Asymmetric Synthesis at Nitrogen by Oxidation of Imines with *m*-Chloroperoxybenzoic Acid in the Presence of Optically Active Alcohols

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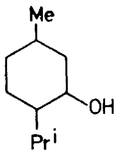
Summary Optically active oxaziridines, stable at the chiral nitrogen atom, have been obtained in 1—19% optical yields, by oxidation of imines with *m*-chloroperoxybenzoic acid in the presence of optically active alcohols; the absolute stereochemistry of the reaction depends on the chirality of the alcohols used.

In principle, optically active alcohols should be powerful chiral media for asymmetric reactions involving basic prochiral substrates and achiral reagents. Nevertheless, although optically active alcohols are commonly used as solvents in n.m.r. spectroscopy to induce enantiomeric nonequivalence in a variety of dissymmetric compounds,[1] the influence of these chiral media on asymmetric syntheses has not been studied to a great extent.[2,3] It has been reported that asymmetric oxidations of imines are solvent dependent and, in particular, give inversion of the enantiomeric composition of the corresponding optically active oxaziridines in protic as opposed to aprotic solvents.[4,5] We now report the results of oxidation of *N*-methyl-(**1a**) and *N*-t-butyl-diphenylmethylenamine (**1b**) with *m*-chloroperoxybenzoic acid (MCPB) in the presence of (*R*)-(—)-menthol (**2**), (*R*)-(—)- and (*S*)-(+)-octan-2-ol (**3**), (*S*)-(—)-1-phenylethanol (**4**), and (*S*)-(+)-2,2,2-trifluoro-1-phenylethanol (**5**).

$Ph_2C{=}NR$

(1)
a; R = Me
b; R = Bu^t



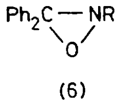
(2)

$Me[CH_2]_5CH(Me)OH$

(3)

RCH(Ph)OH

(4) R = Me
(5) R = CF_3



(6)
a; R = Me
b; R = Bu^t

In a typical experiment, a mixture of the imine (**1a**) or (**1b**) (1 mmol) and the chiral alcohol (5 mmol) was diluted with CH_2Cl_2 (0·4 ml) and treated at −40 °C with a solution of MCPB (1·1 mmol) in CH_2Cl_2 (2 ml). The reaction mixture was kept for 8 h at this temperature, and the solution was then extracted with saturated aq. $NaHCO_3$, washed water with, dried (Na_2SO_4), and evaporated. Oxaziridines (**6a**) and (**6b**) were separated (60—70% yield) from the optically active solvent by column chromatography on silica gel using CH_2Cl_2–n-hexane (7:3) as eluant.

Oxidation of the imines (**1**) with MCPB in the presence of the chiral alcohols (**2**)—(**5**) yields the optically active oxaziridines (**6**). N.m.r. and i.r. spectroscopy, as well as t.l.c. analysis and thermal racemization of (**6a**) and (**6b**), at 120 and 70 °C, respectively, showed that in every case the products obtained were completely free from traces of chiral alcohol.

The results reported in the Table show that: (i) the absolute stereochemistry induced by the oxidation depends on the configuration of the alcohols used, *e.g.* dextro- or laevo-rotatory oxaziridines (**6a**) and (**6b**) were obtained in reactions carried out with (*R*)- or (*S*)-alcohols, respectively; (ii) the optical purity of the reaction products is relatively low when cyclic (**2**) or acyclic (**3**) aliphatic alcohols are used, it increases when the oxidations are carried out in the presence of the aromatic solvents (**4**) and (**5**), and maximum values are achieved for both oxaziridines (**6a**) and (**6b**) with (+)-(**5**); (iii) the influence of temperature is as expected, *e.g.* the optical purity of (**6**) decreases with increasing temperature [Table, reactions carried out with (+)-(**5**)].

The optical yields obtained when (+)-(**5**) was used compare favourably with the values previously reported for asymmetric syntheses of the oxaziridines (**6**) by the chiral peroxyacid oxidation of the imines (**1**) in $CHCl_3$[5] and, very recently, by the photochemical rearrangement in (−)- and (+)-(**5**) of the nitrone isomer of (**6b**);[2] for example, (**6b**) was obtained with an optical purity of 19% at −40 °C (present work), 20% at −60 °C,[5] and 31% at −78 °C,[2] respectively. These results, coupled with the ease of separation of the optically active solvent from the reaction products, suggest that asymmetric inductions in the presence of chiral (**5**) can readily be extended to other prochiral systems.

TABLE

Asymmetric oxidation of imines (**1a**) and (**1b**) with MCPB in the presence of optically active alcohols at −40 °C.[a]

Alcohol[b]	Oxaziridine (**6a**)	(**6b**)	
	$[\alpha]^{20}_{D}/°$	$[\alpha]^{20}_{D}/°$	% Optical purity[c]
(*R*)-(−)-(**2**)	+ 0·9[d]	+ 3·2[d]	1·2
(*R*)-(−)-(**3**)	+ 0·9	+ 4·5	1·7
(*S*)-(+)-(**3**)	− 0·7	− 4·1	1·6
(*S*)-(−)-(**4**)	− 1·5	−23·6	9·1
(*S*)-(+)-(**5**)[e]	+20·9	+49·6	19·2
(*S*)-(+)-(**5**)[e]	+12·8[f]	+19·4[f]	7·5

[a] Reaction mixture composed of imine–alcohol (1:5 mmol) in CH_2Cl_2 (0·4 ml) + MCPB (1·1 mmol) in CH_2Cl_2 (2 ml). [b] Alcohols of 95—100% optical purity were used. [c] Calculated from maximum reported, ref. 5. [d] Reaction mixture dissolved in 2 + 2 ml of CH_2Cl_2. [e] (+)-(*S*)-(**5**) is configurationally related to (+)-(*R*)-(**4**). [f] At +25 °C.

The configurational correlations reported in the Table and the dependence of the optical yield on the nature of the chiral alcohol indicate that this method can also be used to obtain more knowledge about the still debatable problem of the absolute configuration at the asymmetric nitrogen atom of chiral oxaziridines,† as well as about the factors which may control the reported asymmetric synthesis of (**6**). N.m.r. studies[6] seem to indicate that, when secondary alcohols are used, the bonding of the hydroxy hydrogen and/or the *C*HOH hydrogen to the basic sites of the solute may play an active role in determining the conformational behaviour of the diastereoisomeric solvated transition states of the peroxyacid–imine–chiral alcohol system. However, asymmetric reactions show that other effects, including electronic and steric effects, may be operative when solvents with a trifluoromethyl group are used.[7]

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† The absolute stereochemistry at the asymmetric nitrogen centre of optically active oxaziridines has been recently studied by *X*-ray crystal structure analysis (A. Forni, G. Garuti, I. Moretti, G. Torre, G. D. Andreetti, G. Bocelli, and P. Sgarabotto, *J.C.S. Perkin II*, in the press) by a dynamic stereochemistry study of the peroxyacid–imine reaction,[4] and by c.d. spectroscopy (A. Forni, I. Moretti, and G. Torre, *Chimica e Industria*, in the press). All these studies seem to indicate that the configuration at nitrogen of oxaziridines of type (**6**) is (−)-(*S*) and (+)-(*R*), respectively.

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