# Steric Hindrance in the Reaction of Aromatic Sulphonyl Chlorides with Anilines. Effect of 2-Methyl and 2,6-Dimethyl Substituents in Aniline

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The rates of reaction in methanol of substituted benzenesulphonyl chlorides with anilines are retarded by *ortho*-methyl substituents in the aniline. The rates for 2-methyl- and 2,6-dimethyl-aniline deviate from the Brønsted plot established by 3- and 4-substituted anilines. This is attributed to a steric effect. The steric effect, which is a function of the electron-withdrawing power of the substituents in the sulphonyl chloride, decrease in the series $p$-NO$_2$ > $p$-I > $p$-Me > $p$-MeO. This is consistent with the idea that the transition state becomes looser with electron-donating substituents in the sulphonyl chloride.

RATE constants for the reaction of aromatic sulphonyl chlorides with 3- and 4-substituted anilines have been reported.[1] These data were interpreted in terms of a direct nucleophilic displacement mechanism with a transition state becoming progressively looser (decreased bond formation) with increasing electron-donating power of the substituents in the sulphonyl chloride. To extend this work, the rates and activation parameters for the reaction of 2-methyl- and 2,6-dimethyl-aniline with a series of *para*-substituted benzenesulphonyl chlorides have been measured. On the basis of the mechanism mentioned above, a progressive decrease in rate owing to steric interference is expected upon introduction of one and two *ortho*-methyl groups in the nucleophile. Further, since bond formation in the transition state is said to decrease with electron-donating substituents in the sulphonyl chloride, the steric hindrance should also decrease with such substituents.

## EXPERIMENTAL

*Materials*.—The sulphonyl chlorides were as described previously.[1] Aniline, 2-methylaniline, and 2,6-dimethylaniline were commercial samples and were fractionally distilled before use. Methanol containing $\leqslant 0{\cdot}05\%$ water (Merck) was used throughout.

*Rate Measurements*.—Rates were measured conductometrically with a Radiometer Conductivity Meter CDM3 connected to a Sargent Recorder SRL and a Radiometer conductivity cell type PP 1042. The reaction was started by adding 0·010 ml of a solution of the sulphonyl chloride in acetone to 25·0 ml of a solution of the aniline in methanol (aniline concentration 0·05—0·50M; final concentration of sulphonyl chloride *ca.* $4 \times 10^{-4}$M). The observed first-order rate constants were calculated from the resulting conductivity–time curve by Guggenheim's method [2] or by fitting the data to the equation $x = a(1 - e^{-kt})$ by use of an Olivetti Programma 102. Second-order rate constants were calculated from the slopes of plots of the observed first-order rate constants against aniline concentration. Rate constants are estimated to be accurate to ±5% or better. Activation parameters were calculated at 25 °C in the usual way from Arrhenius plots.[3] The estimated precision is *ca.* $\pm 0{\cdot}5$ kcal mol$^{-1}$ in $\Delta H^‡$ and *ca.* $\pm 2$ cal mol$^{-1}$ K$^{-1}$ in $\Delta S^‡$.

Products were not isolated since the well known formation of sulphonanilides from sulphonyl chlorides and anilines [4,5] was confirmed in a previous study.[1]

## RESULTS

The reaction between sulphonyl chlorides and anilines in organic solvents takes place according to equation [4,5] (1).

$$R^1SO_2Cl + 2H_2NR^2 = R^1SO_2{\cdot}NHR^2 + H_3\overset{+}{N}R^2 + Cl^- \quad (1)$$

Sulphonanilides are the predominant product in alcohol since alcoholysis [6,7] of sulphonyl chlorides is slow compared with their reactions with anilines.[1]

The observed rates of reaction with anilines in large excess over sulphonyl chloride were of the first order. Plots of the observed first-order rate constants against concentration of aniline were linear showing that the reaction is of first order in aniline. The second-order rate constants, obtained from the slopes of the plots of the observed first-order rate constants against aniline concentration, together with the activation parameters, are in Table 1.

When the reactions were run to completion (10 half-lives), the infinity value increased slowly with time. This is probably due to reaction of the methyl sulphonate ester with methanol [8,9] and amine.[9] This only affected the kinetics significantly in the case of the slowly reacting 2,6-dimethylaniline, where deviations from first-order kinetics occurred. In these cases the observed first-order rate constants were calculated from the first part (1·5—2 half-lives) of the conductivity–time curve by the computer. The estimated precision of these rate constants is ±5% whereas it is ±3% for the others.

## DISCUSSION

The reaction of aromatic sulphonyl chlorides with anilines has been formulated as a direct one-step nucleophilic substitution at the sulphur atom.[1] The progressive decrease in rate observed upon introduction of one and two *ortho*-methyl groups in aniline (Table 1) is consistent with such a mechanism. This rate reduction could conceivably be caused by either steric strain or steric inhibition to solvation in the transition state. These two possibilities can be distinguished by the effect on $\Delta S^‡$ since steric inhibition to solvation should in-

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TABLE 1

Rate constants and activation parameters for the reaction of aniline (I), 2-methylaniline (II), and 2,6-dimethylaniline (III) with substituted benzenesulphonyl chlorides in methanol

| Sulphonyl chloride | Amine | $10^2k$/l mol$^{-1}$ s$^{-1}$ 15 °C | 25 °C | 35 °C | $\Delta H^‡$/kcal mol$^{-1}$ | $\Delta S^‡$/cal mol$^{-1}$ K$^{-1}$ |
|---|---|---|---|---|---|---|
| $p$-$NO_2\cdot C_6H_4\cdot SO_2Cl$ | (I) | 26·4 | 41·9 | 62·8 | 7·1 | −36 |
| | (II) | 4·43 | 7·48 | 11·5 | 7·8 | −37 |
| | (III) | 0·187 | 0·331 | 0·570 | 9·2 | −39 |
| $p$-$IC_6H_4\cdot SO_2Cl$ | (I) | 7·07 | 11·5 | 18·2 | 7·8 | −36 |
| | (II) | 1·49 | 2·58 | 4·15 | 8·4 | −37 |
| | (III) | 0·0715 | 0·132 | 0·244 | 10·2 | −37 |
| $PhSO_2Cl$ | (I) | 3·98 | 6·86 | 11·5 | 8·8 | −34 |
| | (II) | 0·926 | 1·66 | 2·79 | 9·1 | −36 |
| | (III) | 0·0512 | 0·0959 | 0·185 | 10·7 | −36 |
| $p$-$MeC_6H_4\cdot SO_2Cl$ | (I) | 2·78 | 4·75 | 8·52 | 9·2 | −33 |
| | (II) | 0·648 | 1·19 | 1·98 | 9·3 | −36 |
| | (III) | 0·0422 | 0·0833 | 0·158 | 11·0 | −36 |
| $p$-$MeO\cdot C_6H_4\cdot SO_2Cl$ | (I) | 1·55 | 2·75 | 5·11 | 9·9 | −32 |
| | (II) | 0·406 | 0·783 | 1·32 | 9·8 | −35 |
| | (III) | 0·0344 | 0·0688 | 0·124 | 10·7 | −37 |

crease whereas steric strain should decrease $\Delta S^‡$.[10] In the present case the low precision and small differences in $\Delta S^‡$ make a firm conclusion difficult. There is, however, a trend in the data in that $\Delta S^‡$ for 2,6-dimethylaniline is always less than that for aniline. Thus an explanation in terms of steric strain is favoured.

TABLE 2

Equations for lines generated by plotting log $k$/l mol$^{-1}$ s$^{-1}$ against p$K_a$ (Brønsted plots) for reactions of 3- and 4-substituted anilines with substituted benzenesulphonyl chlorides in methanol at 25 °C. The equations were obtained from a least-squares treatment of data in ref. 1

| Sulphonyl chloride | |
|---|---|
| $p$-$NO_2\cdot C_6H_4\cdot SO_2Cl$ | $\log k = 0·927\ \mathrm{p}K_a - 4·589$ |
| $p$-$IC_6H_4\cdot SO_2Cl$ | $\log k = 0·823\ \mathrm{p}K_a - 4·634$ |
| $PhSO_2Cl$ | $\log k = 0·749\ \mathrm{p}K_a - 4·539$ |
| $p$-$MeC_6H_4\cdot SO_2Cl$ | $\log k = 0·690\ \mathrm{p}K_a - 4·426$ |
| $p$-$MeO\cdot C_6H_4\cdot SO_2Cl$ | $\log k = 0·654\ \mathrm{p}K_a - 4·475$ |

TABLE 3

Deviations [Δ log $k$ = log $k$(calculated) − log $k$(observed)] of 2-methyl- and 2,6-dimethyl-aniline from the Brønsted lines established by the reaction of 3- and 4-substituted anilines with sulphonyl chlorides. The log $k$(calculated) values were obtained from the appropriate equation in Table 2 and a p$K_a$ * of 4·45 and 3·95 for 2-methyl- and 2,6-dimethyl-aniline respectively

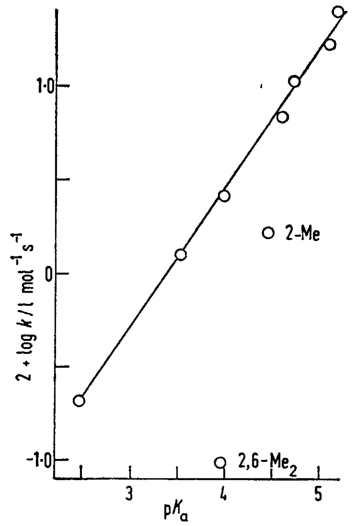
| Sulphonyl chloride | Δ log $k$ 2-Methylaniline | 2,6-Dimethylaniline |
|---|---|---|
| $p$-$NO_2\cdot C_6H_4\cdot SO_2Cl$ | 0·662 | 1·551 |
| $p$-$IC_6H_4\cdot SO_2Cl$ | 0·617 | 1·495 |
| $PhSO_2Cl$ | 0·572 | 1·437 |
| $p$-$MeC_6H_4\cdot SO_2Cl$ | 0·570 | 1·379 |
| $p$-$MeO\cdot C_6H_4\cdot SO_2Cl$ | 0·541 | 1·270 |

* In aqueous solution at 25 °C, from D. D. Perrin, ' Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965.

In the reaction of 3- and 4-substituted anilines with various substituted benzenesulphonyl chlorides,[1] it was found that each sulphonyl chloride gave a Brønsted plot with a slope depending upon the electron-attracting power of the substituent in the sulphonyl chloride.

2-Methyl- and 2,6-dimethyl-aniline show deviations from these Brønsted plots as shown in the Figure for benzenesulphonyl chloride. This is in agreement with the general observation that steric interferences usually causes deviations from linear free-energy relationships.[11]

The vertical displacement of 2-methyl- and 2,6-dimethyl-aniline from the Brønsted line (Figure) is equal to Δ log $k$ = log $k$(calculated) −log $k$(observed). Values of Δ log $k$ for the various sulphonyl chlorides are summarized in Table 3. These values, which decrease steadily from the $p$-nitro- to the $p$-methoxy-compound, show a correlation with the σ values of the sulphonyl chloride substituents.† This means that the Hammett plots generated by $k$(calc.) and $k$(obs.) have different



Brønsted plot, for the reaction of anilines with benzenesulphonyl chloride in methanol at 25 °C, showing the deviation of 2-methyl- and 2,6-dimethyl-aniline from the line established by 3- and 4-substituted anilines. The points falling on the line (from ref. 1) are from the top: 3,4-dimethylaniline, 4-methylaniline, 3-methylaniline, aniline, 4-chloroaniline, 3-chloroaniline, and 3-nitroaniline

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† A least-squares treatment of Δ log $k$ against σ (σ values from ref. 1) gave slopes of 0·104 ± 0·009 ($r$ = 0·990) and 0·226 ± 0·045 ($r$ = 0·946) for 2-methylaniline and 2,6-dimethylaniline respectively.

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[11] L. P. Hammett, ' Physical Organic Chemistry,' McGraw-Hill, New York, 1970, 2nd edn., p. 319.

$\rho$ values. Since similar Hammett plots obtained for reactions of **3**- and 4-substituted anilines, where steric effects are absent, have $\rho$ values linearly related to the $pK_a$ of the aniline,[1] one should on the basis of electronic effects alone expect $\rho$(calc.) = $\rho$(obs.) since $k$(calc.) and $k$(obs.) are based on the same $pK_a$. It seems reasonable, therefore, to assume that the difference in the $\rho$ values arise from a steric effect and that $\Delta \log k$ may be taken as a measure of this effect. The regular variation in $\Delta \log k$ with the sulphonyl chloride substituents thus shows that the steric effect decreases with increasing electron donation to sulphur. This is consistent with a previous conclusion [1] that the transition state becomes looser with electron-donating substituents in the sulphonyl chloride.

I thank Mrs. I. Heggen for experimental assistance.

[1/1471 *Received*, 16*th August*, 1971]