Racemization of Sulphoxides with Halide Ions anchimerically assisted by a Carboxy-group. The Different Behaviour of Chloride and Bromide Ions

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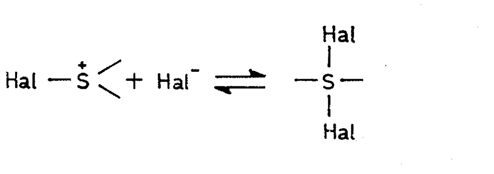
The kinetics of the racemization of (−)-2-isopropylsulphinylbenzoic acid (Ib) catalysed by Cl^- and Br^- have been studied in aqueous perchloric acid, and compared with those of the (−)-methyl analogue (Ia). In racemization with Cl^- the steric effect ($k_{(Ia)}/k_{(Ib)}$ *ca.* 50) is similar to those found in the reactions at sulphur centres, whereas steric retardation is minimized in racemization with Br^- ($k_{(Ia)}/k_{(Ib)}$ *ca.* 6). Moreover the reactivity ratios, k_{Br}/k_{Cl} [3 100 and 500 for (Ib and a), respectively] are much higher than those found in the racemizations of normal sulphoxides (k_{Br}/k_{Cl} *ca.* 3). These results seem to indicate that attack by halide ions in the halogenosulphonium intermediate occurs at sulphur or at halogen depending on the nature of Hal^-.

In recent years the reduction and racemization of sulphoxides catalysed by halide ions (I^-, Cl^-, Br^-) in aqueous acidic media have been studied in detail;[1-8] however the loss of optical activity of the sulphinyl group is still an open question.

The following schemes have been proposed[1-4] to explain racemization (Hal = Br or Cl): (i) formation of sulphide and halogen [equation (1)], with equilibrium (1) largely shifted to the left; (ii) fast halogen exchange of the halogenosulphonium ion [equation (2)]; (iii) formation of an achiral dihalogenosulphurane intermediate [equation (3)].

(1)

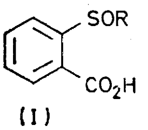
(2)



(3)

Since processes (1)—(3) occur after the rate-determining formation of halogenosulphonium ion for the sulphoxide examined,[1] no kinetic evidence can be found for any of them.

It has been shown[9,10] that in the 2-alkylsulphinylbenzoic acids (I) the reduction and racemization of



(I)

a; R = Me
b; R = Pr^i
c; R = Bu^t

sulphinyl group are anchimerically assisted by the carboxy-group.

We have found[10] that in the racemization of (—)-(Ia) with chloride and bromide ions in aqueous perchloric acid the intervention of a second halide ion, leading to the loss of optical activity, is rate determining.† Therefore with compounds such as (I) it is, in principle, possible to differentiate process (1) from processes (2)

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† This is not the case in the reduction of (Ia) by I^-, where attack by the second halide ion occurs in a relatively fast step.[10]

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

[2] D. Landini, G. Modena, U. Quintily, and G. Scorrano, *J. Chem. Soc.* (*B*), 1971, 2041.

[3] G. Scorrano, *Accounts Chem. Res.*, 1973, **6**, 132.

[4] K. Mislow, T. Simmons, J. T. Melillo, and A. L. Ternay, *J. Amer. Chem. Soc.*, 1964, **86**, 1452.

[5] R. A. Streker and K. K. Andersen, *J. Org. Chem.*, 1968, **33**, 2234.

[6] J. H. Krueger, *Inorg. Chem.*, 1966, **5**, 132.

[7] I. Ookuni and A. Fry, *J. Org. Chem.*, 1971, **36**, 4097.

[8] R. Curci, F. Di Furia, A. Levi, and G. Scorrano, *J.C.S. Perkin II*, 1975, 408.

[9] S. Allenmark and C. E. Hackberg, *Acta Chem. Scand.*, 1968 **22**, 1964.

[10] D. Landini, F. Rolla, and G. Torre, *Internat. J. Sulfur Chem.* (*A*), 1972, **2**, 43.

and (3) by studying the influence of steric factors on the rate of racemization. Indeed pathways (2) and (3), involving attack of the second halide ion at the sulphur atom, must be subject to steric retardation, whereas the latter should be minimized in the case of (1), where attack occurs at halogen.

TABLE 1

pK_a Value of sulphoxide (Ib) in $HClO_4$ from u.v. data at 25°

Acidity function	pK_a [a]	Slope [b] (r)
$H_0 + \log [H^+]$	−1.85	0.56 (9 986)
H_A	−2.25	0.98 (9 976)

[a] The reliability of the data is to be considered within ±0.2.[11] Slopes are evaluated by least squares analysis from plots of log $([SOH^+]/[SO]) + H_0$ *versus* $H_0 + \log [H^+]$ and of log $([SOH^+]/[SO])$ *versus* $-H_A$, respectively.

RESULTS

The rates of chloride and bromide ion racemization of (−)-2-methylsulphinylbenzoic acid (Ia)[10] in aqueous perchloric acid have been compared to those of the (−)-isopropyl analogue (Ib). Unfortunately it was not possible to examine the behaviour of the t-butyl derivative (Ic), since it undergoes an acid-catalysed decomposition faster than the reaction with halide ions.[3]

TABLE 2

Rate constants for racemization of (Ib) with halide ions in aqueous perchloric acid at 25°

Hal⁻	$[H^+]$/M	$-H_0$ [a]	$-H_A$ [a]	$10^5k_{obs}/s^{-1}$	$5 + \log k'$ [b]$/s^{-1}$	α [c] (r)
Cl⁻ [d]	4.10	1.91	1.72	1.64	0.856	1.26 (0.995 3)
	5.19	2.50	2.08	10.4	1.411	
	5.96	2.92	2.35	81.3	2.163	
	6.60	3.32	2.60	244	2.547	
	7.17	3.70	2.84	939	3.072	
Br⁻ [d]	2.09	0.94	0.91	4.39	2.002	1.38 (0.996 1)
	2.59	1.16	1.15	14.0	2.276	
	2.98	1.35	1.31	31.4	2.484	
	3.37	1.54	1.45	99.1	2.860	
	4.10	1.87	1.69	397	3.264	

[a] Corrected for salt effect.[1] [b] The pK_a value used is −2.25. [c] Slopes (α) were evaluated by least squares analysis from plots of log k' *versus* $-H_0$. [d] From sodium chloride (0.4M) and bromide (0.2M).

TABLE 3

Dependence of rate constants for racemization of (Ib) on $[Hal^-]$ in aqueous perchloric acid at 25°

Hal⁻	$[Hal^-]$/M	$[H^+]$/M	$-H_0$ [a]	$10^5k_{obs}/s^{-1}$	$5 + \log k'/s^{-1}$	$-(\log k' + \alpha H_0)$ [b]	s [c] (r)
Cl⁻	0.2	5.19	2.46	2.08	0.729	7.372	2.07 (0.9993)
	0.3	5.19	2.48	4.94	1.097	7.027	
	0.4	5.19	2.50	10.4	1.411	7.637	
	0.5	5.19	2.52	16.9	1.612	6.558	
Br⁻	0.1	2.59	1.14	2.52	1.544	5.033	2.24 (0.9997)
	0.2	2.59	1.16	14.0	2.274	4.327	
	0.3	2.59	1.18	35.6	2.666	3.959	
	0.4	2.59	1.20	72.8	2.963	3.686	

[a] Corrected for salt effect.[1] [b] α = 1.26 and 1.38 for reactions with chloride and bromide ions, respectively (see Table 2). [c] Slopes (s) were evaluated by least squares analysis from plots of $-(\log k' + \alpha H_0)$ *versus* log $[Hal^-]$.

The reactions of (Ib), carried out at 25° with a large excess of halide ion and acid, follow the first-order kinetic equation (4) up to ⩾80% conversion. The experimental rate constant, k_{obs}, strongly depends on the acidity of medium. Since in the range of acid concentration used (2.1—7.2M-$HClO_4$) the sulphoxides are substantially protonated[1,11] the reaction rate should be expressed in equation

$$\text{rate} = k_{obs}[SO]_{st} \tag{4}$$

(5).[*] The amount of protonated sulphoxide (Ib) was

$$\text{rate} = k'[SOH^+] \tag{5}$$

evaluated from its thermodynamic pK_a value and the acidity function H_A.[1] The protonation equilibrium of (Ib) in perchloric acid was measured by a u.v. spectroscopic technique,[11] and thermodynamic pK_a value, evaluated by the Bunnett and Olsen equation[12] and on the H_A scale, is −1.85 and −2.25, respectively.[†] The data are collected in Table 1.

Since a plot of log $([SOH^+]/[SO])$ against $-H_A$ is linear with a slope of *ca.* 1 (Table 1), the H_A acidity function can be used, as a good approximation, to describe the acid-base behaviour of sulphoxide (Ib). Thus the rate constant k', which takes into account protonation of sulphoxide (Ib) was evaluated, as previously reported,[1] from equation (6).

$$k' = k_{obs}(h_A + K_a)/h_A \tag{6}$$

Table 2 shows that the rate coefficient k' still depends on the acidity of the medium. Experimentally we found that log k' against H_0 is linear with slope (α) *ca.* 1, showing that a second proton intervenes before or during the rate-determining step (Table 2). The reaction order in halide ions was evaluated by plotting log $k' + \alpha H_0$ *versus* log $[Hal^-]$, taking into account the salt effect on the H_0 acidity function and the complex dependence of the rate constant on the acidity of the medium, as previously described.[1,10]

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[*] $[SOH^+]$ and $[SO]$ represent the concentration of protonated and free sulphoxide, respectively, and $[SO]_{st}$ stands for the stoicheiometric concentration of sulphoxide.

[†] Similar differences have been found for other sulphoxides. For a discussion of the comparison between the two series of values, see refs. 1 and 11.

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

[12] J. Bunnett and F. P. Olsen, *Canad. J. Chem.*, 1966, **44**, 1899.

Slopes of *ca.* 2 were found for the racemization of (Ib) both with chloride and bromide ions, showing that the reaction is second order in [Hal$^-$]. Pertinent data are collected in Table 3.

TABLE 4

Steric effects on the racemization of sulphoxides (Ia and b) with halide ions in aqueous perchloric acid at 25°

Sulphoxide	[H+]/M	Hal$^-$ [a]	$10^5 k_{obs}/s^{-1}$
(Ia)	5.2	Cl$^-$	241
(Ib)	5.2	Cl$^-$	4.9
(Ia)	2.6	Br$^-$	83.0
(Ib)	2.6	Br$^-$	14.0

[a] From sodium chloride (0.3M) and bromide (0.2M).

TABLE 5

Pseudo-first-order rate constants ($k_{Hal} = k_{obs}$) for the racemization of sulphoxides (Ia and b) with halide ions in aqueous perchloric acid at 25°

Sulphoxide	[H+]/M	$10^5 k_{Br}$	$10^5 k_{Cl}$
(Ia) [a]	2.6	190	0.38
(Ib) [b]	4.1	397	0.13

[a] [NaHal] = 0.3M. [b] [NaHal] = 0.2M.

The steric effect and reactivity ratio, k_{Br}/k_{Cl}, for the racemization of (Ia and b) with chloride and bromide ions can be evaluated from the data reported in Tables 4 and 5, respectively. Due to the large difference in reactivity between Cl$^-$ and Br$^-$, the reaction rates were measured at different perchloric acid concentration (see Tables 4 and 5).

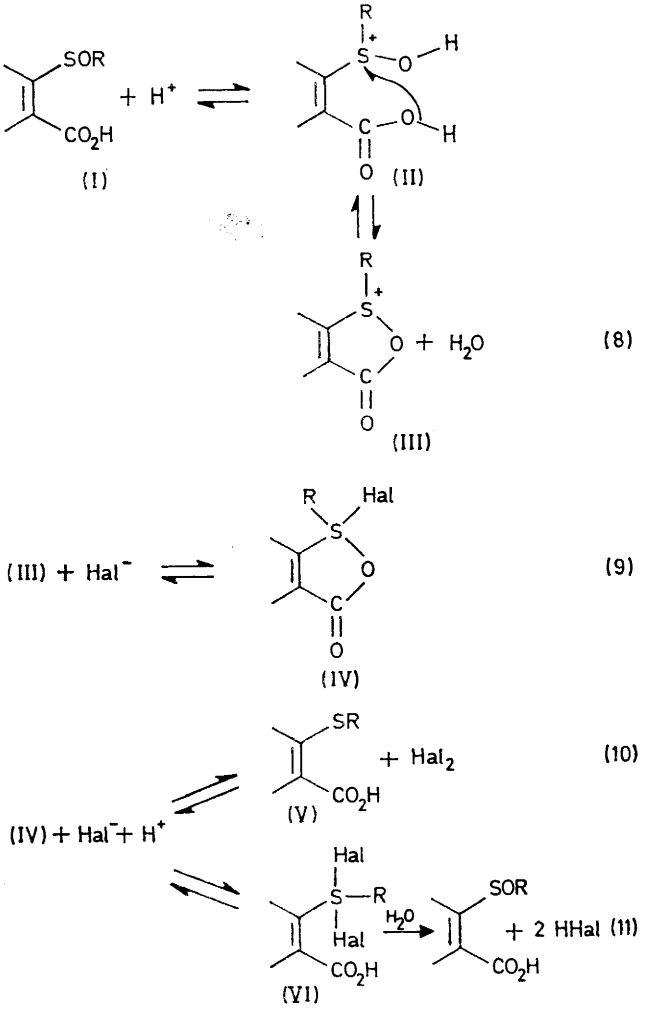
DISCUSSION

The experimental results indicate that the racemization of (—)-2-isopropylsulphinylbenzoic acid (Ib) with chloride or bromide ions in aqueous perchloric acid follows the same kinetic equation (7) as that followed by

$$\text{rate} = k[\text{SO}][\text{Hal}^-]^2 a^2_{\text{H}^+} \qquad (7)$$

the (—)-2-methylsulphinyl derivative (Ia),[10] showing that in the case of (Ib) also the intervention of a second halide ion is rate determining. Therefore for the compounds (Ia and b) the same mechanism must operate, which, on the basis of the kinetic data, can be formulated as reactions (8)—(11).

Elimination of a water molecule by nucleophilic attack of the carboxy-group on the protonated sulphoxide (II) gives the cyclic acyloxy-sulphonium salt (III), which by attack of Hal$^-$ is converted into acyloxy-halogenosulphurane intermediate (IV).* The latter by acid catalysis and reaction with a second halide ion, in the rate-determining step, suffers loss of optical activity through formation either of sulphide (V) [equation (10)] or of a dihalogenosulphurane (VI), which is rapidly hydrolysed to sulphoxide [equation (11)].† Since the reaction always affords the racemic sulphoxide, steps (8)—(10) must be reversible and the equilibria largely shifted to the left.‡



We have found that the rate of racemization of (Ib) with Cl$^-$ is *ca.* 50 times slower than that of (Ia), while with Br$^-$ the ratio $k_{(Ia)}/k_{(Ib)}$ is nearly 6 (Table 4). In other words in the first case steric retardations similar to

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* We do not have any direct evidence of the existence of acyloxy-halogenosulphurane intermediate (IV); however tetraco-ordinate sulphur species have been proposed as intermediates in many reactions, some have been identified in the reaction medium, and a few isolated as stable compounds.[13-15]

† In previous papers,[10,16] on the basis of kinetic data and of experiments of isotopic ^{16}O/^{18}O exchange in (Ia), the reaction scheme was formulated as equations (8)—(10). The present results allow process (11) to be envisaged for the loss of optical activity of sulphoxides (Ia and b).

‡ This assumption is based on the fact that in aqueous medium the overall equilibrium between sulphides and chlorine or bromine, $>\text{S} + \text{Hal}_2 + \text{H}_2\text{O} \rightleftharpoons >\text{SO} + 2\text{HHal}$, is largely shifted toward the sulphoxide.[17-19]

[13] N. E. Hester, *Internat. J. Sulfur Chem.*, 1973, **8**, 119, and references therein.

[14] J. C. Martin and E. F. Perozzi, *J. Amer. Chem. Soc.*, 1974, **96**, 3155.

[15] I. Kapovits and A. Kolmann, *Chem. Comm.*, 1971, 649.

[16] D. Landini and F. Rolla, *J.C.S. Perkin II*, 1972, 137.

[17] G. E. Wilson, jun., and M. M. Y. Chang, *J. Amer. Chem. Soc.*, 1974, **96**, 3155.

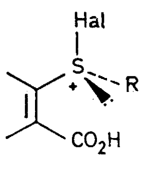
[18] U. Miotti, G. Modena, and L. Sedea, *J. Chem. Soc.* (*B*), 1970, 802.

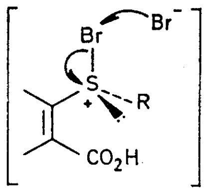
[19] M. Cinquini, S. Colonna, and D. Landini, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 211.

that found in reaction at a sulphur centre[4,5,20-22] are met with, whereas in the second case they are minimized.

Furthermore the reactivity ratio, k_{Br}/k_{Cl}, is *ca.* 500 and 3 100 for (Ia and b), respectively (Table 5). Even if the different steric effect in the reaction of (Ib) with Cl^- and Br^- is taken into account (see above), these values are at least two orders of magnitude higher than those found[1] in the racemization of normal sulphoxides (k_{Br}/k_{Cl} *ca.* 3). Since the latter represents the relative nucleophilicity of Br^- and Cl^- in nucleophilic reactions at sulphinyl sulphur,[1,23] the much higher ratio (k_{Br}/k_{Cl}) found in the racemization of (Ia and b) with chloride and bromide ions shows that the mechanism of attack of the second halide ion must be different for the two halogens.

These results suggest that the second Br^- ion attacks the halogen giving the sulphide [equation (10)] but on the other hand the attack of the second Cl^- ion occurs at sulphur affording the dihalogenosulphurane (VI) [equation (11)]. The attacks must occur on the halogenosulphonium ion (VII) deriving from the acid-catalysed breaking of the S–O bond in intermediate (IV) [formulae (VIII) and (IX)]. A possible alternative involves, in the case of Br^-, a concerted opening of the ring and attack by halide ion.


(VII)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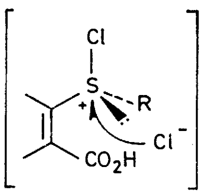
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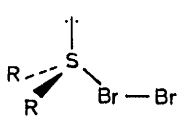
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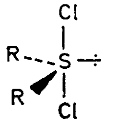
(XI)

The kinetic data we report are for particular sulphoxides, and unfortunately we are not able to extend our consideration to the general case.

The dichotomy of attack at sulphur or at halogen which we propose in the racemization of (Ia and b) is confirmed by investigations on the molecular complexes between sulphides and halogens either in the solid phase or in solution.[24-26] Indeed structures with trico-ordinate pyramidal sulphur (X) and tetraco-ordinate trigonal-bypyramidal sulphur (XI) were found in sulphide-bromine and sulphide–chloride adducts, respectively.

EXPERIMENTAL

Materials and Solvents.—Sodium halides and perchloric acid were AnalaR grade commercial products, used without further purification.

Substrates.—Racemic 2-methylsulphinylbenzoic acid (Ia) was synthesized, as reported,[27] by oxidation of the corresponding sulphide with the stoicheiometric amount of peracetic acid, and carefully purified by repeated crystallization from ethyl acetate, m.p. 178—180° (lit.,[27] 178—180°), yield 75%. Racemic *2-isopropylsulphinylbenzoic acid* (Ib) was obtained in 90% yield, by oxidation of the corresponding sulphide,[28] as described for (Ia), m.p. 136—138° (from 1 : 2 benzene–light petroleum) (Found: C, 56.8; H, 5.8. $C_{10}H_{12}O_3S$ requires C, 56.6; H, 5.7%). (−)-2-Methylsulphinylbenzoic acid (Ia) was obtained from the racemic sulphoxide *via* its brucine salt as previously reported,[27] m.p. 185.5—186°, $[\alpha]_D^{20}$ −227.5° (*c* 1; EtOH). (−)-2-Isopropylsulphinylbenzoic acid (Ib) was similarly prepared from the racemic sulphoxide. Its brucine salt, after four crystallizations from ethanol, had m.p. 191—193°, $[\alpha]_D^{20}$ −108° (*c* 1; EtOH). The optically active sulphoxide (Ib) had m.p. 162—163° (from ethyl acetate), $[\alpha]_D^{20}$ −310° (*c* 1; EtOH).

Products.—The reactions were examined by the method already described.[16] In any case from the reaction mixture of (Ia and b) both with chloride and bromide ions the corresponding racemic sulphoxides were isolated in at least 75% yield.

Acidity Function Measurements.—Perchloric acid solutions were made up by dilution and titrated with standard NaOH. The H_0 values were obtained from published data.[29] The H_A values of perchloric acid solution were provided by Yates.[30] The effect of sodium halide on the acidity was evaluated on the assumption that the effect of bromide is equal to that of chloride.[31] The effect of sodium chloride was evaluated by measuring spectrophotometrically the ionization ratios of suitable indicators at various perchloric acid concentrations, as previously described.[1]

pK_a Value of 2-Isopropylsulphinylbenzoic Acid (Ib).—The pK_a was measured by the u.v. technique already described.[1,11] The values of optical densities at 232 and 245 nm were used. The technique followed in the kinetic experiments has been described in detail elsewhere.[1]

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[20] D. Landini, F. Montanari, G. Modena, and G. Scorrano, *Chem. Comm.*, 1969, 3.

[21] A. Fava, A. Iliceto, and E. Camera, *J. Amer. Chem. Soc.*, 1957, **79**, 833.

[22] A. Fava and A. Iliceto, *J. Amer. Chem. Soc.*, 1958, **80**, 3478.

[23] J. L. Kice, *Accounts Chem. Res.*, 1968, **1**, 58, and references therein.

[24] G. Allegra, G. E. Wilson, jun., E. Benedetti, C. Pedone, and R. Albert, *J. Amer. Chem. Soc.*, 1970, **92**, 4002.

[25] N. C. Baezinger, R. E. Bukles, R. J. Maner, and T. D. Simpson, *J. Amer. Chem. Soc.*, 1969, **91**, 5749.

[26] J. B. Lambert, D. A. Johnson, R. G. Keske, and C. E Mixan, *J. Amer. Chem. Soc.*, 1972, **94**, 8172, and references therein.

[27] G. Barbieri, V. Davoli, I. Moretti, F. Montanari, and G. Torre, *J. Chem. Soc.* (*C*), 1969, 731.

[28] H. Gilman and F. J. Webb, *J. Amer. Chem. Soc.*, 1949, **71**, 4062.

[29] R. S. Ryabova, I. M. Medvetskaya, and M. I. Vinnik, *Russ. J. Phys. Chem.*, 1966, **40**, 182.

[30] K. Yates, personal communication.

[31] M. A. Paul and F. A. Long, *Chem. Rev.*, 1957, **57**, 1.