

through Celite until clear and the filtrate, diluted with ether, was washed with water until the washings were neutral. The ethereal solution was then dried (sodium sulfate), filtered, and rotary evaporated to an oil which was vacuum fractionated to afford 3.65 g (15%) of a mixture of carvotanacetol acetates, bp 79–81° (5 mm), $[\alpha]_D^{25}$ 0.0°.

Selenium Dioxide Oxidation of D-(+)-1-*p*-Menthene (16) in Wet Dioxane in the Presence of Acrylonitrile.—To a solution of 10 g (0.070 mol) of 16 in 80 ml of purified dioxane maintained under an atmosphere of nitrogen was added 2.0 ml (0.03 mol) of acrylonitrile [Eastman practical grade freshly distilled (bp 75–76°) just prior to use to remove inhibitor]. Both the dioxane and 16 were peroxide free as determined by negative test with acidified potassium iodide. To the solution of 16 was added dropwise a solution of 8.0 g (0.07 mol) of selenium dioxide in 200 ml of purified dioxane containing 5.0 ml of distilled water. The reaction was maintained under nitrogen at ambient temperature for several days. Under these conditions, 16 was oxidized to a mixture of *cis*- and *trans*-carvotanacetols, phellandrol, and carvotanacetone (*vide supra*) but no polyacrylonitrile precipitated.

It was determined in control experiments that polyacrylonitrile is highly insoluble in this medium and would have been readily discernible had initiation of polymerization occurred. It was further established that acrylonitrile polymerizes rapidly under the same reaction conditions if a source of free radicals is introduced. Indeed, a solution of 2.0 ml of freshly distilled acrylonitrile in 280 ml of purified dioxane maintained under a nitrogen atmosphere at 40° gave an immediate precipitate when successively treated with 0.3 g of potassium persulfate in 10 ml of aqueous dioxane and 0.15 g of sodium bisulfite in 10 ml of aqueous dioxane.

Registry No.—Selenium dioxide, 7446-08-4; 16, 1195-31-9; 21, 23713-54-4; 26, 23713-55-5; 30, 23713-56-6; 34, 23713-57-7; 39, 23713-58-8; 44, 2001-50-5.

Acknowledgment.—Grateful acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for generous support of this research.

Micellar Effects on the Hydrolysis of 2,4-Dinitrophenyl Sulfate¹

E. J. FENDLER, R. R. LIECHTI, AND J. H. FENDLER

Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15213, and
Radiation Research Laboratories, Mellon Institute, Carnegie-Mellon University, Pittsburgh, Pennsylvania 15213

Received November 3, 1969

Hexadecyltrimethylammonium bromide (CTAB) and poly(oxyethylene)(24)dinonylphenol (DNPE) enhance the rate of neutral hydrolysis of 2,4-dinitrophenyl sulfate by factors of 3.2 and 2.6, respectively, but sodium dodecyl sulfate (NaLS) has no effect on the rate. The rate enhancement arises from a decrease in both the enthalpy and entropy of activation. From the kinetic data at 25.00°, the binding constant between CTAB and 2,4-dinitrophenyl sulfate is calculated to be 1.9×10^5 l. mol⁻¹. The effects of these surfactants on the acid- and base-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate are less specific; both charged and uncharged micelles enhance the rate of the acid-catalyzed reaction, while the base-catalyzed rate is only affected by DNPE. The retardation of the base-catalyzed hydrolysis by DNPE is a manifestation of an increase in both the enthalpy and entropy of activation with respect to the base-catalyzed hydrolysis in the absence of surfactant. Micellar effects on the hydrolyses of sulfate esters are compared with those on aryl phosphates and are discussed in terms of electrostatic and hydrophobic interactions.

The recent vigorous interest in micellar effects on reaction rates has been stimulated by the recognized analogies between protein and micelle structures and between enzymatic and micellar catalysis.² The influence of surfactants on the hydrolysis of aryl phosphates has been shown to be specific. Hexadecyltrimethylammonium bromide (CTAB) increases the rate constants for the dianion hydrolysis of 2,4- and 2,6-dinitrophenyl phosphate by a factor of 25 but does not affect the hydroxide ion catalyzed reaction of the dianion or the hydrolysis of the monoanion of *p*-nitrophenyl phosphate, whereas sodium dodecyl sulfate (NaLS) and poly(oxyethylene)(24)dinonylphenol (Igepal DM-730), a nonionic amphiphile, do not significantly alter the rates of hydrolysis of dinitrophenyl phosphate dianions.³ Since a number of analogies can be made between the mechanisms for the hydrolyses of sulfate⁴ and phosphate esters and since both reactions are of vital importance in biochemical processes, we have undertaken a study of micellar effects on the neutral, acid-catalyzed, and base-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate in order to compare these

two systems and to elucidate the nature of micellar catalysis.

Experimental Section

The preparation and purification of 2,4-dinitrophenyl sulfate has been described.⁴ Hexadecyltrimethylammonium bromide (CTAB) and sodium dodecyl sulfate (NaLS) were purified by the method of Duynstee and Grunwald.⁵ Poly(oxyethylene)(24)dinonylphenol (Igepal DM-730, General Aniline and Film Corp.) was used without further purification⁶ and is denoted as DNPE in the text. Deionized distilled water was used for the preparation of the buffer, the surfactant, and the standard acid and alkali solutions. The pH of the buffer solutions was adjusted by the addition of hydrochloric acid or sodium hydroxide at 25.0° using an Orion Model 801 pH meter. The concentrations of the acid solutions were determined by titration with standard 0.100 or 1.00 M NaOH (BDH) using Lacmoid as the indicator. The alkali solutions were prepared from the 1.00 M NaOH standard by dilution.

The hydrolysis was followed spectrophotometrically on a Beckman DU-2 by measuring the absorbance of the phenoxide ion (360 nm) or the phenol (320 nm).⁴ The temperature of the thermostated baths and the cell compartment was maintained within $\pm 0.05^\circ$, as monitored by NBS thermometers. Good first-order plots were obtained in all cases for at least 75% reaction. The pseudo-first-order rate constants, k_p , for the hydrolysis of 2,4-dinitrophenyl sulfate have been calculated by the Guggenheim method.⁷

(1) Supported, in part, by the Health Research Services Foundation, and by the U. S. Atomic Energy Commission.

(2) For a comprehensive review of micellar effects on reaction rates, see E. J. Fendler and J. H. Fendler, *Advan. Phys. Org. Chem.*, **8**, 271 (1970).

(3) C. A. Bunton, E. J. Fendler, L. Sepulveda, and K.-U. Yang, *J. Amer. Chem. Soc.*, **90**, 5512 (1968).

(4) E. J. Fendler and J. H. Fendler, *J. Org. Chem.*, **32**, 3852 (1968).

(5) E. F. Duynstee and E. Grunwald, *J. Amer. Chem. Soc.*, **81**, 4540 (1959).

(6) We are greatly indebted to Dr. L. W. Burnette of the General Aniline and Film Corp. for providing us with samples of nonionic surfactants.

(7) E. A. Guggenheim, *Phil. Mag.*, **2**, 538 (1926).

Results

The observed pseudo-first-order rate constants, k_{ψ} , for the hydrolysis of 2,4-dinitrophenyl sulfate at pH 8.0 in the presence of a cationic (CTAB), an anionic (NaLS), and an uncharged (Igepal DM-730, DNPE) amphiphile are collected in Table I. Sodium dodecyl sulfate has no effect on the neutral hydrolysis of the substrate, but both hexadecyltrimethylammonium bromide and poly(oxyethylene)(24)dinonylphenol enhance the rate above their critical micelle concentrations (Figure 1). The following critical micelle concentrations are used in the present work: $7.8 \times 10^{-4} M$ for CTAB in $2.5 \times 10^{-3} M$ disodium tetraborate buffer, $8.1 \times 10^{-3} M$ for NaLS, and $4.7 \times 10^{-4} M$ for Igepal DM-730.² The concentrations of 2,4-dinitrophenyl sulfate are $1-6 \times 10^{-5} M$ and in this concentration range the observed rate constants are invariant, within the limits of experimental error, as a function of substrate concentration. The rate constants for micellar catalysis, obtained in the absence of buffers, agree well with those obtained in their presence; $2.5 \times 10^{-3} M$ sodium tetraborate has no influence, therefore, on the micellar catalysis under these conditions.

TABLE I
HYDROLYSIS OF 2,4-DINITROPHENYL SULFATE IN
AQUEOUS MICELLAR SOLUTIONS AT pH 8.00^a

$10^5 c_D, M$	$10^5 k_{\psi}, \text{sec}^{-1}$		
	CTAB	NaLS	DNPE
0.000		2.71 ^b	
0.500			3.82
0.750			4.83
0.925	4.40		
0.950	4.52		
1.00	6.12		4.20
1.05	5.30		
1.10	5.45		
1.25	5.82		
1.50	6.61		5.45
1.75	5.95		
1.75	7.31		
2.00	6.75		
2.25	7.52		
3.00	6.95		
5.00	8.26	2.80	6.28
5.00	8.23 ^c		
6.00	8.30		
6.00	3.34 ^d		
6.00	23.1 ^e		
8.00	8.70		6.80
10.0	8.43		6.85
10.0			19.6 ^f
10.0			45.7 ^g
14.0			6.90
15.0			6.72
20.0	8.65		7.30
20.0			6.40
30.0	8.65		6.50
30.0			7.20
50.0		2.75	

^a In the presence of $2.5 \times 10^{-3} M$ $\text{Na}_2\text{B}_4\text{O}_7$ buffer at 25.00° , unless specified otherwise. ^b $k_0 = 2.71 \times 10^{-5} \text{sec}^{-1}$. ^c In the absence of buffer. ^d At 15.00° . ^e At 35.10° . ^f At 46.50° .

Micellar effects on the acid- and on the base-catalyzed hydrolyses are summarized in Tables II and III, respectively.

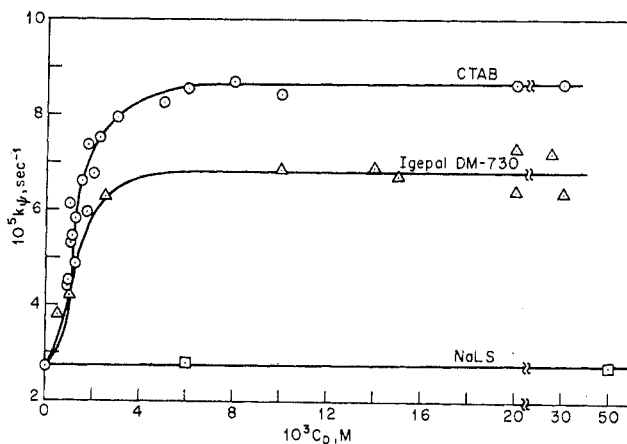


Figure 1.—Plot of the observed pseudo-first-order rate constant, k_{ψ} , against the surfactant concentration, c_D , for the hydrolysis of 2,4-dinitrophenyl sulfate at pH 8.00 and 25.00° .

TABLE II
MICELLAR EFFECTS ON THE ACID-CATALYZED HYDROLYSIS OF
2,4-DINITROPHENYL SULFATE AT 25.00°

[HCl], M	Surfactant	$10^5 k_{\psi}, \text{sec}^{-1}$	$10^5 k_a, M^{-1} \text{sec}^{-1}$ ^a
0.10	None	5.09	23.8
1.00	None	12.57	9.86
0.10	$5 \times 10^{-3} M$ CTAB	11.50	32.4
1.00	$5 \times 10^{-3} M$ CTAB	23.03	14.77
0.10	$5 \times 10^{-2} M$ NaLS	6.05	33.0
1.00	$5 \times 10^{-2} M$ NaLS	15.00	12.25
0.01	$1 \times 10^{-2} M$ DNPE	12.26	54.1

^a $k_a = (k_{\psi} - k_n)/[\text{HCl}]$, where k_n is the observed rate constant for the neutral hydrolysis.

TABLE III
MICELLAR EFFECTS ON THE HYDROXIDE ION CATALYZED
HYDROLYSIS OF 2,4-DINITROPHENYL SULFATE AT 25.00°

Surfactant	$10^4 k_b, M^{-1} \text{sec}^{-1}$ ^a
None	4.48
$5.0 \times 10^{-3} M$ CTAB	5.9
$5.0 \times 10^{-2} M$ NaLS	4.7
$1.0 \times 10^{-2} M$ DNPE	1.65

^a $k_b = \text{slope of plots of } k_{\psi} \text{ vs. } [\text{NaOH}]$ (containing at least four points) in the $0.1-0.4 M$ NaOH concentration range.

The Arrhenius parameters determined for the neutral and the alkaline hydrolyses of 2,4-dinitrophenyl sulfate in the presence and in the absence of surfactants are collected in Table IV. Allowing an overall 5% error in

TABLE IV
ARRHENIUS PARAMETERS FOR THE HYDROLYSIS OF
2,4-DINITROPHENYL SULFATE IN THE PRESENCE OF SURFACTANTS^a

Surfactant	$\Delta H^\ddagger, \text{kcal/mol}$	$\Delta S^\ddagger, \text{eu}^b$
None	18.2	-18.0 ^c
$6.00 \times 10^{-3} M$ CTAB	16.0	-23.3
$1.00 \times 10^{-2} M$ DNPE	16.3	-22.7
None ^d	17.3	-15.0
$1.00 \times 10^{-2} M$ DNPE ^d	19.7	-9.74

^a Neutral hydrolysis, at pH 8.00, unless specified otherwise. ^b Calculated at 25.0° . ^c Data determined previously and given in ref 4. ^d Base-catalyzed hydrolysis; calculated from the second-order rate constants, k_b , at three temperatures.

the individual rate constants, at the temperature interval used, the statistical error for the activation

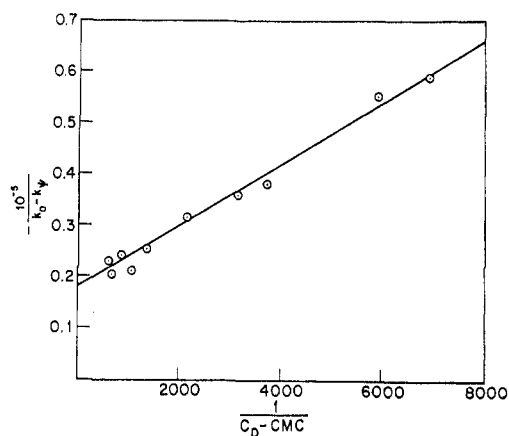


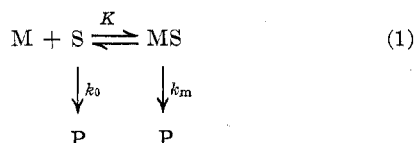
Figure 2.—Plot of $1/(k_0 - k_\psi)$ vs. $1/(c_D - \text{cmc})$ for the interaction of CTAB with 2,4-dinitrophenyl sulfate at pH 8.00 and 25.00°.

enthalpy is ± 0.8 kcal/mol and that for the activation entropy is ± 2.0 eu.⁸

Discussion

Neutral Hydrolysis.—At concentrations greater than their critical micelle concentrations both CTAB and DNPE enhance the rate of the neutral hydrolysis of 2,4-dinitrophenyl sulfate. The rate constants first increase rapidly as a function of surfactant concentration and then reach a value which remains constant over a wide range of surfactant concentration (Figure 1). Similar behavior has been observed in the CTAB-catalyzed hydrolysis of the dianions of 2,4- and 2,6-dinitrophenyl phosphates,³ although the magnitude of the rate enhancement ($k_\psi/k_0 \cong 25$ for CTAB) is considerably greater than that observed for the micellar effects on the neutral hydrolysis of 2,4-dinitrophenyl sulfate ($k_\psi/k_0 = 3.2$ for CTAB and 2.6 for DNPE).

By making a number of assumptions and simplifications,⁹ the kinetic form of micellar catalysis has been successfully treated^{2,3,10-14} in terms of micelle-substrate complex formation and reaction in the aqueous and micellar phase (eq 1), where k_0 and k_m are the rate



constants for product formation in the bulk solvent and in the micellar phase, respectively, and K is the micelle-substrate binding constant. The observed rate constant, k_ψ , for product formation is given^{2,3,10-14} by eq 2. The kinetic behavior for the micelle-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate obeys, at least qualitatively, eq 2 in that k_ψ increases to a constant value

$$k_\psi = \frac{k_0 + k_m K[M]}{1 + K[M]} \quad (2)$$

which represents conditions when $K[M] \gg 1$ and $k_m K[M] \gg k_0$ and the observed rate constant in this plateau region (Figure 1) is due entirely to the reaction in the micellar phase, *i.e.*, $k_\psi = k_m$. Equation 2 can be rearranged to give eq 3,^{2,3,10-14} using the relationship of

$$\frac{1}{k_0 - k_\psi} = \frac{1}{k_0 - k_m} + \left(\frac{1}{k_0 - k_m} \right) \left(\frac{1}{c_D - \text{cmc}} \right) \frac{N}{K} \quad (3)$$

eq 4, where c_D is the total concentration of the surfac-

$$[M] = \frac{c_D - \text{cmc}}{N} \quad (4)$$

tant, cmc is the critical micelle concentration, and N is the aggregation number. A plot of the left-hand side of eq 3 vs. $1/(c_D - \text{cmc})$ should result in a straight line, from which k_m and K/N can be calculated. As expected, such a plot for the CTAB-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate at pH 8.0 is linear (Figure 2). From the intercept, k_m is calculated to be 8.12×10^{-5} sec⁻¹, a value which is in good agreement with the observed rate constant in the plateau region (Figure 1). Assuming an aggregation number of 61 for CTAB,^{2,15} the binding constant, K , for hexadecyltrimethylammonium bromide and 2,4-dinitrophenyl sulfate at pH 8.0 and 25.0° is calculated to be 1.9×10^5 l. mol⁻¹. Since this catalysis by CTAB is relatively small in magnitude and is observed at low surfactant concentrations, the value of K obtained using eq 3 is very sensitive to the actual value used for the cmc. A modified form of eq 3, eq 5, has been suggested to circumvent this problem.¹⁶ A plot of the left-hand side of eq 5 vs. c_D

$$\frac{k_\psi - k_0}{k_m - k_\psi} = \frac{K}{N} (c_D - \text{cmc}) \quad (5)$$

does not involve the cmc and should give a straight line whose slope is K/N . A good straight line is obtained by plotting the data given in Table I according to eq 5 and gives a value of 1.6×10^5 l. mol⁻¹ for K (once again assuming N to be 61). The reasonable agreement between the K values obtained from eq 3 and 5 justifies, at least partially, the approximations used in the derivation of eq 2.^{2,9} From the intercept of the straight line obtained by using eq 5, a value of 3.6×10^{-4} M is obtained for the cmc of CTAB. This cmc value is somewhat lower than that determined by others and used in eq 3 (7.8×10^{-4} M).^{2,3} The lower cmc value determined kinetically can reasonably be attributed to 2,4-dinitrophenyl sulfate induced micellization of the surfactant and hence a decrease in the cmc.^{2,17,18} Similarly, the cmc values obtained, by use of eq 5, for phenyl and 2,4-dimethoxyphenyl hexadecyldimethylammonium bromide in the presence of 2,4-dinitrophenyl phosphate were lower than those obtained in the absence of the phosphate ester.¹⁶

Since the magnitude of the binding constant for 2,4-dinitrophenyl sulfate and CTAB ($K \cong 1.9 \times 10^5$ l. mol⁻¹) is similar to that found for 2,4-dinitrophenyl phosphate and CTAB (1.1×10^5 l. mol⁻¹),³ the greater rate enhancement in the case of phosphate dianion

(8) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).
 (9) A. K. Colter, S. S. Wang, G. H. Megerle, and P. S. Ossip, *J. Amer. Chem. Soc.*, **86**, 3106 (1964).
 (10) F. M. Menger and C. E. Portnoy, *ibid.*, **89**, 4698 (1967).
 (11) T. C. Bruice, J. Katzhendler, and L. R. Fedor, *ibid.*, **90**, 1333 (1968).
 (12) C. A. Bunton and L. Robinson, *ibid.*, **90**, 5972 (1968).
 (13) C. A. Bunton and L. Robinson, *J. Org. Chem.*, **34**, 773 (1969).
 (14) C. A. Bunton and L. Robinson, *ibid.*, **34**, 780 (1969).

(15) E. W. Anacker, R. M. Rush, and J. S. Johnson, *J. Phys. Chem.*, **68**, 81 (1964).
 (16) C. A. Bunton, L. Robinson, and L. Sepulveda, *J. Org. Chem.*, **35**, 108 (1970).
 (17) P. Mukerjee and K. J. Mysels, *J. Amer. Chem. Soc.*, **77**, 2937 (1955).
 (18) P. H. Elworthy, A. T. Florence, and C. B. Macfarlane, "Solubilization by Surface Active Agents and Its Applications in Chemistry and the Biological Sciences," Chapman and Hall, London, 1968.

hydrolysis compared with that for the corresponding sulfate is a manifestation of the higher reactivity of the former in the micellar phase (eq 2).

The acceleration of the rate of the neutral hydrolysis of 2,4-dinitrophenyl sulfate by cationic and nonionic micelles arises from a decrease in both the enthalpy and the entropy of activation (Table IV). In contrast, the catalysis of the dinitrophenyl phosphate dianion hydrolyses by CTAB results almost exclusively from a decrease in the activation energy.

The substrate specificity of the micellar effects are further emphasized by the observed rate enhancement on the neutral hydrolysis of 2,4-dinitrophenyl sulfate by the nonionic surfactant. A straight line is obtained by plotting the data (Table I) for the DNPE-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate at pH 8.0 according to eq 5, from the slope of which we calculate K/N to be $1.3 \times 10^3 M^{-1}$. Since the aggregation number for this amphiphile is unavailable, a direct comparison of the binding constants for the cationic and the nonionic surfactant cannot be made; however, the values of K/N for CTAB (3.1×10^3) and DNPE ($1.3 \times 10^3 M^{-1}$) suggest that 2,4-dinitrophenyl sulfate binds appreciably to the nonionic surfactant irrespective of the exact value of N .

Acid-Catalyzed Hydrolysis.—The rate-determining step in the acid-catalyzed hydrolysis of aryl sulfates probably involves unimolecular fission of a rapidly formed zwitterion;^{4,19} however, acids, in addition to their proton-donating power, exert specific electrolyte effects on both the initial and the transition states of these hydrolyses.⁴

Both charged and uncharged micelles enhance the rate of the acid-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate, the order of effectiveness being DNPE > CTAB \sim NaLS (Table II). The absence of appreciable catalytic specificity in this reaction is obviously uninterpretable solely on the basis of electrostatic effects and indicates the importance of nonelectrostatic factors, such as hydrophobic interactions, and activity coefficient effects in the micellar catalysis

of the acidic hydrolysis. Supporting this postulation is the observation of a significant rate acceleration ($k_v/k_0 = 20$) by nonionic poly(oxyethylene)(20)sorbitan monooleate (Polysorbate 80)²⁰ in the acid-catalyzed hydrolysis of 2,4-dichloronaphthyl sulfate.

Base-Catalyzed Hydrolysis.—The base-catalyzed hydrolysis of sulfate esters is somewhat complex, since this hydrolytic reaction can involve attack of hydroxide ion on both carbon and sulfur.⁴ The observed rate constants may, of course, represent composites of those for these two reaction paths. Neither cationic CTAB nor anionic NaLS influences the base-catalyzed hydrolysis of 2,4-dinitrophenyl sulfate, but nonionic DNPE retards it (Table III). The rate inhibition by the nonionic surfactant is a manifestation of an increase in both the enthalpy and the entropy of activation with respect to the base-catalyzed hydrolysis in the absence of the surfactant (Table IV). The influence of an unchanged surfactant on the base-catalyzed hydrolysis, once again, points strongly to the fact that effects, in addition to those of electrostatic origin, need to be considered in micellar catalysis.

Nature of the Micellar Catalysis.—Micellar catalysis of the hydrolysis of aryl phosphates has been observed only in cases which involve unimolecular phosphorus-oxygen fission in the rate-determining step. Furthermore, catalyst specificity is apparent, since cationic micelles generally accelerate these hydrolyses whereas anionic and nonionic ones either retard them or have little effect.² In these cases the observed catalysis is explicable in terms of relatively simple electrostatic considerations; however, other factors undoubtedly contribute to the catalysis. Conversely, the effects of surfactants on the hydrolyses of aryl sulfates are comparatively much smaller in magnitude and less specific than those for the corresponding aryl phosphates, and nonelectrostatic factors appear to play a significant role in the micellar catalyses.

Registry No.—2,4-Dinitrophenyl sulfate, 17396-93-9; CTAB, 57-09-0.

(19) J. L. Kice and J. M. Anderson, *J. Amer. Chem. Soc.*, **88**, 5242 (1966).

(20) T. H. Baxter and H. B. Kostenbauder, *J. Pharm. Sci.*, **58**, 33 (1969).