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Dephosphorylation in Cationic Micelles and Microemulsions. Effects of Added Alcohols

Clifford A. Bunton,* Francesco de Buzzaccarini, and Fareed H. Hamed

Department of Chemistry, University of California, Santa Barbara, California 93106

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Reaction of *p*-nitrophenyl diphenyl phosphate (pNPDPP) with OH^- in micelles of cetyltrimethylammonium bromide (CTABr) is inhibited by *tert*-amyl alcohol, which reduces the concentration of OH^- in the micelle. Reactivities in these micelles were compared with those in microemulsions containing 1-butanol or benzyl alcohol. *p-tert*-Butylphenoxide ion reacts with pNPDPP in microemulsions containing CTABr, *n*-octane, and *tert*-butyl alcohol, and the first-order rate constants depend on the concentration of phenoxide ion in the microemulsion droplets. Reaction of pNPDPP was also followed in microemulsions of hexadecyl(2-hydroxyethyl)dimethylammonium bromide (**2**), *tert*-amyl alcohol, and *n*-octane. It is faster than in a similar microemulsion containing CTABr but slower than reaction in aqueous micelles of **2**, because of decreased deprotonation of **2**.

Microemulsions are transparent dispersions that can form when a surfactant and a cosurfactant are mixed with oil and water. The cosurfactant is usually an alcohol, although amines can also act as cosurfactant, and oil-in-water (o/w) microemulsion droplets are believed to contain a hydrocarbon core surrounded by surfactant and cosurfactant.[1,2]

Microemulsions, both oil-in-water and water-in-oil, can change reaction rates.[4] In this respect they behave like micelles, and the factors that control chemical reactivity in micelles are also at work in microemulsions. The submiscroscopic aggregates can bring reactants together, or keep them apart, and they can also exert a medium effect. These factors have been analyzed in detail for micellar reactions, and similar treatments are being applied to reactions in microemulsions.[5-7]

Micelle and microemulsion droplets can be regarded as pseudophases, which provide a reaction medium distinct from that of bulk solvent.[8] Their surfaces seem to be similar. For example, they are both somewhat less polar than water, on the basis of spectroscopic estimates of dielectric constant or other solvent parameters, and the reactivity of water molecules at their surfaces is only slightly lower than that of bulk water.[5,6,9-13]

As reaction media, microemulsions have the major advantage over micelles that they can incorporate relatively large amounts of added solute. In addition, the alcohol cosurfactant can be a good nucleophile at high pH.[5,7b]

In this work we used various microemulsions, some containing a functional surfactant. Micelles and comicelles of functional surfactants have been used extensively in nucleophilic addition and substitution.[9,10,14]

The hydroxyl group of the functional surfactants **1** is an effective nucleophile in dephosphorylation, deacylation, and nucleophilic addition at high pH where deprotonation gives the alkoxide moiety **1a**:[10,14-16]

$$\underset{\mathbf{1}}{RN^+Me_2CH_2CH_2OH} \rightleftharpoons \underset{\mathbf{1a}}{RN^+Me_2CH_2CH_2O^-} + H^+$$

In the present work we used the hexadecyl derivative (**2**) hexadecyl(2-hydroxyethyl)dimethylammonium bromide (**2**) whose alkoxide derivative (**2a**) is an effective nucleophile. The substrate was *p*-nitrophenyl diphenyl phosphate (pNPDPP).[15a]

$$\underset{\mathbf{2a}}{n\text{-}C_{16}H_{33}N^+Me_2CH_2CH_2O^-} + (PhO)_2POOC_6H_4NO_2 \rightarrow n\text{-}C_{16}H_{33}N^+Me_2CH_2CH_2OPO(OPh)_2 + {}^-OC_6H_4NO_2$$

A few experiments were carried out with the use of the nonfunctional surfactant cetyltrimethylammonium bromide (CTABr) with hydroxide, alkoxide, or aryloxide ion as nucleophiles, and we also attempted to obtain microemulsions based on the oxime (**3**). In comicelles with CTABr, the oximate (**3**) is an effective dephosphorylating agent.[17]

$$\underset{\mathbf{3}}{n\text{-}C_{12}H_{25}N^+Me_2CH_2CPh{=}NOH} \rightleftharpoons n\text{-}C_{12}H_{25}N^+Me_2CH_2CPh{=}NO^- + H^+$$

Aromatic nucleophilic substitution by OH^- or alkoxide ion upon 2,4-dinitrofluoro- and -chlorobenzene has been examined in microemulsions and in aqueous micelles containing moderately hydrophobic alcohols.[7b,c] These substrates are not very hydrophobic and bind less strongly than pNPDPP to micelles.[18] Comparison of the effects

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(1) Danielsson, I.; Lindman, B. *Colloids Surf.* **1981**, *3*, 391.

(2) There are reports of microemulsions forming without surfactants; cf.: ref 1. These systems have been used as reaction media.[3]

(3) (a) Borys, N. F.; Holt, S. L.; Barden, R. E. *J. Colloid Interface Sci.* **1979**, *71*, 526. (b) Gonzalez, A.; Holt, S. L. *J. Org. Chem.* **1981**, *46*, 2594.

(4) For discussions of microemulsions as reaction media, see ref 3b and 5.

(5) (a) Hermansky, C.; Mackay, R. A. In "Solution Chemistry of Surfactants"; Mittal, K. L., Ed.; Plenum Press: New York, 1979; Vol. 2, p 733 and references cited. (b) Mackay, R. A.; Hermansky, C. *J. Phys. Chem.* **1981**, *85*, 739.

(6) Bunton, C. A.; de Buzzaccarini, F. *J. Phys. Chem.* **1981**, *85*, 3139, 3142.

(7) (a) Bunton, C. A.; de Buzzaccarini, F. *J. Phys. Chem.* **1982**, *86*, 5010. (b) Athanassakis, V.; Bunton, C. A.; de Buzzaccarini, F. *Ibid.* **1982**, *86*, 5002. (c) Bunton, C. A.; de Buzzaccarini, F.; Hamed, F. H., following paper in this issue.

(8) For discussions of micellar effects in thermal reactions, see ref 9 and 10.

(9) Cordes, E. H. *Pure Appl. Chem.* **1978**, *50*, 617.

(10) Bunton, C. A. *Catal. Rev. Sci.-Eng.* **1979**, *20*, 1.

(11) (a) Cordes, E. H.; Gitler, C. *Prog. Bioorg. Chem.* **1973**, *2*, 1. (b) Mukerjee, P.; Cardinal, J. R.; Desai, N. R. In "Micellization, Solubilization and Microemulsions"; Mittal, K. L., Ed.; Plenum Press: New York, 1977; Vol. 1, p 241.

(12) Menger, F. M. *Acc. Chem. Res.* **1979**, *12*, 111. Menger, F. M.; Yoshinaga, H.; Venkatasubban, K. S.; Das, A. R. *J. Org. Chem.* **1981**, *46*, 415.

(13) Al-Lohedan, H.; Bunton, C. A.; Mhala, M. M. *J. Am. Chem. Soc.* **1982**, *104*, 6654.

(14) Tonellato, U. In ref 5a, p 541. Fornasier, R.; Tonellato, U. *J. Chem. Soc., Faraday Trans. 1* **1980**, *76*, 130.

(15) (a) Bunton, C. A.; Ionescu, L. G. *J. Am. Chem. Soc.* **1973**, *95*, 2912. (b) Bunton, C. A.; Diaz, S. *Ibid.* **1976**, *98*, 5663. (c) Pillersdorf, A.; Katzhendler, J. *Isr. J. Chem.* **1979**, *18*, 330. (d) Bunton, C. A.; Gan, L.-H.; Hamed, F. H.; Moffatt, J. R. *J. Phys. Chem.* **1983**, *87*, 336.

(16) Phosphorylation by pNPDPP of the hydroxyl group of **2** in cationic micelles has been demonstrated by identification of the intermediate spectrophotometrically and by TLC.[15d]

(17) Bunton, C. A.; Hamed, F. H.; Romsted, L. S. *J. Phys. Chem.* **1982**, *86*, 2103.

0022-3263/83/1948-2457$01.50/0

Table I. Reaction of pNPDPP with OH^- in Micelles of CTABr-*tert*-Amyl Alcohol[a]

$C_5H_{11}OH$									
%	M	10^3k_Ψ, s^{-1}	β	R	k_M, s^{-1}	V'_m	k'_2, $M^{-1}\ s^{-1}$	V''_m	k''_2, $M^{-1}\ s^{-1}$
		10.3	0.85	1.0	0.29	0.18	0.053	0.36	0.10
0.81	0.092	9.2	0.84	0.93	0.29	0.17	0.050	0.34	0.10
3.33	0.378	6.6	0.78	0.73	0.36	0.16	0.058	0.29	0.10

[a] At 25.0 °C, 0.01 M NaOH and 3.32 wt % CTABr (0.091 M).

Table II. Reactions with Alkoxide Ions[a]

CTABr	octane	alcohol[b]	10^3k_Ψ, s^{-1}	k_Ψ/[OH^-], $M^{-1}\ s^{-1}$
5.0	5.0	10.0	2.52	0.25
8.8	8.8	8.8[c]	8.25	0.83
5.1		10.1	2.31	0.23
		94.1	5.85	0.59

[a] At 25.0 °C and 0.01 M NaOH; other compositions are by wt %. [b] 1-Butanol unless specified. [c] Benzyl alcohol.

of microemulsions upon aromatic nucleophilic substitution and dephosphorylation should provide evidence on the extent to which the overall rate effects depend upon substrate structure and hydrophobicity. In addition, the cosurfactant can be a primary alcohol that can give a nucleophilic alkoxide ion at high pH[5] or a tertiary alcohol that is weakly acidic and gives a weakly nucleophilic alkoxide ion.[7b,19]

Experimental Section

Materials. The preparation and purification of the reagents has been described.[7b,15a]

Kinetics. Formation of *p*-nitrophenoxide ion at 25.0 °C was followed spectrophotometrically at 400 nm. The observed first-order rate constants, k_Ψ, are in reciprocal seconds. All the mixed solvents were made up by weight.

Results

Reactions in Solutions of CTABr. Two sets of conditions were used. In the first we examined the effect of *tert*-amyl alcohol on the rate of reaction of pNPDPP with OH^- in micellized aqueous CTABr, and in the second we used various microemulsions based on CTABr.

Effect of *tert*-Amyl Alcohol. The decrease of k_Ψ on addition of *tert*-amyl alcohol to aqueous CTABr is shown in Table I. A quantitative treatment of these data is given later and is included in this table.

Reactions in Microemulsions. Effects of Alcohols. Reaction of pNPDPP at high pH in microemulsions containing 1-butanol has been studied in detail by Mackay and co-workers,[5] and our general observations accord with theirs, although reaction was slightly faster with our conditions (Table II). Alkoxide ion is the nucleophile in these reactions, but they are often slower than those with OH^- in water where the second-order rate constant is ca. 0.5 M^{-1} s^{-1} at 25.0 °C.[18]

Rate constants are similar in microemulsions and micelles containing similar amounts of 1-butanol but are slower in 1-butanol containing 6% water (Table II). Reaction is faster when the microemulsion contains benzyl alcohol, because it is more acidic than 1-butanol and generates more alkoxide ion.[19]

The small rate increase on addition of 1-butanol, which gives reactive 1-butoxide ion (Table II), contrasts with the rate decrease when *tert*-butyl alcohol is added to water.[18]

Table III. Medium Effects on Spectra of *p*-*tert*-Butylphenol

medium	phenol, M	λ_{max},[a] nm
H_2O	2.5×10^{-4}	273.5
0.1 M CTABr	2.5×10^{-3}	277.0
t-C_4H_9OH	3×10^{-3}	276.5
9% t-C_4H_9OH–hexane	2.5×10^{-3}	276.5 (283)
hexane	2.5×10^{-3}	277 (283)
microemulsion[b,c]	0.08	276.5
microemulsion[b,d]	0.06	276.5
microemulsion[b,e]	0.04	276.5

[a] Values in parentheses are for a shoulder. [b] CTABr: octane:t-C_4H_9OH 1:1:2 w/w. [c] 4.2 wt % CTABr. [d] 3.2 wt % CTABr. [e] 2.3 wt % CTABr.

Table IV. Medium Effects on Spectra of *p*-*tert*-Butylphenoxide Ion

medium	phenoxide, M	λ_{max}, nm
H_2O	2.5×10^{-4}	291.0
0.03 M CTABr	2.5×10^{-3}	298.0
1% H_2O-t-C_4H_9OH	3×10^{-3}	297.0
microemulsion[a]	0.035	298.5
microemulsion[b]	0.08	298.0

[a] CTABr, octane 1.9, t-C_4H_9OH 4.6 wt %. [b] CTABr, octane 4.2, t-C_4H_9OH 8.5 wt %.

Effect of *p*-*tert*-Butylphenol. It is difficult to interpret quantitatively the effects of alcohols upon reaction rates in micelles and microemulsions because of the related problems of the distribution of the alcohol between water and the micelles or droplets[7b,20] and the extent of deprotonation of the alcohol at high pH. Some of these problems are avoided by using aryloxide ions as nucleophiles. Phenols and their anions bind strongly to cationic micelles,[21] and it is easy to measure the extent of deprotonation of phenols. Cationic micelles effectively speed reactions of aryloxide ions with pNPDPP because of the high reactant concentrations in the micellar pseudophase. We used the strongly bound *p*-*tert*-butylphenol, whose anion is an effective dephosphorylating agent.[22]

In order to generate a microemulsion with CTABr containing dilute *p*-*tert*-butylphenol, we had to add *tert*-butyl alcohol as cosurfactant, but then the concentrations of phenol or phenoxide ion could be made low enough for their UV spectra to be observed in 0.1-mm cuvettes.

We saw red shifts with a change of medium from water to micelles or microemulsions of CTABr, and λ_{max} is similar in micelles or microemulsions and in organic solvents (Tables III and IV). These shifts are similar to those observed with a variety of phenols in CTABr micelles.[21]

Reaction of pNPDPP with *tert*-butylphenoxide ion was followed by using the phenol as buffer, so that reaction with OH^- can be neglected (Table V). The values of k_Ψ for reaction of *tert*-butylphenoxide ion depend upon the extent of deprotonation of the phenol, consistent with the apparent pH of the solution.[23]

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(18) Bunton, C. A.; Robinson, L. *J. Org. Chem.* **1969**, *34*, 773, 780.

(19) Hine, J.; Hine, M. *J. Am. Chem. Soc.* **1952**, *74*, 5266.

(20) Hall, D.; Jobling, P. L.; Rassing, J. E.; Wyn-Jones, E. *J. Chem. Soc., Faraday Trans. 2* **1977**, *73*, 1582.

(21) Bunton, C. A.; Sepulveda, L. *J. Phys. Chem.* **1979**, *83*, 680.

(22) (a) Bunton, C. A.; Cerichelli, G.; Ihara, Y.; Sepulveda, L. *J. Am. Chem. Soc.* **1979**, *101*, 2429. (b) Bunton, C. A.; Sepulveda, L. *Isr. J. Chem.* **1979**, *18*, 298.

Table V. Reaction with *p*-*tert*-Butylphenoxide Ion

	CTABr		t-C_4H_9OH				
octane, wt %	wt %	M	wt %	M	$[ArO^-]$, M	10^3k_Ψ, s^{-1}	k_M,[c] s^{-1}
4.19	4.19	0.115	8.39	1.13	0.050[a]	23.6	0.20 (0.09)[d]
4.14	4.14	0.114	8.28	1.12	0.0055[a]	1.19	0.09 (0.04)[e]
2.55	2.56	0.070	5.14	0.69	0.031[b]	23.5	0.14 (0.09)

[a] 1.16 wt % total ArOH. [b] 0.781 wt % total ArOH. [c] Values in parentheses are calculated on the assumption of zero binding of alcohol. [d] pH ≃11.4.[23] [e] pH ≃9.2.[23]

Table VI. Reaction in Microemulsions of 3[a]

CTABr		3					
%	10^2x	%	10^2x	octane, %	$[OH^-]$, M	10^2k_Ψ, s^{-1}	$k_\Psi/[OH^-]$, M^{-1} s^{-1}
17.5	1.77	2.1	0.18	19.6	0.044	1.07	0.25
9.1	0.82	1.07	0.061	10.2	0.030	1.82	0.61

[a] With equal amounts of *n*-octane and 2-methyl-2-pentanol by weight: x is mole fraction, molarity is in terms of total solution volume and percent by weight.

Table VII. Reaction of pNPDPP in Microemulsions of 2[a]

	2		alcohol[b]		CTABr						
run	%	10^2x	%	10^2x	%	10^2x	*n*-octane, %	H_2O, %	$10^2[OH^-]$,[c] M	10^3k_Ψ, s^{-1}	$k_\Psi/[OH^-]$, M^{-1} s^{-1}
1	16.6	1.34	16.7	6.01			16.6	50.0	1.00	8.89	0.89
2	16.6	1.34	16.7	6.01			16.6	50.0	3.00	16.3	0.82
3	16.6	1.34	16.7	6.01			16.6	50.0	4.94	42.6	0.86
4	16.6	1.34	16.7	6.01			16.6	50.0	6.88	57.4	0.83
5	16.6	1.34	16.7	6.01			16.6	50.0	9.76	81.0	0.83
6	26.7	3.96	26.8	17.8			26.7	19.9	1.00	7.26	0.73
7	21.7	2.26	21.8	10.2			21.7	34.9	1.00	7.94	0.79
8	16.7	1.33	25.0	8.95			8.3	50.0	1.00	9.57	0.96
9	13.3	1.24	20.0	7.19			16.7	50.0	1.00	7.22	0.72
10	1.64	0.133	16.7	6.04	16.5	1.31	15.0	50.2	1.00	2.35	0.24
11	0.042	0.003	16.7	5.99	16.6	1.44	16.6	50.2	4.93	4.15	0.084
12			16.7	5.99	16.6	1.44	16.7	50.1	1.00	0.97	0.097
13[d]	16.7	1.36	16.7	6.01			16.7	49.6	1.00	8.02	0.80
14	16.7	1.34	16.7[e]	7.13			16.7	50.0	1.00	10.5	1.05

[a] At 25.0 °C; x = mole fraction, % = percentage by weight. [b] *tert*-Amyl alcohol except where noted. [c] In moles per total volume of solution. [d] 0.39% NaBr added. [e] 1-Butanol instead of *tert*-amyl alcohol.

Reactions in Microemulsions of Functional Surfactants. Two systems were examined. Most of the work involved the hydroxyethyl surfactant (**2**), which readily formed microemulsions with octane and various alcohols, but a few experiments were made with the oxime derived surfactant (**3**).

We could not form microemulsions using **3** as surfactant, but they formed in mixtures of **3** and CTABr, when 2-methylpentan-2-ol was used as cosurfactant, but only over a limited composition range and low $[OH^-]$. The first-order rate constants, k_Ψ, are listed in Table VI, but the study of this system was restricted by phase separation.

Microemulsions of 2. For a given microemulsion, the first-order rate constants, k_Ψ, vary linearly with $[OH^-]$ (Table VII), as for aromatic nucleophilic substitution in these microemulsions,[7c] showing that **2** is not extensively deprotonated; cf. ref 15a,b.

For a given concentration of OH^-, k_Ψ is not very sensitive to the composition of microemulsions containing **2**, although addition of the inert surfactant, CTABr, markedly slows the reaction (Table VII). Replacement of *tert*-amyl alcohol by 1-butanol has little effect on k_Ψ, even though 1-butanol can give nucleophilic 1-butoxide ion,[5,7b] showing that, as in similar systems, **2a** is the active nucleophile.[7c,14,15]

We do not know the extent of deprotonation of **2** in the microemulsions, although the constancy of $k_\Psi/[OH^-]$ up to 0.1 M (Table VII) shows that here K_a(app) of **2** is less than that in aqueous micelles, where $pK_a(\text{app}) \approx 12.4$.[15a,b] This difference between micelles and microemulsion droplets can be ascribed to the decreased binding of counterions, including OH^-, to the latter.[7b,c]

Discussion

Quantitative Treatment of Rate Effects. We cannot estimate the extent of deprotonation of **2** in our microemulsions and treat this dephosphorylation quantitatively. (Reactions in aqueous micelles of **2** have been treated quantitatively.[15a]) Our discussion is therefore restricted to reactions of hydroxide and *p*-*tert*-butylphenoxide ion.

Reaction with *p*-*tert*-Butylphenoxide Ion. For dephosphorylation of pNPDPP in microemulsions containing *tert*-butylphenol, we express the rate constant as

$$k_\Psi = k_M[ArO^-]/([ArO^-] + [ArOH] + [CTABr] + [ROH_M]) \tag{1}$$

where the second-order rate constant, k_M, has concentration written as a mole fraction of aryloxide ion, ArO^-,[10,22] at the surface of the microemulsion droplet, and ROH_M is *tert*-butyl alcohol in the droplet. We assume that *p*-*tert*-butylphenoxide ion will be fully bound to the droplet,[21] but we do not know the extent of binding of the alcohol.

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(23) The apparent pH of the solution was measured on a pH meter calibrated in water, and no allowance was made for medium effects.

We therefore estimate k_M for two limiting cases: (i) we assume that *tert*-butyl and *tert*-amyl alcohol have the same binding constants, Ks = 0.77 M^{-1}, as measured for CTABr micelles with *tert*-amyl alcohol[7b,20] or (ii) we assume Ks ≈ 0, and neglect the concentration of *tert*-butyl alcohol in the droplet. The first assumption gives high, and the second low, limits for k_M (Table V). For a given microemulsion droplet, the two estimates of k_M differ by factors of ca 2, and the magnitude of k_M 0.04–0.2 s^{-1}, is not very different from the value of $k_M = 0.2$ s^{-1} for dephosphorylation by *tert*-butylphenoxide ion in CTABr micelles.[22b]

These values of k_M cannot be compared directly with second-order rate constants having the dimensions of M^{-1} s^{-1}, but, on the basis of an assumed volume of the Stern layer of a CTABr micelle,[10] second-order rate constants in the micelle are approximately half those in water.[22] We cannot readily estimate the volume element of reaction in the microemulsion droplet, in view of uncertainties regarding the distribution of *tert*-butyl alcohol, but our estimates of k_M suggest that second-order rate constants in cationic micelles and microemulsion droplets are not very different.

Reactions with OH^-. The variation of k_Ψ with [CTABr] for reaction of OH^- and pNPDPP can be fitted to the ion-exchange pseudophase model that has been applied to a number of reactions of OH^-.[24-27]

The second-order rate constant, k_M, for the reaction of pNPDPP in the micellar pseudophase can be estimated in terms of the concentration of OH^- in the micelle written as a mole ratio of bound OH^- to cationic head groups in the micelle, and in cationic micelles, $k_M \approx 0.7$ s^{-1}.[28] This rate constant can be converted into a second-order rate constant, k_2^m, M^{-1} s^{-1}, in which the concentration of OH^- is written as molarity on the basis of the molar volume of the micellar Stern layer[10,28] so that

$$k_2^m = 0.14k_M \qquad (2)$$

Alternatively the conversion of k_M into k_2^m can be given in terms of the molar volume of the micelle,[24-27] which approximately doubles k_2^m. Elsewhere the volume element of reaction, V'_m or V''_m, in CTABr micelles in the presence of *tert*-amyl alcohol has been estimated on two assumptions:[7b] in the first, V'_m is assumed to be the sum of the molar volume of bound *tert*-amyl alcohol ROH_M and half that of CTA^+; in the second, V''_m is assumed to be the sum of the molar volumes of bound alcohol and CTA^+ so that

$$k'_2 = k_M/V'_m \text{ and } k''_2 = k_M/V''_m \qquad (3)$$

The treatment of the rate data (Table I) follows that described in detail in ref 7, and the relevant kinetic parameters are included in this Table. The values of β, the fraction of head groups neutralized by counterions, are from ref 7a,b and R is given by

$$R = [\mathrm{CTABr}]/([\mathrm{CTABr}] + [\mathrm{ROH}]_M) \qquad (4)$$

The second-order rate constants, k_M, are little affected by addition of *tert*-amyl alcohol (Table I), as are the related rate constants, k'_2 and k''_2, M^{-1} s^{-1}, although they depend upon the assumptions regarding the volume element of reaction.

Effects of *tert*-Amyl Alcohol on Overall Rate Constants. For both aromatic nucleophilic substitution and dephosphorylation, *tert*-amyl alcohol decreases overall rate constants in micellar solutions (Table I and ref 7b). This decrease could be due to decreased micellar binding of OH^- or substrate, among other factors. But our present results show that decreased micellar binding of substrate is not a major factor in the rate decrease. We find similar rate effects with pNPDPP as with 2,4-dinitrofluorobenzene,[7b] but pNPDPP is so hydrophobic that it should reside largely in the micelle in all conditions.[18,22] Therefore, if partial micellar incorporation of 2,4-dinitrofluorobenzene was a controlling factor, there would be very different effects of *tert*-amyl alcohol in reactions of OH^- with the two substrates. We conclude that a major reason for inhibition by *tert*-amyl alcohol of these two reactions in micelles or microemulsions of CTABr is decreased binding of OH^- to the micelle or droplet, rather than an effect upon the distribution of substrate between water and the micelles or microemulsion droplets.

Medium Effects on Reaction Rates. Quantitative treatments of the effects of micelles, or similar aggregates, upon reactions of anionic nucleophiles or bases derived from weak acids requires estimation of the extent of deprotonation of the acid. We see no simple way of making this estimate for microemulsions of 2. However, we can make some qualitative comments on the factors that control reactivities in the reactions of pNPDPP discussed here, and it is evident that reaction is faster in the presence of a more acidic alcohol, which gives more alkoxide ion (Table II).

There is considerable evidence that concentration of reactants into the small volume of micelles is a major source of rate enhancement of bimolecular reactions,[9,10,24-29] and there are many reactions of ionic reagents for which second-order rate constants in the micelles are similar to those in water. This pattern of behavior also appears to apply to reactions in microemulsion droplets.[5,7] These observations are understandable if reactants are sufficiently hydrophilic to reside, on the average, close to the water-rich micelle–water interface.

However, medium effects of the micelle can be important, as, for example, in spontaneous unimolecular reactions,[10] or water-catalyzed bimolecular reactions, or reactions involving nonionic nucleophiles.[12,13,22a,29] For example, if the micelle stabilizes, or destabilizes, the initial, relative to the transition, state, the rate constant in the micelle should be different from that in water; i.e., the micelle will have a kinetic "solvent" effect.[30]

Typically, reactions of nucleophilic anions are much faster in apolar solvents than in water or hydroxylic solvents, provided that ion pairing of the nucleophile is taken into account.[31] We see the expected behavior for aromatic substitution by OH^-, where addition of a tertiary alcohol sharply speeds reaction and where primary alcohols have an even larger effect because they generate highly nucleophilic alkoxide ion.[7b,32] However, the situation is completely different for reactions of pNPDPP, for exam-

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(24) Romsted, L. S. In ref 11b, Vol. 2, p 509.

(25) Quina, F. H.; Chaimovich, H. *J. Phys. Chem.* **1979**, *83*, 1844. Chaimovich, H.; Bonilha, J. B. S.; Politi, M. J.; Quina, F. H. *Ibid.* **1979**, *83*, 1851.

(26) Al-Lohedan, H.; Bunton, C. A.; Romsted, L. S. *J. Phys. Chem.* **1981**, *85*, 2123.

(27) Funasaki, N.; Murata, A. *Chem. Pharm. Bull.* **1980**, *28*, 805.

(28) Bunton, C. A.; Gan, L.-H.; Moffatt, J. R.; Romsted, L. S.; Savelli, G. *J. Phys. Chem.* **1981**, *85*, 4118.

(29) Martinek, K.; Yatsimirski, A. K.; Levashov, A. V.; Berezin, I. V. In ref 11b, Vol. 2, p 489.

(30) This generalization applies strictly to spontaneous reactions because the rate constants are independent of concentration and therefore of the assumed volume element of reaction, but for other reactions the numerical values of the rate constants depend upon the way in which reactant concentration in the micellar pseudophase is defined.

(31) Parker, A. J. *Chem. Rev.* **1969**, *69*, 1.

(32) Bunnett, J. F. *Q. Rev. Chem. Soc.* **1958**, *12*, 1. Miller, J. "Aromatic Nucleophilic Substitution"; Elsevier: New York, 1968; Chapter 5.

ple, reaction in aqueous OH^- is slowed by added *tert*-butyl alcohol,[18] and in 1-BuOH:H_2O (94:6) reaction is only slightly faster than that in water (Table II), whereas for reaction of 2,4-dinitrofluorobenzene the rate is increased by orders of magnitude.[7b] The organic solvents lower the free energy of the hydrophobic pNPDPP, and this rate-inhibiting effect offsets the rate-enhancing effect of increased nucleophilicity of OH^- with decreasing water content of the solvent.

Spectroscopic probes suggest that the polarity of the Stern layer of a normal micelle, or the surface of an o/w microemulsion droplet, is lower than that of water and similar to that of a primary alcohol.[5,6,11,12] There are considerable uncertainties involved in relating kinetic solvent effects with bulk solvent properties such as dielectric constant, or Z or E_t parameters, but the effects of organic solvents upon reaction of pNPDPP with OH^- suggest that the relatively low polarity of a micelle might slow this reaction but have little effect on reactions of OH^- with less hydrophobic substrates such as carboxylic esters or halonitrobenzenes. There is evidence that micellar second-order rate constants for reaction of pNPDPP with hydroxide or alkoxide ion are slightly smaller, relative to reaction in water, than those for reactions such as deacylation or aromatic nucleophilic substitution.[28,33] However, all these comparisons depend upon the assumed volume element of reaction and the location of reactants at the micelle–water interface. There is also the possibility of reaction of OH^- in water with substrate in the micelle, and there is evidence for such a reaction; cf. ref 28, 34, and 35.

Qualitatively, the comparisons of *overall* rate effects on reactions of pNPDPP in micelles or microemulsion droplets suggest that although the substrate binds effectively to the micelle or droplet, the rate enhancements are small, relative to those for aromatic nucleophilic substitution, for example,[5,7,33]

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Registry No. **2**, 20317-32-2; **3**, 86088-75-7; pNPDPP, 10359-36-1; CTABr, 57-09-0; OH^-, 14280-30-9; *tert*-amyl alcohol, 75-85-4; octane, 111-65-9; benzyl alcohol, 100-51-6; 1-butanol, 71-36-3; water, 7732-18-5; *tert*-butyl alcohol, 75-65-0; hexane, 110-54-3; *p-tert*-butylphenol, 98-54-4; 1-butoxide ion, 26232-84-8; benzylbutoxide ion, 26397-37-5.

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(33) Bunton, C. A. *Pure Appl. Chem.* **1977**, *49*, 969.

(34) Bunton, C. A.; Romsted, L. S.; Savelli, G. *J. Am. Chem. Soc.* **1979**, *101*, 1253.

(35) Nome, F.; Rubiera, A. F.; Franco, C.; Ionescu, L. *J. Phys. Chem.* **1982**, *86*, 1881.

Nucleophilic Aromatic Substitution in Microemulsions of a Hydroxyethyl Surfactant

Clifford A. Bunton,* Francesco de Buzzaccarini, and Fareed H. Hamed

Department of Chemistry, University of California, Santa Barbara, California 93106

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Reactions of 2,4-dinitrochloro- or 2,4-dinitrofluorobenzene in microemulsions of hexadecyl(2-hydroxyethyl)dimethylammonium bromide (1), *n*-octane, and *tert*-amyl alcohol or 1-butanol, and NaOH give an ether by attack of the alkoxide zwitterion of 1. This ether slowly reacts with OH^-, giving 2,4-dinitrophenoxide ion. These reactions are slower than those in aqueous micelles. A Meisenheimer complex is formed by reaction of 1-chloro-2,4-dinitronaphthalene in these microemulsions and in those containing 1-butanol, and it is slowly converted into the naphtholate ion by attack of OH^-.

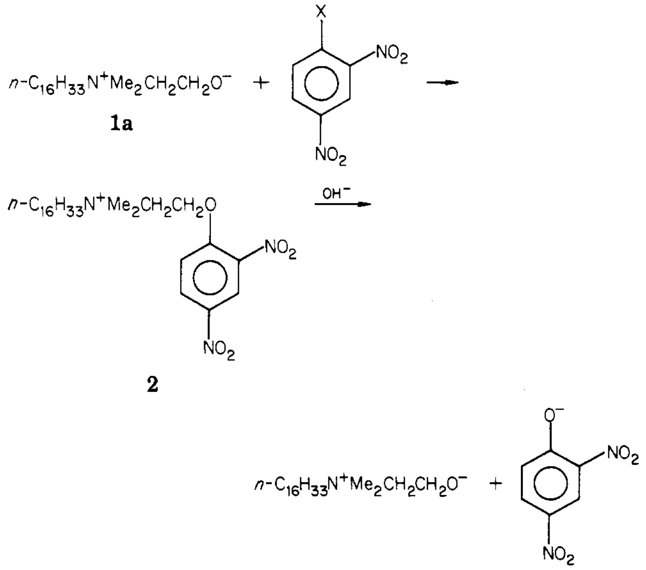
At high pH, an alcohol cosurfactant in a microemulsion can give an alkoxide ion that reacts nucleophilically in dephosphorylation[1] and in aromatic substitution on 2,4-dinitrohalobenzene.[2]

These reactions are mechanistically similar to dephosphorylation and aromatic nucleophilic substitution in micelles of hexadecyl(2-hydroxyethyl)dimethylammonium bromide (**1**) in which the alkoxide moiety of the zwitterion (**1a**) is the reagent and is much more reactive than OH^-.[2b,3]

$$\underset{\textbf{1}}{n\text{-}C_{16}H_{33}N^+Me_2CH_2CH_2OH} + OH^- \rightleftarrows \underset{\textbf{1a}}{n\text{-}C_{16}H_{33}N^+Me_2CH_2CH_2O^-}$$

Reactions of micellized **1** and **1a** with 2,4-dinitrohalobenzenes give an intermediate ether (**2**), which goes forward to 2,4-dinitrophenoxide ion (Scheme I), and both steps can be followed kinetically.[3b]

Scheme I[a]



[a] X = F, Cl.

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(1) (a) Mackay, R. A.; Letts, K.; Jones, C. in "Micellization, Solubilization and Microemulsions"; Mittal, K. L., Ed.; Plenum Press: New York, 1977; p 801. (b) Hermansky, C.; Mackay, R. A. in "Solution Chemistry of Surfactants"; Mittal, K. L., Ed.; Plenum Press: New York, 1979; p 723. (c) Mackay, R. A.; Hermansky, C. *J. Phys. Chem.* **1981**, *85*, 739.

(2) (a) Athanassakis, V.; Bunton, C. A.; de Buzzaccarini, F. *J. Phys. Chem.* **1982**, *86*, 5002. (b) Bunton, C. A.; de Buzzaccarni, F.; Hamed, F., preceding paper in this issue.

(3) (a) Bunton, C. A.; Ionescu, L. G. *J. Am. Chem. Soc.* **1973**, *95*, 2912. (b) Bunton, C. A.; Diaz, S. *Ibid.* **1976**, *98*, 5663. (c) Bunton, C. A.; Gan, L.-H.; Hamed, F. H.; Moffatt, J. R. *J. Phys. Chem.* **1983**, *87*, 336.