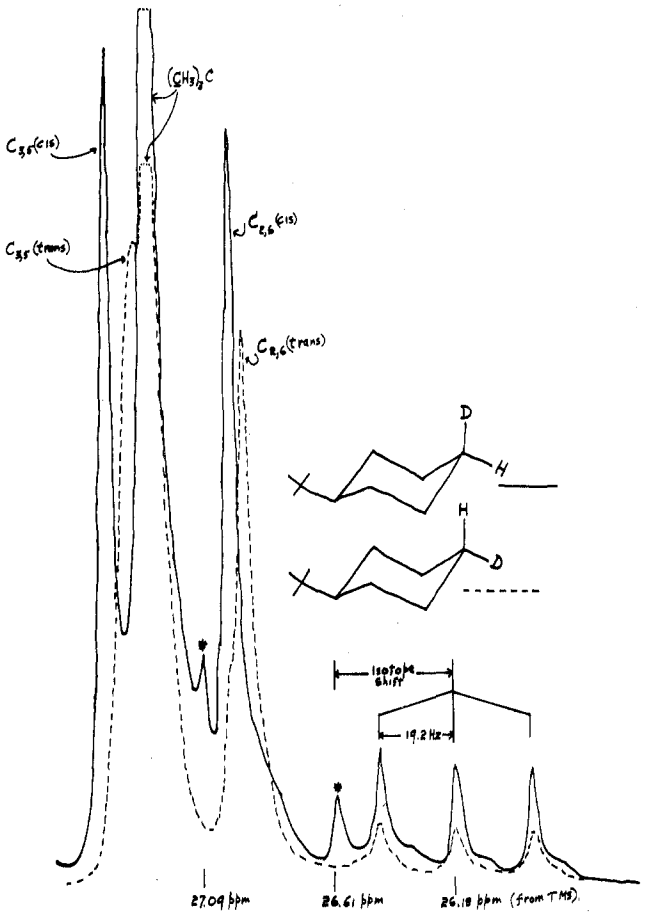

Figure 1. High-field part of the 67.89-MHz ^{13}C spectra (500-Hz expansion) of *trans*-4-*tert*-butylcyclohexane-*1*-d_1 (broken line) and *cis*-4-*tert*-butylcyclohexane-*1*-d_1 (full line). The signals marked with an asterisk correspond to C_1 (at 26.61 ppm) and $C_{2,6}$ (27.09 ppm) in regular (undeuterated) *tert*-butylcyclohexane, admixed (~10%) with the cis isomer. (The degree of deuteration was much higher in the trans case.) The C_1–D triplet ($J_{^{13}C-^2H}$ = 19.2 Hz) is indicated.

Comparison of the shape and position of the $C_{3,5}$ signals in the two isomers (Figure 1) reveals (a) that when ^2H is equatorial (i.e., trans isomer) $C_{3,5}$ is broader and at higher field than when ^2H is axial. The "broadness" was expected as vicinal ^2H coupling to ^{13}C in other systems is substantial for a dihedral angle of 180°,[5,6] which, of course, exists in the trans compound. In addition, it appears that the (γ)-antiperiplanar array of $C_{3,5}$ and ^2H promotes a greater three-bond isotope effect than when a (γ)-syn situation exists, as in the cis isomer.

Previously, Doddrell and Burfitt[8] had examined the effect of ^2H substitution on the ^{13}C spectra of some 1-^2H-1-substituted heptanes, and for the parent hydrocarbon, a one-bond effect (i.e., at C_1) of −0.28 ppm ($J_{^2H-^{13}C}$ = 19.2 Hz) was observed. These results are in line with the present data. More recently, Colli, Gold, and Pearson[7] reported ^2H isotope effects on the ^{13}C NMR spectra of a number of alkyl systems, but generally the compounds were polydeuterated, so that observed effects were combinations of nearest neighbor and more remote interactions. However, their reported (upfield) isotopic shift for perdeuteriocyclohexane of −1.33 ± 0.2 is quite consistent with the values noted here, i.e., (2 × ~0.4) + (4 × ~0.1) ≃ 1.2.

The spectral data are assembled in Table I.

The present results indicate that incorporation of ^2H in a defined way in a cycloalkyl system can be a substantial aid in assignment of carbon signals two and three bonds removed from the site of incorporation.[12] Alternatively, the effect ^2H might have on the spectra could provide insight into the stereochemical location of the ^2H label.

Experimental Section

The compounds examined have been described in detail elsewhere.[2]

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The Effect of Substrate Micellization on the Hydrolysis of *n*-Decyl Phosphate[1]

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Catalysis and inhibition by micelles of added surfactant have been studied extensively,[3-6] but in only a few cases has the effect of substrate micellization been examined.[7-10] However, the rates of hydrolysis of monoalkyl sulfates are markedly affected by substrate micellization which speeds the acid-catalyzed hydrolysis but retards reaction with hydroxide ion.[7] Monoanions of monoalkyl phosphates decompose spontaneously in a reaction which almost certainly involves elimination of metaphosphate ion and proton transfer to the RO– moiety:[11-13]

$$RO{-}PO_3H^- \longrightarrow ROH + PO_3^- \xrightarrow[\text{fast}]{H_2O} Pi$$

At lower pH nucleophilic attack upon the alkyl and phosphoryl groups becomes important. For example, in the acid-catalyzed hydrolysis of a monoalkyl phosphate water can attack the protonated substrate on either the alkyl or phosphoryl group,[12,13] and halide ion can attack the alkyl group.[14]

$$ROPO_3H_2 \overset{H^+}{\rightleftharpoons} ROPO_3H_3^+ \xrightarrow{H_2O} ROH + H_3PO_4 + H^+$$
$$\searrow^{X^-}$$
$$RX + H_3PO_4 + H^+$$
$$(X = Cl, Br)$$

Our aim was to examine the hydrolysis of a hydrophobic monoalkyl phosphate by these various mechanisms at concentrations above and below the critical micelle concentration (cmc). We used *n*-decylphosphoric acid and its monoanion, because they are sufficiently water soluble that a wide concentration range can be used. (We will use the term "alkyl phosphate" without specifying its state of ionization, and refer to the acidic or anionic forms where necessary.)

Experimental Section

Materials. Decanol was converted into *n*-decylphosphoryl dichloride by $POCl_3$, followed by hydrolysis to *n*-decylphosphoric acid in ice water.[15] It was purified by solution in Et_2O and washing with water and after drying (P_2O_5) it had mol wt 236 (by titration) and mp 45.0 °C (lit.[16] 45.0 °C).

Kinetics. The hydrolysis at 100 °C was followed by determination of inorganic phosphate by Fiske and Subba Row's method,[17] or a variant of it, using extraction into 1-butanol, which gave much better results than the simple method, especially for solutions which contained much 1-decanol. Sealed Pyrex ampules were used and for the experiments in which micellized substrate was present only the initial part of the reaction was followed because the products, especially 1-decanol, could change the structure of the substrate micelles. For reaction at pH >4 the sodium salt was used.

Products. We detected no 1-chlorodecane in the products of hydrolysis of 3×10^{-3} M decyl phosphate in 3 M HCl at 100 °C. After ca. 60% reaction $Ba(OH)_2$ was added and the mixture was extracted with redistilled pentane. After drying ($MgSO_4$) the bulk of the pentane was distilled off. Decanol was detected by GLC (12 ft × 0.25 in. 15% Carbowax 20M in 60/80 Chromosorb W, 2% K_2CO_3 at 158 °C). Control tests showed that 5% chlorodecane could have been detected.

Critical Micelle Concentration. The cmc was determined by the surface tension method[18] at 23 °C. Plots of surface tension against log [decyl phosphate] gave sharp breaks at the cmc and there were no minima.

The values of the cmc in water at 23 °C are *n*-$C_{10}H_{21}OPO_3H_2$ (in 0.1 M HCl), 6.9×10^{-4} M; *n*-$C_{10}H_{21}OPO_3HNa$ (pH 4.5), 2.0×10^{-3} M; at pH 6.5, 4.2×10^{-3} M. As expected, the cmc of the undissociated acid is considerably lower than that of the monoanion and at pH 6.5 formation of the dianion further increases the cmc. (For monoalkyl phosphates $pK_2 \sim 6.5$.) Using *n*-decylphosphoric acid and with no control of pH cmc $\sim 2 \times 10^{-3}$ M, showing that under these conditions the acid is extensively dissociated into the monoanion.

Our rate experiments were at 100 °C, and we needed evidence that the values of the cmc at 23 °C would be indicative of micelle formation at higher temperatures. For most surfactants cmc increases slightly with increasing temperature above ca. 30 °C, but the standard compilation gives no values for temperatures >80 °C.[18] We therefore used the solubilization of sparingly soluble Orange OT to show that micelles were present in solutions of monosodium *n*-decyl phosphate at 100 °C. Aqueous solutions of 10^{-3} and 10^{-2} M decyl phosphate were saturated with the dye by shaking at room temperature for 3 days and the increased solubilization in 10^{-2} M decyl phosphate was visible. The solutions were then brought to 100 °C and then rapidly centrifuged, a sample 1 ml was diluted with MeCN (1 ml), and the absorbance was measured at 500 nm. The absorbances were in water, 0.131 (0.097); in 10^{-3} M decyl phosphate, 0.118 (0.100); in 10^{-2} M decyl phosphate, 0.338 (0.233). The values in parentheses were at room temperature.

These results show that the micelles of *n*-decyl phosphate monoanion are not disrupted at 100 °C.

Results and Discussion

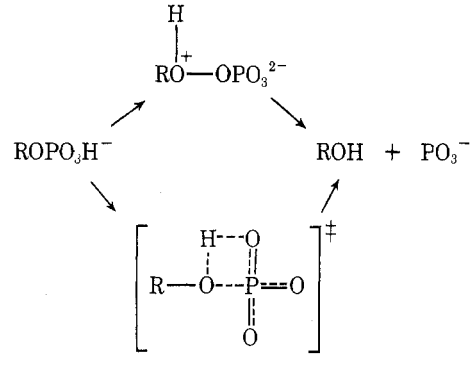
Hydrolysis of the Monoanion. The rate constant for hydrolysis of *n*-decyl phosphate monoanion at pH 4.5 is unaffected by micellization, and is only slightly lower than that for hydrolysis of methyl phosphate monoanion, which is 8.2×10^{-6} s^{-1} at 100 °C. Addition of decanol does not markedly affect the reaction rate (Table I) although it should promote micellization and stabilize a micelle. The dianion is unreactive as expected.[12,13]

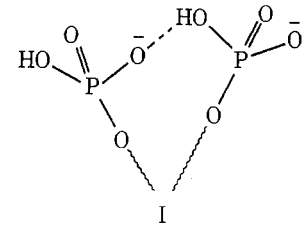
Elimination of metaphosphate ion from a monoanion could be concerted with, or follow, the proton transfer.[11-14,19-21] Our observations are consistent with the insensitivity of rates of hydrolysis of monosubstituted phosphate monoanions to changes in solvent or incorporation into cationic micelles,[11,19-21] although we had expected that the necessity of proton transfer would cause this reaction to be sensitive to substrate micellization. The cmc of the monoanion of 2×10^{-3} M is considerably lower than that of sodium decyl sulfate (3.3×10^{-2} M at 25 °C[18]), and this low cmc of the phosphate monoanion suggests that its micelle is strongly stabilized by hydrogen bonding between adjacent head groups as in I. In this event elimination of metaphosphate ion in the micelle will merely require rearrangement of existing hydrogen bonds.

Table I. Hydrolysis of Monoanionic *n*-Decyl Phosphate[a]

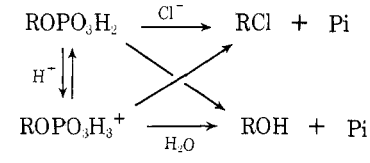
10^3 [*n*-$C_{10}H_{21}OPO_3H^-$], M	$10^6 k_\psi$, s^{-1}	10^3 [*n*-$C_{10}H_{21}OPO_3H^-$], M	$10^6 k_\psi$, s^{-1}
0.6	4.14	15.0	5.70[b]
3.0	4.10	15.0	5.30[c]
4.0	4.13	25.0	5.06
10.0	4.33		

[a] At 100 °C; for hydrolysis of methyl phosphate $k_\psi = 8 \times 10^{-6}$ s^{-1}. [b] Taken to 60% reaction. [c] With 1.5×10^{-2} M 1-decanol.





Hydrolysis at Low pH. At substrate concentrations below the cmc, the rate constants for reaction of *n*-decyl phosphate are similar to those for methyl phosphate.[12,14] Both reactions are catalyzed by strong acid (Table II), and water can attack the methyl and phosphoryl groups of methyl phosphate. For reaction of methyl phosphate halide ion can attack the methyl group of undissociated methyl phosphoric acid or its conjugate acid, e.g.



and at concentrations below the cmc, the attack of chloride ion upon protonated *n*-decylphosphoric acid becomes very important as the hydrogen ion concentration is increased (Table II and Scheme I). (We cannot compare the two systems exactly, because the effect of chloride ion on the reaction of methyl phosphate was examined at constant ionic strength,[14] and we preferred not to use high salt concentrations wherever possible because they can alter micellar structure.)

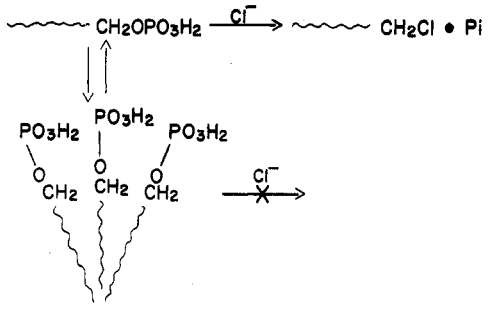
Micellization has a marked effect upon the hydrolysis of undissociated *n*-decylphosphoric acid, and it changes the

Table II. Reaction of *n*-Decyl Phosphate at Low pH[a]

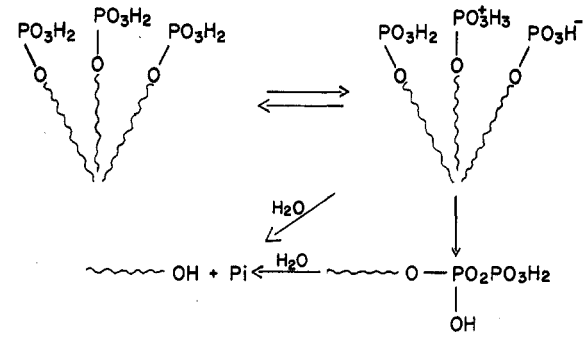
10^3 [n-$C_{10}H_{21}OPO_3H_2$], M	$HClO_4$			HCl		
	0.1 M	1 M	3 M	0.1 M	1 M	3 M
0.10				2.08		
0.53		2.61	8.24		2.67	67.2
2.44		21.5				
3.30	21.7	20.6	9.62	23.1	19.0	9.16

[a] Values of $10^6 k_\psi$, s^{-1} at 100 °C; for reaction of methyl phosphate $10^6 k_\psi$ = 3.45 in 0.1 M HCl; 5.08 in 1 M $HClO_4$ and 39.6 s^{-1} in 2.5 M $HClO_4$ + 1.5 M NaCl.

Scheme I



Scheme II



pattern of hydrogen and chloride ion catalysis. There are several effects at work and some of them can only be separated qualitatively, in part because there is always monomeric substrate in equilibrium with micellized substrate, and added solutes can affect this equilibrium. For monoalkyl phosphates (in the absence of micelles) pK_1 is typically ca. 1.5 and is not especially temperature sensitive,[12,22] so that in 0.1 M strong acid, ca. 80% of the substrate will be as undissociated acid. Thus any rate changes on micellization should not be caused by changes in the relative amounts of *n*-decylphosphoric acid and its monoanion.

Micellization markedly increases the rate of hydrolysis of undissociated *n*-decylphosphoric acid in dilute acid (Table II), but it eliminates the chloride ion promoted reaction and hydrogen ion catalysis of hydrolysis of *n*-decylphosphoric acid.

The absence of hydrogen ion catalysis is understandable, because the hydrogen ions should be almost wholly in the aqueous bulk solvent rather than at the surface of nonionic micelles of *n*-decylphosphoric acid, and formation of any appreciable amount of protonated substrate would create coulombic repulsions at the micellar surface. Attack of chloride ion upon *n*-decylphosphoric acid or its conjugate acid should also be inhibited by micellization, because the alkyl group will be shielded from the hydrophilic chloride ion by the phosphate moiety (Scheme I). We also found that when the concentration of *n*-decylphosphoric acid is well above the cmc the rate constants decrease in going from 1 M to 3 M strong acid, possible because of a change in the micellar structure or reduction in the cmc at high electrolyte concentration.

It is not obvious why micellization promotes hydrolysis of undissociated *n*-decylphosphoric acid. Probably one monomer can assist hydrolysis of its neighbor by partial or complete proton transfer, followed by attack of water (Scheme II), and the lowering of the cmc by interhead group hydrogen bonding was noted earlier. Alternatively a decyl phosphate monoanion could attack its neighbor to give *n*-decyl pyrophosphate which should then be hydrolyzed to alcohol and inorganic phosphate. Proton transfer to a phosphoryl group is shown in Scheme II, but it could be to an alkoxy group, because complete reaction requires loss of ROH. For reaction of methyl phosphate distinction between attack upon the methyl and phosphoryl groups was made isotopically,[12] but this approach is impracticable for the dilute solutions which we use in these experiments. There is considerable attack by water upon the methyl group of methylphosphoric acid, but shielding of the *n*-decyl group in a micelle should hinder attack on the decyl more than upon the phosphoryl group.

Comparison with Reactions of Other Micellized Substrates. There are considerable mechanistic similarities between the mechanisms of hydrolysis of monosubstituted phosphates and sulfates, and these similarities extend to the effects of added micelles on unimolecular reactions of phosphate dianions and sulfate monoanions.[21,23] But there are considerable differences for reactions of micellized monoalkyl phosphates and sulfates because it is the monoanionic alkyl phosphate and the undissociated alkylsulfuric acid which decompose spontaneously.[7,11]

It is difficult to find analogies for the effects of self-micellization of *n*-decyl phosphate at low pH, but the absence of attack of chloride ion upon *n*-decylphosphoric acid, even at relatively high acidities, is similar to the inhibition of attack of hydroxide ion upon *p*-nitrophenyl laurate by substrate micellization,[8] in that in both systems a hydrophilic reagent does not readily attack a micellized nonionic substrate.

Our micellar effects on nucleophilic attack illustrate the way in which substrate micellization can affect reactivity as, for example, in biologically important phosphates.

Registry No. —*n*-Decyl phosphate, 3921-30-0.

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Acid-Catalyzed Hydrolysis of 3-Isopropyloxatriazole

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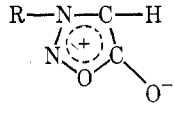
The mechanisms of the acid-catalyzed ring opening of mesoionic 3-aryl- and 3-alkylsydnones (**1**, R = alkyl or aryl) have been studied in some detail.[1,2] In contrast very little is known about the acid-catalyzed decomposition of the analogous (isosteric) oxatriazole system **2**. Boyer and Hernandez observed that cyclohexyloxatriazole (**2a**, R = C_6H_{11}) was re-



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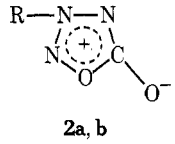

2a, b

sistant to dilute sulfuric acid but decomposed in strong acid to form cyclohexanol, carbon dioxide, and hydrogen azide,[3] whereas the products of hydrolysis of phenyloxatriazole have been reported to be phenyl azide and carbon dioxide.[4] The absence of cyclohexyl azide in the products of decomposition of **2a** reflects the instability of alkyl azides in strong acid.[5] The behavior of oxatriazoles in strong acid seems to be in sharp contrast to that of the sydnones which are converted to the corresponding alkyl and aryl hydrazines. We now report the first kinetic study of the acid-catalyzed ring opening of mesoionic oxatriazoles on 3-isopropyloxatriazole (**2b**, R = *i*-Pr).

The hydrolysis of **2b** only occurs at an appreciable rate at high acidity and high temperature. The first-order rate constants, k_ψ, for the hydrolysis of **2b** in aqueous solutions of mineral acids are shown in Table I.

In spite of the limited range of acidity over which the hydrolysis of **2b** could be studied, a plot of log k_ψ vs. $-H_0$ gives a slope of 1.3.[6] Analysis of the kinetic data in terms of Bunnett's approach[7] leads to a value of w (−0.74) which is in the range associated with reactions in which water does not participate in the rate-determining step. The value of ϕ (−0.30) obtained from the correlation of log k_ψ + H_0 with H_0 + log $[H^+]$[8] leads to a similar conclusion. The value of the entropy

Table I. Hydrolysis Rate, 10^3 k_ψ (min^{-1}), of 2b in Aqueous Mineral Acids

$HClO_4$ Concn, M, at 60 °C						
7.00	7.50	8.00	8.50	9.00	9.50	
1.84	4.69	12.7	38.2	106	460	
H_2SO_4 Concn, M, at 60 °C						
7.00	7.50	8.00	8.50	9.00	9.50	10.0
0.82	1.98	2.87	4.59	7.84	16.2	35.7
HCl Concn, M, at 60 °C						
	8.50	9.00	9.50	10.00		
	0.41	1.53	2.91	6.22		
$HClO_4$ (9.00 M) at Various Temp, °C						
	40.2	45.0	50.0	55.0	60.0	
	10.1	20.0	34.6	65.7	113	

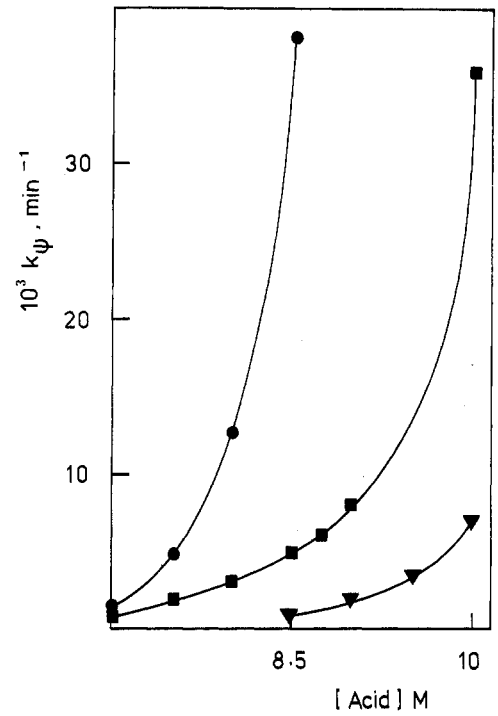

Figure 1. Hydrolysis of **2b** in water at 60 °C: ●, $HClO_4$; ■, H_2SO_4; ▼, HCl.

of activation calculated for 9 M $HClO_4$ ($\Delta S^\ddagger$ = +2.5 eu) is also consistent with an A-1 reaction.[9] The value obtained for the deuterium kinetic solvent isotope effect $[k_\psi(D_2O)/k_\psi(H_2O)$ = 1.42] for the perchloric acid catalyzed hydrolysis of **2b** is characteristic of reactions which proceed via specific hydrogen ion catalysis (although it is perhaps somewhat lower than usually observed for A-1 reactions[10]) and suggests that proton transfer occurs in a preequilibrium step.

The most striking feature of the effect of different acids on the hydrolysis of **2b** (Figure 1) is the order of effectiveness of the acids, viz., $HClO_4 > H_2SO_4 > HCl$. Bunton and his coworkers have suggested that such an order of reactivity is characteristic of A-1 reactions and that the transition states of such reactions are preferentially stabilized by anions of low charge density.[11] All the evidence presently available therefore suggests that the acid-catalyzed hydrolysis of isopropyloxatriazole follows an A-1 mechanism which can be represented as in eq 1. In the absence of any definitive evidence, protonation is assumed to occur on N-2 as has been assumed in the acid-catalyzed hydrolyses of 3-alkylsydnones.[12] Consistent with the proposed mechanism, the major products of hy-