Kinetics of α-Chlorination of Sulphoxides by *N*-Chlorobenzotriazole

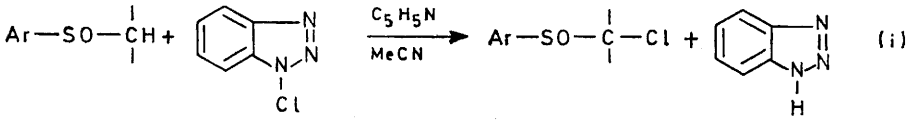
By **Dario Landini** * and **Angela Maia**, Centro C.N.R. and Istituto di Chimica Industriale dell'Università, Via C. Golgi 19, 20133 Milano, Italy

The α-chlorination of aryl methyl and aryl isopropyl sulphoxides with *N*-chlorobenzotriazole in acetonitrile in the presence of pyridine follows second-order kinetics. The reaction is favoured by electron-donating groups and is subject to a noticeable kinetic isotope effect (k_H/k_D). On the basis of the kinetic data a common reaction mechanism is proposed for the two series of sulphoxides, involving formation of an intermediate chloro-oxosulphonium salt which in the rate-determining step collapses on attack by base to give the α-chloro-sulphoxide.

Two opposite stereochemical processes, involving retention and inversion of chirality at sulphur, have been shown [1-3] to occur, respectively, in the α-chlorination of (+)-(*R*)-methyl and (+)-(*R*)-isopropyl *p*-tolyl sulphoxide with (dichloroiodo)benzene or *N*-chlorobenzotriazole in the presence of pyridine, and possible mechanisms have been discussed.[1,2] We wished to discover whether the difference in stereochemical behaviour of aryl methyl (I) and aryl isopropyl sulphoxides (II) was matched by a kinetic difference. We had previously [4] obtained no clear indication from a study of the α-chlorination of the foregoing *p*-tolyl sulphoxides with (dichloroiodo)-benzene, since with these substrates dissociation of the reagent into iodobenzene and chlorine constitutes the rate-determining step.

			Ar–SO–R		
(I)	a	b	c	d	e
R =	Me	CD_3	Me	Me	Me
Ar =	Ph	Ph	*p*-MeC_6H_4	*p*-ClC_6H_4	*m*-ClC_6H_4
(II)	a	b	c	d	e
R =	Pr^i	$CDMe_2$	Pr^i	Pr^i	Pr^i
Ar =	Ph	Ph	*p*-MeC_6H_4	*p*-ClC_6H_4	*m*-ClC_6H_4

We here report a study of the kinetics of α-chlorination of *meta*- and *para*-substituted aryl methyl (I) and aryl isopropyl sulphoxides (II) with *N*-chlorobenzotriazole in the presence of pyridine [equation (i)]. The reactions were carried out in acetonitrile at −10, −20, and −30 °C, and followed iodometrically, by titrating the



(i)

unchanged *N*-chlorobenzotriazole. α-Chloro-sulphoxides were isolated in at least 75% yield.

In the concentration range 3—10 × 10^{-3} mol l^{-1} of substrate and halogenating agent, in the presence of a large excess of pyridine, second-order kinetics [equation (ii)] were observed up to at least 80% conversion.

$$\text{Rate} = k_{obs}[\text{sulphoxide}][N\text{-chlorobenzotriazole}] \quad \text{(ii)}$$

The rate constants (k_{obs}) were independent of pyridine concentration in the range examined (2—6 × 10^{-1} mol l^{-1}) (Table 1).†

With both series of substrates the reaction was favoured by the presence of electron-donating groups. The data fitted the Hammett equation (σ values) and the correlation gave ρ values of −4·35 (r = 0·9992; s = 0·083) and −3·71 (r = 0·9999; s = 0·022) for methyl and isopropyl derivatives, respectively (Table 2).

Comparison of the rates of reaction of compounds (Ia) and (IIa) and of their deuteriated analogues [(Ib) and (IIb)] showed kinetic isotope effects (k_H/k_D) of 3·1

† Comparable yields of α-chloro-sulphoxides were obtained when the reactions were carried out in the absence of pyridine.[3] Preliminary kinetic results indicate that under these conditions, after an induction period of 60—90 s, the reaction is very fast. Furthermore when optically active sulphoxides are used, the reaction products are largely racemized.[3] It seems likely that in the absence of pyridine a different mechanism is operating.

[1] M. Cinquini, S. Colonna, R. Fornasier, and F. Montanari, *J.C.S. Perkin I*, 1972, 1886.
[2] P. Calzavara, M. Cinquini, S. Colonna, R. Fornasier, and F. Montanari, *J. Amer. Chem. Soc.*, 1973, **95**, 7431, and references therein.
[3] M. Cinquini and S. Colonna, *Synthesis*, 1972, 259.
[4] M. Cinquini, S. Colonna, and D. Landini, *J.C.S. Perkin II*, 1972, 296.

and 7·0, respectively (Table 3). Activation parameters obtained from kinetic measurements on (Ia) and (IIa) at three different temperatures are reported in Table 3.

TABLE 1

Rate constants of α-chlorination of sulphoxides (Ia) and (IIa) (3—10 × 10^{-3} mol l^{-1}) by *N*-chlorobenzotriazole (3—10 × 10^{-3} mol l^{-1}) at various concentrations of pyridine in acetonitrile at −10 °C

10^2[pyridine]/ mol l^{-1}	k [a]/l mol^{-1} s^{-1} (Ia)	(IIa)
62·5	2·3	0·21
37·5	2·2	0·22
20·0	2·3	0·22

[a] Average value of at least three runs.

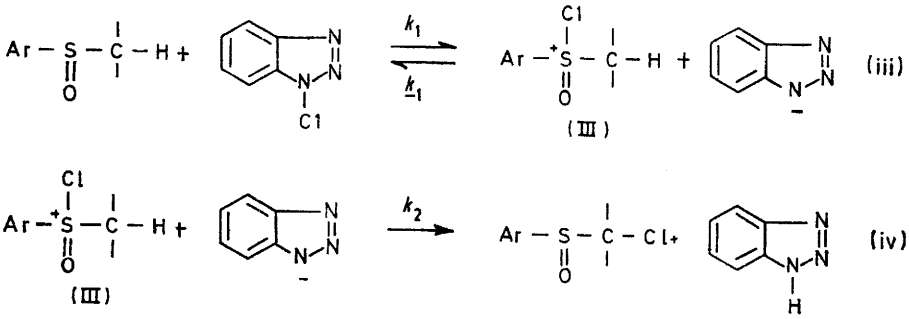


TABLE 2

Electronic effects of substituents in the α-chlorination of compounds (I) and (II) (7 × 10^{-3} mol l^{-1}) by *N*-chlorobenzotriazole (4 × 10^{-3} mol l^{-1}) in the presence of pyridine (0·20 mol l^{-1}) in acetonitrile at −20 °C

Substrate	$10k$ [a]/l mol^{-1} s^{-1}	Substrate	$10k$ [a]/l mol^{-1} s^{-1}
(Ic)	83·7	(IIc)	3·73
(Ia)	14·6	(IIa)	0·895
(Id)	1·8	(IId)	0·122
(Ie)	0·33	(IIe)	0·037

[a] Average value of at least three runs.

TABLE 3

Activation parameters and kinetic isotope effects in the α-chlorination of sulphoxides (I) and (II) by *N*-chlorobenzotriazole in the presence of pyridine (0·20 mol l^{-1}) in acetonitrile

Substrate	$10k$/l mol^{-1} s^{-1} Temp.(°C): −10	−20	−30	$\Delta H^{\ddagger}$ [a]/ kcal mol^{-1}	$\Delta S^{\ddagger}$ [a]/ cal mol^{-1} K^{-1}
(Ia)	23·00	14·6	8·22	6·23 ±0·12	−32·9 ±0·48
(Ib) [b]	7·36				
(IIa)	2·20	0·895	0·357	11·05 ±0·12	−19·30 ±0·49
(IIb) [b]	0·316				

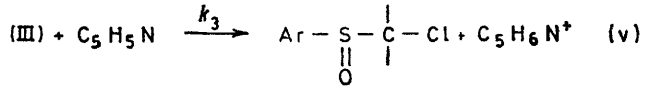
[a] The activation parameters and root mean square deviations are computer-generated (CII 10080) values obtained by using the method of least squares. [b] Compounds (Ib) and (IIb) were 86 and 89% isotopically enriched, respectively.

DISCUSSION

The experimental data demonstrate that α-chlorination of the two series of sulphoxides (I) and (II) with *N*-chlorobenzotriazole in the presence of pyridine follows a common kinetic behaviour. The two different stereochemical processes suggested [2] for the methyl and isopropyl derivatives, respectively, must thus derive from a common mechanism. This, according to the kinetic data, can be formulated as shown in equations (iii) and (iv).* The reaction of the sulphoxide with *N*-chlorobenzotriazole affords an intermediate chloro-oxosulphonium salt (III), which suffers abstraction of an α-proton by benzotriazole anion and migration of chlorine from sulphur to the α-carbon atom. It is thus irreversibly transformed into the α-chloro-sulphoxide. The noticeable kinetic isotope effect (k_H/k_D), together with the absence of H–D exchange with the reaction medium previously found [4] in the α-chlorination

of sulphoxides with (dichloroiodo)benzene, suggests that formation of the carbanion is rate-determining and that abstraction of the α-proton and migration of chlorine from sulphur to the α-carbon atom are probably highly concerted.

Pyridine has no effect on the reaction rate in the concentration range 2—6 × 10^{-1} mol l^{-1} (Table 1). In water the pK_b values of benzotriazole anion [5] and pyridine [6] are 5·8 and 8·8, respectively. In view of the well known properties of dipolar aprotic solvents,[7,8] this difference should be much higher in acetonitrile, so



that the contribution of process (v) to the formation of products should be negligible.

Therefore, if equation (iv) is rate-determining and if we assume that the chloro-oxosulphonium salt (III) is the reactive intermediate, on the basis of the steady-state treatment the kinetic equation (vi) can be obtained, identical to that (ii) found experimentally.

$$\text{Rate} = (k_1k_2/k_{-1})[\text{sulphoxide}][N\text{-chlorobenzotriazole}] \quad \text{(vi)}$$

The high negative values of ρ ($\rho_{Prl} = -3{\cdot}71$; $\rho_{Me} = -4{\cdot}35$) indicate that the rate of the reaction depends on the availability of electrons at the sulphinyl group, which will favour electrophilic attack at sulphur by

* The proposed mechanism is kinetically analogous to that previously reported [4] for the α-chlorination with (dichloroiodo)-benzene.

[5] J. E. Fagel, jun., and G. W. Ewing, *J. Amer. Chem. Soc.*, 1951, **73**, 4360.
[6] H. C. Brown and X. R. Mihm, *J. Amer. Chem. Soc.*, 1955, **77**, 1723.
[7] A. J. Parker, *Quart. Rev.*, 1962, **16**, 163.
[8] A. J. Parker, *Adv. Phys. Org. Chem.*, 1967, **5**, 173.

N-chlorobenzotriazole [equation (iii)] and disfavour the following step (iv). Indeed for the abstraction of the proton [equation (iv)] a positive value of ρ should be expected, but this should be small, since the electronic effect of substituents is transmitted through the sulphur atom.* As a whole, a negative value of ρ should then result.

The difference in values of the isotope effect in the reactions of the methyl sulphoxide (I) and the isopropyl derivative (II) (k_H/k_D 3·1 and 7·0, respectively) clearly indicates that in the transition state of step (iv) the extent of breaking of the C–H bond is different in the two cases. In particular, whereas abstraction of the proton probably corresponds in (II) to an energy maximum,[9] this is not the case with (I).

Two opposite situations could be envisaged for the transition state of the latter: (i) the C–H bond is only slightly loosened; (ii) the bond is considerably stretched.† The hypothesis (i) seems more likely, in agreement with the higher negative value of ρ met with in this series of sulphoxides with respect to (II). In fact if the opposite electronic requirements of steps (iii) and (iv) are taken into account, the appreciable difference in ρ values ($\rho_{Pri} - \rho_{Me} = 0{\cdot}64$) suggests the transition state of the rate-determining step (iv) to be more similar to the intermediate (III) in the case of the methyl derivatives (I) than for the isopropyl compounds (II). This means that the breaking of the C–H bond is less advanced in the former case.

The different negative values of ΔS^* indicate that a greater loss of degrees of freedom is involved on passing from reagents to the activated complex in the methyl than in the isopropyl series. Although it is difficult to evaluate the various factors which determine the entropy of a reaction, and in particular the solvation of the transition state, it seems likely that the difference in ΔS^* is mainly due to a higher conformational freedom in the ground state of the methyl derivatives.

The kinetic data as a whole show that the opposite stereochemical behaviour in the α-halogenations of methyl and isopropyl aryl sulphoxides[1-3] does not result from a substantially different kinetic behaviour. Therefore, either the two opposite stereochemical processes do not involve significant kinetic differences, or a common process is at work and differentiation occurs after the rate-determining step.

EXPERIMENTAL

Solvents and Reagents.—Dry nitrogen was bubbled into commercial acetonitrile, previously saturated with chlorine and kept in the dark for a week, until disappearance of chlorine and hydrochloric acid (iodometric and Volhard tests) was complete. The acetonitrile was then distilled twice over anhydrous potassium carbonate through a Vigreux column. A constant-boiling fraction (b.p. 80·8 °C) was collected for use in kinetic work (water content ≤0·3% from Karl Fischer analysis).

Commercial pyridine was treated with an ethereal solution of chlorine and kept in the dark for a day. The ether was then evaporated off, and the base was distilled over potassium hydroxide, the fraction boiling at 115—116 °C being collected.

N-Chlorobenzotriazole was prepared by a standard method.[10] Iodometric analyses of weighed samples in acetonitrile gave figures generally within 2—3% of the theoretical value.

Substrates.—All sulphides, except 3-chlorophenyl isopropyl sulphide, are known and were prepared by standard methods. The sulphoxides were obtained in more than 80% yield by oxidation with *N*-chlorobenzotriazole [11] and carefully purified by column chromatography (silica gel; light petroleum–ether, 1 : 1) and/or by repeated crystallization. Physical properties and analyses are reported in Table 4.

TABLE 4

Physical properties and analyses of sulphoxides

Sulphoxide	M.p. (b.p.) (°C)	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(Ia)	(144—146 at 15 mmHg) [a]				
(Ic)	42—43 [b]				
(Id)	47—48 [c]				
(Ie)	43—44 [d]				
(IIa)	(97—100 at 0·01 mmHg) [e]				
(IIc)	(111 at 1 mmHg)	65·9	7·75	65·9	7·75
(IId)	(105—107 at 4 mmHg) [f]	53·15	5·5	53·3	5·45
(IIe)	(140—142 at 4 mmHg) [g]	53·35	5·4	53·3	5·45

[a] Lit.,[12] b.p. 75° at 0·01 mmHg. [b] Lit.,[13] m.p. 42—43°. [c] Lit.,[13] m.p. 47—48°. [d] Lit.,[14] m.p. 43—44°. [e] Lit.,[15] b.p. 101—102° at 0·01 mmHg. [f] n_D^{20} 1·5639. [g] n_D^{22} 1·5698.

3-Chlorophenyl Isopropyl Sulphide.—Sodium 3-chlorobenzenethiolate (16·6 g, 0·1 mol) and 2-bromopropane (12·3 g, 0·1 mol) were refluxed for 2 h in methanol (150 ml). Work-up and distillation afforded the *product* (13 g, 70%), b.p. 71—72° at 4 mmHg, n_D^{21} 1·5622 (Found: C, 57·65; H, 5·8. $C_9H_{11}ClS$ requires C, 57·9; H, 5·95%).

Phenyl Trideuteriomethyl Sulphoxide (Ib).—Methyl phenyl sulphoxide (Ia) (2·8 g, 0·02 mol) was dissolved in methan-[^{2}H]ol (15 ml) in the presence of sodium methoxide (0·8 mol) and the mixture was refluxed for 4 days. Work-up afforded the product (2·6 g; b.p. 144—146° at 15 mmHg) 86% isotopically enriched (by ^{1}H n.m.r. spectroscopy).

Phenyl 1-Deuterio-1-methylethyl Sulphoxide (IIb).—Isopropyl phenyl sulphoxide (IIa) (1·7 g, 0·01 mol) was dissolved in methan[^{2}H]ol (10 ml) in the presence of sodium methoxide (0·4 mol) and the mixture was refluxed for 6 days. Work-up afforded the product (1·5 g; b.p. 97—100° at 0·01 mmHg) having a deuterium content of 0·89 atom per molecule (by ^{1}H n.m.r. spectroscopy).

Reaction Products.—A solution of the sulphoxide (0·02 mol), *N*-chlorobenzotriazole (0·02 mol), and pyridine

* A more detailed discussion of this problem has been given previously.[4]

† An analogy, albeit formal, can be found in the classical β-elimination reactions, where a concerted *E*2 process corresponds to a maximum in the isotope effect; the effect is less in the case of an *E*1cb- or *E*1-like process.

[9] K. B. Wiberg, *Chem. Rev.*, 1955, **55**, 713.
[10] C. W. Rees and R. C. Storr, *Chem. Comm.*, 1968, 1305.
[11] W. D. Kingsbury and C. R. Johnson, *Chem. Comm.*, 1969, 365.
[12] D. Barnard, J. M. Fabian, and P. H. Kech, *J. Chem. Soc.*, 1949, 2442.
[13] A. Cerniani and G. Modena, *Gazzetta*, 1959, **89**, 843.
[14] D. Landini, G. Modena, F. Montanari, and G. Scorrano, *J. Amer. Chem. Soc.*, 1970, **92**, 7168.
[15] A. Cerniani, G. Modena, and P. E. Todesco, *Gazzetta*, 1960, **90**, 3.

(0·4 mol) in acetonitrile (50 ml) was kept at −10 °C until disappearance of the halogenating agent was complete (2—48 h). The solvent was then evaporated off and the residue was taken up in dichloromethane (50 ml). The solution was washed with aqueous 5% sodium hydroxide, aqueous 10% sulphuric acid, and water, dried (Na_2SO_4), and evaporated. The crude product was purified by column chromatography (silica gel; ether–light petroleum, 1 : 2) to give the α-chloro-sulphoxide in at least 75% yield. Physical properties and analyses are reported in Table 5.

TABLE 5

Physical properties and analyses of α-chloro-sulphoxides $ArSO{\cdot}CClR^1R^2$

Ar	R^1	R^2	M.p. (b.p.) (°C)	Yield (%)	Found (%) C	Found (%) H	Required (%) C	Required (%) H
Ph	H	H	(78—79 at 0·02 mmHg) [a]	80				
p-MeC_6H_4	H	H	62—63 [b]	85				
p-ClC_6H_4	H	H	86—87 [c]	85				
m-ClC_6H_4	H	H	50—51 [d]	75	39·95	2·75	40·2	2·9
Ph	Me	Me	64—65 [e]	80				
p-MeC_6H_4	Me	Me	65—66 [f]	78	55·45	6·15	55·4	6·05
p-ClC_6H_4	Me	Me	42—43 [f]	75	45·3	4·15	45·6	4·25
m-ClC_6H_4	Me	Me	53—54 [g]	77	45·5	4·25	45·6	4·25

[a] Lit.,[16] 134—137° at 1 mmHg. [b] Lit.,[17] m.p. 61·5—62°. [c] Lit.,[4] m.p. 86—87°. [d] From n-hexane–ether (4 : 1). [e] Lit.,[3] 64—65°. [f] From n-hexane–ether (3 : 1). [g] From n-hexane.

Kinetic Experiments.—The kinetic runs were carried at −10, −20, and −30 °C in a thermostated bath (±0·2 °C). Sulphoxide solutions (A) were prepared by weighing out the substrate into acetonitrile–pyridine stock solutions (25 ml). *N*-Chlorobenzotriazole solutions (B) were prepared immediately before use by dissolving the desired amount of compound in acetonitrile (50 ml). The solutions were titrated iodometrically before use. At zero time solutions (A) and (B) (25 ml each) were mixed by using a Y-tube. Aliquot portions were withdrawn at various times, quenched with an excess of potassium iodide in aqueous 10% sulphuric acid, and titrated iodometrically.

The second-order rate constants (k_{obs}) were obtained by plotting log $(a - x)/(b - x)$ against time, where a is the initial sulphoxide concentration and b the initial concentration of *N*-chlorobenzotriazole.

4/1358 *Received*, 5*th July*, 1974]

[16] G. Tsuchiashi, K. Ogura, S. Iriuchijma, and S. Tomisawa, *Synthesis*, 1971, 89.

[17] G. Tsuchiashi and S. Iriuchijma, *Bull. Chem. Soc. Japan*, 1970, **43**, 2271.