Substituent Effect of the Sulphinyl Group in Electrophilic Aromatic Substitution

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Partial rate factors have been determined for molecular chlorination in nitromethane and protodesilylation in H_2SO_4–AcOH mixtures of methyl phenyl and diphenyl sulphoxide. The electron-activating effect observed in molecular halogenation is interpreted in terms of polarization of the sulphoxide group in the transition state, induced by the electrophilic reagent. In H_2SO_4–AcOH mixtures k_{rel} for protodesilylation at the *para*-position of methyl phenyl sulphoxide is very low, possibly because of hydrogen bonding between the sulphinyl group and the acidic medium. For methyl phenyl sulphide, sulphoxide, and some other compounds the ground state electron densities at the *para*-position have been evaluated from their ^{13}C n.m.r. spectra.

THE effects of sulphinyl groups on the spectra and chemical reactivity of aromatic compounds have already been the subject of many papers.[1] However, in spite of the extensive investigations carried out, the properties of the sulphinyl group are still under debate. The available [2] σ constants and the activation shown in the nucleophilic displacement of *p*-chloro- and *p*-iodo-substituents in diphenyl sulphoxides,[3] indicate that this group is electron withdrawing. On the same grounds Szmant [4] has argued that the substituent effect of the sulphinyl group in electrophilic substitutions should lead mainly to the *meta*-product. However results have been reported in which the sulphinyl group is *para* directing, *e.g.* in nitration in fuming nitric acid [5a] and in molecular bromination.[5b]

In order to assess quantitatively the role of the sulphinyl group in electrophilic aromatic substitutions we have studied the reactivity of methyl phenyl and diphenyl sulphoxide with several electrophiles and the results are reported herein.

RESULTS AND DISCUSSION

The nature of the electrophilic reagent and of the reaction medium are of critical importance in studying the electrophilic substitution of sulphoxides since in many cases sulphones or side products are formed in sizeable amounts making the analysis of the reaction mixture difficult. To avoid such complications, molecular halogenation and protodesilylation have been studied in detail. The isomer distributions for molecular bromination and chlorination in various solvents are reported in Table 1.

Monosubstitution products were obtained (see Experimental section) in high yields; for diphenyl derivatives, minor amounts of *p,p'*-disubstituted derivatives, not exceeding 4%, have been characterized by g.l.c. and mass spectrometric analysis. Chlorination appears more suitable than bromination for a detailed kinetic study; in fact in spite of its lower selectivity [6] molecular chlorination is much faster than bromination, and obeys a simple kinetic law [7] over a wide range of concentrations. The chlorination rates of Ph_2SO, Ph_2S, and other reference compounds have been measured in nitromethane since this solvent offers several advantages such as (i) a large rate acceleration with respect to AcOH and other solvents,[7] (ii) the absence of homolytic reactions,[8] and (iii) the absence of side reactions such as the reduction of the sulphinyl group.[5b] The second-order rate constants for molecular chlorination are collected in Table 2.

TABLE 1

Isomers distributions for non-catalytic halogenation of C_6H_5X

X	Solvent	Electrophile	Temp. (°C)	Isomer distribution (%) *o*	*m*	*p*
SOMe	CCl_4	Bromine	110	2·5		97·5
SOMe	CCl_4–AA [a]	Bromine	110	4		96
SOMe	$MeNO_2$	Bromine	80	1		99
SMe	CCl_4	Bromine	110	6·5		93·5
SOPh	$MeNO_2$	Chlorine	80	5	8	87
SPh	$MeNO_2$	Chlorine	80	20·8	2·7	76·5
Cl	$MeNO_2$	Chlorine	80	29·5		70·5
Br	$MeNO_2$	Chlorine	80	33·5		66·5

[a] 18% w/w Acetic acid.

First-order coefficients have also been determined for the protodesilylation at the *para*-position in methyl phenyl sulphoxide. In the range of acidities explored, however, allowance must be made for the protonation of the sulphoxide group. Previously [9] it has been shown that the ionization of sulphoxides correlates to a

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[8] G. Illuminati and G. Marino, *Gazzetta*, 1954, **84**, 1127.

[9] D. Landini, G. Modena, G. Scorrano, and F. Taddei, *J. Amer. Chem. Soc.*, 1969, **91**, 6703.

good approximation with the H_A acidity function in strong sulphuric acid; the assumption that this relationship also holds in the H_2SO_4–AcOH mixtures used in this study is supported by the good sigmoid curves obtained by plotting the chemical shifts (Δν) of the protonated and unprotonated sulphoxide at various sulphuric acid concentrations against the corresponding H_A functions (see Table 6) and by the slope of the plot log $[BH^+]/[B]$ against H_A which is very close to unity (1·07). The rate constants $k_{\text{free base}}$ can thus

TABLE 2

Second-order rate constants for the non-catalytic chlorination of C_6H_5X in nitromethane at 25°

X	$10^3[ArH]_i$/M	$10^3[Cl_2]_i$/M	10^4k/l mol^{-1} s^{-1}
H	662	28·9	0·068 [a]
	203	26·2	0·070
	123	15·3	0·072
Me	366	35·0	108·00
Cl	338	26·3	0·0063
	441	33·5	0·0060
SOPh [b]	54·2	7·3	3·261
	94·9	16·0	3·086
	91·3	33·3	3·341
SPh [b]	48·27	3·9	5245·0
Br	348	28·2	0·0030
	286	31·3	0·0030

[a] Ref. 6. [b] The observed rate constants have been halved to allow for the availability of two equivalent aromatic rings.

$$\log_{10}k_{\text{free base}} = \log_{10}k_{\text{stoich}} + pK_a - H_A \qquad (1)$$

be calculated from equation (1)[10] where k_{stoich} represents the stoicheiometric monomolecular rate, H_A is the acidity function measured in H_2SO_4–AcOH solution, and the pK_a is given by the H_A value corresponding to half-protonation. The variation with the acidity of k_{stoich} and $k_{\text{free base}}$ is shown in Table 3.

TABLE 3

Variation of the rate of protodesilylation of methyl *p*-trimethylsilylphenyl sulphoxide with acidity at 50 ± 0·3°

H_2SO_4 % [a]	$-H_A$	log k_{stoich}	log $k_{\text{free base}}$
70·18	−2·78	−3·14	−2·61
75·11	−2·90	−2·90	−2·25
76·00	−2·96	−2·84	−2·13
80·54	−3·15	−2·50	−1·60
85·26	−3·35	−2·20	−1·10

[a] Concentration of aqueous acid 7·5 ml of which was mixed with 10 ml of glacial acetic acid.

The ^{13}C n.m.r. spectra of methyl phenyl sulphoxide, sulphide, and related compounds have also been recorded and are listed in Table 4.

TABLE 4

^{13}C Chemical shifts [a] of substituted benzenes in acetone–benzene

X	δ_X	δ_o	δ_m	δ_p	$\delta_p - \delta_m$
OMe [b]	+30·2	−14·7	+0·9	−8·1	−9·0
OH [c]	+26·9	−12·7	+1·4	−7·3	−8·7
SMe	+10·6	−1·77	+0·64	−3·42	−4·06
Cl [b]	+6·4	+0·16	+1·0	−2·00	−3·00
Me	+8·9	+0·7	−0·1	−2·9	−2·8
SOMe	+16·8	−7·04	−1·31	−2·29	−0·98
COMe	+9·17	+0·34	0·0	−4·67	+4·67
NO_2	+20·0	+4·8	+0·9	+5·8	+4·9
SO_2Me	+13·3	+13·3	−1·02	+5·27	+6·29

[a] p.p.m. Relative to internal benzene; positive shifts based on tetramethylsilane convention. [b] See ref. 17*a*. [c] See ref. 17*b*

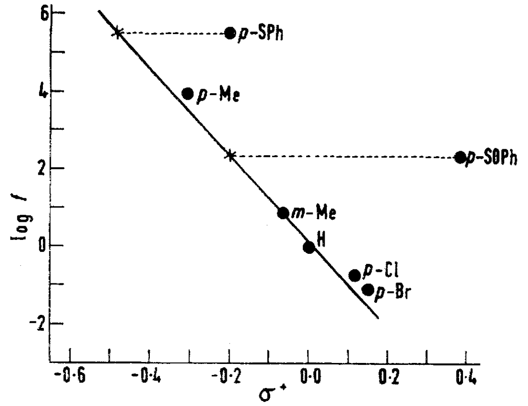
TABLE 5

Partial rate factors for non-catalytic chlorination of C_6H_5X in nitromethane at 25°

	Partial rate factors		
X	f_o	f_m	f_p
SPh			341,600
Me [a]	2430	8·3	9500
SOPh	6·94	11·10	241
Cl	0·08		0·189
Br			0·085

[a] L. M. Stock and H. Himoe, *J. Amer. Chem. Soc.*, 1961, **83**, 4605.

Results in Table 1 show that in molecular halogenation the sulphinyl group exhibits a predominant *ortho*- and *para*-directing effect. Correlation of the partial rate factors (Table 5) derived from Tables 1 and 2 with the electrophilic substituent constants exhibits a linear free energy relationship based on the available[11] σ^+ data (Figure) but a serious discrepancy exists for the *p*-phenylsulphinyl substituent which requires a σ^+ value of −0·19 in striking contrast with that (+0·386) previously[2] reported. The activating effect of the *p*-phenylsulphinyl group in molecular chlorination is in disagreement with the view[4] which places the electron-withdrawing power of the sulphinyl group above that of *m*-halogeno and *m*-formyl substituents and is also incompatible with its activating effect in nucleophilic substitutions.[3] A plausible explanation for the behaviour of the sulphinyl group towards molecular chlorine lies in the importance of polarizability as a factor in the determination of the electrical influences of substituent groups. Recently[12] the polarizability



Plot of log *f* against σ^+ for chlorination by molecular chlorine; σ^+ values are taken from refs. 2 and 11

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[10] C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, and M. Viney, *J. Chem. Soc. (B)*, 1967, 1204.

[11] L. P. Hammett, 'Physical Organic Chemistry,' McGraw-Hill, New York, 1970, p. 356; R. O. C. Norman and R. Taylor, 'Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam, 1965, p. 287.

[12] F. P. Bailey and R. Taylor, *J. Chem. Soc. (B)*, 1971, 1446, and references therein.

of second-row elements has been recognized to be an important factor in the electrophilic reactivity of substrates bearing phenylthio- and methylthio-substituents and it is not unreasonable to assume that this would be true also for the sulphinyl group. For the least reactive electrophiles, molecular halogens, there is in fact a large requirement for an electron pair to be supplied for bond formation in the transition state; this demand for resonance stabilization can greatly enhance the ability of the sulphinyl group to interact mesomerically with the benzene ring to the extent that a net electron supply occurs, giving rise to the activating effect observed in molecular chlorination. The deviation from linearity in the Figure shown by the *para*-phenylthio-substituent can also be explained in terms of the polarizability of second-row element; the σ^+ value required to correlate the chlorination data is $-0{\cdot}50$ in good agreement with that ($-0{\cdot}47$) previously found in detritiation [12] in which the demand for resonance stabilization of the transition state is very large.

The reactivity pattern in protodesilylation offers a different picture from that in halogenation. Protodesilylation rates are generally well correlated by the Yukawa–Tsuno relationship and comparison of results in Table 3 with values obtained in earlier studies,[13] indicates that the value of 0·4 for 10^2k_{rel} for the *p*-methylsulphinyl group lies between those for the *m*-Cl and *m*-CF_3 substituents. Thus the sulphinyl group behaves as an electron-withdrawing substituent in this reaction. The discrepancy observed in relation to the effect of the *p*-sulphinyl group in molecular halogenation and protodesilylation, can, in principle, be the consequence of the different polar character of the media used. The interaction between the acidic medium and the sulphinyl group is not in fact a simple protonation to give the conjugate acid since the ability [14] of the sulphinyl group to participate in hydrogen bonding is likely to increase its electron-withdrawing effect in H_2SO_4–AcOH solution with respect to nitromethane, thus accounting for the observed low reactivity in protodesilylation. The different demand of the two reactions studied on the polarizability of the substituent offers an alternative explanation for the observed discrepancy. However evaluation of the σ constant for protodesilylation by means of the Yukawa–Tsuno equation by using the previous [15] r and ρ values and the σ^+ value (*para*) deduced from chlorination leads to σ_p 1·75 thus indicating that the effect of the differential demand of the two reactions is certainly here overshadowed by the hydrogen bonding effect and cannot be evaluated unambiguously.

Finally the ^{13}C n.m.r. data in Table 4 deserve some comment since they are a very useful measure of π-electron densities in the ground state. From data in Table 4 the corrected *para*-shifts $\delta_p - \delta_m$ which reflect the resonance contribution to the local π electron density in the neighbourhood of the *para*-carbon [16] show a stepwise decrease of electron density at the *para*-position in the order SMe, SOMe, SO_2Me. Comparison with other compounds [16] in Table 4 indicates that the sulphinyl group in the above sequence falls very close to hydrogen. In the aprotic medium a certain amount of polarization of the sulphinyl group towards the phenyl ring is therefore present even in the ground state.

In the absence of specific solvent–substrate interactions, polarization of the aromatic substituent induced by the reagent appears therefore to be of importance for determining the effect of the *p*-sulphinyl group on the reactivity. A significant influence of this kind is also displayed by a *p*-fluorine atom which acts as weakly activating (negative σ^+ value) in bromination [17] and weakly deactivating in nitration.[18] This similarity between the sulphinyl and halogeno-groups has also been observed by Mangini and his co-workers in a spectroscopic study [19] from which the coupling of the unshared electrons of the sulphur atom with the aromatic ring supports a certain amount of electron release by the sulphinyl group, while in the presence of $+M$ substituents electron withdrawal seems to predominate, in line with the effect of this substituent in the transition state.

EXPERIMENTAL

Materials.—Acetic acid and carbon tetrachloride were purified by literature methods.[20] Nitromethane was purified by treatment with chlorine followed by repeated distillations through a Vigreux column as previously described.[6] AnalaR chlorine and bromine were used for halogenation. *Methyl* 4-*trimethylsilylphenyl sulphoxide* was synthesized by oxidation of the parent sulphide [12] with the stoicheiometric amount of *m*-chloroperbenzoic acid in chloroform. After washing with aqueous sodium hydrogen carbonate chloroform was evaporated off and the residual oil distilled under high vacuum to give the sulphoxide (80%), b.p. 120° at 0·1 mmHg (Found: C, 56·8; H, 7·4; S, 15·4. $C_{10}H_{16}OSSi$ requires C, 56·55; H, 7·6; S, 15·1%).

Product Distribution.—The isomer ratios in bromination and chlorination were established by g.l.c. as outlined below. A solution of the sulphide (6 mmol) in nitromethane (5 ml) and a 0·3M-solution of chlorine or bromine (6·6 ml, 2 mmol) in nitromethane in a sealed Carius tube was warmed in the dark at 85° during 8 h. After this period the solvent was evaporated off and the residue was dissolved in CS_2 (10 ml) and analysed by g.l.c. at 190° on a 150 cm (1/8 in) column of 5% Bentone on Chromosorb W (80—100 mesh).

Identification of the peaks was performed by comparison with model chloro- and bromo-sulphides prepared by literature methods.[21]

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[13] C. Eaborn and P. M. Jackson, *J. Chem. Soc.* (*B*), 1969, 21; C. Eaborn and J. F. R. Jaggard, *ibid.*, p. 892.

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[15] C. Eaborn and J. A. Waters, *J. Chem. Soc.*, 1961, 542.

[16] (*a*) G. E. Maciel and J. J. Natterstad, *J. Chem. Phys.*, 1965, **42**, 2427; (*b*) G. L. Nelson, G. C. Levy, and J. D. Cargioli, *J. Amer. Chem. Soc.*, 1972, **94**, 3089.

[17] P. B. de la Mare and P. W. Robertson, *J. Chem. Soc.*, 1948, 100.

[18] N. C. Deno and R. Stein, *J. Amer. Chem. Soc.*, 1956, **78**, 578.

[19] G. Leandri, A. Mangini, and R. Passerini, *J. Chem. Soc.*, 1957, 1386.

[20] A. Weissberger, 'Technique of Organic Chemistry,' Interscience, New York, vol. 17, 1967.

[21] R. C. Passerini, *Boll. sci. Fac. Chim. ind. Bologna*, 1959, **8**, 124.

Small amounts (4% *ca.*) of disubstitution products from the diphenyl derivative were identified by mass spectrometric analysis using a Varian MAT 111 instrument.

Halogenation of sulphoxides was performed similarly but the heating was prolonged for 30 h. No evidence for the formation of halogenosulphides was detected by direct g.l.c. analysis on the halogenation mixture in CCl_4 and $MeNO_2$. All experimental g.l.c. conditions were inadequate for quantitative analysis of the halogenosulphoxides which were determined after reduction of the reaction mixture with sodium iodide in perchloric acid as previously.[22]

The monohalogenation products of chloro- and bromo-benzene were separated and analysed without difficulty directly by g.l.c. at 100° using a 6 ft column (1/8 in) packed with FFAP (5%) on Chromosorb W (80—100 mesh).

The quantitative evaluation of the conversion into mono-substitution products (95%) was obtained by the direct calibration procedure.

Acidity Function and pK_a *Determination*.—The H_A functions for the H_2SO_4–AcOH solutions used in the protodesilylation kinetics have been determined as previously described [23] by using 3-nitro- and 4-methyl-3,5-dinitrobenzamides as indicators. All the u.v. spectra were measured on a 402 Perkin-Elmer spectrophotometer using 1 cm quartz cells and a thermostatically controlled cell-block at 25 ± 0·03°. Following the n.m.r. technique previously described,[24] the chemical shifts for the methyl protons of methyl *p*-trimethylsilylphenyl sulphoxide relative to trimethylammonium ion were measured in H_2SO_4–AcOH solutions. By plotting Δν at various acidities against the corresponding H_A functions a good sigmoid curve was obtained, in which a change in slope occurs within 2—3 H_A units; the H_A value corresponding to half-protonation (−2·25) was taken as the pK_a of methyl *p*-trimethylsilylphenyl sulphoxide (Table 6).

TABLE 6

Chemical shifts (Δν) of protonated methyl *p*-trimethylsilylphenyl sulphoxide in H_2SO_4–AcOH at 25°

H_2SO_4 [a]	$-H_A$	Δν (Hz) [b]
10·05	0·02	+23·5
38·65	1·36	+22·4
54·36	2·02	+11·2
69·93	2·65	−3·2
78·75	3·11	−11·7
87·50	3·50	−14·0
91·21	3·70	−14·6

[a] Concentration of aqueous acid 7·5 ml of which was mixed with 10 ml glacial acetic acid. [b] Values of chemical shifts are relative to Me_3NH^+. Negative indicates a downfield shift.

Kinetic Measurements.—The chlorination experiments were carried out in the dark (aluminium foil) in a constant temperature bath at 25·00 ± 0·03°.

Conventional iodometric procedures were employed.[25] In slower reactions, to avoid loss of chlorine by evaporation, samples (10 ml) of the reaction mixture were sealed in tubes of *ca.* 14 ml capacity. Blank experiments were carried out in all cases to determine whether chlorine was lost other than by reaction with the substrates.

Protodesilylation rates were measured spectrophotometrically at 50 ± 0·2° as previously described.[13]

N.m.r. Measurements.—The ^{13}C n.m.r. spectra were recorded at room temperature on a JEOL JNM PS 100 spectrometer operating at 25·15 MHz, in the continuous wave mode with complete proton decoupling.

Samples (60% w/w) were dissolved in acetone–benzene (9 : 1) the solvent being used as internal standard. Measurements were accurate within 0·1 p.p.m.

[4/306 *Received*, 15*th February*, 1974]

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[25] L. M. Stock and A. Himoe, *J. Amer. Chem. Soc.*, 1961, **83**, 1937.