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Aromatic Sulfonylation. II. Attacking Species under Various Conditions.*[1]

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p-Toluenesulfonylation of toluene and anisole in the presence of $AlCl_3$, $SbCl_5$ or $TiCl_4$ was investigated in methylene chloride, nitromethane and nitrobenzene. Substitution took place at 8.6—13.4% and 86.6—91.4% *para* positions for toluene in methylene chloride, but 42.0—45.7% *ortho* and 54.2—58.0% *para* isomers were obtained in nitromethane and nitrobenzene. Sulfonylation of toluene with *p*-$CH_3C_6H_4SO_2^+$ ClO_4^- afforded 44.8—46.3% *ortho* and 53.7—55.2% *para* isomers. Partial rate factors for toluene were $p_f=52.5$ in methylene chloride, $o_f=12.6\pm0.9$, $p_f=31.4\pm2.0$ in nitromethane, and $o_f=16.0\pm1.7$, $p_f=38.3\pm4.2$ with *p*-$CH_3C_4H_4SO_2^+ClO_4^-$. A plausible mechanism is proposed, in which the attacking species is TsCl-MCl_n complex in methylene chloride, but it is an ion pair, $ArSO_2^+MCl^-_{n+1}$, in nitromethane and nitrobenzene.

In part I of this series we have described the results of kinetic studies on the aluminum chloride-catalyzed *p*-toluenesulfonylation of aromatics in methylene chloride.[1] On the basis of the kinetic data, existence of the kinetic isotope effect and spectroscopic observations, it was concluded that the attacking species of aromatics was TsCl-$AlCl_3$ complex. Jensen and Brown made a kinetic study of Friedel-Crafts sulfonylation of aromatics with aluminum chloride by using nitrobenzene or benzenesulfonyl chloride as solvent, and concluded that either sulfonyl cation or ion pair $ArSO_2^+$ $AlCl_4^-$ was the species which attacked aromatics.[2] Klages and Hoheisel made a study of sulfonyl cations, but did not report the kinetic data of aromatic sulfonylation.[3] In order to clarify the mechanism of sulfonylation, we have investigated the sulfonylation of aromatics with Ts^+ ClO_4^- and with *p*-toluenesulfonyl chloride, using aluminum chloride, antimony pentachloride and titanium chloride as catalysts, and methylene chloride, nitromethane and nitrobenzene as solvents.

Experimental

Materials. The purification of *p*-toluenesulfonyl chloride, toluene, methylene chloride and aluminum chloride was described in a previous paper.[1] Anisole was shaken with sodium carbonate, dried over calcium chloride, and then distilled. Antimony pentachloride and titanium chloride were distilled. Ferric chloride was sublimed. Nitromethane and nitrobenzene were dried over calcium chloride, and then distilled. Silver perchlorate of first grade(Kojima Chemical Co., Ltd.) was used without further prification.

Syntheses of Authentic Samples. *o,p*-Ditolyl sulfone: Reaction between ethyl *p*-toluenesulfinate and *o*-tolylmagnesium bromide, prepared from *o*-bromotoluene and magnesium in ether, gave *o,p*-di-tolyl sulfoxide. Oxidation of sulfoxide, with hydrogen peroxide in acetic acid as solvent, afforded the *o,p*-ditolyl sulfone, mp 55—56°C from methanol(lit, 60°C[4]).

*1 Organic Sulfur Compounds. Part XIX.

1) Aromatic Sulfonylation. I: M. Kobayashi, H. Minato and Y. Kohara, This Bulletin, **43**, 234 (1970).

2) a) F. R. Jensen and H. C. Brown, *J. Amer. Chem. Soc.*, **80**, 4038 (1958). b) F. R. Jensen and H. C. Brown, *ibid.*, **80**, 4042 (1958). c) F. R. Jensen and H. C. Brown, *ibid.*, **80**, 4046 (1958).

3) a) F. Klages and K. Hoheisel, *Chem. Ber.*, **96**, 2057(1963). b) F. Klages and F. E. Malecki, *Ann.*, **691**, 15 (1966).

4) C. Coutot and J. Frenkiel, *Compt. Rend.*, **199**, 557(1934); *Chem. Abstr.*, **29**, 142 (1935).

m,p-Di-tolyl sulfone was prepared in a similar way from *m*-bromotoluene and ethyl *p*-toluenesulfinate, mp 112.5—113.0°C from methanol (lit, 116°C[4]). Di-(*p*-tolyl) sulfone was prepared by aluminum chloride-catalyzed *p*-toluenesulfonylation of toluene in methylene chloride, mp 155°C from methanol(lit, 157—158°C[5]). *p*-Tolyl *o*-methoxyphenyl sulfone: Reaction between sodium *p*-toluenesulfinate and *o*-nitrochlorobenzene in DMSO gave *p*-tolyl *o*-nitrophenyl sulfone. Reduction of the nitro-compound, with hydrochloric acid and stannous chloride, afforded the amino-compound, and hydrolysis of the diazonium chloride in sulfuric acid, prepared from amino-compound, afforded the *p*-tolyl *o*-hydroxyphenyl sulfone. Methylation of hydroxy-compound with dimethyl sulfate gave *p*-tolyl *o*-methoxyphenyl sulfone, mp 118.5—119.0°C from ethanol (lit, 119—120°C[6]). *p*-Tolyl *m*-methoxyphenyl sulfone: A Grignard reagent prepared from 12.5 g of *m*-iodoanisole and 1.3 g of magnesium in 50 m*l* of ether was added drop by drop to 5.0 g of ethyl *p*-toluenesulfinate in 50 m*l* of ether. An excess of dilute hydrochloric acid was then added to the reaction mixture to dissolve the oil. The organic layer was separated, washed with alkali and water, and dried over magnesium sulfate. When the solvent was evaporated, an oily residue was obtained. The oily sulfoxide was purified by elution chromatography over alumina with benzene, and 5.0 g of crystals of *p*-tolyl *m*-methoxyphenyl sulfoxide was obtained (I.R. S-O stretching at 1035 cm^{-1}). To 5.0 g of the sulfoxide in 100 m*l* of acetic acid, 20 g of 30% hydrogen peroxide was added at room temperature, and the reaction mixture was allowed to stand overnight. The solution was warmed to and kept at 50—60°C for about one hour, and the sulfone was extracted with methylene chloride. The solution was evaporated, and the red crystals were purified by elution chromatography over alumina with benzene and ether, and 2.0 g of *p*-tolyl *m*-methoxyphenyl sulfone was obtained, which was recrystallized from methanol, mp 80°C; IR. 1145 cm^{-1}($\nu_s SO_2$), 1285 and 1310 cm^{-1} ($\nu_{as} SO_2$) KBr disc;

Found: C, 63.79; H, 5.55%. Calcd for $C_{14}H_{14}O_3S$: *D*, 64.09; H, 5.39%. *p*-Tolyl *p*-methoxyphenyl sulfone was prepared by aluminum chloride-catalyzed-*p*-toluenesulfonylation of anisole in methylene chloride, mp 103.5—104.0°C from ethanol (lit, 103—104.5°C[7]).

Sulfonylation of Toluene. Two grams of *p*-toluenesulfonyl chloride and 3.0 g of aluminum chloride in 25 m*l* of nitromethane were added to 5.0 g of toluene in 25 m*l* of nitromethane at 10°C. After about 37 hr, a dilute hydrochloric acid was added to the reaction mixture. The residual *p*-toluenesulfonyl chloride was decomposed by steam distillation of organic layer, and then the sulfone which crystallized was extracted with methylene chloride. The isomer ratio of a sulfone obtained was determined by gas-chromatographic analysis on a 2 m column packed with 10% SE-30 on Chromosorb using H_2 as a carrier gas (30 m*l*/min) at 230°C; retention time: *p*-tolyl *o*-tolyl sulfone, 19.9 min, *p*-tolyl *m*-tolyl sulfone, 23.5 min, di-(*p*-tolyl) sulfone, 24.5 min.

Sulfonylation of Anisole. Sulfonylation of anisole was carried out in a manner similar to that used for toluene. Absence of 860 cm^{-1} band showed the absence of *p*-tolyl *m*-methoxyphenyl sulfone in the products. The isomer ratio of a sulfone produced was determined by gas-chromatographic analysis on a 2 m column packed with 10% SE-30 on Chromosorb using H_2 as a carrier gas (30 m*l*/min.) at 250°C; retention time, *p*-tolyl *o*-methoxyphenyl sulfone, 15.8 min, *p*-tolyl *m*-methoxyphenyl sulfone, 16.0 min, *p*-tolyl *p*-methoxyphenyl sulfone, 20.4 min, *p*-tolyl phenyl sulfone, 9.0 min.

Sulfonyation with Sulfonyl Cation. *p*-Toluenesulfonyl perchlorate was prepared from *p*-toluenesulfonyl chloride and silver perchlorate by Klages' method.[3b] The solution of the *p*-toluenesulfonyl perchlorate was added to the solution of an aromatic substrate. The reaction mixture was kept at 10°C overnight, then the sulfone produced was separated by extraction with methylene chloride and analyzed by gas chromatography.

Measurement of Relative Rates by Competitive Sulfonylation. The relative rates were determined by a method similar to that used for measurements of isomer ratios. Gas-chromatographic conditions; 10% SE-30 on Chromosorb, 3 m, H_2 as carrier gas (40 m*l*/min) at 240°C, retention time; *p*-tolyl phenyl sulfone, 15.5 min., *p*-tolyl *o*-tolyl sulfone 19.2 min, *p*-tolyl *m*-tolyl sulfone, 21.0 min, di-(*p*-tolyl) sulfone, 22.5 min.

Results and Discussion

Results concerning the orientation for the *p*-toluenesulfonylation of toluene are summarized in Table 1. The orientation for sulfonylation of toluene with antimony pentachloride and titanium chloride in methylene chloride agreed with the data for aluminum chloride in methylene chloride within the limit of error of gas-chlomatographic analysis. The agreement among the values of orientation for the reactions catalyzed by aluminum chloride, antimony pentachloride or titanium chloride in nitromethane or nitrobenzene is also satisfactory. These values were not in accord with the values obtained in methylene chloride.

Klages and Malecki reported on the formation of sulfonyl cation;[3b] *i.e.* *p*-toluenesulfonyl cation was prepared from *p*-toluenesulfonyl bromide and silver perchlorate in nitromethane. Measurement of electroconductivity indicated that not a free sulfonyl cation but an equilibrium mixture of covalent-bonded(I) and ionized(II) was present in the medium as shown below.

$$\underset{(I)}{Ts\text{-}OClO_3} \rightleftarrows \underset{(II)}{Ts^+ClO_4^-} \xrightarrow{ArH} TsAr + HClO_4 \qquad (1)$$

Sulfonylation of an aromatic substrate with sulfonyl cation (II) took place when the aromatics

5) G. Holt and B. Pagdin, *J. Chem. Soc.*, **1960**, 2508.

6) A. A. Aleykutty and V. Baliah, *J. Indian Chem. Soc.*, **31**, 513(1954); *Chem. Abstr.*, **50**, 219 (1956).

7) H. H. Szmart and G. Suld, *J. Amer. Chem. Soc.*, **78**, 3400 (1956).

TABLE 1. ORIENTATIONS FOR THE *p*-TOLUENESULFONYLATION OF TOLUENE UNDER VARIOUS CONDITIONS AT 10°C

Catalysts \ Solvents		CH_2Cl_2	$PhCH_3$	$PhNO_2$	CH_3NO_2	
$AlCl_3$	*o*	13.4*		42.4	44.6	
	m	0		3.4	—	
	p	86.6		54.2	55.4	
$SbCl_5$	*o*	13.2	31.8	44.1	42.0	
	m	—	—	—	—	
	p	86.8	68.2	55.9	58.0	
$TiCl_4$	*o*	8.6		42.7	45.7	
	m	—		—	—	
	p	91.4		57.3	54.3	
$FeCl_3$	*o*	32.8[a,b]				
	m	—				
	p	67.2				
$Ts^+ClO_4^-$	*o*	35.2[a,b]	37.6[a]	42.7	46.3[a]	44.8
	m	—	—	—	—	—
	p	64.8	62.4	57.3	53.7	55.2

a) at room temperature
b) heterogeneous conditions
* Ref. 1.

was added to this solution.[3b,8]

The orientation for the Lewis acid-catalyzed sulfonylation in nitromethane or nitrobenzene agrees fairly well with the orientation for sulfonylation with tosyl perchlorate solution as seen in Table 1. This fact suggests that the attacking species in the sulfonylation with tosyl perchlorate system was the same as that of the Lewis acid-catalyzed sulfonylation in nitromethane or nitrobenzene, namely sulfonyl cation (II)-like species for both reactions.

Partial rate factors for sulfonylation of toluene are determined by competitive experiments and shown in Tables 2 and 3.

Those values at *para* position were 31.4±2.0 for aluminum chloride-catalyzed sulfonylation in nitromethane and 38.3±4.2 for sulfonylation with sulfonyl cation in nitromethane. The value for the aluminum chloride-catalyzed sulfonylation in methylene chloride was 52.5.[1] Both orientation and partial rate factors clearly indicate that the attacking species in methylene chloride was different from those in nitromethane or nitrobenzene.

TABLE 2. RELATIVE RATES FOR THE ALUMINUM CHLORIDE-CATALYZED *p*-TOLUENESULFONYLATIONS OF TOLUENE AND BENZENE IN NITROMETHANE AT 10°C

Run	$[PhCH_3]_0/[PhH]_0$*	Obs. rel. rate	k_T/k_B
1	0.993	9.00	9.06
2	0.452	4.14	9.15
3	0.263	2.64	10.06

$k_T/k_B = 9.42 \pm 0.64$
$o_f = 12.6 \pm 0.9$, $m_f \fallingdotseq 0$, $p_f = 31.4 \pm 2.0$
* Molar ratio of the initial concentrations.

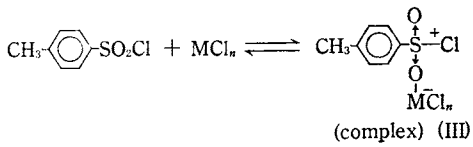
TABLE 3. RELATIVE RATES FOR THE *p*-TOLUENESULFONYLATION OF TOLUENE AND BENZENE WITH *p*-TOLUENESULFONYL CATION IN IN NITROMETHANE AT 10°C

Run	$[PhCH_3]_0/[PhH]_0$*	Obs. rel. rate	k_T/k_B
1	0.981	10.58	10.78
2	0.472	5.36	11.36
3	0.297	3.86	13.00

$k_T/k_B = 11.72 \pm 1.28$
$o_f = 16.0 \pm 1.7$, $m_f \fallingdotseq 0$, $p_f = 38.3 \pm 4.2$
* Molar ratio of the initial concentrations.

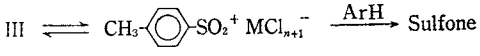
Sulfonylation with a sulfonyl perchlorate in nitromethane and nitrobenzene is less selective than that in methylene chloride and toluene. This finding suggests that the attacking species in the sulfonylation with sulfonyl perchlorate in nitromethane and nitrobenzene were in a relatively free states, whereas the attacking species in methylene chloride or toluene was bulky, less reactive. In order to explain the results of *p*-toluenesulfonylation under various conditions, a plausible mechanism is proposed, which involves several attacking species with various degrees of charge separation. The results of orientation and partial rate factors indicate that; sulfonylations catalyzed by aluminum chloride, antimony pentachloride and titanium chloride in methylene chloride proceed through (2), but sulfonylation in nitromethane and nitrobenzene proceeds through (2), (3) and (4); the

8) H. Burton and H. B. Hopkins, *J. Chem. Soc.*, **1952**, 4457.



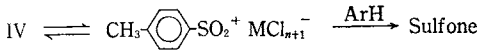
(complex) (III)

$$\xrightarrow{ArH} \text{Sulfone} \quad (2)$$



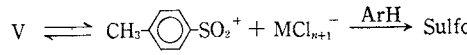
$$\xrightarrow{ArH} \text{Sulfone} \quad (3)$$

(contact ion pair)
(IV)



$$\xrightarrow{ArH} \text{Sulfone} \quad (4)$$

(solvent-separated ion pair)
(V)



$$\xrightarrow{ArH} \text{Sulfone} \quad (5)$$

antimony pentachloride-catalyzed sulfonylation in toluene proceeds through (2) and (3); the aluminum chloride-catalyzed benzenesulfonylation of chlorobenzene in benzenesulfonyl chloride as solvent[2b] proceed through (2), (3), (4) and (5). The energy relationship among these attacking species may be represented by a free energy diagram shown in Fig. 1. The formation of various attacking species could be partially attributed to the difference in solvating power of the solvents. Four attacking species expressed in this diagram, namely the complex, contact ion pair, solvent-separated ion pair and free cation should not be considered to be distinctly differentiated from each other as shown in Fig. 1

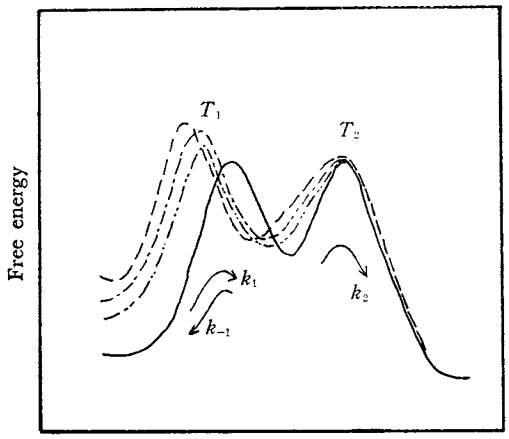


Fig. 1. Free energy diagram for the possible intermediates in the sulfonylation.
——— free cation
——— solvent-separated ion pair
——— contact ion pair
——— complex

and (1)—(5), and the bond strength between sulfonyl group and counter ion varies continuously with the solvents and counter ions. If the aromatic substrate is highly reactive, it can be attacked by sulfonyl chloride-metal chloride complex. Since the reactivity of the complex is low, both its substrate and positional selectivity are high. On the other hand, attacking species similar to free sulfonyl cation is highly reactive and therefore, should have low selectivity. In fact, kinetic evidence supported these suggestions. Kinetic hydrogen isotope effects were observed in sulfonylation with TsCl-$AlCl_3$ complex in methylene chloride,[1] but was not detected in benzenesulfonylation in benzenesulfonyl chloride,[2b] where the sulfonylation was considered to be effected with solvent separated ion pair or free cation. These findings may be explained by the energy diagram in Fig. 1. The difference of energy between reactant and transition states T_1 is small for free cation or ion pair, and considerably large for complex. Transition states T_1 for the complex may be reached in the later stage along the reaction coordinate, where C–H bond length may be stretched much longer than that in T_1 for free sulfonyl cation. On the other hand, the energy difference among transition states T_2 for all attacking species will be very small. Forward rate constant k_2 should be smaller than k_{-1} or at least in comparable order of magnitude with k_{-1} for complex, resulting in kinetic hydrogen isotope effects. For the free cation or solvent-separated ion pair, k_2 should be larger than k_{-1}, and no kinetic isotope effects should be present.

The reaction between arenesulfonyl chloride and such highly reactive aromatics as *m*-dimethoxybenzene in the presence of zinc chloride in aromatic solvent was found to afford a sulfone and attributed to the intermediate formation of the sulfonyl cation.[9] Considering the fact that zinc chloride is a weak Lewis acid and *m*-dimethoxybenzene is a less polar solvent, it seems that a true attacking species was complex or contact ion pair under these reaction conditions.

Orientation for the sulfonylation of anisole is shown in Table 4.

Table 4. Orientation for the sulfonylation of anisole

Catalysts	Solvents	Temp. (°C)	Orientation (%)		
			o-	*m*-	*p*-
$AlCl_3$	CH_2Cl_2	20	38.5	0	61.5
$AlCl_3$	CH_3NO_2	20	40.3	—	59.7
$AlCl_3$	$PhNO_2$	20	42.0	—	58.0
*	CH_3NO_2	10	35.1	—	64.9

* Sulfonylation with $CH_3C_6H_4SO_2^+ClO_4^-$.

9) H. Burton and E. Hoggarth, *ibid.*, **1945**, 14.

The difference in the orientation is less clear than in the cases of other aromatics. It is reasonable that the difference in the reactivity is less clear since anisole is very reactive and reacts with various attacking species of different reactivity more evenly. Partial rate factors for the sulfonylation of anisole catalyzed with aluminum chloride in nitromethane at 10°C were found to be $o_f=50.7$, $m_f \fallingdotseq 0$, $p_f=150$ ($k_{PhOCH_3}/k_{PhH}=41.9$) by competitive experiments. These values are extremely small compared with those of ordinary electrophilic aromatic substitutions ($p_f=1.8\times10^6$ for acetylation[10] and $p_f=1.1\times10^{10}$ for bromination[11]). Plausible explanations for this anomaly is that the reactivity of anisole was depressed by formation of $PhOCH_3$–$AlCl_3$ complex and the concentration of the remaining free anisole was very low for the same reasons.

On the basis of orientation, partial rate factors and other kinetic data, it is concluded that the attacking species varies with the conditions and is a complex, a contact ion pair, a solvent-separated ion pair or a free cation.

10) H. C. Brown and G. Marino, *J. Amer. Chem. Soc.*, **84**, 1658 (1962).

11) L. M. Stock and H. C. Brown, *ibid.*, **82**, 1942 (1960).