Asymmetric Reduction of Sulphoxides with Optically Active Phosphorus Thioacids. Absolute Configuration of *O*-Ethyl Ethylphosphonothioic Acid

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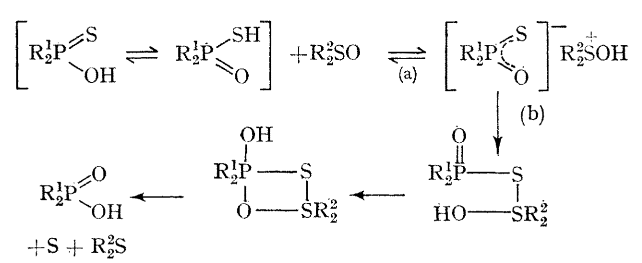
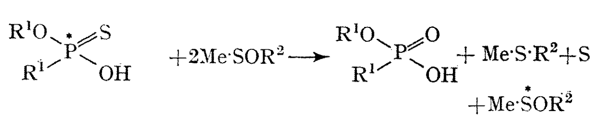
Summary Partial reduction of racemic methyl alkyl sulphoxides with optically active phosphonothioic acids gives recovered sulphoxides that are optically active; the (*R*)-configuration is assigned to (−)-*O*-ethyl ethylphosphonothioic acid.

WE have previously found[1] that phosphorus thioacids react with sulphoxides to afford phosphorus oxyacids, elemental suphur, and sulphides. The available experimental data are consistent with the following reaction course:



SCHEME 1



$$R^1O(R^1)P^*(=S)OH + 2Me{\cdot}SOR^2 \longrightarrow R^1O(R^1)P(=O)OH + Me{\cdot}S{\cdot}R^2 + S + Me{\cdot}\overset{*}{S}OR^2$$

In the present studies, the asymmetric reduction of racemic methyl alkyl sulphoxides with optically active *O*-ethyl ethylphosphonothioic acid (I) and *O*-isopropyl methylphosphonothioic acid (II) was investigated.† In all experiments one mole of thioacid was treated with two moles of sulphoxide and the mixture was kept for several weeks at room temperature. Unreacted sulphoxides were found always to be optically active. The optical yields, the sign, and the absolute configuration of the sulphoxides are shown in the Table.

TABLE

Asymmetric reduction of methyl alkyl sulphoxides with O-*ethyl ethylphosphonothioic acid* (I) *and* O-*isopropyl methylphosphonothioic acid* (II)

	Acid		Sulphoxide			
	$[\alpha]_D$[a] (neat)	R^2	$[\alpha]_D$ (neat)	$[\alpha]_D$ (ethanol)	Optical yield[b] (%)	Absolute configuration
(I)	−13·4	Et	+3·52	+3·47	3·3	(*S*)
	−13·5	Pr^n	+5·27	+4·58	3·5	(*S*)
	−13·5	Pr^i	+1·71	+1·79	3·3	(*S*)
	−14·4	Bu^n	+3·36	+3·97[c]	4·4	(*S*)
	−13·4	Bu^i	+7·54	+7·09	—	(*S*)[d]
	−13·0	$Ph{\cdot}CH_2$[e]	—	+0·45	0·5	(*S*)
	− 7·2	$CH_2{\cdot}CH:CH_2$	−0·17	−0·14	0·9	(*S*)
(II)	−14·0	Et	+1·20	+1·01	1·0	(*S*)
	−14·0	Pr^n	+1·29	+0·76	0·6	(*S*)
	−14·6	Bu^n	+4·36	+5·12[c]	5·7	(*S*)
	−14·0	Bu^i	+4·67	+4·24	—	(*S*)[d]

[a] The optical activity measurements were made with a Perkin-Elmer 141 photopolarimeter (sensitivity ±0·002°). [b] Optical yields were calculated based on the literature data [M. Axelrod, P. Bickart, J. Jacobus, M. M. Green, and K. Mislow, *J. Amer. Chem. Soc.*, 1968, **90**, 4835; K. Mislow, M. M. Hreen, P. Laur, J. Melillo, T. Simmons, and A. L. Ternay, *J. Amer. Chem. Soc.*, 1965, **87**, 1958] and private communication from Professor K. Mislow. [c] In iso-octane. [d] The (*S*)-configuration was assumed for (+)-methyl isobutyl sulphoxide [M. Axelrod, P. Bickart, M. L. Goldstein, M. M. Green, A. Kjær and K. Mislow, *Tetrahedron Letters*, 1968, 3249; W. H. Pirkle and S. D. Beare, *J. Amer. Chem. Soc.*, 1968, **90**, 6250]. Our results can also be considered as a chemical proof for the (*S*)-configuration of (+)-methyl alkyl sulphoxides. [e] Reaction runs under heterogeneous conditions.

The results obtained indicate the clear relationship between the chirality of the remaining sulphoxide and the optically active thioacid. In all cases the sulphoxide enantiomer more slowly consumed by the (−)-acid (I) had the absolute configuration (*S*). Similarly, after reaction with the (−)-acid (II), which is known to possess the (*R*)-configuration,[3] the recovered sulphoxide contained an excess of the enantiomer with the (*S*)-configuration. The same direction of the asymmetric reduction discussed for both (−)-acids (I) and (II) may be reasonably accepted as an indication that they have the same configuration (*R*). The above conclusion is consistent with the results of an o.r.d. study. The shape of the o.r.d. curves of both (−)-acids is almost identical, and a positive Cotton effect at *ca.* 220 nm. is observed.

Since the absolute configuration of both substrates is known, it is possible to suggest a correlation model based on principles of steric control of asymmetric induction (Cram–Prelog approach). According to Scheme 1, the nucleophilic attack of the thioacid anion on sulphoxonium cation [step (b), formation of a sulphur–sulphur bond] is a decisive step in the asymmetric induction. The different rate of the reduction of enantiomeric sulphoxides is due to

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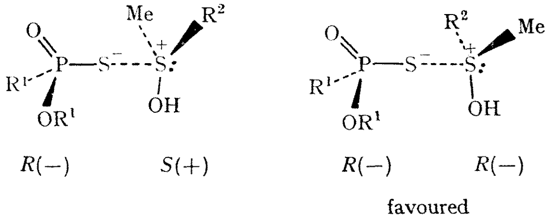
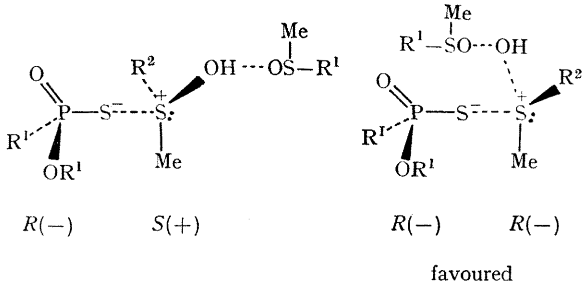
† Balenowic and Bregant[2] have described asymmetric reduction of chiral sulphoxides with optically active thiols.

the nonbonding interactions between substituents attached to the phosphorus and sulphur atoms. The preferred transition states are those where the larger groups at phosphorus (R^1 = OEt, OPr^i) and sulphur (R^2 = alkyl) are positioned away from each other in the staggered conformation. It is also assumed that the lone electron pair on sulphur should occupy the apical position in the trigonal bipyramidal transition state. This situation seems to be favourable from the point of view of charge separation. The suggested diastereoisomeric transition states are depicted below (Scheme 2).



SCHEME 2

In view of the great tendency of sulphoxides to hydrogen-bond formation, another pair of the diastereoisomeric transition states should be taken into account. In these structures an excess of sulphoxide is bonded to a hydroxy-group of the sulphoxonium cation (Scheme 3).



SCHEME 3

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[2] K. Balenovic and N. Bregant, *Chem. and Ind.*, 1964, 1577.

[3] H. P. Benschop, G. R. Van den Berg, and H. L. Boter, *Rec. Trav. chim.*, 1968, **87**, 387.