

## Asymmetric Synthesis at a Pyramidal Nitrogen Centre in a Chiral Medium

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**Summary** Optically active oxaziridines have been synthesised with an optical yield of *ca.* 30% by photochemical rearrangement of isomeric nitrones in (+)- or (-)-2,2,2-trifluoro-1-phenylethanol-fluorotrichloromethane solvent.

CHIRAL solvents have been used previously in asymmetric syntheses but generally yielded products of low optical purity (0–10%).<sup>1</sup> Chiral solvents have also been used to render enantiomeric protons non-equivalent in the n.m.r. spectrum and thus provide a method for determining



optical purity. Thus, (+)- and (-)-2,2,2-trifluorophenylethanol-fluorotrichloromethane (TFPE-FTCM) mixtures have been utilized by Pirkle *et al.*<sup>2,3</sup> to monitor the enantio-

meric homogeneity of a range of structures including amine *N*-oxides.

The chemical similarity between amine *N*-oxides and nitrones (imine *N*-oxides), allied to the availability of (+)- and (-)-2,2,2-trifluorophenylethanol both directly<sup>4</sup> and by synthesis<sup>5</sup> prompted a study of the photochemical rearrangement of nitrones to oxaziridines in Pirkle's solvent.

A typical experiment involved the dissolution of the nitron (0.1 g) in (+)- or (-)-TFPE-FTCM (0.5 ml, 1:1) prior to insertion into a standard n.m.r. tube which was in turn placed in a temperature controlled Dewar type photochemical cell and irradiated (medium pressure u.v. lamp). The reaction was monitored by n.m.r. spectroscopy. Separation of the oxaziridine, nitron, and optically active solvent was achieved by preparative t.l.c. on silica gel using dichloromethane as eluant ( $R_f$  0.7, 0.1, and 0.5, respectively).

Photoisomerization of the nitrones (1a–f) in the asymmetric environment gave optically active oxaziridines (2a–f) illustrating the stability of the nitrogen pyramids in these molecules (Table). In common with other types of asymmetric syntheses, the optical purity of products is

found to increase with decreasing temperature (from 5 to 29%). The rate of photoisomerization of the nitron (1a) to oxaziridine under the present conditions (50% yield after

respectively) showed conclusively that the product was free from traces of chiral solvent.

Maximum enantioselectivity (31%) was obtained using the nitron (1a) at lower temperature (-78 °C) with the (-)-TFPE solvent (of higher optical purity). This result compares favourably with previous optimal values for asymmetric syntheses in chiral media (18%<sup>6</sup> and 23%<sup>7</sup>) and with the value obtained for asymmetric synthesis of this oxaziridine by chiral peroxyacid oxidation of the parent imine (20%).

The relatively high range of optical purity associated with photoisomerization of the benzophenone derived nitrones (1a), (1b), and (1d) (20–31%) contrasts with the values found when a *para*-nitrophenyl substituent is present and may be a reflection of the intimate H-bonding association between the N<sup>+</sup>-O<sup>-</sup> bond of the nitron and the TFPE solvent molecule(s) analogous to that proposed in *S*-oxide-TFPE interaction.<sup>3</sup> Introduction of a second N<sup>+</sup>-O<sup>-</sup> bond into the molecule would be expected to change the solvent-solute interactions and optical purity of the product.

The higher optical yields observed (Table), coupled with the ease of recovery of the solvent suggests that the present chiral solvent method of introducing asymmetry could readily be extended to other systems.

TABLE

Nitron (1)	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	Solvent <sup>a</sup>	[ $\alpha$ ] <sub>D</sub> <sup>20</sup>	Optical purity of (2)/%
<b>a</b>	Ph	Ph	Bu <sup>t</sup>	(+) <sup>b</sup>	+75.9	29 <sup>d</sup>
<b>b</b>	Ph	Ph	Bu <sup>t</sup>	(-) <sup>c</sup>	-80.9	31 <sup>d</sup>
<b>c</b>	Ph	Ph	Bu <sup>t</sup>	(+) <sup>b</sup>	+12.7 <sup>g</sup>	5 <sup>d</sup>
<b>d</b>	Ph	Ph	Pr <sup>t</sup>	(+) <sup>b</sup>	+38.8	20 <sup>d</sup>
<b>e</b>	C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>p</i>	H	Bu <sup>t</sup>	(+) <sup>b</sup>	-5.6	6 <sup>e,f</sup>
<b>f</b>	C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub> - <i>p</i>	Me	Bu <sup>t</sup>	(+) <sup>b</sup>	-2.1	3 <sup>e,f</sup>

<sup>a</sup> TFPE-FTCM (1:1), at -78 °C. <sup>b</sup> Resolved by method in ref. 5, 86% optical purity compared to a commercial sample. <sup>c</sup> Commercial sample, ref. 4. <sup>d</sup> Maximum reported, ref. 8. <sup>e</sup> Maximum reported (J. Bjørge, D. R. Boyd, R. M. Campbell, N. J. Thompson, and W. B. Jennings, *J.C.S. Perkin II*, 1976 606). <sup>f</sup> *E* configuration. <sup>g</sup> At 25 °C.

8 h at -78 °C) indicates that it should be feasible in practice to obtain even higher optical yields at lower temperatures.

While the oxaziridine products obtained directly from the t.l.c. separation appeared to be > 95% pure by i.r. and n.m.r. spectroscopy, thermal racemization of the oxaziridines from the nitrones (1a) and (1b) (at 60 and 120 °C

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