Intramolecular Catalysis by a Carboxy-group in the Reduction and Racemization of Sulphoxides by Halide Ion. $^{16}O/^{18}O$ Exchange as a Test for the Mechanism

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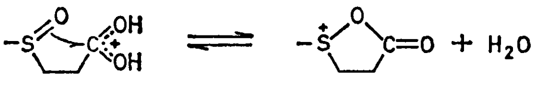
$^{16}O/^{18}O$ Exchange and racemization of the sulphinyl group of *o*-methylsulphinylbenzoic acid have been studied in aqueous perchloric acid both in the presence and in the absence of Br^- and Cl^- ions. Exchange of the sulphinyl oxygen atom is faster than racemization in the presence of halide ions; no exchange occurs at the carboxy-group. These results indicate that, in the reduction and racemization of sulphoxides, intramolecular catalysis by a carboxy-group involves nucleophilic attack by the latter on the sulphur atom of the protonated sulphoxide, with formation of a cyclic acyloxy-sulphonium intermediate.

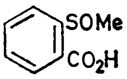
Reduction and racemization of sulphoxides by halide ions (I^-, Br^-, or Cl^-) are intramolecularly catalysed by a carboxy-group, if this is in a favourable position in the molecule.[1-5] Two different mechanisms have been suggested to explain the anchimeric assistance. The first[1] suggests nucleophilic attack by sulphinyl oxygen on the carbon atom of the protonated carboxy-group, with formation of a cyclic acyloxy-sulphonium species (II) [equation (1)]; the second[5] involves formation of (II) *via* nucleophilic attack of the carboxylic oxygen on the sulphur atom of the protonated sulphoxide [equation (2)]. Although the kinetic data[5] on the reduction and racemization of *o*-methylsulphinylbenzoic acid (III) and of the corresponding methyl ester (IV) by halide ions exclude equation (1), they do not definitely prove the second mechanism to be correct. To solve the problem we carried out a series of $^{16}O/^{18}O$ exchanges for compound (III), selectively labelled at the sulphinyl or at the carboxy-group.



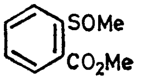
(1)

(I) (II)

(2)



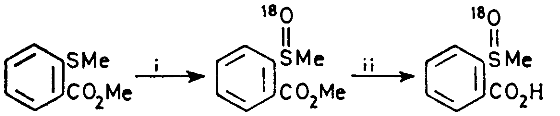
(III)



(IV)

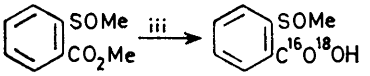
RESULTS

[^{18}O]*o*-Methylsulphinylbenzoic acid (IIIa) (6·8% isotopic content) and *o*-methylsulphinyl[$C^{16}O^{18}OH$]benzoic acid (IIIb) (10% isotopic content) were obtained as shown in equations (3) and (4), respectively.



(3)

(V) (IVa) (IIIa)



(4)

(IV) (III)

Reagents: i, PhICl$_2$–H$_2$^{18}O (ref. 6)–C$_5$H$_5$N, −15°. ii, KOH, EtOH–H$_2$O; iii, Na^{18}OH, dioxan–H$_2$^{18}O

When compound (IIIa), in aqueous perchloric acid (1·3M), was treated with Br^- ion (0·3M) at 25° for 20 min, the ^{18}O content of the sulphinyl group decreased from 6·8 to 5%. Under the same conditions a 7% racemization of compound (III) was observed. The sulphinyl oxygen atom was completely exchanged when the acid (IIIa) was allowed to stand in aqueous perchloric acid (2·5M) at 25° for 4 h, both in the presence and in the absence of chloride ion (0·6M). Under the same conditions a 27% racemization of (III) was observed in the presence of chloride ion (0·6M), whereas in the absence of halide ion no variation in the specific rotation was detected. When the same experiments were carried out on compound (IIIb), no exchange occurred at the ^{18}O-enriched carboxy-group. The data are reported in the Table.

DISCUSSION

The data indicate that exchange at the sulphinyl oxygen atom of *o*-methylsulphinylbenzoic acid (III) is faster than the halide-catalysed racemization and that no exchange occurs at the carboxy-group for the conditions in which the sulphinyl group gives complete exchange and partial racemization.*

On the basis of the relative proportions of racemization

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* It has recently been shown by Oae *et al.*[7] that in 65·7% sulphuric acid *o*-phenylsulphinylbenzoic acid exchanges at the sulphinyl group 10^4 times faster than it racemizes, and that in the same conditions the carboxy-group does not exchange.

[1] S. Allenmark, *Mechanisms of Sulfur Compounds*, 1968, **2**, 173, and previous papers in the series.

[2] S. Allenmark and C. E. Hagberg, *Acta Chem. Scand.*, 1968, **22**, 1664.

[3] S. Allenmark and C. E. Hagberg, *Acta Chem. Scand.*, 1970, **24**, 2225.

[4] D. Landini and G. Torre, *Boll. sci. Fac. Chim. ind. Bologna*, 1969, **27**, 227.

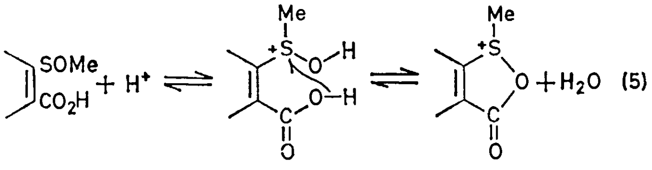
[5] D. Landini, F. Rolla, and G. Torre, *Internat. J. Sulfur Chem. A*, 1972, **2**, 43.

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

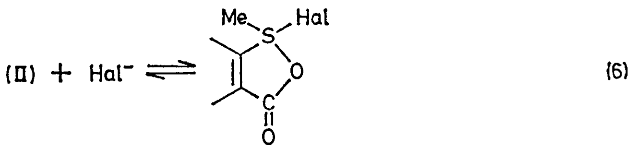
[7] T. Numata, K. Sakai, M. Kise, N. Kunieda, and S. Oae, *Internat. J. Sulfur Chem. A*, 1971, **1**, 1.

(7%) and exchange (26·5%) in perchloric acid (1·3M) in the presence of bromide ion (0·3M), the exchange rate constant ($k_{\text{ex.}}$) is four times the racemization rate constant ($k_{\text{rac.}}$). The ratio $k_{\text{ex.}} : k_{\text{rac.}}$ cannot be evaluated in perchloric acid (2·5M) in the presence of Cl^- (0·6M), since compound (III), recovered after 4 h (in this time a 27% racemization occurs), had fully exchanged its sulphinyl oxygen atom. Since it is known [5] that in the same conditions the racemization catalysed by bromide ion is 6×10^2 times faster than that catalysed by chloride ion, we can assume that $k_{\text{ex.}} : k_{\text{rac.}}$ in the presence of Cl^- must be >4.

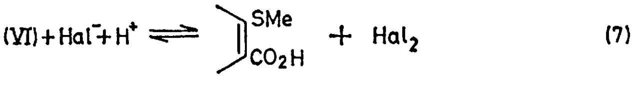
On the basis of the kinetic data [5] the mechanism formulated in equations (5)—(7) had been suggested for the reduction and racemization of (III) by halide ions (I^-, Br^-, or Cl^-).



(III) (I) (II)



(VI)



(VII)

$^{16}O/^{18}O$ Exchange reactions of compounds (IIIa) and (IIIb) in aqueous perchloric acid at 25°

Substrate	$^{18}O(\%)$ [a] Starting material	$^{18}O(\%)$ [a] Recovered material	$[H^+]$/M	Hal^-(M)	Reaction time (min)	Racemization (%)
(IIIa)	6·8	5·0	1·3	Br^- (0·3)	20	7
(IIIa)	6·8	0·0	2·5		240	0
(IIIa)	6·8	0·0	2·5	Cl^- (0·6)	240	27
(IIIb)	10·0	10·0	2·5	Cl^- (0·6)	240	27
(IIIb)	10·0	10·0	2·5		240	0

[a] Probable errors are 2—3%.

The kinetic data indicate all steps are reversible and that the equilibrium is shifted towards the sulphide (VII) in the case of I^- and towards the sulphoxide (III) in the case of Br^- and Cl^-. Moreover, in the reduction, formation of (II) and (VI) proceed at comparable rates and are rate determining, while in the racemization, step (7) is rate determining. The results of $^{16}O/^{18}O$ exchanges are in full agreement with this mechanism, and especially with the formation of intermediate (II) as visualized in equation (5). They exclude nucleophilic attack by the sulphinyl oxygen at the carboxylic carbon atom, which would lead to migration of the ^{18}O oxygen atom from the sulphur to the carboxy-group, and hence to retention of the isotopic content of the molecule, since the carboxy-group does not exchange under the conditions in which racemization occurs. Intermediate (II) must be optically stable; in fact, in the absence of halide ions, exchange but no racemization was observed. Moreover conversions (I) ⟶ (II) and (II) ⟶ (I) must proceed with overall retention, *i.e.* the two processes must both involve retention or inversion. Since nucleophilic substitution at sulphur in the analogous *O*-alkylsulphoxonium salts is known to occur with inversion,[8] it seems likely that reactions (I) ⟶ (II) and (II) ⟶ (I) both proceed with inversion.

EXPERIMENTAL

Mass spectra were recorded with an RMU Itachi 6 D mass spectrometer. Optical activities were measured with a Perkin-Elmer P22 spectropolarimeter in the range 300—320 nm.

Materials and Solvents.—Sodium halides and perchloric acid were AnalaR grade commercial products purified, when necessary by standard methods.

[^{18}O]o-*Methylsulphinylbenzoic Acid* (IIIa).—Methyl [^{18}O]-*o*-methylsulphinylbenzoate (IVa) [5] was obtained in 85% yield by oxidation of the corresponding sulphide (V) [9] with (dichloroiodo)benzene in the presence of pyridine and of 10% ^{18}O-enriched water, as previously reported.[6] Alkaline hydrolysis of (IVa) afforded the acid (IIIa) (90%), m.p. 170—171° (from ethyl acetate) (lit.,[6] 172—173°), ^{18}O content 6·8% (mass spectrum).

o-*Methylsulphinyl*[$C^{16}O^{18}OH$]*benzoic Acid* (IIIb).—This was obtained in 90% yield by hydrolysis of the corresponding methyl ester (IV) [5] in dioxan–10% ^{18}O-enriched water (8 : 2, v/v) in the presence of $Na^{18}OH$ (5 mol. equiv.). It had m.p. 170—171° (from ethyl acetate), ^{18}O content 10·0% (mass spectrum).

$^{16}O/^{18}O$ *Exchanges.*—Sulphoxides (IIIa) or (IIIb) (0·1 g) were dissolved in aqueous perchloric acid (50 ml, 1·3 or 2·5M), in the presence of sodium bromide or sodium chloride (0·3 or 0·6M) (see Table). The reactions were quenched by pouring into a cooled aqueous solution of sodium hydrogen carbonate (final pH 3—4) Extraction with chloroform (8 times) and evaporation of the solvent afforded the product which was purified by crystallization and analysed by mass spectroscopy.

The technique followed in the kinetic experiments has been described elsewhere.[10]

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