Micellar-Catalyzed Hydrolysis of Nitrophenyl Phosphates[1]

C. A. Bunton, Eleanor J. Fendler, L. Sepulveda,[2] and Kui-Un Yang

Contribution from the Department of Chemistry, University of California at Santa Barbara, Santa Barbara, California 93106. *Received March 30, 1968*

Abstract: At concentrations above the CMC, cetyltrimethylammonium bromide catalyzes the hydrolysis of the dianions of 2,4- and 2,6-dinitrophenyl phosphate, but does not affect the rate of attack of hydroxide ion upon them, or the hydrolysis of the monoanion of *p*-nitrophenyl phosphate or the dianion of glucose 6-phosphate. These results suggest that a cationic micelle assists the heterolysis of the dianions of the aryl phosphates to phenoxide and metaphosphate ions, and the effect is largely on the activation energy. Anionic and nonionic detergents do not affect the rate. The micellar catalysis is inhibited by added salts, especially those of arene sulfonates and bulky carboxylate ions. The kinetics can be analyzed in terms of competitive binding of the substrate and the inhibitor to the micelle.

In most kinetic studies of micellar-catalyzed reactions, incorporation of the substrate into the micellar phase brings it into proximity with the reagent which may be attracted to the micelle electrostatically,[3-5] or chemically incorporated in it.[6,7] Because incorporation of the substrate is a prerequisite for both micellar and enzymic catalysis many workers have drawn analogies between the two processes, and we were interested in finding the conditions in which micelles would catalyze the hydrolysis of monosubstituted phosphate esters.

Nitrophenyl phosphates were the preferred substrates, because with mononitrophenyl phosphates the monoanion is the most reactive species,[8] but with dinitrophenyl phosphates reactions of the dianions become important,[9,10] and it is assumed that both reactions generate a short-lived metaphosphate as a reactive intermediate. At high pH 2,4- and 2,6-dinitrophenyl phosphates react also with hydroxide and alkoxide ions,[10] and therefore by appropriate choice of a substrate it is possible to examine micellar effects upon three mechanisms of phosphate monoester hydrolysis.

$$ArOPO_3H^- \longrightarrow ArOH + PO_3^-$$

$$ArOPO_3^{2-} \longrightarrow ArO^- + PO_3^-$$

$$ArOPO_3^{2-} + OH^- \longrightarrow ArO^- + HPO_4^{2-}$$

With the cationic micelles of cetyltrimethylammonium bromide (CTA), there was no catalysis of the hydrolysis of *p*-nitrophenyl phosphate monoanion, but the hydrolyses of 2,4- and 2,6-dinitrophenyl phosphate dianions were markedly accelerated. Anionic and nonionic micelles did not affect the reactions.

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(2) University of Chile–University of California Cooperative Program Fellow.

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Experimental Section

Materials. The preparation and purification of the aryl phosphates has been described,[10,11] and glucose 6-phosphate was a commercial product. Cetyltrimethylammonium bromide (CTA) and sodium lauryl sulfate (NaLS) were purified by the method of Duynstee and Grunwald.[3]

The nonionic detergent was Igepal, a dinonyl phenol condensed with 24 ethylene oxide units (General Aniline and Film Corp.), and is denoted as DNPE in the text. It was kindly supplied by Professor T. C. Bruice and was used without further purification.

Kinetics. The appearance of nitrophenoxide ion was followed spectrophotometrically using a Gilford spectrophotometer as described elsewhere.[10,11] The first-order rate constants, k_ψ, are in units of seconds^{-1}.

The hydrolysis of glucose 6-phosphate was followed by evolution of inorganic phosphate.[12] The cationic detergent interfered with the colorimetric determination of phosphate, and therefore we added sodium perchlorate to portions of the reaction mixture in order to precipitate the cetyl trimethylammonium ions before analysis, but even then we obtained erratic results and could only obtain approximate values for the first-order rate coefficients of 1×10^{-6} at pH 7.0 at 75.0° using 8×10^{-3} *M* phthalate buffer, 8×10^{-3} *M* CTA, and 2×10^{-3} *M* substrate. In the absence of detergent, $k_\psi = 1.25 \times 10^{-6}$ sec^{-1} at pH 7.0.

Results

Kinetics. The cationic micelles of CTA strongly catalyze the hydrolyses of the dianions of 2,4- and 2,6-dinitrophenyl phosphate (Figures 1 and 2), and the rate increases sharply at CTA concentrations greater than the critical micelle concentration (CMC). For CTA in water at pH 9.0 in 2.5×10^{-3} *M* borate buffer, CMC = 0.78×10^{-3} *M* determined by the dye method; *cf.* ref 13. At higher CTA concentrations the rate levels off, with rate enhancements of approximately 25-fold for both substrates. In the absence of detergent, $k_\psi = 8.3 \times 10^{-6}$ sec^{-1} for 2,4- and 4.9×10^{-5} sec^{-1} for 2,6-dinitrophenyl phosphate at 25.0° and pH 9.0.[10] Most of our experiments were carried out with 2,6-dinitrophenyl phosphate, especially in the presence of added salts. As for the spontaneous hydrolysis 2,6- is more reactive than 2,4-dinitrophenyl phosphate when incorporated in CTA micelles.

The rate enhancement arises almost completely from a lowering of the activation energy. In the absence of CTA, E = 25.5 kcal/mol for 2,4- and 26 for 2,6-dinitrophenyl phosphate, and ΔS^* = +2.5 eu for 2,4-

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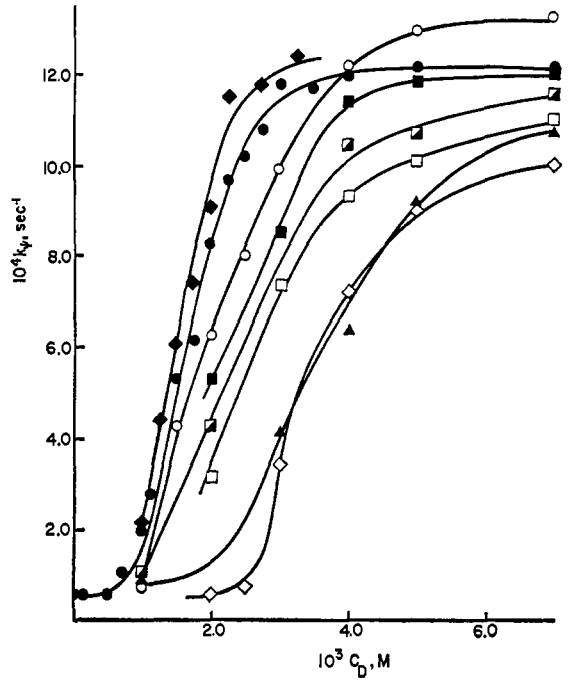

Figure 1. Hydrolysis of 2,6-dinitrophenyl phosphate (9.4×10^{-5} M) in CTA at 25.0° in 2.5×10^{-3} M borate buffer at pH 9.0 unless specified: ●, no added electrolyte; ◆, 1.8×10^{-5} M substrate and no added electrolyte; ○, 0.1 M NaOH; □, 1×10^{-3} M sodium oleate; ◇, 2×10^{-3} M sodium oleate; ■, 2×10^{-3} M disodium phenyl phosphate; ◪, 1×10^{-3} M disodium t-butylphenyl phosphate; ▲, 2×10^{-3} M disodium t-butylphenyl phosphate.

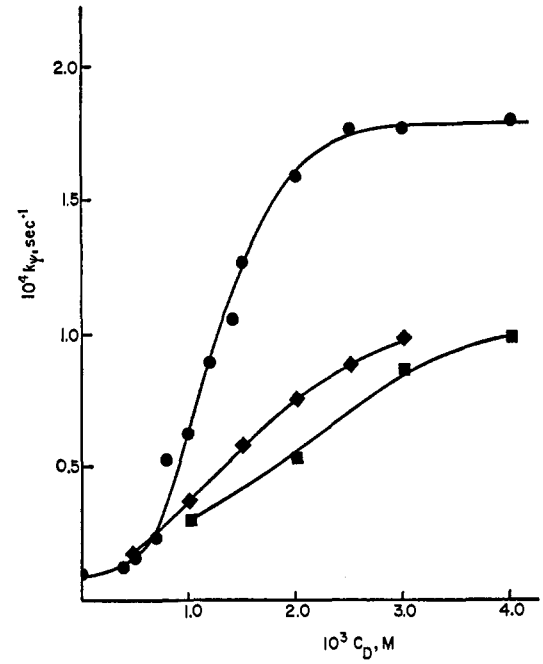

Figure 2. Hydrolysis of 2,4-dinitrophenyl phosphate (6.3×10^{-5} M) in CTA at 25.0° in 2.5×10^{-3} M borate buffer at pH 9.0 unless specified: ●, no added electrolyte; ■, 0.01 M sodium benzoate in 1.5×10^{-3} M borate buffer; ◆, 0.01 M disodium phthalate.

and +6.5 eu for 2,6-dinitrophenyl phosphate.[10] For the plateau at 0.004 M CTA, the figures are E = 23.5 kcal/mol and ΔS^* = 1.7 eu for 2,4- and 23.5 kcal/mol and 5.6 eu for 2,6-dinitrophenyl phosphate. Table I

Table I. Temperature Effects upon the Micellar Catalysis[a]

Substrate	Temp,[d] °C 15.0	25.0	35.0
2,4[b]	4.78	18.6	68.3
2,6[c]	23.2	122	331

[a] Values of $10^5 k_\psi$, sec^{-1}, at pH 9.0 with 2.5×10^{-3} M borate buffer. [b] 6.3×10^{-5} M 2,4-dinitrophenyl phosphate and 4×10^{-3} M CTA. [c] 9.4×10^{-5} M 2,6-dinitrophenyl phosphate and 4×10^{-3} M CTA. [d] The temperature was determined using a NBS calibrated thermometer.

gives the values of the rate constants for the hydrolyses at various temperatures and at micellar concentrations such that all the substrate is wholly incorporated into the cationic micelles of CTA. Each of these rate constants is the mean of two independent values which agreed within 3% of each other.

In all the experiments the substrate concentration was much lower than that of the cationic detergent, and changes in it had slight effects on the rate at the lower detergent concentrations, as shown for the hydrolysis of 2,6-dinitrophenyl phosphate (Figure 1).

The reaction between hydroxide ion and the dianion of 2,6-dinitrophenyl phosphate is not catalyzed by CTA, as can be seen from the results in Figure 1. At detergent concentrations $>5 \times 10^{-3}$ M, where the substrate is wholly incorporated in the micelle, $10^4 k_\psi$ = 13 sec^{-1} in 0.1 M NaOH and 12.2 sec^{-1} at pH 9.0 (Figure 1). In the absence of detergent there is a rate enhancement in the presence of 0.1 M sodium hydroxide.[10]

Absence of Micellar Catalysis. As is to be expected anionic and nonionic detergents do not catalyze the hydrolysis of dinitrophenyl phosphates (Table II), presumably because the dianions are only incorporated into cationic micelles. A monoanion, *e.g.*, of *p*-nitrophenyl phosphate, is not activated by micelles of CTA (Table III) even though it is probably incorporated into it, just like the other aryl phosphate monoanions which can inhibit the hydrolyses of the aryl phosphate dianions. Our experiments with *p*-nitrophenyl phosphate

Table II. Rate Constants of Hydrolysis of 2,6-Dinitrophenyl Phosphate in Anionic and Nonionic Detergents[a]

Detergent	$10^3 C_D$, M 1.0	10.0
NaLS	4.46	4.43
DNPE	4.20	4.30

[a] Values of $10^5 k_\psi$, sec^{-1}, at 25.0° in 2.5×10^{-3} M borate buffer with 9.4×10^{-5} M substrate; in the absence of detergent $10^5 k_\psi$ = 4.90 sec^{-1}, at pH 9.0.[10]

Table III. Hydrolysis of *p*-Nitrophenyl Phosphate in the Presence of Cationic Micelles[a]

C_D, M	pH	$10^6 k_\psi$, sec^{-1}
...	3.7	1.80
0.005	3.0	1.50
0.005	3.3	1.62
0.005	3.7	1.67
0.005	4.1	1.67
0.01	3.0	1.66
0.01	3.3	1.75
0.01	3.7	1.75
0.01	4.1	1.57

[a] At 45.0° with 0.01 M phthalate buffer and cetyltrimethylammonium bromide.

Table IV. Inhibition of the Micellar Catalysis of the Hydrolysis of 2,6-Dinitrophenyl Phosphate[a]

Inhibitor	C_I, M	10^4k_ψ, sec^{-1}
...	...	11.7
NaCl	0.001	11.5[b]
NaCl	0.010	11.2[b]
NaCl	0.030	10.2[b]
NaCl	0.050	8.67[b]
NaCl	0.070	6.73[b]
NaCl	0.100	5.15[b]
Na_2HPO_4	0.002	12.4[b]
CH_3SO_3Na	0.010	10.8
CH_3SO_3Na	0.020	8.73
CH_3SO_3Na	0.035	7.95
CH_3SO_3Na	0.040	7.15
p-$CH_3C_6H_4SO_3Na$	0.002	5.50
p-$CH_3C_6H_4SO_3Na$	0.005	1.72
p-$CH_3C_6H_4SO_3Na$	0.008	1.16
p-$CH_3C_6H_4SO_3Na$	0.010	0.94
p-$CH_3C_6H_4SO_3Na$	0.015	0.85
$C_5H_5CO_2Na$	0.002	7.43
$C_6H_5CO_2Na$	0.007	3.16
$C_6H_5CO_2Na$	0.010	2.25
$C_6H_5CO_2Na$	0.020	1.28
$C_6H_5CO_2Na$	0.040	0.73
o-$C_6H_4CO_2K_2$	0.002	7.07
o-$C_6H_4CO_2K_2$	0.005	5.41
o-$C_6H_4CO_2K_2$	0.010	3.00
o-$C_6H_4CO_2K_2$	0.020	2.09
o-$C_6H_4CO_2K_2$	0.030	1.67
p-$C_6H_4CO_2Na_2$	0.002	6.90
p-$C_6H_4CO_2Na_2$	0.005	4.66
p-$C_6H_4CO_2Na_2$	0.010	2.90
p-$C_6H_4CO_2Na_2$	0.020	1.95
p-$C_6H_4CO_2Na_2$	0.025	1.60
$C_6H_5OPO_3Na_2$	0.001	10.2[c]
$C_6H_5OPO_3Na_2$	0.002	8.50[c]
$C_6H_5OPO_3Na_2$	0.002	9.36
$C_6H_5OPO_3Na_2$	0.004	7.86[c]
$C_6H_5OPO_3Na_2$	0.007	5.76
$C_6H_5OPO_3Na_2$	0.008	5.04[c]
$C_6H_5OPO_3Na_2$	0.012	4.87[c]
$C_6H_5OPO_3Na_2$	0.020	2.98
$C_6H_5OPO_3Na_2$	0.030	2.36
$C_6H_5OPO_3Na_2$	0.040	1.22
$C_6H_5OPO_3Na_2$	0.001	1.83[c,d]
$C_6H_5OPO_3Na_2$	0.001	6.97[c,e]
$C_6H_5OPO_3Na_2$	0.001	11.8[c,f]
$C_6H_5OPO_3Na_2$	0.001	12.5[c,g]
$C_6H_5OPO_3Na_2$	0.001	12.5[c,h]
p-t-$BuC_6H_4OPO_3Na_2$	0.001	7.30[c]
p-t-$BuC_6H_4OPO_3Na_2$	0.0015	4.64[c]
p-t-$BuC_6H_4OPO_3Na_2$	0.002	4.03[c]
p-t-$BuC_5H_4OPO_3Na_2$	0.003	2.18[c]
p-t-$BuC_6H_4OPO_3Na_2$	0.004	1.30[c]
p-t-$BuC_6H_4OPO_3Na_2$	0.005	0.97[c]

[a] At 25.0° with 9.4×10^{-5} M substrate in 3×10^{-3} M CTA at pH 9.0 and 10^{-2} M borate buffer unless specified. [b] 5×10^{-3} M CTA. [c] 2.5×10^{-3} M borate buffer. [d] 1×10^{-3} M CTA. [e] 2×10^{-3} CTA. [f] 4×10^{-3} M CTA. [g] 5×10^{-3} M CTA. [h] 7×10^{-3} M CTA.

were done in the presence of phthalate buffer which inhibits the micellar catalysis simply because we had not observed this inhibition at that time. However, the small amount of phthalate used would not be sufficient to suppress all the catalysis which might have been present, especially at these relatively high concentrations of detergent. Rather surprisingly, CTA does not catalyze the hydrolysis of the dianion of glucose 6-phosphate although for the spontaneous hydrolysis the dianion is considerably more reactive than the monoanion.[14]

Table V. Inhibition of Micellar Catalysis of the Hydrolysis of 2,4-Dinitrophenyl Phosphate[a]

Inhibitor	C_I, M	10^5k_ψ, sec^{-1}
...	...	17.2[b]
...	...	17.7
NaCl	0.005	16.3[c]
NaCl	0.020	16.1[c]
NaCl	0.040	15.0[c]
NaCl	0.060	12.4[c]
NaCl	0.080	10.9[c]
NaCl	0.010	9.27[c]
$C_6H_5CO_2Na$	0.005	10.1
$C_6H_5CO_2Na$	0.010	8.60
$C_6H_5CO_2Na$	0.020	4.35
$C_6H_5CO_2Na$	0.030	3.04
$C_6H_5CO_2Na$	0.040	2.22
o-$C_6H_4CO_2K_2$	0.0075	13.1[c]
o-$C_6H_4CO_2K_2$	0.010	9.90[c]
o-$C_6H_4CO_2K_2$	0.020	6.38[c]
o-$C_6H_4CO_2K_2$	0.030	5.23[c]
o-$C_6H_4CO_2K_2$	0.040	4.56[c]
Catechol	0.010	13.4
Catechol	0.010	10.0[d]
Aspirin	0.010	12.4
Aspirin	0.015	10.6

[a] At 25.0° with 6.3×10^{-5} M substrate in 3×10^{-3} M CTA at pH 9.0 and 0.015 M borate buffer unless specified. [b] 0.0025 M borate buffer. [c] 0.01 M borate buffer. [d] NaOH at pH 12.0.

Salt Effects. Some electrolytes markedly inhibit these micellar catalyses. However, simple salts, *e.g.*, sodium chloride, have only small effects (Tables IV and V), and an increase in the concentration of borate buffer at pH 9.0 from 2.5×10^{-3} M to 15×10^{-3} M only changes the value of 10^5k_ψ from 17.7 to 17.2 sec^{-1} for the hydrolysis of 2,4-dinitrophenyl phosphate in 3×10^{-3} M CTA (Table V), and added sodium phosphate has little effect upon the hydrolysis of 2,6-dinitrophenyl phosphate (Table IV). The large salt inhibitions are observed with sodium toluene-p-sulfonate and sodium salts of carboxylic and substituted phosphoric acids. Most of the studies on these salt effects were made with a constant detergent and varying salt concentration but some experiments were carried out with varying detergent and constant salt concentration (Figures 1 and 2 and Table IV). Small changes in the concentration of borate buffer do not affect the salt inhibition, as is shown by the salt effects of sodium phenyl phosphate in borate buffers (Table IV).

Discussion

Nature of the Catalysis. Only cationic micelles catalyze the hydrolyses of the dianions of the dinitrophenyl phosphates. The rate enhancement for both 2,4- and 2,6-dinitrophenyl phosphate is caused by a 2–3 kcal/mol decrease in the activation energy, and the entropy of activation is almost unaffected.

Kinetic Form of the Catalysis. It is often possible to treat micellar catalysis or retardation by making certain simplifications and assuming that only one substrate molecule is incorporated into a micelle, and that the aggregation number, N, of the micelle is independent of the substrate (*cf.* ref 5 for a discussion of the approximations made in this treatment). There will then be an equilibrium between the substrate in solution, S, and that in the micelle, SD_n.

(14) (a) Ch. Degani and M. Halmann, *J. Amer. Chem. Soc.*, **88**, 4075 (1966); (b) C. A. Bunton and H. Chaimovich, *ibid.*, **88**, 4082 (1966).

$$D_n + S \overset{K}{\rightleftharpoons} SD_n$$
$$\downarrow k^w \qquad \downarrow k^m$$
products

The concentration of the micelles, D_n, is given by

$$C_m = \frac{C_D - CMC}{N} \quad (1)$$

where C_D is the total concentration of detergent, and N the aggregation number. The observed first-order rate constant is given by eq 2, and this equation qualitatively fits the variation of k_ψ with detergent concentration and predicts that $k_\psi = k^m$ when $KC_m \gg 1$ and $k^m KC_m \gg k^w$. Equations 1 and 2 can be combined to give

$$k_\psi = \frac{k^w + k^m KC_m}{1 + KC_m} \quad (2)$$

$$\frac{1}{k^w - k_\psi} = \frac{1}{k^w - k^m} + \left(\frac{1}{k^w - k^m}\right)\left(\frac{N}{K(C_D - CMC)}\right) \quad (3)$$

As predicted by eq 3 plots of $1/(k - k_\psi)$ against $1/(C_D - CMC)$ are linear (Figure 3), but it is obvious that this treatment is oversimplified. Equation 3 predicts that there will be no catalysis for detergent concentrations below the CMC, but the results in Figures 1 and 2 show that there is catalysis with detergent concentrations below the CMC, suggesting that the substrate promotes micellization of the cationic detergent, or that small aggregates of the detergent exist below the CMC, and that they catalyze the hydrolysis. These explanations are not mutually incompatible, and there is extensive evidence from other systems that (i) external agents can promote micellization, (ii) that some aggregation of detergents occurs below the CMC, and (iii) that these small aggregates can be catalytically active.[7,15]

There is another weakness in the treatment. Equation 3 predicts that the intercepts in Figure 3 should give values of $1/(k^w - k^m)$ but the values of k^m, so calculated, are higher than the values of k_ψ in the plateau regions of plots of k_ψ against detergent concentration (Figures 1 and 2). Part of the problems stem from the approximations used in deriving eq 3. In particular, the equation requires that the concentration of micelles be greater than that of substrate, and it is hard to evaluate the seriousness of this approximation at low detergent concentrations. For example, the aggregation number may be greater at higher detergent concentrations than close to the CMC, especially because it is known that submicellar aggregates can form and that micellization can be promoted by foreign agents.[15] In the following discussion we shall assume that k^m is given by the value of k_ψ in the plateau region.

Equation 3 allows us to calculate a binding constant between the cationic micelles and the aryl phosphate monoanions. Using a value for the aggregation number, $N \sim 61$,[16] we obtain $K \sim 1.1 \times 10^5$ and 3.9×10^4 for 2,4- and 2,6-dinitrophenyl phosphates, respectively. These values of K depend critically upon the assumptions made in deriving eq 3, but for the reaction between hydroxide ion and 2,4-dinitrochlorobenzene we obtained fair agreement between the values of K determined kinetically and directly.[17]

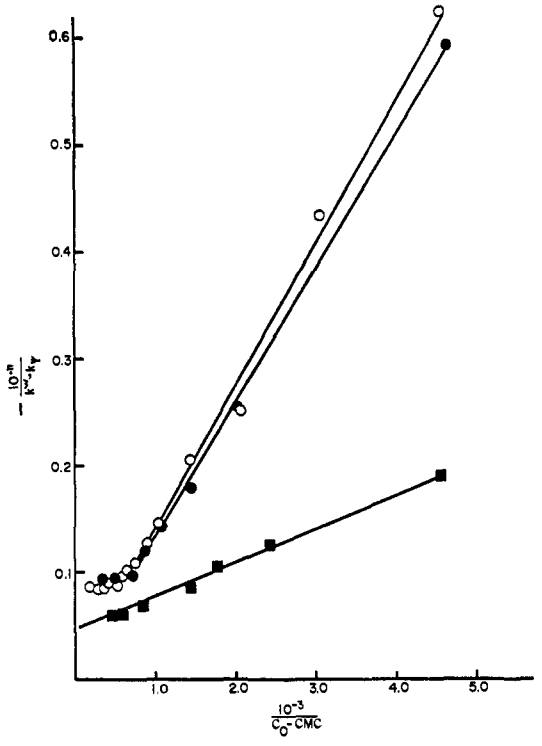

Figure 3. Relation between reaction rate and micelle concentration at pH 9.0 and 25.0°: ●, 1.8×10^{-5} *M* 2,6-dinitrophenyl phosphate; ○, 9.4×10^{-5} *M* 2,6-dinitrophenyl phosphate; ■, 6.3×10^{-5} *M* 2,4-dinitrophenyl phosphate. For 2,6-dinitrophenyl phosphate $n = 4$, and for 2,4-dinitrophenyl phosphate $n = 5$.

In reactions between uncharged substrates and nucleophilic ions catalyzed by cationic micelles a maximum is generally observed in plots of rate constant against detergent concentration,[4,5,17] and similar maxima are observed in reactions between hydroxide ion and 2,4-dinitrofluorobenzene or *p*-nitrophenyl diphenyl phosphate catalyzed by CTA,[18] whereas plateaux are observed in these reactions of phosphate dianions which involve heterolysis of the substrate. These observations agree with the assumption that once the bulk of the substrate is incorporated into the cationic micelle additional detergent merely deactivates the nucleophile.[17]

Inhibition. Simple salts, such as sodium chloride or methanesulfonate, reduce the rate of hydrolysis in the "plateau" region, although a small increase in the concentration of chloride or borate or phosphate ion has little effect (Tables IV and V) and the effects become large only at relatively high electrolyte concentrations. However, the effects of carboxylate ions are very large (Figure 1), *e.g.*, 0.04 *M* benzoate or phthalate buffers almost completely suppress the catalysis at pH 9.0, with a CTA concentration of 3×10^{-3} *M*, and sodium oleate is an even better inhibitor of the micellar catalysis. The dianions of unreactive phosphate esters are also good inhibitors and their efficiency in this role depends

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(16) E. W. Anacker, R. M. Rush, and J. S. Johnson, *J. Phys. Chem.*, 68, 81 (1964).
(17) C. A. Bunton and L. Robinson, *J. Amer. Chem. Soc.*, in press.
(18) L. Robinson, unpublished results.

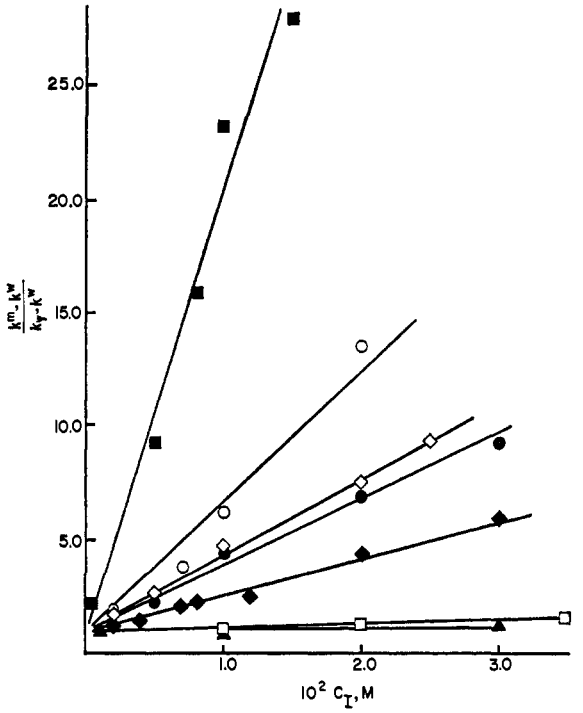


Figure 4. Effect of inhibiting salts upon the hydrolysis of 2,6-dinitrophenyl phosphate in 3×10^{-3} *M* CTA at 25.0° and pH 9.0: ▲, sodium chloride; □, sodium methanesulfonate; ■, sodium toluene-*p*-sulfonate; O, sodium benzoate; ●, dipotassium phthalate; ◇, disodium terephthalate; ◆, disodium phenyl phosphate.

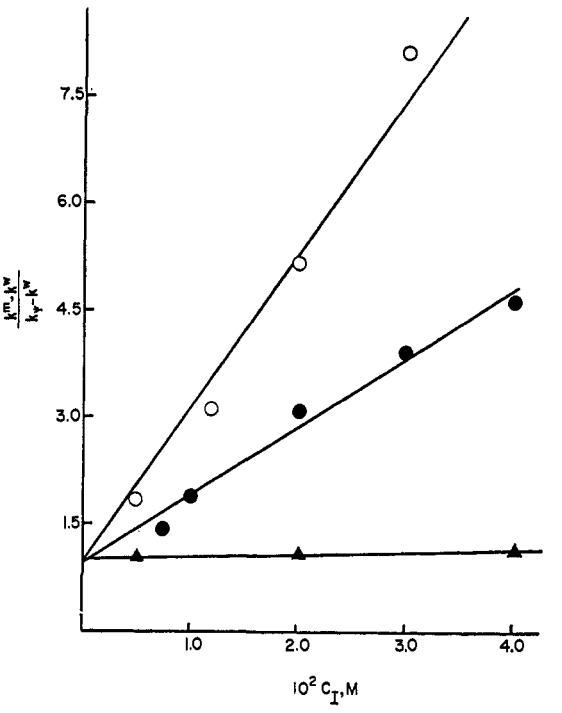


Figure 5. Effect of inhibiting salts upon the hydrolysis of 2,4-dinitrophenyl phosphate in 3×10^{-3} *M* CTA at 25.0° and pH 9.0: ▲, sodium chloride; O, sodium benzoate; ●, dipotassium phthalate.

on the organic residue, *e.g.*, *p-t*-butylphenyl phosphate is a better inhibitor than phenyl phosphate (Figure 1 and Table IV), even though inorganic phosphate is ineffective. Somewhat similarly, sodium tosylate is a much better inhibitor than mesylate in the hydrolysis of 2,6-dinitrophenyl phosphate (Table IV), and phenoxide ions, *e.g.*, of catechol, inhibit the micellar catalysis of the hydrolysis of 2,4-dinitrophenyl phosphate (Table V), even though one might expect them to act as nucleophiles and attack the substrate incorporated in the micelle.

All these results point to the importance of a negative charge and a bulky organic residue in the inhibitor, suggesting that both electrostatic and hydrophobic binding are involved in making the cationic micelles of CTA incapable of incorporating the substrate.

We can assume that the inhibition is competitive, *e.g.*

$$\begin{array}{ccccc} S + D_n & \overset{K}{\rightleftharpoons} & SD_n & \xrightarrow{k^m} & \text{products} \\ I \downarrow\uparrow K_I & & & & \\ ID_n & & & & \end{array}$$

(where I is the inhibiting anion), and if we assume that incorporation of the substrate does not affect the formation of micelles or their interaction with inhibitor we can derive eq 4 which is similar to the equation used to account for competitive enzyme inhibition. In deriving this equation we ignore the effects of added salts upon the aggregation number and CMC of the micelle, and also make the assumptions made in deriving eq 3, and we also assume that incorporation of one inhibitor molecule into the micelle will prevent incorporation of substrate (*cf.* ref 5).

$$\frac{k^m - k^w}{k_\psi - k^w} = 1 + \frac{N}{K(C_D - \text{CMC})} + \frac{K_I C_I N}{K(C_D - \text{CMC})} \quad (4)$$

For a given detergent concentration the second term in this equation is a constant, and can be neglected for the relatively high detergent concentrations used in the present work, and plots of $(k^m - k^w)/(k_\psi - k_*^w)$ against inhibitor concentration are for the most part linear with intercept of unity (Figures 4 and 5). From the slopes of these plots we can calculate the binding constants between inhibitor and the cationic micelles which are given in Table VI. As required by theory these values of K_I are independent of the substrate within

Table VI. Inhibitor Constants[a]

Inhibitor	Substrate 2,4	Substrate 2,6
NaCl	~4[b]	~7[b]
CH_3SO_3Na	...	24
$C_6H_5OPO_3Na_2$	...	230
o-$C_6H_4(CO_2K)_2$	370	410
p-$C_6H_4(CO_2K)_2$	...	470
$C_6H_5CO_2Na$	870	810
p-$C_7H_7SO_3Na$	...	2800

[a] For catalyzed hydrolyses of 2,4- and 2,6-dinitrophenyl phosphates at 25.0° with 3×10^{-3} *M* CTA at pH 9.0. [b] There is considerable uncertainty in these numerical values because of the small salt effect.

experimental error for sodium benzoate and potassium phthalate. Comparison between the values of *K*, the binding constant between substrate and micelle, and K_I, the corresponding binding constants for the inhibiting salts, suggests that the dinitrophenyl phos-

phate dianions are bound much more strongly than phenyl phosphate dianions, and that the nitro groups therefore assist the binding. Comparison of the values of K for 2,4- and 2,6-dinitrophenyl phosphates shows that a nitro group in the *para* position assists binding more than in the *ortho* position.

The linearity of the plots suggests that the approximations made in deriving eq 4 are reasonable. Comparison of inhibition by benzoate and phthalate ions shows that the benzoate monoanion attaches itself to the micelle more strongly than does the phthalate dianion. This conclusion appears surprising if only electrostatic effects are considered, but it is consistent with other observations which show that a monoanion of low charge density binds more strongly to the cationic micelle than does one of high charge density, and the results illustrate the importance of strong hydrophobic binding between a micelle and a bulky ion or molecule.

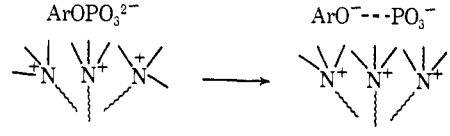
A group *ortho* added to the carboxylate residue reduces the efficiency of an inhibitor, *e.g.*, the acetyl salicylate ion is less effective than benzoate (Table V), presumably for steric reasons, and the difference between phthalate and terephthalate ion (Figure 1) can be explained similarly.

Inhibition by sodium oleate and *t*-butyl phenyl phosphate does not fit eq 4. Plots of $(k^m - k^w)/(k_\psi - k^w)$ against C_I are linear only at low inhibitor concentrations, and at higher concentrations they curve upward. However, a plot of k_ψ against the concentration of sodium oleate is approximately linear (Figure 6), suggesting that the interaction between the oleate and cetyltrimethylammonium ions is so strong that 1 mol of CTA is effectively "neutralized" by every added mole of sodium oleate, presumably to give an uncharged micelle which is catalytically ineffective. The straight line in Figure 6 was drawn on the assumption that 1 mol of CTA is neutralized by 1 mol of sodium oleate, and the results are in reasonable agreement with this prediction.

The behavior of the *t*-butylphenyl phosphate dianion is intermediate between those of sodium oleate and the other salts (*cf.* Table IV and Figure 6), because for this salt plots of k_ψ against inhibitor concentration curve upward at the higher inhibitor concentrations, and plots of $(k^m - k^w)/(k_\psi - k^w)$ against inhibitor concentration also curve upward.

Although inhibition by most of the salts examined fits eq 4 we note one major area of uncertainty in the interpretation. We assume that incorporation of a foreign anion into the micelle prevents incorporation of the substrate, and so makes this micelle completely ineffective as a catalyst, whereas it may simply make it less effective. It is very hard to test this assumption, although we note that the treatments of the kinetic forms of micellar inhibition of anion–molecule reactions which rely on this assumption appear to fit the experimental results quite well.[5,17]

Requirements for Micellar Catalysis of Phosphate Ester Hydrolysis. The kinetic results show that catalysis by a cationic micelle can only occur in certain special circumstances, *e.g.*, there is no micellar catalysis of the hydrolysis of phosphate ester monoanion which involves transfer of a proton so that an alcohol or phenol is released,[8] or of the hydrolysis of the dianion of glucose 6-phosphate which probably involves a proton transfer from the 1-OH group to the phosphate residue.[14b] On the other hand the dinitrophenyl phosphate dianions decompose by splitting into two monoanions,[9,10] and the catalysis of these, but not the other, reactions suggests that the electrostatic energy of two monoanions incorporated into a cationic micelle is greater than that of the dianion from which they are derived. This result may arise simply because each of the monoanionic fragments can interact with a quaternary ammonium ion on the surface of the micelle, *e.g.*



although we note that a simple electrostatic treatment requires that the energy of interaction between a cationic micelle and an anion at a given potential should be proportional to the charge on the anion.

Decomposition of an aryl phosphate dianion into a phenoxide ion and the hypothetical metaphosphate ion should be assisted by any change in the phosphorus–oxygen bond angles toward those of the monomeric metaphosphate ion, and if electrostatic interactions had this effect incorporation of the substrate upon a cationic micelle would assist reaction. The importance of ring strain in increasing the reactivity of some cyclic phosphates has been demonstrated by Westheimer and his coworkers.[19]

An additional effect which could also be significant is that the hydrolysis of dianions of 2,4- and 2,6-dinitrophenyl phosphates increases with decreasing water content of an aqueous organic solvent,[9,10] and transfer

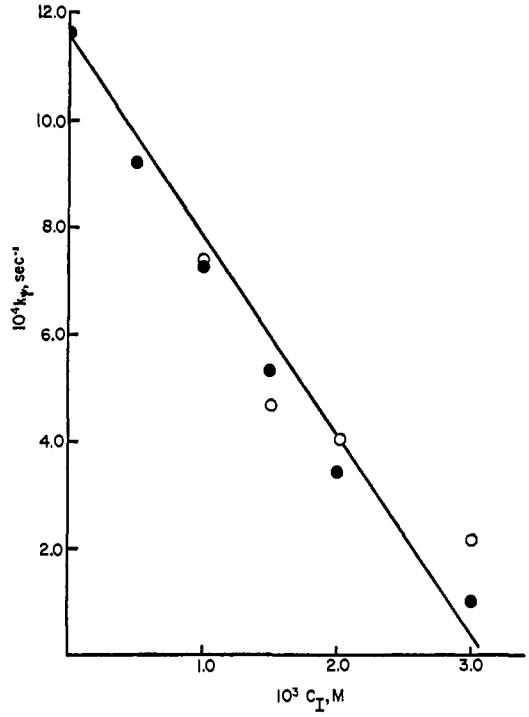


Figure 6. Effects of sodium oleate and disodium *t*-butylphenyl phosphate upon the hydrolysis of 2,6-dinitrophenyl phosphate in 3×10^{-3} M CTA at 25.0° and pH 9.0: ●, sodium oleate; ○, disodium *t*-butylphenyl phosphate.

(19) P. C. Haake and F. H. Westheimer, *J. Amer. Chem. Soc.*, 83, 1102 (1961).

of a dianion from water into the micellar nonaqueous phase could therefore increase its reactivity.

These general explanations of the role of electrostatic effects upon the heterolysis of the phosphorus–oxygen bond are consistent with the observation that the cationic micelle decreases the activation energy of the reaction.

The reaction between hydroxide ion and the aryl phosphate dianion is not assisted to any appreciable extent by CTA micelles. This result is at first sight surprising, but we have observed that incorporation of one anion into the micelle strongly inhibits approach of another, as shown by the inhibition studies. Also the micellar catalysis itself shows that a dianion on the micelle tends to separate into two monoanions, and therefore the micelle should not encourage anions to come together, as would be required for reaction between hydroxide ion and either of the aryl phosphate dianions. In making this assessment of the inability of CTA micelles to catalyze the reaction between hydroxide ion and the dinitrophenyl phosphate dianions we are assuming that sodium hydroxide, acting as an electrolyte, does not have a large inhibiting effect upon the CTA-catalyzed heterolysis of the aryl phosphate dianion to phenoxide and metaphosphate ions. The rate inhibition by added salts decreases markedly with increasing charge density of the anion, *e.g.*; chloride or mesylate is an ineffective inhibitor as compared with the bulkier anions. There are linear relations between the surface potential for monolayers of stearyltrimethylammonium ions and logarithm of the ionic strength of sodium chloride,[20] but the Stern equation takes into account not only ionic strength, but also the size of the ions located around the micelle and interactions such as van der Waal's forces and hydrophobic bonding,[21] and our results suggest that simple ionic atmosphere effects are relatively unimportant for bulky anions.

(20) J. T. Davies and E. K. Rideal, "Interfacial Phenomena," Academic Press Inc., New York, N. Y., 1961, p 76.
(21) O. Stern, *Z. Elektrochem.*, 30, 508 (1924); ref 20, p 85.

Arylation, Methylation, and Carboxyalkylation of Olefins by Group VIII Metal Derivatives

R. F. Heck

Contribution from the Research Center of Hercules Inc., Wilmington, Delaware 19899. *Received December 7, 1967*

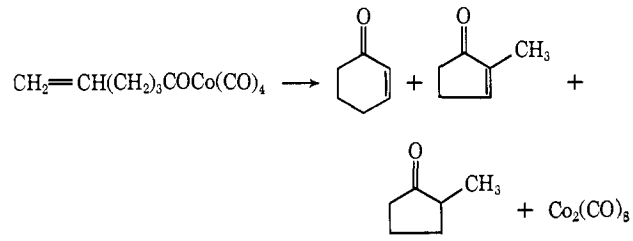
Abstract: Aryl, methyl, and carboxyalkyl derivatives of group VIII metal salts, particularly palladium, rhodium, and ruthenium salts, react with olefins to produce aryl-, methyl-, or carboxyalkyl-substituted olefins, and reduced metal salt or metal. The reaction may be made catalytic with respect to the metal salt by employing cupric chloride or cupric chloride, air, and hydrogen chloride as reoxidants. The reaction is insensitive to oxygen and water and, therefore, provides an extremely convenient method for the synthesis of a wide variety of olefinic compounds.

Addition reactions of nontransition metal alkyls and aryls to olefins are well known. Much less is known about the addition reactions of alkyl and aryl transition metal compounds. Presumably such reactions are responsible for the olefin polymerization reactions caused by combinations of alkylating or arylating agents and titanium, vanadium, or chromium salts. Only a few reasonably clear examples of the addition of transition metal alkyls to olefins without the formation of polymers have been reported. The addition of methylmanganese pentacarbonyl to tetrafluoroethylene[1] and the cyclization of 5-hex-

$$CH_3Mn(CO)_5 + CF_2{=}CF_2 \longrightarrow CH_3CF_2CF_2Mn(CO)_5$$

enoylcobalt tetracarbonyl to a mixture of cyclohexenone, 2-methylcyclopentenone, and 2-methylcyclopentanone[2] are two of the best examples. The present paper reports a study of the reaction of simple aryl and alkyl derivatives of group VIII metals with olefins.

(1) J. B. Wilford, P. M. Treichel, and F. G. A. Stone, *Proc. Chem. Soc.*, 218 (1963).
(2) R. F. Heck, *J. Amer. Chem. Soc.*, **85**, 3116 (1963).



Results and Discussion

Group VIII metal alkyls and aryls have been prepared by reaction of the metal halides with Grignard reagents and alkali metal alkyls. Isolatable products have been obtained only from platinum halides[3] or from phosphine–metal halide complexes[4] and certain other complexes containing "stabilizing" ligands.

Even with these stabilizing ligands, saturated alkyl derivatives (with β-hydrogen substituents) of the group VIII metals are generally unstable with respect to the olefin and the metal hydride.[4] We chose to prepare

(3) M. E. Foss and C. S. Gibson, *J. Chem. Soc.*, 299 (1951).
(4) For example, see J. Chatt and B. L. Shaw, *ibid.*, 4020 (1959); G. Calvin and G. E. Coates, *ibid.*, 2008 (1960).