Reactions of Carbocations with a Nucleophilic Surfactant and Related Alkoxide Ions[1]

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Micelles of 1-hydroxyethyl-2-dimethylhexadecylammonium bromide (I) are effective reagents for the decomposition of malachite green (MG^+) at high pH, giving approximately 600-fold rate enhancement over the hydroxide ion reaction. The decomposition of the tri-*p*-anisylmethyl cation (R^+) at high pH is also strongly catalyzed by micelles of I. This catalysis can be explained in terms of nucleophilic participation by the alkoxide zwitterion of I. At high pH, in the absence of micelles, 2,2,2-trifluoroethanol, propargyl alcohol, and choline are more effective reagents than expected from their dissociation constants, and the reactivities of the alkoxide ions, relative to hydroxide ion follow: $CF_3CH_2O^-$, 2.7 (2.6); $HC{\equiv}CCH_2OH$, 16 (10); $Me_3N^+CH_2CH_2O^-$, 13 (7). The values in parentheses are for reactions of R^+.

Micellar effects upon the equilibrium constants of the reaction of triarylmethyl carbocations with hydroxide ion were rationalized in terms of Coulombic interactions by Hartley and co-workers,[2] and Duynstee and Grunwald showed that the forward reaction was catalyzed by cationic and inhibited by anionic micelles,[3] e.g., for malachite green [bis(4-dimethylaminophenyl)phenylmethyl cation]

$$MG^+ + OH^- \rightleftarrows MGOH$$

More recently the effects of added salts and changes in the lengths of the alkyl group of the surfactant upon the reaction of crystal violet [tris(4-dimethylamino)phenylmethyl cation] have been examined.[4] Micellar catalysis is discussed in ref 5–8.

Functional micelles of surfactants which contain reactive groups are effective nucleophilic or basic reagents,[5–10] but they generally have been used for reactions of organic or inorganic esters. Micelles of surfactants containing a hydroxyethyl head group are effective reagents in reactions of di- and trisubstituted phosphate esters,[10] and our aim was to examine rate enhancements due to micelles of 1-hydroxyethyl-2-dimethylhexadecylammonium bromide (I) because choline is converted into its zwitterion at high pH with $pK_a = 13.9$,[11] and I should give the zwitterion, II.[10,12]

$$\underset{\text{I}}{n\text{-}C_{16}H_{33}N^+Me_2\,CH_2\text{—}CH_2OH} \rightleftarrows$$

$$\underset{\text{II}}{n\text{-}C_{16}H_{33}N^+Me_2CH_2CH_2O^-} + H^+$$

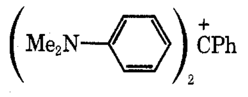
In addition we were interested in the nucleophilicity of the zwitterion (III) of choline and of alkoxide ions of propargyl alcohol and 2,2,2-trifluoroethanol toward carbocations.[13] The rates of nucleophilic attack upon relatively unreactive dye cations have been used to formulate the N^+ scale of nucleophilicity.[14]

$$Me_3N^+CH_2CH_2OH \rightleftarrows \underset{\text{III}}{Me_3N^+CH_2CH_2O^-} + H^+$$

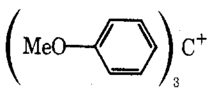
Despite the cationic center, III is a good nucleophile toward phosphate esters[10] and halonitrobenzenes.[17] Bulky alkoxide ions are much better reagents than hydroxide ion in deacylations,[18,19] although in these reactions the partitioning of a tetrahedral intermediate could depend on the nature of the nucleophile, but this is not a problem for an association reaction with a carbocation.

As carbocations we used malachite green (MG^+) and the trianisylmethyl cation, R^+.

In the original work with the relatively stable dye cations, e.g., MG^+, both the rate and equilibrium constants for reaction with hydroxide ion were determined.[3,4] We measure only the forward rate constants because the zwitterion, II, is generated at high pH, where the equilibria are wholly toward MGOH and ROH. The reaction of R^+ with hydroxide ion is only weakly catalyzed by cationic micelles of CTABr, which do not affect the reaction with water.[20]



MG^+



R^+

Micelles of I in alkali effectively speed S_N2[21] and E2[22] reactions at saturated carbon, and it was suggested that this reaction was of hydroxide ions activated by the micelle,[21] but the evidence is equally consistent with II acting as a nucleophile or a general base, and evidence on deacylations catalyzed by micelles of I strongly supports nucleophilic attack by II, although in this system the substrate was in large excess over the surfactant, so that it could control the micellar structure.[23]

Experimental Section

Materials. The alcohols were commercial samples and were crystallized or redistilled before use, and the surfactant was prepared as described.[10] All rate measurements were made using deionized and redistilled water which had been degassed before use for the experiments on the stopped flow spectrophotometer. Choline was added as its chloride and I as its bromide.

Kinetics. The reactions were followed spectrometrically by following the absorbances at 480 nm of R^+ and at 616 nm for MG^+. Gilford spectrophotometers were used for the slower reactions and a Durrum stopped flow spectrophotometer with a Biomation 805 data acquisition unit was used for the faster reactions. Solutions of MG^+ were added at pH 4 and those of R^+ in 0.1 *M* HCl.[15] All reactions were followed at 25.0°. Our values of the second-order rate constants for reactions of R^+ and MG^+ with OH^- are in reasonable agreement with earlier results.[14,15a]

For reactions of R^+ with the surfactant it was generally in one syringe with NaOH and R^+ in HCl was in the other.[15a,20]

Products. Several tests were used to show that the initial products are ethers.

(1) Immediately after complete reaction of MG^+ with 0.1 *M* choline chloride + 0.05 *M* OH^- the pH of the solution was reduced to 7.1 with HCl, and the absorbance due to MG^+ increased from zero to ca. 40% of the initial absorbance and then gradually decreased to an equilibrium value (ca. 25% of the initial absorbance).

Similar observations were made on the products of the reactions of MG^+ with trifluoroethanol and propargyl alcohol, showing that the initially formed ethers gradually decomposed to give the carbocation and then the alcohol under thermodynamic control.

We have similar spectroscopic evidence for ether formation in the reaction of MG^+ with 6×10^{-3} *M* I in 10^{-2} *M* NaOH. After complete reaction the pH was reduced to 7 and the absorbance slowly increased from zero to 10% of that of the original MG^+ and then slowly fell toward the equilibrium value of ca. 2%. The differences in the magnitude of the absorbance changes in this reaction

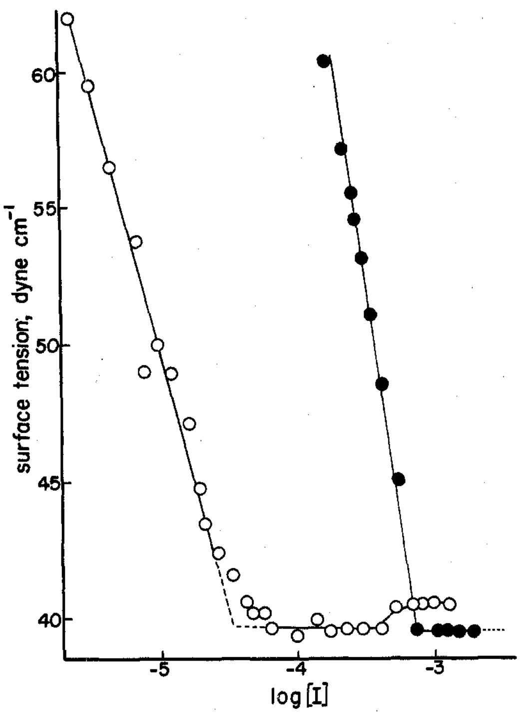


Figure 1. The variation of surface tension with concentration of 1-hydroxyethyl-2-dimethylhexadecylammonium bromide (I): ●, in water; ○, in 0.1 *M* NaOH.

and the corresponding one with choline are due to the effects of the micelle in slowing dissociation of the initially formed ether, *n*-$C_{16}H_{33}N^+Me_2CH_2CH_2OMG$, and speeding the subsequent reaction of MG^+ with OH^-, and in changing the equilibrium between MG^+ and MGOH (cf. ref 3 and 4).

(2) The reaction mixture of MG^+ with 0.1 *M* choline chloride and 0.05 *M* NaOH was spotted, after complete reaction, onto a silica gel plate and the plate was eluted with acetone–H_2O (50:50 v/v), giving a large spot with R_f 0.11 and a small spot at R_f 0.45, which were blue after acidification. After varying periods of time the reaction mixture was reexamined, and the spot with R_f 0.11 gradually decreased in intensity and the other increased, and after 4 hr only the spot with R_f 0.45 was left. This spot was coincident with that of MGOH, and we assume that the spot with the low R_f was that of $Me_3N^+CH_2CH_2OMG$.

A similar experiment was done using R^+ in 0.1 *M* HCl and 0.16 *M* choline chloride and 0.19 *M* NaOH. The mixture was extracted with Et_2O after complete reaction and spotted onto a silica gel plate and the plate was eluted with acetone–H_2O (50:50 v/v). Two yellow spots were observed after acidification, one with R_f 0.05 and a smaller one with R_f 0.93. This second spot was coincident with that of ROH. The ether extraction did not remove all the choline ether from the aqueous reaction mixture, and the yellow color of R^+ developed when this residual water layer was acidified. A control test showed that ROH is wholly extracted by water under these conditions, and addition of 0.3 *M* Me_4NCl did not affect the extraction, so that the material left in the aqueous layer after ether extraction must have been the choline ether.

Critical Micelle Concentrations. The critical micelle concentration of I (as its bromide) in water at 24° was determined from the variation of surface tension with surfactant concentration and a plot of surface tension against log [I] gave a linear plot with a sharp break (Figure 1), and the critical micelle concentration was 8 × 10^{-4} *M*. This value is, as expected, very close to the cmc of CTABr for which values range from 8 to 10 × 10^{-4} *M*.[24] Typically cmc's for similarly charged surfactants are dependent more on the length of the long hydrophobic chain than on the structure of the head group. For the chloride corresponding to I, cmc = 1.2 × 10^{-3} *M* in water at 30°, and this value is close to that of 1.3 × 10^{-3} *M* for CTACl.[24]

The value of the cmc of I was also measured in 0.1 *M* NaOH at 24°, and under these conditions cmc = 3.5 × 10^{-5} *M*. However, a plot of surface tension against log [I] did not give a sharp break (Figure 1), and there was considerable curvature in the plot at concentrations just above the cmc. This curvature is understandable because the composition of the micelle will be changing because of the equilibrium between the cationic surfactant (I) and its zwitterion. This marked decrease is understandable because conversion of I into its zwitterion should markedly reduce the head group repulsions which tend to disrupt a micelle. Our kinetic estimate of pK_a = 12.4 for micellized I suggests that conversion into the zwitterion should be extensive in 0.1 *M* NaOH.[10] Added salts decrease cmc, but effects as large as those we observe with NaOH would not be expected if there was no chemical change because hydrophilic counterions generally have only small effects on micellization.[5–8,24]

Results and Discussion

Reactions in the Absence of Surfactant. Choline, propargyl alcohol, and 2,2,2-trifluoroethanol increase the rates of disappearance of malachite green (MG^+) and the tri-*p*-anisylmethyl cation (R^+) in alkali (Tables I and II). Various effects have to be separated in estimating the reactivities of the choline zwitterion (III) or the alkoxide ions toward the carbocations, because allowance has to be made for the concurrent reactions with hydroxide ion and water.[14–16] Conversion into an alkoxide or zwitterion decreases the hydroxide ion concentration as shown for choline (eq 1), and the concentrations of the alkoxide nucleophiles are estimated using pK_a = 13.9 for choline,[11] 13.55 for propargyl alcohol, and 12.4 for 2,2,2-trifluoroethanol.[25]

$$Me_3N^+CH_2CH_2OH + OH^- \rightleftarrows \underset{\text{III}}{Me_3N^+CH_2CH_2O^-} \quad (1)$$

Attack by nucleophilic anions and water upon R^+ is retarded by most electrolytes, although quaternary ammonium halides in low concentration only slightly retard these reactions but in high concentration speed them.[15,16] However, we neglect these electrolyte effects because of the low

Table I
Reaction of MG^+ in the Presence of 2,2,2-Trifluoroethanol, Propargyl Alcohol, or Choline[a]

R'OH	10^2 $[R'OH]_0$, *M*	10^2 $[OH^-]_0$, *M*	10^3 $[RO^-]$, *M*	10^2 k_ψ, sec^{-1}	10^2 k_ψ^N, sec^{-1} [b]	k_2^N, l. mol^{-1} sec^{-1}
CF_3CH_2OH	2.0	1.73	6.2	4.30	2.5	4.0
	12	1.73	14.2	6.97	6.5	4.5
	20	1.73	15.4	7.41	7.1	4.6
$HC{\equiv}CCH_2OH$	1.0	1.75	0.46	3.85	1.1	23
	2.0	1.75	0.90	4.95	2.2	25
	6.3	1.75	2.45	9.12	6.7	27
	12.1	1.75	4.33	14.4	12.2	28
	20.1	1.75	6.20	17.2	15.3	25
$Me_3\overset{+}{N}CH_2CH_2OH$	2.5	4.16	1.21	9.59	3.0	25
	5.0	4.16	2.35	11.3	4.9	21
	10.0	4.16	4.47	14.3	8.2	18
	10.0	0.83	0.92	3.06	1.9	20
	10.0	2.08	2.3	7.28	4.3	19

[a] At 25.0°. [b] Calculated using k_2^{OH} = 1.64 l. mol^{-1} sec^{-1}.

Table II
Reaction of R^+ in the Presence of 2,2,2-Trifluoroethanol, Propargyl Alcohol, or Choline[a]

R'OH	10^2 $[R'OH]_0$, M	10^2 $[R'O^-]$, M	k_ψ, sec^{-1}	$k_\psi{}^N$, sec^{-1}[b]	10^{-4} $k_2{}^N$, $l. mol^{-1} sec^{-1}$
CF_3CH_2OH	3.0	0.94	252	170	1.8
	6.0	1.33	288	232	1.7
	10	1.57	298	257	1.6
$HC{\equiv}C{-}CH_2OH$	1.0	0.052	188	48	~9
	3.0	0.15	233	99	6.6
	6.0	0.28	286	161	5.8
$Me_3\overset{+}{N}CH_2CH_2OH$	10.0	0.43	412	296	7.0
	10.0[c]	0.27	234	108	4.0
	10.0[d]	0.33	299	177	5.4

[a] At 25.0° with 0.02 M stoichiometric hydroxide ion unless specified. [b] Calculated using $k_2{}^{OH}$ = 6580 l. mol^{-1} sec^{-1}, and k^{H_2O} = 12 sec^{-1}. [c] With 0.025 M stoichiometric hydroxide ion. [d] With 0.03 M stoichiometric hydroxide ion.

concentration of choline chloride (Tables I and II); for example, 0.5 M tetramethylammonium chloride reduces the rate of attack of hydroxide ion upon R^+ by ca. 30%.[15] (The rate increases at higher concentrations of the salt.) The cholinate zwitterion and anions of 2,2,2-trifluoroethanol and propargyl alcohol are good nucleophiles toward the carbocations. The first-order rate constants for the overall reactions are in Tables I and II, and the first- and second-order rate constants ($k_\psi{}^N$ and k^N) for reactions of the alkoxide nucleophiles are calculated using pK_a values after allowing for the contributions of the reactions with water and hydroxide ion. In all these reactions we assume that the hydroxide ion and the other nucleophile, the zwitterion (III) or an alkoxide ion, do not affect each other's reaction (eq 2).

$$k_\psi = k_\psi{}^{H_2O} + k_2{}^{OH}[OH^-] + k_2{}^N[N] \qquad (2)$$

(where N = $Me_3N^+CH_2CH_2O^-$; $CF_3CH_2O^-$; $HC{\equiv}C{-}CH_2O^-$)

The contribution of the water reaction ($k_\psi{}^{H_2O}$) can be neglected for the reaction of MG^+. The values of $k_2{}^N$ are reasonably independent of reagent concentrations, but they inevitably depend upon the pK_a values.

The nucleophilicities toward MG^+ (and R^+ in parentheses) relative to those of hydroxide ion follow: $CF_3CH_2O^-$, 2.7 (2.6); $HC{\equiv}C{-}CH_2O^-$, 16 (10); $Me_3N^+CH_2CH_2O^-$, 13 (7).

The overall rate differences for reactions of hydroxide ion and the alkoxide ions are similar to those found for attack upon p-nitrophenyl esters.[19] However, this similarity is not general for all oxyanions; for example, phenoxide ions are very effective nucleophiles toward R^+,[26] but show no unusual reactivity toward p-nitrophenyl acetate.[19]

The low nucleophilicities of hydroxide ion, and of other high charge density alkoxide ions such as methoxide, relative to their basicity are not unusual. They can be rationalized in terms of hard and soft reagents,[27] and we could also assume that hydroxide and small alkoxide ions merely have unusually high basicities, perhaps because of the ease with which they can transfer protons through a Grotthius chain, and strong solvation of these ions should decrease nucleophilicity more than basicity. However, the bulky organic residues may also act by modifying the solvent structure around the reaction center, or by interacting through dispersive or hydrophobic forces with the organic residues of the substrates.[6,15,16]

The results in Tables I and II, and the evidence for ether formation (Experimental Section), show that the cholinate zwitterion and the alkoxide ions of propargyl alcohol and 2,2,2-trifluoroethanol react as nucleophiles and not as general bases with the carbocations. The ethers are unstable (Experimental Section) and gradually revert to the alcohols, which are the thermodynamically controlled products, presumably by a slow formation of the carbocation, as shown for the choline ether. However, the initial reaction

$$\begin{array}{ccc} Me_3\overset{+}{N}CH_2CH_2O^- + MG^+ & \rightleftharpoons & Me_3\overset{+}{N}CH_2CH_2OMG \\ \downarrow{\scriptstyle OH^-} & & \\ MGOH & & \end{array}$$

goes wholly to the ether, because the absorbance of the solution disappears in the course of the reaction.

Our rate measurements show that the quaternary ammonium moiety does not markedly reduce the nucleophilicity of the cholinate zwitterion (III), whose slightly lower reactivity than the anion of propargyl alcohol may be due to steric effects. Formation of an ion pair intermediate has been postulated in the reactions of relatively stable triarylmethyl carbocations with anions,[14] and it is therefore a little surprising that the cationic center in III has little or no effect on its nucleophilicity toward carbocations. However, there is extensive evidence for the relative unimportance of charge–charge interactions in nucleophilic reactions of charged reactants,[28] which leads us to believe that Coulombic interactions are not especially important in many carbocation–nucleophilic recombinations in aqueous solvents, even though there is evidence for ion pairs, or similar intermediates, in these reactions (cf. ref 15, 16, 26).

Micellar Reactions. Micelles of the hydroxyethyl surfactant effectively speed reactions of the carbocations, and the variations of k_ψ with surfactant concentration are typical of micellar catalysis,[3-8] as shown in Figure 2 for the reaction of MG^+. Very low concentrations of I do not affect

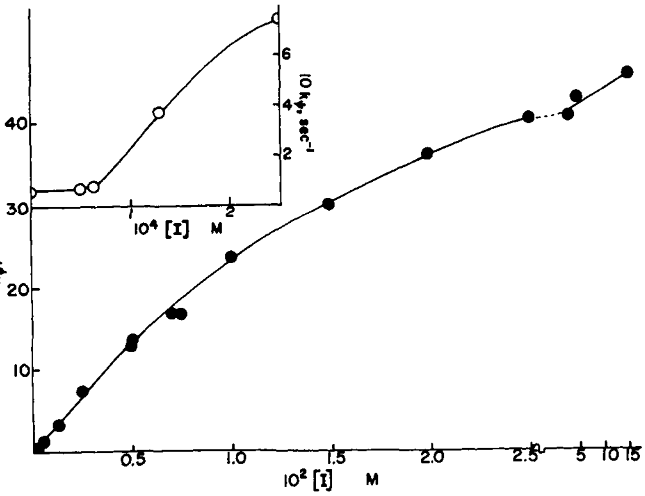


Figure 2. Catalysis of the reaction of MG^+ in 0.042 M NaOH at 25.0° by micelles of I. The inset shows the overall first-order rate constants, k_ψ, at low surfactant concentration.

Table III
Reaction of MG^+ in Micelles of I[a]

10^3 [I], M	10 k_ψ, sec^{-1} 0.005 M OH^-	 0.042 M OH^-
	0.083	0.70
0.30	0.79 (9.5)	9.5 (14)
0.60	1.97 (24)	19 (27)
3.00	5.83 (70)	81 (115)
6.00	23.3 (280)	156 (223)
30.0	39.2 (470)	400 (570)
50.0	47.1 (570)	427 (610)

[a] At 25.0°; MG^+ was added at pH 4. The values of k_ψ in 0.042 M OH^- are interpolated where necessary. The values in parentheses are the rate enhancements relative to reaction in the absence of surfactant.

the rate, but the rate increases at surfactant concentrations well below the cmc, suggesting that reaction is occurring in submicellar aggregates of MG^+ and the surfactant, or that MG^+ sharply lowers the cmc of the surfactant. Similar behavior was found for reactions of crystal violet with hydroxide ion catalyzed by nonfunctional cationic micelles.[4] We did not reach a rate plateau or maximum in reactions of MG^+, suggesting that the surfactant concentration was not high enough for the carbocations to be taken up wholly by the cationic micelles. A rate plateau was found for the reaction of crystal violet with hydroxide ion catalyzed by CTABr,[4] but crystal violet is probably more hydrophobic than MG^+.

The relation between rate and surfactant concentration can be interpreted qualitatively, and occasionally quantitatively, for micellar catalysis in terms of the distribution of substrate between micelle and bulk solvent,[29,30] although for bimolecular reactions there is a complication due to the distribution of the reagent, which is often a hydrophilic ion, between micelle and bulk solvent.[31] The situation is more complicated for these carbocation reactions where the cationic surfactant (I) is converted into the zwitterion (II) at high pH,[10] because incorporation of the cationic substrate into a cationic micelle requires that the favorable hydrophobic and dispersive interactions overcome the Coulombic repulsions, and these Coulombic repulsions decrease with increasing conversion of I into its zwitterion. Thus more substrate should be taken up into the micelle as the pH increases. At the same time the micelle itself should grow because Coulombic repulsions between the cationic head groups should decrease.

However, decreasing micellar charge is not the only reason for the high reaction rates in micelles of I as compared with CTABr, because the rate enhancements of reactions of MG^+ are similar in 5×10^{-3} and 4.2×10^{-2} M NaOH (Table III), and the main differences are at low surfactant concentrations where the effect of hydroxide ion on the cmc (Figure 1) is important.

As is generally found, these functional micelles of the hydroxyethyl surfactant (I) are much better catalysts than nonfunctional micelles of CTABr. For reaction of MG^+ with hydroxide in the presence of CTABr the rate enhancement was by a factor of 20,[3] although slightly larger rate enhancements were found for the reaction of crystal violet.[4] There is almost no catalysis by micellized CTABr of the attack of anions upon the less hydrophobic tri-*p*-anisylmethyl carbocation.[20]

The 600-fold rate enhancement of the reaction of MG^+ by micellized I (Table III) actually underestimates the nucleophilicity of the alkoxide moiety of the zwitterion (II) relative to hydroxide ion in water, because only some of the hydroxyethyl groups are converted into alkoxide.[10]

Table IV
Reaction of R^+ in Micelles of I[a]

10^3 [I], M	10^2 [OH^-], M 0.03	 0.5	 2	 5
	13.9	43.8	140	326
0.05			143	
0.10			188	328
0.10				319[b]
0.30	14.3	96		
0.50			630	
0.60		206		
1.0			~900	~950
1.2		337		
6.0	28		$>10^3$	$>10^3$
50	49			
110	120			

[a] Values of k_ψ, sec^{-1}, at 25.0°. [b] In this experiment the surfactant (I) was in both syringes.

As noted earlier the cholinate zwitterion is a better nucleophile than hydroxide ion, and so much of the high reaction rates in micelles of I at high pH can be ascribed to the high nucleophilicity of the alkoxide moiety in II.[10,23]

As for the nonmicellar reactions with the cholinate and alkoxide nucleophiles, there is no complication due to partitioning of a tetrahedral intermediate in these reactions of the carbocations and micellized I. We could not examine the reaction of R^+ in the presence of micelles of I over a wide range of conditions because with increasing surfactant concentration the reaction became too fast to be followed. Micellized I is an effective reagent toward R^+ (Table IV), and this observation contrasts sharply with the absence of catalysis by micellized CTABr of the reactions of R^+ with hydroxide or azide ion.[20] It is generally assumed that the chemical processes are much slower than incorporation of reagents into the micelle. We tried to test this assumption for reaction of R^+ by having surfactant in both syringes. Unfortunately, cationic micelles sharply decrease the equilibrium formation of R^+, so that we could only do this experiment with low concentrations (10^{-4} M) of I and 0.05 M OH^-, where there is very little micellar catalysis. Although we could not observe rate plateaus in these reactions of R^+, the results in Figure 3 indicate that there is almost no catalysis in very dilute alkali, where the micelle is almost wholly cationic, cf. ref 20, but that it increases sharply as the zwitterionic surfactant (II) is formed with increasing hydroxide ion concentration.

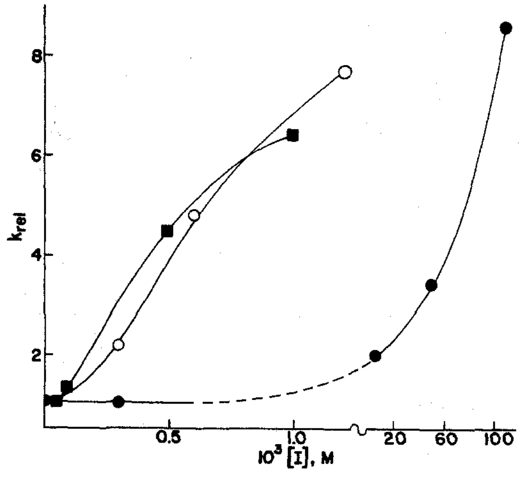


Figure 3. Catalysis of the reaction of R^+ by micelles of I: ●, 3×10^{-4} M OH^-; ○, 5×10^{-3} M OH^-; ■, 2×10^{-2} M OH^-. k_{rel} is relative to k_ψ in the absence of surfactant.

Registry No.—I, 24705-21-3; malachite green, 14426-28-9; trifluoroethanol, 75-89-8; propargyl alcohol, 107-19-7; choline, 62-49-7; tri-*p*-anisylmethyl cation, 14039-13-5.

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Influence of the *o*-Nitro Group on Base Catalysis in Nucleophilic Aromatic Substitution. Reactions in Benzene Solution[1]

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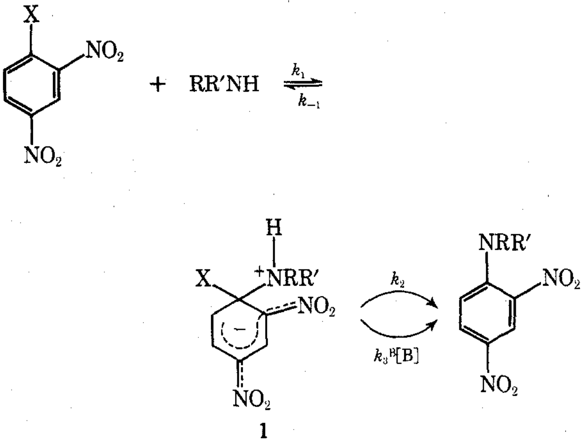
There exist two explanations why nucleophilic aromatic substitutions by secondary amines are frequently more prone to base catalysis than analogous reactions with a primary amine of comparable pK_a. Both are based on the intermediate complex mechanism of eq 1. The first invokes a steric acceleration of the k_{-1} step in the case of secondary amines which reduces k_2/k_{-1} (and k_3^B/k_{-1}) compared to primary amines. The second explanation, initially based on the observation that practically all known examples involved *o*-nitro substituted substrates, invokes intramolecular hydrogen bonding to the *o*-nitro group. Its effect is to lower k_{-1} about equally for primary and secondary amines, but to lower k_2 more for secondary than for primary amines, thus making k_2/k_{-1} larger for primary amines than for secondary amines. Kinetic data on reactions of *n*-butylamine and of piperidine with 1-fluoro-2,4-dinitrobenzene, 1-fluoro-4-nitronaphthalene, and 1-fluoro-4,5-dinitronaphthalene in benzene are presented which support the hydrogen bonding theory. The data are also shown to be most consistent with the SB–GA mechanism of base catalysis in this solvent.

It is well known that some nucleophilic aromatic substitution reactions involving amines as nucleophiles are subject to base catalysis whereas others are insensitive to the addition of base.[3] This has been rationalized in terms of the intermediate complex mechanism where the intermediate may be transformed into products either directly (k_2) or by a base-catalyzed route (k_3^B); eq 1 is representative for the most frequently studied type of substrates, viz., 1-substituted 2,4-dinitrobenzene derivatives. When the product-forming steps are much faster than the reversion of the intermediate to reactants ($k_2 + k_3^B[B] \gg k_{-1}$), intermediate formation (k_1) is rate determining and no base catalysis can be observed. When the rate of the product-forming steps is slower or at least does not greatly exceed the rate of reversion ($k_2 + k_3^B[B] \lesssim k_{-1}$), the net reaction is susceptible to base catalysis.



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