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

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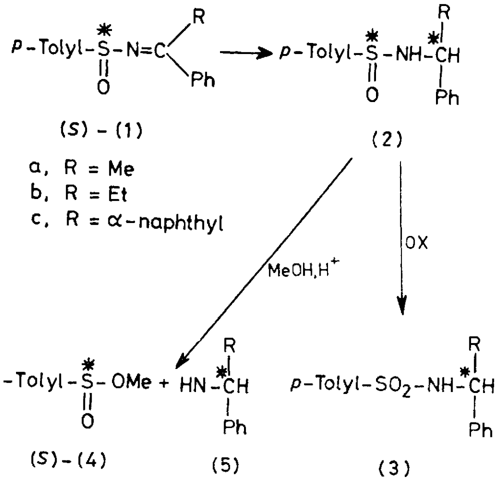
Summary Asymmetric synthesis occurs in the reduction by $LiAlH_4$ of optically active *N*-alkylidenesulphinamides; the sulphinamides thus obtained can be oxidized to optically active sulphonamides or cleaved to optically active amines of high optical purity.

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° ($CHCl_3$), a mixture of optically active sulphinamides (*S*,*S*)-(**2a**) and (*S*,*R*)-(**2a**) was obtained, which was oxidized with *N*-chlorobenzotriazole in methanol[3] to the corresponding optically active sulphonamide (−)-(**3a**). Similarly, reduction of optically active (*S*)-(**1b**), $[\alpha]_D^{25}$ +26·2° ($CHCl_3$) and (*S*)-(**1c**), $[\alpha]_D^{25}$ +7·1° ($CHCl_3$), and subsequent oxidation afforded the optically active sulphonamides (−)-(**3b**) and (+)-(**3c**) (see Table). This confirms that asymmetric induction is occurring in the conversion (**1**) → (**2**).



The sulphonamide (*S*)-(**3a**),[4] $[\alpha]_D^{20}$ −79·3° (benzene), and the diastereomeric sulphinamides (*S*,*S*)-(**2a**),[5] $[\alpha]_D^{25}$ +37·2° ($CHCl_3$), and (*S*,*R*)-(**2a**),[5] $[\alpha]_D^{25}$ +100·9° ($CHCl_3$), had previously been prepared in optically pure form starting from

TABLE. Asymmetric synthesis in the reduction of p-MeC$_6$H$_4$S(O)N=C(Ph)R[a,b]

R	Sulphinamides (**2**)			Sulphonamide (**3**)[c]			Amine (**5**)[c]		
	Yield (%)	$[\alpha]_D^{25d}$	Diast. ratio	Yield (%)	$[\alpha]_D^{25}$	M.p. (°C)	Yield (%)	$[\alpha]_D^{25}$	Optical purity (%)
Me	84	$+42{\cdot}3^\circ$	9:1	64	$-64{\cdot}6^{\circ e}$	88—91	70	$-31{\cdot}3^{\circ f}$	78
Et	80	$+49{\cdot}2^\circ$	8:2	63	$-41{\cdot}7^{\circ d}$	100—102	72	$-12{\cdot}1^{\circ f}$	57
α-Naphthyl	85	$+56{\cdot}0^\circ$	9:1	90	$+3{\cdot}4^{\circ d}$	150 (decomp.)	60	$+52{\cdot}4^{\circ e}$	80

[a] Reactions were carried on in anhydrous diethyl ether at 25 °C with 1 mol of LiAlH$_4$ per mol of substrate. [b] All new compounds gave satisfactory elemental analysis and spectra (i.r., ^{1}H n.m.r.) in agreement with the assigned structure. [c] The absolute configuration of (**3a**—**c**) and of (**5a**—**c**) was (*S*). [d] In CHCl$_3$. [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 method[6] 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 ^{1}H 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*-alkylidenesulphinamides (**1**) and from this to the asymmetric carbon atom of the amines (**5**).

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