Novel Asymmetric Synthesis of Chiral Sulphoxides

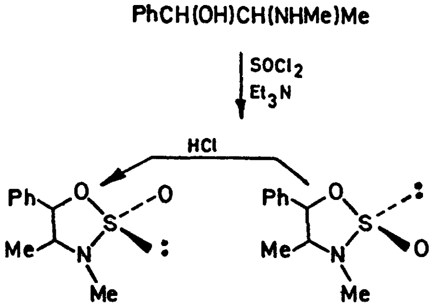
By F. WUDL* and T. B. K. LEE

(*Department of Chemistry, State University of New York at Buffalo, Buffalo, New York* 4214)

Summary A versatile asymmetric synthesis of either enantiomer of open-chain, chiral sulphoxide is described.

WHEN L-ephedrine is allowed to react with thionyl chloride[1] in an asymmetric synthesis, a 60% yield of an 80:20 mixture† of the chiral oxathiazolidine 2-oxide (**1**)‡ is obtained [reaction (1)].

Since diastereomer (**1**) is less soluble than diastereomer (**1a**), the latter can be converted into the former by an application of Herbrandson's work[2] [equation (1)]. Thus, although the asymmetric synthesis step occurs with high efficiency (80%), the overall stereochemical efficiency of reaction (1) may be boosted to 100% of one diastereomer.



(**1**) (**1a**) (1)

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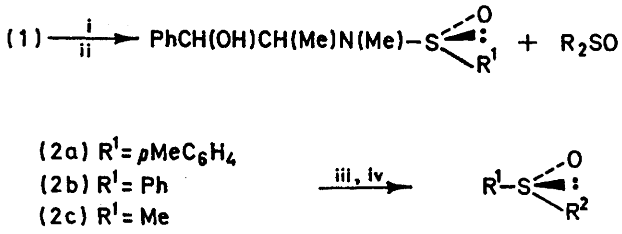
† The absolute configuration at sulphur was assigned by n.m.r. spectroscopy.[1]

‡ All physical and spectroscopic properties, including elemental analysis, agree with the assigned structure.

We found that the S–O bond of (**1**) may be cleaved selectively under specified conditions to afford chiral hydroxy-sulphinamides (**2**). These sulphinamides can in turn be converted into chiral sulphoxides as depicted in the Scheme.



i, R^1MgBr −33°; ii, H_3O^+; iii, R^2Li–THF −70°; iv, H_3O^+

Thus, if steps i and iii in the Scheme are interchanged, either enantiomer of a chiral open-chain sulphoxide can be prepared. The chiral sulphoxides thus prepared were $R^1 = Me$, $R^2 = Ph$ ($[\alpha]_D^{25} - 127{\cdot}5°$, *c* 1·52 EtOH);[3] $R^1 = p$-tolyl, $R^2 = Me$ ($[\alpha]_{546}^{25} + 183°$, *c* 2·1 Me_2CO, lit[3] $[\alpha]_{546}^{25} + 180°$); $R^1 = Ph$, $R^2 = Me$ ($[\alpha]_D^{25} + 128{\cdot}5°$, *c* 1·5 EtOH, lit. $[\alpha]_D^{25} + 149°$).

Steps i and iii (Scheme) proceed with inversion of configuration.†[3] Under certain conditions step i proceeds with incomplete inversion.[4] However, from a synthetic point of view, this is of little consequence since epimers of (**2**) are easily separable.

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[1] Achiral ethanolamines were converted into oxathiazolidine 2-oxides by S. A. Deyrup and C. L. Moyer, *J. Org. Chem.*, 1969, **34**, 175.

[2] H. E. Herbrandson and R. T. Dickerson, *J. Amer. Chem. Soc.*, 1959, **81**, 4102.

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

[4] F. Wudl and T. B. K. Lee, *J. Amer. Chem. Soc.*, submitted for publication.