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Micelles and Reverse Micelles: a Fascinating Micro-reactor

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ABSTRACT

Reactions in micro-heterogeneous systems have been found to be of great interest in the past few decades. Two such micro-heterogeneous aggregates are micelles and reverse micelles, which are formed by surface active agents or surfactants. In numerous chemical reactions, the use of these systems as microreactors increases the rate of the reaction up to 10-100 folds. This chapter will be concentrated on micelles and reverse micelles as catalytic reactors since, in the past few decades, numerous numbers of reactions have been successfully carried out in these systems.

Keywords: *Micelles; Reverse Micelles; Catalysis; Micro-Reactor*

INTRODUCTION

Nature usually prefers self-assembled structures for doing millions of reactions in an efficient manner. Numerous reactions occur on the surface of the cell membrane, DNA, RNA, in the active site of enzymes, etc. All are examples of self-organisation of small units into large supramolecular structures. The process can be mimicked in synthetic supramolecular agglomerates to do the desired reaction in an inefficient manner. Molecular self-assembly is a process in which small molecules spontaneously form larger superstructures by interacting with each other through various attractive forces, which are generally weak non-covalent interactions like van-der Waal force, Coulombic force, hydrophobic interactions, and H-bonding. Cyclodextrins, crown ethers, cryptands, as well as surfactant aggregates like micelles and reverse micelles can be considered as efficient reaction sites or reactors. Among these ordered structures, micelles and reverse micelles are formed by the interactions of small surfactant molecules.

Surfactants are the basic building blocks of the micellar and reverse micellar superstructures. Surfactant is a short form of "surface active agent" that actually means "active at the surface." Surfactant molecules contain two distinct parts: a water-insoluble hydrophobic part and a water-soluble hydrophilic part, which may or may not possess charges (Fendler,1982). Surfactants are mainly of four types. i) cationic surfactant; the cationic portion of the surfactant remains in the hydrophobic unit ii) anionic surfactant; the anionic portion of the surfactant remains in the hydrophobic unit ii) Non-ionic surfactant; there is no formal charge in the molecule but the molecule contains an uncharged hydrophilic part and a hydrophobic part. iv) amphoteric surfactants; both cation and anion exist in the same part of the molecule (Figure 1).

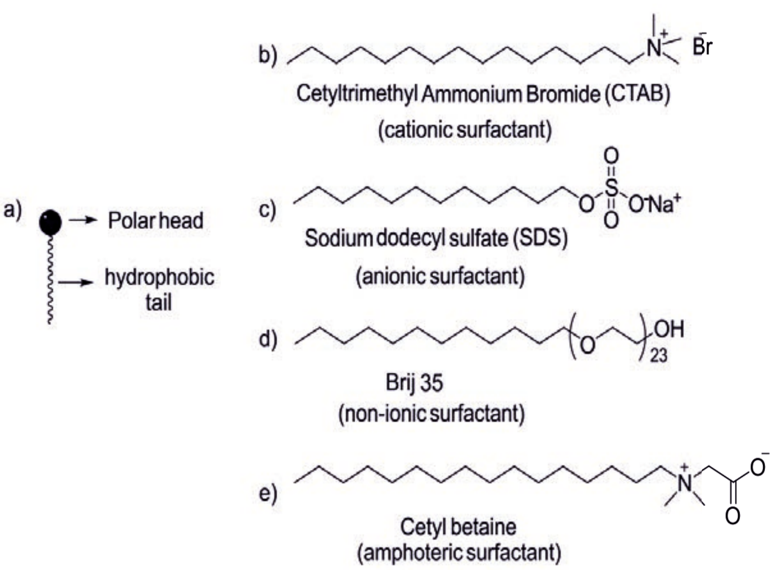

Figure 1: a) Representative structure of a surfactant b) Cationic surfactant c) Anionic surfactant d) Non-ionic surfactant e) Amphoteric surfactant

The simplest forms of supramolecular structures are micelles. When surfactant molecules are dissolved in water, they orient themselves in such a way that the hydrophilic part of the molecule remains in contact with water and the hydrophobic part stays away from water to avoid unfavourable interactions. In this way, a sphere is formed where the hydrophobic parts of many molecules form the hydrophobic core and the hydrophilic parts of those molecules remain in the outer layer of the sphere so that this layer can remain in contact with water (Figure 2). These aggregates are called micelles (Fendler, 1982). For every surfactant, at a particular temperature, there is a minimum concentration above which the micellization process starts. This minimum concentration of the surfactant is called 'critical micellar concentration'(CMC) of that surfactant at that particular temperature. Below CMC, the individual molecules are dissolved like a normal electrolyte. Above CMC, the concentration of surfactant molecules becomes sufficient to form the spherical structure, i.e., micelles. The special feature of micellar solution is that it can solubilise both hydrophilic and hydrophobic materials since micelles have both hydrophobic and hydrophilic domains for solubilisation; a hydrophobic core and a hydrophilic outer layer.

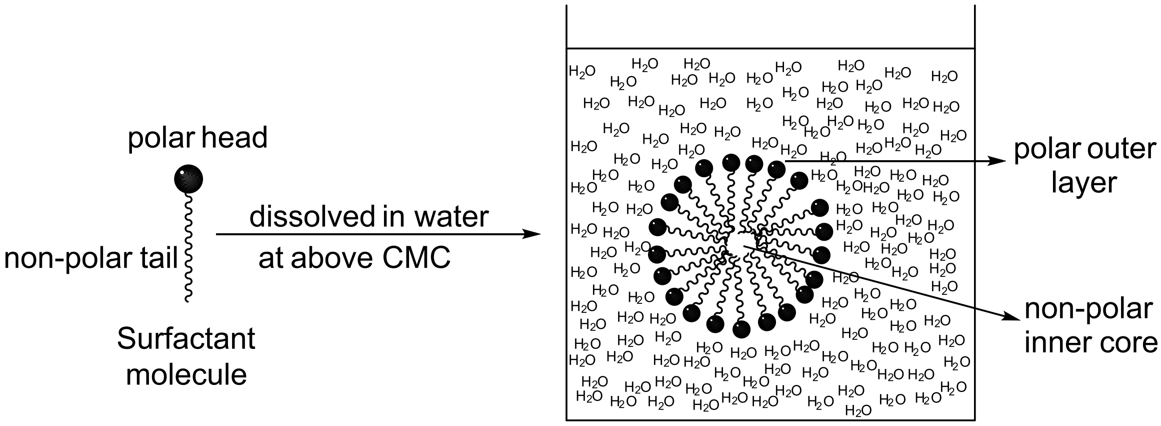

Figure 2: Cross section of micelle structure

LITERATURE REVIEW

In the past few decades, these micellar aggregates have been used efficiently for several chemical transformations in water, and in most of these cases, the rate of the reactions is found to be higher than the reaction with water alone (Paprocki *et al.*, 2018). It has also been found that some reagents cannot do a particular reaction in normal conditions, whereas the reaction can go efficiently in the presence of micellar solution (Bhat & Shairgojray, 2020). These reactions will be discussed later in detail.

Another class of fascinating supramolecular aggregate is reverse micelles. It has been seen that when surfactant molecules are dissolved in bulk water, they form a supramolecular sphere like aggregate where the hydrophobic parts of many molecules form the inner hydrophobic core and the hydrophilic parts form an outer hydrophilic layer which remains in contact with water (Figure 3). But when the

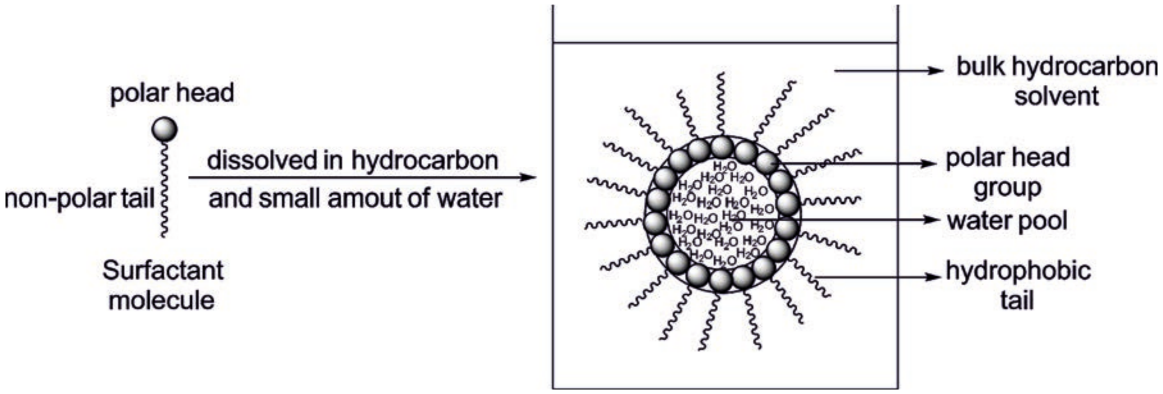

Figure 3: Cross section of reverse micelle structure

medium is changed from bulk water to bulk non-polar solvent in the presence of a small amount of water, the polar heads aggregate themselves into nanometre-scale tiny water droplets where the hydrophobic parts of the molecules are oriented towards the bulk non-polar medium and the hydrophilic parts towards the water droplets, which are known as water pools (Arsene *et al.*, 2021). Thus, the surfactant molecules form the interface between the polar aqueous part and the non-polar oily part. These spherical aggregates are called reverse micelles or water-in-oil microemulsions (Schulman & Prince, 1959).

The important characteristic of reverse micellar solutions is that a large number of bio-molecules, including proteins, enzymes, and nucleic acids, can easily be solubilised without losing their bioactivity (Menger & Yamada, 1979). Actually, these bio-molecules are solubilised in the water pool of the reverse micellar solution and hence they can preserve their biological activity (Mitsou, Xenakis & Zoumpanioti, 2017).

DISCUSSION

In micellar medium, many reactions have been performed in recent years.The demand for the micellar system as a reaction medium has increased in recent times since it also meets the criteria of 'green chemistry' as the solvent used in this system is water, which is a green solvent. In the naked eye, the micellar system seems to be homogeneous, but in reality, it is a microheterogeneous system and the absorbed reactants remain in a micro heterogeneous two-phase system, i.e., oil (hydrophobic inner core) and water. In most of the cases, the rate of the reaction was found to be increased. That's why the reaction in the micellar system is called 'micellar catalysis' when the rate of the reaction increases with respect to water.

Micelle is unique as a micro- or nanoreactor because the reactants are so close together in the polar and nonpolar regions.The effect of micellar structure on reaction rate is due to the following factors (Castanho, Brown & Prieto,1992).

1) The micellar core has a lower dielectric constant than bulk water.Therefore, the different positions of the substrates can create a solvent effect on the reaction rate.

2) The polar head group of the surfactant molecule can stabilise the transition state of the reaction, which actually accelerates the rate of the reaction.

3) The hydrophilic reactants are concentrated more to the bulk water phase through interactions with the highly polar micelle surface. These causes the close proximity of the reactants, which effectively increases the bimolecular collisions between the reactants, leading to an increased rate of bimolecular reactions.

Reactions in micellar solution:

a) Hydrolysis of ester:

It has been found that the micelles formed by cationic surfactants catalyse the reaction of neutral substrate with anionic reagents like hydroxide (^{-}OH), fluoride (F^{-}), thiolate (R-S-), etc. Hydrolysis rates of p-nitrophenyl esters, for example, are found to be 2.3–16.5 times faster in the presence of a small amount of quaternary ammonium ion exchange latex particles than in water alone (Miller *et al.*, 2000). It has been found that the acetates are absorbed strongly by the micellar polymer particles and the concentration of ^{-}OH inside the polymer particles is 10 times higher than the bulk water. These two factors are responsible for the higher reaction rate in the presence of cationic polymeric micellar particles (Figure 4).

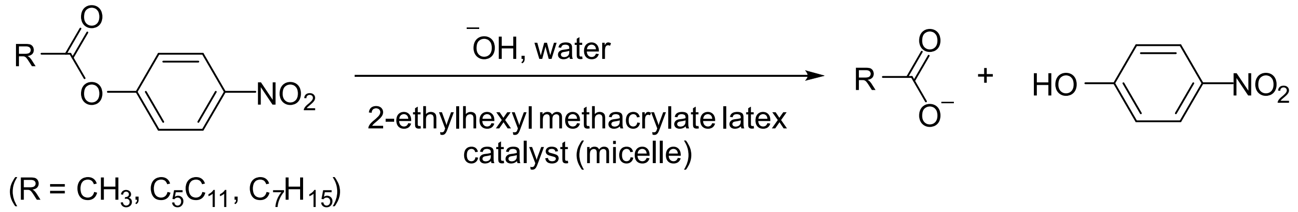

Figure 4: Reaction in polymeric cationic micellar solution

Another ester hydrolysis reaction has been carried out in non-ionic micelles with phosphoryl nitrophenyl esters (Figure 5).

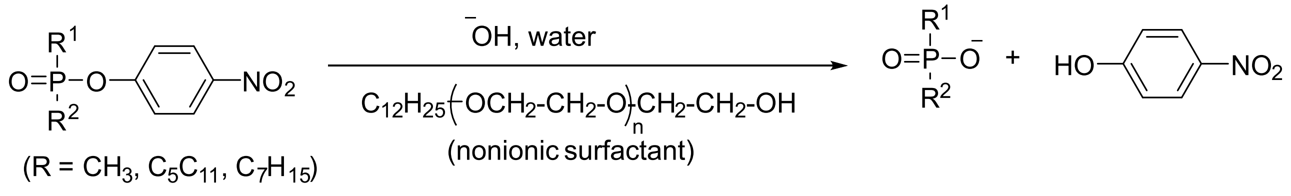

Figure 5: Reaction in nonionic micellar solution

In this case, the rate of the reaction is accelerated due to the formation of alkoxide at the terminal -OH group of the surfactant, which is responsible for easy hydrolysis (Foroudian, Gillitt, & Bunton, 2002).

b) Oxidation:

The rate of chromic acid oxidation of malic acid to oxaloacetic acid was found to be twice as high in CTAB micellar medium than in water alone (Figure 6). Here, the bromide (Br$^-$) counterion of cationic micelles is exchanged with an HCrO4-ion, which increases the local concentration of oxidants and hence increases the rate of the reaction. This acceleration of the rate of the reaction was found to be absent when the CTAB is replaced by a nonionic surfactant (Morshed & Khan, 2004). This proves that the reaction occurs by ion exchange of Br- with $HCrO_4$- at the hydrophilic outer layer of the micelles.

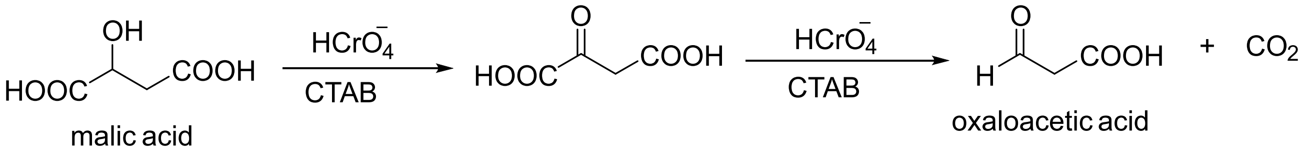

Figure 6: Oxidation of malic acid in a CTAB micellar medium

c) Reduction of esters: $NaBH_4$ can not reduce esters in ambient reaction condition. This is because the electrophilicity of carbonyl carbon of the-COO_2 Et group is less than that of aldehydes and ketones due to the resonance of C=O with the-OR group in esters. Also, the reactivity of $NaBH_4$ is less than the other metal hydride reducing agents like $LiAlH_4$. $NaBH_4$ can reduce the ester groups only at very high temperatures or at very high concentrations of $NaBH_4$. A very efficient method of reduction of ester with $NaBH_4$ at room temperature has been developed using micellar catalytic reaction medium (Das, Roy & Das, 2004). It has been found that when the reaction is done in CTAB micellar medium, a large amount of the reduction product is made. The enhanced yield in the micellar medium is due to an increase in the local concentration of $NaBH_4$ at the micellar surface where the reaction actually takes place. Thus, micellar solution acts as a catalyst in the reaction (Figure 7).

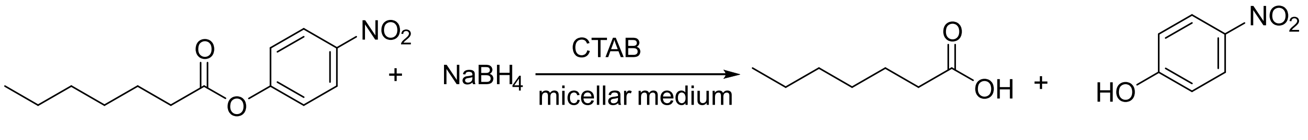

Figure 7: Reduction of ester in CTAB micellar medium

d) Diels-Alder Reactions in Micellar Media: A huge number of Diels-Alder reactions in micellar medium has been done in past few years. Recently, Diels-Alder reaction in micellar medium has been used for the synthesis of pharmacologically relevant 4-amidyl-2-methyl-1,2,3,4-tetrahydroquinolines (THQs) (Arenas, Bonilla & Kouznetsov, 2013). It has been found that the best yield is obtained by the presence of CTAB or sodium dodecyl sulphate (SDS) surfactant solution above its critical micellar concentration (CMC). Here, micelles catalyse the reaction. The explanation for the micellar catalysis is that the micelle has the ability to arrange of stable catalytically active groups which together function as a nanoreactor (Figure 8).

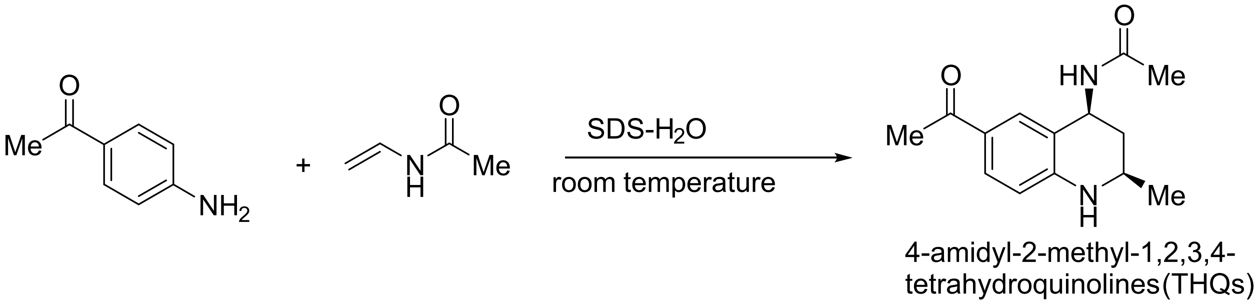

Figure 8: Diels-Alder reaction in a SDS micellar medium

Reactionsin reverse micellar solution:

Reverse micelles are also a very good microreactor for chemical transformation, especially enzyme-catalysed reactions. As already mentioned above, biomolecules like enzymes, DNA, RNA, etc. can preserve their activity when they are dissolved in the water-pool of the reverse micellar system. The examples of some reactions which have been done in reverse micelles are discussed below.

a) Reduction: Ketones have been reduced by $NaBH_4$ in reverse micellar solution (Zhang & Sun, 1996). Here the chiral surfactant has been taken for the formation of reverse micelles and, surprisingly, it is found that the product shows some degree of enantiomeric excess (Figure 9).

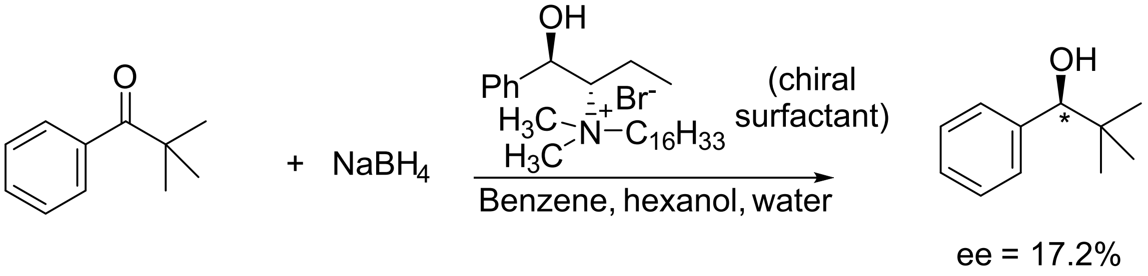

Figure 9: Stereoselective reduction of prochiral ketone in a chiral reverse micellar medium

b) Oxidation: oxidation of toluidine blue by periodatewas done in water and in CTAB based reverse micelles**.** It has been found that the reaction in reverse micelles is 40 times faster than that in water under the identical reaction conditions (Figure 10). In both the solvent systems, the reaction obeys the first order kinetics with respect to both the reactants. The pronounced acceleration of the reaction rate in the reverse micellar system is due to the lower micropolarity of water as well as the higher effective concentration of the substrate and the reactant in the bound water of the water-pool (Nagalakshmia, Shyamala & Rao, 2018).

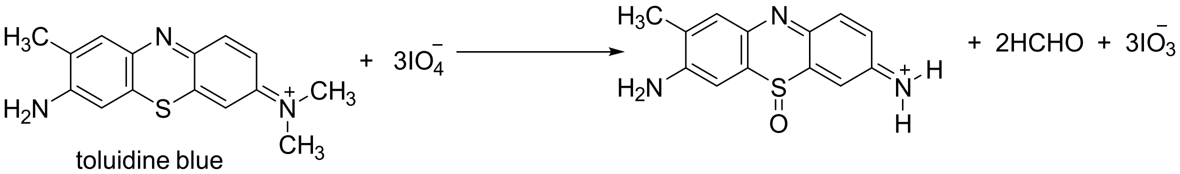

Figure 10: Oxidation reaction in a CTAB based reverse micellar medium

Another reaction of enantioselective sulfoxidation in reverse micelles has been done in the water/CTAB/diacetyltartaric acid/toluene system (Figure 11). Here, prochiral dialkyl sulphides are oxidised with iodoxybenzene ($PhIO_2$) in the mentioned reverse micelles to get a quantitative yield of sulfoxide with an enantiomeric excess (ee) of up to 72%. Here, the chirality of tartaric acid creates the chiral environment in the water-pool, which is actually responsible for enantioselectivity (Tohma *et al.*, 1999).

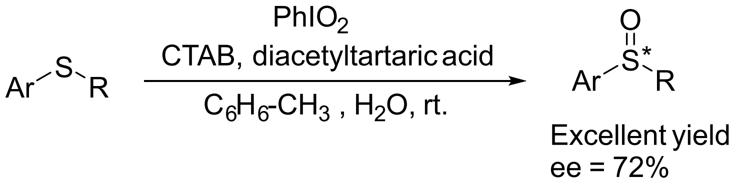

Figure 11: Enantioselective sulfoxidation of prochiral prochiraldialkyl sulphides in a chiral reverse micellar medium

c) Esterification: Lot of esterification reactions have been done by enzyme lipase in reverse micelles (Hayes & Gulari, 1990). In an example, the fatty alcohol and fatty acid are esterified in water/AOT/isooctane reverse micelles (Figure 12). It has been found that the enzyme activity depends on the type and concentration of substrate, H_2O/AOT ratio (w).

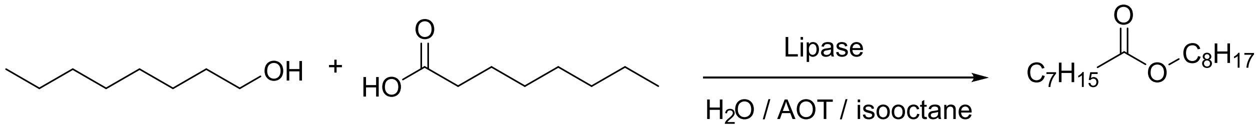

Figure 12: Lipase catalysed esterification of fatty acid and alcohol in reverse micellar medium

CONCLUSION

It has been found that the micellar and reverse micellar solutions serve as fascinating nano/microreactors for a huge number of reactions. In most of the cases, the rate of the reaction was found to be higher than that in water alone. In some cases, stereoselective reactions have also been carried out in chiral micelles or chiral reverse micelles. Faster reaction rates, ambient reaction conditions, and stereoselectivity make these systems highly useful for many organic transformations.

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