Phase-Transfer Agents as Catalysts for a Nucleophilic Substitution Reaction in Microemulsions

Maria Häger*[a, c] and Krister Holmberg[b]

Abstract: The reaction between 4-*tert*-butylbenzyl bromide and potassium iodide was carried out in microemulsions based on different nonionic surfactants, and the reaction rates were compared with those obtained in two-phase systems with added phase-transfer agent, either a quaternary ammonium salt or a crown ether. The reactions were relatively fast in the microemulsions and extremely sluggish in the two-phase systems without additional phase-transfer agent. Addition of a phase-transfer agent did not accelerate the reaction when a hydrocarbon was used as organic solvent, neither in the two-phase system nor in the microemulsion. When a chlorinated hydrocarbon was used as solvent, phase-transfer catalysis became effective and the rate obtained in the two-phase system with an equimolar amount of phase-transfer agent added was higher than that obtained in the microemulsion. When a catalytic amount of phase-transfer agent was used, the rate in the two-phase system was about the same as the rate obtained in the microemulsion without the phase-transfer agent. The combined approach, that is, use of a microemulsion as the reaction medium and addition of a phase-transfer agent, gave the highest reaction rate. The quaternary ammonium salt (tetrabutylammonium hydrogen sulfate) was a more efficient catalyst in the microemulsion system than the crown ether ([18]crown-6).

Keywords: kinetics · microemulsion · nucleophilic substitution · phase-transfer catalysis

Introduction

For a chemical reaction to proceed it is necessary that the reacting species can enter into intimate contact. Most reactions are therefore carried out in homogeneous solutions. However, when the solubility characteristics of the reactants are very different, it may be difficult to find a common solvent for the reacting species. This is, for instance, often the case when ionic species are to react with nonpolar organic compounds. For such and many other cases, polar aprotic solvents, such as DMSO and DMF, offer a simple and efficient solution to the incompatibility. Not only are these liquids excellent solvents, the reactivity when it comes to reactions involving a nucleophilic attack is often high, because the ionic reactant is only slightly solvated in these solvents and consequently obtains a high nucleophilicity. However, for toxicity and price reasons these solvents are unsuitable for large-scale operations. An alternative approach is to use a two-phase system consisting of water and a water-immiscible organic solvent. The incompatible reactants dissolve in the different phases, that is, the ionic reactant in the aqueous phase and the organic compound in the organic phase, and the reaction can take place at the interface between the two phases. The disadvantage with this approach is that the interface is small, which usually causes low reaction rate. Phase-transfer catalysis (PTC) can dramatically improve the situation. In PTC a phase-transfer agent (PTA), usually a quaternary ammonium or phosphonium salt (Q salt) or a crown ether, is added to the two-phase system. These PTAs have the ability to carry the ionic reactant into the organic phase. Once in the organic phase, the reactant becomes highly reactive because the degree of solvation is low; thus, the anion behaves like a 'naked' ion. The choice of organic solvent is often crucial for good extraction efficiency and high nucleophilicity. The best solvents for PTC are those that are aprotic and slightly polar. Chlorinated hydrocar-

---

[a] Dr. M. Häger
Institute for Surface Chemistry
P.O. Box 5607, 114 86 Stockholm (Sweden)
Fax: (+46) 820-8998
E-mail: maria.hager@surfchem.kth.se
maria.hager@chemeng.ntnu.no

[b] Prof. K. Holmberg
Chalmers University of Technology
Department of Materials and Surface Chemistry
412 96 Göteborg (Sweden)
Fax: (+46) 31-160062
E-mail: kh@chem.chalmers.se

[c] Dr. M. Häger
Norwegian University of Science and Technology
Ugelstad Laboratory, Department of Chemical Engineering
7491 Trondheim (Norway)
Fax: (+47) 7359-4080

DOI: 10.1002/chem.200306048

bons, such as dichloromethane and chloroform, are commonly used for this purpose.

Use of a microemulsion as the reaction medium constitutes an alternative to PTC.[1–7] A microemulsion is a thermodynamically stable mixture of water, oil (organic solvent) and surfactant, with the surfactant forming a monolayer that separates the oil and water domains. The curvature of the surfactant film depends on various parameters, such as component (water, oil and surfactant) ratio, temperature and salt concentration. A microemulsion may consist of closed oil domains in water or closed water domains in oil, or it may be bicontinuous, that is, it may contain at the same time continuous oil and water domains. All interfaces are covered by surfactant. The domains are very small, in the nanometer range, which leads to a very large total interfacial area at which the reactants can collide and react.

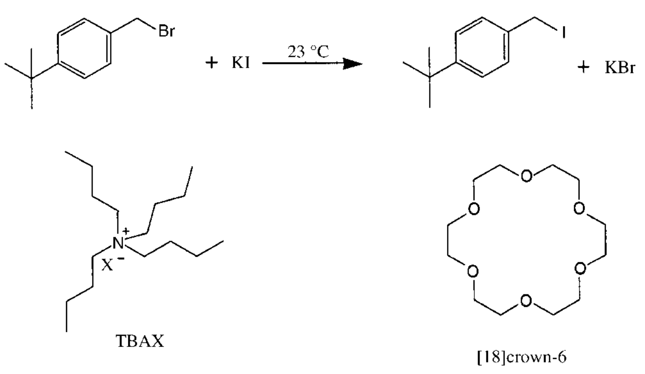
The use of a two-phase system with added PTA and the use of a microemulsion are two alternatives to overcome reagent incompatibility problems in organic synthesis. Both routes have proven useful, but on entirely different accounts. In PTC, the ionic reactant is carried into the organic phase, in which it becomes highly reactive. In the microemulsion approach there is no transfer of reactant from one environment to another; the method relies on the creation of the very large oil–water interface at which the reaction occurs.

In this paper we report results from an attempt to combine the two approaches, that is, using a microemulsion as reaction medium in presence of a PTA. There are only a few reports in the literature on the use of PTAs in combination with microemulsions and none of these have dealt with the issue in a systematic way.[8–9] However, the effect of PTAs in micelles and macroemulsions have been studied in some detail by Battal and co-workers.[10–11] We here show that PTC can indeed be used to accelerate microemulsion-based reactions and we believe that the results presented offer great promise for use of the combined approach in preparative organic chemistry.

Results

The reaction: The reaction studied is a typical nucleophilic substitution involving a lipophilic organic compound and an inorganic salt: the reaction between 4-*tert*-butylbenzyl bromide (4-TBBB) and potassium iodide (KI) (Scheme 1). We have previously investigated this reaction in some detail using both microemulsions and surfactant liquid crystals as reaction media, and we have shown that the reaction proceeds well in such microheterogeneous systems.[12–13] We have also performed the reaction in a range of organic solvents with different polarity (and without surfactant), and by comparing the reaction rates obtained in the different solvents we have been able to establish that the mechanism is that of a second-order nucleophilic substitution reaction.

Phase behaviour: The ternary system D_2O/decane/$C_{12}E_5$ has previously been thoroughly investigated by Olsson and co-workers.[14–18] An L1 phase (oil-in-water microemulsion) exists between 23 and 29 °C. Below 23 °C there is a two-phase area with an L1 phase coexisting with oil (a so-called Winsor I system). Above 29 °C a lamellar liquid crystalline phase (L_α) appears. Addition of the organic reactant, 4-TBBB, moves the L1 region to lower temperatures, as is shown in Figure 1. On the other hand, adding KI or a PTA moves the L1 region to slightly higher temperatures, which is shown in Figure 2.



Scheme 1. Top: Nucleophilic substitution reaction between 4-TBBB and KI. Bottom: Structures of TBAB (X = Br), TBAHS (X = HSO_4) and [18]crown-6.

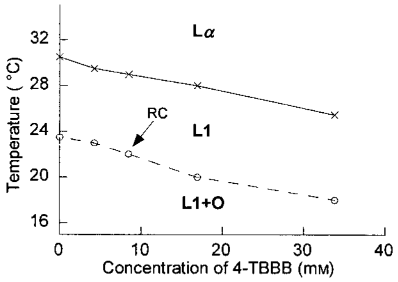


Figure 1. Phase diagram of the ternary $D_2O/C_{12}E_5$/decane system in presence of 4-TBBB. The weight ratio between oil and surfactant is 48/52 and the total weight fraction of oil + surfactant is 0.2. Raising the temperature gives a transition from an oil-in-water microemulsion in equilibrium with excess oil (L1 + O phase) to an oil-in-water microemulsion (L1 phase) and on to a lamellar liquid crystalline phase (L_α phase). The arrow indicates the reaction composition (RC).

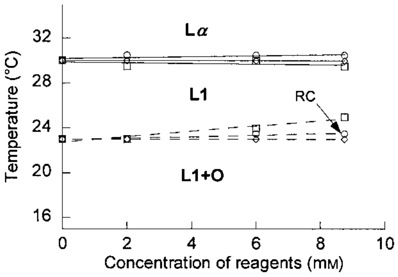


Figure 2. Phase diagram of the ternary $D_2O/C_{12}E_5$/decane system in presence of KI (○), TBAHS (□) and [18]crown-6 (◇). The weight ratio between oil and surfactant is 48/52 and the total weight fraction of oil + surfactant is 0.2. Raising the temperature gives a transition from an oil-in-water microemulsion in equilibrium with excess oil (L1 + O phase) to an oil-in-water microemulsion (L1 phase) and on to a lamellar liquid crystalline phase (L_α phase). The arrow indicates the reaction composition (RC). Addition of the second reactant, 4-TBBB induces a downward slope of both the upper and the lower phase boundary curves (see Figure 1). Thus, the reaction composition lies within the one-phase region in all cases.

The phase behaviour of the system $D_2O/C_{12}E_5$/cyclohexane was characterised and a partial phase diagram is shown in Figure 3. An L2 phase (water-in-oil microemulsion) was found in the oil-rich corner of the ternary phase diagram at 23 °C.

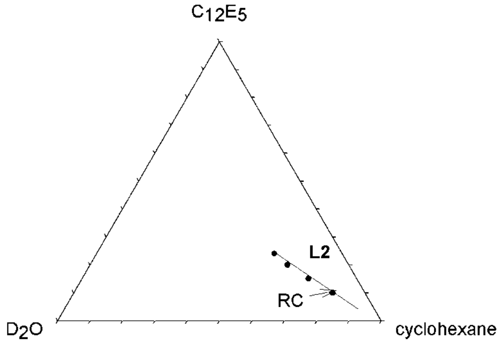


Figure 3. Partial phase diagram of the ternary $D_2O/C_{12}E_5$/cyclohexane system at 23 °C. A water-in-oil microemulsion region (L2 phase) exists in the oil-rich corner of the diagram. The arrow indicates the reaction composition (RC).

The ternary system D_2O/dichloromethane/C_8G_1 at a constant volume fraction of oil based on oil and water (0.5) has been investigated by Egger and co-workers.[19] The phase diagram is dominated by a large bicontinuous microemulsion region, starting at a surfactant weight fraction of 0.2, as is illustrated in Figure 4. The phase diagram was not markedly affected by addition of the two reactants or of a PTA.

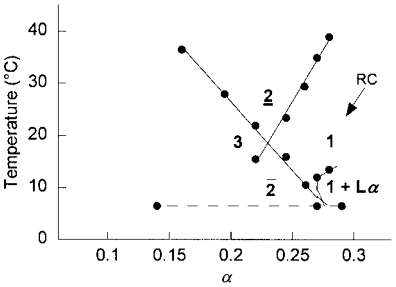


Figure 4. Phase diagram of the ternary $D_2O/C_8G_1/CH_2Cl_2$ system. α is the surfactant weight fraction. The volume fraction of oil to water + oil is 0.5. At low surfactant concentration a three-phase region (3) exists. On increasing the surfactant concentration either an oil-in-water microemulsion in equilibrium with oil ($\underline{2}$) or a water-in-oil microemulsion in equilibrium with water ($\bar{2}$) forms depending on the temperature. At even higher surfactant concentration a one-phase microemulsion (1) appears. At higher concentration and a temperature lower than 15 °C a two-phase region consisting of microemulsion and a lamellar liquid crystalline phase (1 + L_α) is observed. (Redrawn from Ref. [19].) The arrow indicates the reaction composition (RC).

Reaction kinetics: The reaction was monitored by ^{1}H NMR spectroscopy, following the rise of the $-CH_2I$ signal and the decay of the $-CH_2Br$ signal, as described in the Experimental Section and illustrated by Figure 5. The reaction profiles for the reactions in the $D_2O/C_{12}E_5$/decane microemulsion and in the D_2O/decane two-phase system are shown in Figure 6. As can be seen, the reaction runs well in the microemulsion, while in the two-phase system almost no product was formed after 24 h reaction. Addition of an equimolar amount of PTA (tetrabutylammonium hydrogen sulphate (TBAHS), tetrabutylammonium bromide (TBAB) or [18]crown-6) gave no effect, neither on the two-phase reaction nor on the reaction in microemulsion.

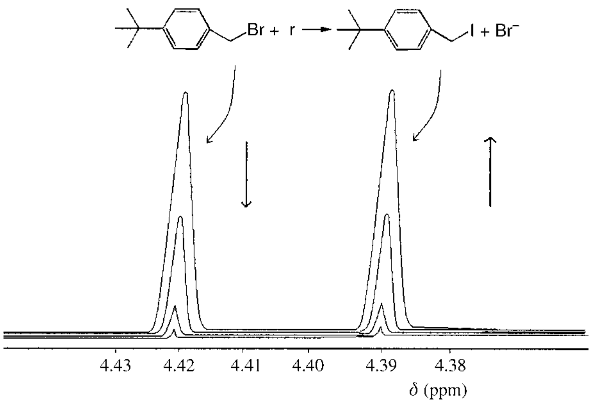


Figure 5. The reaction was monitored by following the decrease of the $-CH_2Br$ signal at 4.42 ppm and the increase of the $-CH_2I$ signal at 4.39 ppm.

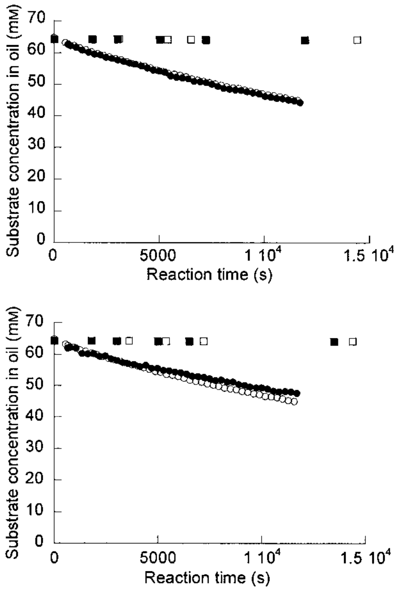


Figure 6. Top: Effect of Q salt (TBAHS or TBAB) on the reaction between 4-TBBB and KI at 23 °C in $D_2O/C_{12}E_5$/decane (○,●) and D_2O/decane (□,■). Bottom: Effect of [18]crown-6 on the reaction between 4-TBBB and KI at 23 °C in $D_2O/C_{12}E_5$/decane (○,●) and D_2O/decane (□,■). In both graphs open symbols denote reactions without PTA and and black symbols reactions with PTA. The overall concentrations of 4-TBBB, KI and [18]crown-6 are all 8.8 mM.

Decane was replaced by cyclohexane in order to enhance the solubilizing power of the organic phase. In doing so, the microemulsion had to be reformulated, and instead of an L1 phase (oil-in-water microemulsion) an L2 phase (water-in-oil microemulsion) was used as reaction medium. Reactions were carried out in the $D_2O/C_{12}E_5$/cyclohexane microemulsion and in the D_2O/cyclohexane two-phase system in the absence and presence of TBAHS. The reaction profiles were very similar to those obtained with decane as oil component. TBAHS did not accelerate the reactions.

The organic phase was changed to dichloromethane in order to further improve the solvency and extraction efficiency. A microemulsion with dichloromethane as organic component cannot be formulated with normal nonionic surfactants of alcohol ethoxylate type, because such surfactants have too high solubility in chlorinated hydrocarbons. Instead, a formulation based on a sugar surfactant, octyl glucoside (C_8G_1), was employed. Figure 7 shows the profiles for the reactions performed in the $D_2O/C_8G_1/CH_2Cl_2$ microemulsion and in the D_2O/CH_2Cl_2 two-phase system in the absence and presence of an equimolar amount of a PTA (TBAHS, TBAB or [18]crown-6). The reaction profiles in the absence of a PTA were similar to those obtained in the decane-based reaction media. The reaction rate in the $D_2O/C_8G_1/CH_2Cl_2$ microemulsion was approximately the same as in the $D_2O/C_{12}E_5$/decane microemulsion, and the two-phase reaction was equally as sluggish as the corresponding reaction in the D_2O/decane system. However, addition of a PTA increased the reaction rate in the two-phase system greatly. This is not unexpected, since chlorinated hydrocarbons are known to function well as solvents for PTC. Addition of a PTA also increased the rate of the reaction in the microemulsion to an appreciable extent.

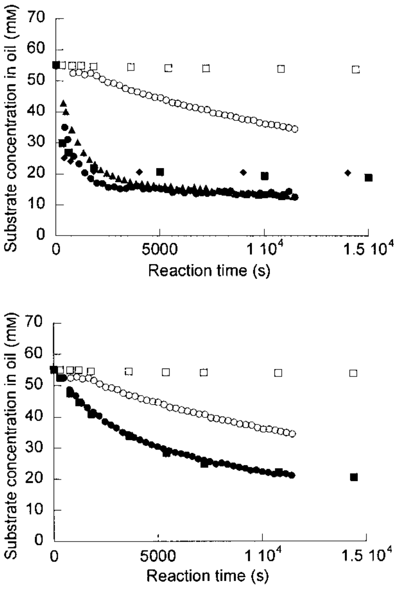


Figure 7. Top: Effect of Q salt on the reaction between 4-TBBB and KI at 23 °C in $D_2O/C_8G_1/CH_2Cl_2$: (○) without Q-salt, (●) with TBAHS, (▲) with TBAB; and in $D_2O\text{-}CH_2Cl_2$: (□) without Q-salt, (■) with TBAHS, (◆) with TBAB. The overall concentrations of 4-TBBB, KI and Q salt are all 20 mM. Bottom: Effect of [18]crown-6 on the reaction between 4-TBBB and KI at 23 °C in $D_2O/C_8G_1/CH_2Cl_2$ (○,●) and D_2O/CH_2Cl_2 (□,■). Open symbols denote reactions without [18]crown-6 and black symbols reactions with [18]crown-6. The overall concentrations of 4-TBBB, KI and [18]crown-6 are all 20 mM.

Phase-transfer catalysis is often performed with a catalytic, rather than an equivalent, amount of PTA. The reactions in the $D_2O/C_8G_1/CH_2Cl_2$ microemulsion and in the D_2O/CH_2Cl_2 two-phase system were therefore repeated with a 0.01 mole equivalent of PTA (based on the reactants). The reaction profiles are shown in Figure 8. Since TBAHS and TBAB gave similar results when used in equimolar amounts, only TBAHS was tested in catalytic amounts. As can be seen, the reactions in both the two-phase system and the microemulsion were considerably slower when the PTA addition was reduced to a catalytic amount. Reaction in the microemulsion without a PTA was approximately as fast as reaction in the two-phase system with a PTA. The combination of a microemulsion as the reaction medium and addition of a PTA gave the highest reaction rate. The Q salt was more effective than the crown ether.

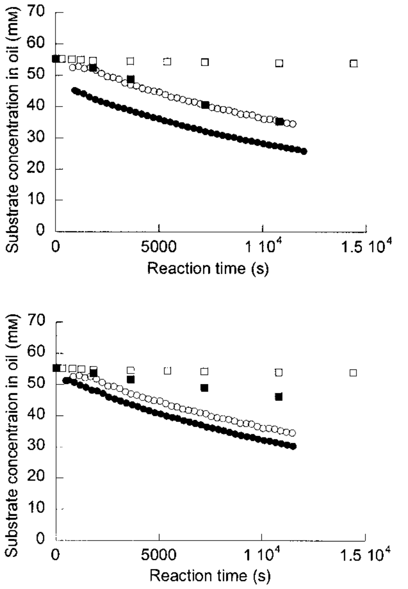


Figure 8. Top: Effect of a catalytical amount of TBAHS on the reaction between 4-TBBB and KI at 23 °C in $D_2O/C_8G_1/CH_2Cl_2$ (○,●) and $D_2O\text{-}CH_2Cl_2$ (□,■). Bottom: Effect of a catalytical amount of [18]crown-6 on the reaction between 4-TBBB and KI at 23 °C in $D_2O/C_8G_1/CH_2Cl_2$ (○,●) and $D_2O\text{-}CH_2Cl_2$ (□,■). In both graphs open symbols denote reaction without PTA and black symbols reactions with PTA. The overall concentrations of both 4-TBBB and KI are 20 mM, and of PTA 0.2 mM.

All rate constants, calculated as the slope from the straight line obtained when plotting the reverse overall concentration of the substrate against reaction time are compiled in Table 1.

Benzyl bromide is known to hydrolyse into benzyl alcohol. This side reaction would distort the monitoring of the reaction, since there would then not be a full equivalence in terms of NMR signals between disappearence of $-CH_2Br$ and appearance of $-CH_2I$. Only in the systems with dichloromethane and with TBAHS present did a peak appear in the NMR spectrum that can be attributed to the alcohol, that is, to $-CH_2OH$ methylene protons (at 4.60 ppm). The $-CH_2Br$ and $-CH_2I$ peaks appear at 4.52 and 4.49 ppm, re-

Table 1. Calculated rate constants for the reaction between equimolar overall amounts of 4-TBBB and KI in absence and in presence of a PTA in both microemulsions and two-phase systems. The volume fraction of oil based on oil and water is denoted ϕ_v and the weight fraction of surfactant based on water, surfactant and oil is denoted α_m. The reactions in microemulsions were carried out at the compositions indicated by arrows in Figures 2–4. All reactions were performed at 23 °C at a stirring rate of around 900 rpm.

Reaction system	$C_{4\text{-TBBB}}$ [10^{-3} mol dm^{-3}]	PTA	C_{PTA} [10^{-3} mol dm^{-3}]	ϕ_V	α_m	$k_{overall}$ [10^{-3} dm^{-3} mol^{-1} s^{-1}]
microemulsion						
$D_2O/C_{12}E_5$/decane	8.75	none		0.12	0.10	4.5
$D_2O/C_{12}E_5$/decane	8.74	[18]crown-6	8.74	0.12	0.10	4.5
$D_2O/C_{12}E_5$/decane	8.75	TBAB	8.74	0.12	0.10	4.5
$D_2O/C_{12}E_5$/decane	8.75	TBAHS	8.75	0.12	0.10	4.9
$D_2O/C_{12}E_5$/cyclohexane	21.01	none		0.92	0.11	2.1
$D_2O/C_{12}E_5$/cyclohexane	21.02	TBAHS	2.1	0.92	0.11	2.1
$D_2O/C_8G_1/CH_2Cl_2$	19.20	none		0.50	0.29	2.8
$D_2O/C_8G_1/CH_2Cl_2$	19.20	[18]crown-6	19.20	0.50	0.29	7.3
$D_2O/C_8G_1/CH_2Cl_2$	19.20	[18]crown-6	0.19	0.50	0.29	3.5
$D_2O/C_8G_1/CH_2Cl_2$	19.20	TBAB	19.20	0.50	0.29	40.6
$D_2O/C_8G_1/CH_2Cl_2$	19.20	TBAHS	19.20	0.50	0.29	61.5
$D_2O/C_8G_1/CH_2Cl_2$	19.20	TBAHS	0.19	0.50	0.29	4.3
two-phase						
D_2O/decane	9.8	none		0.12		
D_2O/decane	9.8	[18]crown-6	9.8	0.12		
D_2O/decane	9.8	TBAB	9.8	0.12		
D_2O/decane	9.8	TBAHS	9.8	0.12		
D_2O/cyclohexane	22.7	none		0.92		
D_2O/cyclohexane	22.7	TBAHS	2.3	0.92		
D_2O/CH_2Cl_2	27.6	none		0.50		0.1
D_2O/CH_2Cl_2	27.6	[18]crown-6	27.6	0.50		6.1
D_2O/CH_2Cl_2	27.6	[18]crown-6	0.28	0.50		0.7
D_2O/CH_2Cl_2	27.6	TBAHS	27.6	0.50		28.6
D_2O/CH_2Cl_2	27.6	TBAHS	0.28	0.50		2.0

spectively, in the system with dichloromethane. The integral of the $-CH_2OH$ peak was approximately 5 % of the combined integrals of the $-CH_2Br$ and $-CH_2I$ peaks; hence, the hydrolysis affects the results only marginally. For all the reactions, except the one in dichloromethane with TBAHS as phase-transfer agent, there was very good agreement between the integrals of the rising $-CH_2I$ peak and the declining $-CH_2Br$ peak. The reason why the side reaction, that is, hydrolysis, occurs when TBAHS and not [18]crown-6 is used as PTA is still unclear. TBAHS did not increase the pH of the water phase.

Discussion

The solubility of 4-TBBB in the aqueous phase is very low. The solubility of the iodide in the organic phase is also extremely low. One may, consequently, assume that the nucleophilic substitution reaction only takes place at the interface, that is, no reaction occurs in the bulk phases. The droplet size in a microemulsion is in the range of 10–50 nm, while the droplet size in a typical (macro)emulsion is in the micrometer range. The droplets obtained during vigorous stirring of the two-phase systems used in this work are probably even larger, since the oil–water interfacial tension is high in such surfactant-free systems. Consequently, the difference in total interfacial area between the two reaction media is very large. It is, thus, not surprising that the reactions performed in the two-phase systems in absence of PTA are much slower than those occurring in the microemulsions. As can be seen from Table 1, the overall rate constants for reactions in the microemulsions based on the different organic solvents are of the same magnitude. One may note that there does not seem to be a direct relationship between the oil–water interfacial area and the reaction rate. The interfacial area of a microemulsion is largely determined by the amount of surfactant in the system. The microemulsions based on decane, cyclohexane and dichloromethane have surfactant weight fractions 0.10, 0.11 and 0.29, respectively. Thus the microemulsion based on the chlorinated solvent has a much larger internal interface than the other two microemulsions; however, the rate constant in this medium is in-between those in decane and in cyclohexane.

An attempt to use a PTA to speed up the reaction in the decane/water two-phase system gave little effect. This is not surprising, since it is known that a solvent such as decane, which has a low dielectric constant ($e = 1.99$), is usually not useful in phase-transfer catalysis. The results are in line with those of a previous work, in which a nucleophilic substitution reaction was performed in a dodecane/water system with added PTA and compared to the reaction in a microemulsion.[20] The poor effect of a PTA in such a system is due to unfavourable extraction equilibrium of the ion pair into the organic phase. ^1H NMR spectroscopy showed that almost no PTA was present in the organic phase after extracting a solution of KI and TBAHS or of tetrabutylammonium iodide (TBAI) in D_2O with decane.

Changing the solvent to cyclohexane, which has a slightly higher dielectric constant ($e = 2.00$), still gave no appreciable effect of the added PTA. Also in this system, ^1H NMR spectroscopy revealed that the extraction equilibrium was very unfavourable.

PTC is known to function well in chlorinated hydrocarbons. Use of dichloromethane, with a dielectric constant of 8.90, as organic solvent resulted in a favourable extraction equilibrium with a high concentration of PTA in the organic phase. Another reason why aprotic and relatively polar liquids, such as dichloromethane, are suitable solvents for PTC-based reactions of the type studied here is that the nucleophile will be poorly solvated and, thus, much higher in nucleophilicity than when present in water or other protic solvents. As is shown in Figure 7, the reaction rate is faster in the two-phase systems with added PTA (used in equimolar amount) than in the microemulsion without PTA. Addition of a PTA to the microemulsion speeds up this reaction to the same level as for the two-phase systems with PTA. The observation that the reaction rates are the same in the two-phase system and in the microemulsion when a PTA is present (in equimolar amounts) indicates that the extraction of the iodide ion into the organic phase is fast and efficient and that the reaction in both systems mostly occurs in the bulk organic phase or domain, not at the interface. Thus, the rate-limiting step is the reaction as such, not the transport of the iodide ion across the interface. The situation may be different for a faster organic reaction. The extraction may then be the rate-limiting step and the much larger interface of the microemulsion may be more important. The situation should also be different in systems with lower extraction efficiency. In such systems the transport of the nucleophile across the interface may be the rate-determining event and the larger oil–water interface of the microemulsion could then be taken advantage of. This reasoning nicely explains results from a previous work in which the ring-opening of a lipophilic epoxide with sodium hydrogen sulfite was studied in a microemulsion and in a two-phase system. The reaction in the microemulsion was much faster than the reaction in the two-phase system when an equimolar amount of PTA was present in both systems.[8] In that reaction system, the extraction constant was considerably lower than in the present system due to two contributing factors. Firstly, the solvent was trichloroethylene, which is less polar than dichoromethane. Secondly the nucleophile was hydrogen sulfite, which is a much more hydrophilic anion than iodide, which means that $Q^+HSO_3^-$ is less readily extracted into the organic phase than Q^+I^-.

In industrial applications of PTC equimolar amounts of the PTA and the nucleophilic reagent is seldom used. Only a catalytic amount of the PTA is usually employed, which means that the Q salt or the crown ether is expected to go back and forth across the interface to pick up and deliver new nucleophiles into the organic phase. One may anticipate that the size of the interface will then be more crucial than when the PTA is used in equimolar amounts. As can be seen in Figure 8, the use of a catalytic, rather than equimolar, amount of either a Q salt or a crown ether slows down the reaction rate both in the D_2O/C_8G_1/dichloromethane microemulsion and in the D_2O/dichloromethane two-phase system. The reduction is more pronounced in the two-phase system. The combined approach, that is, use of a microemulsion as reaction medium and addition of a PTA, gives the fastest reaction. It seems that when the PTA is used in catalytic amount, transport of the nucleophile across the interface becomes a crucial event. An interpretation of the results is that in such a system part of the reaction takes place at the interface, illustrated by the curve for the reaction in the microemulsion in the absence of a PTA, and part of the reaction occurs in the bulk organic phase, as evidenced by the increase in reaction rate when the PTA is added to the microemulsion. In all the reactions, the crown ether was slightly less effective than the Q salts.

The phase behaviour of the system did not change during the course of the reaction, neither for the case of equimolar amount of PTA and nucleophilic reagent nor for the case of catalytic amount of PTA. The mixture remained a clear and low viscous one-phase medium, indicative of a microemulsion.

Conclusions

The present work shows that the reaction between 4-*tert*-butylbenzyl bromide and potassium iodide can be performed at a reasonable rate in a microemulsion based on an aliphatic hydrocarbon. PTC was not effective in such systems. However, when the solvent was changed to a chlorinated hydrocarbon, a PTA accelerated the reaction both in a two-phase system and in a microemulsion. The combined approach of using a microemulsion as reaction medium and addition of a catalytic amount of a PTA resulted in considerably higher reaction rate than either of the approaches alone. This could be of practical interest in preparative organic chemistry in which reagent incompatibility problems often occur and in which PTC is frequently used as a way to bring the reactants into contact.

Experimental Section

Materials: The nonionic surfactants used, penta(ethylene glycol)monododecyl ether ($C_{12}E_5$) and *n*-octyl-β-D-glucopyranoside (C_8G_1), were purchased from Nikko Chemicals and Anatrace, respectively. The solvents, decane, cyclohexane, dichloromethane (CH_2Cl_2) and deuterochloroform ($CDCl_3$), were all from Aldrich. The reagents, potassium iodide (KI) and 4-tert-butylbenzylbromide (4-TBBB), were supplied by Merck and Aldrich, respectively. Deuterium oxide (D_2O), tetrabutylammonium bromide (TBAB), tetrabutylammonium hydrogen sulfate (TBAHS) and tetrabutylammonium iodide (TBAI) were all supplied by Aldrich. The crown ether, [18]crown-6, was from Lancaster. The water was Millipore filtered. All chemicals used had a purity of $\geq 99\%$, except 4-TBBB (97%) and TBAHS (97%). All chemicals were used without any further purification.

Phase diagram: Both the $D_2O/C_{12}E_5$/decane and the $D_2O/C_{12}E_5$/cyclohexane systems were studied directly and through crossed polarisers in a transparent water bath, in which the temperature was regulated by a thermostat. The temperature was varied by one degree at a time and the mixture was allowed to reach equilibrium before determining the self-assembly structure formed. The microemulsion region was determined by titration of D_2O into a stock solution containing surfactant and organic solvent. The titrated amount was controlled by weight with an accuracy of 0.0001 g.

Chemical reaction: The nucleophilic substitution reaction between 4-TBBB and KI was performed at 23 °C in various microemulsions in an NMR tube and in two-phase systems in bottles by using vigorous agitation. The substrate and the nucleophile were always used in equimolar concentration. Stock solutions of KI in D_2O and of 4-TBBB in oil were prepared. The concentration of the PTA was the same as of the reactants, if not otherwise mentioned.

Three different microemulsions were used. The first was based on D_2O, decane and $C_{12}E_5$. The concentration of 4-TBBB in decane was 64.3 mM, giving an overall concentration of 8.8 mM. The microemulsion was made by first mixing the oily stock solution with the surfactant and then adding the aqueous stock solution. The volume fraction of the oil, ϕ_v, based on the oil and water volume, was 0.15. The surfactant weight fraction, α_m, based on total weight was 0.1.

The second microemulsion was D_2O/cyclohexane/$C_{12}E_5$. The concentration of 4-TBBB in cyclohexane was 24.7 mM, giving an overall concentration of 21 mM. The ϕ_V value was 0.92 and the α_m value 0.11. The same formulation procedure as described above was used.

The third microemulsion was D_2O/dichloromethane/C_8G_1. The concentration of 4-TBBB in dichloromethane was 55.2 mM, giving an overall concentration of 20 mM. The ϕ_V value was 0.5 and the α_m value 0.29. The same formulation procedure as described above was used.

The reaction was also performed in two-phase systems based on D_2O and either decane, cyclohexane or CH_2Cl_2 with similar ratio between the oil phase and the aqueous phase as in the microemulsion based on the same organic solvent. Furthermore, the concentrations of reactants and PTAs were the same as well. The reaction was quenched by addition of $CDCl_3$ in a volume ratio of 1:1 $CDCl_3$/reaction mixture after different time intervals. The aqueous phase was removed after centrifugation at 3000 rpm for 5 min and the organic phase was dried by Mg_2SO_4. After filtration the organic phase was analysed by ^1H NMR spectroscopy.

All reactions were analysed by ^1H NMR spectroscopy, by using a 500 MHz Varian Inova spectrometer. The reaction rate was obtained by following the consumption of 4-TBBB and the formation of the product. The specific proton signals that were monitored were the protons of the methylene groups at 4.42 ($-CH_2Br$) and 4.39 ppm ($-CH_2I$), recorded in $D_2O/C_{12}E_5$/decane. In chlorinated hydrocarbons these values were shifted slightly to higher ppm values. The reactions performed in the microemulsions were analysed in situ every five minutes, while the two-phase reactions were analysed after the workup procedure. All reactions were monitored during three hours, at which time the yield was calculated.

Acknowledgement

We would like to thank the Swedish Foundation for Strategic Research for financing M.H. through its Colloid and Interface Technology Programme. M.H. also thanks the Institute for Surface Chemistry AB for financial support. Furthermore, we thank the Swedish NMR Center for granting spectrometer time and Charlotta Damberg at the NMR Center for help with the instruments.

[1] F. M. Menger, J. U. Rhee, H. K. Rhee, *J. Org. Chem.* **1975**, *40*, 3803–3805.

[2] F. M. Menger, A. R. Elrington, *J. Am. Chem. Soc.* **1991**, *113*, 9621–9624.

[3] J. H. Ramsden, R. S. Drago, R. Riley, *J. Am. Chem. Soc.* **1989**, *111*, 3958–3961.

[4] R. Schomäcker, *Nachr. Chem. Tech. Lab.* **1992**, *40*, 1344–1351.

[5] R. Schomäcker, *J. Chem. Res.* **1991**, 92–93.

[6] S. Gutfelt, J. Kizling, K. Holmberg, *Colloids Surf. A.* **1997**, *128*, 265–271.

[7] M. Häger, K. Holmberg, in *Adsorption and Aggregation of Surfactants in Solution* (Eds.: K. L. Mittal, D. O. Shah), Marcel Dekker, New York, **2002**, p. 327.

[8] M. Häger, K. Holmberg, *Tetrahedron Lett.* **2000**, *41*, 1245–1248.

[9] G. Bode, M. Lade, R. Schomäcker, *Chem. Eng. Technol.* **2000**, *23*, 405–409.

[10] C. Siswanto, T Battal, O. E. Schuss, J. F. Rathman, *Langmuir* **1997**, *13*, 6047–6052.

[11] T. Battal, C. Siswanto, J. F. Rathman, *Langmuir* **1997**, *13*, 6053–6057.

[12] M. Häger, K. Holmberg, U. Olsson, Langmuir, **2004**, *20*, 6107–6115.

[13] M. Häger, F. Currie, K. Holmberg, *Colloids Surf.,A* in press.

[14] U. Olsson, P. Schurtenberger, *Langmuir* **1993**, *9*, 3389–3394.

[15] M. S. Leaver, U. Olsson, *Langmuir* **1994**, *10*, 3449–3454.

[16] K. Fukuda, U. Olsson, U. Würz, *Langmuir* **1994**, *10*, 3222–3229.

[17] U. Olsson, H. Wennerström, *Adv. Colloid Interface Sci.* **1994**, *49*, 113–146.

[18] U. Olsson, P. Schurtenberger, *Prog. Colloid Polym. Sci.* **1997**, *104*, 157–159.

[19] H. Egger, T. Sottmann, R. Strey, A. Berkessel, *Tenside, Surfactants, Deterg.* **2002**, *39*, 17–22.

[20] K. Andersson, J. Kizling, K. Holmberg, S. Byström, *Colloids Surf. A* **1998**, *144*, 259–266.

Received: December 19, 2003
Revised: June 21, 2004