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Alkaline Hydrolysis of Aryl Benzenethiolsulfonates

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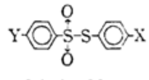
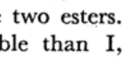
The alkaline hydrolysis of substituted phenyl benzenethiolsulfonates has been investigated. The rate was found to be first order with respect to both hydroxide and ester. The second order rate constant for the unsubstituted ester was found to be $3.2\times10^{3}\ \text{M}^{-1}\ \text{sec}^{-1}$ (water 45°C). The Hammett ρ values were found to be $\rho_{X,Y=H}=2.1$ and $\rho_{Y,X=H}=1.1$ for

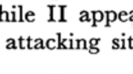


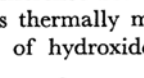
respectively. The reactivities of three esters, *i. e.* phenyl benzenethiolsulfonate, -thiolsulfonate and -sulfonate were compared.

The bond forming and breaking of sulfur-sulfur linkage are very important in biochemistry as well as in organic syntheses. However, the substitution reactions on S^{II}, S^{III}, S^{IV} are relatively unexplored.[1]

In a previous paper, we have shown that the alkaline hydrolysis of substituted phenyl benzenethiolsulfinate (I) is very rapid and proceeds mainly by the attack of hydroxide ion on the sulfinyl sulfur to give sulfinic acid and disulfide.[2] A compound closely related to I is phenyl benzenethiolsulfonate (II) which is known also to give sulfinic acid and disulfide in alkaline hydrolysis.[3] However, there is an important difference between the two esters. While II appears thermally more stable than I, the attacking site of hydroxide is considered to be the sulfenyl sulfur atom in the case of II, unlike the case of I[3] although detailed features of these chemistries are yet to be clarified.


I

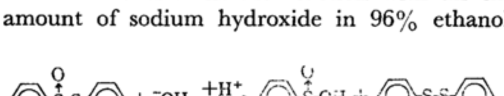

II


III

The present investigation has been undertaken to disclose the nature of the alkaline hydrolysis of the substituted derivatives of II, by means of the kinetic determination of the rates and a comparison with those of I and the related compound III.

Results and Discussion

Product. Phenyl benzenethiolsulfonate (II) was found to give 1.7 mol of benzenesulfinic acid and a small amount of diphenyl disulfide from one mole of the ester in the reaction with an excess amount of sodium hydroxide in 96% ethanol.



(1)

Attempts to confirm the possible formation of the corresponding sulfonic acid have failed as was the case with other workers.[3] The formation of more than equimolar amount of the sulfinic acid from the ester used may be rationalized if one assumes the following consecutive reactions.

$$PhSO_2SPh + OH^- \xrightarrow{-H^+} PhSO_2^- + PhSO^- \quad (2)$$

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[1] J. L. Kice, *Accounts of Chemical Research*, **1**, 58 (1968).

[2] S. Oae, Y. Yoshikawa and W. Tagaki, This Bulletin, **42**, 2899, (1969).

[3] R. Otto and A. Rossing, *Ber.*, **19**, 1235 (1886).

$$2PhSO^- \xrightarrow{+2H^+} PhS(O)SPh + H_2O \quad (3)$$

$$PhS(O)SPh + OH^- \xrightarrow{-H^+} PhSO_2^- + PhS^- \quad (4)$$

$$PhSO_2SPh + PhS^- \longrightarrow PhSO_2^- + PhSSPh \quad (5)$$

Kinetics. From product analysis, the attacking site of hydroxide ion is most likely the sulfenyl sulfur atom. (Eq. (2)). However, there still remains a question as to sulfenic acid. The rates of the alkaline hydrolyses of all the compounds examined were also found to be very rapid. Therefore the kinetic measurements were carried out in a pH-controlled buffer solution. The buffer used was *N*-ethylmorpholine *N*-ethylmorpholine sulfate which did not react with the ester under the same reaction condition and did not precipitate in 60% ethanol-water solution.

The kinetic rates were followed by observing the amounts of disappearance of the starting ester (see experimental). Since the reaction was expected to be complicated as illustrated in Eqs. (2)—(5), only the initial rate was used for the calculation of the rate constants based on

$$\frac{-d(\text{Ester})}{dt} = k_{obs}(E)_0 = [k_0 + k_{OH^-}(OH)_0](E)_0 \quad (6)$$

where k_0 and k_{OH^-} are the rate constants for both spontaneous and alkaline hydrolyses respectively, and $(OH^-)_0$ and $(E)_0$ are the initial concentrations of hydroxide and the ester, respectively.

The first order dependence of the rate on the initial concentration of II and on pH was observed to be similar to that in the hydrolysis of the corresponding sulfinate.[2] In order to obtain an extrapolated value of the rate in water, k_{obs} was plotted against ethanol concentration in the solvent under the same buffer ratio to give a straight line, as shown in Fig. 1.

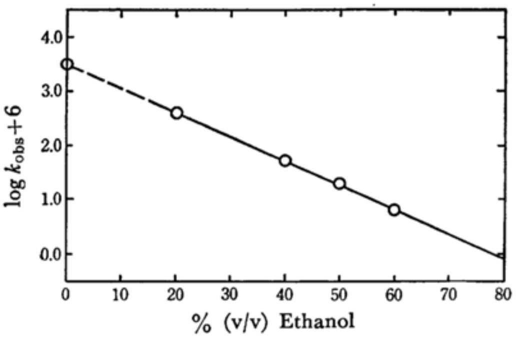


Fig. 1. Plot of pseudo first-order rate constants k_{obs} *vs.* percent of ethanol in the solvent; ester, $PhSO_2SPh$; $(E)_0=3.60\times10^{-3}$; 45°C; pH=7.5 in 60% ethanol-water.

From Fig. 1 the second order rate constant of the alkaline hydrolysis of II in water was calculated to be 3.2×10^3 *l*/mol sec at 45°C. Meanwhile the Arrhenius plot gave E_a and ΔS^* values to be 10 kcal/mol and −13 e.u. (at 45°C), respectively, in 60% ethanol-water. The error involved in the rate constant was within, +5% *i. e.*, the same order of magnitude as in the previous paper.

Substituent Effect. Introduction of an electron-withdrawing substituent at *p*-position of either one of the two benzene rings of the ester accelerated the rate while that of an electron-releasing substituent retarded. The results are shown in Table 1 and their Hammett plot is shown in Fig. 2. From Fig. 2 Hammett ρ values were calculated to be $\rho_X=2.1$ and $\rho_Y=1.1$.

Although the results so far described are not sufficient to allow any detailed discussion on the mechanism of the overall hydrolysis reaction, it is interesting to compare the initial rate of the hydrolysis of the following three closely related esters which are summarized in Table 2.

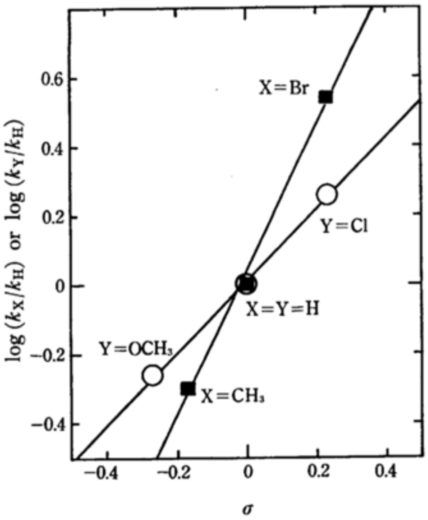
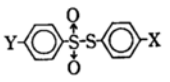


Fig. 2. Hammett plot; plot of $\log(k_X/k_H)$ or $\log(k_Y/k_H)$ for hydrolysis of *p*-substituted phenylbenzenethiolsulfonates in 60% ethanol-water at pH 7.5 and 45°C *vs.* σ.
■ $\rho_X=2.1$, ○ $\rho_Y=1.1$

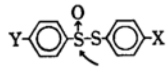
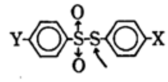
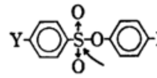
TABLE 1. ALKALINE HYDROLYSIS OF SUBSTITUTED PHENYL BENZENETHIOLSULFONATES



X	Y	10^5 k_{obs} (45°C)
CH_3	H	1.0
H	H	2.1
Br	H	7.3
NO_2	H	1.3*
H	CH_3	1.2
H	Cl	3.8

* pH=6.9
60% (v/v) Ethanol-water, pH=7.5

Table 2. The data for the alkaline hydrolysis of phenyl benzenethiolsulfinate (I), thiolsulfonate (II) and sulfonate (III)

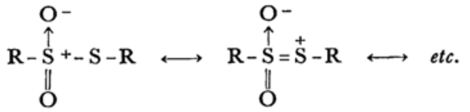
Compound$^{a)}$	k_{OH^-} rel. (50°)$^{b)}$	ρ		E_a kcal/mol$^{b)}$	$\Delta S^{\ddagger}$, e. u.$^{b)}$	Ref.
		Y	X			
 (I)	10^6 $^{c)}$	1.6	2.4	13	−3 (30°C)	2
 (II)	10^5 $^{c)}$	1.1	2.1	10	−13 (45°C)	e
 (III)	1$^{d)}$	2.4	3.0	18	−21 (50°C)	4

a) Arrow indicates the attacking site of hydroxide
b) for X=Y=H
c) In 60% (v/v) ethanol-water
d) In 70% (v/v) dioxane-water
e) This work

In order to correlate the rates and the substituent effects, it is necessary to know the attacking site of hydroxide ion for each of the esters. In the case of sulfonate (III), the attacking site is known to be exclusively the sulfonyl sulfur atom from the ^{18}O tracer study, except for the ester bearing $X=NO_2$ which undergoes significant C–O bond cleavage (about 20%) by the attack of hydroxide ion on the benzenoid carbon of phenolic part.[5]

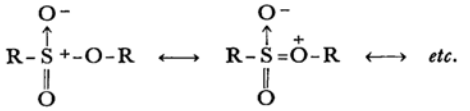
For the other two esters, I and II, the assignment of the attacking site is by no means clear, since in both cases the reactions appear to be so complicated that the product analysis alone cannot give a conclusive answer. However, the assignement is possible if one limits the discussion to only the very initial stage of the reactions. Since no sulfonic acid was detected in the hydrolysis of II, the rate of its initial reaction must be that of the initial attack of hydroxide on the sulfenyl sulfur, whereas in the case of I, the reaction is either an exclusive attack on the sulfinyl sulfur or a competitive attack on both the sulfinyl and the sulfenyl sulfur. Since the hydrolysis products of I are benzenesulfinic acid and diphenyl disulfide, the attack on the sulfenyl sulfur to give the sulfenic acid must be followed by other succeeding reactions. The probable reaction of the sulfenic acid in neutral or acidic media is self-condensation to regenerate the starting ester, I (Eq. (3)). Therefore, the rate of the hydrolysis of I becomes the same as that of the initial attack of hydroxide ion on the sulfinyl sulfur. The ρ_X values are identical for all the three esters in spite of the wide range of their reactivities, while the ρ_Y values vary somewhat more widely. The fact that both ρ_X and ρ_Y are almost the same for sulfonates (III) appears to be in line with the one step S_N2 mechanism which has been suggested from our previous ^{18}O tracer study.[6] The same mechanism might also be applied in the hydrolysis of I and II although the ρ_Y is smaller than ρ_X. A smaller ρ_Y for II could be due to the difference in the attacking site, and the effect of ρ_Y may be weakened by the presence of sulfonyl group inserted between the reaction centers.

The most important finding is an enormous rate difference between the sulfonate and the other two sulfur analogs. Both the heat and entropy of activation seem to be responsible for this rate difference. Unfortunately the data for substituted phenyl benzenesulfinates are not yet available for a comparison with those of thiolsulfinate (I). Both thiolsulfonate (II) and sulfonate (III) are presumed to be stabilized by the following type of resonance that involves an extra π-bond formation with the central sulfur atoms.



$$R-\underset{\overset{\|}{O}}{\overset{\overset{O^-}{\uparrow}}{S}}{}^{+}-S-R \longleftrightarrow R-\underset{\overset{\|}{O}}{\overset{\overset{O^-}{\uparrow}}{S}}=\overset{+}{S}-R \longleftrightarrow etc.$$

II



$$R-\underset{\overset{\|}{O}}{\overset{\overset{O^-}{\uparrow}}{S}}{}^{+}-O-R \longleftrightarrow R-\underset{\overset{\|}{O}}{\overset{\overset{O^-}{\uparrow}}{S}}=\overset{+}{O}-R \longleftrightarrow etc.$$

III

Generally, however, the electron donating conjugation of sulfur is smaller than that of oxygen.[7]

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[4] a) R. V. Vizgert, *Zhur Obshch. Khim.*, **28**, 1873 (1958). b) R. V. Vizgert and E. K. Savchuk, *ibid.*, **26**, 2268 (1956).

[5] S. Oae, T. Fukumoto and R. Kiritani, This Bulletin, **36**, 346 (1963).

[6] D. R. Christman and S. Oae, *Chem. & Ind.*, **1959**, 1251.

[7] C. C. Price and S. Oae, "Sulfur Bonding," Donald Press, New York (1962).

Therefore the S–O bond in III would be stronger than the S–S bond in II, thus resulting in a large rate difference of the rates of the hydrolyses. Sulfonamides are also known to be very stable toward alkali. The higher stability of sulfonamide linkage is also due mainly to the stronger electron donating ability of nitrogen than oxygen and sulfur. In addition to the difference of the bond strengths, the approach of hydroxide anion to the attacking site should be much easier in I and II than in III because of the smaller electrostatic repulsion between sulfonyl oxygen and the hydroxide anion (in II), and also because of the electron accepting ability of the sulfur atom using one of its vacant 3*d*-orbitals.

Experimental

Materal. Substituted phenyl benzenethiolsulfonates were prepared by the reaction of benzenesulfenyl chloride with sulfinic acid in dry ether.[8] The products were recrystallized from methanol or ethanol:
p-$XC_6H_4SSO_2C_6H_5$; X=H, mp 44—45°C (lit[9] 44—45°C); CH_3, 54°C (52—54°C); Br, 85°C; NO_2, 103—105°C (104—105°C).
p-$YC_6H_4SO_2SC_6H_5$: Y=CH_3, 78°C (77—78°C): Cl, 82—82.5°C (81°C), OCH_3, 54°C (54—55°C).

N-Ethylmorpholine buffer and the solvent ethanol were described in the preceding paper.[2]

Product. Unsubstituted ester (2.5 g, 0.01 mol) and potassium hydroxide (1.2 g, 0.2 mol) were dissolved in 50 m*l* of 96% ethanol-water solvent and the mixture was refluxed for 5 hr. Ethanol was removed from the reaction mixture and the residue was dissolved in ether and extracted with water. A part of the water extract was used for the detection of sulfonic acid by converting it to the thiuronium salt.

But no thiuronium salt was formed. The water extract was also titrated with 0.2 N sodium nitrite and the formation of 0.017 mol of sulfinic acid was observed. From the ether layer was isolated 300 mg of diphenyl disulfide which accounted for 14% of the total sulfur, while 0.017 mol of sulfinic acid accounted for 85% of the total sulfur in the starting ester. Thiophenol was not detected in any significant amount either in water or the ether layer. These results clearly indicated that the reaction leads to the quantitative formation of sulfinic acid and disulfide, and the formation of the sulfonic acid was negligible if none at all.

Kinetics. A solution of the thiolsulfonate (3×10^{-3} M) in 30 m*l* of 60% ethanol-water (v/v) and 30 m*l* of the *N*-ethylmorpholine buffer, in 60% ethanol-water were mixed after temperature equilibration in a constant temperature bath. Aliquot (5 m*l*) of this reaction mixture was added to a separating funnel containing 20 m*l* of chloroform and 25 m*l* of acidic water. The chloroform layer was washed and the upper water layer was removed by suction. Two more washings with 25 m*l* each of water were repeated. The optical density of this chloroform solution of the UV absorptions at 270 mμ was recorded and plotted against reaction time. The initial rate was then obtained graphically. The other methods for the treatment of the kinetic data were essentially the same as described in the preceding paper.[2]

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[8] a) F. Klivenyi, *Magyan Kem. Folyoivat*, **64**, 121 (1958); *Chem. Abstr.*, **54**, 16416 (1960). b) G. Kresze and W. Kort, *Chem. Ber.*, **94**, 2624 (1961).