Hydration of Acetaldehyde catalysed by Micellar Triton X-100 in Carbon Tetrachloride

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The spontaneous hydration of acetaldehyde by water and D_2O localized in micellar Triton X-100 in carbon tetrachloride is 1.5×10^4 and 5.4×10^4 times faster than that in bulk water and D_2O, respectively. In the presence of the surfactant, the rates of specific acid-catalysed hydration are between 2.4—1.2 and 3.6—2 times faster than those of perchloric acid-catalysed reactions in bulk water and D_2O, respectively. The rates of the specific acid-catalysed hydration decrease as a function of increasing the concentration of the micelle solubilized water or D_2O.

CATALYSIS by micellar systems is being actively investigated as a model for enzymic catalysis.[1] The observed catalysis has been rationalized in terms of specific binding of the substrate to the micelle and reduction of the activation free energy by electrostatic and hydrophobic interactions.[1,2] In non-aqueous solvents, certain surfactants form ' reversed ' or ' inverted ' micelles.[2] The structure of these reversed micelles is such that the surfactant hydrophilic groups are packed around a polar micellar interior or ' core ' and the hydrophobic tails are in contact with the non-aqueous solvent.[3] Recent results showed that reversed micelles can provide significant information on bio-organic as well as organic reaction mechanisms.[2,4]

The non-ionic surfactant Triton X-100 is used extensively in the assay and purification of enzymes.[5] In some cases it changes the enzymic activity by changing the physical state of the substrate.[6] Little work has been done on catalysis by non-ionic surfactants especially

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[1] E. H. Cordes and C. Gitler, *Bio-org. Chem.*, 1973, **2**, 1; C. A. Bunton, *Progr. Solid-State Chem.*, 1973, **8**, 239.

[2] J. H. Fendler and E. J. Fendler, ' Catalysis in Micellar and Macromolecular Systems,' Academic Press, New York, 1975.

[3] F. M. Fowkes, ' Solvent Properties of Surfactant Solutions,' ed. K. Shinoda, Dekker, New York, 1967.

[4] C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J. Org. Chem.*, 1973, **38**, 3371; *J. Amer. Chem. Soc.*, 1974, **96**, 370; *J.C.S. Dalton*, 1974, 625; W. Hinze and J. H. Fendler, *ibid.*, 1975, 238; J. H. Fendler, F. Nome, and H. C. Van Woert, *J. Amer. Chem. Soc.*, 1974, **96**, 6745.

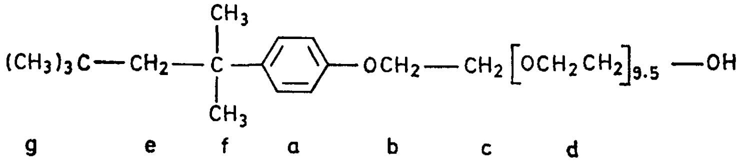
[5] E. A. Dennis and E. P. Kennedy, *J. Lipid Res.*, 1970, **11**, 394; 1972, **13**, 263; W. T. Wickner and E. P. Kennedy, *Fed. Proc.*, 1971, **30**, 1119.

[6] G. H. De Haas, P. O. M. Bonsen, W. A. Pieterson, and L. L. M. Van Deenen, *Biochim. Biophys. Acta*, 1971, **239**, 252.

in non-aqueous solvents.[2] In order to shed more light on the magnitude and mechanism of catalysis by these detergents, the hydration of acetaldehyde in the presence of micellar Triton X-100 in carbon tetrachloride was studied. The choice of this reaction was due to the availability of rate and equilibrium data,[7] and because of the demonstrated importance of substrate hydration in some enzymic reactions.[8]

RESULTS

Triton X-100 is a polydisperse of *p*-t-octylphenoxypolyethoxyethanols (I) with an average chain length of 9—10 oxyethylene units.[9] The ^1H n.m.r. spectrum of a 0.8M solution in carbon tetrachloride shows δ 6.929 (q, *J* 8.6 Hz, ArH), 3.966 (m, CH_2^b), 2.534 (apparent s, $H^{c,d}$), and 1.642, 1·276, and 0.668 (3s, H^{e-g}).



(I)

Acetaldehyde is hydrated in water according to equation (1) where k_h and k_d are the hydration and dehydration rate

$$CH_3CHO + H_2O \underset{k_d}{\overset{k_h}{\rightleftharpoons}} CH_3CH(OH)_2 \qquad (1)$$

constants respectively. The reaction exhibits both general acid and general base catalysis.[7] The ^1H n.m.r. spectrum of aqueous acetaldehyde shows two doublets for the methyl groups of the acetaldehyde and its hydrate as well as two quartets for the CH_3CHO and $CH_3CH(OH)_2$ protons. Hydration and dehydration rate constants can be determined from the linewidth variations of the methyl groups of the aldehyde and its hydrate according to the theory for species exchanging slowly on the n.m.r. time scale and by employing

$$\pi\Delta\nu_{\frac{1}{2}} = \pi\Delta\nu_{\frac{1}{2}}^0 + k_h^\circ(H_2O) + k_h(H^+) \qquad (2)$$

equation (2).[10] Here $\Delta\nu_{\frac{1}{2}}$ and $\Delta\nu_{\frac{1}{2}}^0$ denote the full width at half height of the peak that is being followed (CH_3 group) in the presence and absence of exchange respectively. An equivalent equation can be written for the dehydration reaction except that k_d replaces k_h. Note also that equation (2) is for specific acid catalysis and more terms can be added for the general acid–base catalysis. The equilibrium constant can be determined either from the expression $K = k_h/k_d$ or from the ratio of peak heights of the methyl groups. In a mixture of 0.3M-acetaldehyde and 1.5M-D_2O in 0.8M-Triton X-100 in carbon tetrachloride neither the hydrate doublet nor the $CH_3CH(OH)_2$ proton could be seen because of the strong surfactant absorption. It was only possible, therefore, to calculate k_h. Figures 1 and 2 show representative plots for calculating the spontaneous and specific acid catalysed hydration rates according to equation (2). The effect of water and/or D_2O concentrations on k_h for the specific acid catalysis is shown in Table 1.

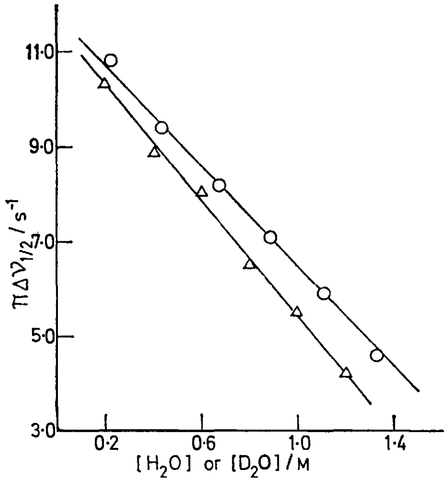


FIGURE 1 Plots of $\pi\Delta\nu_{\frac{1}{2}}$ for the methyl group of acetaldehyde against micelle solubilized water, ○, or D_2O, △, concentration

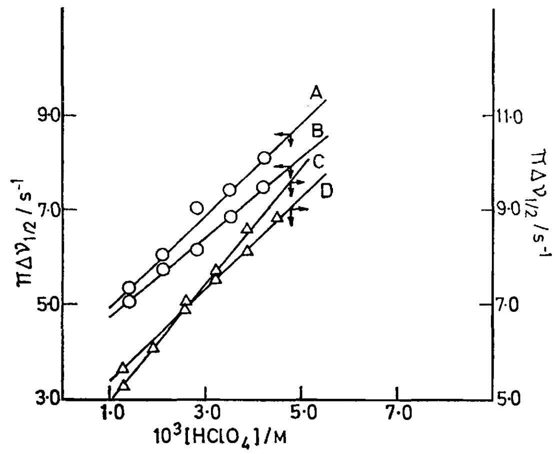


FIGURE 2 Typical plots of $\pi\Delta\nu_{\frac{1}{2}}$ against perchloric acid concentrations at different total water and D_2O. Line A, specific acid catalysis for 1.11M-water; B, for 1.33M-water; C, for 1.0M-D_2O; D, for 1.4M-D_2O

Table 1 shows that the spontaneous hydration is *ca.* 10^4 times faster in the presence of micelle solubilized water and D_2O than in bulk aqueous solvents. Extrapolating the lines in Figure 1 to aqueous concentrations of 55.5M and 50M (molarity of water and D_2O, respectively) yields rate constants that are 81 and 318 times faster than those in water and D_2O at the same temperature. The rates of hydration by micelle solubilized perchloric acid are 2.4—1.2 times

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[7] R. P. Bell, *Adv. Phys. Org. Chem.*, 1966, **4**, 1 and references therein.

[8] D. R. Trentham, C. H. McMurray, and C. I. Pogson, *Biochem. J.*, 1969, **114**, 19; S. J. Reynolds, D. W. Yates, and C. I. Pogson, *ibid.*, 1971, **122**, 285.

[9] 'Rohm and Haas Surfactants, Handbook of Physical Properties, CS-16 G/cd,' Rohm and Haas, Philadelphia, p.6.

[10] P. G. Evans, G. R. Miller, and M. M. Kreevoy, *J. Phys. Chem.*, 1965, **69**, 4325; J. Hine and J. G. Houston, *J. Org. Chem.*, 1965, **30**, 1328; V. S. Griffiths and G. Socrates, *Trans. Faraday Soc.*, 1976, **63**, 673.

faster than those of aqueous acid and 3.6—2 times faster than those catalysed by D^+ in D_2O. Micellar acid-catalysed rates decrease as a function of increasing water and/or D_2O concentration as shown in Table 1.

TABLE 1

Second order rate constants for the spontaneous and specific acid catalysed hydration of acetaldehyde [a,b]

Catalyst	Solvent	t/°C	k_h^0 or k_h	Ref.
H_2O	H_2O	0	1.3×10^{-5}	*j*
		25	1.4×10^{-4}	*k*
		36 [c]	3.6×10^{-4}	
D_2O	D_2O	0	4×10^{-6}	22
		36 [d]	1.1×10^{-4}	
$HClO_4$	H_2O	26	605	10
$HClO_4$	H_2O	36	625 ± 30,	This work
H_2O–Triton	CCl_4	36	5.4 ± 0.3 [e]	This work
D_2O–Triton	CCl_4	36	6.0 ± 0.2 [e]	This work
H^+, H_2O–Triton	CCl_4	36	$1\,500 \pm 70$, [f,g]	This work
			$1\,260 \pm 53$,	
			982 ± 71,	
			860 ± 39	
			730 ± 36	
D^+, D_2O–Triton [h]	CCl_4	36	$1\,750 \pm 110$, [i]	This work
			$1\,383 \pm 42$,	
			$1\,281 \pm 18$,	
			$1\,089 \pm 41$,	
			979 ± 30	

[a] In l mol^{-1} s^{-1}. [b] Concentrations: acetaldehyde 0.3M, Triton X-100 0.8M. [c] Calculated from data at 0 and 25°. E_a 64.8 kJ mol^{-1}. [d] Calculated from data at 0°, E_a is that of hydration in water. [e] Extrapolation to 55.5M-water and 50M-D_2O yields $k_h^\circ = 2.92 \times 10^{-2}$ and 3.5×10^{-2} l mol^{-1} s^{-1}, respectively. [f] Total water concentrations are 0.667, 0.889, 1.11, 1.33, and 1.55M. [g] The rate constant ranges are the standard deviations. [h] Prepared by adding Baker AnalaR perchloric acid to D_2O (99.8% D). [i] Total D_2O concentrations are 0.6, 0.8, 1.0, 1.2, and 1.4M. [j] R. P. Bell and B. de B. Darwent, *Trans. Faraday Soc.*, 1950, **46**, 34. [k] R. P. Bell, M. H. Rand, and K. M. W. Wynne-Jones, *Trans. Faraday Soc.*, 1956, **52**, 1093.

DISCUSSION

By analogy with other nonionic surfactants formed by alkylphenol–polyoxyethylene adducts, for example the Igepal series detergents,[11,*] Triton X-100 forms small aggregates in non-aqueous solvents. An operational critical micelle concentration (c.m.c.) can be determined from breaks in the graph of the chemical shifts of the surfactant discrete protons *versus* its concentration. In dry carbon tetrachloride this c.m.c. value is *ca.* 0.32M and hence kinetic runs were carried out at surfactant concentrations well above the c.m.c. The aggregation of the surfactant can be represented by the stepwise association (3); water solubilization decreases the c.m.c. and increases the % of higher aggregates.[12]

$$\text{monomer} \rightleftharpoons \text{dimer} \rightleftharpoons \text{trimer} \rightleftharpoons \text{-----} \quad (3)$$

Below the c.m.c. value, Triton X-100 solubilizes very little water (<0.1M) whereas above 0.3M the solubility increases noticeably. For example 0.5M-surfactant dissolves 0.61M-water, 0.6M dissolves 0.89M-water, 0.7M dissolves 1.17M-water, and 0.8M dissolves up to 2.0M-water. Micelle solubilized water and/or aqueous acids can be pictured as confined in the micellar core in the form of an aqueous pool surrounded by the surfactant ether oxygen atoms. Chemical shifts of the surfactant protons substantiate this assumption; the results are in Table 2. Only the (CH_2CH_2O) protons shift downfield as a function of added water, D_2O, and/or acid solutions and the shift is higher for water than for D_2O. Solubilization of acetaldehyde by the micellar surfactant can be represented by equation (4) where M represents the micelle,

$$\text{Acetaldehyde} + \text{M} \overset{K}{\rightleftharpoons} \text{Acetaldehyde–M} \quad (4)$$

and K is the acetaldehyde–surfactant association constant. The latter can be calculated from the chemical shift of the solubilizate discrete protons, *e.g.* the CHO proton, as a function of the surfactant concentration according to known procedures.[13,†] From the computed K value (64.5 ± 5 l mol^{-1}), the acetaldehyde concentration in the micellar phase was estimated to be 0.26M. Any contribution from the fraction of acetaldehyde in the solvent to the observed line broadening *i.e.* to the observed hydration can be ruled out because of the negligible solubility of water in carbon tetrachloride.[15] More importantly, the linewidth of the acetaldehyde doublet (concentration 0.3M) was practically constant whether the solvent was dry, or whether it was pre-equilibrated with water and/or with 10^{-3}M-perchloric acid. The preceding discussion shows that acetaldehyde partitions in favour of, and hydrates in, the micellar pseudo-phase.

It has been shown that both macroscopic and microscopic polarities of micelle solubilized water are quite different from those in bulk water.[4,16,17] Moreover the apparent pK_a for several indicators such as Bromophenol Blue and Thymol Blue are much lower in the reversed micelle of Igepal CO-530 (a detergent similar to Triton X-100) than in bulk water.[18] It is also possible that the surfactant itself is protonated since the apparent pK_a value decreases as the Igepal : water ratio increases.

The foregoing discussion shows the unique properties of the aqueous pools entrapped in the micellar core. It is possible that the enhanced spontaneous hydration is due to greater water activity in the core. The decreased

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[*] Comparison of the properties of Triton X-100 with those of the Igepal surfactants is valid. Both surfactants are alkylphenol–ethyleneoxy adducts. Provided that the number of the ethyleneoxy units is the same, both series show identical properties in non-aqueous solvents, *e.g.* c.m.c., water solubilization, *etc.* In addition, Igepal CO-530 catalyses the spontaneous and specific acid hydration of acetaldehyde in carbon tetrachloride.[12]

[†] In calculating K one needs to know the surfactant concentration in the micellar form by using the equation[2] $[M] = (C_D - \text{c.m.c.})/N$ where C_D is the total surfactant concentration, and N is its aggregation number. Following the published procedure for aggregates in non-aqueous solvents,[14] the latter was found to be 4.

[11] P. S. Shieh and J. H. Fendler, personal communication.

[12] O. A. El Seoud, unpublished results.

[13] R. Foster and C. A. Fyfe, *Trans. Faraday Soc.*, 1965, **61**, 1626; W. R. Carper, C. M. Buess, and G. R. Hipp, *J. Phys. Chem.*, 1970, **74**, 4229.

[14] O. A. El Seoud, E. J. Fendler, J. H. Fendler, and R. T. Medary, *J. Phys. Chem.*, 1973, **77**, 1432, 1876.

[15] A. Seidel, 'Solubilities of Organic Compounds,' Van Nostrand, New York, 1941.

[16] F. M. Menger, J. A. Donohue, and R. F. Williams, *J. Amer. Chem. Soc.*, 1973, **95**, 286.

[17] F. M. Menger, G. Saito, G. V. Sanzero, and J. R. Dodd, *J. Amer. Chem. Soc.*, 1975, **97**, 909; J. H. Fendler and L. J. Liu, *ibid.*, p. 999.

[18] F. Nome, S. A. Chang, and J. H. Fendler, personal communication.

rates as a function of increasing water concentration can be due either to a decrease in water activity or simply to dilution of the fraction of acetaldehyde in the micellar core. Alternately, although less likely, when more water is added acetaldehyde is squeezed out of the core and the rate drops. The magnitude of acid catalysis is only modest; however the surfactant can also compete for the protons [18] as shown from Table 2. The decreased k_h values as a function of increasing water or D_2O can be rationalized as for the case of the spontaneous hydration.

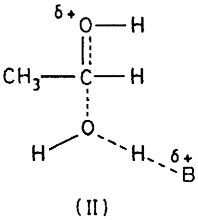
TABLE 2

Chemical shifts of the (CH_2CH_2O) protons of Triton X-100 as a function of water, D_2O, and acid concentration.[a–c]

$[H_2O]$M	$\Delta\delta$/Hz [d]	$[D_2O]$M	$\Delta\delta$/Hz	$10^3[H^+, H_2O]$/M [e]	$\Delta\delta$/Hz	$10^3[D^+, D_2O]$/M [e]	$\Delta\delta$/Hz
0.56	1.0	0.5	0.6	1.4	0.4	1.3	0.2
0.83	1.4	0.75	0.9	2.8	0.8	2.6	0.4
1.11	1.7	1.0	1.2	4.2	1.2	3.8	0.7
1.39	2.0	1.25	1.6	5.6	1.4	5.1	0.9
1.67	2.3	1.5	1.8	7.0	1.6	6.4	1.2

[a] Temperature 31 ± 0.5°. [b] Triton X-100 0.8M in carbon tetrachloride. [c] Chemical shifts for the other protons were constant to ±0.2 Hz. [d] $\Delta\delta$ = Chemical shift in the presence of additive — chemical shift in its absence. Initial chemical shift is 353.4 ± 0.2 Hz. [e] Perchloric acid concentrations are in mol l^{-1} of the solution.

In order to check the similarities between the mechanism of the micellar hydration and that in bulk water the solvent isotope effect was investigated. The observed k_{D_2O}/k_{H_2O} values are *ca.* 1.1—1.2 for both spontaneous and acid-catalysed hydration. These results are in accord with a pre-equilibrium protonation of the aldehyde followed by slow attack of water, a mechanism similar to that proposed for hydration in bulk water.[19] The mechanism of the micellar acid-catalysed reaction can, therefore, be depicted as in (5) and (6). The protonation reaction (5) is fast and the transition state for the rate limiting reaction (6) can be pictured as (II) where B



(II)

$$CH_3CHO + H^+ \rightleftharpoons CH_3CH\overset{+}{O}H \qquad (5)$$

$$B + CH_3CH\overset{+}{O}H + H_2O \rightleftharpoons CH_3CH(HO)_2 + BH \qquad (6)$$

is another molecule of water or the surfactant ether oxygen atom. A similar mechanism involving slow attack of water, or concerted attack of several water molecules, and the participation of the surfactant ether oxygen can be written for spontaneous hydration. On the bases of the slow step depicted above one expects a faster reaction in the case of D_2O and the observed solvent isotope ratio is not far from the expected value of 1.4.[20]

EXPERIMENTAL

Carbon tetrachloride (Merck; Uvasol; maximum water 0.005%) was further dried over activated Linde type 4A molecular sieve for several weeks. Acetaldehyde (Carlo Erba; pure) was distilled under a slow stream of dry, oxygen-free nitrogen and was kept over activated molecular sieve under nitrogen. Acetaldehyde stock solutions in CCl_4 were also prepared under pure nitrogen. No hydrate or any other impurity was detected in the ^1H n.m.r. spectrum of a 3.0M solution of the aldehyde in carbon tetrachloride immediately after preparation or after standing for several hours. Triton X-100 was a gift from Rohm and Haas Co., and was used as received. ^1H N.m.r. spectra were obtained on a Varian model XL-100 spectrometer equipped with a frequency counter and operating at 31 ± 0.5°. Chemical shifts were measured at 500 Hz sweep width and are given on the δ scale relative to internal tetramethylsilane; they are accurate to ±0.2 Hz. Linewidth measurements were obtained from spectra run at 50 Hz sweep width using a Varian T-60 spectrometer operating at 36 ± 0.5°.

Kinetic Measurements.—The reagent stock solutions in carbon tetrachloride were acetaldehyde 3.0M and Triton X-100 1.0M; both were renewed daily. Perchloric acid stock solutions in water and D_2O were 0.35 and 0.32M, respectively. Deuterium oxide (99.8% D; Aldrich; Gold Label) and doubly distilled water were used throughout.

Duplicate runs were carried out as follows. The required volumes of water, D_2O, or acid were added by a microsyringe to several 1 cm^3 volumetric flasks. This was followed by adding Triton X-100 (0.8 cm^3) and acetaldehyde (0.1 cm^3) stock solutions. The mixtures were made up to the mark with dry CCl_4, then shaken, and samples (0.5 cm^3) transferred quickly to the n.m.r. tubes. After equilibration to the T-60 ambient probe temperature (*ca.* 10 min) spectra were recorded under conditions where no peak saturation was observed. The spectrometer was tuned onto the acetaldehyde doublet and each spectrum was recorded by sweeping slowly through this doublet from both directions at least three times. For comparison purposes the resonance line of the surfactant t-butyl group was also recorded. Individual linewidths are accurate to better than ±0.1 Hz. Linewidths of the surfactant t-butyl group were unaffected (±0.1 Hz) by the addition of acetaldehyde, water, or aqueous acid solutions.

In the case of spontaneous hydration, linewidths as a function of increasing water or D_2O concentration were measured. Reciprocal life times ($\pi\Delta\nu_{\frac{1}{2}}/s^{-1}$) were then calculated and second-order rate constants were obtained from graphs of $\pi\Delta\nu_{\frac{1}{2}}$ against the molar concentration of water or D_2O [equation (2), Figure 1]. Second-order rate constants for the specific acid-catalysed hydration were obtained from the slope of graphs of $\pi\Delta\nu_{\frac{1}{2}}$ against the acid concentration

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[19] L. C. Gruen and P. T. Mctigue, *J. Chem. Soc.*, 1963, 5224.

[20] Y. Pocker, *Proc. Chem. Soc.*, 1950, 17.

(Figure 2). In the latter case the acid concentration was varied but the total water and/or D_2O concentration was kept constant. Statistical analysis of the results was carried out on a Hewlett–Packard model 9820A programmable calculator.

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