
7 Organic Reactions in Emulsions and Microemulsions

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CONTENTS

7.1	Introduction	263
7.2	Reaction in Emulsions.....	264
7.3	Reaction in Microemulsions	268
7.3.1	Overcoming Reagent Incompatibility	269
7.3.2	Effect of Surfactant Charge on Reactivity	273
7.3.3	Selectivity in Microemulsion-Based Reactions.....	275
	References	278

7.1 INTRODUCTION

Organic synthesis is normally performed in a homogeneous liquid reaction medium, consisting either of one solvent or of a mixture of solvents. When the reaction involves reactants with widely different polarity, such as a lipophilic organic molecule and an inorganic salt – which is common, for instance in oxidation reactions and in nucleophilic substitution reactions – a two-phase system is often employed. The common practice is to accelerate such a two-phase reaction by addition of a phase transfer catalyst, which may be either a quaternary ammonium salt or a crown ether (1).

Emulsions are oil–water two-phase systems with a large interfacial area stabilized by surfactant. The large interfacial area can be taken advantage of and emulsions have been successfully used as media for organic synthesis. The use of emulsions as vehicles for organic reactions is reviewed in this chapter.

A special case of the use of emulsions as reaction medium is emulsion polymerization, i.e., preparation of lattices. In emulsion polymerization micrometer-sized drops containing the monomer are dispersed in water using a relatively large amount of surfactant in order to obtain a high concentration of surfactant micelles in the bulk aqueous phase. A water-soluble initiator is added and free-radical polymerization is initiated in the aqueous phase. (The monomer has some solubility in water.) The growing oligomers become gradually less water soluble. Since the interfacial area of the many small micelles is orders of magnitude larger than that of the relatively few drops of monomer, the oligomers go into the micelles where continued polymerization occurs. The micelles grow at the expense of the monomer drops and the reaction proceeds until all monomers are consumed. The resulting product, the latex, typically consists of a concentrated dispersion of surfactant-stabilized particles in the size range 70 to 500 nm. Emulsion polymerization is an established process, thoroughly described in the literature (2,3). It is not dealt with further in this review. Free-radical polymerization may also be performed within the drops of a

pre-formed emulsion of a monomer, such as styrene, in water (4,5). Both the free radical initiator and the transfer agent should be oil-soluble. Under these conditions, each particle behaves as an isolated bulk reactor. Because of compartmentalization of the radicals the conversion is fast, much faster than obtained in bulk. The process gives polymer particles of approximately the same size as the size of the starting monomer drops. The molecular weight distribution appears to be similar to that of bulk polymerization.

Microemulsions, i.e., oil–water–surfactant mixtures that unlike emulsions are thermodynamically stable systems, are used as media for a variety of chemical reactions. Microemulsions are macroscopic one-phase systems but microscopically they consist of oil and water domains, separated by a monolayer of surfactant. Depending on the oil-to-water ratio and on the choice of surfactant the interface can be curved towards oil or towards water or the curvature may be small, which is the case for so-called bicontinuous microemulsions. The aqueous droplets of water-in-oil microemulsions have been explored as minireactors for the preparation of nanoparticles of metals and metal salts and particles of the same size as the starting microemulsion droplets can often be obtained (6–8). Polymerization in microemulsions is an efficient way to prepare nanolattices and also to make polymers of very high molecular weight. Both discontinuous and bicontinuous microemulsions have been used for the purpose (9). Microemulsions are also of interest as media for enzymatic reactions. Much work has been done with lipase-catalyzed reactions and water-in-oil microemulsions have been found suitable for ester synthesis and hydrolysis, as well as for transesterification (10,11).

Microemulsions, being microheterogeneous mixtures of oil, water, and surfactant, are excellent solvents for both polar and nonpolar compounds. The capability of microemulsions to solubilize a broad range of substances in a one-phase formulation has been found useful in preparative organic synthesis. Microemulsions are one way, out of several, to overcome the reactant incompatibility problems that are frequently encountered in preparative organic chemistry. The capability of microemulsions to compartmentalize and concentrate reactants can lead to unusual reactivity in organic synthesis. Attempts have also been made to use the oil–water interface of microemulsions as a template to induce regiospecificity of organic reactions. The use of microemulsions as vehicles for organic reactions is reviewed in this chapter and special emphasis is put on the more recent literature.

7.2 REACTION IN EMULSIONS

The term “interfacial synthesis” relates to an organic synthesis performed at the oil–water interface. By using a surface-active catalyst that operates at the interface, interfacial synthesis permits a convenient separation of the product and the catalyst with the view to recover and reuse the latter. The process is somewhat between homogeneous and heterogeneous catalysis; homogeneous in the sense that the catalyst is a soluble molecule that can adopt its conformation in solution, heterogeneous in that the reaction takes place at the boundary between two phases. Performing interfacial synthesis in a system with a large oil–water interface, such as an emulsion, is a way to increase the reaction rate.

Lim and co-workers have performed a range of interfacial syntheses using hydrocarbons or chlorinated hydrocarbons as oil phase and sodium dodecyl sulfate as emulsifier. The reported syntheses include free-radical polymerization (12–14), oxidations (15), and carbonylation reactions (16). Oxidative polymerization of 2,6-dimethylphenol to yield poly(2,6-dimethyl-1,4-phenylene oxide) (Figure 7.1) is a particularly interesting example of the use of the procedure. The reaction has been performed both in toluene–water (13) and in chloroform–water (14) emulsions. Copper is used as the active catalyst and a range of ligands was evaluated to maximize the performance

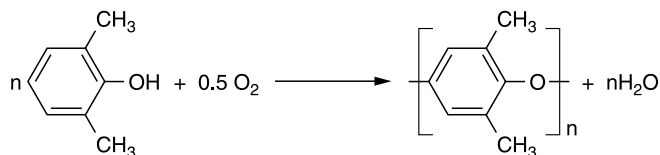


FIGURE 7.1 Oxidative polymerization of 2,6-dimethylphenol.

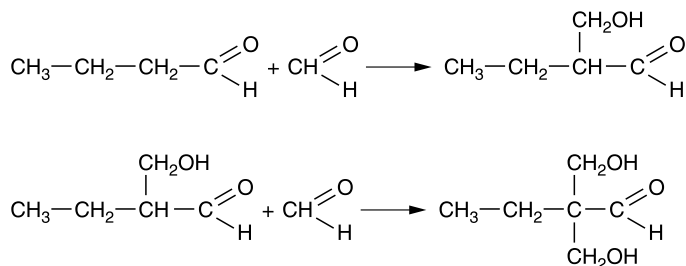


FIGURE 7.2 Crossed aldolization of butyraldehyde and formaldehyde.

of the catalyst at the interface. For the toluene–water system triethyl phosphite gave a proper reaction rate. Much higher reactivity was, however, found in the chloroform–water system when ethylenediamines were used as ligands. Ethylenediamines and substituted ethylenediamines can act as bidentate ligands, capable of forming binuclear copper complexes that can mimic the active site of enzymes that catalyze coupling polymerization of phenols in plants. The highest reactivity, measured as oxygen uptake rate, was obtained with the asymmetrically substituted diamine *N,N*-dibutylethylenediamine. A polymer with a molecular weight of 48,000 was obtained in 95% yield.

It was found that for a series of substituted ethylenediamines the rate of polymerization of 2,6-dimethylphenol correlated well with the surface activity of the copper–ligand complex (14). It is probable that increased surface activity, i.e., increased tendency to reside at the interface, will reduce the diffusion pathway of the reactants in the biphasic system. The surface activity of the complex may also affect the copper (I) → (II) redox cycle.

There are other examples of organic reactions based on a catalytic step that occur at the interface between an aqueous and an oil phase but where that interface has not been enlarged and stabilized by surfactant. The reaction is performed under stirring but without emulsifier the emulsion will be very crude, i.e., the interface will not be very large. A good example of the procedure is reaction between butyraldehyde and formaldehyde, using a solid anion exchange resin, in the form of a fine powder, as catalyst (17). The reaction, a so-called crossed aldolization, takes place in two subsequent steps in which the two α -hydrogens of butyraldehyde are replaced by hydroxymethyl groups (see Figure 7.2). The product formed is an important chemical intermediate. Reduction of the aldehyde group leads to trimethylolpropane, an important building block for alkyds and other polymers.

Butyraldehyde has low solubility in water while formaldehyde is readily water soluble. A liquid–liquid interface will form and the weakly basic catalyst containing tertiary amino groups goes to the boundary. The reaction medium is in effect a three-phase system. The reaction is

believed to start by adsorption of formaldehyde on the catalyst surface; thus, a high surface area and the proximity to the other reactant, butyraldehyde, are parameters that favor the reaction. (Another reason why a high surface area is needed is that a byproduct, ethylacrolein, also adsorbs on the catalyst.) The base-catalyzed aldolization starts with a nucleophilic attack of the base catalyst at the α -carbon of butyraldehyde. The carbanion formed then reacts with formaldehyde. Thus, the reaction is a truly interfacial synthesis. It would be interesting to examine the effect of an increase of the liquid–liquid interfacial area, which could be obtained by addition of a suitable emulsifier.

Organic reactions in emulsions, involving one water-soluble and one oil-soluble reactant, can also be catalyzed by a phase transfer agent. This approach has been applied to the preparation of azo dyes (18). Several azo dyes were prepared in water-in-oil emulsions using chlorinated hydrocarbon as oil phase and with sodium dodecylbenzenesulfonate as emulsifier. Either a quaternary ammonium salt (benzyltrimethylammonium chloride) or a crown ether (dibenzo-18-crown-6) was employed as the phase transfer catalyst.

Attempts have been made to prepare esters of glycerol by base-catalyzed transesterification of fatty acid methyl esters with glycerol using water-in-oil emulsions as reaction medium (19). Monoglyceride was the main reaction product and the yield was moderate. The same reaction, but starting from the fatty acid and using a lipase as catalyst, has been performed in water-in-oil microemulsions (20,21). The product mixture varied with the hydrocarbon used as oil component. When a small hydrocarbon was used, monoglyceride was the main reaction product and only traces of triglyceride were obtained. The reason that triglycerides are not formed in these systems is that the diglyceride formed in the oil–water interfacial zone partitions into the continuous hydrocarbon domain. It is then inaccessible to the enzyme. The yield of triglyceride is increased by using longer hydrocarbons as the oil component. These have poorer solvency for mono- and diglycerides. When the hydrocarbon chain length exceeds that of the glyceride acyl groups, triglyceride was the main reaction product (21). The reaction has also been performed in a monolayer, i.e., at the air–water interface (22,23), as well as in foams (24). The yield of triglyceride is high in both monolayers and foams because the hydrophobic diglyceride intermediate will have no other choice than to stay at the interface. The situation at the oil–water and the air–water interfaces is illustrated in [Figure 7.3](#).

A nucleophilic substitution reaction, preparation of alkyl sulfonate from decyl halide and sodium sulfite, has been performed in water-in-oil emulsions based on the cationic surfactant $R_2(\text{Me})_2\text{N}^+ \text{X}^-$, where R is a long chain alkyl and X is Br or Cl (25,26). For a given amount of decyl halide and a given ratio of halide to sulfite a plot of reaction rate vs. surfactant concentration showed an optimum, as can be seen from [Figure 7.4](#). The results are explained as follows. A certain surfactant concentration is needed to produce a good emulsion. However, increasing the amount of surfactant means increasing the ratio of surfactant counterion (in this case bromide) to reacting ion (sulfite). Since bromide is a large, polarizable anion, it associates with the interface and expels the smaller and less polarizable sulfite ion. Thus, an “unnecessary” large amount of surfactant has a detrimental effect on the reaction rate. [Figure 7.5](#) shows the reaction profiles for different decyl halides. As can be seen, the reaction is fast for decyl iodide, somewhat slower for decyl bromide, and much more sluggish for decyl chloride. This is the expected order of reactivity because iodide is a good leaving group, bromide a slightly less good, and chloride is a poor leaving group. The fact that the order of reactivity is the same as obtained in single-phase systems was taken as an indication that the reaction in the emulsion is kinetically controlled (26).

An indirect way of using emulsions for organic synthesis is the use of foams derived from high internal phase emulsions (HIPE), so-called polyHIPE (27). Such foams are produced from a water-in-oil emulsion with a water-to-oil ratio above 95% and with the oil component being a

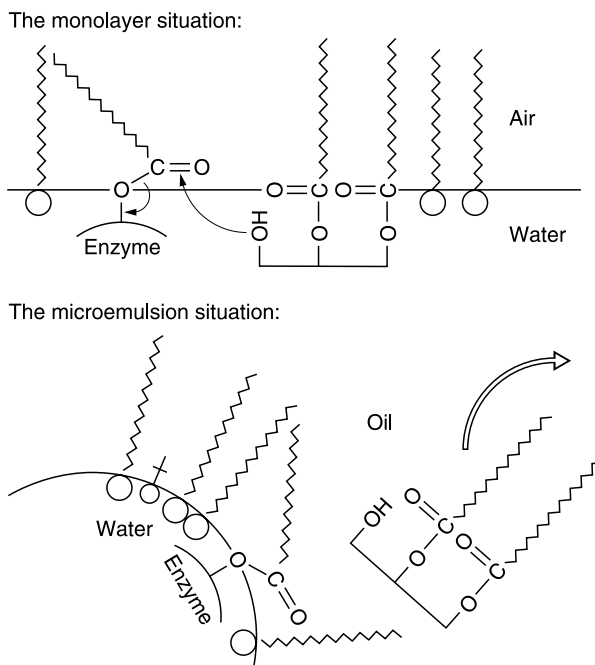


FIGURE 7.3 Arrangements of fatty acids and fatty acid glycerol esters at the air–water and the oil–water interfaces.

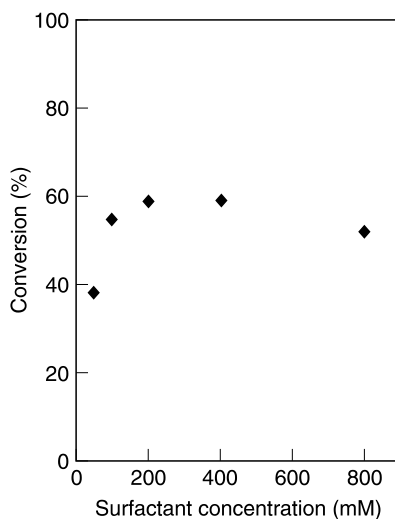


FIGURE 7.4 Conversion of decyl bromide to decyl sulfonate after 9 h at room temperature as a function of surfactant concentration. (Redrawn from Ref. 26.)

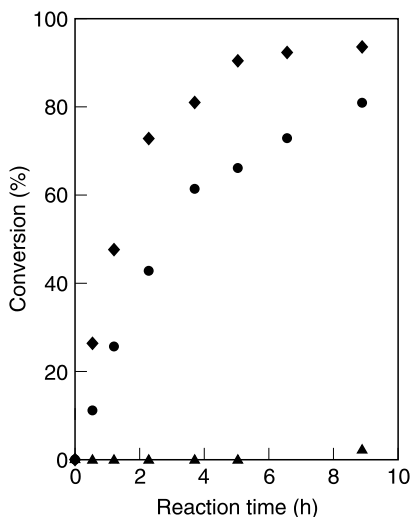


FIGURE 7.5 Conversion of different decyl halides to decyl sulfonate as a function of reaction time. ♦ = iodide, ● = bromide, ▲ = chloride. (Redrawn from Ref. 26.)

polymerizable entity, such as a combination of styrene and divinylbenzene. An oil-soluble emulsifier is used and the free-radical initiator should be water-soluble. An open structure is formed and the water can easily be removed after completed polymerization, resulting in a light foam with the foam lamella consisting of polymer and surfactant. The cells obtained from polymerized divinylbenzene are typically in the range of 10 to 20 μm in diameter, which corresponds rather well with the size of the water drops of the starting water-in-oil emulsion.

Even after completed polymerization there remain many pendant carbon-carbon double bonds. These can be used for derivatization. A range of such derivatized foams has been made from polystyrene/polydivinylbenzene-HIPE using functionalized thiols as derivatization reagents (28). Thiols add to olefins in an anti-Markovnikov fashion by a free-radical mechanism. Amine, alcohol, ester, thiol, halide, acid, and ester groups have been introduced on the foam by this approach. The functionalized HIPE foams can be used as supported catalysts for organic synthesis.

7.3 REACTION IN MICROEMULSIONS

Microemulsions are excellent solvents both for hydrophobic organic compounds and for inorganic salts. Being macroscopically homogeneous yet microscopically dispersed, they can be regarded as something between a solvent-based one-phase system and a true two-phase system. In this context, microemulsions should be seen as an alternative to two-phase systems with phase transfer agents added (29). A very good example, among many, of how effective a properly formulated microemulsion can be in overcoming reagent incompatibility is the detoxification of mustard, $\text{ClCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{Cl}$.

Mustard is a well-known chemical warfare agent. Although it is susceptible to rapid hydrolytic deactivation in laboratory experiments where rates are measured at low substrate concentrations, its deactivation in practice is not easy. Due to its extremely low solubility in water, it remains for months on a water surface. Addition of strong caustic does not markedly increase the

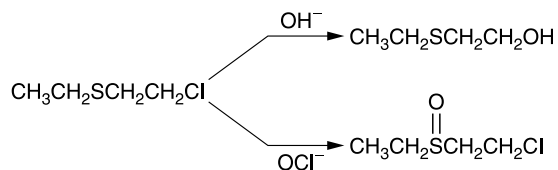


FIGURE 7.6 Transformation of 2-chloroethylethyl sulfide (half-mustard) into 2-hydroxyethylethyl sulfide (by alkali) or into 2-chloroethylethyl sulfoxide (by hypochlorite).

rate of reaction. Menger and Elrington have explored microemulsions as media for both hydrolysis and oxidation of “half-mustard,” $\text{CH}_3\text{CH}_2\text{SCH}_2\text{CH}_2\text{Cl}$, a mustard model (Figure 7.6) (30). Oxidation with hypochlorite turned out to be extremely rapid in both o/w and w/o microemulsions. In formulations based on anionic, nonionic, or cationic surfactant oxidation of the half-mustard sulfide to sulfoxide was complete in less than 15 s. The same reaction takes 20 min when a two-phase system, together with a phase agent, is employed.

A microemulsion can also accelerate the reaction by other means than by supplying a large interfacial area. If the surfactant headgroup carries a charge, as is the case with anionic and cationic surfactants, reagents of opposite charge will be confined to the interior of the droplets of water-in-oil microemulsions. Such a compartmentalization and concentration of the reagents may lead to a rate enhancement, as has been demonstrated in several cases, e.g., in oxidation of iodide by persulfate (31,32). The surfactant monolayer may also accelerate the reaction by attracting reagents of opposite charge situated in the water domain, thus increasing its concentration in the interfacial zone, where the reaction occurs. This type of rate increase has been referred to as microemulsion catalysis in analogy with micellar catalysis for systems without an oil component (33).

Yet another use of microemulsions in organic synthesis is to take advantage of the oil–water interface as a template for one or more of the reagents. The presence of an oil–water interface may induce orientation of reactants in microemulsion systems, which in turn may affect the regioselectivity of organic reactions. All three aspects of the use of microemulsions as medium for organic synthesis, i.e., overcoming reagent incompatibility, providing specific rate enhancement (microemulsion catalysis), and inducing regiospecificity, will be covered in this chapter, which has focused on recent developments in the field. There are several reviews of organic reactions in microemulsions that cover the earlier literature on the topic (7,29,33–38).

7.3.1 OVERCOMING REAGENT INCOMPATIBILITY

Several studies have shown that microemulsions are suitable reaction media for organic reactions involving reactants of widely different polarity. A properly formulated microemulsion can dissolve both reactants and the large oil–water interfacial area enables contact between the two otherwise incompatible species. For some reactions the reactivity in a microemulsion and in a two-phase system with added phase transfer agent is similar (39) but in other instances the reaction is considerably faster in a microemulsion (30,40). The superiority of a microemulsion was particularly pronounced in the synthesis of a surface-active product, decyl sulfonate (39). Decyl bromide and sodium sulfite were used as starting materials and two different microemulsions were tested, one water-in-oil and one bicontinuous. Either a crown ether or a quaternary ammonium salt (Q salt) was employed as phase transfer agent in the two-phase system. As can be seen from Figure 7.7, the reaction proceeded at a reasonable rate in the microemulsions but ceased at an early state in

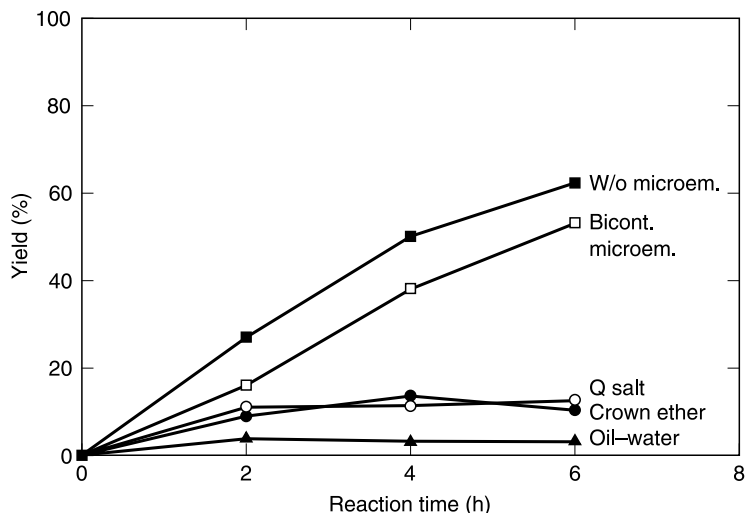


FIGURE 7.7 Reaction profiles for decyl sulfonate synthesis in various reaction media.

the two-phase systems. The poor reactivity in the latter systems has been interpreted as being due to the phase transfer agent partitioning entirely into the hydrocarbon phase due to ion pair formation with the lipophilic anion formed. Too strong association with a lipophilic anion will prevent the Q salt or crown ether to go back into the aqueous phase to pick up another reacting anion and transfer it into the organic phase where the reaction occurs (37,39). This is likely to be a general phenomenon and microemulsions may, thus, constitute a particularly interesting alternative to phase transfer catalysis in cases where the product is a lipophilic anion.

Microemulsions and two-phase systems with added phase transfer agent are both useful means of overcoming reagent incompatibility, but on entirely different accounts. In phase transfer catalysis, the nucleophilic reagent is carried into the organic phase where it becomes poorly solvated and 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. In an attempt to combine the two methods and take advantage of both the high reactivity of a poorly solvated anion in phase transfer catalysis and the very large oil–water interface of a microemulsion, Häger and Holmberg carried out a ring-opening reaction of a lipophilic epoxide in a microemulsion in the presence of a conventional Q salt, tetrabutylammonium hydrogen sulfate (40). Reactions were also performed in a two-phase system with and without added Q salt. It was found that the rate of the Q salt-catalyzed system is increased further when the reaction is carried out in a microemulsion instead of an oil–water two-phase system.

The above reaction was performed in a microemulsion based on a chlorinated hydrocarbon and a combination of two alkylglucoside surfactants was used for formulating the microemulsion. An attempt was also made to accelerate the same reaction performed in a microemulsion based on water, nonionic surfactant, and hydrocarbon oil (41). The reaction was performed in a Winsor III system and the same Q salt, tetrabutylammonium hydrogen sulfate, was added to the formulation. In this case the addition of the phase transfer agent gave only a marginal increase in reaction rate. Similar results had previously been reported for an alkylation reaction performed in different

types of micellar media (42). The addition of a Q salt did not affect a system based on cationic surfactant, a marginal increase in rate for a system based on nonionic surfactant, and a substantial effect when an anionic surfactant was used. The last system, also with Q salt added, gave lower yield than the first two, however, most likely due to electrostatic repulsion of the negatively charged nucleophile by the anionic micelles.

In a more recent work the microemulsion approach and phase transfer catalysis was combined in a nucleophilic substitution, reaction between *t*-butylbenzyl bromide and potassium iodide (43). The microemulsion was based on a chlorinated hydrocarbon and a sugar surfactant, octyl glucoside, which means that there were no counter-ions competing with the nucleophile at the oil–water interface. A quaternary ammonium salt, tetrabutylammonium hydrogen sulfate, was used as phase transfer catalyst, both in an amount equimolar to the iodide and in a catalytic amount. The results are shown in Figure 7.8. As can be seen, the combined approach gives the highest reaction rate in both cases. Use of a phase transfer catalyst in a microemulsion-based reaction can be practically useful.

Reactions in microemulsions have been compared with reactions in liquid crystalline phases. Such comparisons are interesting because they may give information about what is most important for the high reactivity of microemulsion systems: the large oil–water interface or the high dynamics of the system. Both liquid crystalline phases and microemulsions have a high interfacial area but liquid crystals lack the high dynamics of microemulsions. Formation of 2-furfurylthiol from cysteine/furfural and cysteine/ribose mixtures proceeded much more rapidly in both water-in-oil microemulsions (44) and bicontinuous cubic phases (44,45) than in aqueous systems. The reaction was faster in the cubic phase than in the microemulsion, a fact that was mainly attributed to the larger interfacial area in the former system (45).

In another comparison between a liquid crystalline phase and a microemulsion as reaction medium an amphiphilic polymer, a poly(ethylene glycol) with hydrophobic chains at both ends, was synthesized in an oil-in-water microemulsion and in a lamellar liquid crystal. Both systems were based on penta(ethylene glycol)monododecyl ether (C12E5) as surfactant and decane as oil component. Using the same composition and changing only the temperature one could go from a microemulsion (at 22 °C) to a lamellar liquid crystalline phase (at 39 °C). Thus, in this case the interfacial area, which is largely determined by the surfactant content, was about the same in the two systems. The reaction rates in the two systems were approximately the same and very much higher than the rate of the same reaction performed in a two-phase system without neither surfactant, nor phase transfer agent (46).

Figure 7.9 shows yet another example of a comparison between a microemulsion and a liquid crystalline phase as reaction medium (47). The reaction studied, substitution of bromide by iodide, has been discussed above (see Figure 7.8). As can be seen from the figure, the rate in the lamellar liquid crystalline phase is somewhat lower than that in the microemulsion. An interesting observation that can be made from the figure is that the rate in a Winsor I system is very similar to that in the one-phase microemulsion. A Winsor I system is a two-phase system consisting of an oil-in-water microemulsion in equilibrium with excess oil. It was also shown that it was not necessary to stir the Winsor system. The rate with and without stirring was the same. The observation that a Winsor system is just as effective a reaction medium as a one-phase microemulsion has been observed before, for another nucleophilic substitution reaction (48). The fact that a Winsor I system can be used instead of a one-phase microemulsion is practically important. Formulation of a one-phase microemulsion is often a problem, particularly when one wants a high loading of reactants into the oil and water domains, and one may end up with various types of two- or three-phase systems. Evidently, such systems may be just as useful as reaction media, as long as one of the phases is a microemulsion. The excess phase (or phases) can

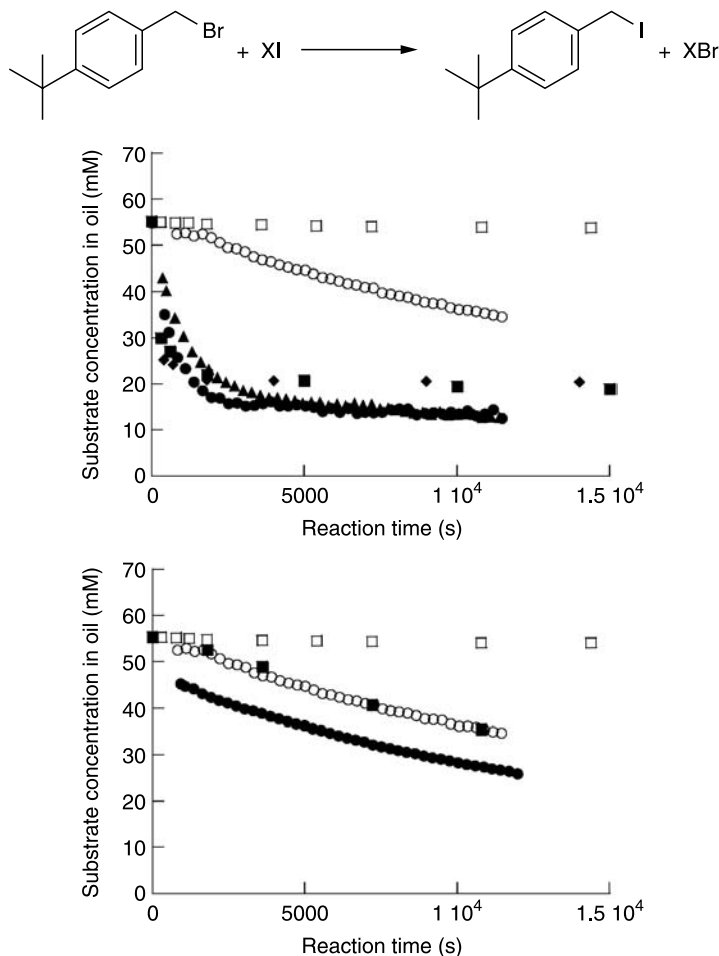


FIGURE 7.8 Reaction profiles for the reaction between 4-*tert*-butylbenzyl bromide and potassium iodide in microemulsion based on dichloromethane, octyl glucoside, and deuterated water using either an equimolar (top) or a catalytic (bottom) amount of tetrabutylammonium hydrogen sulfate (TBAHS) or tetrabutylammonium bromide (TBAB) as phase transfer agent. The reaction was monitored by NMR observing the disappearance of the $-CH_2Br$ signal and appearance of the CH_2I signal. Top: in $D_2O-C_8G_1-CH_2Cl_2$: (○) without Q salt, (●) with TBAHS, (▲) with TBAB; and in $D_2O-CH_2Cl_2$: (□) without Q salt, (■) with TBAHS, (◆) with TBAB. Bottom: in $D_2O-C_8G_1-CH_2Cl_2$: (○) without Q salt, (●) with TBAHS; and in $D_2O-CH_2Cl_2$: (□) without Q salt, (■) with TBAHS.

be regarded as reservoirs for the reactant (or reactants) while the reaction occurs at the oil–water interface of the microemulsion phase.

One of the early examples of the usefulness of microemulsions to overcome the problem of reagent incompatibility was the work by Menger and Elrington on detoxification of mustard; see [Figure 7.6](#) (30). Menger and Rourk have recently revisited the reaction, now exploring the use of cryochemistry for the purpose (49). Microemulsions that resist freezing and phase separation at $-18^\circ C$ were developed using water–propylene glycol as aqueous component and fatty alcohol

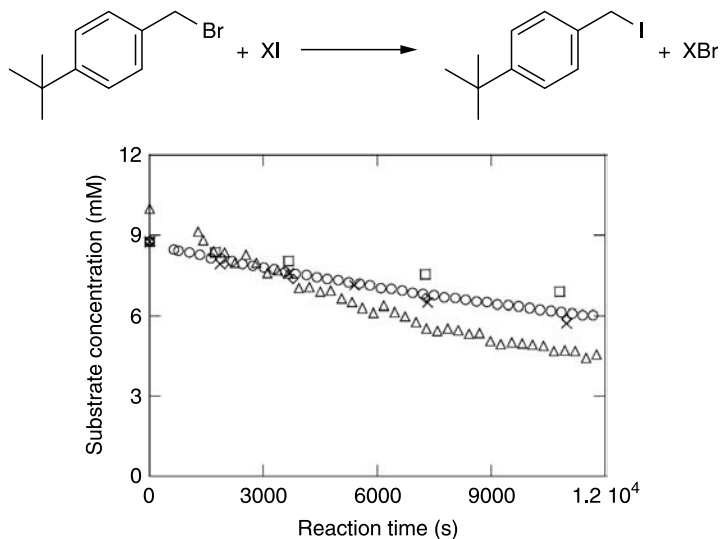


FIGURE 7.9 Reaction profiles for the reaction between 4-*t*-butylbenzyl bromide and potassium iodide performed in lamellar phase (□), oil-in-water microemulsion (○), micellar system (Δ), and Winsor I system (oil-in-water microemulsion in equilibrium with excess oil) (×), all based on alcohol ethoxylate surfactants.

ethoxylates with long polyoxyethylene chains as surfactants. Different types of chemical warfare agents were destroyed by reaction at -18°C , either by hydrolysis or by oxidation.

An attempt was made to correlate the rate of hydrolysis of acetylsalicylic acid with the structure of the microemulsion used as reaction medium (50). Water was added to the formulation and it was found that the reaction rate changed abruptly when the system passed from water-in-oil to bicontinuous and again when the bicontinuous microemulsion was transformed into an oil-in-water microemulsion. For a microemulsion based on a nonionic surfactant the bicontinuous microemulsion gave the highest reaction rate, for a microemulsion based on an anionic surfactant the oil-in-water system was the most reactive, and for a cationics-based microemulsion the water-in-oil system gave the highest reaction rate. Similar results were obtained in another study of the same reaction (51). In previous studies of reactivity in different types of microemulsions based on nonionic surfactants, no large differences in reaction rate were observed, however (52).

Microemulsions have recently been used as medium for hydroformulation reactions (53). Water-soluble rhodium complexes have been found to be highly active in microemulsions based on alcohol ethoxylates. A series of internal olefins have been hydroformylated at temperatures of around 120°C and a pressure of 100 bar. 7-Tetradecene as model alkene was hydroformulated to give 2-hexylnonal at high reaction rate and with a high degree of regioselectivity. It was also shown that the catalyst could be recycled in the work-up process.

7.3.2 EFFECT OF SURFACTANT CHARGE ON REACTIVITY

There are many examples of how the charge of the surfactant headgroup can affect the rate of reaction between a lipophilic organic molecule and a charged, polar nucleophile. The general rule is that cationic surfactants accelerate the reaction involving anionic nucleophiles and vice versa, an effect referred to as microemulsion catalysis. However, it has been found that for cationic

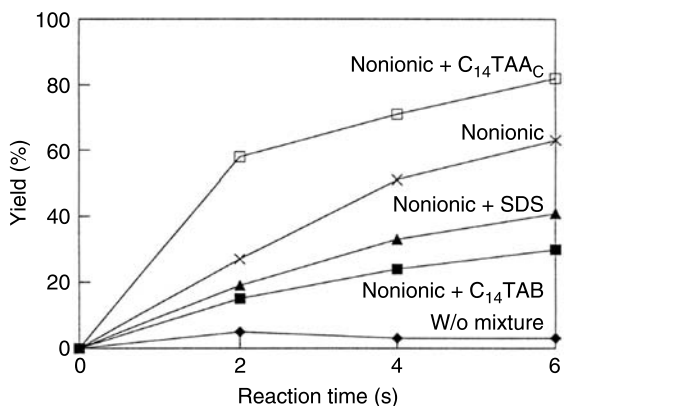


FIGURE 7.10 Effect of addition of ionic surfactant to a microemulsion based on a nonionic surfactant on the rate of formation of decyl sulfonate from decyl bromide and sodium sulfite.

surfactants the choice of counter-ion is decisive of the rate. The choice of counter-ion for anionic surfactants seems to be of less importance.

Oh et al. have shown that the addition of a small amount of the anionic surfactant sodium dodecyl sulfate (SDS) to a nonionics-based microemulsion increased the rate of decyl sulfonate formation from decyl bromide and sodium sulfite (54,55). Addition of minor amounts of the cationic surfactant tetradecyltrimethylammonium salt gave either a rate increase or a rate decrease depending on the surfactant counter-ion. A poorly polarizable counter-ion, such as acetate, accelerated the reaction. A large polarizable counter-ion, such as bromide, gave a slight decrease in reaction rate. The reaction profiles for the different systems are shown in Figure 7.10.

More recently, the effect of surfactant charge on the reaction rate was investigated for the ring opening of 1,2-epoxyoctane with sodium hydrogen sulfite (41). The reaction, which was performed in a Winsor III microemulsion, i.e., a microemulsion in equilibrium with both oil and water, was fast when a nonionic surfactant was used as the sole surfactant and considerably more sluggish when a small amount of SDS was added to the formulation. Another reaction in which the effect of added ionic surfactant was studied related to oxidation of azo dyes by hydrogen peroxide catalyzed by manganese porphyrins. The reaction was fast in a microemulsion based on nonionic surfactant. Addition of a small amount of cationic surfactant speeded up the reaction further while addition of an anionic surfactant led to retardation (56). These results imply that an anionic species is involved in the rate-determining step of the reaction.

An interesting example of a specific ion effect in microemulsions is the strong increase in reactivity found for large, polarizable anions such as iodide and bromide. The tendency for such ions to interact with, and accumulate at, the interface can be taken advantage of for preparative purposes. The increased concentration of such ions in the interfacial zone, where the reaction takes place, will lead to an increase in reaction rate. Expressed differently, the reactivity of iodide and other highly polarizable ions will be very high in such systems. The microemulsions need not be based on cationic surfactants that would drive the anions to the interface by electrostatic attraction. Also microemulsions based on nonionic surfactants display the effect because large, polarizable anions interact with the hydrophobic surface by dispersion forces (57,58). The mechanism of attraction (and the rationale for the increased concentration of reacting species) is, thus, different from that of micellar catalysis, which is basically an ion exchange process.

An illustrative example of the effect of a large polarizable ion at the oil–water interface is the above-mentioned reaction between 4-*t*-butylbenzyl bromide and potassium iodide to give 4-*t*-butylbenzyl iodide. The reaction was performed in a microemulsion based on the nonionic surfactant penta(ethylene glycol)monododecyl ether (C₁₂E₅) and the temperature was varied from 23 to 29 °C, which is the total temperature range of the isotropic oil-in-water region of this system (59). It was found that the reaction rate decreased considerably when the temperature was increased from 23 to 29 °C. ¹²⁵I NMR showed a marked temperature effect on line broadening; the lower the temperature the broader the signals (within the temperature range 23 to 29 °C). This indicates that the iodide ion interacts more strongly with the interface at lower temperature, which is likely to be the reason for the inverse temperature–reactivity relationship. Thus, ion binding to the microemulsion interface can have a pronounced effect on reactivity also in microemulsions based on uncharged surfactants. In another investigation of a nucleophilic substitution reaction in microemulsion, synthesis of 1-phenoxyoctane from 1-bromooctane and sodium phenoxide, no accumulation of the nucleophile at the interface could be observed based on the kinetics data (48,60). This is in line with the view that only the large polarizable anions, such as iodide, become attracted to the interface due to dispersion force interactions (57).

Thus, the use of microemulsions as media for organic substitution reactions can lead to a difference in reaction pattern due to differences in relative nucleophilicity as compared to reactions in homogeneous media. Bunton, Savelli, and others have shown this to be the case for reactions in micellar media (61–65). For instance, the type of reaction medium – homogeneous solution or micellar solution based on cationic surfactant – has been found to be decisive of the reaction of sulfonate esters in the presence of equimolar amounts of bromide and hydroxyl ions. Without surfactant present attack by hydroxyl ions dominates. In the micellar solutions, on the other hand, bromide is the dominating reacting species. Evidently, the larger and more polarizable bromide ion becomes more attracted than the hydroxyl ion to the micellar interface (61).

7.3.3 SELECTIVITY IN MICROEMULSION-BASED REACTIONS

The large oil–water interface of microemulsions can be used as a template for organic reactions. Organic molecules with one more polar and one less polar end will accumulate at the oil–water interface of microemulsions. They will orient at the interface so that the polar part of the molecule extends into the water domain and the nonpolar part extends into the hydrocarbon domain. This tendency for orientation at the interface can be taken advantage of to induce regiospecificity of an organic reaction. A water-soluble reagent will react from the “water side,” i.e., attack the polar part of the amphiphilic molecule, and a reagent soluble in hydrocarbon will react at the other end of the amphiphilic molecule. The principle, although applied to a micellar system, not a microemulsion, is nicely illustrated by an early study of the ability of aqueous micelles to control the regioselectivity of a Diels–Alder reaction in which both reactants were surface active (66). The diene, as well as the dienophile, were lipophilic molecules with a trimethylammonium headgroup. This Diels–Alder system should display no regiochemical preference in the absence of orientational effects since the substituents were close to being both electronically and sterically equivalent with respect to the diene and dienophile reaction centers. When the reactions were run in an organic solvent, i.e., in absence of micellar orientational effects, the two regioisomers were obtained in equal amounts. When, on the other hand, the reactions were carried out in an aqueous buffer in which the reactants form mixed micelles, a regioisomer ratio of 3 was obtained.

Another example, this time in a proper microemulsion, is stereoselective nitration of phenol. It has been claimed that the reaction in an oil-in-water microemulsion gives a preference for ortho nitration whereas conventional nitration in a homogeneous reaction system gives predominantly

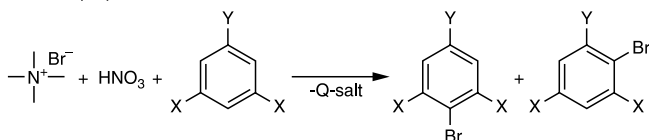
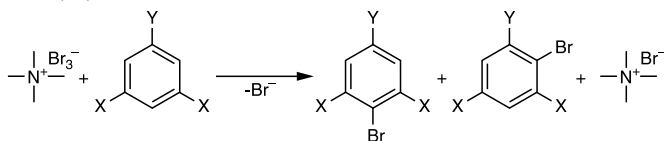
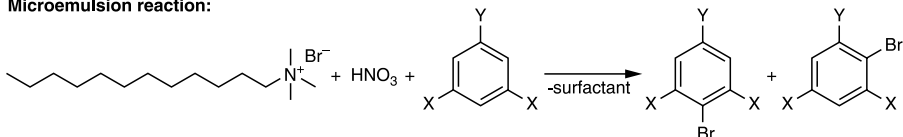
Two-phase reactions:**1. In-situ prepared bromine salt:****2. Pre-prepared bromine salt:****Microemulsion reaction:**

FIGURE 7.11 Reaction approaches used for bromination; $x = \text{H}$ or CH_3 ; $y = \text{CH}_3$, OH , or OCH_3 .

para nitration (67). The results have been questioned, however, since it has not been possible to repeat the experiments (68).

A related reaction, bromination of two phenols and two anisols, has been carried out in a cationic surfactant-based microemulsion using the surfactant counter-ion, i.e., bromide, as reagent (68). The bromide ion was oxidized to elemental bromine by dilute nitric acid, which in turn reacted with the aromatic compound. The results have been compared with two-phase procedures using either an in situ-prepared or a pre-prepared complex between bromine and a quaternary ammonium salt as oxidizing reagent and also with conventional bromination using elemental bromine. The different routes are shown in Figure 7.11. Reaction in the microemulsion gave a more selective para-bromination than the other procedures. In addition, the microemulsion-based reaction proceeded smoothly at room temperature.

Water-in-oil microemulsions have recently been employed to control the regioselectivity of the photocycloaddition of 9-substituted anthracenes (69). Reaction in microemulsion gave very different orientation from that in homogeneous solution. This difference is believed to be due to orientation of the anthracenes at the oil–water interface prior to the irradiation.

Several studies have dealt with the Diels–Alder reaction carried out in micellar media, but not in microemulsions. An early example is given in Ref. 66. Jaeger has continued the work on combining surface-active dienes with surface-active dienophiles and obtained a very high preference for the adduct with the quaternary ammonium groups situated on the same side, obviously due to an orientation in the micelles prior to the cycloaddition (70). The reaction is shown in Figure 7.12.

The adduct with the quaternary ammonium groups situated on the same side was formed predominantly. The regioselectivity is most likely due to the orientation of the diene and dienophile at the micelle–water interface, as illustrated in Figure 7.13.

It has recently been found that microemulsions can be used as a tool to differentiate between the first and the second step of a substitution of symmetrical bifunctional reactants, in this case α,ω -dibromoalkanes (71). In a homogeneous system, where both the lipophilic reactant, the

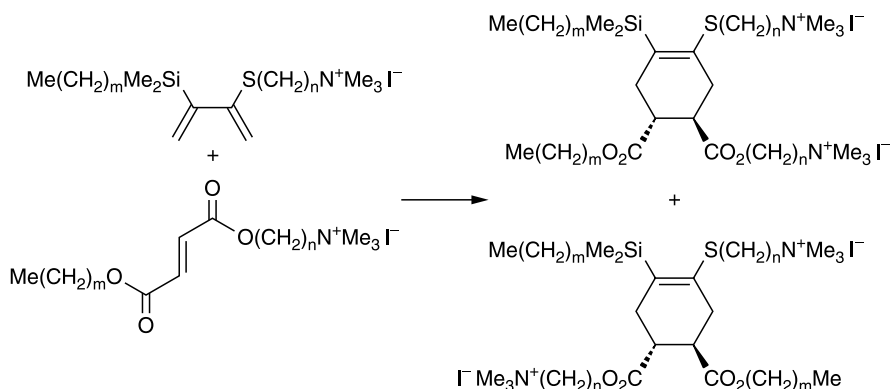


FIGURE 7.12 A Diels–Alder reaction between a surface-active diene and a surface-active dienophile.

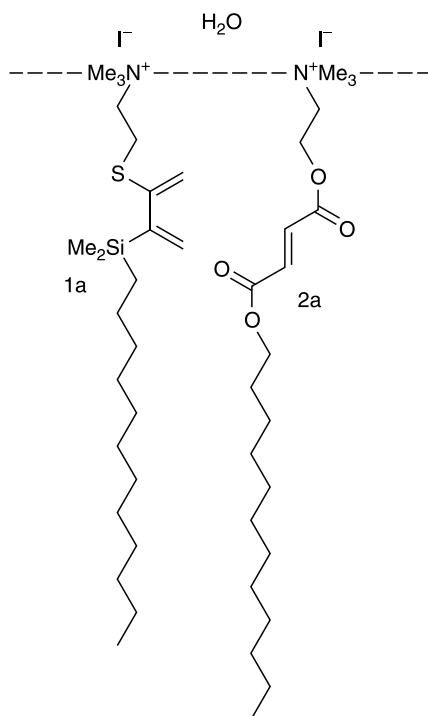


FIGURE 7.13 Preferred orientation of the reactants of Figure 7.12 in a micelle composed of the two surface-active cationic species.

α,ω -dibromoalkane, and the hydrophilic reactant, sodium sulfite, are dissolved the two substitution steps will occur at the same rate. The situation proved to be different in a microemulsion. The intermediate mono-substituted species, a bromoalkanesulfonate, has one polar and one non-polar end; hence, it orients at the interface such that the sulfonate end points into the water domain, leaving the bromo end in the nonpolar environment. Provided that the alignment of

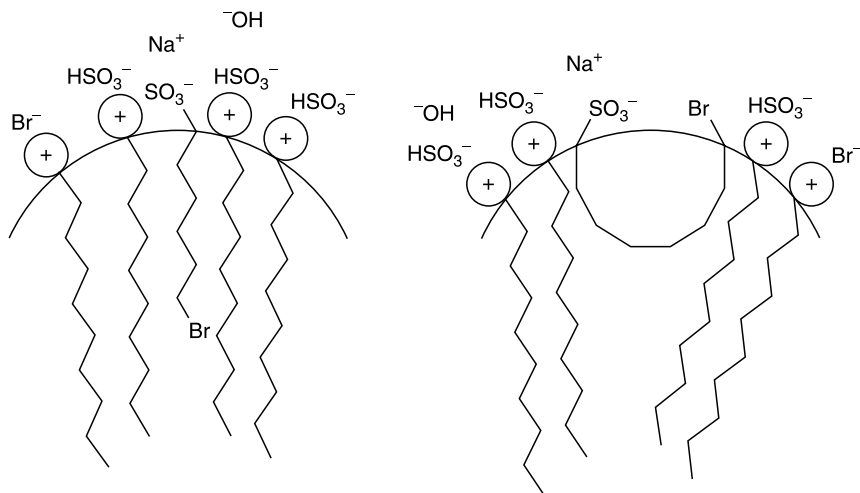


FIGURE 7.14 Alignment of a short-chain (left) and a long-chain (right) bromoalkanesulfonate at the oil–water interface of a microemulsion.

the intermediate is fast compared to the rate of the substitution reaction, such an orientation of the intermediate may protect it from further nucleophilic attack. This turned out to be the case for some of the α,ω -dibromoalkanes. For the species with the shortest alkane chain, 1,4-dibromobutane, there was a pronounced difference in rate of the first and the second substitution step and the intermediate, bromobutanesulfonate could be recovered in high yield. The selectivity decreased with the alkane chain length. Evidently, the second bromide is less protected for the longer derivatives. A likely explanation for the effect is illustrated in Figure 7.14. The more limited regiochemical control for the longer derivatives is probably due to a considerable conformational freedom of these molecules, which allows the remaining bromomethyl group to be exposed at the interface. When the “spacer group” between the sulfonate and the bromomethyl group is short, such folding is more difficult to achieve.

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