

CHAPTER I

Brief Review on Microemulsion as Reaction Media

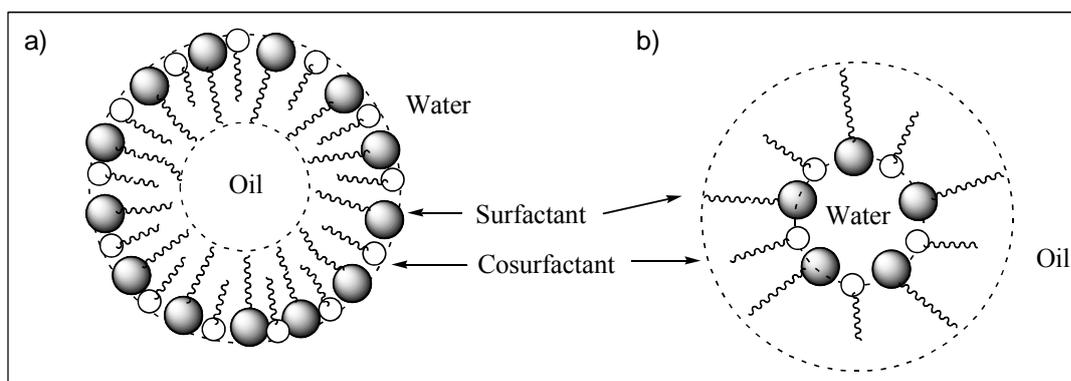
I.A.Introduction

The consciousness over the massive use of organic solvents having some undesirable characteristics as high boiling points, high inflammability, toxicity in synthetic chemistry leads much effort to carry out the reactions in water which is an environmentally benign solvent. But, the potential inconvenience with the application of water is the incompatibility of organic molecules with water. To solve this problem, many attempts have been made, e.g., the application of the “on water” process,¹⁻⁴ the application of hydrophilic cosolvents,^{1,5} the use of phase-transfer catalysis,⁶ pH regulation of the reaction mixture,^{1,7} the use of superheated water^{8,9} or the application of ultrasound or microwave irradiation.⁹ Another interesting way is to study the chemical reactions in microemulsions as excellent solvents both for hydrophobic organic compounds and for inorganic salts.¹⁰

The introduction of microemulsion in the scientific literature is normally ascribed to Schulman. He and his co-workers produced a considerable fraction of the early work regarding their preparation and properties.¹¹⁻¹⁵ In 1943, Hoar and Schulman¹¹ found that a ternary system consisting of sodium stearate-cetane-water became transparent as a straight chain alcohol (*n*-hexyl alcohol) was added. In 1959, Schulman and Stoechnius¹⁵ introduced the term “microemulsion” to describe this four-component system. The straight chain alcohol was called “cosurfactant”. In 1985, Shah *et al.*¹⁶ further gave a complete definition: *i.e.*, microemulsion is a thermodynamically steady isotropic dispersion of two immiscible liquids consisting of micro-domains of one or both liquids, which are stabilized by the interfacial film of surface-active molecules.

The breakthroughs in microemulsions studies have occurred in the past decade. Now-a-days, mEs are generally considered as monodispersed spherically droplets (10-100nm in diameter) of water-in-oil (w/o) or oil-in-water (o/w) type (Scheme I.1) depending on the nature of surfactants and composition of mEs. The w/o microemulsions are grossly differs from reverse micelles (RMs) in terms of water content in the pool. If the water content exceeds the solvation requirement of the amphiphilic head groups, the term “reverse micelle” is replaced by “w/o microemulsion”.¹⁷ The microheterogeneity or compartmentalization of such dispersion with unique physicochemical properties viz. spontaneous formation, clear

appearance, thermodynamic stability, low viscosity, ultra-low interfacial tension, large interfacial area and high solubilization capacity for both hydrophilic and lipophilic compounds, make them useful in biological and technological applications, Such as oil recovery to pharmaceuticals, food technology, photochemical reaction, enzymatic catalysis, nano-particle synthesis, organic and bio-organic reactions etc.¹⁸⁻²⁴The first studies were carried out in the exploration of microemulsions as media for organic reactions by Fendler et al.²⁵ and Menger et al.²⁶ Microemulsions are nowadays grasped as a highly versatile reaction media, which currently find many applications. Two introductory review articles by Sanchez-Ferrer and Garcia-Carmona²⁷ and by Holmberg²⁸ should be cited from the extensive literature. In the first review, reverse micelles are compared with reverse vesicles, which were uniquely described for the first time in 1991.²⁹ Recently, Ghosh et al. has explored a review article in which plausible reaction location in microemulsion has been discussed.³⁰



Scheme-I.1 The two types of microemulsion: a) Direct microemulsion b) Inverse microemulsion

I.B.Characterization of microemulsions

The organic reactions in microemulsion medium have been facilitated by the effect of the microstructure of such complexed fluid. The reaction parameters can also be altered by changing the microenvironment, such as the droplet size, the interfacial area etc. In this way, rapid attention has been paid to focus on the characterisation of composition and physical properties of the different pseudo-phases of the microemulsions. Due to their complexity, namely different types of structures and components involved in these systems, as well as the limitations associated with each technique, the characterization of microemulsions is rather a difficult task. Multiple complementary techniques are required in order to understand and also to manipulate microemulsion behavior. Some of these techniques, starting from phase

behavior to Electron microscopy are presented, in brief, to identify and characterize microemulsions in the following section.¹⁷

I.B.1.Phase behavior of microemulsions

Phase studies are inevitable for the basic understanding of general phase behavior and kinetics of the structural changes of a system.^{31, 32} Phase diagrams for microemulsions are quite complex since there are at least three components; water, oil and surfactant. A map of the locations of different phases in composition space is known as a “phase diagram” of microemulsions.¹⁷ A pictorial representation of “phase diagram” (as a model) considering different phases in composition (of water, surfactant and oil mixtures) has been depicted in Figure-I.1.

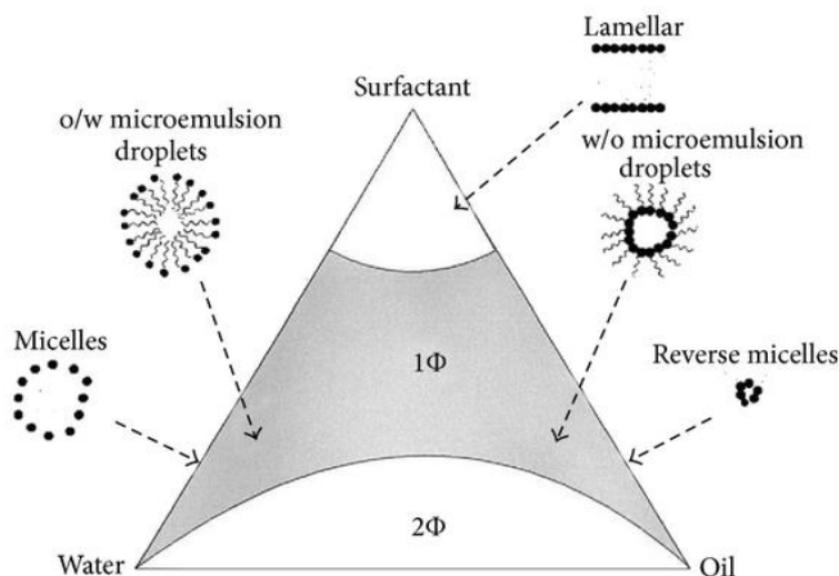


Figure-I.1. Pictorial representation of “phase diagram” of water, surfactant and oil mixtures.

The phase behavior of microemulsions depends on chemical structures of oils and surfactants, temperature, pressure and additives such as salt and polymers etc. Phase diagram provide information on the boundaries of the different phases as a function of composition variables, temperatures, and, more important, structural organization can be inferred. Phase behaviour studies also allow comparison of the efficiency of different surfactants for a given application.¹⁰ In the phase behaviour studies, simple measurement and equipments are required. The boundaries of one-phase region can be assessed easily by visual observation of samples of known composition.

I.B.2. The Schulman's cosurfactant titration at the oil/water interface

(Dilution method)

It is considered that in the formation of water-in-oil (w/o) microemulsion using a blend of surfactant/cosurfactant (amphiphiles), all the surfactant molecules reside at the interface and the cosurfactant molecules are distributed between the bulk oil and the interface depending upon their solubility in water. At fixed water to surfactant composition, a threshold amount of cosurfactant is required for the formation of stable microemulsion, and the size of the dispersed droplets in the dispersion is controlled by the cosurfactant composition. Although direct determination of cosurfactant distribution between the interfacial plane and the bulk oil is difficult, ³³ reports are available in literature using techniques, like SANS, SAXS and DLS,^{34, 35} conductivity,³⁶ interfacial tension.³⁷ To understand chemical reactivity of a single or mixed species either inside the water pool or at the interface of a quaternary w/o microemulsion, the in depth knowledge on (i) interfacial composition such as relative population of surfactant and cosurfactant at the oil/water interface, (ii) the distribution of cosurfactant among the interface and bulk oil phase vis-à-vis the thermodynamics of this transfer process of cosurfactant, (iii) the number and the size of the droplets and (iv) the physicochemical characteristics of the entrapped water, are essential. These parameters are strongly influenced by the type and alkyl chain length of oil and the amphiphiles (surfactant or cosurfactant).³⁶ All these parameters [except (iv), which can be determined from Fourier transform infrared spectroscopy and FTIR measurements],³⁸ can be evaluated (without using sophisticated instruments) from the dilution method which is a pioneering work of Bowcott and Schulman.¹³ This simple but elegant method is accomplished by adding oil at a constant water and surfactant ratio to destabilize an otherwise stable w/o microemulsion and then restabilizing it by adding a requisite amount of cosurfactant (alcohol). For these reasons, the dilution method (which is commonly represents the Schulman's cosurfactant titration of the oil/water interface) has been widely used by a number of workers to estimate the parameters involved in the transfer of alcohol from the bulk oil to the interface.³⁹⁻⁴³ The method provides an understanding of the interfacial compositions of surfactant and cosurfactant as well as distribution of the cosurfactant between the interface and oil, and can quantitatively account for the thermodynamic stability of microemulsion. The mathematical model based on the dilution method and the evaluation of corresponding parameters has been discussed in details in subsequent chapters.

I.B.3. Electrical conductivity

Electrical conductivity is a structure-sensitive property. Nevertheless, the results obtained from conductivity study do not provide a straightforward picture of the microstructure of microemulsions, but transition from water continuous to oil continuous microemulsion can easily be obtained from such measurements, since water continuous formulation (o/w microemulsion) usually shows higher conductance than the oil-continuous formulations (w/o microemulsion).⁴⁴ The low conductance in dilute w/o microemulsion has been explained on the basis of charge fluctuation model.^{45,46} Further, for the w/o microemulsion systems, transition from discrete droplet structure to connected droplet or bicontinuous structure can be envisaged from sharp increase in conductance value (100-1000 times increase) with increasing volume fraction of the polar solvent or temperature. Such phenomenon is called “conductance percolation”.

I.B.4. Viscosity measurement

Microemulsions have varied flow behaviors, for example, lamellar (Newtonian) and non-lamellar (non-Newtonian). Low viscous microemulsions show Newtonian behavior. The Winsor-III and the bicontinuous types are usually non-Newtonian in nature and they can show plasticity.⁴⁷ The viscous properties of microemulsions depend on the type, shape and number density of aggregates present, as well as the interactions between these aggregates. The phenomenon of percolation in microemulsion is associated with droplet clustering and fusion, i.e. internal structure changes and hence, it is reflected in viscosity.

I.B.5. Light scattering techniques

Among the light scattering techniques, dynamic light scattering (DLS), also known as photon correlation spectroscopy, can be used to analyze droplet size of microemulsion via determination of hydrodynamic radius from measurements of the diffusion constants of diluted dispersed phase (droplets) undergoing Brownian motion.⁴⁴ This technique provides the determination of z-average diffusion coefficients (D). If interparticle interaction is assumed to be absent in a system, the hydrodynamic radius of particles (droplets) (d_h) can be obtained from the Stokes-Einstein equation:

$$D = k_B T / 6\pi\eta d_h$$

where, k_B is Boltzmann constant, T is absolute temperature, η is the viscosity of the medium. The DLS technique is useful to characterize size and size distribution of microemulsion droplets, as it monitors the collective diffusive motion in such systems, provided simple diffusion is the sole mechanism responsible for the variation of the scattered intensity.^{48,49} Polydispersity index (PDI) is another important parameter for evaluation of measurement from DLS experiment. The ratio SE/d_h , where SE is the standard error in d_h , is called PDI.⁵⁰ For a mono-dispersed sample, the PDI value is taken to be less than 0.08; whereas the value ranges from 0.08-0.7 is considered as a mid-range polydispersity.⁵¹ Several authors have significantly contributed to the understanding of different interactions in the microemulsion droplet core by measuring the droplet size.^{48, 51, 52}

The interaction between droplets can be investigated by employing Static Light Scattering (SLS) technique, where the intensity of scattered light is generally measured at various angles for different concentrations of microemulsion droplets. At sufficiently low concentrations, the Rayleigh approximation is used provided the particles are small enough.⁵³

I.B.6. Neutron and X-ray scattering techniques

In small angle neutron scattering (SANS), neutrons from a reactor source are scattered by the atomic nuclei of the sample. An advantage of the use of neutrons is that neutrons are non-destructive compare to X-rays, and hence, radiation damage rarely occurs in a neutron based experiment. SANS provides relevant information about structure of microemulsions.⁵⁴⁻⁵⁶ Normal hydrogen and deuterium have significantly different scattering lengths. Thus scattering contrast between heavy water and hydrocarbon is very high. By varying the contrast and even matching the contrast between different components of a mixture, selective portions can be highlighted. By matching the scattering length densities of water and oil, structure of both droplet-type and bicontinuous microemulsions can be established.^{57,58} Radiation wavelength of X-rays (1-10 Å) is smaller than the typical structural length scale in microemulsion. Thus, small angle scattering with X-rays can be very useful to determine the size and shapes of microemulsion droplets from the magnitude and angular dependence of the scattered intensity.^{52, 59, 60} Using synchrotron radiation sources, information about a wide range of systems can be obtained with this technique, including those systems in which the surfactant molecules are poor X-ray scatterers.⁶¹

I.B.7.Spectroscopic probing techniques

Several spectroscopic techniques have been used to study different aspects of structures and properties of microemulsions. The absorption and steady-state emission spectroscopy of probe molecules solubilized in a microemulsion system can probe the polarity of the microemulsion at their solvation location.⁶² Chemiluminescence techniques have also been employed to study transitions between polar and non-polar environments in microemulsion systems. Time-resolved emission spectroscopy provides the information about the dynamics and rotation relaxation of solvent in microemulsions.⁶²⁻⁶⁴ In particular, fluorescence lifetime measurement is a highly sensitive method where the lifetime of a fluorophore can alter in response to changes in the conformational state of the probe molecules or in response to the interaction with local environment in microemulsion systems.⁶⁵ The steady-state anisotropy or polarized fluorescence study provides a simple means of monitoring the processes, in which the microstructure of the microemulsion is affected in some way.⁶⁵

In addition, fluorescence correlation spectroscopy (FCS), which may be considered as a miniaturization of DLS, measures the tiny spontaneous fluctuations in fluorescence intensity of molecules in a very small volume (spot), and quantifies it by temporarily auto-correlating the recorded intensity signal to obtain the variation in local concentration of fluorescent species and hence, their diffusion coefficient.⁶⁶ This technique is an excellent tool for measuring molecular diffusion and size of microemulsion droplets under extremely dilute conditions. In recent experiments, FCS technique has been shown to be applicable to microemulsion systems, where for the w/o AOT system from the diffusion times hydrodynamic radii were determined which compared well to the values obtained in parallel by SANS.⁶⁷

I.B.8.Nuclear Magnetic Resonance (NMR)

This experimental technique provides important information about the microstructure of microemulsions. Proton magnetic resonance has proven to be a useful technique for identifying the structure of water solubilized in reverse micelles. Addition of water to reverse micelles does not significantly affect the chemical shift of other protons, except H₂O. The water proton magnetic resonance exhibits a single peak, indicating the rapid exchange between water protons at various states.^{68, 69} The observed chemical shift results from the weighted average of different water species.

I.B.9. Fourier Transform Infrared Spectroscopy (FTIR) measurements

The knowledge about hydration of surfactants in w/o microemulsions or reverse micelles is helpful for understanding of the dynamics of different physicochemical processes operative within the confined environment (i.e, local interactions in the vicinity of water molecules in w/o microemulsion). Further, it is also helpful and prospective for applications in biological and chemical reactions occurring in w/o microemulsions or reverse micelles.⁷⁰ In order to get a clear understanding of various interactions in the droplet core, including the type of H-bonding which is operative within the water pool, an excellent and non-invasive technique viz., Fourier transform infrared spectroscopy (FTIR) has been introduced. Several authors significantly contributed to the understanding of the water dynamics in single and mixed surfactant derived w/o microemulsion systems by studying the state of water using FTIR method.^{38,39,68} The characteristics of the water molecules confined inside the water pool depend strongly on both water content and the nature or type of the surfactant head group.⁷¹

I.B.10. Electron Microscopy

Transmission Electron Microscopy (TEM) is the most important technique for the study of microstructures of microemulsions because it directly produces images at high resolution and it can capture any co-existent structure and micro-structural transitions.⁷²

There are two variations of the TEM technique for fluid samples.⁷³

1. The cryo-TEM analyses in which samples are directly visualized after fast freeze and freeze fracture in the cold microscope.
2. The Freeze Fracture TEM technique in which a replica of the specimen is imaged under RT conditions

I.C. Effect of the Microenvironment on Reaction

Microemulsions can accelerate the reaction because of their special structural features which can be tuned by proper selection of ingredients in the formulation. The reaction rate is often influenced by the charge at the interface and this charge depends on the surfactant used.¹⁰ The surfactant monolayer attracts reagents of opposite charge situated in the water domain, thus increasing its concentration in the interfacial zone, wherein the reaction occurs. Microemulsion can also induce regioselectivity in organic reactions changing the product

composition compared with the products obtained in a microhomogeneous solution. The induced regioselectivity is believed to be due to the interface acting as a template for reactants having one more polar and one less polar end.⁷⁴ Such a compartmentalization and concentration of the reagents may lead to a rate enhancement.

The dynamic character of these nano-reactors is one of the most important features for chemical reactions carried out in these media.⁷⁵ Dynamic means the continuous motion or movement of a particle not static ones and this is also true in case of microemulsion. The dynamical nature favors contact between the reactant molecules. In motion, several particles collide with each other and exchange of materials can take place. As microemulsion domains are mainly constituted by spherical droplets. All droplet-droplet collision does not effective for the material interchange. The collision between the nanodroplets containing different reactant molecules, the reactant can be transferred and both reactants can be located inside the same droplet. As the reaction takes place, more droplets could contain products and reactants simultaneously.

Again, the character of the oil used in the microemulsion formulation may also influence the reaction at the interface. Luis García-Río et al. investigated a chemical reaction by hydrolysis of anisoyl chloride.⁷⁶ A water-in-oil microemulsion was formulated with an anionic surfactant and a range of organic solvents were explored as oil component. It was found that the hydrolysis reaction proceeded faster with alicyclic hydrocarbons than with cyclic hydrocarbons and smaller alicyclic hydrocarbons gave faster reaction than the longer homologues. Moreover, changing the droplet size one could allow to tune the ratio of unbounded to bounded molecules in nanodroplets and hence its solvation properties. This confinement can enable the reactivity to be controlled. Microemulsion can also influence both reaction kinetics and equilibria.^{10, 77, 78} It has been shown that mEs media can enhance or retard the chemical reaction⁷⁹⁻⁸³ depending on the nature of the surfactant, the nature of the oil phase, and the size of the water pool present in the medium. Hence, Microemulsions are very versatile solvent systems, which also play an outstanding role as reaction media.

I.D.Examples of Reactions in Microemulsion

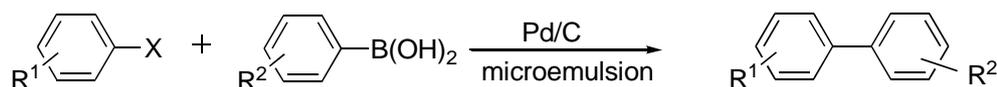
I.D.1.Transition Metal Catalysed C-C Coupling Reaction

Coupling reactions are widely used routes for the formation of carbon-carbon bonds and carbon-heteroatom bonds in particular for the synthesis of biaryl compounds.

I.D.1.1. Homocoupling as well as Suzuki Coupling Reaction

The Suzuki cross-coupling reaction is one of the most widely used reactions for the synthesis of polymers, liquid crystals, agrochemicals, and pharmaceuticals. An enhancement of palladium-catalyzed Suzuki cross-coupling reactions between substrates possessing long-chain alkyl or oxyalkyl substituents in toluene or dimethoxyethane/water mixtures by the addition of sodium dodecylsulfate (SDS) and n-butyl alcohol as co-surfactants is shown by Vashchenko et al.⁸⁴

In 2008, Jiang et al. have presented ligand-free Suzuki reactions catalyzed by Pd/C can be efficiently performed in TX100 microemulsions (Scheme I.2.). A number of aryl halides, including aryl iodides, bromides, and chlorides, were with arylboronic acids smoothly and efficiently to produce good to excellent yields.⁸⁵

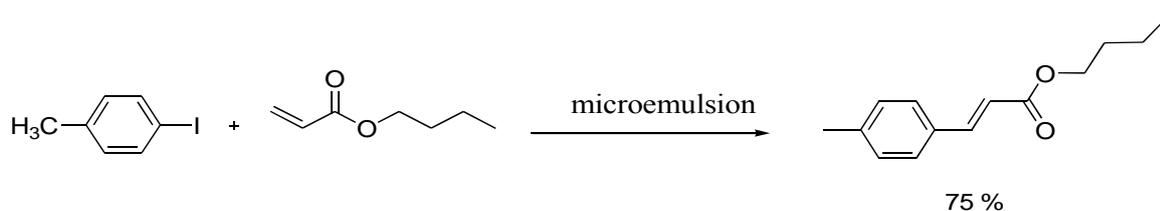


Scheme-I.2. Ligand-free Suzuki reaction catalysed by Pd/C in microemulsion.

I.D.1.2. Heck Reaction

The Heck reaction is one of the most important methods in synthetic organic chemistry for the formation of C–C bonds.⁸⁶ Jiang et al. reported heptane/TX 10/butanol/water/propylene glycol microemulsion containing in situ formed palladium nanoparticles, a very efficient catalyst system for the ligand-free Heck reaction (Scheme I.3).⁸⁷ The results indicated that the aqueous phase concentration, the base concentration, and the temperature played key roles in the conversion of the reaction. Iodobenzene was converted to the corresponding *trans*-stilbene quantitatively within 90–150 min.

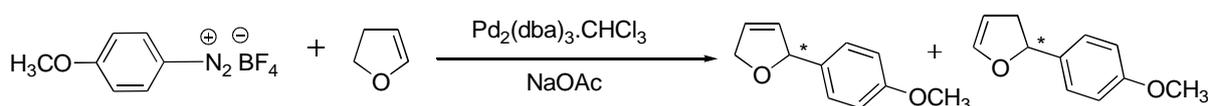
Another report presented by Zhang et al. is Ligand free Heck reaction in the water-in-Ionic Liquid microemulsion [H₂O/TX-100/1-butyl-3-methylimidazolium hexafluoro phosphate ([BMIM]PF₆)]⁸⁸ in which the Pd nanoparticles were prepared *in situ*. Surfactant TX-100 served as the reductant and the stabilizer of the nanoparticles. The TEM images presented that the monodispersed Pd nanoparticles have a mean particle size of 3 nm.



Scheme-I.3. The Heck Reaction in microemulsion media

I.D.1.3. Chiral Synthesis

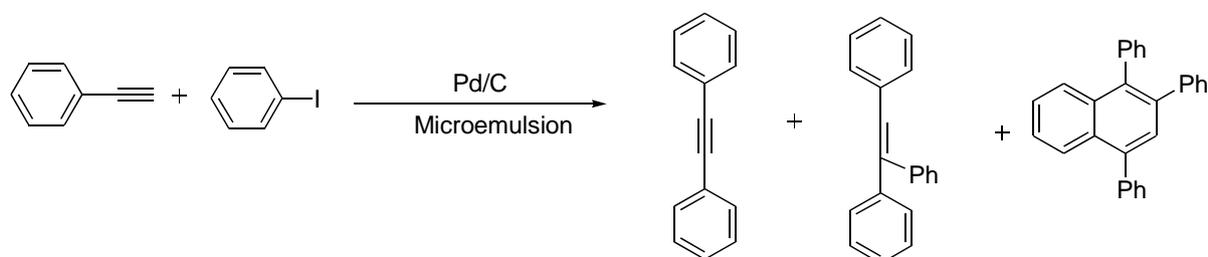
Gayet et al. employs a ternary system BnPyrNTf₂/TX100/toluene as nanoreactors to perform a Matsuda-Heck reaction between p-methoxyphenyl diazonium salt and 2,3-dihydrofuran in the presence of a palladium catalyst at 27^oC. The reaction results the two two regioisomers A and B and their corresponding stereoisomers (Scheme I.4).⁸⁹



Scheme-I.4. Matsuda-Heck reaction between a p-methoxyphenyl diazonium salt and 2,3-dihydrofuran using a palladium catalyst.

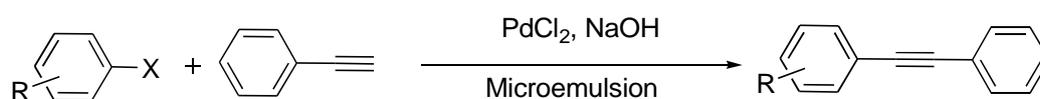
I.D.1.4. Sonogashira Reaction

In absence of ligand, copper or amine, Pd/C catalyzed Sonogashira reactions of aryl iodides and bromides with phenylacetylene were performed well in TX10 microemulsions at 70^oC by Jiang et al. (Scheme-I.5) Aryl iodides and activated aryl bromides were converted to the corresponding diaryl-substituted alkynes quantitatively within 30–150 min and the reactivity in the microemulsion was higher than that in biphasic system.⁹⁰ The “heterogeneously” catalyzed Sonogashira coupling reaction was due to “dissolved Pd-species”.



Scheme-I.5. Sonogashira coupling reaction of iodobenzene with phenylacetylene in TX10 microemulsion

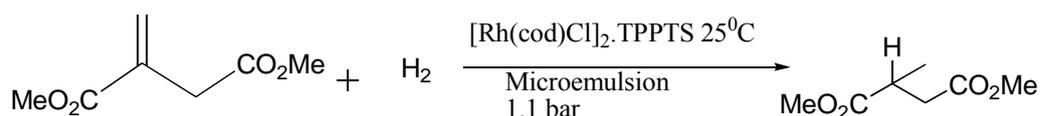
Again, a rapid copper- and ligand-free Sonogashira reaction was performed in an oil-in-water microemulsion (Scheme-I.6) by Jiang et al. Palladium nanoparticles can be in situ formed in the microemulsion, heptane-in-water, without other reductants.⁹¹ Excellent yield of the Sonogashira reaction catalyzed by 0.5 mol% palladium could be achieved at 80°C within 2 min. It has been observed that the ligand-free Sonogashira reaction resulted good yield in microemulsion compared to micelle. The effect of surfactants, alcohols, reaction temperature was also investigated. The reaction in CTAB microemulsion had higher reactivity than that in TX100 microemulsion.



Scheme-I.6. Sonogashira reaction catalysed by PdCl₂ and NaOH in microemulsion.

I.D.2. Catalytic Hydrogenation

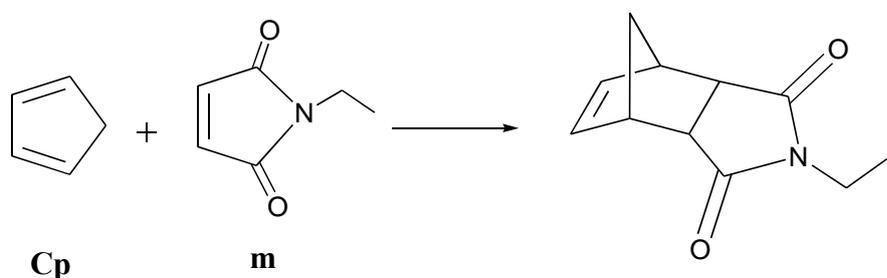
Brusco et al. have studied structural dimensions of two different microemulsions and correlated with the catalytic hydrogenation of dimethyl itaconate (DMI) performed in such media: (a) [Triton X-100-1-pentanol]-cyclohexane-water and (b) Igepal CA-520-cyclohexane-water (Scheme-I.7).⁹² Dynamic light scattering (DLS) and small angle neutron scattering (SANS) measurements were used to determine the characteristic sizes of the Igepal and Triton microemulsions, respectively, showing a linear dependence between the initial hydrogenation rate of DMI and the radius of the micelles. The initial hydrogenation rate of DMI in bulk water is exceeded in both microemulsions. Indications of deformation of the originally spherical Triton X-100 reverse micelles upon addition of the water-soluble catalyst complex Rh-TPPTS were found.



Scheme-I.7. Hydrogenation of dimethyl itaconate formal reaction.

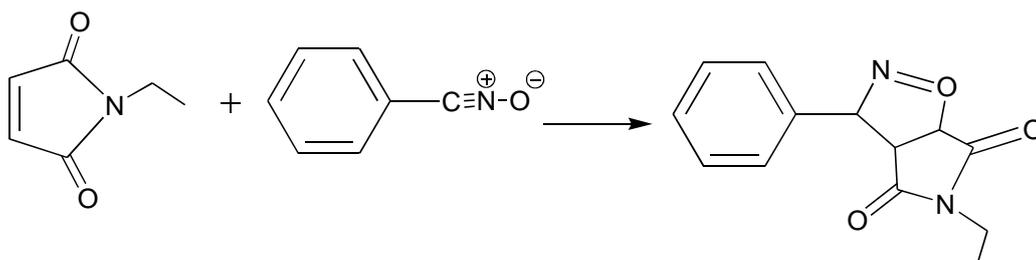
I.D.3. Cycloaddition

Diels-Alder (DA) reactions provide a powerful synthetic tool in organic chemistry and constitute the key step in the preparation of a large number of six-membered rings. The Diels-Alder reaction between *N*-ethylmaleimide and cyclopentadiene in water/AOT/isooctane microemulsions, where AOT denotes sodium bis(2-ethylhexyl)sulfosuccinate, was first studied by Engberts et al. (Scheme-I.8).⁹³ The rate of the reaction was found to be higher than that obtained in pure isooctane, irrespective of the particular microemulsion composition used. On the basis of these results, the reaction takes place simultaneously in the continuous medium and at the microemulsion interface. The favourable arrangement of the reactants at the interface results in more than 95% of the reaction occurring in this microenvironment. The kinetic analysis revealed the rate constant at the microemulsion interface to change with the water content.

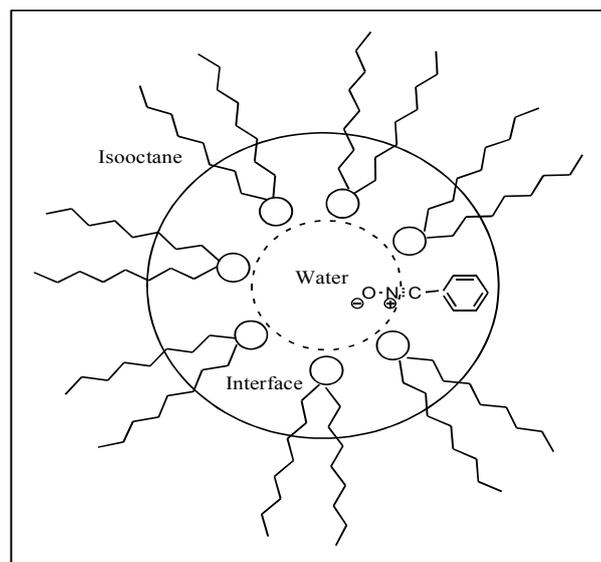


Scheme-I.8. The Diels Alder Reaction between *N*-ethylmaleimide and cyclopentadiene

Further, they have studied the 1, 3-dipolar cycloaddition of benzonitrile oxide to *N*-ethylmaleimide in AOT/isooctane/ water microemulsions at 25.0 °C and found the reaction rate to be roughly 150 and 35 times greater than that in isooctane and pure water, respectively (Scheme-I.9). The accelerating effect of the microemulsion is the combined result of an increase in the local concentrations of the reactants through incorporation into the interface and of the intrinsic rate of the process through electrostatic interactions with the headgroups in the surfactant (Scheme-I.10).⁹⁴

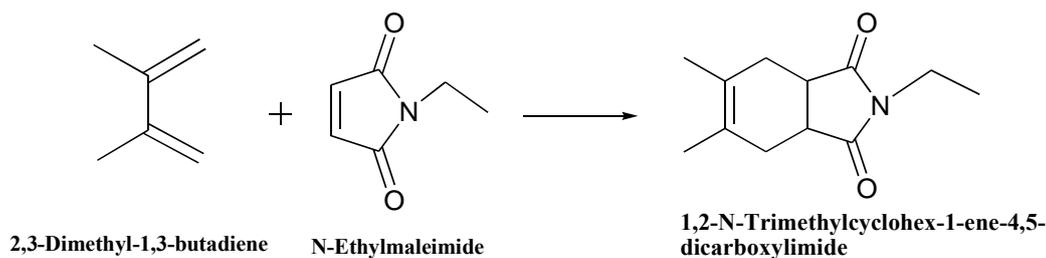


Scheme-I.9. The Diels Alder Reaction between *N*-ethylmaleimide and benzonitrile oxide



Scheme-I.10. Dipolar benzonitrile oxide, in the innermost region of the microemulsion interface

In 2012, Lu et al. have studied Diels-Alder Reaction (DAR) between N-ethylmaleimide and 2,3-dimethyl-1,3-butadiene in microemulsions with ionic liquid (IL) (IL-H₂O/AOT/isooctane) (Scheme-I.11).⁹⁵ The effect of solvent, IL and temperature on the DAR rate was investigated and interpreted. The experimental results showed that the reaction rate in the microemulsion with IL was enhanced and it was faster than that in pure isooctane and in generic AOT microemulsion.

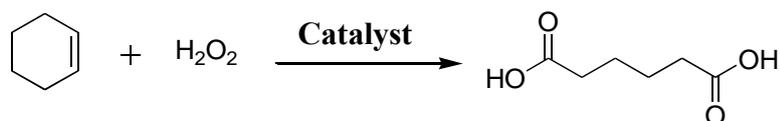


Scheme-I.11. The Diels alder Reaction in IL-microemulsion

I.D.4. Oxidation

Blach et al. have described a recyclable and environmentally friendly process for the oxidation of cyclohexene by hydrogen peroxide in microemulsions, water/ Benzalkonium chlorides (BenzCl)/cyclohexene (Scheme-I.12).⁹⁶ Microemulsion provides homogeneous

media for close contact between the reagents in the hydrogen peroxide phase, leading to a better reactivity without the need for strong stirring or very high temperatures.

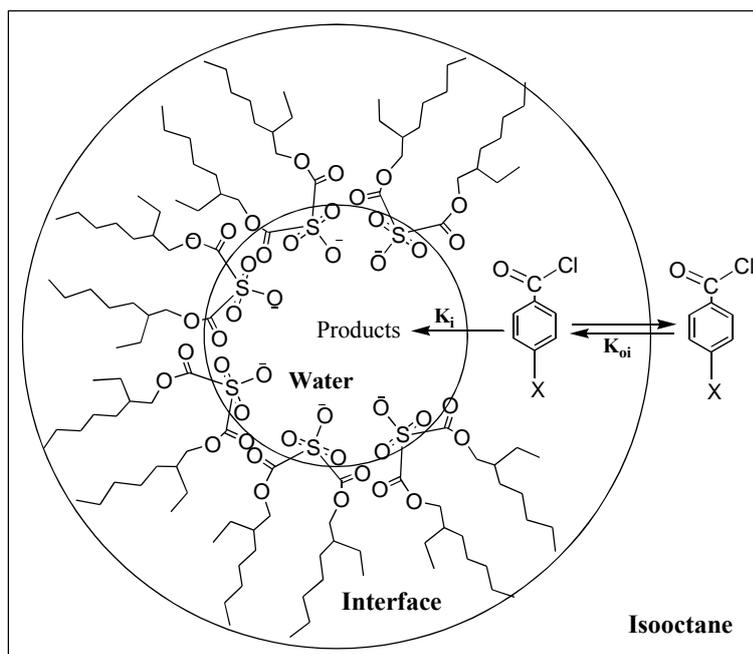


Scheme-I.12. Oxidation of cyclohexane with hydrogen peroxide

I.D.5. Solvolysis

In 2006, Garcia-Rio et al. have demonstrated butylaminolysis of 4-nitrophenyl caprate (NPC) in AOT/chlorobenzene/water microemulsions.⁹⁷ It is shown that the reaction, i.e., nucleophilic attack of butylamine on the ester occurred both at the interface and in the continuous medium simultaneously.

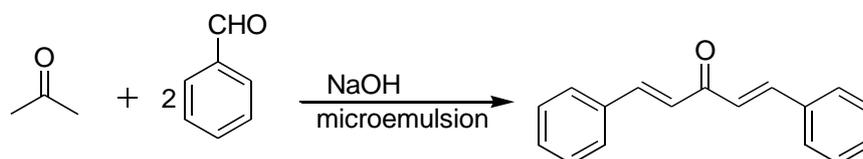
In a review, García-Río et al. shows Solvolysis of substituted benzoyl chlorides in AOT based microemulsion (Scheme-I.13).⁹⁸



Scheme-I.13. Solvolysis of substituted benzoyl chloride

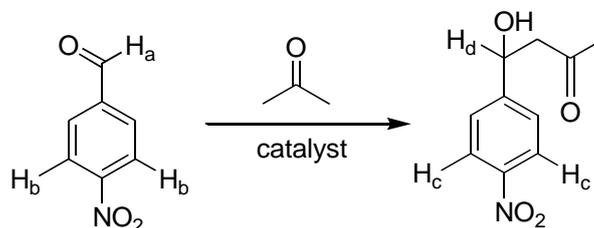
I.D.6. Condensation Reaction

J.J. Shrikhande et al.⁹⁹ have demonstrated the condensation between benzaldehyde and acetone in a cationic surfactant based o/w microemulsion prepared from the combination of n-butanol as co-surfactant, n-hexane as oil and cetyltrimethylammonium bromide (CTAB) as the cationic surfactant (Scheme-I.14). Various parameters influencing the formation of microemulsions, e.g., oil content, surfactant content, oil and co-surfactant ratio were varied and their corresponding effects on the solubilisation of reactants and rate of a condensation reaction were studied. A direct correlation between the droplet size of the microemulsion and rate of the reaction is observed.

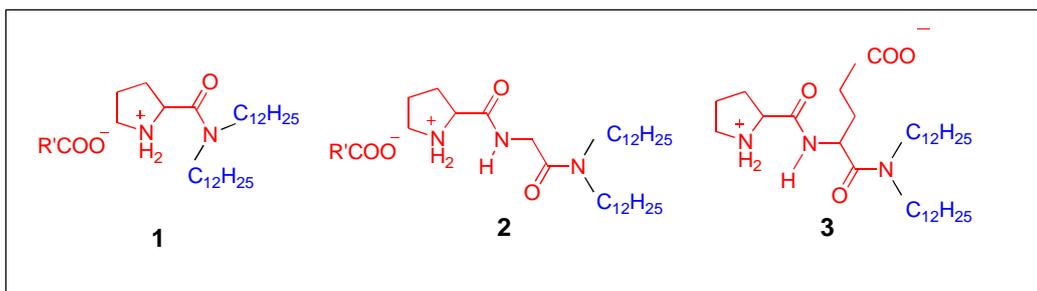


Scheme-I.14. The condensation Reaction in o/w microemulsion

Further a proline catalysed aldol reaction between acetone and p-nitrobenzaldehyde has been studied by P. R. Arivalagan et al. (Scheme-I.15).¹⁰⁰ L-Proline and their derivatives are among the most important class of organic catalysts. Three prolinamide surfactants are designed and synthesized herein. Although the surfactants carried identical catalytic groups (Scheme-I.16), their headgroups contained different functionalities that affected their ability to self-assemble under reverse micelle conditions (DMSO-in-Benzene) and hydrogen-bond with the reactants. The surfactant with a zwitterionic headgroup (catalyst 3) capable of strong aggregation was found to have the highest activity.



Scheme-I.15. Aldol Condensation in acetone and p-nitrobenzaldehyde

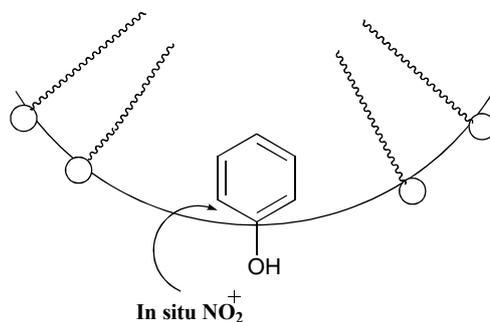


Scheme-I.16. Structures of prolinamide surfactants.

I.D.7. Nitration

M. Hojo reported Nitration of phenol in reversed micelle systems, $\text{CHCl}_3/\text{CTAC}/\text{H}_2\text{O}$ with dilute nitric acid at 35°C to obtain 2- and 4-nitrophenols, where CTAC represents cetyltrimethylammonium chloride. In CTAC and AOT reversed micelle (CHCl_3 or heptane/AOT) medium, 4-methylphenol was converted to 2-nitro-4-methylphenol, where AOT stands for sodium bis (2-ethylhexyl) sulfosuccinate.¹⁰¹

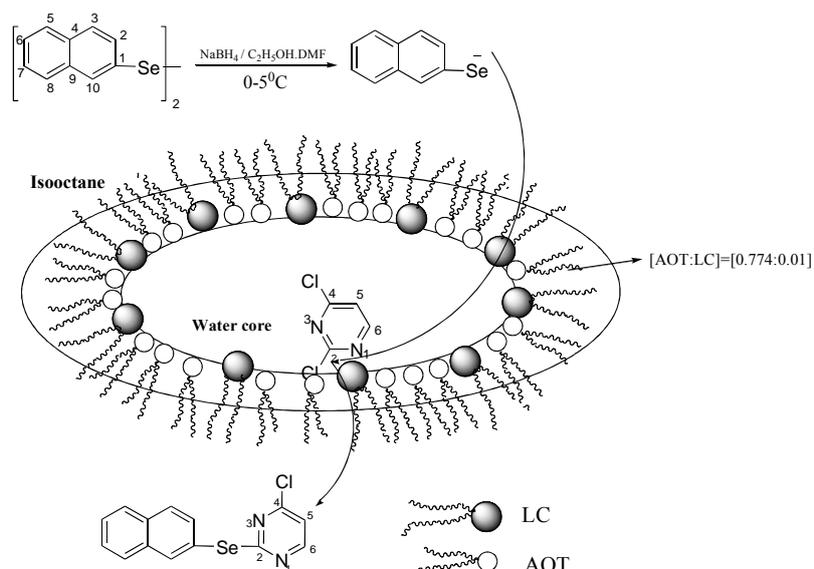
Highly regiospecific mononitration of phenol by the reagent NaNO_3 and dilute sulfuric acid was carried out in a TX100 oil-in-water microemulsion by Jiang et al.¹⁰² (Scheme-I.17). Effects of acid type, surfactant concentration, water content, and alcohol have been investigated.



Scheme-I.17. Nitration of Phenol in O/W microemulsion with dilute Hydrochloric acid and sodium nitrate

I.D.8. Miscellaneous

Mehta et al. have reported a novel synthetic route for preparing organoselenium compounds [4-chloro-2-(naphthalen-2-ylselanyl) pyrimidine] in mixed AOT/lecithin surfactants based reverse isooctane microemulsion (Scheme-I.18).¹⁰³



Scheme-I.18. Probable Mechanism for the Synthesis of 4-Chloro-2-(naphthalene-2-ylselanyl) Pyrimidine

I.E. Microemulsion as Biomimetic Model

It is very complicated to get information about the biomolecular behaviours in locally confined spaces due to the complexities of the biological systems. Reverse micelles (RMs) can perform as a cell membrane-mimetic medium as it provide local hydrophilic moiety in an organic phase resembling to biological membranes of the amphiphilic phospholipids.¹⁰⁴ Again, the radial dimensions of RMs are similar to the confined aqueous compartments in cells and tissues.¹⁰⁵ The dynamics of confined water in the vicinity of biomacromolecules are believed to be responsible for many biological functions, such as molecular recognition and enzymatic catalysis.¹⁰⁶ It can also be used in the field of biochemistry for storing bioactive chemical reagents. Hence, surfactant-based reverse micellar interior is excellent biophysical models to study the confinement effect.¹⁰⁷

In 2008, A. Singha et al.¹⁰⁸ have exhibited a significant improvement in biological hydrogen production achieved by the use of coupled bacterial cells in reverse micellar systems. Two coupled systems (a) *Rhodospseudomonas palustris* CGA009/*Citrobacter* Y19, and (b) *Rhodobacter sphaeroides* 2.4.1/*Citrobacter* Y19 bacteria have been immobilized separately in aqueous pool of the reverse micelles fabricated by various surfactants such as sodium lauryl sulphate (SDS), sodium bis-2-ethylhexyl-sulfosuccinate (AOT), cetylbenzyltrimethylammonium chloride (CBAC) and apolar organic solvents (benzene and isooctane). More than two fold increase in hydrogen production was obtained by the use of Hup₂ mutants instead of

wild-type photosynthetic bacteria together with *Citrobacter* Y19. Addition of sodium dithionite, a reducing agent to AOT/H₂O/ isooctane reverse micellar system with the coupled systems of wild-type photosynthetic bacteria and fermentative bacterium Y19 effected similar increase in hydrogen production rate as it is obtained by the use of mutants. CBAC/H₂O/isooctane reverse micellar system is used for hydrogen production and is as promising as AOT/H₂O/isooctane reverse micellar system. All reverse micellar systems of coupled bacterial cultures furnished encouraging hydrogen production compared to uncoupled bacterial culture. Multi-fold improvement in hydrogen production could be achieved by the use of coupled systems of the photosynthetic bacteria (wild-type or mutated) and the fermentative bacteria entrapped in various reverse micellar systems. Hence, Compartmentalization of the bacterial cells and the enzymes in the reverse micellar systems made the systems very efficient.

Further, S. Pramanik reported the detailed studies of the tetraplex formation in RM to elucidate how these confinements affect the biological function.¹⁰⁷ In this study, they investigated the formation of tetraplex structure from the equimolar mixture of the human telomeric oligonucleotides d[AGGG(TTAGGG)₃] (22AG) and d[(CCCTAA)₃CCCT] (22CT) in bis(2-ethylhexyl)sulfosuccinate (AOT) reverse micelles. The study provides an insight into the formation of G-quadruplexes and i-motif structures under conditions that mimic the interior of the cell. The experimental findings revealed that the Watson–Crick double helix is the predominant form of human telomeric repeat motif (TTAGGG):(CCCTAA) in the dilute solution. However, in AOT RM, which mimics the in-cell confined space; a significant fraction of the equimolar mixture of these complementary strands adopts non-canonical tetraplex structure. It was also demonstrated that the duplex–tetraplex conversion of human telomeric DNA depends on the water pool size i.e. the degree of confinement. Accordingly, fundamental biological functions might be regulated by the degrees of confinement.

I.F. References

References are given in BIBLIOGRAPHY under Chapter I (pp. 101-105).