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Organobase catalysis using 1-(2-pyrimidyl) piperazine in micellar medium: An approach for better performance and reusability of organobase

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Abstract

An organobase-surfactant micellar combined system was investigated for efficient and alkali/ metal free base catalysis and to establish a simple method for separation and reuse of organobase catalyst. Various aqueous organobase-surfactant micellar solutions were studied by using Knoevenagel condensation of salicylaldehyde with active methylene compounds to 3-substituted coumarin as model reaction. The 1-(2-pyrimidyl) piperazine (2-PP) was identified as a highly active organobase and its activity was further improved by using it in aqueous solution of sodium dodecyl sulfate (SDS). The SDS micelles facilitate the reaction in water by solubilizing the 2-PP organobase and the reactants in their active forms. The reactants-SDS interactions in micelles play significant role in promotion of 2-PP catalyzed reaction. The SDS micellar medium not only promotes the 2-PP catalyzed reaction but also provide an easy and practicable protocol for separation and reuse of 2-PP organobase.

Keywords: Organobase; 1-(2-pyrimidyl) piperazine; surfactants; micelles; base catalysis; Knoevenagel condensation; 3-substituted coumarins.

1. Introduction

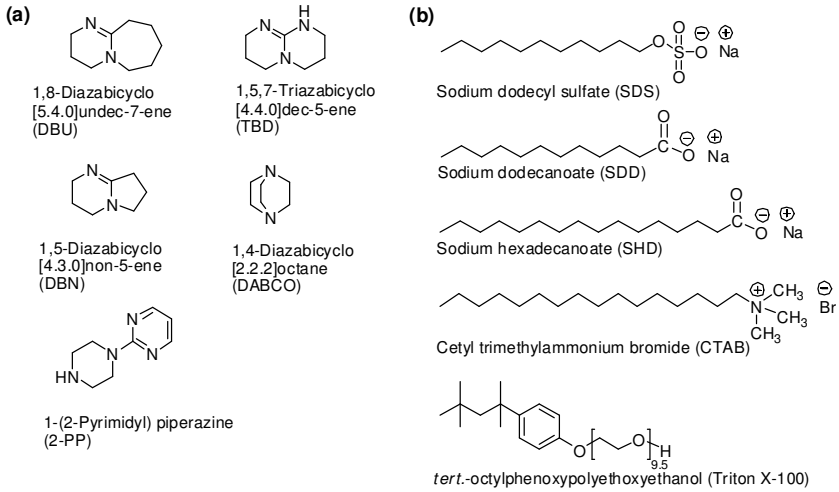
There is a great demand for efficient and alkali/ metal free base catalytic system to be utilized in the organic synthesis. In recent years, the organocatalysis has received much attention to develop metal free and greener route for synthesis of important chemicals,[1] especially for the synthesis of biologically active compounds and intermediates**.** The cyclic organobases (Scheme 1a) such as DBU,[1d,1g-1j] TBD,[1c,1k,1l] DBN,[1m] DABCO,[1f,1n] etc. have been widely explored as non-corrosive, environmentally benign and efficient homogeneous base catalyst for numerous important organic transformations. These organobases have been of special interest for synthetic organic chemistry due to their high basicity: the pKa values of TBD, DBU, DBN and DABCO are 25.96, 24.34, 23.79 and 18.29, respectively.[2] The basicity of guanidine derived bases is higher than amines and amidine bases due to the formation of the number of canonical forms after protonation. The organobase catalysts have been efficient under ambient condition and also in water as solvent. They show excellent activity in homogeneous condition, but their difficult separation and reusability limit their practical applicability. The TBD, a strong bi-cyclic guanidine base, has been demonstrated to be efficient organobase catalyst for aldol reactions.[1c] The polymer supported TBD catalysts were prepared for the easy separation and reusability.[3] The recovery of TBD from homogeneous reaction mixture has been reported by bubbling CO_2 in the reaction mixture at the end of reaction producing a precipitate, which on heating at 130°C under inert atmosphere gave TBD eliminating CO_2.[1c] Cota *et al.*[1g] reported the reusability of DBU in base catalyzed aldol condensation reactions by removing the organic phase containing the product from the aqueous phase (which contains dissolved DBU); however, they required very high concentration of catalyst (DBU-H_2O complex in 1/25 molar ratio) to achieve highest activity.

The organic-aqueous biphasic reaction systems received much interest due to the use of water as inexpensive and environmentally benign solvent and the recovery of water soluble catalyst from

the reaction mass.[4] The use of organobases in organic-aqueous biphasic reactions would be promising for easy separation of organobases as they would be soluble in aqueous phase and after reaction the aqueous phase can be easily separated. The presence of water in many organocatalytic aldol reactions has been found to be useful as co-catalyst in promotion of the reactions.[5,6] However, the insolubility/ incompatibility of hydrophobic organic compounds in water has been found to be major constraint of water mediated or aqueous-organic biphasic reactions showing slow reaction rate.[7-10] Previously, we reported the potential of cationic surfactants to overcome the problem of reagent(s) incompatibility in aqueous reactions showing enhanced reaction rate and selectivity, and also for recovery and reuse of NaOH homogenous catalyst.[11] The reactions in a micellar solution are facilitated by micelles by generating huge interfacial area between oil (reactants) and aqueous phase.[7] This also provides advantages such as solubilization/ localization of reactants in the micelles in special orientation and in active form, and water soluble ionic species (e.g., catalyst) on the micellar surface making the reaction faster and selective.[11-13] In continuation of our work on base catalysis using micellar systems, we were interested in replacement of the NaOH base catalyst by an organobase to develop alkali free micellar system for base catalysis. The organobase catalysis in an appropriate surfactant solution could be an effective approach to have enhanced efficiency of organobase in the aqueous medium as well as for easy separation of organobase for reuse.

The present work was aimed to study the catalytic potential of some important organobases in aqueous surfactant micellar solution to develop an efficient, alkali/ metal free and green catalytic system for base catalysis as well as to establish a simple protocol for recovery and reuse of organobase. We studied five cyclic organobases (Scheme 1a) as well as some inorganic bases (such as NaOH, KOH, Na_2CO_3 and $NaHCO_3$) as catalyst for base catalyzed Knoevenagel condensation of salicylaldehyde and diethyl malonate (DEM) to 3-substituted (ester) coumarin as a model reaction of aldol type reaction under neat, biphasic condition and in micellar

solutions of different surfactants (anionic, cationic and nonionic; Scheme 1b). The 3-substituted coumarins are bioactive compounds exhibiting numerous important pharmacological effects such as analgesic, anti-arthritis, anti-inflammatory, anti-pyretic, anti-viral, anti-cancer, anticoagulant, etc.[14] We found that 1-(2-pyrimidyl) piperazine (2-PP; Scheme 1a) guanidine base, which has not been studied for base catalysis, was highly active for organobase catalysis among the studied organobase catalysts. In aqueous micellar solution of an appropriate surfactant (anionic; SDS), the catalytic performance of 2-PP was observed to be significantly improved. The SDS micelles solubilize the 2-PP organobase catalyst and reactants molecules in water and bring them together for interaction. Furthermore, the favourable interactions between SDS and the reactants in micelles (co-catalytic activity of surfactant) greatly help in catalysis of the reaction. The spent 2-PP-SDS micellar solution could be easily recovered by filtration of crystallized product for reuse.



Scheme 1. Structure of different (a) organic bases and (b) surfactants used in the study.

2. Experimental

2.1. Materials

Salicylaldehyde (>99%), diethyl malonate (DEM; 98%), ethyl acetoacetate (EAA; 98%), sodium hydroxide (99%), potassium hydroxide (99%), sodium bicarbonate (99%), sodium

carbonate (99%), ethyl acetate (99%) and concentrated HCl (35%) were purchased from Merck, India. Cetyl trimethylammonium bromide (CTAB; 98%), sodium dodecyl sulfate (SDS; 98%), Triton X-100 (98%), and toluene (99%) were from S.D. Fine Chemicals, India. Sodium dodecanoate (SDD; 99%), sodium hexadecanoate (SHD; 98.5%), DBU (99%), TBD (99%), 2-PP (99%), DBN (99%) and DABCO (99%) were from Sigma Aldrich. All the chemicals were used without any further purification. The double distilled milli-pore deionized water was used in the reactions.

2.2. Experimental procedure

The catalytic activity of different bases was evaluated by carrying out Knoevenagel condensation reactions of salicylaldehyde and DEM in solvent free condition (neat), in water (biphasic reaction) and in aqueous surfactant solutions. In the reaction tube of reaction station (12 Place Heated Carousel Reaction Station, RR99030, Radleys Discovery Technologies, UK), 5 mL of surfactant aqueous solution was taken and a mixture of salicylaldehyde (2.5 mmol) and DEM (2.5 mmol) was added in the solution under stirring. The base (inorganic/organic) was dissolved in the solution and the reaction mixture was stirred at required temperature for the required period of time. The biphasic reaction (reaction in pure water) was carried out by first dissolving the 2-PP in water (5 mL) followed by addition of reactants mixture in the solution. The details of reaction conditions are also mentioned in the footnote of the tables and figures.

After completion of the reaction, the reaction mixture was neutralized with concentrated HCl and diluted with excess of saturated NaCl solution to reduce the surfactant concentration below the CMC (in case of micellar reactions). The organic phase was extracted with ethyl acetate (10 mL) and was analyzed by gas chromatography (Agilent 5975) having a HP-5 (60 meter, 250 µm diameter) capillary column with a programmed oven temperature from 50 to 280°C, at 1 mL min^{-1} flow rate of N_2 as carrier gas and FID detector. The conversion of DEM was calculated on the basis of its weight percent as follows,

$$\text{Conversion (wt.\%) of DEM} = \frac{100 \text{ X [Initial wt.\% of DEM} - \text{Final wt.\% of DEM]}}{\text{Initial wt.\% of DEM}}$$

The selectivity of the product (3-substututed coumarin) was calculated as below,

$$\text{Selectivity (\%) of 3-substututed coumarin} = \frac{100 \text{ [GC peak area \% of 3-substututed coumarin]}}{\Sigma \text{ Total peak area for all the products}}$$

The products formed in the reactions were characterized by GC–MS analysis and the data were matched with those reported in the literature. GC–MS analysis was carried out using gas chromatograph mass spectrometer (Agilent 5975 GC/MSD with 7890A GC system) having HP-5 capillary column of 60 m length and 250 µm diameter with a programmed oven temperature from 50 to 280°C, at 1 mL min^{-1}flow rate of He as carrier gas and ion source at 230°C.

To recover the surfactant-organobase aqueous solution after the completion of reaction for reuse study, the stirring of reaction mixture was stopped and the solution was allowed for crystallization. The micellar solution was separated by filtration and the surfactant-organobase solution was reused for 1st cycle. In the spent surfactant-organobase solution, the mixture of salicylaldehyde (2.5 mmol) and DEM (2.5 mmol) was added under stirring (700 rpm) and the reaction was further carried out at 30°C for 6 h. The reaction mixture was worked up as previously described. For 2nd and subsequent reaction cycle, the spent surfactant-organobase solution was obtained by filtration of product crystals from reaction mixture of previous cycle. The spent organobase aqueous solution of biphasic reaction (surfactant free) was obtained by phase separation and removing it from the top of the organic phase containing partially crystallized product and unreacted reactants.

The UV-vis spectra of the reactants and 2-PP organobase in water and aqueous surfactant solutions were recorded by using an Agilent, Carry 5000 spectrometer at room temperature. The path length of the quartz cell used in this experiment was 1 cm. The UV absorptions were studied by using separate solutions of base and both reactants (2-PP organobase: 0.18 mM;

salicylaldehyde: 0.8 mM; DEM/ EAA: 2.4 mM) in water and in surfactant solutions. These amounts were found to be completely soluble in the pure water (without surfactant) giving a transparent solution, however, these concentrations of reactants and organobase (2-PP) were different from those used in the catalysis experiments. The ^{1}H NMR analyses of the reactants mixture (salicylaldehyde and DEM/ EAA) and separately of 2-PP organobase in D_2O and surfactant solutions (prepared in D_2O) were carried out using a Bruker Avance III 500 MHz spectrometer. The reactants mixture (in 1:1 molar ratio; 10 µL) was solubilized in 1 mL D_2O or surfactant solution in D_2O. The 2-PP organobase solutions (0.18 mM) prepared in D_2O or in D_2O-surfactant solutions were used for ^{1}H NMR analyses. The number of acquisitions was 32 for each sample. The ^{1}H chemical shifts are reported in δ units (ppm) relative to that of tetramethylsilane (TMS) as external standard.

3. Results and discussion

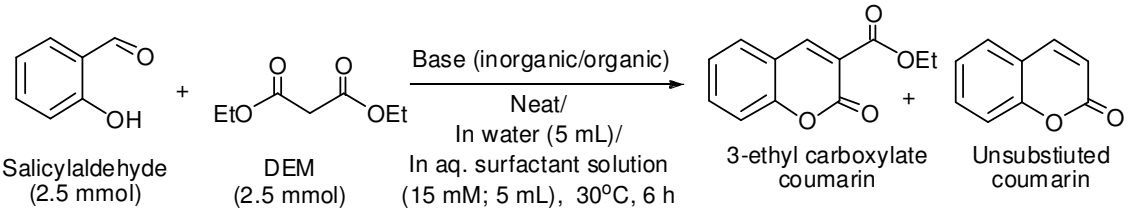
3.1. Catalytic activity of inorganic and organic bases in different reaction media

The control experiments (**ESI; Table S1**) showed that in pure water or in micellar solutions without catalyst (inorganic/ organic base), there was no reaction between salicylaldehyde and DEM/ EAA at room temperature as well as at 60°C. Initially, the reactions of salicylaldehyde and DEM were carried out using 50 mol% of catalyst (inorganic/ organic base) in pure water (biphasic reaction) and in 15 mM CTAB micellar solution at 30°C (Table 1; Entry 1 to 19). The selectivity of the desired product (3-ethyl carboxylate coumarin) was 97-100% and in some reactions, un-substituted coumarin was found as by-product, which could be probably formed due to hydrolysis followed by decarboxylation of 3-substituted coumarin. From the results (Table 1), this is evident that 2-pyrimidyl piperazine (2-PP) is highest in activity than inorganic as well as other organobases giving highest conversion of DEM in water (95%) and in CTAB or SDS micellar solutions (99%). The previously reported organobases such as DBU, TBD, DBN and DABCO in either biphasic condition or micellar media gave lesser conversion than 2-PP.

The higher activity of 2-PP as compared to other organobases may be due to the presence of two basic functionalities in 2-PP molecule: guanidine moiety in aromatic system and secondary amino group in piperazine ring.

The catalytic performance of 2-PP was further examined by reducing its molar amount (from 50 mol% to 10 mol%) in the neat, biphasic and micellar reactions (Table 1; Entry 20 to 28). The biphasic reactions were performed to examine the performance of organobase without surfactant and also to study the separation and reusability of the spent organobase catalyst.[1g] For comparison, the reaction was also carried out using 10 mol% NaOH in CTAB micellar solution (previously studied system for aldol reactions)[11]; the reaction in NaOH-CTAB micellar solution and even in neat condition resulted to very poor conversions (18% and 5%, respectively; Table 1; Entry 27 and 28). In the biphasic reaction using 2-PP organobase, the conversion was found to be decreased to 63% as compared to neat reaction using 2-PP (Table 1; Entry 20). The reduced conversion in biphasic reaction may be due to immiscibility of aqueous phase containing dissolved 2-PP and oil phase of reactants. In addition, the major concern was the reusability of spent 2-PP aqueous solution recovered by phase separation from reaction mass, which has been discussed in detail in section 3.3. The solvent free (neat) reaction using 2-PP base resulted to 84% conversion (Table 1; Entry 21). In the neat condition, 2-PP organobase would be completely soluble in the reaction mixture giving fairly good conversion, however, the recovery of 2-PP from the reaction mass is tedious and requires post reaction work up.

Table 1. Activity of various base catalysts for Knoevenagel condensation of salicylaldehyde and DEM in different reaction media.



Entry	Catalyst	Conv. (wt.%) of DEM	Selectivity (%) of	
			3-ethyl carboxylate coumarin	Un-substituted coumarin
1	NaOH-H_2O	72	98	02
2	NaOH-CTAB	81	99	01
3	KOH-H_2O	61	99	01
4	KOH-CTAB	69	99	01
5	$NaHCO_3$-H_2O	03	100	-
6	$NaHCO_3$-CTAB	12	100	-
7	Na_2CO_3-H2O	48	100	-
8	Na_2CO_3-CTAB	54	100	-
9	DBU-H_2O	52	99	01
10	DBU-CTAB	65	99	01
11	TBD-H_2O	54	99	01
12	TBD-CTAB	69	99	01
13	DBN-H_2O	55	99	01
14	DBN-CTAB	67	99	01
15	DABCO-H_2O	31	100	-
16	DABCO-CTAB	41	99	01
17	2-PP-H_2O	95	99	01
18	2-PP-CTAB	99	98	02
19	2-PP-SDS	99	97	03
20	2-PP-H_2O	63	99	01
21	2-PP (neat)	84	99	01
22	2-PP-CTAB	78	99	01
23	2-PP-SDS	92	99	01
24	2-PP-SDD	89	99	01
25	2-PP-SHD	86	99	01
26	2-PP-Tx-100	66	99	01
27	NaOH-CTAB	18	100	-
28	NaOH (neat)	05	100	-

Entry 1 to 19: 50 mol% base; Entry 20 to 28: 10 mol% base
CTAB: cetyltrimethyl ammonium bromide; SDS: sodium dodecyl sulfate; SDD: sodium dodecanoate ($C_{11}H_{23}COO^-Na^+$); SHD: sodium hexadecanoate ($C_{15}H_{31}COO^-Na^+$).

The reactions using 2-PP organobase in micellar solutions (CTAB, SDS, SDD, SHD, Tx-100; 15 mM) gave increased conversion (66% - 92%; Table 1; Entry 22 to 26) as compared to biphasic reaction. The 2-PP-anionic surfactant (SDS, SDD and SHD) solutions gave higher conversion (86% to 92%) as compared to 2-PP-cationic surfactant (CTAB; 78%) and non-ionic surfactant (Tx-100; 66%) solutions showing higher activity of 2-PP-anionic surfactant solutions. The surfactant molecules in aqueous medium would generate plenty of micelles as the used concentration (15 mM) of the surfactants was far above the critical micellar concentration (CMC) of all the surfactants. The micelles can facilitate the reactions in water by solubilizing the hydrophobic reactants creating huge water-oil (organic reactants) interface in the reaction medium.[7] The ionic micelles are helpful in the aqueous reactions as they accumulate the oppositely charged water soluble catalytic species at interface. The water soluble organobase reacts with water and gets converted into protonated base and OH^- ions as Brønsted base (Scheme 4). Thus the micelles can offer better interaction of water soluble species (protonated base and OH^- ions) and reactants giving enhanced conversion in micellar reactions. The selection of an appropriate surfactant is very important in 2-PP organobase catalysis in micellar media, which is clearly evident from the catalysis results (Table 1; Entry 22 to 26). The surfactant's nature (cationic/ anionic/ non-ionic) is playing crucial role in enhancement of catalytic activity of 2-PP-micellar system. It was anticipation that anionic micelles (SDS, SDD, SHD) might be solubilizing more number of positively charged protonated 2-PP species along with OH^- ion as compared to cationic micelles (CTAB) and therefore, 2-PP-anionic micellar systems showed higher activity. However, our investigations (discussed in the next section) showed that the co-catalytic activity of anionic surfactant (SDS) or surfactant-reactants interaction was greatly responsible for the promotion of the 2-PP catalyzed micellar reaction. As SDS showed highest improvement in 2-PP catalysis and has been widely employed as anionic surfactant in promotion of various catalytic reactions in

water,[15] we selected 2-PP-SDS system for detail investigation. The ionic surfactant's micelles play important role in micellar catalysis, especially when ionic species (catalyst and reaction intermediates) are involved in the reaction; therefore, for comparison 2-PP-CTAB micellar system was also studied.

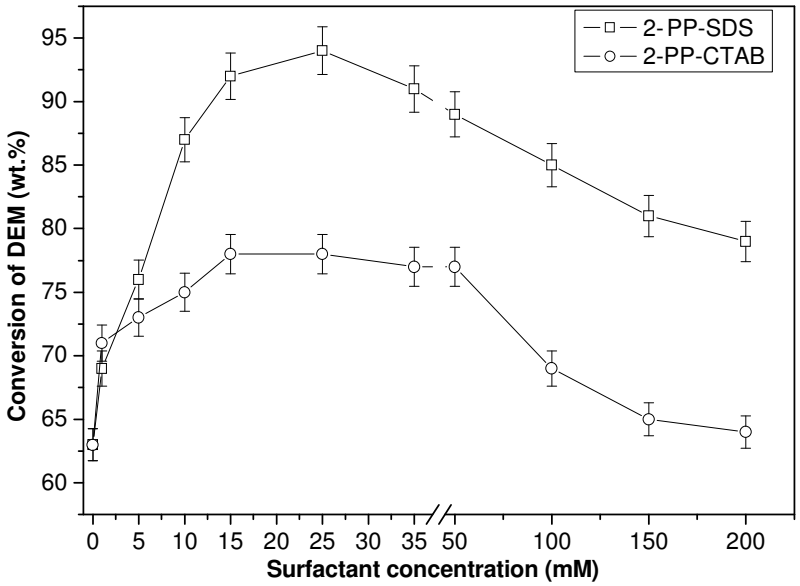


Figure 1. Conversion of DEM in reactions in 2-PP-SDS and 2-PP-CTAB micellar solutions of different surfactant concentrations [Reaction condition: 2.5 mmol salicylaldehyde, 2.5 mmol DEM, 10 mol% 2-PP organobase, 5 mL aqueous SDS/CTAB surfactant solution , 30°C, 6 h].

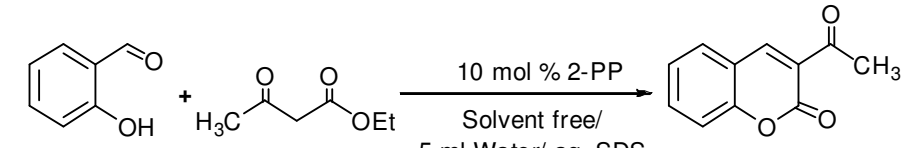
The reaction kinetics of Knoevenagel condensation of salicylaldehyde and DEM in 2-PP-SDS and 2-PP-CTAB micellar solutions at different surfactant concentrations (1 mM to 250 mM; Figure 1) also shows the highest activity of 2-PP-SDS system. All the conversion values reported in Figure 1 are within ±2% precision. Initially, the conversion of DEM increases with increase in the concentration of both the surfactants (from 1 mM) and highest conversion (94%) was obtained with 2-PP-SDS at 25 mM, and 2-PP-CTAB gave highest conversion (78%) at 15 mM. Further increase in the concentration of both the surfactants reduced the conversion of DEM. Thus, the optimum concentration of CTAB and SDS showing highest activity in the

reaction was found to be 15 mM and 25 mM, respectively. The gradual increase in conversion of DEM with CTAB/ SDS concentration up to their optimum concentrations (15 mM/ 25 mM) can be related to the increasing number of micelles in the solution solubilizing more reactants and 2-PP (in protonated form) molecules in the micelles. The significant increased conversion in SDS micellar solutions below CMC (1 mM and 5 mM; SDS CMC is 8 mM) as compared to biphasic reaction is possible with the help of surfactant molecules, presumably in the form of submicellar aggregates. In the SDS solutions below CMC, very likely there will be monomers and submicellar aggregates. This has been reported that in the micellar reactions at below CMC, a small number of surfactant monomers may aggregate with a substrate molecule to form a catalytic micelle (substrate-induced micellization), which contributes in promotion of the reaction.[16] The successive decrease in conversion of DEM with increasing SDS or CTAB concentration, above their optimum concentration (25 mM and 15 mM, respectively), may be attributed to dilution of 2-PP molecules in the micelles slowing down the reaction rate. In addition, the strong solubilization or binding of reactant(s) and/ or organobase molecules may also be one of the reasons for showing reduced conversion at high surfactant concentrations. In many micellar reactions, the decreased reaction rate at high surfactant concentration has been ascribed to dissolution/ strong binding of reactant molecules in the micelles.[16]

The 2-PP-SDS micellar system was also found to be effective in the synthesis of 3-acetyl coumarin by Knoevenagel condensation of salicylaldehyde with EAA to 3-acetyl coumarin in neat as well as in biphasic condition giving good conversion (93% and 90%, respectively, in 6 h) and almost complete conversion in SDS micellar solution (Table 2). The significantly higher conversion of EAA (90%) than DEM (63%) in even biphasic reaction can be attributed to higher reactivity of EAA than DEM. The pKa values of EAA and DEM in dimethyl sulfoxide (DMSO) are 14.4 and 16.4, respectively.[17] It means that EAA is slightly more acidic than DEM i.e., deprotonation of EAA with the help of base catalyst to form its carbanion (enolate; which reacts

with salicylaldehyde) would be easier than DEM, which might be making EAA more reactive in this reaction giving its faster conversion than DEM.

Table 2. Knoevenagel condensation of salicylaldehyde and EAA to 3-acetyl coumarin using 2-PP-SDS micellar solution.[a]



S. No.	Catalytic system	Conv. (wt.%) of EAA	Selectivity (%) of 3-acetyl coumarin
1	2-PP (neat)	93	100
2	2-PP-H_2O	90	100
3	2-PP-SDS	>99	100

The activity of other organobases (DBU, TBD, DBN and DABCO) were also examined for the reaction in aqueous SDS micellar solution (15 mM) using 10 mol% amount of organobases (Table 3). But the 2-PP-SDS system showed highest activity in the reaction giving highest conversion (92%). The room temperature (i.e., 30°C) and 10 mol% 2-PP base was found to be optimum reaction temperature and catalyst amount giving substantial conversion (94%) of DEM (**ESI; Table S2 and S3**).

Table 3. Catalytic activity of various bases in aqueous SDS micellar solution in Knoevenagel condensation of salicylaldehyde and DEM.[a]

Entry	Organobase-SDS system	Conv. (wt.%) of DEM	Selectivity (%) of	
			3-ethyl carboxylate coumarin	Unsubstituted coumarin
1	DBU-SDS	20	99	01
2	TBD-SDS	23	100	-
3	DBN-SDS	26	99	01
4	DABCO-SDS	18	99	01
5	2-PP-SDS	92	100	-

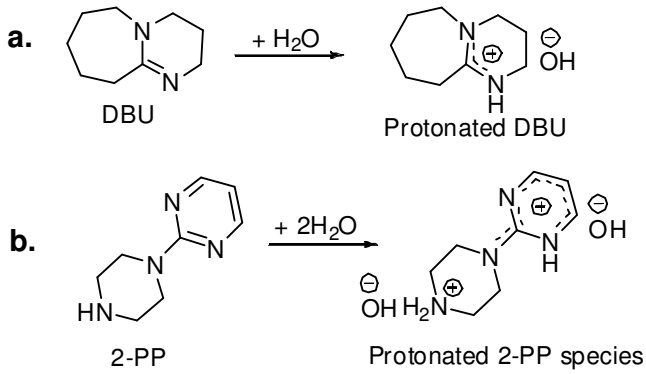
[a]2.5 mmol salicylaldehyde, 2.5 mmol DEM, 10 mol% base, 5 ml aq. SDS surfactant solution (15 mM), 30°C, 6 h.

Numerous acid and base catalysts (homogeneous as well as heterogeneous) have been reported for the Kneovenegal condensation of salicylaldehyde and its derivatives with active methylene compounds to synthesize 3-substituted coumarins.[18] The heterogeneous base catalysts such as metal hydroxides and mixed oxides are known to be best owing to their easy separation and reuse. However, the necessity of metal free processes, reusable catalyst, mild reaction conditions and solvent free or green solvent mediated synthesis are major issues for viable application of homogeneous and heterogeneous base catalysts. The solid acids and bases have been demonstrated to be excellent catalysts for Kneovenegal condensation to synthesize of 3-substituted coumarins owing to their advantageous features (easy separation and reusability), however, they require high temperature[18c-18h] and longer reaction time[18d,18f,18g,18i,18j]. The 2-PP-SDS micellar system was found to be comparable in activity for synthesis of 3-substituted coumarins under ambient condition. Furthermore, the 2-PP-SDS system offers a metal free and green catalytic route for synthesis of biologically active compounds. This study may further explore the wide application of the 2-PP-micellar system in base catalysis and in particular this catalytic system may be of great interest for the synthesis reactions reported with various organobases in homogeneous/ biphasic conditions,[1] inorganic base-surfactant micellar[11,19] and organobase-surfactant micellar solutions.[20]

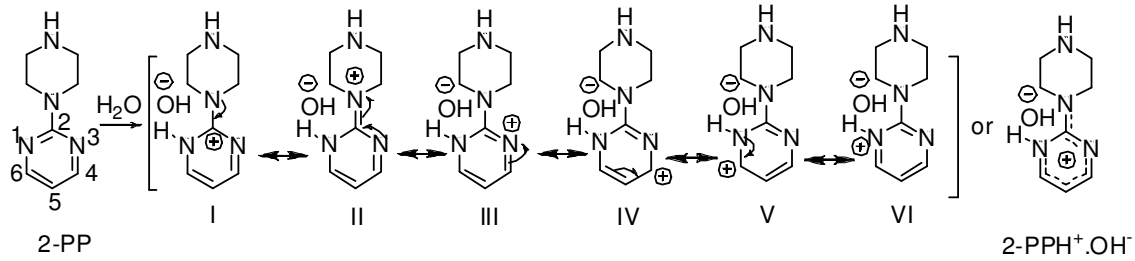
3.2. Role of surfactant's nature (SDS vs. CTAB) on activity of 2-PP-micellar system

The catalysis study (Table 1 and Figure 1) revealed the higher activity of 2-PP-SDS micellar system than 2-PP-CTAB. This result indicates that the nature of surfactant (cationic/ anionic) plays crucial role in promotion of 2-PP catalyzed reaction. Recently, it was shown by NMR studies of DBU-H_2O systems, that the nitrogen atom of DBU (Lewis base) gets protonated by water molecule forming a second resonance structure (positively charged protonated DBU species) with hydroxyl ion (Scheme 4a), which behaves like a Brønsted base catalyst.[1g]

Similarly, the 2-PP molecule (both aromatic guanidine moiety and piperazine secondary amino group) can also get protonated with water molecules in aqueous medium giving a positively charged protonated 2-PP species and associated hydroxyl ions (OH^-) Brønsted base (Scheme 4b). The protonation of 2-PP molecules in aqueous medium was revealed by comparing the ^1H NMR spectra of 2-PP in $CDCl_3$ and D_2O solvents (Figure 3; i & ii). In D_2O, the upfield shifting of the resonance signals for protons at 4^{th} and 6^{th} positions of pyrimidyl ring, the downfield shifting of the resonance signals for proton at 5^{th} position of pyrimidyl ring, and the upfield shifting of the resonance signals for all protons at piperazine ring are indication of protonation of pyrimidyl ring of 2-PP (Scheme 4b). The ^1H NMR results (Figure 3; i & ii) can be explained by using resonating structures of guanidine moiety of protonated 2-PP species given in Scheme 5: structures IV & V exhibit reduced π-electrons density at 4^{th} and 6^{th} positions of pyrimidyl ring of protonated 2-PP showing shielding (upfield shifting) of their protons; comparatively higher electron density over 5^{th} carbon of pyrimidyl ring will cause deshielding (downfield shifting) of its proton; and protonation of pyrimidyl ring or its dearomatization as well as protonation of piperazine secondary amino group would show shielding effect on all protons of piperazine ring causing upfield shifting. *Cota et al.*[1g] also observed in NMR studies of DBU-H_2O complexes that the protonation of DBU leads to a shielding of the carbon atoms directly linked to the basic nitrogen atom.



Scheme 4. Reaction of Lewis bases (a) DBU[1g] and (b) 2-PP with water forming their respective protonated species and hydroxyl ion.



Scheme 5. Resonating structures of guanidine moiety of protonated 2-PP species.

The comparative study on binding/ solubilization of procaine drug (amine.HCl salt) with SDS, CTAB and triton X-100 micelles[21] has demonstrated the higher binding affinity of procaine to SDS than CTAB and triton X-100 owing to the strong electrostatic and hydrophobic interactions between procaine molecules with SDS micelles. Therefore, it was anticipation that higher activity of 2-PP-SDS micellar solution should be related to higher binding/ solubilization of protonated 2-PP species in SDS micelles providing more OH^- ions in micellar phase for reaction. To understand the promotional effect of SDS in the micellar reaction, the solubilization behavior and interaction of both types of micelles (SDS and CTAB) for 2-PP and reactants were studied by using UV and ^1H NMR spectroscopic techniques.

3.2.1. Characterization of 2-PP organobase-surfactant solutions

The UV absorption spectra of 2-PP in CTAB and SDS solutions at different concentrations (Figure 2) clearly depict the solubilization/ association of 2-PP molecules in both the micellar

structures (cationic and anionic) showing gradual increase in the intensity and blue shift of the peak (for 2-PP; λ_{max}: 243 nm) with surfactant concentration.[22] The ^{1}H NMR study has been widely used for probing the solubilization and binding location of aromatic compounds in micelles by observing the aromatic ring induced changes in the chemical shifts of the surfactant.[23] We also observed the aromatic solute induced shift effect by solubilized 2-PP species on SDS and CTAB molecules showing upfield shifting of the signals for different protons of SDS and CTAB (**see ESI; Table S4** & **S5**), which indicates the inclusion of 2-PP species in SDS and CTAB micelles. For CTAB, the major shift for the alkyl chain protons occurs near the head group, whereas in SDS the protons around the middle of the chain are shifted significantly indicating deeper penetration of solubilizate in SDS micelles as compared to CTAB micelles. Our observation was in line of a previous reports[23b] showing the deeper penetration of even a charged solubilizate (i.e., 2-PP species) in SDS micelles. This behavior of SDS has been explained as bending of the alkyl chain of the surfactant toward the aromatic parts of the solubilizate.[23b]

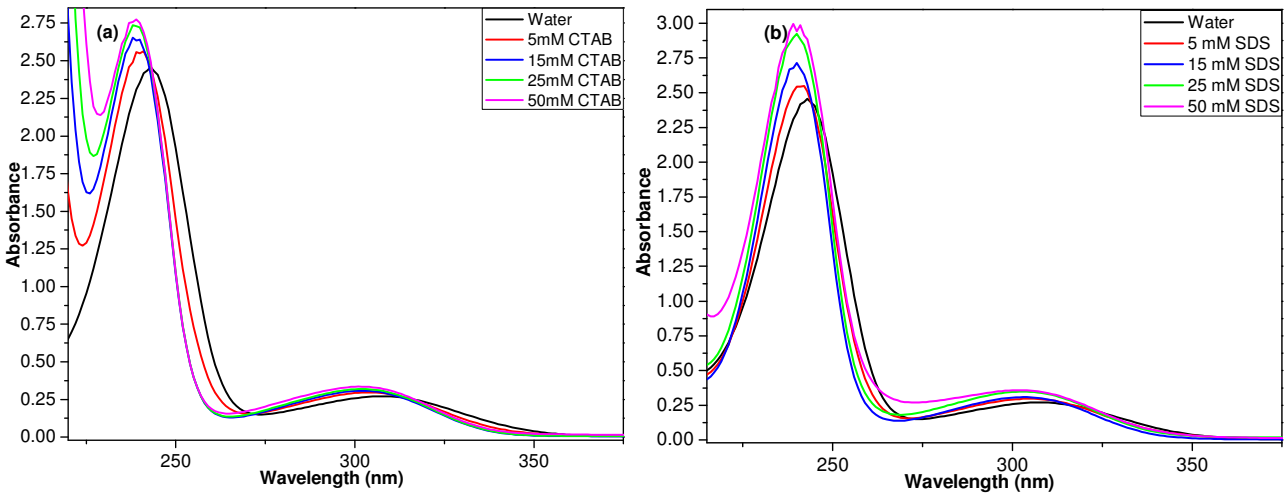


Figure 2. UV absorption spectra of 2-PP in aqueous solutions of (a) CTAB and (b) SDS micellar solutions at different concentrations (0, 5, 15, 25, 50 mM; 2-PP concentration: 0.18 mM).

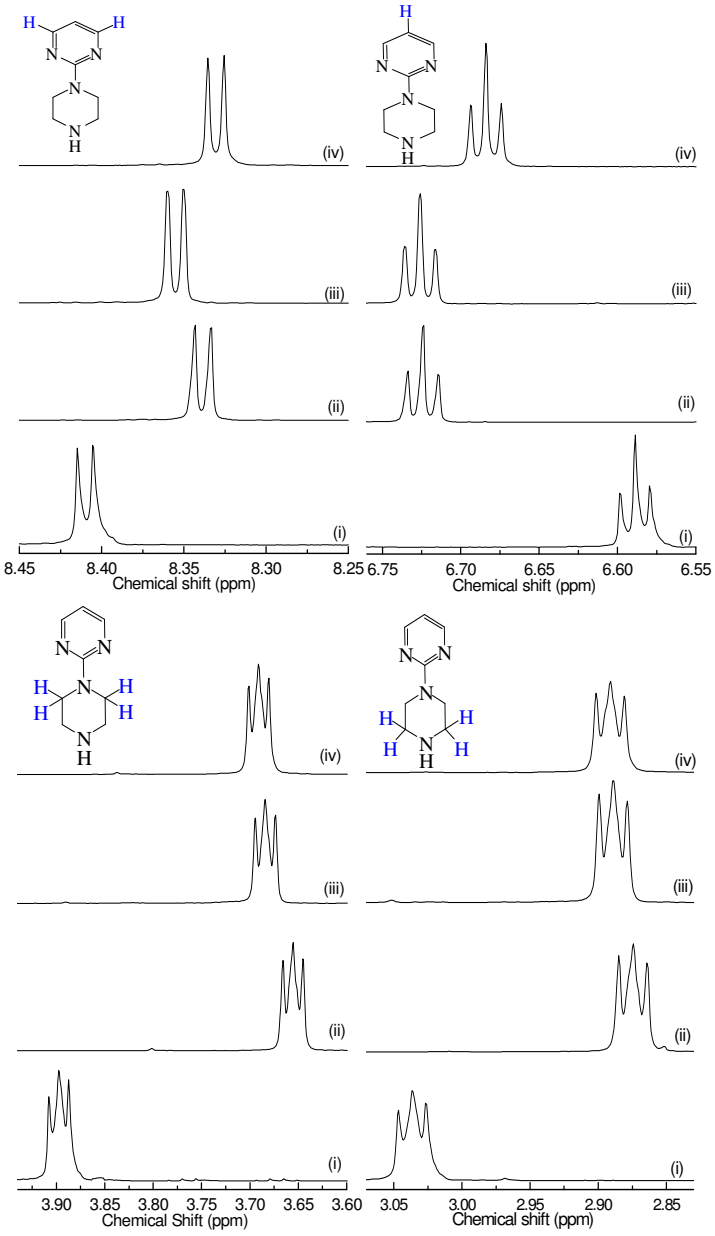
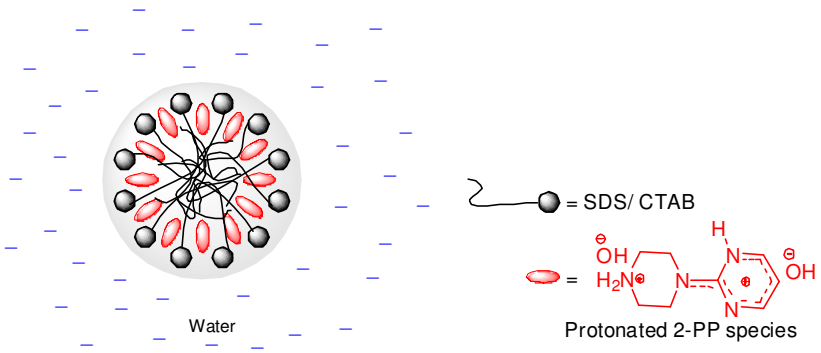


Figure 3. ^{1}H NMR chemical shifts of different protons of 2-PP in (i) $CDCl_3$, (ii) D_2O, (iii) 25 mM CTAB and (iv) 25 mM SDS aqueous solutions.

The solubilization of 2-PP in CTAB and SDS micelles as protonated 2-PP species is also evident from ^{1}H NMR spectrum of 2-PP in micellar solutions showing resemblance with the spectrum in D_2O (Figure 3; iii & iv). However, some spectral differences of 2-PP in micellar and D_2O

solutions can be seen, which are possibly due to presence of 2-PP species in micellar environment. In SDS solution, the slight upfield shifting of the signals for protons of pyrimidyl ring indicates orientation of pyrimidyl group towards core i.e., in non-polar environment, and the slight downfield shifting of the signals for protons of piperazine ring presents its projection towards micellar surface (i.e., polar/ ionic environment). The ^{1}H NMR results (Figure 3; iii & iv) also indicate stronger hydrophobic interaction of pyrimidyl group of 2-PP species with SDS alkyl chain relative to CTAB showing upfield shifting of pyrimidyl protons in SDS solution. The protonated 2-PP species can be localized in the SDS micelles by ionic interaction with sulfate head group of SDS molecules and hydrophobic interaction with surfactant alkyl group. In CTAB micelles, 2-PP species can reside interacting with CTAB head group through the lone pair of electrons of nitrogen atoms and by hydrophobic interaction.[23a] From UV and ^{1}H NMR studies, it can be concluded that 2-PP is solubilized in protonated form in the micelles of both cationic and anionic surfactants (CTAB and SDS) as shown in Scheme 6.

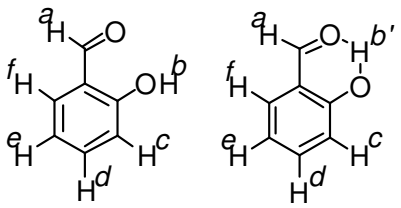


Scheme 6. Solubilization of protonated 2-PP species in SDS/ CTAB micelles.

3.2.2. Micellar solubilization and reactant(s)-surfactant interactions: Co-catalytic activity of SDS

From spectroscopic characterization of 2-PP-surfactant solutions, the role of SDS in 2-PP-SDS systems for promotion of the micellar reaction could not be rationalized as both micellar systems

exhibit excellent solubilization behavior for 2-PP as catalytically active species i.e., protonated 2-PP. In our previous study,[11a] we observed the co-catalytic activity of surfactant molecules (CTAB) in micelles to activate the reacting molecules by favorable surfactant-reactant interactions, which was found to be much supportive in the micellar reaction. In addition to monitoring micellar solubilization of reaction components, ^{1}H NMR can also be used for studying the reaction reactant(s)-surfactant interactions in micelles. The salicylaldehyde molecules may exist in two structural forms (SAL-I & SAL-II) depending upon the nature of environment (Scheme 7): in SAL-I, the phenolic –OH group is in intermolecular hydrogen bonding with solvent molecules (usually in a polar solvent) and in SAL-II, the phenolic –OH has intramolecular hydrogen bonding with aldehyde group within the molecule.[24] The ^{1}H NMR spectrum of salicylaldehyde in D_2O indicates the presence of SAL-I in surfactant free solution showing an intense resonance signal for proton ***b*** at 9.54 ppm (Figure 4i). A weak signal at ~5.4 ppm can be assigned for proton ***b′*** of phenolic –OH group indicating the presence of SAL-II in minor proportion. The signals for aromatic protons (***c***, ***d***, ***e*** and ***f*** protons) of salicylaldehyde can be seen in the range of 6.9 ppm to 7.8 ppm (4 signals; two doublets and two triplets; Figure 4i).



Scheme 7. Different types of protons in SAL-I and SAL-II forms of salicylaldehyde.

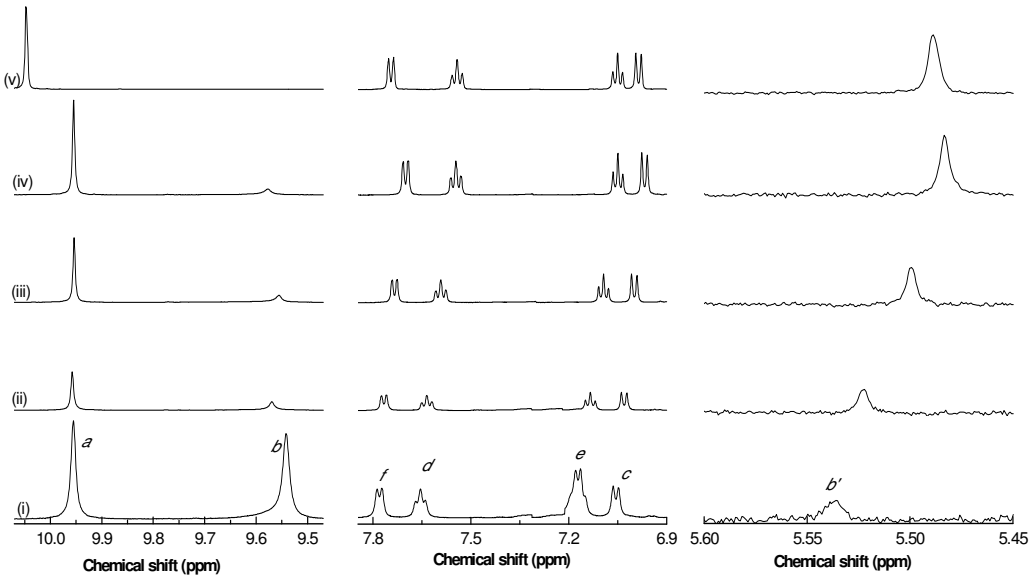


Figure 4. Chemical shifts for different protons of salicylaldehyde in D_2O and in CTAB solutions of different concentrations [i. D_2O, ii. 1 mM CTAB, iii. 25 mM CTAB, iv. 50 mM CTAB, v. 100 mM CTAB].

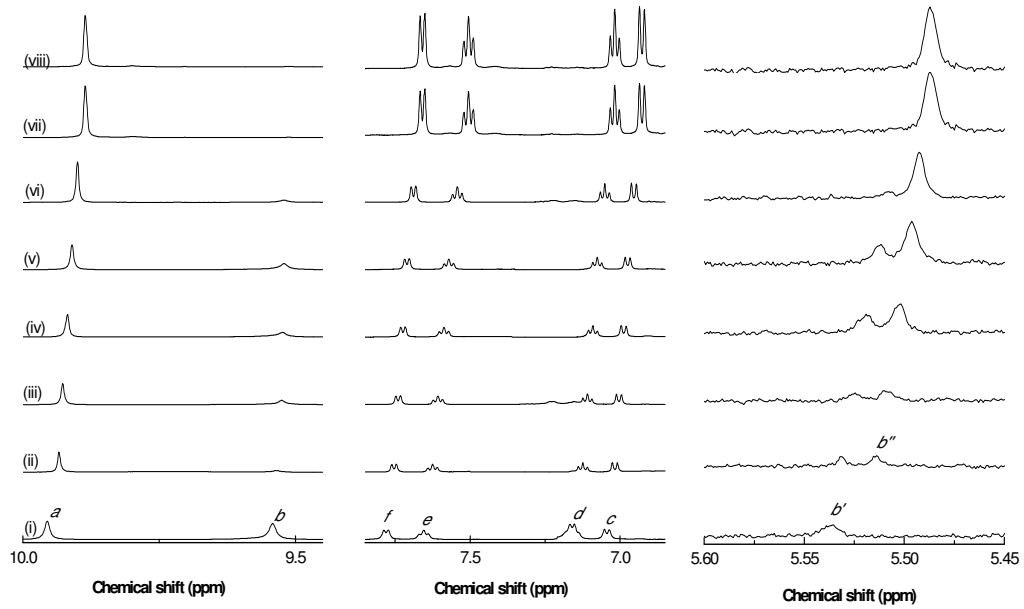


Figure 5. Chemical shifts for different protons of salicylaldehyde in D_2O and in SDS solutions of different concentrations [i. D_2O, ii. 1 mM SDS, iii. 5 mM SDS, iv. 10 mM SDS, v. 15 mM SDS, vi. 25 mM SDS, vii. 50 mM SDS, viii. 100 mM SDS].

The ^{1}H NMR spectra of pure SDS and CTAB in D_2O (25 mM) and their chemical shifts are given in ESI (**Figure S1** & **S2; Table S4-S7**). As compared to pure surfactants (SDS or CTAB; at 25 mM), there was upfield shifting for the protons of both the surfactants in the presence of reactants (**see ESI; Table S6** & **S7**), which is probably due to the hydrophobic effect and aromatic ring induced shifts effect of solubilized reactants.[23] This indicates the existence of solubilized reactants in CTAB and SDS micelles. However, the significantly higher upfield shifting for the protons around the middle of the chain of SDS (**see ESI; Table S6**) reveals the deeper penetration of reactant molecules (salicylaldehyde) in SDS micelles. The significant upfield shifting for the protons near the head group of CTAB indicates the presence of reactant molecules near the head group of CTAB micelles (**see ESI; Table S7**). The ^{1}H NMR spectra of salicylaldehyde in CTAB and SDS solutions (Figure 4 and 5) also show its solubilization and interaction in the micelles. The remarkable spectral changes and shifting of different signals for salicylaldehyde in even below CMC (Figure 5ii & 5iii) was noticed, which can be attributed to the formation of salicylaldehyde-surfactant combined aggregations. Brinchi et al. reported the acceleration of reactions in cationic surfactant solutions at or below CMC (in premicellar solutions) due to either complexation of the substrate with surfactant monomers or pre-micelles or to substrate induced formation of micelles.[16b] The gradual upfield shifting of the signals of salicylaldehyde (except ***a*** and ***b*** protons in CTAB solution) on increasing surfactant concentration is indication of salicylaldehyde solubilization in both CTAB and SDS micelles. The downfield shifting of signals ***a*** and ***b*** of salicylaldehyde with CTAB concentration may arise from ionic interaction of aldehydic and phenolic –OH groups of salicylaldehyde with CTAB head group.[11a] On increasing CTAB concentration, the resonance signal ***b*** was observed to be decreasing in intensity, which completely disappeared in 100 mM CTAB solution, and the signal ***b′*** increased in intensity with upfield shifting. These spectral changes can be related to the existence of salicylaldehyde molecules as SAL-II in CTAB micelles (hydrophobic core). In 100

mM CTAB solution, the significant downfield shifting of ***a*** and ***b′*** indicates the localization of salicylaldehyde molecules in polar part of micelles, i.e., Stern layer, interacting with CTAB head group through of carbonyl group.[11a] The gradual upfield shifting of signals for different protons (***b′***, ***c***, ***d***, ***e*** and ***f***) in CTAB solutions with 1-50 mM concentration and then downfield shifting (which is more significant for aldehydic proton) at 100 mM represents the movement of salicylaldehyde molecules from core of micellar phase to micellar surface and its localization at micellar surface (Stern layer) at high surfactant concentration. In our previous study,[11a] we proposed the localization of aldehyde molecules (benzaldehyde) at interface/ in Stern layer of micellar phase in CTAB solution at high concentrations due to elongation of micelles and the ionic interaction between aldehyde group and CTAB head group. In SDS solution, some significant spectral changes such as disappearance of the signal ***b***, and appearance of the signal ***b′*** and a new signal ***b″*** on increasing SDS concentration was observed (Figure 5). The new upfield resonance signal ***b″*** might have originated due to interaction of ***b′*** type proton of phenolic –OH group of solubilized salicylaldehyde molecules with SDS head group (through sulfate ion group) as shown in Scheme 8. The ***b″*** type proton, interacting with sulfate group of SDS would resonate at higher frequency due to shielding effect of electron rich (negatively charged) sulfate group.

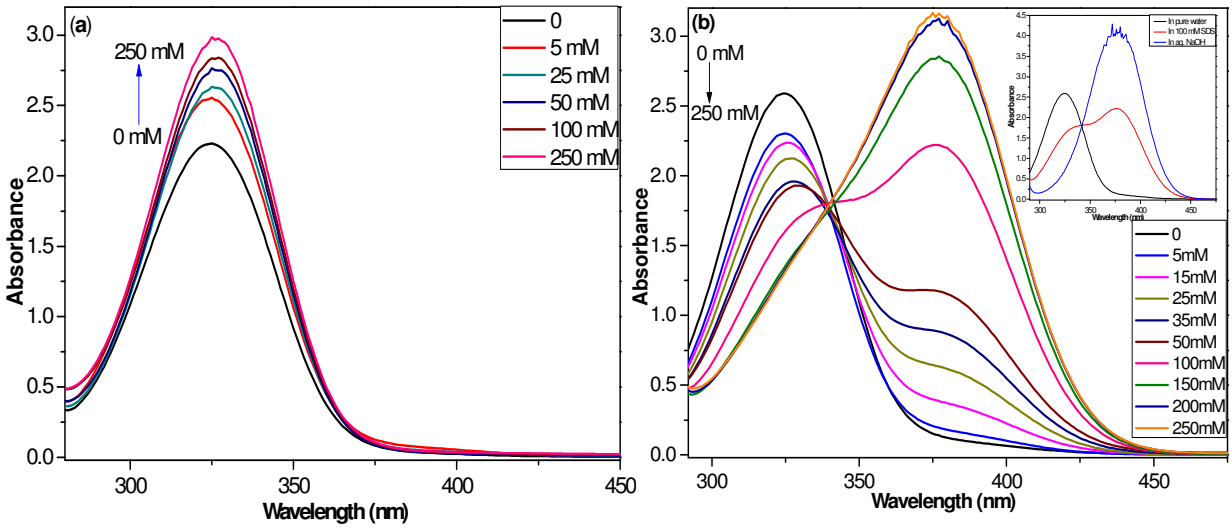
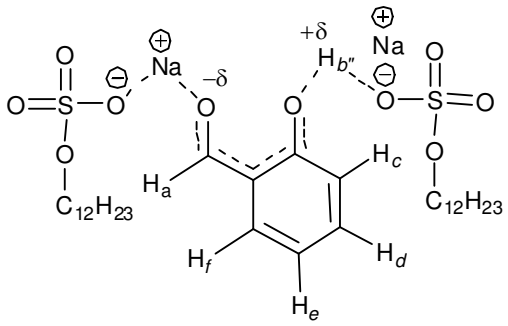


Figure 6. UV absorption spectra of salicylaldehyde in (a) CTAB and (b) SDS solutions (inset: UV absorption spectra of salicylaldehyde in pure water, 100 mM SDS and 0.5 M NaOH aqueous solutions; salicylaldehyde concentration: 0.8 mM).

The UV absorption spectra of salicylaldehyde in CTAB solutions (Figure 6a) indicate its solubilization (localization) in micellar phase showing gradual increase in the peak intensity (~324.5 nm) with surfactant concentration. Interestingly, the spectra of salicylaldehyde in SDS solutions (Figure 6b) showed an additional band at higher wave length (~376.5 nm) on increasing the surfactant concentration. This result supports ^{1}H NMR result showing the interaction of salicylaldehyde molecules solubilized in micelles with SDS molecules. The new band was presumed to be originated from the interaction of salicylaldehyde through its hydroxyl (–OH group) hydrogen atom with head group of SDS molecules forming a phenolate type species as shown in Scheme 8. This was confirmed from the presence of a similar band (at ~376.5 nm) in UV spectrum of salicylaldehyde in aqueous NaOH solution (0.5 M) (Figure 6b; inset), which will have phenolate ion (sodium phenolate) of salicylaldehyde. The phenolate ion of salicylaldehyde can have electronic transition at significantly lower wave length. It was observed that the salicylaldehyde-SDS solution (150-250 mM) resembles the color (yellow) of aqueous NaOH solution of salicylaldehyde and the color intensity gradually increases as SDS

concentration increases from 1 mM to 250 mM (Figure 7). From the spectroscopy studies, it can be concluded that salicylaldehyde molecules are simply solubilized (as SAL-II) in CTAB micelles, and in SDS micelles salicylaldehyde molecules are solubilized as their phenolate species (Scheme 8) interacting with SDS head group.



Scheme 8. Interactions between salicylaldehyde and SDS molecules in SDS micellar solution.

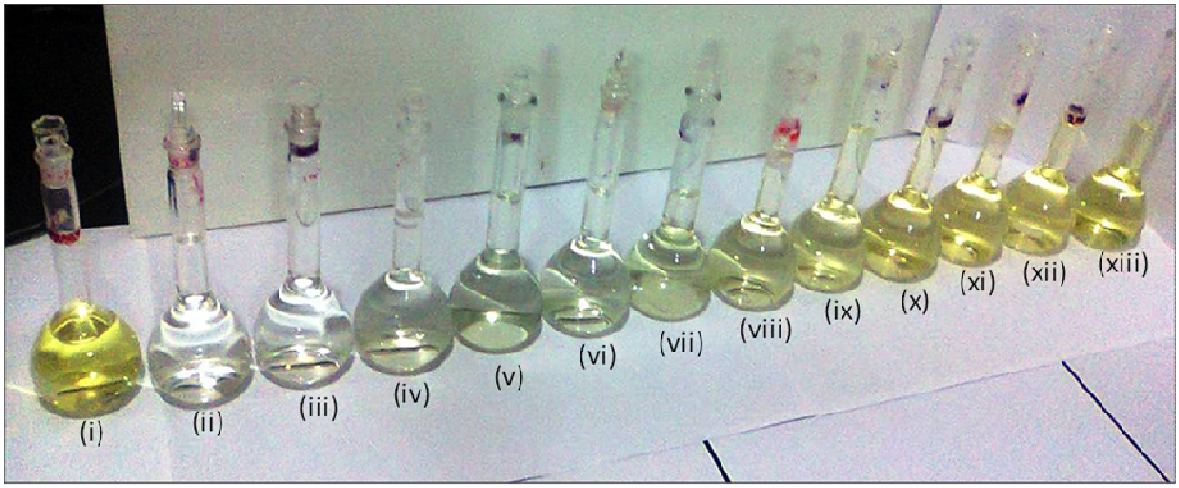


Figure 7. Color of different solutions of salicylaldehyde in (i) aqueous NaOH, (ii) pure water, (iii) 1 mM SDS, (iv) 5 mM SDS, (v) 10 mM SDS, (vi) 15 mM SDS, (vii) 25 mM SDS, (viii) 35 mM SDS, (ix) 50 mM SDS, (x) 100 mM SDS, (xi) 150 mM SDS, (xii) 200 mM SDS and (xiii) 250 mM SDS [salicylaldehyde concentration in all the solutions was 0.8 mM].

Similarly, ^{1}H NMR spectra of DEM in CTAB and SDS solutions revealed its solubilization in both CTAB and SDS micelles showing upfield shifting of resonance signals for different protons of DEM (Figure 8 and 9). The slight shifting of different signals for DEM in dilute SDS micellar solutions (below CMC; 9ii & 9iii) can be attributed to the formation of DEM-surfactant combined micellar aggregates. Interestingly SDS micelles showed strong influence over solubilized DEM; the signals for methylene protons (-CH_2-) of DEM were disappeared in spectra on increasing SDS concentration (Figure 9). The disappearance of the signals for methylene protons could be possible due to interaction of methylene protons (being acidic in nature) of DEM with SDS head group (sulfate ion) of SDS molecules in micelles (Scheme 9), which might have exchanged by deuterium ions in the D_2O solution. Similar results were also obtained with EAA; the disappearance of its methylene protons in SDS solutions with increasing concentration (**see ESI, Figure S3**). The disappearance of the methylene protons of both the methylene active compounds was also observed in ^{1}H NMR spectra of DEM and EAA in the sodium sulfate solution (25 mM in D_2O; **see ESI, Figure S4**) proving that the sulfate group of SDS is the site for the interaction with methylene protons.

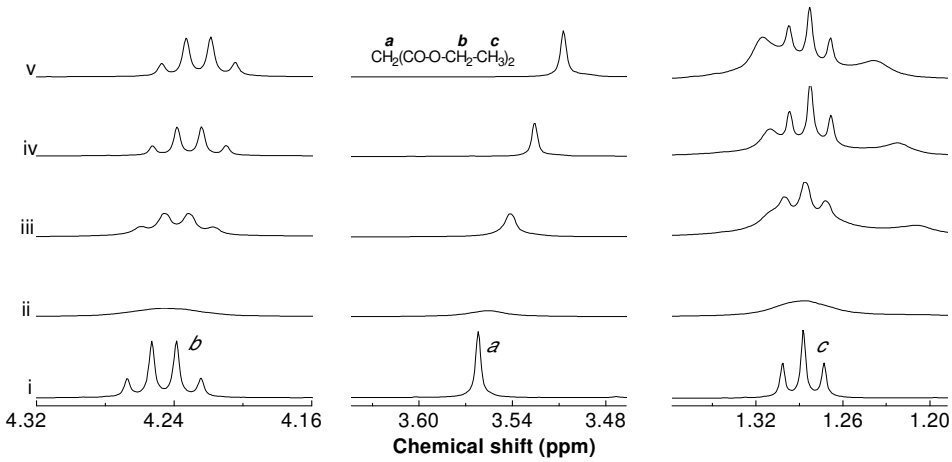


Figure 8. Chemical shifts for different protons of DEM in D_2O and in CTAB solutions of different concentrations (i. D_2O, ii. 1 mM CTAB, iii. 25 mM CTAB, iv. 50 mM CTAB, v. 100 mM CTAB).

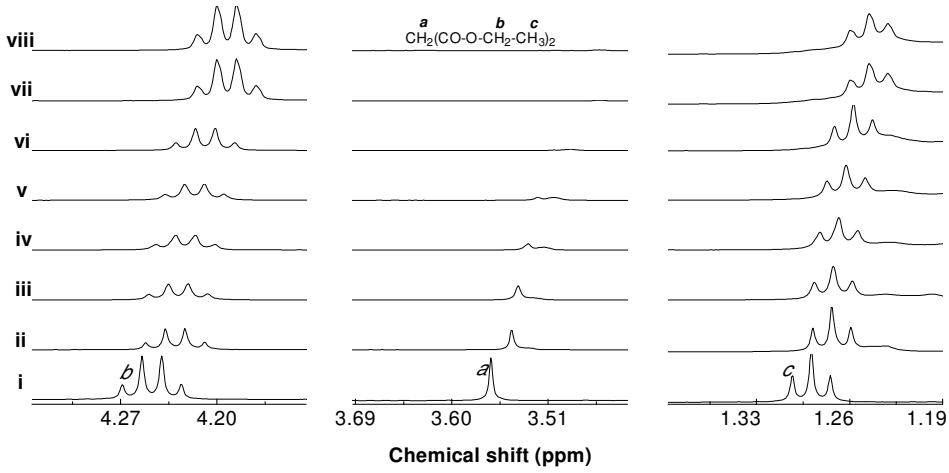
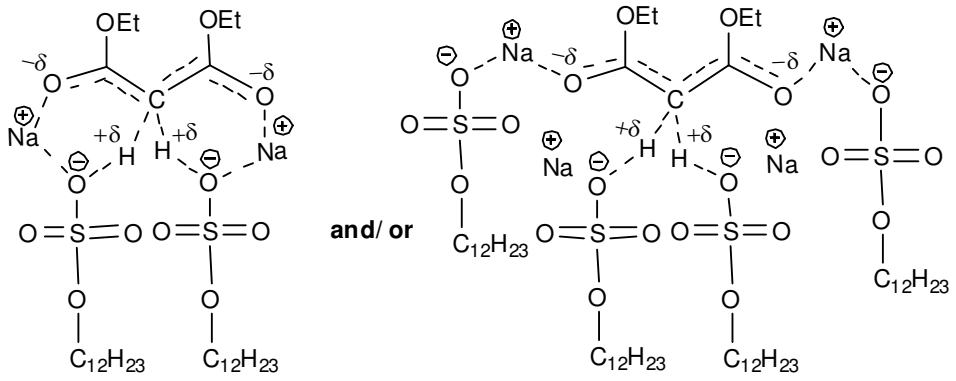


Figure 9. ^{1}H NMR spectra of DEM in D_2O and in SDS solutions of different concentrations [(i) D_2O, (ii) 1 mM SDS, (iii) 5 mM SDS, (iv) 10 mM SDS, (v) 15 mM SDS, (vi) 25 mM SDS, (vii) 50 mM SDS, (viii) 100 mM SDS].



Scheme 9. Interactions of DEM molecule with SDS molecules in SDS micellar solution.

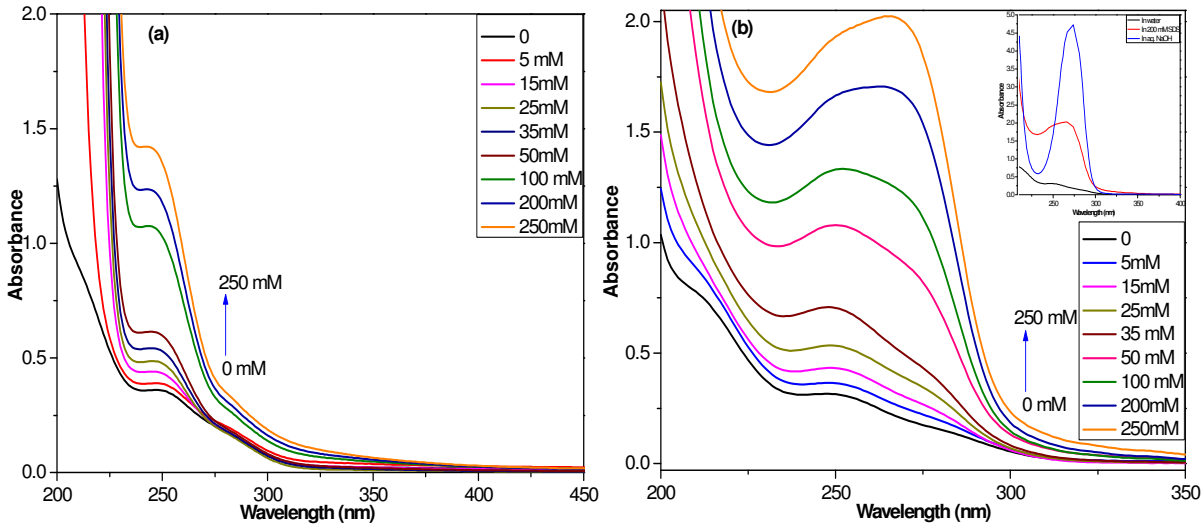


Figure 10. UV absorption spectra of EAA in (a) CTAB and (b) SDS solutions (inset: spectra of EAA in pure water, 200 mM SDS and 0.5 M NaOH aqueous solutions; DEM concentration: 2.4 mM).

The UV absorption spectra of EAA (Figure 10; EAA was used because of its better UV absorbance than DEM) confirms its solubilization in both types of micelles but strong interaction with SDS micelles showing emergence of an additional broad band at higher wave length with surfactant concentration. The interaction of the methylene group of EAA with SDS head group (Scheme 9) will result to their enolate type species bonded (by ionic interaction) with SDS molecules, which will cause the electronic transition at higher wave length. This was confirmed by analyzing EAA in aqueous NaOH solution, which would form sodium salt of its enolate ion.[25] The UV absorption spectrum of this solution exhibits almost a similar band (Figure 10b; inset) as there was a new band in the spectrum of EAA-SDS solution indicating the possibility of the formation of enolate species in SDS solution as a result of the interaction.

From the ^{1}H NMR and UV spectroscopy studies of catalyst-micellar and reactants-micellar solutions, it was found that both 2-PP-SDS and 2-PP-CTAB micellar systems contain solubilized 2-PP species (**protonated form**) and both the reactant molecules (salicylaldehyde

and DEM/ EAA) are solubilized in both CTAB and SDS micellar structures. However, SDS micelles solubilize both the reactants in their active forms (i.e., as phenolate of salicylaldehyde and enolate of DEM/ EAA) required for the reaction. The **hydroxyl ions of protonated 2-PP species** solubilized in SDS micelles can easily remove the protons from thus solubilized salicylaldehyde and DEM/ EAA molecules to produce phenolate and enolate reaction intermediates, respectively. The phenolate and enolate intermediates react (aldol condensation followed by transesterification) to form 3-substituted coumarin product. The solubilization of reactant molecules by SDS micelles in their active forms is the major cause for higher activity of 2-PP-SDS micellar system than 2-PP-CTAB in this reaction. Thus, we found that in addition to solubilization of the reactants and catalyst by SDS micelles, SDS molecules in micelles also show co-catalytic activity to facilitate the reaction. The present study also discloses that SDS micellar solution can be explored as an effective reaction medium for activation of phenolic substrates and methylene active compounds in many reactions.

In our previous studies on NaOH-CTAB catalytic systems,[11a,11c] the activity of NaOH-CTAB micellar solutions (i.e., substrate conversion) was observed to be increasing with surfactant concentration (even up to 200 mM) and the highest activity was achieved at high surfactant concentration (~150 mM) and with equivalent moles of NaOH. With 2-PP-SDS or 2-PP-CTAB, the highest activity was observed at comparatively lesser surfactant concentration (25 mM and 15 mM, respectively; Figure 1) and at 10 mol% amount of 2-PP base. Above the optimum surfactant concentration, the activity of 2-PP-micellar solutions decreases with surfactant concentration (Figure 1), which may be due to decreased concentration of solubilized 2-PP species in the micelles and/ or strong binding of 2-PP species and reactants in the micelles. Contrary to 2-PP-SDS or 2-PP-CTAB, NaOH-CTAB system has free OH^- ions on the micellar surface, which can be exchanged from one micelle to other micelle, and thus on increasing the number of micelles (i.e., surfactant concentration) new micelles do not have deficiency of

surface OH^- ions showing no decrease in the activity at high surfactant concentration. Better performance of 2-PP-SDS micellar system as compared to NaOH-CTAB micellar system at the same loading of both bases (10 mol%; Table 1: Entry 23 and 27) can be attributed to the localized concentration of 2-PP species in the micelles, where solubilized reactants can easily approach the catalytic species (OH^- ions). In NaOH-CTAB system, the OH^- ions are concentrated near the positively charged micellar surface, which are continuously exchanged with Br^- ions. At less loading of NaOH, there would be comparatively lesser availability of OH^- ions near micellar surface in NaOH-CTAB system showing reduced activity in the reaction. In conclusion, the 2-PP-SDS system is an efficient catalyst in comparison to NaOH-CTAB showing better activity at catalytic amount of base (10 mol% 2-PP) and at lower surfactant concentration.

3.3. Reusability of spent 2-PP-SDS micellar solution

We observed that in the reactions carried out using 2-PP-SDS solution (10 mol% 2-PP & 15 mM SDS), after completion of reaction the product was completely crystallized out and settled at the bottom of solution giving transparent aqueous phase (Figure 11). The product crystals were separated by filtration and were re-crystallized from methanol giving 90% yield of 3-ethyl carboxylate coumarin. The spent 2-PP-SDS solution obtained after filtration of product crystals was reused for consecutive three reaction cycles. There was gradual decrease in conversion of DEM from 92% to 78% after third reaction cycle, while the selectivity remained unaffected (Table 4). The possible reason for the decrease in conversion may be due to either presence of unreacted reactants as well as co-products (water and ethanol produced in the reaction) from previous reaction or loss of 2-PP and/ or surfactant (SDS) during product separation. The spent 2-PP-SDS micellar solution was extracted with ethyl acetate after diluting diluted with excess of saturated NaCl solution with water and the organic phase was analyzed by GC, which did not

show any peak for product showing the complete crystallization of product from micellar solution.

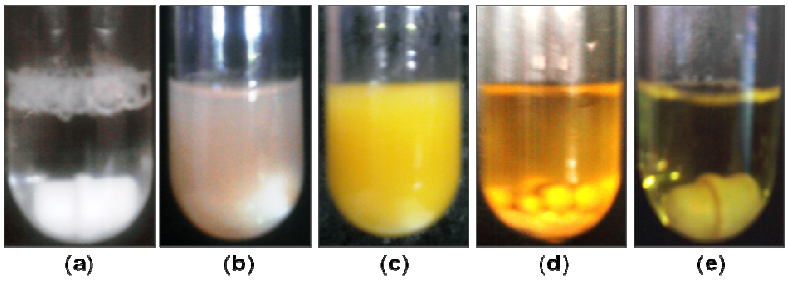


Figure 11. Aqueous SDS (25 mM) solution (a) before addition of reactants and 2-PP, (b) after addition of reactants, (c) after addition of reactants and 2-PP, (d) after reaction (products settled down at the bottom), (e) spent aqueous SDS (25 mM) solution after separation of product by filtration.

Table 4. Reuse study of spent 2-PP-SDS micellar solution.[a]

Reaction cycle	Conversion (wt.%) of DEM	Selectivity (%) of 3-substituted coumarin
Fresh	92	99
1st	85	99
2nd	80	99
3rd	78	99

[a]2.5 mmol salicylaldehyde, 2.5 mmol DEM, 10 mol% 2-PP, 5 ml aq. SDS surfactant solution (15 mM), 30°C, 6 h.

In solvent free (neat) reaction, the reaction mass was in slurry form after completion of reaction. The product could not properly crystallize out probably due to solubility of product in the reaction mixture containing unreacted reactants, dissolved 2-PP and co-products (water and ethanol). The separation of product and 2-PP from this reaction mixture requires post reaction work up using water and ethyl acetate, and so recovery of 2-PP for reuse application becomes tedious. Similarly, in biphasic reaction mixture, the product remains dissolved in organic phase.

The aqueous phase (which contains dissolved 2-PP base) of biphasic reaction could be removed by phase separation. But when this spent aqueous 2-PP solution was reused in next reaction cycle, there was significant decrease in conversion (22%) in first cycle. The decreased conversion was found to be attributed to loss of 2-PP due to partitioning of 2-PP from aqueous phase to oil phase (reactants & product). This was confirmed by GC analysis of the separated organic phase showing presence of 2-PP in significant amount. This shows that the reuse of 2-PP from biphasic reaction by simple removal of aqueous phase is not possible. Cota *et al.*[1g] demonstrated the recovery and reusability of the DBU-H_2O system in the synthesis of jasminaldehyde by removing the aqueous phase containing DBU from the organic reaction mass by phase separation. However, in present work, we could not completely recover 2-PP in aqueous phase (in biphasic reaction); this may be because of more hydrophobic nature of 2-PP molecules partitioning into the organic phase. The reaction of DEM or EAA under biphasic condition seems to be happening in oil phase with the help of 2-PP partitioned from aqueous phase and not under biphasic condition, which is also evident from their substantial conversion in 6 h reaction time (Table 1 & 2). From application point of view, we need a simple method for recovery of 2-PP for reuse, which could be possible with 2-PP-SDS micellar solution. The aqueous micellar solution may not be solubilizing the product and seems to be better medium for product crystallization. The solubilization of 2-PP species by SDS micelles and complete crystallization and easy separation of the product from micellar solution minimize the loss of 2-PP. This is the most advantageous feature of micellar catalytic systems that the reaction product, being insoluble in aqueous micellar medium, either separates out as an oil phase on the top of the solution[11c] or settle down as crystals at the bottom.[11a,11b] Thus the product separation from the micellar solution becomes very easy.

4. Conclusions

The catalytic activity of various aqueous organobase-surfactant micellar systems was evaluated by using Knoevenagel condensation of salicylaldehyde with active methylene compounds to 3-substituted coumarin as model reaction. The 1-(2-pyrimidyl) piperazine (2-PP) was found to be highest in activity as compared to previously reported organobases and its activity was further improved in SDS micellar solution. The SDS micelles solubilize 2-PP organobase and reactants in their active forms for the reaction and SDS molecules show co-catalytic activity. The 2-PP-SDS micellar system can be conveniently recovered after reaction by phase separation for reuse in subsequent reaction cycles. The 2-PP-SDS micellar catalytic system can offer a green, alkali/ metal free and efficient base catalysis processes for the syntheses of bioactive compounds.

Acknowledgement

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Graphical abstract

Organobase catalysis using 1-(2-pyrimidyl) piperazine in micellar medium: An approach for better performance and reusability of organobase

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An efficient and reusable organobase-surfactant micellar catalytic system was formulated for alkali/ metal free base catalysis. The 1-(2-pyrimidyl) piperazine (2-PP) base solubilized in SDS micellar system was demonstrated to be higher in activity as compared to neat/ biphasic/ cationic micellar system for Knoevenagel condensation to synthesize 3-substituted coumarins.