gas chromatograph equipped with a 10 ft by 0.25 in. column packed with 8% SE-30 on 80–100-mesh Chromosorb Q. 1-Methyl-1*H*-tetrazole (**20**) was synthesized by deamination[22] of 5-amino-1-methyl-1*H*-tetrazole.[23] The structures and purity of the compounds studied were verified by their ^1H and ^{13}C NMR spectra.

Spectra. The CW ^1H NMR spectra were determined at 60 MHz with a Perkin-Elmer R-20 or at 100 MHz with a Varian HA-100 NMR spectrometer. The ^{13}C NMR spectra were recorded at 20 MHz, using a Varian FT-80A NMR spectrometer. The ^{13}C spectra were determined at a spectral width of 4 kHz with a 16K data table, applying a 45° pulse with a repetition rate of 2 s and continuous broad-band ^1H decoupling.

The ^{15}N NMR spectra were determined at 8.059 MHz with the Varian FT-80A instrument, using solutions of 750 mg of the azole dissolved in 2 mL of $DCCl_3$ or Me_2SO-d_6. ^{15}N spectra of the NH azoles were recorded with the following conditions: 4 kHz spectral width, 8K data table, 15° or 30° pulse angle, 1-s pulse repetition, and continuous broad-band ^1H decoupling. Then 30 mg of Cr(Acac)$_3$ was added to the NH azole sample and the spectrum was determined with a 4-kHz spectral width, 4K data with 4K of zeros, 15° or 30° pulse angle, 0.5-s aquisition time, and 2.5-s pulse repetition rate. The broad-band ^1H decoupler was on only during the aquisition time to ensure maximum supression of the NOE. The spectra of the *N*-methylazoles were determined in the presence of Cr(Acac)$_3$ and with the appropriate spectrometer conditions. In all cases, it was necessary to accumulate 30 000–60 000 transients in order to obtain spectra with an acceptable signal-to-noise ratio.

The chemical shifts were determined with respect to external nitromethane contained in a 2-mm capillary held concentrically in the sample tube. The nitrogen chemical shifts referenced to nitromethane, $\delta_{CH_3NO_2}$, were then converted to a chemical shift relative to liquid ammonia, δ_{NH_3}, using the following expression:[9,24]

$$\delta_{NH_3} = \delta_{CH_3NO_2} + 380.2 \text{ ppm}$$

No effort was made to correct the chemical shifts for solution magnetic susceptibility differences[9] or magnetic susceptibility changes resulting from the Cr(Acac)$_3$[10] as these result in chemical shift changes that are small in relation to the differences in chemical shifts between the pyrrole- and pyridine-type of nitrogen atoms.

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Registry No. **1**, 109-97-7; **2**, 96-54-8; **3**, 288-32-4; **4**, 616-47-7; **5**, 288-13-1; **6**, 930-36-9; **7**, 271-44-3; **10**, 288-36-8; 11, 16681-65-5; **12**, 18922-69-5; **13**, 95-14-7; **14**, 13351-73-0; **15**, 16584-00-2; **16**, 288-88-0; **17**, 6086-21-1; **18**, 10570-40-8; **19**, 288-94-8; **20**, 16681-77-9; **21**, 16681-78-0.

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On the Mechanism of Ester Aminolysis in the Presence of Alkylammonium Carboxylate Reversed Micelles

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The mechanism of ester aminolysis by alkylammonium carboxylate reversed micelles was examined. There are two possible pathways, one involving the carboxylate group of the surfactant acting as a general base and another in which it is acting as a nucleophile. The latter mechanism involves the formation of a mixed anhydride (derived from the surfactant and the ester) leading, on aminolysis, to two amides. It was not possible to detect the formation of the intermediate anhydride. Careful analysis of the reaction products showed that only one amide, that derived from the ester, is formed. Thus the second mechanism is in error. The nature of the slow step was explored by studying the aminolysis of a series of esters: *p*-X-phenyl acetates (where X = CH_3O, CH_3, H, Br, CN, and NO_2) by dodecylammonium propionate (DAP) and by dodecylamine plus DAP in benzene and in cyclohexane. Excellent correlations between the logarithm of the rate constant and the Hammett (σ^-) values were obtained. This implies that the phenoxide ion is the leaving group and that the slow step probably involves the collapse of the tetrahedral intermediate formed by the attack of the amine on the ester. Thus it appears that ester aminolysis in the micellar pseudophase and that in aprotic solvents proceed with the same mechanism and rate-limiting step.

Catalysis by detergent aggregates in organic solvents (termed reversed micelles) is a subject of increasing importance because of the catalytic efficiency of these species.[1] Reversed micellar catalysis is also relevant to the enzymatic counterpart since the active sites of proteolytic as well as lipolytic enzymes contain hydrophobic regions,[2] whose polarity is similar to that in the micellar water "pools".[1,3] The substrates usually concentrate in the micellar "core" (made of the surfactant hydrophilic groups) where enhanced reactivities, concerted proton transfer, and favorable entropies of activation contribute to the catalysis.[1,3,4]

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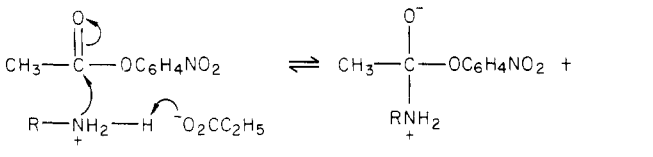
Alkylammonium salts were extensively used as micellar catalysts, especially for acyl-transfer reactions.[1,5,6] As an example, consider the aminolysis of *p*-nitrophenyl acetate by dodecylammonium propionate (DAP) reversed micelles in benzene. The first step of this reaction involves the formation of a tetrahedral intermediate, as shown in eq 1,[6] where R = $C_{12}H_{25}$. More recently it has been argued



$C_2H_5CO_2H$ (1)

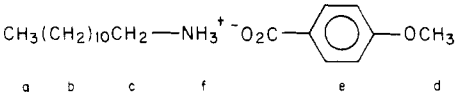
that the carboxylate group of the surfactant is acting not as a general base but as a nucleophile. The slow step was pictured as involving the attack of the R'–CO_2^- group of the detergent on the ester (or the protonated ester) to give a mixed anhydride ($CH_3COOCOC_2H_5$ in the case of the above example).[7] It is relevant, however, that no experimental evidence was given to show the formation of this proposed intermediate or to prove the identity of the formed amides,[7] although many GLC stationary phases are available to specifically indentify these products.[8]

The determination of whether the catalysis is general base type or nucleophilic is an interesting physical organic problem per se. It also bears on the reaction mechanism in reversed micelles relative to that in a reference solvent, e.g., in an organic solvent, and on the similarities between micellar and enzymatic catalysis. By a careful analysis of the products of the reaction of carboxylic esters with alkylammonium carboxylate reversed micelles we were able to show that the nucleophilic catalysis mechanism is not operating, which substantiates our original proposal. The nature of the slow step was also checked by studying the kinetics of the aminolysis of a series of *p*-X-phenyl acetates (X = CH_3O, CH_3, H, Br, CN, NO_2) in the presence of DAP in benzene and in cyclohexane. On the basis of a two-step mechanism involving a tetrahedral intermediate, the kinetic data suggest that the collapse of the intermediate is rate limiting.

Experimental Section

Elemental analyses were performed by the elemental analyses laboratory of this institute. Melting points were not corrected. IR spectra were registered by using a Perkin-Elmer Model 238 spectrometer, and ^1H NMR spectra were obtained with Varian EM-360 or T-60 spectrometers. Chemical shifts are given relative to internal Me_4Si (δ 0). The solvents and reagents were purified as described elsewhere[9] and, when needed, were further dried on Linde Type 4A molecular sieves.

DAP and dodecylammonium *p*-anisate (DAPA) were prepared by heating equimolar amounts of dodecylamine and the appropriate acid in hexane, followed by recrystallization of the crude product from the same solvent: DAP, mp 55–56 °C (lit.[10] mp 54.5–55.5 °C); DAPA, mp 49–50 °C. Anal. Calcd for $C_{20}H_{35}NO_3$: C, 71.17; H, 10.45; N, 4.15. Found: C, 71.17; H, 10.55; N, 4.23. The structure of DAPA is



and the ^1H NMR spectrum (CCl_4) showed the following: δ 0.89 (t, 3 H, a), 1.17 (s, 20 H, b), 2.77 (t, 2 H, C), 3.75 (s, 3 H, d), 7.23 (q, 4 H, e), 8.62 (s, 3 H, f).[11]

The amides CH_3CONHR and C_2H_5CONHR were prepared by refluxing the appropriate anhydride and dodecylamine (DA; molar ratio 1:2) in chloroform for 4 h. The solution was cooled, washed with 0.01 M NaOH solution, water, 0.01 M hydrochloric acid solution, and water, and dried, and the solvent was evaporated. The crude products were recrystallized from hexane. *N*-Dodecylacetamide: mp 54–55 °C (lit.[13] mp 53–54 °C); IR (Nujol)

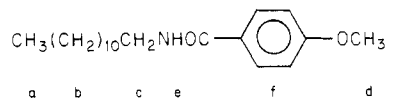
$$\underset{a}{CH_3}(\underset{b}{CH_2})_{10}\underset{d}{CH_2}\underset{e}{NH}\underset{c}{OCCH_3}$$

3270, 1635 cm^{-1}; ^1H NMR (CCl_4) δ 0.89 (t, 3 H, a), 1.24 (s, 20 H, b), 1.85 (s, 3 H, c), 3.16 (m, 2 H, d), 6.61 (t, 1 H, e).

The corresponding C_2H_5CONHR gave a melting point of 52–53 °C (lit.[13] mp 53–53.5 °C) and showed the expected peaks in the IR spectrum (Nujol) at 3300 and 1635 cm^{-1}. Its ^1H NMR spectrum

$$\underset{a}{CH_3}(\underset{c}{CH_2})_{10}\underset{e}{CH_2}\underset{t}{NH}\underset{d}{OCCH_2}\underset{b}{CH_3}$$

(CCl_4) showed the following: δ 0.89 (t, 3 H, a), 1.11 (t, 3 H, b), 1.30 (s, 20 H, c), 2.11 (q, 2 H, d), 3.13 (m, 2 H, e), 6.56 (t, 1 H, f). *N*-Dodecyl-*p*-anisamide was prepared by refluxing DA and *p*-anisoyl chloride (molar ratio 1:2) in chloroform for 4 h, and the reaction mixture was worked up as given for the above amides; mp 89–90 °C. Anal. Calcd for $C_{20}H_{33}NO_2$: C, 75.19; H, 10.41; N, 4.38. Found: C, 75.20; H, 10.29; N, 4.47. The IR spectrum (Nujol) showed peaks at 3320 and 1635 cm^{-1}, and the ^1H NMR spectrum ($CDCl_3$) showed the following: δ 0.88 (t, 3 H, a), 1.25



(s, 20 H, b), 3.38 (m, 2 H, c), 3.80 (s, 3 H, d), 6.22 (t, 1 H, e), 7.26 (q, 4 H, f).

Acetic propionic anhydride was prepared by refluxing acetyl chloride and sodium propionate (prepared in situ from NaH and propionic acid) in THF for 5 h. The solvent was then distilled off, dichloromethane added, the precipitated sodium chloride filtered, and the solvent removed. The product had a boiling point of 52–55 °C (17 mm) [lit.[14] bp 52–55 °C (17 mm)]. The IR spectrum (neat) showed the characteristic anhydride peaks at 1810 and 1745 cm^{-1}. The ^1H NMR (CCl_4) showed the following: δ 1.19 (t, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 2.48 (q, 2 H, CH_2). Attempts to prepare acetic *p*-anisic anhydride by the same procedure gave, however, a solid product whose ^1H NMR spectrum showed that it is *p*-anisic anhydride, probably produced by disproportionation of the mixed anhydride.[15] The desired compound was prepared by refluxing a mixture of sodium *p*-anisate and acetyl chloride for 6 h. The excess acid chloride was removed at room temperature (water pump), leaving a semisolid white product which reacts with anhydrous methanol to give a mixture of methyl acetate and methyl *p*-anisate: ^1H NMR ($CDCl_3$) δ 2.40 (s, 3 H,

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CH_3), 3.94 (s, 3 H, CH_3), 7.58 (q, 4 H, aromatic protons).

The reaction between each of the above-prepared anhydrides and DA was carried out by stirring 5 mmol of the anhydride and 12.5 mmol of the amine in 20 mL dichloromethane at room temperature for several hours. The solution workup was similar to that used in the preparation of the amides. The reaction with DAP or with DAPA was carried out similarly, except that the anhydride concentration was half that used in the reaction with DA.

The esters $CH_3CO_2C_6H_4X$ (X = CH_3, CH_3O, Br, CN) were prepared by refluxing acetyl chloride and the appropriate phenol in chloroform, followed by purification. The products gave the expected physical constants and ^1H NMR spectra. *p*-Nitrophenyl acetate (Aldrich) and phenyl acetate (BDH) were purified before use.

The reaction between *p*-nitrophenyl and/or *p*-tolyl acetate (5 mmol) and DAP or DAPA (25 mmol) was carried out in chloroform (40 mL) in a way similar to that used for the reaction of these surfactants with the mixed anhydrides, and the products were identified by their ^1H NMR and IR spectra.

The kinetics of ester aminolysis by DAP and by DA plus DAP in benzene and in cyclohexane were carried out as given elsewhere[6] by using a Zeiss PM6KS UV–vis spectrophotometer equipped with a thermostated cell holder whose temperature was controlled to within ±0.05 °C. All experiments were carried out under pseudo-first-order conditions, and the reactions were monitored by following the absorption of the liberated phenols (X, λ in nm: CH_3, 290; CH_3O, 305; H, 283; Br, 295; CN, 250; NO_2, 320). It was not possible to monitor the formation of *p*-cyanophenol in benzene because of the strong solvent absorption. Pseudo-first-order rate constants (k_{obsd}) were determined from the absorbance–time data by using a Burroughs 6700 computer. Good first-order kinetics were observed in all cases, and the percentage relative standard deviation of k_{obsd} (i.e., the standard deviation × $100/k_{obsd}$) was <2%.

Results and Discussion

The basic difference between the two proposed mechanisms lies in the intermediate formation of a mixed anhydride. We tried to detect the formation of this species by recording the IR spectrum of a chloroform solution which was 0.025 M in *p*-nitrophenyl acetate and 0.1 M in DAP as a function of time. The only observable change in the carbonyl region was the disappearance of the ester (CO) peak at 1755 cm^{-1} and the appearance of a peak due to the amide carbonyl group at 1650 cm^{-1}. The fact that the characteristic broad doublet of the anhydride was not observed is, however, not surprising since if it is a reactive intermediate, then its concentration may be too low to be detected.

A mixed anhydride formation, however, must be followed by aminolysis to give two different amides. The products will be CH_3CONHR and C_2H_5CONHR or CH_3CONHR and $CH_3OC_6H_4CONHR$ for the reaction of an acetate ester with DAP and DAPA, respectively. Since the anhydride cannot be directly observed, we decided to prove its formation by a careful analysis of the reaction products.

First we showed that a mixture of the two amides (e.g., $CH_3OC_6H_4CONHR$ and CH_3CONHR) once formed is stable under the experimental conditions.[16] The subsequent results are best explained with the aid of Figure 1 for the reaction with DAPA. Figure 1A shows the ^1H NMR spectrum of an equimolar mixture of **CH_3**$CONHR$ and **$CH_3OC_6H_4$**$CONHR$. Note the presence of the two singlets at δ 1.99 and 3.80 for the above boldface methyl groups and the quartet of the aromatic protons. Figure 1B shows the spectrum of the products of the reaction of $CH_3COOCOC_6H_4OCH_3$ with DAPA. It is identical with part A, showing that if a mixed anhydride is formed, then two amides must be obtained. Figure 1C shows the spectrum of the product(s) of the reaction of *p*-nitrophenyl acetate and DAPA. The absence of the singlet at 3.80 ppm and any peaks in the aromatic region of the spectrum clearly shows that the amide $CH_3OC_6H_4CONHR$ is absent. Actually this spectrum is that of CH_3CONHR; i.e., only one amide was formed. The same conclusion can be also reached in the case of DAP. Thus the reaction between $CH_3COOCOC_2H_5$ and the surfactant produced a mixture of the amides CH_3CONHR and C_2H_5CONHR. On the other hand, ^1H NMR spectra showed that the only product of the reaction between DAP and *p*-nitrophenyl acetate was CH_3CONHR.

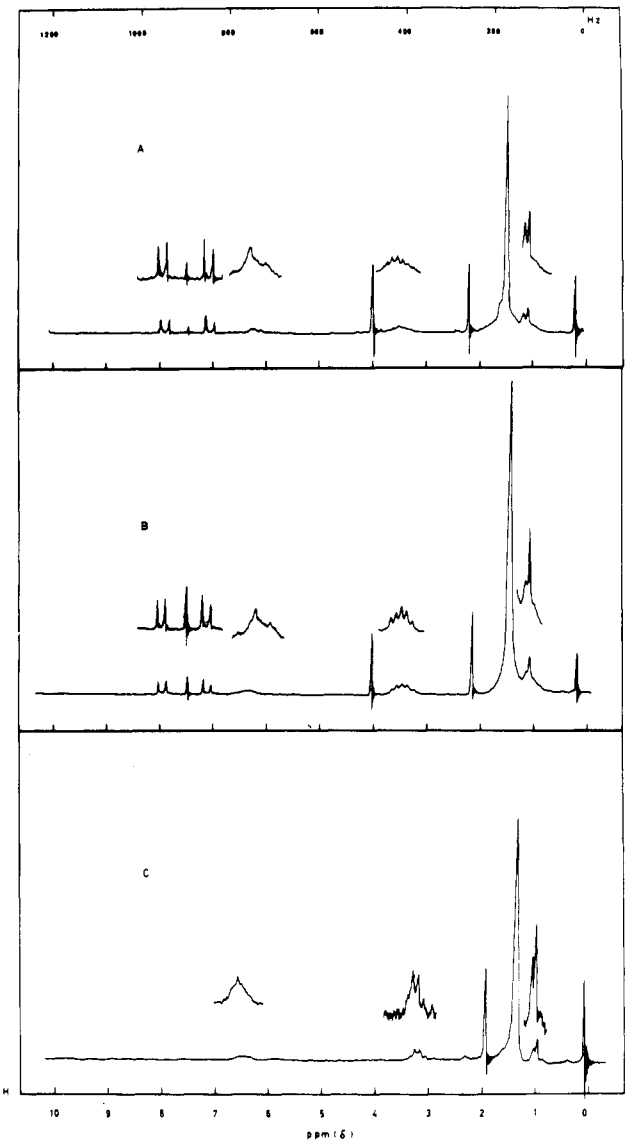


Figure 1. ^1H NMR spectra of an equimolar mixture of *N*-dodecylacetamide and *N*-dodecyl-*p*-anisamide (A) and of the products of the reaction of DAPA with acetic *p*-anisic anhydride (B) and with *p*-nitrophenyl acetate (C).

The above results demonstrate, unequivocally, that no mixed anhydride is formed as an intermediate in the aminolysis under study; hence the nucleophilic mechanism[7] can be ruled out. This is not surprising, since the car-

(16) A mixture of 2.5 mmol of CH_3CONHR, 2.5 mmol of $CH_3OC_6H_4$-CONHR, and 12.5 mmol of DAPA in 30 mL of chloroform was stirred at room temperature for several hours. The mixture workup was similar to that used for the reaction of an ester with DAPA (see the Experimental Section). The ^1H NMR spectrum showed that the two amides were recovered essentially unchanged. A similar result was obtained in an experiment in which an equimolar mixture of CH_3CONHR and C_2H_5CONHR was stirred with DAP in chloroform.

Table I. Rate Constants and Hammett (ρ) Values for the Reversed Micelle-Catalyzed Ester Aminolysis in Benzene and in Cyclohexane at 25 °C

	k_{obsd}[a] in benzene		k_{obsd}[a] in cyclohexane		
X	DAP (0.20 M)	DA + DAP[b]	DAP (0.10 M)	DAP (0.20 M)	DA + DAP[b]
CH_3O	8.7	10.0	12.3	19.6	25.8
CH_3	9.6	11.3	13.2	21.7	28.4
H	13.9	17.3	18.9	31.4	42.7
Br	24.0	32.4	49.0	82.9	124.9
CN	[c]	[c]	307.5	734.2	1378.7
NO_2	170.7	298.6	786.9	2112.3	4277.2
ρ[d]	0.89 ± 0.04	1.01 ± 0.05	1.25 ± 0.04	1.41 ± 0.03	1.54 ± 0.03
CC[e]	0.997	0.996	0.998	0.999	0.999

[a] $10^{-5}k_{obsd}$, s^{-1}. [b] [DA] = 0.025 M and [DAP] = 0.20 M. [c] Not available due to the solvent absorption. [d] Based on the σ^- values, taken from ref 26. [e] Correlation coefficient.

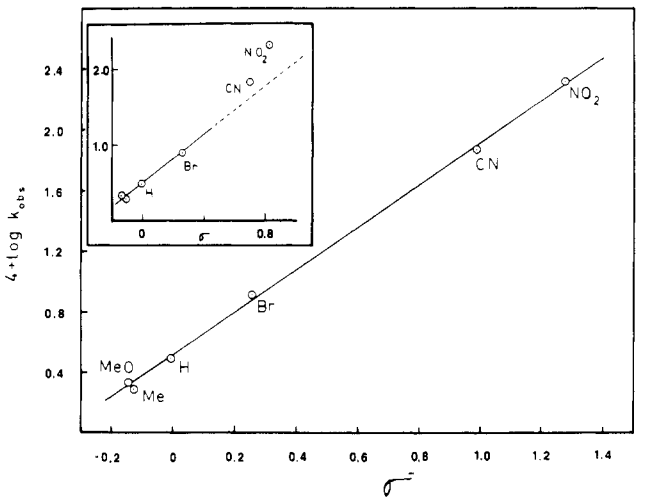
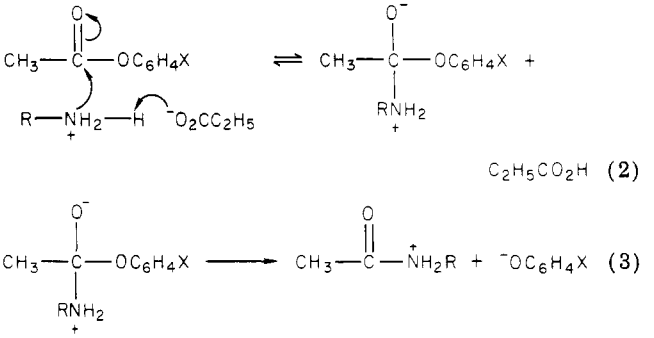


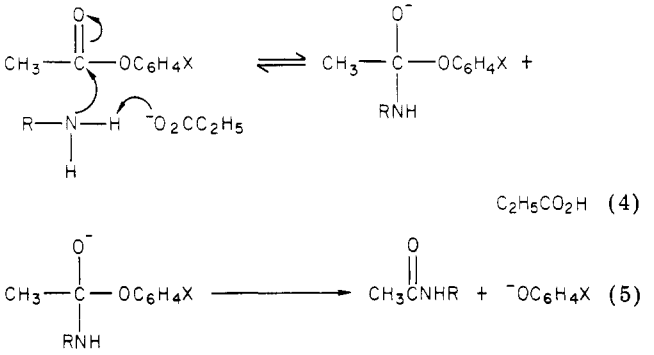
Figure 2. Hammett equation plot between log k_{obsd} and σ^- for the aminolysis of $XC_6H_4O_2CCH_3$ by 0.2 M DAP in cyclohexane. The insert is for the same correlation with σ.

boxylate ion can hardly be assumed to be a "bare" species (hence a good nucleophile) when hydrogen-bond donors are present.[17,18] In the special case where the carboxylate group can only act as a nucleophile,[19] the reaction is strongly inhibited by the addition of protic solvents, due to its strong solvation.[20]

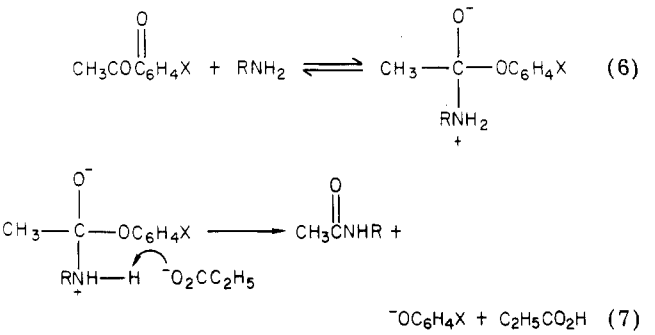
On the basis of the established mechanism for ester aminolysis in aprotic solvents,[18,21] the reaction of an ester, $CH_3CO_2C_6H_4X$, with a detergent, e.g., DAP, can be represented by eq 2 and 3. This scheme predicts that the reaction is first order in DAP, a result which was obtained in the case of the aminolysis in benzene.[6,22] The slow step



can be the formation of the zwitterionic intermediate (eq 2) or its collapse (eq 3). Ester aminolysis by an alkylamine (e.g., DA) in a nonpolar solvent is also catalyzed by these detergents. It is possible to write two schemes (differing only in the timing of the proton transfer) to represent this catalysis. In the first (eq 4) the carboxylate group accepts



a proton from the attacking amine, leading to a negatively charged intermediate which then collapses to products as shown in eq 5. It is also possible that the carboxylate group accepts a proton from the zwitterionic intermediate (eq 7), thereby impairing the back-reaction to the reactants



(i.e., eq 7 is rate limiting).[21] Both mechanisms agree with the fact that the reaction is first order in the amine and in the detergent.[23]

In order to get some insight into the nature of the rate-limiting step, and hence the mechanism of catalysis, we studied the kinetics of the aminolysis of a series of esters, $CH_3CO_2C_6H_4X$, by DAP and by DA plus DAP in benzene and in cyclohexane. Table I shows the values of k_{obsd} for the reaction in the two solvents, along with the corresponding Hammett ρ values.[24] Figure 2 shows the

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(22) The results of the present work agree with those of others[5,7] that the reaction with DAP in cyclohexane is second order in the surfactant. The lower the solvent polarity the less will be the interaction between the surfactant head ions and the solvent. consequently, its hydrophilic groups will interact more with the species present in the micellar core. The second-order dependence on DAP can be taken to indicate that the intermediate is probably strongly hydrogen bonded to the surfactant.

(23) The dependence of k_{obsd} on the surfactant and/or on the amine concentration has been verified both in benzene[6] and in cyclohexane. The reaction was studied as a function of DAP in the presence of a constant DA concentration (0.02 M), and the following rate constants were obtained [DAP concentration, M (10^{-4} k_{obsd}), s^{-1})]: 0.02, (37.1), 0.04 (68.2), 0.06 (99.0), 0.08 (133.5), 0.10 (168.6), 0.12 (199.1), 0.14 (238.2). A plot of k_{obsd} vs. [DAP] gave a straight line (correlation coefficient = 0.999) with a nonzero intercept, showing that $k_{obsd} = k_1[RNH_2] + k_2[RNH_2][DAP]$. The value of k_1 is 1.3×10^{-4} s^{-1}, and that of k_2 is 16.7×10^{-2} M^{-1} s^{-1}.

Hammett equation plot between log k_{obsd} and the σ^- values[26] for the reaction in cyclohexane. The insert in Figure 2 shows the corresponding correlation between log k_{obsd} and the σ values.[26] It is clear that the latter scale is not appropriate since the points for X = CN and NO_2 deviate considerably from the straight line. On the other hand, an excellent correlation with σ^- was obtained, as shown in Figure 2 and from the statistical data in Table I.

The correlation with σ^- rather than σ implies that XC_6H_4–O^- is the leaving group and that the collapse of the intermediate is rate limiting. This is similar to the conclusions drawn concerning the mechanism of ester aminolysis in chlorobenzene and in acetonitrile.[21] That is, it appears that the micellar reaction is similar, both in the mechanism and in the rate-limiting step to its counterpart in aprotic solvents.[27]

Of the two possibilities proposed to explain the role of the carboxylate ion as a general-base catalyst (eq 4 and 7), we think that the former is more plausible for the following reasons. First, eq 4 is similar to eq 2. The latter is probably the most reasonable way to explain the reaction with DAP since the carboxylate group is the strongest base available to accept a proton from the ammonium ion.[28] Note that ^1H NMR studies demonstrated that there exists a strong hydrogen bonding between the ammonium and the carboxylate ions of DAP.[10] Thus the mode of action of the general base is the same in both cases.[29] Ester aminolysis by DA in benzene, as well as in other aprotic solvents, is second order in the amine.[6,21] The DAP-catalyzed reaction is, however, first order in both DA and DAP, showing that the latter probably substitutes the second amine molecule as a general base.[6] On the other hand, eq 6 rests on the assumption that the attacking amine is not hydrogen bonded to the surfactant head ions which form the micellar core. In view of the demonstrated association of hydrogen bond donors with alkylammonium carboxylates,[30] the above-mentioned assumption seems unlikely. Finally, eq 4, which pictures the attacking species as $(RCO_2$–$H_2NR)^-$ and not as RNH_2, is in agreement with the mechanism given to explain the catalytic role of the carboxylate group in the esterolysis reaction in benzene[18] and is similar to the charge-relay mechanism for enzymatic catalysis.[31]

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Registry No. $CH_3CO_2C_6H_4$-*p*-OCH_3, 1200-06-2; $CH_3CO_2C_6H_4$-*p*-CH_3, 140-39-6; $CH_3CO_2C_6H_5$, 122-79-2; $CH_3CO_2C_6H_4$-*p*-Br, 1927-95-3; $CH_3CO_2C_6H_4$-*p*-CN, 13031-41-9; $CH_3CO_2C_6H_4$-*p*-NO_2, 830-03-5; $CH_3(CH_2)_{10}CH_2NHOCH_3$, 3886-80-4; $CH_3(CH_2)_{10}CH_2NHOCCH_2CH_3$, 62855-82-7; CH_3-$(CH_2)_{10}CH_2NHOCC_6H_4$-*p*-$OCH_3$, 1854-15-5; $CH_3COOCOCH_2CH_3$, 13080-96-1; $CH_3COOCOC_6H_4$-*p*-OCH_3, 83511-12-0; DAPA, 83511-11-9; DAP, 17448-65-6; dodecylamine, 124-22-1.

(24) Our (k_{obsd}) values in cyclohexane are higher than those reported before.[25] It is possible that the lower rates were obtained because of the presence of residual moisture in the surfactant solution. It was reported that the solubility limit of DAP in cyclohexane at 25 °C is <0.10 M.[25] We were able, however, to prepare a 0.25 M DAP solution at the same temperature. On drying, DAP looses between 1.3% and 1.5% of its weight. In one experiment we tried to prepare a 0.25 M DAP solution using a partially dried surfactant (weight loss 0.6%); a turbid solution was obtained.

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(27) The micellar ρ values are smaller than those observed for ester aminolysis by pyrrolidine in aprotic solvents.[21] The fact that the reaction is carried out in a medium with very different properties (the micellar microenvironment) probably plays a role in determining the value of ρ. It is relevant, however, that Menger's rate data[21] correlate with σ^- much better than with σ. The use of the former scale results in a substantial decrease in the value of ρ.

(28) This is in contrast to another mechanism in which the ester CO group, acting as a base, accepts this proton.[7]

(29) The intermediate shown in eq 4 must revert back to reactants faster than it goes to products; i.e., eq 5 is rate limiting. According to the principle of microscopic reversibility this can be established by protonating the nitrogen atom of the intermediate by the formed propionic acid.

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Hofmann Degradation of β-Hydroxy Ammonium Salts. α- and β-Hydroxylaudanosine, 7-Hydroxyglaucine, and 13-Hydroxyxylopinine

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The four related β-hydroxy ammonium methiodide salts of α-hydroxylaudanosine (**2a**), β-hydroxylaudanosine (**2b**), 7-hydroxyglaucine (**5a**), and 13-hydroxyxylopinine (**8a**) have been subjected to Hofmann degradation. Although precedent dictates that such materials should form either epoxides or ketones, these are not found. Only products of (a) fragmentation and elimination (from **2a** and **2b**), (b) dehydration and elimination (from **5a**), and (c) elimination and oxidation (from **8a**) are obtained. The results are accounted for by consideration of the molecular geometries of the β-hydroxy ammonium salts as experimentally determined from single-crystal X-ray studies and the geometric requirements for epoxide and ketone formation.

Late-stage oxidation (often with introduction of oxygen) of alkaloids has been proposed to account for, in part, structural modifications in the elaborated bases.[1,2] In some cases, biosynthetic work has supported such speculation by delineating the relationship between coisolated or biogenetically "related" but separately found materi-

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