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The Mechanism of the Alkaline Fusion of Halodiphenyl Sulfone and Halobenzenesulfinic Acids[1]

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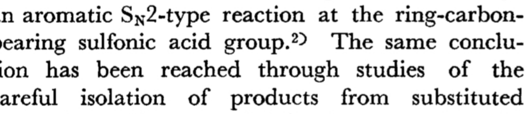
The alkaline fusion of 2-chlorophenyl phenyl sulfone afforded phenol, benzene and chlorobenzene. The initial step of the reaction appears to be the aromatic S_N2-type replacement of chlorine to form 2-hydroxyphenyl phenyl sulfone upon which the hydroxide ion further attacks both phenyl carbon-1 and the sulfur atom of the sulfone group to form the final products. The ^{14}C tracer experiment indicates that the preference of the nucleophilic-attacking site of the hydroxide ion appears to vary with the reaction temperature. A similar alkaline fusion of 2-bromo-4-tolyl phenyl sulfone gave not only benzene, bromotoluene, and phenol, but also *o*- and *m*-cresol, indicating that the reaction proceeds through a somewhat different path. Meanwhile, the alkaline fusion of 2-chlorobenzenesulfinic acid appears to proceed through the *o*-sulfinic benzyne formation; thus 2-bromo-4-tolylsulfinic acid gave equal amounts of *o*- and *m*-cresols.

Previously we have shown, mainly through ^{14}C and ^{18}O tracer experiments, that the alkaline fusion of benzenesulfonic acid proceeded through an aromatic S_N2-type reaction at the ring-carbon-bearing sulfonic acid group.[2] The same conclusion has been reached through studies of the careful isolation of products from substituted aromatic sulfonic acids.[3,4] Subsequently, the mechanism of the alkaline fusion of diphenyl sulfone has been studied by means of the ^{14}C-tracer technique[5]; this study suggests that the reaction proceeds through a simple S_N2-type path, and not one involving benzyne formation. However, an unanswered question has remained as to the site of the nucleophilic attack of the hydroxide ion. The successful isolation of benzenesulfonic acid during the reaction by Ingold and Jessop[6] and the strong affinity of the negative hydroxide ion toward the positively-charged sulfur atom of the sulfone group seem to favor the nucleophilic attack of the hydroxide ion on the sulfone group, as is shown below Mechanism A:



$$C_6H_5SO_2C_6H_5 + \overset{\ominus}{O}H \rightleftharpoons \left[C_6H_5-\overset{O\;\;O}{\underset{OH}{S}}-C_6H_5 \right]^{\ominus} \rightarrow C_6H_5SO_3^{\ominus} + C_6H_6$$

(Mechanism A)

Another mechanism, an aromatic S_N2 reaction on the carbon-atom-bearing sulfonyl group (Mechanism B), cannot be ruled out, however, since a similar alkaline fusion of benzenesulfonic acid is apparently a part of the aromatic S_N2 process, and benzenesulfinic acid has actually been isolated from the alkaline fusion of diphenyl sulfone.[7]

(Mechanism B)

$$C_6H_5SO_2C_6H_5 + \overset{\ominus}{O}H \longrightarrow C_6H_5SO_2^{\ominus} + C_6H_5OH$$

Although there is no easy way to make a choice between the above two mechanisms, the alkaline fusion of *o*-halophenyl phenyl sulfone is an interesting problem in this connection, since the process involving the initial nucleophilic attack of the hydroxide ion on the sulfone group (Mechanism I) may lead to the formation of a benzyne intermediate, as in the reaction of *o*-chlorobenzophenone with potassium amide,[8] and the products formed will be somewhat different from those expected from the attack on the carbon atom. A more clear-cut difference in the distribution of products will be observed when 2-halo-4-tolylsulfone is used, as in the aminolysis of *o*-halobenzophenone. Another interesting problem is the behavior of *o*-halobenzenesulfinate ion in the alkaline fusion, since it will be one of the intermediate formed if the reaction follows the mechanism B.

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[1] Phenols and Phenolic Esters. XIV.

[2] S. Oae, N. Furukawa, M. Kise and M. Kawanishi, This Bulletin, **39**, 1212 (1966).

[3] W. Pritzkow, P. Grothkoph, R. Hoering, H. Gross and W. Fuerhring, *Z. Chem.*, **5**, 300 (1965).

[4] L. R. Buzbee, *J. Org. Chem.*, **31**, 3289 (1966).

[5] S. Oae and N. Furukawa, This Bulletin, **39**, 2260 (1966).

[6] C. K. Ingold and J. A. Jessop, *J. Chem. Soc.*, **1930**, 708.

[7] Professor M. Kobayashi, unpublished.

[8] J. F. Bunnett and B. H. Hrutfiord, *J. Org. Chem.*, **27**, 4152 (1962).

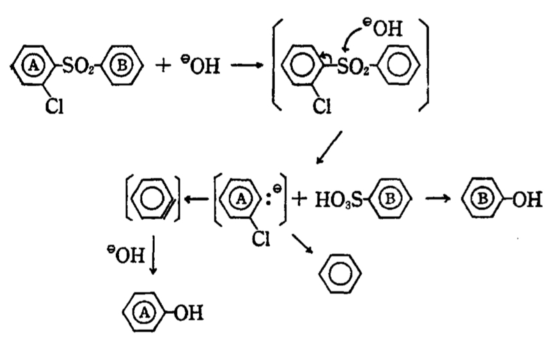
Thus, we have studied the alkaline fusion of 2-chlorophenyl phenyl sulfone, 2-bromo-4-tolyl phenyl sulfone, 2-chloro-benzenesulfinic acid, and 2-bromo-4-tolylsulfinic acid. The results we have obtained are somewhat different from what we anticipated, but they appear to suggest clearly that the nucleophilic attack of the hydroxide ion takes place at both the sulfone group and the aromatic ring carbon-1. By the use of 2-chlorophenyl phenyl-1′-^{14}C sulfone, the relative ratio of the nucleophilic attack of the hydroxide ion at the sulfone group and the aromatic ring carbon was estimated.

This paper will describe our experimental observations and discuss the mechanisms of these reactions.

Results and Discussion

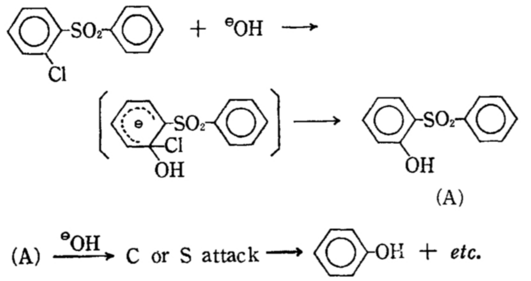
The reaction was generally carried out by heating a mixture of a starting compound with an excess of potassium hydroxide at around 300°C for several minutes in a nickel crucible under a slow stream of nitrogen gas; the products were analyzed by introducing them to their corresponding known derivatives or by a comparison of their gas chromatographic behavior and infrared spectra with those of the authentic samples.

***o*-Halophenyl Phenyl Sulfone.** While the alkaline fusion of diphenyl sulfone takes place slowly at below 300°C, that of the *o*-halo derivative is quite facile. A similar phenomenon was observed in the aminolyses of *o*-halobenzophenone and benzophenone, where the *o*-chloro compound undergoes a much facile cleavage, apparently forming a benzyne intermediate.[8] It appears that the substitution of the electron-withdrawing chloro group facilitates the nucleophilic attack of hydroxide on the molecule. When the alkaline fusion of *o*-chlorophenyl phenyl sulfone was carried out, the products identified were phenol, benzene, and chlorobenzene. This means that unlike the aminolysis of *o*-halobenzophenone the reaction does not seem to proceed only through the formation of benzyne (Mechanism I), since the mechanism involving the formation of benzyne would require phenol and chlorobenzene to be the only products of this reaction. Actually, the formation of a small amount of chlorobenzene suggests that at least a portion of the nucleophilic attack of the hydroxide ion takes place on the sulfone group (Mechanism I).



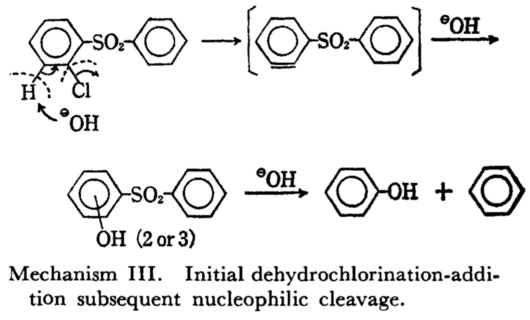
Mechanism I. Attack on the sulfone group.

The complete lack of catechol among the products suggests that the initial nucleophilic attack of hydroxide does not occur at the carbon-1 position of the A ring. This is rather strange, since the A ring would be more susceptible to nucleophilic attack because of its electron-withdrawing *o*-chloro group. However, since chloride is a better leaving group than the benzenesulfinate group, the initial nucleophilic attack on the A ring may take place at the 2-position, replacing chloride ion (Mechanism II).



Mechanism II. Initial chloride replacement subsequent nucleophilic cleavage.

In fact, the *o*-chloro group is highly activated by the phenylsulfonyl group and is susceptible to nucleophilic attack.[9] When *o*-chlorophenyl phenyl sulfone was treated with aqueous potassium hydroxide in dimethyl sulfoxide, *o*-hydroxyphenyl phenyl sulfone was isolated in a high yield. Thus, *o*-hydroxyphenyl phenyl sulfone is a very likely intermediate in this reaction, and the lack of catechol formation may be ascribed to the negative field effect of the hydroxyl group, which suppresses the nucleophilic attack at the A ring. Another possible mechanism is the one that involves the prior formation of *o*-sulfonyl benzyne (Mechanism III). Though the formation of a small



Mechanism III. Initial dehydrochlorination-addition subsequent nucleophilic cleavage.

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[9] S. Oae and Y. Khim, This Bulletin, **40**, 1716 (1967).

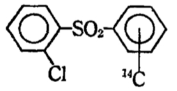
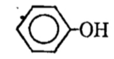
TABLE 1. THE REACTION CONDITIONS AND THE PRODUCTS

Compound	Products (yield %)	Reaction temp. °C
o-Cl-$C_6H_4SO_2Na$	C_6H_5OH (40)	260—330
p-Cl-$C_6H_4SO_2Na$	C_6H_5OH (70)	260—330
2,4-Br(CH_3)$C_6H_3SO_2Na$	o,m-$CH_3C_6H_4OH$* (70), C_6H_5OH	300—350
o-Cl-$C_6H_4SO_2C_6H_5$	C_6H_5OH (65), C_6H_5Cl, C_6H_6	260—300
2,4-Br(CH_3)$C_6H_3SO_2C_6H_5$	o,m-$CH_3C_6H_4OH$**, C_6H_5OH (60)	240—330

* The products ratio was 1 : 1 : 0.5 (*o*-cresol : *m*-cresol : phenol).
** *o*-cresol : *m*-cresol : phenol = trace: 7 : 1

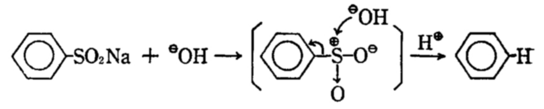
amount of chlorobenzene cannot be explained by this mechanism, it is possible that a portion of the reaction may proceed through this process. In order to test these possibilities, 2-bromo-4-tolyl phenyl sulfone was subjected to alkaline fusion. If the reaction follows the path of the III mechanism, one would expect to obtain nearly equal amounts of *o*- and *m*-cresols. As shown in Table 1, we did find *o*-cresol, but the amount was less than 1/20th that of *m*-cresol. The formation of such a small amount of *o*-cresol suggests that although a tiny fraction of the reaction actually goes through the III mechanism, it is by no means the major path of the reaction. The lack of *p*-cresol among the products is noteworthy, since it indicates that the initial benzyne formation through the nucleophilic attack of the hydroxide ion on the sulfone group does not occur in this reaction; however, the formation of a small amount of *m*-bromotoluene clearly suggests that the process involving the nucleophilic attack of the hydroxide ion on the sulfone group (Mechanism I) cannot be excluded. Moreover, the formation of 4-methylcatechol was not noticed in this reaction. Probably, here also, the major path of the reaction is the one involving the initial chloride replacement (Mechanism II).

TABLE 2. ^{14}C-TRACER STUDY

Compound	Reaction temp. °C	Activities cpm
	—	679
 (as tribromide)	270 270—290 300—330	812 806 681

As has been shown above, phenol was the major product of the alkaline fusion of *o*-chlorophenyl phenyl sulfone. In order to shed further light on the reaction, 2′-chlorophenyl phenyl-1-^{14}C sulfone was subjected to the alkaline fusion. If the source of phenol is limited to either A or B ring, the specific activity of the resulted phenol is expected to be either nil or twice the ^{14}C activitiy of the original sulfone. Indeed, as shown in Table 2, the phenol obtained was found to have nearly the same specific activity as that of the starting sulfone, suggesting that the phenol comes from both A and B rings nearly in the same extent. However, when the alkaline fusion was carried out at somewhat lower temperatures, the specific activity of the phenol formed was found to show a somewhat higher value, suggesting that there is a preference in attacking site in the nucleophilic attack of the hydroxide ion. If the portion of the reaction that proceeds through the I mechanism increases at lower temperatures, it will increase the activity of the phenol formed. However, detailed analyses of the preference of the attacking site of the hydroxide ion will have to await further investigation.

***o*-Halobenzenesulfinic Acids.** In the foregoing discussion, the alkaline fusion of benzenesulfinate was presumed to give only benzene, as was reported previously.[10] In fact, when this reaction was repeated, we found only the formation of benzene. Undoubtedly the nucleophilic attack of the hydroxide ion takes place only at the sulfonyl group, as is illustrated below:



This desulfination is quite facile and is usually completed in a few minutes at around 300°C.

When *o*-chlorobenzenesulfinic acid was treated with an excess of potassium hydroxide, phenol was obtained, but the yield was not impressive; however, *p*-chlorobenzenesulfinic acid in the same reaction also afforded phenol in a much higher yield. In neither case chlorobenzene was isolated. The complete lack of chlorobenzene formation suggests that the nucleophilic attack in the sulfinate group to form chlorobenzene is not the initial process of this reaction; rather, the replacement of the chloro group by the hydroxide ion seems to follow the alkaline cleavage of the sulfinate group. This is clearly demonstrated in the alkaline fusion

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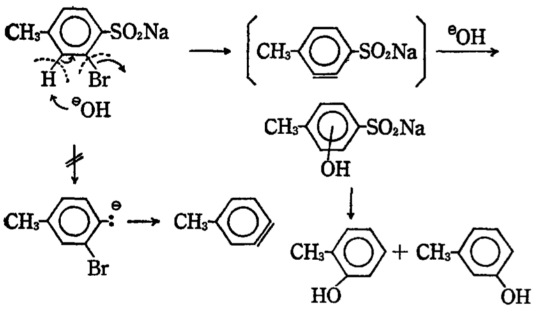
10) R. Otto, *Ann*, **145**, 322 (1868).

of 2-bromo-4-toluenesulfinate, in which both *o*- and *m*-cresols were obtained as the main products; their yields were nearly equal. The results are shown in Table 1. The total absence of *p*-cresol suggests that the replacement reaction of bromine by hydroxyl takes place prior to the alkaline cleavage of the sulfinate group and that *m*-bromotoluene is not the intermediate, since the alkaline fusion of *m*-bromotoluene, presumably proceeding *via* the formation of benzyne,[11] would give not only *o*- and *m*-cresols, but also *p*-cresol. Thus, the equal distribution of *o*- and *m*-cresols suggests that the initial reaction is the dehydrobromination to form the benzyne intermediate, which upon the addition of hydroxide, forms both 2- and 3-hydroxytoluenesulfinates which in the succeeding step undergoes desulfination to afford *o*- and *m*-cresols, as is shown below:



The formation of a small amount of phenol appears to be due to the demethylation of cresols during the alkaline fusion, though its mechanism is not fully understood.

Experimental

The Preparation of *o*-Halosulfinic Acid and *o*-Halosulfone. *o*-Chlorobenzene Sulfinic Acid. *o*-Chloroaniline (12.8 g) was diazotized with 7.6 g of sodium nitrite in a mixture of 16 m*l* of concentrated sulfuric acid and 200 m*l* of water. Into the diazotized solution sulfur dioxide gas was bubbled until the weight of the mixture increased by 50 g. Then copper powder was then added into the solution to decompose the diazotized compound. The precipitate was washed with ether three times. The filtrate was extracted with ether, and the combined ether solution was extracted with a 5% sodium hydroxide solution. The alkaline extract was acidified with concentrated hydrochloric acid. Thus, the sulfinic acid (12.5 g) was obtained in a 90% yield; mp 108—110°C.

o-Bromotoluenesulfinic acid was prepared similarly from 9.5 g of 2-bromo-4-methylaniline in a 72% yield; mp 115—117°C.

***o*-Chlorophenyl Phenyl Sulfone.** *o*-Chlorophenyl phenyl sulfide (33 g), prepared by the reaction of thiophenolate with *o*-chlorobenzene diazonium sulfate, was oxidized with 47.4 g of potassium permanganate in 200 m*l* of acetic acid at a temperature below 50°C. The sulfone thus obtained was recrystallized from benzene - *n*-hexane. The yield was 30 g (80%); mp 106-107°C.

2-Bromo-4-tolyl Phenyl Sulfone. 2-Bromo-4-tolyl phenyl sulfide (10.1 g), prepared by the reaction of a 2-bromo-4-tolyl diazonium solution with thiophenolate, was oxidized with 12.0 g of potassium permanganate in 75 m*l* of acetic acid. After the reaction, the mixture was quenched with a large amount of water; then SO_2 gas was introduced to decompose the excess potassium permanganate. The gummy solid cake was dried and recrystallized from 95% ethanol. The yield was 10.5 g (90%) mp 112—113°C, after repeated recrystallizations from 95% ethanol. The sulfone has characteristic IR absorption bands at 1150 and 1350 cm^{-1}.

The Alkaline Fusion of Sulfinic Acid and Sulfone. *A Typical Example of Alkaline Fusion.* The alkaline fusion of *o*-chlorosulfinic acid was carried out as follows. Sodium *o*-chlorobenzenesulfinate (5.5 g) was added to molten potassium hydroxide (15 g) placed in a nickel crucible, at a temperature kept between 260—300°C under nitrogen stream. Vigorous foaming occurred immediately. After the addition, temperature was kept at 300—330°C for 5 min, and then the vessel was cooled rapidly with running water. The solidified mixture was dissolved into water and acidified with concentrated hydrochloric acid, and the aqueous solution was distilled with steam. Into the distillate bromine water was added until the solution turned slight yellow. The tribromide thus obtained was filtered and washed with water. The yield of tribromophenol was 2.0 g; mp 94°C.

In some cases, the distillate was extracted with ether and directly gas chromatographed. The conditions of G. L. C. were as follows: Temp., 130°C; H_2 35 m*l*/min; column, silicone grease coated on Celite 545, 2 m long.

The results of the alkaline fusion of the other sulfinic acids are listed in Table 1; the conditions were nearly the same.

The Alkaline Fusion of o-Chlorophenyl Phenyl Sulfone. *o*-Chlorophenyl phenyl sulfone (3.0 g) was mixed with 15 g of potassium hydroxide and heated in a nickel crucible at a temperature between 300—350°C with a silicone oil bath. The liquid was trapped and then analyzed by G. L. C. After several minutes of heating, the vessel was cooled. The solidified product was dissolved into water and acidified with concentrated hydrochloric acid. The acidified solution was then distilled with steam. The distillate was extracted with ether, and the ethereal solution was dried over magnesium sulfate. After ether was removed, the residue was distilled. The yield was 1.46 g (91%). The products were analyzed by G. L. C., the conditions of which were the same as in the case of the sulfinic acid. The compounds identified were benzene and phenol; catechol could not be detected by G. L. C.

The Alkaline Fusion of 2-Bromo-4-tolyl Phenyl Sulfone. This compound was treated similarly; from 3.0 g of the sulfone, 0.6 g of phenols and 1.0 g of an unidentified solid were obtained.

The liquid products were analyzed by G. L. C.; benzene, toluene, phenol, *m*-cresol, and a tiny peak of *o*-cresol were found. The ratio of the products is shown in Table 1.

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11) A. T. Bottini and J. D. Roberts, *J. Am. Chem. Soc.*, **79**, 1458 (1957).

o-Chlorophenyl Phenyl Sulfone with Potassium Hydroxide in DMSO. The sulfone (2.5 g) and 5.0 g of potassium hydroxide in 20 m*l* of DMSO containing 5 m*l* of water was refluxed over an oil bath for 24 hr. After cooling, the mixture was poured onto ice water. The aqueous solution was acidified with concentrated hydrochloric acid, and extracted with water. The ether extract was washed with water and dried over sodium sulfate. The ether was removed and the crystalline residue was recrystallized from benzene- *n* -hexane. The crystals were identified as *o*-hydroxyphenyl phenyl sulfone. The yield was 1.8 g (78.2%); mp 97—98°C.

2-Chlorophenyl Phenyl Sulfone-1-^{14}C. The synthesis of the sulfone was performed by the method described for unlabelled sulfone. From 2.0 g of aniline-1-^{14}C and *o*-chlorothiophenol prepared from *o*-chloroaniline and potassium xanthate, 2.5 g of 2′-chlorophenyl phenyl sulfide-1-^{14}C was obtained. The sulfide (2.5 g), when oxidized with potassium permanganate, gave 2.2 g of the titled sulfone. The alkaline fusion was performed as in the case of the unlabeled sulfone. The reaction conditions and products are listed in Table 1. The ^{14}C activity measurements were carried out by the Van Slyke wet combustion method by converting the samples as usual to barium carbonate pellets; the activities were recorded by a 2π gas-flow G. M. counter.