

β -Asymmetric Induction in the Reduction of *N*-Alkylidenesulphinamides. Synthesis of Optically Active Amines

By MAURO CINQUINI and FRANCO COZZI

(Centro C.N.R. e Istituto di Chimica Industriale dell'Universita', Via C. Golgi 19, 20133 Milano, Italy)

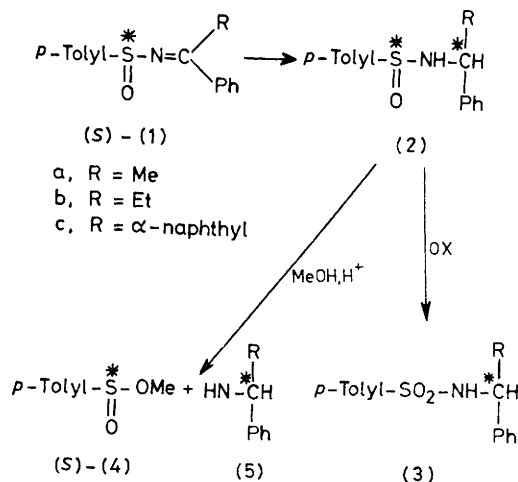
Summary Asymmetric synthesis occurs in the reduction by LiAlH_4 of optically active *N*-alkylidenesulphinamides; the sulphinamides thus obtained can be oxidized to optically active sulphonamides or cleaved to optically active amines of high optical purity.

OPTICALLY active *N*-alkylidenesulphinamides (**1**) are easily accessible by the reaction of a Grignard reagent with a nitrile and subsequent reaction with an optically active sulphinate.¹ In compounds (**1**) the four ligands on the chiral sulphur atom are very different from each other: a lone pair, and oxygen, nitrogen, and carbon atoms. It seemed likely, by analogy with other sulphur derivatives, especially sulphoxides,² that the chiral centre of *N*-alkylidenesulphinamides could give rise to an high degree of asymmetric induction.

We report that the derivatives (**1a—c**) are reduced in high yield by lithium aluminium hydride to afford unequal amounts of the corresponding stereoisomeric sulphinamides (**2a—c**), the diastereomeric ratio being in the range 9:1 to 8:2 (evaluated by ^1H n.m.r. spectroscopy) in the cases examined.

Starting from optically pure (*S*)-(**1a**), $[\alpha]_D^{25} + 98.0^\circ$ (CHCl_3), a mixture of optically active sulphinamides (*S,S*)-(**2a**) and (*S,R*)-(**2a**) was obtained, which was oxidized with *N*-chlorobenzotriazole in methanol³ to the corresponding optically active sulphonamide (—)-(**3a**). Similarly, reduction of optically active (*S*)-(**1b**), $[\alpha]_D^{25} + 26.2^\circ$ (CHCl_3)

and (*S*)-(**1c**), $[\alpha]_D^{25} + 7.1^\circ$ (CHCl_3), and subsequent oxidation afforded the optically active sulphonamides (—)-(**3b**) and (+)-(**3c**) (see Table). This confirms that asymmetric induction is occurring in the conversion (**1**) \rightarrow (**2**).



The sulphonamide (*S*)-(**3a**),⁴ $[\alpha]_D^{20} - 79.3^\circ$ (benzene), and the diastereomeric sulphinamides (*S,S*)-(**2a**),⁵ $[\alpha]_D^{25} + 37.2^\circ$ (CHCl_3), and (*S,R*)-(**2a**),⁵ $[\alpha]_D^{25} + 100.9^\circ$ (CHCl_3), had previously been prepared in optically pure form starting from

TABLE. Asymmetric synthesis in the reduction of *p*-MeC₆H₄S(O)N=C(Ph)R^{a,b}

R	Sulphinamides (2)			Sulphonamide (3) ^c			Amine (5) ^c		
	Yield (%)	[α] _D ^{25d}	Diast. ratio	Yield (%)	[α] _D ²⁵	M.p. (°C)	Yield (%)	[α] _D ²⁵	Optical purity (%)
Me	84	+42.3°	9:1	64	-64.6° ^e	88-91	70	-31.3° ^f	78
Et	80	+49.2°	8:2	63	-41.7° ^d	100-102	72	-12.1° ^f	57
α-Naphthyl ..	85	+56.0°	9:1	90	+3.4° ^d	150 (decomp.)	60	+52.4° ^e	80

^a Reactions were carried on in anhydrous diethyl ether at 25 °C with 1 mol of LiAlH₄ per mol of substrate. ^b All new compounds gave satisfactory elemental analysis and spectra (i.r., ¹H n.m.r.) in agreement with the assigned structure. ^c The absolute configuration of (3a-c) and of (5a-c) was (S). ^d In CHCl₃. ^e In benzene. ^f Neat.

optically pure α-phenylethylamine (5a). Since reduction of (1) does not effect the chiral sulphur atom, a comparison of the values of the optical rotations of the mixture of (S,S)-(2a) and (S,R)-(2a) and of (-)-(S)-(3a) with those reported in the literature^{4,5} established that the prevailing isomer obtained from (S)-(1a) has the (S,S)-(2a) absolute configuration and that the value of asymmetric induction is in this case 80%. The sulphinamides (2a-c) were subjected to acid methanolysis according to Mikolajczyk's method⁶ to give the optically active amines (-)-(5a), (-)-(5b), and (+)-(5c), respectively, and the optically active methyl toluene-*p*-sulphinate (-)-(S)-(4).

In all cases the optical purity of the amines (5) thus obtained was in excellent agreement with the extent of asymmetric synthesis determined by ¹H n.m.r. spectral

evaluation of the diastereomeric ratio of the starting sulphinamides (2) (see Table). The signs of the optical rotations of (5a-c) indicate that the absolute configurations of the predominating diastereomeric sulphinamide are (S,S)-(2a), (S,S)-(2b), and (S,S)-(2c).

The series of reactions reported here allows the transformation of an achiral precursor, a nitrile, into a chiral amine of high, and known, optical purity. In the process asymmetry is transferred from menthol to the sulphur atom of the sulphinate ester and of *N*-alkyldenesulphinamides (1) and from this to the asymmetric carbon atom of the amines (5).

(Received, 8th July 1977; Com. 693.)

¹ M. Cinquini and F. Cozzi, *J.C.S. Chem. Comm.*, 1977, 502.

² F. Montanari in 'Organic Sulphur Chemistry,' ed. C. J. M. Stirling, Butterworths, London, 1975, p. 181.

³ E. U. Jonsson, C. C. Bacon, and C. R. Johnson, *J. Amer. Chem. Soc.*, 1971, **93**, 5306, and references therein.

⁴ M. B. Watson and G. W. Youngson, *J. Chem. Soc.*, 1954, 2145.

⁵ T. R. Williams, A. Nudelman, R. E. Booms, and D. J. Cram, *J. Amer. Chem. Soc.*, 1972, **94**, 4684.

⁶ M. Mikolajczyk, J. Drabowicz, and B. Bujnicki, *J.C.S. Chem. Comm.*, 1976, 568.