

CHAPTER-V

Synergistic Interaction of Surfactant Blends in Aqueous Medium Reciprocates in Non-polar Medium with Improved Efficacy as Nanoreactor

V.A. Introduction

In recent years, the study of the physicochemical properties of mixed surfactant systems turns out to be a topic of interest in the area of self-assembly molecular systems.¹ Organized assemblies *viz.* micelles and microemulsions,² based on mixed surfactants offers substantial alteration in solubilization behaviour, enzyme kinetics, nanoparticle synthesis and chemical activity.³⁻⁷ The interaction between surfactants in mixtures produces marked interfacial effects due to changes in adsorption as well as in the charge density of the surface.⁸⁻¹² In most cases different types of surfactants are mixed for synergistic performance and it is utilized to reduce the total amount of surfactant used in particular applications for reduction of cost and environment impact.^{13,14} However, a proper justification of such modified mixing behaviour is still demands and needs a more generalized approach to optimize the mixing stoichiometry in order to yield the maximum effect. Research to date includes numerous attempts to explore combined physicochemical studies of micro-heterogeneous assemblies with interest not only in elemental aspects but also in their wide applications.¹⁵

The Heck reaction,^{16,17} now-a-days, receives much interest in recent years as it offers a versatile process for the generation of new carbon-carbon bonds,¹⁸ and holds much more promise in many industrial processes, especially in the synthesis of fine chemicals and active pharmaceutical intermediates.¹⁹ In view of current economic and environmental fate, continuous efforts are now being made to develop new templates for carrying out the Heck reaction. One approach is to consider inexpensive amphiphiles as potential additives that upon self-assembly into micelles, accommodate otherwise insoluble organic substrates and catalysts within the lipophilic cores.²⁰ Further, microemulsions might be another, much cheaper with more potentially universal approach to this problem, based on the well-known solubilization phenomena.²¹ Very recently, Heck reaction has been successfully performed in water/cetyltrimethylammonium bromide (CTAB)/1-propanol/1-dodecane based oil-in-water (o/w) microemulsion and two phase region as well at 353K.²²

These findings driven us to extend the use of micelle as well as water-in-oil (w/o) microemulsion based on mixed cationic/non-ionic surfactants as a chemical reaction media for the Heck reaction at ambient temperature. To fulfill this objective, a comprehensive behaviour of the formation and physicochemical properties of micellization and microemulsion blends of CTAB and polyoxyethylene (20) cetyl ether (C₁₆E₂₀) including individual constituent is carried out. The structural features of these systems are investigated via interfacial and bulk routes by employing tensiometry, conductometry and also, by zeta potential, viscosity, dynamic light scattering (DLS), fluorescence lifetime, Fourier transform infrared spectroscopy (FTIR), and field emission scanning electron microscopy (FESEM) measurements. The choice of surfactants in this study is not arbitrary. Although the literature is dominated by studies of microemulsions formed with anionic, sodium bis(2-ethylhexyl) sulfosuccinate (AOT), there is interest in microemulsions formed with other surfactants, particularly cationic CTAB. CTAB is of increasing interest because the head group is a good model for the lipid, phosphatidylcholine.²³ Further, commercially available non-ionic surfactants such as Brij's are extensively used in pharmaceutical formulations as solubilizers and emulsifiers to improve dissolution and absorption of poorly soluble drugs.²⁴ Heptane (Hp) and decane (Dc) were used as oil and 1-pentanol (Pn) was used as cosurfactant. After careful evaluation of various physicochemical and thermodynamic parameters, a model C-C cross coupling reaction (Heck reaction) is performed between n-butylacrylate and 4-iodotoluene in presence of palladium acetate and triethylamine, TEA (base) in mixed surfactant based micellar and w/o microemulsion media. To provide proper explanation of this study, we also perform the Heck reaction in media of individual constituents, which are used for the formation of these organized systems. An attempt is also made to rationalize the yield of the Heck products from the viewpoints of physicochemical and thermodynamic parameters of their formation during the course of the reaction. It is believed that the findings of this study are expected to improve the basic understanding of the formation, characterization and application of mixed micelles and w/o microemulsions.

V.B. Results and Discussion

Before going to discuss about the outcome of Heck reaction in micellar or microemulsion medium, first we emphasize on the formation of single and mixed micellar and microemulsion systems from the thermodynamic point of view and their microstructural, microenvironmental and morphological characteristics and also, interaction between the

constituents. In view of this, we divide this section in four parts; where first part of this section contains summary of formation and characterization of micellar systems in single and mixed surfactants both by experimentally and theoretically. In the second part, reaction site and yields of the Heck reaction are rationalized in terms of the interaction parameter, and Gibbs free energy of micellization. Further, the formation and microstructural characteristics of mixed microemulsions along with yields and possible location of reaction at oil/water interface are discussed in last two parts. Finally, a comparative result of reaction yield has been provided between mixed micellar and microemulsion systems along with individual constituents.

V.B.1. Formation and Characterization of Single and Mixed Micelles

The amphiphilic behaviour in terms of critical micellar concentration (CMC) of pure CTAB, $C_{16}E_{20}$ and their mixture at equimolar composition (1:1) in water is determined from the sharp inflection point in the surface tension (γ) against \log [surfactant] and specific conductivity against [surfactant] plots at 303 K as shown in Figure-V.1A and B.

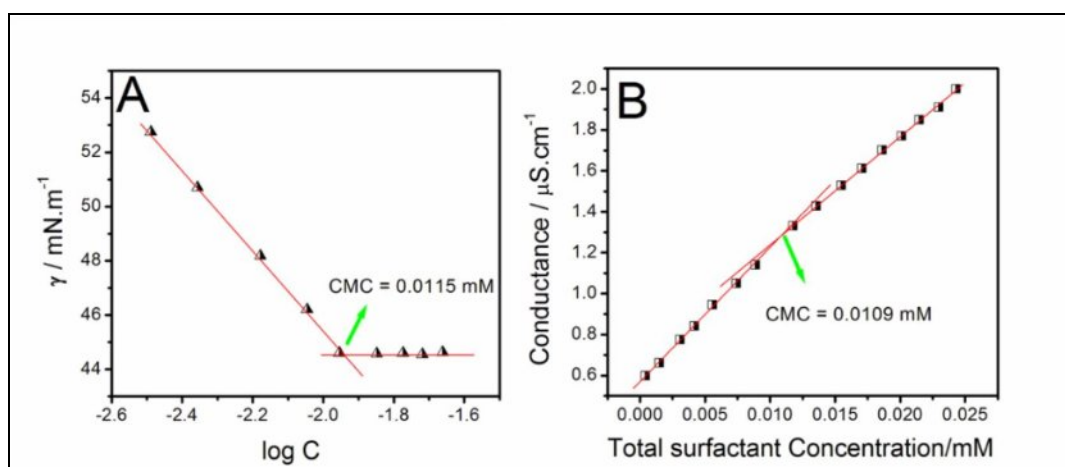


Figure-V.1. Tensiometric (A) and Conductometric (B) determination of CMC of mixed aqueous CTAB/ $C_{16}E_{20}$ systems at equimolar composition at 303K.

Further, a representative illustration of CMC for aqueous $C_{16}E_{20}$ system is presented in Figure-D.S1(Appendix D). The CMC values of these systems are also presented in Table-D.S1 (Appendix D). Lower CMC for CTAB/ $C_{16}E_{20}$ mixtures compared to pure CTAB attributes to the formation of a pseudo-double chain complex arising from the strong electrostatic interaction between the quaternary ammonium cationic segment (CTA^+) and the POE of $C_{16}E_{20}$. In addition, there also exists an enhanced hydrophobic interaction between

the hydrocarbon chains, which favours formation of the mixed micelle and decreases the CMC.²⁷

For ideal mixing of cationic-non-ionic surfactant systems, CMC values have been calculated using the Clint equation,²⁸

$$1/CMC_{ideal} = \alpha_1/CMC_1 + \alpha_2/CMC_2 \quad (2)$$

Where, α_1 and α_2 are the stoichiometric mole fractions of CTAB and C₁₆E₂₀, respectively. For the mixed systems, lower experimental CMC values (CMC₁₂) than those expected from Clint's equation are obtained (Table-D. S1). This observation indicates non-ideal behaviour of aqueous solution and also, demonstrates favourable synergism between the constituent surfactants in mixed micelles.

The nature and strength of interactions between the CTAB and C₁₆E₂₀ molecules in the mixed micelles are evaluated from the interaction parameter by employing Rubingh's approach, based on regular solution theory,²⁹

$$\frac{[(X_1^m)^2 \ln(CMC_{12}\alpha_1/CMC_1X_1^m)]}{(1 - X_1^m)^2 \ln[CMC_{12}(1 - \alpha_1)/CMC_2(1 - X_1^m)]} = 1 \quad (3)$$

Where, X_1^m is the micellar mole fraction of the CTAB incorporated in the mixed micelle. The interaction parameter, β^m is an indicator of the degree of interaction between two surfactants in mixed micelles and accounts for deviation from ideality, which is given by;²⁹

$$\beta^m = [\ln(CMC_{12}\alpha_1/CMC_1X_1^m)]/(1 - X_1^m)^2 \quad (4)$$

For binary system (1:1), β^m values are found to be negative (Table-V.1), which also indicates a synergistic interaction between the component surfactants. According to Rubingh model, the activity coefficient, f_i^m of individual surfactants within the mixed micelles is related to the interaction parameter through the following equations,^{29,30}

$$f_1^m = \exp[\beta^m(1 - X_1^m)^2] \quad (5)$$

$$f_2^m = \exp[\beta^m(X_1^m)^2] \quad (6)$$

Where, $f_i^m = 1$ indicates an ideal mixed system.³⁰ The significance of other terms is discussed earlier. It is seen from Table 1 that both the values of f_1^m and f_2^m are lower than unity, which

indicates the formation of mixed micelles and reflects the non-ideality of a multicomponent mixed system. Further, the maximum surface excess concentration at the air-water interface (Γ_{max}) and the minimum area per surfactant head group adsorbed at the interface (A_{min}) are calculated from the surface tension data by fitting the Gibbs adsorption isotherm,³¹

$$\Gamma_{max} = -\frac{1}{2.303nRT} \left(\frac{d\gamma}{d\log C} \right) \quad (7)$$

$$A_{min} = 10^{18} / \Gamma_{max} N_a \quad (8)$$

Herein, $d\gamma/d\log C$ is the slope of the plot of γ versus $\log C$ (where C represents the concentration of the surfactant). Here, for mixed micelles of cationic/non-ionic surfactants, the value of n (the number of species produced by an amphiphile and whose concentration at the interface varies with the surfactant concentration in the solution) is 3. The values of Γ_{max} and A_{min} are presented in Table 1 and followed the order; $C_{16}E_{20} > CTAB > CTAB/C_{16}E_{20}$ and $C_{16}E_{20} < CTAB < CTAB/C_{16}E_{20}$, respectively. At equimolar composition of mixed $CTAB/C_{16}E_{20}$, minimum Γ_{max} (and thus maximum A_{min}) values are obtained due to the intercalation of POE of $C_{16}E_{20}$ within the positively charged CTAB surfactant molecules which also reduces the repulsion among them.³² The steric hindrance due to long POE chains of $C_{16}E_{20}$ also causes higher A_{min} values for $CTAB/C_{16}E_{20}$ combinations.³²

Another parameter that directly proves the effectiveness of surface tension reduction is the surface pressure at the CMC i.e., Π_{CMC} . It indicates the maximum reduction of surface tension caused by the dissolution of the amphiphilic molecules and is usually defined as;

$$\Pi_{CMC} = \gamma_{sol} - \gamma_{CMC} \quad (9)$$

Where γ_{sol} and γ_{cmc} represent surface tensions of pure water, and surfactant solution at CMC, respectively. As per Table 1, the aqueous $CTAB-C_{16}E_{20}$ mixtures display higher values of Π_{CMC} than their individual counterparts in accordance with their higher surface activity as mentioned earlier, although their efficiency to bring about a reduction in the surface tension of water varies only slightly with the mixture composition.³³

Table-V.1. Interfacial, Thermodynamic and Interaction Parameters of Single and Mixed Surfactants.

(A) Interfacial and Thermodynamic^a parameters						
System	T/K	$\Pi_{cmc} * 10^3 /$	$10^6 \Gamma_{max} /$	$A_{min} /$	$-\Delta G_m^0 /$	$\Delta G_{ads}^0 /$
		N.m⁻¹	mol.m⁻²	nm².molecule⁻¹		kJ.mol⁻¹
CTAB	303	32.0 ^b	1.31 ^b	1.27 ^b		40.5 ^b
64.9 ^b						
CTAB/C ₁₆ E ₂₀	303	34.7	0.86	1.93		71.03
99.74						
C ₁₆ E ₂₀	303	27.64	2.25	0.7379		39.5
51.78						
(B) Interaction^c parameters for CTAB/C₁₆E₂₀ (1:1)						
CMC	CMC	CMC (Avg.)	α and g	β	f_1	
					f_2	
0.0109	0.0115	0.0112	0.829 and 0.171	-4.58 ^d	0.0114 ^c	
0.89 ^c						

^a The average errors in ΔG_m^0 and ΔG_{ads}^0 are $\pm 3\%$; ^b Ref;²⁸ For interaction parameters; ^c CTAB = 1 & C₁₆E₂₀ = 2 and ^d C₁₆E₂₀ = 1 & CTAB = 2.

The standard free energy of micelle formation per mole monomer unit (ΔG_m^0) for these systems is evaluated from the relation;³⁴

$$\Delta G_m^0 = (1 + g)RT \ln X_{cmc} \quad (10)$$

where, X_{cmc} and g are the CMC expressed in mole fraction unit and the fraction of counter ions bound to the micelle, respectively. The fraction of counter-ion binding is related to;³⁴

$$g = \left(1 - \frac{S_{mic}}{S_{mn}} \right) \quad (11)$$

The lower values of g in mixed CTAB/C₁₆E₂₀ (i.e., 0.171) compared to pure CTAB micelle (i.e., 0.47) signify lowering of effective surface charge density in the mixed micelles.³⁵ The

standard free energy of interfacial adsorption (ΔG_{ads}^0) at the air/water interface of micelle is also evaluated from the relation;³⁶

$$\Delta G_{ad}^0 = \Delta G_m^0 - \left(\frac{\Pi_{cmc}}{\Gamma_{max}} \right) \quad (12)$$

The values of ΔG_m^0 and ΔG_{ads}^0 are represented in Table-V.1. Both ΔG_m^0 and ΔG_{ads}^0 values are found to be more negative in binary mixture compared to pure micelle, which indicate that the micellization as well as adsorption processes are more favourable compared to the individual surfactant. Further, more negative ΔG_{ads}^0 values compared to ΔG_m^0 values suggests that the adsorption process is more spontaneous than micelle formation. Micelle formation in the bulk is a secondary process and less spontaneous than interfacial adsorption.^{35,37} In order to get more insight on the surface charge and structural characteristics of pure and mixed micelles, we perform zeta potential, DLS, and FESEM measurements, which are dealt in subsequent paragraphs.

It is already established that zeta potential (ζ) is a very good indicator for the interaction and stability of colloidal systems.³⁸ In view of this, the effect of concentration of the amphiphile(s) on the surface charge of aqueous CTAB, C₁₆E₂₀ and CTAB/C₁₆E₂₀ systems is investigated by measuring the ζ parameter, which is presented in Figure-V.2(A). The positive ζ value for cationic CTAB increases with increasing concentration of CTAB. However, non-ionic C₁₆E₂₀ shows a negative potential, possibly due to the large number of oxygen atoms in POE groups.³⁹ Interestingly, the ζ values for CTAB/C₁₆E₂₀ mixtures are found to be higher than that of single CTAB, which also proves the synergistic interaction between them.⁴⁰

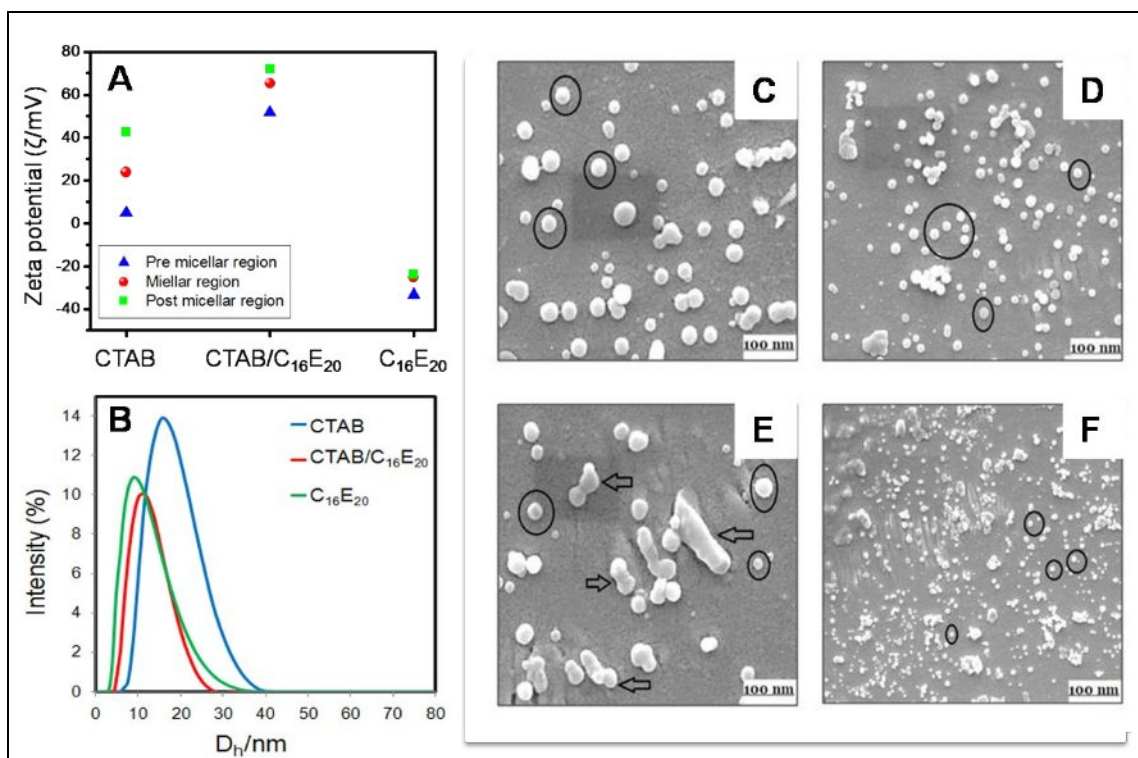


Figure-V.2. (A) Measurement of zeta potential of single and binary (equimolar) surfactants in aqueous medium at 303K. (B) Hydrodynamic diameter (D_h) of micellar systems at 303 K. FESEM images of (C) CTAB/water and (D) CTAB/C₁₆E₂₀/water at micellar region, (E) CTAB/C₁₆E₂₀/water at post-micellar region, and (F) C₁₆E₂₀/water at micellar region.

The DLS technique is employed to determine the size of the aggregates of CTAB, C₁₆E₂₀, and CTAB/C₁₆E₂₀ binary system at their corresponding CMCs at 303K and is depicted in Figure-V.2(B). DLS data shows a monomodal size distribution with hydrodynamic diameter (D_h) ranging from ~10-15 nm for all systems. The micellar size is observed to follow the trend; C₁₆E₂₀ < CTAB/C₁₆E₂₀ < CTAB. The smaller size of C₁₆E₂₀ micelles originates from the relatively weaker interactions of C₁₆E₂₀ with water in comparison to CTAB.^{5,41} Further, the morphology of the four micellar systems is investigated by FESEM technique and illustrated in Figure-V.2C-2F. Uniformly distributed spherical shaped structure is observed for all these systems at micellar region (Figure-V.2C, 2D and 2F), which is indicated by circles in respective figures. Further, Figure-V.2E represents some agglomerated structures (shown by hollow arrows), which consist of two or three single spherical micro-droplets for binary CTAB/C₁₆E₂₀ systems at post-micellar region.

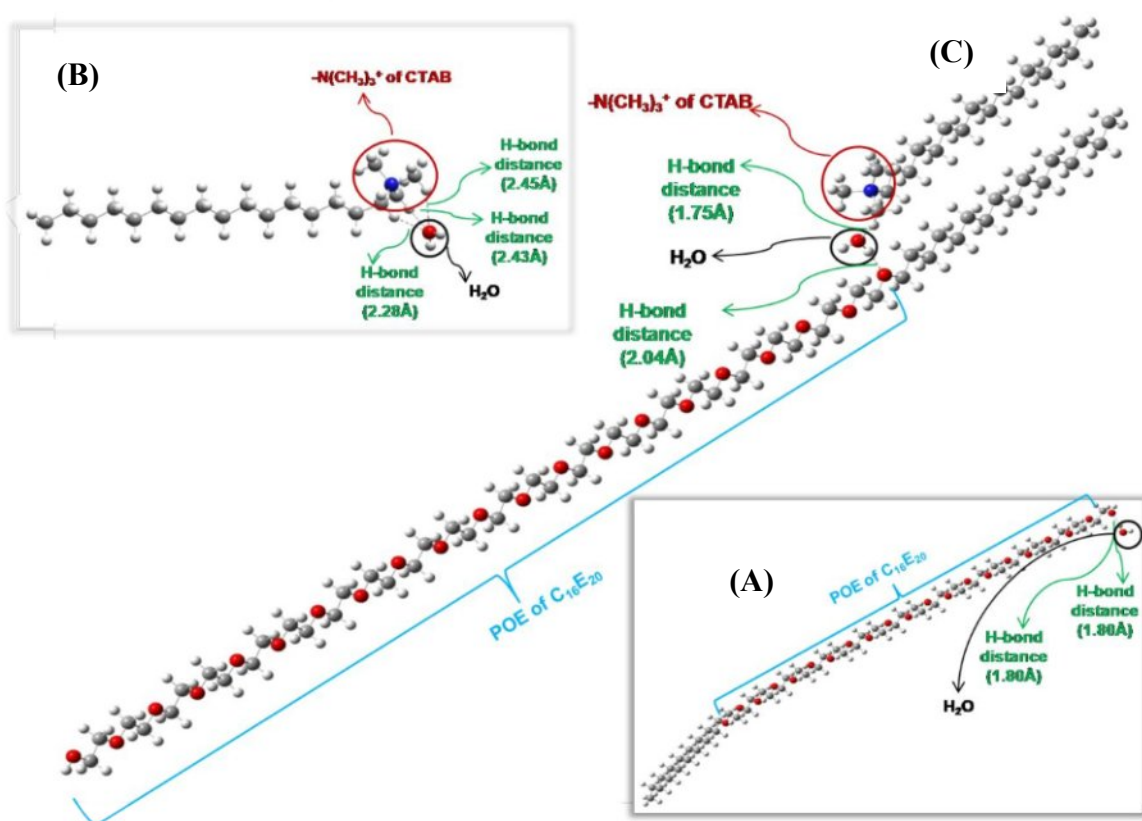


Figure-V.3. Optimized geometries at the B3LYP/6-31G level: (A) $C_{16}E_{20}/H_2O$ complex, (B) CTAB/ H_2O complex, and (C) CTAB/ $C_{16}E_{20}/H_2O$ complex. Colour code for atoms: blue, nitrogen; red, oxygen; dark gray, carbon; and light gray, hydrogen.

In order to understand the interaction of surfactant molecules with solvent qualitatively, we perform quantum chemical DFT calculation. We execute model calculations by using B3LYP functional with the basis set, 6-31G for understanding of the interactions of CTAB, $C_{16}E_{20}$ with H_2O at single and binary (1:1) compositions using Gaussian 09 program. Frequency calculations are also performed to verify that all the optimized geometries correspond to a local minimum which has no imaginary frequency. At the outset, we optimize the structures of the isolated CTAB, $C_{16}E_{20}$ and H_2O , binary complex (1:1) of CTAB and $C_{16}E_{20}$ with H_2O , and ternary complex (1:1:1) of CTAB, $C_{16}E_{20}$ and H_2O . The most stable optimized structures of binary (1:1) and ternary (1:1:1) complexes are presented in Figure-V.3, and their interaction energies (calculated from the difference of stabilization energy between complexes and monomers) are also shown in respective figure. Also, the optimized structures of isolated CTAB, $C_{16}E_{20}$ and CTAB/ $C_{16}E_{20}$ are illustrated in Appendix D (Figure-D.S2). DFT calculation indicates a highly stable ternary complex, CTAB/ $C_{16}E_{20}/H_2O$ with the stabilization energy of -102.09 kJ/mol. The stability of the proposed complexes follows the

order; CTAB/C₁₆E₂₀/H₂O > C₁₆E₂₀/H₂O (-59.09 kJ/mol) > CTAB/H₂O (-41.93 kJ/mol). This result suggests that the stabilization of the CTAB/C₁₆E₂₀/H₂O complex corroborates well the synergism in β parameter, ΔG_m^0 and ΔG_{ads}^0 values (Table-V.1). Similar observation was also reported earlier.^{42,43}

V.B.1.2. C-C cross coupling Heck Reaction in Single and Mixed Micellar Media

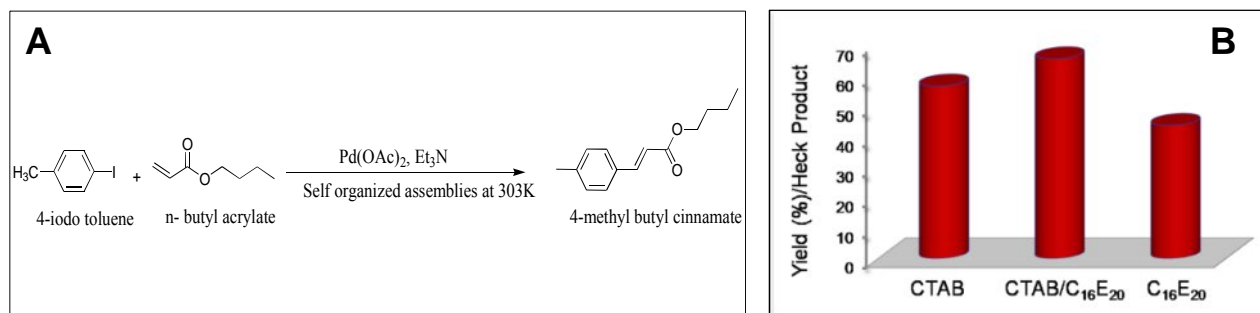


Figure-V.4. (A) Pictorial representation of Heck Reaction in self-organized media; and (B) Yield of Heck reaction in single (CTAB and C₁₆E₂₀) and mixed micelles (CTAB/C₁₆E₂₀, 1:1) at 303K.

Micellar media actually demonstrate that compartmentalization of these systems lead to the formation of the nanoreactor environment in the periphery of the micelle/water pseudo-phase and provide a better sustainability for synthetic organic chemistry.⁴⁴ In this report, repeated trials with a model substrate in characterized single and mixed micelles are explored to articulate the effect of restricted or confined reactor systems in the shed of their physicochemical and thermodynamic properties to rationalize the yield of the Heck reaction product at ambient temperature (303K) (Figure-V.4A). More precisely, it is expected to underline the variation in degree of performance of the Heck reaction from the viewpoints of distinctive features of micellar structure. The results are presented in Figure-V.4 and Table-D.S2 (Appendix D). Various combinations (for example, water, single and mixed micelles of CTAB and C₁₆E₂₀) of the nanoreactor systems (entries 1-4) are explored in order to standardize the best reaction environment from the yield of the desired product of Heck reaction (Table-D.S2). It is clearly evident that yield is very poor in water (7.0%) compares to microheterogeneous systems such as, single CTAB (57%), and C₁₆E₂₀ (44%) or mixed micelle (66.0%). Hence, these results clearly warrant that the envisioned need of a confined environment of aggregated systems which play a significant role in performing the Heck

reaction.⁴⁵ It can be seen from Figure-V.4 and Table-D.S2 that an equimolar composition of mixed micelle exhibits a synergism in yield of the Heck reaction product and consequently, reveals a better reactor than its constituent surfactants. More precisely, mixed micelle possesses some intrinsic properties in its formation that lead to its special characteristics toward performance of the Heck reaction. This is justified from higher negative values of interaction parameter (β^m) and free energy of mixed micelle formation (ΔG_m^0) than individual surfactants (Table-V.1). This suggests formation of the mixed micelle to be most spontaneous as well as functionally operative. Further, it is noted that cationic CTAB-mediated micelle shows higher yield than non-ionic $C_{16}E_{20}$ which corroborates well with spontaneity of formation of respective micelle as designated through the corresponding negative values of both ΔG_m^0 and ΔG_{ads}^0 (Table-V.1).⁴⁶ Surfactant-mediated self-assemblies or micelles are reported to be compatible with the aryl halogens.⁴⁵ Other substrates (excluding Pd^{2+} catalyst, which might be present in the continuous aqueous phase) are expected to be confined in micellar core. Hence, the probable location of micelle-mediated Heck reaction is the micelle/water pseudo-phase whereas the catalysis is likely to be operative.

So far we conclude that due to synergistic interaction between CTAB and $C_{16}E_{20}$ and spontaneous micellization, mixed surfactant based micelle produces an efficient media for performing Heck reaction. Also, the experimentally observed synergistic interaction corroborates well with the quantum chemical DFT calculation. Now, the questions arise that how the synergistic interaction between aforesaid surfactants stimulates in non-polar or non-aqueous medium and also, whether the Heck reaction occurs favorably in this mixed microemulsion system or not? To answer these questions, formation and characterization of mixed microemulsion system at different physicochemical conditions and correlation of the estimated parameters with the reaction mechanism of Heck coupled products are warranted.

V.B.2. Formation and characterization of w/o mixed microemulsions

CTAB requires the presence of a cosurfactant, typically a medium chain alcohol, in order to form a stable microemulsion.⁴⁷ In this study, Pn and Hp (or Dc) are used as cosurfactant and oil, respectively. In w/o microemulsion system, CTAB and $C_{16}E_{20}$ at equimolar composition are considered to populate at the oil/water interface in partial association with the cosurfactant (Pn). On the other hand, Pn further distributes between the interface and the bulk oil, because of its negligible solubility in water.²⁶ Thus, at a fixed [surfactant(s)], a critical concentration of Pn is required for the stabilization of the mixed microemulsions. To estimate

how much amount of (in moles) Pn is distributed in the interface and oil phase for formation of a stable microemulsion, we employ a simple titrimetric technique (known as the dilution method).⁴⁸ The distribution vis-à-vis transfer process of Pn from the continuous oil phase to the interfacial region is discussed in detail in Appendix D, with the help of Figure-D.S3. This method is used for the estimation of various parameters concerning to the formation of CTAB/C₁₆E₂₀ mixed microemulsion systems (with X_{CTAB} or X_{C₁₆E₂₀} = 0.5) in Hp and Dc at 303K and at different molar ratio of water to surfactant ($\omega = 10, 20, 30, 40$ and 50). The estimated parameters, such as number of moles of Pn at the interface (n_a^i), in the oil phase (n_a^o), compositional variations of surfactants and Pn (n_a^i/n_s) at the interface, the distribution constant of Pn between the continuous oil phase and the interface of the droplet (K_d), and standard Gibbs free energy change of transfer of Pn from oil to the interface (ΔG_t^0) are presented in Table-D.S3, Appendix D. It is evident from Figure-V.5A that n_a^i or n_a^i/n_s values decrease with increase in ω for all these systems. Similar trend was reported earlier by Paul et al.⁴⁹ for water/Brij-35/Pn/Dc or Dd and Kundu et al.⁵⁰ for SDS/Brij-58 or Brij-78/Pn/ Hp or Dc microemulsions. At a very low ω , the concentration of Pn at the interface is virtually constant, because long POE chain of C₁₆E₂₀ probably resides at the interface with twisted form due to a strong ion-dipole interaction between compact quaternary ammonium group in CTAB and EO groups in C₁₆E₂₀. With increase in the droplet size by the addition of more water, helically twisted POE-chains unfold and consequently, occupy larger surface area of the droplet.⁵¹ Therefore, unoccupied surface area at the interface reduces to a greater extent and hence, n_a^i is gradually decreases with increase in ω . However, spontaneity of the transfer process further decrease with increase in ω which indicates the trend of Pn transferring from oil to the interface is weakened.⁵⁰ Hp stabilized systems also show higher spontaneity of Pn transfer process than Dc, which is also justified from the higher Pn population at the interface (n_a^i) in former system. Similar observations were reported by Kundu et al.,⁵⁰ Zheng et al.,⁵² and Digout et al.⁵³ for w/o microemulsion systems stabilized by single as well as mixed surfactants. After successful formation of stable mixed microemulsion in conjunction with Pn in Hp or Dc at different ω , it is necessary to understand the microstructural and microenvironmental properties of these systems to reveal the nature of droplet-droplet interaction within these aggregates.

In view of these, size and size distributions of w/o microemulsion droplets are measured by DLS technique. Figure-V.5B depicts variation of the droplet size for mixed microemulsions in both oils as a function of water content ($\omega = 10-50$) at a fixed composition (X_{C₁₆E₂₀} or CTAB

= 0.5), surfactant-cosurfactant mass ratio (= 1:2) and at 303K. The droplet size increases with increase in ω for both oils, keeping other parameters constant, which clearly indicates the swelling behaviour of w/o microemulsions with the addition of water.⁵⁴ The linear variation of droplet size at lower range of ω indicates that the droplets do not interact each other and are probably spherical. The deviation from linearity at higher ω value is due to several factors. Of these, the most relevant ones being enhanced droplet-droplet interaction and shape of the microemulsions. Further, Hp-based systems produce smaller droplet compared to Dc-based systems. It is probable due to the shorter chain of Hp compared to Dc, which easily penetrates to the interface to make it rigid. It can be concluded that with increase in ω , interdroplet interaction increases which is higher for Dc-based system compared to Hp. Both conductance and viscosity measurements in these systems also support the observation from DLS study (Figure-D.S4A and B and inset). The morphology of mixed microemulsions in both oils (Hp and Dc) is also investigated at a fixed $X_{C_{16}E_{20}} = 0.5$, $\omega = 10$ and 303 K by employing FESEM and illustrated in Figure-V.5C-D. The micrographs for Hp based microemulsion (Figure-V.5C) reveal smaller particles arranged in rice grain-like patterns, which produce dispersed spheres of nearly homogeneous type morphology. On the other hand, Dc based microemulsion (Figure-V.5D) produces disintegrated isolated bodies of large globular and near globular particles forming spherical entities. All types of spherical morphology (*viz.* small as well as large) are marked by circles in both figures. For Dc based microemulsion, severe aggregation is occurred and single droplet cannot be discerned distinctly.

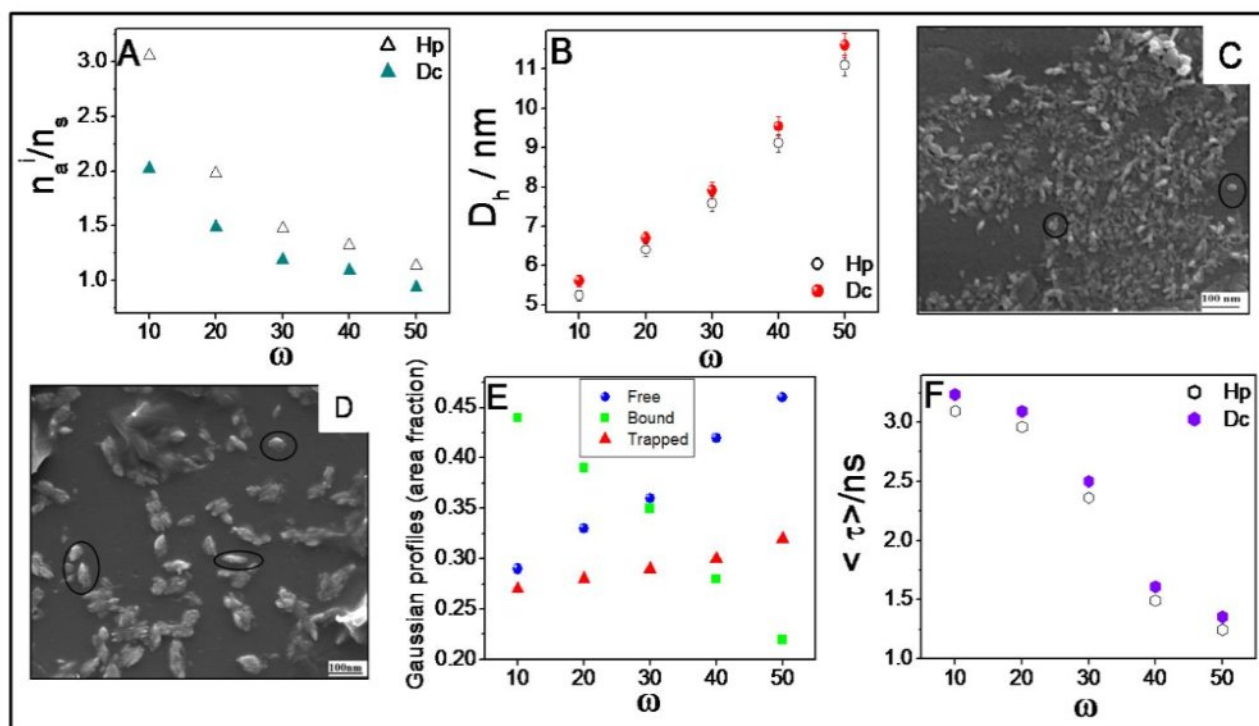


Figure-V.5. (A) Plot of n_a^i/n_s vs. water content (ω) for mixed CTAB/ $C_{16}E_{20}$ microemulsions at equimolar composition comprising 0.5 mmol of mixed surfactant and 14.0 mmol of Hp or Dc stabilized by Pn. (B) Hydrodynamic diameter (D_h) as a function of ω for above mentioned systems. FESEM images of similar systems at a fixed $X_{C_{16}E_{20}} = 0.5$, $\omega = 10$ and 303 K, where (C) Hp and (D) Dc oils. (E) The variation of Gaussian profiles (area fraction) of the normalized spectra of different water species; and (F) Fluorescence lifetime of HCM $\langle \tau \rangle$ ($\lambda_{ex} = 310$ nm) as function of ω in CTAB/ $C_{16}E_{20}$ (1:1)/Pn/ Hp/water microemulsions at 303K.

To understand the dynamics and nature of encapsulated water, we measure mid infrared region (MIR) FTIR spectra of encapsulated water in CTAB/ $C_{16}E_{20}$ (1:1)/Pn/Hp/water microemulsions under varied ω (10→50). We focus our attention in the 3000-3800 cm^{-1} frequency windows as this is a fingerprint region for symmetric and asymmetric vibrational stretch of O-H bonds in water.^{55,56} It is to be noted that a small amount of Pn is used as structure forming cosurfactant in the present study. Hence, the spectra of Pn (at the same concentration) is subtracted from the spectral intensity of O-H stretching band at the corresponding ω in order to eliminate the supplementary IR intensity due to O-H stretching vibration of Pn molecules, and the differential spectra are analysed.^{57,58} Water usually coexists in three ‘states’ or ‘layers’ in the w/o microemulsion.⁵⁸⁻⁶² In view of this, the peaks observed for water O-H are fitted as a sum of Gaussian with the help of Gaussian curve

fitting program, and the vibrational characteristics, particularly the peak area corresponding to each peak, is analyzed using three-state models to unravel the nature of water inside the nanopool and the change in water properties as a function of ω . According to three states model, the solubilized water in microemulsions is identified as free, bound and trapped water molecules and a representative result of deconvolution is depicted in Appendix D, Figure-D.S5. The free water molecules, occupying the core of surfactant aggregates, form strong hydrogen bonds among themselves, that is, possess similar properties to that of bulk water, which shifts the O-H stretching band to lower frequency at about 3250 cm^{-1} (vide. Figure-D.S5).⁵⁸⁻⁶² The bound water i.e. the surfactant head group bound water molecules resonates in the mid frequency region and the IR peak appears at about 3450 cm^{-1} (vide. Figure-D.S5).⁵⁸⁻⁶² Apart from these two types of water species, the water molecules dispersing among long hydrocarbon chains of surfactant molecules are termed as trapped water molecules.⁵⁸⁻⁶² As the trapped water molecules are matrix-isolated dimers or monomeric in nature, they generally absorb in the high frequency region at about 3550 cm^{-1} . The relative abundance [Gaussian profiles (area fraction)] of different water species in these systems as a function of ω is presented in Figure-V.5E. It reveals that the relative abundance of free water increases from 29% to 46% and that of bound water decreases from 44% to 22% with increasing water content ($\omega = 10 \rightarrow 50$) vis-à-vis corresponding increase in droplet size (D_h) from 5.24 nm to 11.10 nm in same ω range. Actually, once water is added to a microemulsion forming system, a portion of the water goes to the interface and hydrates the head groups of surfactants till they become fully hydrated at a certain ω . Further addition of water goes primarily to the inner core, leading to a continuous increase in the fraction of unbounded free water with increase in ω .⁶¹ In addition, the population corresponding to the trapped water molecules (monomers/dimmers) shows an overall weak increasing tendency with the hike of 27% to 32% with increasing ω ($= 10 \rightarrow 50$). It is inferred from this investigation that a few water molecules are displaced from the structured water pool shell to the interfacial region with increasing ω .⁶³

Fluorescence lifetime study of HCM (fluorophore) in mixed surfactant microemulsions is also employed to obtain information about the configuration of the altered interfacial region of mixed amphiphiles interface upon hydration ($\omega = 10 \rightarrow 50$). The choice of the fluorophore (HCM) is based on the fact that the probes residing at the interface and/or facing the polar core upon excitation ($\lambda_{\text{ex}} = 310\text{ nm}$).^{64,65} In the present context, Figure-V.5F depicts that the fluorescence lifetime $\langle \tau \rangle$ of HCM (10^{-5} M) is found to be influenced by the variation of

water content in mixed microemulsions. A regular decreasing trend for $\langle \tau \rangle$ of fluorophore (HCM) is observed for both Hp (3.13 to 1.41 ns) and Dc (3.23 to 1.51 ns) derived systems with increasing ω ($= 10 \rightarrow 50$). Larger droplet size of the microemulsion at $\omega = 50$ compared to $\omega = 10$ results in an increase in the curvature of the surfactant film. Hence a greater fraction of water interacts with the interface; leading to a relatively faster relaxation.⁶⁶ This result is also consistent with findings from FTIR measurements where increase in ω leads to increase in free-water population, which is responsible for observed faster life-time for CTAB/C₁₆E₂₀ (1:1)/Pn/ Hp or Dc/water microemulsions at higher water content.⁶⁷

V.B.2.1. C-C cross coupling Heck Reaction in Mixed Microemulsion

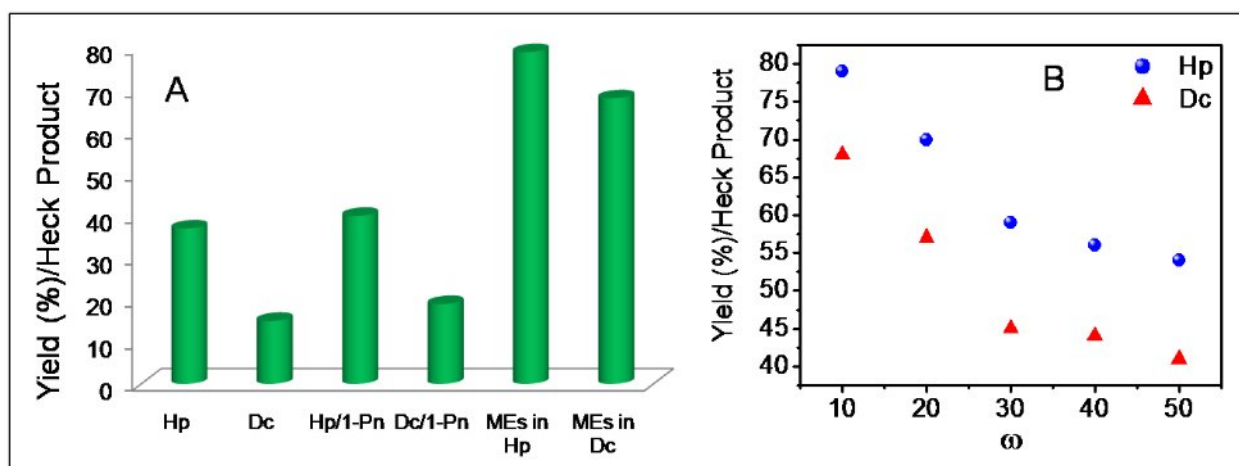
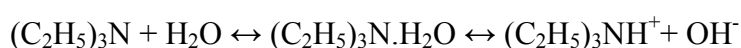


Figure-V.6. Yield of Heck product (A) in individual constituents as well as in w/o mixed microemulsions (MEs), CTAB/C₁₆E₂₀ (1:1)/Pn/ Hp or Dc/water at $\omega = 10$; and (B) variation of yield as a function of ω ($= 10 \rightarrow 50$) in aforementioned MEs at 303K.

In view of the distinctive role of the mixed micelle at equimolar composition for carrying out the Heck reaction, another set of compartmentalized/microheterogeneous systems, water/oil (Hp or Dc) mixed surfactant microemulsions (MEs) stabilized by equimolar (1:1) composition of CTAB/C₁₆E₂₀ and Pn (S: CS = 1:2 wt%), are exploited as a function of ω ($= 10 \rightarrow 50$) (entries 9-18, Table-D.S2 and Figure-V.6). In addition, the yields of the Heck product are also measured in the constituents of these formulations as media (entries 5-8, Table-D.S2). Both oils (Hp and Dc) and oil/Pn mixtures at 1:2 weight ratios (Hp/Pn, and Dc/Pn) show low yield compared to mixed microemulsions, while Hp derived systems show much higher yield than Dc (Figure-V.6A). A profound effect on the overall yield of the Heck product is distinctly validated by changing the template from micelle \rightarrow mixed micelle (1:1)

→ mixed microemulsions (1:1) in Hp and Dc (Table-D.S2). Though, equimolar (1:1) surfactant composition (similar to that of mixed micelle) is fixed in all formulations, yields are found to be dependent on water content (ω), oil type and availability of Pn (as cosurfactant) at the oil/water interface for their stabilization (Figure-V.6B). The highest yield of the desired Heck product is achieved at $\omega = 10$ in Hp and Dc derived microemulsions. Thereafter, a sharp decrease in yield is observed with increasing ω (up to 30) and subsequently, a mild or sluggish decrease achieve still attainment of $\omega = 50$. It is worthy to mention that yield is much higher at lower $\omega = 10$ (ME_{Hp} , 79% and ME_{Dc} , 68%) and 20 (ME_{Hp} , 70% only) than that of mixed micelle (66%), whereas yields are less than that of mixed micelle at rest of the ω 's. However, overall results are rationalized as follows. It is inferred from the yields of the Heck product in microemulsions [ω ranges from 10 → 50 in both oils (ME_{Hp} , 79%→54% and ME_{Dc} , 68%→41%)] in conjugation with the yields in constituent elements *viz.* water (07%), oils (Hp, 37% and Dc, 15%), oil/Pn mixtures (Hp/Pn, 40% and Dc/Pn, 19%) (Figure-V.6A and Table-D.S2) that Heck reaction occurs neither in water nor in oil domain, evidently in the palisade layer of the oil/water interface of the microemulsions. This is well corroborated with previous report, where authors claim that the most plausible reaction location/site was the interfacial region or within the surfactant palisade layer of the w/o microemulsion.^{68,69} In this context, the interaction between two constituents [such as, Pn (cosurfactant) and TEA] of these multicomponent systems plays a decisive role in performance of the Heck reaction leading to formation of the final product. It is worthy to mention that TEA, is an essential reactant of the Heck reaction, which requires a stoichiometric amount of base to neutralize the acid (herein, HI) ensuing from the exchange of a hydrogen atom with a aryl group.^{16,17} In addition, requirement of Pn depends upon composition of the microemulsions, size of polar head group and charge type of surfactant, water content, degree of oil penetration, droplet size/microstructure, etc. and renders overall stability towards multicomponent systems from physicochemical and thermodynamic points of view.^{26,49-53} More precisely, it is deciphered from the viewpoints mentioned above that predominance of the dipole-dipole interaction between Pn and TEA in confined environment enhances the availability of TEA in the vicinity of the interfacial region as well as in confined water with special reference to the bound water. Consequently, formation of OH^- base surrounding the interface proceeds in the following way;^{68,70}



Hence, the penetration of OH⁻ in the palisade layer of microemulsion cannot be ruled out, and subsequently, a basic environment in the vicinity of the interface is likely to be formed, which is essentially required for the Heck reaction.^{68,69} Therefore, most satisfactory yield of the product is achieved at lower ω of 10 or 20 (Figure-V.6 and Table-D.S2), where predominance of Pn in this range of ω is evidenced from characterization of these microemulsions from the dilution method.⁶⁸ It reveals from Figure-V.5A and Table-D.S3 that the interfacial Pn population (n_a^i) and Gibbs free energy of Pn transfer process ($-\Delta G_t^0$) (which is an indicator for spontaneity of microemulsion formation) sharply decrease initially and thereafter mildly with increase in ω . Interestingly, it is worthy to mention that decreasing trends reflected in Figure-V.5A and Figure-V.6B resemblance to each other, which is a strong evidence for decreasing yield with increase in ω . Further, Hp based systems exhibit higher yield than Dc. It can be argued that higher values of n_a^i and $-\Delta G_t^0$ in Hp continuum than Dc continuum (Figure-V.5A and Table-D.S3) are responsible for variation in yield in these two set of systems. Herein, we report a mixed microemulsion mediated Heck coupling reaction which provides comparatively better results than single or mixed micelle validating the spontaneous nature of the reactor framework with a concomitant rapid Pn transfer process ($Pn_{oil} \rightarrow Pn_{interface}$) obtained from the dilution experiments under varied physicochemical environments. In conclusion, CTAB and C₁₆E₂₀ mediated micelles and microemulsions (in single and mixed state) Heck coupling procedure (through generation of new C-C bonds) is developed using ligand-free catalysts, and could be prospective in many industrial processes, especially in the synthesis of fine chemicals and active pharmaceutical intermediates.^{19,71}

Currently, investigations of C-C coupling reactions catalysed by Pd(II) acetate and TEA as base in w/o microemulsions comprising different charge types of surfactants (both in single or mixed state) at different physicochemical conditions (for example, variations in composition of the system, concentration of both base and catalyst, water content, temperature etc.) are underway in our laboratory to probe the reaction mechanism of the Heck reaction in these complex microheterogeneous systems as media.

V.C. Overall Comprehension

In aqueous medium, equimolar composition of CTAB and C₁₆E₂₀ produces several advantages compared to individual surfactant in terms of lower CMC, more attractive

interaction between them and spontaneous micellization (*i.e.*, more negative free energy of micellization) as well as adsorption process at air/water interface. Interestingly, quantum chemical DFT calculation reveals larger interaction energy of equimolar CTAB and C₁₆E₂₀ with water compared to any other combinations. Zeta potential (ζ) values for CTAB/C₁₆E₂₀ mixtures also prove the synergistic interaction between them. Micellar aggregates produce spherical droplets with size ranges from 10 to 15 nm. To understand the distinctive features of micellar structures as chemical nanoreactors, Heck reaction is performed between 4-iodotoluene and *n*-butylacrylate. The reaction yield of Heck coupled product is found to be higher in mixed CTAB/C₁₆E₂₀ micellar solution compared to single CTAB or C₁₆E₂₀ micelle. However, a very poor yield is obtained in pure water. This result certainly proves that strong confinement effect of these assemblies. Also, the higher yield at mixed composition is correlated with spontaneous micellization and adsorption processes. It now stands interesting to further study the behaviour of these surfactants in non-polar solvents. Population of Pn at the oil/water interface of formulated w/o microemulsions vis-à-vis spontaneity of the transfer process is found to be decreased with increase in ω for both oils. Although these parameters are obtained through a straightforward macroscopic measurement, the Gibbs free energies of transfer of Pn from bulk oil to the interface are a sensitive probe of the micro-environment around various solute moieties, and are amenable for the investigation of relatively complex molecular structures. Morphology and size of mixed microemulsion droplets vary with water content as well as oil chain length. The present study also reveals that the relative abundance of free water increases and that of bound water decreases with increasing water content in mixed microemulsions and is well-corroborated with corresponding increase in droplet size under identical ω range. To search for further synergistic performance in non-polar medium in comparison to aqueous, the Heck reaction is carried out in mixed microemulsion media with aforesaid surfactants including individual constituent comprising microemulsion (*viz.* Pn, Hp or Dc). The reaction yields are found to be much higher in microemulsion systems compared to individual constituents. The yield in microemulsion is influenced by population of Pn at the oil/water interface, and chain length of oil. With increase in ω , yield of the Heck product decreases and it is lower for Dc medium compared to Hp. Both of these observations are correlated with spontaneity of Pn transfer process from oil to the interface obtained from the dilution experiment. The reaction in micellar and w/o microemulsion media has been found to be dependent on various physical parameters (such as water content, chain length of oil, composition of surfactants etc.) of these organized media.

V.D. Materials and methods

V.D.1. Materials CTAB (> 99%), C₁₆E₂₀ (> 98.5%) were the products of Sigma Aldrich, USA and Fluka, Switzerland, respectively. The cosurfactant [1-pentanol (Pn, > 98%)] and oils [Hp, (> 98%) and Dc(> 98%)] were products of Fluka, Switzerland, Lancaster, England and E. Merck, Germany, respectively. The dye, 7-hydroxycoumarin (HCM, > 99%) was the product of Chem. Service, West Chester, USA. Palladium acetate [Pd(OAc)₂, ≥ 99.98%] and 4-iodo-toluene (CH₃C₆H₄I, ≥ 99%) were purchased from Sigma Aldrich, USA. (TEA (≥ 99.5%) and n-butyl acrylate were purchased from Merck, Germany. All these chemicals were used without further purification. Doubly distilled water of conductivity less than 3 μS cm⁻¹ was used in the experiments.

V.D.2. Methods

V.D.2.1. Tensiometry Surface tension was measured with a K9 tensiometer (Kruss, Germany) by the platinum ring detachment method. A concentrated surfactant solution was added to a known amount of water, and the surface tension values were measured after thorough mixing and temperature equilibration with an accuracy of ±0.1 mN m⁻¹.

V.D.2.2. Conductance measurements Conductivity measurements were made using an automatic temperature-compensated conductivity meter, Mettler Toledo (Switzerland) Conductivity Bridge, with cell constant of 1.0 cm⁻¹. The instrument was calibrated with a standard KCl solution. A constant temperature (303 ± 0.1 K) was maintained by circulating water through the outer jacket from a thermostatically controlled water bath. The reproducibility of the conductance measurement was found to be within ± 1%.

V.D.2.3. Dynamic light scattering (DLS) and zeta potential measurements Hydrodynamic diameter (D_h) and zeta potential (ξ/mV) measurements of the aggregated systems (single and mixed micelles and w/o mixed microemulsions) were performed using Nano ZS-90 (Malvern, U.K.) dynamic light scattering spectrometer at 303K. The solutions were equilibrated for 2-3 hours before measurement. Solutions were filtered carefully through a 0.22μm MilliporeTM membrane filter loaded to a glass round aperture (PCS8501, Malvern, U.K.) cell of 1.0 cm optical path length for measurement. A He–Ne laser of 632.8 nm was used as the light source, while the scattering angle was set at 90⁰. Temperature was controlled by in built Peltier heating-cooling device (± 0.1 K). D_h of the aggregated system was

estimated from the intensity autocorrelation function of the time-dependent fluctuation in intensity and can be defined as.²⁵

$$D_n = k_B T / 3\pi\eta D \quad (1)$$

Where, k_B , T , η and D indicate the Boltzmann constant, temperature, viscosity and diffusion coefficient of the solution, respectively. Zeta potential were measured using a folded capillary cell (DTS1060, Malvern, U.K.) made of polycarbonate with gold plated beryllium-copper electrodes. One cell was used for a single measurement. To check the reproducibility of the results at least 6 measurements were done.

V.D.2.4. Field Emission Scanning Electron Microscopy (FESEM) measurements A field emission scanning electron microscope (FESEM, HITACHI S-4800) was used to study the morphology of single and mixed micelles and w/o mixed microemulsions. High vacuum ($\sim 10^{-7}$ Torr) field emission setup was applied to deposit the thin film of micelle and microemulsion solution on the glass plates.

V.D.2.5. Formation of microemulsion The formation of microemulsion was accomplished by adding oil (Hp or Dc) at a constant water and surfactant level to destabilize an otherwise stable w/o microemulsion and then restabilizing it by adding a requisite amount of cosurfactant (Pn) with constant composition of interface and continuous phase. The procedure of this experiment with theoretical backgrounds was reported elsewhere.²⁶

V.D.2.6. Viscosity measurements Viscosity measurements were performed using a LVDV-II+PCP cone and plate type rotoviscometer (Brookfield Eng. Lab, USA). The temperature was kept constant (303 K) for viscosity measurement within ± 0.1 K by circulating thermostated water, through a jacketed vessel containing the solution. The reproducibility of the viscosity measurement was found to be within $\pm 1\%$.

V.D.2.7. Fluorescence lifetime measurements The fluorescence lifetime measurements of w/o mixed microemulsions were performed at 303K using a bench-top spectrofluorimeter from Photon Technology International (PTI), USA (Model: Quantamaster-40). The present PTI lifetime instrument employs Stroboscopic Technique (Strobe) for time-resolved fluorescence measurements. In the present experiment, two curves are considered at the measured wavelength (at 450 nm using 310 nano LED as the light source) viz. the instrument response function (IRF) and the decay curve of probe molecules, 7-hydroxycoumarin (10^{-5}

mol dm⁻³). IRF is acquired from a non-fluorescing scattered solution (Herein, Ludox AM-30 colloidal silica, 30 wt.% suspension in water) held in a 1 cm path length quartz cell. The lifetime values of probe molecules are then obtained by convoluting the IRF with a model function and then comparing the result with the experimental decay. Analysis has been made by Felix GX (version 2.0) software. A value of χ^2 in between 0.99-1.22 and a symmetrical distribution of residuals are considered as a good fit.

V.D.2.8. Fourier transform infrared spectroscopy (FTIR) studies FTIR spectra of w/o mixed microemulsions were performed at 303K in the 3000-3800 cm⁻¹ window (mid infrared region) were recorded on a Perkin Elmer Spectrum RXI spectrometer (USA) (Absorbance mode) using a CaF₂-IR crystal window (Sigma-Aldrich) equipped with a Presslock holder with 100 number scans and spectral resolution of 4 cm⁻¹ at 303K. Deconvolution of spectra has been made with the help of Gaussian curve fitting program (Origin software).

V.D.2.9. C-C cross coupling (Heck) reaction in micelles and microemulsions 3 ml of micellar or w/o microemulsion solution and 4.48 mg (0.02 mmol, 4 mol %) Pd(OAc)₂ were taken in a 25 ml round bottom flask and the mixture was placed in a preheated oil bath at 303 K for 30 minutes with constant stirring. Thereafter, 109 mg (0.5 mmol) of 4-iodotoluene, 76.8 mg (0.6 mmol) of *n*-butylacrylate and 101.12 mg (1 mmol) of TEA were introduced into it, and the resulting mixture was further stirred for 60 minutes at 303K. The resulting multicomponent solution (in each case) shows excellent stability towards reagents or otherwise. More precisely, similar experiments were performed in single (CTAB and C₁₆E₂₀) and mixed micelles (at equimolar composition), and mixed microemulsions (at equimolar composition) at different molar ratio of water to surfactant (ω) and also, in other constituents (viz. water, Hp, Dc, Hp/Pn, Dc/Pn) of the microemulsions. Progress of the reaction was monitored by silica gel thin layer chromatography (TLC). After completion, the reaction was quenched with water and the organic part was extracted thrice with diethyl ether. The combined ether layer was dried over anhydrous sodium sulphate and concentrated under vacuum. The yield of the Heck coupled product was determined by HPLC (Agilent Technologies, 1260 Infinity). Further, the product was purified by column chromatography using silica gel where a mixture of petroleum ether and ethyl acetate was used as eluent. Finally, the product was characterized by ¹H-NMR and ¹³C-NMR (Bruker, 300 MHz), which were provided in Appendix D.

V.E. Summary

The present report focuses on the microstructure and properties of micelles and w/o microemulsion systems using similar set of surfactants (CTAB and C₁₆E₂₀) at single and mixed states and also, employment of these organized assemblies as chemical nanoreactor for performing the C-C cross coupling Heck reaction. Equimolar composition of CTAB and C₁₆E₂₀ shows non-ideal solution behaviour in aqueous medium with synergistic interaction between them, which further correlates with gas phase quantum chemical calculation. Understanding the microscopic origins of these mixing properties might facilitate more informed and designed use of such mixed systems in a range of novel formulations from hydrogels to surface coatings.^{72,73} Mixed micellar composition provides efficient medium for carrying out Heck reaction compared to individual micellar and bulk water medium. So far, an operationally simple procedure is developed for carrying out traditional Heck couplings at ambient temperatures in mixed micelle, without resorting to sonication, electrochemistry, or water-soluble phosphine.⁷⁴ Use of inexpensive ionic and non-ionic amphiphiles, allows cross-couplings to take place especially under mild and environmentally attractive conditions. To realize whether the key features responsible for favorable micellization via synergistic interaction reciprocate the interfacial architecture of microemulsions, a multitechnique approach is applied to fully characterize mixed microemulsion systems at different hydration level. The estimation of Pn distribution at oil/water interface and bulk oil phase from dilution method complements more detailed information obtained from more labour-intensive small-angle neutron scattering (SANS) studies of w/o microemulsions.⁷⁵ Further, the droplet size and relaxation dynamics of fluoroprobe inside the confined environment correlates well with variation of different states of water. Knowledge of the such state of solubilized water in w/o microemulsion is important because this bears on the applications of these species, for example, in solubilization, catalysis of chemical reactions,⁷⁶ and in size and polydispersity of nanoparticles synthesized in the microemulsionmedia.⁷⁷ In order to understand the mechanism of Heck reaction in non-polar medium instead of aqueous medium, the formulated w/o microemulsion at different compositions along with individual constituents further used as templates for aforementioned reaction. A profound effect on the overall yield of the Heck product is distinctly validated by changing the template from micelle → mixed micelle (1:1) → mixed microemulsions (1:1), which indicates influence of the nature of the surfactant-solvent interactions, and thus affects the reaction yield.⁷⁸ Herein, it is proposed that the Heck reaction occurs neither in water nor in oil domain, and more precisely, at the

micelle/water pseudo-phase and palisade layer of the oil/water interface of microemulsions. In summary, each amphiphilic nano reactor is analogous to the traditional chemist's flask, with the added advantages of reduced reagent consumption, rapid mixing, automated handling, and continuous processing. Building on advances in continuous flow chemistry,⁷⁹ our study thus provides a new route to regulate and even to enhance the reaction yields in micellar and w/o microemulsion media according to the purpose and could be found useful for future applications in various domains such as enzyme activity, and/or organic synthesis.^{80,81}

V.F. References

References are given in BIBLIOGRAPHY under Chapter V (pp. 113-118).