Asymmetric Induction and Configurational Correlations in Oxidations at Sulphur. Part V.[1] Oxidations of Optically Active Esters of *o*-(Methylthio)benzoic Acid by Achiral Peroxy-acids

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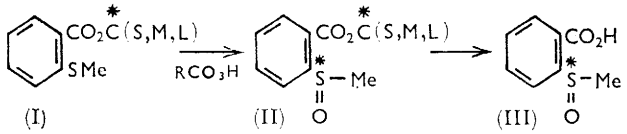
Oxidation of optically active esters of *o*-(methylthio)benzoic acid with achiral peroxy-acids (perbenzoic and 2,4,6-trimethylperbenzoic acids) yields mixtures of the corresponding diastereomeric sulphoxides, enriched in one of the components. Hydrolysis affords optically active *o*-methylsulphinylbenzoic acid. The absolute chirality of the latter depends on the chirality of the inducing alcohol. The optical yields are noticeably higher with the bulkier trimethylperbenzoic acid. The asymmetric induction is interpreted in terms of eclipsing effects of small, medium, and large groups. A correlation model, based on those conformations of the diastereomeric transition states which present the largest difference of steric compression, is suggested.

ASYMMETRIC inductions involving organosulphur compounds have previously been noted in the oxidation of aryl alkyl sulphides [2] and sulphoxides [1] with optically active peroxy-acids. We now report the oxidation of optically active esters of *o*-(methylthio)benzoic acid (I) with achiral reagents, *i.e.*, perbenzoic and 2,4,6-trimethylperbenzoic acid. The reaction yields diastereomerically enriched mixtures of sulphoxides (II), which are subsequently hydrolysed to optically active *o*-methylsulphinylbenzoic acid (III). We have previously described this kind of asymmetric induction for a few cases,[2b] and have developed a correlation model based on principles of steric control similar to those developed by Cram and Prelog for asymmetric syntheses at carbon. Little is known [1,2c] as to whether these principles are applicable to systems other than carbon, and, if so, to what extent. The absolute configuration attributed [2b] to the enantiomers of the acid (III) on the basis of the known configuration of the inducing alcohols turned out to be correct,[3] but the opinion that our model was not reliable was put forward.[4] We therefore thought it necessary to check its validity and its limits with a wider range of experiments.



(I) (II) (III)

R = Ph or 2,4,6-$Me_3C_6H_2$

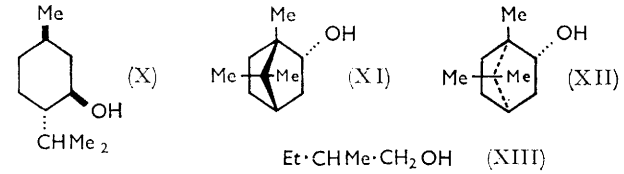
The ten esters listed in Table 1 were prepared by condensation of *o*-(methylthio)-benzoic anhydride or -benzoyl chloride with optically active alcohols (IV)—(XIII). They were oxidized with perbenzoic and trimethylperbenzoic acids in chloroform solution at 0°. Sulphoxides (II) were saponified by heating with sodium hydroxide in aqueous ethanol. The optically pure enantiomers of *o*-methylsulphinylbenzoic acid (III) were obtained by fractional crystallisation of the brucine salts. Their absolute configurations were shown to be (*R*)-(+) and (*S*)-(−) by conversion of (−)-*o*-methylsulphinylaniline into (*S*)-(−)methyl phenyl sulphoxide and the (−)-acid (III).[3]

The sign of rotation of the acid (III) is directly related to the chirality of the inducing alcohol (Table 2); when this can be represented by the stereoformula (XIV), which corresponds to the absolute configuration (*S*) in the cases examined, an excess of the (*R*)-(+)-enantiomer is usually obtained. The opposite enantiomer is obtained when the chirality of the alcohol can be represented by the stereoformula (XV).

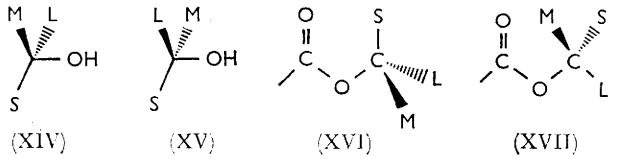
Two exceptions were found in the oxidations with perbenzoic acid: the esters of (−)-borneol (XI) and (−)-isoborneol (XII), both of chirality (XV), lead to the (*R*)-(+)- instead of the (*S*)-(−)-acid (III). Oxidation of the two esters with trimethylperbenzoic acid yielded the expected (*S*)-(−)-enantiomer.

RCHMe·OH

(IV) R = Et
(V) R = Bu^t
(VI) R = C_6H_{11}
(VII) R = Ph
(VIII) R = 2,4,6-$Me_3C_6H_2$
(IX) R = α-$C_{10}H_7$



Et·CHMe·CH_2OH (XIII)



The optical yields of the oxidations with trimethylperbenzoic acid are normally higher than those with perbenzoic acid; a maximum value of 27·7% was found

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[1] Part IV, U. Folli, D. Iarossi, and F. Montanari, *J. Chem. Soc.* (*C*), 1968, 1372.

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TABLE 1

Physical properties and analytical data for optically active esters of *o*-(methylthio)benzoic acid

Alcohol	Formula	C (%) Found	C (%) Reqd.	H (%) Found	H (%) Reqd.	S (%) Found	S (%) Reqd.	M.p. (B.p./μ)	$[\alpha]_D^{20}$ ($CHCl_3$)
(+)-(IV)	$C_{12}H_{16}O_2S$	63·8	64·2	7·1	7·2	14·4	14·3	(93—105°/35—40)	+26·5°
(+)-(V)	$C_{14}H_{20}O_2S$	66·8	66·6	8·5	8·0	12·7	12·6	(98—105/23—25)	+51·3
(+)-(VI)	$C_{16}H_{22}O_2S$	69·6	69·0	8·1	8·0	11·5	11·5	(115—127/10—20)	+17·5
(−)-(VII)	$C_{16}H_{16}O_2S$	69·8	70·5	5·8	5·9	11·6	11·7	(135—138/12)	−50·0
(+)-(VIII) [a]	$C_{19}H_{22}O_2S$	72·4	72·6	7·1	7·0	10·3	10·2	112 [b]	+24·5
(−)-(IX) [a]	$C_{20}H_{18}O_2S$	74·2	74·5	5·5	5·6	9·7	9·9	81—82 [c]	+31·7
(−)-(X)	$C_{18}H_{26}O_2S$	69·9	70·4	8·6	8·5	10·5	10·5	49—50 [b]	−84·0
(−)-(XI)	$C_{18}H_{24}O_2S$	71·0	70·8	8·1	7·9	10·5	10·5	83—84 [b]	−46·5
(−)-(XII)	$C_{18}H_{24}O_2S$	71·0	70·8	7·9	7·9	10·5	10·5	65—66 [b]	−63·5
(−)-(XIII)	$C_{13}H_{18}O_2S$	66·0	65·5	7·7	7·6	13·4	13·5	(120—122/20)	+6·7

[a] From ref. 2*b*; [b] from light petroleum; [c] from ligroin.

TABLE 2

Asymmetric synthesis of *o*-methylsulphinylbenzoic acid [a]

Alcohol: Formula	Alcohol: Chirality	Alcohol: Absolute config.	Oxidations with perbenzoic acid: $[\alpha]_D^{20}$ [b]	Optical yield (%)	Absolute config.: Found	Absolute config.: Expected	Oxidations with trimethylperbenzoic acid: $[\alpha]_D^{20}$ [b]	Optical yield (%)	Absolute config.: Found	Absolute config.: Expected
(IV)	(XIV)	(*S*)-(+)	+1·7°	0·7	(*R*)	(*R*)	+6·4°	2·8	(*R*)	(*R*)
(V)	(XIV)	(*S*)-(+)	+7·4	3·2	(*R*)	(*R*)	+12·3	5·4	(*R*)	(*R*)
(VI)	(XIV)	(*S*)-(+)	+3·0	1·3	(*R*)	(*R*)	+16·1	7·1	(*R*)	(*R*)
(VII)	(XIV)	(*S*)-(−)	+6·0	2·7	(*R*)	(*R*)	+8·5	3·8	(*R*)	(*R*)
(VIII)	(XV)	(*R*)-(+)	−45·4	20·0	(*S*)	(*S*)	−63·0	27·7	(*S*)	(*S*)
(IX)	(XIV)	(*S*)-(−)	+22·3	9·8	(*R*)	(*R*)	+50·5	22·2	(*R*)	(*R*)
(X)	(XV)	(*R*)-(−)	−14·0	6·2	(*S*)	(*S*)	−2·6	1·1	(*S*)	(*S*)
(XI)	(XV)	(*R*)-(−)	+7·7	3·4	(*R*)	(*S*)	−13·5	5·9	(*S*)	(*S*)
(XII)	(XV)	(*R*)-(−)	+3·4	1·5	(*R*)	(*S*)	−5·2	2·2	(*S*)	(*S*)
(XIII)	(XIV)	(*S*)-(−)	0	0		(*R*)	0	0		(*R*)

[a] Oxidations in chloroform at 0°. [b] Measurements in 95% ethanol.

TABLE 3

Influence of solvent on the asymmetric synthesis of *o*-methylsulphinylbenzoic acid

Solvent	Temp. of reaction	Peroxy-acid [a]	From (−)-bornyl ester [b]: $[\alpha]_D^{20}$ [d]	Optical yield (%)	Absolute config.[c]	From (−)-menthyl ester: $[\alpha]_D^{20}$ [d]	Optical yield (%)	Absolute config.[c]
Acetonitrile	0°	B	+9·1°	4·0	(*R*)	−17·7°	7·8	(*S*)
		T	−2·1	0·9	(*S*)	−10·6	4·7	(*S*)
Propan-2-ol	0	B	+6·1	2·7	(*R*)	−14·5	6·4	(*S*)
		T	−3·1	1·4	(*S*)	−11·6	5·1	(*S*)
Chloroform	0	B	+6·2	2·7	(*R*)	−14·0	6·2	(*S*)
		T	−10·0	4·8	(*S*)	−2·6	1·1	(*S*)
Ether	0	B	+6·3	2·8	(*R*)	−17·8	7·8	(*S*)
		T	−4·3	1·9	(*S*)	−15·0	6·6	(*S*)
Benzene	+5	B	+1·0	0·5	(*R*)	−14·0	6·2	(*S*)
		T	−5·3	2·3	(*S*)	−12·9	5·7	(*S*)
Dioxan	+12	B	+3·4	1·5	(*R*)	−10·8	4·8	(*S*)
		T	−5·4	2·4	(*S*)	−10·0	4·4	(*S*)

[a] B = Perbenzoic acid; T = trimethylperbenzoic acid. [b] Prepared from commercial borneol; (−)-borneol, 80%; (+)-isoborneol, 16%; (+)-camphor, 4%. [c] Expected configuration (*S*). [d] Measurements in 95% ethanol.

TABLE 4

Influence of temperature on the asymmetric synthesis of *o*-methylsulphinylbenzoic acid

Temp.	Peroxy-acid [a]	From (+)-1-(α-naphthyl)ethyl ester: $[\alpha]_D^{20}$ [b]	Optical yield (%)	Absolute config.[c]	From (−)-bornyl ester [d]: $[\alpha]_D^{20}$ [b]	Optical yield (%)	Absolute config.[e]
−50°	B	+35·9°	15·8	(*R*)	+8·4°	3·7	(*R*)
	T	+83·0	36·6	(*R*)	−28·5	12·5	(*S*)
0	B	+22·3	9·8	(*R*)	+6·2	2·7	(*R*)
	T	+50·5	22·2	(*R*)	−10·0	4·8	(*S*)
+20	B	+4·8	2·1	(*R*)	+4·6	2·0	(*R*)
	T	+40·6	17·8	(*R*)	−8·1	3·6	(*S*)

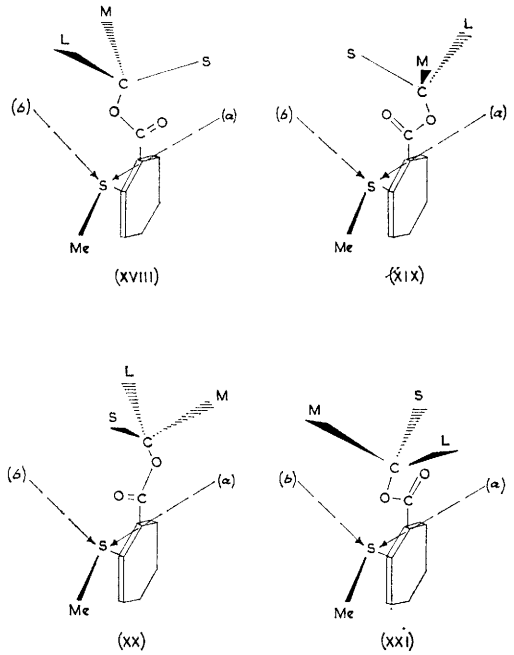
[a] B = Perbenzoic acid; T = trimethylperbenzoic acid. [b] Measurements in 95% ethanol. [c] Expected configuration (*R*). [d] Prepared from commercial borneol: (−)-borneol, 80%; (+)-isoborneol, 16%; (+)-camphor, 4%. [e] Expected configuration (*S*).

for the 1-(2,4,6-trimethylphenyl)ethyl ester. The optical yields are zero for the 2-methylbutyl ester. The diastereomeric esters (II) do not epimerize under the reaction conditions. The effects of solvent and temperature changes in oxidations with the two peroxy-acids are shown in Tables 3 and 4.

DISCUSSION

As for the previous asymmetric inductions at the sulphur atom,[1,2] the stereochemistry of the reaction can be interpreted in terms of eclipsing effects of small (S), medium (M), and large (L) groups bonded to the asymmetric centre. Correct predictions can be made on the basis of the model represented by formula (XVIII): with alcohols of chirality (XIV), attack by peroxy-acid from direction (*a*) is favoured against attack from direction (*b*), thus yielding an excess of acid (*R*)-(+)-(III). According to the model (i) the methyl group bonded to sulphur is in the plane of the aromatic ring and directed away from the ester group, (ii) the CO_2·C*(S,M,L) group is in a conformation (XVI), in which the small group S, which is always the hydrogen atom, is eclipsed with respect to the carbonyl oxygen,* and (iii) the C=O double bond lies in a plane orthogonal to that of the aromatic ring. These conditions result in the M and L groups lying on the same side of plane of the aromatic ring, with the L group closer to the sulphur atom. In conformations (XVIIIa) and (XVIIIb) there is a maximum difference of steric compression between the diastereomeric transition states derived by the attack of the peroxy-acid in the direction of the lone pairs of the sulphur atom. For the purpose of asymmetric induction every other pair of conformations, derived from (XVIIIa and b) by rotation of the ester group around the Ar–CO_2R bond, should be less important: (XIXa and b) and (XXa and b) because of low steric compression, and (XXIa and b) because of high steric compression in both diastereomeric transition states. Therefore, the pair (XVIIIa and b) should determine the stereochemical course and, hence, the actual sign of the acid (III).†

These forecasts are largely speculative. Owing to the great conformational freedom of sulphides (I), the energy differences between the diastereomeric transition states are extremely sensitive to subtle structural variations of the alcohol and peroxy-acid. If the peroxy-acid is small, the steric compression decreases and, as a consequence, the weight of less favourable conformations increases. Some of these, for example (XXIb), lead to a stereochemical result opposite to (XVIIIa), and can



invert the sign of the sulphoxide (III). On this basis, the anomalous trend of the oxidations of bornyl and isobornyl esters with perbenzoic acid could be justified.

If the peroxy-acid is bulky, *e.g.* 2,4,6-trimethylperbenzoic acid, one may expect to find a larger difference between the diastereomeric transition states, *i.e.* an enhanced stereoselectivity of the reaction. This should mean a greater weight of conformations of lesser energy, like (XVIIIa), and, therefore, a greater likelihood of results agreeing with the predictions. The case of menthol is the only one among those studied where the change from use of perbenzoic to use of trimethylperbenzoic acid is accompanied by a decrease in optical activity. Indeed, whereas alcohols (IV)—(IX) are all structurally very similar, menthol (X), with borneol (XI) and isoborneol (XII), is markedly different, and, because of its cyclic structure, does not fit the proposed model so well. The optical yield is zero with 2-methylbutan-1-ol, possibly because the asymmetric centre is farther away from the reaction centre and the steric difference among the S, M, and L groups is small.

Solvent changes have little influence on optical yields and do not alter the stereospecificity of the reactions (Table 3); this fact shows that the conformational equilibrium is more influenced by the size of the peroxy-acid than by the nature of the solvent in this type of

* Under these conditions there is a minimum steric interaction between groups M and L and the carbonyl oxygen, and consequently a maximum freedom of rotation [5] of the same groups around the C–C (asymm.) bonds. This system is essentially analogous to that previously proposed,[2c] conformation (XVII), in which the carbonyl oxygen is flanked by groups S and M. Considerations based on conformations (XVI) or (XVII) are very similar and lead to similar conclusions. However conformation (XVI) also takes into account the fact that the optical yield depends mainly on the relative size of the largest group, L.

† Conformation sets (XVIIIa)—(XXIa) and (XVIIIb)—(XXIb) refer to each one of the two diastereomeric transition states, respectively. Conformations (XVIII)—(XXI) differ from one another by rotations of 90 and 180° around the Ar–CO_2R bond, and can be regarded as representative of all the possible intermediate conformations. The stereochemical result which can be foreseen from each of the pairs of diastereomeric conformations (XVIIIa and b) and (XXa and b) is opposite to the one which can be foreseen from each of the pairs (XIXa and b) and (XXIa and b).

[5] J. D. Morrison, in 'Survey of Progress in Chemistry,' ed. A. F. Scott, Academic Press, New York, 1966, vol. 3, p. 147; see also J. H. Brewster, *Tetrahedron*, 1961, **13**, 106.

asymmetric induction. Temperature changes do not produce any important effects either, at least within the limits considered (Table 4), but the optical yields increase with a decrease of temperature, as expected.

EXPERIMENTAL

Optically Active Alcohols.—Racemic alcohols were resolved by fractional crystallisation of the brucine salts of the respective phthalic monoesters, prepared by conventional methods.[6] Brucine was removed by washing with acid, phthalates were saponified by heating with aqueous or aqueous alcoholic potassium hydroxide, and the optically active alcohols were isolated by steam-distillation or by extraction with ethyl ether.

(S)-(+)-*Butan-2-ol* was obtained by the method of Kantor and Hauser;[7a] $[\alpha]_D^{20}$ +12·2° (1 dm.; neat), b.p. 95—99°, n_D^{20} 1·3957 (lit.,[7b] $[\alpha]_D^{27}$ +13·52°, b.p.[7a] 98—99·5°, n_D^{23} 1·3955).

(S)-(+)-3,3-*Dimethylbutan-2-ol* had $[\alpha]_D^{20}$ +7·0° (1 dm.; neat), b.p. 115—117°, n_D^{20} 1·4148 (lit.,[8] $[\alpha]_D^{20}$ +7·71°, b.p. 119—120°, n_D^{20} 1·4146).

(S)-(+)-1-*Cyclohexylethanol* had $[\alpha]_D^{20}$ +8·0° (*c* 5·1 in ethyl ether), b.p. 83—84°/15 mm., n_D^{20} 1·4648 (lit.,[9a] $[\alpha]_D^{20}$ +8·4°, b.p.[9b] 82—83°/12 mm., n_D^{25} 1·4635).

(S)-(−)-1-*Phenylethanol* had $[\alpha]_D^{20}$ −42·0° (*c* 3·7 in methanol), b.p. 88°/12 mm., n_D^{20} 1·5231 (lit.,[10a] $[\alpha]_D^{23}$ −45·5°, b.p.[10b] 86·5—87·5°/8 mm.).

(R)-(+)-1-(2,4,6-*Trimethylphenyl*)*ethanol* had $[\alpha]_D^{20}$ +47·0° (*c* 1·0 in ethanol), m.p. 49—51° (from light petroleum) (lit.,[11] $[\alpha]_D^{20}$ +52·0°, m.p. 52°).

(S)-(−)-1-(α-*Naphthyl*)*ethanol* had $[\alpha]_D^{20}$ −74·7° (*c* 4·0 in ethanol), b.p. 165°/11 mm. (lit.,[12] $[\alpha]_D^{20}$ −78·9°, b.p.[8] 166°/11 mm.).

(R)-(−)-*Menthol.*—A commercial product was used, m.p. 42—43°, $[\alpha]_D^{20}$ −50° (*c* 5 in ethanol).

(R)-(−)-*Borneol.*—A commercial product, containing (+)-camphor (4%) and (+)-isoborneol (16%) (g.l.c. analysis with a column of 20 M polyethylene glycol on Chromosorb W), was purified by the method of Clark and Read[13] *via* the (−)-bornyloxyacetate. The purified (−)-borneol had $[\alpha]_D^{20}$ −37·7° (*c* 3·5 in toluene), m.p. 203—204° (lit.,[13] $[\alpha]_D$ −37·9°, m.p. 205°).

(R)-(−)-*Isoborneol.*—The commercial racemic isoborneol was resolved by fractional crystallisation of the cinchonine salt of mono-(±)-isobornyl phthalate;[14] $[\alpha]_D^{20}$ −26·6° (*c* 0·6 in ethanol), m.p. 211—213° (lit.,[14] $[\alpha]_D^{16}$ −34·34°, m.p. 214°).

o-(*Methylthio*)*benzoic Acid.*—A solution of anthranilic acid (41·1 g.) in 15% aqueous hydrochloric acid (90 ml.) was diazotised at 0° with sodium nitrite (21 g.) in water (60 ml.), and the diazonium salt was poured with stirring into a solution of potassium xanthogenate (48 g.) and sodium carbonate (96 g.) in water (600 ml.). After 1 hr. at room temperature, 20% aqueous sodium hydroxide (600 ml.) and dimethyl sulphate (28·2 ml.) were added slowly, and the solution was then heated under reflux for 4 hr. Acidification with hydrochloric acid afforded the product, which was filtered off and dried at 100° (35 g., 70%); m.p. 168—169° (from acetic acid) (lit.,[15] 170—171°).

o-(*Methylthio*)*benzoic Anhydride.*—A solution containing *o*-(methylthio)benzoic acid (16·8 g.) and *o*-(methylthio)-benzoyl chloride (18·7 g.), m.p. 74—76°, prepared[16] from the acid and thionyl chloride, in anhydrous pyridine (40 ml.) was heated under reflux for 7 hr. The cooled solution was then diluted with chloroform and acidified with 10% aqueous sulphuric acid. Unchanged *o*-(methylthio)benzoic acid was filtered off, the chloroform layer was separated and the aqueous solution was repeatedly extracted with chloroform. The chloroform solutions were washed with aqueous sodium hydrogen carbonate and with water and dried, and the solvent was evaporated off to give the product (22 g., 63%), m.p. 121—122° (from benzene) (Found: C, 61·2; H, 4·5; S, 19·9. $C_8H_{14}O_3S_2$ requires C, 60·4; H, 4·4; S, 20·2%).

Optically Active Esters of o-(*Methylthio*)*benzoic Acid* (Table 1).—A mixture of optically active alcohol (0·2 mole), *o*-(methylthio)benzoic acid anhydride (0·1 mole) and anhydrous pyridine (0·3 mole) was heated at 90—100° for 7 hr. The mixture was dissolved in light petroleum and acidified with 10% aqueous sulphuric acid. Unchanged *o*-(methylthio)benzoic acid was filtered off, the light petroleum solution was separated, and the aqueous layer was repeatedly extracted with light petroleum. The light petroleum solutions were washed with aqueous sodium hydrogen carbonate and with water, dried, and evaporated. The residue was chromatographed on alumina (Brockmann activity II, III) with benzene as eluant. The ester was recovered from the early fractions (30—50%) and was further purified by distillation in vacuum or crystallisation (see Table). Unaltered alcohol and *o*-(methylthio)benzoic anhydride were recovered from the subsequent fractions.

Perbenzoic Acid.—Chloroform solutions of perbenzoic acid were obtained from benzoyl chloride and hydrogen peroxide, as described by Kergomard and Bigou.[17] For oxidations in other solvents, the chloroform solution of the peroxy-acid was evaporated under vacuum, in the dark, at room temperature. The residue was diluted with light petroleum, undissolved benzoic acid was filtered off, and the solution was cooled at −80°. Perbenzoic acid (80—95% pure) precipitated and was dissolved again in the appropriate solvent to give *ca.* N-solutions.

2,4,6-*Trimethylperbenzoic acid* was prepared from trimethylbenzoic acid *via* the acyl imidazole, as recently described.[18] Solutions in solvents other than chloroform were prepared as described for perbenzoic acid.

Asymmetric Synthesis of o-*Methylsulphinylbenzoic Acid.*—

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A titrated chloroform solution of the peroxy-acid (2 equiv.) was slowly added to a solution of the ester (1—3 mmoles) in chloroform (10 ml.) at 0°. The temperature was kept at 0° until the oxidation was complete (on average, 12 hr. for the oxidations with perbenzoic acid, 3 days for the oxidations with trimethylperbenzoic acid). The acid was extracted with aqueous sodium hydrogen carbonate and the chloroform solution was evaporated to leave the ester. The latter was directly saponified by heating on a steam-bath for 3 hr. (8 hr. for the isobornyl ester) with 5% aqueous alcoholic potassium hydroxide (2·5 equiv.). The solution was diluted with water, extracted with light petroleum until the optically active alcohol had been completely removed, and then acidified with 10% aqueous sulphuric acid. Repeated extractions with chloroform afforded quantitative yields of optically active *o*-methylsulphinylbenzoic acid (see Table 2). Evaporation of the light petroleum solutions gave the unchanged alcohols (quantitative recovery; unchanged optical purity).

For the oxidations in chloroform at −50° (Table 4) the temperature was kept constant with a bath of chloroform–carbon tetrachloride (1 : 1 v/v) saturated with solid carbon dioxide. Oxidations took about 180 hr.

Oxidations in solvents other than chloroform (Table 3) were carried out at 0°. At the end of the reactions, the solvents miscible with water (acetonitrile, propan-2-ol, dioxan) were evaporated off under vacuum, the residues were dissolved in chloroform, and the optically active *o*-methylsulphinylbenzoic acid was isolated as already described. In the other cases the solutions were directly washed with aqueous sodium hydrogen carbonate and the products were isolated in the usual way.

(+)- *and* (−)-o-*Methylsulphinylbenzoic Acid*.—The racemic acid, obtained [19] by oxidation of *o*-(methylthio)benzoic acid with peracetic acid (2 equiv.), had m.p. 178—180° (from ethyl acetate) (lit.,[19] 176—178°). From a solution of the racemic acid (25·8 g.) and brucine (55·2 g.) in boiling absolute ethanol (200 ml.) a brucine salt, m.p. 227—230° (27 g.) was separated by cooling. Four crystallisations from absolute ethanol afforded a salt (12 g.), m.p. 238—239°, $[\alpha]_D^{20}$ +75·3° (*c* 1·1, chloroform), from which, by acidification with 10% aqueous sulphuric acid, (+)-o-(*methylsulphinyl*)-*benzoic acid* (2·8 g.), m.p. 185·5—186° (from ethyl acetate), $[\alpha]_D^{20}$ +227·5° (*c* 1, ethanol) was isolated (Found: C, 52·2; H, 4·3. $C_8H_8O_3S$ requires C, 52·2; H, 4·3%). The mother liquor from the first crystallisation of the brucine salt was evaporated off, and the residue was treated with 10% aqueous sulphuric acid to give (−)-*o*-methylsulphinylbenzoic acid (7·4 g.), m.p. 180—182°, $[\alpha]_D^{20}$ −221·5° (*c* 1, ethanol). After crystallisation from ethyl acetate it had m.p. 185·5—186°, $[\alpha]_D^{20}$ −227·5° (*c* 1, ethanol).

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