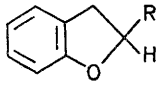
Asymmetric Induction in the Cyclisation of *o*-Allylphenol with Chiral Mercury(II) Carboxylates. The Effect of Dimethyl Sulphoxide

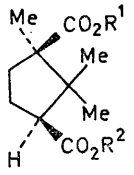
By MICHAEL F. GRUNDON,* DENIS STEWART, and WILLIAM E. WATTS
(*School of Physical Sciences, The New University of Ulster, Coleraine, Northern Ireland*)

Summary The reactions of *o*-allylphenol with mercury(II) salts of a range of chiral carboxylic acids, followed by reductive demercuration, give optically active 2,3-dihydro-2-methylbenzofuran; optical yields are influenced by the addition of dimethyl sulphoxide (DMSO), the maximum effect occurring with 4 mol of DMSO per mol of carboxylate.

WE have extended our interest[1] in asymmetric synthesis as a model for enzymatic reactions by studying the stereospecific intramolecular addition of nucleophiles to alkenes. This type of cyclisation which may be involved, for example, in the biosynthesis of flavonoids and of dihydrofuroquinoline alkaloids, is promoted with mercury(II) acetate. Thus, *o*-allylphenol afforded[2] an organomercurial

(**1a**; R′ = Me), which was reduced[3] ($NaBH_4/HO^-$) to the dihydrobenzofuran (**1b**). Asymmetric solvomercuration has been reported,[4] and we find that when cyclisation of *o*-allylphenol is effected with the mercury(II) salt of an optically active carboxylic acid, the dihydrobenzofuran (**1b**) obtained after demercuration is also optically active. The extent and the direction of asymmetric induction was determined by conversion of the products (**1a**) into compounds of known optical rotation and absolute configuration, *viz.* (**1c**)[5] and $MeCH(OH)CH_2CONHNH_2$.[6]





(**1**) **a**; R = CH_2HgO_2CR'
b; R = Me
c; R = CO_2H
d; R = CH_2HgCl

(**2**) **a**; R^1 = Me, R^2 = H
b; R^1 = H, R^2 = Me

From studies of the reaction using a range of chiral mercury carboxylates, the results may be summarised as follows. (*a*) The extent of asymmetric induction is rather low (< 5% excess of enantiomer), but is reproducible. (*b*) Since treatment of the initial products (**1a**) with aqueous NaCl gives the optically active organomercury chloride (**1d**), production of an excess of one enantiomer must occur during cyclisation. (*c*) For the mercury(II) salt of a particular acid, change in configuration at the chiral centre causes a reversal in the direction of induction; *e.g.* for cyclisation in DMSO followed by reduction, Hg[(*R*)-mandelate]$_2$ gives an excess of (*S*)-(**1b**), while Hg[(*S*)-mandelate]$_2$ furnishes an identical excess of (*R*)-(**1b**). The isomeric mono-methyl esters of (1*R*, 3*S*)-camphoric acid (**2**) were also studied; reaction of the mercury salt of the acid (**2a**) with *o*-allylphenol gives an excess of (*R*)-(**1b**), whereas (*S*)-(**1b**) is formed preferentially from the salt of acid (**2b**). (*d*) A much greater optical yield was achieved with the Hg^{II} salt of an α-amino-acid; *e.g.* for conditions as in (*c*), Hg[(*S*)-valinate]$_2$ produces *ca.* 5% excess of (*R*)-(**1b**) compared with *ca.* 0·5% for Hg[(*S*)-mandelate]$_2$. (*e*) The extent, and occasionally the direction, of induction achieved with a particular mercury carboxylate is sensitive to the nature of the solvent in which cyclisation is conducted; *e.g.* for reactions with Hg[(*S*)-mandelate]$_2$ in CH_2Cl_2, an excess of (*S*)-(**1b**) is obtained after demercuration, whereas in DMSO (*R*)-(**1b**) predominates. A striking specific effect of DMSO was observed in reactions conducted in CH_2Cl_2 containing up to 5% DMSO. Thus, the optical yield of (*R*)-(**1b**) from the (*S*)-mandelate salt approached a maximum when 4 mol of DMSO per mol of carboxylate were present. In reactions with the mercury salt of the methyl camphorate (**2a**), a maximum effect also occurred with 4 mol of DMSO.

Mercurinium ions probably take part in the reactions,[7] and our results suggest that the preferred transition states involve ions solvated with DMSO. Similarly, the higher inductions observed with amino-acids may be related to the known capacity of the amino-group[8] to co-ordinate strongly with mercury. A full mechanistic interpretation is deferred until the results of complementary studies with simple prochiral alkenes are available.

(*Received, 8th June* 1973; *Com.* 821.)

[1] R. M. Bowman, J. F. Collins, and M. F. Grundon, *J.C.S. Perkin I*, 1973, 626.
[2] R. Adams, F. L. Roman, and W. N. Sperry, *J. Amer. Chem. Soc.*, 1922, **44**, 1781.
[3] F. G. Bordwell and M. L. Douglass, *J. Amer. Chem. Soc.*, 1966, **88**, 993.
[4] J. Oda, T. Nakagawa, and Y. Inouye, *Bull. Chem. Soc. Japan*, 1967, **40**, 373; M. Kawana and S. Emoto, *ibid.*, 1967, **40**, 618; R. M. Carlson and A. H. Funk, *Tetrahedron Letters*, 1971, 3661.
[5] W. A. Bonner, N. I. Burke, W. E. Fleck, R. K. Hill, J. A. Joule, B. Sjöberg, and J. H. Zalkow, *Tetrahedron*, 1964, **20**, 1419.
[6] J. H. Ottaway, *Biochem. J.*, 1962, **84**, 11.
[7] D. J. Pasto and J. A. Gontarz, *J. Amer. Chem. Soc.*, 1971, **93**, 6902.
[8] C. A. McAuliffe, J. V. Quagliano, and L. M. Vallarino, *Inorg. Chem.*, 1966, **5**, 1996; T. V. Long and C. M. Yoshida, *ibid.*, 1967, **6**, 1754.