Stereochemical Control in Oxaziridine Synthesis from Nitrones and Imines

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Summary Stereochemistry in the photoisomerization of nitrones or in the peroxy-acid oxidation of imines to oxaziridine diastereomers is deduced from nuclear–nuclear Overhauser effects, and in combination with solvent and temperature studies, leads to a consideration of the oxidation mechanism.

THE non-inverting nature of the nitrogen pyramid in oxaziridines has recently been established by the isolation of enantiomeric[1,2] and diastereomeric oxaziridines.[1,3] We now report that the oxaziridine diastereomer ratio (*cis* : *trans*) resulting from the imine–peroxy-acid reaction and from the photochemical rearrangement of nitrones is markedly dependent on reaction conditions.

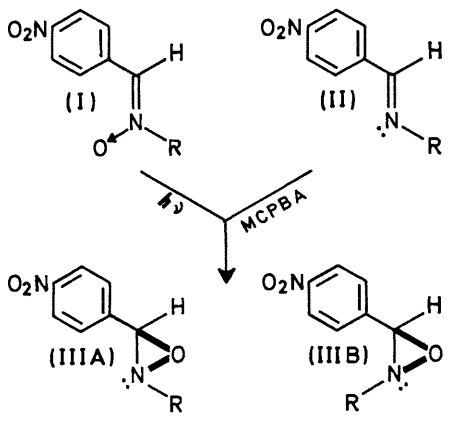
Photolysis of the aldonitrones (I; R = Me, Et, Pr^i) resulted in the formation of a *cis* : *trans* mixture (IIIB and IIIA) of oxaziridines, whose composition depends on solvent (Table 1). Nitrone (I; R = Bu^t) gave only the *trans*-isomer under similar conditions. These results

TABLE 1[a]

Nitrone (I) substituent (R)	(IIIA)	(IIIB)
Me	57 (87[b])	43 (13[b])
Et	73	27
Pr^i	68	32
Bu^t	100	0

[a] Irradiation of nitrone (I) at room temperature, under nitrogen, using a Hanovia U.V.S. 500/A lamp, 80 min. in acetonitrile. [b] Benzene or ethanol solvent.

contrast with previous studies,[4] where the possibility of diastereoisomerism was not considered.



MCPBA = *m*-chloroperoxybenzoic acid

The aldimine–peroxy-acid reaction was studied using imine (II; R = Me), and the results in Table 2, in addition

TABLE 2[a]

Solvent	(IIIA)	(IIIB)
Dichloromethane	61 (43[b])	39 (57[b])
Benzene[e]	57 (39[c])	43 (61[c])
Chloroform	70 (56[d])	30 (44[d])
Acetonitrile, t-butyl alcohol[e]	89	11
Carbon tetrachloride	54	46
Ether	76	24
Ethanol	97	3

[a] Diastereomer ratio (IIIA) : (IIIB (R = Me), resulting from oxidation with *m*-chloroperoxybenzoic acid at −15°, was determined by n.m.r. analysis ($CDCl_3$) of the crude product mixture, which showed no appreciable decomposition or oxaziridine stereomutation. [b] At +41°. [c] At +80°. [d] At +61°. [e] At +20°.

to similar results found with other imines (II; R = Et, Pr^i), show a solvent and temperature-dependent stereoselectivity. A variation of reaction conditions (temperature and solvent) or reactant structure[1] (imine, peroxy-acid, or nitrone) may thus be used, with advantage, in the preferential formation of one diastereomer.

In view of several possible mechanistic interpretations of these solvent and temperature studies an investigation of the stereochemistry of the imines, nitrones, and oxaziridines was attempted using nuclear–nuclear Overhauser effects (NOE).[5] The large NOE's observed (Table 3) confirm the

TABLE 3[a]

R	Imine	Nitrone	Oxaziridines (IIIA)	(IIIB)
Me	27 ± 3%	12 ± 3%[b]	26 ± 2%	0
Bu^t	25 ± 5%	20 ± 3%	34 ± 3%	—

[a] Spectra were measured on a Varian HA-100 n.m.r. spectrometer at +30° in degassed $CDCl_3$ solution, operating in the frequency-sweep mode. % Values refer to the maximum increase in integrated intensity of the α-C–H signal on irradiation of the R signal. [b] In $(CD_3)_2SO$ solution at +60°.

trans-stereochemistry of the oxaziridines (IIIA),[1,6] support the suggestion that the imine (II) is found mainly as the *trans*-isomer,[7] and strengthen the postulation[8] that aldonitrones have the stereochemistry shown (I).

The peroxy-acid and photoisomerization reactions are both kinetically controlled since the *cis*- and *trans*-oxaziridines are not significantly interconverted under the reaction conditions. The *cis*-isomer was converted into the more stable *trans*-isomer (>95%) by heating for 16 h at 130° (in C_2Cl_4 solution) or by photolysis for 200 h at 20° (in $CDCl_3$ solution).†

A concerted electrophilic attack by the peroxy-acid (analogous to the cyclic transition state found in the olefin–peroxy-acid mechanism[9]), or a nucleophilic attack by the peroxy-acid (analogous to the ketone–peroxy-acid mechanism of the Baeyer–Villiger reaction) on the imine have both been suggested as mechanisms for the synthesis of oxaziridines.[10] A recent kinetic study[11] appears to support the former mechanism. The results presented here are difficult to rationalize in terms of a cyclic transition state since there is no direct relationship between the suggested stereochemistry of the imine (II; R = Me) and the derived oxaziridines in some solvents (*e.g. ca.* 60% *cis*-oxaziridine in benzene at +80°).‡ The present results suggest that the mechanism of the imine–peroxy-acid reaction may be more complex or indeed that an alternative mechanism may be operative for solvents which afford a significant proportion of the *cis*-oxaziridine.

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† Equilibrations were carried out in n.m.r. tubes sealed *in vacuo*. The thermal equilibration was accompanied by considerable decomposition into *p*-nitrobenzaldehyde and imine.

‡ Accepting the concerted mechanism, the formation of the *cis*-oxaziridine might be rationalized by assuming that the *trans*-imine is in rapid equilibrium with the *cis*-isomer (not detected by n.m.r. even at low temperature), and that the latter isomer reacts much more rapidly.

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