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ASYMMETRIC SYNTHESIS AND ABSOLUTE CONFIGURATION OF SOME SULPHOXIDES

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THE partial asymmetric synthesis of sulphoxides (I) C_6H_5-SO-Alk,[1] by oxidation of the sulphides with (1S)(+) percamphoric acid (IV),[2] has been previously described. The investigation has now been extended to the corresponding *meta*- and *ortho*-carboxylated derivatives (II) and (III), whose absolute configurations have been determined.

The optically active sulphoxides (II) and (III) have been prepared by oxidation of methyl esters of the sulphides with (1S)(+) perchamphoric acid (IV) and (S)(+) perhydratropic acid (V) ($CHCl_3$, -5°), followed by saponification. The compound (III) has also been prepared by the alternative route of esterification of the sulphide with optically active alcohols [(R)(-) menthol (VI), (R)(+) methyl-mesityl-carbinol (VII), (S)(-) methyl-α-naphtyl-carbi-

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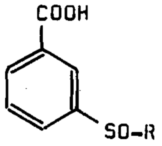
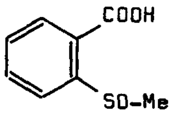
[1] F. Montanari *et al.*, *Gazz.Chim.Ital.* **90**, 739 (1960); *Ricerca Sci.* **30**, 746 (1960). Other works on the same subject have been published at the same time by K. Balenović *et al.*, *Tetrahedron Letters* No. 6, 20 (1960); *Chem. and Ind.* 469 (1961).

[2] Configuration nomenclature after R. S. Cahn, C. K. Ingold and V. Prelog, *Experientia* **12**, 81 (1956).

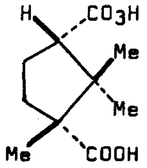
nol (VIII)] , followed by oxidation with perbenzoic acid ($CHCl_3$, -5°) and saponification.



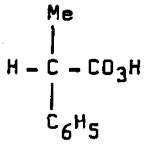
II : R = Me, Et, i-Pr, t-But



III

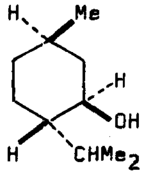


IV

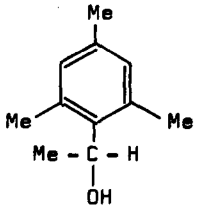


$$\mathrm{H-}\underset{C_6H_5}{\overset{Me}{C}}\mathrm{-CO_3H}$$

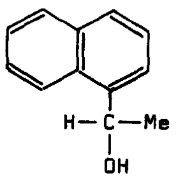
V



VI



VII



VIII

The results, reported in Table 1, are interpreted as follows. The oxidation of sulphides to sulphoxides takes place through an electrophilic attack of the peracid in a perpendicular direction to the sulphide molecule.[3]

Indicating with S, M, L the ligands of small, medium and large size respectively,[4] surrounding the CO_3H group in molecules

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[3] C. G. Overberger and R. W. Cumming, *J.Amer.Chem.Soc.* **75**, 4250 (1953); G. Modena *et al.*, *Gazz.Chim.Ital.* **89**, 834 (1959) and following papers. A tetrahedric direction of attack does not effect our considerations.

[4] V. Prelog, *Bull.Soc.Chim.* 986 (1955); D. J. Cram and F. A. Abd Elhafez, *J.Amer.Chem.Soc.* **74**, 5828 (1952).

Table 1

Peracid or alcohol		Sulphoxide [a]					
Formula	Abs.Conf.n	Formula	R	$\alpha_D^{20°}$ found	$\alpha_D^{20°}$ theor.	Optical yield	Abs.Conf.n
IV	S	II	Me	+4°,9	±114°[b,e]	4,3	R
V	S	II	Me	+3°,1		2,7	R
IV	S	II	Et	+2°,5	±202°[c,e]	1,2	R
V	S	II	Et	+2°,1		1,0	R
IV	S	II	i-Pr	-0°,7	±184°[c,f]	0,4	S
V	S	II	i-Pr	-0°,2		0,1	S
IV	S	II	t-But	-3°,8	±156°[c,g]	2,4	S
V	S	II	t-But	-2°,5		1,6	S
IV	S	III	-	+4°,6	±227°,5[d,h]	2,0	R
V	S	III	-	+3°,0		1,3	R
VI	R	III	-	-14°,0		6,2	S
VII	R	III	-	-46°,6		20,5	S
VIII	S	III	-	+20°,2		8,9	R

[a] Average yields : 90-95% on the sulphide.

[b] MeOH [c] $CHCl_3$ [d] EtOH

[e] P. W. B. Harrison, J. Kenyon and H. Phillips, J.Chem.Soc.,2079 (1926).

[f] M.p. 114°-5°; found : C, 56,39; H, 5,78; S, 14,94. $C_{10}H_{12}O_3S$ requires : C, 56,58; H, 5,70; S, 15,10.

[g] M.p. 148° ; found : C, 58,43; H, 6,31; S, 14,01. $C_{11}H_{14}O_3S$ requires : C, 58,38; H, 6,24; S, 14,17.

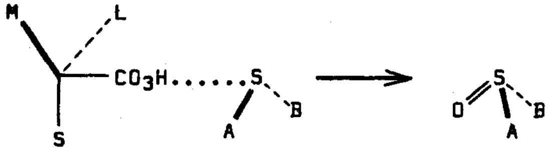
[h] M.p. 186° ; found : C, 52,16; H, 4,42. $C_8H_8O_3S$ requires : C, 52,2; H, 4,35.

(I) to (V), and with A-S-B the sulphide molecules, the most probable conformations in the reaction state are the staggered ones (a) and (b). If A>B, (a) is more favoured since the larger group A is placed in the less hindered position. The yield of the asymmetric synthesis is a function of the predominance of the reaction (a) over (b) and must augment with increasing difference in size among S, M, L, and, for the same oxidizing agent, between A and B. The latter difference must be more relevant in the neighbourhood of sulphur than further away.

In the series (II) all the terms present plain[5] rotatory dispersion curves, which, for equal sign, are almost superimposed in the region 600-300 mμ:[6] this suggests equal absolute configurations.

By oxidation with peracids (IV) and (V) [absolute configuration (S)] , dextro-enantiomers prevail when R = Me, Et, levo- when R = i-Pr, t-But. Being the larger term in the neighbourhood of sulphur the phenyl in the former case, and the alkyl group in the latter, the absolute configuration of sulphoxides (II) must be (S) and (R) respectively. The maximum yield of asymmetric synthesis is in fact observed when R = Me and respectively t-But, as expected when the difference in size between the groups bonded to sulphur is the greatest.

(a)



(S) (R)

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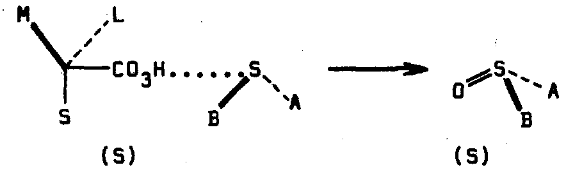
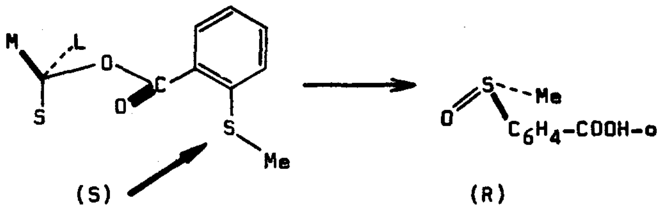
[5] C. Djerassi and W. Klyne, Proc.Chem.Soc. 55 (1957).

[6] We are greatly indebted to Prof. W. Klyne (London) for the determination of the rotatory dispersion curves. For RD curves of sulphoxides see also : W. Klyne, J. Day and A. Kyaer, Acta Chem.Scand. **14**, 215 (1960).

(b)



(c)



The asymmetric synthesis of (III), involving oxidation of optically active esters of the sulphide, can be represented as in (c) (here S, M, L are the small, medium and large groups of the optically active alcohols). The most probable conformation of the sulphide is that where the carbonylic oxygen is placed in the less hindered region, i.e. between S and M.[7] Then, the largest group L shields one of the directions of attack of the peroxide [below the plane in (c)]. This fact agrees with higher optical yields obtained in this way.

The absolute configurations attributed to the enantiomers (III) according to (c) correspond to those derived from (a) and (b).

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[7] Other effects, for instance C=O...H-C interaction, may intervene; however, in the cases here examined, the conclusions are not significantly affected.