Association Phenomena. 2.
Catalysis of the Decomposition of Acetyl Phosphate by Chelate Micelles and by Amine–Ammonium Micelles

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Abstract: The decomposition of acetyl phosphate via hydrolysis and/or aminolysis has been studied with respect to the effects of (a) triethylenetetramine, alone and in the presence of metal ions, in nonmicellar solutions, (b) 5-alkyltriethylenetetramines, alone and in the presence of metal ions, in micellar solutions, (c) ethyltrimethylammonium iodide and butylammonium chloride in nonmicellar solutions, and (d) dodecyltrimethylammonium chloride and dodecylammonium chloride in micellar solutions. The kinetics of acetyl phosphate disappearance have been measured under these various conditions by means of the ferric hydroxamate assay. An analysis of the rate data suggests that in addition to contributions from the uncatalyzed reaction, the amine-catalyzed reaction, and the metal-catalyzed reaction there is also a contribution in both the nonmicellar and micellar systems from a reaction catalyzed by the metal tetramine chelate. In all cases the decomposition proceeds more rapidly in the micellar solutions than in the nonmicellar solutions. Of particular interest is the micellar reaction carried out in the presence of dodecylammonium chloride for which the rate is ~160 times greater than that of the nonmicellar reaction in the presence of butylammonium chloride. On the basis of an optimum rate observed at pH 8 for the micellar process, it is postulated that the catalysis arises from a mixed micelle containing charged and uncharged amine species, the charged species interacting with the anionic centers of acetyl phosphate and the uncharged species acting as a nucleophile toward the carbonyl group of acetyl phosphate.

The first paper in this series, appearing 17 years ago,[1] described the effects of certain cations on the hydrolysis and glycinolysis of acetyl phosphate. The present paper represents an extension of that work and is concerned with the effects of cations in micellar systems on the olysis reactions of acetyl phosphate. Three sets of experiments are discussed: (a) olysis reactions of acetyl phosphate in the presence of triethylenetetramine, with and without metal ions, in nonmicellar solutions; (b) olysis reactions of acetyl phosphate in the presence of 5-alkyltriethylenetetramines, with and without metal ions, in micellar solutions; and (c) olysis reactions of acetyl phosphate in the presence of ethyltrimethylammonium iodide, butylammonium chloride, dodecyltrimethylammonium chloride, and dodecylammonium chloride in nonmicellar and micellar solutions.

Assay Methods. The kinetics of all of the reactions in this study were based on the rate of disappearance of acetyl phosphate as measured by its conversion to ferric hydroxamate. Of the several variations that have been described for this assay, the one reported by Koshland[2] and modified by Pechère and Capony[3] was used. Although this assay can be made quite specific for acyl phosphates, anhydrides, and acyl halides (i.e., very reactive acyl donors), less reactive compounds such as esters, amides, and even carboxylic acids can also slowly acylate hydroxylamine. Advantage was taken of this fact to quantitatively assay not only the unconsumed acetyl phosphate but, when alcohols were present in the reaction mixture, ester as well. Employing the method of Hestrin,[4] unconsumed acetyl phosphate was removed by making the reaction mixture strongly basic before the addition of hydroxylamine and ferric ion. The acetates of ethanol through hexanol yielded good results by this method. The acetates of octanol through hexadecanol produced turbid solutions, but this problem could be avoided by using a 4 M solution of hydrochloric acid in ethanol. Attempts to extend this procedure to the assay of amides, when amines were present in the reaction mixture, were not successful. Because of their much lower reactivity, necessitating rather severe reaction conditions for the formation of the hydroxamate, and because of interference from ester, acetic acid (from acetyl phosphate), and metal ions, amides could be only qualitatively assayed.

Experiments in Nonmicellar Solutions. Decomposition of

Acetyl Phosphate in the Presence of Triethylenetetramine, with and without Metal Ions. A goal of the work described in this paper is to devise a surfactant system that can increase the rate of decomposition of acetyl phosphate by selective nucleophilic attack. One approach involves the formation of mixed micelles containing 1-hexanol as the nucleophile and chelates of 5-alkyltriethylenetetramines and various metals as the primary surfactant. It was hoped that the positively charged micelle would attract the dianionic acetyl phosphate and juxtapose it with the solubilized 1-hexanol in a fashion appropriate to acetyl transfer to the alcohol. Before investigating such systems, however, it was first necessary to provide reference points by carrying out a series of reactions in nonmicellar systems.

The first reference point was obtained by studying the rate of decomposition of acetyl phosphate in aqueous solution (pH 7, temperature 39 °C, ionic strength 0.6) in the presence and absence of a collidine–collidine hydrochloride buffer. A value of $4.0 \pm 0.2 \times 10^{-3}$ min^{-1} was obtained under both conditions, indicating that a buffer is not essential. This is commensurate with the essentially flat pH–rate profile for the hydrolysis of acetyl phosphate in the pH 5–10 region.[2] Values of 4.3×10^{-3} min^{-1}, 4.0×10^{-3} min^{-1}, and 3.78×10^{-3} min^{-1} for acetyl phosphate hydrolysis in buffered solutions[2,5,6] and 4.3×10^{-3} min^{-1} in unbuffered solution[6] have been reported.

To provide further reference points, triethylenetetramine (trien), metal ions, and alcohols were tested individually and in various combinations for their effect on the decomposition of acetyl phosphate. As shown in Table I, trien increases the rate. A plot of $k_{obsd} - k_{uncat}$ vs. trien concentration yields two points; a straight line through these points also passes through the origin and has a slope from which the value of 4.4×10^{-1} min^{-1} for k_{trien} can be calculated. By what pathway(s) trien achieves this rate enhancement is uncertain, for Di Sabato and Jencks[6] have shown that primary and secondary amines can catalyze the decomposition of acetyl phosphate by acid catalysis (e.g., an [amine-H$^+$] term), by nucleophilic catalysis (e.g., an [amine] term), and/or by general base catalysis (e.g., an [amine]^2 term). That at least some of the catalysis by trien is nucleophilic in character is indicated by the formation of acetyltrien, as measured qualitatively by the ferric hydroxamate assay.

More than 20 metals are known to form chelates with trien.

Table I. Effect of trien on the Rate of Decomposition of 0.005 M Acetyl Phosphate[a]

[trien], M	k_{obsd}, 10^{-3} min^{-1}
0	4.0 ± 0.2
0.005	5.9 ± 0.3
0.025	14.6 ± 0.8

[a] pH 7, temperature 39 °C, ionic strength 0.6.

The ions chosen for the present study were Mn^{2+}, Co^{2+}, Zn^{2+}, Ni^{2+}, and Cu^{2+}, because they form 1:1 complexes, are stable to atmospheric oxygen, and form complexes that are soluble in water up to concentrations of 0.025 M. The effect of these ions, alone and in the presence of trien, is shown in Table II. In the absence of trien, precipitates (presumably the metal oxides or hydroxides) formed at the beginning of all of the reactions except those in which Ni^{+2} was the metal ion. Thus, the k_{obsd} values in these cases are for solutions saturated with the particular metal ion. Working at a lower pH (5.8–6.0), Oestreich and Jones[7] did not encounter precipitates in their study of the metal ion-catalyzed hydrolysis of acetyl phosphate.

In the presence of trien no precipitates formed, making it possible to obtain rate data at metal ion concentrations of 0.025 M, as shown in Table II. In these cases $k_{obsd} \simeq k_{uncat.} + k_{metal}[metal] + k_{trien}[trien] + k_{chelate}[chelate]$. However, since all of the solutions except those containing Ni^{2+} are saturated with respect to the metal ion, $k_{uncat.} + k_{metal}[metal]$ can be no greater than k_{obsd} for the reaction in the absence of trien (see Table II). To assess the $k_{trien}[trien]$ term it is necessary to know the concentration of free trien in the reaction mixture, which can be calculated if K_{assoc} for chelate formation at pH 7 is known. This requires that account be taken of the equilibria:

$$trien\text{-}H_4{}^{4+} + 4OH^- \rightleftharpoons trien + 4H_2O$$

$$M^{2+} + trien \rightleftharpoons M(trien)^{2+}$$
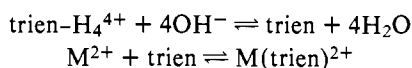
Employing a method described in the literature,[8] the appropriate association constants were found to have the values shown in Table III where K_{eff} applies to systems in which metal hydroxide precipitates are absent.

Using the log K_{eff} values, it can be calculated that when Mn^{2+} is present most of the trien (and Mn^{2+}) is in the *unchelated* form,[10] but that when the other metals are present most of the trien (and metal) is in the *chelated* form. With 0.025 M Mn^{+2} and trien, $k_{uncat.} + k_{metal}[metal] + k_{trien}[trien]$ = 5.4 × 10^{-3} min^{-1} (see Table II) + 14.6 × 10^{-3} min^{-1} (see Table I) = 19.8 × 10^{-3} min^{-1}. This is slightly lower than the observed value of 23.0, suggesting that there is some contribution from the $k_{chelate}[chelate]$ term. With reaction mixtures containing 0.025 M Co^{+2} or Zn^{2+} and trien, essentially all of the trien (and metal) is in the chelated form; so there should be little contribution from $k_{metal}[metal]$ and $k_{trien}[trien]$. The observed values of 19.0 × 10^{-3} min^{-1} and 9.1 × 10^{-3} min^{-1} are significantly greater than the uncatalyzed rate of 4.0 × 10^{-3} min^{-1}, suggesting that here also there is a catalytic effect from chelated species. With Ni^{2+} and Cu^{2+} the rates of reaction show little response to either metal or metal + trien, indicating that the chelated species plays a negligible role in these cases. That portion of the catalysis that is being ascribed to $k_{chelate}[chelate]$ might arise from (a) partially dissociated chelates which can act as nucleophilic species in a fashion comparable with trien itself; (b) partially or fully chelated metal ions which can neutralize the negative charge on acetyl phosphate, facilitating the attack of nucleophiles which may also be associated with the metal atom of the chelate; and/or (c) complex formation between the chelate and acetyl phos-

Table II. Rates of Decomposition of 0.005 M Acetyl Phosphate in the Presence of Metal Ions, with and without trien[a]

Metal	[Metal], M	[trien], M	k_{obsd}, 10^{-3} min^{-1}
Mn	0.005	None	5.4 ± 0.3
	0.005	0.005	7.4 ± 0.4
	0.025	0.025	23.0 ± 1
Co	0.005	None	6.2 ± 0.3
	0.005	0.005	5.7 ± 0.3
	0.025	0.025	19.0 ± 1
Zn	0.005	None	4.6 ± 0.2
	0.005	0.005	5.5 ± 0.3
	0.025	0.025	9.1 ± 0.5
Ni	0.005	None	5.9 ± 0.3
	0.005	0.005	4.5 ± 0.2
	0.025	0.025	6.3 ± 0.3
Cu	0.005	None	4.4 ± 0.2
	0.005	0.005	5.0 ± 0.3
	0.025	0.025	4.8 ± 0.3

[a] pH 7, temperature 39 °C, ionic strength 0.6.

Table III. Association Constants for Metal trien Chelates

Metal ion	Log K_{assoc}, M (40 °C)[9]	Log K_{eff}, M (pH 7)
Mn	5.31	0.01
Co	11.03	5.7
Zn	11.81	6.5
Ni	14.01	8.7
Cu	20.08	14.8

phate, enhancing the leaving ability of metaphosphate and accelerating the decomposition.[12]

The reaction of 0.005 M acetyl phosphate in the presence of ethanol (0.005 M), butanol (0.005 M), or 1-hexanol (0.005 or 0.025 M) showed no enhancement of rate over that of acetyl phosphate alone, and the ferric hydroxamate test gave no indication of the formation of any ester.

Experiments in Micellar Solutions. Decomposition of Acetyl Phosphate in the Presence of 5-Alkyltriethylenetetramines, with and without Metal Ions. 5-Alkyltriethylenetetramines (5-alkyltriens) were synthesized from 1-alkenes by conversion to the corresponding 1,2-dibromoalkanes followed by treatment with ethylenediamine:

$$RCH{=}CH_2 + Br_2 \rightarrow RC(Br)HCH_2Br \xrightarrow{NH_2CH_2CH_2NH_2}$$

$$NH_2CH_2CH_2NHC(R)HCH_2NHCH_2CH_2NH_2$$

$$R = CH_3, n\text{-}C_4H_9, n\text{-}C_6H_{13}, n\text{-}C_8H_{17},$$
$$n\text{-}C_{10}H_{21}, n\text{-}C_{12}H_{25}, n\text{-}C_{14}H_{29}, n\text{-}C_{16}H_{33}$$
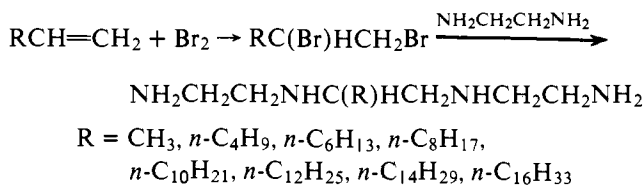
That the 5-alkyltriens closely resemble trien itself with respect to basic properties and chelating ability was shown by comparing the titration curves of the polyamines, alone and in the presence of metals. Plots similar in shape were obtained for trien and the 5-alkyltriens, indicating that the alkyl group has little perturbing effect. The formation of chelates in the presence of Mn^{2+}, Co^{2+}, Zn^{2+}, Ni^{2+}, and Cu^{2+} was clearly demonstrated by the marked differences between the titration curves in the absence and presence of metal ions. The magnitude of these differences increased in the order Mn < Co < Zn < Ni < Cu, in accord with the data in the literature for trien itself (see Table III).

Few precedents appear in the literature for the type of dicationic surfactant represented by the 5-alkyltrien chelates. One whose critical micelle concentration (cmc) has been measured[13] is the bis quaternary ammonium salt obtained from

Table IV. Critical Micelle Concentrations of 5-Hexadecyltrien and the Cu^{2+} Chelates of 5-Octyl-, 5-Decyl-, 5-Dodecyl-, 5-Tetradecyl-, and 5-Hexadecyltrien Determined by Surface Tension and Dye Absorption Measurement

| | Critical micelle concn, M (39 °C) | | | |
| | Surface tension measurement | | Dye absorption measurement | |
Compd	0.6 M NaCl	H_2O	0.6 M NaCl	0.6 M NaCl and 0.025 M 1-hexanol
$Cu(5\text{-octyltrien})^{2+}$	2.5×10^{-2}			
$Cu(5\text{-decyltrien})^{2+}$	3.0×10^{-3}	6.1×10^{-3}	2.8×10^{-3}	2.0×10^{-3}
$Cu(5\text{-dodecyltrien})^{2+}$	2.2×10^{-4}	4.8×10^{-4}	3.2×10^{-4}	1.3×10^{-4}
$Cu(5\text{-tetradecyltrien})^{2+}$	1.6×10^{-5}	$0.95\text{-}1.9 \times 10^{-5}$	$0.90\text{-}1.9 \times 10^{-5}$	$7.6\text{-}9.5 \times 10^{-6}$
$Cu(5\text{-hexadecyltrien})^{2+}$	1.2×10^{-6}			
5-Hexadecyltrien	5.0×10^{-6}			
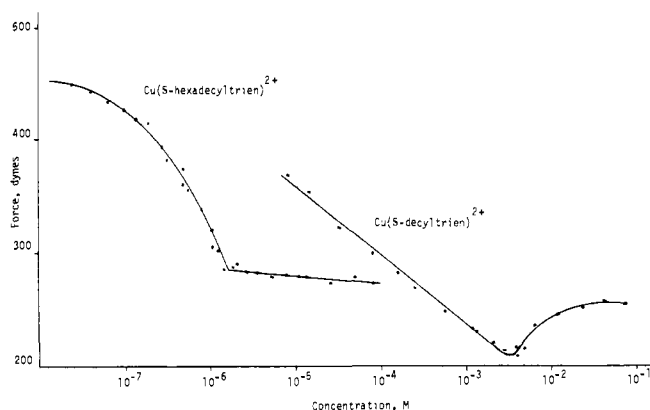
Figure 1. Surface tension measurements of the copper chelates of 5-decyltriethylenetetramine and 5-hexadecyltriethylenetetramine (temperature 39 °C).

Table V. Effect of 5-Dodecyltriethylenetetramine, Alone and in the Presence of Metal Ions, on the Rate of Decomposition of 0.005 M Acetyl Phosphate[a]

Metal	[Metal], M	[5-Alkyltrien], M	k_{obsd}, 10^{-3} min^{-1}
None		0.005	13.7 ± 0.7
		0.025	77 ± 4
Mn	0.005	0.005	8.9 ± 0.5
	0.010	0.010	23 ± 1
	0.025	0.025	150 ± 8
Zn	0.005	0.005	5.7 ± 0.3
	0.010	0.010	7.4 ± 0.4
	0.025	0.025	14.4 ± 0.7
Ni	0.005	0.005	5.8 ± 0.3
	0.010	0.010	6.4 ± 0.3
	0.025	0.025	10.6 ± 0.5
Cu	0.005	0.005	7.8 ± 0.4
	0.010	0.010	8.6 ± 0.4
	0.025	0.025	19 ± 1
	0.050	0.050	50 ± 3

[a] pH 7, temperature 30 °C, ionic strength 0.6.

dimethylhexadecylamine and 1,4-dibromobutane, a value of 3×10^{-5} M being obtained. The critical micelle concentrations for several of the 5-alkyltrien chelates of copper were determined, using surface tension and dye absorption measurements. The results of the surface tension method are shown graphically in Figure 1, and the results of both methods are shown numerically in Table IV. The cmcs of 5-hexadecyl-, 5-decyl-, and 5-octyltrien, as determined by surface tension measurements, are unequivocal, but those of 5-tetradecyl- and 5-dodecyltrien are more difficult to assign because of the unusual shape of the plots. With 5-tetradecyltrien the transition to a constant, reduced value is unexpectedly gradual and might be interpreted as the merger of two transitions. With 5-dodecyltrien two distinct minima occur, separated by a 10-fold range in concentration. These puzzling features are not unique, however, for similar curves have been obtained with the C_{8-18} primary amine hydrochlorides.[14] The occurrence of two or more cmcs is not uncommon and has been attributed to transitions in micelle geometry and/or size.[15] In the present case the higher concentration cmcs were chosen as the more characteristic ones, because these values fall very close to the straight line that is obtained when the log cmc values for the octyl-, decyl-, and hexadecyltriens are plotted vs. the number of carbons in the hydrocarbon chain of the surfactant.[16a] The cmcs for this series of compounds are unusually low. The electrostatic repulsion between the cationic head groups, which might be predicted to lead to high cmcs, is in some manner reduced so that the compounds behave more like nonionic surfactants.[17] The bulkiness of the head group, charge delocalization over the polyamine system, and/or attractive forces between the head groups through hydrogen bonding or polynuclear bridges may account for this.

Experimental difficulties were encountered in attempts to measure the effect of 1-hexanol on the cmcs of the Cu(triens) by surface tension methods. The dye absorption method, therefore, was used, yielding the data shown in Table IV. The

decrease in cmc upon going from water to 0.6 M sodium chloride solution is ascribed to the enhancement of micellization through counterion binding; the further decrease upon the addition of 1-hexanol is ascribed to the formation of mixed micelles.[16b,18] Even though long-chain alcohols do not form micelles by themselves, they are solubilized by other surfactants.[16]

The effect of the chelated metal ion surfactants on the rate of decomposition of acetyl phosphate was investigated by (a) varying the identity of the metal ion, (b) varying the concentration of the metal 5-alkyltrien chelate, and (c) varying the length of the alkyl portion of the 5-alkyltrien in the metal-5-alkyltrien chelate. The results of these studies are shown in Tables V and VI. Unfortunately, the cobalt chelates could not be included, because a heavy red sludge formed when these solutions were adjusted to pH 7, in contrast to the behavior in nonmicellar solutions.

From the rates of reactions carried out in the presence of 5-dodecyltriethylenetetramine in the absence of metal ions (see Table V), a $k_{5\text{-alkyltrien}}$ value of 3.0 min^{-1} can be calculated, a value that is approximately seven times greater than that for k_{trien}. Thus, to the extent that *unchelated* 5-alkyltrien is present in the reaction mixtures containing metal ions, the rates in the micellar systems would be expected to exceed those of the corresponding nonmicellar systems. This is, indeed, what is observed. Employing the same reasoning that is used to interpret the results in the nonmicellar solutions, it can be asserted that there is a contribution from the $k_{chelate}$[chelate] term in the micellar systems also. For example, if it is assumed that in the 0.025 M manganese system the concentration of chelated species is very low (however, see ref 10), the contributions to the rate from $k_{uncat.}$, k_{metal}[metal], and

Table VI. Effect of Length of Alkyl Group of the 5-Alkyltrien in the Cu(5-alkyltrien)- and Mn(5-alkyltrien)-Catalyzed Decompositions of 0.005 M Acetyl Phosphate[a]

No. of carbon atoms in 5-alkyl substituent	Rate constant, 10^{-3} min^{-1}	
	Cu	Mn
0	4.3 ± 0.2	
1	5.0 ± 0.3	
4	4.7 ± 0.2	
6	4.5 ± 0.2	
8	4.2 ± 0.2	6.4 ± 0.3
10	4.1 ± 0.2	7.6 ± 0.4
12	7.8 ± 0.4	8.9 ± 0.5
14	5.8 ± 0.3	9.6 ± 0.5
16	5.9 ± 0.3	11.2 ± 0.6

[a] pH 7, temperature 39 °C, ionic strength 0.6, 5-alkyltrien concentration 0.005 M.

Table VII. Relative Rates for the Decomposition of 0.005 M Acetyl Phosphate in Nonmicellar and Micellar Solutions of Equimolar Amounts of Metal Ions and trien Compound[a]

Metal ion	[Metal] and [trien], M	$k_{obsd}/k_{uncat.}$	
		Nonmicellar (with trien)	Micellar (with 5-alkyltrien)
Mn	0.005	2.0	2.2
	0.025	5.7	38
Zn	0.005	1.4	1.4
	0.025	2.3	3.6
Ni	0.005	1.1	1.5
	0.025	1.6	2.7
Cu	0.005	1.0	2.0
	0.025	1.2	4.8

[a] pH 7, temperature 39 °C, ionic strength 0.6.

$k_{5\text{-alkyltrien}}[5\text{-alkyltrien}]$ should be 5.4×10^{-3} min^{-1} (see Table II) + 77×10^{-3} min^{-1} (see Table V) = 82.4×10^{-3} min^{-1}. The considerably larger observed value of 150×10^{-3} min^{-1}, therefore, indicates a substantial contribution from other sources. Similarly, if it is assumed that in the 0.025 M zinc system the concentration of chelated species is very high, the contribution to the rate from $k_{metal}[metal]$ and $k_{5\text{-alkyltrien}}[5\text{-alkyltrien}]$ should be close to zero and that from $k_{uncat.}$ should be 4.0×10^{-3} min^{-1}. The considerably larger observed value of 14.4×10^{-3} min^{-1} again suggests a contribution from other sources, viz., chelated species. In contrast to the nonmicellar systems containing nickel and copper, where little or no catalysis from any species could be discerned, there is a significant increase in rate in the micellar systems which, by the reasoning just indicated, can be attributed to chelated species.

The comparative data in Table VII show that in almost all cases the decomposition of acetyl phosphate proceeds more rapidly in the micellar solutions than in the corresponding nonmicellar solution. This, taken in conjunction with the data in Table VI, which show an increasing effectiveness of catalysis with increasing chain length of the 5-alkyl group of the 5-alkyltriens, indicates that micellar catalysis is occurring. The rate data, however, do not conform to the equation that frequently applies to micelle-catalyzed reactions,[19] viz.,

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

where k_0 is $k_{uncat.}$, k_ψ is k_{obsd}, k_m is the micelle-catalyzed specific rate, N is the number of surfactant molecules per micelle, K is the association constant between micelles and substrate, C_D is the measured surfactant concentration, and cmc is the critical micelle concentration. Instead, they conform

to the expression

$$\text{rate} = (k_{uncat.} + k_{cat.}C_0^2)[\text{AcPO}_4{}^{2-}] \quad (2)$$

in which C_0 is the total concentration of 5-alkyltrien and metal ion. Failure to conform to expression 1 can probably be attributed to (a) the fact that the number of substrate and surfactant molecules is approximately equal, whereas expression 1 assumes that only one substrate molecule is bound to a given micelle; and (b) the fact that the metal trien chelates have a demonstrated ability to increase the rate of substrate composition, whereas expression 1 assumes that substrate and monomeric surfactant do not complex.

Several modes of action can be suggested to explain the results in micellar solutions, including the following: (a) the positively charged micelles may bind more effectively with acetyl phosphate than do the metal trien chelates; (b) the juxtaposition of the chelated head groups in the micelles may allow tridentate binding of substrate to the chelated surfactants, thus activating the acetyl phosphate to nucleophilic attack, i.e.,
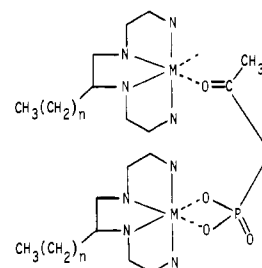
(c) once bound to the micelle, the acetyl phosphate may decompose more rapidly because it is exposed to a higher local concentration of OH$^-$ as a result of the tendency of micelles to reduce their surface charge by counterion binding; (d) decomposition of the substrate may be enhanced by a medium effect in a fashion comparable with that suggested by Bunton[13] for the hydrolysis of nitro-substituted phenyl phosphates by positively charged micelles.

Micellar reactions carried out under the conditions described above and including 1-hexanol in the reaction mixture failed to yield any detectable amounts of ester, indicating that the alcohol does not participate in the hoped for fashion.

Decomposition of Acetyl Phosphate in the Presence of Ethyltrimethylammonium Iodide, Butylammonium Chloride, Dodecyltrimethylammonium Chloride, and Dodecylammonium Chloride. The failure to observe enhancement of acetyl phosphate decomposition via ester formation in the mixed micelle experiments can be ascribed to the low nucleophilicity of alcohols. A 0.025 M solution of 1-hexanol in water has a H_2O/1-hexanol ratio of 2000, which means that, if the nucleophilicities of water and 1-hexanol are comparable, a rate enhancement of $>10^3$ would be necessary for ester formation to be readily detectable. The rate enhancements described in the previous section are probably due, at least in part, to the participation of amino functions, which are considerably stronger nucleophiles than alcohols. To further explore the consequences of nitrogen nucleophiles in micellar systems, experiments have been carried out with some primary amines and quaternary ammonium compounds both in nonmicellar and micellar solutions.

The effects of ethyltrimethylammonium iodide and dodecyltrimethylammonium chloride on the rate of decomposition of acetyl phosphate in aqueous solution were found to be negligible, as indicated in Table VIII. These results, which agree with those of Seltzer[20] and Briggs, Satchell, and White,[21] can probably be ascribed to the low charge density of these compounds, the lone positive charge on each molecule being surrounded by four alkyl groups. In addition, the failure of the

Table VIII. Effect of 0.025 M Quaternary Ammonium Salts on the Rate of Decomposition of 0.005 M Acetyl Phosphate[a]

| Quaternary ammonium salt	Rate constant, 10^{-3} min^{-1}
None	4.0 ± 0.2
$C_2H_5N(CH_3)_3{}^+I^-$	4.1 ± 0.2
$C_{12}H_{25}N(CH_3)_3{}^+Cl^-$	4.1 ± 0.2

[a] pH 7, temperature 39 °C, ionic strength 0.6.

Table IX. Effect of 0.025 M Ammonium Salts on the Rate of Decomposition of 0.005 M Acetyl Phosphate at 39 °C

Ammonium salt	pH	Ionic strength	Rate constant, 10^{-3} min^{-1}	Rel rate
$C_4H_9NH_3{}^+Cl^-$	7	0.3	4.1 ± 0.2	1.0
	8	0.3	4.2 ± 0.2	1.0
	9	0.3	4.2 ± 0.2	1.0
$C_{12}H_{25}NH_3{}^+Cl^-$	7	0.3	30 ± 2	7.5
	7	0.15	47 ± 2	12
	8	0.15	650 ± 30	160
	9	0.15	180 ± 9	45

micellar system from dodecyltrimethylammonium chloride to increase the rate of reaction may also be ascribed to extensive counterion binding in the high ionic strength medium.

More interesting results are obtained with butylammonium chloride and dodecylammonium chloride. Whereas the former has negligible effect on the rate of decomposition of acetyl phosphate, the latter markedly enhances the rate and shows a dependence on both the pH and the ionic strength of the reaction mixture, as illustrated in Table IX. That the ionic strength dependence of the rate is a characteristic feature of the reaction in the presence of a surfactant was shown by experiments carried out in the absence of surfactant. Under this condition the rates of reaction at ionic strengths from 0.6 down to 0.15 are invariant, all being $4.1 \pm 0.2 \times 10^{-3}$ min^{-1}. The sensitivity of the rate of reaction in the presence of surfactant to ionic strength is probably related to the aggregation number of the surfactant which, in the case of dodecylammonium chloride, has been shown to increase from about 100 at very low ionic strength to about 10 000 at an ionic strength of 0.3.[16c] It is postulated[22] that the rapid rise in aggregation number between ionic strengths of 0.05 and 0.3 reflects a change from globular to cylindrical micelles. The present data suggest that the latter are somewhat less effective as catalysts.

The pH dependence of the dodecylammonium chloride catalyzed reaction, with the optimum rate enhancement at pH 8, is ascribed to the dual role played by the amine. In its protonated form the amine interacts electrostatically with the acetyl phosphate, ion binding with its negative charge and, to some extent, increasing its susceptibility to nucleophilic attack. In its free base form the amine can act as a nucleophile, transferring the acetyl group from phosphate to amine, i.e.,
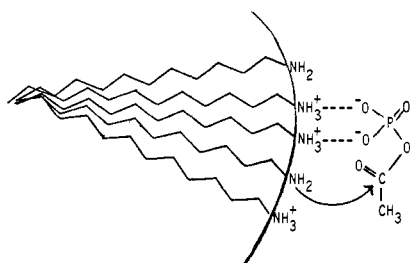
That at least some amide is formed in this reaction was shown by means of the ferric hydroxamate assay (which, for reasons discussed above, cannot be given quantitative significance).

Assuming dodecylamine to have a pK_{BH^+} of 8.7 in the micellar state,[23] the fraction of unprotonated to protonated amine at pH 7, 8, and 9 is 0.02, 0.2, and 2, respectively. It can be argued that at pH 7 the concentration of base is too low for effective acyl transfer to nitrogen to occur and that at pH 9 the charge density on the micelle arising from the protonated amine is extensively altered, the best balance between the requirements of high positive charge density and high nucleophilicity being met in the vicinity of pH 8.

The amine–ammonium system studied in the present investigation represents a simplified version of other mixed micelle systems that have been reported. One of the earliest of these is the combination of N-myristoyl-L-histidine and cetyltrimethylammonium bromide employed by Gitler and Ochoa-Solano[24] to demonstrate catalysis of the hydrolysis of the straight-chain acyl esters of p-nitrophenol. One of the most recent is the combination of dodecylamine and cetyltrimethylammonium bromide employed by Bunton and McAneny[25] to demonstrate catalysis of the decomposition of p-nitrobenzoyl phosphate.

Experimental Section[26]

Dilithium acetyl phosphate was prepared by the method of Stadtman and Lipmann[29] as modified by Kurz.[30] Purification by fractional precipitation gave material of 97% purity which was stored at 4 °C in a desiccator to prevent decomposition.

1,2-Dibromoalkanes were synthesized by bromination of the corresponding 1-alkenes[31] and purified by fractional distillation at reduced pressure to give the products listed in Table X. All of the 1,2-dibromides show absorption bands in the IR at 1149 ± 3 (CH$_2$Br wag), 649 ± 1 (C–Br stretch), and 574 ± 2 cm^{-1} (C–Br stretch) and absorption bands in the NMR at δ 4.4 $\pm$ 0.1 to 3.3 $\pm$ 0.01 (m, 3, CHBrCH$_2$Br), 1.85 $\pm$ 0.15 (m, 3, CH$_2$CHBr), 1.38 $\pm$ 0.10 (m, 2n, (CH$_2$)$_n$), and 0.93 $\pm$ 0.04 ppm (t, 3, CH$_3$).

Triethylenetetramine. Treatment of an ethanolic solution of technical grade trien (Fisher Co.) with concentrated hydrochloric acid yielded material which, after four recrystallizations from absolute ethanol, afforded 20% fine, white crystals, mp 265–266 °C (lit.[32] 265 °C). Thin layer chromatography, using the method of Gnehm, Reich, and Guyer,[37] showed a single spot (R_f 0.09). The mass spectrum of trien shows no parent peak but strong peaks at (P − 30)$^+$ and (P − 73)$^+$ resulting from the loss of –CH$_2$NH$_2$ and –CH$_2$–NHCH$_2$CH$_2$NH$_2$, respectively.[40]

5-Alkyltriethylenetetramines were prepared by modifying the procedure of Jadassohn, Fierz-David, and Vollenweider[41] for the preparation of triethylenetetramine using ethylenediamine and the appropriate 1,2-dibromoalkane. Purification of the 5-methyl- through the 5-dodecyltriethylenetetramines was effected by two fractional distillations under vacuum, the second distillation being from Linde 5-Å molecular sieves. The yields of purified material in these cases were 34 $\pm$ 2%. The 5-tetradecyl- and 5-hexadecyltriethylenetetramines were purified by repeated crystallization from anhydrous ether, yields of only 15% being obtained in these cases. The products were shown to be free of alkenes and halogen compounds by NMR analysis and by the Beilstein flame test. Thin layer chromatography[37,42] showed a single spot for each of the products. The products were characterized as hydrochlorides, nitrates, picrates, or the condensation products obtained with carbon disulfide,[43] as shown in Table XI. The mass spectra of the 5-alkyltriens show no parent peak but strong peaks at (P − 30)$^+$ and (P − 73)$^+$. The (P − 73)$^+$ peak is strong enough that the (P − 72)$^+$ peak can be used to check the molecular formula of this fragment. Also prominent is a peak at (P − 116)$^+$, presumably due to RCH=NH$_2{}^+$ arising from decomposition of the (P − 73)$^+$ fragment. The IR spectra were run neat in all cases; for the amines that are solid at room temperature a sample was melted on the sodium chloride plate. All of the compounds showed absorptions at 3440 $\pm$ 8 (NH stretch), 3360 $\pm$ 30 (NH stretch), 1655 $\pm$ 35 (NH$_2$ bend), 1609 $\pm$ 4 (NH$_2$ bend), 1132 $\pm$ 3 (CN stretch), and 769–909 cm^{-1} (NH$_2$ wag). All of the 5-alkyltriens except 5-methyltrien had ^{1}H NMR absorptions for C-hydrogens at δ 0.95 $\pm$ 0.05 (t, 3, CH$_3$), 1.35 $\pm$ 0.05 (s, n, (CH$_2$)$_n$), and 2.70 $\pm$ 0.05 ppm (m, 11, CH$_2$ and CH of tetramine chain). For spectra measured in CDCl$_3$ or CCl$_4$ absorptions for the N-hydrogens appeared in the δ 1.35 ppm envelope; for spectra

Table X. Physical Properties of 1,2-Dibromoalkanes

Compd	Obsd mp, °C	Lit. mp, °C	Obsd bp, °C (mm)	Lit. bp, °C (mm)	Obsd n^{20}D	Lit. nD (°C)
1,2-Dibromohexane			80–83 (12)	82 (12)[35]	1.5013	1.5012 (19)[38a]
1,2-Dibromooctane			118–19 (15)	118.5 (15)[34]	1.4962	1.4961 (19)[38b]
1,2-Dibromodecane			94.5–5.5 (1)	93 (1)	1.4924	1.4891 (24)[38c]
1,2-Dibromododecane	−17	−15[38e]	104–5 (0.3)		1.4896	
1,2-Dibromotetradecane	−1	0[38e]	143–44 (1)	140–42 (0.3)[32]	1.4876	
1,2-Dibromohexadecane	12.6	13.5[39]	167 (1)	175 (1)[32]	1.4861	
1,2-Dibromooctadecane	22	24[38d]			1.4842	

Table XI. Physical Properties of 5-Alkyltriethylenetetramines

5-Alkyltrien	Bp (mm) or mp, °C	Derivative	Mp, °C	Formula	Calcd, %			Found, %		
					C	H	N	C	H	N
5-Methyl	120–122 (5)[a]	Tetrahydrochloride monohydrate	199	$C_7H_{26}N_4Cl_4O$	25.94	8.09	17.29	26.06	8.01	17.27
5-Butyl	100–103 (0.03)	Tetranitrate hemi-hydrate	175–176	$C_{10}H_{31}N_8O_{12.5}$	25.92	6.74	24.18	26.12	6.53	24.14
		CS_2	191–192	$C_{12}H_{22}N_4S_2$	50.32	7.74	19.56	50.42	7.81	19.55
5-Hexyl	118–122 (0.2)	Dipicrate	140.5–141.5	$C_{24}H_{26}N_{10}O_{14}$	41.86	5.27	20.34	41.62	5.34	20.11
5-Octyl	125–126 (0.03)	Dipicrate	170.5–172.5	$C_{26}H_{40}N_{10}O_{14}$	43.58	5.63	19.54	43.67	5.55	19.84
5-Decyl	138–140 (0.03)	CS_2	178	$C_{18}H_{34}N_4S_2$	58.33	9.25	15.12	58.15	9.31	15.22
5-Dodecyl	150–153 (0.03)	CS_2	177–177.5	$C_{20}H_{38}N_4S_2$	60.25	9.61	14.05	60.25	9.69	14.08
5-Tetradecyl	53–57	CS_2	172.5–173.5	$C_{22}H_{42}N_4S_2$	61.92	9.92	13.13	62.02	9.93	13.07
5-Hexadecyl	57–60	CS_2	167.5–169	$C_{24}H_{46}N_4S_2$	63.38	10.20	12.32	63.32	10.26	12.04

[a] Lit.[44] 122 °C (5 mm).

measured in CD_3OD they appeared at δ 4.59 $\pm$ 0.03 ppm (s, 6, CD_3OH from exchange with NH and NH_2). The ^1H NMR spectrum of 5-methyltrien showed absorptions (in $CDCl_3$) at δ 1.05 (d, 3, CH_3), 1.63 (s, 6, NH and NH_2), and 2.72 ppm (m, 11, CH_2 and CH). The mass, IR, and NMR spectra all indicated the 5-alkyltriens to be in a state of high purity. For purposes of obtaining elemental analytical data, however, the various derivatives listed in Table XI were prepared to minimize the problems arising from the tendency of the free amines to absorb water and carbon dioxide.

1-Hexanol was purified by conversion of commercial material (Aldrich Co.) to the p-hydroxybenzoate followed by saponification[45] to yield shiny, white crystals after recrystallization; mp 52–53 °C (lit.[45] 52.2–52.8 °C). In contrast to the commercial material, the purified product showed only a single peak in the GLC trace.

Metal ion solutions were prepared from 1.98 g of $MnCl_2 \cdot 4H_2O$, 23.80 g of $CoCl_2 \cdot 6H_2O$, 13.63 g of $ZnCl_2$ (and 2 mL of 1 M HCl), 23.77 g of $NiCl_2 \cdot 6H_2O$, and 17.05 g of $CoCl_2 \cdot H_2O$, respectively, in 100 mL of water to give solutions 0.1 M in Mn^{2+} and 1 M in Co^{2+}, Zn^{2+}, Ni^{2+}, and Cu^{2+}. The 1 M solutions were diluted 10-fold immediately before use.

Critical Micelle Concentrations by Surface Tension Measurements.[15b,46,47] Solutions were prepared from the copper-5-alkyltrien complexes in 0.6 N sodium chloride in increasingly high dilutions. A small amount of a given solution was pipetted into a thermostated (at 39 $\pm$ 0.005 °C), jacketed beaker of the surface tension apparatus, the beaker was covered, and the contents were magnetically stirred until thermal equilibrium had been reached. Meanwhile, the platinum blade of the apparatus was cleaned by dipping it in 5 M nitric acid and then in clean water, holding it in the oxidizing part of a Bunsen flame until it turned bright red, and then allowing it to cool to room temperature. The surface tension of the solution was measured, after which the jacketed beaker was cleaned by rinsing four times with 0.6 N sodium chloride in preparation for the next determination. The determinations were made first on the most dilute solutions and then, progressively, on the more concentrated solutions. In this fashion enough points were obtained to ascertain the critical micelle concentration by constructing a plot of the force required to bring the platinum blade to the equilibrium position on the balance vs. the logarithm of the concentration of the surfactant. For each surfactant, duplicate or triplicate determinations of the critical micelle concentrations were made.

Critical Micelle Concentrations by Dye Absorption Measure-

ments.[15b,47,48] A set of solutions containing 10^{-5} M Sky Blue FF dye (Niagara Sky Blue 6B) and various concentrations of copper-5-alkyltrien complex was prepared in (a) water alone, (b) 0.6 N sodium chloride, and (c) 0.6 N sodium chloride containing 0.025 M 1-hexanol. Each of these solutions was added dropwise to 20 mL of a 10^{-5} M solution of the dye in the appropriate solvent, contained in a thermostated (at 39 $\pm$ 0.005 °C), jacketed beaker containing a magnetic stirrer. Surfactant solution was added until the original blue color changed to purple and then back to blue, the second of these color changes being taken as the end point.

Assay Procedures. A. Acetyl Phosphate. A solution containing 1 mL of 28% hydroxylamine hydrochloride, 1 mL of 3.5 M sodium hydroxide, and 2 mL of acetic acid–sodium acetate buffer was prepared in a 10-mL volumetric flask. To this was added a 2-mL aliquot from the reaction mixture. After 10 min, 2 mL of 4 M hydrochloric acid was added, followed by 2 mL of 0.37 M ferric chloride. The absorbance at 505 nm was measured 2 min later.

B. Esters. A 2-mL aliquot from the reaction mixture was added to a 10-mL volumetric flask containing 2 mL of 3.5 M sodium hydroxide. After 10 min, 1 mL of 28% hydroxylamine hydrochloride solution was added and, 2 min later, 3 mL of 4 M hydrochloric acid and 2 mL of 0.37 M ferric chloride were added. The absorbance at 505 nm was measured 2 min later.

C. Amides. A 2-mL aliquot from the reaction mixture was added to a 10-mL volumetric flask containing 1 ml of 3.5 M sodium hydroxide. After 20 min, 2 mL of 40% hydroxylamine hydrochloride was added, and the mixture was heated for 90 min at 90 °C. After cooling, 2 mL of 4 M hydrochloric acid and 2 mL of 0.37 M ferric chloride and 1 mL of water were added and, after 2 min, the absorbance at 505 nm was measured.

Kinetic Measurements. Solutions for kinetic studies were prepared immediately before each run in 50- or 100-mL flasks, depending on the number of aliquots to be removed during the run. Sufficient sodium chloride was added to each solution to bring the ionic strength to 0.6, and other reagents (i.e., trien, 5-alkyltrien, metals, 1-hexanol, etc.) were added as dictated by the specifications of the particular run. The flask was filled to the mark with water, shaken vigorously until only one phase was present, tightly stoppered, and kept in a constant temperature bath at 39 °C until thermal equilibrium was attained. During this time, the electrodes were warmed to 39 °C, the pH meter was calibrated at 39 °C (against Fisher Gram-Pac pH 6.86 buffer),

and the pH of the solution was then measured. If necessary, the pH of the solution was adjusted to 7.00 by the addition of a few drops of standardized sodium hydroxide or hydrochloric acid. The flask was removed from the bath, dilithium acetyl phosphate was added to give a concentration of 0.005 M, the flask was vigorously shaken for 1 min to bring the substrate into solution, and the flask was then put back in the constant-temperature bath. At various times during the course of the reaction 2-mL aliquots were withdrawn and assayed as described above. Reactions were followed to 75–99% completion, times ranging from 10 min to 6 h depending on the rate. Aliquots removed after 24 h gave T_∞ values. At the conclusion of the reaction the pH was again measured in the manner described. A plot of the log of the substrate concentration vs. time yielded straight lines in all but a few cases. Rate constants were determined graphically and by least-squares analysis using a Hewlett-Packard 9100A calculator. The least-squares program[49] also computed the standard deviation of the points from the line and the variance of the slope of the line. The estimated error for the slope (and, correspondingly, for the rate constants) was taken as twice the standard deviation and was $\leq 5\%$. The estimated errors for the rate constants reported in this paper are 5% of the given rate constants.

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(26) Melting points were determined on a Thomas-Hoover Uni-Melt capillary melting point apparatus except those of the 1,2-dibromoalkanes, which were determined by the method of Skaue, Arthur, and Wakenham.[27] Boiling points are uncorrected except for those of the 1,2-dibromoalkanes and for those obtained in capillary tubes by the method of Siwoloboff.[28] Microanalyses were performed by Mikroanalytisches Laboratorium, Vienna, Austria, and by Galbraith Laboratories, Knoxville, Tenn. Infrared spectra of the 1,2-dibromoalkanes were recorded on a Perkin-Elmer Model 457 IR spectrometer; other IR spectra were recorded on a Perkin-Elmer Model 137 Infracord spectrometer. Visible spectra were recorded on a Beckman DB-G spectrometer. Nuclear magnetic resonance spectra were recorded on a Varian A-60A spectrometer with tetramethylsilane as an internal standard, unless otherwise noted. Mass spectra were recorded on a Varian M-66 spectrometer at 70 eV. Gas–liquid chromatographic separations were carried out with an F & M Model 720 dual column programmed temperature instrument using a 2 ft $\times$ ¼ in. column of 20% Carbowax 20M on base-washed firebrick. Thin layer chromatographic separations employed Analtech Uniplates coated with 250 μ silica gel G. pH measurements were made with a Corning Model 12 research meter, using silver–silver chloride triple purpose glass membrane (Corning 476022) and calomel fiber-type reference (Corning 476002) electrodes. Refractive index measurements were made with a Bausch and Lomb Abbe-56 refractometer. Surface tension measurements were made with a Federal Pacific Electric Co. Model LG Rosano surface tensiometer using a platinum blade having a perimeter of 5.3 cm.
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