Transsulfonylations between Aromatic Sulfones and Arenes

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Transsulfonylations between various aromatic sulfones and arenes catalyzed by triflic acid at 150 °C are described. The structural requirements for the occurrence of the transsulfonylations are shown to be similar to those for the transacylations that were described earlier. However, in view of the inherent differences in the properties of aromatic ketones and sulfones with respect to conjugation of the carbonyl and sulfonyl groups with the aromatic ring, a different rationale for the transsulfonylation reactions is offered. A mechanism is suggested that rationalizes the similar structural requirements for transacylations and transsulfonylations in terms of steric relief of strain in the reactions of certain ketones and sulfones.

In a previous paper[1] we described transacylations between various aromatic ketones and arenes catalyzed by aluminum chloride and other Lewis and protonic acids. The presence of two substituents ortho to the acyl function in the ketone and sufficient nucleophilic character in the arene were shown to be required for the transfer of the acyl group. We have now extended this research to a study of possible analogous acid-catalyzed transsulfonylations between alkyl aryl sulfones and arene nucleophiles.

Although the behavior of sulfones in basic media has been explored extensively,[2] there have been few reports of the interaction of sulfones with acids.[3,4] We now report that acid-catalyzed transsulfonylations between aryl sulfones and certain nucleophilic arenes occur, and the structural requirements for the reaction are virtually identical with those of the previously reported transacylations. For example, methyl mesityl sulfone reacted with anisole in the presence of aluminum chloride or triflic acid to produce methyl *p*-anisyl sulfone and mesitylene, but methyl phenyl sulfone did not undergo transsulfonylation with anisole.

The first experiments were carried out with aluminum chloride as catalyst, as in the previous work with ketones,[1] but when triflic acid was found to give similar results, it was adopted as catalyst in the remainder of the work since it gave homogeneous reaction mixtures in all cases. Possible transsulfonylations between seven aryl sulfones and anisole were investigated. The sulfones RSO_2Ar and $Ar'SO_2Ar$ were **1**, R = Me, Ar = phenyl, **2**, R = Me, Ar = *p*-tolyl, **3**, R = Me, Ar = 2,4-dimethylphenyl, **4**, R = Me, Ar = 2,5-dimethylphenyl, **5**, R = Me, Ar = 2,6-dimethylphenyl, **6**, R = Me, Ar = mesityl, and **7**, Ar′ = phenyl, Ar = mesityl. Only the sulfones with two ortho methyl groups (**5–7**) gave transsulfonylations with anisole. The yields as determined by (a) GC/MS, with duplicate runs, and (b) isolation by column chromatography: from **5** (a) 20%, 22%, (b) 18%; from **6** (a) 75%, 77%, (b) 71%; from **7** (a) 77%, 80%, (b) 75%. The lower yield from **5** may be attributed to its partial isomerization to the 2,4- and/or 2,5-dimethylphenyl sulfone.

Reactions of the same seven aryl sulfones with diphenyl ether were similarly tested, with analogous results. Only **5–7** gave transsulfonylation with diphenyl ether as the acceptor of the sulfonyl group, in the following yields: from **5** (a) 22%, 25%, (b) 20%; from **6** (a) 75%, 78%, (b) 71%; from **7** (a) 79%, 82%, (b) 76%.

Various other arene acceptors were also tested in reaction with methyl mesityl sulfone, with the results shown in Table I, which were analogous to those from the reaction of acetylmesitylene with the same arenes.[1] The extent of transsulfonylation appears to be determined by the nucleophilicity of the arene acceptor: benzene gave only a trace of transsulfonylation product, toluene gave 26–30%, and *m*-xylene and the more nucleophilic aromatic ethers gave extensive conversion. It is interesting to note that the reverse of Experiment 3 of Table I was tested, and it was found that methyl 2,4-dimethylphenyl sulfone did *not* react with mesitylene. The reaction of methyl mesityl sulfone with isodurene (experiment 7) gave a reaction mixture that could be shown by capillary GC/MS to contain about 60% of the starting material, methyl mesityl sulfone, and 40% of the product, methyl isoduryl sulfone, but these two very similar compounds could not be isolated by column chromatography.

Table I. Transsulfonylation between Methyl Mesityl Sulfone and Various Arenes[a]

expt no.	arene	transsulfonylation product,[b] % yield GC/MS[c]	isolated[d]
1	benzene	trace	
2	toluene	30, 26	
3	*m*-xylene	75, 75	70
4	anisole	75, 77	75
5	phenetole	78, 75	75
6	diphenyl ether	75, 75	71
7	isodurene	37, 40	

[a] Reaction at 150 °C for 4 h; reactants (molar ratios), sulfone:arene:triflic acid = 1:3:1.5. [b] The products are identified in the Experimental Section. [c] Analysis by GC/MS, duplicate runs. [d] Isolated by column chromatography; see Experimental Section.

These results demonstrated a strong steric effect of *ortho* methyl groups in the aromatic sulfone in determining whether or not the sulfone group would be transferred to another aromatic ring, just as in the case of the acid-catalyzed transacylations described previously.[1] The structural requirements for the analogous reactions in the two systems appear to be very similar, but there are inherent differences between ketones and sulfones which pose an intriguing puzzle.

Although a steric inhibition of resonance in acetylmesitylene that increases the electrophilicity of the carbonyl carbon atom compared to that in the carbonyl in acetophenone provides a reasonable explanation for the transacylations,[1] an analogous explanation of the transsulfonylations is not viable. Molecular orbital (MO) theory,[5] physical evidence,[6] and chemical reactivity data[7]

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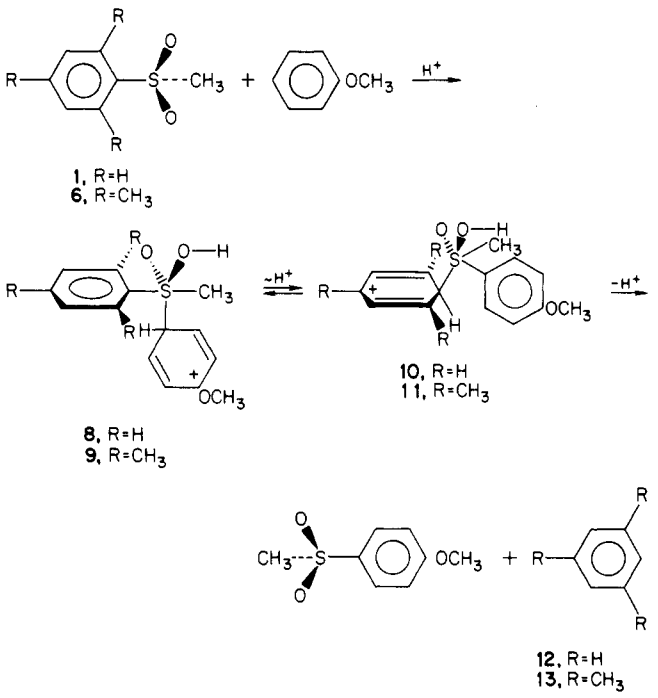
Scheme I



support the view that conjugation of a sulfone group with an aromatic ring does not require coplanarity of the S–O bonds with the ring. Thus another rationale must be sought. We suggest that the one depicted in Scheme I is reasonable. The key to the rationale is the effect of the two ortho methyl groups in methyl mesityl sulfone (**6**) that produces a release of the steric strain in intermediate **9** when the proton is transferred from the anisole ring to the mesitylene ring of **9**. When this happens, the hybridization of the carbon in the mesityl ring attached to the sulfur atom changes from sp^2 (in **9**) to sp^3 (in **11**), which relieves the $A^{1,3}$ strain between the ortho methyl groups and the components of the sulfonyl group in intermediate **9**. Construction of models of compounds **9** and **11** with CPK atomic models indicates severe steric interaction in **9** between the sulfonyl group and the ortho methyl groups of the mesityl ring. In fact, it was impossible to connect the sulfonyl group to the ring carbon atom. On the other hand, the model of **11** could be constructed satisfactorily, since the sulfonyl oxygen atoms are moved away from the ortho methyl groups by the change in the hybridization of the carbon atom.

In the potential (but not realized) reaction of methyl phenyl sulfone with anisole, there is no difference in the energy of **8** and **10** attributable to steric compression, and actually **8** should be considerably more stable than **10** because of the mesomeric interaction of the methoxy group with the positive charge in the anisole ring of **8**. If one assumes that the reaction is under thermodynamic control, owing to the difference in energy of the intermediates **8** or **9** and **10** or **11**, rather than under kinetic control by virtue of the difference in the rates of reaction of **1** and **6** with anisole, one can rationalize the fact that the mesityl sulfone reacts with anisole by transsulfonylation whereas the phenyl sulfone does not. Similar reasoning can be applied to the other reactions in which transsulfonylation from hindered aromatic sulfones to less hindered aromatic rings occurs.

In view of the results of the transsulfonylation reactions described here, we have reassessed the explanation offered in our previous report for the occurrence of transacylation reactions of hindered ketones,[1] which was based solely on steric enhancement of electrophilicity of the carbonyl carbon atom of the hindered ketone. It seems quite possible that a rationale analogous to that offered for the transsulfonylations may also apply to the transacylations. Structures **12** and **14** in the preceding paper are analogous to structures **9** and **11** in the present paper, and it is quite possible that the requirement of two ortho methyl groups in an aromatic ketone for transacylation to occur has more to do with the relief of steric strain in going from **12** to **14** than with a steric inhibition of reasonance that activates the ketone toward reaction with an arene nucleophile.

In an alternative mechanism that should be considered, the sulfonyl (or acyl) group would be cleaved from an intermediate σ complex formed by ipso attack on the aromatic sulfone (or ketone) by a proton, and the sulfonyl (or acyl) group could either reform the starting sulfone (or ketone) or react with the less hindered and more nucleophilic arene to give the transsulfonated (or transacylated) product. Although this alternative mechanism cannot be ruled out on the basis of present experimental data, we believe the mechanism of Scheme I and an analogous mechanism for transacylation is more satisfactory. Part of the argument derives from the transacylation work, in which diarylalkene and triarylmethane derivatives (cf. structures **18** and **2** in the preceding paper[1]) were observed as products of side reactions that accompany the transacylations. The formation of these side products can most plausibly be explained in terms of a "bimolecular" mechanism analogous to Scheme I, since the intermediate formed by nucleophilic attack of the arene on the ketone (structure **12** in the preceding paper[1]) can reasonably lead to all three types of products observed, the transacylated arene, a diarylethene, and a triarylethane.

Another kind of evidence that favors our "bimolecular" mechanism is the strong dependence of the reactions on the nucleophilicity of the arene in its reaction with the ketone or sulfone. For example, methyl mesityl sulfone gives only a trace of reaction with benzene, ca. 28% reaction with toluene, and 75% reaction with *m*-xylene (Table I). Although one may ascribe this trend to the order of reactivity of these arenes with a methylsulfonyl cation (e.g., the alternative mechanism), it would be surprising that virtually no reaction occurred with benzene in view of the ease of sulfonylation of benzene and the fact that any methyl phenyl sulfone should persist in the reaction mixture and be observed, because it has been demonstrated that the unhindered sulfone is stable toward desulfonation under the reaction conditions.

Experimental Section

The GC/MS data were obtained on a Finnigan MAT 4023 spectrometer with an INCOS data system and a J&W Scientific, Inc., 50-m DB1 bonded-phase capillary column (0.25-μm film thickness). The sulfones were prepared according to literature procedures,[8-11] and the purity of each was checked by NMR and GC/MS. All other materials were commercially available; the organic reagents were checked for purity by GC/MS before use.

General Procedure for the Reaction of Sulfones with Anisole. To a 50-mL three-necked flask fitted with a magnetic stirrer and a reflux condenser protected by a drying tube was

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added 5 mmol of the sulfone, 3.0 mL (15 mmol) of anisole, and 0.88 mL (7.5 mmol) of triflic acid. The reaction mixture was stirred at 150 °C for 4 h, allowed to cool to room temperature, and poured over 50 g of ice. The mixture was extracted with chloroform and the chloroform extract was washed sequentially with 40 mL of water, 40 mL of saturated $NaHCO_3$, and 40 mL of water and then dried over $CaCl_2$. The dry chloroform extract was then subjected to quantitative GC/MS analysis. This procedure was repeated as above except that the reaction mixture was separated by column chromatography using silica gel in a 50 cm × 2 cm column. The product sulfone was eluted using a diethyl ether-chloroform (v:v 2:8) mixture. Evaporation of the solvents gave methyl *p*-anisyl sulfone [mp 120–121 °C;[12] mass spectrum, *m/e* 186 (M^+), 171, 123, 107, 94, 77] and phenyl *p*-anisyl sulfone [mp 90–91 °C;[13] mass spectrum, *m/e* 248 (M^+), 177, 123, 107, 77].

General Procedure for the Reaction of Sulfones with Diphenyl Ether. The procedure was exactly as described above except that diphenyl ether was used in place of anisole. Methyl *p*-phenoxyphenyl sulfone [mp 85–86 °C;[14] mass spectrum, *m/e* 248 (M^+), 233, 185, 169, 141, 77] and phenyl *p*-phenoxyphenyl sulfone [mp 92–93 °C;[15] mass spectrum *m/e* 310 (M^+), 233, 217, 185, 169, 77] were obtained as transsulfonylation products. The identity of these known products was confirmed by NMR as well as by melting point and MS.

General Procedure for the Reaction of Methyl Mesityl Sulfone with Various Arenes. The procedure was as described above except that various arenes (15 mmol) were used in reaction with methyl mesityl sulfone (5 mmol) and triflic acid (7.5 mmol). Analyses by GC/MS and column chromatography were carried out as before. The results are presented in Table I. The product sulfones formed by transsulfonylation in experiments 2 and 3 were the same ones used as starting materials in some of the experiments described above. The fact that the retention time in the capillary GC of the product of experiment 2, Table I, was the same as that of the pure methyl *p*-tolyl sulfone used as starting material previously indicated that the product sulfone was indeed the para isomer; there was no indication of more than a trace of other isomers formed in the transsulfonylation. The product sulfones formed by transsulfonylation in experiments 4 and 6, Table I, were the same ones produced in previous experiments. The product sulfone of experiment 5, Table I, ethyl *p*-ethoxyphenyl sulfone, had mp 89–90 °C,[16] mass spectrum, *m/e* 200 (M^+), 185, 137, 121, 77.

Tests for Desulfonylation in the Absence of a Nucleophilic Arene. Each of the seven aryl sulfones was stirred with triflic acid (7.5 mmol) at 150 °C for 3 h and the reaction mixture was worked up as before. Each of the starting sulfones was recovered in almost quantitative yield by evaporation of the chloroform solution.

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Registry No. **5**, 97416-12-1; **6**, 6462-31-3; **7**, 3112-82-1; 4-$MeSO_2C_6H_4OMe$, 3517-90-6; 4-$PhSO_2C_6H_4OMe$, 3112-84-3; 4-$MeSO_2C_6H_4OPh$, 21134-15-6; 4-$PhSO_2C_6H_4OPh$, 47189-05-9; 4-$EtSO_2C_6H_4OEt$, 82961-62-4; 4-$MeSO_2C_6H_4Me$, 3185-99-7; anisole, 100-66-3; diphenyl ether, 101-84-8; toluene, 108-88-3; *m*-xylene, 108-38-3; phenetole, 103-73-1; isodurene, 527-53-7; methyl isoduryl sulfone, 97416-13-2.

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Catalysis of Sulfonate Ester Hydrolysis by Intramolecular Amide Group Assistance

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Kinetics of the alkaline hydrolysis of aryl 2-(acylamino)benzenesulfonates (**1**, X = OAr) obey the equation

$$k_{obsd} = (k_a + k_b[OH^-])/(1 + [H^+]/K_a)$$

Hammett equations correlate the parameters k_a, k_b, and K_a for variation in both amido and leaving phenolate substituents. The values and sign of the ρ values together with entropy of activation data, reactivity, trapping, and oxygen-18 incorporation are consistent with the formation of an intermediate benzoxathiazine *S,S*-dioxide (**2**). The k_a term involves intramolecular attack of the amido anion. The k_b term is consistent with a specific anion effect on k_a. Regular bimolecular $B_{Ac}2$ mechanisms for k_a and k_b are not consistent with the high observed reactivity of these parameters.

The amide group is a well-known intramolecular nucleophilic catalyst for many ester hydrolyses,[1] where it can act in its neutral or conjugate base forms. Previous work from these laboratories has indicated that a neighboring oxyanion is a powerful nucleophile in sulfonyl group transfer.[2,3] We are interested in the amido anion as a potential neighboring group for sulfonyl transfer where the reacting nucleophile is the oxyanion function. Aberlin and Bunton[4] showed that the hydrolysis of 2-acetamido-

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