

Chemical Communications

NUMBER 18/1965

22 SEPTEMBER

Asymmetric Synthesis and Racemization of Disulphide Monoxides

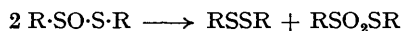
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It is known that oxidation of an unsymmetrically substituted thioether by an optically active peracid can lead to asymmetric synthesis of the corresponding sulphoxide (R·SO·R').¹ S-Oxides of symmetrically or unsymmetrically substituted disulphides (R·SO·S·R or R·SO·S·R') should in theory be resolvable into stereoisomers, and this has been shown to be possible by the recent isolation of the S-monoxides of L-cystine.²

We have found that asymmetric synthesis of disulphide monoxides (thiolsulphinates) can be effected by oxidation of the disulphide with percamphoric acid in chloroform at 0–10°. Under these conditions, the diaryl disulphide monoxides obtained (Ar·SO·S·Ar, Ar = C₆H₅, *p*-Cl-C₆H₄, *p*-Me-C₆H₄ or β-naphthyl) showed some optical activity ($[\alpha]_D^{20}$ ca. 10°, *c* 1 in chloroform), while the corresponding alkyl (dodecyl) or aralkyl (benzyl) compounds were optically inactive. The purity of the products, after successive recrystallizations

from cold chloroform–light petroleum and aqueous acetone, was established by thin-layer chromatography (silica gel, benzene; location by iodine vapour³ or iodoplatinate⁴), which gave satisfactory separation of the disulphide monoxides (R_F ca. 0.5) from initial impurities such as the disulphide (R_F ca. 0.9), the disulphide dioxide (RSO₂SR, R_F ca. 0.7) and camphoric acid (R_F 0). Apart from optical properties, the physical properties (appearance, melting point, and u.v. absorption spectrum) of the diaryl disulphide monoxides agreed well with those of the inactive monoxides prepared by oxidation of the disulphides with perbenzoic acid (*cf.* ref. 5) or by other methods described in the literature.^{6,7,8} Diaryl disulphide monoxides are reported to undergo rather ready disproportionation to the disulphide and disulphide dioxide, either in the solid state on rigorous drying⁷ or in hexane solution.⁵



¹ K. Balenović, N. Bregant, and D. Francetić, *Tetrahedron Letters*, 1960, No. 6, 20; K. Balenović, I. Bregovec, D. Francetić, I. Monković, and V. Tomasić, *Chem. and Ind.*, 1961, 469; A. Mayr, F. Montanari, and M. Tramontini, *Gazzetta*, 1960, 90, 739; A. Maccioni, F. Montanari, M. Secci, and M. Tramontini, *Tetrahedron Letters*, 1961, 607; G. Barbieri, U. Folli, F. Montanari, and G. Torre, *Boll. Sci. Fac. Chim. Ind. Bologna*, 1965, 23, 47.

² W. E. Savige, J. Eager, J. A. Maclaren, and C. M. Roxburgh, *Tetrahedron Letters*, 1964, 3289.

³ "Anfärbereagentien für Dunnschicht- und Papier Chromatographie," E. Merck Co., Darmstadt, Germany, 1961.

⁴ H. M. Winegard, G. Toennies, and R. J. Block, *Science*, 1948, 108, 506.

⁵ H. J. Backer and H. Kloosterziel, *Rec. Trav. chim.*, 1954, 73, 129.

⁶ E. Vinkler and F. Klivénge, *Acta Chim. Acad. Sci. Hung.*, 1957, 11, 15.

⁷ D. Barnard, *J. Chem. Soc.*, 1957, 4675.

⁸ G. Modena and P. E. Todesco, *Ricerca Sci.*, 1960, 30, 1788.

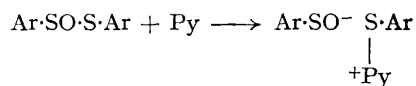
We find that solutions of a monoxide in the common solvents remain stable for at least several days in the dark or in dim light, but rapidly disproportionate in strong light (Pyrex vessels).⁹

These monoxides of symmetrical disulphides show considerable variation of optical stability according to the solvent medium. They appear to be comparatively very stable in certain solvents such as acetonitrile, dioxan, butanone, or acetic acid, where the first-order specific rate for racemization is less than 2×10^{-6} sec.⁻¹ at 50°. In other solvents such as benzene, cyclohexane, or ethanol they appear to racemize fairly easily. In dry benzene at 50°, di-*p*-chlorophenyl disulphide monoxide (all kinetic measurements were made on this compound) racemizes with a half-life of about 1 hr.: $k_{\text{rac}} = 1.9 \times 10^{-4}$ sec.⁻¹ The first-order specific rate appears to be independent of the concentration of the monoxide (in the range 0.07—0.2M). The addition of small amounts of water or ethanol to the benzene strongly decreases the racemization rate. In benzene saturated with water at room temperature (*ca.* 0.03M) the rate is decreased by a factor of about 20. However, the rate is then dependent upon the concentration of monoxide as well, and it increases with increasing [monoxide]/[water] or [monoxide]/[ethanol] ratio.

It is remarkable that although small amounts of ethanol in benzene (up to 0.5M) decrease the racemization rate, pure ethanol ($k_{\text{rac}} = 1.1 \times 10^{-3}$ sec.⁻¹ at 50°) causes racemization faster than pure

benzene. Pyridine is outstanding in that racemization occurs immeasurably fast at room temperature.

The exceptional behaviour of pyridine suggests that racemization may occur in this solvent by way of a special mechanism made possible by its nucleophilic character. In fact, racemization could arise by way of a nucleophilic attack on one of the sulphur atoms, such as



In such a reaction the sulphinyl and pyridinium ions need not become separated, but racemization could occur on collapse of the ion-pair.¹¹

To test the hypothesis of a nucleophilic attack, the effect was determined of a nucleophile such as ionic chloride. It was found that chloride ion has an enormous effect in that in acetonitrile at 25° in the presence of 10⁻⁴M-tetrabutylammonium chloride the first-order specific rate is $k_{\text{rac}} = 6.9 \times 10^{-4}$ sec.⁻¹ Tetrabutylammonium perchlorate was found to have no appreciable effect up to a concentration 10-fold higher. It is likely that this "nucleophilic mechanism" may be operative in ethanol as well. However, some other mechanism must operate in the other solvents, particularly in benzene and in cyclohexane. This matter is currently under investigation.

(Received, August 2nd, 1965; Com. 479.)

⁹ Kice (ref. 10) cites unpublished work by Venier according to which aryl thiolsulphinates in the absence of strong acid decompose only very slowly in solution even at 65°.

¹⁰ J. L. Kice and N. E. Pawlowsky, *J. Amer. Chem. Soc.*, 1964, **86**, 4898.

¹¹ A. Fava, U. Tonnellato, and L. Congiu, *Tetrahedron Letters*, 1965, 1657.