Secondary Valence Force Catalysis. XIV. The Effect of Several Surfactants on the Kinetics of Hydrolysis of a Series of 2-(Substituted phenoxy)tetrahydropyrans[1]

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Dilute aqueous solutions of sodium dodecyl sulfate and sodium hexadecyloxyethyl sulfate catalyze the hydrolysis of a series of 2-(substituted phenoxy)tetrahydropyrans. Rate increases from 15- to 50-fold are observed, depending on the nature of surfactant and substrate. Introduction of a methyl group at the 1 position of the hexadecyloxyethyl sulfate markedly reduces its catalytic effectiveness. Activation parameters for the surfactant-dependent reactions vary nonsystematically from those for the same reactions in 50% dioxane–water or in water. In contrast to the behavior of the anionic surfactants, dodecyltrimethylammonium propanesulfonate and dodecyldimethyl phosphine oxide inhibit the hydrolysis of these substrates.

A growing number of investigations during the last several years have established that a variety of organic reactions are subject to catalysis or inhibition in the presence of dilute aqueous solutions of surfactants.[3,4] Among these reactions are the hydrolysis of acetals and ortho esters[5-9] These studies have established that hydrolysis of acetals derived from benzaldehyde is subject to catalysis by sodium dodecyl sulfate and other anionic surfactants. A variety of aspects of the surfactant-catalyzed reactions have been probed. Because of the importance of acetal hydrolysis or, more exactly, glycoside hydrolysis, in biochemistry, it appears worthwhile to pursue these studies in more detail employing substrates which more closely resemble those found in living systems. For this purpose, we have chosen a series of phenoxytetrahydropyrans. Fife and his coworkers have examined the hydrolysis of these substrates in some detail in the absence of surfactants, providing the basis for an examination of the effect of surfactants.[10,11] The results of this investigation are detailed herein.

Experimental Section

Materials.—Sodium dodecyl sulfate was obtained commercially in a highly purified form. Sodium hexadecyloxyethyl sulfate and sodium hexadecyloxy-1-methylethyl sulfate were generously provided by the Eastern Regional Research Laboratory, Department of Agriculture, Philadelphia, Pa. Dodecyldimethylammonium propanesulfonate and dodecyldimethyl phosphine oxide are the generous gifts of the Miami Valley Laboratories of Procter and Gamble, Inc. 2-(Para-substituted phenoxy)tetrahydropyrans were prepared by simple modifications of the general method of Woods and Kramer.[10,12,13]

Kinetic measurements were made spectrophotometrically employing a Zeiss PMQ II spectrophotometer through which water from a thermostated bath was continuously circulated.[5-9] Except for the measurement of activation parameters, all rate constants were measured at 30°. First- and second-order rate constants were evaluated in the usual way. Excellent pseudo-first-order kinetics were observed throughout. Each first-order rate constant is the average of three determinations. Hydrogen ion activity was calculated from the known amount of added hydrochloric acid. Activation parameters were evaluated from the dependence of second-order rate constants on temperature employing the customary equations.

Results and Discussion

The results of Fife and his coworkers have established some of the basic aspects of the hydrolysis of 2-(para-substituted phenoxy)tetrahydropyrans.[10,11] The hydrolysis of each is subject to specific acid catalysis: the second-order rate constants in 50% dioxane–water are correlated by the Hammett σ constants with a value of ρ of -0.92. The *p*-nitro derivative also exhibits a pH-independent reaction, important above pH 4, and hydrolysis of this substrate is subject to general acid catalysis, $\alpha = 0.5$. Since our studies employing surfactants are best carried out in aqueous solution containing a minimum of organic solvent, we have repeated certain aspects of these studies using water as solvent at a temperature of 30°.

In accord with the earlier results, we observe that hydrolysis of each acetal is subject to specific acid catalysis in the pH range 1–3. Second-order rate constants for these reactions were evaluated at a minimum of five values of pH; the results are collected in Table I. Throughout, the pH was maintained with hydrochloric acid and no inorganic salts were added to maintain constant ionic strength since salts inhibit the surfactant-dependent reactions. The rate constants measured in water are about tenfold greater than those observed by Fife and Jao in 50% dioxane–water at the same temperature.[10] This difference agrees with that found for the same solvent change at 50° by Fife and Brod[11] and for related changes in solvent for hydrolysis of simple acetals.[14] The rate constants are well correlated by the σ constants with a value of ρ of -0.99, nearly the same as that observed in the partially organic solvent.

Hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran in aqueous solution at 30° is subject to general acid cataly-

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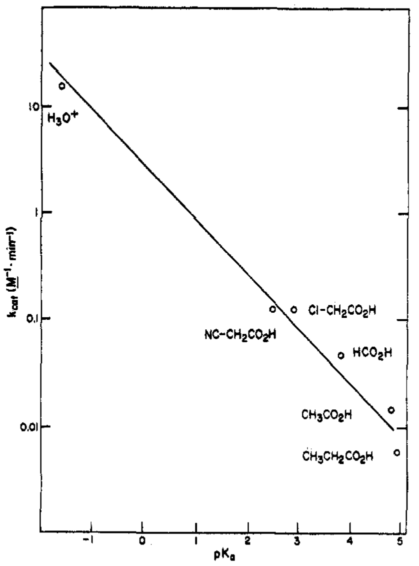

Figure 1.—Catalytic constants of several acids for the hydrolysis of 2-(p-nitrophenoxy)tetrahydropyran in aqueous solution at 30° plotted against the values of pK_a of the acids. The slope of the indicated line is −0.50.

Table I

Kinetics of Hydrolysis of 2-(Para-substituted phenoxy)tetrahydropyrans in the Presence of Aqueous Solutions of Sodium Dodecyl Sulfate at 30°

Substituent	k_0,[a] M^{-1} min^{-1}	k_{max},[b] M^{-1} min^{-1}	k_{max}/k_0	(SDS)$_{max}$,[c] M
p-NO$_2$	15.1	261	17	0.020
p-Cl	45	2100	47	0.015
H	87	2400	32	0.025
p-CH$_3$	138	2900	21	0.015
p-OCH$_3$	159	2400	15	0.020

[a] Second-order rate constant in aqueous solution in the absence of surfactant. [b] Second-order rate constants in the presence of the optimal concentration of sodium dodecyl sulfate. [c] Concentration of sodium dodecyl sulfate at which maximal catalysis is observed.

sis by carboxylic acids. Catalytic constants were evaluated for five such acids over a total buffer concentration range of 0.1-1.0 M. In Figure 1, these catalytic constants, and that for the hydrated proton, are plotted against the appropriate values of pK_a. A satisfactory straight line is obtained, $\alpha = 0.5$, in agreement with the value obtained in 50% dioxane-water.[11] These results establish that the course of hydrolysis of 2-(substituted phenoxy)tetrahydropyrans in water and 50% dioxane-water is similar. The observation of a similar value of ρ and α, for the hydrolysis of the p-nitro derivative, serves to support this point of view.[10,11]

Hydrolysis of each of the substituted acetals is subject to catalysis by dilute aqueous solutions of sodium dodecyl sulfate. In Figure 2, second-order rate constants for these reactions are plotted against the concentration of this surfactant. Although the curves differ in detail, each exhibits the same general features: catalysis up to some optimal concentration followed by inhibition at increasing surfactant concentrations. A similar behavior has previously been observed for catalysis of the hydrolysis of benzaldehyde diethyl acetals and ethyl orthobenzoates by this surfactant.[5-8] Catalysis observed in the present case is not surprising, since the studies of Fife and coworkers have established that these substrates hydrolyze *via* a transition state in which carbonium ion formation occurs.[10,11] Consequently, it would appear that the major part of the catalysis is the result of electrostatic stabilization of the cationic transition state compared to the ground state, the uncharged acetals associated with the micelles and the hydrated proton in the bulk phase. Medium effects and hydrophobic interactions may, of course, contribute to the overall rate of the catalyzed reaction. The maximal rate constant for each substrate and the corresponding concentration of sodium dodecyl sulfate are included in Table I. The maximal rate constants are largely independent of the nature of the polar substituent, except in the case of the p-nitro derivative, which is much less reactive than the others.

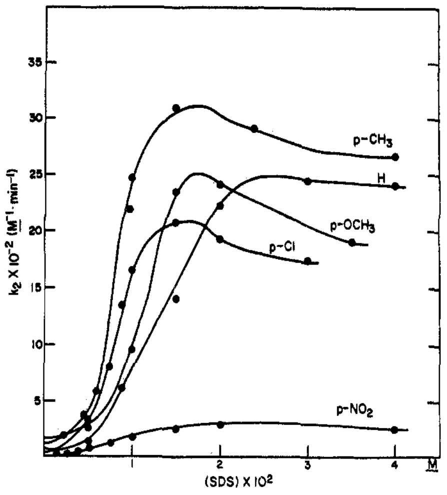

Figure 2.—Second-order rate constants for the hydrolysis of a series of 2-(para-substituted phenoxy)tetrahydropyrans in water at 30° plotted against the concentration of sodium dodecyl sulfate.

Hydrolysis of the 2-(substituted phenoxy)tetrahydropyrans is also subject to catalysis by the anionic surfactant sodium hexadecyloxyethyl sulfate; the pertinent data are collected in Table II. The degree of catalysis observed is about the same as that elicited by sodium dodecyl sulfate except in the case of the p-nitro substrate, which is more sensitive to catalysis by hexadecyloxyethyl sulfate. Note that the latter surfactant is maximally effective at significantly lower concentrations than is sodium dodecyl sulfate.

Table II

Rate Constants for the Hydrolysis of 2-(Para-substituted phenoxy)tetrahydropyrans in the Presence of Aqueous Solutions of Hexadecyloxyethyl Sulfate at 30°

Substituent	k_0,[a] M^{-1} min^{-1}	k_{max},[b] M^{-1} min^{-1}	k_{max}/k_0	(Sur)$_{max}$,[c] M
p-nitro	15.1	562	37	0.005
p-chloro	45	1870	42	0.01
p-methoxy	159	2650	17	0.01

[a] Second-order rate constant in the absence of surfactant. [b] Second-order rate constant at the optimal concentration of surfactant. [c] Surfactant concentration at which optimal catalysis is observed.

Analysis of the data in Tables I and II suggests some regularity in terms of a relation between substrate structure and sensitivity to catalysis. In the case of both sodium dodecyl sulfate and hexadecyloxyethyl sulfate, the extent of catalysis, as judged by the ratio of rate constants in the presence and in the absence of surfactant, increases with increasing electron withdrawal in the polar substituent. This conclusion must be regarded as tentative, since (i) it depends on the use of $k_{\max}/k_0$ values as a measure of sensitivity to catalysis which, although the most reasonable measure, is not the only possible one; and (ii) the correlation for catalysis by hexadecyloxyethyl sulfate is derived from just two points. Moreover, the *p*-nitro substrate does not follow this pattern, being less susceptible to catalysis than would be expected on the basis of the behavior of the other substrates. This may reflect one of two possible causes. First, it has been established that, of the substrates studied here, only that derived from *p*-nitrophenol exhibits a large pH-independent reaction in the absence of surfactant and, moreover, the hydrolysis of only this substrate is markedly subject to general acid catalysis.[10,11] Hence, a mechanistic distinction can be drawn between the hydrolysis of the *p*-nitro substrate and the others: substrate protonation is more important in determining the overall rate of acetal hydrolysis for the *p*-nitro compound than for the other acetals. In light of past studies of acetal and ortho ester hydrolysis,[13,14] this is a reasonable interpretation. Specifically, simple acetals hydrolyze *via* rate-determining carbonium ion formation preceded by rapid and reversible substrate protonation, whereas hydrolysis of the less basic ortho esters occurs with concerted proton transfer and carbonium ion formation in the transition state. Clearly, with less basic acetals, one expects their behavior to eventually change to that of ortho esters. The *p*-nitro substrate is, of course, the least basic one studied here and its behavior does appear to be most nearly like that of an ortho ester. The other possibility for the apparent aberrant behavior of the *p*-nitro compound lies in the disposition of the substrate with respect to the micellar surface. Should this substrate occupy a position distinct from that for the other acetals, one would expect its rate of hydrolysis to be altered. While this explanation is certainly possible, it is difficult to examine experimentally. In any event, let us analyze the results assuming that, for whatever reason, the *p*-nitro compound does behave unusually.

Previous work with both benzaldehyde diethyl acetals and ethyl orthobenzoates has established that substrate sensitivity to catalysis by anionic surfactants increases with increasing electron *donation* of polar substituents.[7,8] This result is apparently the opposite of that observed here. However, all these observations are, in fact, nicely concordant. Recent studies of secondary deuterium isotope effects for acetal hydrolysis reveal that the transition state is reached progressively earlier with increasing electron *donation* from polar substituents for hydrolysis of benzaldehyde acetals and with increasing electron *withdrawal* by polar substituents for hydrolysis of tetrahydropyran acetals.[13] Hence, the important factor in determining susceptibility to electrostatic catalysis appears to be the extent of progress along the reaction coordinate at the time that the transition state is reached. This is reasonable, since increasing progress leads to increasing dispersal of charge and a lessened necessity for electrostatic stabilization.

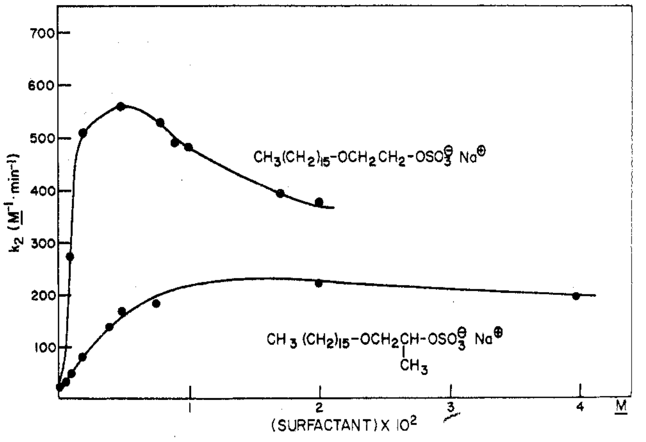

Figure 3.—Second-order rate constants for the hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran in water at 30° plotted against the concentration of the indicated anionic surfactants.

Catalysis of hydrolysis of the tetrahydropyran acetals by anionic surfactants is sensitive to the structure of the surfactant. In Figure 3, second-order rate constants for hydrolysis of 2-(*p*-nitrophenoxy)tetrahydropyran are plotted as a function of the concentration of hexadecyloxyethyl sulfate and 2-hexadecyloxy-1-methylethyl sulfate. Clearly, the minor structural modification has substantially changed the catalytic effectiveness of the surfactant, both in terms of the concentration necessary to elicit optimal catalysis and the maximal rate constant obtained.

A small change in surfactant structure can introduce changes in the surface properties of the micelle which are markedly reflected in the reactivity of adsorbed molecules, in agreement with results of an extensive earlier survey.[7] A comparison between sodium dodecyl sulfate and hexadecyloxyethyl sulfate as catalysts for hydrolysis of the tetrahydropyran acetals reveals that the maximal rate increases achieved are not very different. On the other hand, these maximal changes are attained at much lower concentrations in the case of the latter surfactant compared to the former. This must reflect a difference in equilibrium constant for formation of micelle–substrate complexes in the two cases.

Activation parameters for hydrolysis of the 2-(para-substituted phenoxy)tetrahydropyrans in the presence and absence of anionic surfactants were evaluated from second-order rate constants measured at four temperatures in the range 30–60°. In all cases, the data generated excellent Arrhenius plots. The activation parameters, together with some taken from the work of Fife and Brod,[11] are collected in Table III. The results generate a curious pattern; note, for example, the discordant effects between water and 50% aqueous dioxane for the hydrogen and nitro derivatives. Parts of the observed differences may, of course, be attributed to experimental error. The effects of the anionic surfactants fall into two categories: (i) modest change in enthalpy and entropy of activation making it difficult to judge the source of the surfactant catalysis (methoxy and hydrogen substrates); and (ii) sharply reduced enthalpy of activation coupled with a substantially more negative entropy of activation (chloro and nitro substrates). The latter type of

TABLE III

ACTIVATION PARAMETERS FOR HYDROLYSIS OF 2-(PARA-SUBSTITUTED PHENOXY)TETRAHYDROPYRANS IN THE ABSENCE AND PRESENCE OF ANIONIC SURFACTANTS

Substituent	Solvent	ΔH, kcal/mol	ΔS, eu
Methoxy	Water	12.8	−15.1
	0.02 *M* SDS[a]	11.7	−12.8
Hydrogen	Water	14.3	−11.0
	0.025 *M* SDS[a]	12.1	−11.7
	50% Aqueous dioxane[b]	17.9	−3.0
Chloro	Water	17.3	−2.5
	0.015 *M* SDS[a]	12.1	−12.0
Nitro	Water	17.8	−2.0
	0.02 *M* SDS[a]	13.9	−9.4
	0.005 *M* HDOS[c]	13.4	−9.8
	50% Aqueous dioxane[b]	17.7	−7.6

[a] Sodium dodecyl sulfate, present in the concentration necessary to elicit optimal catalysis. [b] Data from ref 11. [c] Hexadecyloxyethyl sulfate.

TABLE IV

RATE CONSTANTS FOR THE HYDROLYSIS OF A SERIES OF 2-(SUBSTITUTED PHENOXY)TETRAHYDROPYRANS IN THE PRESENCE OF 0.02 *M* SOLUTIONS OF A ZWITTERIONIC AND A NONIONIC SURFACTANT AT 30°

Surfactant	Substituent	k,[a] M^{-1} min^{-1}	k_0/k[b]
Dodecyldimethylammonium propanesulfonate	*p*-NO_2	3.0	5.0
	p-Cl	6.0	7.5
	H	27	3.2
	p-CH_3	37	3.8
	p-OCH_3	49	3.2
Dodecyldimethyl phosphine oxide	*p*-NO_2	2.5	
	H	20	

[a] Second-order rate constant in the presence of 0.02 *M* of the indicated surfactant. [b] Ratio of second-order rate constants for the reaction in the absence and presence of 0.02 *M* surfactant.

result has earlier been observed for benzaldehyde diethyl acetal hydrolysis in the presence of sodium dodecyl sulfate for which a very large favorable enthalpic change is largely compensated by a large unfavorable enthalpic change is largely compensated by a large unfavorable entropic one.[6] It seems likely that even more complex results would be obtained by examining the activation parameters as a function of surfactant concentration.

In contrast with the results observed in the presence of anionic surfactants, both a zwitterionic surfactant and a nonionic surfactant inhibit hydrolysis of the acetals. In Table IV, rate constants for hydrolysis of the series of acetals are collected as a function of the concentration of dimethyldodecylammonium propanesulfonate and dodecyldimethyl phosphine oxide. The two surfactants are approximately equally effective as inhibitors for these reactions.

Zwitterionic surfactants have been little studied in the past, although the one used here has been demonstrated to be an excellent catalyst for the addition of cyanide ion to pyridinium ions.[15] Whatever the source of the rate effects is, they have quite different consequences in the case of these two reactions. There have been several studies of reaction kinetics in the presence of nonionic surfactants. A related study involving hydrolysis of methyl orthobenzoate also revealed, as in the present case, inhibition by nonionic surfactants.[7] These results most likely reflect a medium effect on the hydrolysis rate. Several studies have established that hydrolysis of acetals and ortho esters is retarded in partially organic solvents.[14] However, there have been various examples of catalysis by nonionic surfactants as well. For example, the hydrolysis of certain sulfate esters.[16,17] is subject to substantial catalysis by such surfactants, as are some aromatic nucleophilic addition reactions.[9,18] These results must reflect a complicated pattern of medium effects for the various reactions.

Registry No.—2-(*p*-NO_2 phenoxy)tetrahydropyran, 20443-91-8; 2-(*p*-Cl phenoxy)tetrahydropyran, 20443-90-7; 2-phenoxytetrahydropyran, 4203-50-3; 2-(*p*-CH_3 phenoxy)tetrahydropyran, 13481-09-9; 2-(*p*-OCH_3 phenoxy)tetrahydropyran, 20443-88-3; SDS, 33143-35-0; HDOS, 14858-54-9.

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