Stereoselectivity in Addition of *N*-Nitrenes to Olefins

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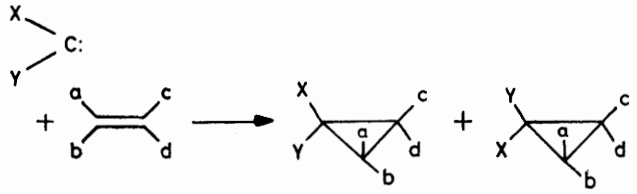
Additions of phthalimidonitrene and 2,3-dihydro-2-oxobenzoxazol-3-ylnitrene to αβ-unsaturated esters, styrenes, and dienes have been examined by n.m.r. at temperatures (< − 20 °C) low enough for kinetically-formed invertomer ratios at nitrogen in the aziridine products to be observed. In many cases, addition is (*a*) stereospecific: only that invertomer having the olefin substituent (CO_2Me, Ph, or $CR{:}CH_2$) *cis* to the heterocycle (phthalimide, benzoxazolone) being observable and (*b*) contrathermodynamic, as can be shown by n.m.r. at temperatures >10 °C when thermodynamic equilibration by inversion at the aziridine ring nitrogen is complete. Some evidence is presented which suggests that the nitrenes add to the s-*cis*- conformations of the dienes, and a possible explanation for the high stereoselectivity is offered.

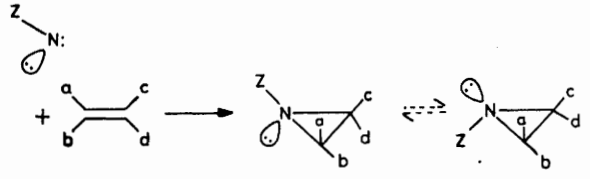
THE addition of a carbene to an olefin results in the creation of up to three chiral centres in the resulting cyclopropane depending upon the substitution pattern of the olefin and the carbene. If addition takes place *via* the carbene singlet state, the configuration of the olefin is retained in the cyclopropane and the ratio of the two stereoisomeric cyclopropanes obtained (Scheme 1) is determined by the relative affinity of X and Y for the two pairs of olefin substituents in the two transition states involved.[1]



SCHEME 1

This ratio is commonly referred to as the 'stereoselectivity' of the carbene :CXY.[2] The stereoselectivities exhibited by some free carbenes are not only surprisingly high † but frequently contrathermodynamic—the larger carbene substituent X or Y being located on the more sterically congested side in the major cyclopropane product.

In a similar fashion, addition of a singlet nitrene to an olefin could produce two stereoisomeric aziridines



SCHEME 2

(Scheme 2) which would be interconvertible by inversion at the aziridine ring nitrogen. There is a dearth of experimental results on stereoselectivity in such cases since (a) few nitrenes can be trapped intermolecularly by olefins [3] and (b) those which can be so trapped (:NCO_2R, :NCN, *etc.*) invariably have very low energy barriers for inversion at the aziridine ring nitrogen, making observation of the kinetically-formed stereoisomeric ratio of aziridines difficult in practice.

Exceptional, however, is an increasing number of *N*-nitrenes [4] whose ground state appears to be the singlet state and which can be trapped intermolecularly by a variety of olefins, often in high yields. Moreover, inversion is seen to be slow on the n.m.r. time-scale at room temperature in the spectra of many of the resulting aziridines. The second nitrogen in these *N*-nitrenes is invariably part of a heterocyclic system.

In this paper [5] we examine the mode of addition of nitrenes derived from *N*-aminophthalimide and *N*-aminobenzoxazolone, two representatives of this class, to a number of olefins at temperatures low enough to ensure that no thermodynamic equilibration between the initially formed aziridine invertomers (Scheme 2) obtains. Nevertheless, ready thermal equilibration, by increasingly rapid nitrogen inversion, is found to occur at temperatures below ambient in the aziridines we have examined. Thus, in a single experiment, it is possible to determine both kinetic and thermodynamic ratios. This is a situation which is advantageous by comparison with studies of stereoselectivity in carbene addition to olefins where thermodynamic equilibration in the resulting cyclopropanes is usually difficult leading to uncertainty as to whether the addition is contrathermodynamic or not.

Addition of Phthalimidonitrene (Phthal-$\dot{N}{:}$, A-$\dot{N}{:}$) *and* 2,3-*Dihydro*-2-*oxobenzoxazol*-3-*ylnitrene* (Benzox-$\dot{N}{:}$, B-$\dot{N}{:}$) *to Methyl Acrylate and Methyl Methacrylate* (*Scheme* 3).—The nitrenes were generated and added to methyl acrylate essentially as described in the literature [6] by oxidation of the appropriate *N*-amino-heterocycle with lead tetra-acetate, but a molar equivalent of the

† Stereoselectivities in carbenoid reactions are usually even higher.

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

[2] 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.

[3] 'Nitrenes,' ed. W. Lwowski, Interscience, New York, 1970.

[4] R. S. Atkinson and S. B. Awad, *J.C.S. Perkin I*, 1977, 346, refs. 1—8.

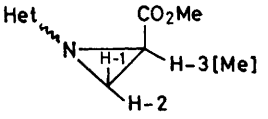
[5] Preliminary reports (*a*) R. S. Atkinson and R. Martin, *J.C.S. Chem. Comm.*, 1974, 386; (*b*) R. S. Atkinson and J. R. Malpass, *ibid.*, 1975, 555.

[6] D. J. Anderson, T. L. Gilchrist, D. C. Horwell, and C. W. Rees, *J. Chem. Soc.* (*C*), 1970, 576.

ester was used instead of the usual excess and the temperature of the methylene chloride solution was maintained between −25 and −30 °C by external cooling. It was subsequently found more convenient to use deuteriochloroform as the solvent. To facilitate examination by n.m.r., the solutions were filtered below −30 °C to remove lead diacetate before being transferred to the probe of the spectrometer without any intermediate warming of the solution. Since most of the aziridines in this work have been prepared previously [6] and are highly soluble in chloroform or dichloromethane at −20 °C, it seems unlikely that adventitious separation of invertomers takes place in this filtration. The ratio of aziridine invertomers kinetically produced was directly measurable under these conditions by n.m.r. integration. The n.m.r. probe was then warmed, typically to above 0 °C; establishment of the thermodynamic ratios then occurred at observable rates. Invariably this latter ratio was unchanged (within experimental error) when the temperature was returned to −30 °C although shifts in peak positions were sometimes apparent. Table 1 shows selected n.m.r. data for aziridines (1A)—(4A) (Het = phthalimide) and (1B)—(4B) (Het = benzoxazolone), and both kinetic and thermodynamic invertomer ratios for addition of Phthal-Ṅ: and Benzox-Ṅ: to methyl acrylate and methyl methacrylate are summarised in Table 2.

TABLE 1

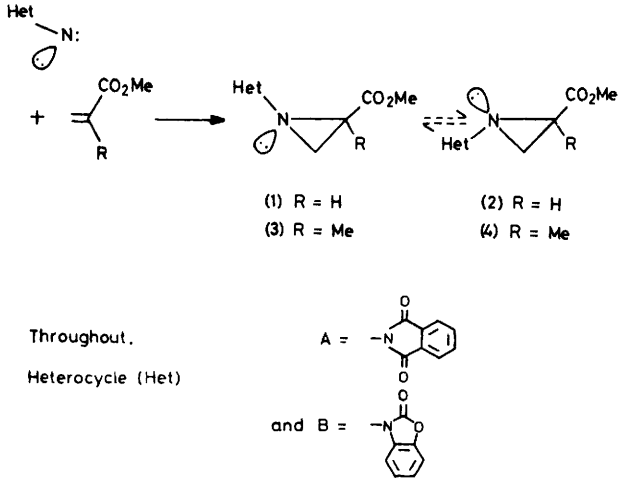
Selected n.m.r. data for methoxy carbonyl aziridines (1)—(4)



Olefin	Aziridine	Solvent	Temp. (°C)	δ Values H-1	H-2	H-3[Me]	CO_2Me	J/Hz
$CH_2{:}CH{\cdot}CO_2Me$	(1A)	CH_2Cl_2 [a,g]	−42	3.22 (dd)	2.96 (dd)	3.35 (dd)	3.64 (s) [f]	$J_{1,2}$ 1.5; $J_{1,3}$ 5.5; $J_{2,3}$ 6.0
	(2A) *	$CDCl_3$ [a]	+25	2.92 (m)	2.92 (m)	3.28 (dd)	3.86 (s)	$J_{1,3}$ 5.7; $J_{2,3}$ 7.4
	(1B)	$CDCl_3$ [b]	−34	3.6 (dd)	2.96 (dd)	3.36 (t)	3.63 (s)	$J_{1,2}$ 1.8; $J_{1,3}$ 6.0; $J_{2,3}$ 6.0
	(2B) *	$CDCl_3$ [b]	−34	2.88 (dd)	3.32 (dd)	2.63 (dd)	3.87 (s)	$J_{1,2}$ 1.3; $J_{1,3}$ 5.0; $J_{2,3}$ 8.0
$CH_2{:}CMe{\cdot}CO_2Me$	(3A)	$CDCl_3$ [a]	−31	3.40 (d)	2.80 (d)	[1.72 (s)]	3.72 (s)	$J_{1,2}$ 1.8
	(4A) *	$CDCl_3$ [a]	−31	3.09 (s)	3.09 (s)	[1.59 (s)]	3.88 (s)	
	(3B)	$CDCl_3$ [b]	−30	3.84br	2.77br	[1.72 (s)]	3.53 (s)	$J_{1,2}$ 2.4 [e]
			+25	3.88 [d]	2.69 (d)	[1.70 (s)]	3.49 (s)	
	(4B) *	$CDCl_3$ [b]	−30	3.14br	3.65br	[1.54 (s)]	3.87 (s)	$J_{1,2}$ 2.7 [e,f]
			+25	3.07br (d)	3.74 (d)	[1.52 (s)]	3.84 (s)	

* Previously prepared (see ref. 6).

[a] Measurements on solutions of purified aziridine(s). [b] Measurements on crude reaction mixture which still contained starting material, acetic acid, *etc.* [c] Spin-decoupling studies confirmed the assignments. [d] Signals which were hidden under other, more intense, signals were positioned with the aid of spin-decoupling experiments. [e] The broad doublet at δ 3.07 sharpened on irradiation at δ 1.52 (Me). [f] Measured at ambient temp. in $CDCl_3$. [g] Data from ref. 5*a*.



SCHEME 3

TABLE 2

Kinetic and thermodynamic ratios for methoxycarbonylaziridines (1)—(4)

Olefin	Nitrene	Aziridine	Kinetic ratio [a] (low temp.)	Thermodynamic ratio [a] (ambient temp.)
$CH_2{:}CH{\cdot}CO_2Me$	Phthal–Ṅ:	(1A)	100	17
		(2A)	0	83
	Benzox–Ṅ:	(1B)	>97	7
		(2B)	<3	93
$CH_2{:}CMe{\cdot}CO_2Me$	Phthal–Ṅ:	(3A)	100	64
		(4A)	0	36
	Benzox–Ṅ:	(3B)	86	35
		(4B)	14	65

[a] Measured by direct n.m.r. integration and/or the cut-and-weigh technique.

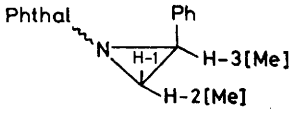
Assignment of structures from n.m.r. data in this work is based on the following established [7] observations. The heterocycles have a shielding effect on *cis*-aziridine ring methyl and *cis*-ester methyl resonances; aziridine ring protons tend to be deshielded when *cis* to the heterocyclic ring and particularly so when a methoxycarbonyl

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

or phenyl group on the adjacent carbon is also *cis*. Most of the n.m.r. spectra were pseudo-first-order and it can be seen that the aziridine ring proton signals appear between δ *ca.* 2.6 and 4.3, conveniently clear of signals due to acetic acid, starting materials, and solvent. Assignments generally follow from relative chemical deuteriochloroform at −30 °C, the n.m.r. spectrum of the solution, run at −30 °C, showed the presence of (2A) only. The 17% of *cis*-invertomer (1A) present at equilibrium makes its appearance only on raising the temperature. Evidently crystallisation of this aziridine, prepared at room temperature, results in complete

TABLE 3

Selected n.m.r. data for phenylaziridines (5A)—(10A)



Olefin	Aziridine	Solvent [a]	Temp. (°C)	δ Values H-1	H-2[Me]	H-3[Me]	J/Hz
CH_2:CHPh	(5A)	CH_2Cl_2	−30	3.74 (m)	2.97 (dd)	3.74 (m)	$J_{1,2}$ *ca.* 2.5; $J_{2,3}$ *ca.* 5.8 [c]
	(6A) *	CH_2Cl_2	−30	2.72 (dd)	2.86 (dd)	3.52 (dd)	$J_{1,2}$ 2.5; $J_{1,3}$ 5.9; $J_{2,3}$ 8.0
CH_2:CHMePh	(7A)	$CDCl_3$ [b]	+25	4.27 (d)	2.68 (d)	[1.83 (s)]	$J_{1,2}$ 3.5
	(8A)	$CDCl_3$ [b]	+25	2.86br (d)	3.13 (d)	[1.63 (s)]	$J_{1,3}$ 2.5 [d]
			−30	2.95br (d)	3.10 (d)	[1.66 (s)]	
MeCH:CHPh	(9A)	$CDCl_3$	−30	4.00 (quint)	[1.61 (d)]	3.61 (d)	$J_{1,3}$ 6.1; $J_{1,Me}$ 6.0
			+25	4.01 (quint)	[1.58 (d)]	3.55 (d)	
	(10A)	$CDCl_3$	−30	3.03 (quint)	[1.46 (d)]	3.69 (d)	$J_{1,3}$ 6.0; $J_{1,Me}$ 6.0
			+25	2.95 (quint)	[1.45 (d)]	3.75 (d)	

* Previously prepared (see ref. 6).

[a] Measurements on the crude reaction mixture obtained as described in the Experimental section [except in the case of (7A) and (8A); see footnote *b*]. [b] The isomer (8A) crystallised preferentially from solution. N.m.r. measurements quoted here were made on essentially pure material dissolved at −30 °C and on the equilibrium mixture of (7A) and (8A) obtained at +25 °C. [c] The spectrum was second-order and highly temperature-dependent. [d] The broad doublet at δ 2.86 sharpened on irradiation at δ 1.63 (Me) (and *vice versa*).

shifts and the characteristic coupling constants, J_{gem} 1—3.5, $J_{vic(trans)}$ 4.5—6.1, and $J_{vic(cis)}$ 5.8—8.0 Hz.[8]

As can be seen from Table 2, the additions of both nitrenes to methyl acrylate are stereospecific * and contrathermodynamic with the ester and heterocycle *cis* in the kinetically formed aziridine invertomer. The transformation of the *cis*-invertomer (1A), from Phthal-N: addition to methyl acrylate, into the previously reported 17:83 thermodynamic equilibrium ratio of *cis*-(1A) and *trans*-(2A) forms which can be followed by n.m.r. leaves little doubt of its structure. Moreover, this *cis*-invertomer (1A) could be crystallised from the cold dichloromethane solution by addition of cold light petroleum and further cooling. The crystalline material thus obtained had a (first-order) aziridine ring splitting pattern identical with that present in the spectrum of the reaction mixture. It is of interest that inversion at the aziridine ring nitrogen is considerably retarded in the crystalline form of (1A). After 4 days at room temperature only 13% of the *trans*-invertomer (2A) was present as shown by re-dissolution and re-measuring the n.m.r. spectrum at −30 °C. In contrast, inversion in solution at room temperature was too fast to be measured by n.m.r.

A further observation was that if a sample of the above aziridine was prepared at room temperature, crystallised from chloroform–light petroleum, and then dissolved in conversion into the more abundant (2A), through preferential crystallisation of the latter with consequent re-establishment of the *cis–trans*-equilibrium in solution.

Phthal-N: adds also stereospecifically to methyl methacrylate, giving exclusively the invertomer with ester and heterocycle *cis* (3A).† However, addition of Benzox-N: to the same ester was not stereospecific (but still highly stereoselective): an 86 : 14 *cis–trans*-ratio [(3B) : (4B)] was obtained reproducibly. Clearly simple steric effects are not responsible for this reduced stereoselectivity since addition of this nitrene to methyl acrylate is more *cis*-selective than addition to methyl methacrylate, *i.e.* in the opposite sense to that anticipated on steric grounds.

Addition of Phthalimidonitrene to Styrenes (*Scheme* 4).—It was of interest to determine whether the above unexpected mode of addition occurred in nitrene addition to other substituted olefins. Low temperature addition of Phthal-N: to styrene gave only the *cis*-invertomer (5A); the thermodynamic equilibrium in this case appeared to be completely on the side of the *trans*-invertomer (6A). Addition to α-methylstyrene was also stereospecific whilst the addition to β-methylstyrene, though not stereospecific, was still highly stereoselective. N.m.r. assignments and observed ratios are given in Tables 3 and 4 respectively.

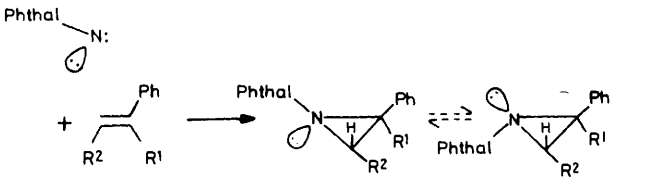
Addition of Phthal-N: *and* Benzox-N: *to Dienes*.—Our most exhaustive examination has been on the addition

* Since stereoselectivity reaches 100%, the addition may be described as stereospecific.

† A reproduction of spectra (in CH_2Cl_2) in this case is given in ref. 5*a*.

[8] S. J. Brois and G. P. Beardsley, *Tetrahedron Letters*, 1966, 5118.

of both nitrenes to the three dienes butadiene, isoprene, and 2,3-dimethylbutadiene (Tables 5 and 6). The room temperature addition of Benzox-N: to these dienes has been reported previously.[9] In the low temperature



(5A) $R^1 = R^2 = H$ (6A) $R^1 = R^2 = H$
(7A) $R^1 = Me, R^2 = H$ (8A) $R^1 = Me, R^2 = H$
(9A) $R^1 = H, R^2 = Me$ (9A) $R^1 = H, R^2 = Me$

SCHEME 4

reactions, the results using butadiene (Scheme 5) were similar to those obtained with styrene: addition of both nitrenes is stereospecific giving only the *cis*-invertomers

TABLE 4

Kinetic and thermodynamic ratios for phenylaziridines (5A)—(10A)

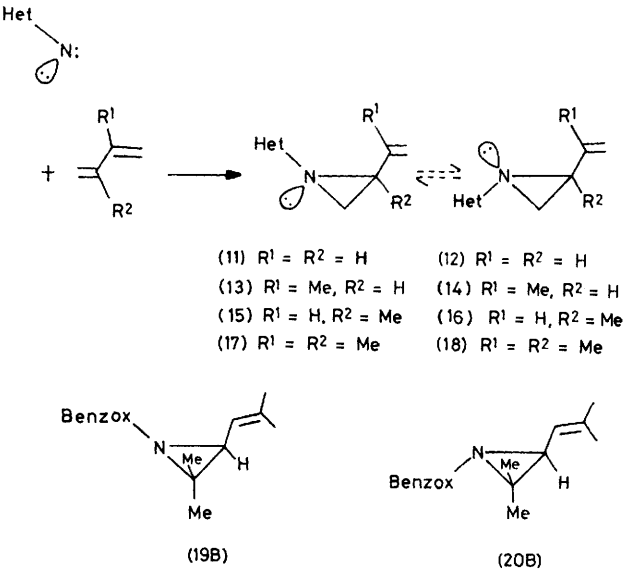
Olefin	Nitrene	Aziridine	Kinetic ratio (low temp.)	Thermodynamic ratio (ambient temp.)
CH_2:CHPh	Phthal–N:	(5A)	100	0
		(6A)	0	100
CH_2:CMePh	Phthal–N:	(7A)	100	15
		(8A)	0	85
trans-CHMe:CHPh	Phthal–N:	(9A)	94	31
		(10A)	6	69

(11A and B) whereas only the *trans*-invertomers (12A and B) are visible in the room temperature spectra.

It is sometimes difficult to exclude the presence of a few percent of the second invertomer by n.m.r. when only one invertomer appears to be present. This is particularly true in systems which do not contain methyl groups (or in the spectra in which the methyl signals are obscured) and where one must rely upon the absence of a coupled aziridine ring proton. A knowledge of exactly where the signals of the absent invertomer are to be expected is of great assistance in this respect.

The vinylaziridine (12A) from this reaction was not isolated previously,[6] but rapid chromatography through alumina and crystallisation from light petroleum gave a crystalline sample, m.p. 99—99.5 °C.

In the addition to isoprene the presence of two double bonds can give rise, in principle, to two pairs of stereoisomers [(13) + (14); (15) + (16); Scheme 5] at temperatures low enough to inhibit inversion at the aziridine ring nitrogen. Previously,[9] two isomeric aziridines have been isolated pure and crystalline by reaction of Benzox-N: with the two different double bonds of isoprene at room temperature. Whereas the n.m.r. spectrum of the isomer obtained by addition to the more substituted double bond shows both invertomers (15B) and (16B) to be present in equilibrium at room temperature, only one invertomer (14B) is observable in the case of the other isomer: this is not surprising considering the increased disparity in size of the substituent groups on the ring. From careful analysis of the low temperature spectrum (Figure 1) of the reaction mixture obtained in the low-temperature addition to isoprene together with that obtained when this reaction mixture was allowed to warm to room temperature (Figure 1) and knowing which peaks were assignable to (14B), (15B), and (16B), the only conclusion to be drawn is that the reaction mixture initially contains (13B), (15B), and (16B); (14B) is conspicuously absent. Furthermore, on gradual warming of the reaction mixture while monitoring the n.m.r. spectrum, the conversion of invertomer (13B) into the thermodynamically more stable (14B) ($t_{\frac{1}{2}}$ *ca.* 20 min at 50 °C) was evidently almost



(11) $R^1 = R^2 = H$ (12) $R^1 = R^2 = H$
(13) $R^1 = Me, R^2 = H$ (14) $R^1 = Me, R^2 = H$
(15) $R^1 = H, R^2 = Me$ (16) $R^1 = H, R^2 = Me$
(17) $R^1 = R^2 = Me$ (18) $R^1 = R^2 = Me$

(19B) (20B)

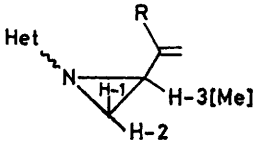
SCHEME 5

complete before observable onset of nitrogen inversion in (15B) and (16B) ($t_{\frac{1}{2}}$ *ca.* 5×10^3 min at 5 °C) with establishment of the thermodynamic balance between the latter. This is a useful result because it shows that the initial ratio of (15B) to (16B) is a true kinetic ratio with no adventitious equilibration having occurred prior to n.m.r. measurement. It is also in agreement with the observations of Brois [10] that increase in size of an aziridine ring substituent lowers the barrier to inversion at the ring nitrogen. The ratio of (14B) to (15B) + (16B) (42 : 58) was consistent with the more substituted (nucleophilic) double bond of isoprene having reacted preferentially. A similar picture emerged in addition of Phthal-N: to isoprene (Table 6).

[9] R. S. Atkinson and C. W. Rees, *J. Chem. Soc.* (*C*), 1969, 772.
[10] S. J. Brois, *J. Amer. Chem. Soc.*, 1967, **89**, 4242; S. J. Brois, *Trans. New York Acad. Sci.*, 1969, **31**, 931; see also D. Felix and A. Eschenmoser, *Angew. Chem. Internat. Edn.*, 1968, **7**, 224.

TABLE 5

Selected n.m.r. data for vinylaziridines (11)—(18) [a]



Olefin	Aziridine	Solvent	Temp. (°C)	δ Values H-1	H-2	H-3[Me]	J/Hz
$CH_2{:}CH{\cdot}CH{:}CH_2$	(11A)	CH_2Cl_2	−30	3.0 (dd)	2.85 (dd)	3.21br (q)	$J_{1,2}$ 2.7; $J_{1,3}$ 5.8; $J_{2,3}$ 5.8; $J_{3,olef.}$ 6.0
	(12A)	CH_2Cl_2	−30	2.56 (dd)	2.71 (dd)	3.14br (q)	$J_{1,2}$ 2.2; $J_{1,3}$ 5.9; $J_{2,3}$ 7.8; $J_{3,olef.}$ 6.2
	(11B)	$CDCl_3$	−30	3.28 (dd)	2.73 (dd)	3.08 (q)	$J_{1,2}$ 2.8; $J_{1,3}$ 5.9; $J_{2,3}$ 6.3
	(12B) *	$CDCl_3$	−30	2.74 (m)	3.05 (m)	3.05 (m)	
$CH_2{:}CH{\cdot}CMe{:}CH_2$	(13A)	$CDCl_3$	−30	3.31 (dd)	2.65—2.8 (complex)		$J_{1,2}$ 3.4; $J_{1,3}$ 6.4
	(14A)	$CDCl_3$	−30	2.57—2.73 (complex)		3.0 (dd)	$J_{1,3}$ 5.6; $J_{2,3}$ 7.4
	(15A)	$CDCl_3$	−30	3.07 (d)	2.63 (d)	[1.54 (s)]	$J_{1,2}$ 3.1
	(16A)	$CDCl_3$	−30	*ca.* 2.7 (d)	2.88 (d)	[1.40 (s)]	$J_{1,2}$ 2.7
	(13B)	$CDCl_3$	−30	3.78 (dd)	*ca.* 2.64 (dd)	3.01 (t)	$J_{1,2}$ 3.5; $J_{1,3}$ 6.2; $J_{2,3}$ 6.2
	(14B) *	$CDCl_3$	−30	2.56 (dd)	2.90 (dd)	3.12 (dd)	$J_{1,2}$ 2.0; $J_{1,3}$ 5.2; $J_{2,3}$ 7.5
	(15B)	$CDCl_3$	−30	3.38 (d)	*ca.* 2.63 (d)	[1.56 (s)]	$J_{1,2}$ 3.0
	(16B) *	$CDCl_3$	−30	*ca.* 2.6 (d)	*ca.* 3.36 (d)	[1.37 (s)]	$J_{1,2}$ 3.0
$CH_2{:}CMe{\cdot}CMe{:}CH_2$	(17A)	$CDCl_3$	−30	3.77 (d)	2.6 (d)	[1.59 (s)]	$J_{1,2}$ 3.5
		$CDCl_3$	0	3.79 (d)	2.53 (d)	[1.57 (s)]	
	(18A)	$CDCl_3$	−30	2.87 (s)	2.87 (s)	[1.45 (s)]	$J_{1,2}$ 2.5, $J_{1,Me}$ < 1
		$CDCl_3$	0	2.79 (d)	2.88 (d)	[1.42 (s)]	
	(17B)	$CDCl_3$	−30	4.43 (d)	2.46 (d)	[1.58 (s)]	$J_{1,2}$ 3.5, $J_{1,Me}$ < 1
	(18B)	$CDCl_3$	−30	2.74br (d)	3.34br (d)	[1.45 (s)]	$J_{1,2}$ 2.5, $J_{1,Me}$ *ca.* 1
		$CDCl_3$	0	2.68 (d)	3.69br (d)	[1.44 (s)]	
$CMe_2{:}CH{\cdot}CH{:}CMe_2$	(20B) [b]*	$CDCl_3$	−31			3.81 (d)	$J_{3,olef.}$ 8.0

[a] All n.m.r. data taken from spectra of crude reaction mixtures. [b] The spectrum in this case was unchanged after warming to ambient and re-cooling. Decoupling experiments identified the vicinal olefinic proton signal at δ 5.10.[9]

* Previously prepared (see ref. 9).

TABLE 6

Kinetic and thermodynamic ratios for vinylaziridines (11)—(20)

Olefin	Nitrene	Aziridine	Kinetic ratio (low temp.)	Thermodynamic ratio [a]
$CH_2{:}CH{\cdot}CH{:}CH_2$	Phthal–$\dot{N}$:	(11A), (12A)	100 : 0	< 5 : > 95
	Benzox–$\dot{N}$	(11B), (12B)	> 95 : < 5	< 5 : > 95
30% ↑ $CH_2{:}CH{\cdot}CMe{:}CH_2$	Phthal–$\dot{N}$:	(13A), (14A)	100 : 0	0 : 100
70% ↑	Phthal–$\dot{N}$:	(15A), (16A)	65 : 35	58 : 42
42% ↑ $CH_2{:}CH{\cdot}CMe{:}CH_2$	Benzox–$\dot{N}$:	(13B), (14B)	100 : 0	0 : 100
58% ↑	Benzox–$\dot{N}$:	(15B), (16B)	75 : 25	61 : 39
$CH_2{:}CMe{\cdot}CMe{:}CH_2$	Phthal–$\dot{N}$:	(17A), (18A)	63 : 37	15 : 85
	Benzox–$\dot{N}$:	(17B), (18B)	74 : 26	13 : 87
$CMe_2{:}CH{\cdot}CH{:}CMe_2$	Benzox–$\dot{N}$:	[(19B), (20B) [b]	0 : 100	0 : 100

[a] Thermodynamic ratios were measured at −30 °C after equilibration at 25 °C. [b] See Table 5, footnote *b*.

Addition to 2,3-dimethylbutadiene under our low temperature conditions was stereoselective for both nitrenes with the heterocycle and isopropenyl group *cis* in the kinetically preferred invertomer. The substituent on the unattacked double bond in these dienes appears to play no role in determining the *cis*-selectivity as judged by comparison of the kinetic ratios in additions to isoprene and 2,3-dimethylbutadiene (Table 6).

DISCUSSION

The pattern which emerges from this work is a consistent preference of the two nitrenes for *cis*-addition to the π-electron containing substituents examined (esters, aromatic rings, and olefins). Stereospecific *cis*-addition is observed whenever the double bond which suffers attack bears no substituent other than hydrogen. Olefins which also carry a methyl group still show this

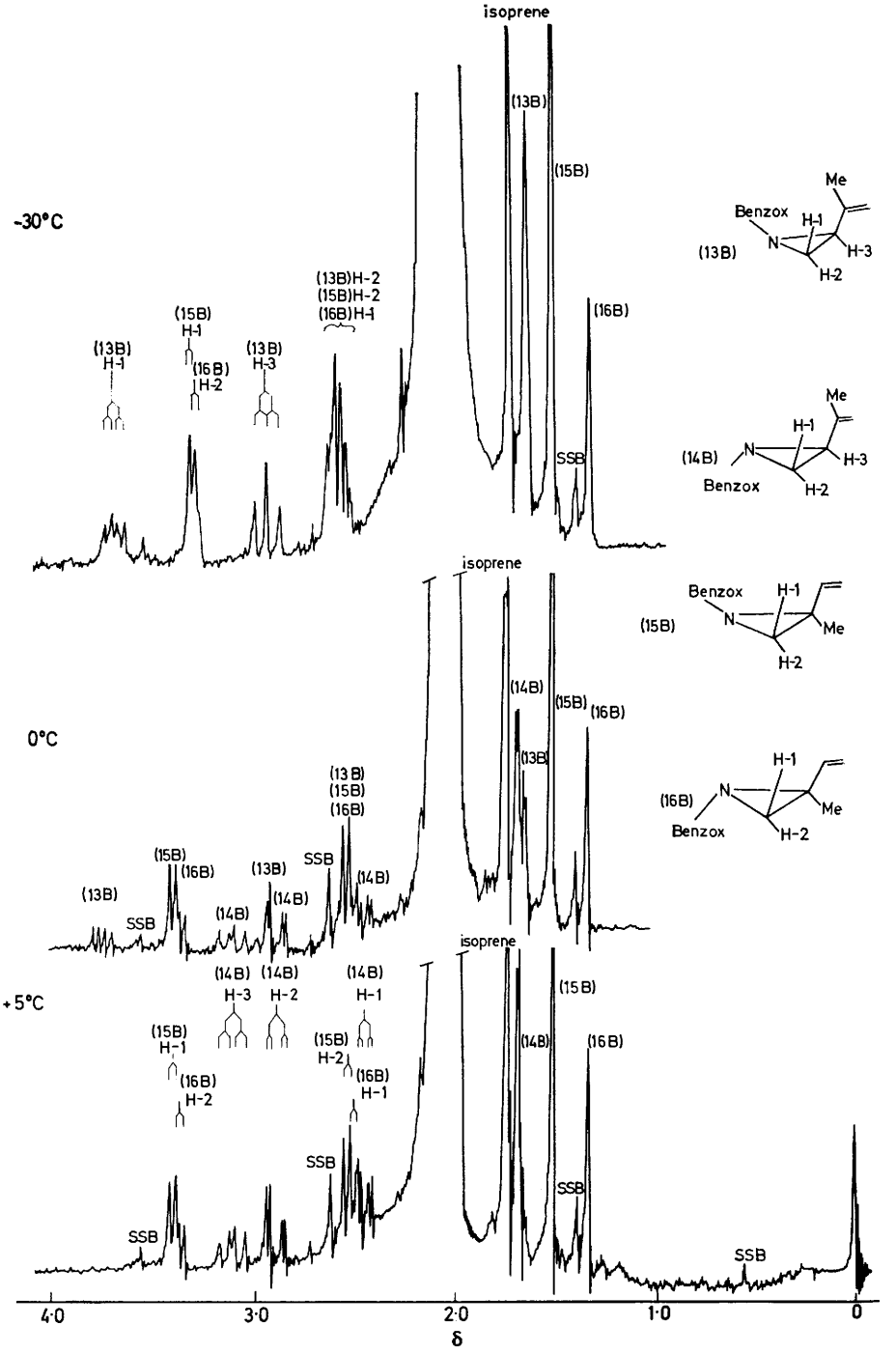


FIGURE 1 Partial n.m.r. spectra of the crude reaction mixture from addition of Benzox-N: to isoprene at −30 °C; changes in invertomer ratios with increase in temperature

preference but the methyl group appears to be able to compete in terms of *cis*-selectivity for the heterocyclic substituent in the kinetically formed aziridines. (This effect varies, and Phthal-Ṅ: addition is still stereospecific even to methyl methacrylate and α-methylstyrene). These generalisations hold over a range of double bond electrophilicities. Although steric effects are evidently of little importance in determining the kinetically formed ratios they are presumably the major factor determining the subsequent thermodynamic ratios.

Person *et al.*[11] have studied the addition of substituted phthalimidonitrenes to various αβ-unsaturated esters and have attempted to correlate increased yields of

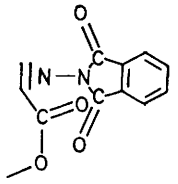


FIGURE 2

aziridines with a favourable secondary orbital interaction between the Phthal-Ṅ: carbonyl carbon and the ester carbonyl oxygen.* These authors did not consider the question of *cis*-selectivity but their model does in fact predict that the *cis*-invertomer will be formed initially in addition to acrylates. This model (Figure 2) also implies that such an interaction will only operate with the s-*cis*-conformation of the ester and it has been suggested [11] that the lack of reactivity of αβ-unsaturated aldehydes may be the result of their adopting an s-*trans*-conformation. Extending this model to addition of the nitrenes to dienes predicts that 2,4-dimethylhexa-2,4-diene would show little *cis*-selectivity since the s-*cis*-conformation of this diene is absent.[12] In the event, addition of Benzox-Ṅ: to this diene under the low temperature conditions gave an n.m.r. spectrum assigned to (20B) (Scheme 5) which was unchanged on warming to room temperature and then re-cooling: there was no evidence for the formation of (19B) in agreement with the prediction above.†

It is noteworthy that an s-*cis*-conformation is always available in the styrenes provided that the vinyl group remains coplanar with the aromatic ring.

To what extent the secondary interaction in Figure 2 is the result of a favourable orbital overlap or of a simple attractive electrostatic interaction is not yet clear. We have earlier suggested that electrostatic interaction between the phthalimide carbonyl carbon and the ester carbonyl oxygen is responsible for some unexpected changes in thermodynamic invertomer ratios in αβ-unsaturated ester-derived aziridines as the size of the ester alkyl group is increased.[7] In terms of the frontier orbital treatment,[13] a rationalisation of the remarkable *cis*-selectivity follows from consideration of Figure 3. Within this HOMO–LUMO pair, the favourable secondary interaction indicated by the shaded lobes is evident. This interaction seems possible for either linear [*sp*-hybridised N (Figure 3)] or non-linear (sp^2-hybridised N) cheletropic addition of the nitrene.

Our attempts to probe the *cis*-selectivity of the methyl group using simple alkenes (propene and *cis*-but-2-ene) were thwarted by the very low yields of aziridines obtained at −30 °C even though an excess of olefin was used and then removed under reduced pressure at −30 °C before n.m.r. measurement. *cis*-But-2-ene gives the corresponding aziridine from Benzox-Ṅ: in 60% yield at 0 °C.[9]

Recent studies using Raman spectroscopy have shown [14] that only 3% of butadiene at room temperature has the s-*cis*-conformation (the fraction will presumably

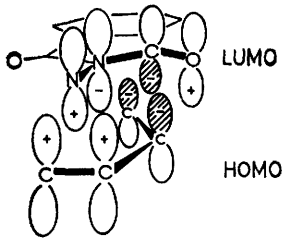


FIGURE 3

be even lower at −25 °C). The corresponding figure for isoprene was calculated to be 11%. Hence both Phthal-Ṅ: and Benzox-Ṅ: must be highly discriminating species if only the s-*cis*-conformation in each case is undergoing attack. As mentioned earlier, the substituent on the unattacked double bond has no effect upon the *cis*-selectivity of addition to these dienes [compare (15A) : (16A) and (17A) : (18A) or (15B) : (16B) and (17B) : (18B)]. One interpretation of this result is that, in the additions to isoprene and 2,3-dimethylbutadiene, the aziridines (16A), (16B), (18A), and (18B) are also formed by reaction of the nitrenes with the dienes in the s-*cis*-conformations. Some support for the lack of reactivity of (monomethyl) s-*trans*-dienes comes from an attempted reaction of 4-methylpenta-1,3-diene with Benzox-Ṅ: and Phthal-Ṅ:, where no aziridine was detectable in solution by n.m.r. using the low temper-

* It is implicit in the French authors' discussion that the secondary orbital interaction between the ester and phthalimido group is dominant. We have shown this to be true in the case of methyl cinnamate in which the ester and phthalimido groups (rather than the phenyl and phthalimido groups) are *cis* in the kinetically formed product.

† Aziridine (20B) was reasonably stable at room temperature (from n.m.r.); in view of the instability of the corresponding phthalimidoaziridine, however, our earlier report [5b] of the presence of 12% of the *cis*(Phthal-butenyl) invertomer present in the kinetically formed product may be an overestimate.

[11] H. Person, C. Fayat, F. Tonnard, and A. Foucaud, *Bull. Soc. chim. France*, 1974, 635.
[12] E. M. Arnett, *J. Org. Chem.*, 1960, **25**, 324.
[13] K. N. Houk, *Accounts Chem. Res.*, 1975, **8**, 361.
[14] D. A. C. Compton, W. O. George, and W. F. Maddams, *J.C.S. Perkin II*, 1976, 1666.

ature conditions. Presumably, the primary HOMO–LUMO (frontier) orbital interaction between the nitrene and the olefin is less favourable when that olefin is part of an s-*trans*-diene rather than an s-*cis*-diene.

EXPERIMENTAL

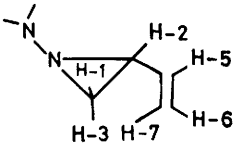
N.m.r. spectra were measured with a JEOL-JNM-PS-100 spectrometer (solutions in CH_2Cl_2 or $CDCl_3$; Me_4Si as internal standard). The general method used for low temperature nitrene addition to the olefins is illustrated by the following.

To a stirred suspension of *N*-aminophthalimide (0.81 g) in dichloromethane (7 ml) containing methyl acrylate (0.43 g) and kept at −25 °C by external cooling was added powdered lead tetra-acetate (2.1 g) over 15 min. The mixture was stirred for a further 45 min at this temperature and then lead salts were filtered off at −40 °C. Examination of the filtrate by n.m.r. at −30 °C with no intermediate warming of the solution above −25 °C showed aziridine ring proton signals at δ 3.24 (dd, *J* 5.5 and 6 Hz, C*H*CO_2Me), 3.04 (dd, *J* 5.5 and 1.5 Hz, H *cis* to CO_2Me and Phthal), and 2.86 (dd, *J* 6 and 1.5 Hz, H *trans* to CO_2Me and Phthal). Careful addition of light petroleum (2 ml) to the filtrate followed by a further filtration, then addition of a further quantity of light petroleum (*ca.* 2 ml) (all these operations carried out at −30 to −40 °C) gave, on further cooling and scratching, a crystalline sample of the aziridine (1A), which was separated, washed with cold 2 : 1 chloroform–light petroleum, and dried under vacuum at −30 °C. Dissolution of this product in $CDCl_3$ at −30 °C gave a solution having δ 7.7—7.4 (m, 4 × ArH), 3.72 (s, CO_2Me), 3.35 (dd, *J* 5.5 and 6 Hz, C*H*CO_2Me) 3.21 (dd, *J* 5.5 × 1.5 Hz, H *cis* to CO_2Me and Phthal), and 2.96 (dd, *J* 6 × 1.5 Hz, H *trans* to CO_2Me and Phthal). An i.r. spectrum of the solid (room. temp.; Nujol) had $\nu_{max.}$ 1 767w, 1 733sh, 1 720sh, 1 708s, and the following peaks which were absent from the spectrum of the *trans*-invertomer (see below): 1 215, 1 175, and 1 015 cm^{-1}.

trans-Methyl 1-phthalimidoaziridine-2-carboxylate (2A), prepared by the method reported and crystallised from chloroform–light petroleum, showed δ (CH_2Cl_2; −32 °C) 3.77 (CO_2Me), and 3.2—3.0 (m) and 2.8—2.7 (m) [3 × aziridine ring H (2nd order)], $\nu_{max.}$ (Nujol) 1 776w, 1 743s, 1 705s, and the following peaks which were absent from the spectrum of the *cis*-invertomer (above): 1 191, 1 092, 838, and 738 cm^{-1}.

1-*Phthalimido*-2-*vinylaziridine* (12A).—The cold methylene chloride solution was poured into saturated sodium hydrogen carbonate solution and the organic layer separated, dried, and evaporated. The residue was filtered through a small column of alumina (Spence type H) in benzene–ethyl acetate 5 : 1 and on evaporation gave (12A) as pale yellow *needles*, m.p. 99—99.5 °C (Found: C, 67.35; H, 4.8; N, 13.15. $C_{12}H_{10}N_2O_2$ requires C, 67.3; H, 4.7; N, 13.1%), δ ($CDCl_3$) [see (A)] 7.60br (s, 4 × ArH), 5.8 (H-5, d × d × d, $J_{5,7}$ 17.1, $J_{5,6}$ 9.3, $J_{6,7}$ 6.2 Hz), 5.51 (H-7, d × d, $J_{7,5}$ 17.1, $J_{7,6}$ 2.7 Hz), 5.34 (H-6, d × d, $J_{6,5}$ 9.3, $J_{6,7}$ 2.7 Hz), 3.09 (H-2, d × d × d, $J_{2,1}$ 7.8, $J_{2,5}$ 6.2, $J_{2,3}$ 5.9 Hz), 2.72 (H-1, d × d, $J_{1,2}$ 7.8, $J_{1,3}$ 2.2 Hz), and 2.51 (H-3, d × d, $J_{3,2}$ 5.9, $J_{3,1}$ 2.2 Hz).

1-*Phthalimido*-2-*methyl*-2-*phenylaziridine* (8A).—This was prepared according to the literature method.[6] The



(A)

product was isolated by column chromatography [basic alumina; eluted by benzene–ethyl acetate (5 : 1) after elution of residual α-methylstyrene with benzene] and crystallised as pale yellow microcrystals from ethanol–water, m.p. 94.5—95 °C (Found: C, 73.25; H, 5.1; N, 10.05. $C_{17}H_{14}N_2O_2$ requires C, 73.35; H, 5.05; N, 10.05%).

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