BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 42 2894—2898 (1969)

Reaction of *p*-Nitrophenyl Benzenesulfonates with Thiophenoxides

Waichiro TAGAKI, Takehiko KURUSU and Shigeru OAE

Department of Applied Chemistry, Faculty of Engineering, Osaka City University, Sumiyoshi-ku, Osaka

(Received December 29, 1968)

The reaction of *p*-nitrophenyl benzenesulfonates has been investigated in dioxane-water solvent. The overall rate constant, k_A, was separated into two composite rate constants, k_{Ar}, and k_{SO_2}, corresponding to the cleavage of C–O and S–O bonds respectively. The reactivities of hydroxide and thiophenoxide in this reaction were compared. The overall rate constant was found to be several times larger with OH^- than with PhS^-. The reactivity of OH^- was largely due to its higher reactivity toward sulfur, while its reactivity toward carbon atom was comparable to that of PhS^-. Substituent effect of the nucleophile, thiophenoxide and of the substrate shed some light on the mechanism of this reaction.

The nucleophilic substitution reaction of sulfonic acid esters is well known. The attacking site of the ester is either the sulfur atom (S–O bond cleavage) or the phenolic or alcoholic carbon atom (C–O bond cleavage), or both, depending on the type of the ester, nucleophiles and reaction conditions. For the substitution reaction on sulfur, there are two possible mechanisms. One is the S_N2 type synchronous mechanism and the other is the two step mechanism, *i.e.* addition and elimination, using a low energy 3*d*-orbital of sulfur atom. The latter possibility, however, has been ruled out for the alkaline hydrolysis of phenyl benzenesulfonate on the basis of our ^{18}O tracer study,[1] and the former S_N2 type substitution has been found to be the main reaction pathway. The C–O bond cleavage is well known in aliphatic compounds. However, for unsubstituted phenyl benzenesulfonate, such C–O bond cleavage is not important, and becomes significant only with *p*-nitrophenyl benzenesulfonte. In an extreme case, Bunnett[2] has shown that 2,4-dinitrophenyl benzenesulfonate undergoes exclusive C–O bond cleavage when thiophenoxide is used as the nucleophile, while such C–O bond cleavage become less significant, when phenoxide is used as the nucleophile. Meanwhile the nucleophilic substitution reaction of 4-nitrohalobenzene has been investigated rather extensively.[3] The most reasonable mechanism for this reaction seems to be the two step mechanism, *i.e.* addition of a nucleophile to the benzene ring (bond forming) followed by the cleavage of the group (bond breaking) to be substituted. According to Bunnett[4] the bond forming step is the rate limiting for most of the substrates and nucleophiles.

During the course of our studies on the mechanism of the nucleophilic reduction of sulfur atom in sulfate and sulfonate by thiol compounds, we became interested in the reaction of *p*-nitrophenyl benzenesulfonate with thiophenol. We began the present study to investigate the following questions: the reactivities of hydroxide and thiophenoxide anions, the relative rate of the reactions on

---

[1] D. R. Christmann and S. Oae, *Chem. & Ind.*, **1959**, 1251.

[2] J. F. Bunnett and J. Y. Bassett, Jr., *J. Am. Chem. Soc.*, **81**, 2104 (1959).

[3] a) A. J. Parker, "Organic Sulfur Compounds," ed. by N. Kharasch, Vol. I (1961), p. 103. b) T. C. Bruice, S. J. Benkovic, "Bioorganic Mechanism," Vol. I, (1966), p. 45; J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 297 (1951).

[4] J. F. Bunnett, *Quart. Revs.*, **12**, 1 (1958).

sulfur and carbon, and the relative importance of bond forming and bond breaking steps. Another purpose was to compare this reaction with the alkaline hydrolysis of thiolsulfinate and thiolsulfonate as described in the preceding two papers.[5]

Results and Discussion

Products. The major reaction pathways can be formulated as in the Eqs. (1)—(3). The product analysis was carried out for the reaction of *p*-nitrophenyl *p*-toluenesulfonate ($X=CH_3$) with thiophenoxide ($Y=H$).

All the possible products shown in Eqs. (1)—(3) except thiolsulfonate III, were identified (Table 1); the tabulated yields are the total yields.

The relative rate of the initial two reactions, k_{SO_2} and k_{Ar} could be judged from the relative yield of *p*-nitrophenol IV, and *p*-nitrophenyl *p*-tolyl sulfide VI, respectively. Although quantitative sepatation of IV and VI was not attempted, it was possible to estimate the amounts of IV and VI and found to be comparable from the measurement of optical density of the UV absorption of the reaction mixture at around 340 mμ. The rate of the reaction of thiolsulfonate III (Eq. (3)) is presumably greater than that of I in view of the fact that III undergoes rapid alkaline hydrolysis.[6] The relative amounts of sulfonic acid salt V and sulfinic acid salt VII, were not determined. However, their amounts should be the same as those of IV and VI.

TABLE 1. PRODUCT ANALYSIS OF THE REACTION OF *p*-NITROPHENYL *p*-TOLUENESULFONATE AND SODIUM THIOPHENOXIDE (Eqs. (1)—(3))[a]

Product		Yield[b] (%)
p-Nitrophenyl phenyl sulfide	(VI)	70
Diphenyl disulfide	(VIII)	
p-Nitrophenol	(IV)	37
p-Toluenesulfonic acid	(V)	90
p-Toluenesulfonic acid	(VII)	

a) In 80% dioxane-water, 50°C, 12 hr, in sealed tube under nitrogen atmosphere.

b) Based on the ester used.

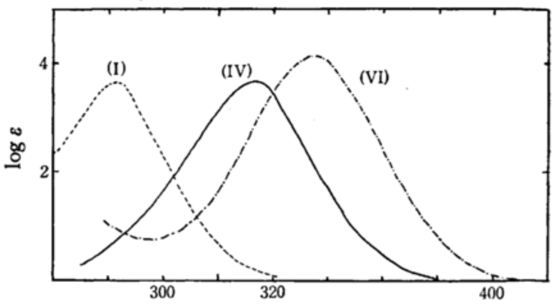
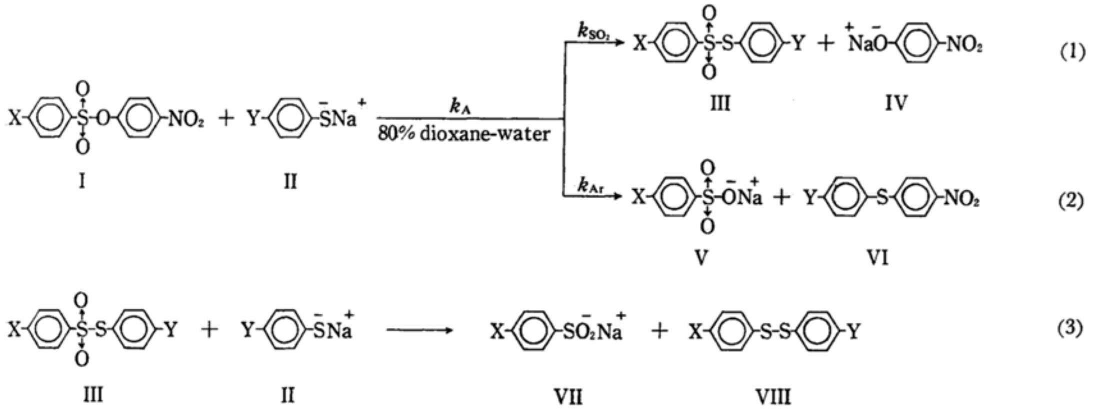


Fig. 1. UV spectra of *p*-nitrophenyl *p*-toluenesulfonate (I); ----, *p*-nitrophenol (IV); ——, and phenyl *p*-nitrophenyl sulfide (VI); —·—, in 0.01 N HCl-ethanol.

Kinetics and Substituent Effects. The UV spectra of the starting ester and the two products, *p*-nitrophenol IV and *p*-nitrophenyl *p*-tolyl sulfide VI, are shown in Fig. 1. Their spectral shapes and the extinction coefficients were nearly the same as for the other substituted compounds.[5] The spectra of the other products, salts V and VII and disulfide VIII, are found in the same spectrum region of the ester, but are different from those of IV and VI. Therefore the rate of the reaction could be followed easily by observing the increase of the optical density near 320 mμ due to the formation of IV and VI (as the total) where the absorption by the ester is negligible. A typical example of the plot of optical density change against the reaction time is shown in Fig. 2. In order to



$k_A=k_{Ar}+k_{SO_2}$ X=Cl, H, CH_3, CH_3O Y=NO_2, Br, H, CH_3, CH_3O

---

[5] See for example: A. Mangini, R. Passerini and S. Serra, *Gazz. Chim. Ital.*, **84**, 47 (1954).

[6] S. Oae, W. Tagaki, R. Nomura and Y. Yohsikawa, This Bulletin, accompanying papers.

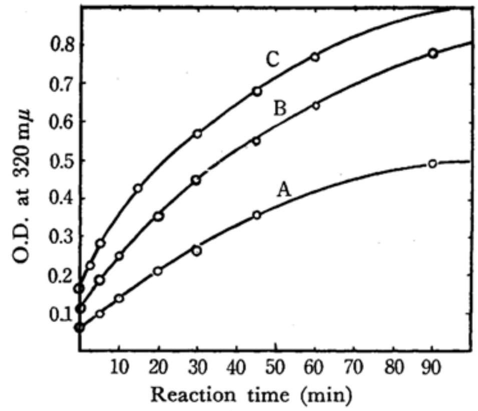


Fig. 2. Plot of optical density *vs.* reaction time, $(RS^-)_0$; 0.01M, $(E)_0$; A, 0.005 M, B, 0.010 M, C, 0.015 M, at 70°C.

avoid complication from the rest of the reactions shown in Eq. (3), only the initial rate was used for the calculation of the rate constant using Eq. (4).

$$\text{Initial rate} = k_A\ (RS^-)_0\ (\text{Ester})_0 \qquad (4)$$

$$k_A = k_{Ar} + k_{SO_2}$$

$(RS^-)_0$ = Initial concentration of thiophenoxide

$(\text{Ester})_0$ = Initial concentration of the ester

Details of the kinetic procedures and the modification of Eq. (4) for the actual calculation are described in the experimental part. In Eq. (4), one needs to know the initial concentration of thiophenoxide anion, $(RS^-)_0$, which is not necessarily the same as that of added salt, sodium thiophenoxide II. In order to calculate the concentration of thiophenoxide ion, the apparent pK_a of unsubstituted thiophenol was determined spectrophotometrically as a function of solvent composition in dioxane-water mixture. The pK_a of thiophenol thus obtained increased substantially as the dioxane content increased: water, 6.65 : 40% dioxane-water (v/v), 7.78; 60% dioxane-water, 8.70. From these values, one can obtain the concentration of the anion when one knows the pH of the reaction mixture. It is also possible to observe the change of the ratio of $(PhS^-)/(PhSH)$ as a function of the concentration of added salt (PhS^-Na^+). These two methods indicate that the added salt exists essentially as dissociated anion even in 80% dioxane-water, provided that the concentration of the added salt is kept around 0.005—0.015 M.

The effect of the composition of dioxane-water mixture on the rate has been examined as shown in Table 2. Although the rate increased as the solvent polarity increased, the effect was rather small. Therefore, the rates were determined for comparison in 80% dioxane-water, in which organic substrates can be readily dissolved.

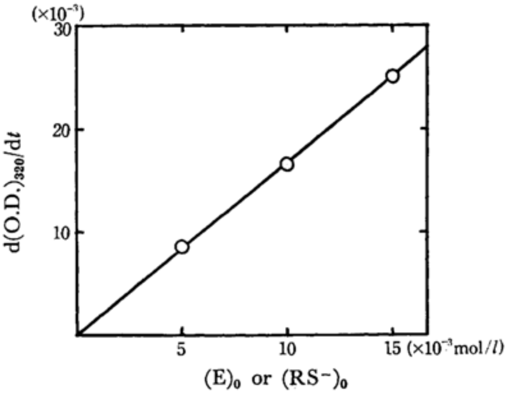


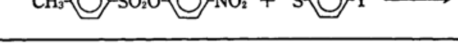
Fig. 3. Plot of initial slope of optical density change against the intial concentration of ester or thiophenoxide in 80% dioxane-water at 70°C.

TABLE 2. EFFECTS OF SOLVENT COMPOSITION OF DIOXANE-WATER MIXTURE ON THE RATE OF THE REACTION OF *p*-NITROPHENYL *p*-TOLUENESULFONATE WITH THIOPHENOXIDE AT 60°C

Dioxane vol. %	$k_A \times 10^3$ *l*/mol sec
50	9.83
60	7.53
70	6.66
80	5.50

The rate constants thus obtained are the overall rate constants including both that of the C–O bond cleavage, k_{Ar}, and that of the S–O bond cleavage, k_{SO_2}. The separation of the two rates was next attempted. The value of k_{Ar} was calculated using the change of optical density at 360 mμ where the absorption by the ester is negligible and that by IV is small compared to that by VI. The rate constant, k_{SO_2}, was then computed by substracting k_{Ar} from the overall rate constant, k_A. Although the reproducibility of k_A was quite satisfactory, high accuracy of the subsequent separation may not be expected, since the absorption at 360 mμ is not

TABLE 3. THE REACTION OF *p*-NITROPHENYL *p*-TOLUENESULFONATE WITH *p*-SUBSTITUTED THIOPHENOXIDE IN 80% DIOXANE-WATER AT 50°C



Y	$\times 10^3$ *l*/mol sec k_A	 k_{Ar}	 k_{SO_2}	k_{SO_2}/k_{Ar}
CH_3O	10.0	7.05	2.95	0.42
CH_3	4.5	3.12	1.38	0.44
H[a]	3.5	1.28	2.20	1.72
Br	2.5	0.58	1.92	3.32

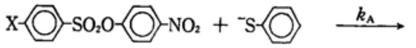
a) $k_A = 1.12 \times 10^{-3}$ *l*/mol sec^{-1} (40°C), 5.5×10^{-3} *l*/mol sec^{-1} (60°C).
$E_a = 16$ kcal/mol $\Delta S^{\neq} = -20$ e.u. (50°C).

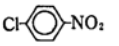
at λ_{max} but at a declinging slope. In spite of this limitation, the results were quite reproducible.

The rate constants observed for the reaction of *p*-nitrophenyl *p*-toluenesulfonate with four different thiophenoxides are shown in Table 3. The rate constants for the reaction of *p*-nitrophenyl *p*-substituted-benzenesulfonate with thiophenoxide are shown in Table 4. The correlation of these rate constants with Hammett σ constants are shown in Figs. 4 and 5.

Table 3 and Fig. 4 indicate that an electron donating substituent at the *p*-position of nucleophile increased the overall rate (k_A), giving Hammett ρ value$=-0.63$. The separation of k_A into k_{Ar} and k_{SO_2} revealed that the overall rate change is caused mainly by the change of k_{Ar} ($\rho=-2.11$). That is, the C–O bond cleavage is more susceptible to the change of nucleophile than the S–O bond cleavage, and the C–O bond cleavage appears to increase with increasing nucleophilicity of the nucleophile. The results in Table 4 and Fig. 5 indicate that the effect of substituent X is larger for the S–O bond cleavage than for the C–O bond cleavage.

TABLE 4. THE REACTION OF *p*-NITROPHENYL *p*-SUBSTITUTED-BENZENSULFONATE WITH THIOPHENOXIDE IN 80% DIOXANE-WATER AT 50°C



X	× 10³ *l*/mol sec			k_{SO_2}/k_{Ar}
	k_A	k_{Ar}	k_{SO_2}	
CH_3	3.50	1.28	2.20	1.72
H	5.47	2.50	2.97	1.19
Cl	10.4	2.73	7.68	2.28
	—	2.43	—	

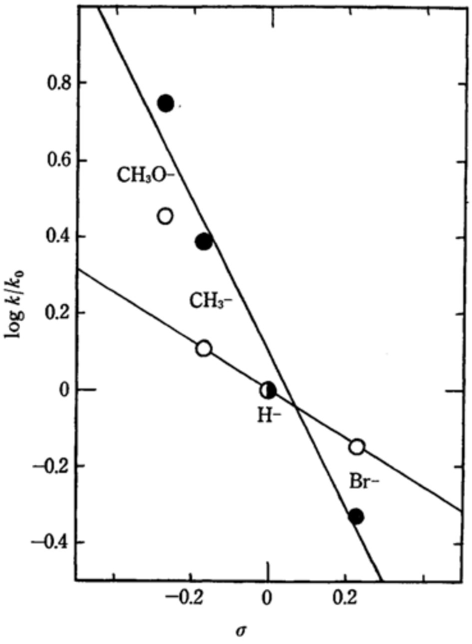


Fig. 4. Hammett plot for the reaction of *p*-substituted thiophenoxides with *p*-nitrophenyl *p*-toluenesulfonate in 80% dioxane-water at 50°C.
○ $\rho=-0.63$ (k_A, the overall rate)
● $\rho=-2.11$ (k_{Ar}, C–O bond cleavage)

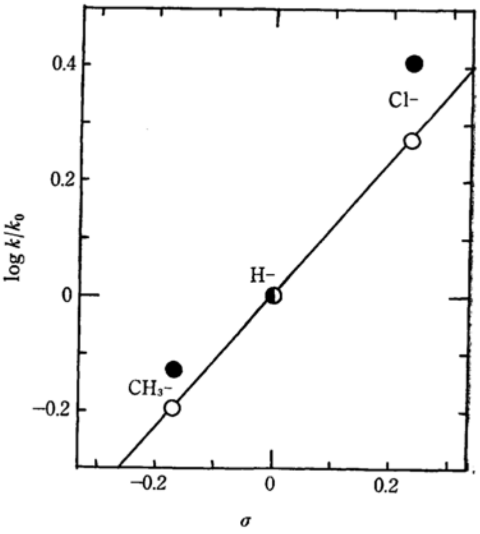


Fig. 5. Hammett plot for the reaction of *p*-nitrophenyl *p*-substituted-benzenesulfonates with thiophenoxide in 80% dioxane-water at 50°C.
○ $\rho=1.18$ (k_A, the overall rate)
● $\rho=1.38$ (k_{SO_2}, S–O bond cleavage)

In nucleophilic substitution reactions of *p*-substituted nitrobenzene derivatives, one of the criteria for the rate limiting step is the effect of the leaving group.[3,4] The rate limiting step would be the bond formation (the addition of nucleophile to the benzene ring), if the reaction is insensitive to the leaving group. According to this criteria, the rate limiting step of this reaction would be also the addition of thiophenoxide anion to the benzene ring in line with the results in Table 4. The bond forming step also seems to be more important in the nucleophilic reaction on the sulfur atom, as the k_{SO_2} increases with an increasing electron withdrawing group (Table 4), although the effect of the nucleophile (Table 3) is not in line with this argument. The reaction of *p*-chloronitrobenzene was also carried out under the same condition. The results (Table 4) indicate that the abilities of chloride and sulfonate anion are comparable with those of the leaving group, suggesting also the indifference of this reaction to the nature of the leaving group.

In Table 5, the rates of the alkaline hydrolysis and the reaction with thiophenoxide are compared. The overall rate of the alkaline hydrolysis is about

3—4 times higher than that of the reaction with thiophenoxide ($X=CH_3$). The separation of the overall rate (from ^{18}O data) then revealed that in alkaline hydrolysis the rate is largely due to the cleavage of the S–O bond, while in the reaction of thiophenoxide the rates of both the C–O and the S–O bond cleavage are of a comparable magnitude.

TABLE 5. REACTION OF HYDROXIDE AND THIOPHENOXIDE TOWARD *p*-NITROPHENYL *p*-TOLUENESULFONATE ($X=CH_3$) AND *p*-NITROPHENYL BENZENESULFONATE ($X=H$), 50°C, 80% DIOXANE-WATER

X	Nucleophile	$\times 10^3$ *l*/mol sec			Ref.
		k_A	k_{Ar}	k_{SO_2}	
CH_3	OH^-	11.5			c)
	PhS^-	3.5	1.28	2.20	c)
H	OH^-	78.6a)	16b)	63b)	8)
	PhS^-	5.47	2.5	2.97	c)

a) 49.5°C; b) Based on the ^{18}O tracer data, 20% C–O bond cleavage in 1% KOH solution;[8] c) Present work.

Experimental

Material. Substituted *p*-nitrophenyl benzenesulfonate was prepared by the reaction of *p*-nitrophenol with substituted benzenesulfonyl chloride in pyridine. The produced esters were recrystallized from ethanol: $p\text{-}XC_6H_4SO_2OC_6H_4NO_2\text{-}p$; X=H, mp 87°C (lit, 88—89°C) $p\text{-}CH_3$, mp 95—96°C (lit, 97°C); *p*-Cl, mp 112—113°C (lit, 110°C). Dioxane was purified just before use by treating with hydrochloric acid and metallic sodium under N_2 gas.[7]

***p*-Substituted Sodium Thiophenoxide.** Thiophenol was dissolved in benzene and to this was added a slightly less amount of sodium hydroxide than that required in order to avoid inclusion of any excess sodium hydroxide in the product. The mixture was refluxed for 3 hr under stirring. The water formed was distilled off with benzene and the resulting white powder was collected by filtration and washed with benzene and dried.

Product Analysis. Reaction of *p*-Toluenesulfonate with Sodium Thiophenoxide in 80% Dioxane-Water. *p*-Nitrophenyl *p*-toluenesulfonate (0.2 g) and thiophenoxide (0.2 g) were dissolved in 80% dioxane-water (10 m*l*) in an ampoule. The ampoule was sealed under N_2 atmosphere and then kept at 50°C for 12 hr. The reaction mixture was made slightly acidic and extracted with ether. Treatment of the ether layer gave 0.21 g of the mixture of *p*-nitrophenol, phenyl *p*-nitrophenyl sulfide and diphenyl disulfide. The water layer gave a mixture of sodium *p*-toluenesulfonate and *p*-toluenesulfinate (0.18 g). The yield of *p*-nitrophenol could also be measured spectrophotometrically in an alkaline solution.

Kinetic Experiment. Solution of both *p*-nitrophenyl benzenesulfonate (0.01—0.02 M), 10 m*l*, and thiophenoxide (0.01—0.02 M) in dioxane-water were kept separately in a constant temperature bath for over 10 min. Then 10 m*l* of thiophenoxide solution was added to the ester solution, and 1 m*l* aliquots of this reaction mixture were pipetted out at suitable time intervals and quenched with 0.01 N HCl - ethanol solution in 50 m*l* volumetric flask to give an assay solution. Thus the concentration of this assay solution was 1/50 of that of the reaction mixture.

Since the reactions were not simple (Eqs. (1)—(3)), only the UV absorption due to the formation of both *p*-nitrophenol (IV) and phenyl *p*-nitrophenyl sulfide (VI) was followed. Figure 1 indicates that both IV and VI give the same molar extinction coefficient at 320 mμ in acidic solution. Therefore the initial change of the optical density of the above assay solution at 320 mμ should be proportional to the change of the total concentration of IV and VI which should then be proportional to the initial concentrations of the ester and thiophenoxide as formulated in

$$\frac{d(\text{O.D. at } 320\,\text{m}\mu)}{dt}=\frac{\varepsilon_0}{\alpha}\frac{d((\text{IV})+(\text{VI}))}{dt} \tag{5}$$

$$\frac{d((\text{IV})+(\text{VI}))}{dt}=\frac{\alpha}{\varepsilon_0}\frac{d(\text{O.D.})}{dt}=k_A\,(\text{RS}^-)_0(\text{E})_0 \tag{6}$$

where $(E)_0$=initial concentration of the ester, $(RS^-)_0$= initial concentration of the thiophenoxide, ε_0=molar extinction coefficient at 320 mμ, α=dilution factor of the reaction mixture for recording of optical density, and k_A=the overall second order rate constant.

A typical example of the plot of optical density change against reaction time is shown in Fig. 2. A plot of the initial slope of optical density change as a function of the initial concentration of ester gives a straight line as shown in Fig. 3, from which one can obtain k_A.

The above k_A is the overall rate constant including both of the C–O and S–O bond cleavages. Their separation was then attempted by recording the absorbance change at 360 mμ which corresponded to the formation of V.

The applicability of the absorption above 320 and 360 mμ for these kinetics was checked for several known mixtures of IV and V at the same total concentrations, and it was confirmed that Beer's law holds and the accuracy is satisfactory. The error involved in the graphical reading of the slope (Fig. 2) sometimes amounted to ±5%. However, the rate constants (k_{obs}) shown in Fig. 3 were surprisingly reproducible; the deviation was generally within ±3%.

The alkaline hydrolysis was also carried out by the same method. The results are shown in Tables 3, 4 and 5.

pK_a of Thiophenol in Dioxane-Water of Different Composition. Undissociated thiophenol has an absorption maximum at around 240 mμ (ε=7425) and the dissociated anion at around 270 mμ (ε=14500). Based on these absorptions the pK_a value of thiophenol was determined spectrophotometrically using phosphate buffer in three different dioxane-water mixtures at 25°C: water, 6.65; 40% dioxane-water (v/v), 7.78; 60% dioxane-water, 8.70.

---

7) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co. (1957).

8) S. Oae and R. Kiritani, This Bulletin, **38**, 765 (1965).