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Aggregation and reactivity in aqueous solutions of cationic surfactants and aromatic anions across concentration scales

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Abstract

The use of aqueous solutions as solvents in synthetic chemistry is one of the pathways towards more sustainable chemical processes. To increase solubility of reactants in aqueous solutions, surfactants can be used. In particular as a result of detailed kinetic studies involving probe reactions, our current understanding of the reaction environment offered by micelles is good to excellent. However, this understanding does not always translate well to reactions on a synthetic scale because concentrations are typically very different from concentrations used in probe reactions. These high concentrations may lead to changes in aggregate morphologies, in particular where aromatic anions are used in combination with cationic surfactants. An overview of aggregation processes and aggregate morphologies across concentration scales is presented together with a discussion of the resulting effects on reactivity in solutions containing cationic surfactants and (reactive) aromatic anions.

1. Introduction

1.1 Water in organic synthesis

Water and aqueous solutions have been advocated as environmentally friendly, green, solvents for synthesis. Further advantages of water as a solvent include it being non-flammable and displaying favourable hydrogen-bonding properties. These hydrogen-bonding properties have been argued to underpin some of the remarkable rate accelerations observed in so-called “on-water” reactions[1] and such effects are thought to play a role in the recent finding of beneficial effects of water on the nucleophilic attack of butyllithium on imines and nitriles.[2] This remarkable finding illustrates the extent to which the author of this article, despite a long-standing interest in aqueous chemistry, underestimated the possibilities of water in organic synthesis when he wrote that “butyllithium and water are simply not compatible.”[3]

1.2 Surfactant-supported synthesis

An argument that is frequently used against the use of water as a solvent involves the lack of solubility of many reactants typically used in organic synthesis. Even this disadvantage can be turned into an advantage, as we have recently shown in a synthetic procedure where a water-ethanol mixture was optimised to dissolve reactants but lead to crystallisation of the desired product.[4] Nevertheless, the usual approach to deal with the solubility challenge is to use solubilising agents such as hydrotropes or surfactants. Hydrotropes are compounds incorporating both a hydrophobic and a hydrophilic moiety which are too small to lead to cooperative formation of assemblies but which nevertheless increase the solubility of hydrophobic materials in aqueous solutions.[5-8] For examples of surfactant-supported syntheses, the reader is referred to the review by Dwars *et al.,*[9] to a review of the development of designer surfactants supporting a wide range of reactions by Lipshutz and Ghorai,[10] and our previous reviews on reactivity in organised assemblies.[11-14]

1.3 Micelle morphologies depend on surfactant shape

In aqueous solutions, surfactants form a variety of aggregates, from spherical micelles, rodlike micelles, wormlike micelles, to bilayers and vesicles. The aggregate morphology can be predicted with good accuracy using the packing parameter P, developed by Israelachvili and Ninham,[15] which describes the shape of a surfactant molecule (equation 1),

$$P = V / (a_0 \times l) \qquad \text{equation 1}$$

where V is the volume of the hydrocarbon chain(s) of the surfactant, a_0 is the effective headgroup surface area, and l is the length of the hydrocarbon chain in the all-trans conformation. For $P < ⅓$, the surfactant is cone-shaped and forms spherical micelles; for $⅓ < P < ½$ the surfactant has the shape of a truncated cone and forms wormlike micelles; for $½ < P < 1$ the surfactant has a cylindrical shape and forms flat bilayers or vesicles; for $P > 1$, the surfactant is an inverted truncated cone and forms inverted micelles.

Structures of selected surfactants discussed in this review, which represent typical cationic surfactants, are shown in Scheme 1.

C_{10}TABr: n=10, X=Br
C_{12}TABr: n=12, X=Br
C_{16}TACl: n=16, X=Cl
etc.

C_{12}mimCl: n=12, X=Cl

Scheme 1

1.4 Micelles as reaction medium according to probe reactions

The many elegant examples of micelle-supported syntheses generate a series of conceptual challenges. The first challenge regards where reactants and products bind in micelles. The general view on this is that the most hydrophobic compounds enter the micellar core, leading to swelling of micelles, while more polar compounds tend to bind in the micellar Stern region. The second challenge involves what micelles look like in terms of reaction medium. This challenge has been addressed by several groups, typically using reactions involving very low concentrations (~ 10 µM) of often neutral reactive chemical probes in combination with higher surfactant concentrations (~ 1-10 mM). For examples, see References [3,16-23]. The combined efforts of multiple groups have now resulted in a good understanding of typical micellar binding sites and what these sites look like in terms of reaction medium for a wide range of surfactant systems.

1.5 Scaling up organic reactions in micellar solutions

For reactions to be synthetically useful, higher concentrations of reactants are required which lead to higher concentrations of products as well. These higher concentrations may affect the micellar reaction medium, with implications for the validity of the reaction medium models derived using low concentrations of reactive probes. In addition, such reaction systems involve significant changes in composition during the reaction. The extent to which this forms a current challenge became clear to us in some of our recent work in which we attempted to exploit our understanding of the reaction environment offered by cationic micelles in the rational optimisation of a palladium-catalysed cross-coupling reaction in aqueous surfactant solution. While studying the kinetics of reactions involving arylboronic acids in micellar solutions of C_{16}TABr, we observed that observed rate constants for these reactions were constant despite the reactions following apparently good first order decay curves. In fact, increasing concentrations of phenylboronic acid resulted in decreases in the observed rate constants. This decrease in observed rate constants suggests that a process involving multiple molecules of phenylboronic acid coming together was causing the observed kinetic effects. We initially suspected that boroxines might form in the micellar solutions but did not find any evidence for this hypothesis. We then noted that the structure of the conjugate base of phenylboronic acid, phenylboronate, is reminiscent of hydrotropes. In addition to the structural similarity, we observed signs of viscoelasticity in some of our solutions containing C_{16}TABr and phenylboronic acid,[24] suggesting the possible formation of wormlike micelles.

We thus became interested in the effects of interactions between aromatic anions and cationic surfactants on aggregate morphology across concentration scales and their potential effects on reaction kinetics, all of course in aqueous solutions.

A key consideration are the concentration ranges of surfactants and aromatic anions involved in these solutions. For convenience, these concentration ranges are defined here relative to the critical micelle concentration (cmc) of the surfactant in water in the absence of additives. The concentration ranges of interest can thus be represented as in Figure 1.

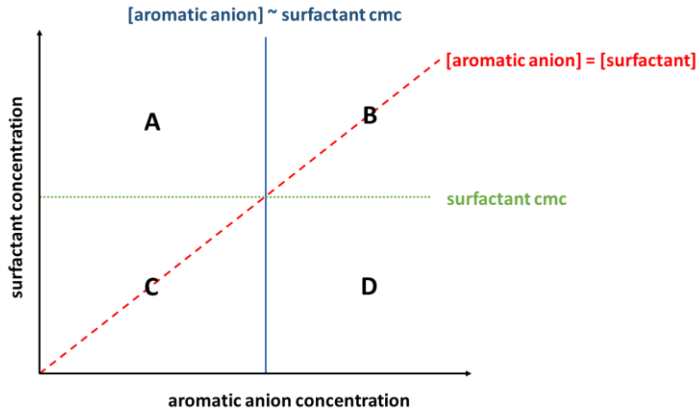


Figure 1: The relative concentration ranges of surfactants and hydrotropes of interest can be divided into four quadrants. The red dashed line indicates equal concentrations of surfactant and hydrotrope.

Figure 1 shows the four quadrants defined by the relative concentrations of surfactant and aromatic anions. Figure 1 also indicates where the concentration of the surfactant equals the concentration of the aromatic anion. Assuming full binding of the aromatic anion, combinations of concentrations on this line for singly charged surfactants and singly charged aromatic anions lead to the formation of “self-assembled zwitterionic surfactants”. We note, however, that many systems that have been studied also include chloride or bromide counteranions, and therefore this line only gives a general indication.

This Review aims to cover what happens across these concentrations regimes. We will first review these regimes in terms of non-reactive systems, followed by a discussion of kinetic effects across the concentration ranges.

2. Aggregate formation across the concentration scales

Before discussing time-dependent reacting systems, we first explore the types of structures formed in the four different quadrants by looking at examples of representative systems.

2.1 Quadrant A – anionic dyes dissolved in micelles

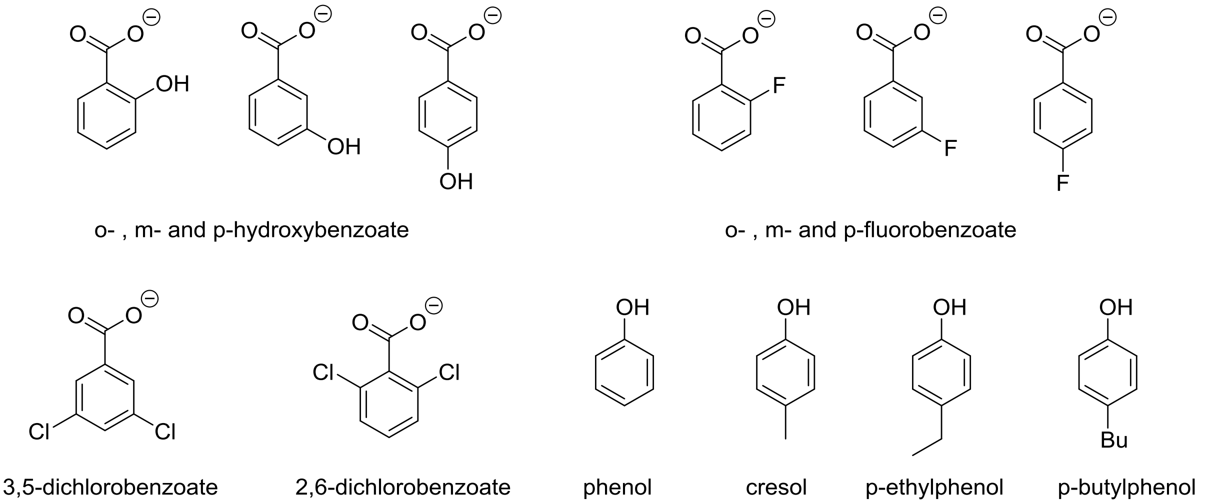
In quadrant A, an excess of surfactant dissolves a far smaller amount of aromatic anions. This concentration range is typically studied using UV-visible spectroscopy. Quadrant A is often represented by the final data points of studies of interactions between aromatic anions and cationic surfactants in quadrant C in which surfactant concentrations are increased while dye concentrations are kept constant. It is commonly assumed that in this range, surfactant aggregate morphologies are not significantly affected by the aromatic anions.

2.2 Quadrant B – at high concentrations of hydrotropes and surfactants above the critical micellar concentration smart materials result from formation of wormlike micelles

At concentrations of hydrotropes and surfactants above the cmc of the surfactant, the addition of aromatic anions to solutions containing cationic surfactants often leads to changes in micellar morphology. Binding of the aromatic counteranions in the micellar Stern region results in a decrease of the effective headgroup surface area a_0 and thus an increase in the packing parameter P. As suggested by the increasing packing parameter, the micellar morphology then changes to elongated structures and may eventually even change to bilayer systems and vesicles. In first instance rodlike micelles are formed. Rodlike micelles are micelles for which the micellar length is shorter than the so-called persistence length; these micelles are too short to show significant flexibility and therefore behave like stiff rods. When the elongated micelles continue to grow, their length will eventually exceed their persistence length so that they become flexible. Such long flexible micelles are referred to as wormlike micelles. Solutions containing wormlike micelles in the dilute regime typically behave as Newtonian fluids, i.e. they behave as one would expect fluids to behave. However, when the wormlike micelles become so long that their length is larger than the intermicellar distances, the wormlike micelles become entangled and this typically leads to significant changes in rheology.

Many different systems can form wormlike micelles and such systems have been reviewed by Dreiss.[25] Of interest here are systems involving surfactants that normally form spherical micelles but for which the addition of oppositely charged components (simple salts, hydrotropes, or cosurfactants) leads to a change in morphology to wormlike micelles. The most studied properties of systems involving wormlike micelles are their bulk properties and the reader is referred to the outstanding introduction by Dreiss to this topic.[26] In particular rheological properties, including viscoelasticity, have attracted much attention. Briefly the viscoelasticity of these solutions is the result of the formation of entangled networks of wormlike micelles. The detailed rheology of these solutions depends strongly on the length of the wormlike micelles, their stiffness (as expressed in persistence length) and the processes by which the entangled networks can be disentangled. Although some of the behaviours of solutions of wormlike micelles may be comparable to solutions of polymers, key differences are that the length of the wormlike micelles follows a broad distribution, wormlike micelles tend to be stiffer, and entanglements can be resolved through breaking and reforming of the wormlike micelles. Micelle length, stiffness and kinetics of breaking and reforming of micelles strongly depend on the precise chemical composition of mixtures. For example, the average length of the wormlike micelles depends on the precise ratio of surfactant to aromatic anion because this ratio determines how many end caps can be formed on the wormlike micelles. Hence the bulk rheological properties can be varied significantly with small changes in the chemical composition.

In addition to the precise molar ratio of surfactant to hydrotrope, the precise molecular structures of the surfactants and aromatic anions is critical as well. The importance of the molecular structure is demonstrated by the remarkable sensitivity to regiochemistry in aromatic anions (Scheme 2).



Scheme 2

It is well known that the addition of *o*-hydroxybenzoate to C_{16}TABr leads to the formation of wormlike micelles, but the addition of *m*- and *p*-hydroxybenzoate does not. For chlorobenzoates, the behaviour is opposite; here the *o*-isomer does not form wormlike micelles whereas the *m*- and *p*-isomer do.[27] Surfactants formed from $C_{14}TA^+$ with fluorobenzoate counteranions also show different behaviour depending on the regiochemistry of the aromatic anion.[28] The *m*- and *p*-isomers first form spherical micelles but at higher concentration undergo a transition to rodlike micelles. On the contrary, surfactant with the *o*-fluorobenzoate counteranion does not form rodlike micelles. The authors attribute the difference to *m*- and *p*-fluorobenzoate binding in the micellar Stern region, bringing the headgroups closer together, whereas the o-fluorobenzoate binds deeper inside the micelles and thus does not cause a morphological change. Analogous experiments using $C_{16}TA^+$ do show formation of rodlike micelles for all three regioisomers.[29] The sensitivity to substitution pattern continues with 3,5-dichlorobenzoate which forms wormlike micelles and viscoelastic solutions with $C_{16}TA^+$ while 2,6-dichlorobenzoate forms spherical micelles and Newtonian solutions.[30]

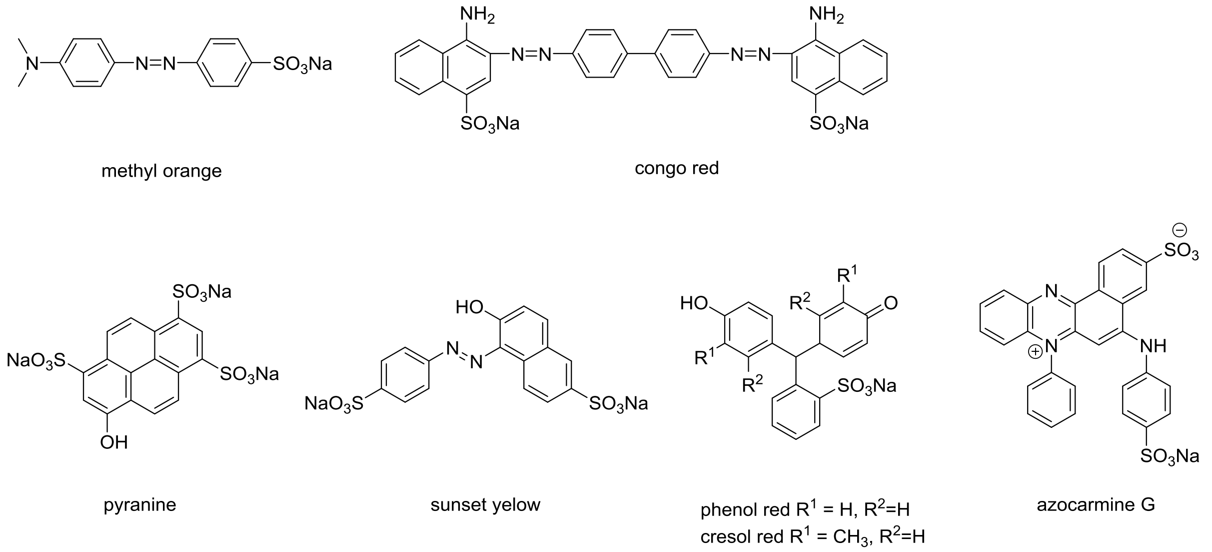
Phenols similarly display variable behaviour. Mixing C_{16}TABr with phenol, cresol, *p*-ethylphenol, *p*-butylphenol and *p*-t-butylphenol showed that phenol and cresol induce transitions to rodlike and eventually wormlike micelles. The more hydrophobic phenols induce transitions to wormlike micelles and then to unilamellar and bilamellar vesicles.[31]

Despite these remarkable effects of the aromatic anions, it is not only the structure of the hydrotropes that controls whether wormlike micelles will be formed. The surfactant structure plays a role as well. The importance of surfactant structure has been illustrated by Lutz-Bueno *et al.*[32] who have shown that the size of the surfactant headgroup matters. Comparison of $C_{16}TA^+$, hexadecylpyridinium and benzyldimethylhexadecylammonium showed that interaction with hydrotropes for surfactants with the largest headgroups cannot sufficiently decrease the effective headgroup surface area and limits the enhancement of viscoelasticity.

In addition to systems such as the examples above, stimulus-responsive wormlike micelles have also been prepared[33,34] including thermoresponsive[35,36] and pH-responsive[37] systems. The literature thus illustrates the remarkable tuneability of systems forming wormlike micelles. However, this tuneability also reflects the challenge in developing a detailed understanding of these systems in particular on the level required for rational design and optimisation of reaction conditions.

2.3. Quadrant C – below the critical micellar concentration anionic dyes interact with cationic surfactants

In quadrant C, concentrations of both surfactants and aromatic anions are low to very low. As a result of these low concentrations, only sufficiently sensitive techniques can be used to study the interactions and it can therefore remain difficult to distinguish between a small amount of precipitate, a pre-micellar aggregate, wormlike micelles and vesicles. The use of anionic dyes (Scheme 3) allows studies involving spectroscopic techniques in a concentration regime where rheology becomes less practical.



Scheme 3

Studies of the interactions between surfactants and anionic dyes identify the importance of the balance between aggregation and aggregation followed by precipitation.[38] In practice, this balance is defined by the Krafft temperature (the temperature below which precipitation occurs and above which surfactant-based assemblies remain in solution).

Buwalda and Engberts[38,39] have studied the addition of the anionic dye methyl orange to solutions of cationic surfactants. Clear spectroscopic changes indicate that aggregates form at very low concentrations. In fact, using electron microscopy, Buwalda *et al.* observe a veritable zoo of aggregates including wormlike vesicular structures, spherical vesicles, and sheets for systems involving dicationic surfactants. Critical aggregation concentrations are also decreased significantly upon the addition of methyl orange. For example, C_{10}TABr has a cmc of 60.2 mM but the critical vesicle concentration in the presence of methyl orange at 50 °C is just 0.84 mM. The authors also demonstrate the importance of both hydrophobic and electrostatic interactions in the formation of the aggregates. Work by Estelrich and co-worker[40] on alkyltrimethylammonium surfactants in the presence of the anionic photoacid pyranine also identifies multiple type of premicellar aggregates which are associated with different critical concentrations. Strikingly, for C_{16}TABr, one of the critical concentrations is as low as 10 µM.

Safavi and coworkers[41] in turn have demonstrated how concentration profiles for the various species involved in solutions containing C_{12}mimCl and anionic dyes azocarmine G and methyl orange, at surfactant concentrations below the cmc in the absence of additives, can be extracted from UV-visible data using chemometric approaches such as multivariate curve resolution – alternating least squares (MCR-ALS). Javadian and co-workers[42] used surface tension, spectroscopy, conductometry and pulsed field gradient NMR to study the interactions between congo red and cationic surfactants. They also observed sub-micellar ion pairing and subsequent aggregation, as did Sohrabi and co-workers for sunset yellow interacting with C_{12}TABr and dicationic gemini surfactants.[43] Finally, Dutta and co-workers[44,45] have shown that the formation of complexes between anionic dyes phenol red, cresol red and cresol purple and cationic surfactants can lead to a further deprotonation of the dye. This deprotonation results in formation of a complex between the dianionic dye and the cationic surfactants.

From the reports discussed above, but also from analogous studies, it is clear that aromatic anions interact with cationic surfactants at concentrations significantly below the cmc of the surfactant alone. Not surprisingly considering the formation of neutral ion pairs, these interactions can lead to a variety of larger aggregates including both soluble and insoluble aggregates. The consensus in the literature appears to be that these species dissolve in surfactant micelles once the surfactant concentration increases above the cmc, i.e. once the systems moves from quadrant C into quadrant A.

2.4 Quadrant D – the forgotten quadrant

To the best of our knowledge, quadrant D, where hydrotrope concentrations are relatively high and surfactant concentrations are low, has not been explored in detail. The paucity of information about this concentration regime is reasonable considering that this quadrant does not represent obvious applications of surfactants. Nevertheless, some experimental techniques lead us through quadrant D. Notably, this includes isothermal titration calorimetry, where surfactant is titrated into a relatively concentrated solution of the hydrotrope. These calorimetric studies show that aggregates are formed at low surfactant concentrations. For example, Šarac *et al.*[46,47] have titrated C_{12}TACl into *o*-, *m*- and *p*-hydroxybenzoate and observed significant lowering of the surfactant cmc, with *o*-hydroxybenzoate having by far the strongest effect. The findings from calorimetry were in agreement with the authors' results from ^{1}H NMR chemical shift changes and pulsed field gradient NMR (diffusion NMR) studies. Similarly, Ito *et al.* have titrated C_{14}TABr into a 1.5 mM *o*-hydroxybenzoate solution. The authors observed that as surfactant concentrations increase the aggregates turn from mixed aggregates to wormlike micelles to spherical micelles.[48] This titration essentially moves from quadrant D into quadrant B as more surfactant is added. As before, in the presence of *o*-hydroxybenzoate, critical aggregation concentrations decrease significantly to below 0.3 mM. The *m*- and *p*-isomers did not produce these effects.

2.5 linking the quadrants

Behaviour in quadrants A and B is well understood in general terms. In quadrant A, aromatic anions are dissolved in a large excess of spherical micelles (where surfactant forming spherical micelles have been used). Quadrant B is challenging in terms of the intricate dependence of aggregate morphology on concentration ratios, chemical structures and temperature but a wide variety of techniques exist to study both bulk and molecular behaviour. Key behaviour in quadrant B involves the formation of rod- and wormlike micelles in the region near charge neutralisation. Behaviour in quadrant D has evoked less interest, but sufficiently sensitive techniques are now being applied to study aggregates in this quadrant as well. These techniques show a clear decrease in critical concentrations of the surfactants and various morphologies, as one would anticipate on the basis of behaviour in quadrant B as well.

This leaves quadrant C where concentrations are very low, hindering the use of several of the available techniques, although spectroscopic techniques clearly still produce useful data. The formation of aggregates in this region is clear as well, but their nature is less obvious. Our current overview, however, renders this concentration regime one of four quadrants. As a result, information from the neighbouring quadrants can be used in the evaluation of the available data. From quadrant D, it is clear that cmcs are significantly lower in the presence of aromatic anions. Quadrant B shows that wormlike micelles are likely to form around the charge neutralisation line. Extrapolating these two observations into quadrant C suggests that aggregates, including rodlike or wormlike micelles, are generally likely to form in this concentration regime as well. This suggests that the electron microscopy observations by Buwalda *et al.* of a variety of different aggregates applies more generally. The idea that critical aggregation concentrations can be far lower than the typical values of 1-10 mM is further confirmed by reports of a surfactant forming spherical micelles displaying a cmc of 11±2 nM.[49]

3. Chemical reactions in micellar systems involving cationic surfactants and aromatic anions

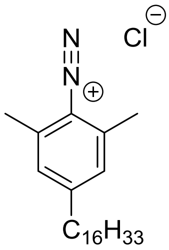
In this section, we explore the effects of aromatic anions on reactions occurring in cationic surfactant solutions. This section is separated into two parts; the first section discusses the effect of morphology changes resulting from added aromatic anions on chemical reactions while the second part discusses what happens if the aromatic anions are either reactants or products.

3.1 Effects of morphological changes on chemical reactions in surfactant aggregates

From a kinetic point of view, the bulk properties of systems in quadrant B involving entangled wormlike micelles are of importance because rheological changes may affect mass transfer processes. Mixing through stirring will be affected but molecular diffusion is typically unhindered unless the diffusing species binds to the aggregates. For reactions where mass transfer is rate limiting, these solutions may therefore display complex reaction kinetics.

Beyond bulk material aspects are the underlying changes in aggregate morphology on the molecular scale. Such changes will strongly affect the local reaction medium in which reactions take place, thus affecting reactivity.

The potential effects of morphological changes on chemical reactivity are illustrated by observations for Romsted’s diazonium probe (Scheme 4) in systems transitioning to wormlike micelles under the influence of 2,6- and 3,5-dichlorobenzoate.[50] For C_{16}TACl micelles with 3,5-dichlorobenzoate, a sharp increase in interfacial concentration of 3,5-dichlorobenzoate and a concomitant decrease in water concentration clearly marked the transition from spherical to wormlike micelles. This transition was not observed for 2,6-dichlorobenzoate.

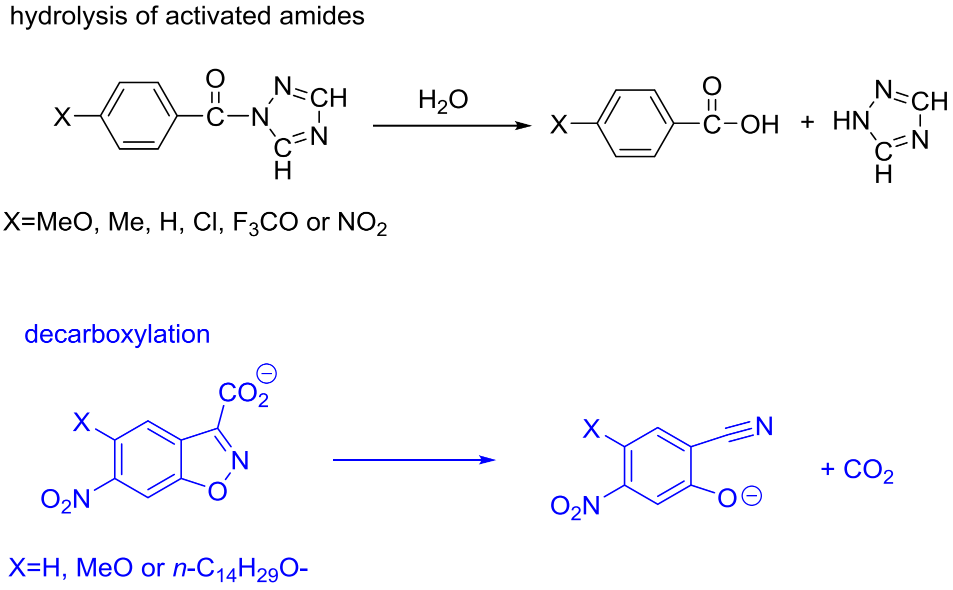


Romsted's diazonium probe

Scheme 4

3.2 Aromatic anions as reactants or products – probe reactions

The first reactions we consider are those carried out on the scale of chemical probe reactions. We and others have long been interested in chemical reactivity in aqueous surfactant solutions and have employed probe reactions to investigate the reaction medium offered by micelles. Studies using probe reactions typically involve very low concentrations of the chemical probes so that the probe does not affect the micellar environment. Typically, these studies are therefore situated in Quadrant A. Our work involving activated amides (Scheme 5) in solutions of cationic surfactants[16,17] is a case in point; had we used higher concentrations of the hydrolytic probes, then the reactions would have generated high concentrations of aromatic carboxylates. These aromatic carboxylates could have affected the morphology of the micellar solutions. Clearly, in this case of chemical probe reactions, the experiments were in fact designed to remain in quadrant A precisely to avoid morphological changes.



Scheme 5

Quadrant C is less forgiving than quadrant A; a molecular probe is not diluted in a large excess of surfactant. Brinchi et al.[51,52] observed catalytically highly active pre-micellar aggregates formed between cationic surfactants and the 5-tetradecyloxy derivative of the 6-nitrobenzisoxazole-3- carboxylate ion (Scheme 5). Based on the enhanced reactivity a rather dry reaction environment in these premicellar aggregates is proposed. Similar pre-micellar accelerations were observed for hydrolyses of dianionic 2,4-dinitrophenyl phosphates in solutions of cationic surfactants,[53] while formation of pre-micellar aggregates between phenylsalicylate (the phenyl ester of o-hydroxybenzoate) and cationic surfactants inhibit hydrolysis of phenylsalicylate in a cooperative manner.[54]

Overall, kinetic behaviour and the underlying aggregation phenomena in Quadrant C are typically ascribed to pre-micellar aggregates. Based on the behaviour of aromatic anions and cationic surfactants as discussed above, we believe that these pre-micellar aggregates may in fact be wormlike micelles or vesicles and we note that this would explain several of the observations, including the drier reaction environment experienced by the 6-nitrobenzisoxazole-3- carboxylate.

3.3 Aromatic anions as reactants or products – synthesis

On the other side of the scale are reactions applied to synthetic challenges where typical concentrations place us in quadrant B. Compounds similar to the hydrotropes shown in Scheme 2 would not be considered unreasonable components of reaction mixtures. For example, phenylboronate is the conjugate base of phenylboronic acid, a well-known reactant in the Suzuki-Miyaura cross-coupling reaction, which led to our interest in the systems reviewed here. For such reactions, it is less important whether the local reaction environment is affected by the changing presence of the reactants or the products, as long as the desired reaction occurs at a reasonable rate. Nevertheless, rational selection of reaction conditions requires an understanding of the changing reaction environment and these potentially changing reaction conditions thus represent an additional step in the translation of results obtained from chemical probe reactions to rational development of syntheses in aqueous surfactant solutions. Little work has been carried out in this area but we note that both the challenges and the potential rewards are significant. The challenges involve the extreme sensitivity of aggregate morphologies to molecular structures. The rewards include the ability to rationally select reaction conditions but also to develop viscoelastic systems with time dependent properties.

Although all effects discussed here have been framed in terms of micelle-forming cationic surfactants in combination with anionic hydrotropes, similar processes also occur for systems involving anionic surfactants and cationic hydrotropes. It also appears reasonable to assume that similar system could be created replacing the surfactants with dendrimers.

4. Conclusions and perspectives

Organic reactions have been studied in aqueous micellar solutions for a considerable time. The use of organic reactivity to probe the micellar structure has convincingly highlighted that surfactant aggregates provide a local reaction medium with distinct properties.

The translation of our understanding as developed using probe reactions to application in organic synthesis is not trivial, however, despite the additional insight gained from the global analysis of aggregation processes across the concentration scales presented here. The main reason why the translation remains non-trivial is the potential of changing morphologies as concentrations of charged species change. Concentrations of species inducing morphology changes might be changed as part of kinetic studies where the concentration of a reactant is changed in order to establish the molecularity of the reaction in that reactant.

Concentrations might also change as a direct result of the reactions themselves, for example in the hydrolysis reactions of amides in which carboxylate anions are formed or in Suzuki-Miyaura cross-coupling reactions where phenylboronic acids are consumed. The resulting interplay between reaction progress, aggregate morphology and reactivity introduces and additional complexity in the analysis of kinetic data for reactions in micellar solution on a synthetic scale but it also introduces new opportunities in generating time-dependent properties. Time-dependent properties complement pH- and temperature-responsive behaviours. Such time-dependent changes could, for example, be exploited in slow release of pharmaceuticals or nutrients, depending on the desired application.

Acknowledgements

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