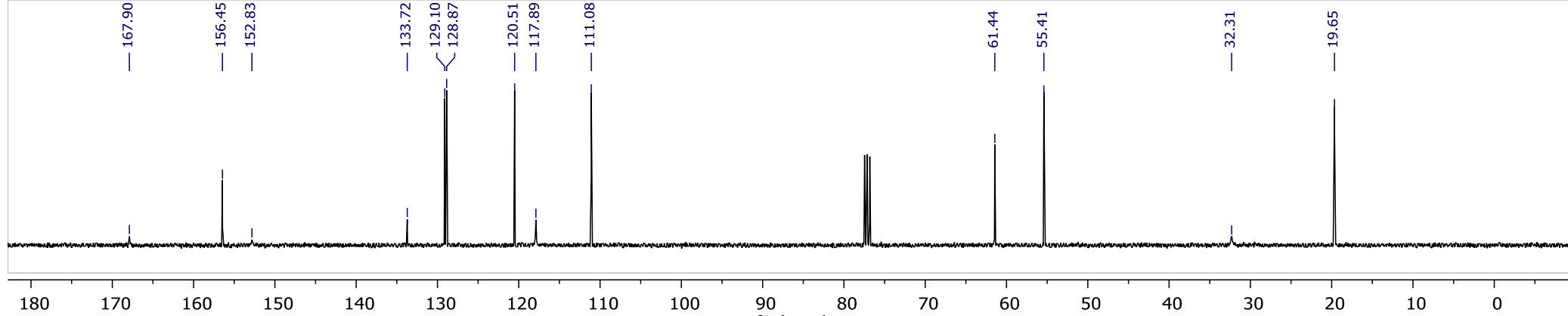


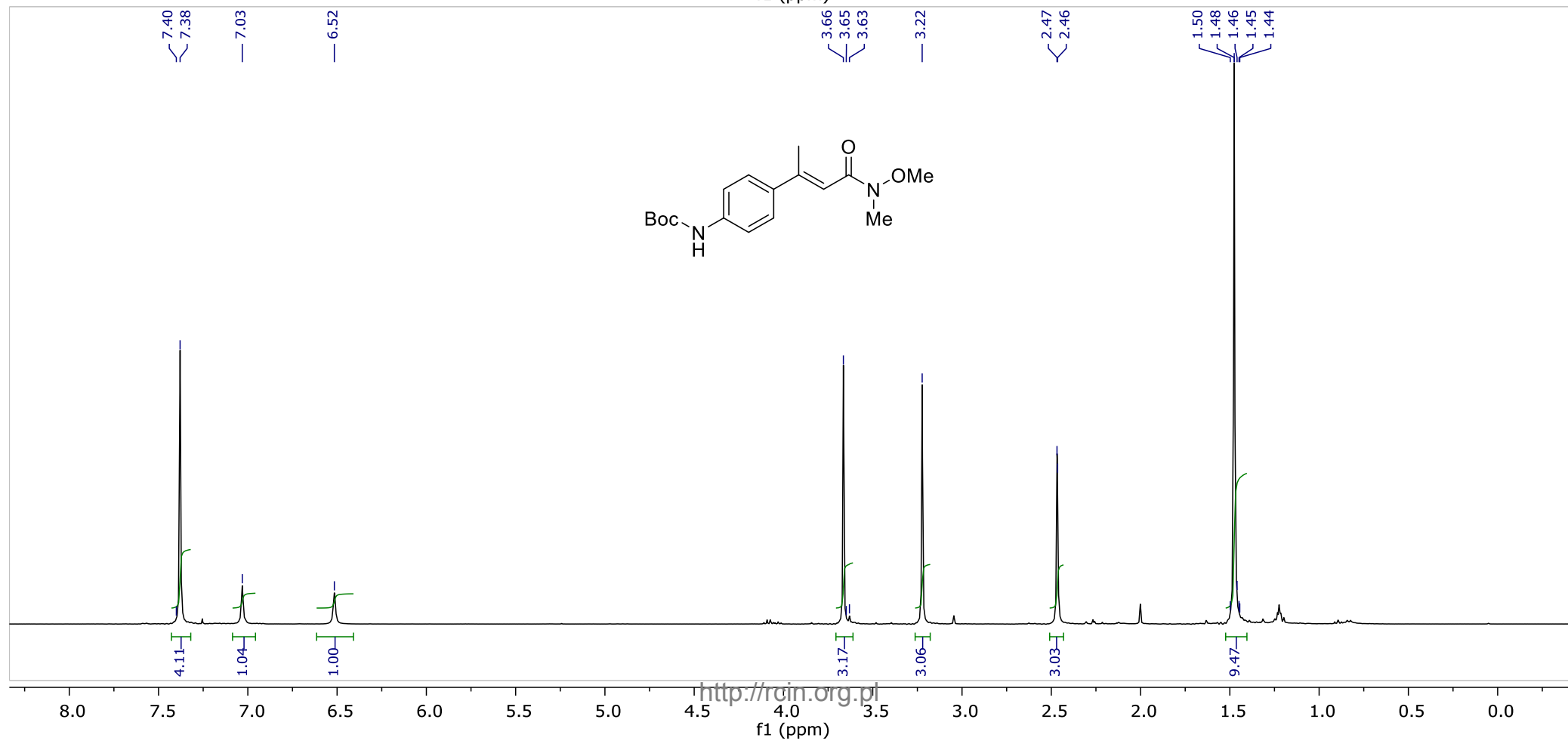
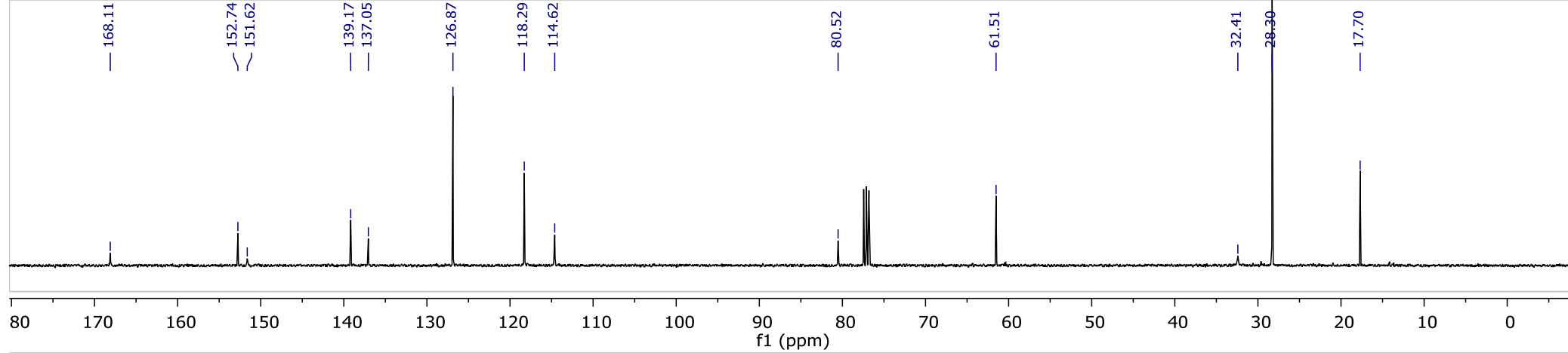




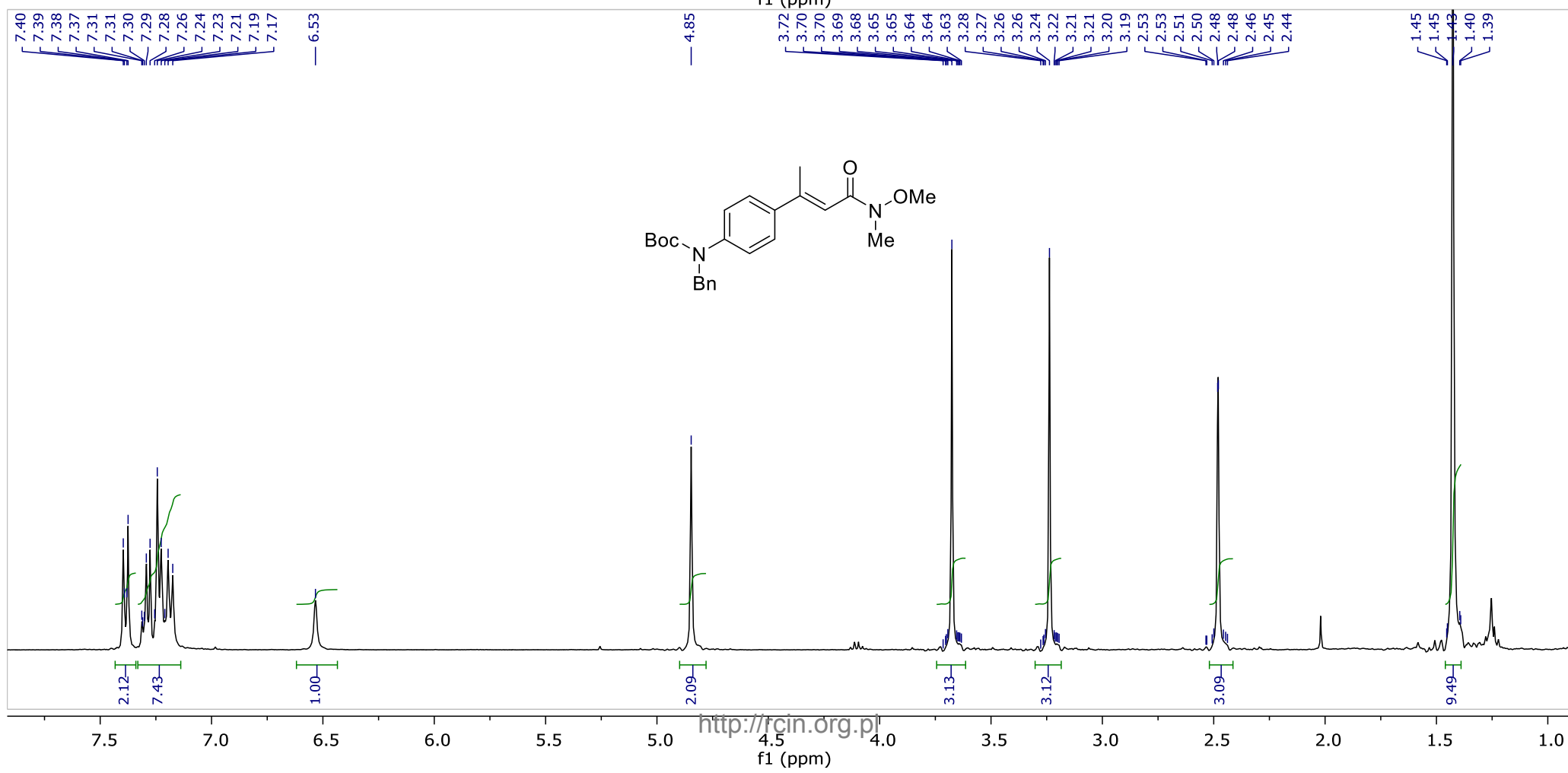
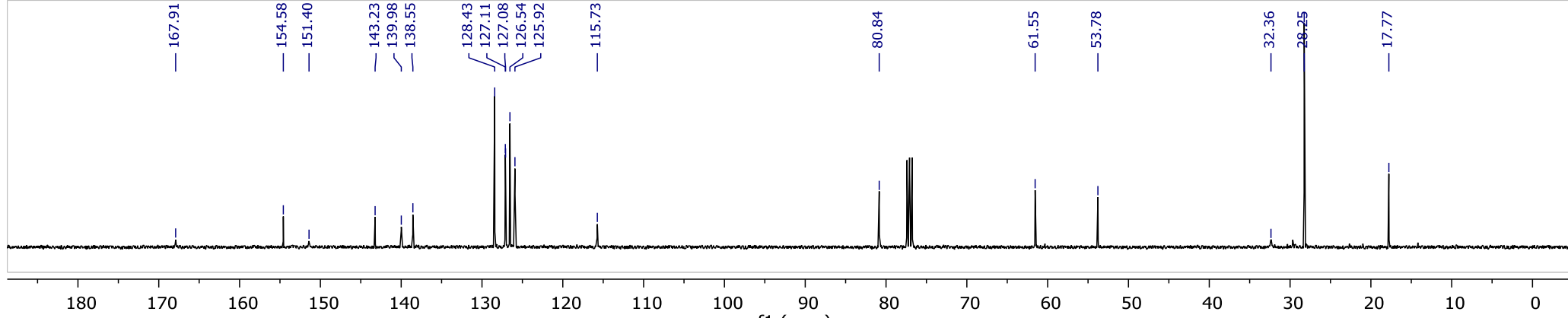


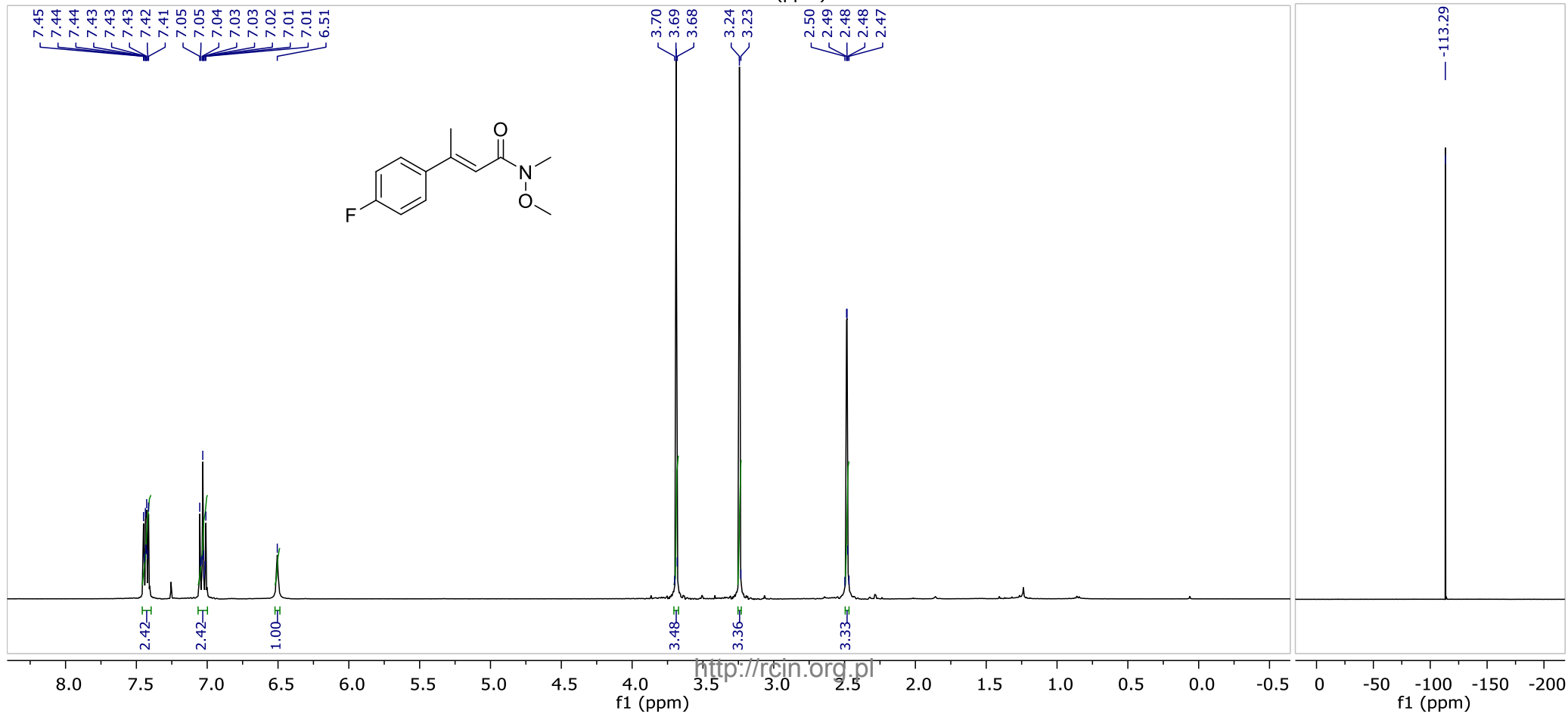
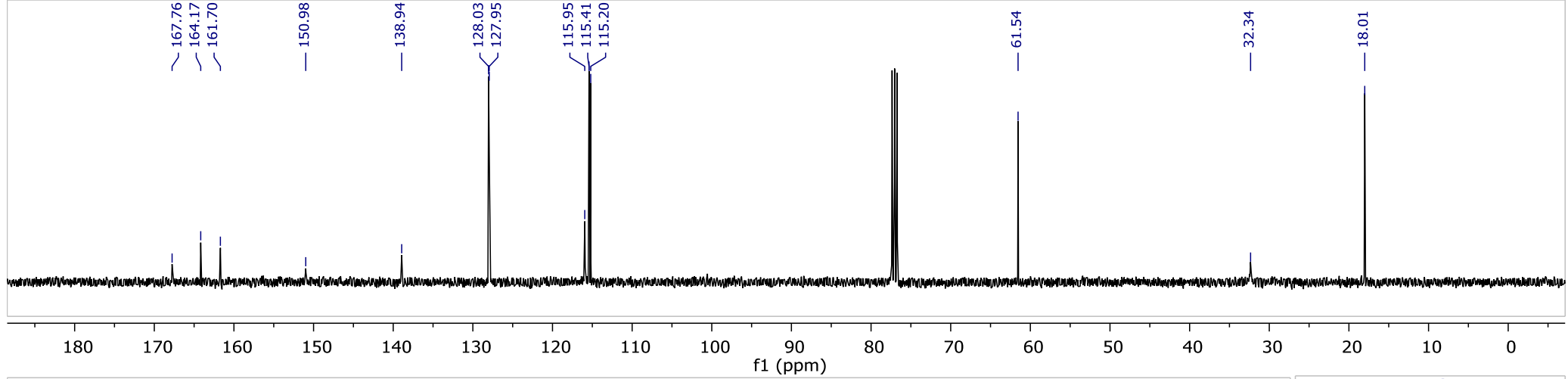


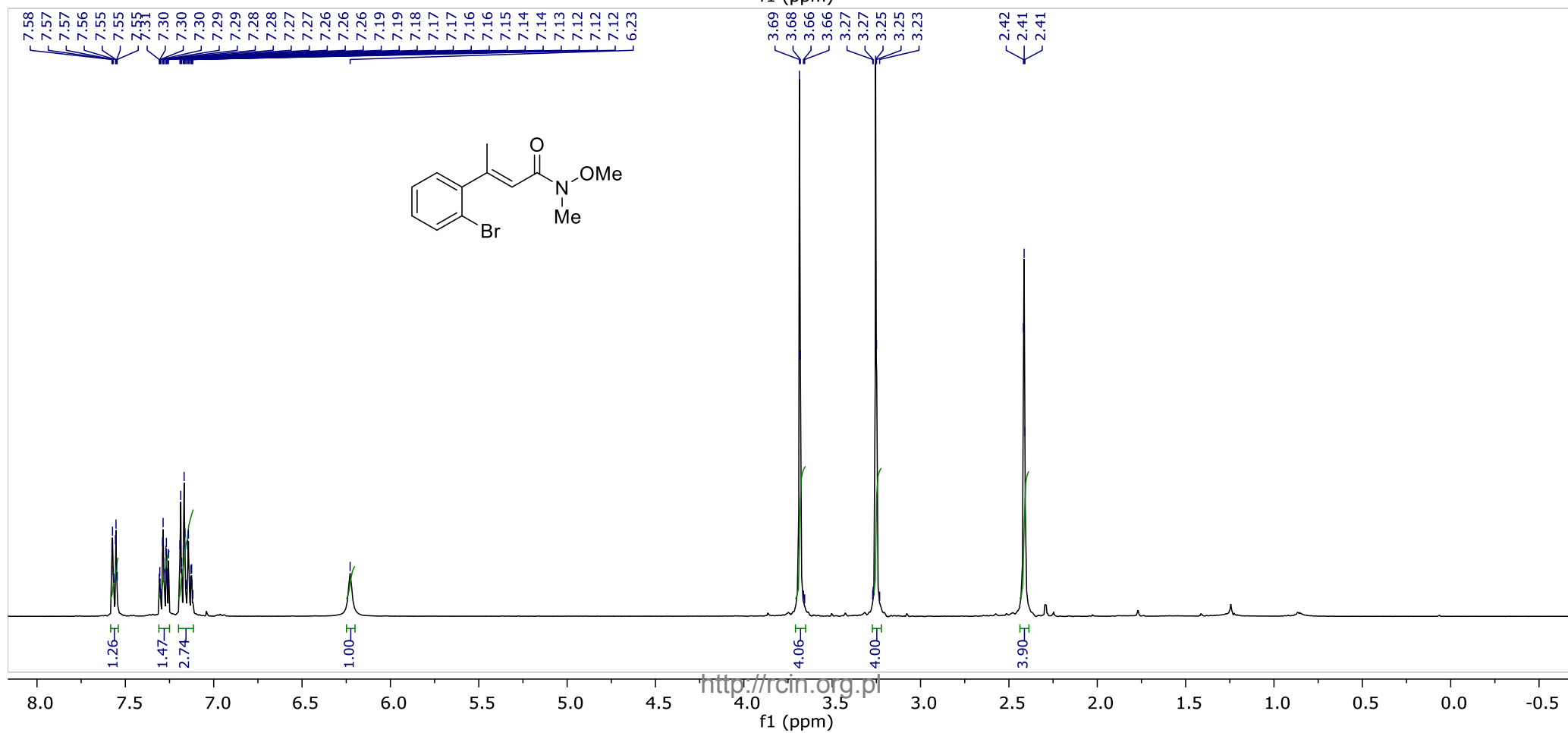
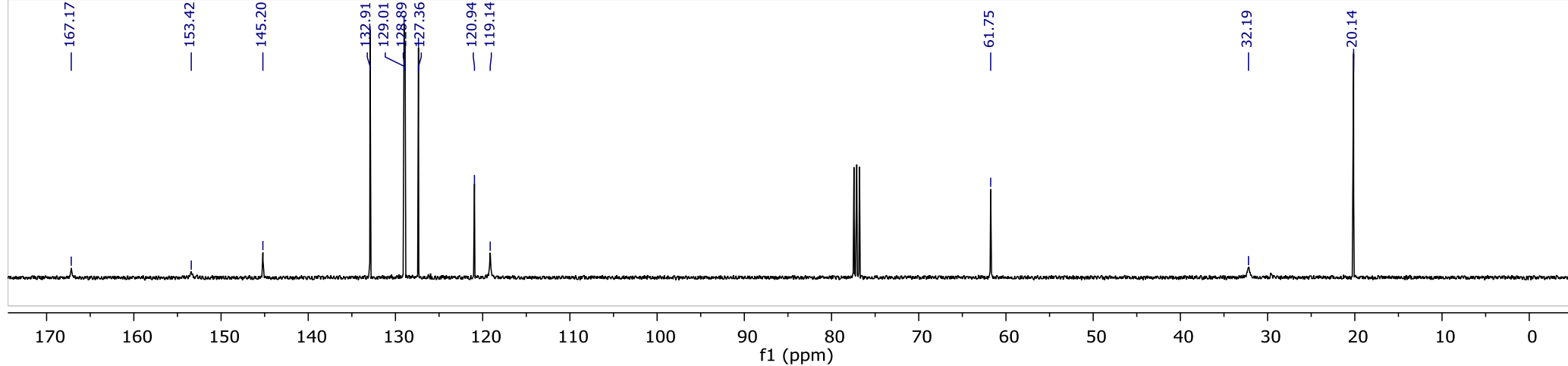


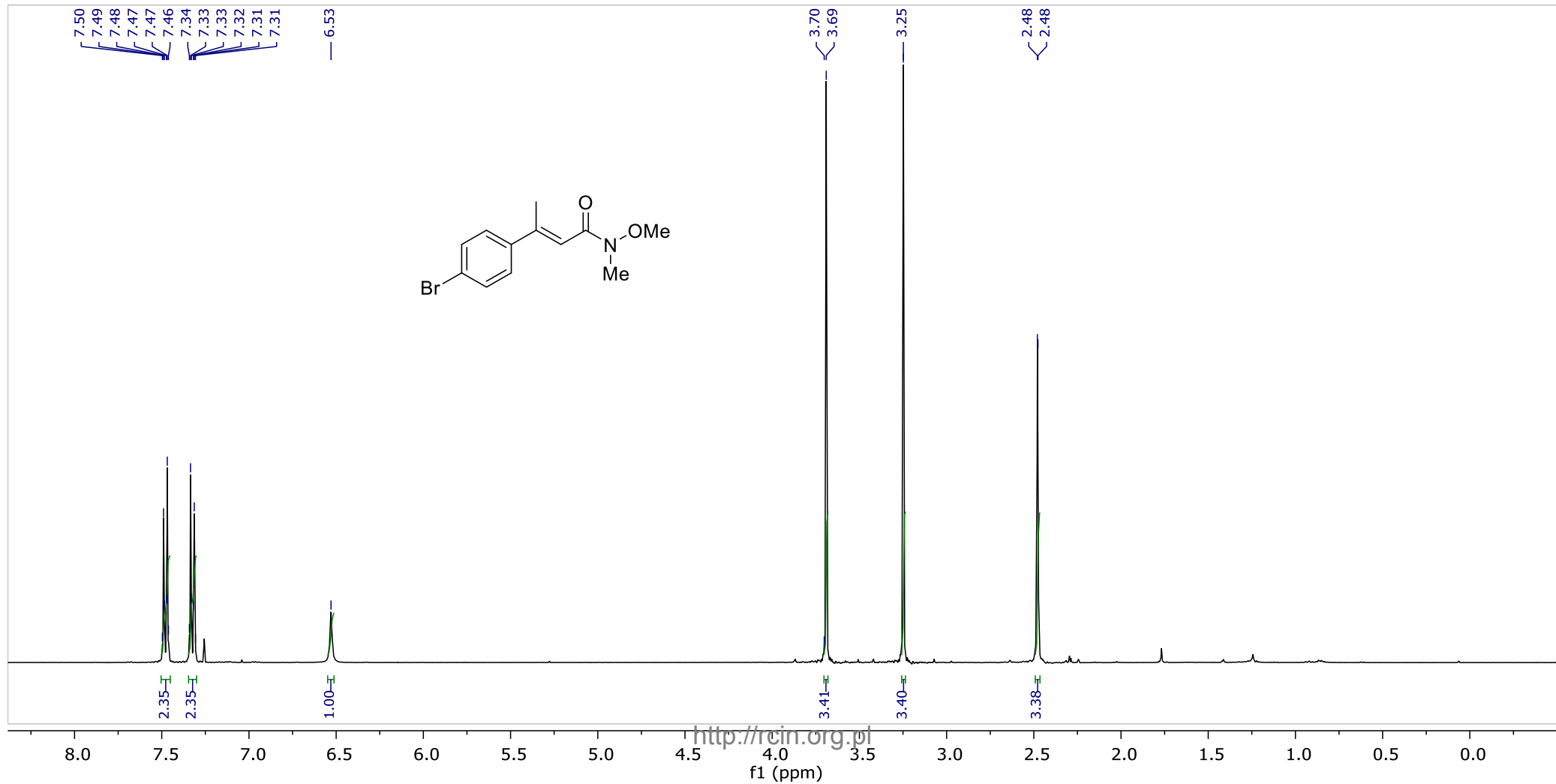
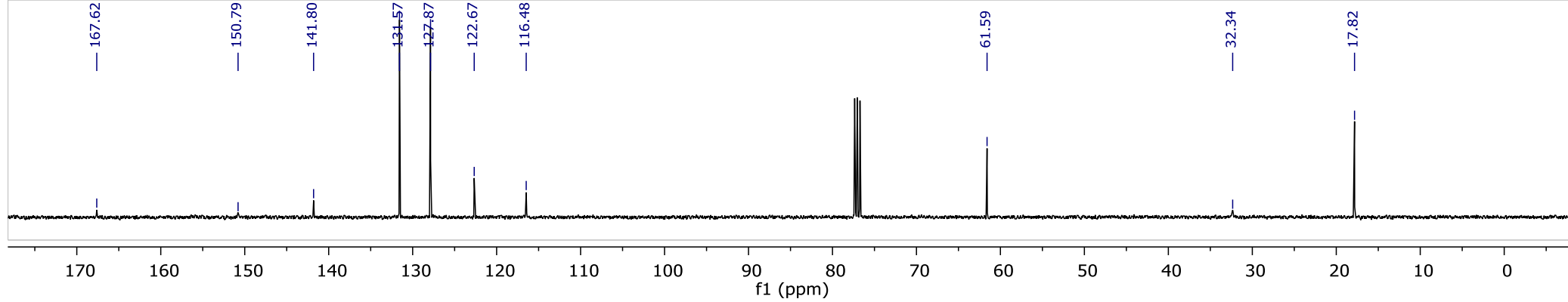


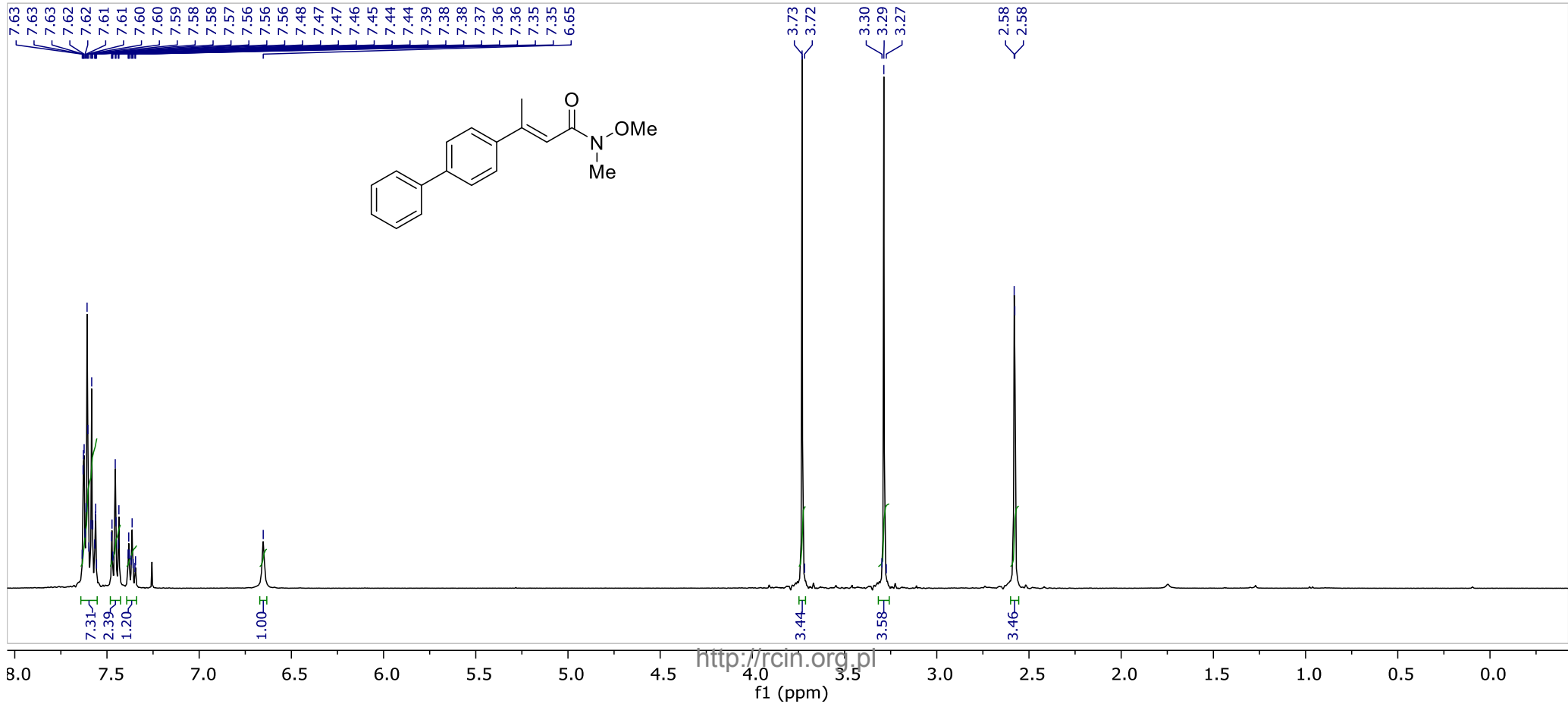
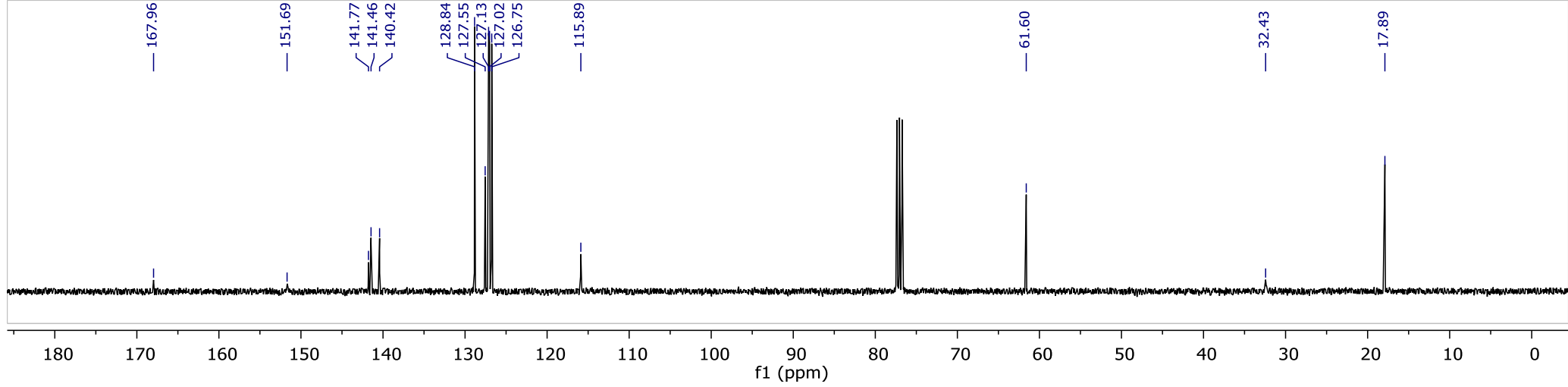


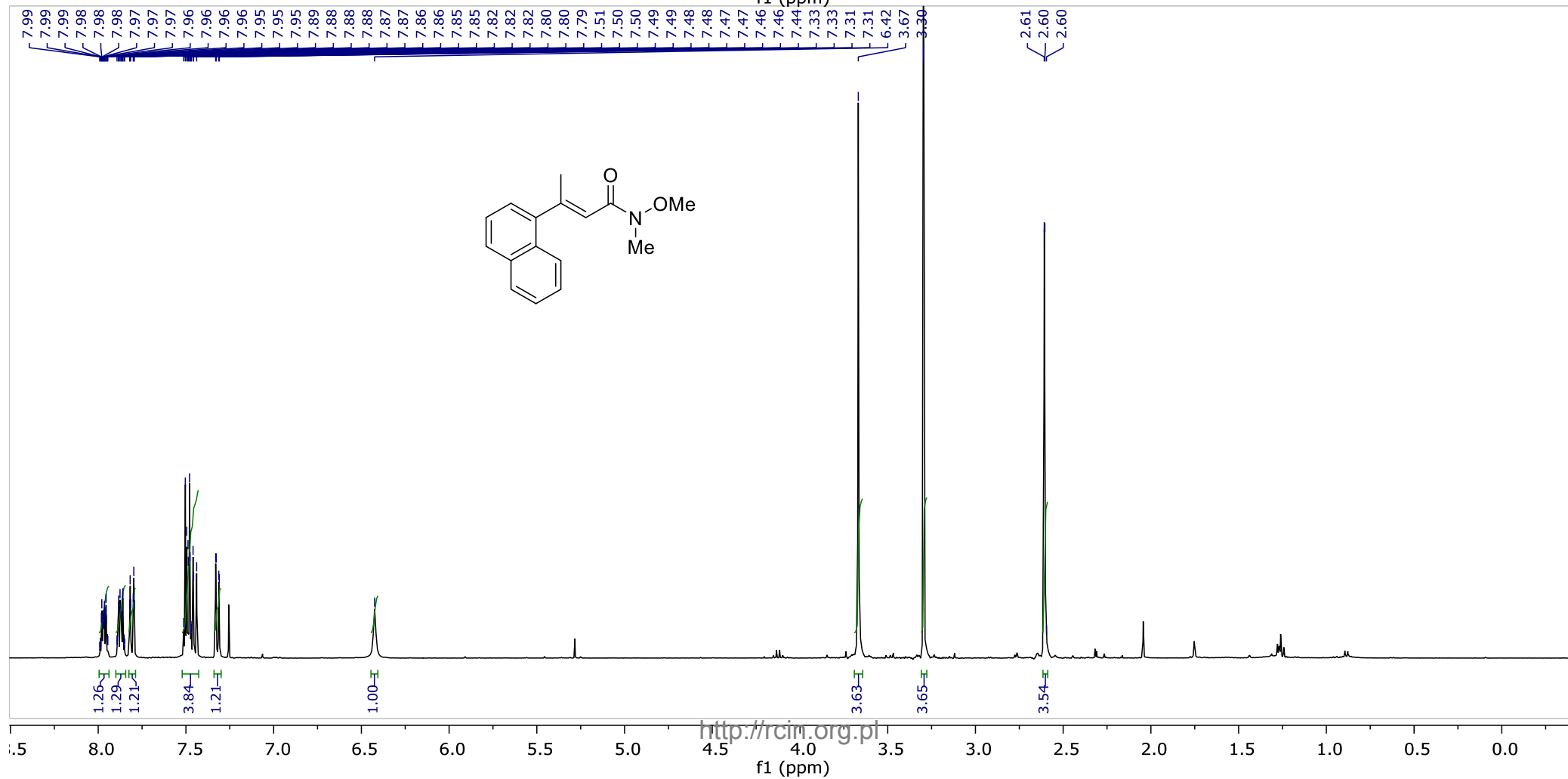
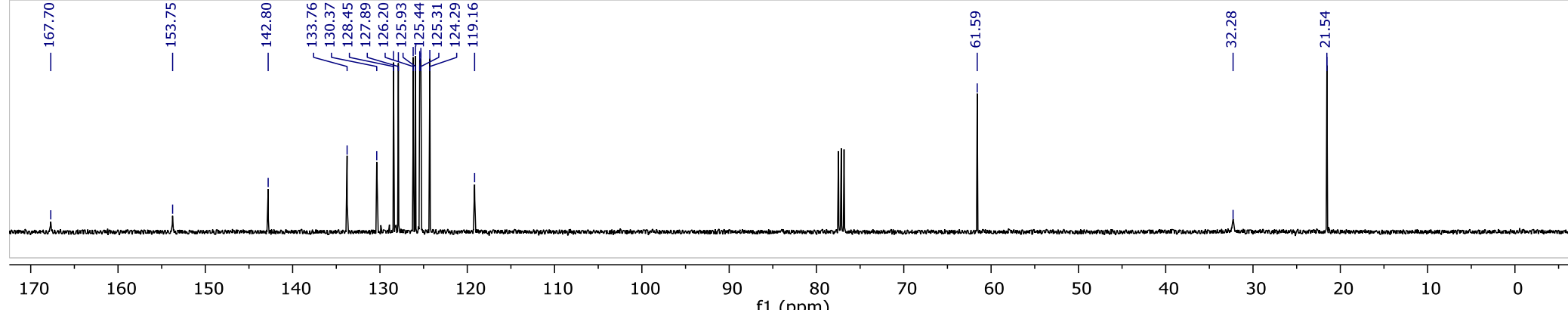


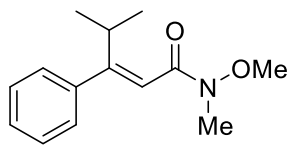
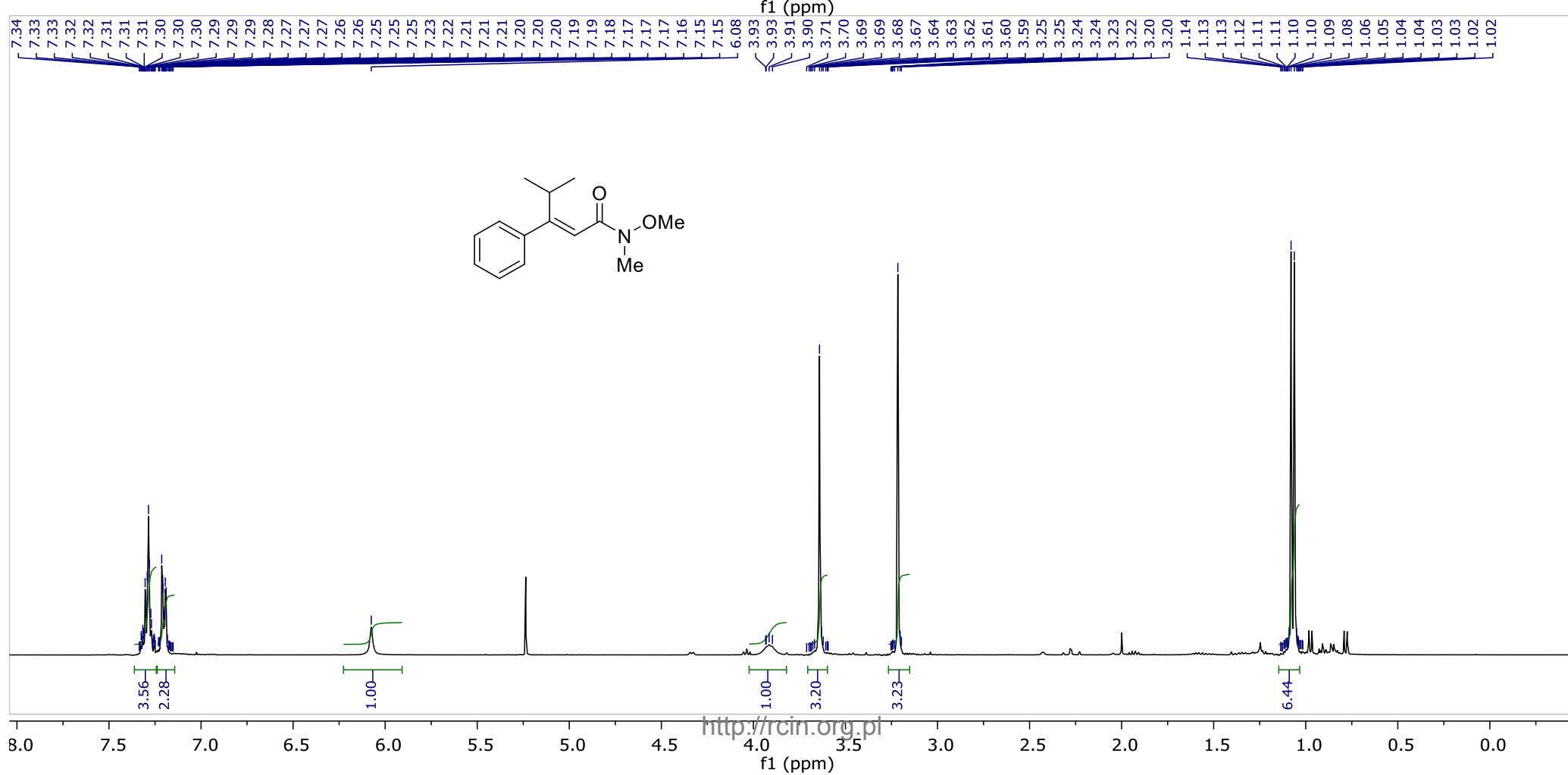
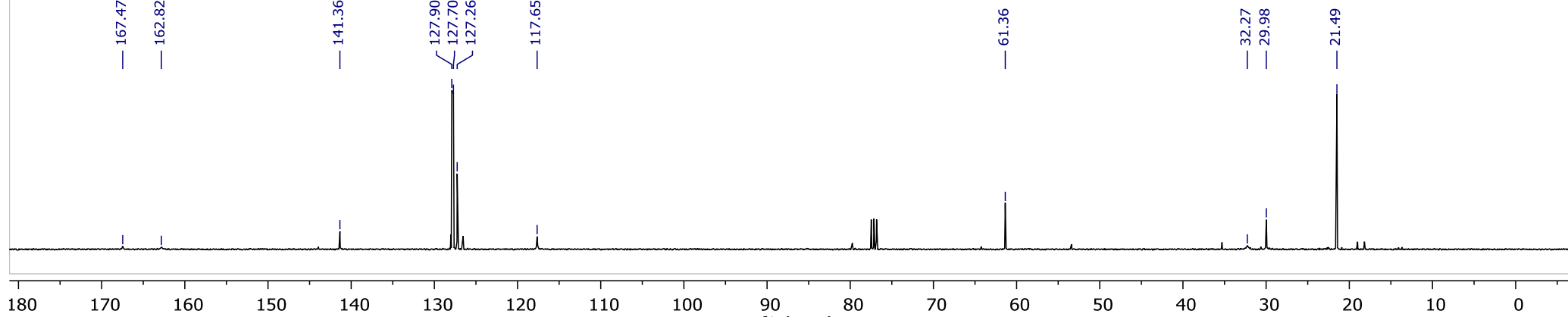


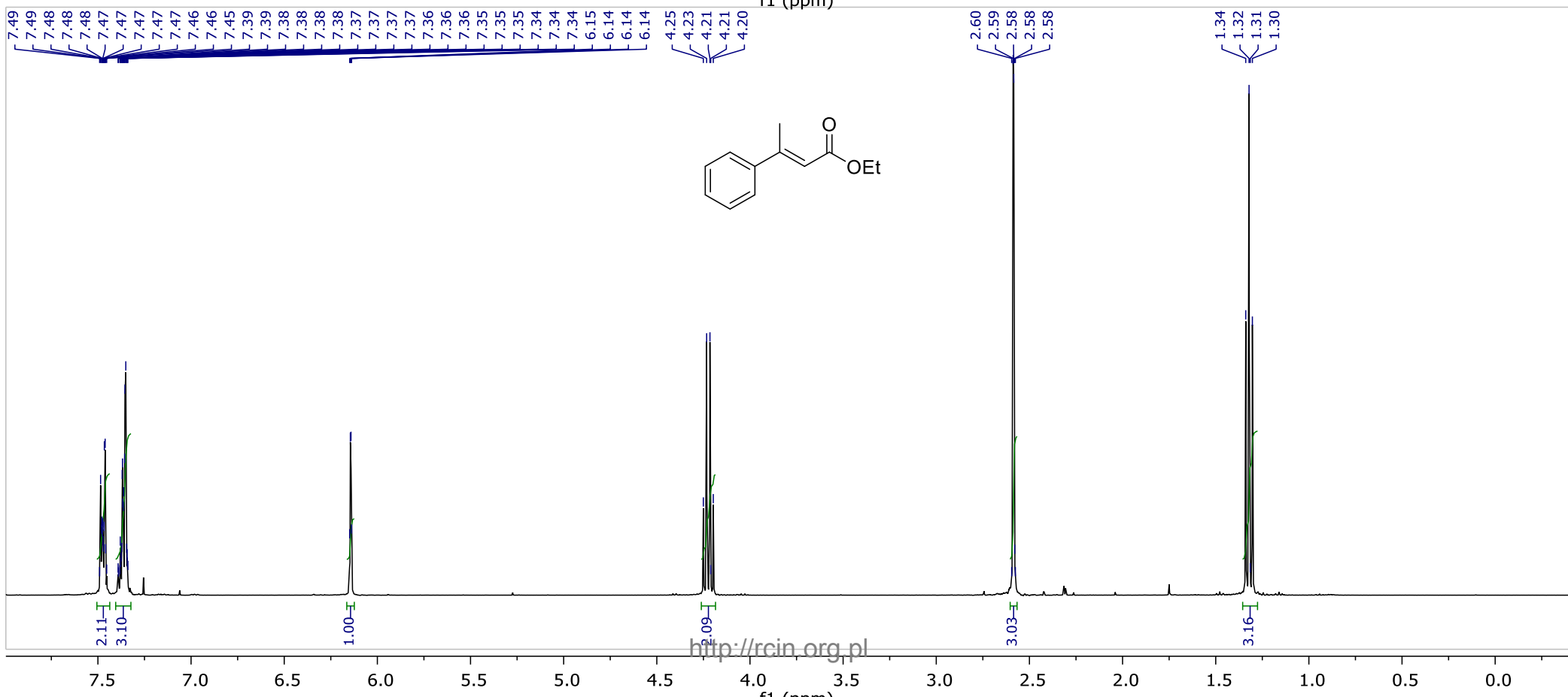
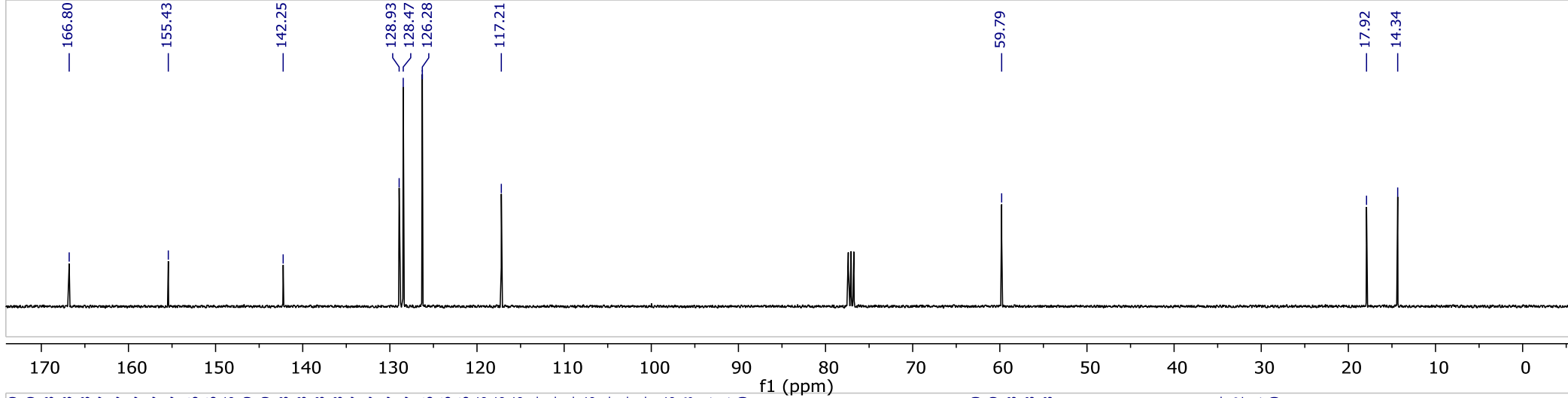




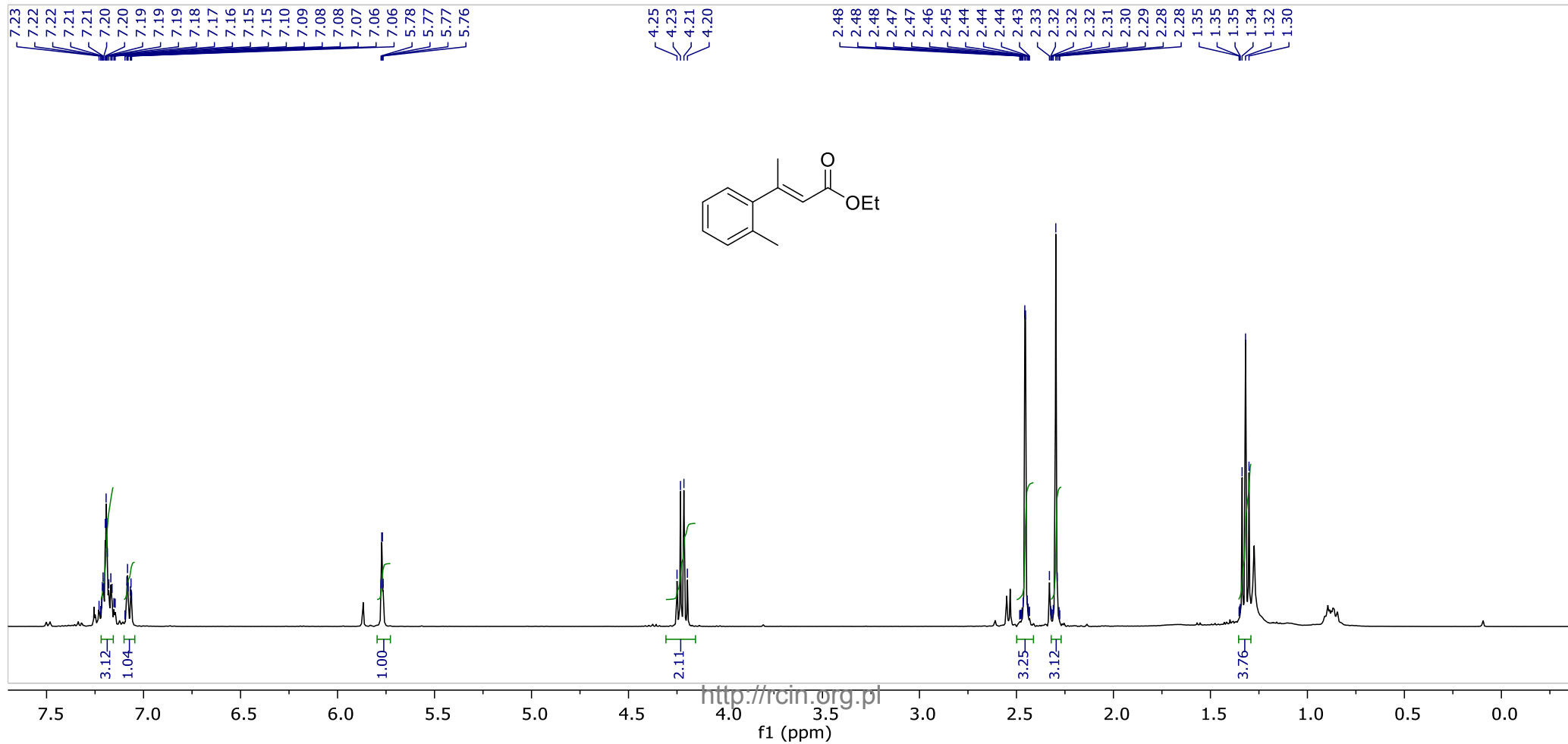
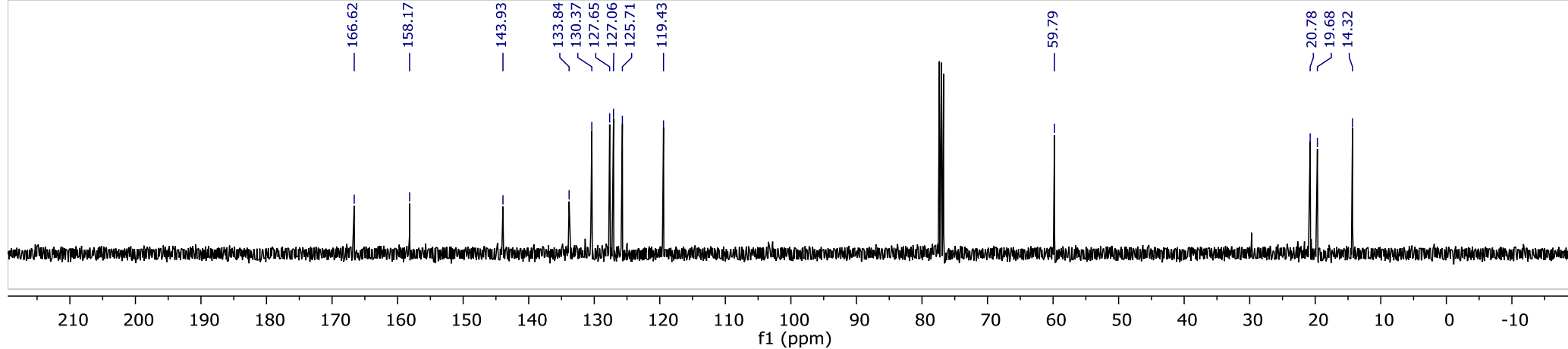


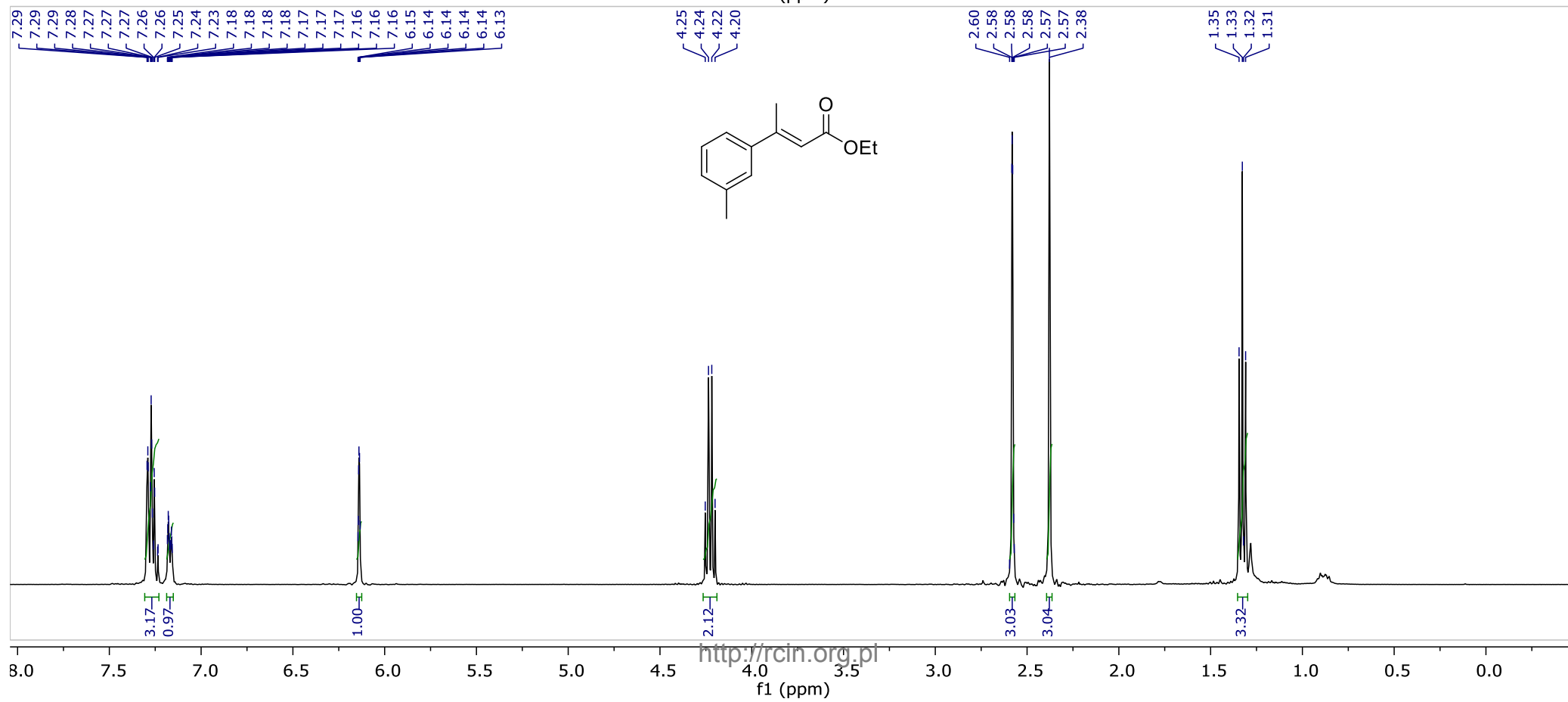
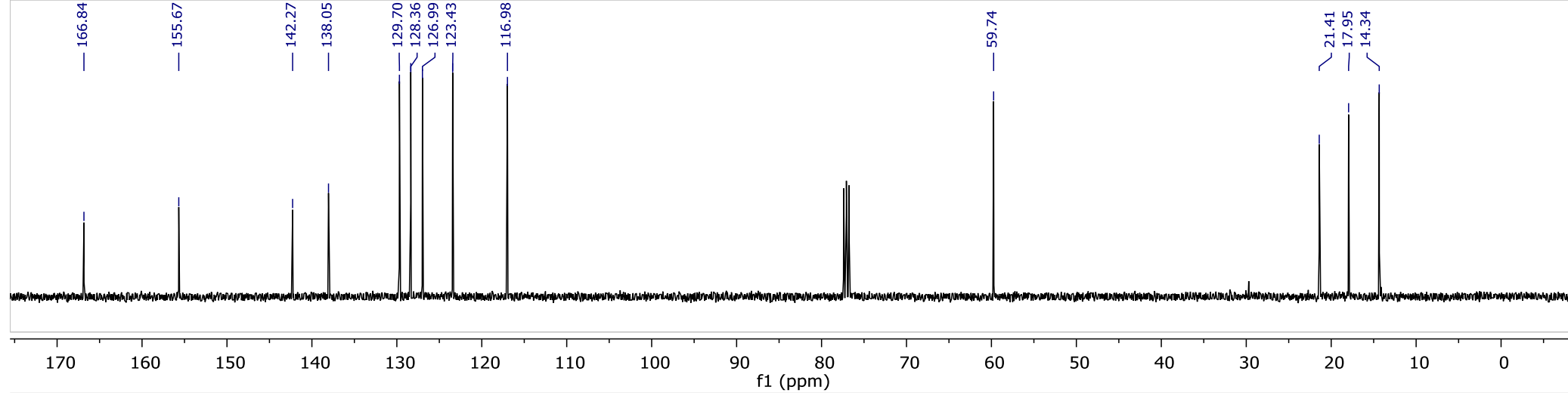


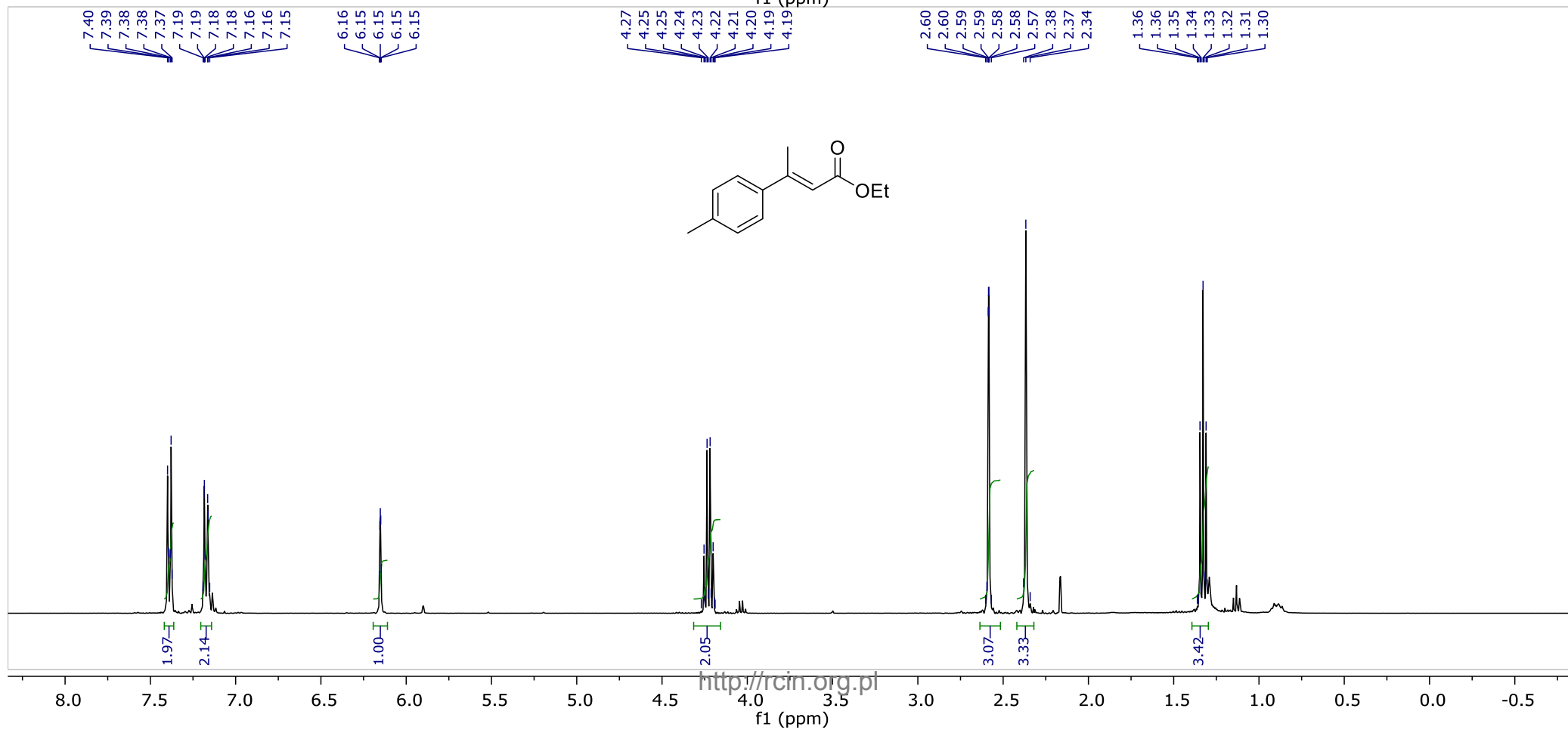
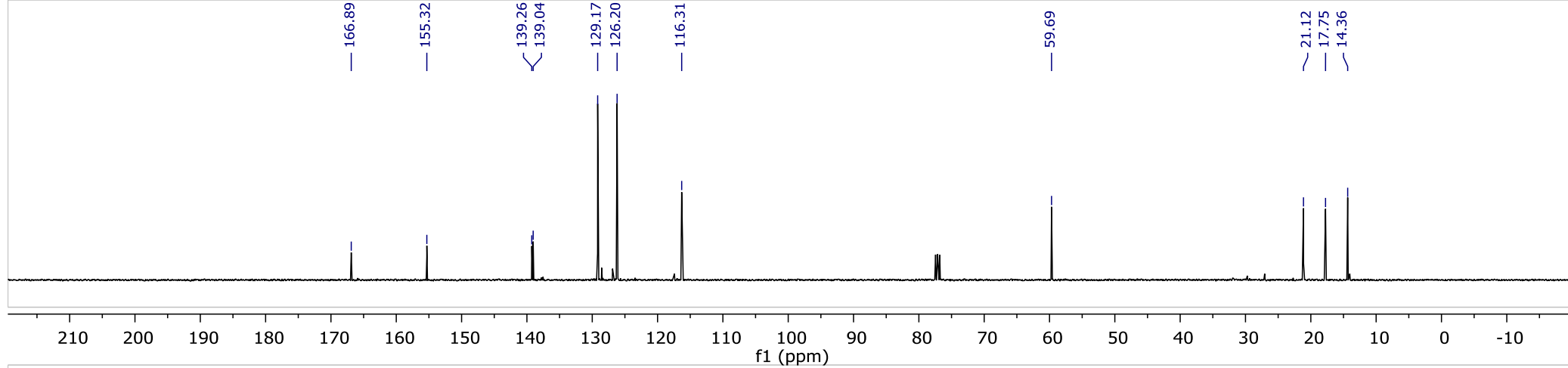


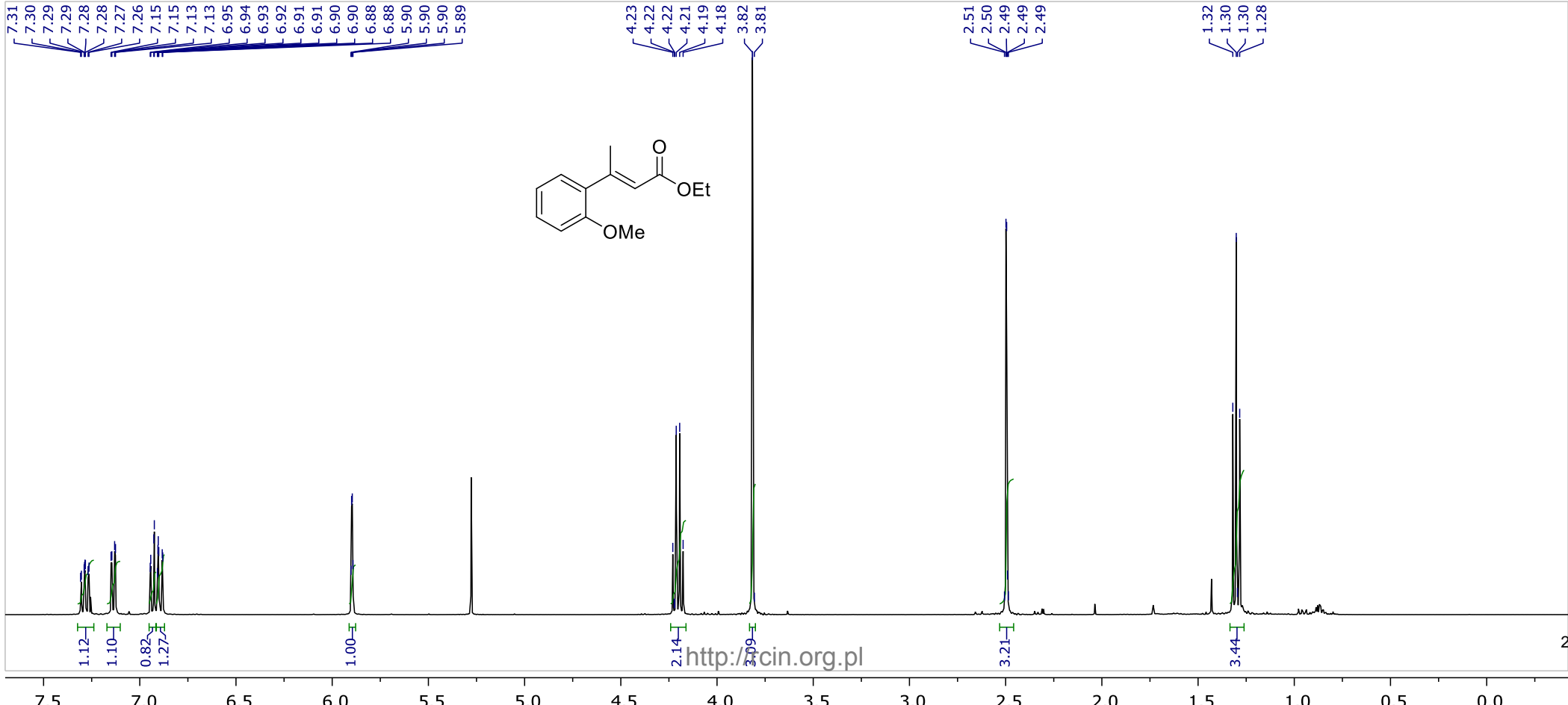
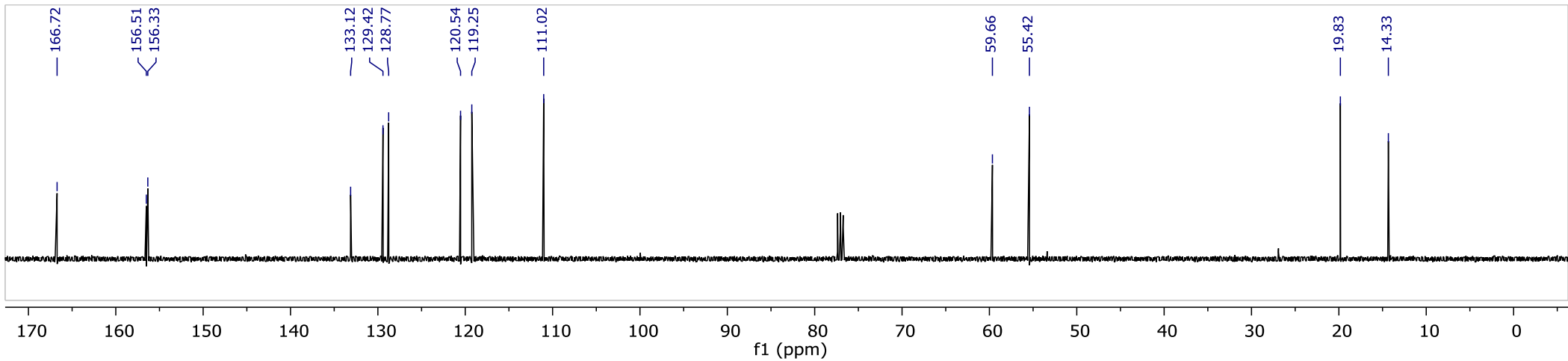


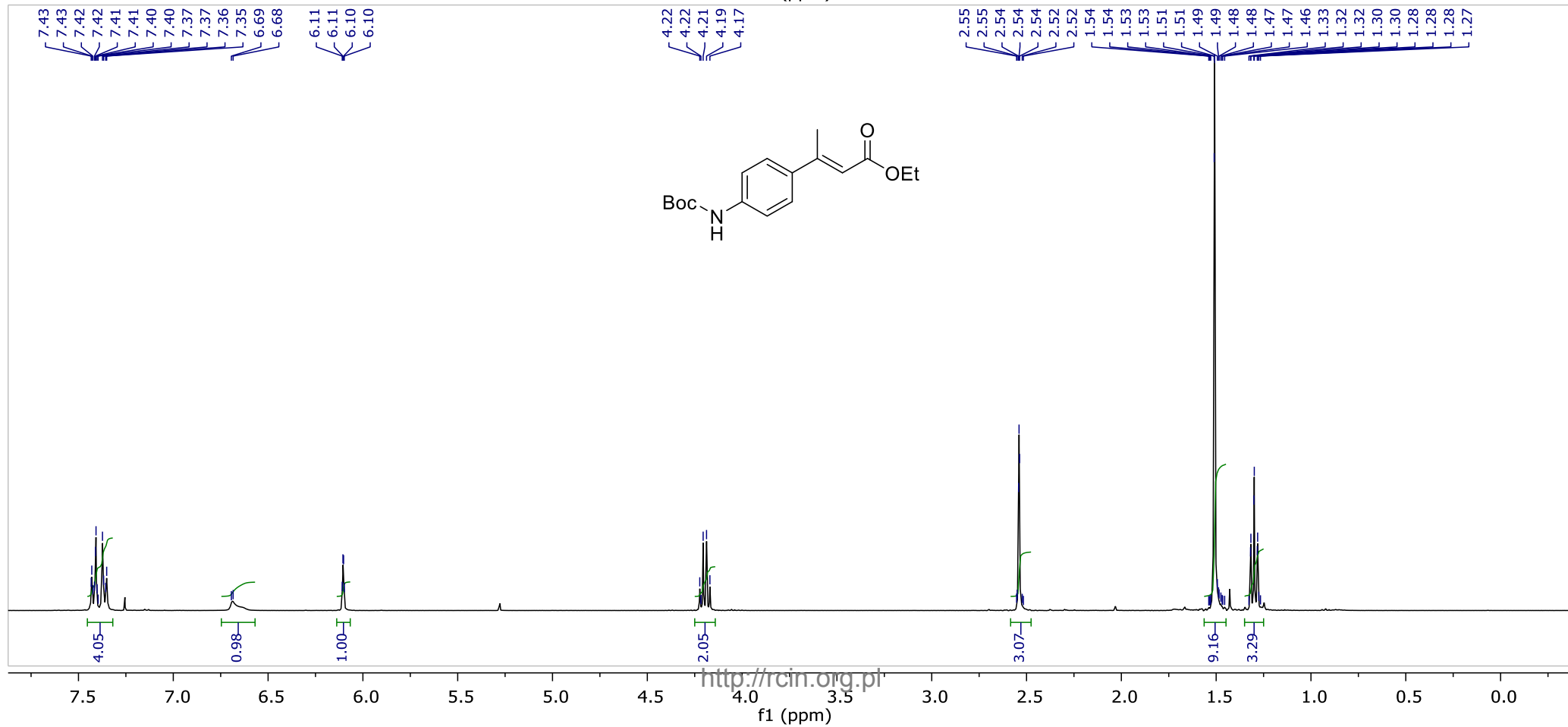
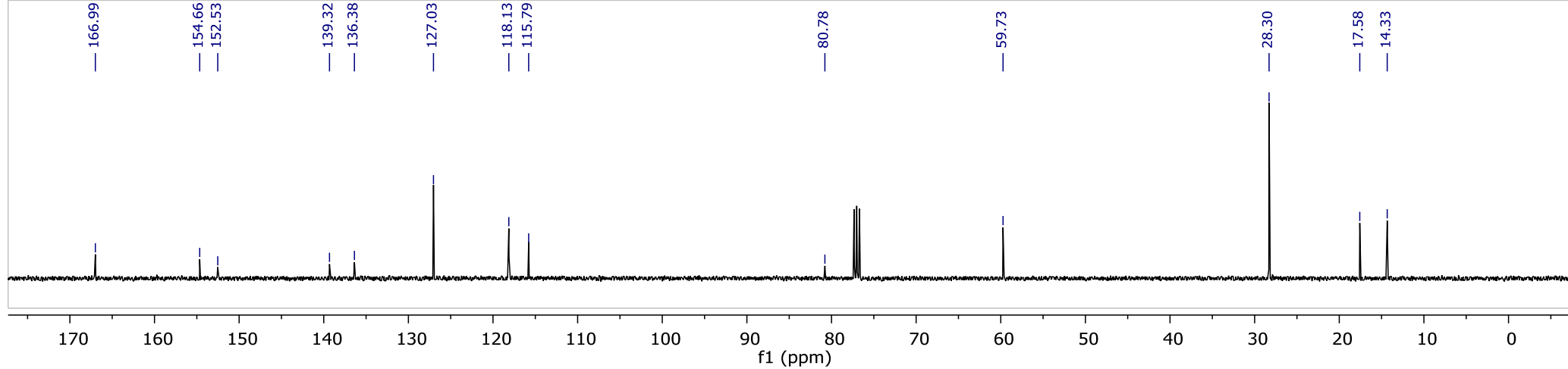


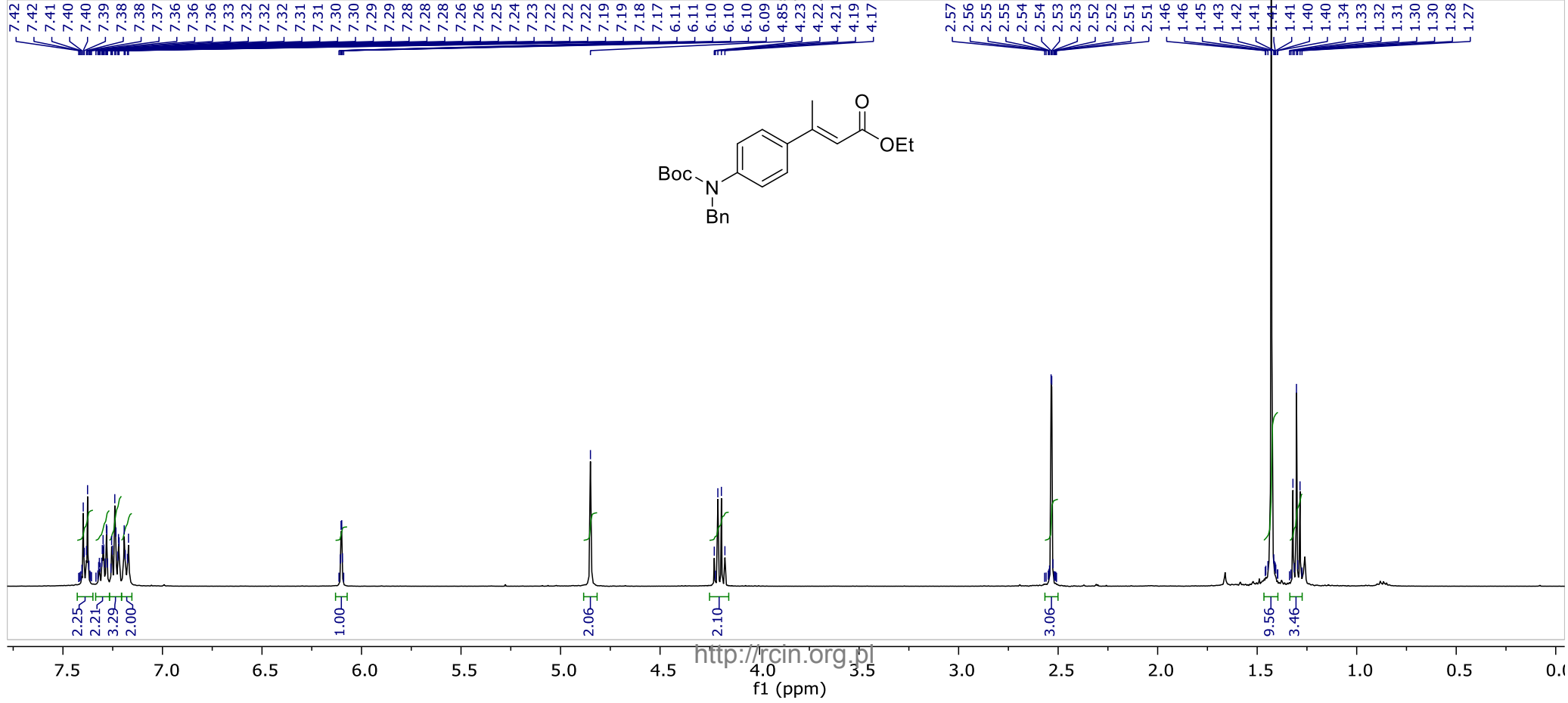
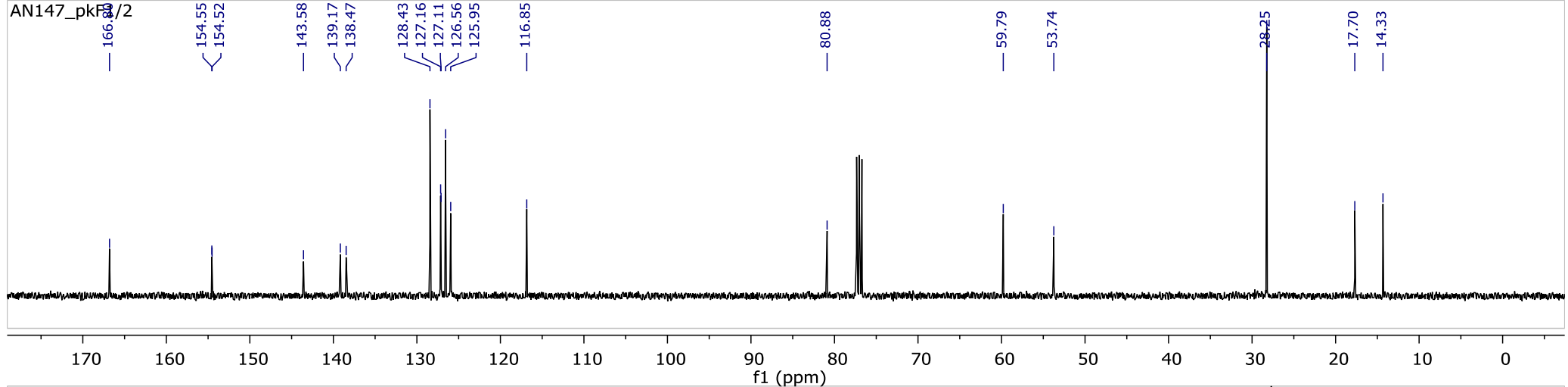


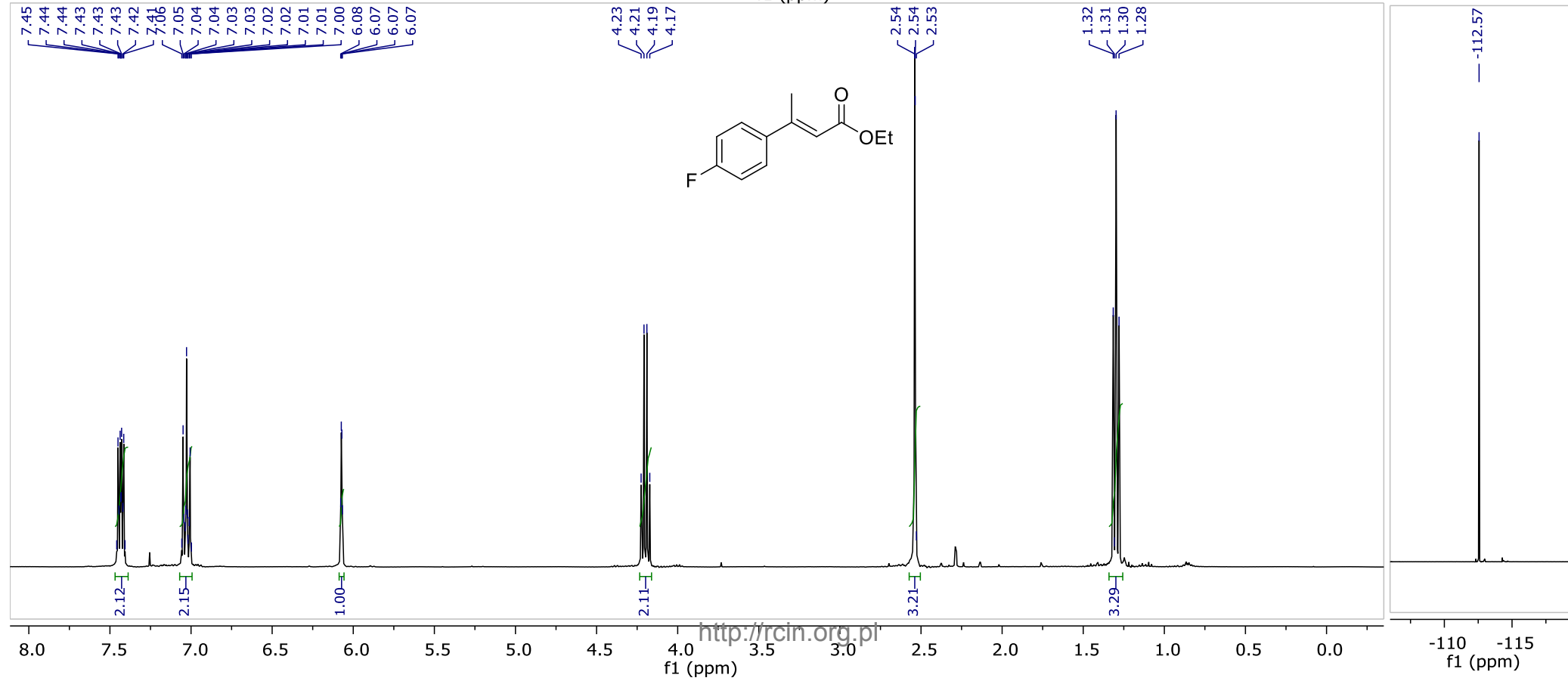
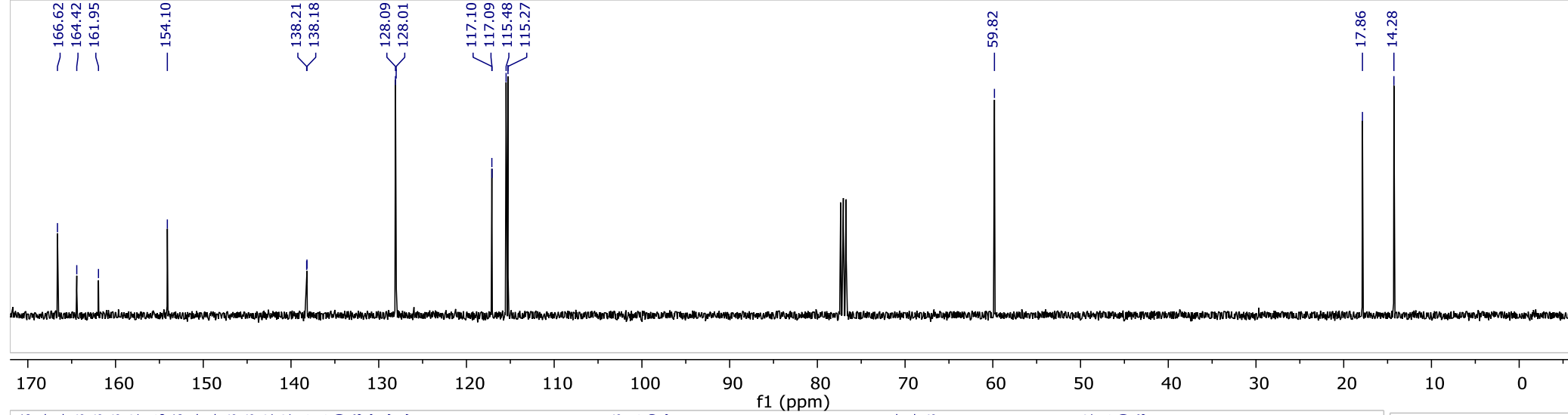


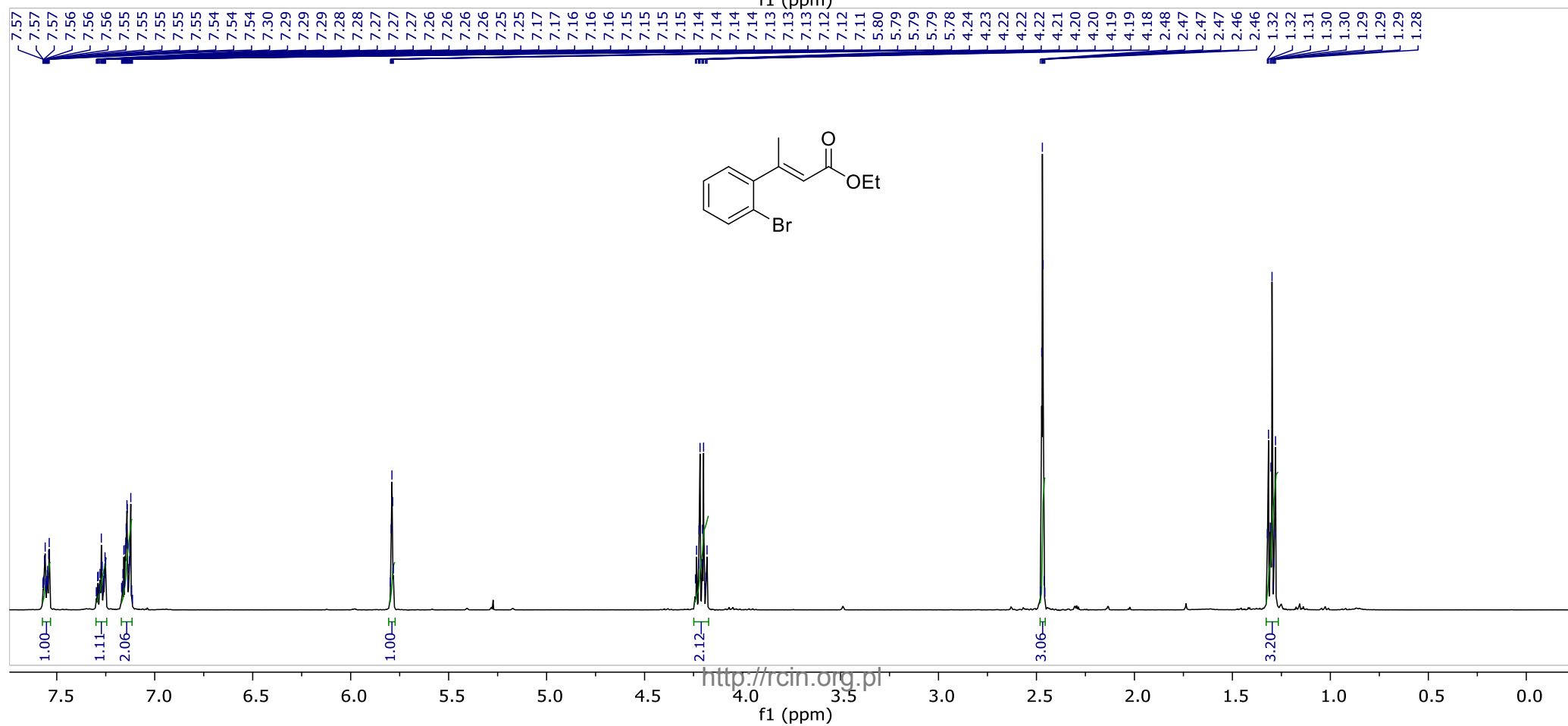
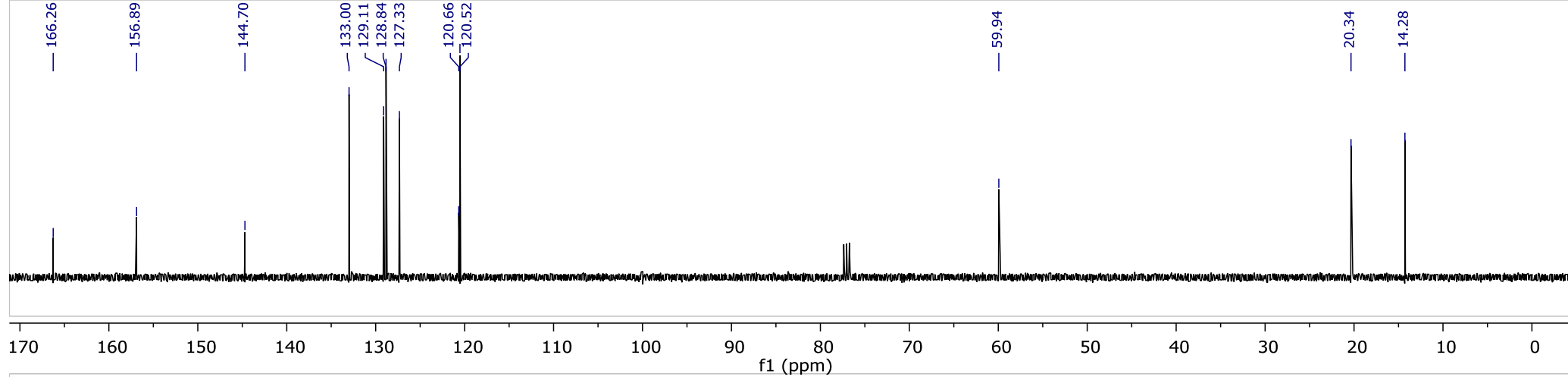




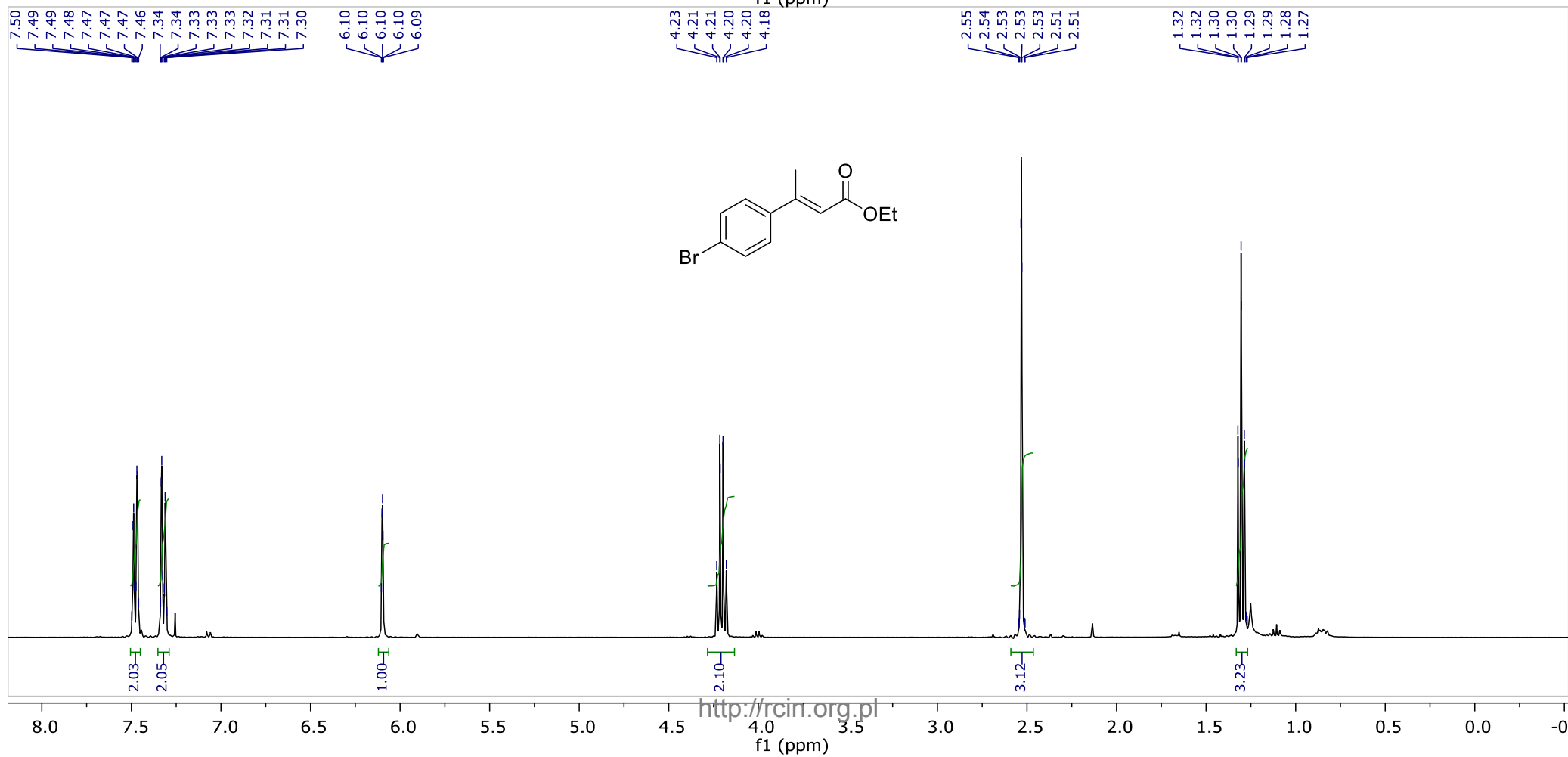
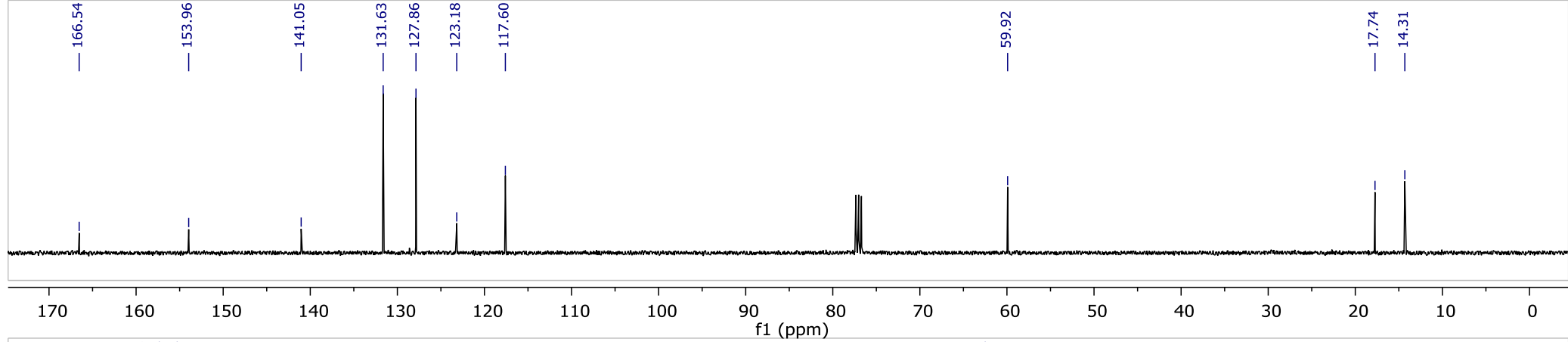


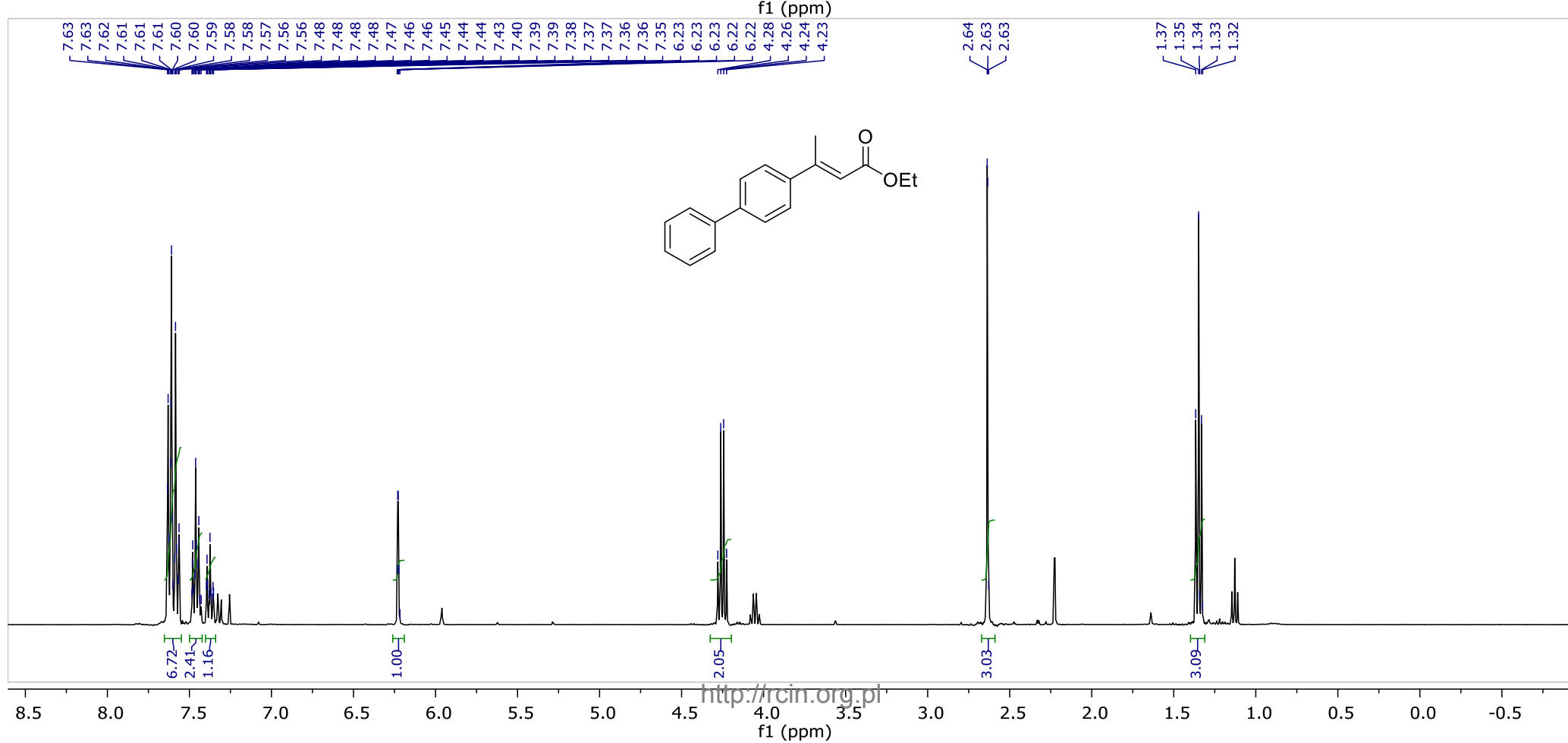
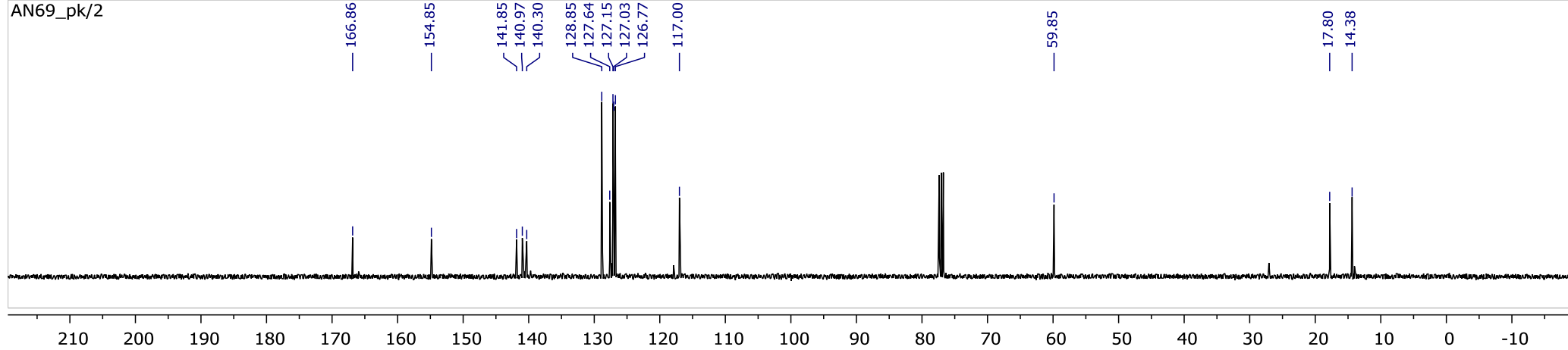


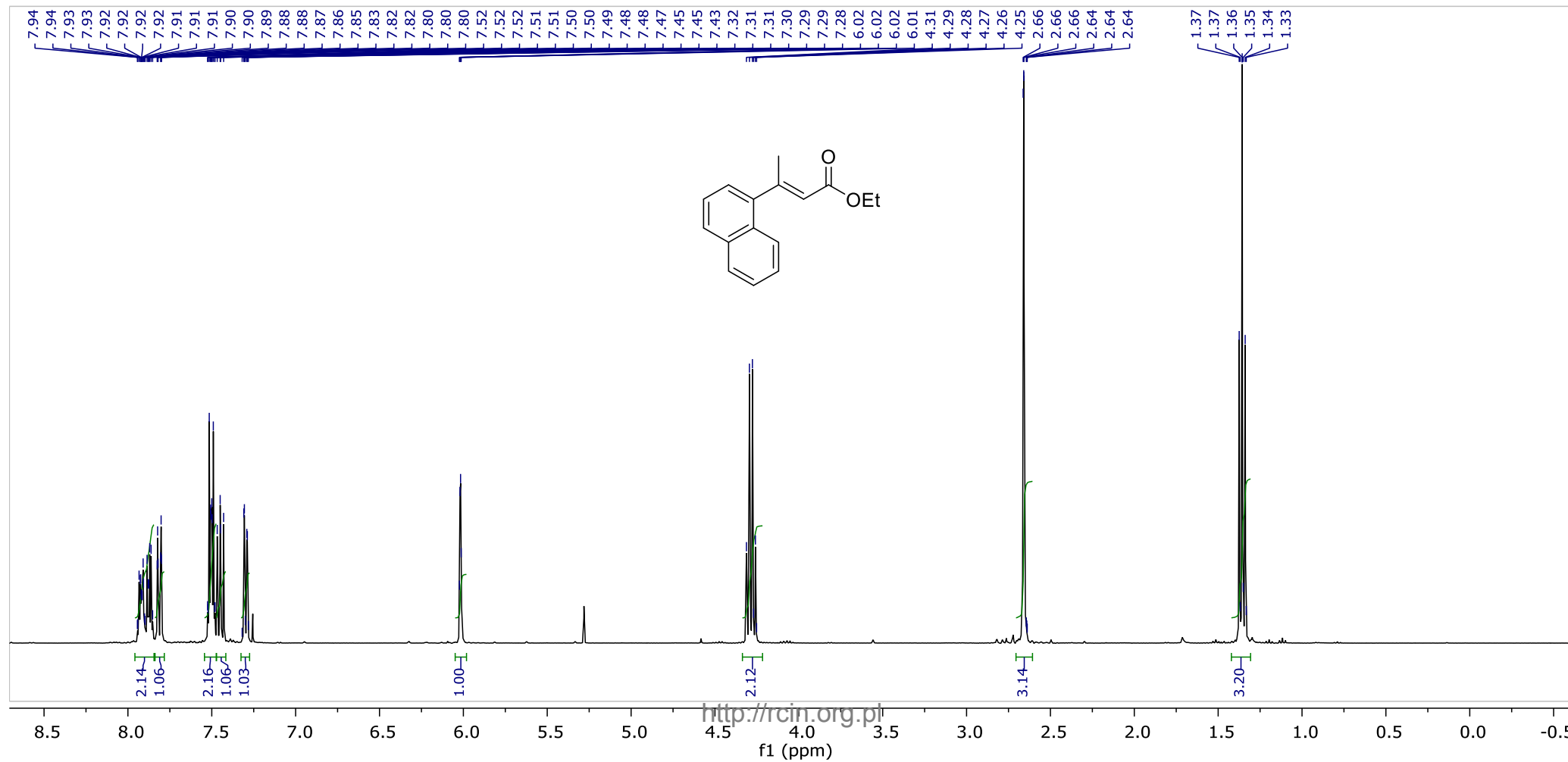
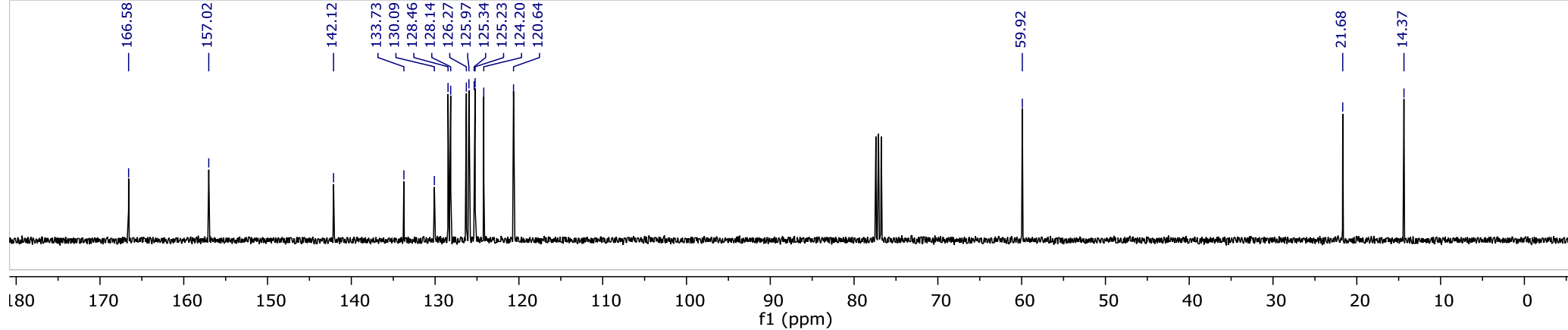


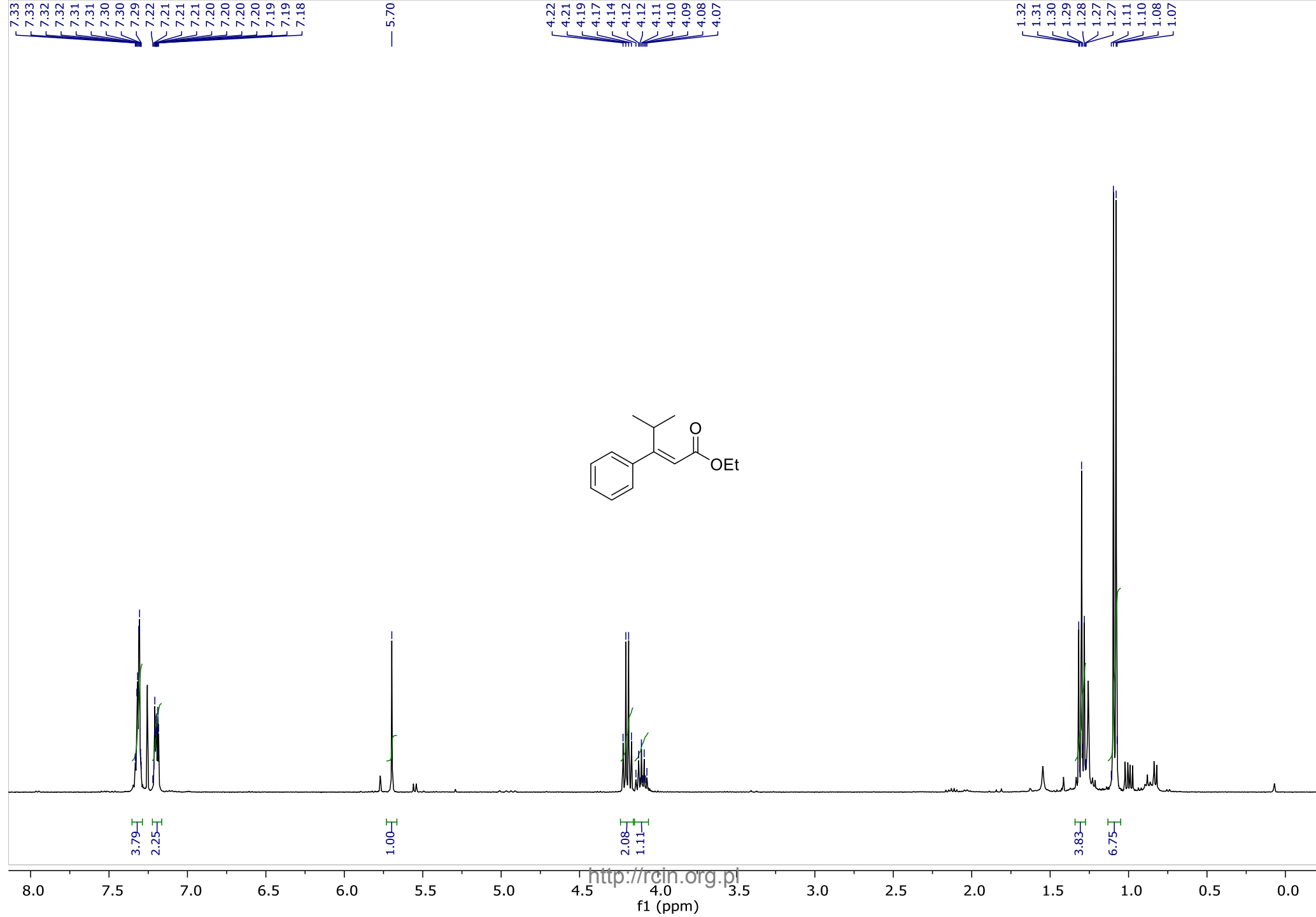














Cite this: *Org. Biomol. Chem.*, 2020, **18**, 1204

Received 15th November 2019,  
Accepted 20th January 2020

DOI: 10.1039/c9ob02472g

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## The synthesis of unnatural $\alpha$ -alkyl- and $\alpha$ -aryl-substituted serine derivatives†

Aleksandra Narczyk  and Sebastian Stecko \*

The synthesis of  $\alpha$ -aryl- and  $\alpha$ -alkyl-substituted serine derivatives *via* [3,3]-sigmatropic rearrangement of allyl carbamates as a key step is reported. Allyl carbamates were obtained from the corresponding allyl alcohols. The former were prepared through three approaches. Aryl-substituted ones were synthesized *via* the Stille coupling reaction of aryl iodides with enantiomerically enriched vinyl stannanes. Conversely, alkyl-substituted allyl alcohols were prepared by an analogous strategy involving the Negishi coupling reaction of enantiomerically enriched vinyl iodides or by enzymatic kinetic resolution of the corresponding racemic alcohols.





















## The synthesis of unnatural $\alpha$ -alkyl- and $\alpha$ -aryl-substituted serine derivatives

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### Electronic Supporting Information

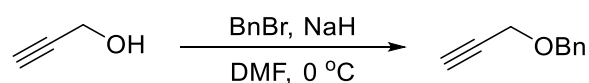
#### Table of contents

1. Experimental procedures .....	2
1.1. Propargyl alcohol derivatives .....	2
1.2. Cu-mediated 1,4-addition to alkynoates .....	6
1.3. The synthesis of Weinreb amides .....	8
1.4. The synthesis of enones <b>9</b> .....	10
1.5. The synthesis of racemic allylic alcohols ( <b>rac-8</b> ) .....	12
1.6. Enzymatic kinetic resolution of racemic allyl alcohols ( <b>rac-8</b> ) .....	14
1.7. Hydrostannylation of propargyl alcohols .....	17
1.8. Enzymatic kinetic resolution of racemic $\beta$ -stannyl allyl alcohol <b>rac-5b</b> .....	18
1.9. The synthesis of allyl alcohols <b>6</b> via Stille coupling reaction .....	19
1.10. Transcarbamoylation of allyl alcohols .....	33
1.11. [3,3]-Sigmatropic rearrangement of allyl carbamates .....	49
1.12. The synthesis of amino acid esters <b>14</b> .....	65
1.13. A large scale synthesis of amino acid <b>15</b> : .....	73
1.14. The synthesis of amino acid <b>16</b> .....	73
1.15. The synthesis of amino ester <b>17</b> .....	74
1.16. The synthesis of amino ester <b>18</b> .....	74
1.17. The synthesis of amino acid <b>19</b> .....	75
1.18. The synthesis of amino acid <b>20</b> .....	76
2. $^1\text{H}$ , $^{13}\text{C}$ , $^{19}\text{F}$ NMR spectra and HPLC chromatograms .....	76

## 1. Experimental procedures

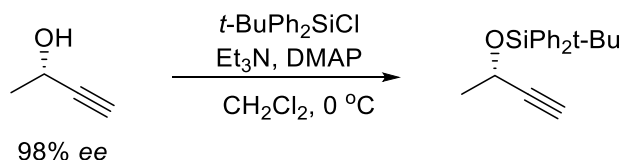
### 1.1. Propargyl alcohol derivatives

#### ((Prop-2-yn-1-yloxy)methyl)benzene (S1):



Propargyl alcohol (52 mmol, 2.9 g, 3.0 mL, 1 equiv.) was added dropwise to a suspension of NaH (60% dispersion in oil, 1.1 equiv., 57 mmol, 2.3 g) in DMF (70 mL) at 0 °C. After 1 h at 0 °C, BnBr (1.1 equiv., 57 mmol, 9.7 g, 6.7 mL) was added and the solution was stirred overnight at rt. Next, water was added and the resulting mixture was extracted with pentane. The combined organic layers were dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvents, the residue was purified by a column chromatography on silica gel (0–5% AcOEt in hexanes) to provide 6.5 g (86%) of benzyl propargyl ether as a yellowish oil; Spectral data in agreement with the literature:<sup>1</sup> H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.44–7.30 (m, 5H), 4.65 (s, 2H), 4.28–4.12 (m, 2H), 2.54–2.46 (m, 1H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 137.4, 128.5, 128.1, 127.9, 79.8, 74.7, 71.6, 57.1.

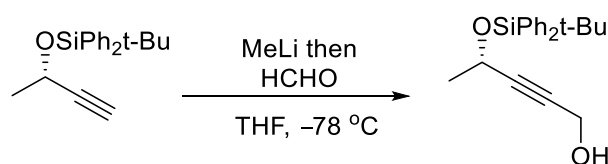
#### (S)-(But-3-yn-2-yloxy)(tert-butyl)diphenylsilane (S2):



A solution of *t*-BuPh<sub>2</sub>SiCl (15.7 mmol, 4.3 g, 4.0 mL) was added dropwise to a solution of (*S*)-but-3-yn-2-ol (14.3 mmol, 1.0 g, 1.1 mL, 98% ee), Et<sub>3</sub>N (28.6 mmol, 2.9 g, 4 mL), DMAP (1.4 mmol, 171 mg) and CH<sub>2</sub>Cl<sub>2</sub> (55 mL) at 0 °C. After stirring overnight, sat. NH<sub>4</sub>Cl was added and the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phase was dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the residue was purified by flash column chromatography on a silica gel (0–5% AcOEt in hexanes). Yield 4.3 g (98%); colourless oil; [α]<sub>D</sub><sup>22</sup> -72.2 (c 1.13, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.82 – 7.68 (m, 4H), 7.49 – 7.35 (m, 6H), 4.50 (qd, *J* = 6.5, 2.1 Hz, 1H), 2.35 (d, *J* = 2.1 Hz, 1H), 1.43 (d, *J* = 6.5 Hz, 3H), 1.12 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 136.0, 135.8, 133.7, 133.5, 129.7, 129.7, 127.6, 127.5, 86.1, 71.5, 59.8, 26.9, 25.2, 19.2.

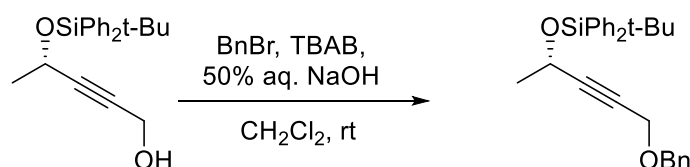


### (S)-4-((*tert*-Butyldiphenylsilyl)oxy)pent-2-yn-1-ol (**S3**):



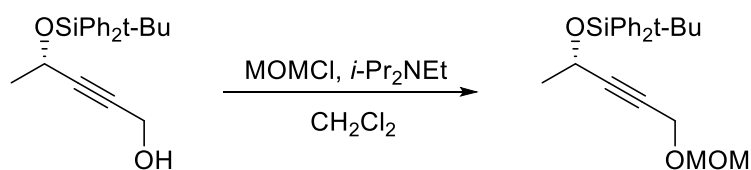
(S)-4-((*tert*-Butyldiphenylsilyl)oxy)pent-2-yn-1-ol **S2** (9.7 mmol, 3.0 g) was dissolved in THF (18 mL), cooled to -78 °C, and a 1.6 M soln. of MeLi in Et<sub>2</sub>O (13.1 mmol, 8.2 mL) was added dropwise. After stirring for 1 h at -78 °C, paraformaldehyde (14.6 mmol, 437 mg) was added portionwise, and the mixture was allowed to warm slowly to rt and left to stand overnight. Next, aq. NH<sub>4</sub>Cl was added, the aqueous phase was extracted with AcOEt, and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the crude residue was purified by flash column chromatography on silica gel (10–20% AcOEt in hexanes). Yield 3.2 g (98%); yellowish oil; [ $\alpha$ ]<sub>D</sub><sup>23</sup> -90.5 (*c* 1.08, CHCl<sub>3</sub>, *ee* 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.83 – 7.74 (m, 2H), 7.74 – 7.67 (m, 2H), 7.47 – 7.35 (m, 6H), 4.62 – 4.50 (m, 1H), 4.09 (s, 2H), 1.42 (d, *J* = 6.5 Hz, 3H), 1.09 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  136.0, 135.8, 134.0, 133.7, 129.7, 129.6, 127.6, 127.4, 88.2, 82.1, 59.9, 51.0, 26.9, 25.0, 19.1.

### (S)-((5-(Benzyloxy)pent-3-yn-2-yl)oxy)(*tert*-butyl)diphenylsilyl ether (**S4a**):



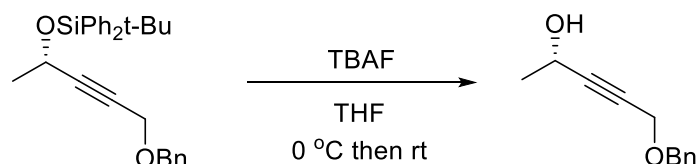
(S)-4-((*tert*-Butyldiphenylsilyl)oxy)pent-2-yn-1-ol **S3** (10.5 mmol, 3.5 g) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (90 mL), next, 50% aq. NaOH (21.0 mmol, 836  $\mu$ l) and TBABr (2.1 mmol, 674 mg) were added at ambient temperature. Next, BnBr (12.5 mmol, 2.1 g, 1.5 mL) was added dropwise and the mixture was left to stand for 48 h. Next, H<sub>2</sub>O was added, the aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub>, and the combined organic layers were dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the crude residue was purified by flash column chromatography on silica gel (1–5% AcOEt in hexanes). Yield 4.3 g (95%); yellowish oil; [ $\alpha$ ]<sub>D</sub><sup>23</sup> -85.6 (*c* 1.01, CHCl<sub>3</sub>, *ee* 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.85 – 7.78 (m, 2H), 7.77 – 7.71 (m, 2H), 7.50 – 7.28 (m, 11H), 4.65 – 4.56 (m, 1H), 4.51 (s, 2H), 4.12 (s, 2H), 1.48 (d, *J* = 6.5 Hz, 3H), 1.13 (s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  137.6, 136.0, 135.8, 133.8, 133.7, 129.7, 129.6, 128.4, 128.1, 127.8, 127.6, 127.5, 89.0, 79.6, 71.2, 60.0, 57.4, 26.9, 25.2, 19.2.

### O-Methoxymethyl (S)-4-((tert-butyl)diphenylsilyloxy)pent-2-yn-1-ol (S4b):



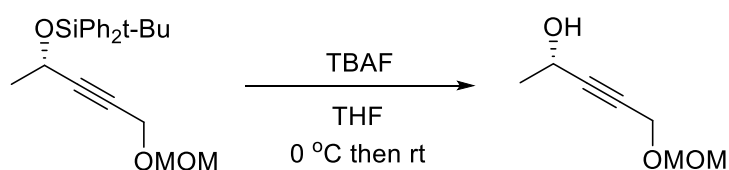
(S)-4-((tert-Butyldiphenylsilyloxy)pent-2-yn-1-ol **S3** (5.7 mmol, 1.9 g) was dissolved in  $\text{CH}_2\text{Cl}_2$  (15 mL), cooled to  $0\text{ }^\circ\text{C}$ , and *i*-Pr<sub>2</sub>NEt (11.4 mmol, 1.5 g, 2 ml) was added. After that, MOMCl (8.6 mmol, 688 mg, 650  $\mu\text{L}$ ) was added dropwise and the mixture was allowed to warm slowly to rt and left to stand overnight. Next, aq.  $\text{NaHCO}_3$  was added, the aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$ , and the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude product was used in next step. Yield 2.2 g (99%); yellowish oil;  $[\alpha]_{\text{D}}^{23} -100.1$  (*c* 1.00,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.82 – 7.72 (m, 2H), 7.71 – 7.65 (m, 2H), 7.47 – 7.32 (m, 6H), 4.61 (s, 2H), 4.52 (qt, *J* = 6.5, 1.7 Hz, 1H), 4.12 (d, *J* = 1.7 Hz, 2H), 3.35 (s, 3H), 1.40 (d, *J* = 6.5 Hz, 3H), 1.07 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  135.9, 135.8, 133.7, 133.6, 129.7, 129.6, 127.6, 127.6, 127.4, 94.6, 88.5, 79.2, 60.0, 55.5, 54.2, 26.9, 26.9, 25.1, 19.2.

### (S)-5-(benzyloxy)pent-3-yn-2-ol (4a):



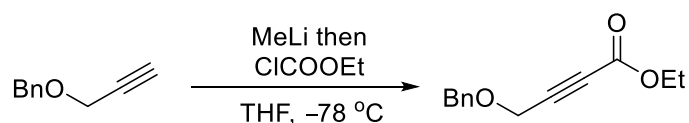
(S)-5-((tert-Butyldiphenylsilyloxy)pent-3-yn-2-yl)oxy)(tert-butyl)diphenylsilane **S4a** (9.3 mmol, 4.0 g) was dissolved in THF (23 mL), cooled to  $0\text{ }^\circ\text{C}$ , and TBAF (1M in THF, 12.1 mmol, 12.1 mL) was added dropwise. The mixture was allowed to warm slowly to rt and left overnight. Next, water was added, the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic phase was dried over  $\text{Na}_2\text{SO}_4$ . After removal of solvents, the crude product was purified by column chromatography on silica gel (10–50% AcOEt in hexanes). Yield 1.5 mg (87%); yellowish liquid;  $[\alpha]_{\text{D}}^{23} -21.7$  (*c* 0.89,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.33 (m, 4H), 7.33 – 7.27 (m, 1H), 4.66 – 4.50 (m, 3H), 4.20 (s, 2H), 2.23 (br s, 1H), 1.46 (d, *J* = 6.6 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  137.4, 128.4, 128.1, 127.9, 88.6, 79.8, 71.7, 58.3, 57.4, 24.3.

**(S)-5-(methoxymethoxy)pent-3-yn-2-ol (4b):**



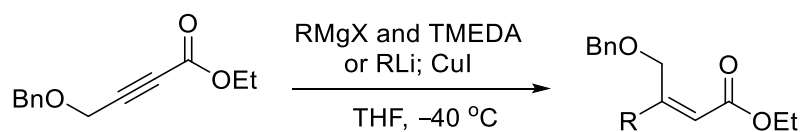
O-Methoxymethyl (S)-4-((*tert*-butyldiphenylsilyl)oxy)pent-2-yn-1-ol **S4b** (5.7 mmol, 2.2 g) was dissolved in THF (22 mL), cooled to 0 °C, and TBAF (1M in THF, 7.4 mmol, 7.4 mL) was added dropwise. The mixture was allowed to warm slowly to rt and left overnight. Next, water was added, the aqueous layer was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phase were dried over Na<sub>2</sub>SO<sub>4</sub>. After removal of solvents, the crude product was purified by a column chromatography on a silica gel (10–50% AcOEt in hexanes). Yield 765 mg (93%); yellowish liquid; [α]<sub>D</sub><sup>23</sup> -24.3 (c 1.09, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.66 (s, 2H), 4.51 (qt, *J* = 6.7, 1.7 Hz, 1H), 4.20 (d, *J* = 1.7 Hz, 2H), 3.34 (s, 3H), 2.64 (br s, 1H), 1.41 (d, *J* = 6.7 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 94.7, 88.4, 79.2, 58.1, 55.5, 54.4, 24.1.

**Ethyl 4-(benzyloxy)but-2-ynoate (10):**



Benzyl propargylether (1.0 equiv., 13.7 mmol, 2.0 g) in THF (18 mL) was cooled to -78 °C, after that MeLi (1.06 equiv., 14.5 mmol, 9.1 mL, 1.6 M in Et<sub>2</sub>O) was added dropwise and the solution was stirred for 30 min followed by addition of ClCOOEt (1.6 g, 1.43 mL, 15.0 mmol, 1.1 equiv.). After 5 minutes, the reaction mixture was allowed to warm to rt and then quenched by addition of saturated aq. NH<sub>4</sub>Cl. The aqueous phase was extracted with Et<sub>2</sub>O, the combined organic phases were dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvents, the residue was purified by a column chromatography on silica gel (10% AcOEt in hexanes) to provide 2.5 g (83%) of **10** as a colourless liquid; Spectral data in agreement with the literature:<sup>1</sup> <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>) δ 7.33–7.19 (m, 5H), 4.53 (s, 2H), 4.24–4.11 (m, 4H), 1.24 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, C<sub>6</sub>D<sub>6</sub>) δ 153.0, 136.7, 128.4, 128.0, 128.0, 83.0, 78.2, 72.0, 62.0, 56.7, 13.9.

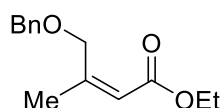
## 1.2. Cu-mediated 1,4-addition to alkynoates



**Method A,<sup>1</sup> general procedure:** CuI (6.0 mmol, 1.1 g) was suspended in THF (16 mL) and cooled to  $-40\text{ }^{\circ}\text{C}$ , next RLi (5.5 mmol) was added. The mixture was stirred at  $-40\text{ }^{\circ}\text{C}$  for 30 min and then cooled to  $-78\text{ }^{\circ}\text{C}$ . A solution of ethyl 4-(benzyloxy)but-2-ynoate (5.5 mmol, 1.2 g) in THF (4 mL) was added portionwise and the resulting suspension was stirred for 4 h at  $-78\text{ }^{\circ}\text{C}$ . The progress of the reaction was followed by TLC. The reaction was quenched by addition of methanol (2 mL), after that the cooling bath was removed and aq.  $\text{NH}_4\text{Cl}$  was added. The aqueous phase was extracted with  $\text{Et}_2\text{O}$ , and the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . After the removal of solvents, the crude residue was purified by a column chromatography on silica gel (5-10% AcOEt in hexanes).

**Method B,<sup>1</sup> general procedure:** CuI (5.0 mmol, 1.0 g) was suspended in THF (30 mL) and cooled to  $-40\text{ }^{\circ}\text{C}$ , next RMgX (4 mmol) was added followed by addition of TMEDA (15.0 mmol, 1.7 g, 2.3 mL). The mixture was stirred at  $-40\text{ }^{\circ}\text{C}$  for 30 min and then cooled to  $-78\text{ }^{\circ}\text{C}$ . A solution of ethyl 4-(benzyloxy)but-2-ynoate (4.0 mmol, 0.9 g) in THF (3 mL) was added portionwise and the resulting suspension was stirred for 4 h at  $-78\text{ }^{\circ}\text{C}$ . The progress of the reaction was followed by TLC. The reaction was quenched by an addition of MeOH (5 mL), after that a cooling bath was removed and aq.  $\text{NH}_4\text{Cl}$  was added. The aqueous phase was extracted with  $\text{Et}_2\text{O}$ , and the combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . After the removal of solvents, the crude residue was purified by a column chromatography on silica gel (5-10% AcOEt in hexanes).

### Ethyl (Z)-4-(benzyloxy)-3-methylbut-2-enoate (11a):

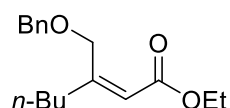


Method A. MeLi (1.6 M solution in  $\text{Et}_2\text{O}$ ) was used. Yield: 1.0 g (overall 99%; *Z/E* ratio >95:5,  $^1\text{H}$  NMR) starting from 1.0 g of ethyl 4-(benzyloxy)but-2-ynoate (**10**); colourless liquid;  $^1\text{H}$

<sup>1</sup> Fischer, D. F.; Xin, Z.-q.; Peters, R., *Angew. Chem. Int. Ed.* **2007**, *46*, 7704-7707

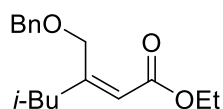
NMR (400 MHz, CDCl<sub>3</sub>) δ 7.39 – 7.32 (m, 4H), 7.32 – 7.23 (m, 1H), 5.77 (h, *J* = 1.5 Hz, 1H), 4.67 (d, *J* = 1.5 Hz, 2H), 4.52 (s, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.01 (d, *J* = 1.5 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 165.9, 156.9, 138.3, 128.3, 127.6, 127.6, 117.3, 72.7, 69.3, 59.8, 21.7, 14.3.

**Ethyl (Z)-3-((benzyloxy)methyl)hept-2-enoate (11b):**



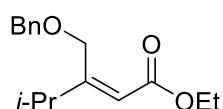
Method A. *n*-BuLi (2.5 M solution in hexane) was used. Yield: 608 mg (overall 96%; *Z/E* ratio >95:5, <sup>1</sup>H NMR) starting from 500 mg of ethyl 4-(benzyloxy)but-2-ynoate (**10**); yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.39 – 7.31 (m, 4H), 7.31 – 7.26 (m, 1H), 5.83 – 5.67 (m, 1H), 4.67 (d, *J* = 1.5 Hz, 2H), 4.52 (s, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.34 (td, *J* = 7.6, 1.2 Hz, 2H), 1.56 – 1.42 (m, 2H), 1.41 – 1.31 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.1, 160.3, 138.3, 128.3, 127.6, 127.5, 116.7, 72.7, 68.1, 59.8, 34.6, 29.9, 22.5, 14.3, 13.9.

**Ethyl (Z)-3-((benzyloxy)methyl)-5-methylhex-2-enoate (11c):**



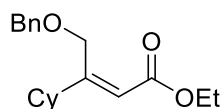
Method B. *i*-BuMgBr (2M solution in Et<sub>2</sub>O) was used. Yield: 502 mg (overall 90%; *Z/E* ratio >95:5 acc. To <sup>1</sup>H NMR spectra) starting from 441 mg of ethyl 4-(benzyloxy)but-2-ynoate (**10**); yellow liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40–7.31 (m, 4H), 7.31–7.25 (m, 1H), 5.73 (s, 1H), 4.66 (d, *J* = 1.6 Hz, 2H), 4.52 (s, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 2.21 (dd, *J* = 7.1, 1.2 Hz, 2H), 2.01–1.84 (m, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.91 (d, *J* = 6.7 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.0, 159.1, 138.4, 128.3, 127.6, 127.5, 117.9, 72.7, 68.0, 59.8, 44.4, 26.6, 22.5, 14.3.

**Ethyl (Z)-3-((benzyloxy)methyl)-4-methylpent-2-enoate (11d):**



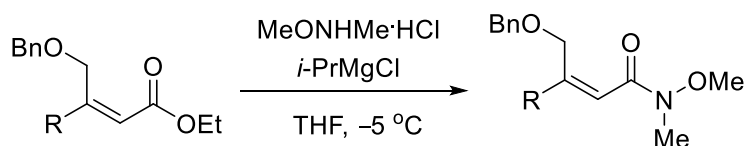
Method B. *i*-PrMgCl (2M solution in THF) was used. Yield: 596 mg (overall 99%; *Z/E* ratio 90:10, <sup>1</sup>H NMR) starting from 500 mg of ethyl 4-(benzyloxy)but-2-ynoate (**10**); yellow liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.41–7.31 (m, 4H), 7.31–7.22 (m, 1H), 5.77 (s, 1H), 4.70 (d, *J* = 1.3 Hz, 2H), 4.54 (s, 2H), 4.15 (q, *J* = 7.2 Hz, 2H), 2.83 (sept, *J* = 6.9 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H), 1.12 (d, *J* = 6.9 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.5, 165.0, 138.4, 128.3, 127.7, 127.5, 115.0, 72.8, 67.5, 59.9, 31.5, 21.5, 14.3.

### Ethyl (*Z*)-4-(benzyloxy)-3-cyclohexylbut-2-enoate (**11e**):



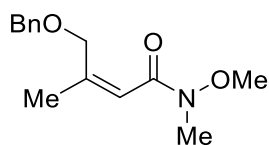
Method B. CyMgCl (1.3M solution in THF/toluene) was used. Yield: 589 mg (overall 85%; *Z/E* ratio 90:10, acc. to <sup>1</sup>H NMR) starting from 500 mg of ethyl 4-(benzyloxy)but-2-ynoate (**10**); colourless liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.40–7.31 (m, 4H), 7.31–7.24 (m, 1H), 5.74 (s, 1H), 4.67 (d, *J* = 1.3 Hz, 2H), 4.52 (s, 2H), 4.14 (q, *J* = 7.1 Hz, 2H), 2.56–2.35 (m, 1H), 1.92–1.62 (m, 5H), 1.40 – 1.30 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.24–1.09 (m, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.6, 164.0, 138.4, 128.3, 127.6, 127.5, 115.6, 72.7, 67.4, 59.8, 41.7, 32.2, 26.6, 26.3, 14.3.

### 1.3. The synthesis of Weinreb amides



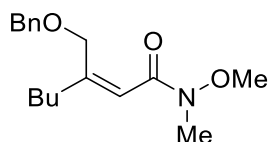
**General procedure:** Suspension of  $\alpha,\beta$ -unsaturated ester (1 equiv) and MeNHOMe·HCl (2 equiv) in dry THF (*c* 0.2-0.3 M) was cooled to  $-5\text{ }^{\circ}\text{C}$  under argon atmosphere, and 2M soln. of *i*-PrMgCl in THF (4 equiv.) was added dropwise. The progress of the reaction was followed by TLC. After stirring at  $-5\text{ }^{\circ}\text{C}$  for 0.5-1 h, the reaction was quenched by the addition of sat. NH<sub>4</sub>Cl. The aqueous phase was extracted with AcOEt and the combined organic phase were washed with brine, and dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvents, the crude residue was purified by a column chromatography on silica gel to provide pure *Z* isomer (10-40% AcOEt in hexanes).

**(Z)-4-(Benzyloxy)-N-methoxy-N,3-dimethylbut-2-enamide (S5a):**



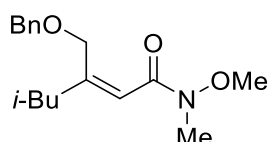
Yield: 749 mg (74%); starting from 952 mg of ester **11a**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37–7.29 (m, 4H), 7.29–7.24 (m, 1H), 6.21 (s, 1H), 4.64 (s, 2H), 4.51 (s, 2H), 3.68 (s, 3H), 3.19 (s, 3H), 2.02 (d,  $J = 1.4$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.1, 153.6, 138.5, 128.3, 127.6, 127.5, 115.9, 72.6, 69.9, 61.4, 32.2, 21.9.

**(Z)-3-((Benzyloxy)methyl)-N-methoxy-N-methylhept-2-enamide (S5b):**



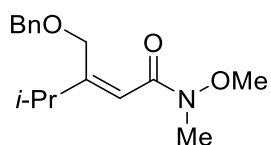
Yield: 474 mg (74%); starting from 608 mg of ester **11b**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40–7.29 (m, 4H), 7.29–7.19 (m, 1H), 6.19 (s, 1H), 4.62 (s, 2H), 4.50 (s, 2H), 3.65 (s, 3H), 3.18 (s, 3H), 2.42–2.27 (m, 2H), 1.57–1.44 (m, 2H), 1.43–1.29 (m, 2H), 0.91 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.3, 156.6, 138.5, 128.3, 127.6, 127.4, 115.6, 72.7, 68.6, 61.4, 34.7, 32.2, 30.1, 22.5, 13.9.

**(Z)-3-((Benzyloxy)methyl)-N-methoxy-N,5-dimethylhex-2-enamide (S5c):**



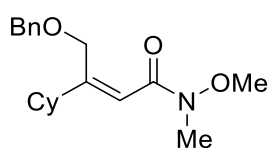
Yield: 273 mg (52%); starting from 498 mg of ester **11c**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.29 (m, 4H), 7.29 – 7.22 (m, 1H), 6.17 (s, 1H), 4.59 (s, 2H), 4.50 (s, 2H), 3.65 (s, 3H), 3.18 (s, 3H), 2.21 (d,  $J = 7.2$  Hz, 2H), 2.01 – 1.83 (m, 1H), 0.91 (d,  $J = 6.7$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.2, 155.3, 138.5, 128.3, 127.6, 127.4, 116.8, 72.6, 68.5, 61.4, 44.6, 32.2, 26.6, 22.6.

**(Z)-3-((Benzyloxy)methyl)-N-methoxy-N,4-dimethylpent-2-enamide (S5d)**



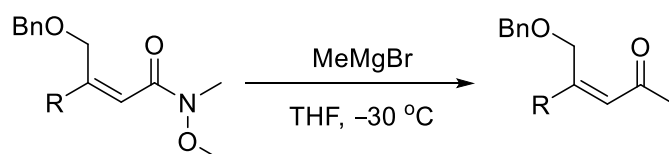
Yield: 318 mg (51%); starting from 596 mg of ester **11d**; colourless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.29 (m, 4H), 7.29 – 7.23 (m, 1H), 6.19 (s, 1H), 4.60 (s, 2H), 4.51 (s, 2H), 3.66 (s, 3H), 3.19 (s, 3H), 2.79 (sept,  $J = 6.8$  Hz, 1H), 1.12 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.8, 160.5, 138.5, 128.3, 127.7, 127.4, 114.3, 72.7, 68.0, 61.3, 32.4, 31.4, 21.6.

#### (Z)-4-(Benzyloxy)-3-cyclohexyl-N-methoxy-N-methylbut-2-enamide (**S5e**)



Yield: 369 mg (75%); starting from 468 mg of ester **11e**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.21 (m, 5H), 6.16 (s, 1H), 4.58 (s, 2H), 4.50 (s, 2H), 3.64 (s, 3H), 3.18 (s, 3H), 2.50 – 2.36 (m, 1H), 1.96 – 1.57 (m, 5H), 1.46 – 1.02 (m, 5H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.8, 159.6, 138.6, 128.3, 127.4, 127.4, 114.9, 72.6, 67.9, 61.3, 41.6, 32.3, 32.3, 26.7, 26.3.

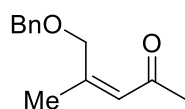
#### 1.4. The synthesis of enones **9**



**General procedure:** A 3 M soln. of  $\text{MeMgBr}$  in THF (1.3 equiv) was slowly added to a solution of Weinreb amide **s1-s5** (1 equiv) in THF (c 0.2-0.3 M) cooled to  $-30$  °C. After addition, the mixture was slowly warmed to  $-5$  °C and stirred for 30-60 min. The progress of the reaction was followed by TLC. Next, sat.  $\text{NH}_4\text{Cl}$  was added and the resulting mixture was extracted with  $\text{AcOEt}$ . The combined organic layers were washed with brine, and dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the residue was purified by a column chromatography on silica gel (10%  $\text{AcOEt}$  in hexanes).

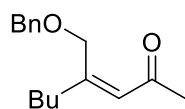
#### (Z)-5-(Benzyloxy)-4-methylpent-3-en-2-one (**9a**):





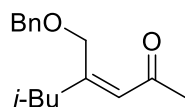
Yield: 338 mg (87%); starting from 479 mg of amide **S5a**; colourless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.31 (m, 4H), 7.31 – 7.23 (m, 1H), 6.19 – 6.11 (m, 1H), 4.61 (s, 2H), 4.51 (s, 2H), 2.17 (s, 3H), 2.01 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.2, 156.5, 138.3, 128.3, 127.6, 124.6, 72.8, 70.3, 31.3, 21.5.

**(Z)-4-((Benzyloxy)methyl)oct-3-en-2-one (9b):**



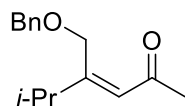
Yield: 296 g (78%); starting from 379 mg of amide **S5b**; colourless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.30 (m, 4H), 7.30 – 7.24 (m, 1H), 6.16 – 6.09 (m, 1H), 4.62 (d,  $J = 1.6$  Hz, 2H), 4.50 (s, 2H), 2.40 – 2.29 (m, 2H), 2.18 (s, 3H), 1.56 – 1.43 (m, 2H), 1.41 – 1.28 (m, 2H), 0.92 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.5, 159.8, 138.3, 128.3, 127.6, 127.5, 123.9, 72.9, 69.1, 34.4, 31.4, 30.2, 22.6, 13.9.

**(Z)-4-((Benzyloxy)methyl)-6-methylhept-3-en-2-one (9c):**



Yield: 161 mg (80%); starting from 238 mg of amide **S5c**; colourless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.30 (m, 4H), 7.30 – 7.22 (m, 1H), 6.09 (s, 1H), 4.60 (d,  $J = 1.7$  Hz, 2H), 4.50 (s, 2H), 2.26 – 2.14 (m, 5H), 2.00 – 1.86 (m, 1H), 0.91 (d,  $J = 6.6$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.3, 158.5, 138.4, 128.3, 127.5, 125.1, 72.8, 69.1, 44.3, 31.4, 26.9, 22.6.

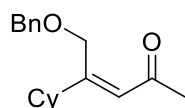
**(Z)-4-((Benzyloxy)methyl)-5-methylhex-3-en-2-one (9d):**



Yield: 210 mg (73%); starting from 343 mg of amide **S5d**; colourless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.30 (m, 4H), 7.30 – 7.23 (m, 1H), 6.11 (s, 1H), 4.62 (d,  $J = 1.6$  Hz, 2H),

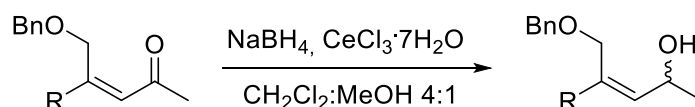
4.51 (s, 2H), 2.87 (sept,  $J = 6.8$  Hz, 1H), 2.21 (s, 3H), 1.11 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.0, 163.9, 138.3, 128.3, 127.6, 127.5, 121.9, 72.9, 68.4, 31.6, 31.1, 21.6.

**(Z)-5-(benzyloxy)-4-cyclohexylpent-3-en-2-one (9e):**



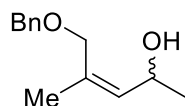
Yield: 291 mg (75%); starting from 448 mg of amide **55e**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.21 (m, 5H), 6.08 (s, 1H), 4.60 (d,  $J = 1.5$  Hz, 2H), 4.50 (s, 2H), 2.59 – 2.39 (m, 1H), 2.20 (s, 3H), 1.96 – 1.57 (m, 5H), 1.48 – 1.01 (m, 5H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.1, 163.0, 138.4, 128.3, 127.6, 127.5, 122.5, 72.9, 68.3, 41.3, 32.3, 31.6, 26.6, 26.3.

**1.5. The synthesis of racemic allylic alcohols (rac-8)**



**General procedure:** To a suspension of enone **9** (3 mmol) and  $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$  (3.6 mmol) in  $\text{CH}_2\text{Cl}_2/\text{MeOH}$  (4:1 v/v, 50 mL),  $\text{NaBH}_4$  (3.6 mmol) was added portionwise. After 2 h at ambient temperature, the reaction mixture was partitioned between  $\text{CH}_2\text{Cl}_2$  and  $\text{H}_2\text{O}$ . The organic layer was separated, and the aqueous one was extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic solutions were dried over anhydr.  $\text{Na}_2\text{SO}_4$ , and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (20%  $\text{AcOEt}$  in hexanes) to afford mixture of alcohols **rac-8**.

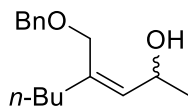
**(Z)-5-(Benzyloxy)-4-methylpent-3-en-2-ol (rac-8a):**



Yield: 200 mg (95%) starting from 210 mg of enone **9a**; colourless liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.22 (m, 5H), 5.44 (d,  $J = 8.5$  Hz, 1H), 4.69 – 4.37 (m, 3H), 4.09 (d,  $J = 11.4$  Hz, 1H), 3.97 (d,  $J = 11.4$  Hz, 1H), 2.12 (br s, 1H), 1.80 (d,  $J = 1.6$  Hz, 3H), 1.22 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.0, 134.3, 133.9, 128.4, 127.7, 72.3, 68.9, 63.8, 23.5, 22.0; FTIR (film)  $\nu$ : 3396, 2970, 2924, 2863, 1451, 1368, 1068, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$

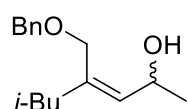
calcd for  $C_{13}H_{18}O_2Na$   $[(M+Na)^+]$  229.1204; found 229.1199; HPLC (racemate) column Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL/min, det. 215 nm; 7.0 min (*R*-enantiomer) and  $R_t$  9.0 min (*S*-enantiomer).

**(Z)-4-((benzyloxy)methyl)oct-3-en-2-ol (*rac*-8b):**



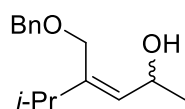
Yield: 239 mg (88%) starting from 271 mg of enone **9b**; colourless liquid;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.39 – 7.32 (m, 4H), 7.32 – 7.26 (m, 1H), 5.45 (d,  $J$  = 8.3 Hz, 1H), 4.64 – 4.52 (m, 1H), 4.50 (d,  $J$  = 2.5 Hz, 2H), 4.11 (d,  $J$  = 11.2 Hz, 1H), 3.94 (d,  $J$  = 11.2 Hz, 1H), 2.19 – 2.05 (m, 2H), 1.97 (br s, 1H), 1.48 – 1.35 (m, 2H), 1.35 – 1.25 (m, 2H), 1.23 (d,  $J$  = 6.3 Hz, 3H), 0.90 (t,  $J$  = 7.1 Hz, 3H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  138.5, 138.0, 133.7, 128.4, 127.8, 127.7, 72.5, 68.0, 63.9, 35.5, 30.1, 23.4, 22.4, 13.9; FTIR (film)  $\nu$  3402, 2959, 2928, 2862, 1454, 1366, 1065, 739, 698  $cm^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $C_{16}H_{24}O_2Na$   $[(M + Na)^+]$  271.1674; found 271.1669; HPLC (racemate) column Chiralcel OD-H, 5% *i*-PrOH in hexanes, flow 0.5 mL/min, det. 215 nm; 14.7 min (*R*-enantiomer) and  $R_t$  16.4 min (*S*-enantiomer).

**(Z)-4-((benzyloxy)methyl)-6-methylhept-3-en-2-ol (*rac*-8c):**



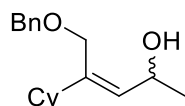
Yield: 197 mg (84%) starting from 233 mg of enone **9c**; colourless oil;  $^1H$  NMR (400 MHz,  $CDCl_3$ )  $\delta$  7.41 – 7.22 (m, 5H), 5.43 (d,  $J$  = 8.2 Hz, 1H), 4.63 – 4.53 (m, 1H), 4.49 (d,  $J$  = 3.5 Hz, 2H), 4.10 (d,  $J$  = 11.2 Hz, 1H), 3.91 (d,  $J$  = 11.2 Hz, 1H), 2.27 (s, 1H), 2.08 – 1.97 (m, 1H), 1.97 – 1.86 (m, 1H), 1.81 – 1.65 (m, 1H), 1.23 (d,  $J$  = 6.3 Hz, 3H), 0.96 – 0.77 (m, 6H);  $^{13}C$  NMR (101 MHz,  $CDCl_3$ )  $\delta$  138.0, 137.0, 135.5, 128.4, 127.8, 127.7, 72.5, 67.9, 63.9, 45.5, 26.3, 23.4, 22.6, 22.3; FTIR (film)  $\nu$  3401, 2955, 2926, 2868, 1454, 1366, 1068, 738, 698  $cm^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $C_{16}H_{24}O_2Na$   $[(M+Na)^+]$  271.1674; found 271.1667; HPLC (for *p*-nitrobenzoate ester, racemate) column Chiralcel OD-H, 5% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm;  $R_t$  7.6 min (*S*-enantiomer) and 9.3 min (*R*-enantiomer).

**(Z)-4-((Benzyloxy)methyl)-5-methylhex-3-en-2-ol (*rac*-8d):**



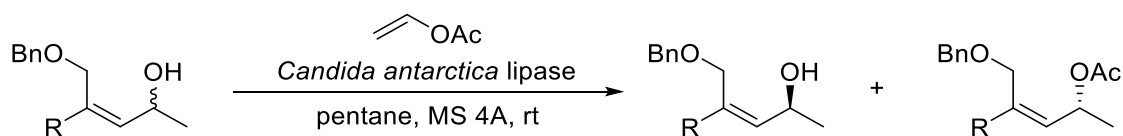
Yield: 182 mg (86%) starting from 210 mg of enone **9d**; yellow oil  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.32 (m, 4H), 7.32 – 7.23 (m, 1H), 5.47 (d,  $J = 8.3$  Hz, 1H), 4.61 – 4.53 (m, 1H), 4.51 (d,  $J = 3.4$  Hz, 2H), 4.13 (d,  $J = 10.9$  Hz, 1H), 3.93 (d,  $J = 10.9$  Hz, 1H), 2.51 – 2.20 (m, 2H), 1.24 (d,  $J = 6.3$  Hz, 3H), 1.06 – 0.99 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.1, 137.9, 132.1, 128.4, 127.9, 127.8, 72.8, 67.4, 63.9, 33.5, 23.2, 21.5, 21.5; FTIR (film)  $\nu$  3405, 2963, 2927, 2870, 1455, 1364, 1066, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{O}_2\text{Na}$  [(M + Na) $^+$ ] 257.1517; found 257.1513; HPLC (for *p*-nitrobenzoate ester, racemate) column Chiralcel OD-H, 5% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm;  $R_t$  7.5 min (*S*-enantiomer) and 10.2 min (*R*-enantiomer).

#### (Z)-5-(Benzyloxy)-4-cyclohexylpent-3-en-2-ol (*rac*-8e):



Yield: 234 mg (80%) starting from 291 mg of enone **9e**; colourless oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.20 (m, 5H), 5.44 (dt,  $J = 8.2, 1.1$  Hz, 1H), 4.62 – 4.52 (m, 1H), 4.50 (d,  $J = 2.0$  Hz, 2H), 4.12 (d,  $J = 10.9$  Hz, 1H), 3.93 (d,  $J = 10.9$  Hz, 1H), 2.41 (br s, 1H), 2.06 – 1.89 (m, 1H), 1.88 – 1.58 (m, 5H), 1.42 – 1.00 (m, 8H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.5, 138.0, 132.6, 128.4, 127.8, 127.7, 72.7, 67.7, 63.9, 43.8, 32.1, 32.0, 26.7, 26.3, 23.3; FTIR (film)  $\nu$  3403, 2925, 2852, 1451, 1067, 737, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{26}\text{O}_2\text{Na}$  [(M + Na) $^+$ ] 297.1830; found 297.1830; HPLC (for *p*-nitrobenzoate ester, racemate) column Chiralcel OD-H, 5% *i*-PrOH in hexanes, flow 1 mL/min, det. 254 nm; 8.0 min (*R*-enantiomer) and  $R_t$  9.7 min (*S*-enantiomer).

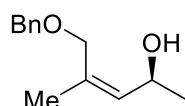
### 1.6. Enzymatic kinetic resolution of racemic allyl alcohols (*rac*-8)



A suspension of racemic alcohol **rac-8** (2.5 mmol), Novozyme 435 (18 mg), 4 Å molecular sieves (100 mg), and vinyl acetate (25 mmol, 2.2 g, 2.3 mL) in pentane (7 mL)

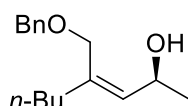
was stirred in room temperature. The progress of the reaction was followed by  $^1\text{H}$  NMR. The reaction mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel (5-20% AcOEt in hexanes).

**(S,Z)-5-(benzyloxy)-4-methylpent-3-en-2-ol (8a):**



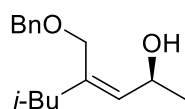
The reaction mixture was stirred for 17 h. Yield: 86 mg (43%) starting from 200 mg of racemic alcohol **rac-8a**; colourless liquid;  $[\alpha]_{\text{D}}^{24}$   $-4.1$  ( $c$  1.15,  $\text{CHCl}_3$ ,  $ee$  99%; (HPLC:  $R_t$  8.7 min));  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.22 (m, 5H), 5.44 (d,  $J$  = 8.5 Hz, 1H), 4.69 – 4.37 (m, 3H), 4.09 (d,  $J$  = 11.4 Hz, 1H), 3.97 (d,  $J$  = 11.4 Hz, 1H), 2.12 (br s, 1H), 1.80 (d,  $J$  = 1.6 Hz, 3H), 1.22 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.0, 134.3, 133.9, 128.4, 127.7, 72.3, 68.9, 63.8, 23.5, 22.0; FTIR (film)  $\nu$ : 3396, 2970, 2924, 2863, 1451, 1368, 1068, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{18}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  229.1204; found 229.1199.

**(S,Z)-4-((Benzyloxy)methyl)oct-3-en-2-ol (8b):**



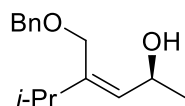
The reaction mixture was stirred for 18 h. Yield: 131 mg (47%) starting from 280 mg of racemic alcohol **rac-8b**; colourless liquid;  $[\alpha]_{\text{D}}^{24}$   $-5.8$  ( $c$  1.06,  $\text{CHCl}_3$ ,  $ee$  97%; (HPLC:  $R_t$  16.4 min));  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.32 (m, 4H), 7.32 – 7.26 (m, 1H), 5.45 (d,  $J$  = 8.3 Hz, 1H), 4.64 – 4.52 (m, 1H), 4.50 (d,  $J$  = 2.5 Hz, 2H), 4.11 (d,  $J$  = 11.2 Hz, 1H), 3.94 (d,  $J$  = 11.2 Hz, 1H), 2.19 – 2.05 (m, 2H), 1.97 (br s, 1H), 1.48 – 1.35 (m, 2H), 1.35 – 1.25 (m, 2H), 1.23 (d,  $J$  = 6.3 Hz, 3H), 0.90 (t,  $J$  = 7.1 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.5, 138.0, 133.7, 128.4, 127.8, 127.7, 72.5, 68.0, 63.9, 35.5, 30.1, 23.4, 22.4, 13.9; FTIR (film)  $\nu$  3402, 2959, 2928, 2862, 1454, 1366, 1065, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{24}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  271.1674; found 271.1669.

**(S,Z)-4-((benzyloxy)methyl)-6-methylhept-3-en-2-ol (8c):**



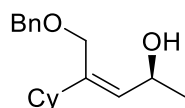
The reaction mixture was stirred for 24 h. Yield: 118 mg (44%) starting from 266 mg of racemic alcohol **rac-8c**; yellowish oil;  $[\alpha]_D^{22} -5.8$  (c 2.49,  $\text{CHCl}_3$ ), *ee* 92%; (determined by HPLC of *p*-nitrobenzoate ester,  $R_t$  7.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.22 (m, 5H), 5.43 (d,  $J = 8.2$  Hz, 1H), 4.63 – 4.53 (m, 1H), 4.49 (d,  $J = 3.5$  Hz, 2H), 4.10 (d,  $J = 11.2$  Hz, 1H), 3.91 (d,  $J = 11.2$  Hz, 1H), 2.27 (s, 1H), 2.08 – 1.97 (m, 1H), 1.97 – 1.86 (m, 1H), 1.81 – 1.65 (m, 1H), 1.23 (d,  $J = 6.3$  Hz, 3H), 0.96 – 0.77 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.0, 137.0, 135.5, 128.4, 127.8, 127.7, 72.5, 67.9, 63.9, 45.5, 26.3, 23.4, 22.6, 22.3; FTIR (film)  $\nu$  3401, 2955, 2926, 2868, 1454, 1366, 1068, 738, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{24}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  271.1674; found 271.1667.

#### (*S,Z*)-4-((Benzyloxy)methyl)-5-methylhex-3-en-2-ol (8d)



The reaction mixture was stirred for 8 days h. Yield: 90 mg (42%) starting from 216 mg racemic alcohol **rac-8d**; yellowish oil;  $[\alpha]_D^{18} -10.7$  (c 1.02,  $\text{CHCl}_3$ ), *ee* 94%; (determined by HPLC of *p*-nitrobenzoate ester:  $R_t$  7.9 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.32 (m, 4H), 7.32 – 7.23 (m, 1H), 5.47 (d,  $J = 8.3$  Hz, 1H), 4.61 – 4.53 (m, 1H), 4.51 (d,  $J = 3.4$  Hz, 2H), 4.13 (d,  $J = 10.9$  Hz, 1H), 3.93 (d,  $J = 10.9$  Hz, 1H), 2.51 – 2.20 (m, 2H), 1.24 (d,  $J = 6.3$  Hz, 3H), 1.06 – 0.99 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.1, 137.9, 132.1, 128.4, 127.9, 127.8, 72.8, 67.4, 63.9, 33.5, 23.2, 21.5, 21.5; FTIR (film)  $\nu$ : 3405, 2963, 2927, 2870, 1455, 1364, 1066, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{22}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  257.1517; found 257.1513.

#### (*S,Z*)-5-(Benzyloxy)-4-cyclohexylpent-3-en-2-ol (8e):

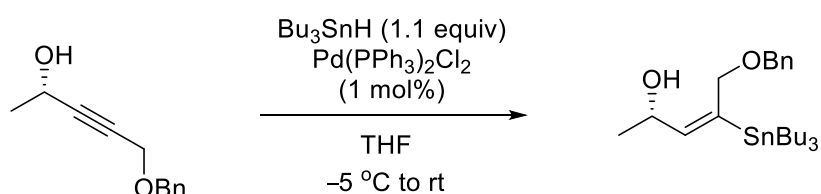


The reaction mixture was stirred for 10 days h. Yield: 124 mg (40%) starting from 312 mg racemic alcohol **rac-8e**; yellowish oil;  $[\alpha]_D^{18} -12.2$  (c 1.11,  $\text{CHCl}_3$ ), *ee* 99%; (determined by

HPLC of *p*-nitrobenzoate ester:  $R_t$  7.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.20 (m, 5H), 5.44 (dt,  $J = 8.2, 1.1$  Hz, 1H), 4.62 – 4.52 (m, 1H), 4.50 (d,  $J = 2.0$  Hz, 2H), 4.12 (d,  $J = 10.9$  Hz, 1H), 3.93 (d,  $J = 10.9$  Hz, 1H), 2.41 (br s, 1H), 2.06 – 1.89 (m, 1H), 1.88 – 1.58 (m, 5H), 1.42 – 1.00 (m, 8H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.5, 138.0, 132.6, 128.4, 127.8, 127.7, 72.7, 67.7, 63.9, 43.8, 32.1, 32.0, 26.7, 26.3, 23.3; FTIR (film)  $\nu$  3403, 2925, 2852, 1451, 1067, 737, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{26}\text{O}_2\text{Na}$  [(M+Na) $^+$ ] 297.1830; found 297.1830.

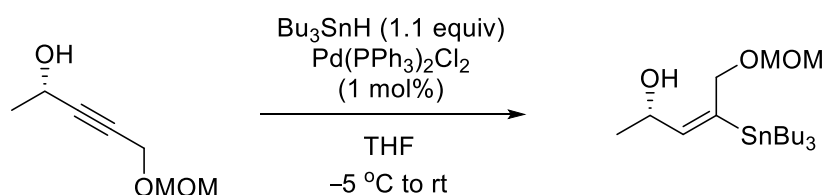
## 1.7. Hydrostannylation of propargyl alcohols

### (*S,E*)-5-(Benzyloxy)-4-(tributylstannyl)pent-3-en-2-ol (**5a**):



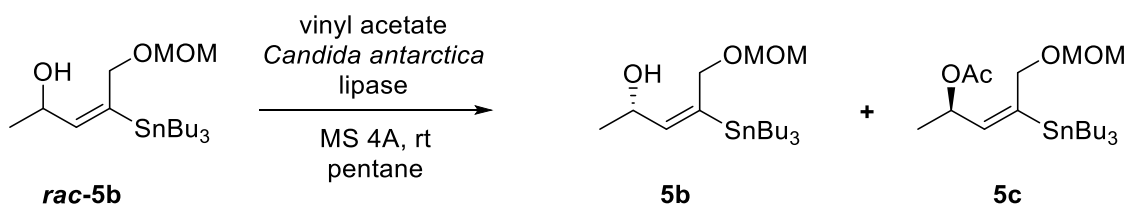
A solution of propargyl alcohol **4a** (5 mmol, 951 mg) and  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  (1 mol %, 0.05 mmol, 35 mg) in THF (10 mL) under an argon atmosphere was cooled to  $-5$  °C. Next,  $\text{Bu}_3\text{SnH}$  (1.1 eq, 5.5 mmol, 1.5 ml) was added very slowly, and the resulting mixture was adjusted to rt. The progress of the reaction was followed by TLC. When the reaction was completed, the solvent was removed and the residue was purified by a flash column chromatography on a silica gel (0–5% AcOEt in hexanes). Yield 1.9 g (80%); yellow oil;  $[\alpha]_D^{22} -10.6$  ( $c$  1.11,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 – 7.20 (m, 5H), 5.62 (d,  $J = 7.6$  Hz, 1H), 4.63 – 4.45 (m, 3H), 4.33 (d,  $J = 12.5$  Hz, 1H), 4.16 (d,  $J = 12.5$  Hz, 1H), 1.68 (s, 1H), 1.58 – 1.38 (m, 6H), 1.37 – 1.25 (m, 12H), 1.22 (d,  $J = 6.4$  Hz, 3H), 1.00 – 0.75 (m, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  145.3, 143.2, 138.1, 128.3, 127.8, 127.6, 72.8, 71.3, 65.0, 29.1, 27.3, 23.2, 13.7, 10.1; FTIR (film)  $\nu$ : 3408, 2956, 2925, 1461, 1151, 1107, 1053, 663  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{42}\text{O}_2\text{SnNa}$  [(M+Na) $^+$ ] 505.2231; found 505.2233.

### (*S,E*)-5-(Methoxymethoxy)-4-(tributylstannyl)pent-3-en-2-ol (**5b**):



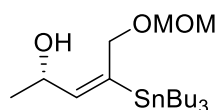
A solution of propargyl alcohol **4b** (5 mmol, 720 mg) and Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (1 mol %, 0.05 mmol, 35 mg) in THF (10 mL) under an argon atmosphere was cooled to -5 °C. Next, Bu<sub>3</sub>SnH (1.1 eq, 5.5 mmol, 1.5 ml) was added very slowly, and the resulting mixture was adjusted to rt. The progress of the reaction was followed by TLC. When the reaction was completed, the solvent was removed and the residue was purified by a flash column chromatography on a silica gel (0–5% AcOEt in hexanes). Yield 1.7 g (79%); yellow oil; [α]<sub>D</sub><sup>24</sup> -11.4 (c 1.21, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.77 – 5.51 (m, 1H), 4.70 – 4.48 (m, 3H), 4.47 – 4.30 (m, 1H), 4.26 – 4.09 (m, 1H), 3.34 (d, *J* = 1.1 Hz, 3H), 2.04 (br s, 1H), 1.60 – 1.36 (m, 6H), 1.35 – 1.12 (m, 9H), 1.00 – 0.73 (m, 15H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 144.2, 143.8, 95.6, 68.4, 64.7, 55.3, 29.0, 27.3, 23.1, 13.6, 10.0; FTIR (film) ν: 3408, 2956, 2925, 1461, 1151, 1107, 1053, 663 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>19</sub>H<sub>40</sub>O<sub>3</sub>SnNa [(M+Na)<sup>+</sup>] 459.1897; found 459.1894.

### 1.8. Enzymatic kinetic resolution of racemic β-stannyl allyl alcohol *rac*-**5b**



A suspension of racemic alcohol *rac*-**5b** (0.6 mmol, 256 mg), Novozyme 435 (4 mg), 4 Å molecular sieves (25 mg), and vinyl acetate (6 mmol, 528 mg, 550 μL) in pentane (1.7 mL) was stirred in room temperature. The progress of the reaction was followed by <sup>1</sup>H NMR. After 5 days, the reaction mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel (5–30% AcOEt in hexanes). Yield: 132 mg (47%) of acetate **Ac-5b** and 118 mg (46%) of alcohol **5b**.

#### (*S,E*)-5-(Methoxymethoxy)-4-(tributylstannyl)pent-3-en-2-ol (**5b**):

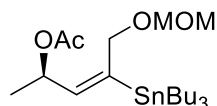


Yield 118 mg (46%); yellow oil; [α]<sub>D</sub><sup>21</sup> -11.0 (c 1.15, CHCl<sub>3</sub>, ee 96%; determined by HPLC: *R*<sub>t</sub> 15.9 min); spectral data in agreement with **5b**; HPLC (racemate) column: Chiralcel OD-H,



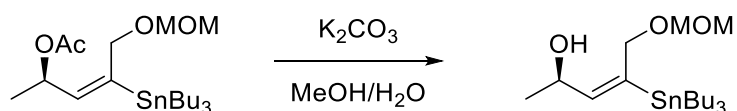
1% *i*-PrOH in hexanes, flow 1 mL min<sup>-1</sup>, det. 210 nm; 12.4 min (*R*-enantiomer) and *R*<sub>t</sub> 15.3 min (*S*-enantiomer).

### (*R,E*)-5-(methoxymethoxy)-4-(tributylstannyl)pent-3-en-2-yl acetate (**5c**)



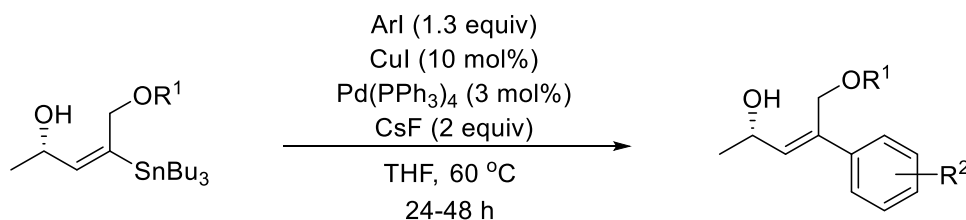
Yield 132 mg (47%); yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.62 – 5.34 (m, 2H), 4.66 – 4.57 (m, 2H), 4.40 (dd, *J* = 13.0, 1.6 Hz, 1H), 4.24 (dd, *J* = 13.0, 1.6 Hz, 1H), 3.35 (s, 3H), 2.02 (s, 3H), 1.57 – 1.16 (m, 15H), 1.00 – 0.71 (m, 15H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 170.1, 146.6, 137.9, 96.0, 68.8, 68.0, 55.3, 29.0, 27.3, 21.3, 20.5, 13.7, 10.2.

### (*R,E*)-5-(Methoxymethoxy)-4-(tributylstannyl)pent-3-en-2-ol (*ent*-**5b**):



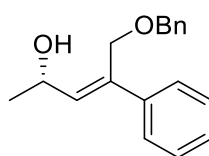
A suspension of acetate **Ac-5b** (0.25 mmol, 118 mg), K<sub>2</sub>CO<sub>3</sub> (0.5 mmol, 70 mg), MeOH (500 μL) and H<sub>2</sub>O (200 μL) was stirred for 24 h at 60 °C. When the reaction was complete, water was added to the mixture. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> and the combined organic phase was dried over sodium sulfate. After the removal of the solvent, the crude product was purified by a column chromatography on a silica gel (5–20% AcOEt in hexanes). Yield 108 mg (99%); yellow oil; [α]<sub>D</sub><sup>24</sup> +12.4 (c 1.10, CHCl<sub>3</sub>, *ee* 98%; determined by HPLC: *R*<sub>t</sub> 12.1 min); spectral data in agreement with **5b**; HPLC (racemate) column: Chiralcel OD-H, 1% *i*-PrOH in hexanes, flow 1 mL min<sup>-1</sup>, det. 210 nm; *R*<sub>t</sub> 12.4 min (*R*-enantiomer) and 15.3 min (*S*-enantiomer).

## 1.9. The synthesis of allyl alcohols **6** via Stille coupling reaction



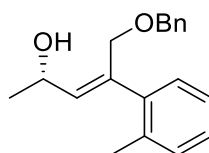
General procedure: Pd(PPh<sub>3</sub>)<sub>4</sub> (5 mol%, 0.05 mmol, 58 mg), CuI (10 mol%, 0.1 mmol, 19 mg) and CsF (2 mmol, 300 mg) were added to a solution of vinyltributylstannane (1 mmol) and aryl iodide (1.3 mmol) in degassed THF (2.2 mL). The resulting mixture was kept at 60–100 °C for 24–48 h. Next, the solvent was removed and the residue was dissolved in AcOEt and washed with 5% aqueous ammonia solution. The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvent, the crude residue was purified by a column chromatography on a silica gel (10–40% AcOEt in hexanes).

**(*S,Z*)-5-(Benzyloxy)-4-phenylpent-3-en-2-ol (6aa):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 51 mg (91%) starting from 100 mg vinylstannane **5a**; waxy solid;  $[\alpha]_D^{23} -21.7$  (c 0.94, CHCl<sub>3</sub>, ee 98%; determined by HPLC:  $R_t$  15.7 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.46 – 7.38 (m, 2H), 7.39 – 7.24 (m, 8H), 5.99 (d,  $J$  = 8.3 Hz, 1H), 4.72 (dq,  $J$  = 8.3, 6.3 Hz, 1H), 4.49 (d,  $J$  = 11.2 Hz, 1H), 4.39 (d,  $J$  = 11.2 Hz, 1H), 2.49 (br s, 1H), 1.35 (d,  $J$  = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  141.0, 137.7, 137.6, 137.3, 128.5, 128.4, 128.0, 127.9, 127.5, 126.4, 72.7, 67.6, 64.3, 23.3; FTIR (film)  $\nu$ : 3397, 3029, 2967, 2925, 2864, 1451, 1364, 1065, 756, 698 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>18</sub>H<sub>20</sub>O<sub>2</sub>Na [(M + Na)<sup>+</sup>] 291.1361; found 291.1355; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; 10.1 min (*R*-enantiomer) and  $R_t$  20.2 min (*S*-enantiomer).

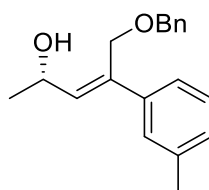
**(*S,Z*)-5-(Benzyloxy)-4-(*o*-tolyl)pent-3-en-2-ol (6ab):**



The reaction mixture was stirred at 60 °C for 48 h. Yield 52 mg (88%) starting from 100 mg vinylstannane **5a**; yellowish oil;  $[\alpha]_D^{20} -6.5$  (c 0.96, CHCl<sub>3</sub>, ee 98%; determined by HPLC:  $R_t$  12.4 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.40 – 7.24 (m, 5H), 7.24 – 7.11 (m, 4H), 5.66 (d,  $J$  = 8.2 Hz, 1H), 4.76 (dq,  $J$  = 8.2, 6.3 Hz, 1H), 4.54 (s, 2H), 4.40 (d,  $J$  = 11.4 Hz, 1H), 4.18 (d,  $J$  =

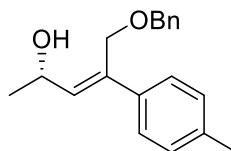
11.4 Hz, 1H), 2.56 (br s, 1H), 2.30 (s, 3H), 1.36 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.0, 139.0, 138.7, 137.7, 135.2, 130.1, 128.8, 128.5, 127.8, 127.8, 127.2, 125.6, 73.0, 69.5, 64.2, 23.1, 20.0; FTIR (film)  $\nu$ : 3403, 3028, 2968, 2925, 2859, 1454, 1363, 1088, 1068, 730, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  305.1517; found 305.1511; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 9.8 min (*R*-enantiomer) and  $R_t$  12.3 min (*S*-enantiomer).

**(*S,Z*)-5-(Benzyloxy)-4-(*m*-tolyl)pent-3-en-2-ol (6ac):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 43 mg (73%) starting from 100 mg vinylstannane **5a**; yellowish oil;  $[\alpha]_D^{24} -23.6$  (c 1.41,  $\text{CHCl}_3$ , *ee* 97%; determined by HPLC:  $R_t$  11.5 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.27 (m, 5H), 7.25 – 7.17 (m, 3H), 7.14 – 7.05 (m, 1H), 5.98 (d,  $J = 8.3$  Hz, 1H), 4.72 (dq,  $J = 8.3, 6.3$  Hz, 1H), 4.57 (d,  $J = 2.3$  Hz, 2H), 4.48 (d,  $J = 11.2$  Hz, 1H), 4.38 (d,  $J = 11.2$  Hz, 1H), 2.36 (s, 3H), 1.35 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  141.0, 137.9, 137.8, 137.8, 137.2, 128.5, 128.2, 128.2, 128.1, 127.9, 127.1, 123.4, 72.7, 67.6, 64.3, 23.3, 21.5; FTIR (film)  $\nu$ : 3398, 2967, 2924, 2862, 1452, 1363, 1065, 785, 739, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  305.1517; found 305.1509; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 8.5 min (*R*-enantiomer) and  $R_t$  11.5 min (*S*-enantiomer).

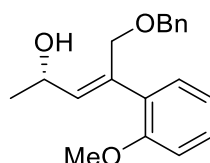
**(*S,Z*)-5-(Benzyloxy)-4-(*p*-tolyl)pent-3-en-2-ol (6ad):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 44 mg (44%) starting from 100 mg vinylstannane **5a**; waxy solid;  $[\alpha]_D^{18} -27.0$  (c 0.99,  $\text{CHCl}_3$ , *ee* 98%; determined by HPLC:  $R_t$  13.8 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.45 – 7.23 (m, 7H), 7.14 (d,  $J = 7.9$  Hz, 2H), 5.97 (d,  $J = 8.3$  Hz, 1H), 4.71 (dq,  $J = 8.3, 6.2$  Hz, 1H), 4.56 (s, 2H), 4.52 – 4.45 (m, 1H), 4.44 – 4.33 (m,

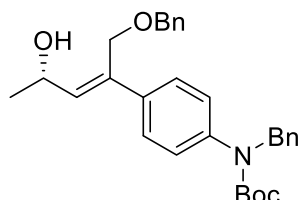
1H), 2.36 (s, 3H), 2.22 (br s, 1H), 1.35 (d,  $J = 6.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.1, 137.8, 137.6, 137.2, 136.5, 129.1, 128.5, 128.0, 127.9, 126.2, 72.6, 67.6, 64.3, 23.3, 21.1; FTIR (film)  $\nu$ : 3399, 2969, 2924, 2865, 2865, 1364, 1067, 816, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  305.1517; found 305.1515; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 9.7 min (*R*-enantiomer) and  $R_t$  14.0 min (*S*-enantiomer).

**(*S,Z*)-5-(Benzyloxy)-4-(2-methoxyphenyl)pent-3-en-2-ol (6ae):**



The reaction mixture was stirred at 60 °C for 48 h. Yield 45 mg (72%) starting from 100 mg vinylstannane **5a**; orange oil;  $[\alpha]_{\text{D}}^{20} -26.0$  ( $c$  1.04,  $\text{CHCl}_3$ ,  $ee$  97%; determined by HPLC:  $R_t$  22.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.18 (m, 7H), 6.95 (t,  $J = 7.5$  Hz, 1H), 6.86 (d,  $J = 8.2$  Hz, 1H), 5.79 (d,  $J = 8.2$  Hz, 1H), 4.75 (dq,  $J = 8.2, 6.3$  Hz, 1H), 4.60 – 4.45 (m, 3H), 4.34 (d,  $J = 11.6$  Hz, 1H), 3.77 (s, 3H), 2.55 (br s, 1H), 1.34 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 138.7, 138.3, 138.0, 131.5, 130.2, 128.8, 128.4, 127.9, 127.7, 120.7, 110.6, 72.6, 68.7, 64.1, 55.3, 23.0; FTIR (film)  $\nu$ : 3409, 2966, 2926, 2862, 1490, 1458, 1244, 1061, 748, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{22}\text{O}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  321.1467; found 321.1461; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 12.0 min (*R*-enantiomer) and  $R_t$  21.7 min (*S*-enantiomer).

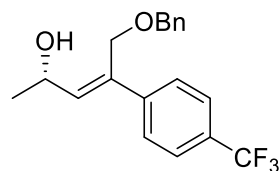
***tert*-Butyl (*S,Z*)-benzyl(4-(1-(benzyloxy)-4-hydroxypent-2-en-2-yl)phenyl)carbamate (6af)**



The reaction mixture was stirred at 60 °C for 24 h. Yield 76 mg (77%) starting from 100 mg vinylstannane **5a**; orange oil;  $[\alpha]_{\text{D}}^{19} -13.2$  ( $c$  1.04,  $\text{CHCl}_3$ ,  $ee$  96%; determined by HPLC:  $R_t$  22.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.20 (m, 12H), 7.12 (d,  $J = 8.2$  Hz, 2H), 5.96 (d,

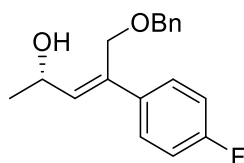
$J = 8.3$  Hz, 1H), 4.84 (s, 2H), 4.69 (dq,  $J = 8.3, 6.3$  Hz, 1H), 4.54 (d,  $J = 2.1$  Hz, 2H), 4.44 (d,  $J = 11.2$  Hz, 1H), 4.35 (d,  $J = 11.2$  Hz, 1H), 2.25 (br s, 1H), 1.44 (s, 9H), 1.33 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.7, 142.1, 138.6, 138.3, 137.7, 137.1, 136.9, 128.5, 128.4, 128.0, 127.9, 127.3, 127.1, 126.5, 126.2, 80.6, 72.6, 67.4, 64.3, 53.9, 28.3, 23.3; FTIR (film)  $\nu$ : 3464, 2975, 2928, 1698, 1513, 1454, 1389, 1366, 1165, 1058, 736, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{30}\text{H}_{35}\text{NO}_4\text{Na}$  [(M+Na) $^+$ ] 496.2464; found 496.2463; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 15.6 min (*R*-enantiomer) and  $R_t$  22.1 min (*S*-enantiomer).

**(*S,Z*)-5-(Benzyloxy)-4-(4-(trifluoromethyl)phenyl)pent-3-en-2-ol (6ag):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 57 mg (82%) starting from 100 mg vinylstannane **5a**; yellowish oil;  $[\alpha]_{\text{D}}^{24} -17.4$  (c 1.13,  $\text{CHCl}_3$ , *ee* 96%; determined by HPLC:  $R_t$  11.1 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (d,  $J = 8.2$  Hz, 2H), 7.49 (d,  $J = 8.2$  Hz, 2H), 7.40 – 7.27 (m, 5H), 6.02 (d,  $J = 8.3$  Hz, 1H), 4.71 (dq,  $J = 8.3, 6.3$  Hz, 1H), 4.55 (d,  $J = 3.0$  Hz, 2H), 4.46 (d,  $J = 11.3$  Hz, 1H), 4.37 (d,  $J = 11.3$  Hz, 1H), 2.28 (br s, 1H), 1.35 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.5, 138.9, 137.4, 136.5, 129.4 (q,  $J = 32.4$  Hz), 128.5, 128.0 (m), 126.7, 124.2 (q,  $J = 271.6, 271.4$  Hz), 125.3 (q,  $J = 3.8$  Hz), 72.8, 67.1, 64.3, 23.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.5; FTIR (film)  $\nu$ : 3398, 2968, 2926, 2859, 1327, 1166, 1122, 1068, 838  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{19}\text{O}_2\text{F}_3\text{Na}$  [(M+Na) $^+$ ] 359.1235; found 359.1227; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 8.9 min (*R*-enantiomer) and  $R_t$  11.2 min (*S*-enantiomer).

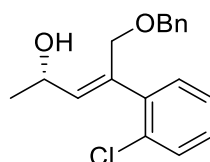
**(*S,Z*)-5-(Benzyloxy)-4-(4-fluorophenyl)pent-3-en-2-ol (6ah):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 43 mg (72%) starting from 100 mg vinylstannane **5a**; yellowish oil;  $[\alpha]_{\text{D}}^{24} -20.3$  (c 1.09,  $\text{CHCl}_3$ , *ee* 96%; determined by HPLC:  $R_t$

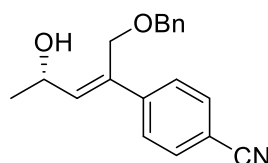
11.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 – 7.27 (m, 7H), 7.00 (t,  $J$  = 8.7 Hz, 2H), 5.92 (d,  $J$  = 8.3 Hz, 1H), 4.70 (dq,  $J$  = 8.3, 6.3 Hz, 1H), 4.55 (d,  $J$  = 2.3 Hz, 2H), 4.45 (d,  $J$  = 11.3 Hz, 1H), 4.35 (d,  $J$  = 11.3 Hz, 1H), 2.26 (br s, 1H), 1.33 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  162.3 (d,  $J$  = 246.4 Hz), 137.6, 137.1 (d,  $J$  = 0.7 Hz), 137.0 (d,  $J$  = 3.3 Hz), 136.7, 128.5, 128.0, 128.0, 128.0, 127.9, 115.3, 115.1, 72.7, 67.4, 64.3, 23.4;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -115.1; FTIR (film)  $\nu$ : 3398, 2968, 2925, 2863, 1509, 1227, 1065, 832, 740, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{19}\text{O}_2\text{FNa}$  [(M + Na) $^+$ ] 309.1267; found 309.1257; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 9.4 min (*R*-enantiomer) and  $R_t$  11.6 min (*S*-enantiomer).

**(*S,Z*)-5-(Benzyloxy)-4-(2-chlorophenyl)pent-3-en-2-ol (6ai):**



The reaction mixture was stirred at 60 °C for 48 h. Yield 50 mg (79%) starting from 100 mg vinylstannane **5a**; yellowish oil;  $[\alpha]_{\text{D}}^{24}$  -18.5 (c 1.83,  $\text{CHCl}_3$ , *ee* 98%; determined by HPLC:  $R_t$  11.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.47 – 7.09 (m, 10H), 5.75 (d,  $J$  = 8.2 Hz, 1H), 4.75 (dq,  $J$  = 8.2, 6.3 Hz, 1H), 4.58 – 4.39 (m, 3H), 4.30 (d,  $J$  = 11.7 Hz, 1H), 2.48 (s, 1H), 1.35 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.9, 140.0, 137.7, 137.5, 132.4, 130.7, 129.5, 128.6, 128.4, 127.8, 127.8, 126.7, 72.8, 68.5, 64.1, 23.0; FTIR (film)  $\nu$ : 3400, 2968, 2925, 2859, 1363, 1064, 753, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{19}\text{O}_2\text{ClNa}$  [(M+Na) $^+$ ] 325.0971; found 325.0963; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 215 nm; 8.5 min (*R*-enantiomer) and  $R_t$  11.2 min (*S*-enantiomer).

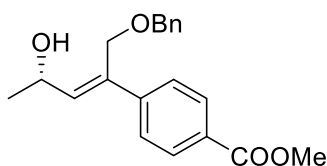
**(*S,Z*)-4-(1-(Benzyloxy)-4-hydroxypent-2-en-2-yl)benzonitrile (6aj):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 45 mg (73%) starting from 100 mg vinylstannane **5a**; yellow oil;  $[\alpha]_{\text{D}}^{24}$  -21.9 (c 1.01,  $\text{CHCl}_3$ , *ee* 98%; determined by HPLC:  $R_t$  23.5 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.64 – 7.52 (m, 2H), 7.53 – 7.42 (m, 2H), 7.42 – 7.20

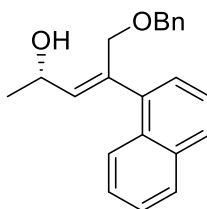
(m, 5H), 6.04 (d,  $J = 8.3$  Hz, 1H), 4.70 (dq,  $J = 8.3, 6.3$  Hz, 1H), 4.54 (d,  $J = 3.1$  Hz, 2H), 4.44 (d,  $J = 11.4$  Hz, 1H), 4.35 (d,  $J = 11.4$  Hz, 1H), 2.33 (br s, 1H), 1.34 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  145.4, 139.7, 137.3, 136.1, 132.1, 128.5, 128.1, 128.0, 127.0, 118.8, 111.0, 72.8, 66.7, 64.3, 23.4; FTIR (film)  $\nu$ : 3409, 2969, 2925, 2864, 2227, 1604, 1364, 1065, 835, 741, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{19}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  316.1313; found 316.1304; HPLC (racemate) column: Chiralpak AD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm;  $R_t$  23.4 min (*S*-enantiomer) and 31.2 min (*R*-enantiomer).

**Methyl (*S,Z*)-4-(1-(benzyloxy)-4-hydroxypent-2-en-2-yl)benzoate (6ak):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 55 mg (81%) starting from 100 mg vinylstannane **5a**; waxy solid;  $[\alpha]_{\text{D}}^{23} -18.2$  (c 1.08,  $\text{CHCl}_3$ , *ee* 97%; determined by HPLC:  $R_t$  19.3 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.05 – 7.94 (m, 1H), 7.92 – 7.83 (m, 1H), 7.79 (d,  $J = 8.1$  Hz, 1H), 7.52 – 7.40 (m, 3H), 7.37 – 7.24 (m, 6H), 5.89 (dd,  $J = 8.1, 1.1$  Hz, 1H), 4.87 (dq,  $J = 8.1, 6.3$  Hz, 1H), 4.64 – 4.47 (m, 3H), 4.30 (d,  $J = 11.2$  Hz, 1H), 2.82 (br s, 1H), 1.41 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.4, 140.2, 138.3, 137.6, 133.7, 131.3, 128.5, 128.4, 127.9, 127.9, 127.7, 126.0, 125.9, 125.8, 125.6, 125.3, 73.2, 70.1, 64.3, 23.1; FTIR (film)  $\nu$ : 3422, 2954, 2925, 2862, 1720, 1606, 1437, 1281, 1109, 1067, 702  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{22}\text{O}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  349.1416; found 349.1411; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 16.1 min (*R*-enantiomer) and  $R_t$  20.2 min (*S*-enantiomer).

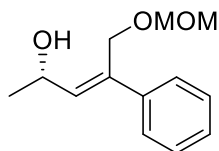
**(*S,Z*)-5-(Benzyloxy)-4-(naphthalen-1-yl)pent-3-en-2-ol (6al):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 50 mg (76%) starting from 100 mg vinylstannane **5a**; yellowish oil;  $[\alpha]_{\text{D}}^{24} -0.4$  (c 1.09,  $\text{CHCl}_3$ , *ee* 97%; determined by HPLC:  $R_t$

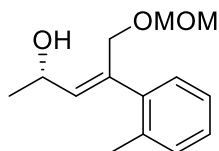
20.2 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.02 – 7.93 (m, 1H), 7.90 – 7.82 (m, 1H), 7.82 – 7.75 (m, 1H), 7.52 – 7.39 (m, 3H), 7.37 – 7.31 (m, 1H), 5.88 (dd,  $J = 8.4, 1.0$  Hz, 1H), 4.92 (dq,  $J = 8.4, 6.3$  Hz, 1H), 4.68 (d,  $J = 6.7$  Hz, 1H), 4.66 – 4.59 (m, 2H), 4.41 (d,  $J = 11.5$  Hz, 1H), 3.32 (s, 3H), 2.59 (br s, 1H), 1.43 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.3, 140.0, 137.3, 133.7, 131.3, 128.4, 127.7, 126.0, 125.8, 125.7, 125.4, 125.3, 95.9, 66.7, 64.2, 55.5, 23.2; FTIR (film)  $\nu$ : 3408, 2965, 2925, 2859, 1453, 1363, 1066, 801, 778, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{22}\text{H}_{22}\text{O}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  341.1517; found 341.1507; HPLC (racemate) column: Chiralcel OD-H, 10% *i*-PrOH in hexanes, flow 1  $\text{mL min}^{-1}$ , det. 215 nm;  $R_t$  20.9 min (*S*-enantiomer) and 25.8 min (*S*-enantiomer).

**(*S,Z*)-5-(Methoxymethoxy)-4-phenylpent-3-en-2-ol (6ba):**



The reaction mixture was stirred at 60 °C for 24 h. Yield 66 mg (87%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{21} -29.2$  ( $c$  0.97,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.58 – 7.40 (m, 2H), 7.40 – 7.19 (m, 3H), 6.02 (d,  $J = 8.5$  Hz, 1H), 4.80 (dq,  $J = 8.5, 6.3$  Hz, 1H), 4.71 – 4.64 (m, 1H), 4.64 – 4.56 (m, 2H), 4.56 – 4.46 (m, 1H), 3.37 (s, 3H), 2.75 (br s, 1H), 1.36 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.5, 137.4, 136.5, 128.4, 127.6, 126.3, 95.1, 64.0, 63.9, 55.5, 23.3; FTIR (film)  $\nu$ : 3410, 2965, 2930, 1445, 1149, 1099, 1049, 920, 761, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{18}\text{O}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  245.1154; found 245.1147.

**(*S,Z*)-5-(Methoxymethoxy)-4-(*o*-tolyl)pent-3-en-2-ol (6bb):**

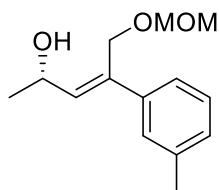


The reaction mixture was stirred at 60 °C for 48 h. Yield 73 mg (91%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{18} -12.1$  ( $c$  1.03,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.25 – 7.03 (m, 4H), 5.63 (d,  $J = 8.3$  Hz, 1H), 4.80 (dq,  $J = 8.3, 6.3$  Hz, 1H), 4.64 (d,  $J =$



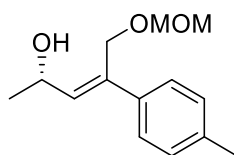
6.7 Hz, 1H), 4.59 (d,  $J = 6.7$  Hz, 1H), 4.47 (d,  $J = 11.6$  Hz, 1H), 4.27 (d,  $J = 11.6$  Hz, 1H), 3.31 (s, 3H), 2.57 (br s, 1H), 2.29 (s, 3H), 1.35 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  141.6, 138.7, 138.0, 135.1, 130.1, 128.8, 127.2, 125.6, 95.8, 66.0, 64.0, 55.4, 23.2, 19.9; FTIR (film)  $\nu$ : 3412, 2959, 2928, 1453, 1150, 1100, 1047, 921, 763, 728  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_3\text{Na}$  [(M+Na) $^+$ ] 259.1310; found 259.1310.

**(S,Z)-5-(methoxymethoxy)-4-(*m*-tolyl)pent-3-en-2-ol (6bc):**



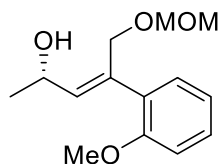
The reaction mixture was stirred at 60 °C for 24 h. Yield 69 mg (86%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_{\text{D}}^{20}$  -25.6 ( $c$  1.19,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 – 7.19 (m, 3H), 7.15 – 7.05 (m, 1H), 6.01 (d,  $J = 8.6$  Hz, 1H), 4.80 (dq,  $J = 8.6, 6.3$  Hz, 1H), 4.68 (d,  $J = 6.7$  Hz, 1H), 4.65 – 4.56 (m, 2H), 4.51 (d,  $J = 11.7$  Hz, 1H), 3.38 (s, 3H), 2.78 (br s, 1H), 2.36 (s, 3H), 1.36 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.5, 137.9, 137.3, 136.5, 128.3, 128.3, 127.1, 123.4, 95.1, 64.0, 63.9, 55.5, 23.3, 21.5; FTIR (film)  $\nu$ : 3415, 2928, 1451, 1369, 1148, 1100, 1049, 921, 786, 702  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_3\text{Na}$  [(M + Na) $^+$ ] 259.1310; found 259.1310.

**(S,Z)-5-(Methoxymethoxy)-4-(*p*-tolyl)pent-3-en-2-ol (6bd):**



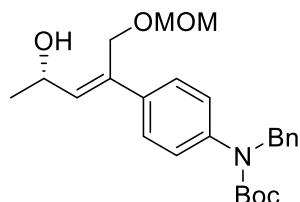
The reaction mixture was stirred at 60 °C for 24 h. Yield 73 mg (90%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_{\text{D}}^{20}$  -30.5 ( $c$  0.95,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.25 (m, 2H), 7.21 – 7.07 (m, 2H), 6.00 (d,  $J = 8.8$  Hz, 1H), 4.88 – 4.74 (m, 1H), 4.72 – 4.44 (m, 4H), 3.37 (s, 3H), 2.76 (br s, 1H), 2.34 (s, 3H), 1.48 – 1.25 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  137.6, 137.3, 136.6, 136.3, 129.1, 126.2, 95.1, 63.9, 63.9, 55.5, 23.3, 21.1; FTIR (film)  $\nu$ : 3413, 2927, 1148, 1099, 1047, 920, 816  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_3\text{Na}$  [(M+Na) $^+$ ] 259.1310; found 259.1299.

**(S,Z)-5-(Methoxymethoxy)-4-(2-Methoxyphenyl)pent-3-en-2-ol (6be):**



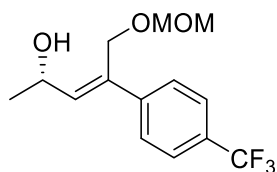
The reaction mixture was stirred at 60 °C for 48 h. Yield 69 mg (81%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{21} -32.2$  ( $c$  1.22,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 – 7.12 (m, 2H), 6.98 – 6.78 (m, 2H), 5.76 (d,  $J$  = 8.5 Hz, 1H), 4.77 (dq,  $J$  = 8.5, 6.3 Hz, 1H), 4.62 (d,  $J$  = 6.6 Hz, 1H), 4.60 – 4.52 (m, 2H), 4.47 (d,  $J$  = 11.8 Hz, 1H), 3.79 (s, 3H), 3.31 (s, 3H), 2.78 (br s, 1H), 1.34 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.7, 138.9, 137.2, 130.9, 130.2, 128.8, 120.7, 110.6, 95.4, 65.1, 63.8, 55.3, 23.0; FTIR (film)  $\nu$ : 3420, 2932, 1490, 1461, 1244, 1149, 1048, 754  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{20}\text{O}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  275.1259; found 275.1252.

**tert-Butyl (S,Z)-benzyl(4-(4-hydroxy-1-(methoxymethoxy)pent-2-en-2-yl)phenyl)carbamate (6bf):**



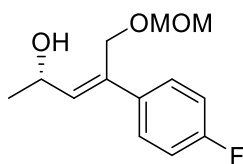
The reaction mixture was stirred at 60 °C for 24 h. Yield 75 mg (77%) starting from 100 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{23} -22.3$  ( $c$  0.97,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.43 – 7.33 (m, 2H), 7.33 – 7.18 (m, 5H), 7.13 (d,  $J$  = 8.2 Hz, 2H), 5.99 (d,  $J$  = 8.6 Hz, 1H), 4.91 – 4.72 (m, 3H), 4.70 – 4.51 (m, 3H), 4.46 (d,  $J$  = 11.8 Hz, 1H), 3.34 (s, 3H), 2.51 (br s, 1H), 1.42 (s, 9H), 1.34 (d,  $J$  = 6.2 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.7, 142.3, 138.6, 137.7, 137.2, 135.8, 128.4, 127.2, 127.0, 126.5, 126.1, 95.1, 80.6, 63.9, 55.5, 53.8, 28.3, 23.2; FTIR (film)  $\nu$ : 3451, 2974, 2930, 1698, 1513, 1388, 1151, 1046, 838, 736  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{25}\text{H}_{33}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  450.2256; found 450.2241.

**(S,Z)-5-(Methoxymethoxy)-4-(4-(trifluoromethyl)phenyl)pent-3-en-2-ol (6bg):**



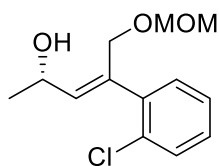
The reaction mixture was stirred at 60 °C for 24 h. Yield 90 mg (91%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{16}$   $-15.1$  ( $c$  1.05,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.64 – 7.49 (m, 4H), 6.06 (d,  $J$  = 8.5 Hz, 1H), 4.80 (dq,  $J$  = 8.5, 6.3 Hz, 1H), 4.69 – 4.56 (m, 3H), 4.50 (d,  $J$  = 12.0 Hz, 1H), 3.35 (s, 3H), 2.76 (br s, 1H), 1.36 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  144.1, 139.0, 135.3, 129.5 (q,  $J$  = 32.4 Hz), 126.6, 125.3 (q,  $J$  = 3.7 Hz), 124.64 (q,  $J$  = 271.8 Hz), 95.2, 63.9, 63.7, 55.5, 23.2;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.6; FTIR (film)  $\nu$ : 3407, 2934, 1616, 1328, 1121, 1048, 838  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{17}\text{O}_3\text{F}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  313.1027; found 313.1020.

**(S,Z)-4-(4-fluorophenyl)-5-(methoxymethoxy)pent-3-en-2-ol (6bh):**



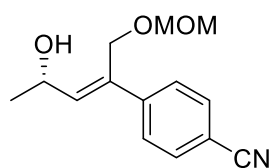
The reaction mixture was stirred at 60 °C for 24 h. Yield 74 mg (90%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{18}$   $-21.9$  ( $c$  1.09,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 – 7.34 (m, 2H), 7.00 (t,  $J$  = 8.6 Hz, 2H), 5.95 (d,  $J$  = 8.5 Hz, 1H), 4.77 (dq,  $J$  = 8.5, 6.2 Hz, 1H), 4.70 – 4.51 (m, 3H), 4.46 (d,  $J$  = 11.9 Hz, 1H), 3.35 (s, 3H), 2.74 (br s, 1H), 1.34 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  162.4 (d,  $J$  = 246.6 Hz), 137.2, 136.52 (d,  $J$  = 3.3 Hz), 135.4, 128.0 (d,  $J$  = 7.9 Hz), 115.22 (d,  $J$  = 21.3 Hz), 95.1, 63.9, 63.9, 55.5, 23.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.9; FTIR (film)  $\nu$ : 3412, 2932, 1510, 1228, 1150, 1099, 1048, 922, 834  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{17}\text{O}_3\text{FNa}$   $[(\text{M}+\text{Na})^+]$  263.1059; found 263.1048.

**(S,Z)-4-(2-Chlorophenyl)-5-(methoxymethoxy)pent-3-en-2-ol (6bi):**



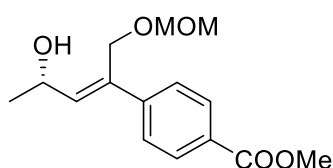
The reaction mixture was stirred at 60 °C for 48 h. Yield 73 mg (83%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{18} -14.2$  (c 1.00, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.39 – 7.31 (m, 1H), 7.28 – 7.16 (m, 3H), 5.72 (d, *J* = 8.4 Hz, 1H), 4.79 (dq, *J* = 8.4, 6.3 Hz, 1H), 4.69 – 4.48 (m, 3H), 4.40 (d, *J* = 11.9 Hz, 1H), 3.30 (s, 3H), 2.66 (br s, 1H), 1.35 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 140.5, 140.1, 136.5, 132.4, 130.7, 129.5, 128.6, 126.7, 95.5, 64.9, 63.9, 55.4, 23.0; FTIR (film) ν: 3418, 2930, 1469, 1150, 1100, 1046, 921, 758 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>13</sub>H<sub>17</sub>O<sub>3</sub>ClNa [(M+Na)<sup>+</sup>] 279.0764; found 279.0762.

**(S,Z)-4-(4-Hydroxy-1-(methoxymethoxy)pent-2-en-2-yl)benzonitrile (6bj):**



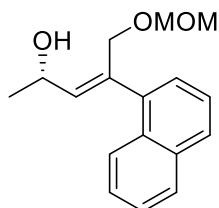
The reaction mixture was stirred at 60 °C for 24 h. Yield 77 mg (91%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{21} -24.9$  (c 1.00, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.65 – 7.48 (m, 4H), 6.07 (d, *J* = 8.5 Hz, 1H), 4.78 (dq, *J* = 8.5, 6.3 Hz, 1H), 4.68 – 4.41 (m, 4H), 3.33 (s, 3H), 2.73 (br s, 1H), 1.34 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 145.1, 139.9, 134.9, 132.2, 127.0, 118.8, 111.0, 95.2, 63.9, 63.4, 55.6, 23.3; FTIR (film) ν: 3430, 2969, 2931, 2227, 1604, 1149, 1100, 1048, 836 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>17</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 270.1106; found 270.1106.

**Methyl (S,Z)-4-(4-hydroxy-1-(methoxymethoxy)pent-2-en-2-yl)benzoate (6bk):**



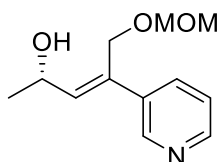
The reaction mixture was stirred at 60 °C for 24 h. Yield 95 mg (95%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{21} -22.6$  (c 1.09, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.09 – 7.87 (m, 2H), 7.59 – 7.38 (m, 2H), 6.09 (d, *J* = 8.5 Hz, 1H), 4.80 (dq, *J* = 8.5, 6.3 Hz, 1H), 4.68 – 4.47 (m, 4H), 3.89 (s, 3H), 3.34 (s, 3H), 2.67 (br s, 1H), 1.35 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.8, 145.0, 139.0, 135.7, 129.7, 129.1, 126.2, 95.2, 63.9, 63.7, 55.5, 52.0, 23.2; FTIR (film) ν: 3427, 2952, 1721, 1437, 1282, 1103, 1048, 773 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>20</sub>O<sub>5</sub>Na [(M+Na)<sup>+</sup>] 303.1208; found 303.1198.

**(S,Z)-5-(methoxymethoxy)-4-(naphthalen-1-yl)pent-3-en-2-ol (6bl):**



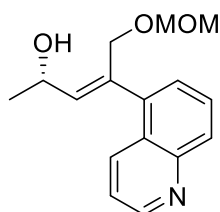
The reaction mixture was stirred at 60 °C for 24 h. Yield 93 mg (95%) starting from 150 mg vinylstannane **5b**; yellowish oil;  $[\alpha]_D^{17} -6.1$  (c 1.01, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.02 – 7.93 (m, 1H), 7.90 – 7.82 (m, 1H), 7.82 – 7.75 (m, 1H), 7.52 – 7.39 (m, 3H), 7.37 – 7.31 (m, 1H), 5.88 (dd, *J* = 8.4, 1.0 Hz, 1H), 4.92 (dq, *J* = 8.4, 6.3 Hz, 1H), 4.68 (d, *J* = 6.7 Hz, 1H), 4.66 – 4.59 (m, 2H), 4.41 (d, *J* = 11.5 Hz, 1H), 3.32 (s, 3H), 2.59 (br s, 1H), 1.43 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 140.3, 140.0, 137.3, 133.7, 131.3, 128.4, 127.7, 126.0, 125.8, 125.7, 125.4, 125.3, 95.9, 66.7, 64.2, 55.5, 23.2; FTIR (film) *v*: 3414, 2929, 1397, 1149, 1100, 1042, 802, 779 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>17</sub>H<sub>20</sub>O<sub>3</sub>Na [(M+Na)<sup>+</sup>] 295.1310; found 295.1303.

**(S,Z)-5-(methoxymethoxy)-4-(pyridin-3-yl)pent-3-en-2-ol (6bm):**



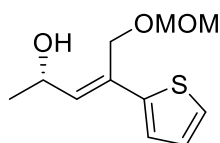
The reaction mixture was stirred at 60 °C for 24 h. Column chromatography: silica gel, 30–80% AcOEt in hexanes. Yield 65 mg (84%) starting from 150 mg vinylstannane **5b** and 3-bromopyridine; yellow oil;  $[\alpha]_D^{26} -7.8$  (c 0.96, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>, mixture of rotamers, data for major rotamer) δ 8.65 (s, 1H), 8.45 (d, *J* = 4.1 Hz, 1H), 7.72 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.21 (dd, *J* = 8.0, 4.8 Hz, 1H), 6.02 (d, *J* = 8.5 Hz, 1H), 4.83 – 4.74 (m, 1H), 4.60 (d, *J* = 6.8 Hz, 1H), 4.57 (d, *J* = 6.8 Hz, 1H), 4.51 (d, *J* = 12.0 Hz, 1H), 4.45 (d, *J* = 12.0 Hz, 1H), 3.31 (s, 3H), 1.33 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 148.4, 147.6, 139.1, 133.7, 133.2, 123.2, 95.3, 63.7, 63.5, 55.5, 23.4; FTIR (film) *v*: 3367, 2966, 2888, 1416, 1149, 1100, 1043, 712 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>12</sub>H<sub>18</sub>NO<sub>3</sub> [(M+H)<sup>+</sup>] 224.1287; found 224.1278.

**(S,Z)-5-(methoxymethoxy)-4-(quinolin-5-yl)pent-3-en-2-ol (6bn):**



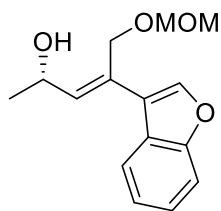
The reaction mixture was stirred at 60 °C for 24 h. Column chromatography: silica gel, 30–80% AcOEt in hexanes. Yield 74 mg (79%) starting from 150 mg vinylstannane **5b** and 5-bromoquinoline; yellow oil;  $[\alpha]_D^{24} +0.4$  (c 1.25, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.91 (br s, 1H), 8.36 (br d, *J* = 8.5 Hz, 1H), 8.05 (br d, *J* = 8.4 Hz, 1H), 7.66 (dd, *J* = 8.5, 7.0 Hz, 1H), 7.42 – 7.36 (m, 2H), 5.84 (d, *J* = 8.4 Hz, 1H), 4.91 (dq, *J* = 8.4, 6.3 Hz, 1H), 4.65 (d, *J* = 6.7 Hz, 1H), 4.59 (d, *J* = 6.7 Hz, 1H), 4.58 (dd, *J* = 11.5, 0.9 Hz, 1H), 4.39 (d, *J* = 11.5 Hz, 1H), 3.27 (s, 3H), 1.42 (d, *J* = 6.3 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 150.0, 148.3, 141.2, 140.2, 135.2, 134.1, 128.9, 128.7, 126.7, 126.1, 120.9, 95.9, 66.5, 64.1, 55.5, 23.5; FTIR (film) *v*: 3361, 2964, 2928, 1499, 1149, 1101, 1045, 806 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>16</sub>H<sub>20</sub>NO<sub>3</sub> [(M+H)<sup>+</sup>] 274.1443; found 274.1438.

**(S,E)-5-(methoxymethoxy)-4-(thiophen-2-yl)pent-3-en-2-ol (6bo):**



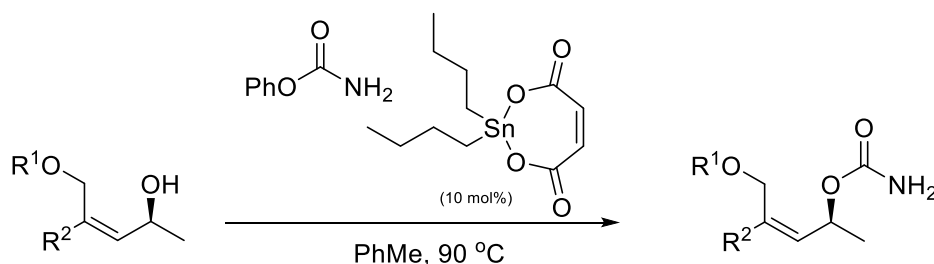
The reaction mixture was stirred at 60 °C for 24 h. Yield 64 mg (81%) starting from 150 mg vinylstannane **5b** and 2-bromothiophene; yellow oil;  $[\alpha]_D^{26} -41.1$  (c 0.97, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.19 – 7.16 (m, 2H), 6.98 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.14 (d, *J* = 8.6 Hz, 1H), 4.78 (dq, *J* = 8.6, 6.2 Hz, 1H), 4.71 (d, *J* = 6.8 Hz, 1H), 4.64 (d, *J* = 6.8 Hz, 1H), 4.60 (d, *J* = 12.0 Hz, 1H), 4.48 (d, *J* = 12.0 Hz, 1H), 3.40 (s, 3H), 2.68 (s, 1H), 1.35 (d, *J* = 6.2 Hz, 3H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 144.1, 135.4, 130.4, 127.5, 124.45, 124.39, 94.8, 63.7, 63.7, 55.5, 23.2; FTIR (film) *v*: 3409, 2967, 2930, 1148, 1099, 1044, 698 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>11</sub>H<sub>16</sub>O<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 251.0718; found 251.0712.

**(S,Z)-4-(benzofuran-3-yl)-5-(methoxymethoxy)pent-3-en-2-ol (6bp):**



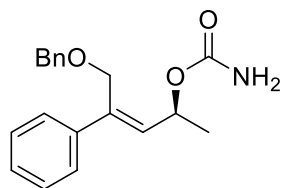
The reaction mixture was stirred at 60 °C for 24 h. Yield 76 mg (84%) starting from 150 mg vinylstannane **5b** and 2-bromothiophene; brown oil;  $[\alpha]_D^{26} -21.1$  (c 0.93,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.95 – 7.63 (m, 2H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.37 – 7.12 (m, 2H), 6.32 (d, *J* = 8.6 Hz, 1H), 4.88 (dq, *J* = 8.6, 6.3 Hz, 1H), 4.76 – 4.56 (m, 3H), 4.45 (d, *J* = 11.8 Hz, 1H), 3.39 (s, 3H), 2.74 (br s, 1H), 1.41 (d, *J* = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.6, 143.0, 137.2, 128.2, 125.8, 124.5, 123.0, 120.9, 120.8, 111.7, 94.8, 64.3, 63.6, 55.5, 23.4; FTIR (film)  $\nu$ : 3400, 2951, 2938, 1132, 1085, 1024, 707  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{15}\text{H}_{18}\text{O}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  285.3116; found 285.3114.

### 1.10. Transcarbamylation of allyl alcohols



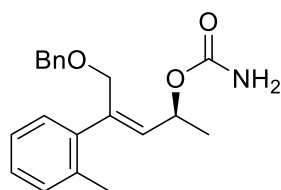
**General procedure:** A solution of alcohol **6** or **8** (0.52 mmol), phenyl carbamate (0.78 mmol), and dibutyltin maleate (16  $\mu\text{mol}$ , 3.0 mol%) in toluene was stirred at 90 °C. The progress of the reaction was followed by TLC. When the reaction was completed, the solution was cooled to 0 °C and diluted with 2 M aqueous NaOH. After stirring at 0 °C for 10 min,  $\text{CH}_2\text{Cl}_2$  and  $\text{H}_2\text{O}$  were added. The organic layer was separated and washed with 2 M aqueous NaOH,  $\text{H}_2\text{O}$ , and brine, dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude residue was purified by a column chromatography on a silica gel deactivated with  $\text{Et}_3\text{N}$  (0–50% AcOEt in hexanes).

#### (*S,Z*)-5-(Benzyloxy)-4-phenylpent-3-en-2-yl carbamate (**3aa**):



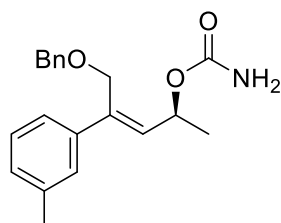
The reaction mixture was stirred for 7 h. Yield 48 mg (90%) starting from 46 mg of alcohol **6aa**; yellowish oil;  $[\alpha]_D^{20}$   $-23.1$  ( $c$  1.04,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 – 7.40 (m, 2H), 7.40 – 7.17 (m, 8H), 5.90 (d,  $J$  = 8.9 Hz, 1H), 5.82 – 5.62 (m, 1H), 4.75 (br s, 2H), 4.62 (d,  $J$  = 11.6 Hz, 1H), 4.53 (s, 2H), 4.44 (d,  $J$  = 11.6 Hz, 1H), 1.40 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 140.4, 138.7, 138.1, 132.2, 128.3, 128.3, 127.9, 127.6, 127.6, 126.6, 72.3, 68.4, 67.2, 21.3; FTIR (film)  $\nu$ : 3348, 2929, 1720, 1599, 1452, 1373, 1058, 758,  $698\text{ cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{21}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  334.1419; found 334.1411.

**(S,Z)-5-(Benzyloxy)-4-(o-tolyl)pent-3-en-2-yl carbamate (3ab):**



The reaction mixture was stirred for 6 h. Yield 49 mg (85%) starting from 50 mg of alcohol **6ab**; yellowish oil;  $[\alpha]_D^{20}$   $-9.1$  ( $c$  1.15,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.06 (m, 9H), 5.80 – 5.66 (m, 1H), 5.50 (dd,  $J$  = 9.0, 1.0 Hz, 1H), 4.74 (br s, 2H), 4.60 – 4.41 (m, 3H), 4.24 (d,  $J$  = 11.8 Hz, 1H), 2.28 (s, 3H), 1.40 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 141.4, 139.8, 138.3, 135.4, 133.4, 130.1, 128.8, 128.3, 127.6, 127.5, 127.2, 125.4, 72.5, 68.9, 68.4, 21.1, 19.9; FTIR (film)  $\nu$ : 3352, 2939, 1719, 1610, 1381, 1152, 1051,  $775\text{ cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{N}$   $[(\text{M}+\text{Na})^+]$  348.1576; found 348.1582.

**(S,Z)-5-(Benzyloxy)-4-(m-tolyl)pent-3-en-2-yl carbamate (3ac):**

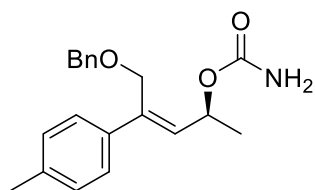


The reaction mixture was stirred for 5 h. Yield 64 mg (75%) starting from 75 mg of alcohol **6ac**; colourless oil;  $[\alpha]_D^{18}$   $-23.7$  ( $c$  3.06,  $\text{CHCl}_3$ ,  $ee$  97%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 –



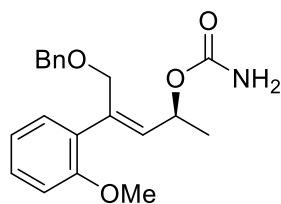
7.17 (m, 8H), 7.14 – 7.06 (m, 1H), 5.88 (d,  $J = 8.9$  Hz, 1H), 5.71 (dq,  $J = 8.9, 6.4$  Hz, 1H), 4.70 (br s, 2H), 4.59 (d,  $J = 11.6$  Hz, 1H), 4.55 (s, 2H), 4.41 (d,  $J = 11.6$  Hz, 1H), 2.35 (s, 3H), 1.40 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 140.5, 138.8, 138.1, 137.8, 132.1, 128.3, 128.2, 128.0, 127.6, 127.3, 123.7, 72.3, 68.4, 67.2, 21.5, 21.3; FTIR (film)  $\nu$ : 3486, 3349, 2926, 1721, 1602, 1454, 1372, 1046, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  348.1576; found 348.1572.

**(S,Z)-5-(Benzyloxy)-4-(*p*-tolyl)pent-3-en-2-yl carbamate (3ad):**



The reaction mixture was stirred for 5 h. Yield 67 mg (81%) starting from 67 mg of alcohol **6ad**; waxy solid;  $[\alpha]_{\text{D}}^{20} -30.5$  (c 1.05,  $\text{CHCl}_3$ ,  $ee$  97%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.19 (m, 7H), 7.13 (d,  $J = 7.8$  Hz, 2H), 5.87 (d,  $J = 9.0$  Hz, 1H), 5.71 (dq,  $J = 9.0, 6.4$  Hz, 1H), 4.69 (br s, 2H), 4.60 (d,  $J = 11.6$  Hz, 1H), 4.53 (s, 2H), 4.42 (d,  $J = 11.6$  Hz, 1H), 2.35 (s, 3H), 1.40 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 138.5, 138.2, 137.5, 137.3, 131.4, 129.0, 128.3, 127.9, 127.6, 126.4, 72.3, 68.4, 67.2, 21.4, 21.1; FTIR (film)  $\nu$ : 3350, 2931, 1732, 1611, 1381, 1147, 1033, 821  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  348.1576; found 348.1579.

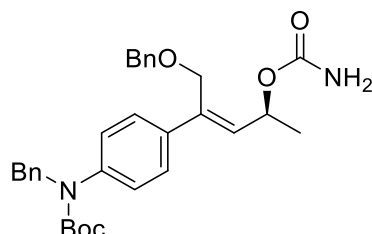
**(S,Z)-5-(Benzyloxy)-4-(2-methoxyphenyl)pent-3-en-2-yl carbamate (3ae):**



The reaction mixture was stirred for 7 h. Yield 36 mg (80%) starting from 40 mg of alcohol **6ae**; yellowish oil;  $[\alpha]_{\text{D}}^{21} -1.2$  (c 3.34,  $\text{CHCl}_3$ ,  $ee$  97%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 – 7.10 (m, 7H), 6.93 (t,  $J = 7.5$  Hz, 1H), 6.85 (d,  $J = 8.2$  Hz, 1H), 5.75 (dq,  $J = 8.8, 6.3$  Hz, 1H), 5.67 (d,  $J = 8.8$  Hz, 1H), 4.70 (br s, 2H), 4.58 (d,  $J = 12.0$  Hz, 1H), 4.49 – 4.37 (m, 3H), 3.75 (s, 3H), 1.39 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.9, 156.4, 139.2, 138.5, 133.2, 130.7, 130.4, 128.8, 128.2, 127.8, 127.4, 120.6, 110.7, 72.1, 68.4, 67.8, 55.4, 21.2; FTIR (film)  $\nu$ :

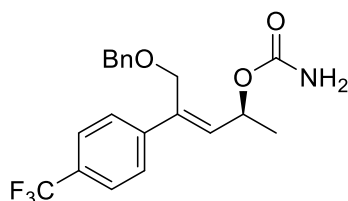
3361, 2930, 1731, 1600, 1495, 1370, 1235, 1041, 771  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{23}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  364.1525; found 364.1518.

***tert*-Butyl (*S,Z*)-benzyl(4-(4-(carbamoyloxy)-1-(methoxymethoxy)pent-2-en-2-yl)phenyl)carbamate (**3af**):**



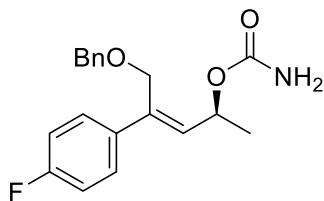
The reaction mixture was stirred for 6 h. Yield 57 mg (70%) starting from 76 mg of alcohol **6af**; yellowish oil;  $[\alpha]_{\text{D}}^{21}$   $-23.6$  (c 1.15,  $\text{CHCl}_3$ , *ee* 96%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 – 6.99 (m, 14H), 5.86 (d,  $J = 8.9$  Hz, 1H), 5.68 (dq,  $J = 8.9, 6.3$  Hz, 1H), 4.83 (s, 2H), 4.66 (br s, 2H), 4.57 (d,  $J = 11.6$  Hz, 1H), 4.50 (s, 2H), 4.39 (d,  $J = 11.6$  Hz, 1H), 1.43 (s, 9H), 1.38 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.2, 154.7, 142.2, 138.6, 138.0, 137.9, 137.7, 132.0, 128.4, 128.3, 127.9, 127.6, 127.4, 127.0, 126.8, 126.1, 80.6, 72.3, 68.3, 67.0, 53.8, 28.3, 21.3; FTIR (film)  $\nu$ : 3349, 2976, 1698, 1387, 1361, 1164, 1046, 739, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{31}\text{H}_{36}\text{N}_2\text{O}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  539.2522; found 539.2531.

**(*S,Z*)-5-(Benzyloxy)-4-(4-(trifluoromethyl)phenyl)pent-3-en-2-yl carbamate (**3ag**):**



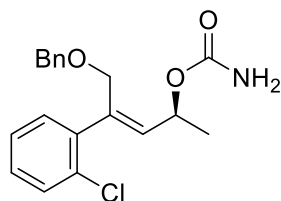
The reaction mixture was stirred for 5 h. Yield 44 mg (89%) starting from 44 mg of alcohol **6ag**; waxy solid;  $[\alpha]_{\text{D}}^{21}$   $-21.2$  (c 1.03,  $\text{CHCl}_3$ , *ee* 96%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.62 – 7.46 (m, 4H), 7.40 – 7.19 (m, 5H), 5.94 (d,  $J = 8.8$  Hz, 1H), 5.70 (dq,  $J = 8.7, 6.4$  Hz, 1H), 4.80 (br s, 2H), 4.61 (d,  $J = 11.7$  Hz, 1H), 4.53 (s, 2H), 4.43 (d,  $J = 11.7$  Hz, 1H), 1.41 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 144.0, 137.8, 137.7, 133.9, 129.5 (q,  $J = 32.4$  Hz), 128.4, 127.9, 127.8, 126.9, 125.19 (q,  $J = 3.8$  Hz), 124.75 (q,  $J = 271.5$  Hz), 72.5, 68.1, 66.8, 21.2;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$   $-62.5$ ; FTIR (film)  $\nu$ : 3362, 2941, 1726, 1611, 1372, 1129, 1039, 843  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{20}\text{NO}_3\text{F}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  402.1293; found 402.1290.

**(S,Z)-5-(benzyloxy)-4-(4-fluorophenyl)pent-3-en-2-yl carbamate (3ah):**



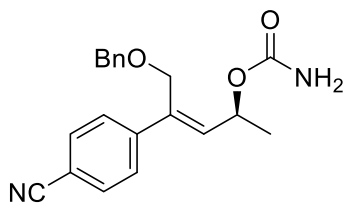
The reaction mixture was stirred for 7 h. Yield 37 mg (79%) starting from 40 mg of alcohol **6ah**; waxy solid;  $[\alpha]_D^{18} -22.2$  (c 1.07,  $\text{CHCl}_3$ , *ee* 96%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.49 – 7.22 (m, 7H), 7.08 – 6.93 (m, 2H), 5.83 (d, *J* = 8.9 Hz, 1H), 5.68 (dq, *J* = 8.9, 6.4 Hz, 1H), 4.71 (br s, 2H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.51 (s, 2H), 4.40 (d, *J* = 11.7 Hz, 1H), 1.39 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  162.4 (d, *J* = 246.6 Hz), 156.2, 138.0, 137.8, 136.4 (d, *J* = 3.3 Hz), 132.0, 128.4, 128.2 (d, *J* = 8.0 Hz), 127.9, 127.7, 115.1 (d, *J* = 21.4 Hz), 72.4, 68.3, 67.1, 21.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -114.9; FTIR (film)  $\nu$ : 3346, 2978, 2930, 2865, 1719, 1601, 1509, 1373, 1227, 1057, 833, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{19}\text{H}_{20}\text{NO}_3\text{FNa}$  [(M+Na) $^+$ ] 352.1325; found 352.1319.

**(S,Z)-5-(Benzyloxy)-4-(2-chlorophenyl)pent-3-en-2-yl carbamate (3al):**



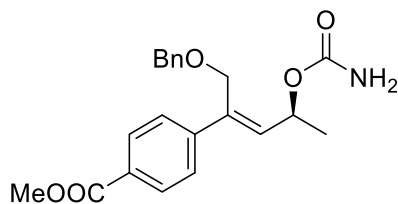
The reaction mixture was stirred for 5 h. Yield 49 mg (85%) starting from 47 mg of alcohol **6al**; yellowish oil;  $[\alpha]_D^{19} +0.2$  (c 0.99,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.33 (m, 1H), 7.32 – 7.18 (m, 8H), 5.72 (dq, *J* = 8.9, 6.4 Hz, 1H), 5.63 (d, *J* = 8.9 Hz, 1H), 4.76 (br s, 2H), 4.58 (d, *J* = 12.2 Hz, 1H), 4.49 (s, 2H), 4.40 (d, *J* = 12.2 Hz, 1H), 1.40 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 140.2, 138.2, 138.2, 134.8, 132.5, 130.8, 129.5, 128.6, 128.3, 127.6, 127.5, 126.5, 72.4, 68.1, 67.9, 21.0; FTIR (film)  $\nu$ : 3353, 2930, 1731, 1375, 1161, 1050, 772  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{19}\text{H}_{20}\text{NO}_3\text{ClNa}$  [(M+Na) $^+$ ] 368.1029; found 368.1026.

**(S,Z)-5-(Benzyloxy)-4-(4-cyanophenyl)pent-3-en-2-yl carbamate (3aj):**



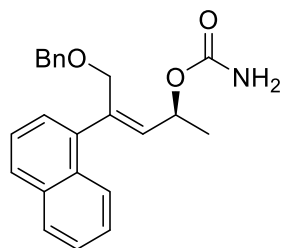
The reaction mixture was stirred for 5 h. Yield 42 mg (91%) starting from 40 mg of alcohol **6aj**; waxy solid;  $[\alpha]_D^{20} -42.6$  (c 1.00, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.64 – 7.55 (m, 2H), 7.54 – 7.46 (m, 2H), 7.38 – 7.21 (m, 5H), 5.94 (d, *J* = 8.8 Hz, 1H), 5.66 (dq, *J* = 8.8, 6.4 Hz, 1H), 4.75 (br s, 2H), 4.58 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 1.6 Hz, 2H), 4.39 (d, *J* = 11.7 Hz, 1H), 1.39 (d, *J* = 6.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.1, 145.0, 137.6, 137.3, 134.8, 132.1, 128.4, 127.9, 127.9, 127.3, 118.9, 111.1, 72.6, 68.1, 66.5, 21.1; FTIR (film) ν: 3484, 3357, 2929, 2227, 1724, 1604, 1373, 1061, 836, 740, 700 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>Na [(M+Na)<sup>+</sup>] 359.1372; found 359.1364.

**Methyl (S,Z)-4-(1-(benzyloxy)-4-(carbamoyloxy)pent-2-en-2-yl)benzoate (3ak):**



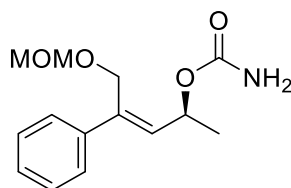
The reaction mixture was stirred for 6 h. Yield 48 mg (89%) starting from 48 mg of alcohol **6ak**; waxy solid;  $[\alpha]_D^{20} -35.1$  (c 1.13, CHCl<sub>3</sub>, ee 97%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.07 – 7.84 (m, 2H), 7.57 – 7.41 (m, 2H), 7.39 – 7.16 (m, 5H), 5.96 (d, *J* = 8.8 Hz, 1H), 5.69 (dq, *J* = 8.8, 6.4 Hz, 1H), 4.76 (br s, 2H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.52 (s, 2H), 4.42 (d, *J* = 11.6 Hz, 1H), 3.91 (s, 3H), 1.38 (d, *J* = 6.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.9, 156.2, 145.0, 137.9, 137.8, 133.9, 129.6, 129.1, 128.4, 127.9, 127.7, 126.5, 72.5, 68.2, 66.8, 52.1, 21.2; FTIR (film) ν: 3361, 2927, 1720, 1606, 1372, 1282, 1108, 1060, 702 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>21</sub>H<sub>23</sub>NO<sub>5</sub>Na [(M+Na)<sup>+</sup>] 392.1474; found 392.1516.

**(S,Z)-5-(Benzyloxy)-4-(naphthalen-1-yl)pent-3-en-2-yl carbamate (3al):**



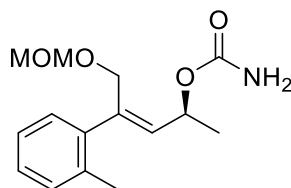
The reaction mixture was stirred for 6 h. Yield 38 mg (74%) starting from 46 mg of alcohol **6a1**; yellowish oil;  $[\alpha]_D^{20}$   $-5.8$  ( $c$  1.11,  $\text{CHCl}_3$ ,  $ee$  97%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.06 – 7.96 (m, 1H), 7.91 – 7.83 (m, 1H), 7.79 (d,  $J$  = 8.2 Hz, 1H), 7.53 – 7.40 (m, 3H), 7.40 – 7.33 (m, 1H), 7.31 – 7.17 (m, 5H), 5.86 (dq,  $J$  = 9.0, 6.3 Hz, 1H), 5.74 (dd,  $J$  = 9.0, 1.1 Hz, 1H), 4.75 (br s, 2H), 4.71 (d,  $J$  = 11.4 Hz, 1H), 4.51 (d,  $J$  = 4.0 Hz, 2H), 4.33 (d,  $J$  = 11.4 Hz, 1H), 1.48 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 139.9, 138.9, 138.2, 135.0, 133.7, 131.5, 128.3, 128.3, 127.6, 127.5, 126.0, 125.9, 125.7, 125.7, 125.2, 72.7, 69.6, 68.6, 21.2; FTIR (film)  $\nu$ : 3348, 2928, 1720, 1593, 1372, 1050, 779  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  338.1368; found 338.1356.

**(S,Z)-5-(Methoxymethoxy)-4-phenylpent-3-en-2-yl carbamate (3ba):**



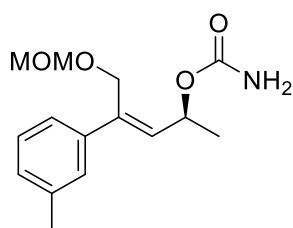
The reaction mixture was stirred for 6 h. Yield 60 mg (86%) starting from 59 mg of alcohol **6ba**; yellowish oil;  $[\alpha]_D^{17}$   $-36.5$  ( $c$  1.07,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 – 7.40 (m, 2H), 7.38 – 7.23 (m, 3H), 5.88 (d,  $J$  = 8.8 Hz, 1H), 5.72 (dq,  $J$  = 8.8, 6.4 Hz, 1H), 4.87 (br s, 2H), 4.71 – 4.58 (m, 3H), 4.50 (d,  $J$  = 11.8 Hz, 1H), 3.34 (s, 3H), 1.40 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 140.4, 138.2, 132.4, 128.3, 127.6, 126.5, 95.6, 68.3, 64.1, 55.4, 21.3; FTIR (film)  $\nu$ : 3354, 2933, 1720, 1601, 1377, 1150, 1043, 762, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{19}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  288.1212; found 288.1196.

**(S,Z)-5-(Methoxymethoxy)-4-(o-tolyl)pent-3-en-2-yl carbamate (3bb):**



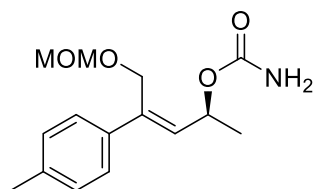
The reaction mixture was stirred for 7 h. Yield 69 mg (91%) starting from 64 mg of alcohol **6bb**; colourless oil;  $[\alpha]_D^{21} -18.3$  (c 0.97,  $\text{CHCl}_3$ ), *ee* 98%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.22 – 7.05 (m, 4H), 5.71 (dq,  $J = 8.9, 6.5$  Hz, 1H), 5.47 (d,  $J = 8.9$  Hz, 1H), 4.86 (br s, 2H), 4.64 – 4.48 (m, 3H), 4.30 (d,  $J = 11.9$  Hz, 1H), 3.24 (s, 3H), 2.28 (s, 3H), 1.40 (d,  $J = 6.5$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 141.3, 139.2, 135.3, 133.4, 130.0, 128.7, 127.2, 125.4, 95.7, 68.2, 65.7, 55.2, 21.2, 19.8; FTIR (film)  $\nu$ : 3355, 2931, 1722, 1602, 1377, 1151, 1046, 765  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  302.1368; found 302.1368.

**(S,Z)-5-(Methoxymethoxy)-4-(*m*-tolyl)pent-3-en-2-yl carbamate (3bc):**



The reaction mixture was stirred for 7 h. Yield 73 mg (91%) starting from 68 mg of alcohol **6bc**; yellowish oil;  $[\alpha]_D^{17} -42.3$  (c 0.93,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.17 (m, 3H), 7.09 (d,  $J = 6.8$  Hz, 1H), 5.86 (d,  $J = 8.8$  Hz, 1H), 5.79 – 5.64 (m, 1H), 4.84 (br s, 2H), 4.74 – 4.59 (m, 3H), 4.49 (d,  $J = 11.7$  Hz, 1H), 3.35 (s, 3H), 2.35 (s, 3H), 1.41 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 140.4, 138.3, 137.9, 132.2, 128.4, 128.2, 127.2, 123.6, 95.6, 68.4, 64.1, 55.4, 21.5, 21.3; FTIR (film)  $\nu$ : 3353, 2931, 1720, 1602, 1376, 1149, 1100, 1042, 785  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  302.1368; found 302.1357.

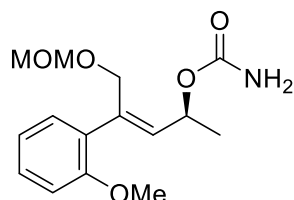
**(S,Z)-5-(Methoxymethoxy)-4-(*p*-tolyl)pent-3-en-2-yl carbamate (3bd):**



The reaction mixture was stirred for 7 h. Yield 69 mg (87%) starting from 67 mg of alcohol **6bd**; yellowish oil;  $[\alpha]_D^{21} -42.4$  (c 1.02,  $\text{CHCl}_3$ ), *ee* 98%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.29 (m, 2H), 7.13 (d,  $J = 7.8$  Hz, 2H), 5.85 (d,  $J = 8.9$  Hz, 1H), 5.78 – 5.64 (m, 1H), 4.83 (br s, 2H), 4.69 – 4.55 (m, 3H), 4.48 (d,  $J = 11.8$  Hz, 1H), 3.34 (s, 3H), 2.33 (s, 3H), 1.45 – 1.35 (m,

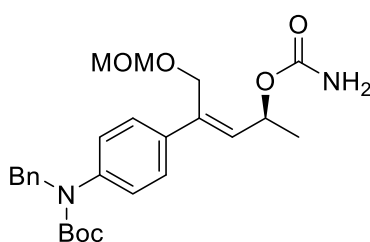
3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 138.0, 137.4, 137.4, 131.5, 129.0, 126.4, 95.5, 68.4, 64.0, 55.4, 21.4, 21.1; FTIR (film)  $\nu$ : 3353, 2932, 1722, 1601, 1377, 1150, 1045, 817  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  302.1368; found 302.1355.

**(S,Z)-5-(Methoxymethoxy)-4-(2-methoxyphenyl)pent-3-en-2-yl carbamate (3be):**



The reaction mixture was stirred for 6 h. Yield 58 mg (78%) starting from 63 mg of alcohol **6be**; yellowish oil;  $[\alpha]_{\text{D}}^{17}$   $-12.0$  ( $c$  1.02,  $\text{CHCl}_3$ ),  $ee$  98%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.32 – 7.20 (m, 1H), 7.21 – 7.12 (m, 1H), 6.98 – 6.79 (m, 2H), 5.78 – 5.67 (m, 1H), 5.63 (d,  $J$  = 8.8 Hz, 1H), 4.81 (br s, 2H), 4.68 – 4.36 (m, 4H), 3.80 (s, 3H), 3.26 (s, 3H), 1.40 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.8, 156.5, 138.6, 133.3, 130.6, 130.4, 128.8, 120.6, 110.7, 95.6, 68.3, 64.8, 55.4, 55.2, 21.3; FTIR (film)  $\nu$ : 3355, 2935, 1721, 1599, 1490, 1376, 1245, 1151, 1047, 756  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  318.1317; found 318.1306.

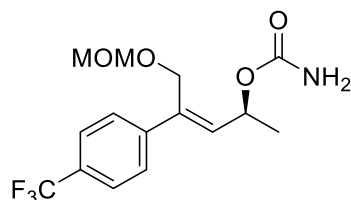
**tert-Butyl (S,Z)-benzyl(4-(4-(carbamoyloxy)-1-(methoxymethoxy)pent-2-en-2-yl)phenyl)carbamate (3bf):**



The reaction mixture was stirred for 6 h. Yield 61 mg (79%) starting from 70 mg of alcohol **6bf**; colourless oil;  $[\alpha]_{\text{D}}^{21}$   $-33.8$  ( $c$  1.10,  $\text{CHCl}_3$ ),  $ee$  98%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.31 (m, 2H), 7.31 – 7.17 (m, 5H), 7.11 (d,  $J$  = 8.2 Hz, 2H), 5.85 (d,  $J$  = 8.8 Hz, 1H), 5.69 (dq,  $J$  = 8.8, 6.3 Hz, 1H), 4.91 – 4.70 (m, 4H), 4.69 – 4.54 (m, 3H), 4.45 (d,  $J$  = 11.8 Hz, 1H), 3.30 (s, 3H), 1.45 – 1.34 (m, 12H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 154.7, 142.3, 138.6, 137.6, 137.4, 132.2, 128.4, 127.3, 127.0, 126.7, 126.1, 95.6, 80.6, 68.3, 64.0, 55.5, 53.8, 28.3, 21.3;

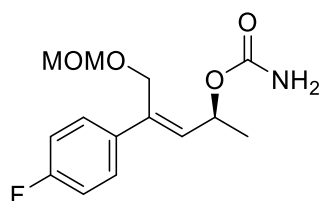
FTIR (film)  $\nu$ : 3356, 2977, 2931, 1698, 1513, 1384, 1152, 1043, 736  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_6\text{Na}$   $[(\text{M}+\text{Na})^+]$  493.2315; found 493.2310.

**(S,Z)-5-(Methoxymethoxy)-4-(4-(trifluoromethyl)phenyl)pent-3-en-2-yl carbamate (3bg):**



The reaction mixture was stirred for 7 h. Yield 78 mg (84%) starting from 82 mg of alcohol **6bg**; waxy solid;  $[\alpha]_{\text{D}}^{17}$   $-29.7$  (c 1.13,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.64 – 7.45 (m, 4H), 5.92 (d,  $J$  = 8.8 Hz, 1H), 5.71 (dq,  $J$  = 8.8, 6.5 Hz, 1H), 4.86 (br s, 2H), 4.69 – 4.56 (m, 3H), 4.49 (d,  $J$  = 12.0 Hz, 1H), 3.33 (s, 3H), 1.41 (d,  $J$  = 6.5 Hz, 1H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 144.0, 137.2, 134.1, 129.6 (q,  $J$  = 32.3 Hz), 126.9, 125.2 (q,  $J$  = 3.8 Hz), 124.7 (q,  $J$  = 271.1 Hz), 95.6, 68.1, 63.8, 55.5, 21.1;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$   $-62.6$ ; FTIR (film)  $\nu$ : 3355, 2937, 1725, 1614, 1378, 1327, 1120, 1049, 839, 604  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{18}\text{NO}_4\text{F}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  356.1086; found 356.1073.

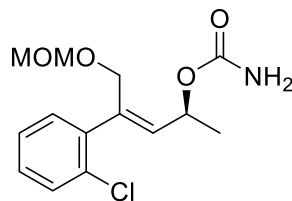
**(S,Z)-4-(4-Fluorophenyl)-5-(methoxymethoxy)pent-3-en-2-yl carbamate (3bh):**



The reaction mixture was stirred for 7 h. Yield 68 mg (93%) starting from 62 mg of alcohol **6bh**; colourless oil;  $[\alpha]_{\text{D}}^{21}$   $-35.5$  (c 1.16,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 – 7.29 (m, 2H), 7.08 – 6.91 (m, 2H), 5.81 (d,  $J$  = 8.8 Hz, 1H), 5.69 (dq,  $J$  = 8.8, 6.3 Hz, 1H), 4.87 (br s, 2H), 4.70 – 4.55 (m, 3H), 4.45 (d,  $J$  = 11.9 Hz, 1H), 3.32 (s, 3H), 1.39 (d,  $J$  = 6.3 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  162.4 (d,  $J$  = 246.6 Hz), 156.4, 137.2, 136.4 (d,  $J$  = 3.3 Hz), 132.2, 128.2 (d,  $J$  = 8.0 Hz), 115.1 (d,  $J$  = 21.4 Hz), 95.6, 68.2, 64.0, 55.5, 21.3;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$   $-114.8$ ; FTIR (film)  $\nu$ : 3355, 2934, 1722, 1602, 1510, 1377, 1228, 1152, 1046, 834  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{18}\text{NO}_4\text{FNa}$   $[(\text{M}+\text{Na})^+]$  306.1118; found 306.1108.

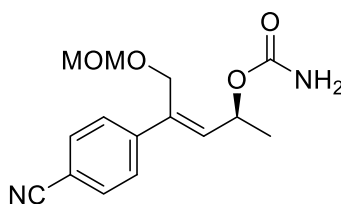


**(S,Z)-4-(2-Chlorophenyl)-5-(methoxymethoxy)pent-3-en-2-yl carbamate (3bi):**



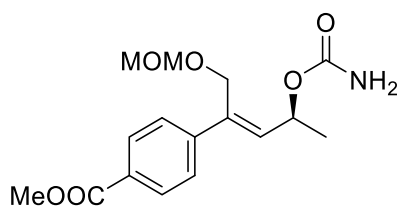
The reaction mixture was stirred for 7 h. Yield 64 mg (87%) starting from 63 mg of alcohol **6bi**; colourless oil;  $[\alpha]_D^{24} -13.4$  (c 1.00,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.30 (m, 1H), 7.25 – 7.15 (m, 3H), 5.70 (dq, *J* = 8.8, 6.4 Hz, 1H), 5.58 (d, *J* = 8.8 Hz, 1H), 4.87 (br s, 2H), 4.61 – 4.50 (m, 3H), 4.43 (d, *J* = 12.2 Hz, 1H), 3.25 (s, 3H), 1.39 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 140.1, 137.6, 134.8, 132.5, 130.8, 129.4, 128.6, 126.5, 95.6, 68.0, 64.7, 55.2, 21.0; FTIR (film)  $\nu$ : 3354, 2933, 1722, 1602, 1376, 1151, 1047, 760  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{14}\text{H}_{18}\text{NO}_4\text{ClNa}$  [(M+Na) $^+$ ] 322.0822; found 322.0809.

**(S,Z)-4-(4-Cyanophenyl)-5-(methoxymethoxy)pent-3-en-2-yl carbamate (3bj):**



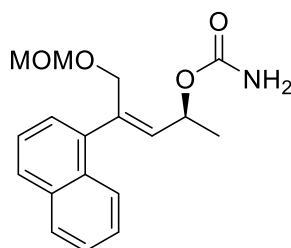
The reaction mixture was stirred for 7 h. Yield 77 mg (98%) starting from 67 mg of alcohol **6bj**; waxy solid;  $[\alpha]_D^{16} -53.5$  (c 1.03,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.70 – 7.41 (m, 4H), 5.93 (d, *J* = 8.7 Hz, 1H), 5.67 (dq, *J* = 8.7, 6.5 Hz, 1H), 4.87 (br s, 2H), 4.71 – 4.53 (m, 3H), 4.46 (d, *J* = 12.0 Hz, 1H), 3.31 (s, 3H), 1.38 (d, *J* = 6.5 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.2, 145.0, 136.8, 134.9, 132.1, 127.2, 118.8, 111.1, 95.7, 68.0, 63.6, 55.6, 21.1; FTIR (film)  $\nu$ : 3359, 2934, 2228, 1723, 1604, 1377, 1151, 1046, 837, 562  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{15}\text{H}_{18}\text{N}_2\text{O}_4\text{Na}$  [(M+Na) $^+$ ] 313.1164; found 313.1153.

**Methyl (S,Z)-4-(4-(carbamoyloxy)-1-(methoxymethoxy)pent-2-en-2-yl)benzoate (3bk):**



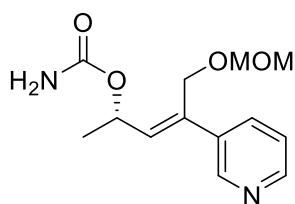
The reaction mixture was stirred for 6 h. Yield 81 mg (83%) starting from 85 mg of alcohol **6bk**; yellowish oil;  $[\alpha]_D^{22} -47.6$  (c 1.10,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.08 – 7.87 (m, 2H), 7.58 – 7.37 (m, 2H), 5.93 (d, *J* = 8.8 Hz, 1H), 5.69 (dq, *J* = 8.8, 6.4 Hz, 1H), 4.91 (br s, 2H), 4.72 – 4.55 (m, 3H), 4.48 (d, *J* = 11.9 Hz, 1H), 3.88 (s, 3H), 3.31 (s, 3H), 1.38 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.8, 156.3, 144.9, 137.4, 134.0, 129.6, 129.2, 126.5, 95.6, 68.1, 63.8, 55.5, 52.0, 21.2; FTIR (film)  $\nu$ : 3361, 2951, 1721, 1606, 1376, 1285, 1151, 1105, 1046, 774  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{16}\text{H}_{21}\text{NO}_6\text{Na}$   $[(\text{M}+\text{Na})^+]$  346.1267; found 346.1261.

**(S,Z)-5-(Methoxymethoxy)-4-(naphthalen-1-yl)pent-3-en-2-yl carbamate (3bl):**



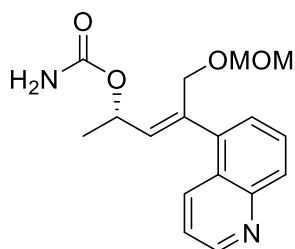
The reaction mixture was stirred for 7 h. Yield 81 mg (86%) starting from 82 mg of alcohol **6bl**; yellowish oil;  $[\alpha]_D^{24} -8.1$  (c 1.07,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.04 – 7.93 (m, 1H), 7.91 – 7.81 (m, 1H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.55 – 7.38 (m, 3H), 7.34 (d, *J* = 7.0 Hz, 1H), 5.84 (dq, *J* = 8.9, 6.4 Hz, 1H), 5.71 (dd, *J* = 8.9, 1.0 Hz, 1H), 4.84 (br s, 2H), 4.71 (dd, *J* = 11.6, 1.0 Hz, 1H), 4.59 (d, *J* = 1.7 Hz, 2H), 4.41 (d, *J* = 11.7 Hz, 1H), 3.23 (s, 3H), 1.48 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 139.7, 138.3, 135.0, 133.7, 131.5, 128.3, 127.7, 126.0, 125.8, 125.7, 125.6, 125.2, 95.9, 68.4, 66.4, 55.3, 21.2; FTIR (film)  $\nu$ : 3353, 2932, 1721, 1597, 1376, 1043, 780  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  338.1368; found 338.1356.

**(S,Z)-5-(methoxymethoxy)-4-(pyridin-3-yl)pent-3-en-2-yl carbamate (3bm):**



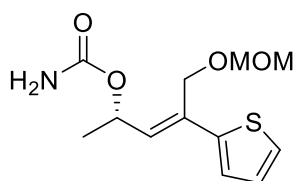
The reaction mixture was stirred for 6 h. Column chromatography: silica gel, 50–100% AcOEt in hexanes. Yield 53 mg (74%) starting from 60 mg of alcohol **6bm**; yellow oil;  $[\alpha]_D^{25}$   $-31.2$  ( $c$  0.94,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , mixture of rotamers, data for major rotamer)  $\delta$  8.65 (d,  $J$  = 2.3 Hz, 1H), 8.48 (d,  $J$  = 4.8 Hz, 1H), 7.78 – 7.65 (m, 1H), 7.29 – 7.14 (m, 1H), 5.88 (d,  $J$  = 8.8 Hz, 1H), 5.68 (dq,  $J$  = 8.8, 6.4 Hz, 1H), 4.93 (br s, 2H), 4.66 – 4.56 (m, 3H), 4.46 (d,  $J$  = 12.0 Hz, 1H), 3.30 (s, 3H), 1.38 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 148.6, 147.8, 135.9, 135.3, 133.9, 133.8, 123.1, 95.7, 68.0, 63.7, 55.5, 21.2; FTIR (film)  $\nu$ : 3351, 2929, 1724, 1609, 1374, 1150, 1043, 713  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  289.1164; found 289.1149.

**(S,Z)-5-(methoxymethoxy)-4-(quinolin-5-yl)pent-3-en-2-yl carbamate (3bn):**



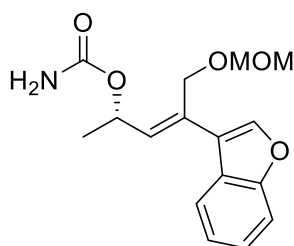
The reaction mixture was stirred for 6 h. Column chromatography: silica gel, 50–100% AcOEt in hexanes. Yield 67 mg (85%) starting from 69 mg of alcohol **6bn**; yellow oil;  $[\alpha]_D^{25}$   $-9.6$  ( $c$  1.27,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , mixture of rotamers, data for major rotamer)  $\delta$  8.99 – 8.81 (m, 1H), 8.35 (d,  $J$  = 8.6 Hz, 1H), 8.10 – 7.96 (m, 1H), 7.72 – 7.58 (m, 1H), 7.44 – 7.31 (m, 2H), 5.79 (dq,  $J$  = 8.9, 6.4 Hz, 1H), 5.66 (dd,  $J$  = 8.9, 1.0 Hz, 1H), 4.78 – 4.63 (m, 3H), 4.56 (s, 2H), 4.38 (d,  $J$  = 11.7 Hz, 1H), 3.19 (s, 3H), 1.46 (d,  $J$  = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 150.1, 148.3, 139.9, 136.8, 135.9, 134.1, 128.9, 128.7, 126.8, 126.0, 121.0, 95.9, 68.2, 66.3, 55.3, 21.1; FTIR (film)  $\nu$ : 3351, 2929, 1724, 1373, 1149, 1099, 1045, 807  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_4$   $[(\text{M}+\text{H})^+]$  317.1501; found 317.1495.

**(S,E)-5-(methoxymethoxy)-4-(thiophen-2-yl)pent-3-en-2-yl carbamate (3bo):**



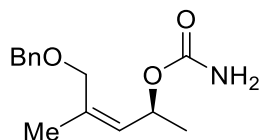
The reaction mixture was stirred for 15 h. Yield 46 mg (67%) starting from 60 mg of alcohol **6bo**; yellow oil;  $[\alpha]_D^{22} -30.3$  (c 1.89,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , mixture of rotamers in ratio 65:35)  $\delta$  7.46 – 7.41 (m, 0.65×1H), 7.36 – 7.22 (m, 0.35×2H), 7.17 (d, *J* = 4.4 Hz, 1H), 6.99 – 6.94 (m, 0.65×1H), 6.01 (d, *J* = 8.9 Hz, 0.65×1H), 5.87 (d, *J* = 8.8 Hz, 0.35×1H), 5.77 – 5.59 (m, 1H), 4.78 (s, 2H), 4.69 – 4.59 (m, 2H + 0.65×1H, 0.35×1H), 4.49 (d, *J* = 11.8 Hz, 0.35×1H), 4.46 (d, *J* = 11.7 Hz, 0.65×1H), 3.39 (s, 0.65×3H), 3.33 (s, 0.35×3H), 1.39 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ , mixture of rotamers)  $\delta$  156.34, 156.27, 143.9, 140.4, 138.2, 132.3, 132.0, 130.4, 128.3, 127.6, 127.4, 126.5, 124.7, 124.6, 95.6, 95.5, 68.4, 68.1, 64.1, 63.9, 55.5, 21.3.; FTIR (film)  $\nu$ : 3354, 2930, 1717, 1601, 1374, 1149, 1043, 700  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{12}\text{H}_{17}\text{NO}_4\text{SNa}$  [(M+Na) $^+$ ] 294.0776; found 294.0766.

**(S,Z)-4-(benzofuran-3-yl)-5-(methoxymethoxy)pent-3-en-2-yl carbamate (3bp):**



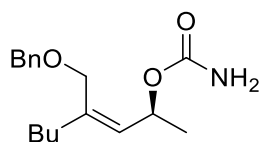
The reaction mixture was stirred for 10 h. Yield 55 mg (65%) starting from 71 mg of alcohol **6bp**;  $[\alpha]_D^{24} -39.7$  (c 3.12,  $\text{CHCl}_3$ , *ee* 98%)  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ , mixture of rotamers, data for major rotamer)  $\delta$  7.81 (s, 1H), 7.80 – 7.72 (m, 1H), 7.53 – 7.46 (m, 1H), 7.33 – 7.20 (m, 2H), 6.18 (d, *J* = 8.9 Hz, 1H), 5.80 (dq, *J* = 8.9, 6.4 Hz, 1H), 4.80 – 4.57 (m, 5H), 4.45 (d, *J* = 11.8 Hz, 1H), 3.38 (s, 3H), 1.45 (d, *J* = 6.4 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.2, 155.5, 143.3, 132.1, 129.8, 126.5, 125.9, 124.5, 122.9, 120.8, 111.7, 95.4, 68.1, 64.5, 55.6, 21.4; FTIR (film)  $\nu$ : 3353, 2930, 1720, 1452, 1375, 1149, 1101, 1043, 748  $\text{cm}^{-1}$ ; HRMS (ESI-TOF) *m/z* calcd for  $\text{C}_{16}\text{H}_{19}\text{NO}_5\text{Na}$  [(M+Na) $^+$ ] 328.1161; found 328.1154.

**(S,Z)-5-(Benzyloxy)-4-methylpent-3-en-2-yl carbamate (3am):**



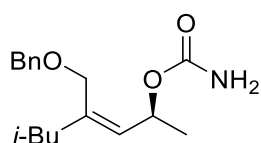
The reaction mixture was stirred for 6 h. Yield 116 mg (99%) starting from 97 mg alcohol **8a**; yellowish oil;  $[\alpha]_D^{19} +34.2$  (c 1.11,  $\text{CHCl}_3$ ), *ee* 99%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.30 (m, 4H), 7.30 – 7.24 (m, 1H), 5.53 (dq,  $J = 9.0, 6.4$  Hz, 1H), 5.36 (dq,  $J = 9.0, 1.4$  Hz, 1H), 4.67 (br s, 2H), 4.47 (s, 2H), 4.18 (d,  $J = 11.7$  Hz, 1H), 4.05 (d,  $J = 11.7$  Hz, 1H), 1.82 (d,  $J = 1.4$  Hz, 3H), 1.28 (d,  $J = 6.4$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.4, 138.4, 136.2, 128.9, 128.3, 127.7, 127.6, 72.1, 68.8, 67.9, 21.5, 21.3; FTIR (film)  $\nu$ : 3348, 2928, 1717, 1375, 1049, 739, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{19}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  272.1263; found 272.1262.

**(S,Z)-4-((benzyloxy)methyl)oct-3-en-2-yl carbamate (3a):**



The reaction mixture was stirred for 5 h. Yield 144 mg (94%) starting from 131 mg alcohol **8b**; yellowish oil;  $[\alpha]_D^{19} +18.4$  (c 1.01,  $\text{CHCl}_3$ , *ee* 97%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.34 (d,  $J = 4.4$  Hz, 4H), 7.31 – 7.24 (m, 1H), 5.55 (dq,  $J = 9.0, 6.4$  Hz, 1H), 5.36 (d,  $J = 9.0$  Hz, 1H), 4.73 (br s, 2H), 4.47 (s, 2H), 4.18 (d,  $J = 11.6$  Hz, 1H), 4.03 (d,  $J = 11.6$  Hz, 1H), 2.20 – 2.08 (m, 2H), 1.46 – 1.36 (m, 2H), 1.36 – 1.22 (m, 5H), 0.90 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 139.9, 138.4, 128.4, 128.3, 127.7, 127.5, 72.3, 68.1, 67.6, 34.7, 29.9, 22.4, 21.4, 14.0; FTIR (film)  $\nu$ : 3349, 2929, 2861, 1718, 1373, 1049, 738, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}_3\text{Na}$   $[(\text{M} + \text{Na})^+]$  314.1732; found 314.1732.

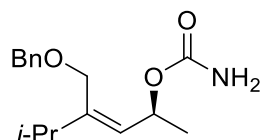
**(S,Z)-4-((Benzyloxy)methyl)-6-methylhept-3-en-2-yl carbamate (3a):**



The reaction mixture was stirred for 6 h. Yield 78 mg (90%) starting from 75 mg alcohol **8c**; waxy solid;  $[\alpha]_D^{19} +13.3$  (c 0.99,  $\text{CHCl}_3$ , *ee* 92%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.21 (m, 5H), 5.64 – 5.48 (m, 1H), 5.33 (d,  $J = 9.0$  Hz, 1H), 4.61 (br s, 2H), 4.47 (s, 2H), 4.16 (d,  $J = 11.7$  Hz, 1H), 4.01 (d,  $J = 11.7$  Hz, 1H), 2.08 – 1.89 (m, 2H), 1.85 – 1.66 (m, 1H), 1.31 (d,  $J = 6.2$

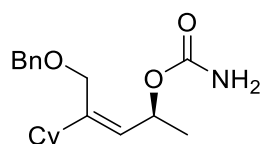
Hz, 3H), 0.86 (d,  $J = 6.6$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 138.6, 138.4, 130.0, 128.3, 127.7, 127.5, 72.2, 68.1, 67.5, 44.7, 26.1, 22.4, 22.4, 21.4; FTIR (film)  $\nu$ : 3350, 2955, 2927, 1718, 1371, 1050, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}_3\text{Na}$  [(M+Na) $^+$ ] 314.1732; found 314.1726.

**(S,Z)-4-((benzyloxy)methyl)-5-methylhex-3-en-2-yl carbamate (3ap):**



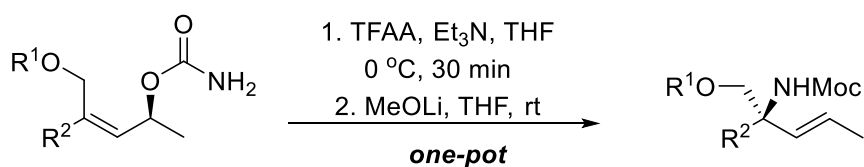
The reaction mixture was stirred for 6 h. Yield 79 mg (95%) starting from 72 mg alcohol **8d**; yellowish oil;  $[\alpha]_{\text{D}}^{23} +22.7$  (c 1.13,  $\text{CHCl}_3$ ,  $ee$  94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.19 (m, 5H), 5.68 – 5.50 (m, 1H), 5.36 (d,  $J = 8.9$  Hz, 1H), 4.58 (br s, 2H), 4.48 (d,  $J = 2.3$  Hz, 2H), 4.20 (d,  $J = 11.3$  Hz, 1H), 4.02 (d,  $J = 11.3$  Hz, 1H), 2.51 – 2.38 (m, 1H), 1.29 (d,  $J = 6.3$  Hz, 3H), 1.04 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 145.1, 138.4, 128.3, 127.7, 127.5, 126.8, 72.4, 68.4, 67.1, 32.3, 21.7, 21.5; FTIR (film)  $\nu$ : 3348, 2962, 1719, 1600, 1373, 1044, 740, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_3\text{Na}$  [(M+Na) $^+$ ] 300.1576; found 300.1572.

**(S,Z)-5-(Benzyloxy)-4-cyclohexylpent-3-en-2-yl carbamate (3aq):**



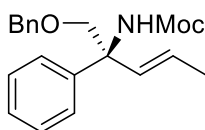
The reaction mixture was stirred for 6 h. Yield 134 mg (98%) starting from 118 mg alcohol **8e**; yellowish oil;  $[\alpha]_{\text{D}}^{23} +10.3$  (c 1.09,  $\text{CHCl}_3$ ,  $ee$  99%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.18 (m, 5H), 5.57 (dq,  $J = 8.9, 6.4$  Hz, 1H), 5.33 (d,  $J = 8.9$  Hz, 1H), 4.72 (br s, 2H), 4.47 (s, 2H), 4.19 (d,  $J = 11.3$  Hz, 1H), 4.01 (d,  $J = 11.3$  Hz, 1H), 2.14 – 1.99 (m, 1H), 1.83 – 1.62 (m, 5H), 1.38 – 1.02 (m, 8H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 144.5, 138.4, 128.3, 127.7, 127.5, 127.3, 72.3, 68.4, 67.2, 42.5, 32.3, 32.1, 26.7, 26.7, 26.3, 21.5; FTIR (film)  $\nu$ : 3348, 2925, 2852, 1719, 1599, 1451, 1374, 1051, 1051  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{27}\text{NO}_3\text{Na}$  [(M+Na) $^+$ ] 340.1889; found 340.1888.

### 1.11. [3,3]-Sigmatropic rearrangement of allyl carbamates



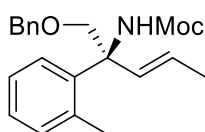
**General procedure:** To a solution of carbamate **3** (0.5 mmol) and Et<sub>3</sub>N (3 mmol, 304 mg, 418  $\mu$ L) in dry THF (10 mL) cooled to 0 °C, TFAA (1 mmol, 210 mg, 139  $\mu$ L) was added. The resulting mixture was warmed slowly to room temperature and stirred for 0.5–1 h. In a separate flask, a 1 M solution of LiHMDS (3 mmol, 3 mL) was added to a solution of MeOH (3 mmol, 96 mg, 121  $\mu$ L) in dry THF (10 mL). After 1 h, the solution of MeOLi was added to the generated allyl isocyanate and the progress of the reaction was followed by TLC. After 2 h, volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (5–10% AcOEt in hexanes).

#### Methyl (*S,E*)-(1-(benzyloxy)-2-phenylpent-3-en-2-yl)carbamate (**13aa**):



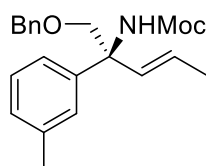
Yield 57 mg (63%) starting from 86 mg of carbamate **3aa**; yellowish oil;  $[\alpha]_D^{23}$  -26.5 (c 0.8, CHCl<sub>3</sub>), *ee* 96%; (determined by HPLC: *R<sub>t</sub>* 18.3 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.48 – 7.17 (m, 10H), 6.01 (d, *J* = 15.7 Hz, 1H), 5.78 – 5.48 (m, 2H), 4.51 (s, 2H), 3.77 (d, *J* = 9.4 Hz, 1H), 3.69 (d, *J* = 9.4 Hz, 1H), 3.61 (s, 3H), 1.78 (d, *J* = 6.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.6, 142.0, 137.7, 131.5, 128.4, 128.1, 127.8, 127.7, 127.1, 126.7, 126.5, 75.3, 73.4, 62.1, 51.8, 18.1; FTIR (film)  $\nu$ : 3348, 3347, 1737, 1501, 1245, 1027, 770 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>20</sub>H<sub>23</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 348.1576; found 348.1572; HPLC (racemate) column Chiralpak AD-H, 5% i-PrOH in hexanes, flow 0.5 mL min<sup>-1</sup>, det. 215 nm; *R<sub>t</sub>* 20.9 min (*S*-enantiomer) and 23.7 min (*R*-enantiomer).

#### Methyl (*S,E*)-(1-(benzyloxy)-2-(*o*-tolyl)pent-3-en-2-yl)carbamate (**13ab**):



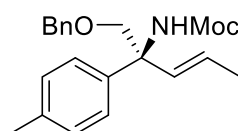
Yield 49 mg (55%) starting from 85 mg of carbamate **3ab**; waxy solid;  $[\alpha]_D^{24} -42.0$  (c 1.1, CHCl<sub>3</sub>, *ee* 95%; determined by HPLC:  $R_t$  13.5 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.43 – 7.26 (m, 6H), 7.20 – 7.08 (m, 3H), 6.10 (d, *J* = 15.8 Hz, 1H), 5.48 – 5.23 (m, 2H), 4.58 (s, 2H), 3.95 (s, 2H), 3.59 (s, 3H), 2.35 (s, 3H), 1.73 (dd, *J* = 6.5, 1.7 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.4, 139.5, 138.0, 136.3, 132.6, 132.2, 128.4, 127.8, 127.7, 127.7, 127.3, 126.2, 125.5, 73.4, 72.9, 62.8, 51.7, 22.1, 17.9; FTIR (film)  $\nu$ : 3331, 2942, 1722, 1501, 1257, 1113, 1044, 762 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>21</sub>H<sub>25</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 362.1732; found 362.1724; HPLC (racemate) column Chiracel OD-H, 5% i-PrOH in hexanes, flow 0.5 mL min<sup>-1</sup>, det. 215 nm;  $R_t$  15.2 min (*S*-enantiomer) and 17.2 min (*R*-enantiomer).

**Methyl (*S,E*)-(1-(benzyloxy)-2-(*m*-tolyl)pent-3-en-2-yl)carbamate (13ac):**



Yield 44 mg (71%) starting from 60 mg of carbamate **3ac**; colourless oil;  $[\alpha]_D^{22} -19.5$  (c 0.8, CHCl<sub>3</sub>, *ee* 93%; determined by HPLC:  $R_t$  15.9 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.41 – 7.11 (m, 8H), 7.09 – 6.98 (m, 1H), 5.99 (d, *J* = 16.0 Hz, 1H), 5.71 – 5.45 (m, 2H), 4.51 (s, 2H), 3.86 – 3.65 (m, 2H), 3.61 (s, 3H), 2.34 (s, 3H), 1.78 (dd, *J* = 6.5, 1.7 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.6, 142.0, 137.8, 137.6, 131.5, 128.4, 128.0, 127.9, 127.7, 127.7, 127.1, 126.5, 123.6, 75.3, 73.4, 62.0, 51.8, 21.7, 18.1; FTIR (film)  $\nu$ : 3348, 2946, 1749, 1479, 1253, 1109, 1038, 783, 714 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>21</sub>H<sub>25</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 362.1732; found 362.1734; HPLC (racemate) column Chiracel OD-H, 5% i-PrOH in hexanes, flow 0.5 mL min<sup>-1</sup>, det. 215 nm;  $R_t$  15.8 min (*S*-enantiomer) and 16.9 min (*R*-enantiomer).

**Methyl (*S,E*)-(1-(benzyloxy)-2-(*p*-tolyl)pent-3-en-2-yl)carbamate (13ad):**

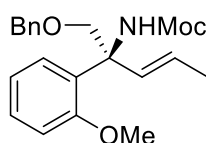


Yield 33 mg (55%) starting from 58 mg of carbamate **3ad**; yellowish oil;  $[\alpha]_D^{24} -23.8$  (c 1.4, CHCl<sub>3</sub>), *ee* 98%; (determined by HPLC:  $R_t$  37.8 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.41 – 7.20 (m, 7H), 7.11 (d, *J* = 7.9 Hz, 2H), 5.97 (d, *J* = 15.7 Hz, 1H), 5.68 – 5.47 (m, 2H), 4.50 (d, *J* = 4.1



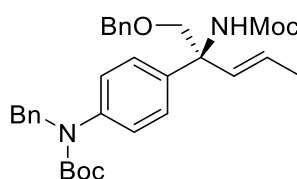
Hz, 2H), 3.79 – 3.63 (m, 2H), 3.59 (s, 3H), 2.31 (s, 3H), 1.76 (dd,  $J = 6.5, 1.8$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 139.0, 137.8, 136.6, 131.6, 128.8, 128.4, 127.7, 127.7, 126.5, 126.4, 75.3, 73.4, 61.9, 51.7, 21.0, 18.1; FTIR (film)  $\nu$ : 3342, 2949, 1726, 1487, 1252, 1111, 1029, 963  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{25}\text{NO}_3\text{Na}$   $[(\text{M} + \text{Na})^+]$  362.1730; found 362.1727; HPLC (racemate) column Chiracel OD-H, 5% i-PrOH in hexanes, flow 0.2 mL  $\text{min}^{-1}$ , det. 215 nm;  $R_t$  41.0 min (*S*-enantiomer) and 51.7 min (*R*-enantiomer).

**Methyl (*S,E*)-(1-(benzyloxy)-2-(2-methoxyphenyl)pent-3-en-2-yl)carbamate (13ae):**



Yield 38 mg (58%) starting from 63 mg of carbamate **3ae**; colourless oil;  $[\alpha]_{\text{D}}^{24} -12.4$  (c 1.4,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.12 (m, 7H), 6.97 – 6.79 (m, 2H), 5.97 (d,  $J = 15.7$  Hz, 1H), 5.72 (br s, 1H), 5.54 (dq,  $J = 15.7, 6.6$  Hz, 1H), 4.50 (s, 2H), 4.09 (d,  $J = 9.3$  Hz, 1H), 3.97 (d,  $J = 9.3$  Hz, 1H), 3.72 (s, 3H), 3.59 (s, 3H), 1.74 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.2, 155.6, 138.3, 132.2, 129.4, 128.9, 128.6, 128.2, 127.7, 127.5, 125.3, 120.5, 112.0, 73.2, 72.8, 61.9, 55.3, 51.6, 18.0; FTIR (film)  $\nu$ : 3435, 3362, 2937, 1741, 1499, 1228, 1018, 766  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{25}\text{NO}_4\text{Na}$   $[(\text{M} + \text{Na})^+]$  378.1681; found 378.1680.

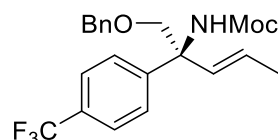
***tert*-Butyl (*S,E*)-benzyl(4-(1-(benzyloxy)-2-((methoxycarbonyl)amino)pent-3-en-2-yl)phenyl)carbamate (13af):**



Yield 49 mg (66%) starting from 72 mg of carbamate **3af**; colourless oil;  $[\alpha]_{\text{D}}^{24} -9.3$  (c 2.1,  $\text{CHCl}_3$ ,  $ee$  93%; determined by HPLC:  $R_t$  14.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.17 (m, 12H), 7.13 (d,  $J = 8.2$  Hz, 2H), 5.95 (d,  $J = 15.8$  Hz, 1H), 5.68 – 5.40 (m, 2H), 4.82 (d,  $J = 3.5$  Hz, 2H), 4.47 (s, 2H), 3.82 – 3.47 (m, 5H), 1.75 (dd,  $J = 6.5, 1.8$  Hz, 3H), 1.41 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.4, 154.8, 141.9, 139.3, 138.8, 137.7, 131.3, 128.4, 128.3, 127.8, 127.7, 127.1, 126.9, 126.9, 126.8, 125.6, 80.6, 75.2, 73.4, 61.9, 53.9, 51.7, 28.3, 18.1; FTIR

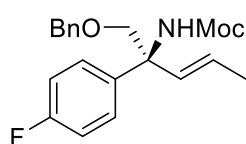
(film)  $\nu$ : 3424, 2928, 1736, 1698, 1496, 1387, 1243, 1166, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{32}\text{H}_{38}\text{N}_2\text{O}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  553.2677; found 553.2684; HPLC (racemate) column Chiracel OD-H, 5% *i*-PrOH in hexanes, flow 1  $\text{mL min}^{-1}$ , det. 215 nm;  $R_t$  17.1 min (*S*-enantiomer) and 23.5 min (*R*-enantiomer).

**Methyl (*S,E*)-(1-(benzyloxy)-2-(4-(trifluoromethyl)phenyl)pent-3-en-2-yl)carbamate (13ag):**



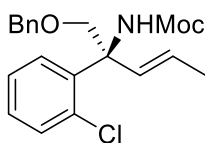
Yield 62 mg (75%) starting from 79 mg of carbamate **3ag**; waxy solid;  $[\alpha]_D^{24}$   $-14.4$  ( $c$  1.7,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.58 (d,  $J$  = 8.3 Hz, 2H), 7.51 (d,  $J$  = 8.3 Hz, 2H), 7.41 – 7.26 (m, 3H), 7.22 (d,  $J$  = 6.2 Hz, 2H), 6.01 (d,  $J$  = 15.8 Hz, 1H), 5.80 – 5.51 (m, 2H), 4.52 (s, 2H), 3.76 (d,  $J$  = 9.3 Hz, 1H), 3.70 – 3.55 (m, 4H), 1.80 (dd,  $J$  = 6.5, 1.7 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 146.2, 137.4, 130.8, 129.3 (q,  $J$  = 32.3 Hz), 128.5, 127.9, 127.7, 127.5, 127.0, 125.1 (q,  $J$  = 3.7 Hz), 124.2 (q,  $J$  = 271.9 Hz), 75.2, 73.5, 62.0, 51.9, 18.1;  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.5; FTIR (film)  $\nu$ : 3341, 2955, 1740, 1498, 1333, 1125, 1069, 831  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{22}\text{NO}_3\text{F}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  416.1449; found 416.1450.

**Methyl (*S,E*)-(1-(benzyloxy)-2-(4-fluorophenyl)pent-3-en-2-yl)carbamate (13ah):**



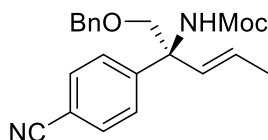
Yield 48 mg (73%) starting from 63 mg of carbamate **3ah**; colourless oil;  $[\alpha]_D^{24}$   $-19.4$  ( $c$  2.0,  $\text{CHCl}_3$ ),  $ee$  98%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.42 – 7.19 (m, 7H), 6.99 (t,  $J$  = 8.7 Hz, 2H), 5.98 (d,  $J$  = 15.8 Hz, 1H), 5.72 – 5.47 (m, 2H), 4.51 (s, 2H), 3.73 (d,  $J$  = 9.4 Hz, 1H), 3.68 – 3.43 (m, 4H), 1.78 (dd,  $J$  = 6.5, 1.7 Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  161.9 (d,  $J$  = 245.6 Hz), 155.5, 137.8, 137.6, 131.2, 128.4, 128.3 (d,  $J$  = 8.0 Hz), 127.8, 127.7, 127.0, 114.9 (d,  $J$  = 21.3 Hz), 75.3, 73.4, 61.7, 51.8, 18.1;  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -116.2; FTIR (film)  $\nu$ : 3336, 2943, 1753, 1518, 1241, 1040, 843  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{22}\text{NO}_3\text{FNa}$   $[(\text{M}+\text{Na})^+]$  366.1481; found 366.1479.

**Methyl (*S,E*)-(1-(benzyloxy)-2-(2-chlorophenyl)pent-3-en-2-yl)carbamate (13ai):**



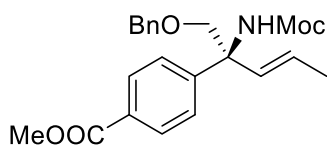
Yield 58 mg (66%) starting from 85 mg of carbamate **3ai**; waxy solid;  $[\alpha]_D^{24} -43.2$  (c 1.2, CHCl<sub>3</sub>, *ee* 97%; determined by HPLC:  $R_t$  36.1 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.50 (dd,  $J = 7.7, 2.0$  Hz, 1H), 7.40 – 7.11 (m, 8H), 5.99 (dq,  $J = 15.8, 1.7$  Hz, 1H), 5.72 – 5.45 (m, 2H), 4.55 (s, 2H), 4.11 (d,  $J = 9.4$  Hz, 1H), 3.98 (d,  $J = 9.4$  Hz, 1H), 3.59 (s, 3H), 1.78 (dd,  $J = 6.5, 1.7$  Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.2, 138.4, 137.8, 132.6, 131.7, 131.4, 129.9, 128.6, 128.4, 127.7, 127.7, 126.6, 126.5, 73.4, 72.7, 62.2, 51.8, 18.0; FTIR (film)  $\nu$ : 3351, 2947, 1729, 1500, 1256, 1031, 771 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>20</sub>H<sub>22</sub>NO<sub>3</sub>ClNa [(M+Na)<sup>+</sup>] 382.1186; found 382.1183; HPLC (racemate): column Chiralpak AS-H, 5% *i*-PrOH in hexanes, flow 0.2 mL/min, det. 215 nm; 36.6 min (*R*-enantiomer) and  $R_t$  38.9 min (*S*-enantiomer).

**Methyl (*S,E*)-(1-(benzyloxy)-2-(4-cyanophenyl)pent-3-en-2-yl)carbamate (13aj):**



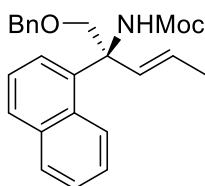
Yield 53 mg (66%) starting from 77 mg of carbamate **3aj**; yellowish oil;  $[\alpha]_D^{22} -7.5$  (c 0.8, CHCl<sub>3</sub>, *ee* 98%; determined by HPLC:  $R_t$  24.6 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.64 – 7.55 (m, 2H), 7.53 – 7.45 (m, 2H), 7.38 – 7.27 (m, 3H), 7.25 – 7.16 (m, 2H), 5.96 (d,  $J = 15.8$  Hz, 1H), 5.74 – 5.56 (m, 2H), 4.50 (s, 2H), 3.73 (d,  $J = 9.3$  Hz, 1H), 3.65 – 3.54 (m, 4H), 1.78 (dd,  $J = 6.5, 1.7$  Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.5, 147.6, 137.2, 131.9, 130.4, 128.5, 128.0, 127.8, 127.7, 127.4, 118.8, 110.9, 75.0, 73.5, 62.0, 52.0, 18.1; FTIR (film)  $\nu$ : 3418, 2918, 2227, 1730, 1500, 1246, 1097, 740 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>O<sub>3</sub>Na [(M+Na)<sup>+</sup>] 373.1528; found 373.1527; HPLC (racemate) column Chiralcel OD-H, 5% *i*-PrOH in hexanes, flow 1 mL/min, det. 215 nm;  $R_t$  23.0 min (*S*-enantiomer) and 27.1 min (*R*-enantiomer).

**Methyl (*S,E*)-4-(1-(benzyloxy)-2-((methoxycarbonyl)amino)pent-3-en-2-yl)benzoate (13ak):**



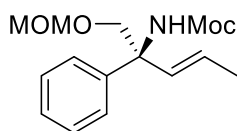
Yield 35 mg (75%) starting from 45 mg of carbamate **3ak**; waxy solid;  $[\alpha]_D^{21} -10.9$  (c 1.03,  $\text{CHCl}_3$ , *ee* 98%; determined by HPLC:  $R_t$  18.7 min);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.1 – 7.9 (m, 2H), 7.5 – 7.4 (m, 2H), 7.4 – 7.2 (m, 3H), 7.2 – 7.1 (m, 2H), 6.0 (d,  $J = 15.9$  Hz, 1H), 5.7 – 5.5 (m, 2H), 4.5 (s, 2H), 3.9 (s, 3H), 3.8 (d,  $J = 9.4$  Hz, 1H), 3.7 – 3.5 (m, 4H), 1.8 (dd,  $J = 6.5, 1.7$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.9, 155.5, 147.3, 137.4, 130.9, 129.4, 128.9, 128.4, 127.9, 127.7, 127.3, 126.6, 75.1, 73.5, 62.1, 52.0, 51.9, 18.1; FTIR (film)  $\nu$ : 3419, 2951, 1724, 1497, 1281, 1105, 703  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{25}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  406.1630; found 406.1627; HPLC (racemate) column Chiracel OD-H, 5% *i*-PrOH in hexanes, flow 1 mL/min, det. 235 nm;  $R_t$  18.7 min (*S*-enantiomer) and 23.4 min (*R*-enantiomer).

#### Methyl (*S,E*)-1-(benzyloxy)-2-(naphthalen-1-yl)pent-3-en-2-ylcarbamate (**13al**):



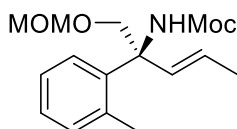
Yield 36 mg (70%) starting from 49 mg of carbamate **3al**; yellowish oil;  $[\alpha]_D^{23} -43.7$  (c 1.1,  $\text{CHCl}_3$ , *ee* 97%; determined by HPLC:  $R_t$  23.7 min);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  8.34 (d,  $J = 7.6$  Hz, 1H), 7.94 – 7.79 (m, 1H), 7.78 (d,  $J = 8.1$  Hz, 1H), 7.64 (d,  $J = 7.4$  Hz, 1H), 7.49 – 7.10 (m, 8H), 6.31 (d,  $J = 15.8$  Hz, 1H), 5.57 (br s, 1H), 5.39 (dq,  $J = 15.8, 6.6$  Hz, 1H), 4.58 (s, 2H), 4.29 – 3.96 (m, 2H), 3.56 (s, 3H), 1.70 (dd,  $J = 6.6, 1.7$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 138.0, 136.8, 134.9, 132.6, 130.7, 129.2, 129.0, 128.4, 127.8, 127.7, 127.2, 126.6, 126.2, 125.1, 124.9, 124.8, 73.4, 73.0, 63.3, 51.7, 18.0; FTIR (film)  $\nu$ : 3339, 2954, 1720, 1500, 1234, 1040, 785  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{24}\text{H}_{25}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  398.1732; found 398.1731; HPLC (racemate) column Chiralpak AD-H, 5% *i*-PrOH in hexanes, flow 0.5 mL/min, det. 215 nm;  $R_t$  22.2 min (*S*-enantiomer) and 25.8 min (*R*-enantiomer).

#### Methyl (*S,E*)-1-(methoxymethoxy)-2-phenylpent-3-en-2-ylcarbamate (**13ba**):



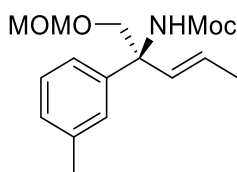
Yield 43 mg (85%) starting from 48 mg of carbamate **3ba**; yellowish oil;  $[\alpha]_D^{22}$   $-21.8$  (c 0.8,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.50 – 7.17 (m, 5H), 6.00 (d,  $J = 15.8$  Hz, 1H), 5.80 – 5.53 (m, 2H), 4.78 – 4.42 (m, 2H), 4.05 – 3.74 (m, 2H), 3.61 (s, 3H), 3.28 (s, 3H), 1.78 (dd,  $J = 6.5, 1.7$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.4, 141.8, 131.5, 128.1, 127.1, 126.7, 126.4, 96.8, 73.4, 61.9, 55.5, 51.8, 18.1; FTIR (film)  $\nu$ : 3341, 3341, 1735, 1497, 1245, 1037, 774, 701  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  302.1368; found 302.1372.

**Methyl (S,E)-1-(methoxymethoxy)-2-(o-tolyl)pent-3-en-2-yl carbamate (13bb):**



Yield 44 mg (74%) starting from 57 mg of carbamate **3bb**; waxy solid;  $[\alpha]_D^{23}$   $-28.9$  (c 1.1,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 – 7.31 (m, 1H), 7.22 – 7.05 (m, 3H), 6.07 (d,  $J = 15.8$  Hz, 1H), 5.49 – 5.24 (m, 2H), 4.66 (s, 2H), 4.09 (s, 2H), 3.59 (s, 3H), 3.35 (s, 3H), 2.39 (s, 3H), 1.72 (dd,  $J = 6.5, 1.7$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.3, 139.4, 136.3, 132.6, 132.2, 127.5, 127.4, 126.4, 125.6, 96.9, 71.1, 62.5, 55.5, 51.7, 22.1, 17.9; FTIR (film)  $\nu$ : 3339, 2948, 1731, 1500, 1247, 1109, 1040, 732  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  316.1525; found 316.1527.

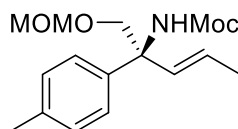
**Methyl (S,E)-1-(methoxymethoxy)-2-(m-tolyl)pent-3-en-2-yl carbamate (13bc):**



Yield 52 mg (74%) starting from 67 mg of carbamate **3bc**; colourless oil;  $[\alpha]_D^{22}$   $-19.5$  (c 0.8,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27 – 7.14 (m, 3H), 7.11 – 6.99 (m, 1H), 5.99 (dd,  $J = 15.7, 1.8$  Hz, 1H), 5.73 – 5.53 (m, 2H), 4.69 – 4.49 (m, 2H), 3.98 – 3.77 (m, 2H), 3.61 (s, 3H), 3.30 (s, 3H), 2.34 (s, 3H), 1.78 (dd,  $J = 6.5, 1.8$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 141.8, 137.6, 131.6, 128.0, 127.9, 127.0, 126.5, 123.5, 96.8, 73.3, 61.8, 55.5, 51.8,

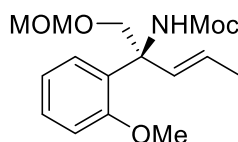
21.6, 18.1; FTIR (film)  $\nu$ : 3344, 2948, 1736, 1498, 1240, 1108, 1038, 780, 704  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{Na}$  [(M+Na) $^+$ ] 316.1525; found 316.1520.

**Methyl (*S,E*)-(1-(methoxymethoxy)-2-(*p*-tolyl)pent-3-en-2-yl)carbamate (13ad):**



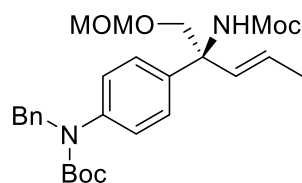
Yield 50 mg (77%) starting from 62 mg of carbamate **3ad**; yellowish oil;  $[\alpha]_{\text{D}}^{22}$  -13.2 (c 1.1,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 – 7.29 (m, 2H), 7.17 (d,  $J$  = 7.9 Hz, 2H), 6.02 (d,  $J$  = 15.4 Hz, 1H), 5.78 – 5.59 (m, 2H), 4.74 – 4.54 (m, 2H), 3.93 (d,  $J$  = 9.9 Hz, 1H), 3.86 (d,  $J$  = 9.9 Hz, 1H), 3.65 (s, 3H), 3.35 (s, 3H), 2.36 (s, 3H), 1.83 (dd,  $J$  = 6.5, 1.8 Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{cdcl}_3$ )  $\delta$  155.4, 138.8, 136.7, 131.6, 128.9, 126.5, 126.3, 96.8, 73.4, 61.6, 55.5, 51.8, 21.0, 18.1; FTIR (film)  $\nu$ : 3343, 2948, 1736, 1499, 1244, 1108, 1038, 972  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_4\text{Na}$  [(M+Na) $^+$ ] 316.1525; found 316.1516.

**Methyl (*S,E*)-(1-(methoxymethoxy)-2-(2-methoxyphenyl)pent-3-en-2-yl)carbamate (13ae):**



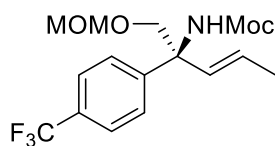
Yield 41 mg (76%) starting from 52 mg of carbamate **3ae**; colourless oil;  $[\alpha]_{\text{D}}^{22}$  -13.9 (c 2.0,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 (d,  $J$  = 7.8 Hz, 1H), 7.29 – 7.20 (m, 1H), 7.00 – 6.85 (m, 2H), 5.96 (dq,  $J$  = 15.7, 1.7 Hz, 1H), 5.75 (br s, 1H), 5.55 (dq,  $J$  = 15.7, 6.5 Hz, 1H), 4.65 – 4.52 (m, 2H), 4.23 (d,  $J$  = 9.7 Hz, 1H), 4.09 (d,  $J$  = 9.7 Hz, 1H), 3.80 (s, 3H), 3.59 (s, 3H), 3.28 (s, 3H), 1.74 (dd,  $J$  = 6.5, 1.7 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.2, 155.5, 132.2, 129.3, 128.7, 125.3, 120.6, 112.1, 96.8, 71.0, 61.7, 55.5, 55.3, 51.6, 17.9; FTIR (film)  $\nu$ : 3430, 3357, 2947, 1734, 1493, 1241, 1038, 755  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_5\text{Na}$  [(M+Na) $^+$ ] 332.1474; found 332.1473.

***tert*-Butyl (*S,E*)-benzyl(4-(3-oxo-5-(prop-1-en-1-yl)-2,7,9-trioxa-4-azadecan-5-yl)phenyl)carbamate (13af):**



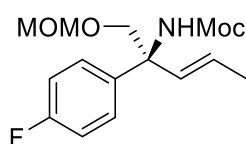
Yield 43 mg (77%) starting from 55 mg of carbamate **3af**; colourless oil;  $[\alpha]_D^{21} -3.3$  (c 1.2,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.33 – 7.25 (m, 4H), 7.25 – 7.18 (m, 3H), 7.13 (d,  $J = 8.3$  Hz, 2H), 5.94 (dd,  $J = 15.8, 1.7$  Hz, 1H), 5.71 – 5.48 (m, 2H), 4.81 (d,  $J = 2.2$  Hz, 2H), 4.66 – 4.47 (m, 2H), 3.84 (d,  $J = 9.8$  Hz, 1H), 3.78 (d,  $J = 9.8$  Hz, 1H), 3.59 (s, 3H), 3.24 (s, 3H), 1.75 (dd,  $J = 6.5, 1.7$  Hz, 3H), 1.40 (s, 9H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.4, 154.8, 141.9, 139.2, 138.8, 131.4, 128.3, 127.1, 126.9, 126.9, 126.8, 125.7, 96.8, 80.6, 73.2, 61.6, 55.5, 53.9, 51.8, 28.2, 18.0; FTIR (film)  $\nu$ : 3345, 2931, 1699, 1511, 1387, 1247, 1165, 1037, 700  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{27}\text{H}_{36}\text{N}_2\text{O}_6\text{Na}$  [(M+Na) $^+$ ] 507.2471; found 507.2482.

**Methyl (S,E)-1-(1-(methoxymethoxy)-2-(4-(trifluoromethyl)phenyl)pent-3-en-2-yl)carbamate (13bg):**



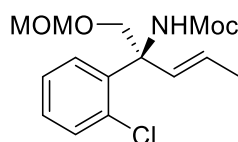
Yield 57 mg (77%) starting from 72 mg of carbamate **3bg**; colourless oil;  $[\alpha]_D^{22} -7.4$  (c 0.8,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.58 (d,  $J = 8.4$  Hz, 2H), 7.52 (d,  $J = 8.3$  Hz, 2H), 5.99 (dd,  $J = 15.9, 1.8$  Hz, 1H), 5.78 – 5.59 (m, 2H), 4.67 – 4.51 (m, 2H), 3.87 (d,  $J = 9.9$  Hz, 1H), 3.77 (d,  $J = 9.9$  Hz, 1H), 3.61 (s, 3H), 3.28 (s, 3H), 1.79 (dd,  $J = 6.5, 1.8$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.5, 146.0, 130.8, 129.3 (q,  $J = 32.4$  Hz), 127.5, 126.9, 125.1 (q,  $J = 3.9$  Hz), 124.2 (q,  $J = 272.2$  Hz), 96.8, 73.4, 61.7, 55.6, 51.9, 18.1;  $^{19}\text{F NMR}$  (376 MHz,  $\text{CDCl}_3$ )  $\delta$  – 62.5; FTIR (film)  $\nu$ : 3336, 2950, 1734, 1501, 1328, 1248, 1123, 1070, 843  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{20}\text{NO}_4\text{F}_3\text{Na}$  [(M+Na) $^+$ ] 370.1242; found 370.1245.

**Methyl (S,E)-2-(4-fluorophenyl)-1-(methoxymethoxy)pent-3-en-2-yl carbamate (13bh):**



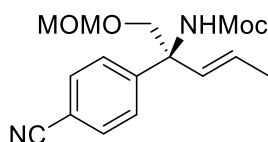
Yield 42 mg (71%) starting from 56 mg of carbamate **3bh**; colourless oil;  $[\alpha]_D^{23} -15.4$  (c 2.1, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.47 – 7.28 (m, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 5.97 (dd, *J* = 15.3, 1.7 Hz, 1H), 5.76 – 5.53 (m, 2H), 4.70 – 4.47 (m, 2H), 3.85 (d, *J* = 9.9 Hz, 1H), 3.76 (d, *J* = 9.9 Hz, 1H), 3.60 (s, 3H), 3.28 (s, 3H), 1.78 (dd, *J* = 6.5, 1.7 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  161.9 (d, *J* = 245.6 Hz), 155.5, 137.6, 131.3, 128.2 (d, *J* = 8.1 Hz), 127.0, 114.9 (d, *J* = 21.3 Hz), 96.8, 73.5, 61.4, 55.5, 51.8, 18.0; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  -116.1; FTIR (film)  $\nu$ : 3337, 2948, 1733, 1508, 1240, 1037, 837 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>4</sub>FNa [(M+Na)<sup>+</sup>] 320.1274; found 320.1273.

**Methyl (S,E)-2-(2-chlorophenyl)-1-(methoxymethoxy)pent-3-en-2-yl)carbamate (13bi):**



Yield 42 mg (76%) starting from 53 mg of carbamate **3bi**; waxy solid;  $[\alpha]_D^{20} -39.2$  (c 1.0, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.50 (d, *J* = 7.7 Hz, 1H), 7.34 (d, *J* = 7.7 Hz, 1H), 7.29 – 7.14 (m, 2H), 5.97 (dd, *J* = 15.8, 1.7 Hz, 1H), 5.74 – 5.50 (m, 2H), 4.71 – 4.55 (m, 2H), 4.25 (d, *J* = 9.8 Hz, 1H), 4.08 (d, *J* = 9.8 Hz, 1H), 3.59 (s, 3H), 3.32 (s, 3H), 1.77 (dd, *J* = 6.6, 1.7 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.2, 138.3, 132.6, 131.8, 131.4, 129.8, 128.7, 126.7, 126.5, 96.8, 71.0, 61.9, 55.5, 51.8, 18.0; FTIR (film)  $\nu$ : 3345, 2949, 1731, 1502, 1246, 1039, 761 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>4</sub>ClNa [(M+Na)<sup>+</sup>] 336.0979; found 336.0983.

**Methyl (S,E)-2-(4-cyanophenyl)-1-(methoxymethoxy)pent-3-en-2-yl)carbamate (13bj):**

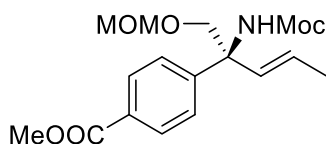


Yield 56 mg (77%) starting from 70 mg of carbamate **3bj**; yellowish oil;  $[\alpha]_D^{22} +0.8$  (c 1.0, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.64 – 7.56 (m, 2H), 7.55 – 7.45 (m, 2H), 5.95 (dq, *J* = 15.7, 1.7 Hz, 1H), 5.81 – 5.57 (m, 2H), 4.65 – 4.48 (m, 2H), 3.83 (d, *J* = 9.9 Hz, 1H), 3.72 (d, *J* = 9.9 Hz, 1H), 3.59 (s, 3H), 3.26 (s, 3H), 1.78 (dd, *J* = 6.5, 1.7 Hz, 3H); <sup>13</sup>C NMR (101



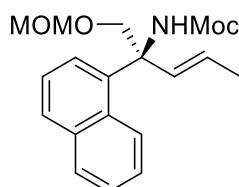
MHz, CDCl<sub>3</sub>)  $\delta$  155.5, 147.5, 131.9, 130.4, 127.8, 127.4, 118.8, 111.0, 96.8, 73.3, 61.7, 55.6, 52.0, 18.1; FTIR (film)  $\nu$ : 3340, 2950, 2228, 1730, 1504, 1249, 1038, 573 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>Na [(M+Na)<sup>+</sup>] 327.1321; found 327.1325.

**Methyl (S,E)-4-(3-oxo-5-(prop-1-en-1-yl)-2,7,9-trioxa-4-azadecan-5-yl)benzoate (13bk):**



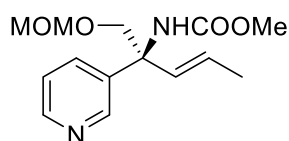
Yield 51 mg (73%) starting from 77 mg of carbamate **3bk**; waxy solid;  $[\alpha]_D^{22}$  -1.9 (c 1.0, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.04 – 7.91 (m, 2H), 7.54 – 7.38 (m, 2H), 5.98 (dd,  $J$  = 15.8, 1.8 Hz, 1H), 5.74 – 5.58 (m, 2H), 4.68 – 4.47 (m, 2H), 3.94 – 3.74 (m, 5H), 3.60 (s, 3H), 3.26 (s, 3H), 1.78 (dd,  $J$  = 6.5, 1.8 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  166.8, 155.5, 147.2, 131.0, 129.4, 129.0, 127.3, 126.5, 96.8, 73.3, 61.8, 55.6, 52.0, 51.9, 18.1; FTIR (film)  $\nu$ : 3348, 2952, 1724, 1504, 1281, 1110, 1038, 776 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>6</sub>Na [(M+Na)<sup>+</sup>] 360.1423; found 360.1429.

**Methyl (S,E)-1-(methoxymethoxy)-2-(naphthalen-1-yl)pent-3-en-2-yl)carbamate (13bl):**



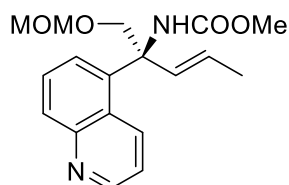
Yield 59 mg (82%) starting from 69 mg of carbamate **3bl**; waxy solid;  $[\alpha]_D^{23}$  -26.2 (c 1.0, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.49 – 8.30 (m, 1H), 7.92 – 7.73 (m, 2H), 7.73 – 7.61 (m, 1H), 7.52 – 7.34 (m, 3H), 6.33 (d,  $J$  = 15.8 Hz, 1H), 5.58 (br s, 1H), 5.41 (dq,  $J$  = 15.8, 6.5 Hz, 1H), 4.70 – 4.65 (m, 2H), 4.39 – 4.20 (m, 2H), 3.57 (s, 3H), 3.35 (s, 3H), 1.71 (dd,  $J$  = 6.5, 1.7 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.4, 136.8, 134.9, 132.6, 130.7, 129.2, 129.0, 127.4, 126.7, 126.0, 125.2, 125.0, 124.8, 97.0, 71.3, 63.0, 55.5, 51.8, 18.0; FTIR (film)  $\nu$ : 3332, 2947, 1727, 1506, 1244, 1039, 779 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>19</sub>H<sub>23</sub>NO<sub>4</sub>Na [(M+Na)<sup>+</sup>] 352.1525; found 352.1530.

**Methyl (S,E)-(1-(methoxymethoxy)-2-(pyridin-3-yl)pent-3-en-2-yl)carbamate (13bm):**



To a solution of carbamate **3bm** (0.2 mmol, 54 mg), PPh<sub>3</sub> (0.3 mmol, 79 mg), and Et<sub>3</sub>N (0.4 mmol, 40 mg, 56  $\mu$ L) in dry CH<sub>2</sub>Cl<sub>2</sub> (4 mL) cooled to 0 °C, CBr<sub>4</sub> (0.32 mmol, 106 mg) was added portionwise. The resulting mixture was warmed slowly to room temperature and stirred for 16 h. After that, dry MeOH (5 mL) and *n*-Bu<sub>3</sub>SnOMe (10 mol%, 0.02 mmol, 6.5 mg) were added to the generated allyl isocyanate and the progress of the reaction was followed by TLC. After 5 h, volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (20–60% AcOEt in hexanes). Yield 43 mg (78%); yellow oil; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>, mixture of rotamers, data for major rotamer) <sup>13</sup>C NMR (101 MHz, DMSO)  $\delta$  156.5, 148.5, 147.5, 134.7, 134.5, 131.9, 129.1, 123.9, 95.5, 66.6, 63.3, 55.3, 46.2, 21.6; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>Na [(M+Na)<sup>+</sup>] 303.1321; found 303.1318.

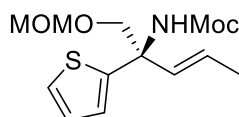
**Methyl (S,E)-(1-(methoxymethoxy)-2-(quinolin-5-yl)pent-3-en-2-yl)carbamate (13bn):**



To a solution of carbamate **3z** (0.25 mmol, 80 mg), PPh<sub>3</sub> (0.38 mmol, 98 mg), and Et<sub>3</sub>N (0.5 mmol, 51 mg, 70  $\mu$ L) in dry CH<sub>2</sub>Cl<sub>2</sub> (5 mL) cooled to 0 °C, CBr<sub>4</sub> (0.4 mmol, 133 mg) was added portionwise. The resulting mixture was warmed slowly to room temperature and stirred for 16 h. After that, dry MeOH (5 mL) and Bu<sub>3</sub>SnOMe (10 mol%) were added to the generated allyl isocyanate and the progress of the reaction was followed by TLC. After 5 h, volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (20–60% AcOEt in hexanes). Yield 49 mg (60%); yellow oil; <sup>1</sup>H NMR (400 MHz, DMSO, mixture of rotamers, data for major rotamer)  $\delta$  8.92 – 8.82 (m, 1H), 8.42 – 8.26 (m, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 7.70 (dd, *J* = 8.4, 7.1 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.46 – 7.37 (m, 1H), 6.51 (s, 2H), 4.65 – 4.55 (m, 1H), 4.48 (s, 2H), 4.35 (d, *J* = 11.9 Hz,

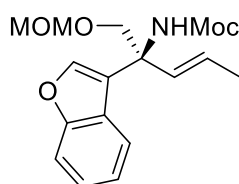
1H), 3.07 (s, 3H), 1.37 (d,  $J = 6.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz, DMSO)  $\delta$  156.7, 150.7, 148.3, 140.3, 136.6, 136.2, 134.1, 129.3, 128.8, 126.7, 126.3, 121.8, 95.7, 66.8, 66.2, 55.1, 21.5; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}_4\text{Na}$  [(M+Na) $^+$ ] 353.1477; found 353.1475.

**Methyl (*R,E*)-(1-(methoxymethoxy)-2-(thiophen-2-yl)pent-3-en-2-yl)carbamate (13bo)**



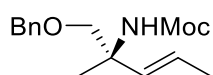
MeOH (5 mL) and  $\text{Bu}_3\text{SnOMe}$  (10 mol%) were used as a nucleophile instead of MeOLi. Yield 72 mg (79%) starting from 88 mg of carbamate **3bo**; yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , mixture of rotamers, data for major rotamer)  $\delta$  7.22 – 7.17 (m, 1H), 7.04 – 6.98 (m, 1H), 6.97 – 6.91 (m, 1H), 5.96 (dq,  $J = 15.5, 1.7$  Hz, 1H), 5.74 – 5.54 (m, 2H), 4.63 (d,  $J = 3.0$  Hz, 2H), 3.91 (d,  $J = 1.7$  Hz, 2H), 3.61 (s, 3H), 3.33 (s, 3H), 1.77 (dd,  $J = 6.5, 1.7$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.3, 146.9, 131.4, 128.1, 127.1, 126.5, 124.6, 96.9, 73.7, 60.1, 55.6, 51.9, 17.9; FTIR (film)  $\nu$ : 3337, 2921, 1736, 1497, 1244, 1148, 1111, 1038, 700  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{19}\text{NO}_4\text{SNa}$  [(M+Na) $^+$ ] 308.0932; found 308.0926.

**Methyl (*S,E*)-(2-(benzofuran-3-yl)-1-(methoxymethoxy)pent-3-en-2-yl)carbamate (13bp)**



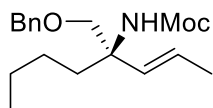
Yield 54 mg (85%) starting from 62 mg of carbamate **3bp**; yellow oil;  $[\alpha]_D^{23} +73.2$  (c 2.4,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.71 – 7.12 (m, 5H), 5.99 (d,  $J = 15.7$  Hz, 1H), 5.79 – 5.46 (m, 2H), 4.63 (s, 2H), 4.17 – 3.92 (m, 2H), 3.59 (s, 3H), 3.30 (s, 3H), 1.76 (d,  $J = 6.6$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 142.9, 131.5, 128.2, 127.6, 126.4, 125.9, 124.2, 122.5, 121.3, 111.7, 96.9, 71.8, 58.1, 55.5, 51.8, 17.9; FTIR (film)  $\nu$ : 3335, 2950, 1733, 1502, 1452, 1244, 1107, 1039, 748  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{21}\text{NO}_5\text{Na}$  [(M+Na) $^+$ ] 342.1317; found 342.1308.

**Methyl (*R,E*)-(1-(benzyloxy)-2-methylpent-3-en-2-yl)carbamate (13am):**



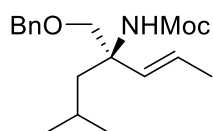
Yield 40 mg (80%) starting from 48 mg of carbamate **3am**; yellowish oil;  $[\alpha]_D^{21} -0.3$  (c 1.0, CHCl<sub>3</sub>, ee 99%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.46 – 7.18 (m, 5H), 5.70 – 5.50 (m, 2H), 5.14 (br s, 1H), 4.53 (d, *J* = 1.7 Hz, 2H), 3.61 (s, 3H), 3.45 (d, *J* = 9.1 Hz, 1H), 3.37 (d, *J* = 9.1 Hz, 1H), 1.77 – 1.63 (m, 3H), 1.42 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.6, 138.1, 133.5, 128.4, 127.7, 127.6, 124.7, 76.0, 73.3, 56.0, 51.5, 22.2, 17.9; FTIR (film)  $\nu$ : 3347, 2935, 1730, 1500, 1247, 1095, 965, 738, 699 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>21</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 286.1419; found 286.1414.

**Methyl (*R,E*)-(4-((benzyloxy)methyl)oct-2-en-4-yl)carbamate (13an):**



Yield 46 mg (84%) starting from 53 mg of carbamate **3an**; yellowish oil;  $[\alpha]_D^{21} -0.7$  (c 1.0, CHCl<sub>3</sub>, ee 97%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.40 – 7.24 (m, 5H), 5.61 – 5.46 (m, 2H), 4.97 (br s, 1H), 4.52 (s, 2H), 3.61 (s, 3H), 3.56 (s, 2H), 1.90 – 1.64 (m, 5H), 1.36 – 1.13 (m, 4H), 0.88 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.5, 138.3, 132.6, 128.3, 127.6, 124.4, 73.5, 73.3, 58.8, 51.5, 35.3, 25.6, 23.0, 18.0, 14.0; FTIR (film)  $\nu$ : 2955, 2930, 1732, 1500, 1244, 1100, 736 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>18</sub>H<sub>27</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 328.1889; found 328.1879.

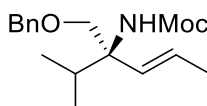
**Methyl (*R,E*)-(4-((benzyloxy)methyl)-6-methylhept-2-en-4-yl)carbamate (13ao):**



Yield 37 mg (75%) starting from 47 mg of carbamate **3ao**; yellowish oil;  $[\alpha]_D^{21} +0.6$  (c 1.7, CHCl<sub>3</sub>, ee 92%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.42 – 7.19 (m, 5H), 5.66 – 5.41 (m, 2H), 4.95 (s, 1H), 4.52 (s, 2H), 3.70 – 3.47 (m, 5H), 1.85 – 1.74 (m, 1H), 1.72 (d, *J* = 4.9 Hz, 3H), 1.70 – 1.59 (m, 2H), 0.90 (d, *J* = 4.5 Hz, 3H), 0.89 (d, *J* = 4.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  155.5, 138.3, 133.2, 128.3, 127.6, 127.6, 124.0, 73.9, 73.3, 59.2, 51.5, 44.0, 24.6, 24.5, 23.8, 18.0;

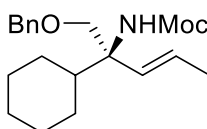
FTIR (film)  $\nu$ : 3425, 3354, 2953, 1731, 1501, 1237, 1100, 737, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{27}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  328.1889; found 328.1887.

**Methyl (*R,E*)-(3-((benzyloxy)methyl)-2-methylhex-4-en-3-yl)carbamate (13ap):**



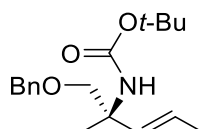
Yield 45 mg (61%) starting from 70 mg of carbamate **3ap**; yellowish oil;  $[\alpha]_{\text{D}}^{21}$   $-11.4$  (c 1.0,  $\text{CHCl}_3$ ), *ee* 94%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.44 – 7.15 (m, 5H), 5.67 – 5.33 (m, 2H), 4.91 (s, 1H), 4.52 (s, 2H), 3.73 (s, 2H), 3.60 (s, 3H), 2.45 – 2.22 (m, 1H), 1.73 (d,  $J = 4.4$  Hz, 3H), 0.98 – 0.68 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.7, 138.4, 130.0, 128.3, 127.6, 127.5, 125.4, 73.4, 70.9, 61.6, 51.5, 32.2, 18.2, 17.1, 16.9; FTIR (film)  $\nu$ : 3353, 2963, 1731, 1501, 1244, 1097, 740  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  314.1732; found 314.1725.

**Methyl (*R,E*)-(1-(benzyloxy)-2-cyclohexylpent-3-en-2-yl)carbamate (13aq):**



Yield 30 mg (57%) starting from 51 mg of carbamate **3aq**; yellowish oil;  $[\alpha]_{\text{D}}^{21}$   $-17.2$  (c 2.8,  $\text{CHCl}_3$ ), *ee* 99%;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.40 – 7.23 (m, 5H), 5.54 – 5.40 (m, 2H), 4.91 (s, 1H), 4.51 (s, 2H), 3.70 (s, 2H), 3.60 (s, 3H), 2.07 – 1.88 (m, 1H), 1.85 – 1.54 (m, 9H), 1.38 – 0.83 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  155.6, 138.4, 130.8, 128.3, 127.6, 127.5, 124.9, 73.3, 70.8, 61.5, 51.5, 42.7, 27.3, 27.0, 26.6, 26.5, 18.1; FTIR (film)  $\nu$ : 3423, 2927, 2854, 1733, 1500, 1235, 1097, 737, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{29}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  354.2045; found 354.2035.

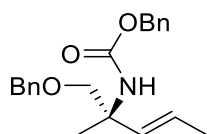
***tert*-butyl (*R,E*)-(1-(benzyloxy)-2-methylpent-3-en-2-yl)carbamate (13ar):**



*t*-BuOH was added instead of MeOH as a nucleophilic agent. Yield 92 mg (75%) starting from 100 mg of carbamate **3am**; yellowish oil;  $[\alpha]_{\text{D}}^{20}$   $+3.9$  (c 1.43,  $\text{CHCl}_3$ ), *ee* 99%;  $^1\text{H}$  NMR

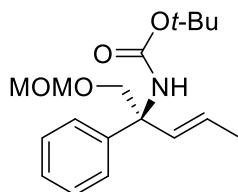
(500 MHz, CDCl<sub>3</sub>)  $\delta$  7.40 – 7.22 (m, 5H), 5.64 – 5.51 (m, 2H), 4.95 (br s, 1H), 4.54 (d,  $J$  = 2.1 Hz, 2H), 3.45 (d,  $J$  = 9.1 Hz, 1H), 3.37 (d,  $J$  = 9.1 Hz, 1H), 1.75 – 1.65 (m, 3H), 1.43 (s, 9H), 1.40 (s, 3H); <sup>13</sup>C NMR (126 MHz, cdcl<sub>3</sub>)  $\delta$  154.7, 138.2, 133.9, 128.4, 127.6, 127.6, 124.3, 78.9, 76.0, 73.3, 55.9, 28.4, 22.3, 17.9; FTIR (film)  $\nu$ : 3432, 2976, 1723, 1493, 1366, 1248, 1169, 1074, 740, 698 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>18</sub>H<sub>27</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 328.1889; found 328.1883.

**Benzyl (*R,E*)-(1-(benzyloxy)-2-methylpent-3-en-2-yl)carbamate (13as):**



BnOH was added instead of MeOH as a nucleophilic agent. Yield 118 mg (87%) starting from 100 mg of carbamate **3am**; yellowish oil;  $[\alpha]_D^{20}$  +4.3 (c 1.32, CHCl<sub>3</sub>, ee 99%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.49 – 7.20 (m, 10H), 5.69 – 5.51 (m, 2H), 5.24 (br s, 1H), 5.07 (s, 2H), 4.53 (d,  $J$  = 2.5 Hz, 2H), 3.47 (d,  $J$  = 9.1 Hz, 1H), 3.40 (d,  $J$  = 9.0 Hz, 1H), 1.71 (d,  $J$  = 4.2 Hz, 3H), 1.45 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  154.9, 138.0, 136.7, 133.4, 128.4, 128.3, 128.0, 127.9, 127.6, 127.5, 124.8, 75.9, 73.3, 66.1, 56.1, 22.2, 17.9; FTIR (film)  $\nu$ : 3423, 3032, 2935, 1729, 1498, 1452, 1242, 1091, 739, 698 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>21</sub>H<sub>25</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 362.1732; found 362.1724.

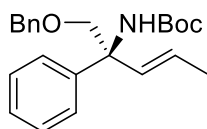
***tert*-butyl (*S,E*)-(1-(methoxymethoxy)-2-phenylpent-3-en-2-yl)carbamate (13bq):**



*t*-BuOH was added instead of MeOH as as a nucleophilic agent. Yield 228 mg (77%) starting from 246 mg of carbamate **3ba**; yellowish oil;  $[\alpha]_D^{22}$  -16.55 (c 1.64, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.43 – 7.35 (m, 2H), 7.35 – 7.26 (m, 2H), 7.26 – 7.18 (m, 1H), 5.97 (d,  $J$  = 15.8 Hz, 1H), 5.62 (dq,  $J$  = 15.8, 6.5 Hz, 1H), 5.39 (br s, 1H), 4.67 – 4.51 (m, 2H), 3.95 – 3.71 (m, 2H), 3.29 (s, 3H), 1.77 (dd,  $J$  = 6.5, 1.7 Hz, 3H), 1.36 (br s, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  154.6, 142.3, 131.9, 128.0, 126.9, 126.4, 126.4, 96.8, 79.2, 73.4, 61.8, 55.5, 28.3, 18.1; FTIR

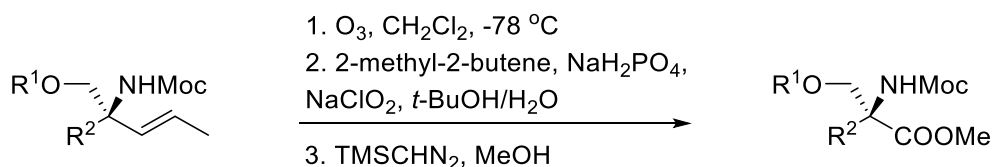
(film)  $\nu$ : 3433, 2974, 1727, 1489, 1365, 1247, 1169, 1042, 701  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{27}\text{NO}_4\text{Na}$   $[(\text{M}+\text{Na})^+]$  344.1838; found 344.1829.

***t*-Butyl (*S,E*)-(1-(benzyloxy)-2-phenylpent-3-en-2-yl)carbamate (13at):**



Yield 285 mg (68%) starting from 356 mg of carbamate **3aa**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.46 – 7.17 (m, 10H), 5.99 (d,  $J$  = 15.8 Hz, 1H), 5.72 – 5.51 (m, 1H), 5.43 (s, 1H), 4.52 (d,  $J$  = 4.3 Hz, 2H), 3.91 – 3.50 (m, 2H), 1.79 (dd,  $J$  = 6.5, 1.7 Hz, 3H), 1.38 (br s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.5, 137.9, 131.8, 128.4, 128.0, 127.7, 127.7, 126.9, 126.5, 126.4, 79.2, 75.4, 73.4, 62.1, 28.3, 18.1; FTIR (film)  $\nu$ : 3429, 2975, 1727, 1701, 1485, 1365, 1245, 1168, 1094, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{23}\text{H}_{29}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  390.2045; found 390.2037.

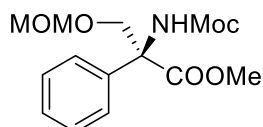
**1.12. The synthesis of amino acid esters 14**



**General procedure:** Ozone was passed through a solution of carbamate **13** (0.5 mmol) in dry  $\text{CH}_2\text{Cl}_2$  (20 mL) at  $-78$  °C until the solution turned blue. Then, excess of ozone was removed by bubbling oxygen through the mixture. After the addition of  $\text{Me}_2\text{S}$  (4 mL), the resulting mixture was warmed to room temperature and stirred for 1 h. Next, the solvent was removed under reduced pressure. The residue was dissolved in *t*-BuOH/ $\text{H}_2\text{O}$  mixture (4 : 1 v/v, 15 mL) followed by an addition of  $\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$  (364 mg, 2.5 mmol), 2-methyl-2-butene (230  $\mu\text{L}$ ) and  $\text{NaClO}_2$  (pur. 80%, 304 mg, 2.5 mmol). The resulting mixture was stirred overnight. Next, the solvent was removed and the crude amino acid was dissolved in dry MeOH, and treated with (trimethylsilyl)diazomethane (3 eq., 2 M soln in  $\text{Et}_2\text{O}$ ). When

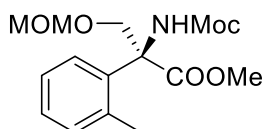
the reaction was complete, the solvent was removed and the crude product was purified by a flash column chromatography.

**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-phenylpropanoate (14a):**



Yield 42 mg (85%) starting from 46 mg of carbamate **13a**; yellowish oil;  $[\alpha]_D^{21} -26.2$  (c 1.8,  $\text{CHCl}_3$ , *ee* 96%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.51 – 7.19 (m, 5H), 6.28 (br s, 1H), 4.65 (s, 2H), 4.60 – 4.51 (m, 1H), 4.48 (d,  $J = 9.4$  Hz, 1H), 3.73 (s, 3H), 3.61 (s, 3H), 3.32 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.5, 154.9, 137.3, 128.6, 128.2, 125.9, 96.7, 68.1, 65.5, 55.3, 53.2, 51.9; FTIR (film)  $\nu$ : 2953, 1729, 1498, 1249, 1070, 1042  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{19}\text{NO}_6\text{Na}$  [(M+Na) $^+$ ] 320.1110; found 320.1110.

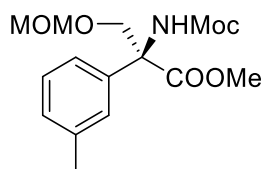
**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-(o-tolyl)propanoate (14b):**



Yield 40 mg (71%) starting from 53 mg of carbamate **13b**; waxy solid;  $[\alpha]_D^{21} +3.0$  (c 2.1,  $\text{CHCl}_3$ , *ee* 95%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.39 – 7.05 (m, 4H), 6.40 (br s, 1H), 4.84 – 4.72 (m, 1H), 4.69 (s, 2H), 4.42 (d,  $J = 8.8$  Hz, 1H), 3.75 (s, 3H), 3.54 (s, 3H), 3.33 (s, 3H), 2.24 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.10, 154.29, 136.11, 135.30, 132.18, 128.14, 127.11, 125.69, 96.66, 68.94, 64.39, 55.28, 53.38, 51.82, 20.04; FTIR (film)  $\nu$ : 3425, 2953, 1730, 1497, 1250, 1073, 1041  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_6\text{Na}$  [(M+Na) $^+$ ] 334.1267; found 334.1259.

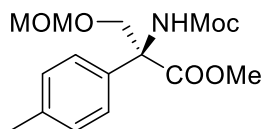
**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-(m-tolyl)propanoate (14c):**





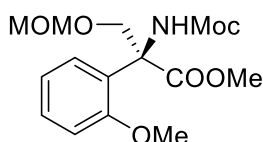
Yield 44 mg (71%) starting from 48 mg of carbamate **13c**; yellowish oil;  $[\alpha]_D^{21}$   $-64.7$  (c 3.6,  $\text{CHCl}_3$ , *ee* 93%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.28 – 7.14 (m, 3H), 7.10 (d,  $J = 7.2$  Hz, 1H), 6.28 (br s, 1H), 4.65 (s, 2H), 4.61 – 4.50 (m, 1H), 4.47 (d,  $J = 9.4$  Hz, 1H), 3.72 (s, 3H), 3.60 (s, 3H), 3.32 (s, 3H), 2.34 (s, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.6, 154.8, 138.2, 137.3, 129.0, 128.5, 126.5, 123.0, 96.7, 68.1, 65.4, 55.3, 53.2, 51.9, 21.6.; FTIR (film)  $\nu$ : 3428, 2953, 1731, 1498, 1251, 1073, 1042  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_6\text{Na}$   $[(\text{M}+\text{Na})^+]$  334.1267; found 334.1267.

**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-(p-tolyl)propanoate (14d):**



Yield 38 mg (90%) starting from 46 mg of carbamate **13d**; yellowish oil;  $[\alpha]_D^{21}$   $-70.0$  (c 2.7,  $\text{CHCl}_3$ ), *ee* 98%;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.30 – 7.22 (m, 2H), 7.14 (d,  $J = 8.0$  Hz, 2H), 6.28 (s, 1H), 4.65 (s, 2H), 4.60 – 4.50 (m, 1H), 4.46 (d,  $J = 9.3$  Hz, 1H), 3.72 (s, 2H), 3.60 (s, 3H), 3.32 (s, 3H), 2.31 (s, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.7, 154.8, 137.9, 134.4, 129.3, 125.8, 96.7, 68.1, 65.3, 55.3, 53.2, 51.9, 21.0; FTIR (film)  $\nu$ : 3428, 2953, 1729, 1501, 1248, 1073, 1041  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_6\text{Na}$   $[(\text{M}+\text{Na})^+]$  334.1267; found 334.1261.

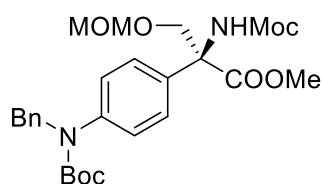
**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-(2-methoxyphenyl)propanoate (14e):**



Yield 31 mg (78%) starting from 37 mg of carbamate **13e**; waxy solid;  $[\alpha]_D^{21}$   $-59.6$  (c 2.6,  $\text{CHCl}_3$ , *ee* 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.36 (d,  $J = 7.8$  Hz, 1H), 7.32 – 7.22 (m, 1H), 6.96

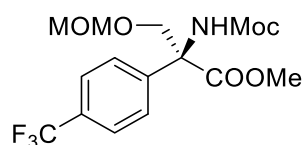
(t,  $J = 7.6$  Hz, 1H), 6.86 (d,  $J = 8.2$  Hz, 1H), 6.44 (br s, 1H), 4.92 (d,  $J = 9.0$  Hz, 1H), 4.67 (s, 2H), 4.22 (d,  $J = 9.0$  Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.52 (s, 3H), 3.31 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.1, 156.3, 154.5, 129.5, 128.0, 126.4, 120.3, 111.4, 96.6, 68.0, 62.2, 55.5, 55.2, 52.9, 51.6; FTIR (film)  $\nu$ : 3429, 2952, 1727, 1497, 1297, 1253, 1073, 1042, 756  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{21}\text{NO}_7\text{Na}$  [(M+Na) $^+$ ] 350.1216; found 350.1208.

**Methyl (S)-2-(4-(benzyl(tert-butoxycarbonyl)amino)phenyl)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)propanoate (14f):**



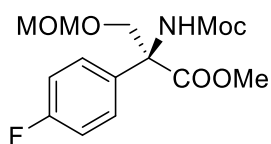
Yield 34 mg (79%) starting from 42 mg of carbamate **13f**; yellowish oil;  $[\alpha]_{\text{D}}^{21} -41.7$  (c 2.5,  $\text{CHCl}_3$ ,  $ee$  93%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.35 – 7.14 (m, 9H), 6.22 (br s, 1H), 4.81 (s, 2H), 4.63 (s, 2H), 4.50 (s, 1H), 4.41 (d,  $J = 9.4$  Hz, 1H), 3.71 (s, 3H), 3.60 (s, 3H), 3.30 (s, 3H), 1.40 (s, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  171.3, 154.9, 154.6, 142.9, 138.7, 128.4, 127.0, 126.9, 126.4, 120.2, 115.3, 96.7, 80.9, 68.1, 65.3, 55.3, 53.8, 53.2, 52.0, 28.2; FTIR (film)  $\nu$ : 3425, 2953, 1730, 1701, 1511, 1386, 1250, 1154, 1041  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_8\text{Na}$  [(M+Na) $^+$ ] 525.2213; found 525.2214.

**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-(4-(trifluoromethyl)phenyl)propanoate (14g):**



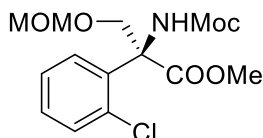
Yield 49 mg (86%) starting from 55 mg of carbamate **13f**; yellowish oil;  $[\alpha]_{\text{D}}^{21} -49.7$  (c 4.0,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.60 (d,  $J = 8.4$  Hz, 2H), 7.53 (d,  $J = 8.4$  Hz, 2H), 6.33 (br s, 1H), 4.65 (s, 2H), 4.51 (s, 1H), 4.46 (d,  $J = 9.2$  Hz, 1H), 3.75 (s, 3H), 3.62 (s, 3H), 3.33 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.8, 154.9, 141.3, 130.3 (q,  $J = 32.4$  Hz), 126.5, 125.56 (q,  $J = 3.8$  Hz), 123.87 (q,  $J = 272.8$  Hz), 96.7, 68.2, 65.4, 55.4, 53.5, 52.1;  $^{19}\text{F}$  NMR (376 MHz,  $\text{CDCl}_3$ )  $\delta$  -62.8; FTIR (film)  $\nu$ : 3427, 2956, 1730, 1501, 1329, 1250, 1124, 1072, 1042  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{18}\text{NO}_6\text{F}_3\text{Na}$  [(M+Na) $^+$ ] 388.0984; found 388.0975.

**Methyl (S)-2-(4-fluorophenyl)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)propanoate (14h):**



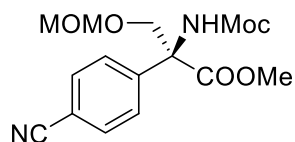
Yield 39 mg (91%) starting from 40 mg of carbamate **13h**; yellowish oil;  $[\alpha]_D^{21} -56.9$  (c 2.8, CHCl<sub>3</sub>, *ee* 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.48 – 7.28 (m, 2H), 7.02 (t, *J* = 8.7 Hz, 2H), 6.28 (br s, 1H), 4.64 (s, 2H), 4.55 – 4.45 (m, 1H), 4.42 (d, *J* = 9.3 Hz, 1H), 3.73 (s, 3H), 3.60 (s, 3H), 3.31 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.3, 162.4 (d, *J* = 247.6 Hz), 154.9, 133.1, 127.9 (d, *J* = 8.2 Hz), 115.5 (d, *J* = 21.7 Hz), 96.7, 68.2, 65.1, 55.3, 53.3, 52.0; <sup>19</sup>F NMR (376 MHz, CDCl<sub>3</sub>)  $\delta$  -113.9; FTIR (film)  $\nu$ : 3425, 2955, 1730, 1509, 1236, 1073, 1041 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>18</sub>NO<sub>6</sub>FNa [(M+Na)<sup>+</sup>] 338.1016; found 338.1002.

**Methyl (S)-2-(2-chlorophenyl)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)propanoate (14i):**



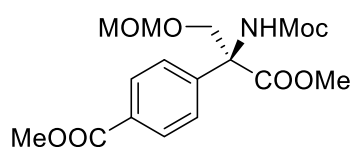
Yield 37 mg (87%) starting from 40 mg of carbamate **13i**; waxy solid;  $[\alpha]_D^{21} -2.4$  (c 3.1, CHCl<sub>3</sub>, *ee* 97%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.61 – 7.07 (m, 4H), 6.49 (br s, 1H), 4.81 (d, *J* = 9.0 Hz, 1H), 4.68 (s, 2H), 4.33 (d, *J* = 9.0 Hz, 1H), 3.77 (s, 3H), 3.54 (s, 3H), 3.33 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  171.0, 154.3, 135.2, 133.0, 130.8, 129.4, 129.2, 126.3, 96.7, 68.3, 63.8, 55.3, 53.5, 51.8; FTIR (film)  $\nu$ : 3427, 2953, 2893, 1726, 1499, 1296, 1249, 1150, 1111, 1072, 1042, 751 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>18</sub>NO<sub>6</sub>ClNa [(M+Na)<sup>+</sup>] 354.0720; found 354.0710.

**Methyl (S)-2-(4-cyanophenyl)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)propanoate (14j):**



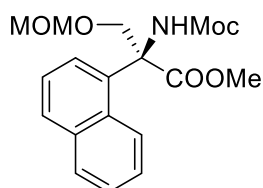
Yield 43 mg (78%) starting from 52 mg of carbamate **13j**; yellowish oil;  $[\alpha]_D^{21} -61.0$  (c 3.4, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.69 – 7.60 (m, 2H), 7.57 – 7.48 (m, 2H), 6.32 (br s, 1H), 4.64 (s, 2H), 4.52 – 4.36 (m, 2H), 3.75 (s, 3H), 3.61 (s, 3H), 3.32 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.4, 154.9, 142.5, 132.3, 127.0, 118.3, 112.2, 96.7, 68.3, 65.5, 55.4, 53.6, 52.2; FTIR (film)  $\nu$ : 3418, 2955, 2230, 1730, 1504, 1251, 1073, 1041 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>6</sub>Na [(M+Na)<sup>+</sup>] 345.1063; found 345.1053.

**Methyl (S)-4-(5-(methoxycarbonyl)-3-oxo-2,7,9-trioxa-4-azadecan-5-yl)benzoate (14k):**



Yield 37 mg (81%) starting from 43 mg of carbamate **13k**; yellowish oil;  $[\alpha]_D^{21} -61.8$  (c 2.8, CHCl<sub>3</sub>), ee 98%; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.01 (d,  $J = 8.2$  Hz, 2H), 7.47 (d,  $J = 8.2$  Hz, 2H), 6.32 (br s, 1H), 4.65 (s, 2H), 4.59 – 4.40 (m, 2H), 3.89 (s, 3H), 3.73 (s, 3H), 3.60 (s, 3H), 3.32 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  170.9, 166.5, 154.8, 142.2, 130.0, 129.8, 126.1, 96.7, 68.2, 65.5, 55.4, 53.4, 52.1, 52.0; FTIR (film)  $\nu$ : 3423, 2954, 1727, 1503, 1437, 1283, 1250, 1113, 1073, 1041 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>8</sub>Na [(M+Na)<sup>+</sup>] 378.1165; found 378.1162.

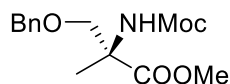
**Methyl (S)-2-((methoxycarbonyl)amino)-3-(methoxymethoxy)-2-(naphthalen-1-yl)propanoate (14l):**



Yield 33 mg (61%) starting from 51 mg of carbamate **13l**; waxy solid;  $[\alpha]_D^{21} +6.8$  (c 3.0, CHCl<sub>3</sub>, ee 97%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  8.23 – 8.01 (m, 1H), 7.97 – 7.71 (m, 2H), 7.63 – 7.34 (m, 4H), 6.63 (br s, 1H), 4.90 (d,  $J = 8.6$  Hz, 1H), 4.74 (s, 2H), 4.56 (d,  $J = 8.6$  Hz, 1H), 3.64 (s, 3H), 3.45 (s, 3H), 3.37 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  172.8, 154.3, 134.3, 132.4, 130.7, 129.5, 129.4, 126.4, 125.4, 125.4, 124.7, 123.5, 96.7, 69.3, 64.4, 55.3, 53.5, 51.7; FTIR

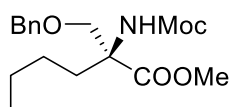
(film)  $\nu$ : 3421, 2953, 1728, 1496, 1250, 1075, 1040, 782  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_6\text{Na}$   $[(\text{M}+\text{Na})^+]$  370.1267; found 370.1257.

**Methyl (S)-3-(benzyloxy)-2-((methoxycarbonyl)amino)-2-methylpropanoate (14m):**



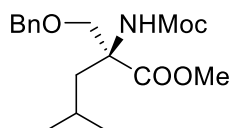
Yield 36 mg (90%) starting from 38 mg of carbamate **13m**; yellowish oil;  $[\alpha]_{\text{D}}^{21}$   $-0.7$  (c 2.6,  $\text{CHCl}_3$ ,  $ee$  99%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.52 – 7.09 (m, 5H), 5.67 (br s, 1H), 4.66 – 4.36 (m, 2H), 3.85 – 3.76 (m, 1H), 3.73 (s, 3H), 3.69 (d,  $J = 9.2$  Hz, 1H), 3.64 (s, 3H), 1.54 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  173.1, 155.7, 137.7, 128.4, 127.7, 127.6, 73.3, 72.7, 60.3, 52.7, 51.8, 20.2; FTIR (film)  $\nu$ : 3360, 2952, 1728, 1508, 1453, 1251, 1090, 742  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{19}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  304.1161; found 304.1144.

**Methyl (S)-2-((benzyloxy)methyl)-2-((methoxycarbonyl)amino)hexanoate (14n):**



Yield 34 mg (82%) starting from 39 mg of carbamate **13n**; yellowish oil;  $[\alpha]_{\text{D}}^{21}$   $+2.0$  (c 2.8,  $\text{CHCl}_3$ ,  $ee$  97%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.15 (m, 5H), 5.77 (br s, 1H), 4.54 (d,  $J = 12.3$  Hz, 1H), 4.44 (d,  $J = 12.3$  Hz, 1H), 4.18 – 3.98 (m, 1H), 3.74 (s, 3H), 3.70 – 3.49 (m, 4H), 2.16 (s, 1H), 1.80 – 1.58 (m, 1H), 1.40 – 1.16 (m, 4H), 1.11 – 0.91 (m, 1H), 0.85 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.8, 155.0, 138.0, 128.3, 127.6, 127.5, 73.2, 71.2, 64.5, 52.7, 51.7, 31.5, 25.6, 22.5, 13.8; FTIR (film)  $\nu$ : 3426, 2956, 2865, 1726, 1504, 1244, 1093  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  346.1630; found 346.1627.

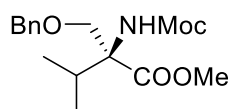
**Methyl (S)-2-((benzyloxy)methyl)-2-((methoxycarbonyl)amino)-4-methylpentanoate (14o):**



Yield 11 mg (65%) starting from 16 mg of carbamate **13o**; yellowish oil;  $[\alpha]_{\text{D}}^{21}$   $+5.8$  (c 0.7,  $\text{CHCl}_3$ ,  $ee$  92%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.16 (m, 5H), 5.94 (br s, 1H), 4.54 (d,  $J =$

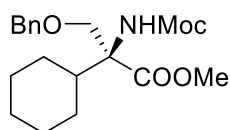
12.4 Hz, 1H), 4.41 (d,  $J = 12.4$  Hz, 1H), 4.10 (d,  $J = 9.2$  Hz, 1H), 3.74 (s, 3H), 3.63 (s, 3H), 3.58 (d,  $J = 9.2$  Hz, 1H), 2.26 – 2.17 (m, 1H), 1.66 – 1.49 (m, 2H), 0.88 (d,  $J = 6.3$  Hz, 3H), 0.76 (d,  $J = 6.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  173.4, 154.9, 138.0, 128.3, 127.6, 127.5, 73.1, 71.8, 64.0, 52.6, 51.7, 39.7, 24.0, 23.8, 22.4; FTIR (film)  $\nu$ : 3426, 2955, 2928, 1726, 1503, 1245, 1092  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  346.1631; found 346.1628.

**Methyl (S)-2-((benzyloxy)methyl)-2-((methoxycarbonyl)amino)-3-methylbutanoate (14p):**



Yield 28 mg (66%) starting from 40 mg of carbamate **13p**; waxy solid;  $[\alpha]_{\text{D}}^{21} -13.1$  (c 2.4,  $\text{CHCl}_3$ ,  $ee$  94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.48 – 7.09 (m, 5H), 5.69 (br s, 1H), 4.55 (d,  $J = 12.3$  Hz, 1H), 4.46 (d,  $J = 12.3$  Hz, 1H), 4.30 (d,  $J = 9.3$  Hz, 1H), 3.88 (d,  $J = 9.3$  Hz, 1H), 3.73 (s, 3H), 3.63 (s, 3H), 2.53 – 2.33 (m, 1H), 1.00 – 0.81 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.0, 155.4, 138.3, 128.2, 127.5, 127.5, 73.2, 69.0, 67.3, 52.4, 51.8, 31.9, 17.7, 17.5; FTIR (film)  $\nu$ : 3366, 2956, 1723, 1509, 1255, 1069, 746  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{23}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  332.1474; found 332.1474.

**Methyl (S)-3-(benzyloxy)-2-cyclohexyl-2-((methoxycarbonyl)amino)propanoate (14q):**



Yield 21 mg (71%) starting from 28 mg of carbamate **13q**; yellowish oil;  $[\alpha]_{\text{D}}^{21} -26.2$  (c 1.8,  $\text{CHCl}_3$ ,  $ee$  99%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.41 – 7.16 (m, 5H), 5.71 (br s, 1H), 4.55 (d,  $J = 12.3$  Hz, 1H), 4.45 (d,  $J = 12.3$  Hz, 1H), 4.39 – 4.25 (m, 1H), 3.87 (d,  $J = 9.2$  Hz, 1H), 3.73 (s, 3H), 3.63 (s, 3H), 2.16 – 1.96 (m, 1H), 1.89 – 1.44 (m, 5H), 1.37 – 0.98 (m, 3H), 0.98 – 0.77 (m, 1H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  172.2, 155.3, 138.3, 128.2, 127.5, 73.2, 68.7, 67.2, 52.4, 51.7, 42.0, 27.8, 27.7, 26.4, 26.4, 26.1; FTIR (film)  $\nu$ : 3419, 2930, 2854, 1727, 1504, 1234,

1072  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{27}\text{NO}_5\text{Na}$   $[(\text{M}+\text{Na})^+]$  372.1787; found 372.1779.

### 1.13. A large scale synthesis of amino acid 15:

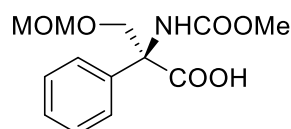
**Step 1 (synthesis of alcohol 6ba):** Yield 1.39 g (6.24 mmol, 89%) starting from 3.04 g (7 mmol) of vinyl stannane **5b**.

**Step 2 (synthesis of carbamate 3ba):** Yield 1.39 g (5.24 mmol, 84%) starting from 1.39 g (6.24 mmol) of alcohol **6ba**.

**Step 3 (synthesis of allylamine 13b):** Yield 1.22 g (4.35 mmol, 83%) starting from 1.39 g (5.24 mmol) of carbamate 3ba. Dehydration was performed at  $-10\text{ }^\circ\text{C}$ .

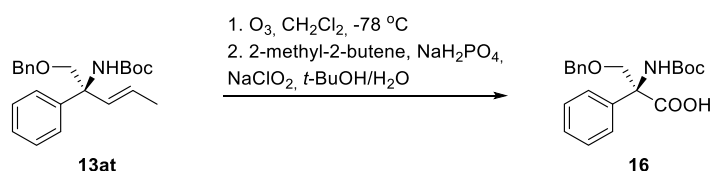
**Step 4 (oxidation to carboxylic acid 15):** Yield 1.02 g (3.61 mmol, 83%) starting from 1.22 g (4.35 mmol) of allyl amine **13b**. Acid **15** was isolated and purified by extraction with AcOEt.

#### (S)-2-((Methoxycarbonyl)amino)-3-(methoxymethoxy)-2-phenylpropanoic acid (15)



$^1\text{H}$  NMR (400 MHz,  $\text{MeOH-}d_4$ )  $\delta$  7.49 – 7.41 (m, 2H), 7.38 – 7.23 (m, 3H), 4.81 (s, 1H), 4.67 – 4.59 (m, 2H), 4.51 – 4.40 (m, 2H), 3.58 (s, 3H), 3.31 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{MeOH-}d_4$ )  $\delta$  172.3, 155.7, 138.0, 128.1, 127.6, 125.9, 96.3, 67.8, 65.1, 54.3, 51.1; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{17}\text{NO}_6\text{Na}$   $[(\text{M}+\text{Na})^+]$  306.0954; found 306.0953.

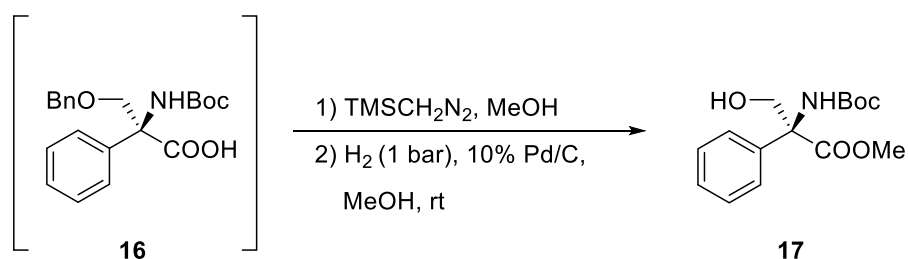
### 1.14. The synthesis of amino acid 16



**General procedure:** Ozone was passed through a solution of carbamate **13at** (0.27 mmol, 100 mg) in dry  $\text{CH}_2\text{Cl}_2$  (11 mL) at  $-78\text{ }^\circ\text{C}$  until the solution turned blue. Then, excess of ozone was removed by bubbling oxygen through the mixture. After the addition of  $\text{Me}_2\text{S}$  (2 mL), the resulting mixture was warmed to room temperature and stirred for 1 h. Next, the solvent was removed under reduced pressure. The residue was dissolved in  $t$ -

BuOH/H<sub>2</sub>O mixture (4 : 1 v/v, 8 mL) followed by an addition of NaH<sub>2</sub>PO<sub>4</sub>·H<sub>2</sub>O (1.4 mmol, 154 mg), 2-methyl-2-butene (125 μL) and NaClO<sub>2</sub> (pur. 80%, 1.4 mmol, 154 mg). The resulting mixture was stirred overnight. Next, the solvent was removed. The crude amino acid **16** was subjected to the further transformations or purified by a reverse phase flash column chromatography (RP-C18; 10-80% MeOH in H<sub>2</sub>O). Yield 81 mg (80%); waxy solid; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ 7.62 – 7.06 (m, 10H), 6.68 (br s, 1H), 4.52 (s, 2H), 4.25 (s, 2H), 1.35 (s, 9H); <sup>13</sup>C NMR (101 MHz, DMSO-*d*<sub>6</sub>) δ 172.7, 154.1, 138.7, 128.6, 128.5, 127.9, 127.8, 126.6, 78.9, 73.0, 70.8, 65.2, 28.6; FTIR (film) ν: 3302, 2977, 2594, 1726, 1649, 1496, 1367, 1248, 1165, 1060, 698 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>21</sub>H<sub>25</sub>NO<sub>5</sub>Na [(M+Na)<sup>+</sup>] 394.1630; found 394.1616.

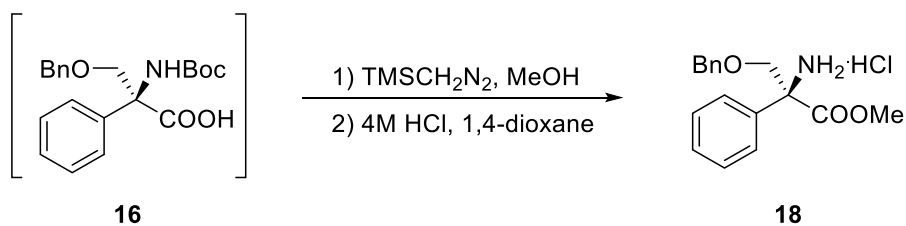
### 1.15. The synthesis of amino ester **17**



The crude amino acid **16** was dissolved in dry MeOH (8 mL), and treated with (trimethylsilyl)diazomethane (3 eq., 2 M soln in Et<sub>2</sub>O). When the reaction was complete, the solvent was removed and the residue was purified by flash column chromatography on a silica gel (5–20% AcOEt in hexanes). After that, the product was redissolved in MeOH (5 mL), 10% Pd/C (10 mg) was added and the resulting mixture was saturated by hydrogen (ballon) at rt. When the reaction was completed, a catalyst was removed by filtration. The solvent and volatiles were removed to provide product **17**. Yield 71 mg (88%) starting from 100 mg of carbamate **13at**; yellowish oil; <sup>1</sup>H NMR (400 MHz, MeOH-*d*<sub>4</sub>) δ 7.63 – 7.05 (m, 5H), 4.78 (s, 3H), 4.32 (br s, 1H), 3.69 (s, 3H), 1.41 (s, 9H); <sup>13</sup>C NMR (101 MHz, MeOH-*d*<sub>4</sub>) δ 172.0, 155.1, 137.9, 128.0, 127.5, 126.0, 79.5, 66.9, 63.9, 51.9, 48.3, 48.1, 47.8, 47.6, 47.4, 47.2, 47.0, 27.2; FTIR (film) ν: 3424, 2977, 2928, 1719, 1493, 1392, 1244, 1166, 1056, 698 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>21</sub>NO<sub>5</sub>Na [(M+Na)<sup>+</sup>] 318.1317; found 318.1308.

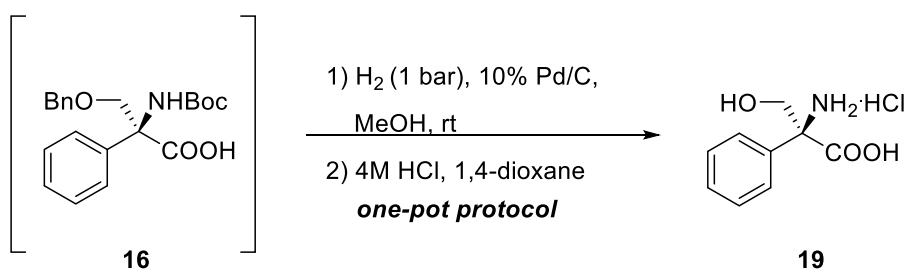
### 1.16. The synthesis of amino ester **18**





The crude amino acid **16** was dissolved in dry MeOH (8 mL), and treated with (trimethylsilyl)diazomethane (3 eq., 2 M soln in Et<sub>2</sub>O). When the reaction was complete, the solvent was removed and the residue was purified by flash column chromatography on a silica gel (5–20% AcOEt in hexanes). After that, the product was redissolved in 4M HCl in 1,4-dioxane (5 mL). After 16 hr solvents and volatiles were removed to provide amino ester hydrochloride **18**. Yield 77 mg (88%) starting from 100 mg of amino acid **16**; yellowish oil; <sup>1</sup>H NMR (400 MHz, MeOD) δ 7.54 – 7.40 (m, 5H), 7.40 – 7.26 (m, 5H), 4.81 (s, 3H), 4.74 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 4.29 (d, *J* = 10.0 Hz, 1H), 4.14 (d, *J* = 10.0 Hz, 1H), 3.82 (s, 3H); <sup>13</sup>C NMR (101 MHz, MeOH-*d*<sub>4</sub>) δ 168.7, 136.8, 132.4, 129.8, 129.2, 128.2, 127.9, 127.9, 125.6, 73.4, 70.6, 66.7, 53.0, 48.3, 48.1, 47.9, 47.6, 47.4, 47.2, 47.0; FTIR (film) ν: 2871, 1752, 1593, 1516, 1452, 1242, 1101, 736, 697 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>17</sub>H<sub>19</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 308.1263; found 308.1256.

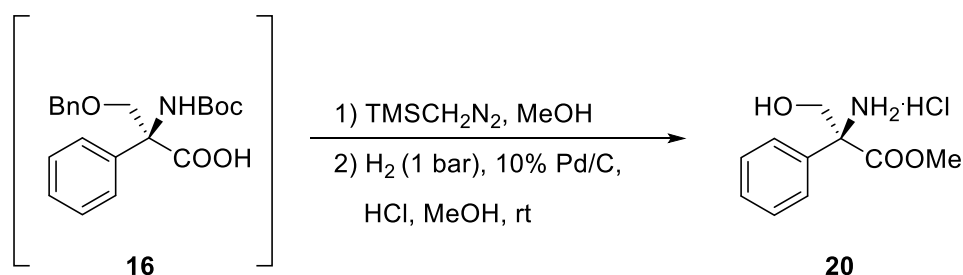
### 1.17. The synthesis of amino acid **19**



The amino acid **16** (0.22 mmol, 81 mg) was dissolved in dry MeOH (5 mL), 10% Pd/C (10 mg) was added and the resulting mixture was saturated by hydrogen (ballon) at rt. When the reaction was completed, a catalyst was removed by filtration and the solvent and volatiles were removed. The residue was redissolved in 4M HCl in 1,4-dioxane (5 mL). After 16 hr solvents and volatiles were removed to provide amino acid hydrochloride **19**. Yield 47 mg (99%) starting from 81 mg of amino acid **16**; waxy solid; <sup>1</sup>H NMR (400 MHz, MeOH-*d*<sub>4</sub>) δ 7.66 – 7.28 (m, 5H), 4.92 (s, 3H), 4.43 (d, *J* = 11.0 Hz, 1H), 4.13 (d, *J* = 11.0 Hz, 1H); <sup>13</sup>C NMR (101 MHz, MeOD) δ 170.0, 133.3, 129.4, 129.0, 125.7, 66.7, 63.7, 48.3, 48.1, 47.9, 47.7, 47.5,

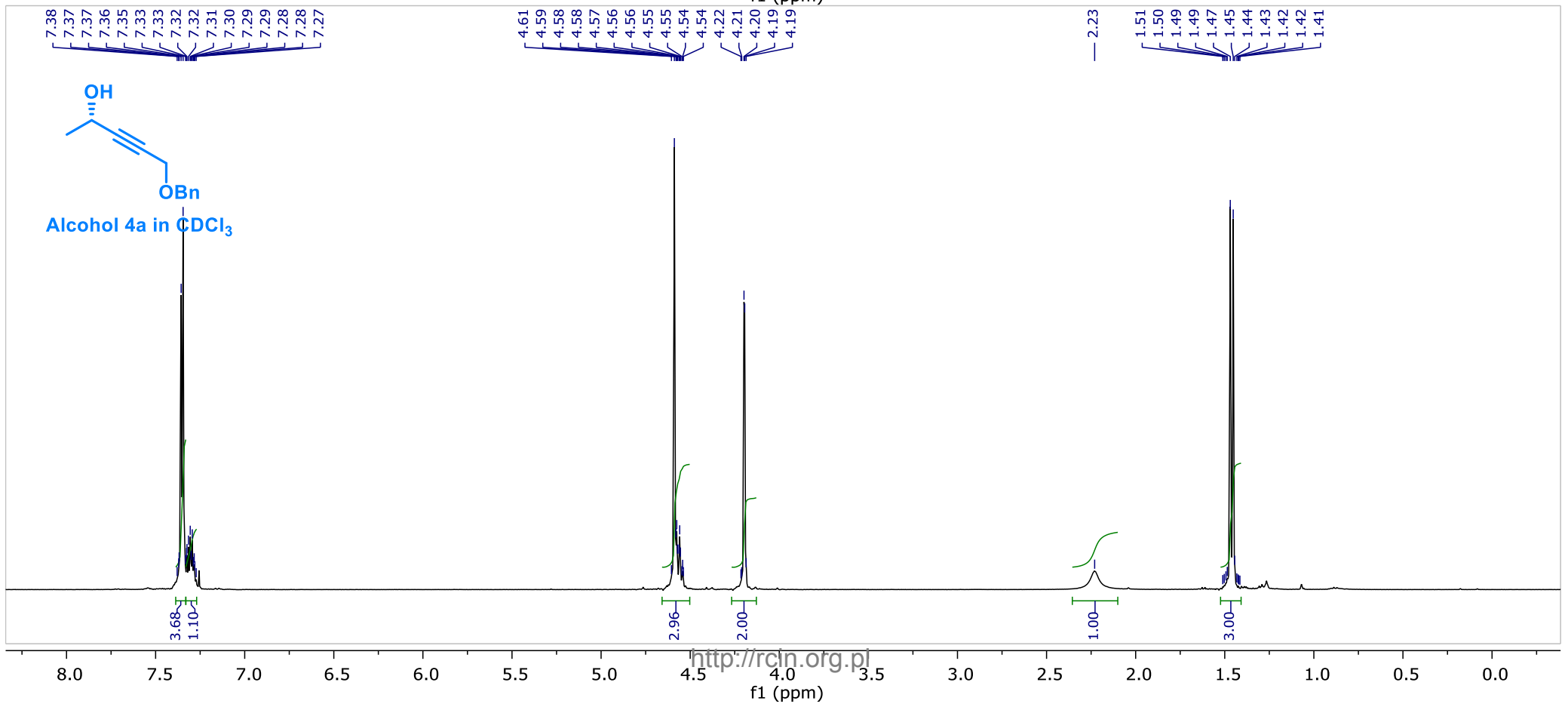
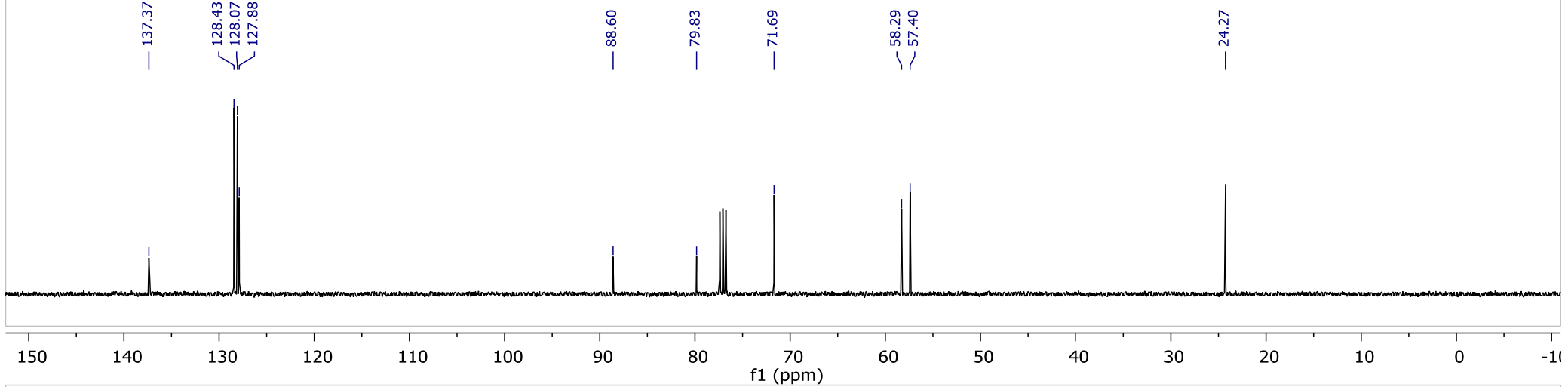
47.2, 47.0; FTIR (film)  $\nu$ : 3348, 2920, 2851, 1742, 1588, 1516, 1380, 1190, 1056, 862, 695, 559  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_9\text{H}_{10}\text{NO}_3$  [(M-H)] 180.0661; found 180.0657.

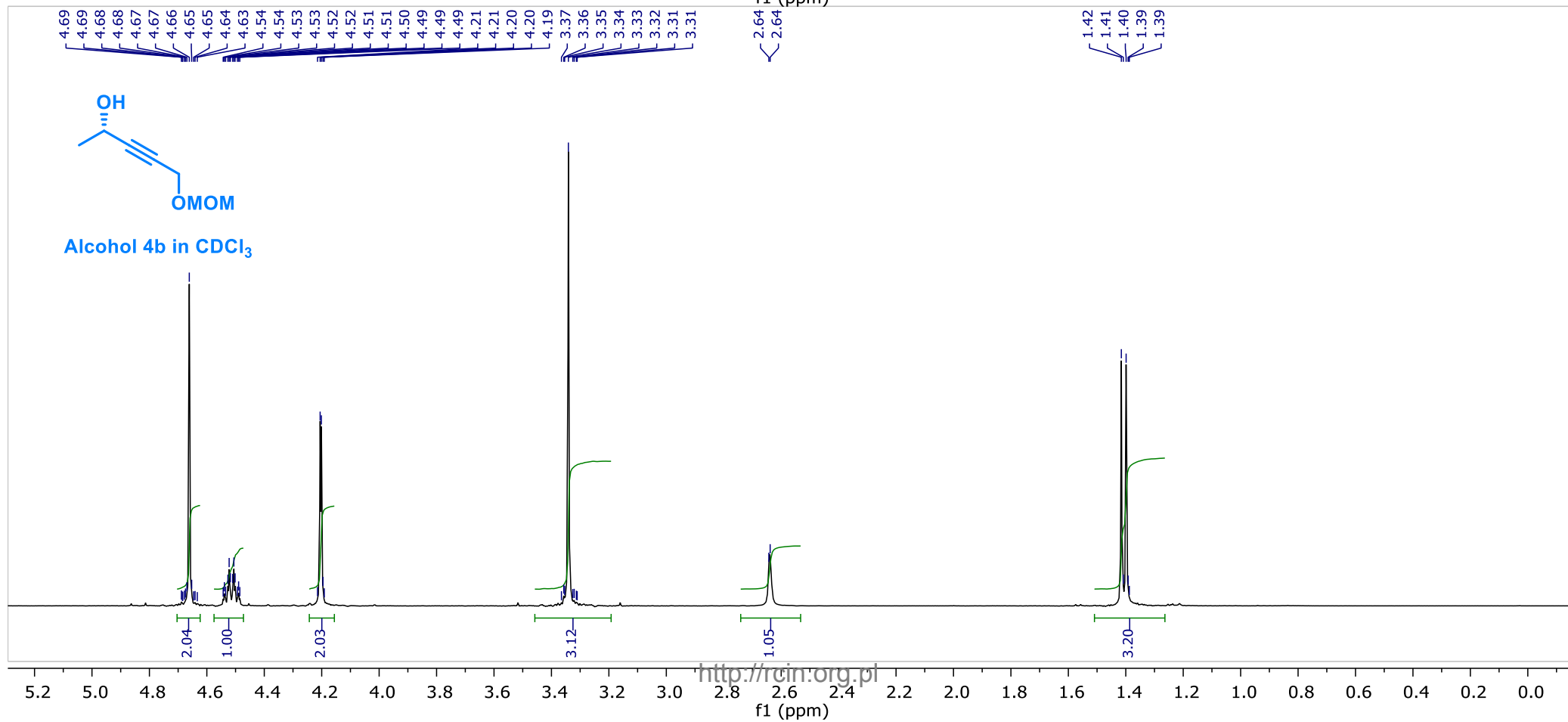
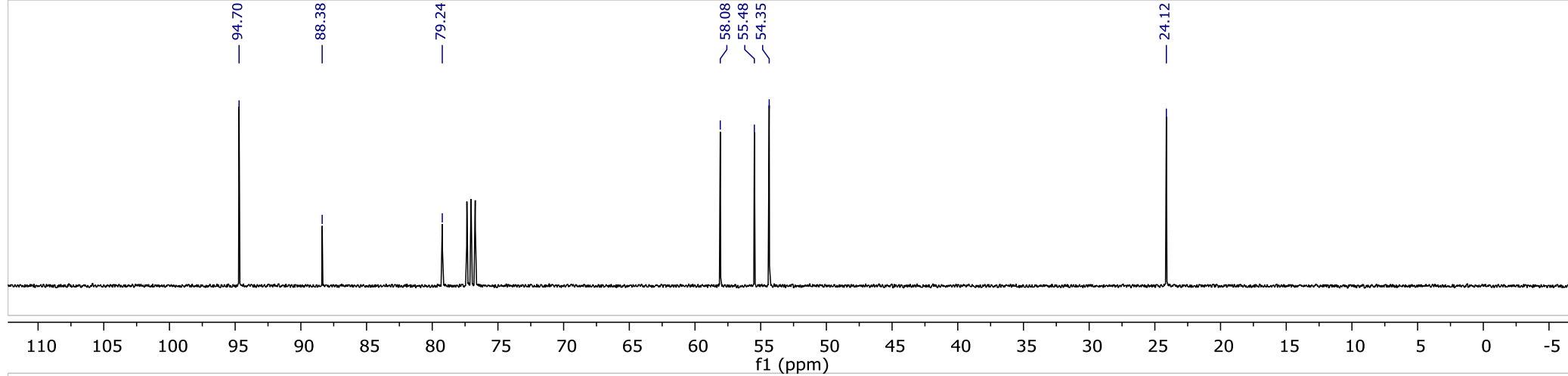
### 1.18. The synthesis of amino acid **20**

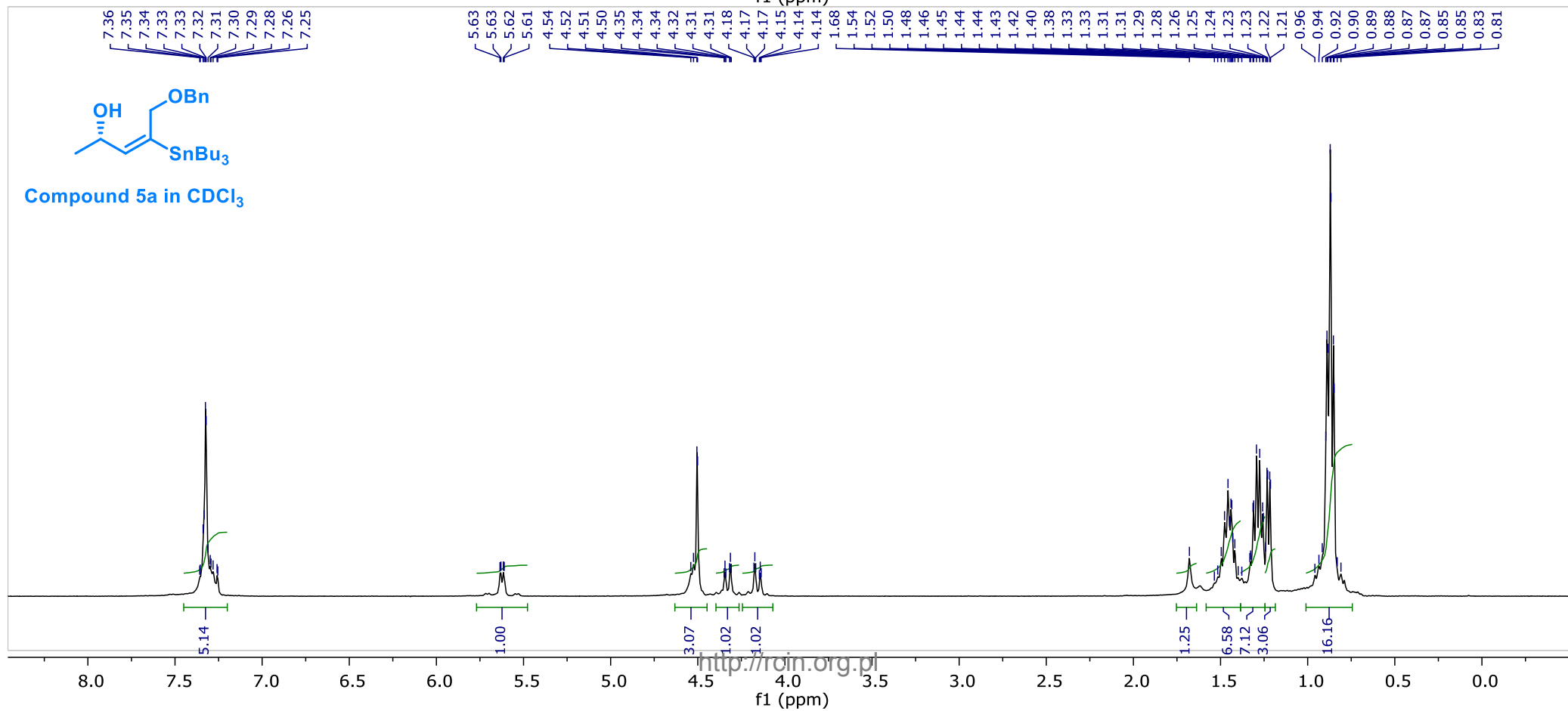
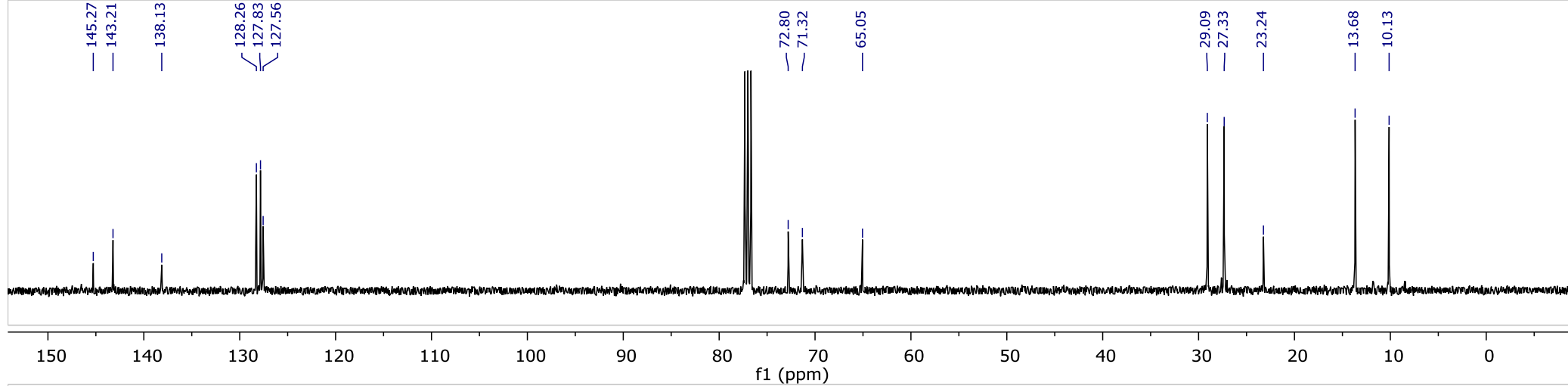


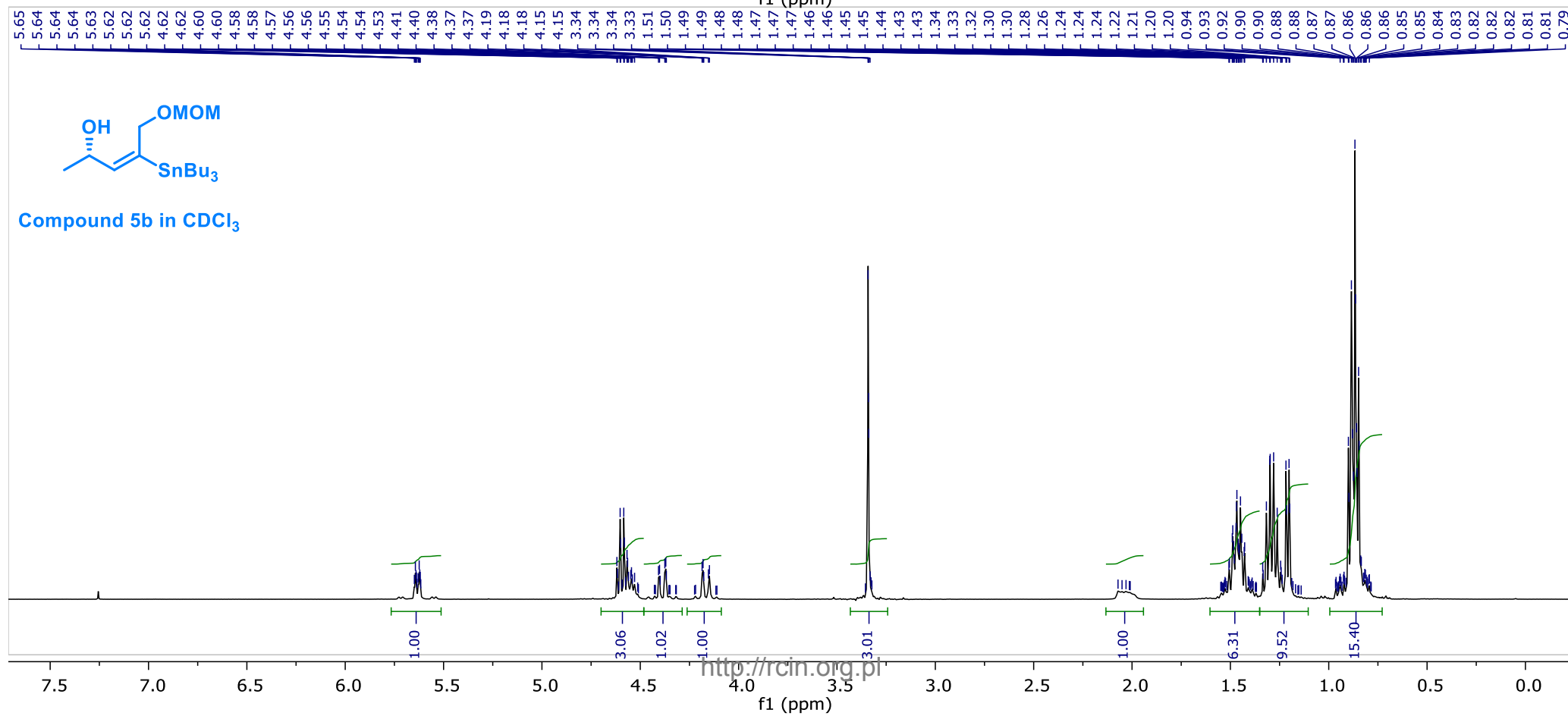
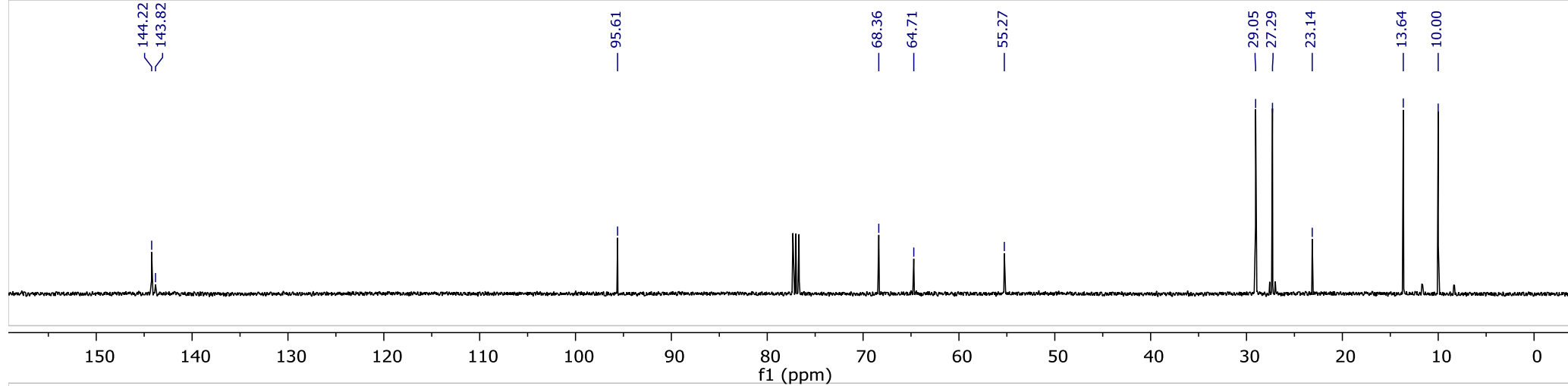
The crude amino acid **16** was dissolved in dry MeOH (8 mL), and treated with (trimethylsilyl)diazomethane (3 eq., 2 M soln in  $\text{Et}_2\text{O}$ ). When the reaction was complete, the solvent was removed and the residue was purified by flash column chromatography on a silica gel (5–20% AcOEt in hexanes). After that, the product was redissolved in MeOH (5 mL), 10% Pd/C (10 mg) and 1 mL of 4M HCl in 1,4-dioxane was added and the resulting mixture was saturated by hydrogen (balloon) at rt. When the reaction was completed, a catalyst was removed by filtration. The solvent and volatiles were removed to provide product **17**. Yield 65 mg (87%) starting from 100 mg of carbamate **13at**;  $^1\text{H}$  NMR (500 MHz,  $\text{MeOH-}d_4$ )  $\delta$  7.52 – 7.44 (m, 8H), 4.44 (d,  $J = 11.6$  Hz, 1H), 4.12 (d,  $J = 11.6$  Hz, 1H), 3.87 (s, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{MeOH-}d_4$ )  $\delta$  170.6, 134.2, 131.0, 130.5, 127.0, 68.3, 65.1, 54.2; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{10}\text{H}_{14}\text{NO}_3$  [(M+H) $^+$ ] 196.0974; found 196.0972.

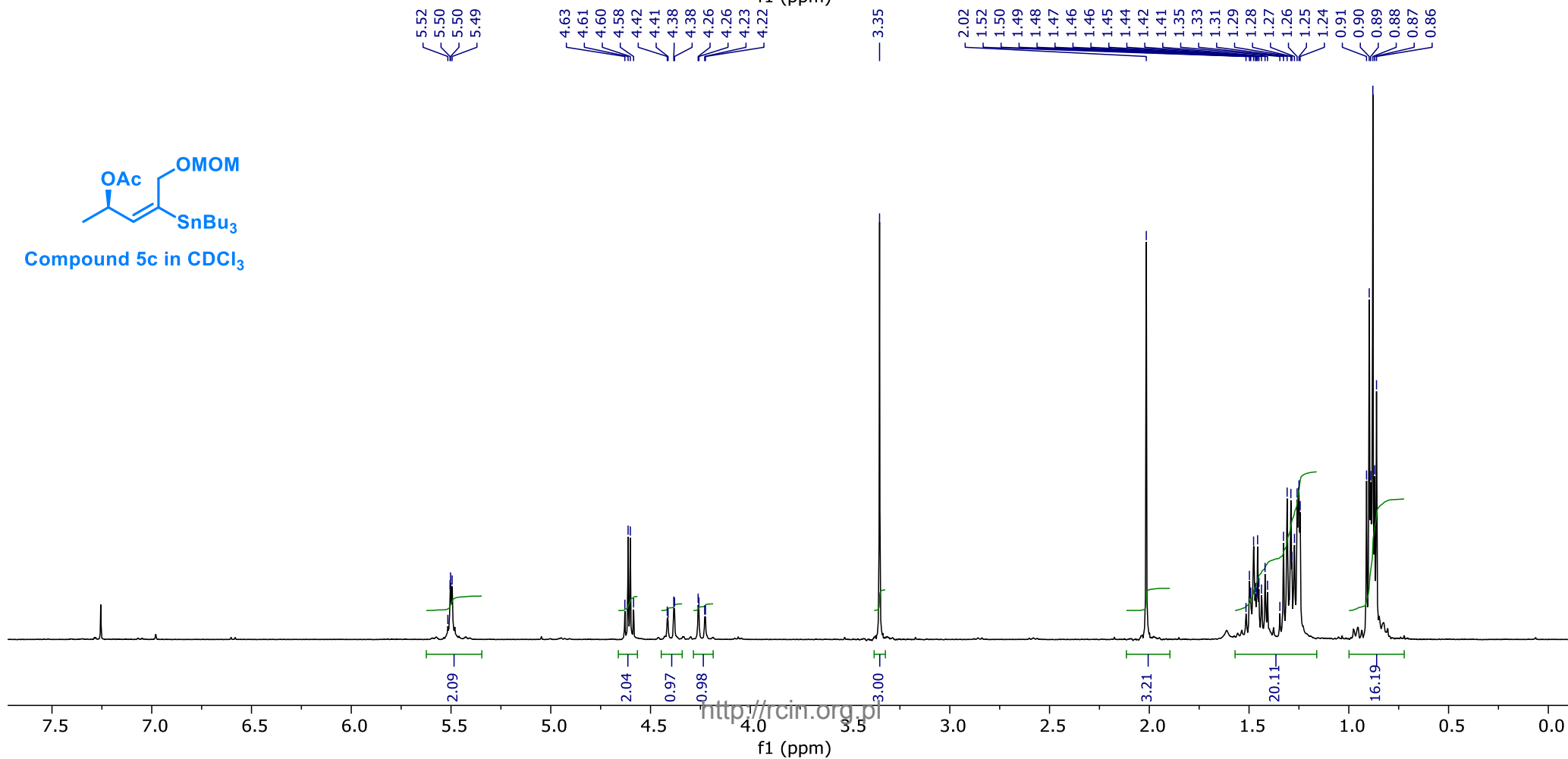
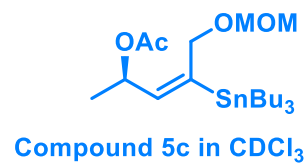
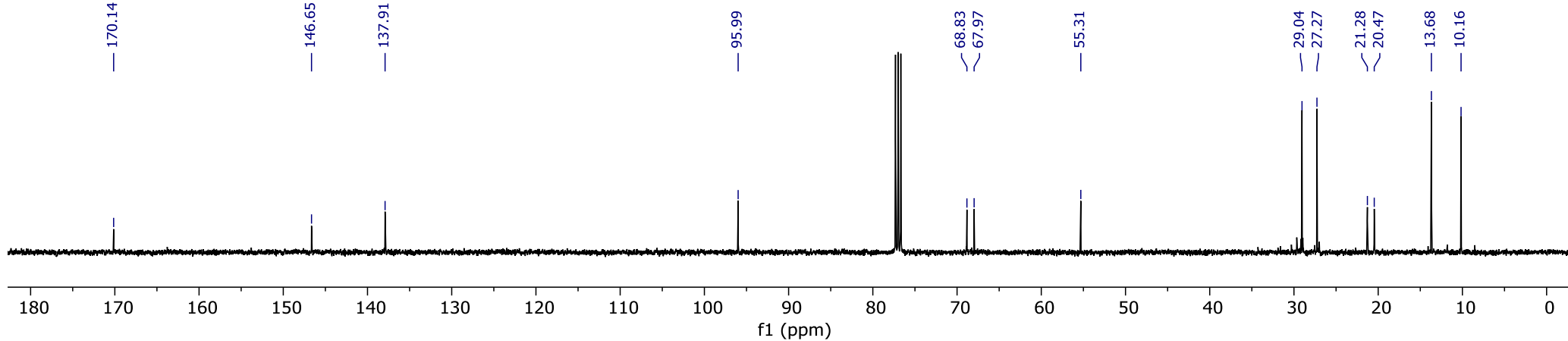
## 2. $^1\text{H}$ , $^{13}\text{C}$ , $^{19}\text{F}$ NMR spectra and HPLC chromatograms





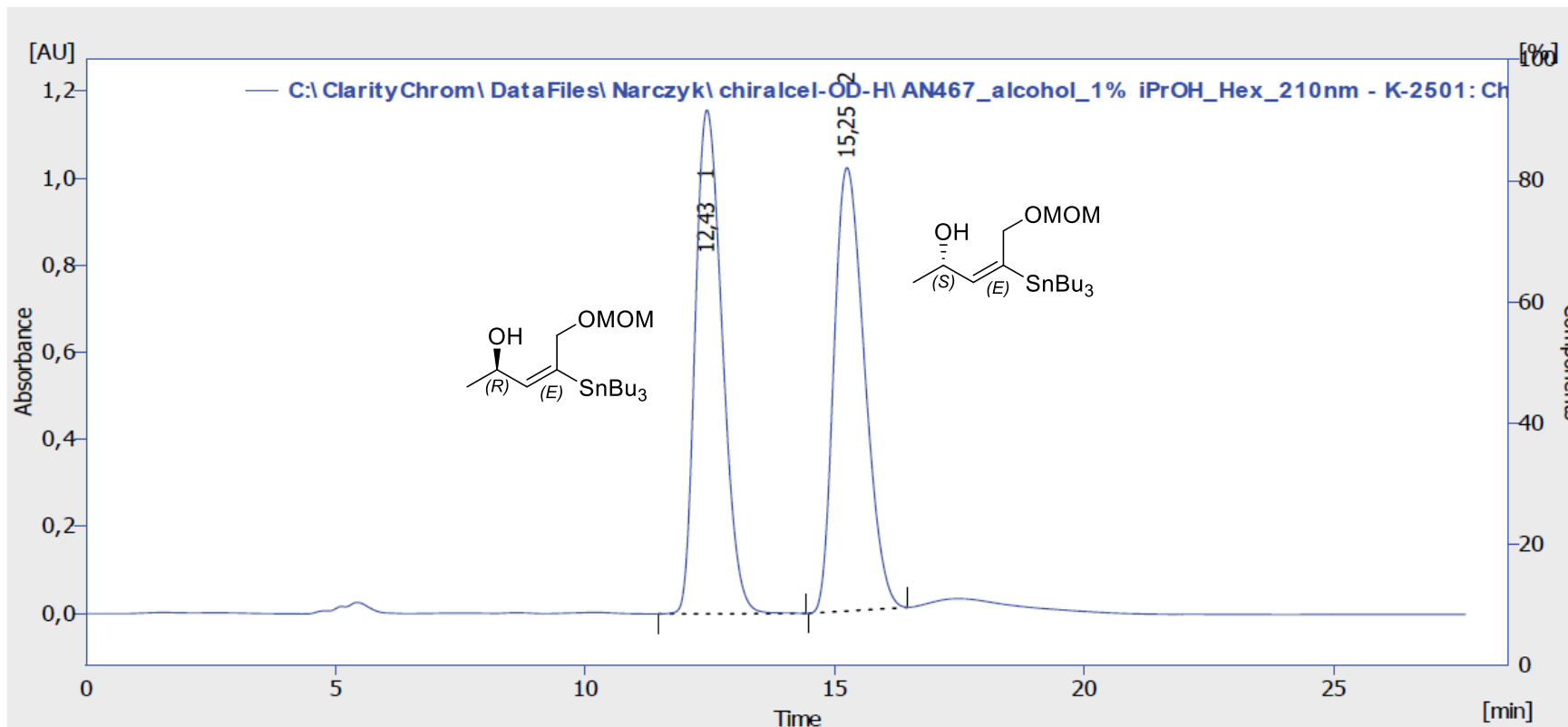






## HPLC chromatogram of compound *rac*-5b

Conditions: column Chiralcel OD-H, 1% *i*-PrOH in hexanes, 1mL/min, detection: UV, 210 nm



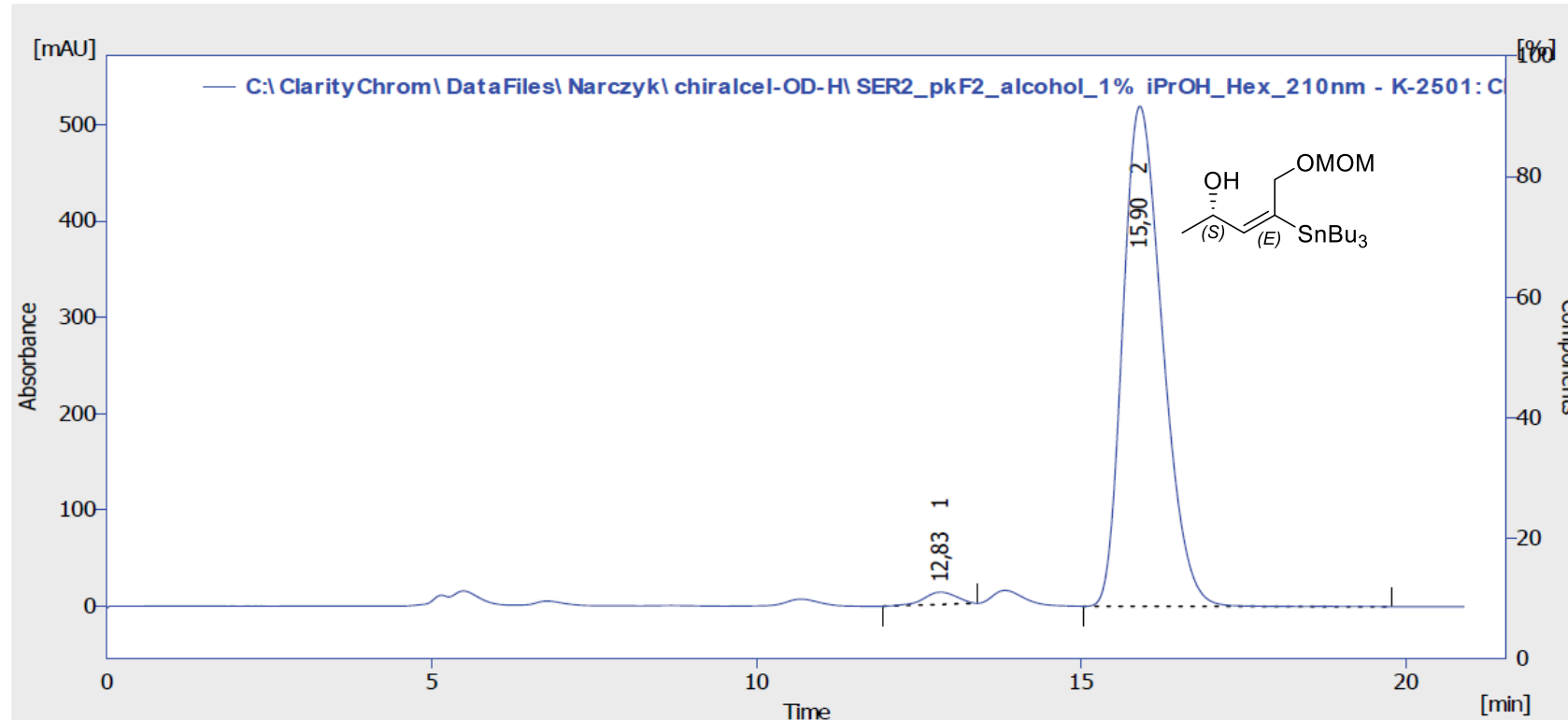
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN467\_alcohol\_1% iPrOH\_Hex\_210nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12,433	43385,355	1157,266	50,1	53,2	0,62	
2	15,250	43232,968	1018,681	49,9	46,8	0,68	
	Total	86618,324	2175,947	100,0	100,0		



## HPLC chromatogram of compound 5b

Conditions: column Chiralcel OD-H, 1% *i*-PrOH in hexanes, 1mL/min, detection: UV, 210 nm

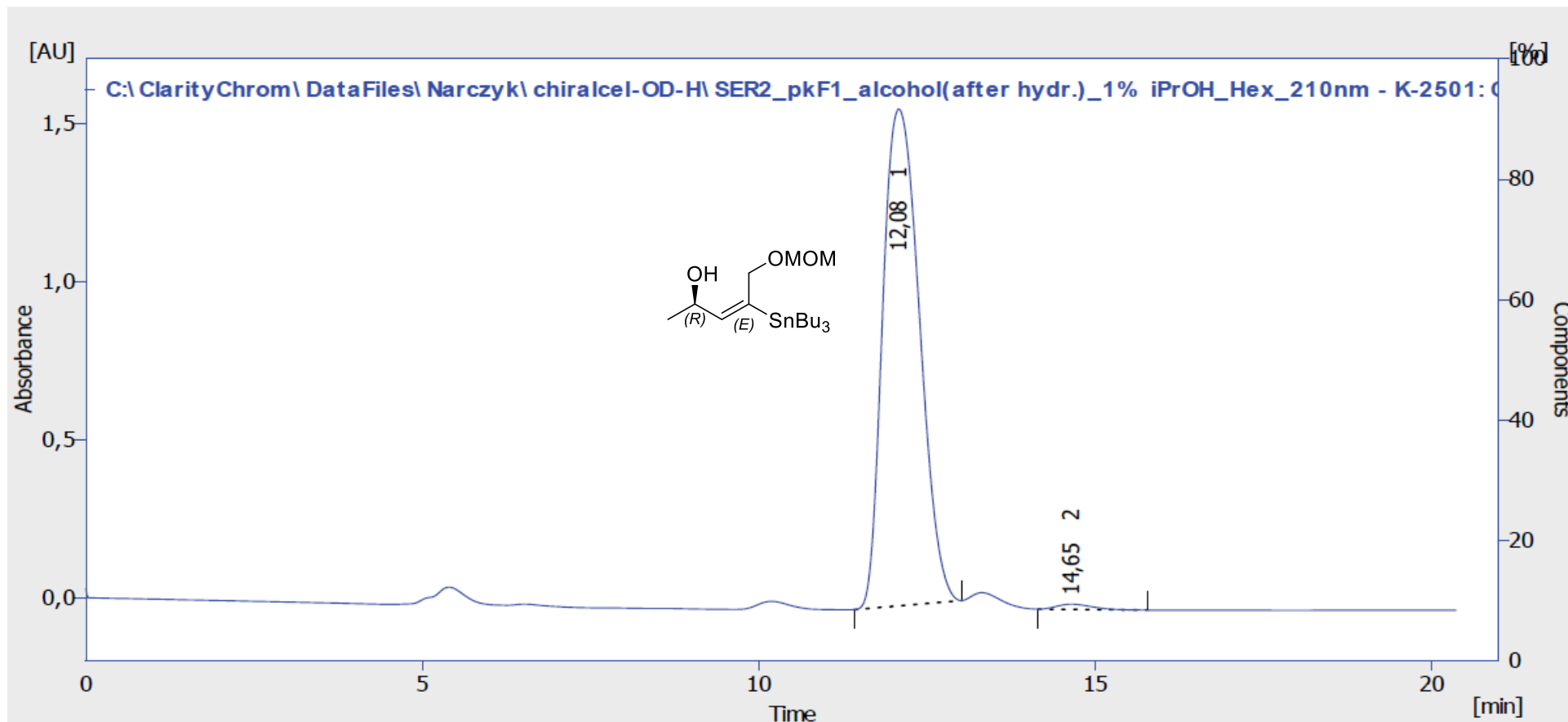


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER2\_pkF2\_alcohol\_1% iPrOH\_Hex\_210nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12,833	443,049	12,755	2,0	2,4	0,58	
2	15,900	22083,832	519,226	98,0	97,6	0,68	
	Total	22526,881	531,982	100,0	100,0		

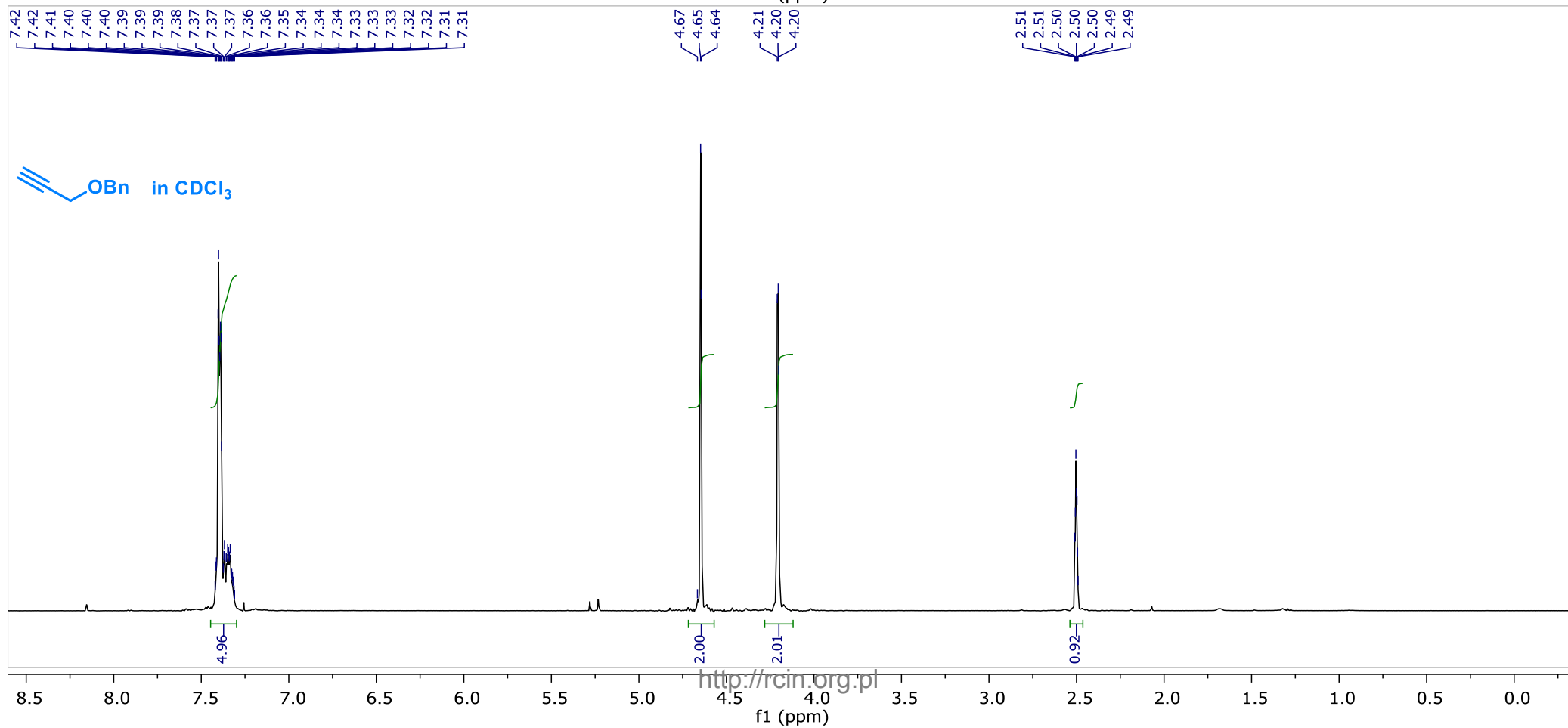
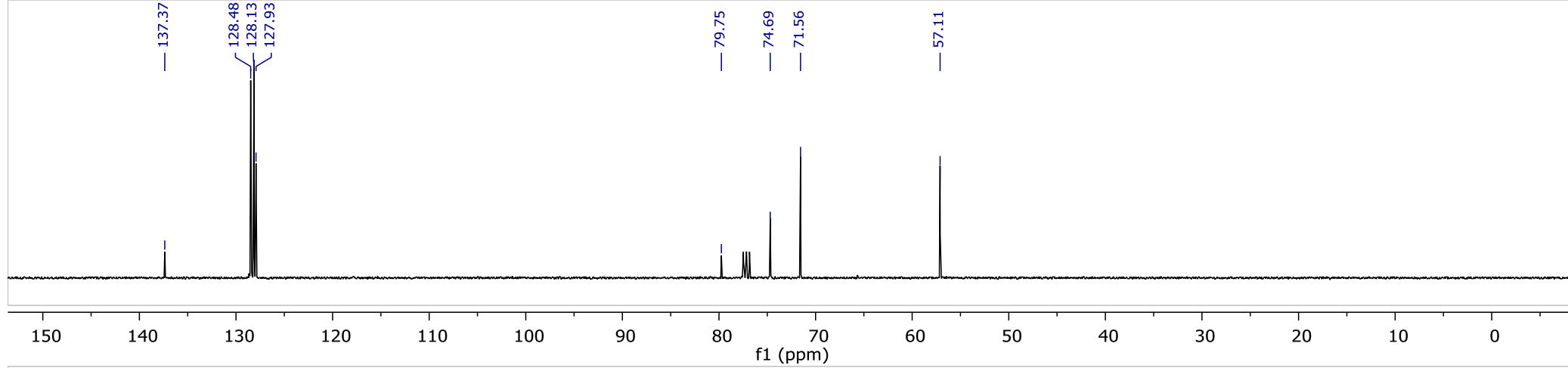
## HPLC chromatogram of compound *ent*-5b

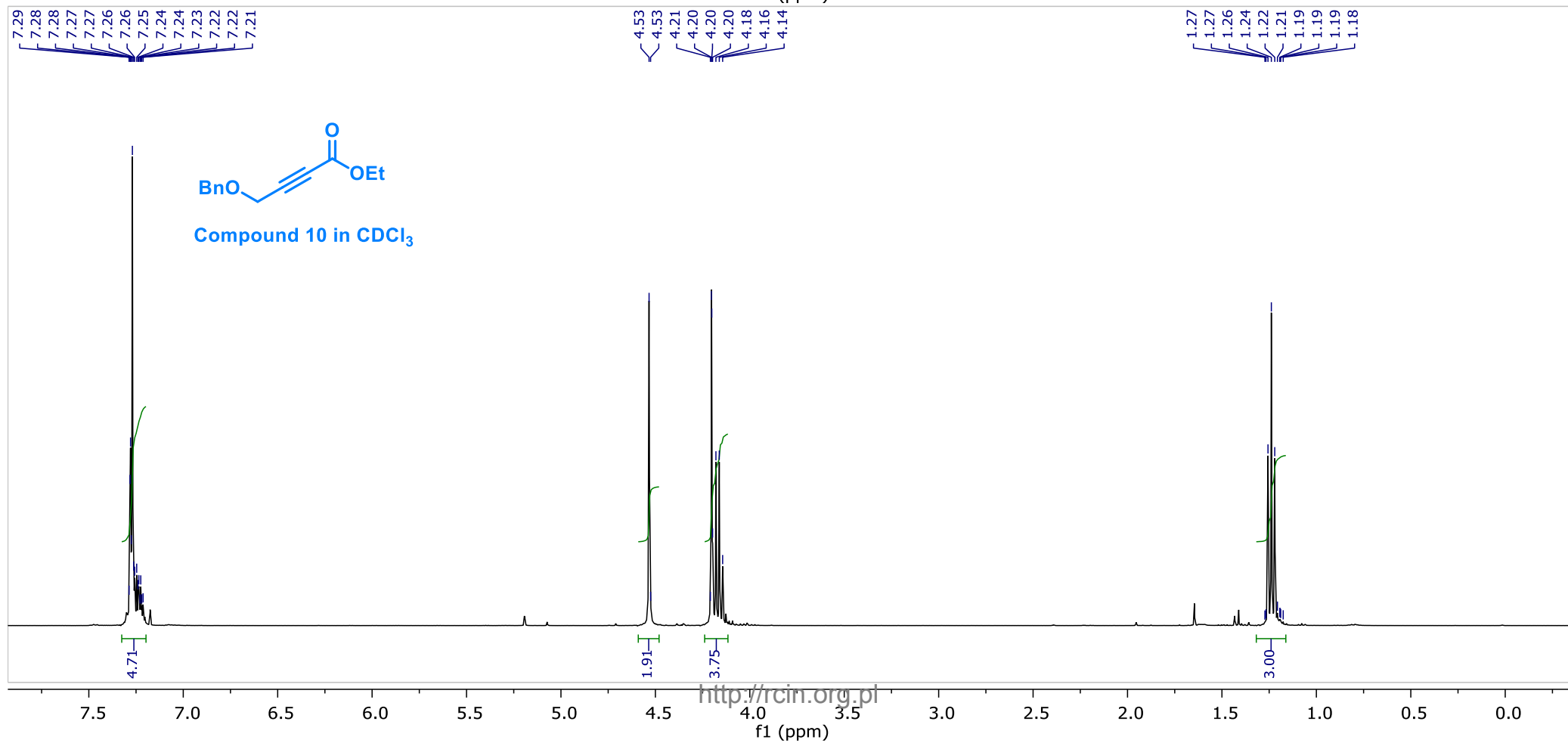
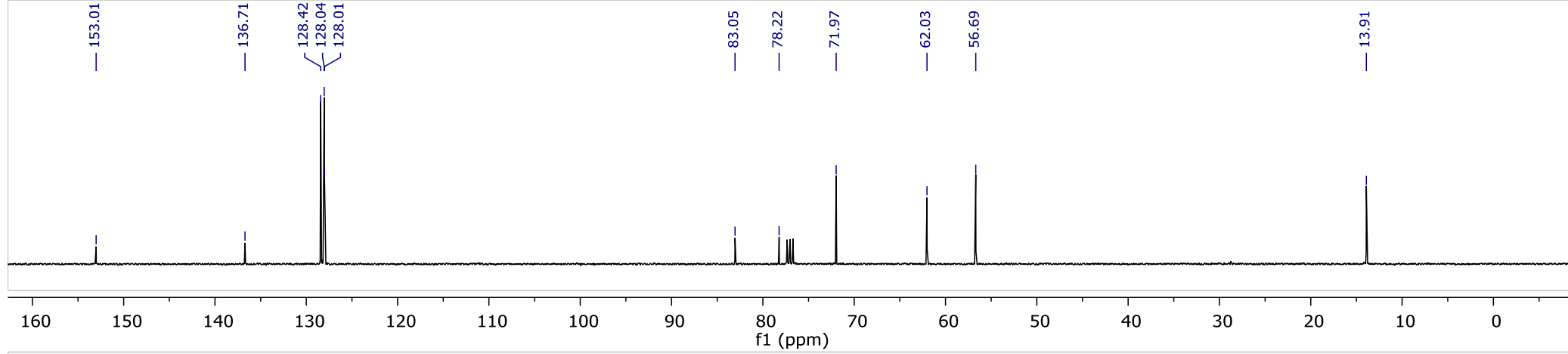
Conditions: column Chiralcel OD-H, 1% *i*-PrOH in hexanes, 1mL/min, detection: UV, 210 nm

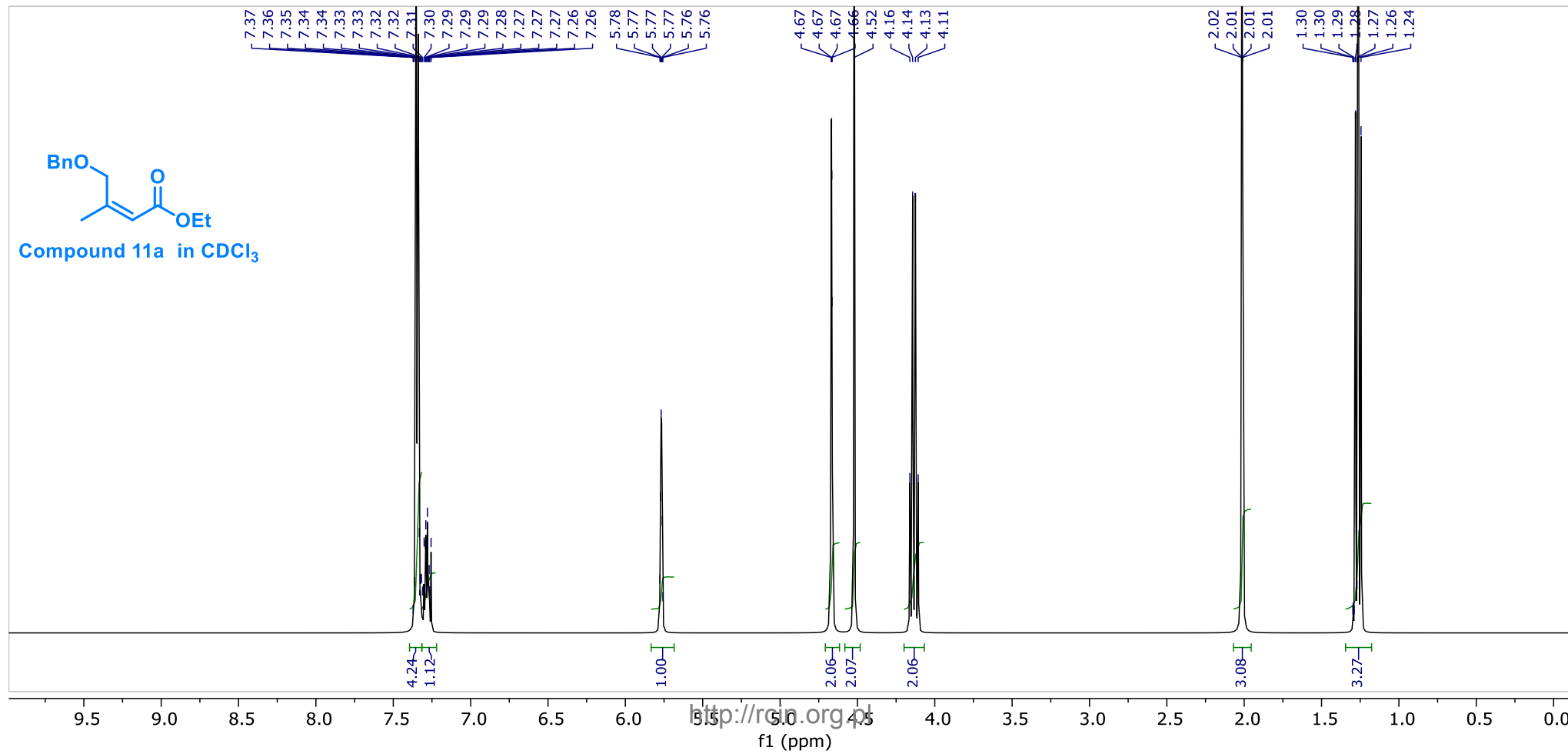
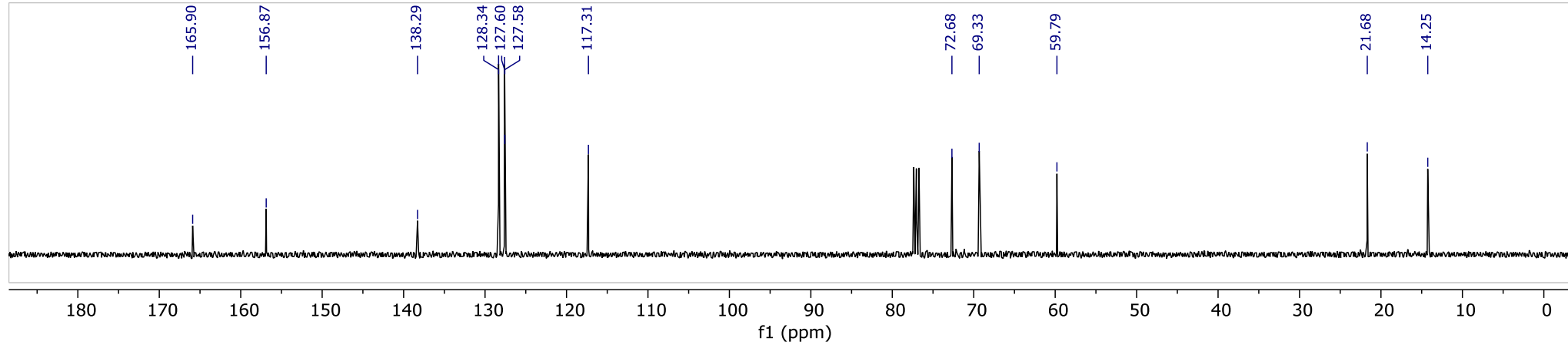


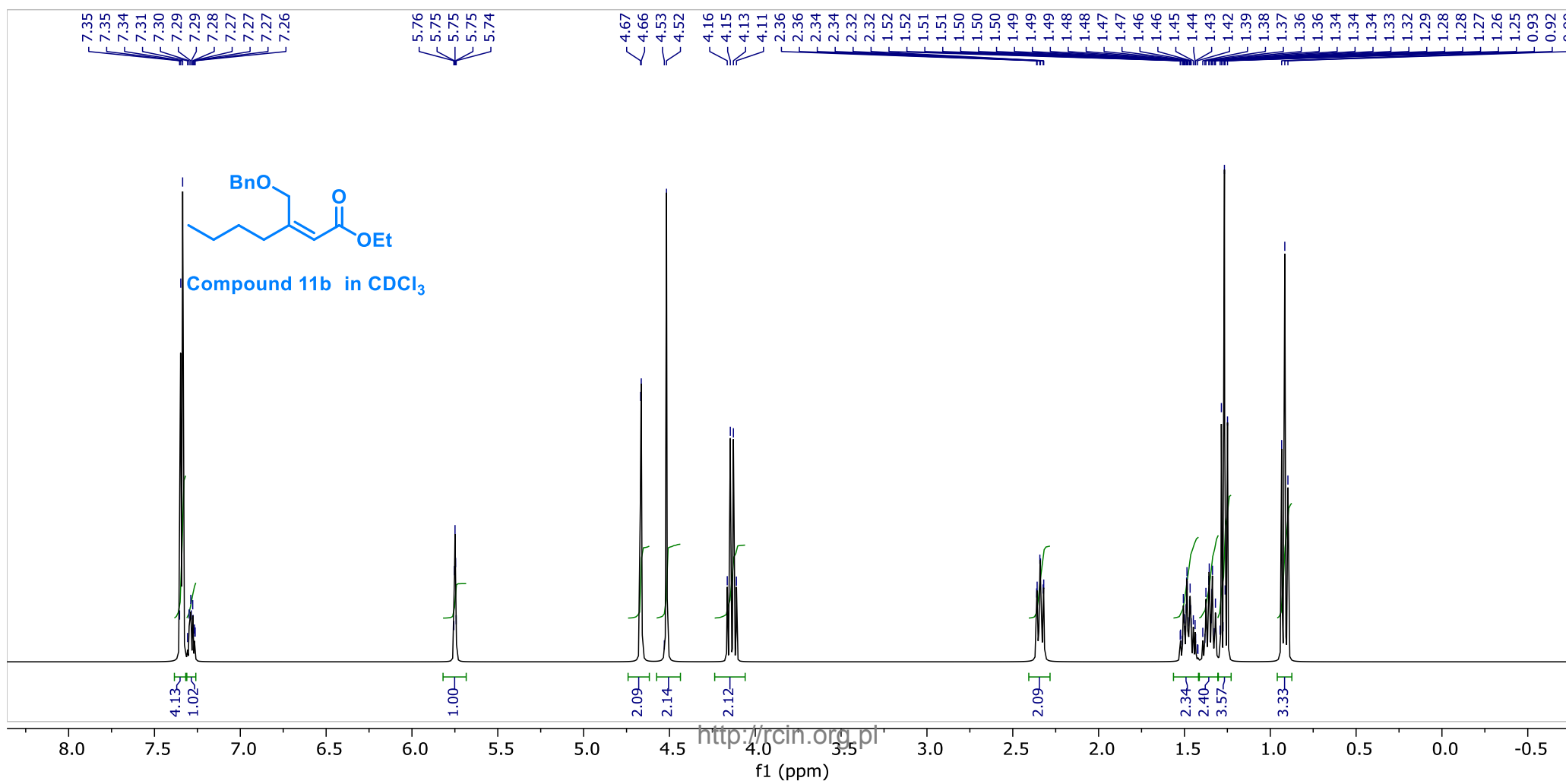
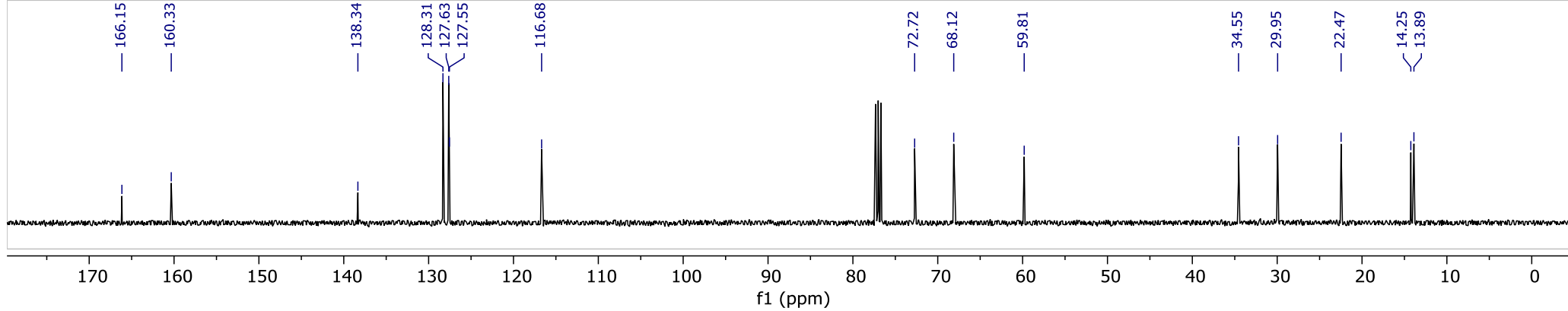
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER2\_pkF1\_alcohol(after hydr.)\_1% iPrOH\_Hex\_210nm - K-2501: Channel 1)

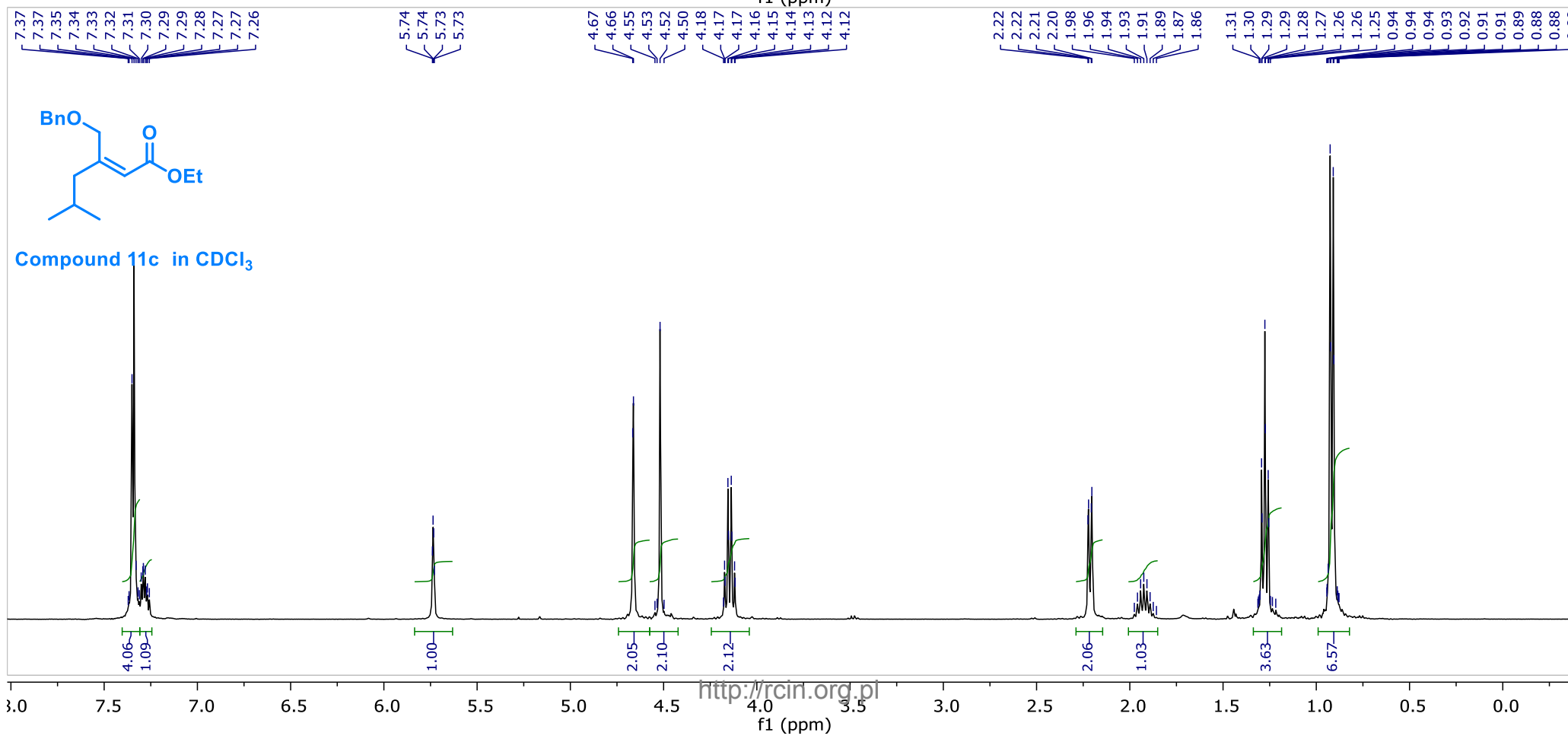
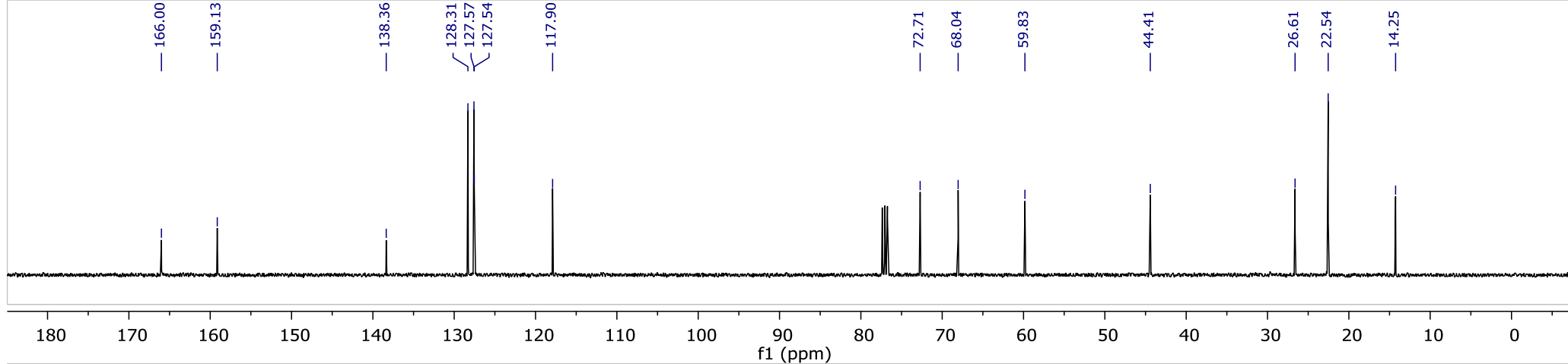
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12,083	59572,954	1573,337	99,0	99,0	0,63	
2	14,650	593,705	16,562	1,0	1,0	0,58	
	Total	60166,659	1589,899	100,0	100,0		

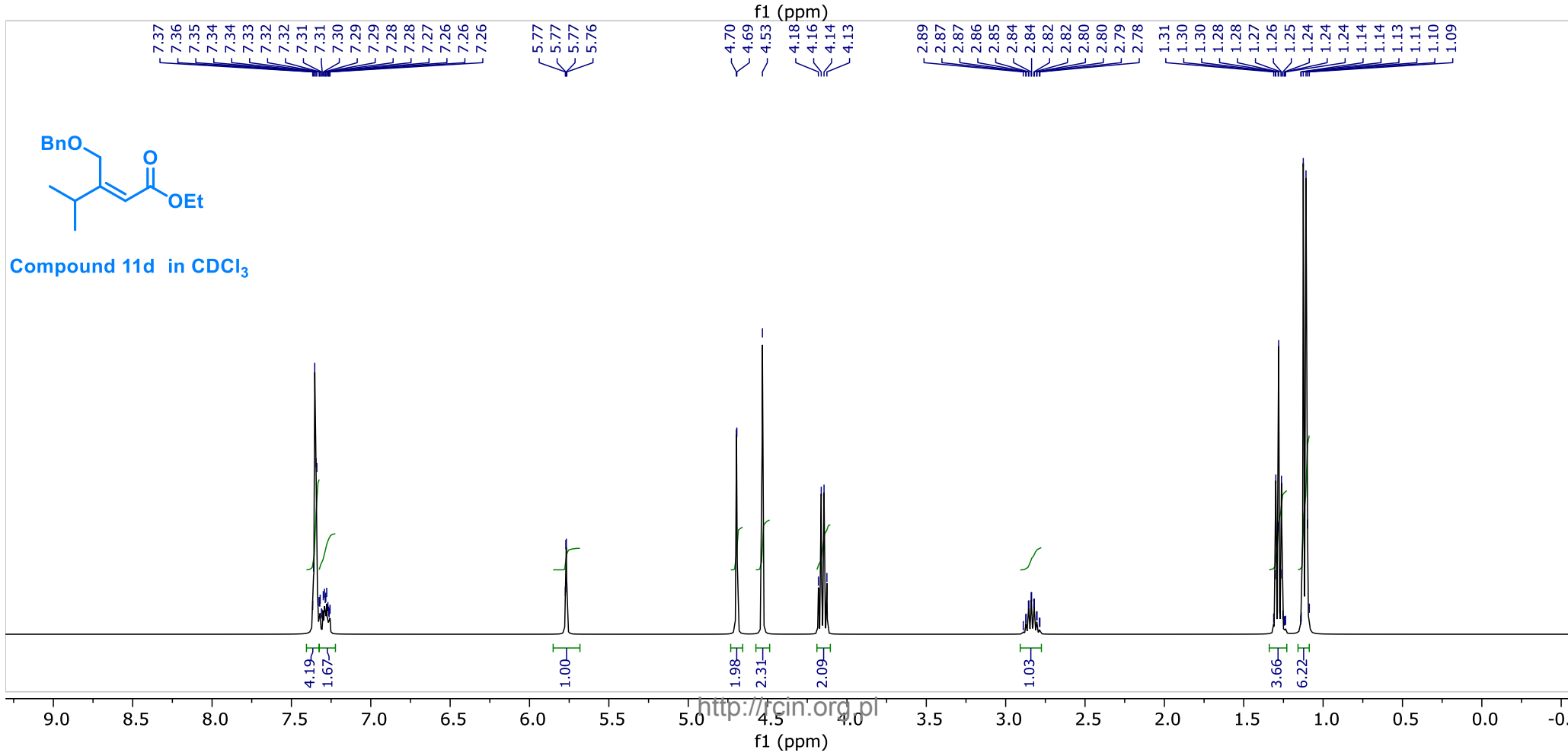
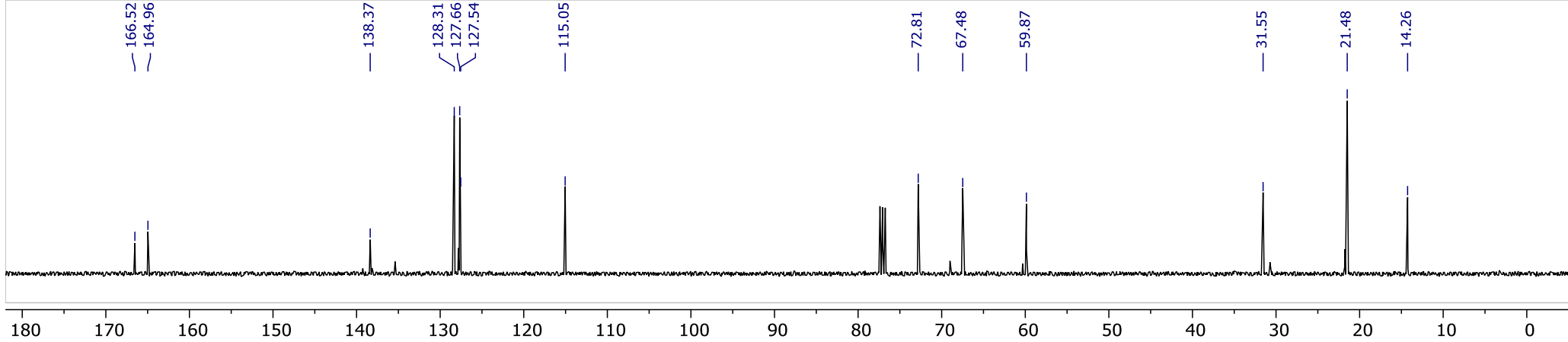




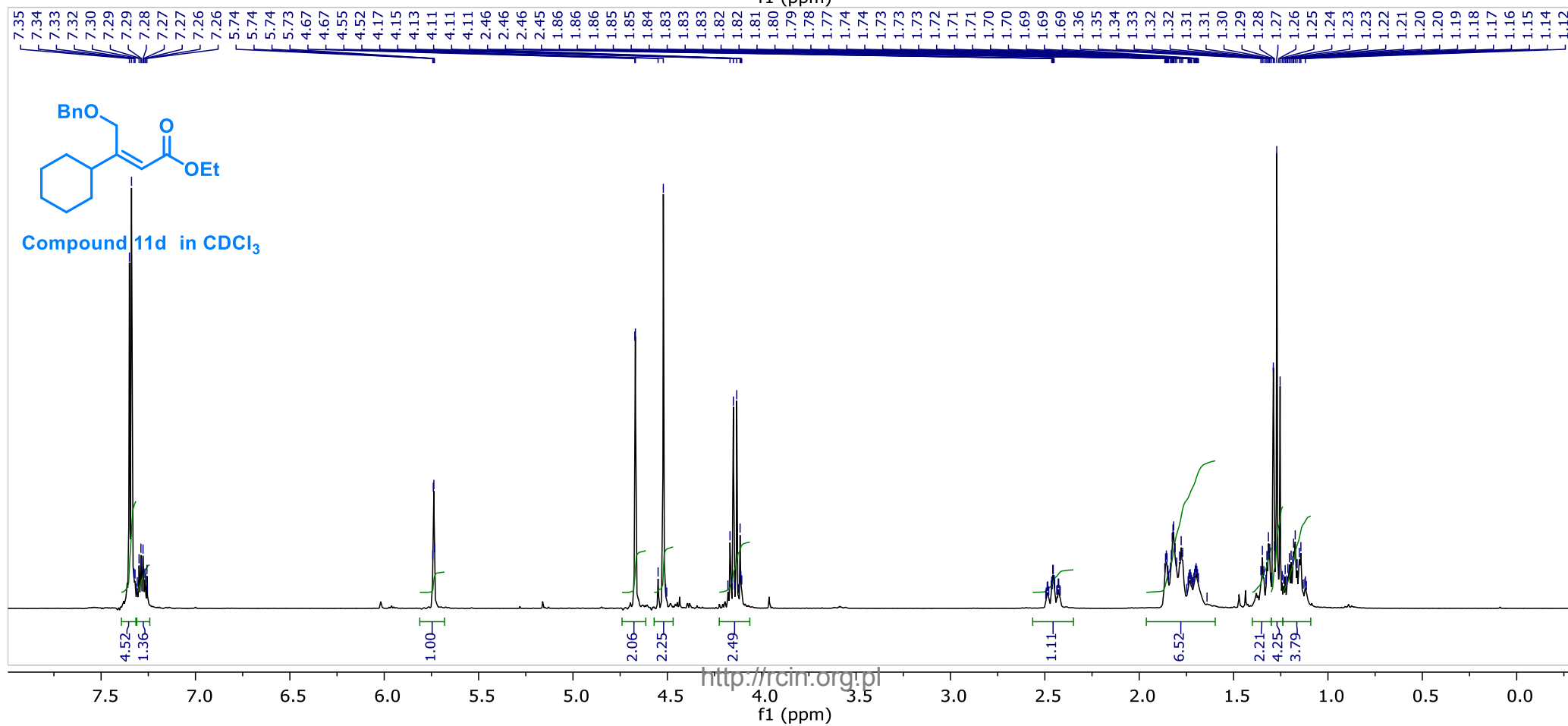
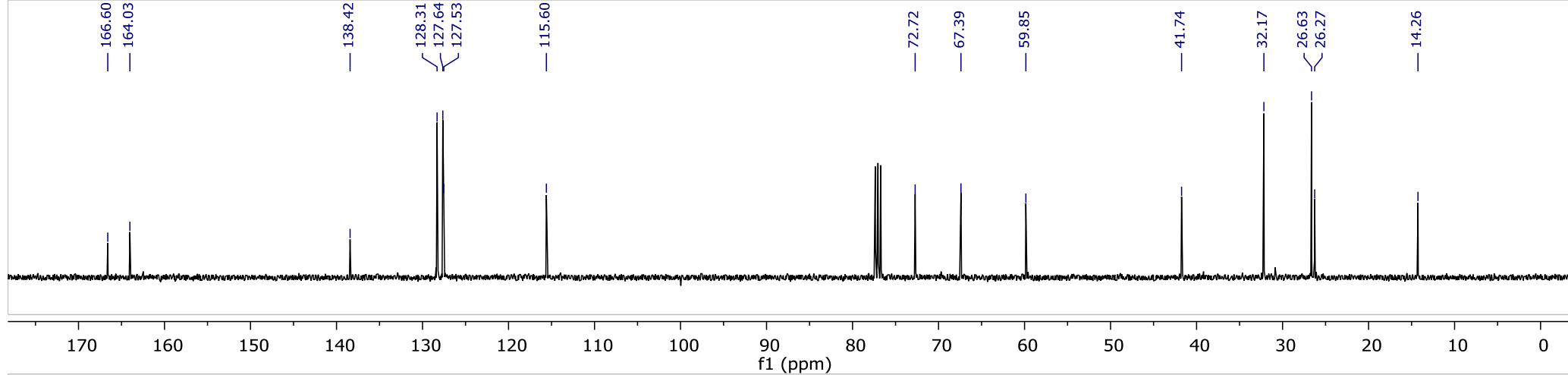


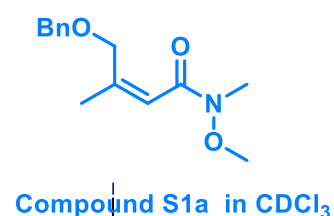
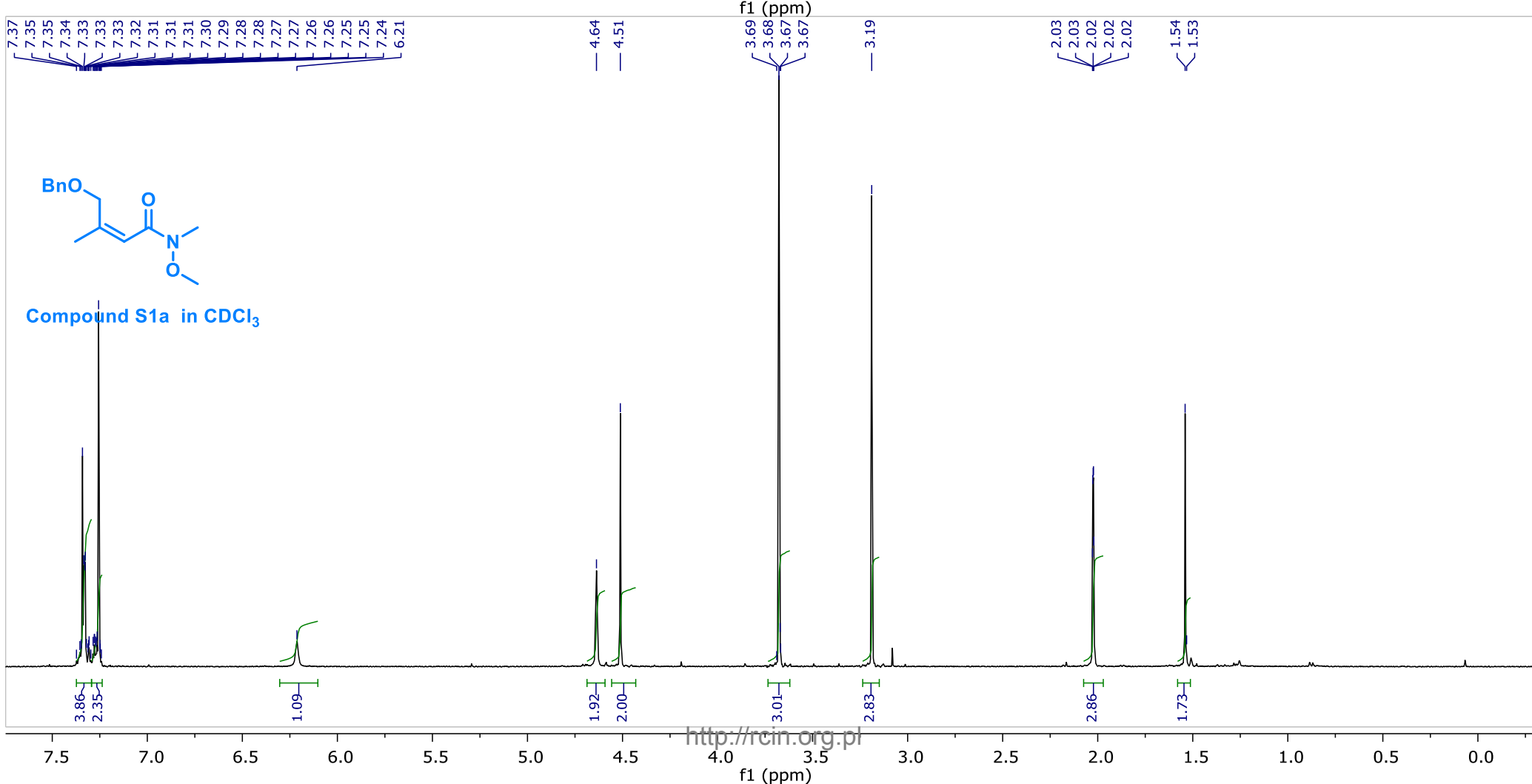
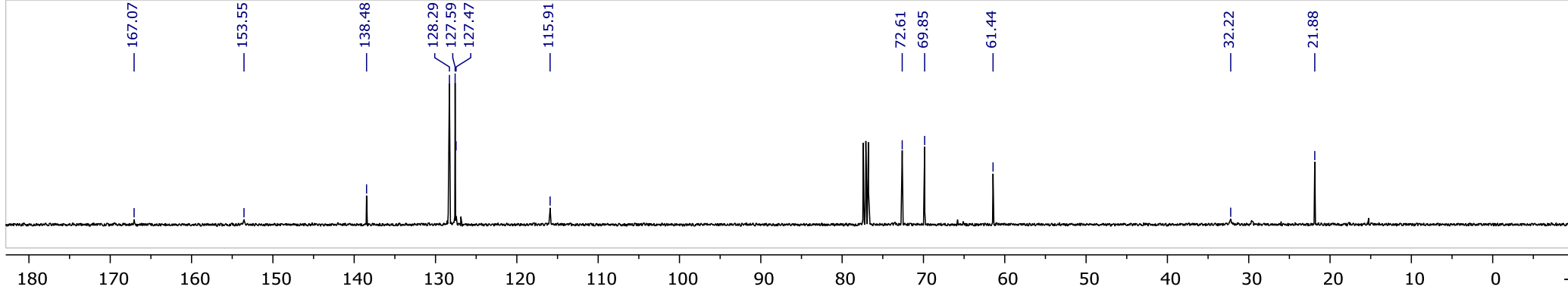


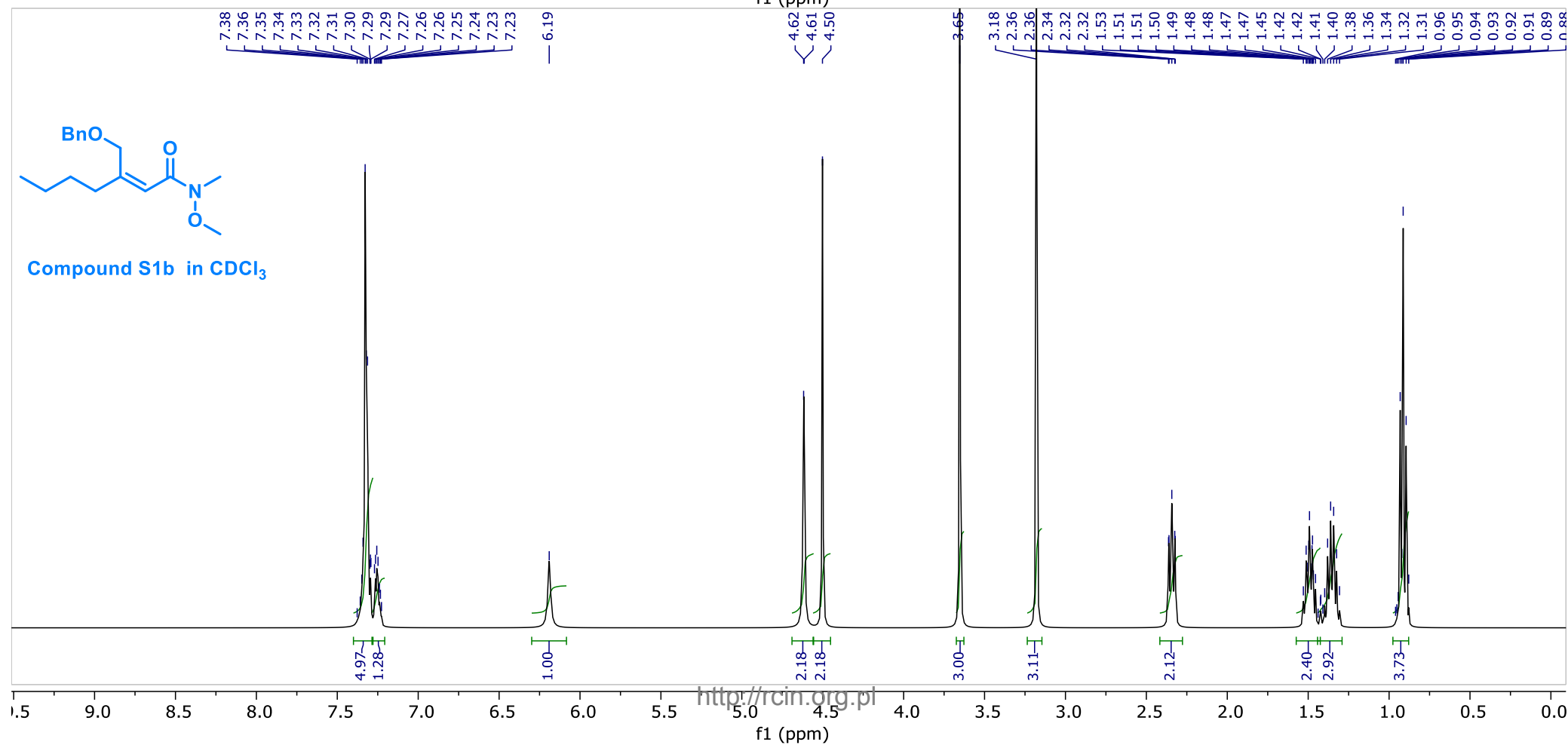
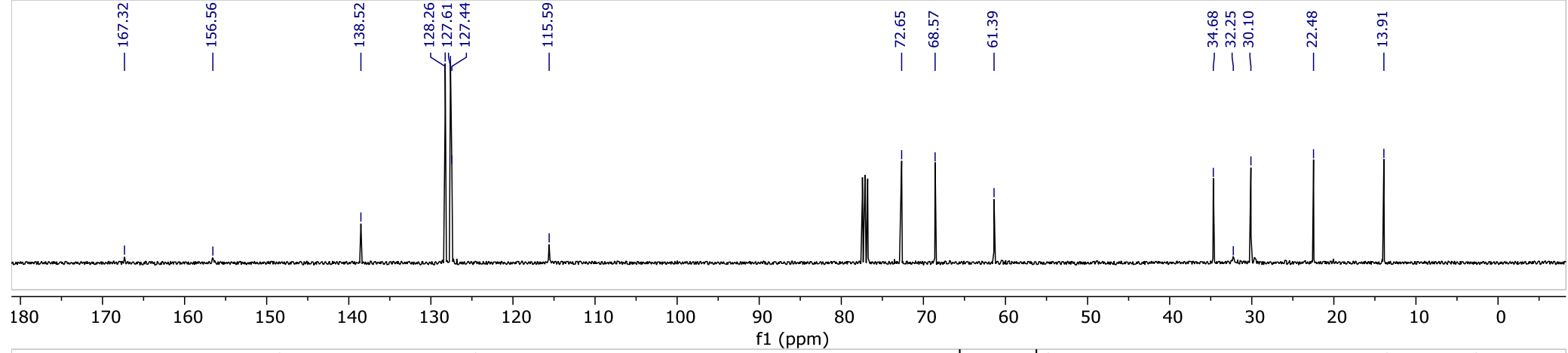


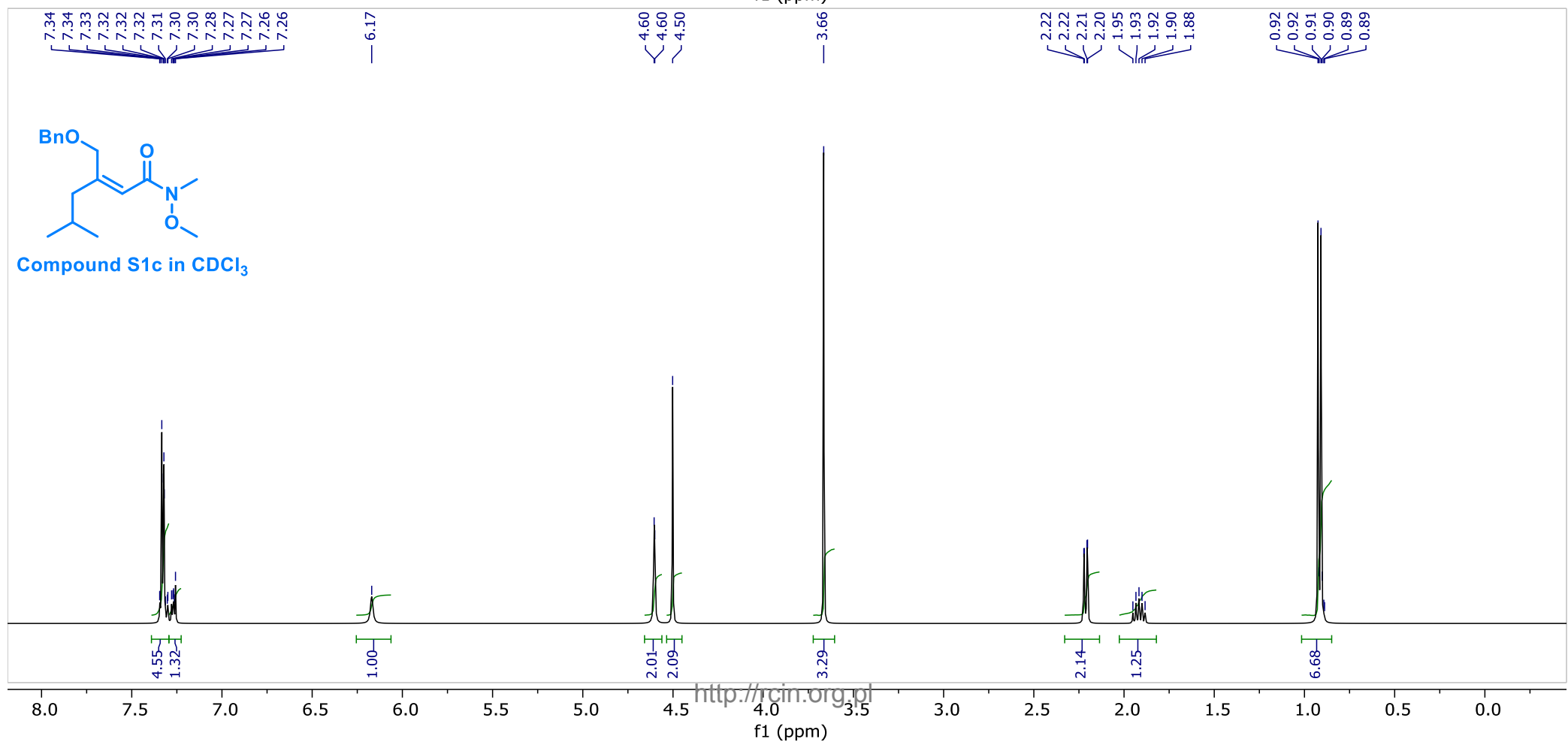
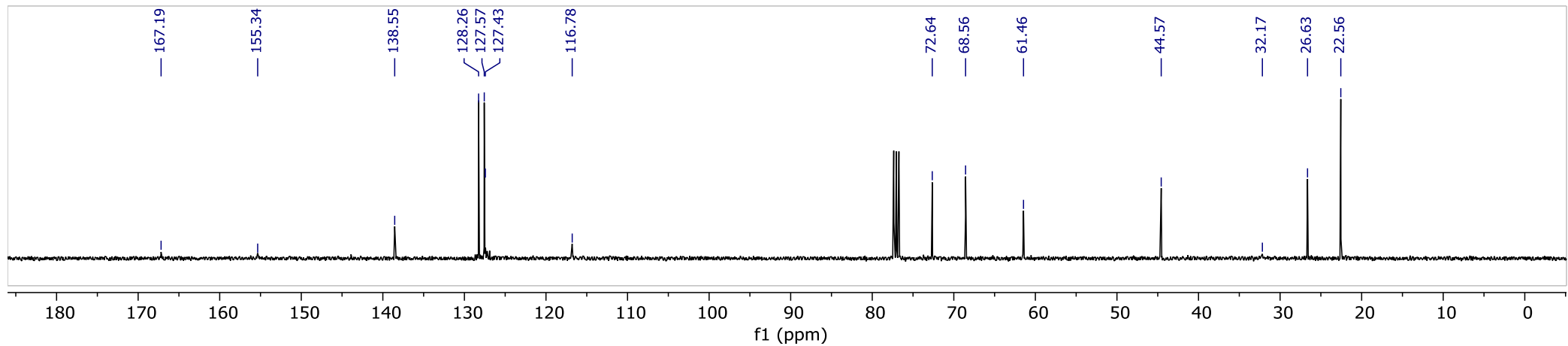


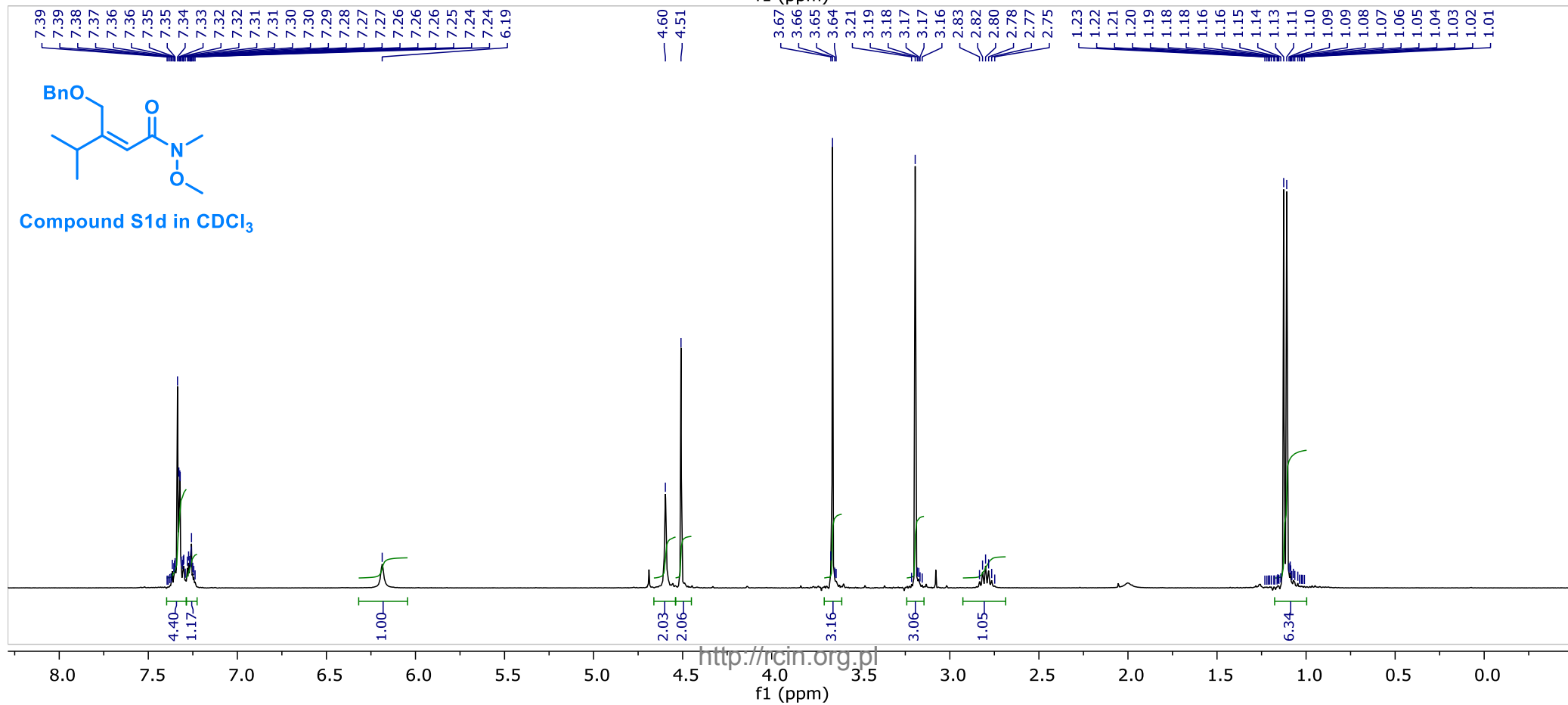
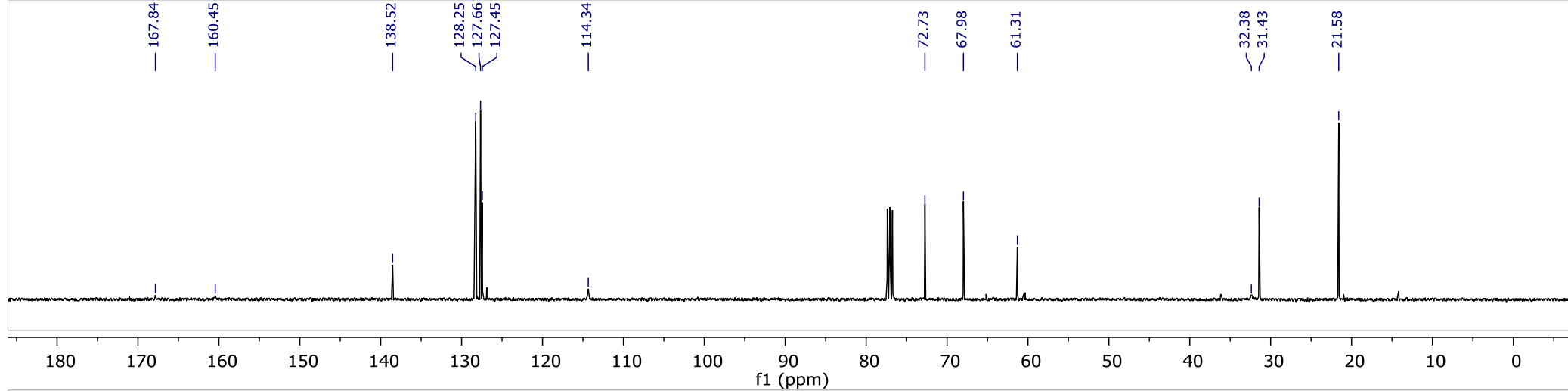


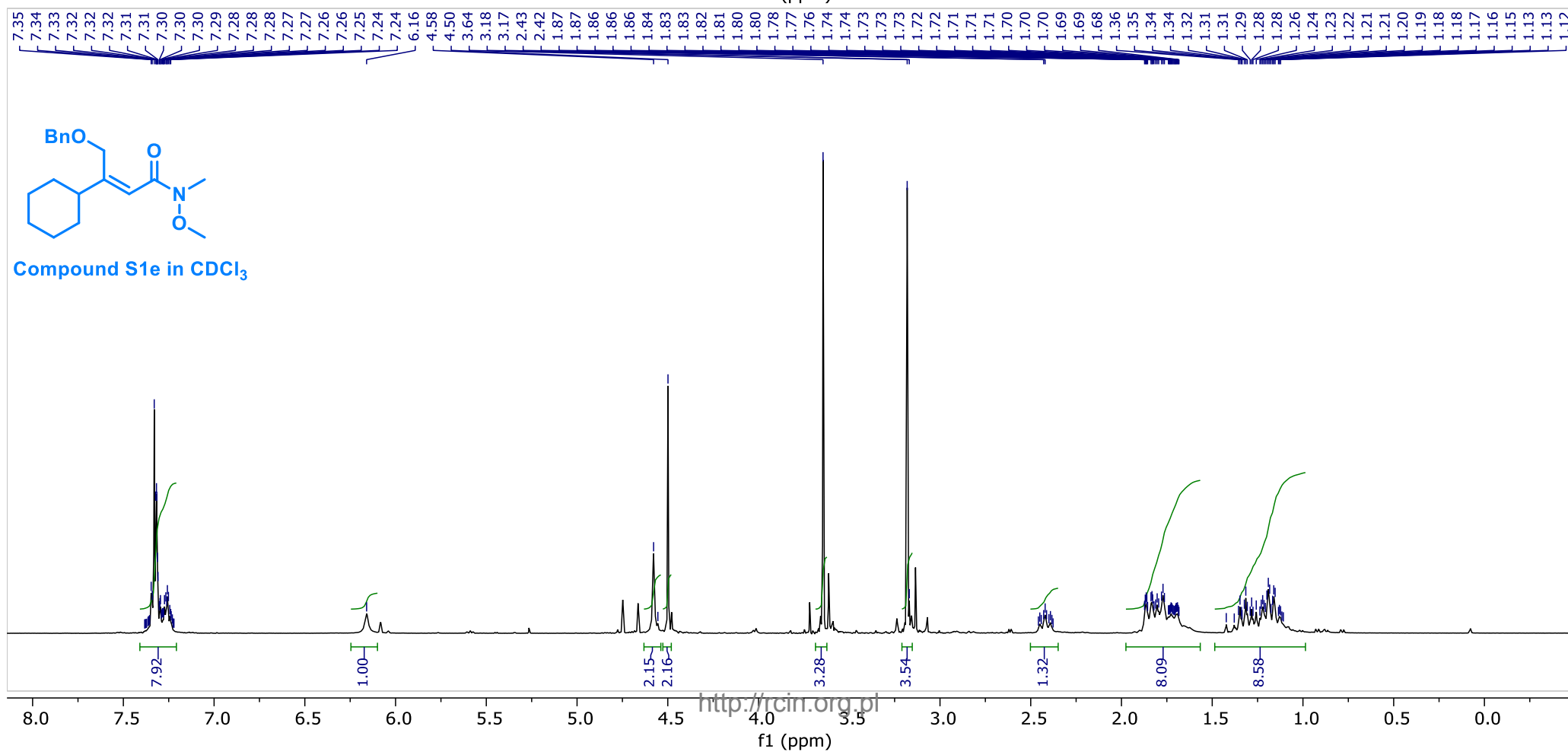
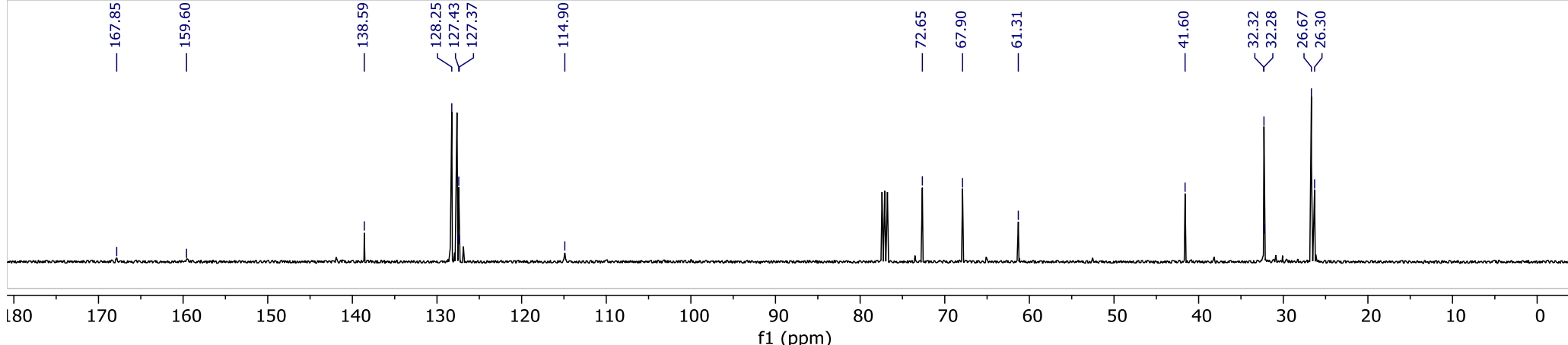


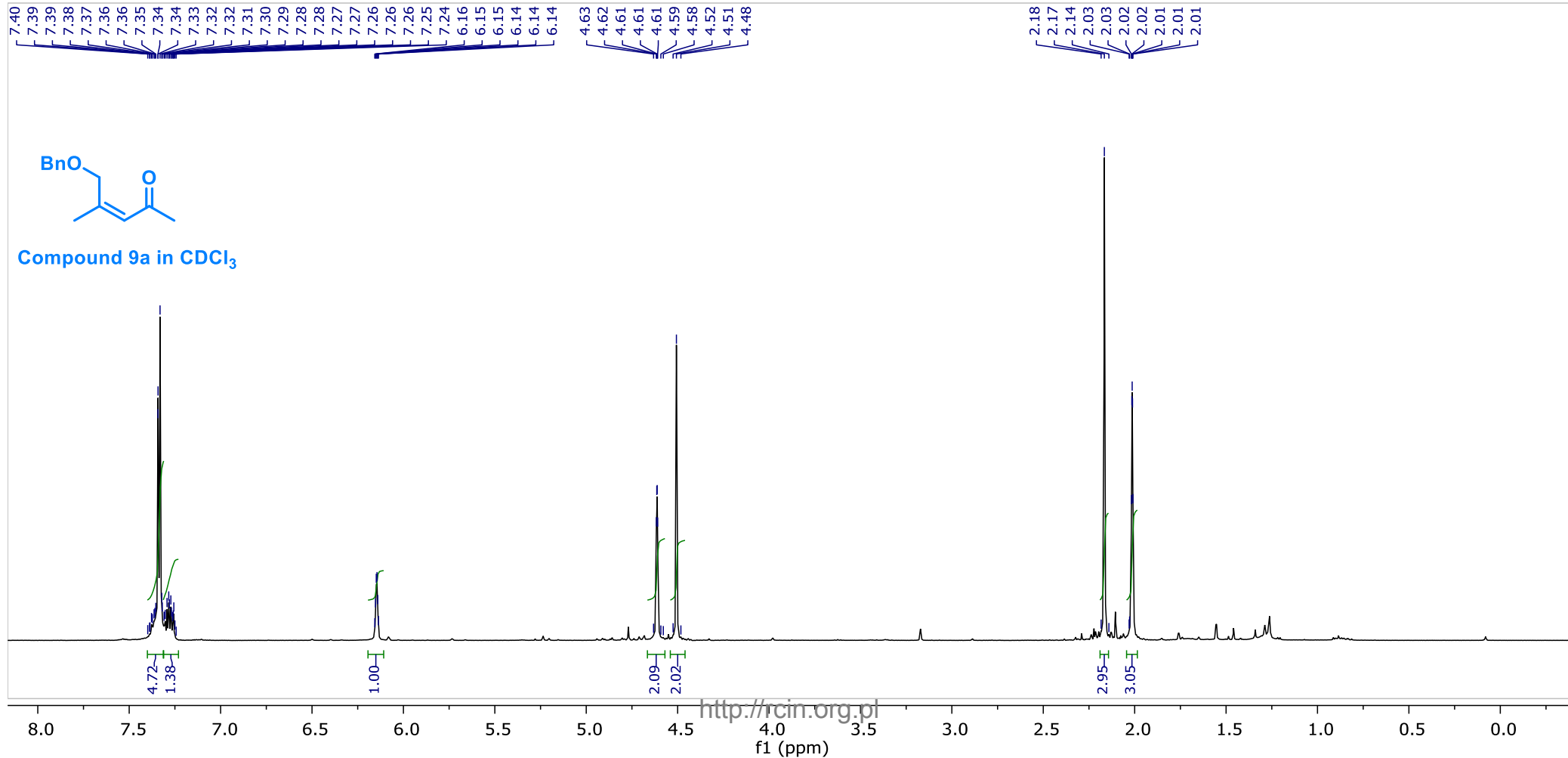
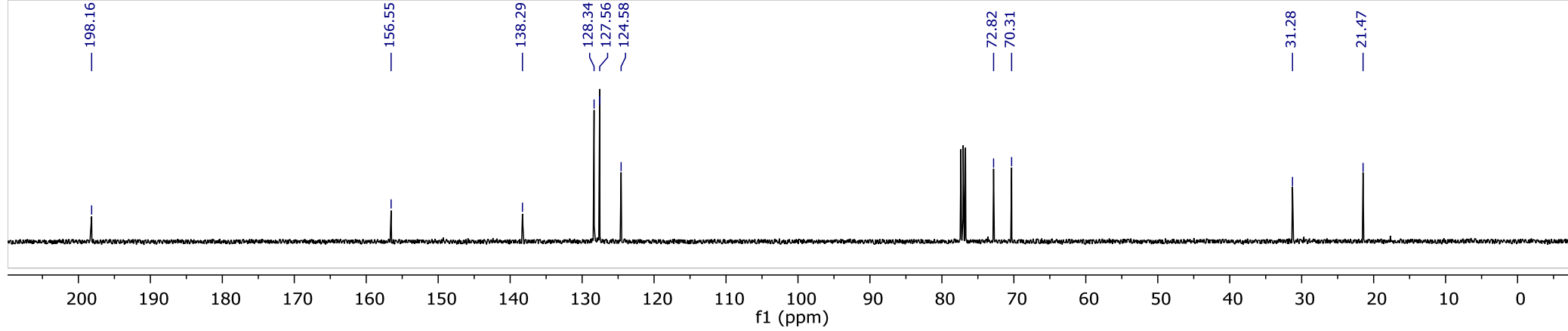


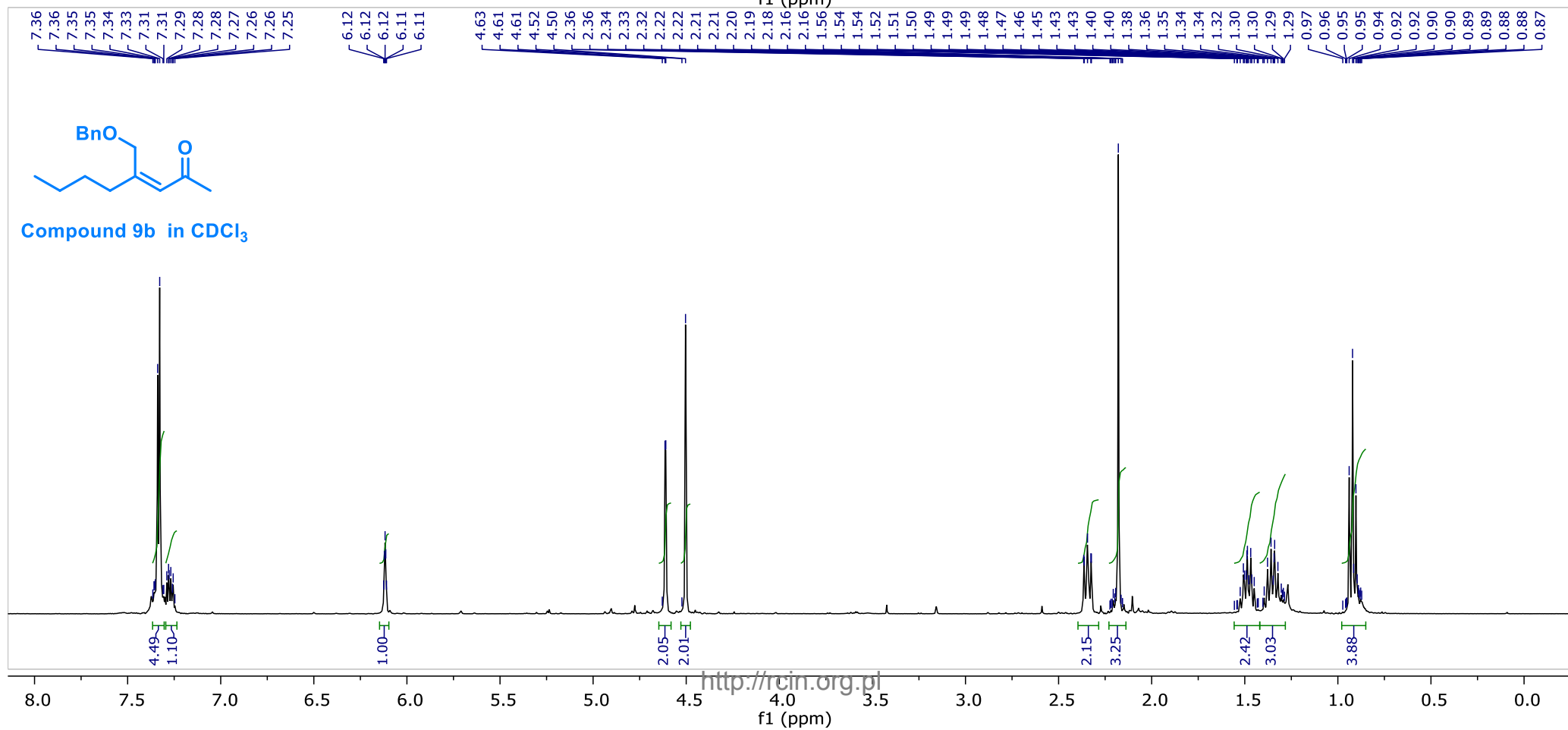
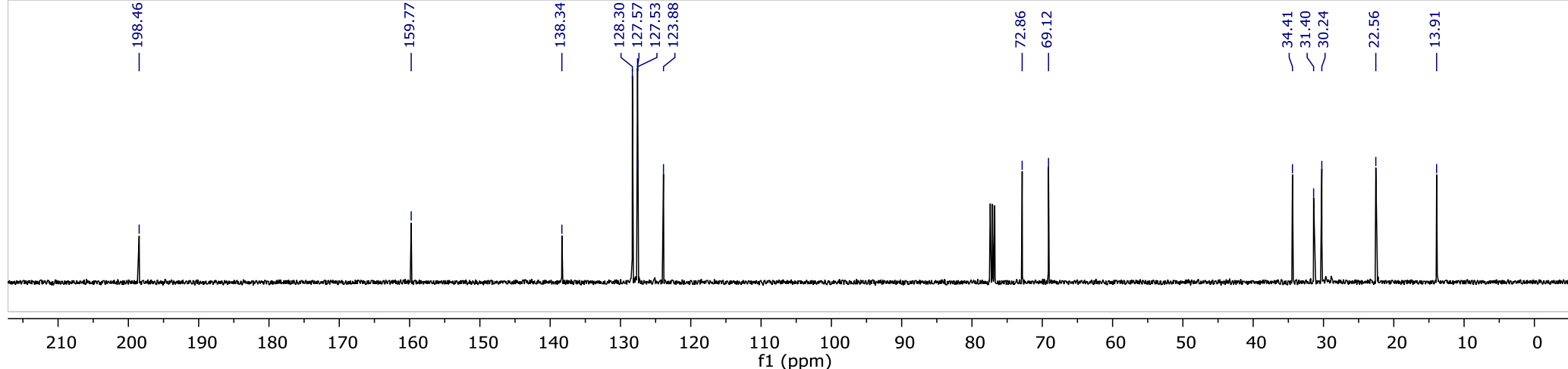




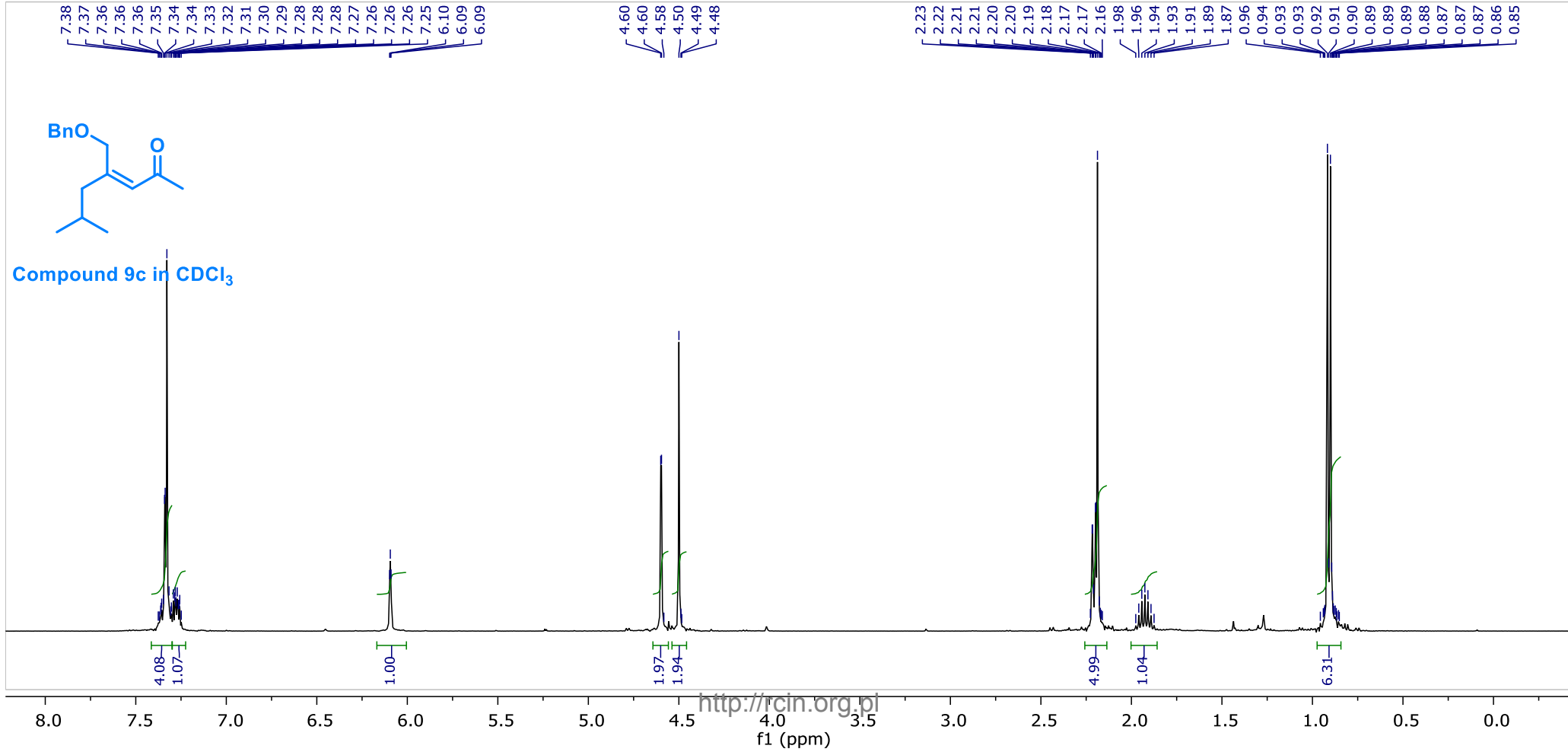
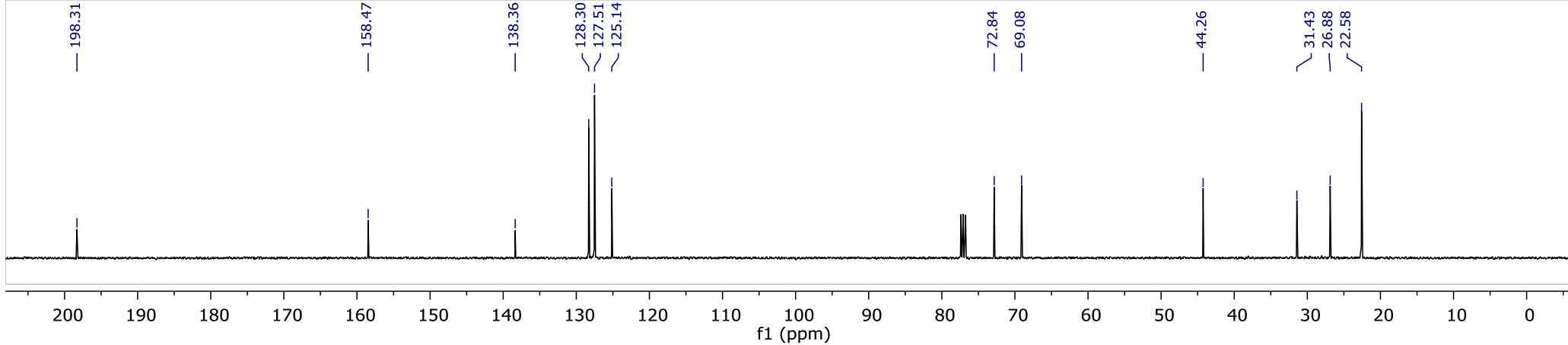


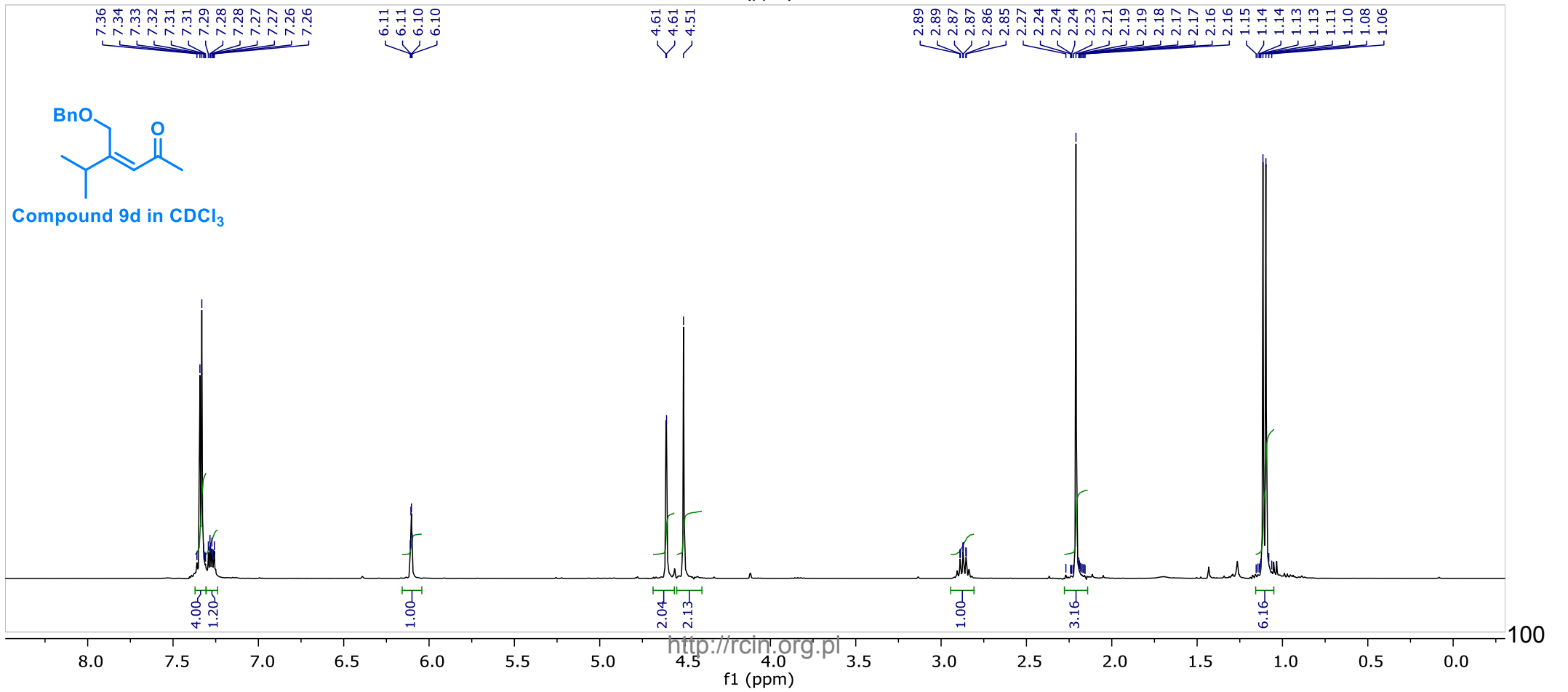
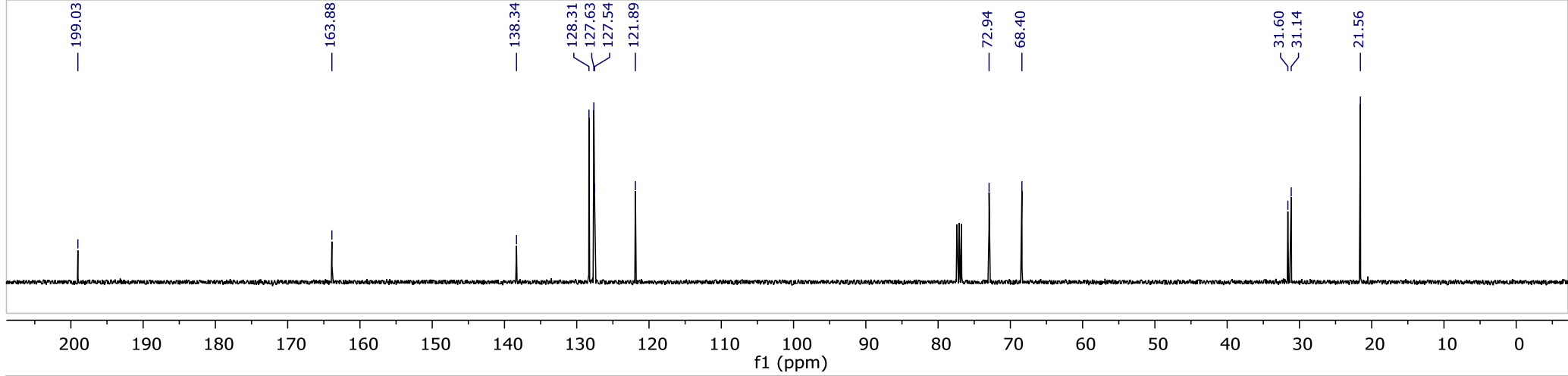


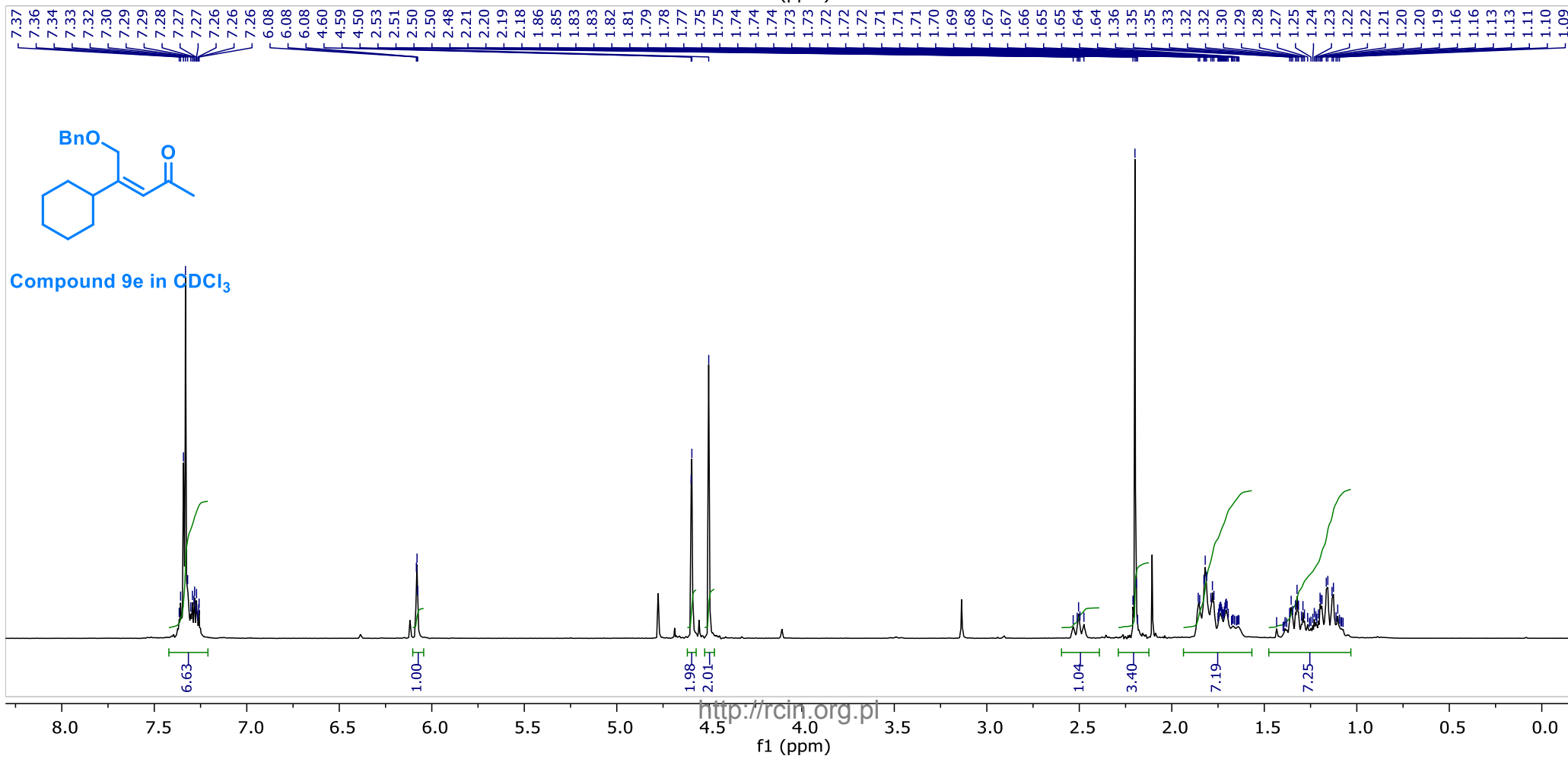
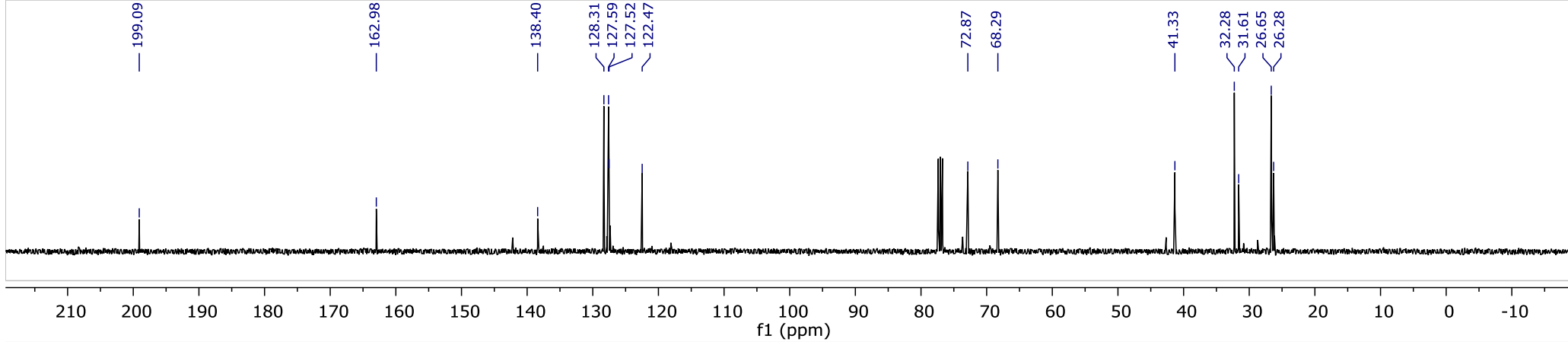


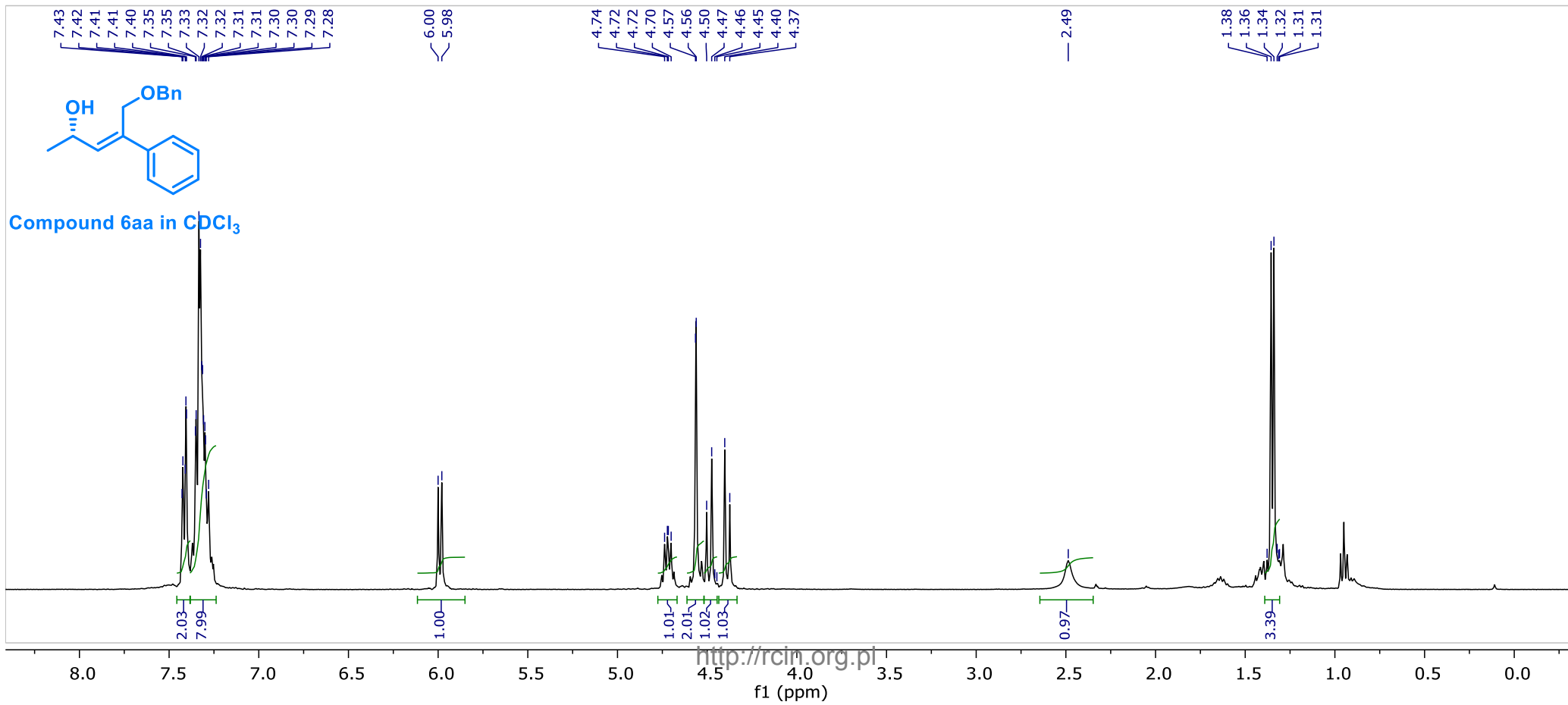
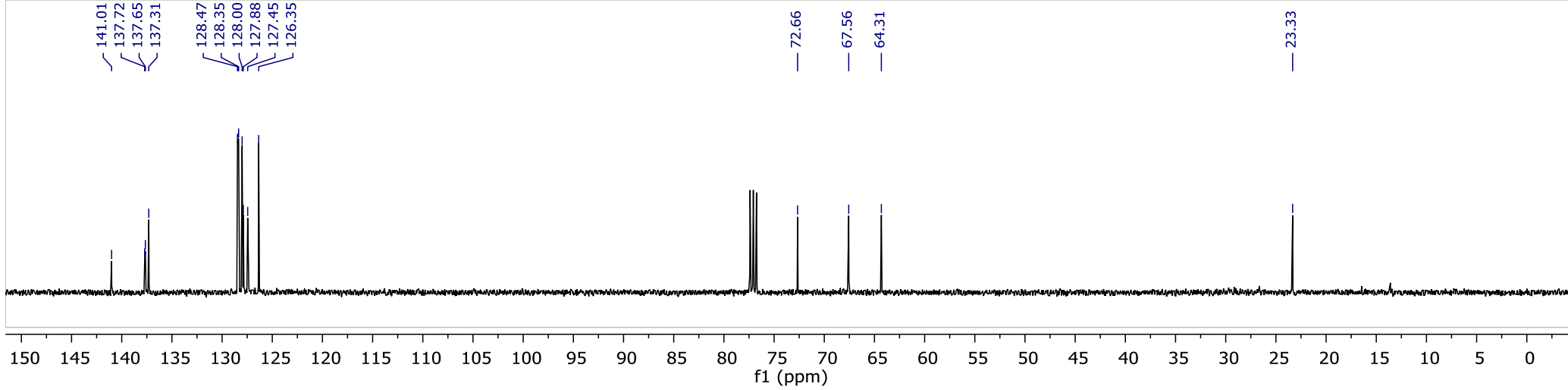


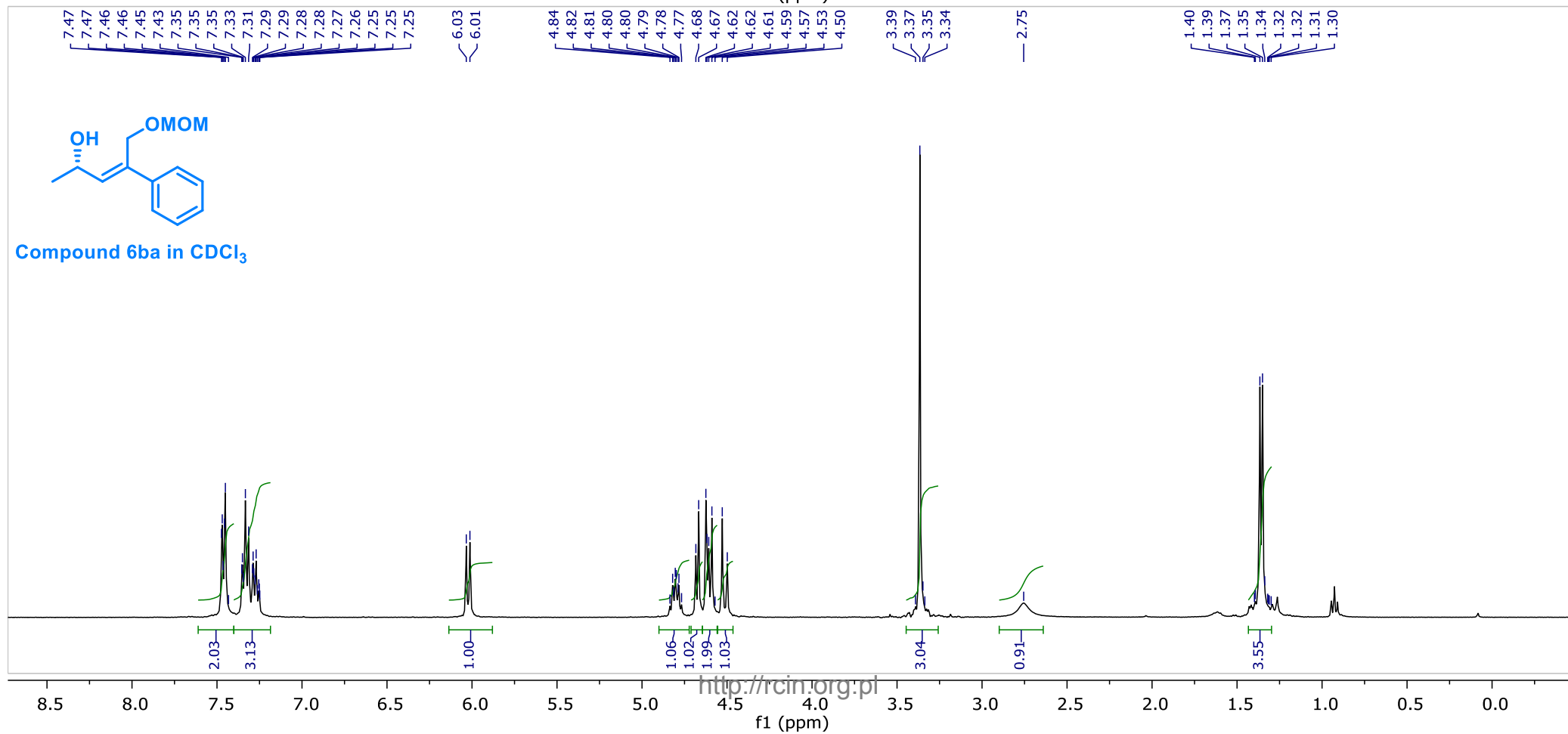
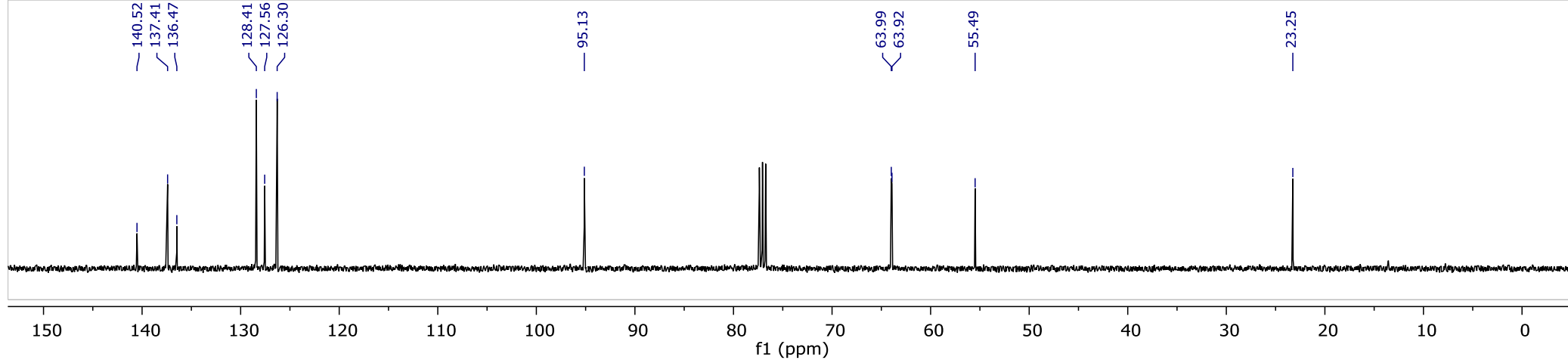






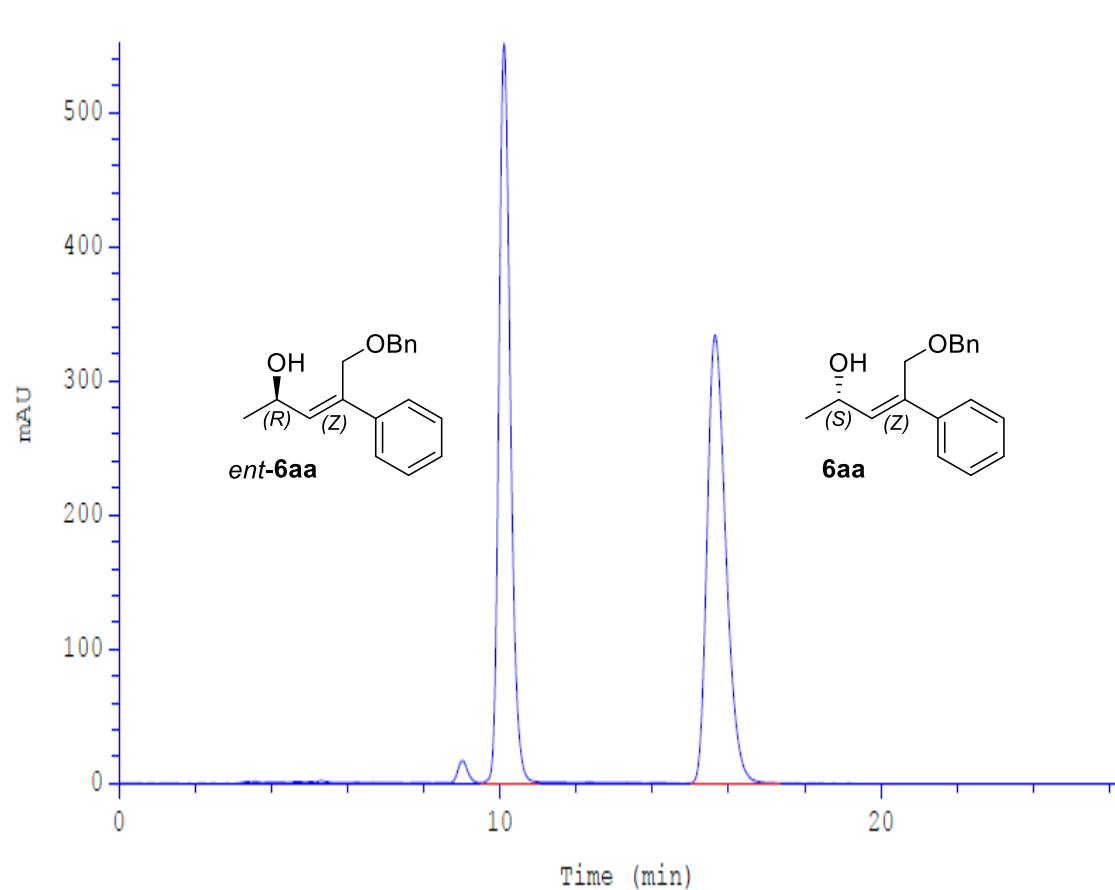




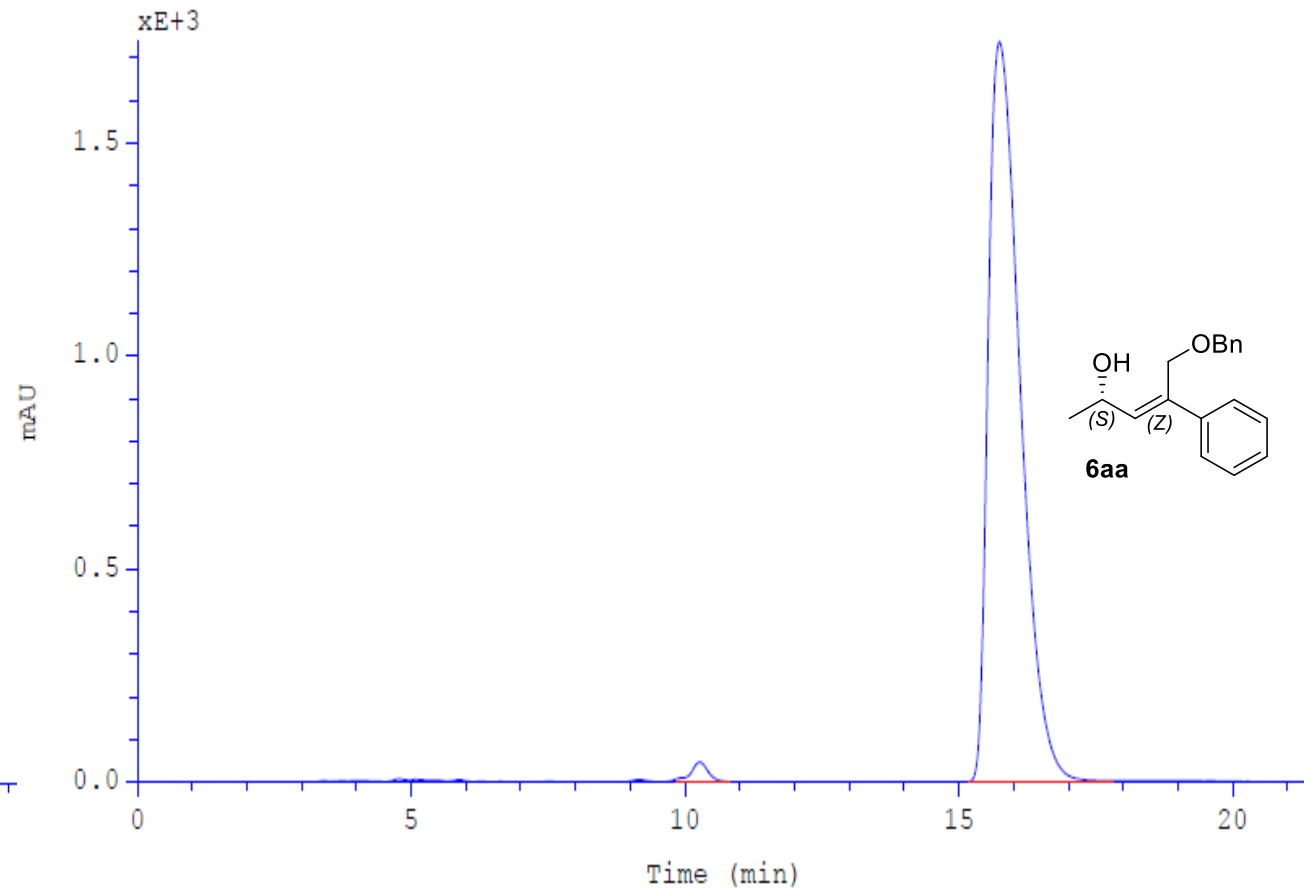


## HPLC chromatogram of compound *rac*-6aa and 6aa

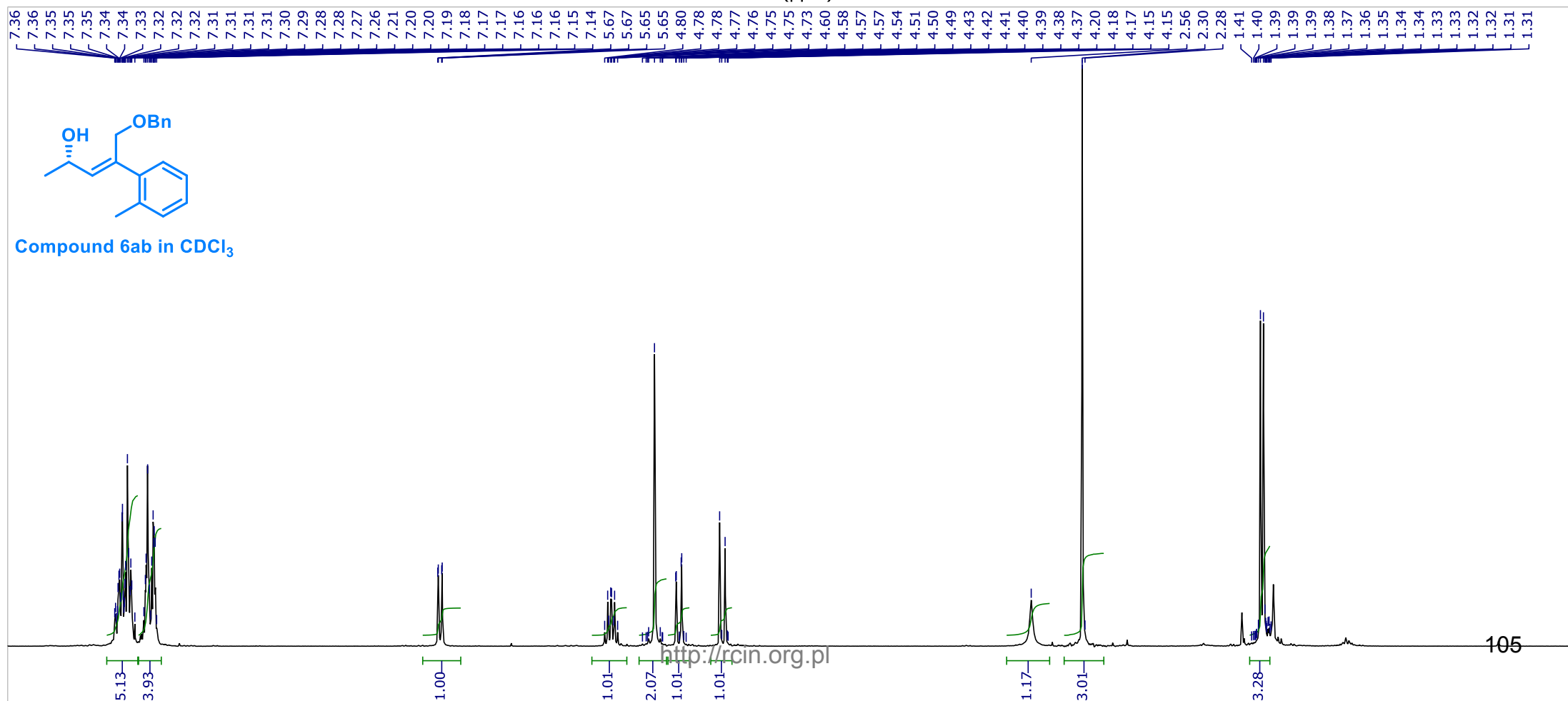
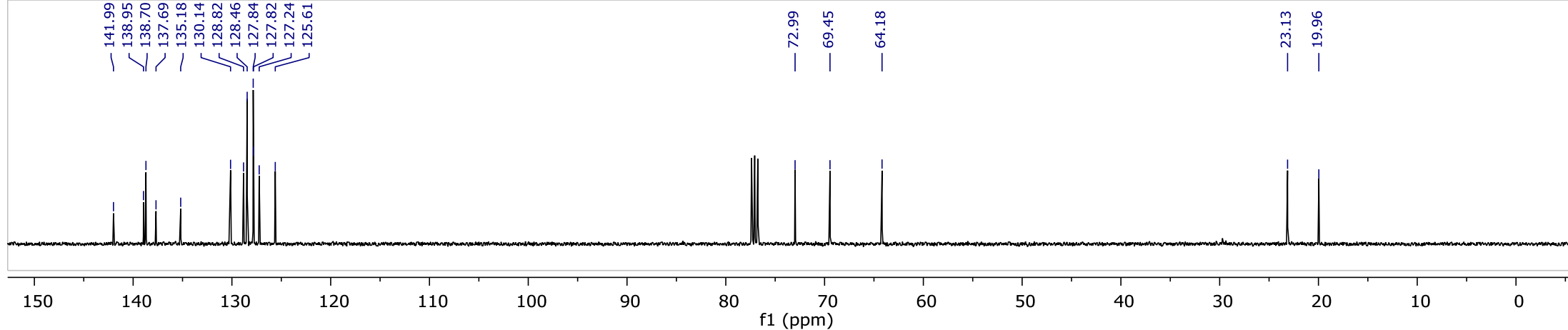
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

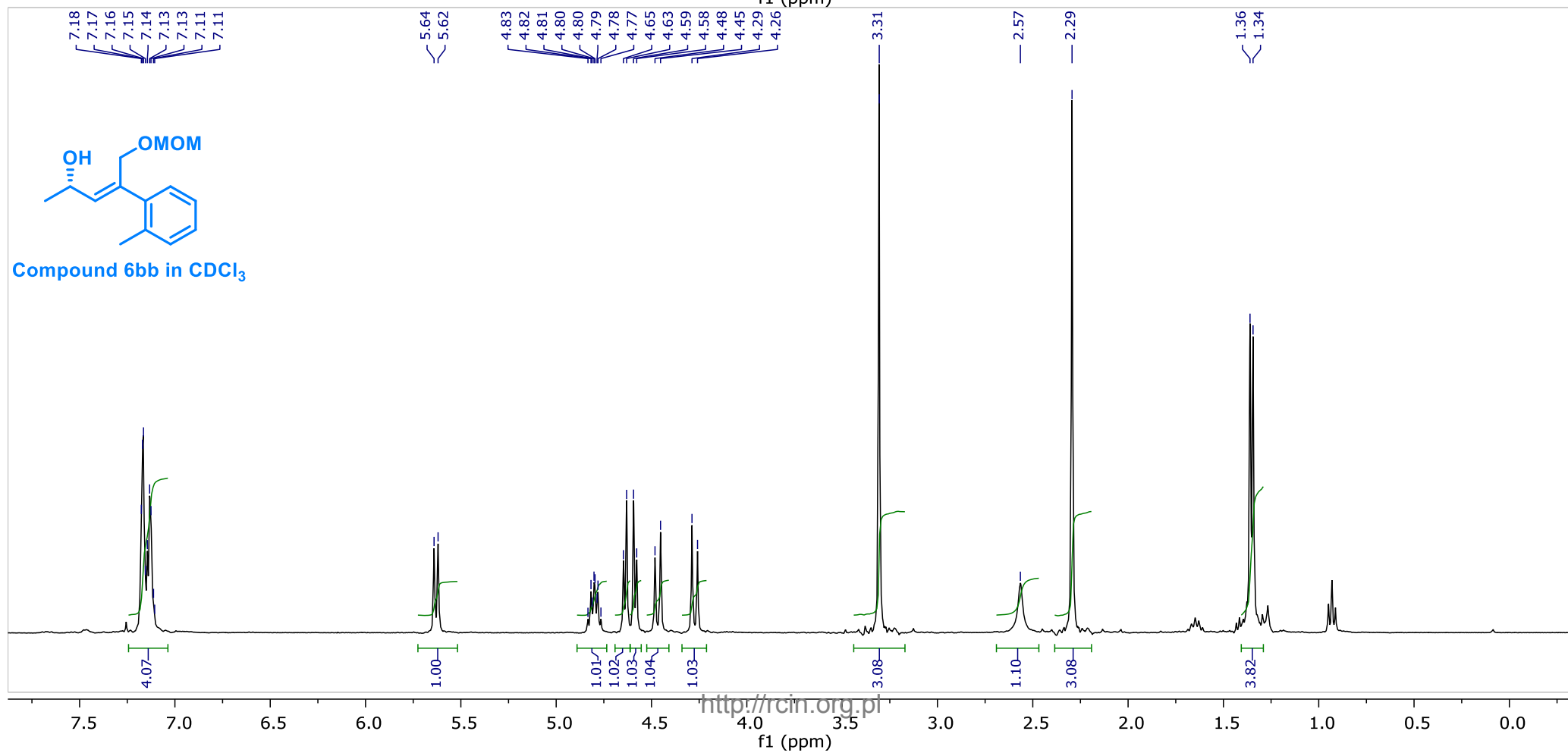
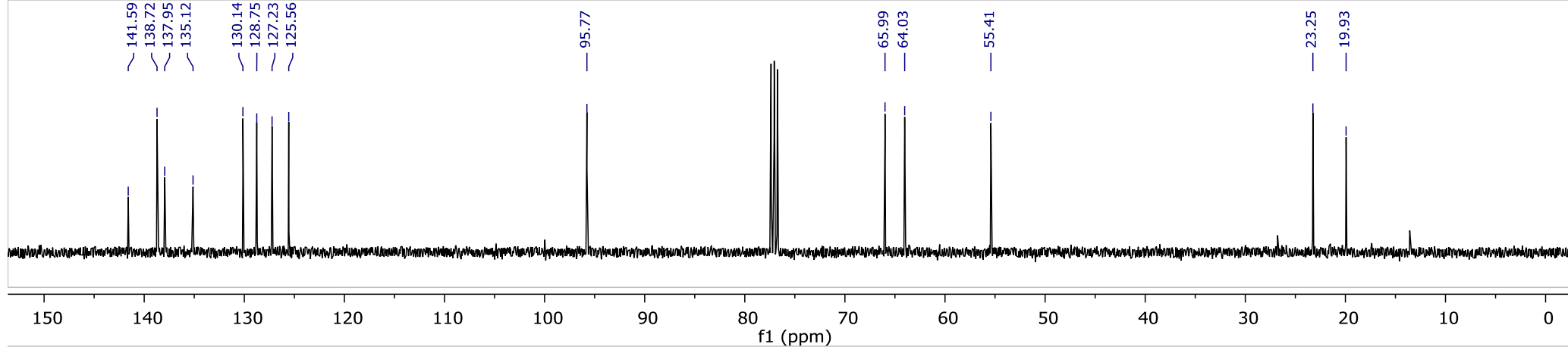


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.103	9.58	10.83	190.61	549.551	50.3871	0.319
2	15.639	14.90	16.71	187.681	333.034	49.6129	0.522



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.272	9.91	10.67	12.1894	40.7783	1.0274	0.282
2	15.741	15.15	17.58	1174.2	1736.39	98.9726	0.631

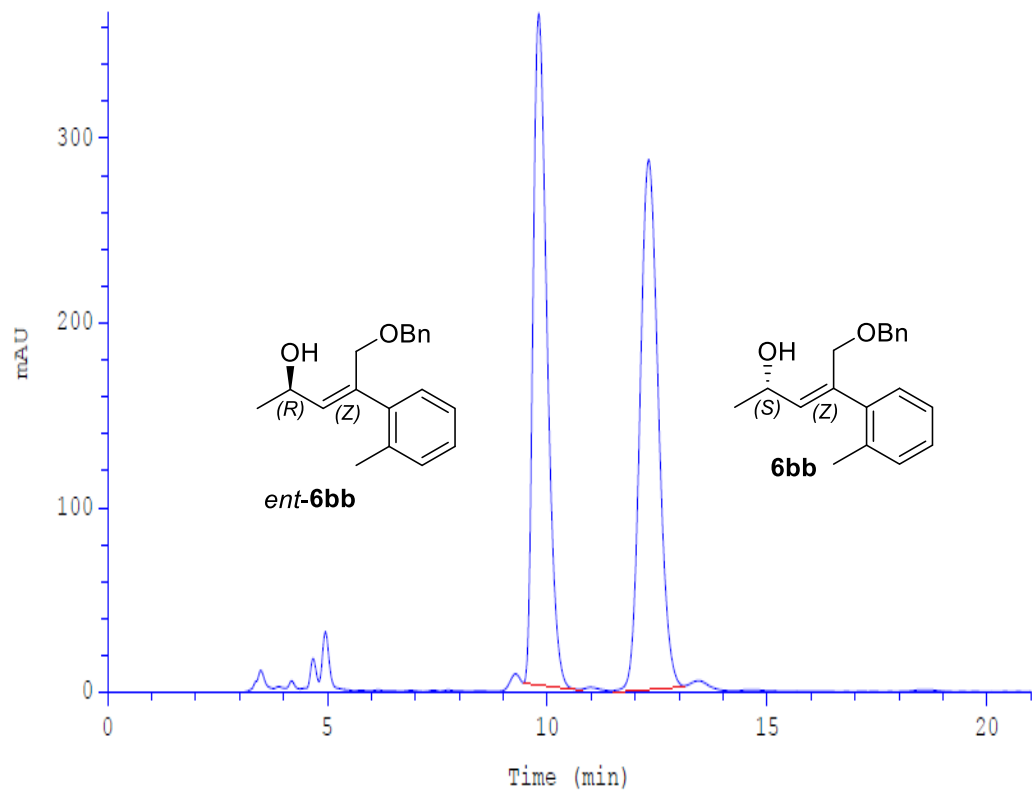




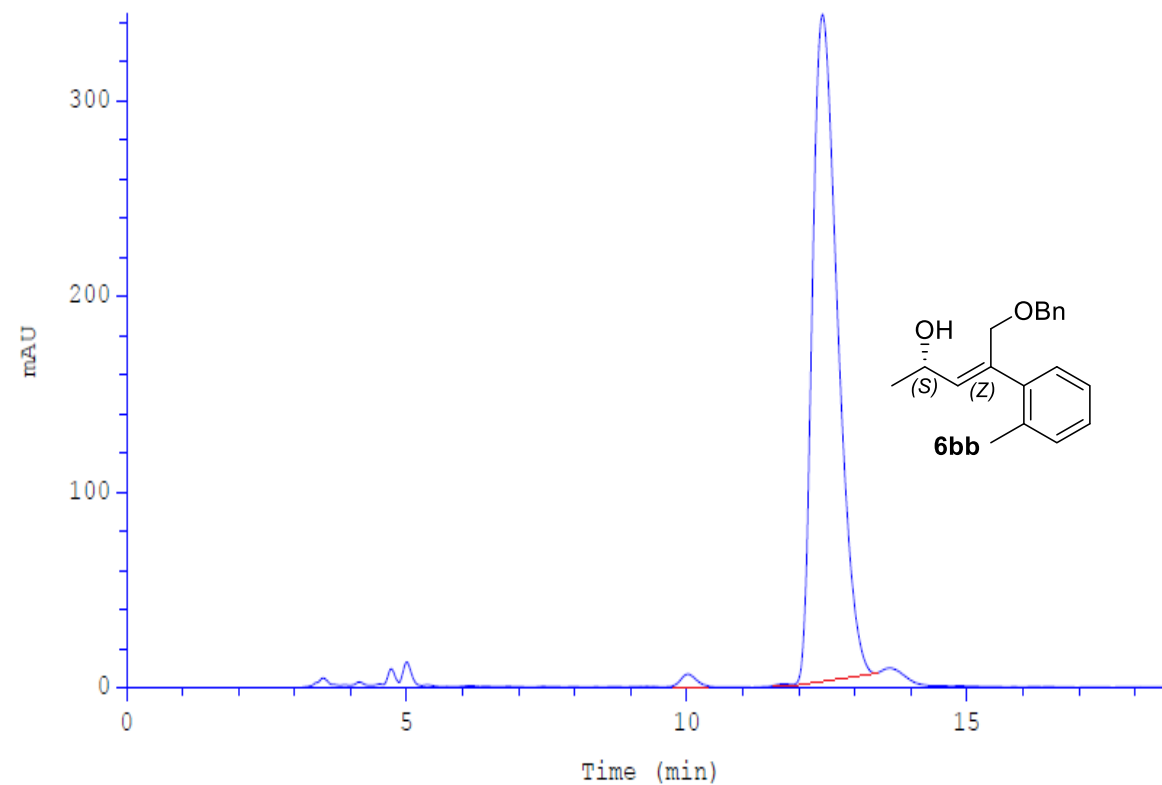


## HPLC chromatogram of compound rac-6cbb and 6bb

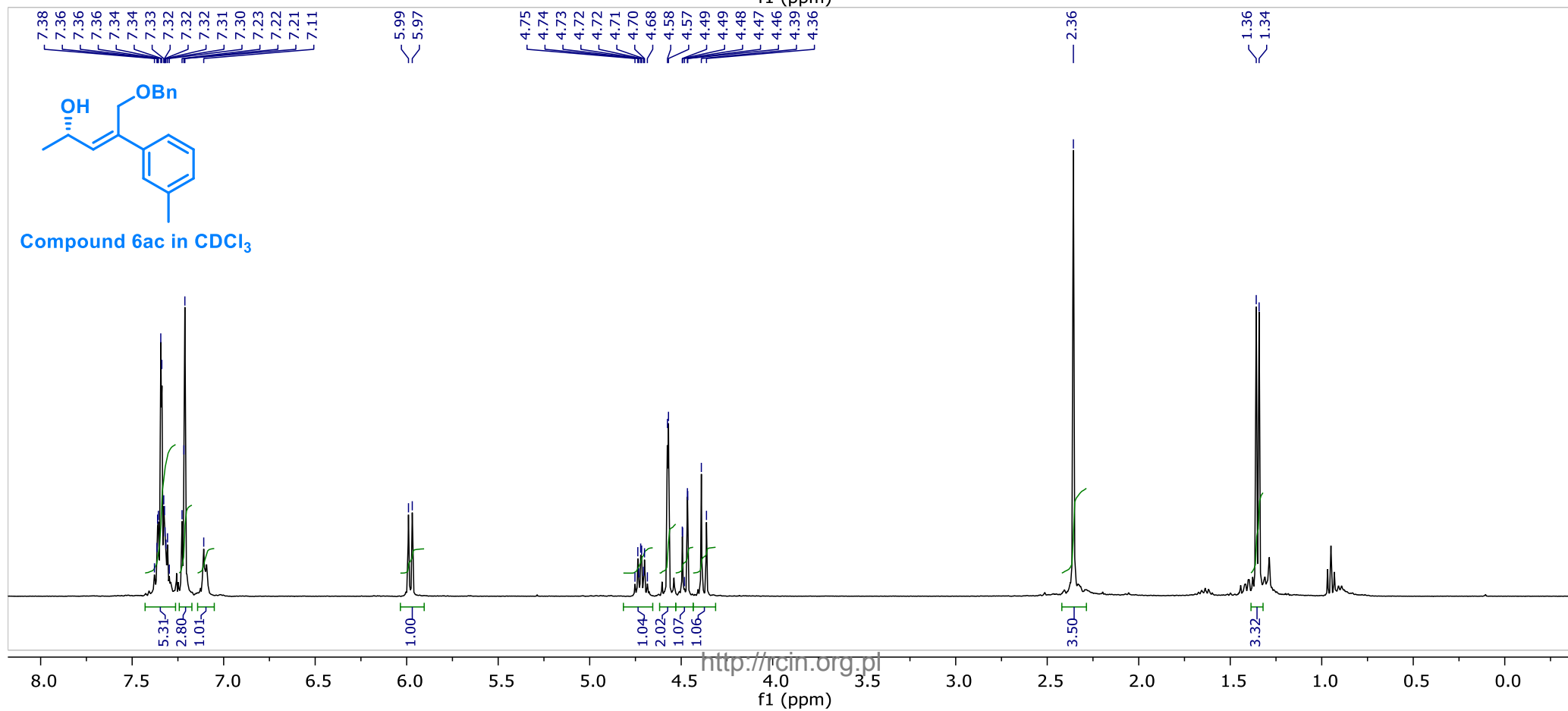
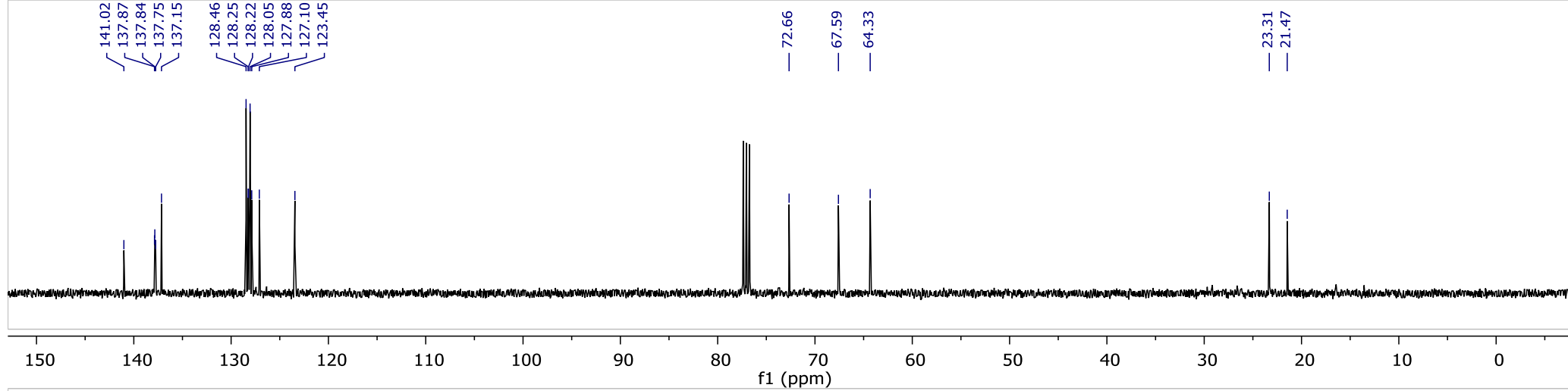
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

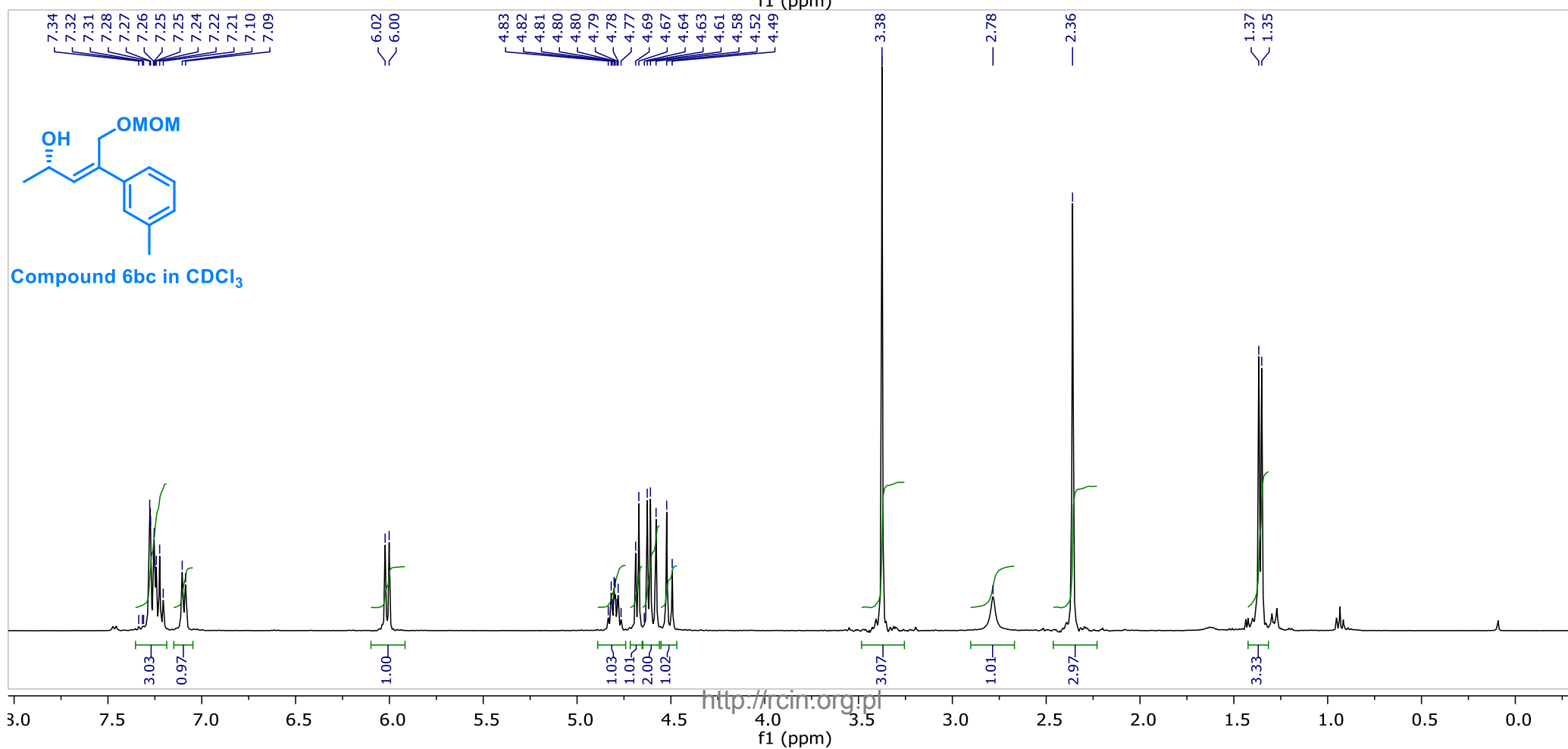
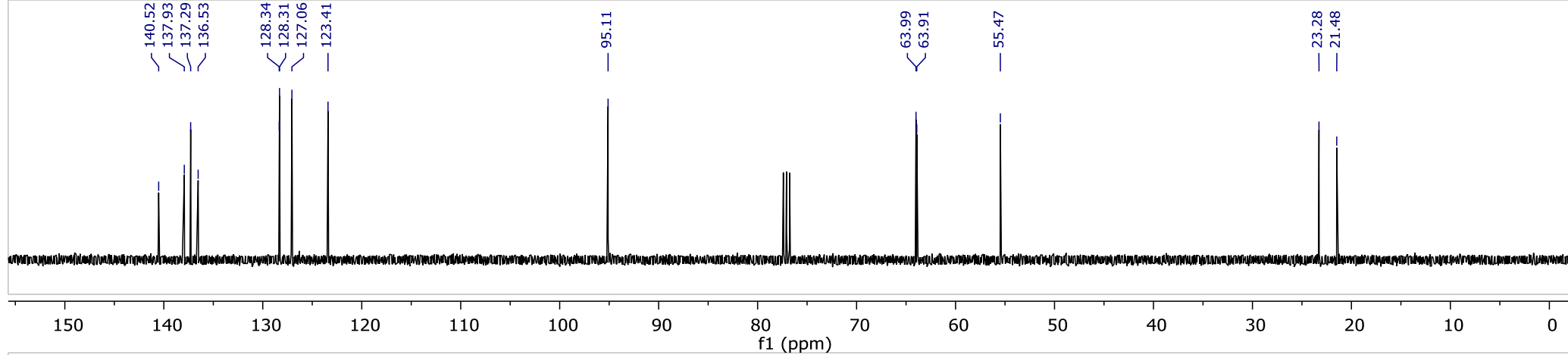


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.806	9.46	10.66	132.873	363.435	49.2021	0.342
2	12.307	11.47	13.11	137.183	286.182	50.7979	0.447



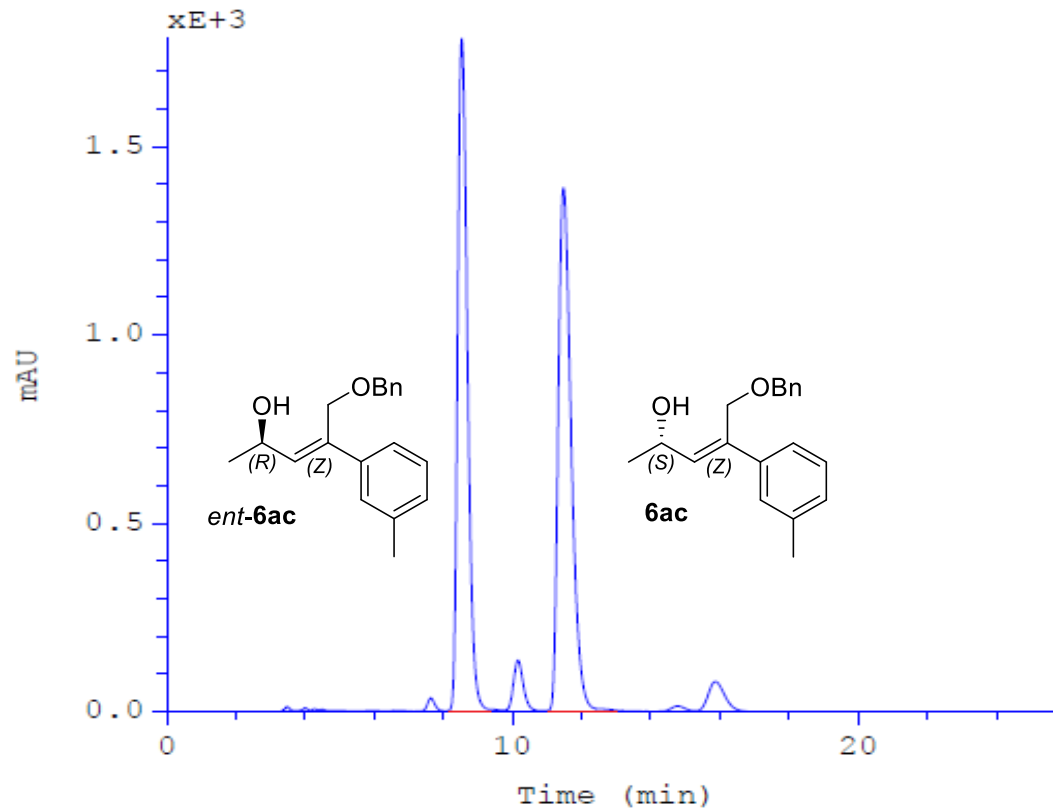
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	10.024	9.77	10.33	1.6106	5.65254	0.9000	0.277
2	12.425	11.59	13.40	177.342	339.581	99.1000	0.492



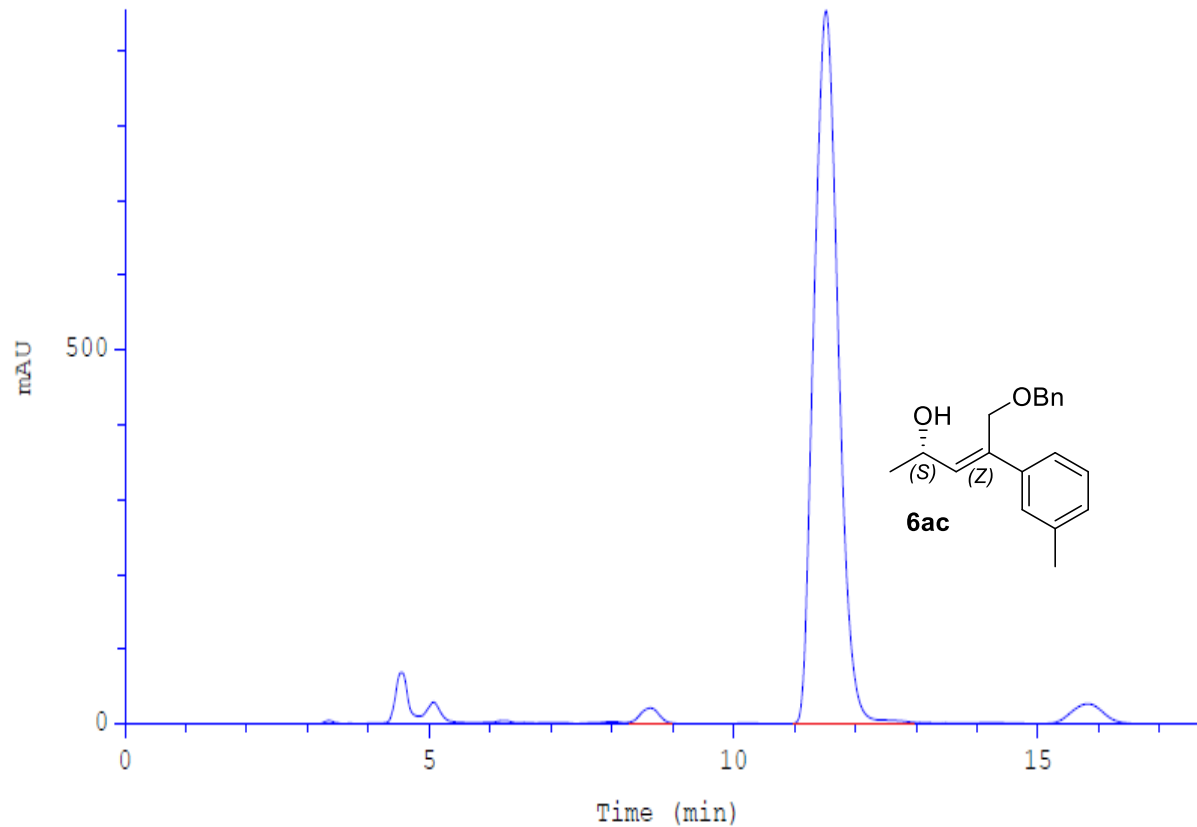


## HPLC chromatogram of compounds rac-6ac and 6ac

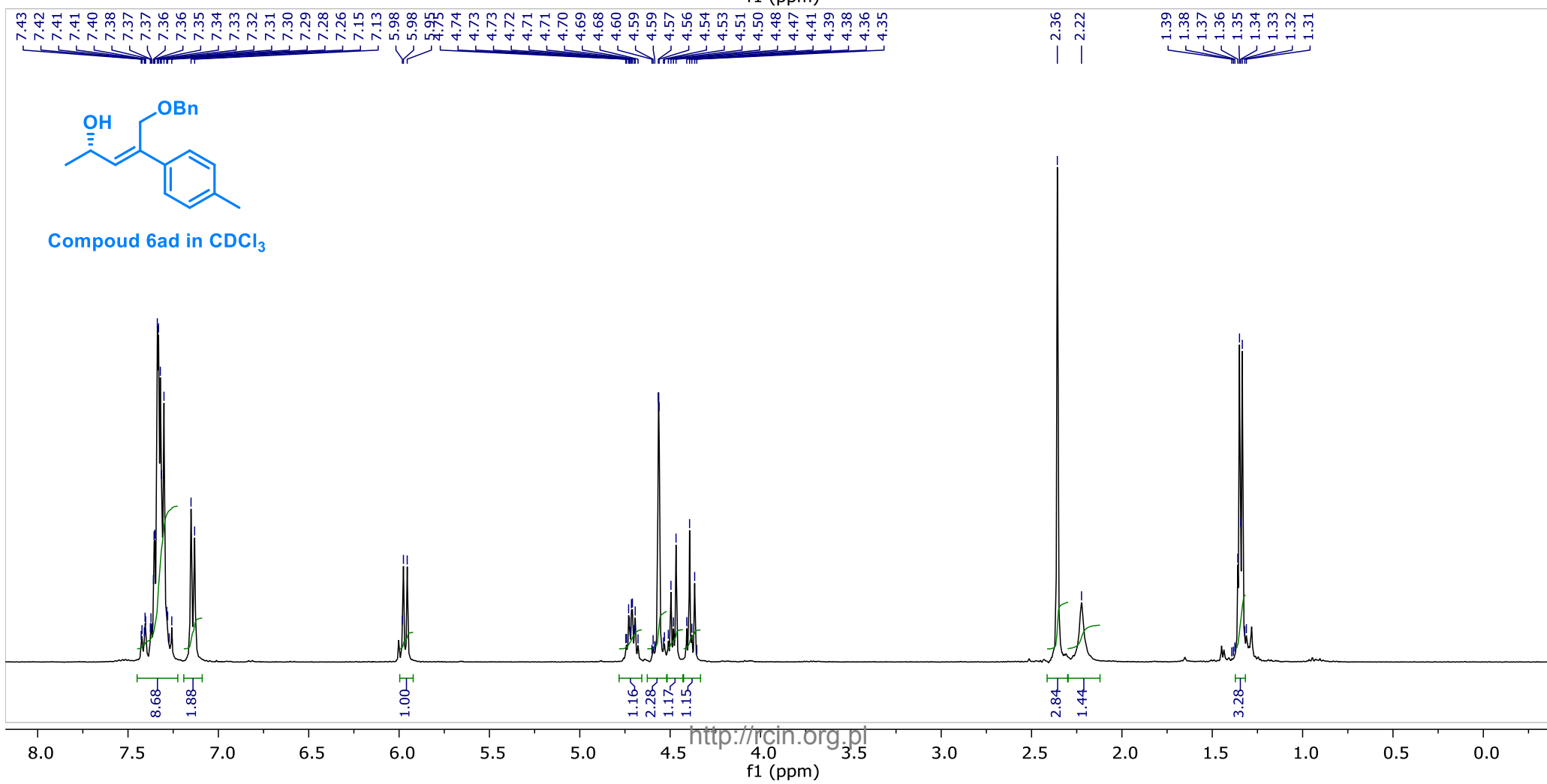
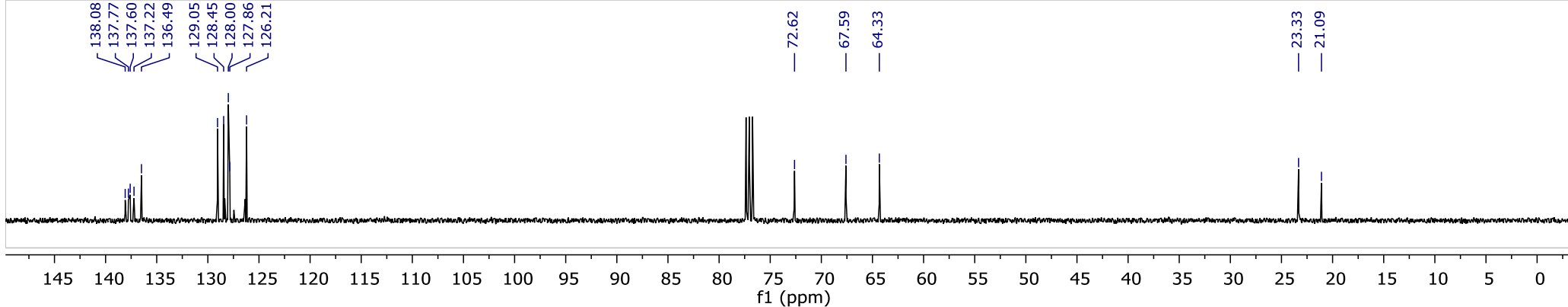
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

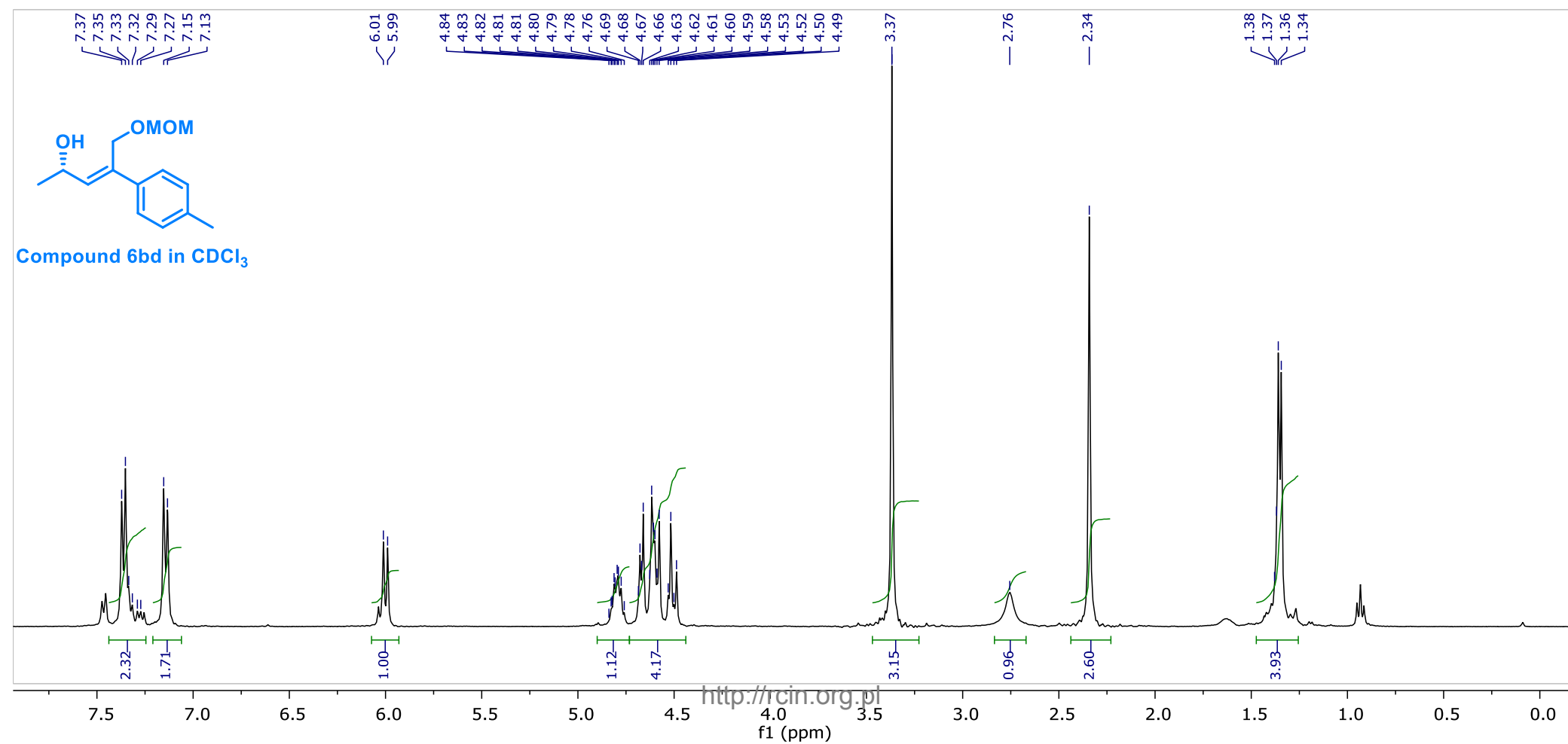
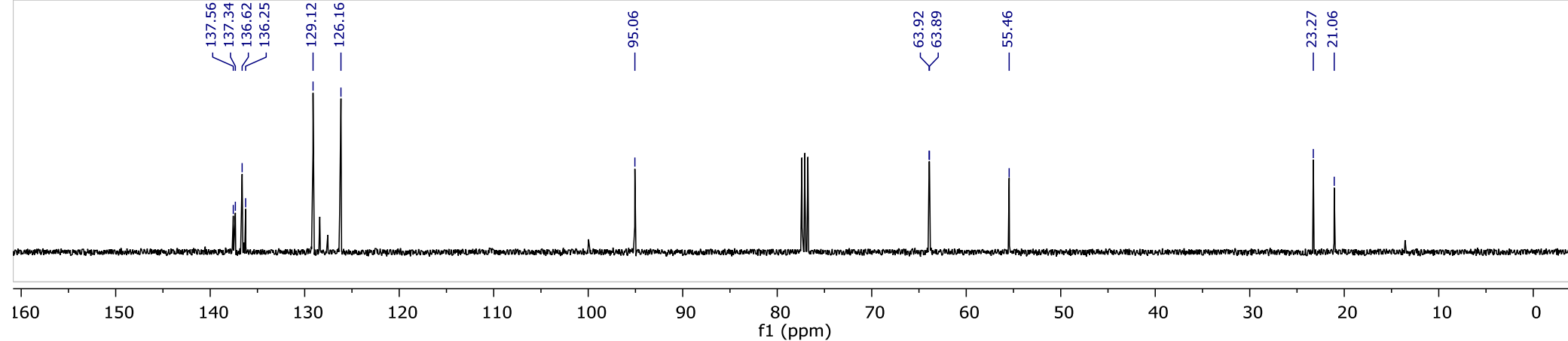


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.535	8.08	9.24	584.45	1781.6	49.3268	0.305
2	11.469	10.97	13.01	600.404	1386.94	50.6732	0.399



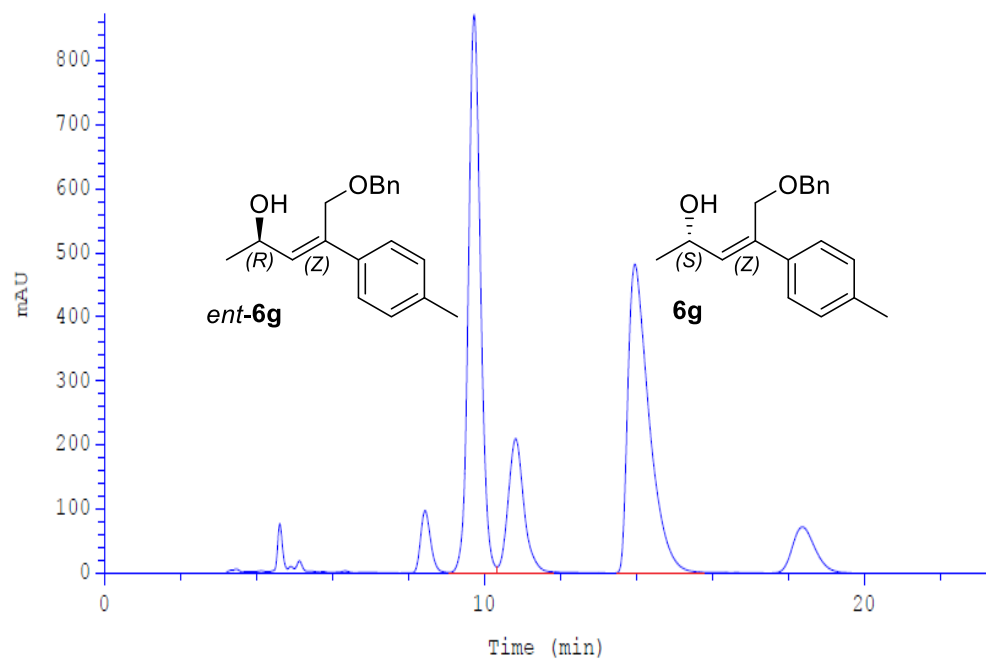
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.640	8.30	8.94	6.28518	19.0359	1.4107	0.327
2	11.525	10.97	12.95	439.239	952.273	98.5893	0.440



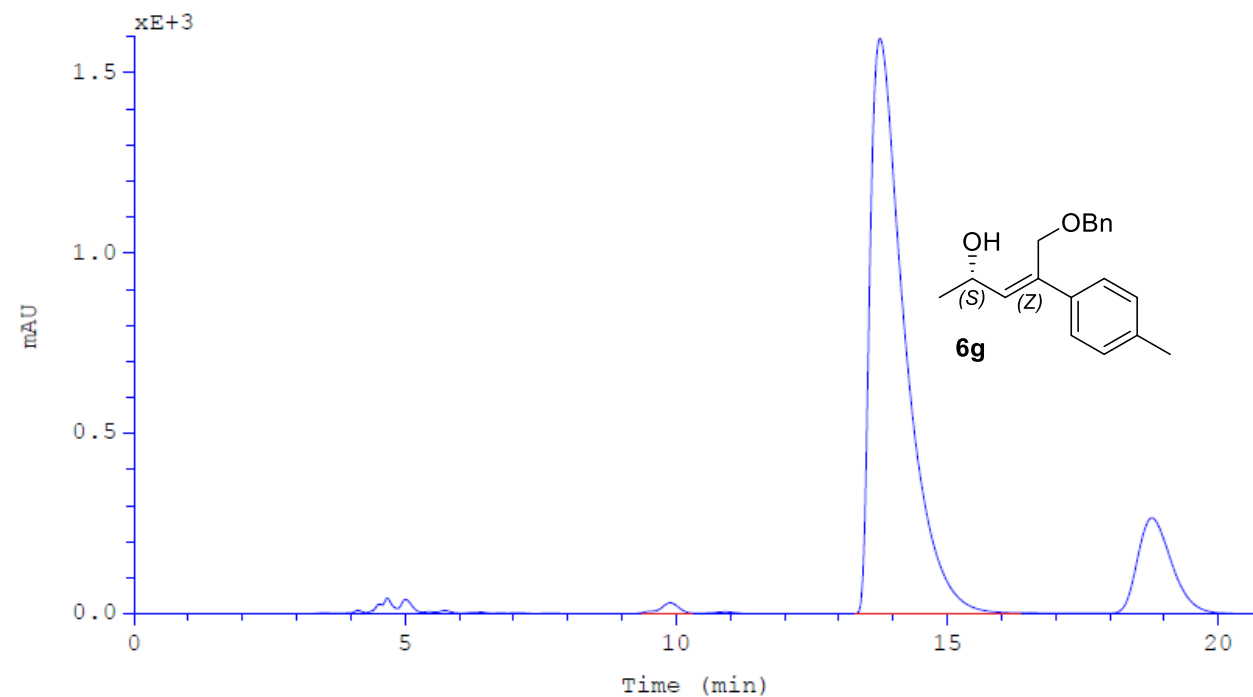


## HPLC chromatogram of compounds rac-6ad and 6ad

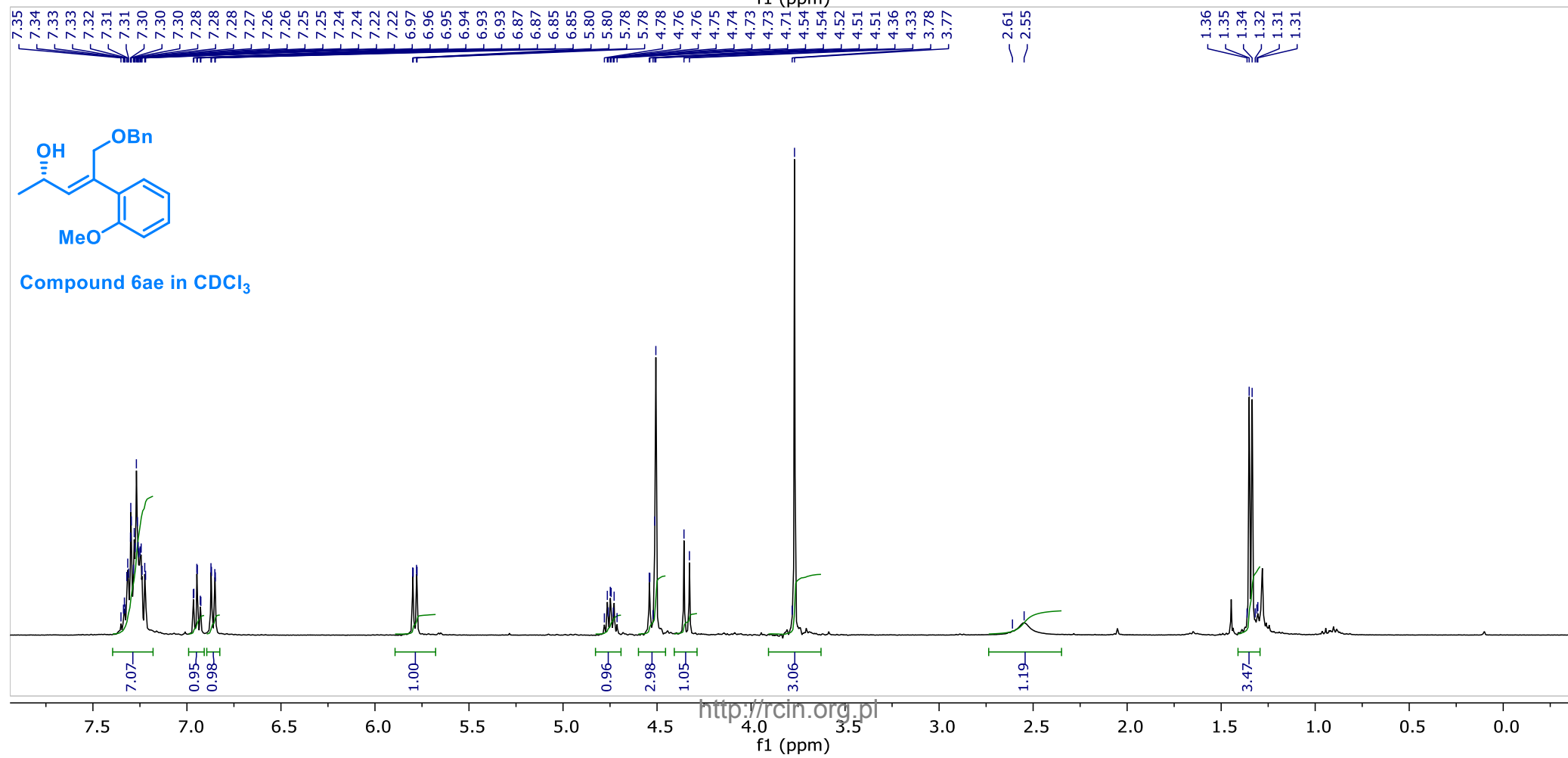
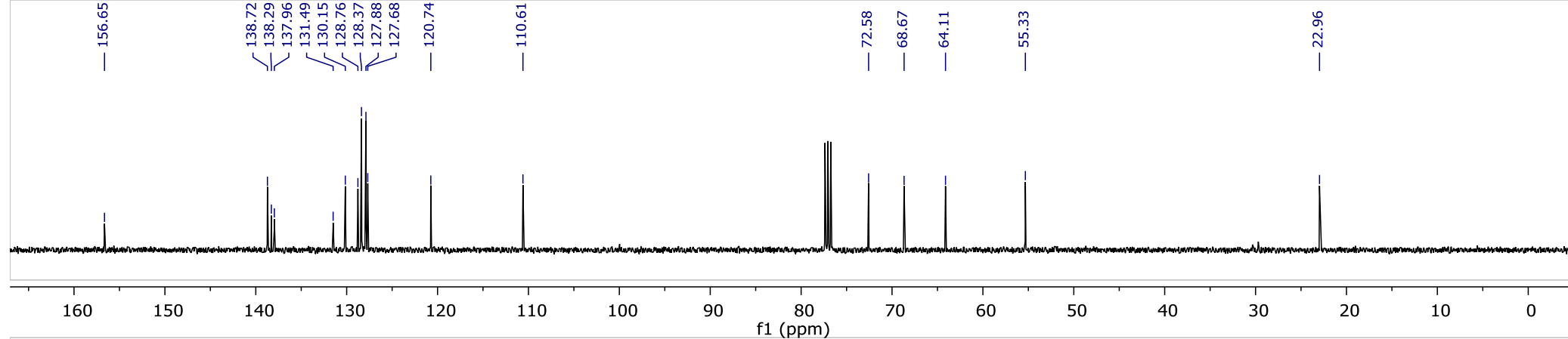
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm



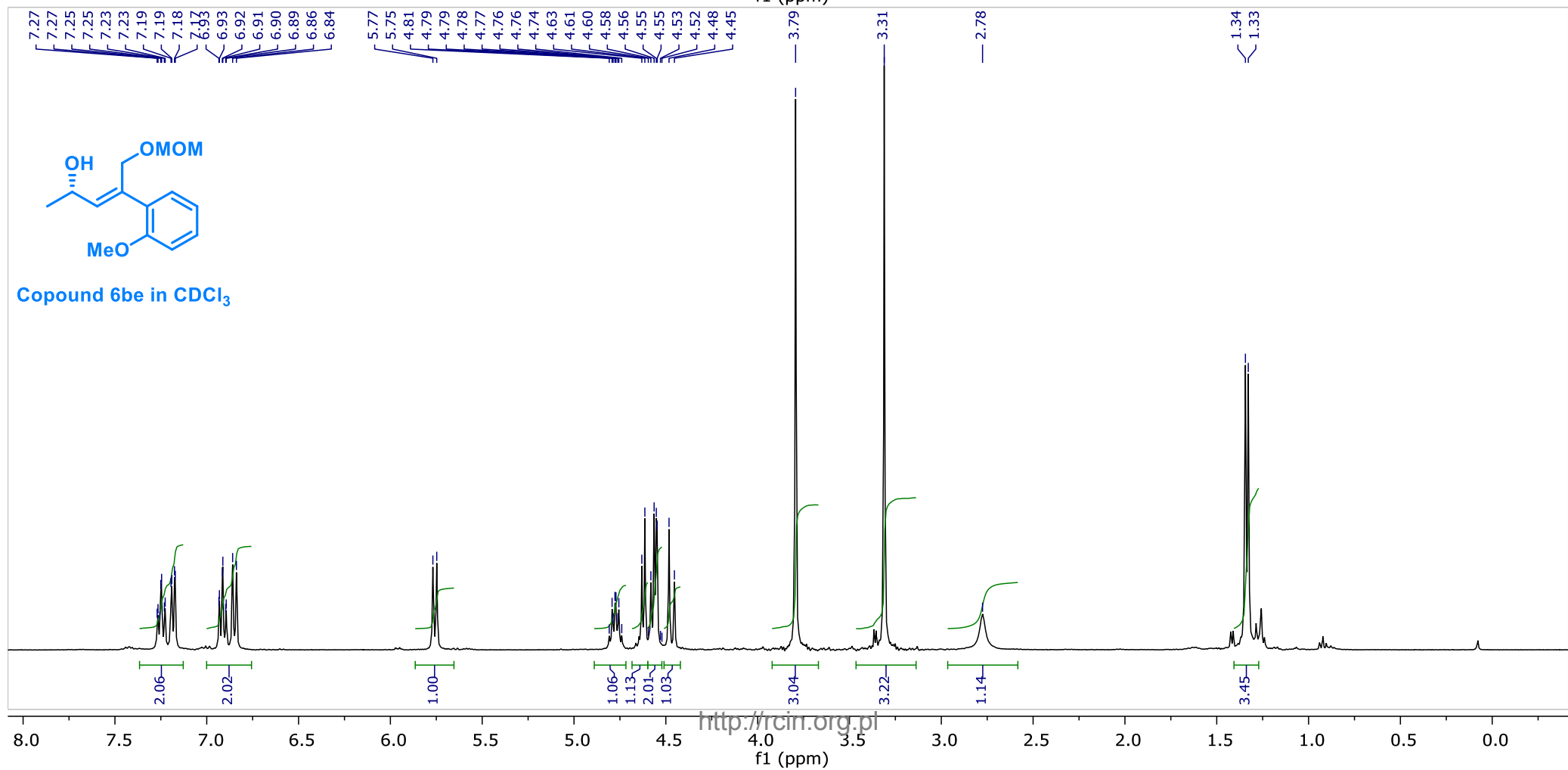
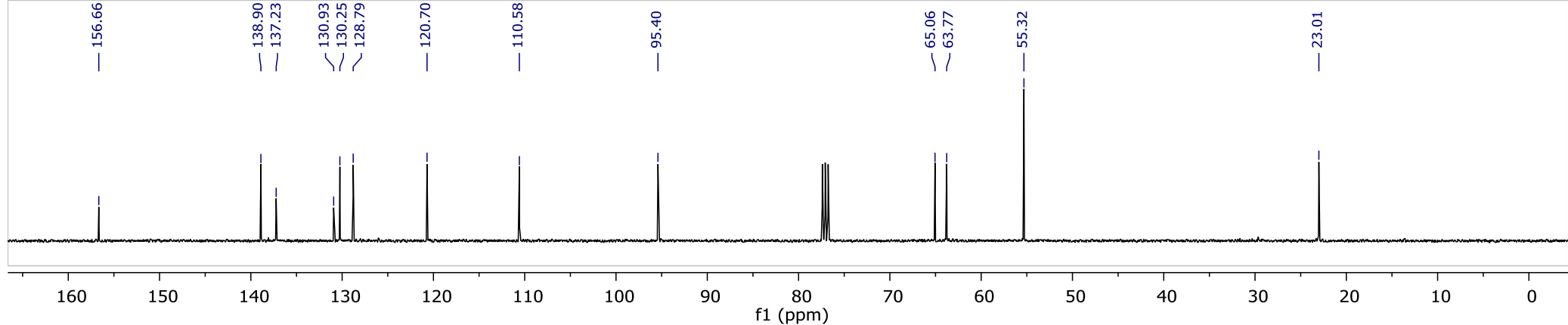
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.738	9.15	10.37	320.01	868.917	43.9579	0.334
2	10.821	10.37	11.77	98.3449	207.651	13.5091	0.420
3	13.973	13.47	15.63	309.637	480.475	42.5330	0.584



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.889	9.35	10.23	10.1067	27.63	0.8512	0.322
2	13.759	13.24	16.17	1177.21	1594.65	99.1488	0.654

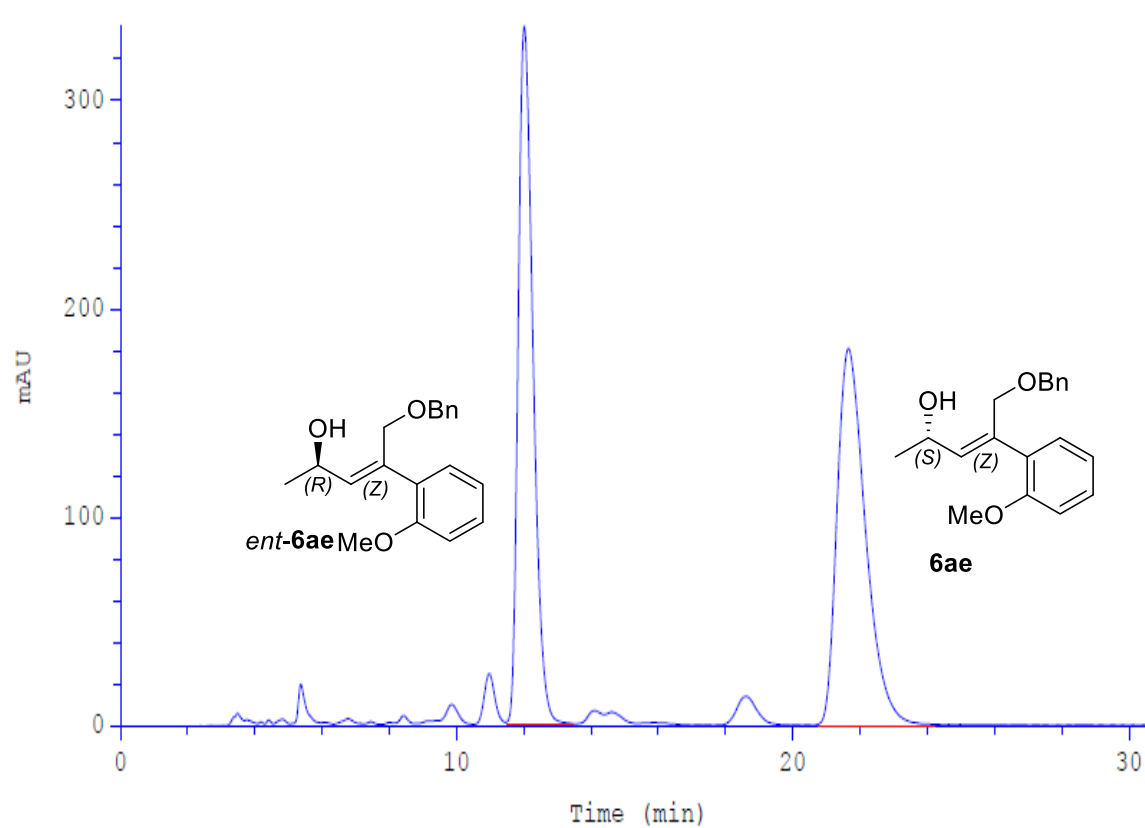




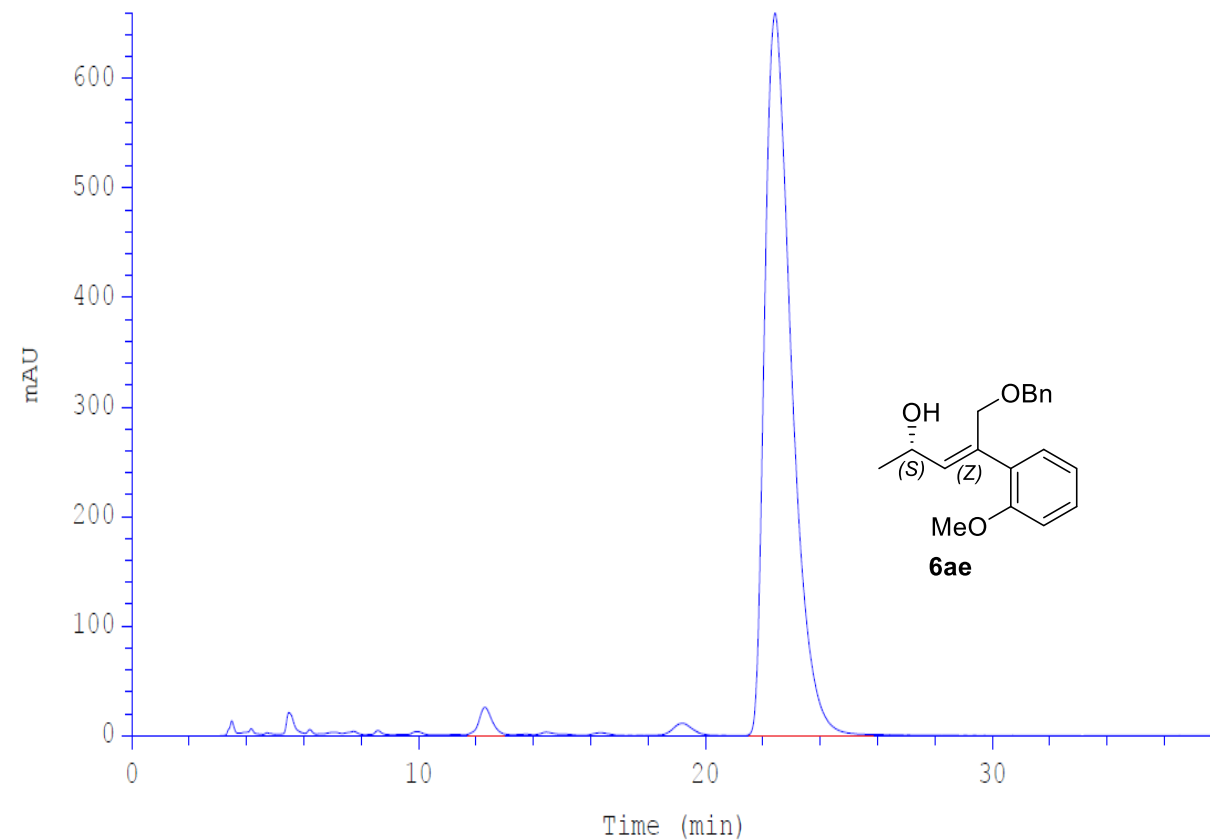


## HPLC chromatogram of compounds rac-6ae and 6ae

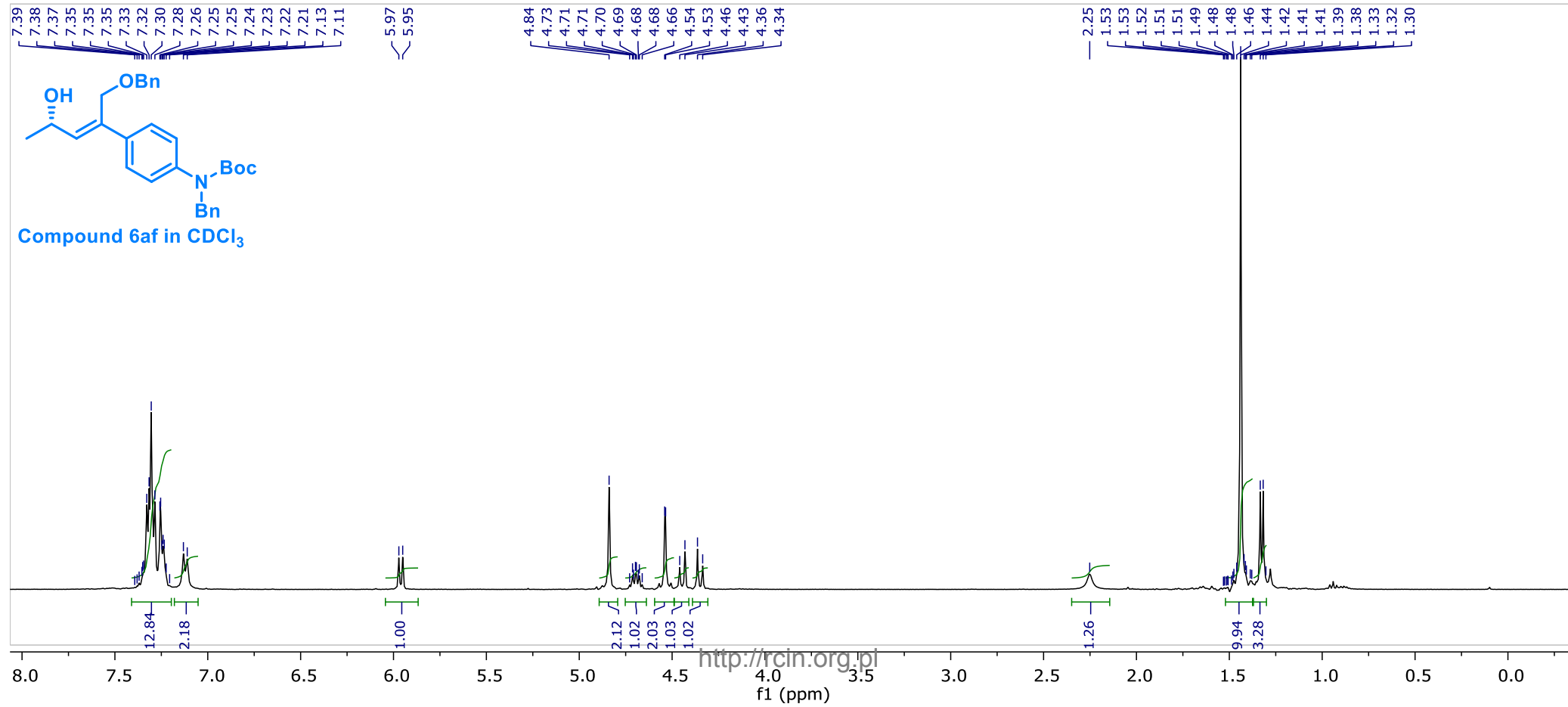
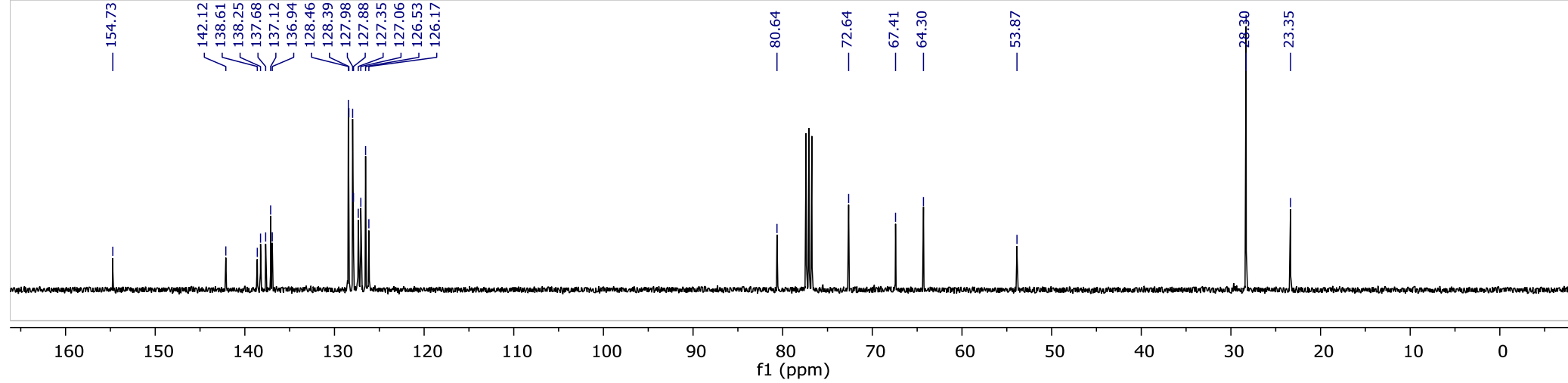
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

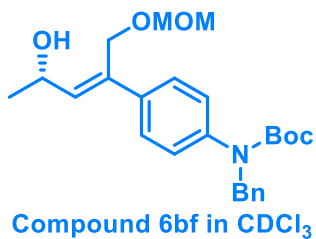
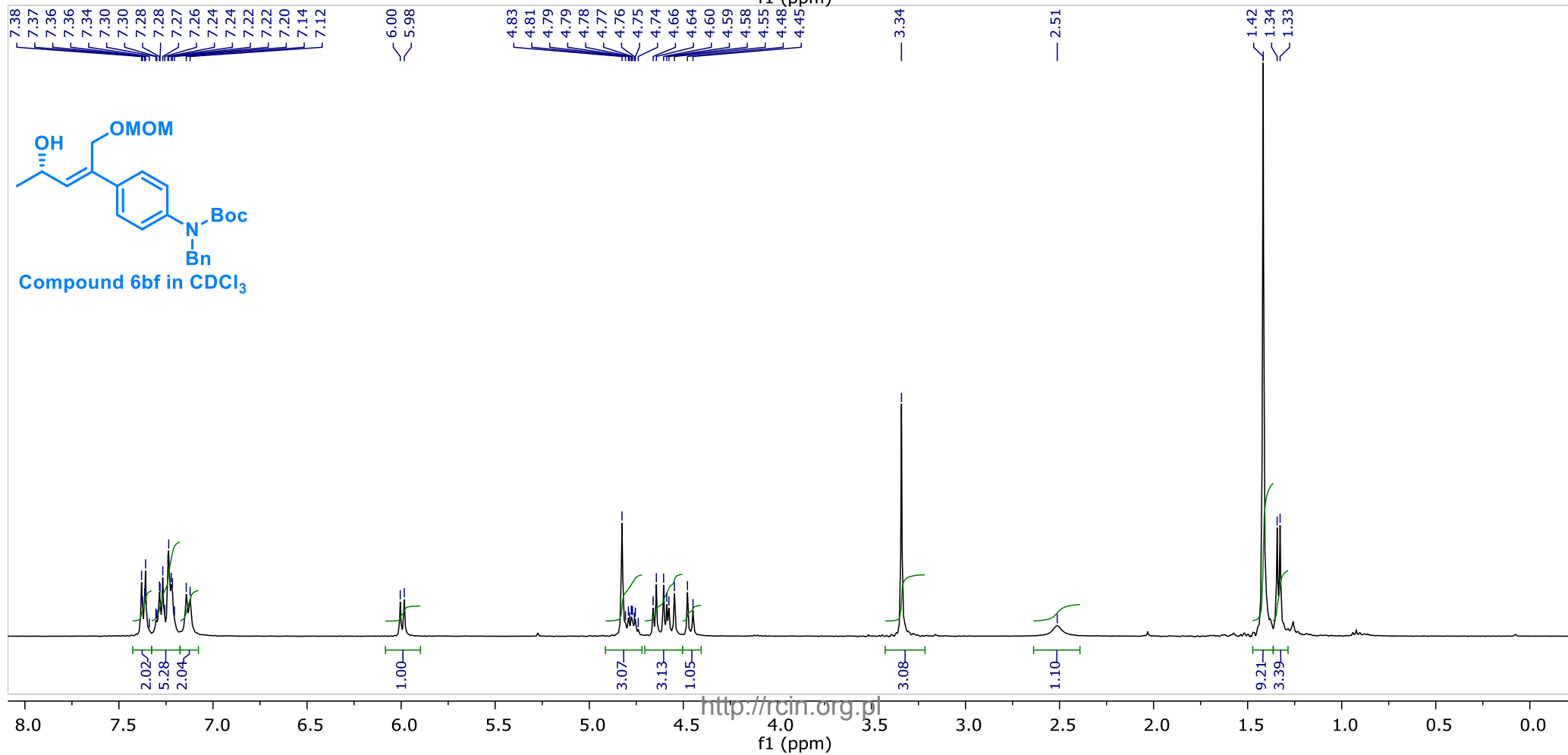
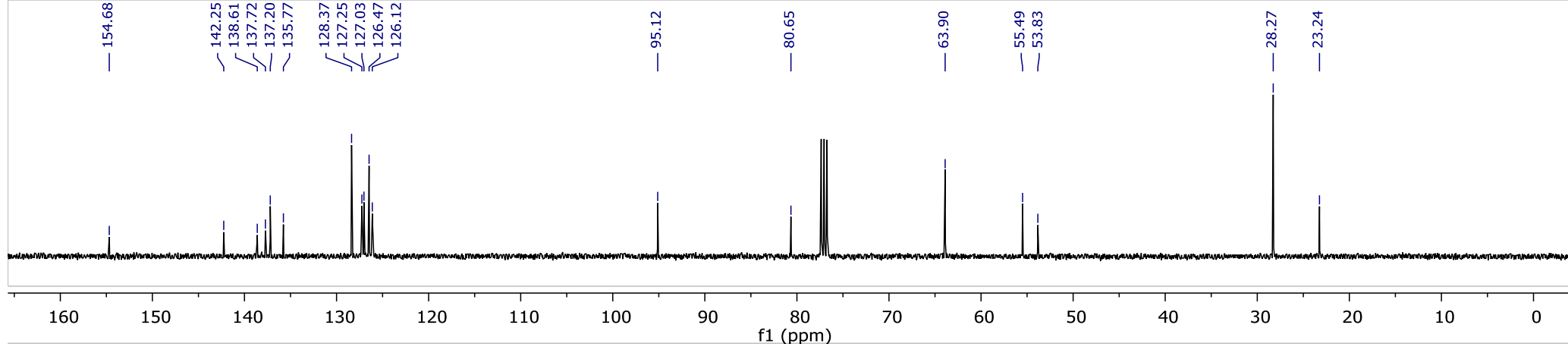


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	12.021	11.47	13.42	169.751	333.591	49.0608	0.474
2	21.658	20.61	24.19	176.249	180.513	50.9392	0.899



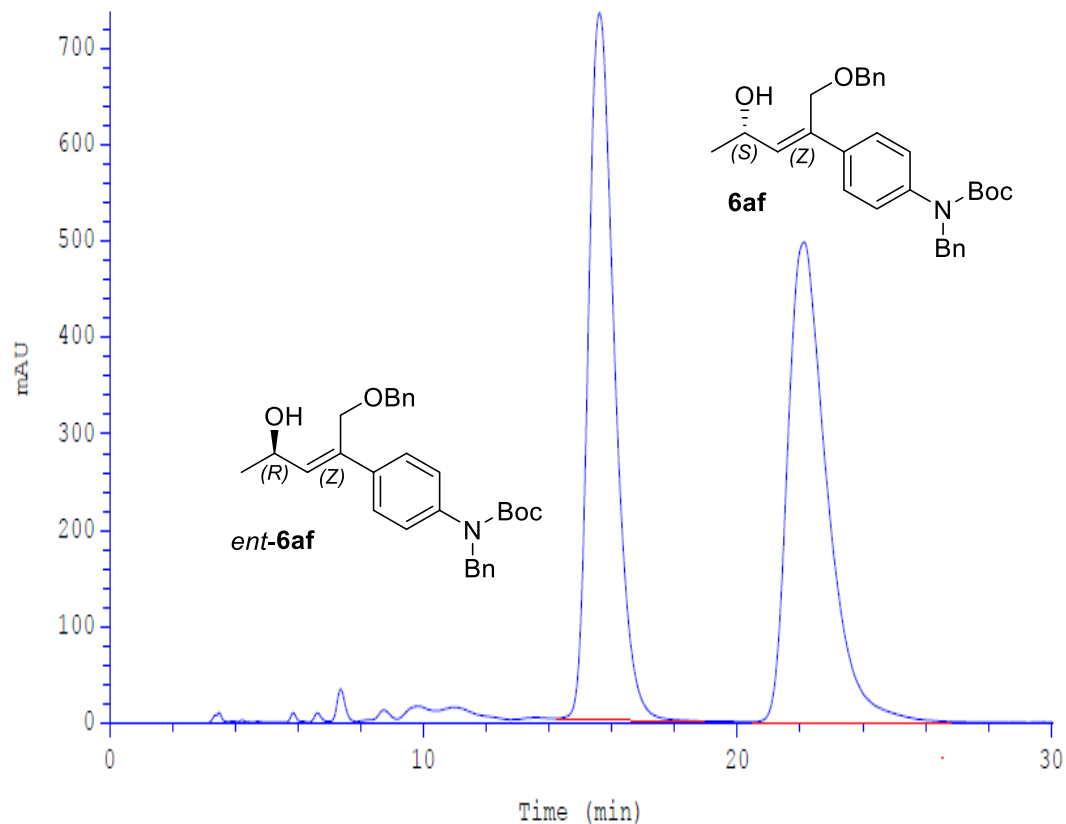
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	12.320	11.90	12.86	10.232	22.558	1.4294	0.430
2	22.422	21.52	24.98	705.567	658.137	98.5705	0.984



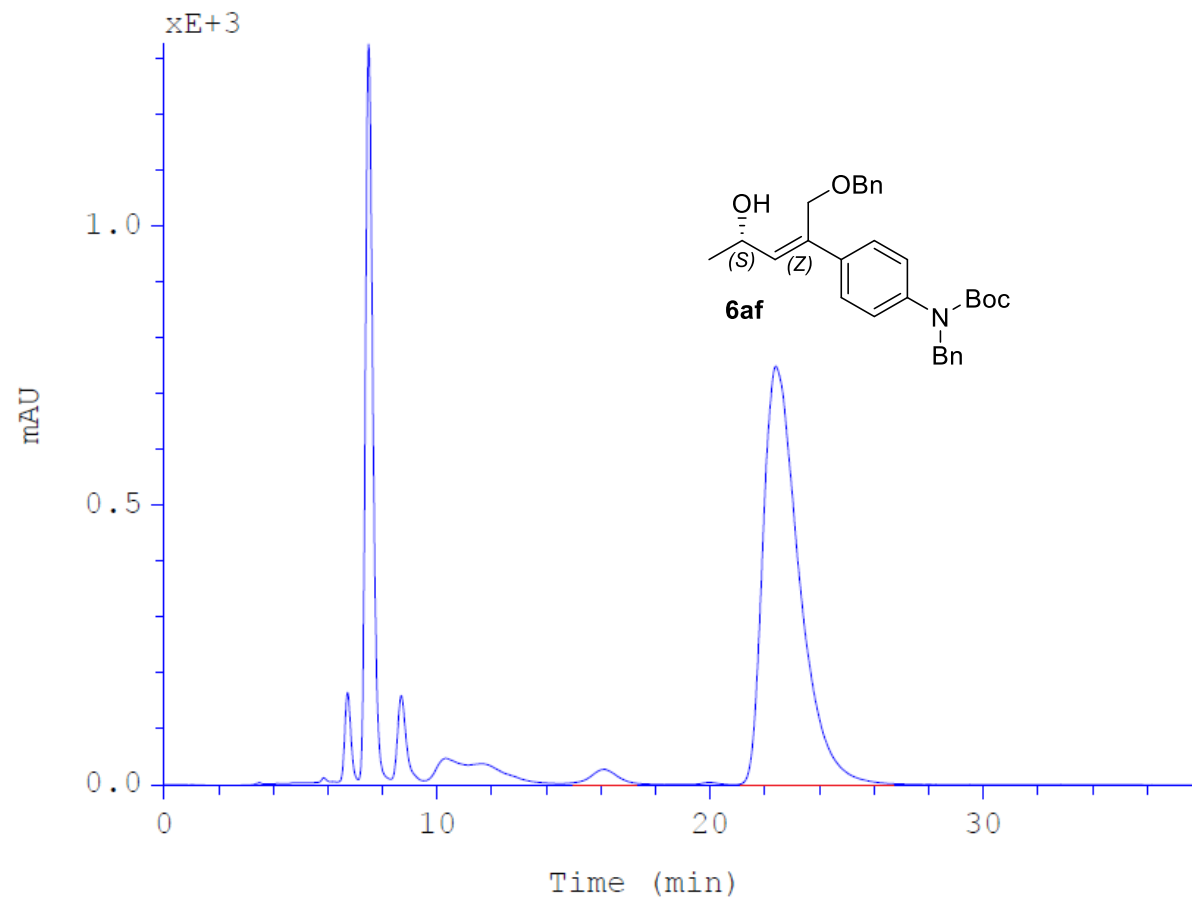


## HPLC chromatogram of compounds rac-6af and 6af

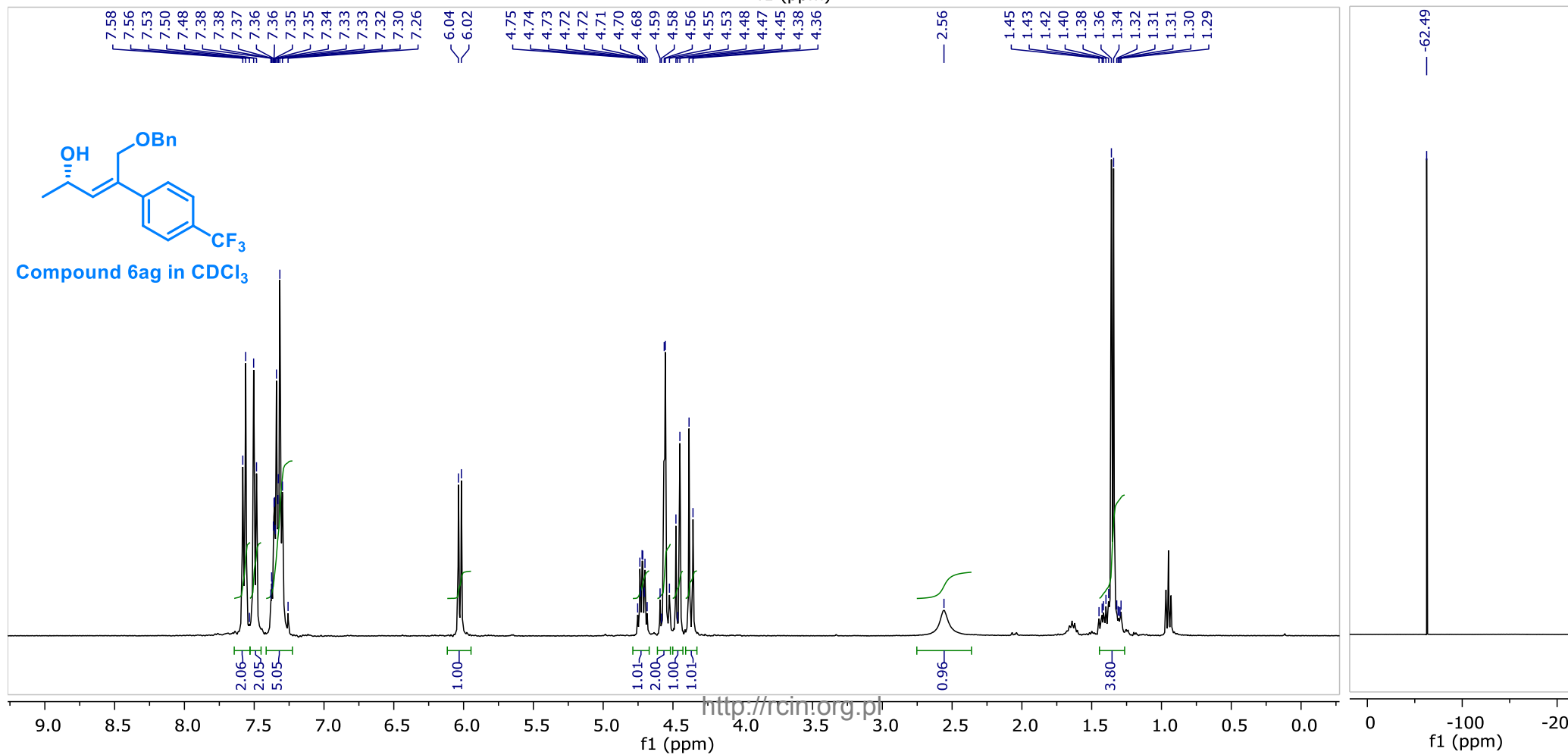
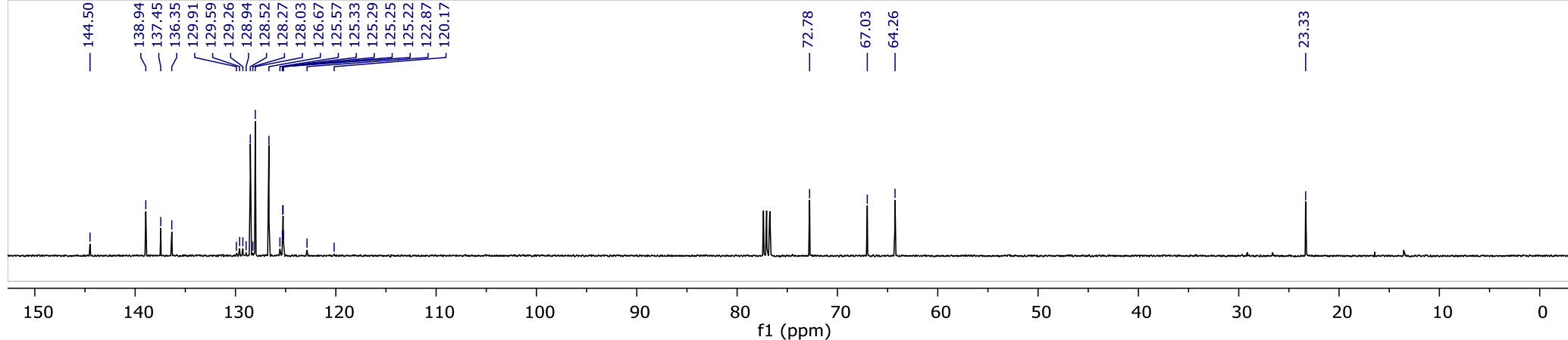
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

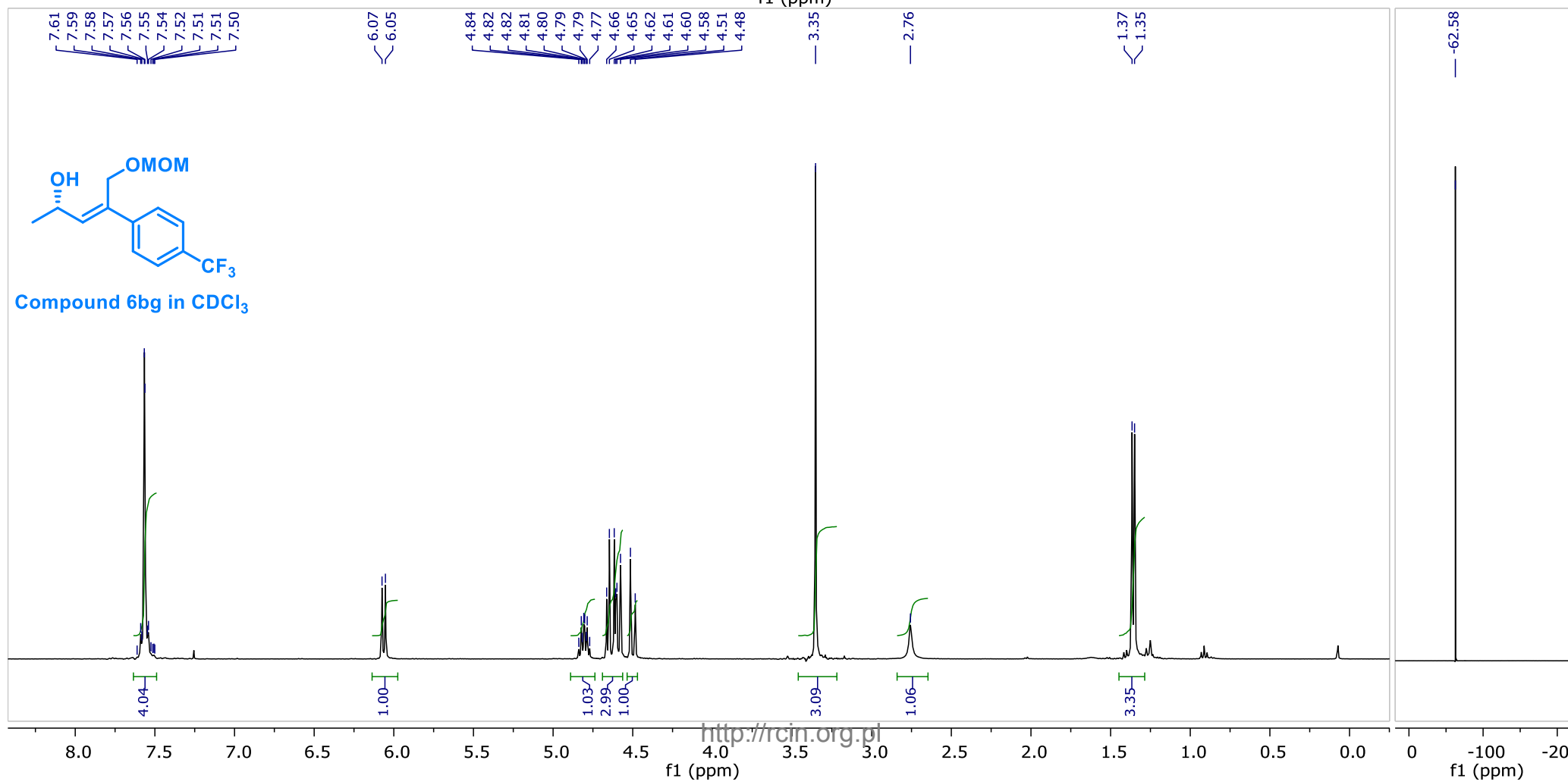
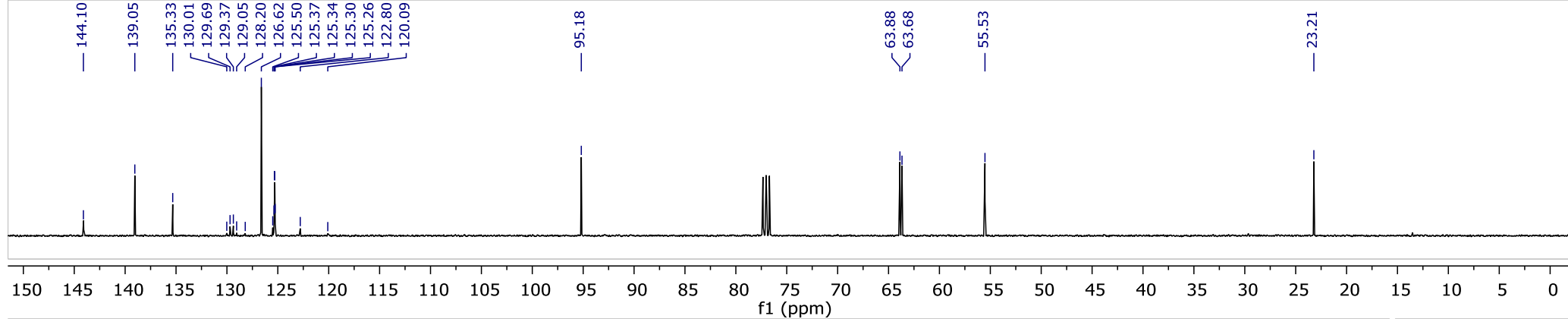


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.606	14.11	18.91	701.171	732.056	49.5518	0.880
2	22.125	20.52	26.73	713.855	497.09	50.4482	1.292



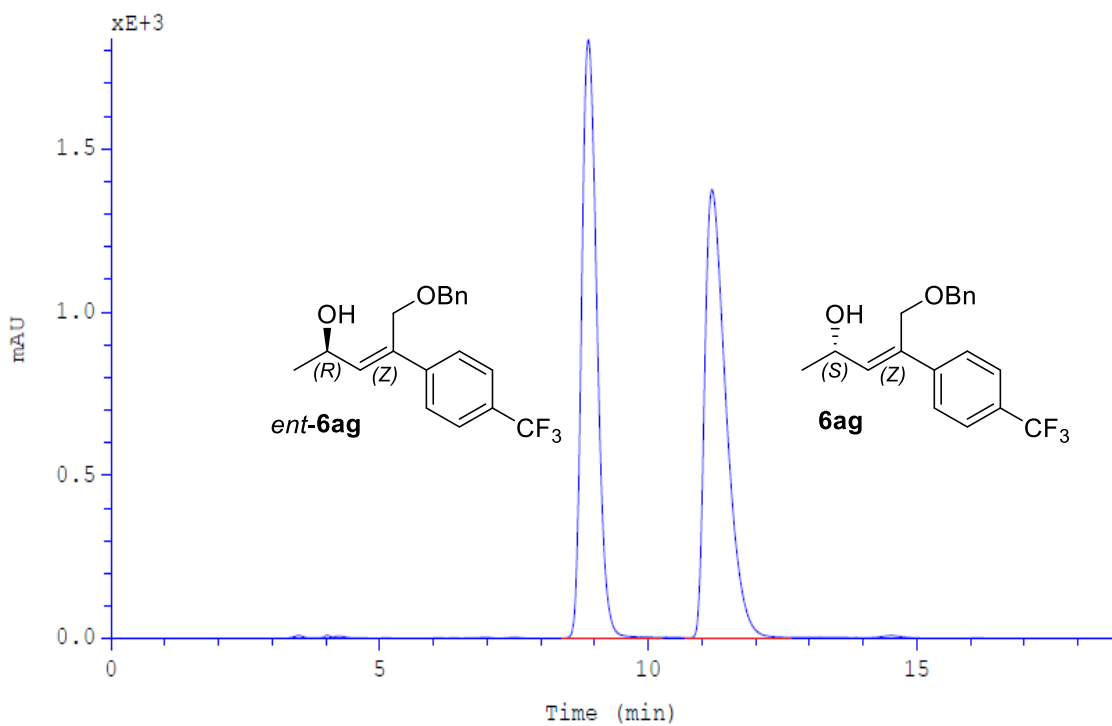
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	16.119	15.08	17.13	22.9296	23.4914	1.9812	0.936
2	22.403	21.14	26.32	1134.45	746.937	98.0188	1.376



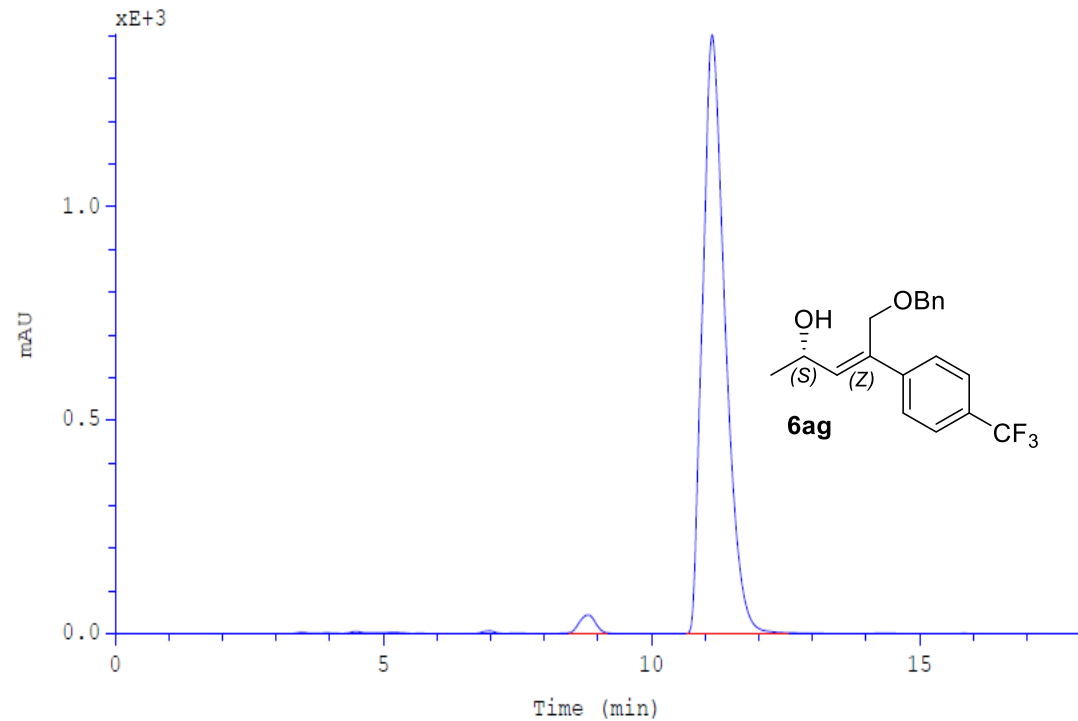


## HPLC chromatogram of compounds rac-6ag and 6ag

Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

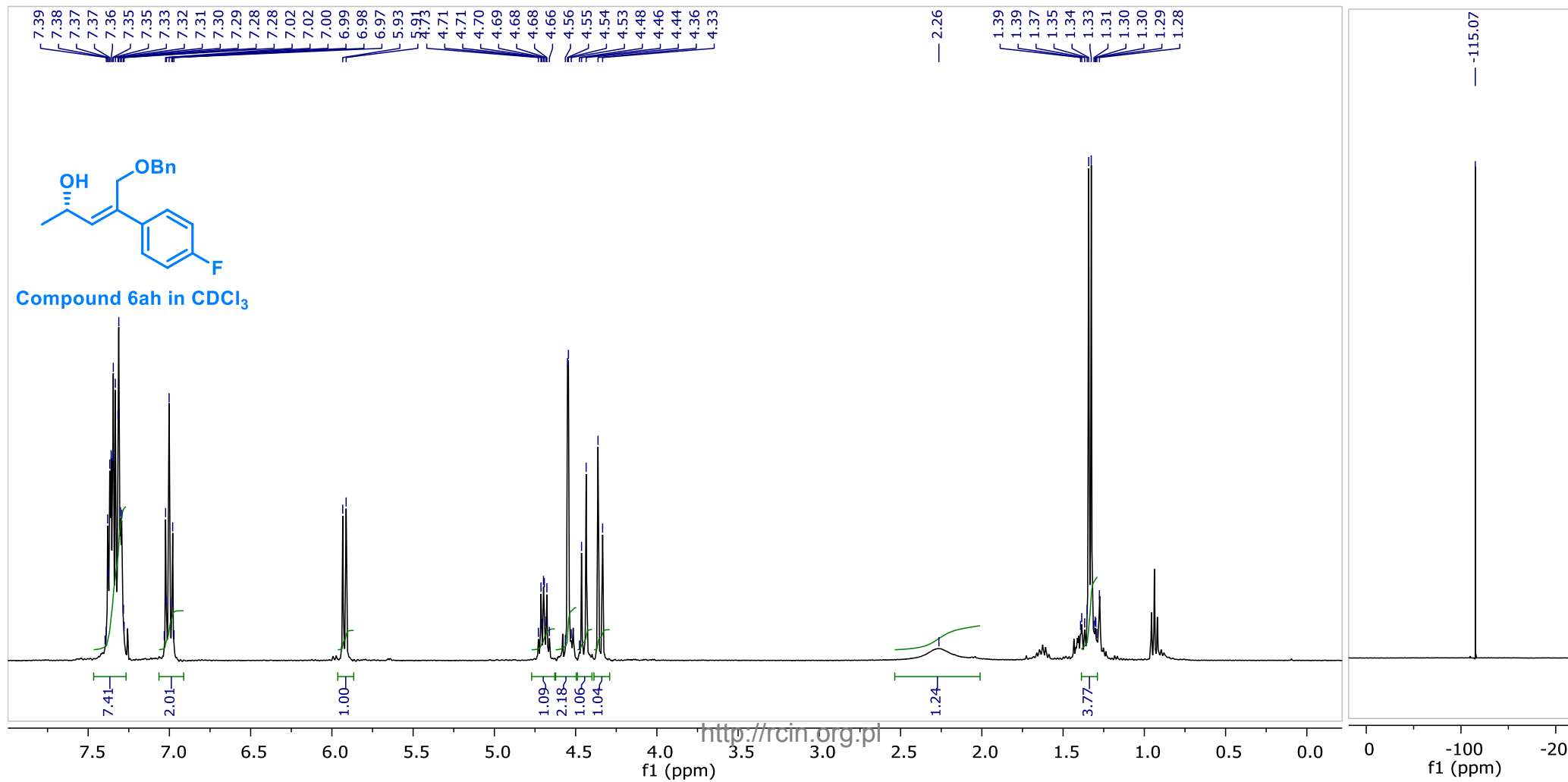
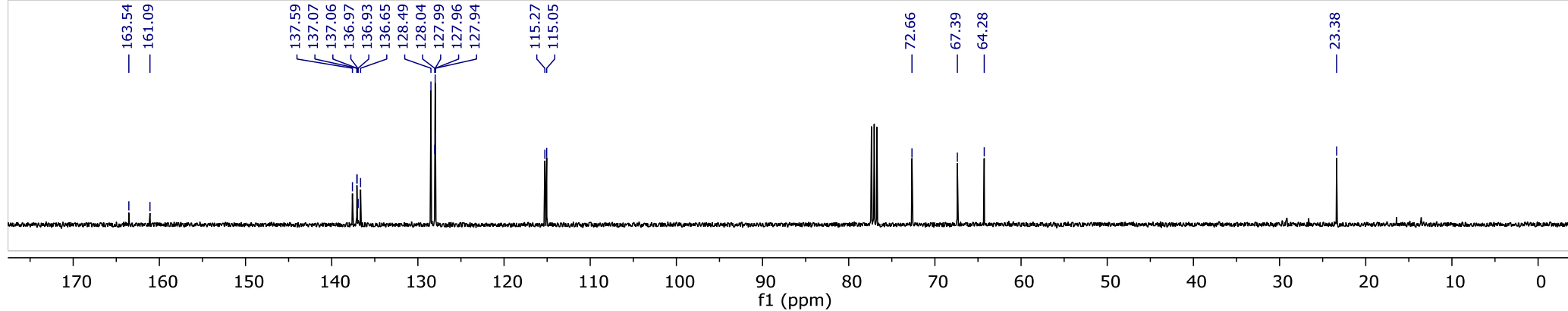


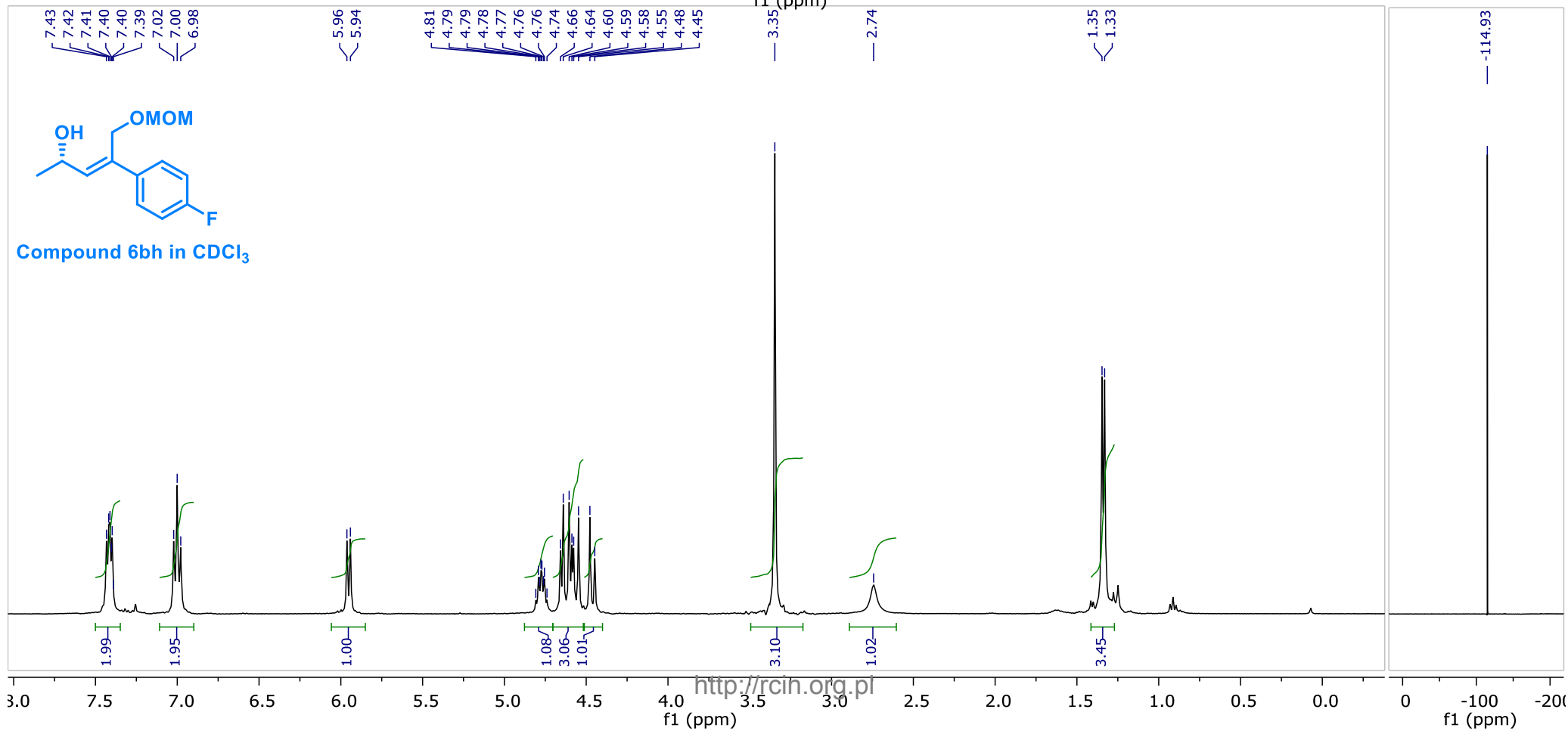
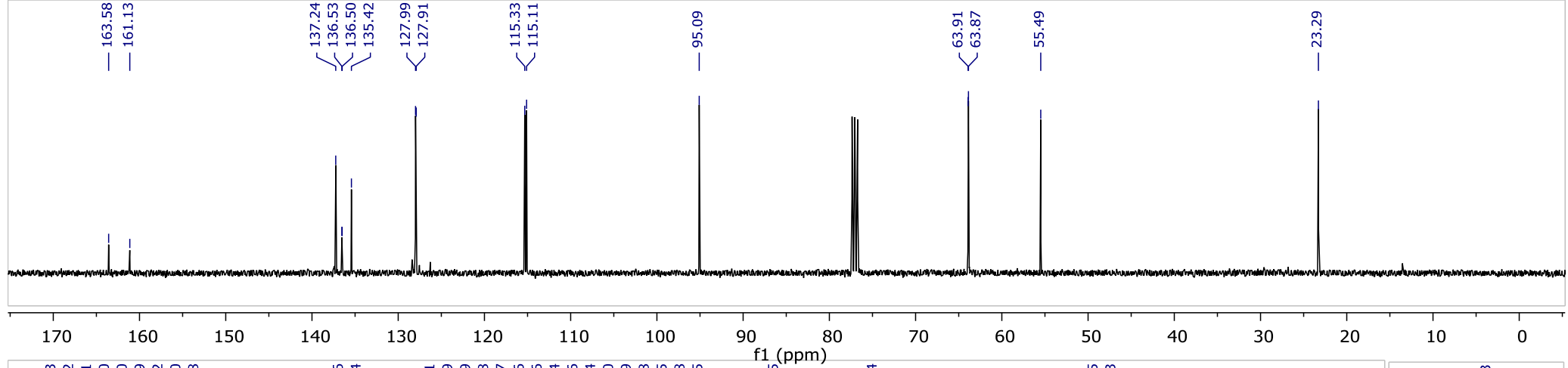
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.890	8.36	10.19	602.48	1832.6	48.8396	0.306
2	11.191	10.76	12.58	631.11	1373.61	51.1604	0.423



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.823	8.50	9.13	13.1239	40.3799	1.8953	0.325
2	11.125	10.65	12.43	679.326	1401.39	98.1047	0.449

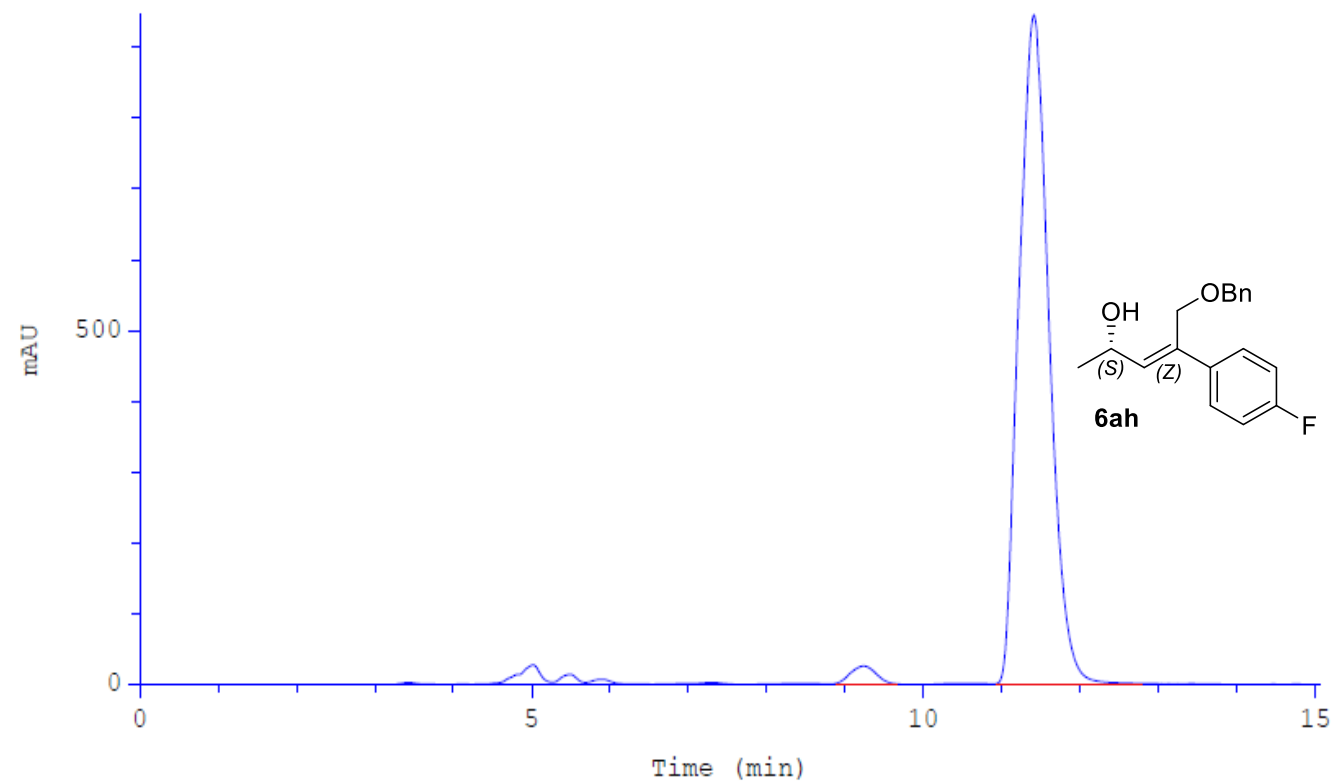
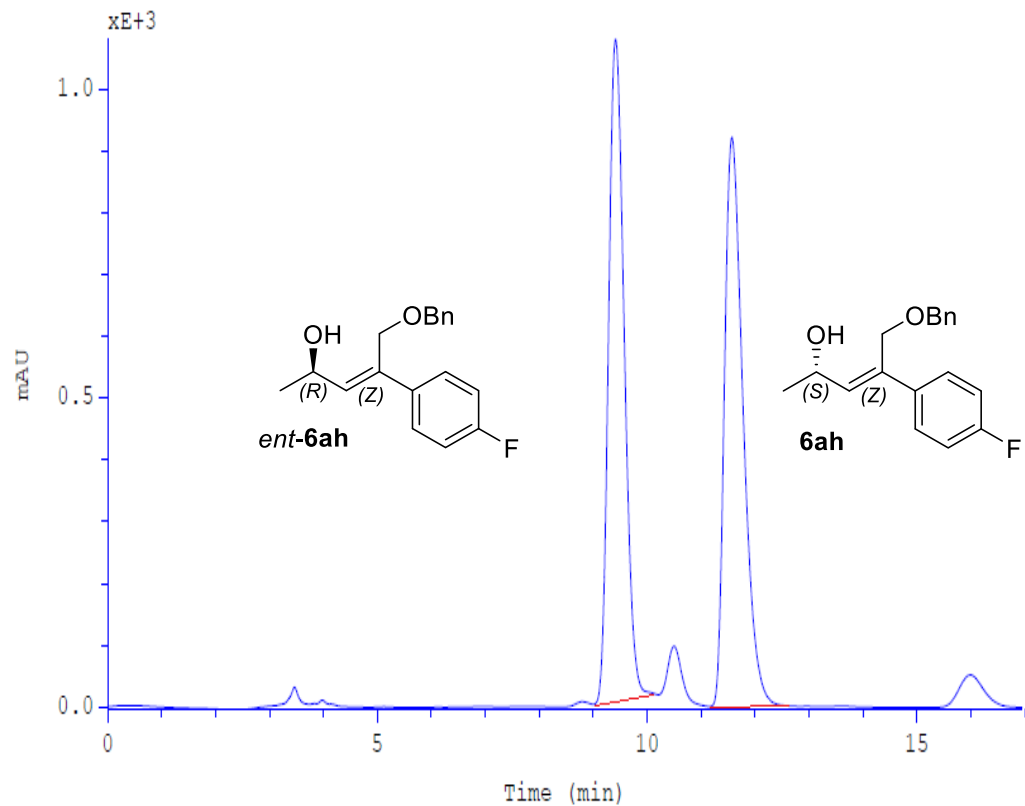






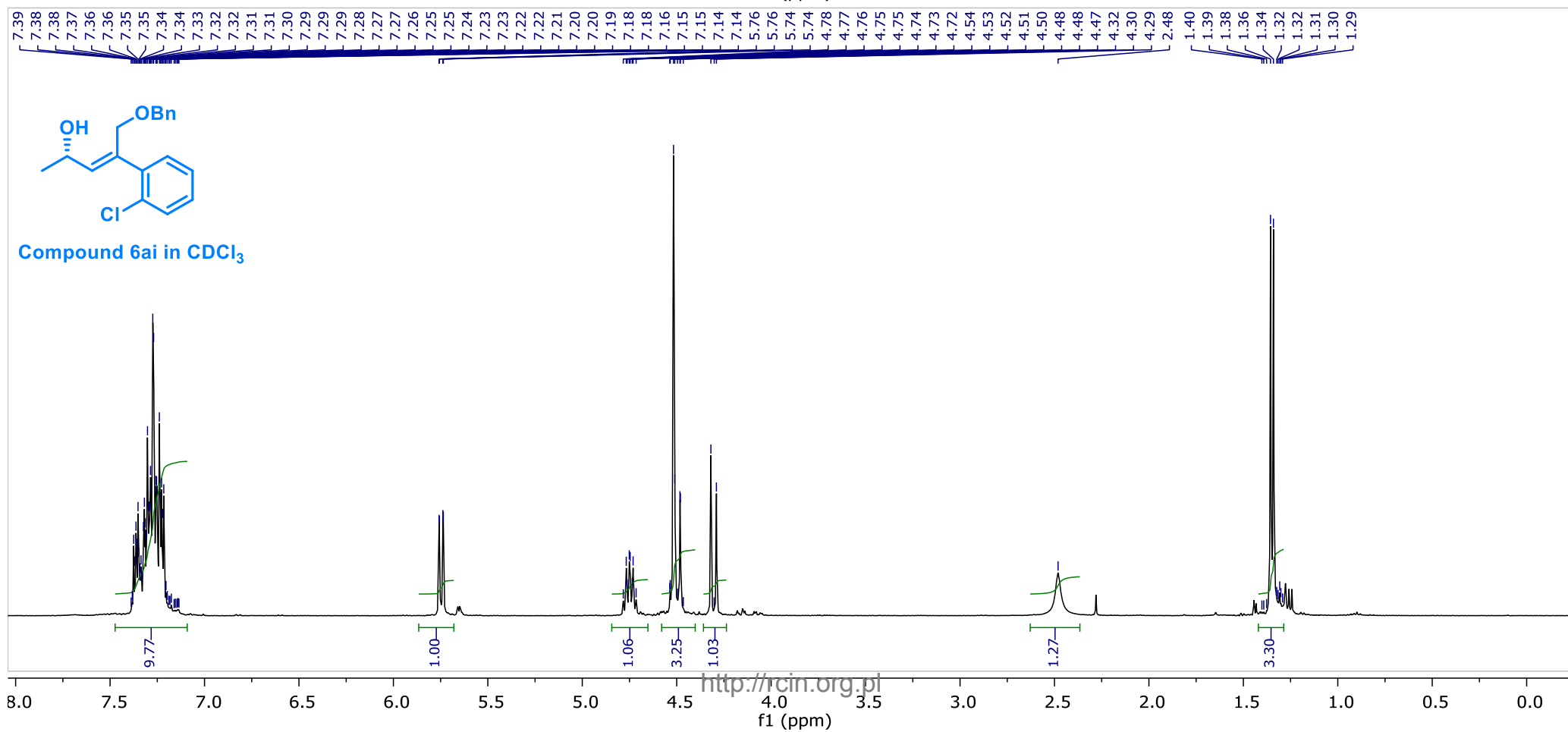
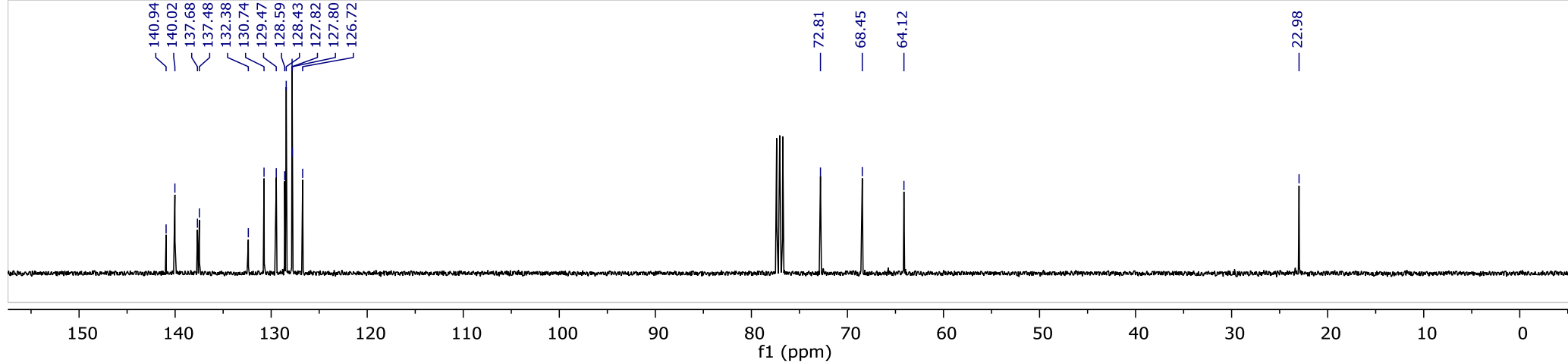
## HPLC chromatogram of compounds rac-6ah and 6ah

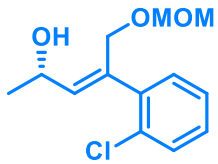
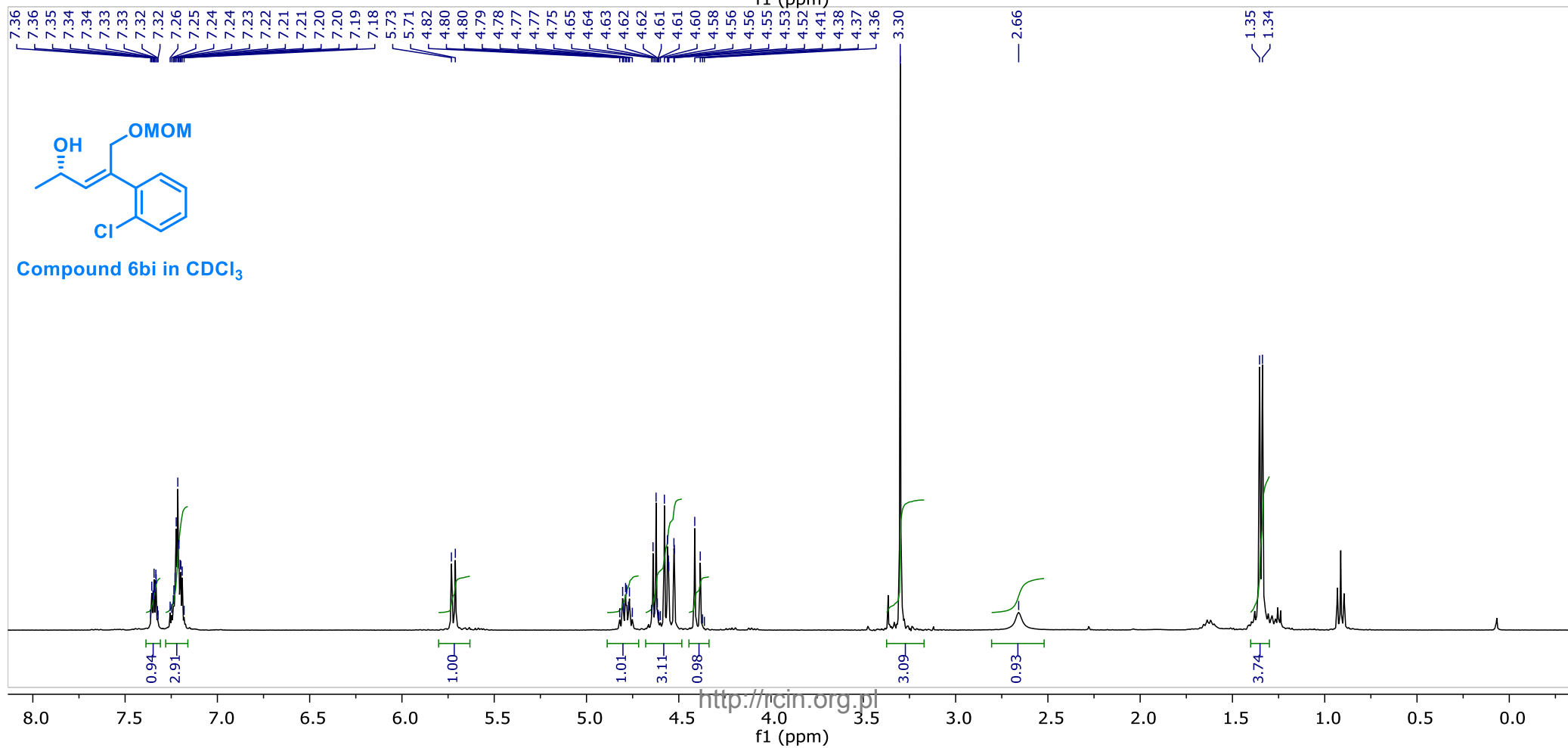
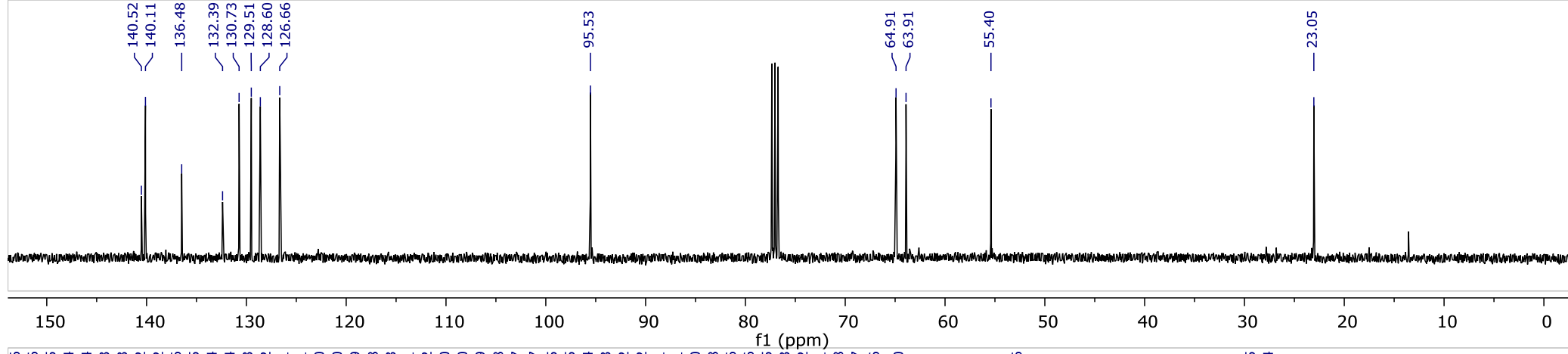
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.408	9.04	10.13	359.65	1070.84	49.5195	0.315
2	11.576	11.17	12.48	366.63	921.878	50.4805	0.368

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	9.242	8.89	9.59	8.82102	24.3448	2.0631	0.357
2	11.411	10.87	12.79	418.734	944.629	97.9369	0.425

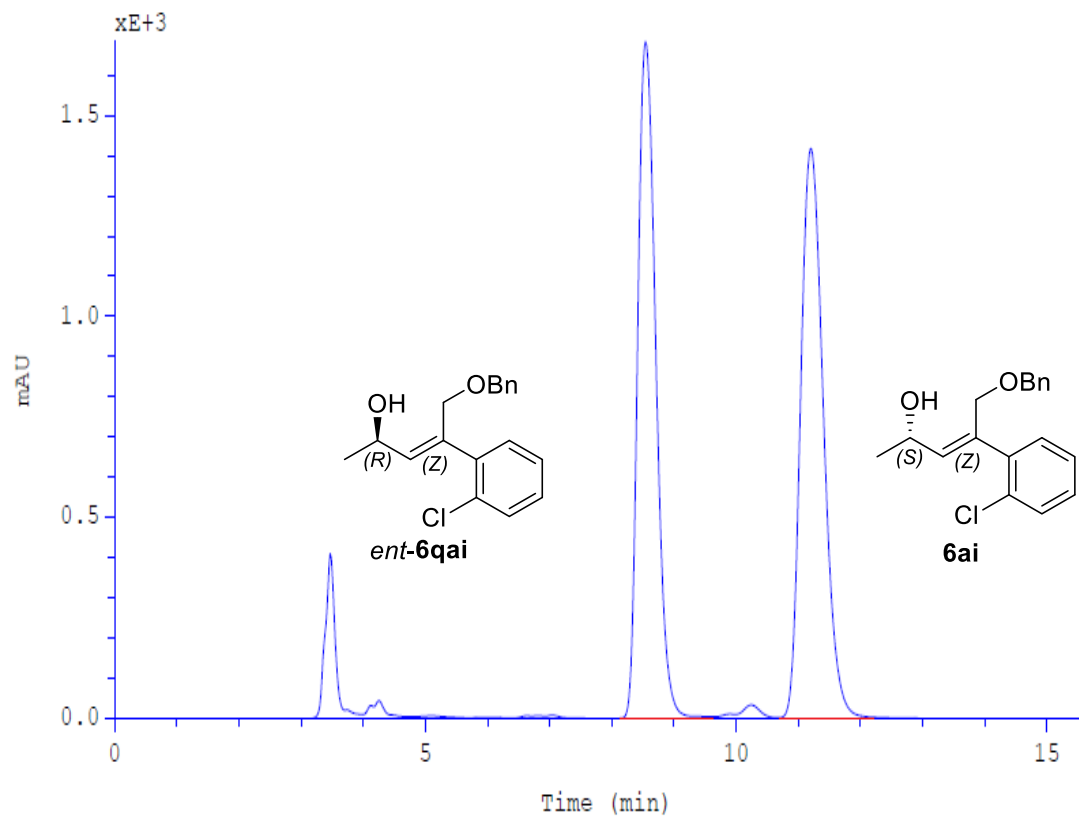




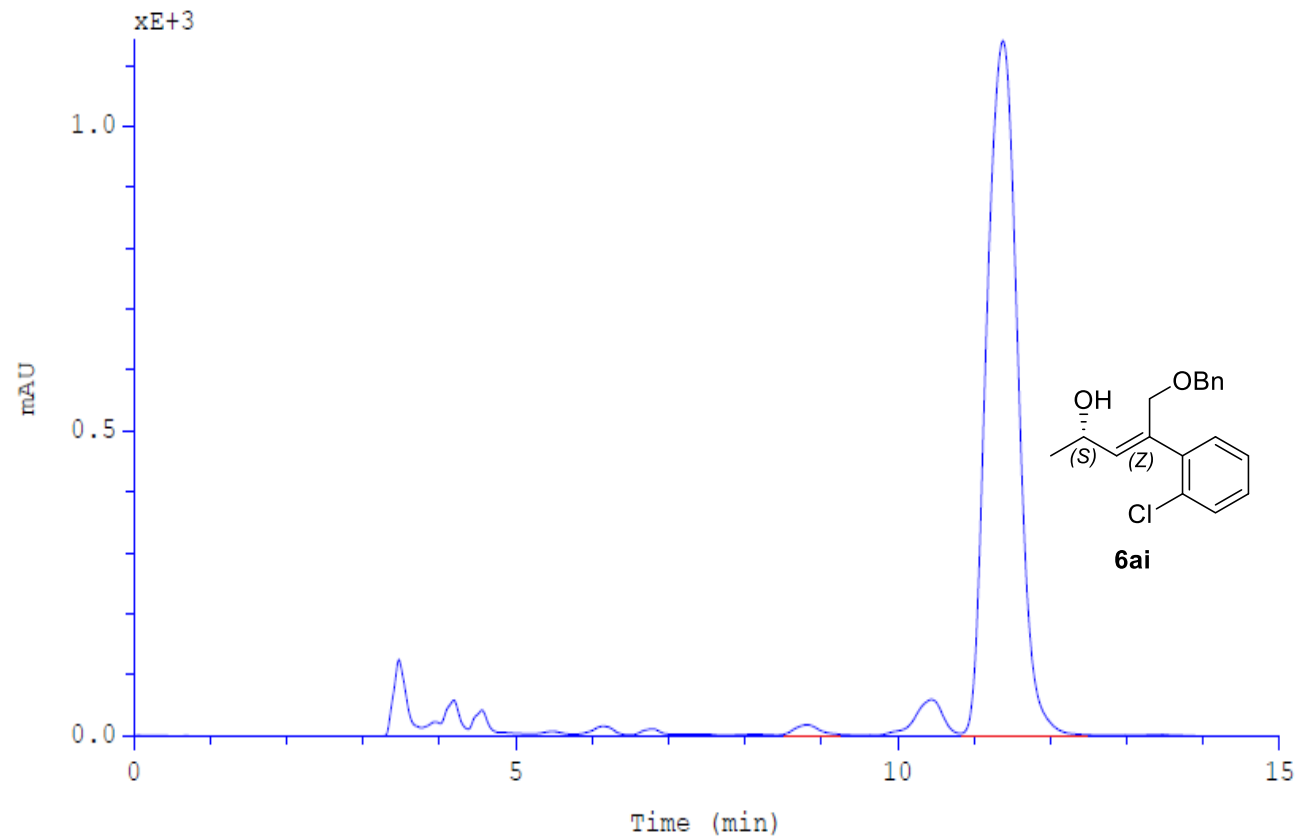
Compound 6bi in CDCl<sub>3</sub>

## HPLC chromatogram of compounds rac-6ai and 6ai

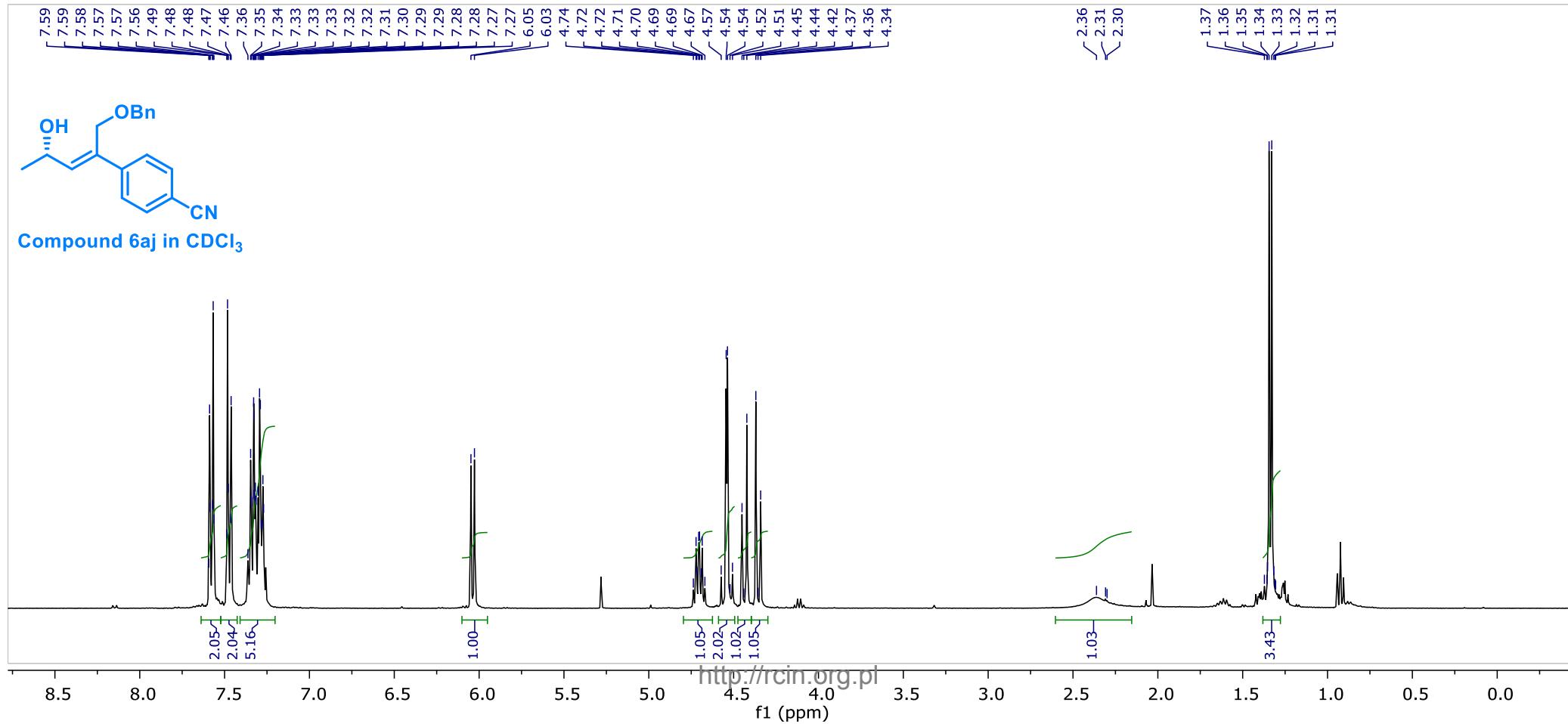
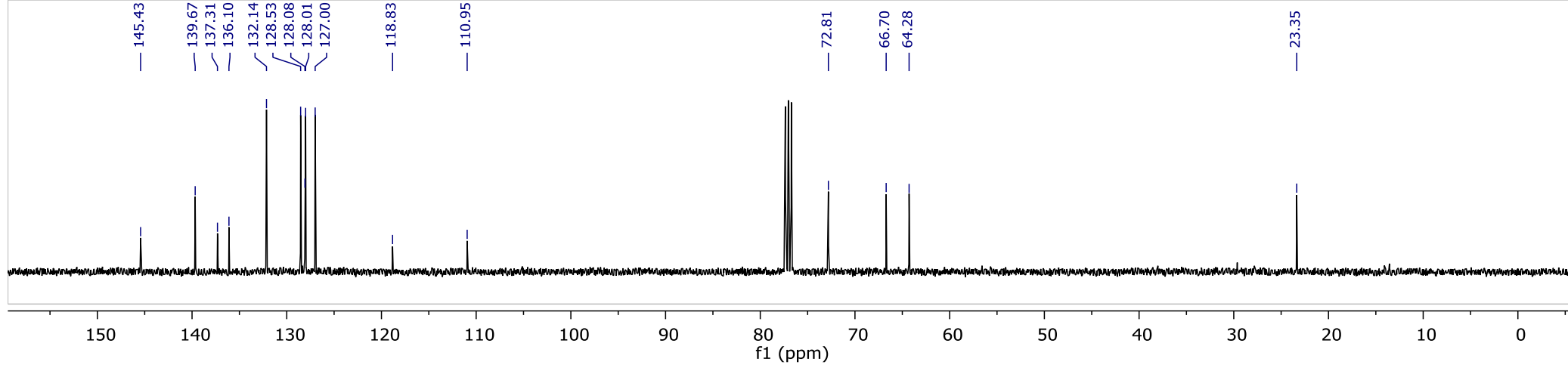
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 215 nm

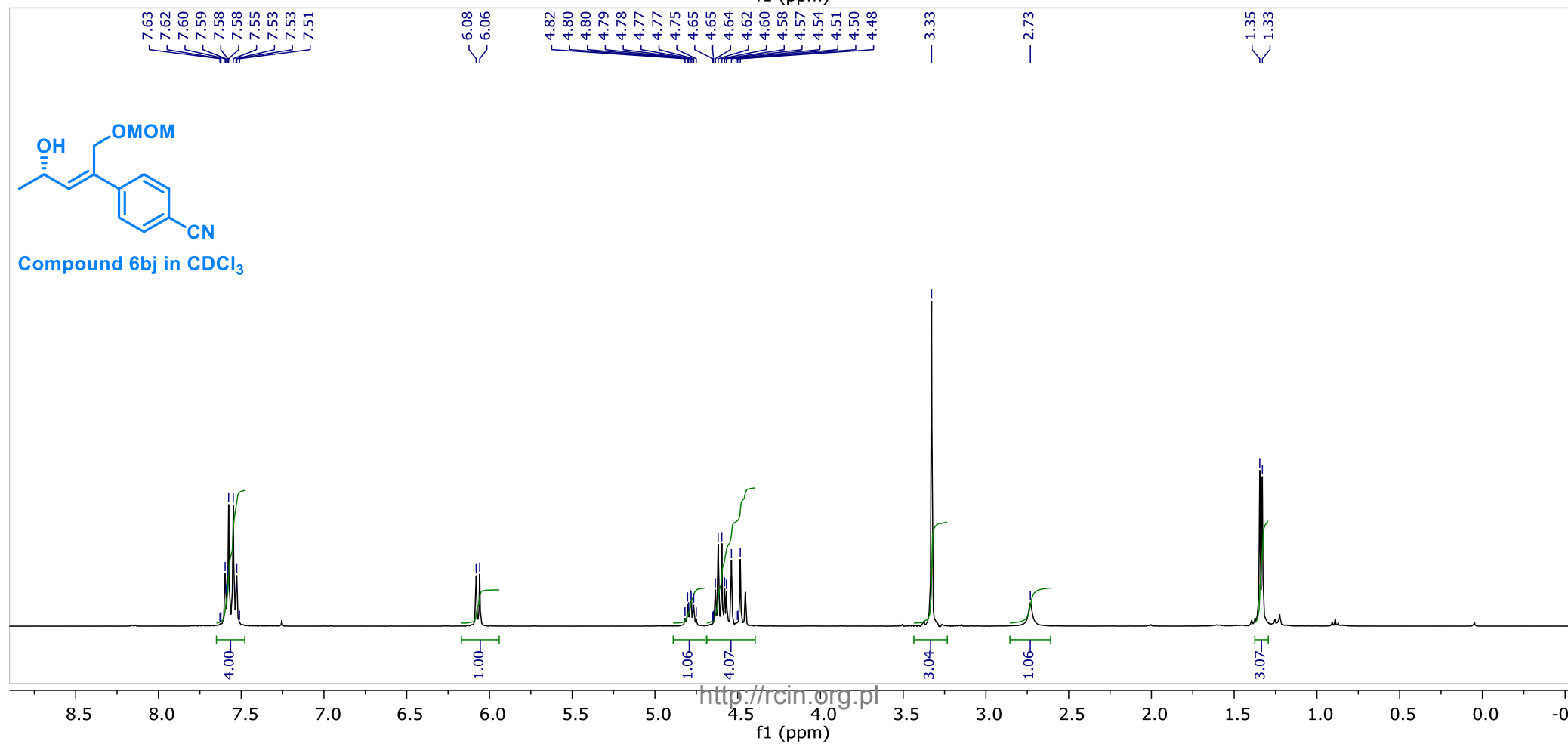
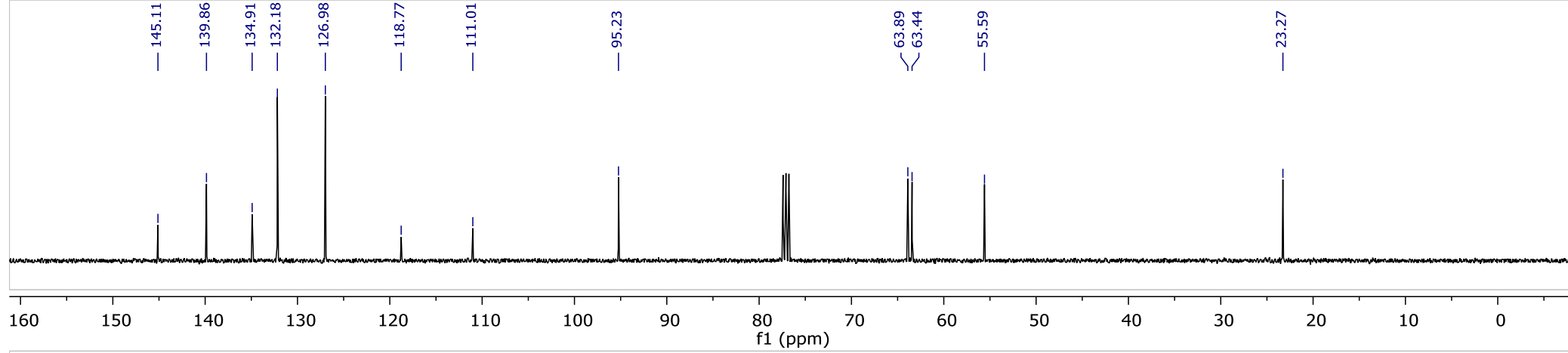


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.541	8.13	9.59	563.336	1682.15	48.6523	0.314
2	11.193	10.67	12.12	594.547	1415.02	51.3477	0.394



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.808	8.54	9.17	4.66577	14.5617	0.8715	0.309
2	11.377	10.82	12.35	530.728	1137.43	99.1285	0.449

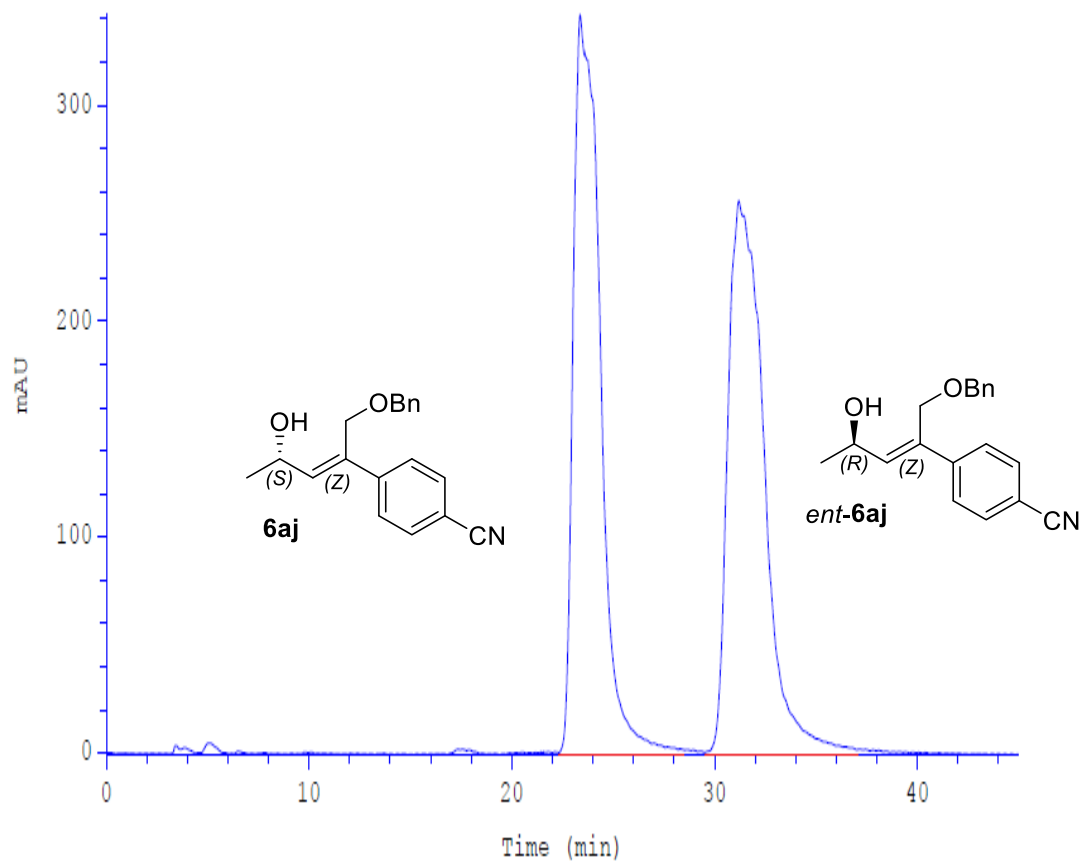




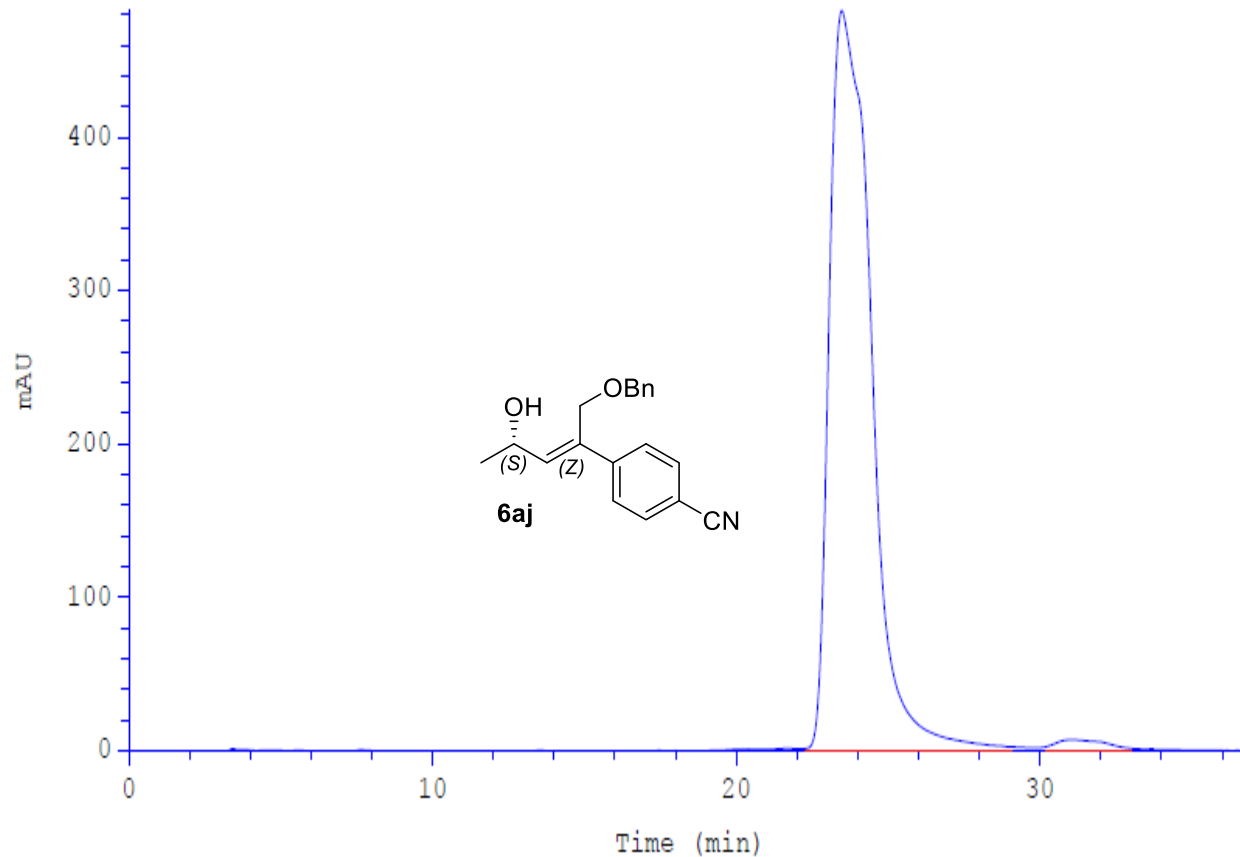


## HPLC chromatogram of compounds rac-6aj and 6aj

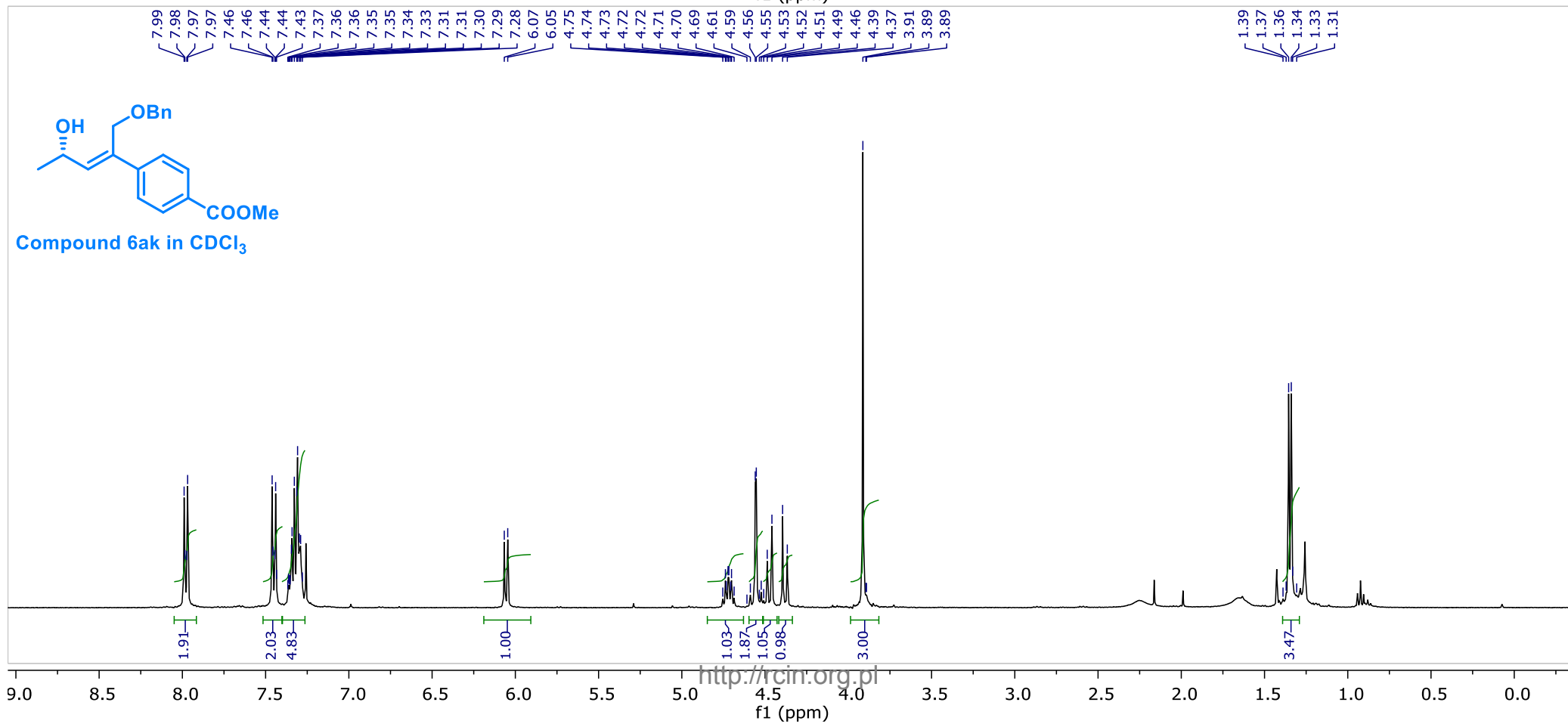
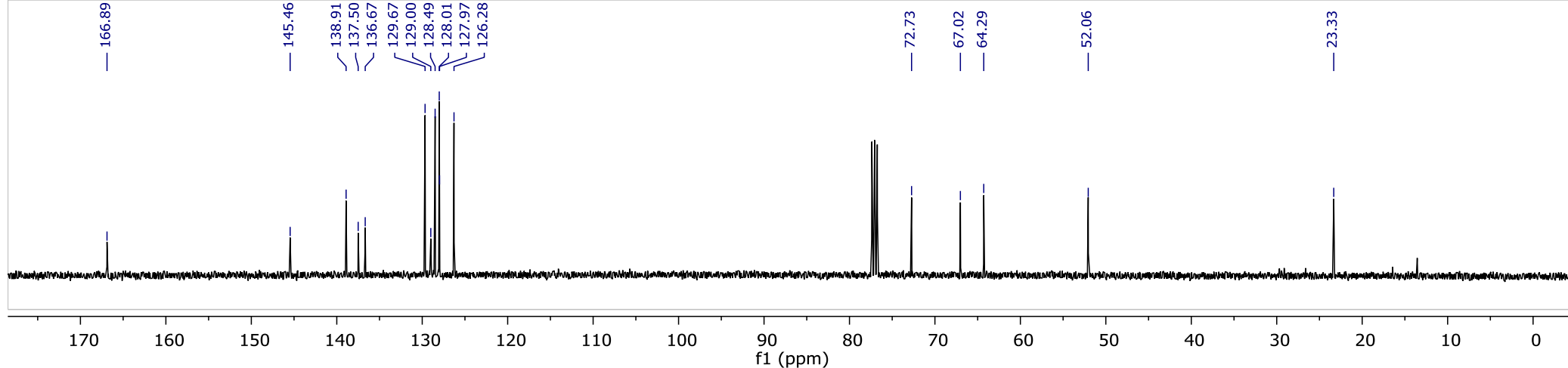
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

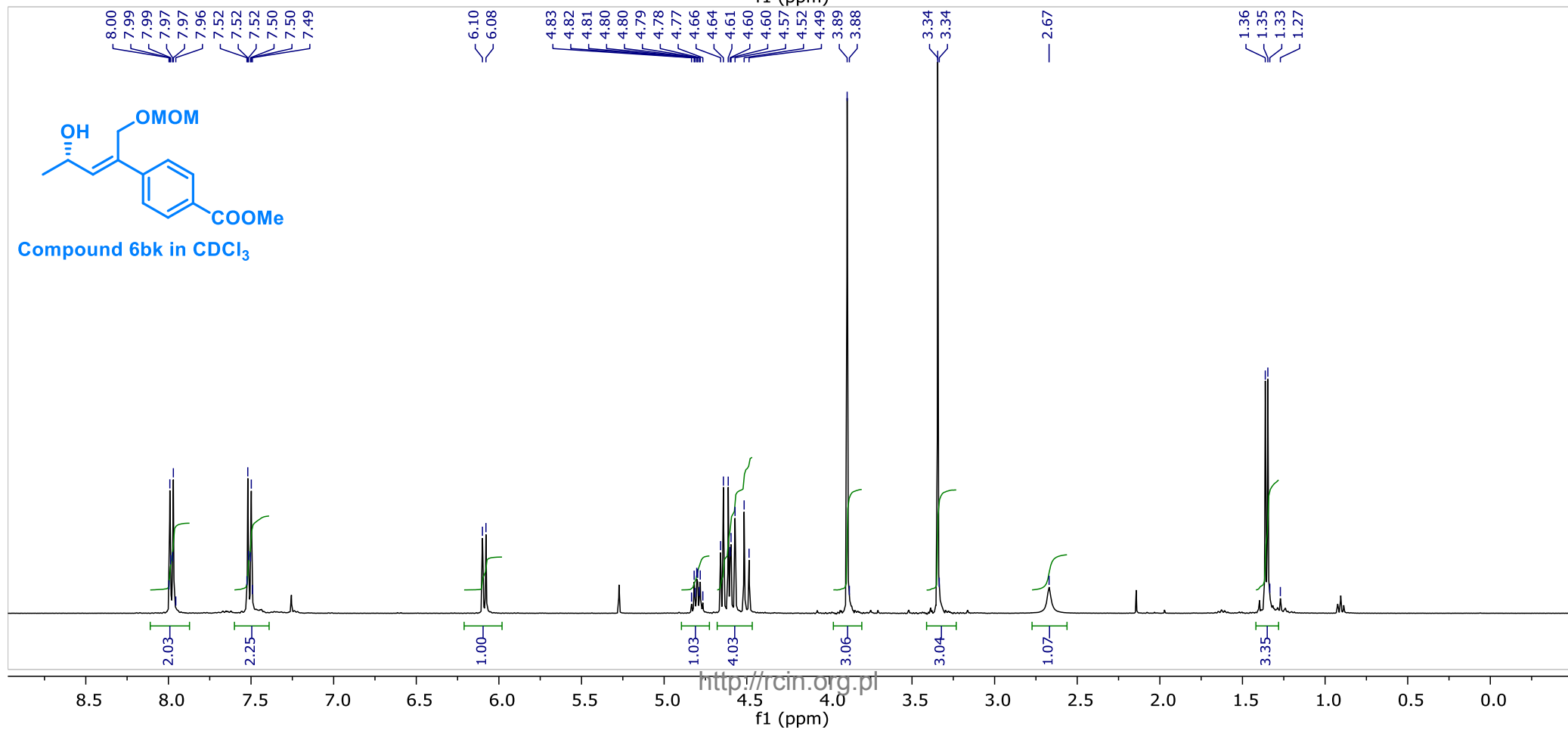
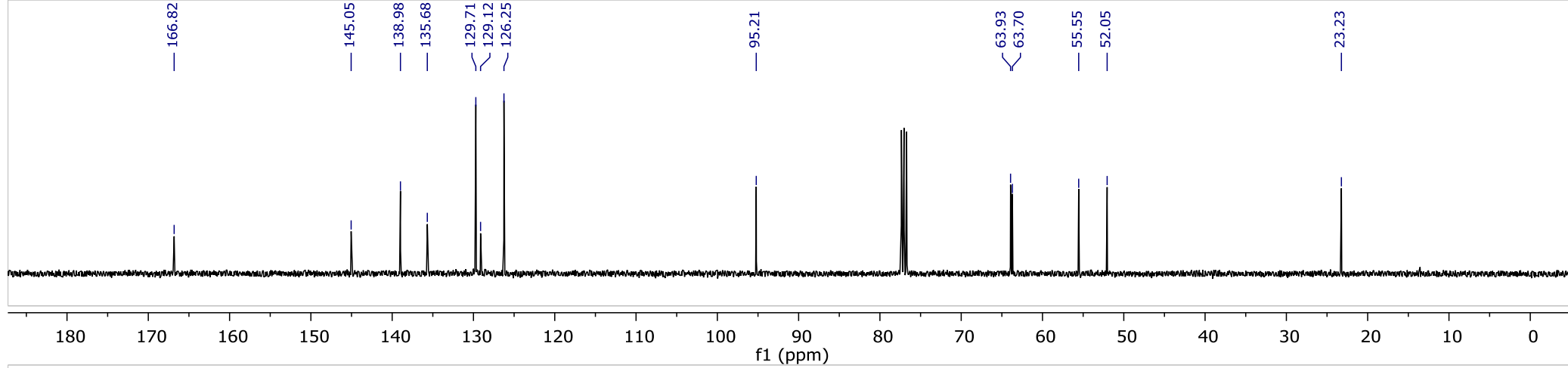


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	23.371	22.28	28.19	518.719	341.339	50.1355	1.438
2	31.189	29.75	36.93	515.916	254.59	49.8645	1.926



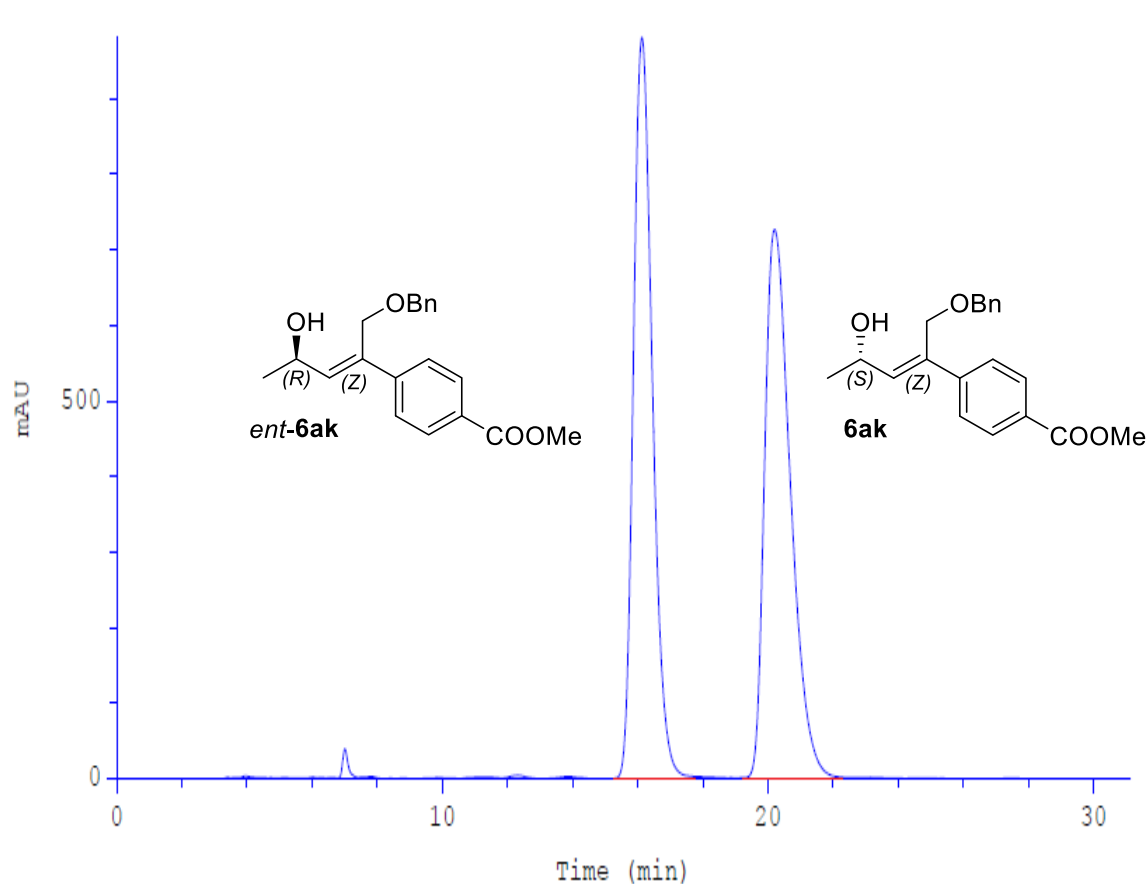
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	23.471	22.22	28.69	757.213	480.783	98.9833	1.492
2	31.039	30.14	32.70	7.77761	4.90156	1.0167	1.692



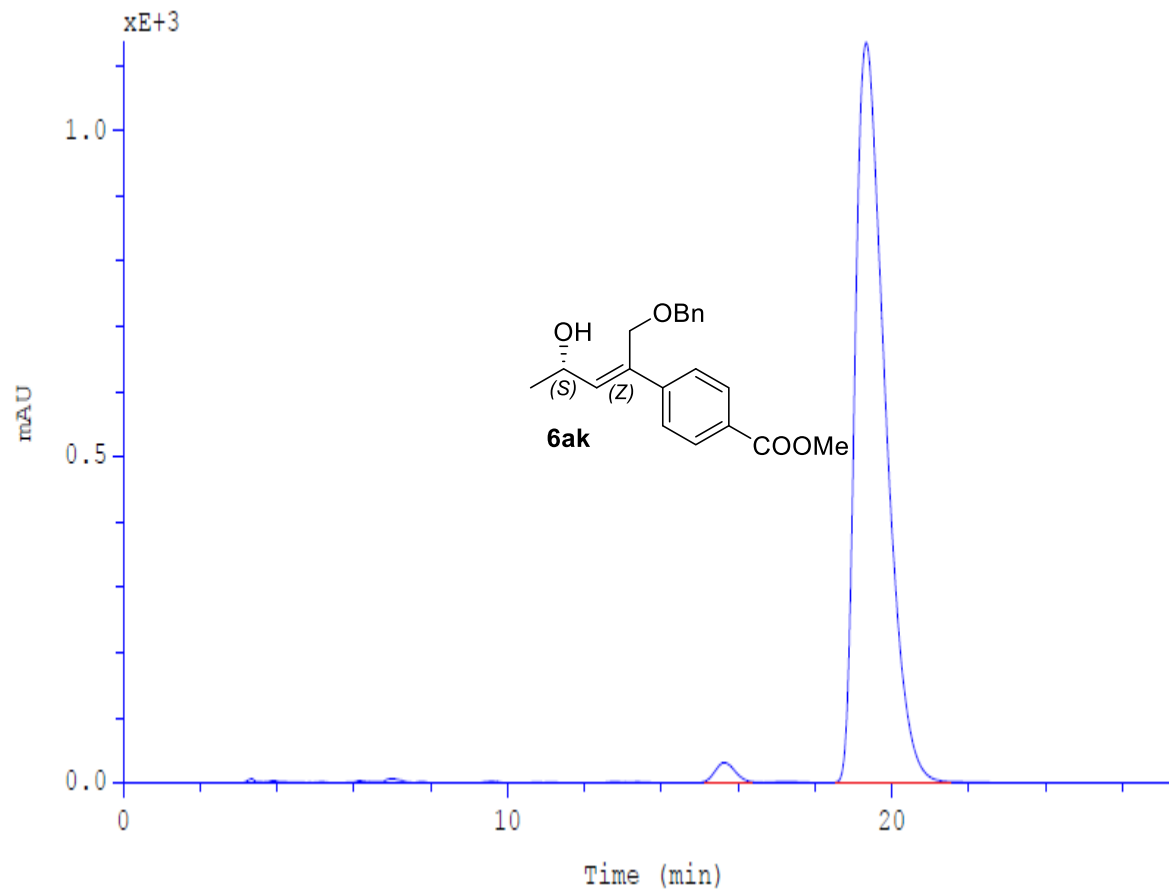


# HPLC chromatogram of compounds rac-6ak and 6ak

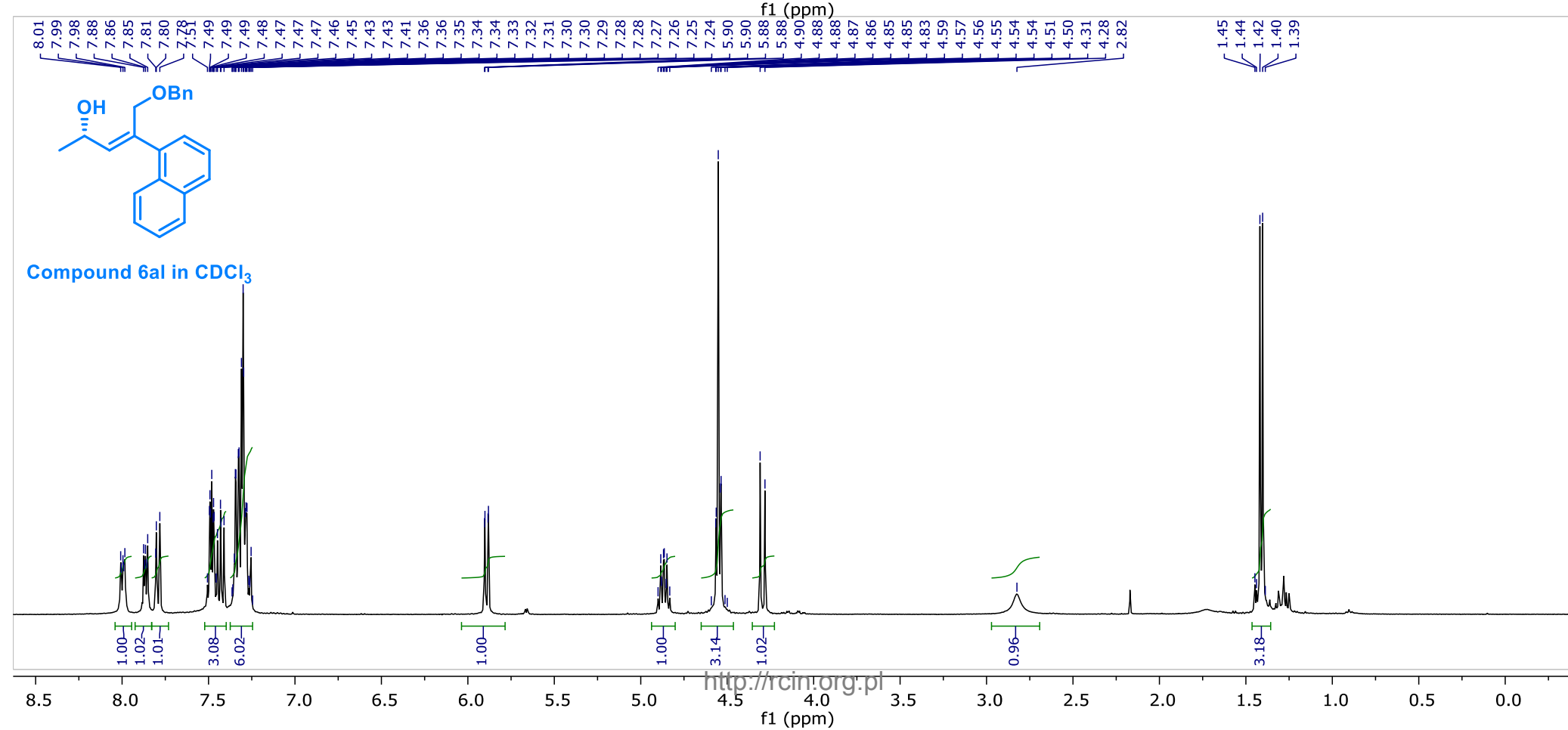
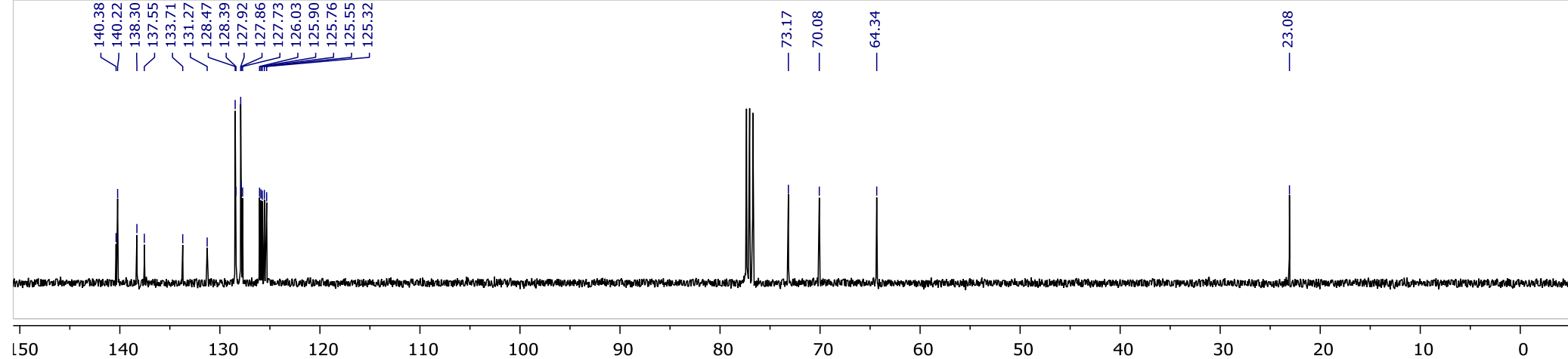
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

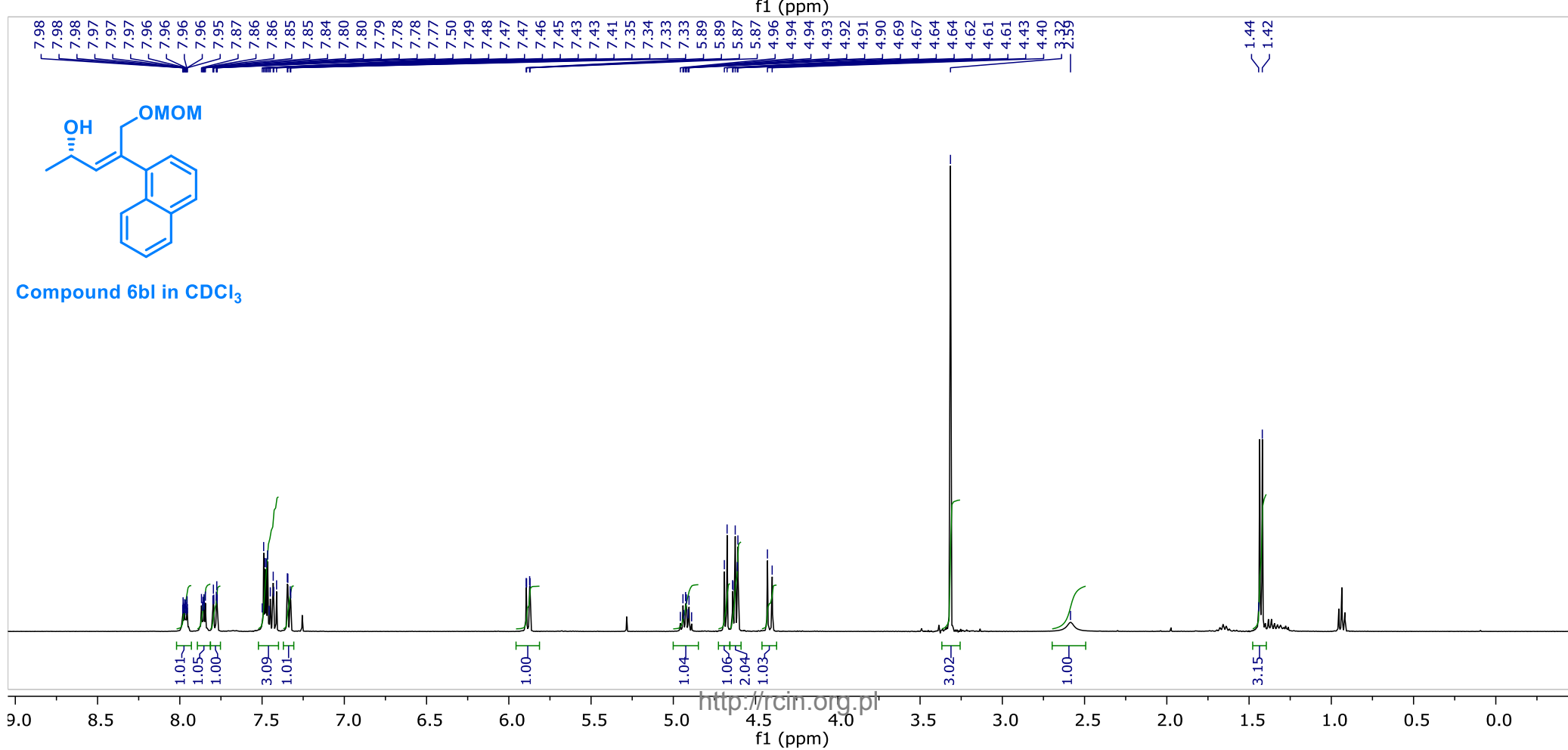
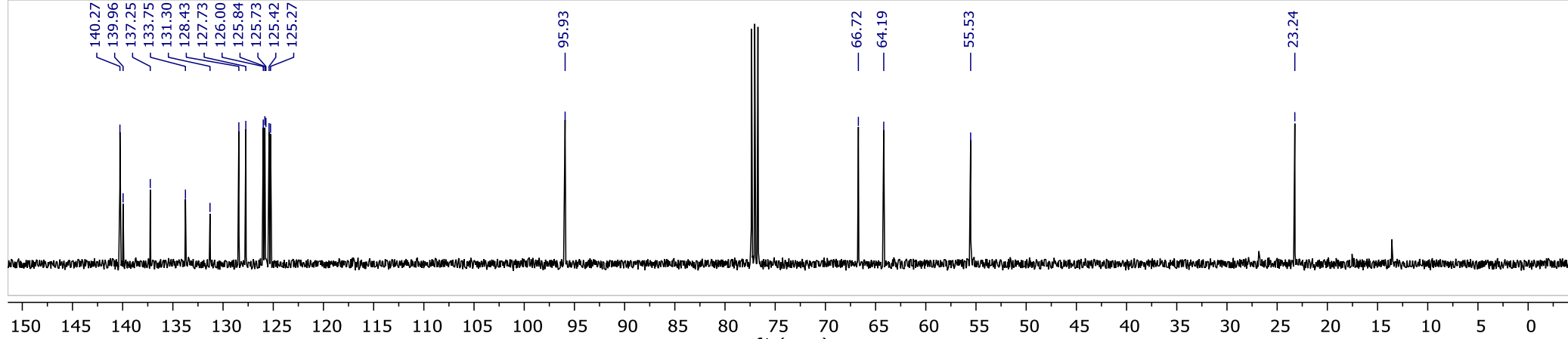


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	16.121	15.12	17.75	660.041	979.073	49.8990	0.627
2	20.205	19.30	22.14	662.714	724.685	50.1010	0.853



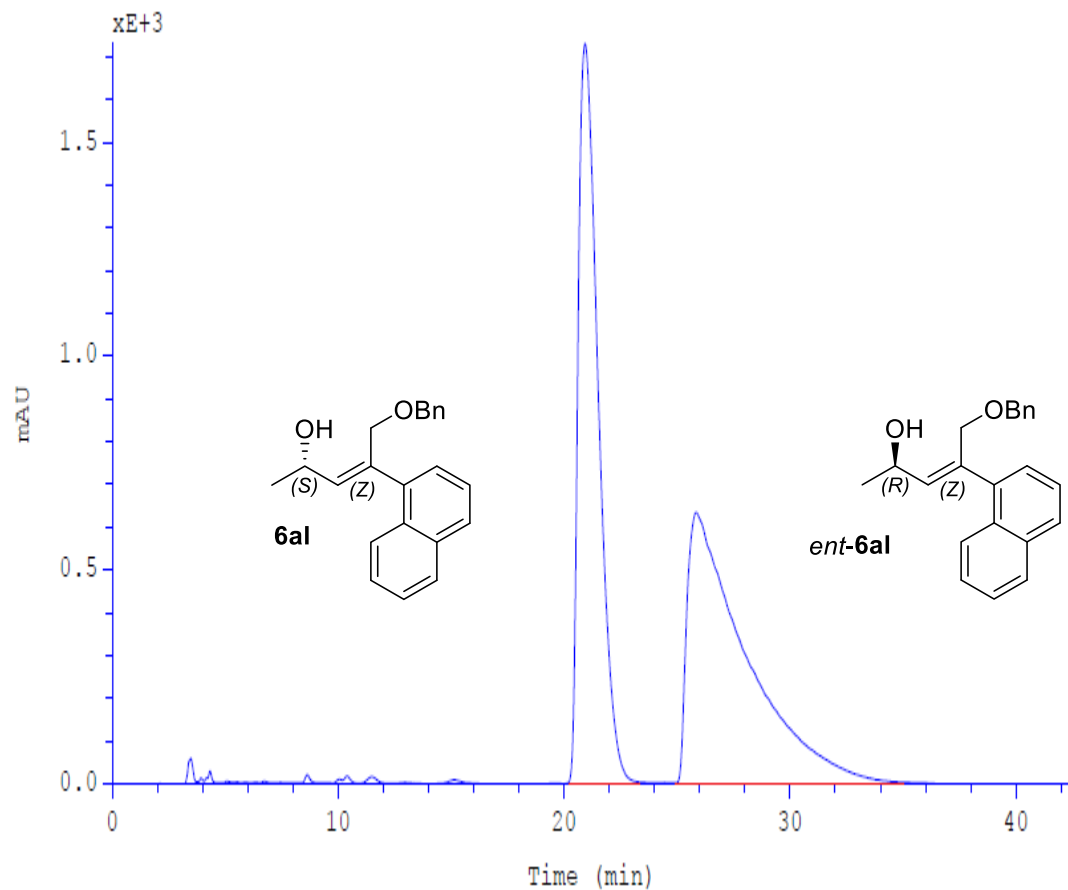
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.638	15.16	16.25	15.8395	28.3027	1.5347	0.541
2	19.340	18.47	21.60	1016.28	1134.52	98.4653	0.833



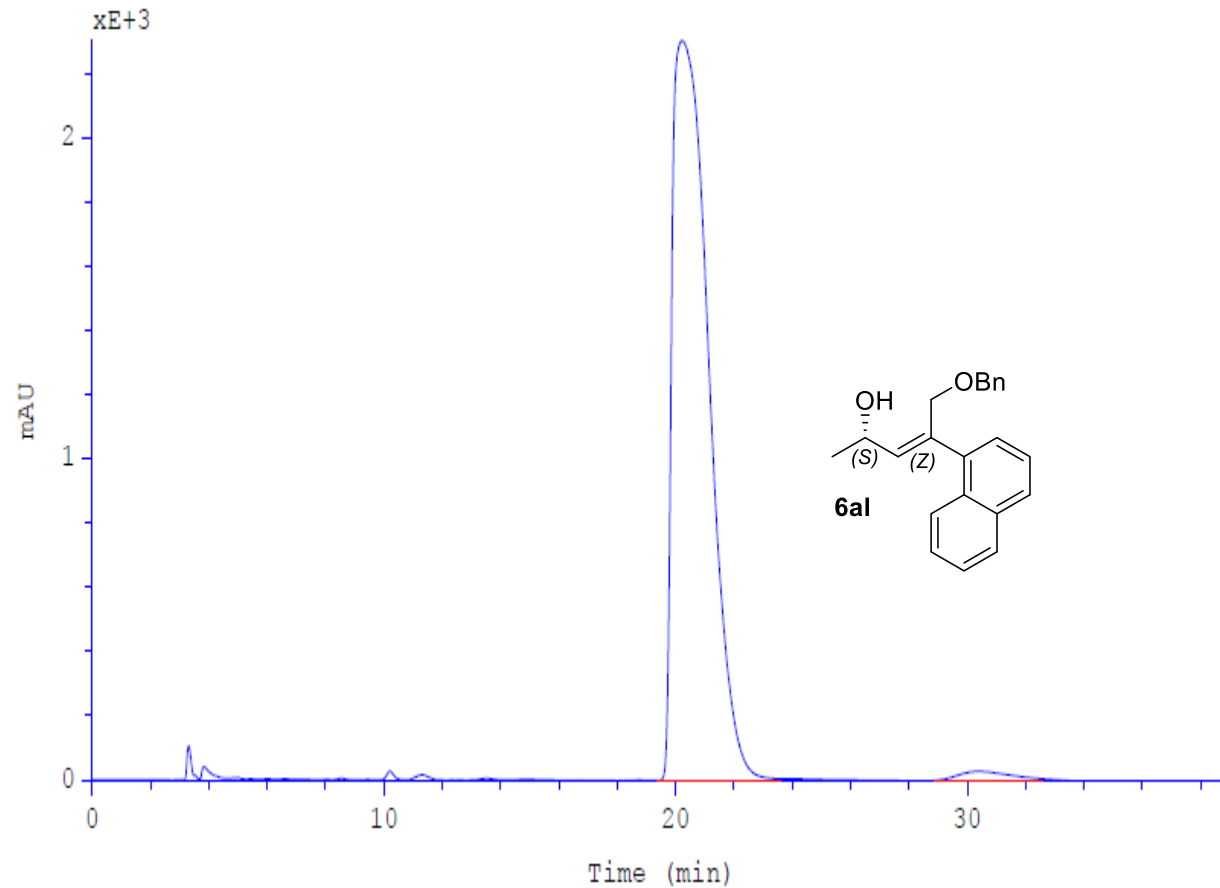


## HPLC chromatogram of compounds rac-6al and 6al

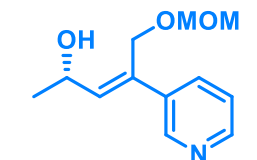
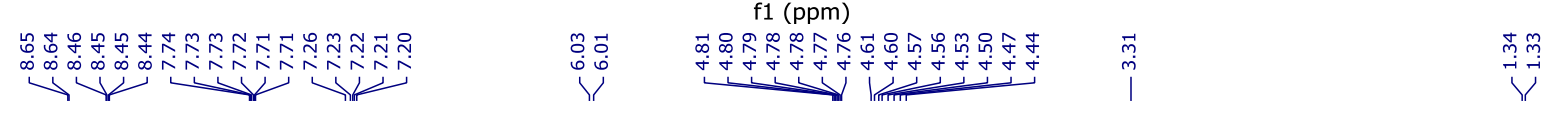
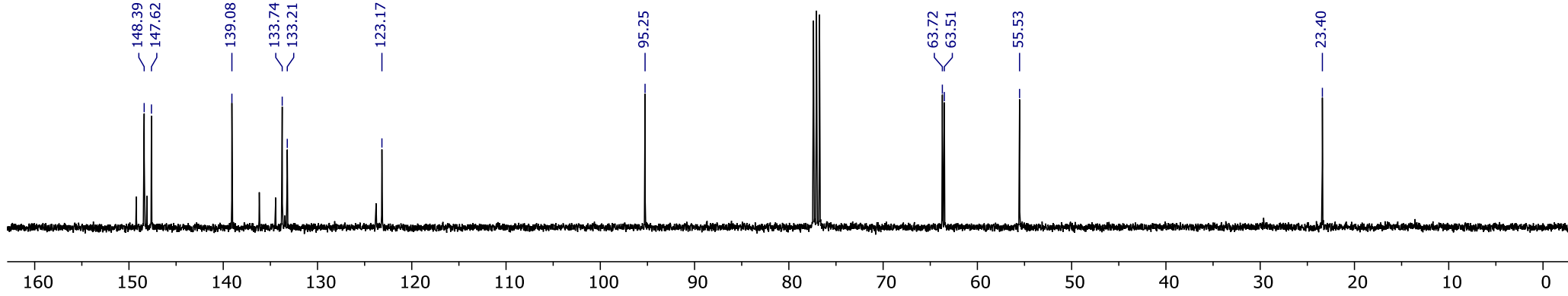
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 215 nm



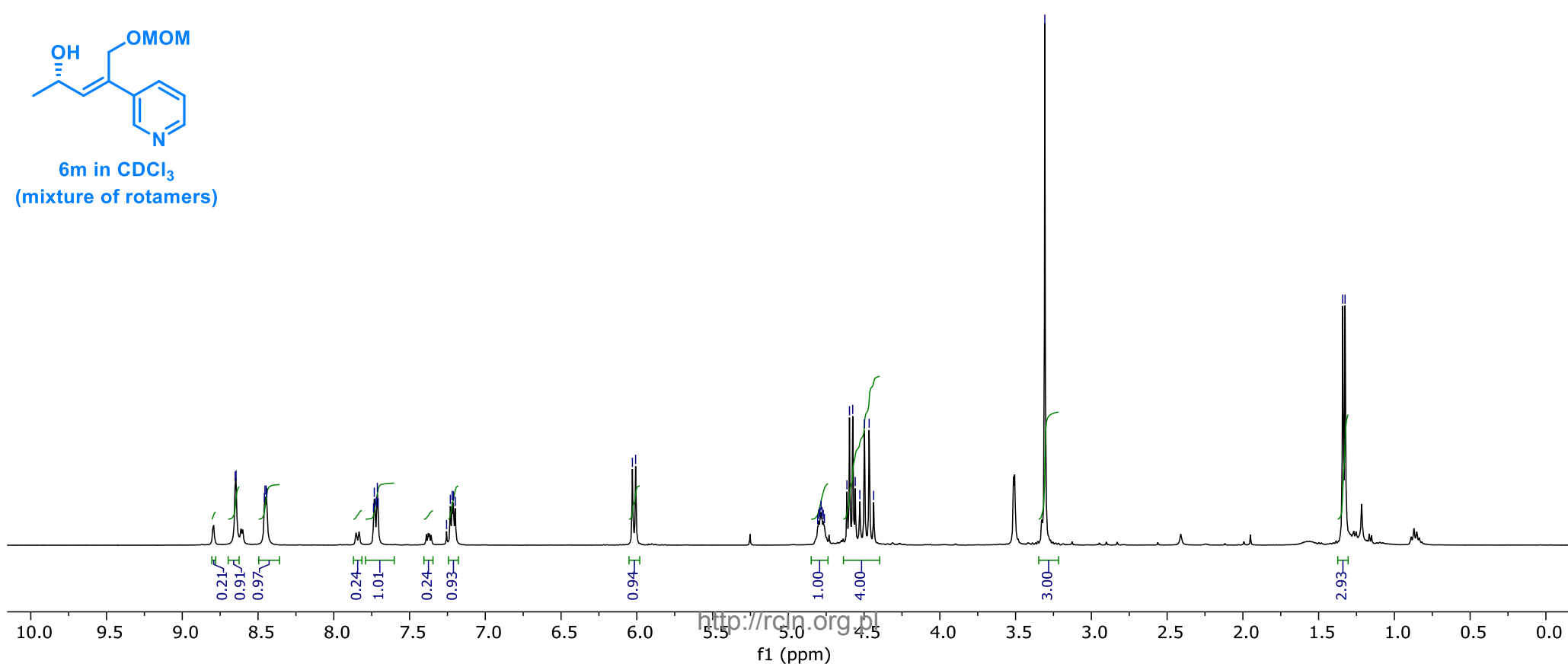
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	20.921	20.11	23.28	1771.41	1728.51	48.3087	0.959
2	25.839	24.90	34.76	1895.44	631.934	51.6913	2.506



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	20.222	19.34	23.42	3317.22	2302.15	98.6203	1.379
2	30.424	28.86	32.39	46.4081	25.6184	1.3797	1.795



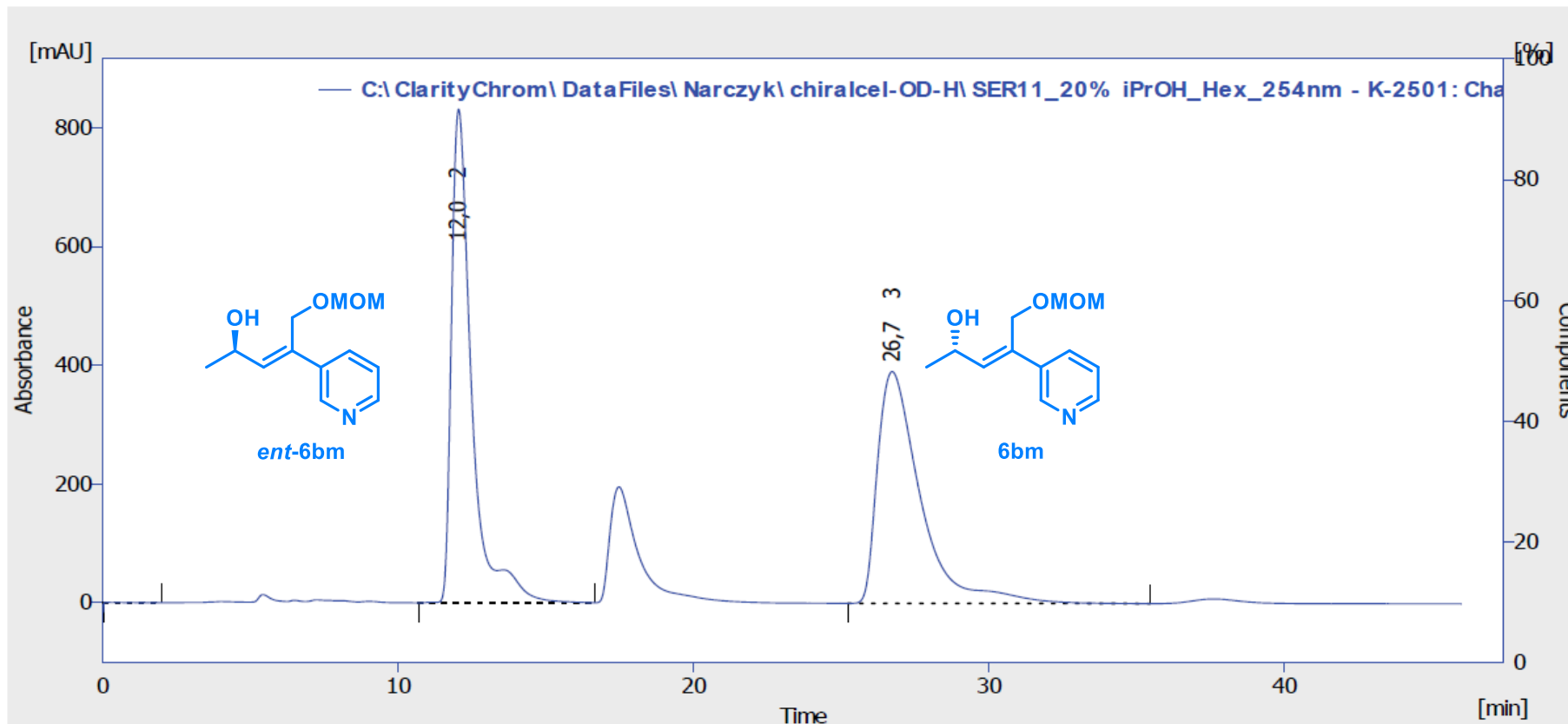
6m in CDCl<sub>3</sub>  
(mixture of rotamers)





## HPLC chromatogram of compounds *rac*-6bm

Conditions: column Chiralcel OD-H, 20% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

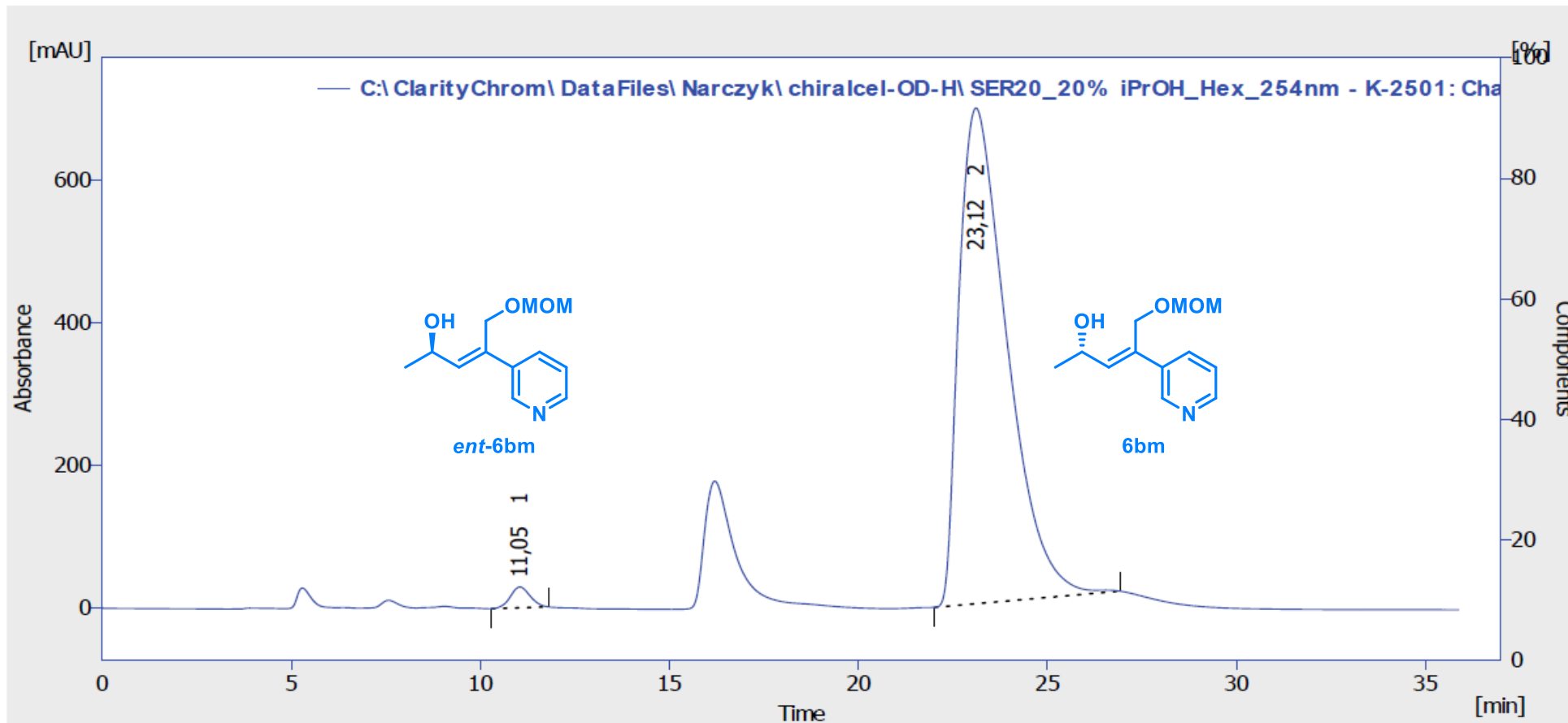


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER11\_20% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	0,150	11,807	0,562	0,0	0,0	0,12	
2	12,033	39696,279	831,648	50,1	68,0	0,67	
3	26,717	39596,551	390,452	49,9	31,9	1,47	
	Total	79304,638	1222,662	100,0	100,0		

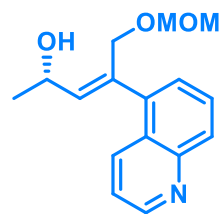
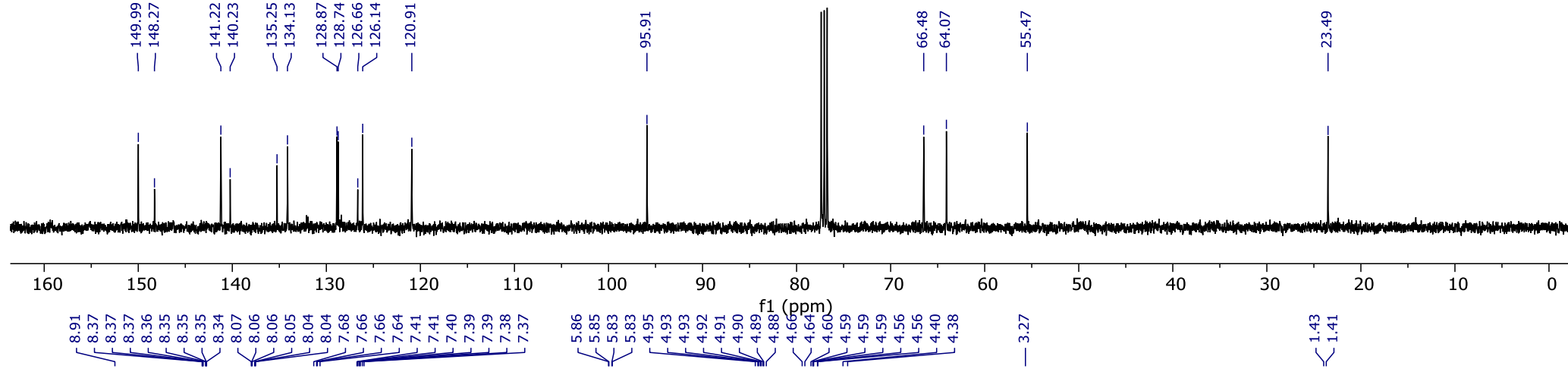
## HPLC chromatogram of compounds 6bm

Conditions: column Chiralcel OD-H, 20% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

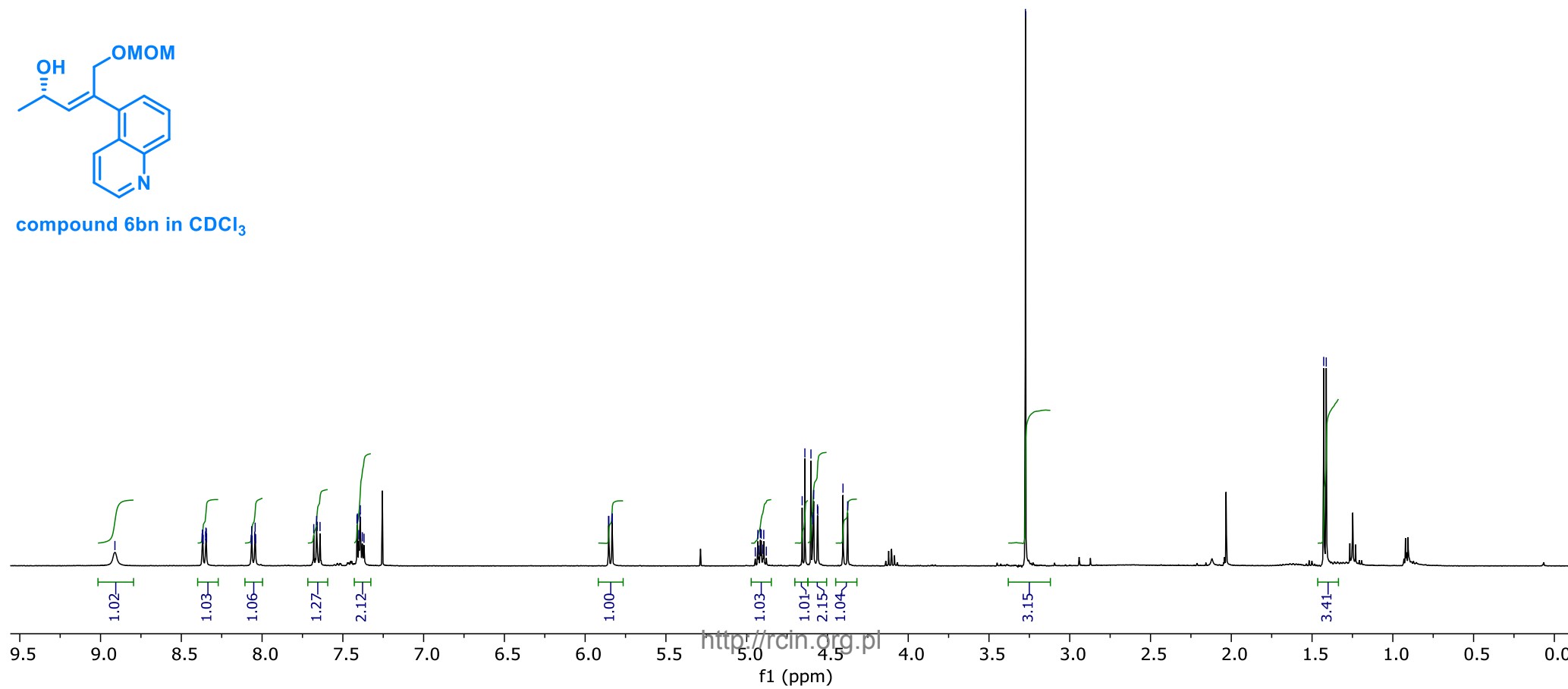


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER20\_20% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11,050	1064,865	29,176	1,7	4,0	0,60	
2	23,117	61312,185	694,281	98,3	96,0	1,40	
	Total	62377,050	723,457	100,0	100,0		

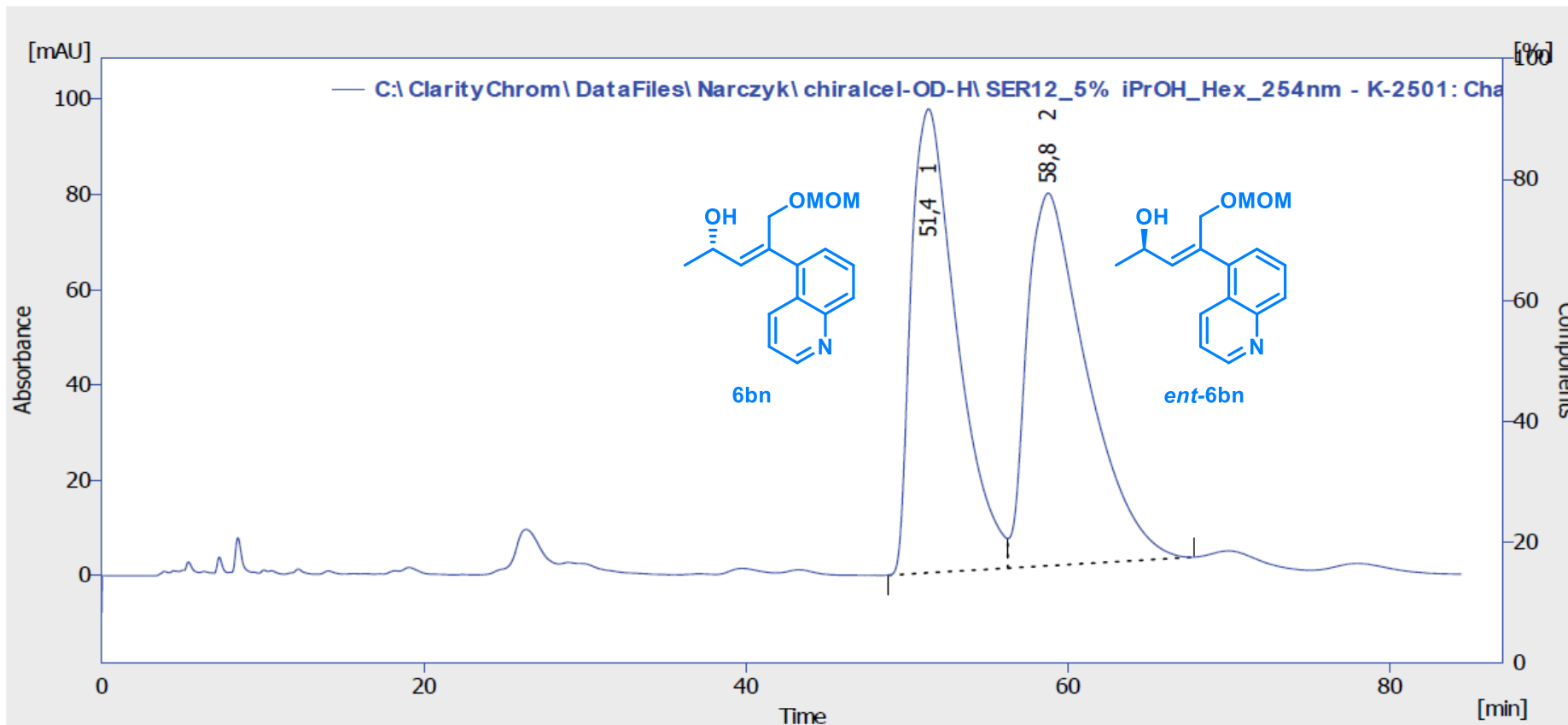


compound 6bn in CDCl<sub>3</sub>



## HPLC chromatogram of compounds *rac*-6bn

Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

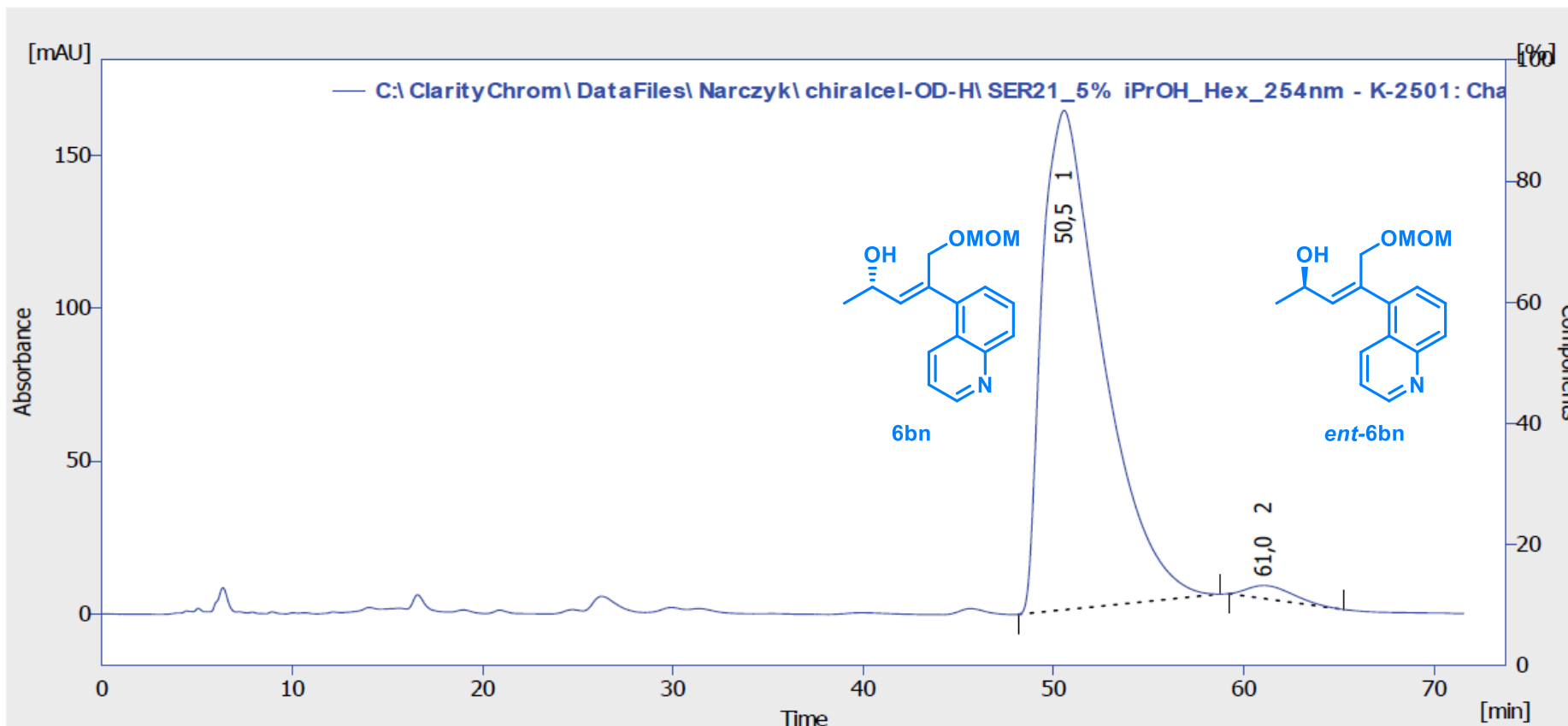


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER12\_5% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	51,350	19215,249	97,393	48,6	55,5	3,08	
2	58,767	20333,000	78,228	51,4	44,5	4,05	
	Total	39548,248	175,621	100,0	100,0		

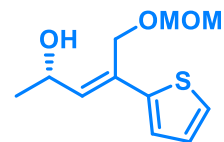
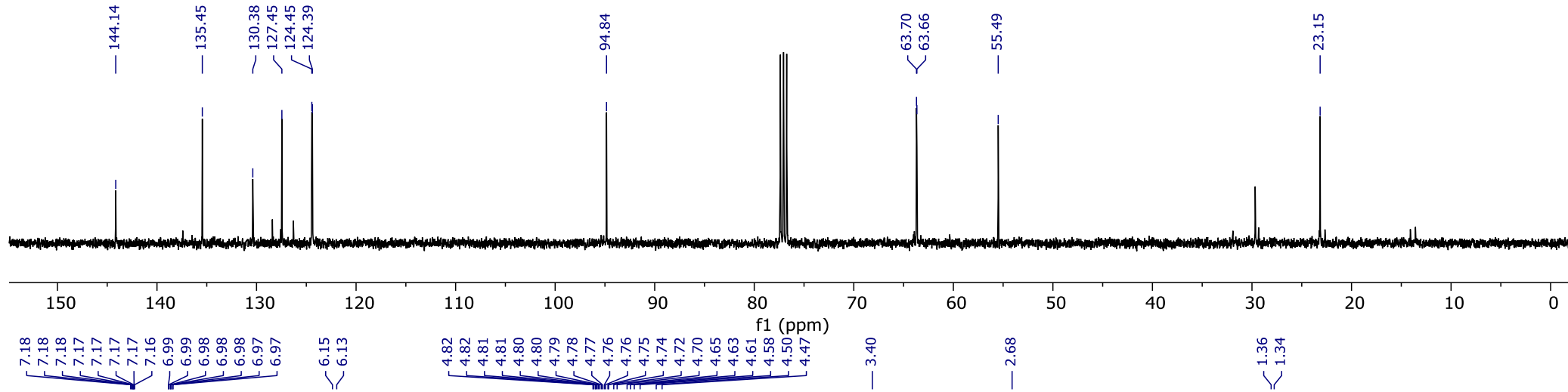
## HPLC chromatogram of compounds 6bn

Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

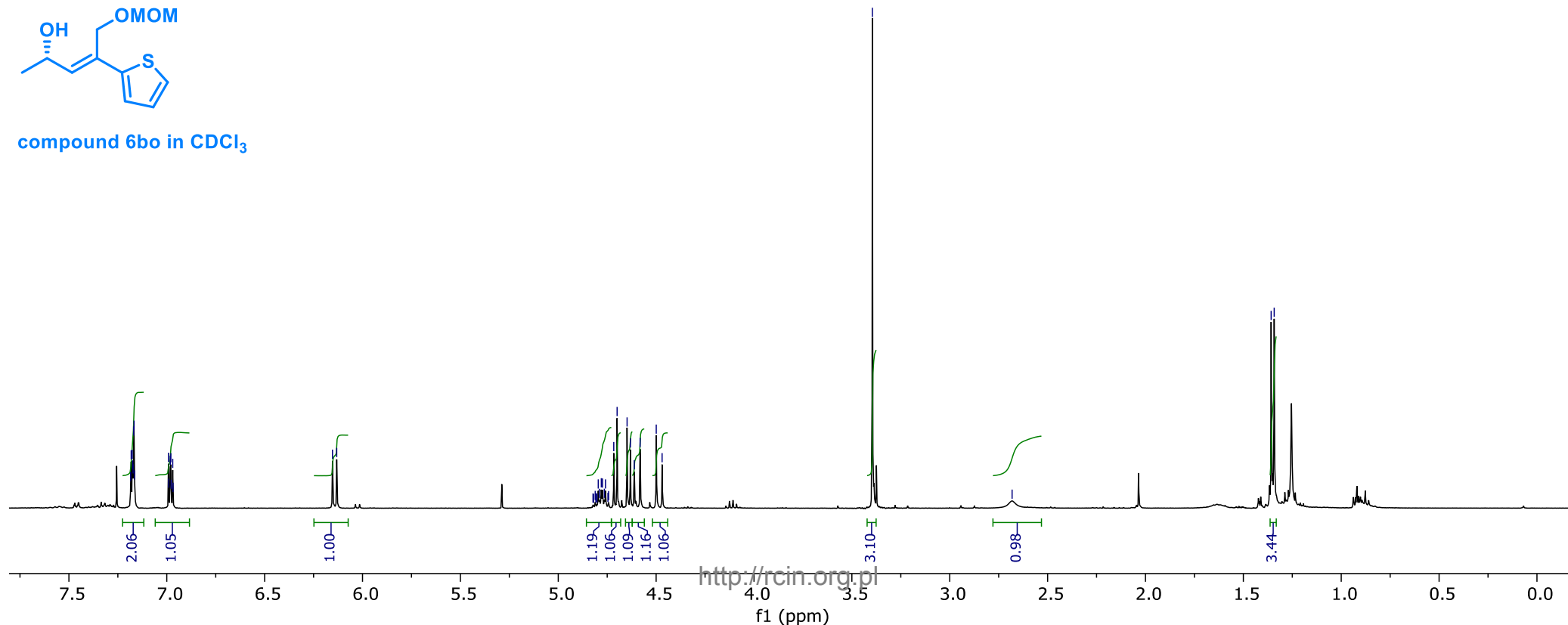


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER21\_5% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	50,550	36031,722	163,223	98,0	97,5	3,45	
2	61,050	731,299	4,257	2,0	2,5	2,63	
	Total	36763,022	167,480	100,0	100,0		

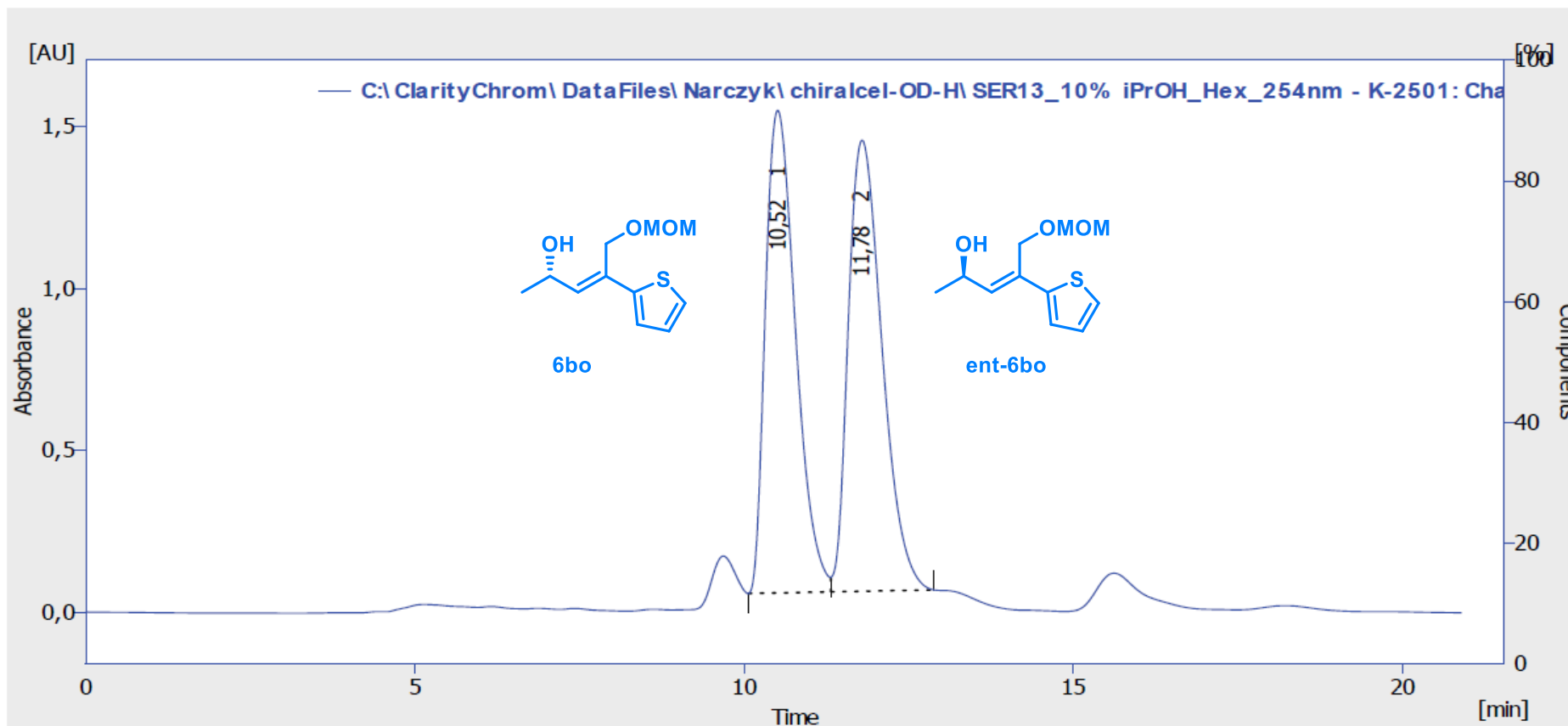


compound 6bo in CDCl<sub>3</sub>



## HPLC chromatogram of compounds rac-6bo

Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

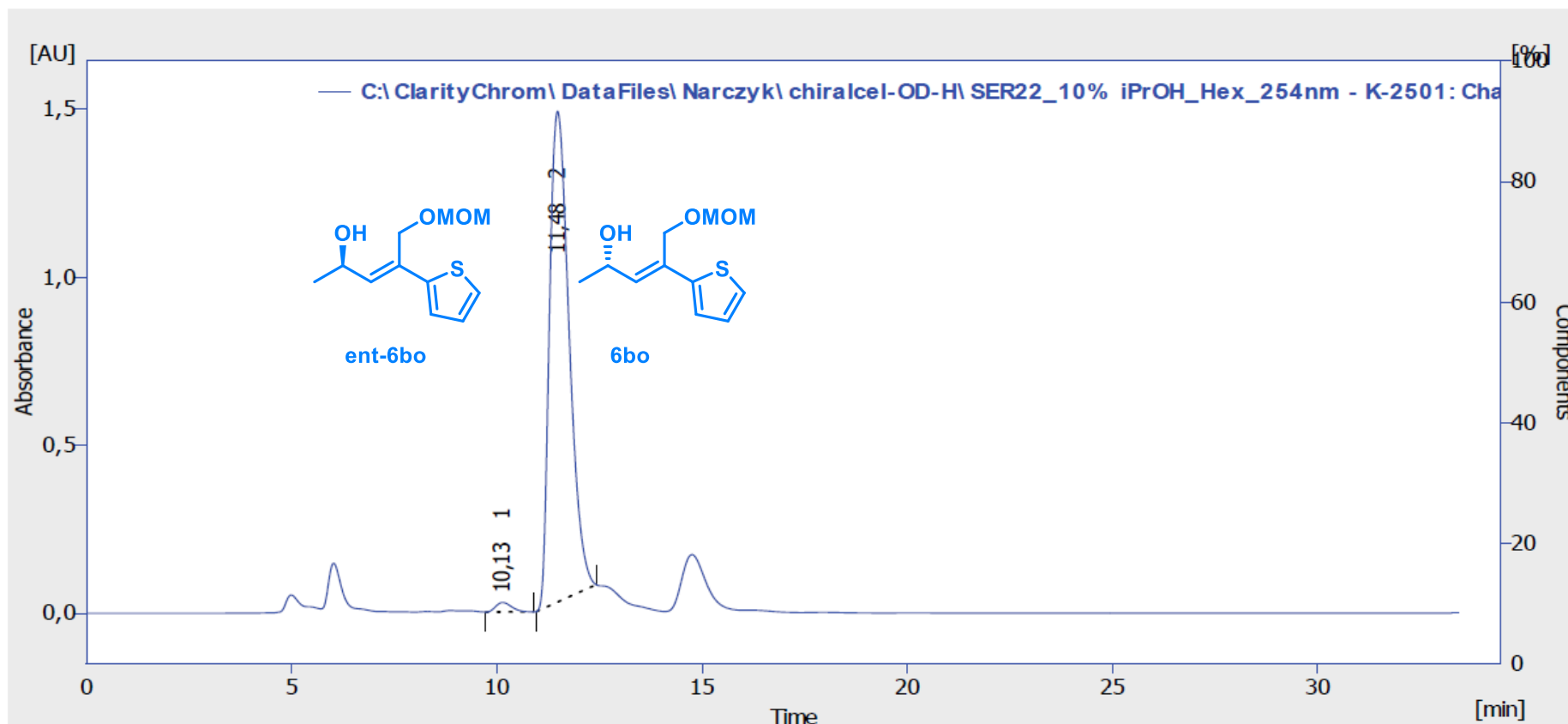


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER13\_10% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10,517	47629,647	1491,942	48,8	51,7	0,53	
2	11,783	49900,399	1394,931	51,2	48,3	0,57	
	Total	97530,046	2886,873	100,0	100,0		

## HPLC chromatogram of compounds rac-6bo

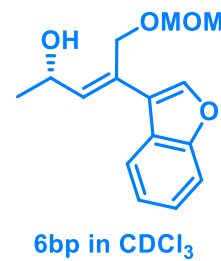
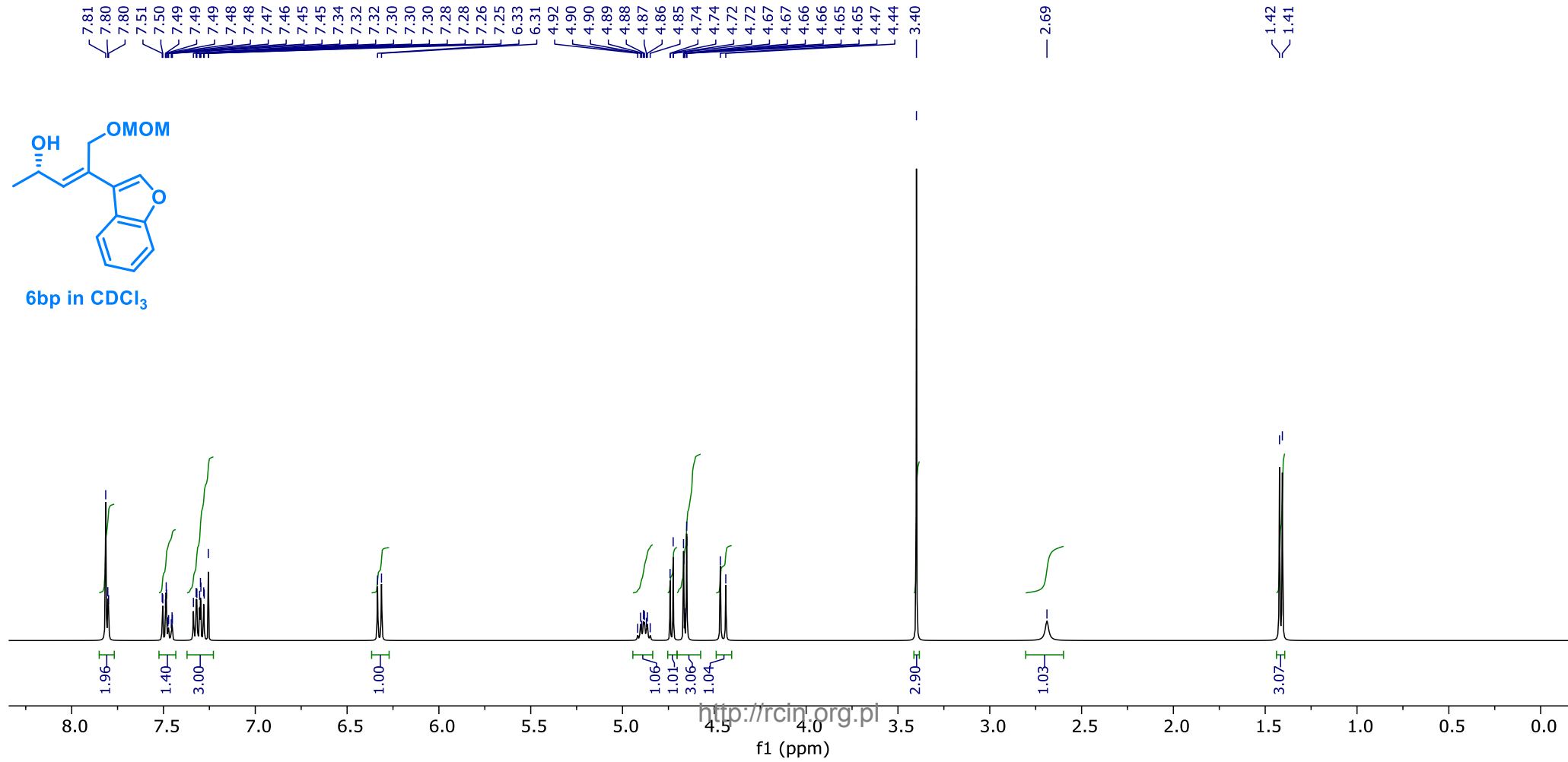
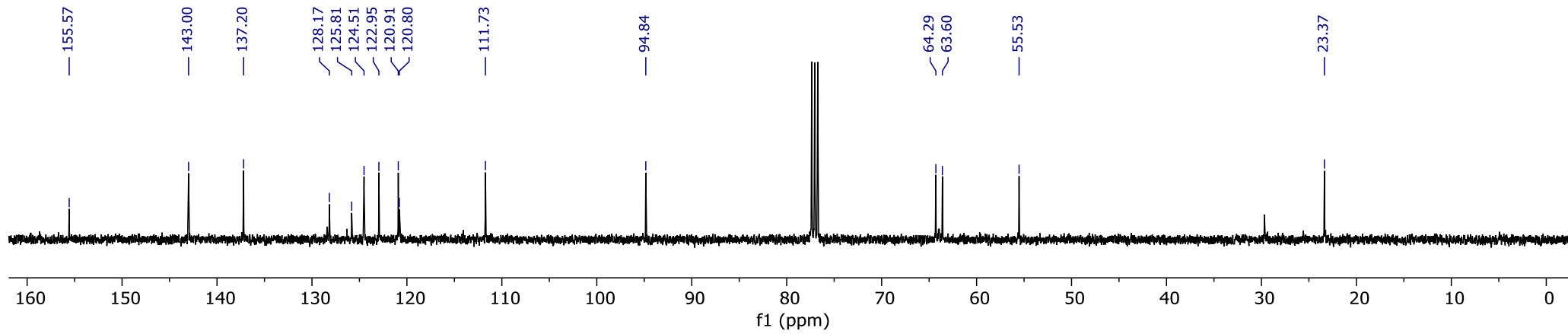
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm



Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER22\_10% iPrOH\_Hex\_254nm - K-2501: Channel 1)

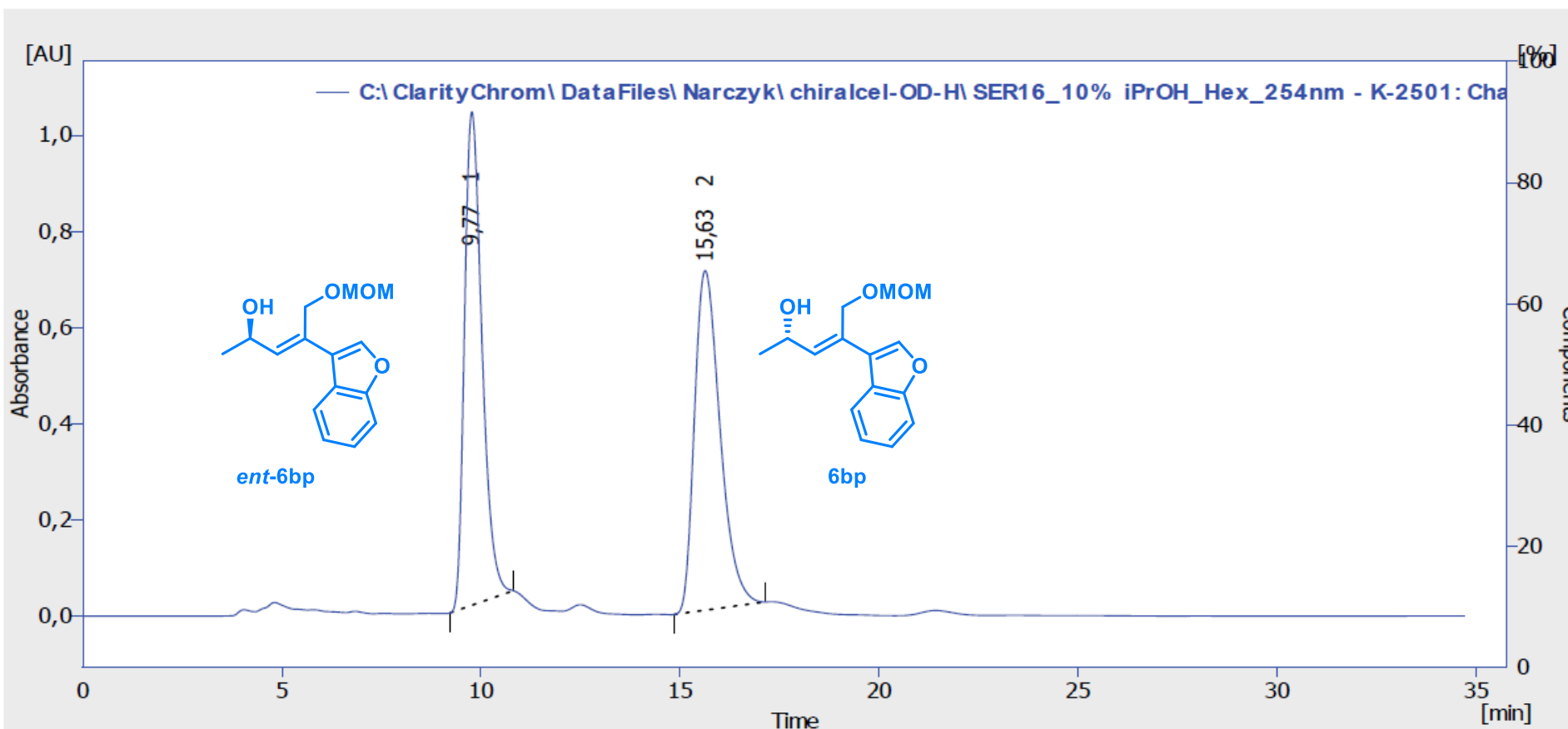
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10,133	763,791	28,358	1,6	1,9	0,43	
2	11,483	48441,697	1460,926	98,4	98,1	0,55	
	Total	49205,488	1489,284	100,0	100,0		





## HPLC chromatogram of compounds rac-6bp

Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm

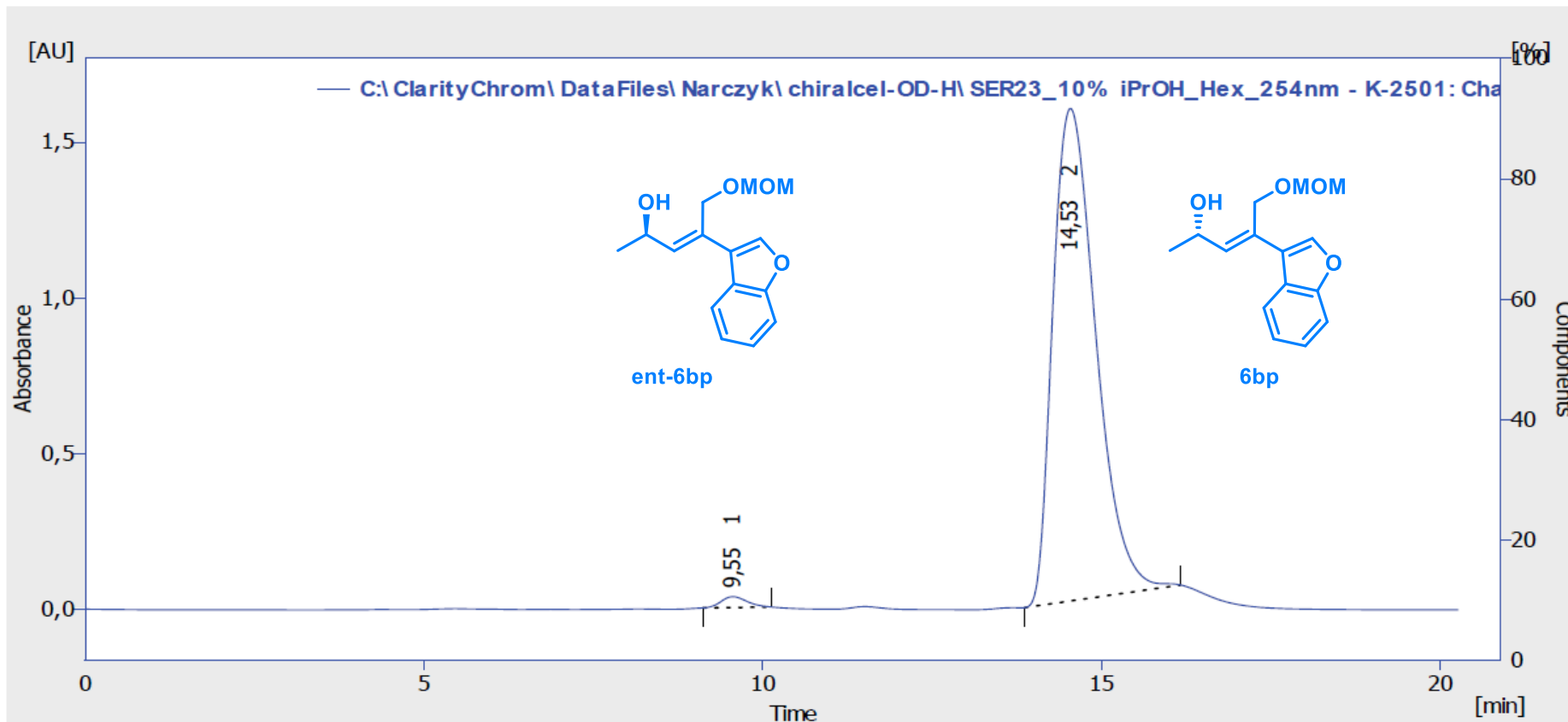


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER16\_10% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	9,767	31298,040	1026,431	49,8	59,2	0,48	
2	15,633	31543,240	706,565	50,2	40,8	0,70	
	Total	62841,280	1732,997	100,0	100,0		

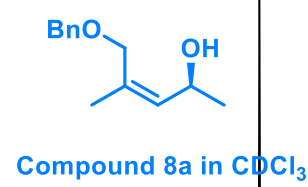
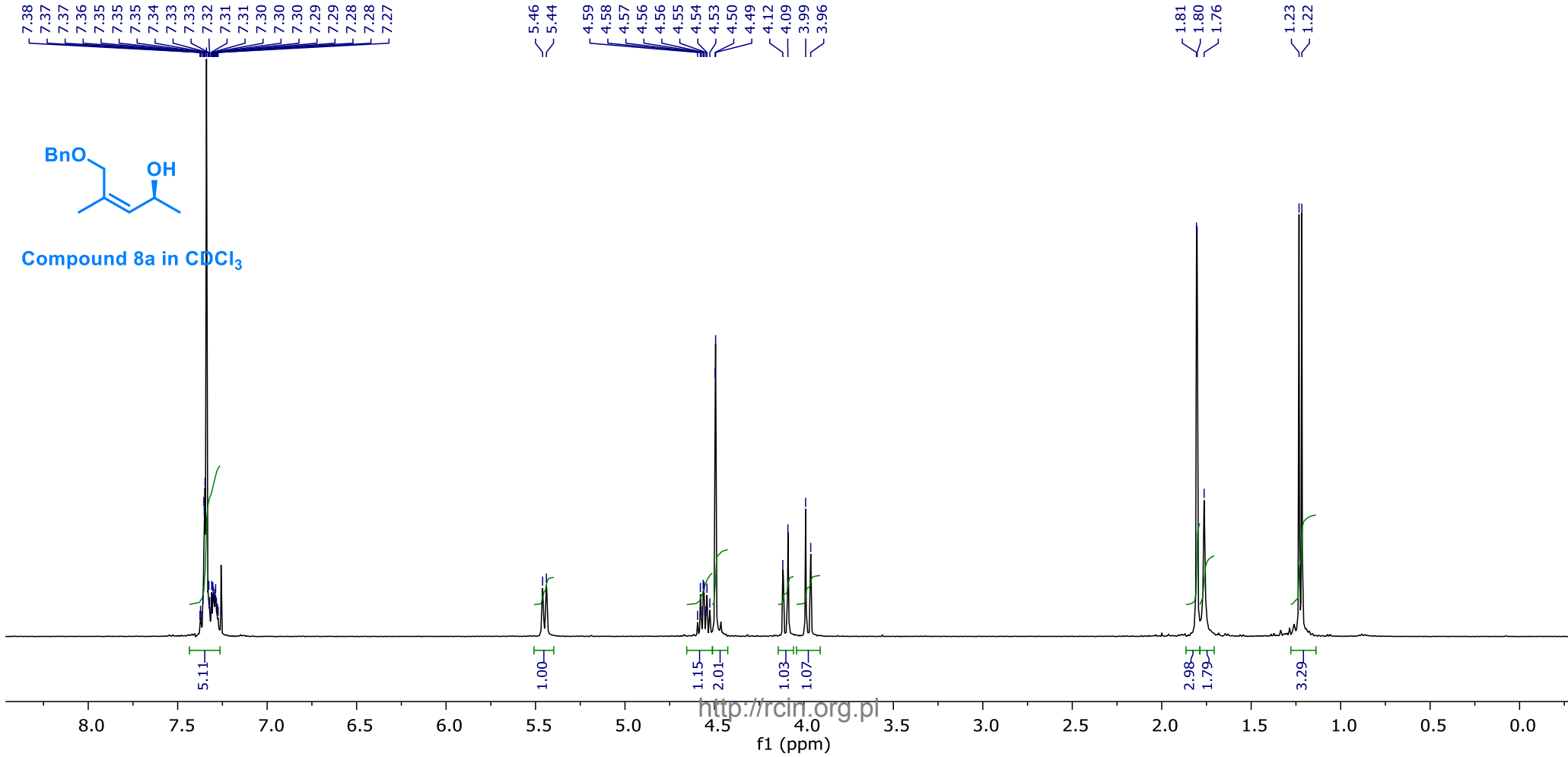
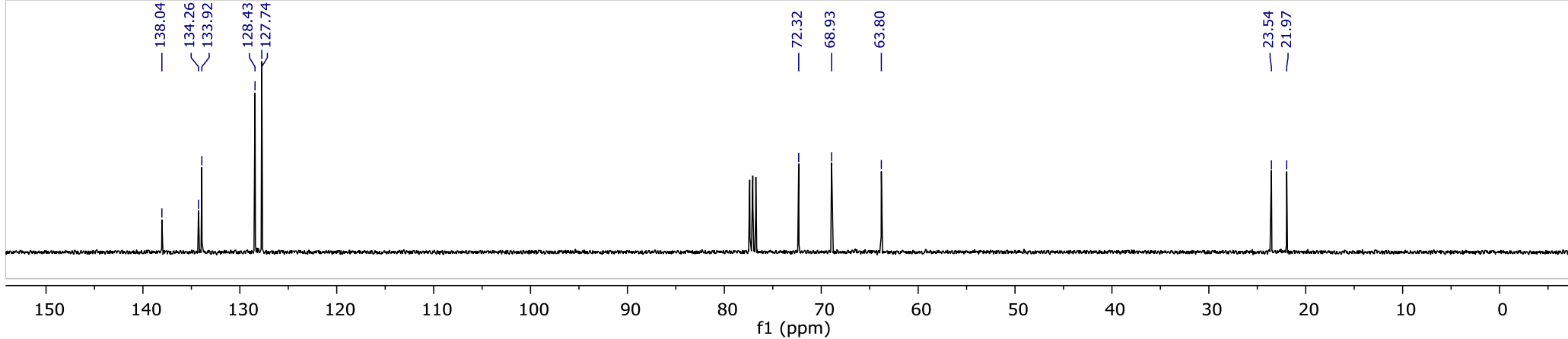
## HPLC chromatogram of compounds 6bp

Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1mL/min, detection: UV, 254 nm



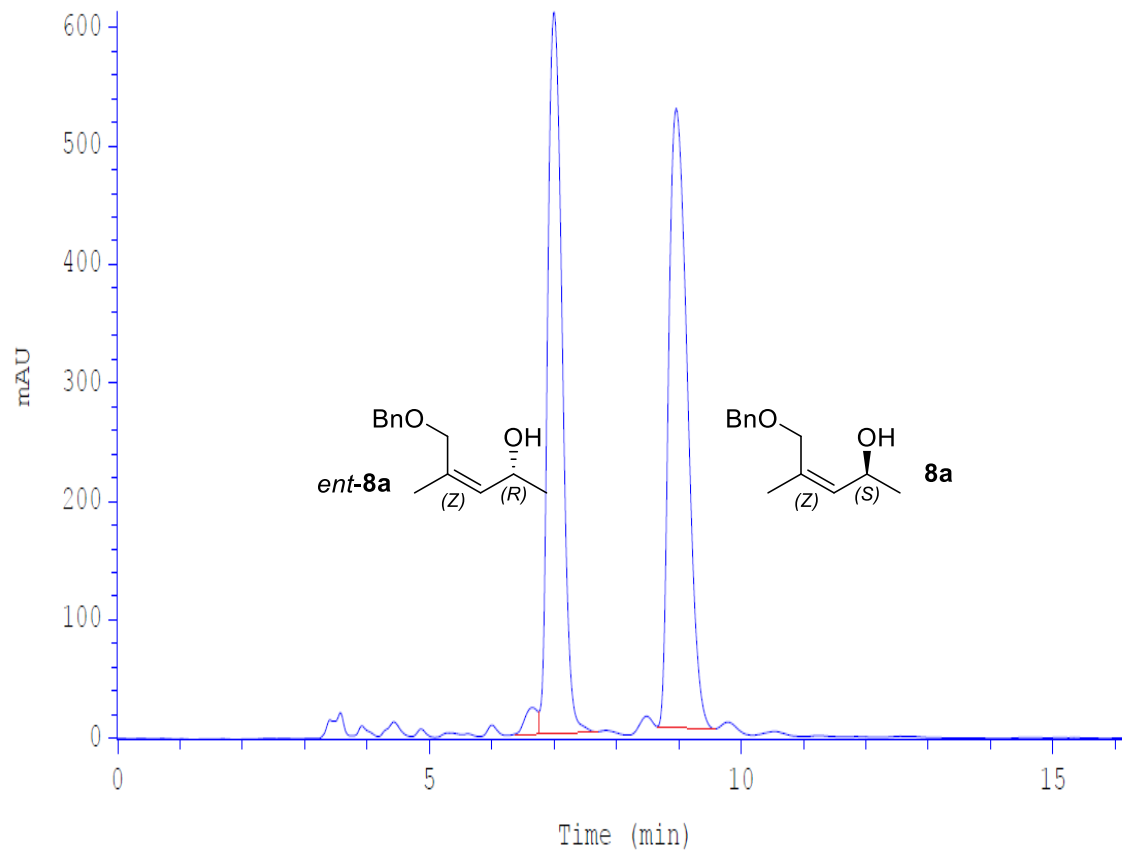
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\SER23\_10% iPrOH\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	9,550	926,602	34,863	1,3	2,2	0,43	
2	14,533	69770,083	1582,049	98,7	97,8	0,72	
	Total	70696,684	1616,912	100,0	100,0		

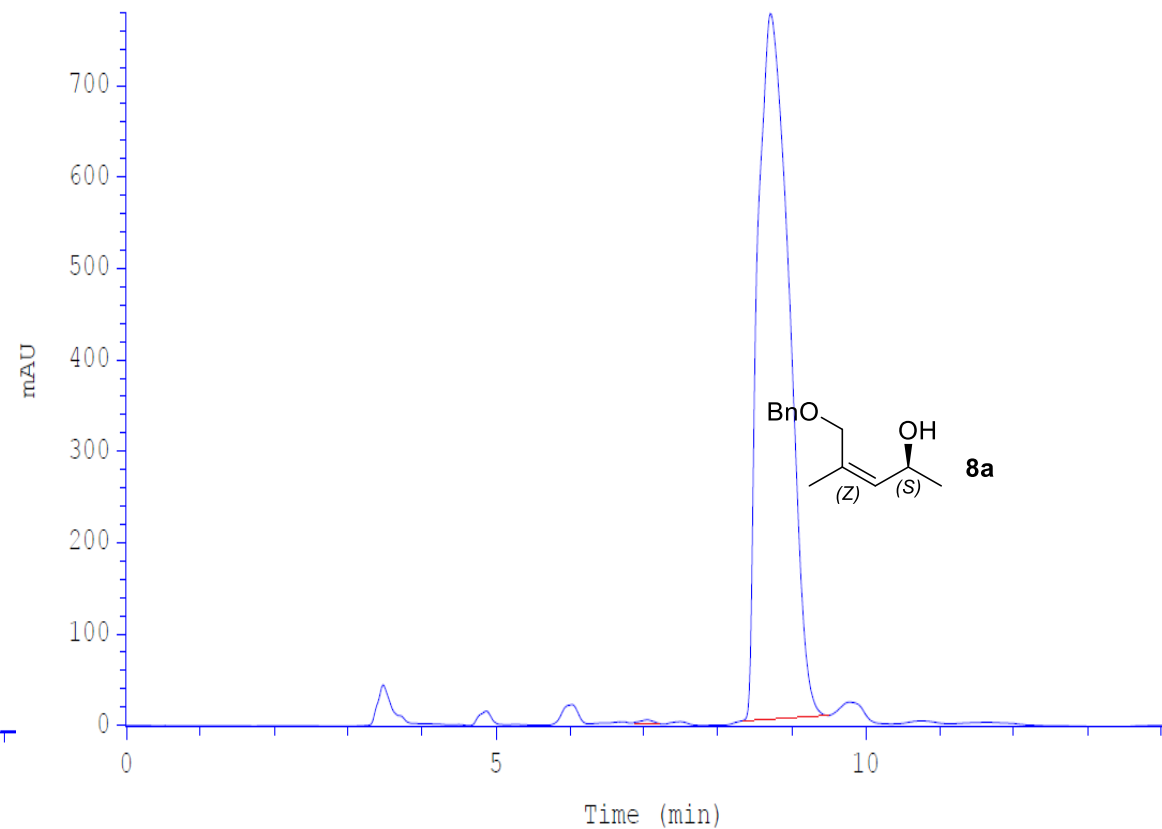


## HPLC chromatogram of compounds *rac*-8a and 8a

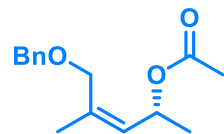
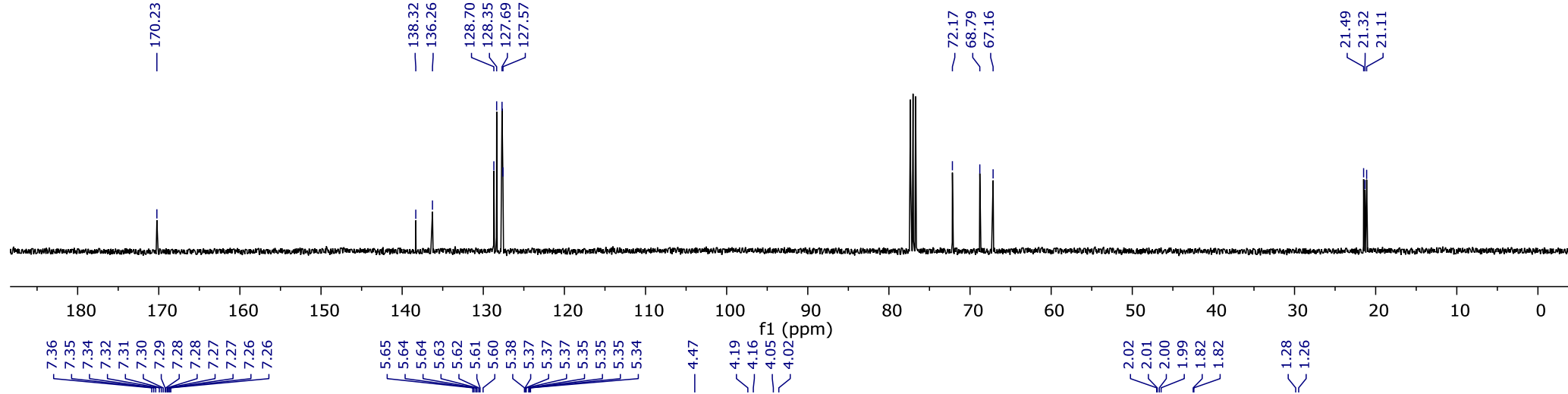
Conditions: column Chiralcel OD-H, 10% *i*-PrOH in hexanes, 1 mL/min, detection: UV, 215 nm



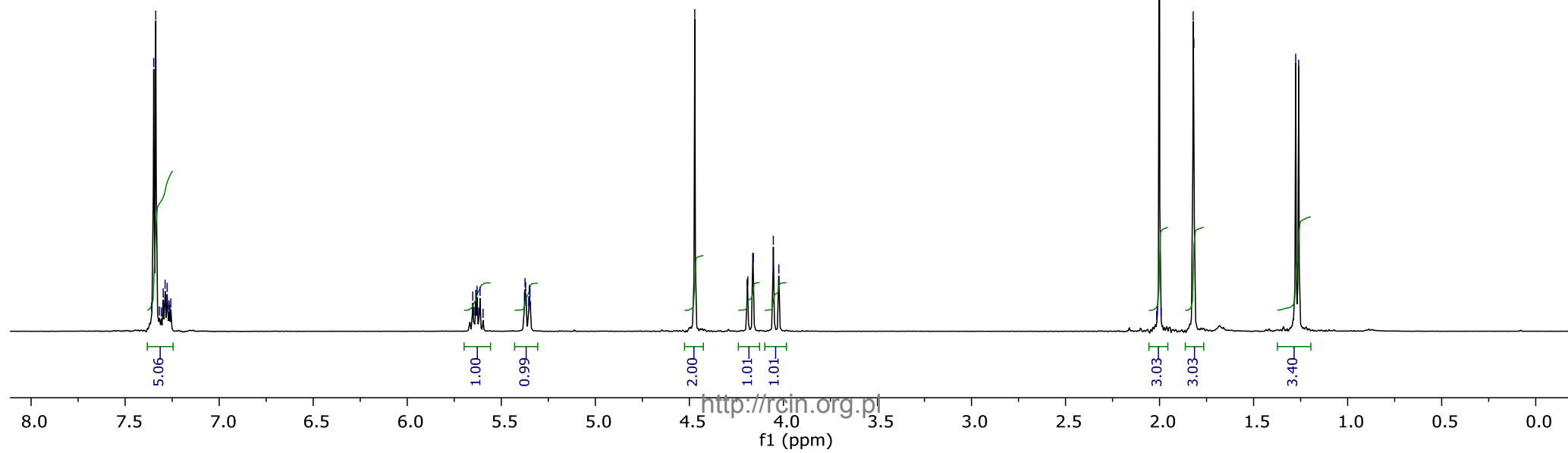
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.656	6.27	6.76	5.46644	22.7194	1.5780	0.198
2	7.006	6.76	7.67	163.005	609.049	47.0542	0.254
3	8.958	8.63	9.66	177.948	522.021	51.3678	0.331

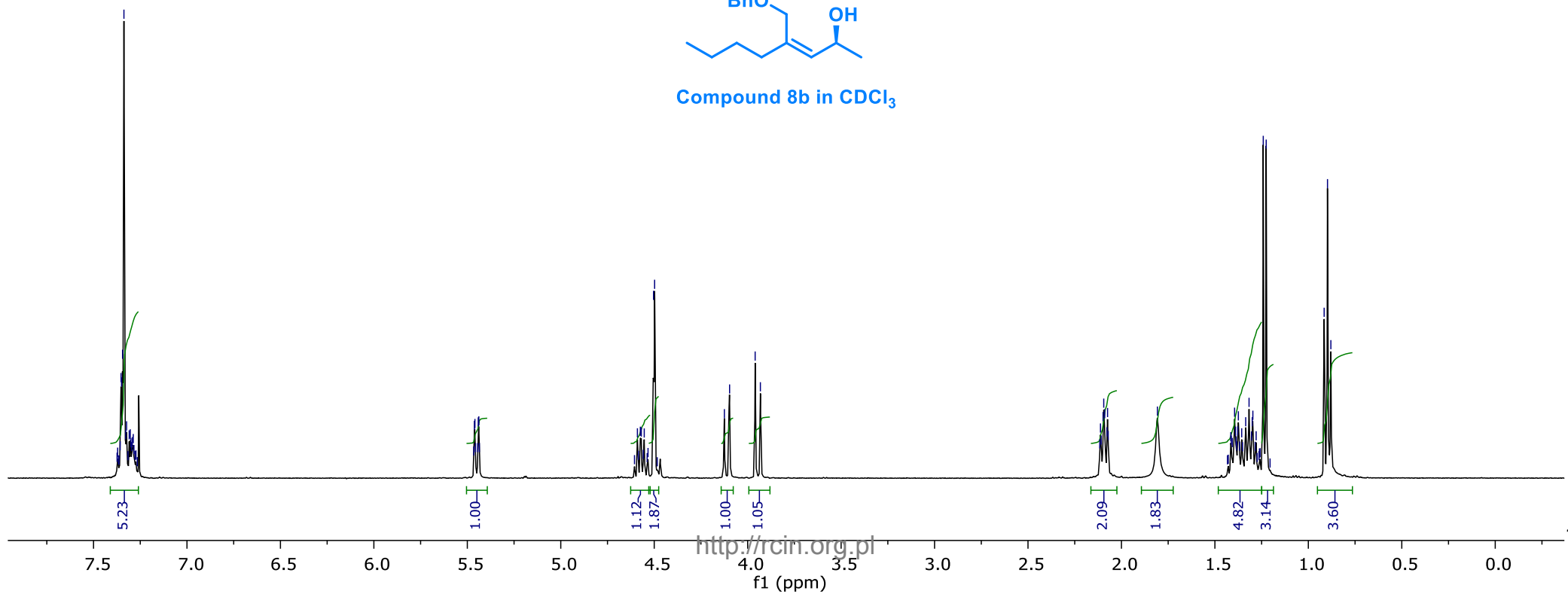
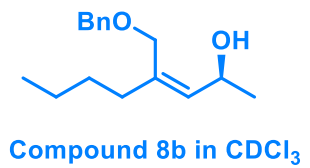
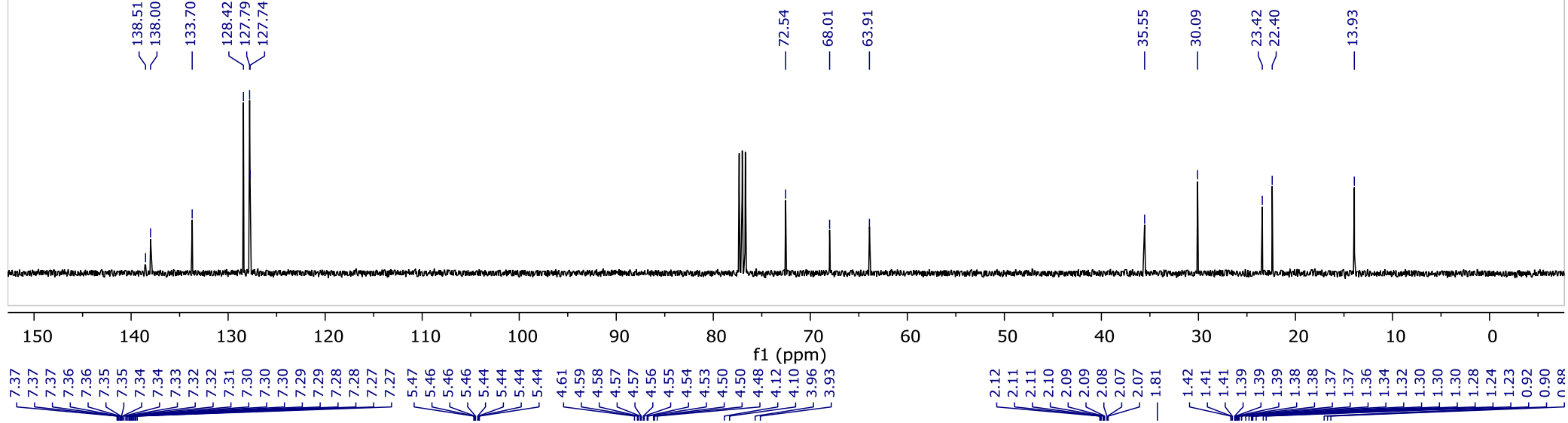


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.707	6.49	6.83	0.234908	1.37233	0.0623	0.186
2	8.709	8.21	9.55	376.566	772.701	99.9377	0.509



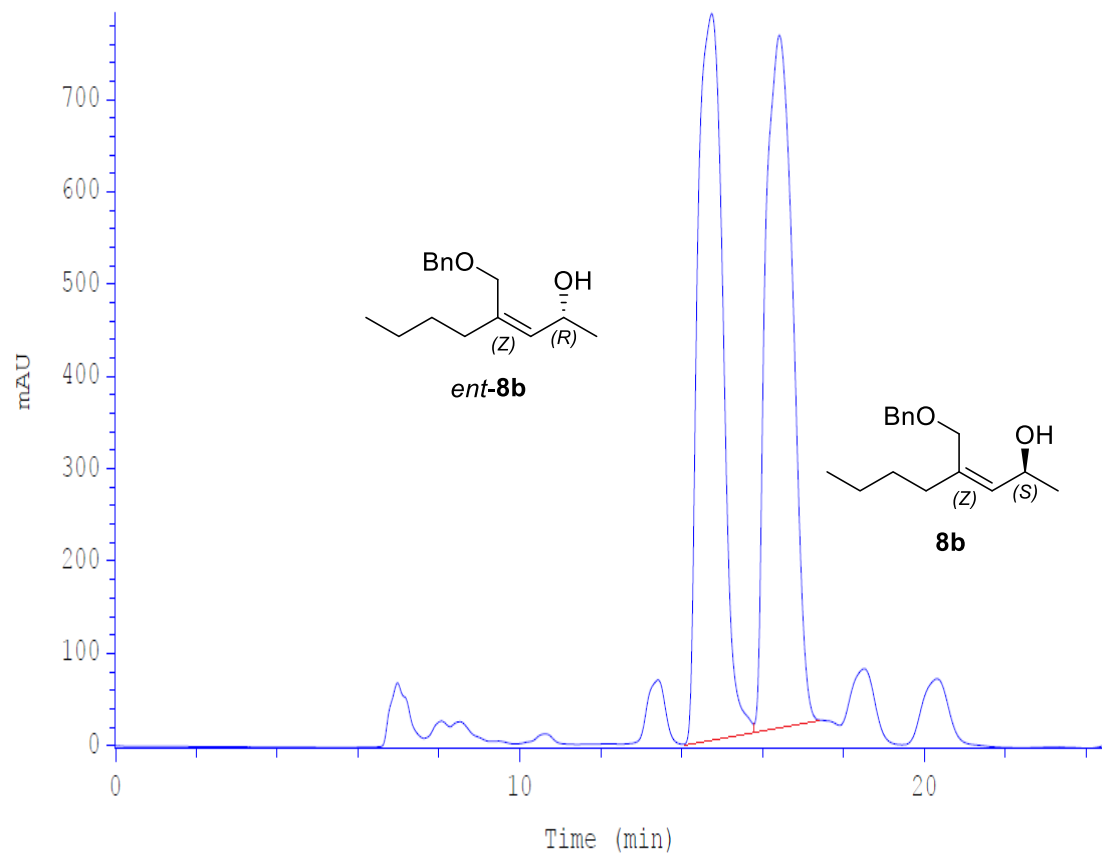
Compound 12a in CDCl<sub>3</sub>



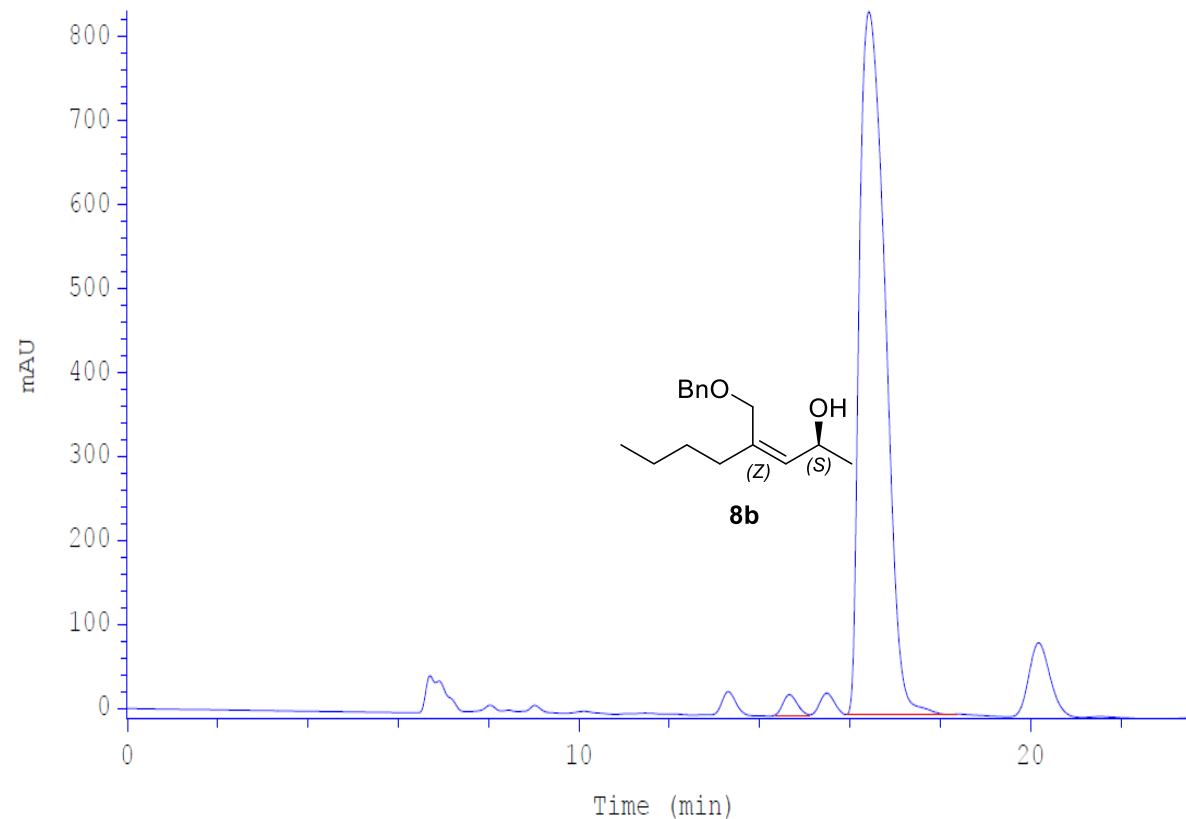


## HPLC chromatogram of compounds rac-8b and 8b

Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 0.5 mL/min, detection: UV, 215 nm

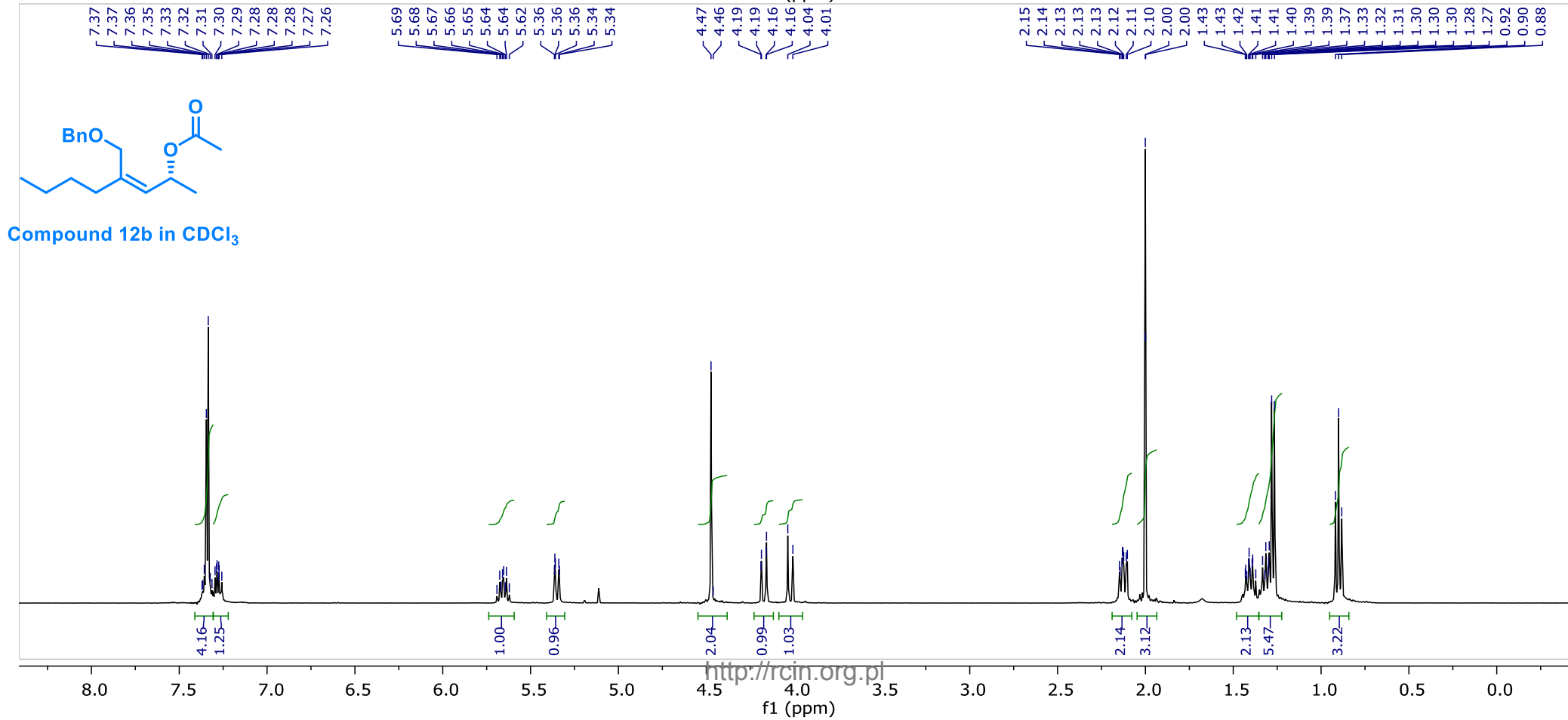
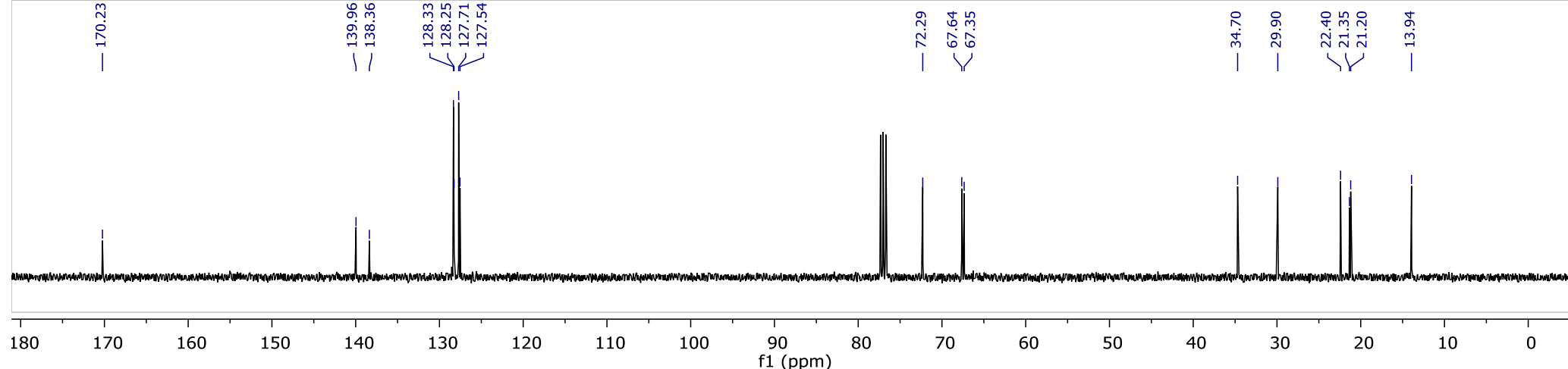


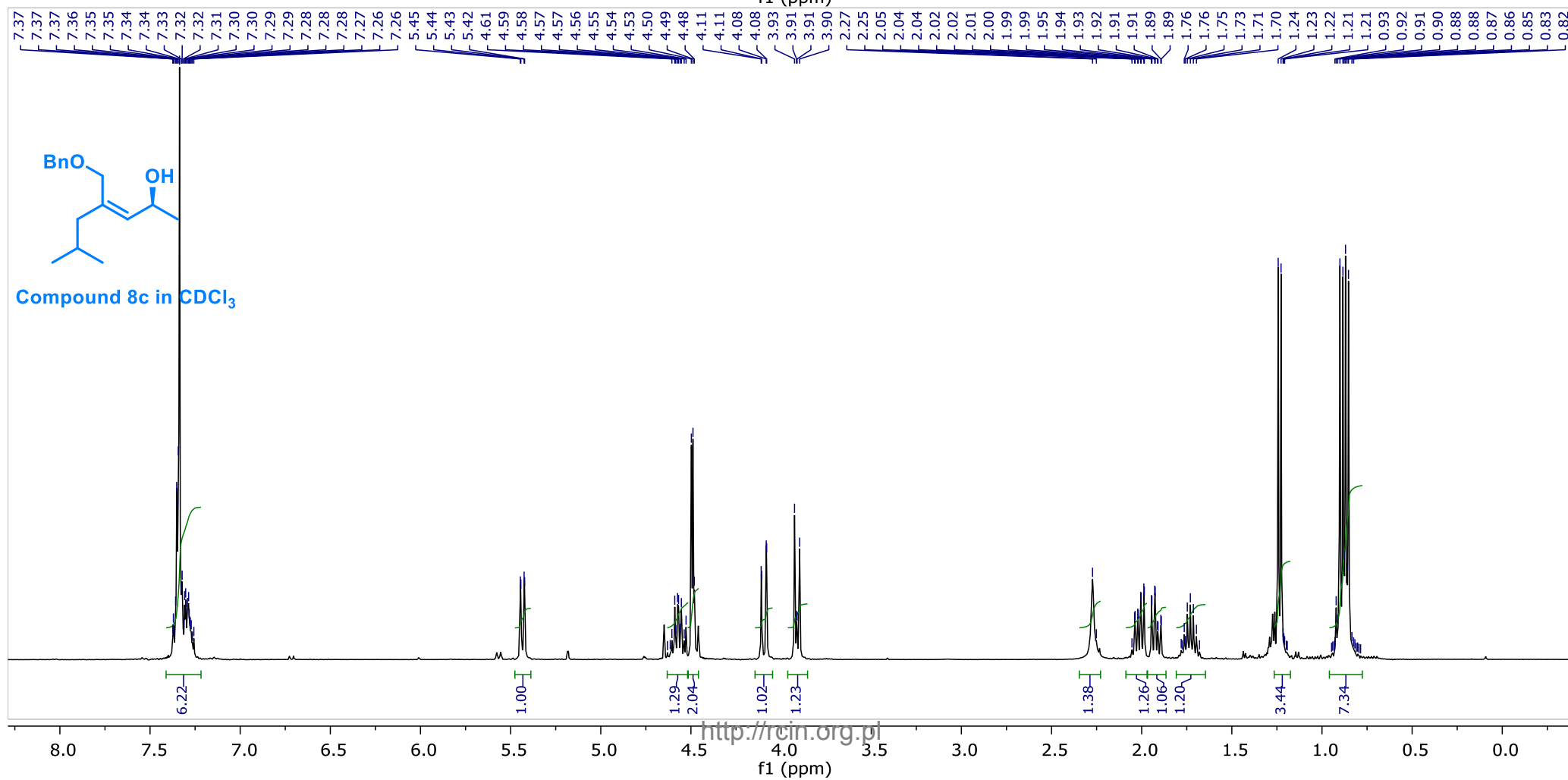
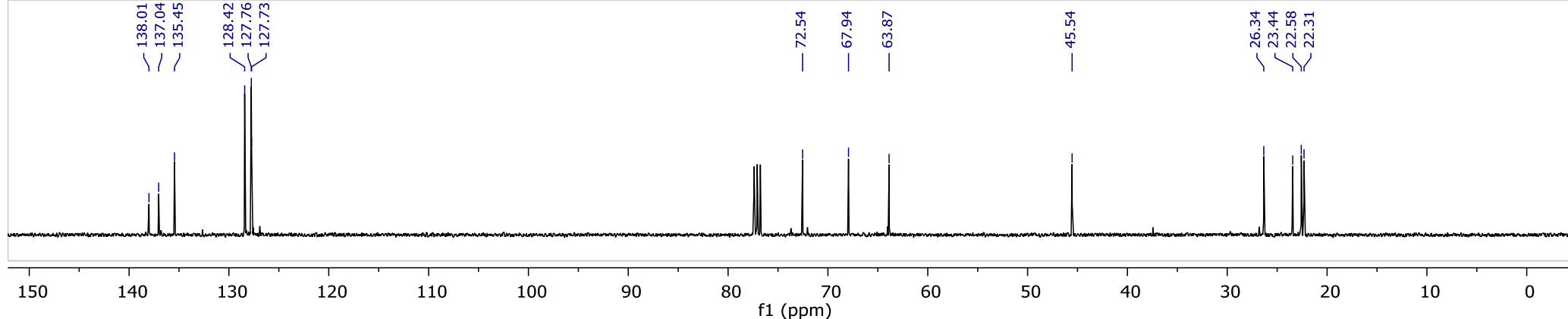
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	14.739	14.07	15.79	556.689	783.135	49.1124	0.707
2	16.423	15.79	17.38	576.81	744.837	50.8876	0.799



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	14.656	14.31	15.09	8.88969	24.5827	1.5856	0.346
2	16.407	15.89	18.74	551.752	837.12	98.4144	0.652

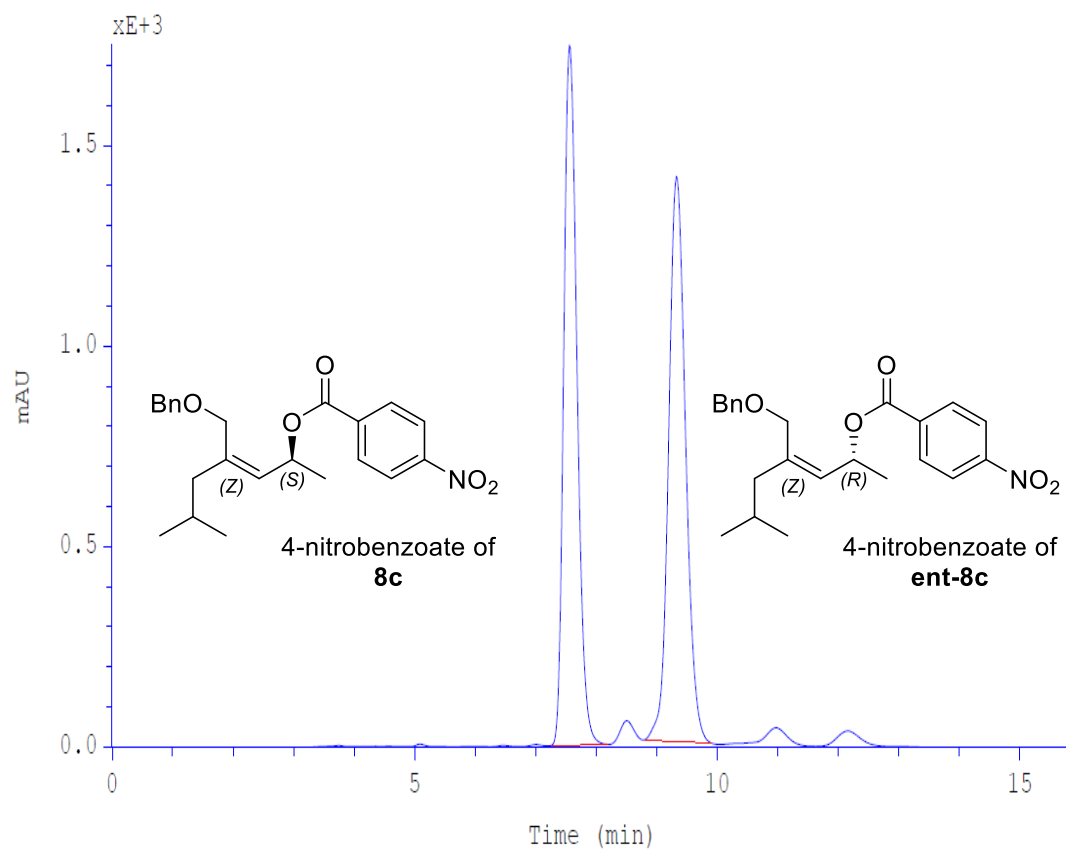




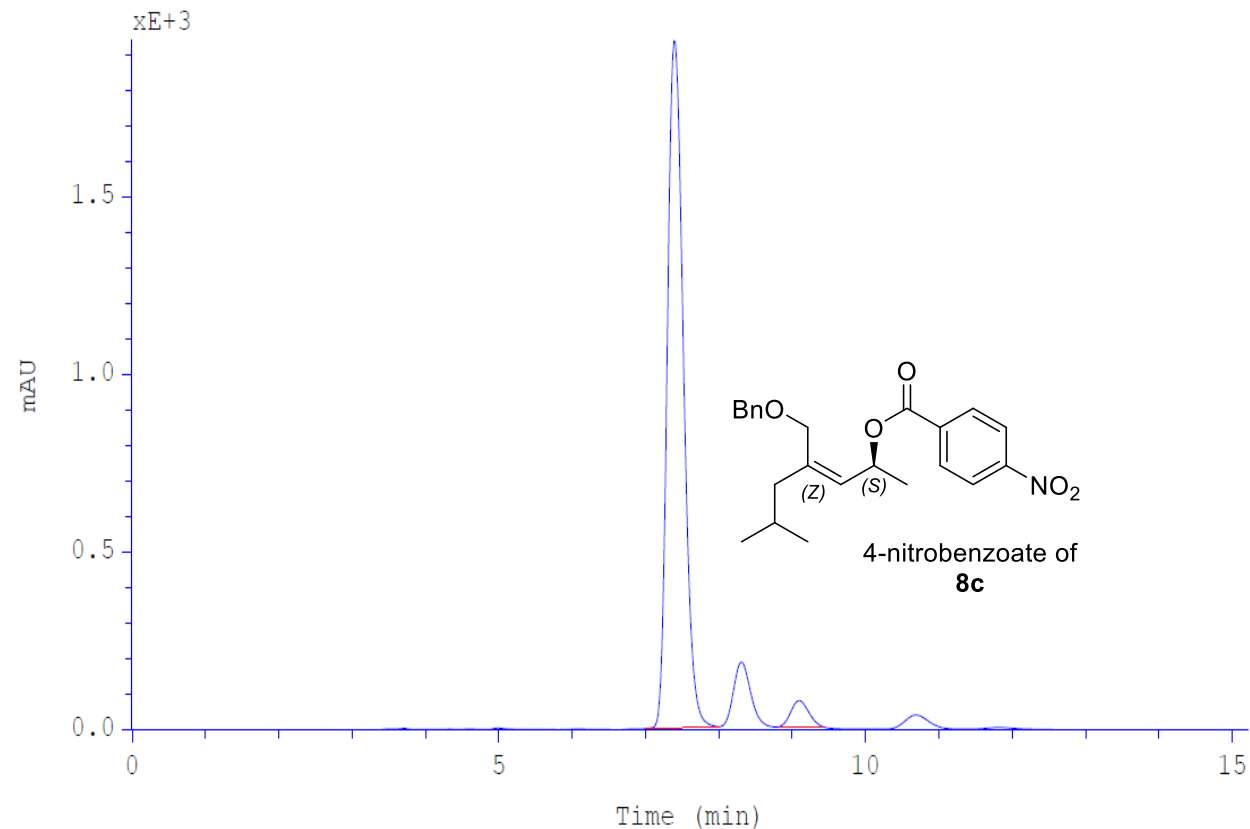


## HPLC chromatogram of compounds rac-8c and 8c

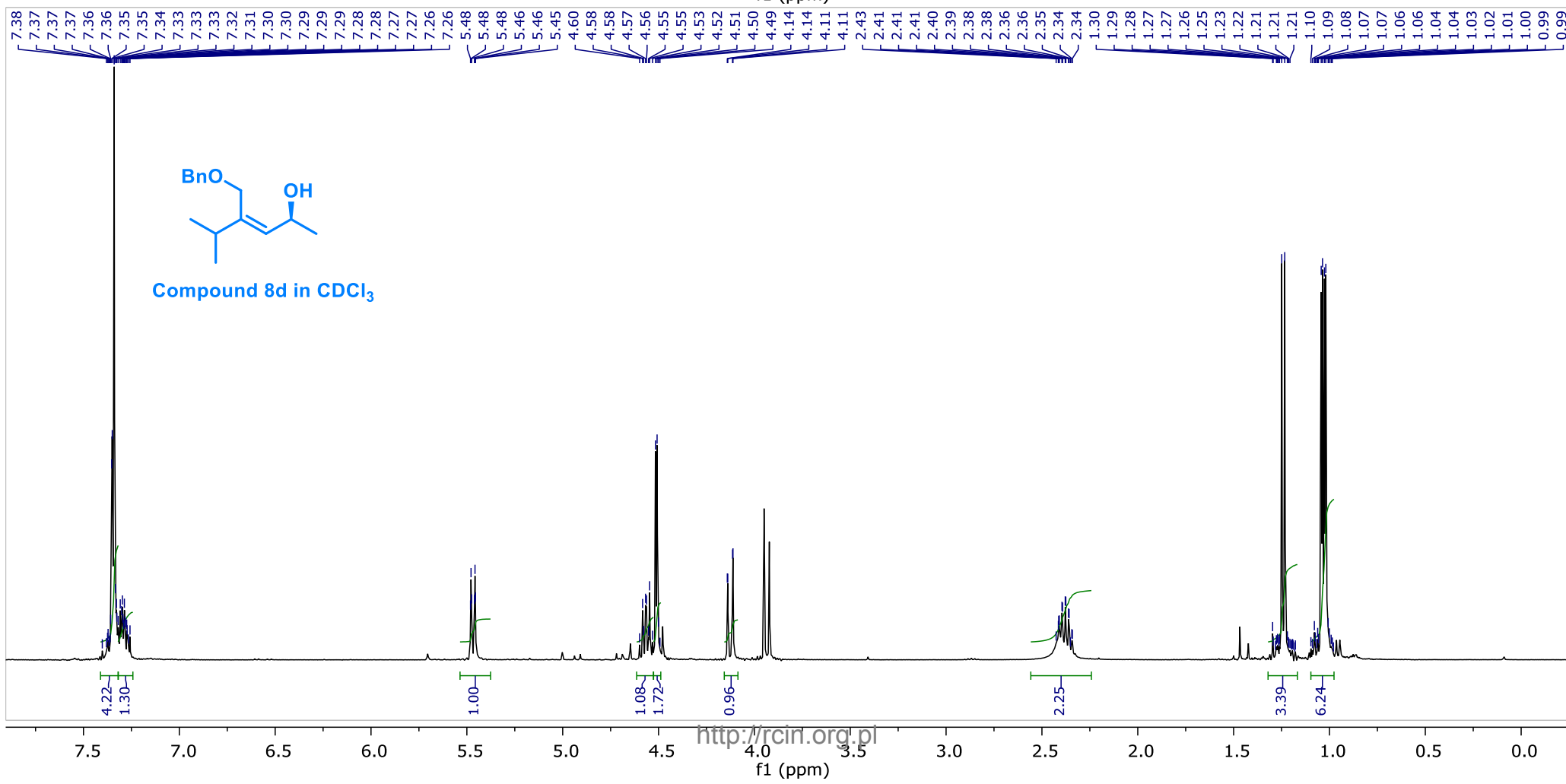
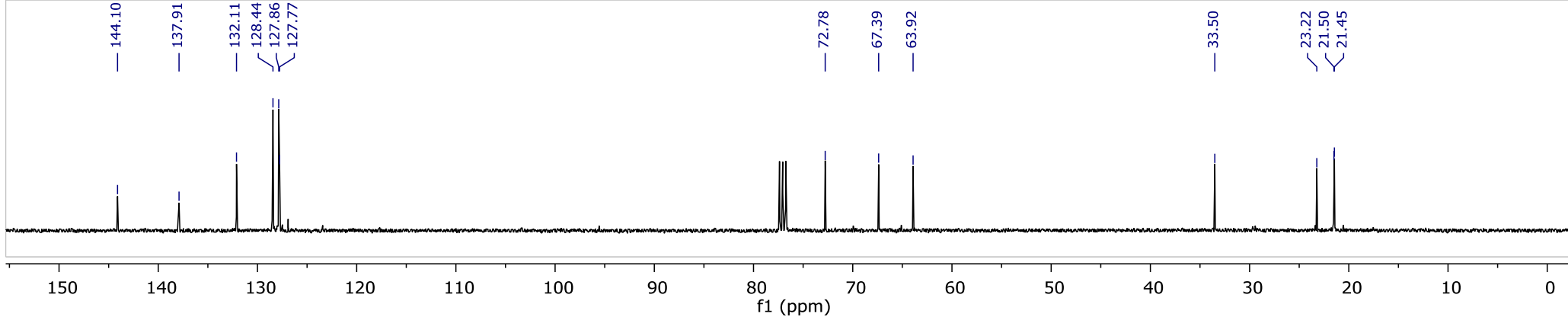
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1 mL/min, detection: UV, 254 nm



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.556	7.18	8.13	441.829	1745.55	49.0605	0.235
2	9.324	8.80	9.97	458.751	1410.89	50.9395	0.298

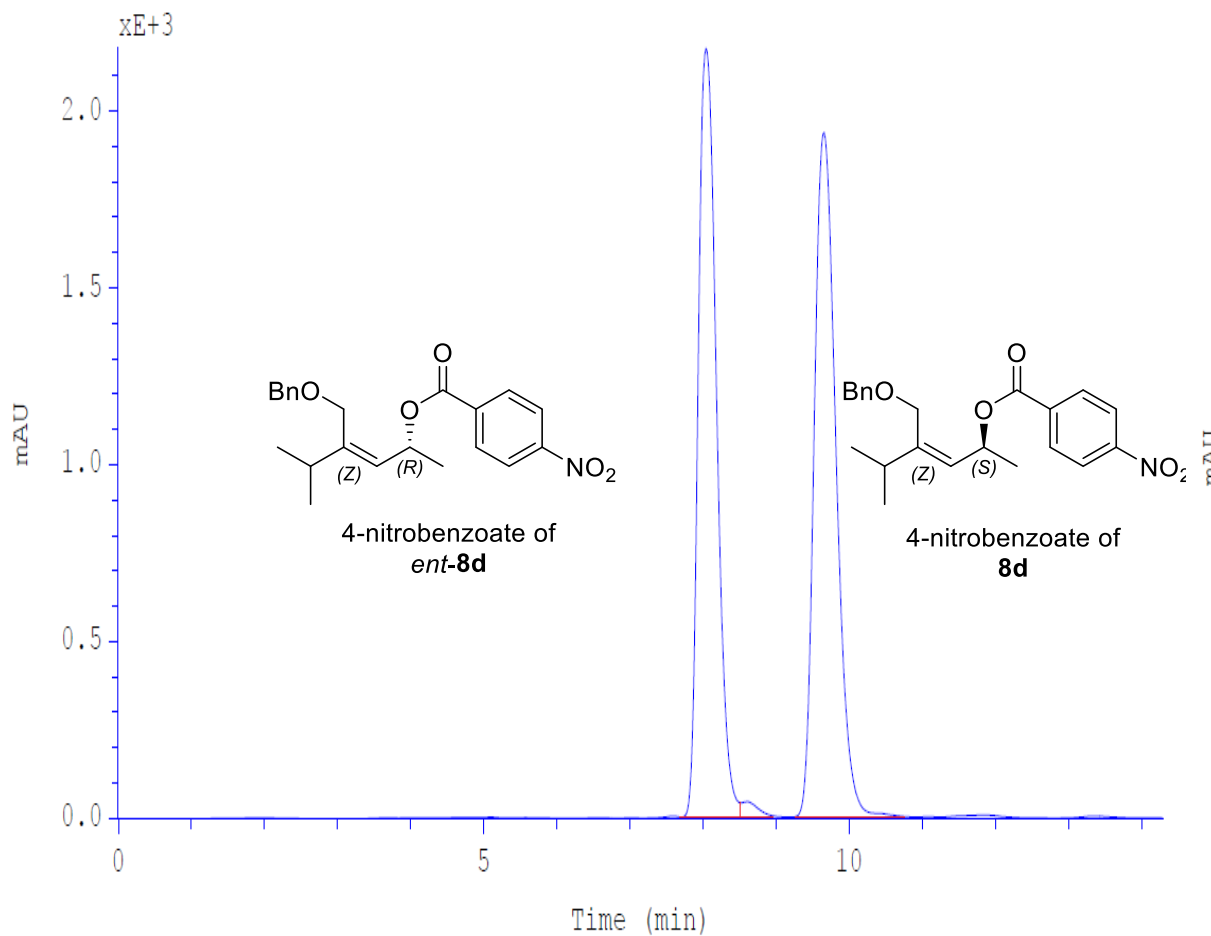


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.389	6.99	7.99	489.611	1934.52	95.7684	0.236
2	9.091	8.80	9.47	21.6341	75.3065	4.2316	0.272

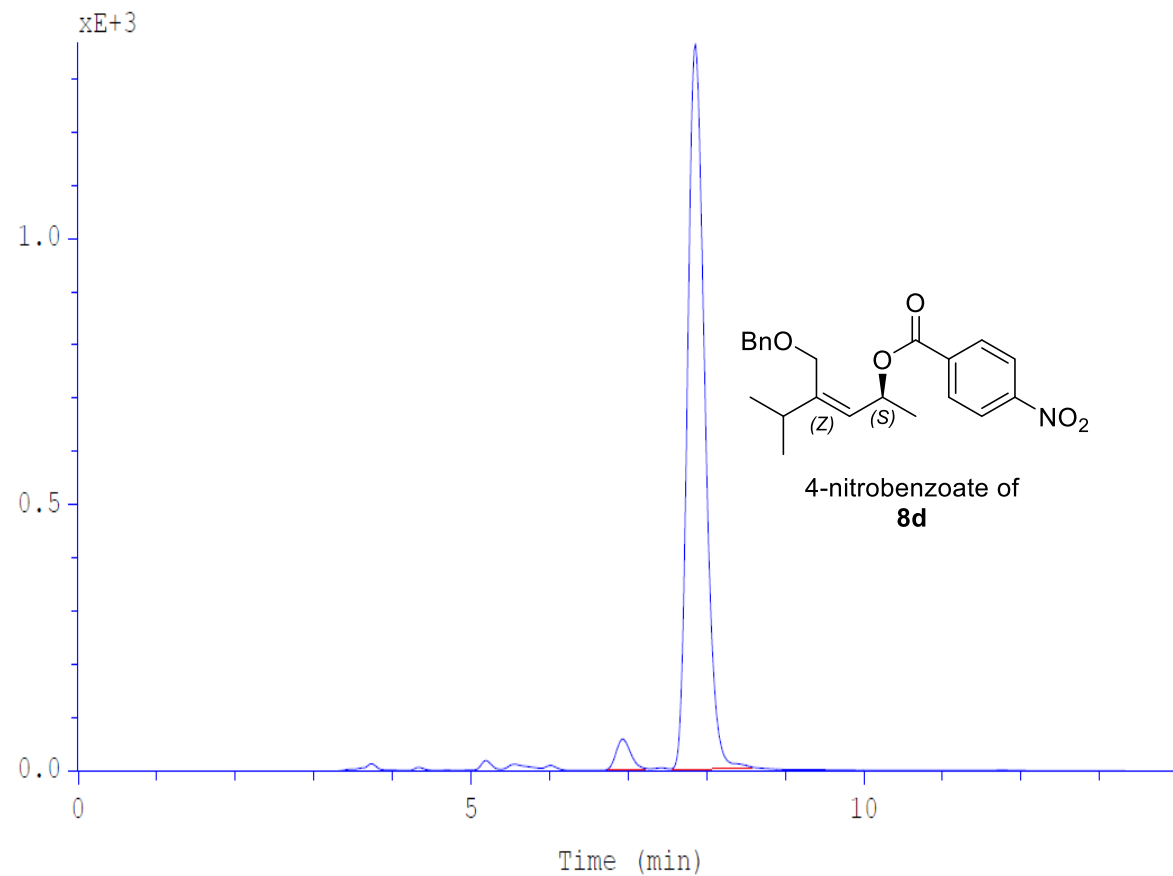


## HPLC chromatogram of compounds rac-8d and 8d

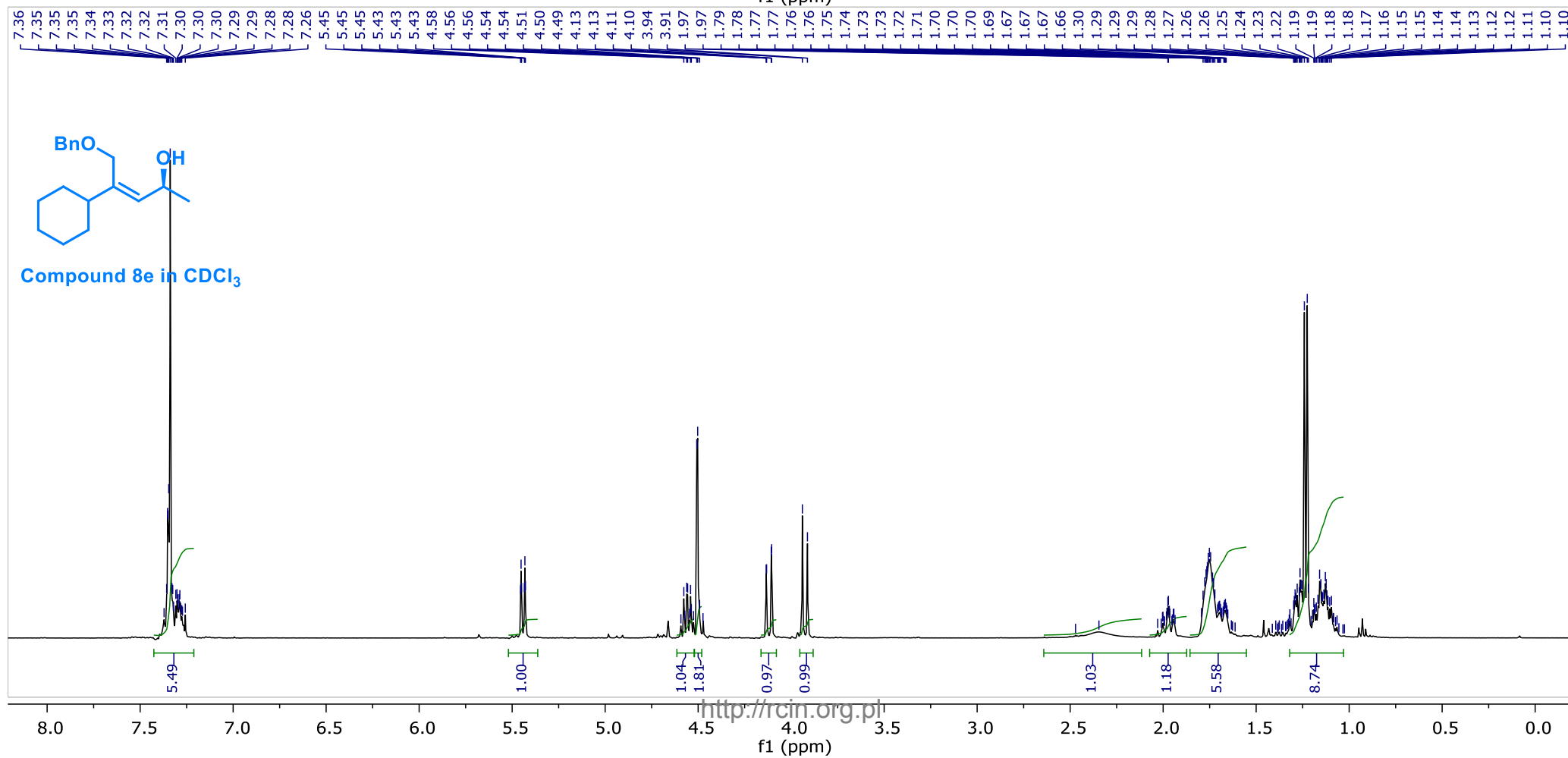
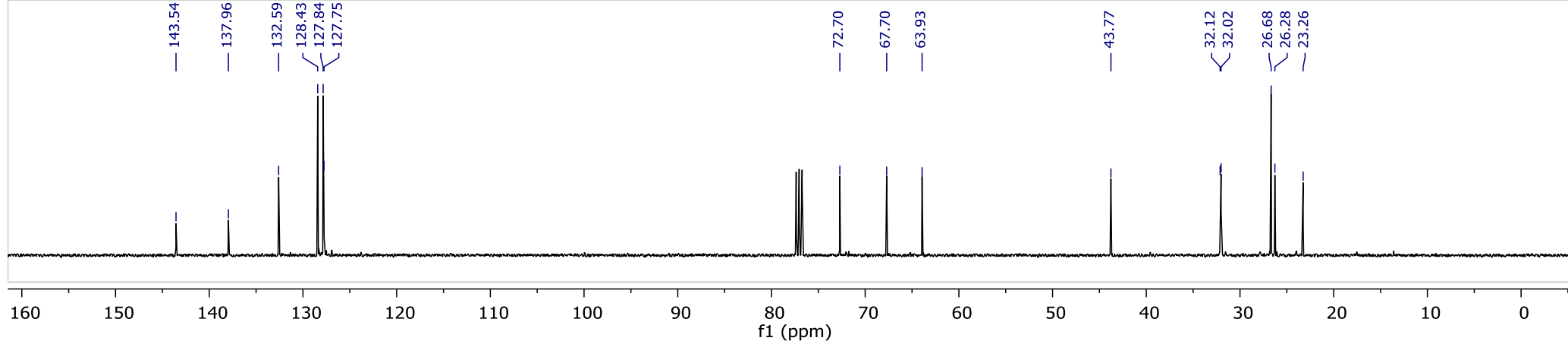
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1 mL/min, detection: UV, 254 nm



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	8.040	7.71	8.53	630.22	2173.52	48.3556	0.270
2	8.608	8.53	8.94	9.66638	40.3015	0.7417	0.192
3	9.659	9.24	10.59	663.417	1933.8	50.9028	0.319

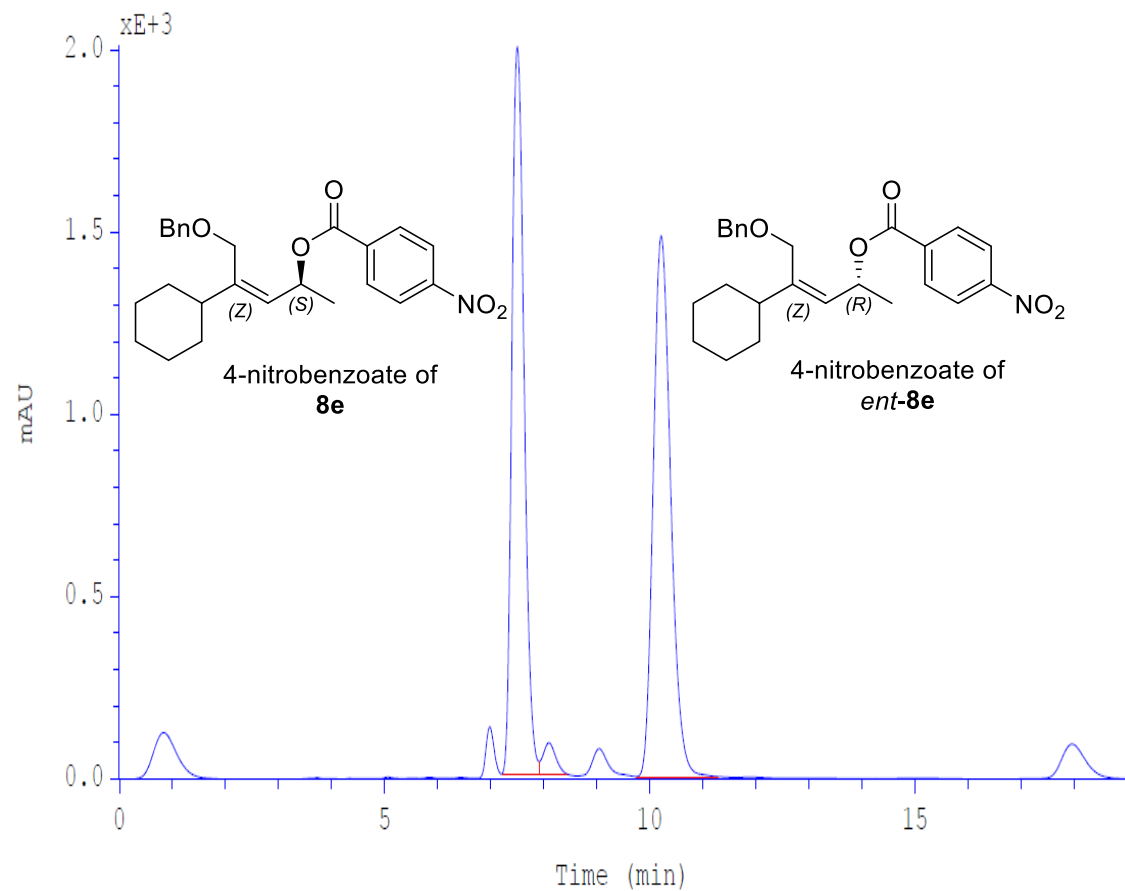


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	6.940	6.72	7.16	11.0193	54.5897	3.0977	0.192
2	7.857	7.54	8.77	344.703	1362.36	96.9023	0.233

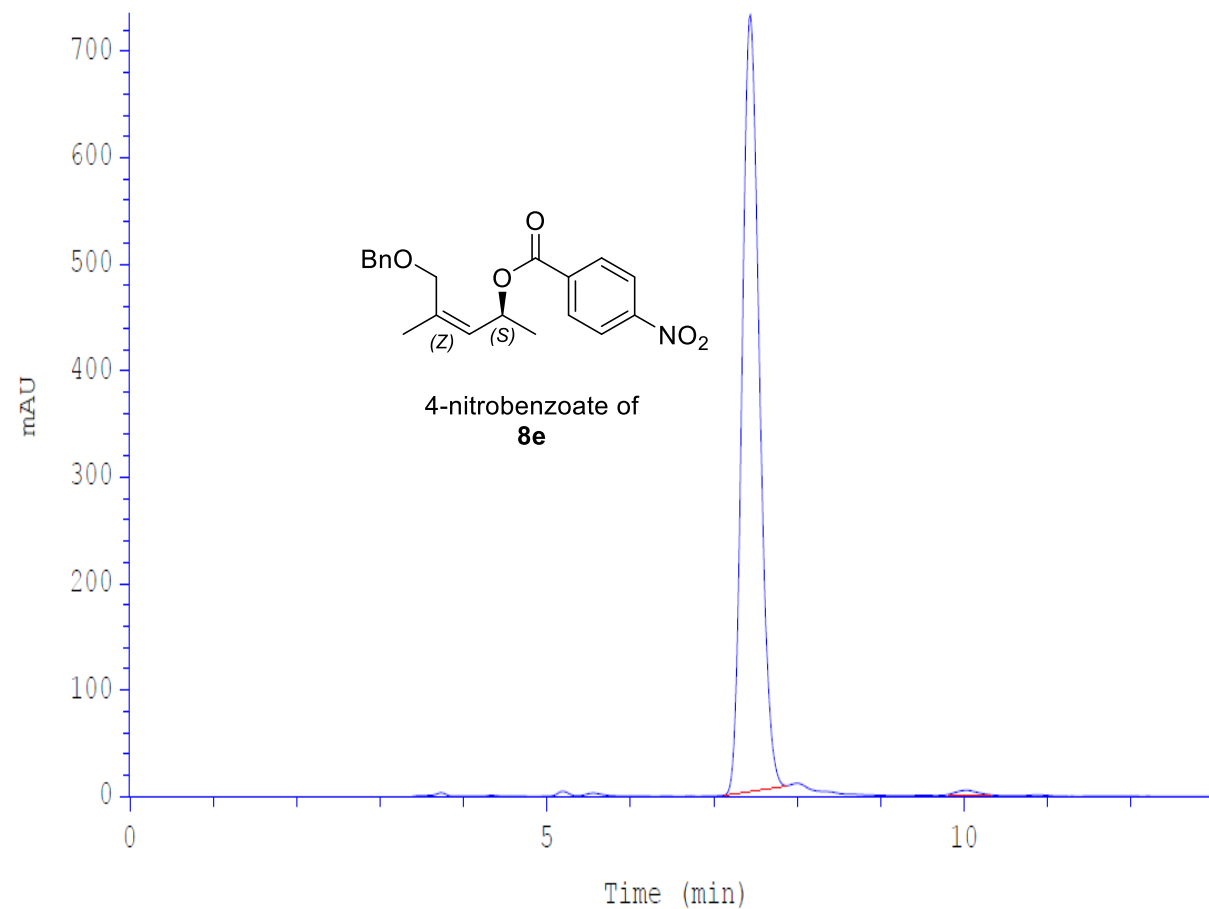


## HPLC chromatogram of compounds rac-8e and 8e

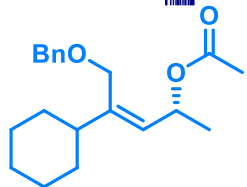
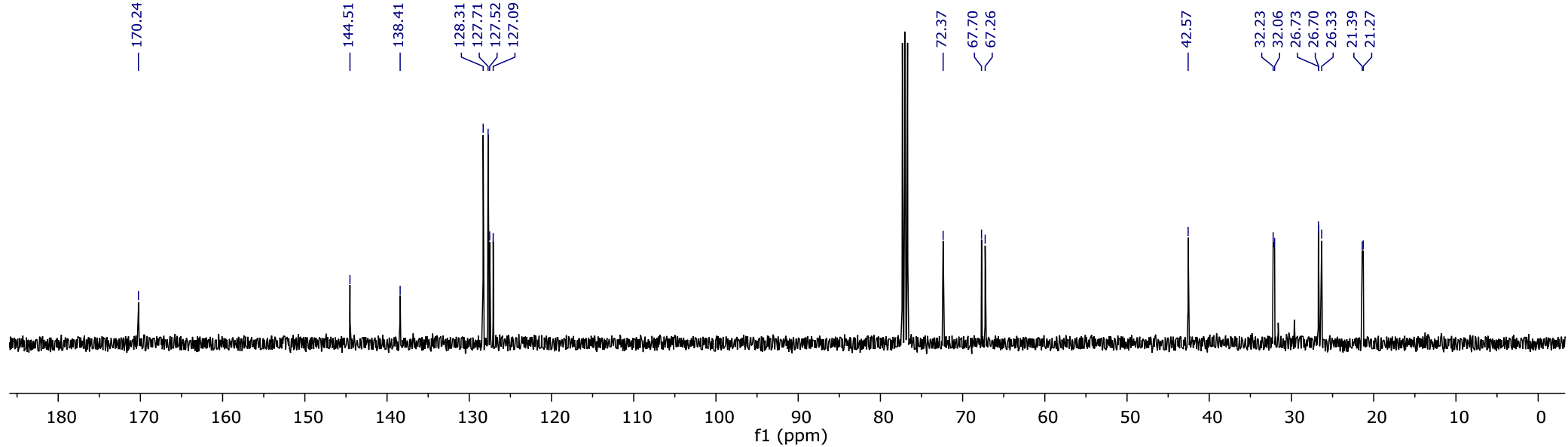
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1 mL/min, detection: UV, 254 nm



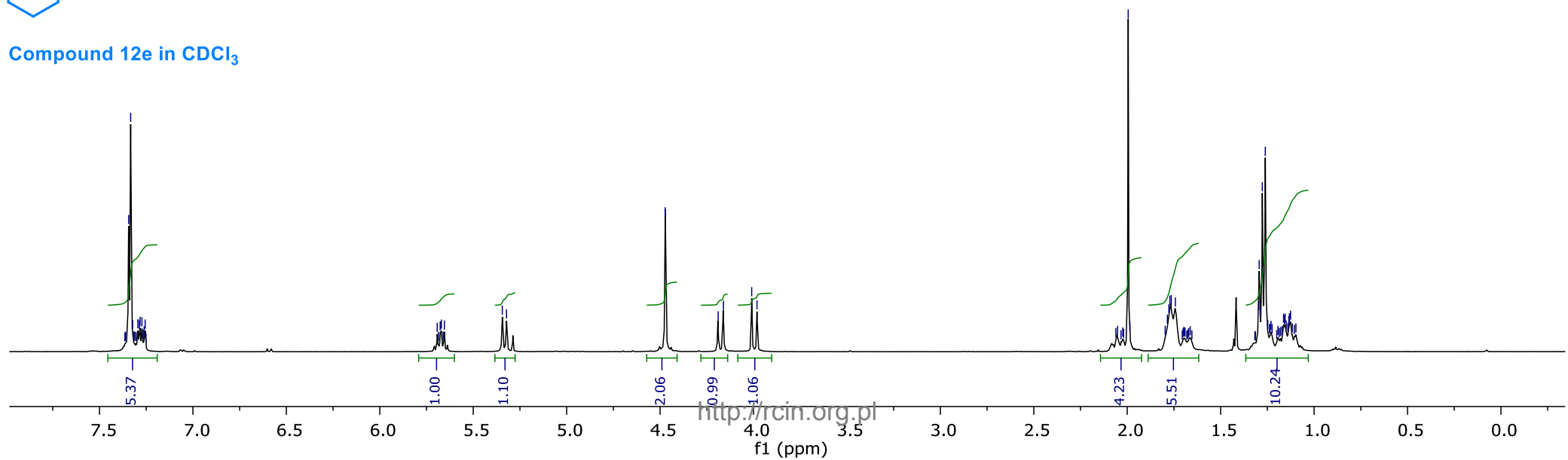
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.505	7.21	7.91	535.253	1997.94	47.6420	0.250
2	8.105	7.91	8.55	26.2584	89.2974	2.3372	0.238
3	10.206	9.75	11.11	561.978	1482.06	50.0208	0.352



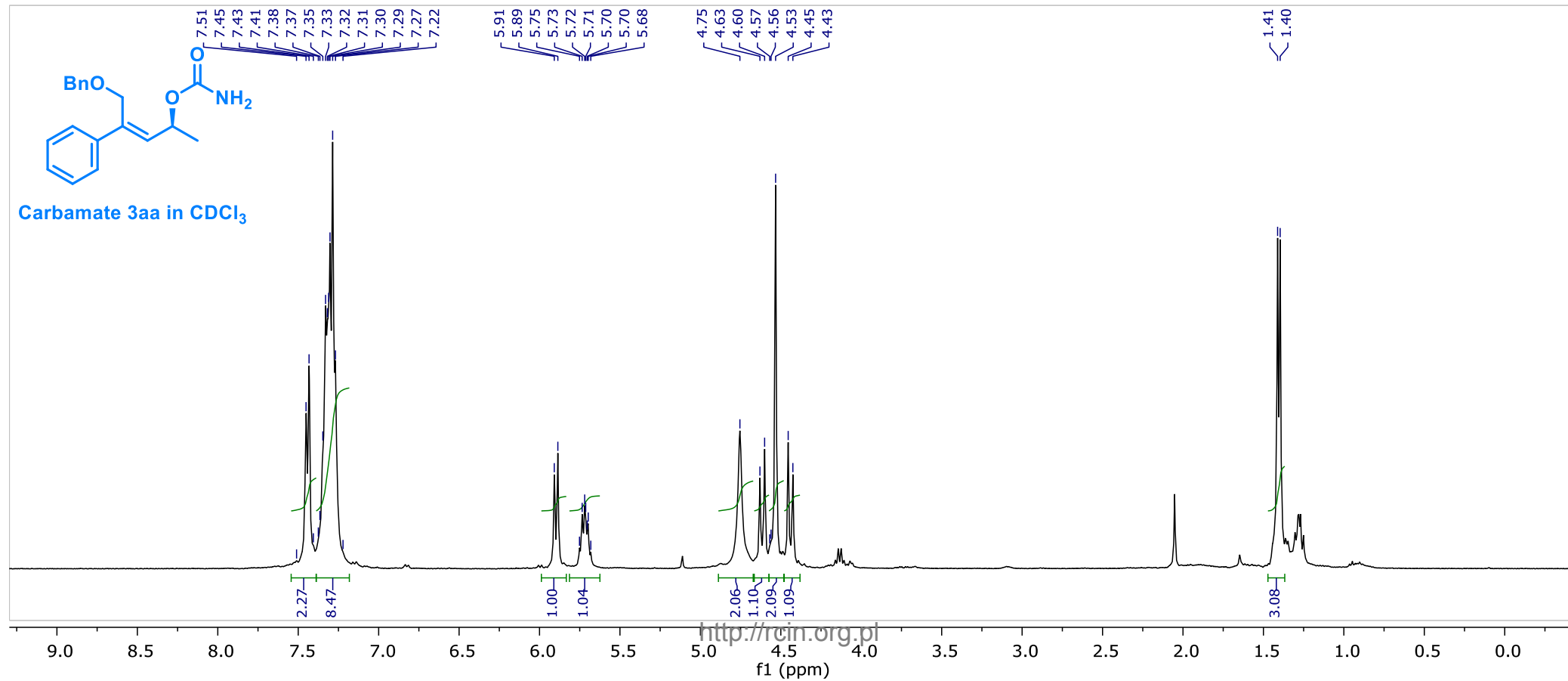
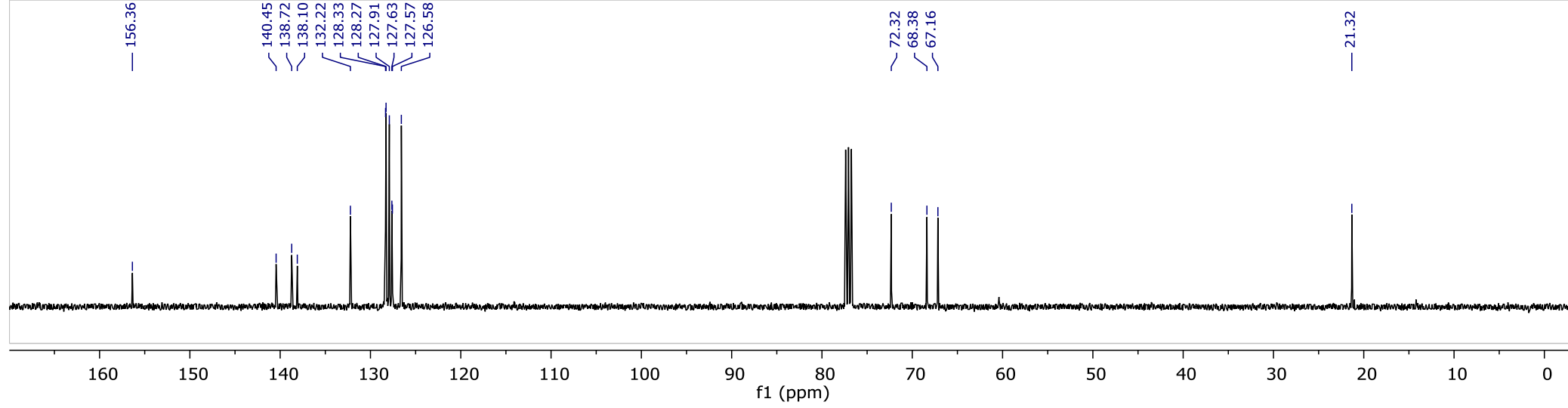
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	7.441	7.12	7.90	175.636	729.531	99.4191	0.224
2	10.027	9.80	10.26	1.02616	3.89274	0.5809	0.254

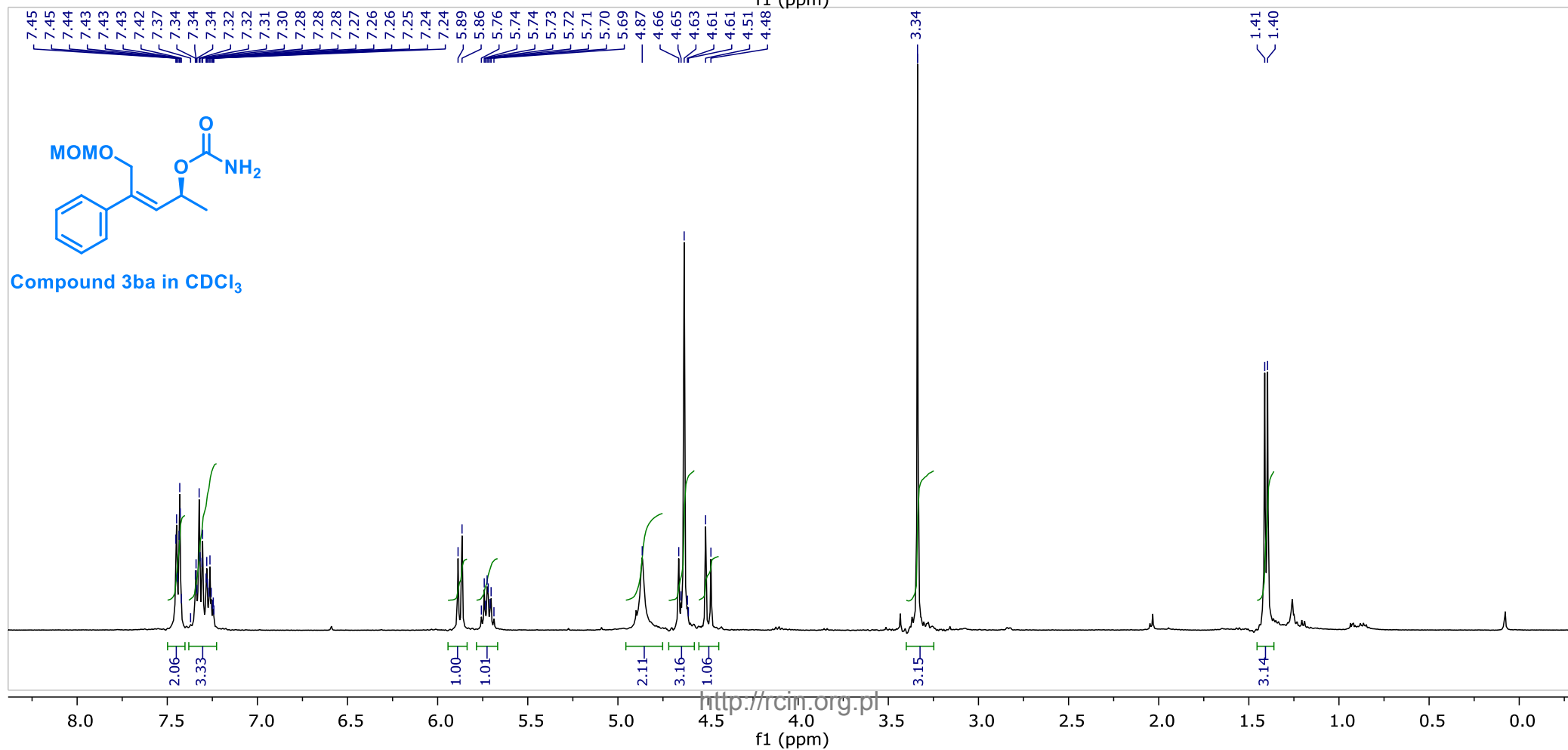
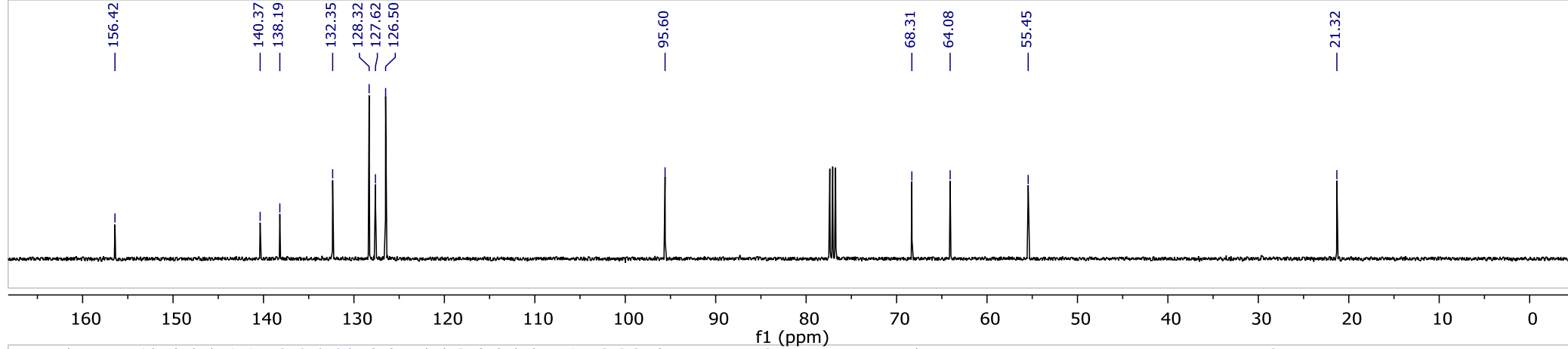


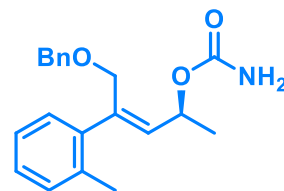
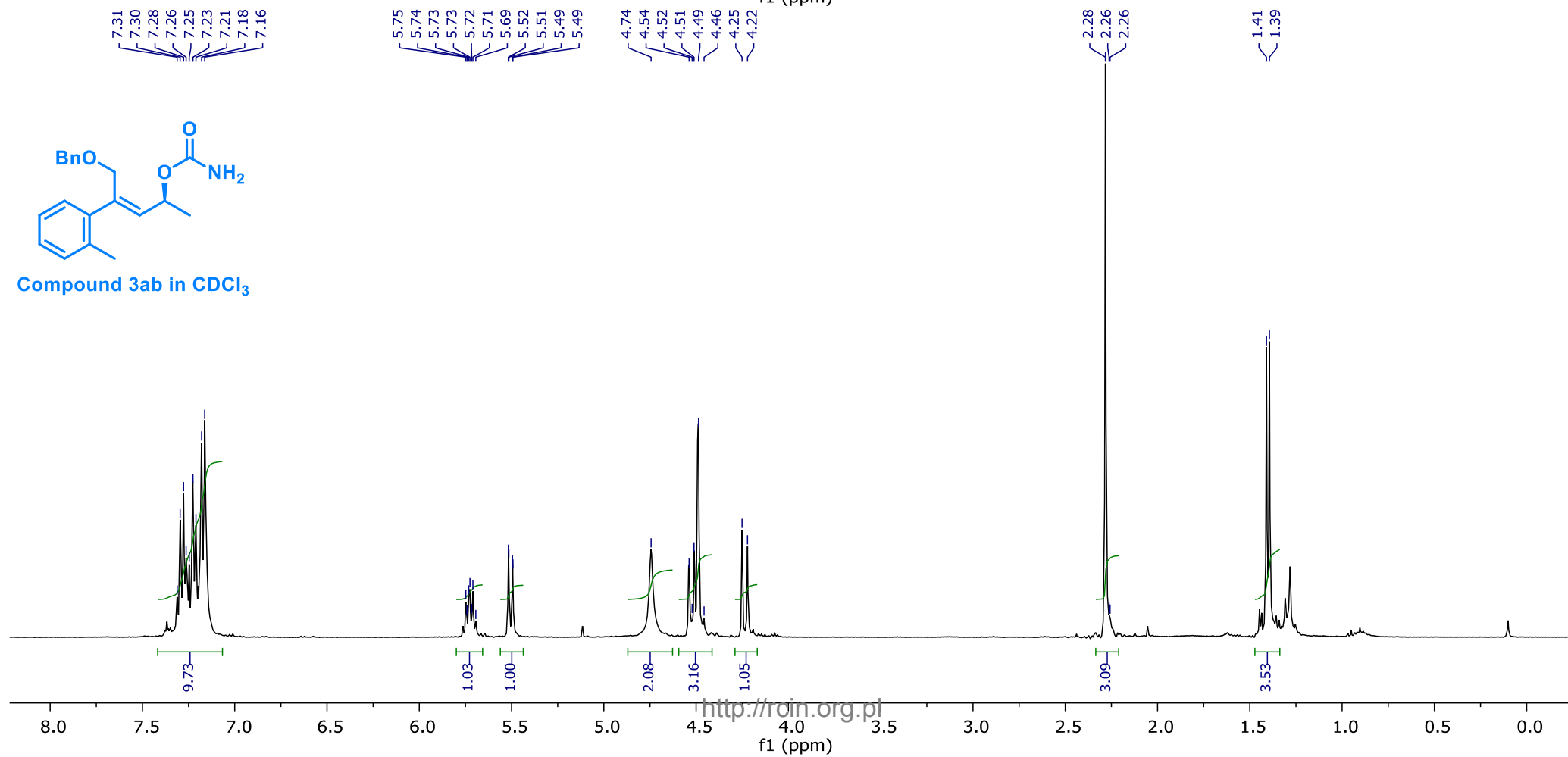
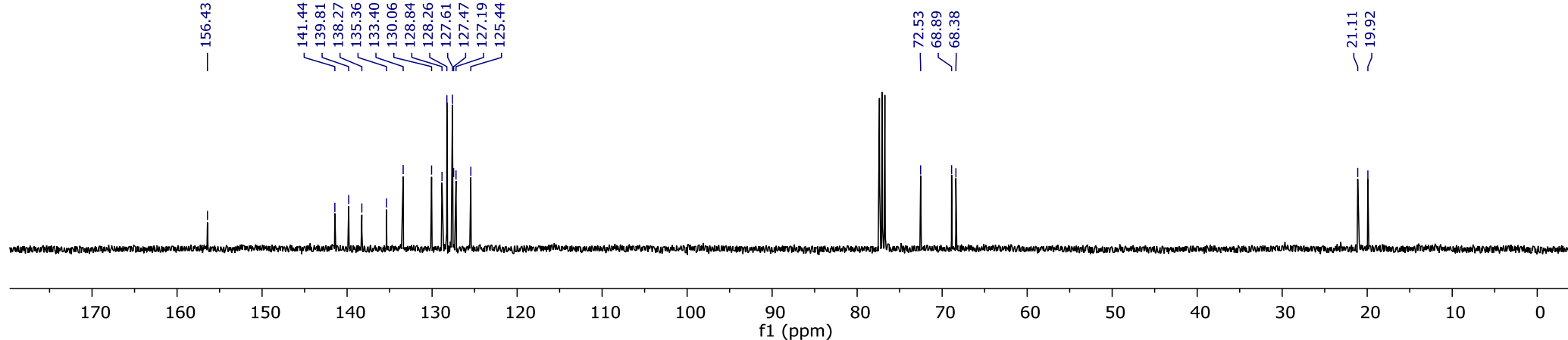
Compound 12e in CDCl<sub>3</sub>



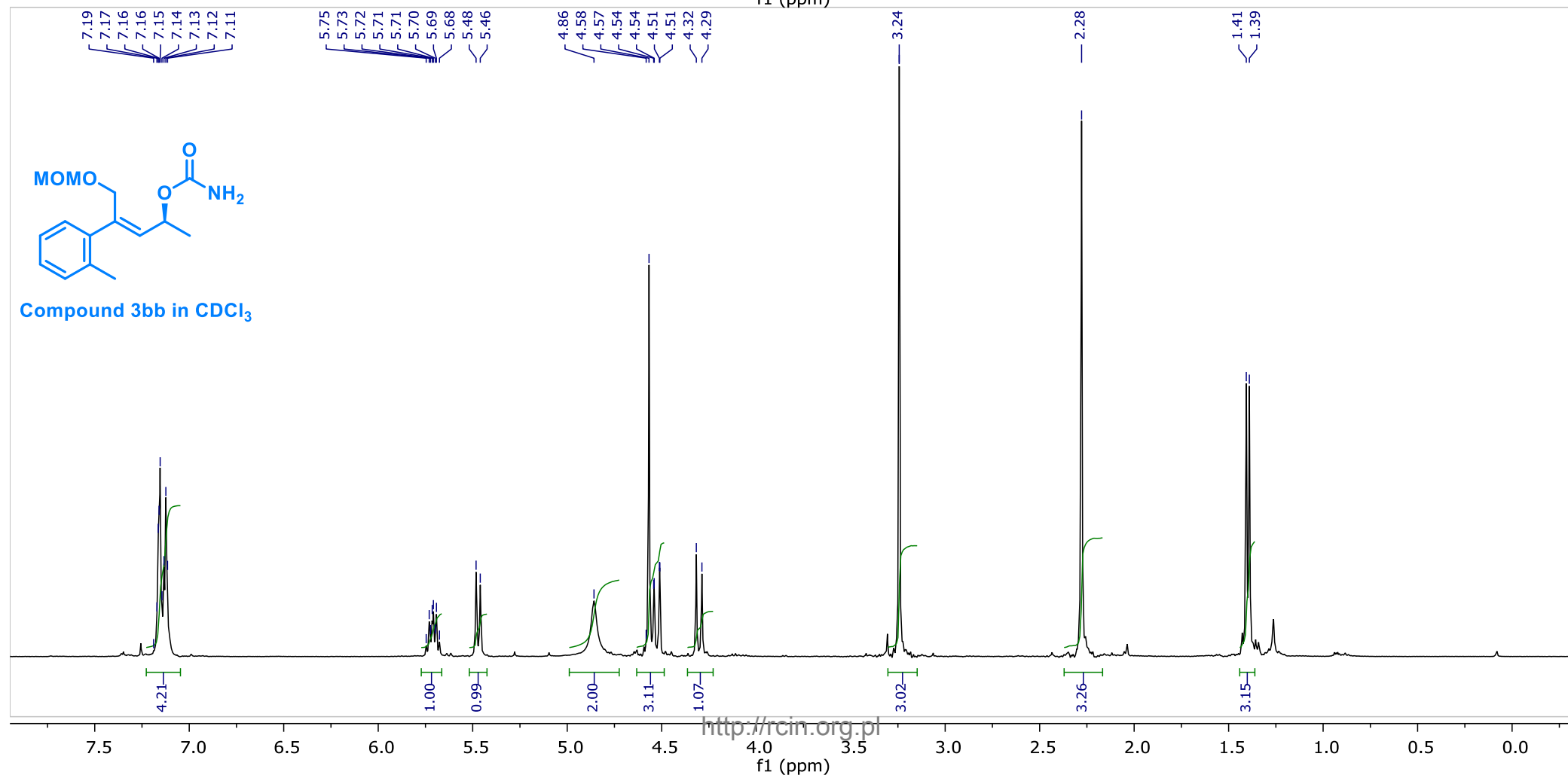
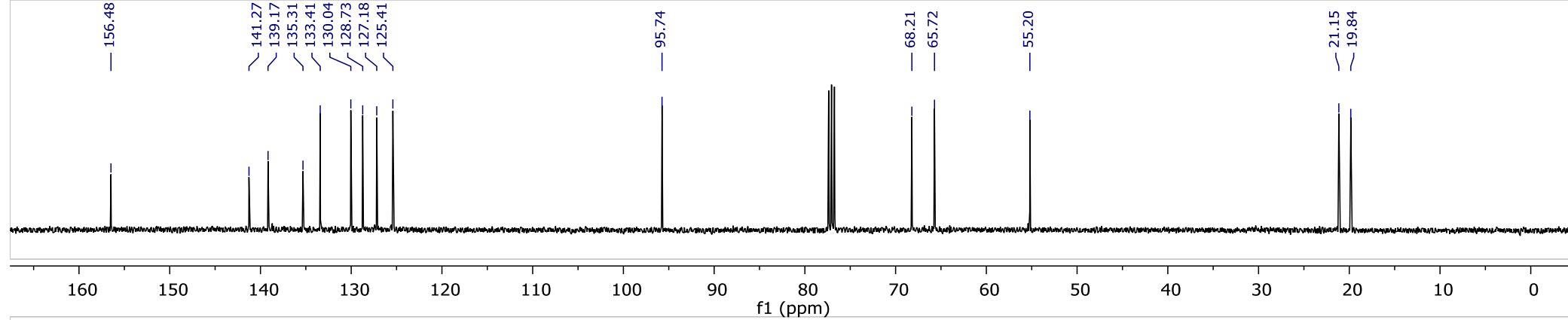


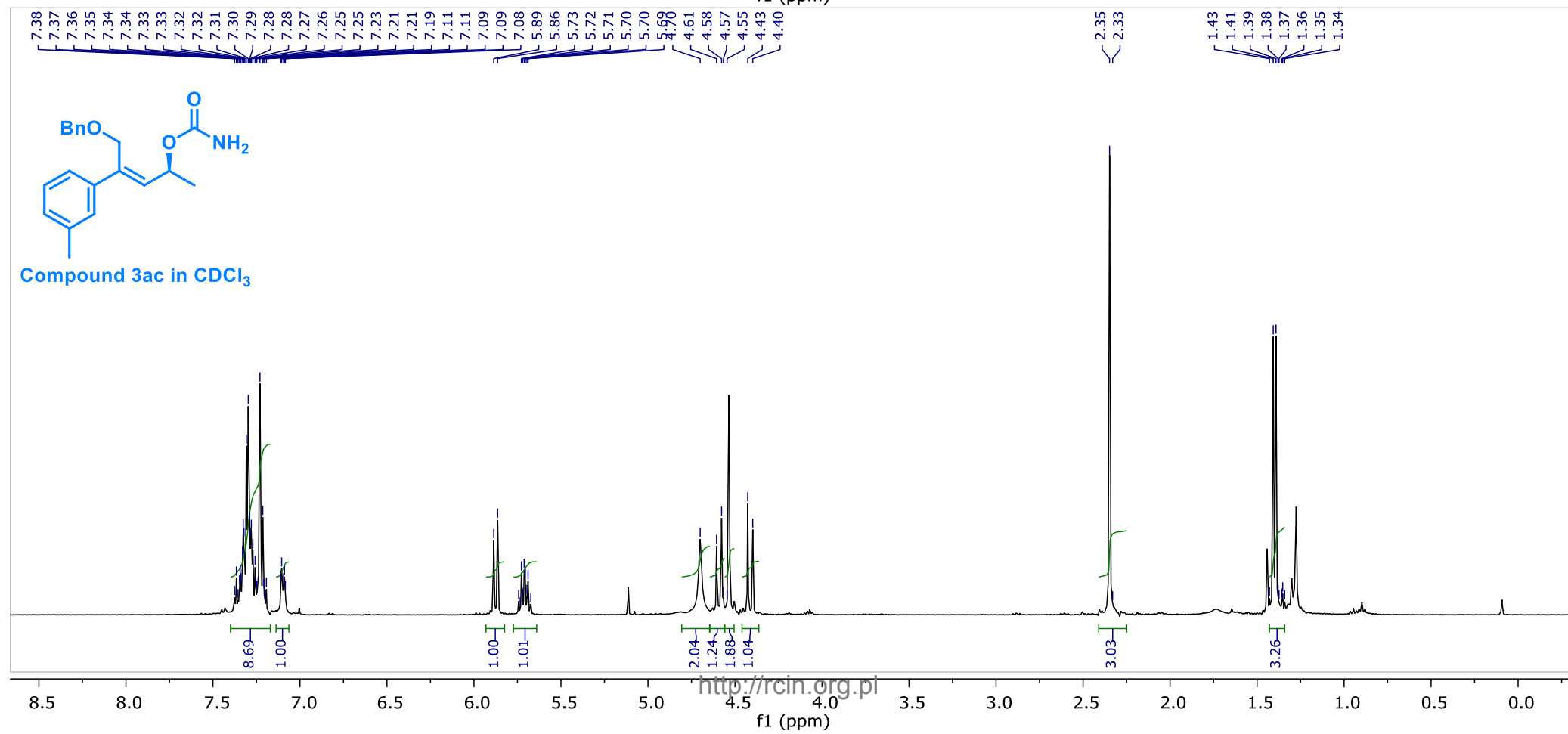
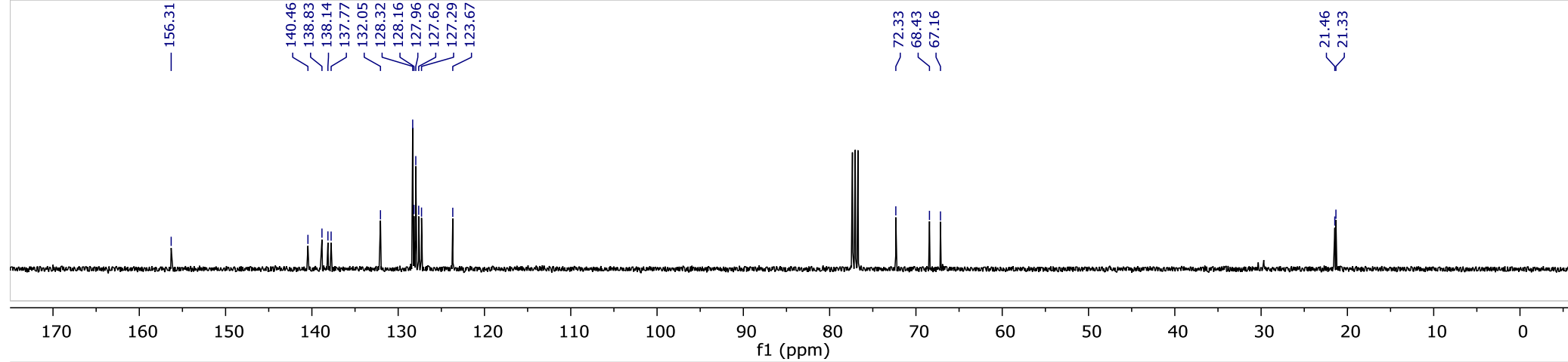


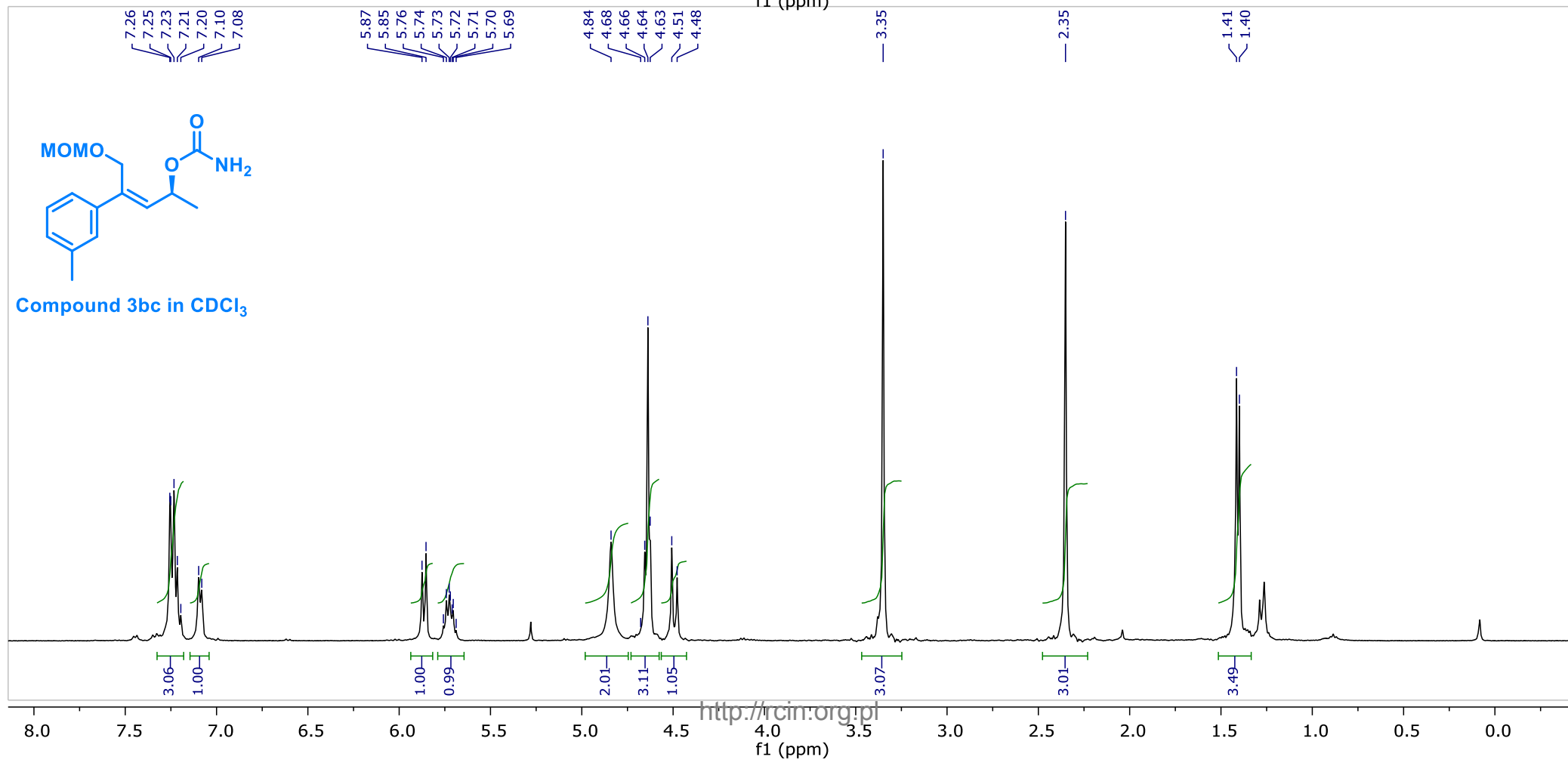
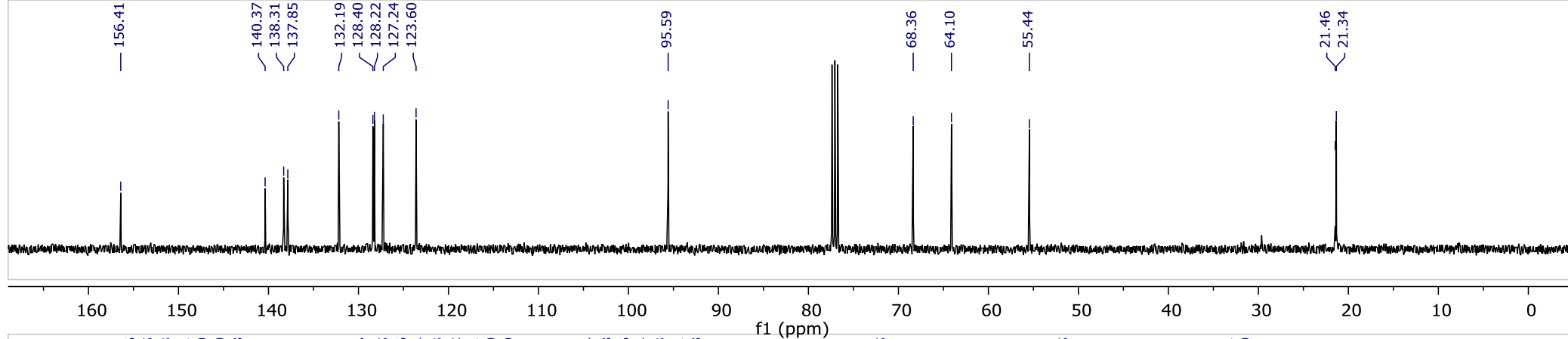


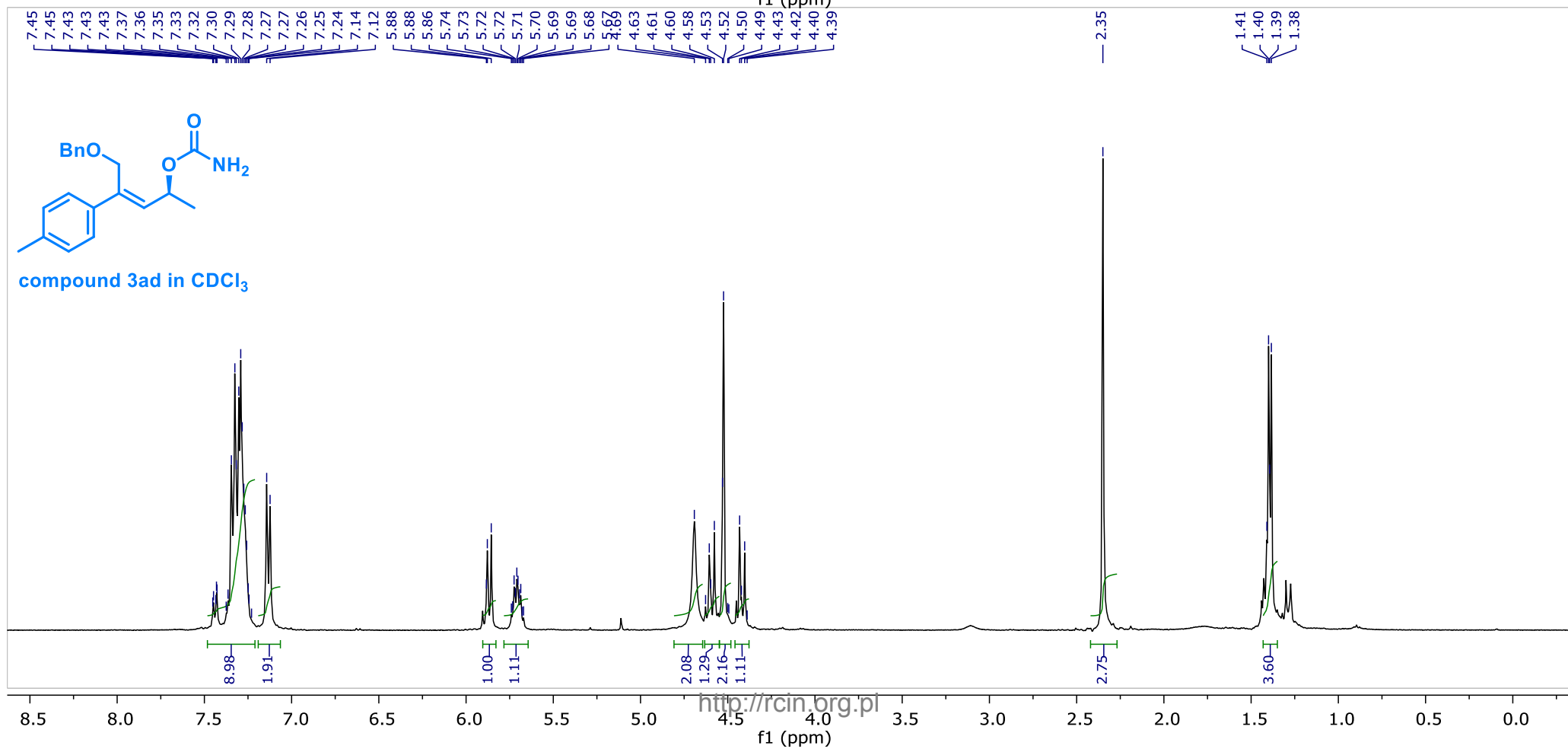
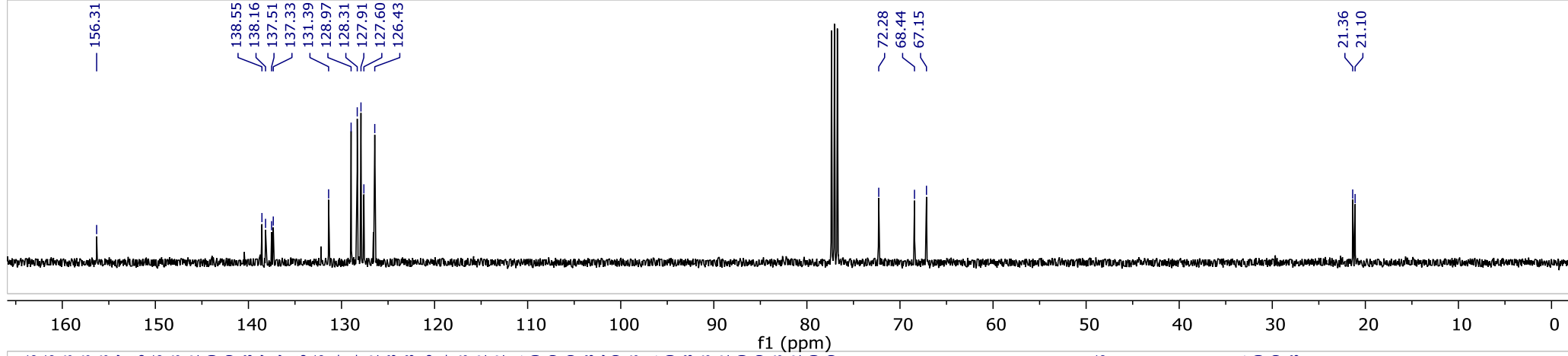


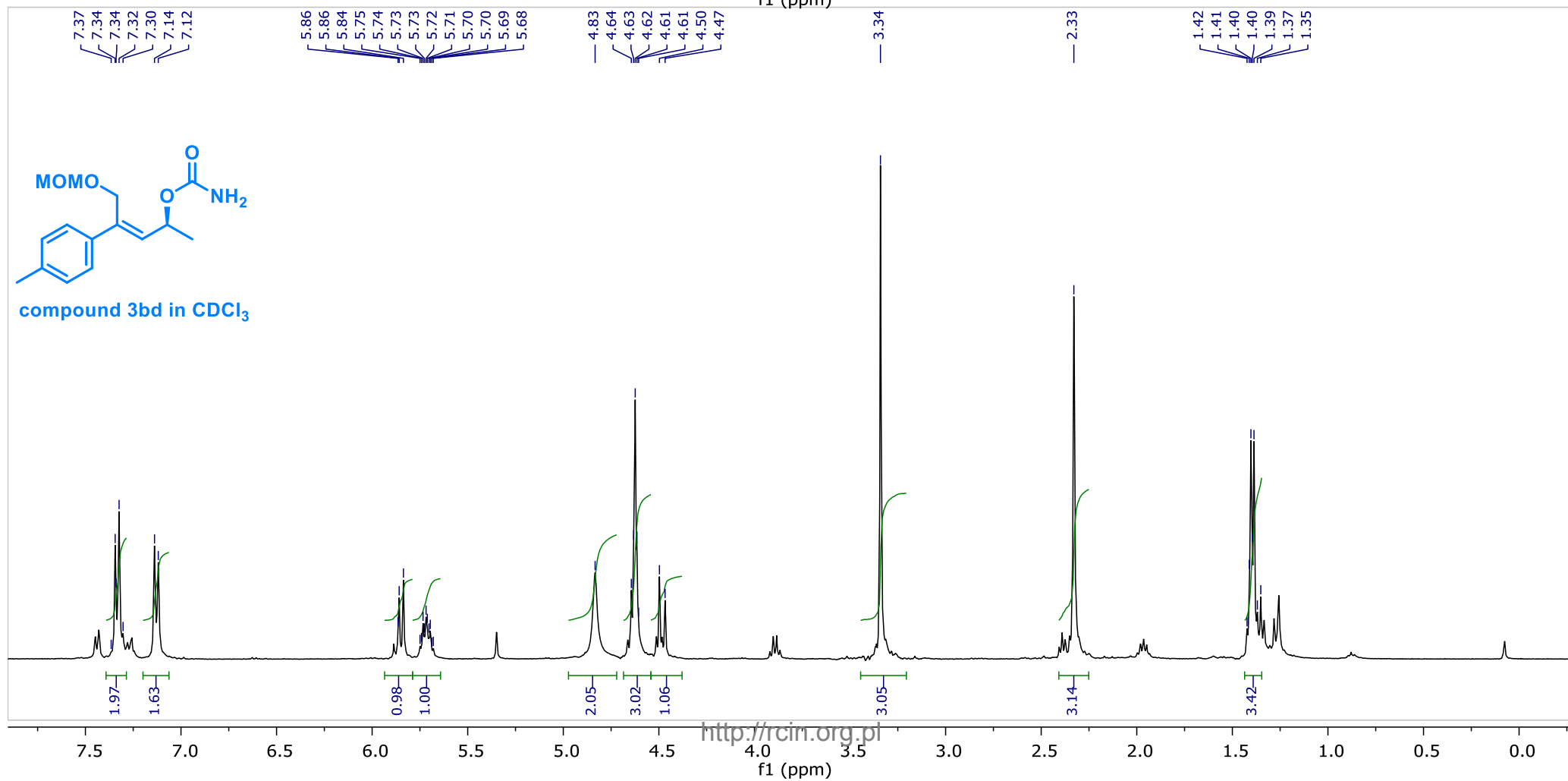
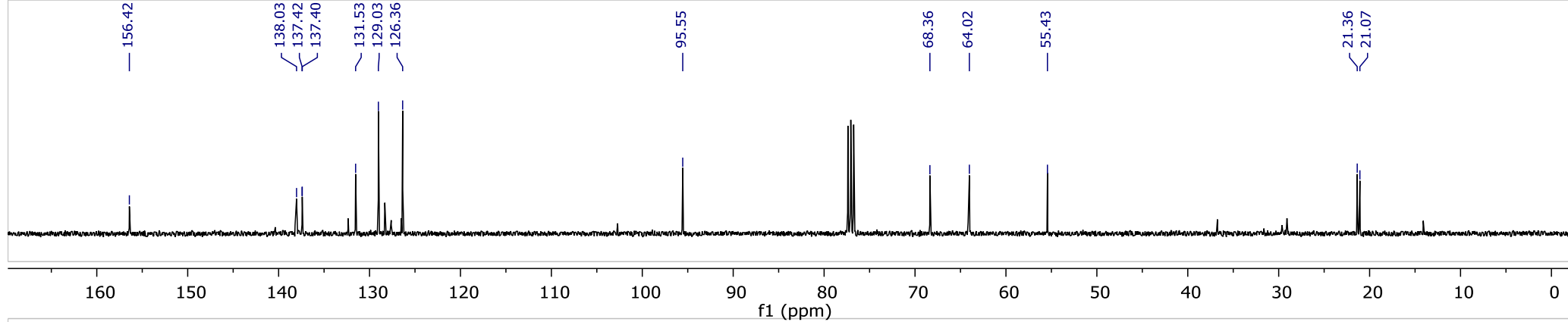
Compound 3ab in CDCl<sub>3</sub>



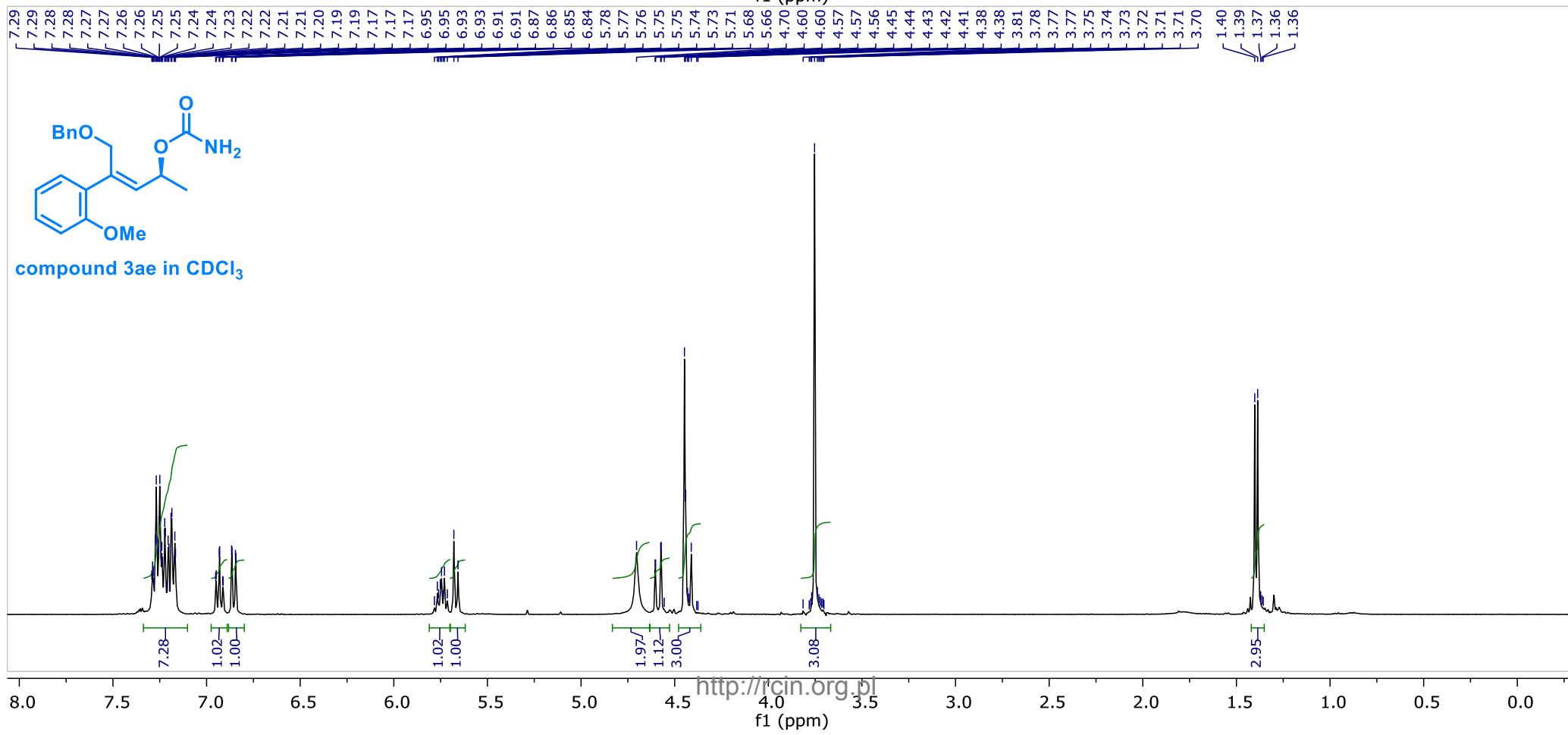
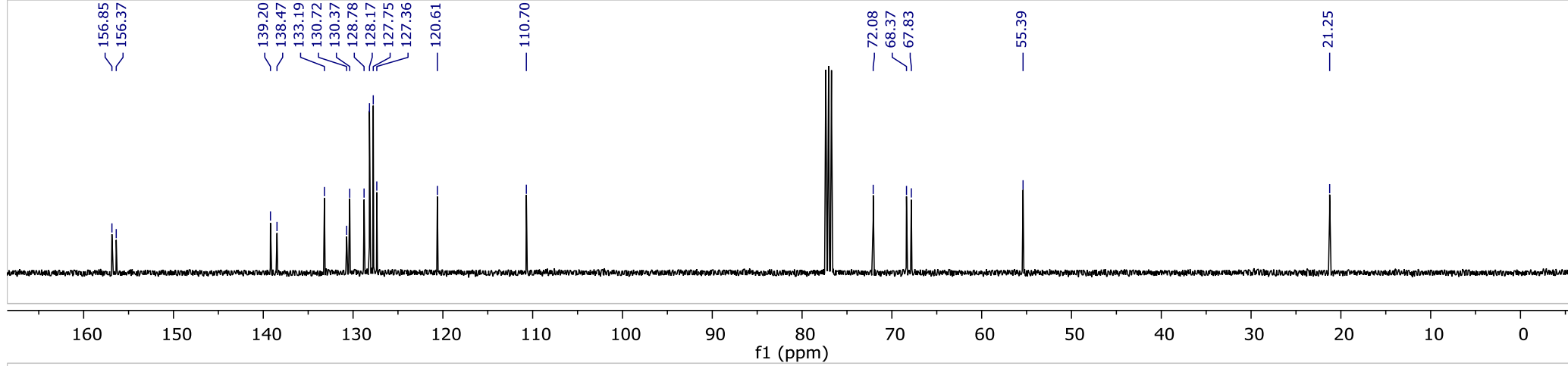


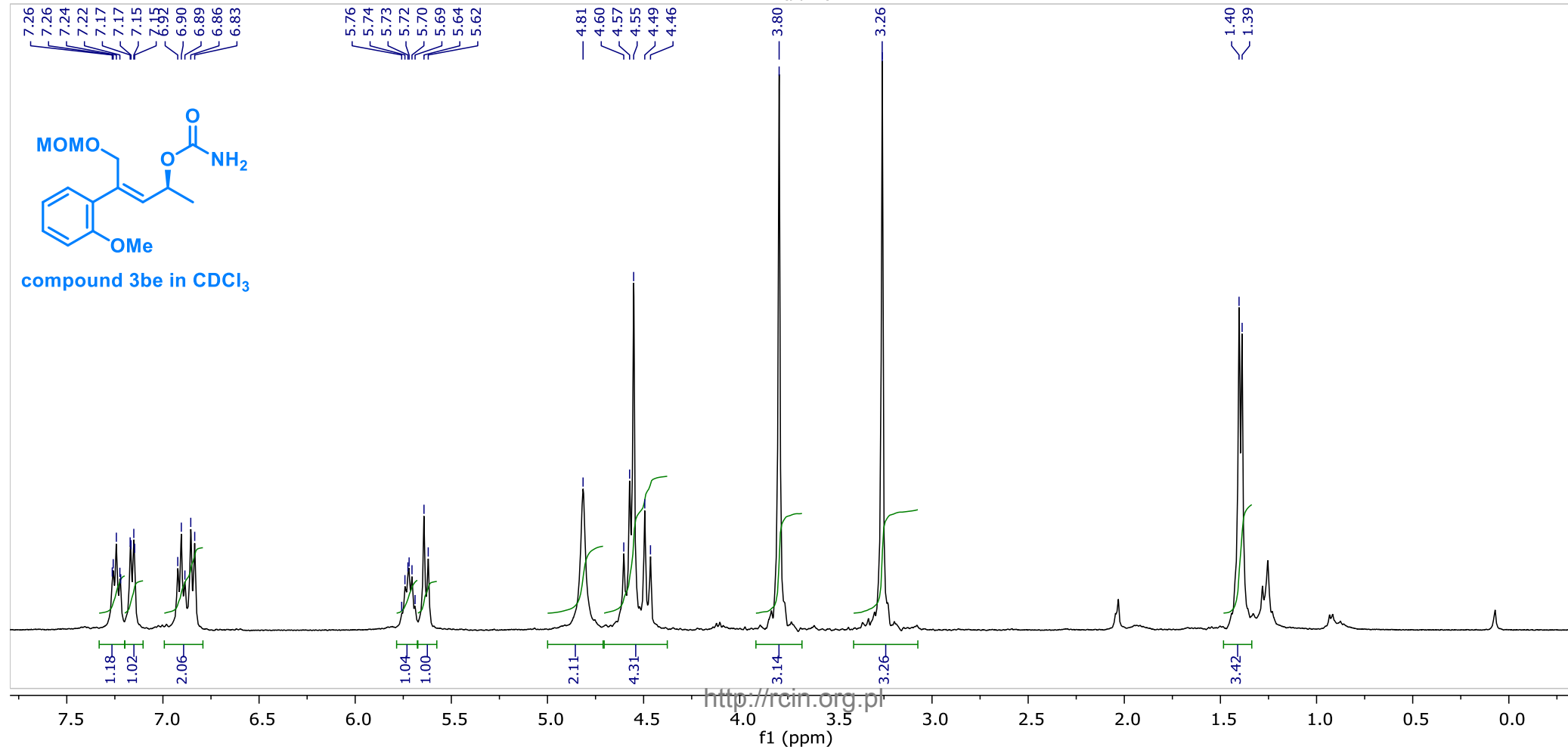
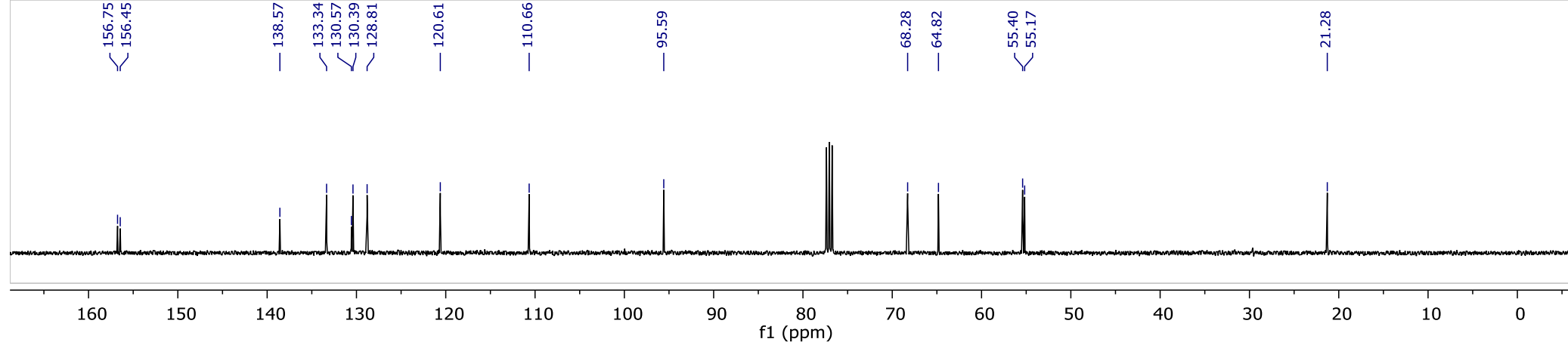


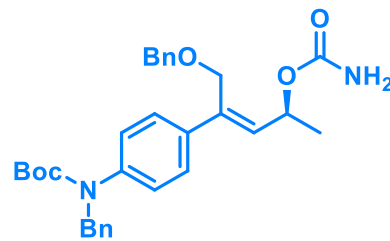
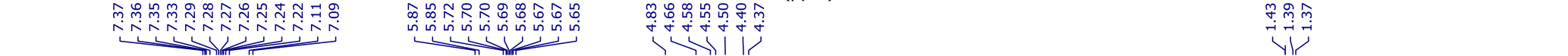
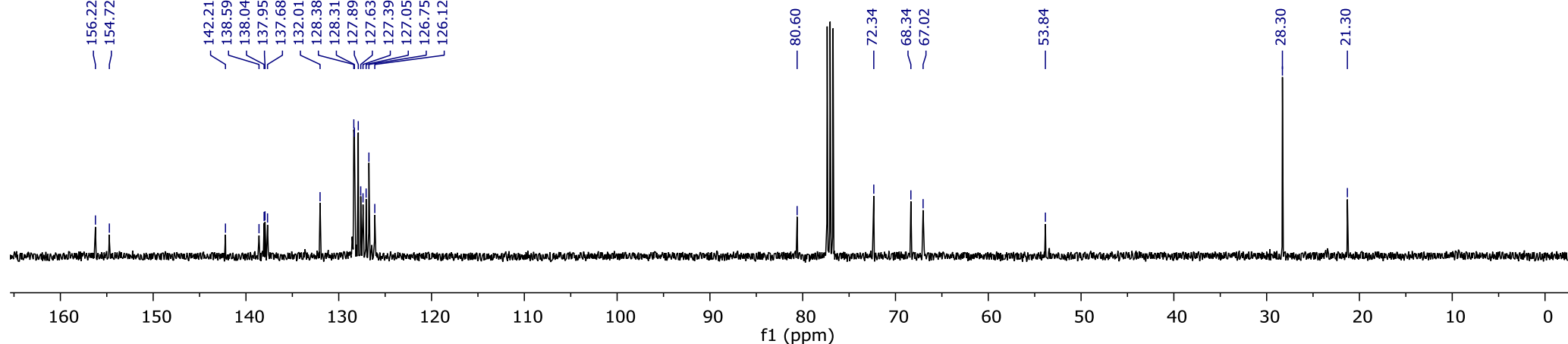




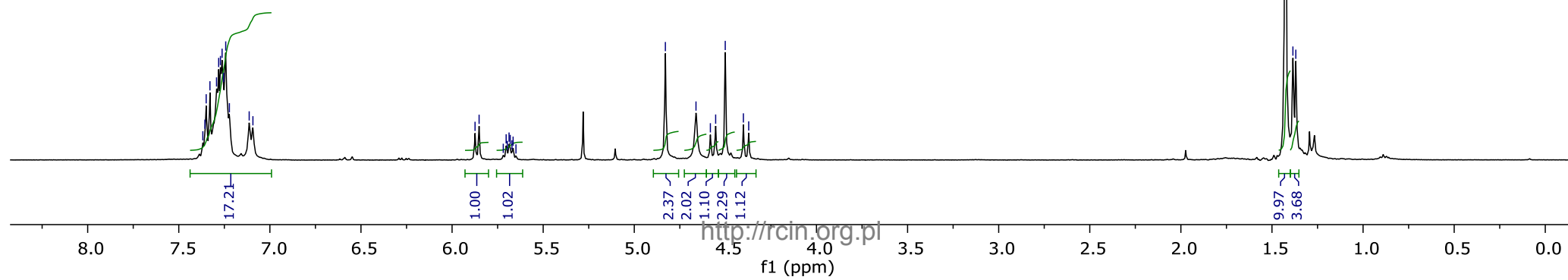


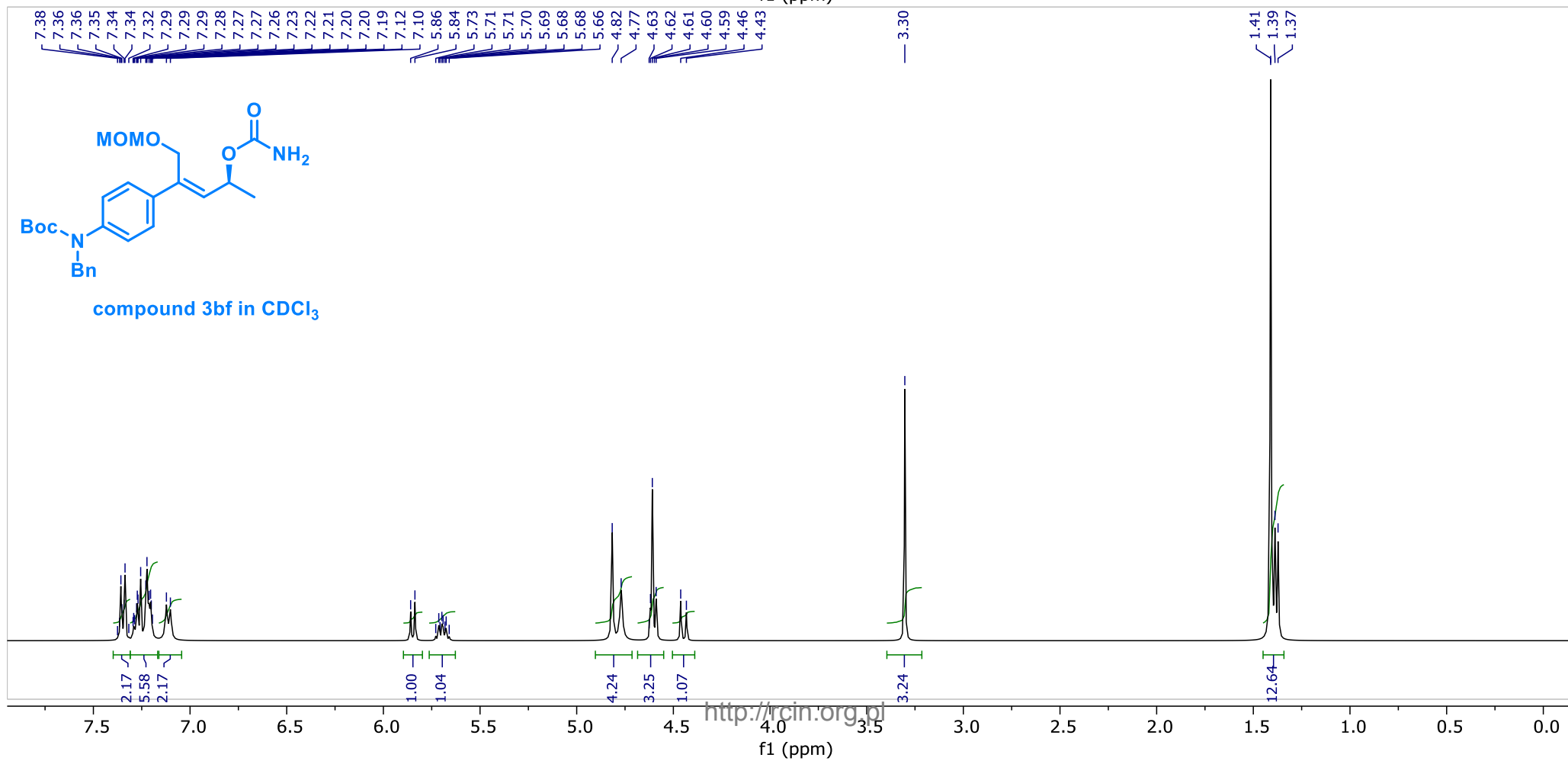
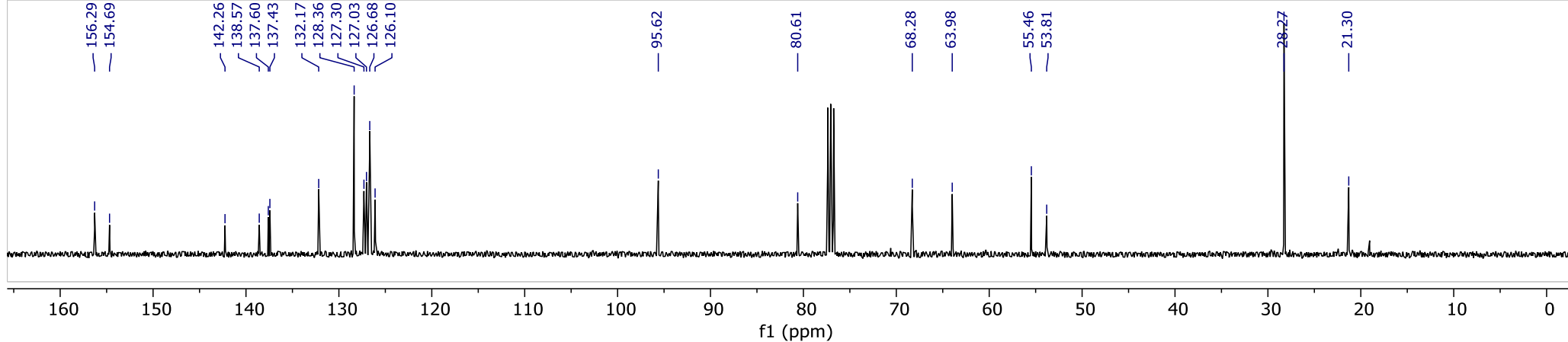


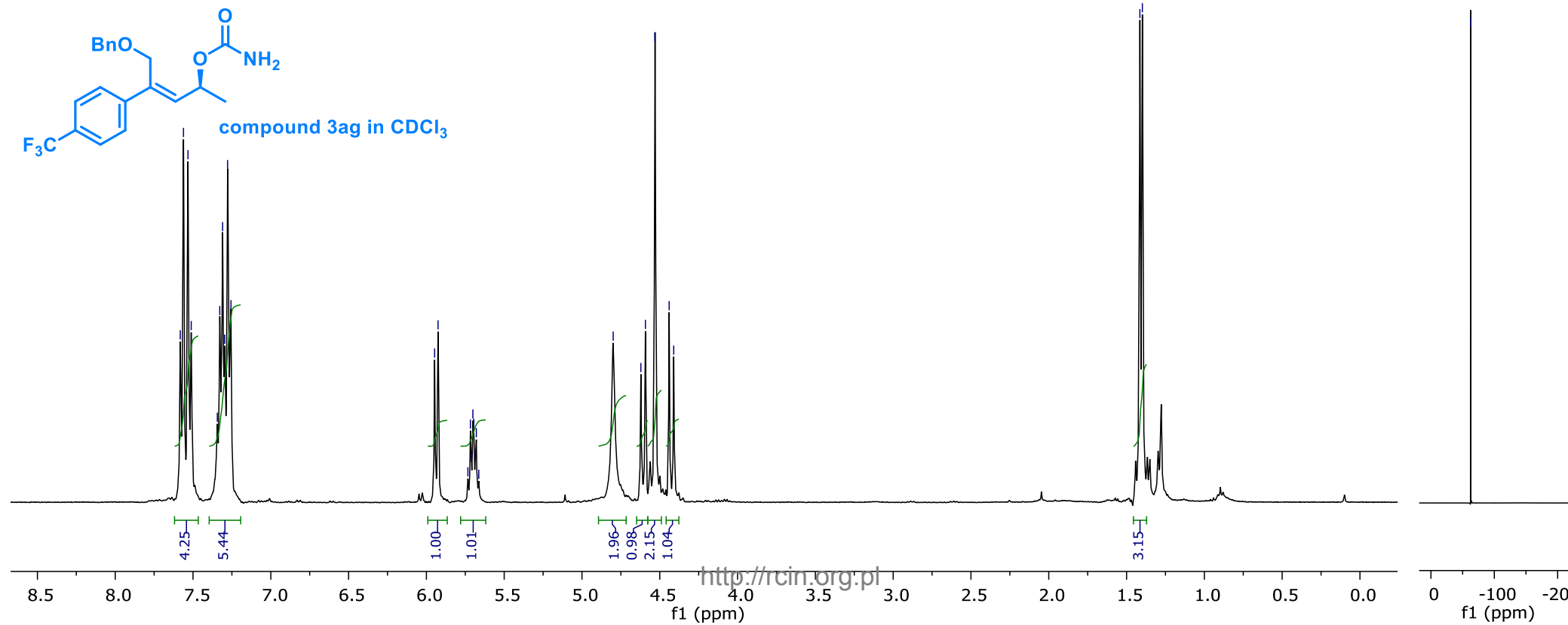
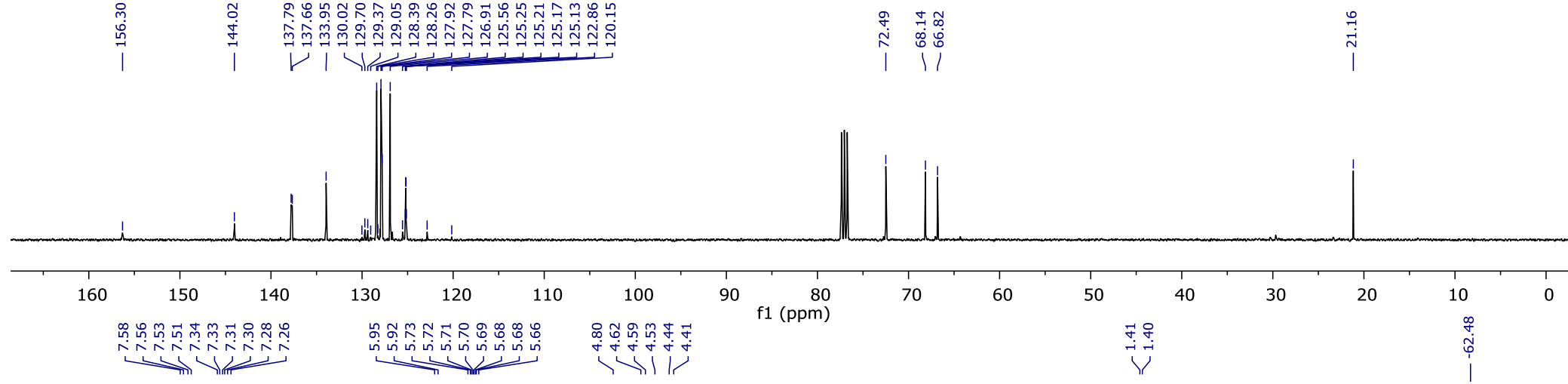


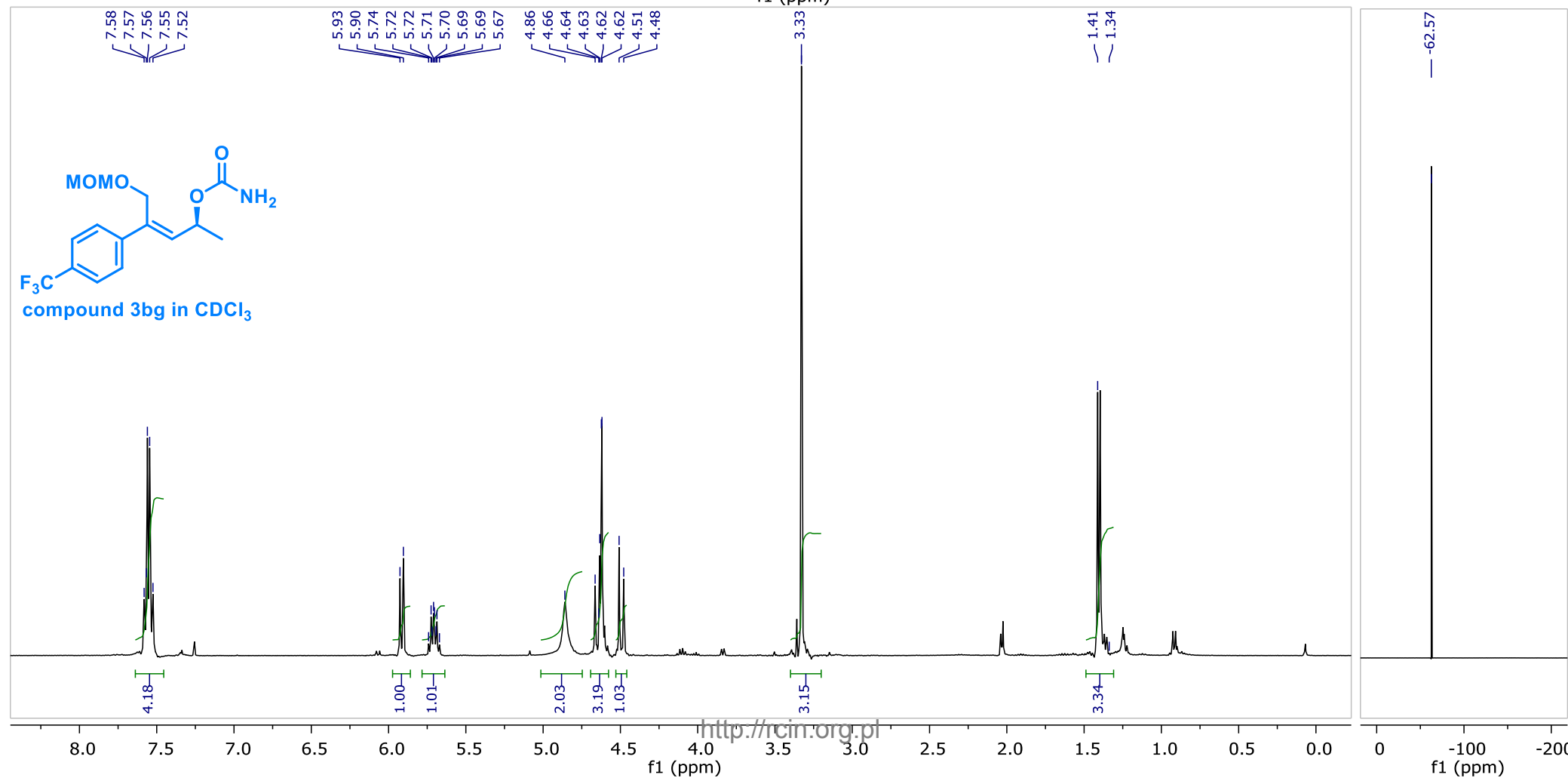
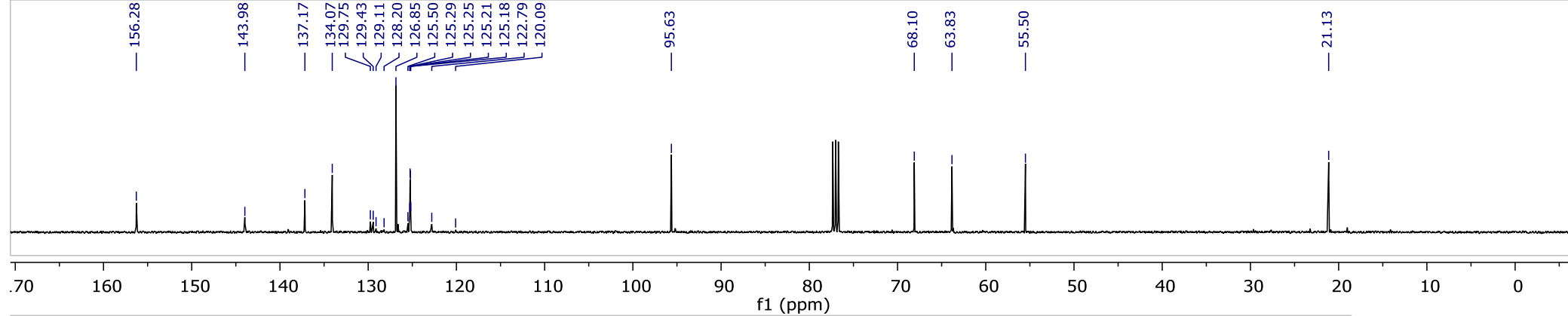


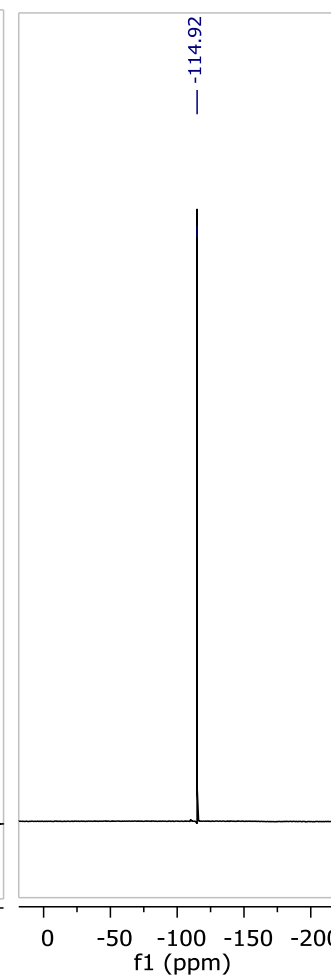
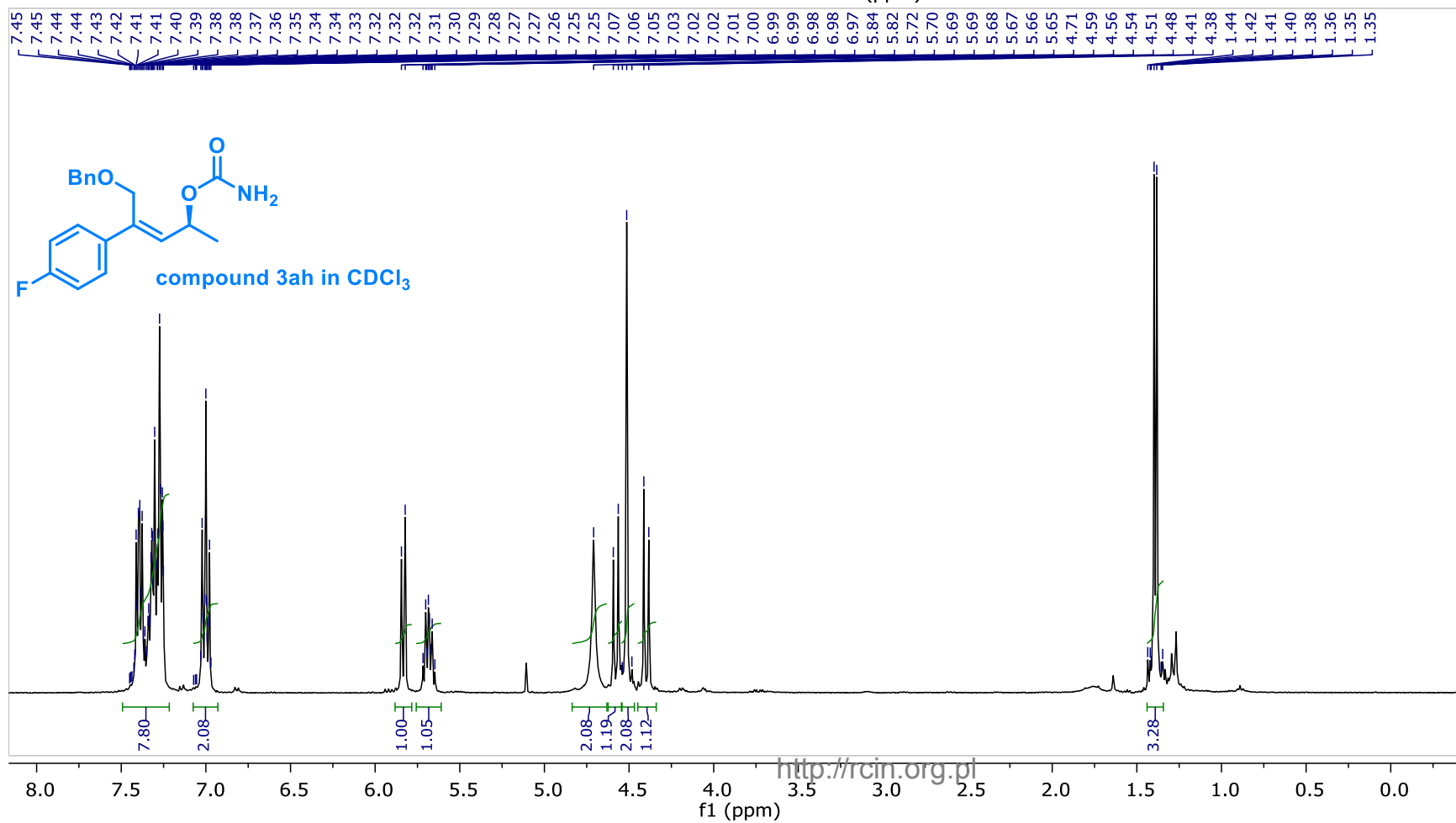
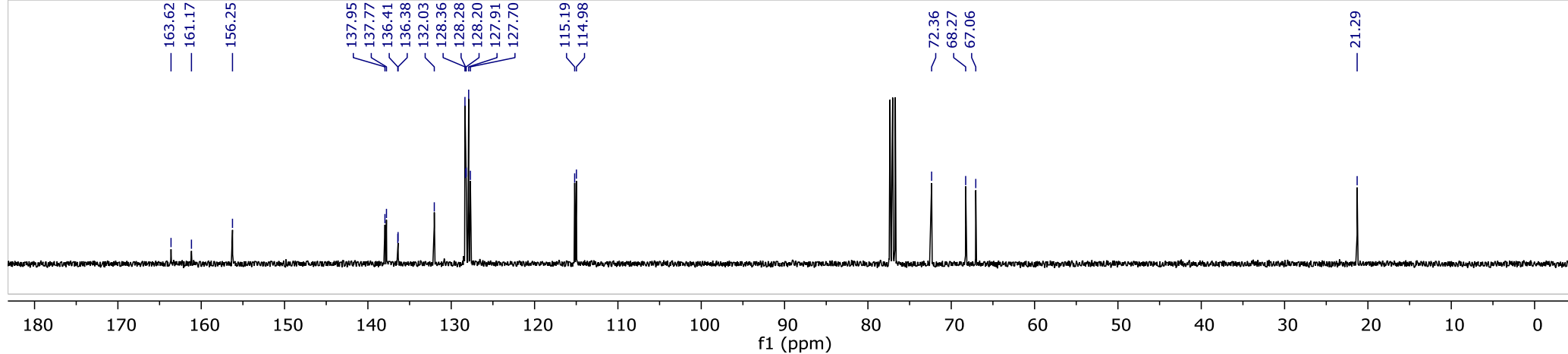
compound 3af in CDCl<sub>3</sub>

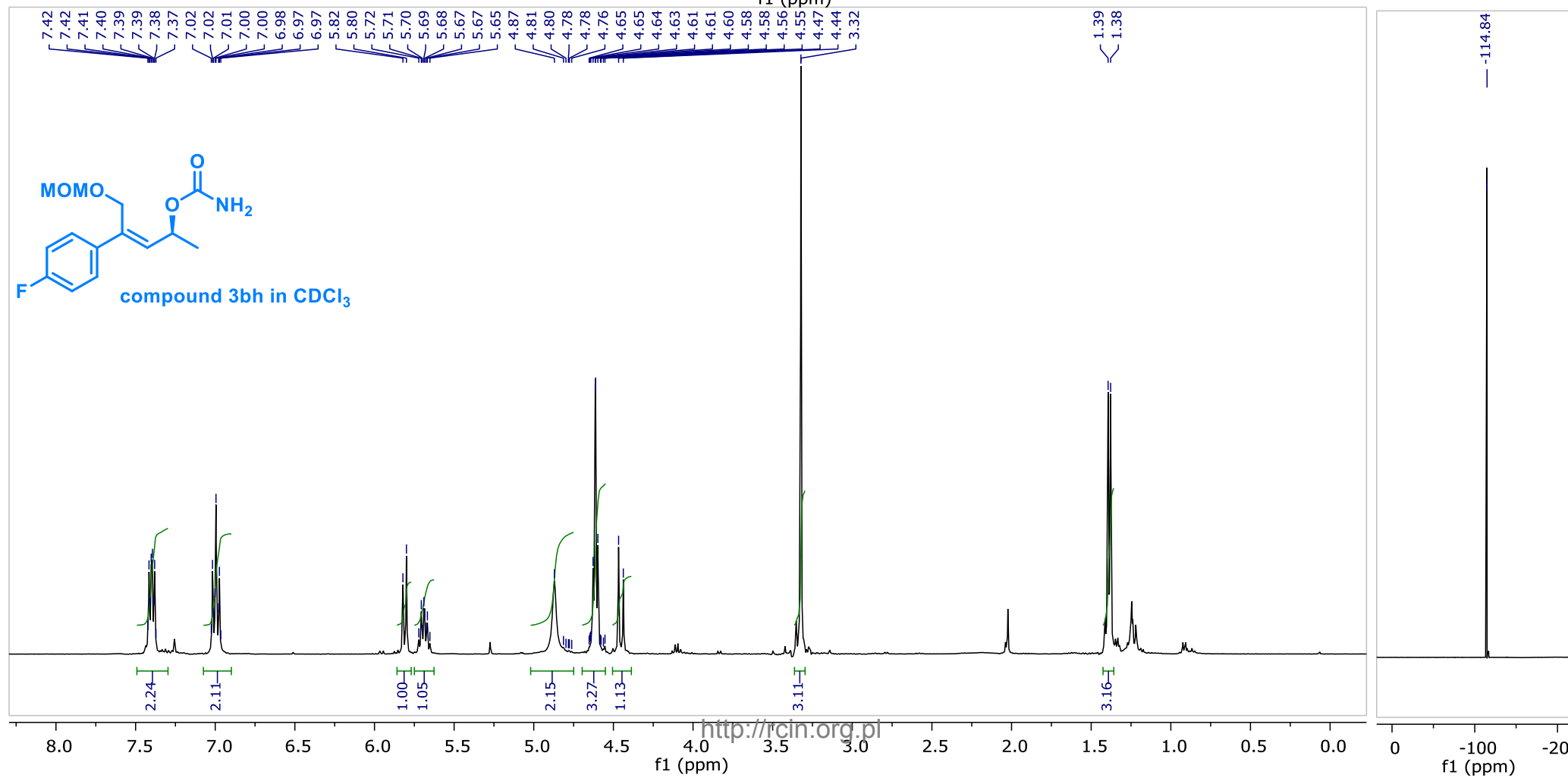
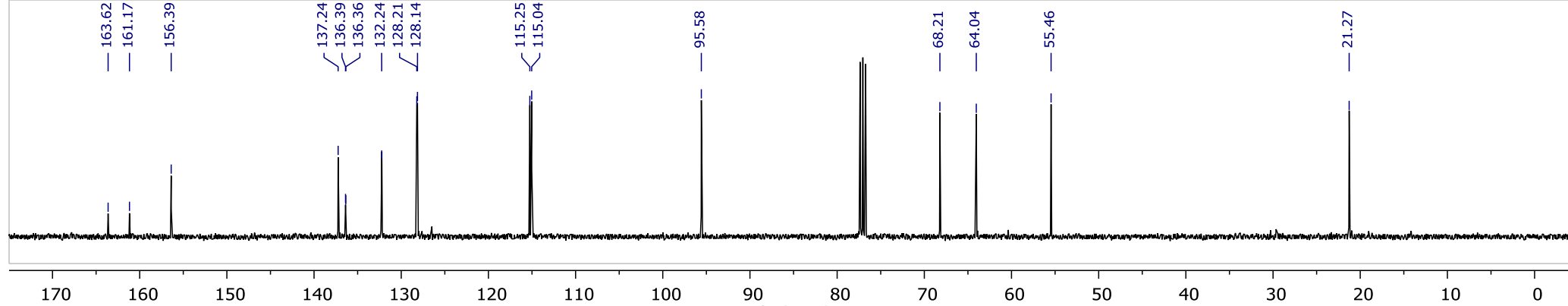




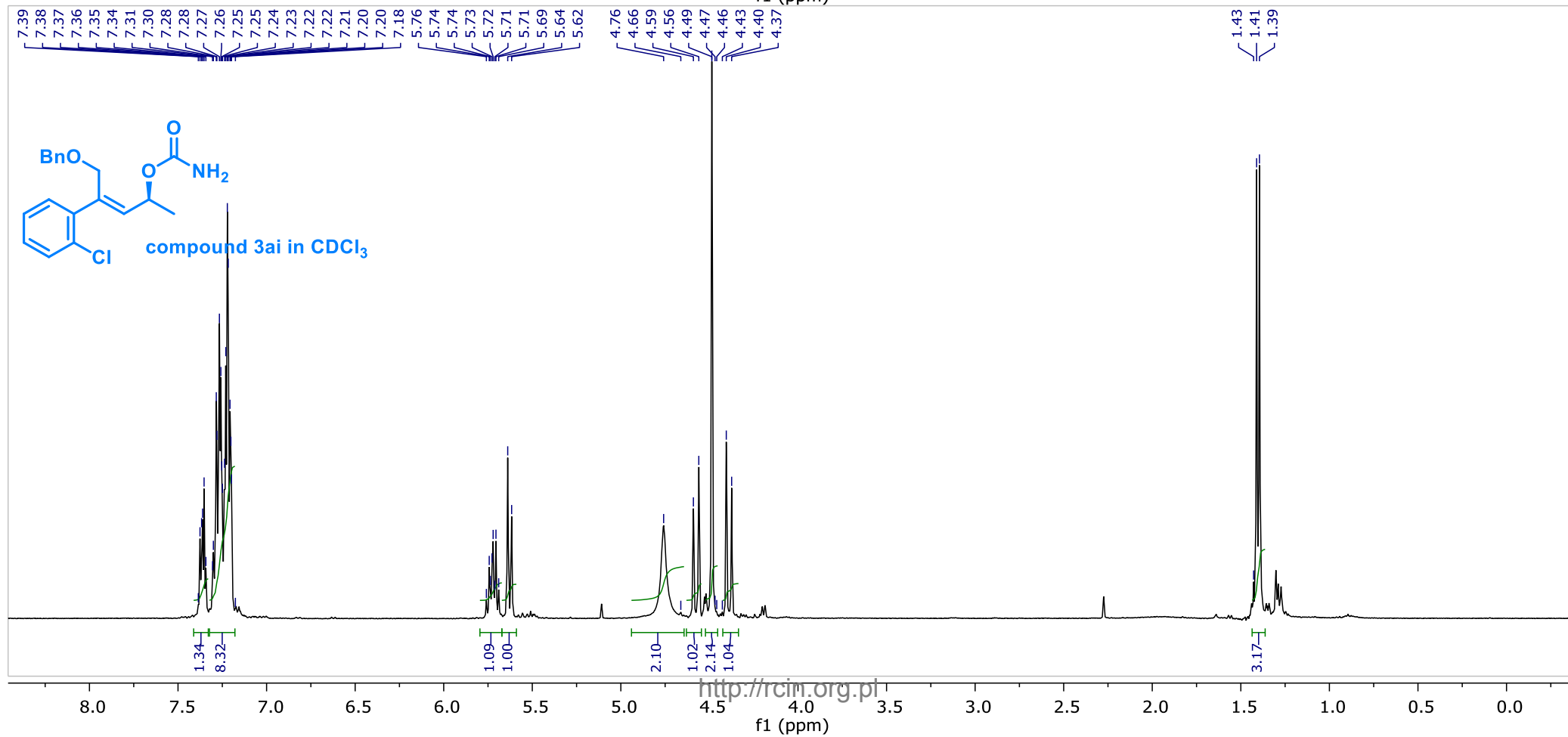
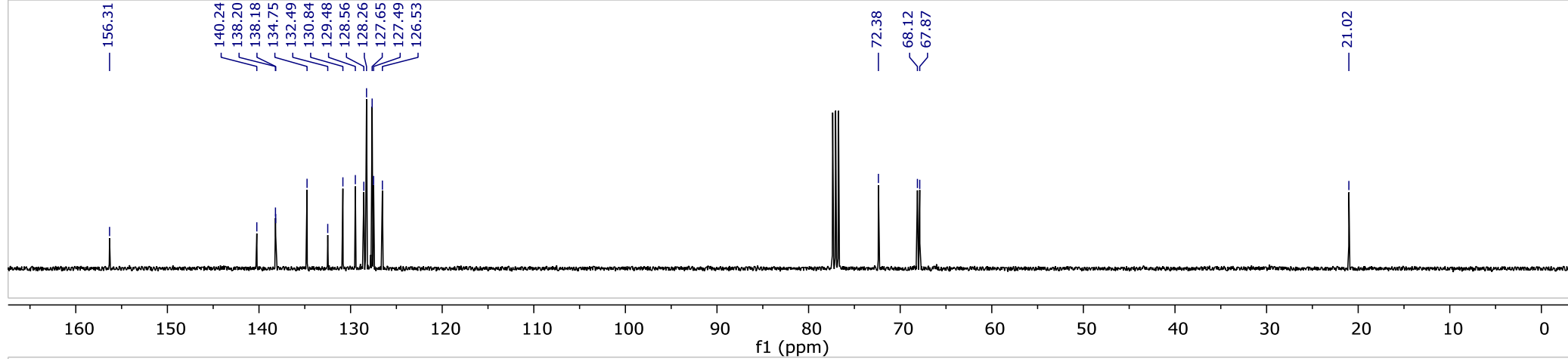


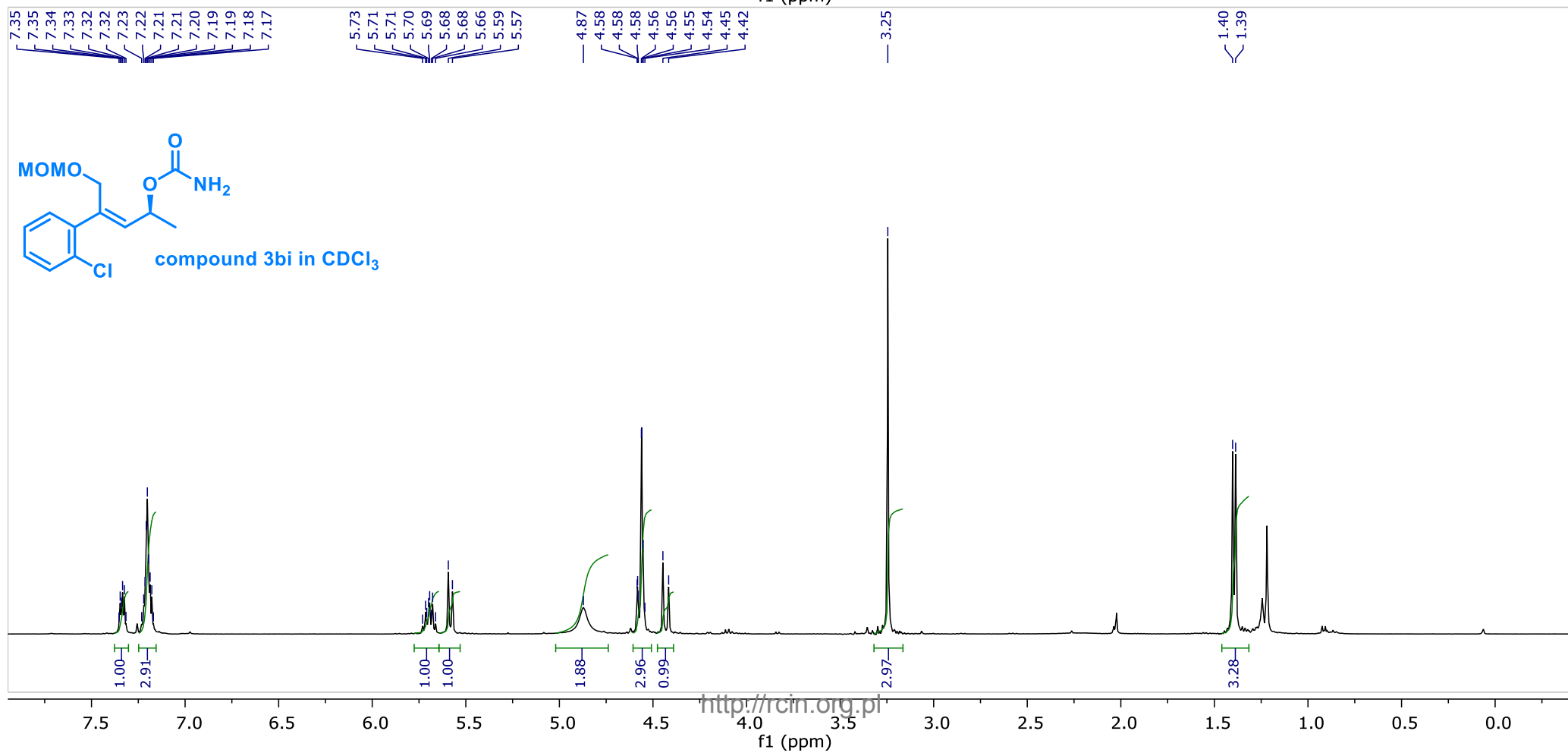
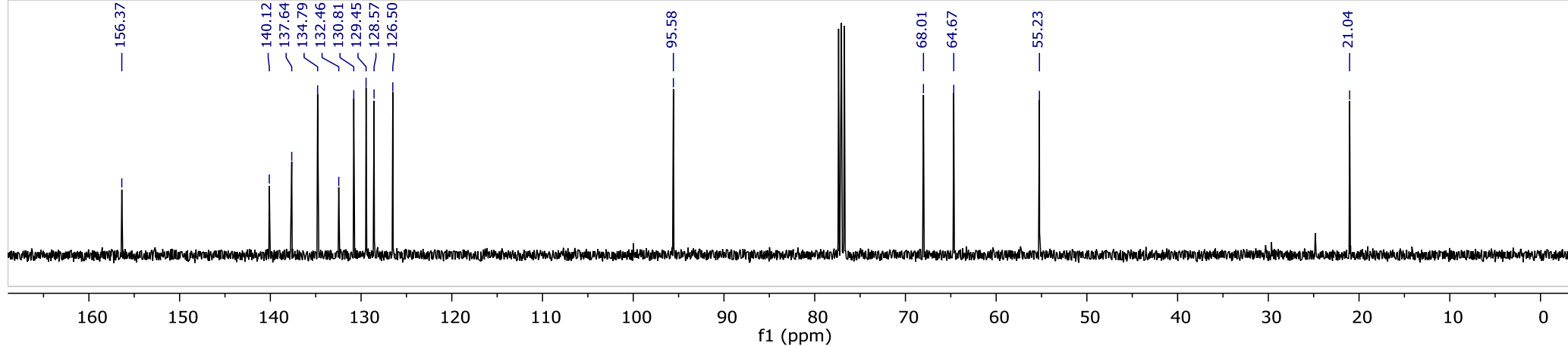


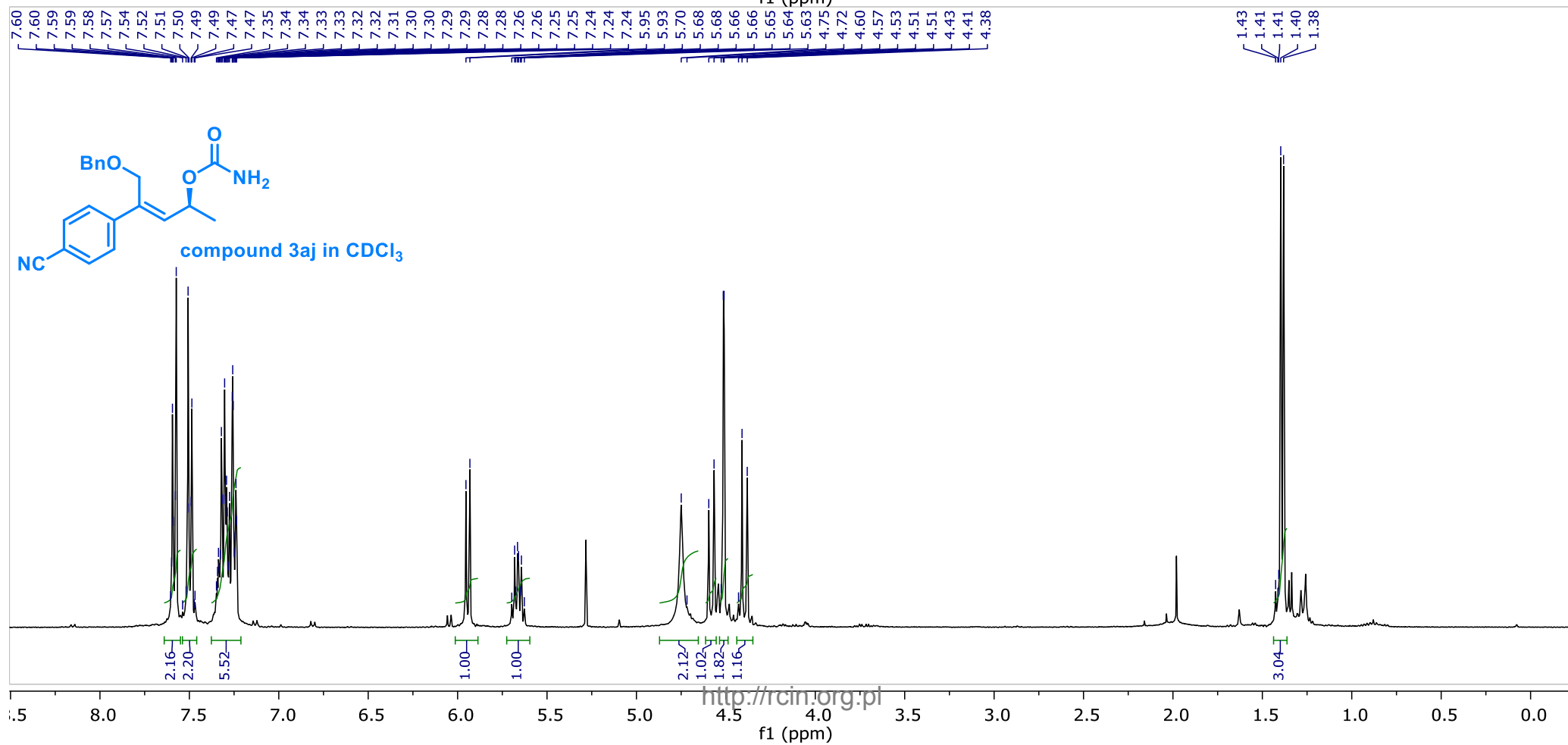
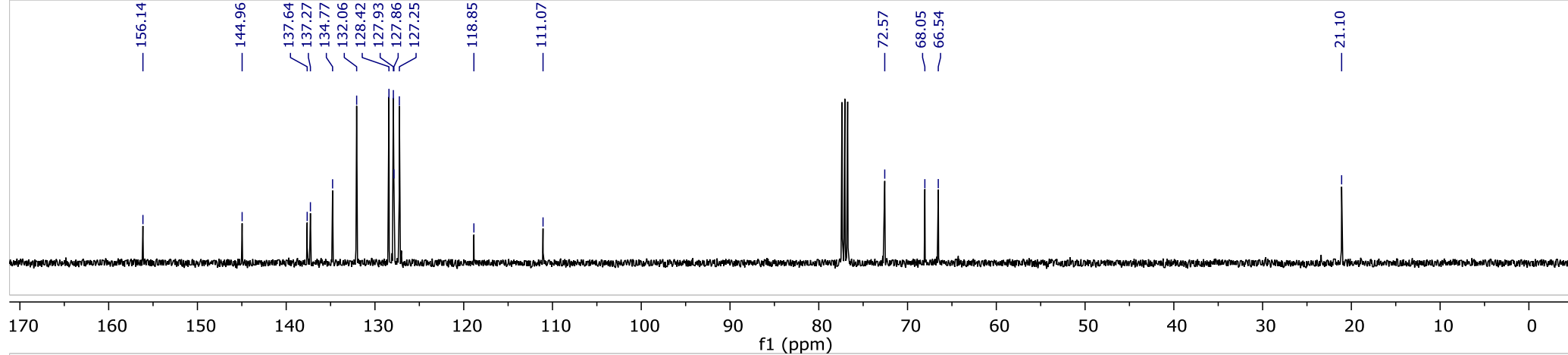


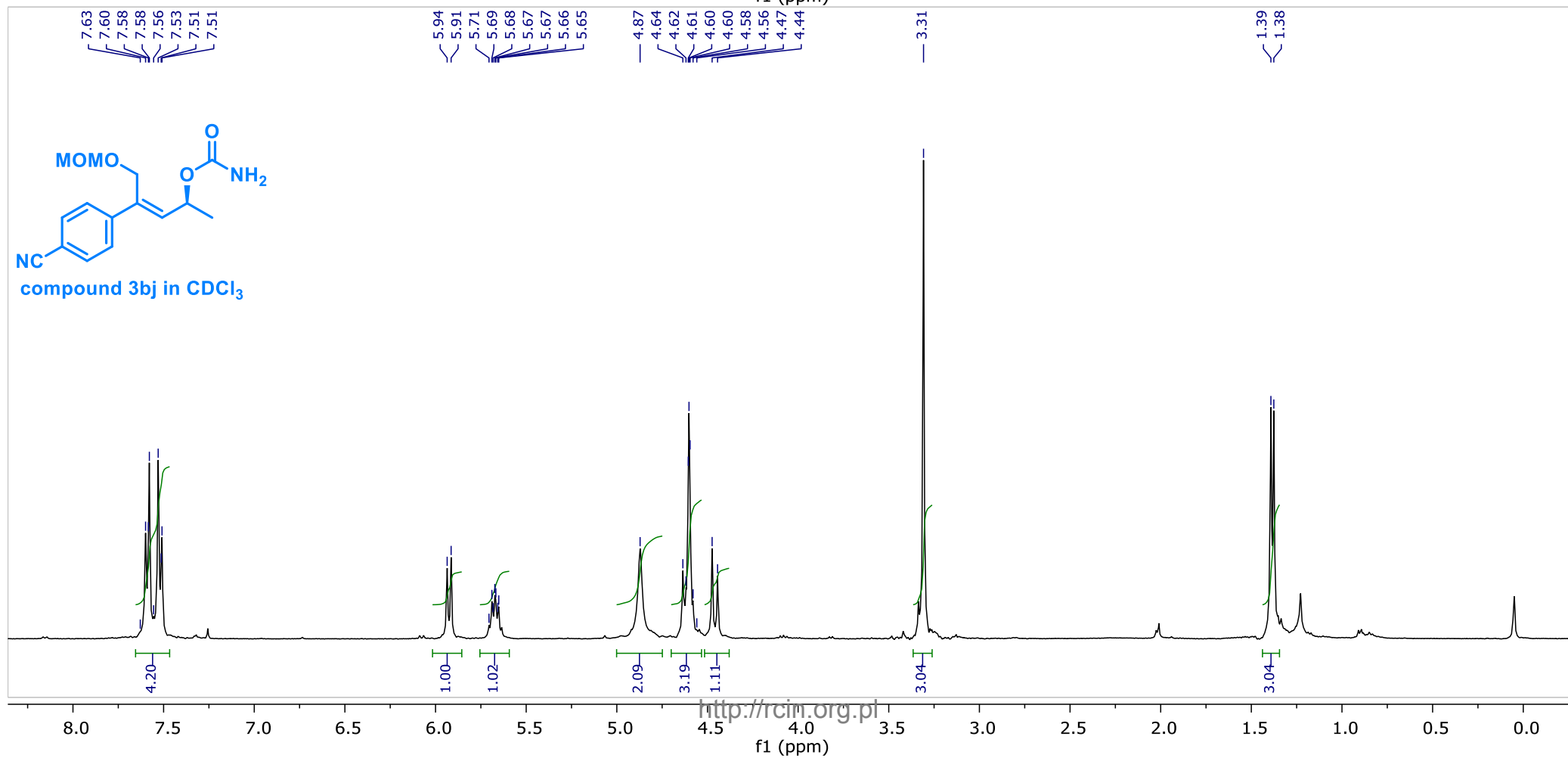
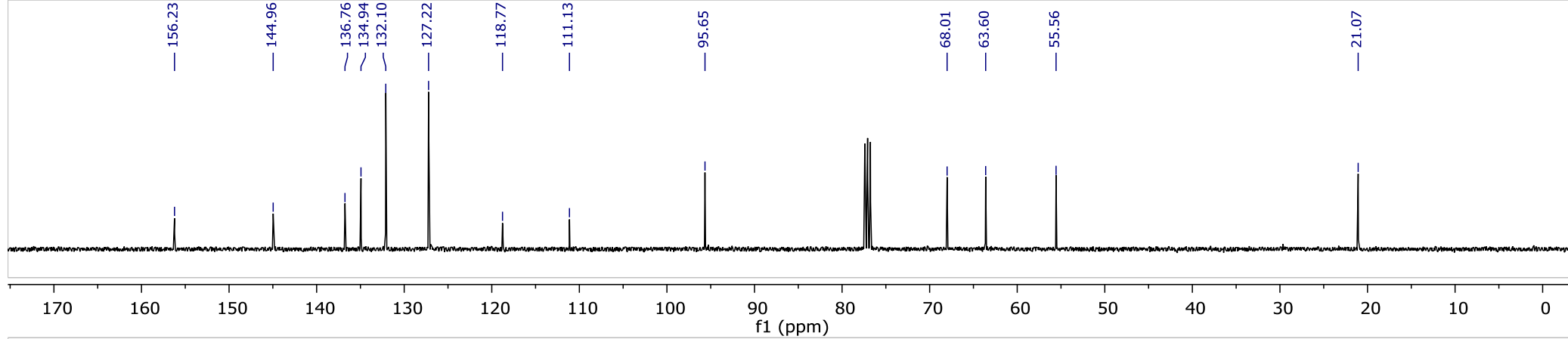


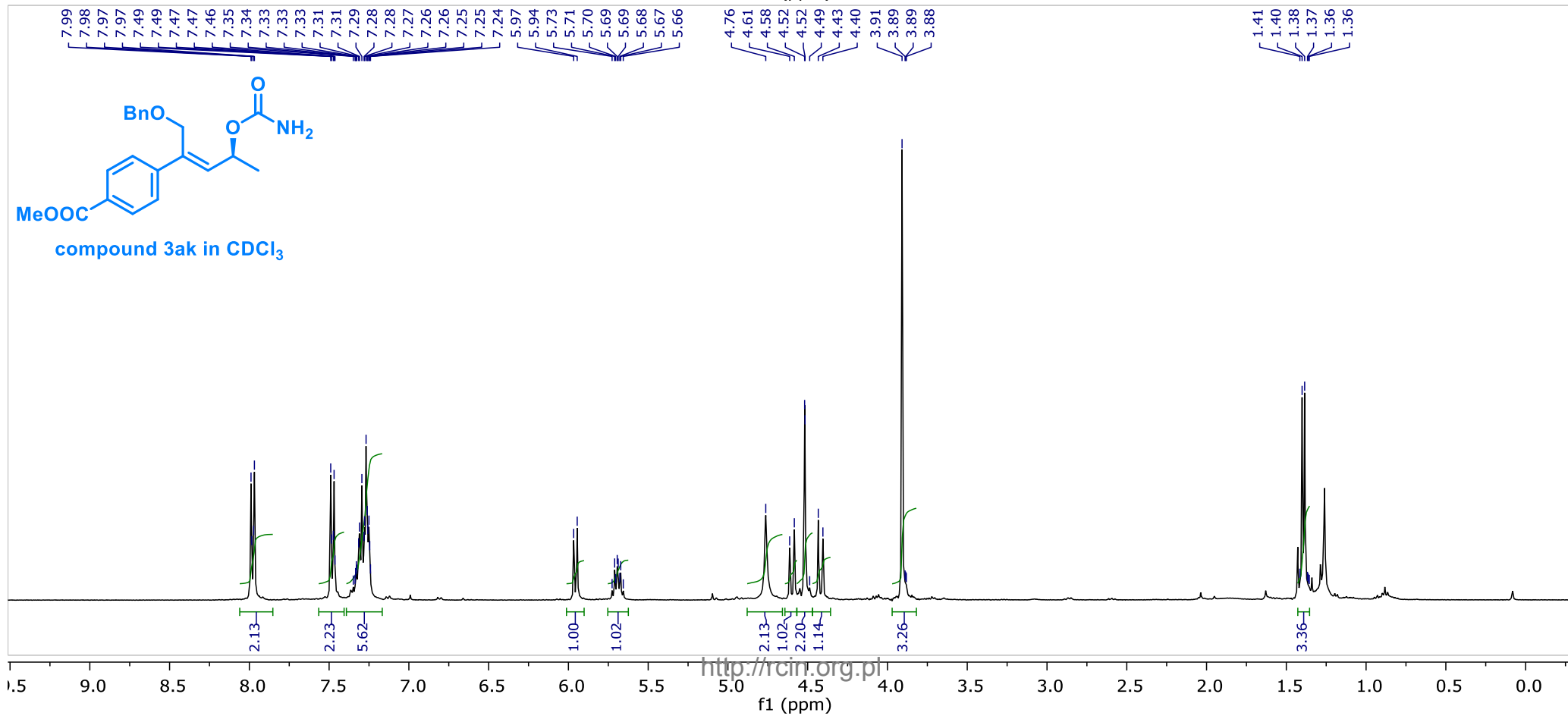
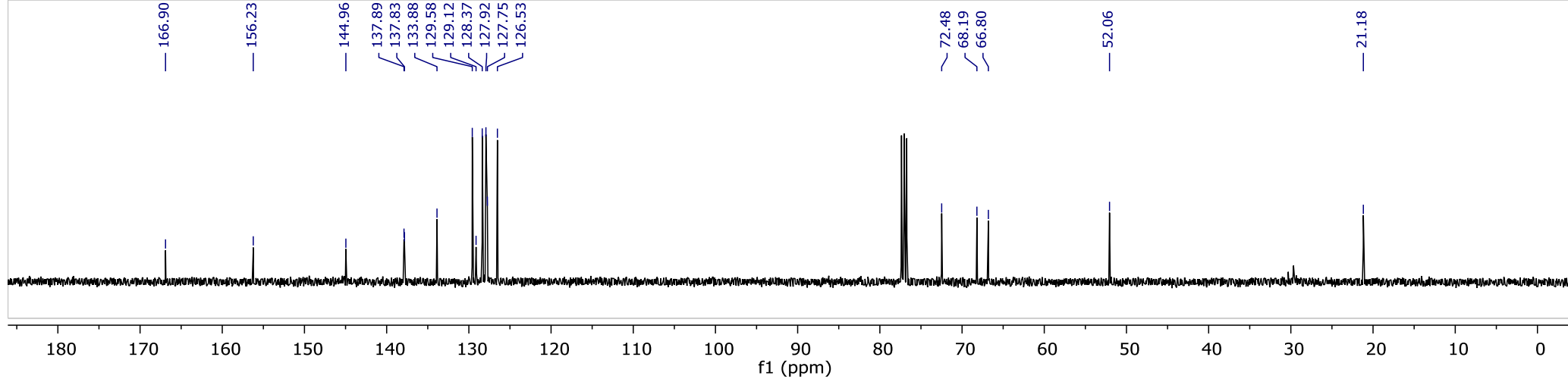


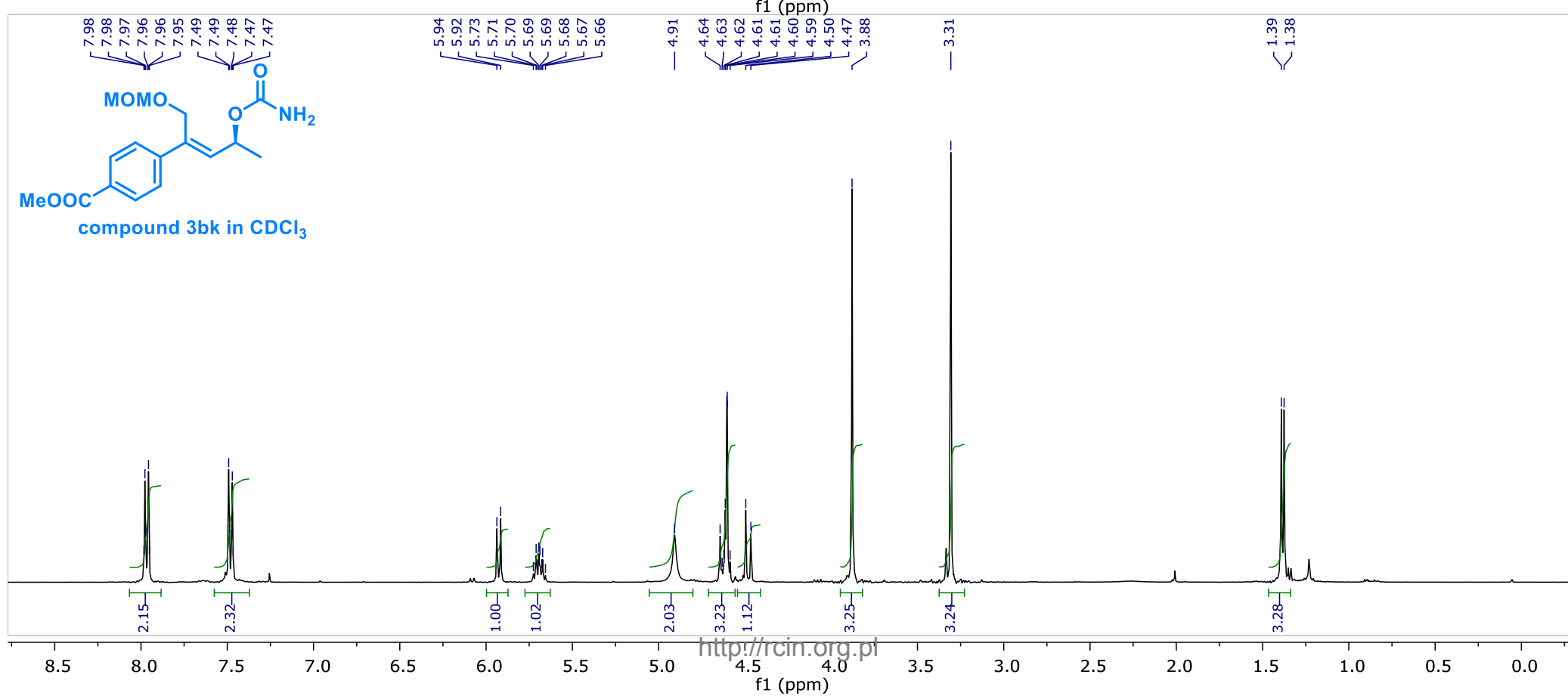
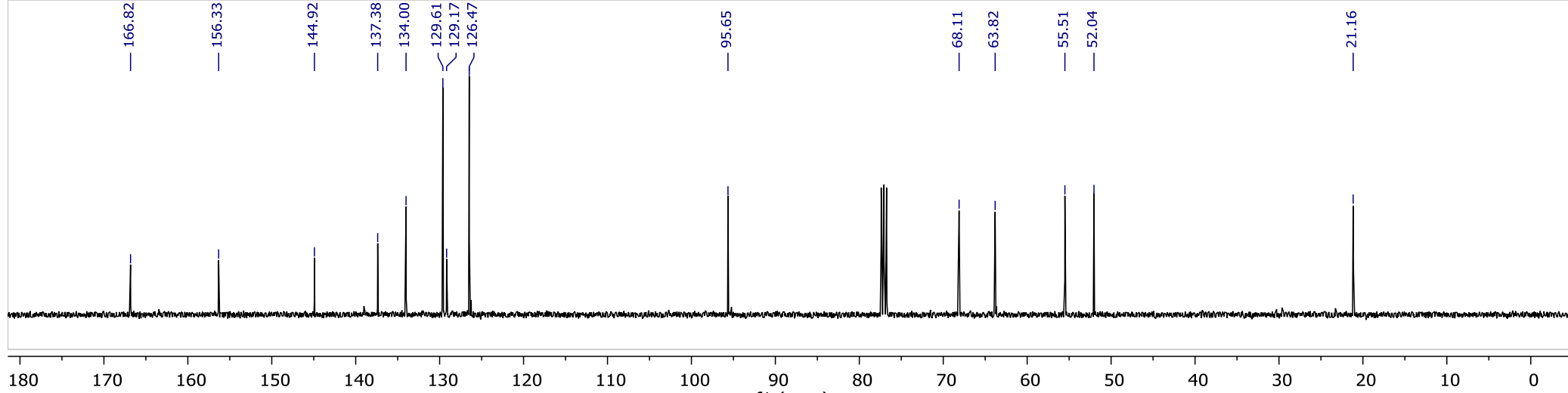


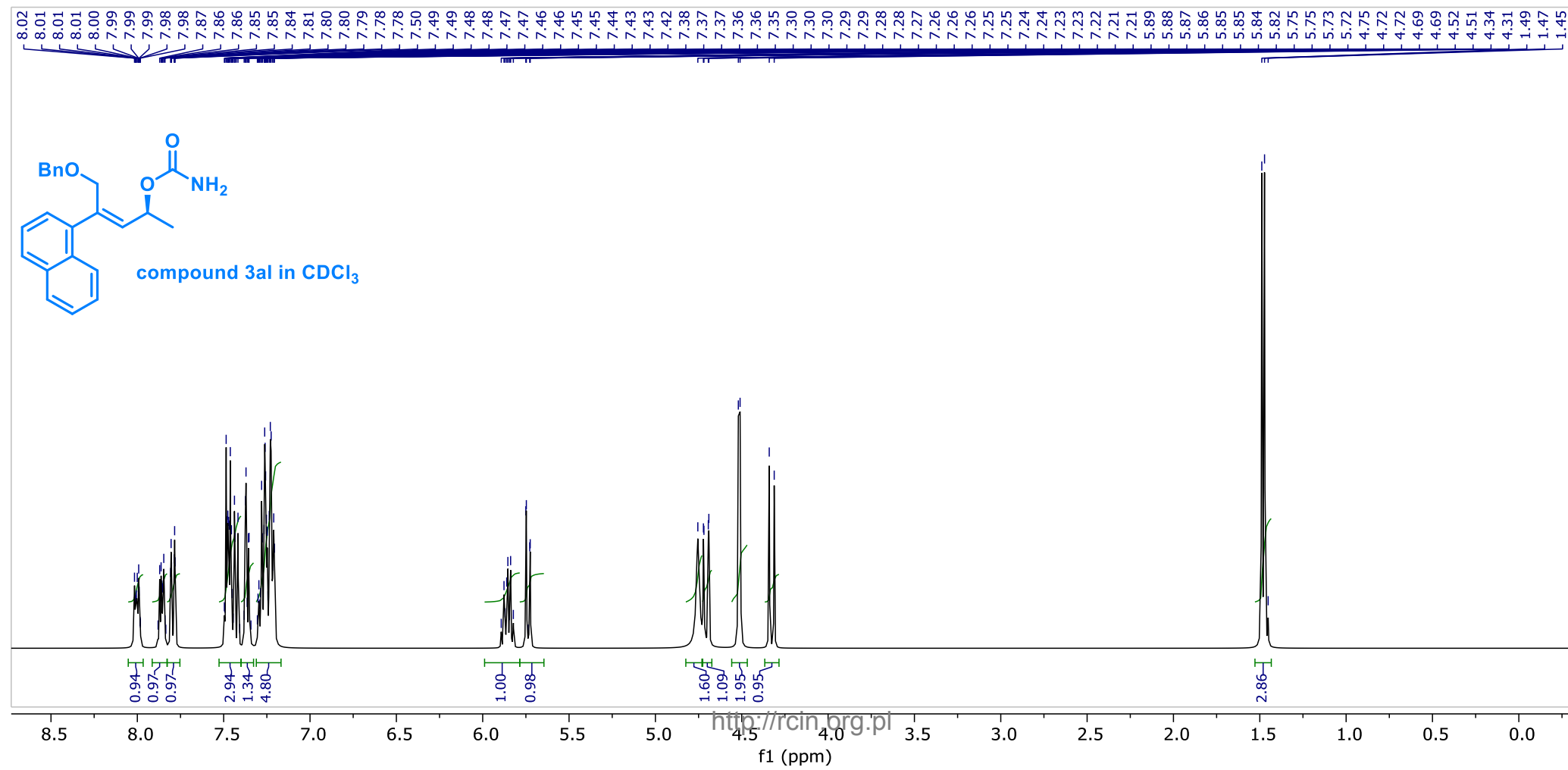
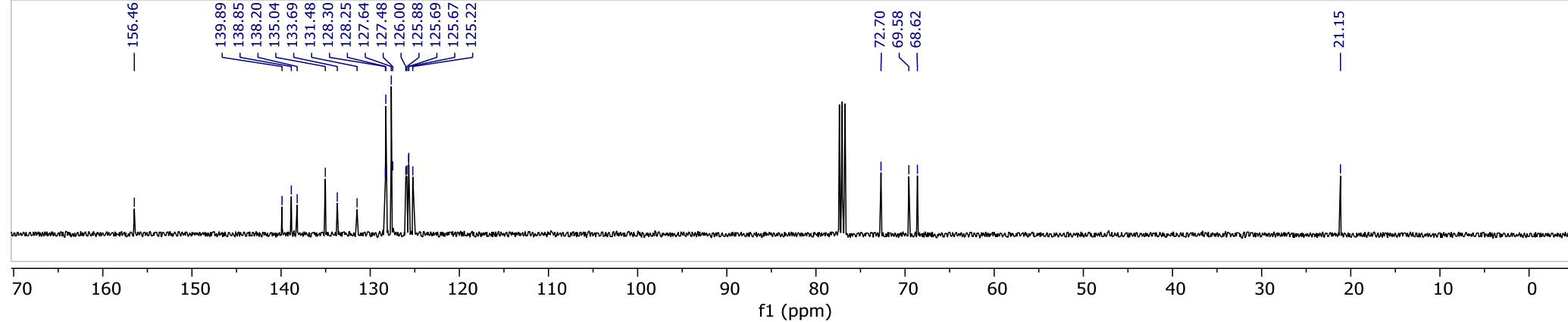


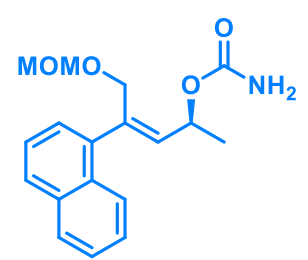
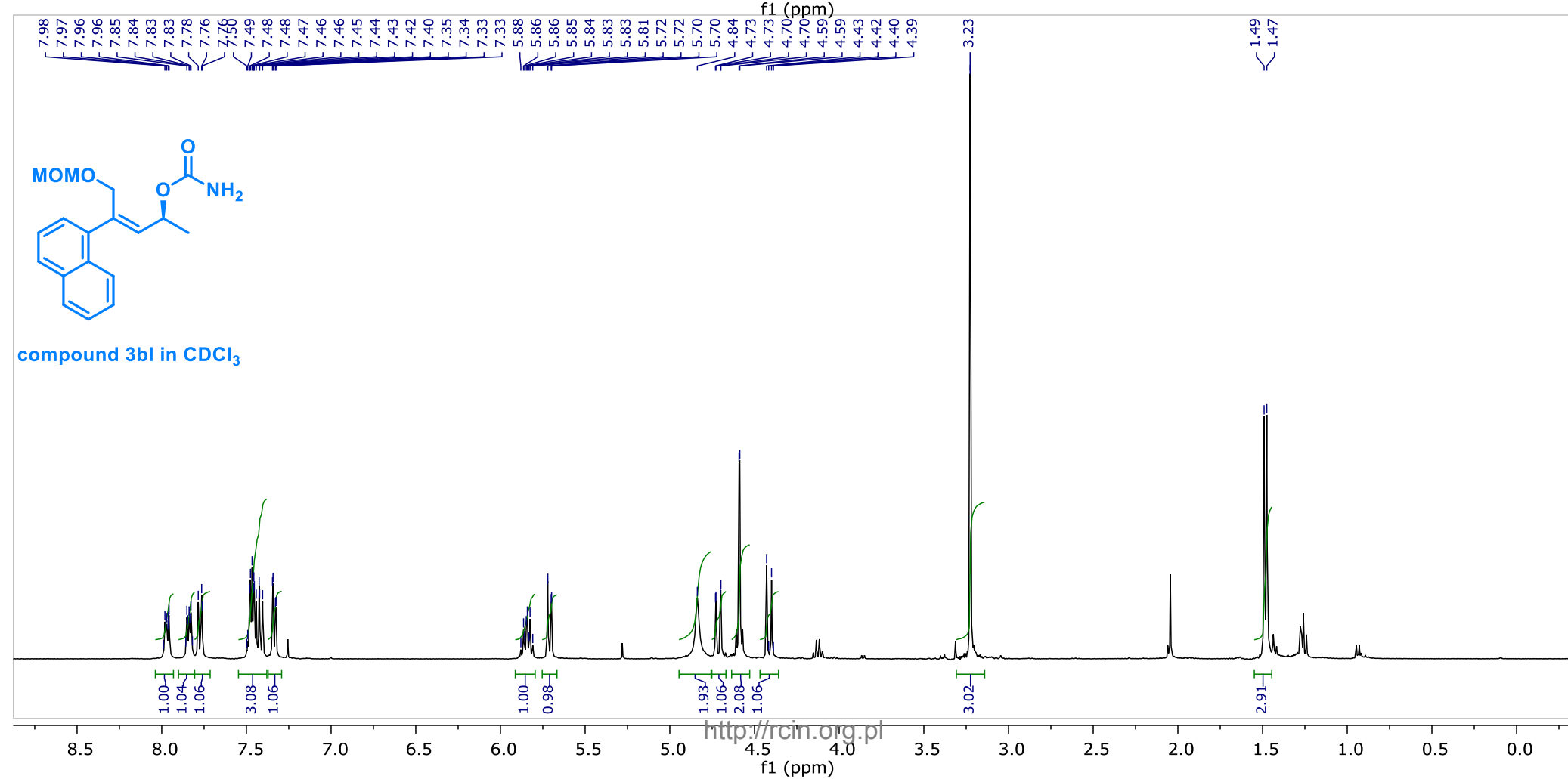
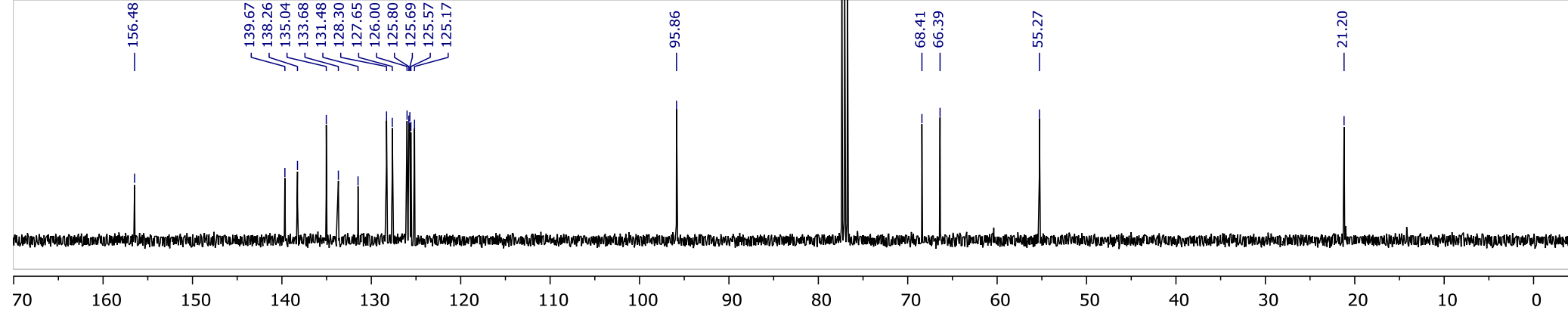






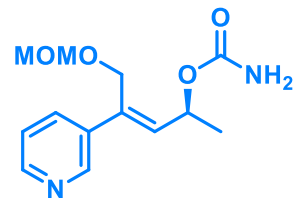
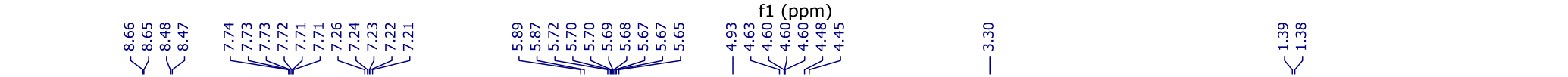
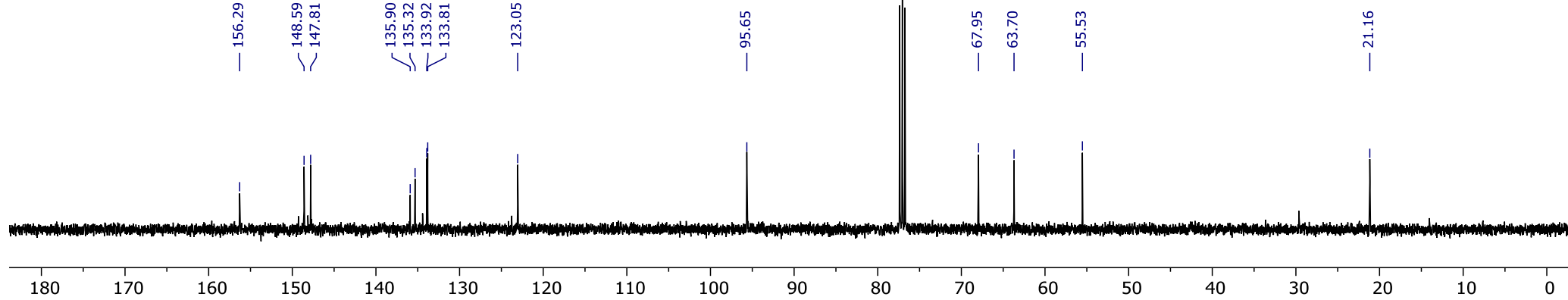




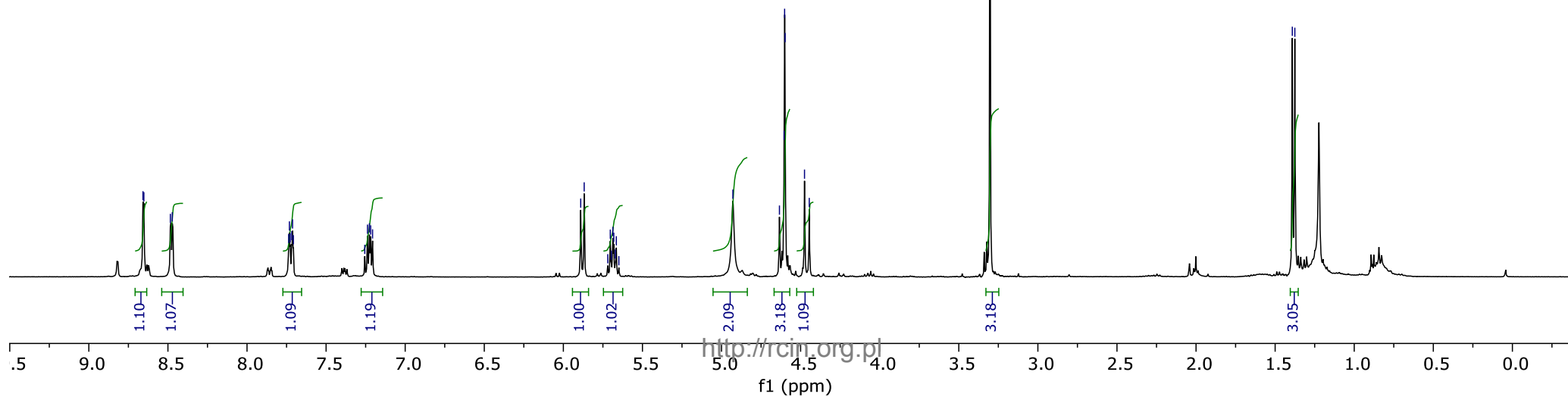


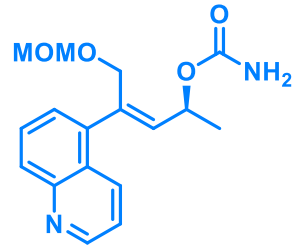
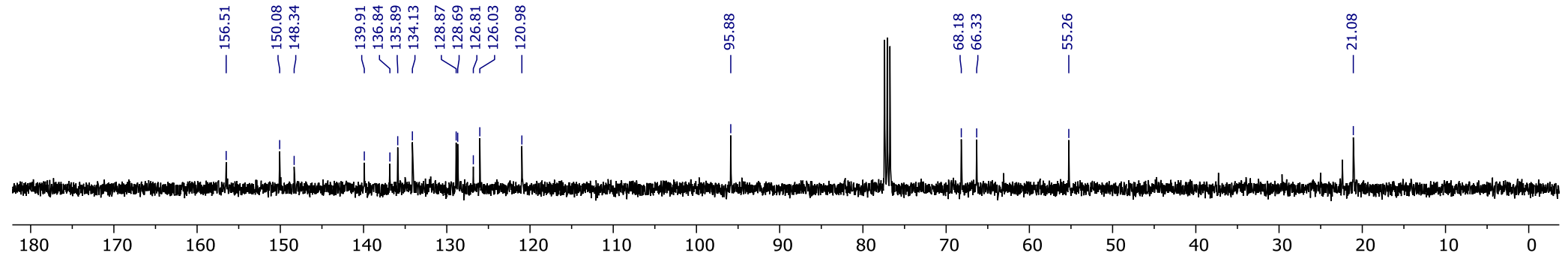
compound 3bl in CDCl<sub>3</sub>



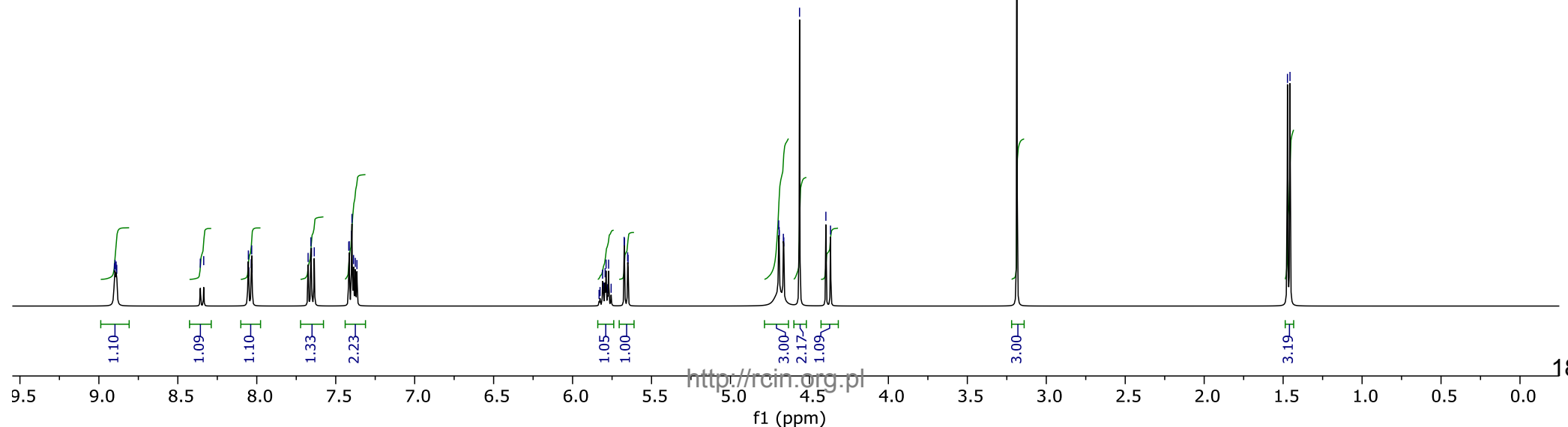


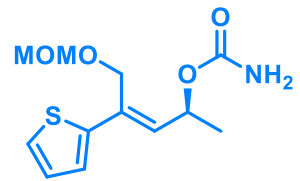
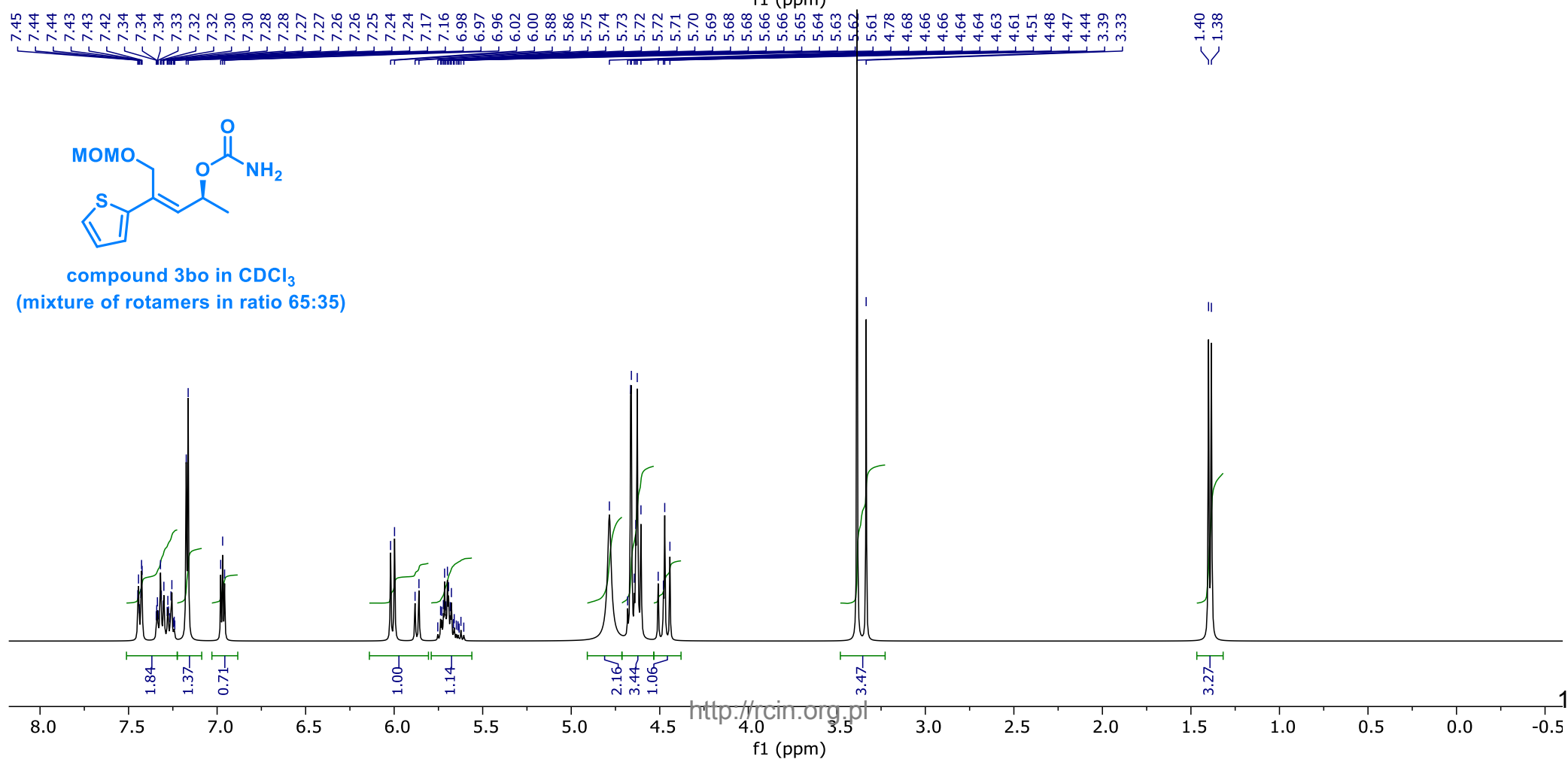
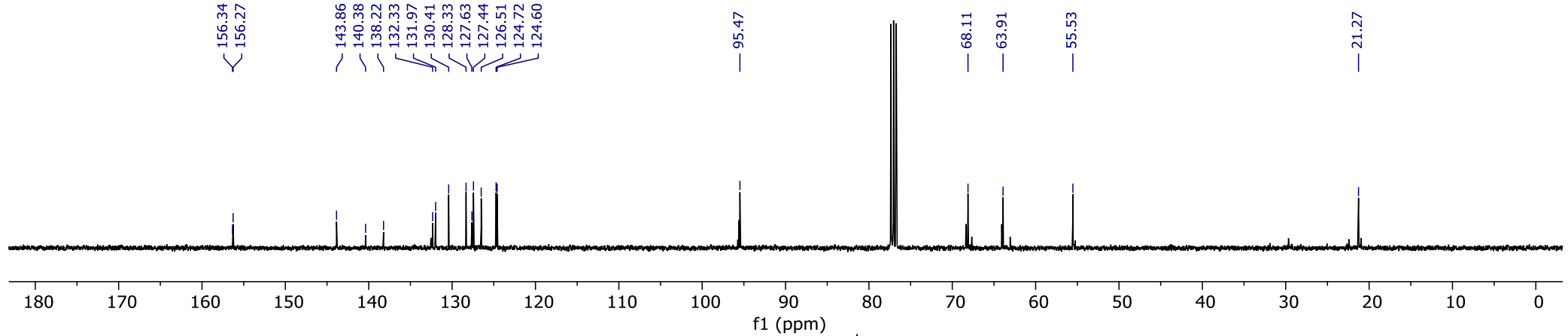
compound 3bm in CDCl<sub>3</sub>  
(mixture of rotamers)



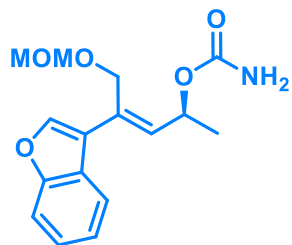
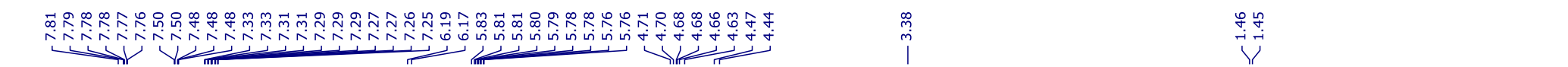
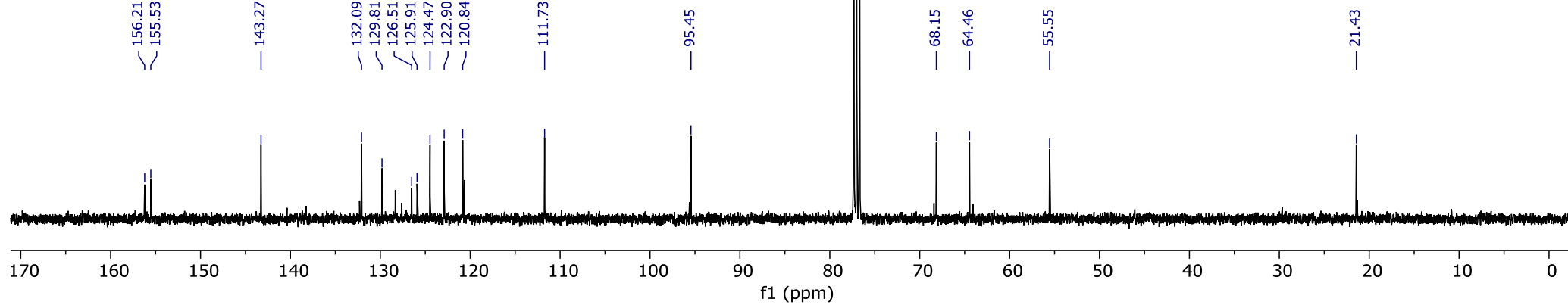


compound 3bn in CDCl<sub>3</sub>

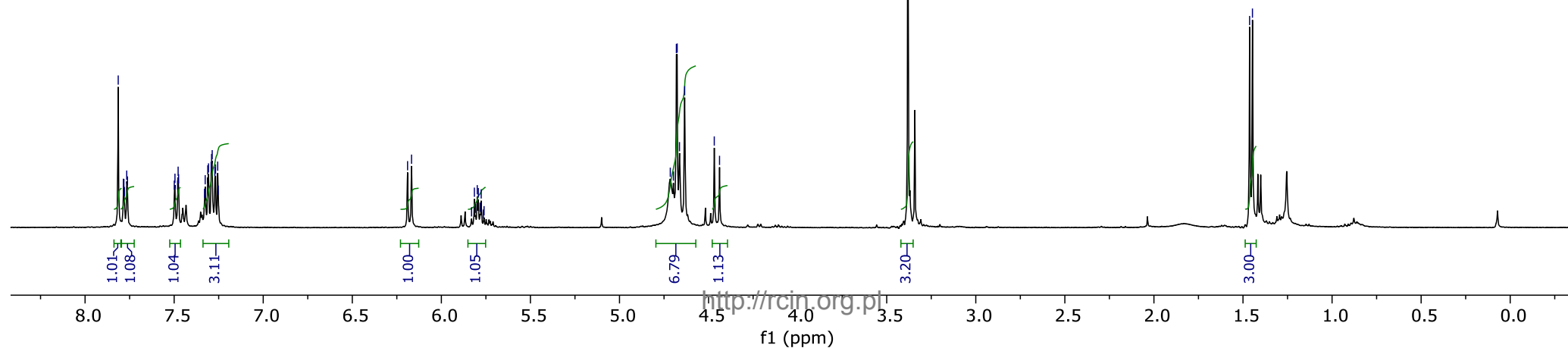


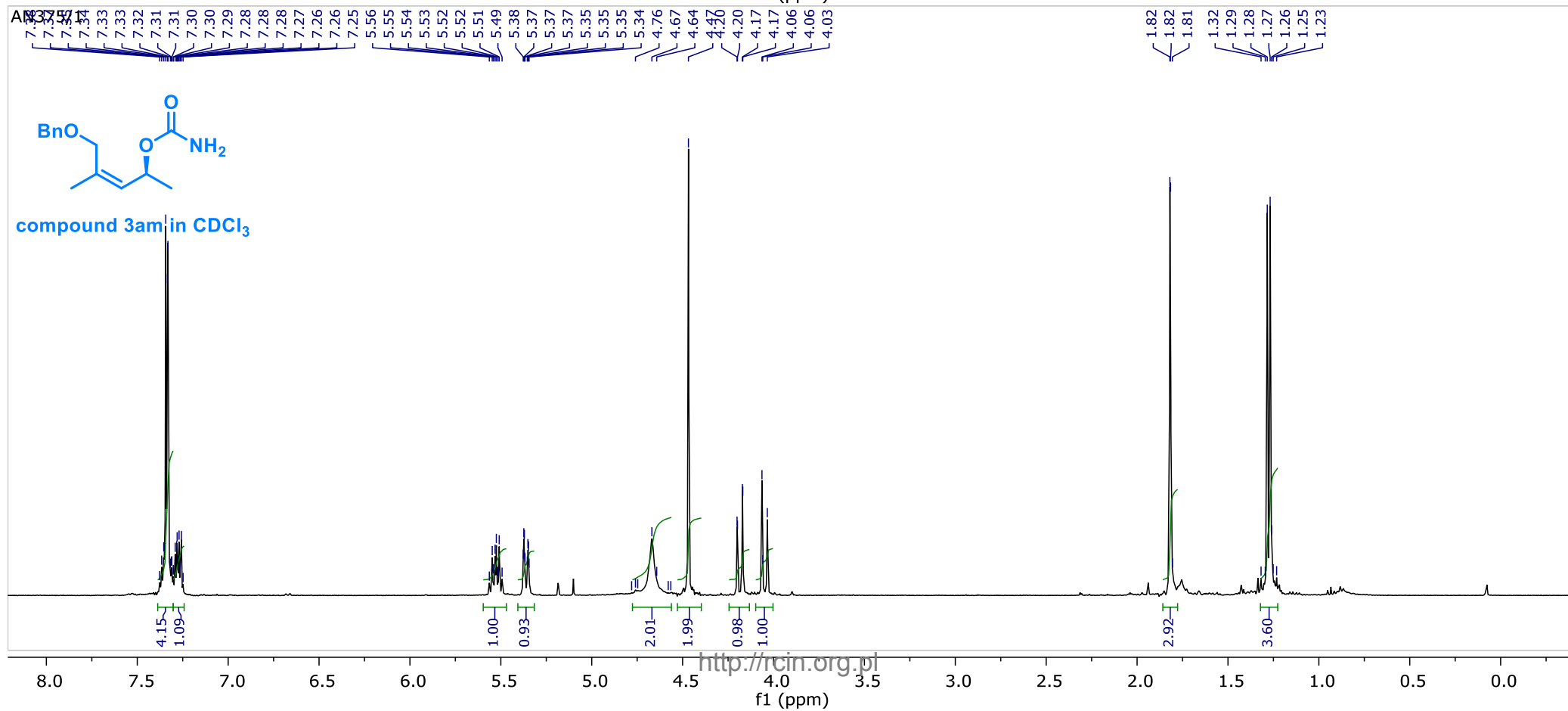
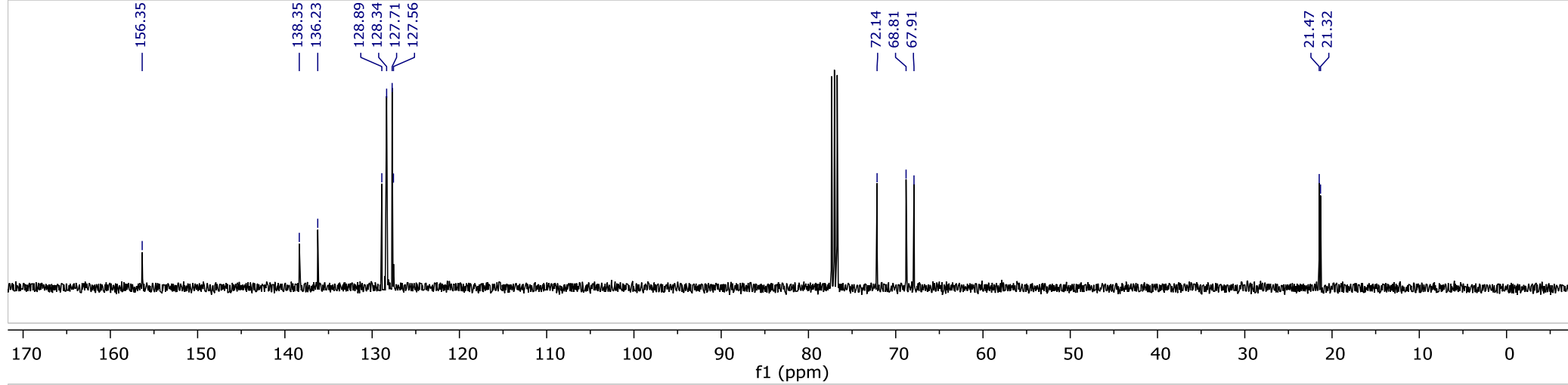


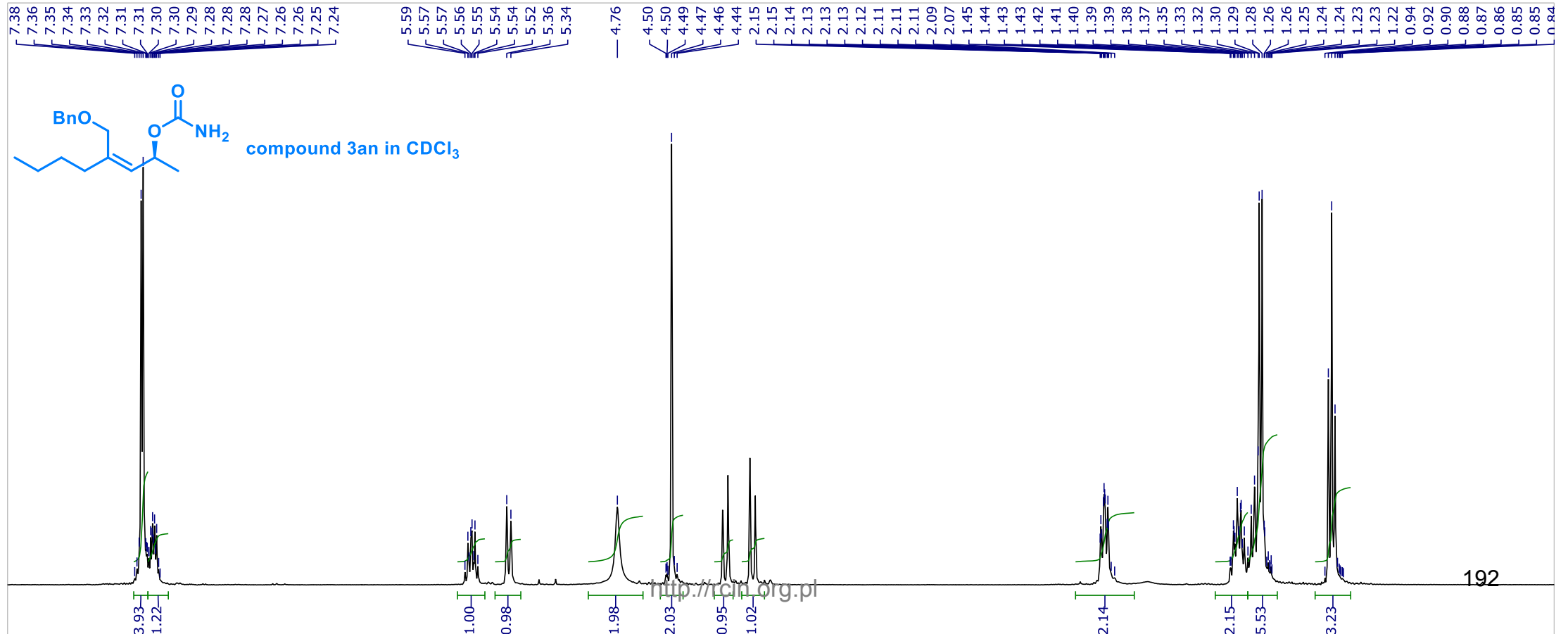
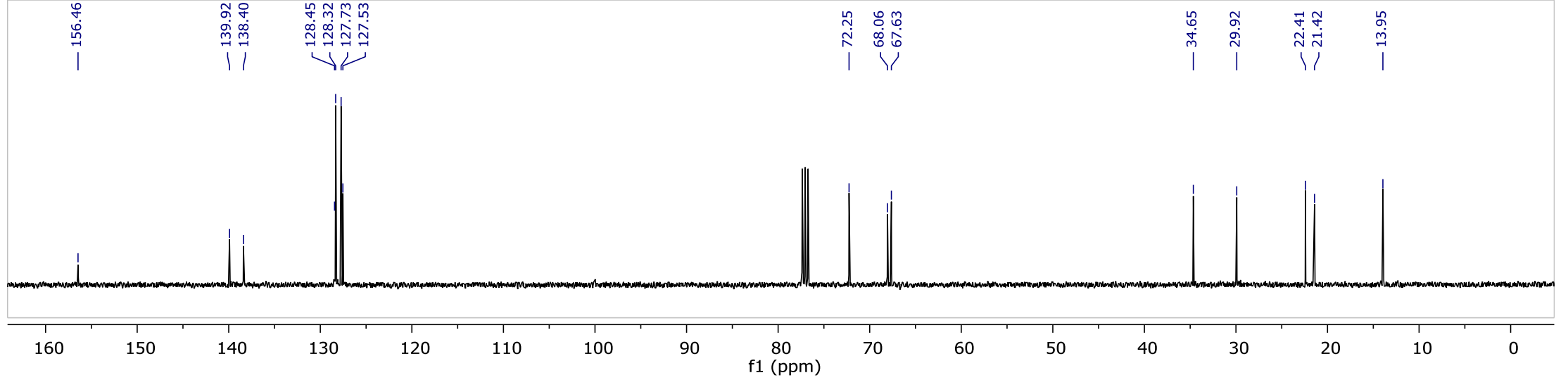
compound 3bo in CDCl<sub>3</sub>  
(mixture of rotamers in ratio 65:35)

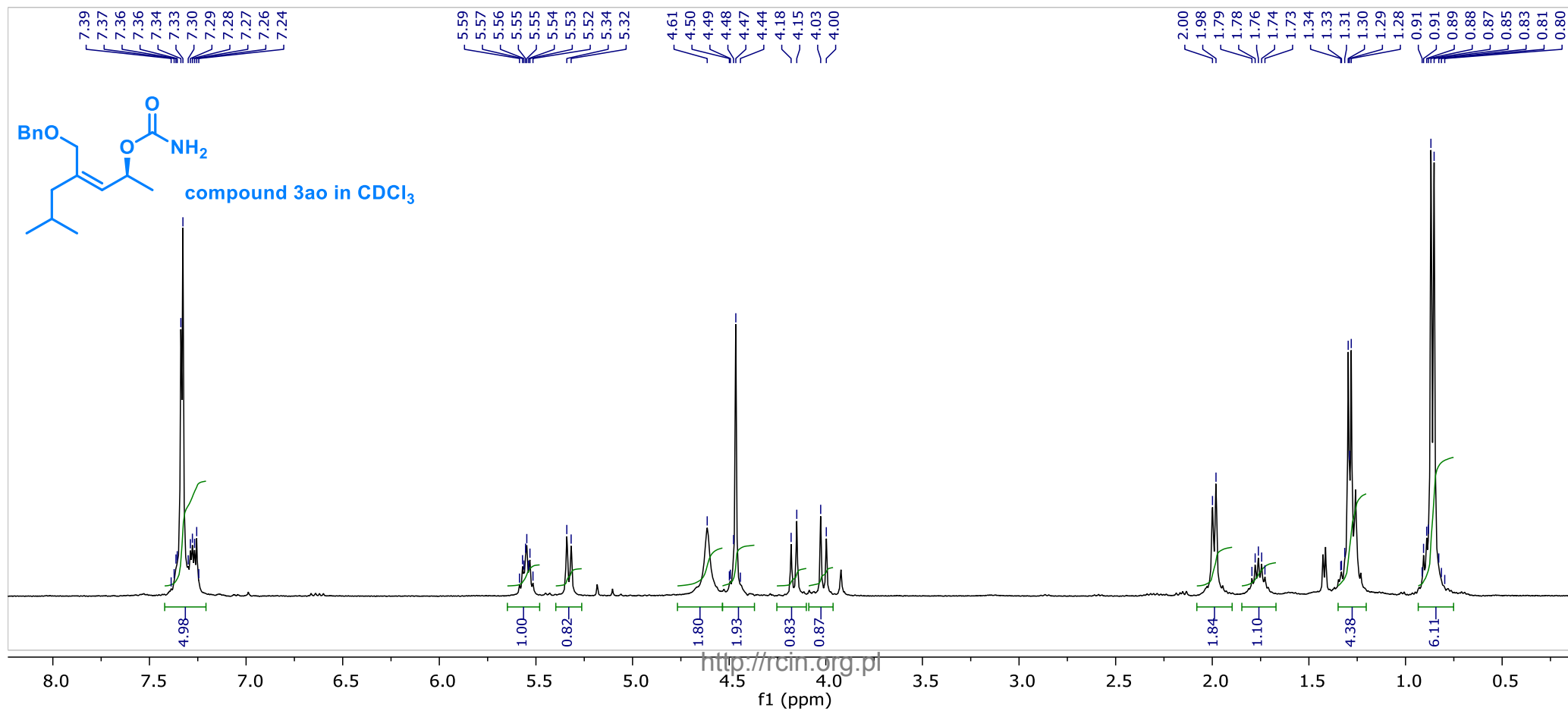
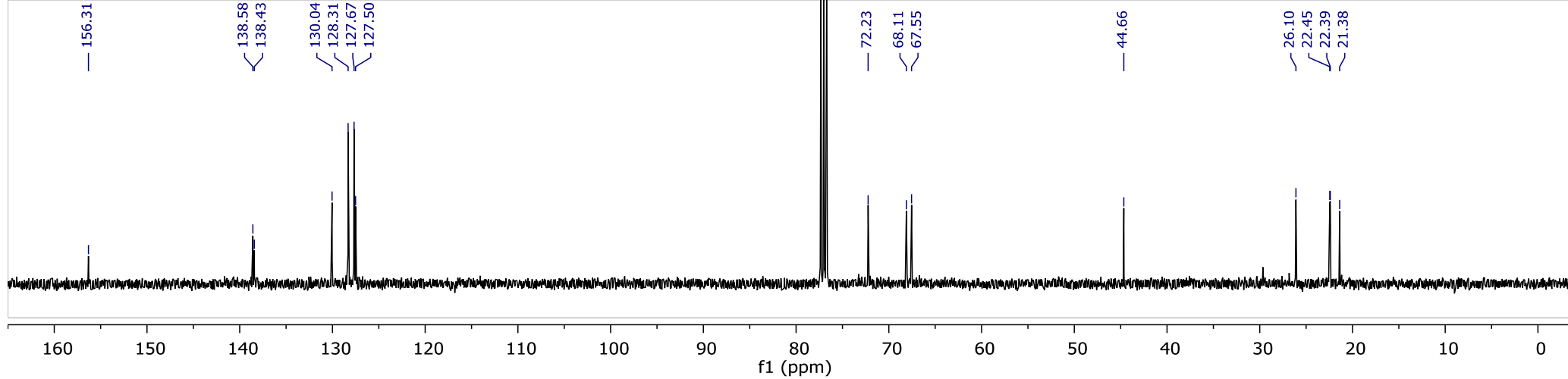


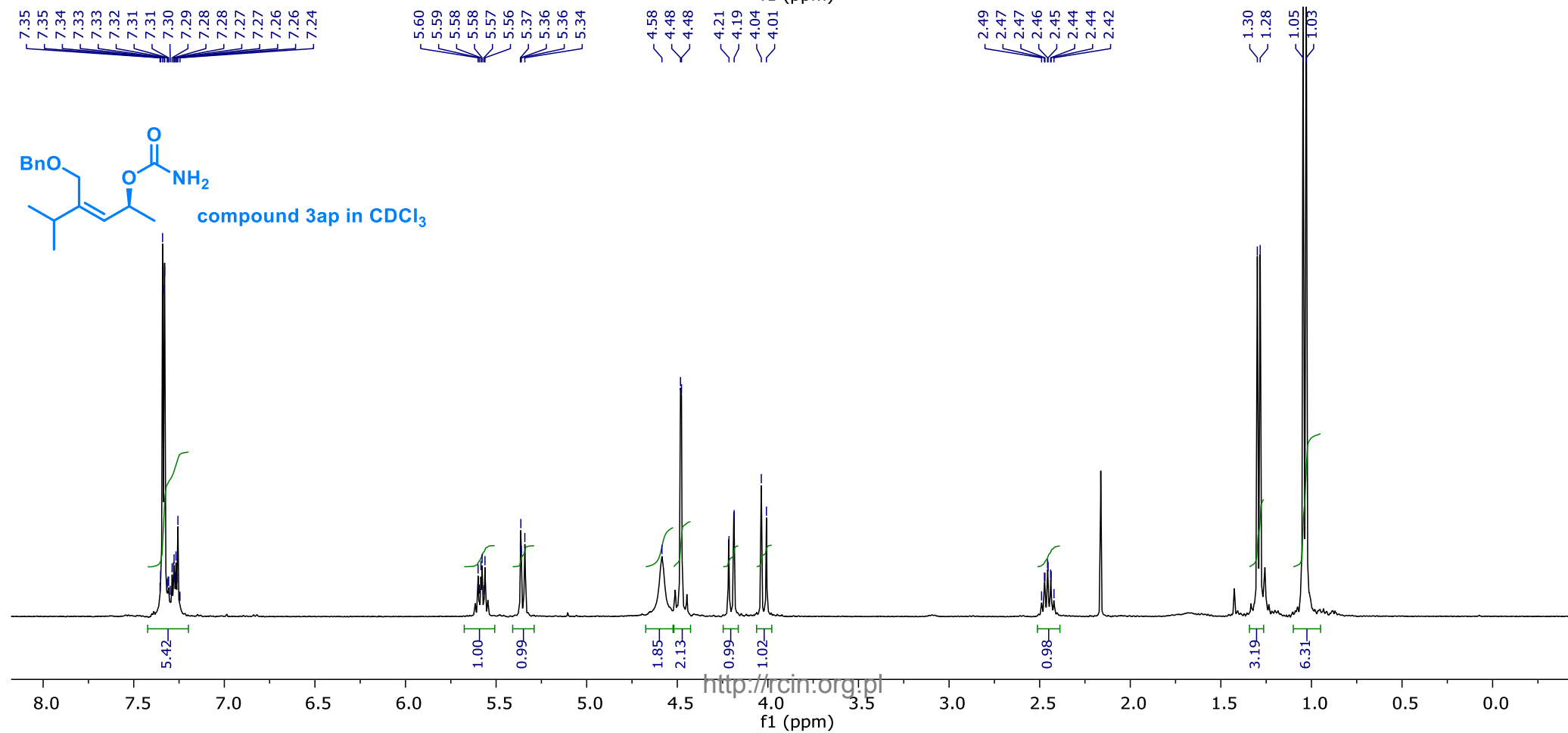
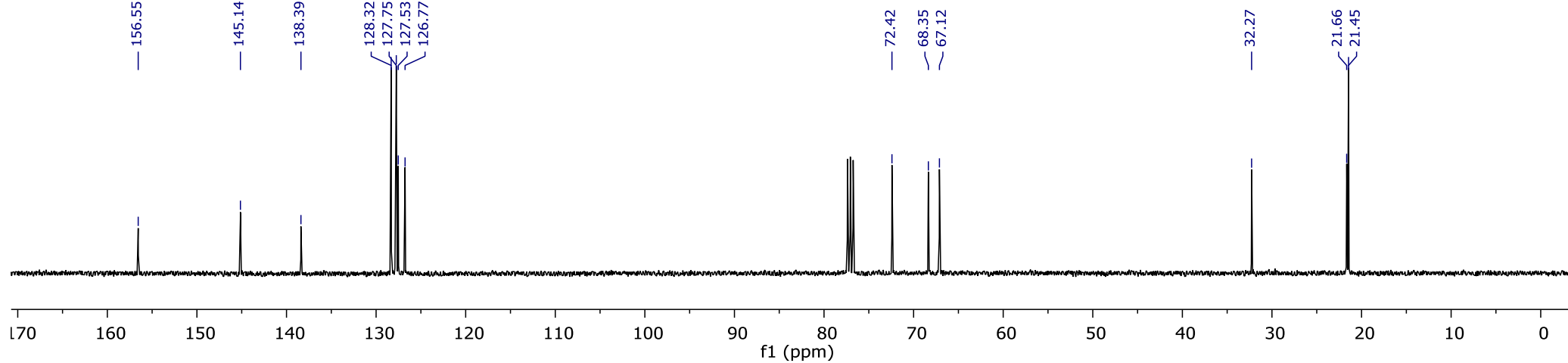
compound 3bp in CDCl<sub>3</sub>  
(mixture of rotamers)



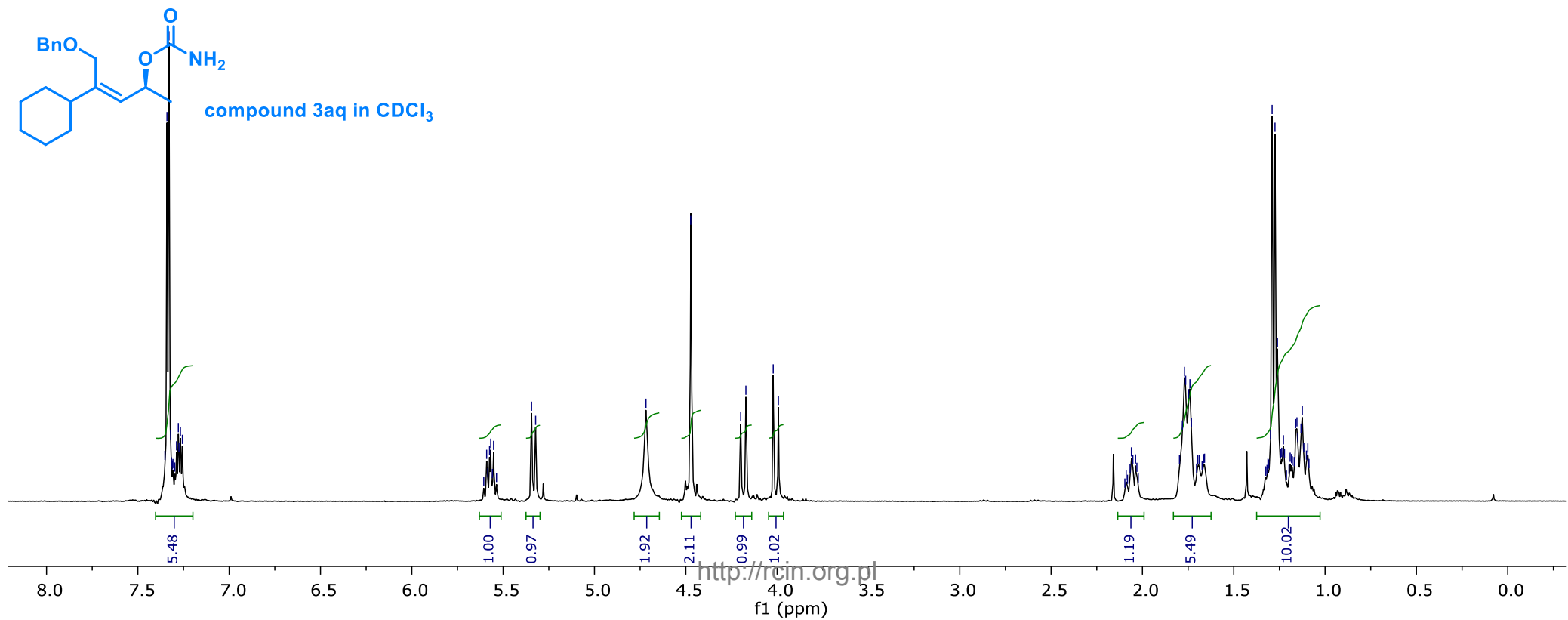
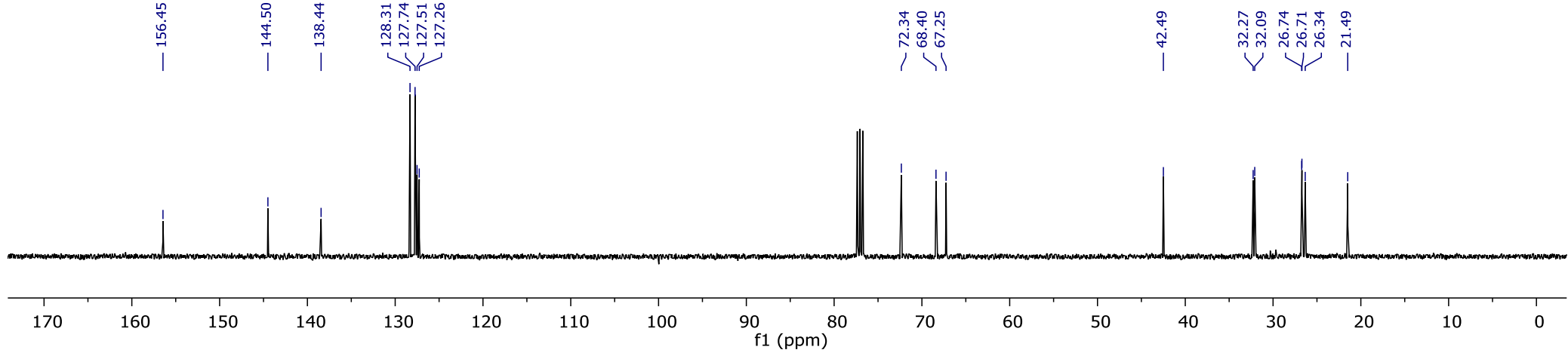


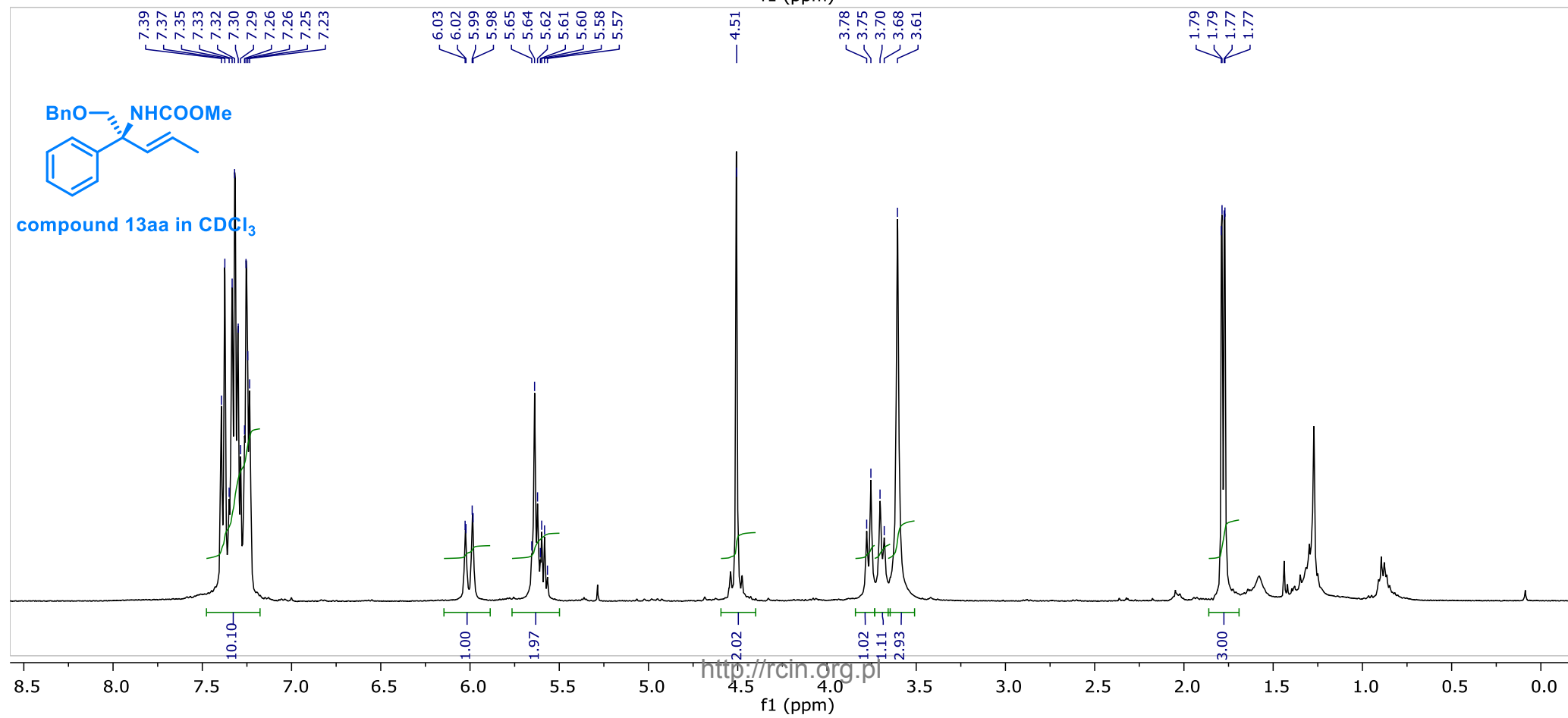
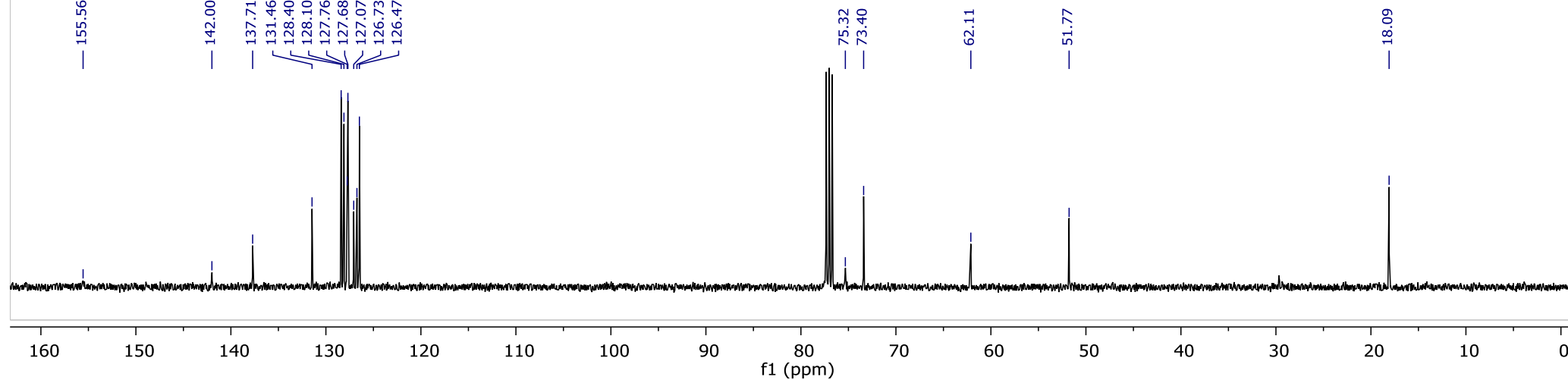


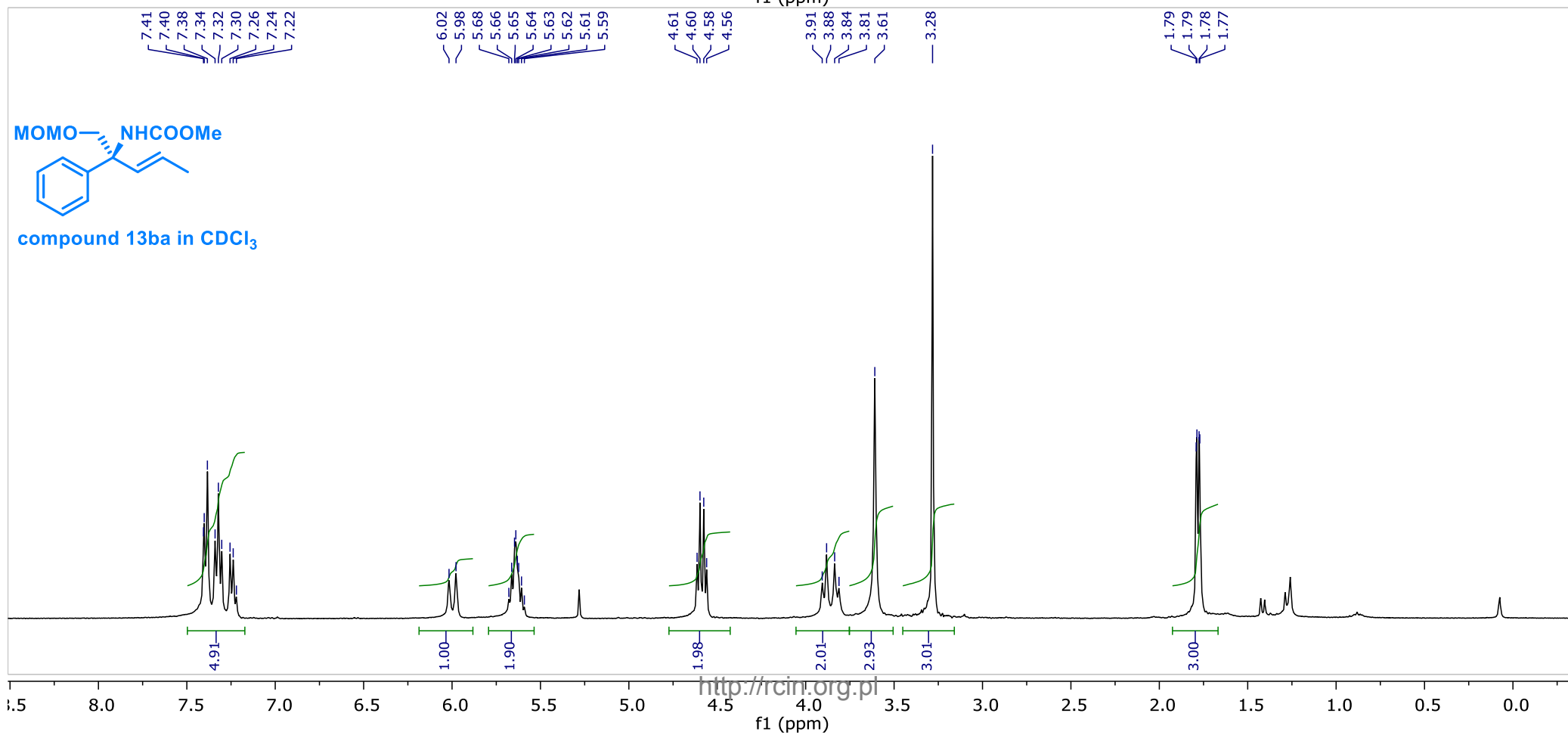
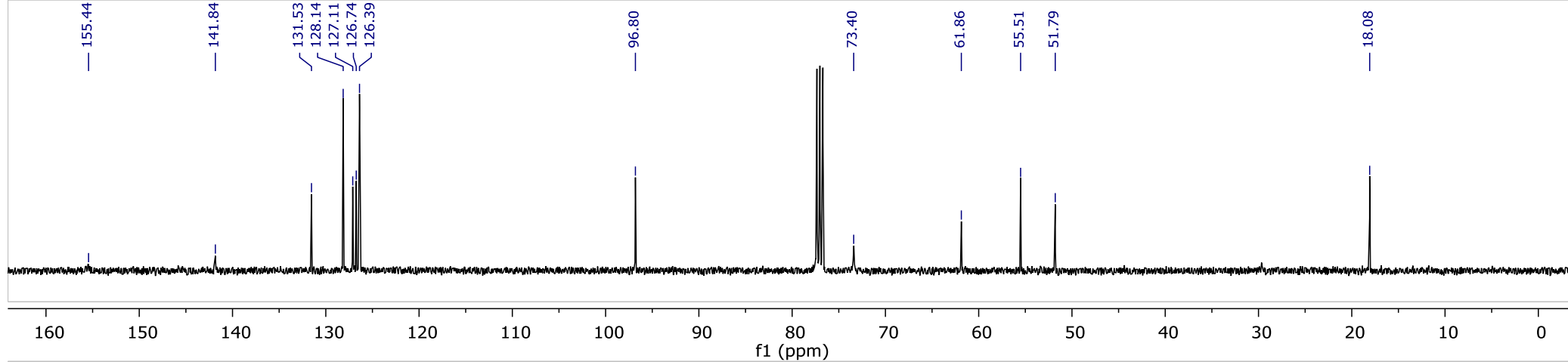






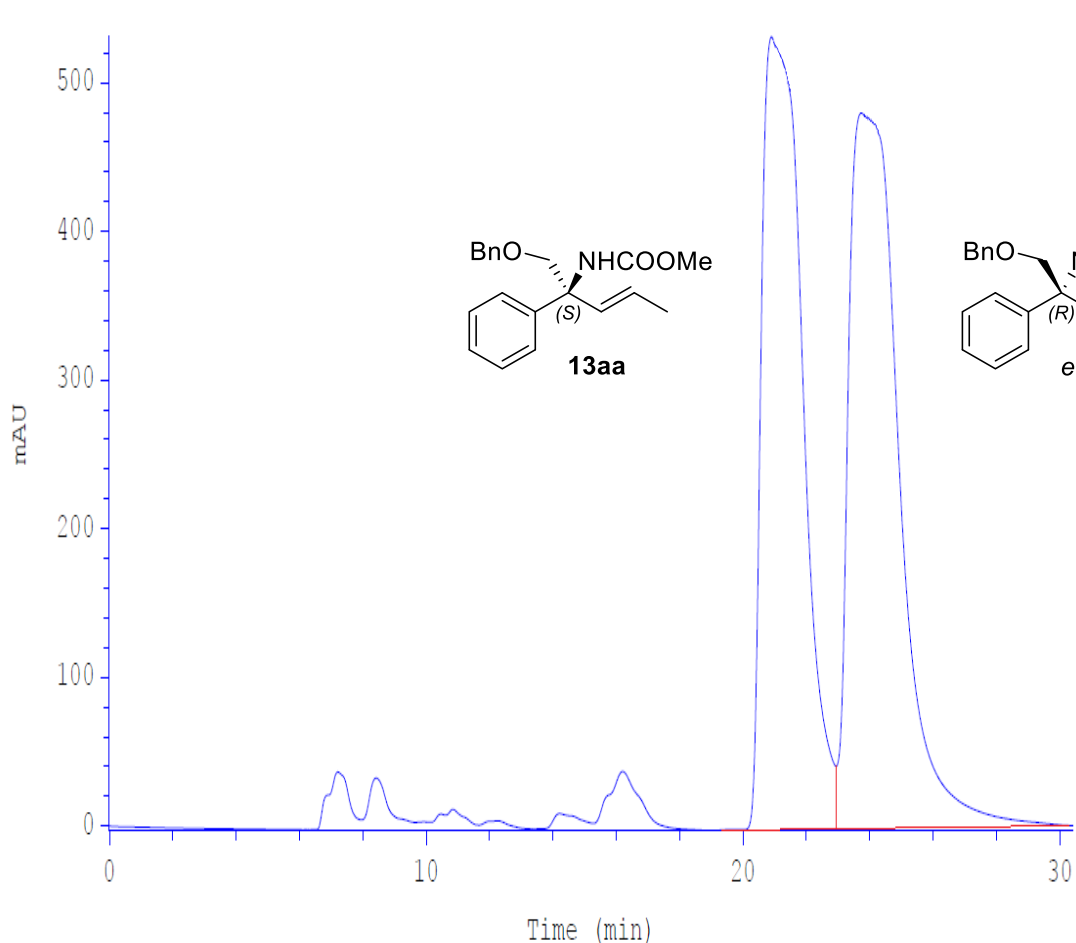




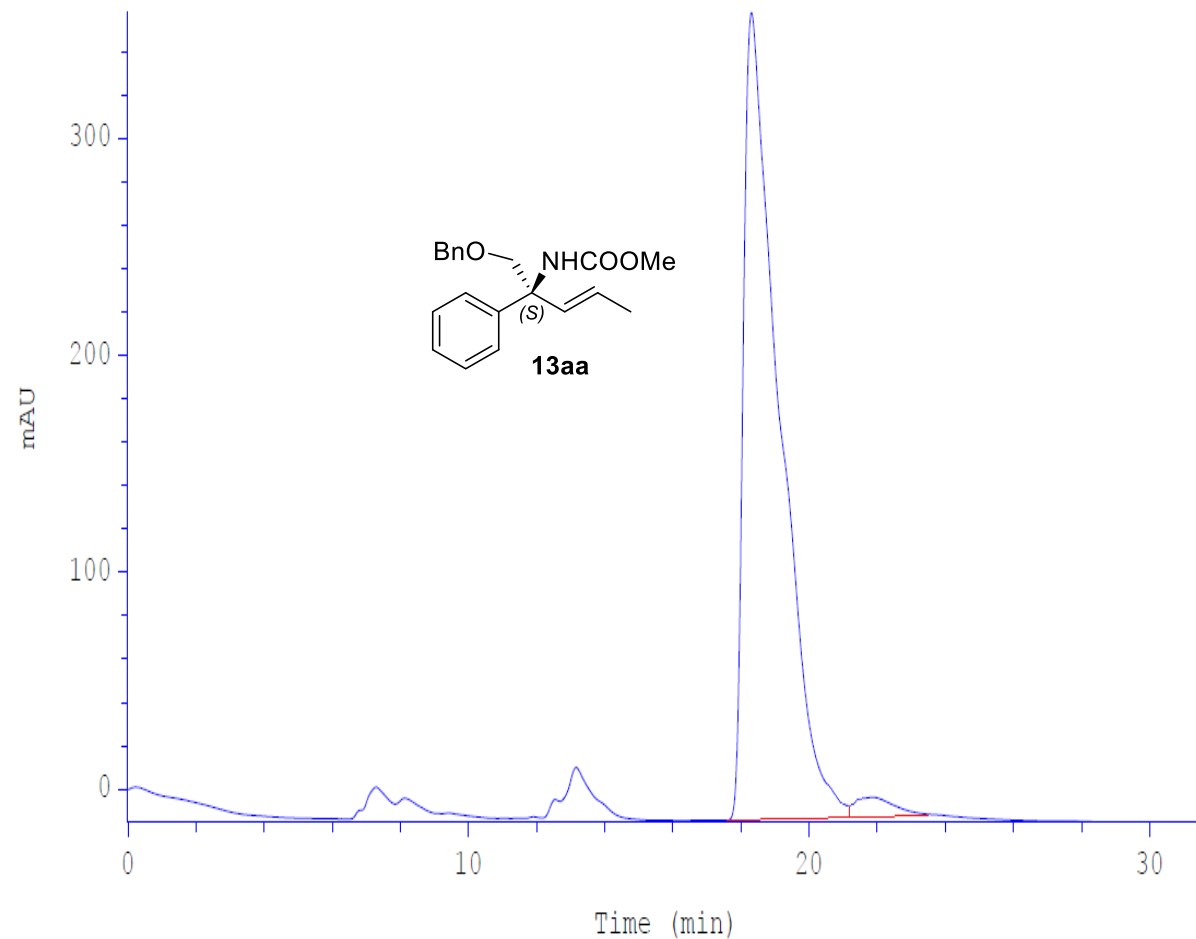


## HPLC chromatogram of compounds rac-13aa and 13aa

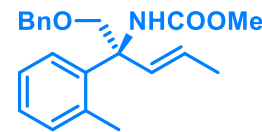
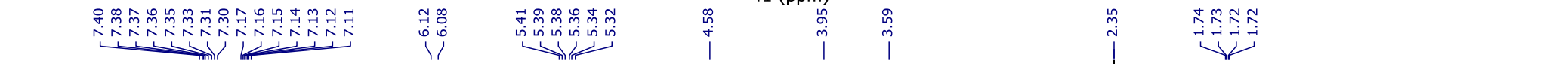
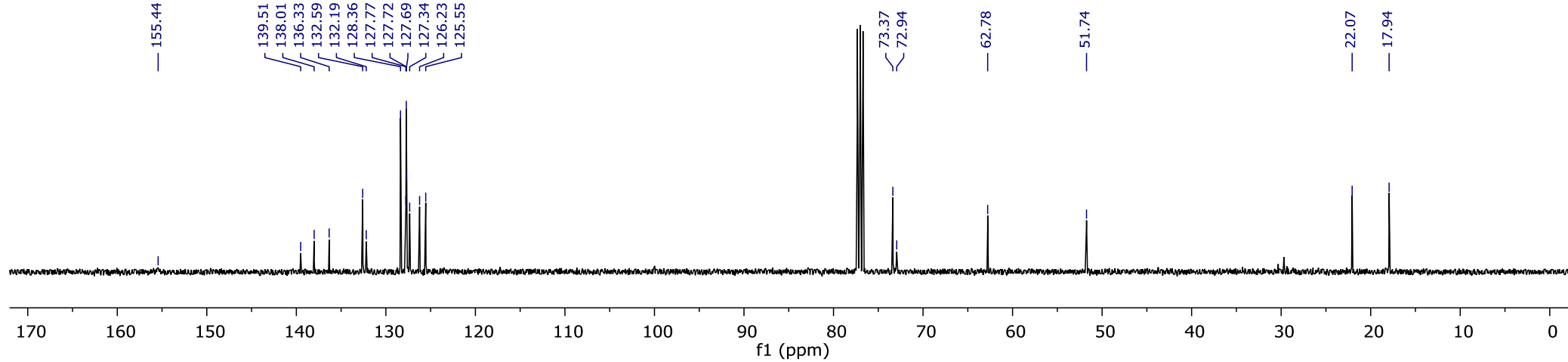
Conditions: column Chiralpak AD-H, 5% *i*-PrOH in hexanes, 0.5 mL/min, detection: UV, 215 nm



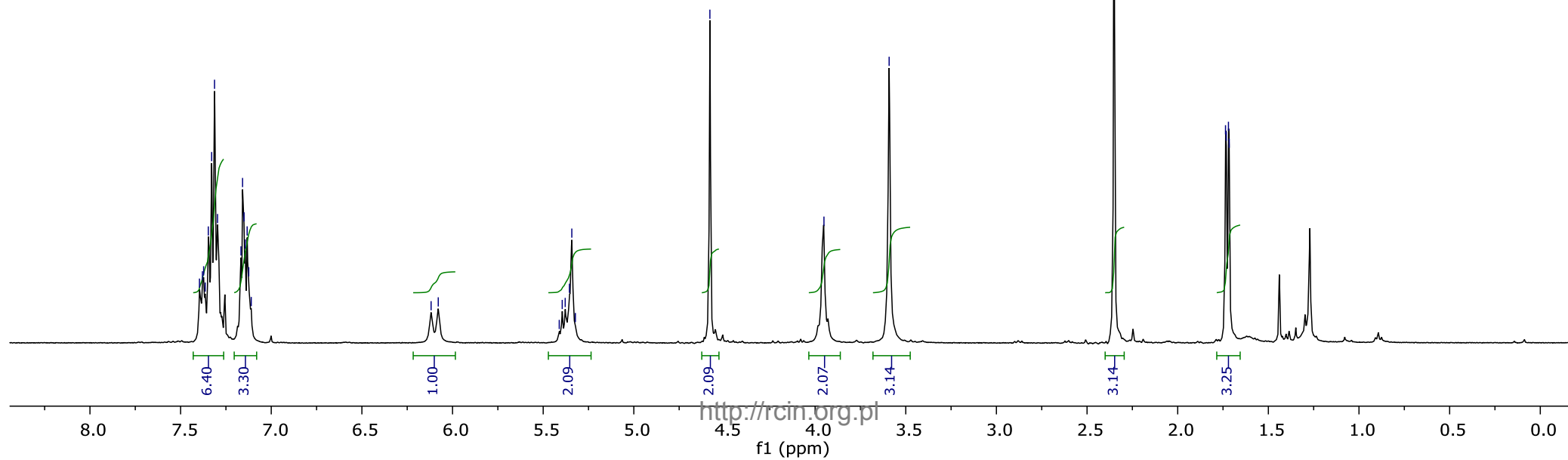
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	20.906	19.09	22.94	789.047	532.985	47.0451	1.382
2	23.740	22.94	30.37	888.168	481.202	52.9549	1.649

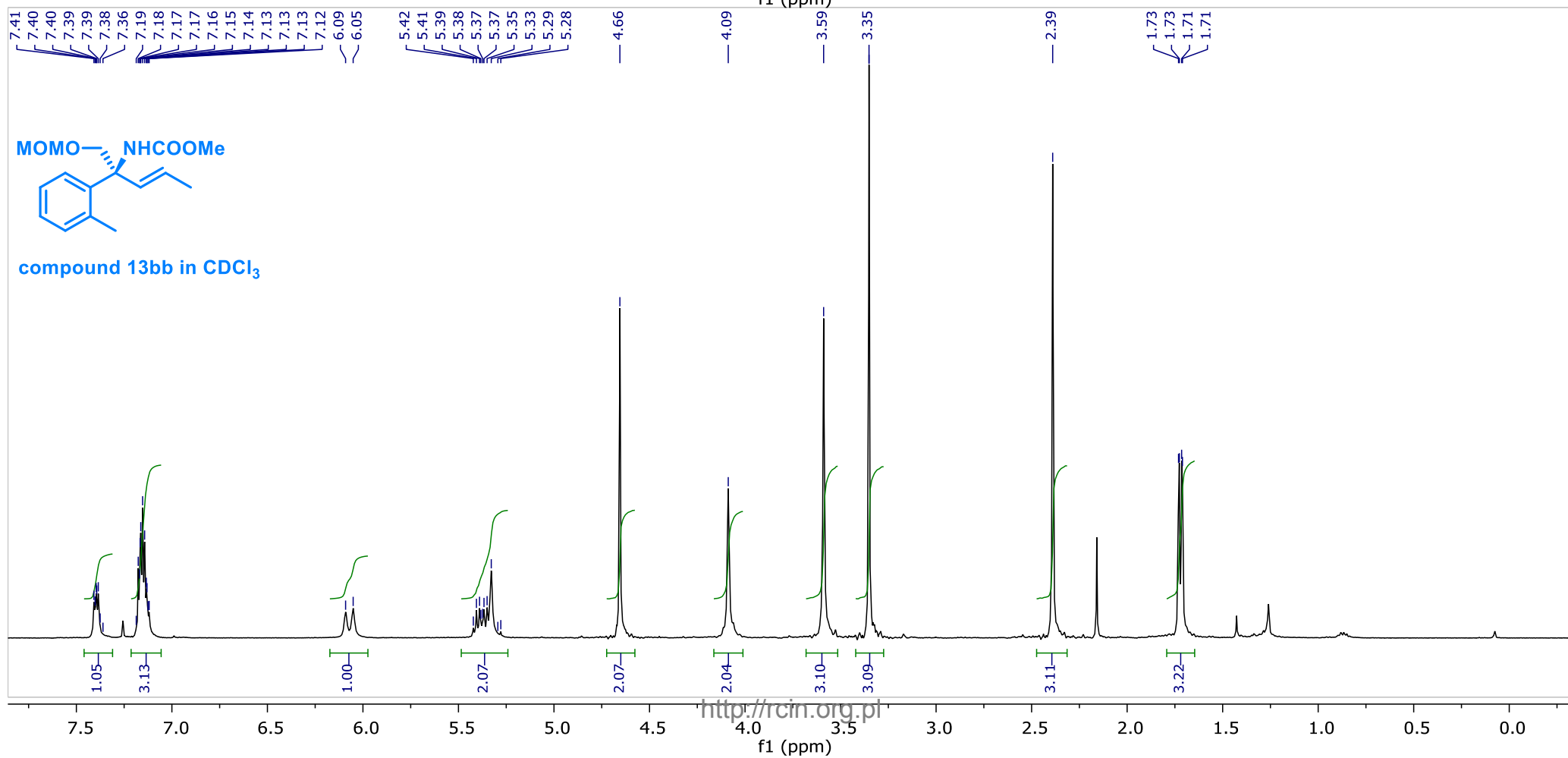
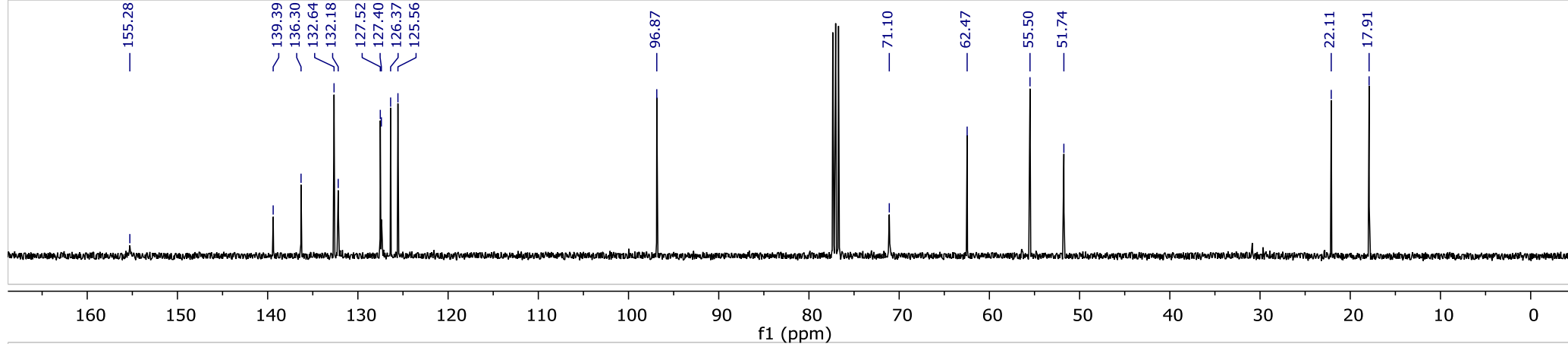


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	18.305	17.60	21.50	457.155	371.738	98.0626	1.052
2	21.872	21.50	23.45	9.03176	8.46852	1.9374	1.087



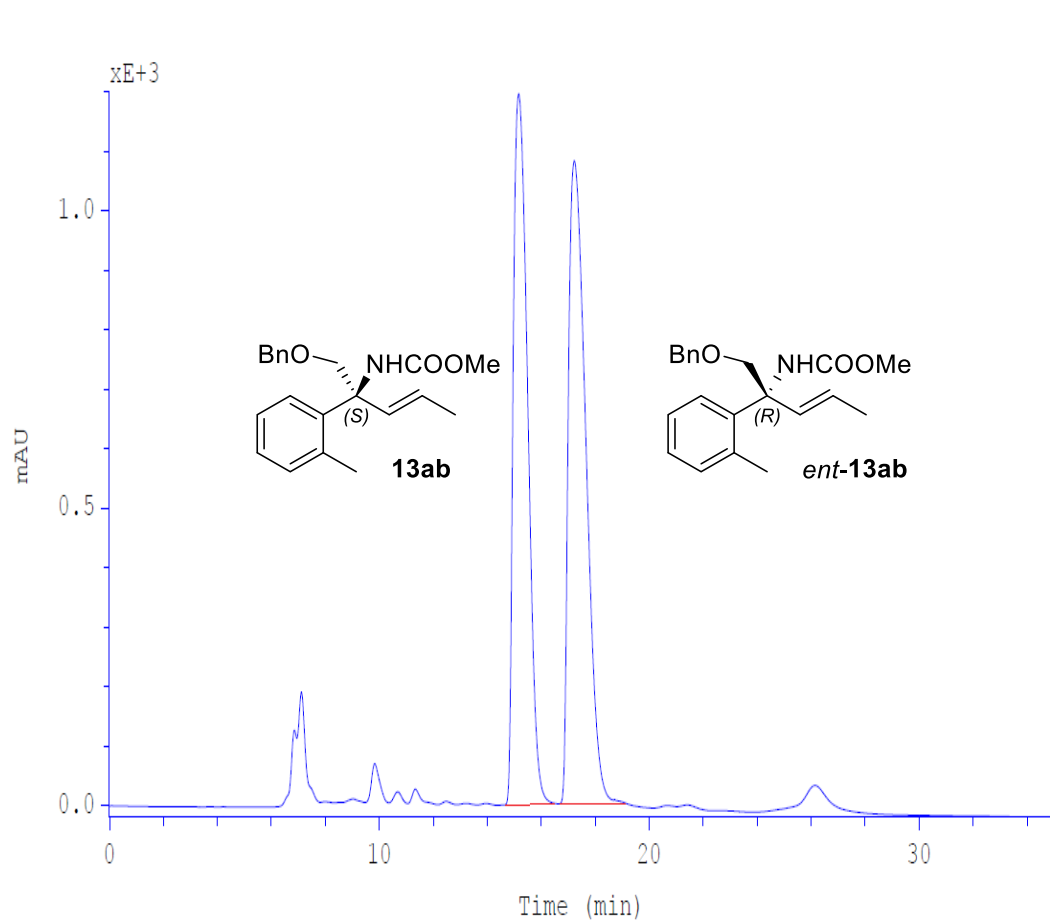
compound 13ab in CDCl<sub>3</sub>



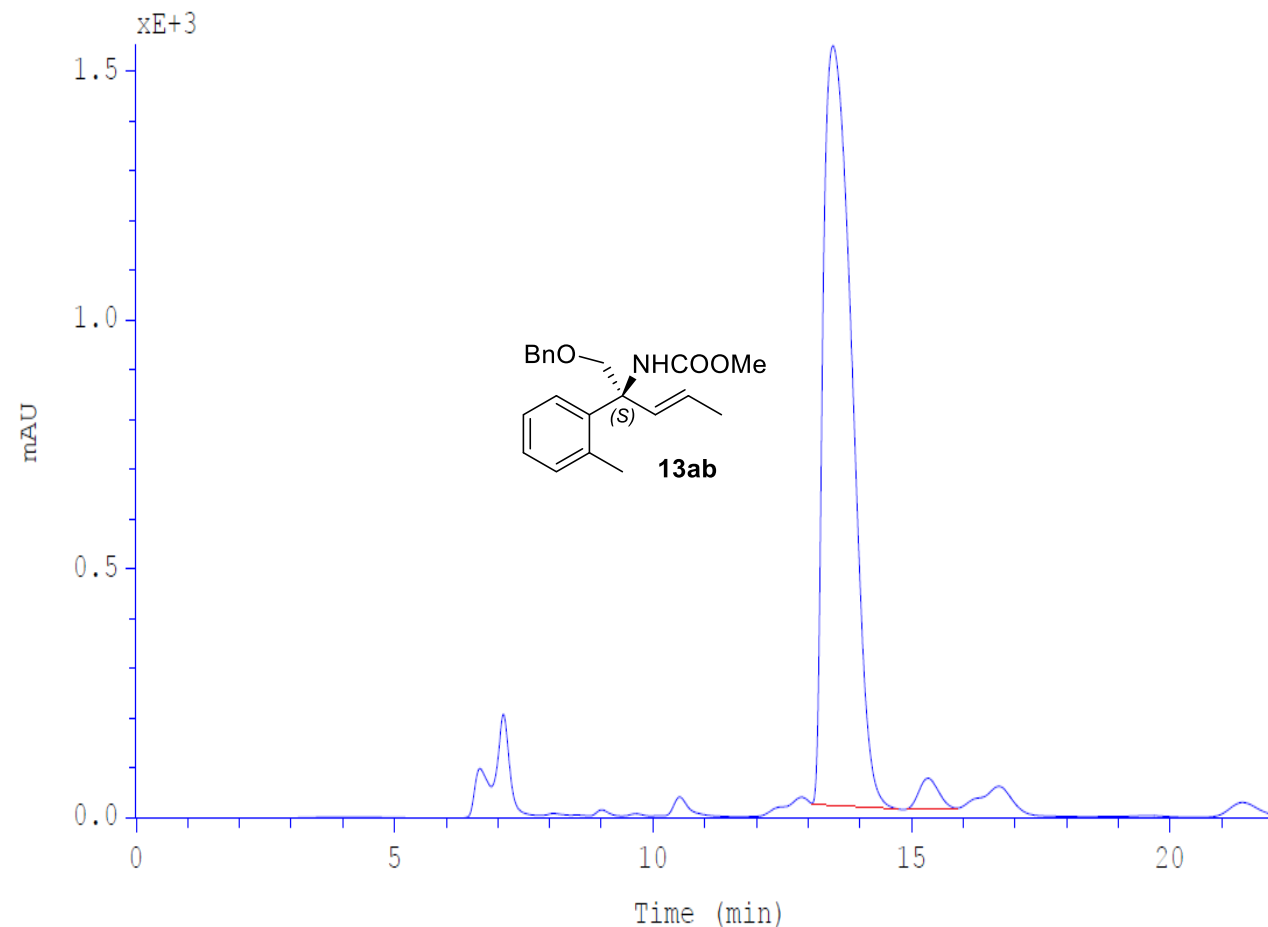


## HPLC chromatogram of compounds rac-13ab and 13ab

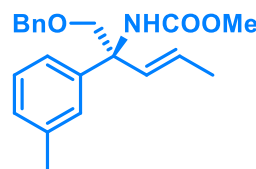
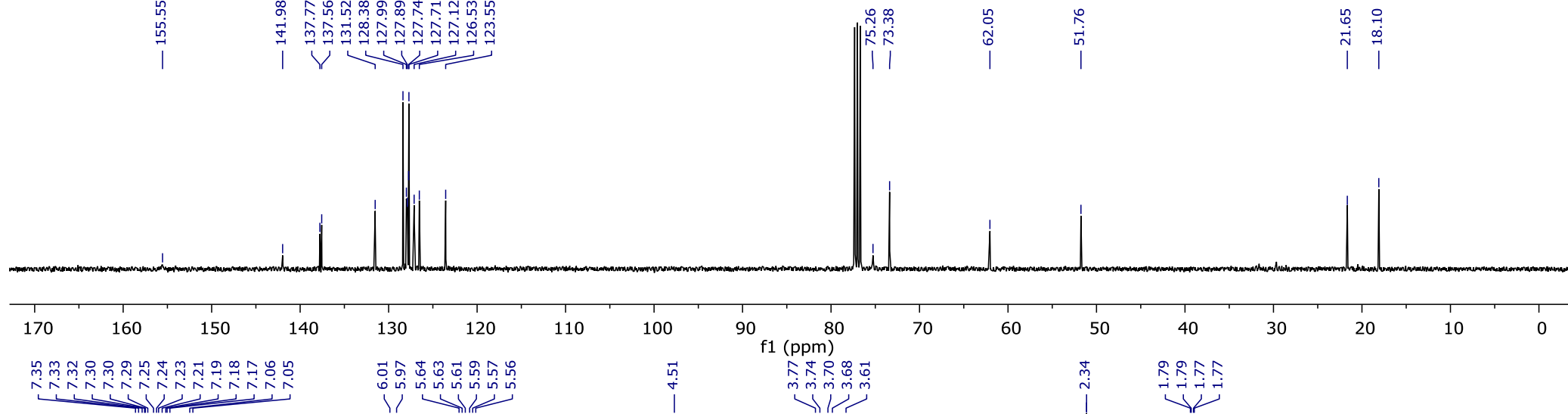
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 0.5 mL/min, detection: UV, 215 nm



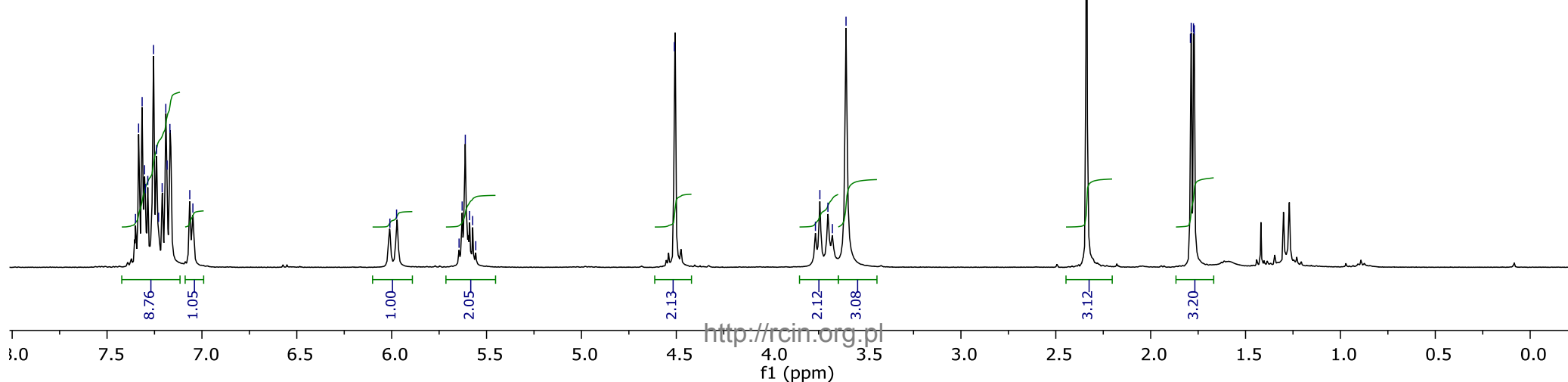
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.170	14.40	16.64	740.093	1195.11	47.7570	0.604
2	17.220	16.65	18.99	809.613	1080.18	52.2430	0.727



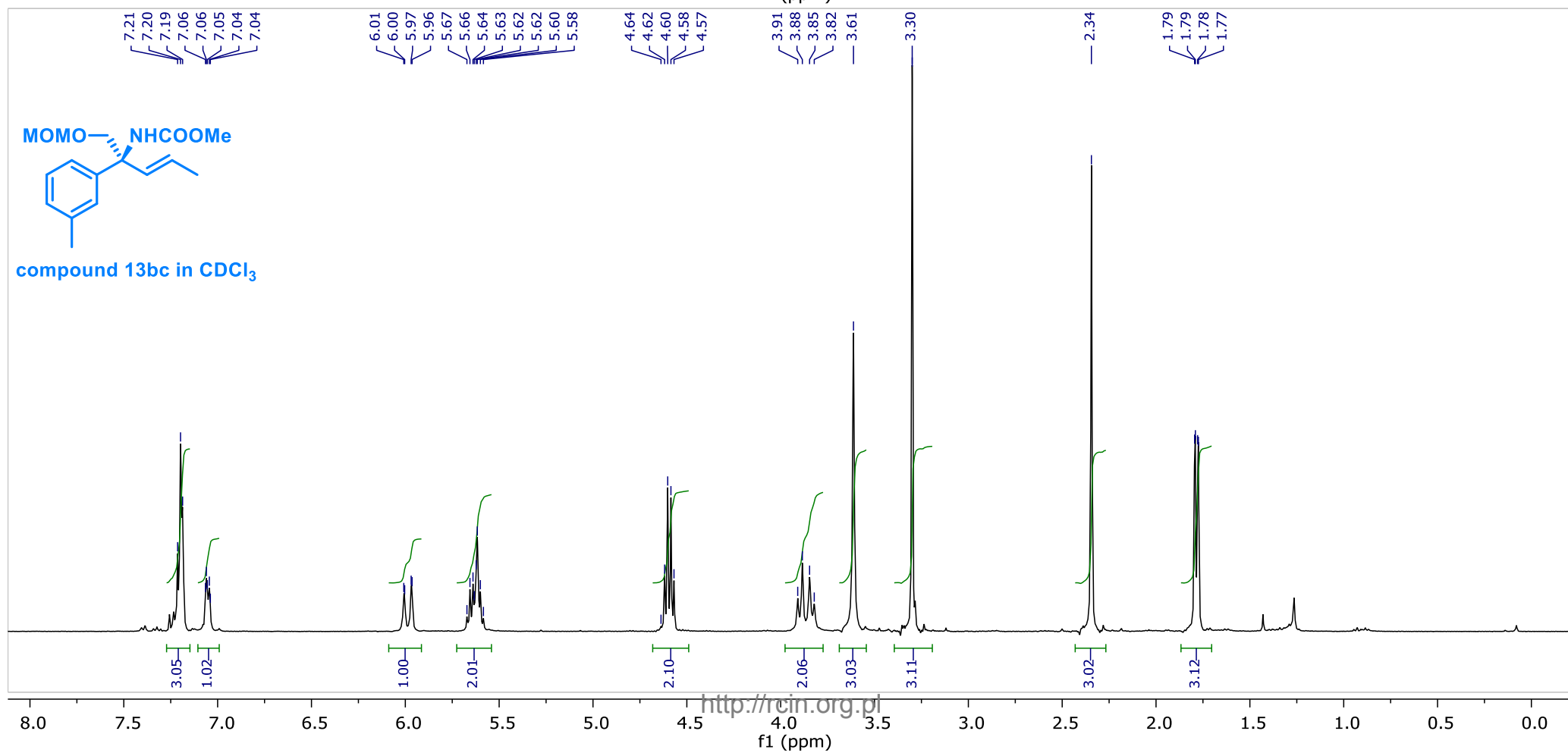
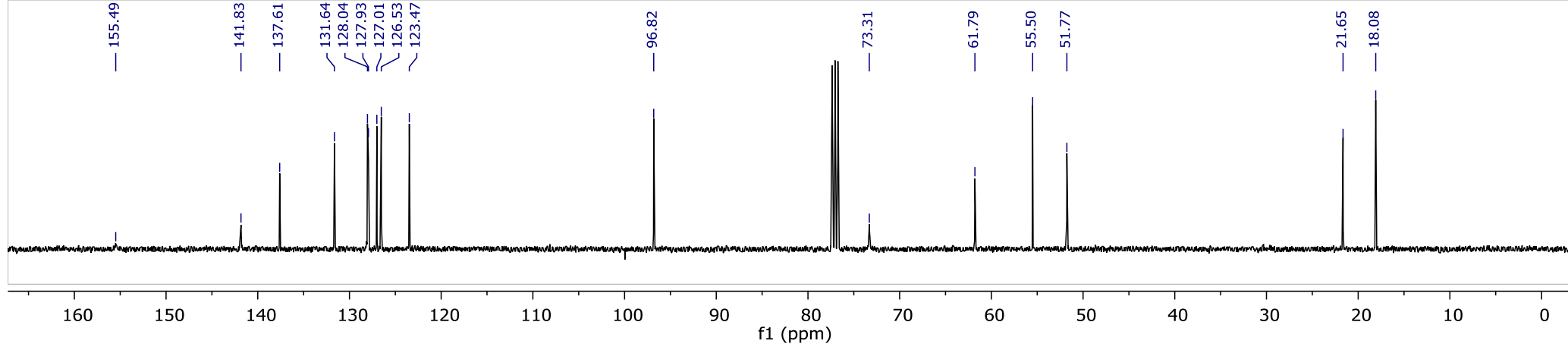
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	13.490	13.06	14.76	971.464	1525.87	97.5206	0.634
2	15.324	14.96	15.79	24.6989	59.0103	2.4794	0.407



compound 13ac in CDCl<sub>3</sub>

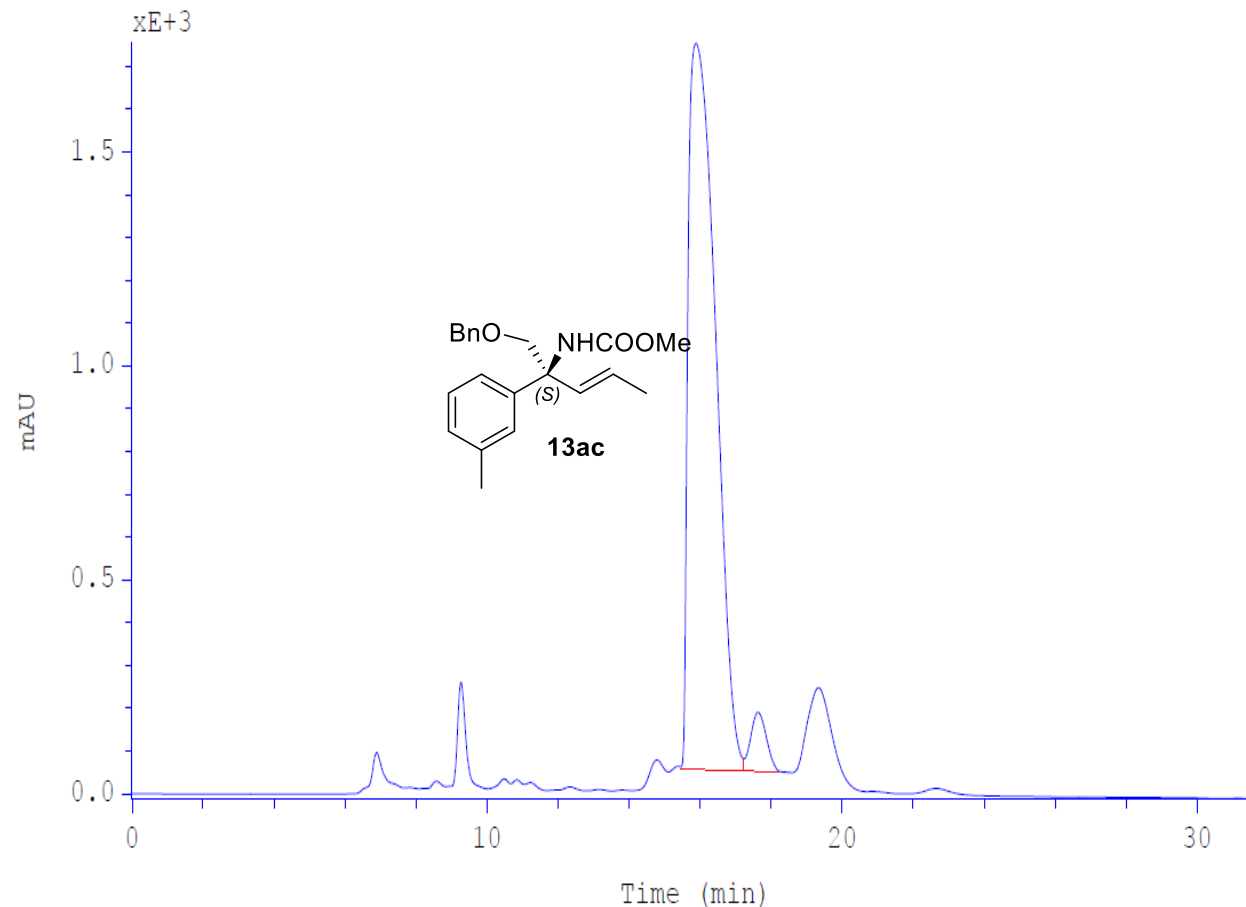
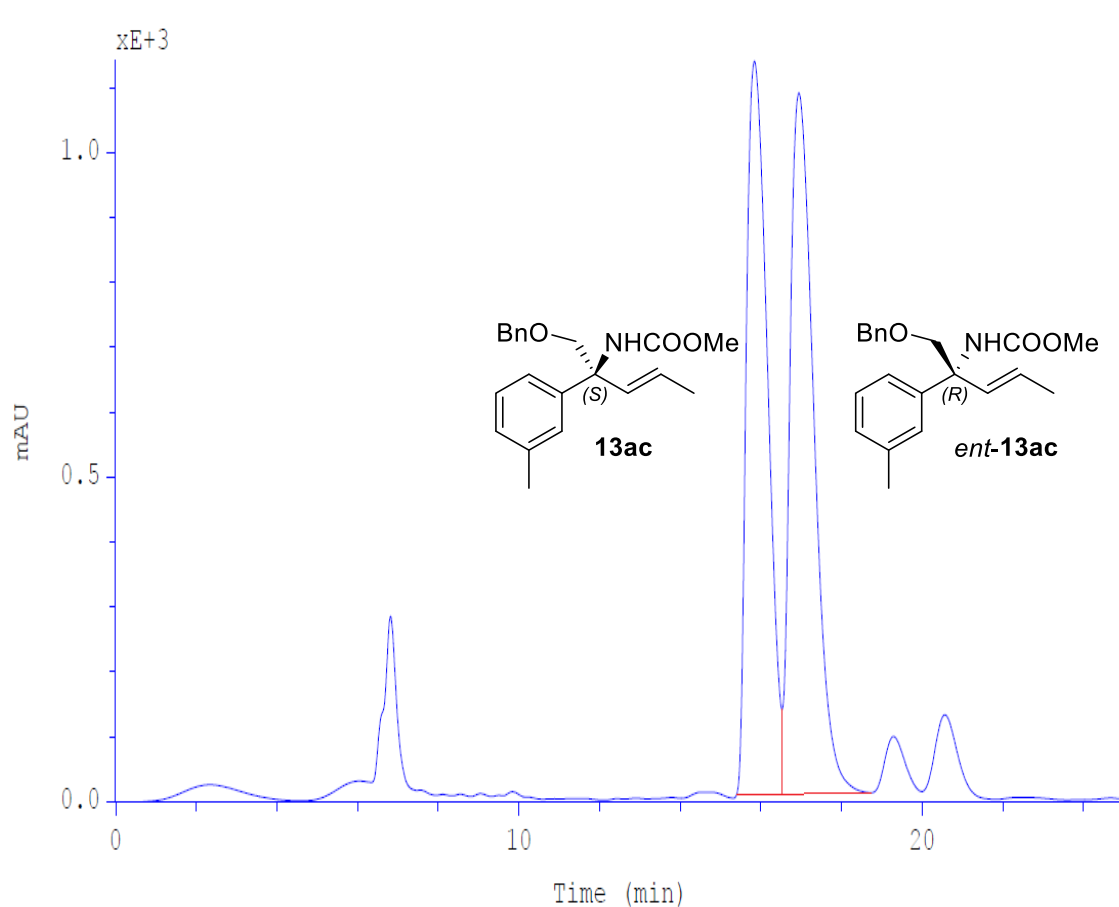






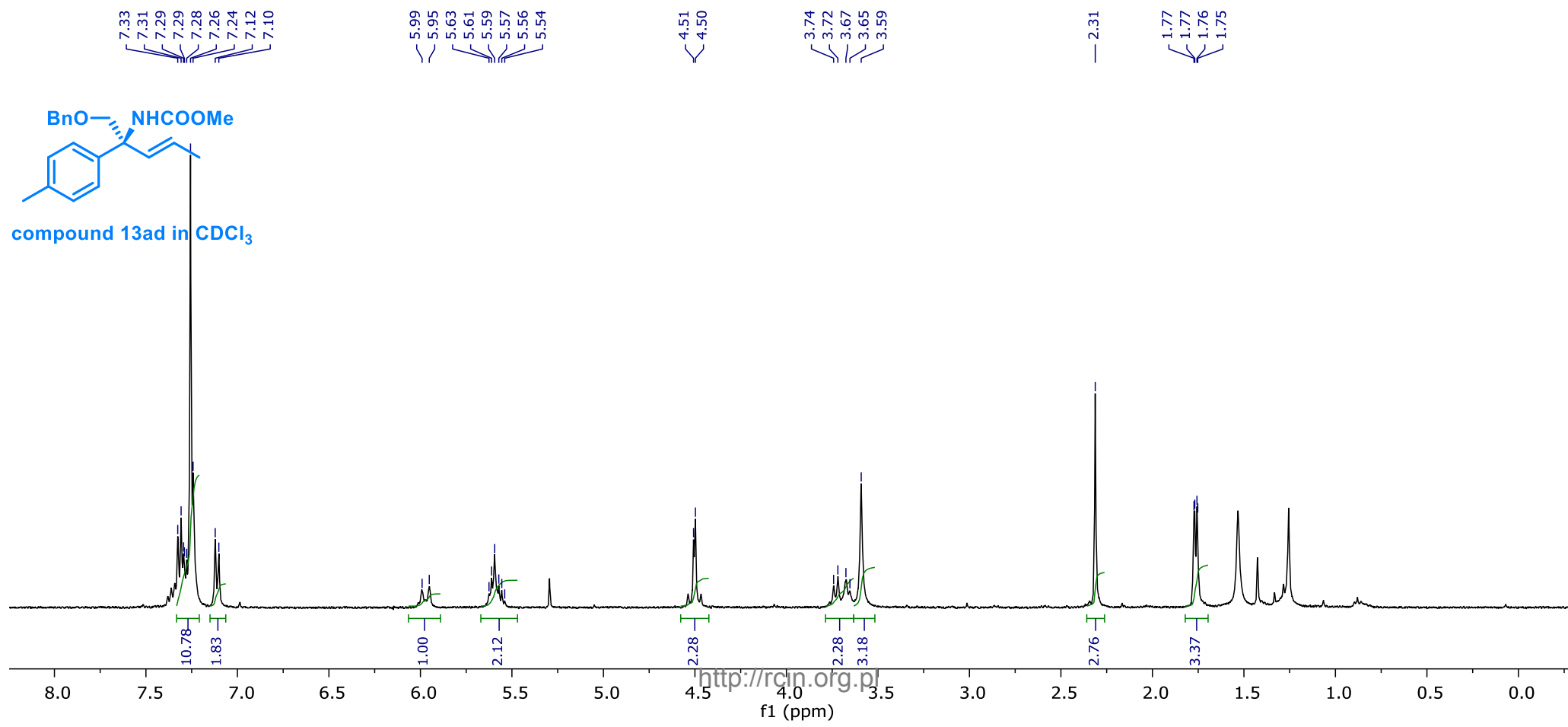
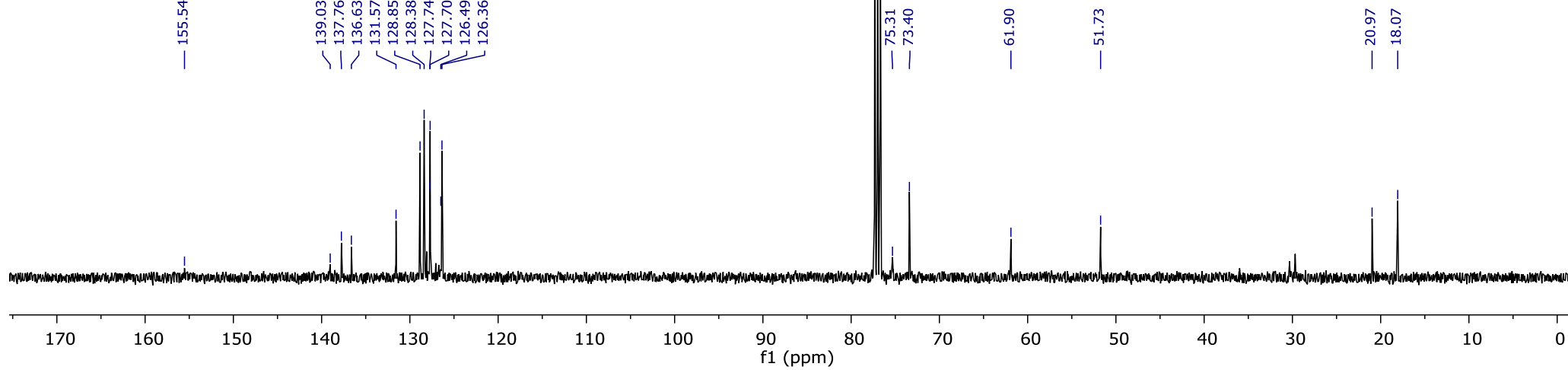
## HPLC chromatogram of compounds rac-13e and 13e

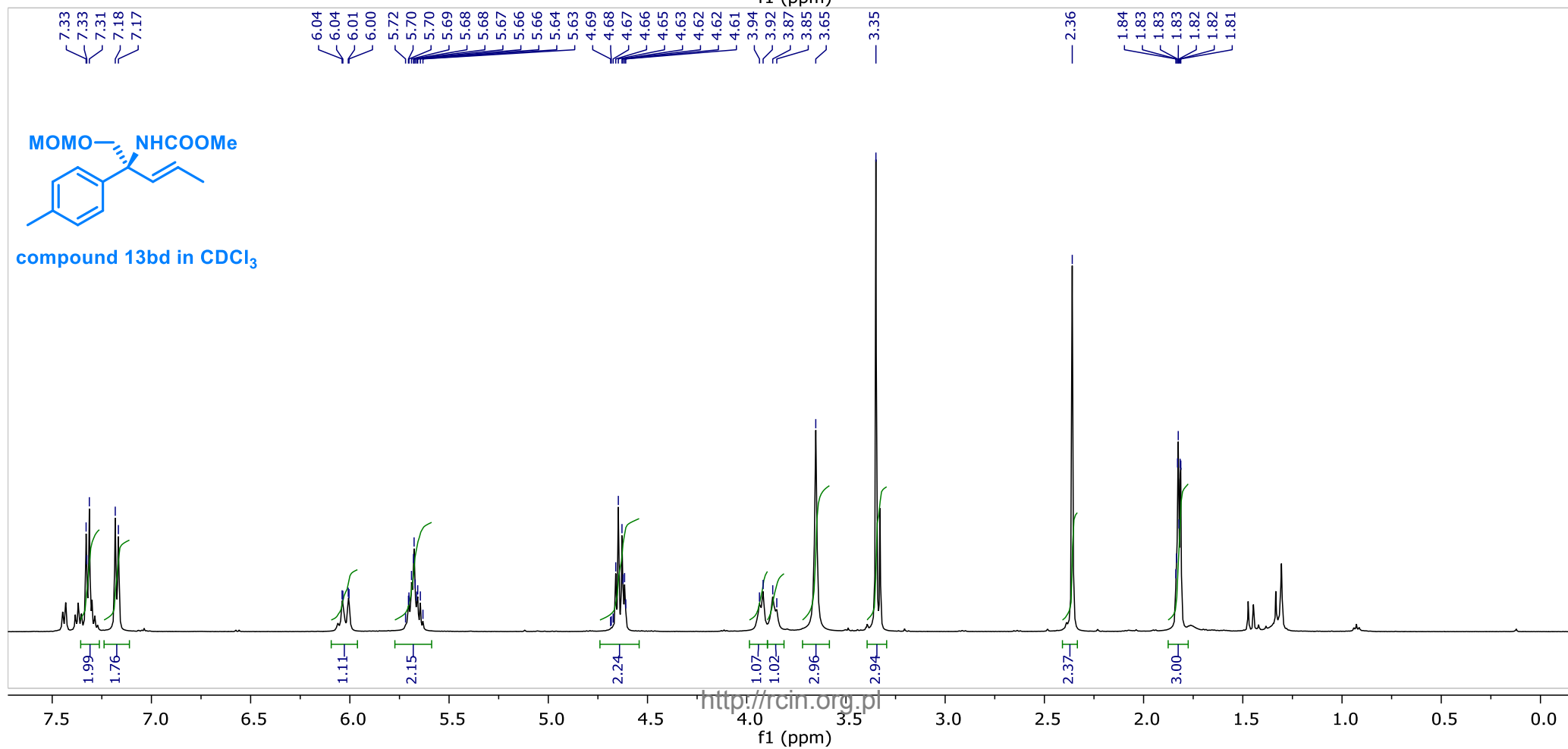
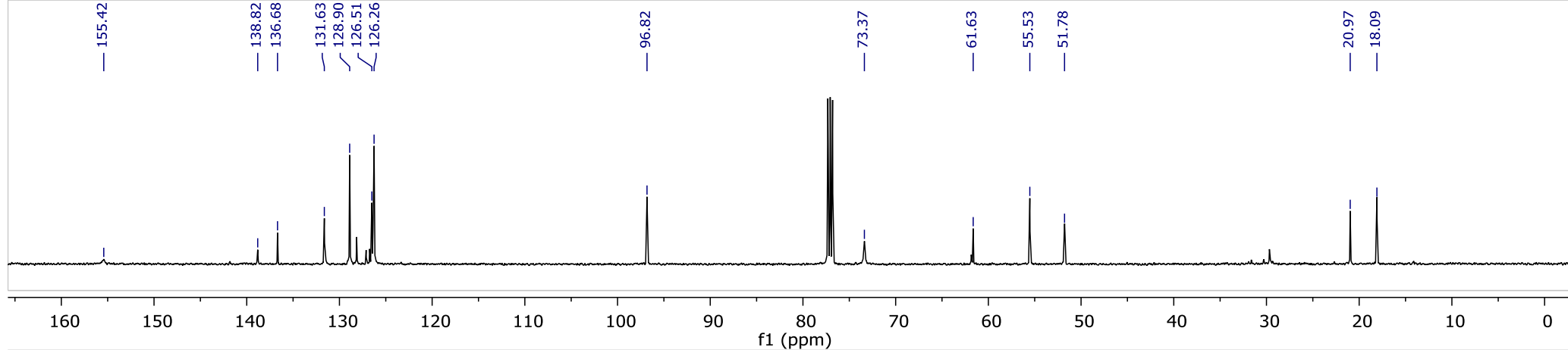
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 0.5 mL/min, detection: UV, 215 nm



	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.839	15.32	16.54	691.334	1134.73	48.1662	0.568
2	16.940	16.54	18.66	743.975	1083.43	51.8338	0.629

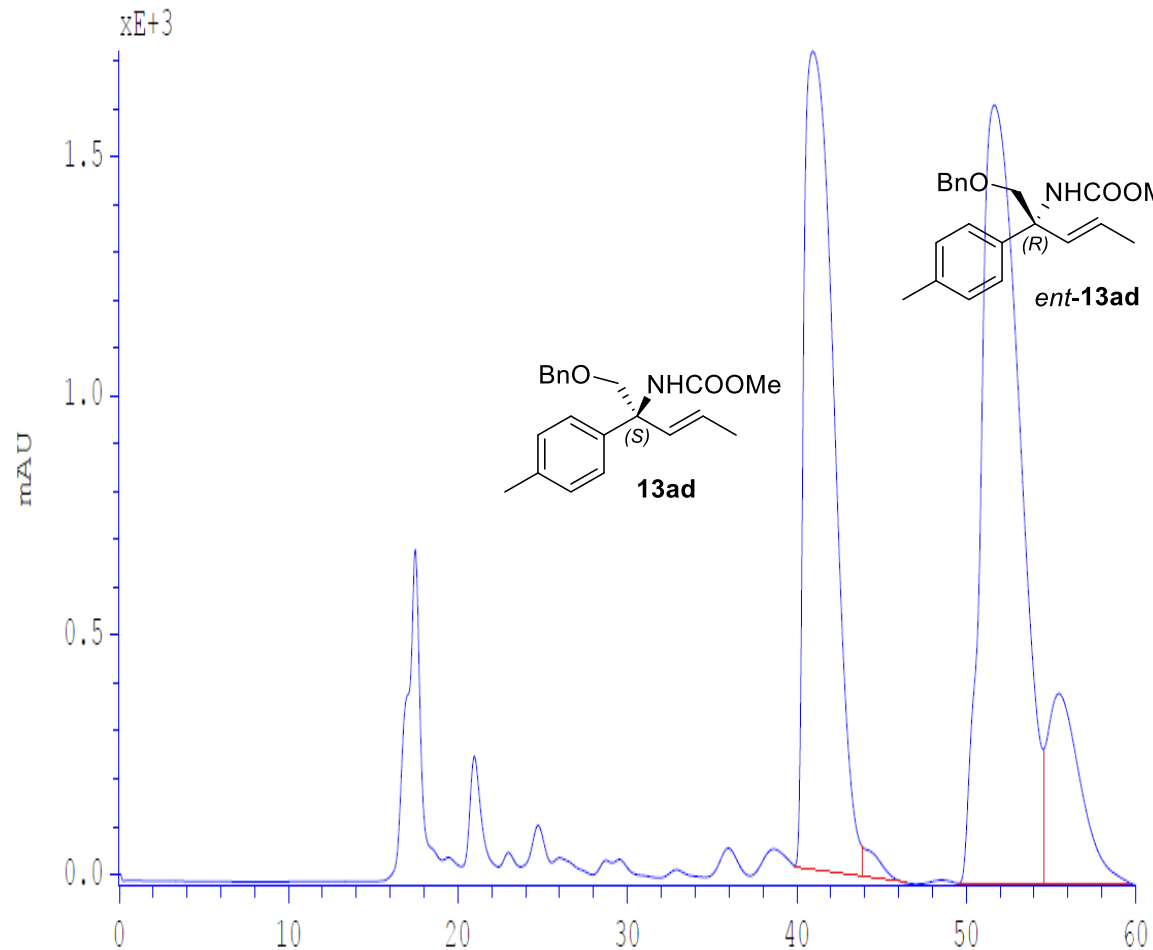
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	15.887	15.46	17.21	1482.01	1686.44	96.3422	0.882
2	17.621	17.25	18.30	56.2669	119.542	3.6578	0.464



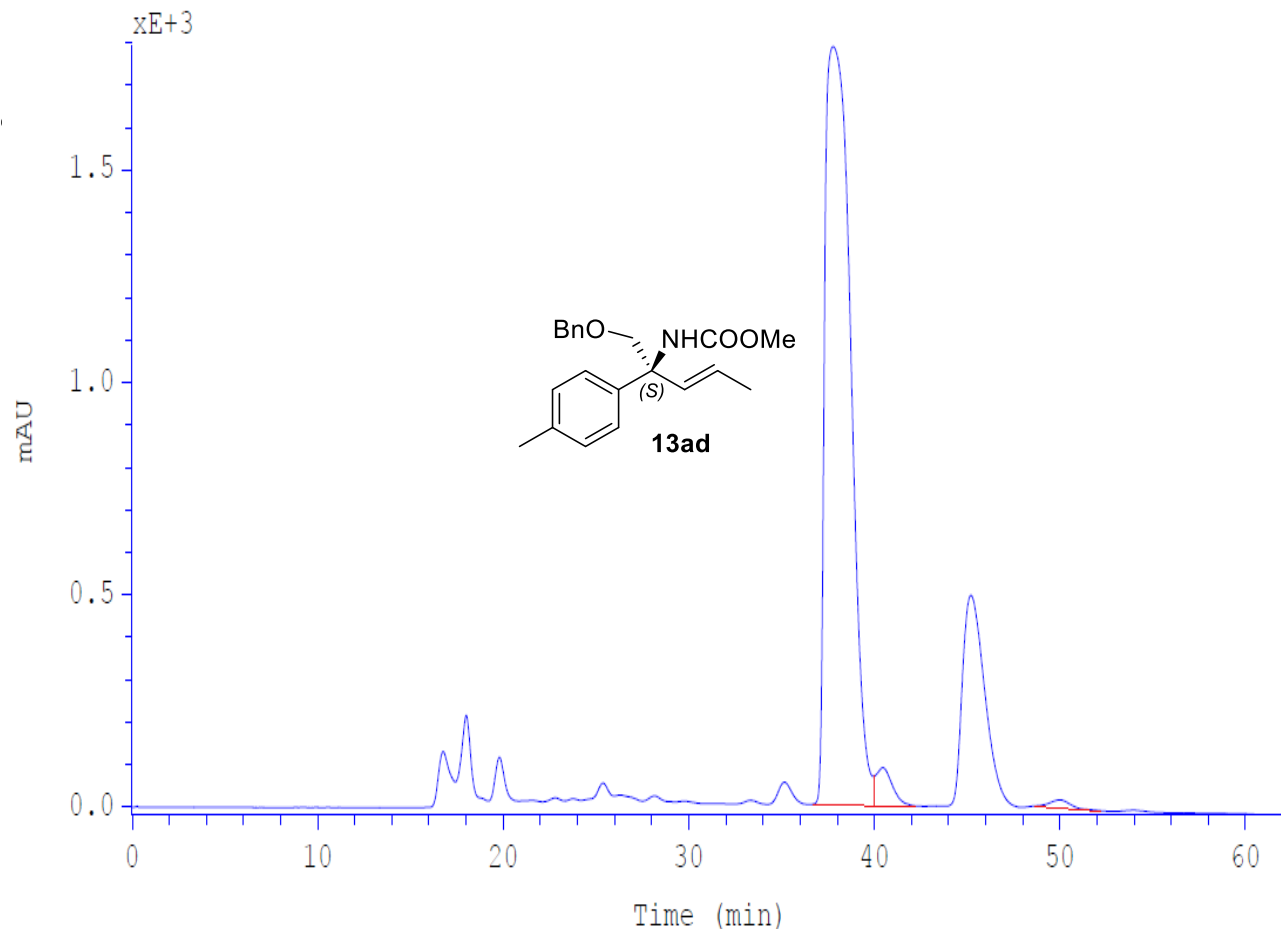


## HPLC chromatogram of compounds rac-13ad and 13ad

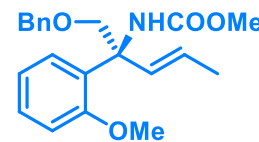
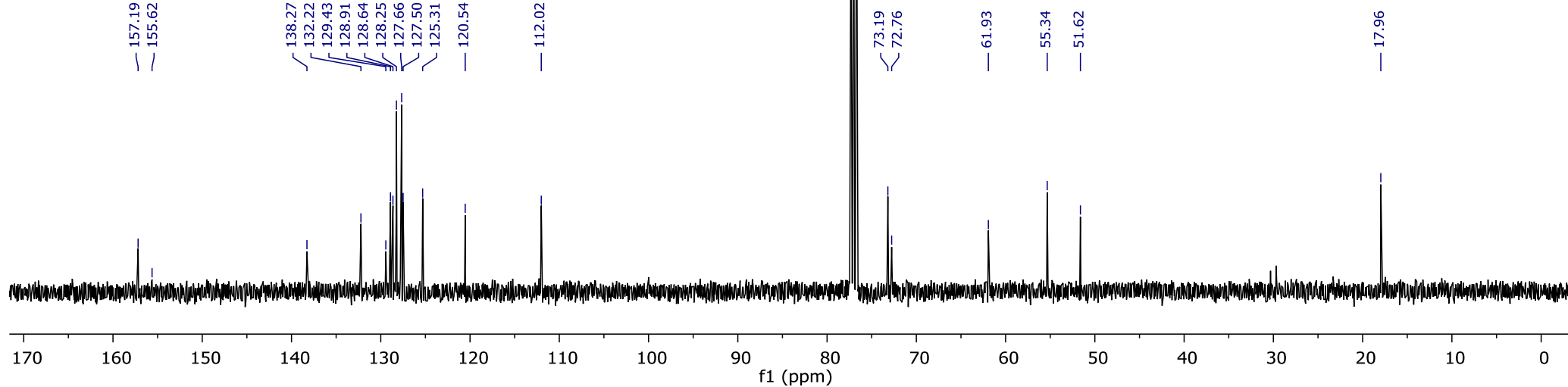
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 0.2 mL/min, detection: UV, 215 nm



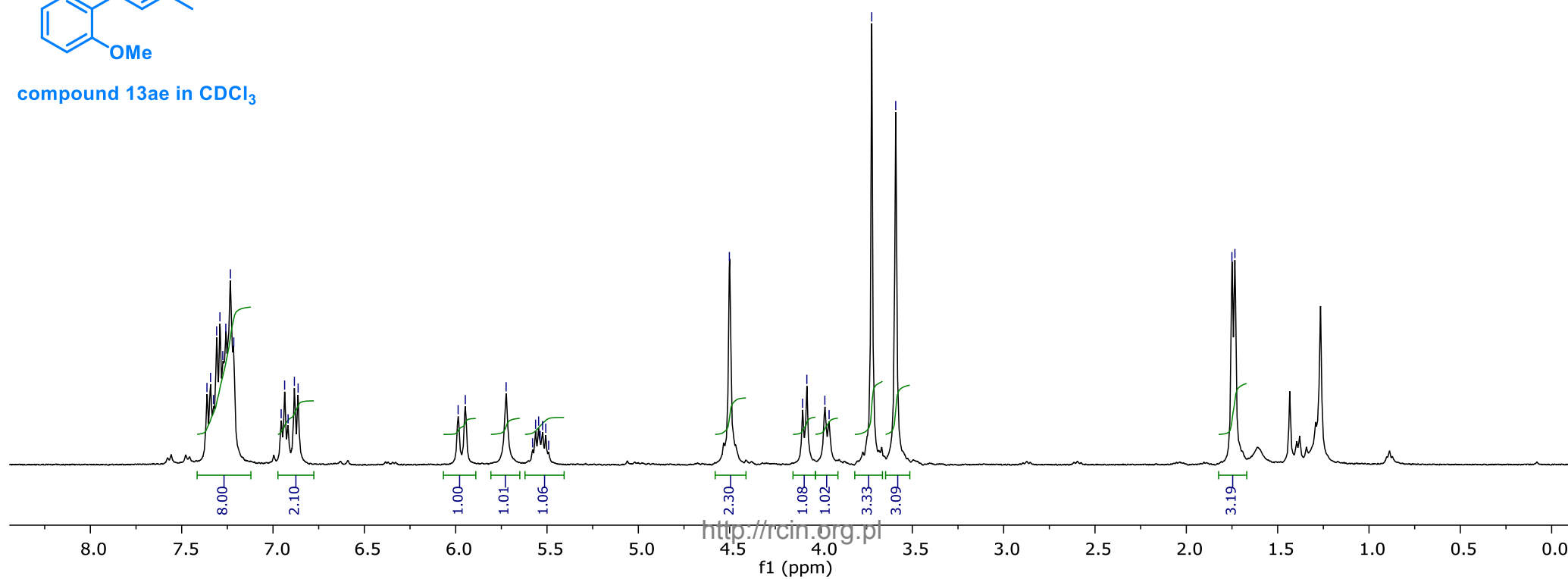
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	40.967	39.77	43.87	3454.48	1706.09	39.5169	1.948
2	43.883	43.87	46.46	70.4806	61.6068	0.8062	1.155
3	51.667	49.64	54.48	4296.63	1625.31	49.1505	2.314
4	55.467	54.48	59.58	920.19	395.01	10.5263	1.853

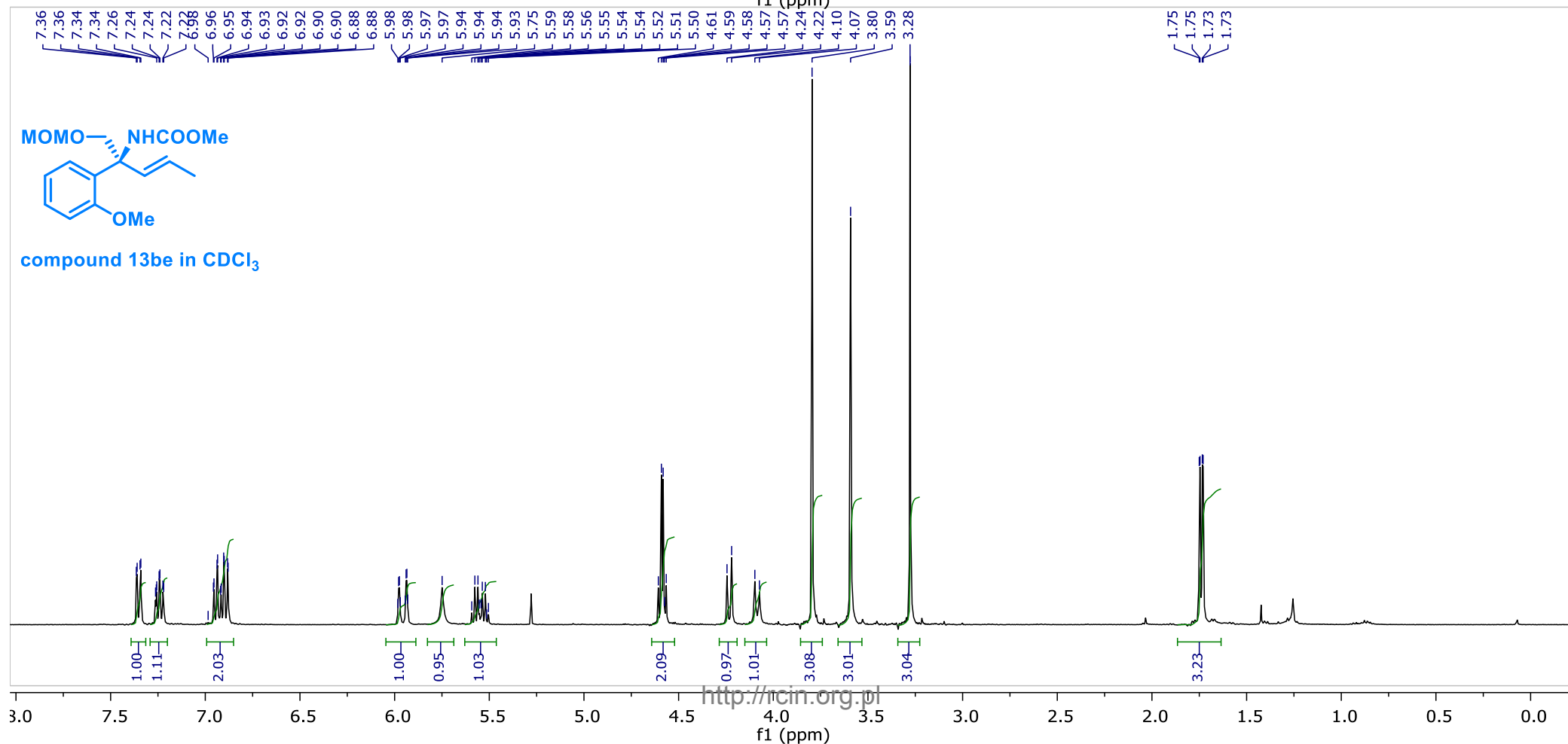
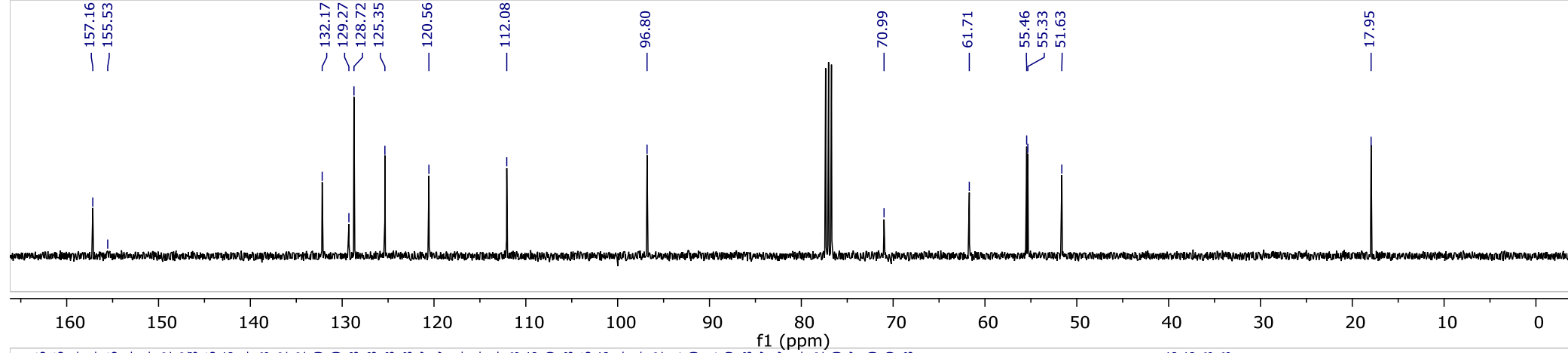


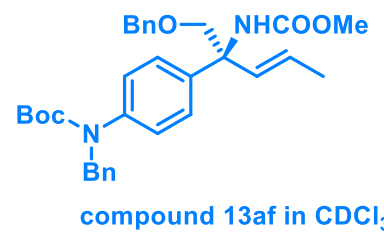
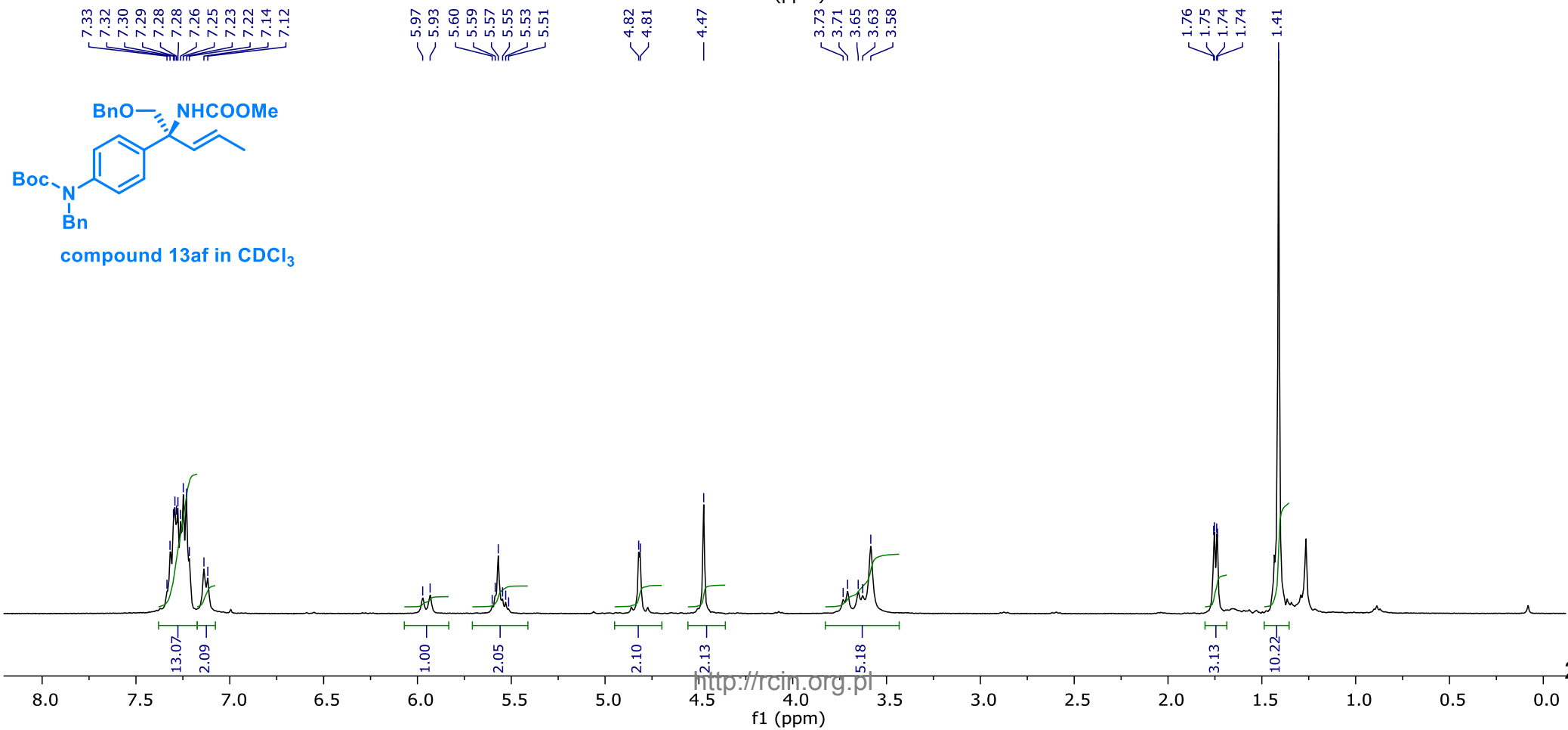
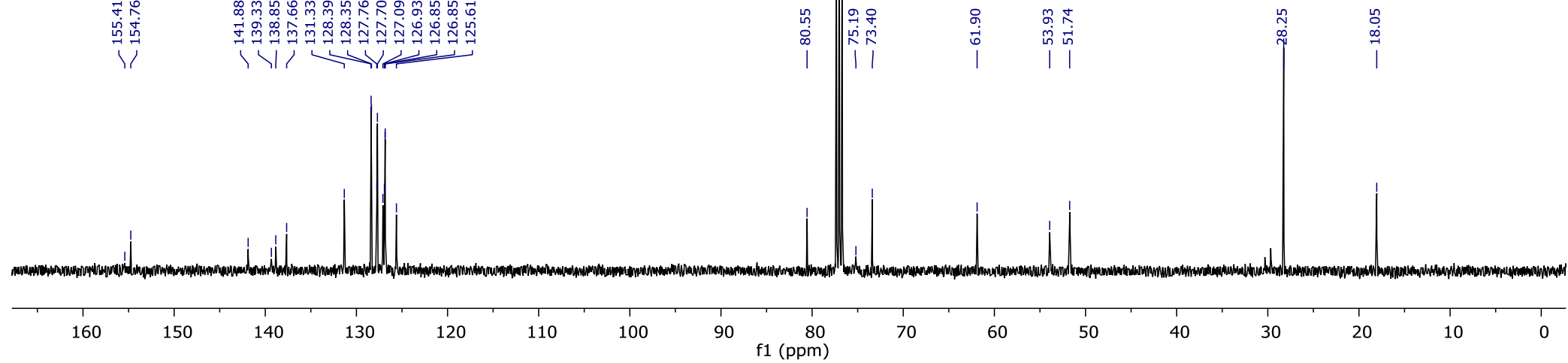
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	37.788	36.65	39.88	2857.29	1786.24	95.8366	1.545
2	40.472	39.88	42.22	99.5322	89.4168	3.3384	0.788
3	49.956	48.57	52.36	24.5958	18.9717	0.8250	1.236



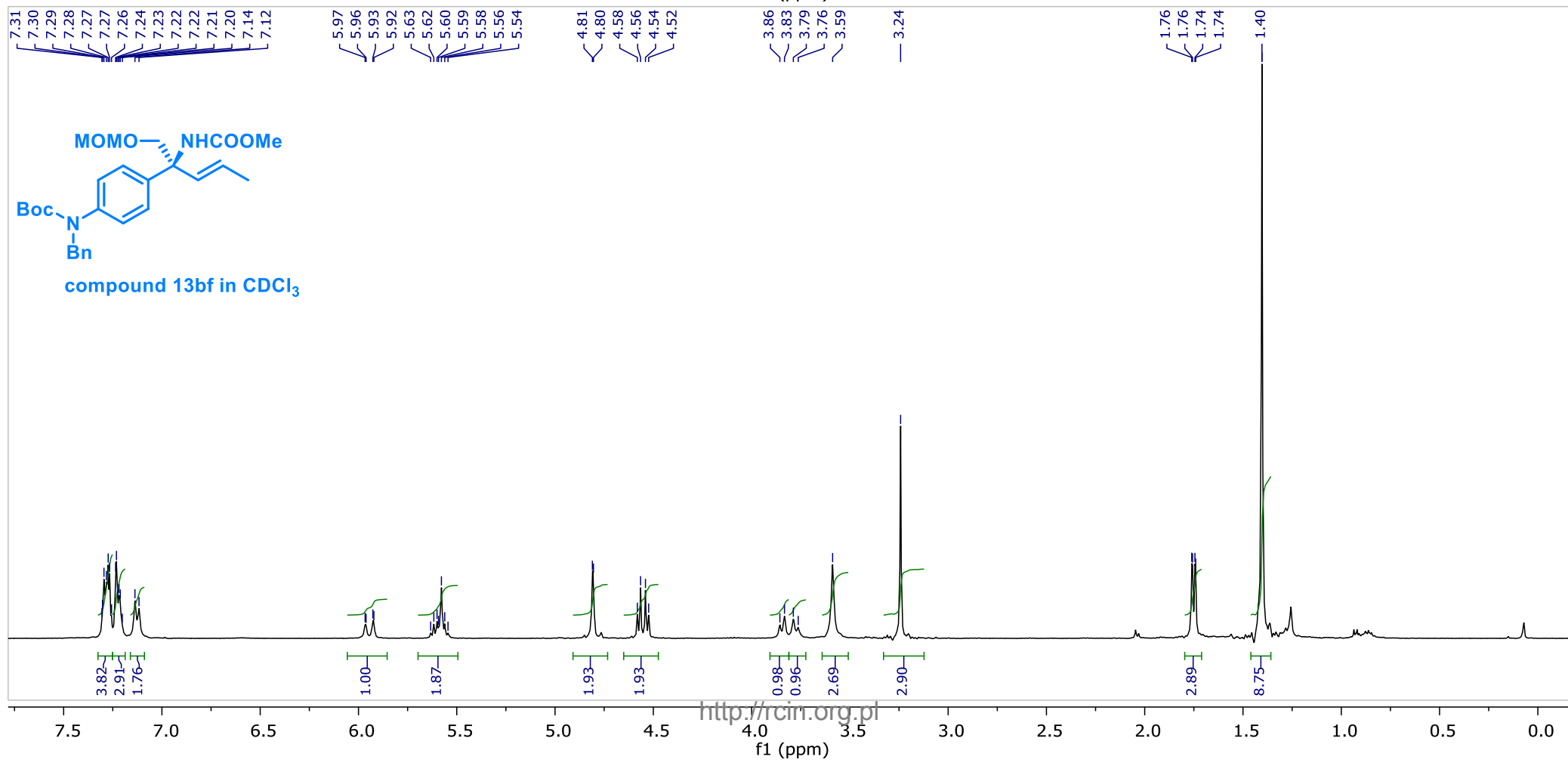
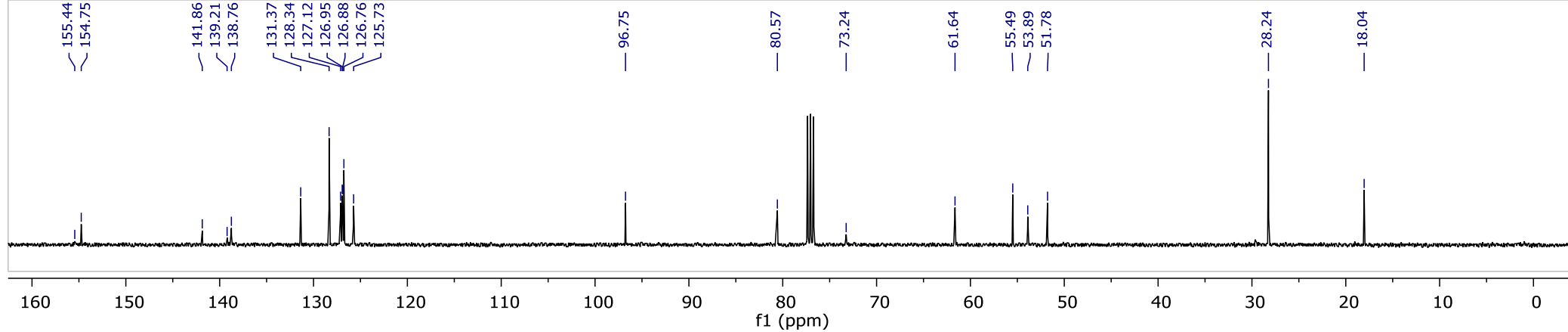
compound 13ae in CDCl<sub>3</sub>





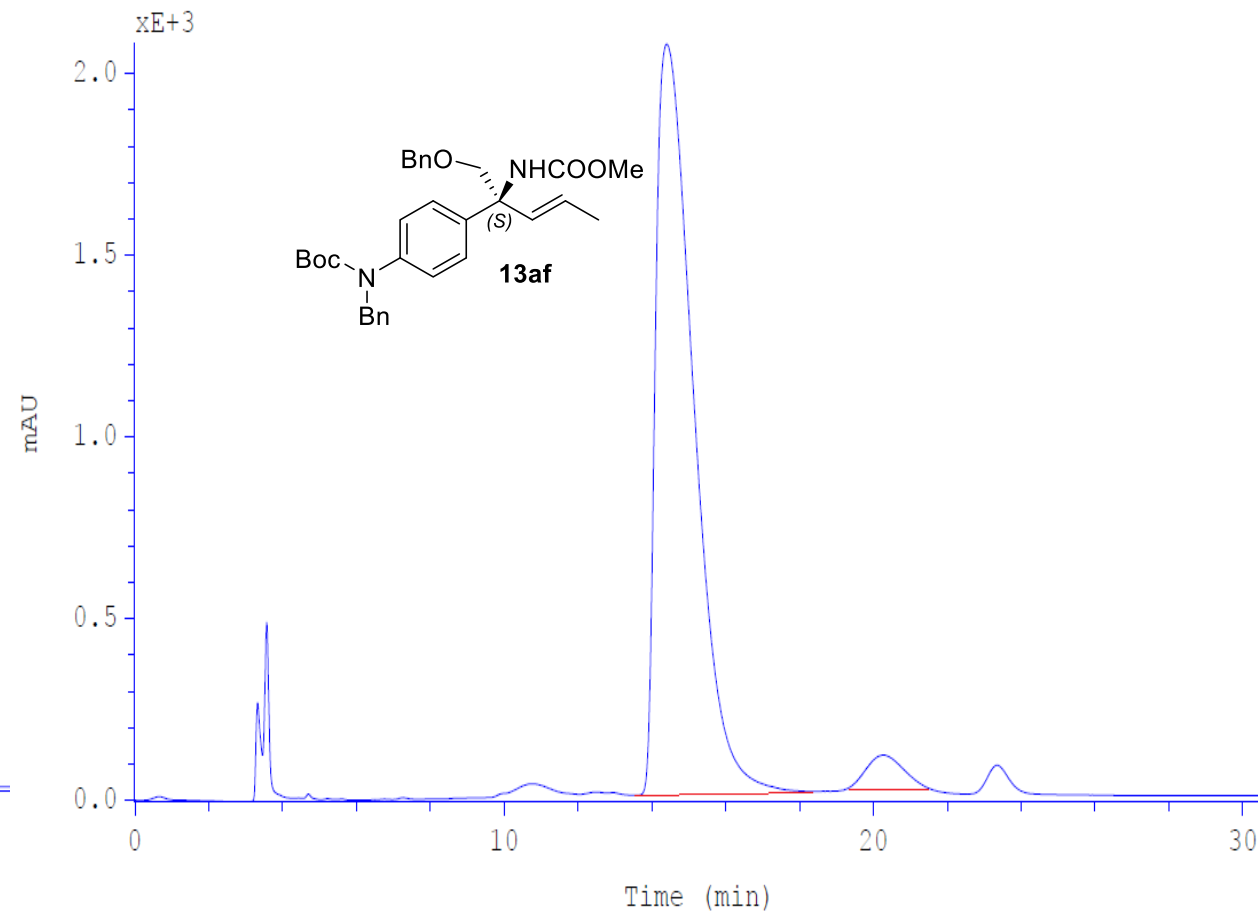
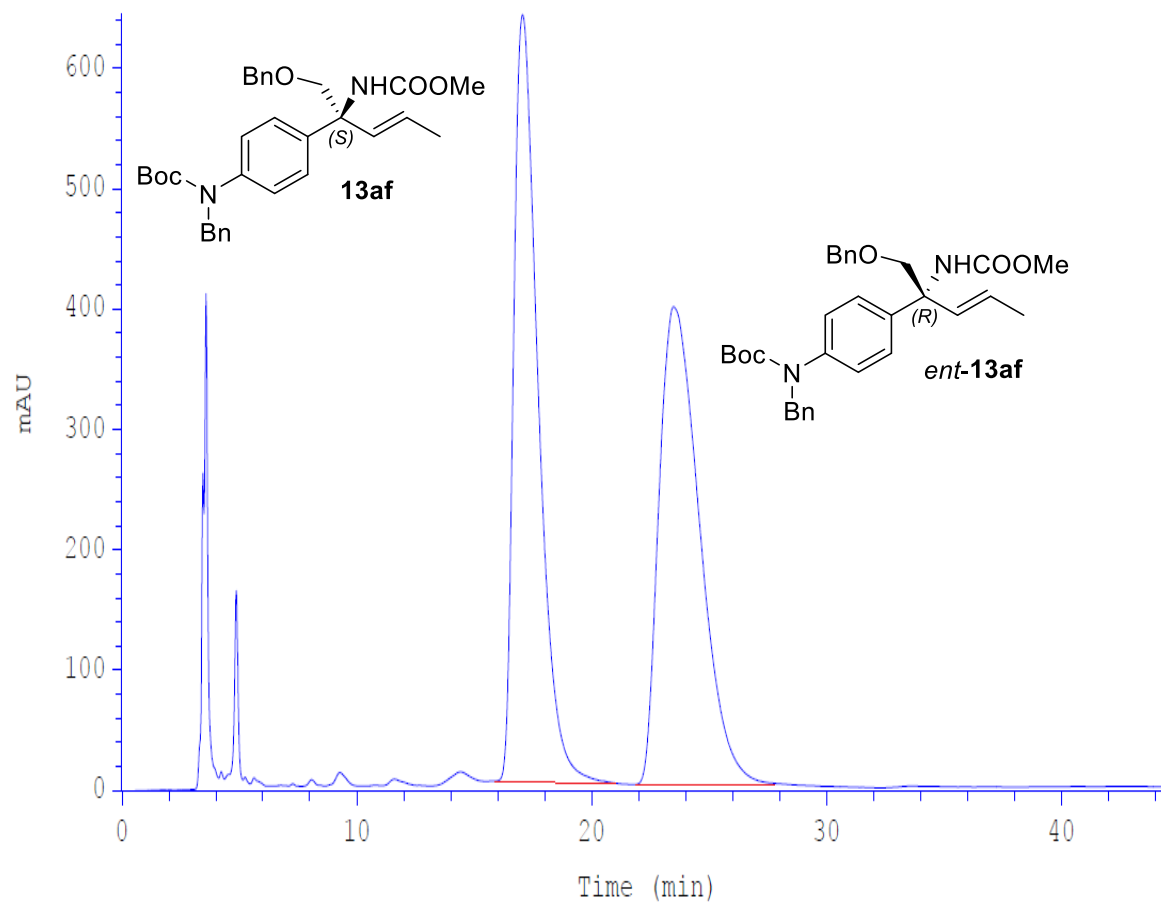






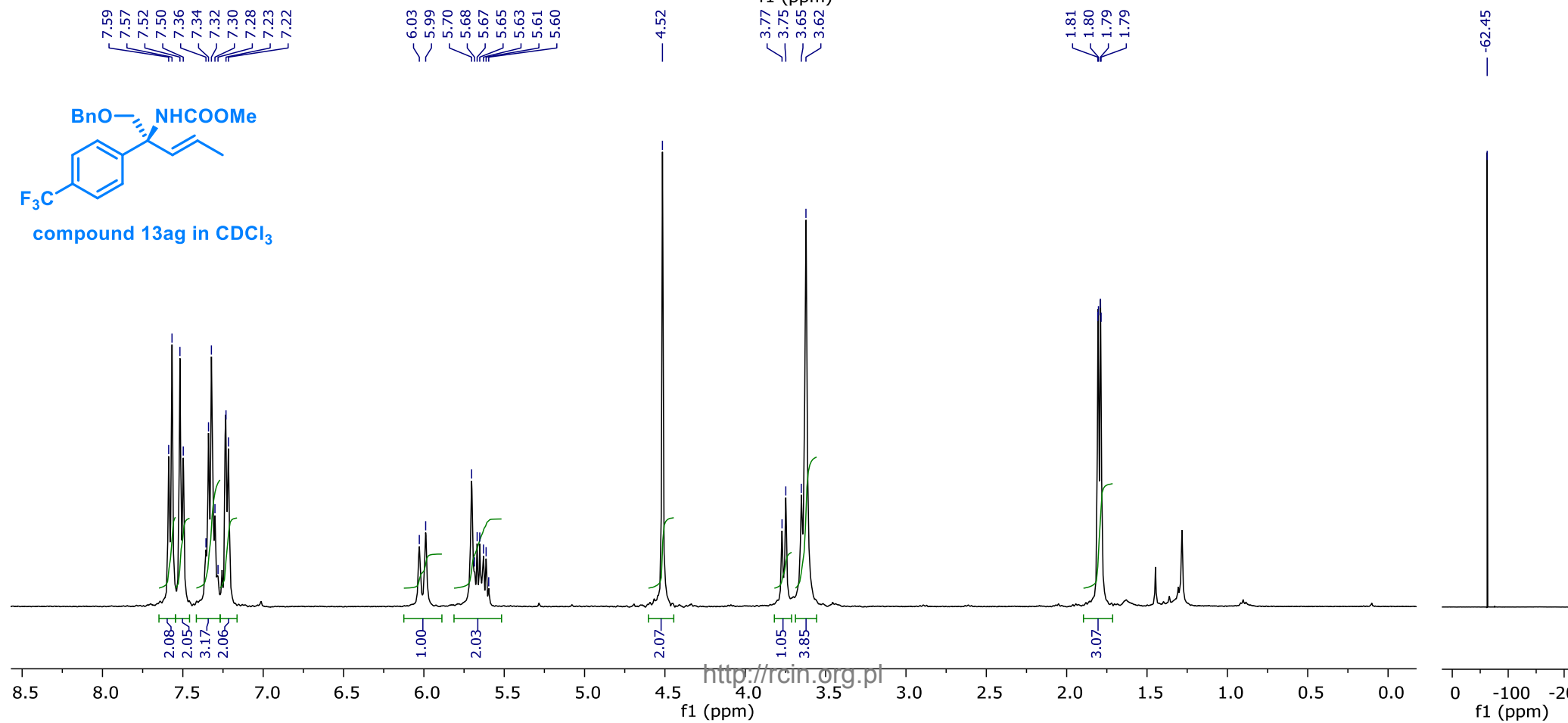
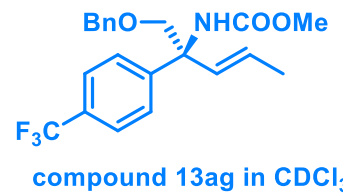
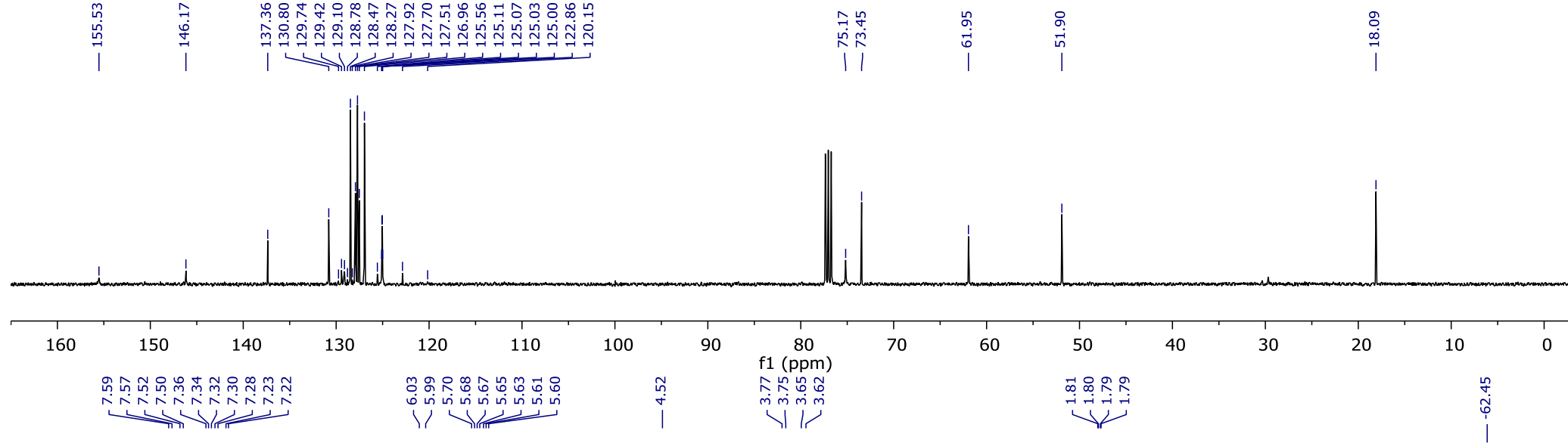
## HPLC chromatogram of compounds rac-13af and 13af

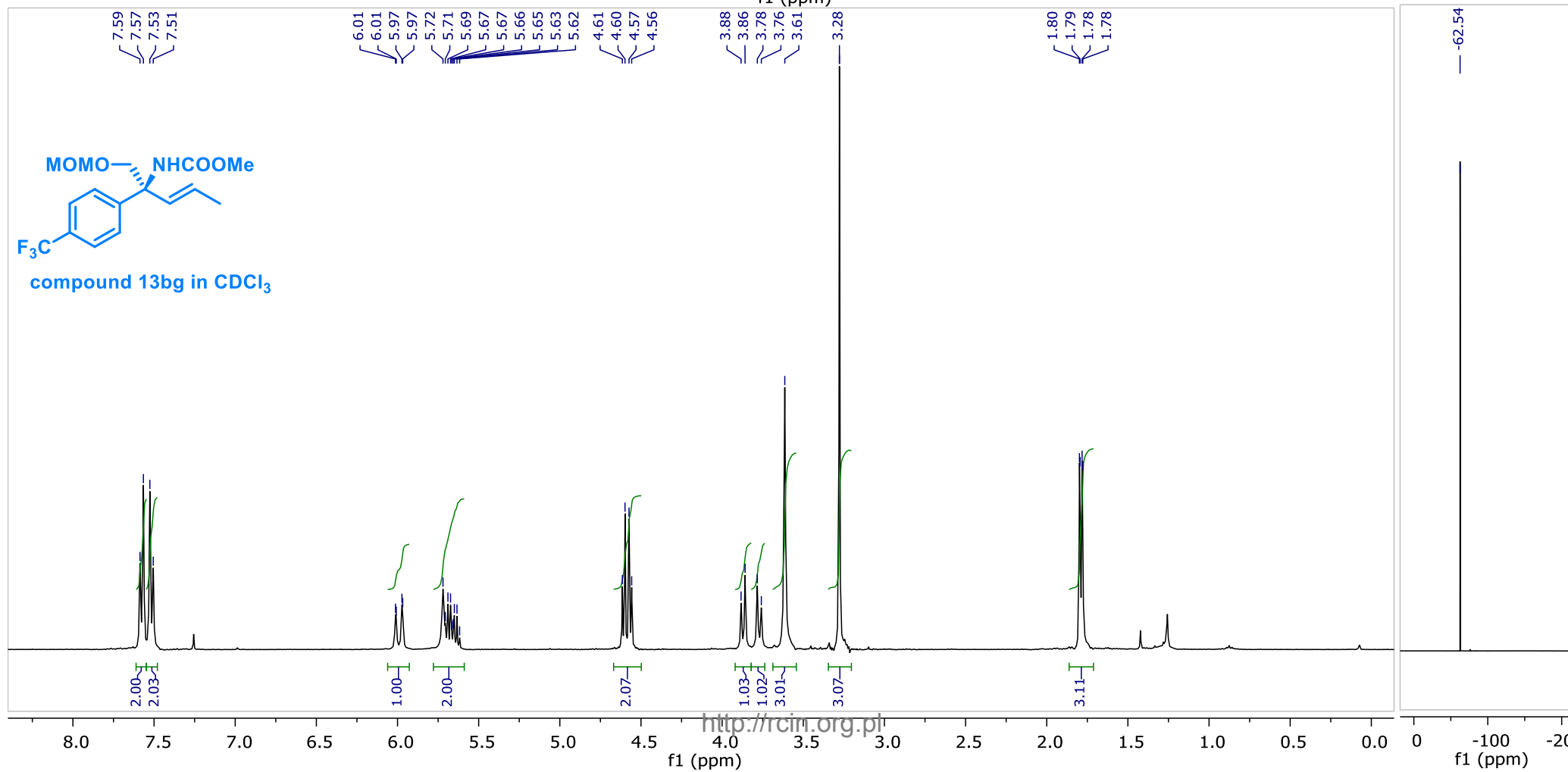
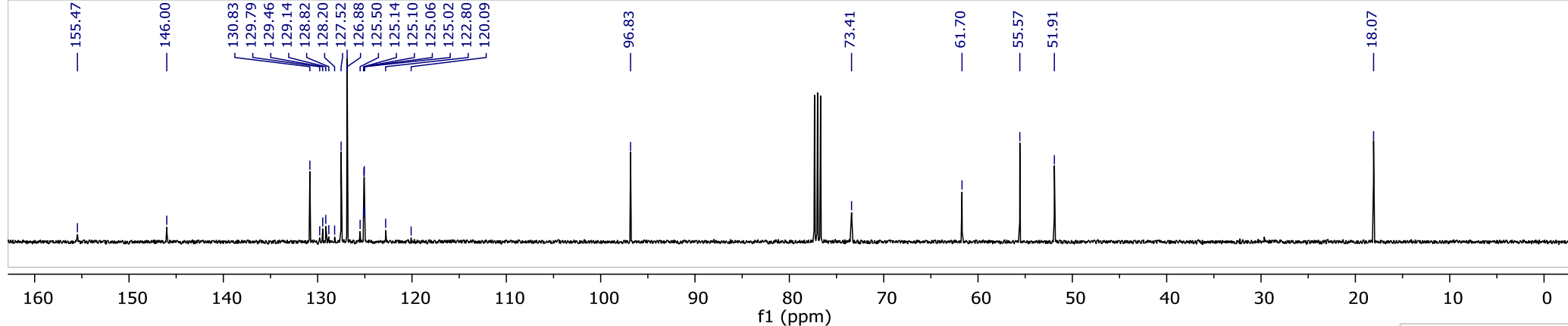
Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1 mL/min, detection: UV, 215 nm

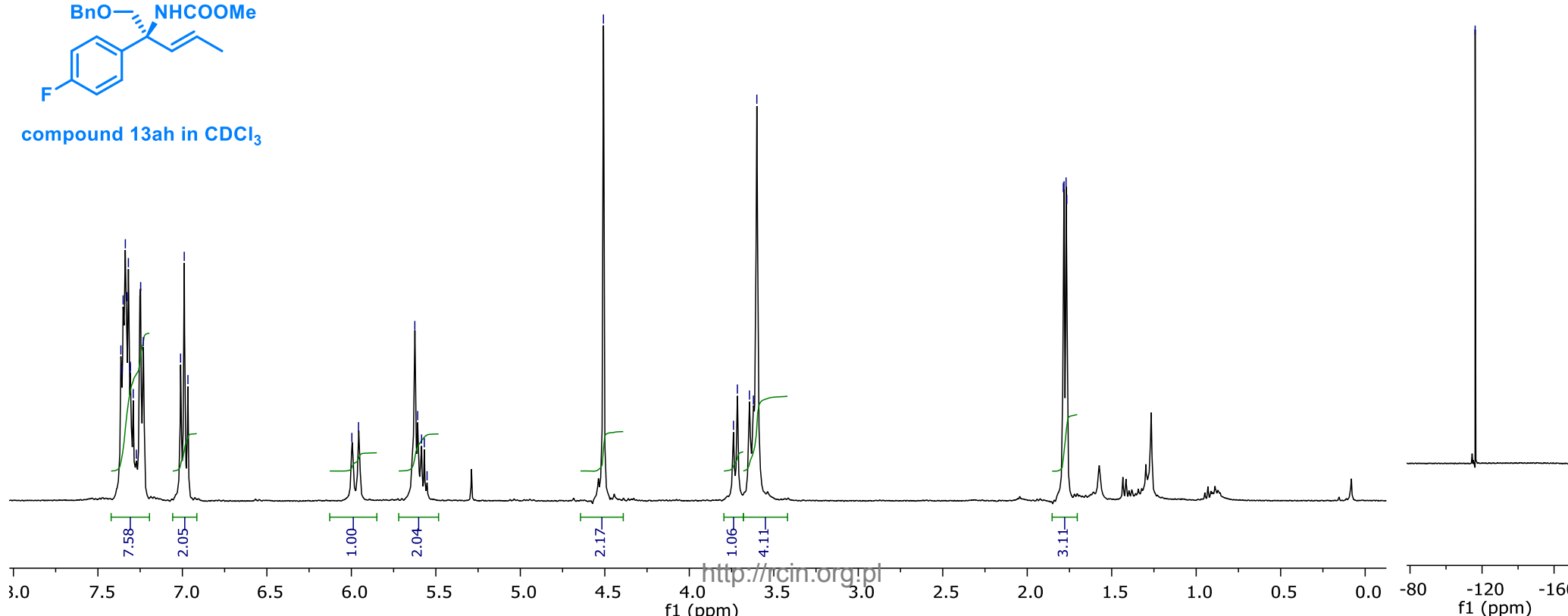
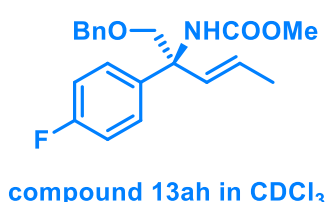
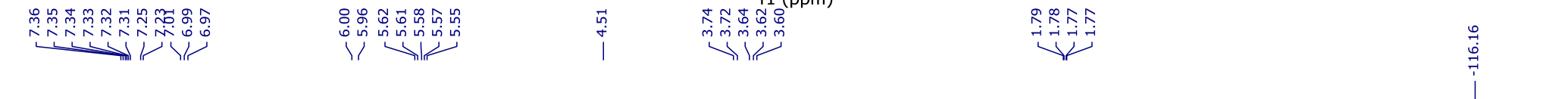
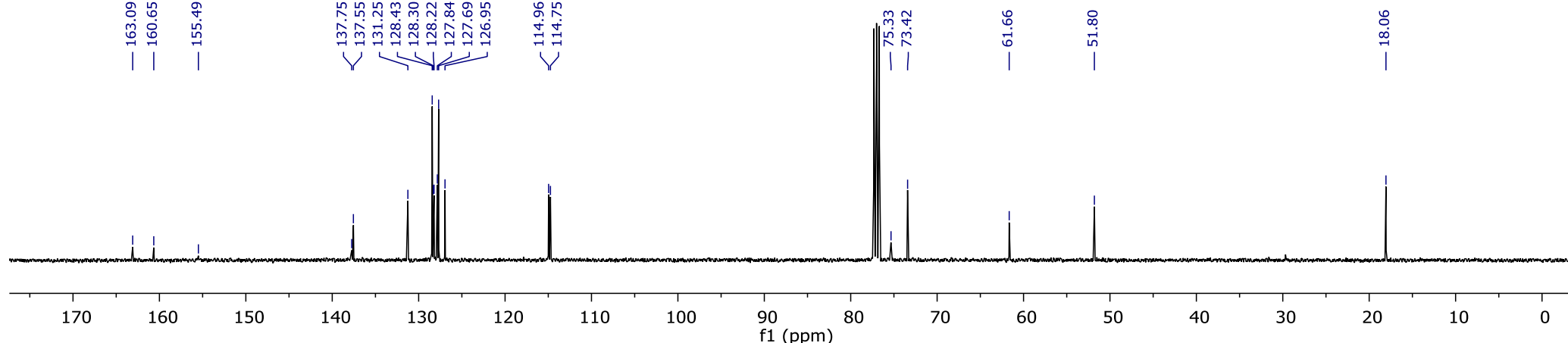


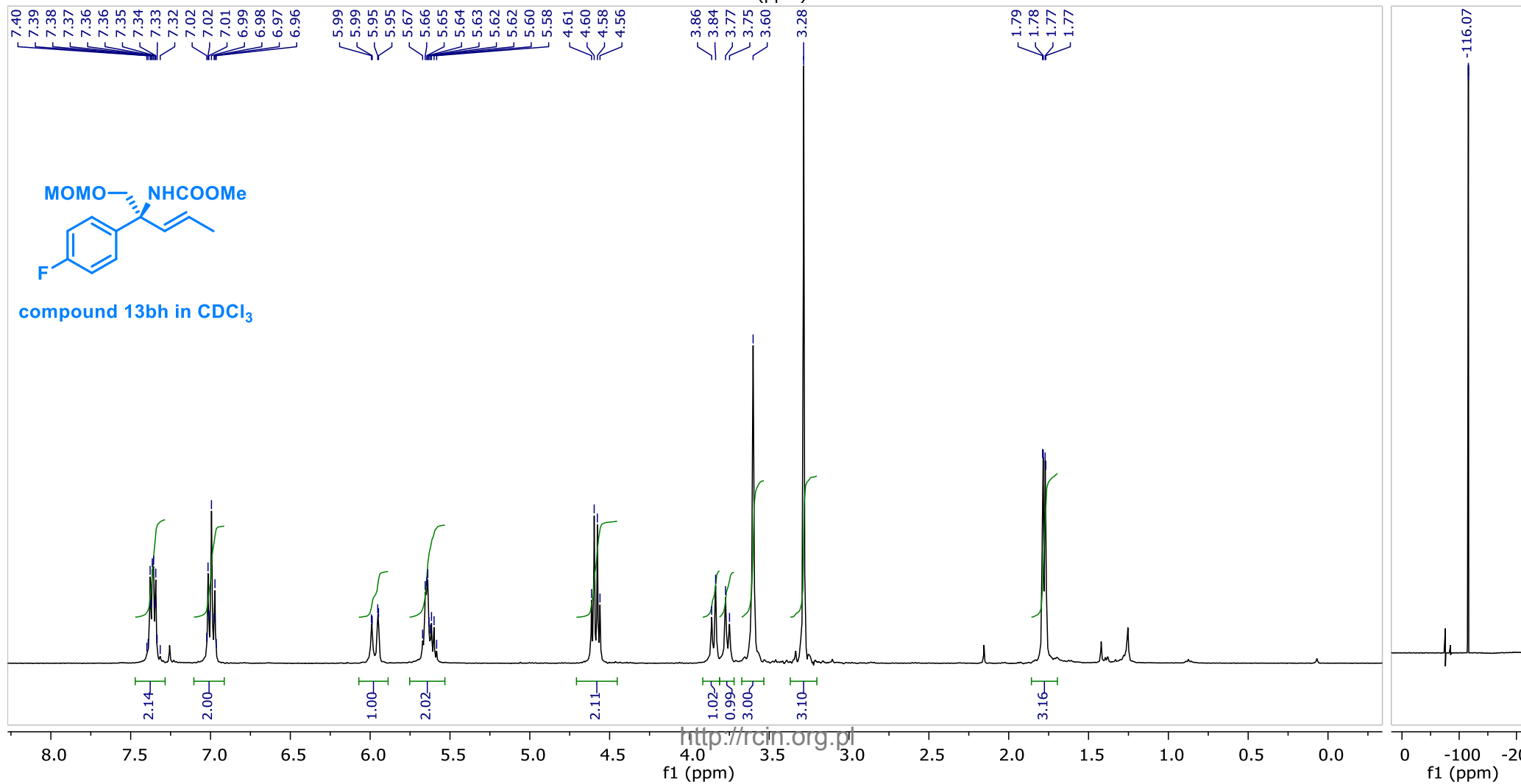
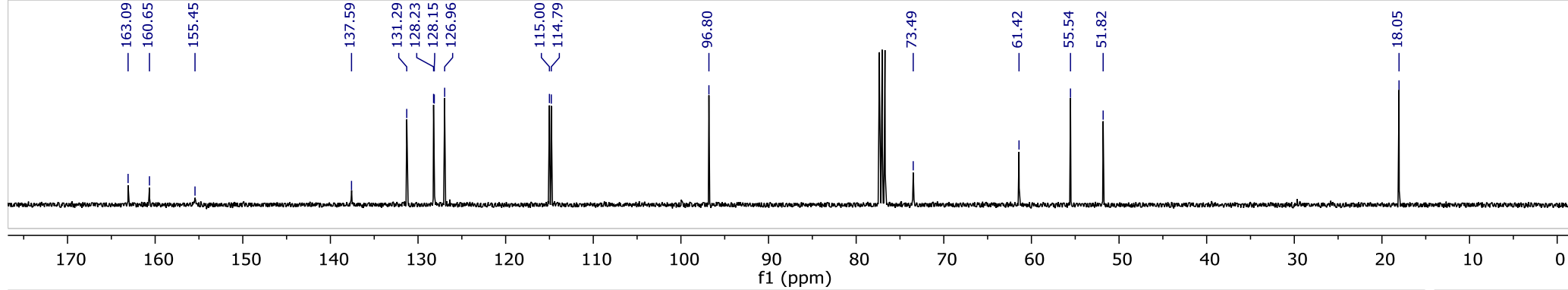
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	17.052	15.78	21.13	768.791	637.323	49.2832	1.100
2	23.486	21.80	27.90	791.155	396.696	50.7168	1.896

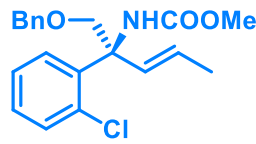
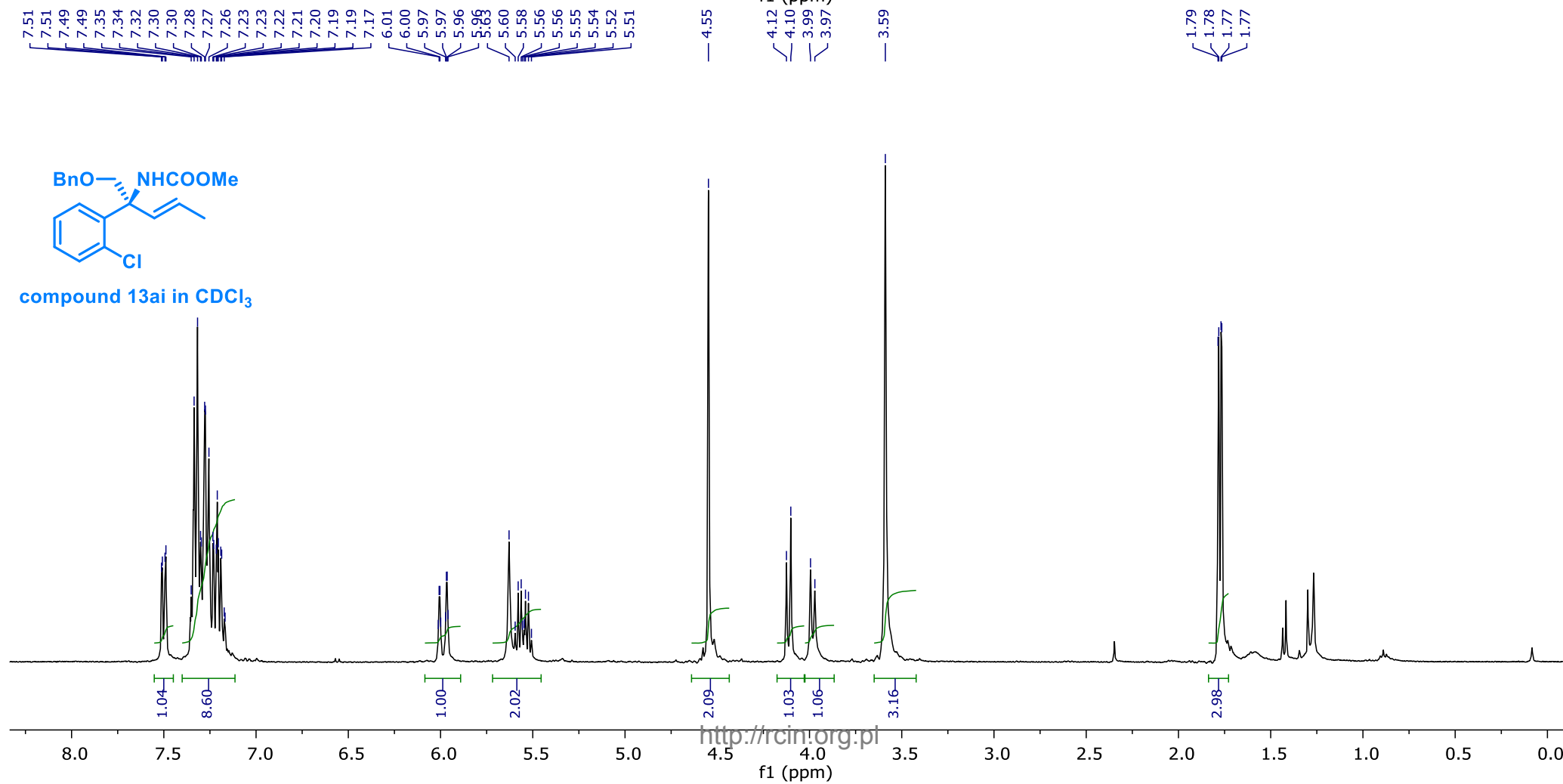
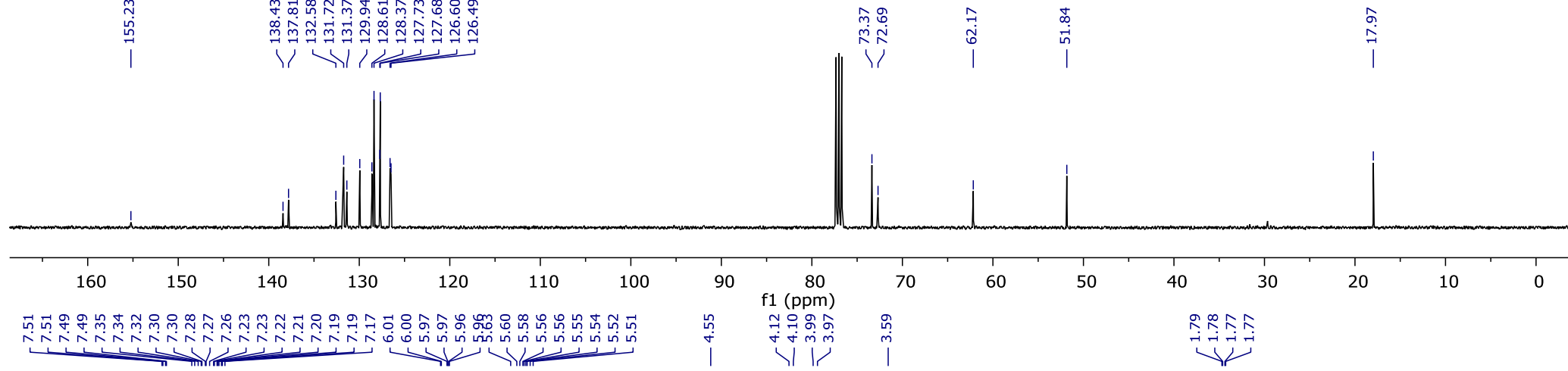
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	14.404	13.49	18.46	2457.39	2065.24	96.1323	1.103
2	20.255	19.40	21.52	98.8686	88.0847	3.8677	1.110



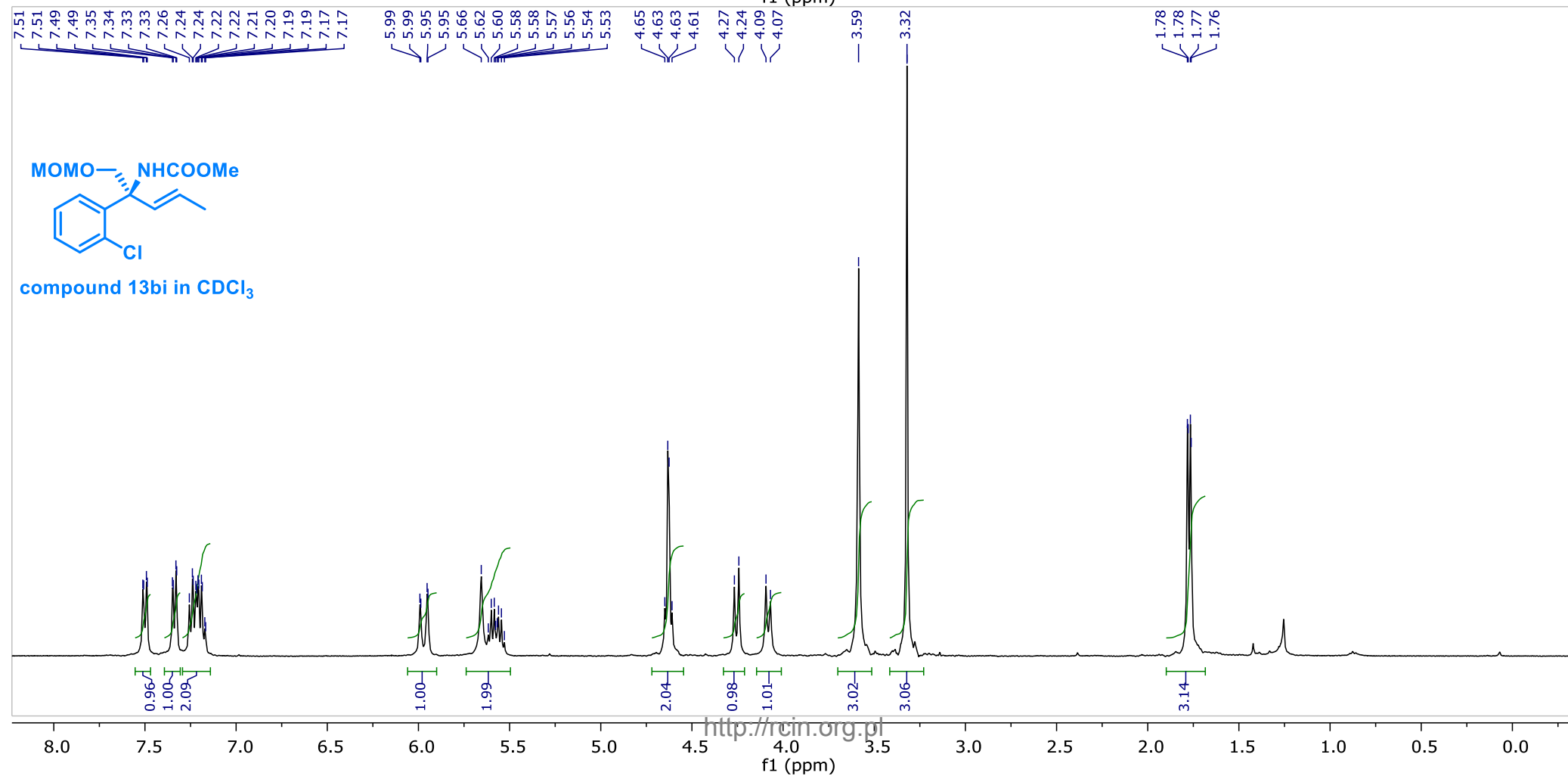
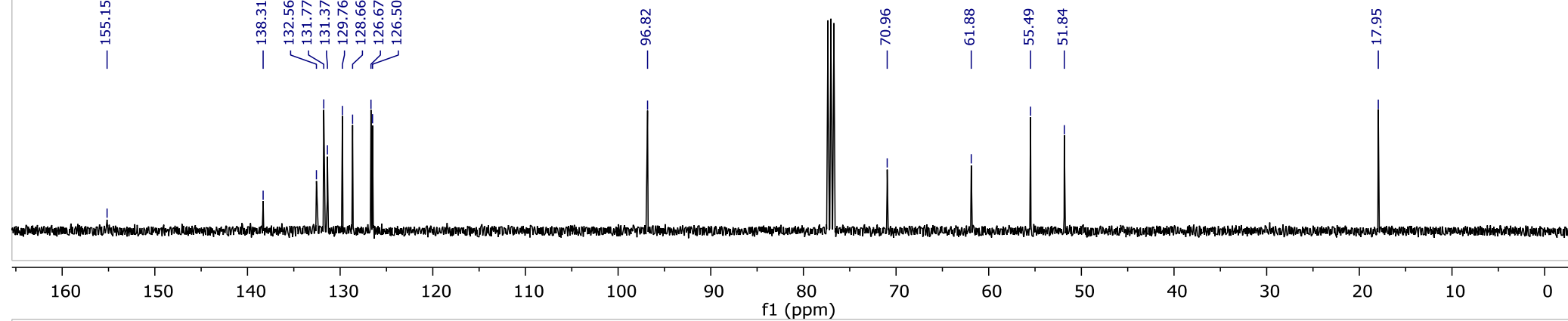








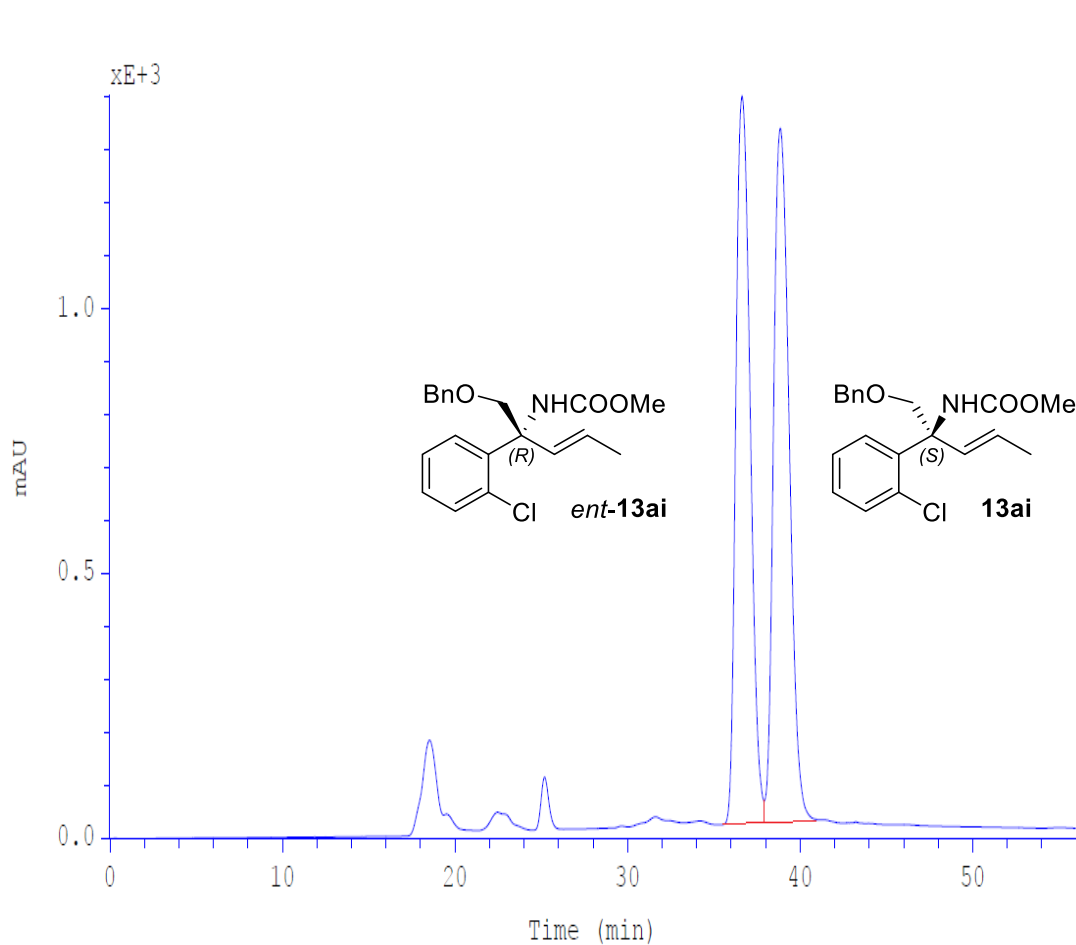
compound 13ai in CDCl<sub>3</sub>



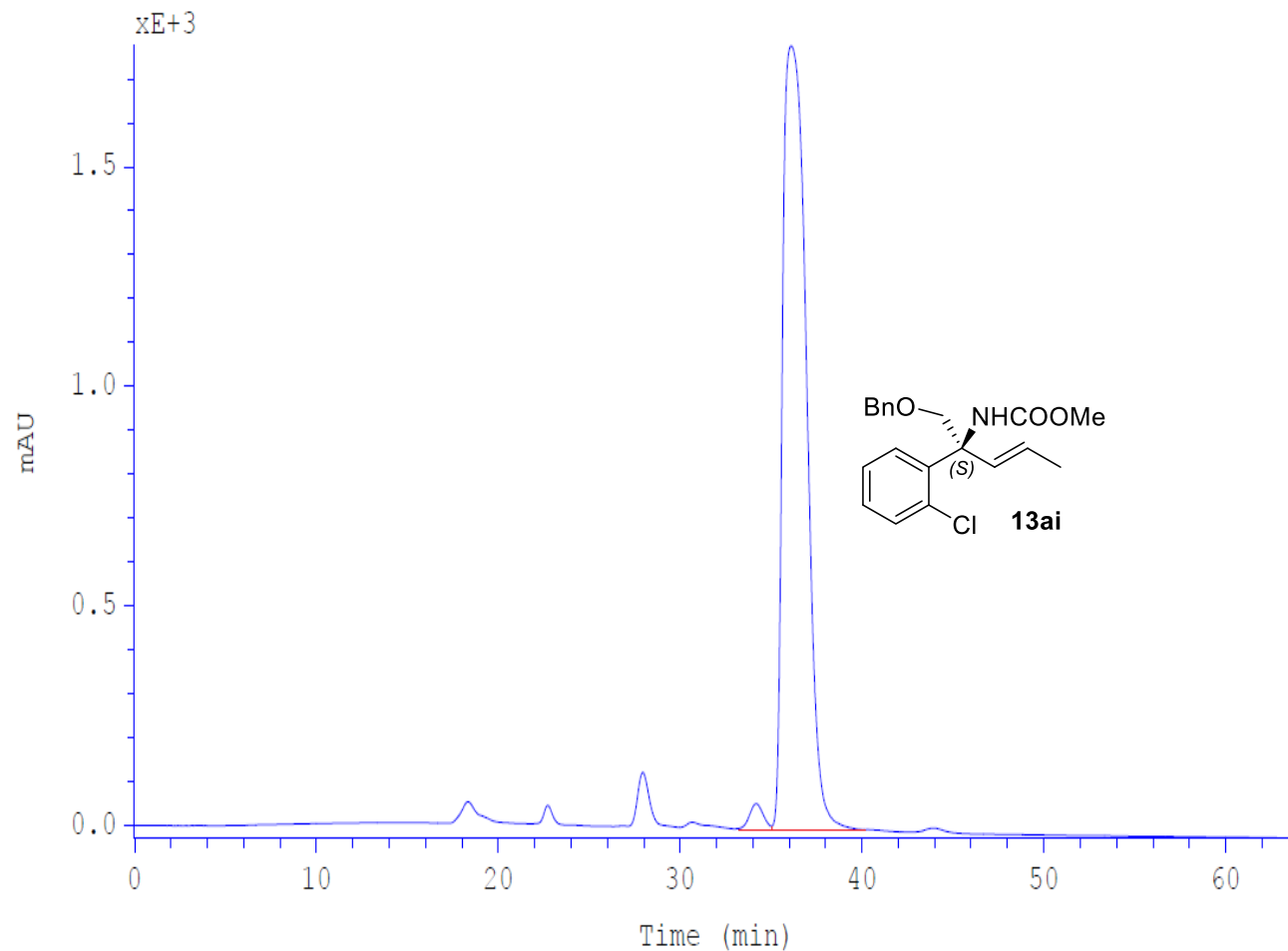


## HPLC chromatogram of compounds rac-13ai and 13ai

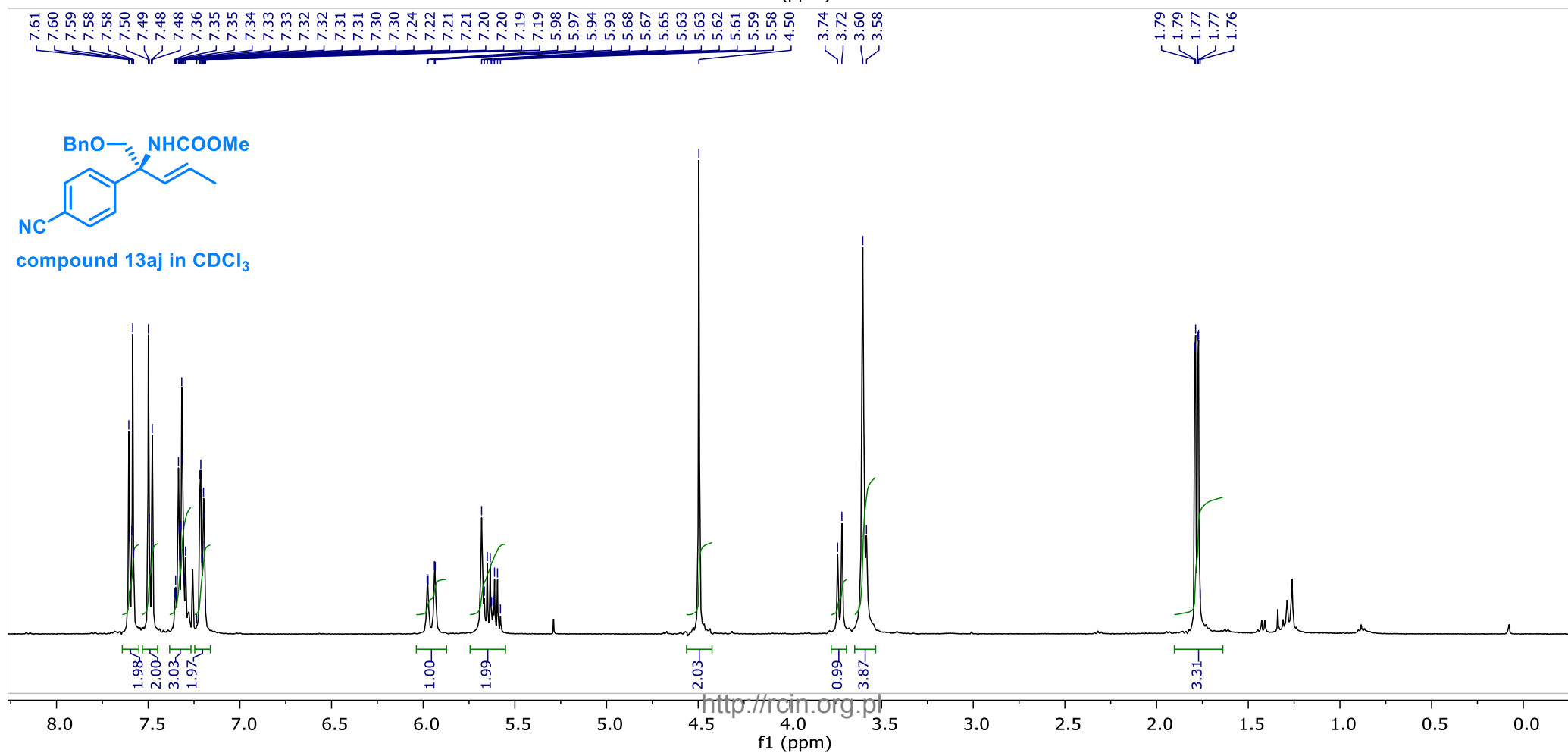
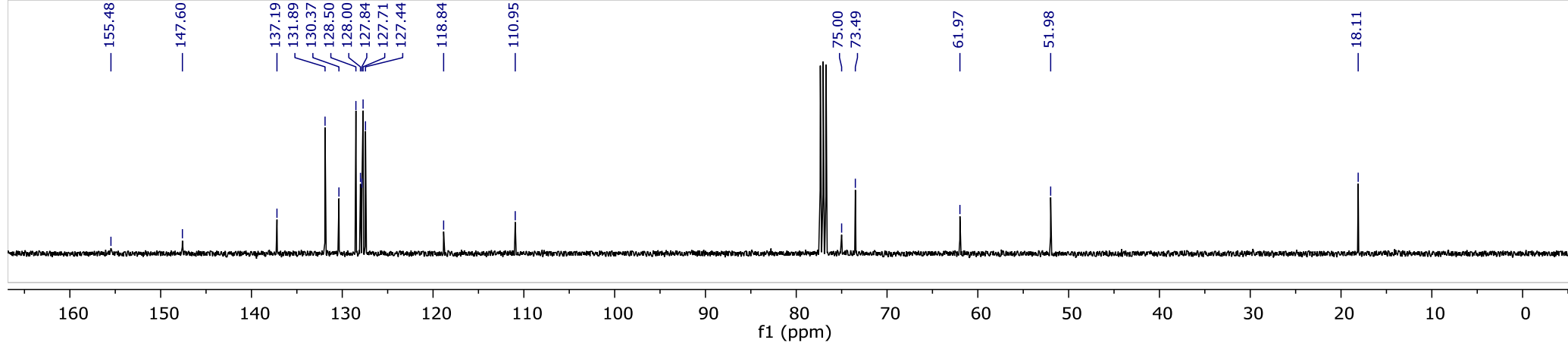
Conditions: column Chiralcel AS-H, 5% *i*-PrOH in hexanes, 0.2 mL/min, detection: UV, 215 nm

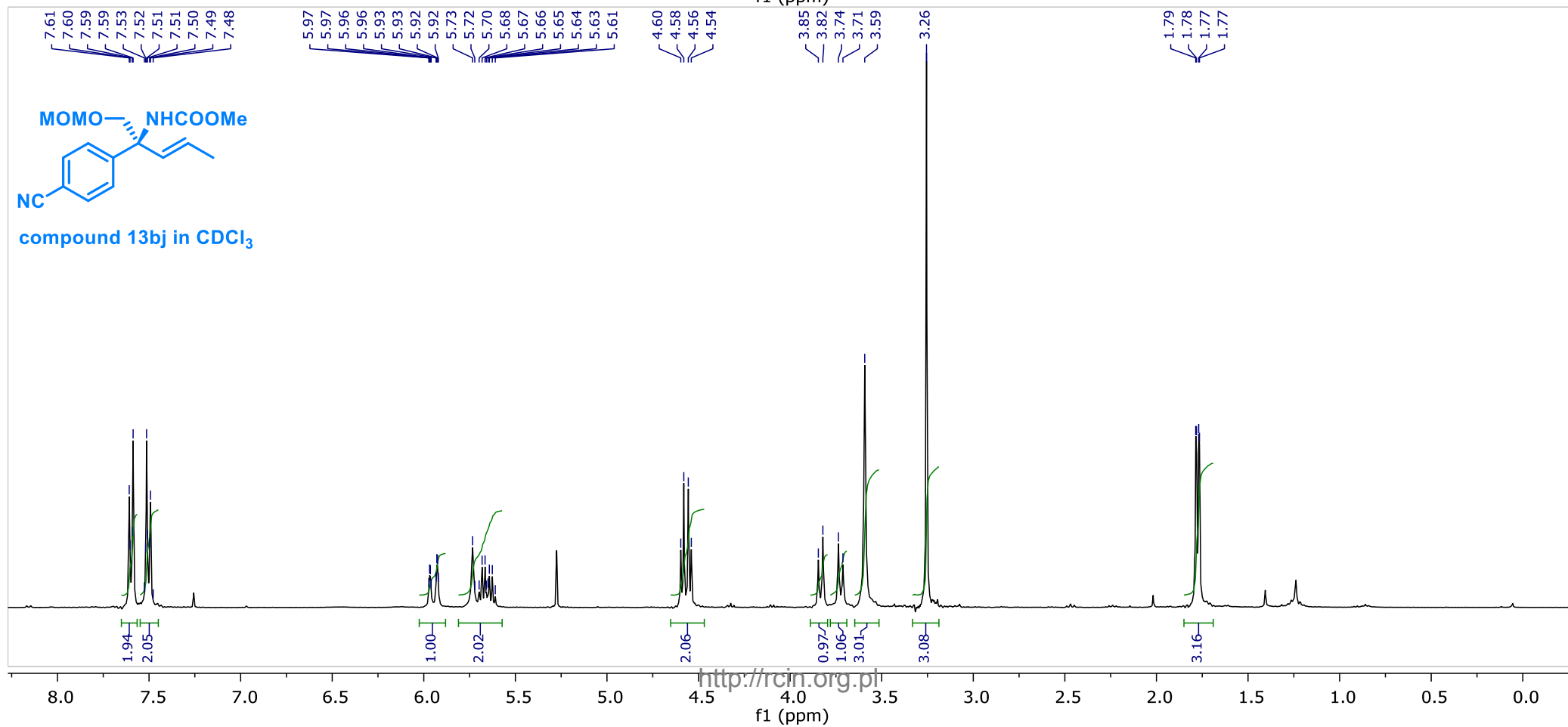
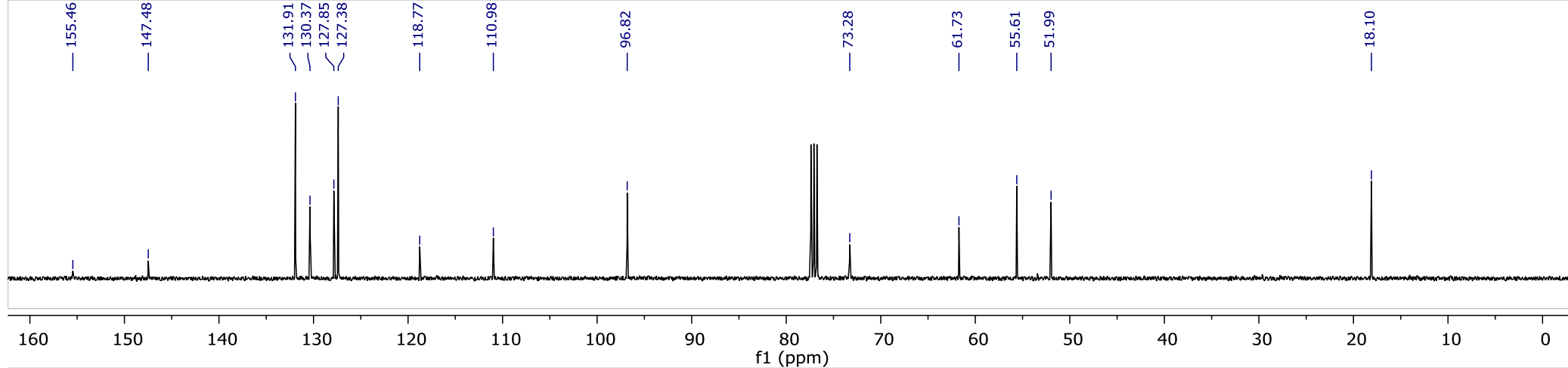


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	36.639	35.37	37.88	1326.88	1375.16	48.8256	0.914
2	38.856	37.88	41.57	1390.7	1311.45	51.1744	0.995



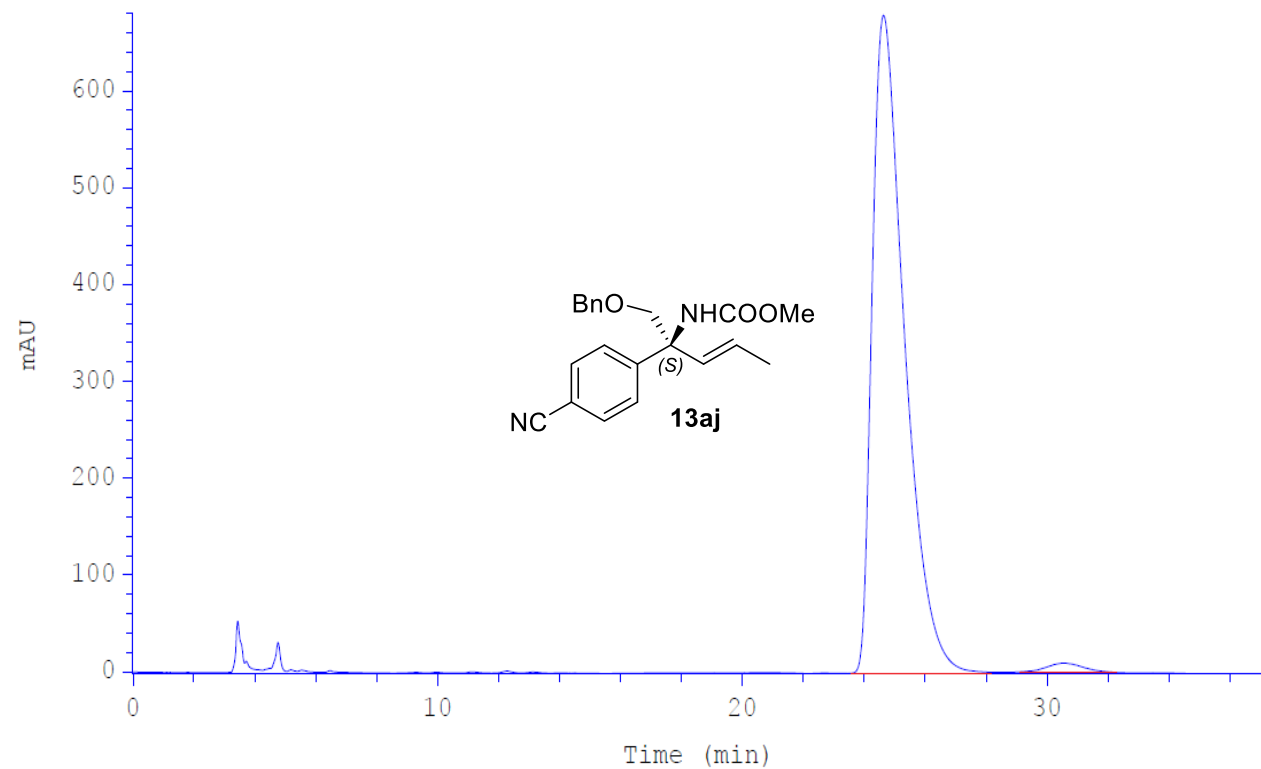
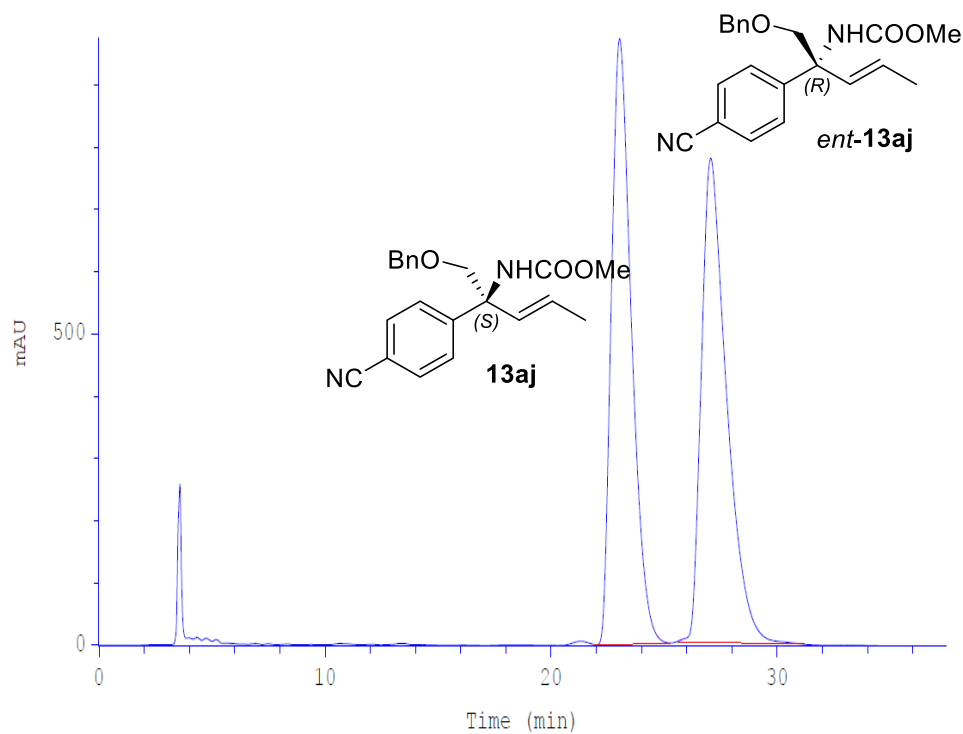
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	34.187	33.42	34.92	39.3659	51.153	1.4537	0.758
2	36.121	35.01	40.11	2668.54	1778.46	98.5463	219.454





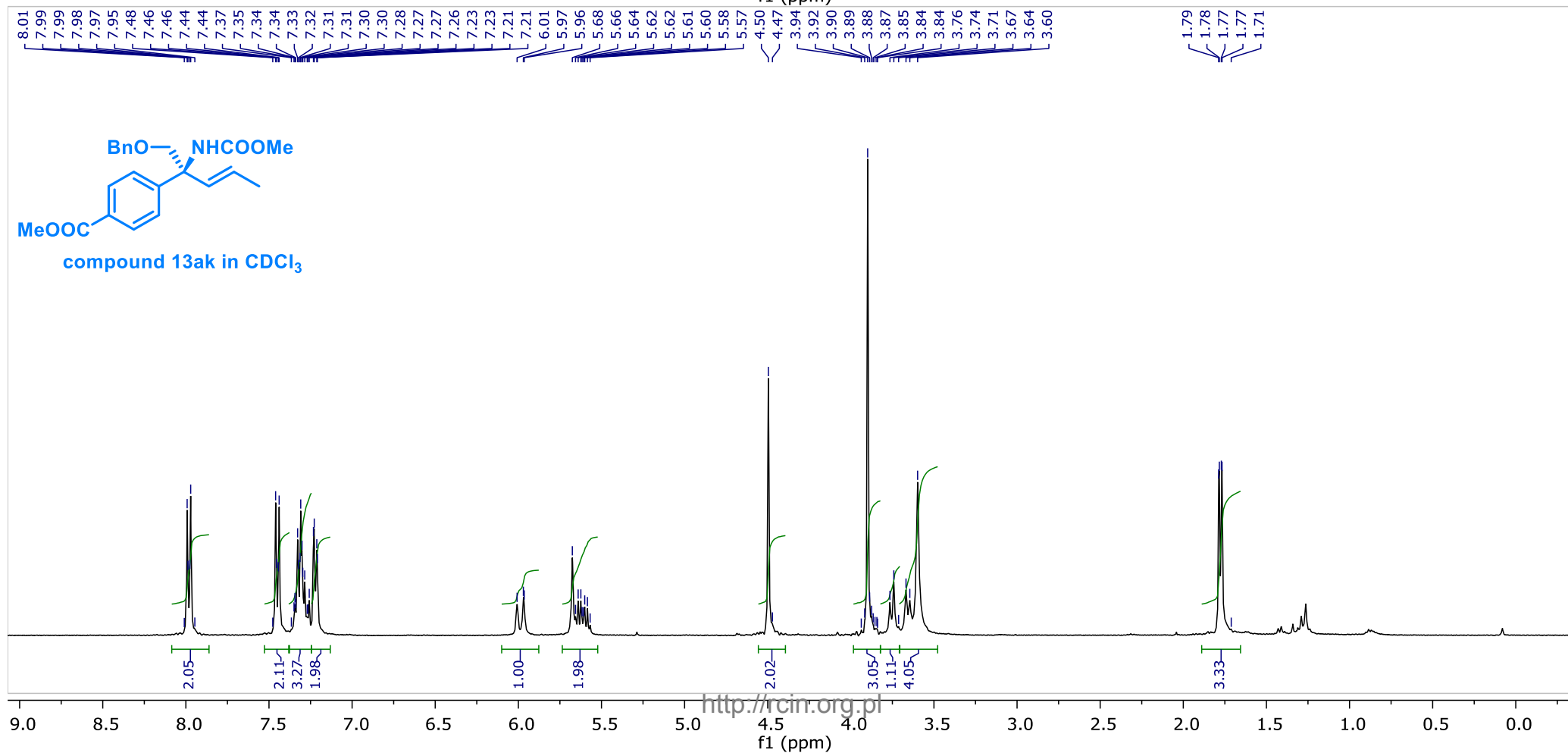
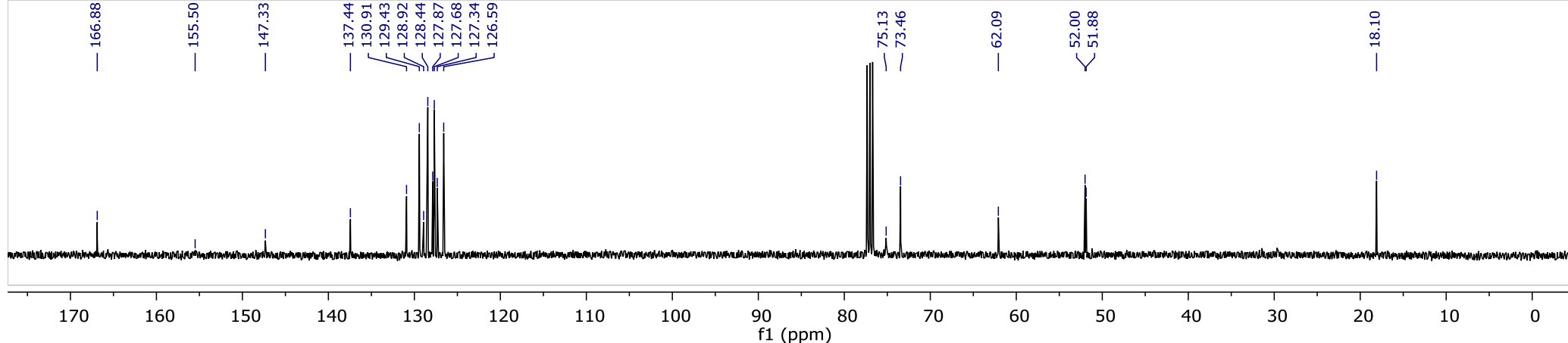
## HPLC chromatogram of compounds rac-13aj and 13aj

Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1mL/min, detection: UV, 215 nm



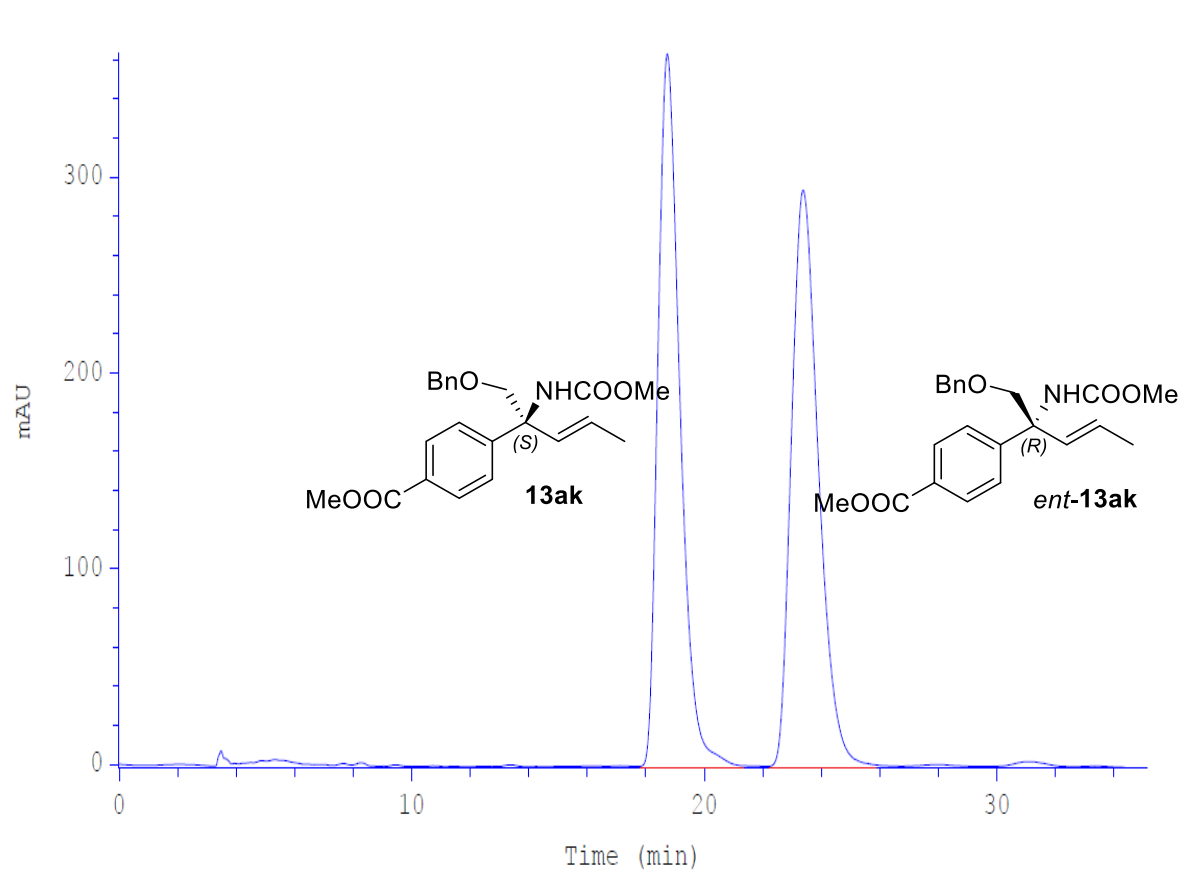
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	23.037	21.90	25.04	995.05	971.575	49.7215	0.959
2	27.055	25.51	30.97	1006.2	778.094	50.2785	1.178

	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	24.638	23.47	28.24	833.507	679.575	98.9761	1.121
2	30.555	29.66	31.75	8.62284	7.64392	1.0239	1.136



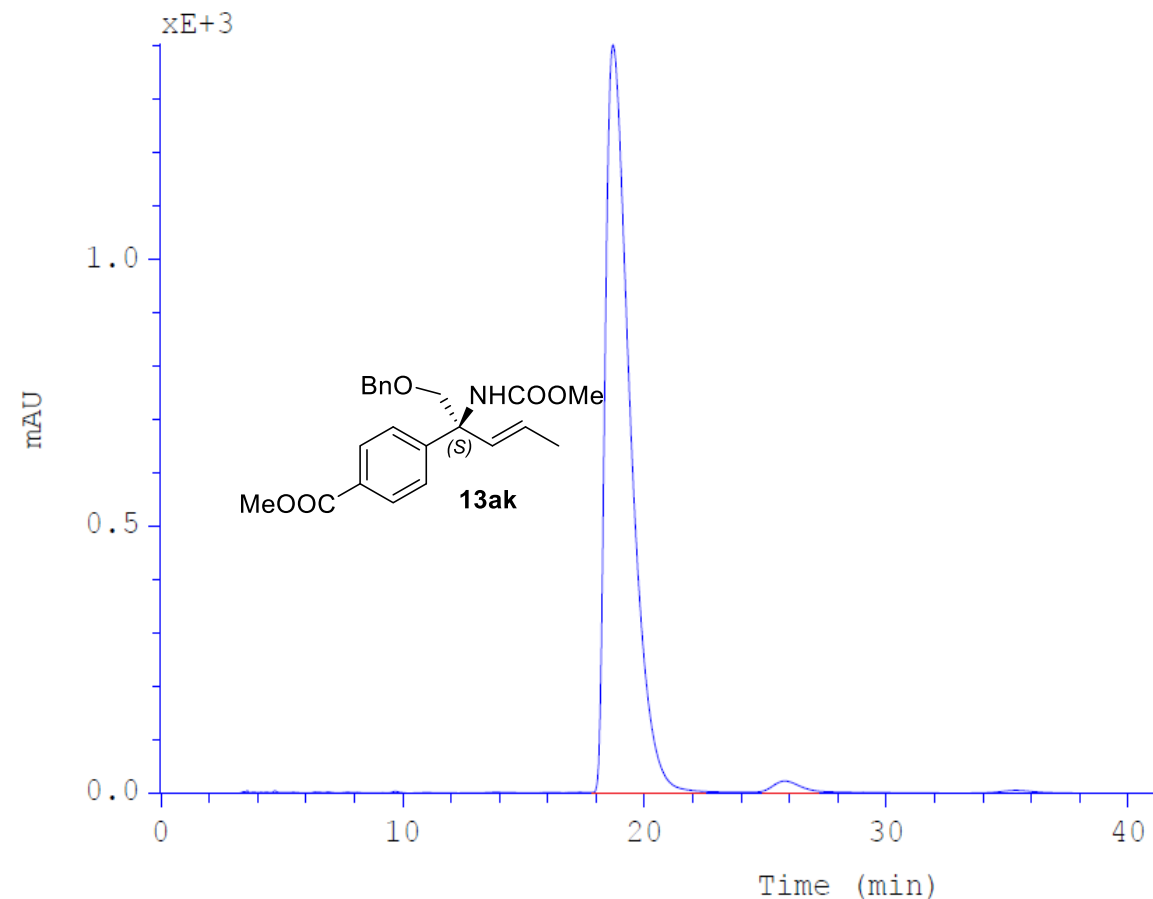
## HPLC chromatogram of compounds rac-13ak and 13ak

Conditions: column Chiralcel OD-H, 5% *i*-PrOH in hexanes, 1mL/min, detection: UV, 235 nm

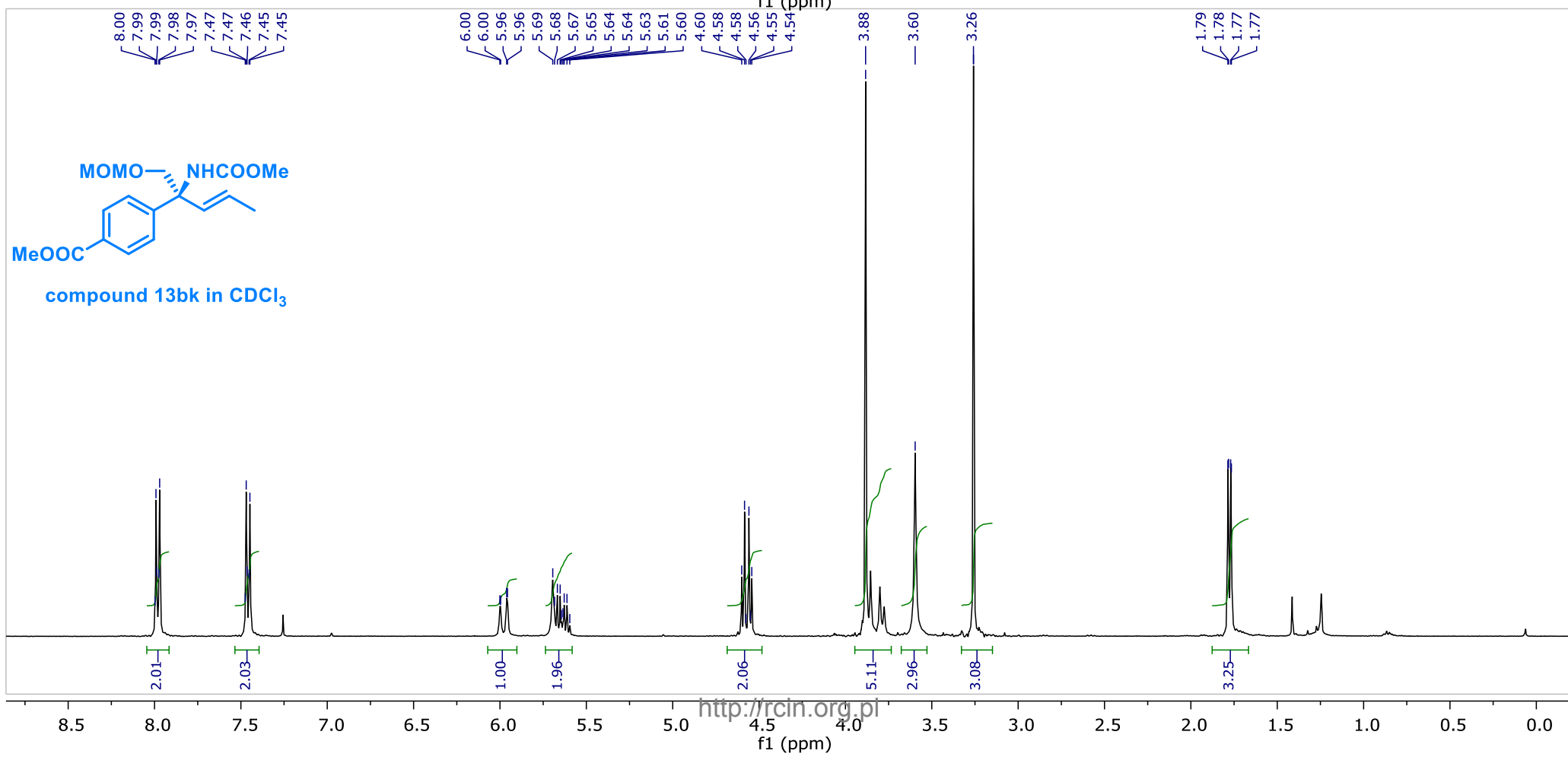
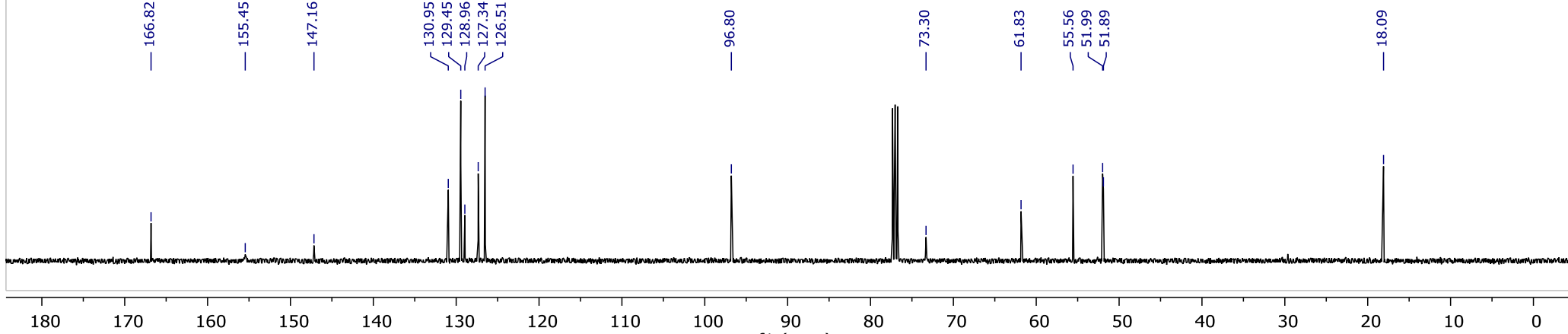


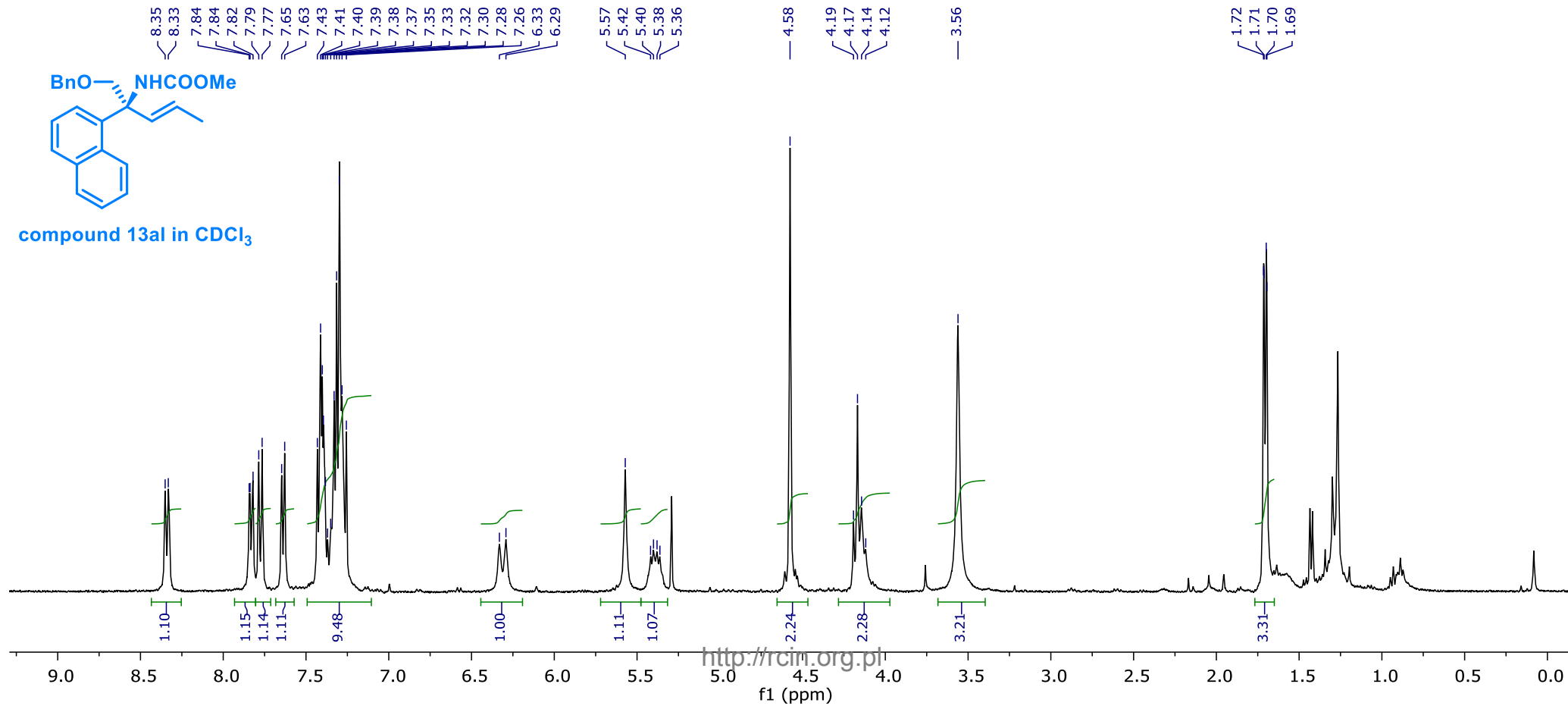
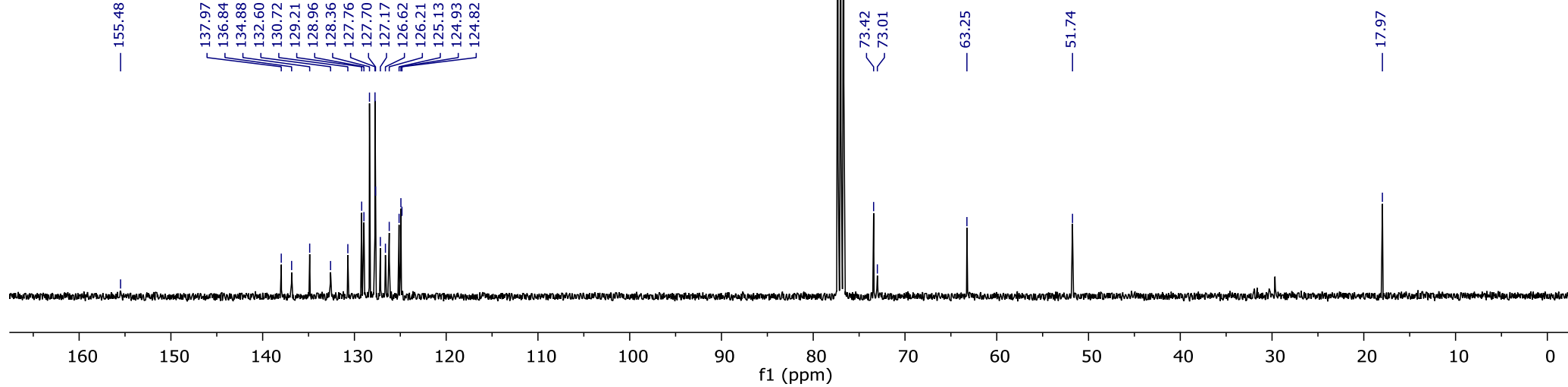
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	18.737	17.80	21.14	316.327	363.879	50.2708	0.799
2	23.371	22.27	25.82	312.919	294.056	49.7292	0.991

<http://rcin.org.pl>

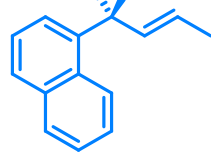


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	18.700	17.82	22.39	1655.15	1400.8	98.7510	1.078
2	25.800	24.95	27.18	20.9348	18.5042	1.2490	1.105



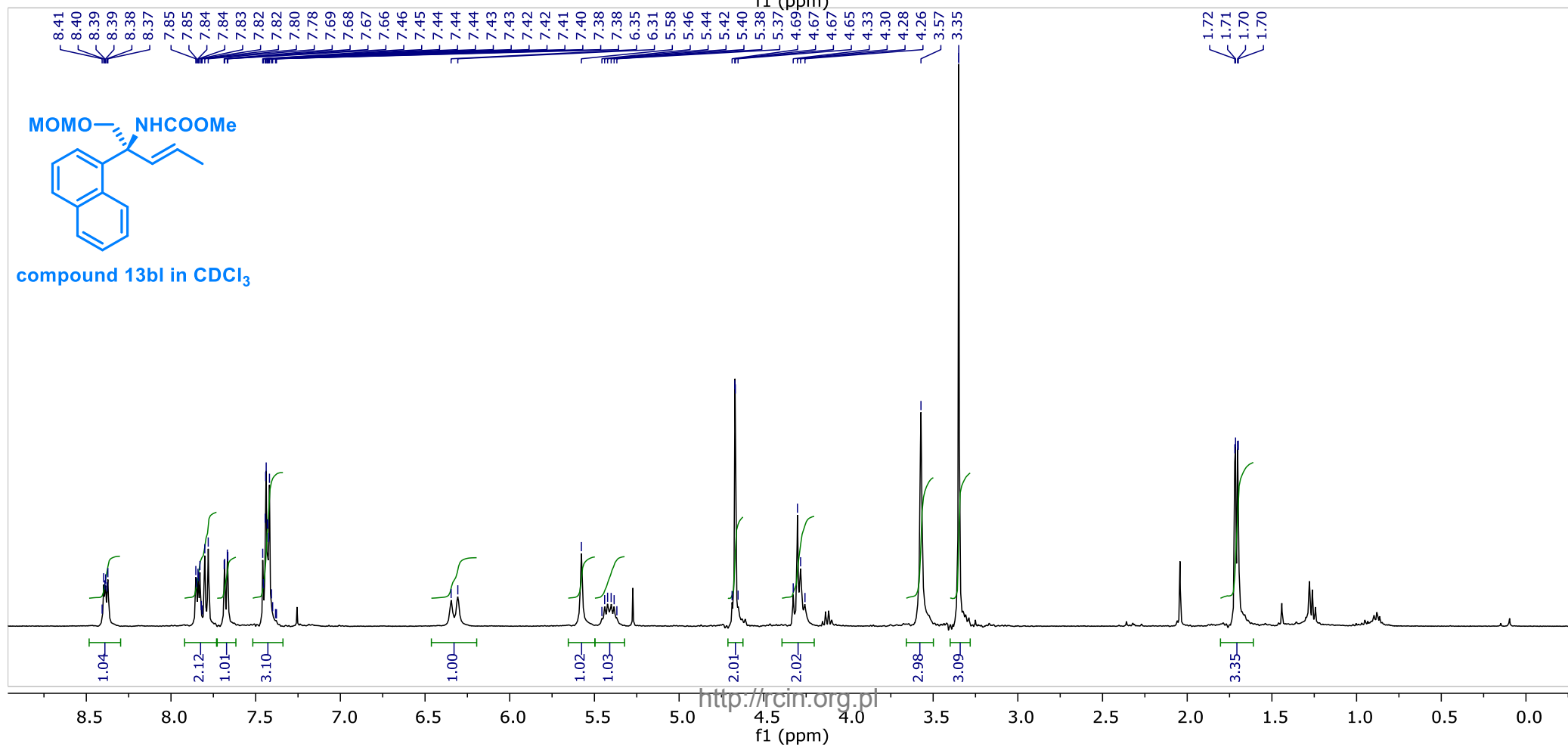
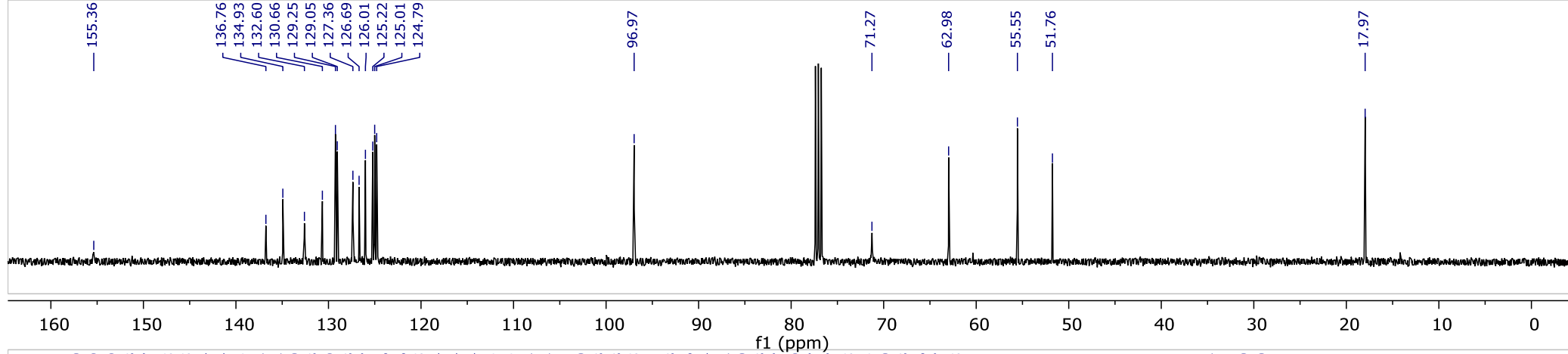


BnO—NHCOOMe



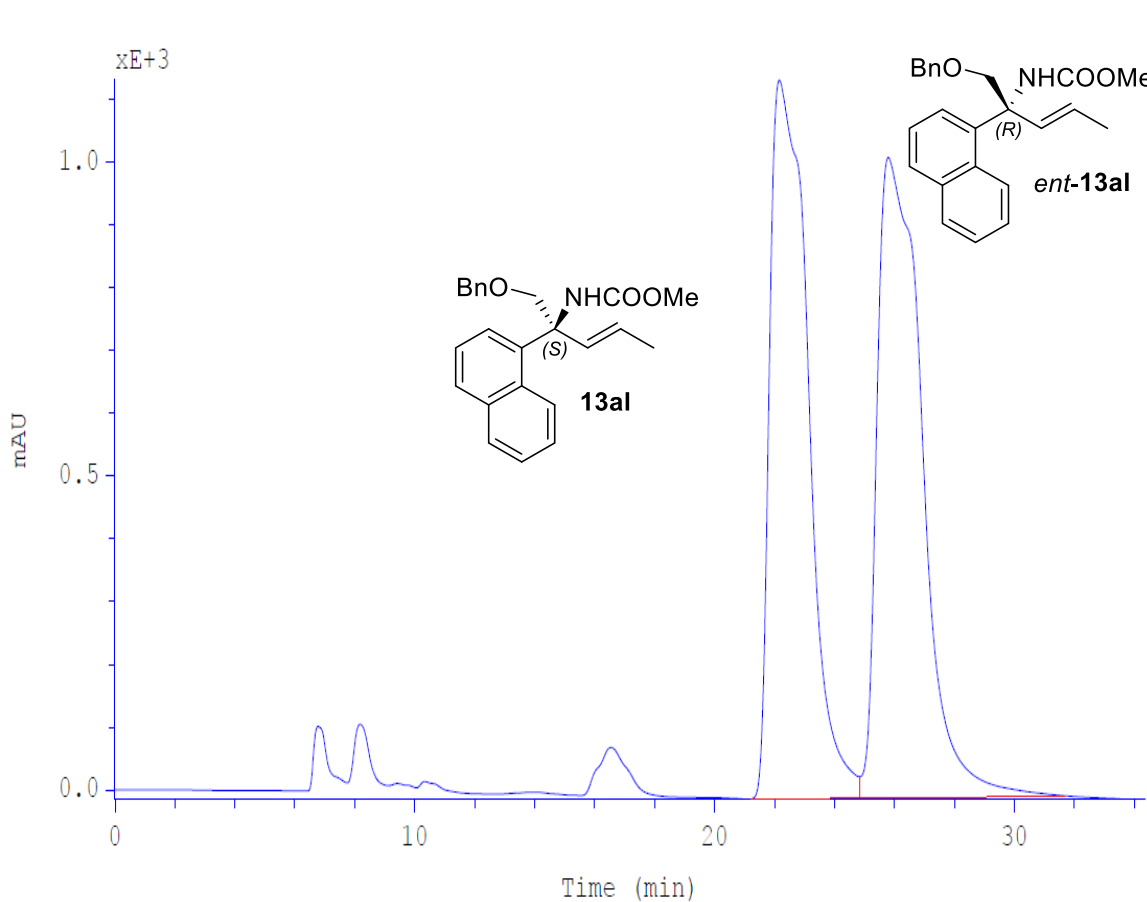
compound 13a in CDCl<sub>3</sub>



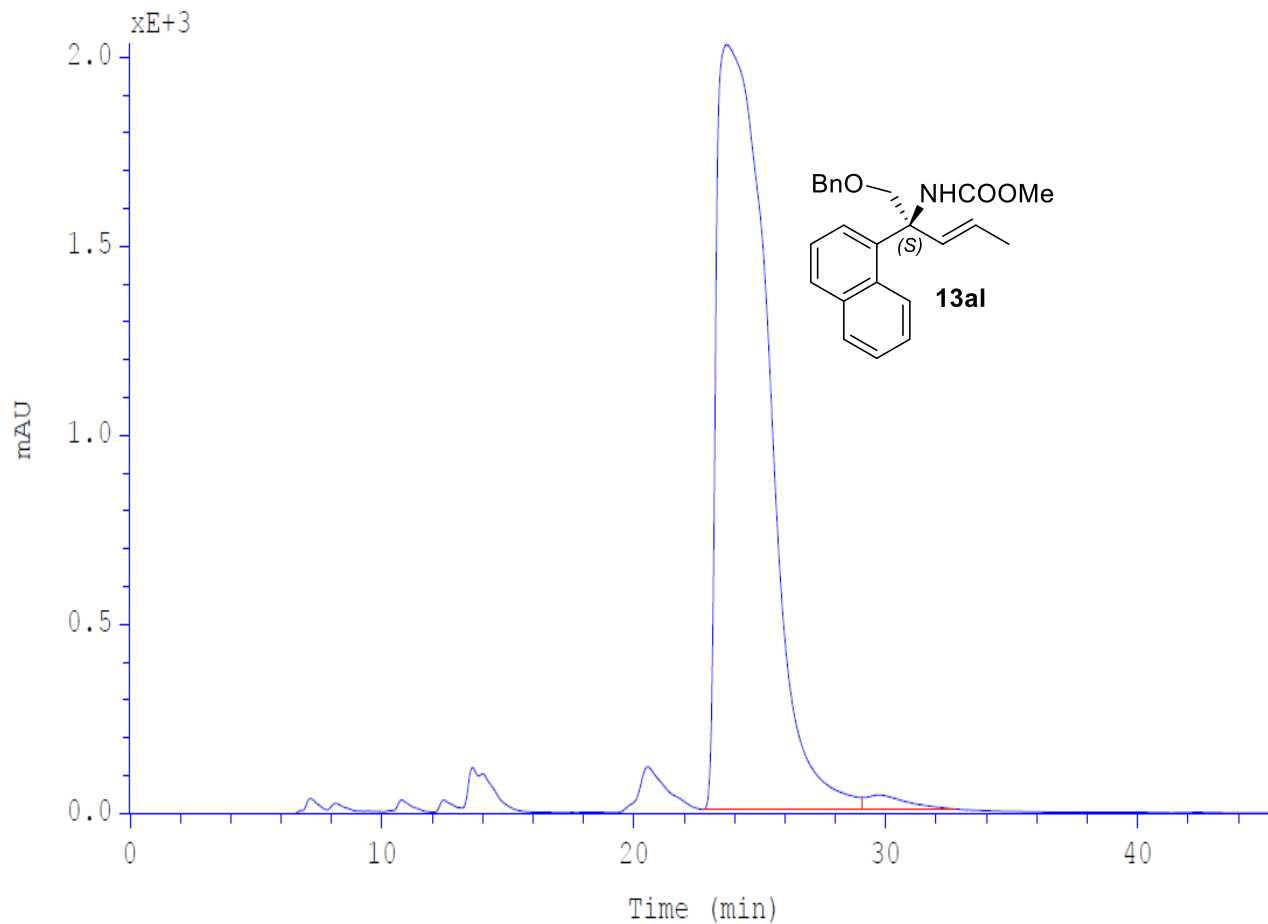


## HPLC chromatogram of compounds rac-13al and 13al

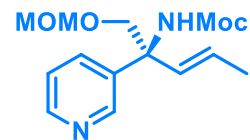
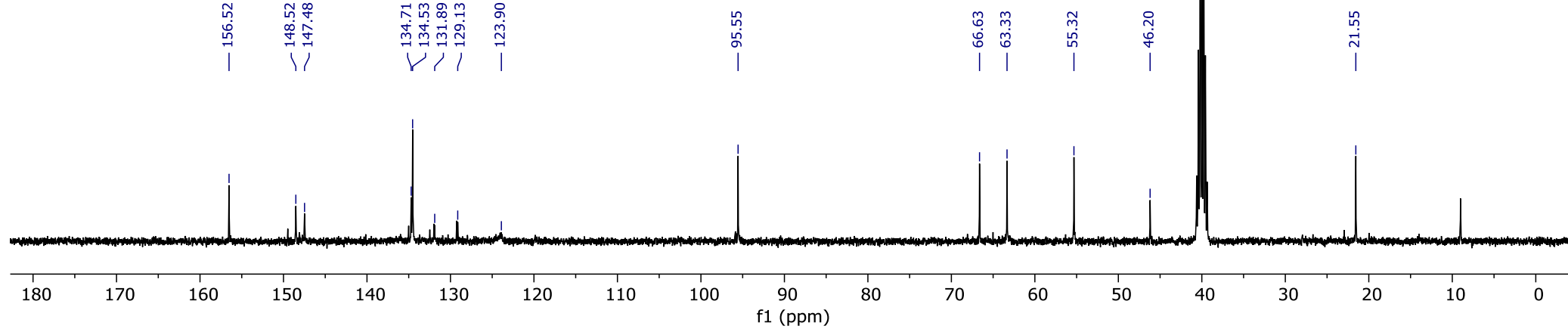
Conditions: column Chiralpak OA-H, 5% *i*-PrOH in hexanes, 0.5 mL/min, detection: UV, 215 nm



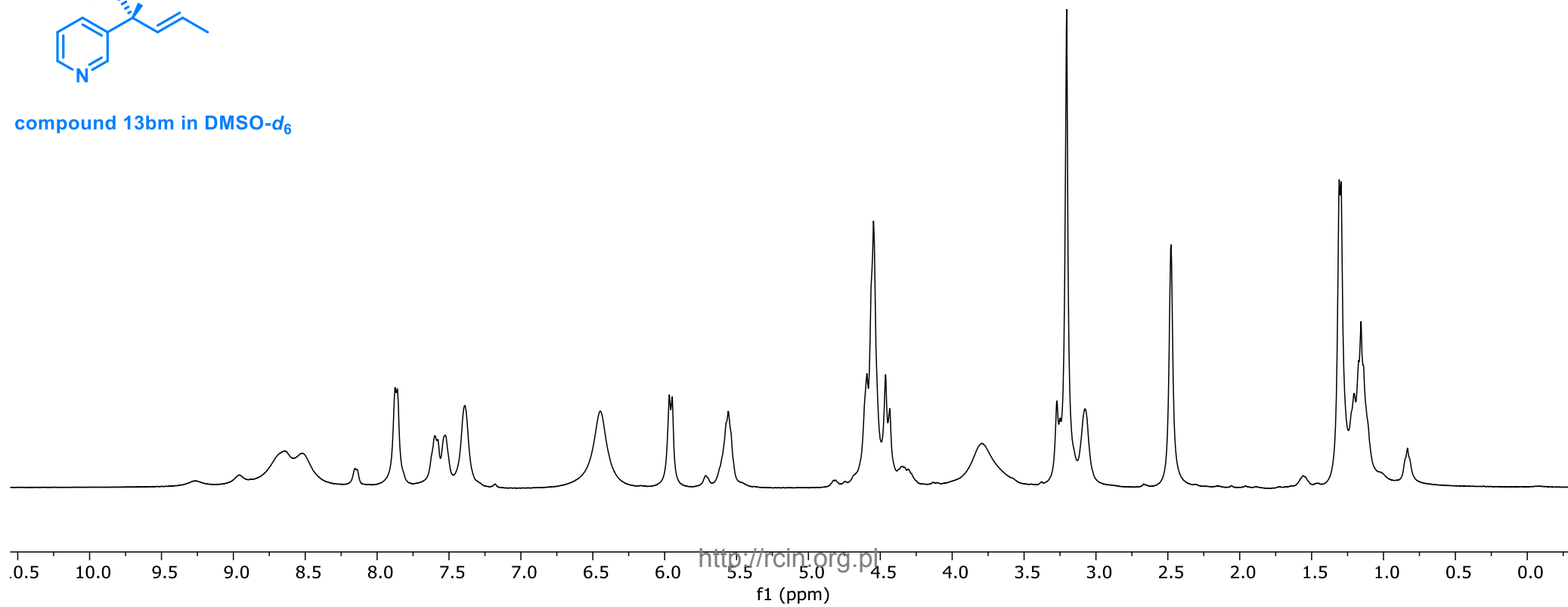
	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	22.155	21.15	24.91	1696.81	1144.95	48.9625	1.399
2	25.789	24.91	31.68	1768.72	1020.18	51.0375	1.614

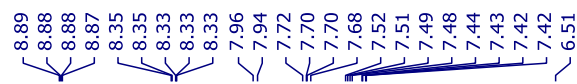
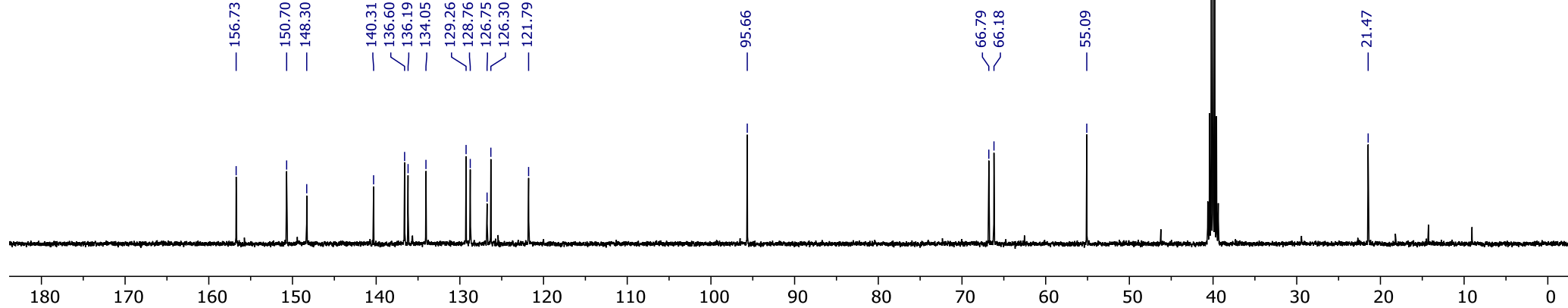


	Ret.time [min]	Start [min]	End [min]	Area [mAU*min]	Height [mAU]	% Area	Width [min]
1	23.702	22.77	29.07	4781.11	2022.06	98.7435	2.274
2	29.736	29.07	32.28	60.8405	34.9882	1.2565	1.353

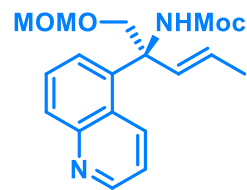
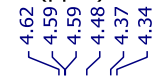


compound 13bm in DMSO-d<sub>6</sub>

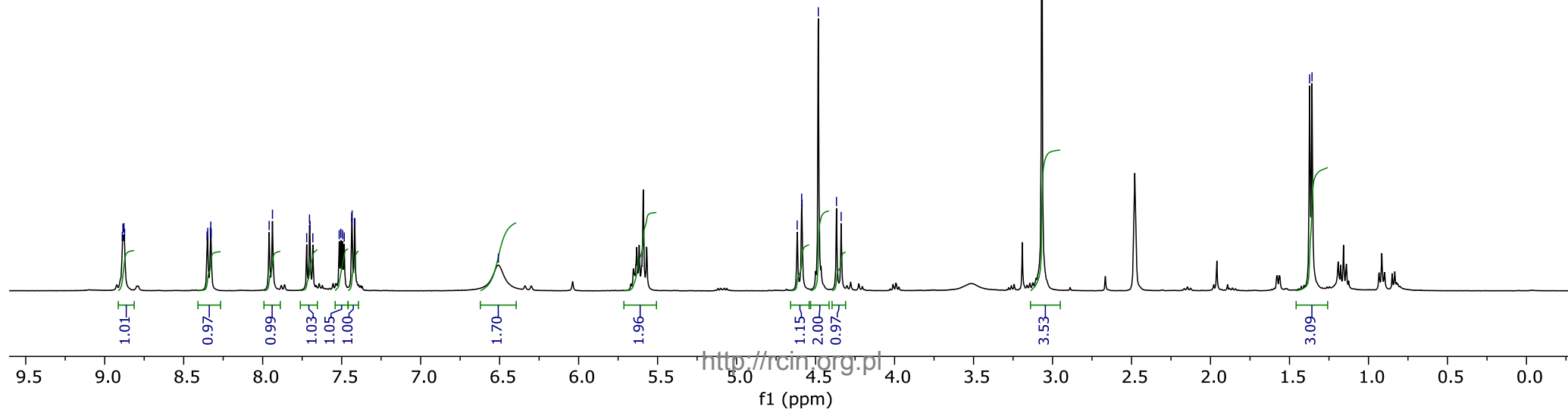


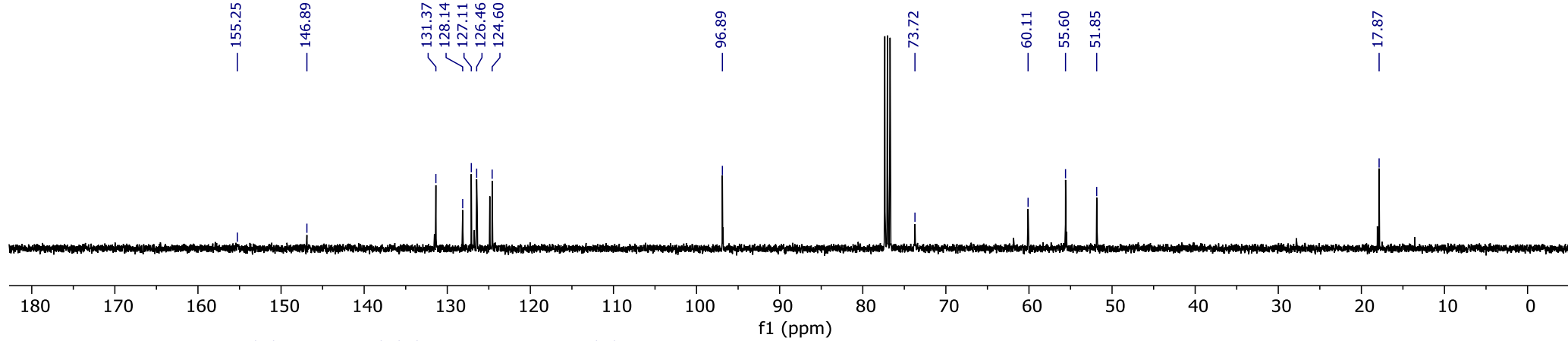


f1 (ppm)

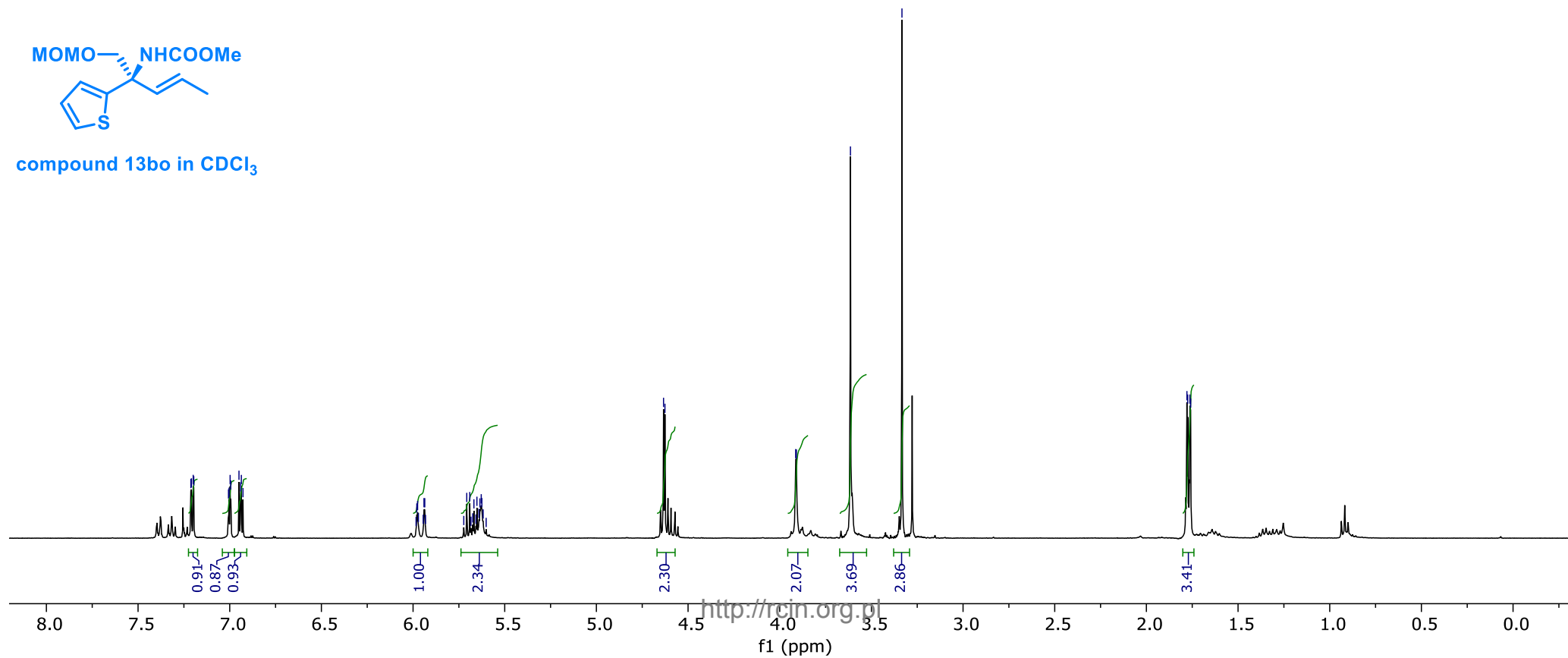
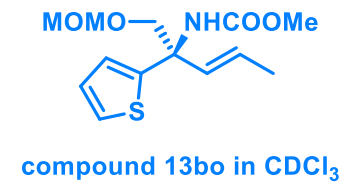


compound 13bm in CDCl<sub>3</sub>

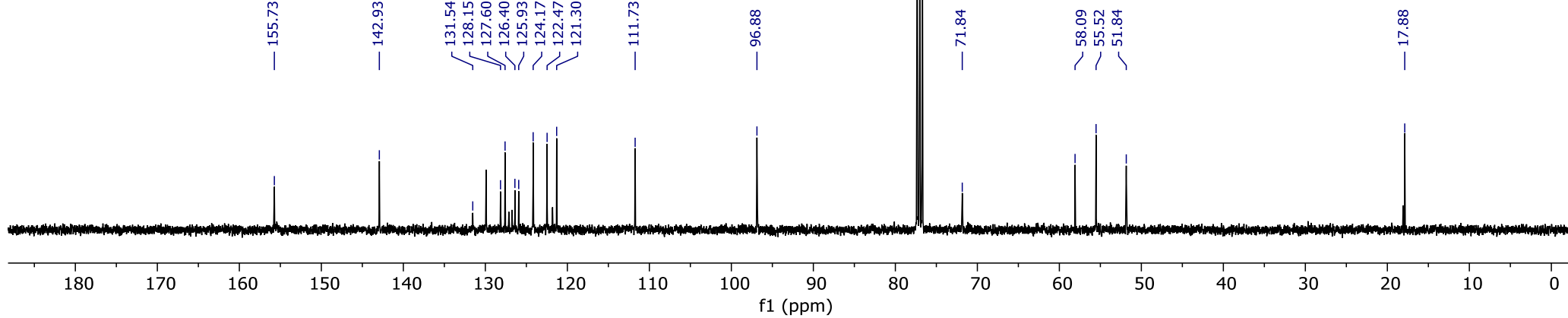




155.25, 146.89, 131.37, 128.14, 127.11, 126.46, 124.60, 96.89, 73.72, 60.11, 55.60, 51.85, 17.87, 7.21, 7.21, 7.20, 7.20, 7.01, 7.00, 6.99, 6.95, 6.94, 6.93, 5.98, 5.98, 5.97, 5.94, 5.94, 5.94, 5.93, 5.72, 5.71, 5.69, 5.68, 5.67, 5.66, 5.65, 5.64, 5.63, 5.62, 5.60, 4.63, 4.63, 3.91, 3.91, 3.61, 3.33, 1.78, 1.77, 1.76, 1.76



0.91, 0.87, 0.93, 1.00, 2.34, 2.30, 2.07, 3.69, 2.86, 3.41



7.65  
7.63  
7.56  
7.47  
7.45  
7.40  
7.38  
7.34  
7.32  
7.30  
7.28  
7.26  
7.24  
7.21  
7.19  
7.17

6.01  
5.97  
5.73  
5.71  
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4.63

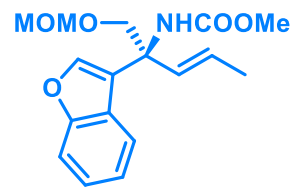
f1 (ppm)

4.07  
4.05  
4.01  
3.99

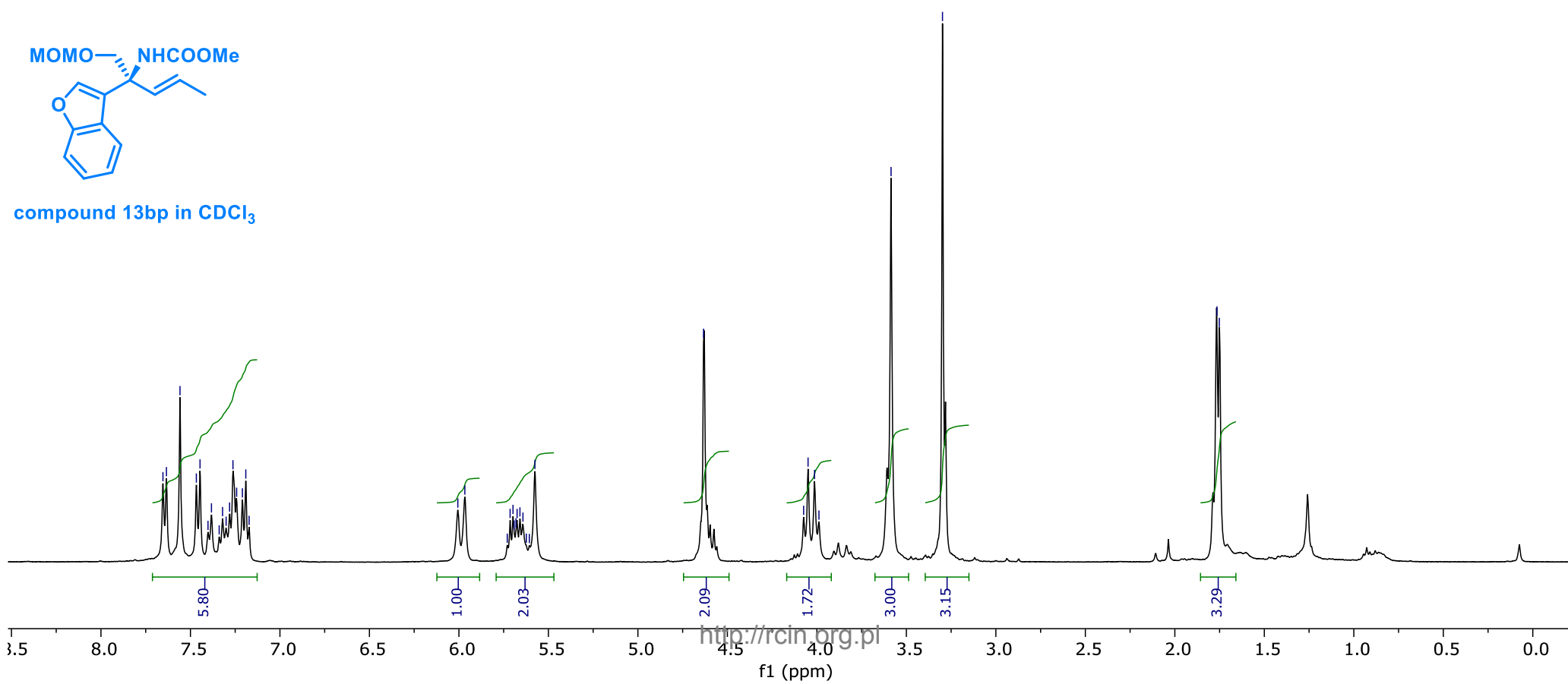
3.59

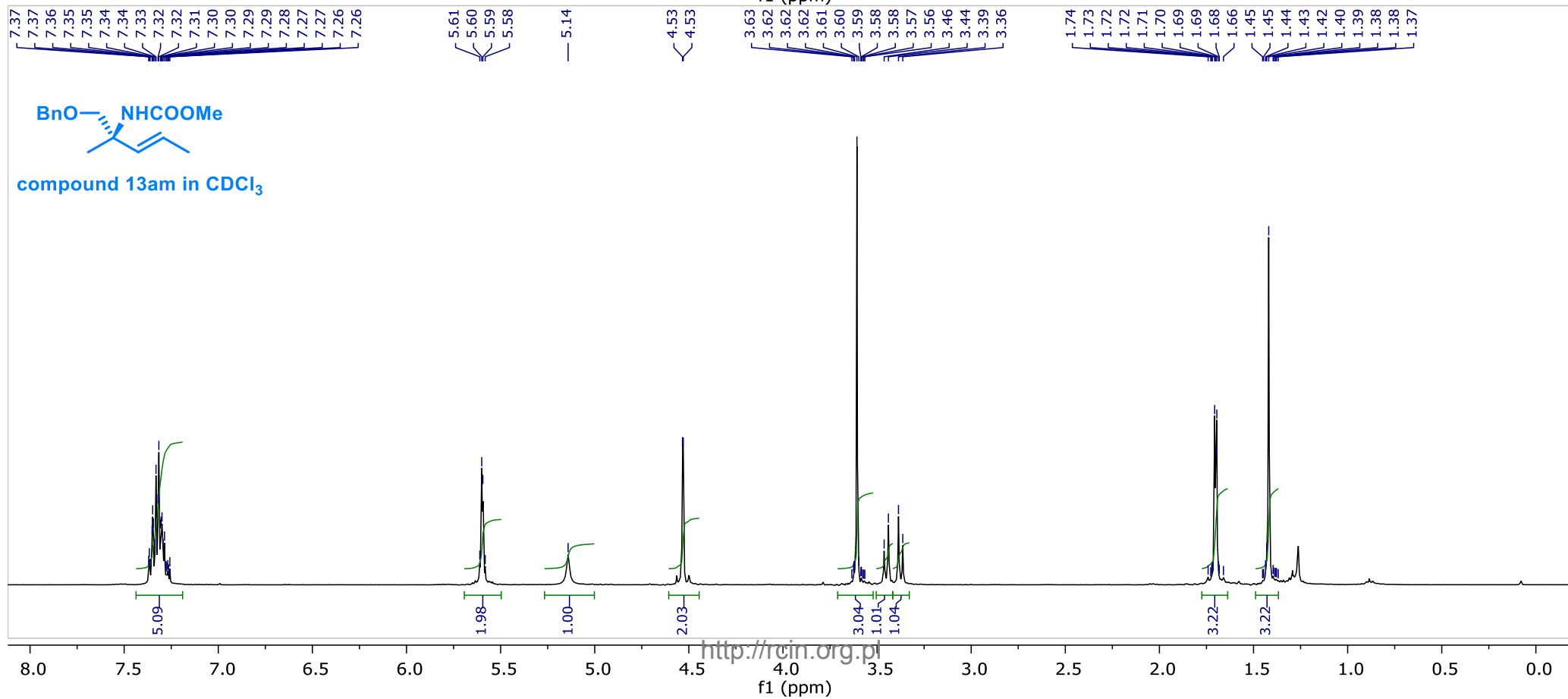
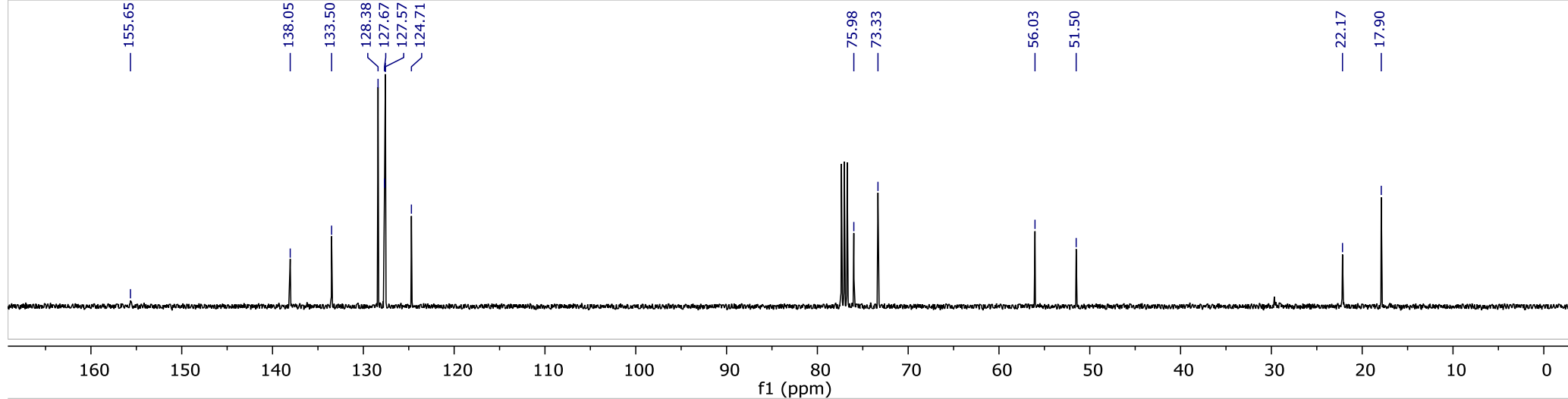
3.30

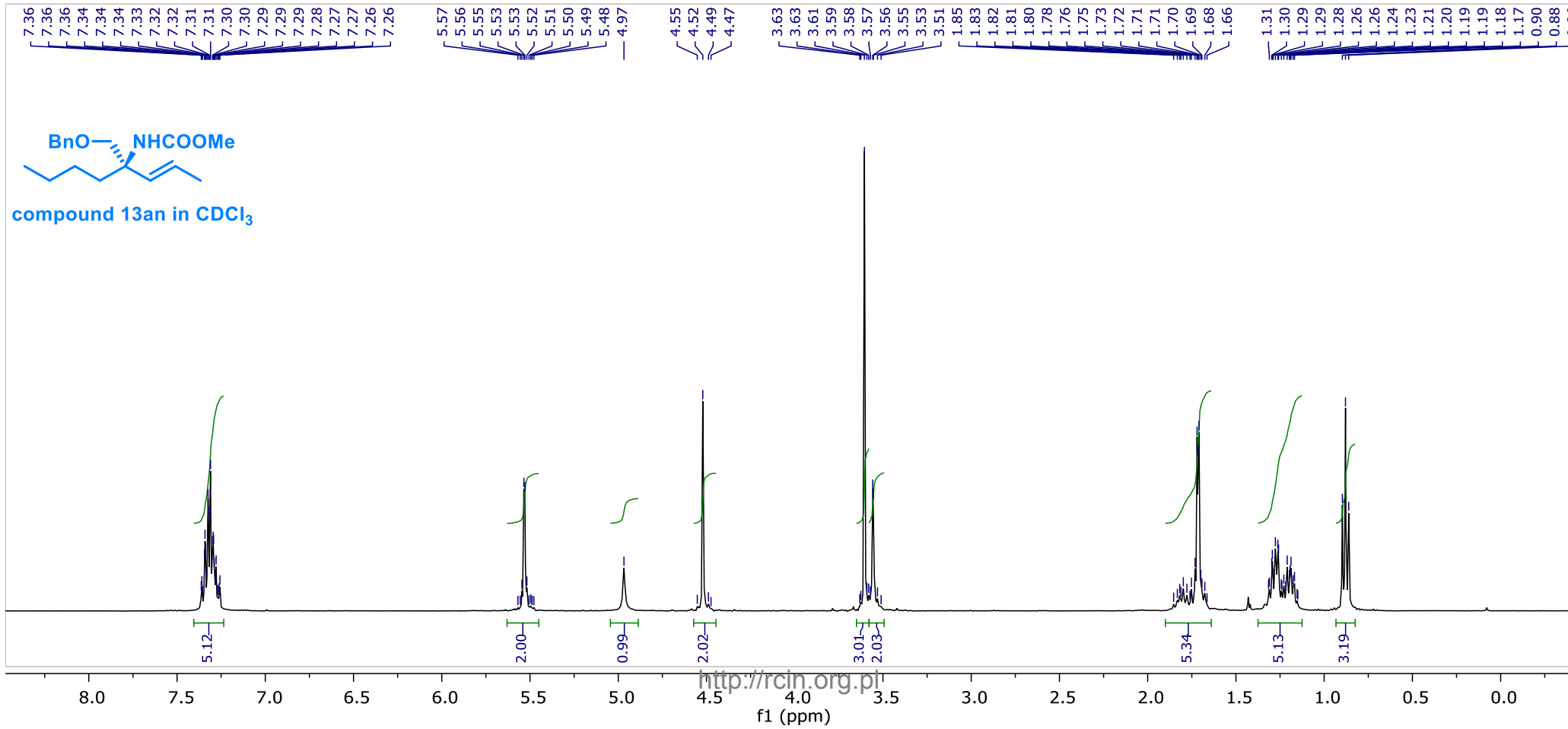
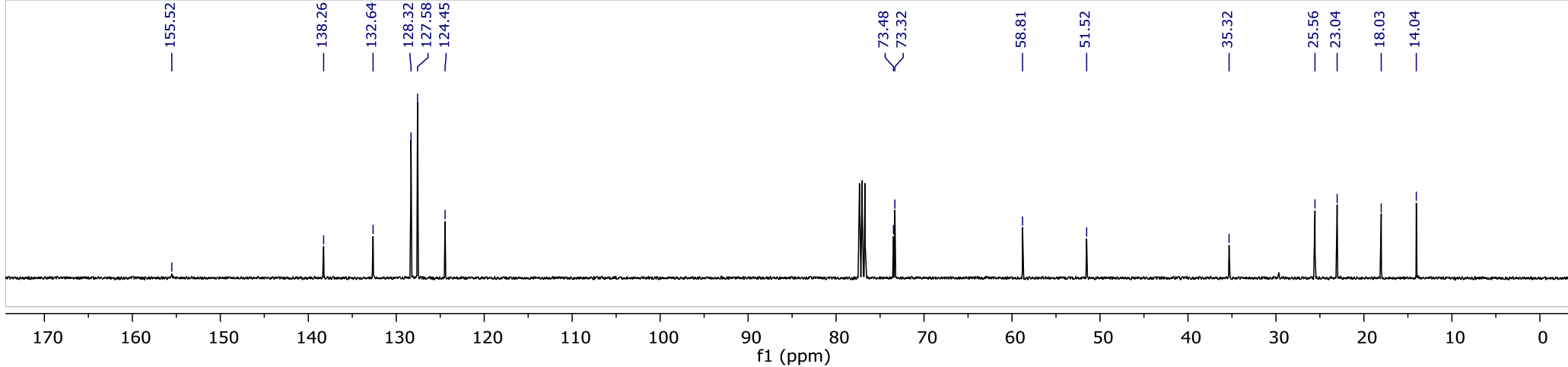
1.76  
1.75



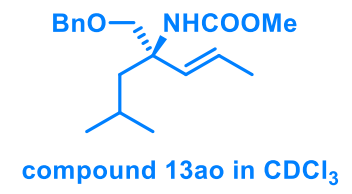
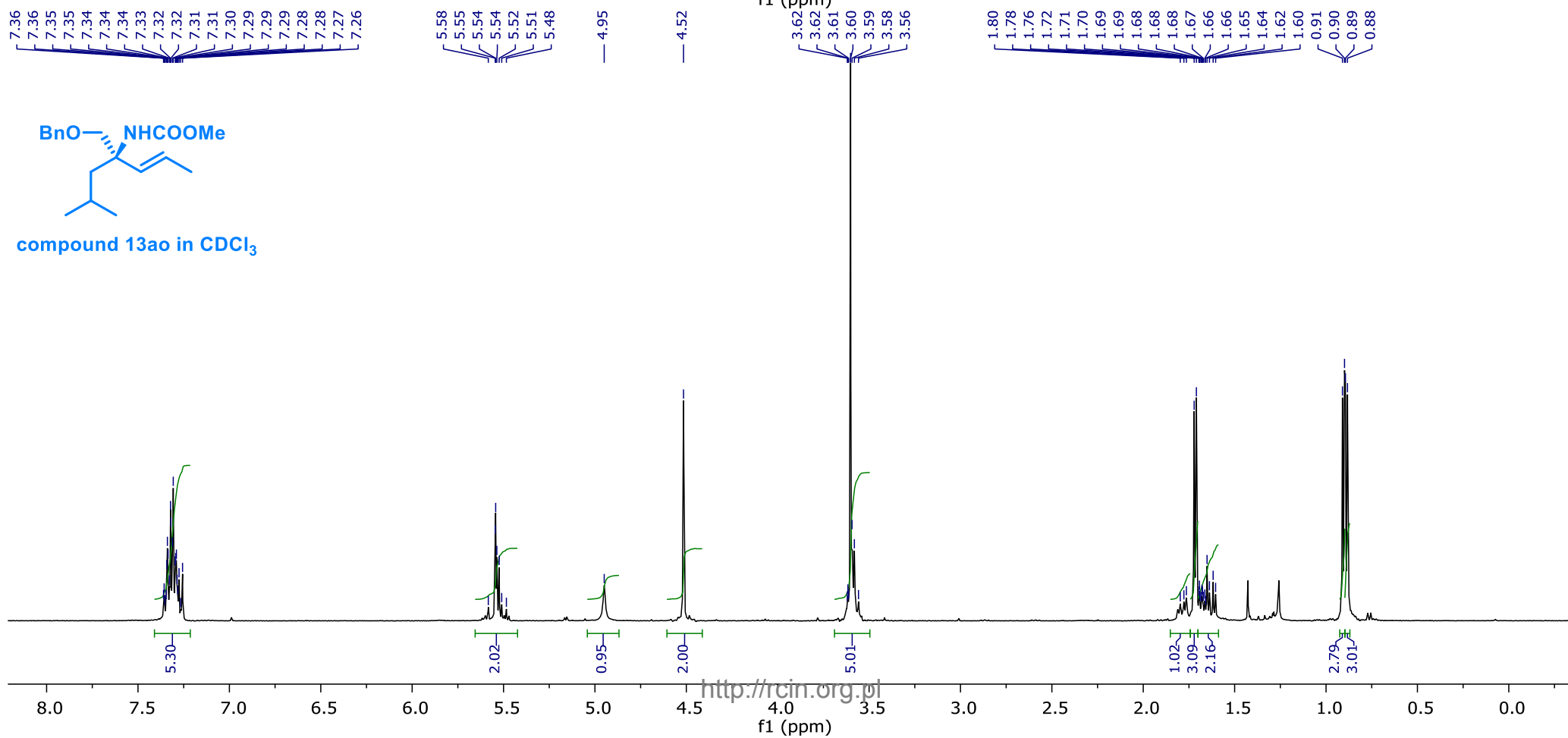
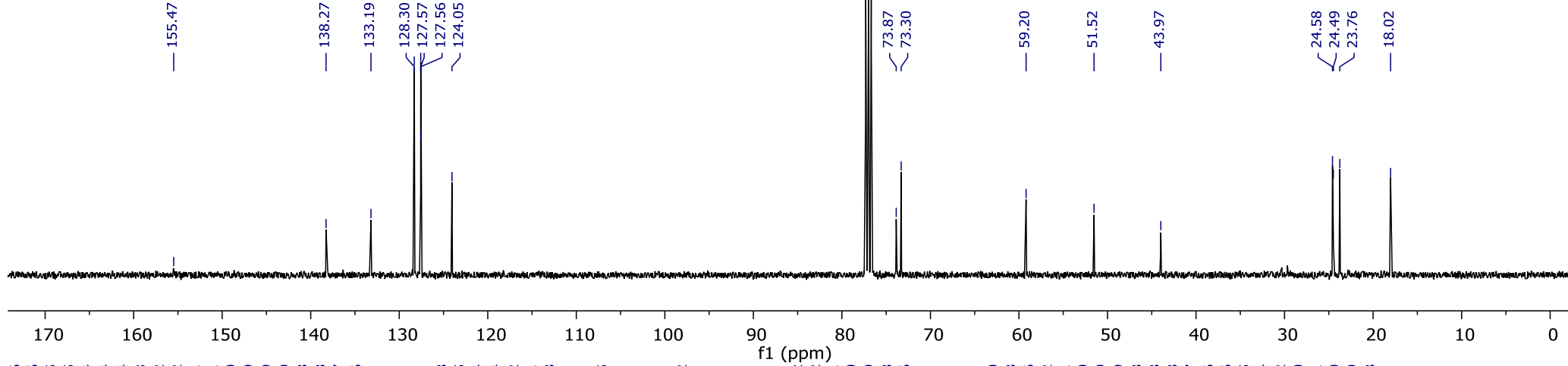
compound 13bp in CDCl<sub>3</sub>

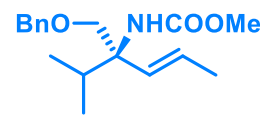
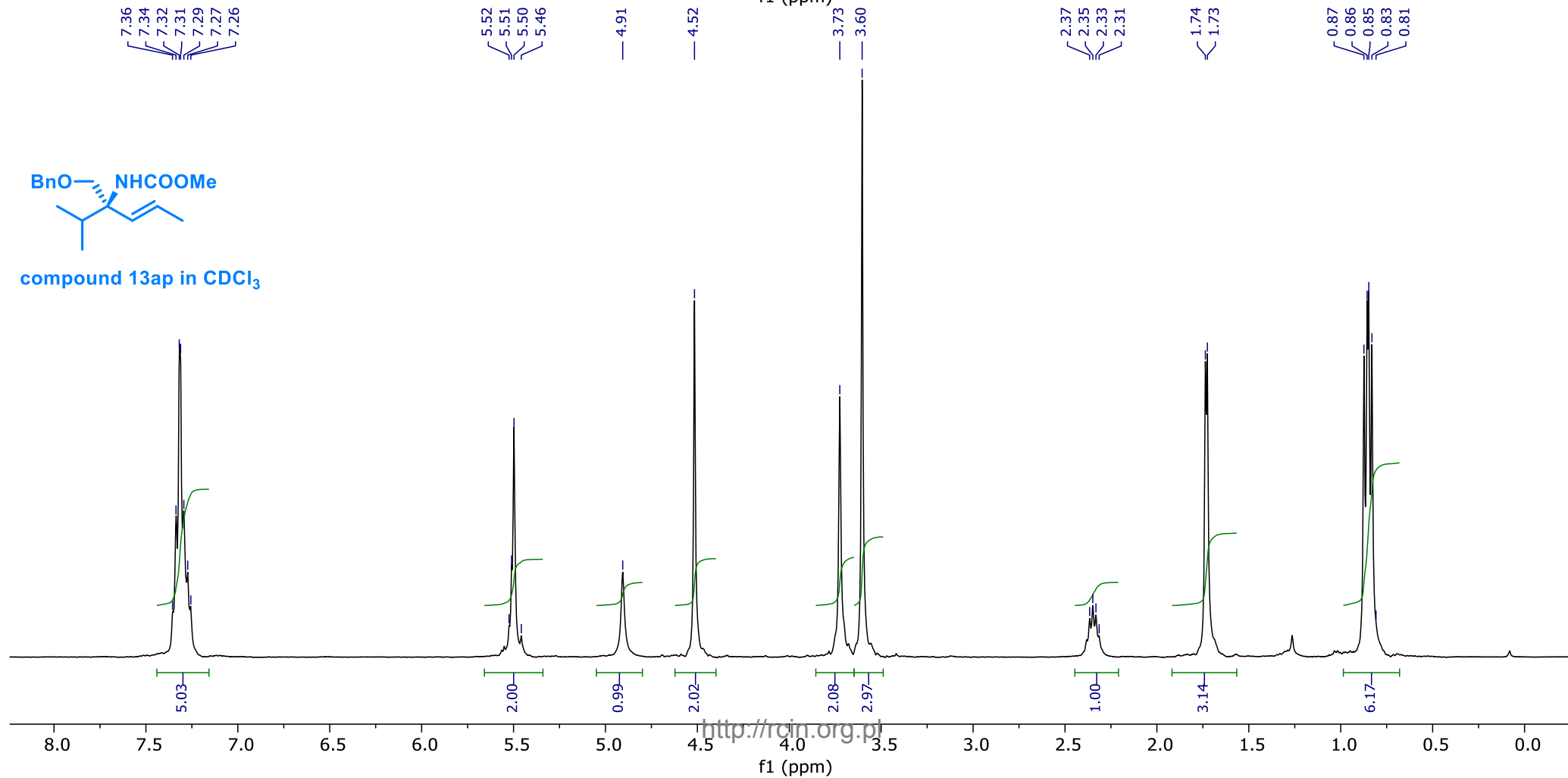
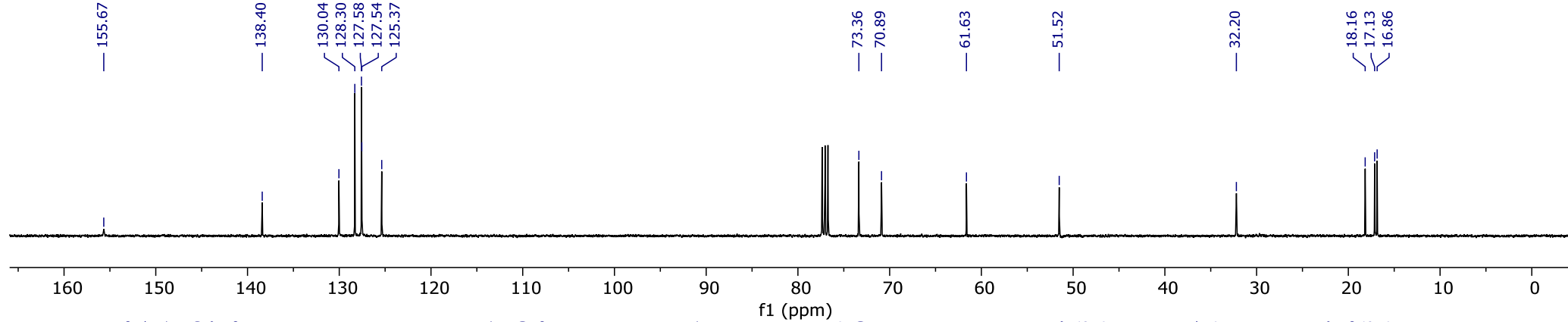




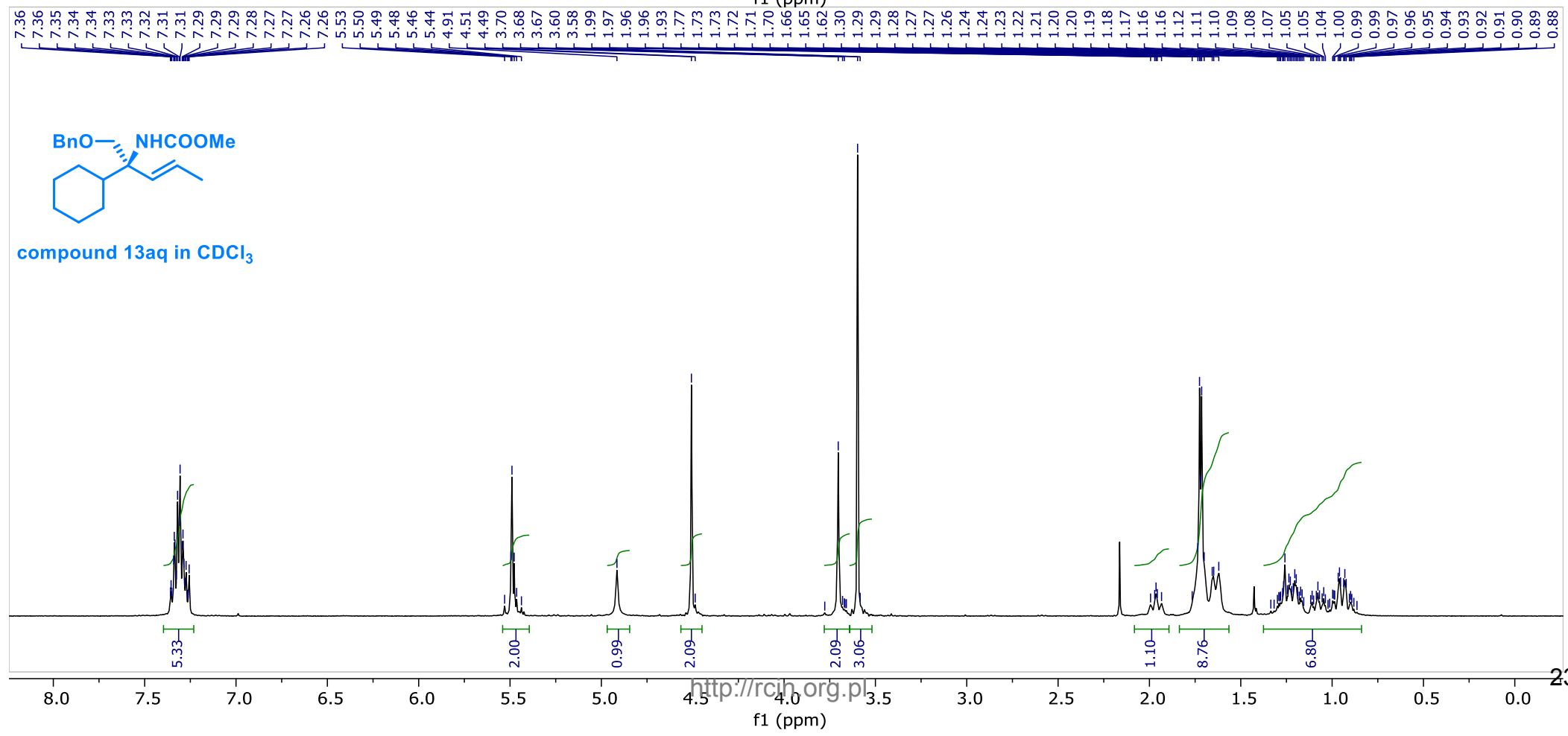
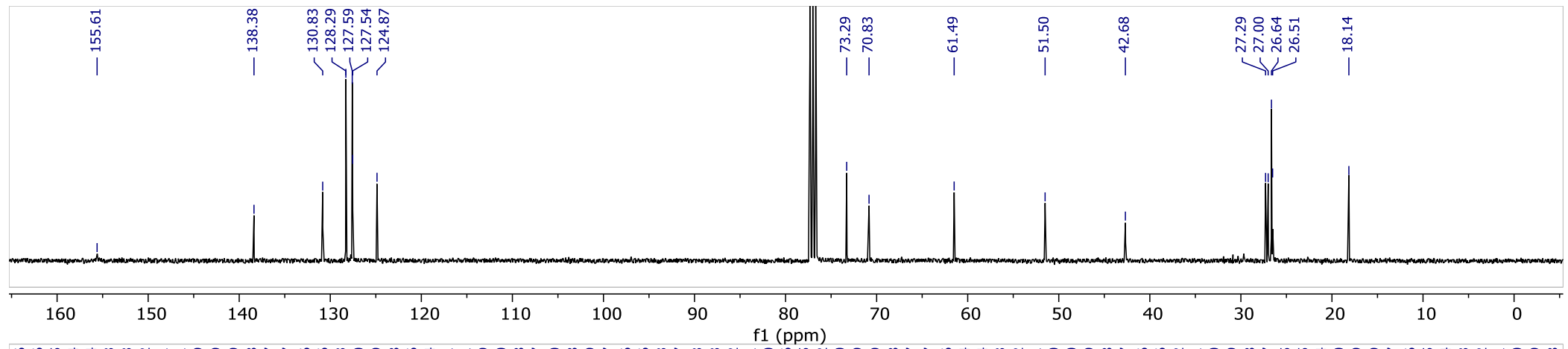


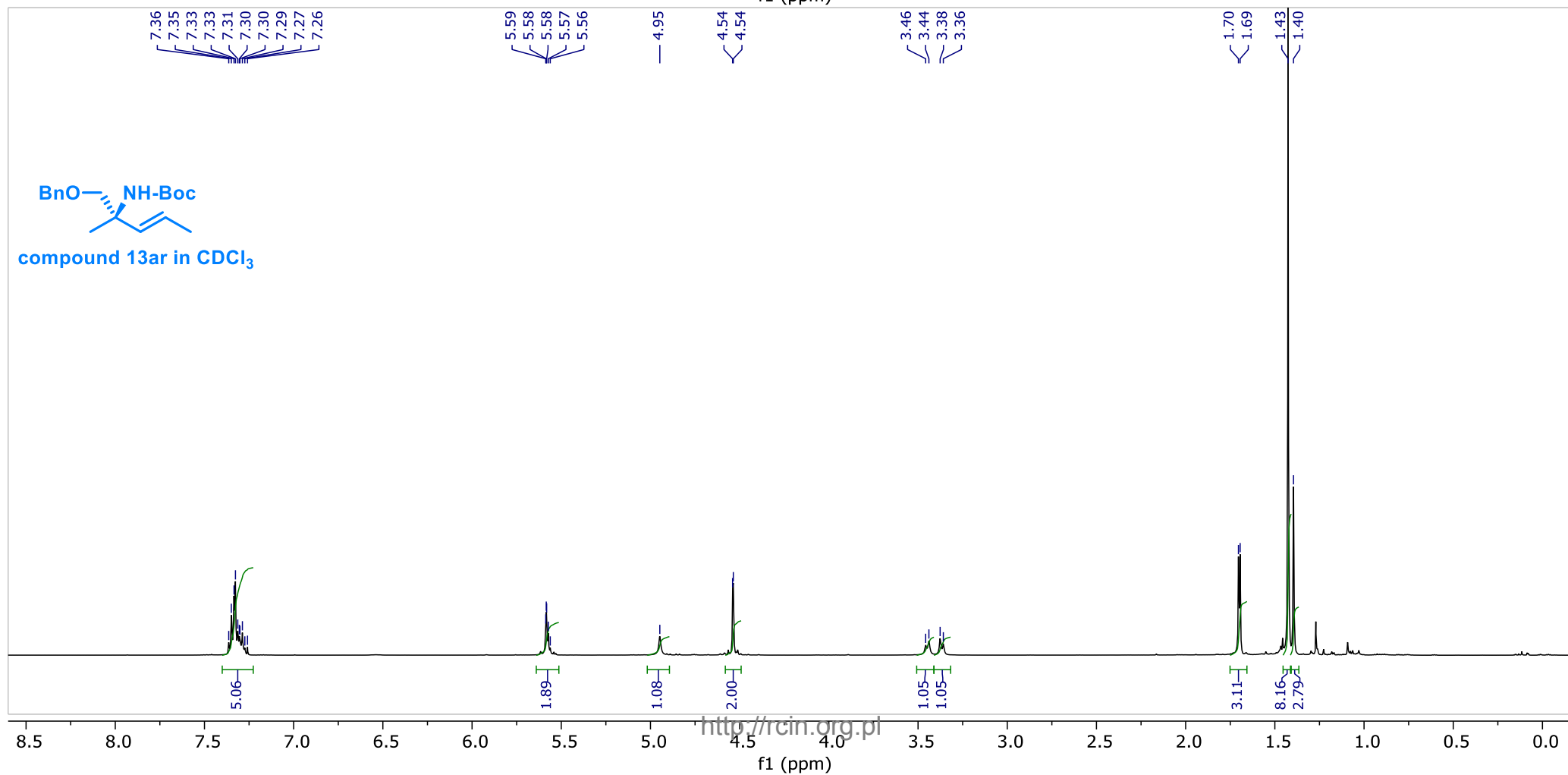
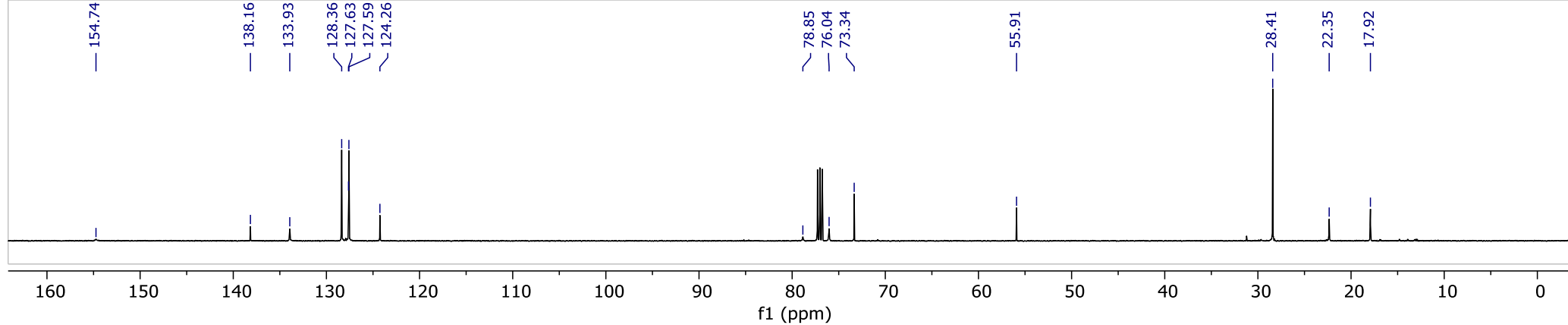


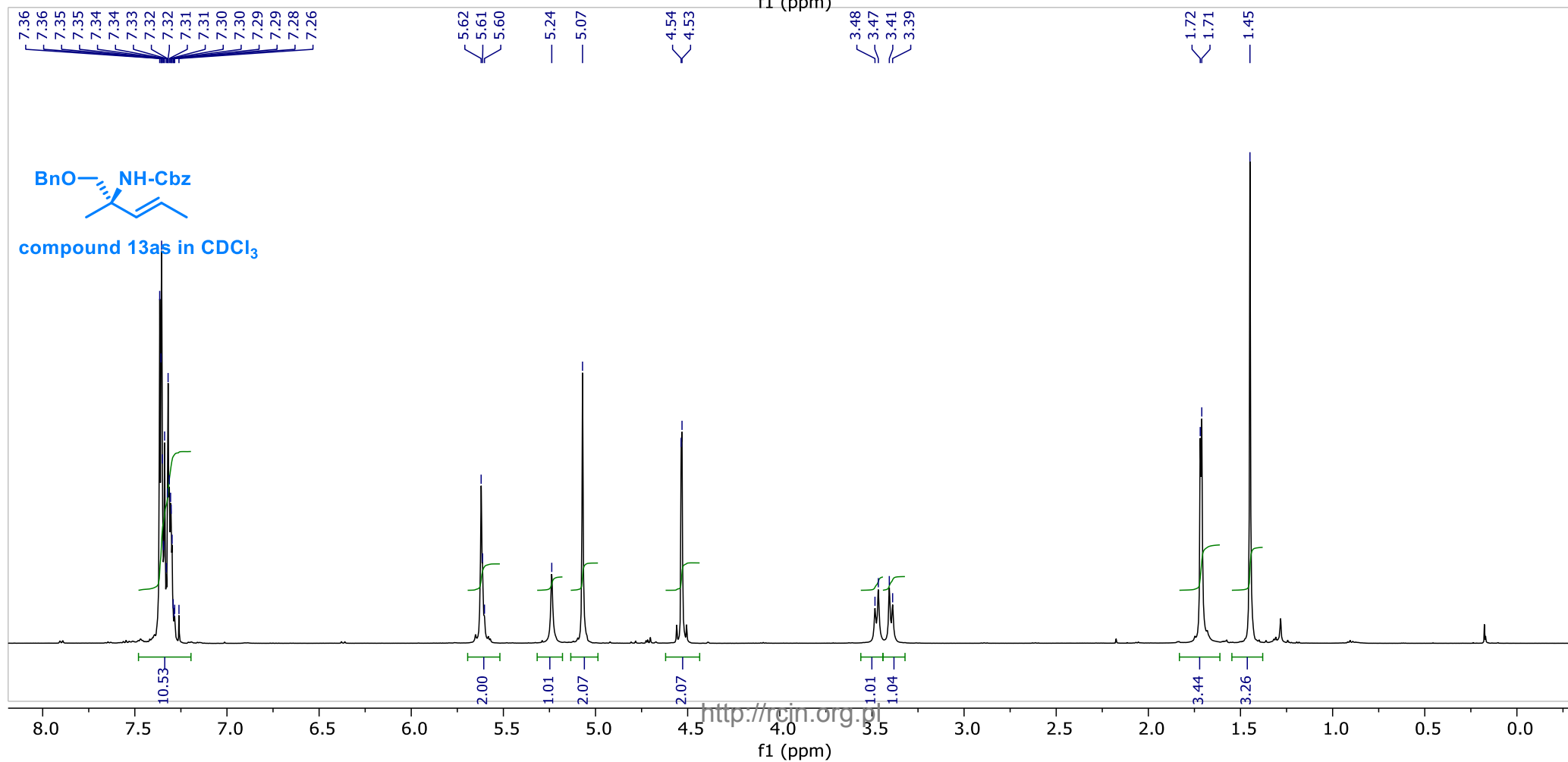
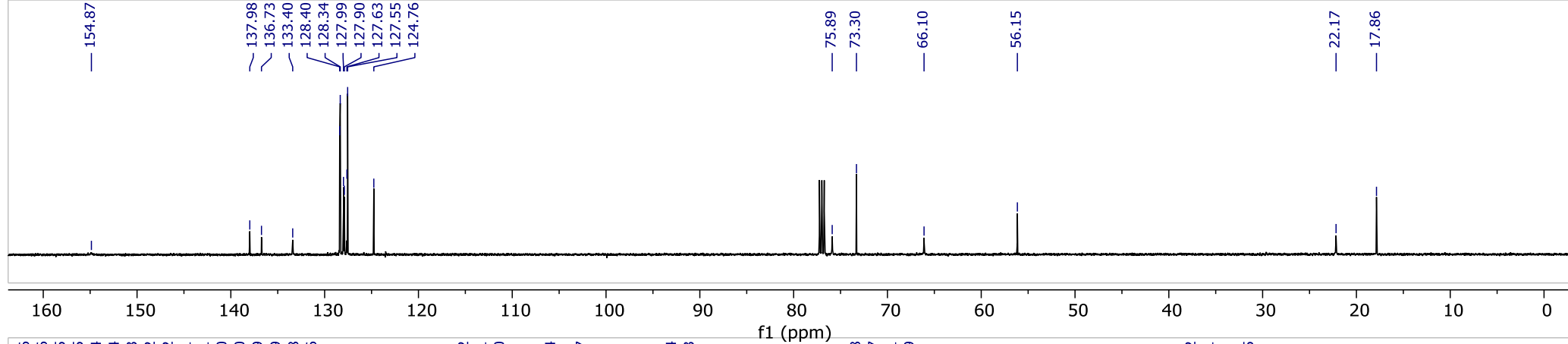


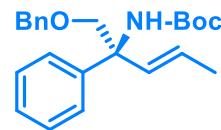
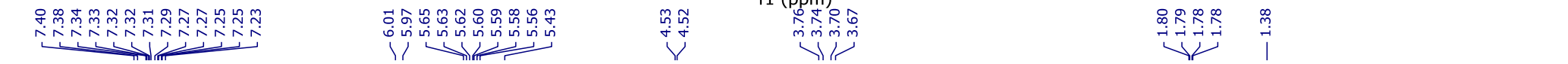
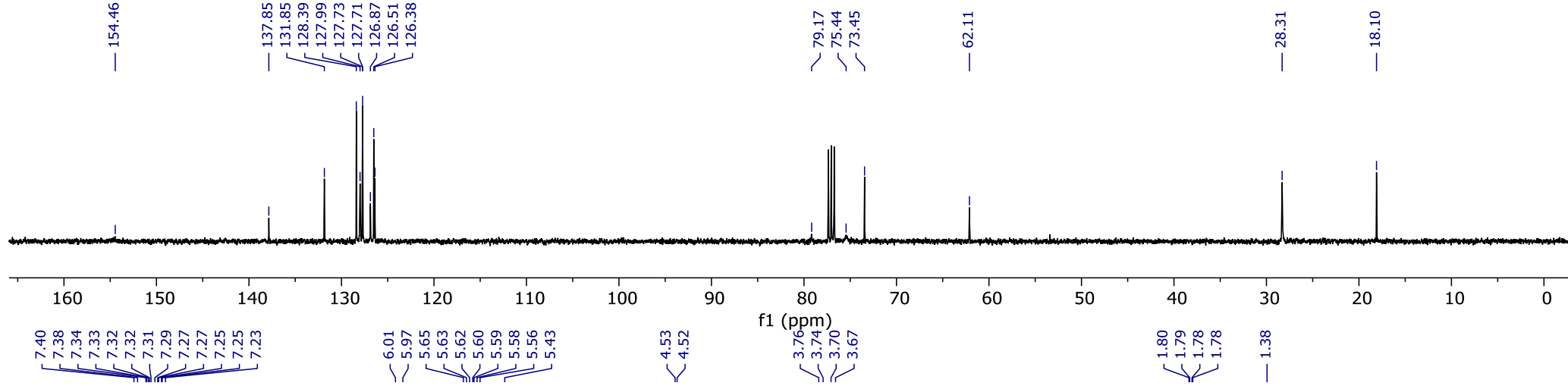


compound 13ap in CDCl<sub>3</sub>

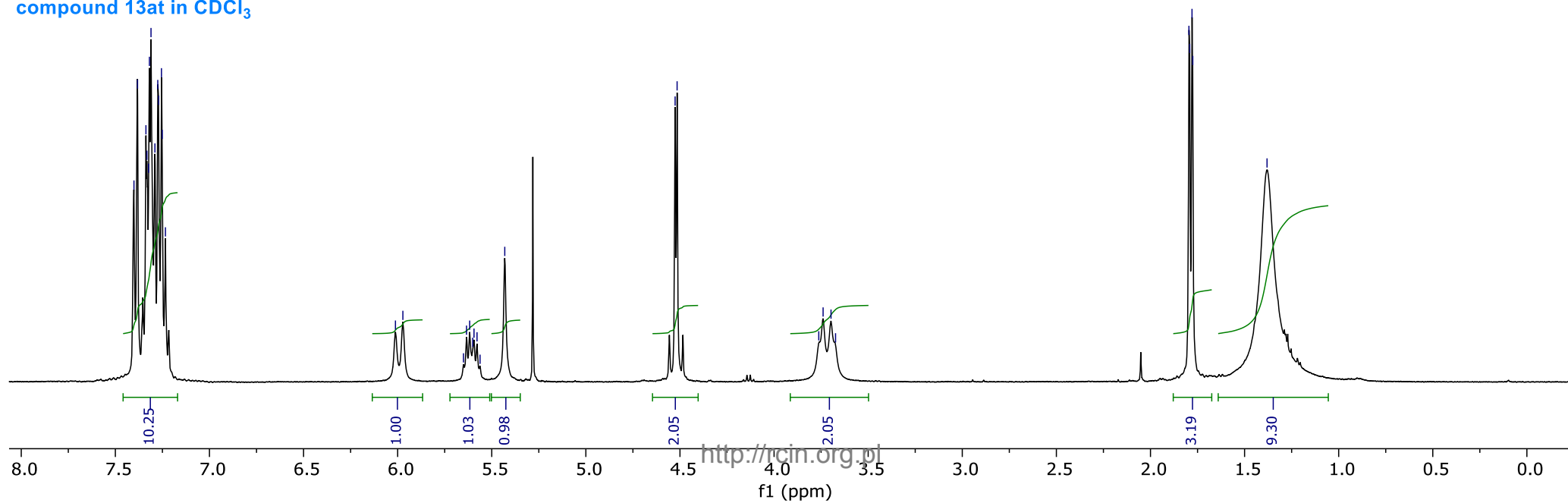


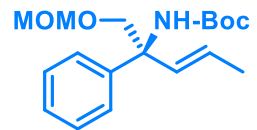
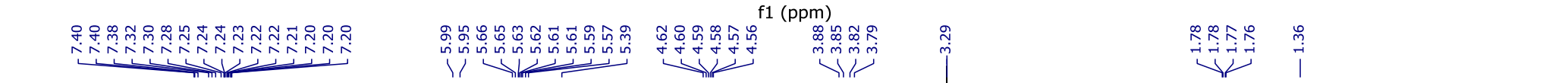
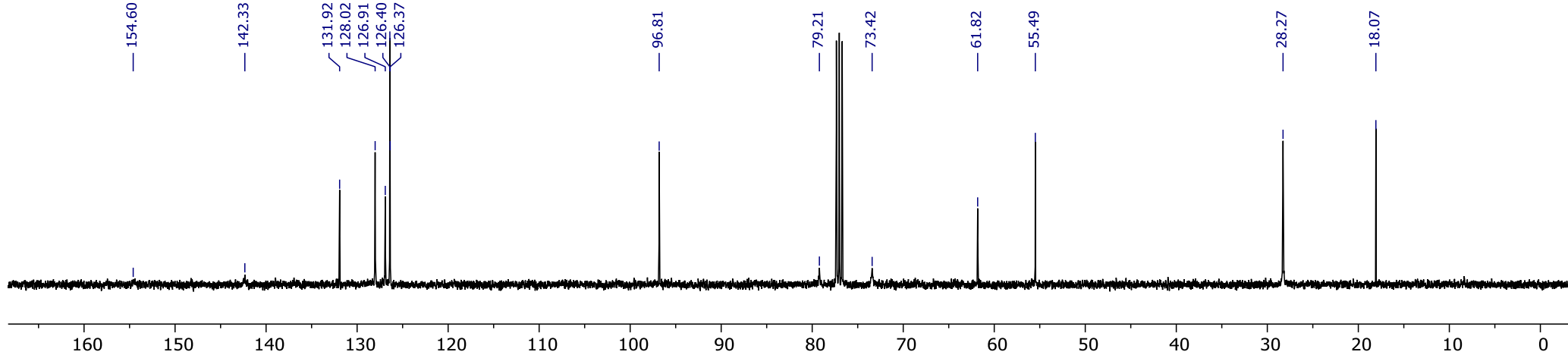




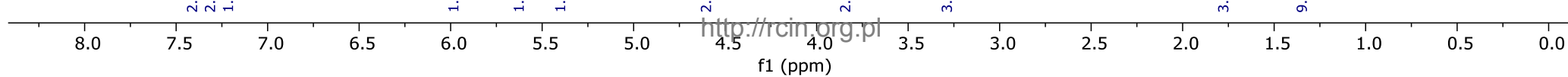


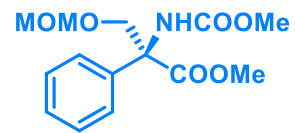
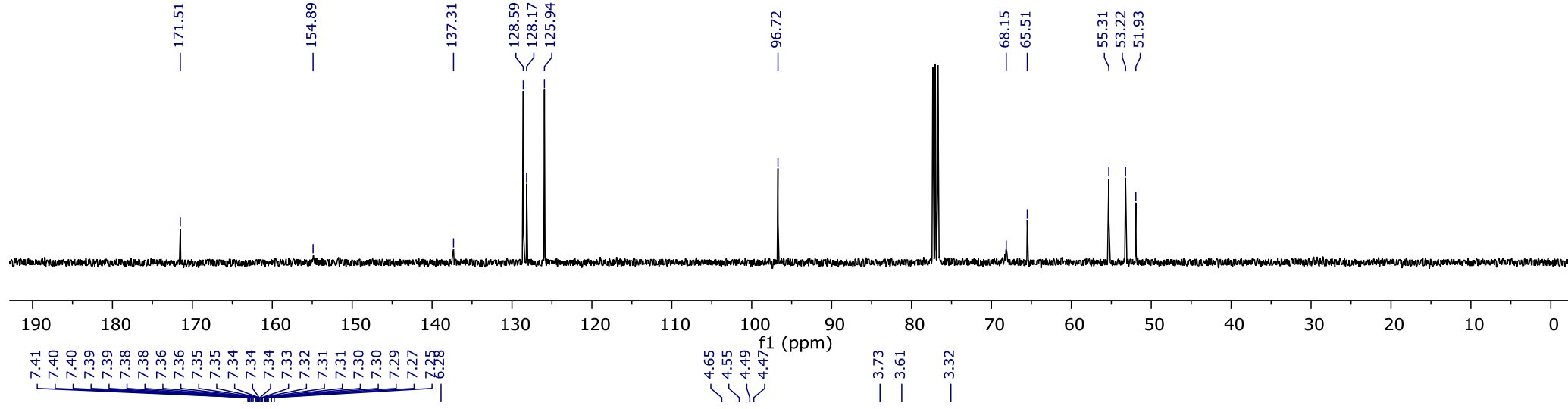
compound 13at in CDCl<sub>3</sub>



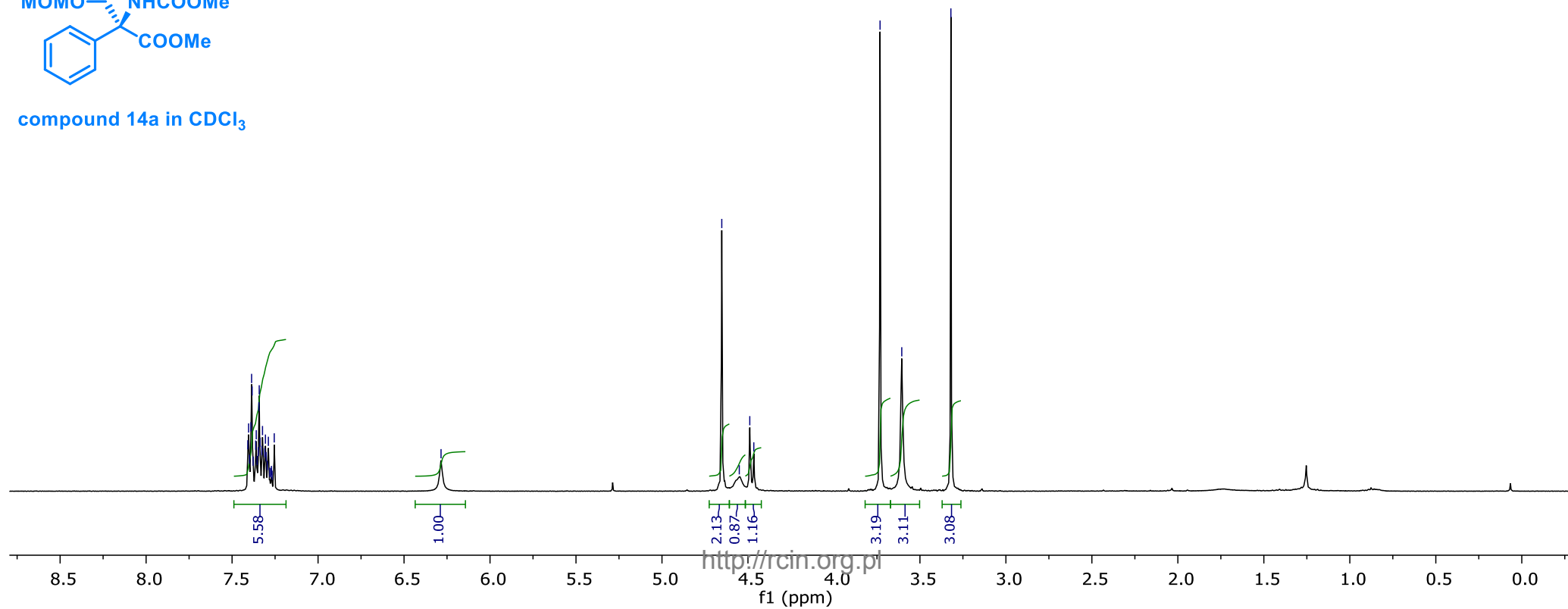


compound 13bq in CDCl<sub>3</sub>

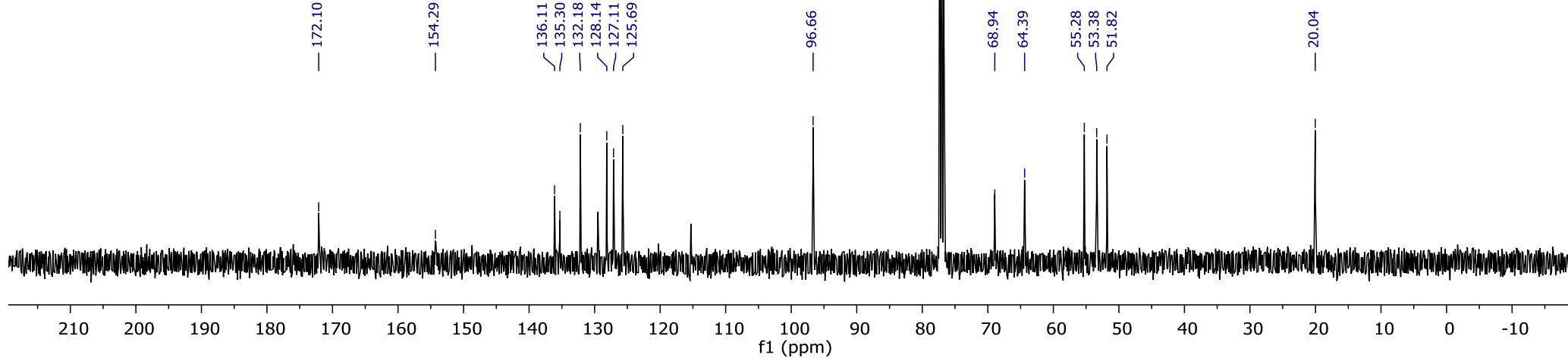




compound 14a in CDCl<sub>3</sub>







7.31, 7.26, 7.25, 7.25, 7.22, 7.21, 7.21, 7.20, 7.19, 7.13, 7.12

6.40

4.76, 4.69

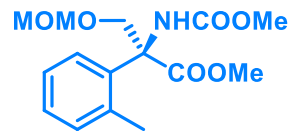
4.43, 4.41

3.75

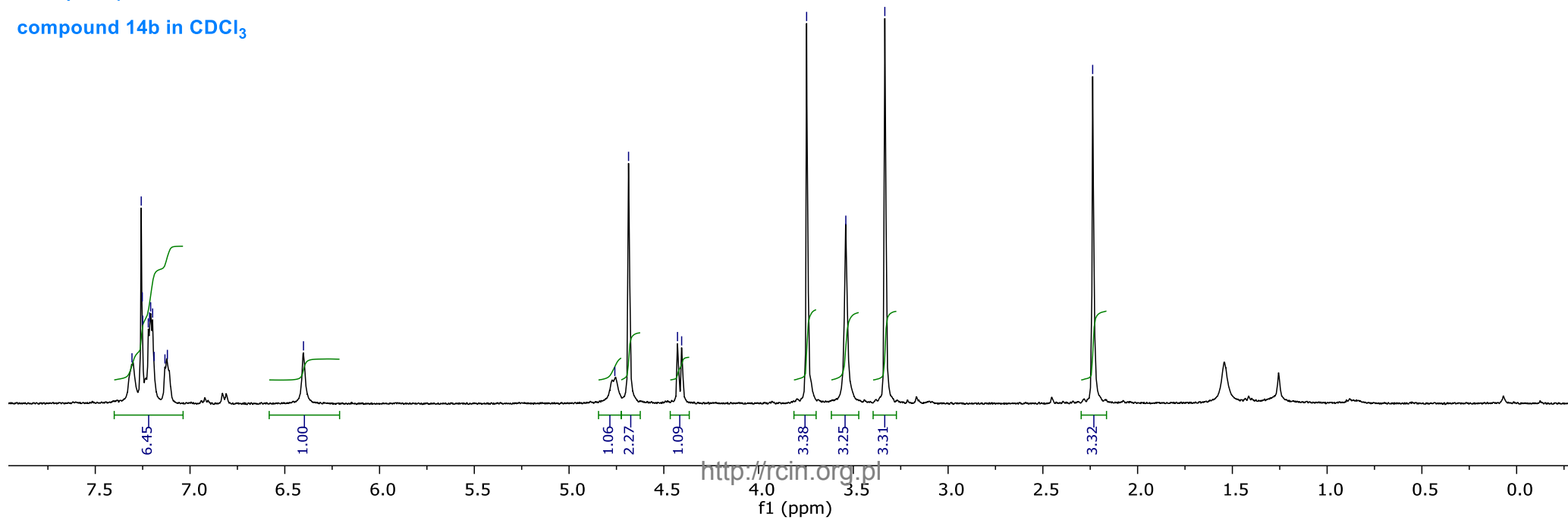
3.54

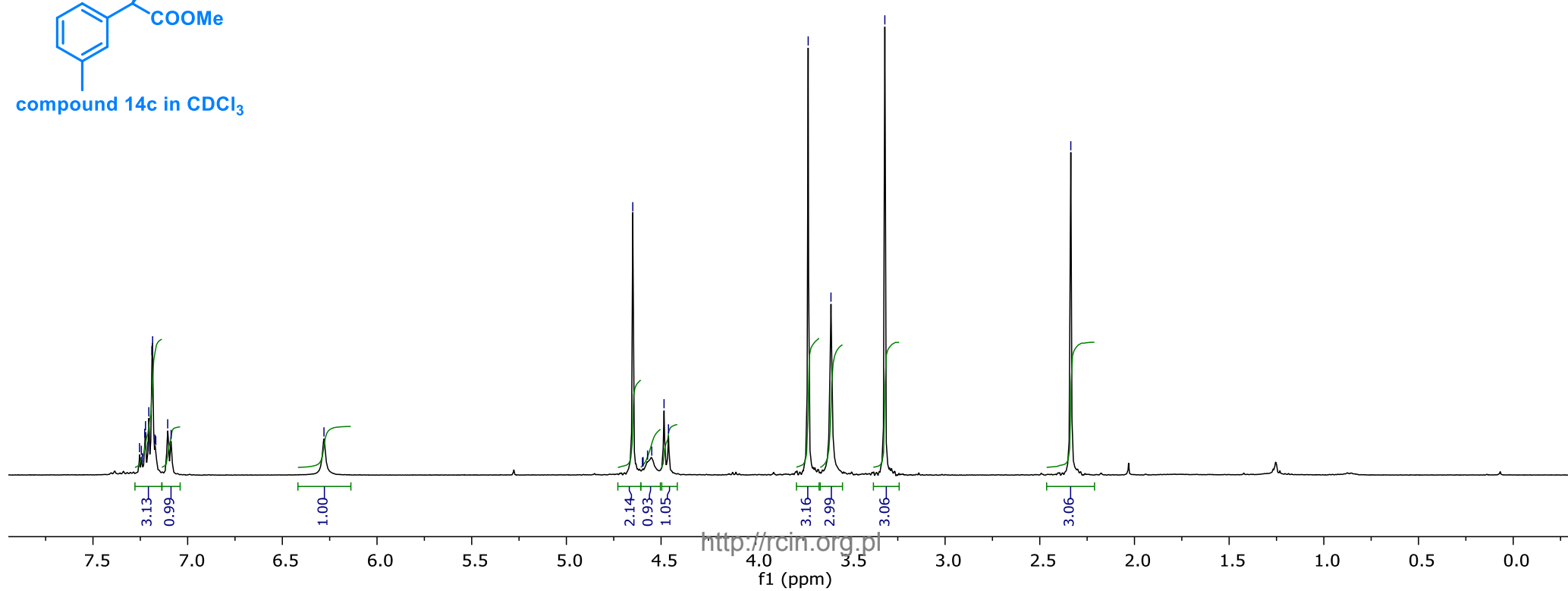
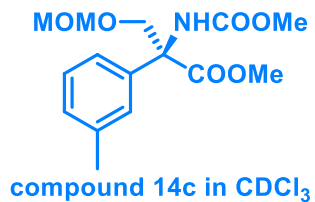
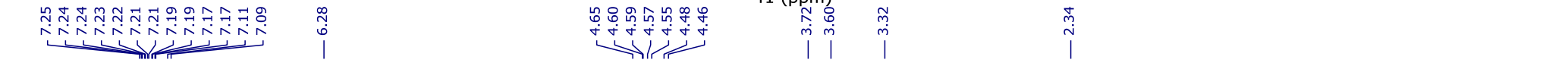
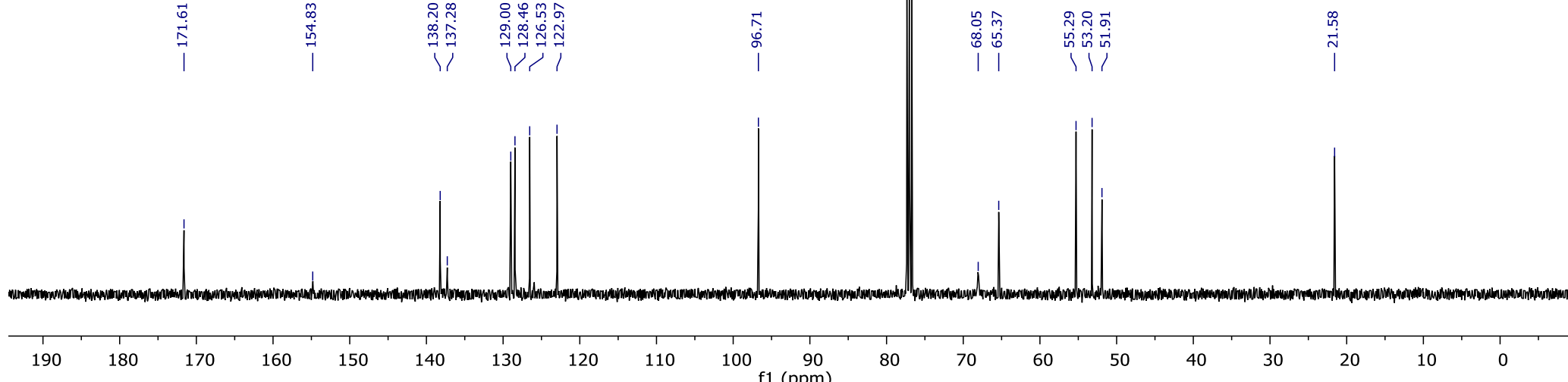
3.33

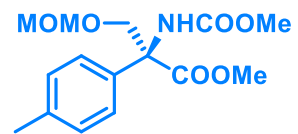
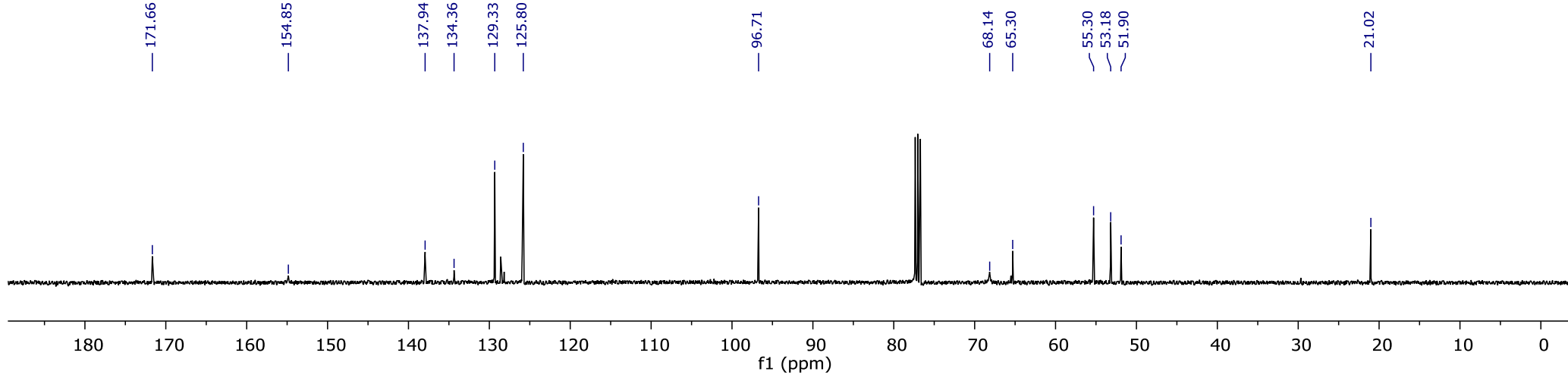
2.24



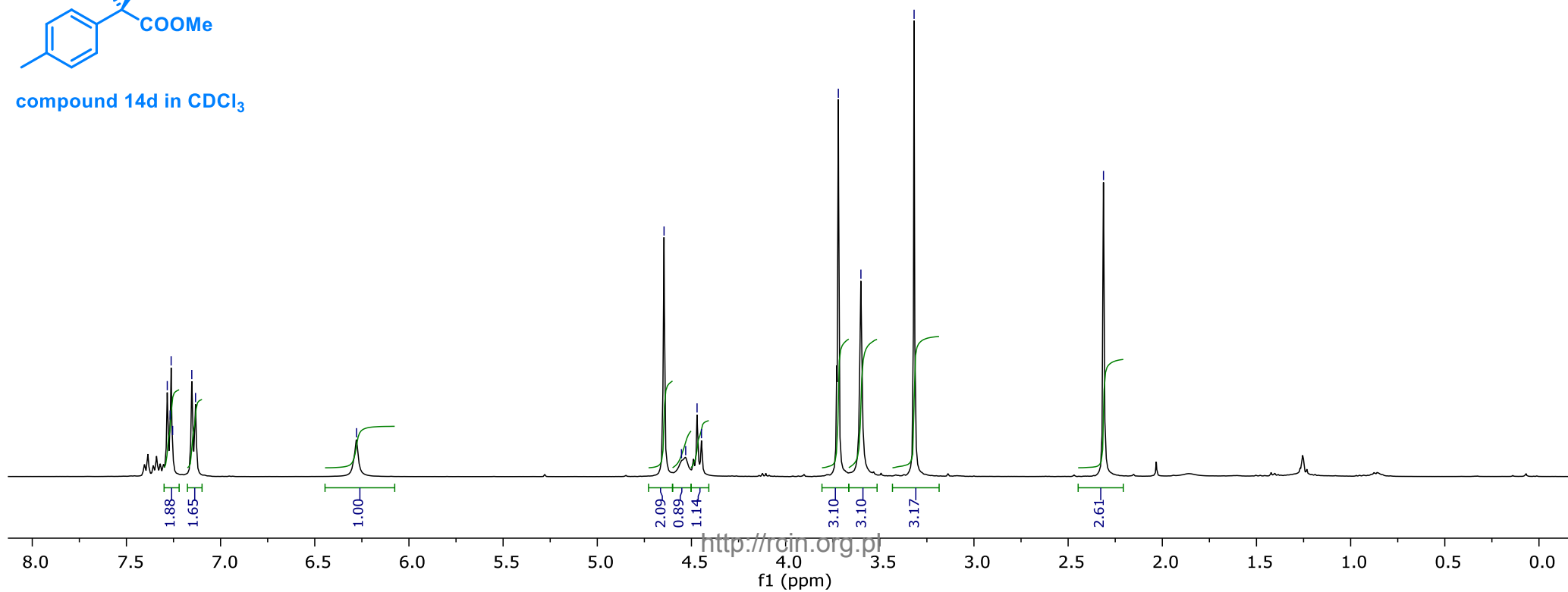
compound 14b in CDCl<sub>3</sub>

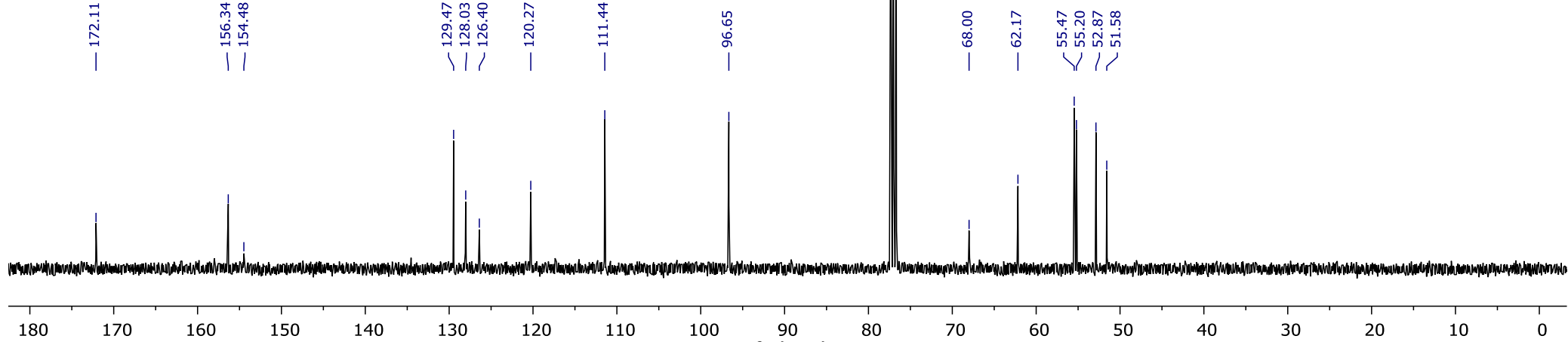






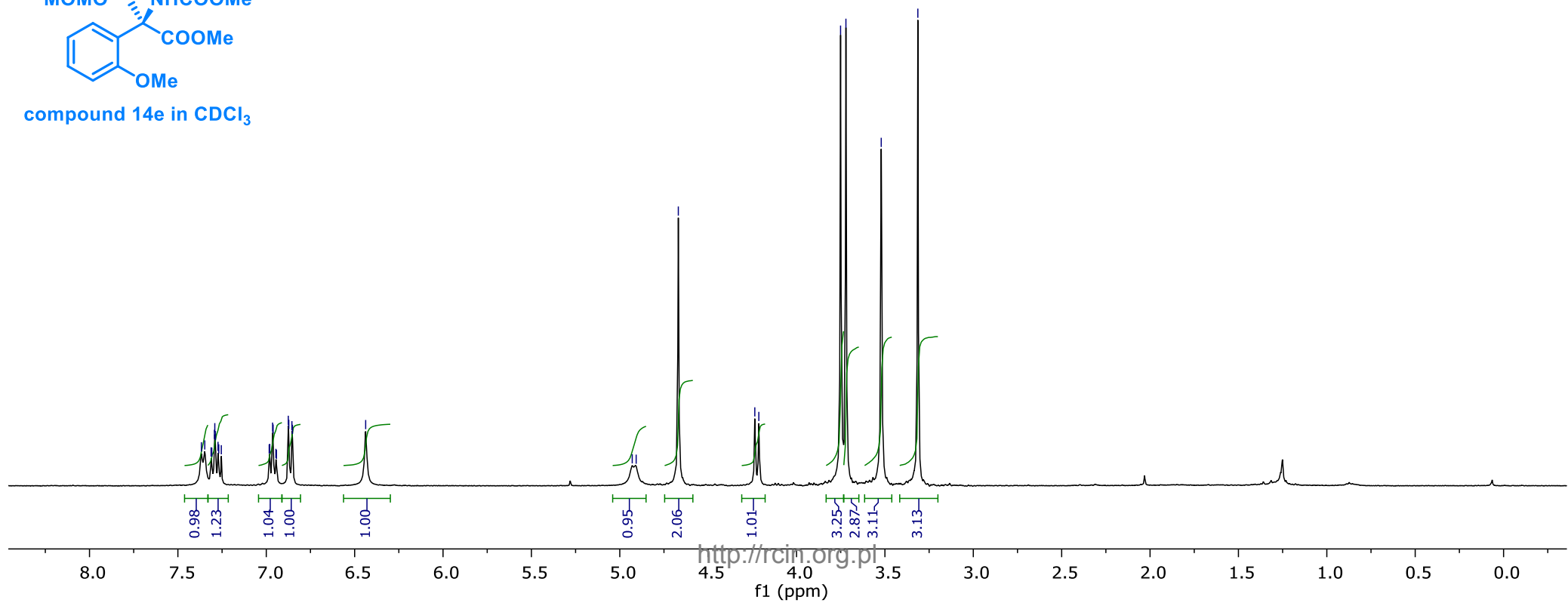
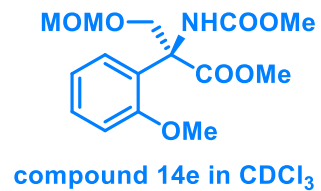
compound 14d in CDCl<sub>3</sub>

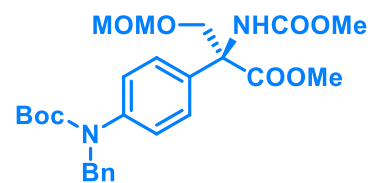
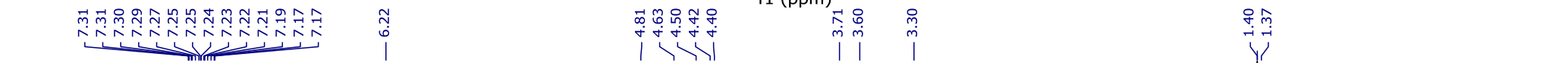
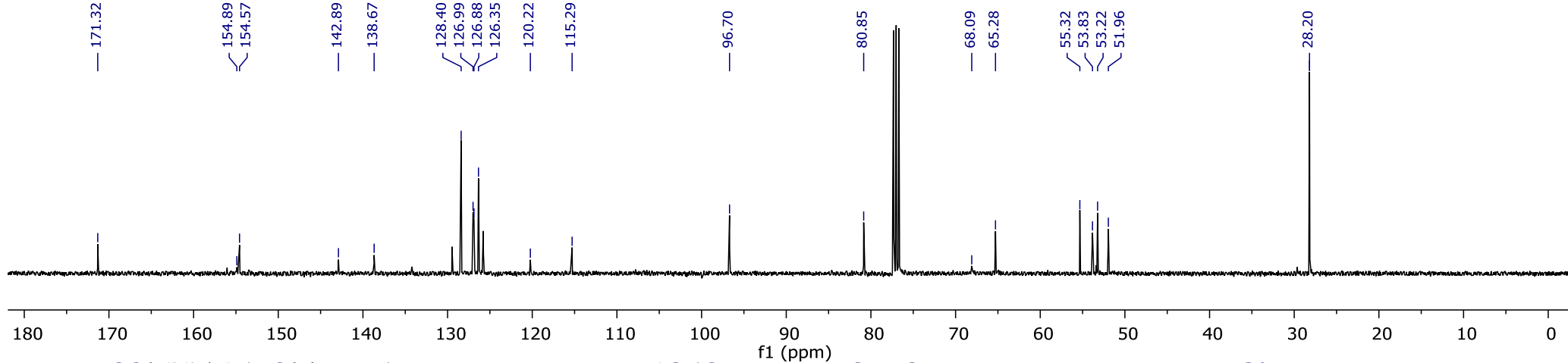




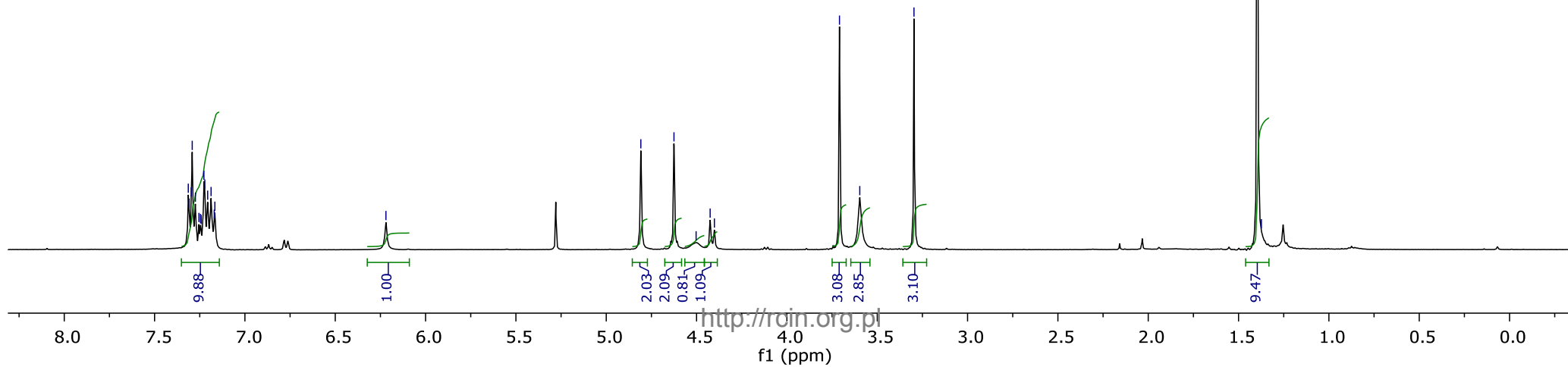
7.37  
7.35  
7.31  
7.31  
7.29  
7.29  
7.27  
7.27  
7.25  
6.98  
6.96  
6.96  
6.95  
6.94  
6.88  
6.87  
6.85  
6.85  
6.44

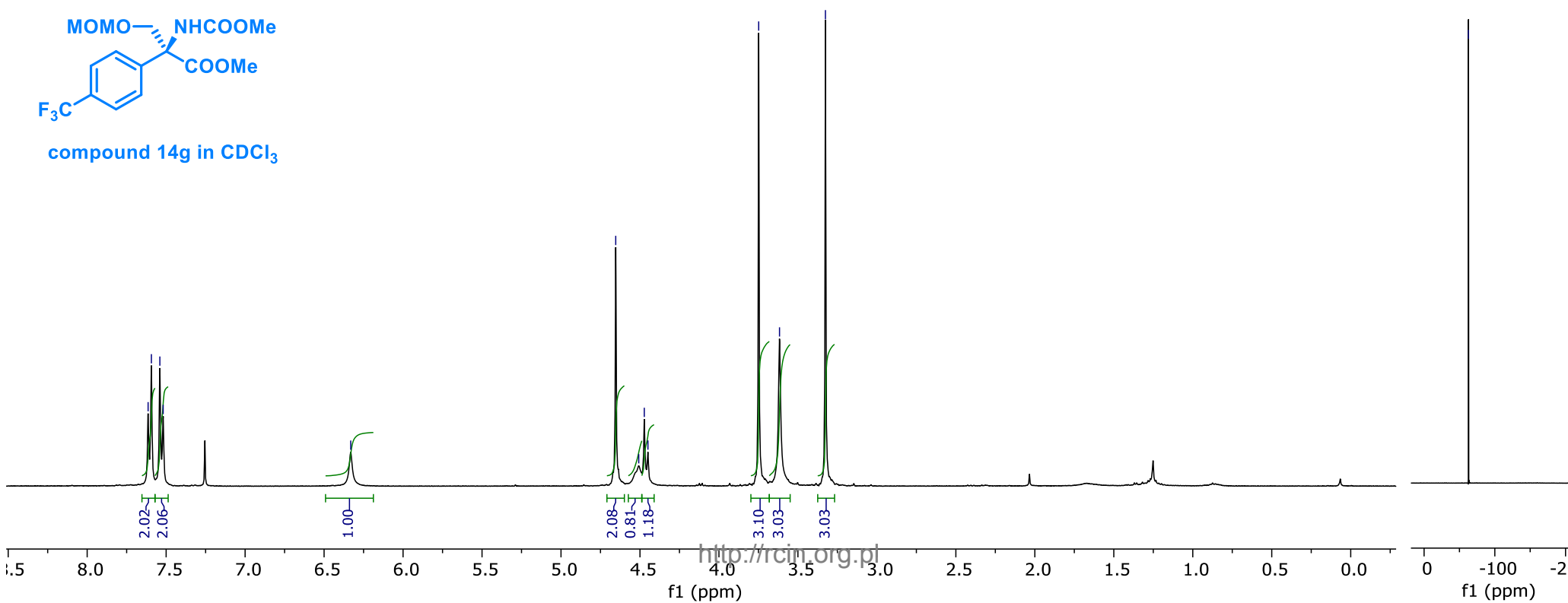
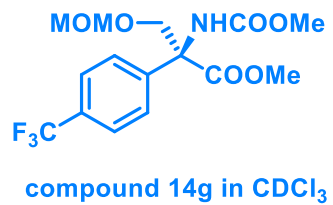
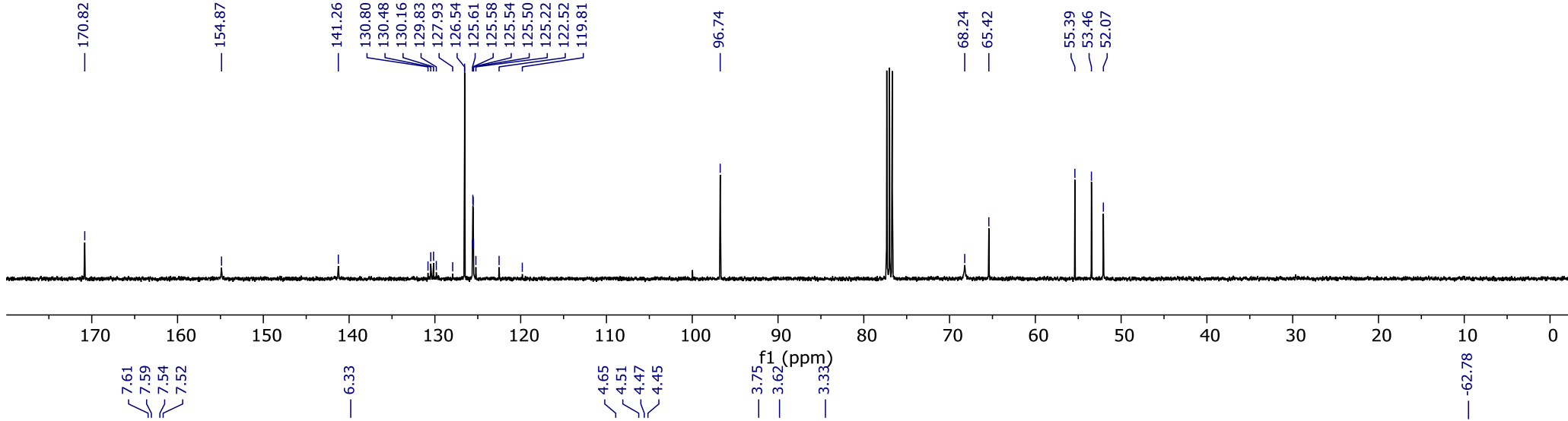
4.93  
4.91  
4.67  
4.24  
4.21  
3.75  
3.72  
3.52  
3.31

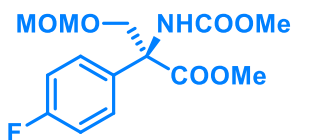
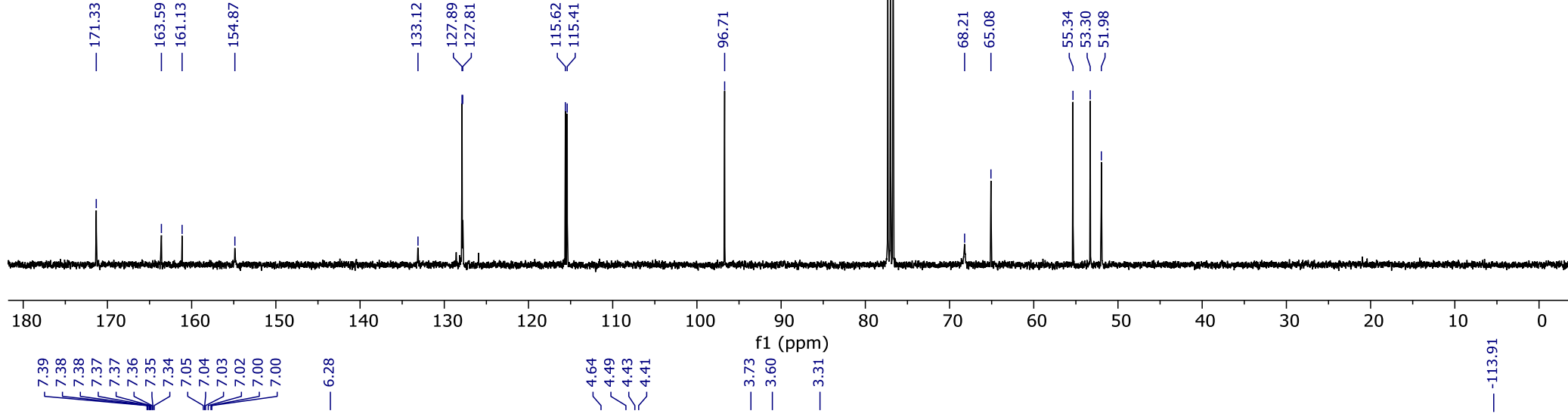




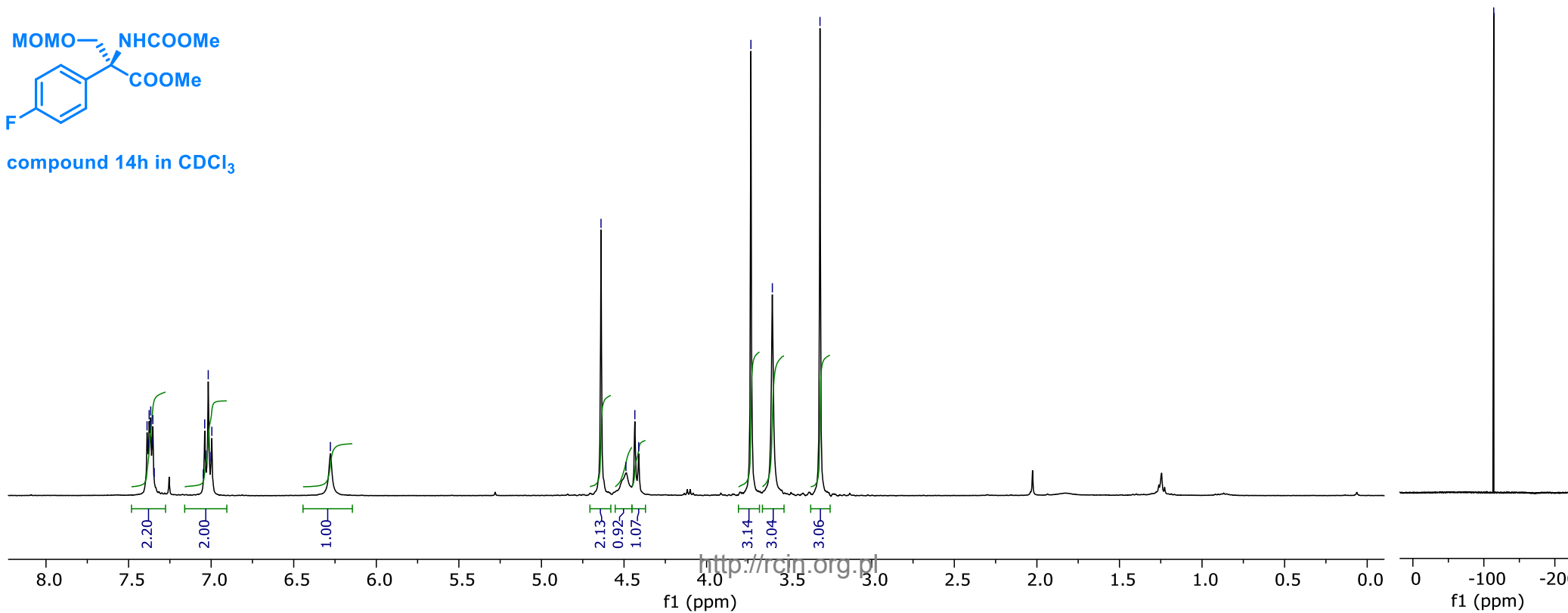
compound 14f in CDCl<sub>3</sub>

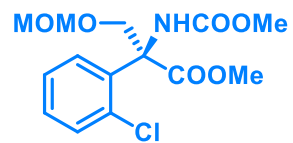
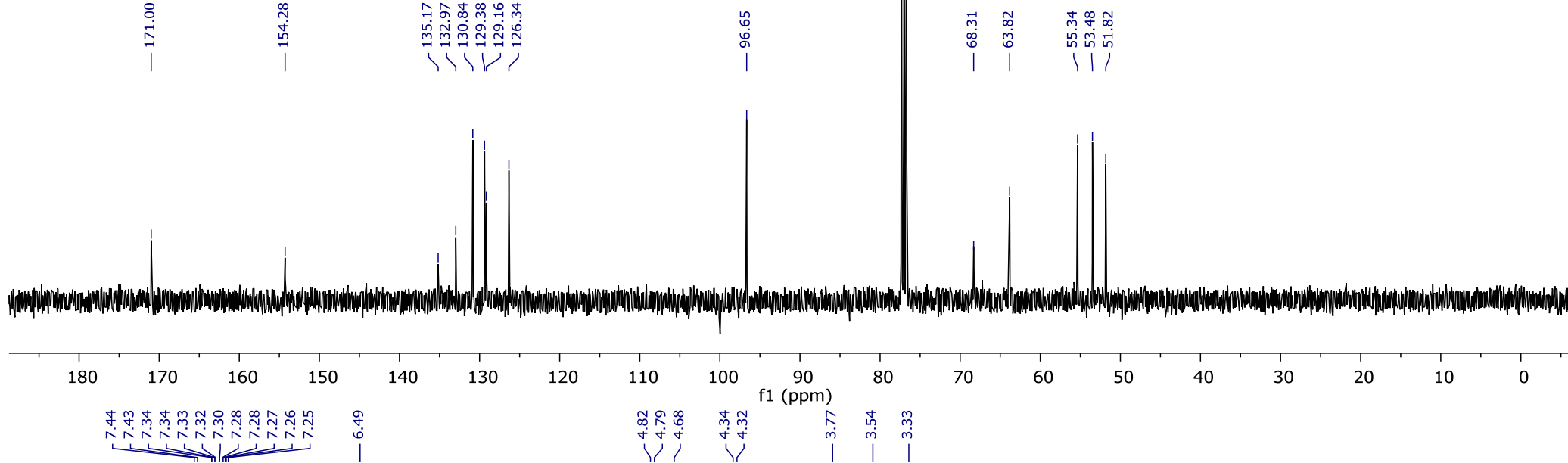




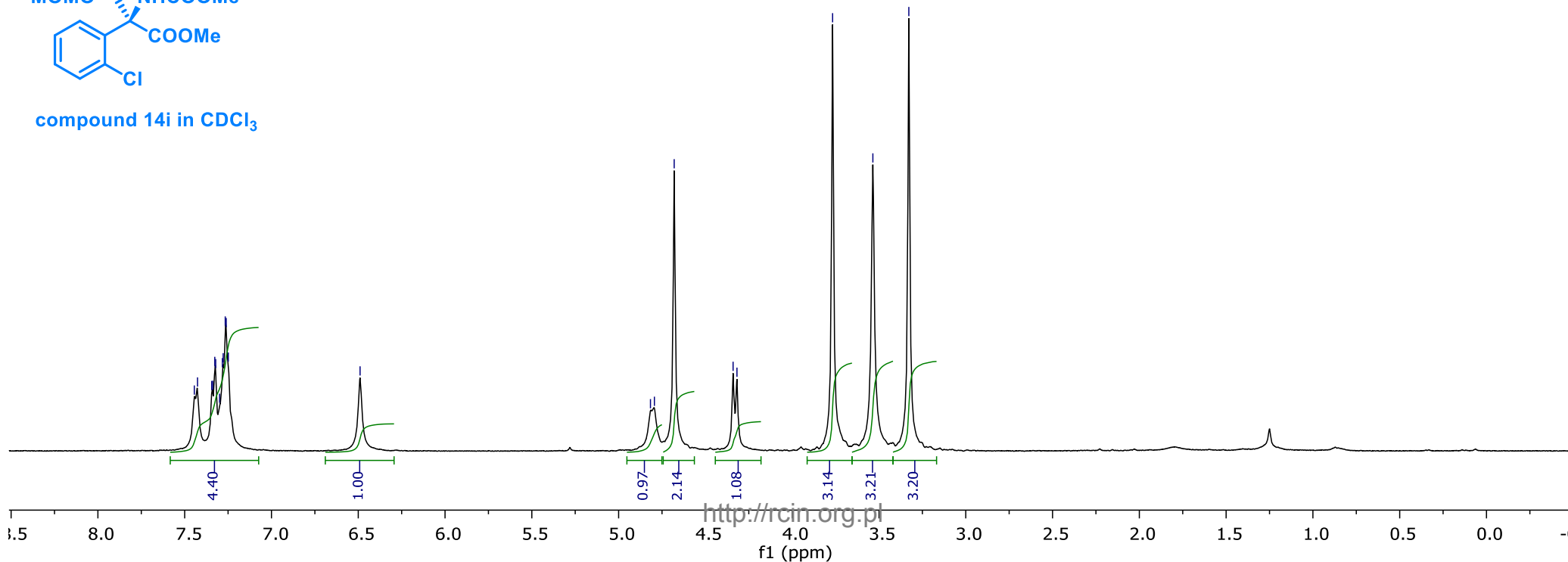


compound 14h in CDCl<sub>3</sub>

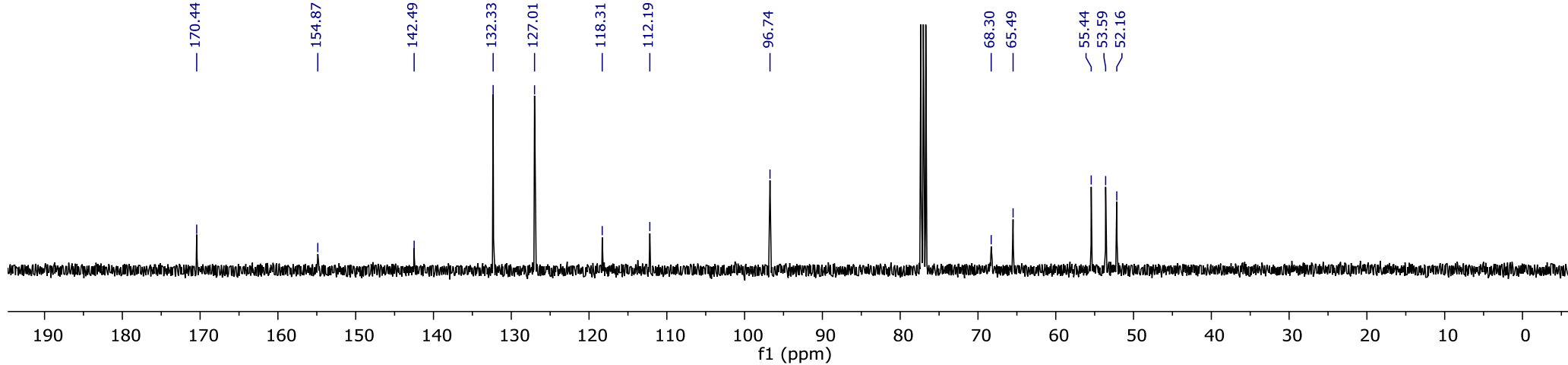




compound 14i in CDCl<sub>3</sub>







7.66  
7.65  
7.65  
7.63  
7.62  
7.54  
7.54  
7.53  
7.52  
7.52  
7.51

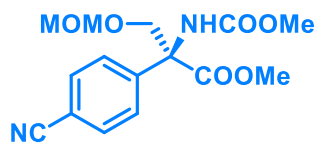
6.32

4.64  
4.45  
4.43  
4.41

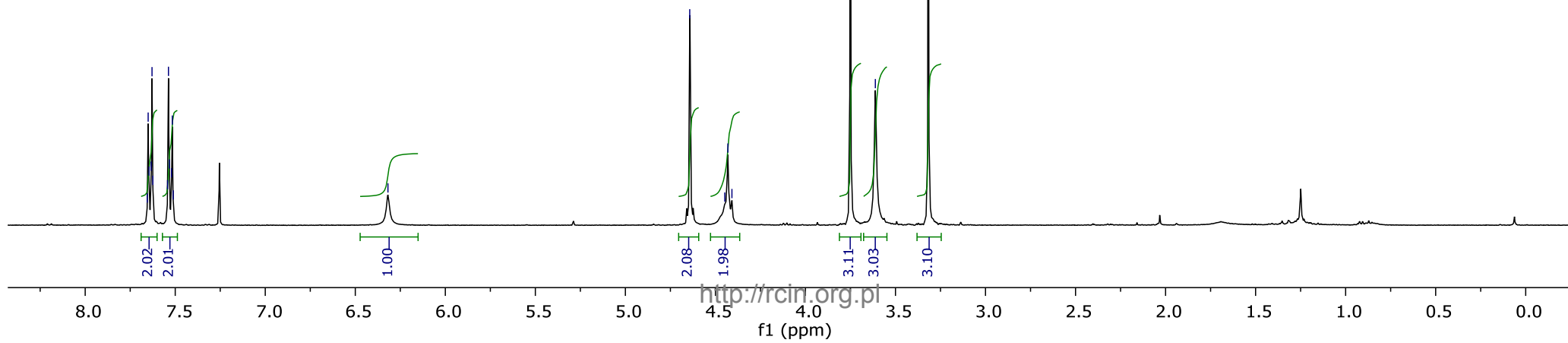
3.75

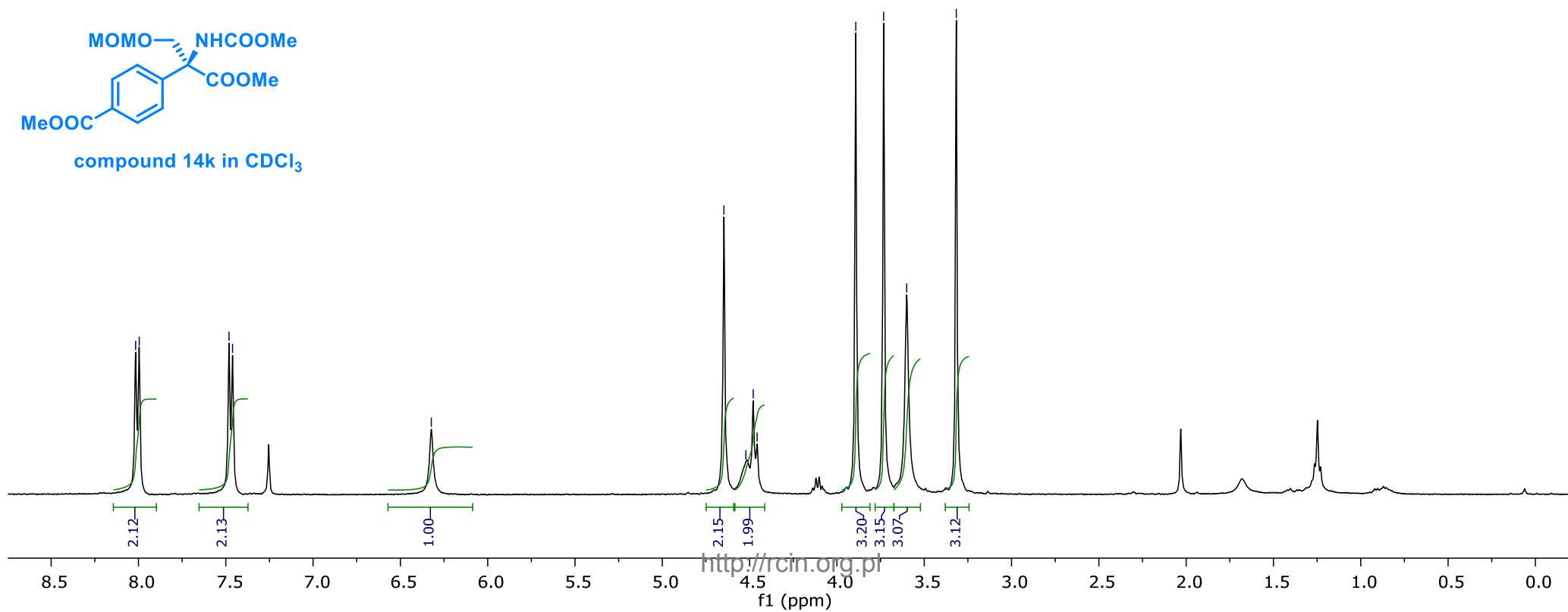
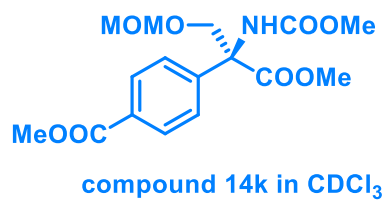
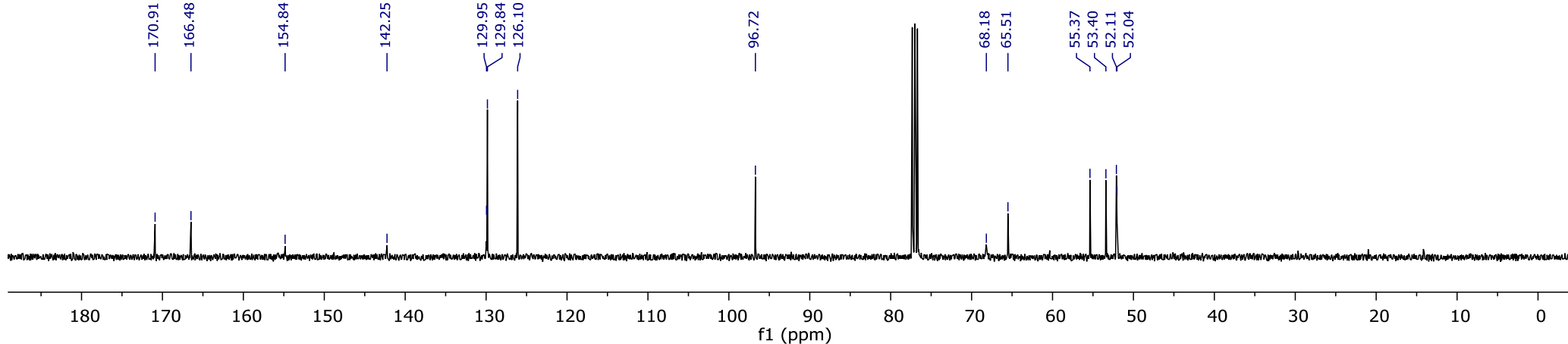
3.61

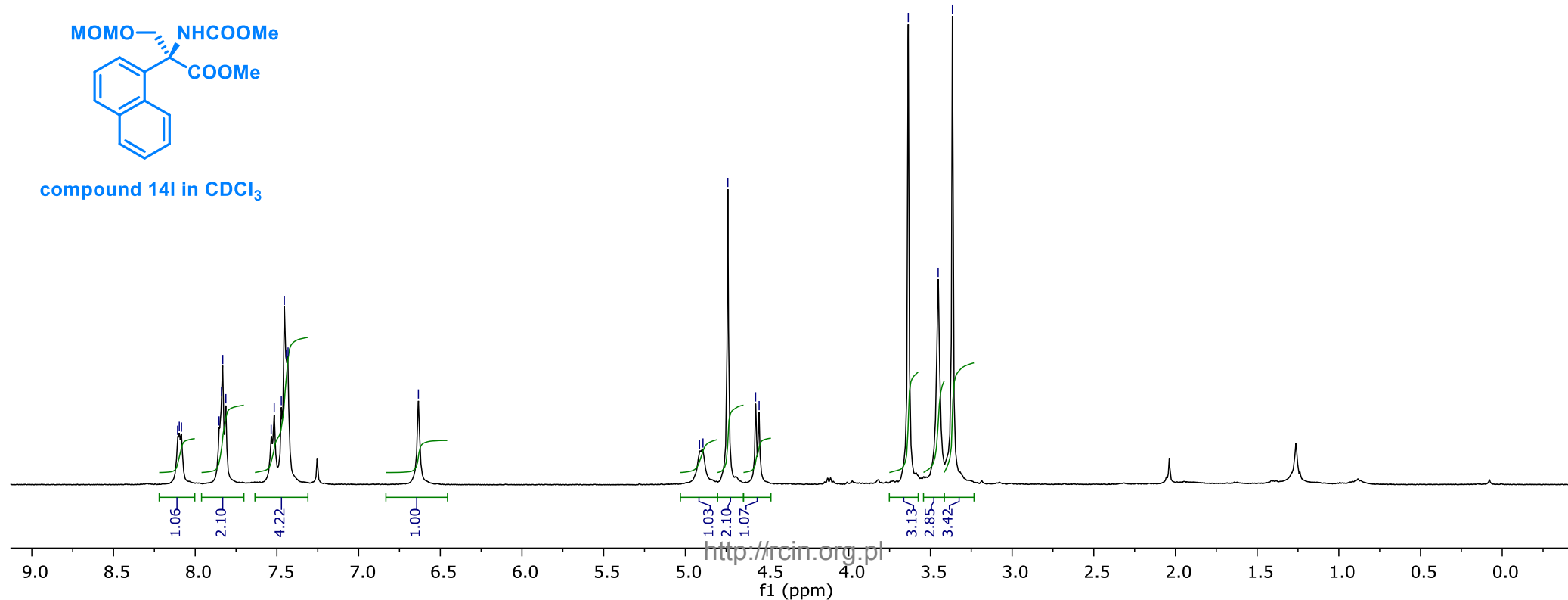
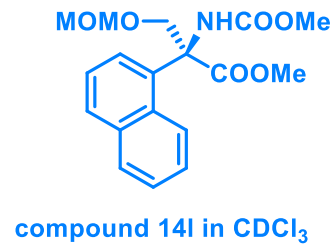
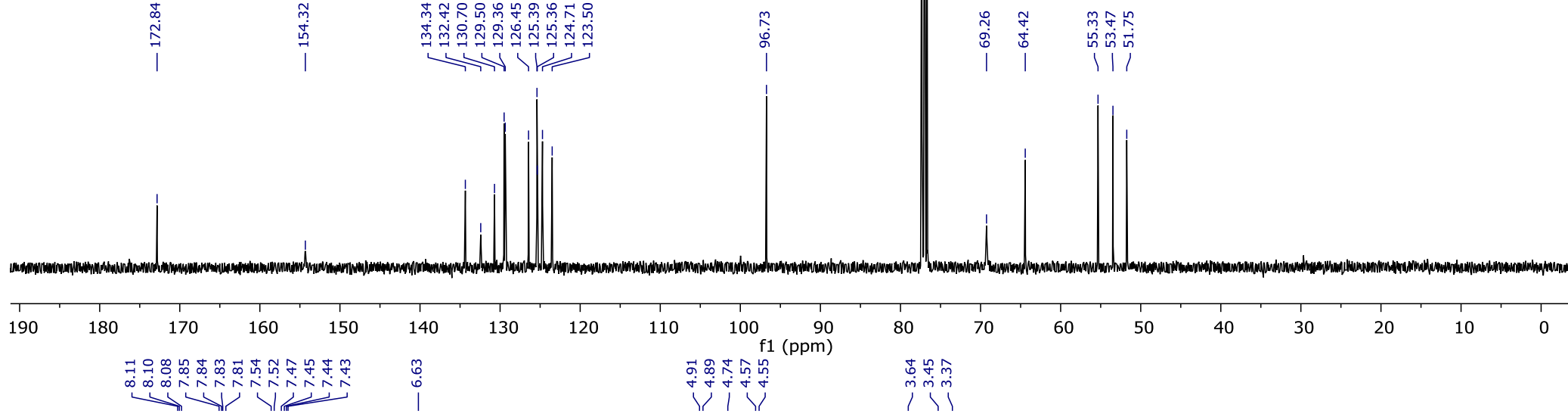
3.32

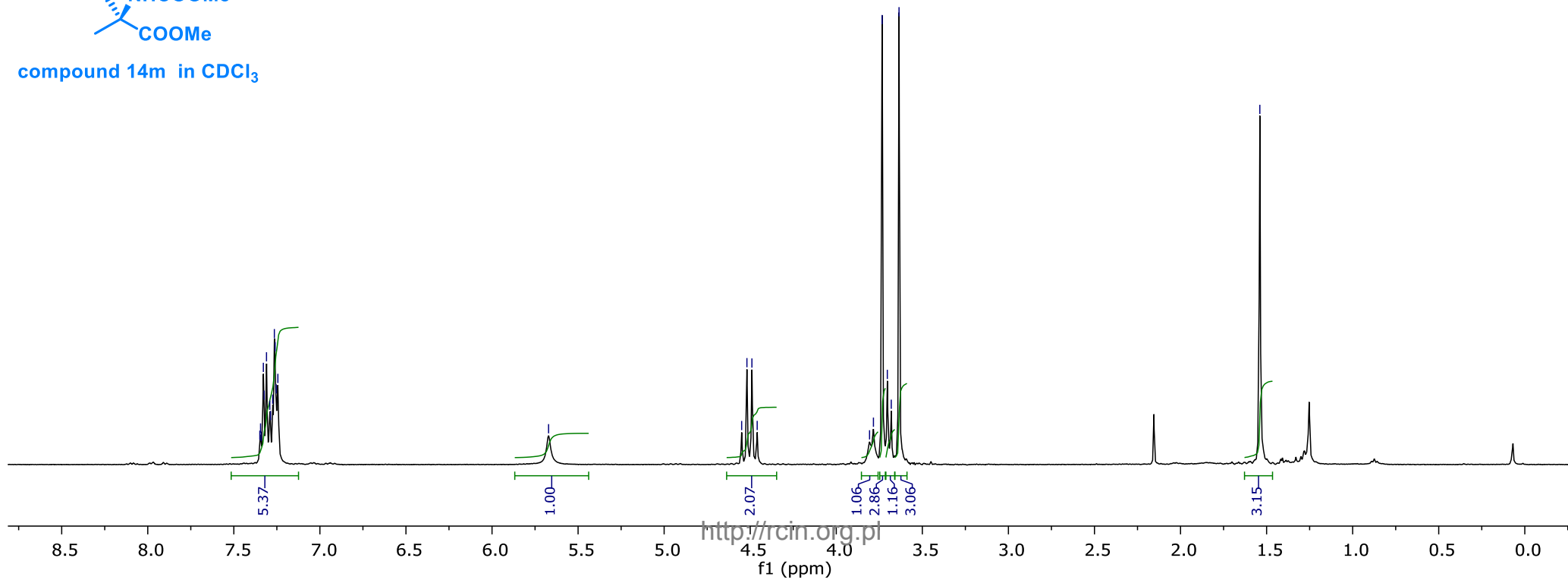
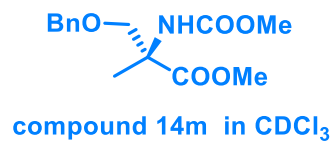
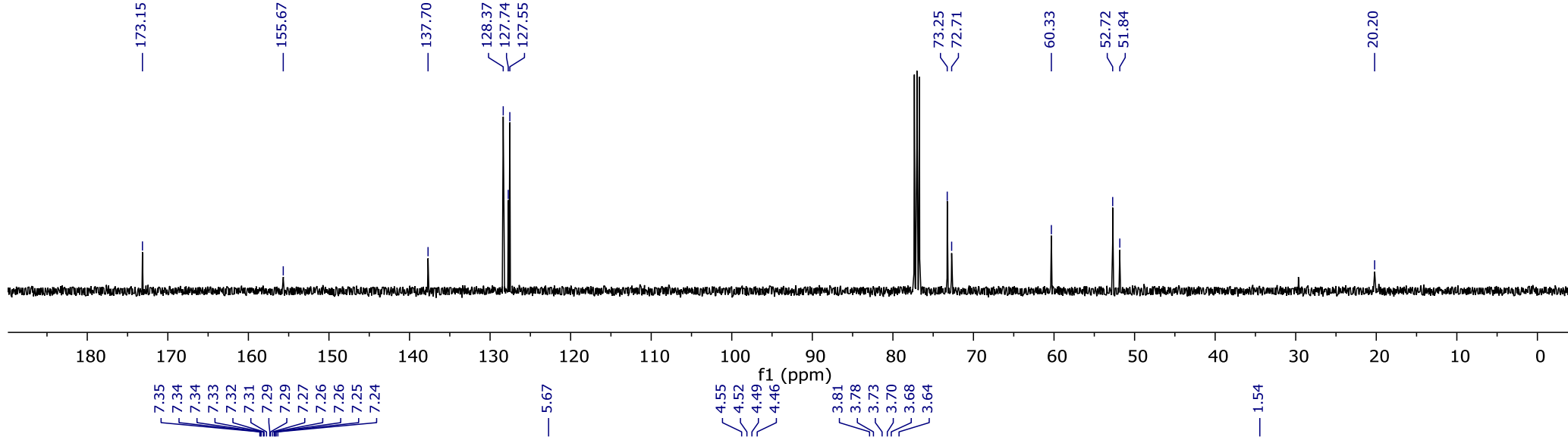


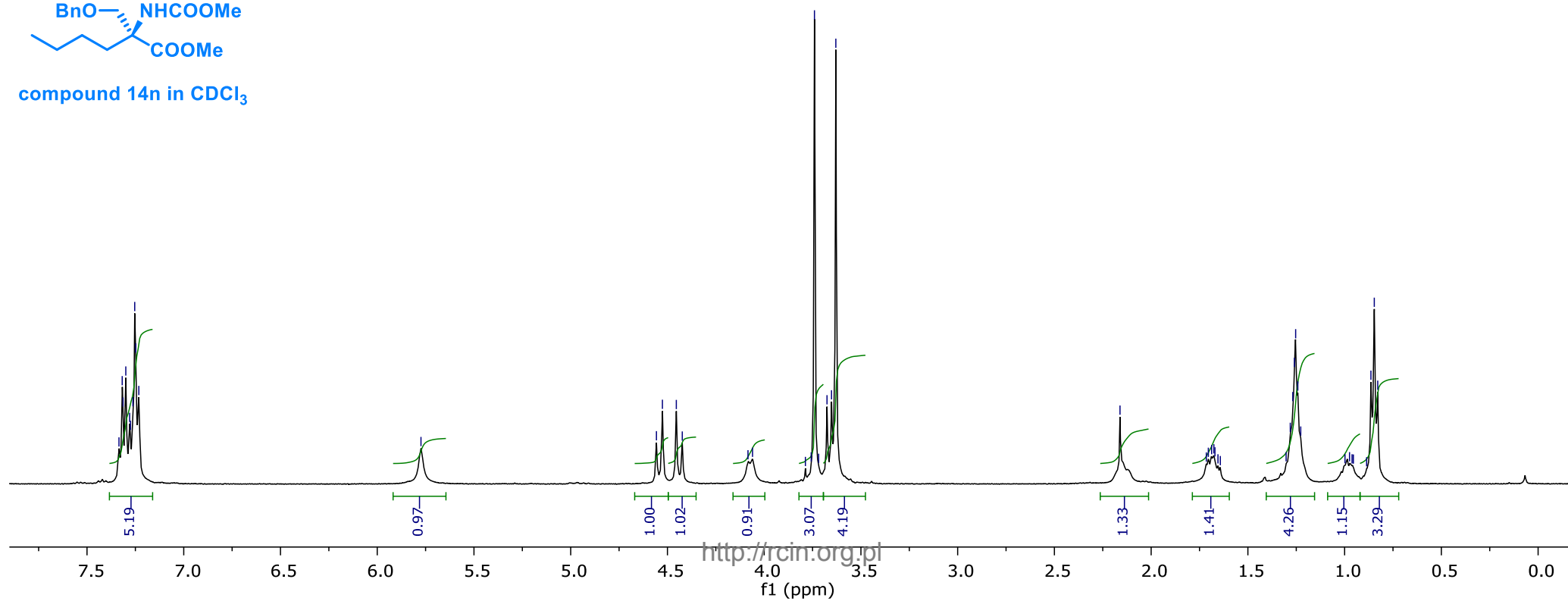
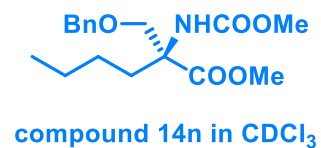
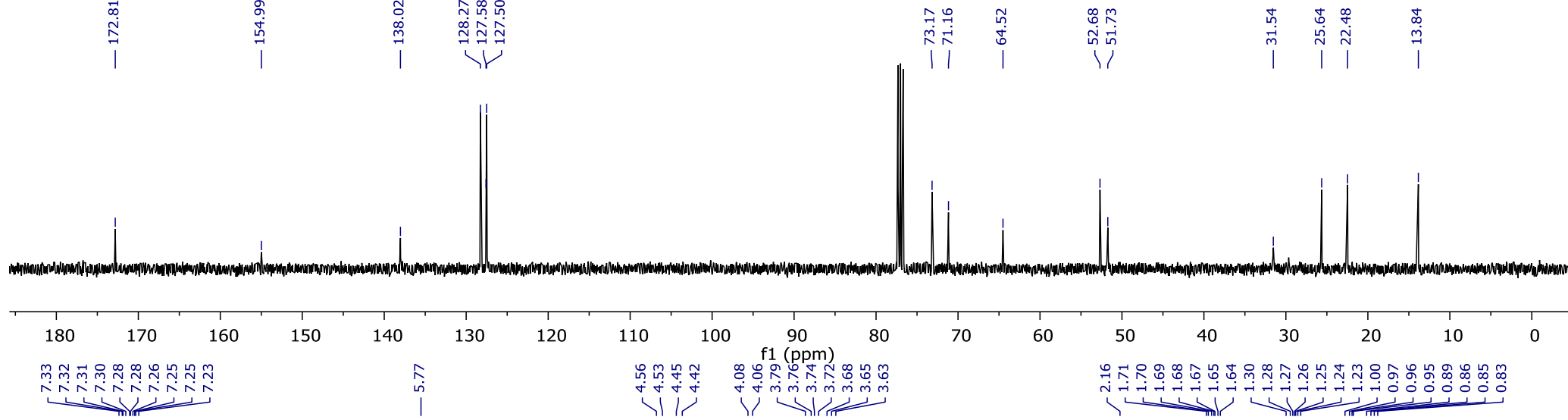
compound 14j in CDCl<sub>3</sub>

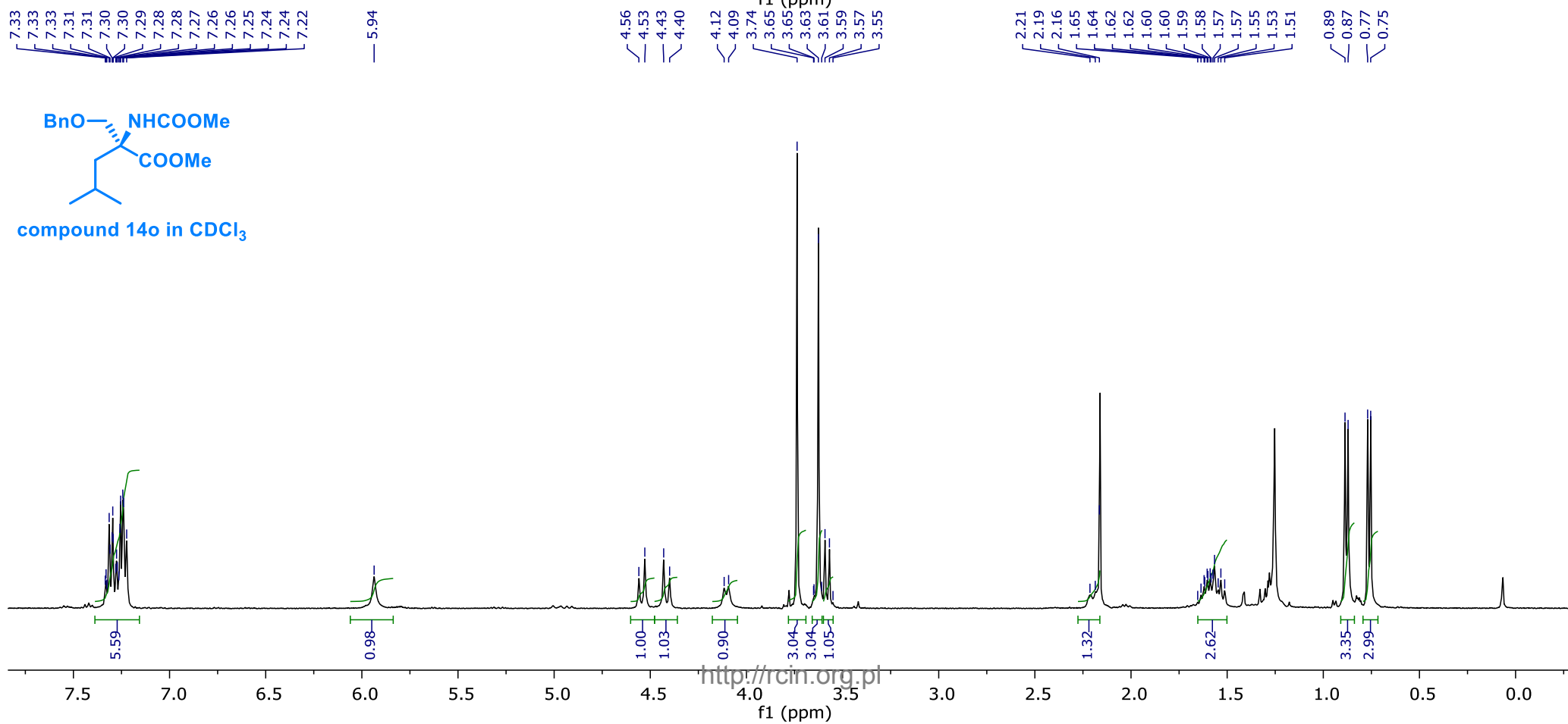
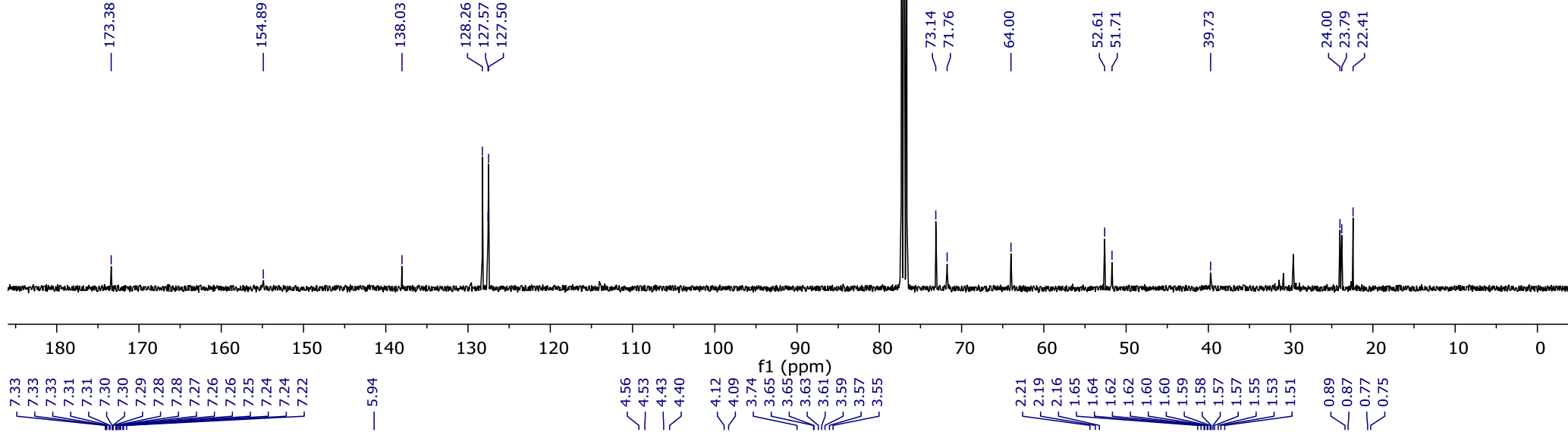


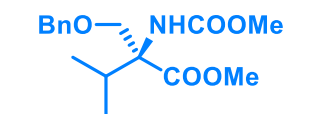
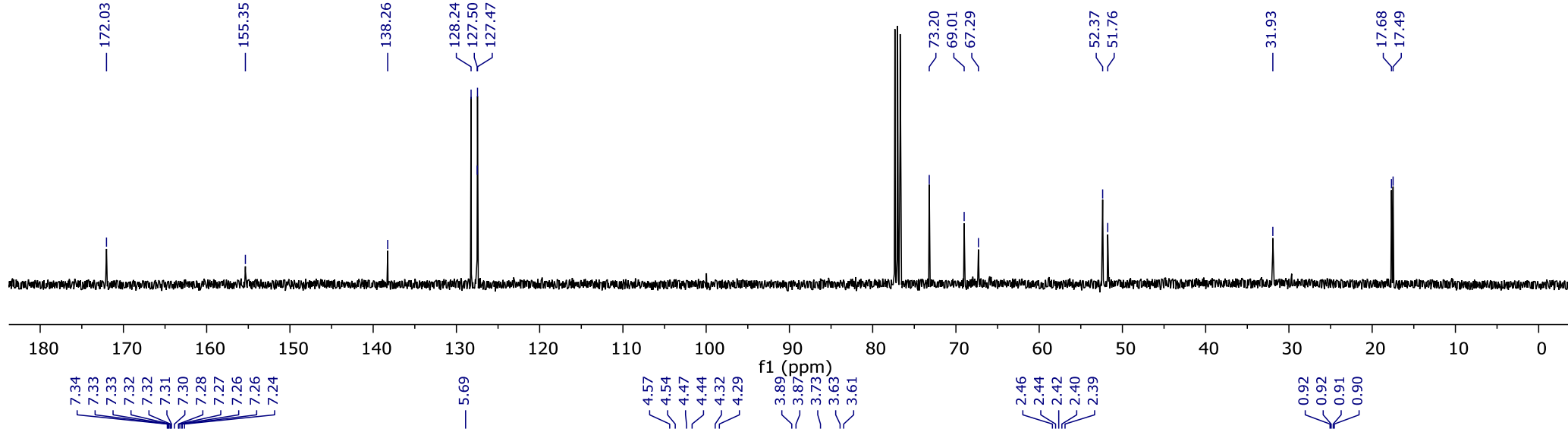




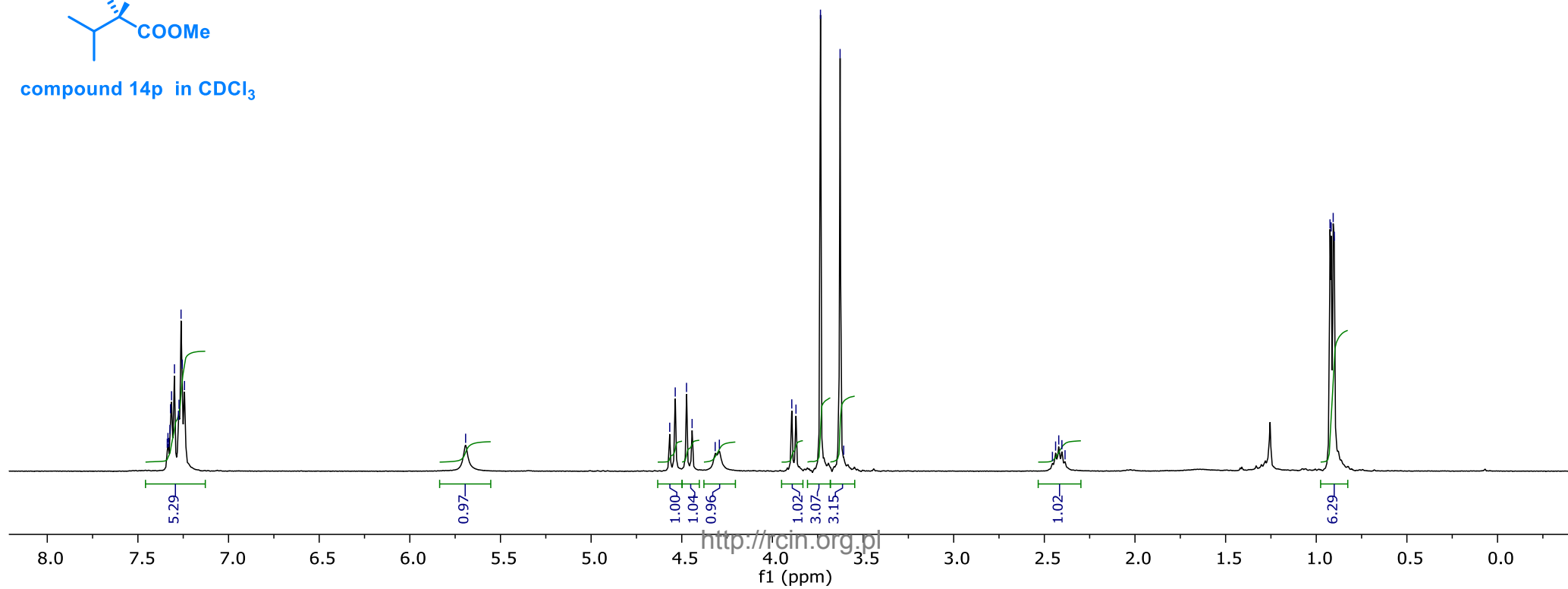


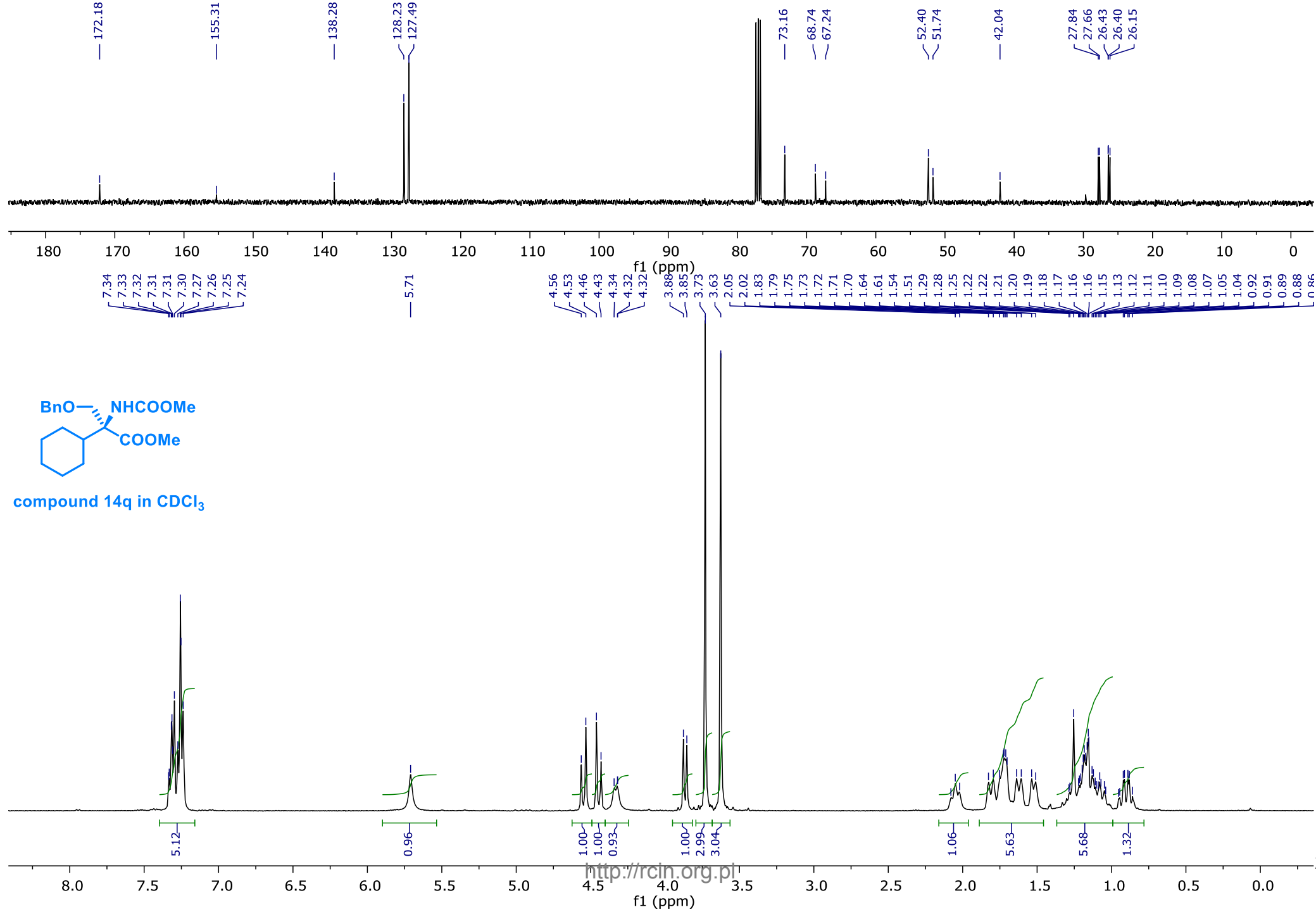




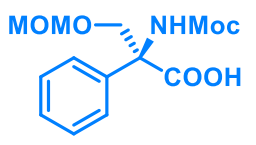
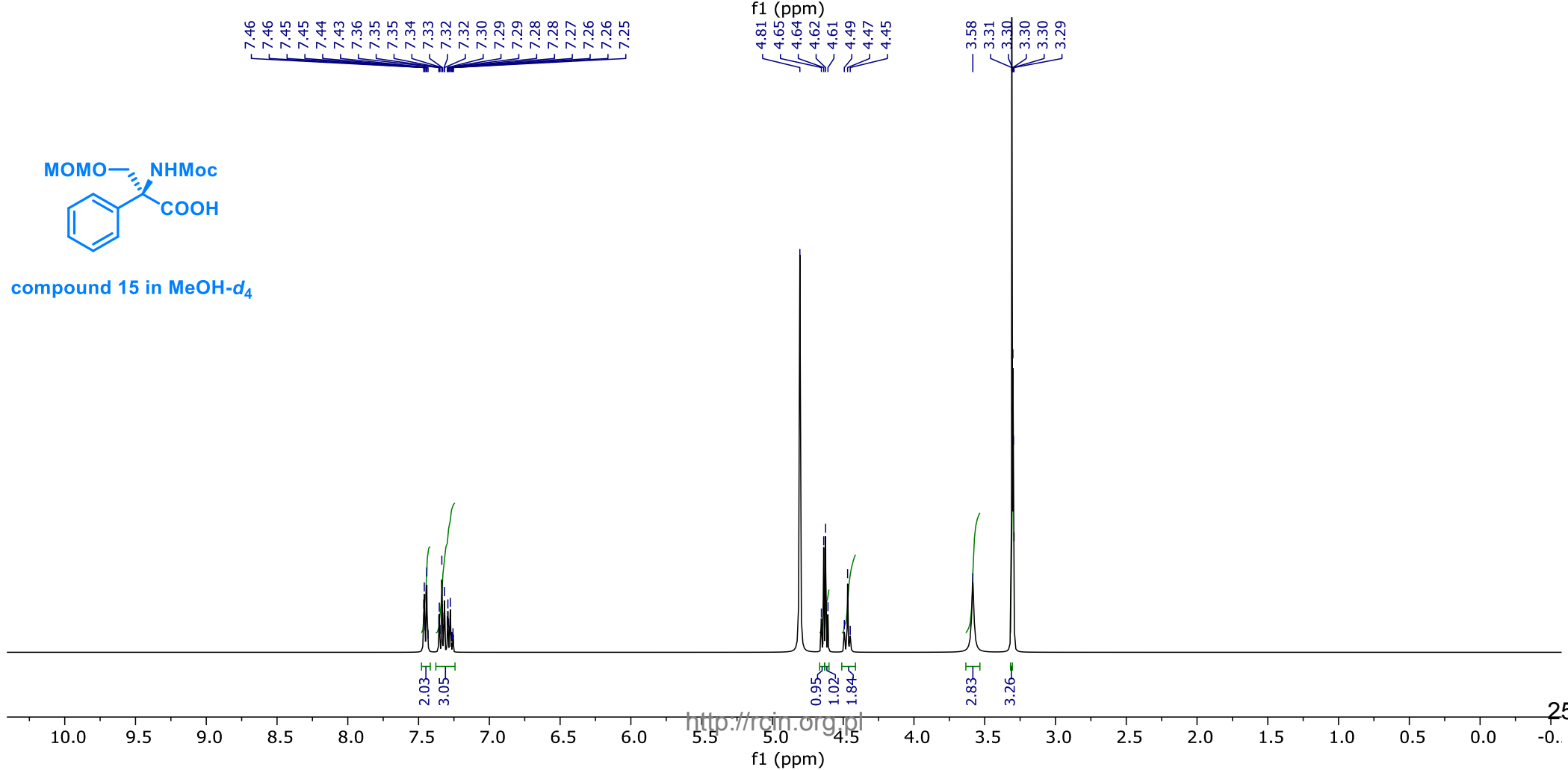
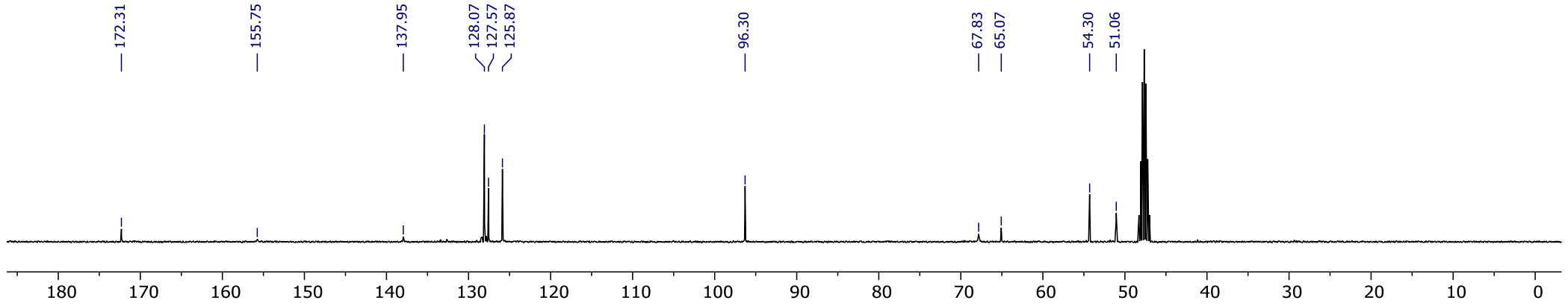


compound 14p in CDCl<sub>3</sub>

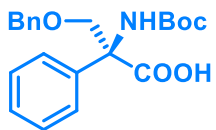
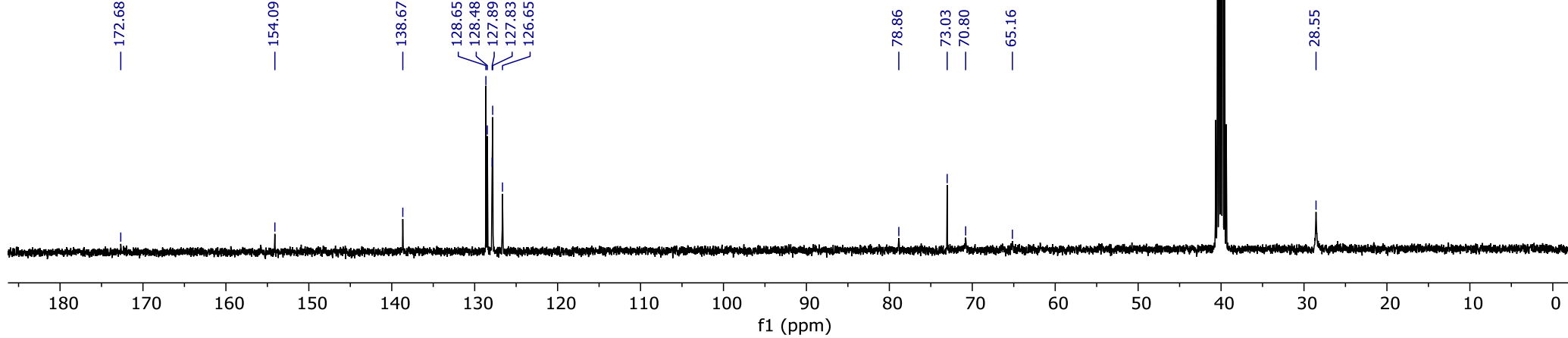




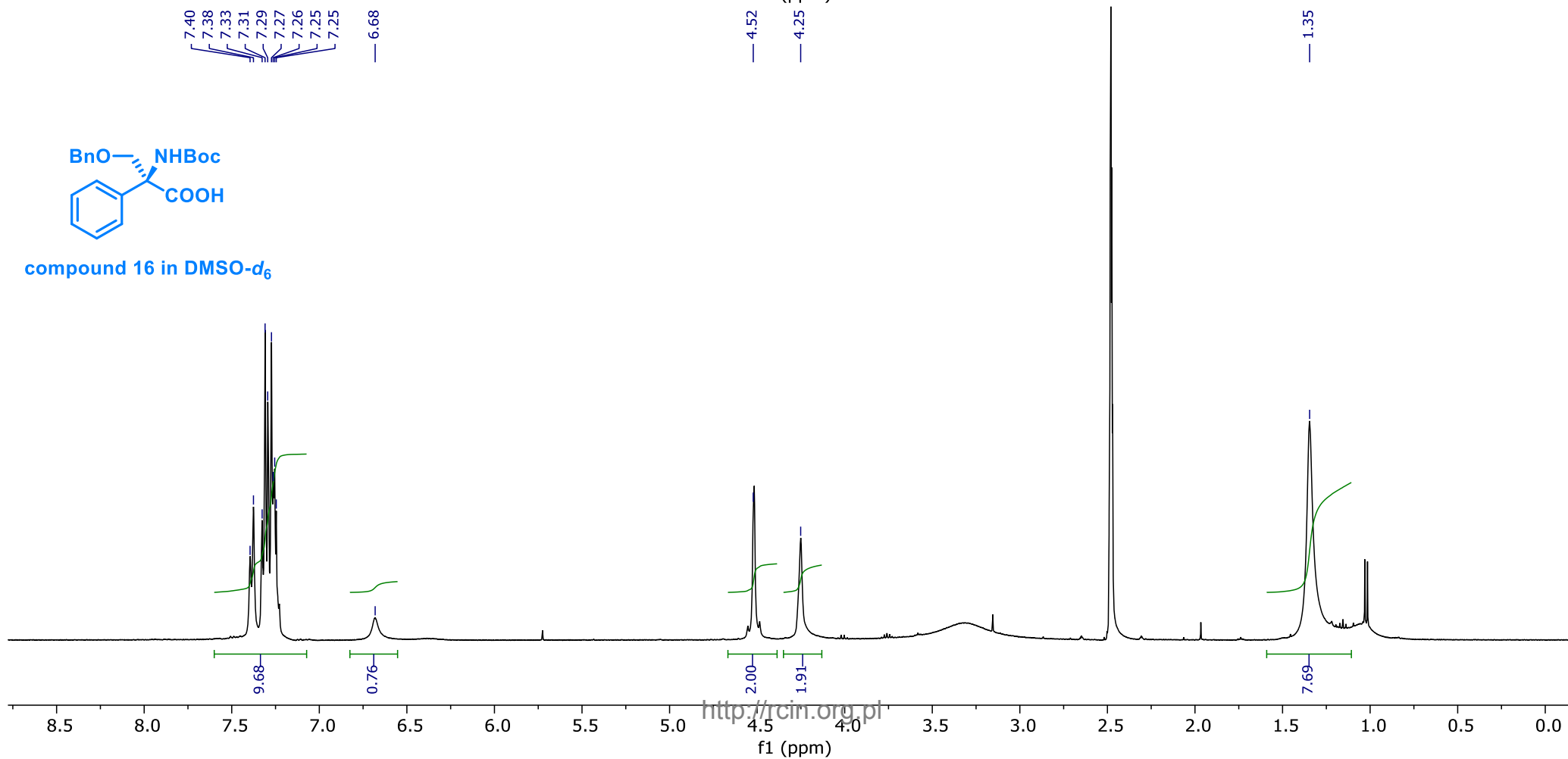


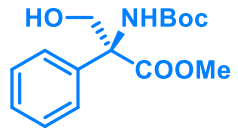
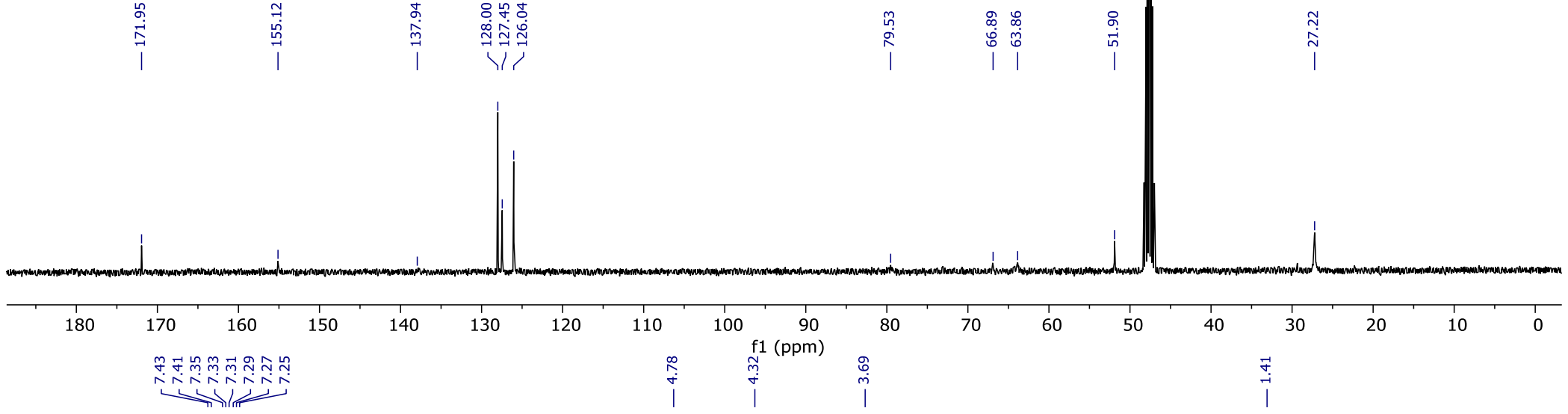


compound 15 in MeOH-d<sub>4</sub>

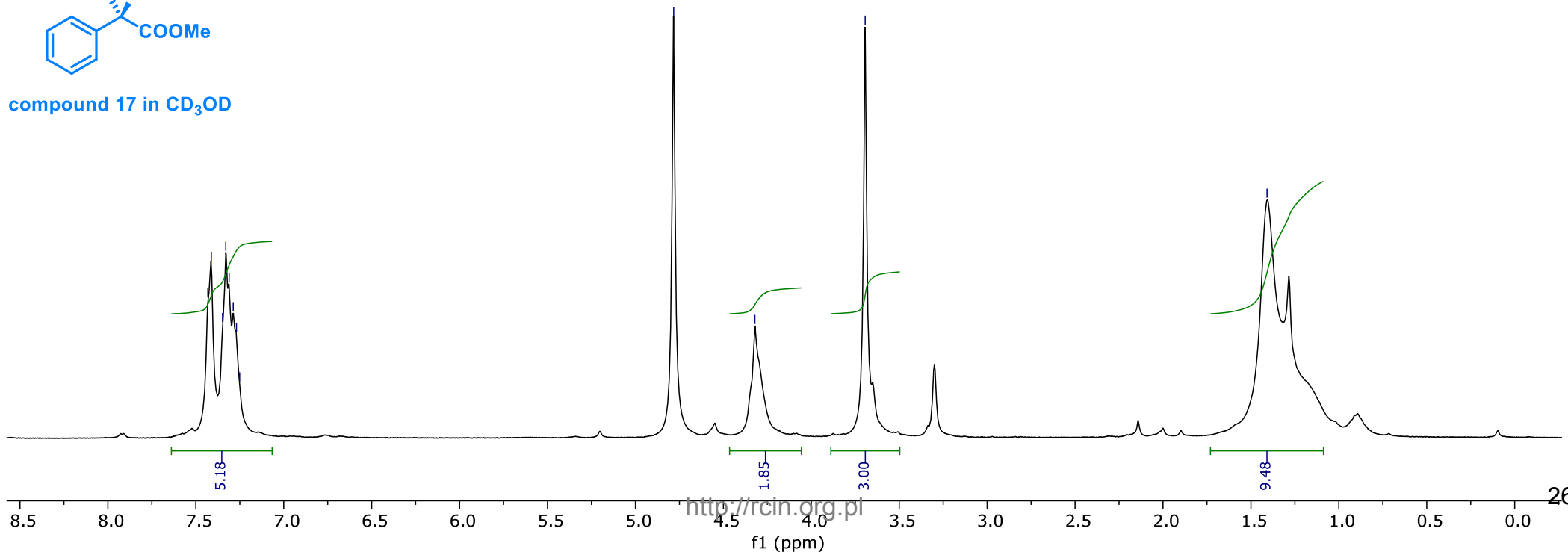


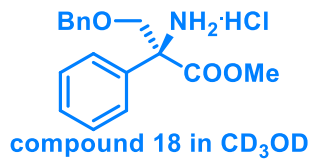
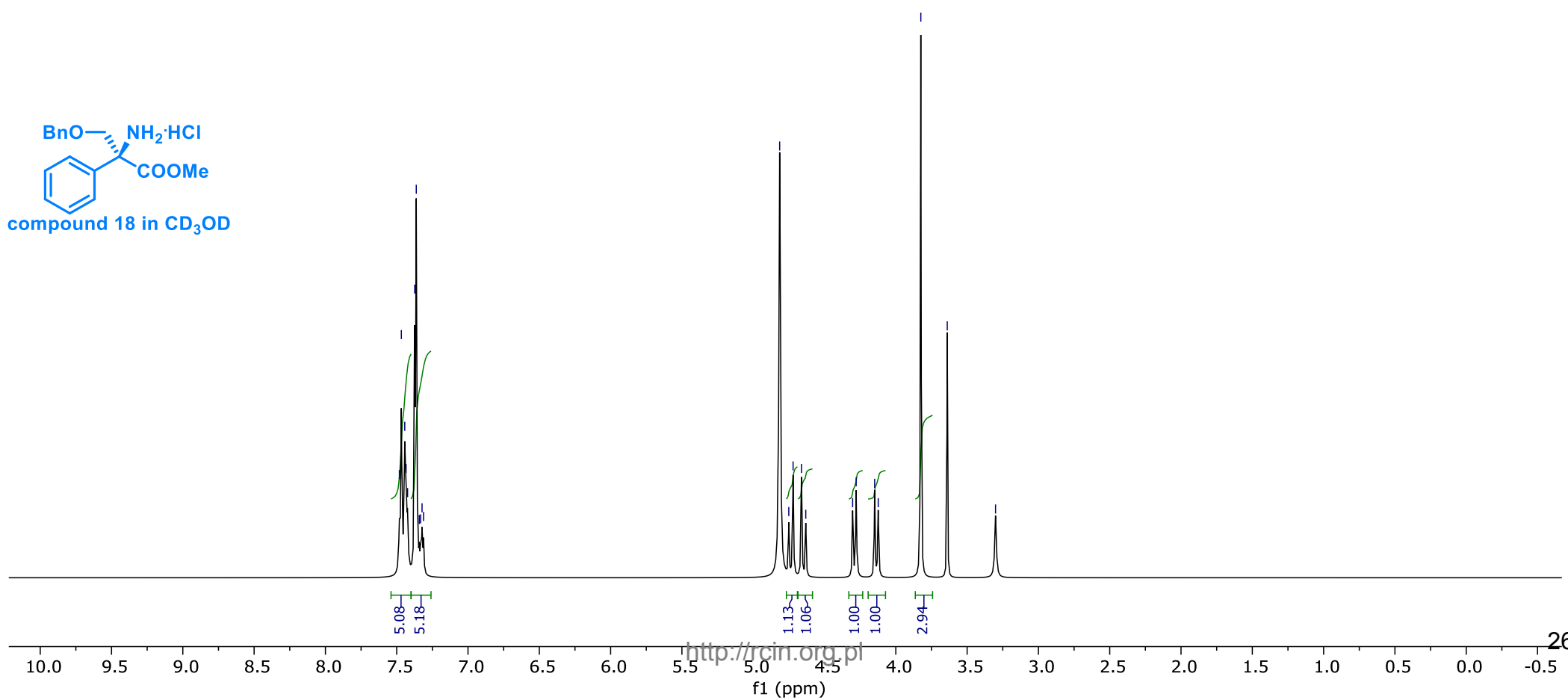
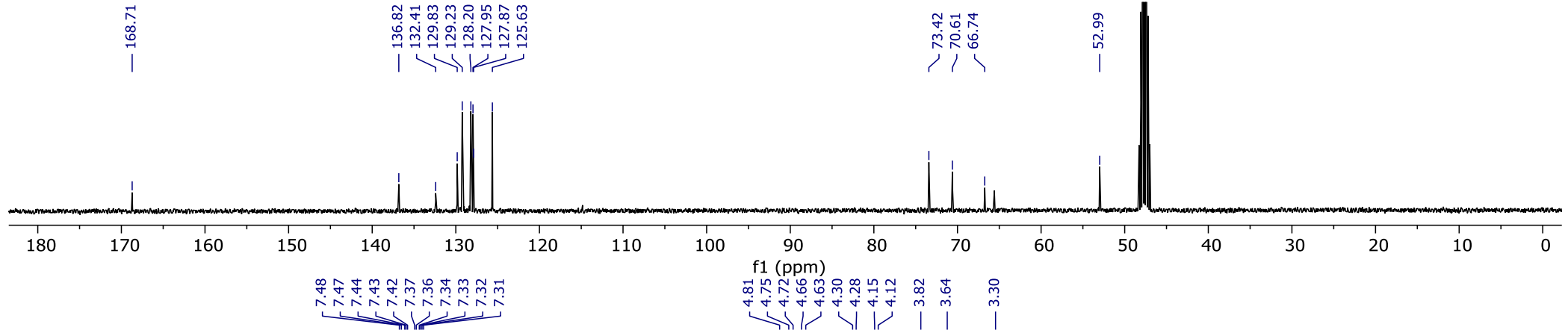
compound 16 in DMSO-d<sub>6</sub>

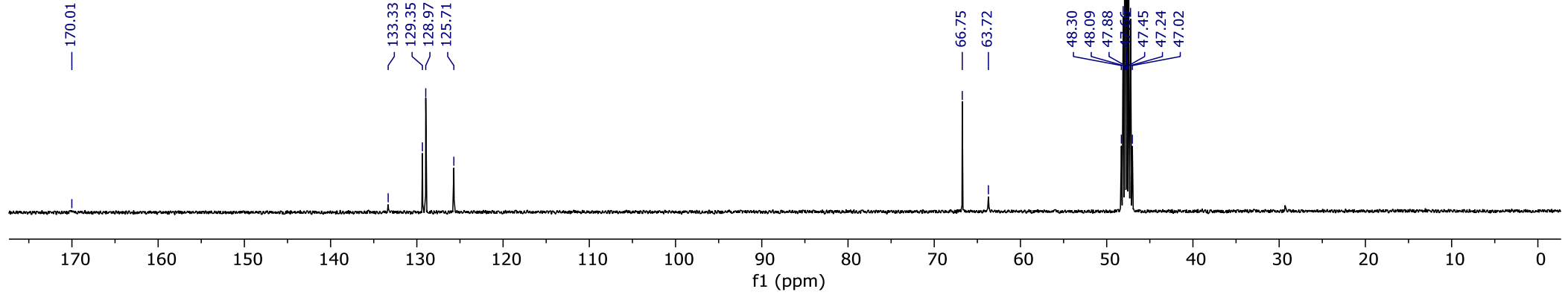




compound 17 in CD<sub>3</sub>OD



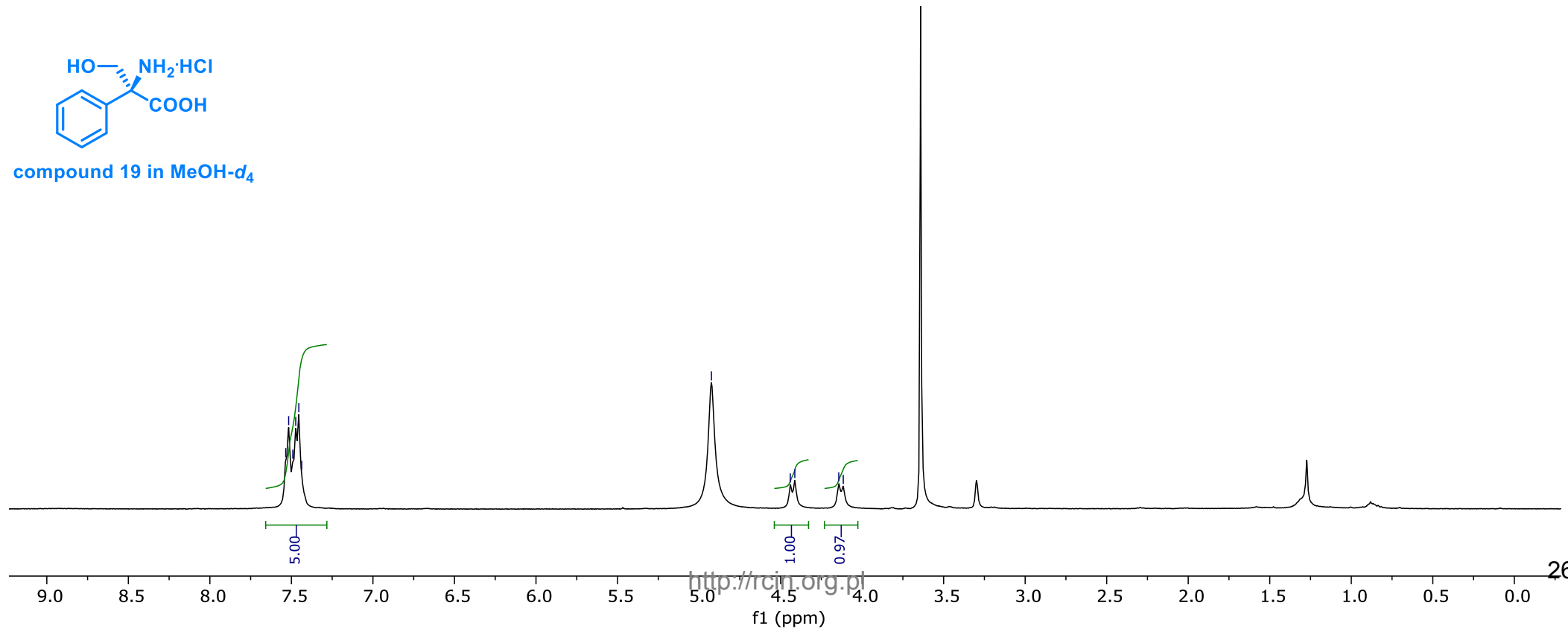
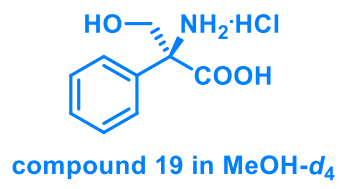


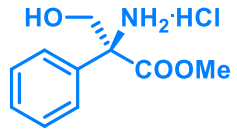
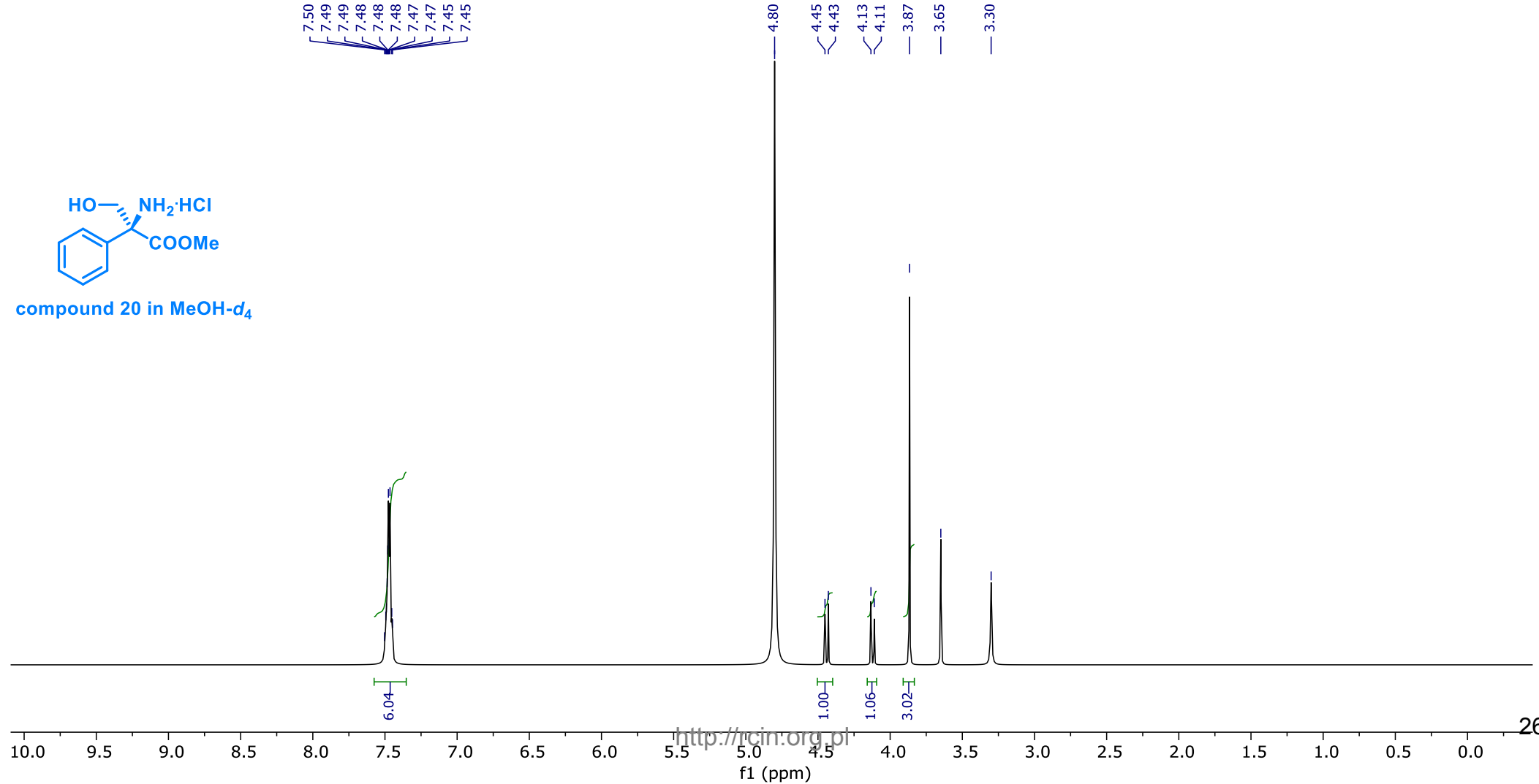
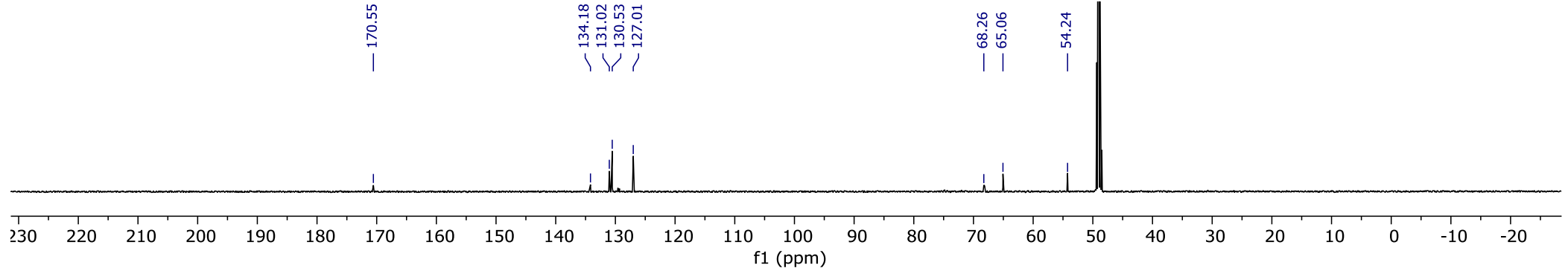


7.53  
7.52  
7.49  
7.47  
7.45  
7.44

4.92

4.44  
4.41  
4.14  
4.12





compound 20 in MeOH-d<sub>4</sub>

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# An entry to non-racemic $\beta$ -tertiary- $\beta$ -amino alcohols, building blocks for the synthesis of aziridine, piperazine, and morpholine scaffolds

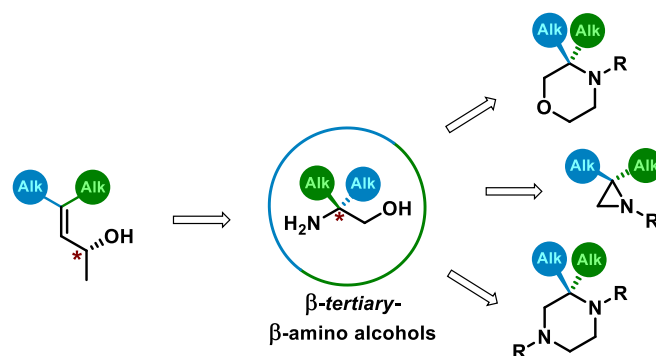
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## Graphical abstract



## Abstract

A method for the preparation of enantiopure  $\beta$ -*tert*-amino alcohols bearing a tetrasubstituted C-stereocenter, as well as their conversion into selected medicinally privileged heterocyclic systems (morpholines, aziridines, piperazines) is reported. These compounds were obtained through enantiospecific sigmatropic rearrangement of allyl carbamates as a key step. The latter were prepared from the corresponding  $\beta,\beta'$ -dialkyl-substituted non-racemic allyl alcohols. In addition, an asymmetric synthesis of such highly substituted allylic alcohols via either enantioselective 1,2-reduction of enones, enzymatic kinetic resolution, or a functionalization of chiral propargyl alcohols, with discussion of scope and limitations of each method is reported.

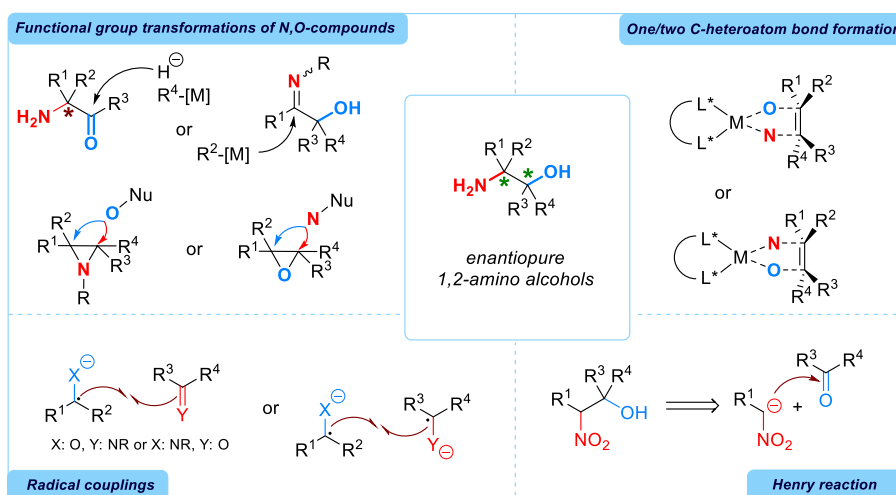


## Keywords

1,2-amino alcohols, sigmatropic rearrangements, heterocycles, aziridines, morpholines, piperazines

## Introduction

The 1,2-amino alcohol unit is an important structural motif in various natural products, medicinally active compounds, chiral auxiliaries, and privileged ligands. Nowadays, over 300,000 compounds containing this unit are known, including more than 2000 natural products, almost 100 FDA-approved drugs, and hundreds of drug candidates.<sup>1, 2</sup> The formation of these structures has therefore received widespread attention from the synthetic organic chemistry community (Scheme 1).<sup>1, 2</sup>

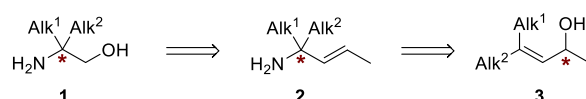


Scheme 1

The synthesis of such compounds has stimulated continuing interest and extensive efforts (Scheme 1).<sup>1-11</sup> Standard methods for the synthesis of enantiopure vicinal amino alcohols involve various addition reactions which mostly require non-racemic substrates or reagents (Scheme 1). Most common strategies are based on functional group transformation of vicinal N,O-compounds (e.g. reduction of natural amino acids),<sup>4-6</sup> addition of N/O-heteroatoms to substrates,<sup>3, 8-10</sup> and transformation of

nitro aldol (Henry) reaction products.<sup>11, 12</sup> These strategies, including their catalytic enantioselective variations, suffer from either structurally limited substrates/products or relatively low regio- and stereoselectivity. Difficulties in the control of regioselectivity are also an issue in the ring opening of aziridines and epoxides.

Recently, several radical cross-coupling strategies between amine and alcohol moieties have been reported.<sup>7</sup> Among them, protocols involving  $\text{SmI}_2$ -mediated reductive cross-coupling of imine derivatives<sup>11, 13, 14</sup> or nitrones<sup>15-18</sup> with aldehydes or ketones have been developed. Unfortunately, the use of stoichiometric amounts of  $\text{SmI}_2$  as reductant is a substantial limitation and challenge for enantioselective variants with the use of chiral ligands.<sup>11, 19</sup> An additional disadvantage are the unavoidable side-reactions (e.g. pinacol-type homocoupling or reduction of substrates). An interesting alternative are visible light-mediated transformations,<sup>20-27</sup> although there are only a few reports on enantioselective protocols involving photocatalyst-merged dual catalyst systems with chiral phosphoric acid organocatalyst<sup>20</sup> or chiral rhodium Lewis acid,<sup>22</sup> or bifunctional Lewis acid/photoredox catalyst<sup>23</sup> of chiral-at-metal iridium complex.<sup>21</sup> In 2018, Huang and co-workers<sup>24</sup> reported the reductive cross-coupling reaction of aldonitrones with aromatic aldehydes via the synergistic catalysis of Ru-photocatalyst and chiral  $\text{Sc}(\text{OTf})_3/N,N$ -dioxide complex. The reaction proceeded also for ketonitrones, but only ketonitrones derived from symmetric ketones were tested. Nevertheless, all of the mentioned methods relied heavily on specially designed substrates.



*Scheme 2*

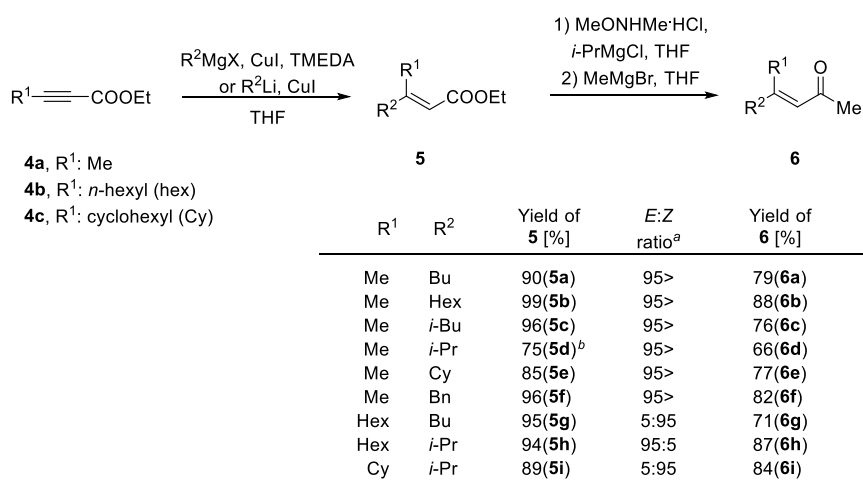
None of the above fit perfectly for a synthesis of type **1** enantiopure vicinal amino alcohols (Scheme 2). Their synthesis through functional group transformation requires an access to enantiopure quaternary amino acids or aziridines, whose preparation in enantiopure form is a challenging task in itself. Also, the synthesis of **1** by radical coupling can be problematic since the generation of formaldehyde-derived radical species is not straightforward. The use of formaldehyde as a reagent for such a process, as well as others processes, e.g. the Henry reaction, is problematic from the stereochemical point of view, since very often for these transformation, the carbonyl partner is a significant contributor of asymmetric induction at the transition state. For such a small and achiral reagent, the developed protocols have to involve complex chiral systems to provide sufficient levels of enantioselectivity.

Therefore, establishing a protocol for direct and efficient preparation of enantiopure amino alcohols **1** is still required. We sought to investigate the preparation of **1** through [3,3]-sigmatropic rearrangement of allyl alcohols to **2** derivatives. In general, sigmatropic rearrangements are an excellent tool for the creation of stereogenic centers, particularly those of high steric hindrance.<sup>28-30</sup> The reason for that is the intramolecular course of the process and its concerted mechanism. In consequence, these reactions allow for highly stereoselective generation of stereogenic centers through chirality transfer along the allylic system.

## Results and discussion

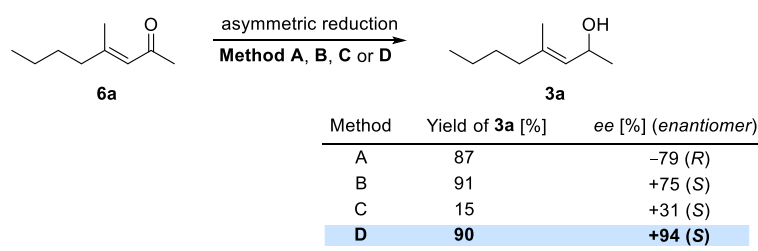
In order to investigate the feasibility of this proposal, in the initial attempt, we began with the synthesis of  $\beta,\beta$ -dialkyl substituted allyl alcohols **3**. The synthesis of enantiopure type **3** alcohols is rather challenging and only a few examples, including enzymatic<sup>31</sup> and catalytic<sup>32</sup> kinetic resolution of racemates, addition of organometallics

to chiral aldehydes<sup>33</sup> or sequential functionalization of enantiopure propargyl alcohols,<sup>34-36</sup> are known. We decided to prepare these compounds through a less explored enantioselective 1,2-reduction<sup>37-41</sup> of the corresponding enones **6**. The latter were prepared through a 1,4-addition reaction of organocopper reagents to alkynes **4**. The addition reaction provided  $\alpha,\beta$ -unsaturated esters **5** as single isomers in most cases (Scheme 3). Then, esters **5** were readily converted into Weinreb amides which, upon treatment with MeMgBr, gave the corresponding unsaturated ketones **6**. As mentioned, the 1,4-addition step provided mainly single isomers (*E* or *Z*). In a few cases, slight contamination with the side isomer was readily removed through column chromatography of the corresponding Weinreb amides.



<sup>a</sup> Determined by <sup>1</sup>H NMR; <sup>b</sup> Lower yield due to the volatility of the product.

Scheme 3

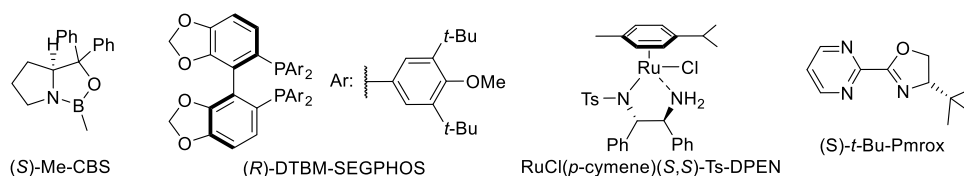


**Method A:** (S)-(-)-2-Methyl-CBS-oxazaborolidine (25 mol%), BH<sub>3</sub>·SMe<sub>2</sub>

**Method B:** Cu(OAc)<sub>2</sub> (3 mol%), (*R*)-DTBM-SEGPHOS (3 mol%), DEMS, Et<sub>2</sub>O, -25 °C

**Method C:** RuCl(*p*-cymene)(*S,S*)-Ts-DPEN (10 mol%), HCOOH:Et<sub>3</sub>N 5:2, rt

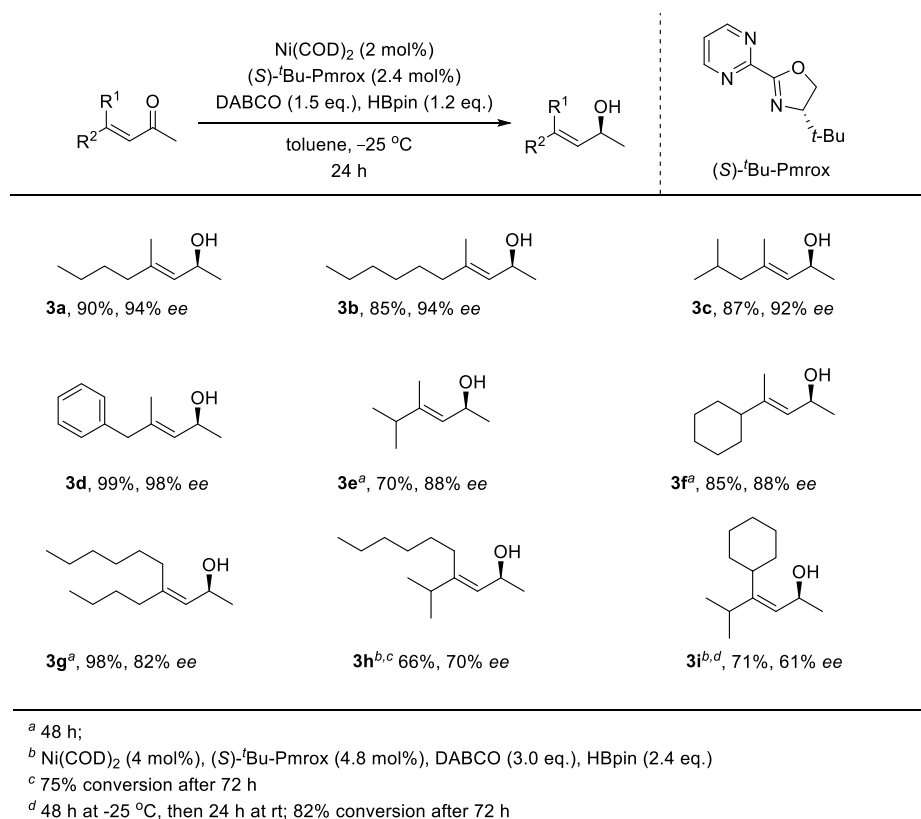
**Method D:** Ni(COD)<sub>2</sub> (2 mol%), (*S*)-*t*-Bu-Pmrox (2.4 mol%), DABCO, pinBH, toluene, -25 °C



### Scheme 4

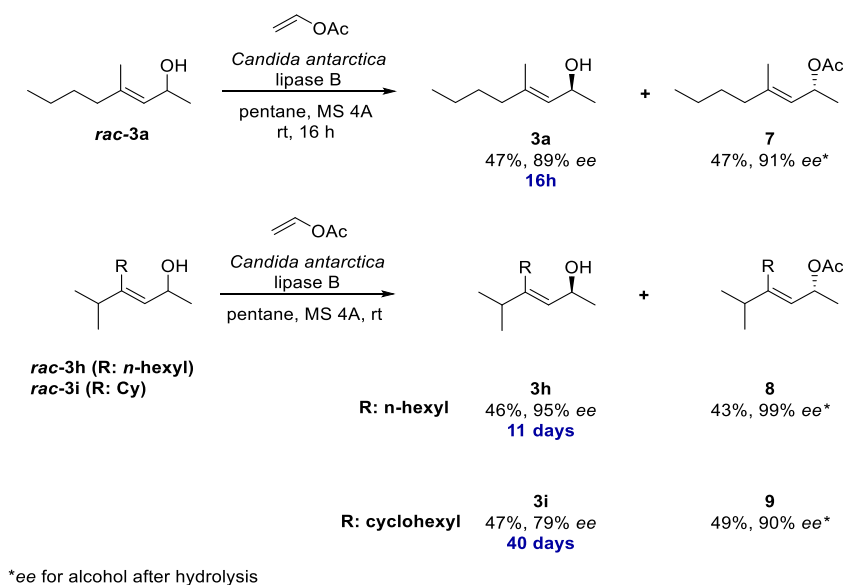
With a series of  $\beta,\beta$ -disubstituted enones **6** in hand, studies on their enantioselective reduction were conducted. The CBS reduction of model enone **6a** with BH<sub>3</sub>·Me<sub>2</sub>S in the presence of a chiral (*S*)-(-)-Me-oxazaborolidine (Scheme 4, Method A) provided the corresponding alcohol (***R***-**3a**) with good yield (87%) and average enantioselectivity (79% *e.e.*).<sup>42</sup> The Cu-catalyzed hydrosilylation (Scheme 4, Method B), which we have successfully utilized in the past,<sup>35</sup> proceeded efficiently, but the level of enantioselectivity was still insufficient. Disappointingly, transfer hydrogenation of **6a** in the presence of Noyori-type catalysts (Scheme 4, Method C) failed and mostly the starting material was recovered. The isolated product had poor enantiopurity. The best results were achieved when enone **6a** was subjected to (*S*)-*t*-Bu-Pmrox/Ni-mediated 1,2-reduction with pinBH under conditions reported by Chen and co-workers.<sup>38</sup> Under conditions presented in Scheme 4 (method D), the desired alcohol **3a** was obtained in 90% yield (over 95% conversion of starting material) and in very high enantioselectivity (94% *ee*).

The reduction proceeded efficiently also for other simple  $\beta,\beta$ -disubstituted enones bearing *n*-butyl (**3a**), *n*-hexyl (**3b**), *i*-butyl (**3c**), and benzyl (**3d**) substituents (Scheme 5). Reduction of enones bearing hindered alkyl groups such as *i*-propyl or cyclohexyl ones, proceeded still efficiently, though the reaction time had to be extended up to 48 h. In addition, their reduction provided the corresponding allyl alcohols **3e** and **3f** with slight lower enantiopurity (Scheme 5). The replacement of R<sup>1</sup> = Me group in **3a** by *n*-hexyl, as in **3g**, caused the same effect. Also, in this case, extension of reaction time to 48 h was required. The introduction of a bulky group as R<sup>1</sup> strongly affected the reduction process. In the case of the synthesis of alcohols **3h** and **3i**, even a 3-fold increase of reaction time did not result in complete conversion of the starting material. Moreover, in both cases, a significant decrease of enantioselectivity was observed. Further attempts at re-optimization of the reaction did not enhance the process.



Scheme 5

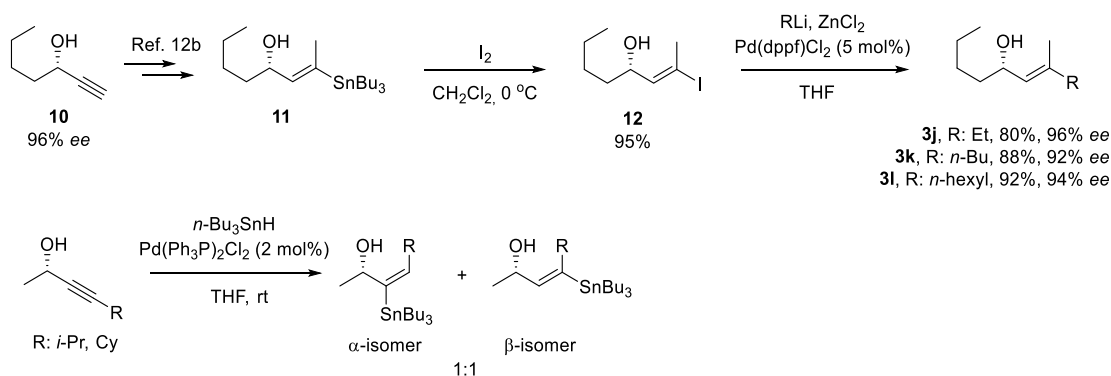
The observed difficulties in the synthesis of enantiopure alcohols **3h** and **3i** encouraged us to attempt to prepare them *via* kinetic resolution of racemates. Initially, the effectiveness of this approach was tested for model alcohol **rac-3a** (Scheme 6). Its treatment with vinyl acetate in the presence of lipase B from *Candida antarctica* provided, after 16 h, the corresponding (*S*)-allyl alcohol (**3a**) in 47% yield and with high 89% *ee* enantiopurity. The accompanying (*R*)-acetate **7** was isolated in 47% yield and its enantiopurity was 91% *ee*. Kinetic resolution of **rac-3h** and **rac-3i** required dramatic increase in reaction time to 11 days, for the former, and to 40 days(!) for the latter. These two examples clearly show how challenging the synthesis of enantiopure type **3h/3i** allyl alcohols bearing sterically hindered substituents is.



Scheme 6

Recently, we have demonstrated that a sequential functionalization of propargyl alcohols is an efficient method for the preparation of complex allyl alcohols.<sup>35, 36, 43</sup> Therefore, we decided to check whether the developed protocols will be suitable for the current studies. Initially, easily available (*S*)-hept-1-yn-3-ol (**10**) was transformed to  $\beta$ -vinylstannane **11** following our previous protocol (Scheme 7).<sup>35</sup> After Sn-halogen exchange, the resulting vinyl iodide **12** was subjected to the Negishi cross-coupling

reaction. The cross-coupling with simple alkyl organozinc reagents proceeded smoothly (in ca. 3-4 h), with complete conversion of the starting material, and without the formation of a protodehalogenation side product when Pd(dppf)Cl<sub>2</sub> was used as the catalyst.<sup>44</sup> Disappointingly, this process was limited to the introduction of simple linear alkyl groups such as methyl, ethyl or *n*-butyl. In the case of alcohols bearing a secondary alkyl group (e.g. *i*-Pr or Cy, Scheme 7), the corresponding vinylstannanes were formed non-selectively to provide difficult to separate mixtures of  $\alpha$  and  $\beta$  isomers.

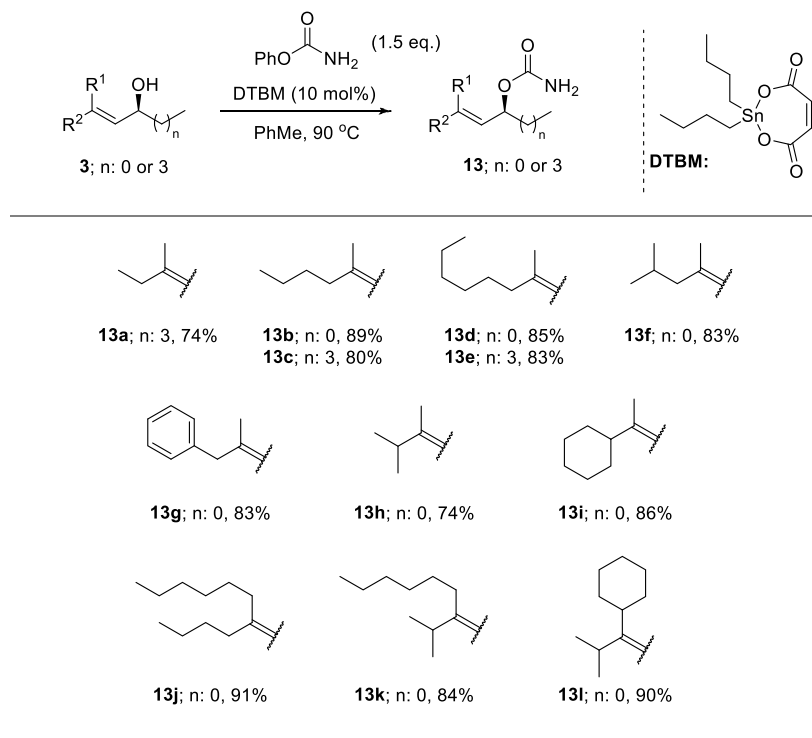


Scheme 7

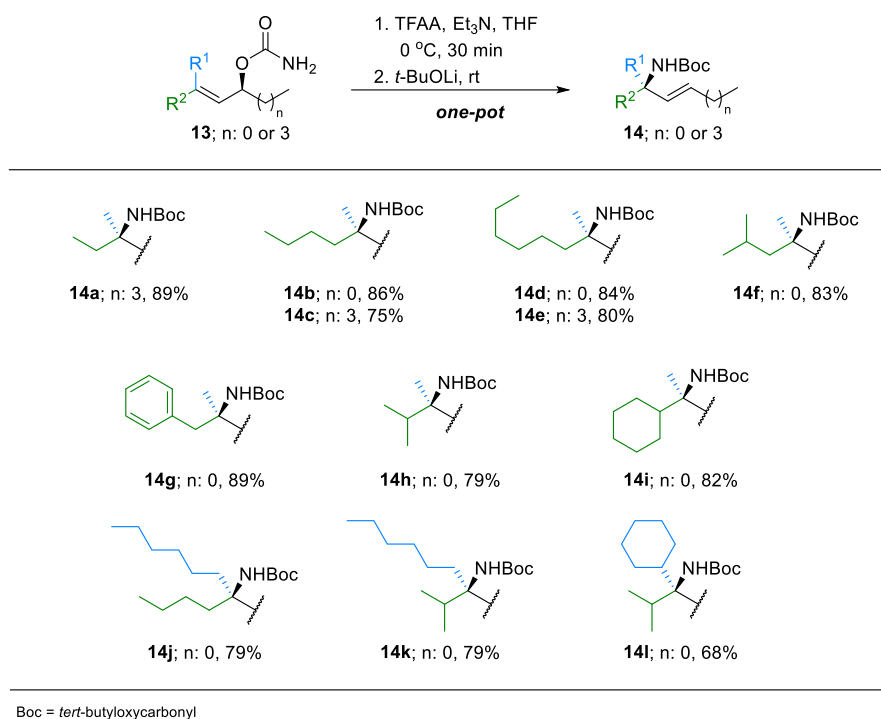
In the next step,  $\beta,\beta$ -dialkyl substituted allyl alcohols **3** were transformed into *tert*-allylamines through the [3,3]-sigmatropic Ichikawa rearrangement reaction.<sup>45, 46</sup> First, they were carbamoylated by the treatment with phenyl carbamate in the presence of dibutyltin maleate (DBTM) as a catalyst (Scheme 8).<sup>47, 48</sup> The resulting carbamates **13** were treated with TFAA (2 equiv.) in the presence of Et<sub>3</sub>N (6 equiv.). After 30 min, *t*-BuOLi was added to provide *N*-Boc protected allylamines **14** with high overall yields after 3 steps. The rearrangement proceeded efficiently for a wide range of alkyl substituents regardless of whether they were simple linear groups or sterically hindered substituents. Importantly, the rearrangement proceeded stereoselectively



with complete chirality transfer and generated the new tetrasubstituted carbon stereocenter enantiospecifically (Scheme 9).



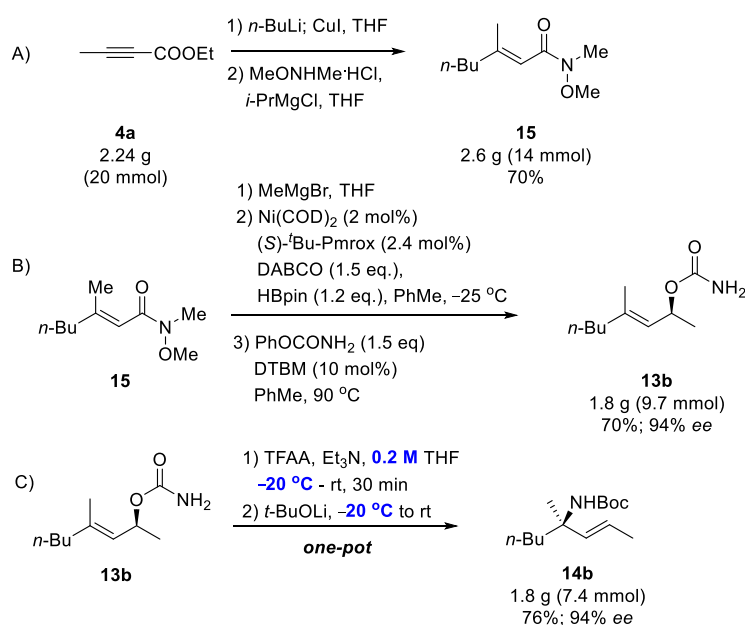
*Scheme 8*



*Scheme 9*

The transformations presented above, leading to  $\alpha,\alpha$ -dialkyl substituted allyl amines, proceeded smoothly not only on a small scale (<1 mmol) but are easily scalable. This was exemplified by a gram-scale synthesis of allylamine **14b** (Scheme 10). To maximize the efficiency of the process and minimize any loss of intermediates, the individual steps were combined in three blocks, and intermediate isolation/purification was mostly limited to a simple extraction. Thus, 20 mmol (2.24 g) of alkyne **4a** was transformed into Weinreb amide **15**. Next, it was subjected to Grignard reagent addition and, after simple extraction, to the enantioselective reduction. The crude alcohol was transcarbamoylated to provide product **13b**. Finally, the carbamate was rearranged to amine **14b**. As a result, the presented formal 7-step synthesis required only three chromatographic purification operations: 1) amide **15** (to eliminate slight contamination with the *Z* isomer), 2) carbamate **13b** (slight impurities can affect the efficiency of the rearrangement), and 3) final amine **14b**. The remaining

steps required only simple extraction. The Ichikawa transformation was also efficient on a larger scale, although, in order to facilitate the process, the reaction temperature was decreased to  $-20\text{ }^{\circ}\text{C}$  (to avoid overheating of the reaction mixture during the addition of a larger amount of TFAA). Moreover, in case of the gram-scale synthesis, reaction concentration could be increased from 0.05 M (for <1 mmol scale) to 0.2 M, which allowed to reduce the amount of solvent and, as a result, the amount of waste. Thus, starting from 20 mmol (2.24 g) of alkyne **4a**, 1.8 g (7.4 mmol) of product **14b** was obtained with overall yield 37% (Scheme 10).

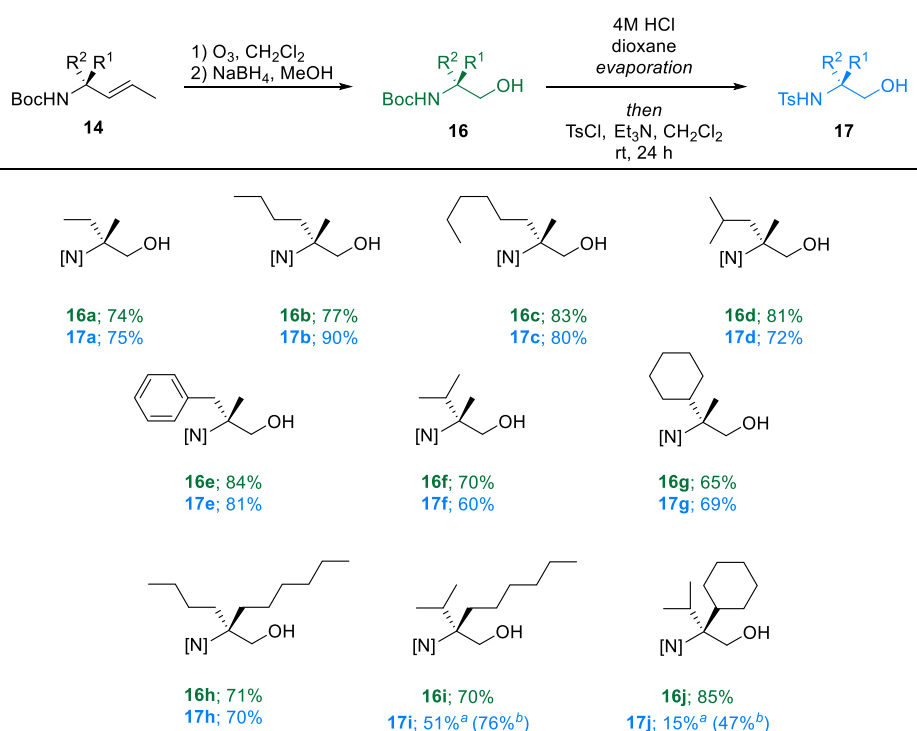


Scheme 10

It should be stressed that the reported strategy, based on sigmatropic rearrangement of allyl carbamates **13**, allows for the preparation of vast classes of *N*-functionalized allylamine derivatives. As we already demonstrated in the past,<sup>35</sup> a simple replacement of *t*-BuOLi by other nucleophilic agents, including alkoxides (or alcohols), *C*-nucleophiles (organometallics, enolates), *N*-nucleophiles (amines, hydrazines, oximes etc.), *H*-nucleophiles, enables direct access to carbamates, amides, and urea derivatives.

Finally, the resulting allylamines **14** were ozonolyzed, followed by NaBH<sub>4</sub> reduction to provide *N*-Boc protected enantiopure vicinal amino alcohols **16**. (Scheme 11) in very good yield after 2 steps. In addition, type **16** amino alcohols can be easily transformed into their *N*-Ts congeners **17** by treatment of **16** with 4M HCl in dioxane followed by tosylation of the crude amine with *p*-TsCl in the presence of Et<sub>3</sub>N, as demonstrated in Scheme 11. For more hindered amino alcohols **16i,j**, the tosylation under standard conditions was less effective. However, the replacement of the base with TMEDA and the solvent with MeCN enhanced the process. Both types of these β-amino alcohols were proved to be highly valuable building blocks in target-oriented synthesis as well as valuable organocatalysts, chiral auxiliaries, and chiral templates.<sup>5</sup>

49-51



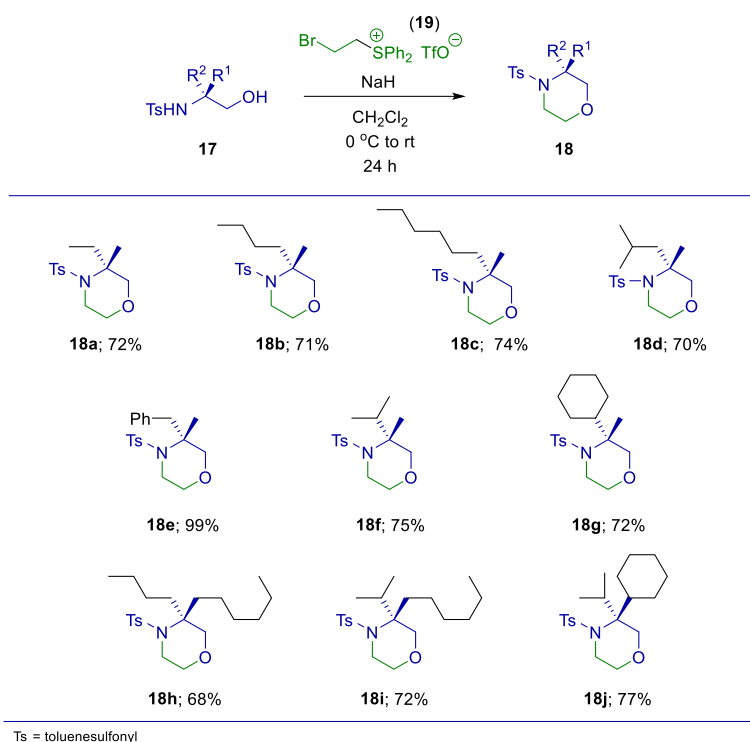
Boc = *tert*-butoxycarbonyl; Ts = toluenesulfonyl

<sup>a</sup> reaction time: 3 days; <sup>b</sup> Tosylation was performed by using TsCl (1 eq.), TMEDA (7 eq.) in MeCN at rt for 3 days.

Scheme 11

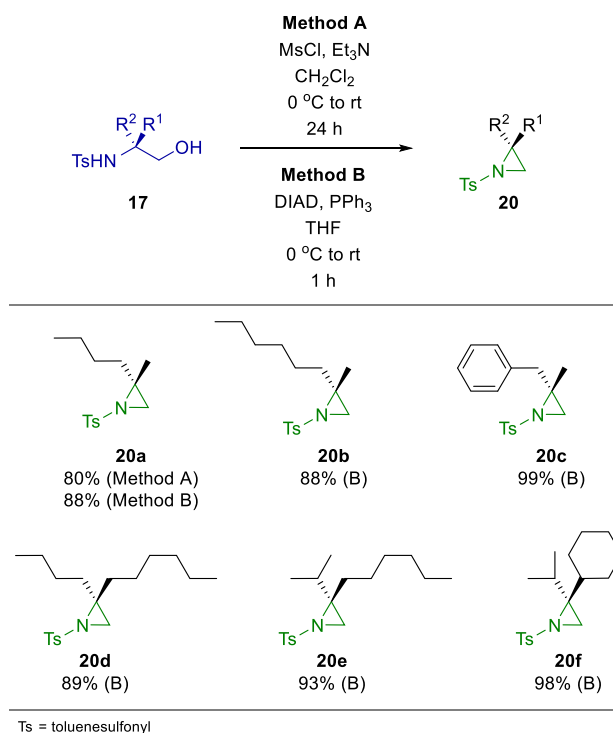
Nitrogen-containing heterocycles with a morpholine,<sup>52-58</sup> piperazine<sup>55-60</sup> or aziridine<sup>61,62</sup> ring are important pharmacophores in medicinal chemistry. Although vast number of synthetic protocols for the preparation of the mentioned heterocyclic scaffolds are known, less attention has been devoted to develop approaches for C-substituted analogues, particularly those bearing tetrasubstituted carbon stereocenters, due to limited access to suitable starting materials or efficient, highly stereoselective synthetic protocols. From this point of view, the reported protocol for the preparation of enantiopure  $\beta$ -*tert*-amino alcohols should be highly attractive as a tool for synthetic and medicinal chemists. Thus, to demonstrate the utility of the reported strategy for the preparation of enantiopure  $\beta$ -*tert*-amino alcohols, their conversion into the mentioned heterocyclic scaffolds was performed.

As already mentioned, the morpholine scaffold has been classified as a privileged structural motif in drug discovery and continues to have increasing presence in lifesaving medications.<sup>52-58</sup> Morpholines are also valuable building blocks. Therefore, we decided to transform amino alcohols **16** or **17** into enantiopure *gem*-disubstituted heterocycles **18**. An intuitive approach based on the cyclization of **16/17** with a dielectrophilic synthon such as dihalide is rather less efficient and often provides side elimination products. For this reason, we turned our attention to more efficient annulation agents such as bromoethylsulfonium salts reported by Aggarwal and co-workers.<sup>63</sup> In the presence of salt **19** and NaH as a base, compounds **17** were easily cyclized to non-racemic morpholines **18** in very good yields (Scheme 12).



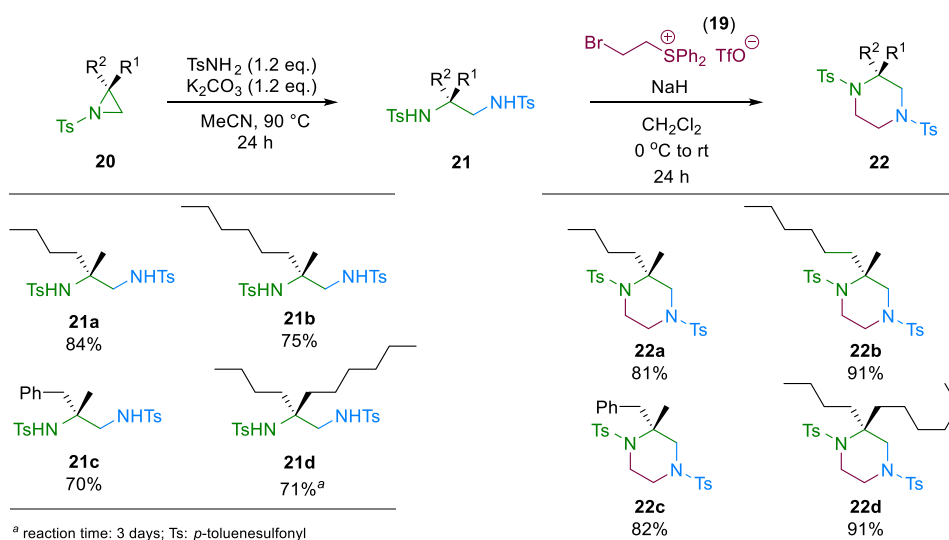
*Scheme 12*

Next, the conversion of 1,2-amino alcohols **17** into the corresponding aziridines **20** was performed. Two synthetic protocols were tested. In the first approach, amino alcohol **17b** was treated with MsCl in the presence of Et<sub>3</sub>N. In the second approach, the cyclization was performed under Mitsunobu reaction conditions. The latter reaction provided the desired product in higher yield, thus these conditions were applied for other amino alcohols **17**. In all cases, the desired enantiopure aziridines **20** were obtained in excellent yields (Scheme 13).



*Scheme 13*

The final demonstration of the utility of amino alcohols **16/17** in the synthesis of medically important heterocycles was the transformation of selected compounds **17** into the corresponding piperazine systems, which, as already mentioned, are important systems for organic and medicinal chemistry.<sup>55-60</sup> Thus, aziridines **20** were subjected to ring-opening with TsNH<sub>2</sub> to furnish diamine derivatives **21** (Scheme 14). Next, in the presence of sulfonium salt **19** and base, diamines **21** underwent a cyclization process to provide enantiopure piperazines **22** bearing a tetrasubstituted carbon stereocenter in high yields.



Scheme 14

## Conclusions

In summary, a method for the preparation of enantiopure  $\beta$ -*tert*-amino alcohols bearing a tetrasubstituted C-stereocenter was reported. These compounds were obtained through enantiospecific sigmatropic rearrangement of allyl carbamates as a key step. The latter were prepared from the corresponding  $\beta,\beta$ -dialkyl substituted non-racemic allyl alcohols. In addition, the asymmetric synthesis of such highly substituted allylic alcohols via either enantioselective 1,2-reduction of enones, enzymatic kinetic resolution, or functionalization of chiral propargyl alcohols, with a discussion of the scope and limitations of each method, was reported. The mentioned rearrangement step proceeded efficiently to provide the desired products (allylamines) in high yields and with complete chirality transfer; these were next easily transformed into target enantiopure  $\beta$ -*tert*-amino alcohols. It is worth to highlight that the reported method allowed for the preparation of complex non-racemic  $\alpha$ -*tert*-allylamines and, in turn,  $\beta$ -*tert*-amino alcohols (bearing tetrasubstituted C-stereocenter) either on a small (<1 mmol) or on a gram scale (>7 mmol), starting from



simple, commercially available alkynes. Finally, the importance of the developed method was demonstrated by the synthesis of selected heterocyclic scaffolds (morpholines, aziridines, and piperazines) starting from the synthesized  $\beta$ -*tert*-amino alcohols.

### Supporting information

The Electronic Supporting Information (ESI): Experimental procedures, characterization of organic compounds, copies of  $^1\text{H}$ ,  $^{13}\text{C}$  spectra and HPLC data for selected compounds.

### Acknowledgements

The authors are grateful to the National Science Centre of Poland for financial support of the project (research grant OPUS 2014/15/B/ST5/04398 and PRELUDIUM No. 2018/29/N/ST5/01388). A. Narczyk is grateful to the National Science Centre of Poland for ETIUDA doctoral scholarship (No. 2018/28/T/ST5/00267).

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**An entry to non-racemic  $\beta$ -tertiary- $\beta$ -amino alcohols, building blocks for  
the synthesis of aziridine, piperazine, and morpholine scaffolds**

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**Electronic supplementary materials**

**Table of contents**

1. General info.....	2
2. The synthesis of alkynes.....	2
3. The Cu(I)-mediated 1,4-addition to alkynoates .....	3
4. The synthesis of Weinreb amides .....	8
5. The synthesis of enones 6 .....	12
8. Enzymatic kinetic resolution of racemic allyl alcohols.....	20
9. The hydrolysis of acetates 8 and 9.....	23
10. The synthesis of ( <i>S,E</i> )-2-iodooct-2-en-4-ol.....	24
12. Transcarbamoylation of allyl alcohols.....	27
13. [3,3]-Sigmatropic rearrangement of allyl carbamates.....	33
14. A large scale synthesis of allylamine 14b .....	38
15. The synthesis of 1,2-amino alcohols 16.....	41
16. Synthesis of 1,2-amino alcohols 17.....	45
17. The synthesis of morpholines 18 .....	50
20. The synthesis of piperazines 22 .....	60
21. References.....	63
22. <sup>1</sup> H, <sup>13</sup> C NMR spectra and HPLC chromatograms.....	64

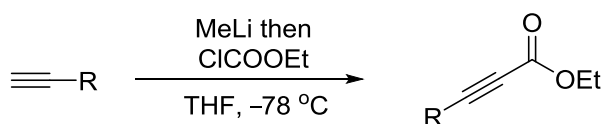
## 1. General info

NMR Spectra ( $^1\text{H}$ ,  $^{13}\text{C}$ ) were performed at 298 K.  $^1\text{H}$  NMR spectra were referenced to residual non-deuterated chloroform ( $\delta$  7.26 ppm) in  $\text{CDCl}_3$  and residual  $\text{DMSO}-d_5$  ( $\delta$  2.50 ppm) in  $\text{DMSO}-d_6$ .  $^{13}\text{C}$  NMR spectra were referenced to  $\text{CDCl}_3$  ( $\delta$  77.2 ppm) and  $\text{DMSO}-d_6$  ( $\delta$  39.5 ppm). Data is presented as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant  $J$  (Hz) and integration.

Reactions were monitored by HPLC,  $^1\text{H}$  NMR, and/or by TLC on silica gel plates (TLC Silica gel 60 F254, Aluminium sheets). TLC analysis was performed using hexanes/EtOAc as the eluent and visualized using UV light, and  $\text{KMnO}_4$  of cerium/molybdenum stains. Column chromatography was performed by using silica gel from Merck (Silica gel 60, 40-63  $\mu\text{m}$ ). Flash chromatography was accomplished using an automated system (Reveleris X2, with ELSD and UV (235 and 254 nm) detection) with silica cartridges (Merck, Silica gel 60, 40-63  $\mu\text{m}$ ). Solvents were purified by use of drying cartridges through a solvent delivery system. Melting points ( $^\circ\text{C}$ ) are uncorrected.

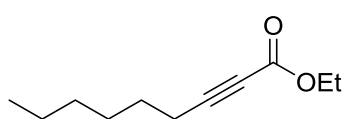
Ethyl 2-butynoate [4341-76-8] was purchased from Fluorochem, phenyl carbamate [622-46-8] was purchased from Alfa Aesar, and dibutyltin maleate [78-04-6] was purchased from TCI.

## 2. The synthesis of alkynes 4b and 4c

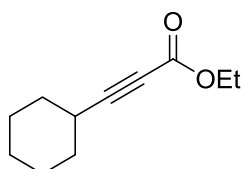


**General procedure:** A solution of alkyne (1.0 equiv., 18.1 mmol) in THF (24 mL) was cooled to  $-78\text{ }^\circ\text{C}$ , and MeLi (1.06 equiv., 19.0 mmol, 11.9 mL, 1.6 M in  $\text{Et}_2\text{O}$ ) was added dropwise. After 30 min ethyl chloroformate (2.2 g, 1.9 mL, 20.0 mmol,

1.1 equiv.) was added and after 5 min. a cooling bath was removed and the reaction mixture was allowed to warm to rt. Next, reaction was quenched by addition of sat. aq.  $\text{NH}_4\text{Cl}$ . The aqueous layer was separated and extracted with  $\text{Et}_2\text{O}$ . The combined organic phases were dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the residue was purified by a column chromatography on silica gel (0-10%  $\text{AcOEt}$  in hexanes).

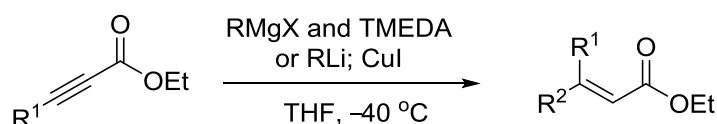


**Ethyl non-2-ynoate (4b):** Yield: 3.2 g (98%) starting from 2.0 g of oct-1-yne; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.17 (q,  $J = 7.0$  Hz, 2H), 2.29 (t,  $J = 7.1$  Hz, 2H), 1.60 – 1.48 (m, 2H), 1.42 – 1.32 (m, 2H), 1.32 – 1.19 (m, 7H), 0.86 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.8, 89.3, 73.1, 61.6, 31.1, 28.5, 27.5, 22.4, 18.6, 14.0, 13.9; Elem. Anal Found: C, 72.53; H, 10.01; N, 7.59%,  $\text{C}_{11}\text{H}_{18}\text{O}_2$  requires C, 72.49; H, 9.95%.



**Ethyl 3-cyclohexylpropiolate (4c):** Yield: 2.8 g (85%) starting from 2.0 g of ethynylcyclohexane; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.17 (q,  $J = 7.1$  Hz, 2H), 2.57 – 2.40 (m, 1H), 1.88 – 1.75 (m, 2H), 1.74 – 1.61 (m, 2H), 1.57 – 1.40 (m, 3H), 1.37 – 1.19 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.0, 92.7, 73.1, 61.6, 31.4, 28.8, 25.6, 24.6, 14.0; Elem. Anal Found: C, 73.28; H, 8.94%,  $\text{C}_{11}\text{H}_{16}\text{O}_2$  requires C, 73.30; H, 8.95%.

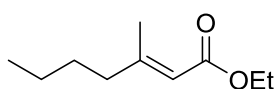
### 3. The Cu(I)-mediated 1,4-addition to alkynoates 5



**Method A, general procedure:**<sup>1</sup> A suspension of CuI (11.0 mmol, 2.1 g) in THF (30 mL) was cooled to  $-40\text{ }^{\circ}\text{C}$ , and RLi (10.6 mmol) was added. The resulting mixture was stirred at  $-40\text{ }^{\circ}\text{C}$  for 30 min and then cooled to  $-78\text{ }^{\circ}\text{C}$ . A solution of ethyl alkynoate (10.0 mmol) in THF (1 mL) was added portionwise and the resulting mixture was stirred for 2 h at  $-78\text{ }^{\circ}\text{C}$ . The progress of the reaction was followed by TLC. Next, the reaction was quenched by an addition of aq.  $\text{NH}_4\text{Cl}$  at  $-78\text{ }^{\circ}\text{C}$ , after that the cooling bath was removed and the mixture was left to adjust to rt. The reaction mixture was filtrated through a short pad of Celite. The collected solids were rinsed with  $\text{Et}_2\text{O}$ . After that, the aqueous phase was separated and extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of solvents, the crude residue was purified by a column chromatography on silica gel (1-10%  $\text{Et}_2\text{O}$  in pentanes).

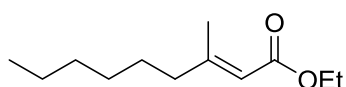
**Method B, general procedure:**<sup>1</sup> A suspension of CuI (15.0 mmol, 2.9 g) in THF (90 mL) was cooled to  $-40\text{ }^{\circ}\text{C}$ , and  $\text{RMgX}$  (12 mmol) and TMEDA (45.0 mmol, 5.1 g, 6.8 mL) were added. The mixture was stirred at  $-40\text{ }^{\circ}\text{C}$  for 30 min and then cooled to  $-78\text{ }^{\circ}\text{C}$ . A solution of ethyl alkynoate (12.0 mmol) in THF (2 mL) was added portionwise and the resulting suspension was stirred for 4 h at  $-78\text{ }^{\circ}\text{C}$ . The progress of the reaction was followed by TLC. The reaction was quenched by addition of aq.  $\text{NH}_4\text{Cl}$ . The cooling bath was removed and mixture was left to adjust to rt. The reaction mixture was filtrated through a short pad of Celite. The collected solids were rinsed with  $\text{Et}_2\text{O}$ . After that, the aqueous phase was separated and extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over  $\text{Na}_2\text{SO}_4$ . After the removal of solvents, the crude residue was purified by a column chromatography on silica gel (1-10%  $\text{Et}_2\text{O}$  in pentanes).

**Ethyl (*E*)-3-methylhept-2-enoate (5a):**



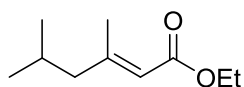
Method A. *n*-BuLi (2.5 M solution in hexane) was used. Yield: 1.5 g (90%; *E/Z* ratio >95:5, acc. <sup>1</sup>H NMR) starting from 1.1 g (9.8 mmol) of ethyl but-2-ynoate; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.70 – 5.56 (m, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.20 – 2.01 (m, 5H), 1.51 – 1.37 (m, 2H), 1.35 – 1.18 (m, 5H), 0.89 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.9, 160.2, 115.4, 59.4, 40.6, 29.5, 22.3, 18.7, 14.3, 13.8; Elem. Anal Found: C, 70.52; H, 10.69%, C<sub>11</sub>H<sub>18</sub>O<sub>2</sub> requires C, 70.55; H, 10.66%.

### Ethyl (*E*)-3-methylnon-2-enoate (5b):



Method A. *n*-HexLi (2.3 M solution in hexane) was used. Yield: 2.4 g (99%; *E/Z* ratio >95:5, <sup>1</sup>H NMR) starting from 1.3 g (11.6 mmol) of ethyl but-2-ynoate; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.64 (q, *J* = 1.2 Hz, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.17 – 2.06 (m, 5H), 1.51 – 1.39 (m, 2H), 1.35 – 1.20 (m, 9H), 0.87 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.9, 160.2, 115.4, 59.4, 40.9, 31.6, 28.8, 27.3, 22.5, 18.7, 14.3, 14.0; Elem. Anal Found: C, 72.71; H, 11.22%; C<sub>12</sub>H<sub>22</sub>O<sub>2</sub> requires C, 72.68; H, 11.18%.

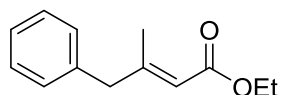
### Ethyl (*E*)-3,5-dimethylhex-2-enoate (5c):



Method B. *i*-BuMgBr (2 M solution in Et<sub>2</sub>O) was used. Yield: 1.9 g (96%; *E/Z* ratio >95:5, acc. <sup>1</sup>H NMR) starting from 1.3 g (11.6 mmol) of ethyl but-2-ynoate; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.67 – 5.53 (m, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.11 (d, *J* = 1.3 Hz, 3H), 2.02 – 1.93 (m, 2H), 1.91 – 1.77 (m, 1H), 1.26 (t, *J* = 7.1 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 166.7, 159.1, 116.7, 59.4, 50.5, 26.2, 22.4, 18.6, 14.3; Elem. Anal Found: C, 72.53; H, 10.01%, C<sub>10</sub>H<sub>18</sub>O<sub>2</sub> requires C, 70.55; H, 10.66%.

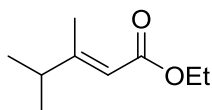


### Ethyl (*E*)-3-methyl-4-phenylbut-2-enoate (5f):



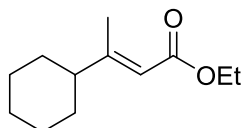
Method B. *BnMgCl* (1 M solution in  $\text{Et}_2\text{O}$ ) was used. Yield: 2.5 g (96%; *E/Z* ratio >95:5, acc.  $^1\text{H}$  NMR) starting from 1.3 g (11.6 mmol) of ethyl but-2-ynoate; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.38 – 7.07 (m, 5H), 5.79 – 5.60 (m, 1H), 4.15 (q,  $J = 7.1$  Hz, 2H), 3.52 – 3.31 (m, 2H), 2.12 (d,  $J = 1.3$  Hz, 3H), 1.27 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.7, 158.2, 137.8, 129.1, 128.5, 126.7, 117.3, 59.6, 47.1, 18.6, 14.3 Elem. Anal Found: C, 76.48; H, 7.95%,  $\text{C}_{13}\text{H}_{16}\text{O}_2$  requires C, 76.44; H, 7.90%.

### Ethyl (*E*)-3,4-dimethylpent-2-enoate (5d):



Method B. *i*-PrMgCl (2 M solution in THF) was used. Yield: 938 mg (overall 75%; *E/Z* ratio >95:5, acc.  $^1\text{H}$  NMR) starting from 897 mg (8.0 mmol) of ethyl but-2-ynoate; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.73 – 5.54 (m, 1H), 4.12 (q,  $J = 7.1$  Hz, 2H), 2.41 – 2.27 (m, 1H), 2.10 (d,  $J = 1.3$  Hz, 3H), 1.25 (t,  $J = 7.1$  Hz, 3H), 1.04 (d,  $J = 6.8$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.1, 165.3, 113.6, 59.4, 38.1, 20.8, 16.3, 14.3; Elem. Anal Found: C, 69.14; H, 10.30; %,  $\text{C}_9\text{H}_{16}\text{O}_2$  requires C, 69.19; H, 10.32%.

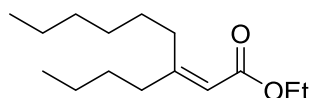
### Ethyl (*E*)-3-cyclohexylbut-2-enoate (5e):



Method B. *CyMgCl* (1.3 M solution in THF/toluene) was used. Yield: 2.0 g (85%; *E/Z* ratio >95:5, acc.  $^1\text{H}$  NMR) starting from 1.3 g (11.6 mmol) of ethyl but-2-ynoate; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.73 – 5.52 (m, 1H), 4.13 (q,  $J = 7.1$  Hz, 2H), 2.13 (d,  $J = 1.3$  Hz, 3H), 2.01 – 1.90 (m, 1H), 1.84 – 1.63 (m, 5H), 1.35 – 1.07 (m,

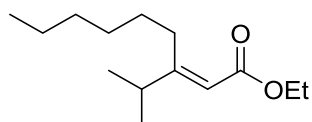
8H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  167.3, 164.8, 113.9, 59.4, 48.7, 31.4, 26.4, 26.1, 17.3, 14.3. Elem. Anal Found: C, 73.40; H, 10.24; %,  $\text{C}_{12}\text{H}_{20}\text{O}_2$  requires C, 73.43; H, 10.27%.

#### Ethyl (Z)-3-butylnon-2-enoate (5g):



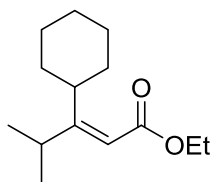
Method A. *n*-BuLi (2.5 M solution in hexane) was used. Yield: 1.25 g (overall 95%; *Z/E* ratio 95:5,  $^1\text{H}$  NMR) starting from 1.0 g (5.5 mmol) of ethyl non-2-ynoate (**4b**); yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.60 (s, 1H), 4.12 (q,  $J = 7.2$  Hz, 2H), 2.64 – 2.46 (m, 2H), 2.20 – 2.01 (m, 2H), 1.51 – 1.38 (m, 4H), 1.37 – 1.20 (m, 10H), 0.95 – 0.79 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  166.6, 164.8, 115.1, 59.3, 38.1, 32.1, 31.7, 29.8, 29.6, 28.6, 22.6, 22.4, 14.3, 14.0, 13.9; Elem. Anal Found: C, 74.91; H, 11.69%,  $\text{C}_{15}\text{H}_{28}\text{O}_2$  requires C, 74.95; H, 11.74%.

#### Ethyl (E)-3-isopropylnon-2-enoate (5h):



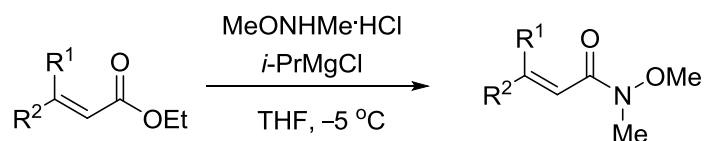
Method B. *i*-PrMgCl (2 M solution in THF) was used. Yield: 1.2 g (94%; *E/Z* ratio 95:5, acc.  $^1\text{H}$  NMR) starting from 1.0 g (5.5 mmol) of ethyl non-2-ynoate (**4b**); yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.61 (s, 1H), 4.13 (q,  $J = 7.1$  Hz, 2H), 2.61 – 2.48 (m, 2H), 2.41 – 2.29 (m, 1H), 1.49 – 1.17 (m, 11H), 1.06 (d,  $J = 6.8$  Hz, 6H), 0.91 – 0.79 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.5, 166.9, 113.0, 59.4, 36.1, 31.8, 31.7, 29.8, 29.3, 22.6, 21.6, 14.3, 14.0; Elem. Anal Found: C, 74.33; H, 11.62%,  $\text{C}_{14}\text{H}_{26}\text{O}_2$  requires C, 74.29; H, 11.58%.

#### Ethyl (Z)-3-cyclohexyl-4-methylpent-2-enoate (5i):



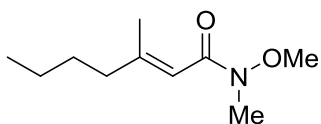
Method B. CyMgCl (1.3 M solution in THF/toluene) was used. Yield: 1.5 g (89%; *Z/E* ratio 95:5,  $^1\text{H}$  NMR) starting from 1.4 g (7.8 mmol) of ethyl 3-cyclohexylpropiolate (**4c**); yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.62 (s, 1H), 4.13 (q,  $J = 7.1$  Hz, 2H), 3.79 – 3.59 (m, 1H), 2.64 – 2.48 (m, 1H), 1.83 – 1.63 (m, 3H), 1.62 – 1.50 (m, 2H), 1.42 – 1.31 (m, 3H), 1.27 (t,  $J = 7.1$  Hz, 3H), 1.24 – 1.07 (m, 1H), 1.04 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  175.4, 167.2, 112.8, 59.4, 40.9, 30.3, 30.0, 26.3, 26.1, 23.9, 14.3; Elem. Anal Found: C, 75.02; H, 10.82; %,  $\text{C}_{14}\text{H}_{24}\text{O}_2$  requires C, 74.95; H, 10.78%.

#### 4. The synthesis of Weinreb amides **S1**



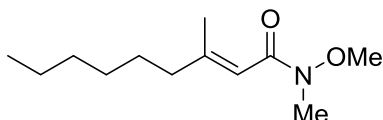
**General procedure:** A suspension of  $\alpha,\beta$ -unsaturated ester **5** (1 equiv) and  $\text{MeNHOMe}\cdot\text{HCl}$  (2 equiv) in dry THF (c 0.2-0.3 M) was cooled to  $-5$  °C under argon atmosphere, and 2M soln. of *i*-PrMgCl in THF (4 equiv.) was added dropwise. The progress of the reaction was followed by TLC. After stirring at  $-5$  °C for 30-60 min, the reaction was quenched by an addition of sat.  $\text{NH}_4\text{Cl}$ . The aqueous phase was separated and extracted with AcOEt. The combined organic phases were washed with brine, and dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the crude product was purified by a column chromatography on silica gel to provide pure *E* or *Z* isomer (10-30% AcOEt in hexanes).

**(*E*)-*N*-Methoxy-*N*,3-dimethylhept-2-enamide (**S1a**):**



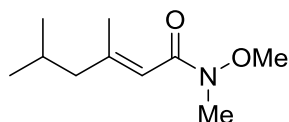
Yield: 1.4 g (92%) starting from 1.4 g (8.2 mmol) of ester **5a**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.08 (s, 1H), 3.65 (s, 3H), 3.18 (s, 3H), 2.19 – 1.97 (m, 5H), 1.51 – 1.37 (m, 2H), 1.38 – 1.22 (m, 2H), 0.90 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.2, 156.8, 113.8, 61.3, 40.8, 32.2, 29.7, 22.3, 18.6, 13.8; Elem. Anal Found: C, 64.87; H, 10.38; N, 7.59%,  $\text{C}_{10}\text{H}_{19}\text{NO}_2$  requires C, 64.83; H, 10.34; N, 7.56%.

**(E)-N-Methoxy-N,3-dimethylnon-2-enamide (S1b):**



Yield: 2.3 g (92%) starting from 2.3 g (8.2 mmol) of ester **5b**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.07 (s, 1H), 3.64 (s, 3H), 3.17 (s, 3H), 2.23 – 1.92 (m, 5H), 1.56 – 1.36 (m, 2H), 1.36 – 1.12 (m, 6H), 0.95 – 0.73 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.2, 156.7, 113.8, 61.3, 41.1, 32.3, 31.6, 28.9, 27.5, 22.6, 18.6, 14.0; Elem. Anal Found: C, 67.60; H, 10.86; N, 6.61 %,  $\text{C}_{12}\text{H}_{23}\text{NO}_2$  requires C, 67.57; H, 10.87; N, 6.57%.

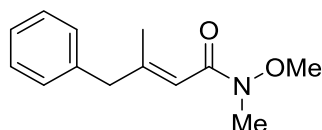
**(E)-N-Methoxy-N,3,5-trimethylhex-2-enamide (S1c)**



Yield: 1.8 g (90%) starting from 1.9 g (11.2 mmol) of ester **5c**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.05 (s, 1H), 3.64 (s, 3H), 3.17 (s, 3H), 2.07 (d,  $J = 1.4$  Hz, 3H), 1.99 (dd,  $J = 7.6, 0.8$  Hz, 2H), 1.92 – 1.76 (m, 1H), 0.87 (d,  $J = 6.5$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  168.1, 155.6, 115.0, 61.3, 50.8, 32.2, 26.2, 22.4, 18.5; Elem.

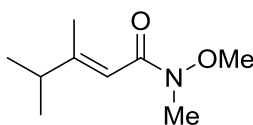
Anal Found: C, 64.85; H, 10.31; N, 7.59 %, C<sub>10</sub>H<sub>19</sub>NO<sub>2</sub> requires C, 64.83; H, 10.34; N, 7.56%.

**(E)-N-Methoxy-N,3-dimethyl-4-phenylbut-2-enamide (S1f):**



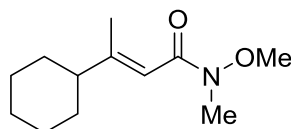
Yield: 1.4 g (87%) starting from 1.5 g (7.3 mmol) of ester **5f**; yellowish oil; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.35 – 7.12 (m, 5H), 6.10 (s, 1H), 3.61 (s, 3H), 3.44 (d, *J* = 1.3 Hz, 2H), 3.18 (s, 3H), 2.08 (d, *J* = 1.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.0, 154.7, 138.3, 129.1, 128.4, 126.5, 115.9, 61.4, 47.2, 32.3, 18.6; Elem. Anal Found: C, 71.25; H, 7.83; N, 6.41 %, C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub> requires C, 71.21; H, 7.81; N, 6.39%.

**(E)-N-Methoxy-N,3,4-trimethylpent-2-enamide (S1d)**



Yield: 1.3 g (85%) starting from 1.4 g (9.0 mmol) of ester **5d**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.07 (s, 1H), 3.62 (s, 3H), 3.16 (s, 3H), 2.41 – 2.25 (m, 1H), 2.04 (d, *J* = 1.4 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 168.5, 161.5, 112.1, 61.2, 38.1, 32.3, 21.0, 16.0; Elem. Anal Found: C, 63.15; H, 9.98; N, 8.21 %, C<sub>9</sub>H<sub>17</sub>NO<sub>2</sub> requires C, 63.13; H, 10.01; N, 8.18%.

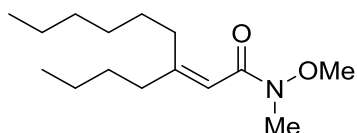
**(E)-3-Cyclohexyl-N-methoxy-N-methylbut-2-enamide (S1e):**



Yield: 1.4 g (90%) starting from 1.4 g (7.1 mmol) of ester **5e**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.06 (s, 1H), 3.64 (s, 3H), 3.17 (s, 3H), 2.06 (d, *J* = 1.4 Hz, 3H), 2.00 – 1.90 (m, 1H), 1.84 – 1.62 (m, 4H), 1.37 – 1.05 (m, 6H); <sup>13</sup>C NMR (101 MHz,

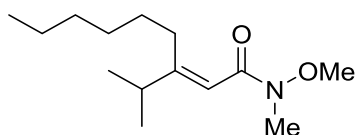
CDCl<sub>3</sub>)  $\delta$  168.6, 160.9, 112.4, 61.3, 48.7, 32.3, 31.5, 26.5, 26.1, 17.1; Elem. Anal Found: C, 68.41; H, 9.97; N, 6.58 %, C<sub>12</sub>H<sub>21</sub>NO<sub>2</sub> requires C, 68.21; H, 10.02; N: 6.63%.

**(Z)-3-Butyl-N-methoxy-N-methylnon-2-enamide (S1g)**



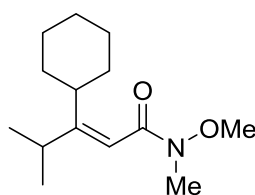
Yield: 1.2 g (92%) starting from 1.2 g (5.0 mmol) of ester **5g**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.04 (s, 1H), 3.65 (s, 3H), 3.17 (s, 3H), 2.62 – 2.40 (m, 2H), 2.19 – 2.06 (m, 2H), 1.50 – 1.19 (m, 12H), 0.95 – 0.75 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  168.0, 161.0, 113.5, 61.3, 38.0, 32.3, 32.0, 31.7, 30.0, 29.6, 28.7, 22.6, 22.4, 14.0, 13.9; Elem. Anal Found: C, 70.49; H, 11.48; N, 5.50 %, C<sub>15</sub>H<sub>29</sub>NO<sub>2</sub> requires C, 70.54; H, 11.45; N, 5.48%.

**(E)-3-Isopropyl-N-methoxy-N-methylnon-2-enamide (S1h):**



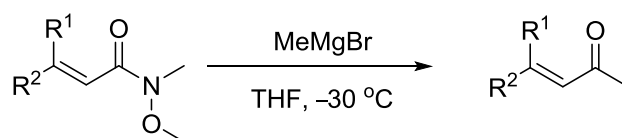
Yield: 1.1 g (92%) starting from 1.3 g (5.7 mmol) of ester **5h**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.06 (br s, 1H), 3.65 (s, 3H), 3.18 (s, 3H), 2.57 – 2.46 (m, 2H), 2.43 – 2.30 (m, 1H), 1.51 – 1.38 (m, 2H), 1.38 – 1.21 (m, 6H), 1.07 (d, *J* = 6.8 Hz, 6H), 0.92 – 0.78 (m, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  168.4, 166.6, 111.5, 61.2, 35.7, 32.5, 31.7, 31.7, 29.9, 29.4, 22.6, 21.9, 14.0; Elem. Anal Found: C, 69.70; H, 11.31; N, 5.78 %, C<sub>14</sub>H<sub>27</sub>NO<sub>2</sub> requires C, 69.67; H, 11.28; N, 5.80%.

**(Z)-3-Cyclohexyl-N-methoxy-N,4-dimethylpent-2-enamide (S1i):**

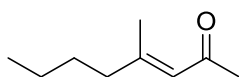


Yield: 1.4 g (92%) starting from 1.4 g (6.2 mmol) of ester **5i**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.03 (s, 1H), 3.63 (s, 3H), 3.50 – 3.30 (m, 1H), 3.18 (s, 3H), 2.60 – 2.43 (m, 1H), 1.84 – 1.50 (m, 5H), 1.44 – 1.08 (m, 5H), 1.04 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.2, 168.7, 112.0, 61.2, 41.4, 32.6, 30.5, 29.7, 26.2, 26.1, 24.2; Elem. Anal Found: C, 70.28; H, 11.55; N, 5.83 %,  $\text{C}_{14}\text{H}_{25}\text{NO}_2$  requires C, 70.25; H, 10.53; N, 5.85%.

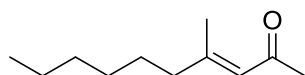
## 5. The synthesis of enones **6**



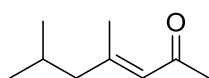
**General procedure:** A 3 M soln. of  $\text{MeMgBr}$  in  $\text{THF}$  (1.3 equiv) was slowly added to a pre-cooled ( $-30\text{ }^\circ\text{C}$ ) solution of Weinreb amide **S1** (1 equiv) in  $\text{THF}$  (c 0.2-0.3 M). Next, the mixture was slowly warmed to  $-5\text{ }^\circ\text{C}$  and stirred for 30-60 min. The progress of the reaction was followed by TLC. Next, sat.  $\text{NH}_4\text{Cl}$  was added and the resulting mixture was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed with brine, and dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the residue was purified by a column chromatography on silica gel (1-10%  $\text{Et}_2\text{O}$  in pentanes).



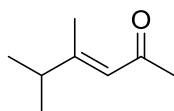
**(E)-4-Methyloct-3-en-2-one (6a):** Yield: 1.7 g (86%) starting from 2.6 g (14.0 mmol) of amide **S1a**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.05 (q,  $J = 1.3$  Hz, 1H), 2.15 (s, 3H), 2.12 – 2.06 (m, 5H), 1.50 – 1.38 (m, 2H), 1.36 – 1.26 (m, 2H), 0.90 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.8, 158.9, 123.4, 40.9, 31.7, 29.6, 22.3, 19.2, 13.8; Elem. Anal Found: C, 77.11; H, 11.53%,  $\text{C}_9\text{H}_{16}\text{O}$  requires C, 77.09; H, 11.50%.



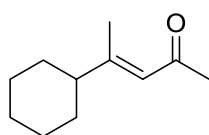
**(E)-4-Methyldec-3-en-2-one (6b):** Yield: 1.7 g (96%) starting from 2.3 g (10.8 mmol) of amide **S1b**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.04 (q,  $J = 1.3$  Hz, 1H), 2.14 (s, 3H), 2.11 – 2.05 (m, 5H), 1.51 – 1.38 (m, 2H), 1.35 – 1.21 (m, 6H), 0.93 – 0.80 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.7, 158.9, 123.4, 41.2, 31.7, 31.6, 28.9, 27.4, 22.5, 19.2, 14.0; Elem. Anal Found: C, 78.56; H, 12.03%,  $\text{C}_{11}\text{H}_{20}\text{O}$  requires C, 78.51; H, 11.98%.



**(E)-4,6-Dimethylhept-3-en-2-one (6c):** Yield: 717 mg (82%) starting from 1.2 g (6.5 mmol) of amide **S1c**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.02 (q,  $J = 1.3$  Hz, 1H), 2.16 (s, 3H), 2.09 (d,  $J = 1.3$  Hz, 3H), 2.00 – 1.93 (m, 2H), 1.91 – 1.78 (m, 1H), 0.87 (d,  $J = 6.4$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  198.6, 157.7, 124.7, 50.8, 31.7, 26.3, 22.4, 19.1; Elem. Anal Found: C, 77.12; H, 11.52%,  $\text{C}_9\text{H}_{16}\text{O}$  requires C, 77.09; H, 11.50%.



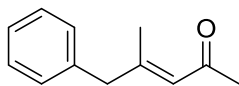
**(E)-4,5-Dimethylhex-3-en-2-one (6d):** Yield: 691 mg (78%) starting from 1.2 g (7.0 mmol) of amide **S1d**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.24 – 5.82 (m, 1H), 2.37 – 2.25 (m, 1H), 2.15 (s, 3H), 2.07 (d,  $J = 1.3$  Hz, 3H), 1.04 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.2, 163.9, 121.4, 38.2, 31.8, 20.9, 16.7; Elem. Anal Found: C, 76.18; H, 11.22%,  $\text{C}_8\text{H}_{14}\text{O}$  requires C, 76.14; H, 11.18%.



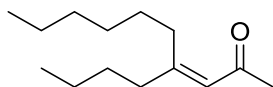
**(E)-4-Cyclohexylpent-3-en-2-one (6e):** Yield: 983 mg (86%) starting from 1.4 g (6.6 mmol) of amide **S1e**; yellowish liquid;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.17 – 5.81 (m, 1H), 2.15 (s, 3H), 2.09 (d,  $J = 1.3$  Hz, 3H), 2.01 – 1.87 (m,



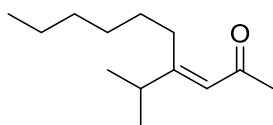
1H), 1.83 – 1.74 (m, 2H), 1.75 – 1.62 (m, 3H), 1.34 – 1.08 (m, 5H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 199.3, 163.3, 121.8, 48.9, 31.8, 31.4, 26.4, 26.1, 17.7; Elem. Anal Found: C, 79.50; H, 10.95%, C<sub>11</sub>H<sub>18</sub>O requires C, 79.46; H, 10.91%.



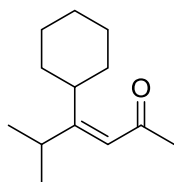
**(E)-4-Methyl-5-phenylpent-3-en-2-one (6f):** Yield: 1.0 g (94%) starting from 1.4 g (6.4 mmol) of amide **S1f**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.36 – 7.08 (m, 5H), 6.15 – 5.94 (m, 1H), 3.41 (s, 2H), 2.17 (s, 3H), 2.09 (d, *J* = 1.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.8, 156.6, 137.8, 129.1, 128.6, 126.7, 125.0, 47.2, 31.8, 19.1; Elem. Anal Found: C, 82.68; H, 8.06%, C<sub>12</sub>H<sub>14</sub>O requires C, 82.72; H, 8.10%.



**(Z)-4-Butyldec-3-en-2-one (6g):** Yield: 820 mg (89%) starting from 1.1 g (4.3 mmol) of amide **S1g**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.00 (s, 1H), 2.60 – 2.47 (m, 2H), 2.21 – 2.02 (m, 5H), 1.51 – 1.23 (m, 12H), 0.89 (dt, *J* = 15.6, 7.1 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.3, 163.7, 123.0, 38.4, 32.4, 31.8, 31.6, 29.9, 29.6, 28.6, 22.6, 22.5, 14.0, 13.9; Elem. Anal Found: C, 79.90; H, 12.41%; C<sub>14</sub>H<sub>26</sub>O requires C, 79.94; H, 12.46%.

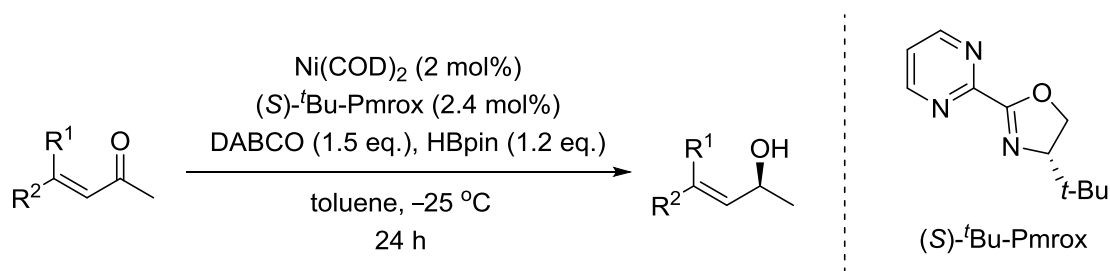


**(E)-4-Isopropyldec-3-en-2-one (6h):** Yield: 705 mg (95%) starting from 921 mg (3.8 mmol) of amide **S1h**; yellowish liquid; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 6.01 (s, 1H), 2.56 – 2.45 (m, 2H), 2.40 – 2.29 (m, 1H), 2.16 (s, 3H), 1.46 – 1.22 (m, 8H), 1.06 (d, *J* = 6.8 Hz, 6H), 0.91 – 0.79 (m, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 198.6, 169.3, 120.6, 36.3, 32.0, 31.9, 31.6, 29.8, 29.2, 22.6, 21.6, 14.0, 14.0; Elem. Anal Found: C, 79.49; H, 12.27%, C<sub>13</sub>H<sub>24</sub>O requires C, 79.53; H, 12.32%.



**(Z)-4-Cyclohexyl-5-methylhex-3-en-2-one (6i):** Yield: 1.0 g (91%) starting from 1.4 g (5.8 mmol) of amide **51i**; yellowish liquid;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  6.00 (s, 1H), 3.69 – 3.46 (m, 1H), 2.65 – 2.47 (m, 1H), 2.16 (s, 3H), 1.82 – 1.61 (m, 3H), 1.59 – 1.45 (m, 2H), 1.42 – 1.25 (m, 4H), 1.23 – 1.07 (m, 1H), 1.03 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  199.3, 173.6, 120.8, 40.9, 32.1, 30.3, 29.8, 26.2, 26.1, 23.9; Elem. Anal Found: C, 80.31; H, 11.37%,  $\text{C}_{13}\text{H}_{22}\text{O}$  requires C, 80.35; H, 11.41%.

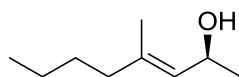
## 6. NiH-catalyzed 1,2-reduction of $\alpha,\beta$ -unsaturated ketones **6**



**General procedure:**<sup>2</sup> A flask was charged with  $\text{Ni}(\text{COD})_2$  (4  $\mu\text{mol}$ , 2.0 mol %, 1.1 mg),  $(S)\text{-}^t\text{Bu-Pmrox}$  (4.8  $\mu\text{mol}$ , 2.4 mol%, 1.0 mg) and DABCO (1.5 equiv, 0.3 mmol, 33.6 mg) under an Ar atmosphere. Toluene (0.8 mL) was added and the mixture was stirred for 10 min before pinBH (1.2 equiv, 0.24 mmol, 30.7 mg, 35  $\mu\text{L}$ ) was added. Next, the reaction mixture was cooled to  $-25$   $^\circ\text{C}$  and a solution of enone **6** (1.0 equiv, 0.2 mmol) in 0.2 mL toluene was added by syringe. The reaction mixture was left to stir at this temperature. The progress of the reaction was followed by TLC. When the reaction was completed, a saturated solution of  $\text{NH}_4\text{F}$  in MeOH (1 mL) was added and cooling bath was removed. The mixture was stirred at rt for 30 min followed by an addition of  $\text{H}_2\text{O}$  (2 mL) and  $\text{Et}_2\text{O}$  (3 mL). The aqueous phase was separated and extracted with  $\text{Et}_2\text{O}$  (2x) and dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the crude residue was purified by a

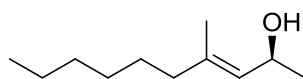
column chromatography on silica gel (0-20% Et<sub>2</sub>O in pentanes). The enantiomeric excess of product (% *ee*) was determined by HPLC analysis for the corresponding *p*-nitrobenzoate ester derivatives.

### (*S,E*)-4-Methyloct-3-en-2-ol (**3a**)



The reaction mixture was stirred for 24 h. Yield: 498 mg (90%) starting from 544 mg of ketone **6a**; yellowish oil;  $[\alpha]_D^{21}$  -24.5 (*c* 1.02, CHCl<sub>3</sub>, *ee* 94%; HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 6.1 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.19 (dq, *J* = 8.4, 1.3 Hz, 1H), 4.55 (dq, *J* = 8.4, 6.3 Hz, 1H), 1.96 (td, *J* = 7.5, 1.2 Hz, 2H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.45 (br s, 1H), 1.41 – 1.32 (m, 2H), 1.31 – 1.23 (m, 2H), 1.21 (d, *J* = 6.3 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 137.9, 128.9, 64.7, 39.1, 29.8, 23.6, 22.3, 16.3, 13.9; FTIR (film) *v*: 3347, 2960, 2928, 1670, 1456, 1380, 1099, 1058, 866 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>9</sub>H<sub>18</sub>O [*M*] 142.1358; found 142.1364; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralpak AS-H, 5% *i*-PrOH in hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; 6.0 min (*R*-enantiomer) and *R*<sub>t</sub> 7.5 min (*S*-enantiomer).

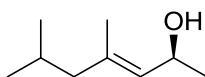
### (*S,E*)-4-Methyldec-3-en-2-ol (**3b**):



The reaction mixture was stirred for 24 h. Yield: 605 mg (85%) starting from 700 mg of ketone **6b**; yellowish oil;  $[\alpha]_D^{21}$  -21.2 (*c* 1.13, CHCl<sub>3</sub>), *ee* 94%; HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 30.4 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.19 (dq, *J* = 8.4, 1.3 Hz, 1H), 4.56 (dq, *J* = 8.4, 6.2 Hz, 1H), 2.03 – 1.87 (m, 2H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.49 – 1.33 (m, 3H), 1.33 – 1.12 (m, 9H), 0.95 – 0.77 (m, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 138.0, 128.9, 64.8, 39.4, 31.7, 28.9, 27.6, 23.6, 22.6, 16.3, 14.0; FTIR (film) *v*: 3340, 2960, 2928, 2857, 1670, 1456, 1379, 1104, 1059, 866 cm<sup>-1</sup>; HRMS (EI) *m/z*

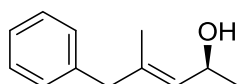
calcd for C<sub>11</sub>H<sub>22</sub>O [M] 170.1671; found 170.1676; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; *R*<sub>t</sub> 27.3 min (*S*-enantiomer) and 30.9 min (*R*-enantiomer).

**(*S,E*)-4,6-Dimethylhept-3-en-2-ol (3c):**



The reaction mixture was stirred for 24 h. Yield: 444 mg (87%) starting from 438 mg of ketone **6c**; yellowish oil; [α]<sub>D</sub><sup>22</sup> -20.3 (c 0.99, CHCl<sub>3</sub>), *ee* 92%; HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 24.7 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.18 (dq, *J* = 8.4, 1.3 Hz, 1H), 4.56 (dq, *J* = 8.4, 6.2 Hz, 1H), 1.90 – 1.68 (m, 3H), 1.63 (d, *J* = 1.3 Hz, 3H), 1.40 (s, 1H), 1.21 (d, *J* = 6.2 Hz, 3H), 0.88 – 0.78 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 136.7, 130.5, 64.8, 49.2, 25.9, 23.6, 22.5, 22.1, 16.2; FTIR (film) *v*: 3342, 2954, 2925, 2869, 1669, 1464, 1383, 1367, 1102, 1057, 864 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>9</sub>H<sub>18</sub>O [M] 142.1358; found 142.1363; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; *R*<sub>t</sub> 22.1 min (*S*-enantiomer) and 26.2 min (*R*-enantiomer).

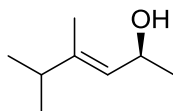
**(*S,E*)-4-methyl-5-phenylpent-3-en-2-ol (3d):**



The reaction mixture was stirred for 24 h. Yield: 701 mg (99%) starting from 700 mg of ketone **6f**; yellowish oil; [α]<sub>D</sub><sup>22</sup> -25.1 (c 0.98, CHCl<sub>3</sub>), *ee* 98%; HPLC for free alcohol *R*<sub>t</sub> 39.1 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.33 – 7.23 (m, 2H), 7.25 – 7.12 (m, 3H), 5.33 (dq, *J* = 8.4, 1.4 Hz, 1H), 4.59 (dq, *J* = 8.4, 6.3 Hz, 1H), 3.29 (s, 2H), 1.62 (d, *J* = 1.4 Hz, 3H), 1.50 (br s, 1H), 1.27 (d, *J* = 6.3 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 139.5, 136.7, 131.1, 128.9, 128.3, 126.2, 64.8, 46.0, 23.6, 16.2; FTIR (film) *v*: 3346, 2969, 2923, 1669, 1602, 1494, 1452, 1381, 1058, 742, 699 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>12</sub>H<sub>16</sub>O [M] 176.1201; found 176.1200; HPLC (racemate) column: Chiralcel OD-

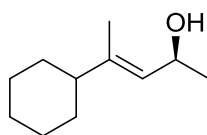
H, 1% *i*-Pr in hexanes, flow 1 mL min<sup>-1</sup>, det. 210 nm; *R*<sub>t</sub> 40.1 min (*S*-enantiomer) and 47.6 min (*R*-enantiomer).

**(*S,E*)-4,5-dimethylhex-3-en-2-ol (3e):**



The reaction mixture was stirred for 48 h. Yield: 328 mg (70%) starting from 461 mg of ketone **6d**; yellowish oil;  $[\alpha]_{\text{D}}^{22}$  -23.9 (*c* 0.92, CHCl<sub>3</sub>), *ee* 88%; HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 28.7 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.21 (dq, *J* = 8.3, 1.3 Hz, 1H), 4.57 (dq, *J* = 8.3, 6.3 Hz, 1H), 2.32 – 2.10 (m, 1H), 1.63 (d, *J* = 1.3 Hz, 3H), 1.39 (s, 1H), 1.22 (d, *J* = 6.3 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 143.4, 126.8, 64.7, 36.5, 23.6, 21.2, 13.8; FTIR (film) *v*: 3347, 2963, 2928, 1666, 1463, 1379, 1053, 857 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>6</sub>H<sub>16</sub>O [M] 128.1201; found 128.1200; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; *R*<sub>t</sub> 26.3 min (*S*-enantiomer) and 30.6 min (*R*-enantiomer).

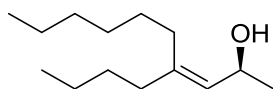
**(*S,E*)-4-cyclohexylpent-3-en-2-ol (3f):**



The reaction mixture was stirred for 48 h. Yield: 602 mg (85%) starting from 700 mg of ketone **6e**; yellowish oil;  $[\alpha]_{\text{D}}^{22}$  -23.5 (*c* 1.09, CHCl<sub>3</sub>), *ee* 88%; HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 35.5 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.18 (dq, *J* = 8.3, 1.3 Hz, 1H), 4.57 (dq, *J* = 8.3, 6.3 Hz, 1H), 1.87 – 1.58 (m, 9H), 1.40 (br s, 1H), 1.33 – 1.04 (m, 9H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 142.9, 127.2, 64.7, 47.0, 31.7, 31.7, 26.6, 26.3, 23.6, 14.7; FTIR (film) *v*: 3335, 2925, 2852, 1448, 1058 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>11</sub>H<sub>20</sub>O [M] 168.1514; found 168.1517; HPLC (for *p*-nitrobenzoate ester,

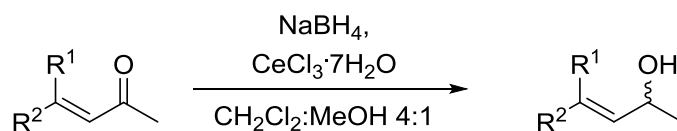
racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; *R*<sub>t</sub> 33.9 min (*S*-enantiomer) and 37.7 min (*R*-enantiomer).

**(*S,Z*)-4-butyldec-3-en-2-ol (3g):**



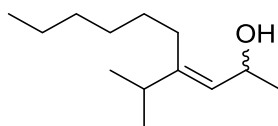
The reaction mixture was stirred for 48 h. Yield: 495 mg (98%) starting from 500 mg of ketone **6g**; yellowish oil; [α]<sub>D</sub><sup>22</sup> -9.0 (c 0.92, CHCl<sub>3</sub>, *ee* 82%; determined by HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 15.5 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.17 (d, *J* = 8.7 Hz, 1H), 4.58 (dq, *J* = 8.7, 6.2 Hz, 1H), 2.14 – 1.89 (m, 4iH), 1.47 – 1.14 (m, 16H), 0.97 – 0.77 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 142.5, 128.9, 64.4, 36.3, 31.7, 30.6, 30.2, 29.4, 28.9, 23.9, 22.6, 22.5, 14.0, 14.0; FTIR (film) *ν*: 3334, 2958, 2927, 2858, 1464, 1055 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>14</sub>H<sub>28</sub>O [M] 212.2140; found 212.2136; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralpak AS-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; 10.5 min (*R*-enantiomer) and *R*<sub>t</sub> 14.8 min (*S*-enantiomer).

**7. The synthesis of racemic allylic alcohols (*rac*-3)**



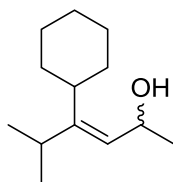
**General procedure:** To a suspension of enone **6** (3 mmol) and CeCl<sub>3</sub>·7H<sub>2</sub>O (3.6 mmol) in CH<sub>2</sub>Cl<sub>2</sub>/MeOH (4:1 v/v, 50 mL), NaBH<sub>4</sub> (3.6 mmol) was added portionwise. After 2 h at ambient temperature, the reaction mixture was partitioned between CH<sub>2</sub>Cl<sub>2</sub> and H<sub>2</sub>O. The organic layer was separated, and the aqueous one was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic solutions were dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (5-20% AcOEt in hexanes) to afford alcohol **rac-3**.

### (E)-4-isopropyldec-3-en-2-ol (*rac*-3h)



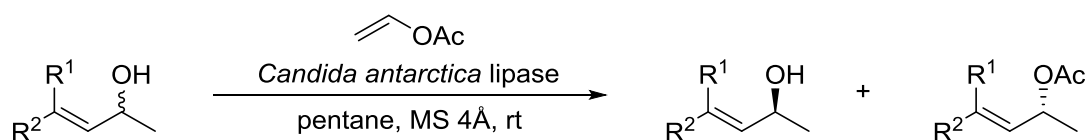
Yield: 379 mg (94%) starting from 400 mg of ketone **6h**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.17 (d,  $J = 8.8$  Hz, 1H), 4.57 (dq,  $J = 8.8, 6.2$  Hz, 1H), 2.29 – 2.14 (m, 1H), 2.14 – 1.95 (m, 2H), 1.47 – 1.15 (m, 12H), 1.05 – 0.95 (m, 6H), 0.92 – 0.78 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  148.4, 126.5, 64.6, 33.9, 31.7, 30.1, 30.1, 29.7, 23.8, 22.6, 22.0, 22.0, 14.0; FTIR (film)  $\nu$ : 3333, 2960, 2928, 2860, 1465, 1057  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{26}\text{O}$  [M] 198.1984; found 198.1989; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 21.1 min (*S*-enantiomer) and 23.1 min (*R*-enantiomer).

### (Z)-4-Cyclohexyl-5-methylhex-3-en-2-ol (*rac*-3i):



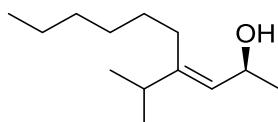
Yield: 330 mg (99%) starting from 330 mg of ketone **6i**; yellow oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.16 (d,  $J = 8.7$  Hz, 1H), 4.72 (dq,  $J = 8.7, 6.2$  Hz, 1H), 2.45 – 2.35 (m, 1H), 2.29 (hept,  $J = 6.9$  Hz, 1H), 1.83 – 1.09 (m, 14H), 1.05 – 0.92 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.3, 126.3, 64.0, 41.3, 31.6, 29.9, 26.7, 26.6, 26.1, 24.1, 24.1, 24.0; FTIR (film)  $\nu$ : 3332, 2961, 2926, 2853, 1448, 1047  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{24}\text{O}$  [M] 196.1827; found 196.1829; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm; 25.6 min (*S*-enantiomer) and 36.5 min (*R*-enantiomer).

## 8. Enzymatic kinetic resolution of racemic allyl alcohols (*rac*-3)



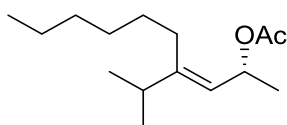
**General procedure:** A suspension of racemic alcohol **rac-3** (2.5 mmol), Novozyme 435 (18 mg), 4 Å molecular sieves (100 mg), and vinyl acetate (25 mmol, 2.2 g, 2.3 mL) in pentane (7 mL) was stirred in room temperature. The progress of the reaction was followed by  $^1\text{H}$  NMR. The reaction mixture was filtered through Celite, and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel (0-20% Et<sub>2</sub>O in pentanes).

**(*S,E*)-4-Isopropyldec-3-en-2-ol (3h):**



The reaction mixture was stirred for 11 days. Yield: 172 mg (46%) starting from 374 mg of racemic alcohol **rac-3h**; yellowish oil;  $[\alpha]_{\text{D}}^{22} -12.7$  (c 0.88, CHCl<sub>3</sub>), *ee* 95%; HPLC of *p*-nitrobenzoate ester:  $R_t$  21.9 min);  $^1\text{H}$  NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.17 (d,  $J = 8.8$  Hz, 1H), 4.57 (dq,  $J = 8.8, 6.2$  Hz, 1H), 2.29 – 2.14 (m, 1H), 2.14 – 1.95 (m, 2H), 1.47 – 1.15 (m, 12H), 1.05 – 0.95 (m, 6H), 0.92 – 0.78 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  148.4, 126.5, 64.6, 33.9, 31.7, 30.1, 30.1, 29.7, 23.8, 22.6, 22.0, 22.0, 14.0; FTIR (film)  $\nu$ : 3333, 2960, 2928, 2860, 1465, 1057 cm<sup>-1</sup>; HRMS (EI)  $m/z$  calcd for C<sub>13</sub>H<sub>26</sub>O [M] 198.1984; found 198.1989; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm;  $R_t$  21.1 min (*S*-enantiomer) and 23.1 min (*R*-enantiomer).

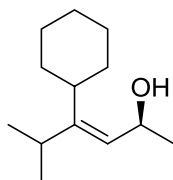
**(*R,E*)-4-Isopropyldec-3-en-2-yl acetate (8):**





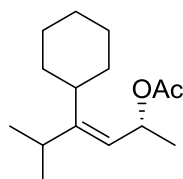
The reaction mixture was stirred for 11 days. Yield: 196 mg (43%) starting from 374 mg of racemic alcohol **rac-3h**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.59 (dq,  $J = 9.1, 6.3$  Hz, 1H), 5.11 (d,  $J = 9.1$  Hz, 1H), 2.30 – 2.07 (m, 2H), 2.05 – 1.90 (m, 4H), 1.42 – 1.17 (m, 11H), 1.04 – 0.93 (m, 6H), 0.86 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.2, 150.0, 122.1, 68.0, 33.9, 31.7, 30.2, 29.7, 29.6, 22.6, 22.0, 21.9, 21.4, 21.3, 14.0; Elem. Anal Found: C, 74.99; H, 11.77%,  $\text{C}_{15}\text{H}_{28}\text{O}_2$  requires C, 74.95; H, 11.74%.

**(S,Z)-4-cyclohexyl-5-methylhex-3-en-2-ol (3i):**



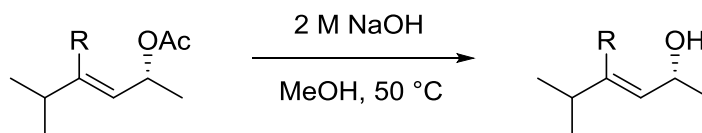
The reaction mixture was stirred for 40 days; after each 7 days the fresh portion of enzyme was added. Yield: 159 mg (47%) starting from 341 mg of racemic alcohol **rac-3i**; yellow oil;  $[\alpha]_{\text{D}}^{24} -12.2$  ( $c$  0.62,  $\text{CHCl}_3$ ,  $ee$  79%), HPLC of *p*-nitrobenzoate ester:  $R_t$  21.6 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.16 (d,  $J = 8.7$  Hz, 1H), 4.72 (dq,  $J = 8.7, 6.2$  Hz, 1H), 2.45 – 2.35 (m, 1H), 2.29 (hept,  $J = 6.9$  Hz, 1H), 1.83 – 1.09 (m, 14H), 1.05 – 0.92 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  153.3, 126.3, 64.0, 41.3, 31.6, 29.9, 26.7, 26.6, 26.1, 24.1, 24.1, 24.0; FTIR (film)  $\nu$ : 3332, 2961, 2926, 2853, 1448, 1047  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{24}\text{O}$  [M] 196.1827; found 196.1829; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL  $\text{min}^{-1}$ , det. 254 nm;  $R_t$  25.6 min (*S*-enantiomer) and 36.5 min (*R*-enantiomer).

**(R,Z)-4-Cyclohexyl-5-methylhex-3-en-2-yl acetate (9):**



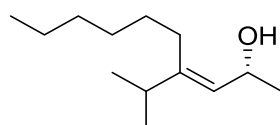
The reaction mixture was stirred for 40 days; after each 7 days the fresh portion of enzyme was added. Yield: 207 mg (50%) starting from 341 mg of racemic alcohol **rac-3i**; yellowish oil;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.71 (dq,  $J = 8.9, 6.3$  Hz, 1H), 5.11 (d,  $J = 8.9$  Hz, 1H), 2.50 – 2.36 (m, 1H), 2.29 (hept,  $J = 6.7$  Hz, 1H), 1.98 (s, 3H), 1.79 – 1.60 (m, 3H), 1.56 – 1.47 (m, 1H), 1.46 – 1.08 (m, 9H), 1.02 – 0.90 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  170.3, 155.0, 121.7, 67.6, 41.5, 31.1, 31.1, 29.3, 26.5, 26.5, 26.1, 24.4, 24.0, 21.5, 21.4; Elem. Anal Found: C, 75.62; H, 11.02; %,  $\text{C}_{15}\text{H}_{26}\text{O}_2$  requires C, 75.58; H, 10.99%.

### 9. The hydrolysis of acetates **8** and **9**



**General procedure:** A mixture of allyl acetate (1.0 mmol), MeOH (5 mL) and 2 M aq. NaOH (2 mL) was stirred for 24 h at 50 °C. When the reaction was complete, water was added to the mixture. The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  and the combined organic phase was dried over sodium sulfate. After the removal of the solvent, the crude product was used without a purification.

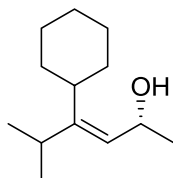
#### (*R,E*)-4-Isopropyldec-3-en-2-ol (**ent-3h**):



Yield: 180 mg (99%) starting from 196 mg of acetate **8**; yellow oil;  $[\alpha]_{\text{D}}^{24} +12.5$  ( $c$  0.61,  $\text{CHCl}_3$ ,  $ee$  99%; determined by HPLC of *p*-nitrobenzoate ester:  $R_t$  19.8 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.17 (d,  $J = 8.8$  Hz, 1H), 4.57 (dq,  $J = 8.8, 6.2$  Hz, 1H), 2.29 – 2.14 (m, 1H), 2.14 – 1.95 (m, 2H), 1.47 – 1.15 (m, 12H), 1.05 – 0.95 (m, 6H), 0.92 – 0.78 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  148.4, 126.5, 64.6, 33.9, 31.7, 30.1, 30.1, 29.7, 23.8, 22.6, 22.0, 22.0, 14.0; FTIR (film)  $\nu$ : 3333, 2960, 2928, 2860, 1465, 1057  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{26}\text{O}$  [M] 198.1984; found 198.1989; HPLC (for *p*-

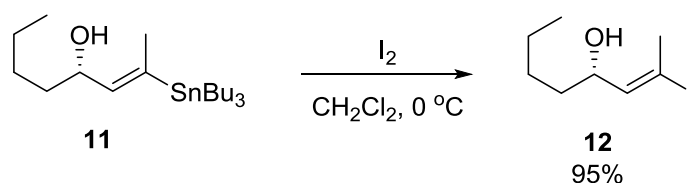
nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow: 1 mL min<sup>-1</sup>, det. 254 nm; 21.1 min (*S*-enantiomer) and *R*<sub>t</sub> 23.1 min (*R*-enantiomer).

**(*R,Z*)-4-Cyclohexyl-5-methylhex-3-en-2-ol (*ent*-3i):**



Yield: 169 mg (99%) starting from 207 mg of acetate **9**; yellow oil; [α]<sub>D</sub><sup>24</sup> +15.7 (*c* 1.20, CHCl<sub>3</sub>), *ee* 90%; determined by HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 26.8 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.16 (d, *J* = 8.7 Hz, 1H), 4.72 (dq, *J* = 8.7, 6.2 Hz, 1H), 2.45 – 2.35 (m, 1H), 2.29 (hept, *J* = 6.9 Hz, 1H), 1.83 – 1.09 (m, 14H), 1.05 – 0.92 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 153.3, 126.3, 64.0, 41.3, 31.6, 29.9, 26.7, 26.6, 26.1, 24.1, 24.1, 24.0; FTIR (film) ν: 3332, 2961, 2926, 2853, 1448, 1047 cm<sup>-1</sup>; HRMS (EI) *m/z* calcd for C<sub>13</sub>H<sub>24</sub>O [M] 196.1827; found 196.1829; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1 mL min<sup>-1</sup>, det. 254 nm; 25.6 min (*S*-enantiomer) and *R*<sub>t</sub> 36.5 min (*R*-enantiomer).

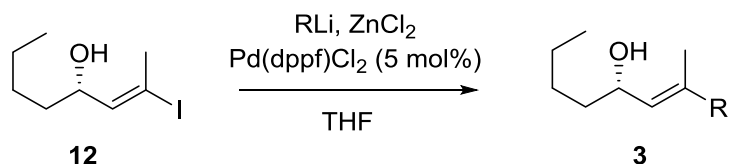
**10. The synthesis of (*S,E*)-2-iodooct-2-en-4-ol**



In a darkness, β-vinyltributylstannane **11**<sup>3</sup> (4.8 mmol, 2.0 g) was dissolved in dry CH<sub>2</sub>Cl<sub>2</sub> (0.1 M, 48 mL) and cooled to 0 °C, and next, I<sub>2</sub> (1.2 equiv., 5.8 mmol, 730 mg) was added portionwise. The progress of the reaction was followed by a TLC. After 1 h at 0 °C, the resulting mixture was washed with sat. aq. KF, followed by an addition of sat. aq. Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>. The organic phase was dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvents, the crude residue was purified by a column chromatography on a silica gel deactivated with Et<sub>3</sub>N (0-10% AcOEt in hexanes) to

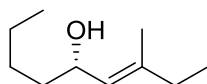
provide  $\beta$ -vinyl iodine **12** (1.2 g, 95%) as yellowish oil;  $[\alpha]_D^{23} +8.1$  (*c* 1.19, CHCl<sub>3</sub>, 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.17 (dq, *J* = 8.7, 1.5 Hz, 1H), 4.40 – 4.21 (m, 1H), 2.44 (d, *J* = 1.5 Hz, 3H), 1.71 (br s, 1H), 1.62 – 1.51 (m, 1H), 1.50 – 1.39 (m, 1H), 1.38 – 1.18 (m, 4H), 0.89 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  144.0, 97.5, 69.6, 36.7, 28.3, 27.3, 22.6, 14.0; FTIR (film)  $\nu$ : 3327, 2955, 2929, 2858, 1637, 1465, 1377, 1131, 1065, 1023, 646 cm<sup>-1</sup>; Elem. Anal Found: C, 37.85; H, 5.63; I, 50.0%, C<sub>8</sub>H<sub>15</sub>I O requires C, 37.81; H, 5.59; I, 49.94%. HRMS (EI) *m/z* calcd for C<sub>8</sub>H<sub>15</sub>O<sup>+</sup> [M-] 127.1117; found 127.1115.

### 11. The synthesis of $\beta,\beta$ -disubstituted allyl alcohols via Negishi coupling



A soln. of RLi (3 equiv., 2.4 mmol) was added to a 1M soln. of ZnCl<sub>2</sub> in THF (3 equiv., 2.4 mmol, 2.4 mL), pre-cooled to -30 °C. After stirring for 1 h at rt, the resulting mixture was transferred to the mixture of vinyl iodide **12** (1 equiv., 0.79 mmol, 200 mg) and Pd(dppf)Cl<sub>2</sub> (5 mol %, 29 mg) in dry and degassed THF pre-cooled to 0 °C. Mixture was left to stand overnight at rt. The progress of the reaction was followed by TLC. After removal of solvent, the crude residue was purified by column chromatography.

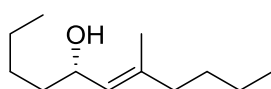
#### (*S,E*)-3-Methylnon-3-en-5-ol (**3j**):



Column chromatography: silica gel, 0–20% Et<sub>2</sub>O in pentanes. Yield: 97 mg (80%) starting from 200 mg of vinyl iodide **12**; yellowish oil;  $[\alpha]_D^{22} -16.0$  (*c* 1.08, CHCl<sub>3</sub>), *ee* 96%; HPLC of *p*-nitrobenzoate ester: *R*<sub>t</sub> 27.8 min); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.14 (dq, *J* = 8.7, 1.4 Hz, 1H), 4.34 (dt, *J* = 8.7, 6.5 Hz, 1H), 2.08 – 1.93 (m, 2H), 1.67 (d, *J* = 1.4 Hz, 3H), 1.62 – 1.49 (m, 1H), 1.49 – 1.17 (m, 6H), 1.00 (t, *J* = 7.5 Hz, 3H),

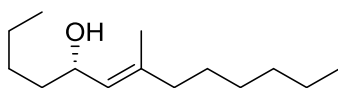
0.89 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  140.2, 126.7, 68.6, 37.5, 32.2, 27.6, 22.7, 16.5, 14.0, 12.4; FTIR (film)  $\nu$ : 3339, 2956, 2929, 2858, 1637, 1464, 1378, 1065, 1023, 1007, 646  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{10}\text{H}_{20}\text{O}$  [M] 156.1514; found 156.1519; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1  $\text{mL min}^{-1}$ , det. 254 nm;  $R_t$  28.6 min (*S*-enantiomer) and 33.5 min (*R*-enantiomer).

**(*S,E*)-7-Methylundec-6-en-5-ol (3k):**



Column chromatography: silica gel, 5–20% AcOEt in hexanes. Yield 126 mg (88%) starting from 200 mg of vinyl iodide **12**; yellowish oil;  $[\alpha]_{\text{D}}^{23} -10.1$  ( $c$  1.12,  $\text{CHCl}_3$ ), *ee* 92%; HPLC of *p*-nitrobenzoate ester:  $R_t$  21.4 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.15 (dq,  $J = 8.7, 1.4$  Hz, 1H), 4.35 (dt,  $J = 8.7, 6.5$  Hz, 1H), 2.05 – 1.92 (m, 2H), 1.66 (d,  $J = 1.4$  Hz, 3H), 1.63 – 1.52 (m, 1H), 1.49 – 1.18 (m, 10H), 0.90 (t,  $J = 7.1$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.8, 127.9, 68.6, 39.2, 37.5, 29.9, 27.6, 22.7, 22.3, 16.5, 14.0, 13.9; FTIR (film)  $\nu$ : 3341, 2957, 2929, 2859, 1466, 1379, 998  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{24}\text{O}$  [M] 184.1827; found 184.1832; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1  $\text{mL min}^{-1}$ , det. 254 nm;  $R_t$  21.4 min (*S*-enantiomer) and 24.1 min (*R*-enantiomer).

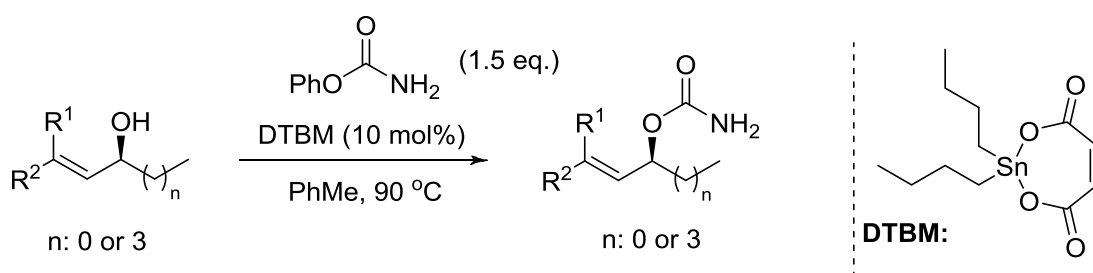
**(*S,E*)-7-Methyltridec-6-en-5-ol (3l):**



Column chromatography: silica gel, 5–20% AcOEt in hexanes. Yield 152 mg (92%) starting from 200 mg of vinyl iodide **12**; yellowish oil;  $[\alpha]_{\text{D}}^{23} -9.7$  ( $c$  1.00,  $\text{CHCl}_3$ ), *ee* 94%; HPLC of *p*-nitrobenzoate ester:  $R_t$  20.7 min);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.14 (d,  $J = 8.7$  Hz, 1H), 4.34 (dt,  $J = 8.7, 6.6$  Hz, 1H), 2.17 – 1.83 (m, 2H), 1.73 – 1.50 (m, 4H), 1.50 – 1.10 (m, 15H), 1.02 – 0.73 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  138.8,

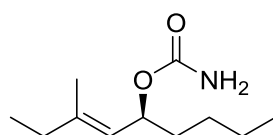
127.9, 68.7, 39.6, 37.5, 31.7, 28.9, 27.6, 22.7, 22.6, 16.5, 14.0; FTIR (film)  $\nu$ : 3341, 2957, 2928, 2857, 1465, 1379, 1004  $\text{cm}^{-1}$ ; HRMS (EI)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{28}\text{O}$  [M] 212.2140; found 212.2133; HPLC (for *p*-nitrobenzoate ester, racemate) column: Chiralcel OD-H, 100% hexanes, flow 1  $\text{mL min}^{-1}$ , det. 254 nm;  $R_t$  20.6 min (*S*-enantiomer) and 23.6 min (*R*-enantiomer).

## 12. Transcarbamylation of allyl alcohols **3**



**General procedure:**<sup>4</sup> A solution of allyl alcohol **3** (0.52 mmol), phenyl carbamate (0.78 mmol), and dibutyltin maleate (53  $\mu\text{mol}$ , 10 mol%) in toluene (*c* 0.2 M) was stirred at 90 °C. The progress of the reaction was followed by TLC. When the reaction was completed, the solution was cooled to 0 °C and diluted with 2 M aqueous NaOH. After stirring at 0 °C for 10 min,  $\text{CH}_2\text{Cl}_2$  and  $\text{H}_2\text{O}$  were added. The organic layer was separated and washed with 2 M aqueous NaOH,  $\text{H}_2\text{O}$ , and brine, dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude residue was purified by a column chromatography on a silica gel deactivated with  $\text{Et}_3\text{N}$  (0–30% AcOEt in hexanes).

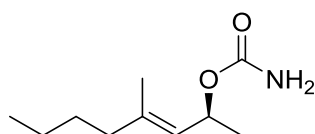
### (*S,E*)-3-Methylnon-3-en-5-yl carbamate (**13a**):



The reaction mixture was stirred for 8 h. Yield: 84 mg (74%) starting from 89 mg of alcohol **3j**; waxy solid;  $[\alpha]_{\text{D}}^{23} +5.9$  (*c* 1.14,  $\text{CHCl}_3$ , *ee* 96%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.38 (dt,  $J = 9.1, 6.7$  Hz, 1H), 5.08 (dq,  $J = 9.1, 1.3$  Hz, 1H), 4.56 (br s, 2H),

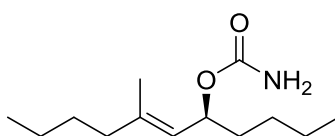
2.13 – 1.90 (m, 2H), 1.77 – 1.58 (m, 4H), 1.54 – 1.41 (m, 1H), 1.40 – 1.18 (m, 5H), 1.00 (t,  $J = 7.5$  Hz, 3H), 0.88 (t,  $J = 7.0$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.9, 142.1, 122.4, 72.4, 34.9, 32.2, 27.2, 22.5, 16.8, 14.0, 12.4; FTIR (film)  $\nu$ : 3433, 3330, 3261, 3212, 2959, 2929, 2860, 1681, 1611, 1404, 1044  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{21}\text{NO}_2\text{Na}$  [(M+Na) $^+$ ] 222.1470; found 222.1465.

**(*S,E*)-4-Methyloct-3-en-2-yl carbamate (13b):**



The reaction mixture was stirred for 4 h. Yield: 567 mg (89%) starting from 490 mg of alcohol **3a**; white solid; m.p. 68-70 °C;  $[\alpha]_{\text{D}}^{20} -7.2$  ( $c$  1.20,  $\text{CHCl}_3$ ,  $ee$  94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.46 (dq,  $J = 8.7, 6.3$  Hz, 1H), 5.12 (dq,  $J = 8.7, 1.4$  Hz, 1H), 4.87 (br s, 2H), 2.02 – 1.89 (m, 2H), 1.66 (d,  $J = 1.4$  Hz, 3H), 1.43 – 1.15 (m, 7H), 0.87 (t,  $J = 7.2$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.9, 139.8, 124.5, 68.9, 39.1, 29.7, 22.3, 21.1, 16.5, 13.9; FTIR (film)  $\nu$ : 3433, 3330, 3261, 3210, 2962, 2929, 1681, 1612, 1405, 1047  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{10}\text{H}_{19}\text{NO}_2\text{Na}$  [(M+Na) $^+$ ] 208.1313; found 208.1307.

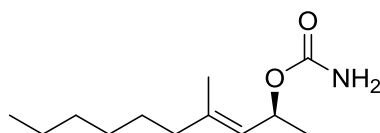
**(*S,E*)-7-Methylundec-6-en-5-yl carbamate (13c):**



The reaction mixture was stirred for 5 h. Yield: 113 mg (80%) starting from 115 mg of alcohol **3k**; waxy solid;  $[\alpha]_{\text{D}}^{22} +1.4$  ( $c$  1.38,  $\text{CHCl}_3$ ,  $ee$  92%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.37 (dt,  $J = 9.0, 6.7$  Hz, 1H), 5.09 (dq,  $J = 9.1, 1.3$  Hz, 1H), 4.48 (br s, 2H), 2.12 – 1.89 (m, 2H), 1.77 – 1.60 (m, 4H), 1.53 – 1.11 (m, 9H), 0.98 – 0.75 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.8, 140.7, 123.6, 72.4, 39.2, 34.9, 29.8, 27.2, 22.5, 22.3,

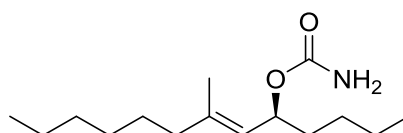
16.7, 14.0, 13.9; FTIR (film)  $\nu$ : 3346, 2957, 2930, 2861, 1711, 1383, 1310, 1039  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{25}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  250.1783; found 250.1783.

**(*S,E*)-4-Methyldec-3-en-2-yl carbamate (13d):**



The reaction mixture was stirred for 4 h. Yield: 624 mg (85%) starting from 585 mg of alcohol **3b**; white solid; m.p. 61-62 °C;  $[\alpha]_{\text{D}}^{22}$  -9.2 ( $c$  1.44,  $\text{CHCl}_3$ ,  $ee$  94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.48 (dq,  $J$  = 8.7, 6.3 Hz, 1H), 5.13 (dq,  $J$  = 8.7, 1.3 Hz, 1H), 4.70 (br s, 2H), 2.03 – 1.90 (m, 2H), 1.68 (d,  $J$  = 1.3 Hz, 3H), 1.46 – 1.30 (m, 2H), 1.33 – 1.14 (m, 9H), 0.87 (t,  $J$  = 6.9 Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.7, 139.9, 124.5, 68.9, 39.4, 31.7, 28.9, 27.5, 22.6, 21.1, 16.6, 14.0; FTIR (film)  $\nu$ : 3435, 3261, 2929, 1683, 1612, 1404, 1046  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{23}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  236.1626; found 236.1620.

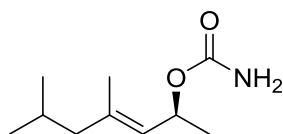
**(*S,E*)-7-Methyltridec-6-en-5-yl carbamate (13e):**



The reaction mixture was stirred for 5 h. Yield: 140 mg (83%) starting from 140 mg of alcohol **3i**; waxy solid;  $[\alpha]_{\text{D}}^{22}$  -0.4 ( $c$  1.00,  $\text{CHCl}_3$ ,  $ee$  94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.37 (dt,  $J$  = 9.0, 6.7 Hz, 1H), 5.08 (dq,  $J$  = 9.0, 1.3 Hz, 1H), 4.51 (br s, 2H), 2.05 – 1.95 (m, 2H), 1.77 – 1.54 (m, 4H), 1.53 – 1.17 (m, 13H), 0.96 – 0.76 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.6, 140.8, 123.6, 72.5, 39.5, 34.9, 31.7, 28.8, 27.6, 27.2, 22.6, 22.6, 16.7, 14.0, 14.0; FTIR (film)  $\nu$ : 3439, 3343, 2956, 2928, 2857, 1682, 1648, 1399, 1038, 581  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{29}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  278.2096; found 278.2097.

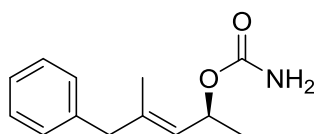


**(*S,E*)-4,6-Dimethylhept-3-en-2-yl carbamate (13f)**



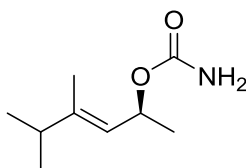
The reaction mixture was stirred for 4 h. Yield: 349 mg (83%) starting from 322 mg of alcohol **3c**; white solid; m.p. 85-87 °C;  $[\alpha]_{\text{D}}^{22} -5.3$  (c 0.94, CHCl<sub>3</sub>, ee 92%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.48 (dq, *J* = 8.7, 6.4 Hz, 1H), 5.12 (dq, *J* = 8.7, 1.4 Hz, 1H), 4.69 (br s, 2H), 1.91 – 1.68 (m, 3H), 1.66 (d, *J* = 1.4 Hz, 3H), 1.26 (d, *J* = 6.4 Hz, 3H), 0.91 – 0.73 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.7, 138.6, 126.1, 68.9, 49.2, 25.9, 22.5, 22.1, 21.1, 16.5; FTIR (film) *v*: 3433, 3331, 3262, 3208, 2952, 2925, 1681, 1611, 1404, 1046 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>10</sub>H<sub>19</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 208.1313; found 208.1311.

**(*S,E*)-4-Methyl-5-phenylpent-3-en-2-yl carbamate (13g):**



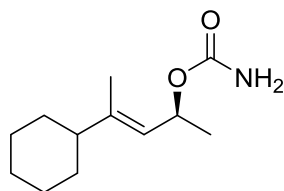
The reaction mixture was stirred for 4 h. Yield: 702 mg (83%) starting from 678 mg of alcohol **3d**; white solid; m.p. 105-107 °C;  $[\alpha]_{\text{D}}^{20} -30.5$  (c 1.27, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.34 – 7.10 (m, 5H), 5.51 (dq, *J* = 8.6, 6.4 Hz, 1H), 5.27 (dq, *J* = 8.6, 1.4 Hz, 1H), 4.83 (br s, 2H), 3.30 (d, *J* = 3.2 Hz, 2H), 1.66 (d, *J* = 1.4 Hz, 3H), 1.30 (d, *J* = 6.4 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.8, 139.3, 138.5, 128.9, 128.3, 126.9, 126.2, 68.9, 45.9, 21.1, 16.5; FTIR (film) *v*: 3426, 3330, 3263, 3205, 2976, 1681, 1614, 1409, 1044, 695 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>13</sub>H<sub>17</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 242.1157; found 242.1156.

**(*S,E*)-4,5-Dimethylhex-3-en-2-yl carbamate (13h):**



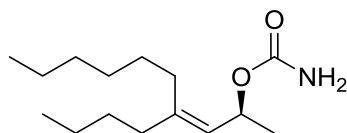
The reaction mixture was stirred for 3 h. Yield: 322 mg (74%) starting from 326 mg of alcohol **3e**; waxy solid;  $[\alpha]_D^{21} -3.7$  (c 1.27, CHCl<sub>3</sub>, ee 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.47 (dq, *J* = 8.6, 6.4 Hz, 1H), 5.13 (dq, *J* = 8.6, 1.4 Hz, 1H), 4.84 (br s, 1H), 2.19 (hept, *J* = 6.9 Hz, 1H), 1.64 (d, *J* = 1.4 Hz, 3H), 1.24 (d, *J* = 6.4 Hz, 3H), 0.97 (d, *J* = 6.9 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.9, 145.1, 122.5, 68.9, 36.4, 21.2, 21.1, 14.1; FTIR (film) *v*: 3443, 3332, 3195, 2963, 1720, 1385, 1315, 1041, 1011 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>9</sub>H<sub>17</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 194.1157; found 194.1154.

**(*S,E*)-4-Cyclohexylpent-3-en-2-yl carbamate (13i):**



The reaction mixture was stirred for 4 h. Yield: 561 mg (86%) starting from 518 mg of alcohol **3f**; white solid; 88-100 °C;  $[\alpha]_D^{21} -15.0$  (c 1.07, CHCl<sub>3</sub>, ee 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.47 (dq, *J* = 8.6, 6.3 Hz, 1H), 5.12 (dq, *J* = 8.6, 1.3 Hz, 1H), 4.83 (br s, 2H), 1.89 – 1.56 (m, 9H), 1.34 – 1.01 (m, 8H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.9, 144.6, 122.9, 68.9, 47.0, 31.7, 31.6, 26.6, 26.6, 26.3, 21.2, 15.0; FTIR (film) *v*: 3440, 3331, 3258, 2926, 2854, 1683, 1612, 1404, 1044 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>12</sub>H<sub>21</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 234.1470; found 234.1463.

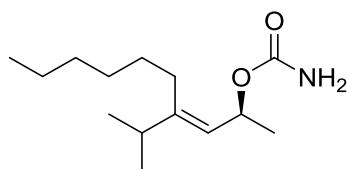
**(*S,Z*)-4-Butyldec-3-en-2-yl carbamate (13j):**



The reaction mixture was stirred for 5 h. Yield: 427 mg (91%) starting from 391 mg of alcohol **3g**; waxy solid;  $[\alpha]_D^{22} +12.5$  (c 0.90, CHCl<sub>3</sub>, ee 82%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 5.49 (dq, *J* = 9.0, 6.3 Hz, 1H), 5.11 (d, *J* = 9.0 Hz, 1H), 4.75 (br s, 2H), 2.23 – 2.08 (m, 1H), 2.07 – 1.88 (m, 3H), 1.49 – 1.14 (m, 15H), 0.96 – 0.75 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.7, 144.3, 124.4, 68.6, 36.2, 31.7, 30.8, 30.0, 29.4, 28.6, 22.6,

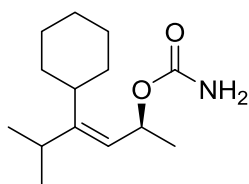
22.4, 21.5, 14.0, 13.9; FTIR (film)  $\nu$ : 3339, 2956, 2929, 2859, 1713, 1373, 1317, 1043  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{29}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  278.2096; found 278.2097.

**(*S,E*)-4-Isopropyldec-3-en-2-yl carbamate (13k):**



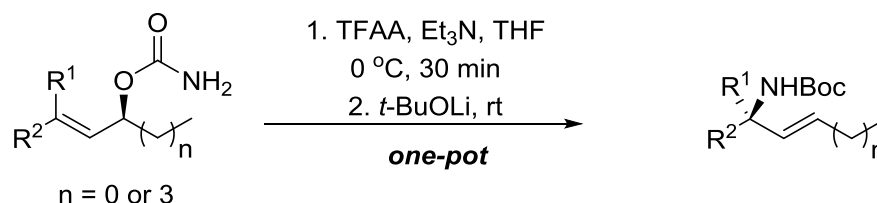
The reaction mixture was stirred for 4 h. Yield: 162 mg (84%) starting from 159 mg of alcohol **3h**; waxy solid;  $[\alpha]_{\text{D}}^{24} +8.4$  ( $c$  1.70,  $\text{CHCl}_3$ ,  $ee$  95%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.49 (dq,  $J = 9.0, 6.3$  Hz, 1H), 5.11 (dd,  $J = 9.0, 1.0$  Hz, 1H), 4.78 (br s, 2H), 2.28 – 2.08 (m, 2H), 2.07 – 1.93 (m, 1H), 1.43 – 1.19 (m, 11H), 1.04 – 0.94 (m, 6H), 0.91 – 0.80 (m, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.7, 150.1, 122.2, 68.8, 33.8, 31.7, 30.2, 29.7, 29.6, 22.6, 22.0, 21.9, 21.6, 14.0; FTIR (film)  $\nu$ : 3336, 2959, 2930, 2871, 1711, 1601, 1466, 1374, 1315, 1037  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{27}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  264.1939; found 264.1931.

**(*S,Z*)-4-Cyclohexyl-5-methylhex-3-en-2-yl carbamate (13l)**



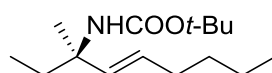
The reaction mixture was stirred for 6 h. Yield: 138 mg (90%) starting from 125 mg of alcohol **3i**; waxy solid;  $[\alpha]_{\text{D}}^{24} -2.5$  ( $c$  0.68,  $\text{CHCl}_3$ ,  $ee$  79%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.70 – 5.50 (m, 1H), 5.11 (d,  $J = 8.7$  Hz, 1H), 4.79 (br s, 2H), 2.53 – 2.37 (m, 1H), 2.30 (hept,  $J = 6.5$  Hz, 1H), 1.80 – 1.05 (m, 13H), 1.05 – 0.88 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.8, 155.0, 121.8, 68.4, 41.4, 31.2, 29.3, 26.5, 26.4, 26.1, 24.4, 24.1, 21.8; FTIR (film)  $\nu$ : 3343, 2927, 2853, 1713, 1378, 1040  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{25}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  262.1783; found 262.1776.

### 13. [3,3]-Sigmatropic rearrangement of allyl carbamates **13**



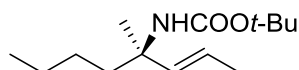
**General procedure:** A solution of carbamate **13** (0.5 mmol) and Et<sub>3</sub>N (3 mmol, 304 mg, 418  $\mu$ L) in dry THF (10 mL) was cooled to 0 °C, and TFAA (1 mmol, 210 mg, 139  $\mu$ L) was added. The resulting mixture was warmed slowly to room temperature and stirred for 0.5–1 h. After that, the *t*-BuOLi (3 mmol, 240 mg) was added portionwise to the generated allyl isocyanate. The progress of the reaction was followed by TLC. After 1 h, volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (2–20% AcOEt in hexanes).

#### ***tert*-Butyl (*R,E*)-(3-methylnon-4-en-3-yl)carbamate (**14a**):**



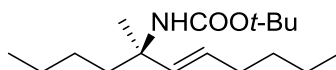
Yield 91 mg (89%) starting from 81 mg of carbamate **13a**; colourless oil;  $[\alpha]_D^{25} -6.7$  (c 1.08, CHCl<sub>3</sub>, *ee* 96%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.56 – 5.28 (m, 2H), 4.46 (br s, 1H), 2.12 – 1.91 (m, 2H), 1.79 – 1.53 (m, 2H), 1.42 (s, 9H), 1.38 – 1.18 (m, 7H), 0.88 (t, *J* = 7.0 Hz, 3H), 0.81 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  154.4, 135.2, 128.2, 78.6, 55.8, 32.6, 32.0, 31.6, 28.4, 24.7, 22.1, 13.8, 8.1; FTIR (film)  $\nu$ : 3362, 2966, 2928, 1725, 1699, 1492, 1366, 1247, 1171, 1079 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>29</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 278.2096; found 278.2083.

#### ***tert*-Butyl (*R,E*)-(4-methyloct-2-en-4-yl)carbamate (**14b**):**



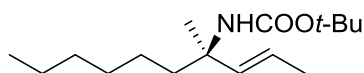
Yield 617 mg (86%) starting from 552 mg of carbamate **13b**; yellowish oil;  $[\alpha]_D^{23} - 9.0$  (c 1.12,  $\text{CHCl}_3$ , *ee* 94%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.60 – 5.36 (m, 2H), 4.46 (br s, 1H), 1.72 – 1.56 (m, 5H), 1.39 (s, 9H), 1.34 – 1.09 (m, 7H), 0.86 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.3, 136.8, 122.3, 78.5, 55.5, 39.8, 28.3, 26.0, 25.0, 22.9, 17.7, 14.0; FTIR (film)  $\nu$ : 3359, 2961, 2931, 1725, 1698, 1492, 1365, 1249, 1172, 1083  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{27}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  264.1939; found 264.1931.

***tert*-Butyl (*R,E*)-(5-methylundec-6-en-5-yl)carbamate (14c):**



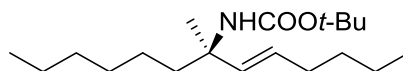
Yield 98 mg (75%) starting from 105 mg of carbamate **13c**; colourless oil;  $[\alpha]_D^{25} - 5.6$  (c 1.08,  $\text{CHCl}_3$ , *ee* 92%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.56 – 5.33 (m, 2H), 4.46 (br s, 1H), 2.12 – 1.89 (m, 2H), 1.75 – 1.53 (m, 2H), 1.41 (s, 9H), 1.37 – 1.09 (m, 11H), 0.88 (t,  $J = 7.1$  Hz, 6H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.4, 135.6, 128.0, 78.6, 55.6, 39.9, 32.0, 31.6, 28.4, 26.1, 25.2, 23.0, 22.1, 14.0, 13.8; FTIR (film)  $\nu$ : 3364, 2958, 2929, 2861, 1727, 1697, 1490, 1365, 1172 1082, 1046, 969  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{33}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  306.2409; found 306.2406.

***tert*-Butyl (*R,E*)-(4-methyldec-2-en-4-yl)carbamate (14d):**



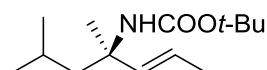
Yield 640 mg (84%) starting from 600 mg of carbamate **13d**; yellowish oil;  $[\alpha]_D^{23} - 8.3$  (c 1.16,  $\text{CHCl}_3$ , *ee* 94%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.56 – 5.35 (m, 2H), 4.46 (br s, 1H), 1.68 – 1.51 (m, 5H), 1.37 (s, 9H), 1.31 – 1.08 (m, 11H), 0.89 – 0.76 (m, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.2, 136.8, 122.4, 78.5, 55.6, 40.1, 31.7, 29.5, 28.4, 25.0, 23.7, 22.5, 17.7, 14.0; FTIR (film)  $\nu$ : 3361, 2960, 2929, 2858, 1725, 1698, 1491, 1453, 1365, 1248, 1172  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{31}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  292.2252; found 292.2245.

***tert*-Butyl (*R,E*)-(7-methyltridec-5-en-7-yl)carbamate (**14e**):**



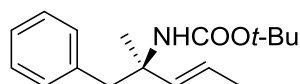
Yield 132 mg (80%) starting from 135 mg of carbamate **13e**; colourless oil;  $[\alpha]_D^{25} - 5.9$  (*c* 1.09, CHCl<sub>3</sub>, *ee* 94%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.55 – 5.30 (m, 2H), 4.46 (br s, 1H), 2.12 – 1.91 (m, 2H), 1.71 – 1.53 (m, 2H), 1.41 (s, 9H), 1.38 – 1.10 (m, 15H), 0.96 – 0.76 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  154.4, 135.6, 128.0, 78.6, 55.6, 40.2, 32.0, 31.8, 31.6, 29.5, 28.4, 25.2, 23.8, 22.6, 22.1, 14.0, 13.9; FTIR (film)  $\nu$ : 3362, 2957, 2927, 2857, 1725, 1698, 1490, 1366, 1247, 1170, 1052 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>19</sub>H<sub>37</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 334.2722; found 334.2710.

***tert*-Butyl (*R,E*)-(4,6-dimethylhept-2-en-4-yl)carbamate (**14f**):**



Yield 356 mg (83%) starting from 328 mg of carbamate **13f**; yellowish oil;  $[\alpha]_D^{24} - 10.4$  (*c* 0.95, CHCl<sub>3</sub>, *ee* 92%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  5.61 – 5.33 (m, 2H), 4.48 (br s, 1H), 1.75 – 1.47 (m, 6H), 1.38 (s, 9H), 1.33 – 1.15 (m, 3H), 0.87 (d, *J* = 6.5 Hz, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  154.2, 137.4, 122.0, 78.6, 55.9, 48.3, 28.4, 25.8, 24.6, 24.5, 24.1, 17.7; FTIR (film)  $\nu$ : 3364, 2957, 2930, 1725, 1698, 1492, 1366, 1243, 1168, 1083 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>27</sub>NO<sub>2</sub>Na [(M+Na)<sup>+</sup>] 264.1939; found 264.1934.

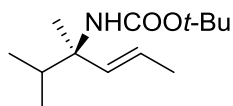
***tert*-Butyl (*R,E*)-(2-methyl-1-phenylpent-3-en-2-yl)carbamate (**14g**):**



Yield 558 mg (89%) starting from 500 mg of carbamate **13g**; yellowish oil;  $[\alpha]_D^{24} + 19.6$  (*c* 0.95, CHCl<sub>3</sub>, *ee* 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.32 – 7.18 (m, 3H), 7.19 – 7.09 (m, 2H), 5.65 (dq, *J* = 15.6, 1.6 Hz, 1H), 5.46 (dq, *J* = 15.6, 6.4 Hz, 1H), 4.41 (br s, 1H), 3.15 (d, *J* = 13.2 Hz, 1H), 2.95 (d, *J* = 13.2 Hz, 1H), 1.71 (dd, *J* = 6.4, 1.6 Hz, 3H),

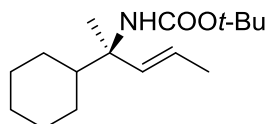
1.48 (s, 9H), 1.32 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.5, 137.6, 136.5, 130.8, 127.8, 126.3, 123.0, 78.9, 55.9, 44.8, 28.5, 25.7, 17.8; FTIR (film)  $\nu$ : 3362, 2976, 2930, 1719, 1495, 1365, 1249, 1168, 702  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{25}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  298.1783; found 298.1772.

***tert*-Butyl (*R,E*)-(2,3-dimethylhex-4-en-3-yl)carbamate (14h):**



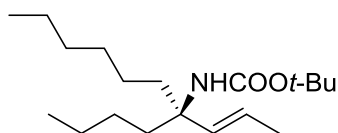
Yield 314 mg (79%) starting from 300 mg of carbamate **13h**; yellowish oil;  $[\alpha]_{\text{D}}^{24}$  -12.4 ( $c$  0.90,  $\text{CHCl}_3$ ,  $ee$  88%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.63 – 5.38 (m, 2H), 4.48 (br s, 1H), 2.10 (s, 1H), 1.70 (d,  $J$  = 4.8 Hz, 3H), 1.41 (s, 9H), 1.31 (s, 3H), 0.88 – 0.80 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.4, 134.5, 123.5, 78.5, 58.6, 35.2, 28.4, 21.0, 17.8, 17.2, 17.1; FTIR (film)  $\nu$ : 3360, 2969, 2931, 1725, 1696, 1493, 1452, 1389, 1367, 1250, 1170 1081, 975  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{13}\text{H}_{25}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  250.1783; found 250.1778.

***tert*-Butyl (*R,E*)-(2-cyclohexylpent-3-en-2-yl)carbamate (14i):**



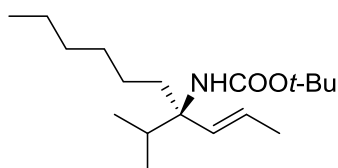
Yield 416 mg (82%) starting from 400 mg of carbamate **13i**; yellowish oil;  $[\alpha]_{\text{D}}^{24}$  -14.0 ( $c$  0.97,  $\text{CHCl}_3$ ,  $ee$  88%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.58 – 5.34 (m, 2H), 4.46 (br s, 1H), 1.80 – 1.56 (m, 9H), 1.39 (s, 9H), 1.29 (s, 3H), 1.28 – 0.80 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.5, 135.1, 123.2, 78.6, 58.5, 45.8, 28.4, 27.4, 27.3, 26.7, 26.5, 21.5, 17.8; FTIR (film)  $\nu$ : 3359, 2975, 2928, 2854, 1724, 1694, 1491, 1450, 1366, 1240, 1171  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{29}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  290.2096; found 290.2092.

***tert*-Butyl (*S,E*)-(5-(prop-1-en-1-yl)undecan-5-yl)carbamate (14j):**



Yield 287 mg (79%) starting from 300 mg of carbamate **13j**; yellowish oil;  $[\alpha]_D^{23} +2.5$  (c 1.13,  $\text{CHCl}_3$ , ee 82%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.4 (dq,  $J = 15.9, 6.0$  Hz, 1H), 5.3 (d,  $J = 15.9$  Hz, 1H), 4.4 (br s, 1H), 1.9 – 1.7 (m, 2H), 1.7 (dd,  $J = 6.0, 1.3$  Hz, 3H), 1.6 – 1.4 (m, 2H), 1.4 (s, 9H), 1.3 – 1.1 (m, 12H), 0.9 – 0.8 (m, 6H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.2, 136.0, 122.6, 78.4, 58.5, 37.4, 37.2, 31.8, 29.5, 28.3, 25.6, 23.3, 22.9, 22.5, 17.8, 14.0, 14.0; FTIR (film)  $\nu$ : 3363, 2957, 2928, 2860, 1727, 1696, 1490, 1365, 1246, 1172, 1090, 969  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{37}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  334.2722; found 334.2719.

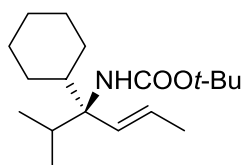
**tert-Butyl (R,E)-(4-isopropyldec-2-en-4-yl)carbamate (14k):**



Yield 131 mg (79%) starting from 135 mg of carbamate **13k**; colourless oil;  $[\alpha]_D^{25} +14.9$  (c 0.50,  $\text{CHCl}_3$ , ee 95%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.62 – 5.08 (m, 2H), 4.44 (br s, 1H), 2.26 (s, 1H), 1.96 (s, 1H), 1.71 (d,  $J = 6.1$  Hz, 3H), 1.67 – 1.54 (m, 1H), 1.40 (s, 9H), 1.31 – 1.09 (m, 8H), 0.85 (t,  $J = 6.5$  Hz, 3H), 0.80 (d,  $J = 6.9$  Hz, 6H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.3, 132.3, 123.9, 78.4, 61.7, 34.3, 34.0, 31.8, 29.6, 28.4, 23.6, 22.6, 18.0, 17.3, 17.2, 14.0; FTIR (film)  $\nu$ : 2961, 2928, 2860, 1726, 1696, 1491, 1366, 1245, 1170, 1090  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{35}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  320.2565; found 320.2561.

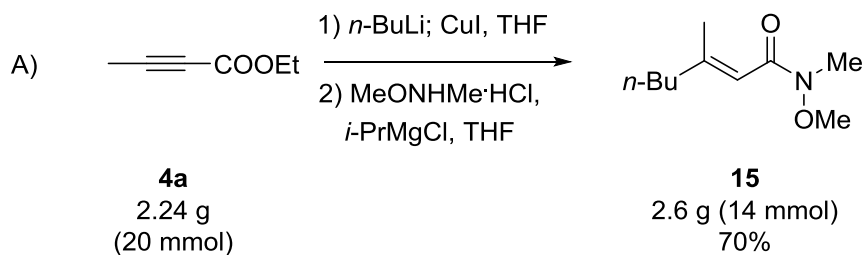
**tert-Butyl (S,E)-(3-cyclohexyl-2-methylhex-4-en-3-yl)carbamate (14l):**





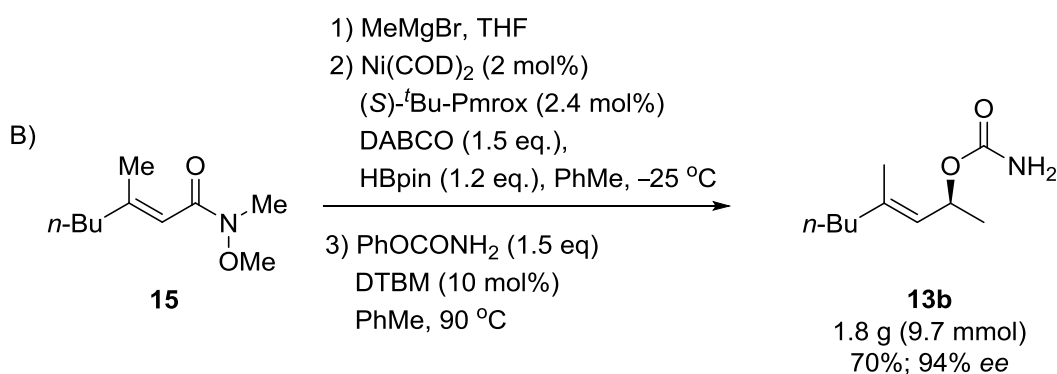
Yield 100 mg (68%) starting from 121 mg of carbamate **13l**; colourless oil;  $[\alpha]_D^{25} +8.9$  ( $c$  0.71,  $\text{CHCl}_3$ ,  $ee$  79%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.50 – 5.10 (m, 2H), 4.24 (br s, 1H), 2.50 (br s, 1H), 2.08 – 1.89 (m, 1H), 1.84 – 1.55 (m, 8H), 1.40 (s, 9H), 1.32 – 0.88 (m, 5H), 0.85 (d,  $J = 6.8$  Hz, 3H), 0.79 (d,  $J = 6.8$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  154.9, 133.7, 123.7, 78.0, 65.0, 43.2, 31.3, 28.4, 28.0, 27.5, 27.0, 26.8, 17.9, 17.5, 17.2; FTIR (film)  $\nu$ : 2971, 2928, 2854, 1731, 1689, 1494, 1365, 1237, 1168  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{33}\text{NO}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  318.2409; found 318.2400.

#### 14. A large scale synthesis of allylamine **14b**



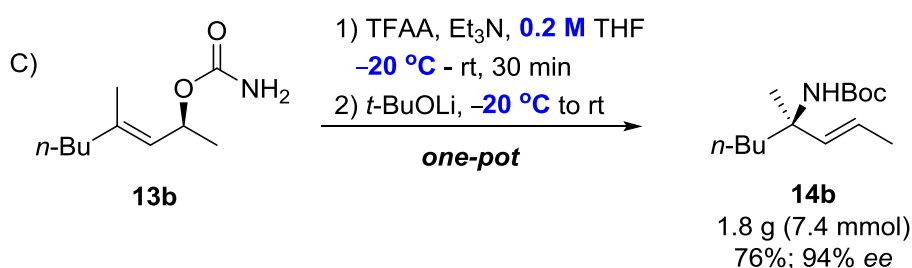
A block: A suspension of  $\text{CuI}$  (22.0 mmol, 4.2 g) in THF (60 mL) was cooled to  $-40$   $^\circ\text{C}$ , and 2.5 M solution of  $\text{BuLi}$  in hexane (21.2 mmol, 8.5 mL) was added. The resulting mixture was stirred at  $-40$   $^\circ\text{C}$  for 30 min and then cooled to  $-78$   $^\circ\text{C}$ . A solution of ethyl but-2-ynoate (**4a**) (20.0 mmol, 2.2 g, 2.3 mL) in THF (2 mL) was added portionwise and the resulting mixture was stirred for 2 h at  $-78$   $^\circ\text{C}$ . The progress of the reaction was followed by TLC. Next, the reaction was quenched by an addition of aq.  $\text{NH}_4\text{Cl}$  at  $-78$   $^\circ\text{C}$ , after that the cooling bath was removed and the mixture was left to adjust to rt. The reaction mixture was filtrated through a short pad of Celite. The collected solids were rinsed with  $\text{Et}_2\text{O}$ . After that, the aqueous phase was separated and extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude

product was used in the next step without further purification. A suspension of crude  $\alpha,\beta$ -unsaturated ester **5a** and MeNHOMe·HCl (2 equiv., 40 mmol, 3.9 g) in dry THF (0.3 M, 67 mL) was cooled to  $-5\text{ }^{\circ}\text{C}$  under argon atmosphere, and 2M soln. of *i*-PrMgCl in THF (4 equiv., 80 mmol, 40 mL) was added dropwise. The progress of the reaction was followed by TLC. After stirring at  $-5\text{ }^{\circ}\text{C}$  for 60 min, the reaction was quenched by an addition of sat.  $\text{NH}_4\text{Cl}$ . The aqueous phase was separated and extracted with AcOEt. The combined organic phases were washed with brine, and dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of the solvents, the crude product was purified by a column chromatography on silica gel (10-30% AcOEt in hexanes) to provide pure *E* isomer of **15** (70%; after 2 steps, 14 mmol, 2.6 g).



B block: A 3 M soln. of MeMgBr in THF (1.3 equiv., 18.2 mmol, 6.1 mL) was slowly added to a pre-cooled ( $-30\text{ }^{\circ}\text{C}$ ) solution of Weinreb amide **13b** (1 equiv., 14 mmol, 2.6 g) in THF (0.3 M, 47 mL). Next, the mixture was slowly warmed to  $-5\text{ }^{\circ}\text{C}$  and stirred for 60 min. The progress of the reaction was followed by TLC. Next, sat.  $\text{NH}_4\text{Cl}$  was added and the resulting mixture was extracted with  $\text{Et}_2\text{O}$ . The combined organic layers were washed with brine, and dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude product was used in the next step without further purification. Next, a flask was charged with Ni(COD)<sub>2</sub> (280  $\mu\text{mol}$ , 2.0 mol %, 77 mg), (*S*)-*t*Bu-Pmrox (336  $\mu\text{mol}$ , 2.4 mol%, 70.0 mg) and DABCO (1.5 equiv, 21 mmol, 2.4 g) under an Ar atmosphere. Toluene (56 mL) was added and the mixture was stirred for 10 min before pinBH (1.2 equiv, 16.8 mmol, 2.1 g, 2.5 mL)

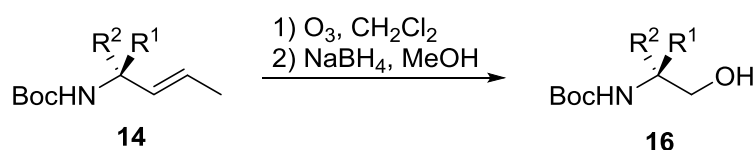
was added. Next, the reaction mixture was cooled to  $-25\text{ }^{\circ}\text{C}$  and a solution of crude enone **6** in 14 mL toluene was added by syringe. The reaction mixture was left to stir at this temperature for 24 h. The progress of the reaction was followed by TLC. When the reaction was completed, a saturated solution of  $\text{NH}_4\text{F}$  in MeOH was added and cooling bath was removed. The mixture was stirred at rt for 30 min followed by an addition of  $\text{H}_2\text{O}$  and  $\text{Et}_2\text{O}$ . The aqueous phase was separated and extracted with  $\text{Et}_2\text{O}$  (2x) and dried over anhydr.  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude product was used in the next step without further purification. Next, a solution of crude allyl alcohol **3a**, phenyl carbamate (1.5 equiv., 21 mmol, 2.9 g), and dibutyltin maleate (1.4 mmol, 10 mol%, 486 mg) in toluene (0.2 M, 70 mL) was stirred at  $90\text{ }^{\circ}\text{C}$  for 6 h. The progress of the reaction was followed by TLC. When the reaction was completed, the solution was cooled to  $0\text{ }^{\circ}\text{C}$  and diluted with 2 M aqueous NaOH. After stirring at  $0\text{ }^{\circ}\text{C}$  for 10 min,  $\text{CH}_2\text{Cl}_2$  and  $\text{H}_2\text{O}$  were added. The organic layer was separated and washed with 2 M aqueous NaOH,  $\text{H}_2\text{O}$ , and brine, dried over  $\text{Na}_2\text{SO}_4$ . After the removal of the solvent, the crude residue was purified by a column chromatography on a silica gel deactivated with  $\text{Et}_3\text{N}$  (0–30% AcOEt in hexanes) to provide carbamate **13b** (70%; after 3 steps, 94% ee, 9.7 mmol, 1.8 g).



C block: A solution of carbamate **13b** (9.7 mmol, 1.8 g) and  $\text{Et}_3\text{N}$  (58.2 mmol, 5.9 g, 8.1 mL) in dry THF (0.2 M, 49 mL) was cooled to  $-20\text{ }^{\circ}\text{C}$ , and TFAA (19.4 mmol, 4.1 g, 2.7 mL) was added. The resulting mixture was warmed slowly to room temperature and stirred for 1 h. After that, the mixture was re-cooled to  $-20\text{ }^{\circ}$  and the  $t\text{-BuOLi}$  (19.4 mmol, 4.7 g) was added portionwise to the generated allyl

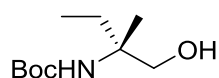
isocyanate. The resulting mixture was warmed slowly to room temperature and stirred for 1 h. The progress of the reaction was followed by TLC. After that, the volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (2–20% AcOEt in hexanes) to provide carbamate **14b** (76%; after 1 step, 94% *ee*, 7.4 mmol, 1.8 g).

## 15. The synthesis of 1,2-amino alcohols **16**



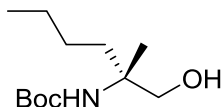
**General procedure:** Ozone was passed through a solution of carbamate **14** (0.5 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) at –78 °C until the solution turned blue. Then, excess of ozone was removed by bubbling oxygen through the mixture. After that, MeOH (5 mL) and NaBH<sub>4</sub> (2.5 mmol, 95 mg) was added portionwise and the resulting mixture was slowly warmed to room temperature and stirred for 2 h. When the reaction was complete, the solvent was removed under reduced pressure and the crude product was purified by a flash column chromatography (5–30% AcOEt in hexanes).

### ***N*-Boc (*R*)-2-amino-2-methylbutan-1-ol (**16a**):**



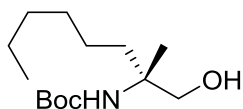
Yield 51 mg (74%) starting from 88 mg of carbamate **14b**; waxy solid;  $[\alpha]_D^{23} +6.2$  (*c* 1.07, CHCl<sub>3</sub>, *ee* 96%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 4.60 (br s, 1H), 3.74 – 3.50 (m, 2H), 1.82 – 1.63 (m, 1H), 1.61 – 1.48 (m, 1H), 1.41 (s, 9H), 1.13 (s, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 156.2, 79.7, 69.4, 57.0, 29.1, 28.3, 22.0, 7.8; FTIR (film)  $\nu$ : 3412, 3314, 2973, 2927, 2881, 2855, 1685, 1502, 1458, 1366, 1251, 1169, 1082 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>10</sub>H<sub>21</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 226.1242; found 226.1247.

***N*-Boc (*R*)-2-amino-2-methylhexan-1-ol (16b):**



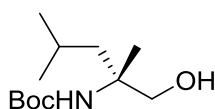
Yield 147 mg (77%) starting from 200 mg of carbamate **14b**; waxy solid;  $[\alpha]_D^{23} +6.2$  (*c* 1.07, CHCl<sub>3</sub>, *ee* 94%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.65 (br s, 1H), 3.73 – 3.39 (m, 2H), 1.74 – 1.43 (m, 2H), 1.40 (s, 9H), 1.34 – 1.08 (m, 9H), 0.88 (t, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  156.2, 79.7, 69.6, 56.8, 36.3, 28.3, 25.6, 23.1, 22.4, 14.0; FTIR (film)  $\nu$ : 3415, 3333, 2941, 2920, 2857, 1728, 1681, 1512, 1463, 1369, 1241, 1180, 1062 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>12</sub>H<sub>25</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 254.1732; found 254.1729.

***N*-Boc (*R*)-2-amino-2-methyloctan-1-ol (16c):**



Yield 238 mg (83%) starting from 300 mg of carbamate **14d**; waxy solid;  $[\alpha]_D^{23} +12.7$  (*c* 0.43, CHCl<sub>3</sub>, *ee* 94%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.60 (br s, 1H), 3.69 – 3.51 (m, 2H), 1.77 – 1.61 (m, 1H), 1.55 – 1.43 (m, 1H), 1.42 (s, 9H), 1.34 – 1.22 (m, 8H), 1.15 (s, 3H), 0.87 (t, *J* = 6.8 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  156.2, 79.7, 69.6, 56.8, 36.6, 31.7, 29.6, 28.3, 23.4, 22.5, 22.4, 14.0; FTIR (film)  $\nu$ : 3410, 3334, 2956, 2928, 2858, 1720, 1683, 1502, 1466, 1366, 1252, 1172, 1067 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>29</sub>NO<sub>3</sub>Na [(M+Na)<sup>+</sup>] 282.2045; found 282.2039.

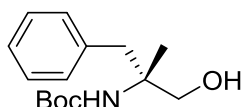
***N*-Boc (*R*)-2-amino-2,4-dimethylpentan-1-ol (16d):**



Yield 123 mg (81%) starting from 160 mg of carbamate **14f**; waxy solid;  $[\alpha]_D^{24} +2.8$  (*c* 1.00, CHCl<sub>3</sub>, *ee* 92%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.56 (br s, 1H), 3.66 (d, *J* = 11.4 Hz, 1H), 3.55 (d, *J* = 11.4 Hz, 1H), 1.82 – 1.67 (m, 2H), 1.42 (s, 9H), 1.25 (s, 1H), 1.18

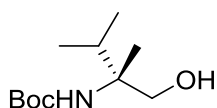
(s, 3H), 0.96 (t,  $J = 6.0$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.1, 79.6, 70.3, 57.1, 44.3, 28.3, 25.0, 24.4, 23.7, 23.1; FTIR (film)  $\nu$ : 3406, 3347, 2956, 2929, 2871, 1688, 1502, 1366, 1250, 1170, 1066, 1045  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{12}\text{H}_{25}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  254.1732; found 254.1728.

***N*-Boc (*R*)-2-amino-2-methyl-3-phenylpropan-1-ol (16e):**



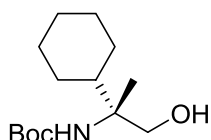
Yield 243 mg (84%) starting from 300 mg of carbamate **14g**; waxy solid;  $[\alpha]_{\text{D}}^{24} +84.9$  (c 1.08,  $\text{CHCl}_3$ ,  $ee$  98%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.37 – 7.11 (m, 5H), 4.50 (br s, 1H), 3.68 (s, 2H), 3.17 (d,  $J = 13.5$  Hz, 1H), 2.81 (d,  $J = 13.5$  Hz, 1H), 1.46 (s, 9H), 1.07 (s, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.2, 137.1, 130.6, 128.1, 126.5, 79.8, 69.5, 57.2, 41.0, 28.4, 22.9; FTIR (film)  $\nu$ : 3275, 3071, 2979, 2929, 1678, 1557, 1288, 1174, 1069, 699  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{15}\text{H}_{23}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  288.1398; found 288.1380.

***N*-Boc (*R*)-2-amino-2,3-dimethylbutan-1-ol (16f):**



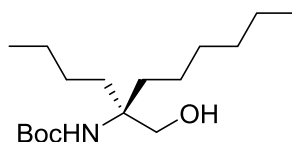
Yield 120 mg (70%) starting from 180 mg of carbamate **14h**; waxy solid;  $[\alpha]_{\text{D}}^{24} +1.1$  (c 0.94,  $\text{CHCl}_3$ ,  $ee$  88%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.61 (br s, 1H), 3.72 (d,  $J = 11.8$  Hz, 1H), 3.62 (d,  $J = 11.8$  Hz, 1H), 2.31 (hept,  $J = 6.9$  Hz, 1H), 1.42 (s, 9H), 0.99 (s, 3H), 0.95 – 0.85 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 79.8, 68.7, 59.9, 31.0, 28.3, 18.4, 17.2, 16.7; FTIR (film)  $\nu$ : 3286, 2980, 2929, 1679, 1556, 1450, 1366, 1288, 1253, 1173, 1088, 1064  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{11}\text{H}_{23}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  240.1576; found 240.1567.

***tert*-Butyl (*R*)-(2-cyclohexyl-1-hydroxypropan-2-yl)carbamate (16g):**



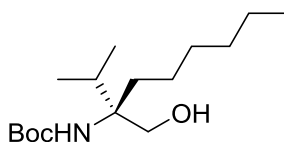
Yield 125 mg (65%) starting from 200 mg of carbamate **14i**; waxy solid;  $[\alpha]_D^{25} +10.5$  (c 2.81,  $\text{CHCl}_3$ , ee 88%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.59 (br s, 1H), 3.72 (d,  $J = 11.8$  Hz, 1H), 3.61 (d,  $J = 11.8$  Hz, 1H), 2.00 – 1.85 (m, 1H), 1.84 – 1.60 (m, 4H), 1.42 (s, 9H), 1.34 – 1.18 (m, 3H), 1.17 – 0.81 (m, 6H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.5, 79.8, 68.6, 59.8, 41.5, 28.3, 27.5, 26.8, 26.7, 26.6, 26.6, 19.5; FTIR (film)  $\nu$ : 3275, 2924, 2852, 1679, 1561, 1446, 1289, 1177, 1066, 737, 703  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{27}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  280.1889; found 280.1883.

#### ***N*-Boc (S)-2-amino-2-butylcyclohexan-1-ol (16h)**



Yield 96 mg (71%) starting from 140 mg of carbamate **14j**; waxy solid;  $[\alpha]_D^{25} -1.9$  (c 0.95,  $\text{CHCl}_3$ , ee 82%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.51 (br s, 1H), 3.74 – 3.54 (m, 2H), 1.62 – 1.43 (m, 4H), 1.43 (s, 9H), 1.36 – 1.12 (m, 12H), 0.95 – 0.79 (m, 6H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  156.3, 79.6, 67.9, 59.3, 34.2, 34.0, 31.7, 29.7, 28.3, 25.3, 23.1, 23.0, 22.5, 14.0, 14.0; FTIR (film)  $\nu$ : 3410, 3332, 2956, 2930, 2862, 1685, 1501, 1366, 1251, 1172, 1070, 1054  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{17}\text{H}_{35}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  324.2515; found 324.2513.

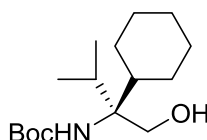
#### ***N*-Boc (R)-2-amino-2-isopropylcyclohexan-1-ol (16i):**



Yield 74 mg (70%) starting from 110 mg of carbamate **14k**; waxy solid;  $[\alpha]_D^{25} -6.9$  (c 0.99,  $\text{CHCl}_3$ , ee 95%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.58 (br s, 1H), 3.75 (d,  $J = 12.1$  Hz, 1H), 3.67 (d,  $J = 12.1$  Hz, 1H), 2.22 – 2.07 (m, 1H), 1.67 – 1.36 (m, 11H), 1.34 –

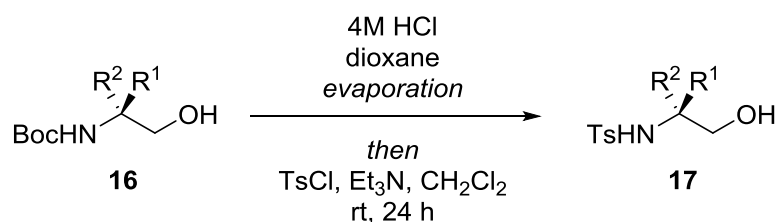
1.10 (m, 8H), 0.98 – 0.74 (m, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.0, 79.8, 66.9, 61.5, 32.2, 31.7, 31.4, 30.0, 28.3, 22.7, 22.6, 17.0, 16.6, 14.0; FTIR (film)  $\nu$ : 3265, 2927, 2857, 1679, 1555, 1463, 1366, 1287, 1253, 1175, 1069, 721  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{33}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  310.2358; found 310.2350.

### ***N*-Ts (*S*)-2-amino-2-cyclohexyl-3-methylbutan-1-ol (**16j**):**



Yield 69 mg (85%) starting from 84 mg of carbamate **14i**; waxy solid;  $[\alpha]_{\text{D}}^{24}$   $-4.6$  ( $c$  1.30,  $\text{CHCl}_3$ ,  $ee$  79%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  4.49 (br s, 1H), 3.96 – 3.73 (m, 2H), 2.11 – 1.92 (m, 1H), 1.89 – 1.53 (m, 6H), 1.42 (s, 9H), 1.32 – 1.07 (m, 5H), 1.03 – 0.83 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  157.2, 79.5, 65.2, 63.4, 44.4, 32.7, 28.4, 27.9, 27.7, 27.4, 27.1, 26.6, 18.1, 17.7; FTIR (film)  $\nu$ : 3277, 2925, 2853, 1681, 1554, 1284, 1176, 1069, 1001, 718, 698  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{31}\text{NO}_3\text{Na}$   $[(\text{M}+\text{Na})^+]$  308.2202; found 308.2196.

### **16. Synthesis of 1,2-amino alcohols **17****



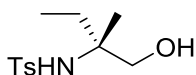
**Method A, general procedure:** *N*-Boc protected amino alcohol **16** (0.5 mmol) was dissolved in 4 M HCl/dioxane (1 mL) under an argon atmosphere. The progress of the reaction was followed by TLC. After 1 h, solvent was evaporated and crude residue was dissolved in  $\text{CH}_2\text{Cl}_2$  (0.2 M). Next,  $\text{Et}_3\text{N}$  (2 mmol, 202 mg, 279  $\mu\text{L}$ ) was added and reaction mixture was stirred for 10 min. After that, TsCl (0.5 mmol, 95 mg) was added portionwise and reaction was left to stand overnight. Next,



volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (5–30% AcOEt in hexanes).

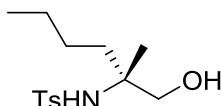
**Method B, general procedure:** *N*-Boc protected amino alcohol **16** (0.5 mmol) was dissolved in 4 M HCl/dioxane (1 mL) under an argon atmosphere. The progress of the reaction was followed by TLC. After 1 h, solvent was evaporated and crude residue was dissolved in MeCN (0.15 M). Next, TMEDA (3.5 mmol, 407 mg, 528  $\mu$ L) was added and reaction mixture was stirred for 10 min. After that, TsCl (0.5 mmol, 95 mg) was added portionwise and reaction was left to stir for 3 days. Next, volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (5–30% AcOEt in hexanes).

***N*-Ts (*R*)-2-amino-2-methylbutan-1-ol (17a):**



Method A. Yield 41 mg (75%) starting from 43 mg of *N*-Boc amino alcohol **16a**; colourless oil;  $[\alpha]_D^{25}$  -0.7 (c 1.22, CHCl<sub>3</sub>, ee 96%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.87 – 7.69 (m, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 4.77 (br s, 1H), 3.59 – 3.41 (m, 2H), 2.42 (s, 3H), 1.57 – 1.45 (m, 2H), 1.04 (s, 3H), 0.79 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  143.3, 139.8, 129.6, 127.0, 68.0, 61.1, 30.3, 21.5, 20.6, 7.6; FTIR (film)  $\nu$ : 3490, 3287, 2951, 2939, 1476, 1321, 1321, 1154, 1101, 1051, 664 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>12</sub>H<sub>19</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 280.0983; found 280.0989.

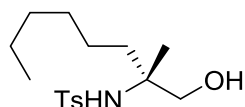
***N*-Ts (*R*)-2-amino-2-methylhexan-1-ol (17b)**



Method A. Yield 88 mg (90%) starting from 80 mg of *N*-Boc amino alcohol **16b**; colourless oil;  $[\alpha]_D^{25}$  -0.1 (c 1.30, CHCl<sub>3</sub>, ee 94%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.79 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 5.06 (br s, 1H), 3.68 – 3.33 (m, 2H), 2.41 (s,

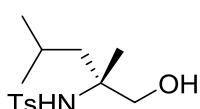
3H), 1.50 – 0.99 (m, 9H), 0.78 (t,  $J = 6.5$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.2, 139.9, 129.6, 127.0, 68.4, 60.9, 37.3, 25.4, 22.9, 21.5, 21.3, 13.9; FTIR (film)  $\nu$ : 3496, 3279, 2955, 2931, 1466, 1322, 1304, 1151, 1094, 1048, 815, 663, 551  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  308.1296; found 308.1293.

***N*-Ts (*R*)-2-amino-2-methyloctan-1-ol (17c):**



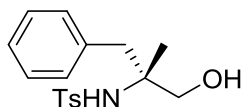
Method A. Yield 145 mg (80%) starting from 150 mg of *N*-Boc amino alcohol **16c**; colourless oil;  $[\alpha]_{\text{D}}^{25} -5.2$  (c 2.21,  $\text{CHCl}_3$ ,  $ee$  94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.84 – 7.75 (m, 2H), 7.33 – 7.26 (m, 2H), 4.89 (br s, 1H), 3.54 (d,  $J = 11.6$  Hz, 1H), 3.46 (d,  $J = 11.6$  Hz, 1H), 2.41 (s, 3H), 1.47 – 1.05 (m, 10H), 1.05 (s, 3H), 0.84 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 139.8, 129.6, 127.1, 68.4, 61.0, 37.5, 31.7, 29.5, 23.2, 22.5, 21.5, 21.4, 14.0; FTIR (film)  $\nu$ : 3498, 3278, 2928, 2858, 1322, 1304, 1153, 1094, 1055, 815, 663, 551  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{27}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  336.1609; found 336.1605.

***N*-Ts (*R*)-2-amino-2,4-dimethylpentan-1-ol (17d):**



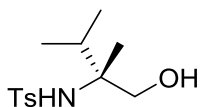
Method A. Yield 89 mg (72%) starting from 100 mg of *N*-Boc amino alcohol **16d**; colourless oil;  $[\alpha]_{\text{D}}^{22} +1.2$  (c 4.40,  $\text{CHCl}_3$ ,  $ee$  92%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 (d,  $J = 8.0$  Hz, 2H), 7.27 (d,  $J = 8.0$  Hz, 2H), 5.04 (br s, 1H), 3.47 (s, 2H), 2.65 – 2.44 (m, 1H), 2.40 (s, 3H), 1.79 – 1.51 (m, 1H), 1.49 – 1.21 (m, 2H), 1.08 (s, 3H), 0.97 – 0.71 (m, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.2, 140.0, 129.6, 127.0, 68.7, 61.4, 46.7, 24.8, 24.7, 23.6, 21.5, 21.1; FTIR (film)  $\nu$ : 3490, 3273, 2945, 2934, 1469, 1320, 1314, 1150, 1089, 1043, 811, 666, 554  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{23}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  308.1296; found 308.1288.

***N*-Ts (*R*)-2-amino-2-methyl-3-phenylpropan-1-ol (17e):**



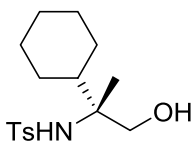
Method A. Yield 127 mg (81%) starting from 130 mg of *N*-Boc amino alcohol **16e**; waxy solid;  $[\alpha]_D^{25} +1.7$  (c 0.81, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.76 – 7.67 (m, 2H), 7.34 – 7.12 (m, 7H), 4.79 (br s, 1H), 3.64 – 3.37 (m, 2H), 2.85 (d, *J* = 3.9 Hz, 2H), 2.41 (s, 3H), 1.01 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 143.3, 139.9, 136.0, 130.7, 129.6, 128.3, 126.9, 126.8, 67.3, 60.8, 43.9, 21.5, 20.7; FTIR (film) ν: 3505, 3276, 2925, 1454, 1304, 1153, 1093, 1052, 988, 664 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>17</sub>H<sub>21</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 342.1140; found 342.1133.

***N*-Ts (*R*)-2-amino-2,3-dimethylbutan-1-ol (17f):**



Method A. Yield 76 mg (60%) starting from 102 mg of *N*-Boc aminoalcohol **16f**; colourless oil;  $[\alpha]_D^{25} +1.4$  (c 1.00, CHCl<sub>3</sub>, ee 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.79 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 4.90 (br s, 1H), 3.58 (s, 2H), 2.41 (s, 3H), 1.99 – 1.80 (m, 1H), 0.94 (s, 3H), 0.81 (s, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 143.2, 139.8, 129.6, 127.0, 66.9, 63.9, 33.3, 21.5, 17.0, 16.7, 16.0; FTIR (film) ν: 3479, 3271, 2929, 2849, 1327, 1311, 1155, 1097, 1051, 816, 664 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>13</sub>H<sub>21</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 294.1140; found 294.1145.

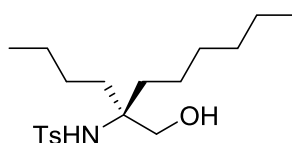
***N*-Ts (*R*)-2-amino-2-cyclohexylpropan-1-ol (17g):**



Method A. Yield 84 mg (69%) starting from 106 mg of *N*-Boc aminoalcohol **16g**; waxy solid;  $[\alpha]_D^{24} -2.6$  (c 1.86, CHCl<sub>3</sub>, ee 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.78 (d, *J*

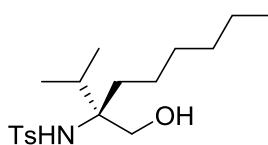
= 8.0 Hz, 2H), 7.28 (d,  $J = 8.0$  Hz, 2H), 4.85 (br s, 1H), 3.71 – 3.44 (m, 2H), 2.41 (s, 3H), 1.81 – 1.41 (m, 5H), 1.35 – 0.70 (m, 9H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.2, 139.9, 129.6, 127.1, 66.7, 63.8, 43.5, 27.2, 26.8, 26.5, 26.4, 26.3, 21.5, 17.5; FTIR (film)  $\nu$ : 3501, 3280, 2926, 2854, 1449, 1305, 1153, 1093, 663, 553  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{25}\text{NO}_3\text{SNa}$  [(M+Na) $^+$ ] 334.1453; found 334.1444.

### ***N*-Ts (S)-2-amino-2-butyloctan-1-ol (17h)**



Method A. Yield 73 mg (78%) starting from 82 mg of *N*-Boc aminoalcohol **16h**; waxy solid;  $[\alpha]_{\text{D}}^{24} +3.2$  ( $c$  1.40,  $\text{CHCl}_3$ ,  $ee$  82%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (d,  $J = 8.0$  Hz, 2H), 7.28 (d,  $J = 8.0$  Hz, 2H), 4.77 (s, 1H), 3.56 (s, 2H), 2.63 (br s, 1H), 2.41 (s, 3H), 1.47 – 0.92 (m, 16H), 0.83 (t,  $J = 7.2$  Hz, 3H), 0.77 (t,  $J = 6.7$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 139.7, 129.6, 127.1, 65.9, 64.2, 33.7, 33.5, 31.6, 29.4, 24.9, 22.8, 22.7, 22.6, 21.4, 14.0, 13.8; FTIR (film)  $\nu$ : 3357, 3310, 2922, 2852, 1659, 1632, 1467, 1154  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{19}\text{H}_{33}\text{NO}_3\text{SNa}$  [(M+Na) $^+$ ] 378.2079; found 378.2078.

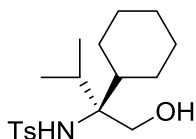
### ***N*-Ts (R)-2-amino-2-isopropyloctan-1-ol (17i):**



Method B. Yield 90 mg (76%) starting from 100 mg of *N*-Boc aminoalcohol **16i**; waxy solid;  $[\alpha]_{\text{D}}^{25} +10.0$  ( $c$  0.66,  $\text{CHCl}_3$ ,  $ee$  95%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 (d,  $J = 8.0$  Hz, 2H), 7.28 (d,  $J = 8.0$  Hz, 2H), 4.79 (br s, 1H), 3.86 – 3.52 (m, 2H), 3.03 (br s, 1H), 2.41 (s, 3H), 1.98 – 1.77 (m, 1H), 1.51 – 0.62 (m, 19H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 139.8, 129.5, 127.0, 66.6, 65.8, 32.9, 32.6, 31.6, 29.7, 22.8, 22.6, 21.5, 17.1,

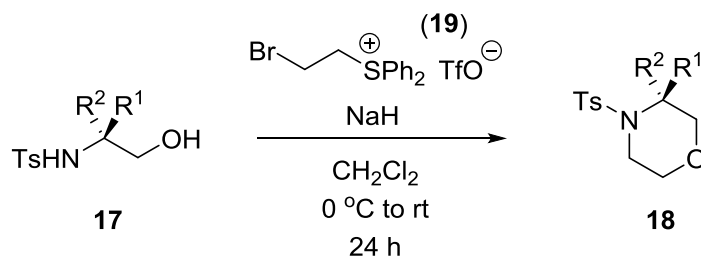
16.6, 14.0; FTIR (film)  $\nu$ : 3359, 3312, 2932, 2858, 1665, 1636, 1462, 1151  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{31}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  364.1922; found 364.1929.

### ***N*-Ts (*S*)-2-amino-2-cyclohexyl-3-methylbutan-1-ol (**17j**):**



Method B. Yield 56 mg (47%) starting from 100 mg of *N*-Boc aminoalcohol **16j**; waxy solid;  $[\alpha]_{\text{D}}^{26} -3.0$  ( $c$  0.79,  $\text{CHCl}_3$ ,  $ee$  79%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.72 (d,  $J$  = 8.2 Hz, 2H), 7.22 (d,  $J$  = 8.2 Hz, 2H), 4.42 (s, 1H), 3.82 (d,  $J$  = 12.6 Hz, 1H), 3.74 (d,  $J$  = 12.6 Hz, 1H), 2.82 (br s, 1H), 2.35 (s, 3H), 1.89 (hept,  $J$  = 6.9 Hz, 1H), 1.78 – 1.40 (m, 6H), 1.28 – 0.93 (m, 5H), 0.88 (d,  $J$  = 6.9 Hz, 3H), 0.73 (d,  $J$  = 6.9 Hz, 3H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.2, 139.9, 129.5, 126.9, 69.6, 63.6, 44.6, 33.2, 28.3, 27.9, 27.2, 26.9, 26.4, 21.5, 18.4, 17.9; FTIR (film)  $\nu$ : 3500, 3275, 2927, 2861, 1451, 1315, 1155, 1092, 549  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{29}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  362.1766; found 362.1761.

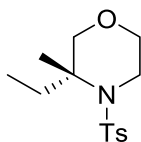
## **17. The synthesis of morpholines **18****



**General procedure:**<sup>5</sup> NaH (3.5 equiv., 0.56 mmol, 60% in mineral oil, 22 mg) and then bromoethylsulfonium triflate **19** (1.2 equiv, 0.19 mmol, 85 mg) were slowly added to a stirred solution of **17** (1 equiv, 0.16 mmol) in  $\text{CH}_2\text{Cl}_2$  (0.02 M) at 0 °C. The reaction was stirred at 0 °C for 2 h, then warmed to room temperature and stirred overnight. The mixture was quenched by addition of water and then extracted with  $\text{CH}_2\text{Cl}_2$ . The combined organic phases were dried over anhydrous

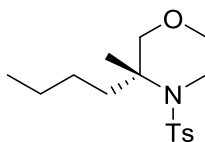
Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvents, the residue was purified by a column chromatography on silica gel (5-20% AcOEt in hexanes).

***N*-Ts (*R*)-3-ethyl-3-methyl-morpholine (18a):**



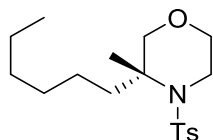
Yield 29 mg (72%) starting from 36 mg of **17a**; yellow oil;  $[\alpha]_D^{24} -10.1$  (*c* 0.70, CHCl<sub>3</sub>, *ee* 96%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.71 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 3.86 – 3.74 (m, 1H), 3.67 – 3.47 (m, 3H), 3.46 – 3.35 (m, 1H), 3.18 (d, *J* = 11.7 Hz, 1H), 2.42 (s, 3H), 1.99 – 1.71 (m, 2H), 1.25 (s, 3H), 0.87 (t, *J* = 7.5 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  143.0, 139.8, 129.5, 127.0, 74.3, 67.2, 61.0, 42.9, 26.6, 21.5, 20.5, 8.5; FTIR (film)  $\nu$ : 2962, 2923, 2853, 1459, 1330, 1159, 1123, 955, 814, 680, 551 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>14</sub>H<sub>21</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 306.1140; found 306.1129.

***N*-Ts (*R*)-3-butyl-3-methyl-morpholine (18b):**



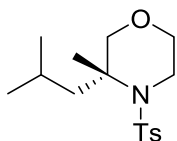
Yield 31 mg (71%) starting from 41 mg of **17b**; yellowish oil;  $[\alpha]_D^{24} -30.1$  (*c* 0.73, CHCl<sub>3</sub>, *ee* 94%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.70 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 3.91 – 3.70 (m, 1H), 3.67 – 3.35 (m, 4H), 3.16 (d, *J* = 11.6 Hz, 1H), 2.41 (s, 3H), 1.92 – 1.66 (m, 2H), 1.46 – 1.11 (m, 7H), 0.86 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  143.0, 139.8, 129.5, 127.0, 74.8, 67.3, 60.7, 43.0, 33.8, 26.2, 23.1, 21.4, 21.1, 13.9; FTIR (film)  $\nu$ : 2956, 2927, 2859, 1459, 1333, 1160, 1124, 957, 814, 684, 549 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>16</sub>H<sub>25</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 334.1453; found 334.1447.

***N*-Ts (*R*)-3-hexyl-3-methyl-morpholine (18c):**



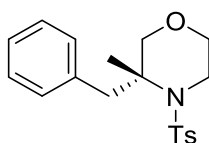
Yield 40 mg (74%) starting from 50 mg of **17c**; yellowish oil;  $[\alpha]_D^{24}$   $-31.9$  (c 1.20,  $\text{CHCl}_3$ , ee 94%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (d,  $J = 8.0$  Hz, 2H), 7.27 (d,  $J = 8.0$  Hz, 2H), 3.86 – 3.73 (m, 1H), 3.64 – 3.34 (m, 4H), 3.16 (d,  $J = 11.6$  Hz, 1H), 2.41 (s, 3H), 1.93 – 1.65 (m, 2H), 1.34 – 1.12 (m, 11H), 0.6 (t,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.0, 139.8, 129.5, 127.0, 74.7, 67.3, 60.7, 43.0, 34.0, 31.7, 29.7, 24.0, 22.6, 21.4, 21.1, 14.0; FTIR (film)  $\nu$ : 2954, 2926, 2856, 1460, 1333, 1161, 1124, 956, 684, 549  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{29}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  362.1766; found 362.1760.

#### ***N*-Ts (*R*)-3-isobutyl-3-methyl-4-tosylmorpholine (**18d**):**



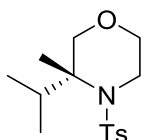
Yield 33 mg (70%) starting from 43 mg of **17d**; waxy solid;  $[\alpha]_D^{24}$   $-29.3$  (c 0.84,  $\text{CHCl}_3$ , ee 92%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.69 (d,  $J = 8.1$  Hz, 2H), 7.27 (d,  $J = 8.1$  Hz, 2H), 3.89 – 3.74 (m, 1H), 3.65 – 3.45 (m, 3H), 3.45 – 3.30 (m, 1H), 3.14 (d,  $J = 11.7$  Hz, 1H), 2.41 (s, 3H), 1.78 – 1.71 (m, 2H), 1.69 – 1.59 (m, 1H), 1.33 (s, 3H), 0.92 (d,  $J = 6.6$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.0, 140.0, 129.5, 127.0, 75.1, 67.2, 61.1, 43.0, 42.2, 25.0, 24.8, 24.0, 21.8, 21.4; FTIR (film)  $\nu$ : 2956, 2927, 2869, 1329, 1162, 1125, 957, 686, 549  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{25}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  334.1453; found 334.1444.

#### ***N*-Ts (*R*)-3-benzyl-3-methyl-morpholine (**18e**):**



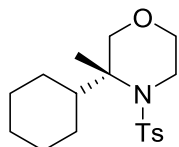
Yield 55 mg (99%) starting from 50 mg of **17e**; waxy solid;  $[\alpha]_D^{24} +26.5$  (c 1.27, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.75 (d, *J* = 8.0 Hz, 2H), 7.43 – 7.06 (m, 7H), 4.00 (d, *J* = 8.8 Hz, 1H), 3.85 – 3.51 (m, 3H), 3.50 – 3.30 (m, 2H), 3.06 – 2.78 (m, 2H), 2.42 (s, 3H), 1.19 (s, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  143.2, 139.8, 136.9, 130.8, 129.6, 128.1, 127.0, 126.5, 73.2, 67.5, 60.7, 43.0, 38.7, 21.5, 21.2; FTIR (film)  $\nu$ : 2925, 2854, 1457, 1326, 1161, 1122, 956, 708, 686, 555 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>19</sub>H<sub>23</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 368.1296; found 368.1283.

### ***N*-Ts (*R*)-3-isopropyl-3-methyl-morpholine (18f)**



Yield 40 mg (75%) starting from 48 mg of **17e**; yellow oil;  $[\alpha]_D^{24} -37.1$  (c 1.22, CHCl<sub>3</sub>, ee 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.71 (d, *J* = 8.0 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 3.90 – 3.58 (m, 3H), 3.55 – 3.35 (m, 2H), 3.07 (d, *J* = 11.8 Hz, 1H), 2.70 (hept, *J* = 7.2 Hz, 1H), 2.41 (s, 3H), 1.21 (s, 3H), 1.02 (d, *J* = 6.9 Hz, 3H), 0.89 (d, *J* = 6.9 Hz, 3H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  142.7, 140.9, 129.5, 126.7, 73.1, 66.8, 64.3, 42.8, 28.4, 21.4, 17.6, 17.1, 16.2; FTIR (film)  $\nu$ : 2966, 2926, 1331, 1157, 1124, 957, 677, 553 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>15</sub>H<sub>23</sub>NO<sub>3</sub>SNa [(M+Na)<sup>+</sup>] 320.1296; found 320.1289.

### ***N*-Ts (*R*)-3-cyclohexyl-3-methyl-morpholine (18g):**

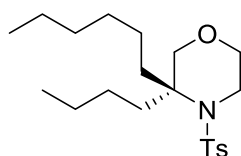


Yield 39 mg (72%) starting from 50 mg of **17g**; waxy solid;  $[\alpha]_D^{25} -59.9$  (c 1.24, CHCl<sub>3</sub>, ee 88%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.70 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 8.1 Hz, 2H), 3.89 – 3.57 (m, 2H), 3.52 – 3.33 (m, 2H), 3.02 (d, *J* = 11.8 Hz, 1H), 2.41 (s, 3H), 2.33 – 2.17 (m, 1H), 1.95 – 1.81 (m, 2H), 1.81 – 1.55 (m, 3H), 1.40 – 0.98 (m, 8H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  142.6, 141.1, 129.5, 126.6, 72.8, 66.8, 64.3, 42.9, 38.5, 28.0, 27.0,



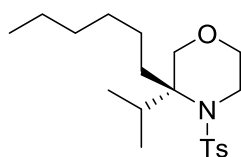
26.9, 26.8, 26.4, 21.4, 17.5; FTIR (film)  $\nu$ : 2927, 2852, 1452, 1334, 1293, 1157, 1120, 958, 689, 545  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{21}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  360.1609; found 360.1599.

### ***N*-Ts (*S*)-3-butyl-3-hexyl-morpholine (18h)**



Yield 29 mg (68%) starting from 40 mg of **17h**; colourless oil;  $[\alpha]_{\text{D}}^{25}$   $-0.7$  ( $c$  0.60,  $\text{CHCl}_3$ ,  $ee$  82%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.73 (d,  $J = 8.1$  Hz, 2H), 7.27 (d,  $J = 8.1$  Hz, 2H), 3.73 – 3.55 (m, 2H), 3.48 (s, 2H), 3.41 – 3.26 (m, 2H), 2.41 (s, 3H), 2.05 – 1.83 (m, 2H), 1.83 – 1.63 (m, 2H), 1.49 – 1.05 (m, 12H), 0.87 (t,  $J = 6.8$  Hz, 6H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.1, 139.0, 129.4, 127.4, 72.7, 66.8, 64.5, 43.4, 33.9, 33.6, 31.7, 29.9, 26.2, 24.0, 23.3, 22.6, 21.4, 14.1, 14.0; FTIR (film)  $\nu$ : 2955, 2928, 2860, 1461, 1330, 1160, 1127, 1095, 684  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{35}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  404.2235; found 404.2225.

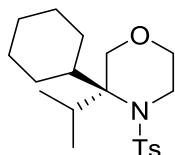
### ***N*-Ts (*R*)-3-hexyl-3-isopropyl-morpholine (18i)**



Yield 46 mg (72%) starting from 60 mg of **17i**; colourless oil;  $[\alpha]_{\text{D}}^{25}$   $-9.0$  ( $c$  0.84,  $\text{CHCl}_3$ ,  $ee$  95%);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.75 (d,  $J = 8.0$  Hz, 2H), 7.28 (d,  $J = 8.0$  Hz, 2H), 3.80 – 3.65 (m, 2H), 3.65 – 3.55 (m, 1H), 3.51 (d,  $J = 12.1$  Hz, 1H), 3.43 – 3.25 (m, 2H), 2.88 – 2.71 (m, 1H), 2.41 (s, 3H), 2.19 – 2.02 (m, 1H), 1.66 – 1.51 (m, 1H), 1.50 – 1.09 (m, 8H), 1.07 – 0.93 (m, 6H), 0.87 (t,  $J = 6.8$  Hz, 3H);  $^{13}\text{C}$  NMR (101 MHz,  $\text{CDCl}_3$ )  $\delta$  142.9, 138.7, 129.4, 127.3, 70.4, 67.9, 66.2, 43.7, 33.6, 32.3, 31.8, 30.1, 24.4, 22.7, 21.4, 19.1, 17.9, 14.1; FTIR (film)  $\nu$ : 2956, 2926, 1464, 1329, 1160, 1095, 950,

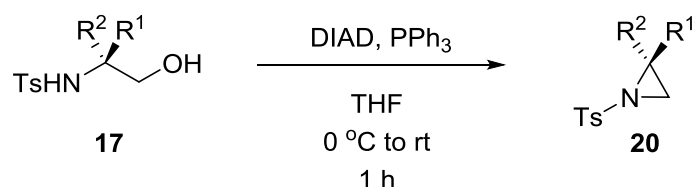
677, 552  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{33}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  390.2079; found 390.2073.

### ***N*-Ts (*S*)-3-cyclohexyl-3-isopropyl-morpholine (18j):**



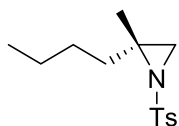
Yield 38 mg (77%) starting from 46 mg of **17j**; waxy solid;  $[\alpha]_{\text{D}}^{25} -7.3$  ( $c$  0.95,  $\text{CHCl}_3$ ,  $ee$  79%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 (d,  $J = 8.0$  Hz, 2H), 7.28 (d,  $J = 8.0$  Hz, 2H), 3.81 (d,  $J = 12.4$  Hz, 1H), 3.71 (d,  $J = 12.4$  Hz, 1H), 3.67 – 3.49 (m, 2H), 3.39 – 3.11 (m, 2H), 2.97 – 2.75 (m, 1H), 2.53 – 2.27 (m, 4H), 2.22 – 1.96 (m, 2H), 1.88 – 1.62 (m, 3H), 1.44 – 0.98 (m, 11H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.1, 138.3, 129.5, 127.6, 71.4, 68.6, 65.7, 43.7, 43.6, 31.9, 30.0, 29.2, 27.4, 27.3, 26.7, 21.4, 20.2, 18.9; FTIR (film)  $\nu$ : 2925, 2858, 1442, 1337, 1290, 1150, 1121, 942, 667  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{20}\text{H}_{31}\text{NO}_3\text{SNa}$   $[(\text{M}+\text{Na})^+]$  388.1922; found 388.1928.

### **18. The synthesis of aziridines 20**



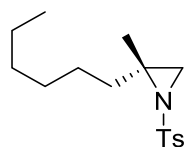
**General procedure:** DIAD (1.1 equiv, 0.19 mmol, 38 mg, 37  $\mu\text{L}$ ) was added dropwise to a stirred solution of 1,2-amino alcohol **17** (1 equiv, 0.175 mmol) and  $\text{Ph}_3\text{P}$  (0.19 mmol, 50 mg) in THF (0.1 M) at 0  $^\circ\text{C}$ . After that, the reaction was slowly warmed to room temperature and stirred for 1 h. Next, volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (2–20% AcOEt in hexanes).

### ***N*-Ts (*R*)-2-butyl-2-methyl-aziridine (20a):**



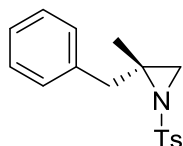
Yield 41 mg (88%) starting from 50 mg of **17b**; colourless oil;  $[\alpha]_D^{26} -12.5$  (c 0.91,  $\text{CHCl}_3$ , ee 94%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81 (d,  $J = 7.9$  Hz, 2H), 7.29 (d,  $J = 7.9$  Hz, 2H), 2.53 (s, 1H), 2.41 (s, 3H), 2.27 (s, 1H), 1.73 – 1.51 (m, 5H), 1.47 – 1.19 (m, 4H), 0.88 (t,  $J = 7.1$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.6, 138.2, 129.4, 127.3, 51.1, 41.4, 37.5, 27.9, 22.5, 21.5, 18.6, 13.9; FTIR (film)  $\nu$ : 2955, 2933, 2862, 1451, 1331, 1168, 949, 711, 569  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{14}\text{H}_{21}\text{NO}_2\text{SNa}$   $[(\text{M}+\text{Na})^+]$  290.1191; found 290.1195.

***N*-Ts (R)-2-hexyl-2-methyl-1-tosylaziridine (20b):**



Yield 42 mg (88%) starting from 50 mg of **17c**; colourless oil;  $[\alpha]_D^{27} -16.8$  (c 0.97,  $\text{CHCl}_3$ , ee 94%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.81 (d,  $J = 7.9$  Hz, 2H), 7.29 (d,  $J = 7.9$  Hz, 2H), 2.53 (s, 1H), 2.42 (s, 3H), 2.27 (s, 1H), 1.81 – 1.10 (m, 13H), 0.87 (t,  $J = 6.4$  Hz, 3H);  $^{13}\text{C NMR}$  (101 MHz,  $\text{CDCl}_3$ )  $\delta$  143.6, 138.2, 129.4, 127.3, 51.1, 41.4, 37.8, 31.6, 29.0, 25.7, 22.5, 21.5, 18.6, 14.0; FTIR (film)  $\nu$ : 2954, 2930, 2858, 1457, 1321, 1160, 947, 831, 710, 574  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{16}\text{H}_{25}\text{NO}_2\text{SNa}$   $[(\text{M}+\text{Na})^+]$  318.1504; found 318.1496.

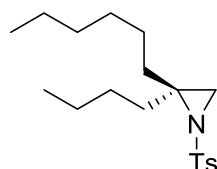
***N*-Ts (R)-2-benzyl-2-methyl-aziridine (20c):**



Yield 47 mg (99%) starting from 50 mg of **17e**; yellowish oil;  $[\alpha]_D^{29} -41.5$  (c 0.95,  $\text{CHCl}_3$ , ee 98%);  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )  $\delta$  7.89 – 7.73 (m, 2H), 7.38 – 7.11 (m, 7H), 2.94 (s, 2H), 2.60 (s, 1H), 2.43 (s, 3H), 2.41 (s, 1H), 1.58 (s, 3H);  $^{13}\text{C NMR}$  (101 MHz,

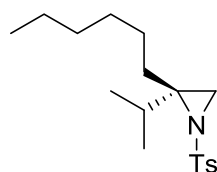
CDCl<sub>3</sub>)  $\delta$  143.8, 137.9, 136.9, 129.5, 129.5, 128.4, 127.4, 126.8, 50.8, 44.0, 40.3, 21.6, 18.4; FTIR (film)  $\nu$ : 3062, 3029, 2980, 2928, 1732, 1453, 1319, 1158, 821, 708, 570 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>17</sub>H<sub>19</sub>NO<sub>2</sub>SNa [(M+Na)<sup>+</sup>] 324.1034; found 324.1027.

#### ***N*-Ts (*S*)-2-butyl-2-hexyl-aziridine (20d)**



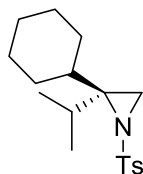
Yield 45 mg (89%) starting from 53 mg of **17h**; yellowish oil;  $[\alpha]_D^{24}$  +0.1 (c 1.00, CHCl<sub>3</sub>, ee 82%); <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.81 (d,  $J$  = 7.9 Hz, 2H), 7.30 (d,  $J$  = 7.9 Hz, 2H), 2.42 (s, 3H), 2.39 (s, 2H), 1.91 – 1.78 (m, 2H), 1.78 – 1.64 (m, 2H), 1.53 – 1.15 (m, 11H), 1.00 – 0.73 (m, 6H); <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>)  $\delta$  143.5, 138.4, 129.4, 127.3, 54.9, 41.0, 32.8, 32.5, 31.7, 29.1, 28.1, 25.9, 22.6, 21.5, 14.0, 14.0; FTIR (film)  $\nu$ : 2956, 2943, 2859, 1450, 1311, 1164, 942, 710, 544 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>19</sub>H<sub>31</sub>NO<sub>2</sub>SNa [(M+Na)<sup>+</sup>] 360.1973; found 360.1977.

#### ***N*-Ts (*R*)-2-hexyl-2-isopropyl-aziridine (20e)**



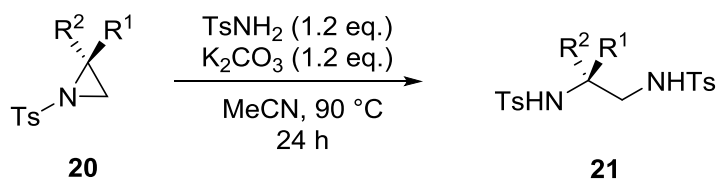
Yield 35 mg (93%) starting from 40 mg of **17i**; colourless oil;  $[\alpha]_D^{25}$  -7.3 (c 0.94, CHCl<sub>3</sub>, ee 95%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.75 (d,  $J$  = 8.0 Hz, 2H), 7.23 (d,  $J$  = 8.0 Hz, 2H), 2.44 (s, 1H), 2.36 (s, 3H), 2.26 (s, 1H), 2.07 – 1.82 (m, 2H), 1.45 – 1.11 (m, 5H), 0.93 (d,  $J$  = 6.8 Hz, 3H), 0.87 – 0.70 (m, 6H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  146.3, 141.4, 132.2, 130.1, 61.5, 41.7, 34.6, 33.6, 32.8, 32.2, 29.6, 25.4, 24.4, 22.1, 20.7, 16.9; FTIR (film)  $\nu$ : 2957, 2940, 2865, 1452, 1310, 1174, 949, 699, 544 cm<sup>-1</sup>; HRMS (ESI-TOF)  $m/z$  calcd for C<sub>18</sub>H<sub>29</sub>NO<sub>2</sub>SNa [(M+Na)<sup>+</sup>] 346.1817; found 346.1820.

### ***N*-Ts (*S*)-2-cyclohexyl-2-isopropyl-aziridine (**20f**):**



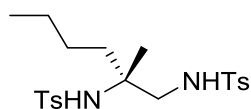
Yield 38 mg (98%) starting from 42 mg of **17j**; waxy solid; *ee* 79%;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.82 (d,  $J = 8.1$  Hz, 2H), 7.30 (d,  $J = 8.1$  Hz, 2H), 2.43 (s, 3H), 2.39 (s, 2H), 2.30 (hept,  $J = 7.0$  Hz, 1H), 1.96 – 1.83 (m, 1H), 1.83 – 1.68 (m, 4H), 1.65 (d,  $J = 13.2$  Hz, 1H), 1.47 – 1.16 (m, 5H), 1.15 – 0.92 (m, 8H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 138.7, 129.3, 127.3, 63.7, 39.4, 38.9, 31.6, 30.5, 30.4, 26.6, 26.4, 26.1, 21.5, 21.2, 19.6; FTIR (film)  $\nu$ : 2951, 2943, 2867, 1443, 1315, 1161, 974, 713, 546  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{18}\text{H}_{27}\text{NO}_2\text{SNa}$  [( $\text{M}+\text{Na}$ ) $^+$ ] 344.1660; found 344.1663.

### **19. The synthesis of 1,2 diamines **21****



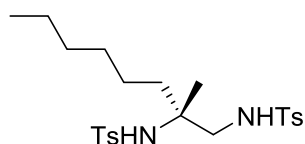
**General procedure:**<sup>6</sup> A suspension of aziridine **20** (1 equiv, 0.2 mmol), *p*-toluenesulfonamide (1.2 equiv, 0.24 mmol, 41 mg) and potassium carbonate (1.2 equiv, 0.24 mmol, 33 mg) in acetonitrile (0.1 M, 2 mL) was heated at 90 °C for 24–72 h. The progress of the reaction was followed by TLC. After the complete consumption of a starting material, the reaction mixture was cooled to rt. After that, the volatiles were removed under reduced pressure. The residue was purified by a flash chromatography on a silica gel (5–40% AcOEt in hexanes).

### ***N,N'*-diTs (*R*)-2-methylhexane-1,2-diamine (**21a**)**



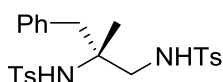
The reaction was kept at 90 °C for 24 h. Yield 60 mg (84%) starting from 43 mg of aziridine **20a**; colourless oil;  $[\alpha]_{\text{D}}^{28} -3.9$  (c 0.58,  $\text{CHCl}_3$ , ee 94%);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.79 – 7.64 (m, 4H), 7.31 (d,  $J = 7.9$  Hz, 2H), 7.27 (d,  $J = 7.5$  Hz, 2H), 5.22 (t,  $J = 7.1$  Hz, 1H), 4.74 (s, 1H), 3.08 – 2.89 (m, 2H), 2.43 (s, 3H), 2.42 (s, 3H), 1.50 – 0.94 (m, 9H), 0.76 (t,  $J = 6.9$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 143.3, 139.7, 137.1, 129.7, 129.6, 126.9, 126.9, 59.5, 50.8, 37.9, 25.1, 22.6, 22.5, 21.4, 21.4, 13.7; FTIR (film)  $\nu$ : 3282, 2955, 2932, 2871, 1454, 1426, 1326, 1159, 1092, 815, 664, 553  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{21}\text{H}_{30}\text{N}_2\text{O}_4\text{S}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  461.1545; found 461.1537.

***N,N'*-diTs (*R*)-2-methyloctane-1,2-diamine (21b):**



The reaction was kept at 90 °C for 24 h. Yield 43 mg (75%) starting from 36 mg of aziridine **20b**; colourless oil;  $[\alpha]_{\text{D}}^{28} -5.6$  (c 0.48,  $\text{CHCl}_3$ , ee 94%);  $^1\text{H NMR}$  (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.78 – 7.50 (m, 4H), 7.34 – 7.00 (m, 4H), 5.36 (t,  $J = 7.0$  Hz, 1H), 5.00 (s, 1H), 2.96 (dd,  $J = 13.2, 7.0$  Hz, 1H), 2.88 (dd,  $J = 13.2, 7.0$  Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H), 1.47 – 0.80 (m, 13H), 0.75 (t,  $J = 7.3$  Hz, 3H);  $^{13}\text{C NMR}$  (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.3, 143.3, 139.6, 137.2, 129.7, 129.6, 126.9, 126.9, 59.5, 50.9, 38.1, 31.6, 29.2, 23.0, 22.5, 22.5, 21.5, 21.4, 14.0; FTIR (film)  $\nu$ : 3289, 2961, 2931, 2861, 1459, 1423, 1320, 1165, 1096, 819, 666, 552  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{23}\text{H}_{34}\text{N}_2\text{O}_4\text{S}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  489.1858; found 489.1851.

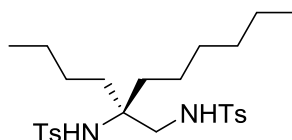
***N,N'*-diTs (*R*)-2-methyl-3-phenylpropane-1,2-diamine (21c):**



The reaction was kept at 90 °C for 24 h. Yield 49 mg (70%) starting from 45 mg of aziridine **20c**; waxy solid;  $[\alpha]_{\text{D}}^{26} +26.0$  (c 0.78,  $\text{CHCl}_3$ , ee 98%);  $^1\text{H NMR}$  (500 MHz,

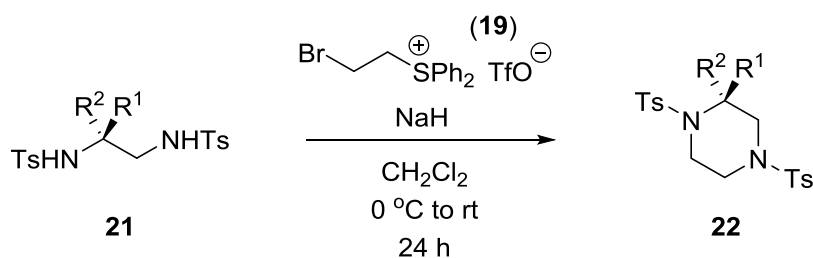
CDCl<sub>3</sub>) δ 7.6 (d, *J* = 7.9 Hz, 2H), 7.5 (d, *J* = 8.0 Hz, 2H), 7.3 – 7.0 (m, 9H), 5.2 (t, *J* = 7.0 Hz, 1H), 4.9 (s, 1H), 2.9 (d, *J* = 7.0 Hz, 2H), 2.8 (d, *J* = 13.5 Hz, 1H), 2.7 (d, *J* = 13.5 Hz, 1H), 2.3 (s, 3H), 2.3 (s, 3H), 0.9 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 143.5, 143.4, 139.5, 136.7, 135.2, 130.7, 129.7, 129.6, 128.4, 127.1, 127.0, 126.4, 59.2, 50.7, 44.8, 22.2, 21.5, 21.4; FTIR (film) *v*: 3275, 2925, 2855, 1454, 1329, 1160, 1092, 814, 664, 552 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>24</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>Na [(M+Na)<sup>+</sup>] 495.1388; found 495.1382.

### *N,N'*-diTs (*S*)-2-butyloctane-1,2-diamine (**21d**):



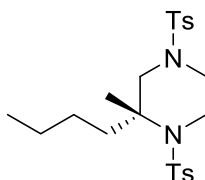
The reaction was kept at 90 °C for 72 h. Yield 43 mg (71%) starting from 40 mg of aziridine **20d**; colourless oil; [α]<sub>D</sub><sup>31</sup> +4.4 (c 0.64, CHCl<sub>3</sub>, *ee* 82%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.68 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.18 (d, *J* = 8.2 Hz, 2H), 5.30 (t, *J* = 7.1 Hz, 1H), 4.70 (s, 1H), 2.95 (d, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 2.33 (s, 3H), 1.44 – 0.78 (m, 16H), 0.76 (t, *J* = 7.3 Hz, 3H), 0.68 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 143.4, 143.2, 139.5, 137.2, 129.7, 129.6, 127.0, 62.6, 48.2, 34.1, 33.8, 31.6, 29.2, 24.6, 22.6, 22.6, 22.5, 21.5, 21.4, 14.0, 13.8; FTIR (film) *v*: 3293, 2965, 2928, 2865, 1451, 1427, 1321, 1091, 828, 667, 551 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>26</sub>H<sub>40</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>Na [(M+Na)<sup>+</sup>] 531.2327; found 531.2321.

## 20. The synthesis of piperazines **22**



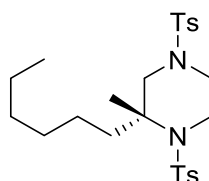
**General procedure:**<sup>5</sup> NaH (3.5 equiv., 0.56 mmol, 60% in mineral oil, 22 mg) and then bromoethylsulfonium triflate **19** (1.2 equiv, 0.19 mmol, 85 mg) were slowly added to a stirred solution of the diamine **21** (1 equiv, 0.16 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.02 M) at 0 °C. The reaction was stirred at 0 °C for 2 h, then warmed to room temperature and stirred overnight. The mixture was quenched by addition of water and then extracted with CH<sub>2</sub>Cl<sub>2</sub>. The combined organic phases were dried over anhydr. Na<sub>2</sub>SO<sub>4</sub>. After the removal of the solvents, the residue was purified by a column chromatography on silica gel (5-30% AcOEt in hexanes).

***N,N'*-diTs (*R*)-2-butyl-2-methyl-piperazine (**22a**):**



Yield 36 mg (81%) starting from 42 mg of diamine **21a**; colourless oil;  $[\alpha]_D^{25} +10.8$  (c 0.98, CHCl<sub>3</sub>, ee 94%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.64 – 7.39 (m, 4H), 7.25 (d, *J* = 7.9 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 3.85 – 3.71 (m, 1H), 3.50 – 3.31 (m, 2H), 3.14 (d, *J* = 11.8 Hz, 1H), 2.57 – 2.45 (m, 1H), 2.37 (s, 3H), 2.32 (s, 3H), 2.25 (d, *J* = 11.7 Hz, 1H), 1.75 – 1.55 (m, 2H), 1.25 (s, 3H), 1.22 – 0.94 (m, 4H), 0.77 (t, *J* = 7.0 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>) δ 143.9, 143.2, 139.5, 132.7, 129.8, 129.5, 127.6, 127.0, 61.0, 54.7, 46.1, 42.6, 34.2, 25.8, 22.9, 22.7, 21.5, 21.4, 13.8; FTIR (film) *v*: 2956, 2929, 1345, 1165, 1096, 960, 660, 604, 551 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>23</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>Na [(M+Na)<sup>+</sup>] 487.1701; found 487.1688.

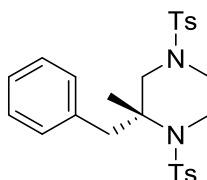
***N,N'*-diTs (*R*)-2-hexyl-2-methyl-piperazine (**22b**):**





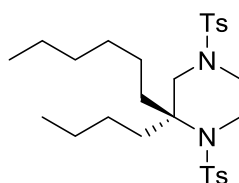
Yield 36 mg (91%) starting from 38 mg of diamine **21b**; waxy solid;  $[\alpha]_D^{25} +9.5$  (c 0.87, CHCl<sub>3</sub>, ee 94%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.60 – 7.45 (m, 4H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 3.86 – 3.72 (m, 1H), 3.48 – 3.31 (m, 2H), 3.14 (d, *J* = 11.7 Hz, 1H), 2.58 – 2.47 (m, 1H), 2.37 (s, 3H), 2.32 (s, 3H), 2.25 (d, *J* = 11.8 Hz, 1H), 1.65 (t, *J* = 7.8 Hz, 2H), 1.25 (s, 3H), 1.23 – 0.95 (m, 8H), 0.80 (t, *J* = 7.1 Hz, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  143.9, 143.2, 139.6, 132.7, 129.8, 129.5, 127.6, 127.0, 61.1, 54.7, 46.1, 42.6, 34.5, 31.6, 29.5, 23.6, 22.8, 22.5, 21.5, 21.4, 14.0; FTIR (film)  $\nu$ : 2962, 2937, 1355, 1162, 1091, 662, 603 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>25</sub>H<sub>36</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>Na [(M+Na)<sup>+</sup>] 515.2014; found 515.2019.

***N,N'*-diTs (*R*)-2-benzyl-2-methyl-piperazine (22c):**



Yield 40 mg (82%) starting from 46 mg of diamine **21c**; waxy solid;  $[\alpha]_D^{24} +102.3$  (c 1.82, CHCl<sub>3</sub>, ee 98%); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.57 (d, *J* = 8.3 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.24 – 7.11 (m, 7H), 4.01 – 3.88 (m, 1H), 3.70 – 3.59 (m, 1H), 3.58 – 3.46 (m, 1H), 3.38 – 3.19 (m, 2H), 2.64 (d, *J* = 13.0 Hz, 1H), 2.46 – 2.35 (m, 4H), 2.32 (s, 3H), 1.94 (d, *J* = 11.7 Hz, 1H), 1.13 (s, 3H); <sup>13</sup>C NMR (126 MHz, CDCl<sub>3</sub>)  $\delta$  144.2, 143.5, 139.4, 136.1, 131.9, 131.0, 129.8, 129.7, 128.2, 127.9, 127.0, 126.8, 61.1, 53.9, 46.7, 42.6, 38.8, 23.5, 21.5, 21.5; FTIR (film)  $\nu$ : 2922, 1596, 1454, 1342, 1159, 687, 597, 548 cm<sup>-1</sup>; HRMS (ESI-TOF) *m/z* calcd for C<sub>26</sub>H<sub>30</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>Na [(M+Na)<sup>+</sup>] 521.1545; found 521.1536.

***N,N'*-diTs (*S*)-2-butyl-2-hexyl-piperazine (22d):**



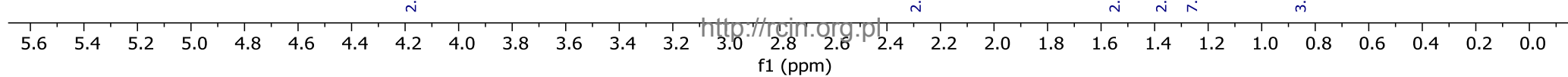
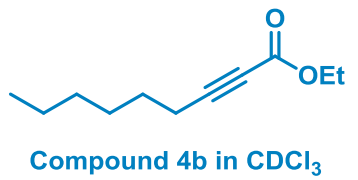
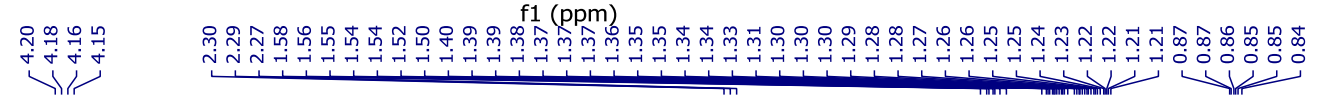
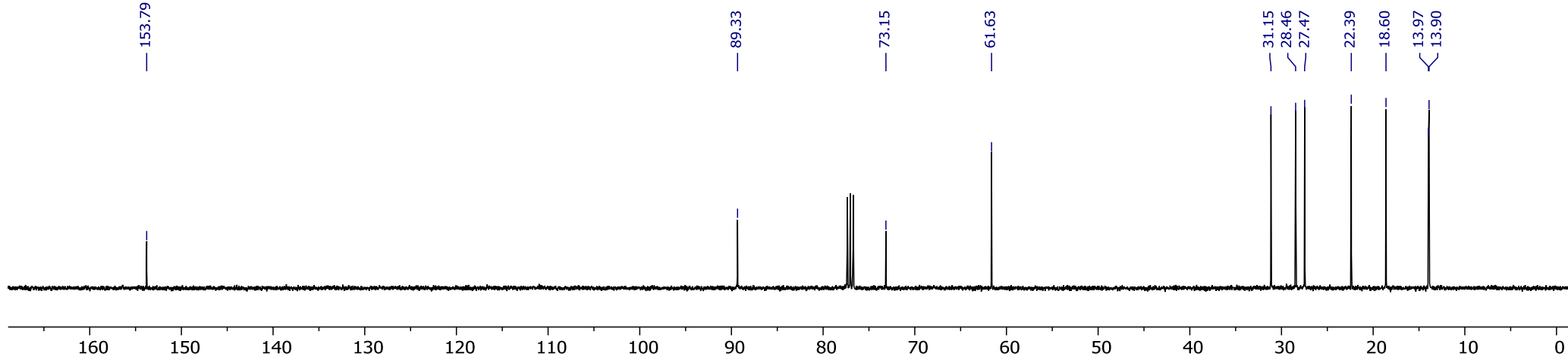
Yield 34 mg (91%) starting from 36 mg of diamine **21d**; yellow oil;  $[\alpha]_D^{24} +0.1$  (c 1.21,  $\text{CHCl}_3$ , ee 82%);  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.56 (d,  $J = 8.0$  Hz, 2H), 7.52 (d,  $J = 7.9$  Hz, 2H), 7.25 (d,  $J = 7.9$  Hz, 2H), 7.16 (d,  $J = 8.0$  Hz, 2H), 3.50 (t,  $J = 5.3$  Hz, 2H), 2.93 (t,  $J = 5.3$  Hz, 2H), 2.84 (s, 2H), 2.37 (s, 3H), 2.32 (s, 3H), 1.87 – 1.62 (m, 4H), 1.36 – 0.95 (m, 12H), 0.90 – 0.61 (m, 6H);  $^{13}\text{C}$  NMR (126 MHz,  $\text{CDCl}_3$ )  $\delta$  143.9, 143.3, 139.3, 132.8, 129.8, 129.4, 127.6, 127.3, 65.2, 52.2, 45.8, 42.8, 33.9, 33.6, 31.6, 29.6, 25.8, 23.6, 23.0, 22.6, 21.5, 21.4, 14.0, 13.9; FTIR (film)  $\nu$ : 2971, 2923, 1341, 1181, 1101, 966, 607, 559  $\text{cm}^{-1}$ ; HRMS (ESI-TOF)  $m/z$  calcd for  $\text{C}_{28}\text{H}_{42}\text{N}_2\text{O}_4\text{S}_2\text{Na}$   $[(\text{M}+\text{Na})^+]$  557.2484; found 557.2481.

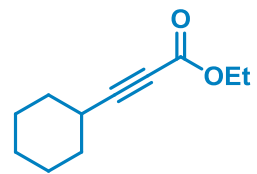
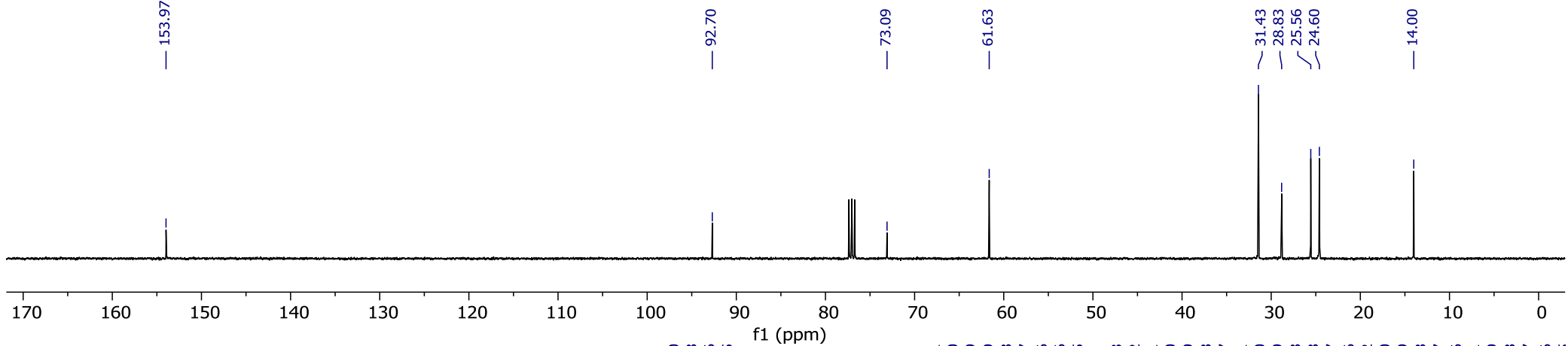
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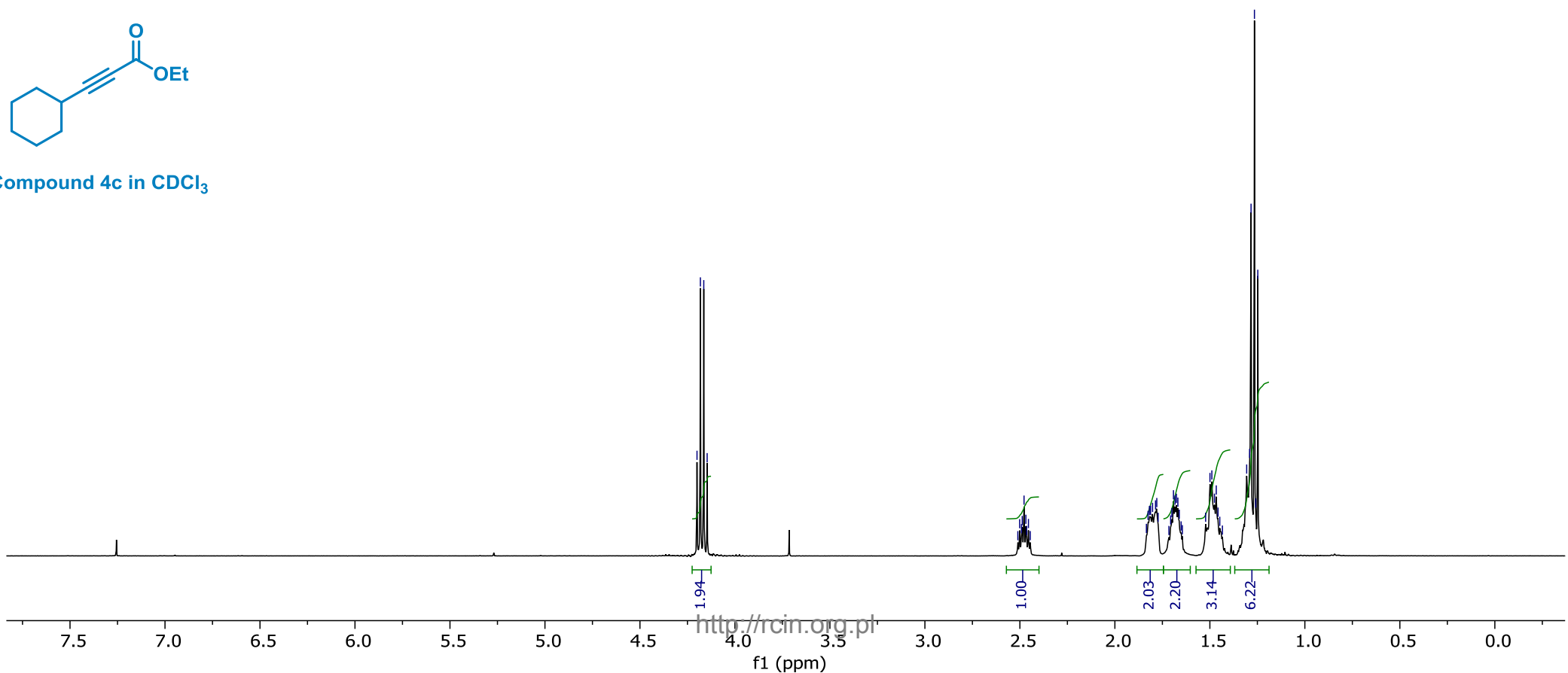
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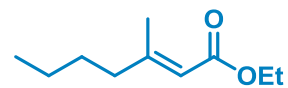
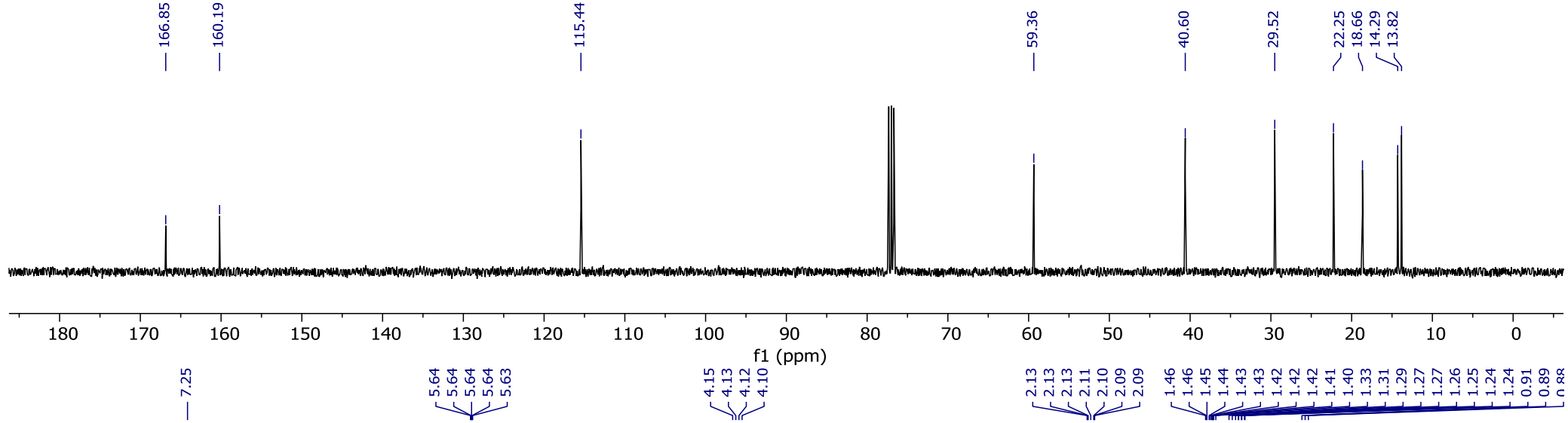
## 22. $^1\text{H}$ , $^{13}\text{C}$ NMR spectra and HPLC chromatograms



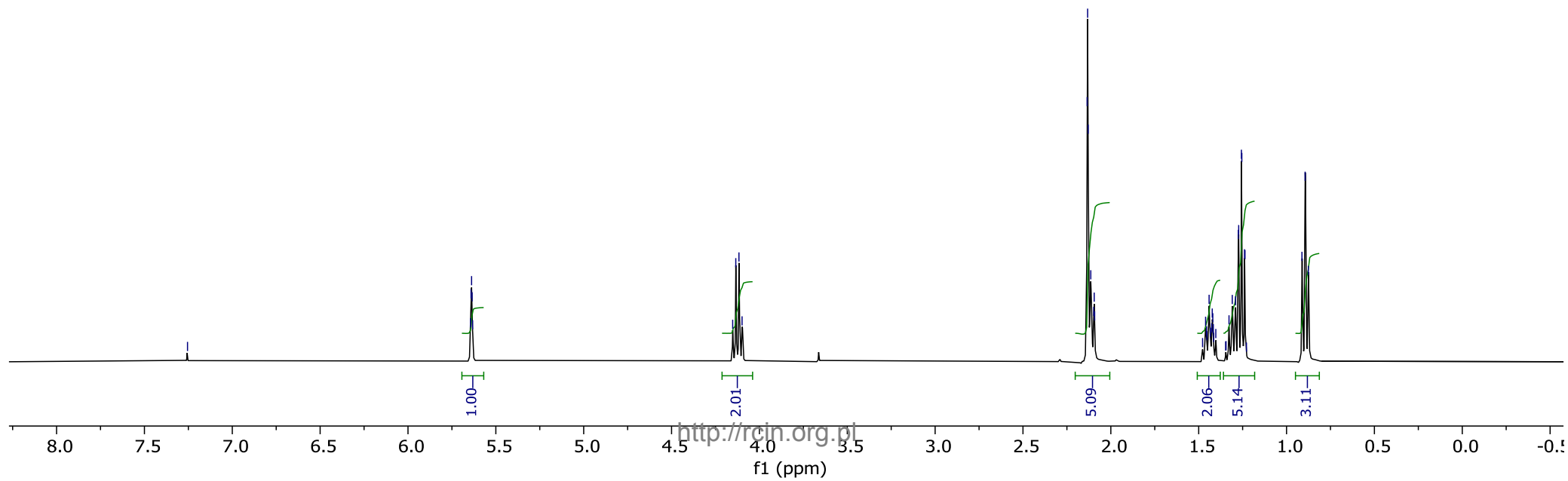


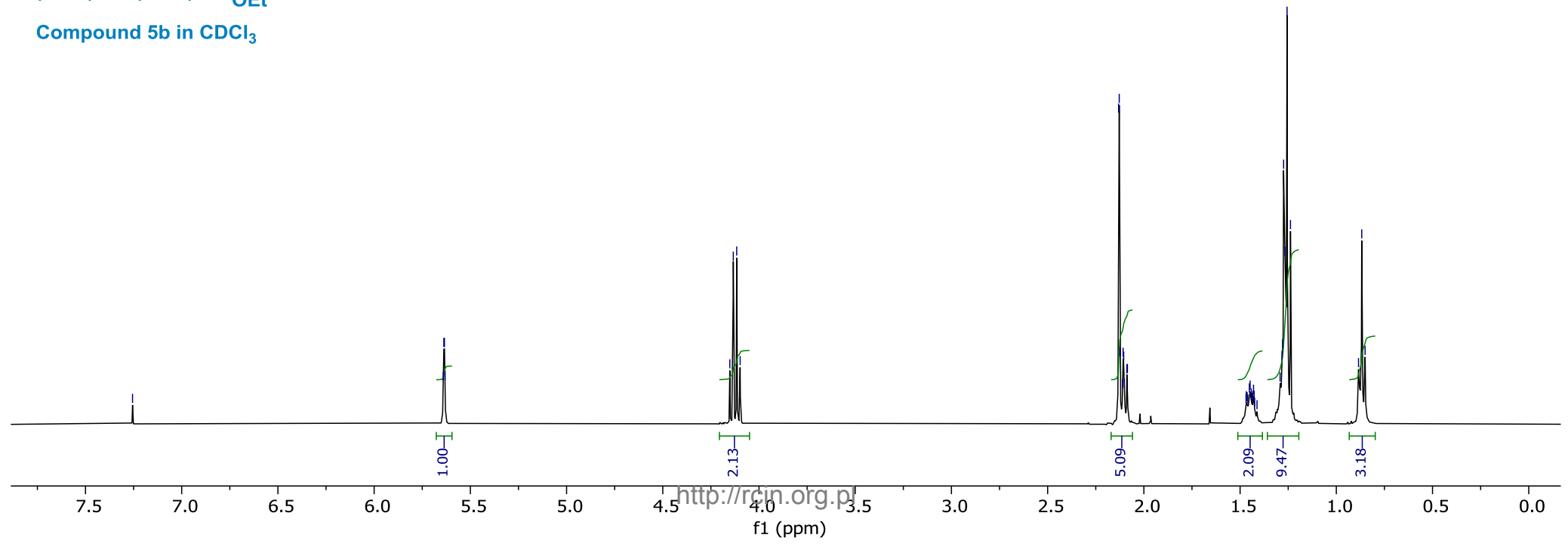
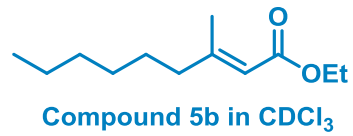
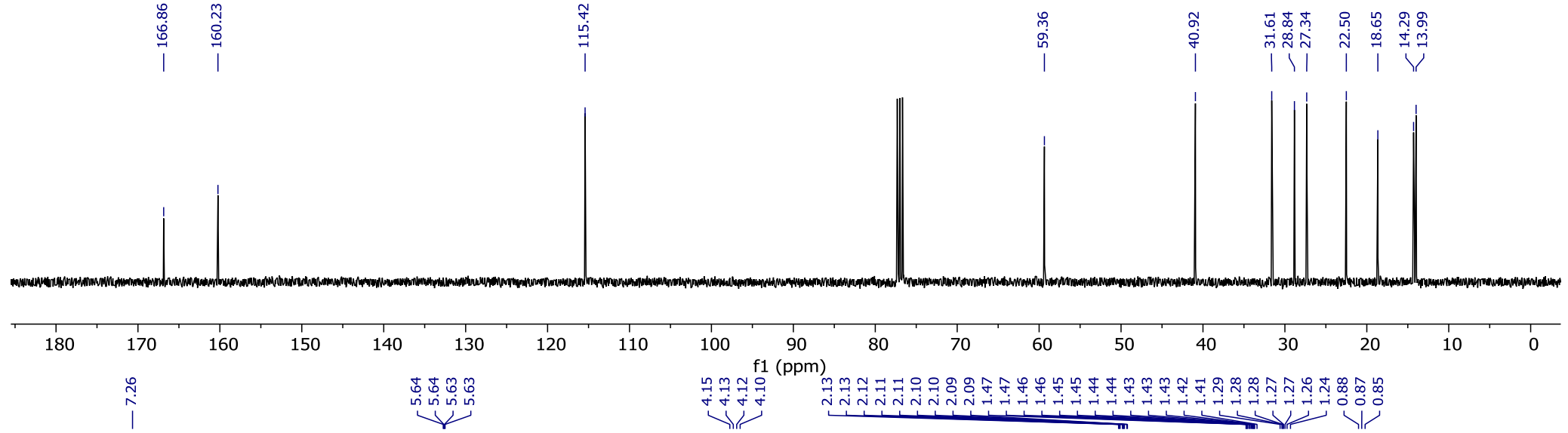
Compound 4c in CDCl<sub>3</sub>

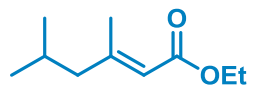
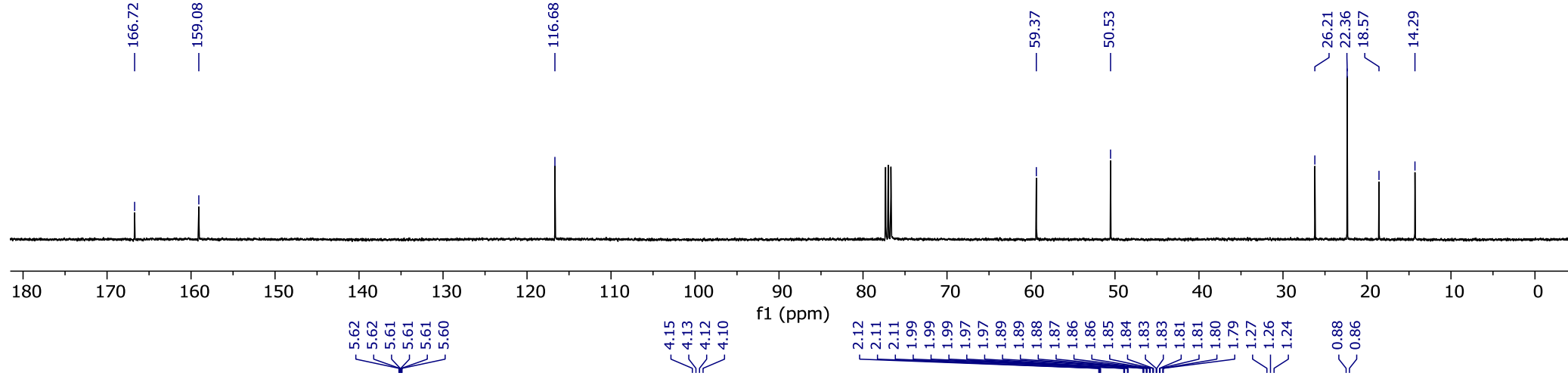




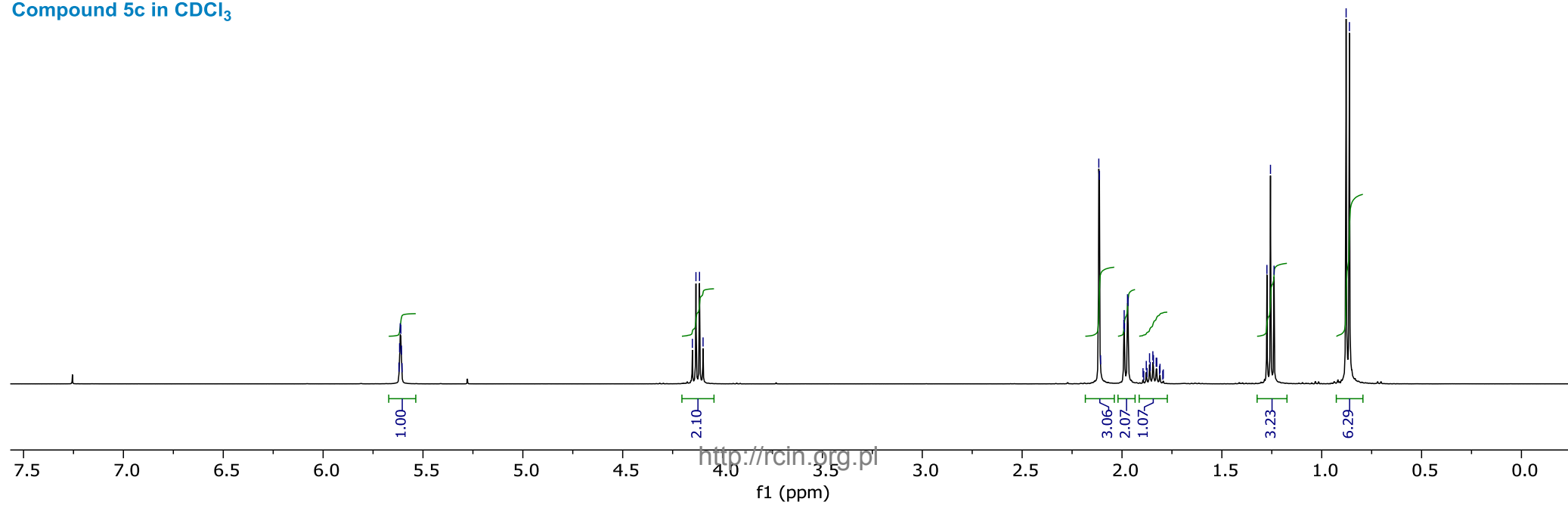
Compound 5a in CDCl<sub>3</sub>



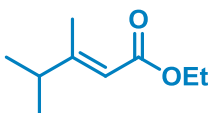
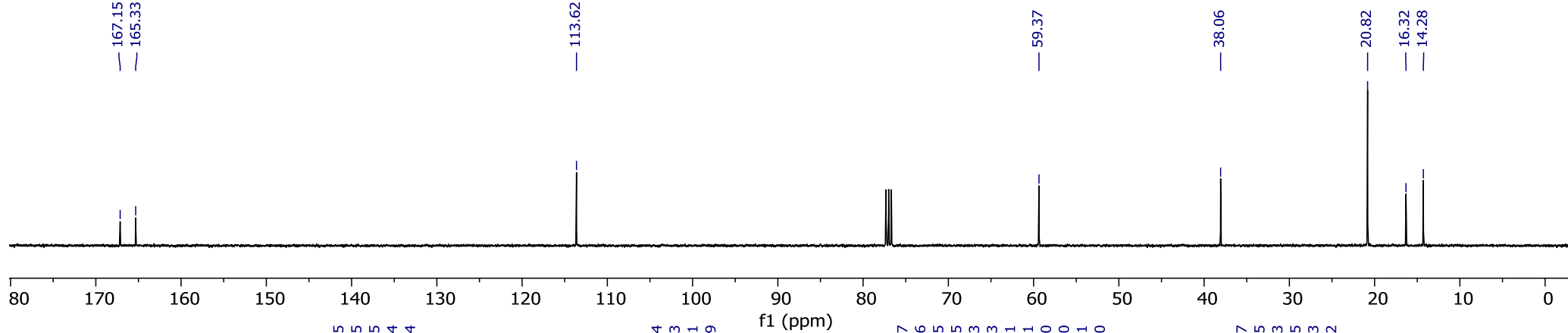




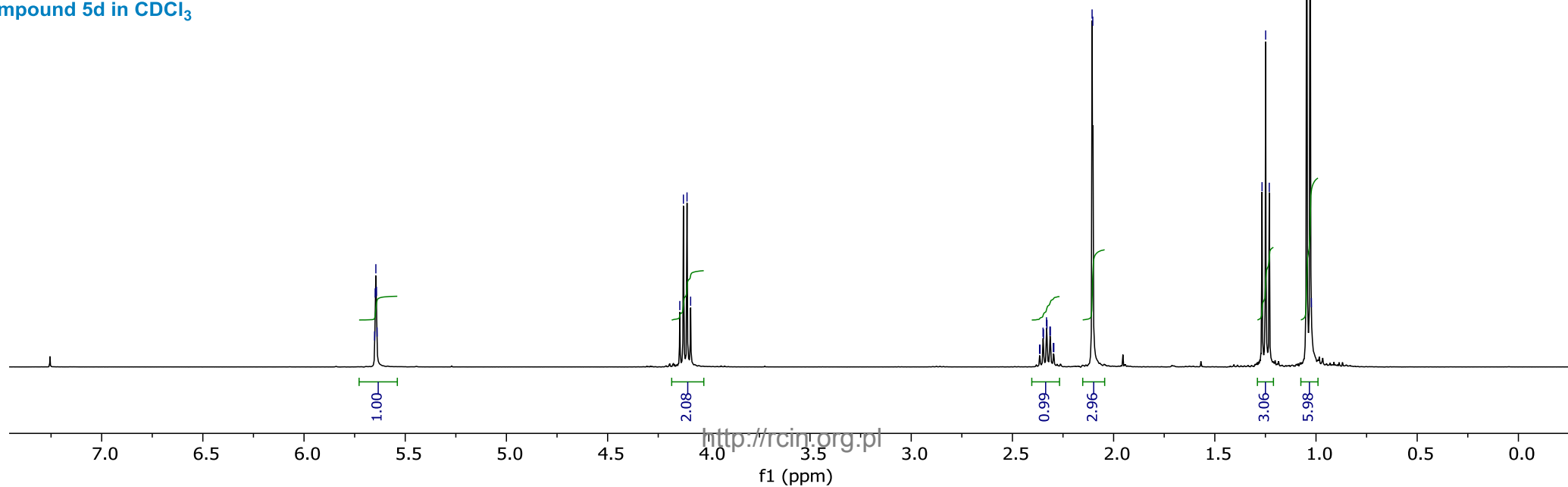
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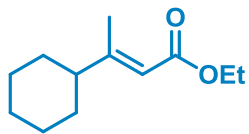
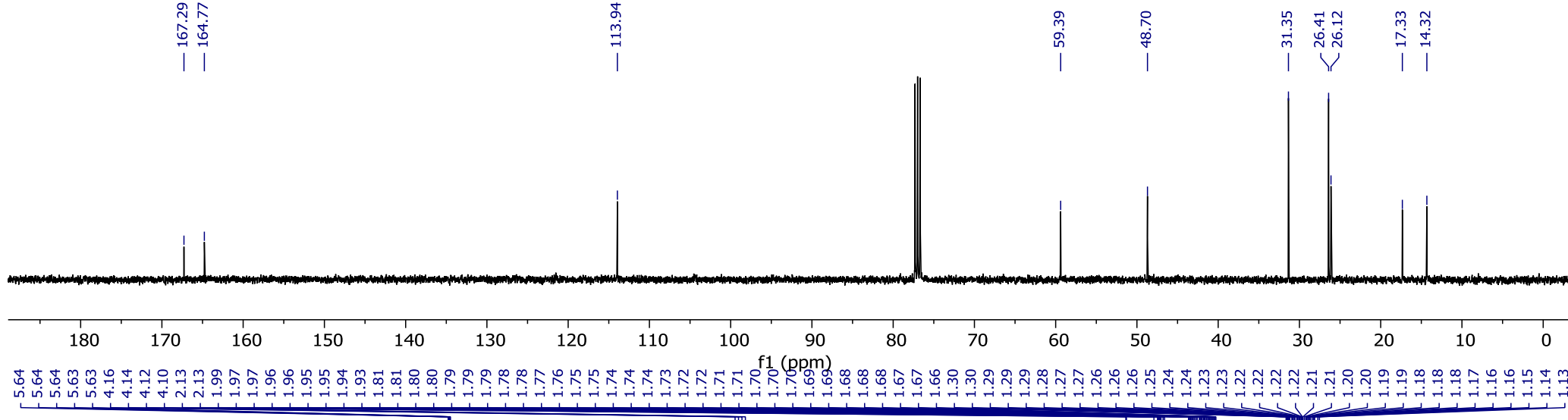




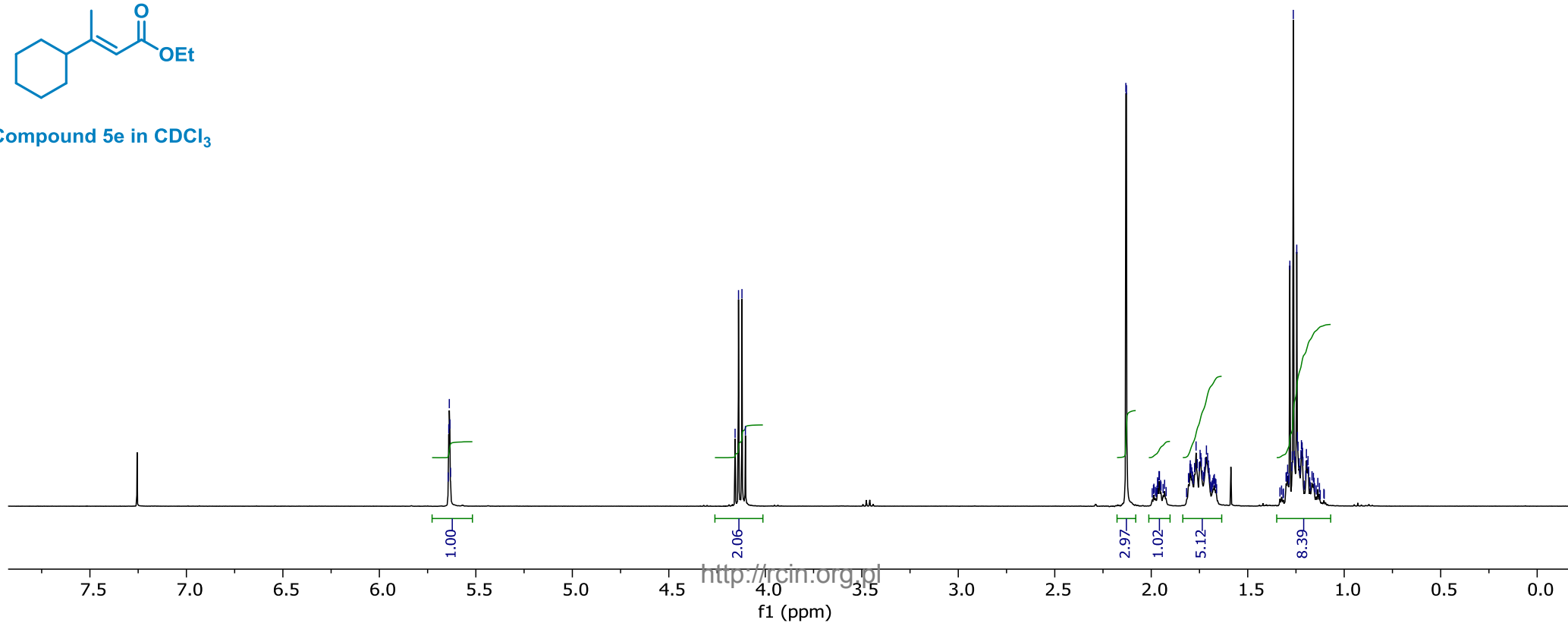


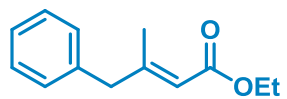
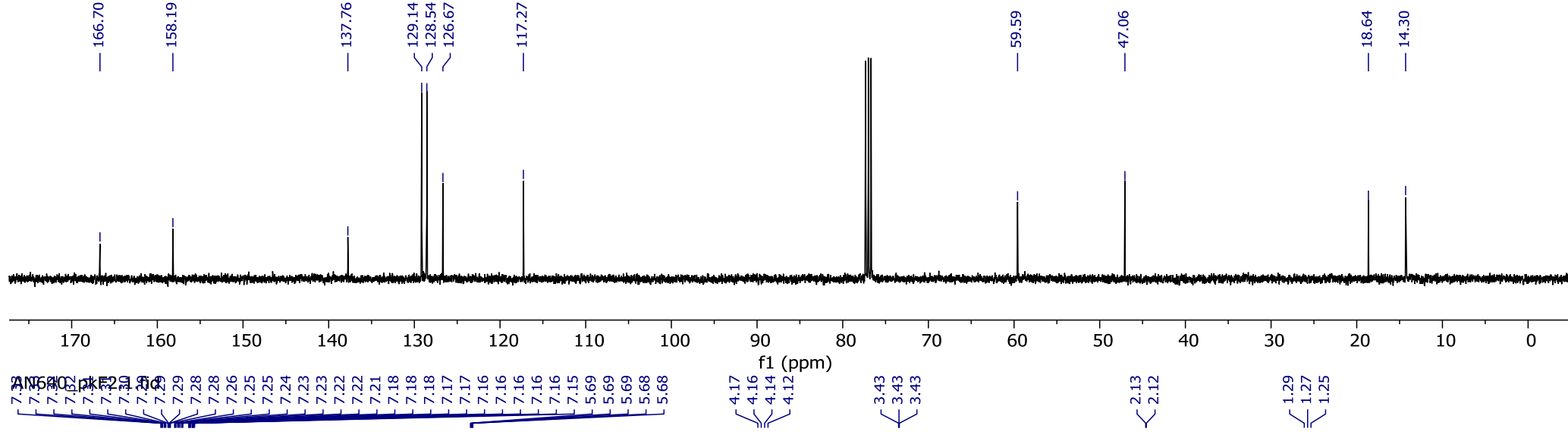
Compound 5d in CDCl<sub>3</sub>



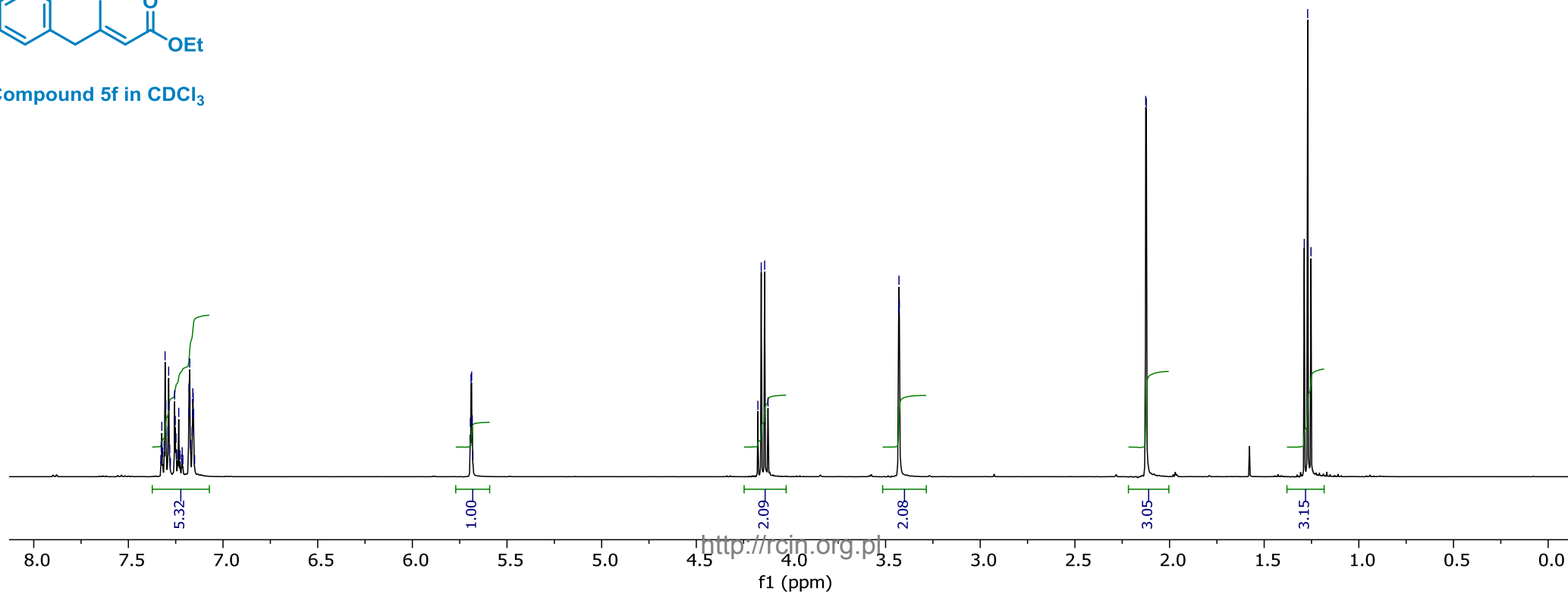


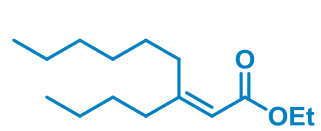
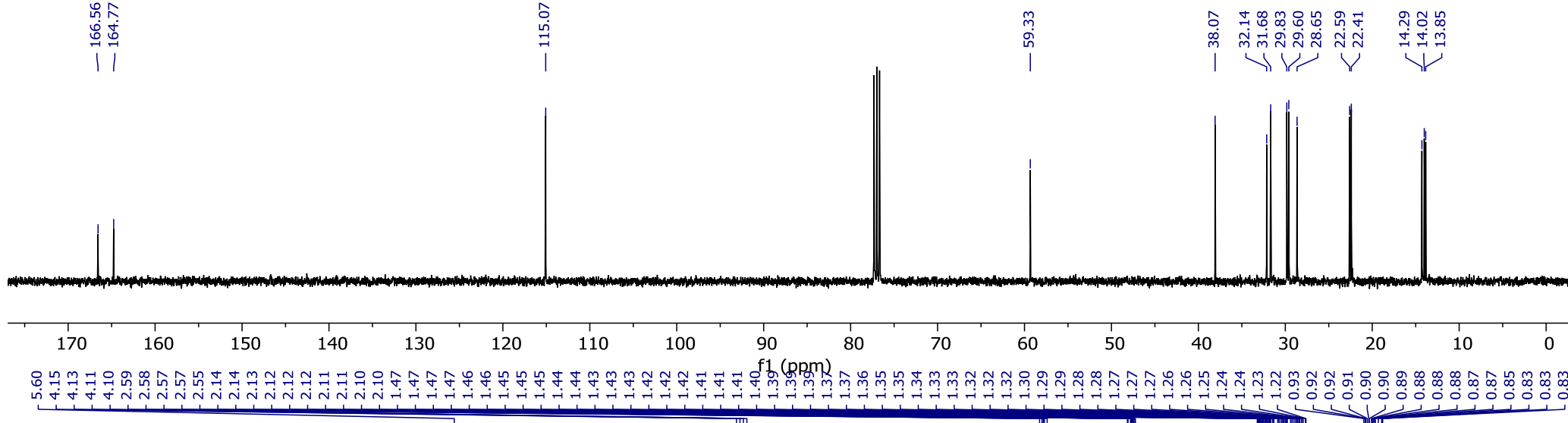
Compound 5e in CDCl<sub>3</sub>



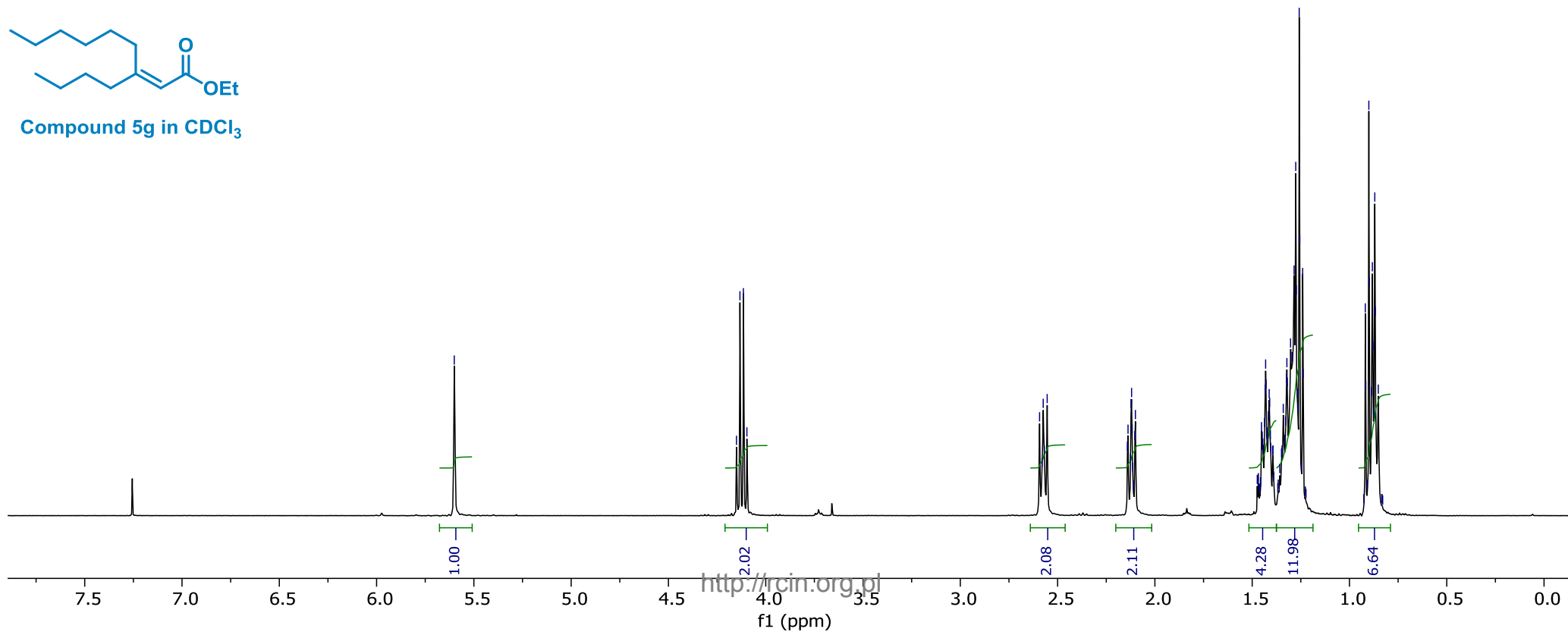


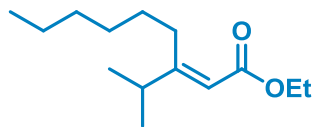
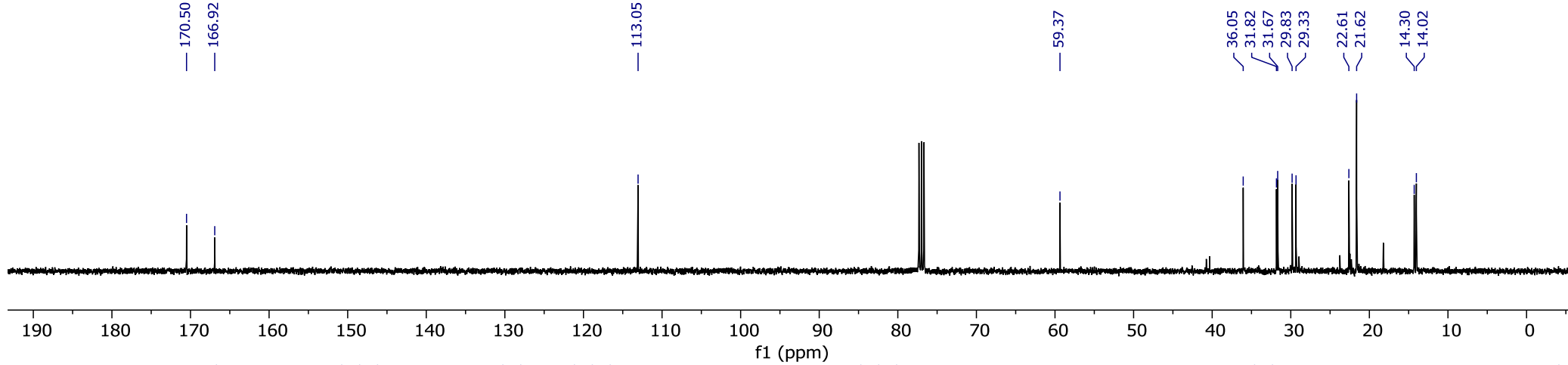
Compound 5f in CDCl<sub>3</sub>



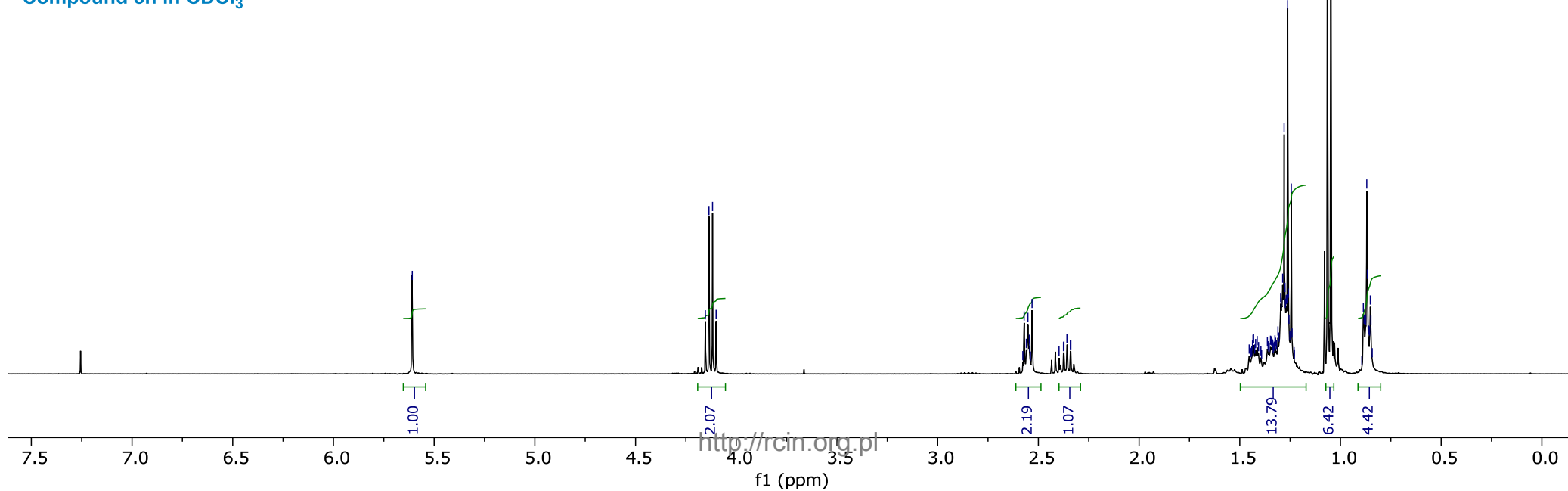


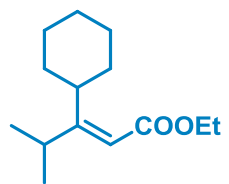
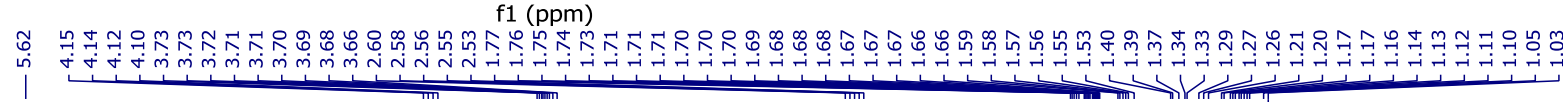
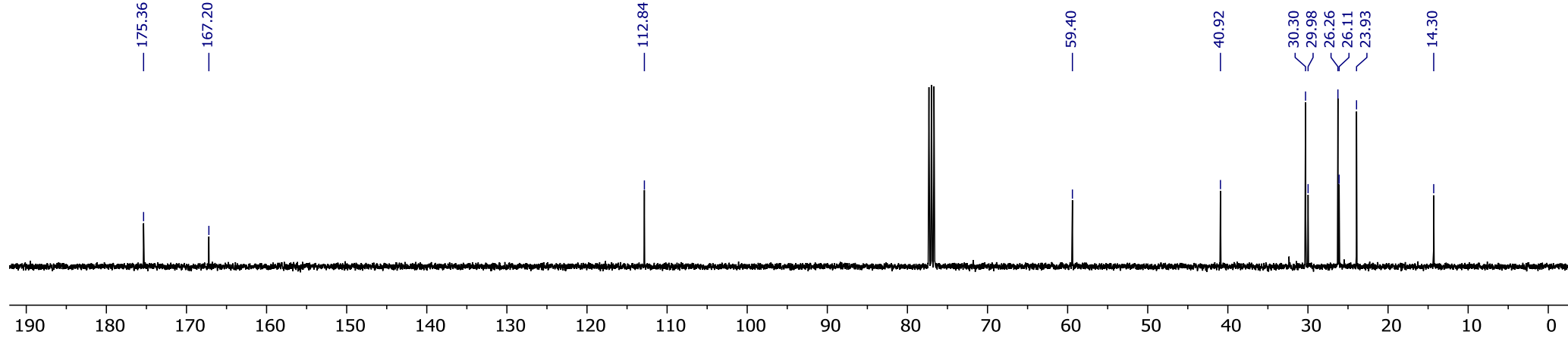
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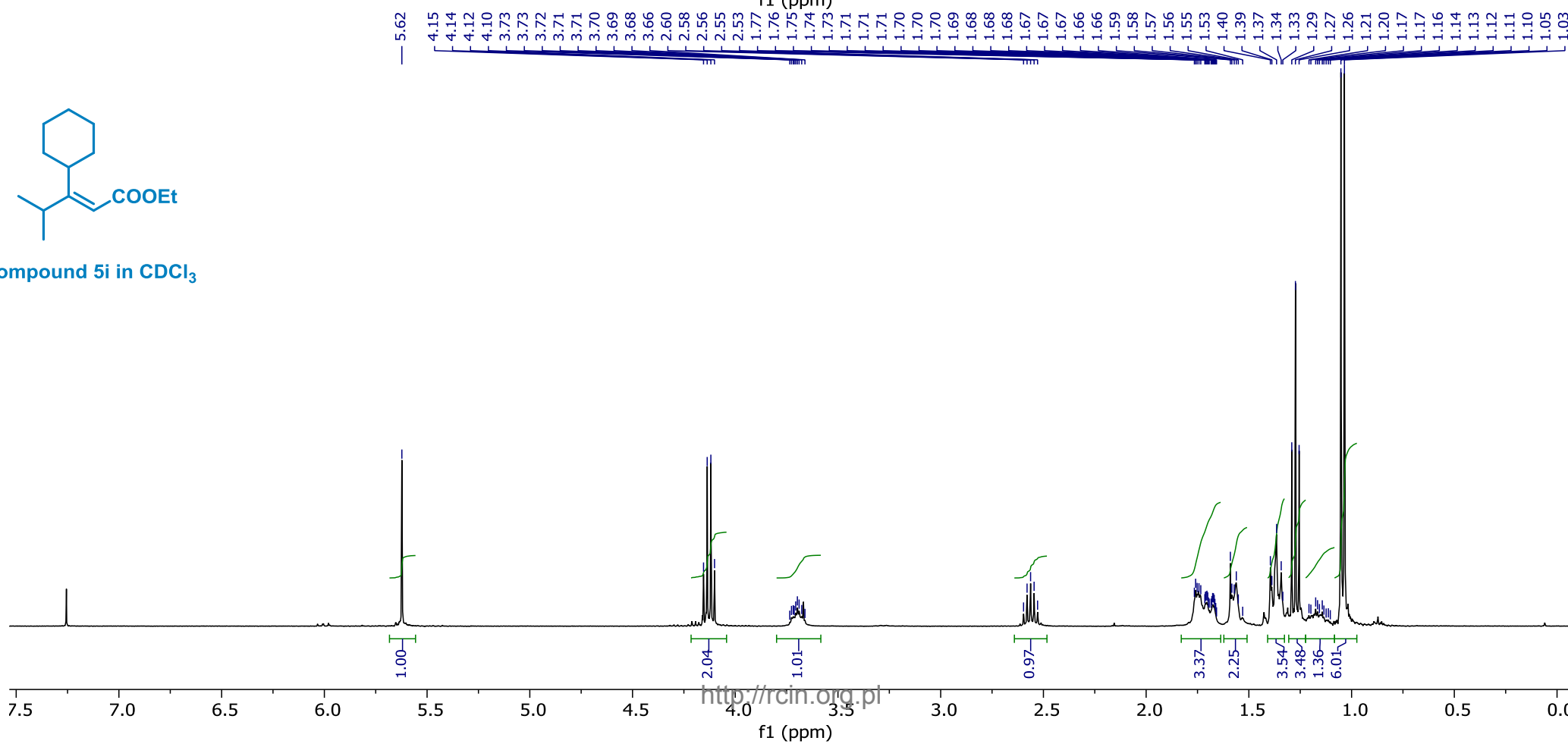


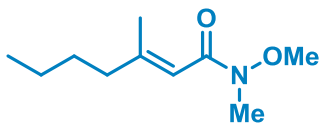
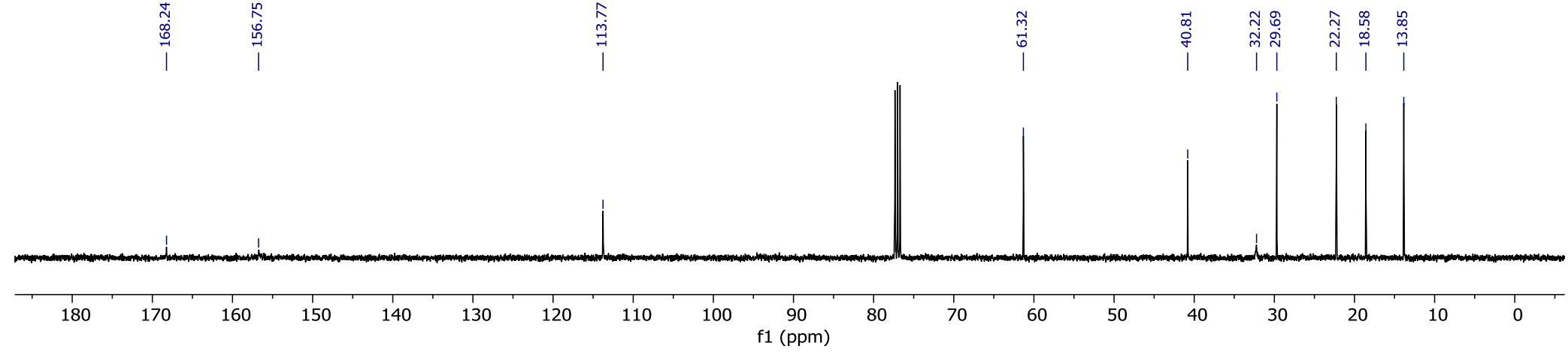
Compound 5h in CDCl<sub>3</sub>



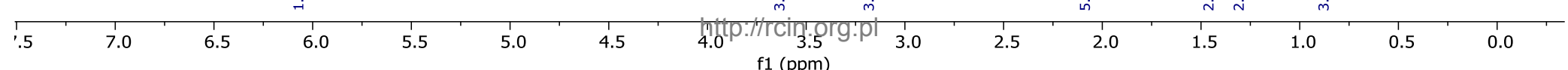


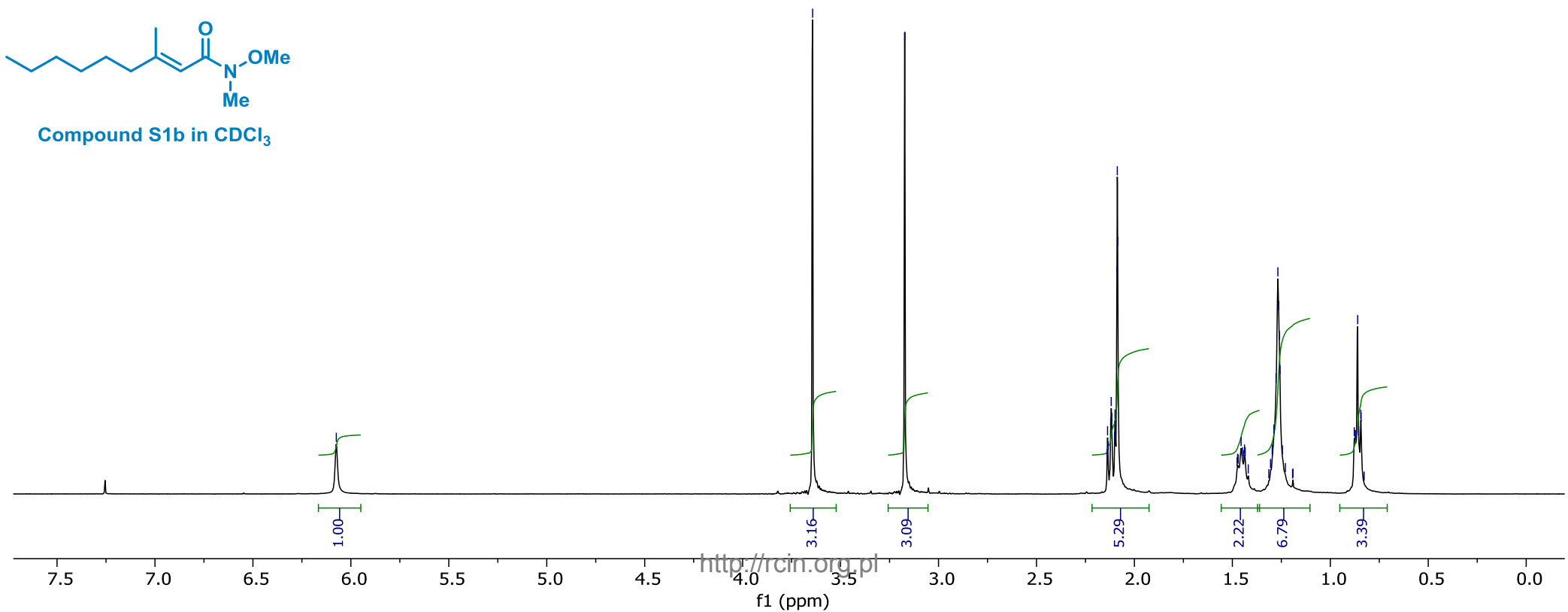
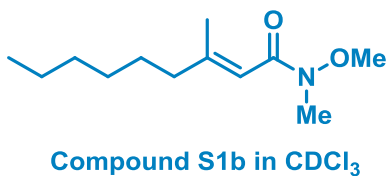
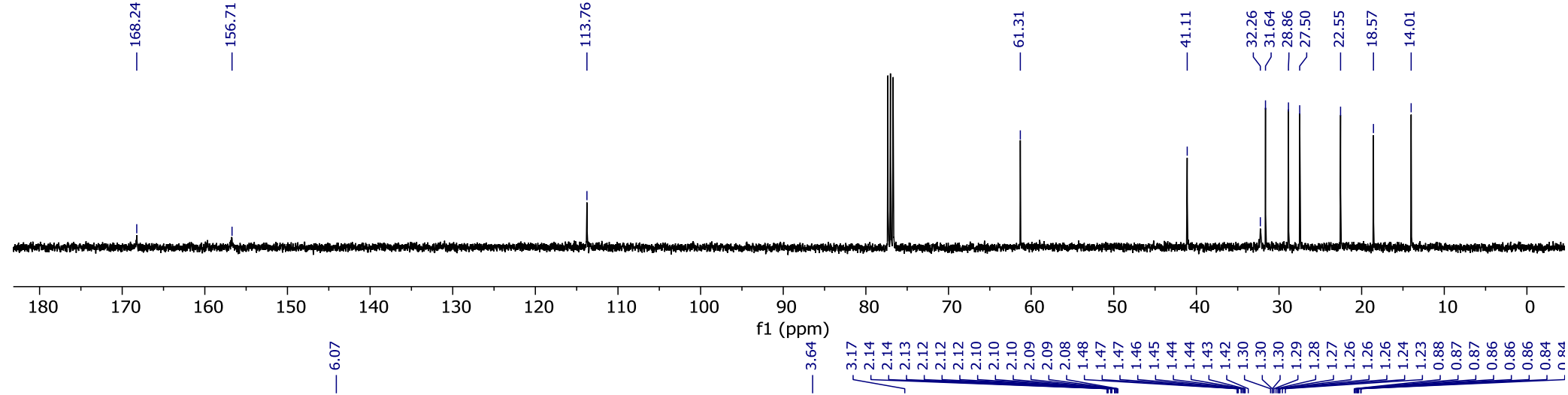
Compound 5i in CDCl<sub>3</sub>



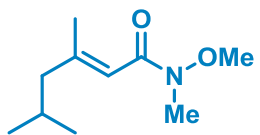
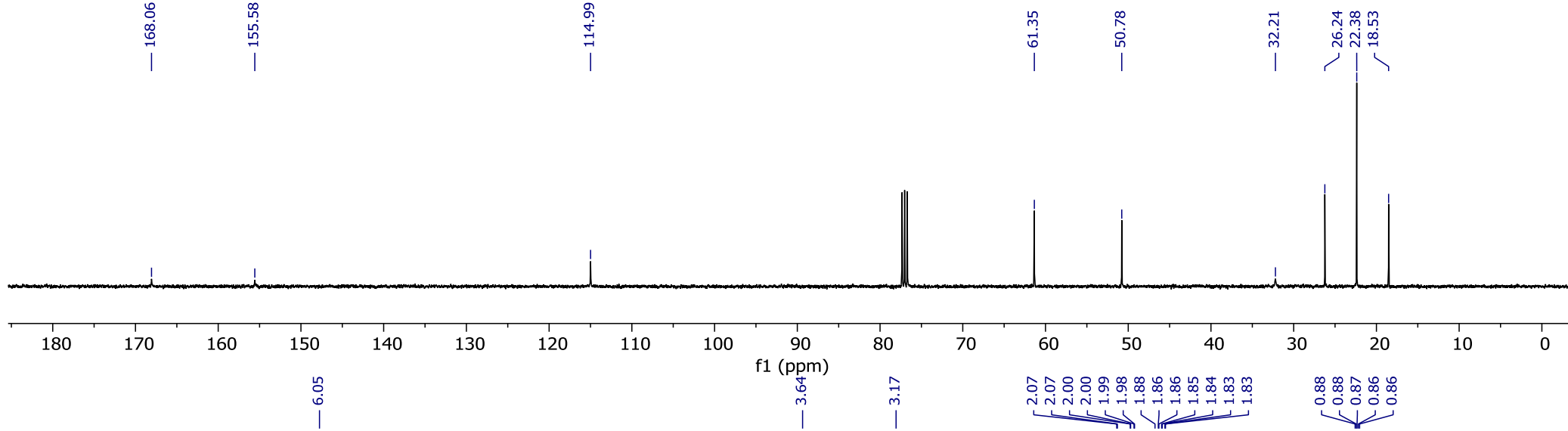


Compound S1a in CDCl<sub>3</sub>

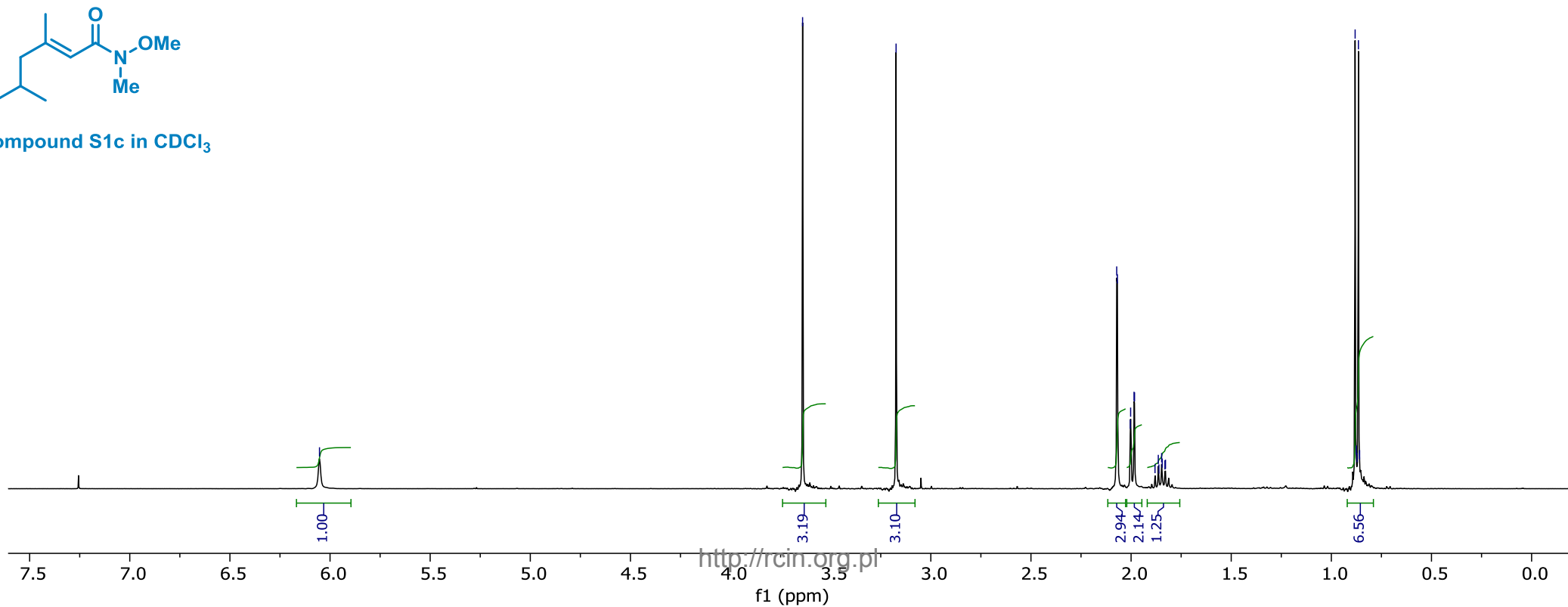


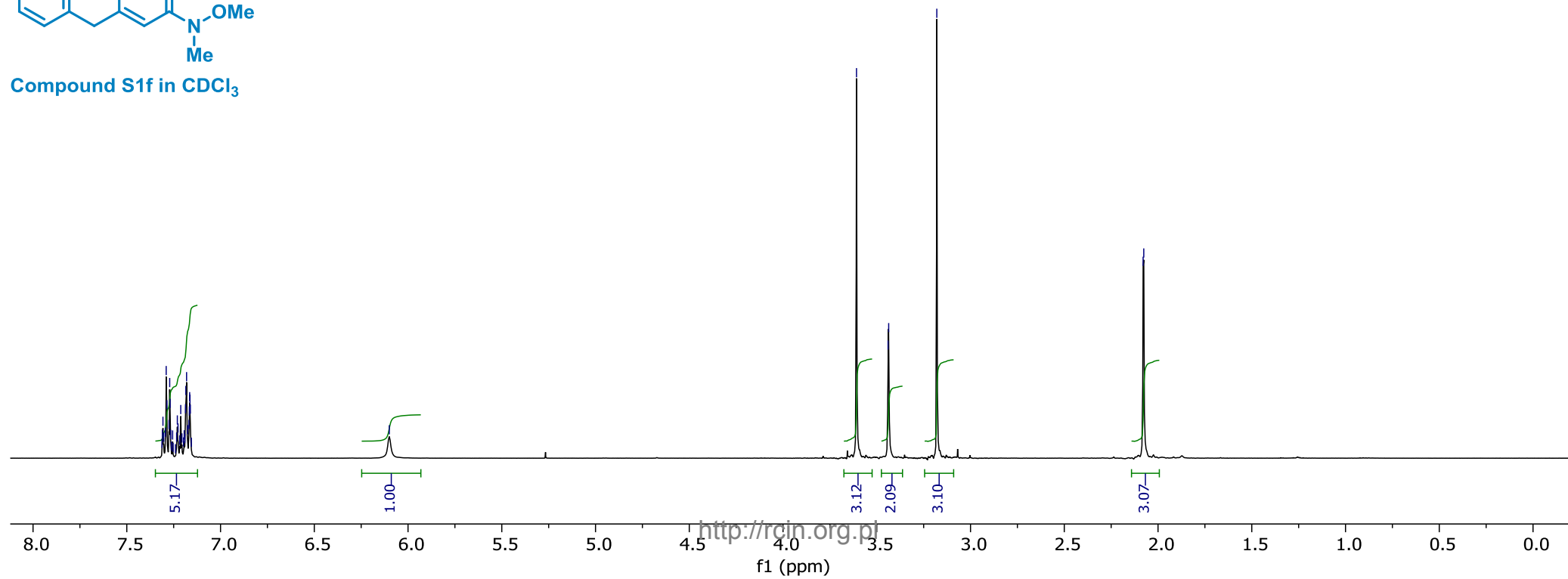
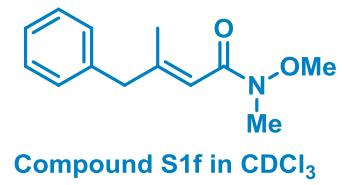
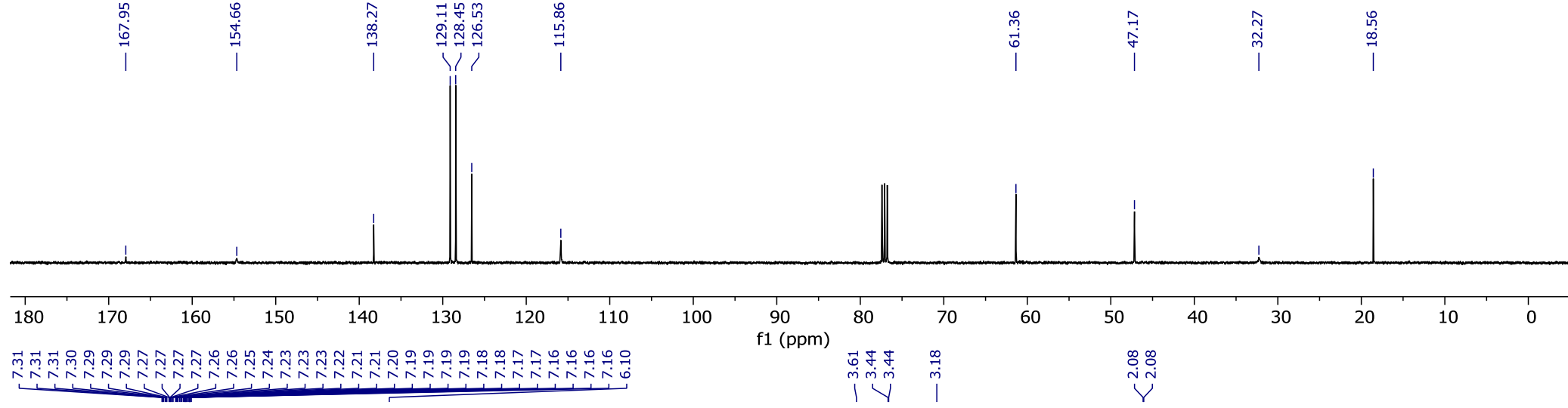


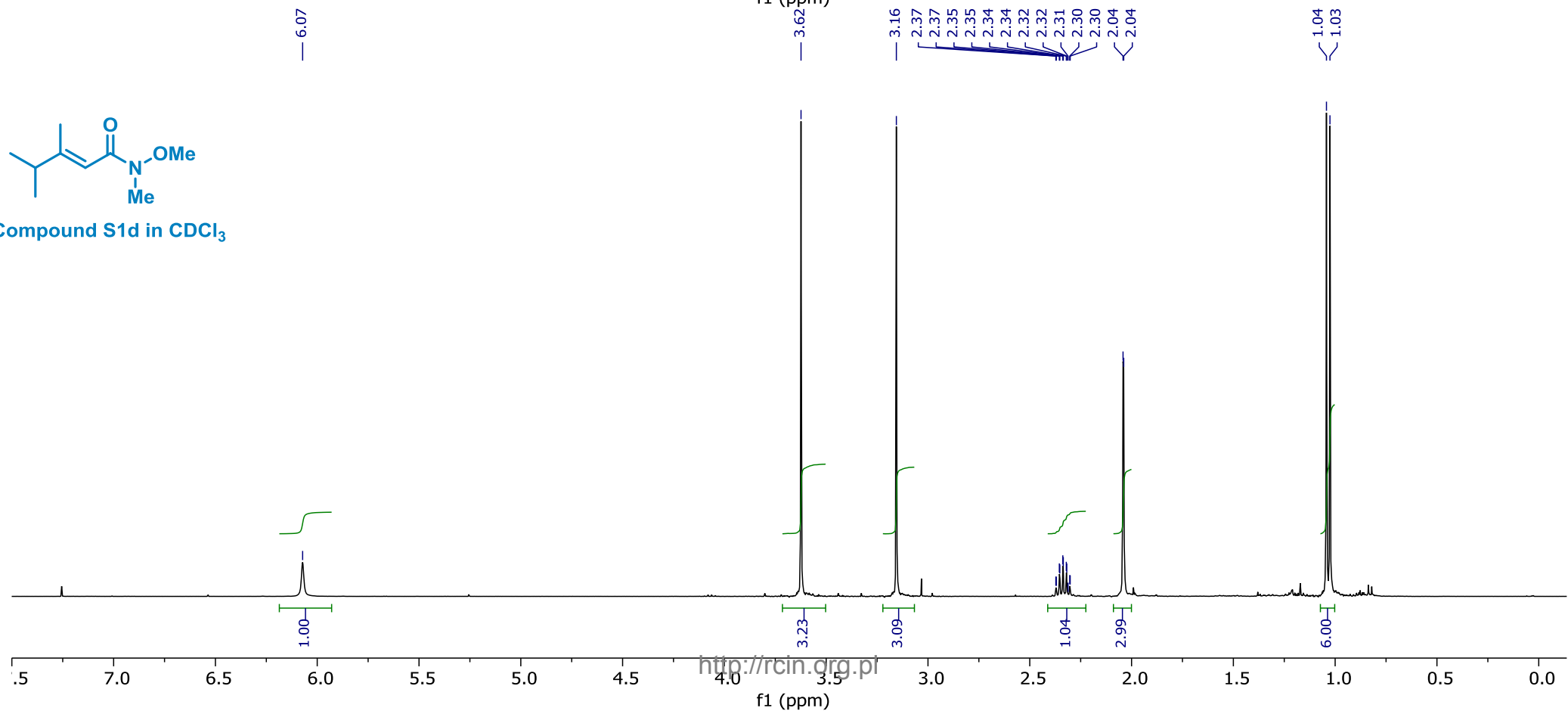
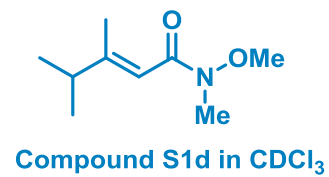
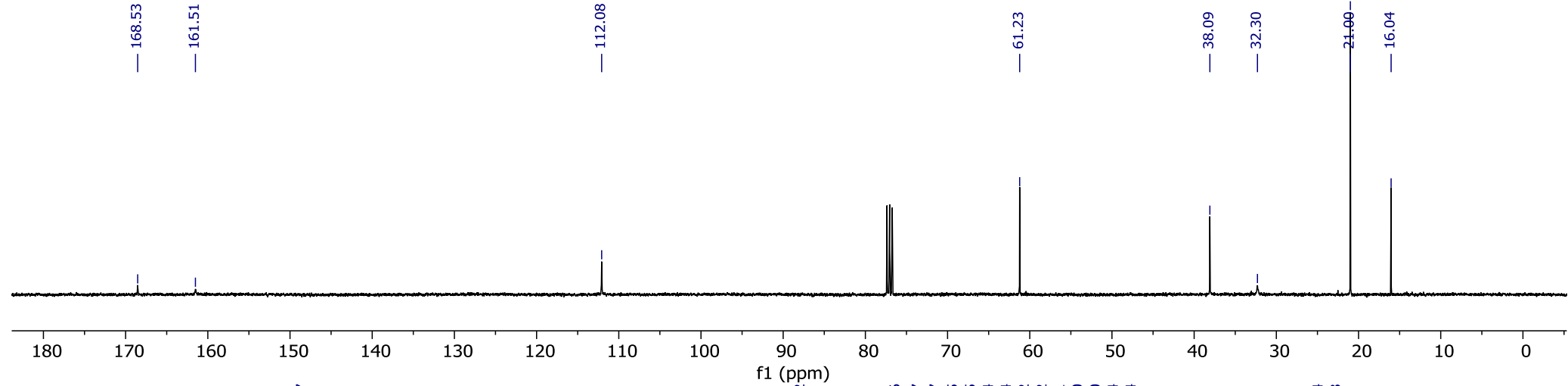


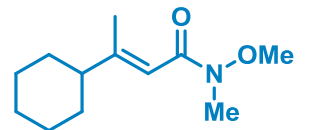
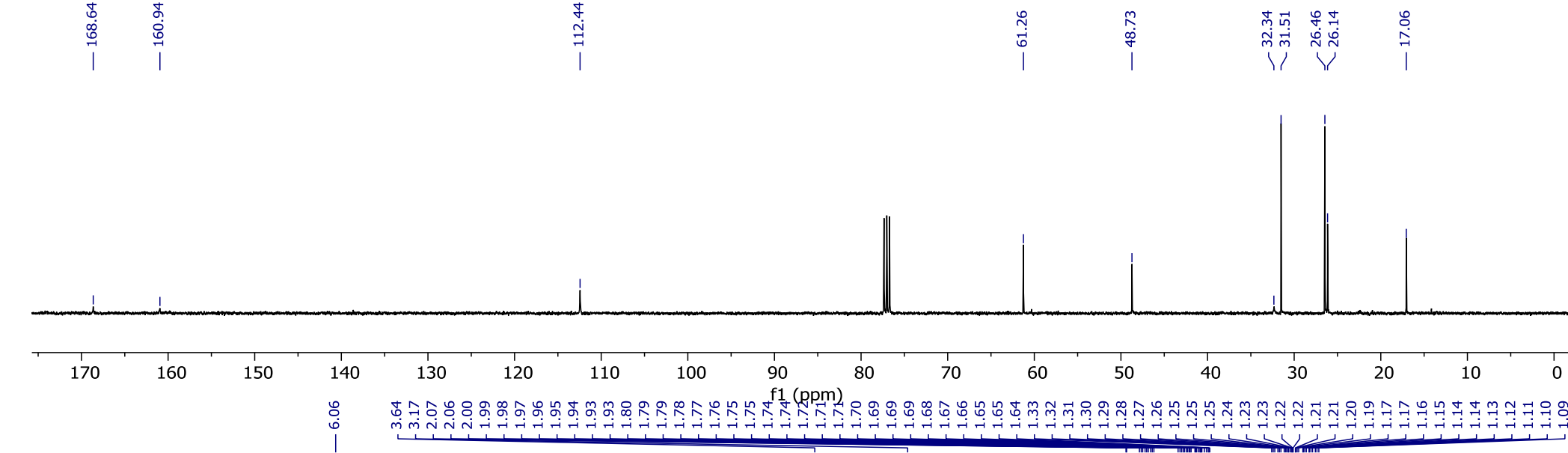


Compound S1c in CDCl<sub>3</sub>

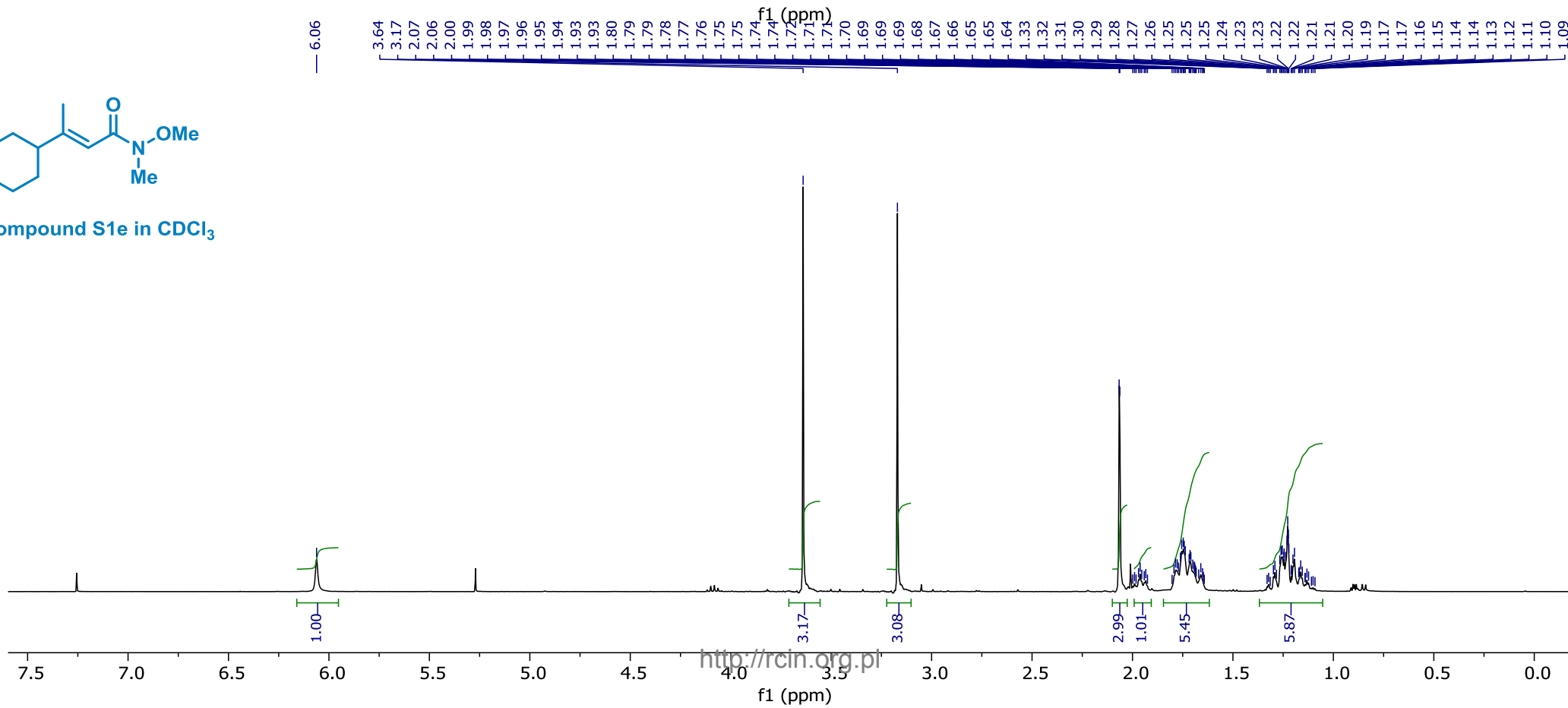


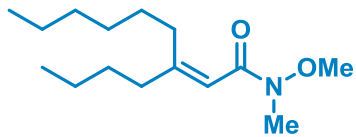
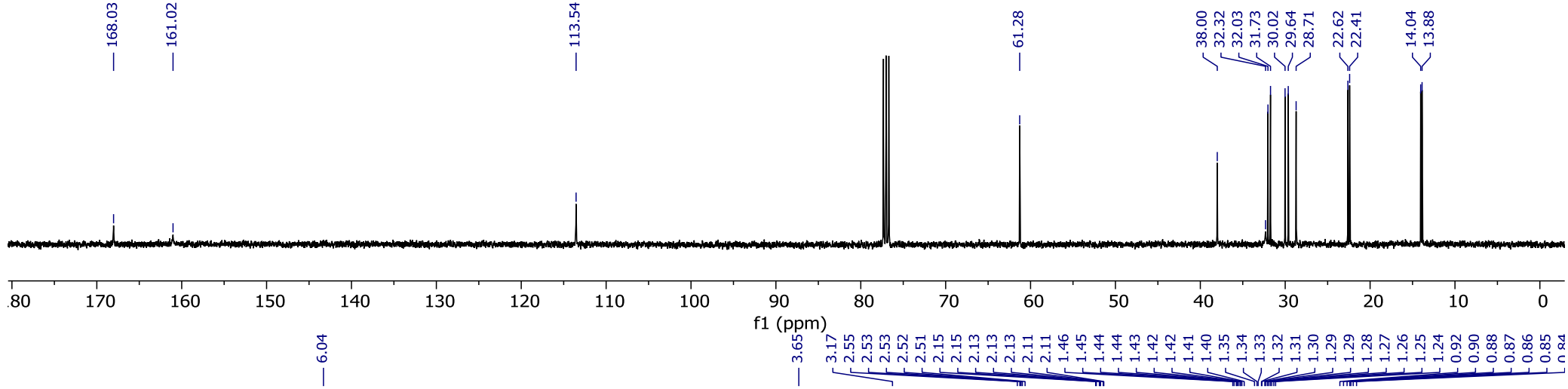




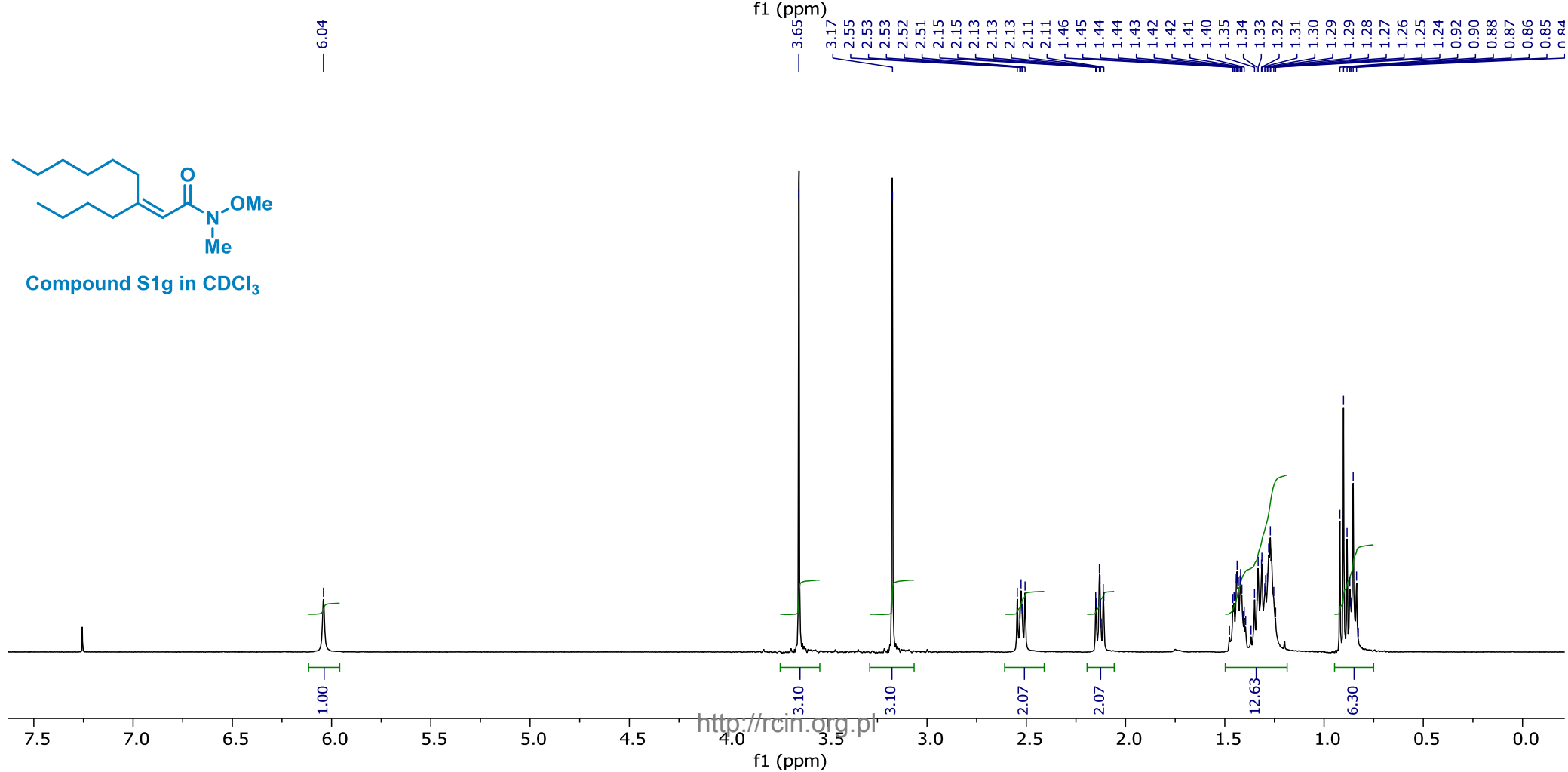


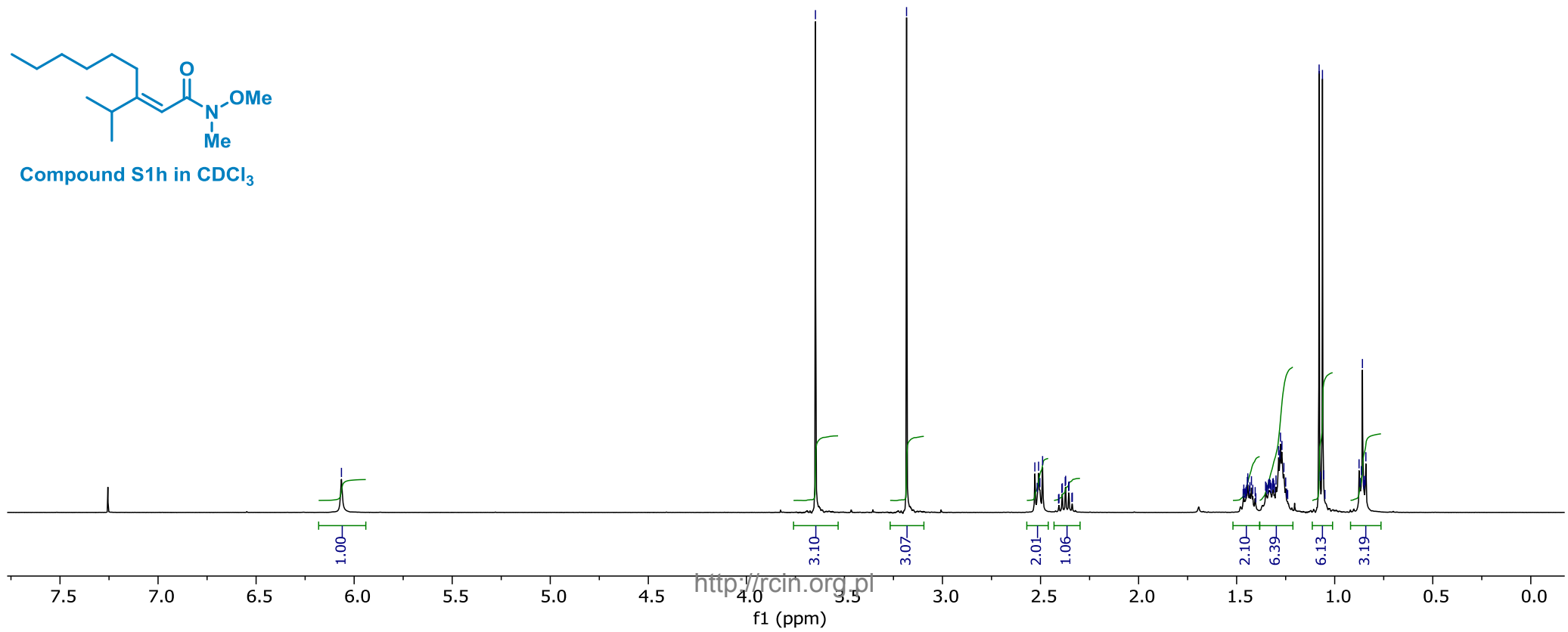
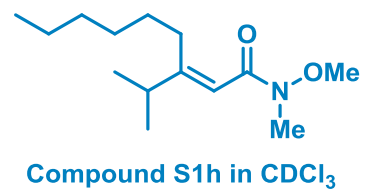
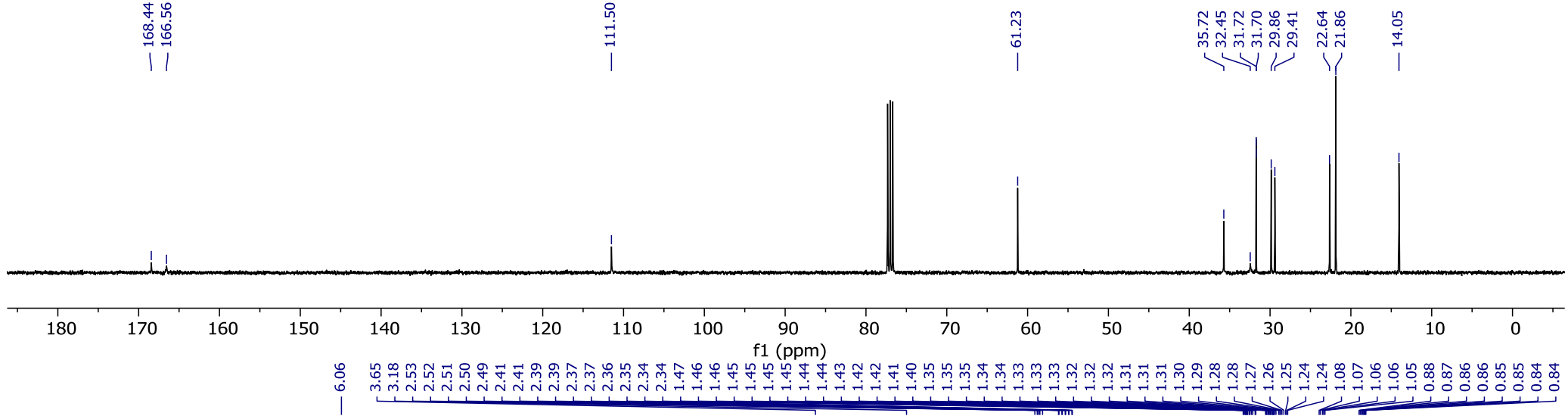
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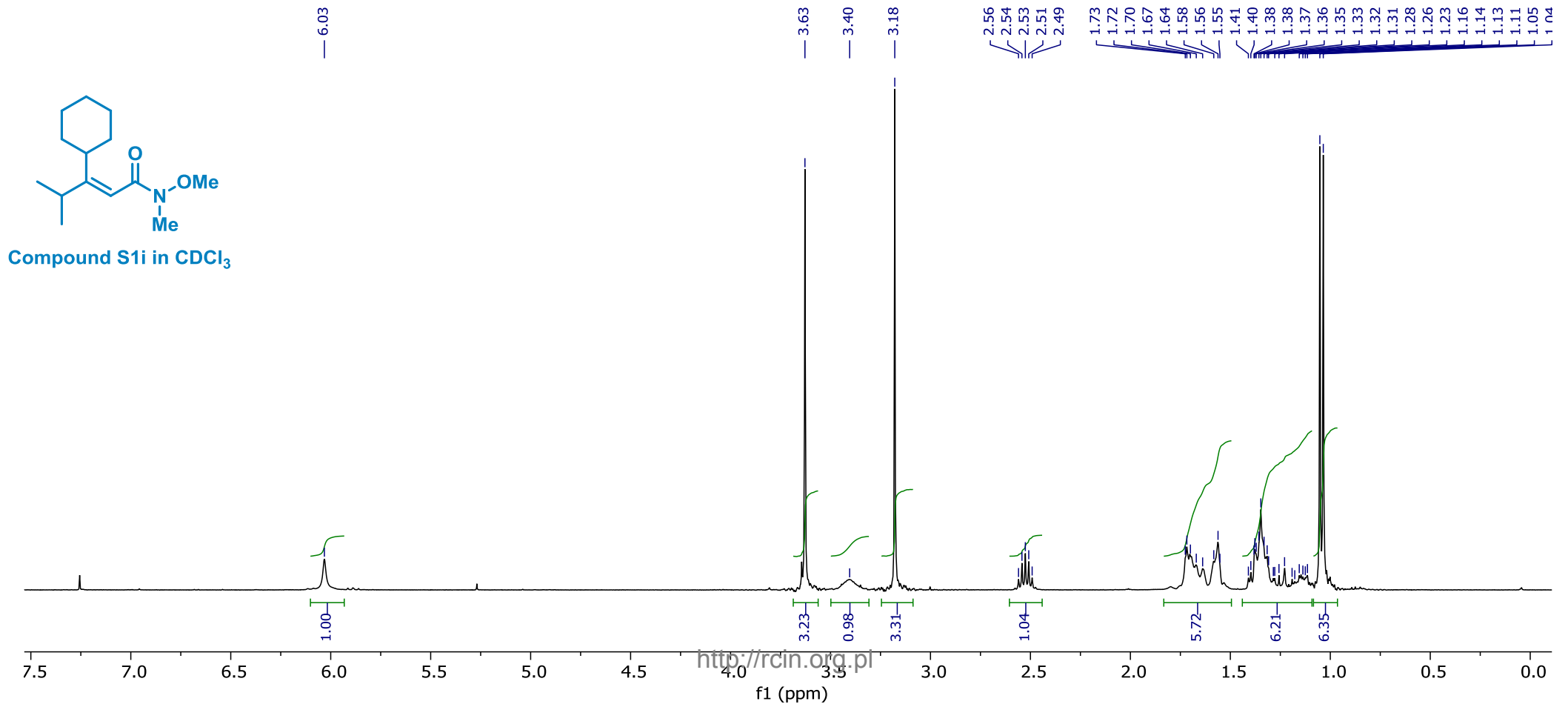
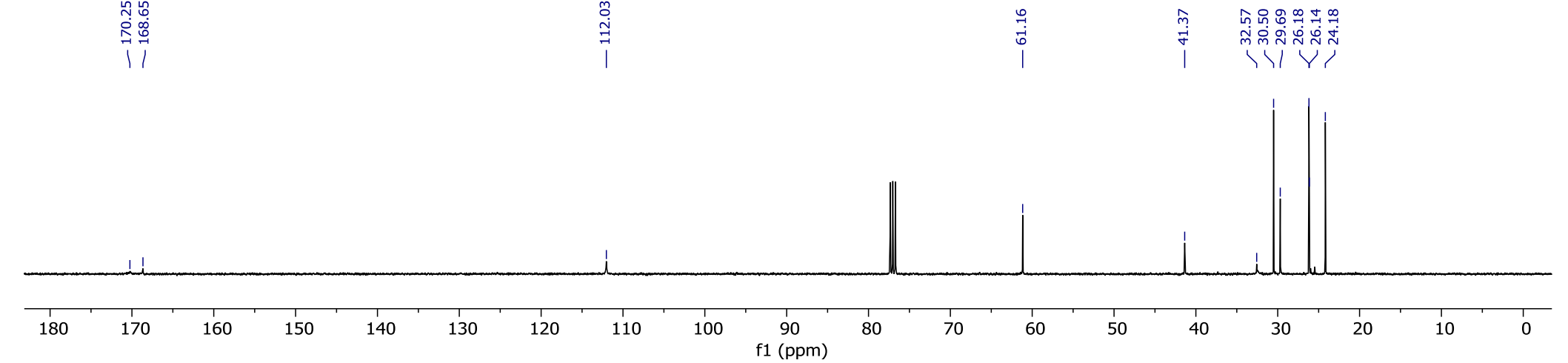


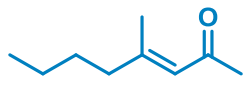
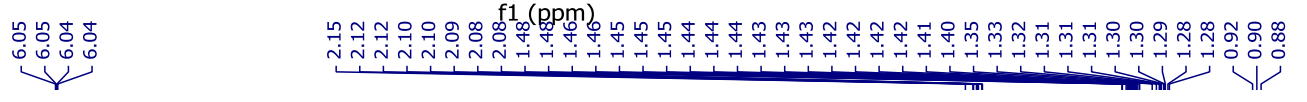
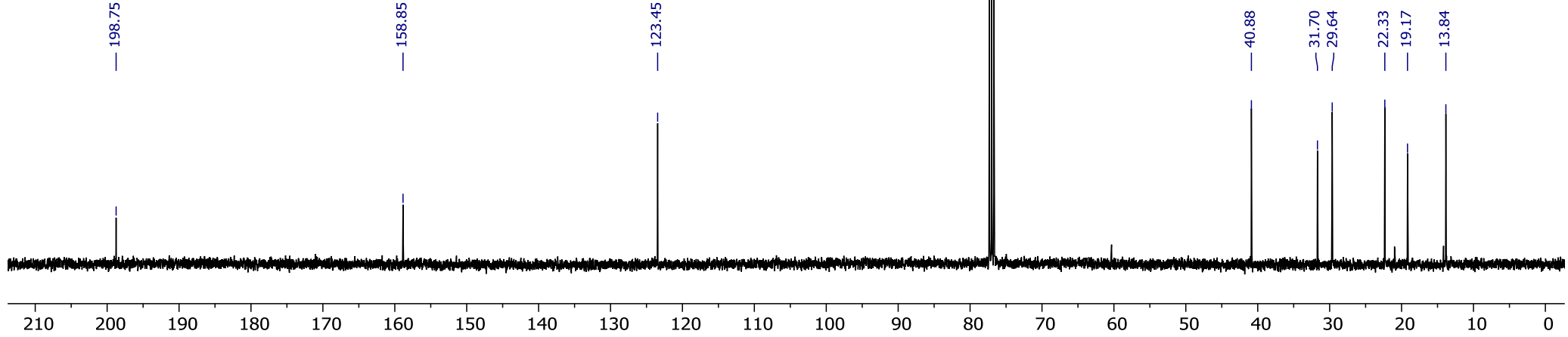
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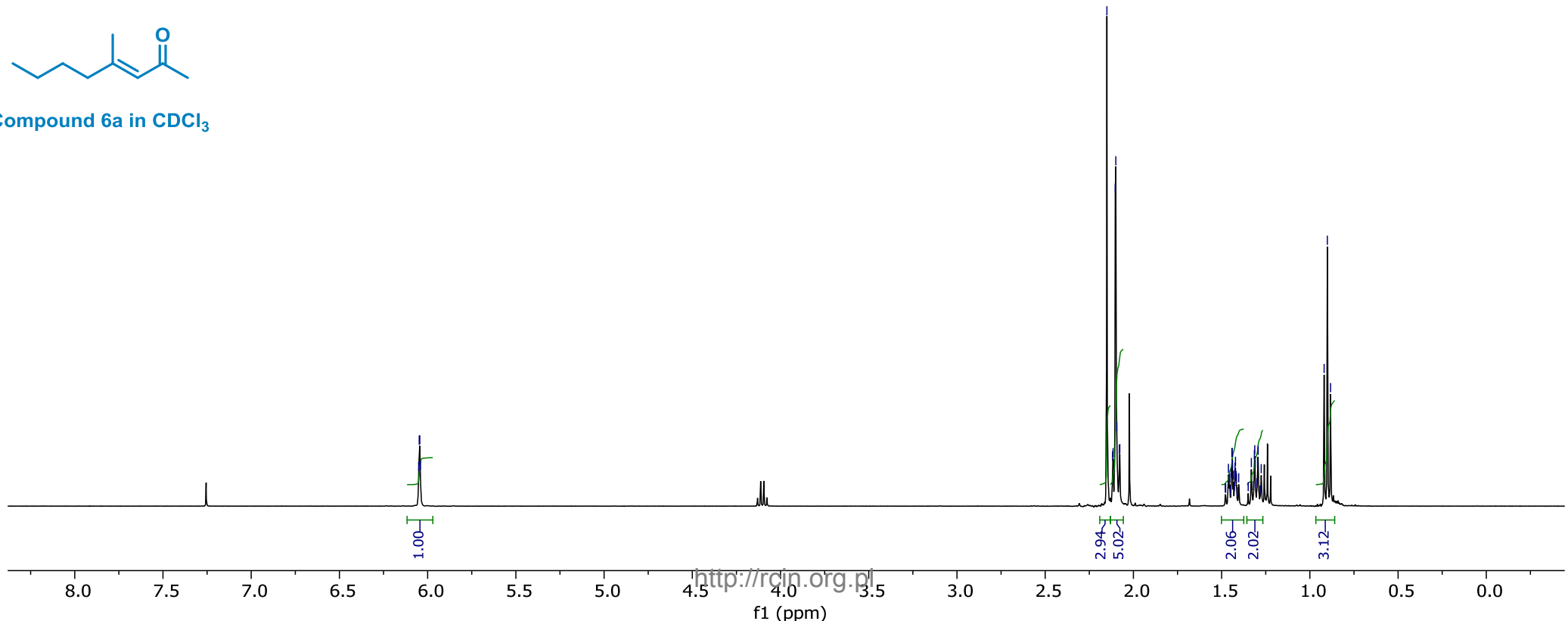


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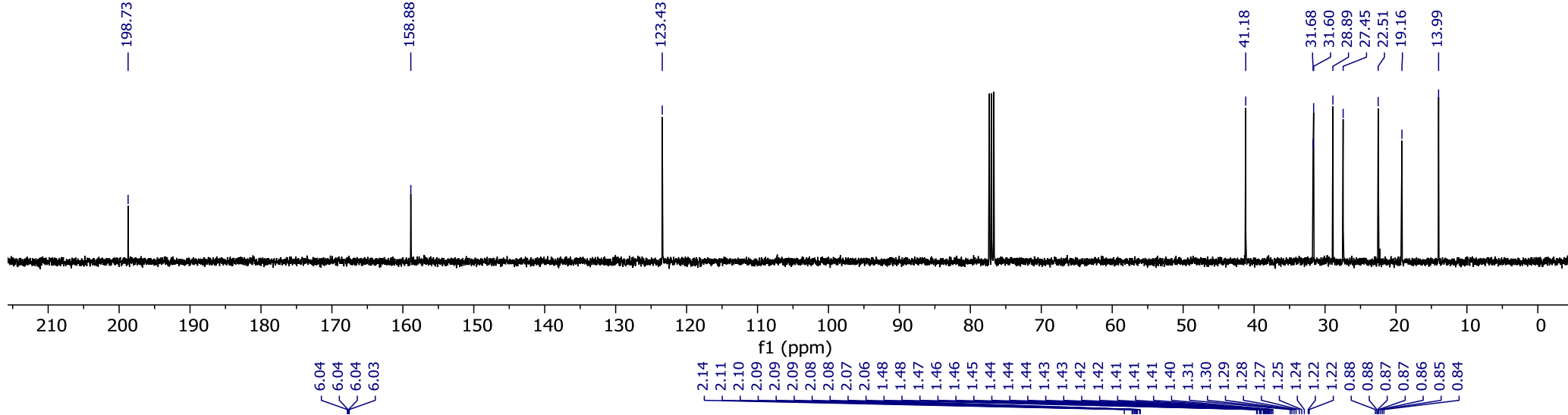




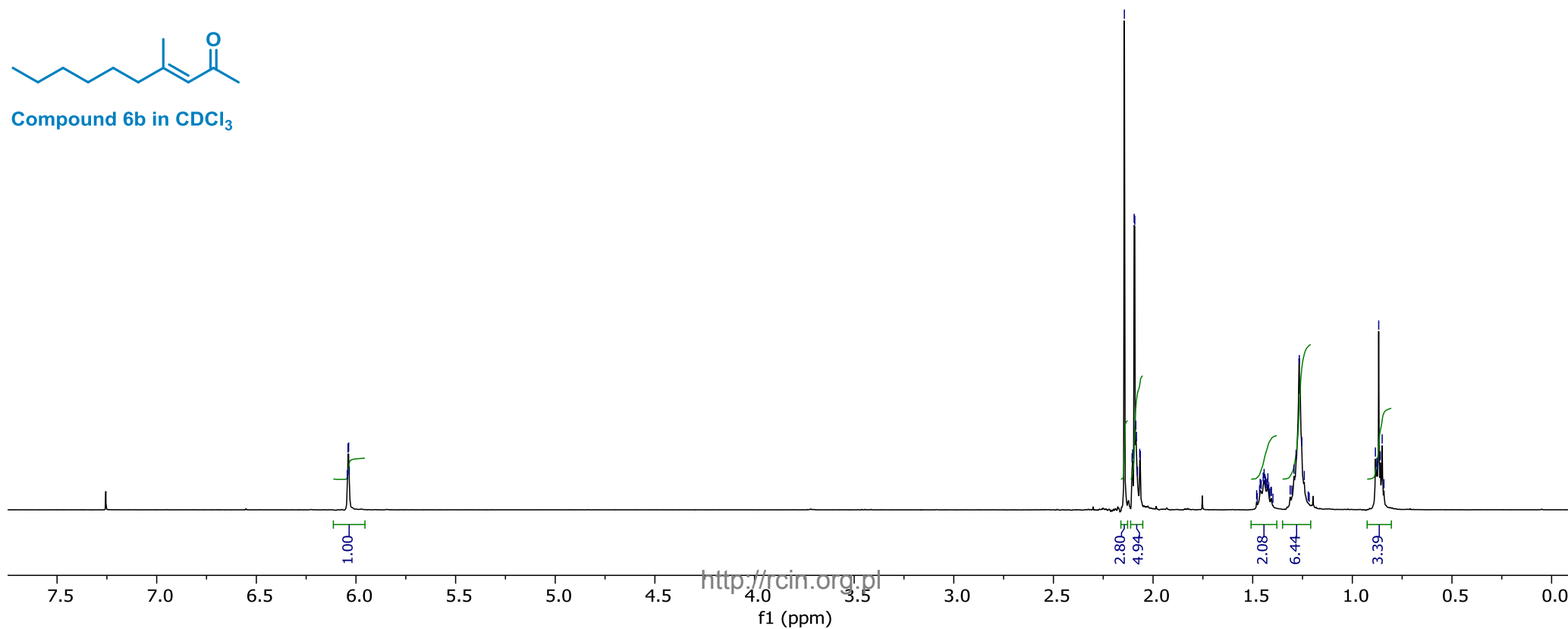
Compound 6a in CDCl<sub>3</sub>

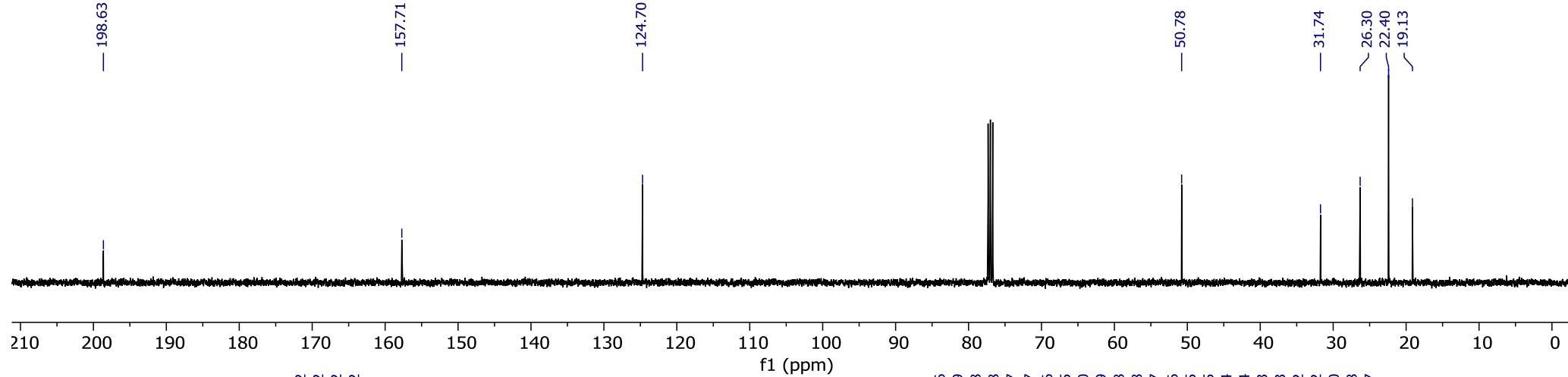






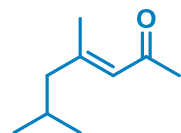
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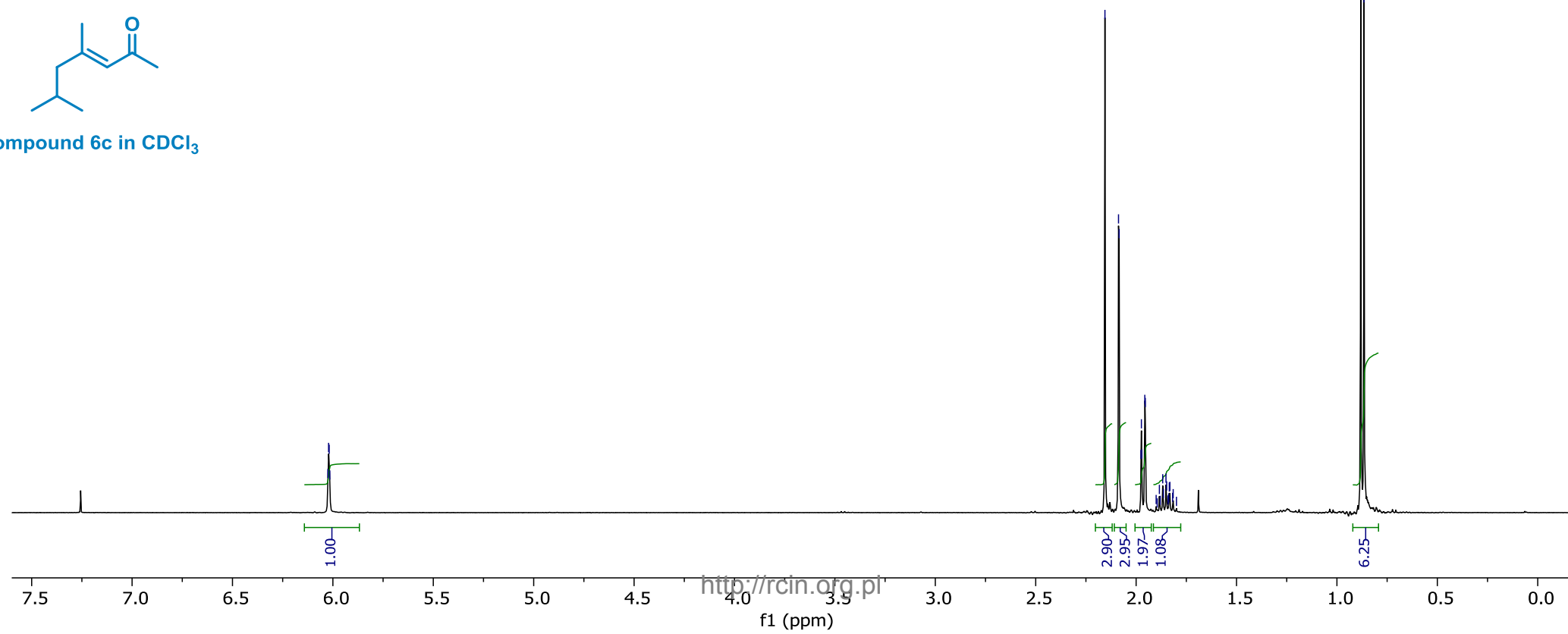


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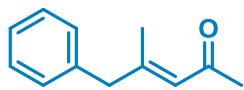
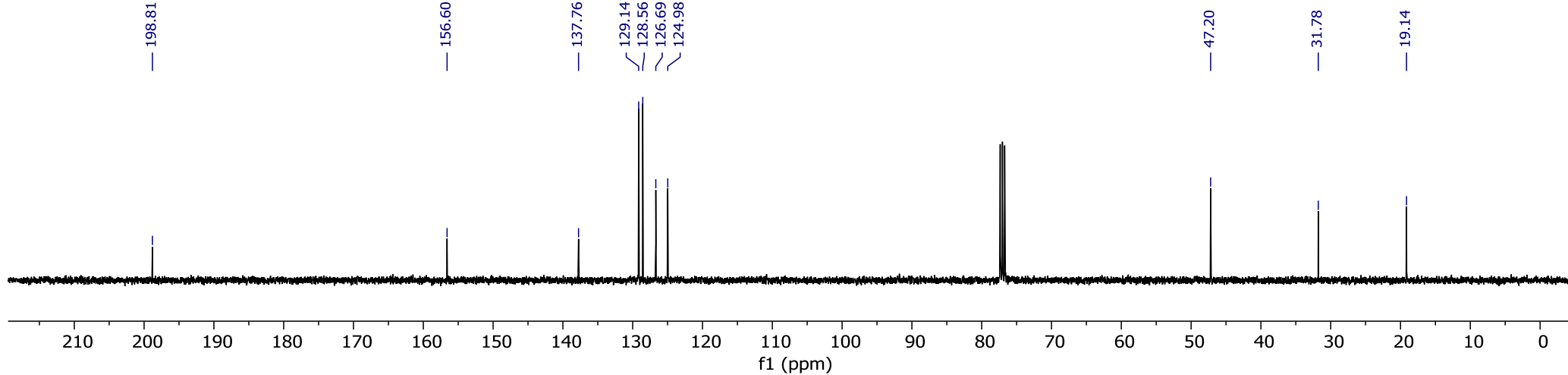
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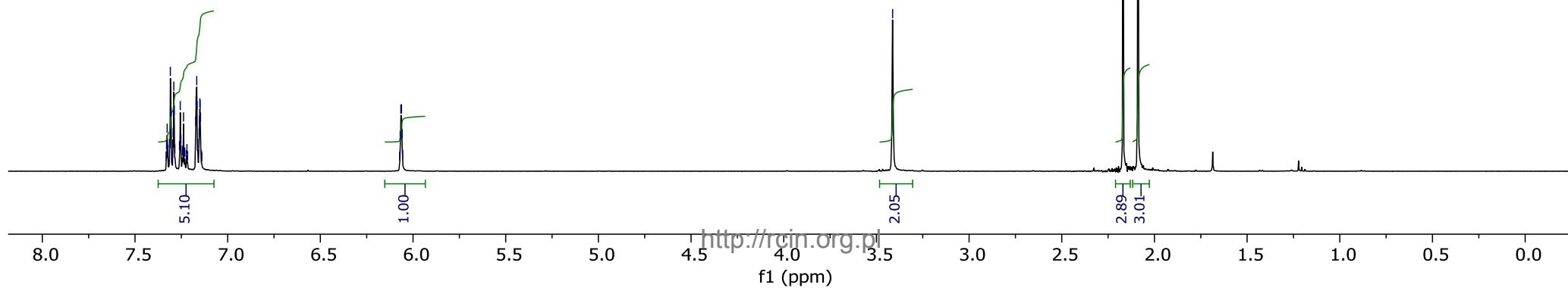
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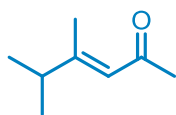
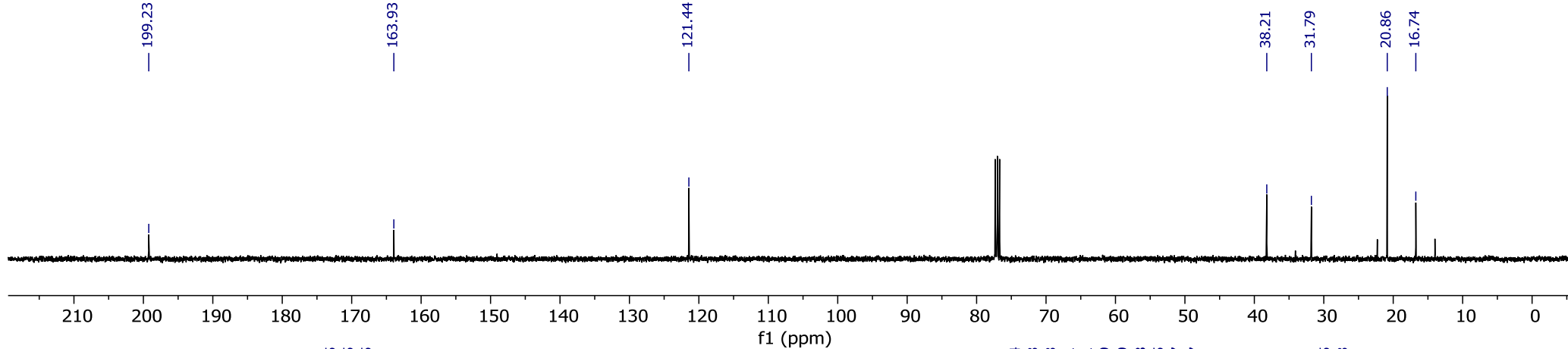


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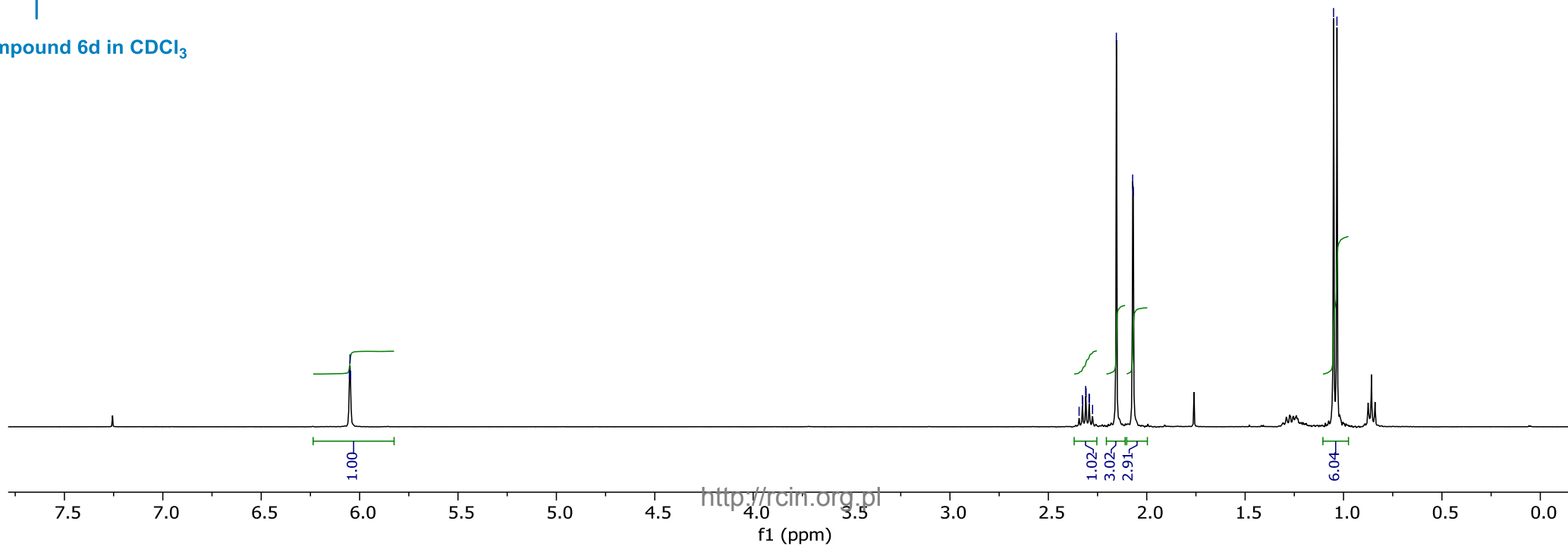


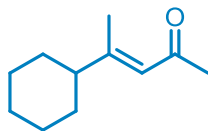
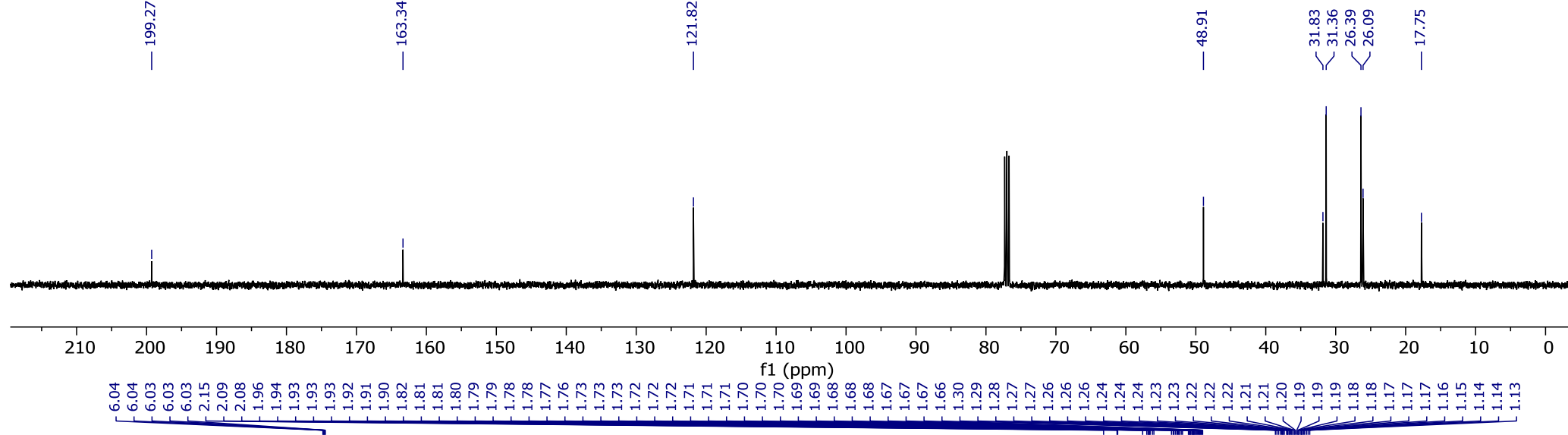
Compound 6f in CDCl<sub>3</sub>



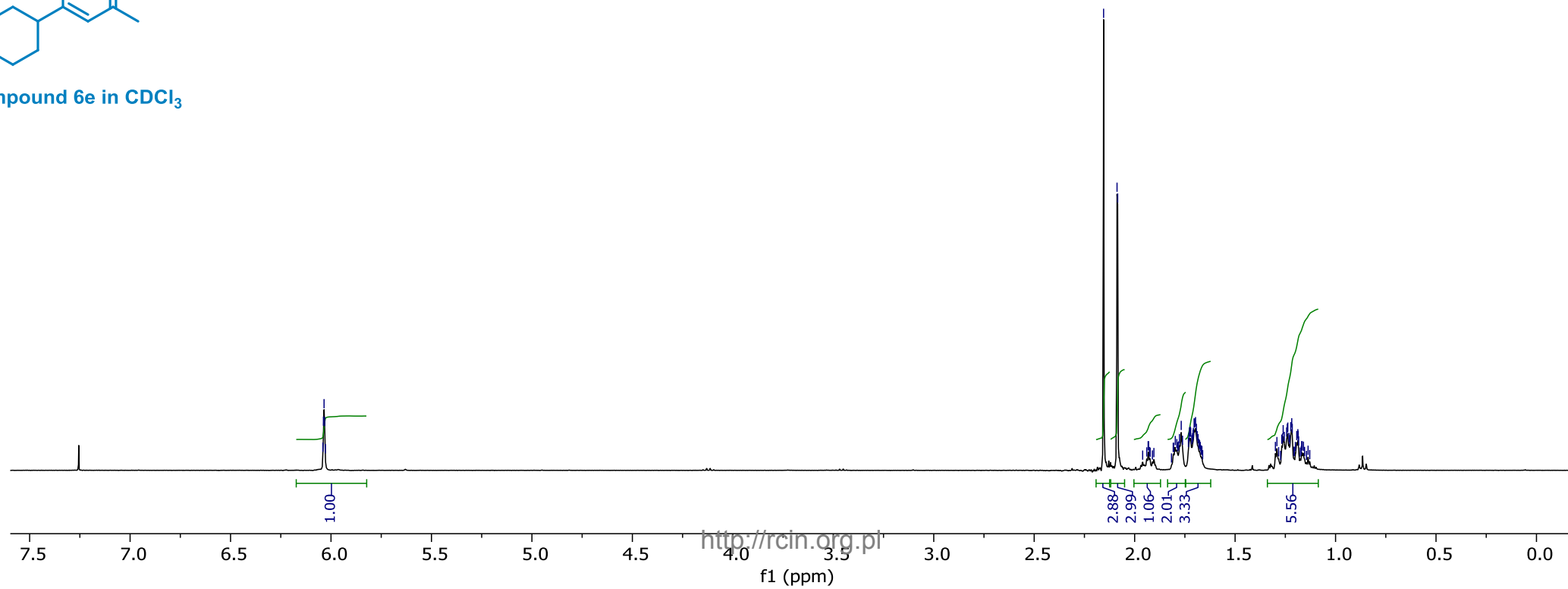


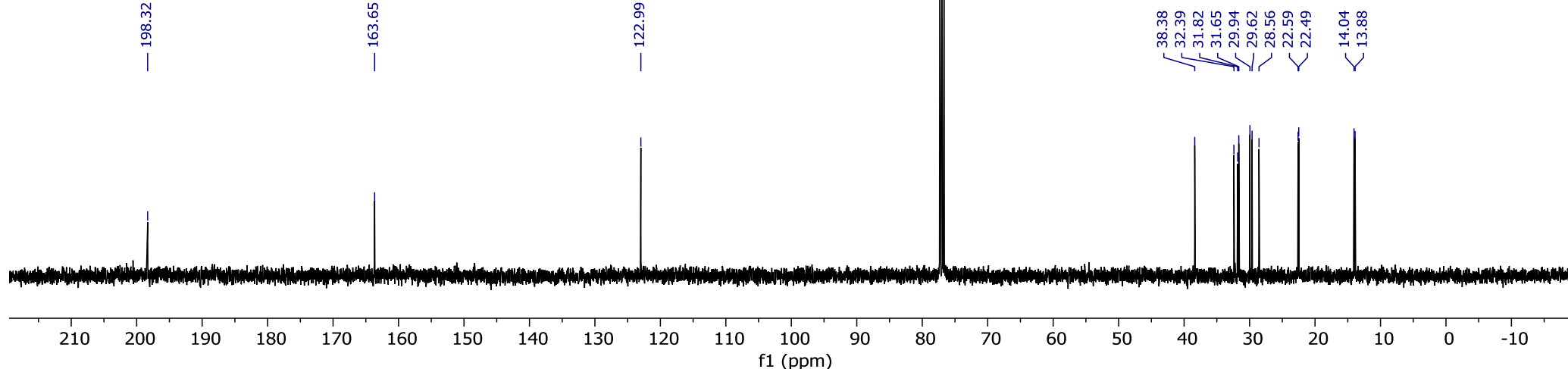
Compound 6d in CDCl<sub>3</sub>



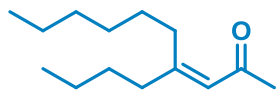


Compound 6e in CDCl<sub>3</sub>

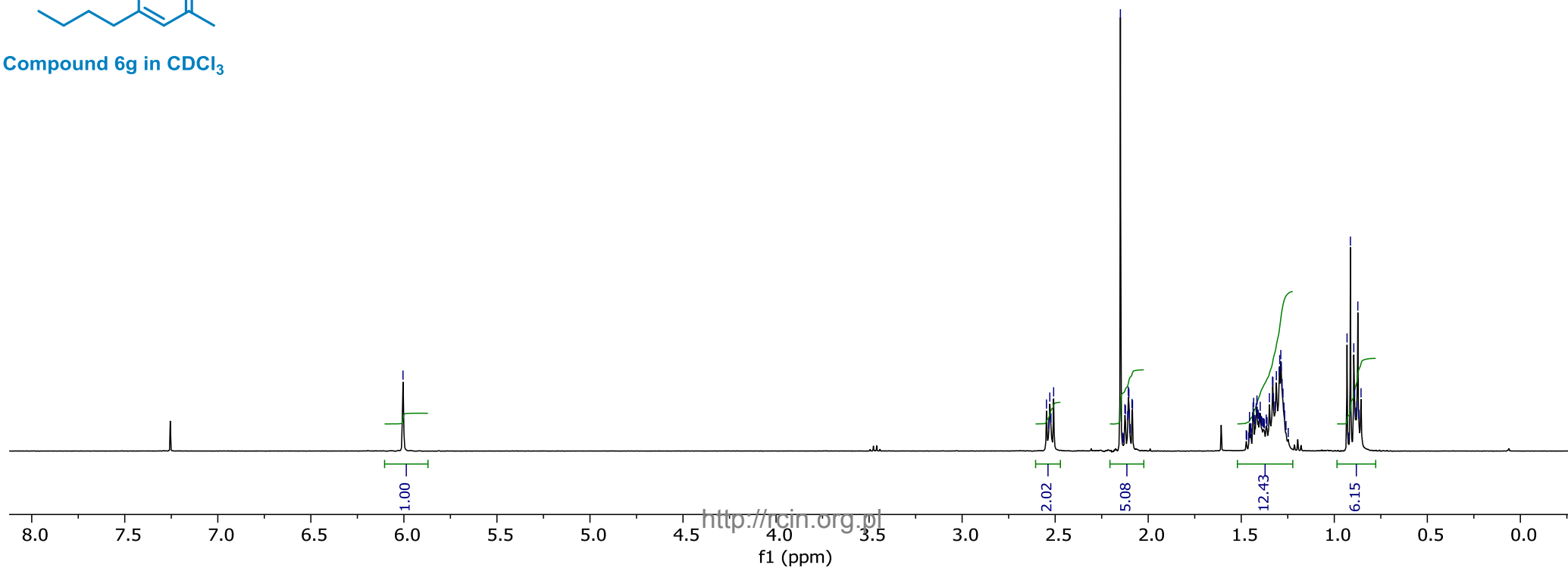


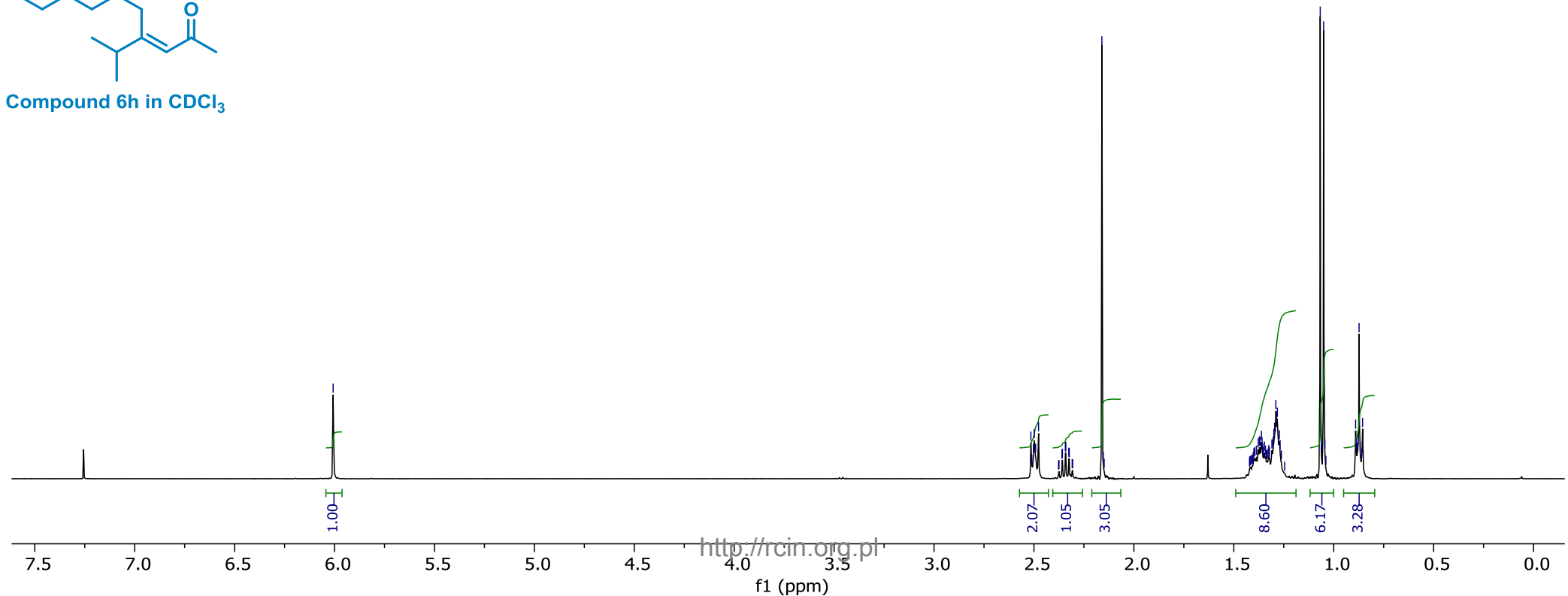
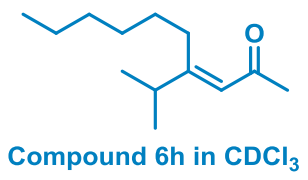
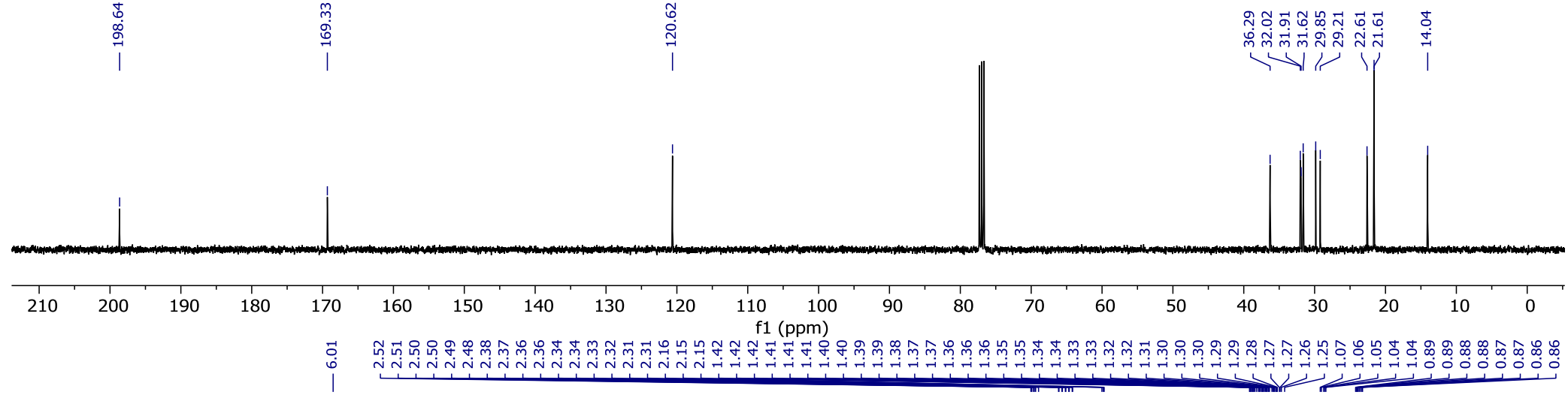


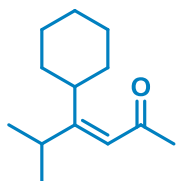
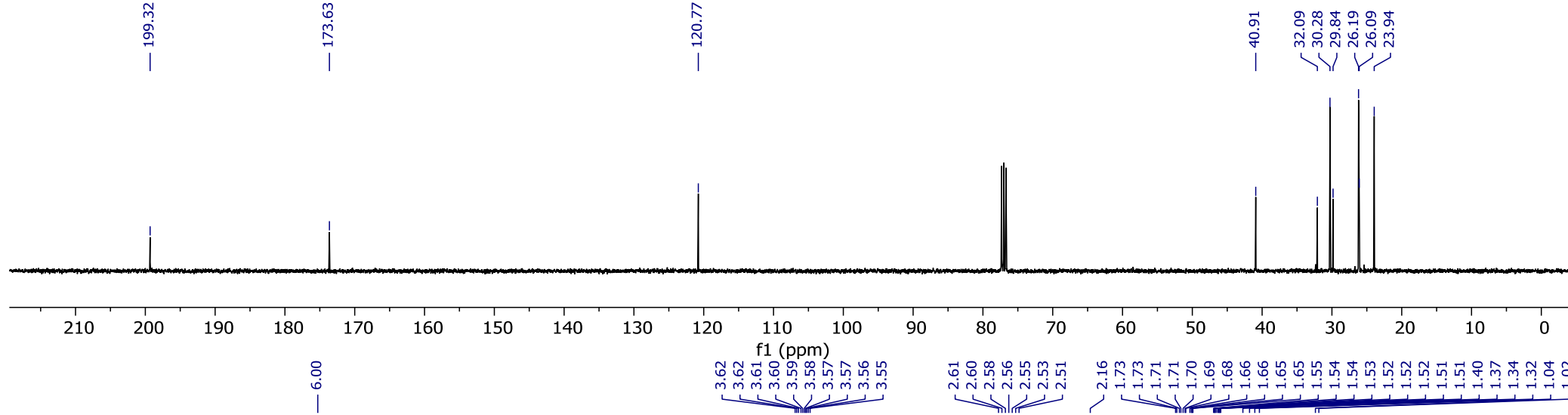
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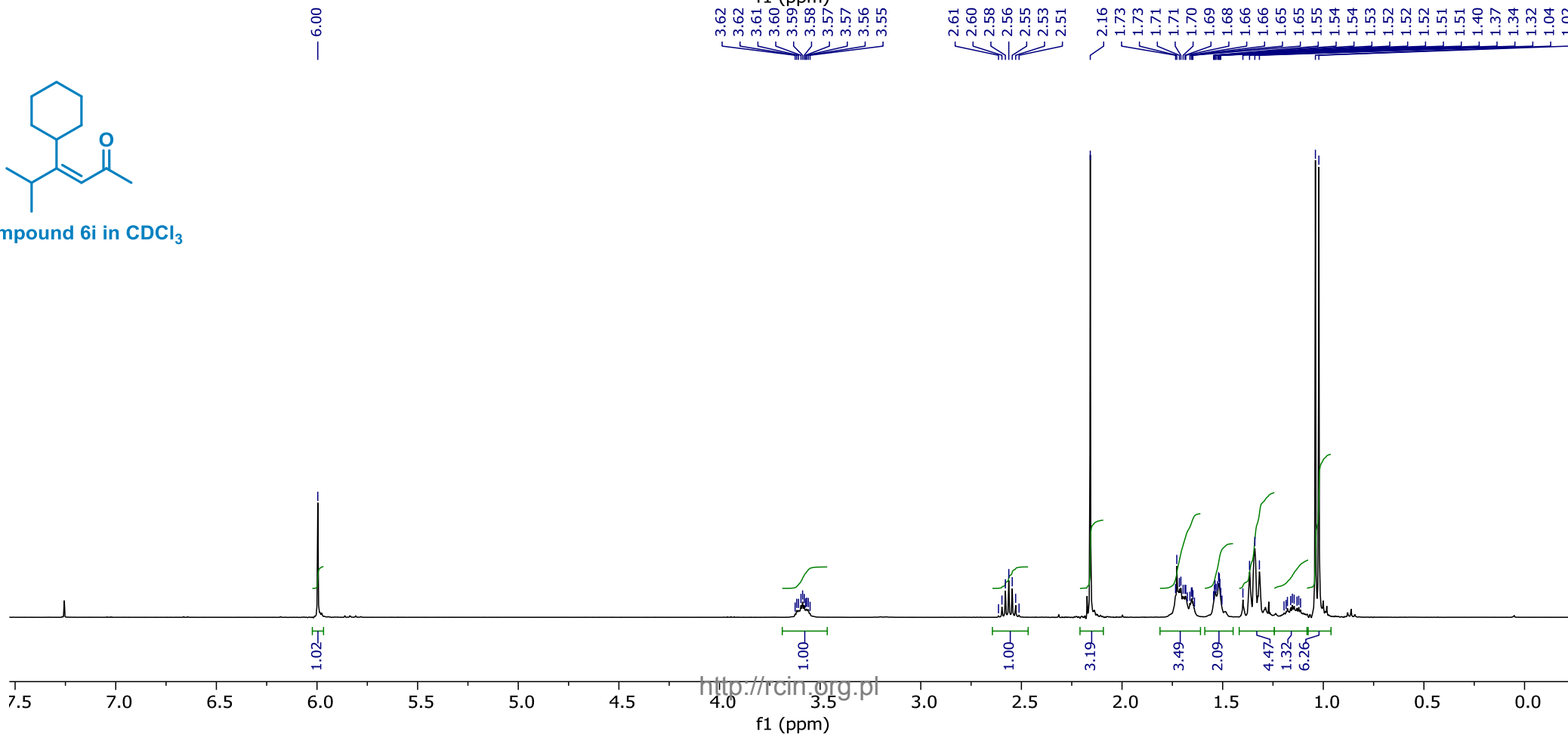
Compound 6g in CDCl<sub>3</sub>



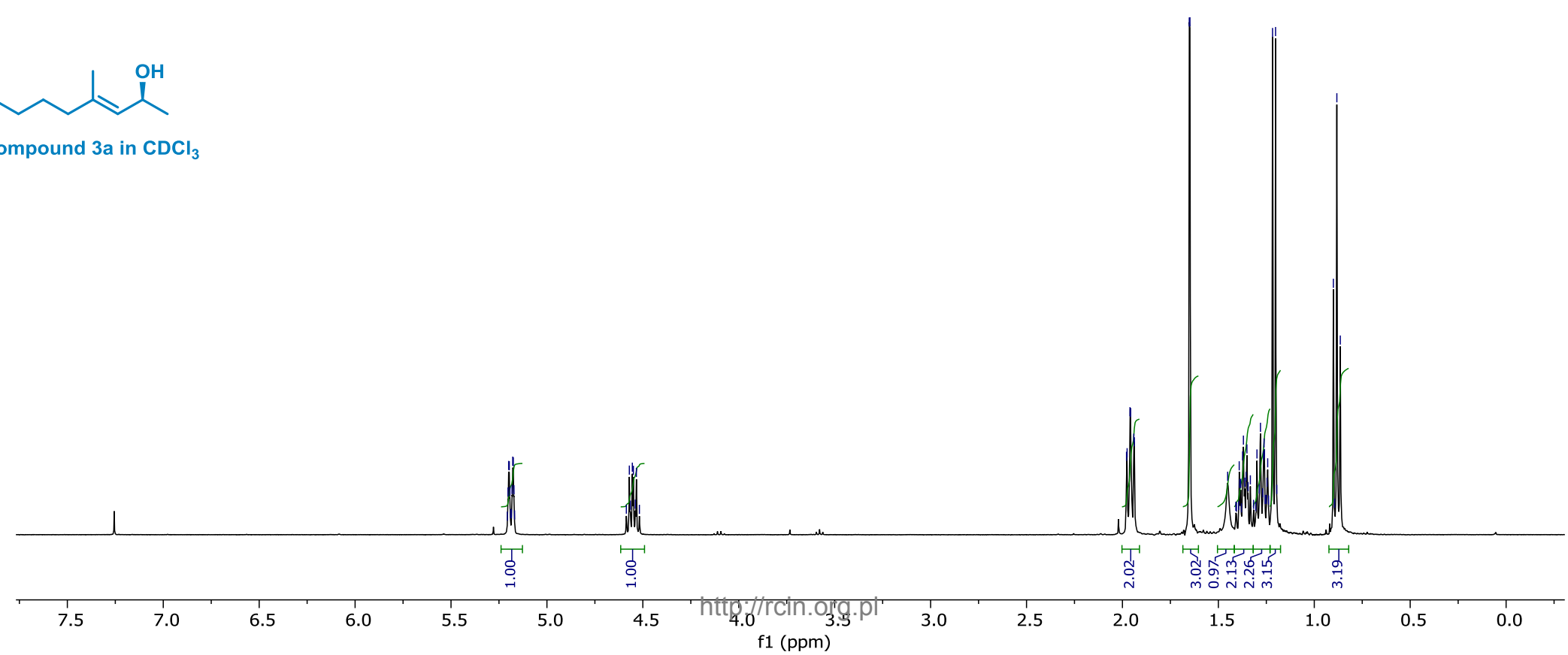
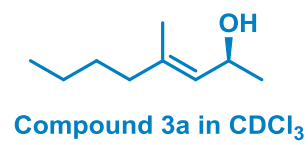
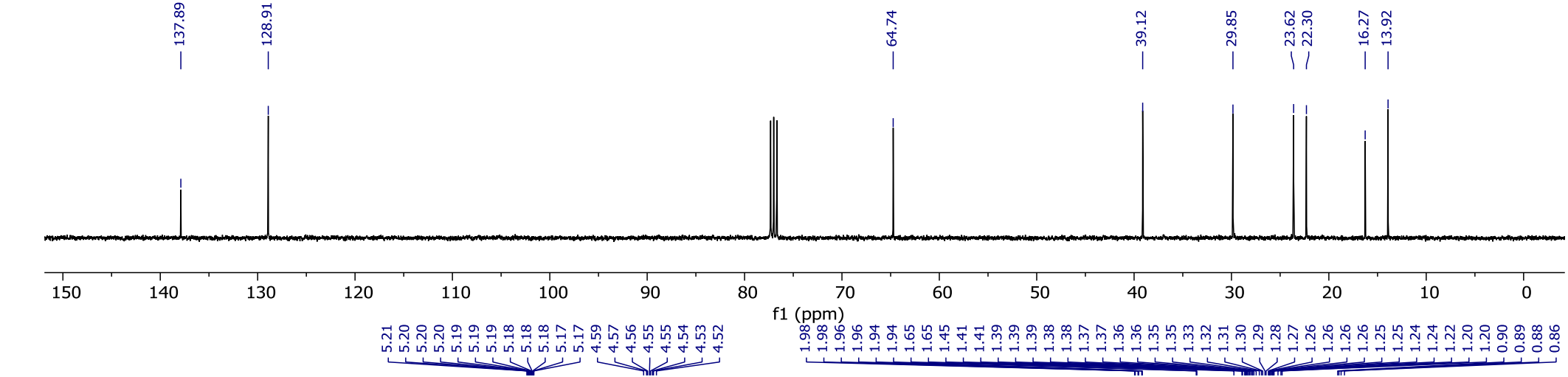


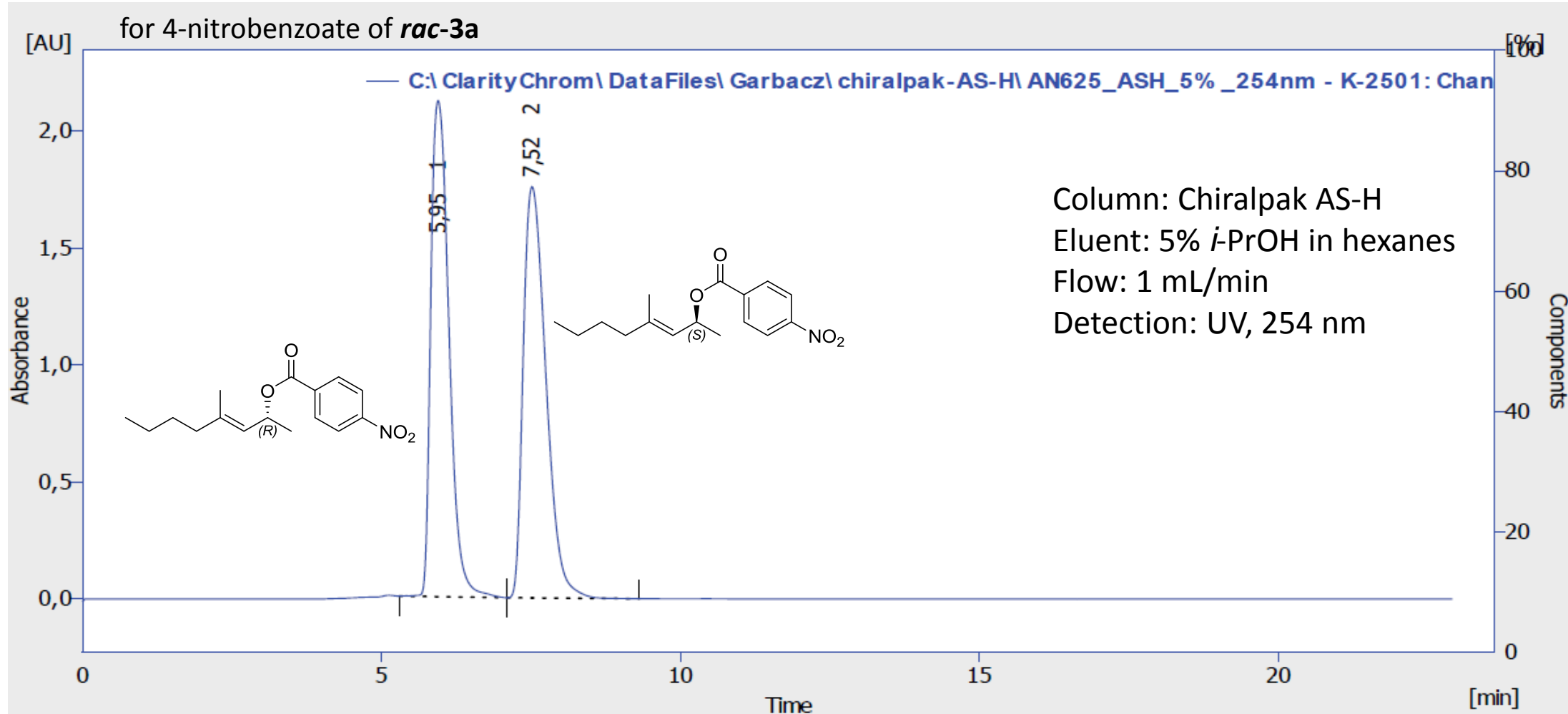


Compound 6i in CDCl<sub>3</sub>



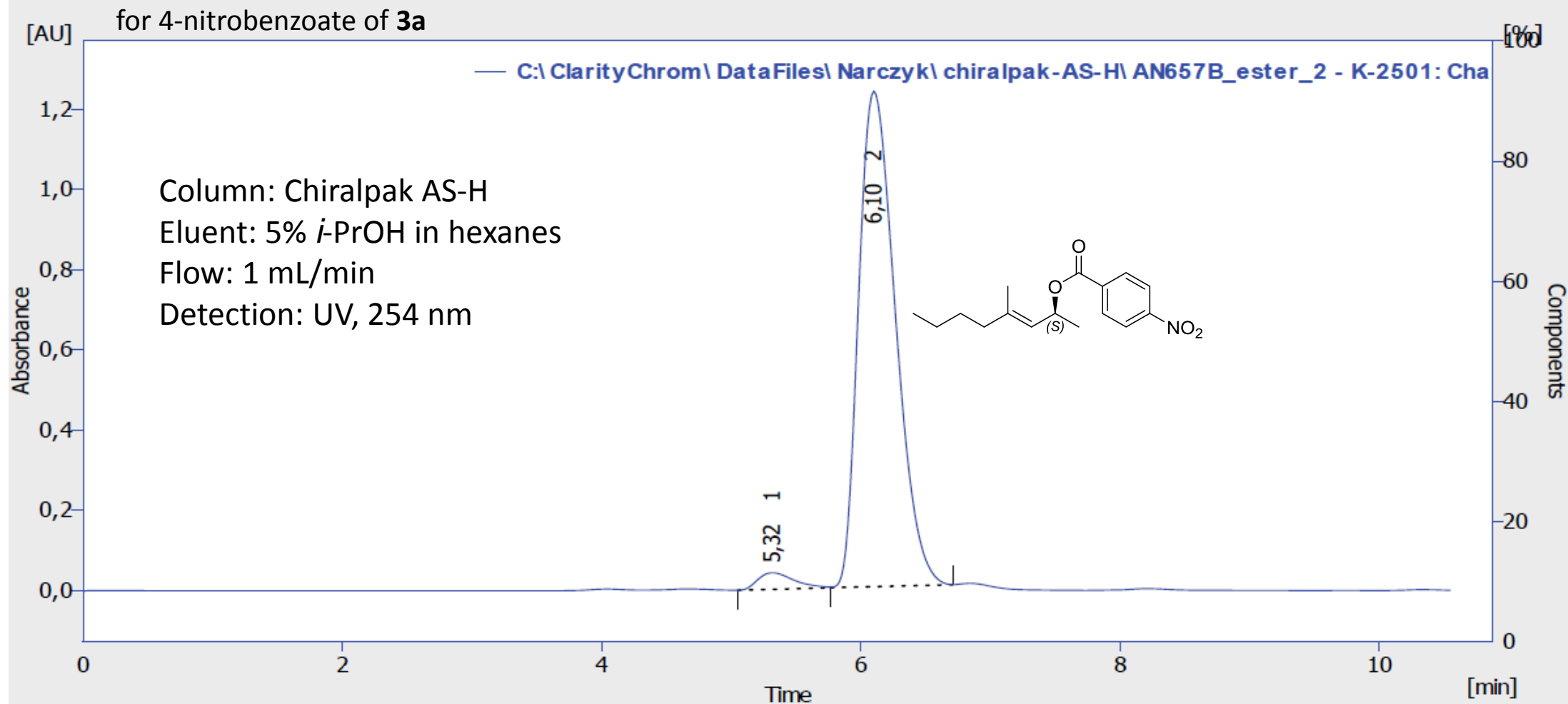






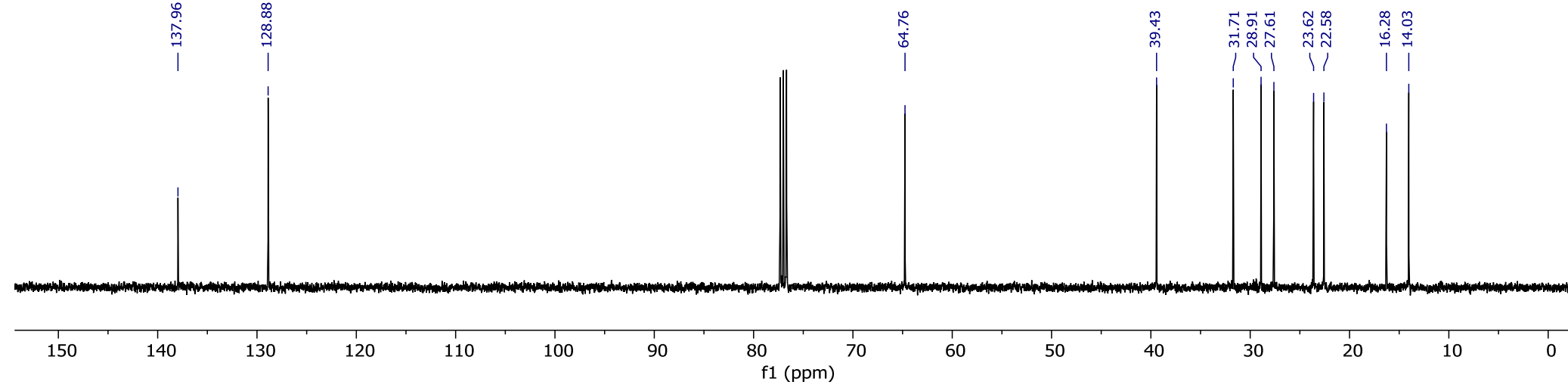
Result Table (Uncal - C:\ClarityChrom\DataFiles\Garbacz\chiralpak-AS-H\AN625\_ASH\_5%\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5,950	44767,975	2121,819	49,2	54,7	0,35	
2	7,517	46262,793	1759,162	50,8	45,3	0,43	
	Total	91030,768	3880,980	100,0	100,0		

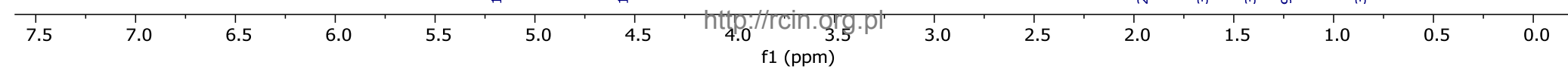


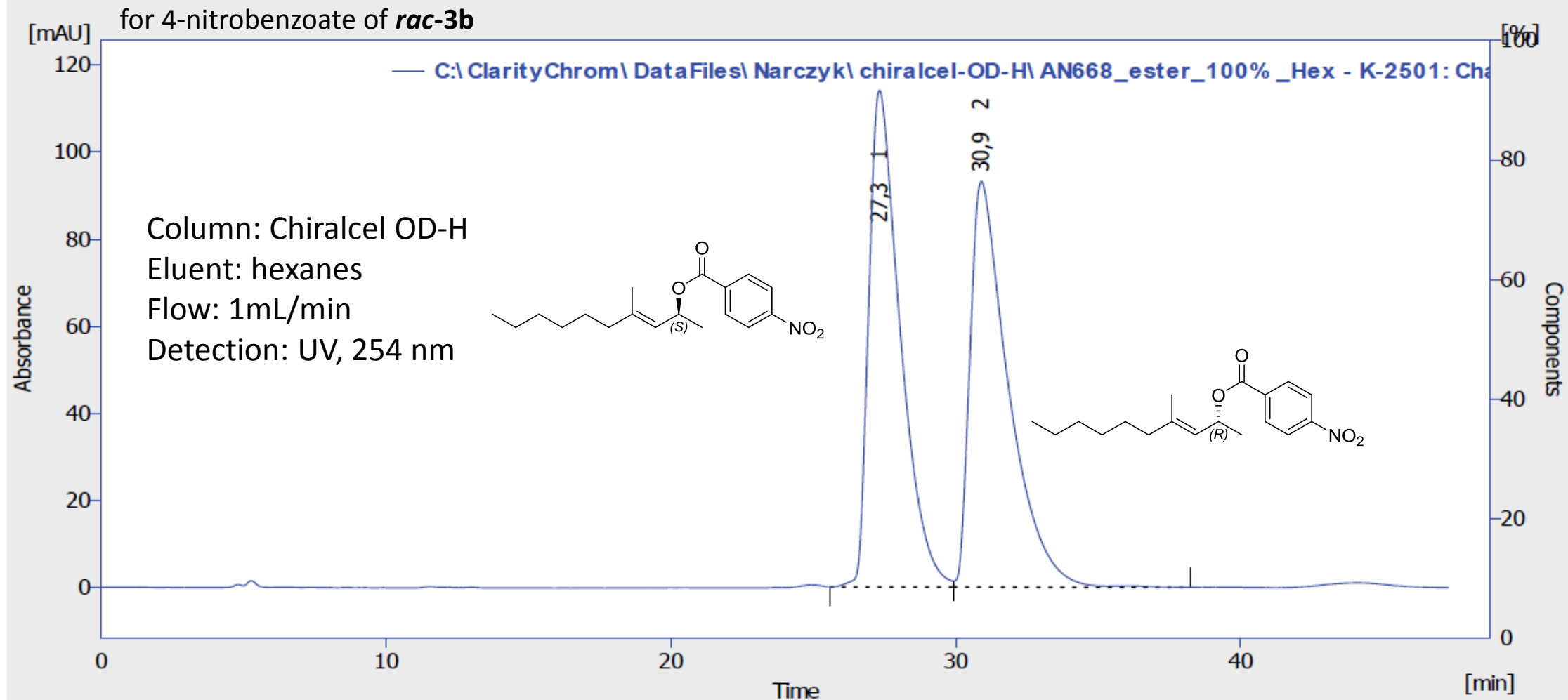
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralpak-AS-H\AN657B\_ester\_2 - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5,317	797,080	41,276	3,2	3,2	0,33	
2	6,100	24335,231	1235,657	96,8	96,8	0,32	
	Total	25132,311	1276,934	100,0	100,0		



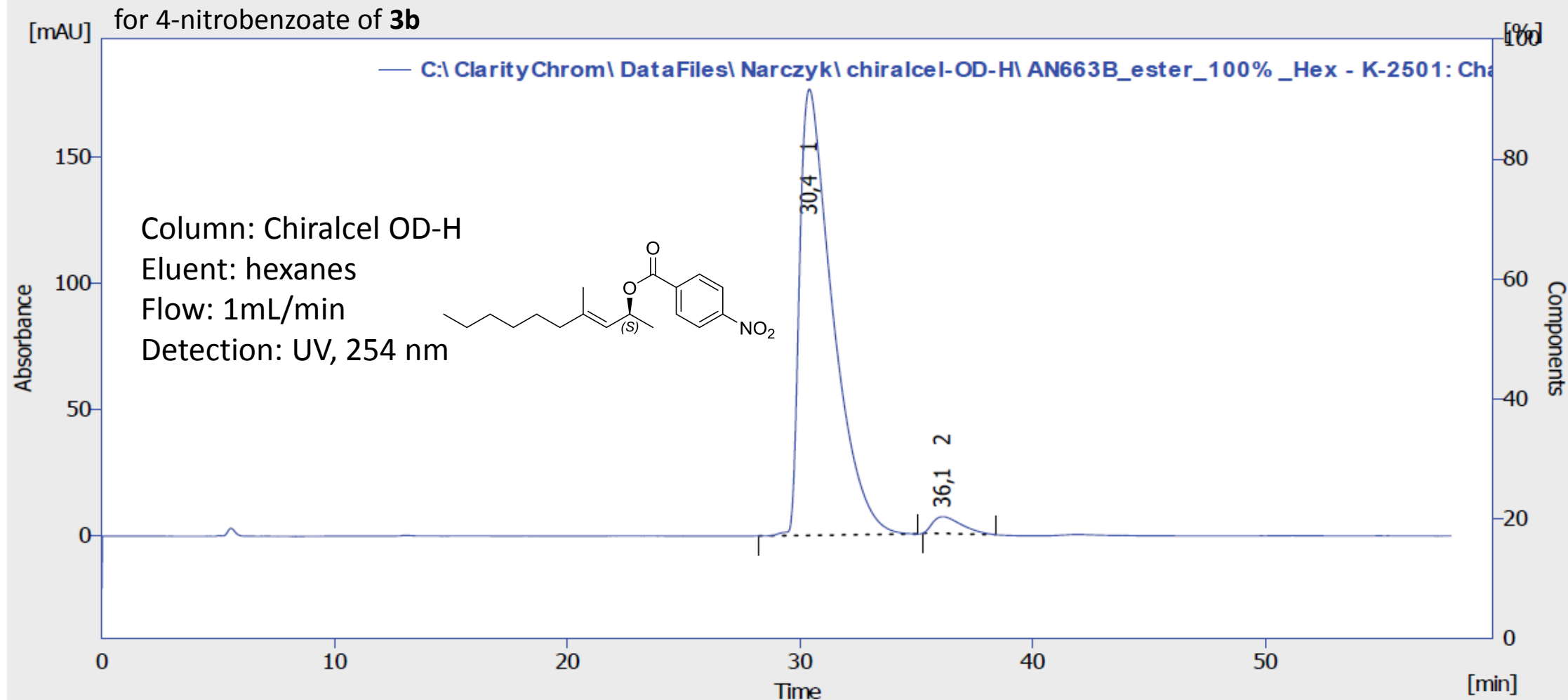
Compound 3b in CDCl<sub>3</sub>





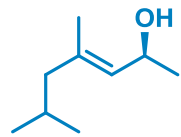
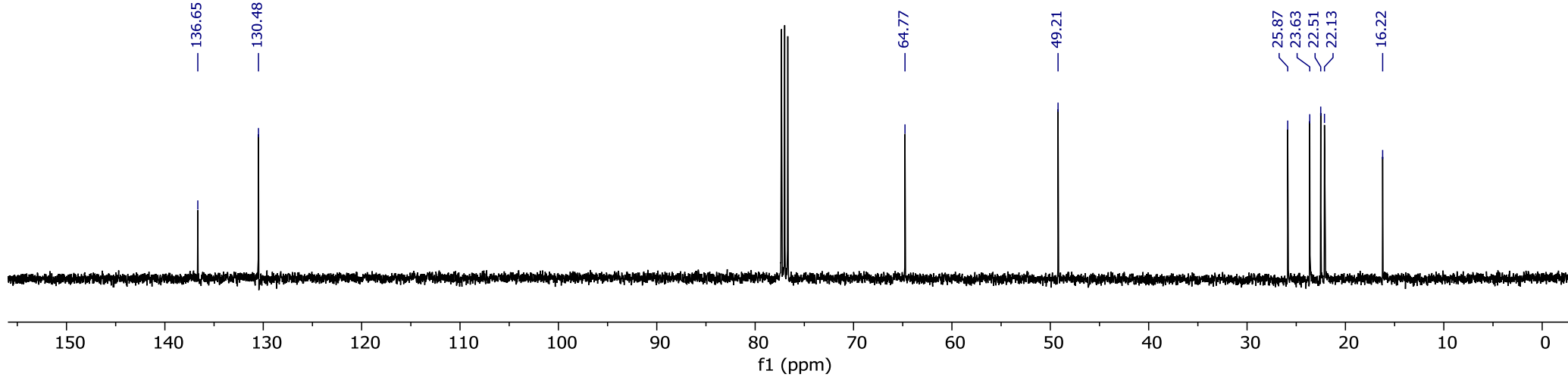
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN668\_ester\_100%\_Hex - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	27,333	8775,738	114,167	50,0	55,0	1,18	
2	30,900	8768,887	93,255	50,0	45,0	1,40	
	Total	17544,625	207,422	100,0	100,0		

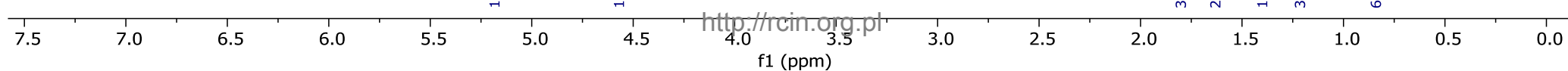


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN663B\_ester\_100%\_Hex - K-2501: Channel 1)

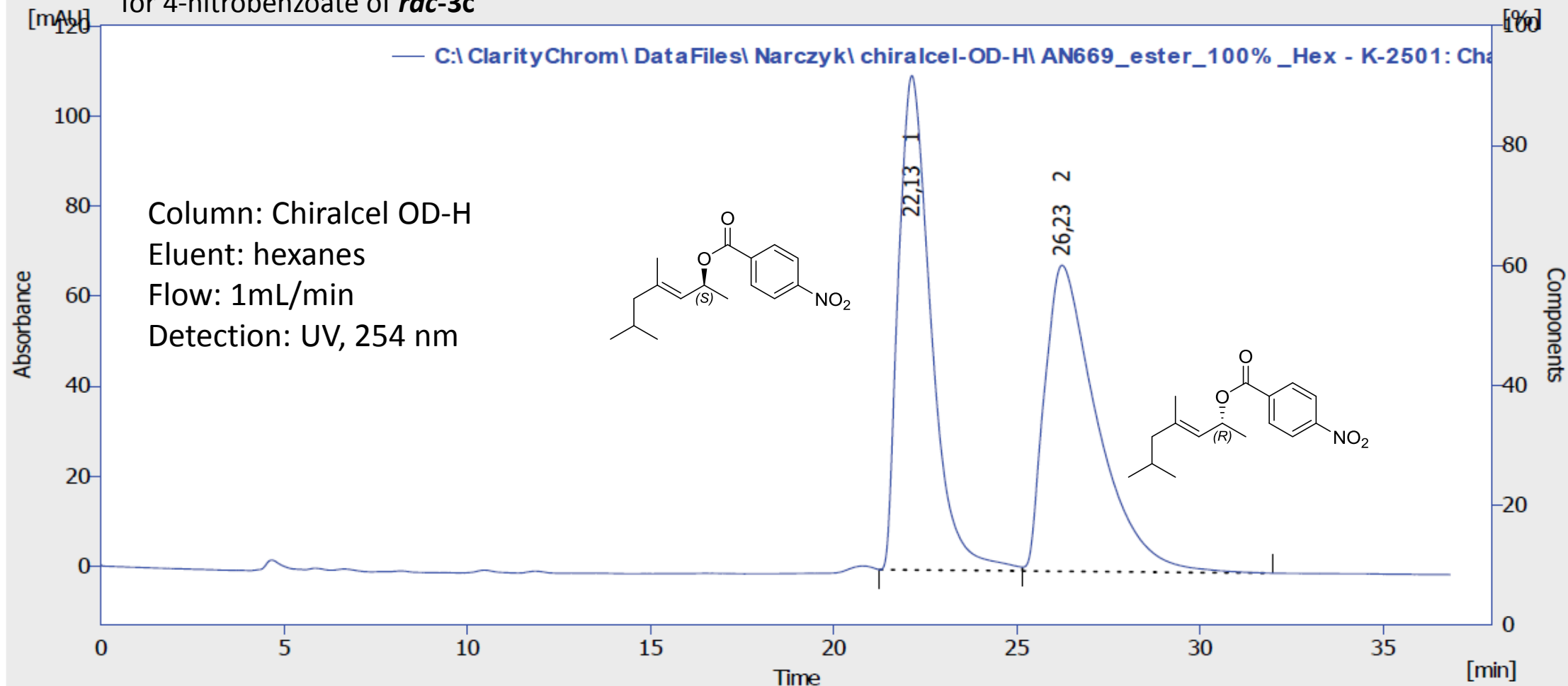
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	30,400	17356,062	176,363	96,8	96,4	1,48	
2	36,133	576,797	6,642	3,2	3,6	1,38	
	Total	17932,859	183,005	100,0	100,0		



Compound 3c in CDCl<sub>3</sub>



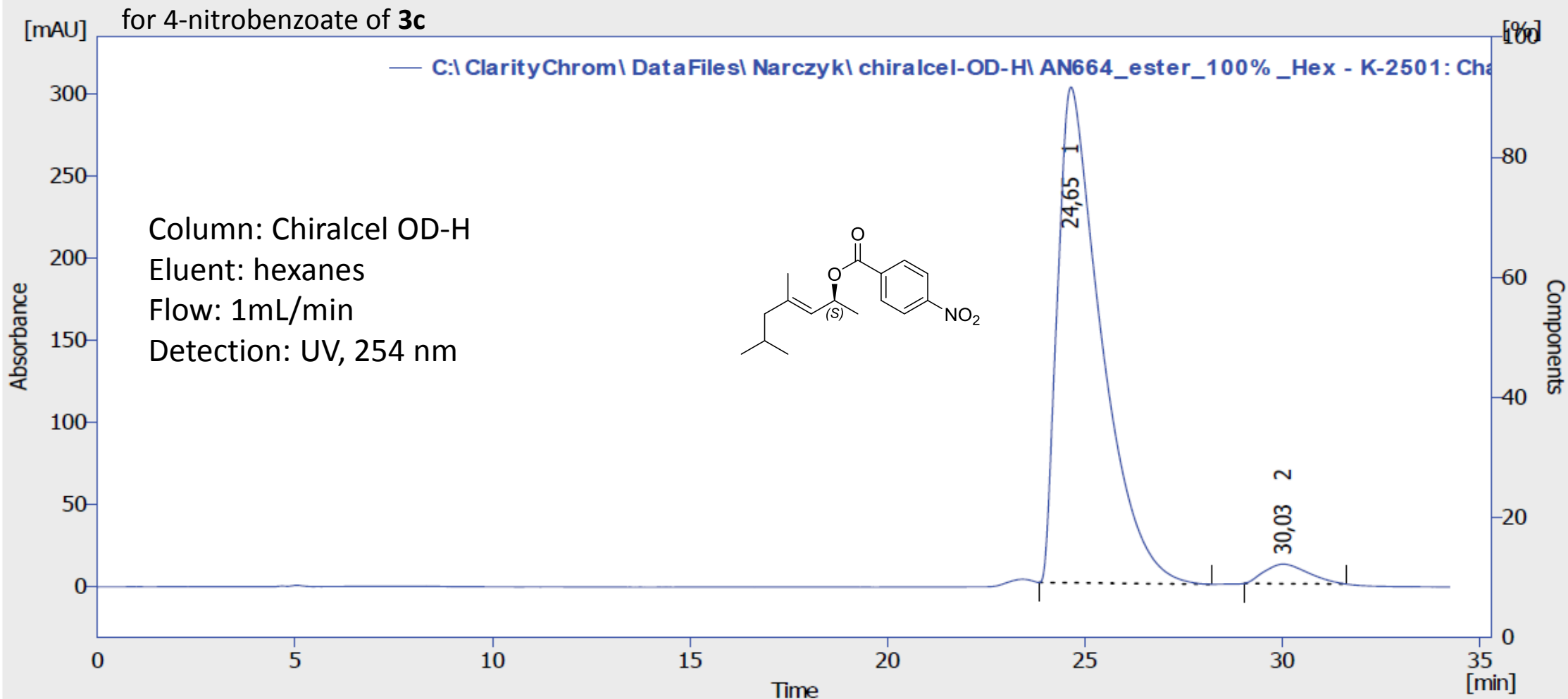
for 4-nitrobenzoate of *rac*-3c



Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN669\_ester\_100%\_Hex - K-2501: Channel 1)

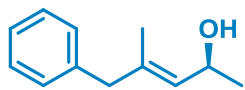
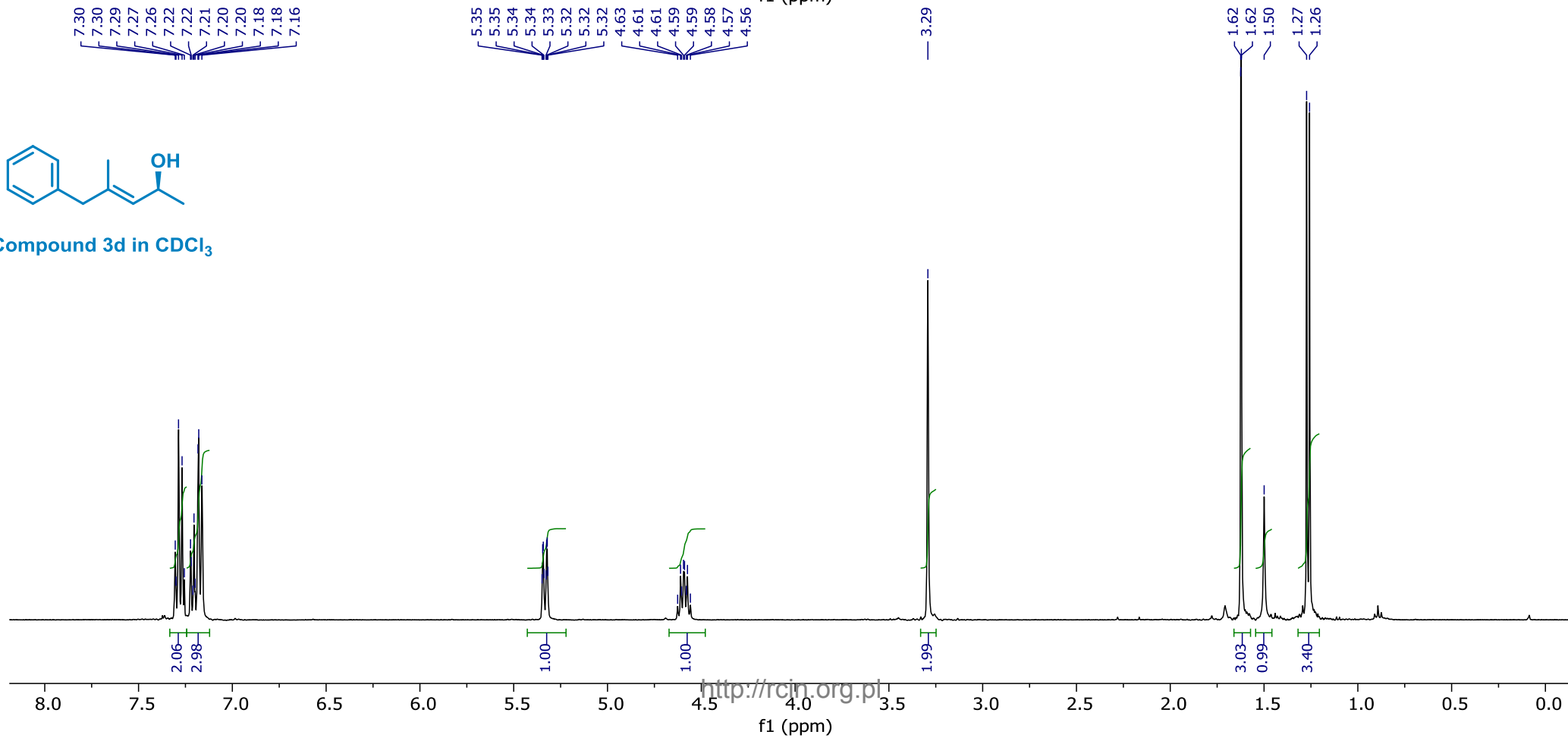
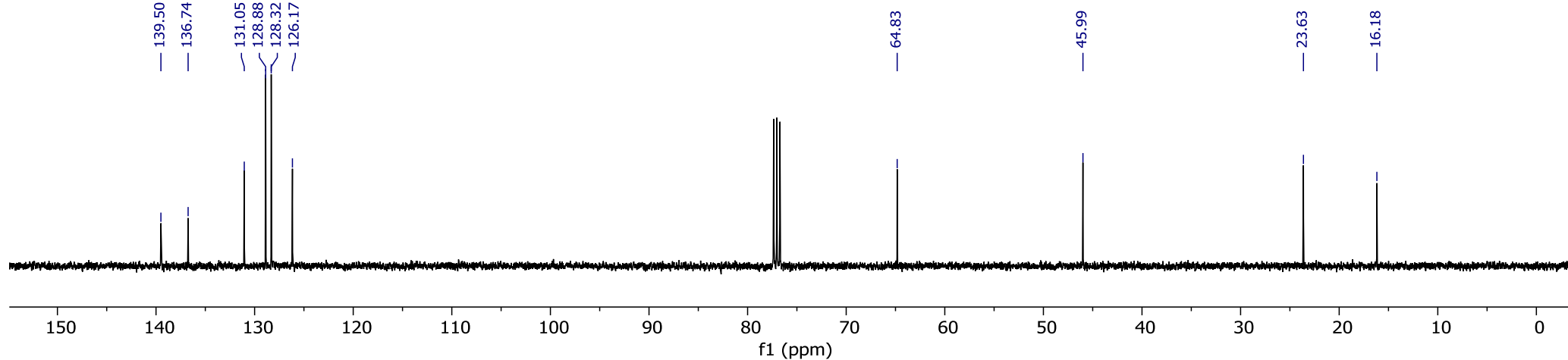
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22,133	6795,309	109,858	50,0	61,8	0,97	
2	26,233	6792,114	68,008	50,0	38,2	1,52	
	Total	13587,424	177,866	100,0	100,0		



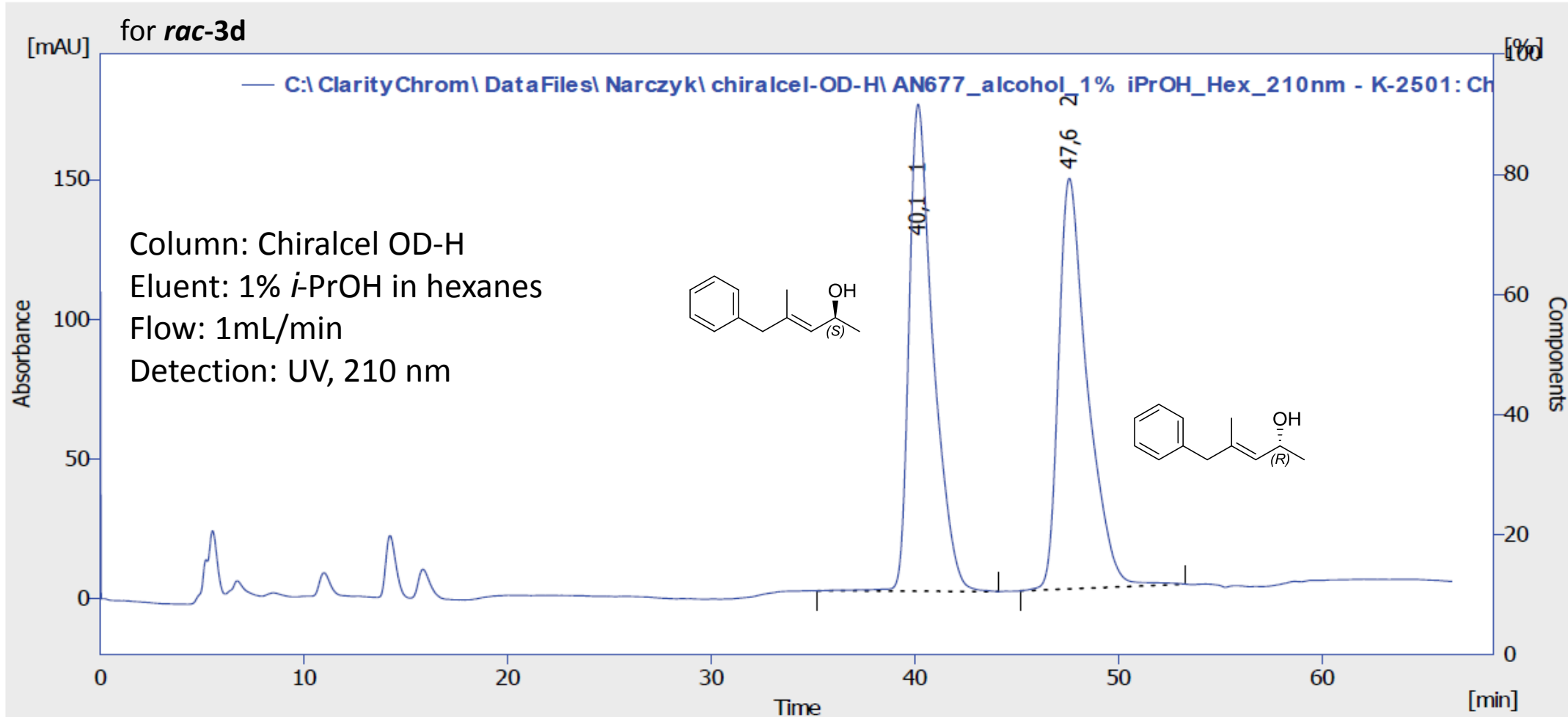


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN664\_ester\_100%\_Hex - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	24,650	23134,109	301,574	96,2	96,2	1,18	
2	30,033	920,188	11,876	3,8	3,8	1,28	
	Total	24054,297	313,450	100,0	100,0		

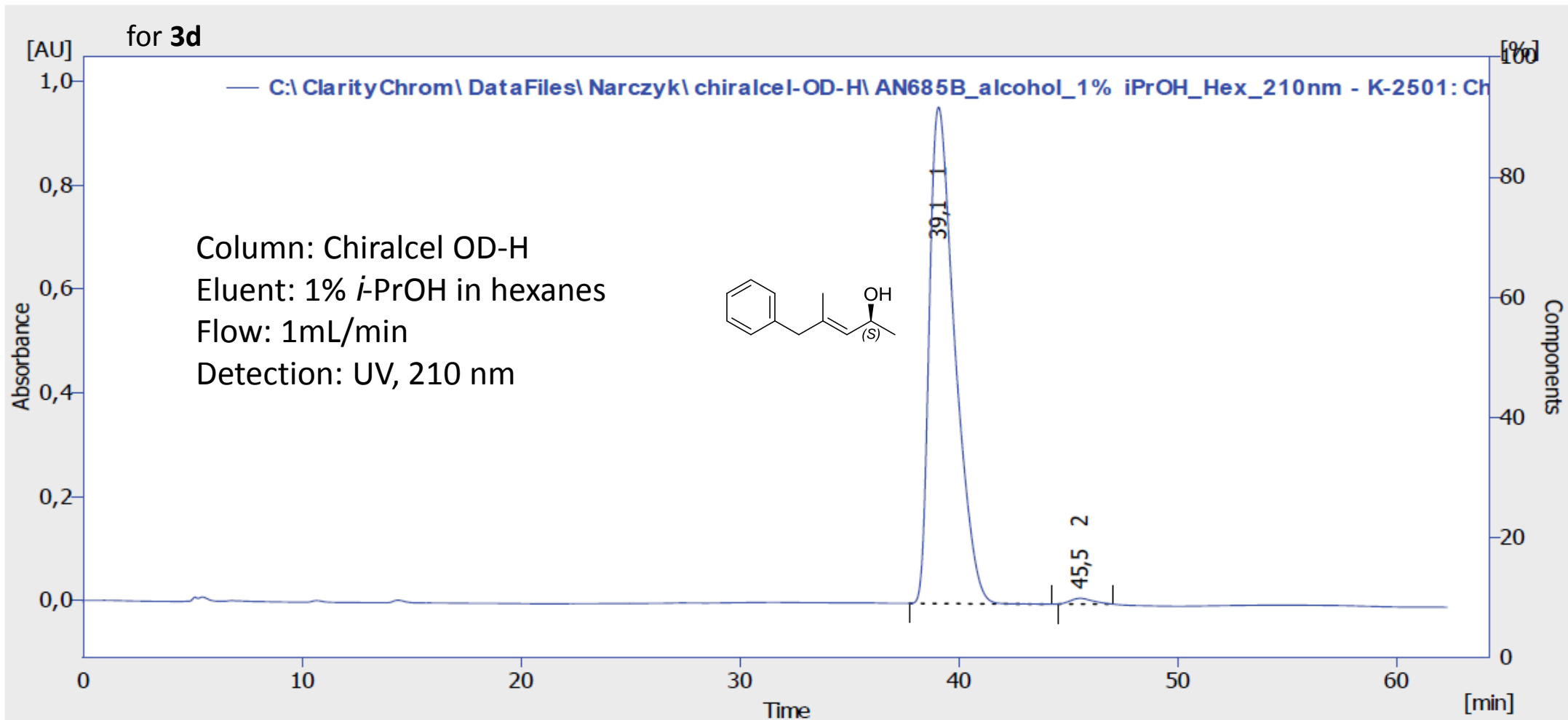


Compound 3d in CDCl<sub>3</sub>



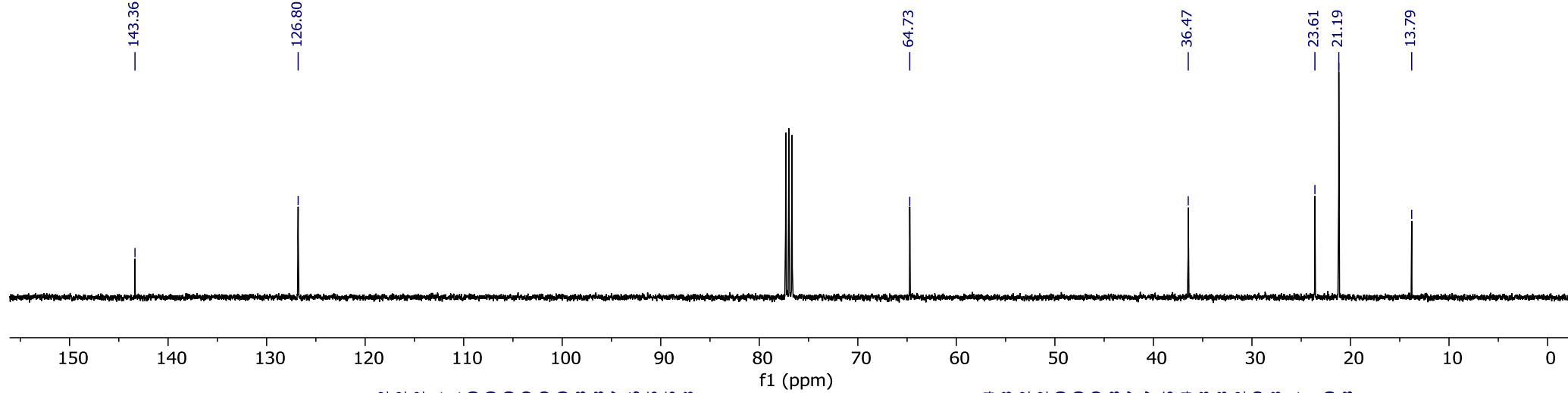
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN677\_alcohol\_1% iPrOH\_Hex\_210nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	40,150	14400,527	174,180	49,8	54,3	1,23	
2	47,583	14512,956	146,834	50,2	45,7	1,47	
	Total	28913,482	321,014	100,0	100,0		



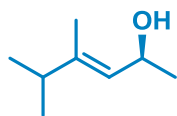
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN685B\_alcohol\_1% iPrOH\_Hex\_210nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	39,083	77222,401	957,204	99,0	98,9	1,25	
2	45,550	801,594	11,074	1,0	1,1	1,15	
	Total	78023,995	968,278	100,0	100,0		

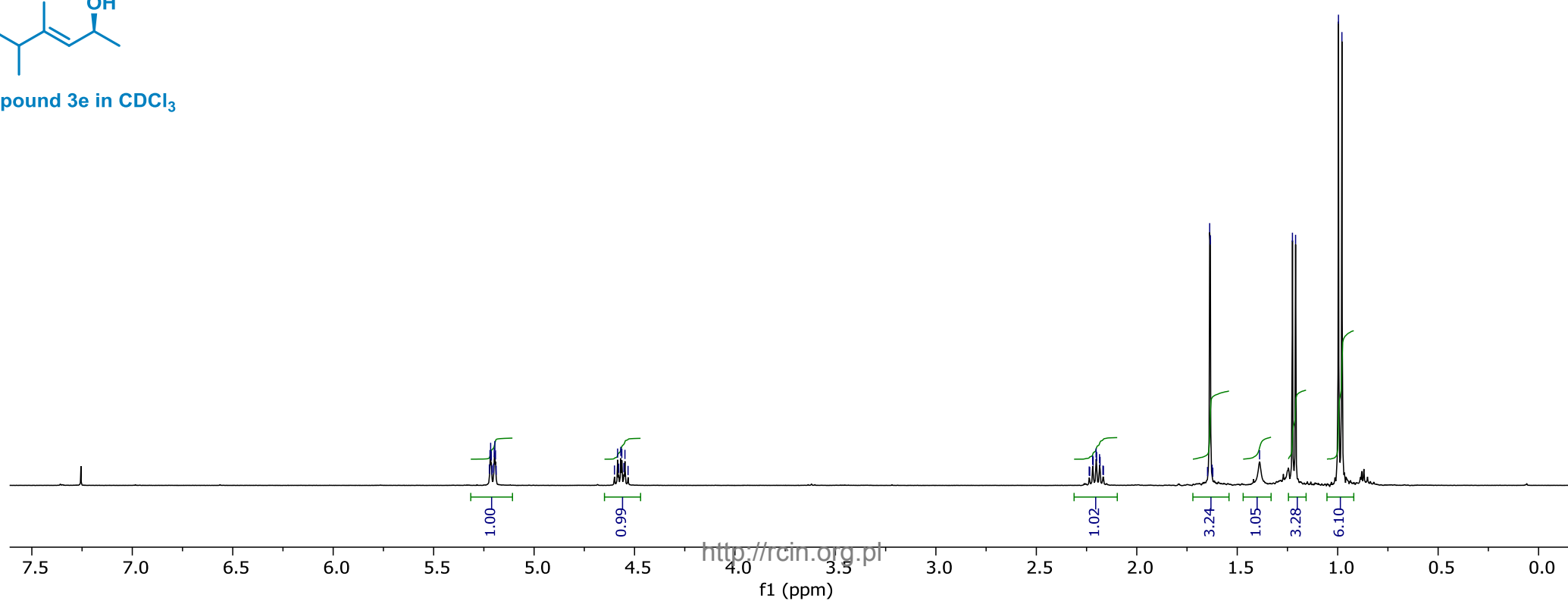


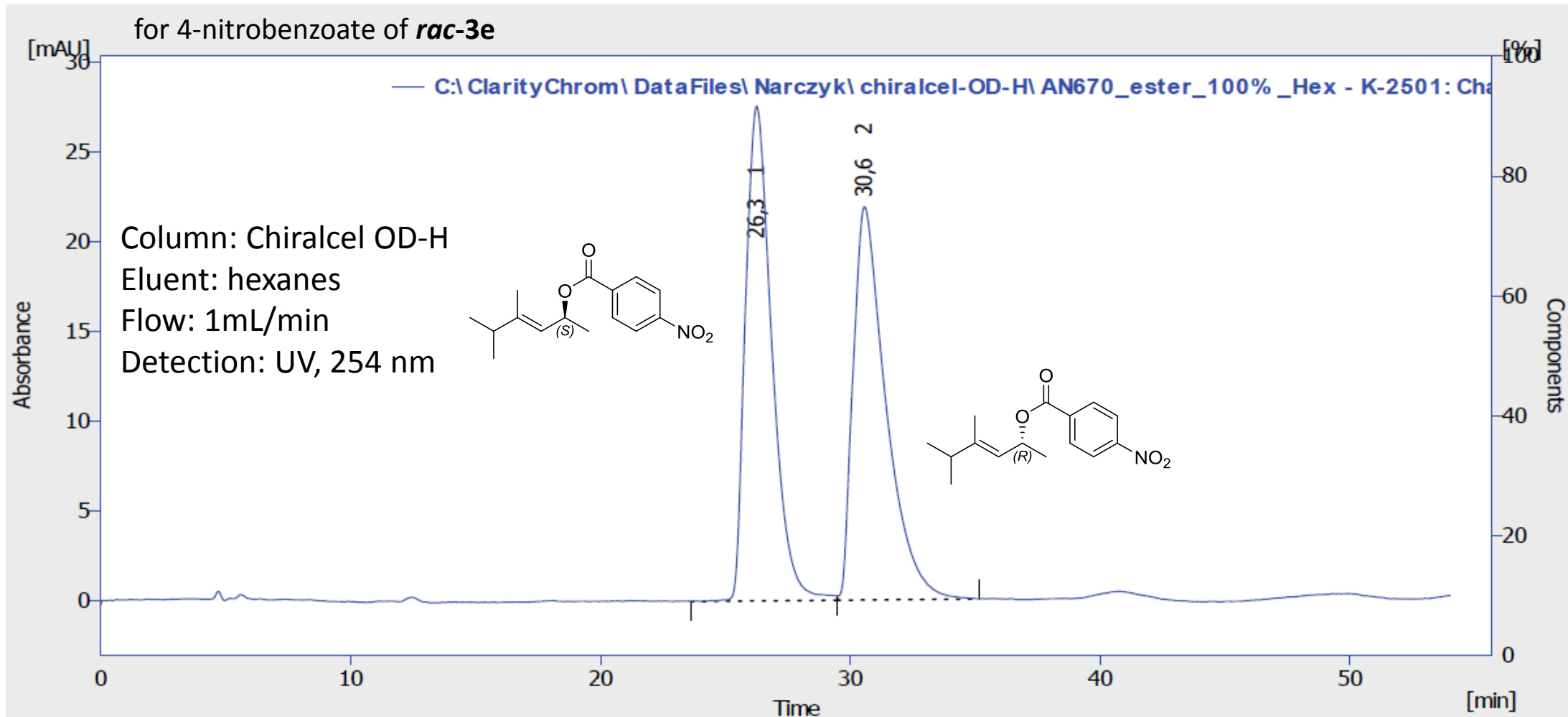
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1.63  
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1.23  
1.21  
1.00  
0.98



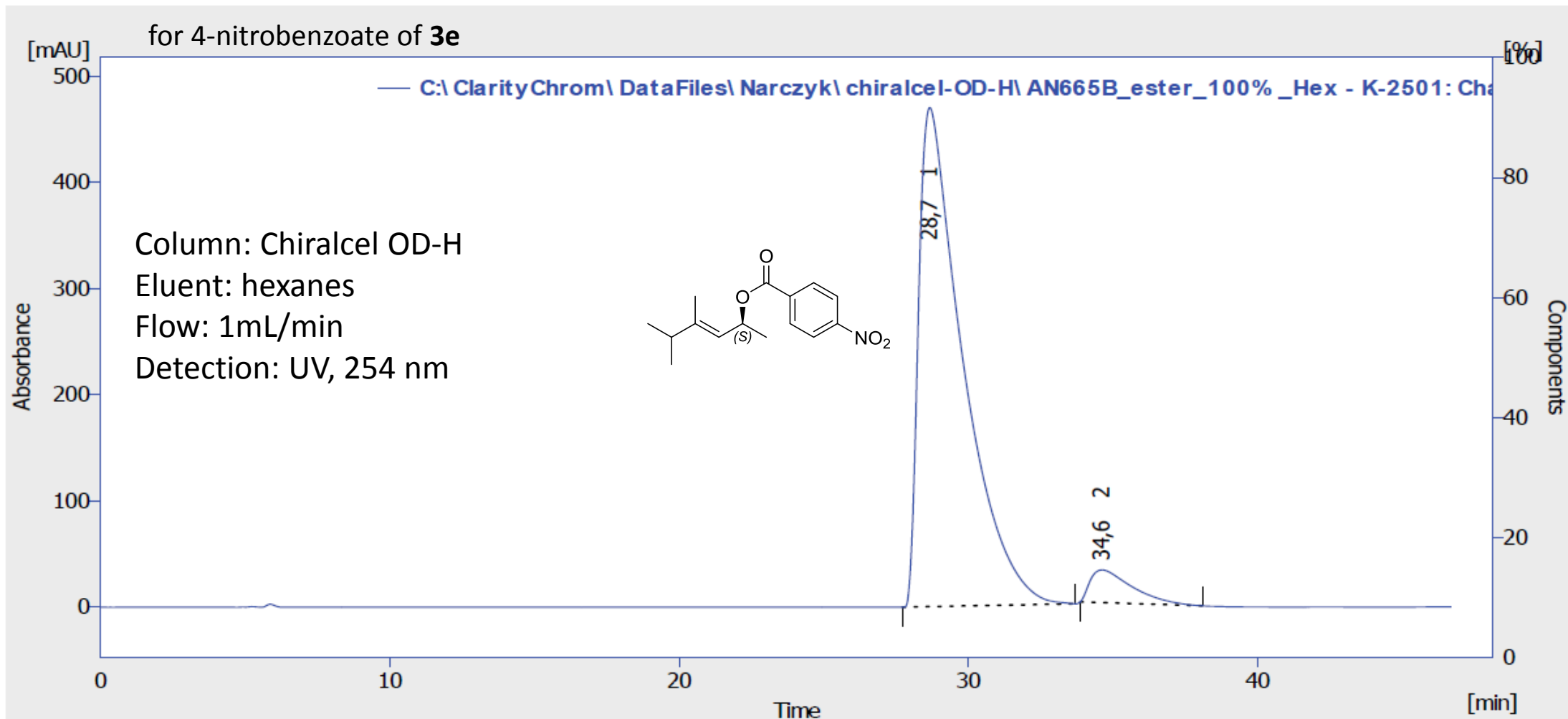
Compound 3e in CDCl<sub>3</sub>





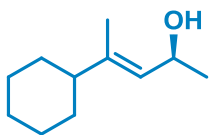
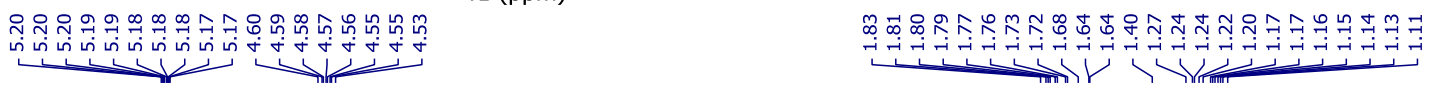
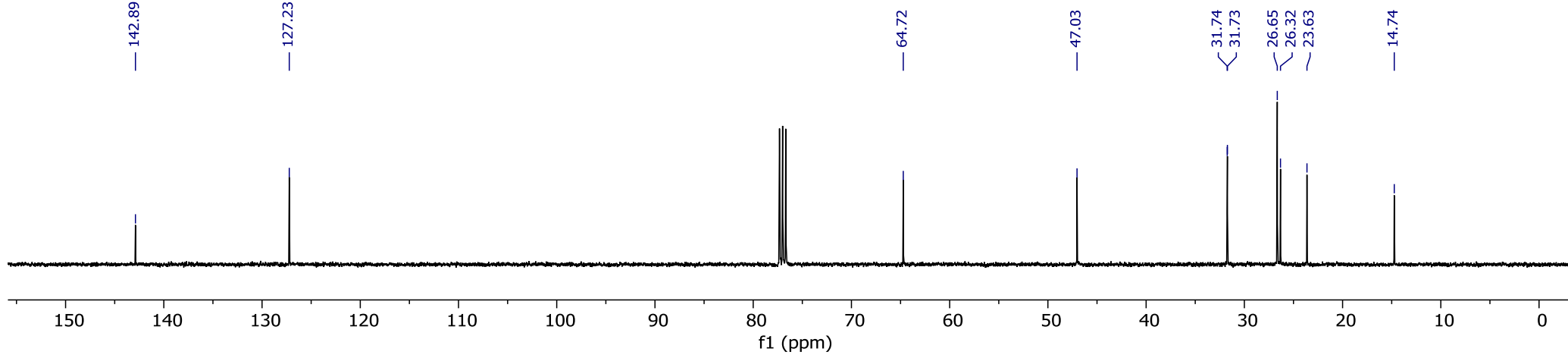
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN670\_ester\_100%\_Hex - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	26,250	2033,156	27,603	50,4	55,7	1,15	
2	30,567	2004,322	21,934	49,6	44,3	1,40	
	Total	4037,477	49,537	100,0	100,0		

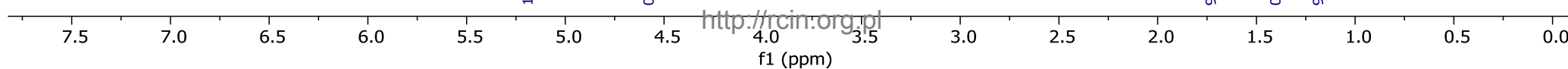


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN665B\_ester\_100%\_Hex - K-2501: Channel 1)

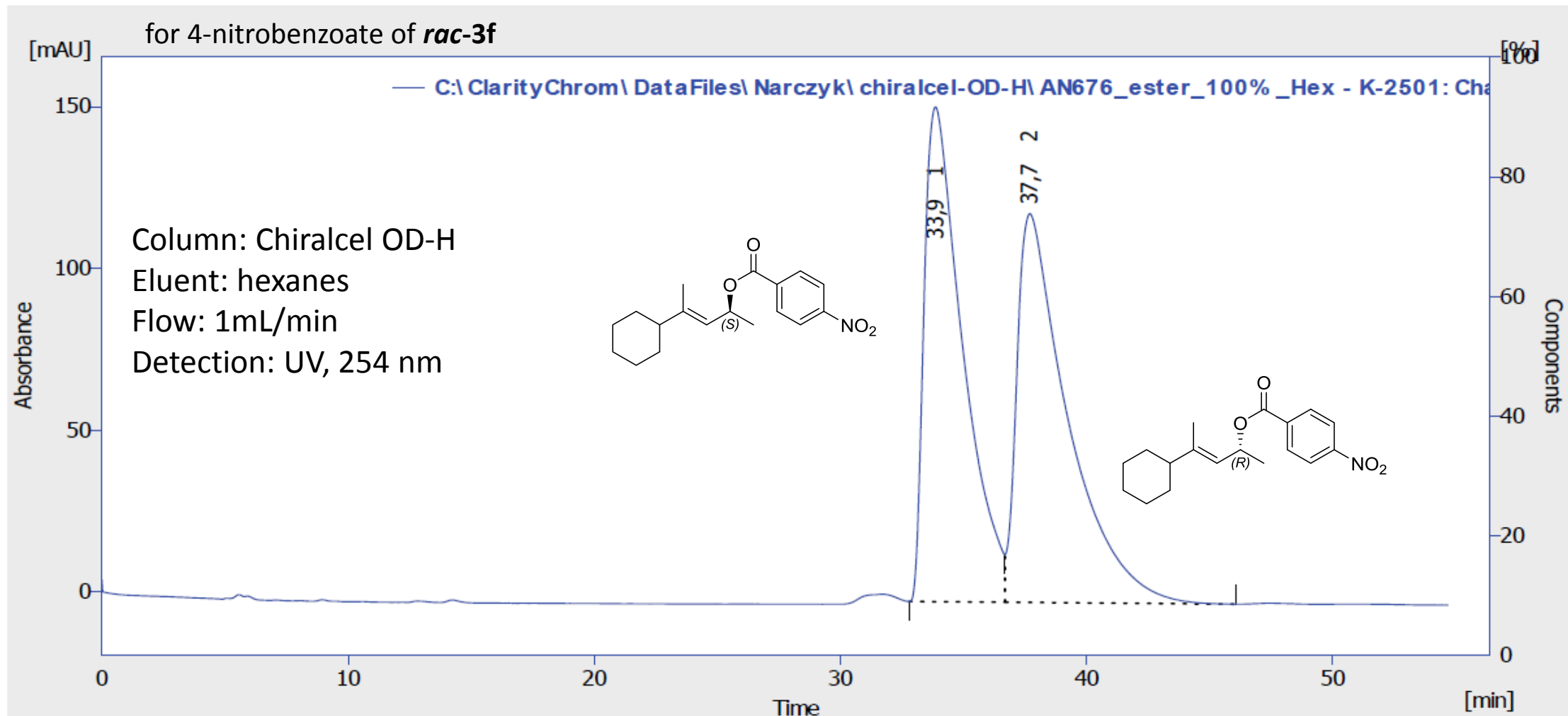
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	28,667	49732,684	469,898	94,1	93,8	1,57	
2	34,617	3114,321	30,803	5,9	6,2	1,53	
	Total	52847,005	500,701	100,0	100,0		



Compound 3f in CDCl<sub>3</sub>

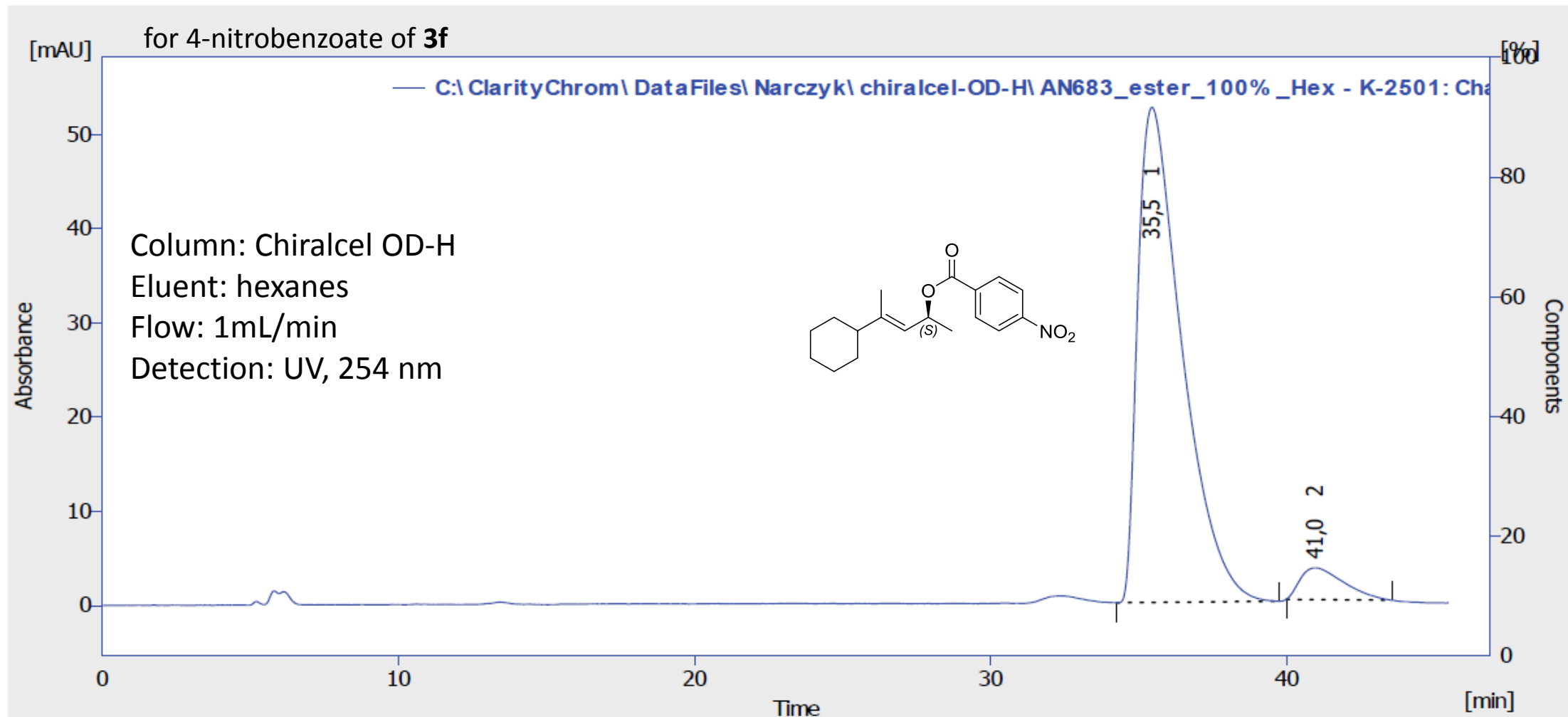






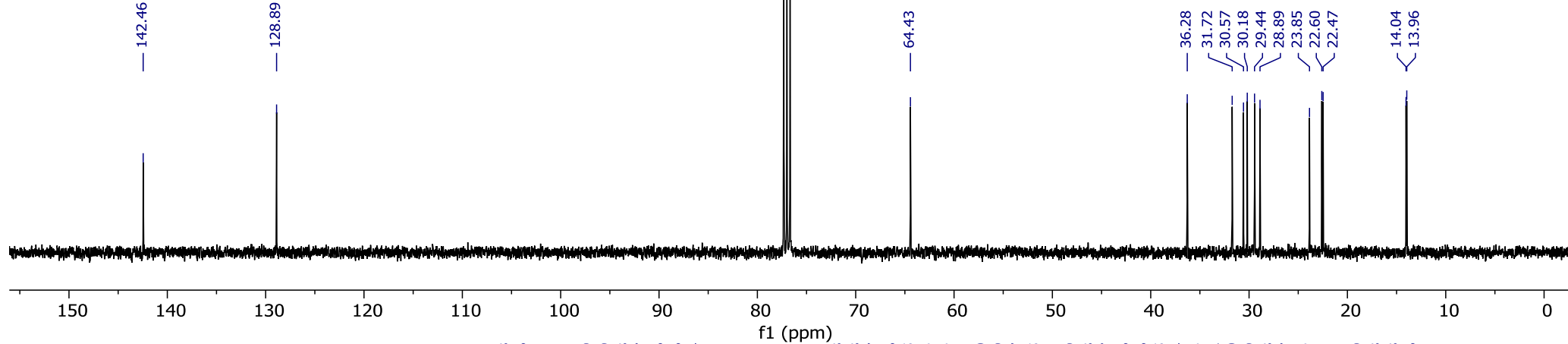
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN676\_ester\_100%\_Hex - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	33,867	16671,769	152,939	49,1	56,0	1,68	
2	37,700	17309,085	120,195	50,9	44,0	2,05	
	Total	33980,854	273,134	100,0	100,0		



Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN683\_ester\_100%\_Hex - K-2501: Channel 1)

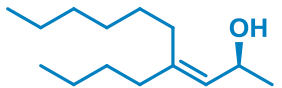
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	35,450	5457,342	52,563	94,0	94,0	1,60	
2	40,967	345,734	3,363	6,0	6,0	1,67	
	Total	5803,076	55,925	100,0	100,0		



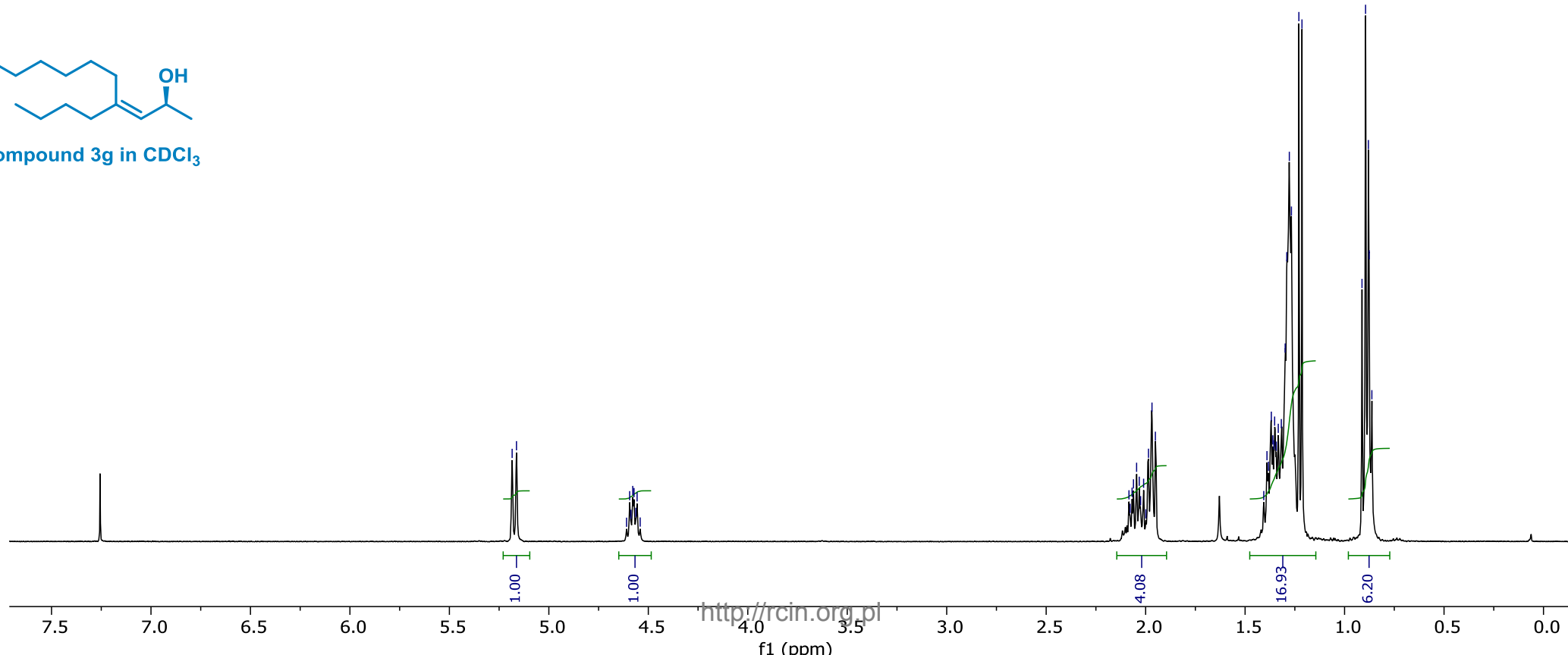
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14.04  
13.96

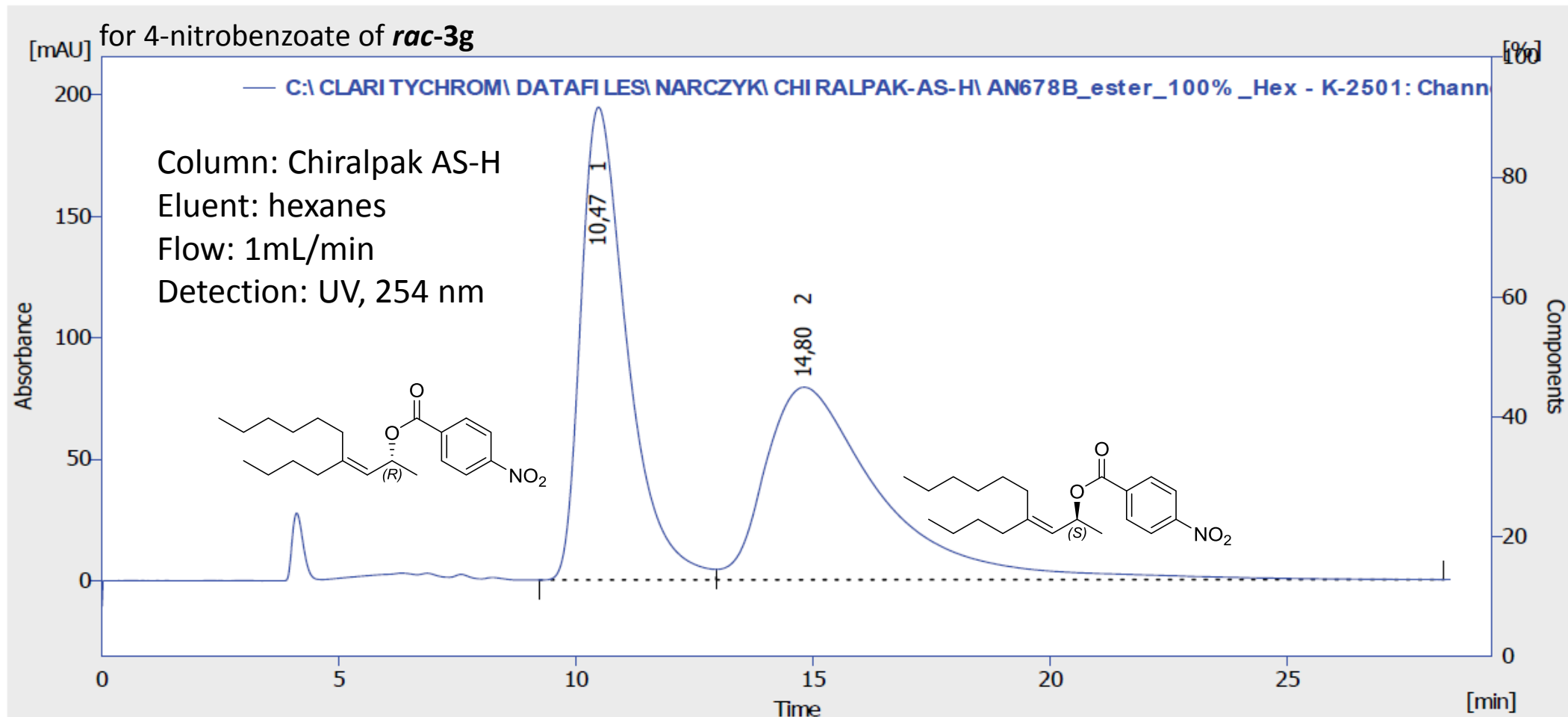
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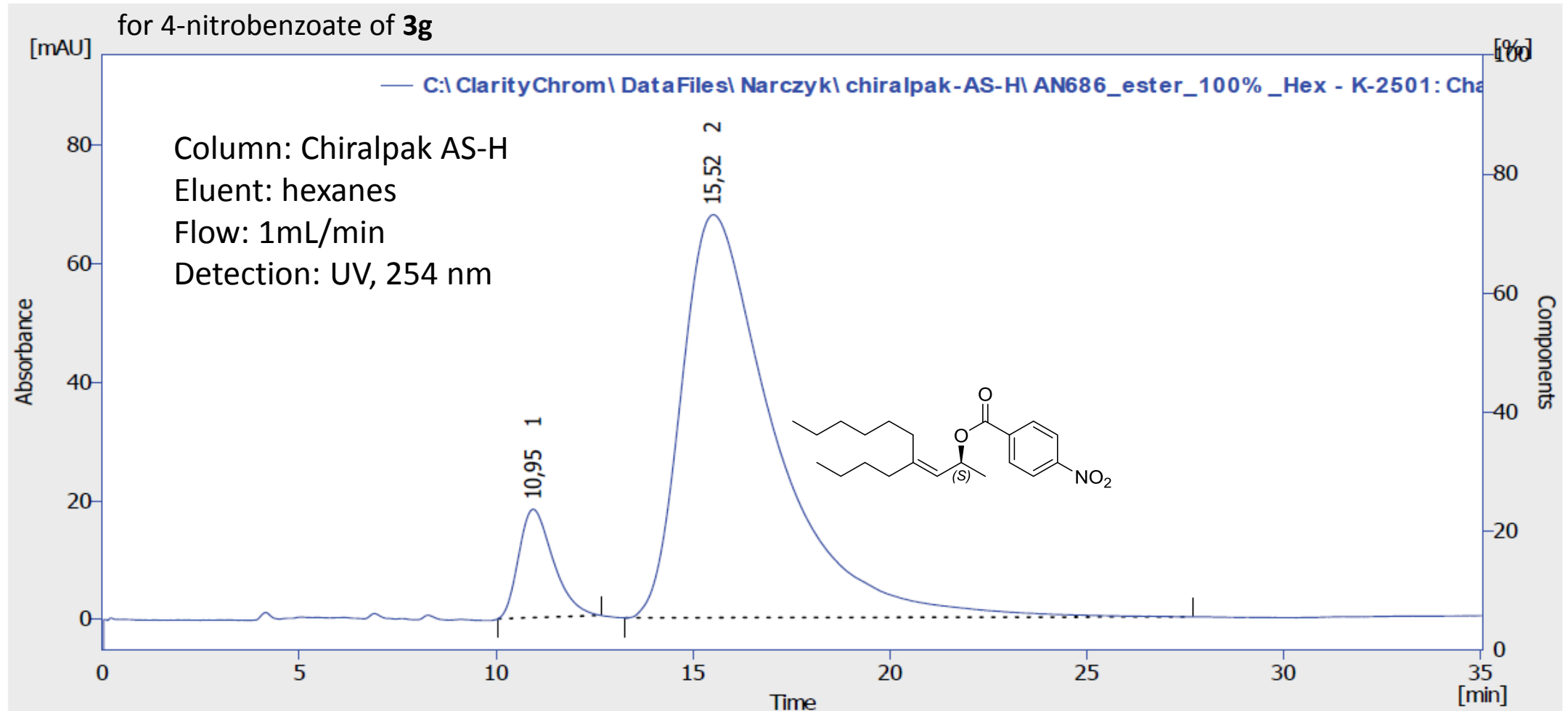
Compound 3g in CDCl<sub>3</sub>





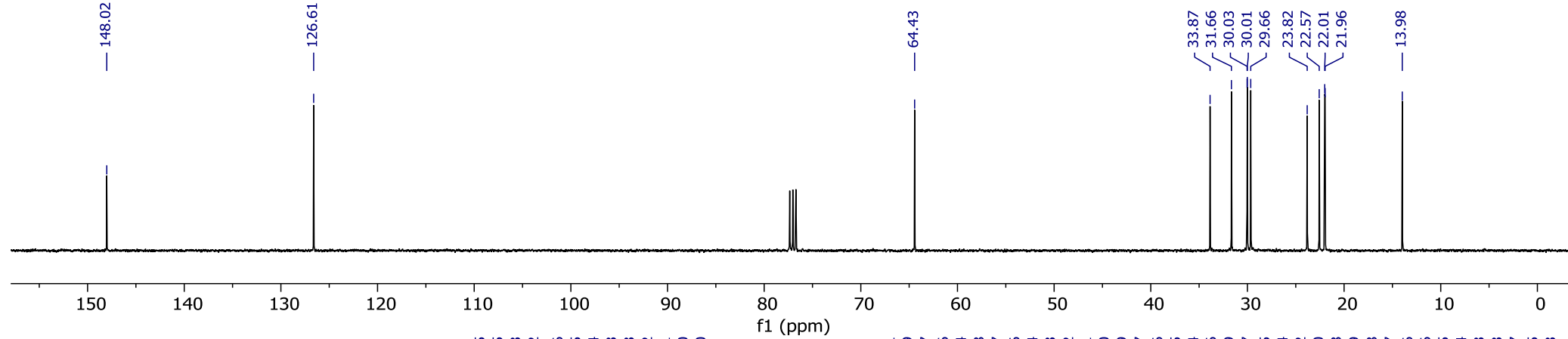
Result Table (Uncal - C:\CLARITYCHROM\DATAFILES\NARCZYK\CHIRALPAK-AS-H\AN678B\_ester\_100%\_Hex - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10,467	13281,105	194,611	49,6	71,0	1,03	
2	14,800	13492,339	79,299	50,4	29,0	2,38	
	Total	26773,443	273,910	100,0	100,0		



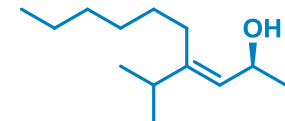
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralpak-AS-H\AN686\_ester\_100%\_Hex - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10,950	1111,599	18,248	9,0	21,2	0,95	
2	15,517	11177,051	67,880	91,0	78,8	2,33	
	Total	12288,650	86,128	100,0	100,0		

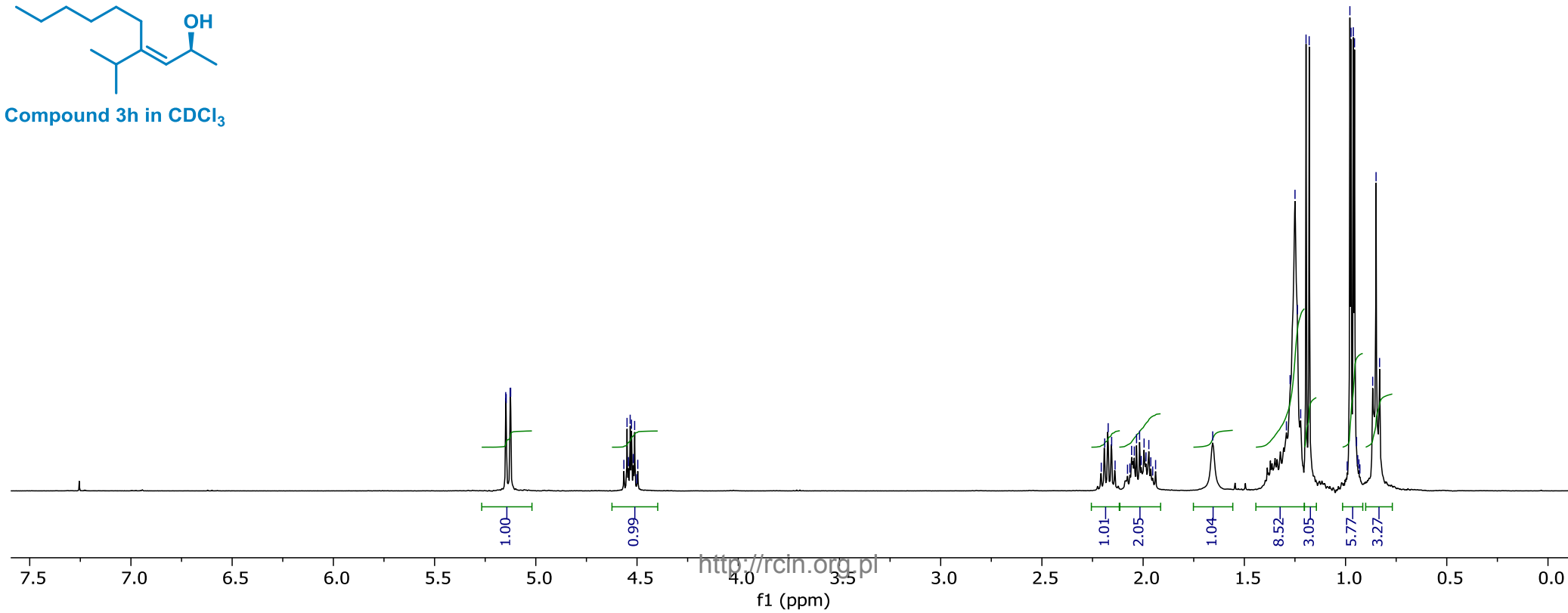


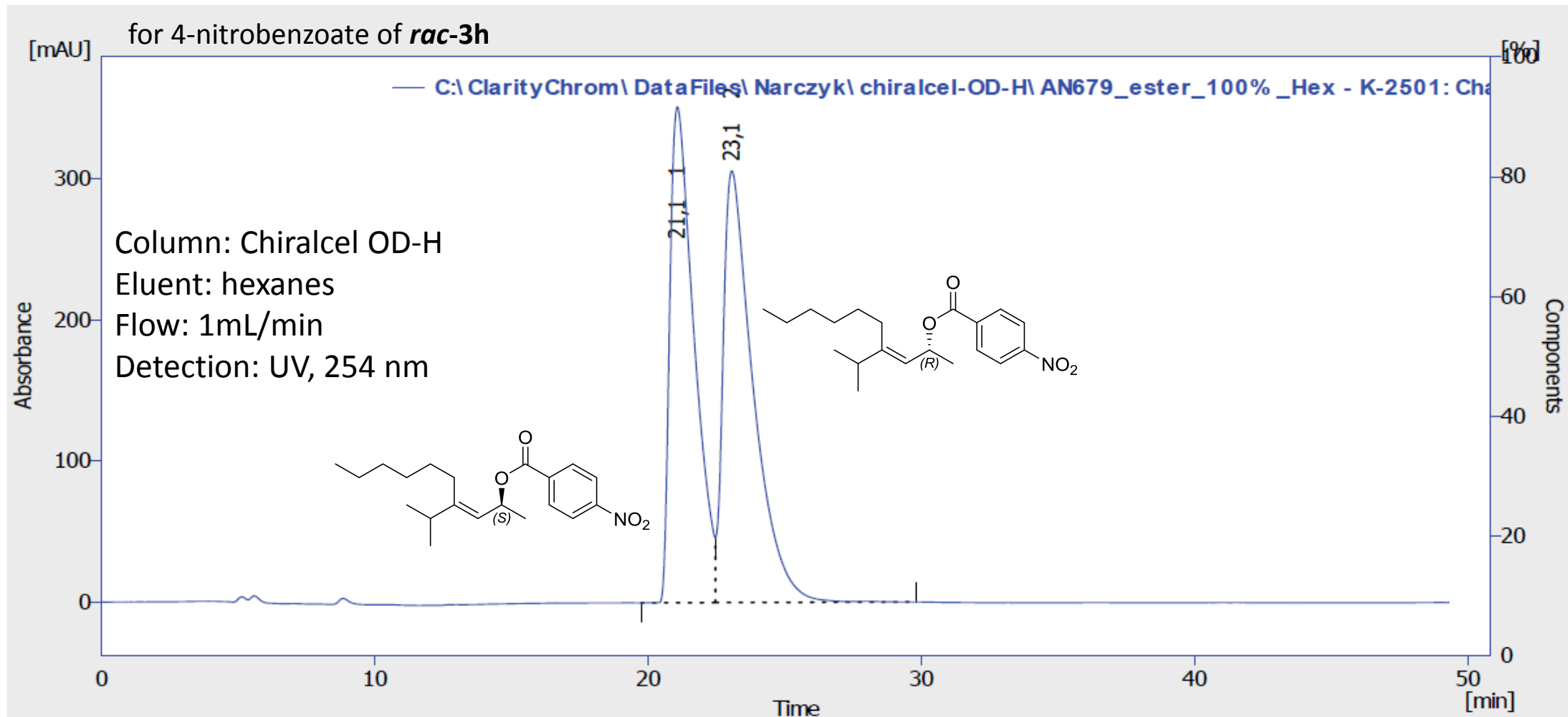
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1.97  
1.96  
1.95  
1.94  
1.66  
1.29  
1.27  
1.25  
1.24  
1.22  
1.20  
1.18  
0.99  
0.98  
0.97  
0.96  
0.96  
0.95  
0.94  
0.93  
0.93  
0.87  
0.85  
0.83



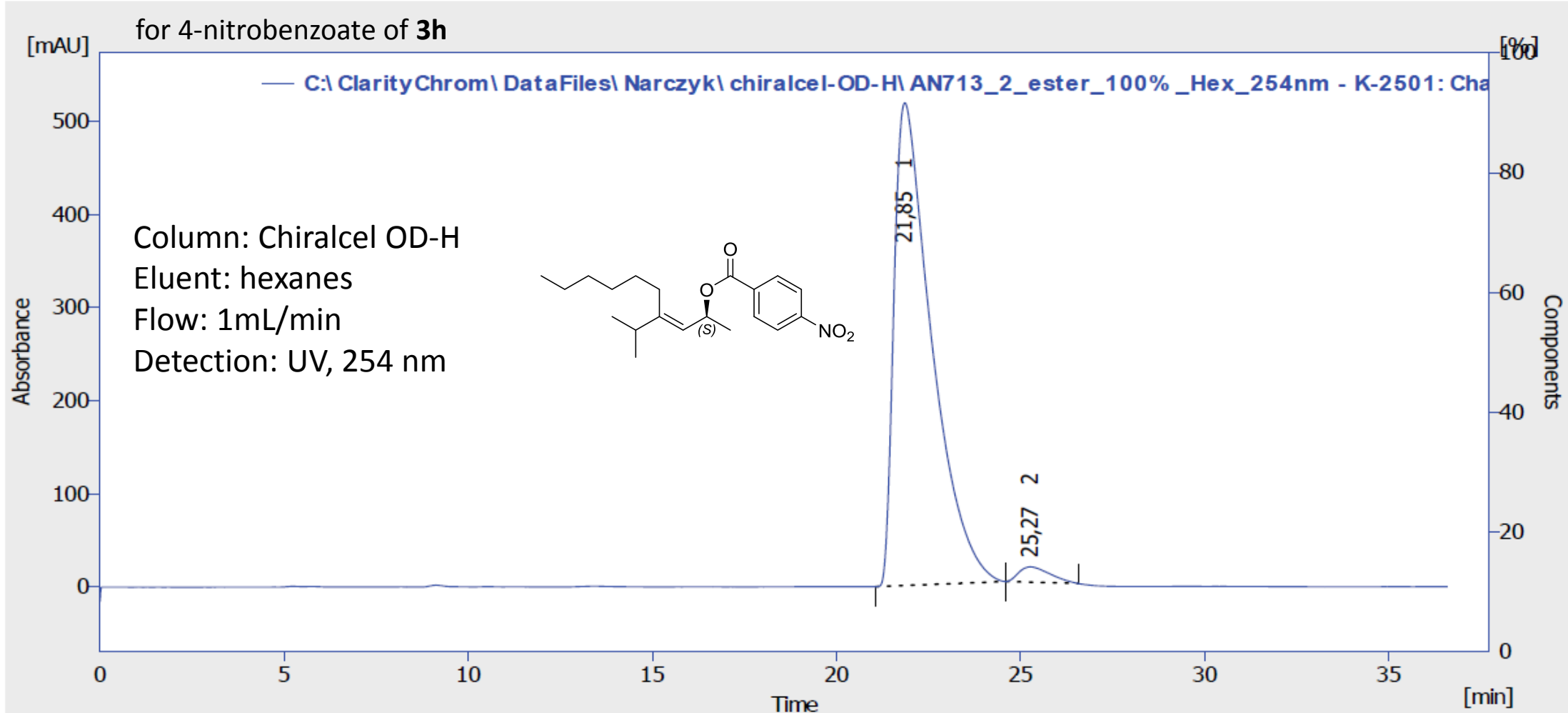
Compound 3h in CDCl<sub>3</sub>





Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN679\_ester\_100%\_Hex - K-2501: Channel 1)

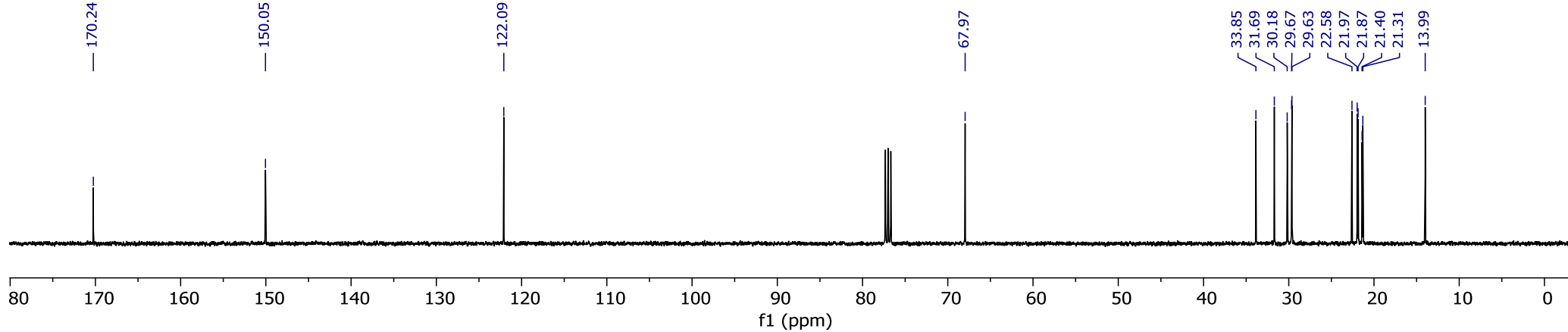
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21,067	21685,002	351,532	47,9	53,5	0,98	
2	23,067	23598,541	305,993	52,1	46,5	1,15	
	Total	45283,544	657,525	100,0	100,0		



Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN713\_2\_ester\_100%\_Hex\_254nm - K-2501: Channel 1)

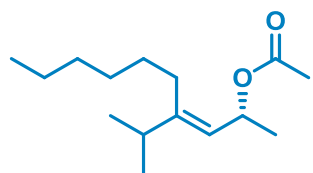
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21,850	36725,197	518,106	97,4	96,9	1,10	
2	25,267	970,552	16,394	2,6	3,1	0,97	
	Total	37695,749	534,501	100,0	100,0		



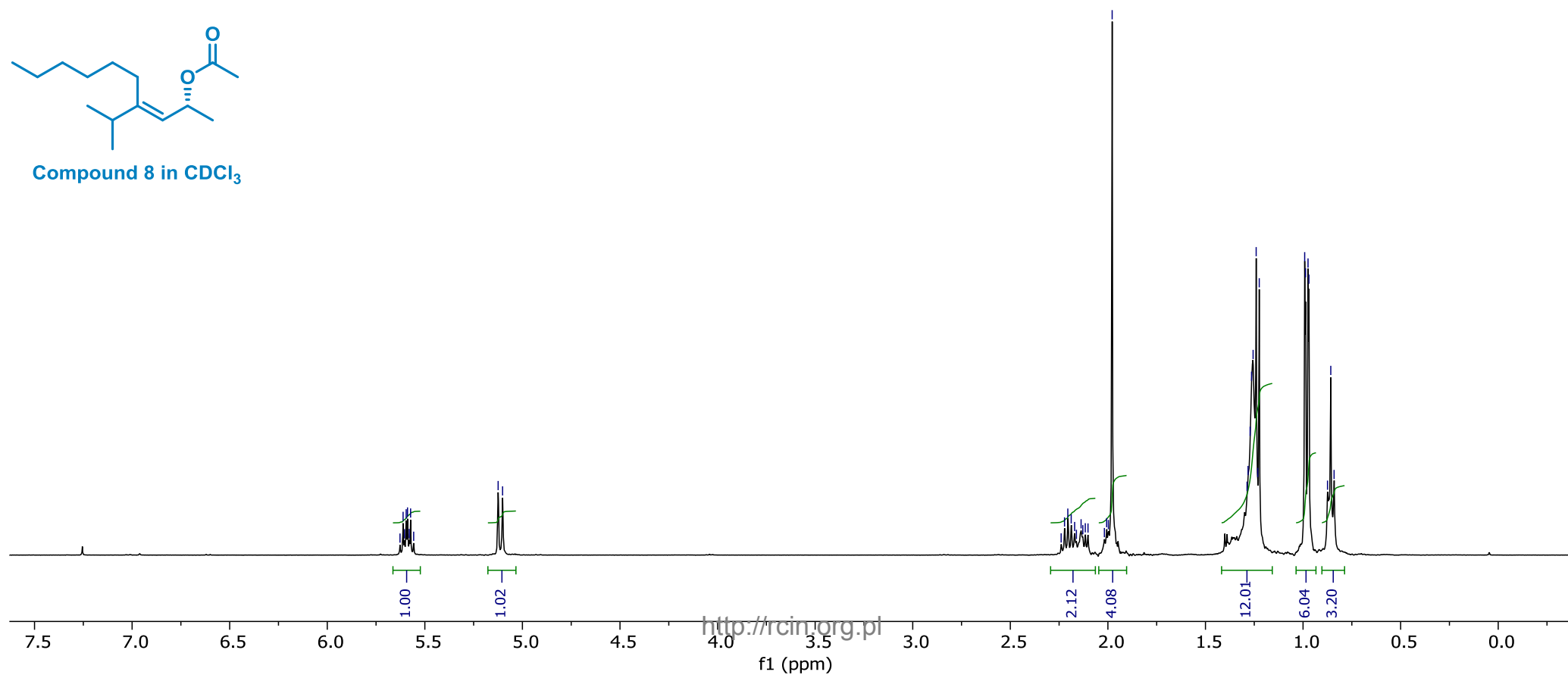


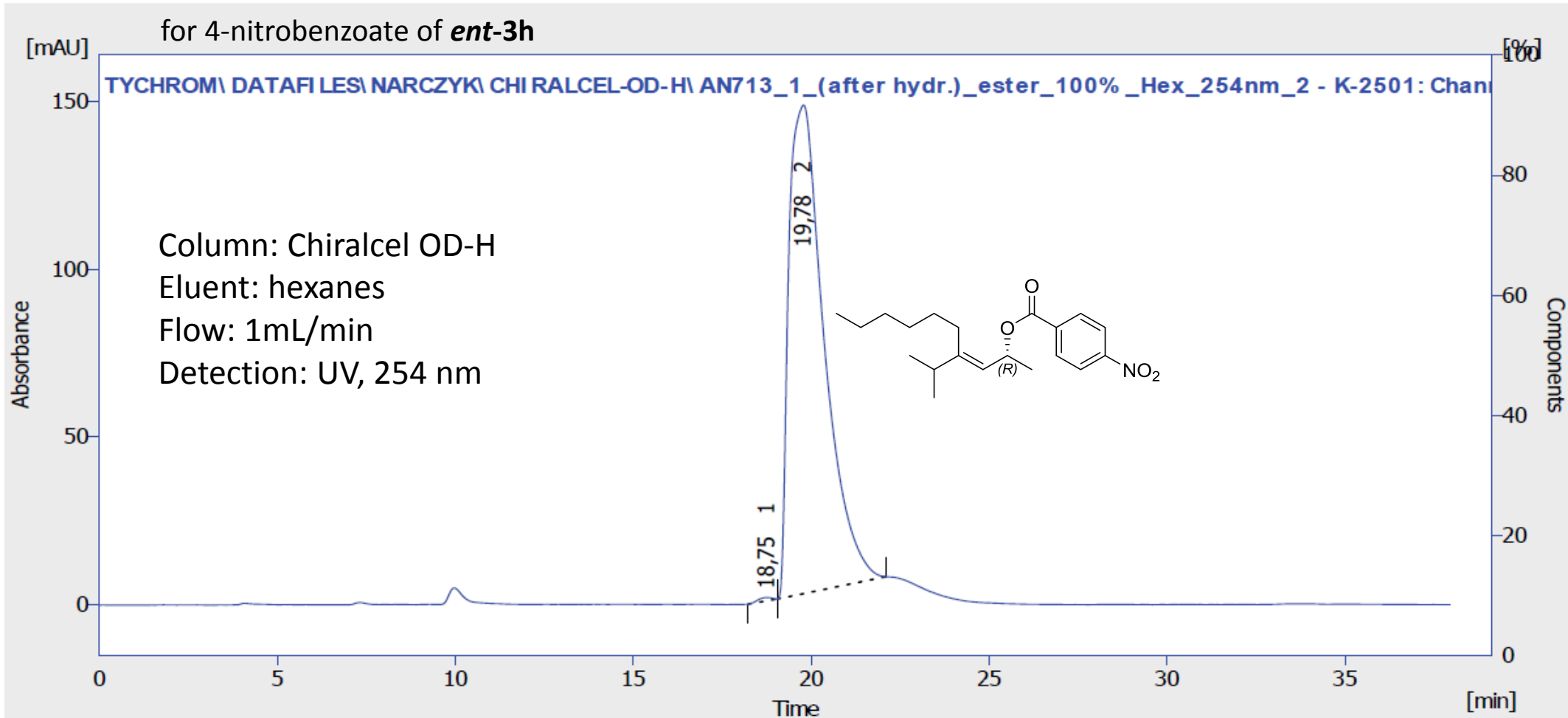
5.63  
5.61  
5.60  
5.59  
5.58  
5.57  
5.56  
5.12  
5.10

2.24  
2.22  
2.21  
2.19  
2.17  
2.16  
2.14  
2.13  
2.12  
2.10  
2.02  
2.01  
2.00  
1.98  
1.29  
1.28  
1.27  
1.26  
1.26  
1.24  
1.23  
1.22  
0.99  
0.99  
0.97  
0.87  
0.86  
0.84



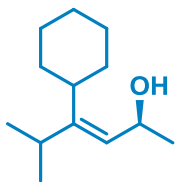
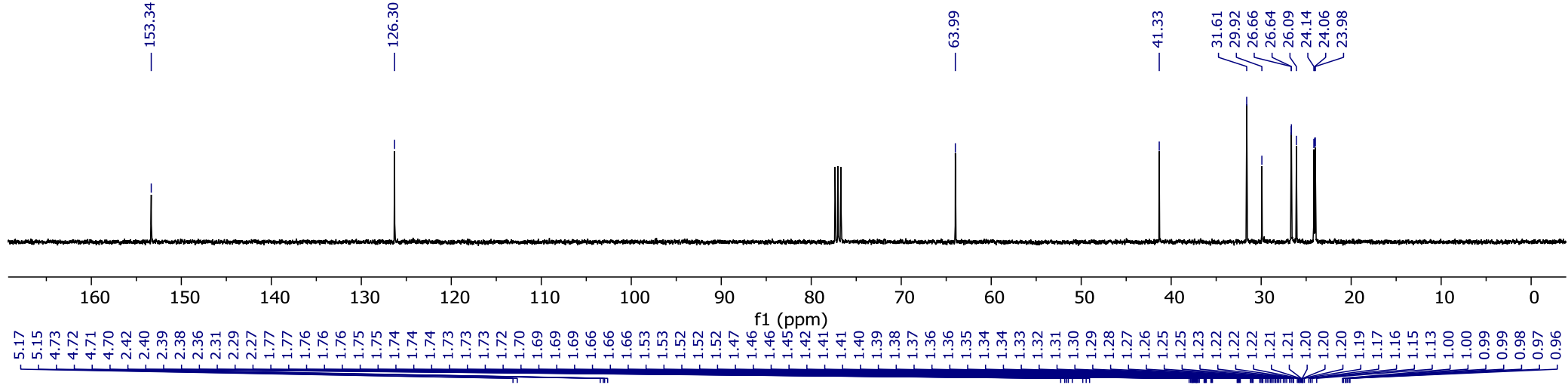
Compound 8 in CDCl<sub>3</sub>



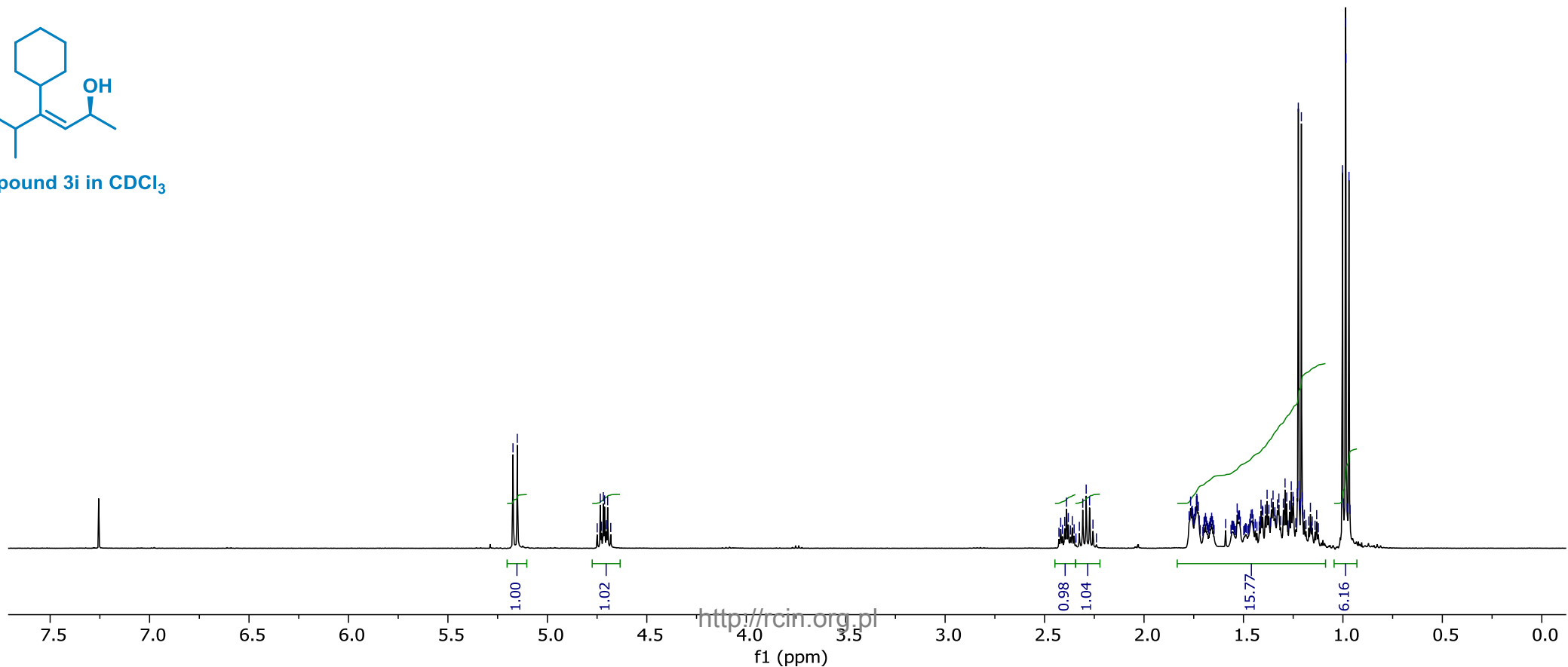


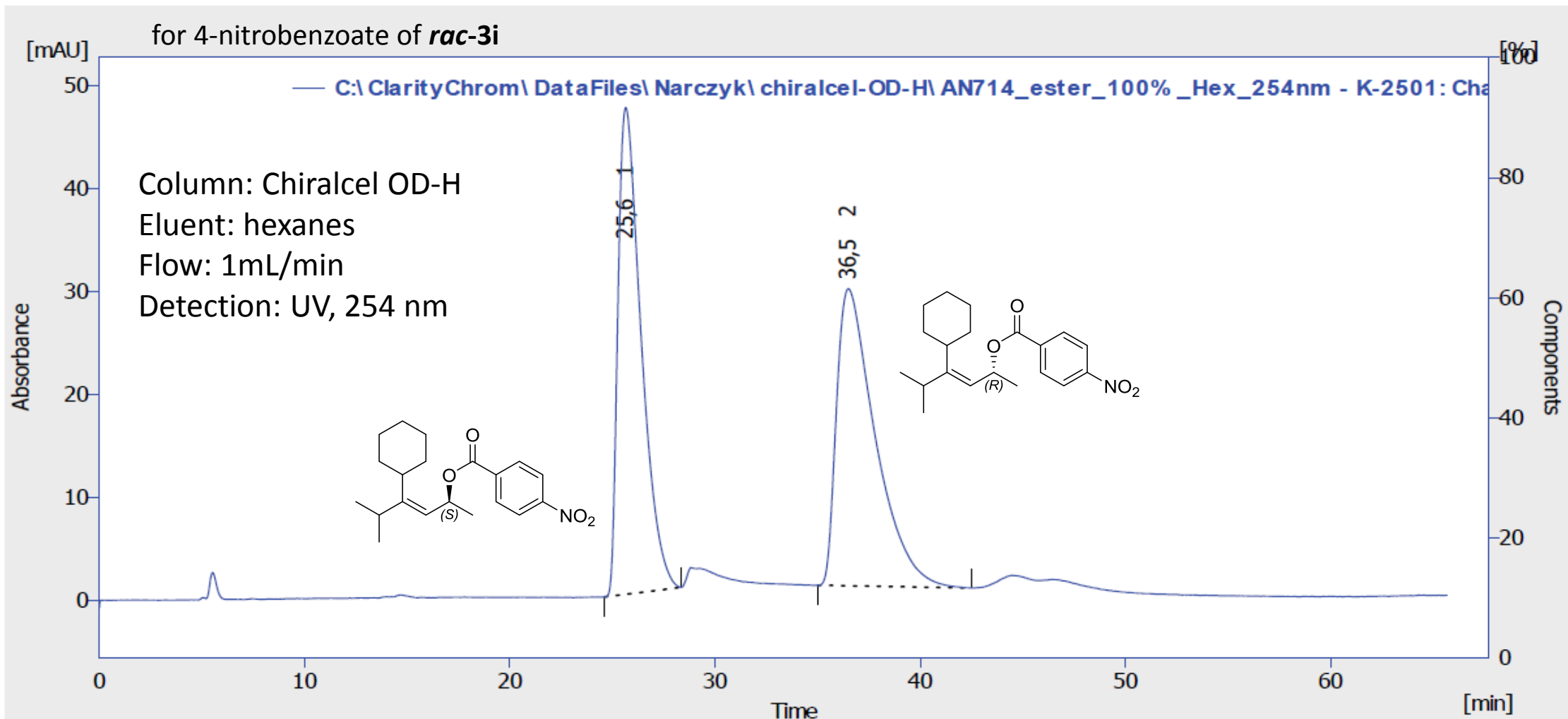
Result Table (Uncal - C:\CLARITYCHROM\DATAFILES\NARCZYK\CHIRALCEL-OD-H\AN713\_1\_(after hydr.)\_ester\_100%\_Hex\_254nm\_2 - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	18,750	28,011	1,010	0,3	0,7	0,52	
2	19,783	10063,408	145,455	99,7	99,3	1,10	
	Total	10091,419	146,465	100,0	100,0		



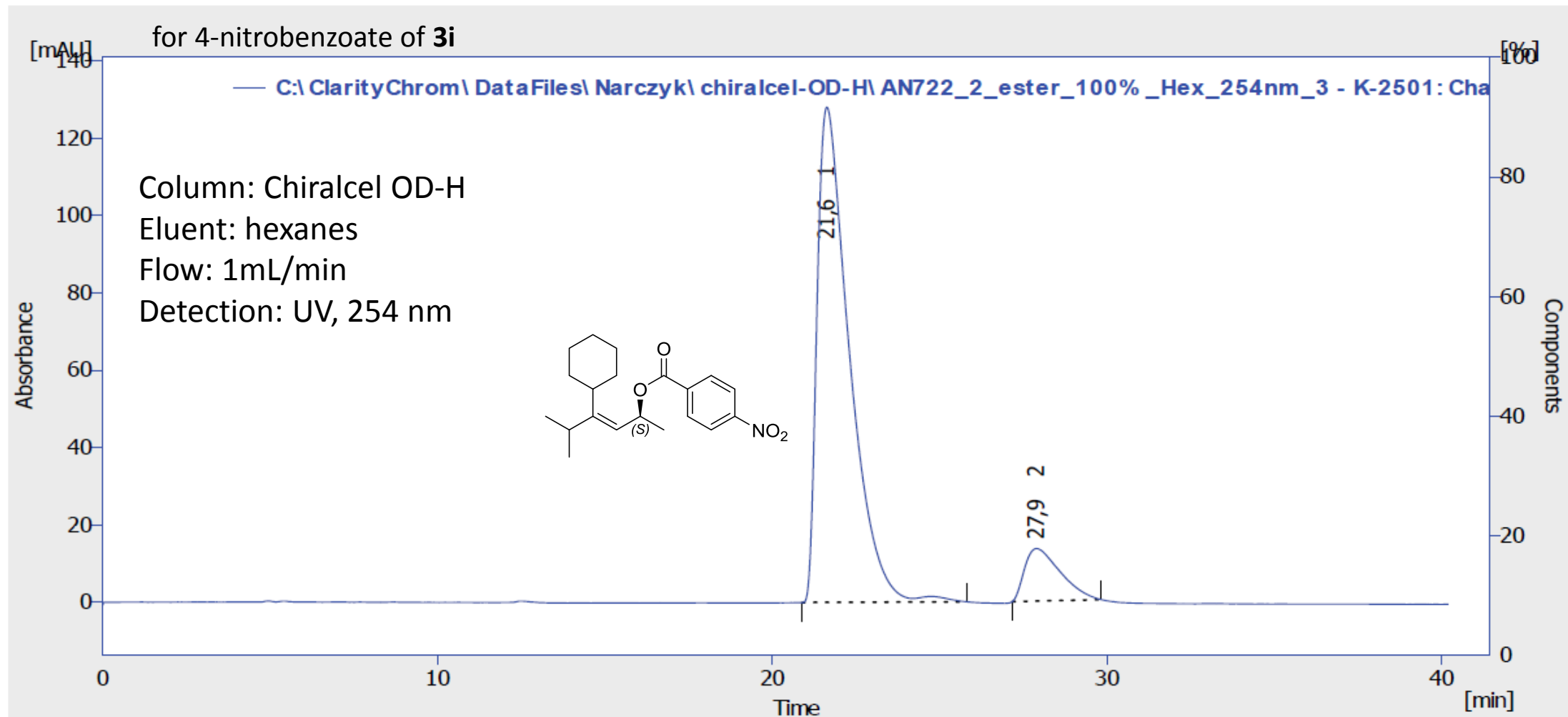
Compound 3i in CDCl<sub>3</sub>





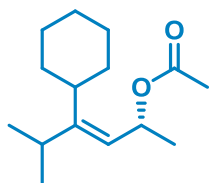
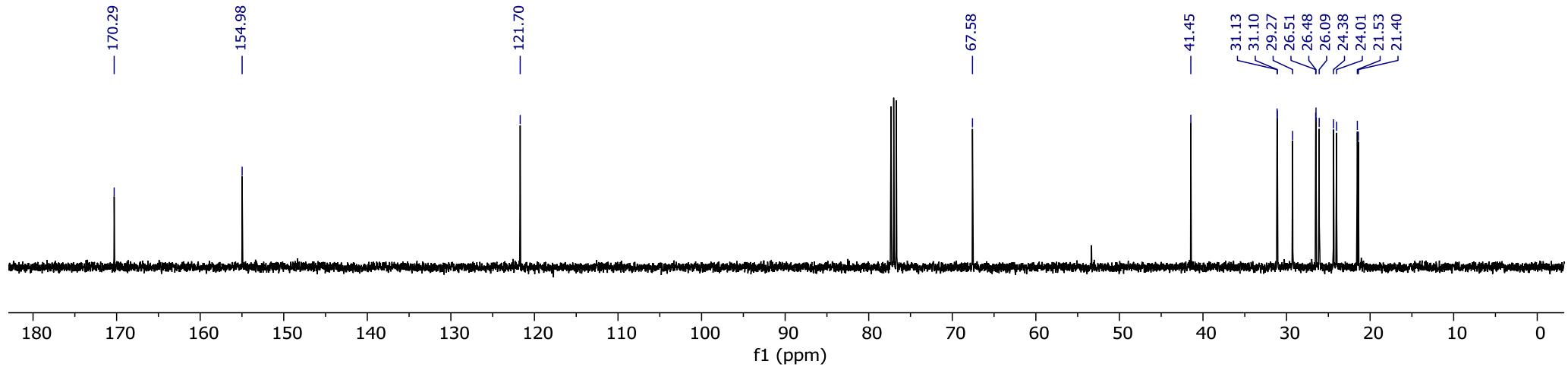
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN714\_ester\_100%\_Hex\_254nm - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	25,650	3715,077	47,311	49,6	62,1	1,23	
2	36,500	3782,532	28,885	50,4	37,9	1,98	
	Total	7497,610	76,196	100,0	100,0		

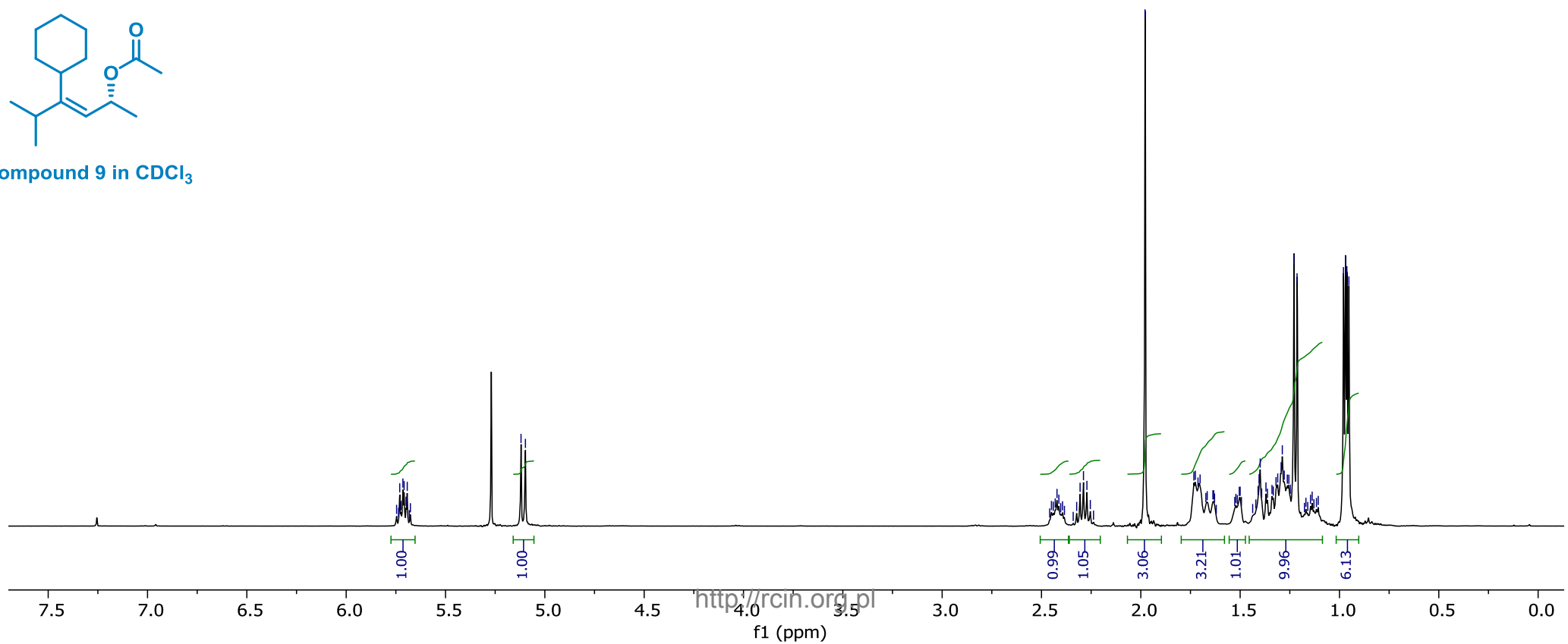


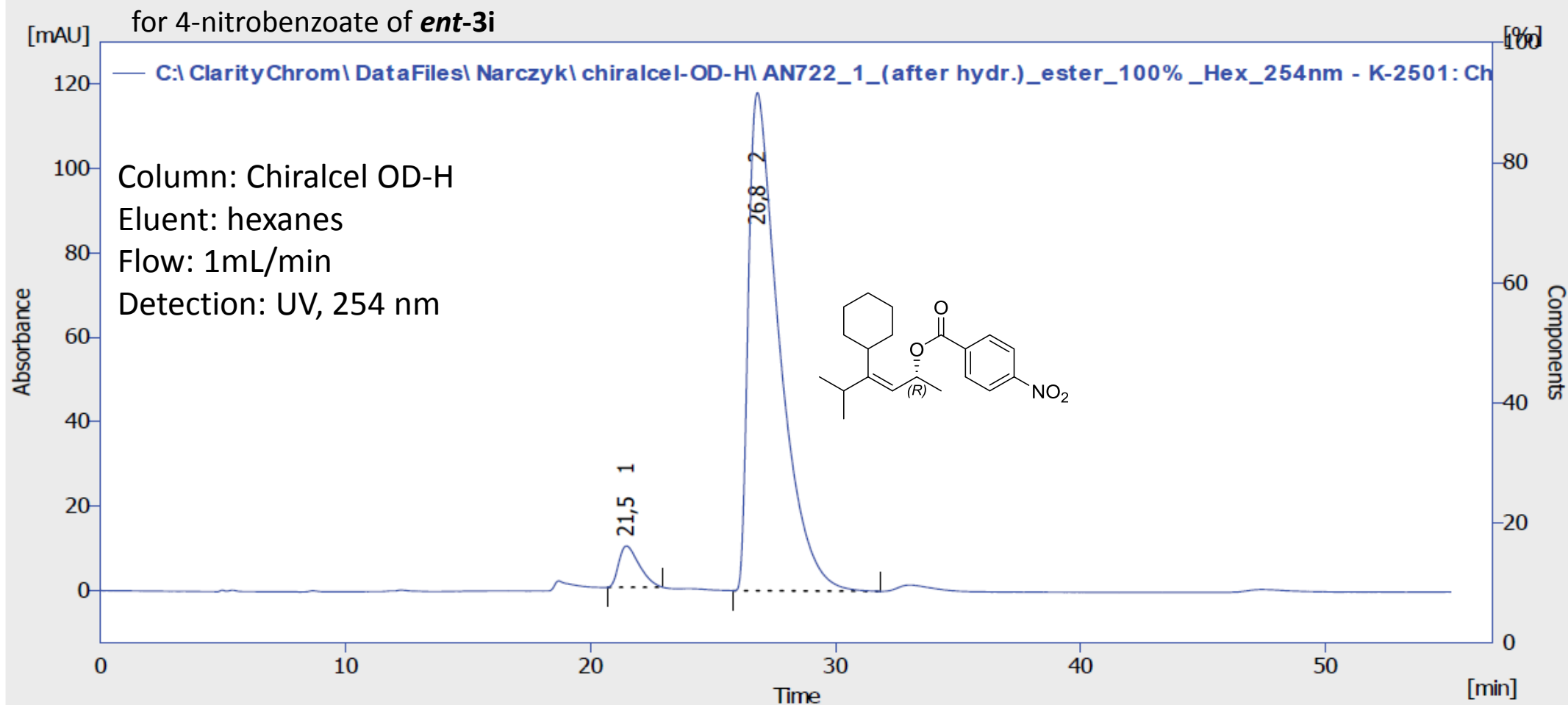
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN722\_2\_ester\_100%\_Hex\_254nm\_3 - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21,633	8594,579	128,076	89,5	90,4	1,02	
2	27,900	1006,784	13,574	10,5	9,6	1,20	
	Total	9601,363	141,650	100,0	100,0		



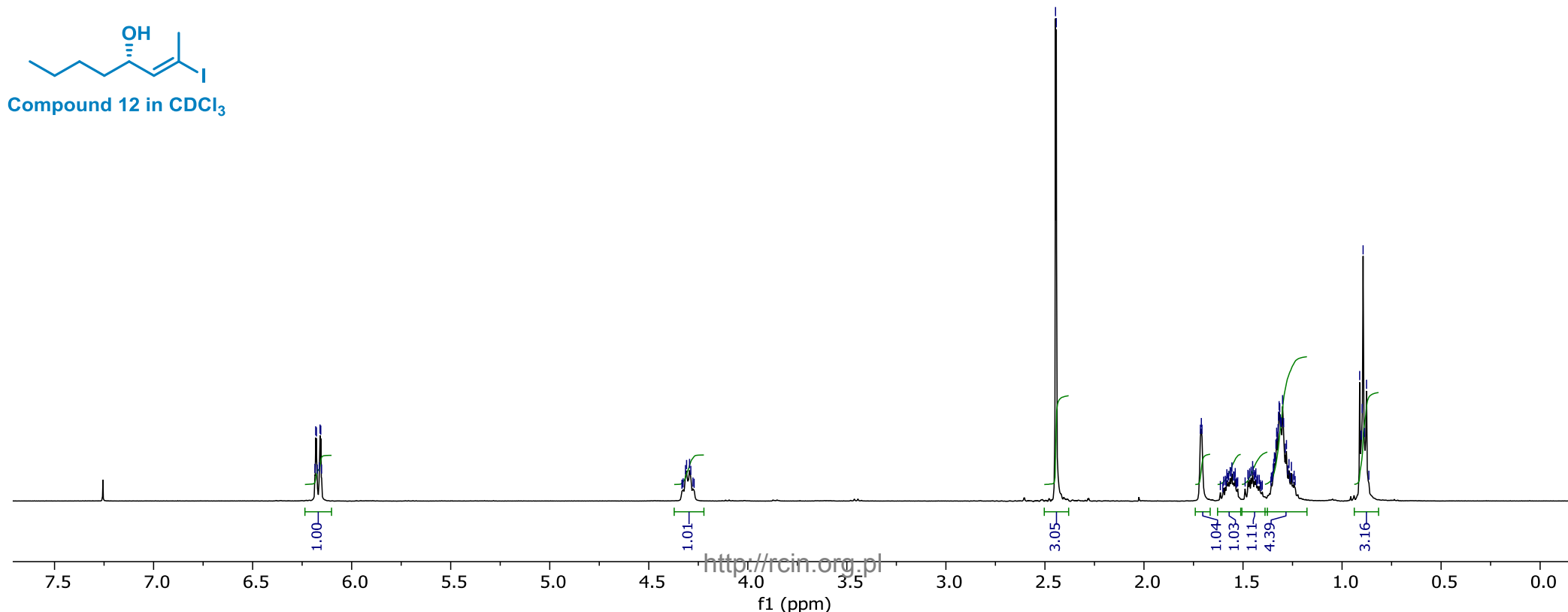
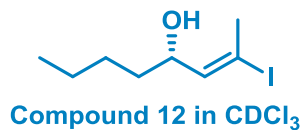
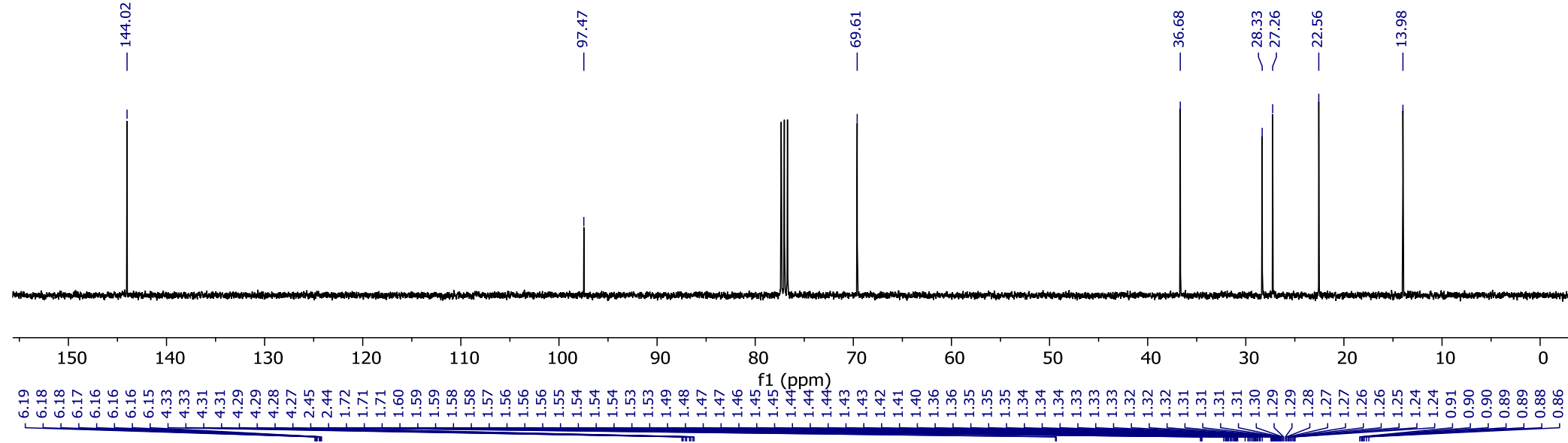
Compound 9 in CDCl<sub>3</sub>



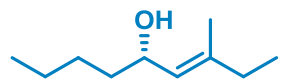
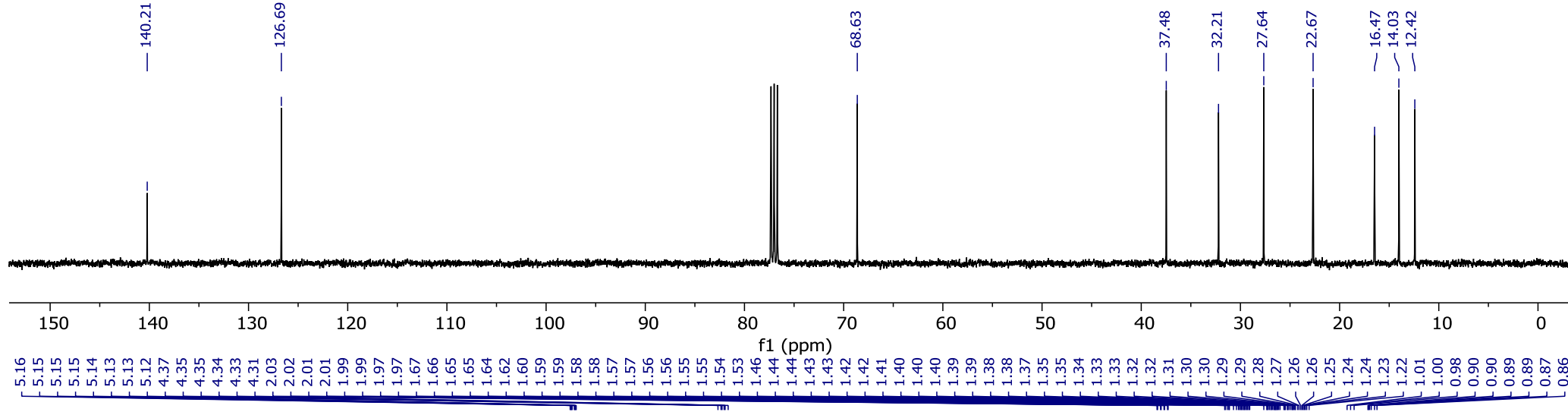


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN722\_1\_(after hydr.)\_ester\_100%\_Hex\_254nm - K-2501: Channel 1)

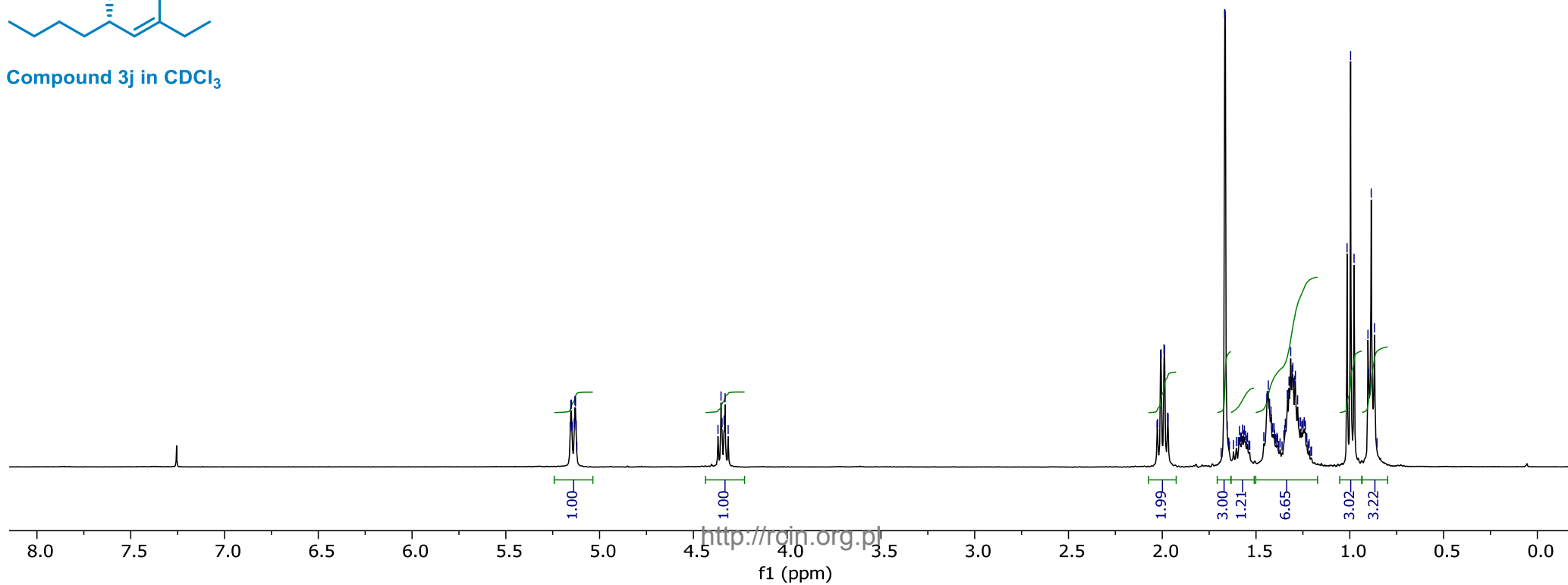
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21,467	571,259	9,803	5,2	7,7	0,93	
2	26,817	10370,883	117,971	94,8	92,3	1,32	
	Total	10942,142	127,774	100,0	100,0		

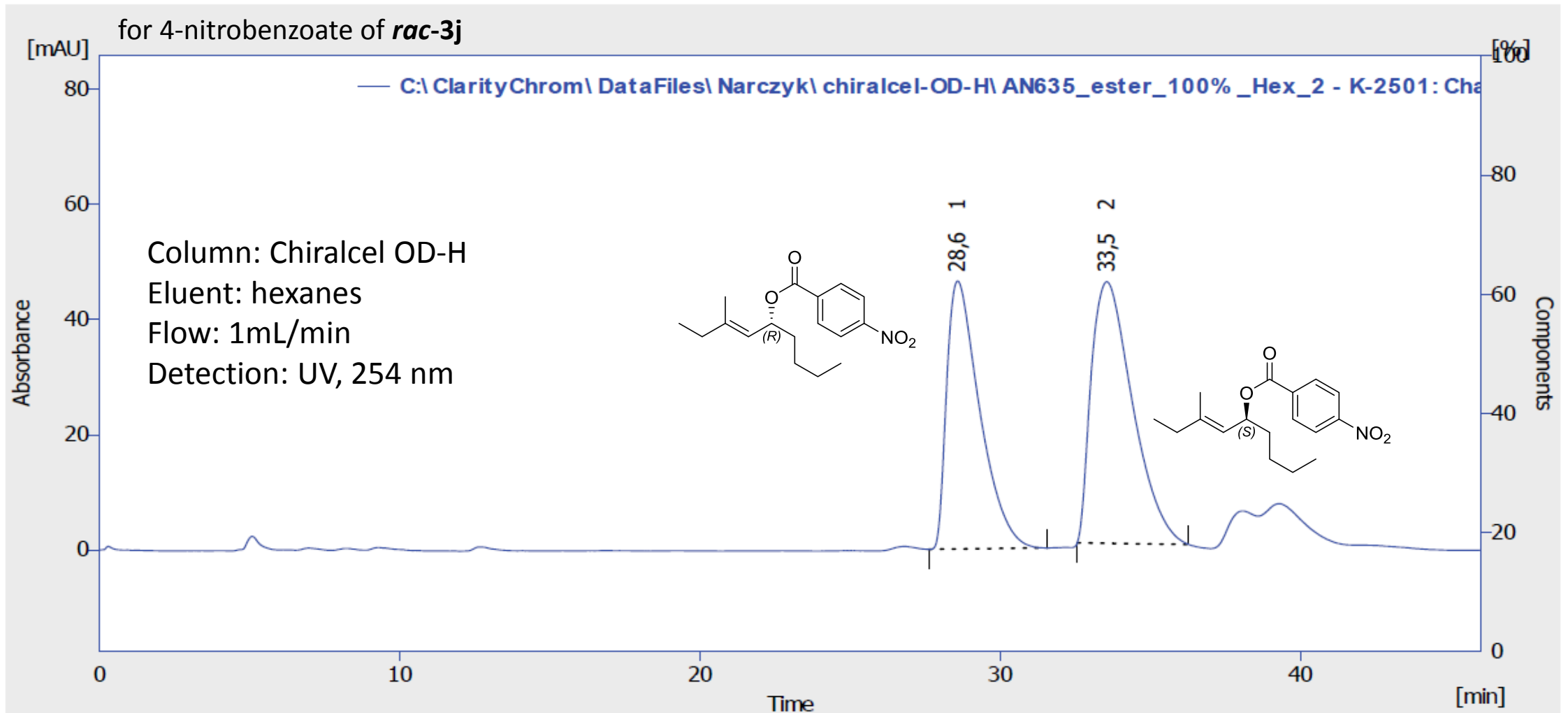






Compound 3j in CDCl<sub>3</sub>

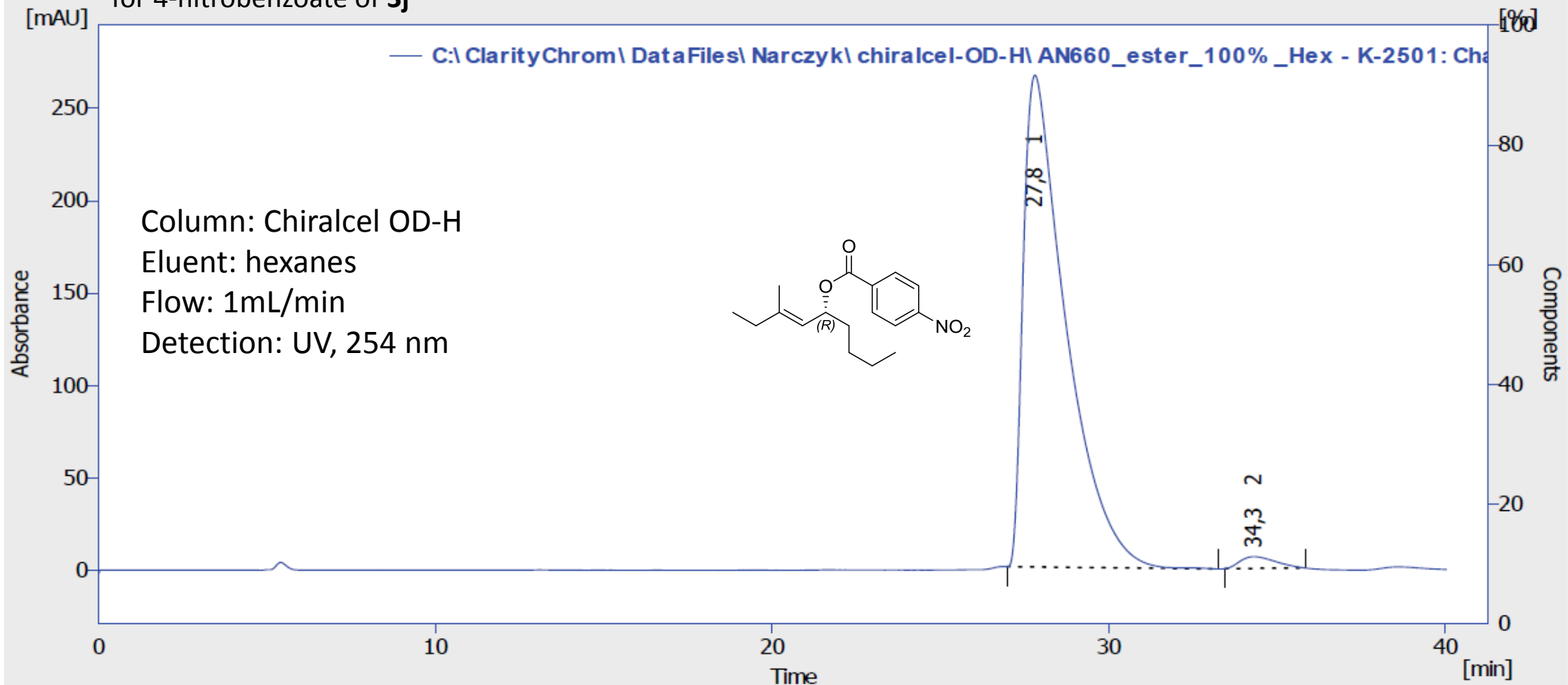




Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN635\_ester\_100%\_Hex\_2 - K-2501: Channel 1)

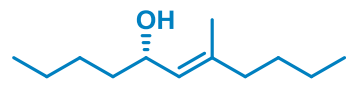
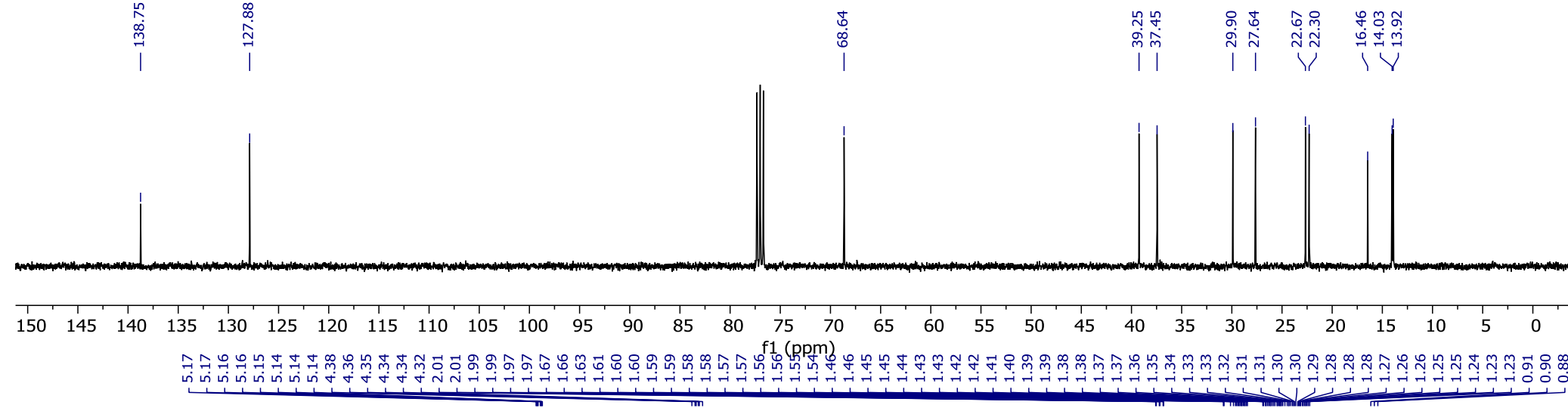
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	28,583	3557,583	46,534	45,0	50,6	1,18	
2	33,550	4348,385	45,422	55,0	49,4	1,53	
	Total	7905,969	91,957	100,0	100,0		

for 4-nitrobenzoate of **3j**

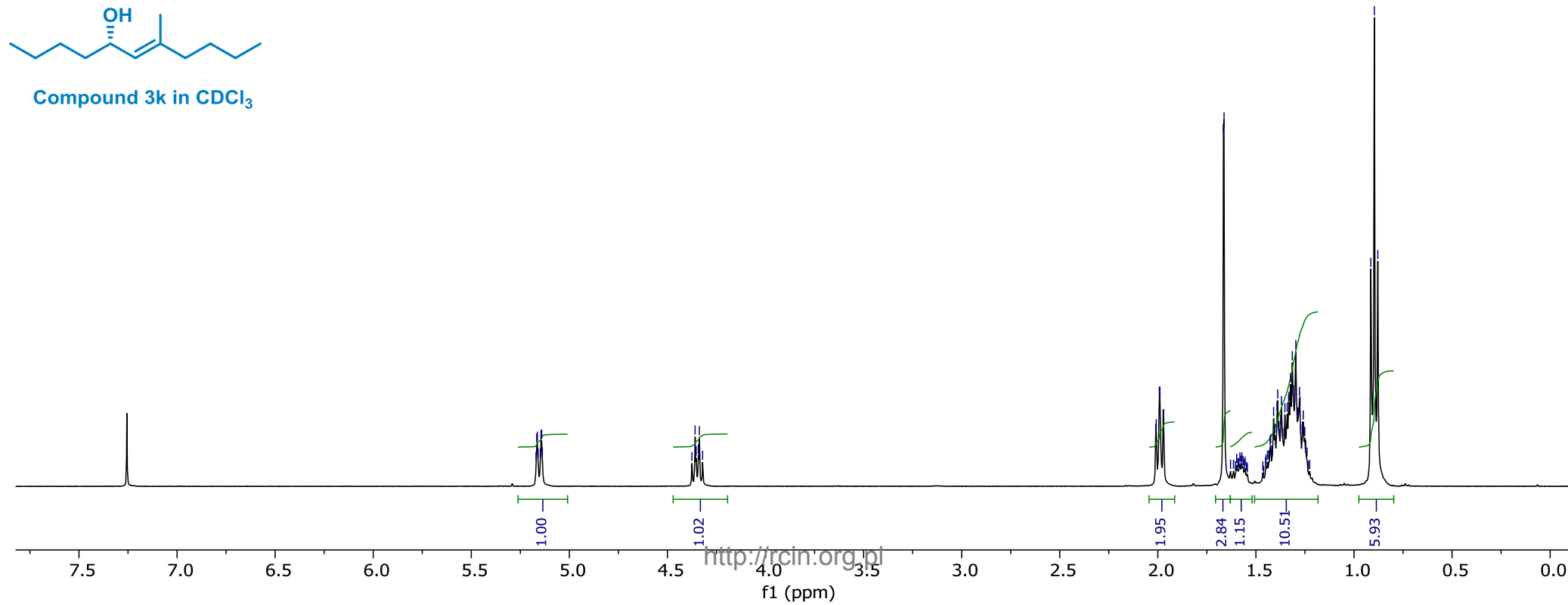


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN660\_ester\_100%\_Hex - K-2501: Channel 1)

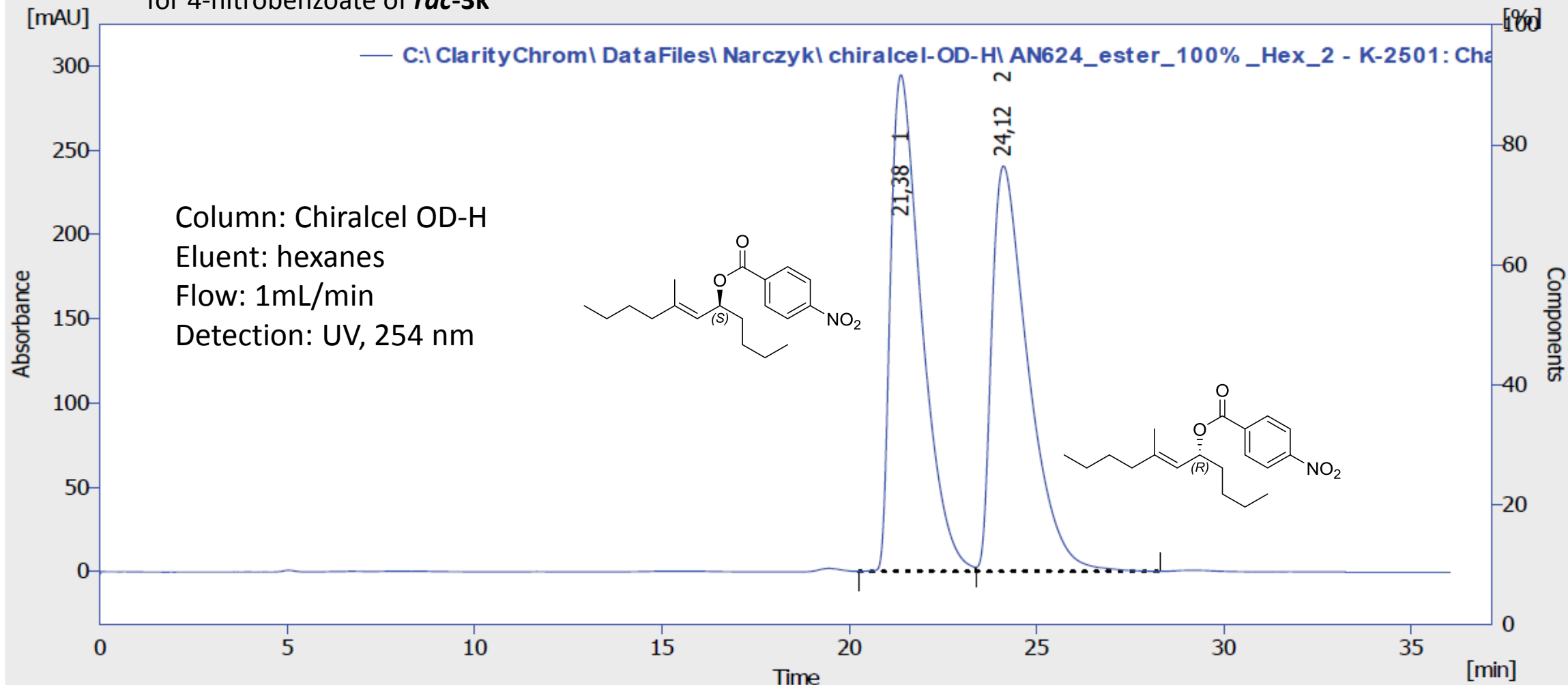
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	27,800	23492,146	266,332	98,1	97,7	1,32	
2	34,300	466,416	6,371	1,9	2,3	1,22	
	Total	23958,561	272,703	100,0	100,0		



Compound 3k in CDCl<sub>3</sub>

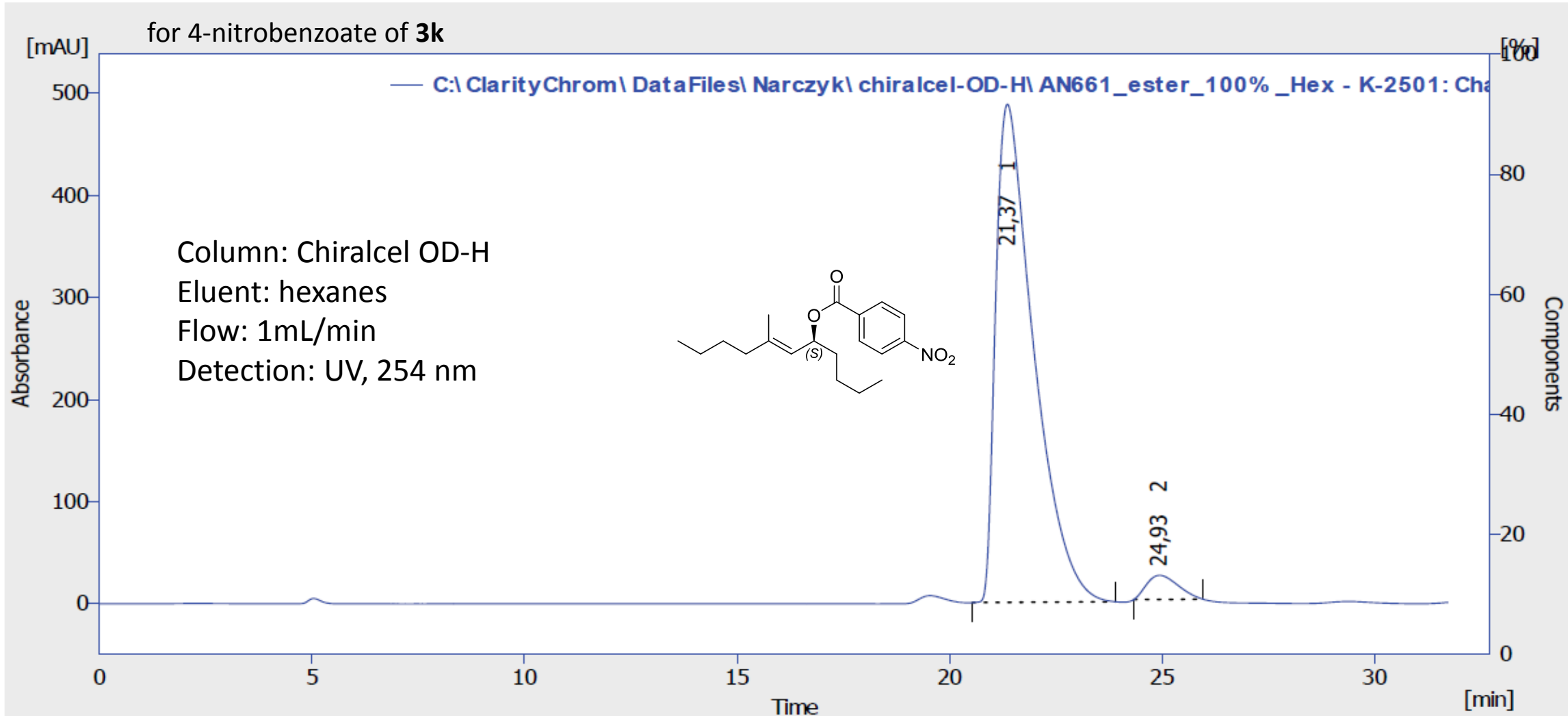


for 4-nitrobenzoate of *rac*-3k



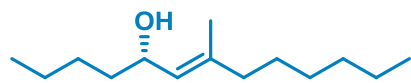
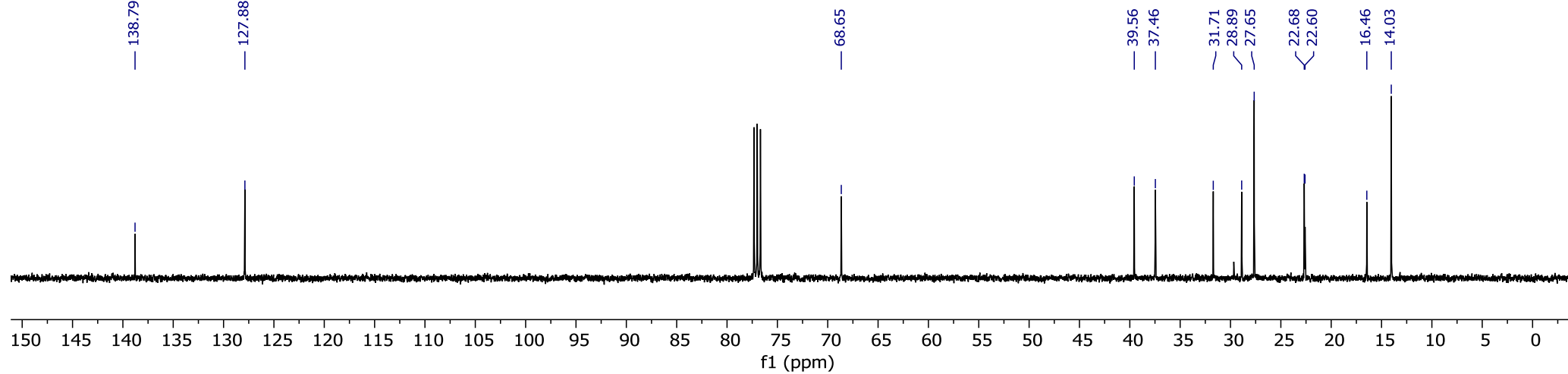
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN624\_ester\_100%\_Hex\_2 - K-2501: Channel 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21,383	16896,782	294,412	51,0	55,1	0,88	
2	24,117	16210,264	240,385	49,0	44,9	1,05	
	Total	33107,046	534,797	100,0	100,0		

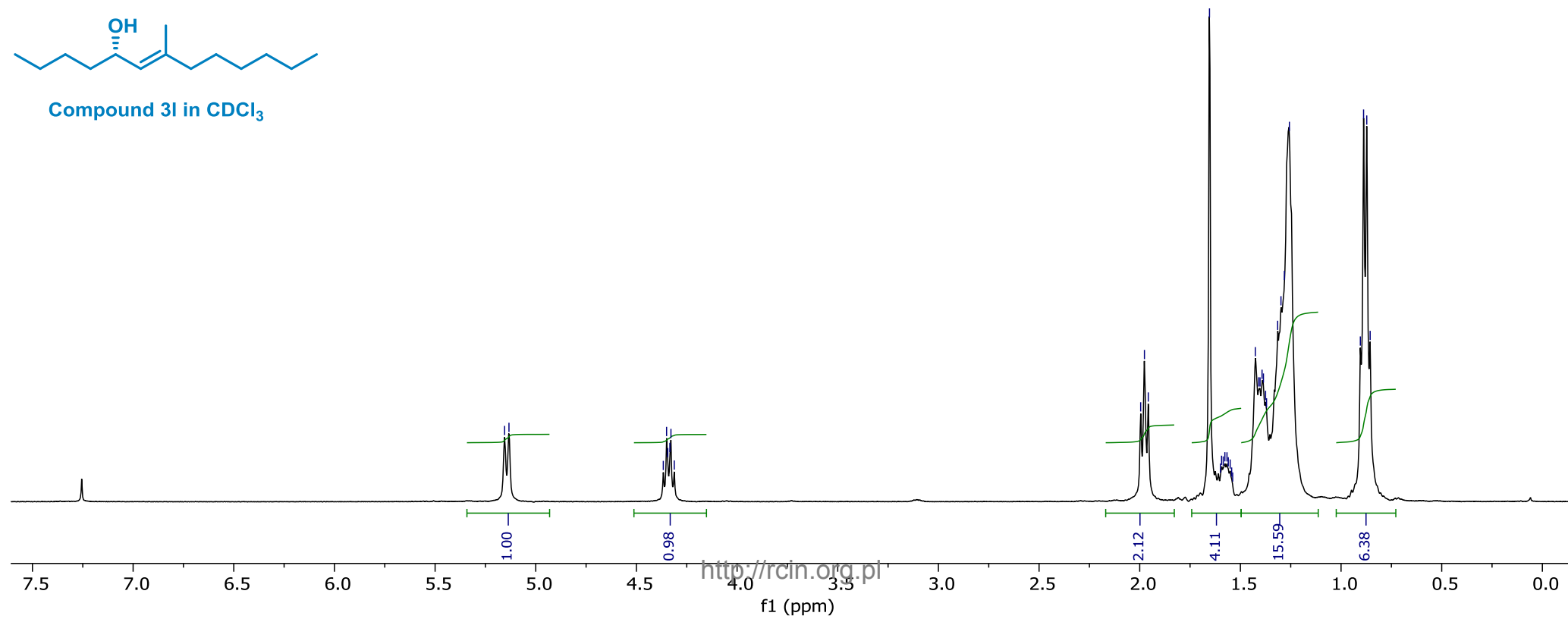


Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN661\_ester\_100%\_Hex - K-2501: Channel 1)

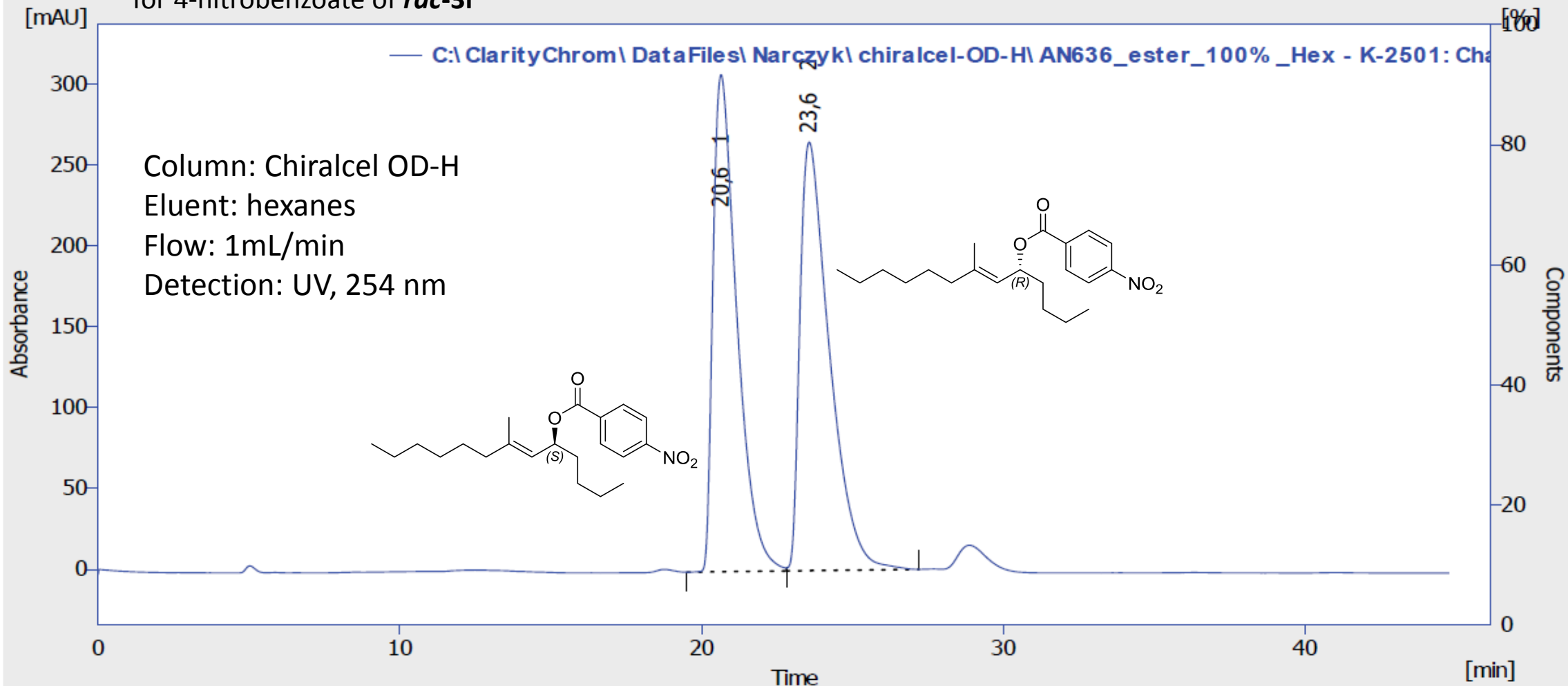
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21,367	30320,013	487,972	96,1	95,4	0,97	
2	24,933	1221,122	23,700	3,9	4,6	0,87	
	Total	31541,135	511,672	100,0	100,0		



Compound 3l in CDCl<sub>3</sub>



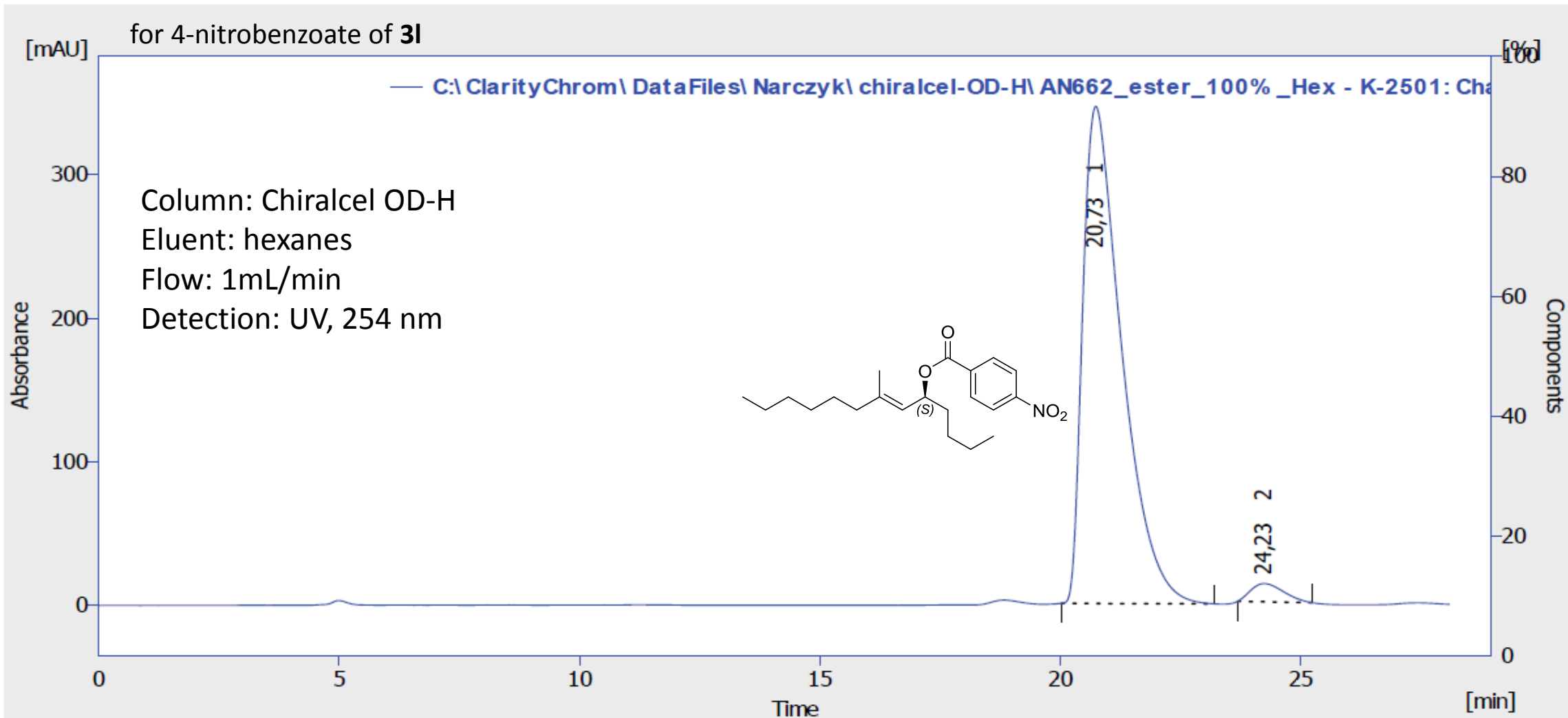
for 4-nitrobenzoate of *rac*-3I



Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN636\_ester\_100%\_Hex - K-2501: Channel 1)

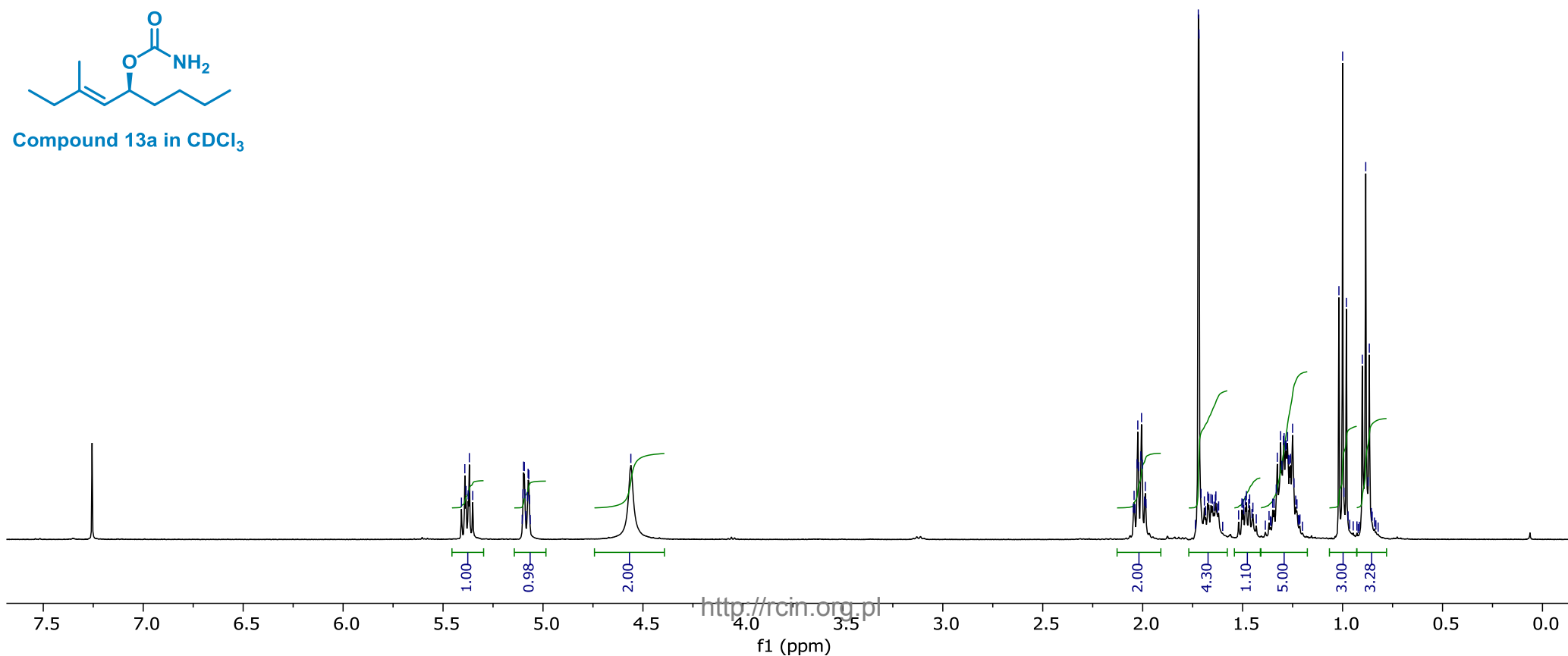
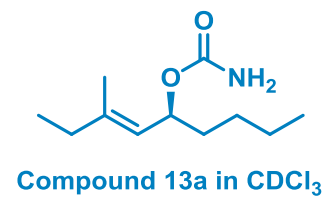
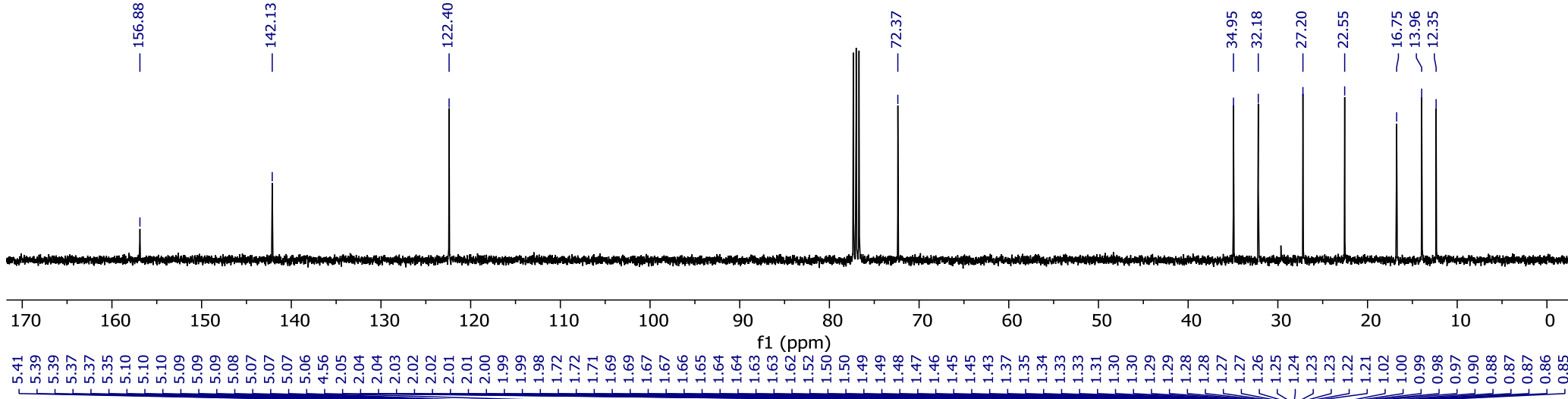
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	20,650	16973,950	307,587	48,4	53,7	0,87	
2	23,567	18085,819	265,187	51,6	46,3	1,05	
	Total	35059,769	572,774	100,0	100,0		

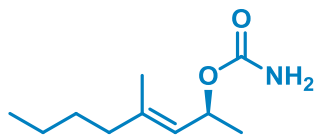
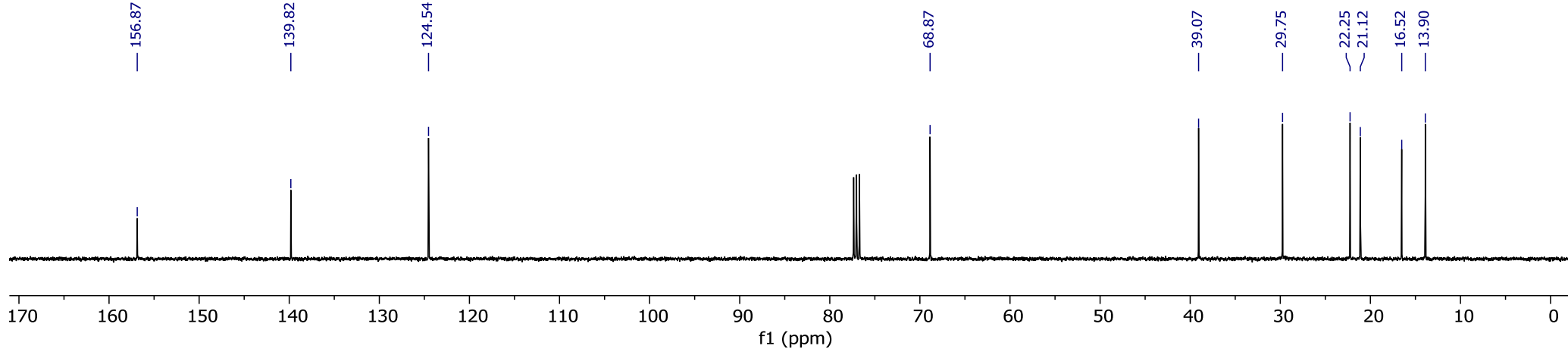




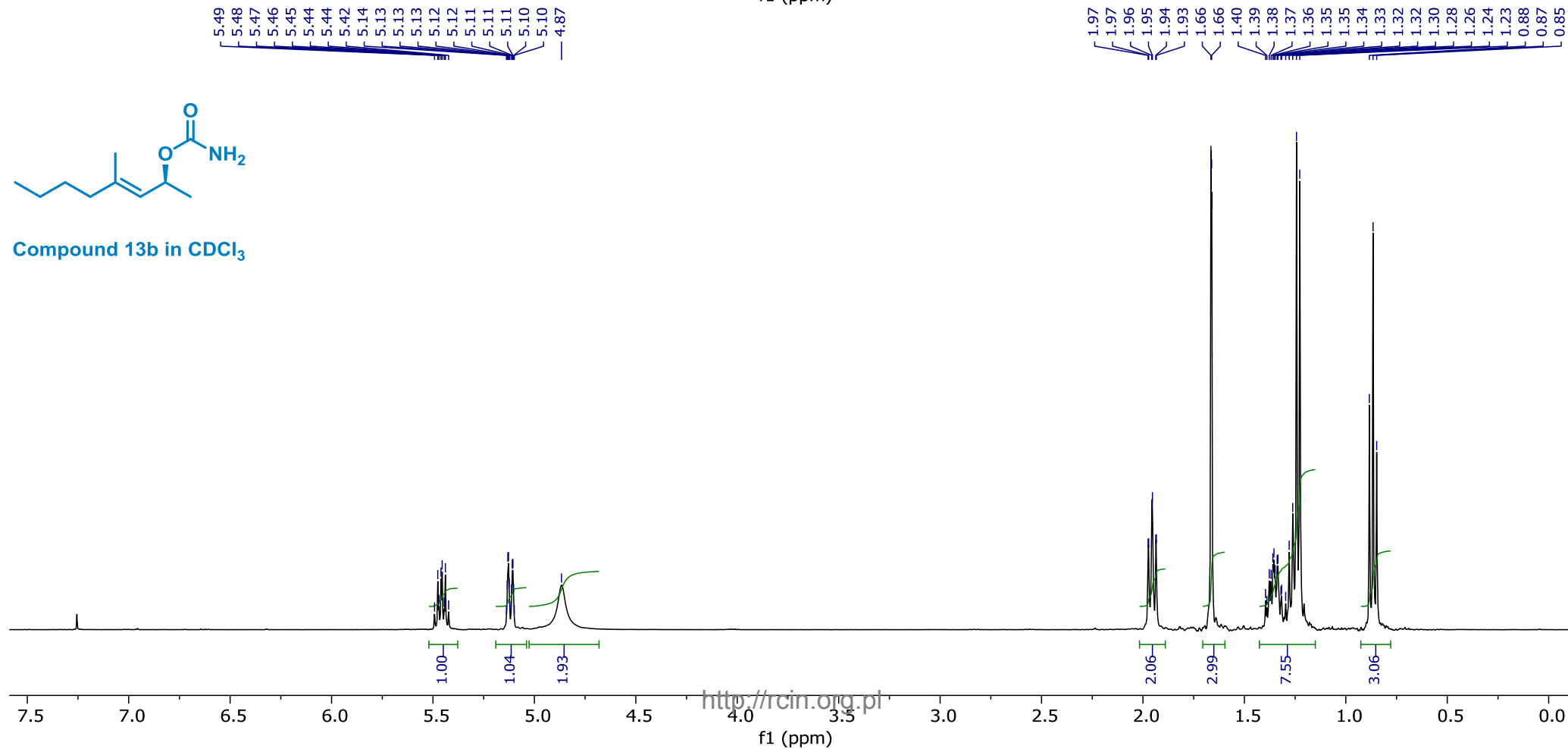
Result Table (Uncal - C:\ClarityChrom\DataFiles\Narczyk\chiralcel-OD-H\AN662\_ester\_100%\_Hex - K-2501: Channel 1)

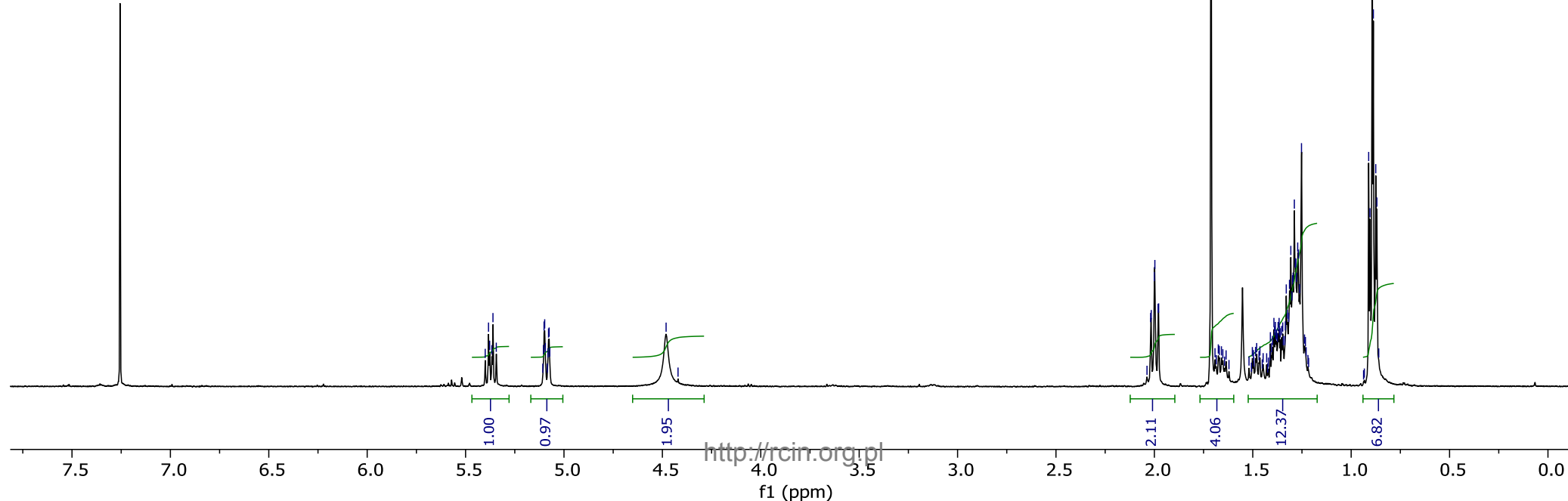
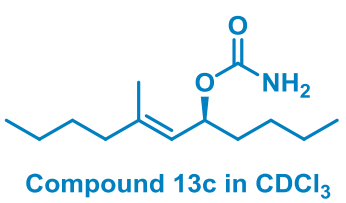
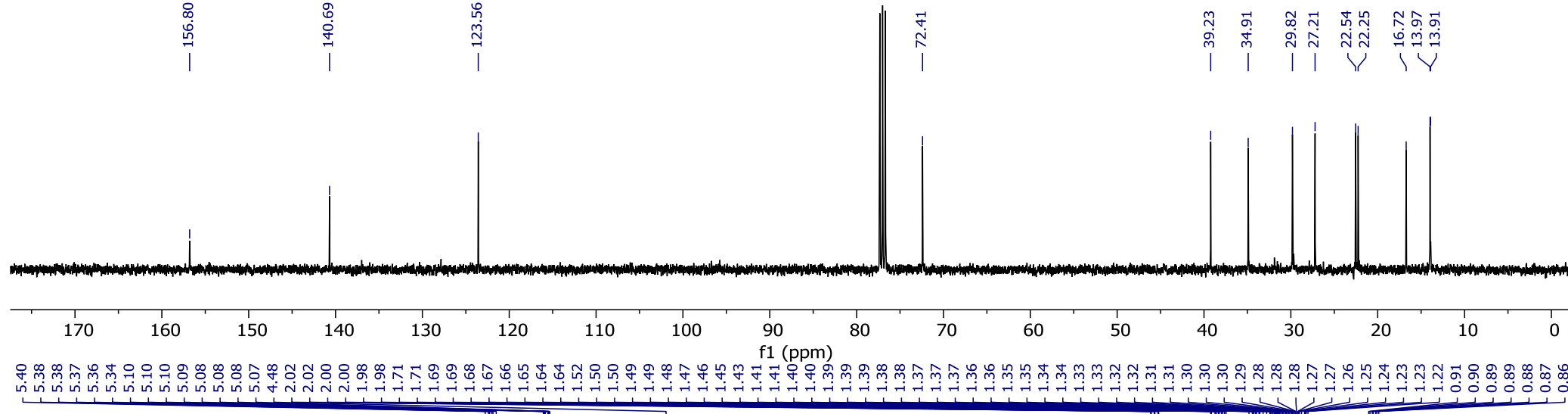
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	20,733	19508,479	346,365	97,0	96,4	0,88	
2	24,233	606,732	12,761	3,0	3,6	0,78	
	Total	20115,210	359,126	100,0	100,0		

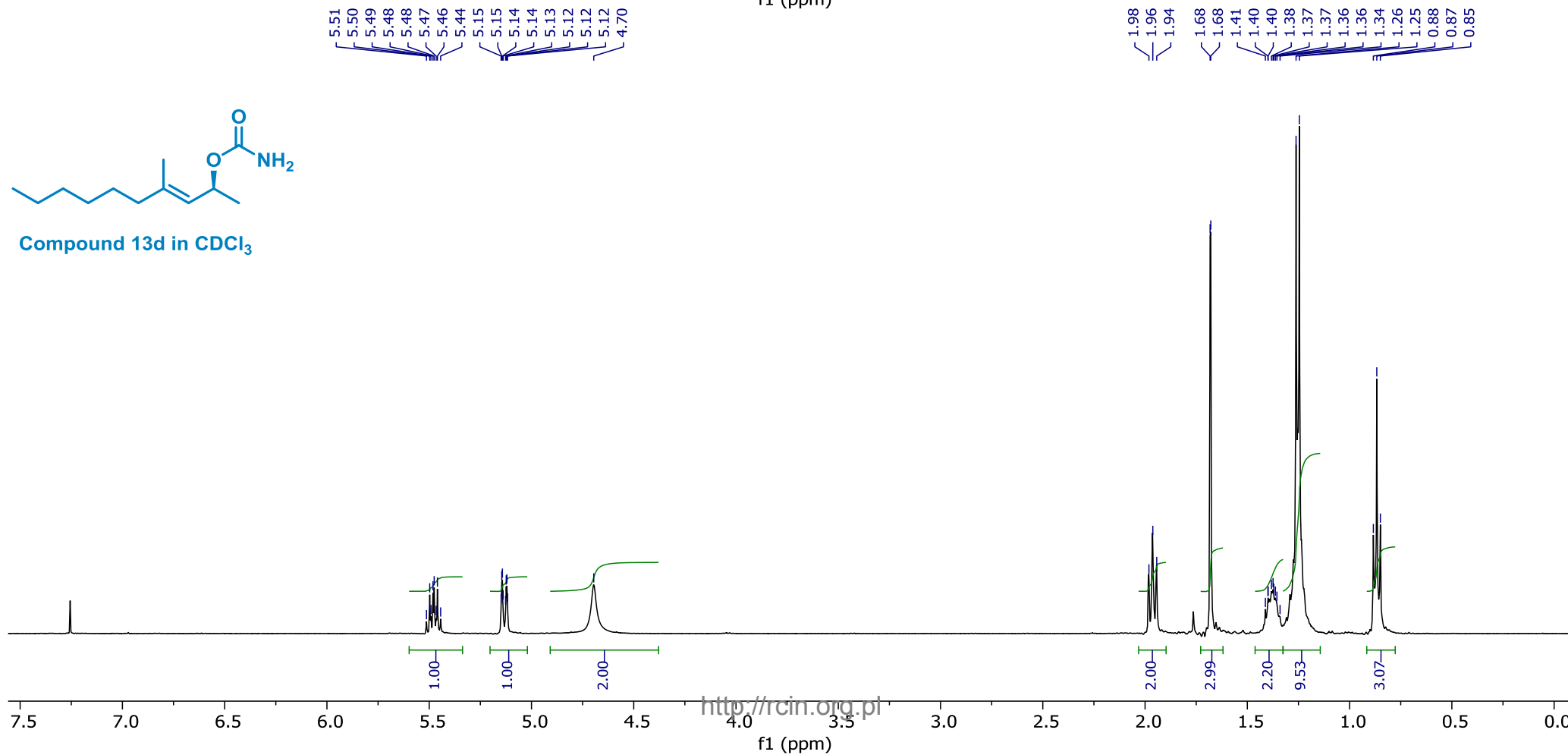
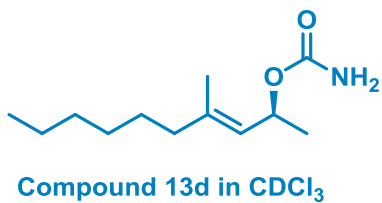
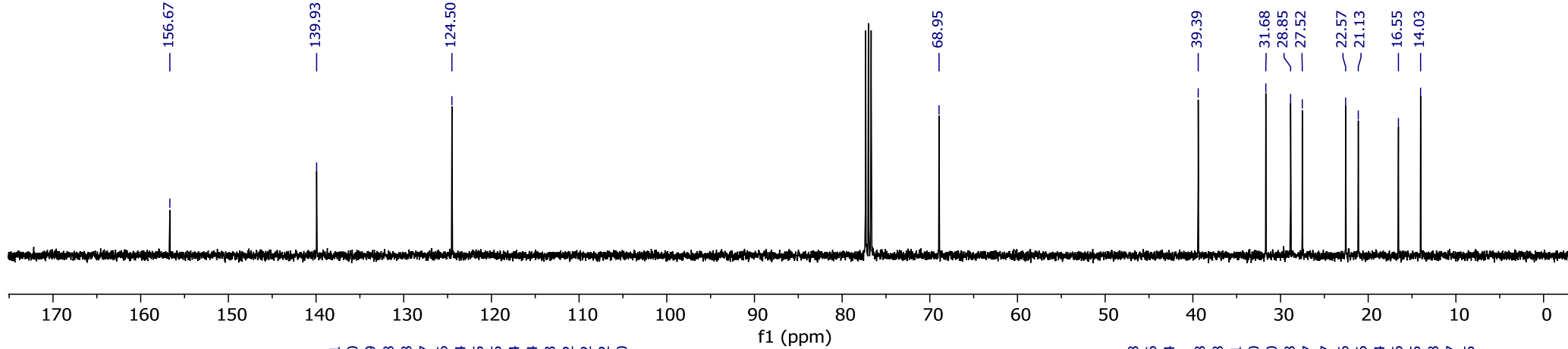


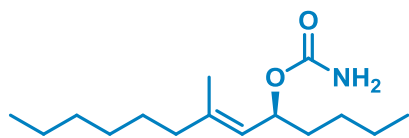
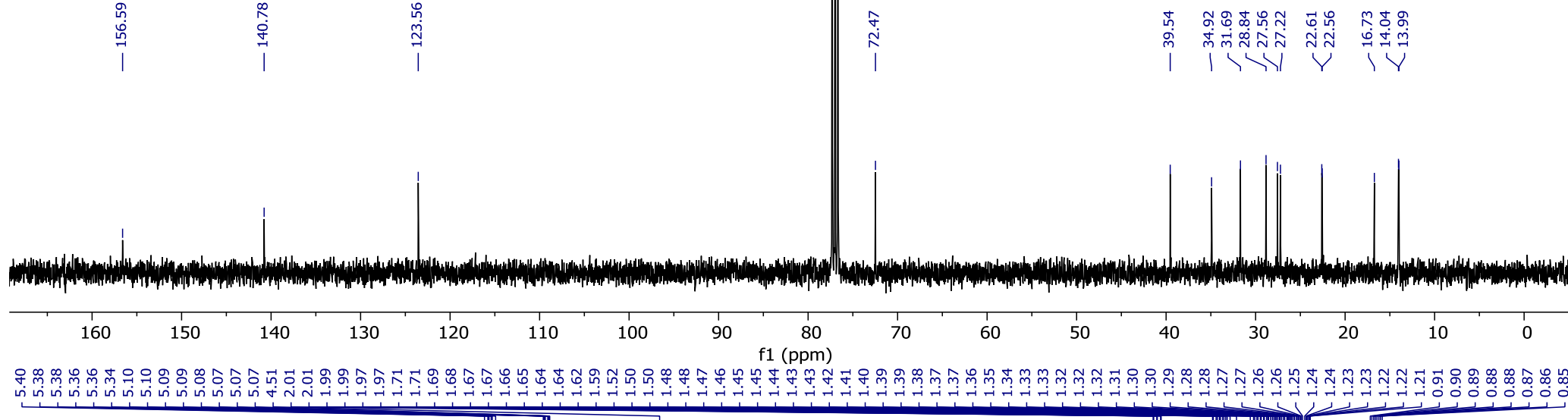


Compound 13b in CDCl<sub>3</sub>

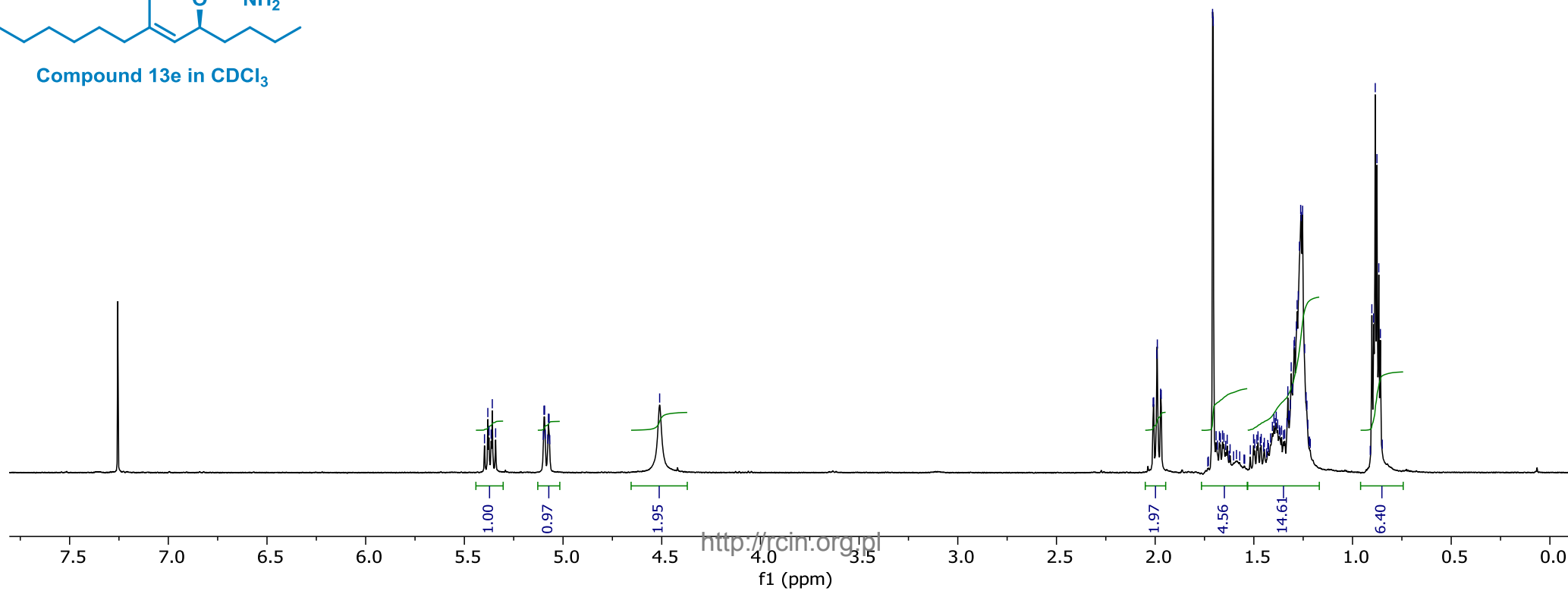


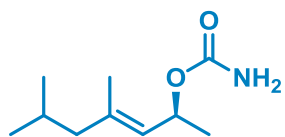
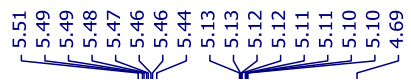
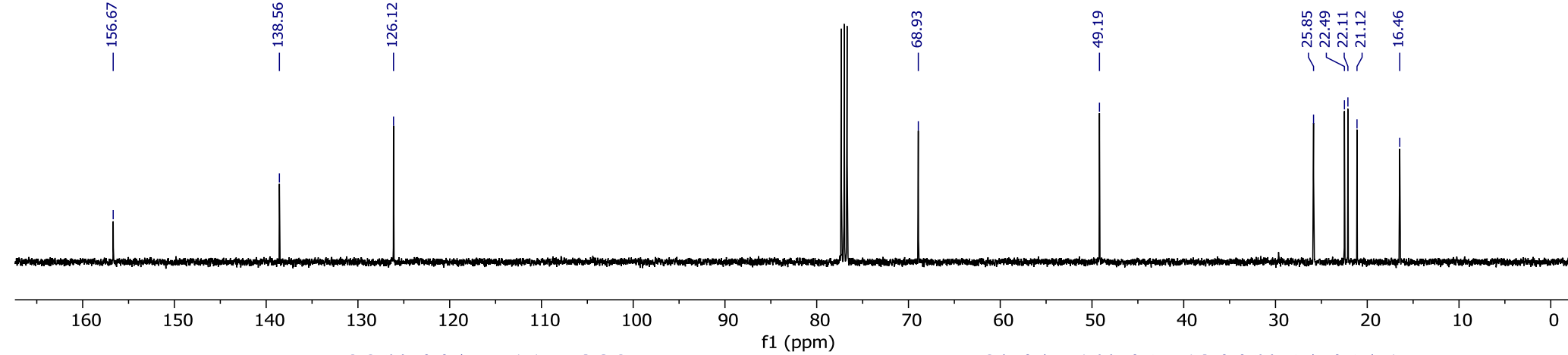




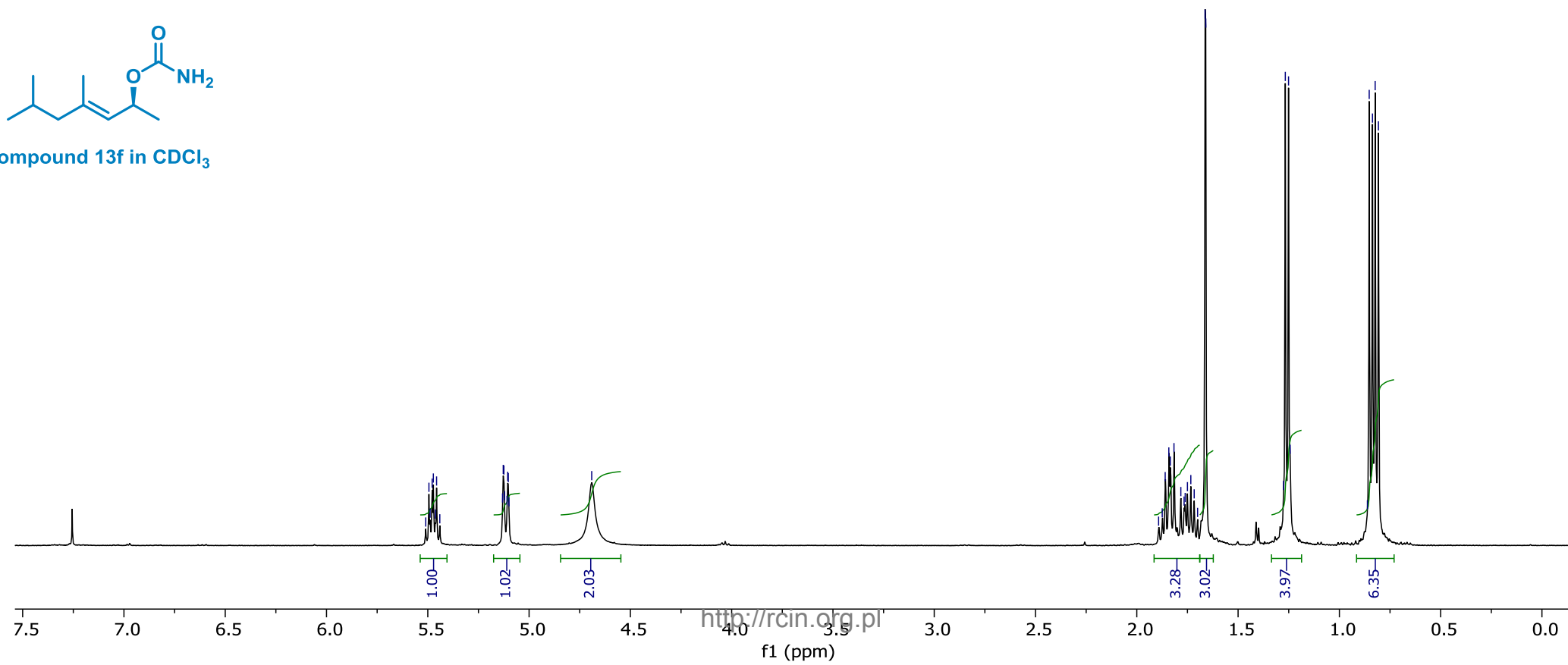


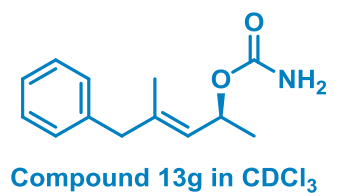
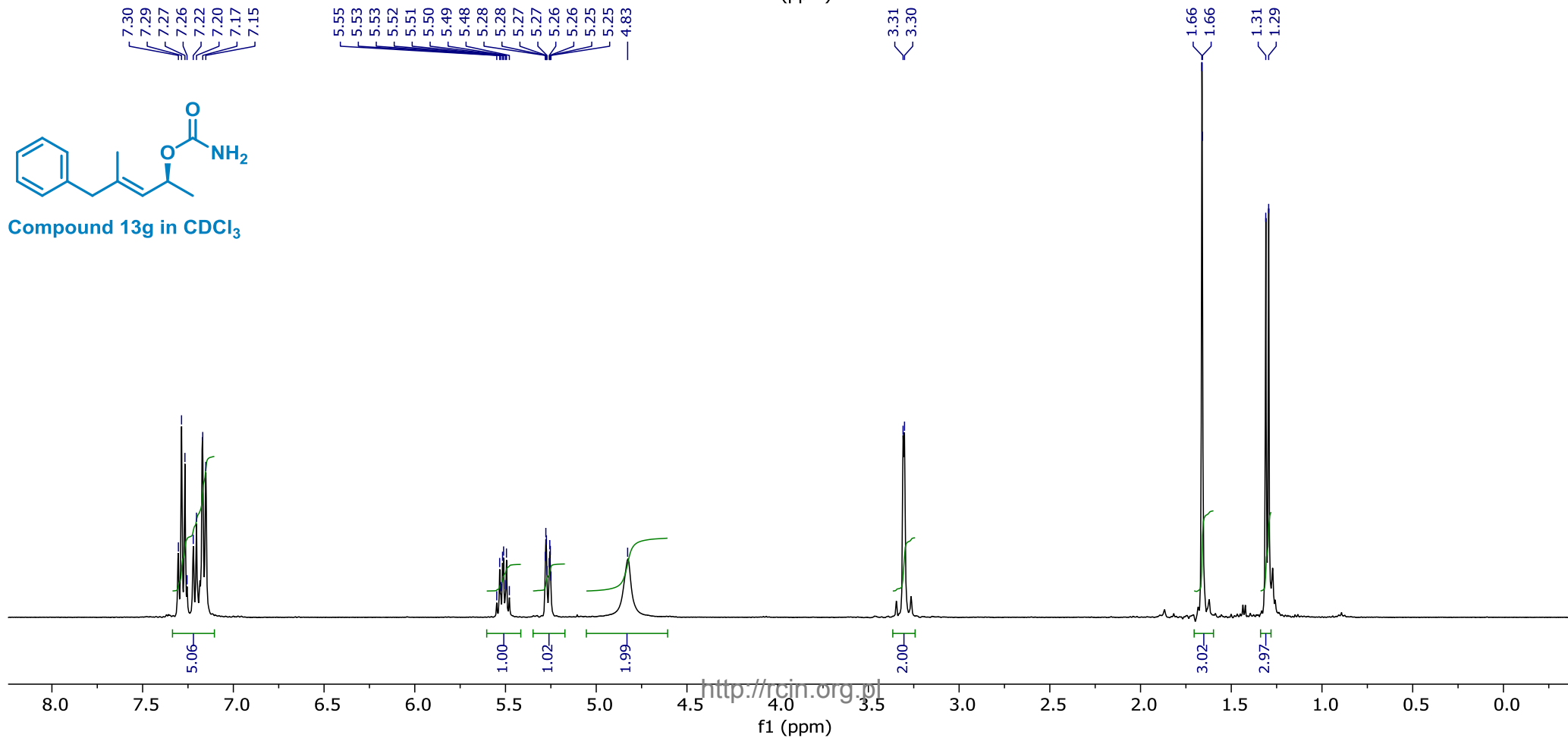
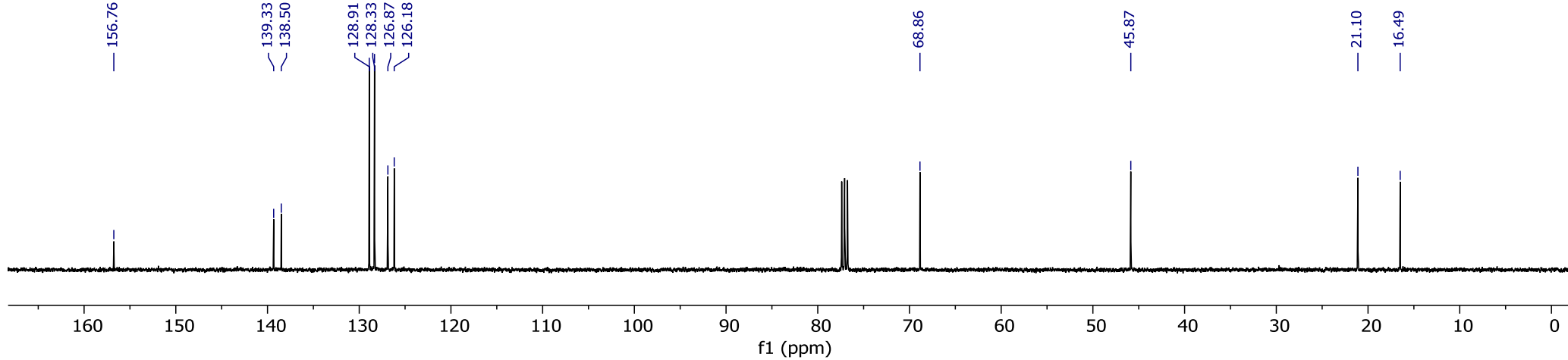
Compound 13e in CDCl<sub>3</sub>



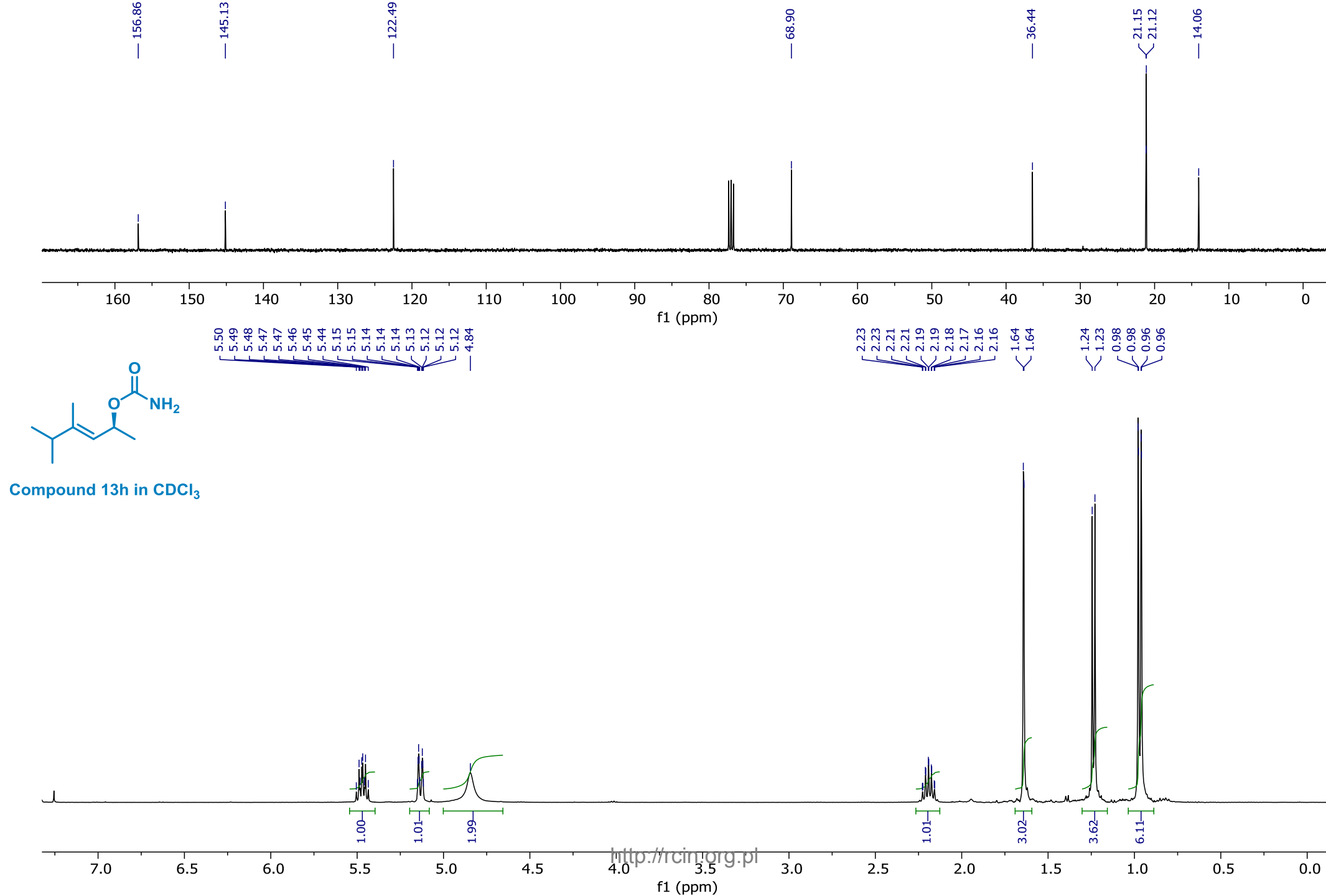


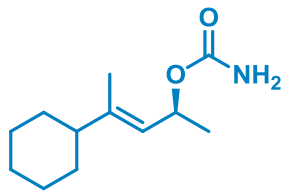
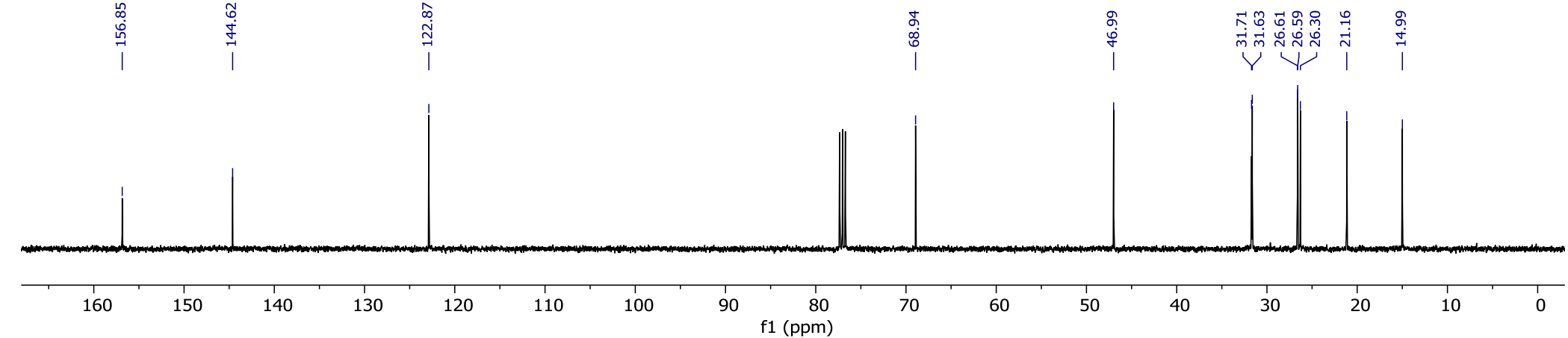
Compound 13f in CDCl<sub>3</sub>



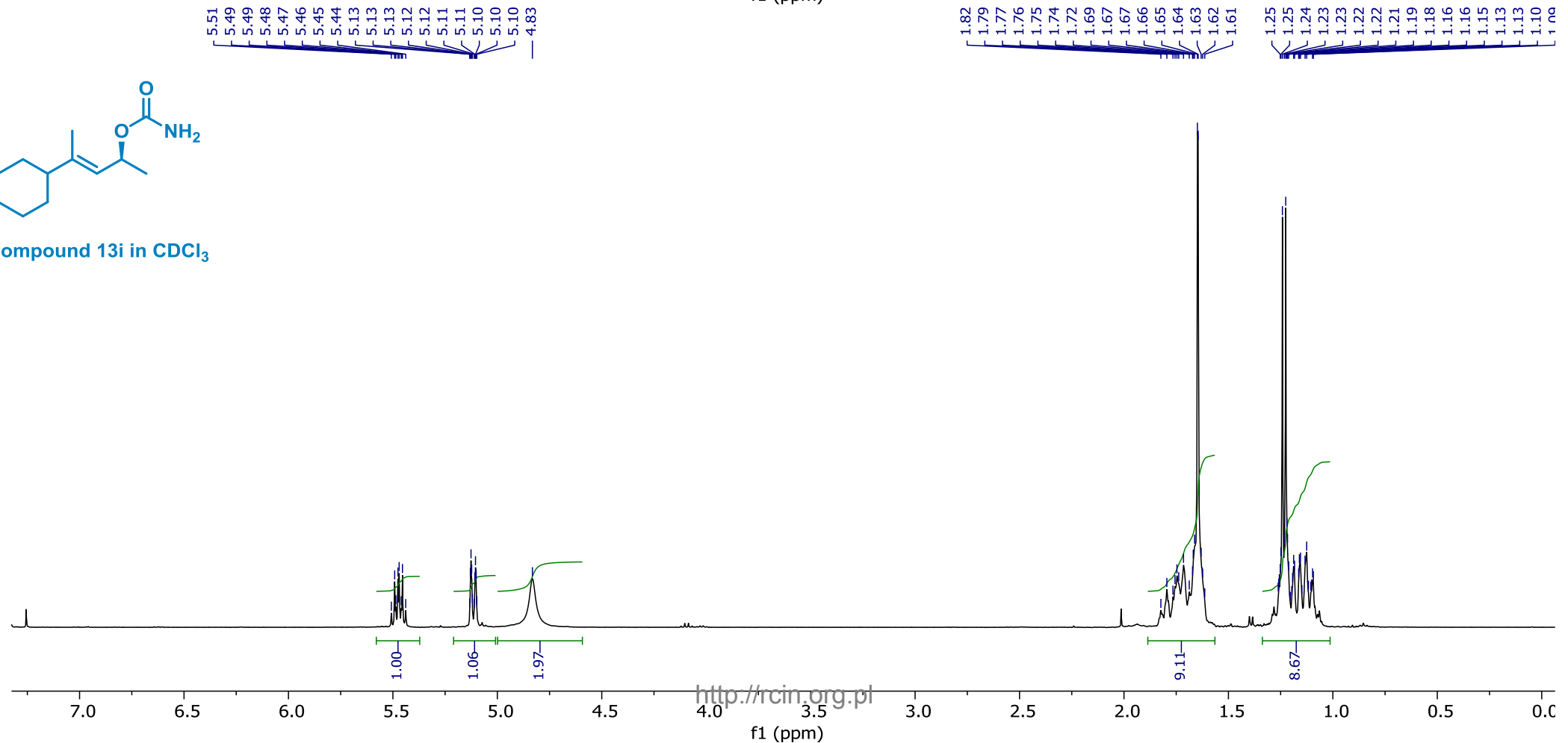


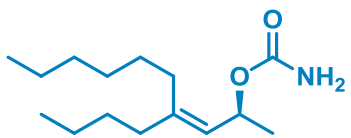
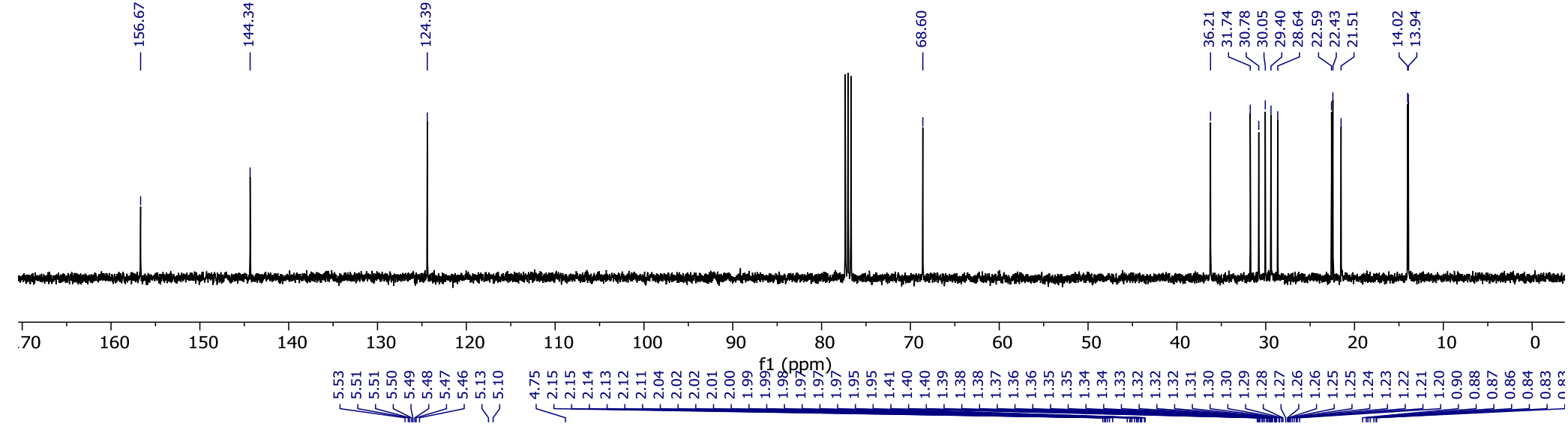




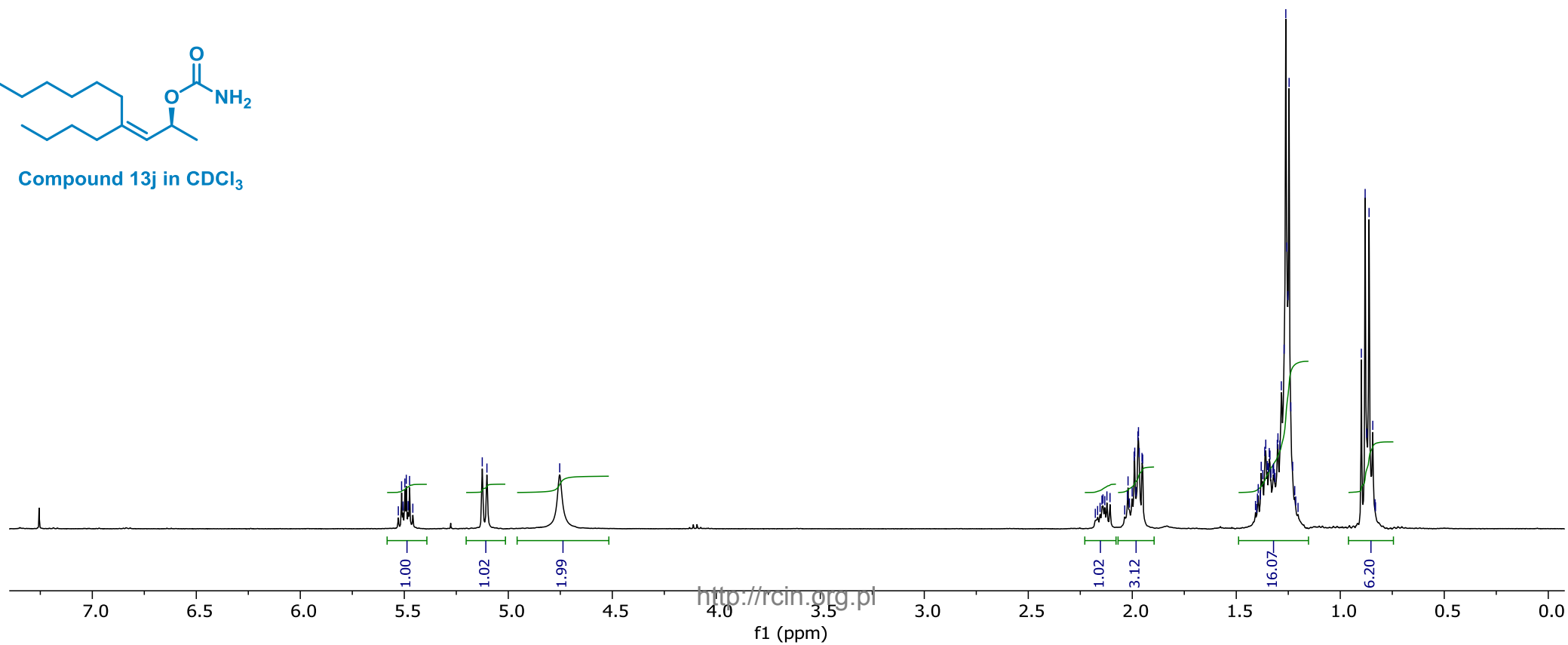


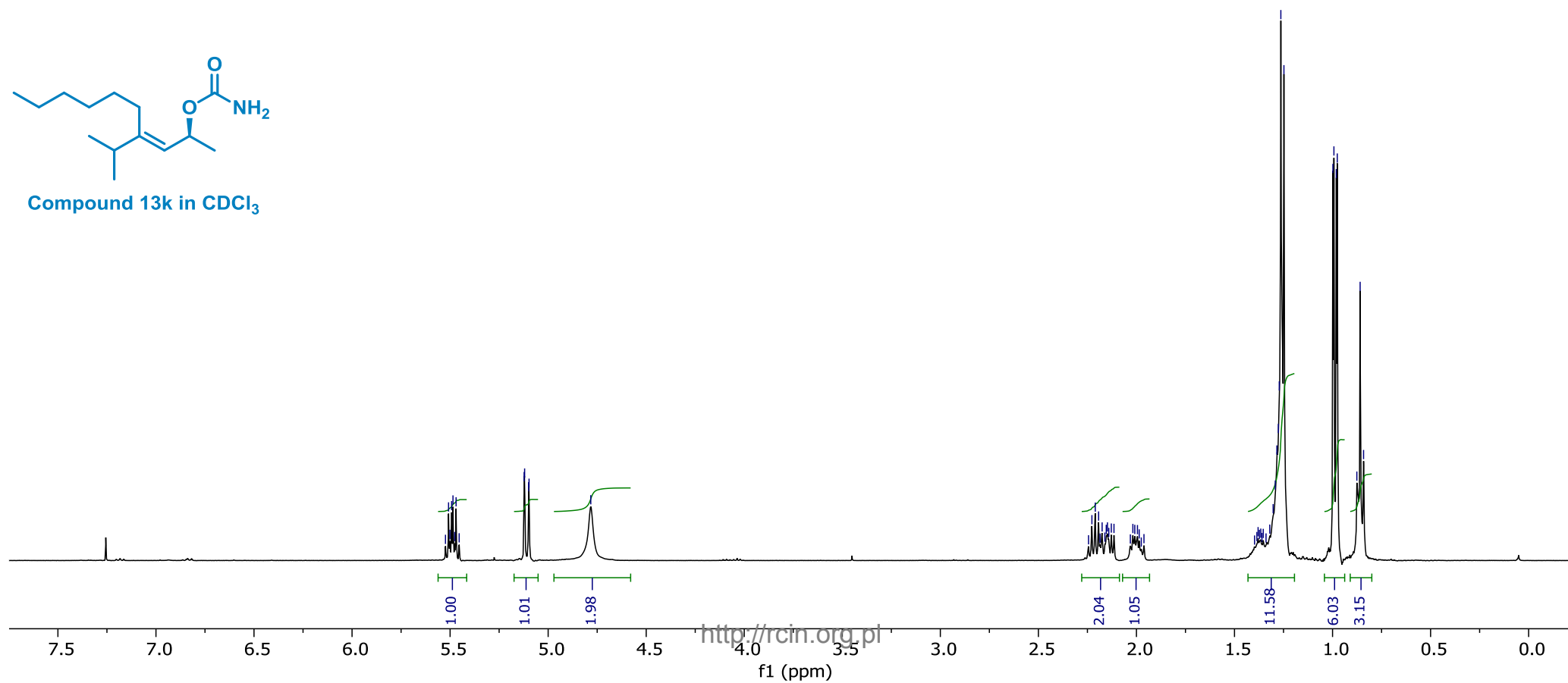
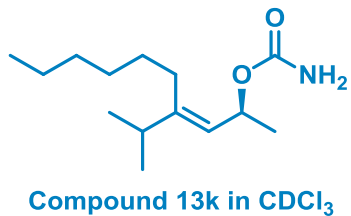
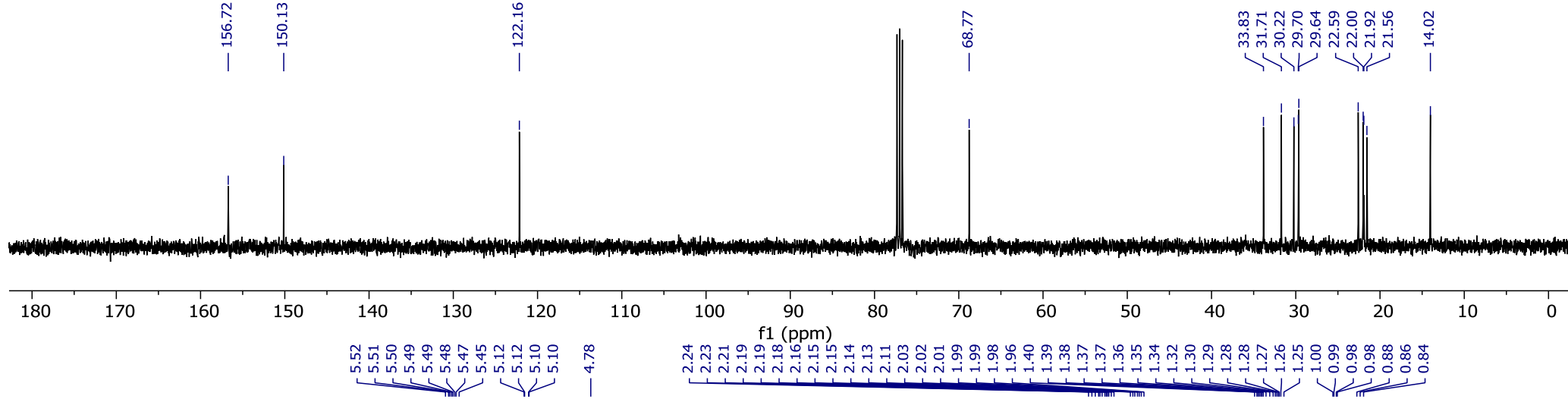
Compound 13i in CDCl<sub>3</sub>

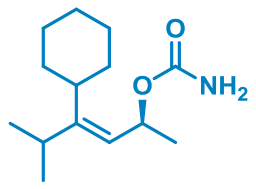
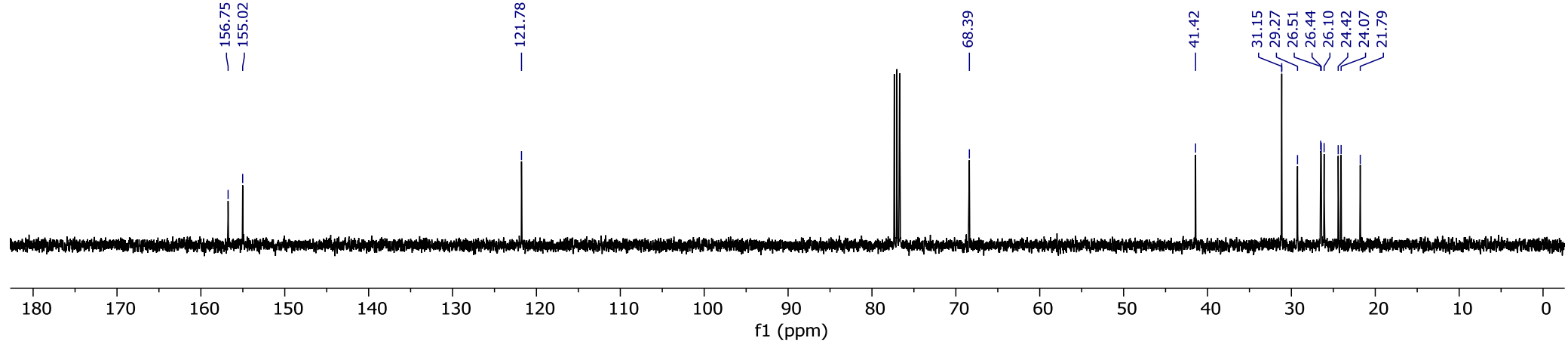




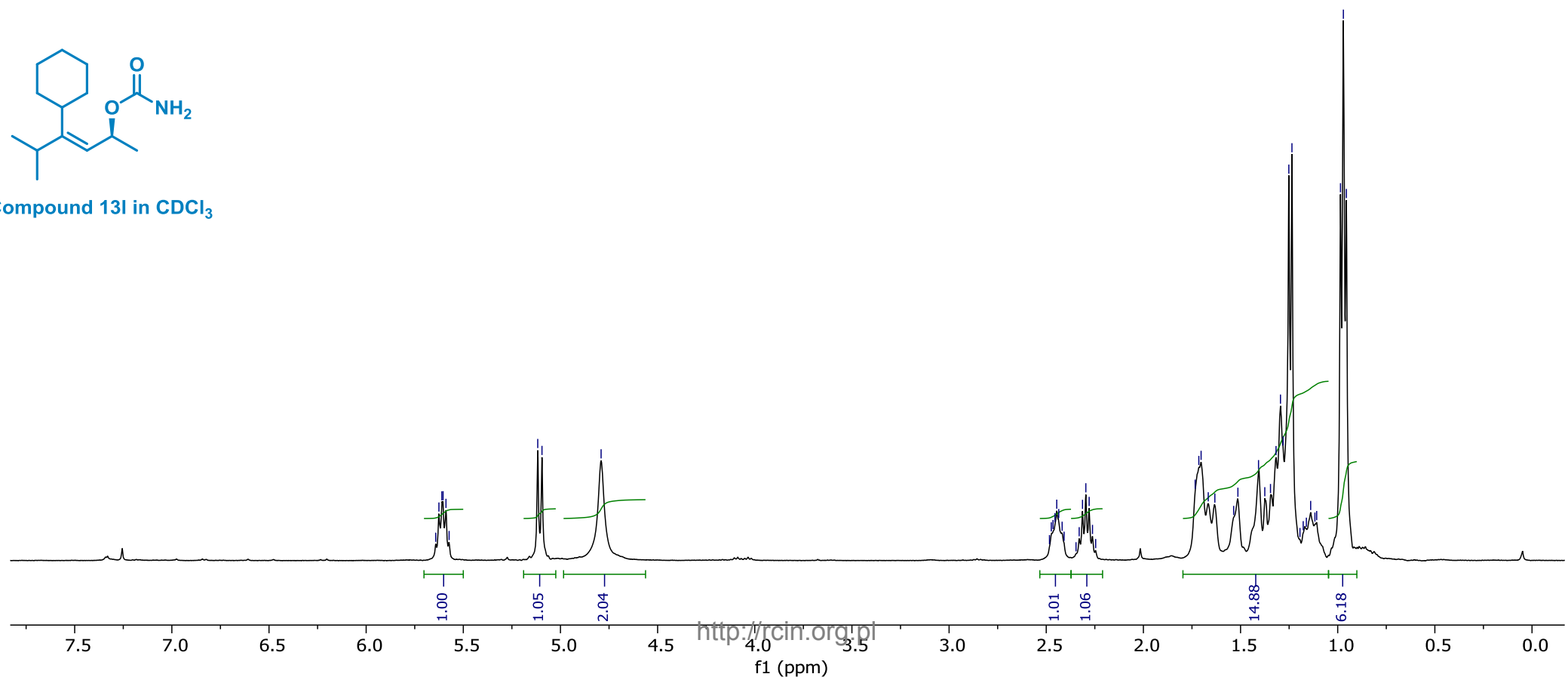
Compound 13j in CDCl<sub>3</sub>

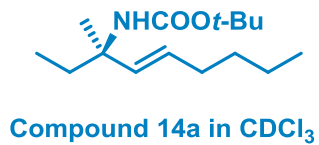
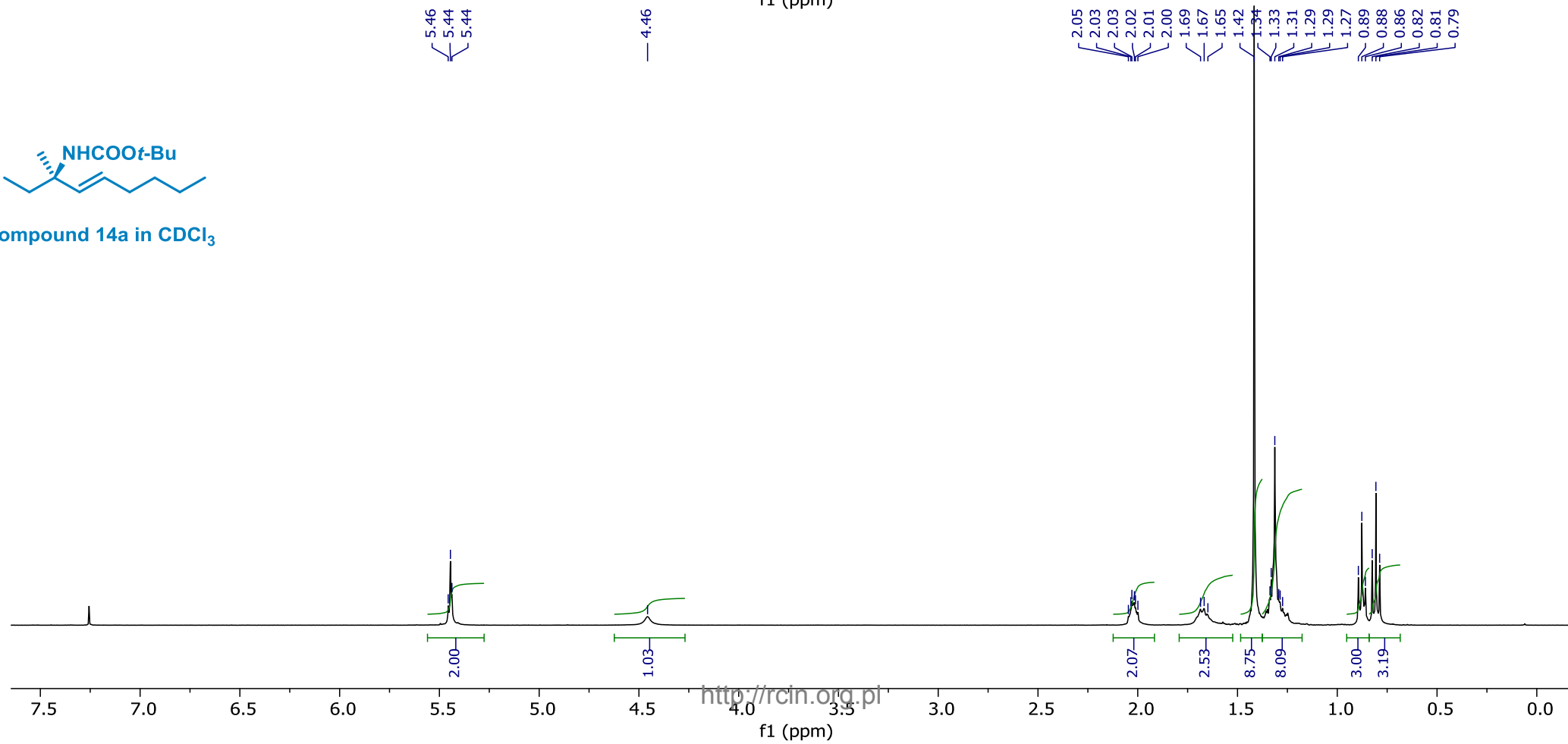
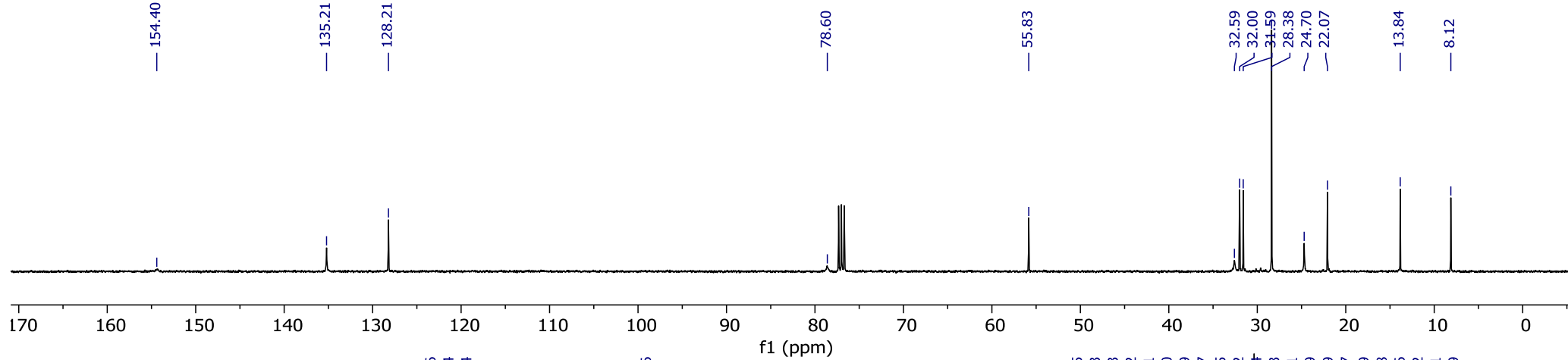


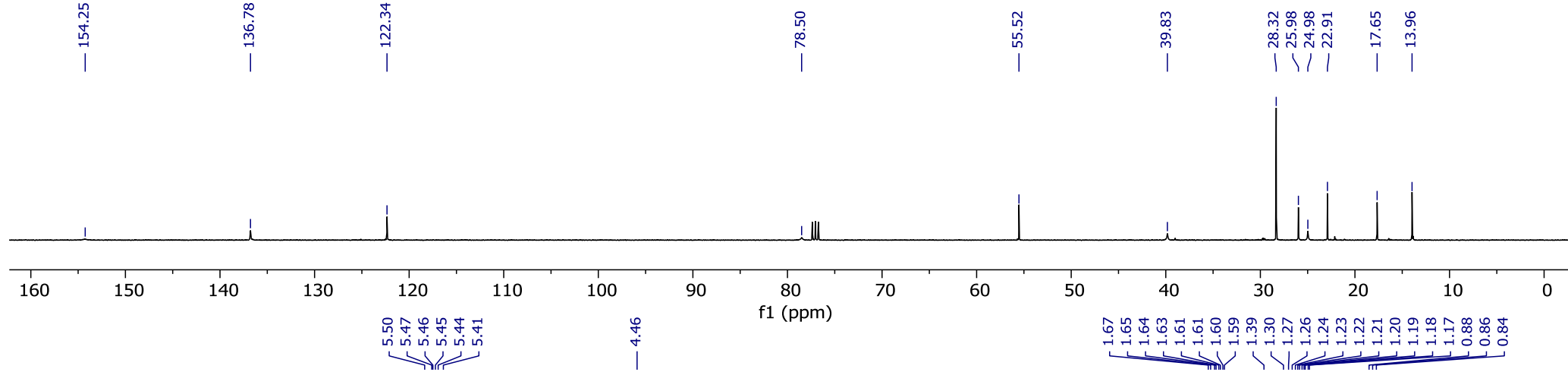




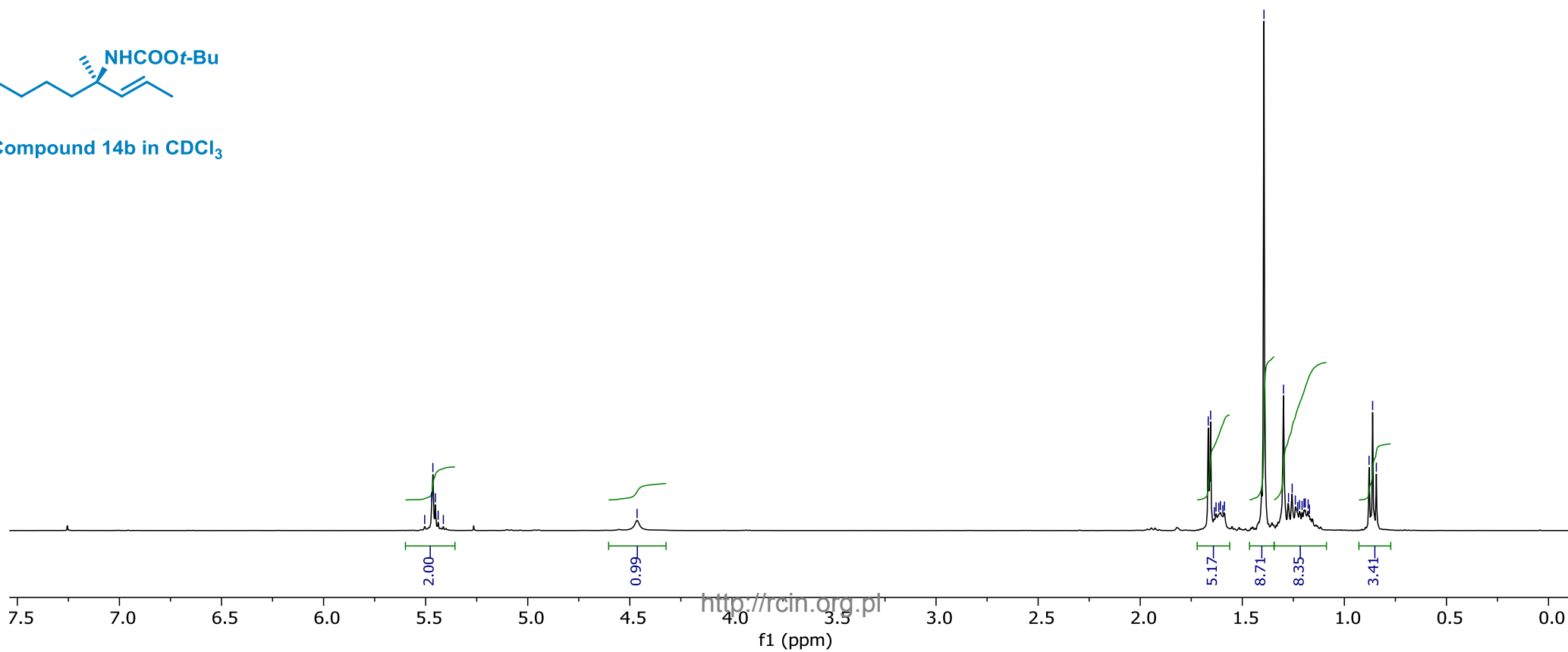
Compound 13l in CDCl<sub>3</sub>

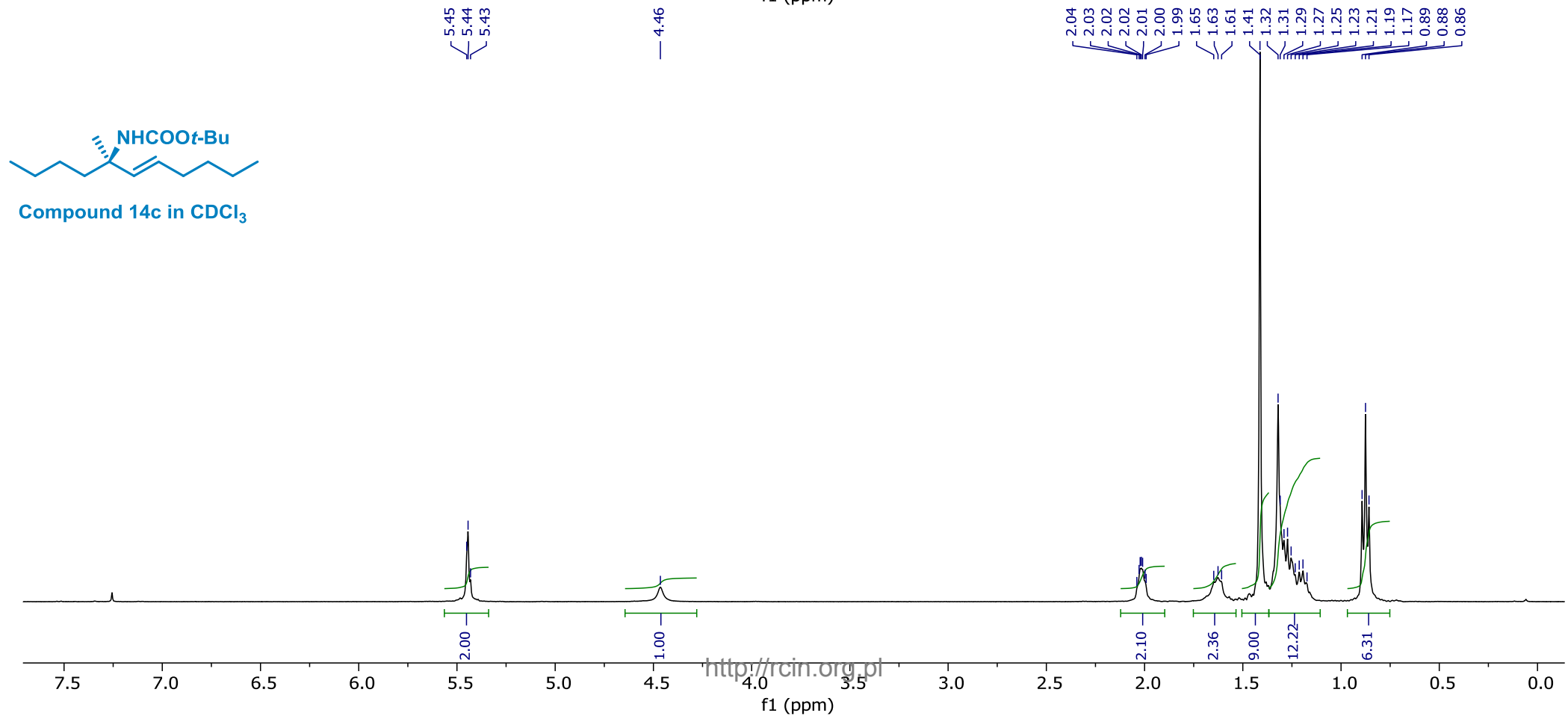
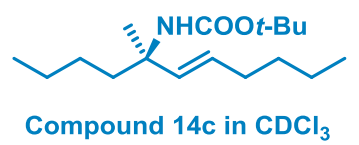
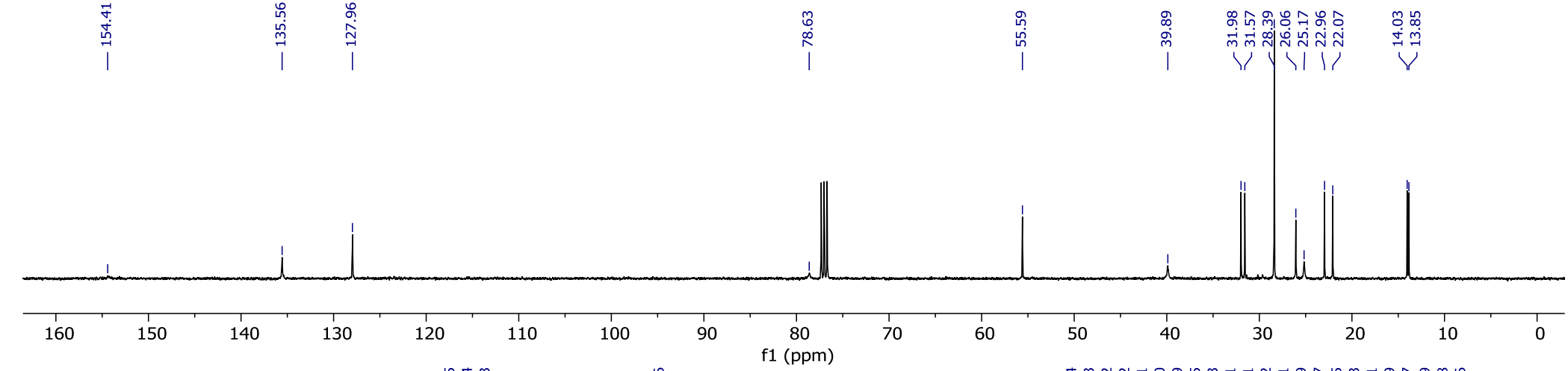




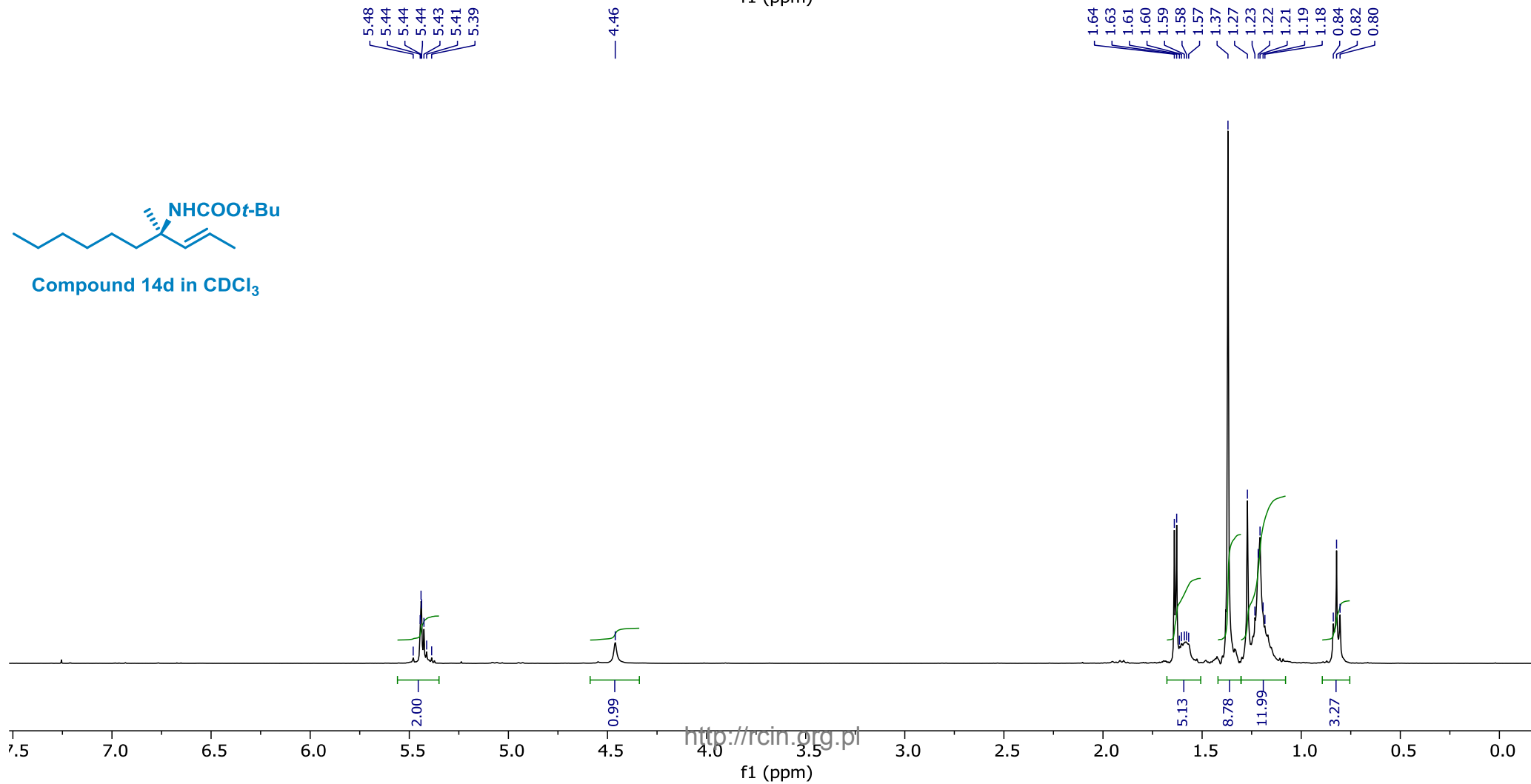
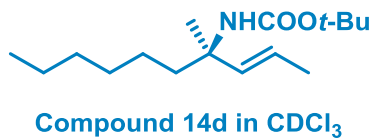
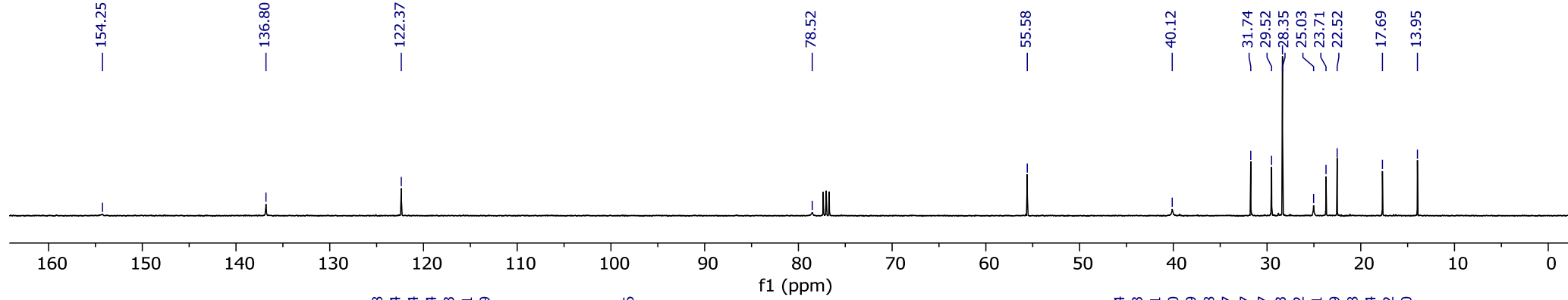


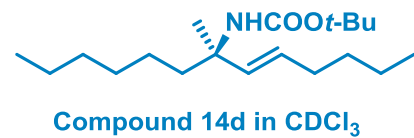
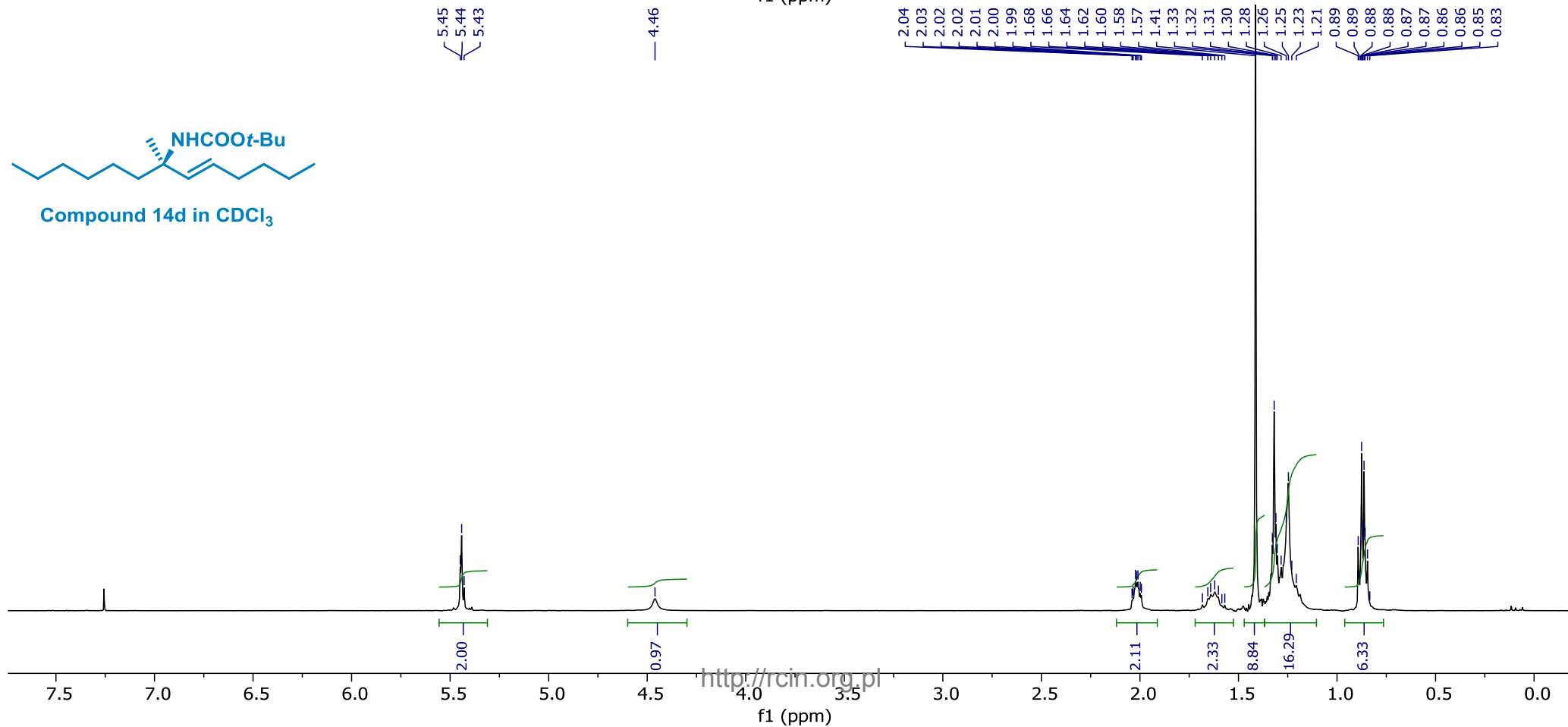
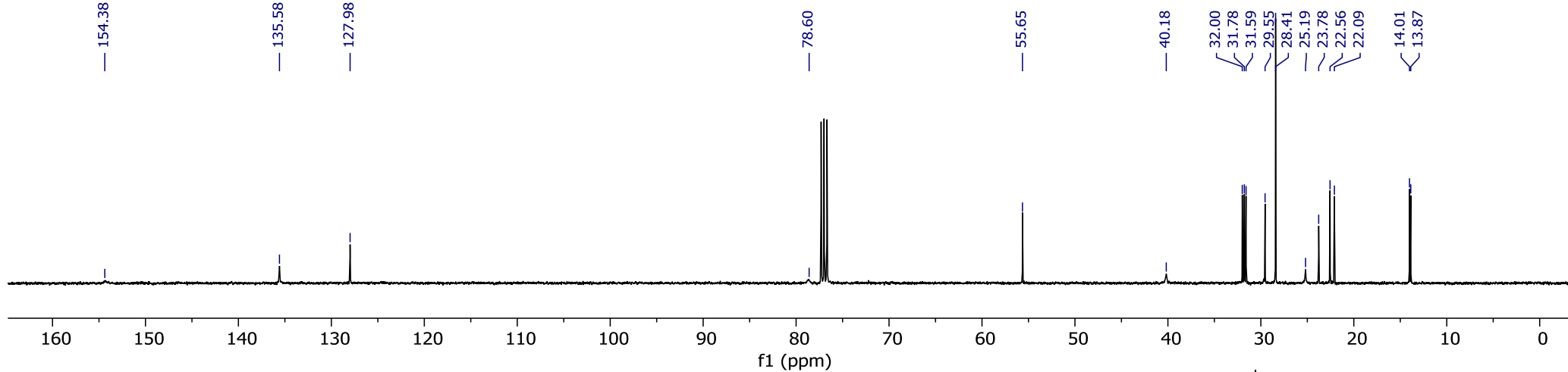
Compound 14b in CDCl<sub>3</sub>

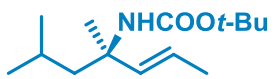
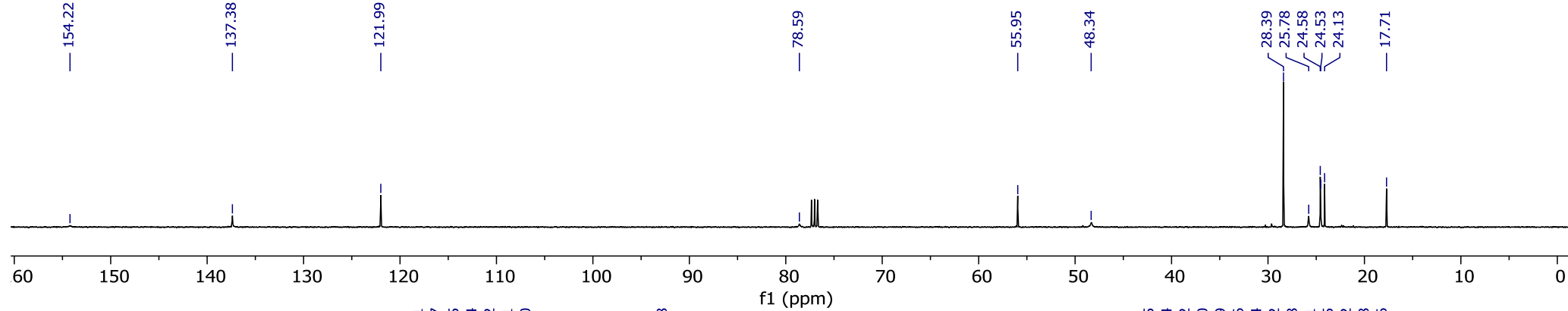




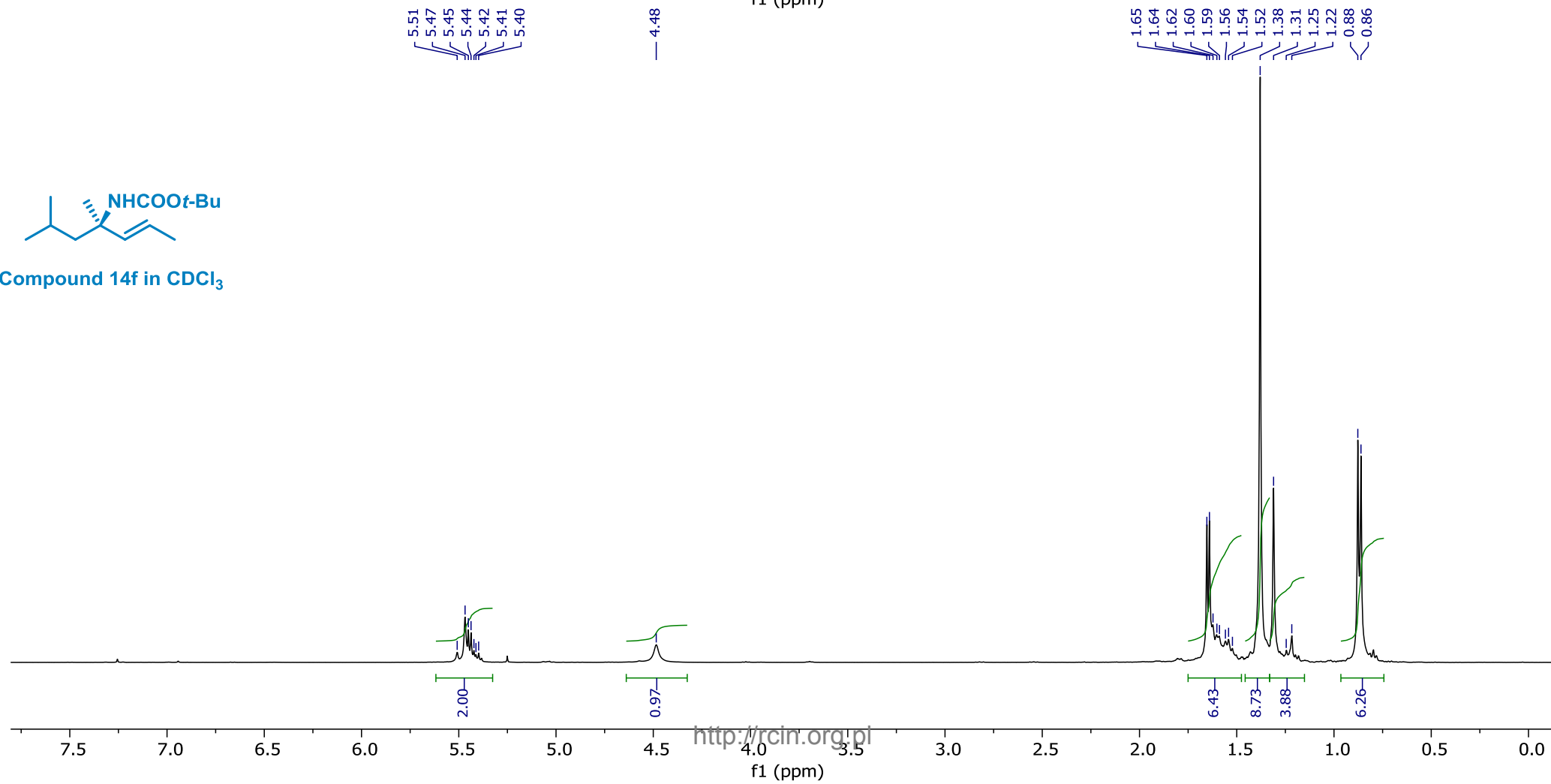


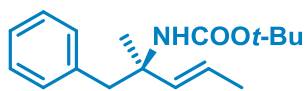
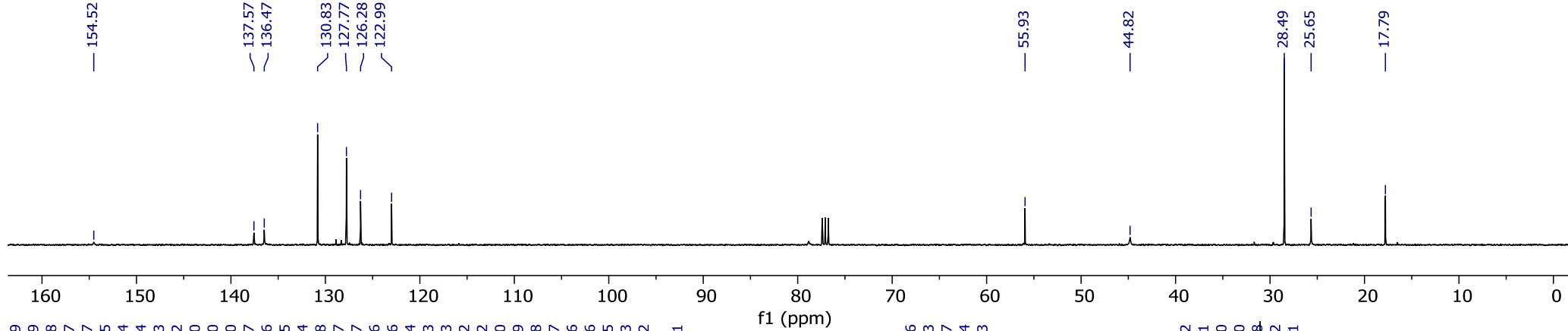




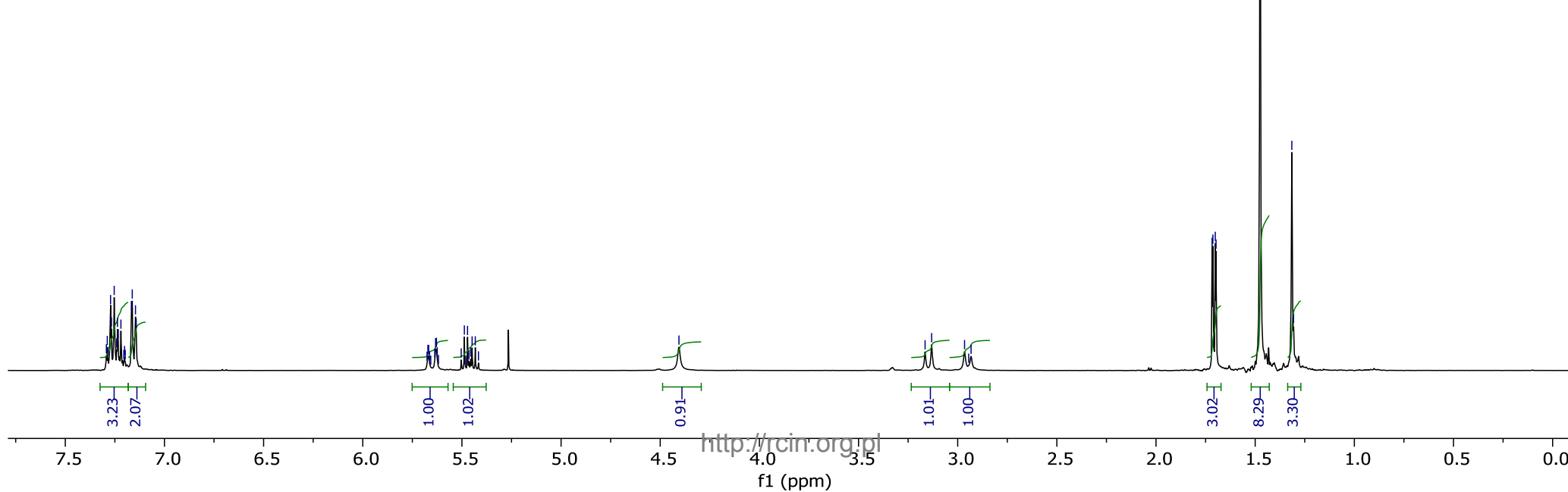


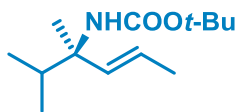
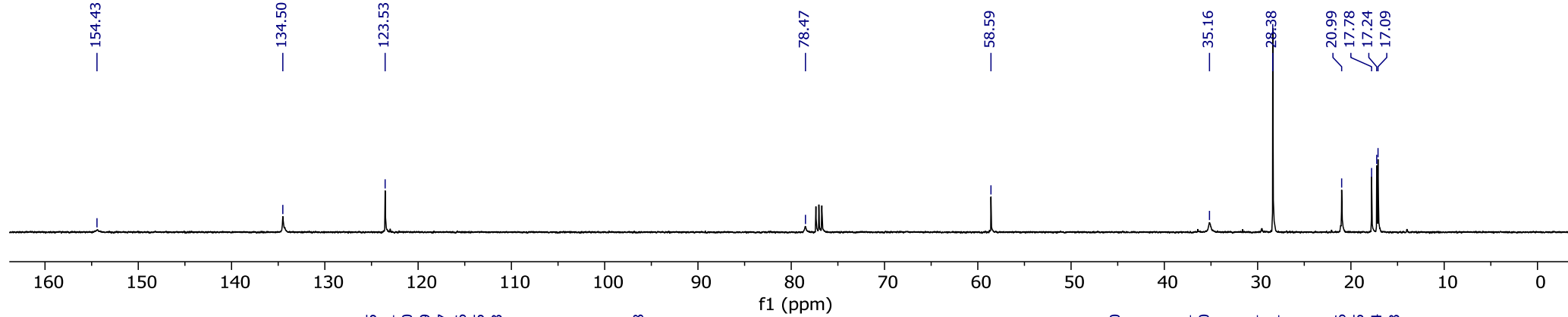
Compound 14f in CDCl<sub>3</sub>



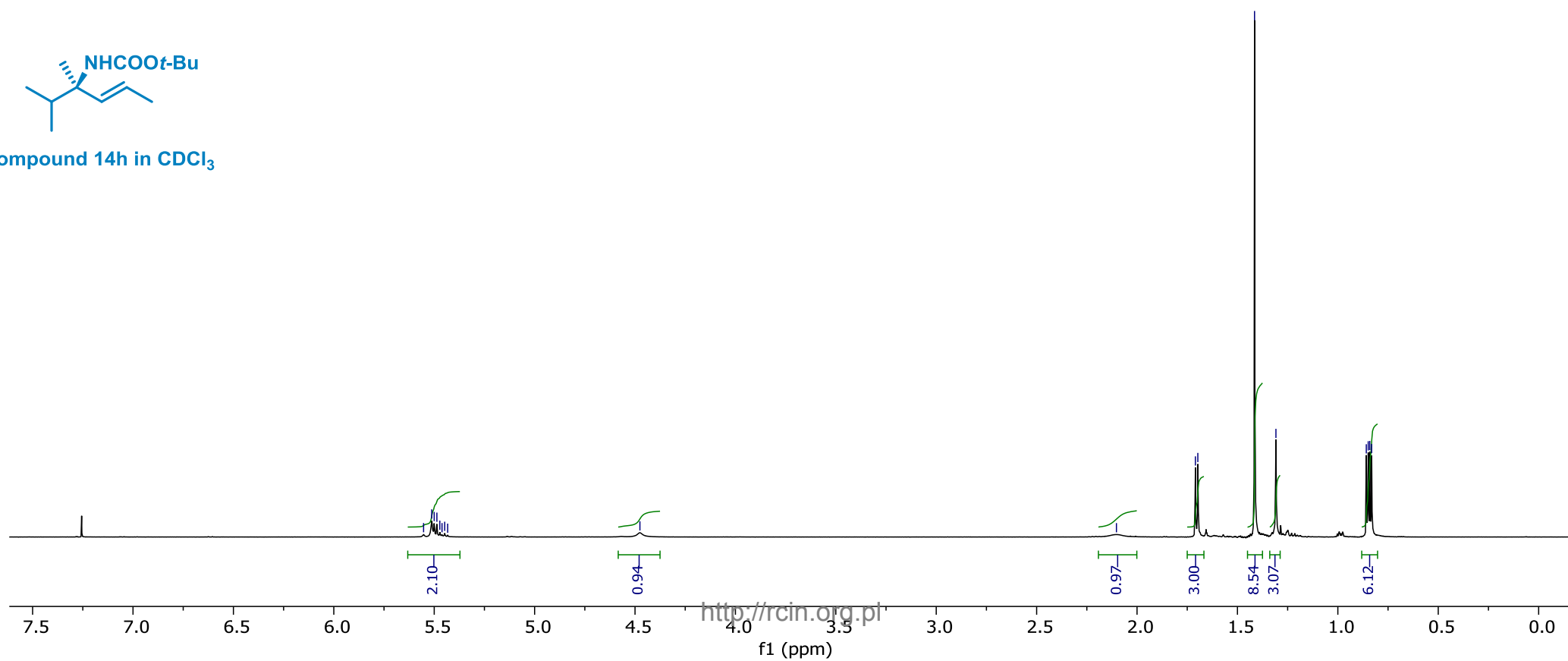


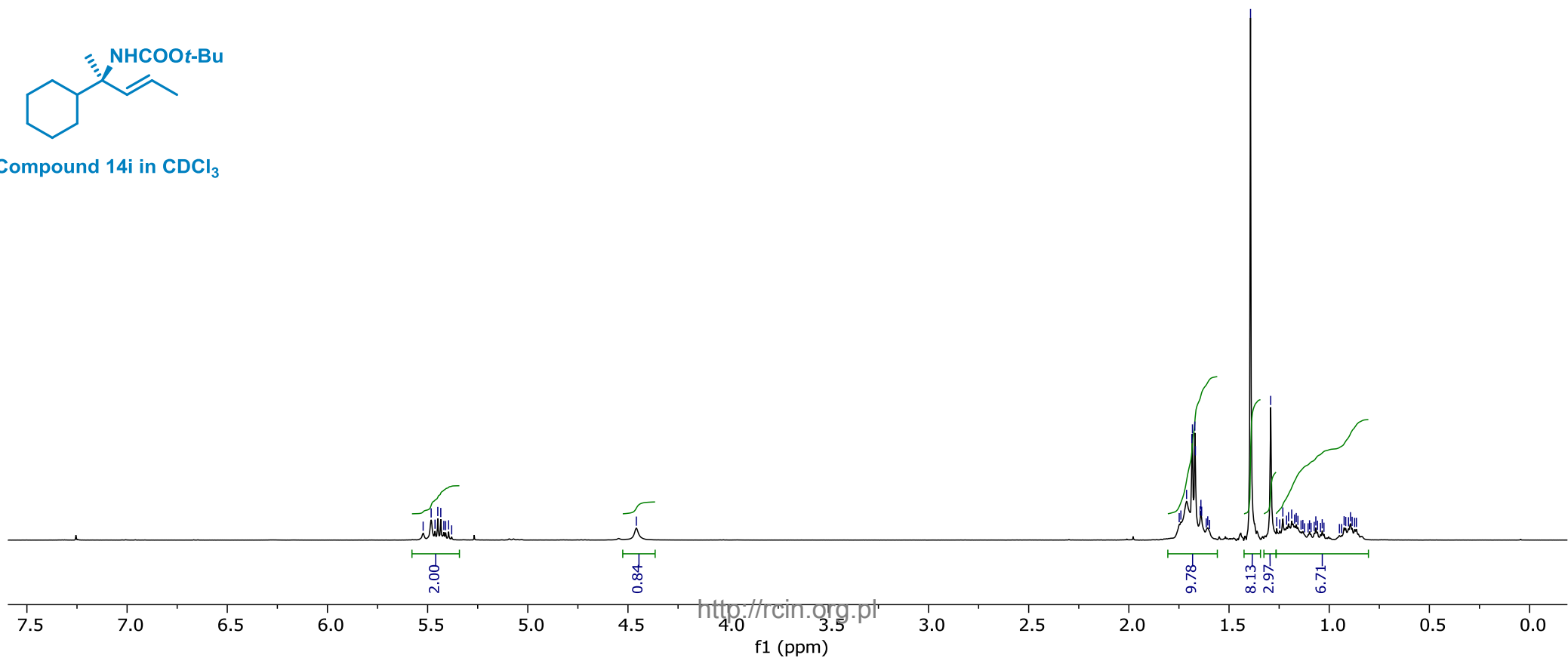
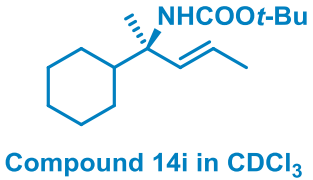
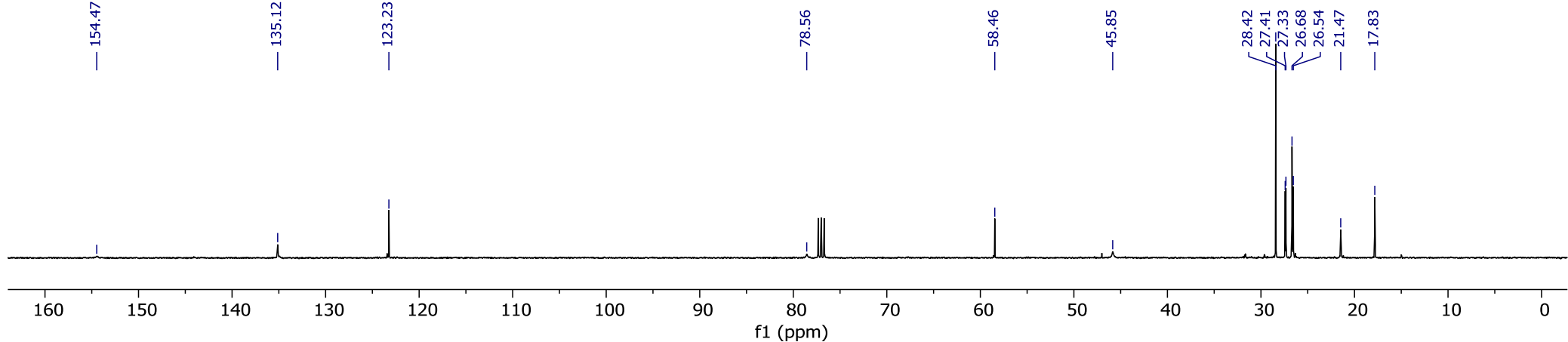
Compound 14g in CDCl<sub>3</sub>

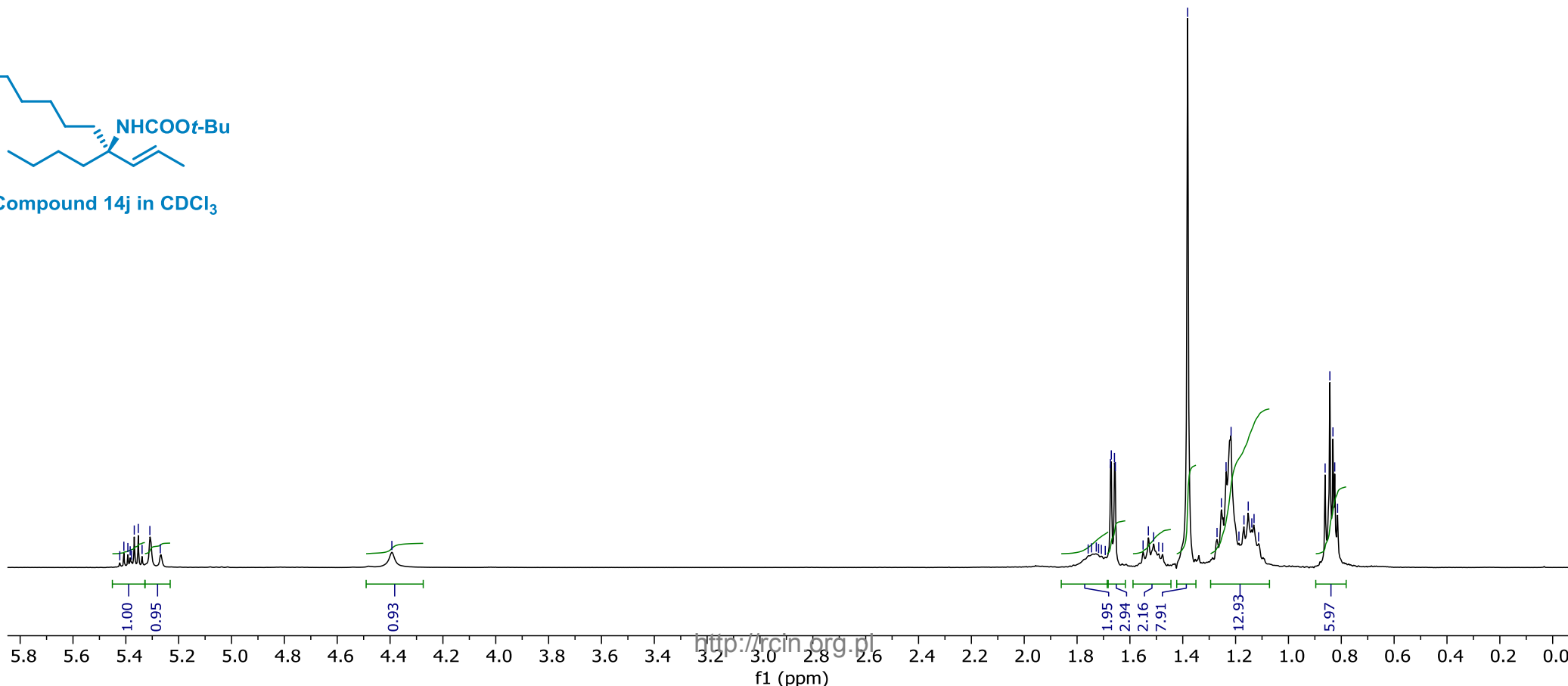
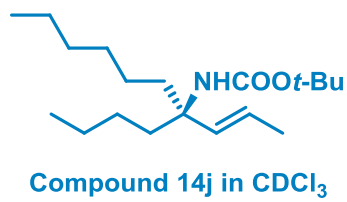
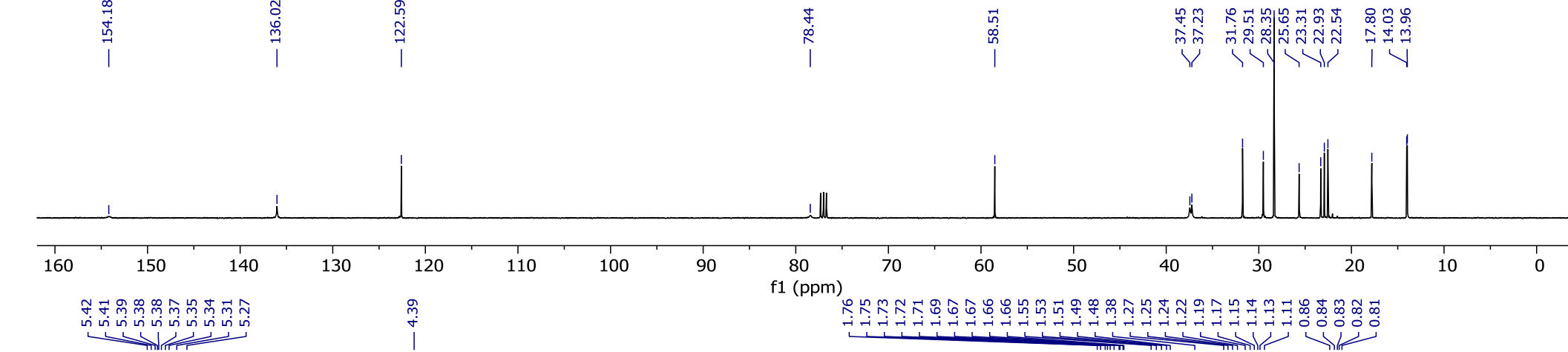


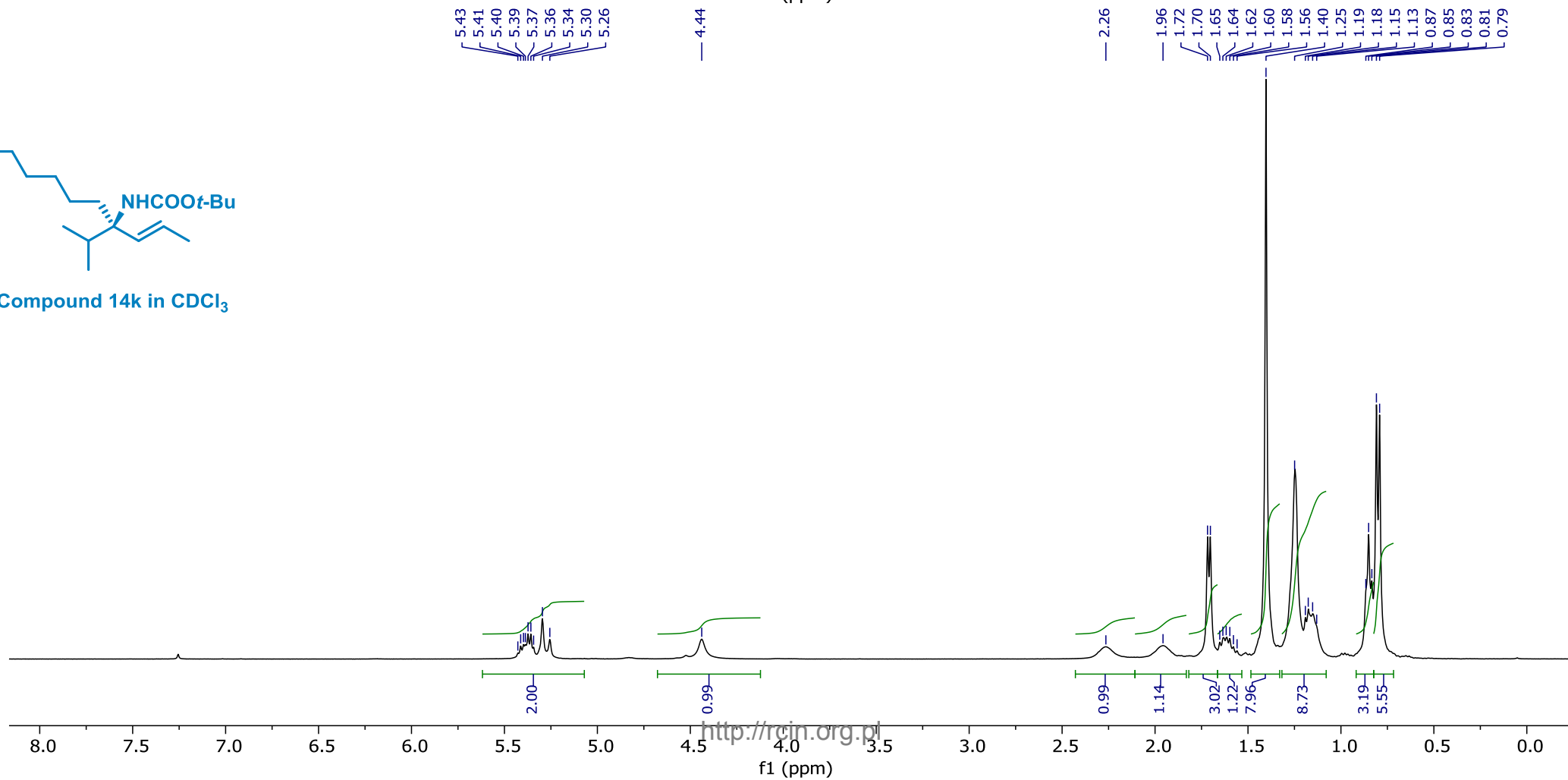
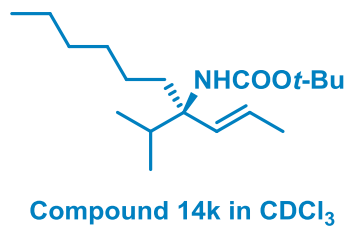
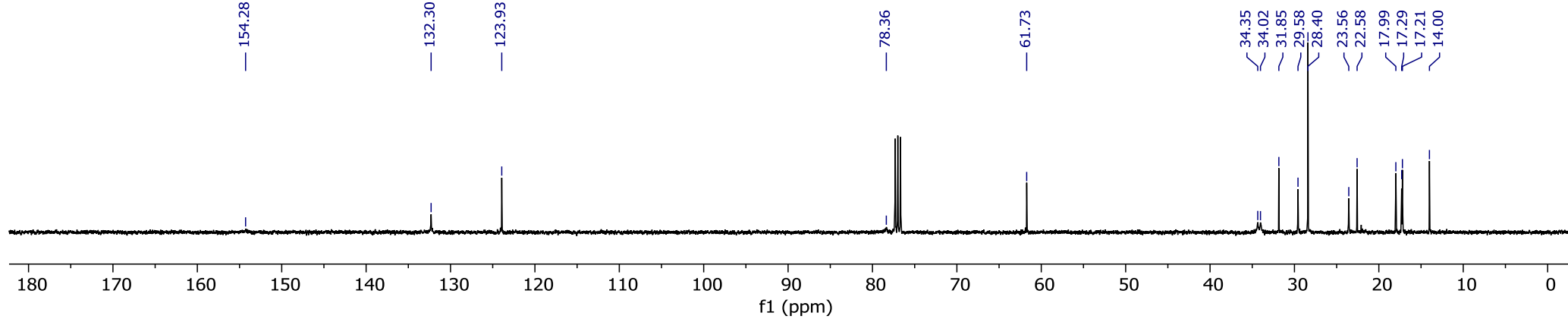


Compound 14h in CDCl<sub>3</sub>

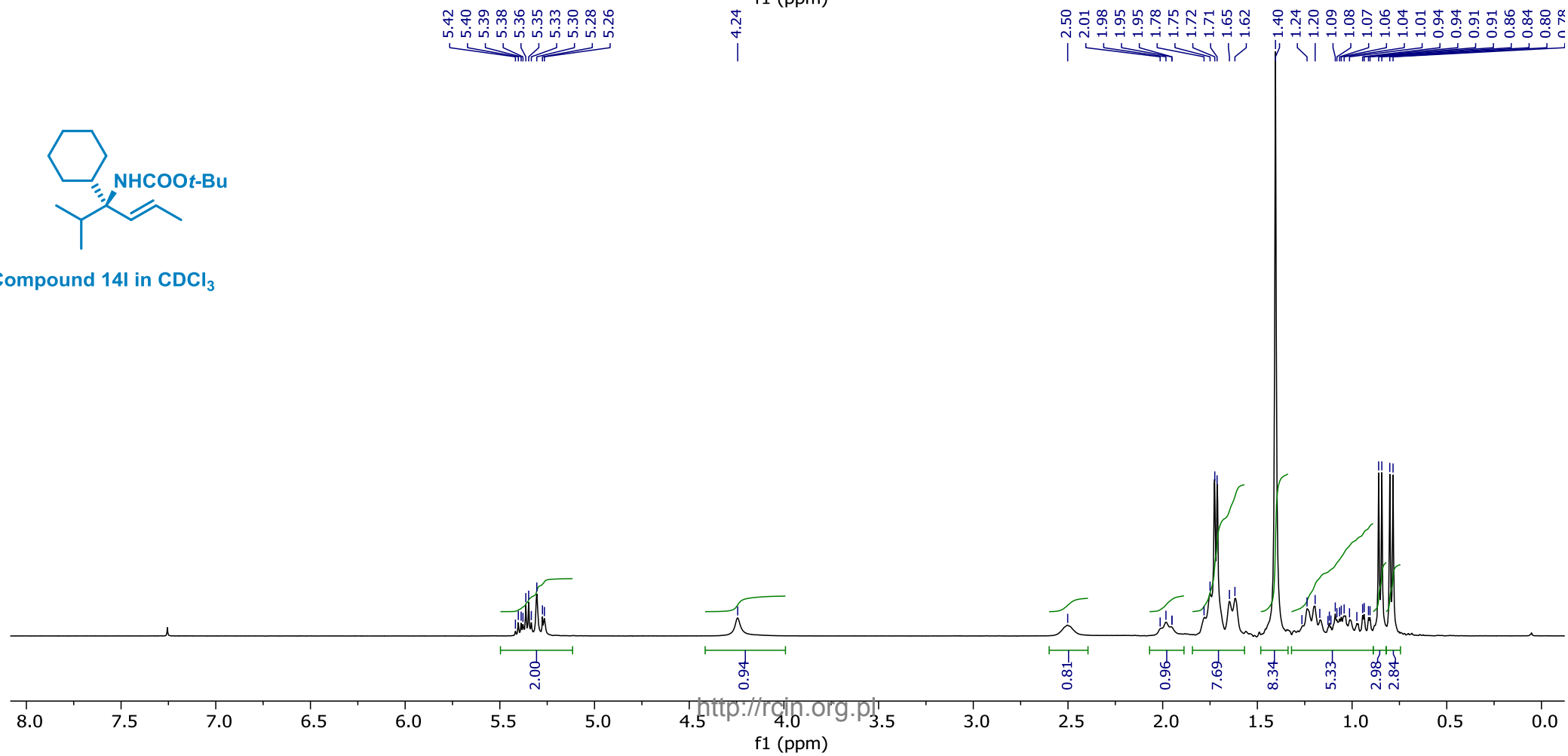
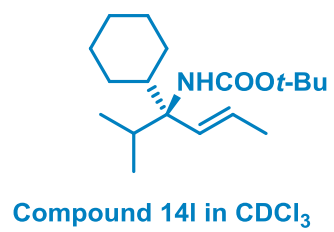
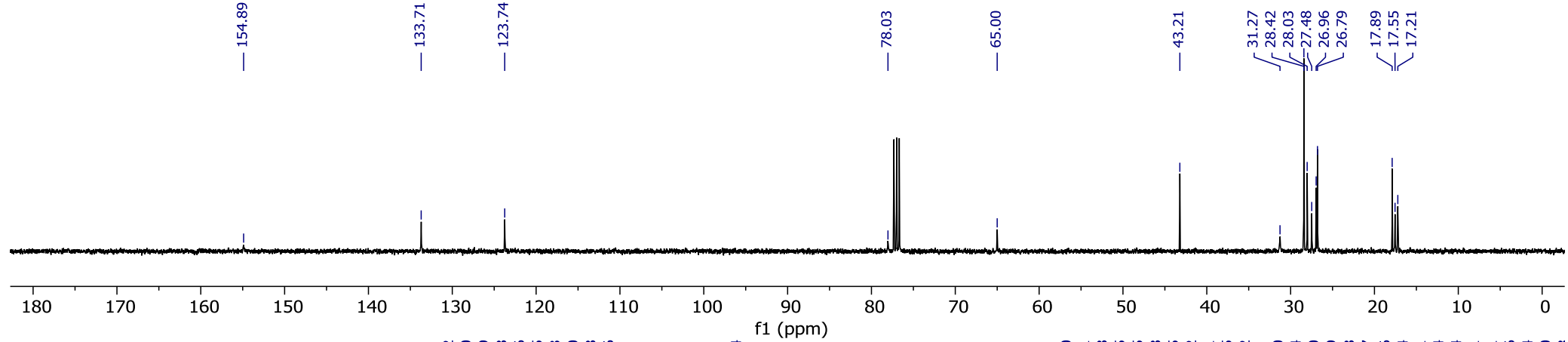


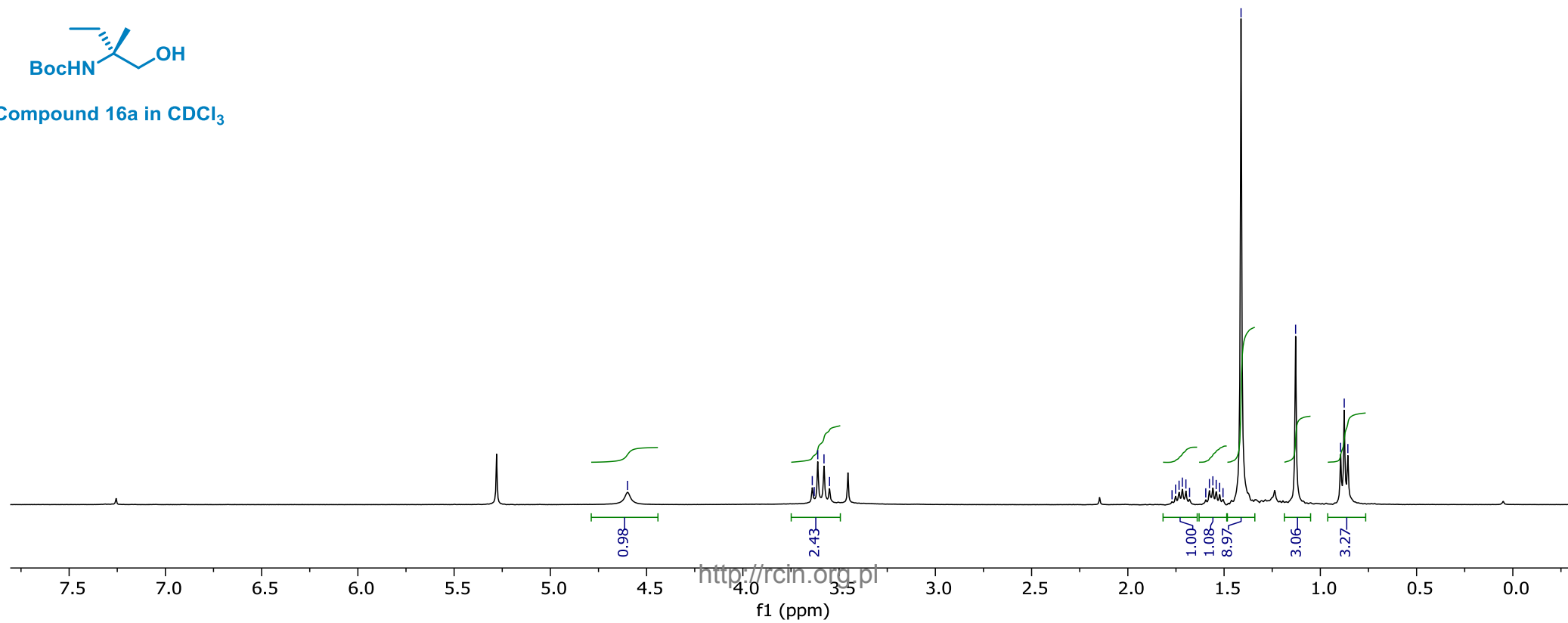
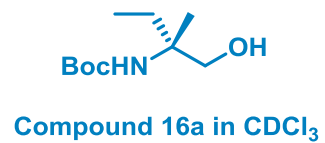
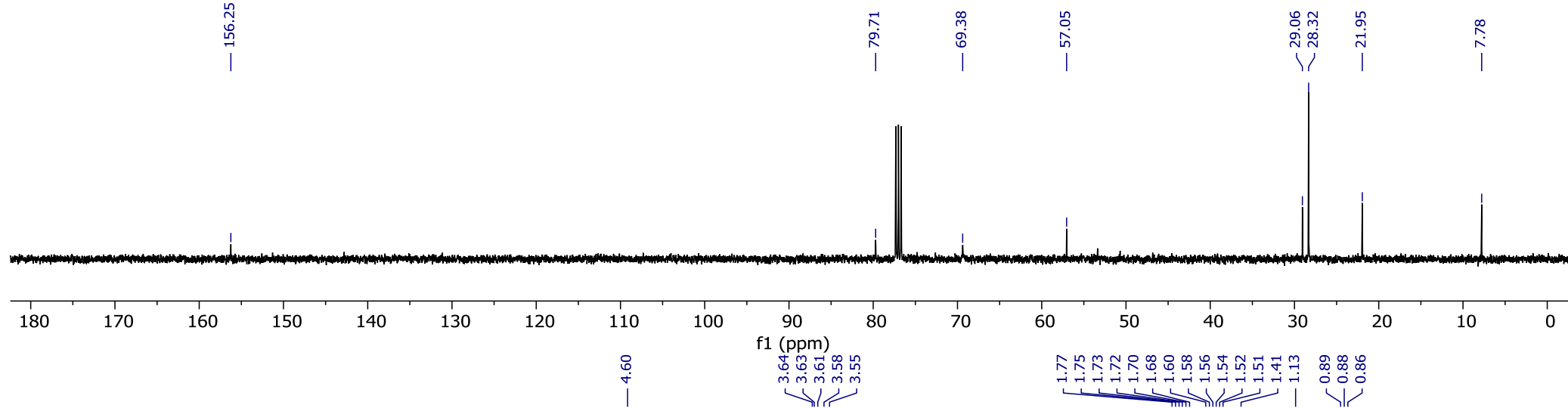


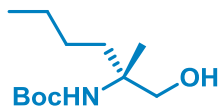
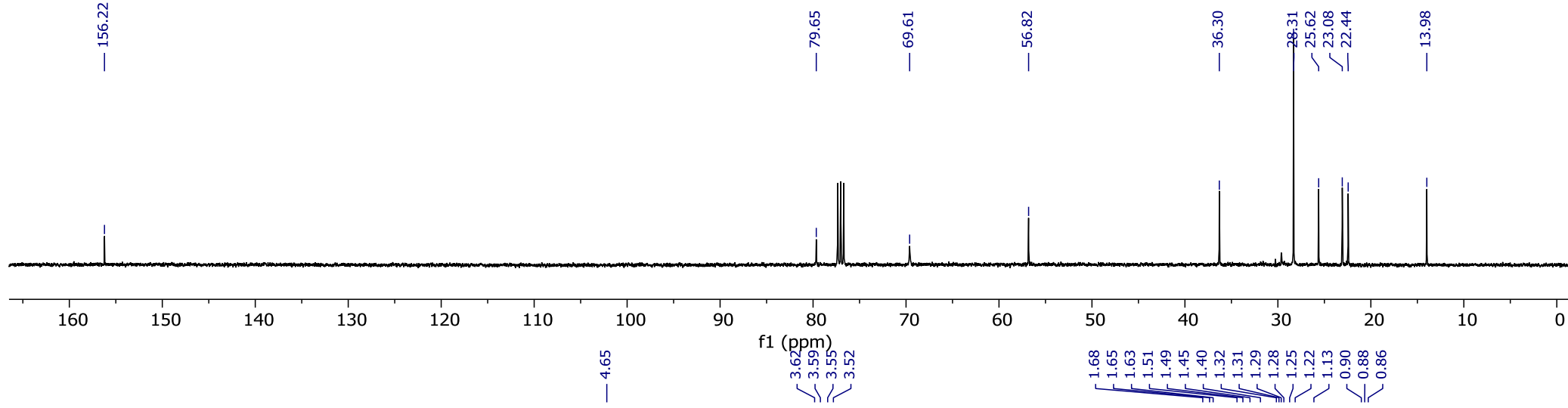




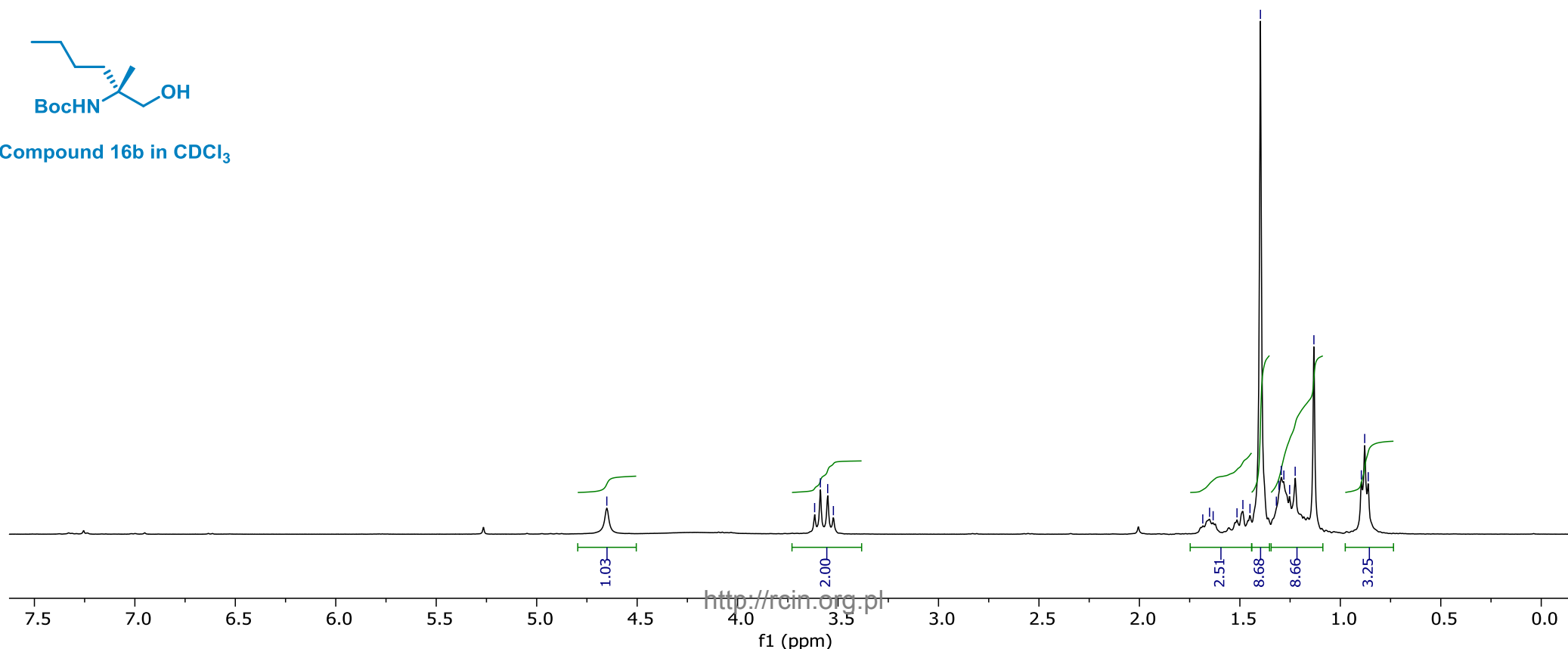


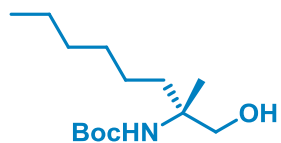
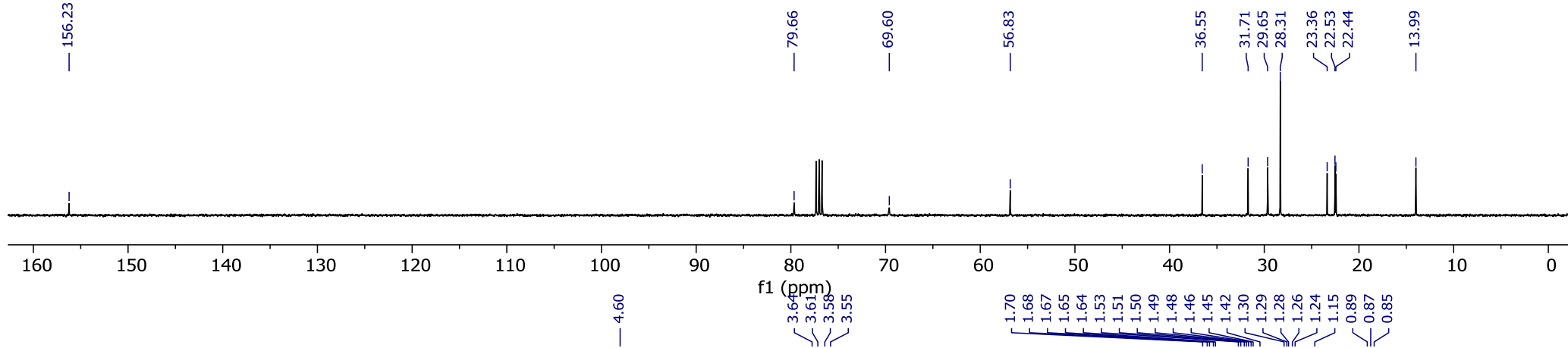




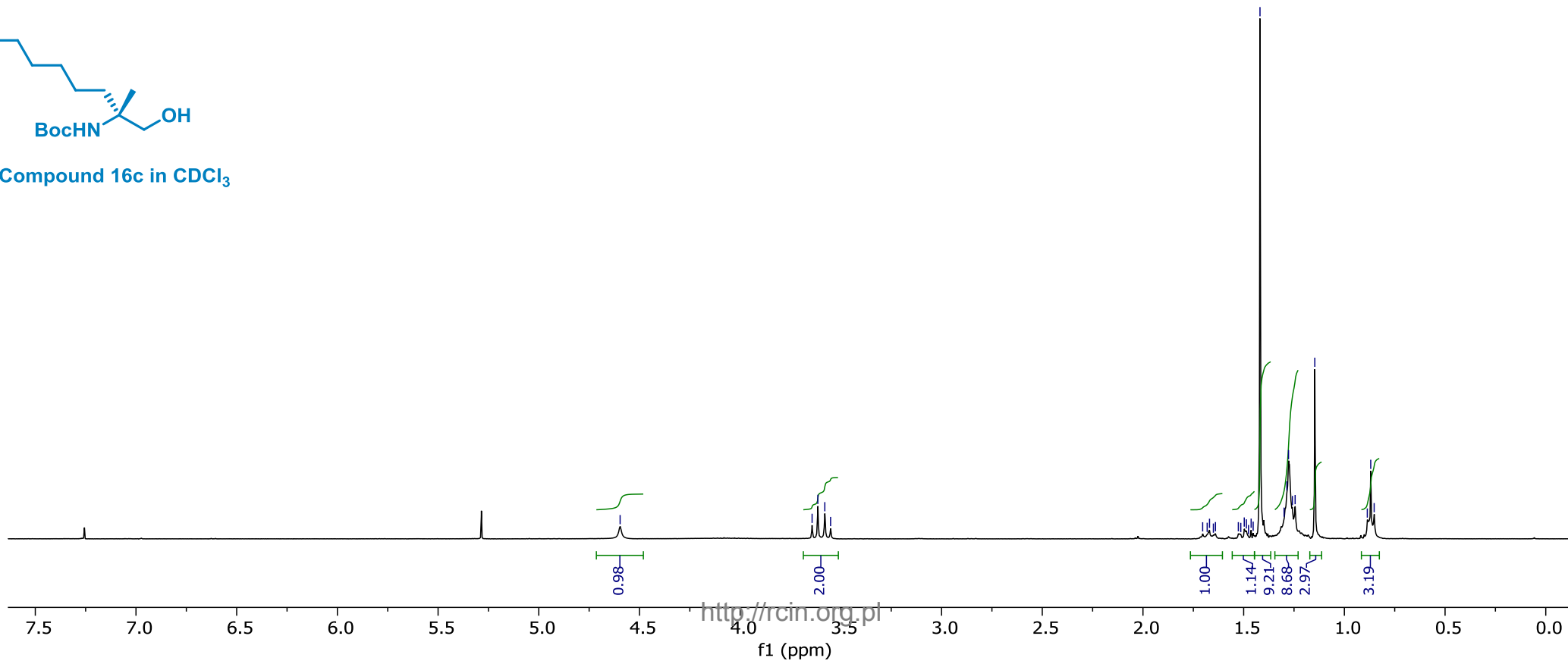


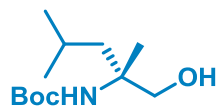
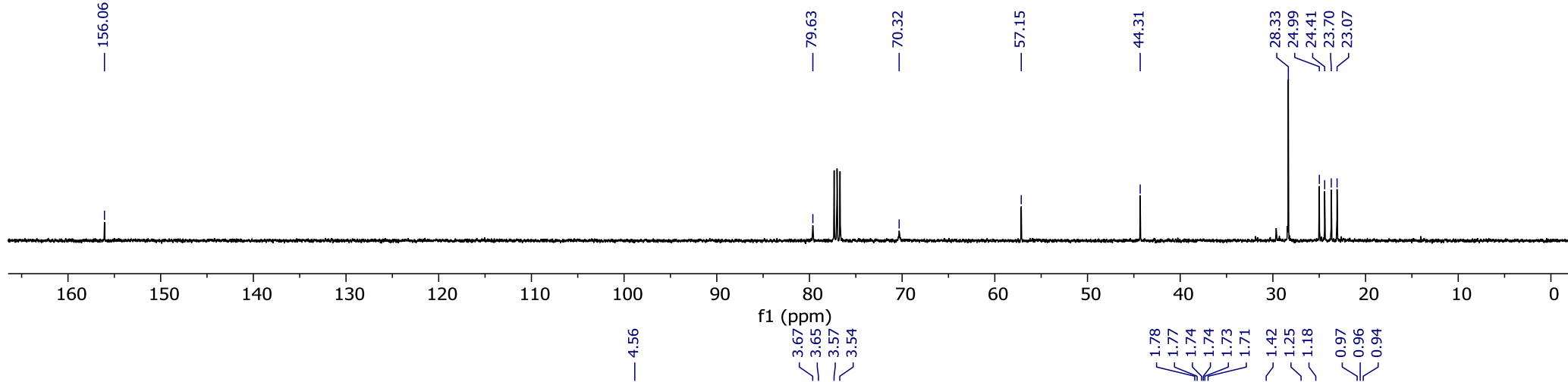
Compound 16b in CDCl<sub>3</sub>



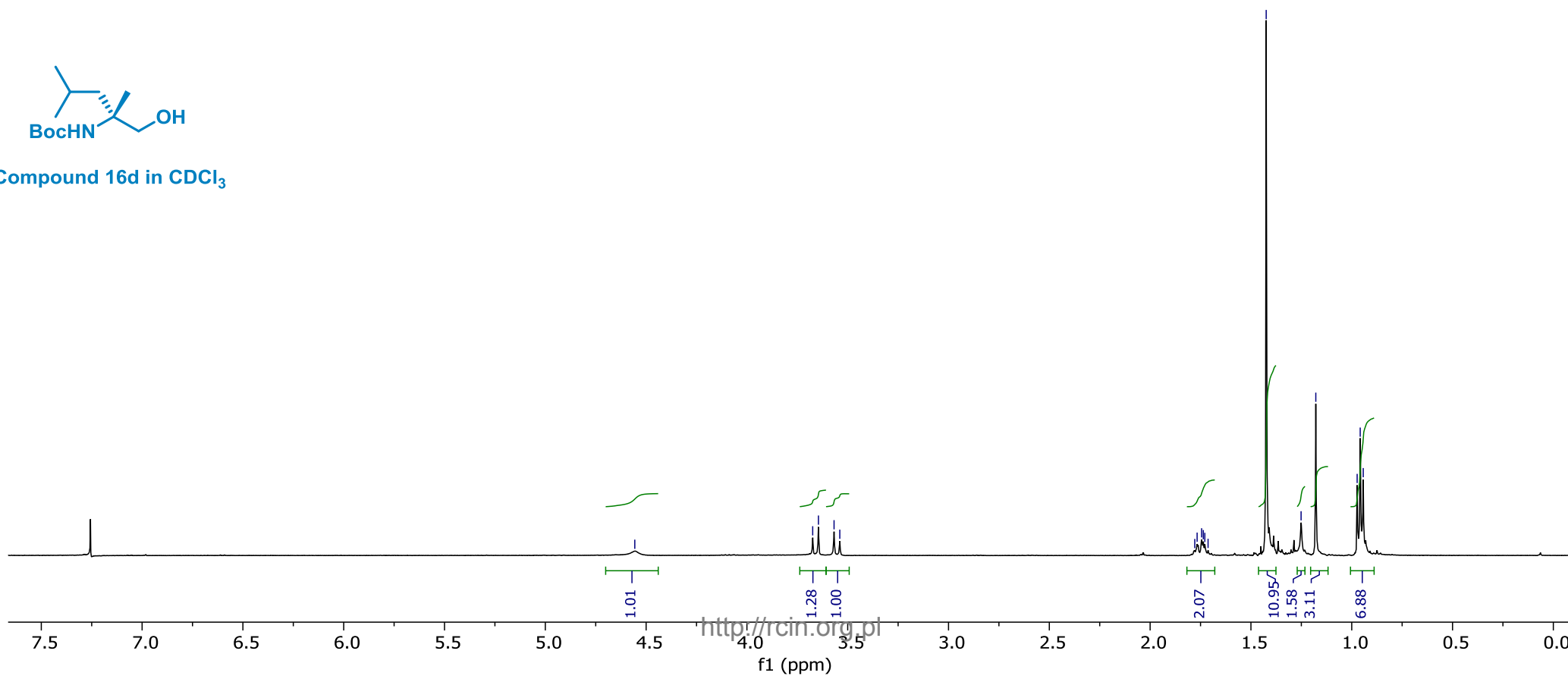


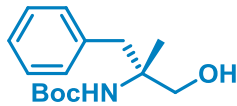
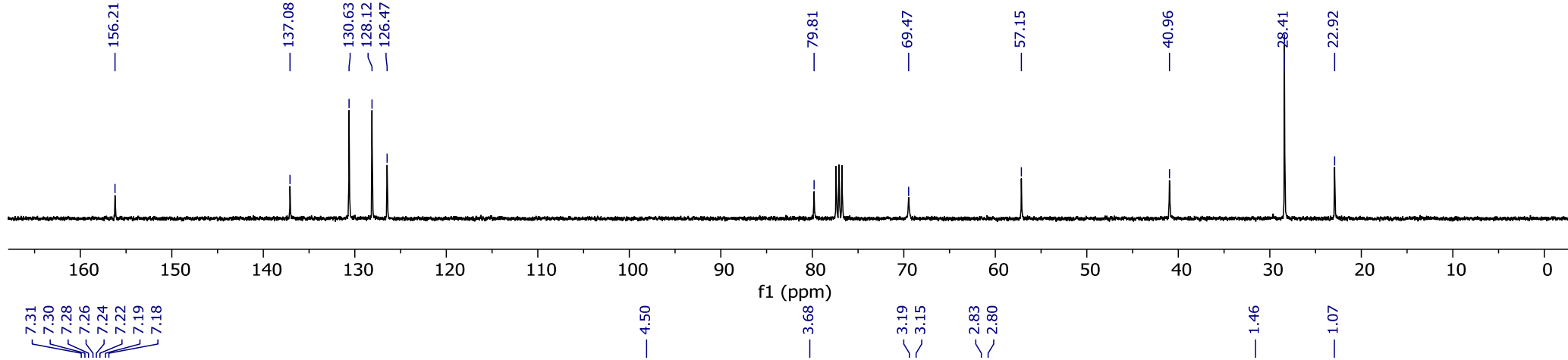
Compound 16c in CDCl<sub>3</sub>



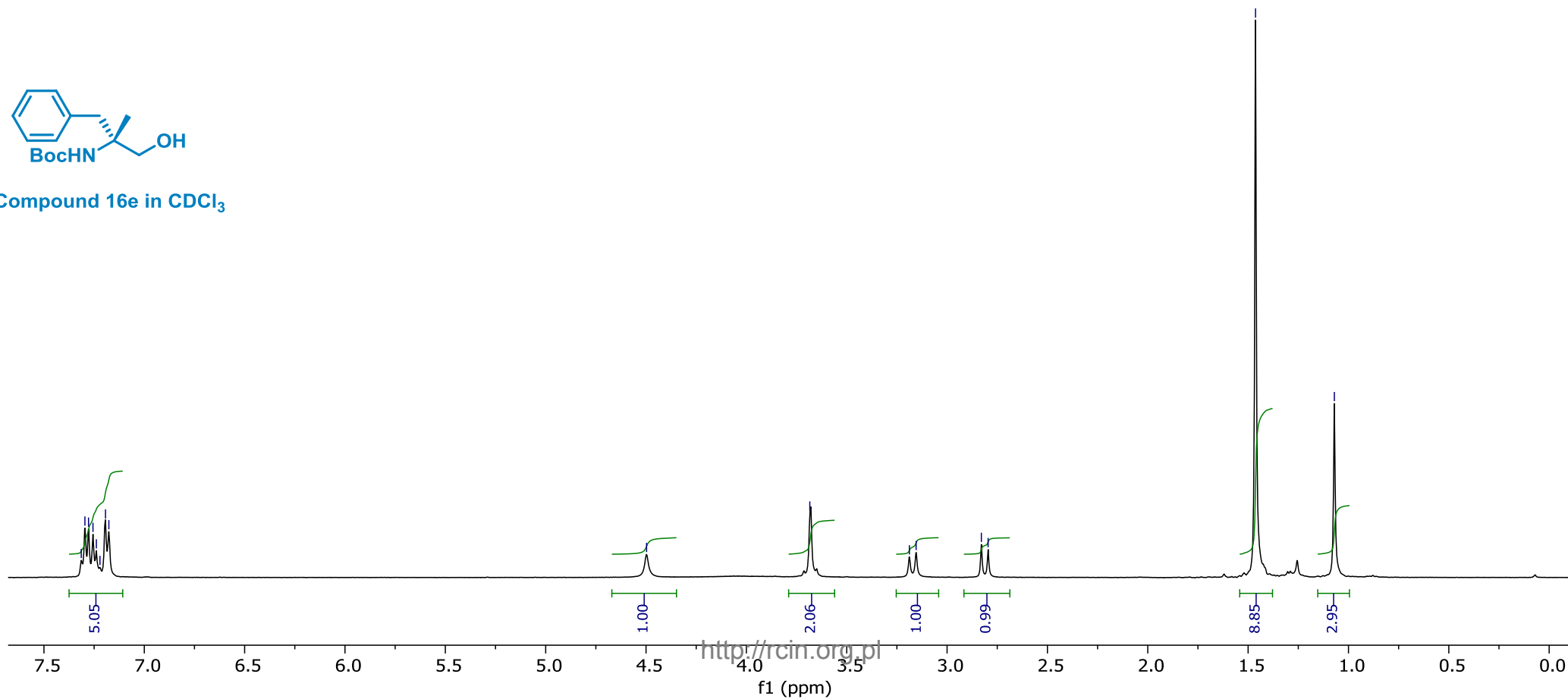


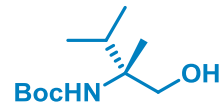
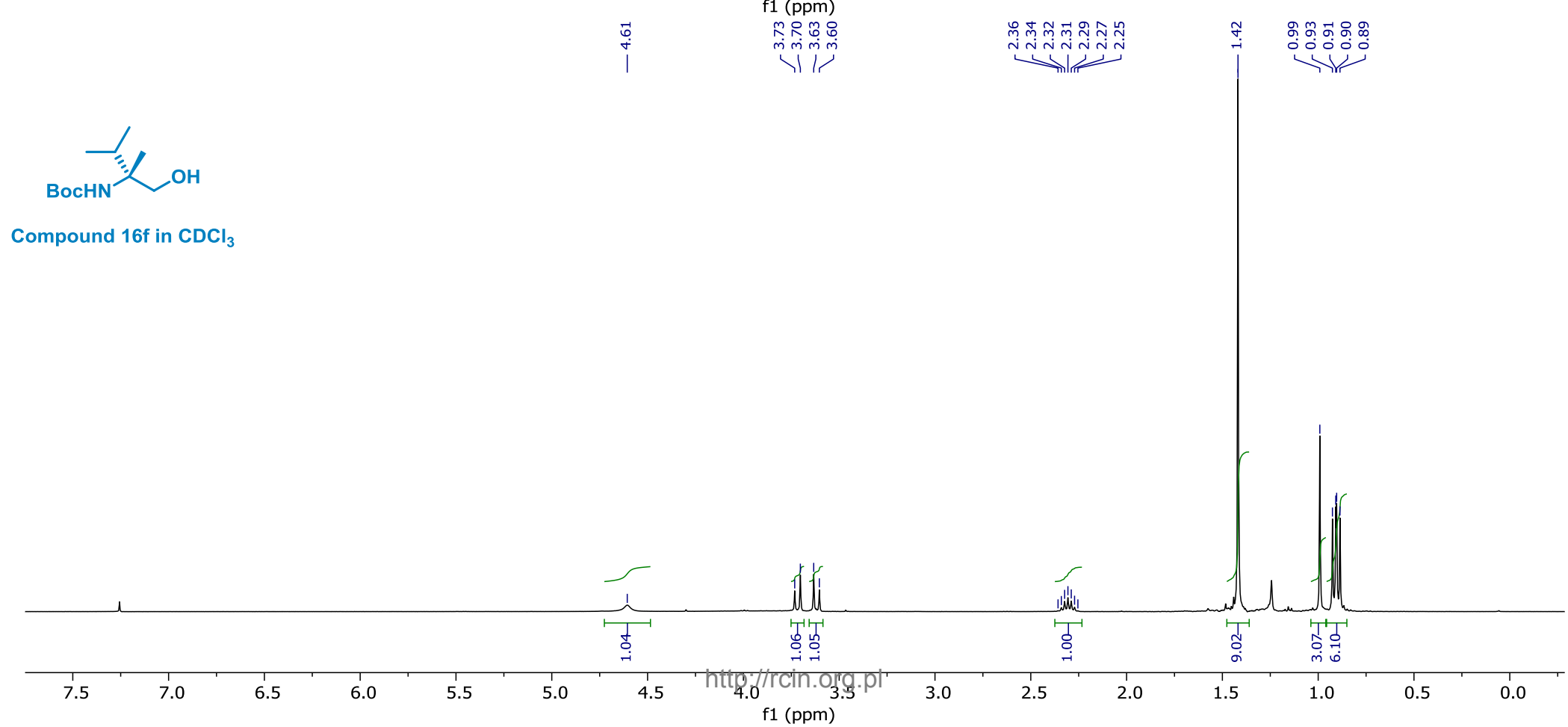
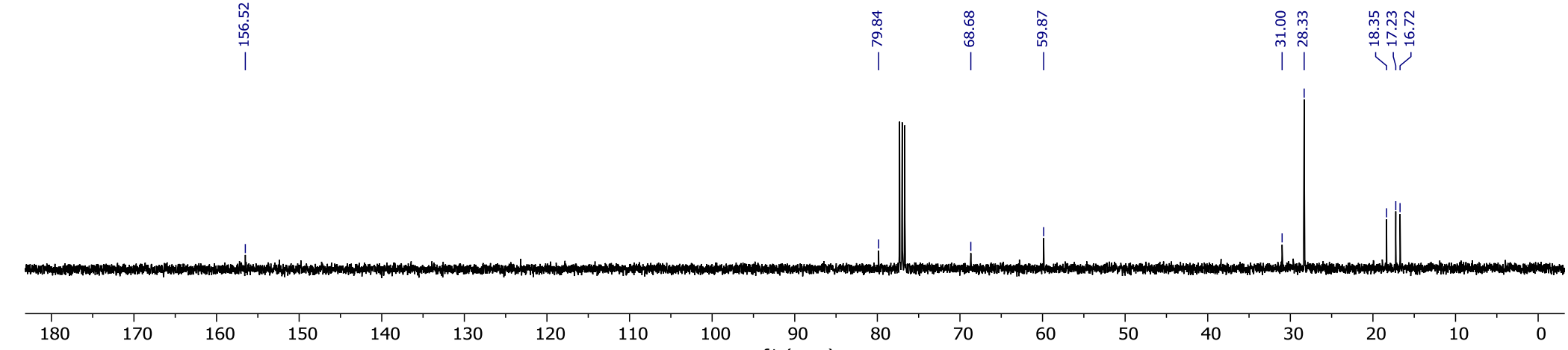
Compound 16d in CDCl<sub>3</sub>



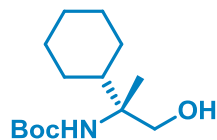
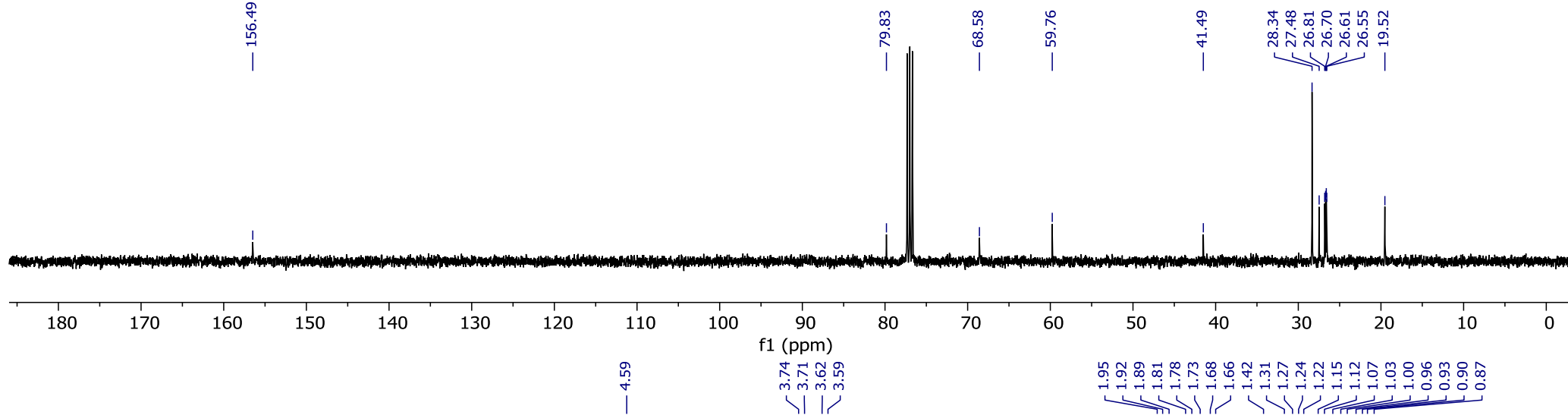


Compound 16e in CDCl<sub>3</sub>

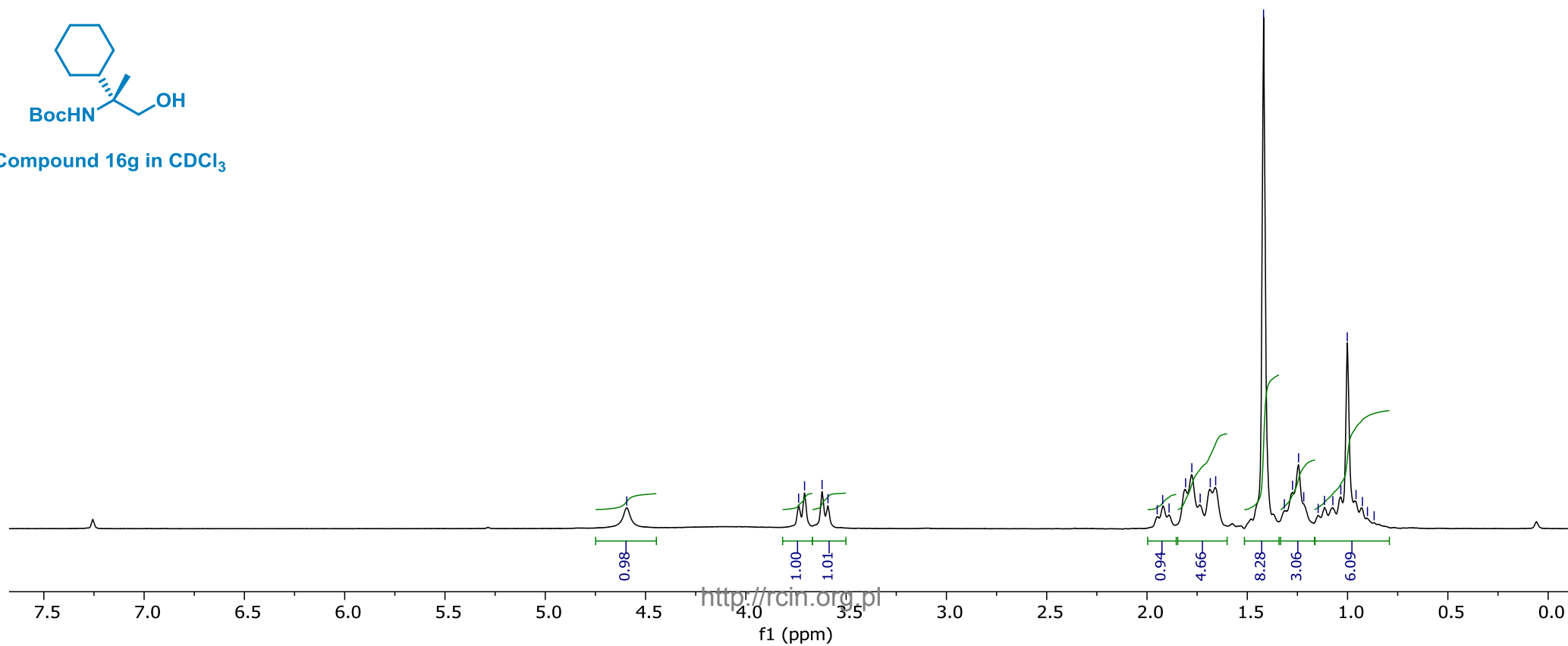




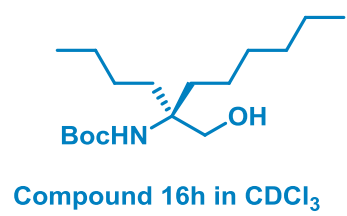
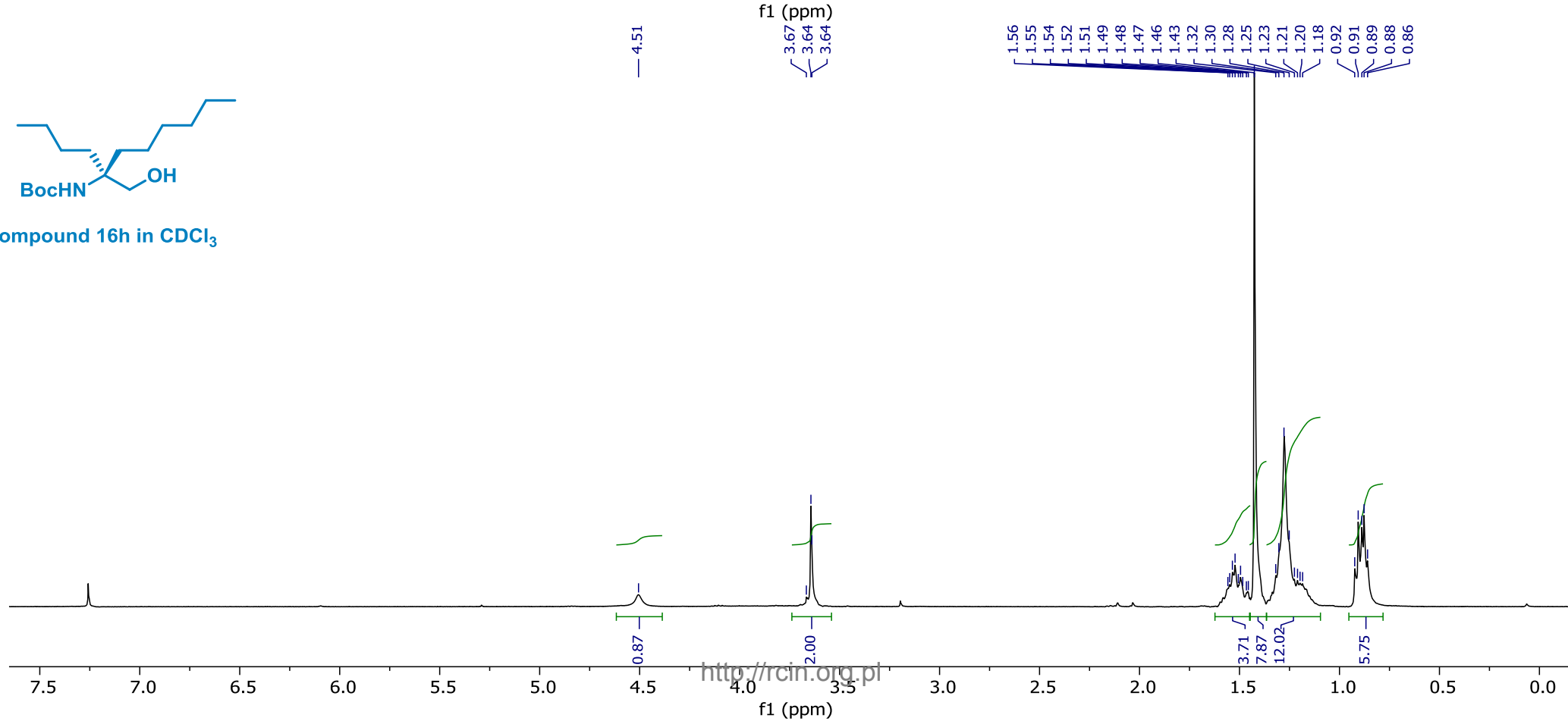
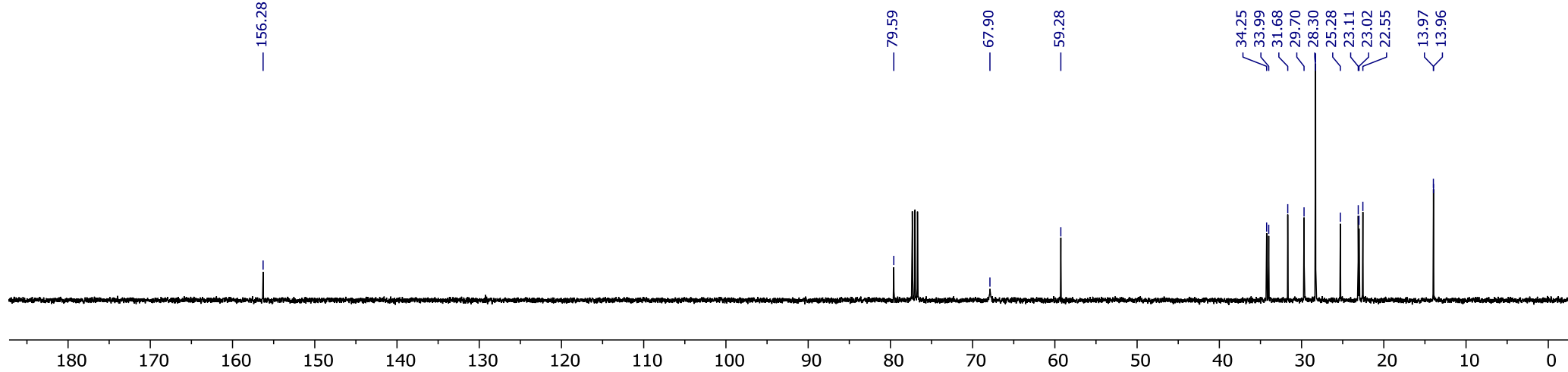
Compound 16f in CDCl<sub>3</sub>

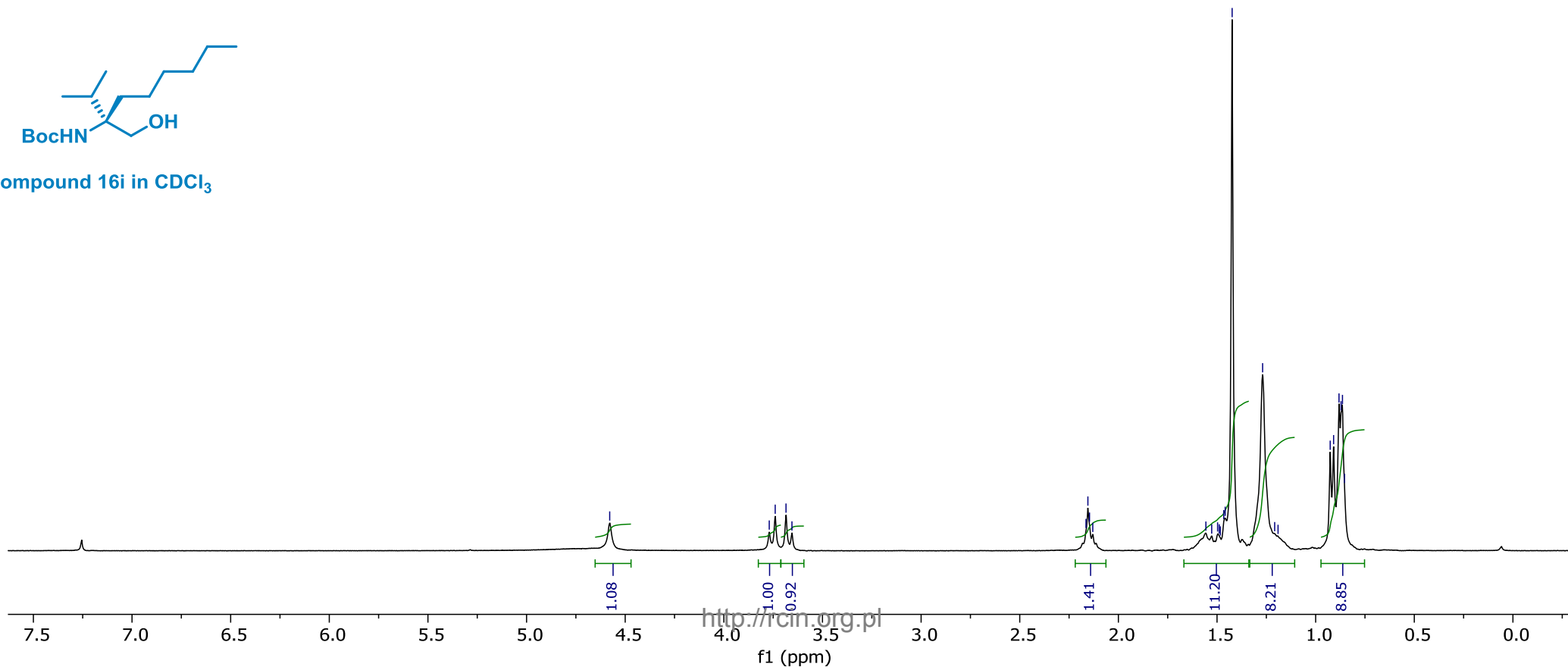
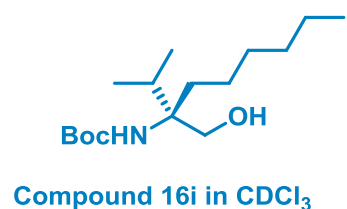
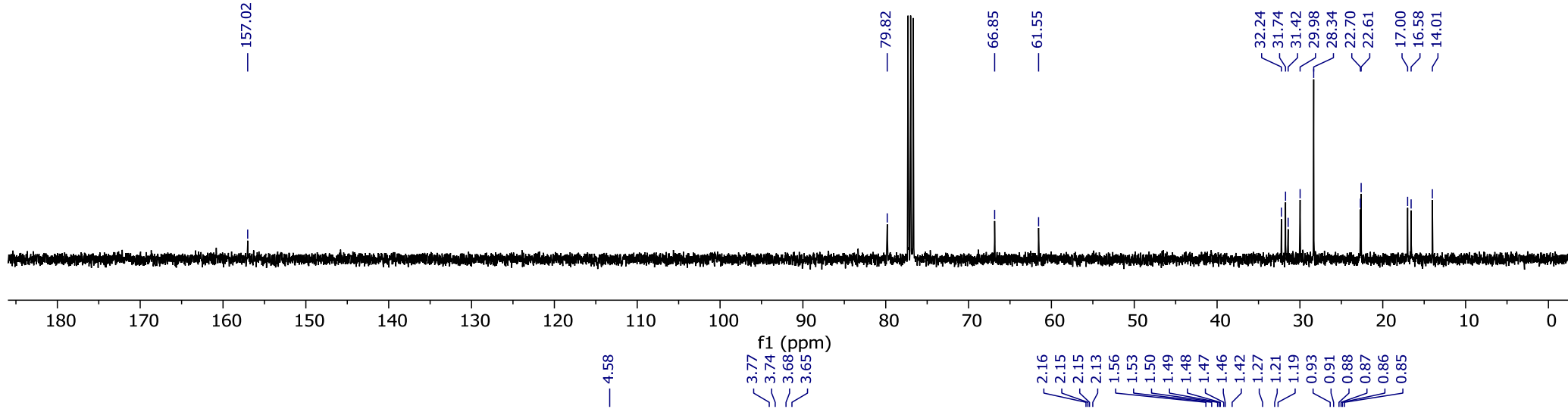


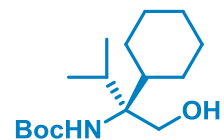
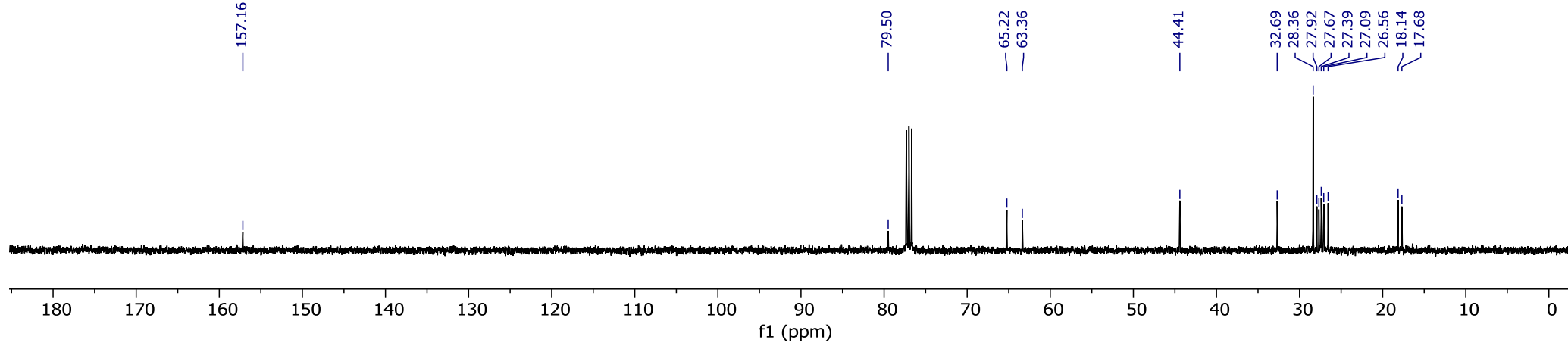
Compound 16g in CDCl<sub>3</sub>



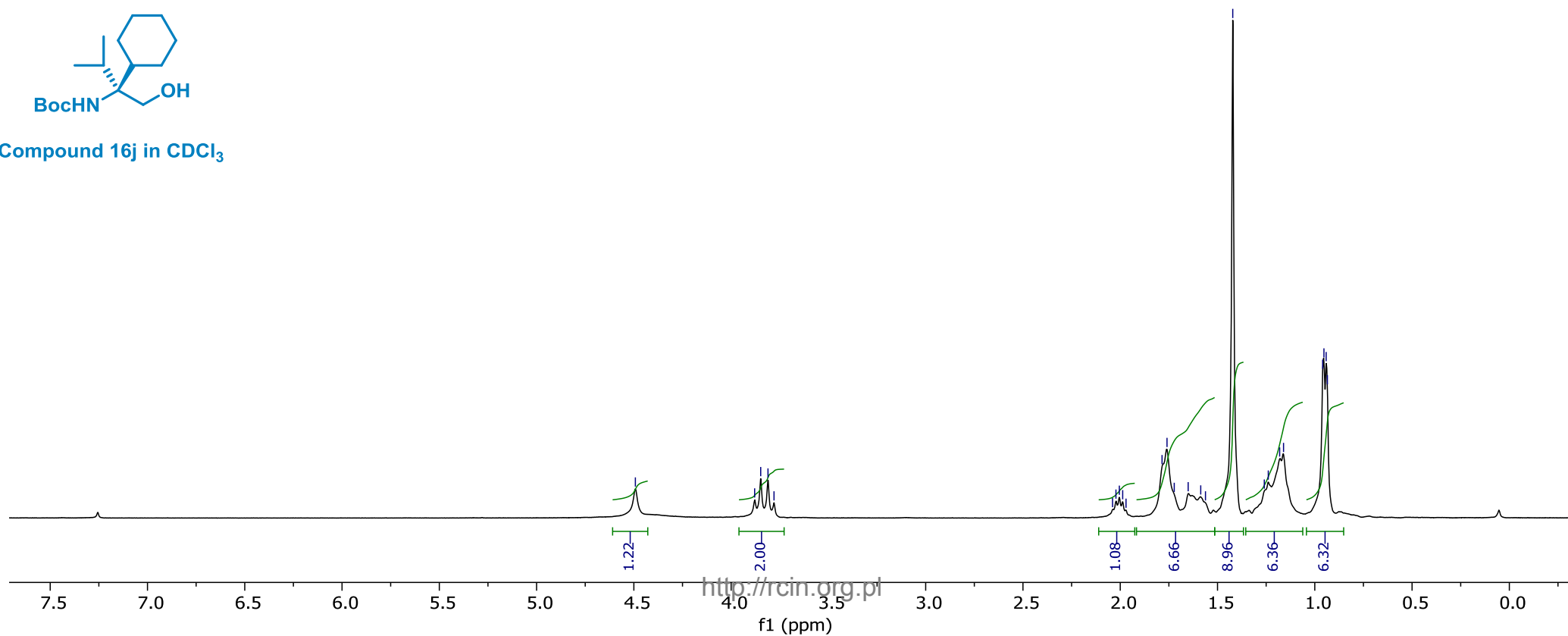


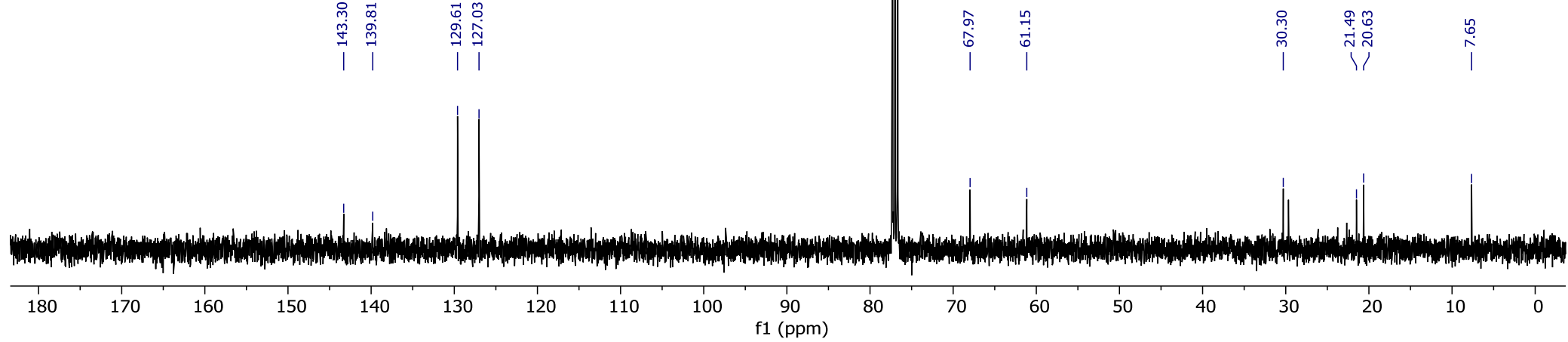




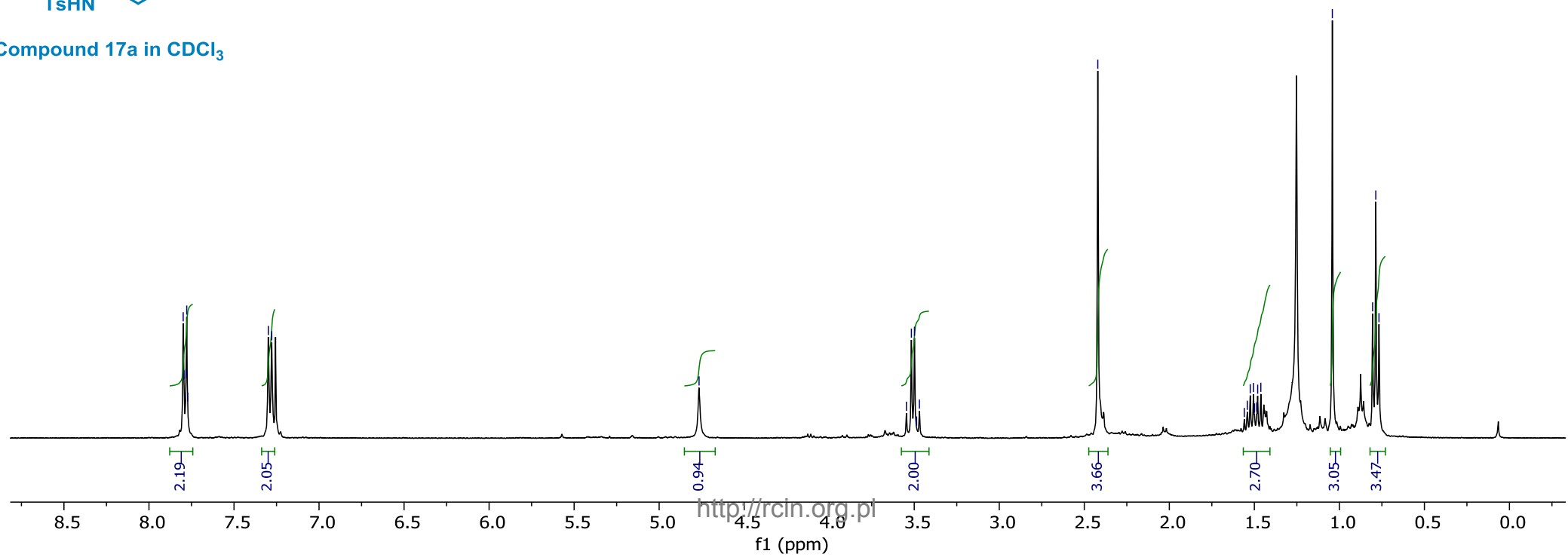


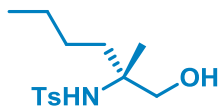
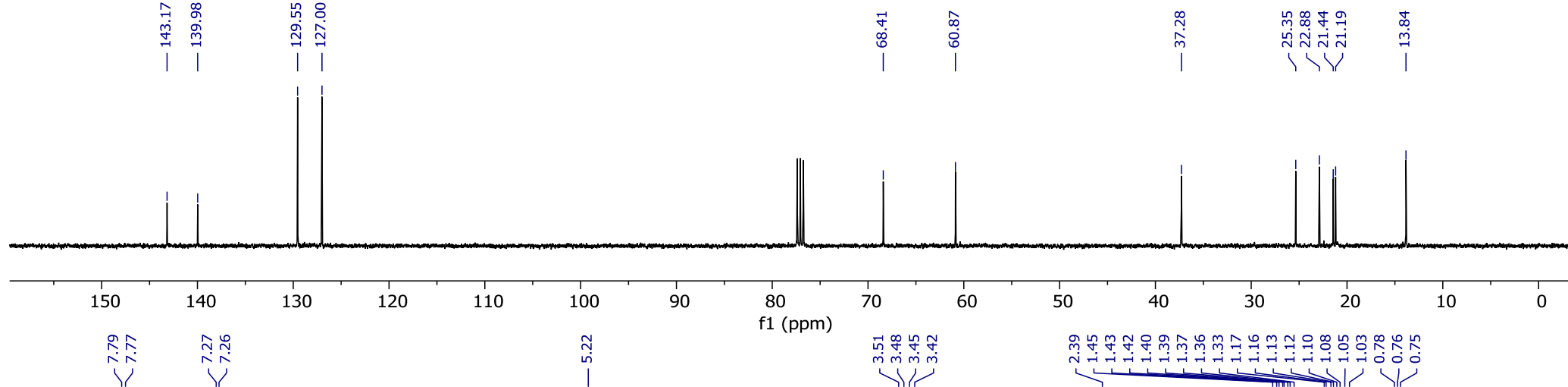
Compound 16j in CDCl<sub>3</sub>



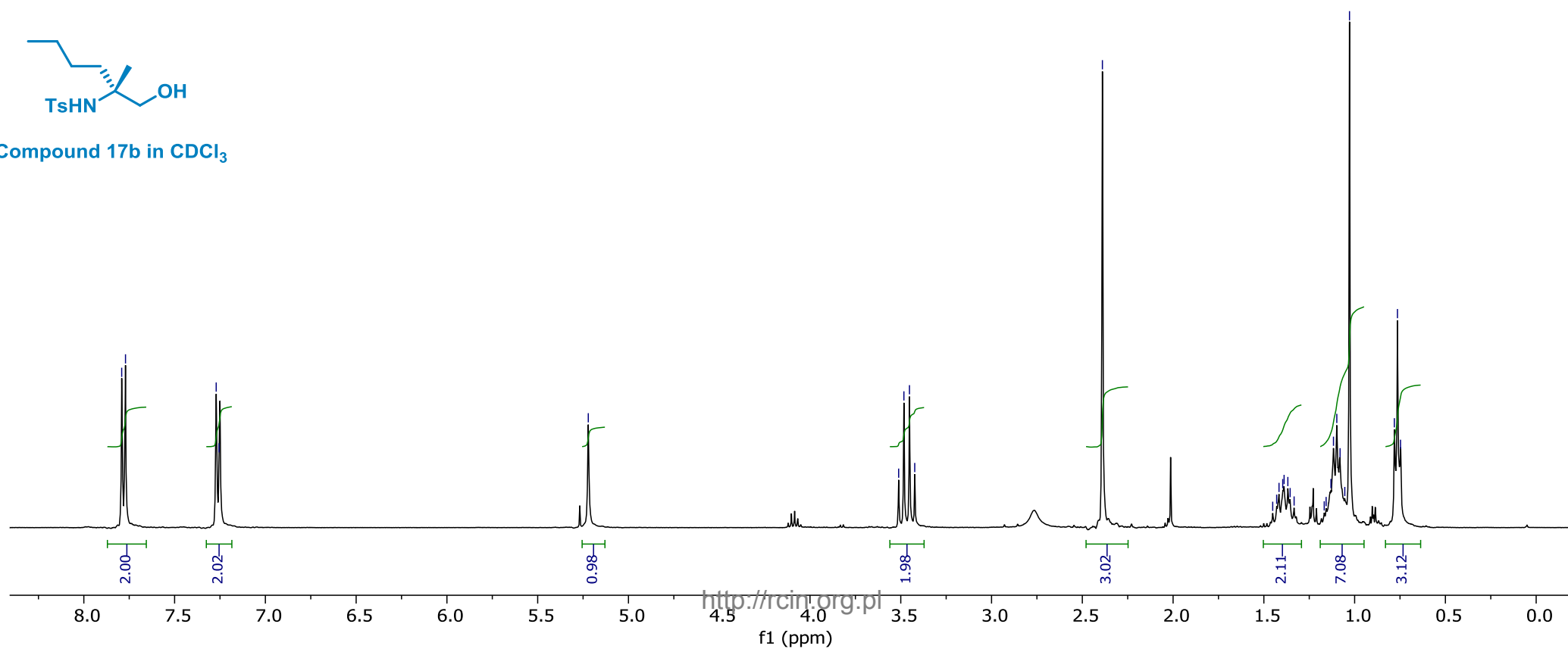


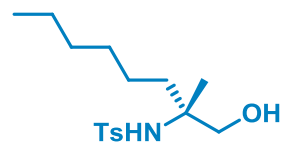
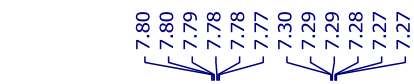
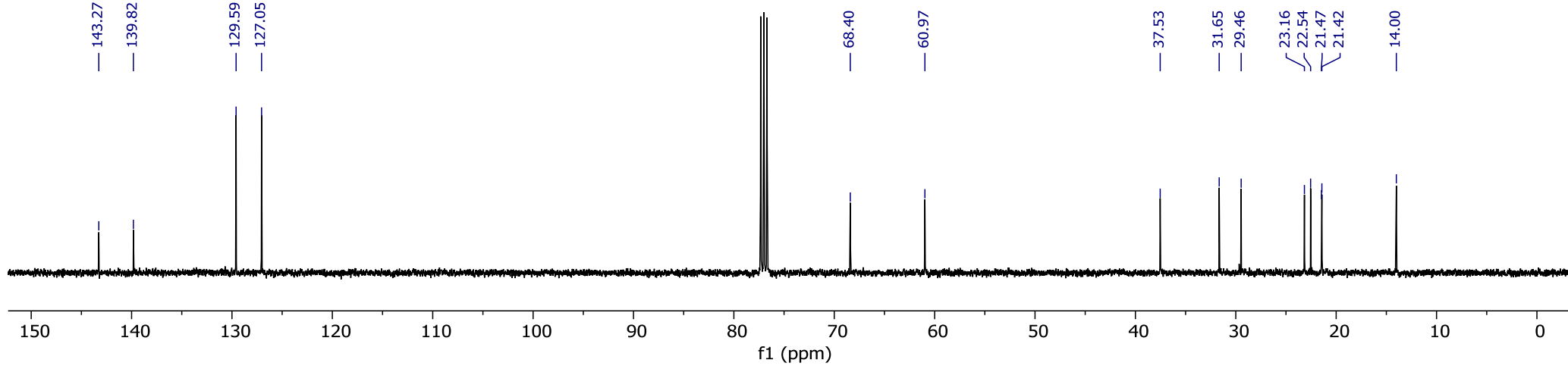
Compound 17a in CDCl<sub>3</sub>



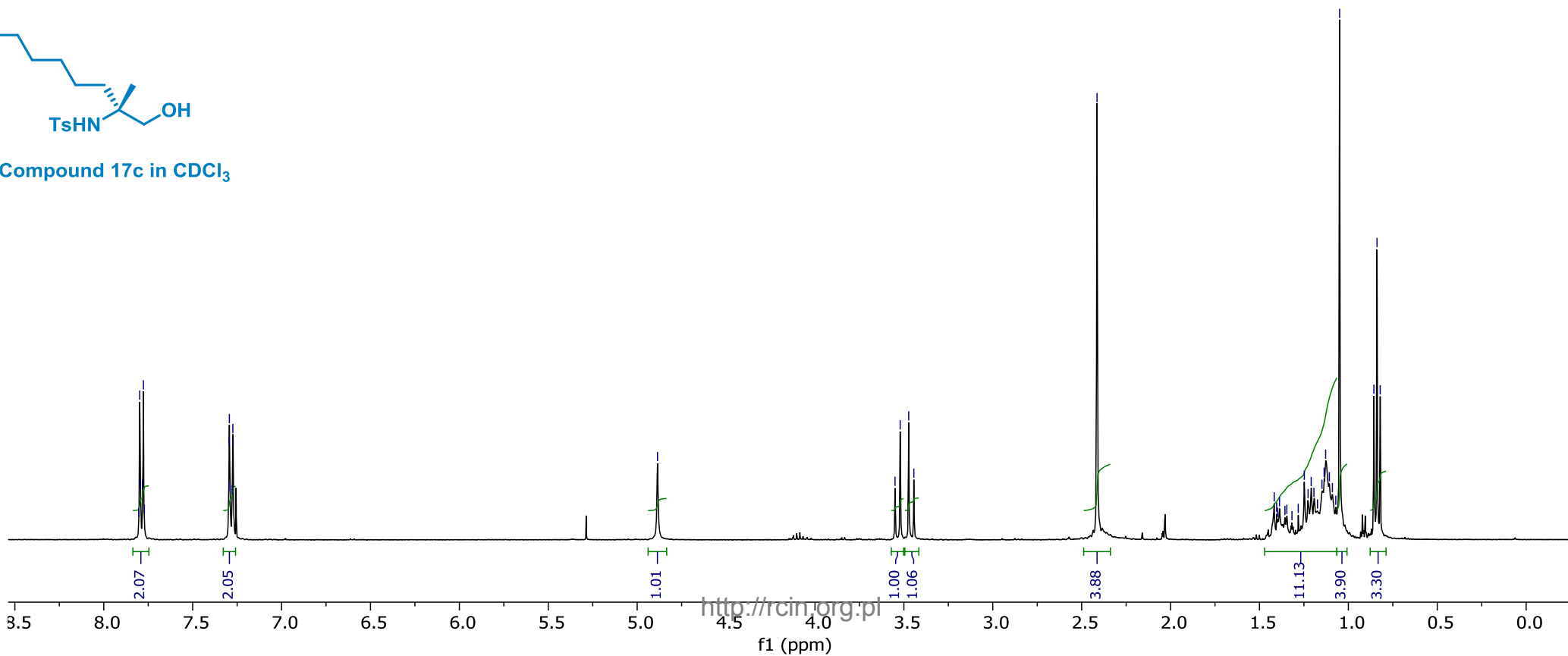


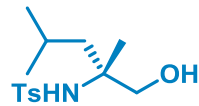
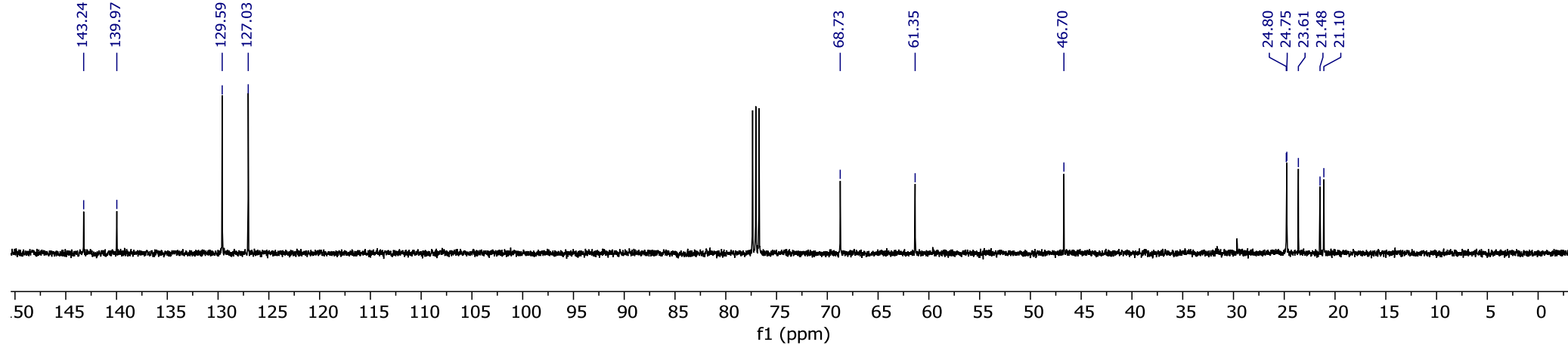
Compound 17b in CDCl<sub>3</sub>



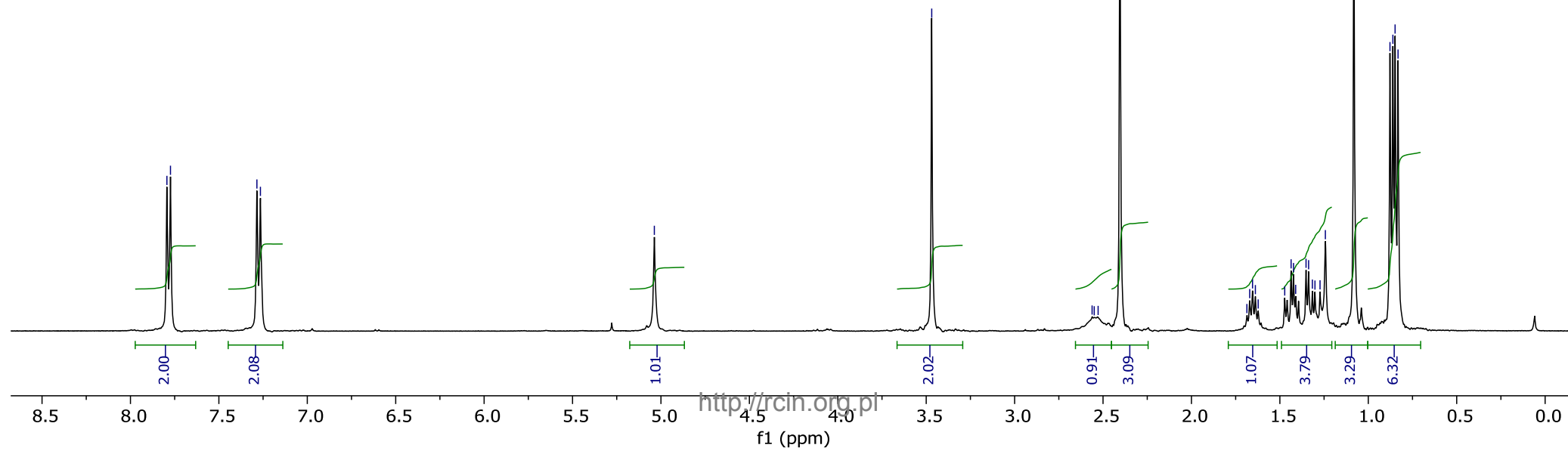


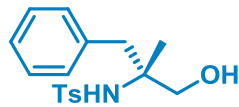
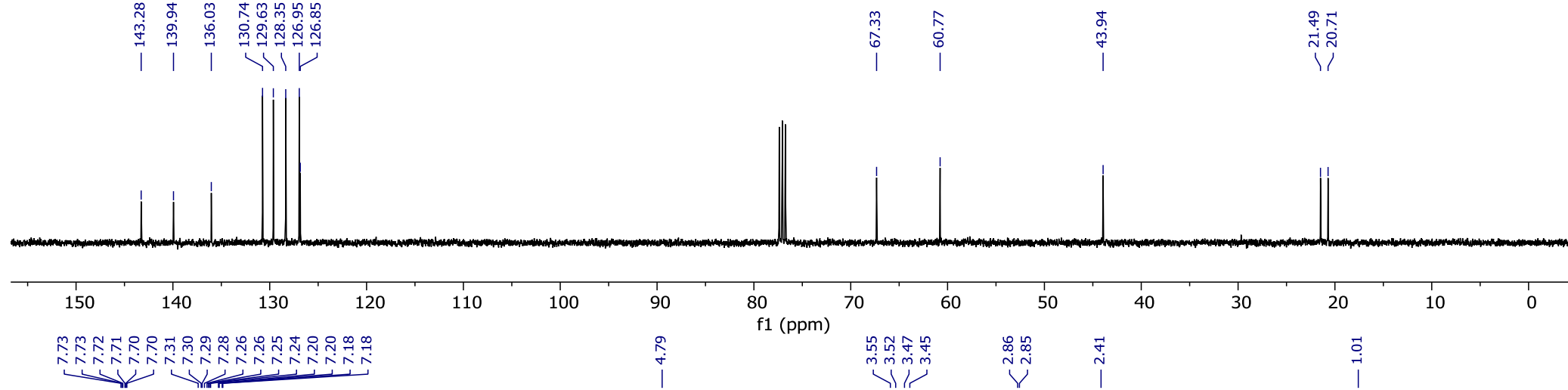
Compound 17c in CDCl<sub>3</sub>



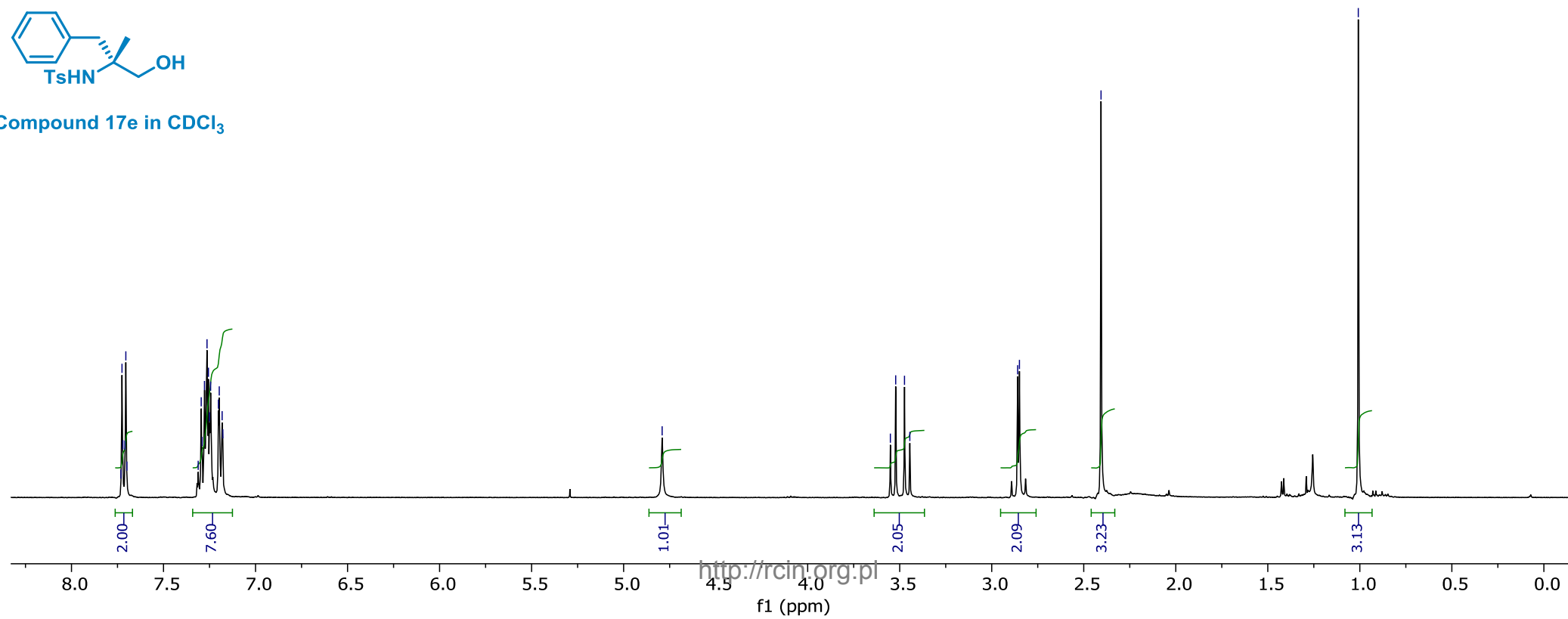


Compound 17d in CDCl<sub>3</sub>

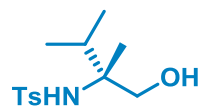
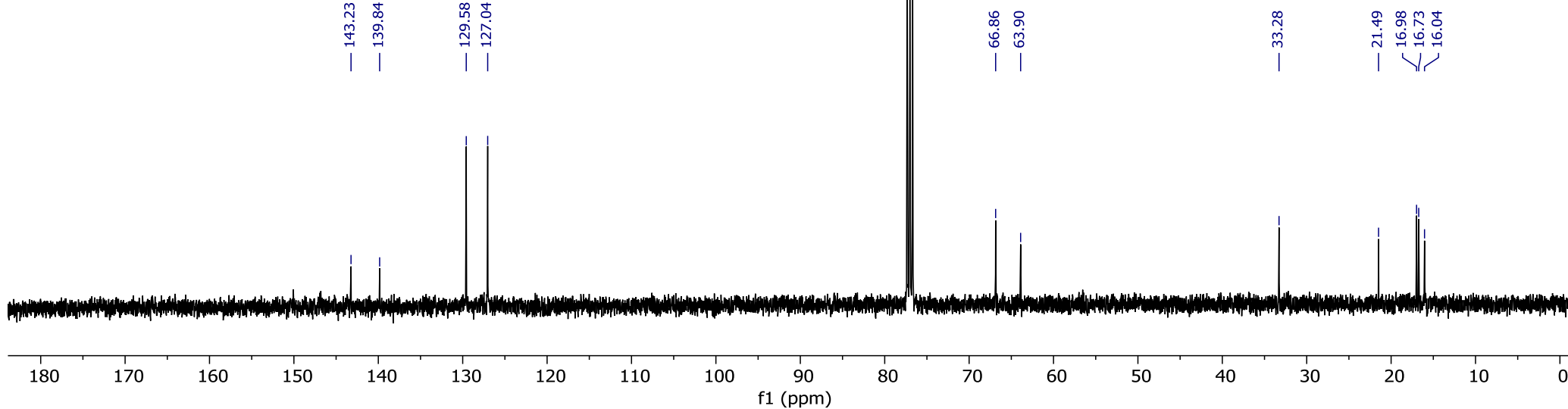




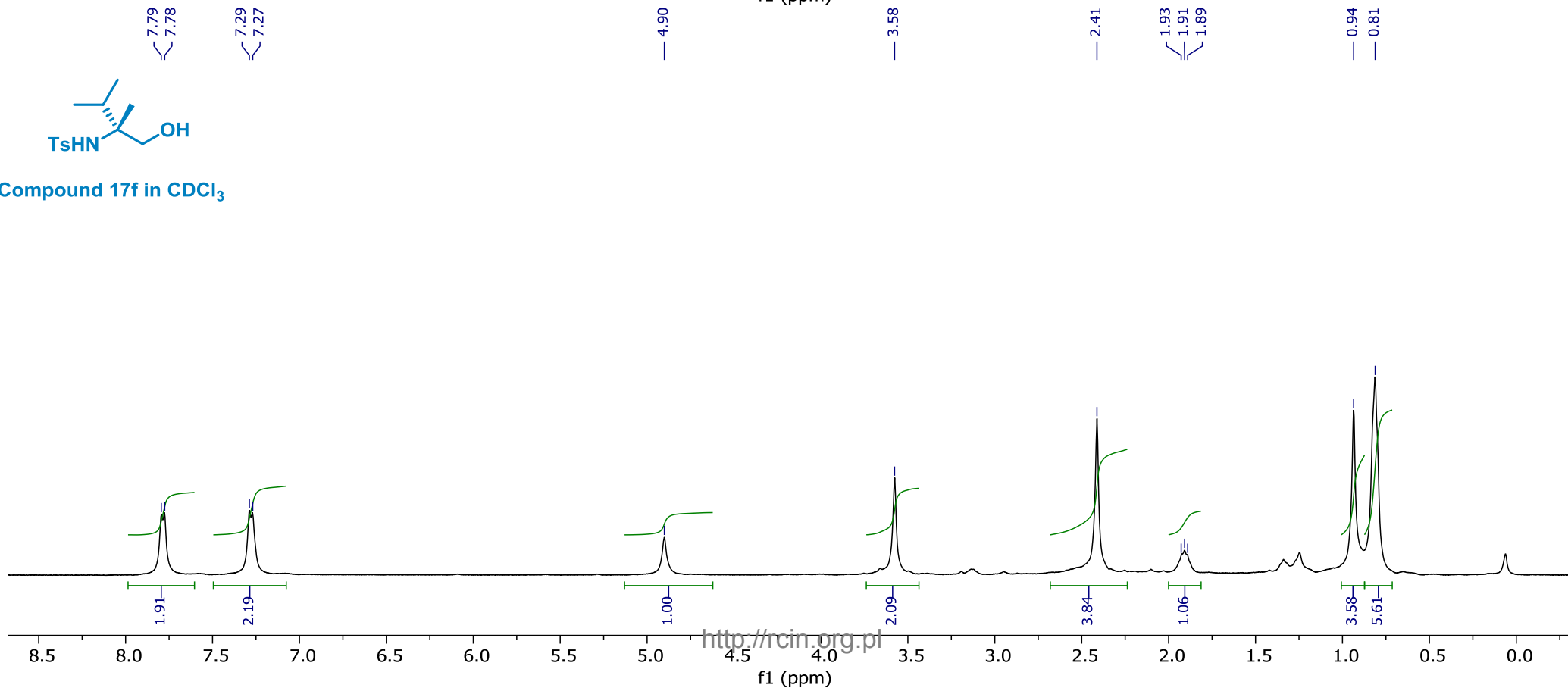
Compound 17e in CDCl<sub>3</sub>

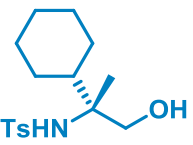
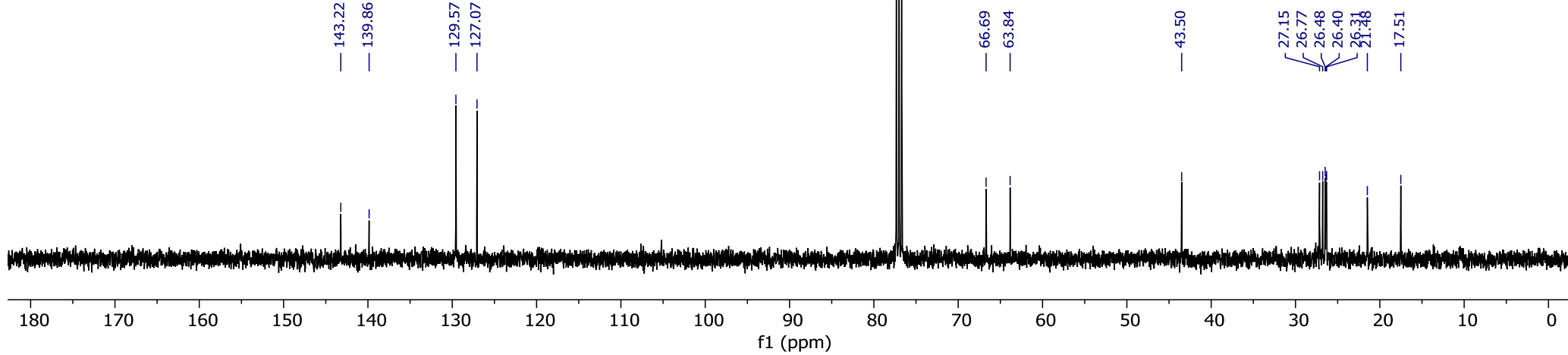




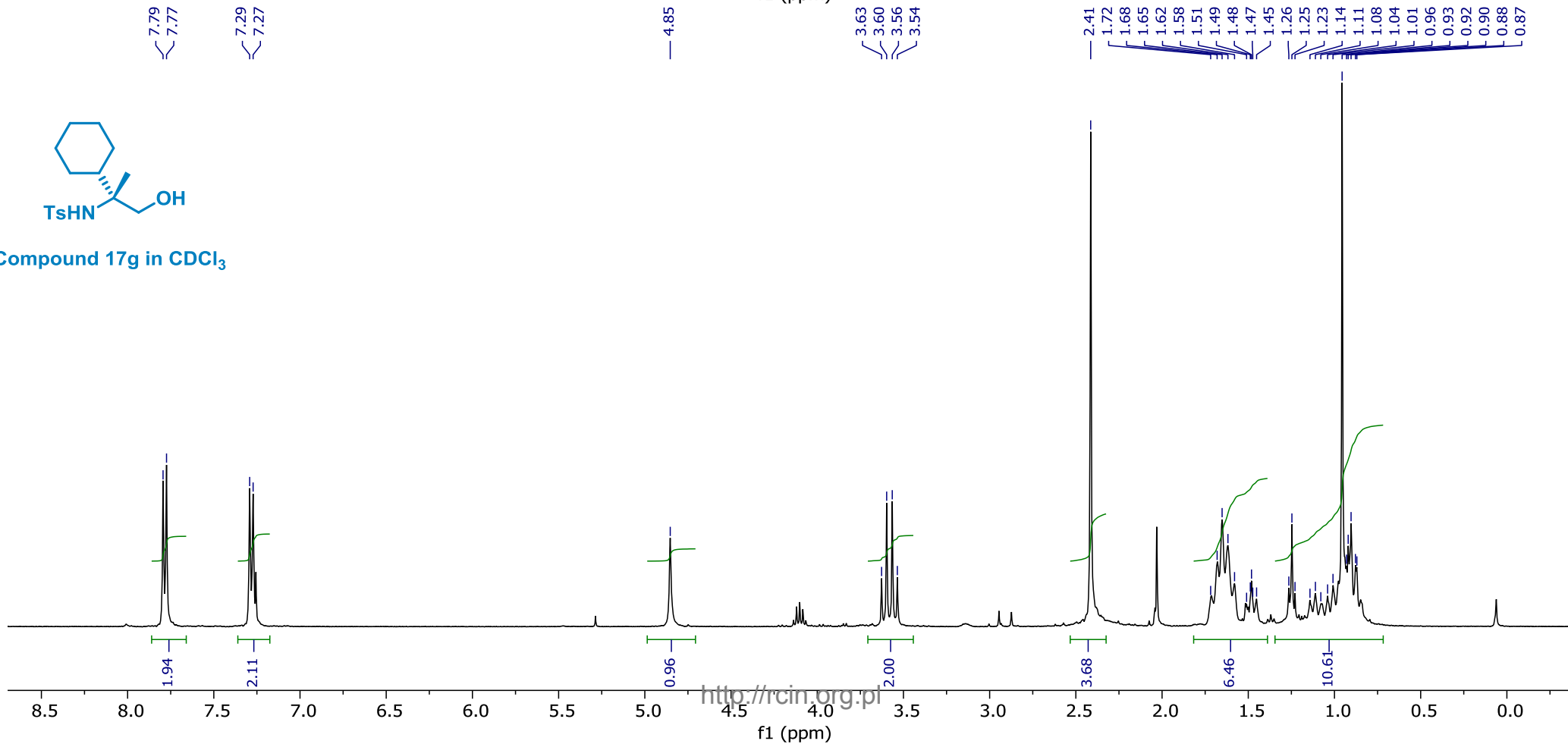


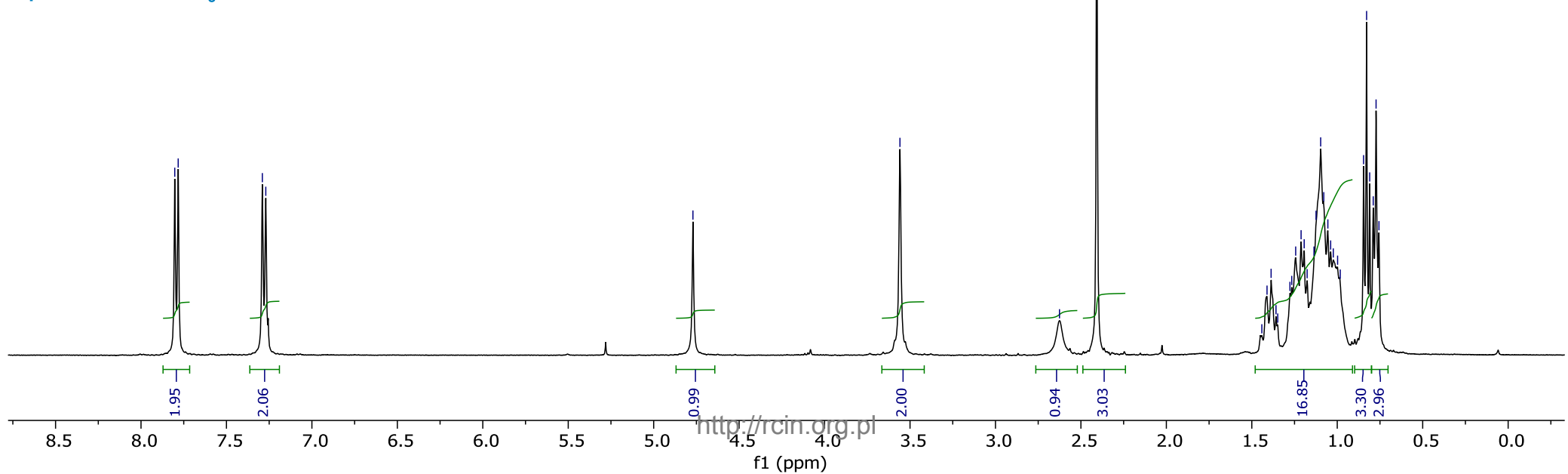
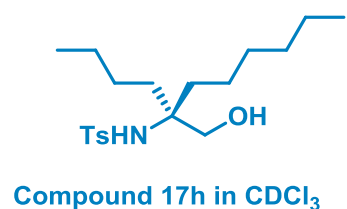
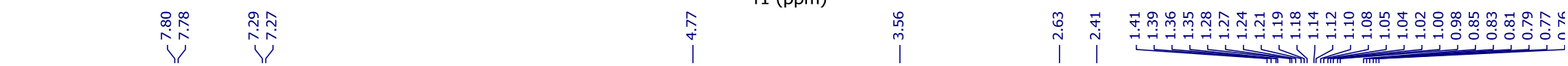
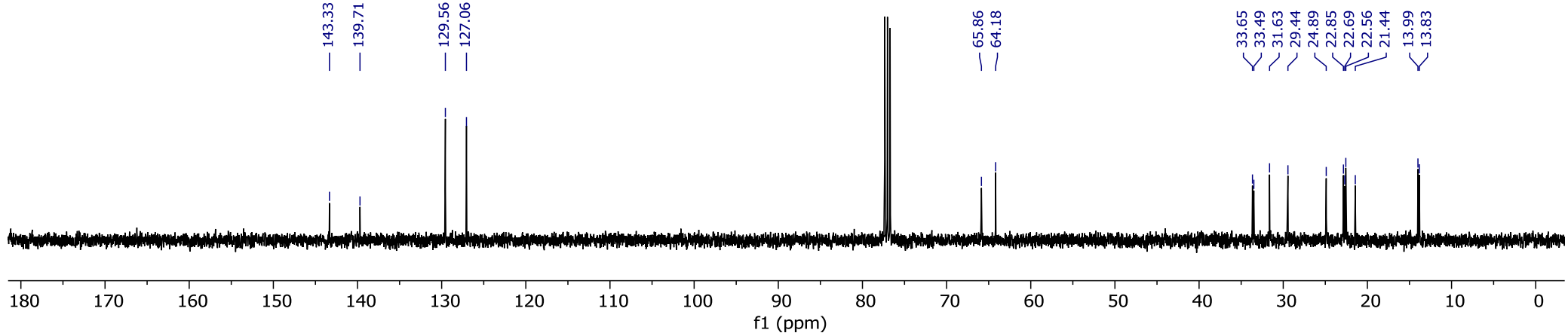
Compound 17f in CDCl<sub>3</sub>

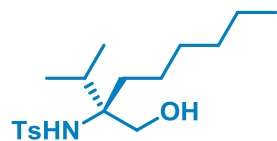
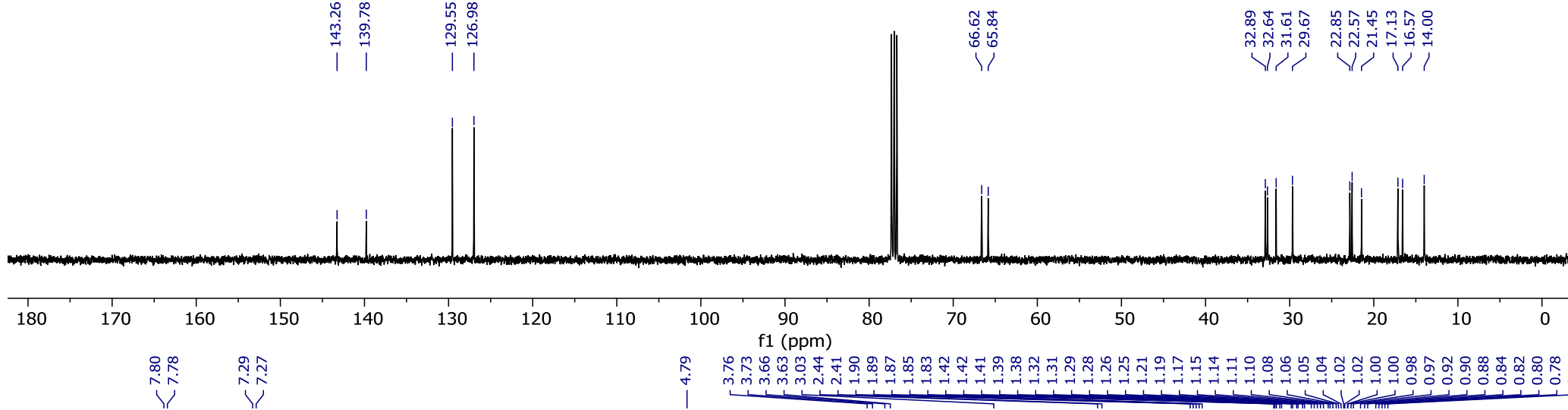




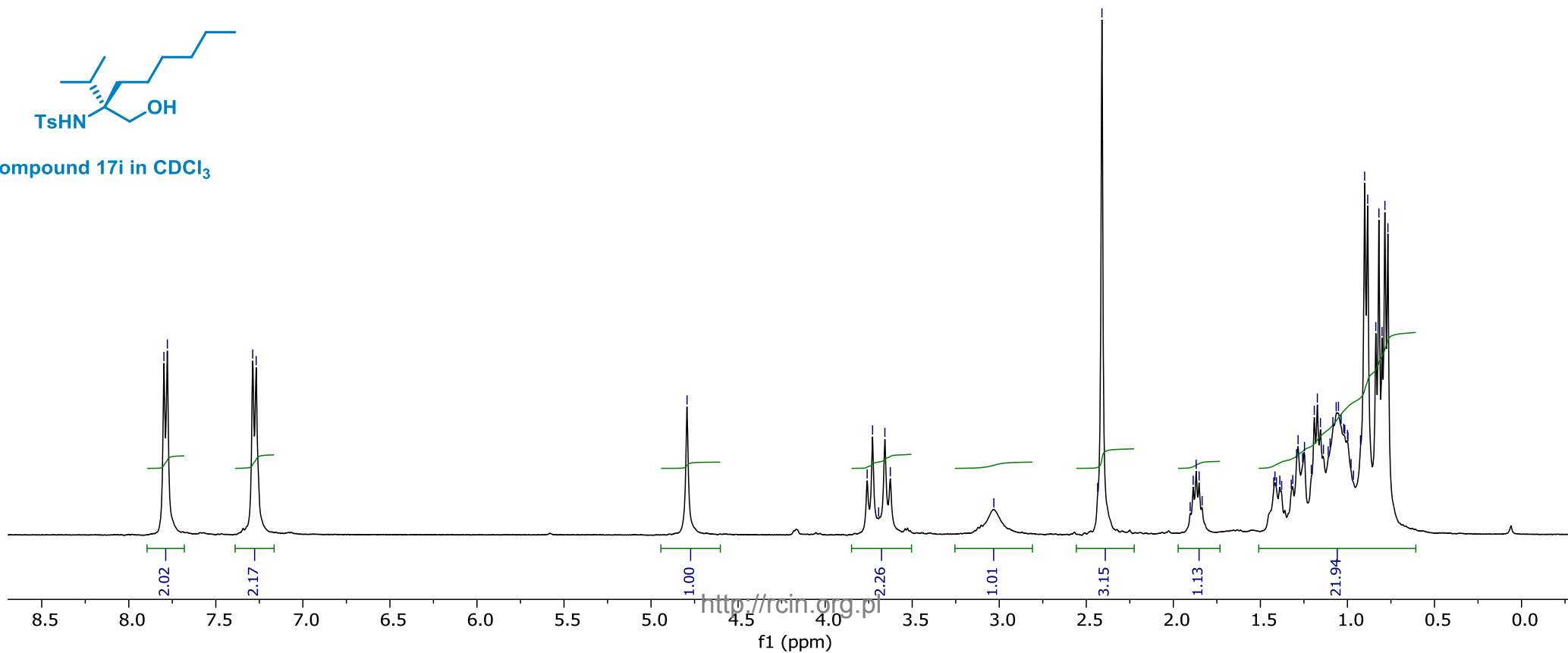
Compound 17g in CDCl<sub>3</sub>

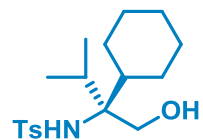
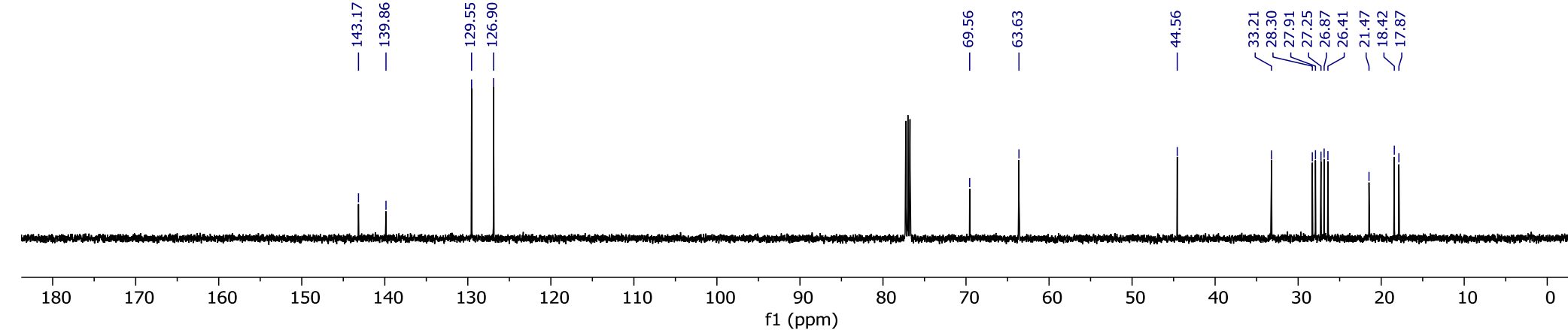




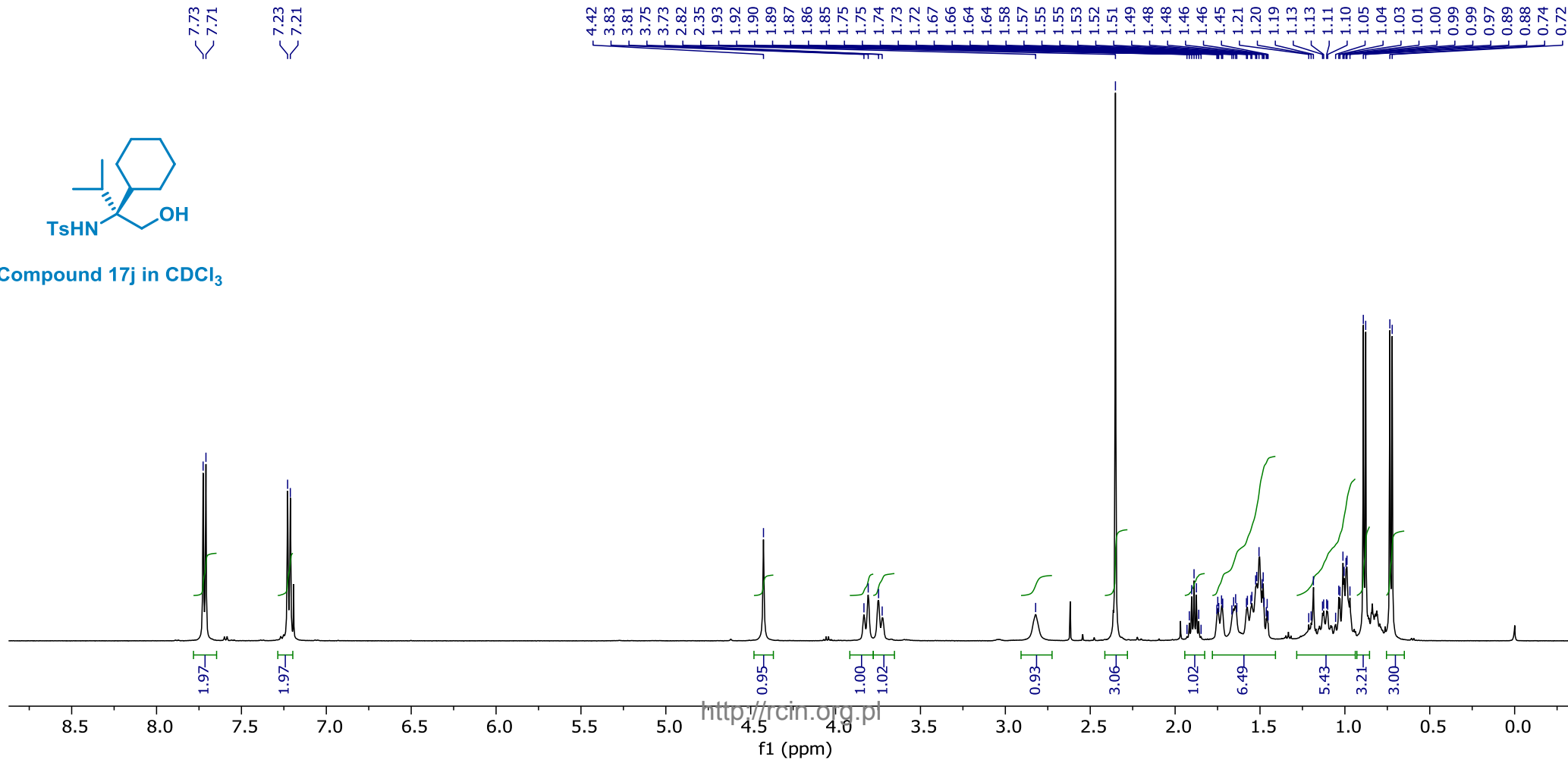


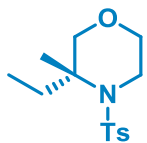
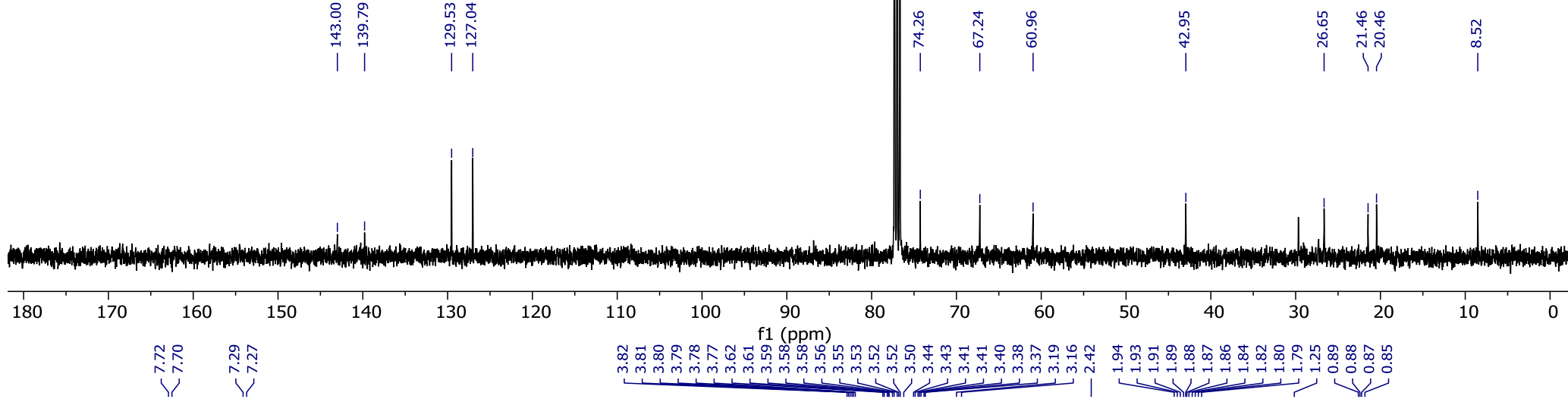
Compound 17i in CDCl<sub>3</sub>



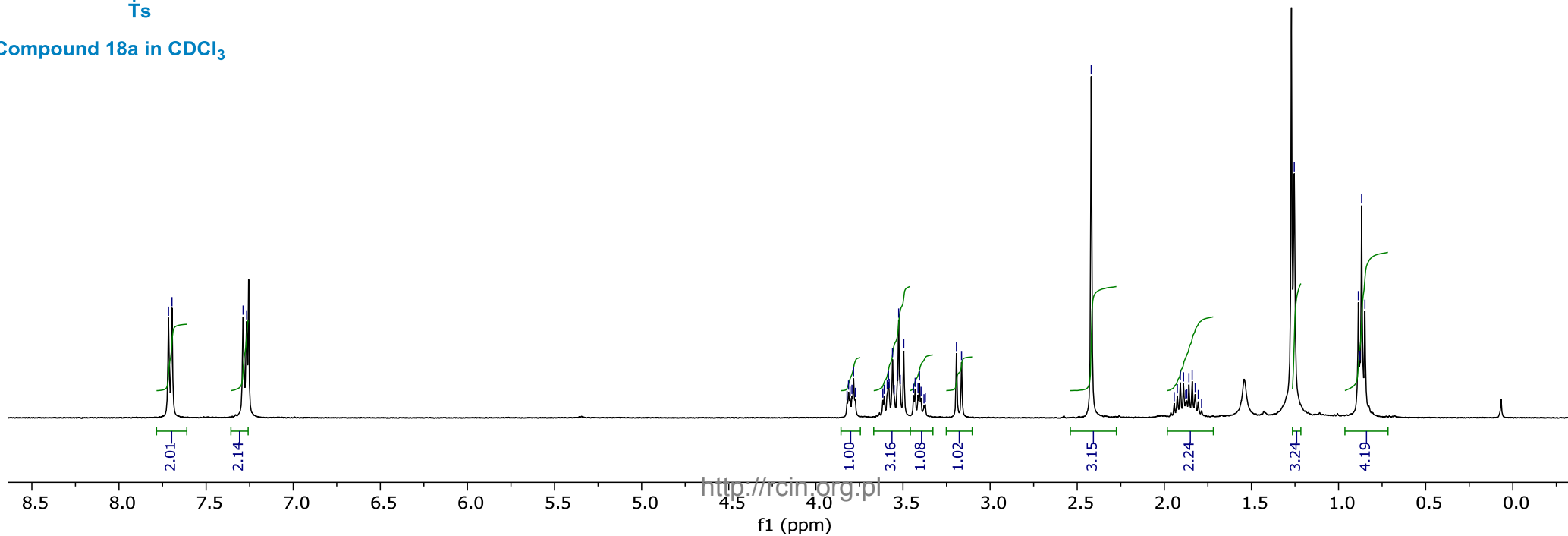


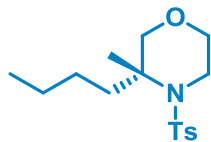
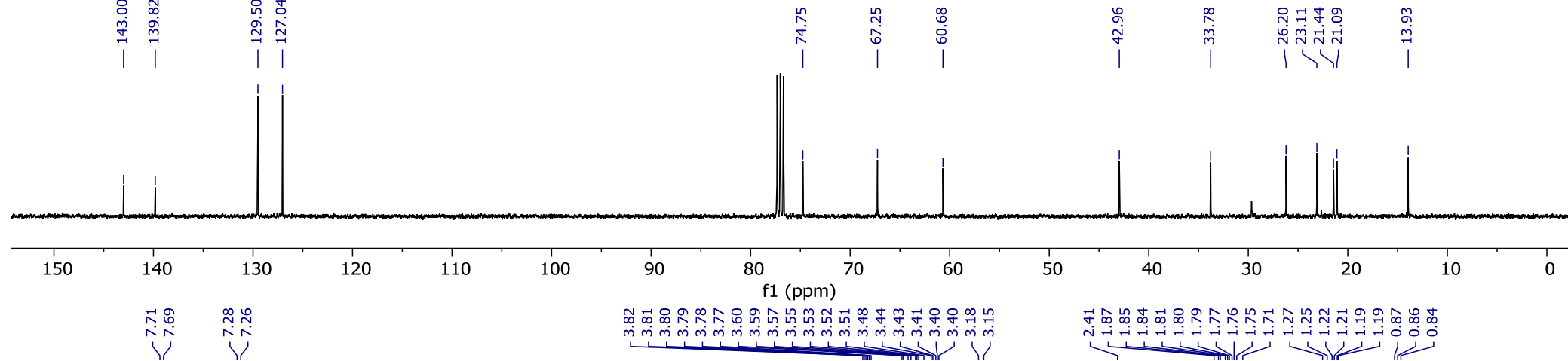
Compound 17j in CDCl<sub>3</sub>



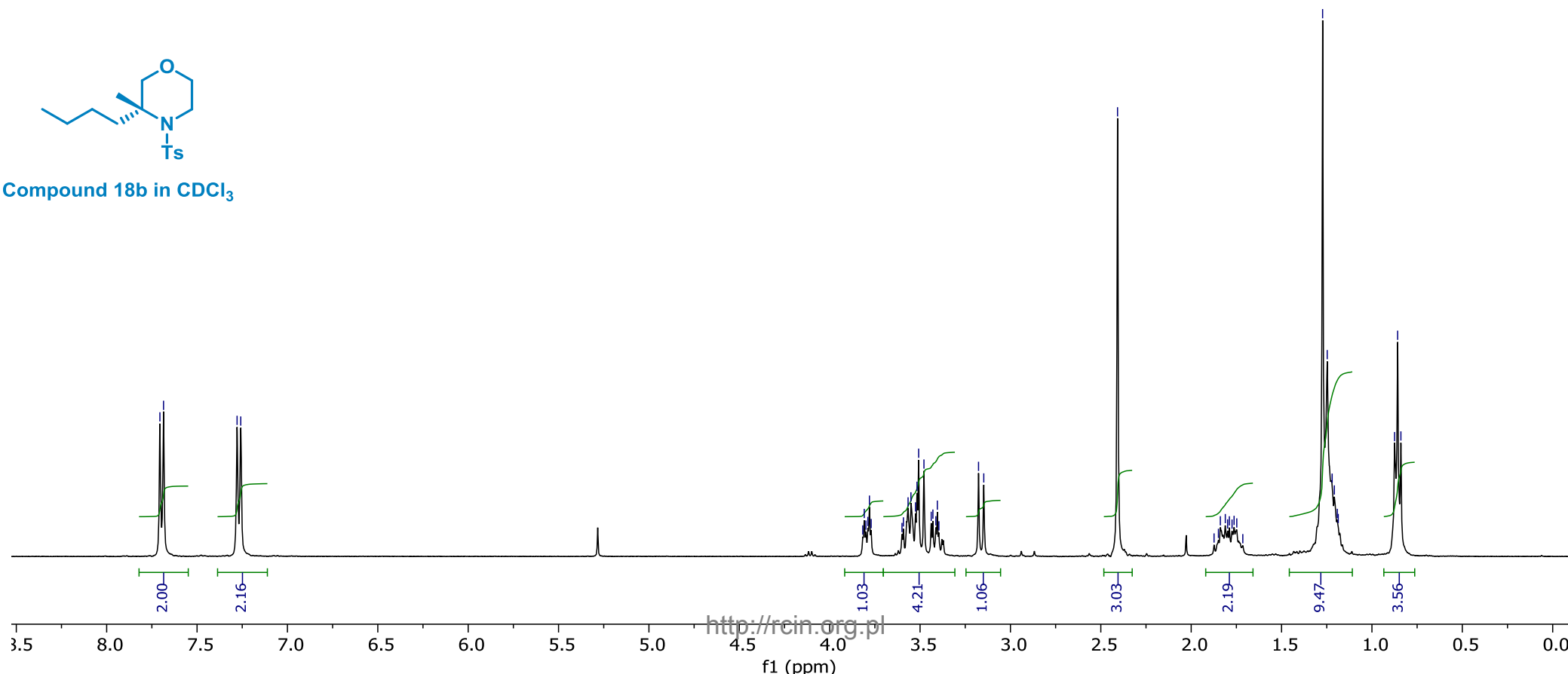


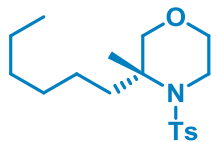
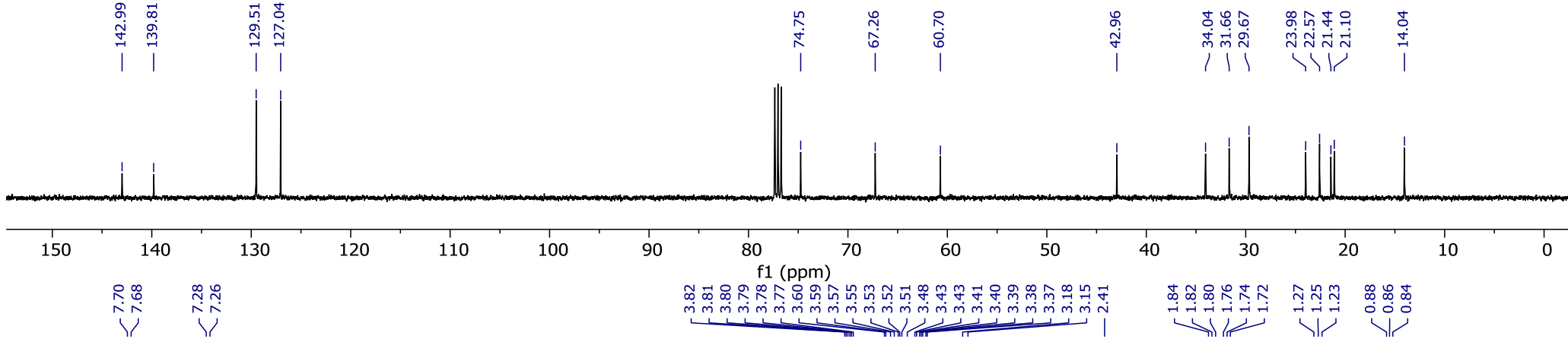
Compound 18a in CDCl<sub>3</sub>



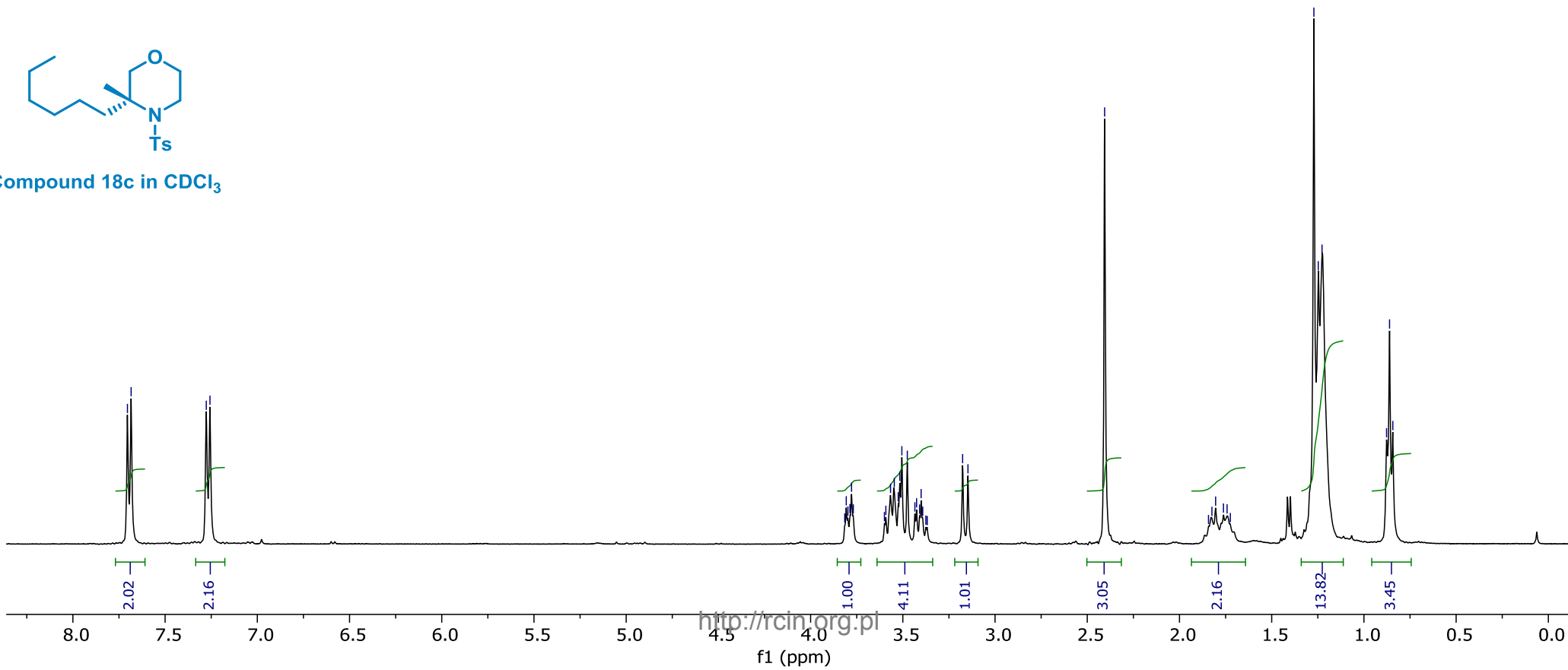


Compound 18b in CDCl<sub>3</sub>

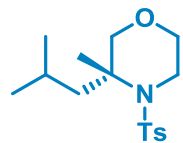
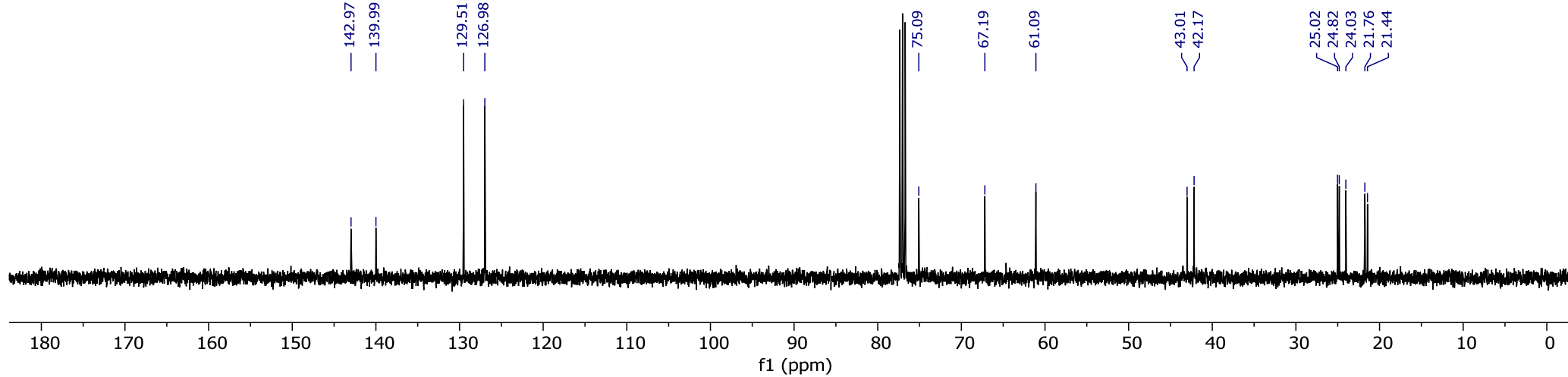




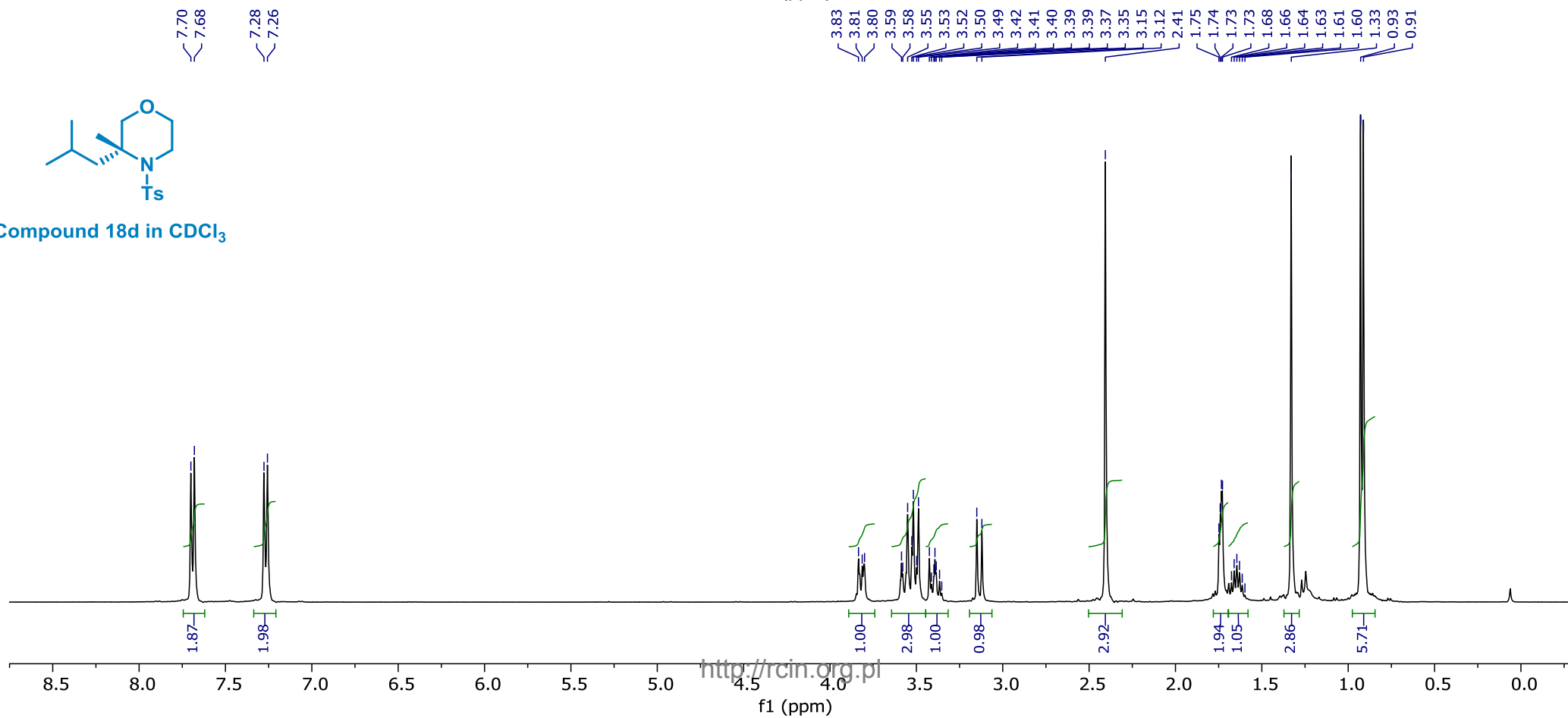
Compound 18c in CDCl<sub>3</sub>

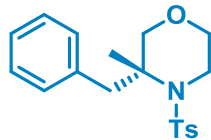
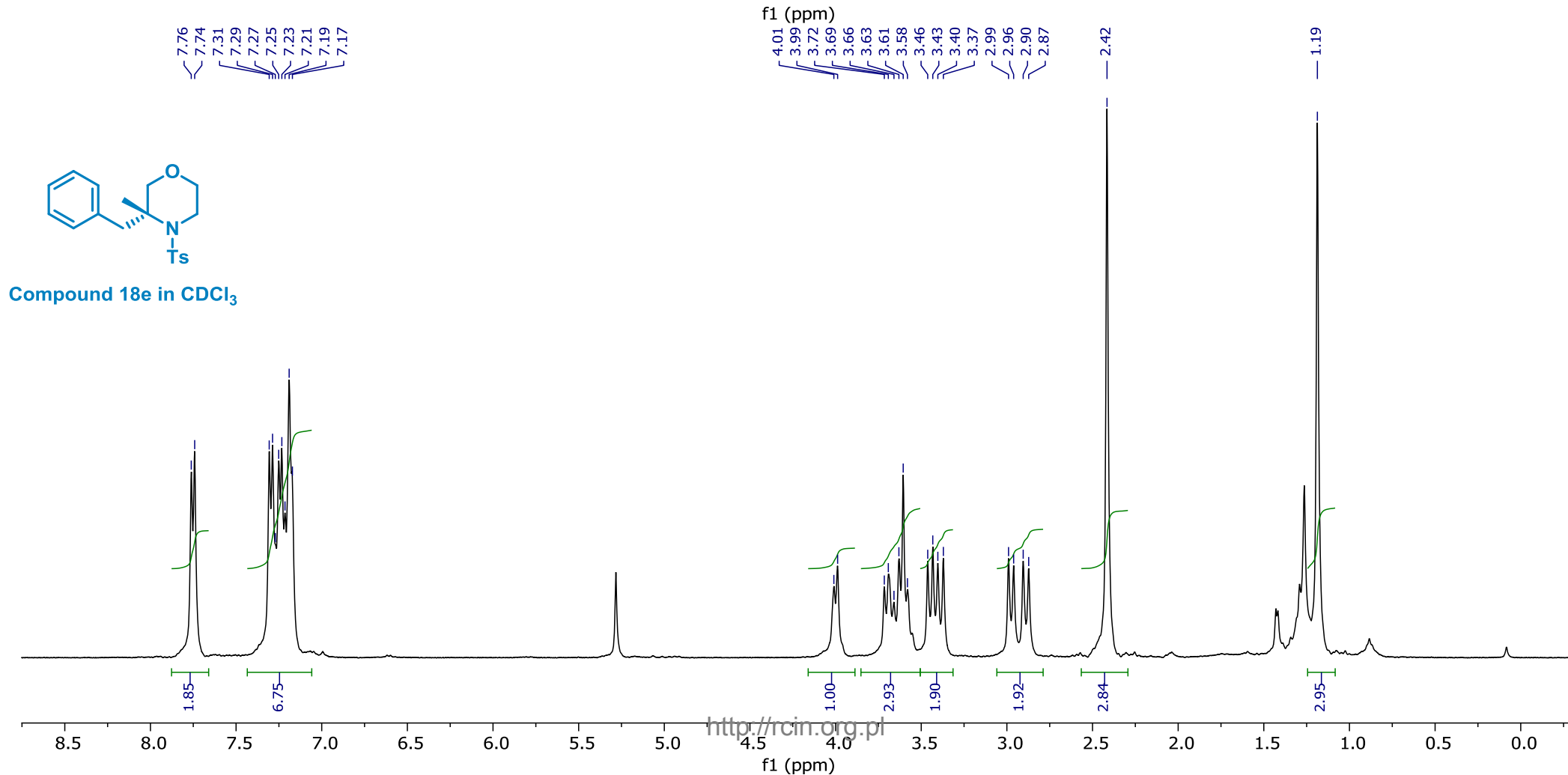
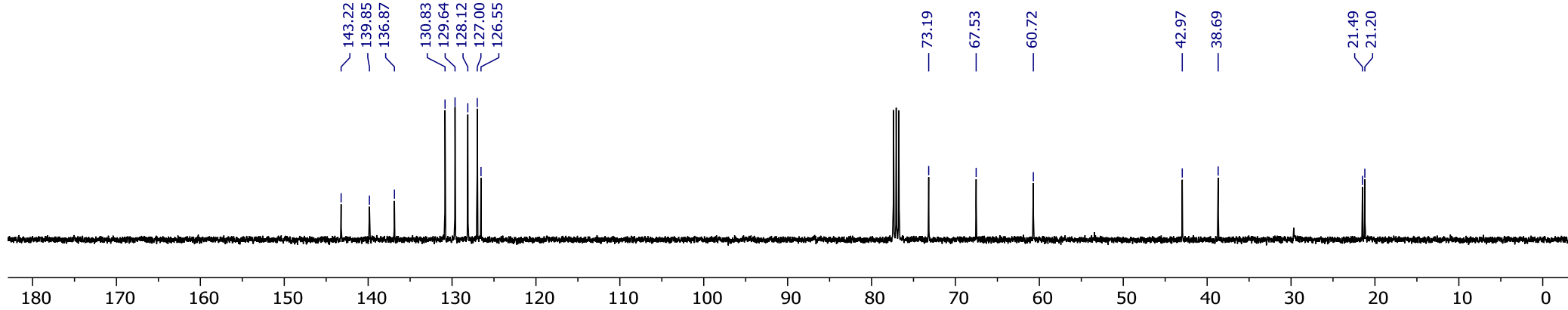




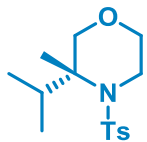
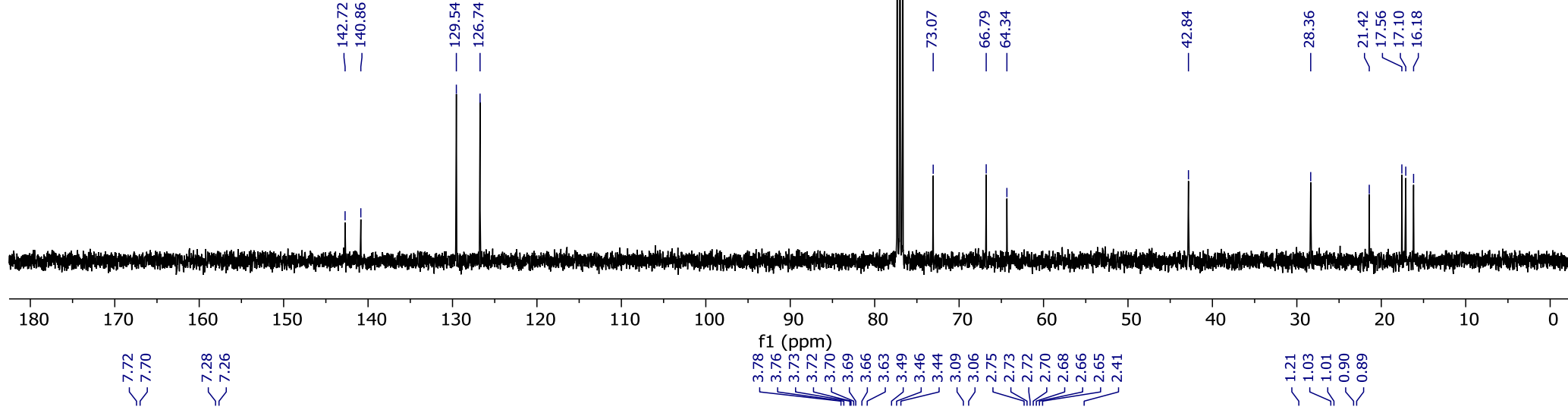


Compound 18d in CDCl<sub>3</sub>

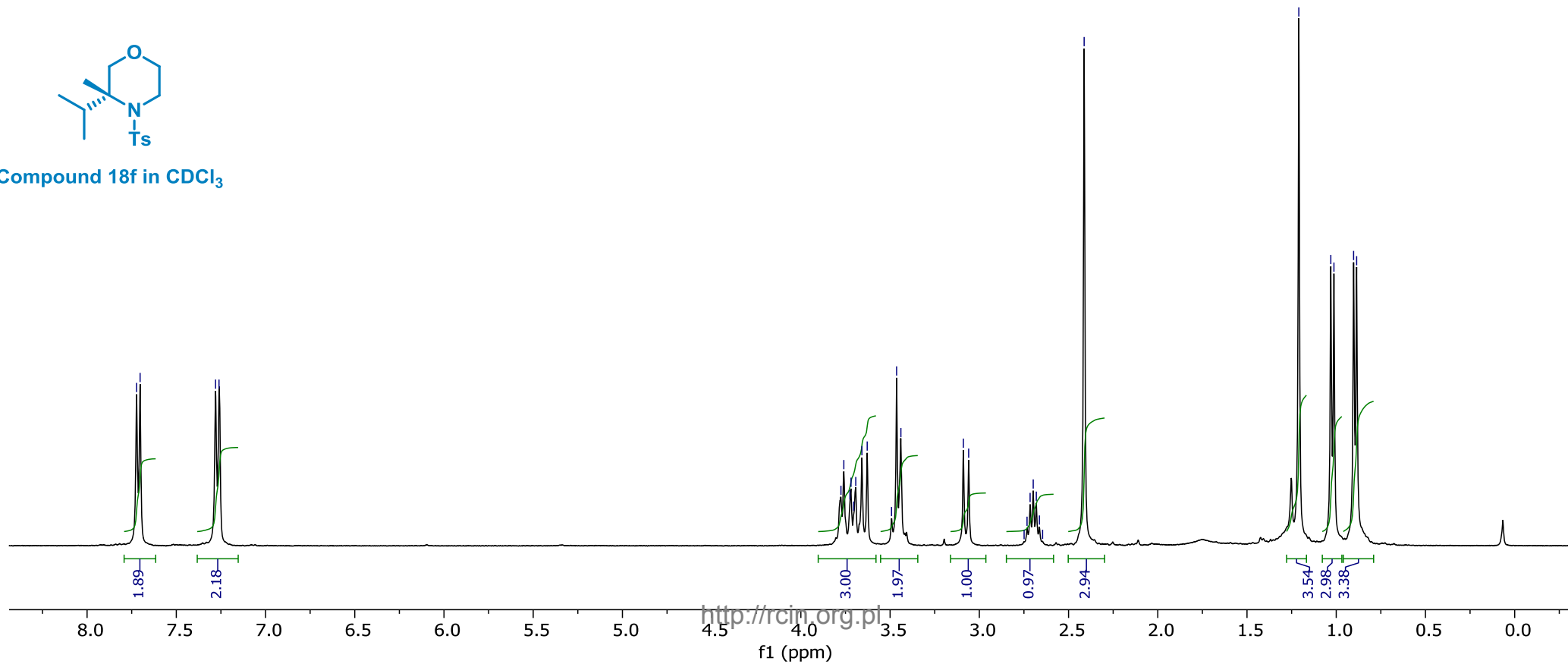


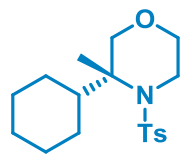
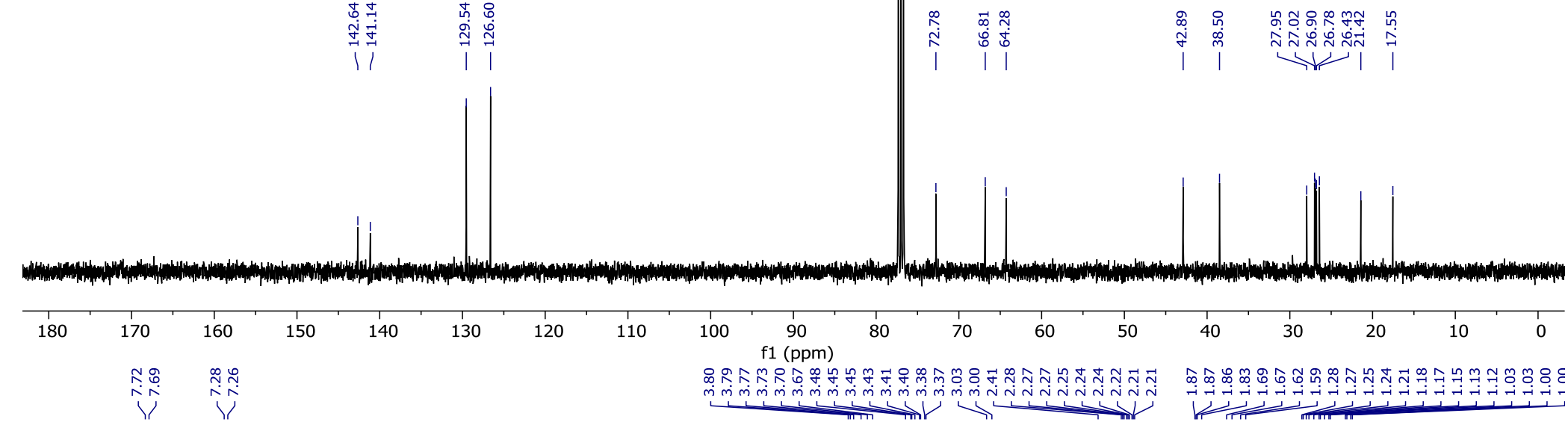


Compound 18e in CDCl<sub>3</sub>

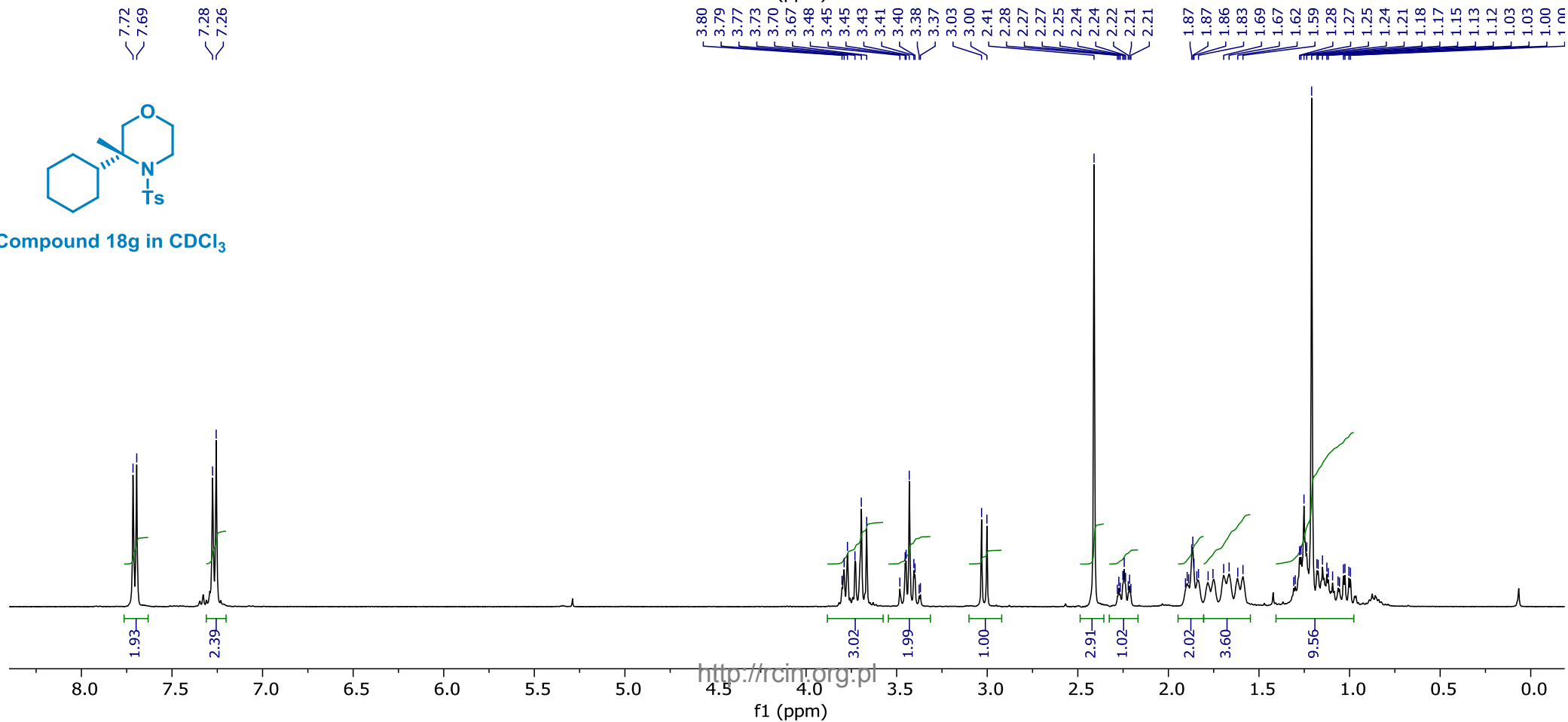


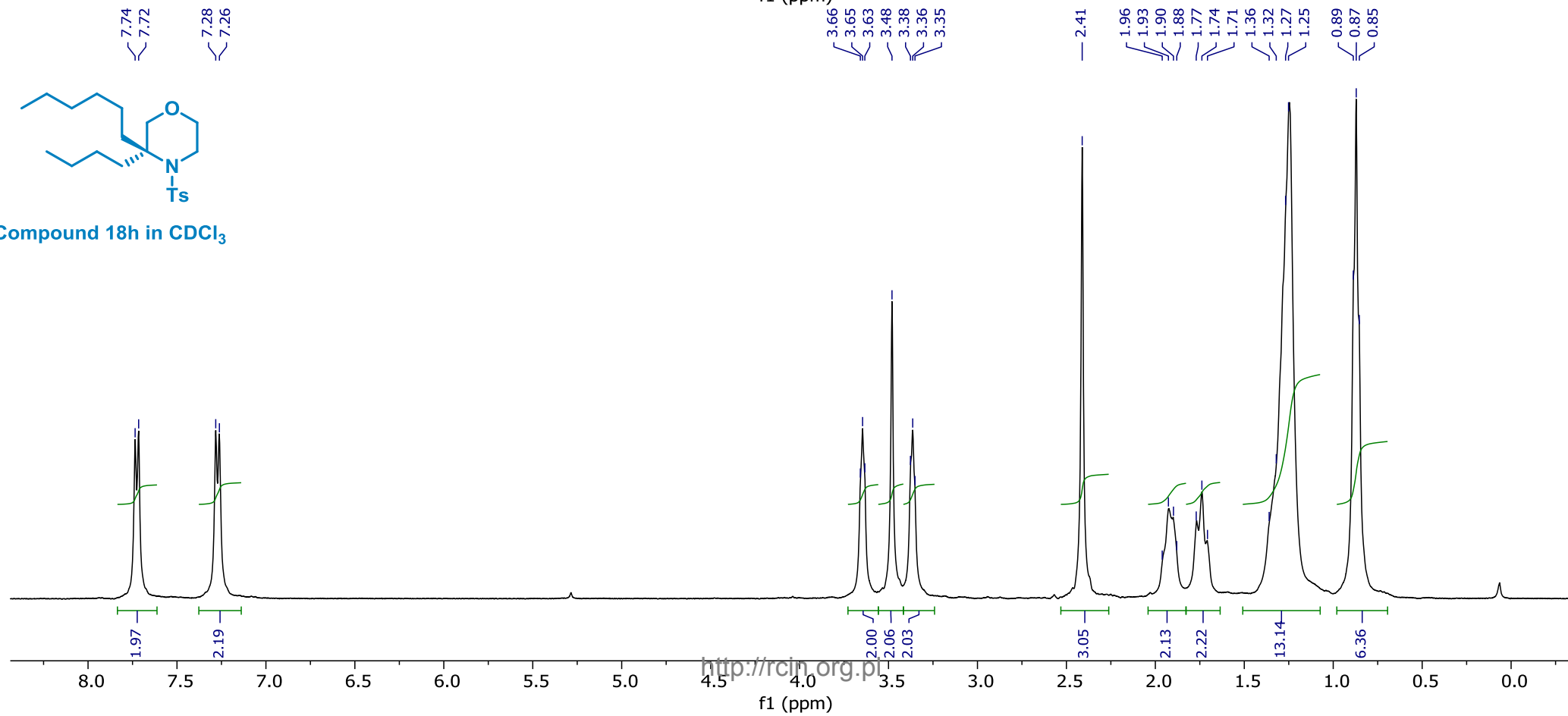
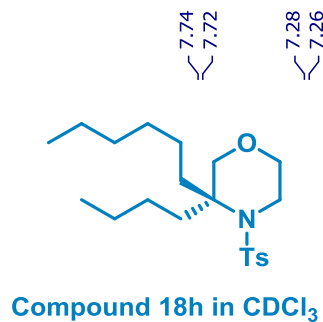
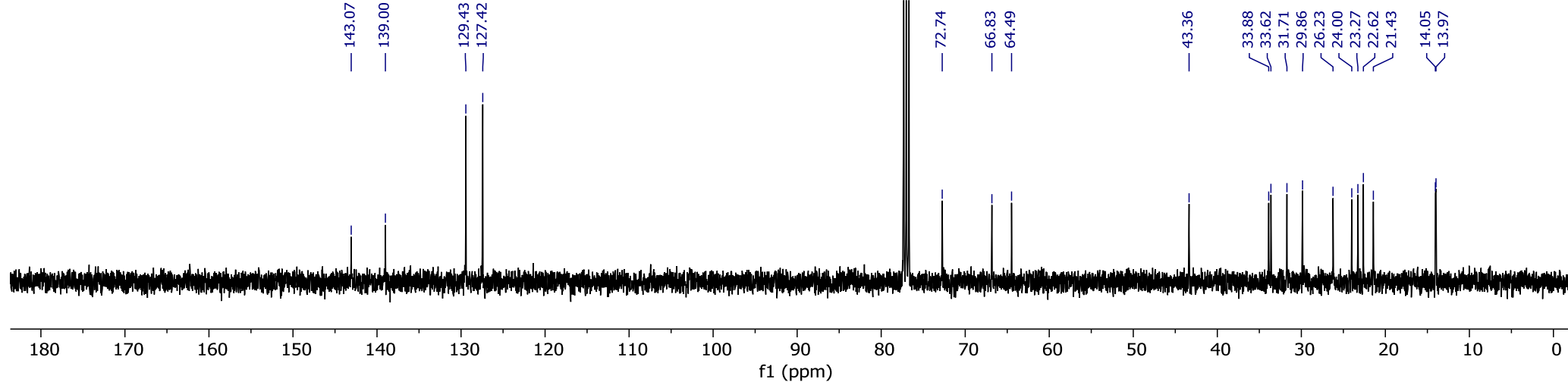
Compound 18f in CDCl<sub>3</sub>

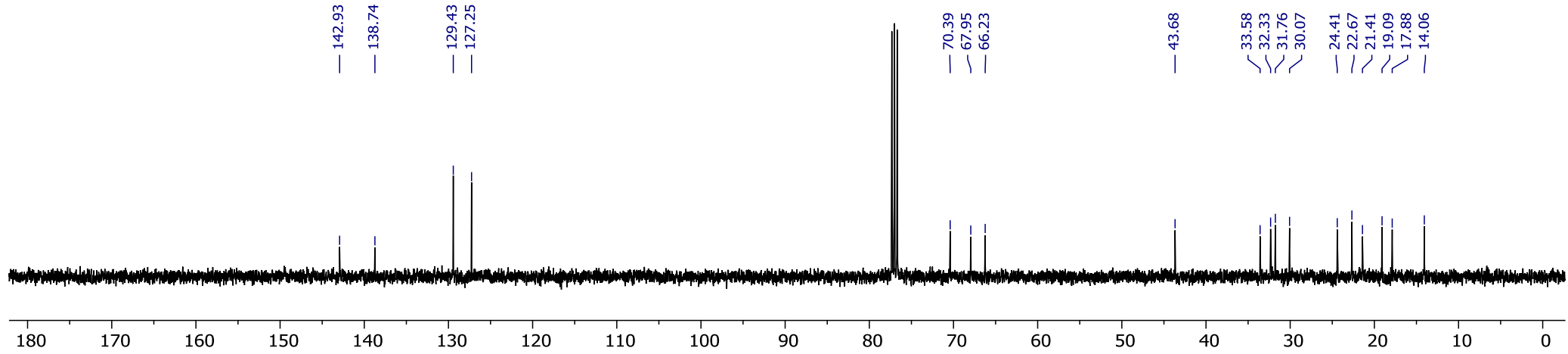




Compound 18g in CDCl<sub>3</sub>



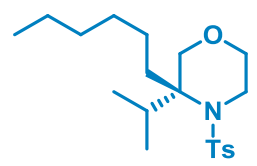




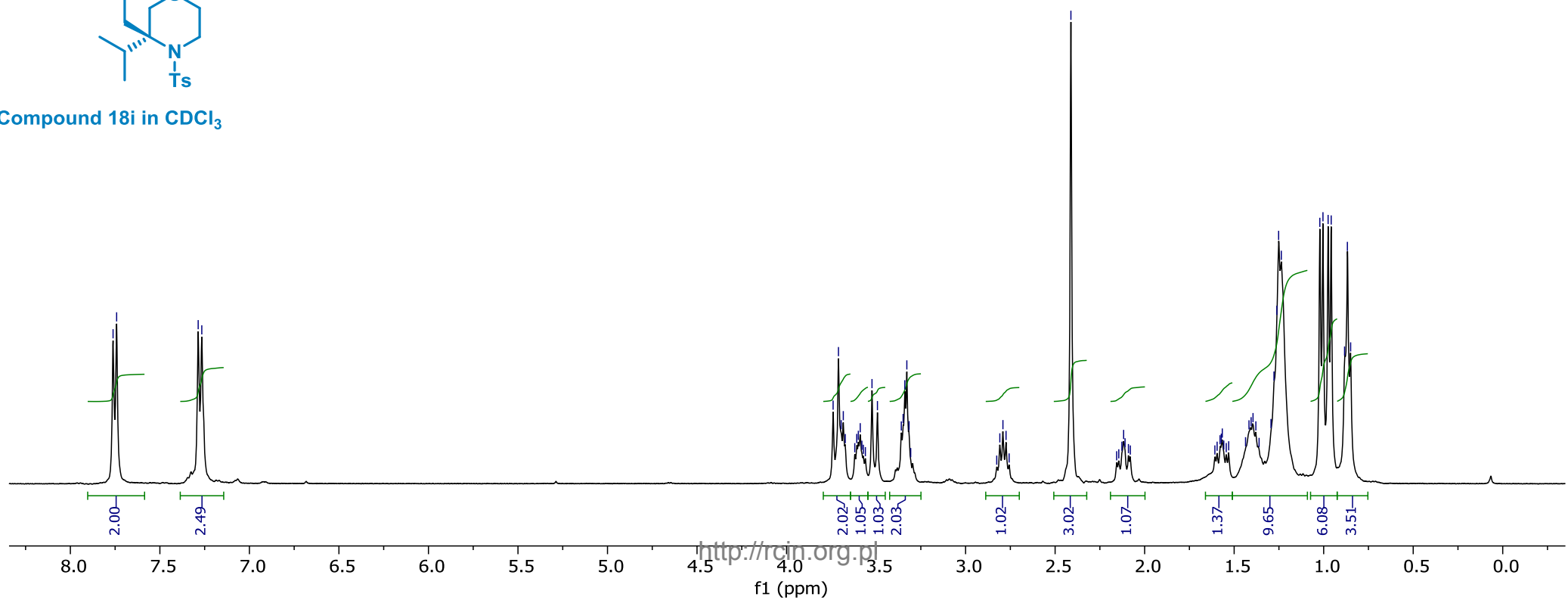
142.93  
138.74  
129.43  
127.25  
70.39  
67.95  
66.23  
43.68  
33.58  
32.33  
31.76  
30.07  
24.41  
22.67  
21.41  
19.09  
17.88  
14.06

7.76  
7.74  
7.29  
7.27

3.74  
3.71  
3.70  
3.68  
3.67  
3.62  
3.61  
3.60  
3.59  
3.58  
3.56  
3.52  
3.49  
3.36  
3.35  
3.34  
3.33  
3.32  
3.31  
2.83  
2.81  
2.79  
2.77  
2.76  
2.41  
2.13  
2.12  
2.11  
1.60  
1.58  
1.57  
1.57  
1.56  
1.53  
1.44  
1.42  
1.41  
1.39  
1.38  
1.36  
1.29  
1.28  
1.26  
1.25  
1.24  
1.02  
1.00  
0.98  
0.88  
0.87  
0.85



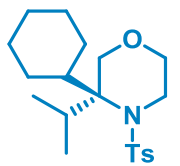
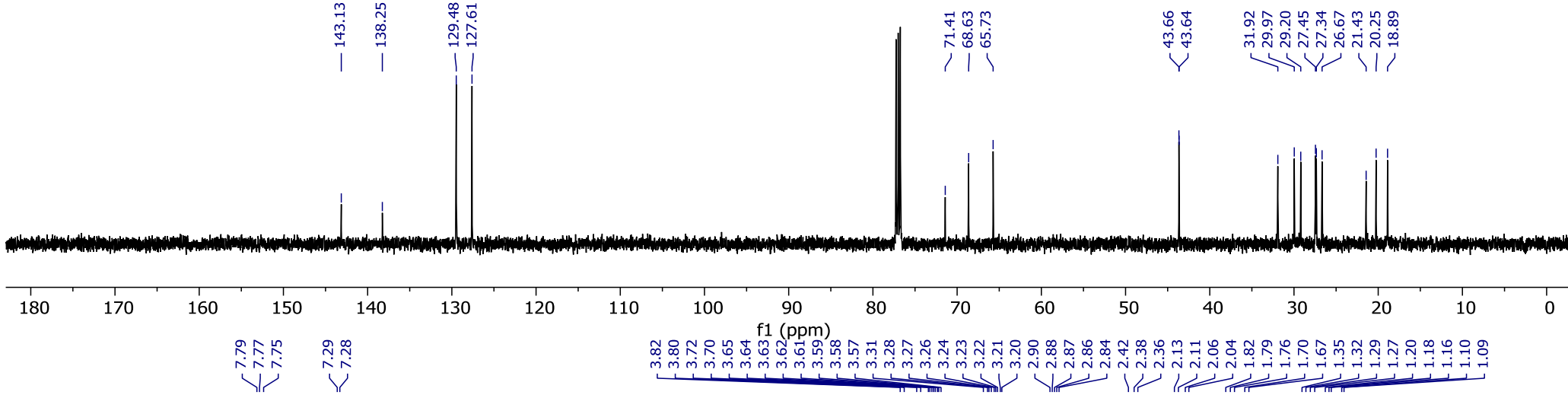
Compound 18i in CDCl<sub>3</sub>



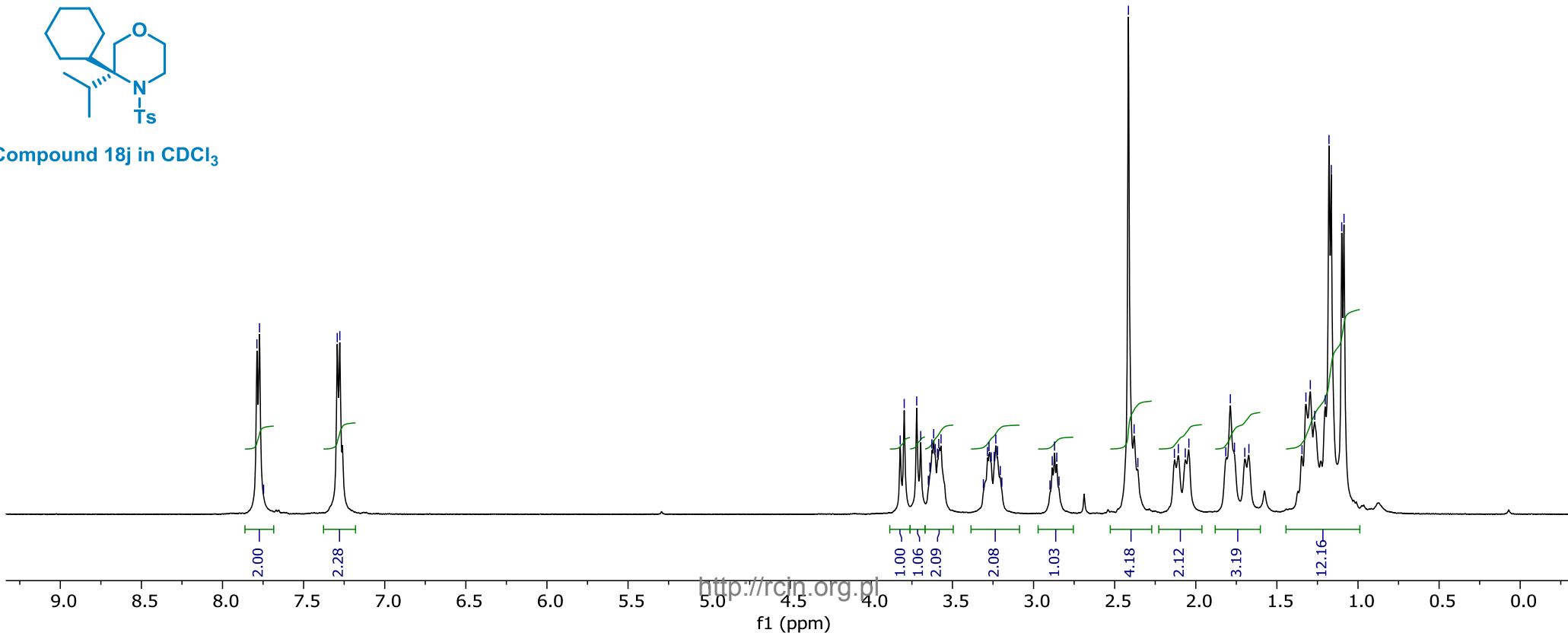
2.00  
2.49

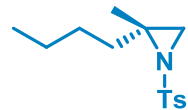
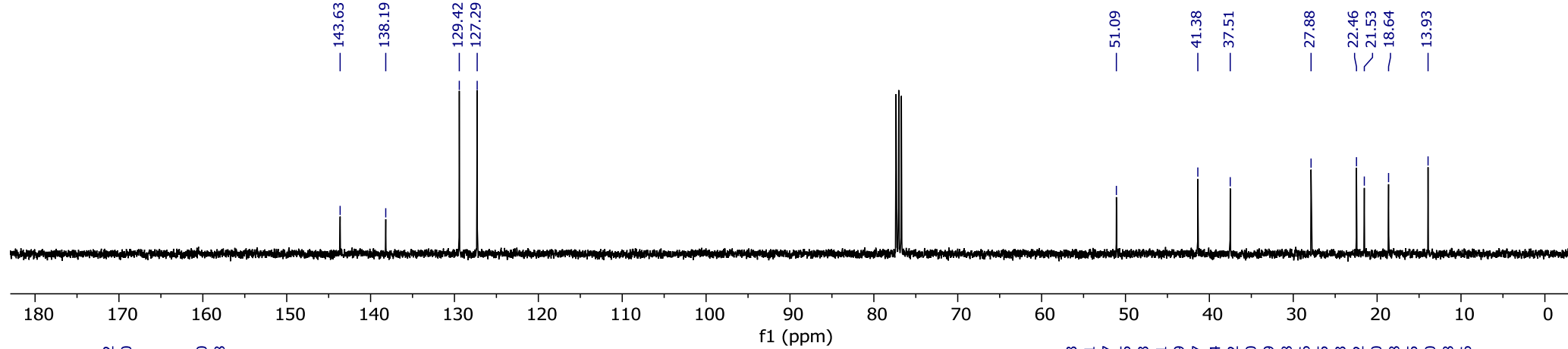
2.02  
1.05  
1.03  
2.03  
1.02  
3.02  
1.07  
1.37  
9.65  
6.08  
3.51

<http://rcin.org.pl>

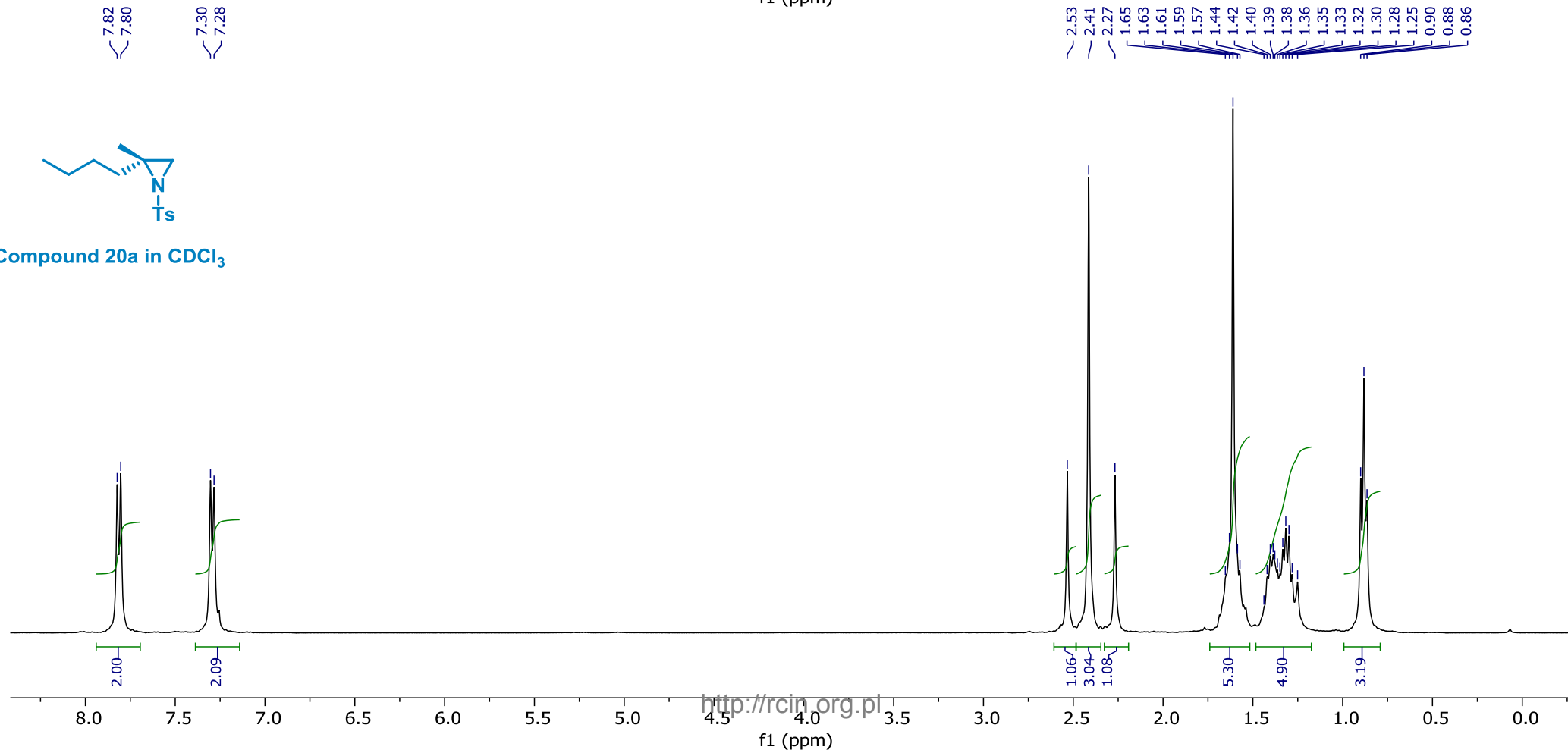


Compound 18j in CDCl<sub>3</sub>

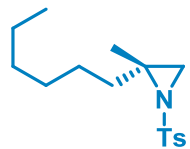
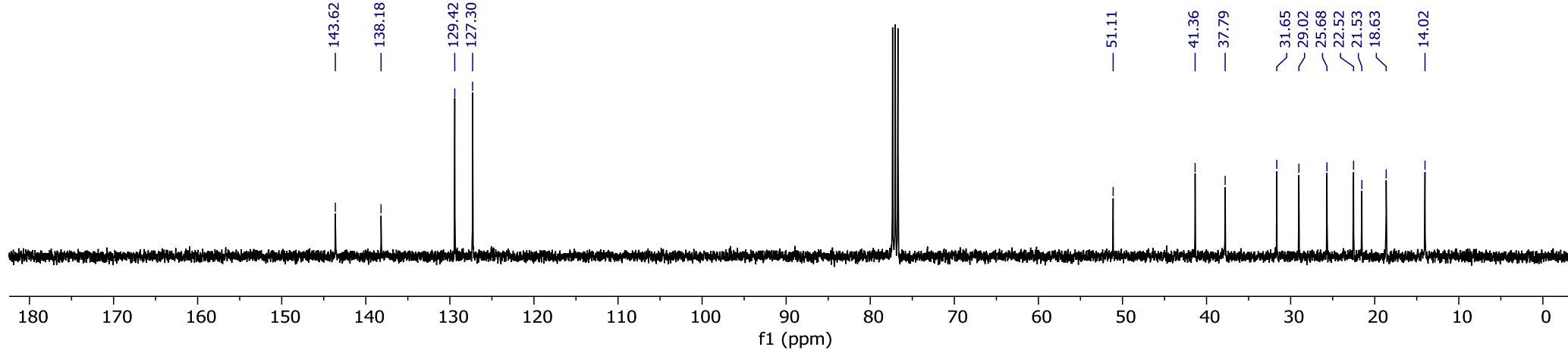




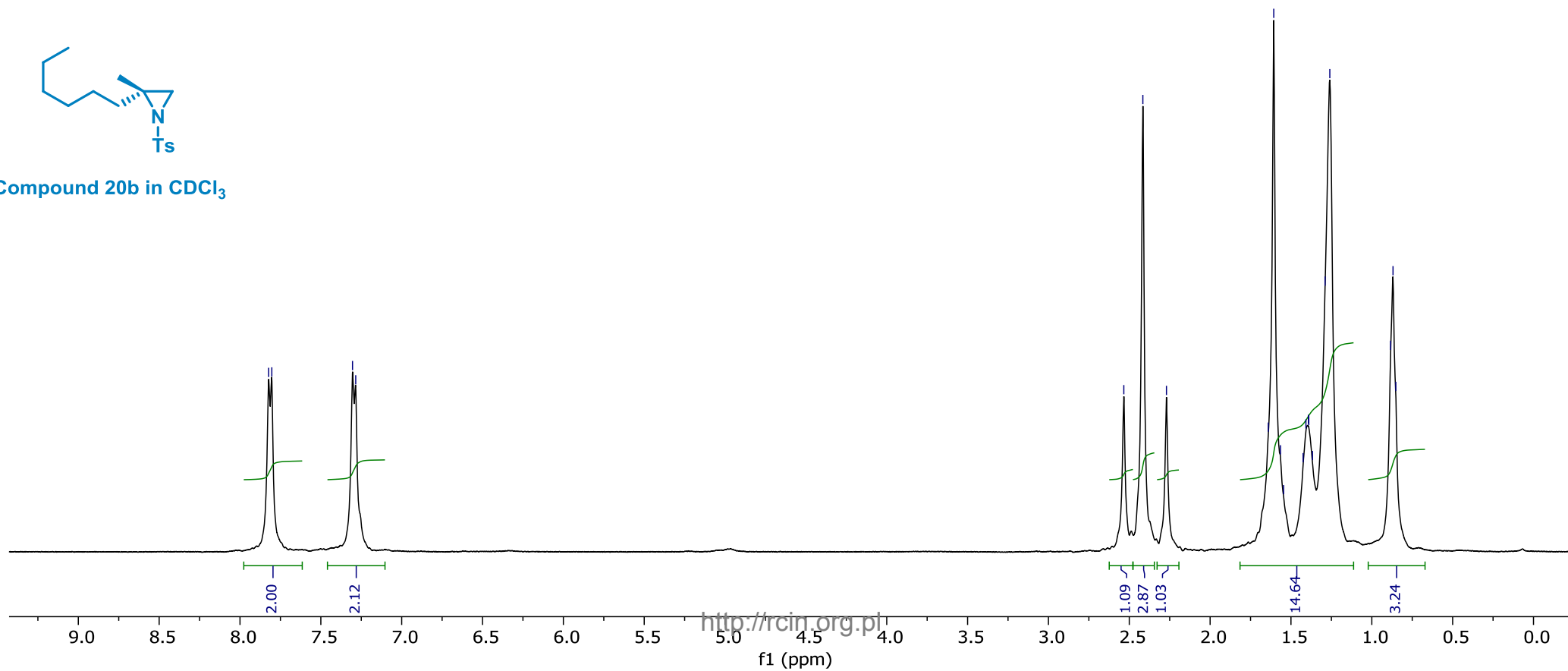
Compound 20a in CDCl<sub>3</sub>

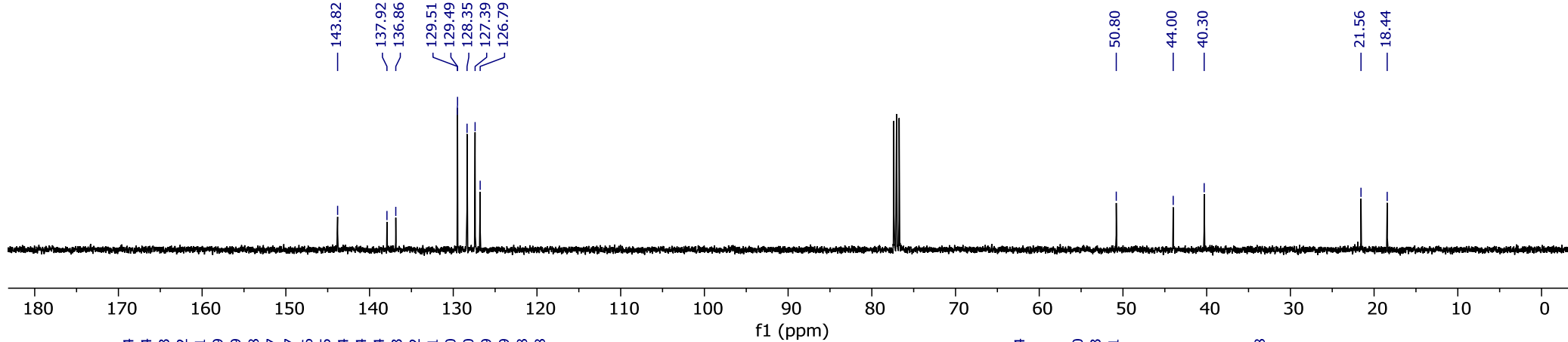






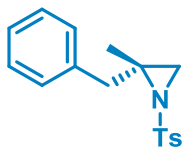
Compound 20b in CDCl<sub>3</sub>



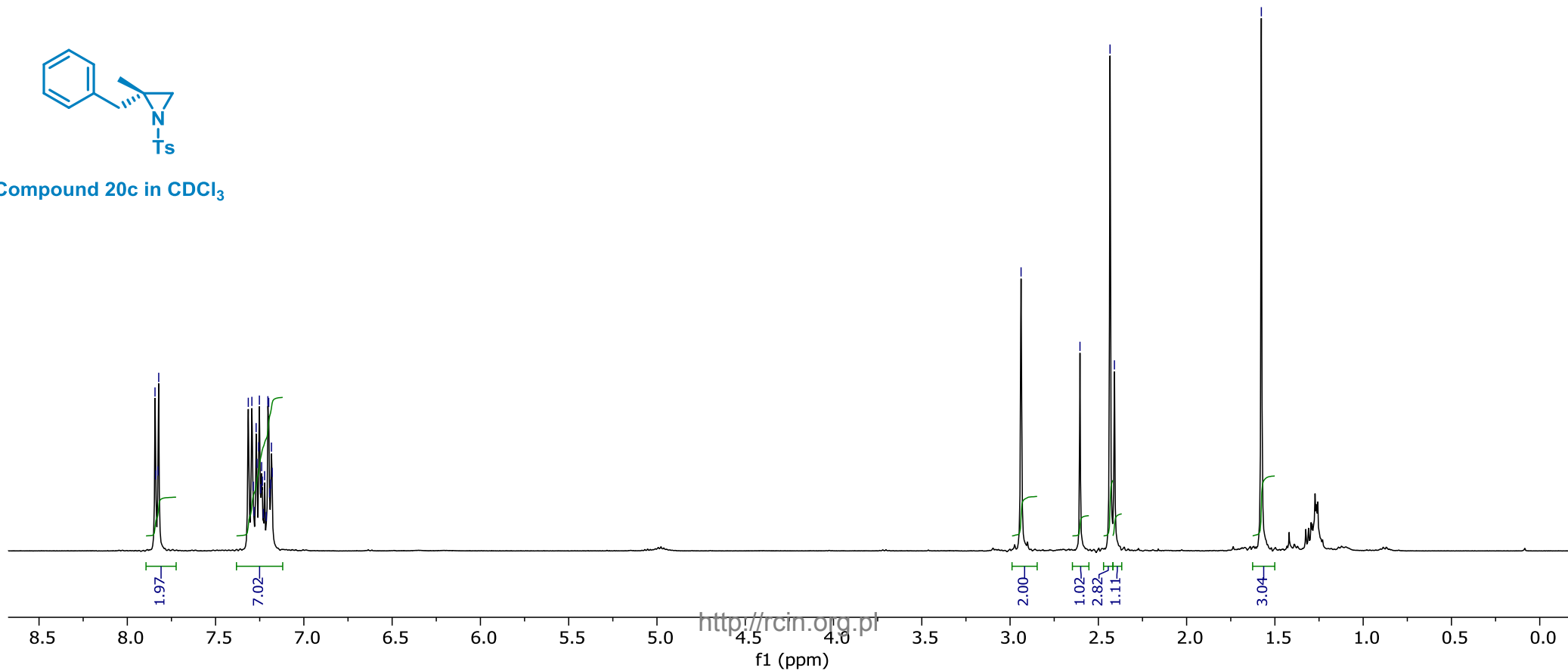


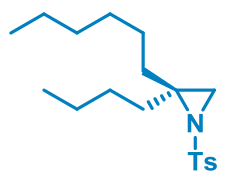
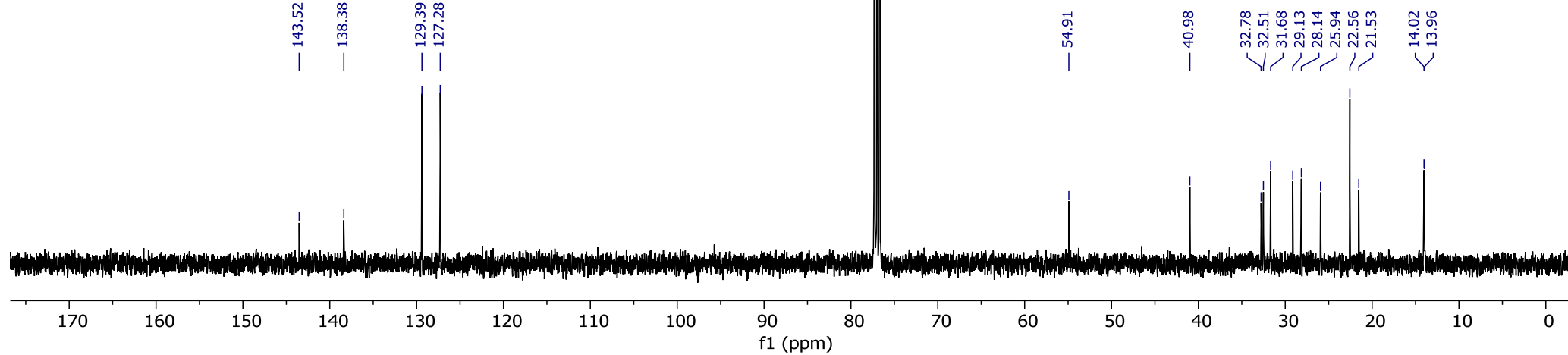
7.84  
7.84  
7.83  
7.82  
7.31  
7.29  
7.29  
7.28  
7.27  
7.27  
7.26  
7.25  
7.24  
7.24  
7.24  
7.23  
7.22  
7.21  
7.20  
7.20  
7.19  
7.19  
7.18

2.94  
2.60  
2.43  
2.41  
1.58

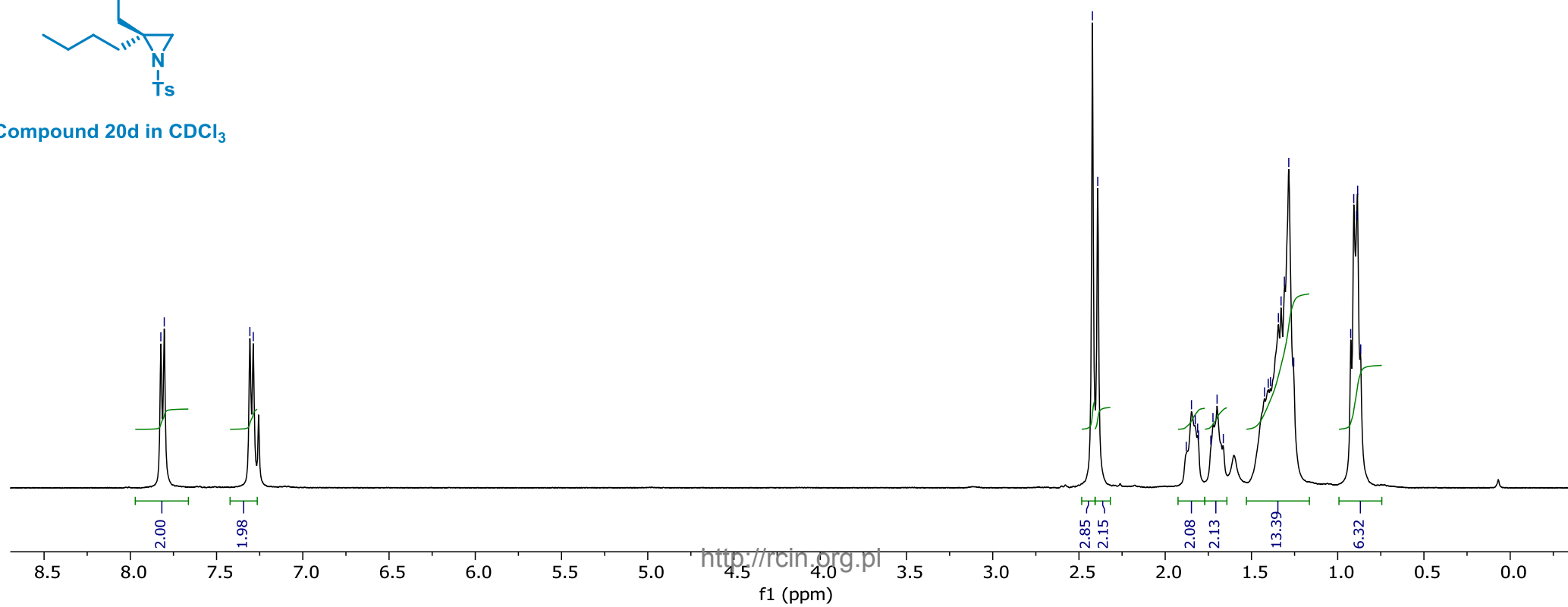


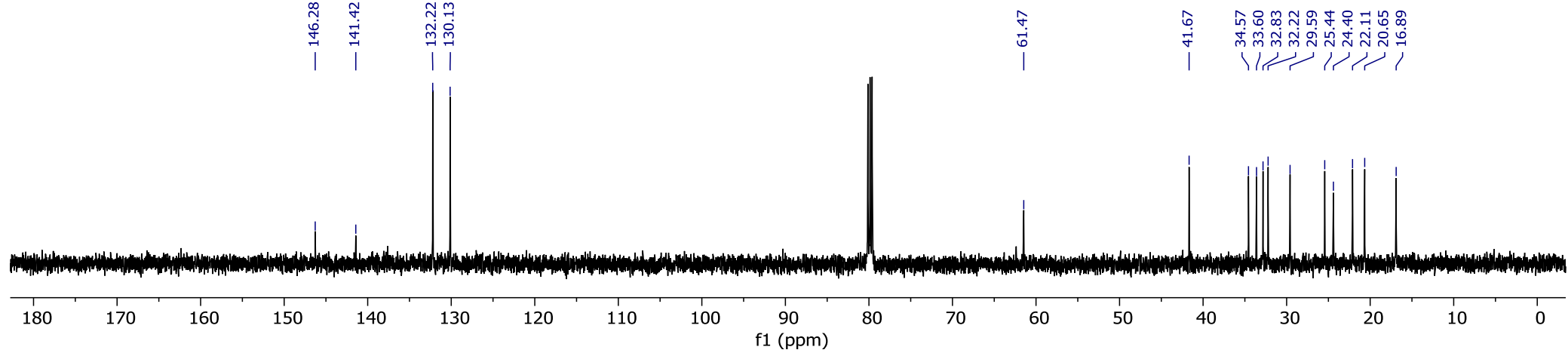
Compound 20c in CDCl<sub>3</sub>





Compound 20d in CDCl<sub>3</sub>



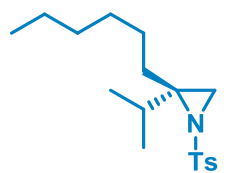


7.76  
7.74  
7.72

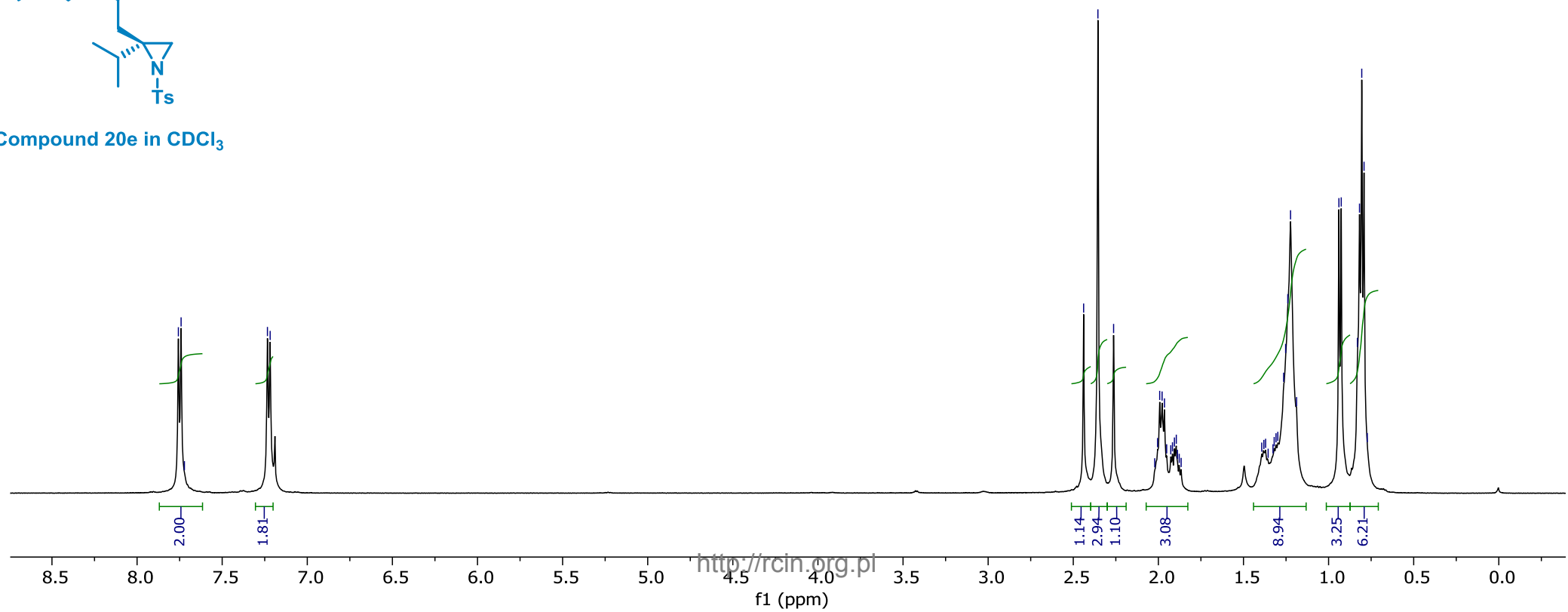
7.23  
7.22

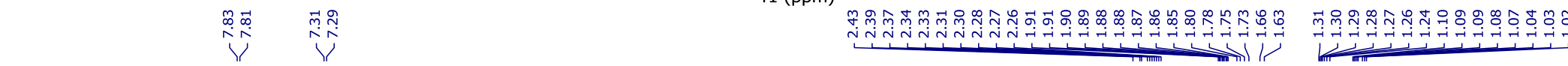
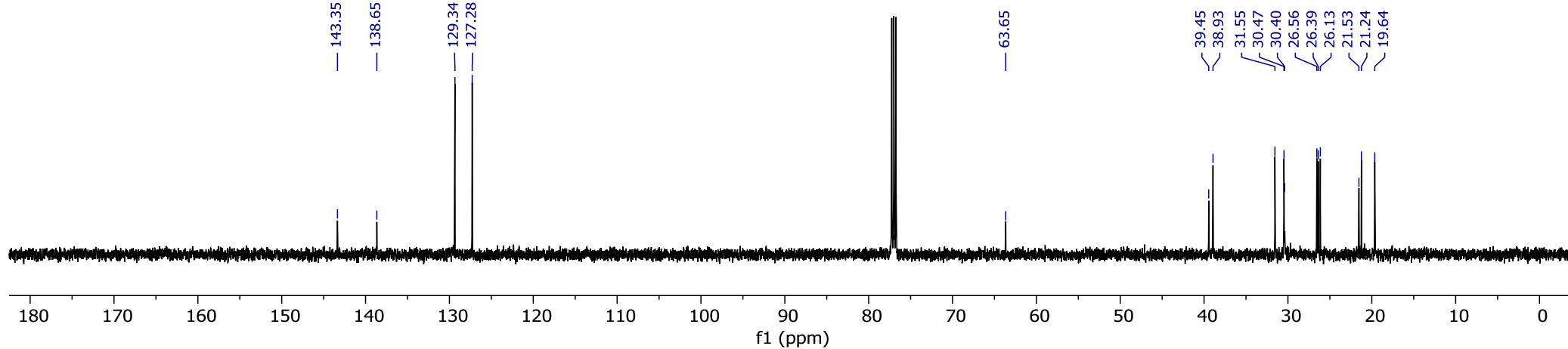
2.44  
2.36  
2.26  
2.02  
2.00  
1.99  
1.98  
1.96  
1.95  
1.93  
1.92  
1.91  
1.89  
1.88  
1.87

1.39  
1.38  
1.37  
1.33  
1.32  
1.31  
1.30  
1.26  
1.25  
1.24  
1.22  
1.19  
0.94  
0.93  
0.83  
0.82  
0.81  
0.79  
0.77

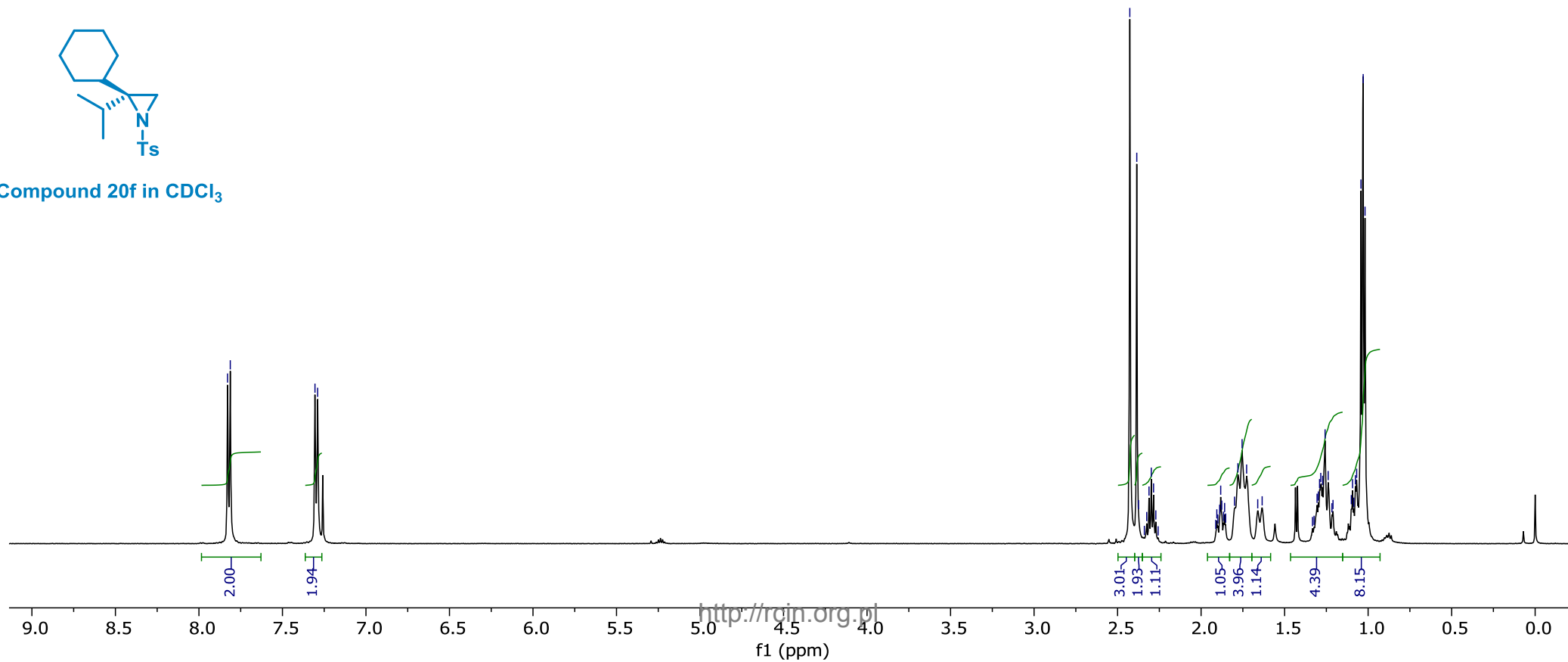


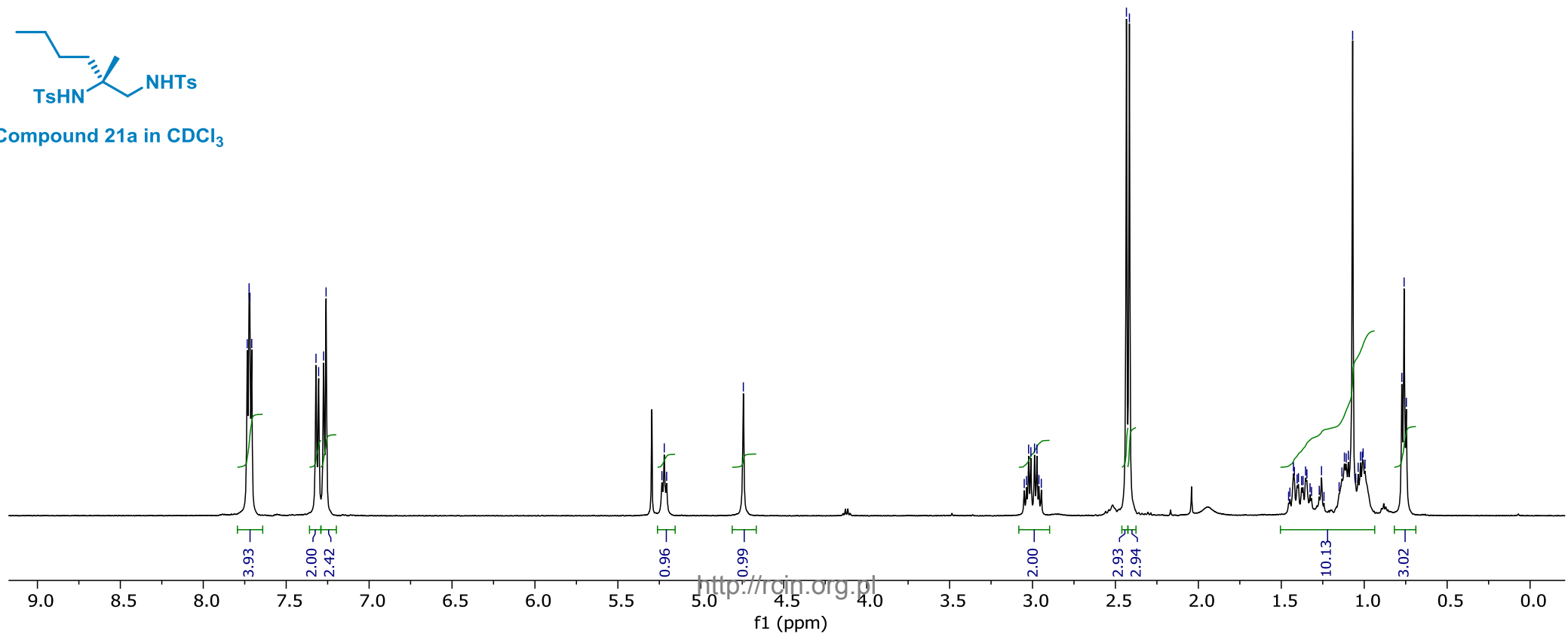
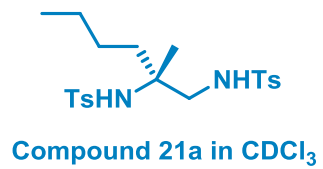
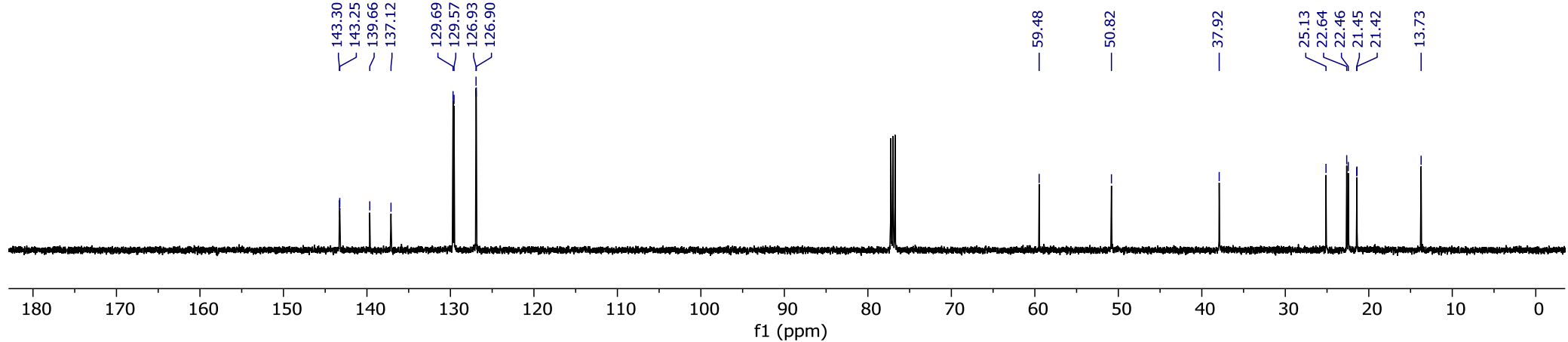
Compound 20e in CDCl<sub>3</sub>

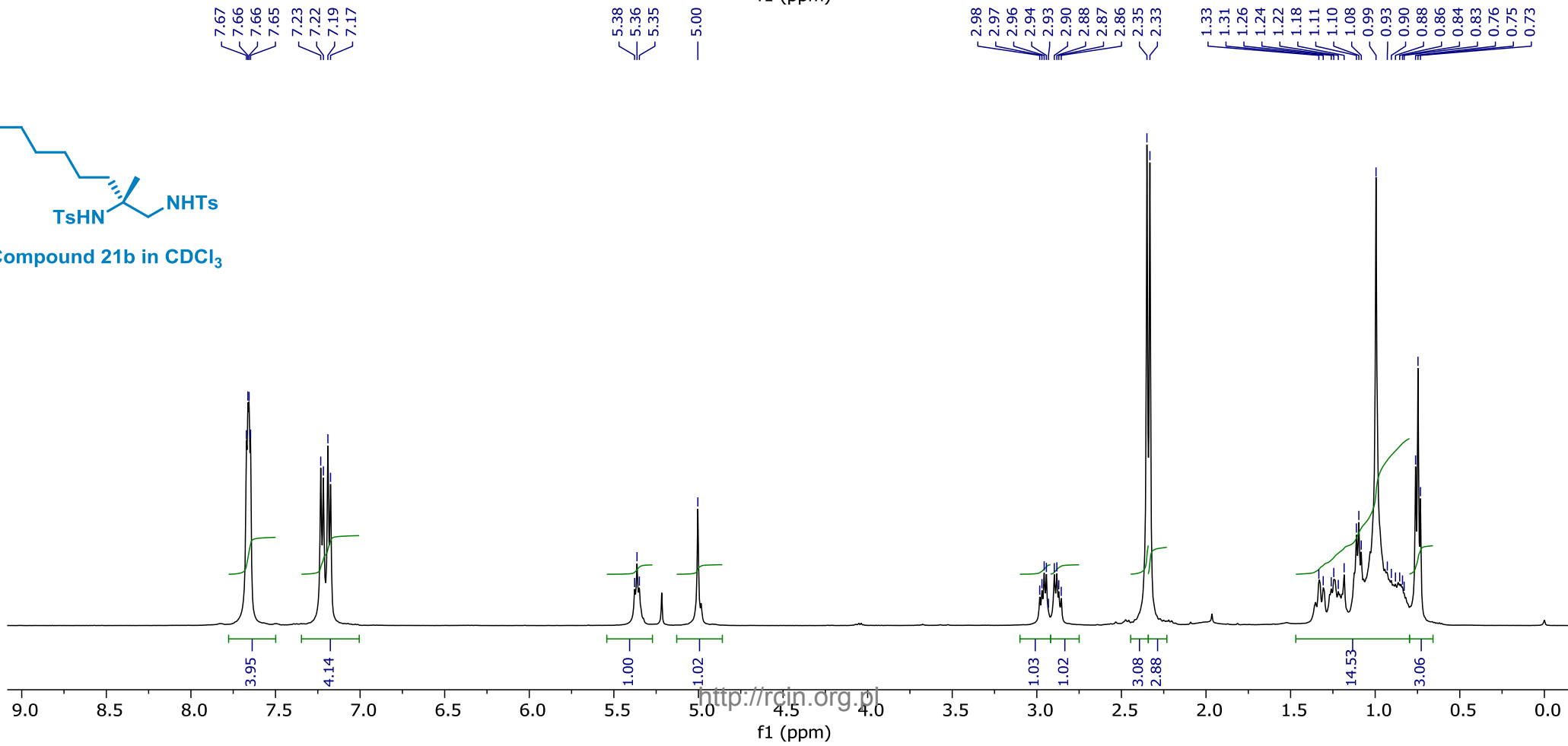
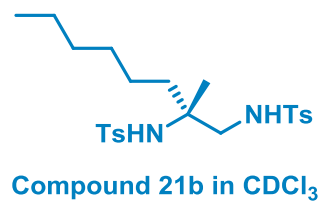
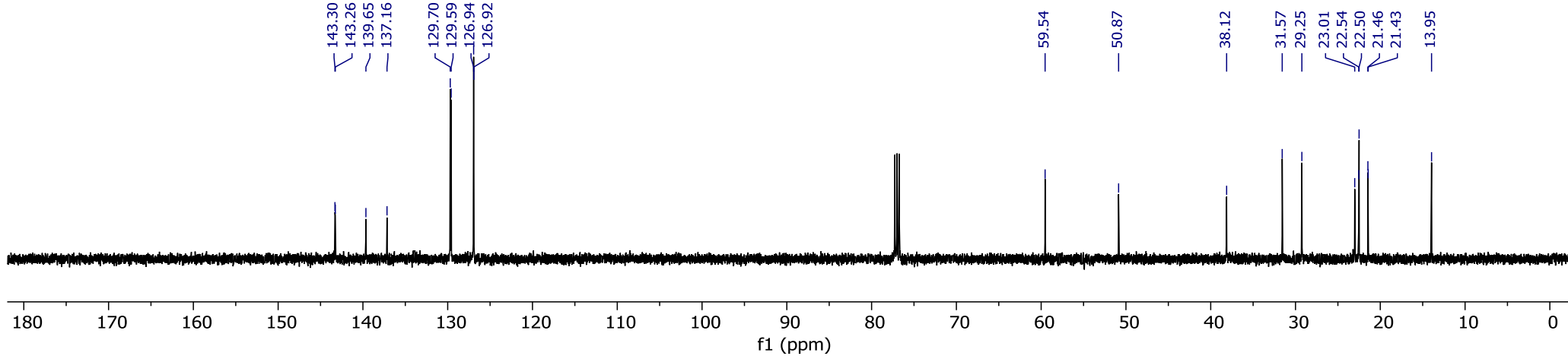


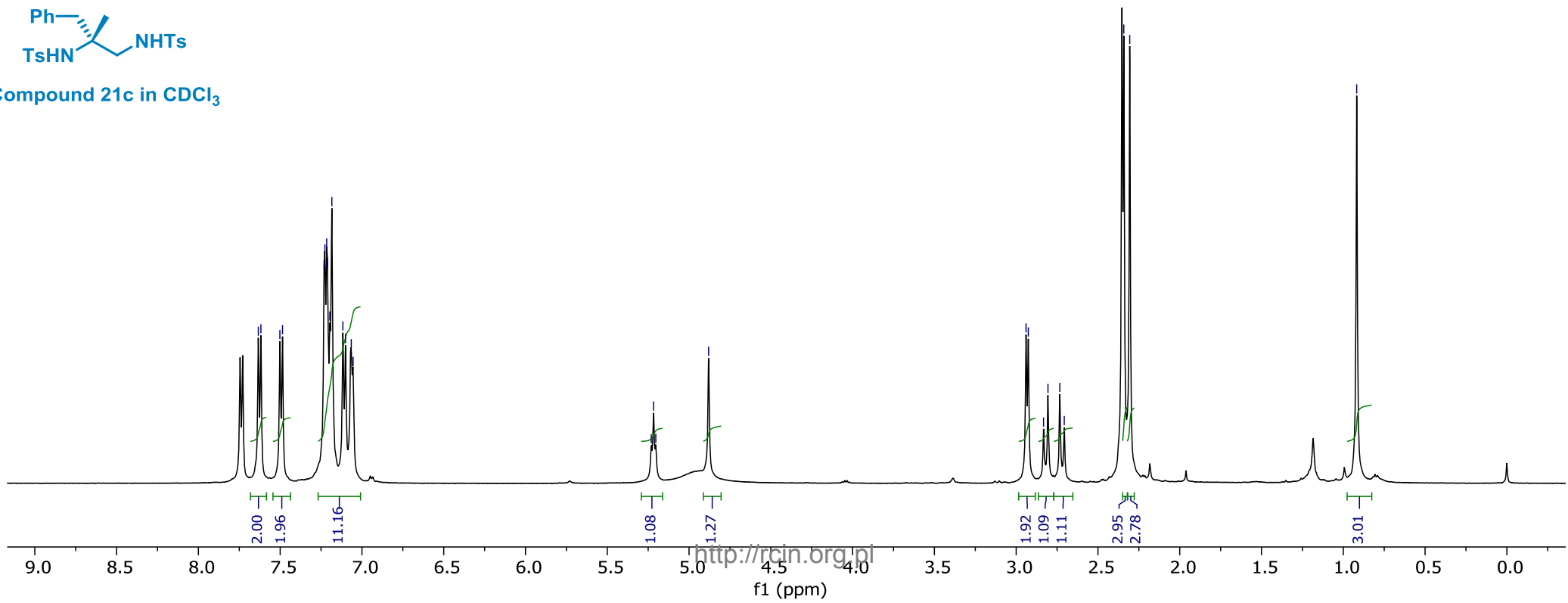
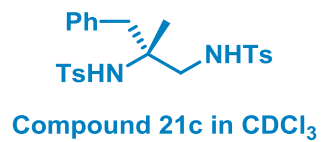
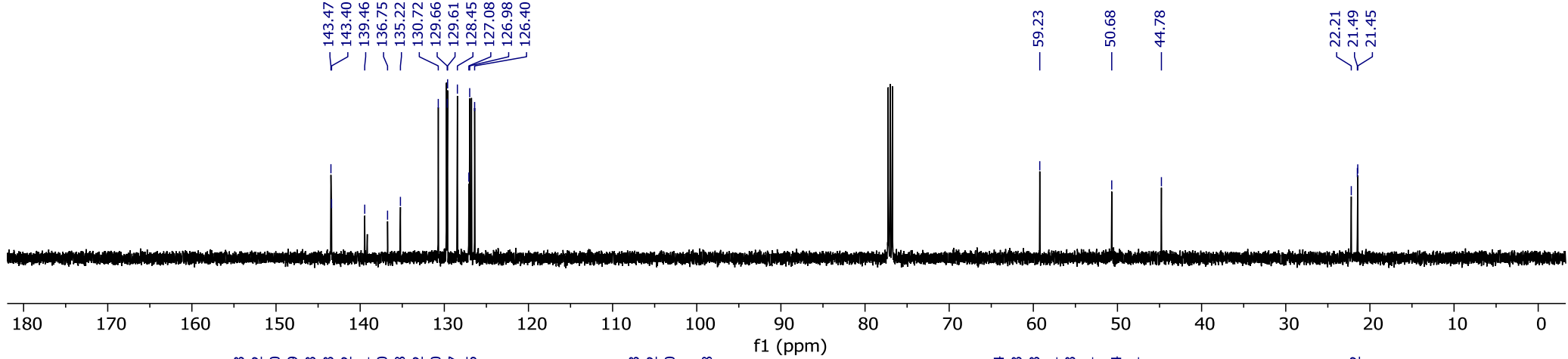


Compound 20f in CDCl<sub>3</sub>

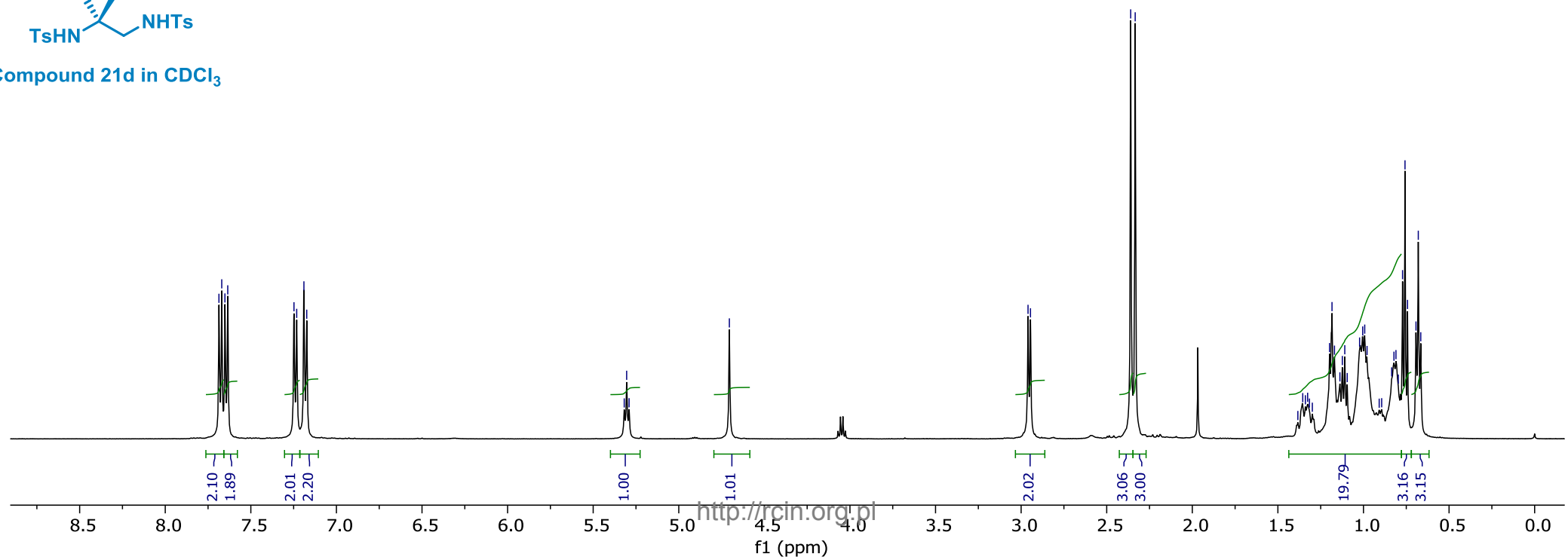
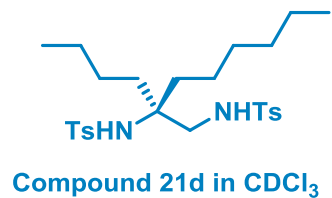
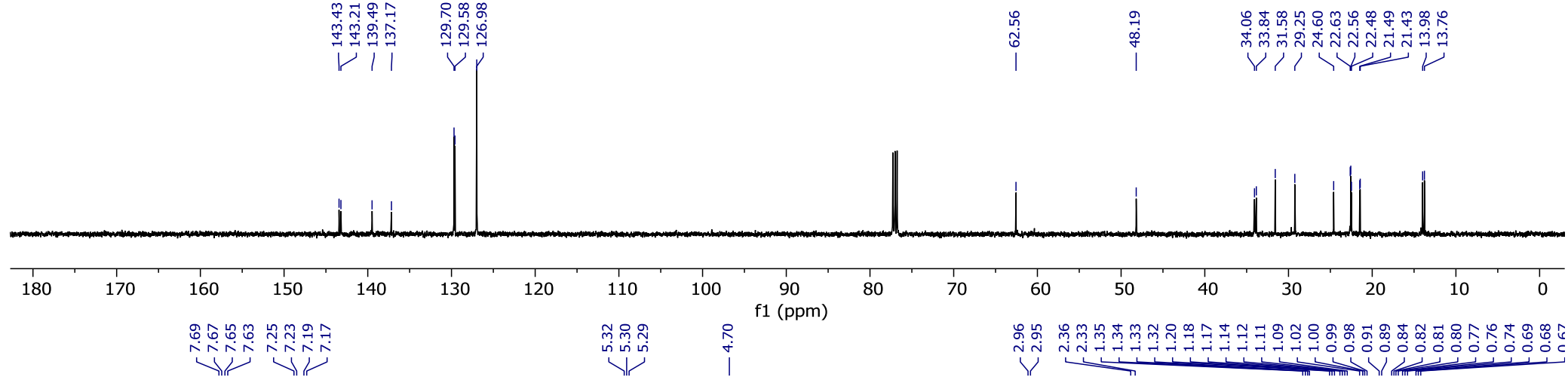


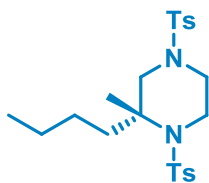
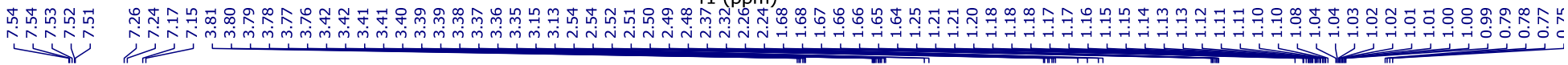
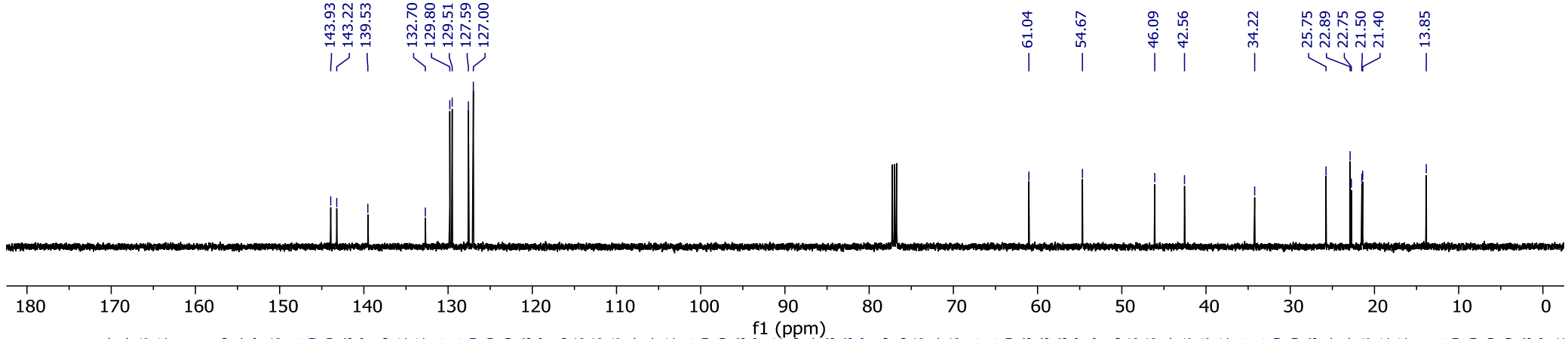




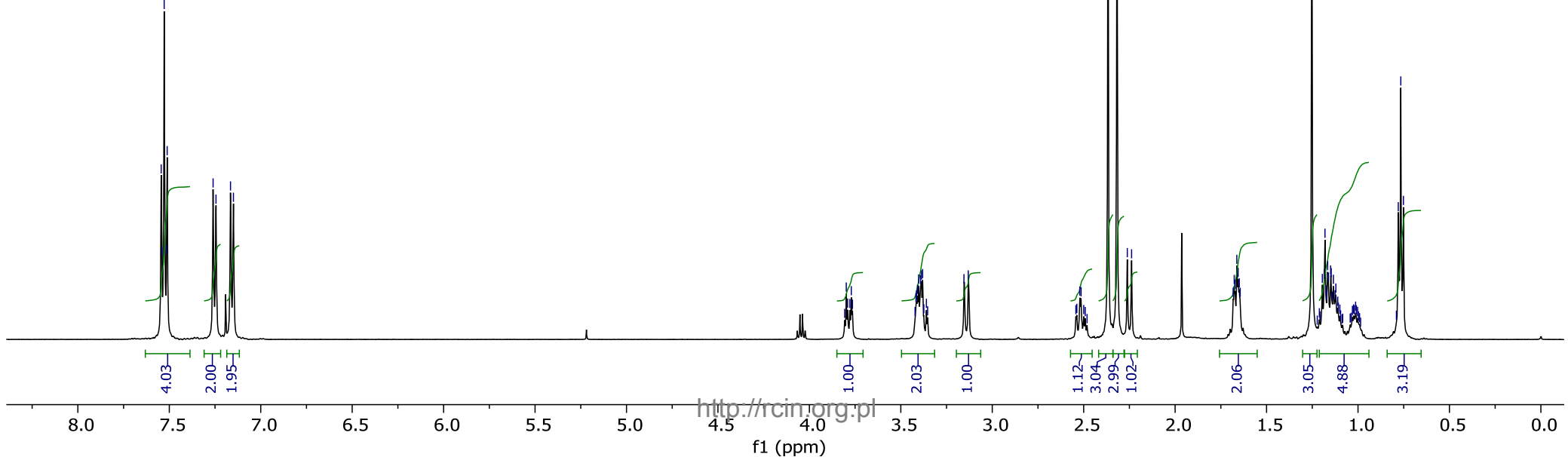


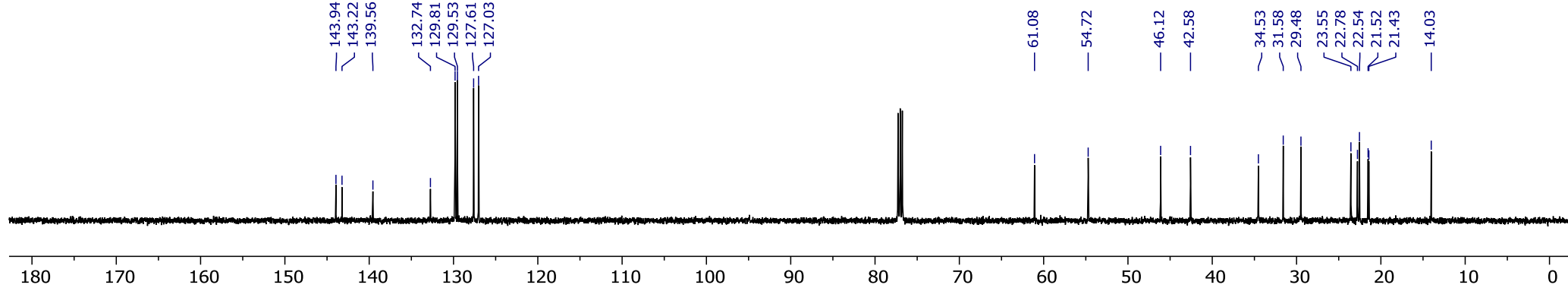






Compound 22a in CDCl<sub>3</sub>

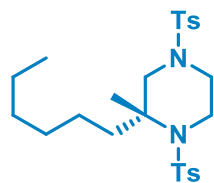




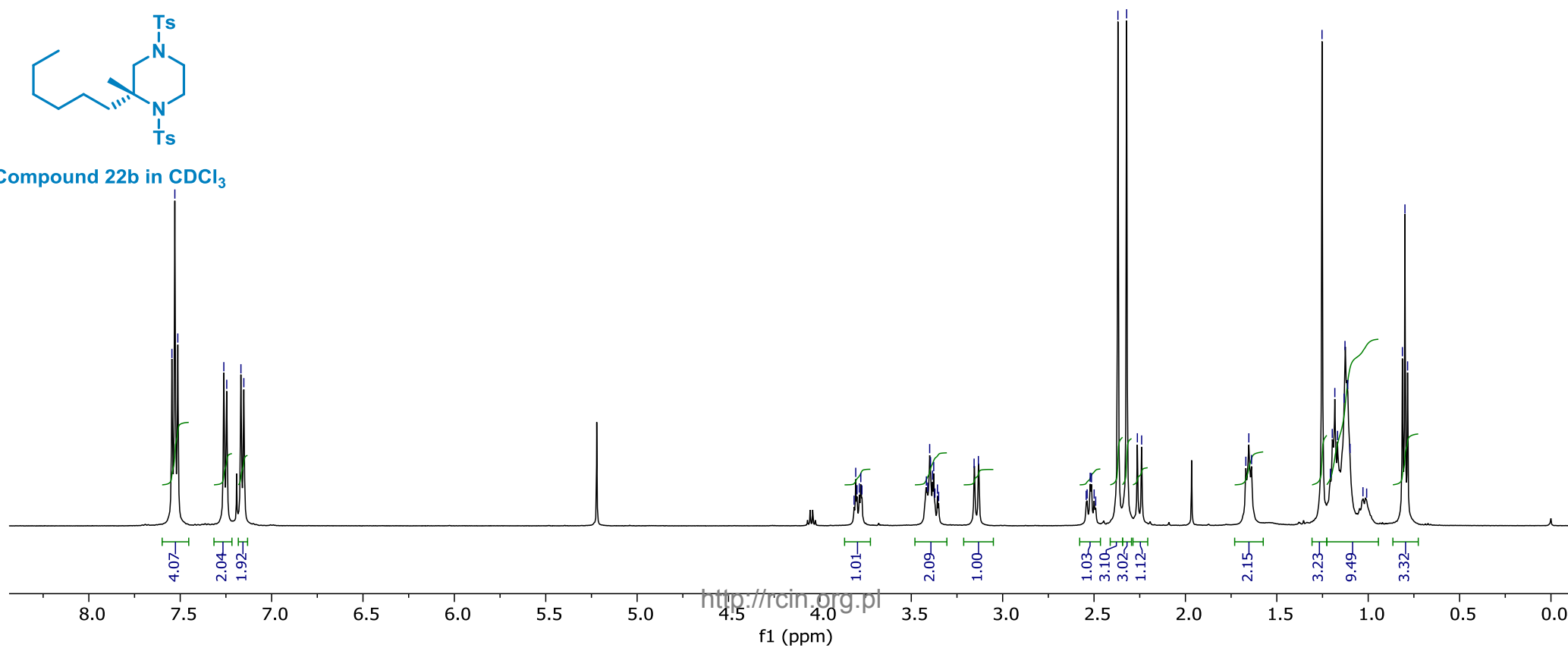
7.55  
7.53  
7.51  
7.26  
7.25  
7.17  
7.15

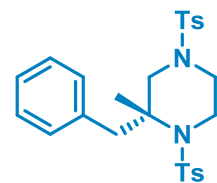
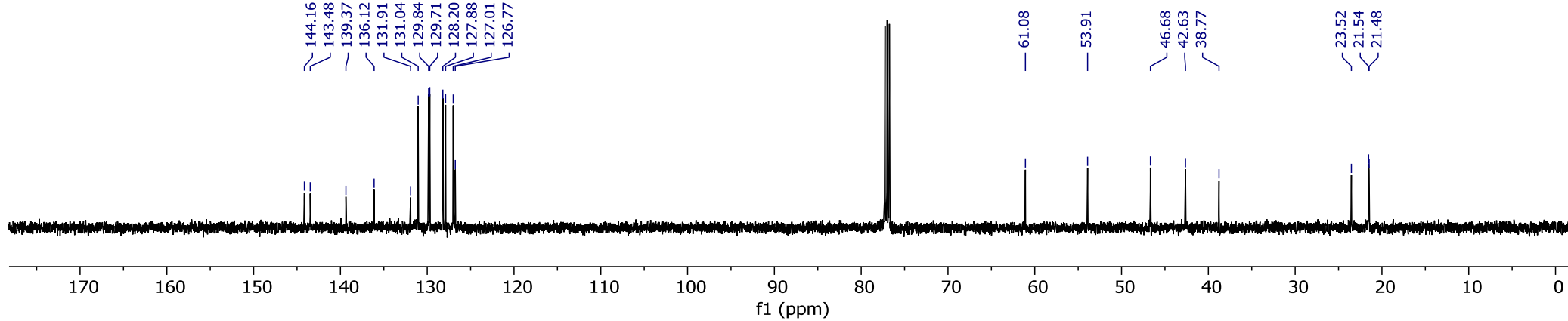
f1 (ppm)

3.81, 3.80, 3.80, 3.78, 3.78, 3.77, 3.42, 3.41, 3.40, 3.39, 3.38, 3.38, 3.37, 3.36, 3.35, 3.16, 3.13, 2.54, 2.54, 2.52, 2.51, 2.50, 2.49, 2.37, 2.32, 2.26, 2.24, 1.67, 1.65, 1.64, 1.25, 1.21, 1.20, 1.18, 1.17, 1.13, 1.13, 1.11, 1.10, 1.03, 1.01, 0.81, 0.80, 0.78

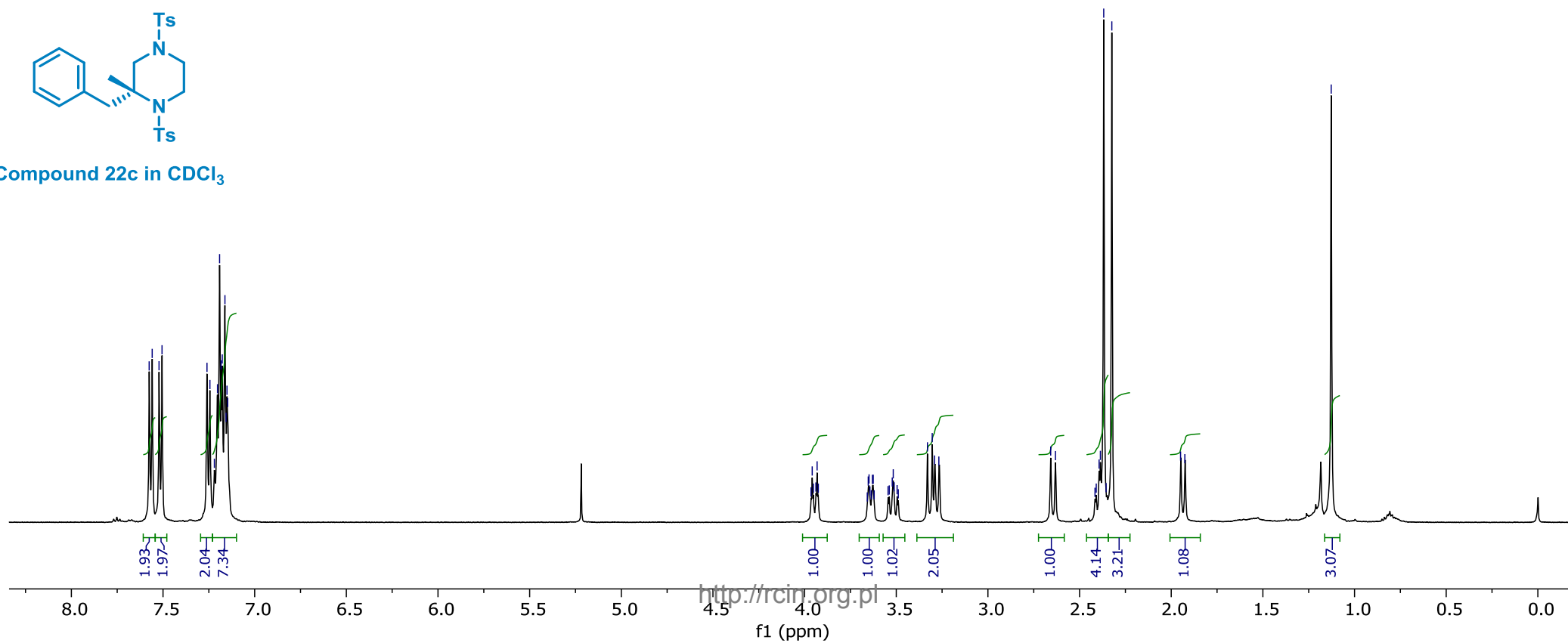


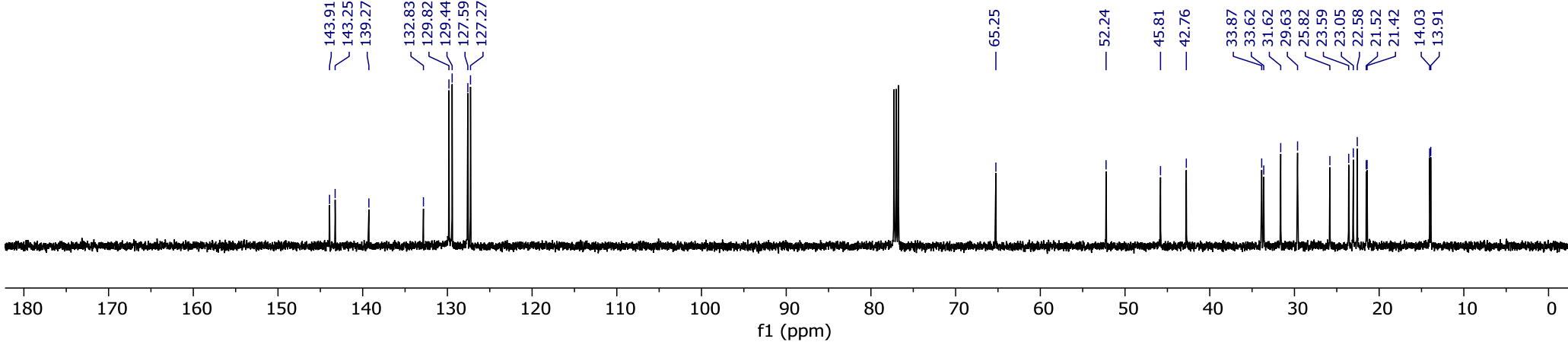
Compound 22b in CDCl<sub>3</sub>





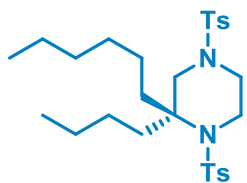
Compound 22c in CDCl<sub>3</sub>



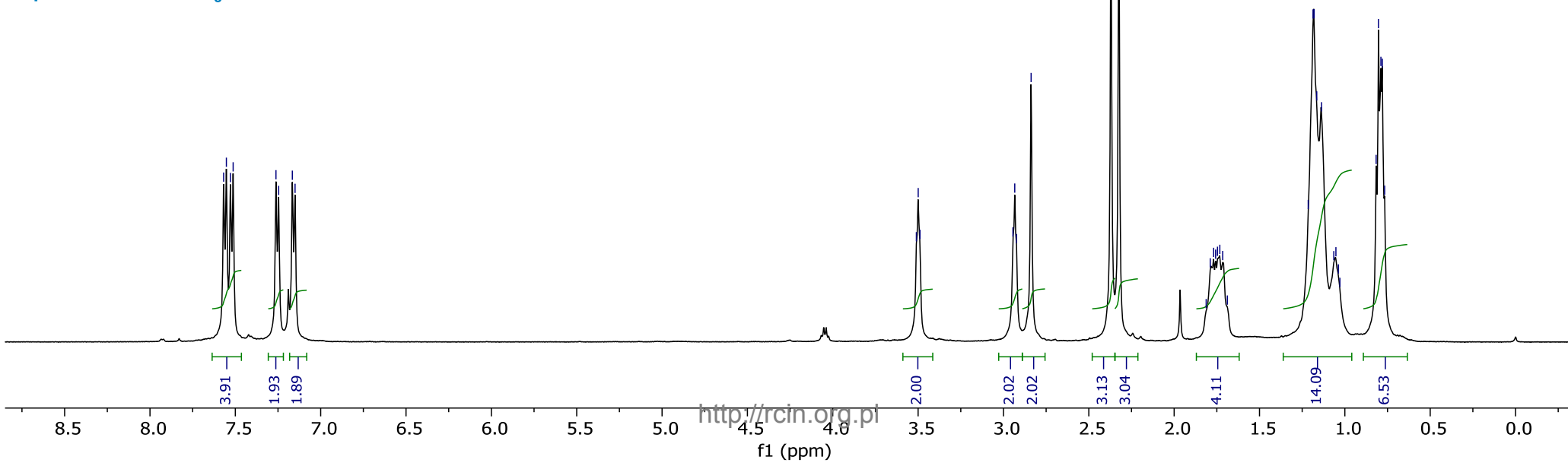


7.57, 7.55, 7.53, 7.51, 7.26, 7.25, 7.17, 7.15

3.51, 3.50, 3.49, 2.94, 2.93, 2.92, 2.84, 2.37, 2.32, 1.81, 1.79, 1.77, 1.76, 1.75, 1.73, 1.72, 1.69, 1.21, 1.19, 1.18, 1.16, 1.14, 1.06, 1.05, 1.04, 1.03, 0.82, 0.80, 0.79, 0.78, 0.77



Compound 22d in CDCl<sub>3</sub>



## **7. OŚWIADCZENIA WSPÓŁAUTORÓW PUBLIKACJI**



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Warszawa, dn. 22 czerwca 2020 r.

## OŚWIADCZENIE

Niniejszym oświadczam, że mój wkład w powstanie artykułów wchodzących w skład rozprawy doktorskiej:

1. M. Pieczykolan, A. Narczyk, S. Stecko, *The synthesis of chiral  $\beta,\beta$ -diaryl allylic alcohols and their use in the preparation of  $\alpha$ -tertiary allylamines and quaternary  $\alpha$ -amino acids*, *J. Org. Chem.* **2017**, *82*, 5636-5651,

był następujący: uczestniczyłam w opracowywaniu koncepcji badań oraz planowaniu eksperymentów, zsyntetyzowałam, wyizolowałam i zanalizowałam typowymi metodami spektralnymi ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS i IR) związki **6g-I**, **8**, **ent-10**, **11**, **12**, **ent-13** podane w publikacji. Zinterpretowałam uzyskane wyniki i uczestniczyłam w przygotowaniu manuskryptu.

2. A. Narczyk, M. Pieczykolan, S. Stecko, *The synthesis of non-racemic  $\beta$ -alkyl- $\beta$ -aryl-disubstituted allyl alcohols and their transformation into quaternary allylamines and amino acids*, *Org. Biomol. Chem.*, **2018**, *16*, 3921-3946,

był następujący: uczestniczyłam w opracowywaniu koncepcji badań oraz zaplanowałam eksperymenty, zsyntetyzowałam, wyizolowałam i zanalizowałam typowymi metodami spektralnymi ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS i IR) wszystkie związki podane w publikacji. Zinterpretowałam uzyskane wyniki i brałam udział w przygotowaniu manuskryptu.

3. A. Narczyk, S. Stecko, *The synthesis of unnatural  $\alpha$ -alkyl- and  $\alpha$ -aryl-substituted serine derivatives*, *Org. Biomol. Chem.*, **2020**, *18*, 1204-1213,

był następujący: uczestniczyłam w opracowywaniu koncepcji badań oraz planowaniu eksperymentów, zsyntetyzowałam, wyizolowałam i zanalizowałam typowymi metodami spektralnymi ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS i IR) wszystkie związki podane w publikacji. Zinterpretowałam uzyskane wyniki i uczestniczyłam w przygotowaniu manuskryptu.

4. A. Narczyk, S. Stecko, *An entry to enantiopure  $\beta$ -tertiary- $\beta$ -amino alcohols, building blocks for synthesis of aziridine, piperazine, and morpholine scaffolds* (w recenzji).

był następujący: uczestniczyłam w opracowywaniu koncepcji badań oraz planowaniu eksperymentów, zsyntetyzowałam, wyizolowałam i zanalizowałam typowymi metodami spektralnymi ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS i IR) wszystkie związki podane w publikacji. Zinterpretowałam uzyskane wyniki i uczestniczyłam w przygotowaniu manuskryptu.

Aleksandra Narczyk

Powyższy opis wkładu doktorantki w powstanie artykułów jest zgodny ze stanem faktycznym.

A handwritten signature in blue ink, reading "Sebastian Stecko". The signature is written in a cursive, flowing style.

Sebastian Stecko





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### OŚWIADCZENIE

Niniejszym oświadczam, że mój wkład w powstanie artykułów:

1. M. Pieczykolan, A. Narczyk, S. Stecko, *The synthesis of chiral  $\beta,\beta$ -diaryl allylic alcohols and their use in the preparation of  $\alpha$ -tertiary allylamines and quaternary  $\alpha$ -amino acids*, *J. Org. Chem.* **2017**, 82, 5636-5651;
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3. A. Narczyk, S. Stecko, *The synthesis of unnatural  $\alpha$ -alkyl- and  $\alpha$ -aryl-substituted serine derivatives*, *Org. Biomol. Chem.*, **2020**, 18, 1204-1213;
4. A. Narczyk, S. Stecko, *An entry to enantiopure  $\beta$ -tertiary- $\beta$ -amino alcohols, building blocks for synthesis of aziridine, piperazine, and morpholine scaffolds* (w recenzji).

polegał na opracowaniu koncepcji badań, prowadzeniu nadzoru merytorycznego nad realizacją projektu, uczestniczyłem także w analizie wyników eksperymentalnych oraz przygotowaniu tekstu publikacji.

Sebastian Stecko



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był następujący: uczestniczyłem w opracowywaniu koncepcji badań oraz planowaniu eksperymentów, zsyntetyzowałem, wyizolowałem i zanalizowałem typowymi metodami spektralnymi ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS i IR) związki **4**, **5**, **6a-f**, **9**, **10**, **13**, przedstawione w publikacji. Zinterpretowałem uzyskane wyniki i uczestniczyłem w przygotowaniu manuskryptu.

2. A. Narczyk, M. Pieczykolan, S. Stecko, *The synthesis of non-racemic  $\beta$ -alkyl- $\beta$ -aryl-disubstituted allyl alcohols and their transformation into quaternary allylamines and amino acids*, *Org. Biomol. Chem.*, **2018**, *16*, 3921-3946,

był następujący: uczestniczyłem w opracowywaniu koncepcji badań, planowaniu eksperymentów oraz interpretacji uzyskanych wyników związanych z syntezą alkoholi alilowych **2a**, **2n**, **2o**, **2p** (Tabela 1 w manuskrypcie) poprzez reakcję sprzęgania Negishiego. Uczestniczyłem w przygotowaniu manuskryptu.

Michał Pieczykolan



B. Org. 420/20

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