Optical Resolution of Chiral *N*-Alkyl-3,3-bismethoxycarbonyloxaziridines

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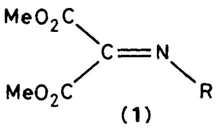
Classical optical resolution by fractional crystallization of diastereoisomeric salts obtained from the reaction of racemic *N*-t-butyl- **(3a)** and *N*-isopropyl-oxaziridine-3,3-dicarboxylic acid monomethyl ester **(3b)** with (*R*)-(+)- and (*S*)-(−)-1-phenylethylamine, followed by methylation of the optically active **(3a)** and **(3b)**, affords chiral oxaziridines **(2a)** and **(2b)** whose asymmetry is due solely to the nitrogen atom.

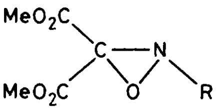
The first synthesis of optically active oxaziridines, whose molecular asymmetry is due solely to a pyramidal nitrogen atom, was achieved by asymmetric induction.[1] We now report that optical resolution of *N*-alkyloxaziridine-3,3-dicarboxylic esters of type (**2**)[2,3] can be effected by using the classical fractional crystallization of the diastereoisomeric salts obtained from the reaction of the corresponding monomethyl esters (**3**) with (*R*)-(+)- and (*S*)-(−)-1-phenylethylamine (PEA).

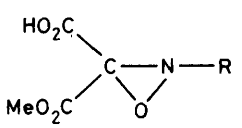
The racemic oxaziridines (**2a**) and (**2b**) were synthesized by oxidation of the imines (**1a**) and (**1b**) at 0 °C in $CHCl_3$ with *m*-chloroperoxybenzoic acid. The saponification of (**2a,b**) with an equimolecular amount of KOH in MeOH, followed by treatment with toluene-*p*-sulphonic acid hydrate in MeOH at 20 °C, afforded stereospecifically the corresponding *N*-alkyloxaziridine-3,3-dicarboxylic acid monomethyl esters (**3a,b**) in a single diastereoisomeric form (as indicated by ^1H n.m.r. spectroscopy).

The reaction of the racemic monoacids (**3a,b**) with an equimolecular amount of (*R*)-(+)-PEA in diethyl ether provided a mixture of diastereoisomeric salts, which on crystallization (×4) from ethyl acetate to constant melting points and optical rotations, gave the diastereoisomerically pure (+) forms in 20—25% yield. Likewise, treatment with (*S*)-(−)-PEA of the monomethyl esters (**3**) recovered from the more soluble diastereoisomeric fractions led to the optically pure (−) salts.

Removal of the PEA moiety was achieved by addition of toluene-*p*-sulphonic acid hydrate in MeOH to each fraction. Finally, we obtained the enantiomeric (−) and (+) pairs of (**2a**) and (**2b**) by esterification of optically active (**3a**) and (**3b**) with ethereal diazomethane. The ^1H n.m.r. spectra of these compounds, recorded in the presence of a 5 molar excess of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol, suggest that the enantiomeric purities are not less than 94%.


(**1**)


(**2**)


(**3**)

a; R = Bu^t
b; R = Pr^i

Table 1. Physical properties of compounds (**2a**) and (**2b**).

Oxaziridine	B.p., *t*/°C (*p*/mmHg)	$[\alpha]_D^{20}$ [a]	% Enantiomeric excess
(**2a**)	72 (0.020)	+74.1° −76.4°	95[b]
(**2b**)	84 (0.045)	+60.6° −61.7°	98[b]

[a] In chloroform solution. [b] Determined from n.m.r. spectra recorded in $CDCl_3$ solution and in the presence of a 5-fold excess of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol.

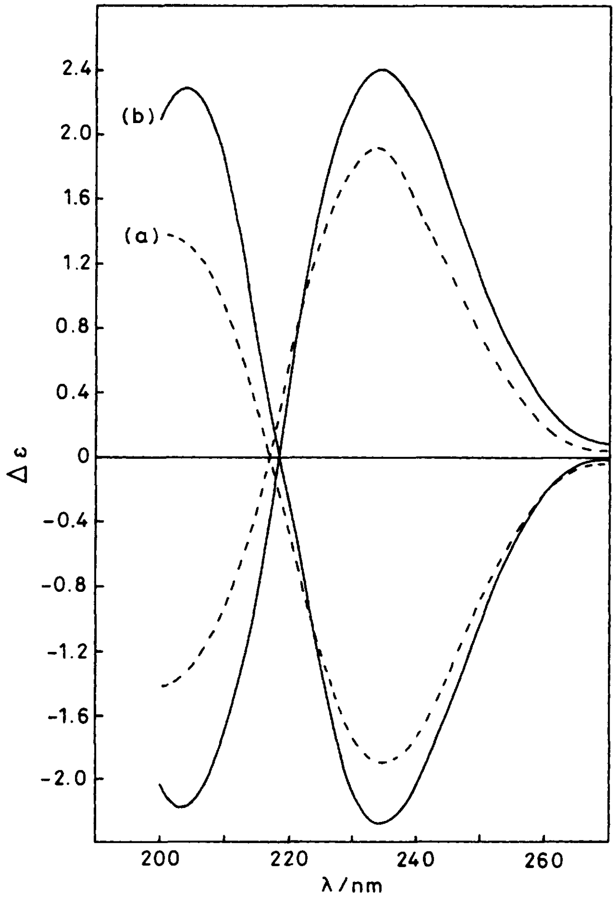


Figure 1. C.d. spectra of the enantiomeric species of (a) (**2a**) and (b) (**2b**), in iso-octane solution.

The properties of the oxaziridines (**2a**) and (**2b**) are reported in Table 1; the corresponding c.d. spectra are in Figure 1. (−)-(**2a**) and -(**2b**) show a clear positive Cotton effect centred at 234—235 nm, and a negative band at lower wavelengths, and specular behaviour is also observed for (+)-(**2a**) and -(**2b**). According to theoretical[4] and experimental[5] studies, this chiroptical behaviour is consistent with the (−)-(*S*) and (+)-(*R*) configurations of the derivatives (**2**).

Although several examples of highly optically pure three-membered heterocycles containing a chiral nitrogen atom have been reported, which have been obtained by fractional crystallization of partially optically active solid samples,[6] to the best of our knowledge this is the first example of enantiomeric resolution of chiral oxaziridines having a tercovalent nitrogen as the sole asymmetric centre.†

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† Experimental[7] and theoretical[8] studies indicate that the ring substituents have an important influence on the chemical stability of the oxaziridine ring. In this respect, it is noteworthy that oxaziridines of type (**2**) and (**3**) are quite stable under the acidic and basic conditions employed in the present work.