The Synthesis of Optically Active Sulphoxides from Sulphinamides

By JOHN JACOBUS and KURT MISLOW*
(*Princeton University, Princeton, New Jersey* 08540)

OPTICALLY ACTIVE SULPHOXIDES are conveniently prepared from sulphinates by the Grignard synthesis.[1,2] The synthesis of racemic sulphoxides from sulphinamides by reaction with alkyl-lithium reagents has been previously described[3,4]; we now report that optically active sulphoxides are generated by reaction of organolithium reagents with diastereomerically enriched sulphinamides.

Addition of benzenesulphinyl chloride in ether to (+)-(*S*)-deoxyephedrine[5] {*N*-methyl-1-phenyl-2-propylamine, $[\alpha]_{D}^{23}$ +17·6° (water) as the hydrochloride} at 0° affords a mixture of diastereomeric *N*-methyl-*N*-(1-phenyl-2-propyl)benzenesulphinamides which are separable by fractional crystallization from petroleum ether (60—70°). The properties of the two components† are: diastereomer (A), m.p. 84—85°, $[\alpha]_{D}^{23}$ +96°, n.m.r. τ 8·63 (C-CH_3, d, *J* 6·5 Hz), 7·68 (N-CH_3, s), 7·00—7·50 (PhCH_2, m), 5·66—6·17 (C-*H*, m), 2·34—3·00 (aromatic, m), and 2·70 (aromatic, s); diastereomer (B), m.p. 79—80°, $[\alpha]_{D}^{23}$ +118°, n.m.r. τ 8·70 (C-CH_3, d, *J* 6·5 Hz), 7·46 (N-CH_3, s), 6·84—7·34 (PhCH_2, m), 6·00—6·58 (C-*H*, m), 2·16—3·00 (aromatic, m), 2·58 (aromatic, s). Reaction of the diastereomerically pure (by n.m.r.) sulphinamides (A) and (B) with methyl-lithium in ether at −70° afforded (+)-(*R*)-methyl phenyl sulphoxide,[4] $[\alpha]_{D}^{23}$ +137° (ethanol), and the (−)-(*S*) isomer, $[\alpha]_{D}^{23}$ −135° (ethanol), respectively. Since

---

† Satisfactory elemental analyses (±0·3%) were obtained for both diastereomers. Optical rotations refer to 1—2% solutions in ethanol. N.m.r. spectra were measured on a Varian A-60A spectrometer and refer to 5% solutions in deuteriochloroform with tetramethylsilane as internal standard.

the highest rotation reported for methyl phenyl sulphoxide is $[\alpha]_D$ 149° (ethanol),[4] the product of reaction is at most only 90—92% optically pure. Three interpretations are readily envisaged: the starting deoxyephedrine might be optically impure, the displacement reaction might be less than completely stereospecific, or the sulphoxide produced might be partially racemized under the reaction conditions. Though not excluding the first two possibilities, we rank the last explanation first in importance since this observation is consistent with prior findings.[4] Particularly noteworthy is the observation that the displacement reaction fails to occur, in the present instance, when methyl-magnesium bromide is employed as a reagent under conditions which are successful in the Grignard synthesis of sulphoxides from sulphinates.[1,2]

If, by analogy with the stereochemistry of the Grignard synthesis,[1,2] the present displacement reaction occurs predominantly with inversion of configuration, it follows that diastereomers (A) and (B) have the (*R*)- and (*S*)-configuration at sulphur, respectively.

In contrast to the asymmetric synthesis of sulphinates,[2,6] the asymmetric synthesis of (A) and (B) is strongly temperature dependent and becomes more stereospecific with increasing temperature in the range 0 to −70°: thus, reaction of benzenesulphinyl chloride (1 mole) with deoxyephedrine (2 moles) at 0° affords a **3** : **1** mixture of diastereomers with (A) predominating, whereas at −70° a **1** : **1** mixture is obtained.

Support by the Air Force Office of Scientific Research is gratefully acknowledged.

(*Received, December 22nd,* 1967; *Com.* 1370.)

---

[1] K. K. Andersen, *Tetrahedron Letters*, 1962, 93; K. K. Andersen, *J. Org. Chem.*, 1964, **29**, 1953; K. K. Andersen, W. Gaffield, N. E. Papanikolaou, J. W. Foley, and R. I. Perkins, *J. Amer. Chem. Soc.*, 1964, **86**, 5637; P. Bickart, M. Axelrod, J. Jacobus, and K. Mislow, *ibid.*, 1967, **89**, 697.

[2] K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, jun., *J. Amer. Chem. Soc.*, 1965, **87**, 1958.

[3] E. J. Corey and T. Durst, *J. Amer. Chem. Soc.*, 1966, **88**, 5656.

[4] J. Jacobus and K. Mislow, *J. Amer. Chem. Soc.*, 1967, **89**, 5228.

[5] P. Karrer and K. Ehrhardt, *Helv. Chim. Acta*, 1951, **34**, 2202; W. Leithe, *Ber.*, 1932, **65**, 660.

[6] M. M. Green, M. Axelrod, and K. Mislow, *J. Amer. Chem. Soc.*, 1966, **88**, 861.