Absolute Stereochemistry of the Peroxy-acid–Imine Route to Optically Active Oxaziridines

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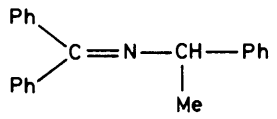
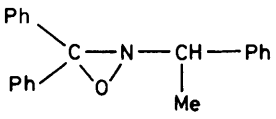
The stereochemistry of oxidation of optically active or racemic *N*-diphenylmethylene-α-methylbenzylamine with chiral or achiral peroxy-acids to oxaziridines of known absolute configuration over a range of reaction conditions has been studied. The diastereoselectivity depends only on temperature, whereas the enantioselectivity depends on the chirality of the peroxy-acid, the temperature, and the solvent. Oxidation of racemic imine with *S*-peroxy-acids yields, under kinetic control, two optically active negative diastereoisomers with a predominance of (2*S*,α*R*)- and (2*R*,α*S*)-products over (2*S*,α*S*)- and (2*R*,α*R*)-isomers. The results are discussed in conjunction with the problem of one- and two-step mechanisms and with the question of absolute configuration at chiral nitrogen in optically active oxaziridines.

MUCH work has hitherto been devoted to obtaining optically active oxaziridines, stable at the chiral nitrogen atom, by oxidation of imines with optically active or achiral peroxy-acids.[1-12] Nevertheless, the nature of the absolute stereochemistry of this asymmetric oxidation is still debatable.

The synthesis of the diastereoisomeric (−)-(2*S*)- and (+)-(2*R*)-*N*-[(*R*)-α-methylbenzyl]diphenyloxaziridines, and knowledge of their physical properties and *X*-ray crystal structures[13] has enabled us to study in detail the absolute stereochemistry of the peroxy-acid–imine route to optically active oxaziridines. In particular, we have studied the effects of changes in peroxy-acid, solvent, and temperature (reaction conditions are generally known to have a great influence on the asymmetric inductions of chiral oxaziridines)[2-5] on the oxidation of optically active and racemic *N*-diphenylmethylene-α-methylbenzylamine (1) to the corresponding diastereoisomeric oxaziridines (2a and b).



(1)



(2a and b)

RESULTS

Oxidations of (−)-(*R*)- or (+)-(*S*)-imine (1) were performed with an equimolecular amount of *m*-chloroperoxybenzoic acid (3), (+)-(1*S*)-peroxycamphoric acid (4), or (+)-(*S*)- or (−)-(*R*)-2-phenylperoxypropionic acid (5). Oxidations of racemic imine (1), on the other hand, were carried out under conditions of kinetic control, with an insufficient amount (0.5 mol. equiv.) of the chiral peroxy-acid (4) or (5). These processes constitute a more complex version of asymmetric syntheses and kinetic resolutions, for one can expect the enantiomeric species of (1) to react at different rates with chiral peroxy-acids (4) and (5), each *via* two diastereoisomeric transition states, thus giving not only different amounts of (2a) and (2b) but also optically active oxaziridines.

The results of oxidations in chloroform at various temperatures are reported in Tables 1 and 2. The effect of solvent upon oxidation of the optically active imine (1) with the achiral peroxy-acid (3) at +20 °C, and with (+)-(4) at −30° are shown in Tables 3 and 4. Table 5 gives the corresponding results of oxidation of racemic (1) at +40 °C with (+)-(4).

TABLE 1

Effect of different peroxy-acids on oxidation of optically active imine (1) at −30 °C in $CHCl_3$

		Oxaziridine (2a)			Oxaziridine (2b)
Imine	Peroxy-acid	% [a]	Abs. config.	$[\alpha]_D$ (°) [b]	% [a]
(−)-(*R*)-(1)	(3)	95	(2*S*,α*R*)	−94.0	5
	(4)	94	(2*S*,α*R*)	−95.5	6
	(−)-(*R*)-(5)	96	(2*S*,α*R*)	−93.6	4
	(+)-(*S*)-(5)	97	(2*S*,α*R*)	−94.2	3
(+)-(*S*)-(1)	(−)-(*R*)-(5)	96	(2*R*,α*S*)	+94.5	4
	(+)-(*S*)-(5)	97	(2*R*,α*S*)	+94.8	3

[a] Estimated by n.m.r. integration of the diastereotopic methyl signals in CCl_4 solution (±3%). [b] Product oxaziridines were separated and purified by column chromatography prior to optical rotation measurement in chloroform solution (*c* 2—3).

The results in Tables 1, 3, and 4 show that asymmetric induction at the tercovalent nitrogen of the optically active (1) imine does not depend on the nature or chirality of the peroxy-acid or on the solvent. At −30 °C in chloroform solution the product separated in 80—90% yield from unchanged imine (1) consists essentially of one diastereoisomer (2a), with (−)-(2*S*,α*R*) or (+)-(2*R*,α*S*) absolute chirality depending on the *R*- or *S*-configuration of the starting imine (Table 1). The configuration of (2a) remains the same whether the achiral oxidant (3) or the more complex

[1] S. J. Brois, *J. Amer. Chem. Soc.*, 1968, **90**, 506.
[2] F. Montanari, I. Moretti, and G. Torre, *Chem. Comm.*, 1968, 1694; 1969, 1086.
[3] D. R. Boyd, *Tetrahedron Letters*, 1968, 4561.
[4] D. R. Boyd and R. Graham, *J. Chem. Soc.* (*C*), 1969, 2648, 2650.
[5] F. Montanari, I. Moretti, and G. Torre, *Gazzetta*, 1973, **103**, 681.
[6] J. Bjørgo and D. R. Boyd, *J.C.S. Perkin II*, 1973, 1575.
[7] C. Bełżecki and D. Mostowicz, *J.C.S. Chem. Comm.*, 1975, 244.
[8] C. Bełżecki and D. Mostowicz, *J. Org. Chem.*, 1975, **40**, 3878.
[9] D. R. Boyd, D. C. Neil, C. G. Watson, and W. B. Jennings, *J.C.S. Perkin II*, 1975, 1813.
[10] M. Bucciarelli, I. Moretti, G. Torre, G. D. Andreetti, G. Bocelli, and P. Sgarabotto, *J.C.S. Chem. Comm.*, 1976, 60.
[11] J. Bjørgo, D. R. Boyd, R. M. Campbell, N. J. Thompson, and W. B. Jennings, *J.C.S. Perkin II*, 1976, 606.
[12] M. Bogucka-Ledóchowska, A. Konitz, A. Hempel, Z. Dauter, E. Borowski, C. Bełżecki, and D. Mostowicz, *Tetrahedron Letters*, 1976, 1025.
[13] A. Forni, G. Garuti, I. Moretti, G. Torre, G. D. Andreetti, G. Bocelli, and P. Sgarabotto, *J.C.S. Perkin II*, in the press.

optically active peroxy-acids (4) and (*R*)- or (*S*)-(5) are used as oxidants. At higher temperatures, there is a decrease in diastereoselectivity: the amount of (2b) goes from 2—3% at −30 °C to 12—13% at +20 or +40 °C. The relative amounts of (2a) and (2b) do not change significantly when the solvent is changed (Tables 3 and 4). These results are confirmed by the results of oxidations of the racemic imine (Tables 2 and 5). These data indicate that in the oxidation of the imine (1) with organic peroxy-acids the (2*R*,α*S*)- and (2*S*,α*R*)-structures are much more favoured than the (2*R*,α*R*)- and (2*S*,α*S*)-forms.

The oxidations of racemic (1) with 0.5 mol. equiv. of chiral peroxy-acid (4) or (5) gave oxaziridines with the expected predominance of one enantiomeric species. The results (Tables 2 and 5) show that the sign of the optical activity of this prevalent enantiomer is negative in both (2a) and (2b) when chloroform is used as solvent with (4) or (*S*)-(5) as oxidant. A positive rotation was found with (*R*)-(5) as oxidant. Enantioselectivity is not particularly high even in reactions carried out at −65 °C. Finally, Table 5 reveals a marked solvent effect on the enantiomeric composition of the oxaziridines (2), in contrast with the lack of solvent effect on diastereoselectivity.

From the data in Table 2 we can summarize both qualitative and quantitative aspects in the synthesis of chiral oxaziridines (2) from racemic imine (1) and (+)-(*S*)-(5) as shown in the Figure. This Figure clarifies the absolute stereochemistry of transition states in an imine–chiral peroxy-acid route to optically active oxaziridines. The results reported in Tables 1—5 are thus of great interest in connection not only with possible mechanisms of reaction but also with the problem of the absolute configuration at the chiral nitrogen atom of optically active oxaziridines.

TABLE 2

Oxidation of racemic imine (1) with 0.5 mol. equiv. of (*R*)- or (*S*)-2-phenylperoxypropionic acid in chloroform

		Oxaziridine							
		(2a)				(2b)			
Peroxy-acid	Temp. (°C)	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.	Optical yield [c]	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.	Optical yield [c]
(−)-(*R*)-(5)	−65	>99	+6.3	(2*R*,α*S*)	6.5				
(+)-(*S*)-(5)	−65	>99	−6.2	(2*S*,α*R*)	6.4				
(+)-(*S*)-(5)	+40	88	−2.7	(2*S*,α*R*)	2.8	12	−12.5	(2*S*,α*S*)	4.9

[a,b] As Table 1. [c] Based on the maximum optical value found after recrystallization of (2a) and (2b): (2a) $[\alpha]_D^{25}$ ±97.0° ($CHCl_3$), (2b) $[\alpha]_D^{25}$ ±256.0 ($CHCl_3$).[13]

TABLE 3

Dependence of oxidation of (*S*)-(1) with *m*-chloroperoxybenzoic acid on solvent at 20 °C

	Oxaziridine					
	(2a)			(2b)		
Solvent	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.
CH_2Cl_2	86	+94.6	(2*R*,α*S*)	14	−248.6	(2*S*,α*S*)
C_6H_6	87	+94.8	(2*R*,α*S*)	13	−250.3	(SS,α*S*)
Et_2O	88	+95.2	(2*R*,α*S*)	12	−249.0	(2*S*,α*S*)
MeOH	88	+96.0	(2*R*,α*S*)	12	−249.7	(2*S*,α*S*)

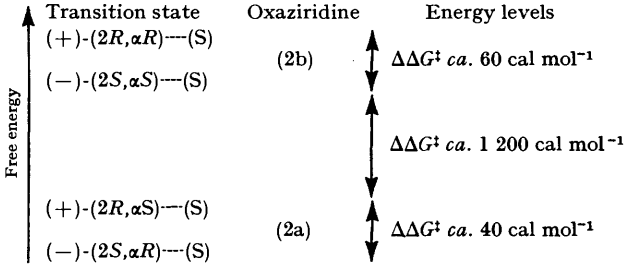
[a,b] As Table 1.

TABLE 4

Dependence of oxidation of (*R*)-(1) with (*S*)-peroxycamphoric acid on solvent at −30 °C

	Oxaziridine			
	(2a)			
	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.	(2b) % [a]
$CHCl_3$	94	−95.5	(2*S*,α*R*)	6
MeOH	93	−93.6	(2*S*,α*R*)	7

[a,b] As Table 1.



Energy relationship and absolute stereochemistry of the four diastereoisomeric transition states in the racemic imine (1)–(*S*)-peroxy-acid (5) route to optically active oxaziridines (2a and b) in chloroform at +40 °C

DISCUSSION

Interpretation of Stereochemical Results on the Basis of Kinetic Mechanisms.—The mechanism of the imine–peroxy-acid reaction is of current interest in view of

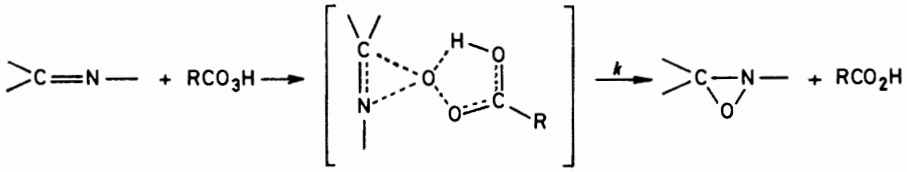
TABLE 5

Effect of solvent upon oxidation of racemic (1) with 0.5 mol. equiv. of (*S*)-peroxycamphoric acid at +40 °C

	Oxaziridine							
	(2a)				(2b)			
Solvent	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.	Optical yield [c]	% [a]	$[\alpha]_D$ (°) [b]	Abs. config.	Optical yield [c]
$CHCl_3$	88	−3.3	(2*S*,α*R*)	3.4	12	−2.7	(2*S*,α*S*)	1.0
MeOH	89	+1.3	(2*R*,α*S*)	1.3	11	+16.1	(2*R*,α*R*)	6.3

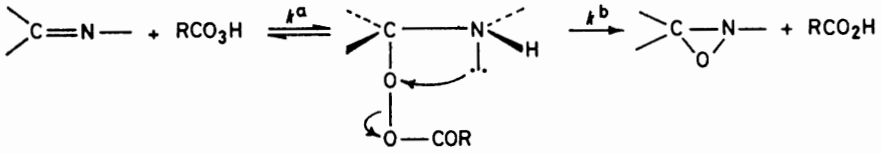
[a,b] As Table 1. [c] As Table 2.

conflicting interpretations of kinetic studies. Both one-[14] and two-step[15] mechanisms have been postulated: (*a*) the one-step mechanism (Scheme 1) involves a concerted electrophilic attack of the peroxy-acid on the electrons of the C=N bond with a symmetric cyclic transition state (6) analogous to that widely on the peroxide bond. In this mechanism the intermediacy of conformers of type (7) is assumed. These two mechanisms have been widely examined, more recently, by dynamic stereochemical studies of imines.[8,9,17] The results seem to be more consistent with the stepwise imine–peroxy-acid mechanism.



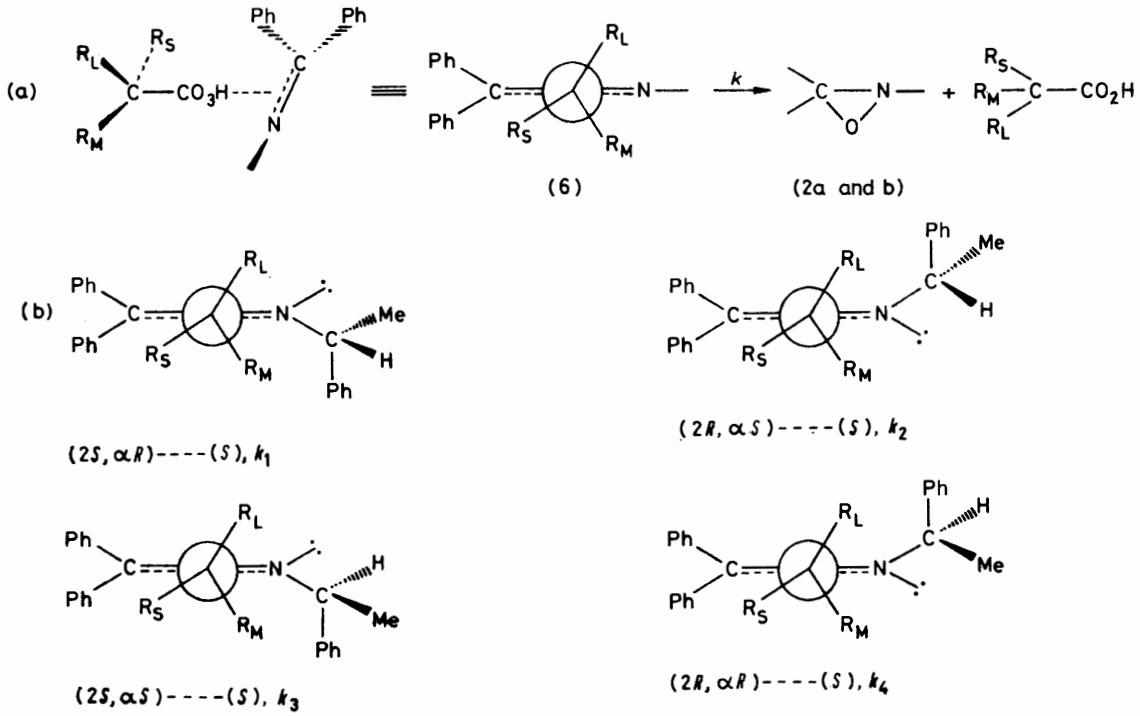
(6)

SCHEME 1 One-step mechanism



(7)

SCHEME 2 Two-step mechanism



SCHEME 3 (a) One-step mechanism of peroxy-acid (4) or (*S*)-(5)–racemic imine (1) route to oxaziridines (2a and b) in chloroform; (b) absolute stereochemistry of the diastereoisomeric transition states (6); $k_1 > k_2 \ggg k_3 > k_4$

accepted for the epoxidation of olefins;[16] (*b*) the two-step mechanism (Scheme 2) proceeds by addition of the peroxy-acid to the bonding of the imine followed by an internal nucleophilic attack of the basic nitrogen atom

We will now examine the implications of our stereochemical results with respect to both one- and two-step mechanisms.

(i) *One-step mechanism.* On the basis of the concerted

[14] V. Madan and L. B. Clapp, *J. Amer. Chem. Soc.*, 1969, **91**, 6078; 1970, **92**, 4902.

[15] Y. Ogata and Y. Sawaki, *J. Amer. Chem. Soc.*, 1973, **95**, 4687.

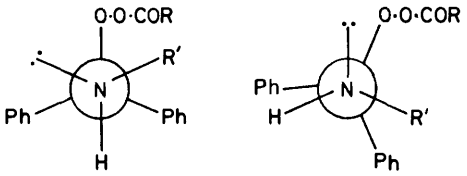
[16] For a review on stereochemistry of epoxide synthesis, see G. Berti, *Topics Stereochem.*, 1973, **7**, 93.

[17] K. Grant Taylor, Min-Shong Chi, and M. S. Clark, jun., *J. Org. Chem.*, 1976, **41**, 1131.

mechanism (Scheme 1) we can devise the cyclic transition-state models of Scheme 3 to rationalize the stereochemical results obtained in oxidation of the imine (1) in chloroform with the (*S*)-peroxy-acids (4) and (5) (Tables 2 and 5 and Figure).* In these models we denote as R_L, R_M, and R_S the groups directly linked to the asymmetric carbon atom of the peroxidant with large, medium, and small steric requirements, respectively [19] [*e.g.* for the 2-phenylperoxypropionic acid (5), R_L = Ph, R_M = Me, R_S = H]. In the transition state (6) of Scheme 3, R_S of the oxidant is considered eclipsed and R_M and R_L staggered with respect to the imine double bond. In the same model the phenyl substituent of the asymmetric carbon atom of the imine is in the plane of the double bond, whereas the other groups (H and Me) are staggered on either side of the same plane [Scheme 3(b)]. According to these models, the highly stereospecific synthesis of the diastereoisomeric form (2a) as opposed to (2b) could be explained by the favoured direction of addition of the peroxy-acids being towards the face of the carbon–nitrogen double bond which is least hindered. In the case of Scheme 3 this would result in the approach of the reagent from the side of the hydrogen, not (or much less so) from that of the methyl group, and we should therefore expect $k_1,k_2 \ggg k_3,k_4$. On the other hand, from the same models the prevalence of the enantiomer having the absolute *S*-configuration at nitrogen in both (2a) and (2b) is controlled by non-bonded steric interactions between the substituents at the chiral carbon of the peroxidant and the *N*-substituents of the imines. Obviously, these interactions can be revealed only by using racemic (1) and, in accord with the order R_M---CHPhMe < R_L---CHPhMe, they should give $k_1 > k_2$ and $k_3 > k_4$.

In our opinion the cyclic models of the transition state (6) depicted in Scheme 3 and, in consequence, the one-step mechanism, rationalize many of the stereochemical aspects of the syntheses of oxaziridines (2), especially from the qualitative point of view, but fail to account entirely for certain other experimental findings: for instance, it seems difficult to explain, on the basis of this concerted mechanism, the highly favoured formation of (2a) *vs.* (2b) and the observed lack of dependence of diastereoselectivity on the nature and the chirality of the peroxy-acid and on the solvent.†

(ii) *Two-step mechanism.* In the two-step mechanism of Scheme 2 the ground-state conformational preference for the intermediates (7) is assumed by some authors to be close to the staggered conformation of type (8), and elimination of the free acid from the intermediate (8) during the second step is considered to require a transition-state preference similar to the eclipsed conformation (9).[8,9] Therefore, rationalization of our results in terms of the two-step mechanism has to take into account the fact that stereospecific interactions between



(8) (9)

the peroxy-acid substituents and the imine groups, which contribute to the stereochemical course, may be involved both during the first-step approach of the two reagents and, intramolecularly, in intermediates and transition states of types (8) and (9), respectively. In addition, other effects (solvent, hydrogen bonding, *etc.*) can modify the relative energy levels derived from steric factors alone.

An exhaustive rationalization of the results obtained in chloroform can be given in terms of the two-step mechanism, if we make the following three assumptions. (*a*) The enantiomeric composition of (2a) and (2b) is controlled by the relative non-bonded interactions between the reagents during the first-step approach of the peroxy-acid at the imine carbon atom. According to the model (10) (Scheme 4), these interactions should follow the order R_M---CHPhMe < R_L---CHPhMe and give $k_1^a > k_2^a$ and $k_3^a > k_4^a$. (*b*) The enantiomeric composition of (2a) and (2b) is not greatly modified, qualitatively speaking, by non-bonded interactions which may control the conformational free-energy levels of intermediates of type (8). This assumption can be considered substantially correct provided that the rate of ring closure (k^b) is at least 100 times greater than those of processes which would lead to the species (8). At present there is no conclusive information available regarding the relative values of either the rate of formation of (8) (which may involve among other things rotation about the C–N bond, inversion at nitrogen, or more complex bond-making and -breaking phenomena) or the rate of ring closure which characterizes the second step.‡ (*c*) The stereospecific non-bonded interactions between the substituents of the peroxy-

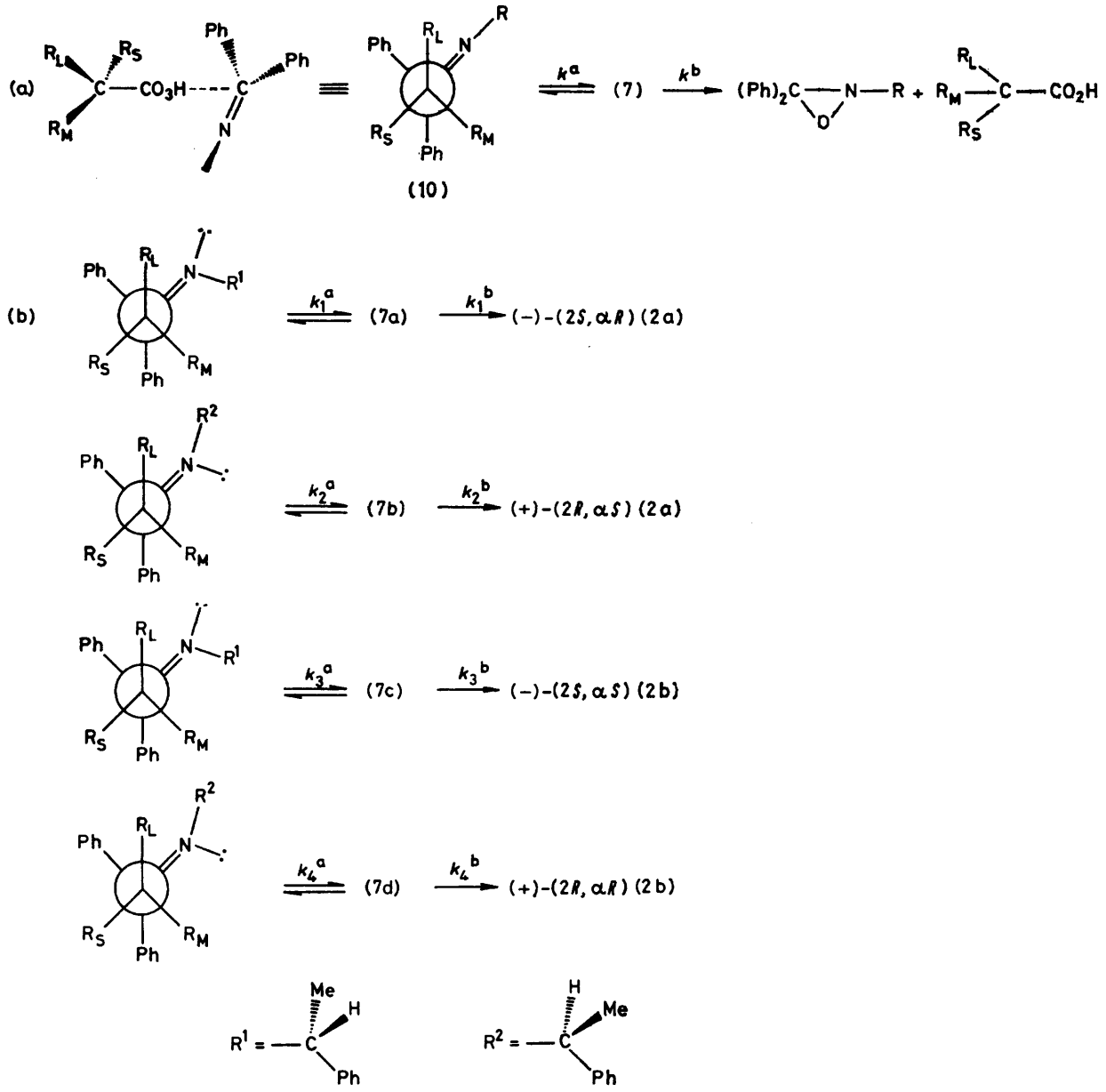
* As frequently pointed out for other asymmetric transformations,[18] there is no suggestion that the models of Schemes 3 and 4 are accurate descriptions of the real transition states in the peroxy-acid–imine route to oxaziridines; these models at best constitute approximations which, of the factors that can influence the stereoselectivity of these reactions, take specific account only of non-bonding steric interactions.

† For example the cyclic transition state (6) should possess a certain rigidity and would therefore be expected to be more sensitive to variations in peroxidant non-bonded steric effects than was the case.

‡ Kinetic studies seem to indicate that k^b of Scheme 4 should be high in reactions of oxidation of acyclic imines (k^b will vary from 10^3 to 10^{13}—10^{15} l mol^{-1} s^{-1}).[15] On the other hand, calculated and observed energy barriers to fast processes of inversion and/or rotation in simple acyclic amines,[20] more hindered trialkylamines,[21] and cyclic amines,[20] lie roughly in the range 3—15 kcal mol^{-1}, which correspond to k values of 10^{10}—10^2 s^{-1}, respectively, at room temperature.

[18] J. D. Morrison and H. S. Mosher, 'Asymmetric Organic Reactions,' Prentice–Hall, Englewood Cliffs, New Jersey, 1971.
[19] Ref. 18, p. 340.
[20] J. B. Lambert, *Topics Stereochem.*, 1971, **6**, 19.
[21] C. H. Bushweller, W. G. Anderson, P. E. Stevenson, D. L. Burkey, and J. W. O'Neil, *J. Amer. Chem. Soc.*, 1974, **96**, 3892.

acids and the imine groups are still weaker in the second-step S_Ni process of ring closure. In other words, the stereochemical results of the present work may not necessarily imply a stereospecific intramolecular elimination of the acid by a concerted process of bond making and this is in good agreement with the calculated difference in activation energies for the formation of the two oxaziridine diastereoisomers given in the Figure. Therefore, it seems reasonable that the high diastereoselectivity observed in our experiments could depend,

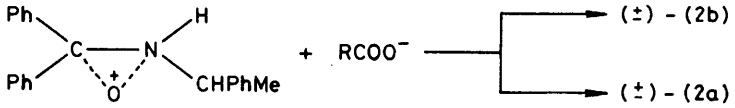


SCHEME 4 (a) Two-step mechanism of peroxy-acid (4) or (*S*)-(5)–racemic imine (1) route to oxaziridines (2a and b) in chloroform; (b) absolute stereochemistry of the diastereoisomeric transition states (10); $k_1^a > k_2^a, k_3^a > k_4^a$; $k_1^b, k_2^b \ggg k_3^b, k_4^b$

and breaking as depicted in structure (7) of Scheme 2. This assumption, which accounts not only for the enantiomeric composition of (2a) and (2b), obtained in the reaction of racemic (1) with the chiral reagents (4) and (5), but also, and in particular, for the lack of peroxy-acid effect on the diastereoselectivity, is based on the finding [13] that oxaziridines of structure (2b) are less stable than the isomers (2a) by *ca.* 1.3 kcal mol^{-1}, from a quantitative point of view also, upon the difference in free-energy levels of two transition-state conformations which, during the ring-closure step, assume a structure of type (11) which is very similar to that of the final products (2a and b), without any interference by the acid substituents. In this case, and according to the Curtin–Hammett principle, we must expect the two transition states to reflect the differences between

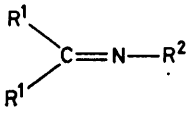
the ground-state stabilities of the diastereoisomers (2a and b), insomuch as whatever unfavourable interactions exist in (2b) should exist to a similar extent in the transition state leading to it.

Finally, the two-step mechanism can also explain the observed solvent effect, for the absence of this effect on the predominance of one diastereoisomeric form over the other (Tables 3 and 4), and the inversion in the enantiomeric composition of (2a) and (2b) obtained in methanol as opposed to chloroform (Table 5), can be understood if we assume that the solvent effect is exerted primarily at the first step of asymmetric transformation. Therefore, on the one hand, the variation in magnitude and sign of the optical rotations of the oxaziridines (2) under the conditions reported in Table 5 may be interpreted as a measure of the variation in ' effective bulk ' of both reagents by solvation of their ground-states, as suggested also by kinetic results,[15] while, on the other hand, the constancy of the diastereoisomeric ratio might indicate that solvation is not effective at a second-step level or, if it is, is masked by the pronounced difference in free-energy levels of the epimeric transition states (11) that lead to oxaziridines (2).



(11)

Absolute Configuration at the Chiral Nitrogen Atom in Optically Active Oxaziridines.—Before considering the possibility of extending the present absolute configuration correlations to other chiral oxaziridines it is timely to re-examine the stereochemical aspects of asymmetric oxidations of imines, for they are largely dependent not only on the reaction conditions but, more particularly, on the nature and configuration of the imines. It therefore seems appropriate to analyse separately the results obtained from the asymmetric oxidations (*a*) of imines derived from symmetrical ketones (12) and (*b*) of imines derived from aldehydes or unsymmetrical ketones (13).



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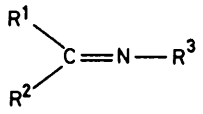
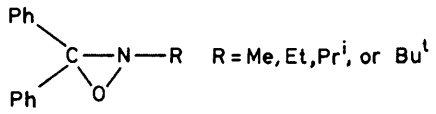


(13)



(14)

Asymmetric oxidations of imines (12) are characterized either by a relatively low enantioselectivity or by a very high diastereoselectivity, depending on whether the imines carry an alkyl substituent [5] or a chiral group [7,10] on nitrogen. These results are in good agreement with the data obtained in the present work. Another important point of correlation is related to the qualitative aspects of these oxaziridine syntheses. Previous oxidations of imines (12; R^1 = Ph and R^2 = Me, Et, Pr^i, or Bu^t) with optically active peroxy-acids gave results very similar to those reported in Tables 2 and 5, showing a marked solvent effect on the enantiomeric composition and giving oxaziridines (14) which show negative or positive plain o.r.d. curves in the wavelength region 589—350 nm, according to whether peroxy-acids with absolute *S*- or *R*-configuration, respectively, are used.[5] The correlation between the chiroptical properties of the oxaziridines (2) and (14) (even if at present restricted to a rather low spectral range) is important, providing that the contribution to the optical activity of the diphenyl three-membered ring chromophore is dominant with respect to that of the chiral carbon centre in structures (2). The opposite rotatory power of the epimers (2*S*,α*R*) *vs.* (2*R*,α*R*) or (2*R*,α*S*) *vs.* (2*S*,α*S*) seems to indicate that this is the case, and it is therefore reasonable to assume that the chiroptical properties of the oxaziridines (2) and (14) should depend upon the chirality at nitrogen. In conclusion, both quantitative and qualitative aspects of the syntheses of optically active oxaziridines (2) and (14) agree with regard to the extension to the asymmetric syntheses of (14) of the stereochemical models (10) of Scheme 4 (where R^1 = R^2 = Me, Et, Pr^i, or Bu^t) and to the nitrogen atom of (14) of the (−)-(S), (+)-(*R*) absolute configuration found for the oxaziridines (2a) and (2b) in the present work.

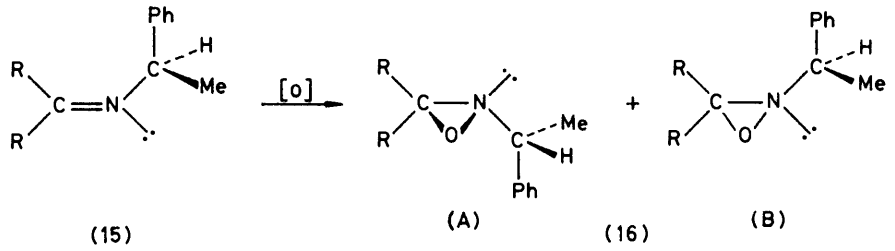
Other available findings for oxaziridines similar to the diastereoisomers (2a and b) are reported in Table 6. They were obtained by oxidation with *m*-chloroperoxybenzoic acid of aliphatic imines of type (12) formed from (+)-(*R*)-methylbenzylamine.[7] By contrast with the rotatory behaviour of our diphenyl compounds [Table 6, compound (16d)], the epimeric forms (A) and (B) of the aliphatic (R = Me) or cycloaliphatic (R_2 = $[CH_2]_4$ or $[CH_2]_5$) chiral oxaziridines reported in Table 6 show optical rotation values which are both positive at 436 nm. The rotatory powers of the diastereoisomers (A) derived from imines (15a—c) are in any case lower than the corresponding values of (B). Unfortunately, no rotations at other wavelengths are reported for these compounds, so at present it is impossible to find out if the lower optical activity of (A) with respect to (B)

corresponds to a general negative trend of the o.r.d. curves of (A), at least in the 589—350 nm region, as found for the negative enantiomeric forms of (2a and b). Nevertheless, even without this correlation, the agreement of the quantitative aspects of reactions of Table 6 is, in our opinion, enough to indicate that the absolute configuration of the prevalent diastereoisomeric form of (2) [(2*S*,α*R*) or (2*R*,α*S*)] can also be extended to the epimer (A) derived from oxidations of imines of type (15).

Correlation between the present results and those obtained in asymmetric oxidations of imines derived from aldehydes or unsymmetrical ketones (13) is more problematical. It is interesting that most of the stereochemical aspects found in the syntheses of the oxaziridines (2) and (14) are also observed in the reactions of imines (13) with chiral peroxy-acids, namely, marked solvent and temperature effect on enantioselectivity and negative plain o.r.d. curves for oxaziridines obtained by oxidation with (+)-(1*S*)-peroxycamphoric acid.[3-4,11] Despite these similarities, extension of the stereochemical models (10) of Scheme 4 to the oxidation route of systems (13) must be carried out with great caution, for the molecular environment of imines (13) deviates from that of compounds (1) and (12), for which the model (10) was proposed. This deviation can be appreciable in some cases and thus its effect on the stereoselectivity of the asymmetric syntheses and on the chiroptical properties due to the chiral nitrogen centre of the three-membered ring may differ from that observed by us for the compounds in question. Any clarification of these matters will require a much more complete knowledge than we possess at present.

TABLE 6

Oxidations of imines of type (12) with *m*-chloroperoxybenzoic acid



Imine		% Oxaziridine (16) diastereoisomers (A)	(B)	$[\alpha]_{436}$ (°) ($CHCl_3$) (A)	(B)	Abs. config. (A)	(B)
(15a) R = Me [a]	(16a)	82	18	+98.5	+271.9		
(15b) $R_2 = [CH_2]_4$ [a]	(16b)	87	13	+66.0	+295.4		
(15c) $R_2 = [CH_2]_5$ [a]	(16c)	97	3	+118.5	+205.4		
(15d) R = Ph [b]	(16d)	86	14	−198.7	+547.0	(2*S*,α*R*)	(2*R*,α*R*)

[a] Data from ref. 7; reactions conducted in CH_2Cl_2 at 0—5 °C. [b] Data from present work; reaction conducted in CH_2Cl_2 at +20 °C.

EXPERIMENTAL

Optical rotations were measured with a Perkin-Elmer 141 automatic photoelectric polarimeter with 1 or 10 cm path length cells. I.r. spectra were determined for solutions in CCl_4 with a Perkin-Elmer 257 instrument, and ^1H n.m.r. spectra for solutions in CCl_4 (Me_4Si as internal standard) with a JEOL C-60-HL spectrometer. Microanalyses were performed with a Perkin-Elmer 240 elemental analyser.

Imine Syntheses.—Racemic and optically active *N*-diphenylmethylene-α-methylbenzylamines were obtained in 45—60% yield by titanium tetrachloride-catalysed condensation [22] of benzophenone with free racemic or (−)-(*S*)- or (+)-(*R*)-α-methylbenzylamine in benzene solution at room temperature. The imines were purified by column chromatography on silica with ether–light petroleum (50 : 50) as eluant, followed by crystallization from pentane. The racemic and optically active imines show identical i.r. and ^1H n.m.r. spectra: $\nu_{max.}$ 1 620 cm^{-1} (C=N); τ (CCl_4) 2.7 (15 H, m), 5.5 (1 H, q), and 8.5 (3 H, d). (±)-N-(*diphenylmethylene*)-α-*methylbenzylamine* had m.p. 49—50 °C; (+)-(S)- or (−)-(R)-N-(*diphenylmethylene*)-α-*methylbenzylamine* had m.p. 63—64 °C; $[\alpha]_D^{25}$ ±15.5°, $[\alpha]_{436}^{25}$ ±67.2° (*c* 2.2 in $CHCl_3$) [Found for (−)-(*R*): C, 83.35; H, 6.85; N, 5.15. $C_{21}H_{19}N$ requires C, 83.4; H, 6.7; N, 4.9%].

Oxaziridine Syntheses.—Ten or five mmol of peroxy-acid was used to oxidize 10 mmol of the optically active or racemic imine (1), respectively. A titrated solution of the peroxy-acid in chloroform was dropped into a stirred solution of the imine at a specific temperature and the mixture was kept for 9 h at this temperature. The chloroform solution was then repeatedly extracted with saturated aqueous sodium hydrogen carbonate, washed with water, dried (Na_2SO_4), and evaporated.

When methanol was used as solvent it was evaporated off under vacuum at the end of the reaction; the residue was dissolved in chloroform and the solution was treated as above.

In every case oxaziridines were separated from unchanged imines in 80—90% yield. The relative amounts of the diastereoisomeric oxaziridines were determined by ^1H n.m.r. spectroscopy of the crude products, by integration of the diastereotopic methyl signals.

The crude products of reactions carried out at −30 °C with optically active imine (1) were purified by column chromatography on silica [CH_2Cl_2–hexane (70 : 30) as

[22] I. Moretti and G. Torre, *Synthesis*, 1970, 141.

eluant] to give as pure product only (−)-(2*S*)-*N*-[(*R*)- or (+)-(2*R*)-*N*-[(*S*)-α-methylbenzyl]diphenyloxaziridine. After recrystallization from pentane the enantiomeric forms of (2a) showed m.p. 78—79 °C; $[\alpha]_D^{25}$ ±97.0, $[\alpha]_{436}^{25}$ ±198.7° (*c* 2.0 in $CHCl_3$); τ (CCl_4) 2.80 (15 H, m), 6.91 (1 H, q), and 8.48 (3 H, d).[13] Pure (−)-(2*S*)-[*N*-(*S*)- or (+)-(2*R*)-*N*-[(*R*)-α-methylbenzyl]diphenyloxaziridine was obtained from the reactions carried out at +20 °C with optically active imine (1) and *m*-chloroperoxybenzoic acid as described elsewhere.[13] The products show m.p. 60—61 °C; $[\alpha]_D^{25}$ ±256.0°, $[\alpha]_{436}^{25}$ ±547.0° (*c* 2.0 in $CHCl_3$); τ (CCl_4) 2.65 (15 H, m), 6.88 (1 H, q), and 8.81 (3 H, d).[13]

The crude products of the reactions carried out with racemic imine (1) contained *ca.* 42% of oxaziridines (2). The optically active diastereoisomeric forms (2a and b) were separated and purified by column chromatography on silica [CH_2Cl_2–hexane (70 : 30)] prior to optical rotation measurement in chloroform solution (*c* 2—3).

Unchanged imine was recovered by column chromatography from the reactions carried out under conditions of kinetic control at −65 °C and analysed. polarimetrically. It showed the expected (−)-(*R*) {$[\alpha]_{436}$ −3.1 (*c* 2.5 in $CHCl_3$)} or (+)-(*S*) {$[\alpha]_{436}$ +3.6 (*c* 3.1 in $CHCl_3$)} optical activity when (+)-(2*R*,α*S*)-(2a) or (−)-(2*S*,α*R*)-(2a), respectively, was obtained.

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