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The Alkaline Hydrolyses of·Chlorophenyl Phenyl Sulfoxides and Sulfones[1]

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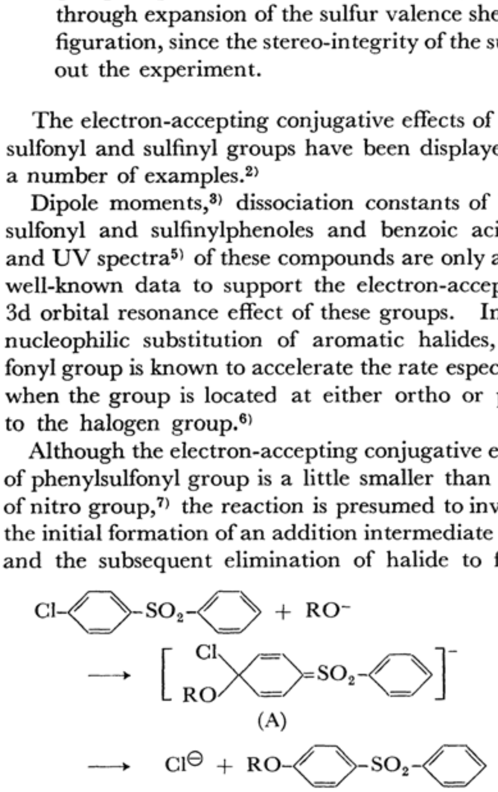
Both phenylsulfonyl and phenylsulfinyl group have been shown to activate the nucleophilic substitution of aromatic chloride from ortho- and para-positions, however, the effect of phenylsulfonyl group was substantially larger than that of phenylsulfinyl group. The activation by these sulfur groups is presumably due to the conjugative stabilization by the phenylsulfonyl or -sulfinyl groups through expansion of the sulfur valence shell. The addition complex is presumed to retain its configuration, since the stereo-integrity of the sulfoxide group has been shown to be maintained throughout the experiment.

The electron-accepting conjugative effects of both sulfonyl and sulfinyl groups have been displayed in a number of examples.[2]

Dipole moments,[3] dissociation constants of both sulfonyl and sulfinylphenoles and benzoic acids,[4] and UV spectra[5] of these compounds are only a few well-known data to support the electron-accepting 3d orbital resonance effect of these groups. In the nucleophilic substitution of aromatic halides, sulfonyl group is known to accelerate the rate especially when the group is located at either ortho or para to the halogen group.[6]

Although the electron-accepting conjugative effect of phenylsulfonyl group is a little smaller than that of nitro group,[7] the reaction is presumed to involve the initial formation of an addition intermediate (A), and the subsequent elimination of halide to form the final product, like in the case of *o*- and *p*-nitrohalobenzene in which an addition intermediate can be actually detected.[8]



In view of the formation of the *m*-methylsulfonylaniline in the treatment of *o*-methylsulfonylbromobenzene with soda amide,[9] halophenylsulfone in a strong alkaline condition could lead to the prior formation of " sulfonylbenzyne " intermediate. However, we have found that when *o*-,[10] *m*-, and *p*-chlorophenyl phenyl sulfones were treated with potassium hydroxide in aqueous dimethyl sulfoxide, *o*-, *m*-, and *p*-hydroxyphenyl phenyl sulfones were the only isolable products respectively. Therefore, the reactions appear to proceed through a clean-cut aromatic S_N2 process.

The acidity constants of *p*-methylsulfinyl- and *m*-methylsulfonyl-phenols[4c] reveals that the sulfinyl group can display a relatively strong electron-accepting 3d orbital resonance effect, only a little smaller than that of the sulfonyl group. Therefore, in the nucleophilic substitution of aromatic halides, the sulfinyl group when substituted either at ortho- or para-position is also considered to accelerate the rate.

Unfortunately there is no reliable and quantitative data to support it, though there is a report indicating that *p*-iodophenyl phenyl sulfoxide was affected by the treatment of caustic alkali where the meta isomer was not.[11]

Here, too, there is a possibility that the replacement proceeds through " benzyne " intermediate. When, however, *o*- and *p*-chlorophenyl phenyl sulfoxide

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[1] Phenols and phenolic esters XV; paper XIX on Sulfoxides.

[2] C. C. Price and S. Oae, " Sulfur Bonding," Ronald Press N.Y., (1962), Chapters 3 and 4.

[3] C. W. N. Cumpa, G. H. Jefferey and S. Walker, *Trans. Faraday Soc.*, **52**, 193 (1956).

[4] a) F. G. Bordwell and G. D. Cooper, *J. Am. Chem. Soc.*, **74**, 1058 (1952); b) C. C. Price and J. J. Hydock, *ibid.*, **74**, 1943 (1952); c) F. G. Bordwell and P. J. Boutan, *ibid.*, **79**, 717 (1957).

[5] a) E. A. Fehnel and M. Carmack, *ibid.*, **71**, 231 (1949); b) H.P. Koch, *J. Chem. Soc.*, **1949**, 408 ; c) S. Oae and C. Zalut, *J. Am. Chem. Soc.*, **82**, 5359 (1960); d) S. Oae, M. Yoshihara and W. Tagaki, This Bulletin, **40**, 951 (1967).

[6] H. R. Todd and R. L. Shriner, *J. Am. Chem. Soc.*, **56**, 1382 (1934).

[7] a) R. L. Heppolette and J. Miller, *Chem.* & *Ind.*, **1954**, 1457; b) R. L. Heppolette and J. Miller, *J. Chem. Soc.*, **1956**, 2329.

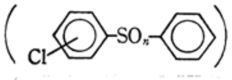
[8] a) J. F. Bunnett and R. J. Marath, *J. Am. Chem. Soc.*, **77**, 5051 (1955); b) W. Greizerstein and J. A. Brieux, *ibid.*, **84**, 1032 (1962); c) R. R. Bishop, E. A. S. Canell and N. B. Chapman, *J. Chem. Soc.*, **1952**, 437.

[9] G. A. Martin, Jr., *Iowa State Coll.*, *J. Sci.*, **21**, 38 (1946); *Chem. Abstr.*, **41**, 952 (1947).

[10] N. Furukawa and S. Oae, This Bulletin, to be published.

[11] D. L. Hamide and R. B. Williams, *J. Chem. Soc.*, **1938**, 211.

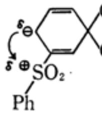
Table 1. The rates of hydrolyses of chlorophenyl phenyl sulfones and sulfoxides in aqueous dimethyl sulfoxide[a)] at 158±0.1°C

Compound 		k_2 ($l\cdot mol^{-1}\cdot sec^{-1}$)	Relative rates (Total)	Relative rates within the isomers
SO_n	Cl			
SO	*m*-Cl	$(4.18\pm0.140)\times10^{-7}$	1	1
SO	*p*-Cl	$(3.34\pm0.08)\times10^{-5}$	81	81
SO	*o*-Cl	$(1.93\pm0.09)\times10^{-5}$	66	66
SO_2	*m*-Cl	$(1.88\pm0.11)\times10^{-4}$	450	1
SO_2	*p*-Cl	$(3.74\pm0.06)\times10^{-3}$	9000	20
SO_2	*o*-Cl	$(1.93\pm0.13)\times10^{-3}$	4600	10

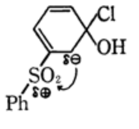
a) The volume ratio of H_2O and DMSO in the reaction with sulfoxides was 1 : 2.
The volume ratio of H_2O and DMSO in the reaction with sulfones was 1 : 3.2.

were treated with potassium hydroxide in aqueous dimethyl sulfoxide, both *o*- and *p*-hydroxyphenyl phenyl sulfoxides were the major and the only isolable products, indicating that the reaction proceeds through a typical aromatic S_N2 path. Now that the analyses of products suggest that the reaction of these compounds are clean-cut aromatic S_N2 processes, we have carried out kinetic experiments in order to compare the relative magnitudes of the activating effects of both phenylsulfonyl and phenylsulfinyl groups in the alkaline hydrolysis of aryl chlorides. The results are shown in Table 1.

When the relative rates of the sulfoxides are compared with those of the sulfones, the activating effect of phenylsulfinyl group is much smaller than that of phenylsulfonyl group. Even the least reactive sulfone, *i.e.* *m*-chlorophenyl phenyl sulfone is more than 5 times more reactive than the most reactive sulfoxide, *p*-chlorophenyl phenyl sulfoxide. This means that either the Coulombic attractive force of phenylsulfonyl group is very strong, or the incipient addition intermediate from the meta isomer is sufficiently stabilized by the nonbonding interaction as shown below:



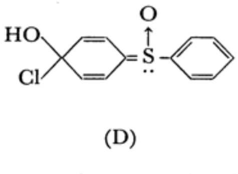
or



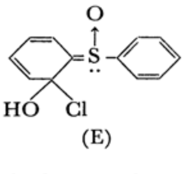
(B) (C)

In the case of chlorophenyl phenyl sulfones, the *p*-isomer is the most reactive and the relative rate is 20 times as that of the *m*-isomer, clearly indicating the strong electron-accepting conjugative effect of *p*-phenylsulfonyl group. In the previous work on the ethanolysis of chlorophenyl methyl sulfones with sodium ethoxide the relative rate of the para isomer was found to be 21 times of that of the meta isomer[6)] but a little less than that of the ortho isomer, though the difference is very small. The steric bulkiness of phenyl group might be reducing the reactivity of otherwise reactive *o*-chlorophenyl phenyl sulfone, whereas such a steric hindrance could be relatively small in the ethanolysis of *o*-chlorophenyl methyl sulfone.

In the case of chlorophenyl phenyl sulfoxide too, the para isomer is the most reactive, and about 80 times more reactive than the meta isomer. The difference is more pronounced not only than that between *m*- and *p*-chlorophenyl phenyl sulfones but also than that between *m*- and *p*-chloro-nitrobenzenes. (46.5 fold).[6)] Here again, *o*-chlorophenyl phenyl sulfone is also very reactive, but somewhat less reactive than the para isomer due perhaps to the steric hindrance. The markedly increased reactivities of the ortho and the para isomers over that of the meta isomer is undoubtedly associated with the 3d orbital conjugative effect of the phenylsulfonyl group to stabilize the incipient addition intermediate (D and E) in the reaction.

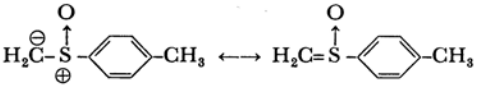


(D)



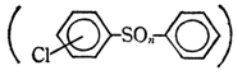
(E)

Here again a question is raised as to the steric configuration around the sulfoxide group during the hydrolysis, as in the base-catalyzed hydrogen isotopic reaction of an optically active methyl-*p*-tolyl sulfoxide, in which the incipient carbanion would be stabilized by a similar 3d orbital resonance shown below:[12)]



[12)] Y. H. Khim, W. Tagaki, M. Kise, N. Furukawa and S. Oae, This Bulletin, **39**, 2556 (1966).

TABLE 2. THE NUCLEOPHILIC SUBSTITUTION OF CHLOROPHENYL PHENYL SULFOXIDES AND SULFONES WITH POTASSIUM HYDROXIDE IN AQUEOUS DIMETHYL SULFOXIDE

Compound		Mp (°C) or bp (°C/mmHg) (lit.)	Product phenol			
			Time hr	OH	Yield %	Mp (°C) (lit.)[15]
SO_n	Cl					
SO_2	*m*-Cl	113—114	18	*m*-OH	73	163—164 (163—163.5)
SO_2	*p*-Cl	90—91 (91)	2	*p*-OH	93	135—136 (136—137)
SO_2	*o*-Cl	108—109 (105)	2	*o*-OH	85	98—99 (98—99)
SO	*m*-Cl	180—182/3 (190-192/5)	125	*—	—	
SO	*p*-Cl	45—46 (45—46)	16	*p*-OH	75	145—146 (144—145)
SO	*o*-Cl	61—62 (60—61)	18	*o*-OH	80	164—165 (164—165)

* *m*-Hydroxyphenyl phenyl sulfoxide could not be isolated: After a prolonged heating for several days this compound apparently decomposed.

An optically active sulfoxide, *i.e.*, (+)*p*-chlorophenyl phenyl sulfoxide, $[\alpha]_D^{20}+4.5°$, was synthesized by first reacting optically active (−)menthyl *p*-chlorobenzenesulfinate with phenylmagnesium bromide and then subjecting to the hydrolysis with potassium hydroxide in aqueous dimethyl sulfoxide. The product, *p*-hydroxyphenyl phenyl sulfoxide, obtained in more than 75% yield, was found to retain its optical integrity $[\alpha]_D^{20}+5.0°$, suggesting that no concurrent racemization takes place during the reaction. This may serve as another evidence to support the concept that 3d orbital resonance does not require any particular angular arrangement such as coplanarity which an ordinary resonance by the overlapping of 3p orbitals does.

Experimental

Preparations of the Starting Materials. All the three chlorophenyl phenyl sulfides *i.e.*, *o*-, *m*-, and *p*-isomers were prepared by reacting the corresponding chlorobenzenediazonium salts with thiophenolate.

The sulfides (*o*-isomer bp 132—133°C/1 mmHg, *p*-isomer bp 140—142°C/2 mmHg, *m*-isomer bp 118—120°C/1 mmHg) were oxidized as usual with hydrogen peroxide in glacial acetic acid containing a few drops of concentrated sulfuric acid to the corresponding sulfones in nearly quantitative yields and these sulfones were recrystallized from benzene - petroleum ether; the *o*-isomer, mp 108—109°C, the *m*-isomer, mp 113—114°C, the *p*-isomer, mp 90—91°C.

p-Chlorophenyl phenyl sulfide and the *m*-isomer were oxidized with bromine in aqueous acetic acid containing pyridine, by the procedure developed in these laboratories[13] to the corresponding sulfoxides in yields exceeding 75%, while *o*-chlorophenyl phenyl sulfide was oxidized as usual with hydrogen peroxide in glacial acetic acid containing a few drops of concentrated sulfuric acid at room temperature to the *o*-chlorophenyl phenyl sulfoxide in yield 90%.

The *p*- and *o*-isomers were recrystallized from benzene-petroleum ether and the *m*-isomer was redistilled; *o*-isomer mp 61—62°C, *p*-isomer mp 45—56°C, *m*-isomer bp 180—182°C/3 mmHg.

(+)*p*-Chlorophenyl Phenyl Sulfoxide. The titled compound was prepared by treating 10.5 g of (−)-menthyl *p*-chlorobenzenesulfinate (mp 82—83°C, $[\alpha]_D^{20}$ −183°, *c* 2.0 ethanol) with the Grignard reagent prepared from 12.8 g of bromobenzene and 2.6 g of magnesium in 80 m*l* of ether. The usual work up[14] of the reaction mixture afforded 5.5 g of (+) *p*-chlorophenyl phenyl sulfoxide which was recrystallized from *n*-hexane - ether in 70% yield. Mp 70—71°C, $[\alpha]_D^{25}$ +4.5° (*c* 0.58 ethanol).

Alkaline Hydrolyses of Chlorophenyl Phenyl Sulfones and Sulfoxides. *p*-Chlorophenyl phenyl sulfone (1.3 g) was gently refluxed with 0.95 g of potassium hydroxide in 29 m*l* of aqueous dimethyl sulfoxide (22 m*l* DMSO +7 m*l* H_2O) for 2 hr, the mixture was poured into a large amount of cold water, acidified with hydrochloric acid, extracted with ether and the ether extract was dried over sodium sulfate. After ether was evaporated, the crystalline residue was directly recrystallized from benzene and petroleum ether and 1.1 g of *p*-hydroxyphenyl phenyl sulfone was obtained.

By similar treatments, other products were also isolated. The results are tabulated in Table 2.

Hydrolysis of Optically Active (+)*p*-Chlorophenyl Phenyl Sulfoxide. The title compound was treated similarly and (+)*p*-hydroxyphenyl phenyl sulfoxide obtained in 75% yield was subjected to the usual measurement of optical rotation, the detail of which was reported in our previous paper.[12]

The Kinetic Experiment. Dimethyl sulfoxide was purified first by distillation after keeping with barium oxide for 8 hr at about 100°C, then dried over molecular sieve for 3 days and again by fractionation, and the fraction boiling at 56—57°C/5 mmHg was collected and used.

Kinetic measurements and rate calculations were made as follows. " Zero " time was taken as 3 min

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13) S. Oae, Y. Ohnishi, S. Kozuka and W. Tagaki, This Bulletin, **39**, 364 (1966).

14) K. K. Andersen, W. Gaffield, N. E. Papanikolaou, J. W. Foley and R. I. Perkins, *J. Am. Chem. Soc.*, **86**, 5637 (1964).

15) C. Y. Meyers, *Gazz. Chim. Ital.*, **93**, 1208, 1209 (1963).

after the ampoules containing 1 m*l* of aryl chloride, DMSO and H_2O solution respectively were introduced into the thermostat. From time to time the ampoule was broken, and washed out with pure 20 m*l* water and 30 m*l* ether in a flask containing 2 m*l* of 2 N nitric acid. The aqueous part was separated into a 200 m*l* glass stoppered Erlenmyer flask containing 3 m*l* of 0.1 N silver nitrate solution and the ethereal layer was washed with 20 m*l* portion of water, and the combined mixture of the aqueous solution was placed into an Erlenmeyer flask.

The excess of silver ion was then titrated by the usual Volhard method.

Each run was carried out using ampoules, while the concentrations of both an aryl chloride and potassium hydroxide were maintained at 1.76×10^{-4} N and 5.63×10^{-4} N, respectively.