Dynamic Stereochemistry of Imines and Derivatives. Part 13.[1] The Stereochemistry of the Products from Peroxyacid Oxidation of Bis-*N*-Alkylaldimines

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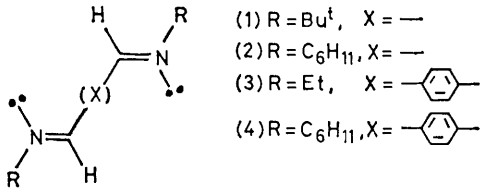
Bis-*N*-alkylimines derived from glyoxal (1) and (2) and terephthalaldehyde (3) and (4) have been oxidised with *m*-chloroperoxybenzoic acid to give stereoisomeric mixtures of bis-oxaziridines. The bis-oxaziridines obtained from (1) have been separated and unequivocally assigned *trans,trans* [racemic] (5a) and *trans,trans* [*meso*] (5b) configurations by a combination of n.m.r. methods and asymmetric synthesis. Bis-oxaziridine products resulting from oxidation of the bis-imines (3) and (4) are also configurationally stable at nitrogen, and are formed as diastereoisomeric mixtures. Analysis of the bis-oxaziridine product mixture by ^{1}H and ^{13}C n.m.r. indicates that the major components have the *trans,trans* and *cis,trans* stereochemistry though traces of the *cis,cis* isomer are probably present. Each of these components may be a mixture of *meso* and racemic isomers which are unresolved in the n.m.r. spectra. ^{1}H and ^{13}C shifts and some ^{13}C–H coupling constants are reported for the bis-oxaziridines.

OXAZIRIDINES have remarkably high configurational stability at nitrogen and can exist in isolable *cis*- and *trans*-forms.[2,3] Accordingly, bis-oxaziridines should have intriguing stereochemical possibilities. However, few studies of these systems have been reported in the literature [4-6] and in only one case has the stereochemistry been considered.[6] In this outstanding early investigation of oxaziridine chemistry Emmons [6] isolated two isomeric bis-oxaziridines from the peroxyacetic acid oxidation of the bis-imine (1) and assigned, *a priori*, a *meso*-configuration to the higher-melting isomer and a racemic configuration to the other. However, at the time of this work (1958) the configurational stability at the nitrogen atom of oxaziridines had not been established, and the terms *meso* and racemic merely referred to the relative configurations at carbon. Similarly, the peroxyacetic acid oxidation of bis-imines (2), (3), and (4) has been reported to yield in each case one bis-oxaziridine of unspecified stereochemistry.[4]

In view of the non-inverting nature of the nitrogen atom in many mono-oxaziridines at ambient temperature, we anticipated that bis-oxaziridines derived from

[1] Part 12, J. Bjørgo, D. R. Boyd, W. B. Jennings, P. M. Muckett, and L. C. Waring, *J. Org. Chem.*, in the press.
[2] D. R. Boyd, R. Spratt, and D. M. Jerina, *J. Chem. Soc.*, (*C*), 1969, 2650.
[3] J. Bjørgo, D. R. Boyd, R. M. Campbell, N. J. Thompson, and W. B. Jennings, *J.C.S. Perkin II*, 1976, 606.
[4] L. Horner and E. Jürgens, *Chem. Ber.*, 1957, **90**, 2184.
[5] H. Krimm, *Chem. Ber.*, 1958, **91**, 1057.
[6] W. D. Emmons, *J. Amer. Chem. Soc.*, 1957, **79**, 5739.

the imines (1)—(4) should exist in enantiomeric and diastereomeric forms (5a—d)—(8a—d).



Bis-imines of the type (1) and (2) have been considered to exist with a preference for the *trans,trans* conformation shown.[7,*] More recent studies on the preferred geometry of aldimines [8,9] would again be in concurrence with these conclusions.

Oxidation of the bis-imine (1) with *m*-chloroperoxybenzoic acid (MCPBA) gave a mixture of bis-oxaziridines which was separated by short column chromatography [10] on silica gel. The initially eluted compound (5b) had a higher melting point (83—84 °C) than the more strongly held isomer (5a), m.p. 46—47 °C. The n.m.r. signals from the equivalent ring hydrogens and ring carbon in (5b) were distinguishable from the corresponding signals of (5a) (Table 1).

The *trans,trans* configuration of the isomeric mixture (5a, b) was confirmed by irradiation of the *N*-t-butyl signal and observation of the ring-proton signals using a degassed sample. The observed nuclear–nuclear Overhauser enhancement on the CH signals was 40% due to the close proximity of the t-butyl group.

The n.m.r. spectra do not allow an unequivocal assignment of the *meso* and racemic isomers. However, this proved to be possible by asymmetric synthesis using (+)-peroxycamphoric acid (PCA) as oxidant.† This chiral oxidant has previously been used to distinguish disulphoxide stereoisomers [12] and azoxy-oxadiaziridine structural isomers [13] and the present application further demonstrates the versatility of this reagent.

Chromatographic separation of the products from the (+)-PCA oxidation of compound (1), as before, yielded two products. The bis-oxaziridine m.p. 83—84 °C was found to be devoid of optional activity and was, therefore, identified as the *trans,trans* (*meso*) form (5b). The other product, m.p. 46—47 °C, gave a small but reproducible optical rotation $[\alpha]_{589}$ —2.1°, $[\alpha]_{436}$ —4.1° in $CHCl_3$ as expected for the *trans,trans* (racemic) configuration (5a).

The crude product from the MCPBA oxidation of (2) also appeared by ^1H and ^{13}C n.m.r. analysis to be a mixture of stereoisomers (6a) and (6b) by analogy with the spectra of (5a) and (5b) (Table 1). The isomer ratio was virtually unchanged by recrystallisation from

TABLE 1

^1H and ^{13}C n.m.r. data for bis-imines and their oxidation products [a]

Compd.	Vinylic or ring proton [b]	Vinylic or ring carbon	Acrylic N–C
(1)	7.95 (2H)	157.93	58.17
(2)	7.94 (2H)	160.07	69.34
(3)	8.29 (t, J 1.5 Hz, 2H)	159.87	55.89
(4)	8.31 (d, J 0.5 Hz, 2H)	157.99	69.99
(5a)	3.705 [3.73] (2 H)	74.15 [72.14]	58.10 [55.57]
(5b)	3.71 [3.78] (2 H)	73.89 [71.94]	58.23 [55.76]
(6a)	3.52 [3.50] (2 H)	79.22 [79.48]	69.41 [69.89]
(6b)	3.53 [3.57] (2 H)	79.03 [79.35]	69.21 [69.15]
(7a,b)	4.48 [4.06] (2 H)	80.07 [80.26]	56.74 [56.93]
(7c,d)	4.52 (1 H), 5.22 (1 H) [4.08 (1 H), 5.03 (1 H)]	79.42, 79.94 [79.55, 80.26]	47.70, 56.74 [48.16, 56.93]
(7e,f)	5.25 [5.03] (2 H)	79.42 [c] [79.55] [c]	47.70 [c] [48.16] [c]
(8a,b)	4.52 [4.17] (2 H)	79.35 [79.42]	70.06 [70.06]
(8c,d)	4.57 (1 H), 5.25 (1 H) [4.17 (1 H), 5.11 (1 H)]	78.83, 79.22 [79.29, 79.42]	59.21, 70.06 [59.46, 70.06]
(8e,f)	5.30 [5.09] (2 H)	*d*	59.66 [c] [59.89] [c]
(10a; R = Et)	4.55 (1 H), 9.97 (1 H) [e]	80.07, 191.67	56.74
(10b; R = Et)	5.27 (1 H, 10.00 (1 H) [e]	*d*	*d*
(10a; R = C_6H_{11})	4.59 (1 H), 9.99 (1 H) [e]	79.35, 191.67	65.64
(10b; R = C_6H_{11})	5.31 (1 H), 10.03 (1 H) [e]	*d*	*d*

[a] Chemical shifts are given in δ units relative to $SiMe_4$. Open figures refer to deuteriochloroform solution, and data in square brackets were obtained in deuteriobenzene solution. [b] d = doublet, t = triplet; other signals were singlets. [c] Assignment uncertain. [d] Signals were too weak to detect. [e] Aldehydic proton.

All *N*-t-butyloxaziridines with a proton directly attached to the ring have to date been found to exist exclusively in the *trans*-configuration, as a result of steric interactions.[2,8,11] Thus isomers (5c—f) were neither expected nor detected (by n.m.r.) in the product mixture.

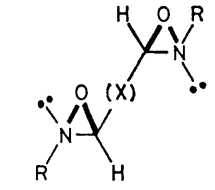
* Throughout this paper *cis*- and *trans*-stereochemistry is assigned in accordance with the sequence rules, *i.e. cis* = *seq cis* and *trans* = *seq trans*.

† A recent paper (W. H. Pirkle and P. L. Rinaldi, *J. Org. Chem.*, 1977, **42**, 2080) has implied that the PCA used in previous asymmetric synthesis work may have been an unpurified mixture of isomers. The (+)-PCA used in the present investigation and in our previous studies was recrystallised according to the procedure described by J. F. Collins and M. A. McKervey (*J. Org. Chem.*, 1969, **34**, 4172).

[7] J. M. Kliegman and R. K. Barnes, *Tetrahedron Letters*, 1969, 1953.
[8] D. R. Boyd, W. B. Jennings, R. Spratt, and D. M. Jerina, *Chem. Comm.*, 1970, 745.
[9] J. Bjørgo, D. R. Boyd, C. G. Watson, W. B. Jennings, and D. M. Jerina, *J.C.S. Perkin II*, 1974, 1081.
[10] B. J. Hunt and W. Rigby, *Chem. and Ind.*, 1967, 1868.
[11] D. R. Boyd, D. C. Neill, C. G. Watson, and W. B. Jennings, *J.C.S. Perkin II*, 1975, 1813.
[12] R. Louw and H. Nieuwenhuyse, *Chem. Comm.*, 1968, 1561.
[13] F. D. Greene and S. S. Hecht, *Tetrahedron Letters*, 1969, 575.

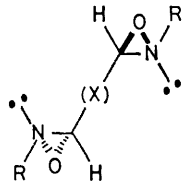
methanol and the m.p. 120—122 °C was similar to that previously reported by Horner and Jürgens [4] (123 °C). It therefore seems reasonable to suggest that this product [4] was in fact also a mixture of isomers.

The isomer ratio of bis-oxaziridines (5a) : (5b) and (6a) : (6b) formed under identical conditions was found to be similar, *i.e.* 46—47% racemic : 54—53% *meso*. There seems therefore to be little preference for peroxy-acid addition to either face of the double bond in the mono-oxaziridine intermediate (9a; X = —). However, the preferred conformation around the central



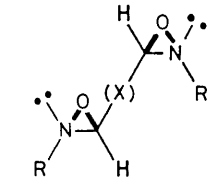
(a)

trans, *trans (racemic)*



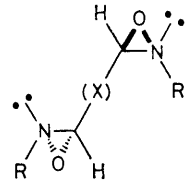
(b)

trans,trans (meso)



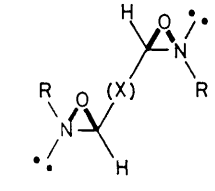
(c)

trans,cis (racemic)



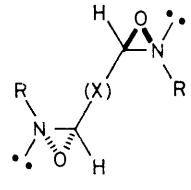
(d)

trans,cis (racemic)



(e)

cis,cis (racemic)



(f)

cis,cis (meso)

(5) R = Bu^t, X = —

(6) R = C_6H_{11}, X = —

(7) R = Et, X = 

(8) R = C_6H_{11}, X = 

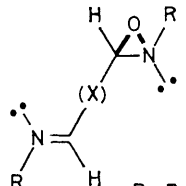
TABLE 2

Product distribution from MCPBA oxidation of bis-imines (3) and (4) in dichloromethane at 0 °C

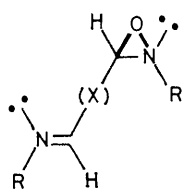
Imine	Bis-oxaziridine	%	Aldehyde oxaziridine	%
(3)	*trans,trans*-(7a,b)	46	*trans*-(10a; R = Et)	10
	trans,cis-(7c,d)	34	*cis*-(10b; R = Et)	3
	cis,cis-(7a–f)	7		
(4)	*trans,trans*-(8a,b)	55	*trans*-	
	trans,cis-(8c,d)	13	(10a; R = C_6H_{11})	26
	cis,cis-(8e—f)	1	*cis*-(10b; R = C_6H_{11})	5

CH–CH bond in the diastereoisomeric transition states for the addition of the second oxygen atom may differ and need not be transoid as shown in (9a).

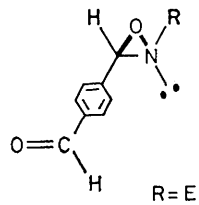
The stereochemistry about the carbon–nitrogen double bond in the aromatic bis-imines (3) and (4) can be assumed to be exclusively *trans,trans* since they are devoid of the *ortho*-substituents which are normally associated with detectable amounts of *cis*-aldimines.[9] In principle, ten stereoisomers of the bis-oxaziridines



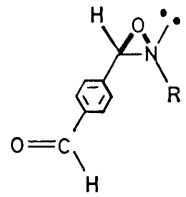
(9a) R = Bu^t or C_6H_{11}



(9b)



(10a) R = Et or C_6H_{11}



(10b)

(7) or (8) could be produced by peroxyacid oxidation of (3) or (4). Previous results with *trans*-imines of aromatic aldehydes from these laboratories [2,3] showed that appreciable quantities of both *cis*- and *trans*-oxaziridines were formed on oxidation. Accordingly the product mixture from the oxidation of aromatic bis-aldimines might be expected to contain *trans,trans*, *cis,trans*, and *cis,cis* isomers.

In practice, t.l.c. and n.m.r. analysis of the product mixture from MCPBA oxidation of (3) and (4) showed the presence of at least two bis-oxaziridines. The ring proton chemical shift in *C*-aryloxaziridines is very characteristic of the stereochemistry about the CN bond, *viz. ca.* δ 4.5 for the *trans*-isomer and *ca.* δ 5.2 for the *cis*-isomer (in $CDCl_3$).[2] The crude reaction mixture showed two reproducible signals in each of these regions plus an additional pair of weak signals of variable intensity, depending on the oxidation conditions. In addition, two aldehyde signals of variable intensity were observed at *ca.* δ 10.0 which showed the same integrated intensity as the extra oxaziridine CH signals. These resonances are assigned to the *trans* and *cis* formyloxaziridines (10a) and (10b) (see Table 1), presumably produced by decomposition of the bis-oxaziridines.

Attempts to separate the bis-oxaziridine mixture (7) by column and preparative t.l.c. were unsuccessful because of decomposition and the large number of products. However, recrystallisation of the product mixtures from (3) and (4) gave crystalline compounds, m.p. 87—90 °C (lit.,[4] 93 °C) and 162—166 °C (lit.,[4] 161 °C) respectively which appear to be identical to those reported previously. These compounds each gave a singlet for the oxaziridine ring proton at δ 4.48 and 4.52 respectively (in $CDCl_3$) as anticipated for the pure *trans,trans* isomers (7a,b) and (8a,b). In view of the large separation between the two oxaziridine fragments in (7) and (8), and the observation that imines (1) and (2)

give rise to an equimolar *meso* : racemic *trans,trans* bis-oxaziridine mixture, it would seem likely that the *trans,-trans* bis-oxaziridines formed from (3) or (4) should also be a *meso* (7b) or (8b)–racemic (7a) or (8a) mixture. However it was not possible to resolve the signals of these *trans,trans* bis-oxaziridines into two components in either the ^1H or ^{13}C spectra (even with the aid of a 220 MHz ^1H spectrum). Possibly this is a consequence of the large separation between the oxaziridine moieties in (7) or (8) which reduces the *meso*-racemic signal splitting compared with (5) and (6).

Further evidence for the *trans,trans* stereochemistry comes from observations on the ^{13}C satellites of the ring proton signal. Values of ^1J (^{13}CH) of 178 Hz for both (7a,b) and (8a,b) are similar to those found for comparable *trans*-mono-oxaziridines (177—180 Hz).[14]

In addition to the major *trans,trans* components, the oxidation mixture from (3) and (4) showed signals consistent with the *trans,cis* structures of (7c,d) and (8c, d). Several factors support this conclusion. (i) Two signals were observed close to the values of δ 4.5 and 5.2 normally found for *trans*- and *cis*-mono-oxazidines respectively with similar ring substituents (Table 1);[2] (ii) the two signals were of equal intensity; (iii) two equal intensity singlets were observed in the ^{13}C n.m.r. spectrum for the ring carbon atoms; and (iv) the measured $^1J(^{13}CH)$ couplings of 178 and 183 Hz for the signals of (7c,d) at δ 4.52 and 5.22 (in $CDCl_3$) indicate *trans*- and *cis*-oxaziridine stereochemistry respectively.[14]

A relatively minor, but reproducible, signal at δ 5.25 ($CDCl_3$) in the ^1H spectrum of the crude product mixture from (3) has been tentatively identified as the *cis,cis* isomer (7e,f). This isomer should be the least stable since *cis*-oxaziridines tend to decompose with time. Decomposition was more evident in the case of the cyclohexyl compound (8) as judged by the presence of more intense formyloxaziridine signals and the very small proportion of the *cis,cis* bis-oxaziridine (8e,f). In addition to equally intense aldehydic and oxaziridine CH signals (Table 1), the formyloxaziridines (10; R = Et and C_6H_{11}) exhibited an $[AB]_2$ pattern for the aromatic hydrogens, δ_A 7.56 and δ_B 7.86 in $CDCl_3$, consistent with the unsymmetrical ring substitution.

The oxidation product distribution for both bis-imines is given in Table 2. The selective decomposition of the *cis*-oxaziridine rings, particularly in the case of (8) makes it difficult to quantitatively interpret the bis-oxaziridine ratios. However, it is probable that (10a) has originated mainly from the *trans,cis* bis-oxaziridines (7c,d) and (8c,d), and (10b) mainly from the *cis,cis* compounds (7e,f) and (8e,f). On this basis the corrected bis-oxaziridine ratios prior to decomposition should be *trans,trans* : *trans,cis* : *cis,cis* = 46 : 44 : 10 for (7) and 55 : 39 : 6 for (8). However, the unsymmetrical *trans,cis* bis-oxaziridines have a statistical bias of 2 since they can be formed from both the *trans* and *cis* mono-oxaziridines (9a) and (9b). Therefore on energetic grounds the *trans*-orientation is favoured by a factor of *ca.* 2.1 in the case of (7) and *ca.* 2.8 for (8). These estimates are similar irrespective of whether they are derived from the *trans,-trans* : *trans,cis* or *trans,cis* : *cis,cis* ratios (after statistical correction). The slightly lower proportion of *cis*-orientated oxaziridine moieties in (8) as compared to (7) probably results from increased steric destabilisation of the transition state leading to *cis*-orientation in the cyclohexyl case. The observation of a high proportion of *cis*-oxaziridine residues on oxidation of *trans,trans* bis-imines further emphasises the lack of stereospecificity of the imine–peroxyacid reaction.[11]

In conclusion, it is evident from the present study that the oxidation of bis-imine (1) which was previously assumed to give a mixture of *meso* and racemic isomers was basically correct. The isomeric bis-oxaziridines obtained from the imines (1) and (2) have now been identified as having a *trans,trans* (*meso*) and *trans,trans* (racemic) configuration. The previous report of one bis-oxaziridine product being obtained from bis-imines (3) and (4) can now be clarified in terms of the initial formation of a mixture of stereoisomers due to the configurational stability at the oxaziridine nitrogen atom.

EXPERIMENTAL

^1H N.m.r. spectra were obtained at 100 MHz on a Varian XL-100 continuous wave spectrometer or at 90 MHz on a Bruker WH-90 Fourier instrument. ^{13}C Spectra were recorded at 22.6 or 15.0 MHz using Bruker WH-90 or JEOL FX-60 Fourier spectrometers respectively.

The bis-imines (1)—(4) were prepared by the literature methods [4,15] and had similar physical properties to those reported (Table 3). Bis-oxaziridines were obtained by MCPBA oxidation of the bis-imines in dichloromethane. Typically, MCPBA (1.0 g) in dichloromethane (25 cm^3) was added dropwise to the imine (3) (0.43 g, 2.3×10^{-3} mol) in dichloromethane (50 cm^3) at 0 °C. The solution was stirred for 2 h at 0 °C prior to the normal work-up procedure.[11]

The bis-oxaziridines (5a) and (5b) (*ca.* 5 g) were separated by column chromatography [10] using silica gel (1 000 g, Kieselgel G Type 80, Merck) in a column of 12 cm diameter and a 9 : 1 mixture of light petroleum (b.p. 40—60 °C): ether as eluant. The products were recrystallised from pentane. The procedure was repeated using (+)-peroxy-

TABLE 3

Physical properties of bis-imines and bis-oxaziridines

Compd.	M.p. (°C)	Lit. m.p. (°C)	Ref.[a]
(1)	51—52	52—53	15
(2)	151—152	150	4
(3)	55—56	—	4
(4)	125—129	131—132	4
(5a)	46—47	42—43	6
(5b)	83—84	82—84	6
(6a,b)	120—122	123	4
(7a,b)	87—90	93	4
(8a,b)	162—166	160—161	4

[a] See references to main text.

[14] W. B. Jennings, D. R. Boyd, C. G. Watson, E. D. Becker, R. B. Bradley, and D. M. Jerina, *J. Amer. Chem. Soc.*, 1972, **94**, 8501.

[15] P. Clopath and A. V. Zelewsky, *Helv. Chim. Acta.*, 1972, **55**, 52.

camphoric acid as chiral oxidant at −78 °C.[3] The physical properties of the recrystallised bis-oxaziridines (Table 3) correspond well with values reported in the literature.

Attempts to separate the complex mixture of bis-oxaziridines (7) or (8) and the formyloxaziridine decomposition products (10) were unsuccessful. Analytical t.l.c. on silica gel (eluting with dichloromethane) of the product mixture showed at least four spots, two of which gave a positive iodine test when sprayed with aqueous KI followed by benzoic acid in chloroform. The recrystallised product (from methanol) gave only one spot which was the bis-oxaziridine (7a,b) (R_F 0.26) or (8a,b) (R_F 0.38). It is probable that the lower R_F spots in the crude mixtures were the isomers (7c,d) (R_F 0.19) and (8c,d) (R_F 0.26) since *cis*-mono-oxaziridines have lower R_F values under these t.l.c. conditions.[2] Preparative t.l.c. and column chromatography of the mixture, followed by recrystallisation, allowed pure samples of (7a,b) and (8a,b) to be isolated but other fractions were mixtures of isomers and decomposition products.

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