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A substitution reaction in an oil-in-water microemulsion catalyzed by a phase transfer catalyst

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Abstract

A lipophilic epoxide was reacted with sodium sulfite in a microemulsion using a phase transfer agent as reaction promoter. The microemulsion was based on an aqueous buffer, a chlorinated hydrocarbon and alkyl glycoside surfactants. The reaction was fast compared to the same reaction performed in a two-phase system with the same phase transfer agent. © 2000 Elsevier Science Ltd. All rights reserved.

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It is common practice to take advantage of phase transfer catalysis in nucleophilic substitution reactions involving incompatible reactants.^{1,2} In many reactions of this type, the substrate is a lipophilic organic molecule insoluble in water and other polar solvents while the nucleophile is usually an anion which is not soluble in the substrate or in nonpolar solvents. Such reactions may be performed in a two-phase system in the presence of a phase transfer agent (PTA) such as a quaternary ammonium salt or a crown ether. The role of the PTA is to transfer the nucleophilic anion from the aqueous to the organic phase. Once in the organic phase, the nucleophile becomes highly reactive because (i) the degree of solvation is low, and (ii) the large cations used as PTAs do not form strong ion pairs with the nucleophile in the organic phase; thus, the anion behaves as a 'naked' ion. The choice of organic solvent is often crucial for good extraction efficiency and high nucleophilic reactivity. Chlorinated hydrocarbons are known to function well in this respect.

Use of a microemulsion as a reaction medium constitutes an alternative to phase transfer catalysis.^{3,4} A microemulsion is a thermodynamically stable mixture of organic solvent, water and surfactant.⁵ Depending on the relative volumes of oil and water and on the type of surfactant used, the microemulsion can have the structure of oil-in-water or of water-in-oil or it can be bicontinuous, i.e. consist of infinitely long channels of oil and water. Regardless of the structure, the cross-over dimensions of the oil and water domains of a microemulsion are very small, typically of the order of 5–20 nm. This means that

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the oil–water interfacial area, which is stabilized by a monolayer of surfactant, is extremely large. The interest in microemulsions as reaction media for organic synthesis is derived from their ability to dissolve, in a one-phase system, both lipophilic organic molecules and inorganic species. The lipophilic molecules go into the oil domains and the water-soluble species go into the aqueous domains. Since the interface between the two compartments is so large and since the system is a highly dynamic one with interfaces disintegrating and reforming at the time-scale of milliseconds, there are ample opportunities for the two otherwise incompatible reagents to meet and react at the interface. We have successfully used the microemulsion approach to prepare a long-chain hydroxysulfonate by ring-opening of a lipophilic α -epoxide with sodium hydrogen sulfite.⁶

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

The aim of the present work is to combine the two approaches into one; i.e. to carry out a nucleophilic substitution reaction in a microemulsion in the presence of a conventional PTA, tetrabutylammonium hydrogen sulfate. The reaction is the same as the one we have previously investigated using a microemulsion as a reaction medium but without added PTA. As a reference, the reaction is also carried out in a normal two-phase system with the same PTA added. The reaction under study shown below was previously performed in a microemulsion based on dodecane, water and different types of surfactant.⁶ The reaction rate depended on the choice of surfactant and at optimum conditions all the epoxide had been consumed after 2 h at a reaction temperature of 75°C. At the same reaction time and temperature only 20% of the epoxide was consumed when the reaction was carried out in a surfactant-free dodecane–water two-phase system (without added PTA).



We have now performed the same reaction in an oil-in-water microemulsion (often denoted L1) based on chlorinated hydrocarbon, water and surfactant with tetrabutylammonium hydrogen sulfate added to the formulation.

A combination of two alkylglucoside surfactants was needed to formulate a suitable microemulsion based on the aqueous buffer and trichloroethylene (TCE). Fig. 1 shows the extension of the isotropic L1 region in the absence and presence of the reactants and the PTA. As can be seen, neither the hydrophobic epoxide nor the inorganic salt affects the phase behavior appreciably. Neither does the PTA markedly affect the phase boundary of the L1 region.

The aqueous phase consisted of 5% sodium sulfite in 0.1 M citrate buffer of pH 4. The oil component was a solution of 1,2-epoxyoctane in TCE (1195 g/l). The surfactants used were technical products, AG 6262 (octyl glucoside from Akzo Nobel Surface Chemistry, Sweden) and Simulsol SL 26 (dodecyl/hexadecyl glucoside from Seppic, France) in a ratio of 3:1.

The reaction was performed in an L1 microemulsion at 22°C with PTA added in an equimolar amount to the inorganic salt. The weight ratio of oil:surfactant:water was 1:2:7 giving equimolar amounts of the reagents. The reaction was stopped by addition of water and CH_2Cl_2 , which led to an instantaneous destabilization of the microemulsion. The mixture was centrifuged and the oil phase was washed with water and dried with Mg_2SO_4 . The chlorinated solvent was evaporated to yield an oily residue to which dodecane was added. The solution was filtered to remove traces of surfactant. The reaction was monitored

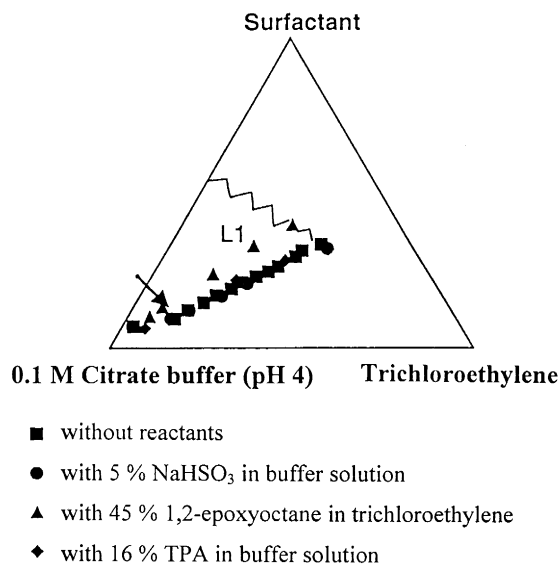


Fig. 1. Pseudo-ternary phase diagram. The arrow indicates the reaction composition

by TLC (7:1 CH_2Cl_2 :MeOH) and consumption of the epoxide was quantified by ^1H NMR, using a 400 MHz Varian UNITY 500 spectrometer. All ^1H NMR measurements were carried out at 20°C in CDCl_3 . Samples were taken at different time intervals during the course of 48 h and the signals from the oxirane ring protons at δ 2.39 ppm (dd), 2.66 ppm (m) and 2.84 ppm (m) were used for the analysis.

For comparison, the reaction was also performed in a two-phase aqueous buffer:TCE system with a weight ratio of 7:1, in the presence and absence of PTA. The work-up, apart from the evaporation of CH_2Cl_2 , and the analysis procedure, were the same as above.

The reaction profiles of all reactions are shown in Fig. 2. The reaction performed in the microemulsion with added PTA was rapid considering the low reaction temperature with only 10% epoxide remaining

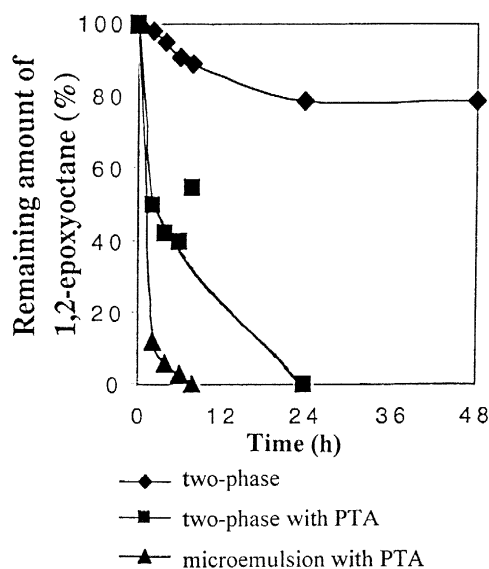


Fig. 2. Reaction profiles as determined from disappearance of epoxide

after 2 h. At the final stage of the reaction, a phase separation into an oil-in-water microemulsion in equilibrium with oil, a so-called Winsor 1 system, occurred. The reaction in the two-phase system with PTA was more sluggish, but complete conversion of the epoxide was obtained after 24 h. Reaction in the two-phase system without added PTA gave only 20% conversion after 48 h reaction time.

Thus, this study shows that a substitution reaction performed in a microemulsion can be greatly accelerated by addition of a PTA.

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