The Stereochemistry of the Reaction of α-Lithio-sulphoxides (α-Sulphinyl Carbanions) with Ketones

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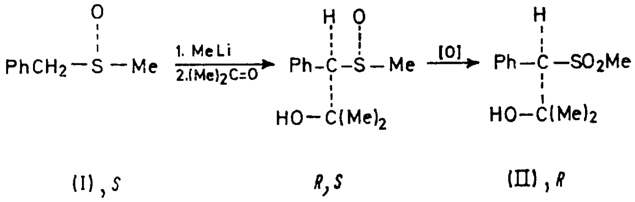
Summary Metallation of *S*-benzyl methyl sulphoxide followed by quenching with acetone gives a mixture of diastereomers in a 15:1 ratio; the major isomer is shown to have the *R* configuration at carbon and a synthesis of optically active epoxides from optically active sulphoxdes is described.

WE have shown that the lithio-derivatives of a number of sulphoxides of the type $R^1CH_2S(O)R^2$ (R^1 and/or R^2 = aryl or alkyl) react with an excess of various electrophiles to give a mixture of diastereomeric products, the ratio being essentially constant for each electrophile and characteristic of each sulphoxide.[1] We have also carried out these reactions using optically active benzyl methyl and benzyl t-butyl sulphoxides and shown that the stereochemical course of the reaction producing the major isomer in the deuteriation was opposite to that observed in the methylation reaction.[1] Since deuteriation probably occurred with retention of the carbanion configuration,[2] methylation must have occurred with inversion.[1,3]

The reaction of α-lithio-sulphoxides with ketones was expected to occur with retention of the carbanion configuration.[4] Application of this reaction to the synthesis of compounds having optical activity at carbon requires a definite knowledge of its stereochemical course; we have therefore verified the above expectation.

Optically pure *S*-benzyl methyl sulphoxide, (I), α_D 96° (*c* 0·8 in EtOH)[5] was metallated (MeLi, THF, −60°), quenched with acetone and the crude product $[\alpha]_D$ −121° (*c* 1·5 in $CHCl_3$)] oxidized with excess of *m*-chloroperbenzoic acid yielding the sulphone (II),† (Scheme 1) m.p. 120—121°; α_D −45·6° (*c* 1·9, in EtOH); n.m.r. ($CDCl_3$), δ 1·37 (s, 3H), 1·46 (s, 3H), 2·66 (s, 3H), 3·88 (s, 1H, OH), 4·27 (s, 1H) and 7·2—7·7 (m, 5H).

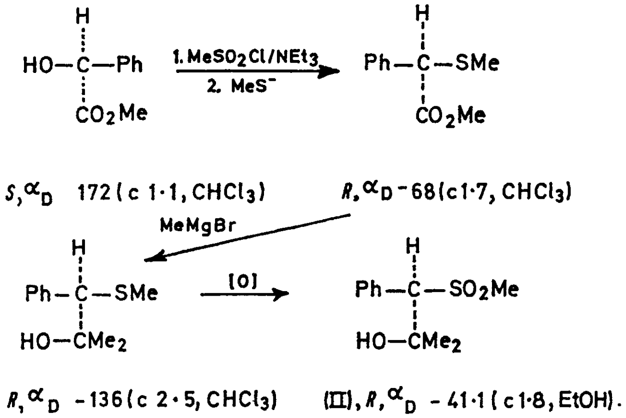


SCHEME 1

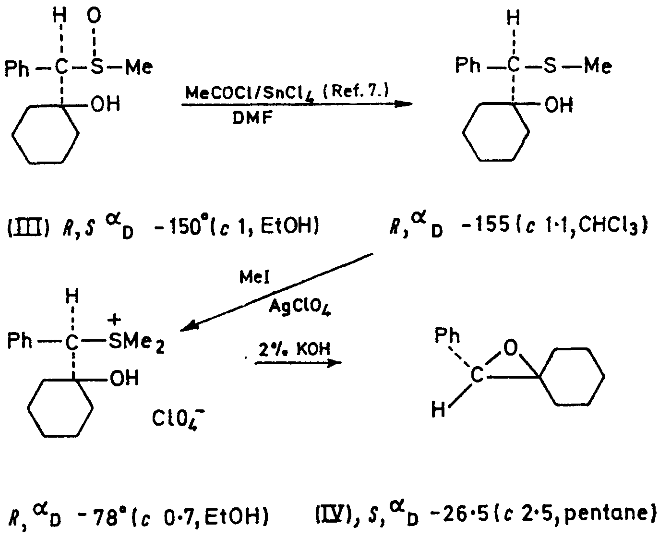
The same sulphone having α_D −41·1° (*c* 1·8 in EtOH), *R* configuration at carbon, was produced from *S*-mandelic acid α_D 147° (*c* 2·5 in H_2O) *ca.* 94% optical purity as shown in Scheme 2.‡ The reactions involved were straightforward with only the displacement by MeS^- involving any stereochemical change in the asymmetric centre.[6] The rotations and absolute configurations are given in Scheme 2.

The major isomer produced from the α-lithio-sulphoxide of (I) thus had the *R* configuration at carbon as expected on the basis of retention of configuration. Thus the steric course of the hydroxy-alkylation step is identical with that of deuteriation and opposite to that of methylation.

We have developed a three-step synthesis of epoxides from β-hydroxy sulphoxides. Application of this sequence to (III), the product from cyclohexanone and the lithio-salt of optically pure (I) yielded the epoxide (IV) (60% overall yield), α_D −26·5° (*c* 2·7 in pentane).§ The assignment of the epoxide configurations as *S* follows from the stereochemistry of the condensation reaction and the inversion of configuration in the cyclization step (Scheme 3). Extension of these studies to the preparation of other optically active epoxides and the potential use of the lithio-salts of optically active sulphoxides in the synthesis of other compounds having known asymmetry at carbon is in progress.



SCHEME 2



SCHEME 3

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† All new compounds had spectroscopic properties consistent with their structure assignment. Crystalline compounds gave Satisfactory combustion analysis.

‡ The sulphone prepared in this way is probably less than 94% optically pure. Partial racemization could have occurred in the CH_3S^- displacement or the Grignard reaction.

§ The epoxide (IV) should be optically pure since a purification was carried out on (III) and the subsequent steps do not involve the carbon asymmetry or are stereospecific.

[1] T. Durst, R. Viau, and M. R. McClory, *J. Amer. Chem. Soc.*, 1971, **93**, 3077.

[2] (a) A. Rauk, E. Buncel, R. Y. Moir, and S. Wolfe, *J. Amer. Chem. Soc.*, 1965, **87**, 5498; (b) T. Durst, R. R. Fraser, M. R. McClory, R. B. Swingle, R. Viau, and Y. Y. Wigfield, *Canad. J. Chem.*, 1970, **48**, 2148.

[3] Electrophic substitution with inversion has rarely been observed. For recent examples see H. C. Brown and C. F. Lane, *Chem. Comm.*, 1971, 521.

[4] The prediction is based on the analogy that base-catalysed cleavage of an optically active β-hydroxy sulphone into a carbonyl compound and an optically active sulphone occurs with retention of configuration at the carbon α to the sulphone. D. J. Cram and A. S. Wingrove, *J. Amer. Chem. Soc.*, 1963, **85**, 1100.

[5] K. Mislow, M. M. Green, and M. Raban, *J. Amer. Chem. Soc.*, 1965, **87**, 2761.

[6] A. Streitweiser, jun., "Solvolytic Displacement Reactions", McGraw-Hill Inc., New York, N.Y., 1962. Chapter III.

[7] G. V. Kaiser, R. D. J. Cooper, R. E. Koehler, C. F. Murphy, J. A. Webber, I. G. Wright, and E. M. Van Heymingen, *J. Org. Chem.*, 1970, **35**, 2430.