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❚ **Phase-Transfer Catalysis**

Interfacial Generation of a Carbanion: The Key Step of PTC Reaction Directly Observed by Second Harmonic Generation

Michal Hamkalo,*[a, b] Piotr Fita,[b] Michal Fedorynski,[c] and Mieczyslaw Makosza*[d]

Abstract: We present the first unambiguous evidence of the interfacial mechanism of phase-transfer catalysis (PTC) by direct observation of the formation of carbanions in the interfacial region between the aqueous and the organic phase by using a surface-sensitive spectroscopic method known as second harmonic generation (SHG). Ion exchange of carbanions adsorbed at the surface after addition of lipophilic tetraalkylammonium salts (TAA) to organic phase and transport of the lipophilic ion-pairs to the organic phase is observed. Results allow for the formulation of a more detailed mechanism of PTC.

Phase-transfer catalysis (PTC) is a general methodology for organic reactions that proceed between anionic species and non-charged lipophilic partners.[1] The PT catalyzed reactions are usually carried out in two immiscible liquid–liquid phase systems (organic and aqueous) or liquid–solid systems. The catalytic process consists of a continuous formation of the ion pairs of the lipophilic cations of the catalyst, usually tetraalkylammonium (TAA) cations, with the reacting anionic species. These species can be inorganic anions initially dissolved in an aqueous phase as sodium or potassium salts or organic anions—for example, carbanions—generated by deprotonation of appropriate precursors by aqueous solution of sodium hydroxide. Particularly valuable are PTC reactions of carbanions generated by action of saturated aqueous sodium hydroxide on a variety of C–H acids.[1] For many years, two alternative mechanisms of PTC were considered: the extraction mechanism proposed by Starks,[2] according to which TAA cations

continuously transfer inorganic anions from the aqueous into the organic phase in which further reactions take place, and the interfacial mechanism proposed by Makosza for reactions of carbanions,[1a,b] in which the key step is deprotonation of the carbanion precursors in the interfacial region with the aqueous sodium hydroxide. The subsequent ion exchange with the TAA salts in the interfacial region produces lipophilic ion pairs that migrate into the organic phase where further reactions take place.

The initially speculative interfacial mechanism of PTC was supported experimentally by studies of concentration changes, of stereochemical outcomes of reactions, the isotope exchange studies and other criteria.[3] Subsequently, the unified interfacial mechanism was formulated.[4] The key steps of both variants of PTC take place at the phase boundary (interfacial region), in which the ion exchange between the organic phase containing the TAA salts of the catalyst and the inorganic salts dissolved in water takes place. Similarly deprotonation of CH acids (and other weak organic acids) by aqueous NaOH solution and ion-exchange with interfacially generated carbanions takes place to form lipophilic ion pairs that are transferred to the organic phase.

Recently, an interesting analysis of the rate limiting steps of PTC alkylation of carbanions based on the interfacial mechanism was published.[5] A direct observation of carbanions adsorbed at the phase boundary would provide the final confirmation of the interfacial mechanism of PTC reactions of these species. Such observations so far were not reported, because of lack of adequate spectral methods that could distinguish between species in solution and species adsorbed on the liquid phase boundary.

In this paper, we report first direct observation of carbanions generated at the interface between organic solvents (chlorobenzene, toluene) and aqueous solutions of strong bases, in particular 50% $NaOH_{(aq.)}$, using a surface sensitive spectroscopic method, second harmonic generation (SHG).

SHG is a well-established surface-sensitive spectroscopic technique.[6–12] In this method, the surface between two immiscible liquids is illuminated with intense laser pulses (more details are given in the supporting information), which results in nonlinear generation of light with twice the frequency (half the wavelength) of the incident wave, the second harmonic (SH) light. Only molecules located in the interfacial region affect this process because SH generation is forbidden in bulk liquid due to symmetry reasons.[7] The maxima of SHG spectra (defined here as a dependence of the maximum of the SH generation yield on half of the wavelength of the incident

[a] M. Hamkalo
Institute of Physical Chemistry, Polish Academy of Sciences
Kasprzaka 44/52, 01-224 Warsaw (Poland)
E-mail: mhamkalo@ichf.edu.pl

[b] M. Hamkalo, Dr. P. Fita
Institute of Experimental Physics, Faculty of Physics
University of Warsaw, Pasteura 5, 02–093 Warsaw (Poland)

[c] Prof. M. Fedorynski
Department of Chemistry, Warsaw University of Technology
00-661 Warsaw (Poland)

[d] Prof. M. Makosza
Institute of Organic Chemistry, Polish Academy of Sciences
Kasprzaka 44/52, 01-224 Warsaw (Poland)
E-mail: mikem@icho.edu.pl

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light) for each species adsorbed at the surface are located at similar wavelengths as the maxima of electronic absorption spectra of these species in solution. It is thereby possible to selectively probe species adsorbed at the surface by tuning the incident beam to match electronic spectra of particular molecules. The intensity of the generated SH light is proportional to the square of the surface concentration of molecules contributing to the process and to the square of the incident light intensity, which can be expressed by Equation (1):

$$I(2\omega) \quad \sim \quad C_{surf}^2 \bullet I^2(\omega) \tag{1}$$

in which $I(2\omega)$ is the intensity of the second harmonic signal, $I(\omega)$ is the intensity of the fundamental beam, and C_{surf} is the surface concentration of contributing molecules. Therefore, changes in the surface concentration of a selected species can be monitored by measurements of SH light intensity. This concept has been proved in the previous work, in which reliable detection of thymolphthalein anions and measurements of their concentration at the boundary between organic (chlorobenzene) and aqueous (50% NaOH solution) phases was demonstrated.[10]

In this work we aimed to record SHG spectra of carbanions at the surface by appropriately tuning the incident beam and to obtain results which would verify formation of carbanions in the interfacial region, the key process in most of PTC chemical reactions.

Arylacetonitriles were most often used as the carbanion precursors in studies of interfacial generation and reactions of carbanions.[3] However, in the preliminary experiments we have found that phenylacetonitrile and 2-phenylpropionitrile were unsuitable for our purpose, because their carbanions are insufficiently stable and their optical properties are not tailored to the experimental system. Looking for a proper model carbanion precursor we have found, after some experimentation, that p-nitrobenzyl phenyl sulfide 1 has the appropriate CH acidity and forms carbanions of sufficient stability that have the absorption spectrum well matched to our experimental setup. For studies of the interfacial ion-exchange and migration of the lipophilic ion-pairs, we selected two tetraalkylammonium salts (TAA): tetrapropylammonium bromide 2, and trioctylmethylammonium bromide 3. It should be mentioned that 2 and 3 have different lipophilicity defined as the number of carbon atoms. Compound 2, having $\Sigma C = 12$ was much less lipophilic than 3, ($\Sigma C = 25$). For all experiments chlorobenzene was used as the organic phase (Figure 1).

The experiments were carried out in a cubic glass cuvette, first filled with the aqueous phase, onto which the organic solution was carefully poured. Measurements were started after the system stabilized mechanically and the interface was
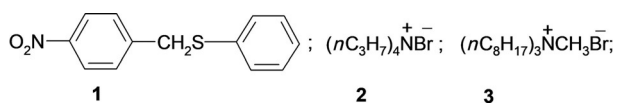
smooth and motionless. Exposure of a 0.01 M solution of 1 in chlorobenzene to 50% NaOH(aq.) did not result in any visible changes. The absorption spectra of the solution before the exposure and a few minutes after the exposure were identical and show the spectrum of neutral 1, indicating that the sodium salt of the carbanion was not transferred into the organic phase. However, when such two-phase system was illuminated by the laser beam, a second harmonic (SH) signal at a range of 510–525 nm of substantial intensity was detected indicating that the carbanion molecules derived from 1 were generated at the interface (Figure 2). It should be mentioned
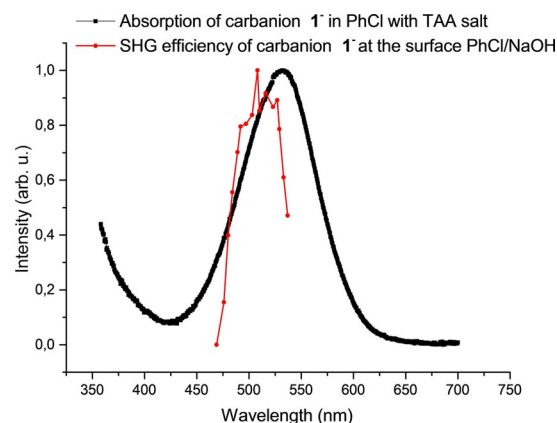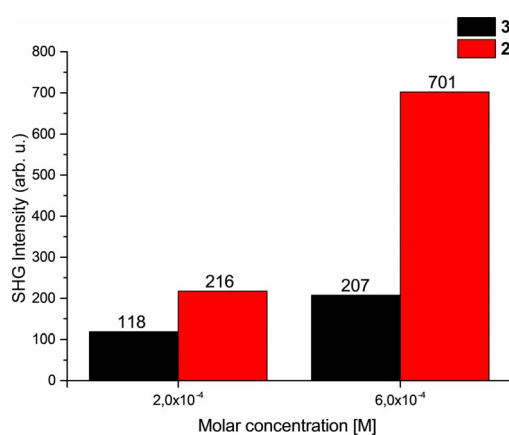
Figure 2. Absorption spectrum of the carbanion 1^- in chlorobenzene (PhCl, black line) compared with the SHG spectrum (red line) recorded at the chlorobenzene/NaOH(aq.) interface with 1 dissolved in the organic phase. Maxima of both spectra are close enough to each other to conclude that the carbanion 1^- is present at the interface.

that the illumination of the two-phase system comprising pure chlorobenzene and 50% (by weight) aqueous sodium hydroxide did not result in the observation of any SH signals. The separately prepared carbanion 1 in the form of tetrapropylammonium salt in chlorobenzene had the absorption maximum at 525 nm. Solution of 1 in chlorobenzene exposed to 50% NaOH(aq.) was colorless for a long time, but upon addition of a TAA salt, it gradually became colored due to interfacial formation of soluble ion-pairs TAA$^+1^-$ that migrated into the organic phase. Absorption spectra of such solution after separation of the organic phase revealed a strong absorption at 520 nm (Figure 2) due to the carbanion 1^-. In this way, the identity of anionic species detected by SHG on the phase boundary as sodium salt of 1^- was confirmed. Thus, carbanions generated at the liquid–liquid phase interface were observed spectroscopically for the first time.

In the next set of experiments, a given amount of 2 and 3 (20 μL) of 0.01 M solution in chlorobenzene was introduced on the top of the organic phase during SHG measurements. We observed that such addition resulted in the slow coloration of the organic phase and in enhancement of the SH signal (Figure S5 in the Supporting Information), indicating an increase of the interfacial concentration of the carbanion.

The signal that reflects an increase of a surface concentration of the carbanion had a direct connection to the type of

Figure 1. Model carbanion precursor 1 and TAA salts 2, 3 selected for optical studies of carbanions formation and transport.

the added salt. Addition of the less lipophilic salt **2** resulted in a larger increase of the SH signal (this corresponded to the higher concentration of the carbanion in the interfacial region). It should be noted that in the motionless two-phase systems transfer of the TAA salts added at the top of the organic phase to the phase boundary proceeds by diffusion. Considering that there are fluctuations of concentration due to the Brown movements when the SH signal is collected from small surface fragments, there are small fluctuations of intensity particularly during high sensitivity measurements. To compare the enhancement of the SH signal by TAA salts of different lipophilicity not affected by such fluctuations due to diffusion the salts were dissolved in the solution of **1** before exposing it to the NaOH solution. Comparison of the intensity of the SH signal in these systems is shown in Figure 3

Figure 4. The equilibrium of carbanion generation and behavior at the interface between two phases based on experimental results.

Figure 5. The equilibrium processes at the interface after addition of catalyst (TAA salt) based on experimental results.
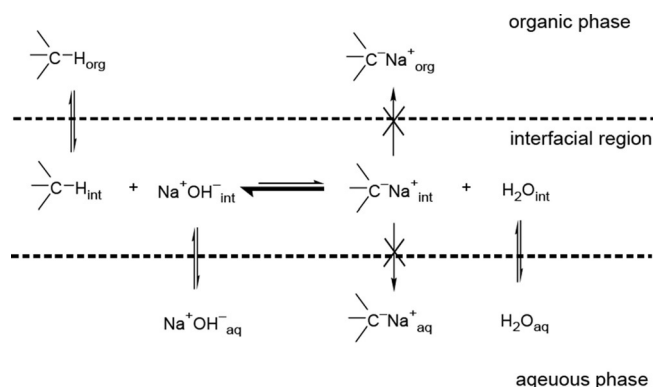
Figure 3. SH light intensity measured with two different concentrations of **1** in chlorobenzene over 50% NaOH aqueous solution and less (**2**) and more (**3**) lipophilic TAA salts added to the organic phase.
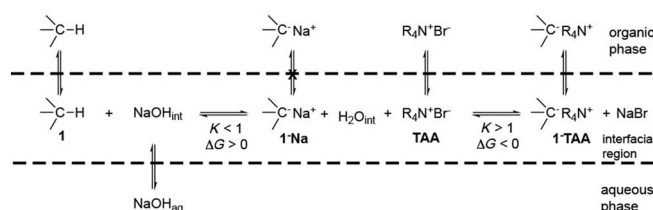
Based on these results we propose the following mechanism of phase transfer catalysis. In the two-phase system (aqueous NaOH and an organic phase) carbanions are generated (and stay) only in the interfacial region. Their surface concentration is relatively low but detectable (the equilibrium of the surface reaction is shifted to the left side), furthermore, they cannot migrate into either the organic or into the aqueous phase. This is usually the first step of a PT catalyzed reaction (Figure 4).

In the second step of the PTC process the catalyst, that is, the TAA salt enters into an ion exchange with the carbanions (associated with the sodium cations) adsorbed at the surface that results in the formation of lipophilic ion pairs of **1**$^-$ with TAA cations (Figure 5). This process shifts the deprotonation equilibrium to the right, because the hydration energy of TAA cations is much weaker than of sodium cations.

Considering that diffusional transfer of the lipophilic ion-pairs from the interfacial region into solution is slower than the abstraction of the proton from **1**, the addition of **2** and **3** to the system results not only in migration of the ion-pairs into solution (indicated by the coloration of the organic phase) but also in the increase of the SH signal. The migration of the less lipophilic ion-pairs into the solution is slower, therefore

the interfacial concentration of the carbanions upon addition of **2** is higher than upon addition **3**. To confirm this reasoning, we studied interfacial formation of carbanions with the hydrophilic tetramethyl ammonium hydroxide. Density of the commercial 40% aqueous solution of Me$_4$N$^+$OH$^-$ (TMA) was lower than chlorobenzene and the ion-pair **1**$^-$ Me$_4$N$^+$ was somewhat soluble in this solvent. Therefore, to create a two-phase system with a proper phase boundary, we used toluene as the organic phase. For comparison the SH signal of **1**$^-$ in the two-phase system toluene, 50% aqueous NaOH was also determined. The results are shown in Figure 6.

Measurements of the intensity of the SH signal in the two-phase system comprising a solution of **1** in toluene and 40% Me$_4$N$^+$OH$^-$ or 50% NaOH$_{(aq.)}$ gave surprising results. Basicity of OH$^-$ in aqueous solutions is a function of hydration. In the 50% aqueous solution of NaOH (ca. 12.5 м), there is approximately one molecule of water for each ion (Na$^+$ and OH$^-$). On the other hand, in the 40% solution of Me$_4$N$^+$OH$^-$ (ca. 3.6 м), there are approximately 3 molecules of water for each ion. One should therefore expect that the basicity of the OH$^-$ anions in the TMA solution should be lower than in 50% aq. NaOH, hence interfacial concentration of **1**$^-$ anions in the former case should be lower than in the case of NaOH solution, whereas, as shown in Figure 6, it is just the opposite. It appears therefore that the factor deciding on interfacial concentration of **1**$^-$ is mostly energy of hydration of cations, which is much lower for Me$_4$N$^+$ than Na$^+$. In the interfacially located ion-pairs, the cations should be partially dehydrated which is energetically more favorable for Me$_4$N$^+$ cations. This reasoning is supported by the observation that the intensity of
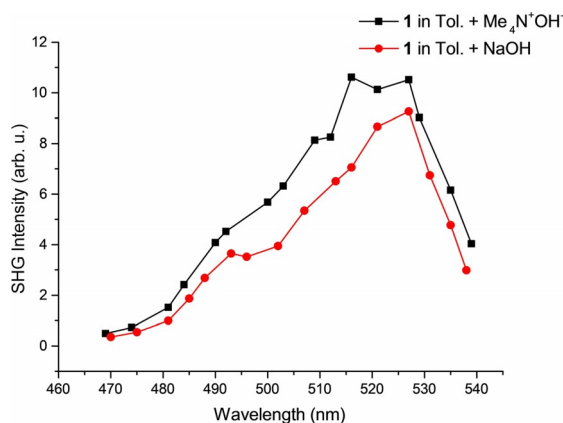
Figure 6. Comparison of SHG spectra recorded in the system consisting of **1** in toluene over different aqueous phases: 50% NaOH$_{(aq.)}$ (red) and 40% TMA$_{(aq.)}$ (black).

the SH signal in the system comprising solution of **1** in chlorobenzene with 50% aq. NaOH is weaker than with 60% aq. KOH of similar molarity (Figure 7).
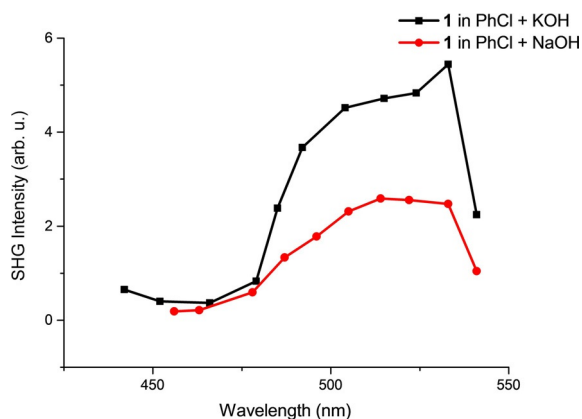
Figure 7. Comparison of SHG spectra recorded in the system consisting of **1** in chlorobenzene over different aqueous phases: 50% NaOH$_{(aq.)}$ (red) and 60% KOH$_{(aq.)}$ (black).

Hydration energy of Me$_4$N$^+$ cations (-208 kJ mol^{-1})[13] is much weaker than hydration energy of Na$^+$ cations (-416 kJ mol^{-1})[13] hence the interfacial location of the ion-pairs **1**$^-$Me$_4$N$^+$ is much more favorable than **1**$^-$Na$^+$ in spite of the lower concentration of OH$^-$ anions in the former solution. Similarly, the hydration energy of potassium cation (-334 kJ mol^{-1})[13] is weaker than of sodium cation, hence the interfacial concentration of **1**$^-$K$^+$ in the system comprising solution of **1** in chlorobenzene with 60% KOH is higher than with 50% NaOH. Both of these solutions are of similar molarity. This conclusion is in agreement with many observations that aqueous KOH in the PTC generation of carbanions is more efficient than aqueous NaOH.[16] From these results one can conclude that the effectiveness of interfacial generation of carbanions is strongly affected by energy of hydration of the cations associated with hydroxide anions in the aqueous phase. Further ion-exchange of interfacially located carbanions with lipo-

philic TAA salts results in the formation of the lipophilic ion-pairs that migrate into the organic phase. Effects of the structure and lipophilicity of these salts on the rates of ion-exchange and the migration need further studies.

We have shown that the surface-sensitive second harmonic generation spectroscopy is an efficient tool for observation of interfacially generated carbanions. Using this spectral method, we have confirmed that in the two-phase system of 50% aq. NaOH and a solution of the carbanion precursor in a nonpolar solvent, carbanions are indeed generated, stay at the interface and their spectra can be recorded. Furthermore, we have shown that using this spectral technique, we can observe the interfacial ion-exchange. We have also observed that effectiveness of interfacial deprotonation of CH acids and concentration of carbanions is strongly affected by energy of hydration of the cations associated with OH$^-$ anions in the aqueous phase. For instance, aqueous KOH is more efficient than NaOH. Introduction of the catalyst results in an interfacial ion-exchange followed by migration of the lipophilic ion-pairs into the organic phase and shifts the interfacial acid-base equilibrium so the concentration of carbanions at the interface becomes higher. Moreover, we have demonstrated that the less lipophilic the catalyst is, the higher the interfacial concentration of the carbanions. The results provided direct confirmation of the interfacial mechanism of PT catalyzed reactions of carbanions, the methodology widely used in chemical synthesis which still remains a target of modern research.[14]

Experimental Section

p-Nitrobenzyl phenyl sulfide **1** was obtained according to the literature.[13] Tetraalkylammonium salts, chlorobenzene, toluene, and all bases used in the experiments were commercial and used without purification.

A scheme of the experimental system is shown in Figure 8. The incident laser beam is generated by a tunable femtosecond optical parametric amplifier (Coherent Opera Solo) seeded by a 5 kHz repetition rate Ti:Sapphire femtosecond system (Coherent Legend Elite Duo). The beam is focused onto the interface between the organic and aqueous phases. The generated second harmonic beam is filtered from the fundamental light and directed to a monochro-
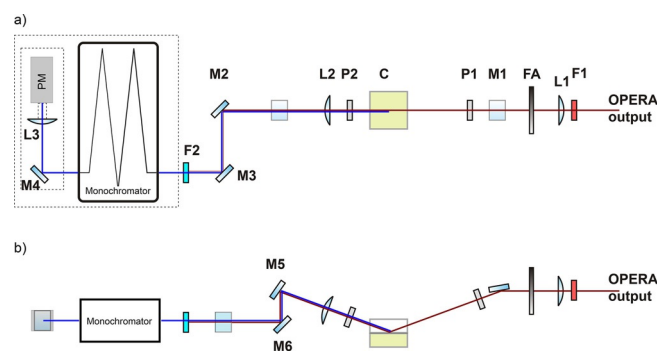
Figure 8. a) Simplified top view of the experimental setup for SHG measurements: F1, long pass filter; L1-L3, lenses; FA, adjustable neutral density filter; P1, P2, polarizers; C, sample cell; M1-M6, mirrors; F2, short pass filter; PM, photomultiplier; b) side view of the same setup.

mator. The output of the monochromator is coupled to a photo-multiplier module (Hamamatsu H9305-04) connected to a lock-in amplifier synchronized with the repetition frequency of the laser. Details of the setup are presented in the Supporting Information and reference [10].

All SHG experiments were carried out in a cubic glass cuvette ($3 \times 3 \times 3$ cm^3). A solution of the appropriate base (3 mL) was first poured into the cuvette and subsequently a solution of **1** in chlorobenzene or toluene (5 mL) was carefully added on top of the aqueous phase. The sample was ready for measurements after 1–2 min, when the system attained mechanical equilibrium. In selected experiments small amounts of TAA salts **2**, **3** dissolved in chlorobenzene were instilled into the organic phase either before or after it was poured onto the aqueous phase.

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Conflict of interest

The authors declare no conflict of interest.

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