Catalysis by Reversed Micelles in Nonpolar Solvents. Mutarotation of 2,3,4,6-Tetramethyl-α-D-glucose in Benzene and in Cyclohexane[1]

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Abstract: Micellar dodecylammonium propionate (DAP), dodecylammonium benzoate (DABz), and dodecylammonium butyrate (DAB) enhance the rate of 2,3,4,6-tetramethyl-α-D-glucose mutarotation in benzene at 24.6° by factors of 380, 457, and 688, respectively. The corresponding rate enhancement by DAP in cyclohexane is 863. These micellar catalyses are considerably greater than those due to hydronium ions or water in aqueous solutions. Kinetic analysis of the data suggests that the extent of binding between 2,3,4,6-tetramethyl-α-D-glucose and these micellar surfactants parallels their catalytic efficiencies. Proton nmr investigations of the chemical shifts due to the protons of the surfactants as functions of 2,3,4,6-tetramethyl-D-glucose concentration provided evidence for strong interactions between the hydrophilic groups of the micellar surfactants and 2,3,4,6-tetramethyl-D-glucose solubilized in the core of the "reversed" micelles.

Rates of reactions in the presence of aqueous micellar surfactant solutions have been extensively studied and reviewed.[2-5] The structural similarities between globular proteins and spherical micelles and the analogies between enzymatic and micellar catalysis[2-4] have prompted recent investigations of micellar systems as possible models for the micro environment of the active site of enzymes. Although in some cases the kinetics for micellar catalysis obey the Michaelis–Menten equation and competitive inhibition has been observed, micelles in aqueous solutions rarely enhance the rates of reactions by factors greater than 10^2 and show relatively limited substrate specificity.[2-4] Micelles, unlike enzymes, are in a dynamic equilibrium with the monomeric surfactant and have comparatively mobile structures in water.[6] Additionally, micelles, unlike enzymes, do not bind the substrate in a rigid configuration with a specific orientation. It appears, therefore, that the aqueous micellar systems investigated to date provide somewhat poorer models for enzymatic interactions than originally anticipated.

Recent approaches to enhancement of the catalytic power of aqueous micelles included the attachment of the substrate and/or a catalytic group to the surfactants forming the micelle, *i.e.*, the study of functional micelles[7-10] and the examination of multiply charged detergents[11] as analogs to flexible chain polymers carrying a large number of ionic groups attached to the macromolecular backbone.[5] Since the active sites of many enzymes are in a relatively hydrophobic environment and since X-ray crystallographic studies indicated ion-pair and hydrogen-bonding interactions in polar regions of some proteolytic enzymes,[12,13] model studies in apolar solvents [14] and at interfaces[15] have provided a better understanding of the mechanisms involved. The hydrolysis of *p*-nitrophenyl dodecanoate has recently been examined in hexanol systems containing water and hexadecyltrimethylammonium bromide under conditions where formation of micelles, "reversed" micelles, and liquid crystalline phases have been demonstrated.[16,17] Rate accelerations of *ca.* 20-fold have been found in the regions where water is solubilized in the polar interior of the reversed micelle. This rate enhancement was analogous to that observed previously for the reaction of *p*-nitrophenyl dodecanoate in *aqueous* micellar hexadecyltrimethylammonium bromide solution[18] indicating that solubilization of the hydrolyzing agent results in catalytic efficiency similar to that for substrate solubilization. An alternative approach is to rely exclusively on the solubilization of polar substrates in the hydrophilic interior of reversed micelles in two-component (surfactant, apolar solvent) systems. Such reversed micelles contain the charged hydrophilic groups in their interior while the hydrophobic hydrocarbon portion of the surfactants form the outer layer of the micelle in contact with the nonpolar solvent.[6,19,20] The size of these reversed micelles is generally considerably smaller than that of micelles in water.[19,20] It is not too unreasonable,

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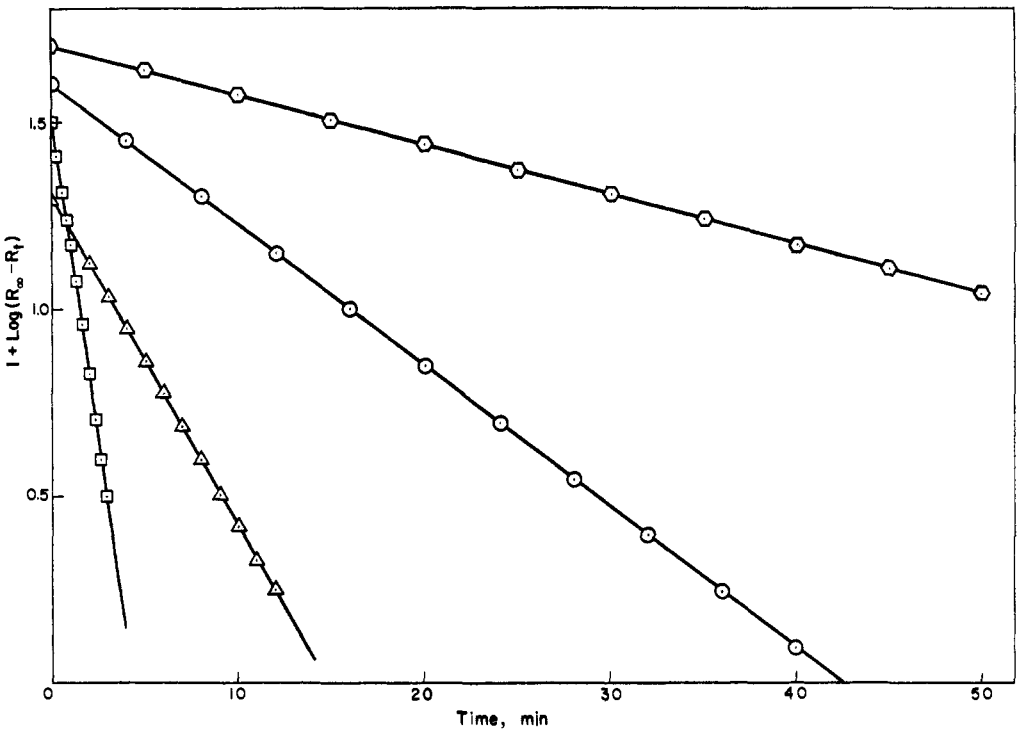

Figure 1. Typical plots of log ($R_\infty - R_t$) *vs.* time for the mutarotation of 1.7×10^{-2} *M* 2,3,4,6-tetramethyl-α-D-glucose at 24.6°: ⊙, 1.00×10^{-2} *M* HCl in water; ⊙, 1.00×10^{-3} *M* DAP in benzene; △, 3.00×10^{-3} *M* DABz in benzene; ⊡, 1.00×10^{-3} *M* DAP in cyclohexane.

therefore, to assume that the polar interior of reversed micelles is correspondingly smaller and consequently polar substrates solubilized therein would be held more rigidly than substrates in aqueous micelles. To test these hypotheses we have initiated structural and kinetic investigations of a variety of reactions in the presence of reversed micelles in nonpolar solvents.

The expected favorable partitioning of 2,3,4,6-tetramethyl-α-D-glucose between the polar micellar and apolar bulk phases as well as the significance of bifunctional catalysis for its mutarotation rate by 2-pyridone in benzene[21-24] led us to initiate our investigations with a study of this reaction. We observed no micellar, bifunctional, or micelle-induced bifunctional catalysis of the mutarotation in water. We observed, however, substantial rate accelerations of this reaction by reversed micelles in apolar benzene and cyclohexane.

Experimental Section

Reagent grade benzene (<0.02% water) and cyclohexane were dried and stored over Linde Type 5A molecular sieve.

2,3,4,6-Tetramethyl-α-D-glucose was prepared by a slightly modified procedure of West and Holden.[25] It was found advantageous to carry out the entire procedure as rapidly as possible which was facilitated by vacuum rotary evaporation of the chloroform solution from the final extraction, to extract with at least six portions of chloroform in both cases, and to stop the procedure, if necessary, after the first chloroform extractions and store the solution at *ca.* 0° overnight. Three different samples were used which differed slightly in melting point and specific rotation but not in the rate of mutarotation, presumably due to different amounts of the β isomer.

Dodecylammonium propionate (DAP) and dodecylammonium butyrate (DAB) were prepared by the method of Kitahara.[26] After at least two recrystallizations from hexane, DAP melted at 54.5–56.9° (lit.[20] 54–56°), and after at least four recrystallizations from hexane, DAB melted at 40–41.5° (lit.[26] 39–41°). Dodecylammonium benzoate (DABz) was prepared analogously,[27] but the procedure was modified in that the crystalline salt was washed with reagent grade acetonitrile in order to remove any free benzoic acid after which a melting point of 38–40° (lit.[27] 40–42°) was obtained. The surfactants were dried *in vacuo* over P_2O_5 for at least 12 hr immediately prior to making up the stock solutions in benzene or cyclohexane.

The spectrophotometric determinations of the critical micelle concentrations were carried out on a Beckman DU spectrophotometer by measuring the absorbance of the surfactant at an appropriae wavelength as a function of its concentration. The wavelengths used were 218 nm for DAP and DAB in cyclohexane and 271 nm for DABz in benzene. Blank solutions were identical with those of the sample minus the surfactant.

Rates for the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose were followed in 50-mm thermostated cells using a Bendix automatic recording polarimeter. Pseudo-first-order rate constants for the mutarotation, k_ψ ($k_\psi = k_{forward} + k_{reverse}$), have been calculated from linear plots of log [$R_\infty - R_t$) *vs.* time. Such typical plots are illustrated in Figure 1.

The 60-MHz proton nuclear magnetic resonance spectra were obtained on Varian Associates T-60 and modified A-60 spectrometers; those at 100 MHz were obtained on a modified Varian Associates HA-100 spectrometer with a Hewlett-Packard Model 200 ABR audio oscillator and frequency counter. Each spectrum was recorded at least three times after equilibration to ambient probe temperature (HA-100, 32°; A-60, 42.5°; T-60, 32°) or to the desired temperature (26, 34, and 37.5°), maintained with a V6040 variable-temperature controller on the A-60 spectrometer. All spectra were determined on freshly prepared solutions in benzene, benzene-d_6, or cyclohexane and were measured relative to a 10% solution of tetramethylsilane (TMS) in chloroform contained in a sealed capillary inserted in the tube (at 60 MHz) or in a Wilmad 520-2 internal coaxial capillary tube (at 100 MHz). No difference between the two types of standards could be detected at 60 MHz. Chemical shifts were generally obtained from spectra recorded at 100-Hz (T-60 and A-60) and 250-Hz (HA-100) sweep widths and are given on the δ scale in parts per million relative to the "external" TMS (δ = 0 ppm). Individual measurements are accurate to

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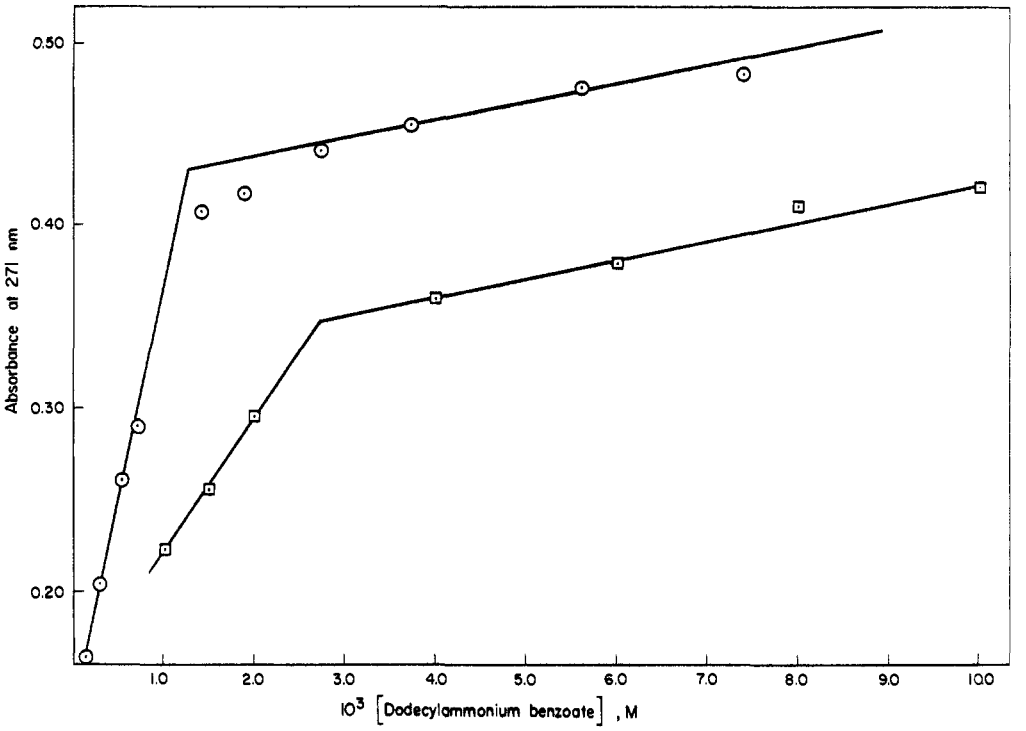

Figure 2. Cmc plots of the absorbance of DABz at 271 nm as a function of its molar concentration in the absence (⊡) and the presence (⊙) of 1.7×10^{-2} *M* 2,3,4,6-tetramethyl-D-glucose.

±0.01 at 100 MHz and ±0.02 at 60 MHz. The samples used for determination of the 2,3,4,6-tetramethyl-D-glucose concentration dependence of the surfactant chemical shifts contained mutarotated 2,3,4,6-tetramethyl-α-D-glucose, *i.e.*, an equilibrium mixture of the α and β isomers.

Results

Critical Micelle Concentrations. Critical micelle concentrations, cmc's, have been determined from the discontinuity in plots of the uv absorbance or the proton magnetic resonance frequency of the CH_2 protons *vs.* surfactant concentration. The lack of higher wavelength absorption maxima coupled with the absorption due to benzene limited the spectrophotometric cmc determinations to DABz in this solvent. Addition of 1.7×10^{-2} *M* 2,3,4,6-tetramethyl-D-glucose lowers the critical micelle concentration of this surfactant by a factor of 2 (Figure 2). The cmc of DAP in cyclohexane has been determined similarly. Advantage has been taken of the breaks in plots of the CH_2 proton magnetic resonance chemical shifts as a function of concentration to determine cmc values for DAP, DAB, and DABz in benzene. Experimental limitations under our conditions precluded, however, the determination of cmc values below 10^{-3} *M*. We assumed, therefore, that 2,3,4,6-tetramethyl-α-D-glucose lowers the cmc values of DAP and DAB by the same factor as it does for DABz. Table I contains the cmc values of the surfactants in the apolar solvents in which the kinetic investigations have been carried out.

Kinetic Investigations of 2,3,4,6-Tetramethyl-α-D-glucose Mutarotation. Rate constants for the mutarotation of tetramethyl-α-D-glucose have been obtained in water at 24.6° (Table II). In order to avoid complications in the examination of the effects of micellar surfactants in water, the use of buffers or electrolytes has been avoided. Since the concentration of 2,3,4,6-tetramethyl-α-D-glucose was kept at 10^{-2} *M*, no appreciable deviations from previously reported rate constants[28] have been observed. pH values were

Table I. Critical Micelle Concentrations, Relative Rate Enhancements, and Substrate–Micelle Association Parameters

Surfactant	Solvent	Cmc, *M*[a]	k_m/k_0	K/N^b	K/N^c
DAP	Benzene	5.0×10^{-4}	380	390	417
DABz	Benzene	1.3×10^{-3}	457	325	429
DAB	Benzene	1.0×10^{-3}	688	420	780
DAP	Cyclohexane	1.7×10^{-4}	863	620	1130

[a] Determined or calculated values in the presence of 1.7×10^{-2} *M* 2,3,4,6-tetramethyl-D-glucose. [b] Calculated from eq 5; see Discussion. [c] Calculated from eq 4; see Discussion.

Table II. Mutarotation of 2,3,4,6-Tetramethyl-α-D-glucose in Water at 24.6° [a]

pH[b] or acid[b]	Catalyst	$10^4 k_\psi$, sec^{-1}
5.43		3.45
4.52		3.33
1.0×10^{-2} *M* HCl		3.68
1.0×10^{-1} *M* HCl		7.71
	Hydronium ion	43.1[c] (50.9)[d]
5.25	2.0×10^{-2} *M* CTAB[e]	2.95
5.35	4.0×10^{-2} *M* DDAPS[f]	3.13
5.60	1.0×10^{-2} *M* NaLS[g]	3.63
5.30	1.0×10^{-2} *M* 2-pyridone	4.08
5.23	1.0×10^{-2} *M* 2-pyridone + 2.0×10^{-2} *M* DDAPS	3.33

[a] Initial concentration of 2,3,4,6-tetramethyl-α-D-glucose = 1.7×10^{-2} *M*. [b] In the absence of any buffers or electrolytes. [c] Second-order rate constant, $(k_\psi - 3.4 \times 10^{-4}\ sec^{-1})/[HCl]$. [d] Taken from ref 28. [e] Hexadecyltrimethylammonium bromide. [f] 3-(Dimethyldodecylammonio)propane-1-sulfonate. [g] Sodium dodecyl sulfate.

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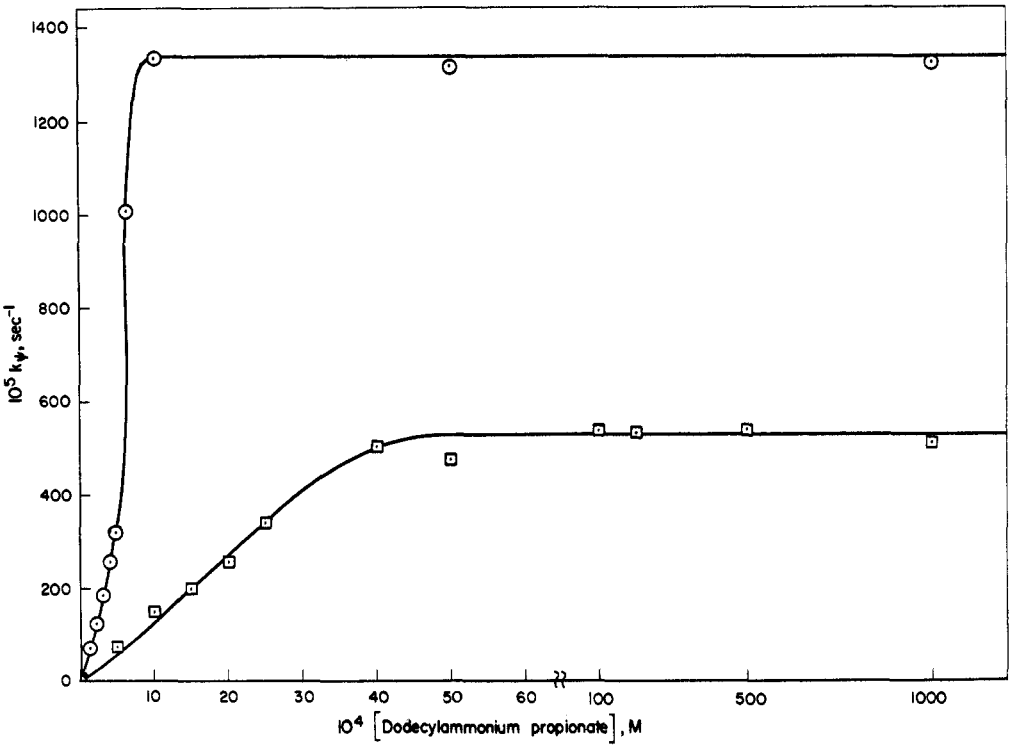

Figure 3. Pseudo-first-order rate constants for the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose in cyclohexane (⊙) and in benzene (⊡) at 24.6° as a function of DAP concentration.

monitored on the same solutions parallel with rate measurements. Those runs with greater than ±0.20 pH unit change were discarded. In agreement with previous postulates,[29] it is apparent that no bifunctional catalysis by 2-pyridone is observed in water. Mutarotation rates are equally unaffected by the presence of cationic, anionic, or zwitterionic micellar surfactants. The high solubility of 2,3,4,6-tetramethyl-α-D-glucose in water is likely to prevent its solubilization by the hydrophobic surfactants. This factor is presumably also responsible for the lack of micelle-induced bifunctional catalysis by 2-pyridone.

Rate constants for the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose in pure benzene or in pure cyclohexane showed only slight variations. The mean value in benzene at 24.6° ($k_\psi = 1.40 \times 10^{-5}$ sec^{-1}) agrees well with those given in the literature.[28] No appreciable change in this rate constant has been observed for the different preparations or for repeatedly repurified samples of 2,3,4,6-tetramethyl-α-D-glucose.

The formation of a complex between 2,3,4,6-tetramethyl-α-D-glucose and 2-pyridone in benzene has been substantiated by the observed abnormally high specific rotations in these solutions.[21] Since we used very low concentrations of 2,3,4,6-tetramethyl-α-D-glucose and since the half-life for the mutarotation in benzene or in cyclohexane in the presence of reversed micelles is very short, our attempts to determine specific rotations were unsuccessful.

The presence of surfactants capable of forming reversed micelles in apolar solvents enhance the rate of mutarotation substantially. Rate constants in the presence of DAP, DAB, and DABz in benzene are given in Table III and those in the presence of DAP in cyclohexane in Table IV. Figure 3 illustrates the catalysis by DAP in benzene and in cyclohexane.

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Table III. Mutarotation of 2,3,4,6-Tetramethyl-α-D-glucose in Benzene in the Presence of Surfactants at 24.6° [a]

10^4[surfactant], M	$10^5 k_\psi$, sec^{-1} DAP	DABz	DAB
0.00		1.40 (1.80)[b]	
0.10	1.80		
1.00	12.8		
5.00	73.6	134	
10.0	146	122	253
15.0	193	187	187
20.0	253	218	283
25.0	335	239	282
30.0	311	299	325
35.0	512	368	360
40.0	472		
50.0		429	601
60.0		700	
80.0		650	
100	556	680	980
200	525	630	963
500	553	640	953
1000	518	638	965

[a] Initial concentration of 2,3,4,6-tetramethyl-α-D-glucose = 1.7×10^{-2} M. [b] In "wet" (water-saturated) benzene.

Table IV. Mutarotation of 2,3,4,6-Tetramethyl-α-D-glucose in Cyclohexane in the Presence of DAP at 24.6° [a]

10^4[DAP], M	$10^5 k_\psi$, sec^{-1}	10^4[DAP], M	$10^5 k_\psi$, sec^{-1}
0.00	1.6	4.00	255
0.10	13.6	5.0	519
1.00	73.9	10.0	1340
1.50	207	50.0	1320
2.00	126	1000	1358
3.00	182		

[a] Initial concentration of 2,3,4,6-tetramethyl-α-D-glucose = 1.7×10^{-2} M.

Table V. Chemical Shifts of Detergents and Their Dependence on the Concentration of 2,3,4,6-Tetramethyl-D-glucose[a]

Surfactant	$-CH_3CH_2-$		$CH_3(CH_2)_nCO_2^-$		$-(CH_2)_n-$		$-(CH_2)_n-$		$-CH_2CO_2^-$		$-CH_2NH_3^+-$		$-ArH_{2,6}$		$-ArH_{3,4,5}$		$-NH_3^+$	
	δ_0	a	δ_0	a	δ_0	a	δ_0	a	δ_0	a	δ_0	a	δ_0	a	δ_0	a	δ_0	a
DAP	0.772[b]	+0.08[b]					1.14[b]	+0.16[b]	2.27[b]	+0.05[b]	2.60[b]	+0.84[b]					8.82[b]	−3.02[b]
										+0.16[b]	2.60	+0.75					8.77	−2.94
DAP[d]	0.343						0.700		1.83		2.21						8.83	
DAB	0.775	0,	0.94	−0.04,			1.14	0	2.28	0,	2.61	+0.82					8.76	−3.50
		+0.12		−0.06						−0.02								
DABz	0.775	0			0.890	+0.24	1.13	0			2.55	+0.97	8.25	−0.20			9.13	−4.17
																	9.12	
DABz[d]	0.275	0			0.417	0	0.625	0			2.08	+0.97	7.33	−0.15			8.59[b]	−4.05
DABz[f]	0.758	0			0.873	+0.29	1.12	0			2.53	+0.98	8.25	−0.09	7.11	0	9.29	−4.23
DABz[d,f]	0.278	0			0.427	+0.30	0.627	0,			2.07	+0.93	7.74	−0.12	6.63	0	8.73	−4.68
								+0.04										
DABz[g]											2.94	+0.43	8.12	+0.15	7.39	+0.13	9.30	−4.88

[a] At 100 MHz in benzene unless specified otherwise; see Experimenal Section for details. [b] [Detergent] = 0.50 M unless specified otherwise; [2,3,4,6-tetramethyl-D-glucose] = 0–1.0 × 10^{-1} M. [c] 0.51 M. [d] At 60 MHz. [e] Temperature dependent (t, °C, ν_0 Hz): 26.0, 520.5; 34.0, 518.5; 37.5, 515.5; 42.5, 514.0. [f] In benzene-d_6. [g] In cyclohexane.

The proton nmr chemical shifts of DAP, DAB, and DABz in benzene, benzene-d_6, and cyclohexane as well as their dependence on the concentration of mutarotated 2,3,4,6-tetramethyl-α-D-glucose are given in Table V.

Discussion

The catalysis of the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose by micelle-forming surfactants in apolar solvents is very similar to that generally observed in aqueous solutions.[2-4] The rate constant–concentration profile for each surfactant exhibits a sigmoidal dependence followed by a plateau (Figure 3). In the plateau region the rate constants for the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose in benzene in the presence of DAP, DABz, and DAB are factors of 380, 457, and 688 greater than those in the pure solvent. The rate enhancement by DAP in cyclohexane is a factor of 863. The magnitude of these rate enhancements is considerably greater than those generally observed in aqueous micellar systems.[2-4] It is also noteworthy that micellar effects in cyclohexane are considerably more pronounced than those in benzene. In fact, rates of mutarotation in cyclohexane in the presence of DAB and DABz became so rapid that, under our conditions, no reliable rate constants could be obtained. Our qualitative observation that the solubility of 2,3,4,6-tetramethyl-α-D-glucose is less in cyclohexane than in benzene suggests a more favorable partitioning between the polar micellar phase and the bulk apolar solvent in the former than in the latter.

The rate acceleration of the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose in benzene is not due to the presence of small amounts of water in the benzene, since the rate constant in "wet" benzene is only slightly greater than that in dry benzene (Table III). More significantly, k_ψ value in water at pH 5.43 (34.5 × 10^{-5} sec^{-1}) is smaller by factors of 15, 18, and 28 than that in benzene in the presence of micellar DAP, DABz, and DAB, respectively. Catalysis of the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose in benzene by DAP, DABz, and DAB at the beginning of the plateau is, in fact, factors of 210, 260, and 370 greater than that by hydronium ions in water. In cyclohexane the same factor is 3000. The present kinetic data clearly imply, therefore, that substrates oriented specifically in the polar regions of a nonpolar medium, a situation not too different from some enzyme–substrate systems,[12,13] can react faster than in completely aqueous environments.

The observed kinetic form of the catalysis suggests the possibility of evaluating the extent of the micelle–substrate binding as had been shown for many cases in aqueous micellar solutions.[2-4] If micelle–substrate association follows 1:1 stoichiometry, then the rate constant for the mutarotation in the bulk apolar solvent, k_0, and that in the polar micellar phase, k_m, is expressed by eq 1, where M, S, and MS represent the

$$\begin{array}{ccc} M + S & \overset{K}{\rightleftharpoons} & MS \\ \downarrow k_0 & & \downarrow k_m \end{array} \qquad (1)$$

micelle, substrate, and micelle–substrate complex, respectively, and K is the binding, or association, constant. The observed pseudo-first-order rate con-

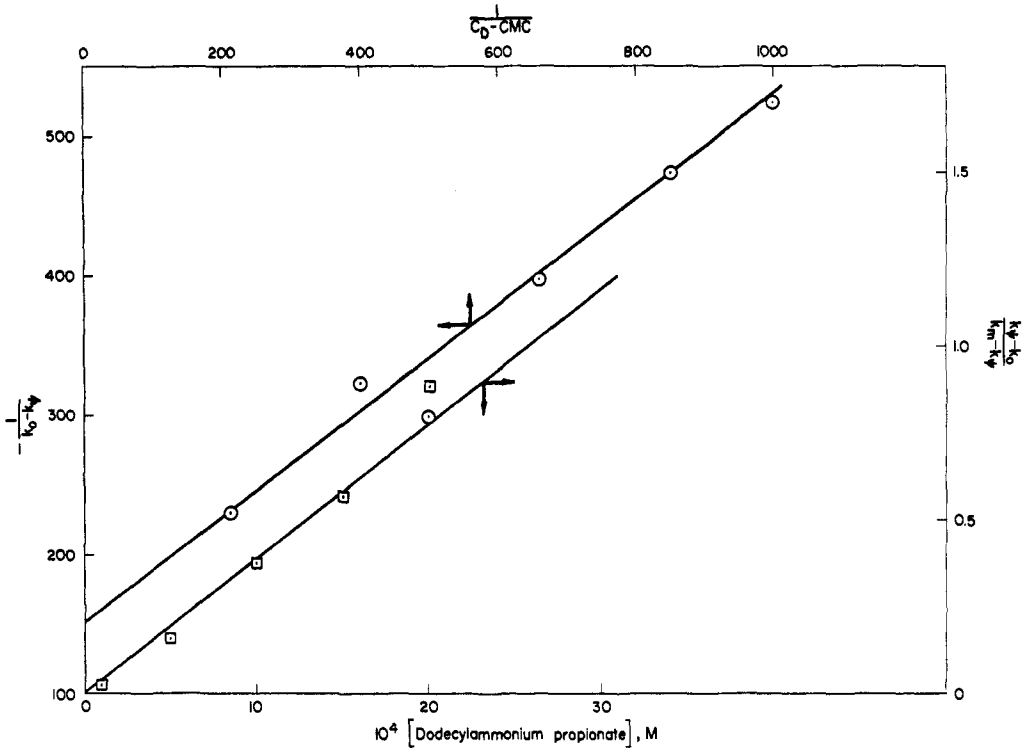


Figure 4. Micelle–substrate association (binding) constant plots for 2,3,4,6-tetramethyl-α-D-glucose (1.7×10^{-2} *M*) and DAP in benzene according to eq 4 (⊙) and eq 5 (⊡).

stant for the mutarotation, k_ψ, can be shown[2-4] to be described by

$$k_\psi = \frac{k_0 + k_m K[M]}{1 + K[M]} \quad (2)$$

where $[M]$ is the concentration of the micelles and is related to the stoichiometric concentration of the surfactant, C_D, the critical micelle concentration, cmc, and the aggregation number, N, by

$$[M] = (C_D - \text{cmc})/N \quad (3)$$

Combination of eq 2 and 3 and rearrangement gives

$$\frac{1}{k_0 - k_\psi} = \frac{1}{k_0 - k_m} + \frac{1}{k_0 - k_m}\left(\frac{1}{C_D - \text{cmc}}\right)\frac{N}{K} \quad (4)$$

Plots of the left-hand side of eq 4 against $1/(C_D - \text{cmc})$ should give straight lines from the slopes of which K/N can be calculated. All the surfactant systems gave reasonably good linear plots (Figure 4), indicating the validity of the assumptions[2-4] made in deriving eq 4. Perhaps it should be pointed out that this is the first instance in which association constants have been evaluated for substrate–micelle interactions in nonpolar solvents. It is likely, therefore, that the gross behavior of catalysis by reversed micelles is analogous to that by "normal" micelles formed in water.

An alternative rearrangement of eq 2 and 3 gives

$$\frac{k_\psi - k_0}{k_m - k_\psi} = \frac{K}{N}(C_D - \text{cmc}) \quad (5)$$

The advantage of eq 5 over eq 4 is that knowledge of the cmc is not required; plots of the left-hand side of eq 5 *vs.* C_D give straight lines with slopes of K/N. Its disadvantage is that only a limited range can be used, since erroneous values are obtained for points when $k_\psi \simeq k_0$ or when $k_\psi \simeq k_m$.[3] With these limitations, all systems gave good linear plots according to eq 5 (*e.g.*, see Figure 4). Considering the assumptions made in the derivation (4) and (5) and the inherent inaccuracies in cmc values, the agreement between the independently obtained K/N values are satisfactory (Table I). The order of increasing K/N values, DAP in benzene < DABz in benzene < DAB in benzene < DAP in cyclohexane, is the same using either eq 4 or 5, but the differences tend to be more pronounced as the magnitude of K/N increases (Table I). Reported values for the aggregation numbers of these surfactants in benzene and in cyclohexane range between 5 and 20.[19,20] If the assumption is made that the aggregation numbers of DAP, DAB, and DABz in benzene are not too dissimilar, then the obtained rate enhancements parallel the extent of interaction between 2,3,4,-6-tetramethyl-α-D-glucose and the surfactants (Table I). This relationship is most apparent in comparing the effects of DAP in benzene with that in cyclohexane. Considering the observed solubility behavior it is tempting, therefore, to propose that 2,3,4,6-tetramethyl-α-D-glucose binds to DAP more effectively in cyclohexane than in benzene.

Pronounced catalysis occurs at surfactant concentrations below the respective apparent critical micelle concentration (Tables I–III). For example, even 1.0×10^{-5} *M* DAP in cyclohexane causes an eightfold rate enhancement of the mutarotation of 2,3,4,-6-tetramethyl-α-D-glucose. The paucity of the available data on the possible formation of small aggregates below the cmc does not allow us to ascribe the catalysis to this factor or to the alternative effect of ion pairing by the monomeric surfactants.

In order to probe the interactions between the surfactants and 2,3,4,6-tetramethyl-D-glucose in benzene

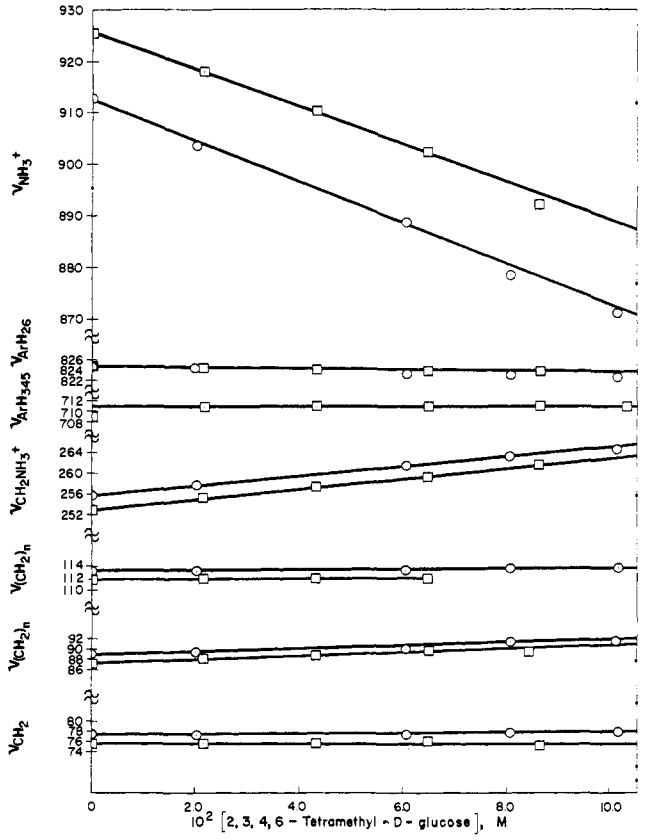


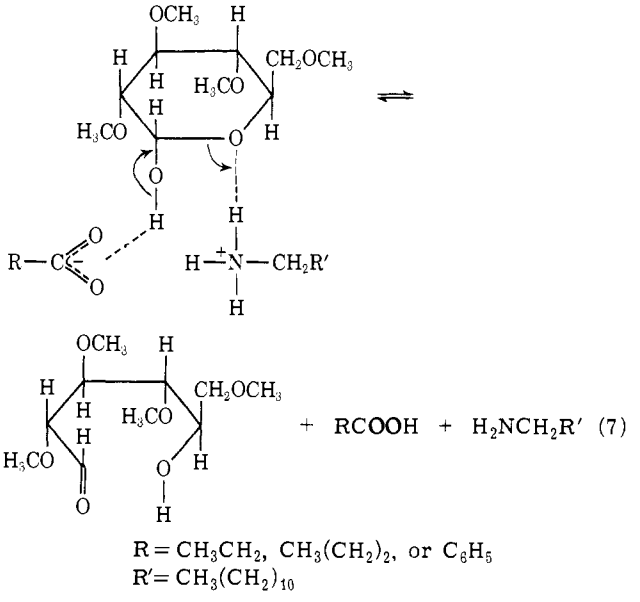
Figure 5. Plots of the observed chemical shifts (ν, Hz) at 100 MHz and 32° of 0.50 M DABz in benzene (○) and benzene-d_6 (□) as a function of the concentration of 2,3,4,6-tetramethyl-D-glucose.

and cyclohexane, we investigated the proton nmr spectra of these systems. The spectra of DAP and DAB in benzene consist of a fairly sharp triplet for the terminal methyl protons of the long hydrocarbon chain, an unresolved broad resonance for the intermediate methylene protons of the dodecylammonium ion, a broad NH_3^+ resonance, and multiplets for the protons of the methylene groups adjacent to the carboxyl and ammonium ions. A second upfield triplet is discernible in the spectra of DAB and can be ascribed to the terminal methyl protons of the butyrate ion (see Table V). The resonances for the dodecylammonium ion in the spectra of DABz are similar to those of DAP and DAB with the exception that the resonance for the intermediate methylene protons consists of two overlapping broad peaks (relative intensity *ca.* 8:8) which are possibly the consequence of shielding of the methylene protons closest to the ammonium ion by the π electrons of the benzoate ion. Well-resolved multiplets for the ortho and for the meta and para protons of the benzoate ion are observed in the spectra of DABz in benzene-d_6 and cyclohexane; however, that for the latter protons is obscured by the solvent in benzene. Likewise the upfield methyl and methylene resonances could not be observed in cyclohexane under our conditions. The chemical shifts (δ_0) of the proton resonances of DAP and DAB in benzene and of DABz in benzene, benzene-d_6, and cyclohexane are given in Table V.

The observed chemical shifts (δ) of the DAP, DAB, and DABz protons are linear functions of the concentration of added 2,3,4,6-tetramethyl-D-glucose, and consequently were fitted to the equation

$$\delta = \delta_0 + a[X] \quad (6)$$

where δ and δ_0 are the observed and limiting chemical shifts and X is the solubilizate. Values for a, the concentration dependence, were calculated from linear plots of δ *vs.* [2,3,4,6-tetramethyl-D-glucose], M (*e.g.*, see Figure 5). Similar concentration dependencies were found for organic compounds and substrates solubilized by "normal" micelles in aqueous systems.[30] This analogous, but reversed, proton nmr behavior in aqueous and nonpolar micellar systems, like the kinetic results, suggests that the basic mode of micellar catalysis is similar in the two media. It is apparent from Table V and Figure 5 that significantly large a values are found only for the protons immediately adjacent to the hydrophilic groups. Indeed, the magnitude of the a values for the protons of the micellar surfactants decreases with increased separation from the charged atom or atoms, *i.e.*, $NH_3^+ > H_3N^+-CH_2 > {}^-O_2C-CH_2$ or ${}^-O_2C-Ar(H_{26})$. Since the ammonium and carboxylate ions are oriented in the interior of the micellar pseudo-phase, these results (Table V and Figure 5) distinctly indicate that tetramethyl-D-glucose is solubilized in the hydrophilic micellar core in close proximity to these groups. On the other hand, for cases in which the organic additive is not solubilized in the micellar phase, *e.g.*, *p*-chloronitrobenzene, the a values for all of the surfactant protons are either negligible or very small.[31] By analogy, the hydrophilic micellar core does not incorporate the benzene or cyclohexane solvent. It is also highly probable, *via* hydrogen bonding and other interactions, that the sugar is held in a relatively rigid configuration in the micellar core or "cavity." Double hydrogen bonding has been proposed, based on activation parameters, in the bifunctional catalysis of the mutarotation of tetramethyl-α-D-glucose by 2-pyridone in benzene,[22,23] and this conclusion is strongly supported by recent CNDO/2 MO calculations.[32] The latter results



R = CH_3CH_2, $CH_3(CH_2)_2$, or C_6H_5
R′ = $CH_3(CH_2)_{10}$

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also indicate that the double hydrogen bond is stronger than two separate single hydrogen bonds. It is tempting to postulate that the mutarotation in the micellar core involves hydrogen bonding both between the dodecylammonium ion and the heterocyclic oxygen atom and between the 1-hydroxyl group and the carboxylate ion of the surfactant, thereby facilitating ring opening (eq 7). The large upfield shift observed for the ammonium protons as a function of tetramethylglucose concentration supports such a postulate. A functional catalytic mechanism of this type is consistent with the observed kinetic results if the ring opening reaction is rate determining and the surfactant *via* hydrogen bonding facilitates this step. The probability of double hydrogen bonding with the surfactant is predictably far greater in the core of the micellar phase than in the bulk solvent.

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Electrochemical Reduction of Pyrazine in Aqueous Media[1]

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Abstract: The reactions associated with the reduction of pyrazine (I) in aqueous media are highly dependent upon solution pH. In 1 *M* $HClO_4$ three polarographic waves are observed. The first two waves are successive reversible one-electron steps yielding the radical cation of 1,4-dihydropyrazine (II) and 1,4-dihydropyrazine (III), respectively. Controlled potential coulometry is characterized by a mass transport process with *n* values of 2.00 ± 0.01. A rapid and reversible reaction between I and III yielding II is observed at pH <2. The third wave is a catalytic hydrogen wave with a species derived from III serving as the catalyst. The decomposition of III is first order and is acid–base catalyzed. Above pH 2 a single diffusion-controlled two-electron reduction is observed. The reversibility of this wave decreases with increasing pH. Coulometric *n* values are dependent upon stirring rate, concentration of I, and pH. Functional group tests indicate that the decomposition of III involves ring opening at an N–C site yielding $H_2NCH{=}CHNHCH_2CHO$ (IV), which subsequently polymerizes. In phosphate buffers a polymer of $-CH{=}NCH_2-$ precipitates. Spectral evidence indicates that the carbonyl group of IV or a polymer of IV is reduced during exhaustive electrolysis. Uv data indicate the above mechanism is valid up to pH 7.

Of the three unsubstituted isomeric aromatic diazines, pyrimidine is the most thoroughly studied, probably because the purine, adenine, and other derivatives are of great importance in the biological sciences. Derivatives of pyrazine, some of which occur naturally, have found use as pharmaceuticals.[2] Pyridazine derivatives, none of which occur naturally, are used as antifungicidal agents for stored food stuffs. Other derivatives have found some use as pharmaceuticals.[3]

The redox behavior of these compounds has received modest attention. Elving and coworkers[4] have devoted considerable effort to the electrochemical reduction of pyrimidine and its derivatives. Detailed mechanisms have been presented for several compounds.[5] Fragmentary results for the reduction of pyrazine have been reported,[6-10] but these studies *in toto* are incomplete and contradictory. The work reported herein is a detailed investigation of the electrochemical reduction of pyrazine in well-buffered aqueous media.

Experimental Section

Pyrazine (I), Puriss grade from Aldrich Chemicals (Milwaukee, Wis.), was used without further purification. Uv and ir spectra confirmed its purity and identity. All other chemicals were reagent grade quality and used without further purification. Perchloric acid and phosphate buffers (C_{PO_4} = 0.37 *M*) were used to control pH. $NaClO_4$ was used to maintain the ionic strength of the final test solutions at 1.0.

Polarographic data were obtained with a stabilized Heath (Benton Harbor, Mich.) Polarographic System. For detailed wave-shape and half-wave potential studies the potential axis was expanded such that the cell potential could be read directly from the polarogram to the nearest 0.5 mV.

For cyclic voltammetric and chronoamperometric studies an all-solid-state operational amplifier potentiostat designed similar to the one reported by Smith, *et al.*,[11] was used. An X–Y recorder or

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