Addition of *N*-Nitrenes to αβ-Unsaturated Esters: Investigation of Kinetically formed Invertomer Ratios

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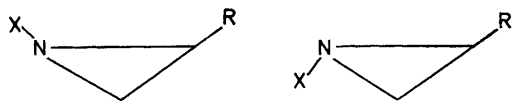
Summary *N*-Aminophthalimide is oxidised in methylene dichloride solution at −35 °C with lead tetra-acetate in the presence of methyl acrylate to yield methyl 1-phthalimidoaziridine-2-carboxylate in which the initially formed invertomer at nitrogen is that which is thermodynamically less stable, with the ester and phthalimido-groups *syn*.

STEREOSELECTIVITY in the cyclopropanation of unsymmetrical olefins by carbenes RR'C: is the result of different orientations of the carbene in the addition.[1] The ratio of isomers (*syn*:*anti*) obtained often bears little relation to values expected from their ground-state strain, revealing that other criteria determine the ordering of the two transition stages involved.[2]

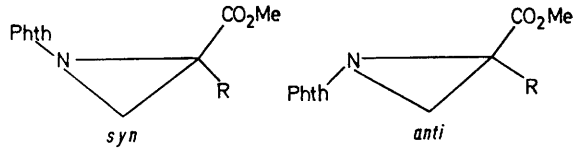
Addition of any singlet nitrene $X\ddot{N}$: to an unsymmetrical olefin could similarly result in *syn*- and *anti*-isomers [(A) and (B)]. However, the kinetically produced ratio $(A:B)_{kin.}$ may be masked by a subsequent equilibration of these two diastereoisomers by rapid inversion at nitrogen. The situation could be turned to advantage if the *N*-substituent X were chosen so as to raise the inversion barrier sufficiently for $(A:B)_{kin.}$ to be measured but also to permit thermodynamic equilibration at a slightly higher temperature.[3]



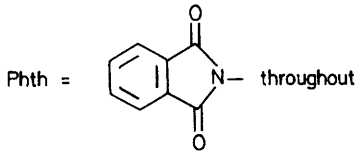
Oxidation of various *N*-amino-heterocycles in the presence of olefins gives aziridines.[4a,b] *N*-Aminophthalimide was oxidised with $Pb(OAc)_4$ in the presence of methyl methacrylate (1 mol. equiv.) using CH_2Cl_2 as solvent at −35 °C. Part of the n.m.r. spectrum of the filtered (−40 °C) CH_2Cl_2 solution at −32 °C is shown in Figure 1(a). On warming to room temperature the spectrum changes irreversibly to Figure (b) which contains all the peaks observed in the room temperature spectrum of the aziridine (**1**). This aziridine is known to exist as a 1·8:1 mixture of *syn*- and *anti*-invertomers [4b] with the peak assignments as indicated in Figure (b).

Allowing for impurities, Figure (a) corresponds to the spectrum expected for the pure *syn*-isomer of (**1**); the

absence of the aziridine ring proton singlet and highest field methyl group of Figure (b) indicates that none of the *anti*-invertomer of (**1**) is present in the kinetically formed reaction product.



(1) R = Me
(2) R = H



More impressive is the result of a similar oxidation of *N*-aminophthalimide in the presence of methyl acrylate, all operations being carried out at *ca.* −40 °C. The n.m.r. spectrum of the total filtered† solution at −42 °C was consistent with the presence of only the *syn*-invertomer of the aziridine (**2**); the thermodynamically more stable *anti*-isomer is adjudged to be totally absent since none of its characteristic ester methyl peak is visible. An irreversible change in the spectrum occurs as the temperature is raised and the growth of the ester peak of the *anti*-invertomer can be clearly observed (separation between ester peaks 0·15 p.p.m.). By room temperature the spectrum is identical with that from a sample of the aziridine (**2**) prepared by the literature method[4b] and known to contain a 1:5 ratio of *syn*- and *anti*-invertomers. Crystallisation of the cold filtered solution above by addition of light petroleum and cooling to − 78 °C gave the pure *syn*-invertomer of (**2**) whose aziridine ring proton signals were superimposable upon those from the total cold solution spectrum, with δ 2·96 (dd, 1H, *J* 6 and 1·5 Hz, H *trans* to ester and phthalimide), 3·21 (dd, 1H, *J* 5·5 and 1·5 Hz, H *cis* to ester and phthalimide), 3·35 [dd (overlapping), 1H, *J* 5·5 and 6 Hz, H *gem* to ester]. Thus the exclusive product of the putative nitrene intermediate to methyl acrylate is the less stable *syn*-invertomer.

These results support the suggestion made recently[5] that in formation of the aziridines (**1**) and (**2**) there is a face-to-face orientation of phthalimido-nitrene and α,β-unsaturated ester with a favourable secondary interaction between the phthalimido-carbonyl carbon and ester carbonyl oxygen. We have also noted some curious ground-state effects in aziridine esters *N*-substituted with heterocyclic groups which have been explained by an attractive interaction between the same groups.[6]

Preliminary investigations show that the ester-*syn*-selectivity above is also exhibited by other *N*-nitrenes. Additionally, reaction of styrene with phthalimidonitrene produces 2-phenyl-*N*-phthalimidoaziridine with phenyl *syn* to the heterocycle, as the kinetically formed product. Large

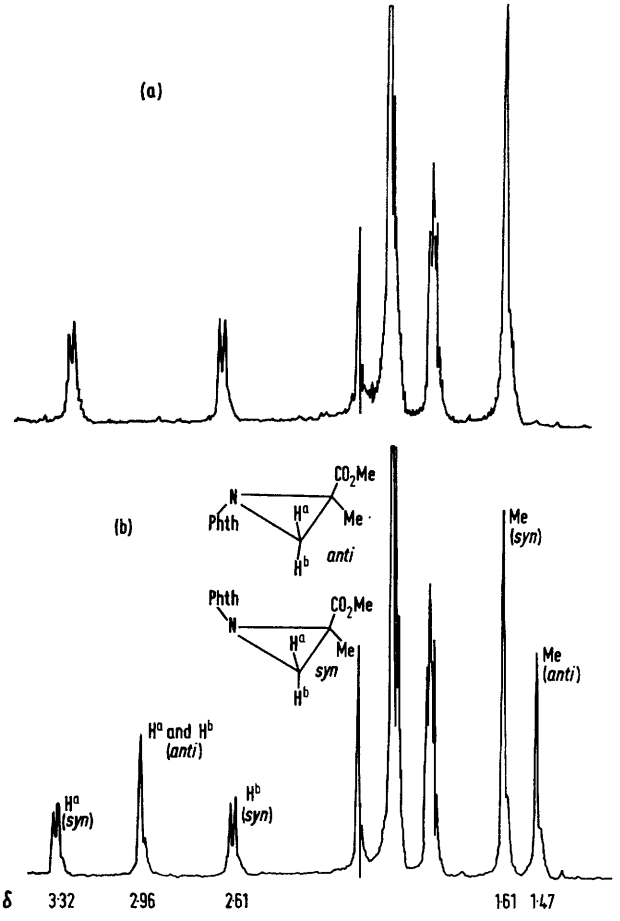


FIGURE. Part of the n.m.r. spectrum (100 MHz) at −32 °C of the solution [after filtering off $Pb(OAc)_2$] obtained from oxidation at −35 °C of *N*-aminophthalimide with $Pb(OAc)_4$ in the presence of methyl methacrylate using CH_2Cl_2 as solvent. (b) The same solution after warming to room temperature. This spectrum is unchanged on re-cooling to −32 °C except for some small shifts in peak positions.

syn-selectivities in cyclopropanation are more characteristic of carbenoids rather than free carbenes but a free *N*-nitrene in the present case could be a highly discriminating species.

Many of the *N*-heterocyclic aziridines previously prepared (ref. 4a,b), we now suspect to crystallise exclusively as one invertomer. This has been proved in a number of cases; thus crystallisation of (**2**) from chloroform–light petroleum at room temperature and n.m.r. measurements at −30 °C

† We can discount any adventitious separation of *syn*- and *anti*-isomers as a result of this filtration in which $Pb(OAc)_2$ is removed.

(dissolving at *ca.* −30 °C) shows that only the *anti*-isomer is present. This does not invalidate previous measurements of invertomer ratios[6] since the thermodynamic equilibrium is rapidly re-established at room temperature. In the crystalline state, the *syn*-isomer of (**2**) is converted slowly and incompletely into the *anti*-isomer at room temperature over a period of weeks.

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[1] W. Kirmse, 'Carbene Chemistry,' 2nd edn., Academic Press, New York, **1971**, p. 288; R. A. Moss in 'Selective Organic Transformations,' ed., B. S. Thyagarajan, vol. **1**, Wiley, New York, 1970, p. **35**.

[2] R. Hoffmann, C. C. Levin, and R. A. Moss, *J. Amer. Chem. Soc.*, **1973**, **95**, 629.

[3] Thermal equilibration of cyclopropanes is possible only in simple cases and usually requires high (>300 °C) temperatures; N. E. Howe, E. W. Yankee, and D. J. Cram, *J. Amer. Chem. Soc.*, **1973**, **95**, **4230**; A. B. Chmurny and D. J. Cram, *ibid.*, p. **4237** and references therein.

[4] (a) R. S. Atkinson and C. W. Rees, *J. Chem. Soc.* (*C*), **1969**, **772**; (b) D. J. Anderson, T. L. Gilchrist, D. C. Horwell, and C. W. Rees, *ibid.*, **1970**, **576**.

[5] H. Person, F. Tonnard, A. Foucard, and C. Fayat, *Tetrahedron Letters*, **1973**, **2495**.

[6] D. J. Anderson, D. C. Horwell, and R. S. Atkinson, *J. Chem. Soc.* (*C*), **1971**, **624**.