Compartmentalization of reactants in supercritical fluid micelles

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Received (in Montpellier, France) 1st February 2002, Accepted 8th April 2002
First published as an Advance Article on the web 29th July 2002

The hydrolysis of acetylsalicylic acid, a model reaction, in sodium bis(2-ethylhexyl) sulfosuccinate (AOT)/supercritical ethane reverse micelles has been studied in the presence of imidazole catalyst using *in situ* UV-vis spectroscopy. An increase of rate constant by 55 times was observed in AOT/supercritical ethane micellar medium compared to the reaction carried out in aqueous buffer. The reaction had a strong dependence on the water content of micelles, which decelerated to a large extent when the water content of the micelles was increased. The acceleration of the reaction in micelles compared to aqueous buffer and the water content dependence of the reaction rate have been confirmed to be due to compartmentalization of the water-soluble reactant and catalyst in the aqueous core of the micelles. The local concentration of substrate and catalyst increases when they are enclosed in the aqueous core of the micelles, resulting in an increase in the rate constant and shortening of the reaction time, rather than the existence of a diluted solution in the aqueous buffer. No pressure dependence of the reaction has been found in the pressure range of 27 to 44 MPa at 310 K.

Supercritical fluids (SCFs) have widely been used for various chemical processes from separation[1] and extraction[2,3] to inorganic[4] and organic synthesis.[5,6] The advantages of using SCFs are their higher diffusivities and lower viscosities compared to conventional solvents,[7] which results in improved mass transfer properties important for extraction, separation, and reaction processes. The solvent strength of SCFs can easily be manipulated by changing the temperature and pressure of the system. SCFs that have relatively low critical points such as carbon dioxide ($T_c = 304.1$ K and $P_c = 7.38$ MPa) and ethane ($T_c = 305.2$ K and $P_c = 4.88$ MPa) are ideal vehicles for those chemical processes where low temperatures are required to avoid any possible thermal degradation. The limitation to using SC CO_2 and ethane is that they are poor solvents because of their nonpolar characteristics.[8,9] However, by the addition of small amounts of polar cosolvents such as acetone and methanol their solvent strength can be improved significantly in terms of extraction efficiency, selectivity, yield, and reduction in the operating pressure of the system. Ekart *et al.*[10] achieved the difficult separation of polar organic solutes using SC CO_2, ethane, and fluoroform by the addition of a variety of polar cosolvents. Nevertheless, the major limitation to the broader use of these SCFs is due to their inability to dissolve a wide range of hydrophiles and in particular ionic species. This problem was first overcome when reverse micelles were prepared in SC ethane and propane by using a surfactant AOT.[11] The synthesis of reverse micelles in SCFs provided an opportunity to host a variety of solutes from polar and nonpolar organic compounds[12] to inorganic salts[13] in a system mostly consisting of the supercritical phase since there exists a combination of aqueous, interfacial, and nonpolar environments in reverse micellar solutions. Over the last 14 years, because of their unique properties, SCF reverse micelles have been used as potential reaction, extraction, and separation media where a proper phase contact between water- and oil-soluble solutes is absolutely necessary. A very recent review article[14] has described the preparation, properties and applications of reverse micelles prepared in SC CO_2, ethane, and propane using a variety of surfactants.

In this article, we have investigated, using *in situ* UV-vis spectroscopy, the hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles with imidazole as the catalyst as a function of the water content of the micelles and ethane pressure. From this study, we have shown first that in SCF micelles much faster kinetics and shorter reaction times could be achieved compared to the reaction carried out in aqueous solution as a result of the compartmentalization of the water-soluble substrate and catalyst inside the aqueous core of the reverse miscelles.

Results and discussion

Fig. 1 is the reaction profile of hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles at 40.2 MPa and 310 K. The kinetics of the reaction show that there is a significant decrease in the rate of hydrolysis of acetylsalicylic acid upon increasing the water content of the micelles from $W_0 = 1$ to $W_0 = 3$. Fig. 2 shows the pseudo-first-order rate constants (k/s^{-1}) for hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles and in aqueous buffer solution. Increasing the water content (W_0) of micelles containing imidazole decelerated the reaction.

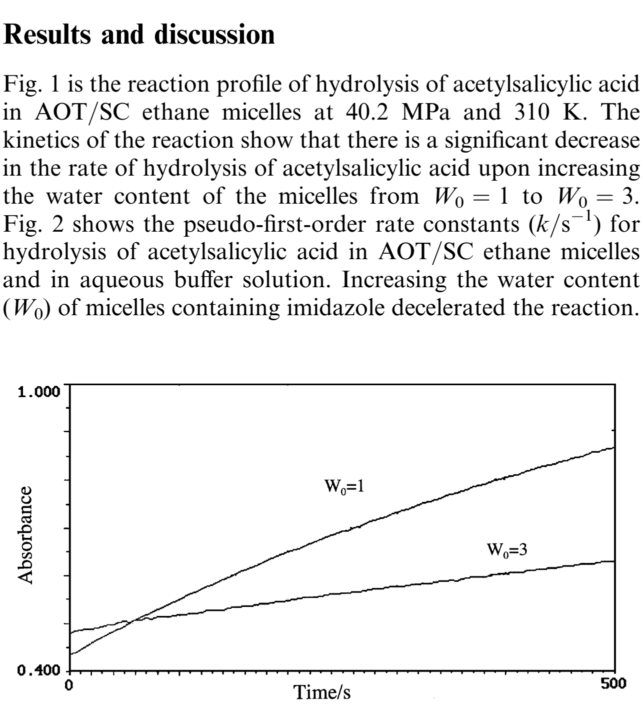

Fig. 1 Time course of the formation of salicylic acid in SC ethane micelles in the presence of imidazole catalyst at $W_0 = 1$ and $W_0 = 3$; $P = 40.2$ MPa and $T = 310$ K.

DOI: 10.1039/b201435c

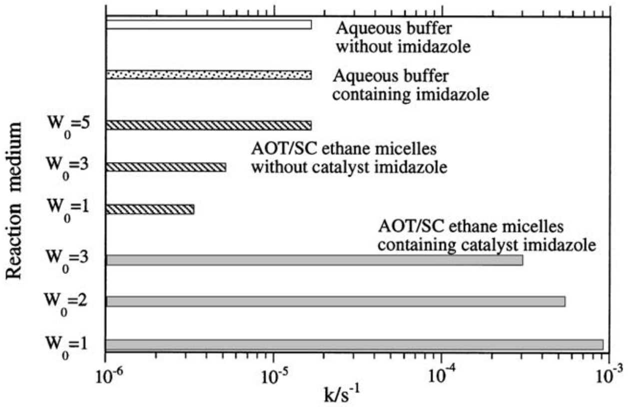

Fig. 2 Rate constants (k/s^{-1}) for hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles ($P = 40.2$ MPa) and in aqueous buffer with and without addition of imidazole at 310 K.

The reaction rate was enhanced greatly when carried out in AOT/SC ethane micelles as compared to aqueous buffer in the presence of imidazole catalyst. Fig. 2 also shows that the incorporation of imidazole in aqueous solution does not influence the reaction, whereas the addition of imidazole increases the reaction rate remarkably in micelles. The percent conversion of acetylsalicylic acid to salicylic acid at different reaction times in the presence of imidazole revealed that 100% conversion was obtained within 33 min in micelles with $W_0 = 1$, while in aqueous solution it took 61 h to complete the reaction. The time taken to complete the reaction increased with increasing amount of water in the micelles (Fig. 3). The shorter reaction times and higher rate constants in micelles as compared to aqueous solution could be explained by the compartmentalization of the water-soluble imidazole catalyst and acetylsalicylic acid substrate inside the aqueous core of the micelles, thus increasing the local concentration of reactants, whereas in aqueous medium the reactants are diluted resulting in longer reaction times and lower reaction rates. Increasing the amount of water in the micelles containing imidazole decreases the concentration of reactants in the aqueous core of the micelles and reduces the rate constant. The increase in the rate constant as a result of compartmentalization of reactants in the core of the micelles was confirmed by investigating the concentration dependence of the reaction in micelles and in aqueous buffer solution. In both reaction media the rate constant increased with increasing concentration of catalyst and substrate (Fig. 4), which proves that the compartmentalization of reactants in the aqueous domain of the micelles is indeed the reason for the acceleration of the reaction in micelles.

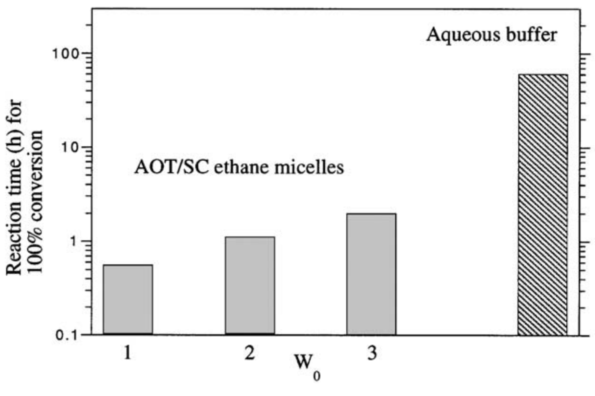

Fig. 3 Bars comparing the reaction time for hydrolysis of acetylsalicylic acid in the presence of imidazole in AOT/SC ethane micelles ($P = 40.2$ MPa) and in aqueous solution at ambient pressure and 310 K.

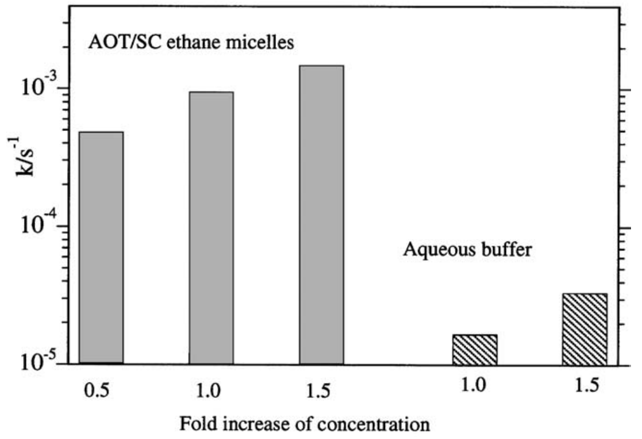

Fig. 4 Rate constant *vs.* n-fold increase in the concentration of imidazole and acetylsalicylic acid in micelles ($W_0 = 1$ and $P = 35.6$ MPa) and in aqueous buffer at 310 K. One-fold of imidazole and acetylsalicylic acid is 2.5×10^{-2} and 2.5×10^{-4} M, respectively.

The reactions in micelles and aqueous solution were conducted using 100 mM phosphate buffer of pH 7.0. To check the influence of a pH jump observed when the initial buffer is injected into the micelles[15,16] on the reaction kinetics, the reaction in AOT/SC ethane micelles was carried out by solubilizing the initial buffers in three different pH (*viz* 5.5, 7.0, and 9.27) solutions. No influence due to changing pH could be noticed on the reaction. This confirms that the acceleration of the reaction in micelles is not due to a change in the pH of the starting buffer but instead it is solely due to compartmentalization of the reactants inside the smaller volume water pool of the micelles.

A comparison has been made of the rate constants of hydrolysis of acetylsalicylic acid in the presence of imidazole for $W_0 = 1$ in AOT/SC ethane micelles ($P = 40.2$ MPa) and normal AOT/isooctane micelles. The rate constant was found to be 1.3 times higher in SC ethane micelles, which is attributed to the higher diffusivities of the reactants in the SC ethane phase.

The hydrolysis of acetylsalicylic acid is characterized by the general acid-base catalysis of imidazole.[17] In the first transition state, the transfer of a proton from water to imidazole occurs to from the intermediate imidazolium cation and the formation of a negatively charged ester takes place by the attack of hydroxide ion on the acyl carbonyl group of the acetyl of acetylsalicylic acid. In the second transition state, the proton from the imidazolium cation is transferred to the alcohol group and finally the fission of the acid–alcohol bond yields the products salicylic acid and acetic acid.

The intramolecular hydrolysis of acetylsalicylic acid was also investigated in AOT/SC ethane micelles without the addition of imidazole catalyst. The results were contrary to those of the reaction carried out in the presence of imidazole. The rate constant increased with increasing water content of the micelles (Fig. 2). At $W_0 = 5$, the value of the rate constant approached that observed in aqueous solution. The intramolecular catalyzed hydrolysis reaction depends on the availability of water molecules. In micelles of low water content, the initially added water molecules are used for the hydration of sodium counter ions and sulfosuccinate head groups of the surfactant AOT molecule.[18] Therefore, in low water content micelles, the rate constant of hydrolysis is lower. As the amount of water increases, more water molecules are available for the hydrolysis of acetylsalicylic acid, thus a higher reaction rate is observed.

The effect of pressure on the hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles has also been investigated in terms of the rate constant (Fig. 5) and time taken for the completion

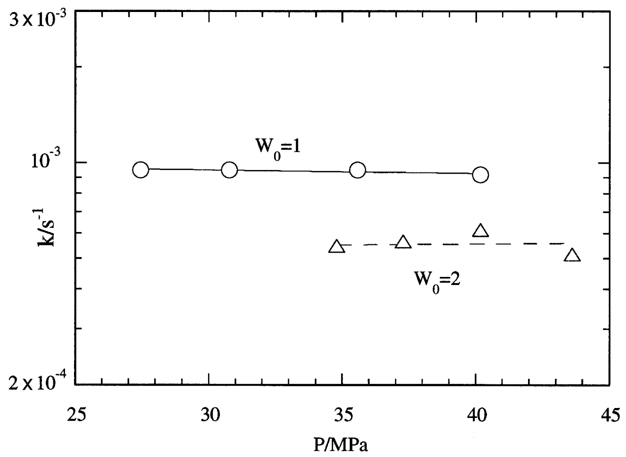

Fig. 5 Pressure dependence of the rate constant of hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles at 310 K.

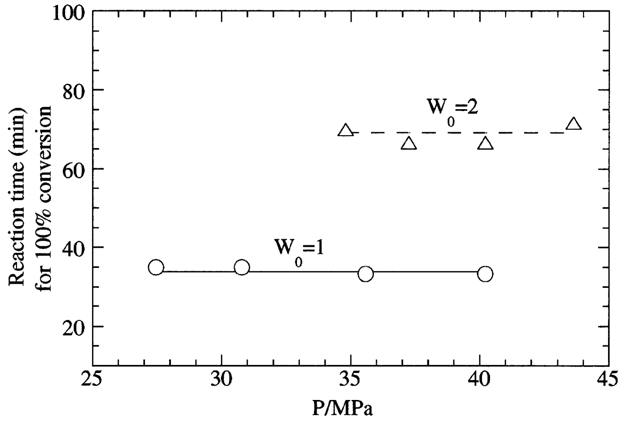

Fig. 6 Plot of reaction time *vs.* pressure for 100% conversion of acetylsalicylic acid to salicylic acid in AOT/SC ethane micelles at 310 K.

of the reaction (Fig. 6). Increasing the pressure of ethane does not influence the kinetics of the reaction, which is contrary to the pressure dependence observed in normal AOT/octane micelles for enzyme catalysed hydrolysis reactions[19] and attributed to the stability of the enzyme in structurally ordered micelles at higher octane pressure. In contrast to the large enzyme molecules, which are in efficient contact with the micellar interface, the smaller imidazole molecules are located in the micelles core and far from the interface; therefore, they do not experience any change when the pressure of the system is increased and the reaction rate remains independent of pressure. A pressure dependence of the esterification of acetic acid with ethanol was observed in compressed CO_2 and conversion reached a maximum at the critical pressure of the reaction system.[20] At the critical pressure and above critical temperature, the conversion and kinetics parameters for several other reactions[21–23] carried out in compressed CO_2 have also been found to reach a maximum because the solubility and diffusivity of the reactants are highest in this region. In the present study of hydrolysis of acetylsalicylic acid in AOT/SC ethane micelles, the supercritical conditions of ethane continuous phase of micelles have been maintained throughout the course of the reaction; thus, no influence of pressure on the kinetics of the reaction was observed.

Conclusions

Supercritical fluid micelles can be used as reaction media for hydrolysis reactions with enhancement of the reaction rate compared to aqueous medium. The water content of the micelles has strong influence on the hydrolysis of acetylsalicylic acid in the presence of imidazole catalyst. The reaction rate decelerates with increasing water content of the micelles as a result of dilution of the reactants. The acceleration of the reaction in micelles and the influence of water content has been confirmed to be due to compartmentalization of the water-soluble imidazole catalyst and acetylsalicylic acid substrate in the aqueous core of the micelles. No influence of increasing pressure of supercritical ethane was observed on the kinetics of the reaction; therefore, reactions can be carried out efficiently in the low-pressure region of supercritical ethane.

Experimental

Chemicals

AOT was obtained from Fluka and was purified by the method of Politi *et al.*[24] Ethane (> 99.7%) was procured from Nippon Sanso Corporation. Acetylsalicylic acid and imidazole were obtained from Wako Pure Chemical Industries Ltd. and Tokyo Chemical Industry Co. Ltd., respectively, and were used as received. Disodium hydrogen phosphate and sodium dihydrogen phosphate, obtained from Nacalai Tesque, Inc., were used for phosphate buffer preparation. Deionized distilled water procured from Wako Pure Chemical Industries Ltd. was used for sample preparation.

Apparatus and measurements

A 2.2 ml high pressure UV cell was used as a reactor, consisting of a stainless steel cylinder fitted with a pair of sapphire windows. All the experiments were carried out at a fixed temperature of 310 K, which was controlled within ±0.2 °C with a temperature controller attached to the high pressure cell. For sample preparation, the measured amounts of AOT, acetylsalicylic acid, imidazole, and water were loaded into the high pressure cell. The cell was then closed and the micelle solution prepared by filling pre-cooled ethane inside the cell at the desired pressure (27–44 MPa). The concentrations of AOT, acetylsalicylic acid, and imidazole were taken as 0.1, 2.5×10^{-4} and 2.5×10^{-2} M, respectively, and were with respect to the total volume of micelle or aqueous buffer solution. The amount of water added to prepare the micelles is represented by W_0, which is the molar ratio of water-to-AOT. Phosphate buffer (100 mM) was used as an aqueous reaction medium and also to adjust the water content of the micelles. In the case of concentration dependent experiments, the concentrations of acetylsalicylic acid and imidazole were varied in the range of 0.5 to 1.5 of the standard concentrations given above.

For the rate constant determinations, the increase in the absorbance of the salicylic acid product was recorded at 298.6 nm *vs.* reaction time with a Jasco V-570 spectrometer. The conversion rate (%) was determined by recording the spectrum of the product at various reaction times. The reaction time for apparent 100% conversion in buffer was rather longer as it took 61 h. This was similarly determined by recording the spectrum at different times until no further increase in the absorbance was observed. The absorbance at 100% conversion reached a similar value as that of pure salicylic acid dissolved in the media.

The reaction mixtures were stirred continuously during the measurements by a Teflon-coated bar driven by an outside magnet attached to the cell. The homogeneity of all reverse micellar solutions was confirmed by looking across the windows of the high pressure UV cell. The reactions in aqueous buffer were carried out at ambient pressure.

References

1 Y. Yamini and N. Bahramifar, *J. Chem. Eng. Data*, 2000, **45**, 1129.

2 B. A. Benner, Jr., *Anal. Chem.*, 1998, **70**, 4594.

3 J. M. Becnel and K. M. Dooley, *Ind. Eng. Chem. Res.*, 1998, **37**, 584.

4 T. Adschiri, Y. Hakuta and K. Arai, *Ind. Eng. Chem. Res.*, 2000, **39**, 4901.

5 Y. Ikushima, K. Hatakeda, O. Sato, T. Yokoyama and M. Arai, *J. Am. Chem. Soc.*, 2000, **122**, 1908.

6 B. M. Kabyemela, T. Adschiri, R. M. Malaluan and K. Arai, *Ind. Eng. Chem. Res.*, 1999, **38**, 2888.

7 E. Klesper, *Angew. Chem., Int. Ed. Engl.*, 1978, **17**, 738.

8 A. Wesch, N. Dahmen and K. H. Ebert, *Ber. Bunsenges. Phys. Chem.*, 1996, **100**, 1368.

9 *Handbook of Chemistry and Physics*, ed. D. R. Lide, CRC Press, Boca Raton, FL, 78th ed., 1997.

10 M. P. Ekart, K. L. Bennett, S. M. Ekart, G. S. Gurdial, C. L. Liotta and C. A. Eckert, *AIChE J.*, 1993, **39**, 235.

11 R. W. Gale, J. L. Fulton and R. D. Smith, *J. Am. Chem. Soc.*, 1987, **109**, 920.

12 R. D. Smith, J. L. Fulton, J. P. Blitz and J. M. Tingey, *J. Phys. Chem.*, 1990, **94**, 781.

13 Y. Ikushima, N. Saito and M. Arai, *J. Colloid Interface Sci.*, 1997, **186**, 254.

14 Z. Shervani and Y. Ikushima, in *Encyclopedia of Surface and Colloid Science*, ed. A. Hubbard, Marcel Dekker, New York, 2002, pp. 3413–3422.

15 F. M. Menger and K. Yamada, *J. Am. Chem. Soc.*, 1979, **101**, 6731.

16 R. E. Smith and P. L. Luisi, *Helv. Chim. Acta*, 1980, **63**, 2302.

17 G. Schmeer, C. Six and J. Steinkirchner, *J. Solution Chem.*, 1999, **28**, 211.

18 M. Wong, J. K. Thomas and M. Gratzel, *J. Am. Chem. Soc.*, 1976, **98**, 2391.

19 R. V. Rariy, N. Bec, J. L. Saldana, S. N. Nametkin, V. V. Mozhaev, N. L. Klyachko, A. V. Levashov and C. Balny, *FEBS Lett.*, 1995, **364**, 98.

20 Z. Hou, B. Han, X. Zhang, H. Zhang and Z. Liu, *J. Phys. Chem. B*, 2001, **105**, 4510.

21 H. Kawanami and Y. Ikushima, *Chem. Commun.*, 2000, 2089.

22 S. Fujita, B. M. Bhanage, Y. Ikushima and M. Arai, *Green Chem.*, 2001, **3**, 87.

23 T. Mori and Y. Okahata, *Chem. Commun.*, 1998, 2215.

24 M. J. Politi, O. Brandt and J. H. Fendler, *J. Phys. Chem.*, 1985, **89**, 2345.