

## Research Article

# Acid Hydrolysis of Bromazepam Catalyzed by Micelles, Reverse Micelles, and Microemulsions

Ferdousi Begum,<sup>1</sup> M. Yousuf A. Mollah,<sup>1</sup>  
M. Muhibur Rahman,<sup>2</sup> and Md. Abu Bin Hasan Susan<sup>1</sup>

<sup>1</sup>Department of Chemistry, University of Dhaka, Dhaka 1000, Bangladesh

<sup>2</sup>University Grants Commission of Bangladesh, 29/1 Agargaon, Dhaka 1207, Bangladesh

Correspondence should be addressed to Md. Abu Bin Hasan Susan; [susan@du.ac.bd](mailto:susan@du.ac.bd)

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Kinetics of the acid hydrolysis of bromazepam (Bz) has been investigated in micelles, reverse micelles, and microemulsions of cetyltrimethylammonium bromide (CTAB) by spectrophotometric method. The rate of the acid hydrolysis of Bz was found to be enhanced both below and above the critical micelle concentration (CMC) of CTAB in aqueous solution. The pseudo-first-order rate constant ( $k'$ ) shows an initial decrease for both low and high  $H^+$  concentrations. With further increase in [CTAB], at low  $[H^+]$ , the  $k'$  attains an almost constant value, while, at high  $[H^+]$ , the  $k'$  passes through a maximum and then decreases. The kinetic data for catalysis by micelles of CTAB was interpreted with the pseudophase ion exchange (PIE) model. In CTAB/cyclohexane/1-butanol/water microemulsions, as the water to surfactant ratio ( $w_o$ ) increases, the physicochemical properties and droplet sizes of microemulsions significantly change and distinct changes in reaction environment can be marked. The rate of the hydrolysis reaction exhibits excellent correlation with the physicochemical properties and droplet sizes of the microemulsions and reverse micelles of CTAB. At  $[H^+] = 0.001$  M, in reverse micelles and microemulsions of CTAB, the  $k'$  of the acid hydrolysis of Bz decreases sharply followed by a slight increase with increasing  $w_o$ .

## 1. Introduction

Supramolecular self-assembly, in other words, self-organization, is the spontaneous and reversible association of two or more components under equilibrium conditions into stable, structurally well-defined aggregates joined by noncovalent bonds [1]. A wide variety of nanometer or micrometer scale structures and assemblies have been generated, including micelles [2], microemulsions [2], and vesicles [3, 4]. These organizations from molecular self-assemblies to controllable architectures and materials with advanced functions may meet the requirement of many objectives in science and technology such as catalysis of chemical reactions, sensors, and electronic and electromechanical devices [5–10]. The rate of a chemical reaction significantly changes in supramolecular self-organized media, specifically in surfactant-based organized media involving hydrophobic interactions, such as micelles, reverse micelles, and microemulsions. This has

resulted in a surge of interest in the kinetics of reactions involving different substrates solubilized in such organized media with a view to the fundamental understanding of the mechanism of reaction in different environments for their potential applications.

Research to date includes numerous attempts to explore the catalysis of hydrolysis reactions by supramolecular self-assembled systems such as micelles, reverse micelles, and microemulsions using a wide variety of substrates, including esters [11, 12], dyes [13–20], and drugs [11, 21–35]. Bromazepam (Bz) is used as a psychotropic drug which undergoes acid/base hydrolysis in aqueous solution and study of this reaction, within the physiological pH range, is of great importance because the absorption of these drugs in the gastrointestinal tract is affected by the nature of the chemical species involved.

Sodium decyl (SdeS), dodecyl (SDS), and tetradecyl (STS) sulfate have been reported to produce an inhibitory

effect in the kinetics of the acid hydrolysis of aqueous diazepam, bromazepam, and flunitrazepam drugs, while negligible effects were observed in the cases of polyoxyethylene-23-dodecanol and cetyltrimethylammonium bromide (CTAB) [24]. The presence of *N*-cetyl-*N*-ethyl-*N,N*-dimethylammonium bromide has been found to cause inhibition of the basic hydrolysis of triflusal [25]. The hexadecylphosphocholine micelles inhibit the basic hydrolysis of the indomethacin and acemetacin [26]. The presence of CTAB micelles enhances the rate of alkaline hydrolysis of penicillin [27]. The rate-[surfactant] profiles for the hydrolysis of indomethacin show rate inhibition in the presence of SDS and rate enhancement in the presence of CTAB [28]. At pH 13, curcumin undergoes rapid degradation by alkaline hydrolysis in the SDS micelles whereas it is greatly suppressed in the presence of either CTAB or dodecyltrimethylammonium bromide micelle [29]. The effect of cationic surfactants with varying hydrophobic chains and with different head groups and anionic surfactant (SDS) on the rate of alkaline hydrolysis of the carsalam and its *N*-substituted derivatives have been investigated by Al-Ayed et al. [30]. The plots of observed rate constant ( $k_{\text{obs}}$ ) versus [surfactants] for degradation of indomethacin under alkaline condition were curved with negative slopes for ethoxylated lanolin, polysorbate 80; but, with the cetrimonium bromide, the plots showed a marked positive change in  $k_{\text{obs}}$  as the [surfactant] passed through the CMC [31]. The intramolecular degradation of Cephaclo was catalyzed 25-fold by micelles of CTAB [32]. The rate of the hydrolysis of isatin and its derivatives of different hydrophobicities increased on increasing the [cetyltrimethylammonium chloride] and, after reaching a maximum, it started decreasing; conversely, micelles of SDS inhibited the rate of hydrolysis of isatin and its derivatives [33]. Cationic micelles enhanced the rate of alkaline hydrolysis of acetylsalicylic acid and triflusal at low surfactant concentrations, although inhibited the reactions at high surfactant concentrations, while anionic micelles show a catalytic effect and zwitterionic and nonionic micelles show inhibitory effect at all concentrations [34]. The basic hydrolysis of carbofuran was catalyzed in the presence of colloidal aggregates with positive surface charge and large inhibition by anionic and nonionic surfactants [35].

In spite of numerous studies, there have been no reports on the investigation of the kinetics of the acid hydrolysis of Bz in reverse micelles and microemulsions. To understand the mechanism of this reaction under different reaction environments, microemulsion may serve as a very potential medium and kinetic studies need to be systematically and intensively conducted for its exploration. In the present work, we investigated the kinetics of the acid hydrolysis of Bz in absence and presence of micelles, reverse micelles, and microemulsions of CTAB and the kinetic results in these different media have been compared with those in aqueous solution. In addition, kinetic profile for the reaction catalyzed by CTAB was treated quantitatively by pseudophase ion exchange (PIE) model. We have also studied the physicochemical properties and droplet sizes of reverse micelles and microemulsions of CTAB and correlated the physicochemical properties and *Z*-average diameters with kinetic results of the acid hydrolysis of Bz.

## 2. Materials and Methods

**2.1. Reagents.** Bromazepam (generously received from ACI Limited), cetyltrimethylammonium bromide (CTAB) (E. Merck), 1-butanol (Merck), cyclohexane (Merck), sodium hydroxide (NaOH), and hydrochloric acid (HCl) solution were each reagent grade material and used as received without further purification.

**2.2. Preparation of Microemulsions and Reverse Micelles of CTAB.** The CTAB/1-butanol/cyclohexane/water microemulsions were prepared at fixed CTAB (20% wt.) and cyclohexane (0 and 3.4% wt.) with different water and 1-butanol contents that ranged from high water to high alcohol content using deionized double distilled water following the procedure reported earlier [36].

**2.3. Apparatus.** Kinetic measurements and spectral analysis were carried out in a double beam Shimadzu UV-visible spectrophotometer model UV1650C (equipped with a thermoregulated cell compartment) and a rectangular quartz cell of path length 1 cm was used throughout the investigation. The reproducibility of the results in all cases has been checked through replicate measurements. The results, reproducible in the range of  $\pm 1\%$ , were only used for kinetic profiles. Specific conductivities, viscosities, and refractive indices of different CTAB microemulsions and reverse micelles were measured with a Jenway 4510 conductivity meter (equipped with a dip-type precalibrated cell), AntonPaar-Lovis 2000 M/ME microviscosimeter (measure viscosity by rolling ball principle with an accuracy of  $\pm 10^{-6}$  mPa s), and Abbemat 300 refractometer (high resolution optical sensor), respectively. The *Z*-average diameters of different CTAB microemulsions and reverse micelles droplets were measured using a Zetasizer Nano ZS90 (ZEN3690, Malvern Instruments Ltd., UK) by dynamic light scattering (DLS) method. The particle size detection limit was about 0.3 nm–5  $\mu\text{m}$  (diameter) and accuracy of the *Z*-average diameter determined has been  $\pm 2\%$ . A He-Ne laser of 633 nm wavelength was used and the measurements were made at a fixed scattering angle of  $90^\circ$ . Samples were filtered using VALUPREP 0.45  $\mu\text{m}$  polytetrafluoroethylene (PTFE) filter and the *Z*-average diameters were determined from cumulants mean of the intensity average of 50 runs and the reproducibility was checked from at least 3 measurements. The temperature of the apparatus was controlled automatically within  $\pm 0.01$  K by a built-in Peltier device.

**2.4. Acid Hydrolysis of Bz.** The rate of acid hydrolysis of Bz in aqueous solution was measured spectrophotometrically by monitoring the absorbance at the  $\lambda_{\text{max}}$  ( $= 235$  nm) of Bz with the progress of the reaction. In the cases of kinetic measurements absorbance at the  $\lambda_{\text{max}}$  of Bz in micelles, reverse micelles, and microemulsions of CTAB was monitored since the  $\lambda_{\text{max}}$  was found to shift slightly in the presence of these media. The kinetic studies were conducted at controlled temperature. The acid hydrolysis of Bz follows second-order kinetics. The hydrolysis was therefore carried out by using a large excess of  $[\text{H}^+]$  (more than 10-fold) in aqueous and

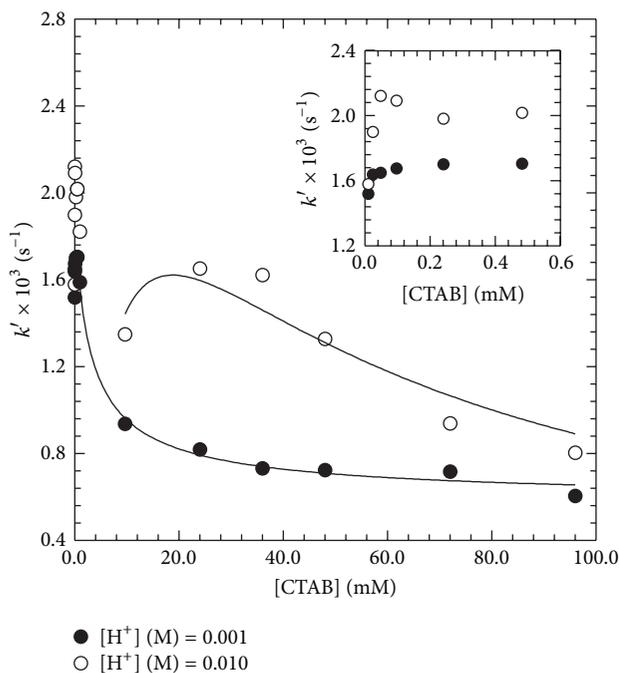


FIGURE 1: The  $k'$  as a function of [CTAB] for acid hydrolysis of  $2.21 \times 10^{-5}$  M Bz. Inset shows the values of the  $k'$  at [CTAB] below the CMC.

different supramolecular systems of CTAB, that is, under pseudo-first-order conditions of  $[\text{H}^+] \gg [\text{Bz}]$ . Assuming absorbance at 235 nm of the reaction mixture to be due to Bz only, we obtain,  $\ln[(A_0 - A_\infty)/(A - A_\infty)] = k't$ ; here,  $k'$  is the pseudo-first-order rate constant,  $A$  is the absorbance at any time,  $t$ , and  $A_0$  and  $A_\infty$  are the absorbance at  $t = 0$  and  $t = \infty$ , respectively, which depend on the molar absorptivity and the initial and final concentrations of the Bz. The values of  $k'$  were evaluated from a least square fit of the plot of  $\ln[(A_0 - A_\infty)/(A - A_\infty)]$  versus  $t$ .

### 3. Results and Discussions

**3.1. Critical Micelle Concentration (CMC) of CTAB in Aqueous Solution.** The variation in specific conductivity with change in concentration of CTAB in aqueous media CTAB was measured to determine the CMC of CTAB. The experimental specific conductivity values of CTAB lie on two straight lines and their point of intersection gave the CMC value for CTAB in aqueous solution. The CMC value at  $25^\circ\text{C}$  has been found to have a value of 0.87 mM for CTAB in aqueous solution, which is in good agreement with literature data [15, 36].

**3.2. Hydrolysis in the Presence of CTAB.** The  $k'$  versus [CTAB] profile for the acid hydrolysis of Bz in the presence of CTAB is shown in Figure 1 for  $[\text{H}^+] = 0.001$  and  $0.01$  M. The standard deviation in  $k'$  for aqueous solution was below  $\pm 0.0014 \text{ s}^{-1}$  and, for micelles, it was below  $\pm 0.0020 \text{ s}^{-1}$ . From Figure 1, it is apparent that, below the CMC, the  $k'$  increases for both

low and high  $[\text{H}^+]$ . For low  $[\text{H}^+]$ , at high [CTAB] (up to the CMC), the  $k'$  becomes almost constant; however, for high  $[\text{H}^+]$ , the  $k'$  decreases as the [CTAB] increases further. Above the CMC, the  $k'$  shows an initial decrease for both low and high  $[\text{H}^+]$ . As the [CTAB] continues to increase above the CMC, the  $k'$  at low  $[\text{H}^+]$  attains an almost constant value; while, at high  $[\text{H}^+]$ , the  $k'$  passes through a maximum and then decreases. This corresponds to the change in reaction mechanism during the course of the reaction depending on  $[\text{H}^+]$ . In fact, the mechanism of the hydrolysis of Bz changes with change in pH. At high pH, that is, low  $[\text{H}^+]$ , the breakage of the ring occurs at the 1,2-amidic bonds, which is considered to be reversible and, at low pH, that is, high  $[\text{H}^+]$ , the rupture takes place in the remaining 1,2-amidic or 4,5-azomethine group and the final hydrolysis products, the 2-amino-5-substituted benzophenones and glycine derivatives [24], are formed.

The  $k'$  for the acid hydrolysis of Bz in aqueous solution at  $[\text{H}^+] = 0.001$  and  $0.01$  M is  $1.07 \times 10^{-3} \text{ s}^{-1}$  and  $1.69 \times 10^{-3} \text{ s}^{-1}$ , respectively. Under identical experimental conditions, the  $k'$  has the value of  $1.58 \times 10^{-3} \text{ s}^{-1}$  and  $1.82 \times 10^{-3} \text{ s}^{-1}$  in the presence of 0.96 mM CTAB (just above the CMC), while the  $k'$  has the value of  $1.70 \times 10^{-3} \text{ s}^{-1}$  and  $2.02 \times 10^{-3} \text{ s}^{-1}$  for 0.49 mM CTAB (below the CMC) and for  $[\text{H}^+] = 0.001$  and  $0.01$  M, respectively. It is clear that the values of the  $k'$  in presence of CTAB are higher than in aqueous solution. CTAB, thereby, enhances the acid hydrolysis of Bz and serves as a positive catalyst both below and above the CMC.

At very high [CTAB], the values of the  $k'$  have been found to be smaller than the corresponding value in aqueous solution for both high and low  $[\text{H}^+]$ . This indicates that, at concentrations far above the CMC of CTAB, the rate of reaction is ultimately inhibited. This may be explained in terms of two facts: *Firstly*, with increasing [CTAB], the number of micelles increases and when the number of micelles exceeds that required to solubilize all of Bz, there is a dilution of the concentration of Bz per micelle as the [CTAB] is increased further. This causes a reduction in the rate constant. *Secondly*, the charged surface of CTAB in aqueous solution may cause the repulsion of similar-charged reactant,  $\text{H}^+$ , or even the solubilization of the  $\text{H}^+$  into the micelle. Such repulsion or solubilization of the  $\text{H}^+$  will result in a decrease in its activity in the solution phase. An increase in the [CTAB] over that required to affect complete solubilization of the Bz may therefore result in a decrease in the rate constant, even for the cases where rate enhancement by micelles occurs.

In the cases of our kinetic runs, we have always used the concentration of CTAB as 20% wt., which corresponds to a value of ca. 0.5 M. The kinetics of the acid hydrolysis of Bz has, therefore, been studied in aqueous solution using 0.5 M of CTAB and the result has been compared with those in aqueous solution. The  $k'$  in 0.5 M CTAB is lower ( $0.74 \times 10^{-3} \text{ s}^{-1}$ ) than the corresponding value in aqueous solution ( $1.07 \times 10^{-3} \text{ s}^{-1}$ ) under identical experimental conditions. This is indicative of interaction between the micellar head groups and Bz.

The enhancement and inhibition of the rate of the hydrolysis of Bz by CTAB micelles were treated by PIE model [37].

According to PIE model the apparent rate constant is given by the following equation:

$$k' = \frac{k_W [H^+] + (k_M K_S - k_W) m_H [M]}{1 + K_S [M]} \quad (1)$$

Here,  $[M]$  is the concentration of micellized surfactant which is given by  $[M] = ([S] - \text{CMC})/N$ , where  $[S]$  is the concentration of the surfactant and  $N$  is the aggregation number (61 for CTAB in aqueous solution at 25°C). The  $k_M$  refers to the second-order rate constant in the micellar pseudophase. The  $K_{\text{Br}}^{\text{H}}$  and  $K_S$  are the ion exchange equilibrium constant and the binding constant of the substrate, Bz, to the micelles, respectively. The fraction of micellar head groups neutralized by  $\text{H}^+$  ions ( $m_H$ ) were obtained by solving [37]

$$m_H^2 + m_H \left\{ \frac{[H^+] + K_{\text{Br}}^{\text{H}} [\text{Br}^-]}{(K_{\text{Br}}^{\text{H}} - 1) [M]} - \beta \right\} - \frac{\beta [H^+]}{(K_{\text{Br}}^{\text{H}} - 1) [M]} = 0 \quad (2)$$

The experimental data were fitted to both (1) and (2) simultaneously, using  $k_M$ ,  $K_S$ , and  $K_{\text{Br}}^{\text{H}}$  as adjustable parameters. Results of computer simulation for the data at the concentration of  $\text{H}^+ = 0.001$  and 0.01 M are shown in Figure 1. The values of  $k_M$ ,  $K_S$ , and  $K_{\text{Br}}^{\text{H}}$  obtained with best fitting at  $[\text{H}^+] = 0.001$  and 0.01 M are shown in Table 1.

From Table 1, it is apparent that the values of  $K_{\text{Br}}^{\text{H}}$  are independent of  $[\text{H}^+]$  and the  $K_S$  and  $k_M$  depend on the  $[\text{H}^+]$ . This may be due to the fact that as the concentration of Bz is constant, at low and high  $[\text{H}^+]$ , the concentration of the reactant,  $\text{H}^+$ , is different in the micellar pseudophase and the bulk phase.

**3.3. Hydrolysis in CTAB/Cyclohexane/1-Butanol/Water Microemulsions and CTAB/1-Butanol/Water Reverse Micelles.** Figure 2 represents the  $k'$  versus water to surfactant ratio ( $w_o$ ) profiles for CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles at  $[\text{H}^+] = 0.001$  M. The standard deviations in  $k'$  for  $w/o$  and  $o/w$  microemulsions were maximum  $\pm 0.0056$  and  $\pm 0.0029$   $\text{s}^{-1}$ , respectively, and that for reverse micelles ranged from  $\pm 0.0032$  to  $\pm 0.0050$   $\text{s}^{-1}$ . Figure 2 shows that the rate constants are greatly affected by CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles, which is clear indication of catalysis of the acid hydrolysis of Bz by these organized media.

As the  $w_o$  in CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles increases, the  $k'$  sharply decreases first and then becomes almost constant; however, at higher value of the  $w_o$  ( $>50$ ), a gradual increase is apparent. The rate constants attain value much higher than the corresponding value in aqueous solution under identical experimental conditions.

From Figure 2, in the region "ab" of the curve ( $w_o < 20$ ), the rate constant decreases with increasing value of  $w_o$  which should correspond to the region of reverse micelles of CTAB in 1-butanol where the incorporation of water into the CTAB reverse micelles inhibits the reaction. Part "cd" of the curve

TABLE 1: The optimized values of  $k_M$ ,  $K_S$ , and  $K_{\text{Br}}^{\text{H}}$  for  $[\text{H}^+] = 0.001$  and 0.01 M for acid hydrolysis of  $2.21 \times 10^{-5}$  M Bz in micelles of CTAB using PIE model.

$[\text{H}^+]$ (M)	$k_M$ ( $\text{s}^{-1}$ )	$K_{\text{Br}}^{\text{H}}$	$K_S$ ( $\text{M}^{-1}$ )
0.010	0.016	1.00	200
0.001	0.370	1.00	187

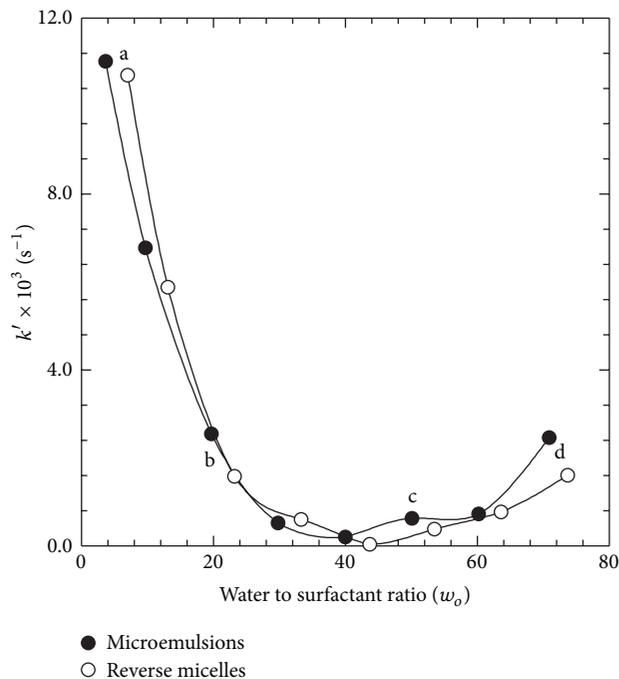


FIGURE 2: The  $k'$  versus  $w_o$  profiles for the acid hydrolysis of  $2.21 \times 10^{-5}$  M Bz in CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles at  $[\text{H}^+] = 0.001$  M.

( $w_o > 50$ ) should correspond to the reaction in CTAB micelles in water where a decrease in 1-butanol produces a slight increase in the rate of reaction. Part "bc" of the curve ( $w_o = 20 \sim 50$ ) should correspond to the cluster formation of the CTAB reverse micelles ( $w/o$  microemulsions) in 1-butanol and CTAB micelles ( $o/w$  microemulsions) in water that is bicontinuous microemulsions (BC).

**3.4. Comparative Study for the Acid Hydrolysis of Bz in Aqueous Solution, Micelles, Reverse Micelles, and Microemulsions of CTAB.** Figure 3 compares the  $k'$  for different supramolecular self-assembled systems based on CTAB at  $[\text{CTAB}] = \text{ca. } 0.5$  M with that in aqueous solution under identical experimental conditions. From Figure 1, it can be seen that, at concentrations far above the CMC of CTAB, the reaction rate is ultimately inhibited which may be correlated with change in binding constant between CTAB and acid dissociation constant of Bz.

The  $w/o$  microemulsions (lower value of  $w_o$ ) have been found to bring about an increase in the reaction rate where high 1-butanol content dominates CTAB/1-butanol reverse micelles whereas, in  $o/w$  microemulsions (higher value of

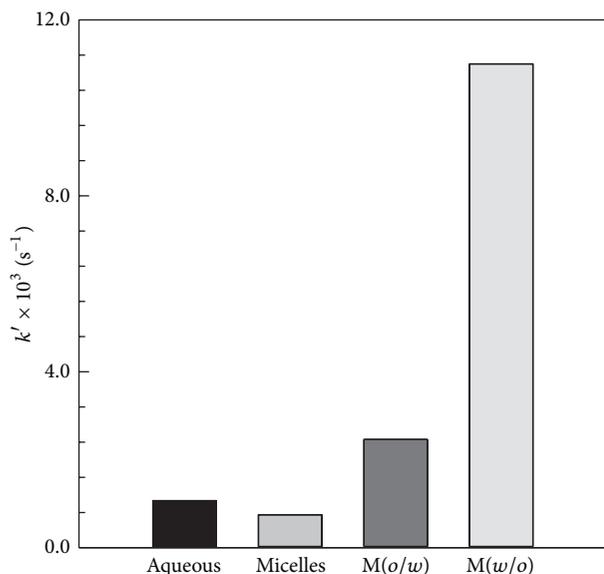


FIGURE 3: The  $k'$  for aqueous and different self-assembled systems based on CTAB;  $[\text{Bz}] = 2.21 \times 10^{-5} \text{ M}$  and  $[\text{H}^+] = 0.001 \text{ M}$ . Micelles ( $[\text{CTAB}] = \text{ca. } 0.5 \text{ M}$ );  $o/w$  ( $w_o = 70.9$ ) and  $w/o$  ( $w_o = 3.64$ ) microemulsions.

$w_o$ ), the rate constant is higher as compared to aqueous solution and the corresponding micelles but lower than that in  $w/o$  microemulsions. It should correspond to the region of direct CTAB micelles in water where the lower content of 1-butanol was incorporated into the CTAB micelles. The schematic diagram of the acid hydrolysis of Bz in different self-assembled systems is shown in Scheme 1.

### 3.5. Physicochemical Properties of

#### CTAB/Cyclohexane/1-Butanol/Water Microemulsions and CTAB/1-Butanol/Water Reverse Micelles

**3.5.1. Viscosity.** Figure 4 shows the change of viscosities with the  $w_o$  for CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles. The viscosity of the microemulsions is very low, less than 120 mPa s. In CTAB/1-butanol/cyclohexane/water microemulsions (Figure 4(a)), at  $w_o < 20$ , the viscosity increases slightly while, for  $w_o = 20\sim 50$ , it increases gradually whereas, at  $w_o > 50$ , a sharp increase is apparent. In CTAB/1-butanol/water reverse micelles (Figure 4(b)), at  $w_o < 20$ , the viscosity increases slightly while, for  $w_o = 20\sim 50$ , it shows a slight decrease and, at  $w_o > 50$ , a sharp increase is noticeable. This increase in viscosity with the addition of water has been ascribed to the increasing diameter of water filled conduits in the bicontinuous and  $o/w$  microemulsions [38]. The initial increase in viscosity profile should correspond to the aggregation and attractive interaction of water droplets in CTAB/1-butanol reverse micelles ( $w/o$  microemulsions). With further increasing  $w_o$  up to 50, the water and 1-butanol droplets of CTAB micelles and reverse micelles coagulate to form clusters (i.e., the bicontinuous region) in which the gradual increase for microemulsion and decrease for reverse

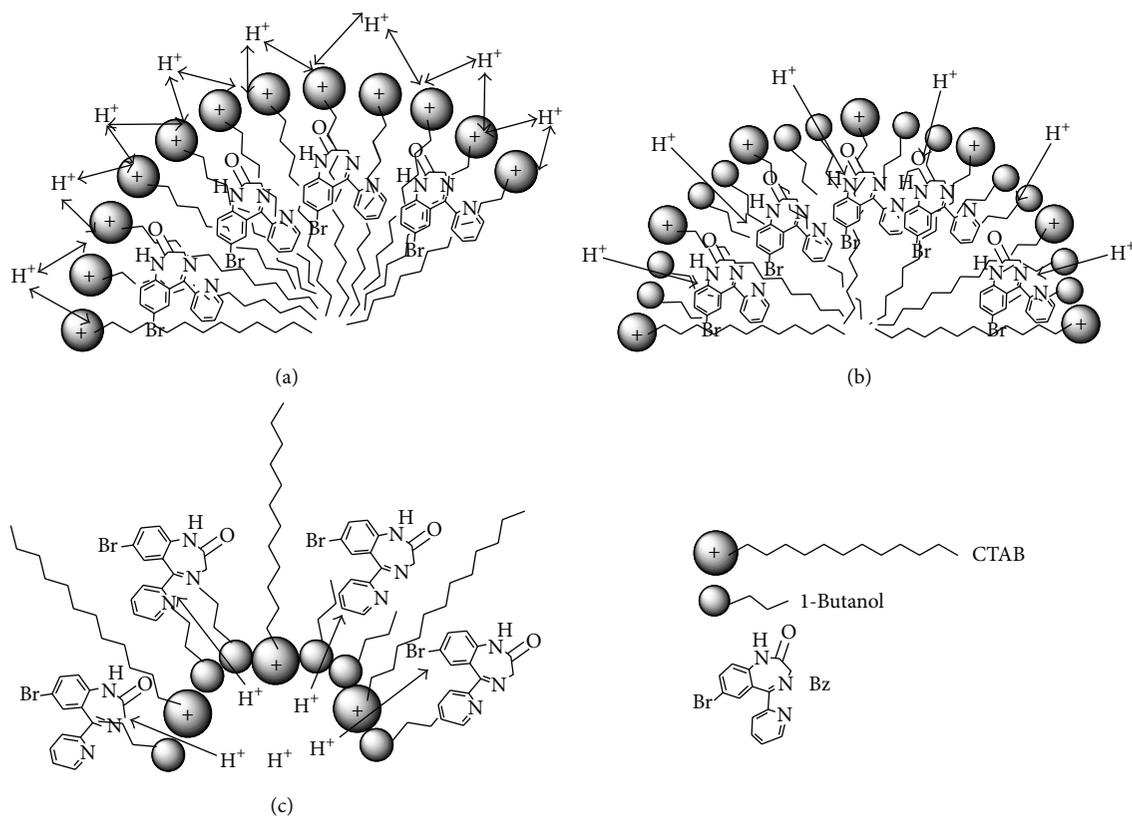
in viscosity are apparent [39]. Above  $w_o = 50$ , the sharp rise in viscosity corresponds to the 1-butanol droplets in CTAB/water micelles ( $o/w$  microemulsions) as the viscosity of water is higher than the 1-butanol.

**3.5.2. Specific Conductivity.** Figure 5 shows specific conductivities of CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles against the  $w_o$ . The conductivity of the microemulsions and reverse micelles increases with the  $w_o$ . This indicates an increase in the number of conducting species in the systems [39]. At lower value of the  $w_o$ , the conductivity value is low to indicate that the hydrophilic trimethylammonium ion and counterion  $\text{Br}^-$  of CTAB in contact with the water droplets of CTAB/1-butanol reverse micelles ( $w/o$  microemulsions) are not easily dissociated. At higher value of the  $w_o$ , CTAB micelles ( $o/w$  microemulsions) are formed in water and the orientation of the CTAB changes where the hydrophilic trimethylammonium ion and the counterion,  $\text{Br}^-$ , are freely dissociated in water and increase the specific conductivity. In the middle portion, the conductivity increases that should be corresponding to the network of the conductive channel (bicontinuous microemulsions) formed by the interaction of water and 1-butanol droplets of the CTAB/1-butanol reverse micelles and CTAB/water micelles, respectively [39].

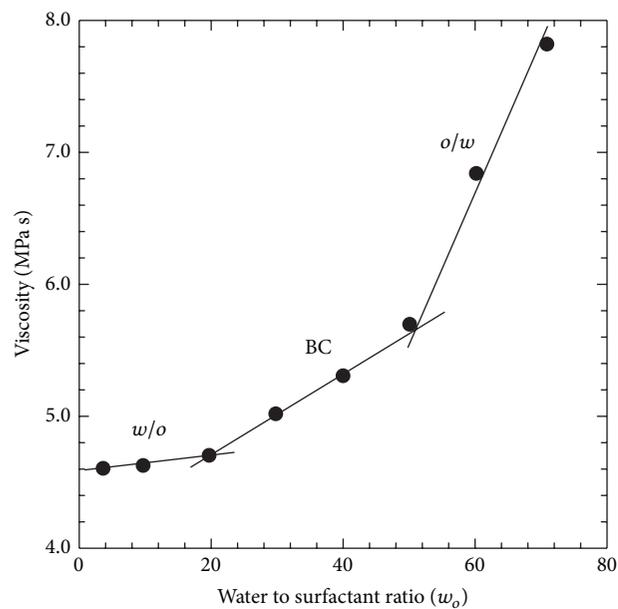
**3.5.3. Refractive Index.** Figure 6 shows the change of refractive index of CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles with the  $w_o$ . The refractive index specifies the transparency of the microemulsions. With increasing  $w_o$ , the refractive index decreases monotonically. As the refractive index is a property sensitive to structural transitions, the results suggest that no structural modifications are involved [40]; that is, water and 1-butanol remain encapsulated into the CTAB/1-butanol reverse micelles (low  $w_o$ ) and CTAB/water micelles (high  $w_o$ ), respectively.

**3.5.4. Correlations of Physicochemical Properties of CTAB/Cyclohexane/1-Butanol/Water Microemulsions and CTAB/1-Butanol/Water Reverse Micelles with Kinetic Results of Acid Hydrolysis of Bz.** As the  $w_o$  increases, the physicochemical properties such as viscosity, density, specific conductivity, and refractive index of CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles change. The viscosity, density, and specific conductivity increase and refractive index decreases with the  $w_o$ . The changes in physicochemical properties with  $w_o$  suggest that properties are dependent on different microstructure regions of reverse micelles and microemulsions. The viscosity versus  $w_o$  profile shows different patterns for change in the  $w_o$ . Increase in viscosity at  $w_o < 20$ ,  $w_o = 20\sim 50$ , and  $w_o > 50$  corresponds to the  $w/o$ , bicontinuous, and  $o/w$  microemulsions, respectively (Figure 4). Thus, increase in the  $w_o$  causes change in reaction environment that also causes change in reaction rate of the acid hydrolysis of Bz (Figure 2).

Figures 2 and 4 show that as the  $w_o$  increases, the reaction rate decreases up to  $w_o < 20$ ; then the rate becomes

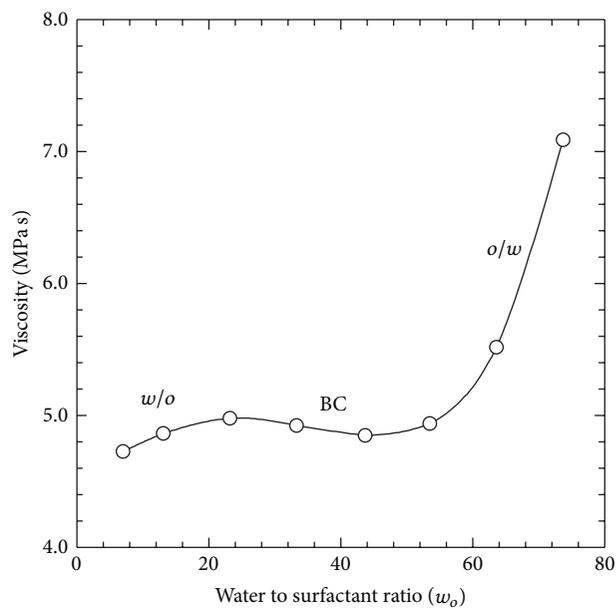


SCHEME 1: Acid hydrolysis of Bz in (a) micelles ( $[CTAB] = \text{ca. } 0.5 \text{ M}$ ); (b)  $o/w$  ( $w_o = 70.9$ ) and (c)  $w/o$  ( $w_o = 3.64$ ) microemulsions.



● Microemulsions

(a)



○ Reverse micelles

(b)

FIGURE 4: Viscosities as a function of  $w_o$  for (a) CTAB/1-butanol/cyclohexane/water microemulsions and (b) CTAB/1-butanol/water reverse micelles.

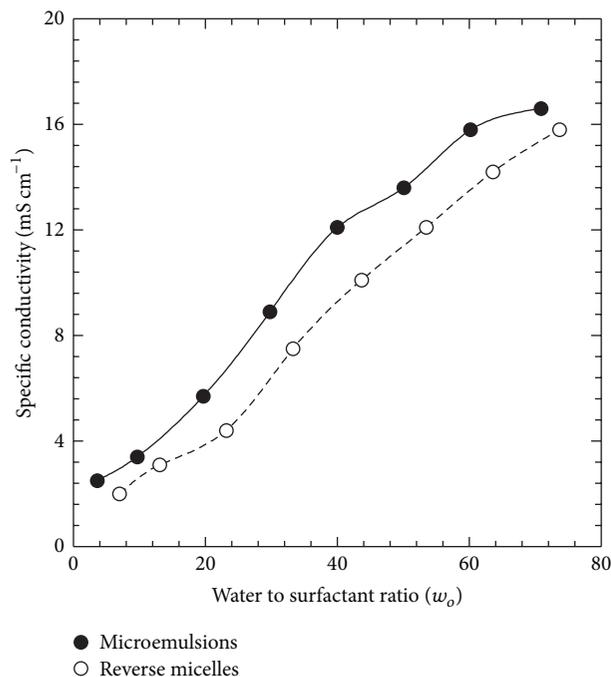


FIGURE 5: Specific conductivities of CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles.

almost constant at  $w_o = 20\sim 50$  and at  $w_o > 50$  a gradual increase is apparent which correlates well with viscosity and conductivity results. Again, the conductivity versus  $w_o$  profile shows the increase in conductivity with increase in the  $w_o$  which is also associated with viscosity of microemulsions and reverse micelles of CTAB. At  $w_o > 50$ , the CTAB/water micelles of sufficient numbers collide and produce a channel that carries ions leading to increase in conductivity and viscosity increases due to the presence of micelle core [30]. At  $w_o < 20$ , the CTAB/1-butanol reverse micelles are formed that allow transport of ions through the water that filled cores and the viscosity slightly increases due to the interaction of water droplets [39]. In the middle region,  $w_o = 20\sim 50$ , the bicontinuous microemulsions are formed where water and 1-butanol droplets collide to form network structure. Thus, the viscosity increases due to the collision of different droplets and the conductivity increases for the transport of ions in the conductive channel produced by water as well as 1-butanol droplets.

**3.6. Droplet Sizes of CTAB/Cyclohexane/1-Butanol/Water Microemulsions and CTAB/1-Butanol/Water Reverse Micelles.** Figure 7 shows the Z-average diameter versus  $w_o$  for CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles. The droplet sizes of all the microemulsions and reverse micelles are less than 100 nm [41]. It can be seen from Figure 7 that the Z-average diameters of CTAB/1-butanol/water reverse micelles are higher than the corresponding CTAB/1-butanol/cyclohexane/water microemulsions and decrease with increasing  $w_o$ . The larger size at  $w_o = 3.64$  is due to the formation of CTAB reverse

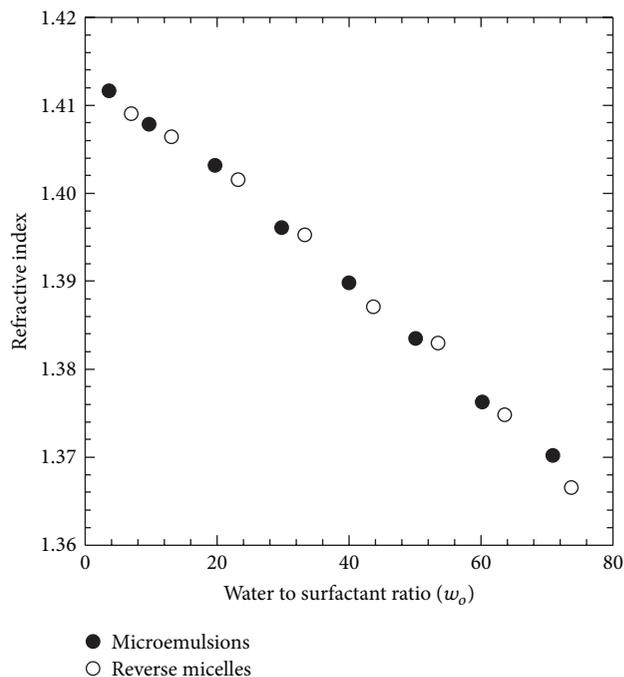


FIGURE 6: Refractive indices of CTAB/1-butanol/cyclohexane/water microemulsions and CTAB/1-butanol/water reverse micelles.

micelles ( $w/o$  microemulsions) in 1-butanol where the electrostatic repulsion between the polar heads is screened by 1-butanol and facilitates the formation of aggregates as well as larger size of the droplets [42]. As the  $w_o$  increases, the droplet sizes decrease possibly due to the decrease in the number of reverse micelles. At  $w_o = 70.9$ , the droplet sizes are so small and correspond to the CTAB micelles ( $o/w$  microemulsions) in water. Additionally, in the middle region, the droplet sizes are almost constant that correspond to the transition from reverse micellar phase to micellar phase, via bicontinuous microemulsions.

The polydispersity index (PDI), a width parameter, has been calculated from a Cumulants analysis of the DLS measured intensity autocorrelation function. In general, values smaller than 0.1 indicate reasonably narrow distribution and values greater than 0.7 indicate that the sample has a very broad size distribution. The PDI values in our measurements have been evaluated for CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles. It has been found that the PDI values range from 0.107 to 0.354 and 0.226 to 0.499 for reverse micelles and microemulsions of CTAB, respectively. In all cases, the PDI values are within the range of 0.1–0.7 which indicates that the droplets of reverse micelles and microemulsions are reasonably uniform in their distribution.

The standard deviations in Z-average diameters,  $d$ , of CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles have been calculated and these depend on the  $w_o$  for all cases, such as  $w_o = 3.64$  ( $d = 2.72$  nm) and  $w_o = 70.9$  ( $d = 0.30$  nm); the standard deviations in Z-average diameters of microemulsions were  $\pm 0.682$  and

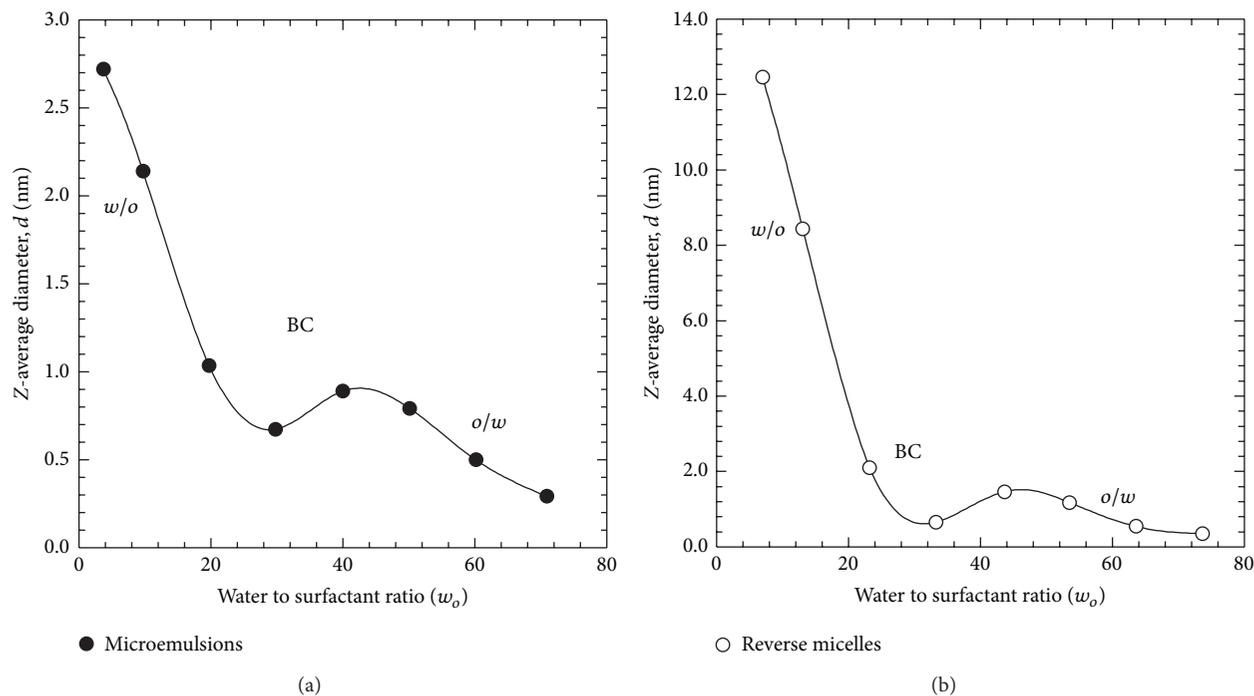


FIGURE 7: Z-average diameters of (a) CTAB/1-butanol/cyclohexane/water microemulsions and (b) CTAB/1-butanol/water reverse micelles.

$\pm 0.004$  nm, respectively, while at  $w_o = 7.00$  ( $d = 12.46$  nm) and  $w_o = 73.7$  ( $d = 0.35$  nm), the standard deviations in Z-average diameters of reverse micelles were  $\pm 0.614$  and  $\pm 0.003$  nm, respectively. Thus, for both reverse micelles and microemulsions of CTAB, at high value of  $w_o$ , the results tend to be very close to the expected values that indicate relatively narrow distribution of droplet sizes and, at low value of  $w_o$ , the results are spread out at a relatively wider range of values.

*3.7. Correlation of Droplet Sizes of CTAB/Cyclohexane/1-Butanol/Water Microemulsions and CTAB/1-Butanol/Water Reverse Micelles with Kinetic Results of Acid Hydrolysis of Bz.* The droplet sizes of the CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles as well as the rate constants of acid hydrolysis of Bz decrease with increasing  $w_o$  as shown in Figures 2 and 7. For lower values of  $w_o$  (larger droplet sizes and less viscous media), the values of the  $k'$  are higher due to the presence of CTAB/1-butanol reverse micelles which accelerate the reactions. In contrast, the formation of CTAB/water micelles at higher  $w_o$  values (smaller droplet sizes and more viscous media) inhibits the reaction and lowers the reaction rate. The bicontinuous microemulsions are formed for intermediate values of the  $w_o$  where both water and 1-butanol droplets merge to provide complex microstructures and the values of the  $k'$  as well as the size of the droplets become almost constant. The rate constants for bicontinuous systems are less than the corresponding values in w/o, o/w microemulsions and the aqueous solutions.

## 4. Conclusions

Micelles, reverse micelles, and microemulsions of CTAB influence the rate of the acid hydrolysis of Bz. The kinetic profiles vary depending on the change in the reaction environment due to different assembly and orientation of the surfactants in micelles, reverse micelles, and microemulsions. In micellar solution, the profiles also exhibit pH dependence. The kinetic data showed good fit to the PIE model for the title reaction with reasonable values of the parameters. The  $k'$  versus  $w_o$  profiles for CTAB/cyclohexane/1-butanol/water microemulsions and CTAB/1-butanol/water reverse micelles show a sharp decrease in the  $k'$  followed by a gradual increase with increasing  $w_o$  to indicate a transition from w/o to o/w via bicontinuous microemulsions. The physicochemical properties and droplet sizes of these media are also greatly affected by change in the  $w_o$  which correlates with kinetic results with change in the microenvironment for different orientations of CTAB.

## Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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