Kinetics of α-Chlorination of Sulphoxides by Iodobenzene Dichloride

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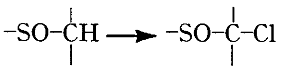
The kinetics of the reaction of sulphoxides with iodobenzene dichloride and pyridine in acetonitrile to give α-chlorosulphoxides has been studied. The data indicate that the reaction proceeds through α-chlorosulphoxonium salts which by attack of base collapse to α-chlorosulphoxides. The last step is rate-determining for substrates deactivated by electron-withdrawing and sterically hindered groups.

THE reaction of sulphoxides with reagents such as iodobenzene dichloride,[1-3] nitrosyl chloride,[4] t-butyl hypochlorite,[5] chlorine,[6] and sulphuryl chloride [7] allows, in the presence of base, the introduction (1) of a chlorine atom α to the sulphinyl group, overcoming Pummerer-type rearrangement. While the Pummerer reaction



$$-\mathrm{SO{-}CH} \longrightarrow -\mathrm{SO{-}C{-}Cl} \qquad (1)$$

has been the subject of much mechanistic speculation,[8] no investigation has been reported on the mechanism of α-chlorination. The kinetics of the reaction of sulphoxides with iodobenzene dichloride and pyridine in acetonitrile to give α-chlorosulphoxides are reported here.

The reactions were carried out in acetonitrile at 0 °C, and followed iodometrically, by titrating the unchanged iodobenzene dichloride. The reaction products were isolated in at least 70% yield.

In the case of *para*-X-substituted alkyl phenyl sulphoxides (I)—(V) the reaction follows first-order kinetics up to 80—90% conversion. The rate is independent of the nature and concentration of the substrate and depends only on the dissociation of iodobenzene dichloride into iodobenzene and chlorine (Table 1).

Pyridine has no effect on the reaction rate, the rate constant being inversely proportional to the concentration of iodobenzene. In the case of substrates deactivated by electron-withdrawing groups and sterically hindered, the reaction follows more complex kinetics.

$4\text{-}XC_6H_4\cdot SO\cdot R$

Compound	(I)	(II)	(III)	(IV)	(V)
X	H	Me	H	H	Cl
R	Me	Me	Et	Pr^i	Me

$4\text{-}X\text{-}2\text{-}ClC_6H_3\cdot SO\cdot R$

Compound	(VI)	(VII)	(VIII)	(IX)	(X)
X	H	H	Me	Cl	Ac
R	Me	CD_3	Me	Me	Me

A detailed kinetic investigation was carried out on *o*-chlorophenylmethyl sulphoxide (VI). The reaction was studied in the concentration range 4—10 × 10^{-3}M. In the presence of an excess of pyridine and iodo-

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[1] G. Barbieri, M. Cinquini, S. Colonna, and F. Montanari, *J. Chem. Soc.* (*C*), 1968, 659.

[2] M. Cinquini, S. Colonna, and F. Montanari, *Chem. Comm.*, 1969, 607.

[3] M. Cinquini, S. Colonna, and D. Iarossi, *Boll. sci. Fac. chim. ind. Bologna*, 1969, **27**, 197.

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[6] G. Tsuchihashi and S. Iriuchijima, *Bull. Chem. Soc. Japan*, 1970, **43**, 2271.

[7] (*a*) K. C. Tin and T. Durst, *Tetrahedron Letters*, 1970, 4643; (*b*) G. Tsuchiashi, K. Ogura, S. Iriuchijima, and S. Tomisawa, *Synthesis*, 1971, 89.

[8] C. R. Johson and W. G. Phillips, *J. Amer. Chem. Soc.*, 1969, **91**, 682, and references therein.

TABLE 1

Rate constants for the α-chlorination of compounds (I)—(V) by $PhICl_2$ ($5{\cdot}0 \times 10^{-3}$M) and pyridine ($1{\cdot}5 \times 10^{-1}$M) in MeCN at 0 °C

Substrate	10^3[sulphoxide]/M	$10^3k/s^{-1}$
(I)	13·3	3·1
(I)	5·8	3·2
(II)	10·8	3·2
(II)	6·1	3·2
(III)	11·5	3·2
(III)	6·3	3·0
(IV)	10·1	3·2
(IV)	6·0	3·1
(V)	9·5	3·0
(V)	5·2	3·1

TABLE 2

Effect of the concentration of PhI on the rate constants of the α-chlorination of compounds (VI) and (VII) (4—10 × 10^{-3}M) by $PhICl_2$ (4—10 × 10^{-3}M) and pyridine (3 × 10^{-1}M) in MeCN at 0 °C

Substrate	[PhI]/M	10^2k_{obs}/l mol^{-1} s^{-1}
(VI)	0·1	17·6
(VI)	0·15	11·9
(VI)	0·3	5·9
(VI)	0·4	4·5
(VII) [a]	0·3	1·1

[a] Deuterium content 0·86 atom per molecule.

TABLE 3

Effect of the concentration of pyridine on the rate constants of the α-chlorination of compound (VI) (4—10 × 10^{-3}M) by $PhICl_2$ (4 × 10^{-3}M) in the presence of PhI (1 × 10^{-1}M) in MeCN at 0 °C

[Pyridine]/M	10^2k_{obs}/l mol^{-1} s^{-1}
0·1	4·0
0·2	7·9
0·3	11·9
0·4	15·6

TABLE 4

Electronic effects of substituents in the α-chlorination of compounds (VI) and (VIII)—(X) ($8{\cdot}0 \times 10^{-3}$M) by $PhICl_2$ ($5{\cdot}0 \times 10^{-3}$M) and pyridine ($1{\cdot}2 \times 10^{-1}$M) in the presence of PhI ($1{\cdot}0 \times 10^{-1}$M) in MeCN at 0 °C

Substrate	10^2k_{obs}/l mol^{-1} s^{-1}
(VIII)	25·0
(VI)	7·6
(IX)	1·8
(X)	0·47 [a]

[a] Value obtained by extrapolation of runs carried at a pyridine concentration equal to 4·1 × 10^{-1}M.

benzene, with not less than 20 mol per mol of sulphoxide and $PhCl_2$, second-order kinetics were observed up to 80% conversion. The rate constants (k_{obs}) for the reaction are inversely proportional to the concentration of iodobenzene (Table 2) and directly proportional to the concentration of pyridine (Table 3). Comparison of the rates of reaction of (VI) and of its trideuteriomethyl analogue (VII) showed a kinetic isotope effect $k_H/k_D = 5{\cdot}5$ * (Table 2).

The electronic effects of substituents were studied in a series of 4-substituted 2-chlorophenyl methyl sulphoxides (Table 4). The reaction is favoured by electron-donating and disfavoured by electron-withdrawing groups. The data fit the Hammett equation by use of Hammett's σ values and the correlation gives a ρ value of $-2{\cdot}55$ ($r = 0{\cdot}9977$).

DISCUSSION

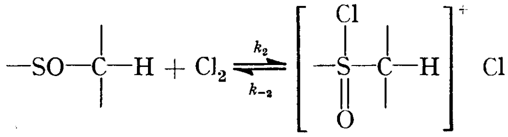
The experiments indicate that in the α-chlorination of sulphoxides iodobenzene dichloride acts only as a controlled source of chlorine, which is the real halogenating agent.† Dissociation of $PhICl_2$ into its components is the first step. With substrates such as (I)—(V), this is the rate-determining step. This process is rate-determining also in the oxidation of sulphides to sulphoxides [10] and in the chlorination of aromatic hydrocarbons [11] by $PhICl_2$.

To gain information about the mechanism, it was necessary to study kinetics with substrates such as the sulphoxide (VI) where the dissociation of $PhICl_2$ is not the slow step. Then the kinetic equation experimentally found is (2). On the basis of the kinetic data the

$$\text{Rate} = \frac{k[\text{Sulphoxide}][\text{PhICl}_2][\text{py}]}{[\text{PhI}]} \qquad (2)$$

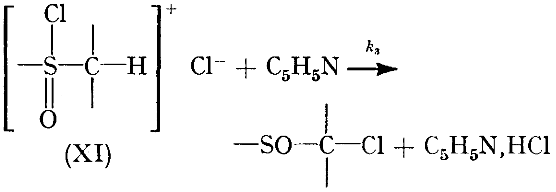
mechanism can be formulated as in equations (3)—(5).

$$\text{PhICl}_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{PhI} + \text{Cl}_2 \qquad (3)$$



$$-\text{SO}-\overset{|}{\underset{|}{\text{C}}}-\text{H} + \text{Cl}_2 \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \left[-\overset{\text{Cl}}{\underset{\text{O}}{\overset{|}{\underset{\|}{\text{S}}}}}-\overset{|}{\underset{|}{\text{C}}}-\text{H}\right]^+ \text{Cl}^- \qquad (4)$$

(XI)



$$\left[-\overset{\text{Cl}}{\underset{\text{O}}{\overset{|}{\underset{\|}{\text{S}}}}}-\overset{|}{\underset{|}{\text{C}}}-\text{H}\right]^+ \text{Cl}^- + \text{C}_5\text{H}_5\text{N} \xrightarrow{k_3} -\text{SO}-\overset{|}{\underset{|}{\text{C}}}-\text{Cl} + \text{C}_5\text{H}_5\text{N,HCl} \qquad (5)$$

(XI)

On the basis of the steady-state treatment the rate of formation of the α-chlorosulphoxide is given by equation (6). Since equation (5) is rate-limiting, and

$$\frac{d[\alpha\text{-Chlorosulphoxide}]}{dt} = k_3[\text{XI}][\text{py}] = \frac{k_2k_3[\text{Sulphoxide}][\text{Cl}_2][\text{py}]}{k_3[\text{py}] + k_{-2}} \qquad (6)$$

since no accumulation of the intermediate (XI) has been observed, equilibrium (4) is shifted to the left. Therefore $k_{-2} \gg k_3[\text{py}]$, and the last equation may be simplified to equation (7).

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* Minimum value measured for compound (VII) with a deuterium content of 0·86 atom per molecule.

† α-Chlorination can be carried out with chlorine as such in the presence of pyridine.[6,9]

[9] M. Cinquini, S. Colonna, and D. Landini, unpublished results.

[10] M. Cinquini, S. Colonna, and D. Landini, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 211.

[11] R. M. Keefer and L. J. Andrews, *J. Amer. Chem. Soc.*, 1957, **79**, 4348.

$$\frac{d[\alpha\text{-Chlorosulphoxide}]}{dt} = \frac{k_2k_3}{k_{-2}}[\text{Sulphoxide}][\text{Cl}_2][\text{py}] \quad (7)$$

The chlorine concentration is given by (8) and the

$$[\text{Cl}_2] = \frac{k_1[\text{PhICl}_2]}{k_{-1}[\text{PhI}]} \quad (8)$$

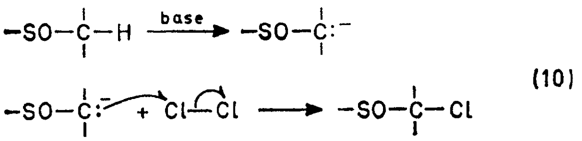
kinetic expression becomes (9), equal to that experimentally found.

$$\frac{d[\alpha\text{-Chlorosulphoxide}]}{dt} = \frac{k_1k_2k_3}{k_{-1}k_{-2}}\frac{[\text{Sulphoxide}][\text{PhICl}_2][\text{py}]}{[\text{PhI}]} \quad (9)$$

The reaction proceeds through attack of chlorine at the sulphinyl group with formation (4) of an intermediate chlorosulphoxonium salt (XI). Hydrogen abstraction by the base at a carbon α to the sulphur atom leads then to migration of the chlorine atom from the sulphinyl group to the carbon atom, with formation (5) of the chlorosulphoxide. Step (5) is rate-determining in the case of substrates deactivated by electron-withdrawing groups and sterically hindered, in agreement with the kinetic expression (2) and with the large isotope effect.

Hydrogen abstraction and migration of chlorine from the sulphinyl group to the α-carbon atom must proceed through a concerted process. Working in the presence of an excess of D_2O and H_2O (more than 200 mol per mol of sulphoxide) respectively, and stopping the halogenation of compounds (VI) and (VII) at 50% conversion, we found no H–D exchange either in the recovered sulphoxides or in the products. Isotope exchange accompanied by a smaller value of the isotope effect should be predicted if attack by base would lead to the reversible formation of a carbanion.

The large negative value of ρ (—2·55) shows the reaction to be strongly favoured by an increased electron-availability at the sulphinyl group. However the suggested mechanism indicates that while the electrophilic attack (4) by chlorine at the sulphinyl group must be favoured by electron-donating groups, the next step (5) must be favoured by electron-withdrawing groups. In fact the ease of abstraction of the hydrogen must depend on its acidity, and for this process one should expect a positive value of ρ. Moreover, this value should be small, since the electronic effect of substituents is transmitted through the sulphur atom. An indication is given by the value ($\rho = +1{\cdot}05$; $+1{\cdot}1$, in CCl_4) found in the α-chlorination of benzylic sulphides by *N*-chlorosuccinimide.[12,13] According to this, the experimental value of ρ indicates that the transition state in the rate-limiting step is like the intermediate (XI). Tsuchihashi and Iriuchijima[6] suggested the mechanism (10) for the α-chlorination of sulphoxides. This is not in


(10)

agreement with our data, since a positive value of ρ should be expected. Moreover sulphones do not react in these conditions, although hydrogen atoms α to a sulphonyl group are more acidic than those α to a sulphinyl group.[14]

The relatively large value of ρ suggests attack by chlorine at sulphur rather than at oxygen. Analogous values of ρ were found in reactions involving electrophilic attack at sulphur, as in the α-chlorination of aryl methyl sulphides by *N*-chlorosuccinimide ($\rho = -3$ in CCl_4)[15] and in the oxidation of sulphides by bromine ($\rho = -3{\cdot}2$ in H_2O–MeOH)[16] and by chlorine ($\rho = -2{\cdot}6$ in MeCN).[17] A comparison, albeit indirect, with a reaction involving attack at the sulphinyl oxygen, can be found in the protonation of sulphoxides, for which $\rho = -0{\cdot}72$.[18]

It thus seems reasonable to attribute to the reaction intermediate (XI) the structure of an *S*-chlorosulphoxonium salt, instead of that of an *O*-chlorosulphoxonium salt. A further indication is that diaromatic sulphoxides react with iodobenzene dichloride to afford the corresponding sulphones.[1] It seems likely that the last reaction proceeds through the same intermediate,* as indicated by the reaction of alkyl aryl sulphoxides with *N*-chlorobenzotriazole which, depending on the solvent, leads either to α-chlorination (in CH_2Cl_2) or to oxidation to sulphones (in MeOH).[20]

EXPERIMENTAL

Commercial acetonitrile was saturated with chlorine and kept in the dark for a week. Chlorine was removed by bubbling dry nitrogen for 4 h and distilling the mixture 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 ⩽3%, from Karl–Fischer analysis).

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

Commercial iodobenzene was fractionally distilled and had b.p. 189 °C.

Iodobenzene dichloride was made by the standard method[21] in small lots which were used immediately.

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* The same intermediate was suggested by Oae *et al.*[19] for the oxidation of sulphoxides to sulphones by t-butyl hypochlorite.

[12] D. L. Tuleen, *J. Org. Chem.*, 1967, **32**, 4006.

[13] D. L. Tuleen and T. B. Stephen, *J. Org. Chem.*, 1969, **34**, 31.

[14] C. C. Price and S. Oae, ' Sulfur Bonding,' The Ronald Press Co., New York, 1962, p. 136.

[15] D. L. Tuleen and V. C. Marcum, *J. Org. Chem.*, 1967, **32**, 204.

[16] U. Miotti, G. Modena, and L. Sedea, *J. Chem. Soc.* (*B*), 1970, 802.

[17] M. Cinquini, S. Colonna, and D. Landini, unpublished results.

[18] D. Landini, F. Montanari, G. Modena, and G. Scorrano, *J. Amer. Chem. Soc.*, 1970, **92**, 7168.

[19] K. Kikukawa, W. Tagaki, N. Kunieda, and S. Oae, *Bull. Chem. Soc. Japan*, 1969, **42**, 831.

[20] M. Cinquini and S. Colonna, unpublished results.

[21] H. J. Lucas and E. R. Kennedy, *Org. Synth.* Coll.Vol. III, 1955, p. 482.

Iodometric analysis of weighed samples of the product in acetonitrile solution were generally within 2% of the theoretical value.

All the sulphides, except the sulphide (XIII) are known and were prepared by standard methods. The sulphoxides were obtained in more than 80% yield by the sodium metaperiodate [22] oxidation of the corresponding sulphides and carefully purified by column chromatography (silica gel; eluant ether–light petroleum, 1 : 1) and by repeated crystallization. Physical properties and analyses are reported in Table 5.[23-25]

TABLE 5

Physical properties and analyses of sulphoxides

Substrate	M.p. (b.p.) (°C)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
(I)	(148—150 at 17 mmHg) [a]					
(II)	42—43 [b]					
(III)	(101—102 at 1 mmHg) [c]					
(IV)	(97—100 at 0·01 mmHg) [d]					
(V)	47—48 [e]					
(VI)	(121 at 3 mmHg)	C_7H_7ClOS	48·31	4·09	48·14	4·04
(VIII)	(113—114 at 0·8 mmHg)	C_8H_9ClOS	51·05	4·90	50·92	4·81
(IX)	96—97 [f]	$C_7H_6Cl_2OS$	39·95	2·90	40·21	2·89
(X)	81—82 (decomp.) [g]	$C_9H_9ClO_2S$	49·89	4·19	49·87	4·27

[a] Lit.,[23] b.p. 75° at 0·01 mmHg. [b] Lit.,[24] m.p. 42—43°. [c] Lit.,[25] b.p. 101—102° at 1 mmHg. [d] Lit.,[25] b.p. 101—102° at 0·01 mmHg. [e] Lit.,[24] m.p. 47—48°. [f] From n-hexane. [g] From cyclohexane.

TABLE 6

Physical properties and analyses of α-chlorosulphoxides 2–X–4–Y–C_6H_3·SO·CClR¹R²

X	Y	R¹	R²	M.p. (b.p.) (°C)	Yield (%)	Formula	Found (%) C	Found (%) H	Required (%) C	Required (%) H
H	H	H	H	(78—79 at 0·02 mmHg) [a]	80					
H	Me	H	H	61—62 [b]	82					
H	H	Me	H	(82 at 0·03 mmHg) [c]	75					
H	H	Me	Me	64—65 [d]	80					
Cl	H	H	H	53—54 [e]	78	$C_7H_6Cl_2OS$	40·12	2·84	40·20	2·89
Cl	Me	H	H	52—53 [e]	70	$C_8H_8Cl_2OS$	43·03	3·55	43·11	3·61
Cl	Cl	H	H	90—91·5 [f]	77	$C_7H_5Cl_3OS$	34·70	2·00	34·50	2·05
Ac	Cl	H	H	148—149 (decomp.)	75	$C_9H_8Cl_2O_2S$	43·20	3·19	43·04	3·20
H	Cl	H	H	86—87 [f]	85	$C_7H_6Cl_2OS$	40·40	2·86	40·20	2·89

[a] Lit.,[7b] 134—137° at 1 mmHg. [b] Lit.,[6] m.p. 61·5—62°. [c] Lit.,[7b] b.p. 90° at 0·2 mmHg. [d] Lit.,[7b] m.p. 64·5—65·5°. [e] From diethyl ether–light petroleum. [f] From light petroleum–benzene.

2-Chloro-4-(methylthio)phenyl Methyl Ketone (XII).—2-Chlorophenyl methyl sulphide [26] (15·9 g, 0·1 mol) was acetylated with acetyl chloride (0·25 mol) in the presence of aluminium trichloride (0·12 mol) in carbon disulphide at 0 °C for 20 min. Work-up afforded, after crystallization from cyclohexane, 13 g (65%) of *product*, m.p. 57—58° (Found: C, 53·74; H, 4·39. C_9H_9ClOS requires C, 53·86; H, 4·52%).

2-Chlorophenyl Trideuteriomethyl Sulphoxide (VII).—2-Chlorophenyl methyl sulphoxide (VI) (2·1 g, 0·01 mol) was dissolved in deuteriomethanol (20 ml) in the presence of sodium methoxide (0·4 mol) and the mixture was refluxed for 49 h. Work-up afforded 1·9 g of product (b.p. 120—121° at 3 mmHg). ^{1}H N.m.r. spectroscopy showed a deuterium content of 0·86 atom per molecule.

Reaction Products.—A solution of the sulphoxide (0·03 mol), iodobenzene dichloride (0·03 mol), and pyridine (0·1 mol) in acetonitrile (100 ml) was kept in the dark at 0 °C until the complete disappearence of the halogenating agent (12—48 h). After evaporation of the solvent the residue was taken up with chloroform (50 ml), washed with 10% aqueous sulphuric acid, and with water, dried ($CaCl_2$), and evaporated. The crude product was purified by column chromatography (silica gel; eluant ether–light petroleum, 1 : 1) to give the α-chlorosulphoxides in at least 70% yield. Physical properties and analyses are reported in Table 6.

α-Chlorinations of Compounds (VI) *and* (VII) *in the presence of* D_2O *and* H_2O.—(*a*) 2-Chlorophenyl methyl sulphoxide (VI) and iodobenzene dichloride were allowed to react in acetonitrile–deuterium oxide (95 : 5, v/v) in conditions similar to the kinetic ones. The reaction was stopped at 50% conversion by adding an excess of potassium iodide dissolved in 10% aqueous sulphuric acid. The mixture was extracted four times with methylene dichloride. The organic layer was washed with 10% aqueous sulphuric acid, then with 10% aqueous sodium thiosulphate, and dried ($CaCl_2$). Evaporation of the solvent and column chromatography (silica gel; eluant ether–light petroleum, 1 : 1) afforded the unchanged sulphoxide (which had the lower R_F value) and the α-chlorosulphoxide. ^{1}H N.m.r. analysis showed no H/D exchange.

(*b*) 2-Chlorophenyl trideuteriomethyl sulphoxide (VII) and iodobenzene dichloride reacted in acetonitrile–water (95 : 5, v/v) in the same conditions as in (*a*). By quenching the reaction at 57% conversion, no D/H exchange was observed either in the starting material or the product. In both case (*a*) and (*b*) the recovered material and the α-chlorosulphoxide accounted for an almost quantitative yield.

Kinetic Experiments.—The kinetic runs were carried in

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[22] N. J. Leonard and C. R. Johson, *J. Org. Chem.*, 1962, **27**, 282.

[23] D. Barnard, J. M. Fabian, and H. P. Kech, *J. Chem. Soc.*, 1949, 2442.

[24] A. Cerniani and G. Modena, *Gazzetta*, 1959, **89**, 843.

[25] A. Cerniani, G. Modena, and P. Todesco, *Gazzetta*, 1960, **90**, 3.

[26] G. A. Martin, jun., *Iowa State Coll. J.Sci.*, 1946, **21**, 38 (*Chem. Abs.*, 1947, **41**, 952*e*).

the dark at 0 °C. Sulphoxide solutions were prepared by weighing out the sulphoxide into 25 ml of acetonitrile–pyridine stock solutions. Iodobenzene dichloride solutions were prepared immediately before use by dissolving the desired amount of the compound in 50 ml of an iodobenzene–acetonitrile stock solution. The solutions were titrated iodometrically before use. At zero time 25 ml of the iodobenzene dichloride solutions were added to the sulphoxide solutions. Aliquot portions were withdrawn at various times, quenched by addition of an excess of potassium iodide in 10% aqueous sulphuric acid, and titrated iodometrically.

The first-order rate constants were obtained by plotting log [$PhICl_2$] against time and determining the slope of the line. The pseudo-second-order rate constants were obtained in a similar way by plotting log $(a-x)/(b-x)$ against time, where a is the initial sulphoxide concentration and b the initial concentration of iodobenzene dichloride.

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