Thermal Elimination Reactions of Nitrones. Part 2.[1] A Mechanistic Study based on Substituent and Solvent Effects

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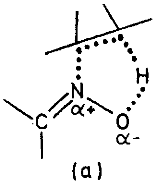
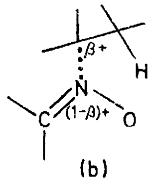
The rates of thermal elimination of isobutene from a series of *N*-(diarylmethylene)-t-butylamine *N*-oxides have been measured by u.v. spectroscopy. Activation parameters derived for *N*-(fluoren-9-ylidene)-t-butylamine *N*-oxide in decalin and t-butyl alcohol solvents are consistent with an intramolecular concerted mechanism involving a highly ordered cyclic transition state. Kinetic results from the thermal elimination of *para*-substituted *N*-(diarylmethylene)-t-butylamine *N*-oxides in protic and aprotic solvents however suggest that the reaction proceeds *via* a non-synchronous concerted mechanism in contrast to the Cope elimination of tertiary amine oxides.

SEVERAL reports have recently been published on the thermal cleavage of *N*-(diarylmethylene),[1-3] and *N*-(arylmethylene)alkylamine *N*-oxides[4] to alkenes and oximes. This reaction on superficial examination appears to be closely analogous to the Cope elimination of amine oxides, differing formally only in the presence of an sp^2 rather than an sp^3 hybridised nitrogen atom. However, the first comparative kinetic studies[1] on nitrone eliminations have revealed a very different pattern of reactivity from that shown by amine oxides, suggesting significant differences in the nature of the transition states for the two processes.

The transition state for nitrone elimination may resemble one of four extreme electronic distributions (a)—(d). Transition state (a) represents a synchronous pericyclic process, while (b) and (c) correspond to the internal analogues of E_1 and E_{1cb} reactions respectively, and (d) corresponds to a homolytic process leading to a radical pair. In transition states (b)—(d) a discrete intermediate *might* be involved; but it could equally well be that the reaction, while formally concerted, involves a transition state which resembles one of these possible intermediates. In the present paper the electronic nature of the transition state for thermal elimination of nitrones will be discussed.



(a)



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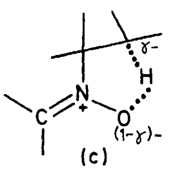

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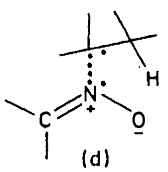
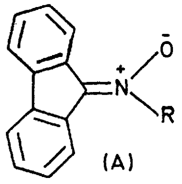


(d)

RESULTS

The comparative kinetic studies in Part 1[1] dealt mainly with the rates of olefin elimination from a series of ketonitrones of general structure (A).

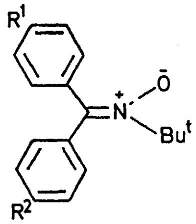


(A)

R = Et, CHMePh, Pr^i, Bu^t, Me_2EtC

The relative rates were measured by n.m.r. spectroscopy. When allied to the relative distribution of isomeric olefin products, the combined data were rationalised in terms of statistical and steric factors, olefin stabilisation, and charge development in the transition state. With the kinetic data available[1] it was not possible to investigate fully the last important factor.

More accurate kinetic data have now been obtained using u.v. spectroscopy to follow the rate of thermal fragmentation of *N*-(fluoren-9-ylidene)-t-butylamine *N*-oxide (1) into isobutene and fluorenone oxime over a range of solvents. In order to probe the electron distribution in the transition-state a series of *para*-substituted *N*-(diarylmethylene)-t-butylamine *N*-oxides (2)—(6) were also synthesised.



(2) $R^1 = R^2 = MeO$
(3) $R^1 = R^2 = Me$
(4) $R^1 = R^2 = H$
(5) $R^1 = H$, $R^2 = NO_2$
(6) $R^1 = R^2 = NO_2$

Nitrone (1) was synthesised by direct peroxy-acid oxidation of the parent imine.[1] Nitrones (2)—(4) were obtained by $LiAlH_4$ or $NaBH_4$ reduction of the present imines,[5] followed by peroxy-acid oxidation of the secondary amine products to nitrones using the method recently reported by

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[1] Part 1, D. R. Boyd and D. C. Neill, *J.C.S. Perkin I*, 1977, 1308.

[2] D. R. Boyd, *Tetrahedron Letters*, 1973, 3467.

[3] W. M. Leyshon and D. A. Wilson, *J.C.S. Perkin I*, 1975, 1920.

[4] M. H. Goodrow, J. A. Villarreal, and E. J. Grubbs, *J. Org. Chem.*, 1974, **39**, 3447.

[5] W. B. Jennings, S. A. Showiman, D. R. Boyd, and R. M. Campbell, *J.C.S. Perkin II*, 1976, 1501.

Beckett.[6] Nitrones (5) and (6) were obtained by photochemical rearrangement of the corresponding oxaziridines using the experimental conditions reported for the synthesis of other nitrones.[7] Nitrone (5) is assumed to consist of almost equal concentrations of both *E*- and *Z*-isomers under the thermal elimination conditions.

Nitrones (1)—(6) all showed the characteristic π–π^* transition band in the 280—370 nm region of the u.v. spectrum, whereas the product oximes showed only weak absorption bands above 260 nm. The kinetics were thus followed by u.v. using thermostatically controlled cells. It was possible to measure reaction rates in the range 30—90 ($\pm$0.1) °C.

A comprehensive kinetic study was carried out using nitrone (1) (*ca.* 3×10^{-5}M) in purified t-butyl alcohol and decalin solvents by following the absorbance decrease at 354 nm. Measurements were recorded at seven temperatures in the range 52—88 °C and plots of log $(A_t - A_\infty)$ against time gave the rate constants (Table 1). A plot of log k/T against $1/T$ was linear and a least squares statistical analysis of these results gave a correlation coefficient of 0.9999 and 0.9991 respectively for t-butyl alcohol and decalin. The resulting activation parameters are: t-butyl alcohol, $\Delta H^\ddagger$ 25.8 $\pm$ 0.2 kcal mol^{-1}, ΔS -1.7 ± 0.6 cal mol^{-1} K^{-1}; decalin, $\Delta H^\ddagger$ 25.8 $\pm$ 0.5 kcal mol^{-1}, ΔS -0.4 ± 1.5 cal mol^{-1} K^{-1}. In all cases the only observed products were isobutene and fluorenone oxime and the kinetics were strictly first order. The kinetic measurements on (1) were repeated in the solvents decalin, methanol, ethanol, and t-butyl alcohol at 63.0 °C (Table 2).

TABLE 1

Rates of elimination of nitrone (1)

t-Butyl alcohol		Decalin	
t/°C	10^4k/s^{-1}	t/°C	10^4k/s^{-1}
88.1	7.76	85.5	12.50
74.7	1.97	84.0	9.04
72.5	1.56	77.6	5.45
69.5	1.08	72.2	2.91
66.0	0.72	66.1	1.47
59.0	0.315	60.5	0.72
52.0	0.13	56.0	0.41

TABLE 2

Rate of elimination of nitrone (1) in a range of solvents at 63.0 °C

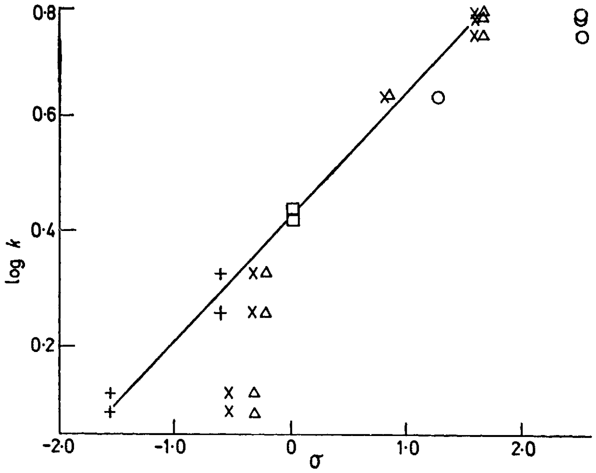
Solvent	5 + log(k/s^{-1})
Decalin	1.15
t-Butyl alcohol	0.67
Ethanol	0.54
Methanol	0.48

Nitrones (2)—(6) were similarly pyrolysed in solution in purified t-butyl alcohol, decalin, or *o*-dichlorobenzene and the kinetics followed as for nitrone (1). The logarithms of the rate constants found are presented in Table 3. These logarithmic quantities were plotted against various sets of substituent parameters (σ°, σ^+, σ^-, and σ_p).[8] The Figure shows this plot for the results in t-butyl alcohol; the data from the other solvents are fewer and less accurate but show a qualitatively similar result. A good correlation exists with σ^+ (σ^0 for electron-withdrawing substituents) giving a value of 0.22 for ρ, but attempted correlations with σ^- or σ_p fail badly.

TABLE 3

Rates of elimination of nitrones (2)—(6)

Solvent (t/°C)	Bu^{t}OH (63)	Decalin (63)	*o*-Dichlorobenzene (50)
Compound		5 + log(k/s^{-1})	
(2)	0.114, 0.079	1.174	1.459
(3)	0.255, 0.322	1.303	1.602
(4)	0.431, 0.415	1.364	1.663
(5)	0.633		
(6)	0.771, 0.778, 0.690	1.412	2.217



Hammett plots for the elimination of nitrones (2)—(6) in Bu^{t}OH at 63 °C □ $\sigma = 0$ (common to all scales); + σ^+; × σ_p; △ σ^0; ○ σ^-

DISCUSSION

Of the four possible transition state types (a)—(d) the homolytic mechanism (d) appears to be most easily excluded on the presently available evidence. Grubbs *et al.*[4,9-11] have shown that with compound (7) where elimination is impossible, thermal decomposition of the nitrone takes place, but at a higher temperature than would be expected for a comparable elimination reaction. This reaction shows the characteristics of a radical process; products attributable to radical coupling are observed,

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[6] A. H. Beckett, R. T. Coutts, and F. A. Ogunbona, *Tetrahedron*, 1973, **29**, 4189.

[7] J. Bjørgo, D. R. Boyd, D. C. Neill, and W. B. Jennings, *J.C.S. Perkin I*, 1977, 254.

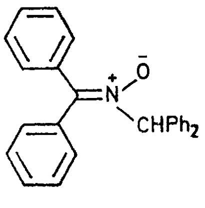
[8] O. Exner in 'Advances in Linear Free Energy Relationships,' Plenum, London, 1972, p. 1.

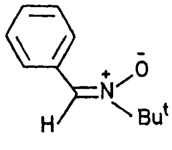
[9] T. S. Dobashi and E. J. Grubbs, *J. Amer. Chem. Soc.*, 1973, **95**, 5070.

[10] J. S. Vincent and E. J. Grubbs, *J. Amer. Chem. Soc.*, 1969, **91**, 2022.

[11] E. J. Grubbs, J. A. Villarreal, J. D. McCullough, jun., and J. S. Vincent, *J. Amer. Chem. Soc.*, 1967, **89**, 2234.

and the activation entropy $\Delta S^\ddagger$, of $+14.5 \pm 0.8$ cal $\mathrm{mol^{-1}\ K^{-1}}$,[4] is typical of such homolytic fragmentations.


(7)


(8)

During the course of the present studies Grubbs *et al.*[4] reported that from the thermal elimination reaction of nitrone (8) in t-butyl alcohol solvent a value for $\Delta S^\ddagger$ of $-0.3 + 0.9$ cal $\mathrm{mol^{-1}\ K^{-1}}$ was obtained. Our results gave values for $\Delta S^\ddagger$ of -1.7 ± 0.6 ($\mathrm{Bu^tOH}$) and -0.4 ± 1.5 (decalin) cal $\mathrm{mol^{-1}\ K^{-1}}$ and are also consistent with those previously reported[12] for a cyclic concerted mechanism. $\Delta S^\ddagger$ Values for thermal elimination of olefins are typically -5 (xanthate esters[13]), $+1$ to -11 (amine oxides[14,15]), -11 to -16 cal $\mathrm{mol^{-1}\ K^{-1}}$ (sulphoxides[16]).

From the kinetic data previously reported[1] for the thermal elimination reaction of *N*-(fluoren-9-ylidene)-alkylamine *N*-oxides the E_a values are found to lie in the range 23—24 kcal $\mathrm{mol^{-1}}$. Activation energies for homolytic cleavage of nitrones have been found[4,11] to occur in the range 38—51 kcal $\mathrm{mol^{-1}}$. Thus, in accord with the observations of Grubbs *et al.*[4] the activation energies for thermal elimination of our nitrones are consistently lower than those anticipated for a homolytic fragmentation-disproportionation route to oxime and olefin. Furthermore, products of coupling or disproportion, frequently associated with a homolytic reaction, were not detected during pyrolysis of nitrones (1)—(6).

The present and other[4] results suggest that the radicals observed[17] by e.s.r. during the pyrolysis of (8) (and *para*-substituted analogues) arise from a very minor side reaction. In further support of this view it was recorded that the yields of benzaldoxime from (8)[4] and fluorenone oxime from (1)[1] were essentially quantitative ($\geqslant 97\%$).

It seems that two discrete thermal processes may occur, one, an elimination which is almost certainly a concerted pericyclic process, and the other, a homolytic fission which cannot in our series compete effectively with the elimination. Leyshon and Wilson[3] have found examples of nitrones where such competition exists, but these involve sulphur-containing leaving groups which might be expected to form more stable radicals. An analogous competitive situation occurs in thermal sulphoxide eliminations.[18]

Substituent Effects.—It is fortunate that the homolytic transition state (d) can be excluded in our systems, because an unequivocal interpretation of substituent effects would be difficult if iminoxyl radicals, like those observed when elimination is impossible,[10] were involved. However, it is possible to predict the consequences of substitution in the aryl groups of nitrones (2)—(6) on the reaction rate for transition states of types (a)—(c).

Transition state (b) differs from the starting material chiefly in a diminution of positive charge on the nitrogen atom. This will have two consequences: primarily, a reduction in its electron-withdrawing power, and secondarily, an indirect increase in the electron-donating power of the oxygen. These would both lead to a positive ρ value. Furthermore, if the (conjugative) electron withdrawal by nitrogen is the predominant interaction mode, a correlation with σ^+ rather than σ_p or σ^- is expected.

Transition state (c) would have precisely the opposite consequences. Here, the reduction of negative charge on the oxygen will diminish its (conjugative) electron-donating power, and indirectly increase the electron-withdrawing power of the nitrogen, leading to a negative ρ value; again assuming that the primary interaction mode is more important than the indirect effect, a correlation with ρ^- might be expected.

Transition state (a) has characteristics intermediate between (b) and (c). In principle, there could exist a 'neutral' transition state where the stabilisation of negative charge on oxygen and that of positive charge on nitrogen assume equal importance, and the reaction would then be insensitive to substitution.

Excluding a homolytic mechanism, and comparing the predicted substituent effects with experiment it appears that the data fit a transition state resembling (b) rather than (c). The small value of ρ suggests, however, that the loss of positive charge on the nitrogen atom is less than complete. The most consistent view of the reaction is therefore that it is concerted but not synchronous, with N–C bond breaking considerably in advance of O–H bond making.

Earlier results obtained from these laboratories are in line with this conclusion.[1] Alkyl substitution of the β-carbon atom (from which a hydrogen atom is lost) had little effect on the reaction rate, since the relative proportions of isomeric olefin products varied little from expectations based on purely statistical factors. In contrast, alkyl (or aryl) substitution on the α-carbon atom (directly attached to nitrogen) had a marked effect on the reaction rate. Thus the rates fell neatly into groups according to whether the α-carbon atom was primary, secondary, benzylic, or tertiary. The last category was faster by a factor of *ca.* 10^6 than the first at 60 °C.

Solvent Effects.—In the present work (Tables 1—3), the reaction rates in decalin are *ca.* 2—10 fold faster than in t-butyl alcohol at the same temperature. This is

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[12] W. H. Saunders and A. F. Cokerill in 'Mechanism of Elimination Reactions,' Wiley, New York, 1973, ch. V.

[13] G. L. O'Connor and H. R. Nace, *J. Amer. Chem. Soc.*, 1952, **74**, 5454.

[14] G. C. Smith and E. Siber, *J. Org. Chem.*, 1973, **38**, 4172.

[15] M. R. V. Sahyum and D. J. Cram, *J. Amer. Chem. Soc.*, 1963, **85**, 1263.

[16] D. W. Emerson and T. J. Korniski, *J. Org. Chem.*, 1969, **34**, 4115.

[17] K. Sommermeyer, W. Seiffert, and W. Wilker, *Tetrahedron Letters*, 1974, 1821.

[18] C. A. Kingsbury and D. J. Cram, *J. Amer. Chem. Soc.*, 1952, **74**, 5454.

considerably smaller than the difference in rates between non-hydroxylic and hydroxylic solvents in the Cope elimination of tertiary amine oxides (10^6 fold difference).[15] The inverse correlation between the rates of elimination and the hydrogen-bonding aptitude of the solvent probably reflects hydrogen bonding to the negative oxygen atom. Thus the very small solvent effect we observe lends further support to the proposal that O–H bond-making involvement in the transition state is much less during thermal elimination of nitrones than in the Cope elimination.

Comparison with Other Reactions.—Certain data are of fundamental significance for a theoretical discussion: (i) the accelerations on successive alkyl substitution at the α-carbon atom; (ii) the ratio of the rate increase between secondary and tertiary compared to that between primary and secondary.

Large values of the acceleration on alkyl substitution can be taken as indicating significant charge development at the α-carbon atom in the transition state. The accelerations are moderate to large for many elimination[19–22] (and solvolysis[23]) reactions including the nitrone elimination but very small for the Cope[24] and Hofmann[25] eliminations.

The tertiary/secondary : secondary/primary rate ratio X is close to 1 for the alkyl halide pyrolyses[19,20] (and also the Cope elimination[24]) which would be consistent with a nearly constant development of charge in the transition state, *i.e.* each successive substitution resulting in a similar stabilisation. This is in accord with the proposed mechanism for halide pyrolysis, in which the transition state resembles an incipient ion pair. This ratio X for the nitrone elimination compares better with that found for solvolysis reactions[23] in water with a much greater rate increase on going from secondary to tertiary than on going from primary to secondary. It is considered that in the case of aqueous solvolysis, this effect corresponds to a mechanistic shift from S_N2-like to S_N1-like transition states * and we propose that a similar interpretation may be placed on our nitrone elimination results.

Thus, it is probable that the nitrone elimination is more nearly synchronous for primary than for tertiary alkyl groups. The present substituent effect data apply to a tertiary leaving group, where charge development should be maximised. For nitrone eliminations the kinetic data can therefore be most easily rationalised in terms of a ' variable transition state '. On this basis the internal elimination reactions may be arranged in the following order of decreasing variability of transition state:

$$\text{nitrone} > \text{acetate} > \text{halide, amine oxide.}$$

In comparison the solvolyses in hydroxylic solvents show high variability, while the Hofmann elimination (and the sulphonium analogue) show relatively small changes. The Hofmann elimination closely resembles the Cope elimination at similar temperatures, while the sulphonium elimination shows more charge development, as expected for the better leaving group.

It is proposed that variability in the transition state should arise where neither the leaving group nor the hydrogen abstracting basic centre is totally dominant in determining the mechanism. If, as in the Cope elimination, the leaving group is poor, and is a strong base, a ' constant ' synchronous mechanism is observed (an internal analogue of the E_2 reaction); if, as in the halide pyrolyses, the leaving group is good, and is a weak base, a ' constant ' ion-pair-like mechanism is observed (an internal analogue of the E_1 reaction). With the nitrones and acetates the leaving group abilities and their base-strengths are intermediate; the nature of the transition state may then reasonably be expected to be a more sensitive function of substitution.

Further work on the nitrone systems is in progress in order to explore more fully the relevance of these ideas.

EXPERIMENTAL

N.m.r. spectra were recorded at 60 MHz using a Varian A-60 instrument. Unless stated otherwise chemical shift positions for protons were obtained in $CDCl_3$ solution using tetramethylsilane as reference. All solvents were dried and purified by distillation for kinetic runs.

Nitrone (1) was synthesised by the route reported previously.[1] Nitrones (2)—(4) were obtained in good yield (70—85%) using either $LiAlH_4$ or $NaBH_4$ reduction of the parent imines which were available from an earlier study.[27] The product secondary amines were oxidised by *m*-chloroperbenzoic acid at 0—25 °C in anhydrous acetone over two days and product nitrones were isolated in 70—90% yield.[6]

The physical properties, microanalytical data, and chemical shifts for nitrones (2)—(4) and the corresponding secondary amines are given in Table 4.

Nitrones (5) and (6) were isolated after u.v. irradiation (253.7 nm) of the isomeric oxaziridines (0.02M) in chloroform. The crude nitrones were separated from unchanged

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* However, in the much less nucleophilic solvent acetonitrile solvolytic rate constants are logarithmically linearly related (for secondary, benzylic, and tertiary bromides) to alkyl halide pyrolysis.[26]

[19] D. H. R. Barton and F. P. Onyon, *Trans. Faraday Soc.*, 1949, **45**, 725; D. H. R. Barton and K. E. Mowlett, *J. Chem. Soc.*, 1949, 155; D. H. R. Barton and A. J. Mead, *Trans. Faraday Soc.*, 1950, **46**, 114.

[20] P. J. Thomas, *J. Chem. Soc.*, 1959, 1192; A. T. Blades and G. W. Murphy, *J. Amer. Chem. Soc.*, 1952, **74**, 6219; A. T. Blades, *Canad. J. Chem.*, 1958, **36**, 1043; A. Maccoll and P. J. Thomas, *J. Chem. Soc.*, 1955, 979; G. D. Harden and A. Maccoll, *ibid.*, p. 2545.

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[23] A. Streitwieser in ' Solvolytic Displacement Reactions,' McGraw-Hill, New York, 1962, p. 43; S. Winstein, E. Grunwald, and M. W. Jones, *J. Amer. Chem. Soc.*, 1951, **73**, 2700; E. D. Hughes, C. K. Ingold, S. Masterman, and B. J. McNulty, *J. Chem. Soc.*, 1940, 899.

[24] A. C. Cope and E. R. Turnbull, *Org. Reactions*, 1960, **11**, 361.

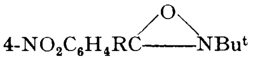
[25] P. V. Banthorpe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 1960, 4054.

[26] H. M. R. Hoffman and A. Maccoll, *J. Amer. Chem. Soc.*, 1965, **87**, 3774.

[27] W. B. Jennings, S. A. Showiman, D. R. Boyd, and R. M. Campbell, *J.C.S. Perkin II*, 1976, 1501.

TABLE 4

Physical properties and microanalytical data

Secondary armines $(4\text{-}XC_6H_4)_2CH\cdot NHBu^t$		Found (%)				Required (%)			$\delta(CHCl_3)$		
X	M.p. (°C)	C	H	N	Formula	C	H	N	CHN	X	Bu^t
MeO	59—60	76.0	8.7	4.9	$C_{19}H_{25}NO_2$	76.2	8.4	4.7	4.96	3.69	1.03
Me	140 (0.005) [a]	85.6	9.35	5.2	$C_{19}H_{25}N$	85.3	9.4	5.2	4.92	2.12	1.04
H	52—54	85.1	8.9	5.72	$C_{17}H_{21}N$	85.3	8.8	5.85	5.00		1.02
Oxaziridines  $4\text{-}NO_2C_6H_4RC(O)NBu^t$											
R											
Ph [b]	64—94	68.4	6.0	9.2	$C_{17}H_{18}N_2O_3$	68.4	6.1	9.4			1.04
$4\text{-}NO_2C_6H_4$	142 [c]										1.08
Nitrones											
(2)	108—109	72.65	7.4	4.5	$C_{19}H_{23}NO_3$	72.8	7.4	4.5		3.77	1.42
(3)	102—103	81.2	8.1	4.8	$C_{19}H_{23}NO$	81.1	8.2	5.0		2.33	1.43
(4)	82—84	80.6	7.7	5.3	$C_{17}H_{19}NO$	80.6	7.6	5.5			1.42
(5) [b]	75—79	68.7	6.3	9.3	$C_{17}H_{18}N_2O_3$	68.4	6.1	9.4			1.46
(6)	106—107	59.4	5.0	12.2	$C_{17}H_{17}N_3O_5$	59.5	5.0	12.2			1.48

[a] B.p. (°C) (*p*/mmHg). [b] *cis–trans* mixture. [c] Lit.,[26] 143°.

oxaziridine by trituration with pentane followed by rapid t.l.c. purification. These nitrones were found to isomerise slowly to oxaziridines on silica-gel. Nitrone (5) and the isomeric oxaziridine are assumed to exist as a *cis–trans*-mixture at the elevated temperatures required for m.p. determination or thermal elimination.

We thank Messrs. W. J. Swindall and B. McKnight for microanalytical data, Dr. M. G. Burnett for providing the u.v. kinetic equipment and helpful advice, and the Northern Ireland Ministry of Education for financial support (to D. C. N.).

[7/115 *Received, 24th January,* 1977]