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STUDIES ON THE CONFIGURATION AT CHIRAL NITROGEN IN 2-(S-1-PHENYLETHYL)-3-p-BROMOPHENYL OXAZIRIDINE

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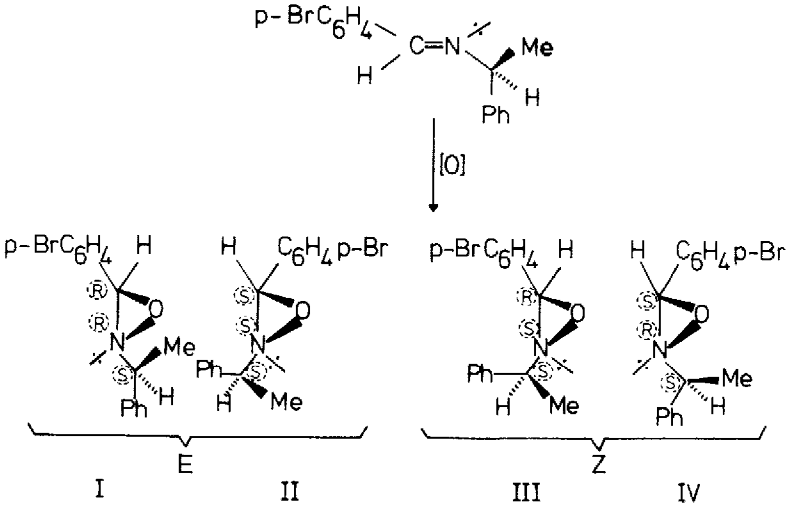
Oxaziridines with stable chiral nitrogen atom can be obtained highly stereospecifically by m-chloroperbenzoic acid oxidation of the Schiff's bases formed from achiral carbonyl compounds and chiral R(+)-α-phenylethylamine.[1] The Schiff base of configuration E obtained from this amine and benzaldehyde, when oxidized under these conditions yields all possible nonracemic diastereoisomers, with the isomers of configuration E in excess [2]:

$$\text{diastereoisomers of configuration E} \begin{bmatrix}\text{RRR}\\ \text{SSR}\end{bmatrix} \qquad \text{diastereoisomers of configuration Z} \begin{bmatrix}\text{RSR}\\ \text{SRR}\end{bmatrix}$$

The separation of diastereoisomers and the determination of their physical properties did not permit the establishment of the absolute configuration of the chiral nitrogen and carbon atoms in the oxaziridine ring. This problem has been solved by x-ray crystal structure analysis of a model compound.

E(+)-N-p-bromobenzylidene-α-phenylethylamine, obtained from S(-)-α-phenylethylamine, was oxidized with m-chloroperbenzoic acid. The composition of the mixture of four diastereoisomers was determined by integration of the C(3)-proton signals. By analogy, [3] the E configuration was ascribed to I and II and Z



to III and IV. The diastereoisomers were separated chromatographically (SiO_2, hexane-ether = 95:5) and characterized (Table 1).

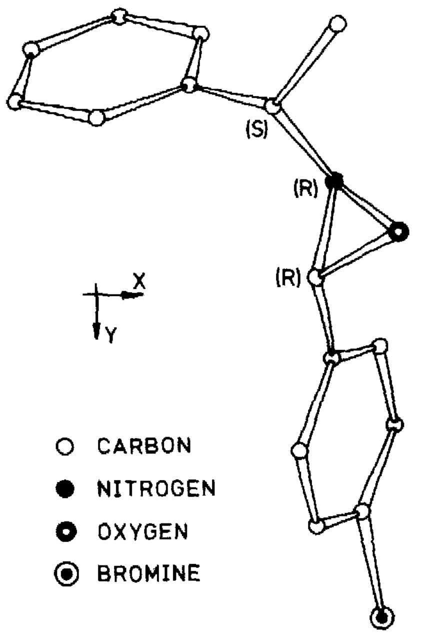
Table 1.

Diastereo-isomer	m.p. (°C)	α_D^{20}	c ($CHCl_3$)	δ (ppm) H-C(3)	% in the mixture
I	128-129	+128.6	1.026	4.325	58.5
II	58-59	-60.4	1.050	4.380	20.7
III	84-85	-224.6	1.460	5.000	15.9
IV	109.5-110.5	-292.6	1.004	5.150	4.9

The diastereoisomer I, formed predominantly, was submitted to x-ray analysis.

The x-ray crystallographic study of a single crystal of diastereoisomer I confirmed the structure and, by reference to the S configuration of the α-phenylethylamine asymmetric centre used in the synthesis, established the absolute configuration.

<u>Crystal data</u>: $C_{15}H_{14}NOBr$, MW =304, Orthorhombic, Space Group $P2_12_12_1$, $\underline{a}$=7.73(1), $\underline{b}$=29.83(2), $\underline{c}$=5.92(1) Å, V=1367 $Å^3$, D_m=1.40, D_x=1.47 $g\cdot cm^{-3}$, Z=4, F(000)=616.



The intensity data were collected on a Syntex $P2_1$ four-circle fully automatic diffractometer with graphite-monochromated CuK_α radiation. A total of 1133 independent reflexions were measured. Of these, 983 were considered as observable and used in calculations. Lorentz and polarization corrections were applied. No absorption correction was made. The computations were performed with the Syntex Software system and NRC crystallographic programmes.[4]

The structure was solved by the heavy-atom method. The coordinates of all non-hydrogen atoms were derived from a Fourier map and refinement was performed by the least-squares method with anisotropic temperature factors. All the hydrogen atoms were found on a difference map. Final R index is 4.7% for 983 reflexions. The structure is as shown in the Figure, which illustrates the c axis projection of the molecule. The hydrogen atoms are not included.

The Z direction points downwards.

The results obtained establish that the diastereoisomer I is (+)-2R,3R-2(S-1-phenylethyl)-3-p-bromophenyloxaziridine. The absolute configurations of oxaziridines have not been reported in the literature before: the only information available deals with the relative configuration of these compounds.[5,6]

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