NEW SYNTHESES OF

AZIRIDINES AND AZIRINES

By

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STATEMENT

The work described in this thesis was carried out by the author in the Department of Chemistry at the University of Leicester under the supervision of Professor C.W. Rees and Dr T.L. Gilchrist. No part of it is concurrently being submitted for any other degree.

October 1967 - August 1970

Signed

D.J. Anderson.

(D.J. ANDERSON)

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ABSTRACT

The work presented in this thesis concerns the oxidation of N-amino compounds and the interception of the reactive intermediates, the postulated amino-nitrenes.

The Introduction has been divided into three parts concerning (1) the synthesis of aziridines from nitrenes and olefins (2) nitrogen inversion as studied by N.M.R. spectroscopy (3) synthetic approaches to 2H-azirines.

The preparation of one new N-amino compound, N-aminophthalimidine is reported and the oxidations of that compound and of N-aminophthalimide, N-aminonaphthalimide, 3-aminobenzoxazolin-2(3H)-one and N-aminocarbazole are reported. The oxidation of the N-amino compounds alone leads to a variety of products, a major one frequently being the deaminated compound. The mechanism of oxidative deamination is discussed and an intermediate in the reaction, a tetrazane, has been isolated.

Oxidations in the presence of olefins and sulphoxides generally give aziridines and sulphoximines.

The N.M.R. spectra of most aziridines studied showed the presence of invertomers at room temperature. The implications of slow nitrogen inversion as a tool for conformational analysis are discussed.

Several chloro- and bromo-substituted aziridines were found to undergo a facile thermal rearrangement with ring opening to give hydrazones.

Sulphoximines and certain aziridines substituted in the 2-position with an unsaturated group were shown to produce the amino-nitrenes upon photolysis.

When N-aminophthalimide was oxidised in the presence of acetylenes, 2H-azirines and not 1H-azirines were isolated. The mechanism of this novel rearrangement is discussed, and other attempted syntheses of the 1H-azirine system are reported.

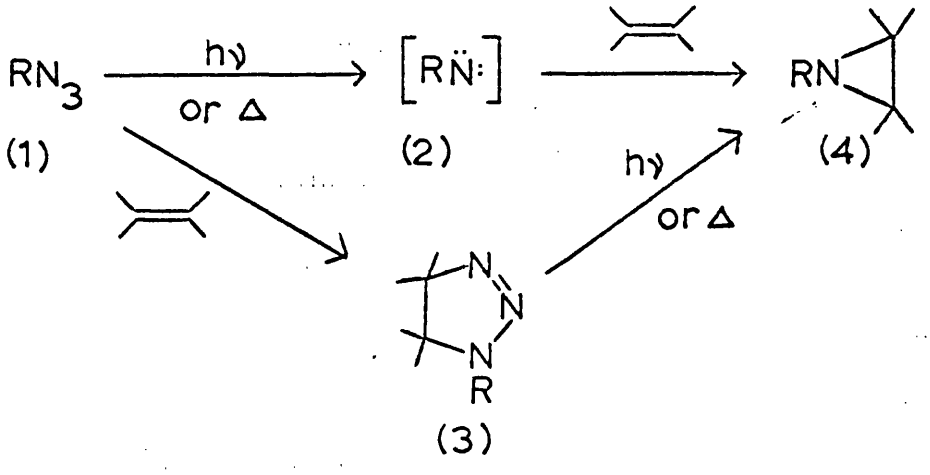
CONTENTS

INTRODUCTION

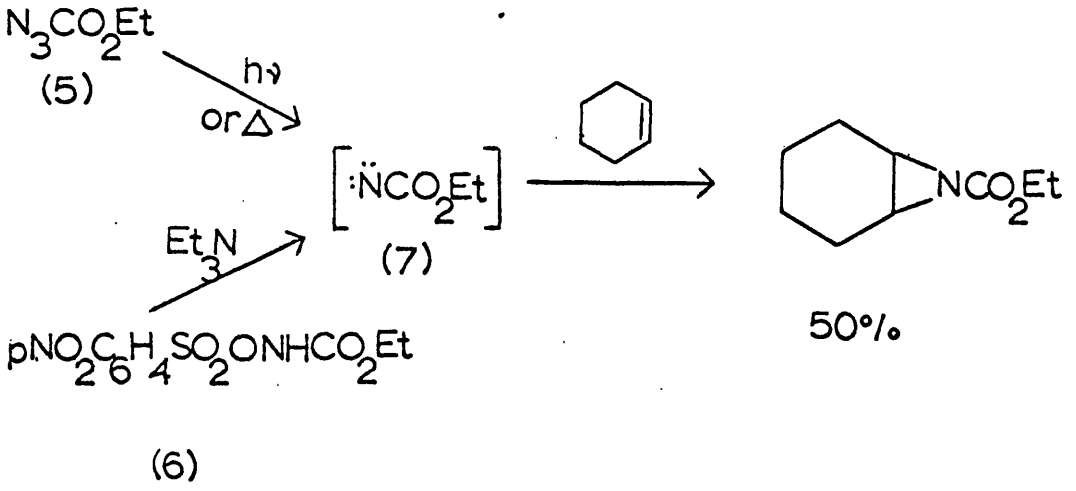
This section is an attempt to outline and cover some of the major advances, in three particular fields, pertinent to certain aspects of the work described later in this thesis.

1. Formation of Aziridines from Nitrenes and Olefins

The most utilised source of nitrenes[1–4] has been the thermolysis and photolysis of organic azides.[5] However when considering the addition of nitrenes derived from azides (1) to olefins to give aziridines (4), it is not always possible to prove from product analysis whether a nitrene (2) or an initial azide adduct, a triazoline (3), has been involved. Only if the suspected nitrene can be generated from other sources and gives the same final product analyses can it be rationalised that a nitrene is the reacting species.



Lwowski and coworkers[6–9] recognised that the same yields of aziridines and other products could be obtained by: (a) the photolysis[6,7] and (b) the pyrolysis of ethylazidoformate (5)[7] (c) the α-elimination of p-nitrobenzenesulphonic acid from its N-hydroxyurethane ester (6).[8,9]



These observations are conclusive with nitrene (7) addition to the olefin. As yet no triazolines have been isolated from the reaction of azidoformates and olefins, and there is no reaction in the absence of light and heat.

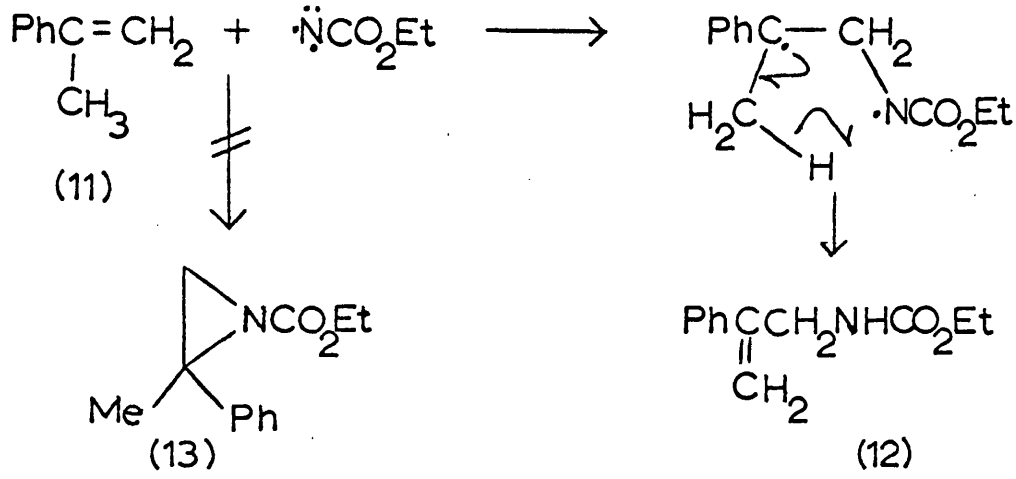
Stereospecific addition of ethoxycarbonylnitrene (7) to olefins has been briefly studied by Hafner et al.[10] and Japanese workers[11] using cis- and trans-but-2-ene (8) and β-methylstyrene (9) respectively. It has been thoroughly studied by the Lwowski group[12–14] using cis- and trans-4-methylpent-2-ene (10) from which the corresponding aziridines

MeCH = CHMe	PhCH = CHMe	Me_2CHCH = CHMe
(8)	(9)	(10)

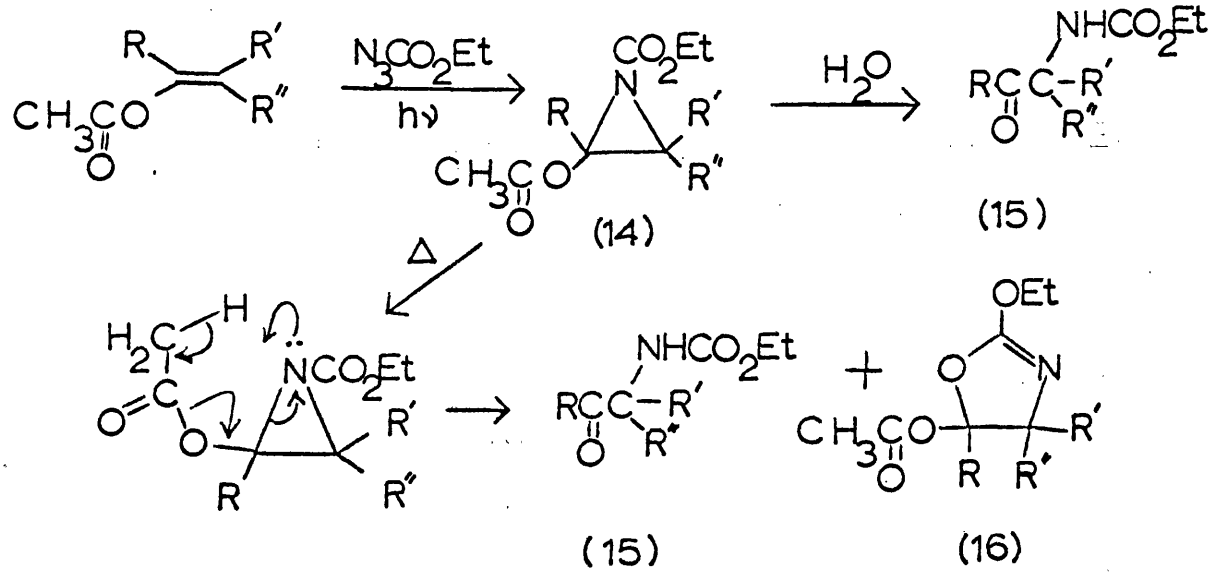
were isolated in high yield. Consequently the stereochemistry of the reactions of singlet and triplet nitrenes have now been well established and are analogous to those of singlet and triplet carbenes as proposed by Skell,[16,17] and treated theoretically by Hoffmann[18] and Anastassiou.[19]

Briefly, singlet nitrenes are responsible for stereospecific addition to olefins and C-H bond insertion, and triplet nitrenes add to

olefins to form aziridines in a non stereospecific manner by a two step process. Ethoxycarbonylnitrene[14] generated photolytically consists of about one third triplet and two thirds singlet. Triplet nitrene can be selectively trapped out with α-methylstyrene (11) to give the urethane (12) and none of the aziridine (13).

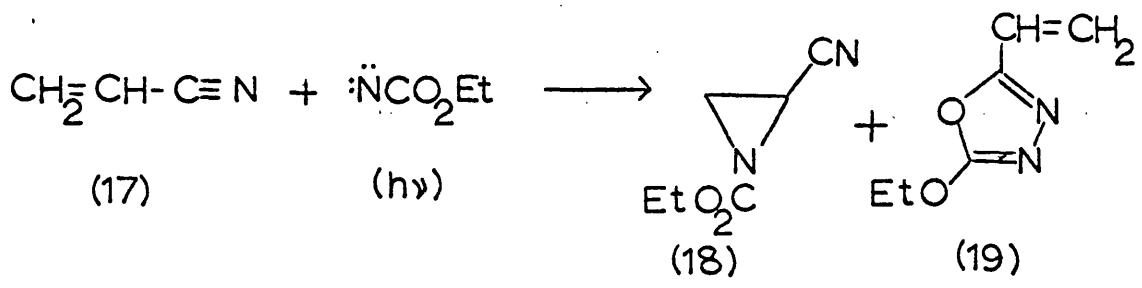


A small amount of work has been done on the addition of ethoxycarbonylnitrene to 'electron rich' olefins such as dihydropyran[20] and the enol acetates.[21] The resultant aziridines have proved to be very labile both to thermolysis and to hydrolysis, which has often hampered their isolation in a pure state.[21] For example, aziridines (14) could be obtained in excellent yield although impure and were converted very readily to the ketourethanes (15) either by a trace of water or on

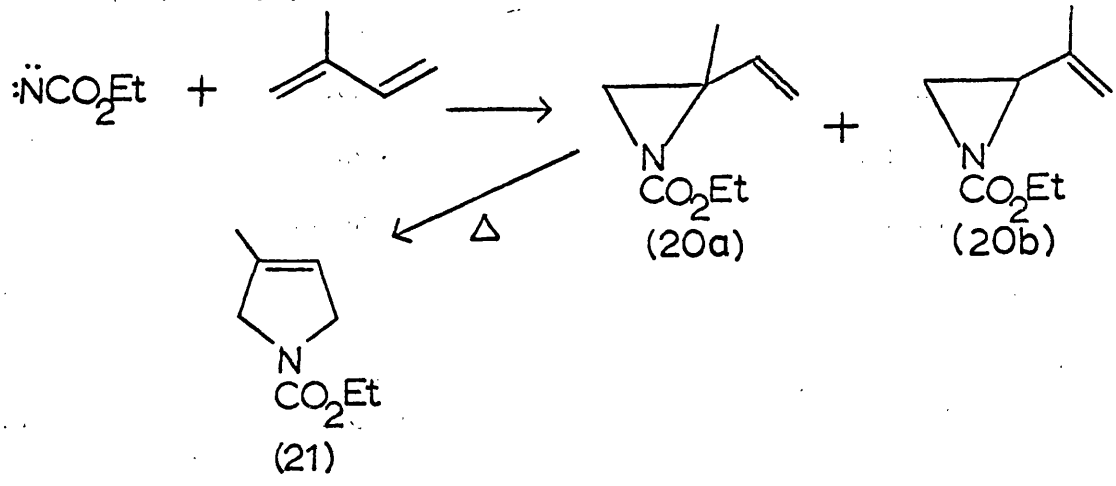


warming. Similarly the dihydrooxazole (16) could be obtained on heating (14), a reaction characteristic of N-carboalkoxyaziridines.[22]

Ethoxycarbonylnitrene has been shown to readily undergo 1,3-dipolar additions to acetylenes and nitriles to give oxazoles and oxadiazoles respectively.[5] However if the nitrene can compete, by 1,2-cycloaddition to an olefin to give an aziridine then this is the predominant reaction.[23,24] Similarly 1,2-cycloaddition is preferred to C-H bond insertion.[25] If acrylonitrile (17) is used as the olefin and dipolarophile, then the 2-cyanoaziridine (18) is produced in five times the yield of the oxadiazole (19).

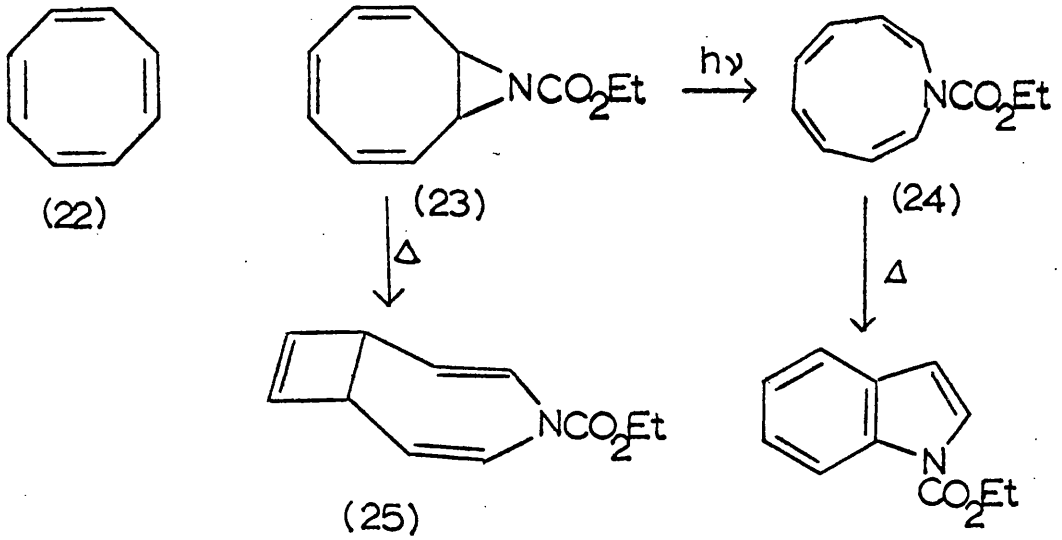


Ethoxycarbonylnitrene also adds 1,2 to dienes to give 2-vinylaziridines (20).[10,22] No 1,3 or 1,4 addition to dienes has ever been observed as a primary product.



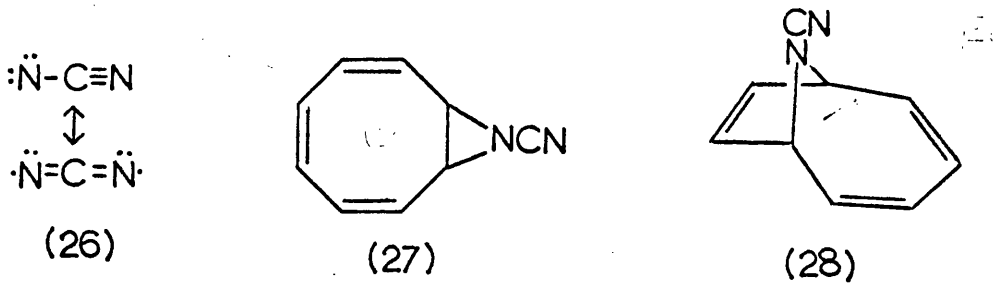
Pyrolysis of the vinylaziridine (20a) yielded the pyrroline (21).

Reaction of ethoxycarbonylnitrene with cyclooctatetraene (22) gives the aziridine (23) which can undergo further photolytic and pyrolytic



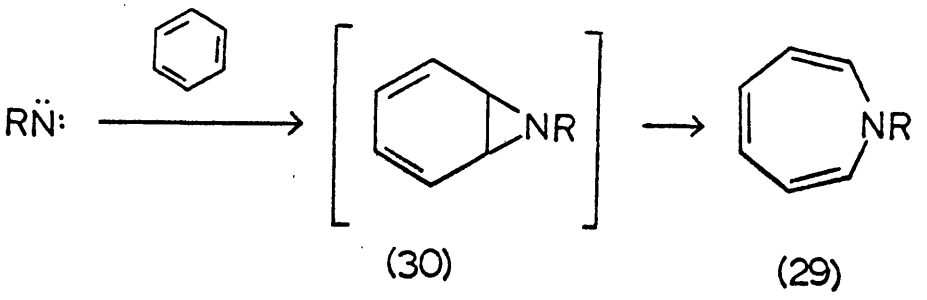
rearrangements to give (24) and (25) respectively.[26,28]

On the other hand cyanonitrene (26)[29] adds both 1,2 and 1,4 to cyclooctatetraene to give (27) and (28) respectively. (28) is thought



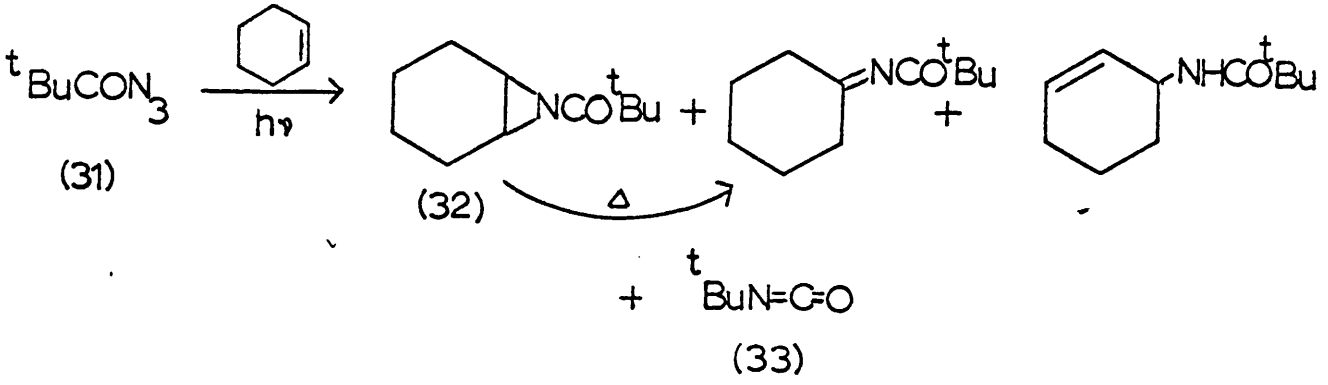
to be a primary product since it is not formed from the aziridine (27) under the reaction conditions. It is thought to be due to triplet nitrene addition.

Alkoxycarbonylnitrenes, cyanonitrene and azidocarbonylnitrene all add to benzene to give azepines (29),[5] presumably via the intermediate aziridine (30) although this has never been isolated or detected.[38]



(30) (29)

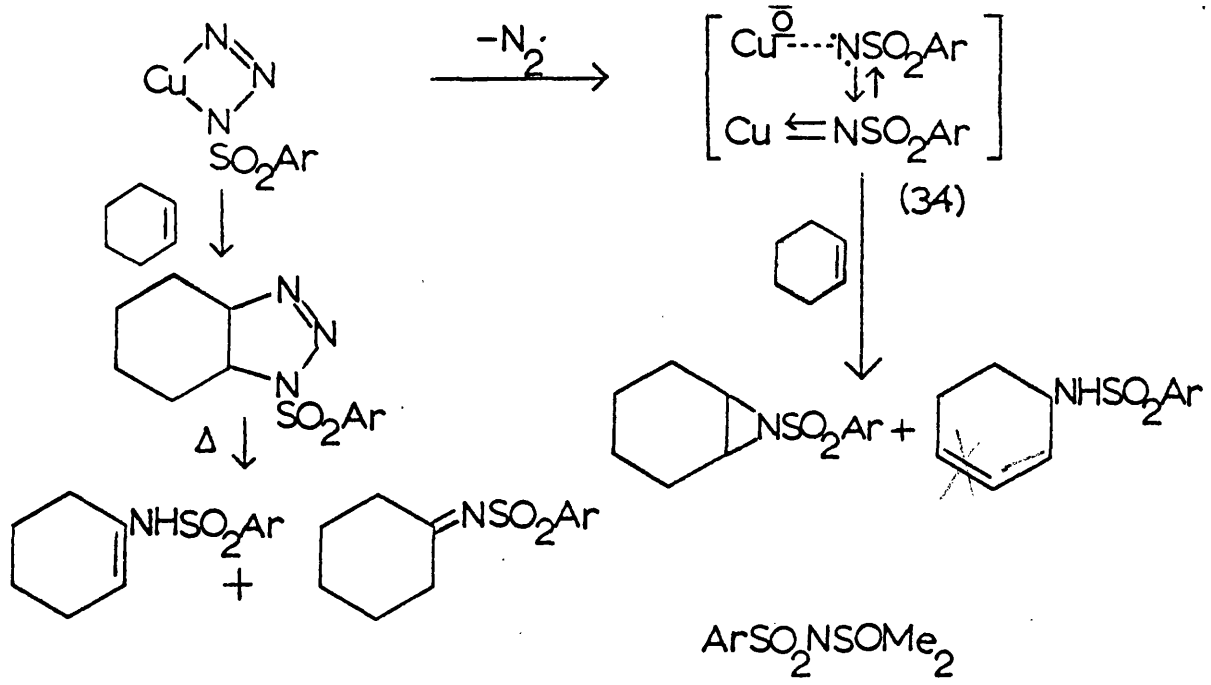
The nitrene derived from the photolysis of pivaloyl azide (31)[15,30] can be trapped with cyclohexene to give the aziridine (32) and other products. However thermolysis of pivaloylazide gives quantitative



(31) (32) (33)

isocyanate (33) and allows no trapping of the possible nitrene intermediate. This suggests that the nitrene is not the source of isocyanate in the Curtius reaction.

Although it is generally assumed that the reaction of sulphonylazides with olefins to give aziridines proceeds via the triazoline (often isolable), there has been one report[31] that during the copper catalysed decomposition of arylsulphonylazides, a copper-nitrenoid intermediate (34) is involved:

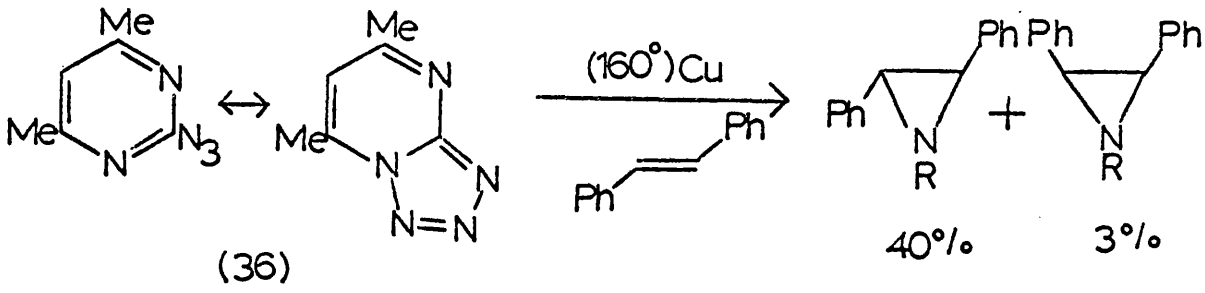


(35)

Addition of dimethylsulphoxide to the cyclohexene traps the nitrene selectively as the sulphoximine (35).

There is one report[32] of the generation of a phosphorus nitrene from a phosphazene azide, and trapping a 1:1 adduct with cyclopentadiene. However there is no conclusive evidence that the adduct is an aziridine.

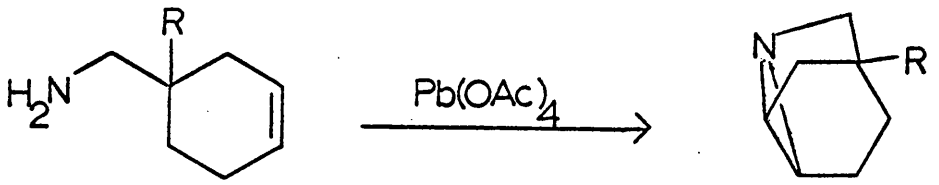
There is also only one reported example[33] of the trapping of a C-nitrene, from the copper catalysed decomposition of 2-azido-4,6-dimethyl-pyrimidine (36) in the presence of trans-stilbene. The reaction was mainly stereospecific.



(36)

Nitrene[34] itself has been added to ethylene at 4°K in a solid argon matrix to give ethylenimine.

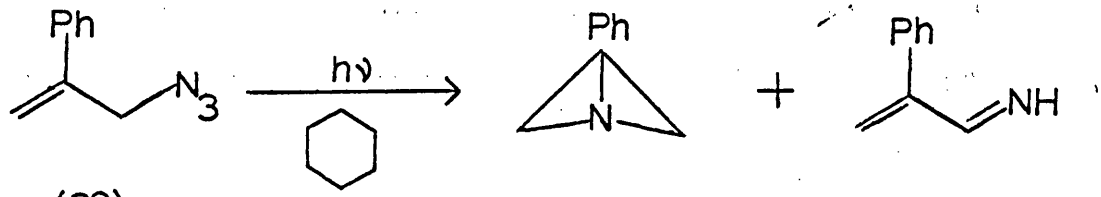
There are several examples of intramolecular addition of nitrenes to double bonds to give aziridines, the most striking being that of Nagata[35] et al: the unsaturated primary amine (37), when oxidised with



(37) (38)

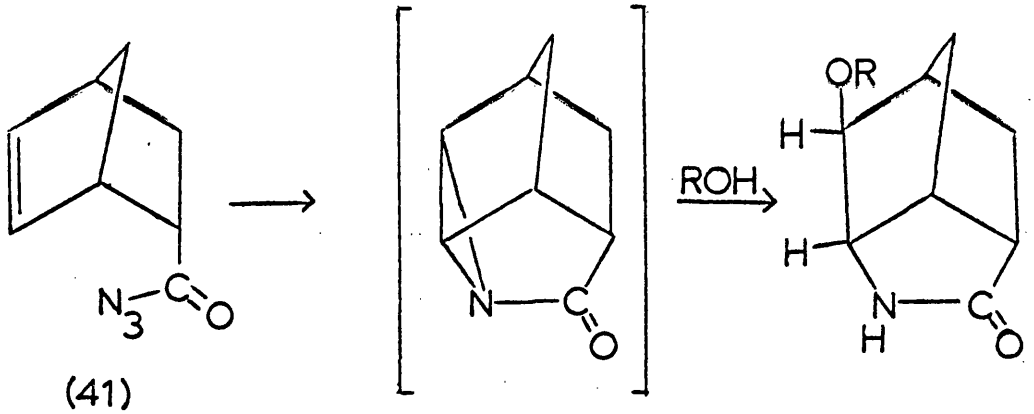
lead tetraacetate gave a high yield of the aza-tricyclooctane (38).

The allyl azide (39)[36] similarly yielded the azabicyclobutane (40) on photolysis.



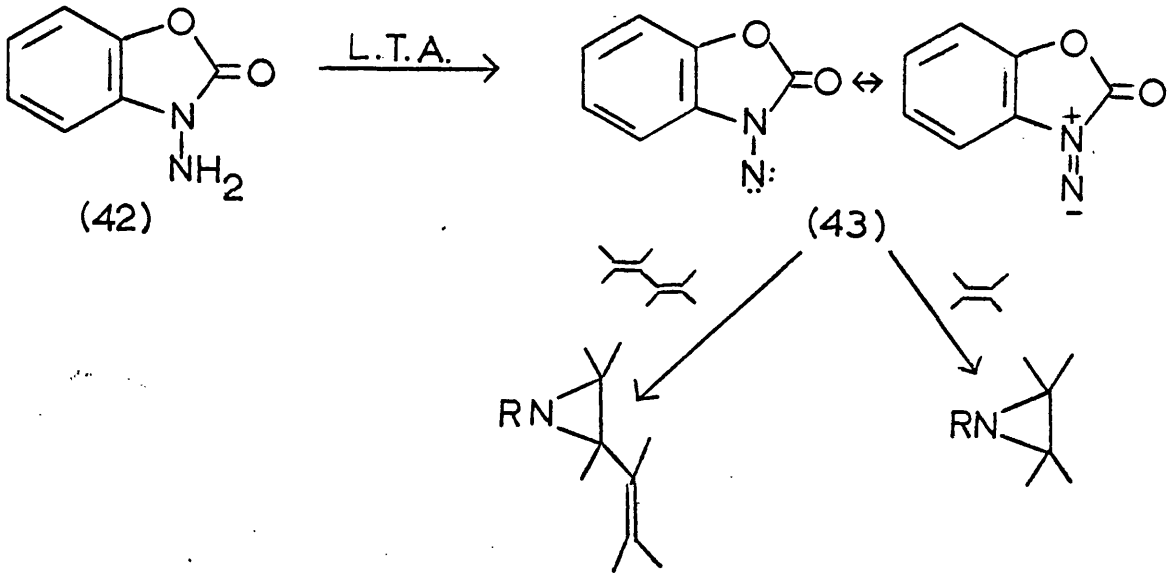
(39) (40)

From certain acyl azides (41) Edwards et al.[37] were able to detect the presence of aziridines and isolate their hydrolysis products.



(41)

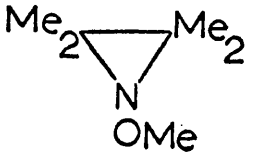
Rees and Atkinson[39,40] showed that aziridines could be isolated in the oxidation of N-aminobenzoxazolin-2-one (42) by lead tetraacetate in the presence of olefins and dienes. Greater than 95% stereospecific addition was observed with cis- and trans-but-2-ene even at very low olefin concentration, suggesting that the nitrene (43) is generated and trapped in its singlet state which is probably stabilised by electron delocalisation as shown.



(42) (43)

Very recently this method of generating nitrenes has been extended by Brois.[41] The oxidation of methoxyamine (44) by lead tetraacetate in the presence of tetramethylethylene led to the isolation of the N-methoxyaziridine (45).

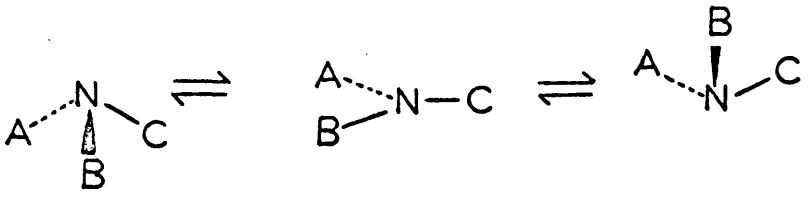
(44)



(45)

2. Retarded Nitrogen Inversion as studied by N.M.R. Spectroscopy

Nitrogen inversion in amines has received considerable attention especially during the last decade.[42] The process involves the rehybridisation of the electrons on the nitrogen from pyramidal sp^3, through the planar sp^2 transition state, and finally to the inverted sp^3 pyramid.



A necessary condition for observation of nitrogen inversion by N.M.R. spectroscopy is that a particular nucleus (usually a proton) should have different chemical shifts in the two invertomers. The larger the chemical shift difference, then the easier is its detection. If inversion is very fast then the N.M.R. spectrum would show a time-average position for a particular proton, the non-equivalence only being resolved when the rate of inversion has been reduced to say ca. 60 $sec.^{-1}$ and lower.

N.M.R. spectroscopy allows access to intramolecular processes which involve activation energies of the order of ca. 5-25 kc. $mole.^{-1}$. These figures being determined by the lowest (ca. -170°) and the highest (ca. 220°) temperatures at which high resolution spectra can be obtained. In this range of activation energies, the processes are so fast that separation of isomers is impossible at room temperature.

The process of inversion in primary amines is generally sufficiently fast not to allow its detection by N.M.R. methods. The activation energy

for ammonia and many primary amines has been calculated to be $\leqslant 6$ kc. mole.$^{-1}$.

Free energy of activation for inversion ($\Delta G^{\ddagger}$) has been calculated using the relationships adopted by Gutowsky and Holm[43] utilising the coalescence temperature (Tc) and the maximum chemical shift difference ($\Delta\nu_{AB}$) of the same proton in different invertomers.

$$\text{Rate of inversion} \quad K_r \approx \frac{\pi\Delta\nu_{AB}}{\sqrt{2}} \approx \frac{K_B Tc}{h} e^{\frac{-\Delta G^{\ddagger}}{RTc}}$$

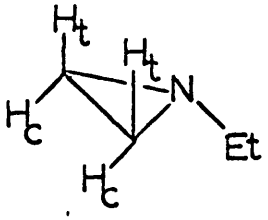
For the separation of actual nitrogen invertomers at room temperature, then $\Delta G^{\ddagger}$ must be $\geqslant 25$ kc. mole.$^{-1}$, which follows from earlier predictions.[44]

When the amine nitrogen atom is incorporated in a ring, the process of inversion becomes less frequent and is satisfactorily studied by N.M.R. techniques. Frequently the room temperature spectra, especially of aziridines, will show the presence of both invertomers.

This fact can be explained by considering the planar transition state where the hybridisation of the nitrogen is sp^2, and the bond angles at optimum geometry are 120°. In aziridine rings the internal nitrogen bond angle is just >60°, consequently, if in the transition state this angle tends to 120° then considerable strain is introduced i.e. the activation energy is increased and the process becomes less favourable.

In the case of 4-,[45] 5-,[46,47] 6-,[48–50] and 7-,[47] membered rings, invertomers can often be observed upon running the spectrum at low temperature. However N.M.R. studies of piperidine derivatives are not completely unambiguous since there is also the competing process of ring inversion.

Bottini and Roberts[51] were the first to show experimentally that the rate of inversion in N-alkyl substituted aziridines was sufficiently slow for it to be detected by N.M.R. techniques. The 40Mc. spectrum of 1-ethylaziridine (46) at room temperature showed two distinct bands for the aziridine ring protons, separated by 27c.p.s..



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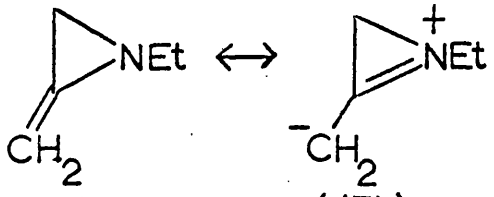


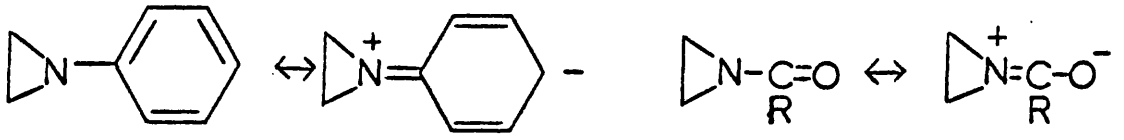
(47a) (47b)

The high and low field signals have been assigned to the protons cis-(Hc) and trans-(Ht) to the N-ethyl group respectively.[52] That the geminal protons showed non-equivalence indicated that inversion was slow on the N.M.R. time scale. The two bands coalesced to a broad singlet at ca. 110°, at the mean position. Upon cooling, the original spectrum was obtained.

In contrast to (46), the N.M.R. spectrum of 1-ethyl-2-methylene-aziridine (47) at room temperature showed a single band for the aziridine ring protons. However on cooling to -80° and below, this was resolved into two bands of equal intensity separated by ca. 30c.p.s. The coalescence temperature was found to be between -60° and -70°. It follows that the barrier to inversion in (47) is considerably less than that of (46). This is thought to be due to the contribution of the electron delocalised form (47b), greatly favouring the planar transition state.

These observations were followed[53] by a study of the effect of various N-alkyl and aryl substituents on the rate of inversion, and have received more reliable attention by Brois.[52,54,55] The outcome of these observations is that the attachment of bulky groups, such as t-butyl, to

the nitrogen atom does not increase the rate of inversion as much as was first thought,[53] except in the cases where these groups can delocalise the nitrogen lone pair by a conjugative effect, as in (48), (49) and (50). The small increase in rate that is observed with non-



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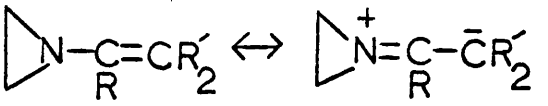


(50)

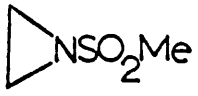
conjugative bulky groups is due to the fact that the transition state of the molecule is less sterically crowded than the ground state.

Early observations were hindered mainly by the low operating frequencies, often as low as 20.5Mc.,[56] when the chemical shift difference of geminal aziridine ring protons was small in comparison to the rate of inversion.

The electronic effect of the N-substituent plays an important role in the frequency of inversion. Studies[53,56–62] have shown that electron attracting substituents increase the rate of inversion by electron delocalisation of the nitrogen lone pair, hence stabilising the planar transition state. This effect accounts also for the fact that nitrogen inversion in amides is so rapid that it has so far eluded detection by N.M.R. spectroscopy. The conjugative effect previously mentioned is also important.

For N-sulphonylaziridines[56,57,59,60] the increase in rate observed has been accounted for by the dpπ planar overlap enhancing the attainment

of the planar transition state, similar to the pπ overlap described for 1-phenylaziridine (48).[57,59] That the size of the substituent in N-sulphonylaziridines does not alter the rate of inversion or activation energy appreciably may be seen by comparing 1-methylsulphonylaziridine (51)[58] and 1-phenylsulphonylaziridine (52).[59]



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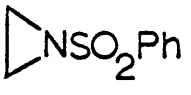
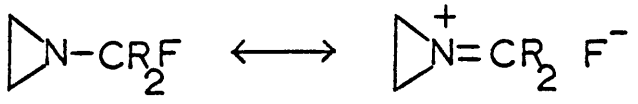


(52)

$\Delta G^{\ddagger}$	=	14.0 kc. mole.$^{-1}$	$\Delta G^{\ddagger}$	=	12.4 kc. mole.$^{-1}$
Tc	=	-25°	Tc	=	-30°
K_r	=	25 sec.$^{-1}$	K_r	=	36 sec.$^{-1}$

Similarly the high rate of inversion of N-fluoro-alkylaziridines[63,64] with respect to the alkyl aziridines, has been attributed to 'negative hyperconjugation':-



The effect of an electronegative 'hetero' atom, particularly O, N, Cl and S, attached directly to the nitrogen atom of amines profoundly alters the rate of inversion since the effect can operate in two ways:

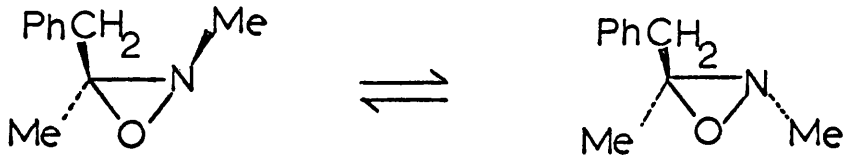
(i) With increasing electronegativity of the N-substituent, the p-character of the nitrogen lone-pair is reduced, favouring the pyramidal ground state.

(ii) Lone pair - lone pair steric interactions between the nitrogen and 'hetero' atom are less in the pyramidal ground state than in the planar transition state.

The overall effect is thus to increase the energy of activation and to reduce the rate of inversion.

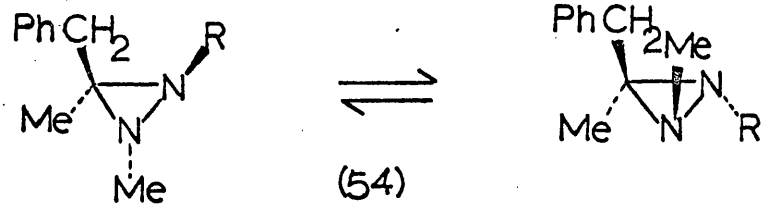
Consequently it is not surprising to find that the inversion of even acyclic (a) hydroxylamine[65–67] and (b) hydrazine[68,69] derivatives has been observed by N.M.R. methods, as well as for the cyclic derivatives of (a)[70–72] and (b).[73,74]

The effect is especially important in oxaziridines and diaziridines where the 'hetero' atom effect and the ring strain have been combined. This combination has allowed the separation of stable invertomers at room temperature,[75–78] e.g. of 2,3-dimethyl-3-benzyloxaziridine (53),[77]



(53)

and of the analogous diaziridine (54),[78] and the isolation of an optically



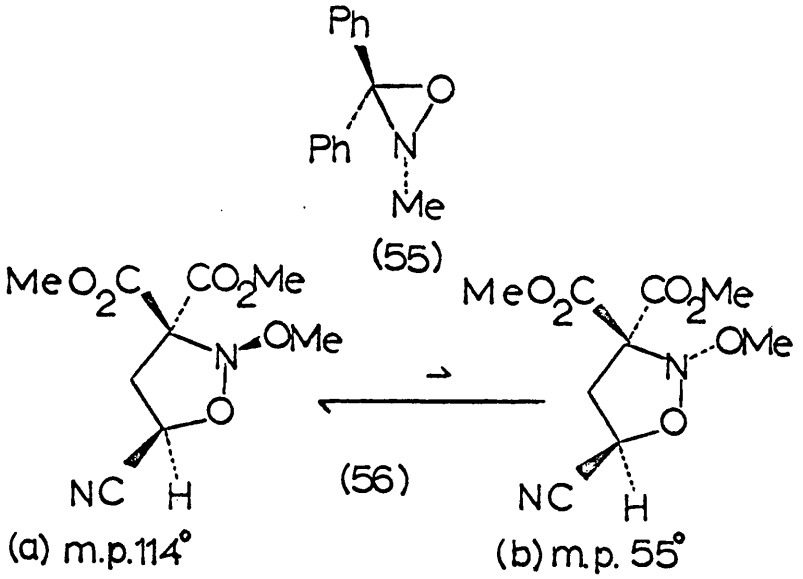
(54)

(i) R = -H $\Delta G^{\ddagger}$ ca. 26.7 kc. mole.$^{-1}$

(ii) R = $-CH_2Ph$ $\Delta G^{\ddagger}$ ca. 27.3 kc. mole.$^{-1}$

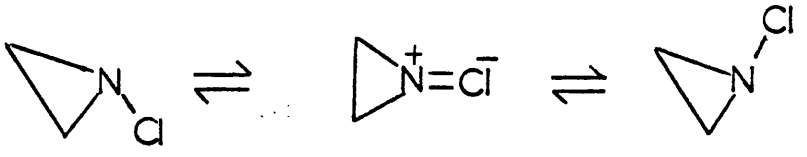
active oxaziridine (55),[79] as a result of non-inverting nitrogen.

There is also one remarkable report by Eschenmoser[72] on the separation, at room temperature, of invertomers of a 1,2-oxazolidine derivative (56).



The less stable isomer (56b) has been confirmed by X-ray analysis to have the trans-configuration.[80] Presumably this isolation has been possible because of the internal and external 'hetero' atom effect and should be compared with the observations of Lehn[70] and Griffith[71] on simple N-alkyl substituted 1,2-oxazolidines where $\Delta G^{\ddagger}$ is 10-15 kc. mole.$^{-1}$.

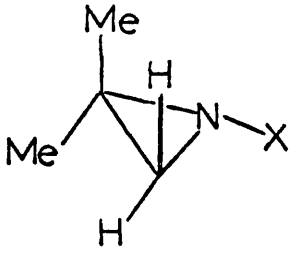
Initial observations[56] of the 20.5Mc. N.M.R. spectrum of N-chloroaziridine (57) suggested that the rate of inversion was rapid even at -100° and it was suggested that the contribution from (57b) could



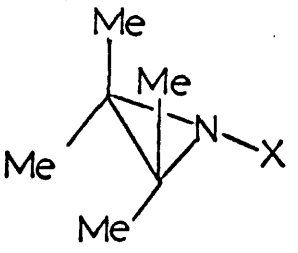
(57a) (57b) (57c)

stabilise the transition state via d-orbital resonance - similar to that

suggested for N-benzyl-N-methylchloramine.[65] That the inversion of (57), on the N.M.R. timescale, was fast, was also the later conclusion of Anet et al.[59] They were however not completely convinced since they predicted that N-chloroaziridine (57) should have a low rate of inversion due to the high electronegativity of the chlorine and the lone-pair repulsions between the chlorine and nitrogen atoms. These predictions were soon realised by Brois[81] with the synthesis of 1-halogeno-2,2-dimethylaziridine (58) and 1-halogeno-2,2,3,3-tetramethyl-aziridine (59).



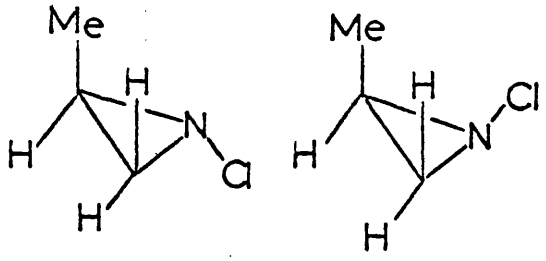
(58) (a) X=Cl
(b) X=Br



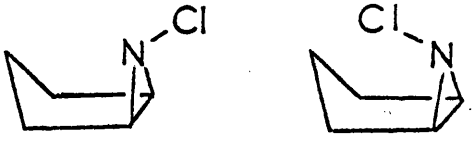
(59)(a) X = Cl
(b) X= Br

The N.M.R. spectra of (58) showed non-equivalent methyl groups and aziridine ring protons; (59) showed two types of methyl groups present; both observations are consistent with slow inversion at nitrogen.

So effective is the retardation of the inversion by N-halogen substitution that, in suitably designed aziridines, the separate invertomers can be isolated,[82–84] e.g. 1-chloro-2-methylaziridine (60)[82] and 7-chloro-7-azabicyclo[4,1,0]heptane (61).[83]



(60)

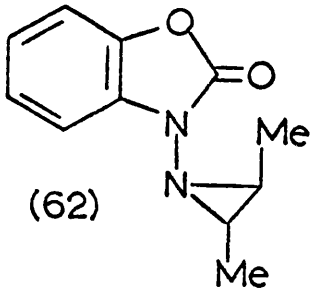


(61)

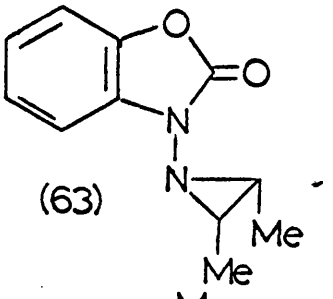
Determination of the coalescence temperatures for N-chloroaziridines is hampered by their thermal instability but reported values of Tc and $\Delta G^{\ddagger}$ for 1-chloro-2,2-dimethylaziridine (59a) are >180° and >23.5 kc. mole.$^{-1}$ respectively.

A reinvestigation[85] of earlier work[56] by Russian workers on N-halogenoaziridines studied now at 60Mc. agrees with the observations of Brois and Eschenmoser that the inversion is slow.

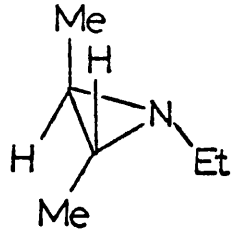
Atkinson[40,86] recognised that inversion in N-aminoaziridines was sufficiently slow to be detected, in the study of the benzoxazolinone substituted aziridines (62) and (63).



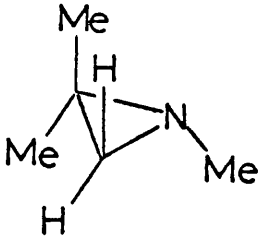
(62)



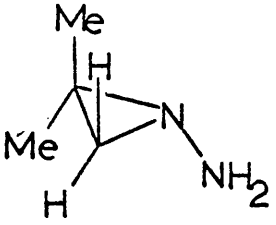
(63)



(64)



(65)



(66)

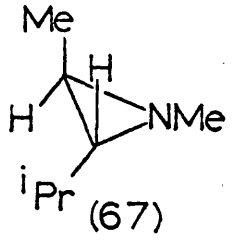
The room temperature spectrum of (62) exhibited non-equivalence of the ring protons and the C-methyls. The coalescence temperature was ca. 150°; this is higher than that reported (ca. 60°) for trans-2,3-dimethyl-1-ethylaziridine (64) and 1,2,2-trimethylaziridine (65), and lower than that reported[45] (>180°) for 1-chloro-2,2-dimethylaziridine (58a). In terms of electronegativity of the N-'hetero' atom, this is precisely as anticipated.

It was subsequently shown[87] that the methyl groups in 1-amino-2,2-dimethylaziridine (66) still showed non-equivalence at ca. 150°: determination of the exact Tc again being thwarted by the thermal instability of (66).

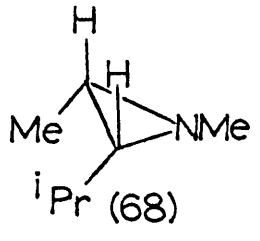
It seemed a logical conclusion that 1-methoxy-2,2,3,3-tetramethylaziridine (45)[41] should exhibit retarded nitrogen inversion with Tc >130° and $\Delta G^{\ddagger}$ >22 kc. mole.$^{-1}$.

Most of the values of $\Delta G^{\ddagger}$ reported for aziridines have been obtained using the expression stated earlier. However the validity of the comparison of $\Delta G^{\ddagger}$'s obtained by this method is open to question, since they are obviously obtained at different temperatures. Roberts[88] has questioned the validity of the approach, suggesting that line shape parameters as a function of temperature give more accurate values, an improvement on line-width parameters.[89] The first value reported[89] of $\Delta G^{\ddagger}$ for 1,2,2-trimethylaziridine (65) was ca. 19 kc. mole.$^{-1}$, this compares with the more recent value[88] of ca. 24 kc. mole.$^{-1}$.

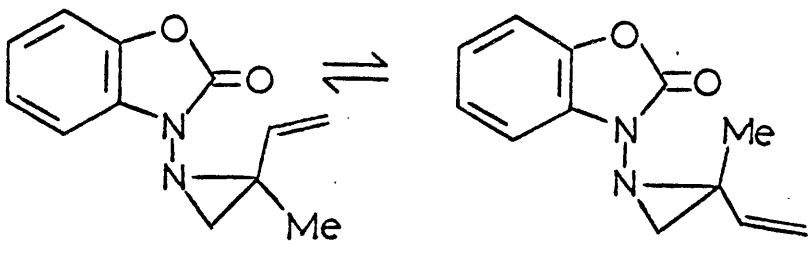
The use of the slow inversion phenomenon in suitably N-substituted aziridines has received little attention as a tool for conformational analysis. Bottini et al.[90,91] studied the quaternisation of aziridines (67) and (68) with methyl iodide and found that the quaternary salts



(67)



(68)



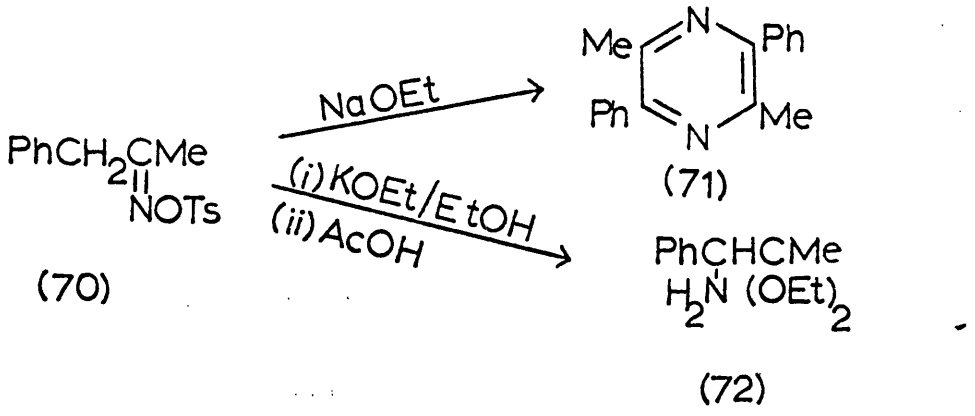
(69)

isolated did not necessarily reflect the invertomer ratios as indicated by N.M.R. spectra. This was later shown[92] to be due to halide ion catalysed equilibration of the tetraalkylaziridinium ions. More reliable results were obtained using methyl benzenesulphonate[93] for quaternisation.

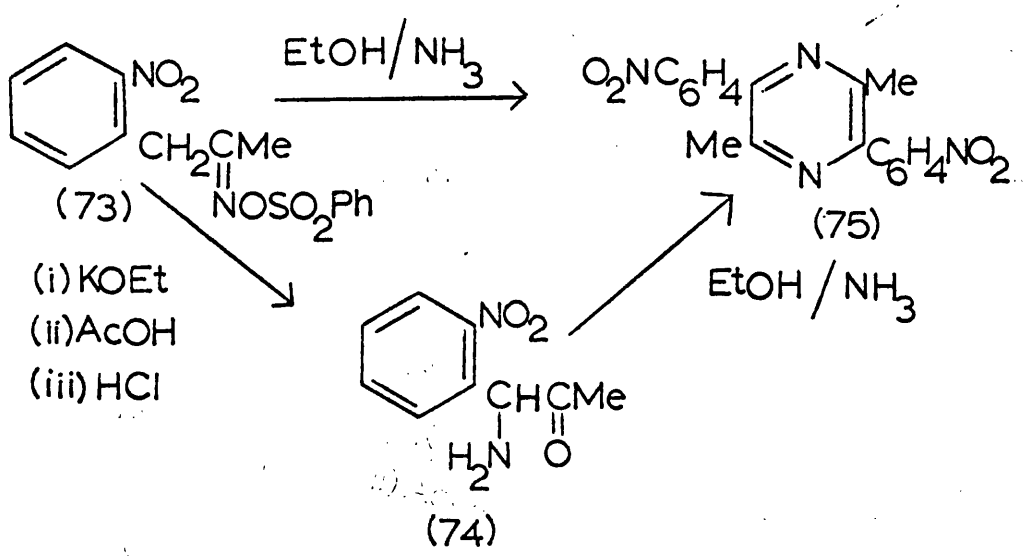
Atkinson[40] has demonstrated from analysis of invertomer ratios in aziridine (69), that the vinyl group is less sterically demanding than the methyl group, in harmony with the conformational analysis results in the cyclohexane ring system.[94]

3. Synthetic Approaches to 2 H -Azirines

(i) In 1923 Neber and Friedolsheim[95] whilst studying the Beckmann Rearrangement, observed the abnormal behaviour of certain benzylketoxime arylsulphonates. Treatment of 1-phenyl-2-propanoneoximetosylate (70) with sodium ethoxide gave 2,5-dimethyl-3,6-diphenylpyrazine (71), whereas potassium ethoxide in ethanol followed by acetic acid gave the α-aminoketal (72). Similarly with 1-(2-nitrophenyl)-2-propanone oxime



benzenesulphonate (73), the α-aminoketone (74) and the pyrazine (75)

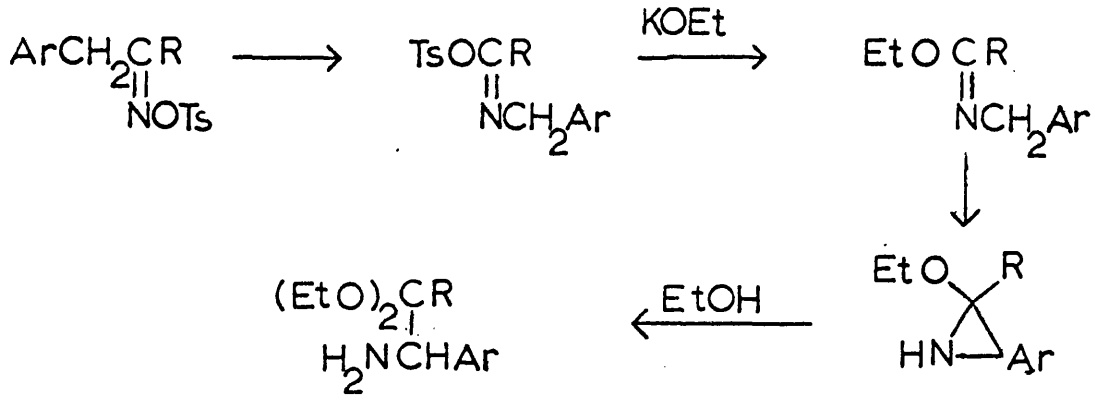


could be isolated under certain reaction conditions as indicated above, the α-aminoketone undergoing self intermolecular condensation to give the pyrazine.

The ketoximebenzenesulphonate derived from dibenzylketone[96] behaved analogously to (73).

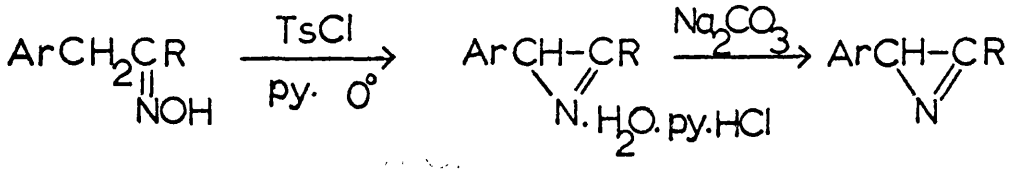
This useful synthesis of α-aminoketones from ketoximearylsulphonates has had numerous synthetic applications[97] and has consequently been termed the 'Neber Rearrangement'.

An early attempt by Neber[95] to explain the mechanism involved a Beckmann type rearrangement.



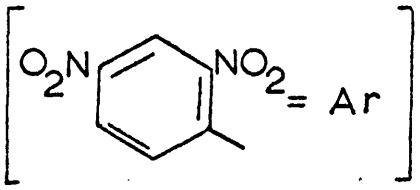
However, subsequent observations[98,99] showed that the rearrangement could be effected during the addition of the sulphonylchloride to the ketoxime in pyridine at 0°.

Salt-like intermediates were isolated, for which the structures (76)[98] and (77)[99] were proposed. The free azirines (78) and (79) could be isolated upon treatment of the salts with dilute sodium carbonate solution.

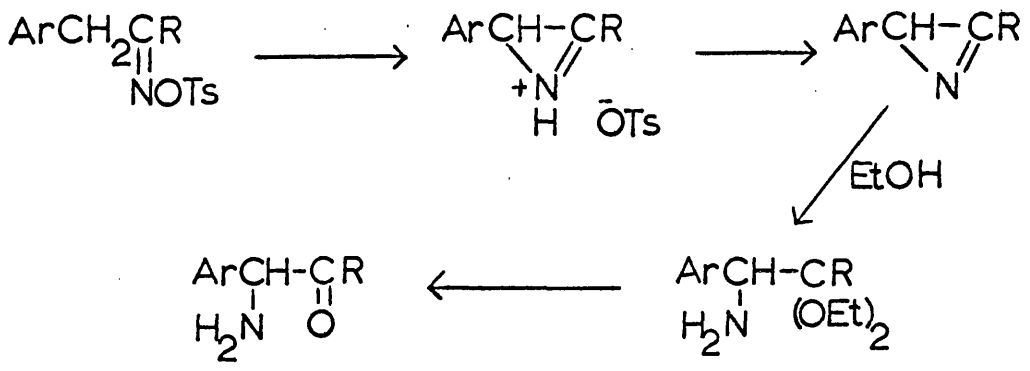


(76) R= Me
(77) R= Ph

(78) R=Me
(79) R=Ph



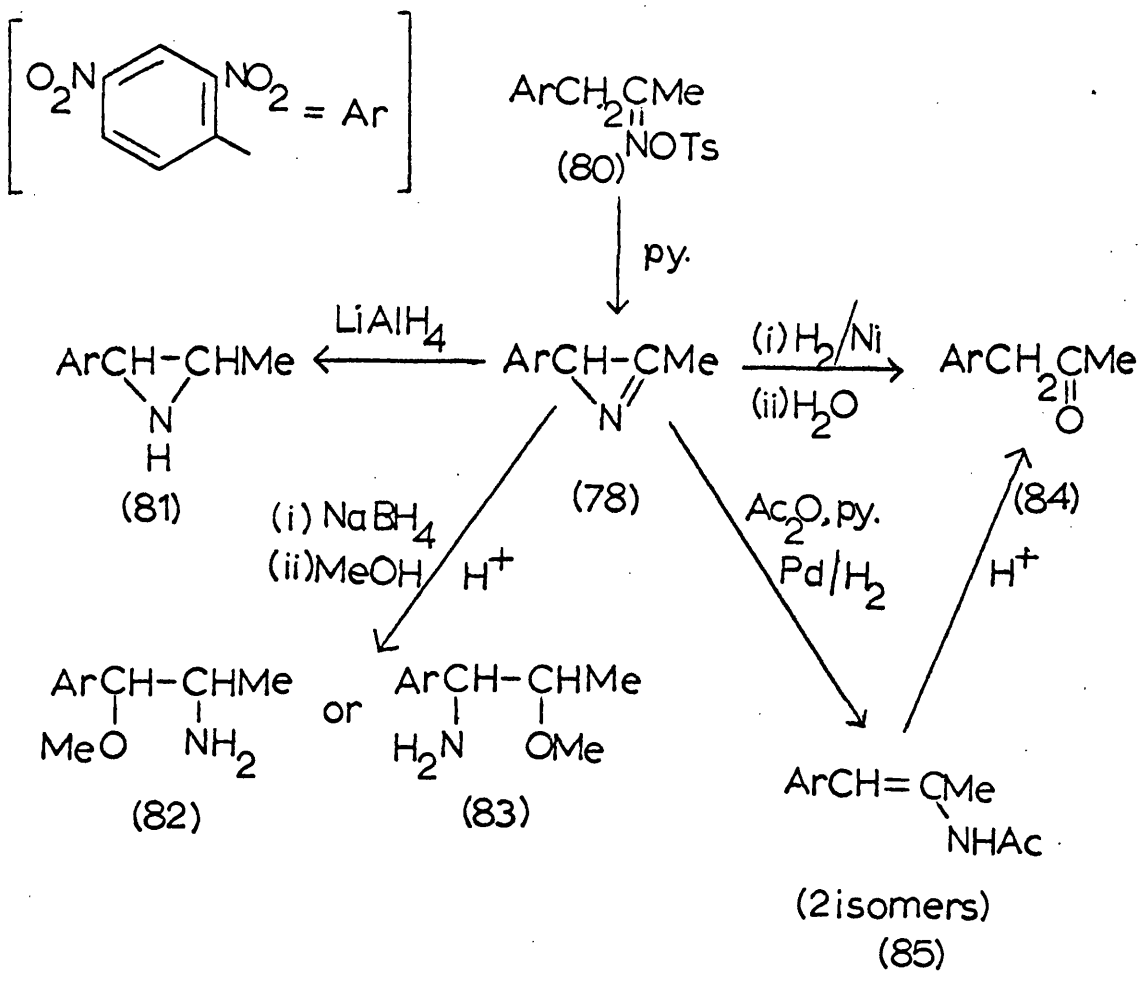
Upon more vigorous hydrolysis, the azirine complexes (76) and (77) gave either the dihydropyrazine or the α-aminoketone. Consequently the isolation of these complexes warranted a review of the mechanism, shown below. The Neber rearrangement received negligible attention after



Neber's last extension of it in 1936,[100] until 1953 when Cram and Hatch published their critical examination on the mechanism[101] and scope[102] of the reaction. They prepared the oximetosylate (80) in the absence of pyridine, using instead dioxan-water-sodium bicarbonate. When subjected to Neber's original conditions i.e. pyridine, (80) was found to give the same azirine (78) as observed earlier.[98] Besides confirming all of Neber's earlier observations on the reactions of (78), they also added further evidence for the structure as outlined.

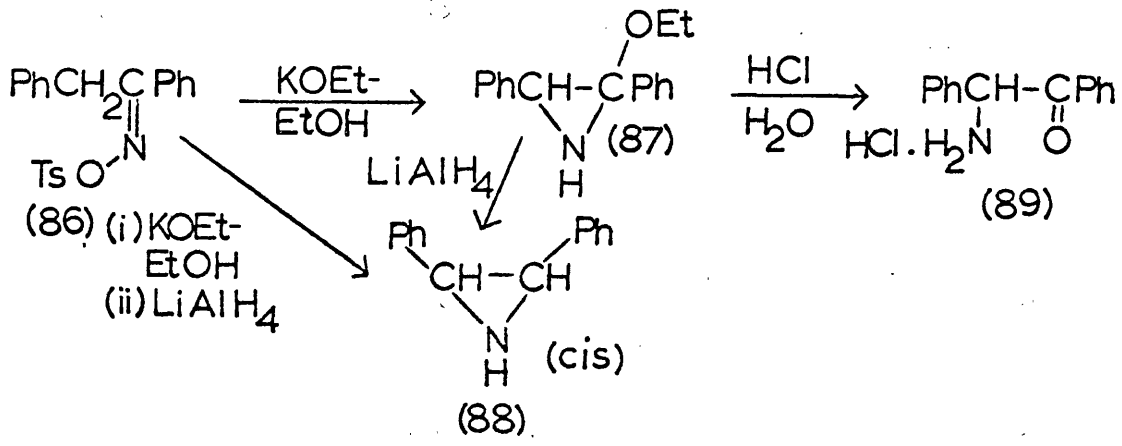
Treatment of the azirine (78) with lithium aluminium hydride gave a small yield of the aziridine (81); sodium borohydride in methanol gave the β-aminoether (82) or (83).

Hydrogenation in the presence of Raney nickel catalyst produced the ketone (84) in ca. 50% yield, hydrogenation in acetic anhydride/pyridine medium with palladium on charcoal catalyst produced the two isomeric vinyl acetamide compounds (85) which on acid hydrolysis yielded the ketone (84).



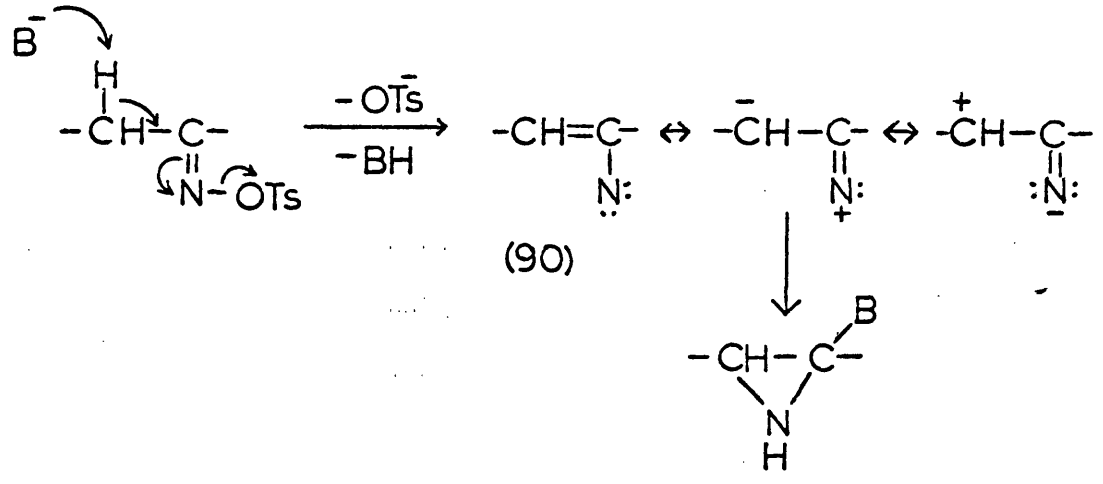
Spectroscopic evidence was also presented, notably the C=N vibration in the I.R. spectrum of (78) at ca. 1800 $cm.^{-1}$; absent in the aziridine (81).

However they did not feel that the dinitrophenylacetone system was typical of the reaction since the benzylic proton is very acidic due to the two nitro groups, so that it can be removed by pyridine. Furthermore the resultant azirine would be considerably stabilised by the presence of the nitro groups. Consequently[102] they reinvestigated the reaction of the ketoxime-p-toluenesulphonate (86) derived from desoxybenzoin, with potassium ethoxide in ethanol. The reaction sequence is shown below.



Although they were unable to isolate the azirine, they were able, using low temperature techniques, to isolate the unstable 2-ethoxyaziridine (87) which on treatment with lithium aluminium hydride yielded cis-2,3-diphenylaziridine (88). (Neber and Huh[99] succeeded in isolating only desylaminehydrochloride (89)). Similar results were obtained for the p,p'-dichlorodesoxybenzoin derivative, although only the reduced aziridine, and not the 2-ethoxyaziridine could be isolated.

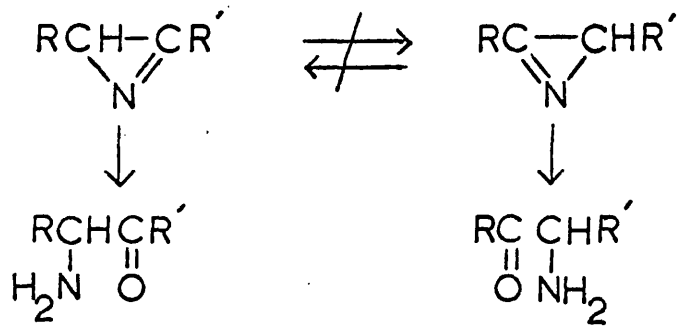
They proposed the mechanism shown below, an extension of Neber's revised form.



The initial step is the base induced elimination of an α-proton followed by (or synchronous with) the loss of the tosyloxy function, with subsequent ring closure. The existence of the vinyl nitrene species (90) was purely speculative, but it cannot be excluded in view of its likely participation in the pyrolysis and photolysis of vinyl azides (described later).

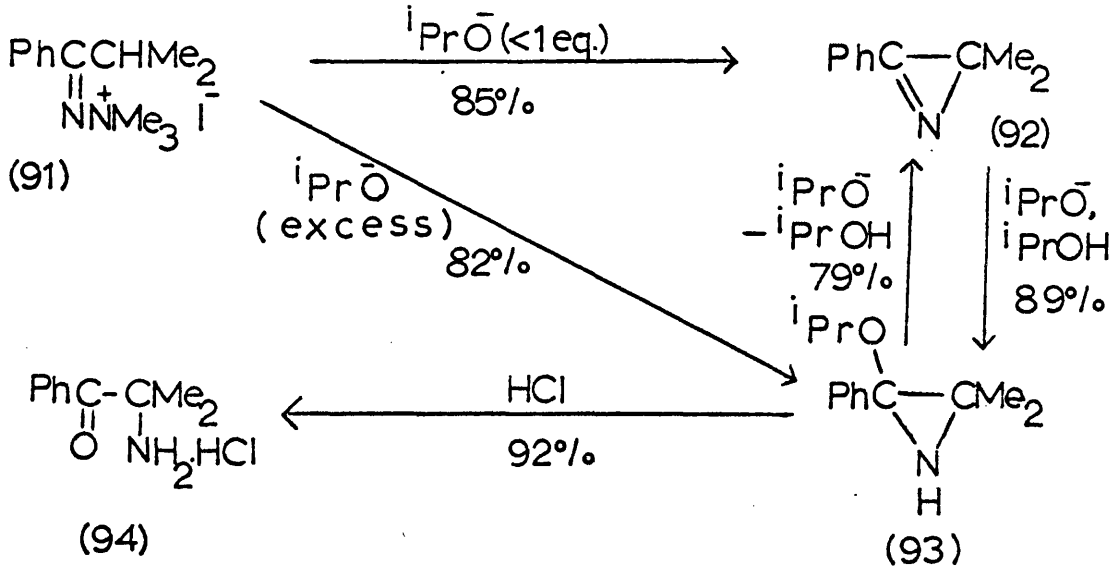
It was subsequently demonstrated[103] that the rearrangement does not depend upon the configuration of the oximetosylate and that cyclisation occurs with removal of the more acidic proton if the two carbon atoms α to the ketoxime linkage both possess protons. Similarly it was shown that the carbonyl carbon atom in the resulting α-aminoketone was the same

as the carbon of the carbon-nitrogen double bond of the ketoxime, eliminating any possible tautomerisation of the intermediate azirine of the type indicated below.



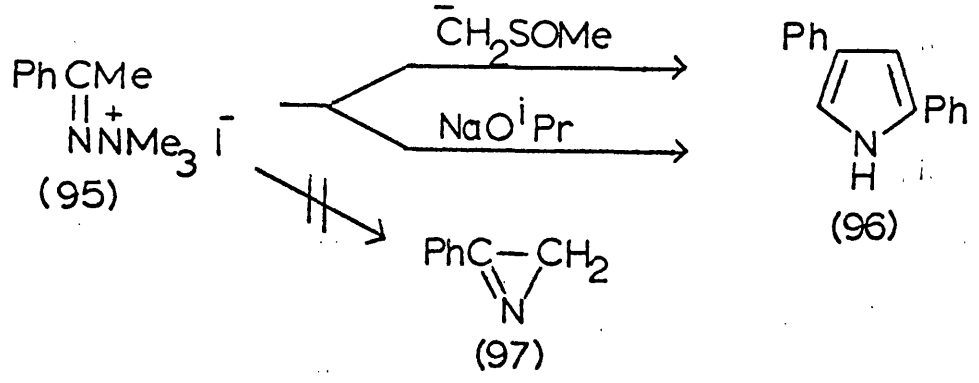
The mechanistic conclusion[103] was in harmony with that of Cram and Hatch.[102] The resultant 2-alkoxyaziridine was derived from the addition of alcohol to the intermediate azirine (cf. ref. [104]).

(ii) A reaction of parallel mechanism to the Neber rearrangement is the base catalysed rearrangement of dimethylhydrazone methiodides bearing α-hydrogen atoms, to the corresponding α-aminoketone.[105] The reaction is perhaps best demonstrated with the methiodide (91),[104] where the intermediate azirine proved to be very stable.

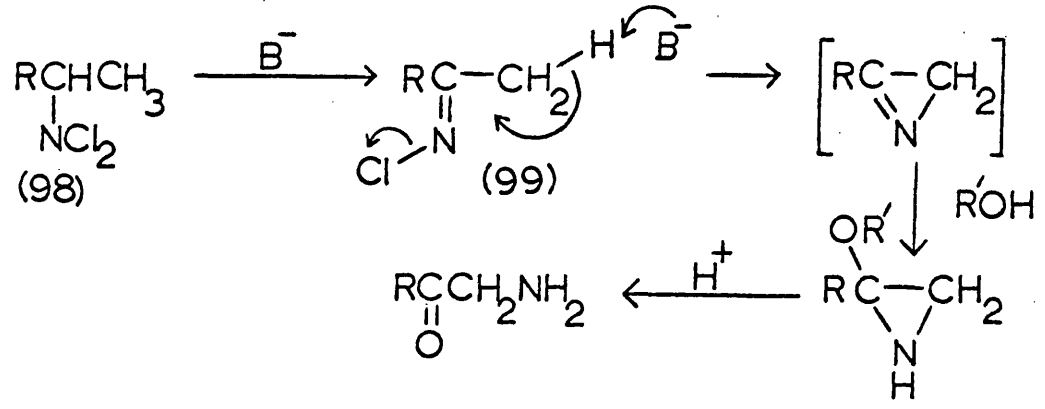


When the dimethylhydrazone methiodide (91) was treated with just less than one equivalent of base, the azirine (92) was isolated in high yield. When treated with excess base, the 2-alkoxyaziridine (93) was similarly isolated. The azirine (92) was found to react readily with excess base in alcohol to give the aziridine (93) which could be converted back to the azirine (92) by treatment with a catalytic amount of base and removal of the alcohol. Both the azirine (92) and the aziridine (93) on acid hydrolysis gave the α-aminoketone (94), the aziridine being the more labile.

The above reaction has subsequently been utilised in the synthesis of a steroidal azirine[106,107] and has received a brief examination of its scope by Sato.[108] He concluded that:- (a) if the α-hydrogen was on a tertiary carbon atom, then azirines could be isolated in good yield; (b) when on a secondary carbon atom, the azirine produced was generally unstable and dimerised to the pyrazine or added alcohol to give a 2-alkoxyaziridine; (c) when the α-position was a primary carbon atom, then he could isolate none of the usual products (whereas Smith and Most[105] isolated phenacylaminehydrochloride (35%) by treatment of (95) with sodium ethoxide!). Instead, for example, acetophenonedimethylhydrazone methiodide (95)[109] yielded 2,4-diphenylpyrrole (96), resulting[108] from the reaction of 2-phenylazirine (97)[110] with the carbanion of acetophenone.



(iii) A second reaction similar to that of the Neber rearrangement, and worthy of comment, is that discovered by Baumgarten[111] in which a N,N-dichloro-sec-amine, when treated with base, yields an α-aminoketone. The initial step has been shown[112,113] to be the base catalysed dehydrochlorination of the dichloroalkylamine (98) to give the

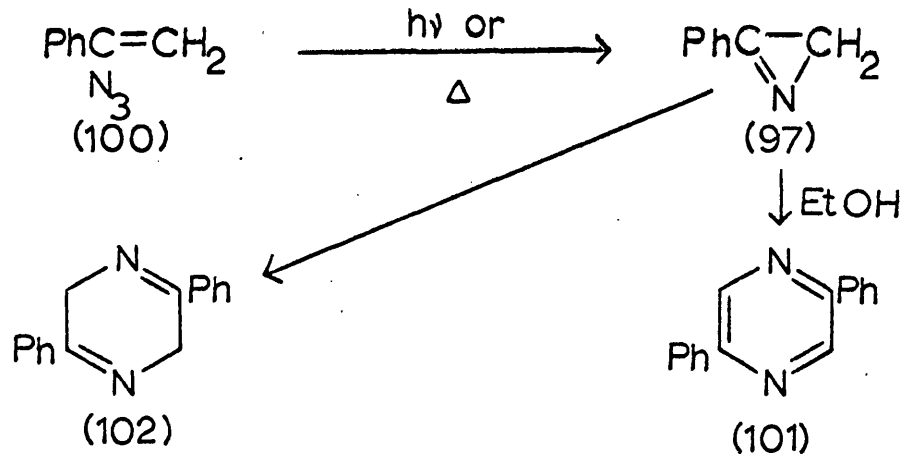


N-chloroketimine (99). The second stage was believed to proceed via a similar mechanism to that proposed by Cram and Hatch for the Neber rearrangement since the same cis-2,3-diphenylaziridine (88) could be isolated by Baumgarten[114,115] as by Cram and Hatch.[102] However no azirines as yet have been isolated from N,N-dichloro-sec-amines.

When the Neber rearrangement[102] and the N,N-dichloro-sec-amine[111] rearrangement were extended to aldoximes and primary amines respectively, they yielded nitriles as the major products. These were thought to have been formed via an E_2 mechanism. These observations can be compared with the pyrolysis and photolysis of terminal vinyl azides (discussed later), where often the major product is the nitrile.

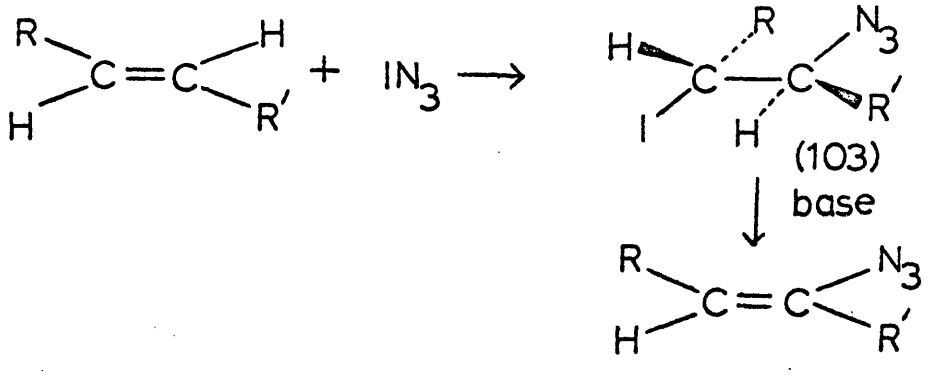
(iv) Perhaps the most useful synthesis of azirines involves the pyrolysis and photolysis of vinyl azides.[5] Smolinsky[116,117] found that the vapour phase pyrolysis (350-360°; 0.1-0.3 mm.) of α-azidostyrene (100) gave,

in high yield, 2-phenylazirine (97), which was converted in boiling ethanol to 2,5-diphenylpyrazine (101).



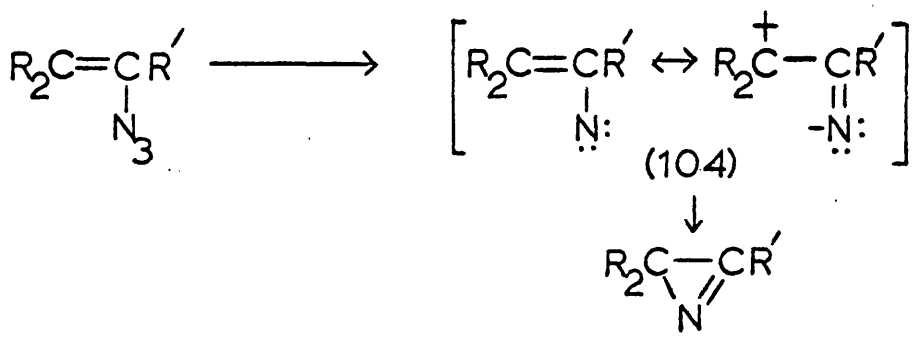
The subsequent photolysis of (100) by Horner[110] yielded the azirine (97) which on standing in vacuo. dimerised to the 3,6-dihydropyrazine (102).

The general accessibility of vinyl azides has been made feasible by the discovery by Hassner et al.[118–121] that iodine azide adds stereospecifically trans- to olefins in good yield. Stereospecific dehydroiodination of the resultant vicinal iodoazide (103) can readily be accomplished, yielding the vinyl azide; except in the cases of five and six membered rings where allyl azides are obtained.



Photolysis[122] of the resultant vinyl azides is generally preferred to pyrolysis, giving excellent yields of azirines as shown in Table 1 on the next page.

A possible intermediate in both the photolysis and pyrolysis of vinyl azides is the vinyl nitrene (104).[5]



Although this would be expected to have some dipolar character as hinted at earlier,[102] attempts to trap it with the usual 1,3-dipolarophiles have failed.[122] This could perhaps be due to the fact that intramolecular ring closure is favoured over 1,3-dipolar addition, and may be compared with the formation of cyclopropenes from alkenylcarbenes.[128–131]

When terminal vinyl azides (105) are pyrolysed or photolysed, the most usual product is the nitrile (106),[124,132–137] thought[135,136] to be formed via the ketimine (107). However Japenese[138] workers presented spectroscopic evidence for the discrete existence of the azirines (108) unsubstituted in the 3-position, in the low temperature (-50°) photolysates of terminal vinyl azides.

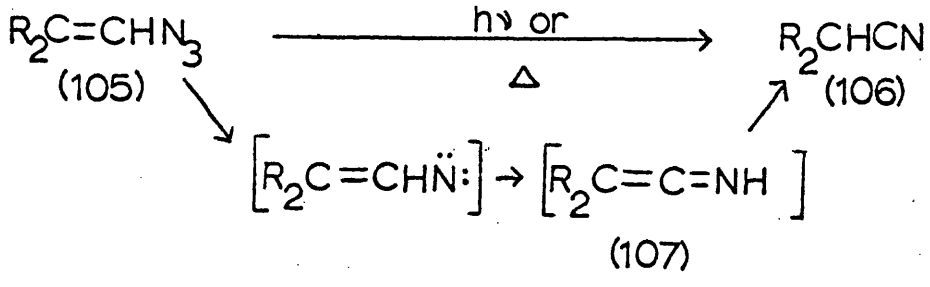
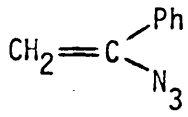
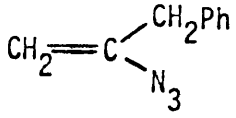
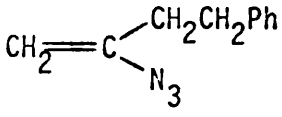
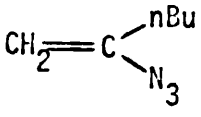
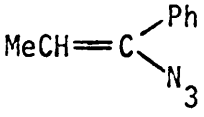
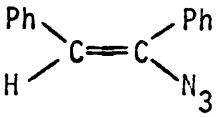
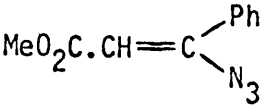
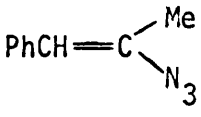
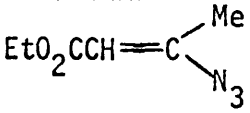
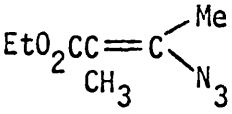
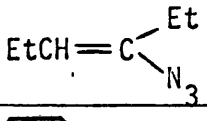
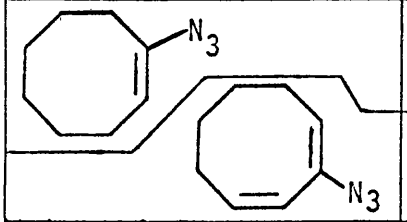
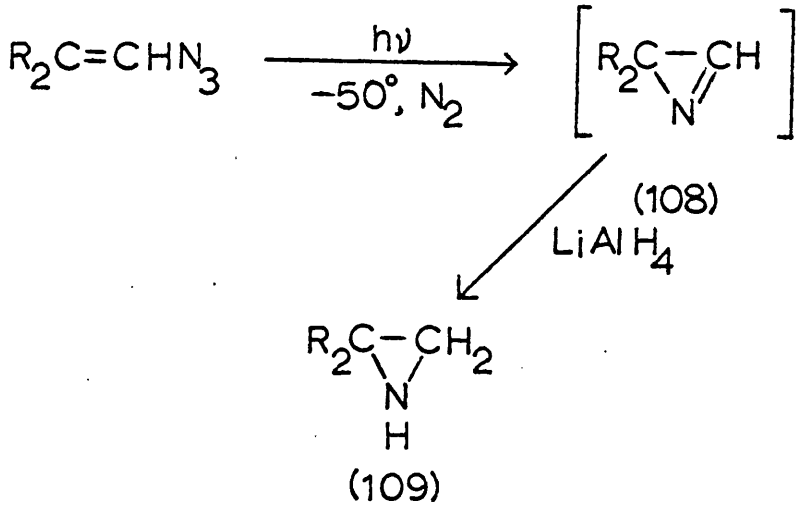
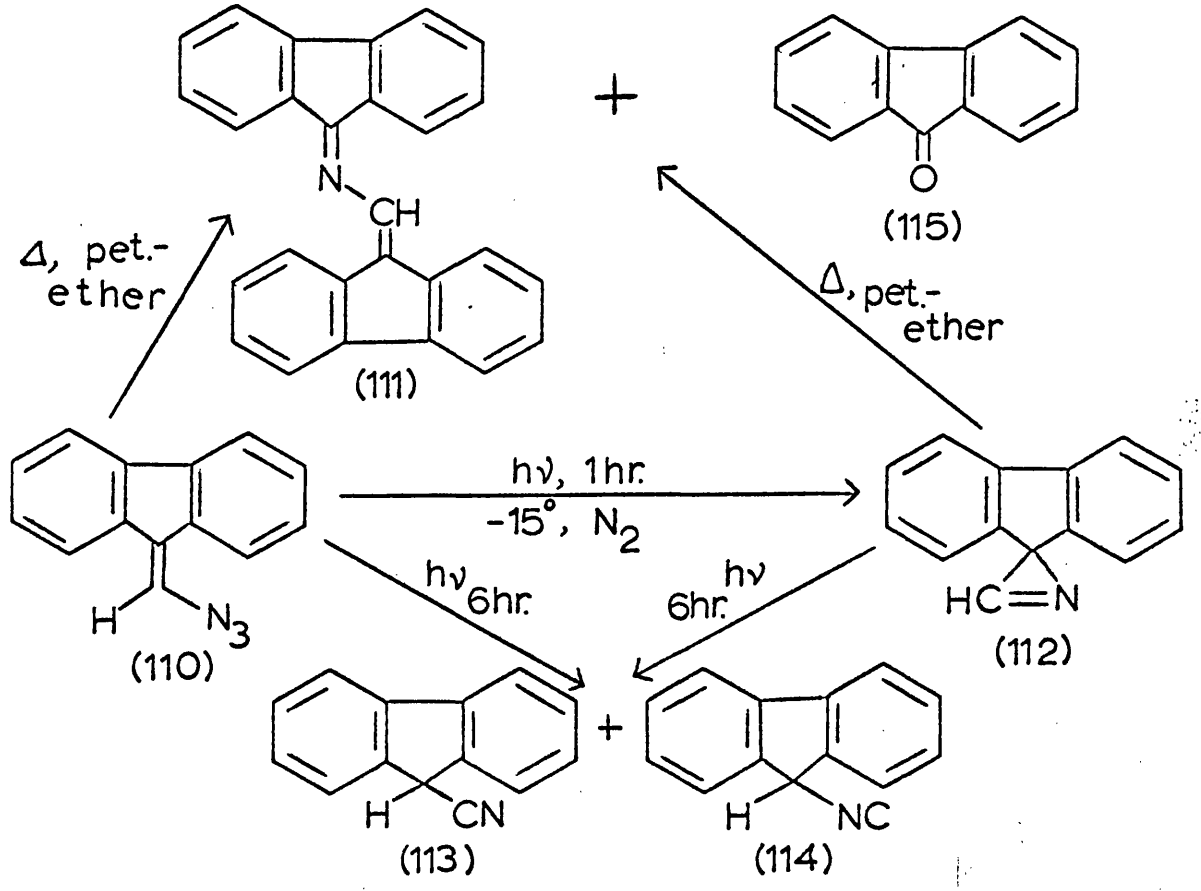


TABLE 1

Vinyl Azide	% Yield of Azirine	Ref.
	(hν) 58 (Δ) 80 (hν) 94 (hν) 85	110 117 122 123
	(hν) 100	122
	(hν) 93	122
	(hν) 81 (Δ) 29	122 117
	(hν) 94	121
	(Δ) 94	120
	(hν) 45	122
	(hν) 100 (Δ) 100	124 124
	(hν) 70	125
	(hν) 65	125
	(hν) 55	122
	(hν) 93 (hν) 100	122 122
$CF_3CF=CFN_3$	Δ(20°) 36 Δ(20°) 25	126 127



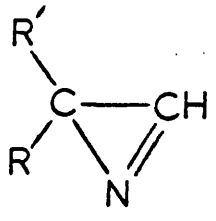
Treatment of the photolysate with lithium aluminium hydride produced the aziridine (109). This led to a careful reinvestigation by Hafner and Bauer[139] of some original work by Smolinsky,[137] who had been able to isolate only (111) in ca. 25% yield from the pyrolysis of (110) in boiling benzene.

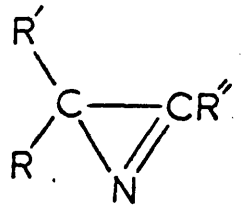


However the careful photolytic approach of Hafner and Bauer enabled the azirine (112) unsubstituted in the 3-position, to be isolated. This on further photolysis produced 9-cyano- (113) and 9-isocyanofluorene (114) as did extended photolysis of azide (110). Gentle thermolysis of both (110) and (112) produced (111) and fluorenone (115).

Compound (111) was considered to have been formed from the reaction of the carbene, 9-fluorenylidene [produced via HCN elimination from azirine (112)] with azirine (112). Fluorenone (115) was thought to be produced by the reaction of the carbene and oxygen.

The discrepancy of C=N vibration between type A and type B azirines has not been explained, but only compared to the similar behaviour in the analogous cyclopropenes.[128]

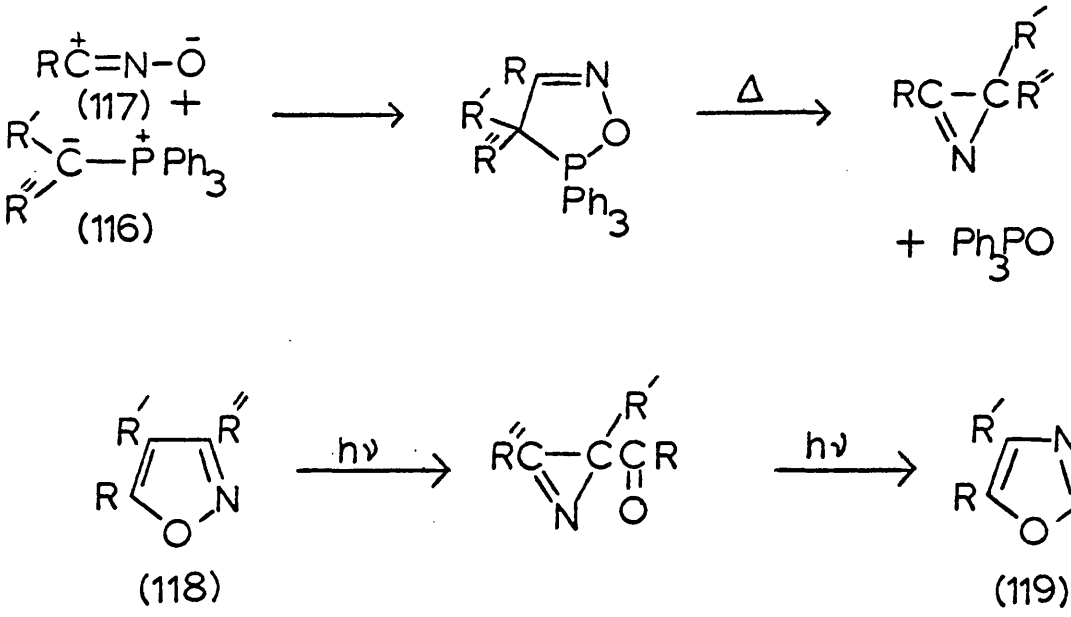




ν_{max} C=N ca. 1660 cm.$^{-1}$ ν_{max} C=N ca. 1770 cm.$^{-1}$

A B

(v) The addition of phosphonium ylides (116) to nitrile oxides (117), followed by the elimination of phosphine oxide has led to azirines.[140–143] The general scheme is presented below.



(vi) The photolysis of isoxazoles (118) to oxazoles (119) has led to the isolation of azirines as intermediates.[144–146]

Instrumentation and Experimental Techniques

1. Infrared (I.R.) spectra were recorded in the range 4000-625 $cm.^{-1}$ on Perkin-Elmer 237 and 257 spectrophotometers. Solid samples were run as nujol mulls unless otherwise indicated, and liquids as thin films, using polystyrene as reference.

2. Ultraviolet (U.V.) spectra were recorded in the range 200-450 nm. on a Unicam S.P. 800 spectrophotometer. Solvents used are indicated in the text.

3. Nuclear magnetic resonance (N.M.R.) spectra were recorded on Varian A60, Varian T60 and Bruker 90 machines. Spin decoupling was carried out using a Varian DA60 machine at 56.4 Mc.. Solvents are indicated in the text and tetramethylsilane was used as an internal standard.

4. Routine mass spectra were recorded on an A.E.I. MS9 spectrometer, and metastable peaks are indicated by asterisks in the text. Accurate mass spectra were recorded on an A.E.I. MS 902 spectrometer.

5. Melting point (m.p.) determinations were carried out on a Kofler Micro Heating Stage using corrected thermometers.

6. Elemental analyses were conducted by Rapid Elemental Analysis and by Strauss.

7. Thin layer chromatography (t.l.c.) was used extensively as a qualitative guide during reactions and for assessing the purity of compounds. Samples were run in suitable solvent mixtures on glass plates coated with a 250μ layer of Kieselgel G (E. Merck) or Aluminiumoxid G (Type E, pH 7.5) (E. Merck). The plates were observed under ultraviolet light or developed by spraying with iodine.

8. Preparative thin layer chromatography (prep. t.l.c.) was used to separate small amounts of reaction mixtures by a similar technique to that of t.l.c.; 20 x 20 and 100 x 20 cm. glass plates coated with a 1 mm. layer of Kieselgel PF254 or Aluminiumoxid PF254 with a fluorescent indicator were used.

9. Column chromatography was carried out using silica gel M.F.C. (B.D.H.), and deactivated basic alumina (Spence type H) (prepared by deactivation of basic alumina with 6% by weight of water in a ball mill). The mixture to be chromatographed was adsorbed on to the support from a suitable solvent, by evaporation using a rotary evaporator. Columns were packed under petroleum and then eluted with solvent mixtures of gradually increasing polarity. Only fractions containing significant amounts of material have been recorded.

10. Solvents were purified as follows.

    Benzene and other aromatic solvents, methylene chloride, tetrahydrofuran and dimethoxyethane were dried by refluxing over calcium hydride, distilled and stored over molecular seives (type 4A), except tetrahydrofuran which was stored over sodium wire. Anhydrous ether was stored over sodium wire.

    Dimethyl sulphoxide was distilled and stored over molecular seives (type 4A).

    Acetonitrile was dried by refluxing over phosphorus pentoxide, distilled and stored over molecular seives (type 4A).

    Methanol used was Karl Fischer Reagent grade.

11. Petroleum used during this work refers to light petroleum, b.p. 40-60°, unless otherwise stated.

12. Lead tetraacetate (L.T.A.) (B.D.H. or Hopkin and Williams) was freed from acetic acid by filtration, washed with a little dry ether and stored over concentrated sulphuric acid.

13. Hydroxylamine-O-sulphonic acid (H.O.S.) was prepared by the method of Goesl and Meuwsen[147] and stored in an air tight bottle.

14. Chloramine was prepared in ether solution by a modification[148] of the method of Theilacker and Wegner,[149] and gave a chloramine concentration of approx. 0.17 M.

15. Where possible, compounds were characterised by comparison of their melting points (m.p.) and mixed melting points (m.m.p.), I.R. and N.M.R. spectra with those of authentic specimens. Literature m.p. and b.p. values are given with references except for well authenticated compounds for which the values quoted are those given in the Heilbron Dictionary of Organic Compounds (4th Edition).

EXPERIMENTAL

Preparation of N-Amino Compounds.

3-Aminobenzoxazolin-2(3H)-one.

Benzoxazolin-2(3H)-one (13.5 g., 0.1 mole.) and anhydrous sodium carbonate (37.5 g., 0.3 mole.) were dissolved in water (250 ml.) at 60°. Hydroxylamine-O-sulphonic acid (22.6 g., 0.2 mole.) was added in small portions to the solution, the temperature being kept below 70°. After 45 min. the crystalline precipitate of 3-aminobenzoxazolin-2(3H)-one (7.5 g., 50%) was filtered, washed with water and dried, m.p. 168-9° (lit.[40] 168-171°). Recrystallisation of the product from dichloromethane did not raise the m.p.. The yield was not improved when four equivalents of hydroxylamine-O-sulphonic acid were used.

N-Aminophthalimide.

This was prepared by the method of Drew and Hatt,[150] from phthalimide and hydrazine hydrate. The crude product was recrystallised from ethanol to give colourless needles (35-40%), m.p. 200-202° (lit.[150] 200-205°).

N-Aminonaphthalimide.

This was prepared by the procedure of Carpino et al.[151] from 1,8-naphthalic anhydride and hydrazine hydrate in D.M.F. and obtained directly as bright yellow needles (90%) m.p. 263-7° (lit.[151] 265-6°).

Phthalimidine.

Phthalimide (50 g., 0.34 mole.) and granulated tin (85 g., 0.72 mole.) were mixed with water (75 ml.) and heated on a steam bath with stirring.

Concentrated hydrochloric acid (250 ml.) was added dropwise over 30 min.. After stirring for a further 1 hr. the reaction mixture was filtered and allowed to cool. Extraction with chloroform (3 x 125 ml.) and removal of solvent yielded the crude product. Recrystallisation from ethanol afforded colourless needles of pure phthalimidine (30.6 g., 70%) m.p. 151° (lit. 150°).

N-Aminophthalimidine.

Phthalimidine (10.0 g., 75 m.mole.) was dissolved in dry dichloromethane (150 ml.) and a 50% dispersion of sodium hydride (5.4 g., 112 m.mole.) in oil added with caution. When gas evolution had ceased a solution (0.15 M) of chloramine (750 ml., 112 m.mole.) was added to the stirred reaction mixture. After 60 hr. the brown precipitate was filtered off and the yellow filtrate evaporated to dryness, yielding an oily yellow solid. The majority of the oil was removed by washing with petroleum. Charcoaling of the residual yellow solid (8.8 g.) in dichloromethane solution followed by recrystallisation from benzene-petroleum afforded N-aminophthalimidine (4.5 g., 40%), m.p. 96° (Found: C, 64.4; H, 5.4; N, 18.7. $C_8H_8N_2O$ requires C, 64.8; H, 5.4; N, 18.9%); ν_{max} 3280 (w), 3257 (w), 3148 (vw), 1706 (sb), 1465, 1450, 958, 729 and 721 $cm.^{-1}$; λ_{max} (EtOH) 222 (log ε 4.0), 229 (3.9), 272sh (3.5) and 279 nm. (3.4); τ ($CDCl_3$) 5.53 (4H), and 2.80-2.00 (m, 4H); τ ($CDCl_3$ + D_2O) 5.53 (2H), and 2.80-2.00 (m, 4H); m/e 148(P) (base), 133, 132, 120, 119, 118, 105, 104 and 90. Benzylidene derivative: colourless flakes m.p. 206° (lit.[152] 206°).

Preparation of N-aminophthalimidine on a larger scale (30 g.) afforded a product difficult to purify. Conversely preparation on a small scale (1 g.) afforded a product which was easily purified.

Attempted amination of phthalimidine with H.O.S. (4 equiv.) using sodium hydroxide base at 60°, or with hydrazine hydrate (neat and equimolar in ethanol, at room temperature and at reflux) resulted in a quantitative recovery of phthalimidine.

Treatment of phthalide (6.7 g., 50 m.mole.) in ethanol (50 ml.) with hydrazine hydrate (2.5 ml.) under reflux for 30 min., afforded on cooling, o-hydroxymethylbenzhydrazide (3.7 g., 45%) m.p. 130° (lit. 128°).

N-Aminocarbazole.

N-Nitrosocarbazole[153] (30.0 g., 0.153 mole.) was dissolved in dry ether (300 ml.) and added dropwise to a stirred suspension of lithium aluminium hydride (10.0 g., 0.25 mole.) in dry ether (600 ml.) over $2\frac{1}{2}$ hr. Excess reagent was destroyed by the addition of water and the solids filtered off. The ether layer was dried with anhydrous sodium sulphate and evaporated to dryness yielding crude N-aminocarbazole (25.0 g., 90%). Recrystallisation from ethanol afforded colourless needles of pure N-aminocarbazole (20.8 g., 75%) m.p. 150° (lit.[154,155] 151°).

Oxidation of the N-Amino Compounds alone.

N-Aminophthalimide and Lead tetraacetate.

Lead tetraacetate (2.8 g., 6.3 m.mole.) was added, with stirring, to N-aminophthalimide (1.0 g., 6.2 m.mole.) in dry dichloromethane (20 ml.) during 5-10 min.. After 15 min. the reaction mixture was filtered and the insoluble solids washed with dichloromethane (20 ml.). Removal of the solvent afforded a pale yellow solid (0.85 g.) which on recrystallisation from ethanol afforded pure phthalimide (70-80%) as colourless needles m.p. 230° (lit. 238°).

In a subsequent experiment the combined filtrate and washings were extracted with 1% sodium hydroxide solution (4 x 50 ml.) and water (50 ml.). After drying the organic layer with anhydrous sodium sulphate, the solvent was removed yielding a pale yellow solid (75 mg.) which still contained a little phthalimide. Recrystallisation from chloroform gave pale yellow crystals of 1,4-bisphthaloyltetrazene m.p. 277-80° dec. (Found: C, 59.6; H, 2.3; N, 17.3. $C_{16}H_8N_4O_4$ requires C, 60.0; H, 2.5; N, 17.5%); ν_{max} 1789 (w), 1740 (s), 1280 (s), 1270 (s), 1076, 877, 800 (w), 790 (w) and 707 $cm.^{-1}$; m/e 320 (P), 292, 278, 174, 147, 146 (base), 104, 90 and 76; m* 320 → 278 = 242, 174 → 146 = 122.5, 104 → 76 = 55.5.

N-Aminophthalimide and Iodosobenzene diacetate.

Iodosobenzene diacetate (2.0 g., 6.2 m.mole.) was added to a stirred suspension of N-aminophthalimide (2.0 g., 12.4 m.mole.) in dichloromethane (50 ml.). Complete solution was obtained after about half the oxidant had been added; further addition caused precipitation . After ca. 10 min. the reaction mixture was filtered and the very insoluble colourless amorphous 1,4-bisphthaloyltetrazane (1.36 g., 68%) m.p. 210-212° was washed with dichloromethane and ether. [Attempted recrystallisation from benzene,

dichloromethane, chloroform, ethylacetate, ethanol or water yielded only phthalimide]. (Found: C, 58.9; H, 3.0; N, 17.0. $C_{16}H_{10}N_4O_4$ requires C, 59.6; H, 3.1; N, 17.4%); ν_{max} 3270 (s. N-H), 1784 (w), 1758 (w), 1722 (sb), 1370 (sb), 1058, 980, 783, 758, 707, 700 and 676 $cm.^{-1}$.

Subsequent oxidation of the tetrazane (1 mol.) with iodosobenzene diacetate (1 mol.) afforded phthalimide (50%) and 1,4-bisphthaloyltetrazene (40%).

Oxidation of the tetrazane (1 mol.) with lead tetraacetate afforded 1,4-bisphthaloyltetrazene (80%).

Treatment of the tetrazane with a few drops of triethylamine in chloroform afforded phthalimide (95%).

N-Aminophthalimide and N-Chlorobenzotriazole.

N-Chlorobenzotriazole[156] (1.5 g., 10 m.mole.) was added to a stirred suspension of N-aminophthalimide (0.8 g., 5 m.mole.) in dichloromethane (25 ml.) during 15 min.. After about half of the N-chlorobenzotriazole had been added the mixture became very exothermic and gas was evolved. The precipitated benzotriazole hydrochloride (0.75 g., 99%) was filtered off after ca. 30 min. and washed with a little dichloromethane. Removal of the solvent yielded a yellow sticky solid, which was dissolved in chloroform. Precipitation with petroleum afforded a bright yellow solid (0.60 g.). Attempted recrystallisation of this yellow solid from boiling ethanol (25 ml.) gave a bright yellow solution and a pale yellow precipitate. The ethanol solution deposited colourless needles of phthaloyl bisbenzotriazole (20%) m.p. 195-7° (Found: C, 65.4; H, 3.1; N, 22.5. $C_{20}H_{12}N_6O_2$ requires C, 65.2; H, 3.3; N, 22.8%); ν_{max} 1722 (s), 1703 (s), 1375 (sb), 941, 936 and 751 $cm.^{-1}$; λ_{max} (MeCN) 242 (log ε 4.5), 260 sh (4.3) and 302 nm.(4.1); m/e 368 (P), 322, 250, 222 (base), 104 and 76; m* 368 → 250 = 170.

The solid insoluble in boiling ethanol was recrystallised from chloroform to give pale yellow crystals of 1,4-bisphthaloyltetrazene (15%) m.p. 273-75° dec..

Benzotriazole and Phthaloyl chloride.

Benzotriazole (6.0 g., 25 m.mole.) was dissolved in 10% sodium hydroxide solution (25 ml.) and phthaloyl chloride (5.5 g., 27 m.mole.) added. The mixture was shaken for 10 min. then filtered, giving a cream solid (3.2 g.). Recrystallisation from ethanol afforded colourless needles of phthaloyl bisbenzotriazole m.p. 195-7° m.m.p. 195-6° with specimen from N-aminophthalimide and N-chlorobenzotriazole.

N-Aminonaphthalimide and Lead tetraacetate.

Lead tetraacetate (2.1 g., 4.7 m.mole.) was added during 10 min. to a stirred suspension of N-aminonaphthalimide (1.0 g., 4.7 m.mole.) in dry dichloromethane (50 ml.). After 15 min. the reaction mixture was filtered and the solids washed with dry dichloromethane (50 ml.) to give a pale green solution. Removal of the solvent afforded a pale brown solid (0.40 g., 41%) of crude naphthalimide. Extraction of the solids filtered from the reaction mixture, with acetone (100 ml.) afforded more naphthalimide (0.20 g., 20%). Recrystallisation from chloroform gave pale yellow needles of pure naphthalimide m.p. 299° (lit. 300°).

N-Aminophthalimidine and Lead tetraacetate.

Lead tetraacetate (2.3 g., 5.2 m.mole.) was added to N-aminophthalimidine

(0.75 g., 5 m.mole.) in dry dichloromethane (25 ml.) during 5-10 min.. There was a vigorous gas evolution. The reaction mixture was filtered after 20 min. and the solid washed with a little dichloromethane. Removal of the solvent afforded a sticky solid. Chromatography [basic alumina] afforded phthalide [petroleum-ether (1:1)] (trace) m.p. 73° (lit. 75°); biphthalimidine [ether-ethyl acetate (1:1)] (68 mg., 10%) as colourless rods from chloroform-petroleum m.p. 283-288° (lit.[157] 280-290°); ν_{max} 1720 (s), 1690, 1205, 747 and 738 cm.$^{-1}$; m/e 264 (P), 236, 133, 132 (base), 105, 104, 90, 89 and 77; m* 264 → 236 = 211; N-acetylaminophthalimidine [ethyl acetate-methanol (10:1)] (140 mg., 14%) as colourless prisms from chloroform-petroleum m.p. 207° (Found: C, 63.2; H, 5.2; N, 14.7. $C_{10}H_{10}N_2O_2$ requires C, 63.15; H, 5.3; N, 14.7%); ν_{max} 3200, 1715 (s), 1670 (s), 1528, 1296, 1167, 1016 and 734 cm.$^{-1}$; τ ($CDCl_3$) 7.86 (3H), 5.31 (2H), 2.46 (m, 3H), 2.15 (m, 1H) and 0.50 (broad, 1H); m/e 190 (P), 148 (base), 132, 120, 118, 104 and 90; m* 118 → 104 = 91.7.

N-Aminocarbazole and Lead tetraacetate.

Lead tetraacetate (3.1 g., 7.0 m.mole.) was added during 15 min. to a stirred solution of N-aminocarbazole in dry acetonitrile (20 ml.). After ca. 50 min. the green-grey solid (3.1 g.) was filtered off to give a black filtrate. The solid was washed with cold water (200 ml.) and dried, affording crude bisbiphenyltetrazene (0.80 g., 81%) as a green-grey amorphous powder. Recrystallisation (with difficulty) from diglyme afforded pale green crystals of the pure tetrazene m.p. 212° dec. (lit.[153,155] 216°); ν_{max} 1432, 1214, 1146, 1069 (w), 932, 746 (s) and 715 cm.$^{-1}$.

3-Aminobenzoxazolin-2(3H)-one and Lead tetraacetate.

(i) L.T.A. (9.0 g., 20.3 m.mole.) was added during 10 min. to a suspension of the N-amino compound (2.8 g., 18.7 m.mole.) in dry benzene (100 ml.). After 3 hr. the brown solid was filtered off. Extraction with boiling chloroform (2 x 100 ml.) followed by removal of the solvent, afforded a bright yellow solid (0.5 g., 18%). Recrystallisation from dichloromethane-benzene afforded bright yellow granules of cis-3,3'-azobis-(benzoxazolin-2(3H)-one) m.p. 197-199° dec. (Found: C, 57.2; H, 2.7; N, 18.7. $C_{14}H_8N_4O_4$ requires C, 56.8; H, 2.7; N, 18.9%); ν_{max} 1773, 1728, 1250, 1032, 772, 759 and 749 $cm.^{-1}$; λ_{max} (EtOH) 210 (log ε 3.8), 225 sh (3.5), 247 (3.2), 272 (3.4) and 397 nm. (3.2); m/e 296 (P), 135 (base), 120, 92 and 79.

(ii) L.T.A. (4.5 g., 10.2 m.mole.) was almost completely dissolved in dry dichloromethane (60 ml.) and a solution of the N-amino compound (1.5 g., 10.0 m.mole.) in dichloromethane (150 ml.) was added dropwise, with stirring during 3 hr.. The reaction mixture changed colour from bright yellow to dark brown. After 4 hr. the insoluble material was filtered off and washed with dichloromethane until the washings were colourless. Evaporation of the solution to small bulk (ca. 30 ml.) afforded a dirty yellow solid (0.23 g., 15%). This was filtered off and recrystallised from glacial acetic acid to give colourless plates of trans-3,3'-azobis(benzoxazolin-2(3H)-one)m.p. 220-222° dec. (Found: C, 56.4; H, 2.6; N, 18.7. $C_{14}H_8N_4O_4$ requires C, 56.8; H, 2.7; N, 18.9%); ν_{max} 1790 (b), 1470, 1247, 1022, 999 and 760$cm.^{-1}$; λ_{max} (EtOH) 225-246 (log ε 2.8) and 329 nm. (2.9); m/e 296 (P), 135 and 134 (base).

The filtrate was evaporated to smaller bulk (ca. 10 ml.) and allowed to stand overnight. The chocolate brown solid which separated out (0.11 g.,

7%) was filtered off and recrystallised from dichloromethane-benzene to give cis-3,3'-azobis(benzoxazolin-2(3H)-one) m.p. 195-7° dec..

Examination of the residues from (i) and (ii) by t.l.c. showed them to be very complex.

Small amounts of the trans-tetrazene could also be isolated during reaction (i) with L.T.A., and also from the homogeneous oxidations with iodosobenzene diacetate and potassium bromate-hydrochloric acid.

3-Aminobenzoxazolin-2(3H)-one and Activated Manganese Dioxide[158]

Activated manganese dioxide (25.9 g., 0.3 mole.) was added to the N-amino compound (3.0 g., 0.02 mole.) in dry ether (200 ml.). The reaction mixture was stirred for 24 hr. then filtered. The orange filtrate was evaporated to dryness and the residue chromatographed over silica. The following compounds were eluted: diphenyl carbonate (0.08 g., 4%) [petroleum-ether (50:1)] m.p. 76° (lit. 79°); phenol (0.25 g., 13%) [petroleum-ether (10:1)] characterised as its p-nitrobenzoate m.p. 126-8° (lit. 126°); benzoxazolin-2(3H)-one (1.0 g., 37%) [petroleum-ether (1:1)] m.p. 140° (lit. 141-2°); and o-azidophenol (0.1 g., 4%) [ether-methanol (20:1)] as a black oil characterised as its benzoate m.p. 43° (lit.[159] 43°).

Preparation of Aziridines from N-Amino compounds and Olefins.

General Procedure.

The N-amino compound (1 mol.) was stirred with dry dichloromethane (15 ml. per gram.) and the olefin (5 mol.) was added. Lead tetraacetate (1.1 mol.) was then added to the stirred suspension at room temperature during 10 min.. After a further 15 min. the mixture was filtered, the solid was washed with dichloromethane and the combined filtrate and washings were evaporated to dryness. The residue was examined by t.l.c. to determine the subsequent purification procedure, which is indicated for each aziridine.

The following aziridines were prepared in this manner:-

From N-Aminophthalimide.

cis-2,3-Dimethyl-1-phthalimidoaziridine.

This was made from N-aminophthalimide and cis-but-2-ene, isolated (19%) by column chromatography [basic alumina; petroleum-ether (9:1)], and gave pale yellow granules from benzene-petroleum; m.p. 102° (Found: C, 66.0; H, 5.7; N, 13.1. $C_{12}H_{12}N_2O_2$ requires C, 66.6; H, 5.6; N, 13.0%); ν_{max} 1784 (w), 1760 (w), 1730 (s), 1706 (sb), 1183, 1153, 1100, 1020, 883, 790 and 708 (s) $cm.^{-1}$; τ ($CDCl_3$) 8.61 (d, J = 4 c.p.s., Me cis-to phthalimido) and 8.57 (d, J = 4 c.p.s., Me trans-to phthalimido) (total 6H), 7.40 (m, 2H) and 2.27 (4H).

trans-2,3-Dimethyl-1-phthalimidoaziridine.

This was obtained from N-aminophthalimide and trans-but-2-ene, isolated (36%) by column chromatography [basic alumina; petroleum-ether

(9:1)], and gave yellow needles from benzene-petroleum; m.p. 72° (Found: C, 66.1; H, 5.6; N, 13.0. $C_{12}H_{12}N_2O_2$ requires C, 66.6; H, 5.6; N, 13.0%); ν_{max} 1789 (w), 1765 (w), 1735 (sb). 1185, 1140, 1030, 890, 782, 710 and 700 cm.$^{-1}$; τ ($CDCl_3$) 8.68 (d, J = 6 c.p.s., 3H, Me cis-to phthalimido), 8.59 (d, J = 6 c.p.s., 3H, Me trans-to phthalimido), 7.52 (q, J = 6 c.p.s., 1H, trans-to phthalimido), 7.42 (q, J = 6 c.p.s., 1H, cis-to phthalimido) and 2.27 (4H).

3-t-Butyl-2,2-dimethyl-1-phthalimidoaziridine.

This was prepared from N-aminophthalimide and 2,4,4-trimethylpent-2-ene, isolated (61%) by column chromatography [basic alumina; petroleum-ether (4:1)]; and gave yellow needles from ethanol, m.p. 76° (Found: C, 70.3; H, 7.6; N, 10.4. $C_{16}H_{20}N_2O_2$ requires C, 70.6; H, 7.4; N, 10.3%); ν_{max} 1772 (w), 1726 (s, b) 1151, 1078, 981, 891, 779 and 700 (s) cm.$^{-1}$; τ ($CDCl_3$) 8.84 (9H), 8.74 (3H, Me trans-to t-Bu), 8.43 (3H, Me cis-to t-Bu), 7.23 (1H) and 2.22 (4H); m/e 272 (P), 268, 217 (base), 149, 131, 127, 104 and 76; m* 149 → 131 = 115, 217 → 149 = 102.

The use of a non-chromatographic work up procedure similar to that described for 7-phthalimido-7-azabicyclo[4.1.0]heptane did not improve the yield of aziridine and phthalimide (23%) was also isolated.

7-Phthalimido-7-azabicyclo[4.1.0]heptane.

This was made from N-aminophthalimide and cyclohexene and isolated (40%) by column chromatography [basic alumina; petroleum-ether (9:1)] to give yellow granules from ethanol m.p. 137° (Found: C, 69.3; H, 5.8; N, 11.7. $C_{14}H_{14}N_2O_2$ requires C, 69.4; H, 5.8; N, 11.6%); ν_{max} 1782 (w),

1763 (w), 1710 (sb), 1155, 992, 889, 718 and 710 cm.$^{-1}$; λ_{max} (EtOH) 212 (log ε 4.3), 239 (4.5) and 296 nm. (3.0); τ ($CDCl_3$) 8.66 (m, 4H), 7.90 (m, 4H), 7.28 (m, 2H) and 2.29 (4H); m/e 242 (P), 214, 213, 201, 188, 163, 162, 148, 147, 130, 105, 104, 96 (base) and 76. Use of 4 mol. of olefin instead of 5 mol. gave a yield of 36%; with 2 mol. it was 20% and with 1 mol. of cyclohexene the yield was 13%.

In a subsequent experiment, phthalimide was removed from the crude reaction mixture by washing with 1% aqueous sodium hydroxide, and the organic solution was then washed with water, dried, and evaporated to give the crude aziridine (87%) m.p. 110-127°. One recrystallisation from petroleum gave the aziridine (60%) as yellow granules, m.p. 135-6°.

When the pure aziridine was absorbed on a column of basic alumina and eluted after 2 hr., only 20% was recovered.

When iodosobenzene diacetate (1 mol.) was used as the oxidant, the same yield of aziridine could be isolated by column chromatography as with L.T.A..

2-Phenyl-1-phthalimidoaziridine.

This was obtained directly from N-aminophthalimide and styrene by recrystallisation of the crude mixture from ethanol (42%) as pale yellow needles m.p. 152° (Found: C, 72.4; H, 4.5; N, 10.4. $C_{16}H_{12}N_2O_2$ requires C, 72.7; H, 4.6; N, 10.6%); ν_{max} 1782 (w) 1763 (w) 1710 (sb), 1150, 980, 887, 747 and 700 cm.$^{-1}$; τ ($CDCl_3$) 7.26 (2d, J = 2 and 6 c.p.s., 1H cis- to phenyl), 7.14 (2d, J = 2 and 8 c.p.s., 1H trans- to phenyl), 6.40 (2d, J = 6 and 8 c.p.s., 1H gem- to phenyl), 2.60 (m, 5H) and 2.28 (m, 4H); m/e 264 (P), 173, 162, 147, 118, 104 (base), 91 and 76.

2,3-Benzo-6-phthalimido-6-azabicyclo[3,1,0]hexane.

This was isolated (18%) from N-aminophthalimide and indene by column chromatography [basic alumina; petroleum-ether (1:1)] and gave pale yellow needles from ethanol m.p. 189° (Found: C, 73.5; H, 4.2; N, 10.1. $C_{17}H_{12}N_2O_2$ requires C, 73.9; H, 4.4; N, 10.1%); ν_{max} 1754 (w), 1712 (s), 1242 (m), 892, 755, 712 (s) and 705 (s) cm.$^{-1}$; τ ($CDCl_3$) 6.63 (m, 2H), 6.22 (m, 1H), 5.82 (d, J = 6 c.p.s., 1H), 2.73 (m, 3H) and 2.48-2.05 (m, 5H); m/e 276 (P) (base), 258, 247, 147, 130, 129, 116, 115, 104 and 76; m* 276 - 258 = 241.

The same aziridine could be isolated in low yield using a non-chromatographic work up.

3-Acetyl-2,2-dimethyl-1-phthalimidoaziridine.

This was prepared from N-aminophthalimide and mesityl oxide, and isolated (88%) by crystallisation of the crude reaction mixture from petroleum to give pale yellow needles m.p. 67-69° (Found: C, 65.1; H, 5.3; N, 10.85. $C_{14}H_{14}N_2O_3$ requires C, 65.1; H, 5.5;.N, 10.85%); ν_{max} 1779 (w), 1712 (sb), 1150, 1071, 881, 786 and 709 cm.$^{-1}$; λ_{max} (EtOH) 214 (log ε 4.3), 239 (4.5) and 290 nm. (3.1); τ ($CDCl_3$) 8.57 (6H, 2 aziridine ring methyls), 7.62 (3H), 6.58 (1H) and 2.20 (4H); N.M.R. at -60°: τ ($CDCl_3$) 8.53 and 8.47 (2 broad lines, total 6H, methyls respectively cis- and trans- to phthalimido), 7.52 (3H), 6.44 (1H) and 2.20 (4H); m/e 258 (P), 243, 216, 148 (base), 147, 130, 104 and 76; m* 147 → 130 = 114; 258 → 148 = 101.5; 104 → 76 = 55.5.

Methyl 1-phthalimidoaziridine-2-carboxylate.

This was made from N-aminophthalimide and methyl acrylate and

obtained (73%) by recrystallisation of the reaction mixture from ethanol to give very pale yellow needles, m.p. 172° (Found: C, 58.6; H, 4.4; N, 11.2. $C_{12}H_{10}N_2O_4$ requires C, 58.5; H, 4.1; N, 11.4%); ν_{max} 1782 (w), 1762 (w), 1750 (w), 1710 (sb), 1238, 1080, 945, 886 and 710 cm.$^{-1}$; m/e 246 (P), 215, 214, 187, 160, 147, 130, 104 (base) and 76. For N.M.R. assignments see Table (4) of the discussion.

Ethyl 1-phthalimidoaziridine-2-carboxylate.

This was made directly from ethyl acrylate and N-aminophthalimide and gave colourless needles (65%) from ethanol m.p. 160° (Found: C, 60.0; H, 4.7; N, 10.5. $C_{13}H_{12}N_2O_4$ requires C, 60.0; H, 4.65; N, 10.8%); ν_{max} 1775 (w), 1761 (w), 1747 (s), 1710 (sb), 1230, 1200, 1118, 1082, 973, 881, 786 and 710 cm.$^{-1}$.The N.M.R. assignments are given in Table (4) of the discussion.

Isopropyl 1-phthalimidoaziridine-2-carboxylate.

This was prepared directly (90%) from isopropyl acrylate and N-aminophthalimide and recrystallised from ethanol to give colourless needles, m.p. 97° (Found: C, 61.1; H, 5.2; N, 10.3. $C_{14}H_{14}N_2O_4$ requires C, 61.3; H, 5.15; N, 10.2%); ν_{max} 1786 (w), 1764 (w), 1743 (w), 1707 (sb), 1228 (s), 1196 (s), 1112, 1090, 978, 885, 783 and 706 (s) cm.$^{-1}$. The N.M.R. assignments are given in Table (4) of the the discussion.

t-Butyl 1-phthalimidoaziridine-2-carboxylate.

This was made from N-aminophthalimide and t-butyl acrylate and obtained directly (90%) by recrystallisation from ethanol to give colourless needles, m.p. 127° (Found: C, 62.2; H, 5.7; N, 9.7. $C_{15}H_{16}N_2O_4$ requires C, 62.5; H, 5.6; N, 9.7%); ν_{max} 1778 (w), 1767 (w), 1726 (sb), 1247, 1178, 1165, 1157, 974, 897, 883 and 706 (s) cm.$^{-1}$. The N.M.R. assignments are given in Table (4) of the discussion.

Methyl 2-methyl-1-phthalimidoaziridine-2-carboxylate.

This was made from N-aminophthalimide and methyl methacrylate, and obtained (100%) by trituration of the reaction mixture with petroleum followed by recrystallisation from petroleum to give pale yellow needles, m.p. 106° (Found: C, 59.7; H, 4.8; N, 10.6. $C_{13}H_{12}N_2O_4$ requires C, 60.0; H, 4.65; N, 10.8%); ν_{max} 1782 (w), 1762 (w), 1720 (sb), 1710 (sb), 1210, 1099, 1082, 891, 883, and 704 cm.$^{-1}$; m/e 260 (P), 228, 201, 200, 147, 104 (base) and 76; m* 228 → 200 = 176; 104 → 76 = 55.5. For N.M.R. assignments see Table (3) of the discussion.

Ethyl 2-methyl-1-phthalimidoaziridine-2-carboxylate.

This was made from N-aminophthalimide and ethyl methacrylate and was obtained (70%), after considerable trituration with petroleum, as yellow crystals from chloroform-petroleum, m.p. 69° (Found: C, 61.1; H, 5.1; N, 10.1. $C_{14}H_{14}N_2O_4$ requires C, 61.3; H, 5.15; N, 10.2%); ν_{max} 1760 (w), 1720 (sb), 1705 (s), 1187, 1160, 1111, 1027, 890, 777, 709 and 702 cm.$^{-1}$. For N.M.R. assignments see Table (3) of the discussion.

Isopropyl 2-methyl-1-phthalimidoaziridine-2-carboxylate.

This was prepared from N-aminophthalimide and isopropyl methacrylate (80%) and recrystallised from chloroform-petroleum to give pale yellow crystals, m.p. 106° (Found: C, 62.5; H, 5.4; N, 9.7. $C_{15}H_{16}N_2O_4$ requires C, 62.5; H, 5.6; N, 9.7%); ν_{max} 1787 (w), 1767 (w), 1725 (sb), 1710 (s), 1204, 1186, 1110 (sb), 994, 796, and 713 $cm.^{-1}$. For N.M.R. assignments see Table (3) of the discussion.

t-Butyl 2-methyl-1-phthalimidoaziridine-2-carboxylate.

This was prepared from N-aminophthalimide and t-butyl methacrylate directly (80%), and recrystallised from chloroform-petroleum as lemon yellow crystals, m.p. 100° (Found: C, 63.5; H, 5.9; N, 9.2. $C_{16}H_{18}N_2O_4$ requires C, 63.7; H, 6.0; N, 9.3%); ν_{max} 1765 (w), 1725 (sb), 1713 (s), 1165, 1130, 1074, 906, 856 and 721 $cm.^{-1}$. For N.M.R. assignments see Table (3) of the discussion.

trans-Methyl 2-methyl-1-phthalimidoaziridine-3-carboxylate.

This was made from N-aminophthalimide and methyl crotonate and gave yellow needles (90%) from ethanol, m.p. 99° (Found: C, 59.5; H, 4.8; N, 10.8. $C_{13}H_{12}N_2O_4$ requires C, 60.0; H, 4.65; N, 10.8%); ν_{max} 1773 (w), 1760 (w), 1710 (s), 1222, 1141, 987, 880 and 707 $cm.^{-1}$; m/e 260 (P), 245, 228, 201, 174, 147, 130, 114, 104 (base) and 76. For N.M.R. assignments see Table (6) of the discussion.

(See p.63 for ethyl ester)

trans-Isopropyl 2-methyl-1-phthalimidoaziridine-3-carboxylate.

This was prepared from N-aminophthalimide and isopropyl crotonate directly (90%), and recrystallised from chloroform-petroleum as yellow crystals, m.p. 81° (Found: C, 62.3; H, 5.4; N, 9.7. $C_{15}H_{16}N_2O_4$ requires C, 62.5; H, 5.6; N, 9.7%); ν_{max} 1786 (w), 1772 (w), 1720 (sb), 1216, 1146, 1125, 1111, 994, 891 and 716 (s) cm.$^{-1}$. For N.M.R. assignments see Table (6) of the discussion.

trans-t-Butyl 2-methyl-1-phthalimidoaziridine-3-carboxylate.

This was prepared from N-aminophthalimide and t-butyl crotonate directly (90%) and recrystallised from ethanol to give lemon yellow granules, m.p. 144° (Found: C, 63.6; H, 6.1; N, 9.3. $C_{16}H_{18}N_2O_4$ requires C, 63.6, H, 6.0; N, 9.3%); ν_{max} 1765 (w), 1720 (sb), 1233, 1151, 1122, 1082, 1004, 983, 886, 782, 712 and 706 cm.$^{-1}$. For N.M.R. assignments see Table (6) of the discussion.

Methyl 2,2-dimethyl-1-phthalimidoaziridine-3-carboxylate.

This was made from N-aminophthalimide and methyl 3,3-dimethylacrylate and isolated (75%) by recrystallisation of the crude mixture from ethanol to give yellow leaflets, m.p. 102° (Found: C, 61.0; H, 5.3; N, 10.1. $C_{14}H_{14}N_2O_4$ requires C, 61.3; H, 5.15; N, 10.2%); ν_{max} 1760 (w), 1734 (s), 1710 (sb), 1197, 1180, 1166, 1157, 1080, 867, 789 and 702 cm.$^{-1}$; τ (CCl_4) 8.66 (3H, Me cis- to phthalimido), 8.60 (3H, Me trans- to phthalimido), 6.76 (1H), 6.26 (3H) and 2.30 (4H); m/e 274 (P), 258, 242, 214, 173, 148, 147, 130, 128, 104 (base) and 76; m* 104 → 76 = 55.5.

Diethyl 1-phthalimidoaziridine-trans-2,3-dicarboxylate.

This was obtained from N-aminophthalimide and diethyl fumarate, and was isolated (20%) by column chromatography [basic alumina; petroleum-ether (4:1)] to give pale yellow needles from ethanol m.p. 70° (Found: C, 58.2; H, 4.8; N, 8.3. $C_{16}H_{16}N_2O_6$ requires C, 57.8; H, 4.85; N, 8.4%); ν_{max} 1785 (w), 1767 (w), 1742 (sb), 1720 (sb), 1215, 1045, 1025, 984, 899, 884 and 710 (s) $cm.^{-1}$; τ (CCl_4) 8.72 and 8.63 (2t, J = 7.5 c.p.s., 3H each, ester methyls respectively cis- and trans- to phthalimido), 6.55 (d, J = 5 c.p.s., 1H trans- to phthalimido), 6.25 (d, J = 5 c.p.s., 1H cis- to phthalimido); 5.83 and 5.70 (2q, J = 7.5 c.p.s., each 2H, respectively ester methylenes cis- and trans- to phthalimido) and 2.27 (4H); m/e 332 (P), 259, 214, 147, 127, 104 (base) and 76.

The same aziridine was isolated (1%) by column chromatography from the reaction of N-aminophthalimide and diethyl maleate, but none of the expected maleate derived aziridine.

2-Acetoxy-1-phthalimidoaziridine.

This was obtained directly (85%) from N-aminophthalimide and vinyl acetate by recrystallisation of the crude product from either ethanol or carbon tetrachloride, giving off-white crystals, m.p. 128° (Found: C, 58.2; H, 4.0; N, 11.2. $C_{12}H_{10}N_2O_4$ requires C, 58.5; H, 4.1; N, 11.4%); ν_{max} 1763 (s. acetoxy C=O), 1705 (vs. phthalimido C=O), 1204 (s), 930, 890, 710 and 703 $cm.^{-1}$; τ ($CDCl_3$) 7.80 (3H), 7.20 (2d, J = 3.5 and 3.0 c.p.s., 1H cis- to acetoxy), 6.83 (2d, J = 5.8 and 3.0 c.p.s., 1H trans- to acetoxy), 4.10 (2d, J = 5.8 and 3.5 c.p.s., 1H gem- to acetoxy) and 2.20 (4H); m/e 246 (P), 218, 204, 176, 175 (base), 148, 147, 130, 104 and 76; m* 204 → 175 = 150, 147 → 130 = 114.

trans-2,3-Dichloro-1-phthalimidoaziridine.

This was isolated (60%) from N-aminophthalimide and trans-1,2-dichloroethylene by recrystallisation of the reaction mixture from benzene-petroleum or ethanol to give colourless needles m.p. 127° (Found: C, 47.0; H, 2.35; Cl, 27.4; N, 10.9. $C_{10}H_6Cl_2N_2O_2$ requires C, 46.5; H, 2.4; Cl, 27.85; N, 10.85%); ν_{max} 1773 (w), 1730 (sb), 1244, 1218, 1141, 990, 899, 833, 827, 811, 790 and 710 cm.$^{-1}$; τ ($CDCl_3$) 4.78 (2H) and 2.17 (4H); N.M.R. at -60°:- τ ($CDCl_3$) 5.22 (d, J = 2.5 c.p.s., 1H trans- to phthalimido), 4.24 (d, J = 2.5 c.p.s., 1H cis- to phthalimido) and 2.12 (4H); m/e 260 (P), 258 (P), 256 (P), 221, 172, 147, 104 (base) and 76; m* 104 → 76 = 55.5.

2,2,3-Trichloro-1-phthalimidoaziridine.

This was obtained from N-aminophthalimide and trichloroethylene giving cream needles (90%) from ethanol, m.p. 97° (Found: C, 40.9; H, 1.5; N, 9.4. $C_{10}H_5Cl_3N_2O_2$ requires C, 41.2; H, 1.7; N, 9.6%); ν_{max} 1786 (w), 1730 (sb), 1140, 1096, 1081, 994, 925, 881, 828, 786 and 709 cm.$^{-1}$; τ ($CDCl_3$) 3.83 (1H) and 2.23 (4H).

trans-2,3-Dichloro-2,3-dimethyl-1-phthalimidoaziridine.

This was obtained from trans-2,3-dichlorobut-2-ene[160] and N-amino-phthalimide by recrystallisation (with charcoaling) of the reaction product from chloroform-petroleum, giving cream crystals (29%) m.p. 142° (Found: C, 50.4; H, 3.4; Cl, 24.7; N, 9.9. $C_{12}H_{10}Cl_2N_2O_2$ requires C, 50.5; H, 3.5; Cl, 24.9; N, 9.8%); ν_{max} 1730 (sb), 1095 (s), 889, 721 and 713 cm.$^{-1}$;

τ ($CDCl_3$) 7.90 (6H) and 2.23 (4H); m/e 286 (P), 284 (P), 249, 213, 187 (base), 147, 104 and 76.

2-Bromo-1-phthalimidoaziridine.

This was obtained directly (48%) from N-aminophthalimide and vinyl bromide by recrystallisation (with charcoaling) of the crude reaction product from dichloromethane-petroleum, as cream needles m.p. 147-8° (Found: C, 44.9; H, 2.8; Br, 29.2; N, 10.4. $C_{10}H_7BrN_2O_2$ requires C, 44.9; H, 2.6; Br, 30.0; N, 10.5%); ν_{max} 1786 (w), 1765 (w), 1725 (sb), 1285 (s), 1160, 977, 887, 801 and 713 $cm.^{-1}$; τ ($CDCl_3$) 7.13 (dd, J = 4.0 and 3.5 c.p.s., 1H cis- to bromine), 6.85 (dd, J = 7.0 and 3.5 c.p.s., 1H trans- to bromine), 5.04 (dd, J = 7.0 and 4.0 c.p.s., 1H gem- to bromine) and 2.20 (4H).

N-Aminophthalimide and Tetramethylallene.

The general oxidation procedure was used and the residue chromatographed over silica. Phthalimide (39%) [petroleum-ether (1:1)] was eluted first followed by a colourless solid (30%) [petroleum-ether (1:3)] which on recrystallisation from chloroform-petroleum afforded colourless rods of 4-acetoxy-3-(N-aminophthalimide)-2,4-dimethylpent-2-ene m.p. 163° (Found: C, 64.9; H, 6.3; N, 8.9. $C_{17}H_{20}N_2O_4$ requires C, 64.5; H, 6.4; N, 8.85%); ν_{max} 3425 (s), 1800 (w), 1733 (sb), 1687 (s), 1214, 1073, 880 and 718 $cm.^{-1}$; τ ($CDCl_3$) 8.55 (3H), 8.34 (3H), 8.09 (3H), 7.89 (3H), 7.80 (3H), 4.74 (1H) and 2.18 (4H); m/e 316 (P), 298, 274, 256, 241, 216, 175, 148 (base), 147, 130, 110, 108, 104, 94 and 76; m* 316 → 256 = 207.5, 148 → 130 = 114.

From N-Aminonaphthalimide.

7-Naphthalimido-7-azabicyclo[4,1,0]heptane.

This was isolated (44%) from the reaction of N-aminonaphthalimide and cyclohexene, using column chromatography [basic alumina; petroleum-ether (1:1)], and gave yellow crystals from chloroform-petroleum m.p. 167° (Found: C, 73.7; H, 5.7; N, 9.8. $C_{18}H_{16}N_2O_2$ requires C, 73.9; H, 5.5; N, 9.6%); ν_{max} 1700 (s), 1662 (sb), 1233, 1202, 903, 784 and 772 cm.$^{-1}$; τ ($CDCl_3$) 8.50 (m, 4H), 7.73 (m, 4H), 7.30 (m, 2H) and 2.43-1.29 (m, 6H); m/e 292 (P), 263, 249, 223, 212, 198, 180, 154, 126, 96 and 95 (base); m* 198 → 180 = 164.

Methyl 2-methyl-1-naphthalimidoaziridine-2-carboxylate.

This was obtained from N-aminonaphthalimide and methyl methacrylate after washing a chloroform solution of the crude product with 1% sodium hydroxide solution. Evaporation of the solvent and recrystallisation from chloroform-petroleum yielded yellow granules m.p. 218-20° (Found: C, 65.6; H, 4.6; N, 8.9. $C_{17}H_{14}N_2O_4$ requires C, 65.8; H, 4.6; N, 9.0%); ν_{max} 1728 (s. ester C=O), 1694 (s. imide C=O), 1662 (sb. imide C=O), 1594, 1248, 1208, 1173, 1109, 844 and 776 (s) cm.$^{-1}$; τ ($CDCl_3$) 8.47 and 8.20 (total 3H, ratio 1:5, ring methyl respectively cis- and trans- to imide), 7.24 and 7.04 (each d, J = 2.0 c.p.s., total 1H, ratio 1:5, aziridine ring proton trans- to ester respectively cis- and trans- to imide), 6.75 and 6.64 (each d, J = 2.0 c.p.s., total 1H, ratio 5:1, aziridine ring proton cis- to ester respectively cis- and trans- to imide), 6.42 and 6.13 (total 3H, ratio 5:1, ester methyl respectively cis- and trans- to imide) and 2.46-1.30 (m, 6H).

From 3-Aminobenzoxazolin-2(3H)-one.

Methyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)aziridine-2-carboxylate.

This was prepared from 3-aminobenzoxazolin-2(3H)-one and methyl acrylate, isolated (96%) by column chromatography [basic alumina; petroleum-ether (4:1)], colourless needles from chloroform-petroleum, m.p. 83-85° (Found: C, 56.4; H, 4.3; N, 11.8. $C_{11}H_{10}N_2O_4$ requires C, 56.4; H, 4.3; N, 12.0%); ν_{max} 1775, 1767, 1730, 1253, 1233, 1177, 1136, 1010, 982, 755 and 747 cm.$^{-1}$ The N.M.R. assignments are given in Table (4) of the discussion.

Methyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)-2-methylaziridine-2-carboxylate.

This was made from 3-aminobenzoxazolin-2(3H)-one and methyl methacrylate, isolated (61%) by column chromatography [basic alumina; petroleum-ether (4:1)], and crystallised from chloroform-petroleum as colourless plates, m.p. 95° (Found: C, 58.1; H, 4.9; N, 11.4. $C_{12}H_{12}N_2O_4$ requires C, 58.1; H, 4.9; N, 11.3%); ν_{max} 1783, 1775, 1767, 1724, 1252, 1205, 1167, 1122, 1012, 983, 742 and 696 cm.$^{-1}$. The N.M.R. assignments are given in Table (3) of the discussion.

Ethyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)-2-methylaziridine-2-carboxylate.

This was isolated from 3-aminobenzoxazolin-2(3H)-one and ethyl methacrylate by column chromatography [basic alumina; petroleum-ether (2:1)] as an oil (57%). (Found: m/e 262.0953. $C_{13}H_{14}N_2O_4$ requires m/e = 262.0950); ν_{max} 1780 (sb), 1727 (s), 1257 (s), 1184, 1010 and 744 cm.$^{-1}$. The N.M.R. assignments are given in Table (3) of the discussion.

t-Butyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)-2-methylaziridine-2-carboxylate.

This was isolated (46%) from t-butyl methacrylate and 3-aminobenzoxazolin-2(3H)-one by column chromatography [basic alumina; petroleum-ether (3:1)]. Recrystallisation from petroleum afforded very pale yellow needles m.p. 71-2° (Found: C, 62.2; H, 6.2; N, 9.7. $C_{15}H_{18}N_2O_4$ requires C, 62.1; H, 6.2; N, 9.6%); ν_{max} 1775 (sb), 1720 (s), 1254 (s), 1155 (sb), 1120, 1008, 980, 846 and 756 $cm.^{-1}$. The N.M.R. assignments are given in Table (3) of the discussion.

trans-Methyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)-3-methylaziridine-2-carboxylate.

This was isolated (56%) by column chromatography [basic alumina; petroleum-ether (3:1)] from 3-aminobenzoxazolin-2(3H)-one and methyl crotonate. Crystallisation from chloroform-petroleum afforded colourless granules m.p. 59-62° (Found: C, 58.2; H, 5.0; N, 11.5. $C_{12}H_{12}N_2O_4$ requires C, 58.1; H, 4.9; N, 11.3%); ν_{max} 1773 (sb), 1723 (s), 1480, 1255, 1208 (s), 1079, 1024 and 750 $cm.^{-1}$. The N.M.R. assignments are given in Table (6) of the discussion.

From N-Aminocarbazole.

N-Aminocarbazole and 2-Methylbut-2-ene.

The general oxidation procedure was used and the residue chromatographed (basic alumina). The following fractions were obtained. N,N'-Dicarbazolyl (100% petroleum) (<1%) m.p. 220-224° (lit. 220°); N-nitrosocarbazole [petroleum-ether (20:1)] (20%) m.p. 78° (lit. 84°); 2,3,3-trimethyl-1-carbazolylaziridine [petroleum-ether (9:1)] (7%) as colourless needles from petroleum m.p. 77-79° (Found: C, 81.0; H, 7.4; N, 11.4. $C_{17}H_{18}N_2$ requires C, 81.6; H, 7.25; N, 11.2%); ν_{max} 1600 (w), 1235, 745 (s) and 725 cm.$^{-1}$; τ ($CDCl_3$) 8.78 (3H, Me cis- to aziridine ring H), 8.44 (3H, Me trans- to aziridine ring H), 8.43 (d, J = 7 c.p.s., 3H, Me gem- to aziridine ring H), 6.94 (q, J = 7 c.p.s., 1H), 2.92-2.36 (m, 6H) and 1.89 (d, J = 6 c.p.s., 2H); m/e 250 (P), 180 (base), 179, 166, 165 and 152; m* 250 → 180 = 219.6, 180 → 152 = 128.4.

N-Aminocarbazole and Styrene.

Using the general oxidation procedure and chromatography (basic alumina), the following products were isolated. N,N'-Dicarbazolyl (100% petroleum) (<1%) m.p. 220-222° (lit. 220°); N-nitrosocarbazole [petroleum-ether (20:1)] (15%) m.p. 76-78° (lit. 84°); 2-phenyl-1-carbazolylaziridine [petroleum-ether (7:1)] as colourless needles (4%) from ether-petroleum m.p. 127-9° (Found: C, 84.6; H, 5.75; N, 9.7. $C_{20}H_{16}N_2$ requires C, 84.5; H, 5.7; N, 9.85%); ν_{max} 1599 (w), 1236, 749, 738 (s), 721 and 713 cm.$^{-1}$; τ ($CDCl_3$) 7.20 (d, J = 5.5 c.p.s., 1H cis- to phenyl), 6.86 (d, J = 9.0 c.p.s., 1H trans- to phenyl), 6.30 (dd, J = 9.0 and 5.5 c.p.s., 1H gem- to phenyl), 3.10-2.35 (m, 11H) and 1.92 (d, J = 6.0 c.p.s., 2H); m/e 284 (P), 182, 180, 167, 166, 152 and 104 (base).

N-Aminophthalimidine and Cyclohexene.

The general oxidation procedure was adopted followed by chromatography of the residue (silica). The following products were isolated: N-nitrosophthalimidine [petroleum-ether (2:1)] (8%) m.p. 147° (lit. 150°); biphthalimidine [ether-ethyl acetate (1:1)] (7%) m.p. 283-8° (lit.[157] 280-90°); and N-acetylaminophthalimidine (14%) m.p. 207°.

trans-Ethyl 2-methyl-1-phthalimidoaziridine-3-carboxylate

This was obtained from N-aminophthalimide and ethyl crotonate directly (75%) and recrystallised from petroleum to give pale yellow crystals m.p. 62° (Found: C, 61.1; H, 5.0; N, 10.4. $C_{14}H_{14}N_2O_4$ requires C, 61.3; H, 5.1; N, 10.2%); ν_{max} 1783, 1775, 1765 (w), 1725 (sb), 1714 (sb), 1208 (s), 1143, 1038, 889, 712 and 707 cm.$^{-1}$. For N.M.R. assignments see Table (6) of the discussion.

Rearrangements of Halogenoaziridines.

2,3-trans-Dichloro-1-phthalimidoaziridine.

The dichloroaziridine m.p. 127° (100 mg.) was heated in a sublimation tube at 170° for 10 min.. Sublimation of the residue at 120°/0.1 mm. gave 2,2-dichloroethylideneaminophthalimide (94 mg., 94%) m.p. 150° (Found: C, 46.3; H, 2.4; Cl, 27.9; N, 10.8. $C_{10}H_6Cl_2N_2O_2$ requires C, 46.5; H, 2.4; Cl, 27.85; N, 10.85%); ν_{max} 1795 (w), 1758 (w), 1726 (s), 1300, 1130, 1076, 936, 879 and 710 $cm.^{-1}$; τ ($CDCl_3$) 3.67 (d, J = 8 c.p.s., 1H), 2.11 (m, 4H), 0.96 (d, J = 8 c.p.s., 1H); m/e 260 (P), 258 (P), 256 (P), 221, 172 (base), 147, 104 and 76.

2,2,3-Trichloro-1-phthalimidoaziridine.

The trichloroaziridine m.p. 97° (100 mg.) was heated in a sublimation tube at 150° for 10 min.. Sublimation of the residue at 130°/0.1 mm. afforded 2,2,2-trichloroethylideneaminophthalimide (97 mg., 97%), m.p. 171° (Found: C, 40.95; H, 1.9; Cl, 36.8; N, 9.7. $C_{10}H_5Cl_3N_2O_2$ requires C, 41.2; H, 1.7; Cl, 36.5; N, 9.6%); ν_{max} 1786 (w), 1759 (w), 1733 (s), 1300, 1129, 922, 881, 721 and 706 $cm.^{-1}$; τ ($CDCl_3$) 2.10 (m, 4H) and 0.65 (1H).

Synthesis of 2,2,2-trichloroethylideneaminophthalimide.

N-Aminophthalimide (1.2g., 7.4 m.mole.) and chloral (25 ml.) were heated under reflux for 2 hr.. Chloral hydrate solidified in the condenser. Excess of chloral was removed by distillation in vacuo. and the solid residue was washed with ether to give 2,2,2-trichloroethylideneaminophthalimide (1.75 g., 81%), m.p. 169°, m.m.p. 168-169° with specimen from the rearrangement.

N-Aminophthalimide and trans-1,2-dibromoethylene.

Lead tetraacetate (6.6 g., 15 m.mole.) was added to a stirred suspension of N-aminophthalimide (2.4 g., 15 m.mole.) in dichloromethane (30 ml.) containing trans-1,2-dibromoethylene (14 g., 75 m.mole.), during 15 min.. The mixture was filtered after 30 min. and the solid washed with a little chloroform. The filtrate and washings were evaporated yielding an oily residue, which was redissolved in chloroform (70 ml.). The solution was washed with 1% aqueous sodium hydroxide (3 x 200 ml.) and water (100 ml.). Drying of the chloroform layer with anhydrous sodium sulphate followed by evaporation of the solvent, gave a solid (1.65 g.). Recrystallisation (with charcoaling) from chloroform-petroleum gave pale pink plates of 2,2-dibromoethylideneaminophthalimide (1.10 g., 21%), m.p. 162-3° (Found: C, 34.7; H, 2.2; Br, 45.7; N, 8.1. $C_{10}H_6Br_2N_2O_2$ requires C, 34.7; H, 1.7; Br, 46.2; N, 8.1%); ν_{max} 1790 (w), 1757 (w), 1735 (s), 1304, 1176, 965, 881, 705 and 650 $cm.^{-1}$; τ ($CDCl_3$) 3.71 (d, J = 8 c.p.s., 1H), 2.10 (m, 4H) and 0.73 (d, J = 8 c.p.s., 1H).

Rearrangement of 2-Bromo-1-phthalimidoaziridine.

The aziridine (149 mg.) was dissolved in pure o-dichlorobenzene (7.5 ml.) and heated under reflux for 20 min.. Removal of the solvent in vacuo. (1 mm.) afforded off-white crystals (131 mg. 87%). Recrystallisation from dichloromethane-petroleum afforded cream needles of 2-bromoethylideneaminophthalimide m.p. 124° (Found: C, 45.0; H, 2.7; Br, 28.8; N, 10.4. $C_{10}H_7BrN_2O_2$ requires C, 44.9; H, 2.6; Br, 30.0; N, 10.5%); ν_{max} 1785 (w), 1765 (w), 1724 (sb), 1312 (sb), 887 and 714 $cm.^{-1}$; τ ($CDCl_3$) 5.80 (d, J = 6 c.p.s., 2H), 2.13 (m, 4H) and 1.09 (t, J = 6 c.p.s., 1H).

Attempted Reduction of Aziridines.

Hydrazinolysis of 2,2-Dimethyl-1-phthalimido-3-t-butyl-aziridine.

Hydrazine hydrate (0.33 ml., 6.6 m.mole.) was added to a solution of the aziridine (0.90 g., 3.3 m.mole.) in ethanol (7 ml.) at room temperature. There was a slightly exothermic reaction and a gas was evolved. After 3 min. a colourless solid was precipitated. The mixture was stirred for 24 hr. and filtered. The precipitate (0.60 g.) was shaken with water (100 ml.) and chloroform (100 ml.). The chloroform layer yielded N-aminophthalimide (0.20 g., 36%) on evaporation. Acidification of the aqueous layer gave phthalazine-1,4-dione (0.045 g., 16%). The filtrate from the hydrazinolysis was adsorbed on basic alumina and the column was eluted with petroleum, ether, and ethanol, but no significant amounts of material were obtained on evaporation of the fractions.

Attempted hydrogenolysis of 7-phthalimido-7-azabicyclo-[4,1,0]heptane.

The aziridine (726 mg., 3 m.mole.) was dissolved in ethyl acetate and 10% palladium on charcoal catalyst (95 mg.) added. The mixture was hydrogenated at room temperature and pressure. After 4 days it appeared that the theoretical amount of hydrogen (66 ml.) had been taken up. The catalyst was filtered off and the solvent removed to yield a yellow solid. t.l.c. indicated that this contained a very small amount of phthalimide, which was removed by washing a chloroform solution of the residue with 1% sodium hydroxide solution (2 x 100 ml.). After drying the organic layer over anhydrous sodium sulphate, the solvent was removed to give crude 7-phthalimido-7-azabicyclo[4,1,0]heptane m.p. 125-130° (550mg. 76%). Recrystallisation from petroleum afforded pure aziridine m.p. 135° m.m.p. 134° with authentic specimen.

Oxidation of N-Amino compounds in the presence of Sulphoxides.

N-Aminophthalimide and Dimethyl sulphoxide.

Lead tetraacetate (2.8 g., 6.3 m.mole.) was added during 10 min. to N-aminophthalimide in dry dimethyl sulphoxide (17 ml.) with stirring. After 40 min. the pale yellow solution was poured into ether (300 ml.). The precipitated white solid was filtered off and extracted with boiling chloroform (150 ml.). Removal of the chloroform in vacuo. yielded a colourless solid (1.3 g., 75%). Recrystallisation from chloroform afforded pure N-phthalimido-S,S-dimethylsulphoximine as colourless needles m.p. 208° (Found: C, 50.2; H, 4.1; N, 11.7; S, 13.6. $C_{10}H_{10}N_2O_3S$ requires C, 50.4; H, 4.2; N, 11.8; S, 13.5%); ν_{max} 1778 (w), 1745 (w), 1708 (sb), 1203 (s), 1188, 1041 (s), 880, 711 and 708 $cm.^{-1}$; ν_{max} ($CHCl_3$) 1785 (w), 1740 (w), 1720 (sb), 1380, 1115, 1040 (s) and 885 $cm.^{-1}$; λ_{max} (EtOH) 227 (log ε 4.3), 294 (3.1) and 302 nm. (3.1); τ ($CDCl_3$) 6.72 (6H) and 2.15 (4H); m/e 238 (P), 147, 104 (base) and 76.

N-Aminophthalimide and Methyl phenyl sulphoxide.

N-Aminophthalimide (0.75 g., 4.6 m.mole.) was suspended in dry dichloromethane (10 ml.) containing methyl phenyl sulphoxide (2.1 g., 13.1 m.mole.). Lead tetraacetate (2.2 g., 5.0 m.mole.) was added to the rapidly stirred suspension during 10 min.. After 30 min. the mixture was filtered and the filtrate taken to dryness. Chromatography (basic alumina) of the residue afforded phthalimide (270 mg., 40%) [petroleum-ether (1:2)], methyl phenyl sulphoxide (1.25 g., 60%) [100% ether] and N-phthalimido-S-methyl-S-phenylsulphoximine (400 mg., 20%) [ether-methanol, (20:1)] as colourless flakes from ethanol m.p. 153° (Found: C, 59.6; H, 4.0; N, 9.1; S, 10.6.

$C_{15}H_{12}N_2O_3S$ requires C, 60.0; H, 4.0; N, 9.3; S, 10.7%); ν_{max} 1780 (w), 1740 (w), 1714 (s), 1216 (s), 1188, 1091, 1079, 1036, 1004, 877, 765 and 705 cm.$^{-1}$; ν_{max} ($CHCl_3$) 1785 (w), 1744 (w), 1720 (s), 1375, 1113, 1090, 1035, 1010 and 885 cm.$^{-1}$; τ ($CDCl_3$) 6.67 (3H), 2.60-2.00 (m, 7H) and 1.50-1.80 (m, 2H); m/e 300 (P), 147, 140, 124 (base), 104 and 76.

N-Aminophthalimide and Diphenyl sulphoxide.

Lead tetraacetate (1.5 g., 3.4 m.mole) was added, during 10 min. to N-aminophthalimide (0.5 g., 3.1 m.mole.) in dichloromethane (15 ml.) containing diphenyl sulphoxide (2.5 g., 12.4 m.mole). After 30 min. the reaction mixture was filtered and the filtrate taken to dryness. Chromatography (basic alumina) of the residue afforded a mixture of phthalimide and diphenyl sulphoxide [petroleum-ether (1:3)], and N-phthalimido-S,S-diphenylsulphoximine (200 mg., 18%) [ether-methanol (1:1)] as pale yellow crystals from ethanol m.p. 220° (Found: C, 66.7; H, 3.8; N, 7.7; S, 8.9. $C_{20}H_{14}N_2O_3S$ requires C, 66.4; H, 3.8; N, 7.7; S, 8.8%); ν_{max} 1782 (w), 1760 (w), 1745 (w), 1713 (sb), 1462, 1234 (s), 1194, 1082, 1047, 883, 860, 737 and 710 cm.$^{-1}$; ν_{max} ($CHCl_3$) 1784 (w), 1745 (w), 1720 (sb), 1450, 1372, 1095 (s), 1085 (s), 1008, 999 and 883 cm.$^{-1}$; m/e 362 (P), 202, 185 (base), 162, 147, 104 and 76.

3-Aminobenzoxazolin-2(3H)-one and Dimethyl sulphoxide.

3-Aminobenzoxazolin-2(3H)-one (0.5 g., 3.3 m.mole.) was dissolved in dry dimethyl sulphoxide (15 ml.) and lead tetraacetate (1.5 g., 3.4 m.mole.) added during 5 min.. After 20 min. the deep red reaction

mixture was poured into water (150 ml.) and extracted with chloroform (5 x 50 ml.). The chloroform extracts were washed with water (3 x 50 ml.) and dried over anhydrous sodium sulphate. Removal of the solvent afforded a dark brown solid (0.45 g., 60%). Recrystallisation (with charcoaling) from chloroform-petroleum afforded light-brown crystals of N-(Benzoxazolin-2-on-3-yl)-S,S-dimethylsulphoximine m.p. 164-5° (Found: C, 48.2; H, 4.4; N, 12.3; S, 14.1. $C_9H_{10}N_2O_3S$ requires C, 47.8; H, 4.5; N, 12.4; S, 14.0%); ν_{max} 1760 (sb), 1480, 1254, 1209 (s), 1102, 1092, 1040, 1012 and 746 cm.$^{-1}$; τ (d_6DMSO) 6.64 (6H) and 2.81 (4H); m/e 226 (P), 150, 135, 120, 92 and 78 (base).

N-Aminonaphthalimide and Dimethyl sulphoxide.

Lead tetraacetate (4.2 g., 9.5 m.mole.) was added, during 10 min., to a stirred suspension of N-aminonaphthalimide (2.0 g., 9.4 m.mole.) in dry dimethyl sulphoxide (30 ml.). After stirring for 20 min. the resultant yellow solution was poured into water (200 ml.) and the precipitated solid (2.4 g., 70%) was collected and dried. The aqueous layer was extracted with chloroform (3 x 100 ml.), and the combined chloroform extracts washed with water (3 x 100 ml.). After drying over anhydrous sodium sulphate, the chloroform layer afforded, on evaporation, more solid (0.3 g., 29%). Recrystallisation of the combined solids from ethanol afforded pale yellow needles of N-naphthalimido-S,S-dimethylsulphoximine m.p. 205° (Found: C, 58.1; H, 4.4; N, 10.0; S, 11.2. $C_{14}H_{12}N_2O_3S$ requires C, 58.3; H, 4.2; N, 9.7; S, 11.1%); ν_{max} 1702 (s), 1664 (sb), 1237 (s), 1203 (s), 1066 (s), 1056 (s), 889 and 775 cm.$^{-1}$; τ ($CDCl_3$) 6.64 (6H) and 2.40-1.40 (m, 6H).

N-Aminophthalimidine and Dimethyl Sulphoxide.

Lead tetraacetate (3.0 g., 6.75 m.mole.) was added during 5-10 min. to the N-amino compound (1.0 g., 6.75 m.mole.) in dry D.M.S.O. (15 ml.). The reaction mixture was poured into methylene chloride (200 ml.) and extracted with water (2 x 200 ml.) to leave a pale green organic solution. After drying over anhydrous sodium sulphate, the organic layer was evaporated to yield a yellow oil which rapidly crystallised to give crude N-phthalimidinyl-S,S-dimethylsulphoximine (0.8 g., 53%) m.p. ca. 160° dec. then crystals form in melt with m.p. >320°. ν_{max} 1685 (s), 1210, 1196 (s), 1176, 1040 (s), 982 and 733 cm.$^{-1}$; τ ($CDCl_3$) 6.76 (6H), 5.38 (4H), 2.70-2.40 (m, 3H) and 2.30-2.00 (m, 1H); m/e no parent (224), 148, 147, 133, 132, 118, 90 and 78 (base). Attempted recrystallisation from ethanol afforded 2,2'-azobisphthalimidine as colourless plates m.p. >320°, subliming from 290°. (Found: C, 65.3; H, 4.0; N, 19.0. $C_{16}H_{12}N_4O_2$ requires C, 65.75; H, 4.1; N, 19.2%); ν_{max} 1720 (s), 1470, 1454, 1366, 1212, 1202 and 741 cm.$^{-1}$; τ (CF_3CO_2H) 5.63 (4H), 3.30-2.80 (m, 6H) and 2.75-2.50 (m, 2H); m/e 292 (P), 160, 133, 132 (base), 118, 104, 90 and 77.

In a subsequent experiment the original reaction mixture was poured into water and extracted with chloroform. After washing the chloroform extracts with water and drying over anhydrous sodium sulphate, the tetrazene (44%) was obtained directly with no trace of the sulphoximine.

Generation of N-Phthalimido Nitrene by Photolysis.

From N-Phthalimido-S,S-dimethylsulphoximine.

The sulphoximine (500 mg., 2.1 m.mole.) was dissolved in acetonitrile (15 ml.) containing cyclohexene (15 ml.). The solution was photolysed at 254 nm. in a quartz apparatus for 24 hr.. Removal of the solvent followed by chromatography [basic alumina; petroleum-ether (1:1)] afforded 7-phthalimido-7-azabicyclo[4,1,0]heptane (105 mg., 20%) m.p. 135° m.m.p. 134° with specimen from N-aminophthalimide and cyclohexene.

From 3-Acetyl-2,2-dimethyl-1-phthalimidoaziridine.

The aziridine (500 mg., 1.94 m.mole.) was dissolved in acetonitrile (90 ml.) containing cyclohexene (11.5 ml.). The solution was photolysed in a Hanovia Reactor using a pyrex filter for 20 hr., then a quartz filter for 20 hr.. Removal of the solvent afforded a viscous yellow oil which was purified by prep. t.l.c. [silica gel; petroleum-ether (1:1)]. 7-Phthalimido-7-azabicyclo[4,1,0]heptane (190 mg., 40%) and 3-acetyl-2,2-dimethyl-1-phthalimidoaziridine (123 mg., 23%) were obtained.

Photolysis of 7-Phthalimido-7-azabicyclo[4,1,0]heptane.

The aziridine (1.0 g., 4.1 m.mole.) was dissolved in acetonitrile (80 ml.) containing 2,4,4-trimethylpent-2-ene (20 ml.). The solution was photolysed for 24 hr. in a Hanovia Reactor using a quartz apparatus. Removal of the solvent afforded 7-phthalimido-7-azabicyclo[4,1,0]heptane (0.95 g., 95%). There was no t.l.c. evidence for the aziridine derived from the substituted pentene.

Preparation of 2H-Azirines from N-Aminophthalimide and Acetylenes.

General Procedure.

Lead tetraacetate (1.1 mol.) was added in portions to the N-amino compound (1 mol.) and the acetylene (> 5 mol.) in dry dichloromethane. After stirring for 15-30 min., lead diacetate was filtered off and washed with a little dichloromethane. Removal of the solvent yielded mainly phthalimide (60-80%) plus the azirine. The majority of the azirine was leached out with a little ether. The resultant ether solution was chromatographed on deactivated basic alumina to give the pure azirine. Residual phthalimide was eluted directly after the azirine.
The following azirines were prepared in this manner:-

3-Methyl-2-phthalimido-2H-azirine.

This was isolated (1%) by chromatography [basic alumina; ether-petroleum (1:3)] from the oxidation of N-aminophthalimide in the presence of prop-1-yne at -15°. Recrystallisation from ether-petroleum gave colourless needles m.p. 131° (Found: C, 66.0; H, 4.0; N, 14.2. $C_{11}H_8N_2O_2$ requires C, 66.0; H, 4.0; N, 14.0%); ν_{max} 1776 (w), 1730 (s), 1137, 960, 728 (s), 720 and 708 cm.$^{-1}$; τ ($CDCl_3$) 7.24 (3H), 6.16 (1H) and 2.25 (m, 4H); m/e 200 (P), 185, 161, 147, 132, 104 (base) and 76; m* 104 → 76 = 55.5.

2-Phthalimido-3-n-propyl-2H-azirine.

This was isolated from N-aminophthalimide and pent-1-yne by chromatography [basic alumina: ether-petroleum (1:3)] as an oil (5%). Scratching gave pale yellow crystals m.p. 38-44°. Recrystallisation from ether-petroleum gave colourless needles m.p. 46-7° (Found: C, 67.7; H, 5.3;

N, 12.3. $C_{13}H_{12}N_2O_2$ requires C, 68.4; H, 5.3; N, 12.3%); ν_{max} 1778 (w), 1720 (sb), 1138, 733 and 725 cm.$^{-1}$; τ ($CDCl_3$) 8.89 (t, J = 7 c.p.s., 3H), 8.08 (sx., J ~ 7 c.p.s., 2H), 6.90 (t, J = 7 c.p.s., 1H) 6.85 (t, J = 7.5 c.p.s., 1H), 6.12 (1H) and 2.24 (4H); [Irradiation of the multiplet at τ 8.08 caused the signals at τ 6.90 and 6.85 to collapse to two singlets separated by 2.5 c.p.s.]; m/e 228 (P), 200, 185, 160, 147, 122, 104 (base) and 76; m* 228 → 200 = 175.5, 104 → 76 = 55.5.

3-n-Butyl-2-phthalimido-2H-azirine.

This was obtained (2%) as a colourless oil from N-aminophthalimide and hex-1-yne by chromatography [basic alumina: ether-petroleum (1:4)]; (analysis was not obtained); ν_{max} 1772 (w), 1720 (sb), 1131, 979 (w), 730 and 722 cm.$^{-1}$; τ (CCl_4) 9.20-8.00 (m, 7H), 6.95 (m, 2H), 6.23 (1H) and 2.25 (m, 4H).

2,3-Dimethyl-2-phthalimido-2H-azirine.

This was obtained as a colourless oil (7%) from N-aminophthalimide and but-2-yne by chromatography [basic alumina: ether-petroleum (1:7)]. Prolonged scratching gave a pale yellow solid which on recrystallisation from ether-petroleum gave colourless crystals m.p. 78° (Found: C, 67.0; H, 4.5; N, 12.8. $C_{12}H_{10}N_2O_2$ requires C, 67.3; H, 4.7; N, 13.1%); ν_{max} 1778 (w), 1758 (w), 1712 (s), 1390 (s), 1134, 884, 720 and 716 cm.$^{-1}$; τ ($CDCl_3$) 8.23 (3H), 7.24 (3H) and 2.22 (4H); m/e 214 (P), 173, 147, 132, 104 (base) and 76.

2,3-Diethyl-2-phthalimido-2H-azirine.

This was isolated (10-15%) as a colourless oil from N-aminophthalimide and hex-3-yne by chromatography [basic alumina: ether-petroleum (1:2)]. (Analysis was not obtained); ν_{max} 1780 (w), 1760 (w), 1720 (sb), 1370 (s), 1122, 1080, 879 and 719 (s) $cm.^{-1}$; τ (CCl_4) 9.23 (t, J = 7 c.p.s., 3H), 8.60 (t, J = 7 c.p.s., 3H), 7.92 (q, J = 7 c.p.s., 1H), 7.72 (q, J = 7 c.p.s., 1H), 6.95 (q, J = 7 c.p.s., 1H), 6.90 (q, J = 7 c.p.s., 1H) and 2.27 (4H); m/e 242 (P), 224, 211, 209, 187, 158, 132, 104 (base) and 76; m* 242 → 187 = 144.5, 187 → 132 = 93, 104 → 76 = 55.5.

Catalytic hydrogenation of 2-Phthalimido-3-n-propyl-2H-azirine.

10% Palladium on charcoal (30 mg.) was added to the azirine (100 mg., 0.44 m.mole.) in ethyl acetate (6 ml.) and the mixture hydrogenated at room temperature until just more than the theoretical quantity of hydrogen (12 ml., 0.53 m.mole.) had been taken up. Filtration and removal of the solvent yielded a yellow oil which crystallised on scratching to a pale yellow solid (95 mg., 95%) m.p. 72-82°. Recrystallisation from ether-petroleum yielded colourless needles of 1-(N-phthalimido)pentan-2-one m.p. 83-4° (Found: C, 67.4; H, 5.8; N, 6.1. $C_{13}H_{13}NO_3$ requires C, 67.5; H, 5.7; N, 6.0%); ν_{max} (KBr) 1774 (w), 1720 (sb), 1420 (b), 940, 725 and 715 $cm.^{-1}$; τ ($CDCl_3$) 9.06 (t, J = 7 c.p.s., 3H), 8.34 (m, 4H), 7.54 (t, J = 7 c.p.s., 2H), 6.58 (2H), and 2.24 (m, 4H); m/e 231 (P), 162, 161, 160, 104 and 71 (base); m* 231 → 162 = 113.5, 231 → 160 = 111.

Preparation of 1-(N-phthalimido)pentan-2-one.

A mixture[161] of 1- and 3- bromopentan-2-one was obtained from the bromination of pentan-2-one.

Potassium phthalimide (15.0 g., 81 m.mole.) was added with stirring to the bromoketone mixture (12.5 g., 76 m.mole.) in dimethylformamide (60 ml.). The exothermic reaction mixture was stirred until it had cooled to room temperature, then poured into water (300 ml.) and extracted with chloroform (3 x 50 ml.). The combined chloroform extracts were washed with 1% sodium hydroxide solution (60 ml.) and water (2 x 50 ml.). After drying the chloroform solution with anhydrous sodium sulphate, the solvent was removed yielding a black tar. Chromatography [basic alumina: ether-petroleum (1:1)] afforded 1-(N-phthalimido)pentan-2-one (2.25 g., 13%) m.p. 83-4° m.m.p. 82-3° with a specimen from the catalytic hydrogenation of 2-phthalimido-3-n-propyl-2H-azirine. Identical I.R. and N.M.R. spectra were also obtained.

1-(N-Phthalimido)propan-2-one.

This was prepared (40%) by the literature[162] method from potassium phthalimide and chloroacetone in dimethylformamide.

1-(N-Phthalimido)propan-2-one oxime.

This was obtained (79%) as colourless needles from ethanol m.p. 192-7° (lit. 172°[163] and 191-2°[164]), (Found: C, 60.5; H, 4.5; N, 12.8. $C_{11}H_{10}N_2O_3$ requires C, 60.5; H, 4.6; N, 12.8%); ν_{max} 3250 (b), 1768 (w), 1700 (sb), 1112, 1020, 725 and 708 cm.$^{-1}$.

1-(N-Phthalimido)propan-2-one oxime p-toluenesulphonate.

N-Phthalimidopropan-2-one oxime (12.5 g., 57 m.mole.) was dissolved in dry pyridine (50 ml.) and cooled in an ice-water bath. Pure p-toluenesulphonyl chloride (11.5 g., 60 m.mole.) was added and the solution stirred for 3 hr.. The reaction mixture became opaque and viscous, and was poured into water (450 ml.). The solid was filtered off, dried and recrystallised from benzene, affording colourless granules of the p-toluenesulphonate (13.5 g., 63%) m.p. 146-7° (Found: C, 58.6; H, 4.4; N, 7.5; S, 8.7. $C_{18}H_{16}N_2O_5S$ requires C, 58.1; H, 4.3; N, 7.5; S, 8.6%); ν_{max} 1784 (w), 1727 (sb), 1196 (s), 1185 (s), 870, 800, 729, 717 and 675 cm.$^{-1}$.

1-(N-Phthalimido)propan-2-one oxime p-toluenesulphonate and potassium t-butoxide.

Potassium t-butoxide (0.6 g., 5.35 m.mole.) was added to the p-toluenesulphonate (3.0 g., 8.07 m.mole.) in dry benzene (180 ml.) and the reaction mixture heated under reflux with stirring. Further portions of t-butoxide (2 x 0.6 g.) were added after 2 hr. and 4 hr.. After 10 hr. more t-butoxide (1.0 g., 8.93 m.mole.) was added. The reaction was followed continuously by t.l.c. [silica gel; ether-petroleum (1:1)]. The reaction mixture was allowed to cool after 10.5 hr. and the solids filtered off. Evaporation of the filtrate yielded an oily solid. The solid (mainly unreacted tosylate) was washed with ether and the solvent evaporated, yielding crude azirine (550 mg., 34%). Recrystallisation from ether-petroleum yielded 3-methyl-2-phthalimido-2H-azirine (150 mg., 9%) m.p. 125°, m.m.p. 123° with a specimen from N-aminophthalimide and prop-1-yne. Identical I.R. and N.M.R. spectra were also obtained.

N-Aminophthalimide and Di-t-butylacetylene.

Di-t-butylacetylene b.p. 113.0-114.0°, 763 mm. (lit.[165] 111.9°, 746 mm.) was prepared by the literature method[165] from t-butylacetylene.

The general oxidation procedure was adopted, using a six fold excess of the acetylene. Phthalimide (47%) was isolated. The ether solution was washed with 1% sodium carbonate solution and dried with anhydrous sodium sulphate. Removal of the solvent afforded a yellow oil which crystallised to a yellow solid (35%) m.p. 70-85°. Recrystallisation from ether-petroleum afforded lemon-yellow crystals of 2-(3,3-dimethylbut-1-ynyl)-2-methyl-1-phthalimidoaziridine m.p. 97-8° (Found: C, 72.3; H, 6.2; N, 10.2. $C_{17}H_{18}N_2O_2$ requires C, 72.3; H, 6.4; N, 9.9%); ν_{max} 1786 (w), 1766 (w), 1723 (s), 1707 (s), 1286, 1195, 1172, 1080, 1060, 985, 887, 709 and 703 $cm.^{-1}$; τ ($CDCl_3$) 9.09 (9H), 8.44 (3H), 7.40 (d, J = 2.5 c.p.s., 1H trans- to ring methyl), 6.55 (d, J = 2.5 c.p.s., 1H cis to ring methyl) and 2.23 (4H); m/e 282 (P), 267, 175, 173, 147, 122, 120, 107 (base), 104, 91 and 76.

Further rectification of the di-t-butylacetylene still afforded small amounts of the aziridine, but no azirine.

N-Aminocarbazole and Hex-3-yne.

The general oxidation procedure was adopted followed by chromatography of the residue (basic alumina). The following compounds were isolated: N-nitrosocarbazole [petroleum-ether (20:1)] (18%) m.p. 77-79° (lit. 84°) and carbazole [petroleum-ether (5:1)] (33%) m.p. 240° (lit. 246°).

Attempted Dechlorination of 2,3-Dichloroaziridines.

trans-2,3-Dichloro-1-phthalimidoaziridine and Sodium Iodide-Acetone.[166]

The aziridine (0.50 g., 1.95 m.mole.) was dissolved in acetone (10 ml.) containing sodium iodide (1.5 g., 10 m.mole.) and heated under reflux for 1½ hr., then allowed to cool. The insoluble sodium chloride (0.22 g., 93%) was filtered off and the deep red filtrate was evaporated to dryness. The resultant dark solid was treated with chloroform (60 ml.) and the solution washed with 1% sodium thiosulphate solution (2 x 75 ml.). After drying over anhydrous sodium sulphate, the chloroform layer yielded an orange solid (0.23 g., 38%) on evaporation. Rapid recrystallisation from chloroform-petroleum afforded orange crystals of 2-iodoethylideneamino-phthalimide m.p. 117° (Found: C, 37.8; H, 1.9; N, 9.1. $C_{10}H_7IN_2O_2$ requires C, 38.2; H, 2.2; N, 8.9%); ν_{max} 1783 (w), 1760 (w), 1730 (sb), 1468, 1310 (s), 1118, 885 and 711 $cm.^{-1}$; τ ($CDCl_3$) 5.90 (d, J = 6 c.p.s., 2H), 2.30-1.90 (m, 4H) and 1.07 (t, J = 6 c.p.s., 1H); m/e 314 (P), 187, 162, 161, 160, 147 (base), 130, 104 and 76.

Prolonged heating in a solvent caused rapid darkening of the solution.

The iodo compound was also obtained in the same yield from 2,2-dichloroethylideneaminophthalimide, using the above reaction conditions.

Preparation of Sodium Naphthalene.[167]

Pure naphthalene (6.4 g., 0.05 mole.) was dissolved in pure T.H.F. (50 ml.) under nitrogen. Small clean lumps of sodium (1.25 g., 0.055 mole.) were added during 10 min.. There was a small induction period after the addition of the first portion of sodium of ca. 5 min., then the intense

green colouration of the reagent appeared. The mixture was stirred for 2 hr. when a portion was removed and titrated against 0.1 M hydrochloric acid. The average strength of the reagent was ca. 1 M.

trans-2,3-Dichloro-1-phthalimidoaziridine and Sodium Naphthalene in the presence of Furan.

A solution (5 ml., 4.75 m.mole) of 0.95 M sodium naphthalene was added during 1 min. to a stirred solution of the aziridine (1.0 g., 3.90 m.mole.) in T.H.F. (40 ml.) containing furan (10 ml.) at -60°. The dark green colour of the reagent was instantly discharged and the reaction mixture acquired a deep red colouration. After 2 hr. at -60° the mixture was allowed to warm to room temperature for 16 hr.. A further amount (4 ml., 3.80 m.mole.) of reagent was added at room temperature and stirring continued for 2 hr.. Naphthalene was the sole product by t.l.c. analysis. Filtration of the reaction mixture followed by evaporation of the solvent afforded a brown amorphous solid, which was chromatographed over alumina. Naphthalene (1.05 g., 95%) (100% petroleum) was the only product eluted.

trans-2,3-Dichloro-1-phthalimidoaziridine and Sodium Naphthalene in the presence of Cyclopentadiene.

The experimental conditions were the same as for the preceding experiment but cyclopentadiene (10 ml.) was used instead of furan.

Chromatography (alumina) again afforded only naphthalene contaminated with the cyclopentadiene dimer.

trans-2,3-Dichloro-2,3-dimethyl-1-phthalimidoaziridine and Di-iron enneacarbonyl.[168]

The aziridine (0.50 g., 1.75 m.mole.) was dissolved in dry benzene (20 ml.). Di-iron enneacarbonyl (1.0 g., 2.75 m.mole.) was added to the stirred solution in one portion. Stirring was continued for 7 hr.. From t.l.c. analysis the aziridine was the sole product. Preparative t.l.c. [1 m.; silica; ether-petroleum (1:1)] afforded the pure aziridine (0.25 g., 50%).

In a subsequent experiment T.H.F. was used as the solvent and the reaction was conducted at 60° for 4 hr.. Again t.l.c. evidence indicated no new products and the aziridine (45%) was recovered as before.

trans-2,3-Dichloro-1-phthalimidoaziridine and Disodium iron tetracarbonyl.[169]

Iron pentacarbonyl (1 ml., 7.4 m.mole.) was added to a suspension of sodium borohydride (0.5 g., 13.2 m.mole.) in dry dimethoxyethane (30 ml.). After 20 min. methanol (10 ml.) was added to decompose excess borohydride. When gas evolution had ceased, the aziridine (1.05 g., 4.1 m.mole.) was added in one portion to the deep crimson mixture. Stirring at room temperature was continued for 24 hr.. The buff coloured solids (0.35 g.) were filtered off from the deep crimson filtrate. Removal of the solvent afforded a dark brown solid which was shown by t.l.c. (both silica and alumina) to contain trace amounts of tri-iron dodecacarbonyl only. The solid was chromatographed over florisil support, eluting with petroleum, ether, and ethyl acetate. No significant amounts of identifiable material were eluted.

trans-2,3-Dichloro-2,3-dimethyl-1-phthalimidoaziridine and Disodium iron tetracarbonyl.[169]

Sodium borohydride (0.45 g., 8.4 m.mole.) was suspended in dry dimethoxyethane (25 ml.) and iron pentacarbonyl (0.9 ml., 6.7 m.mole.) was added to the stirred mixture. After 20 min. methanol (9 ml.) was added to the deep crimson mixture to decompose excess borohydride. When gas evolution had ceased, a solution of the aziridine (0.50 g., 1.75 m.mole.) in T.H.F. was added dropwise over 30 sec.. After stirring at room temperature for 25 hr. the buff coloured solids (450 mg.) were filtered off and the solvent removed. A dark purple oily solid was obtained which was leached with benzene (100 ml.) and ether (100 ml.). Removal of the mixed solvent afforded a dark purple oily solid which was applied to a prep. t.l.c. plate (1m., alumina). The plate was eluted with ether-petroleum (1:1), and the intense yellow band at R_f 0.4 removed and washed from the support with ether. Removal of the solvent afforded a dark orange oily solid (50 mg.), which was shown [t.l.c., silica; benzene-dichloromethane (1:1)] to be a mixture of two yellow components. The oily solid was applied to a prep. t.l.c. plate (20 cm., silica) and eluted with benzene-dichloromethane (1:1). The faster running orange band was removed from the plate and washed with ether, yielding a golden orange solid (1 mg.) m.p. 147° dec. ν_{max} (KBr) 2041, 2017, 2003, 1994, 1978, 1950 (w), 1799 (w), 1747 (s), 1706 (s), 1270, 880 (w), 718 (w) and 710 $cm.^{-1}$; m/e 494, 466, 438, 410, 382, 354, 326, 285, 259, 147 (base), 104 and 76; m* 326 → 285 = 249, 285 → 259 = 235. Removal of the slower running band afforded a small amount of an impure brown oily solid m.p. 85-115° dec. contaminated with colourless flakes; ν_{max} (KBr) 3185 (wb), 2074, 2034 (b), 2010 (b), 1960 (s), 1976 (w), 1729 (sb), 1306 (s), 1125, 885 and 716 (s) $cm.^{-1}$; m/e 216, 201,

187, 162, 147 (base), 130, 104 and 76.

It is thought that the low yields of products are due to deterioration during chromatography.

1,2,3-Triazole-4,5-dicarboxylic acid.

Chloroform (400 ml.) was added to a slurry of sodium azide (65 g.) in water (65 ml.) cooled to 0°. Concentrated sulphuric acid (50 ml.) was added dropwise to the mixture with stirring. After 45 min. the pale green chloroform layer (less dense) was decanted off and poured through a filter paper. Acetylene dicarboxylic acid (18 g.) in ether (200 ml.) was added in one portion and the whole gently heated under reflux for 6 hr.. The reaction mixture was cooled to 0° and the solids filtered off (5.3 g.). The residual solution was poured into petroleum (500 ml.) and the precipitated solids filtered off (8.0 g.). Recrystallisation of the solids from ether afforded the triazole (6 g.) m.p. 190-5° (lit.[170] 200°).

1,2,3-Triazole-4,5-dicarboxylic acid and Acetic anhydride.

The triazole (3 g.) and acetic anhydride (20 ml.) were heated under reflux for 1 hr.. The acetic anhydride was removed on a rotary evaporator, yielding an oily brown solid. The residual oil was removed in vacuo. (1 mm.) leaving a brown solid, which sublimed at an oil bath temperature of ca. 120°. The sublimate was removed and resublimed to yield colourless granules (50 mg.) of 2-methyloxazole-4-carboxylic acid m.p. 183° (lit.[171] 183-4°) ν_{max} 3170 (w), 3125 (w), 2550 (vb), 1720 (sb), 1596, 1590, 1300 (s), 1218, 1170 (s), 1113, 995 (w), 931, 777 (w), 761, 750 and 675 (w) $cm.^{-1}$; m/e 127 (P) (base), 110, 99, 85 and 83.

DISCUSSION

Foreword

Oxidation of simple 1,1-dialkyl or -diaryl hydrazines proceeds via a variety of pathways,[172] two of the major ones being tetrazene formation and loss of nitrogen to give dialkyls and diaryls.

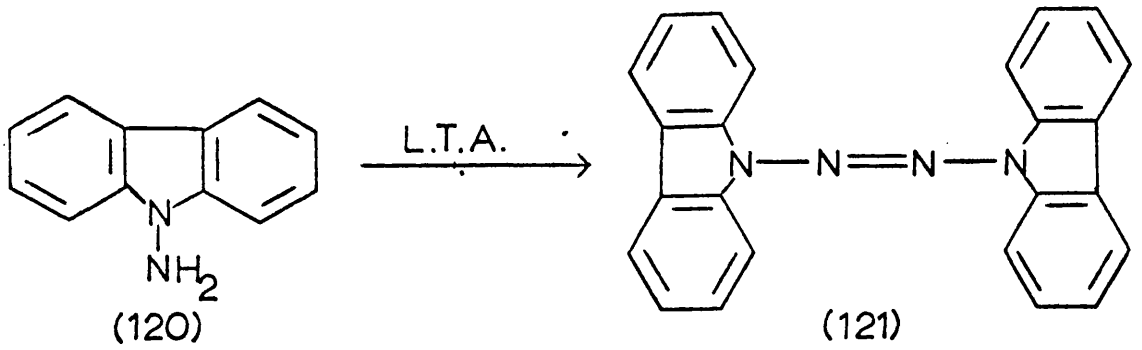
N-Aminoheterocyclic compounds may be conveniently treated as 1,1-disubstituted hydrazines and may be loosely classified into two broad groups: (i) those which on oxidation undergo mainly intermolecular reactions such as deamination and tetrazene formation, and (ii) those which on oxidation undergo mainly intramolecular reactions such as rearrangement and extrusion.

Examples of the first class are N-aminocarbazole (120)[155] and 1-aminobenzimidazole (122),[173] undergoing tetrazene (121) formation and deamination (123) respectively.

Examples of the second class are 1-aminobenzotriazole (124)[174] which extrudes nitrogen to give biphenylene (126) via benzyne (125); and 1-amino oxindole (127)[175,176] which rearranges to 3-cinnolinol (128).

Intermediates postulated in several of the reactions have been amino-nitrenes, of which it is claimed[177] that a conjugate acid has been isolated as the perchlorate salt (129).

It was subsequently demonstrated[39,40] that aziridines could be isolated from the oxidation of 3-aminobenzoxazolin-2(3H)-one (42) in the presence of olefins, (see Pt.(1) of Introduction), thus adding more evidence to the existence of amino-nitrenes.



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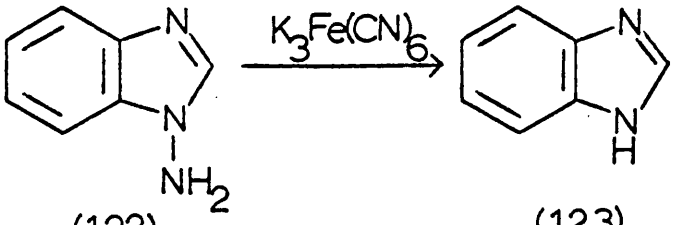

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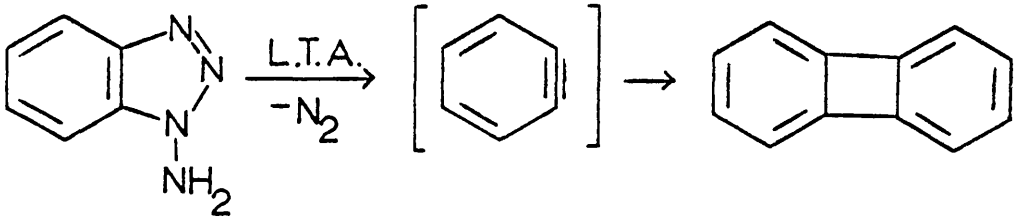

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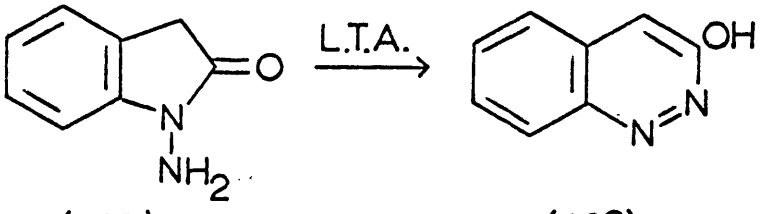

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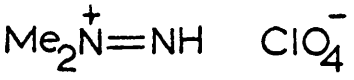
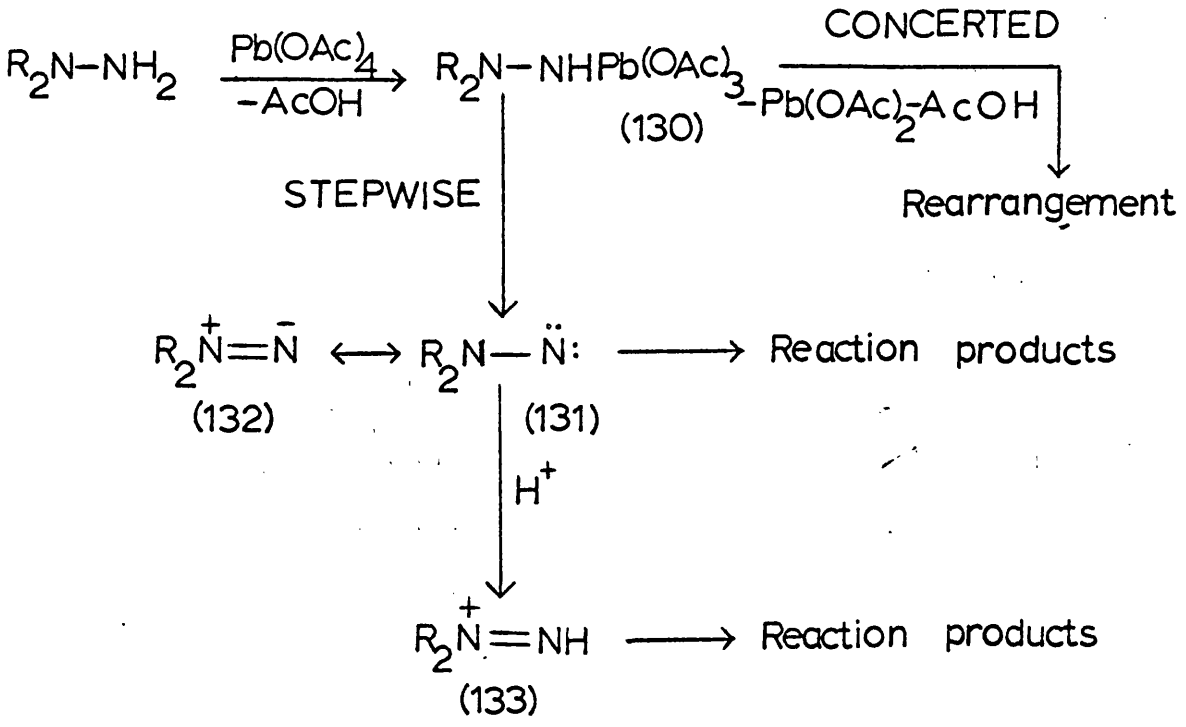


(129)

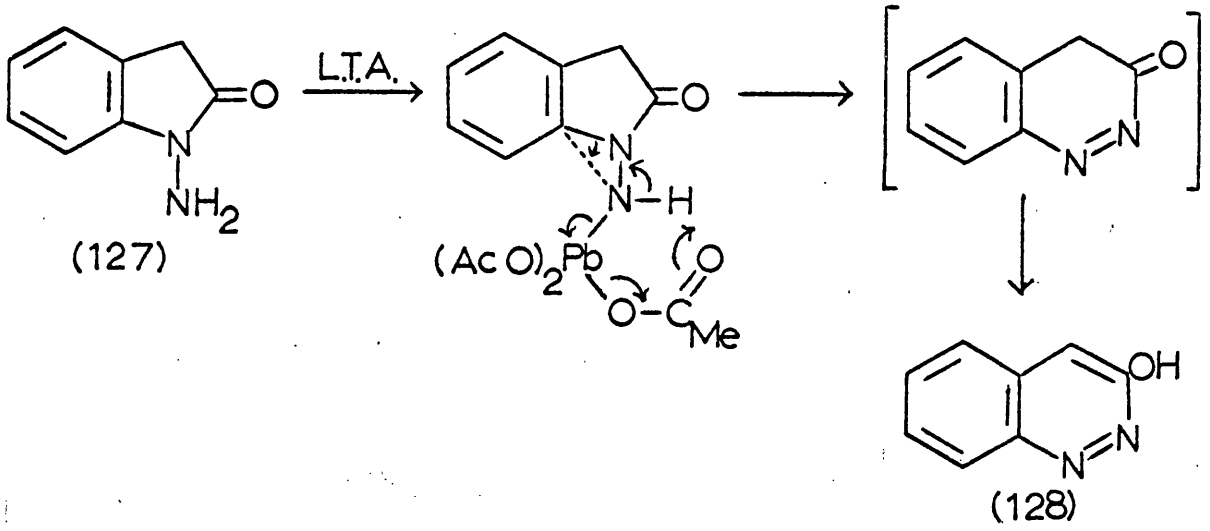
These latter observations encouraged an investigation of the factors which distinguish the group of compounds which undergo intramolecular reactions from those which undergo intermolecular reactions. The choice of N-amino compounds was somewhat influenced by the desire to have readily available starting materials.

The Nature of the Intermediate

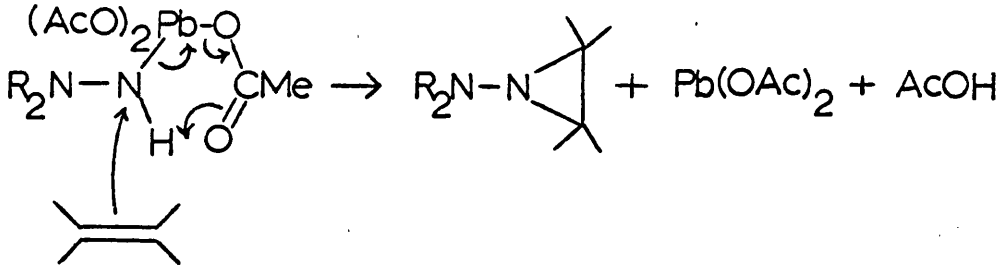
It is necessary first of all to consider the course of reaction of the N-amino compounds with L.T.A.. It is generally agreed that the initial reaction is the formation of the lead complex (130). This has two possible pathways open to it; either reaction can be concerted with loss of lead diacetate and acetic acid, or reaction can be stepwise, the amino-nitrene (131) being an intermediate. This might then give the products directly or could undergo prior protonation in the acid medium to give the nitrenium ion (133).



Baumgarten[176] favours the concerted pathway. He has noted the fact that $-Pb(OAc)_3$ is a good leaving group and has proposed that the initial L.T.A.-amine adduct (130) serves as a nitrenoid intermediate in the oxidation of N-aminooxindole (127) to 3-cinnolinol (128). He has also suggested that this type of mechanism could be operative in our 'trapping' experiments, reported later.

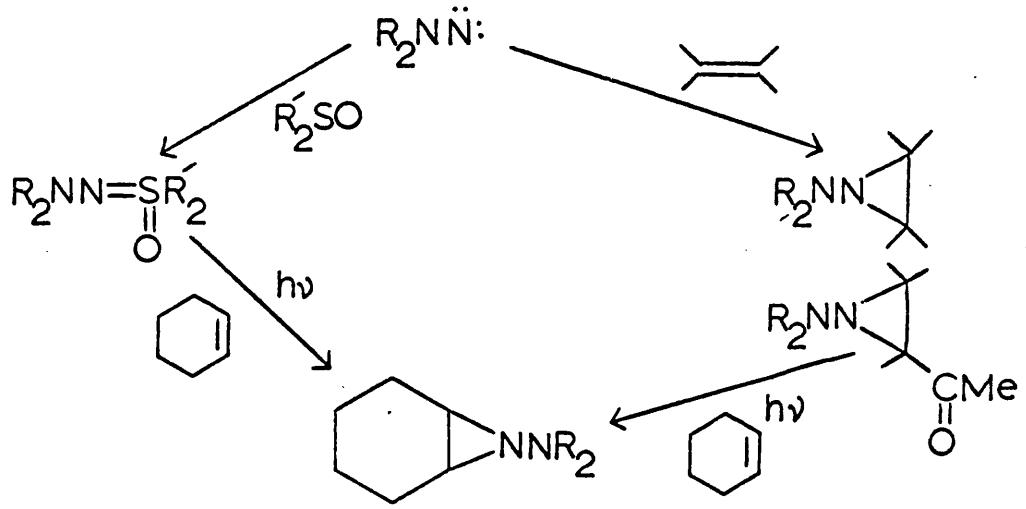


While his proposed mechanism is acceptable in accounting for the rearranged product (128), it is unlikely that this mechanism is operative in the absence of any rearrangement products. However consideration must be paid to the intramolecular 'trapping' experiment reported in the Introduction Pt.(1). The amine (37), when oxidised with L.T.A., was 'trapped' intramolecularly by the olefinic double bond to give the fused aziridine (38). The double bond may have provided assistance for the concerted loss of lead diacetate and acetic acid with aziridine formation. This mechanism could possible account for aziridine formation in our cases. The reaction would however be intermolecular and possibly less favourable.



The second route open to the initial lead complex (130) is the formation of the discrete amino-nitrene (131). This would be expected to receive some stability in its singlet state from the electron delocalised form (132), the lone pair on the tervalent nitrogen being delocalised into the vacant p-orbital of the univalent nitrogen. A similar suggestion has been made for methoxy-nitrene.[41]

Intramolecular pathways could well involve the nitrenoid but intermolecular pathways are more likely to involve the free nitrene. We believe that our 'trapping' experiments with olefins and sulphoxides as outlined, are highly suggestive that the nitrene is the reacting species. Furthermore the photolyses of dimethyl sulphoximines and of aziridines substituted in the 2-position with unsaturated groups, in the presence of cyclohexene also give high yields of the corresponding aziridine.



The only likely common intermediate in all three reactions is the amino-nitrene.

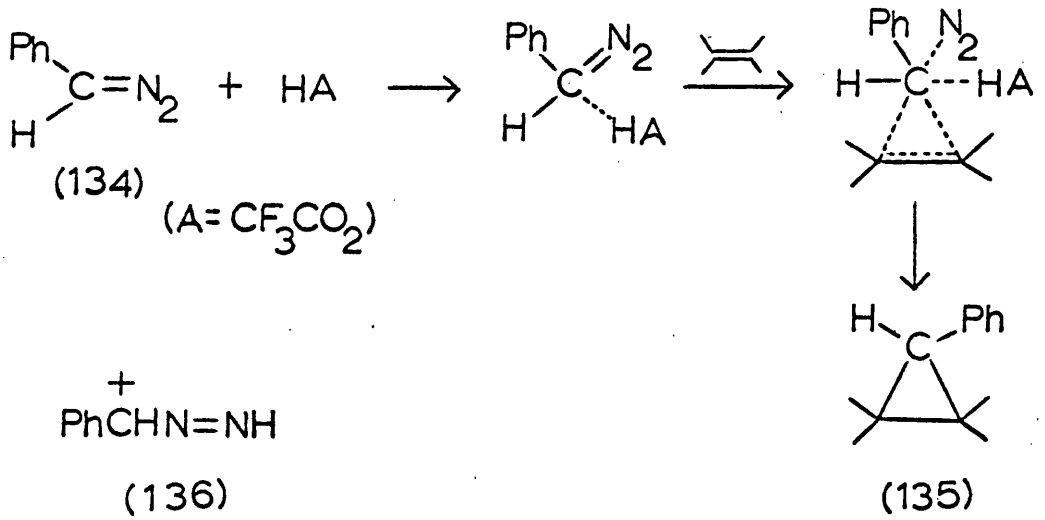
A comparison may be made between the initial lead complex and azides. In the latter the decomposition and rearrangement can be concerted e.g. Curtius rearrangement; or stepwise, by loss of nitrogen to give the nitrene. It is possible that both Baumgarten's[176] and our interpretations

are correct, and that the reaction is concerted where rearrangement or intramolecular reaction is observed, but otherwise it is stepwise.

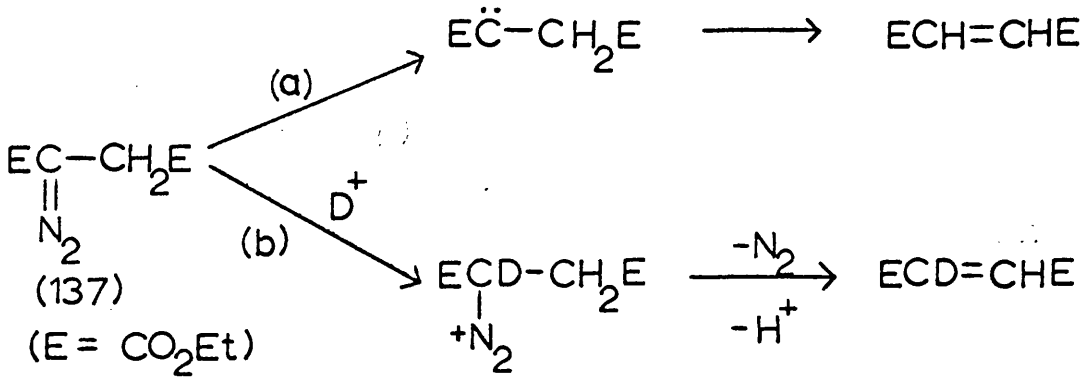
For every molecule of oxidant used, two molecules of acetic acid are formed. Consequently the reactive species is produced in an acidic medium, but experiments have indicated that the course of the oxidation of N-amino compounds by L.T.A. is unaffected by the presence of calcium carbonate.

However with the current fashionable interest in nitrenium ions,[178-180] it is necessary to consider whether the protonated nitrene species (133) could be playing an important role in determining the course of the reaction. This is the same proposal as was made earlier.[177] The electron delocalised form (132) bears a striking similarity to simple diazo compounds. Protonation would lead to (133).

However in the acid (CF_3CO_2H) catalysed decomposition of phenyl diazomethane (134) in olefins to give cyclopropanes (135) and other products, it is not thought[181] necessary to go through the protonated diazo species (136). A more satisfactory mechanism has been invoked to explain the product distribution and the deuterium incorporation (with CF_3CO_2D), not involving the protonated diazo compound. In view of the non-polar nature of the reaction medium it is considered that the diazo carbon atom acts as an acceptor in hydrogen bond formation with the acid, and that complete protonation is slow or comparable with the rate of the following steps.



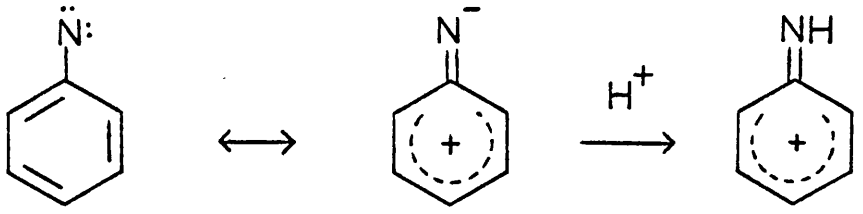
Subsequent studies[182] on the decomposition of diethyl diazosuccinate (137) in various solvents, have shown that even in acetic acid d_1 two thirds of the reaction proceeds via the carbenic pathway (a). In DCl/D_2O medium the reaction follows pathway (b) completely. In ethanol d_1 and cyclohexanol d_1 80-90% of the product is attributable to route (a).



An important conclusion was that the carbenic decomposition and protonation of the diazo compound compete with each other in most protic solvents but that the relative extents of both processes depend upon the pk_a of the solvent; the larger the pk_a then the larger the extent of the carbenic process.

Similar results have been obtained[183] for diaryldiazomethanes with alcohols. It was shown that the addition of alcohols had little effect upon the rate of decomposition, indicating that they were probably not reacting before decomposition.

It has been noted[184] that the deoxygenation of nitro- and nitroso-benzenes by triethyl phosphite takes a different reaction path in the presence and absence of acetic acid. This has been attributed to the participation of phenyl nitrenium ion (138), which can undergo nucleophilic attack in the ortho and para positions.



(138)

There is however no report of the decomposition of phenyl azides in the presence of acetic acid.[5] The acid catalysed decomposition of 2-azidobiphenyls has been briefly studied[185] in acetic acid containing hydrogen bromide. In the non catalysed decompositions, carbazoles or furoxans are formed, whereas the hydrogen bromide catalysed decompositions give rise to 2-aminobiphenyls. Furthermore the ortho and para positions with respect to the original azido function are brominated if they are vacant. The rate determining step is the decomposition of the conjugate acid of the azide. It was shown that bromination of the resultant amine was accomplished by bromine as outlined in the scheme.

$$ArN_3 + H^+ \longrightarrow ArNH - N_2^+$$

$$ArNH - N_2^+ + Br^- \longrightarrow ArNHBr + N_2$$

$$ArNHBr + HBr \longrightarrow Br_2 + ArNH_2 \quad \underset{\rightleftharpoons}{\overset{HBr}{\searrow}} \quad ArNH_3^+ Br^-$$

$$ArNH_2 + Br_2 \longrightarrow Br - ArNH_2.HBr$$

In the light of modern mechanistic attitudes it may even be contrived that a nitrenium ion is involved here!

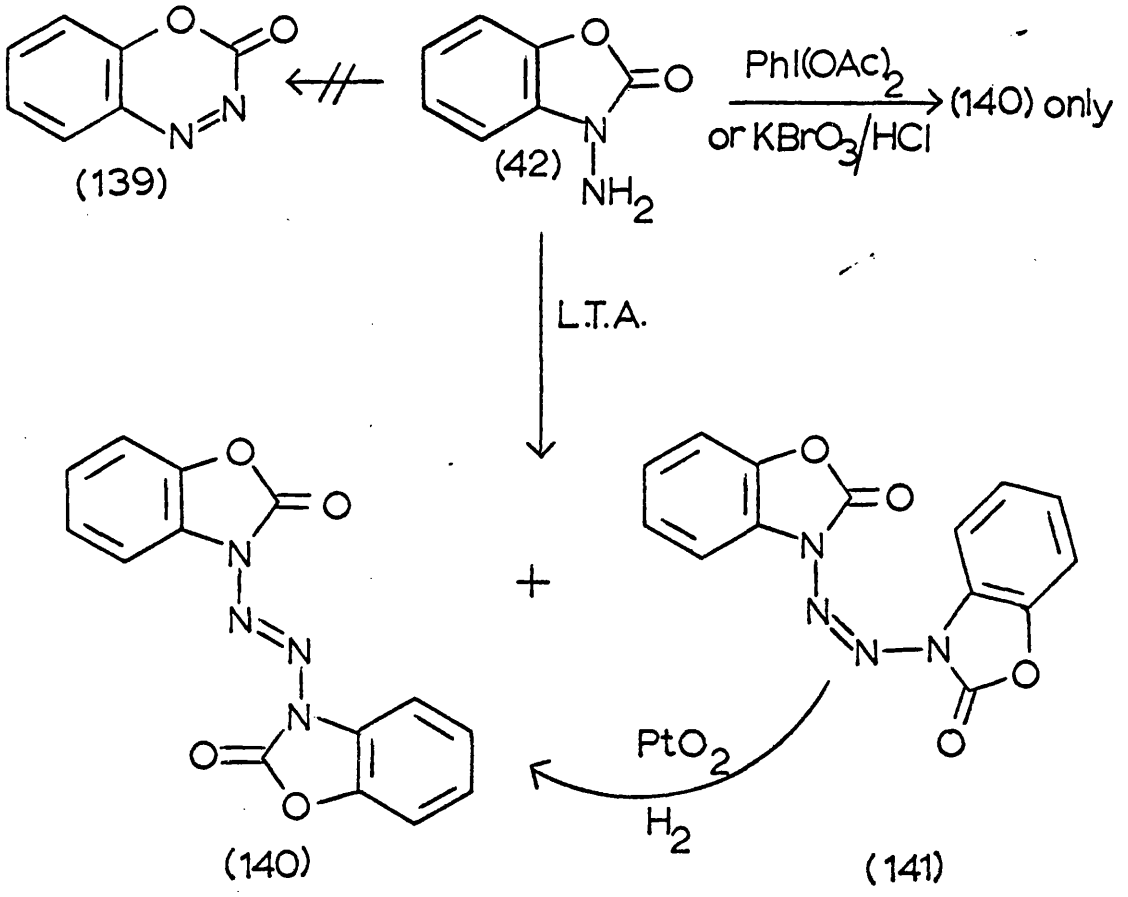
The possible nitrenium ion that would be produced in our reactions would be destabilised either by the adjacent electrophilic carbon atom(s) of the lactam or imide carbonyl(s), or by the resultant loss of hetero-aromaticity of the ring in which it is situated e.g. N-carbazolyl nitrenium ion. Moreover our oxidations are conducted in non-protic solvents such as dichloromethane-olefin mixtures with an anticipated very high pka. These theories, taken in context with the dependence of pka of the solvent upon the decomposition pathway of diethyl diazosuccinate, would suggest that the oxidation of our N-amino compounds do involve discrete amino-nitrenes and not nitrenium ions as the major reaction pathway.

Preparation and Oxidation of the N-Amino Compounds

3-Aminobenzoxazolin-2(3H)-one

The title compound was prepared by an improvement of the literature method[40] by the amination of benzoxazolin-2(3H)-one with two equivalents of H.O.S. instead of one.

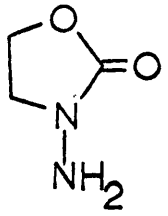
By analogy with 1-aminooxindole (127), 3-aminobenzoxazolin-2(3H)-one (42) might be expected to give the ring inserted compound (139) which could fragment by losing nitrogen and carbon dioxide, to give benzyne. However this was never detected; instead oxidation with L.T.A. afforded two tetrazenes (140) and (141) assigned to the trans- and cis- configuration respectively.



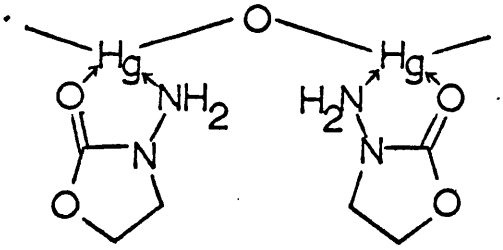
The ratio of the yields of the tetrazenes varied according to the conditions employed. If essentially homogeneous oxidation was used, then the trans- form was the major one isolated. However if the oxidation was conducted under heterogeneous conditions, with the majority of the L.T.A. initially out of solution, then the cis- form was the major product isolated with only minor amounts of the trans- form. The total amount of tetrazenes isolated only accounted for ca. 20% of the starting material. The remainder of the reaction mixture was extremely complex by t.l.c. analysis as noted earlier.[40]

The assignment of the configuration of the tetrazenes is aided by their I.R. spectra. That assigned to the trans- form has a single carbonyl absorption at 1790 $cm.^{-1}$, and the cis- form has two strong absorptions at 1773 and 1728 $cm.^{-1}$, as anticipated from their structures shown in (140) and (141). Their U.V. spectra were not very indicative; the cis- form exhibited a very complicated series of absorptions whereas the trans- form spectrum was relatively simple. This may possibly have been expected. Only the trans- form was isolated from the homogeneous oxidations with iodosobenzene diacetate and potassium bromate-hydrochloric acid. It is thought that an important criterion for cis- tetrazene formation is a reactive surface such as that of an insoluble oxidant. Confirmatory evidence was provided by Atkinson[186] who noted that attempted hydrogenation of the cis- form produced the trans- form.

In retrospect these results are parallel to those of Forgione et al.,[187] who found that oxidation of 3-amino-2-oxazolidinone (142) with homogeneous reagents produced a trans- tetrazene whereas mercuric oxide produced both the cis- and trans- forms, the cis- form predominating. The isomerisation of the cis- to the trans- was accomplished by U.V. light. The trans- tetrazene was stable to hydrogenation whereas the cis- form gave the deaminated 2-oxazolidinone.



(142)

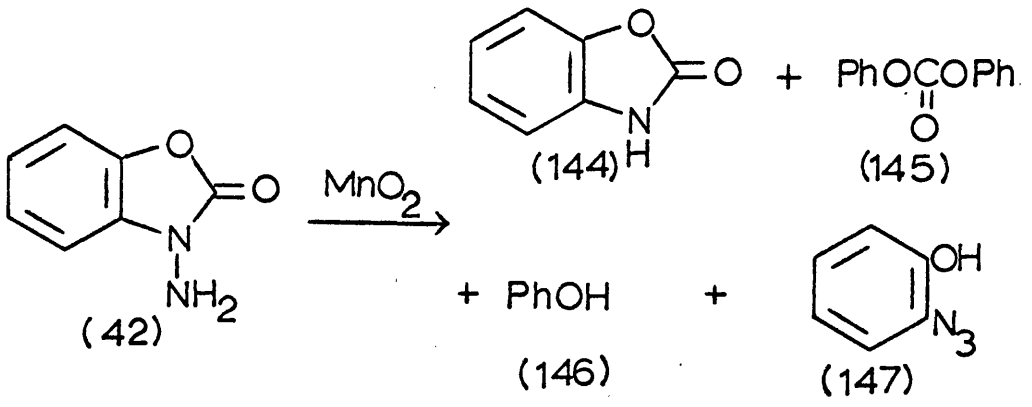


(143)

The formation of the cis- tetrazene from (142) with mercuric oxide, has been suggested to involve a metal-amine chelate complex (143) which then undergoes oxidation. N-Aminolactams are known[188,189] to form copper chelates, by coordinating as bidentate ligands.

It is uncertain whether the same type of intermediate is involved during L.T.A. oxidations since the structure of L.T.A. has yet to be determined.

It was noted[40] that benzoxazolin-2(3H)-one, the product of oxidative deamination, was only recovered in low yield from reaction with L.T.A.. However it did not react with manganese dioxide. Oxidation of the N-amino compound (42) with manganese dioxide did in fact produce benzoxazolin-2(3H)-one (144) as the major product. Minor products, diphenyl carbonate (145), phenol (146) and o-azidophenol (147) were also isolated. From t.l.c. analysis these minor products were also present in the oxidation with L.T.A..



(42) $\xrightarrow{MnO_2}$ (144) + (145) + PhOH (146) + (147)

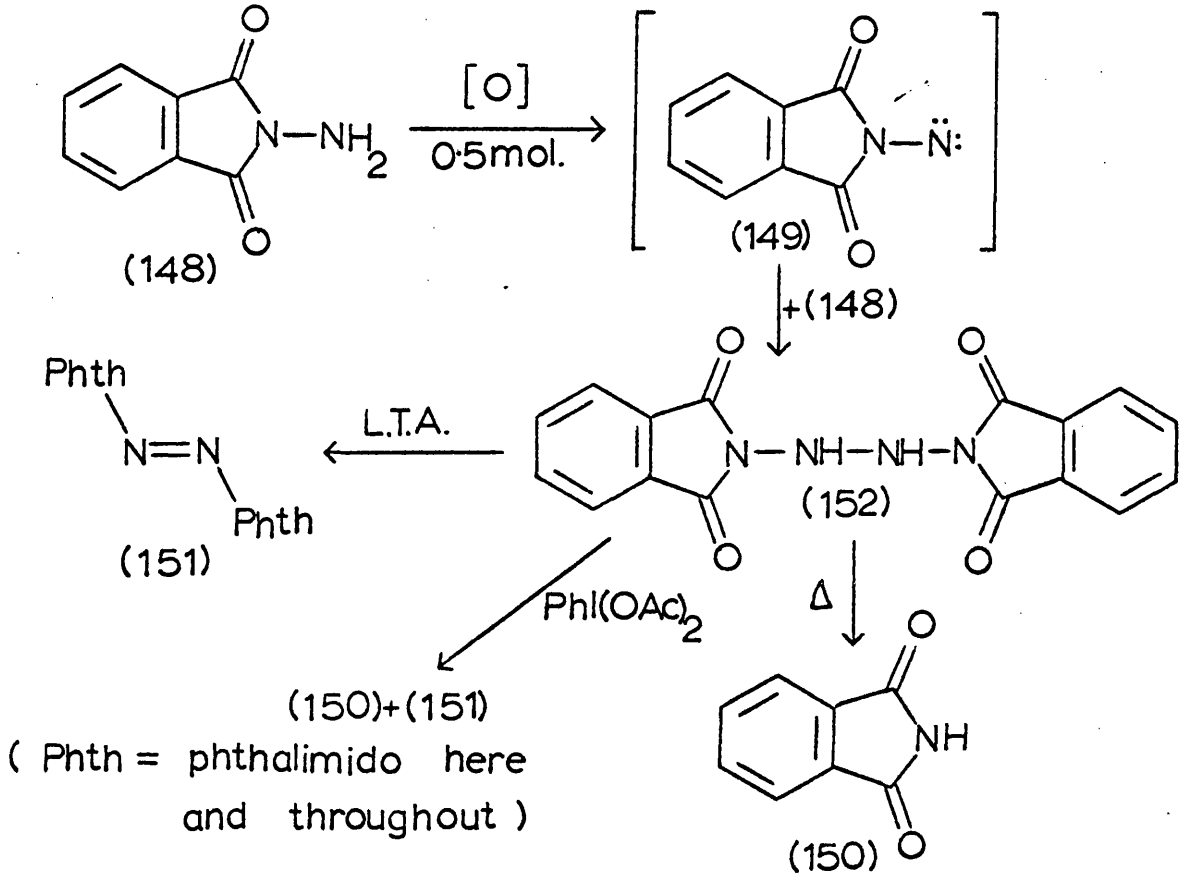
The latter three minor products were shown (by t.l.c. only) to be formed by both cis- and trans- tetrazene oxidation with manganese dioxide.

It has subsequently been noted[190] that the oxidation of N,N-dibenzylhydrazine with L.T.A. produced some benzylazide. This was shown to be formed from further oxidation of the intermediate 1,1,4,4-tetrabenzyltetrazene.

N-Aminophthalimide

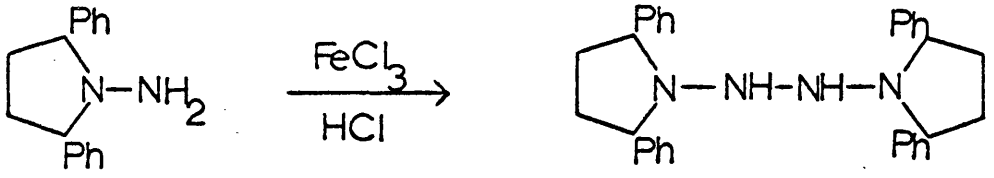
This N-amino compound (148) is perhaps the most readily available, being prepared from phthalimide and hydrazine hydrate in a simple one step reaction.

Oxidation with L.T.A. gave two products, phthalimide (150) and the trans- tetrazene (151), in yields of 70-80% and 5% respectively.



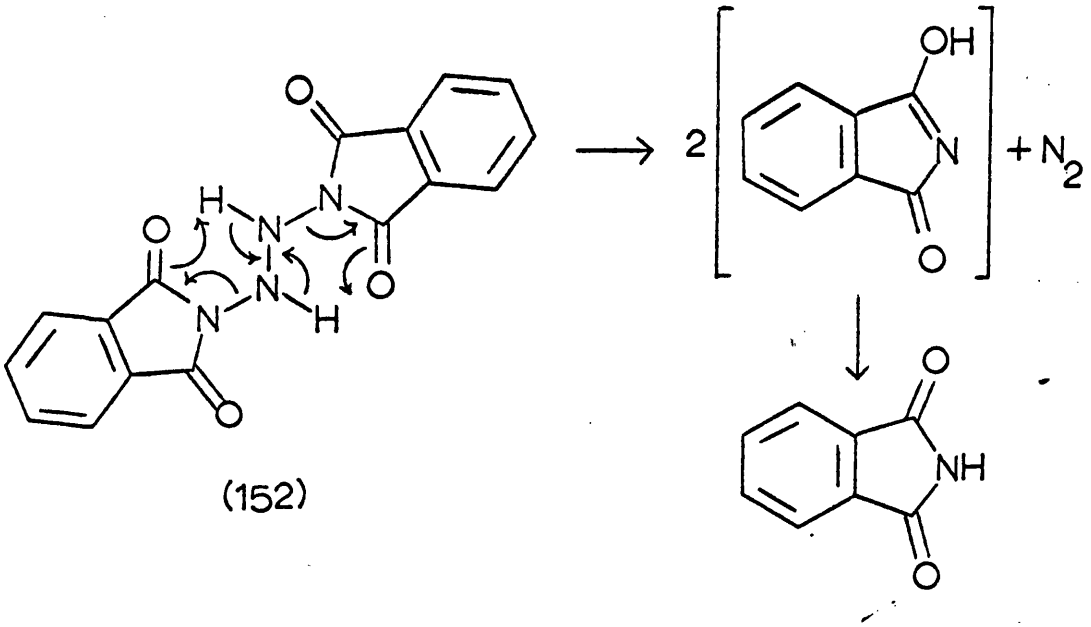
Oxidation with iodosobenzene diacetate (1 mol.) also led to the isolation of phthalimide and the tetrazene but in approximately equal amounts. Careful observation of the reaction indicated that an isolable intermediate was being formed. The oxidant was added to a suspension (approx. 25% in solution) of N-aminophthalimide (148) in dichloromethane. After about a quarter of the oxidant had been added, complete solution was obtained. Further addition of oxidant caused immediate precipitation which reached a maximum when 0.5 mol. had been added. (Addition of 1 mol. of oxidant caused complete solution again). Spectral and chemical evidence indicated that the precipitated solid was the tetrazane (152). Attempted recrystallisation afforded phthalimide only. It was subsequently found that the tetrazane deteriorated on storage to phthalimide. The m.p. recorded (210-12°) could be that of impure phthalimide. The mass spectrum showed only a parent peak for phthalimide. The I.R. spectrum exhibited a single strong N-H peak and the rest of the spectrum was very similar to the tetrazene (151). When treated with triethylamine, phthalimide was immediately formed. Excess iodosobenzene diacetate produced about equal amounts of phthalimide and tetrazene, whereas L.T.A. produced solely the tetrazene.

The tetrazane (152) is considered to be formed from the reaction of N-phthalimido nitrene (149) with N-aminophthalimide (148). A similar suggestion[191] has been made for the formation of the tetrazane (154) from N-amino-2,5-diphenylpyrrolidine (153).



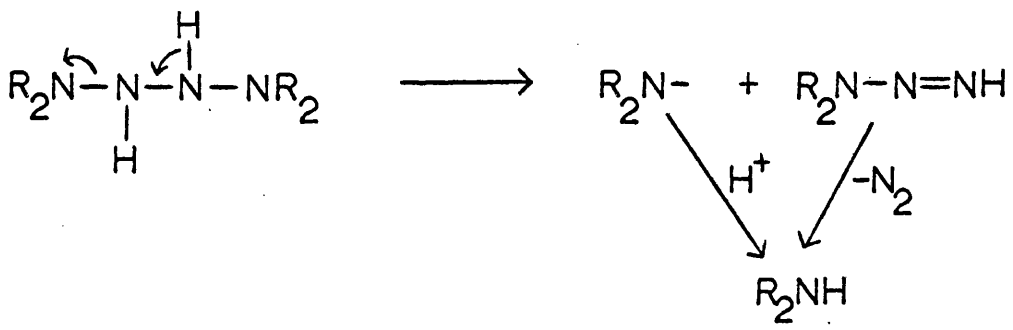
(153) (154)

Dreiding has proposed[192] that the tetrazane (152), which he only postulated as an intermediate and did not isolate, rapidly undergoes 1,5-hydrogen shifts, as shown, to give the enol form of phthalimide and nitrogen. This is an extremely attractive mechanism for oxidative deamination of N-aminolactams. However, as mentioned earlier, 1-aminobenzimidazole (122) on oxidation with ferricyanide gives benzimidazole (123) which is also a product from L.T.A. oxidation.[188]



(152)

In this case it is only possible to involve a similar 1,5-hydrogen shift mechanism if the ring nitrogen adopts a sp^3 geometry, which is highly unlikely. Perhaps a more general oxidative deamination mechanism is that outlined below, the ease with which the reaction proceeds, depending upon the stability of the anion produced.

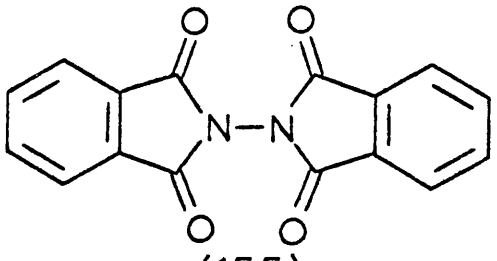


Both deamination mechanisms proposed require the tetrazane as an intermediate. However oxidation of the tetrazane with L.T.A. produced only the tetrazene. This may have been due to the reaction conditions. If the reaction were conducted at low temperature then the major product is expected to be the tetrazene. This has also been suggested diagramatically by Dreiding.[192]

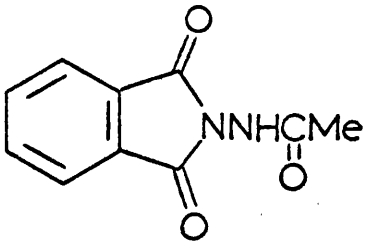
A less plausible mechanism of oxidative deamination involves oxidation of the amine to the nitroso compound. Disproportionation of the latter would generate the deaminated species and oxides of nitrogen. However this mechanism would require 2 mol. of L.T.A. whereas 1 mol. has been shown to be sufficient. Furthermore the gas evolved during our oxidations has been shown to be nitrogen.[188] On the other hand, the N-nitroso compound could deaminate remaining N-amino compound in an analogous way to the deamination of 3-aminobenzoxazolin-2(3H)-one with N-nitrosodiphenylamine.[40]

Tetrazene formation has been shown to be a consequence of tetrazane oxidation. It has also been suggested[192] that it occurs by nitrene dimerisation, since it was found that more tetrazene than phthalimide was formed if the addition of L.T.A. was rapid. Similar suggestions have also been made for other examples.[3,172]

Phthalimido-phthalimide (155) and N-acetylaminophthalimide (156) have also been isolated[192] in low yield from L.T.A. oxidation of N-aminophthalimide.



(155)

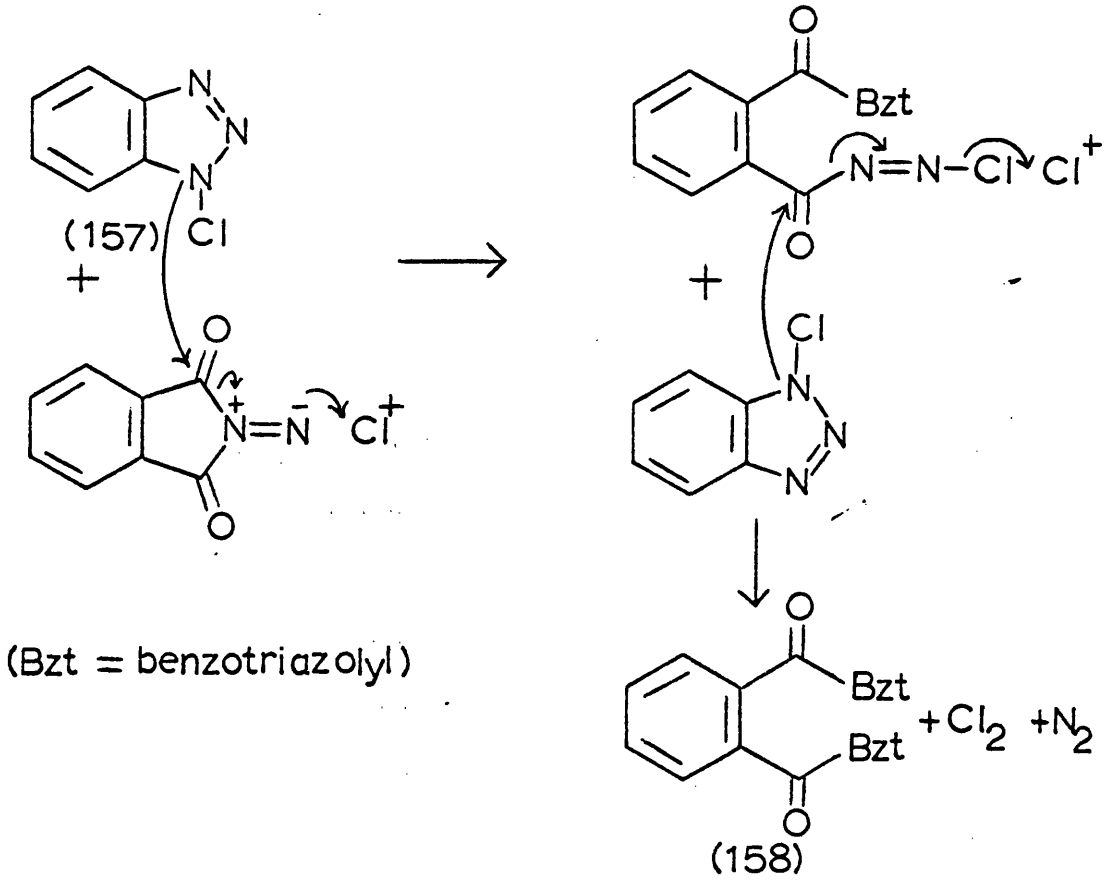


(156)

It was established that (155) was the result of a trans-imidation reaction between phthalimide and N-aminophthalimide with loss of ammonia.

N-Acetylaminophthalimide may have been a by-product of the primary oxidation of the N-amino compound with L.T.A..

Oxidation of N-aminophthalimide (1 mol.) with N-chlorobenzotriazole (157) (2 mol.) yielded two products, the tetrazene (151) and phthaloyl-bisbenzotriazole (158) in approximately the same amounts. The latter compound (158) was independently synthesised from phthaloyl chloride and benzotriazole.

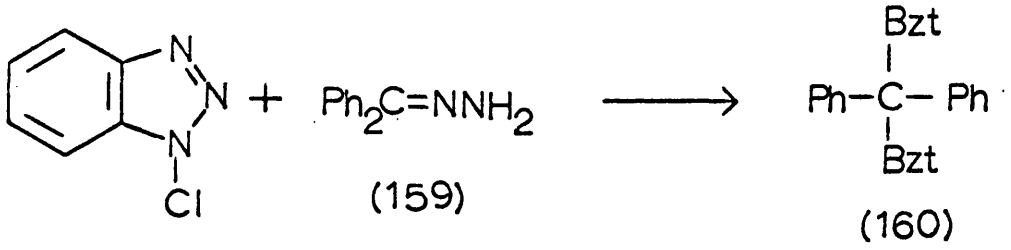


(Bzt = benzotriazolyl)

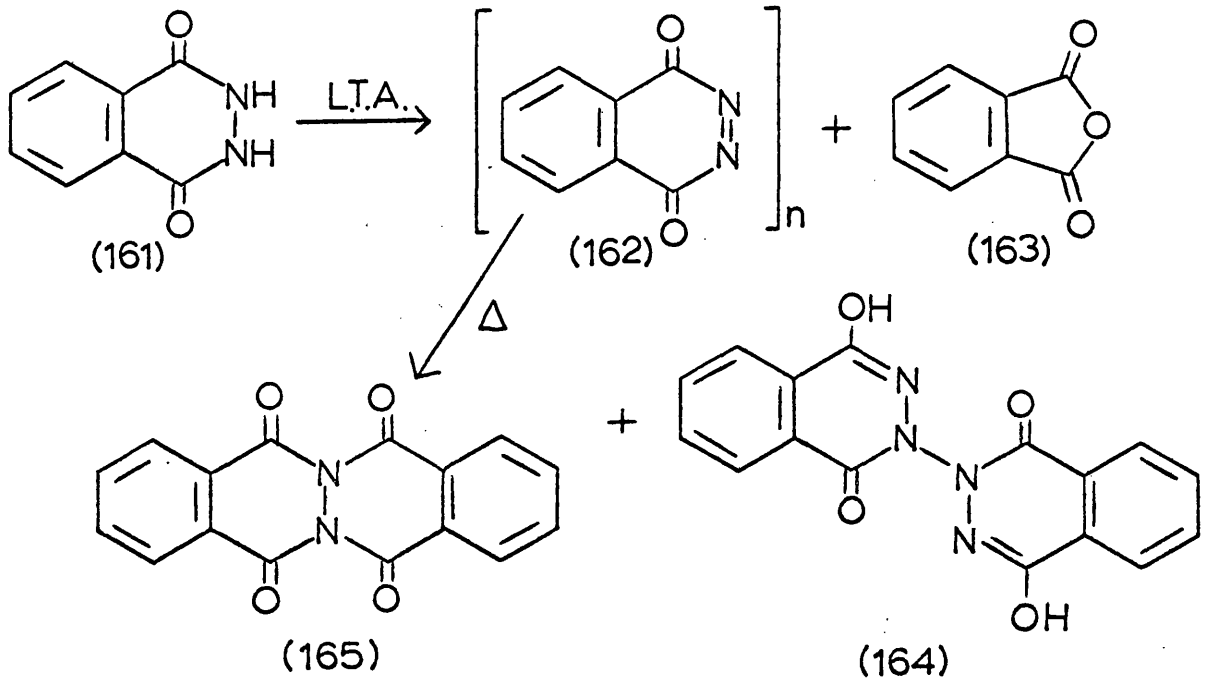
The substitution of the benzotriazole ring is uncertain, but comparison of U.V. spectra with other benzotriazole derivatives[174] indicates 1-substitution.

A possible mechanism for the formation of (158) under oxidative conditions is outlined. It was subsequently shown[193] that the oxidation

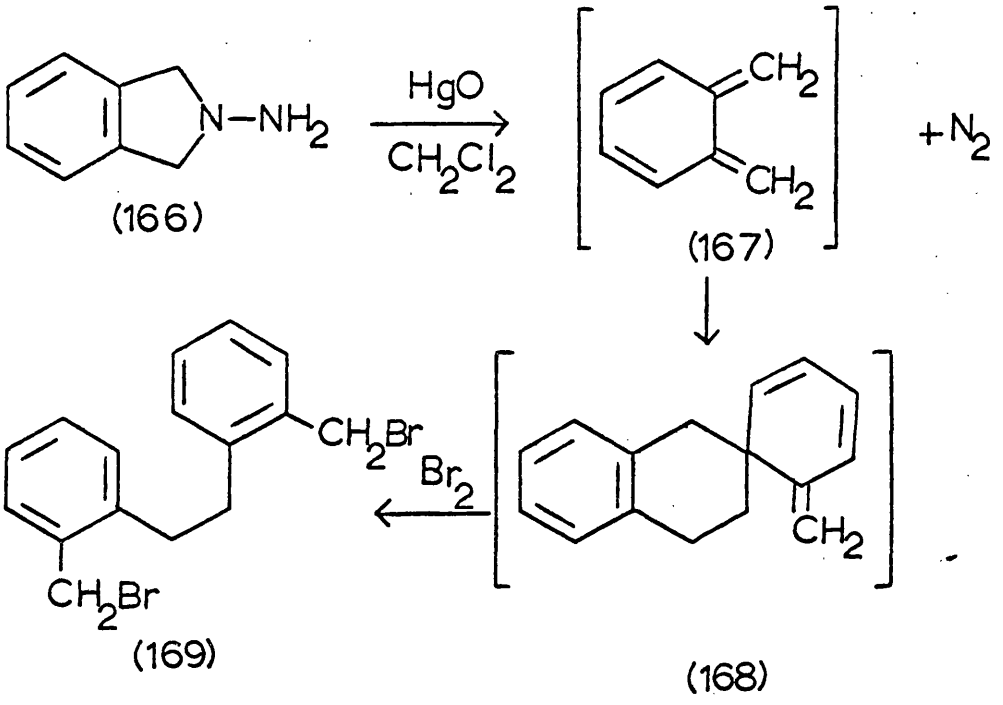
of benzophenone hydrazone (159) with N-chlorobenzotriazole gave dibenzotriazolyldiphenylmethane (160) by an analogous mechanism.



Phthalhydrazide (161) is an isomer of N-aminophthalimide and the oxidation of both could possibly proceed through a common intermediate. Examination of the literature revealed[194] that the oxidation of phthalhydrazide (161) with L.T.A. gives mainly a polymeric product (162) with lesser amounts of phthalic anhydride (163) and the bis-hydrazide (164). On heating, the polymer (162) is converted smoothly to the compound (165).



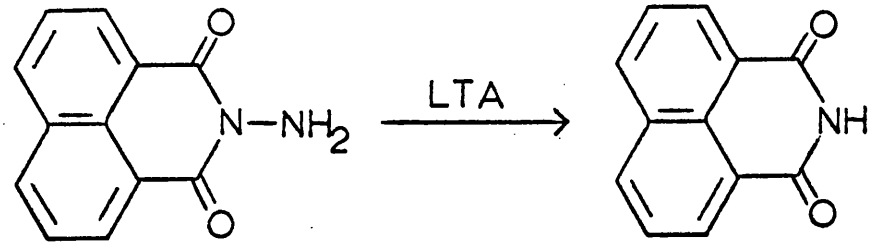
A comparison may also be made with the oxidation of N-amino-isoindoline (166) by mercuric oxide.[195] Several minor products are formed but the major one is a dimer (168) of the presumed o-xylylene intermediate (167). The dimer was isolated as its dibromide (169).



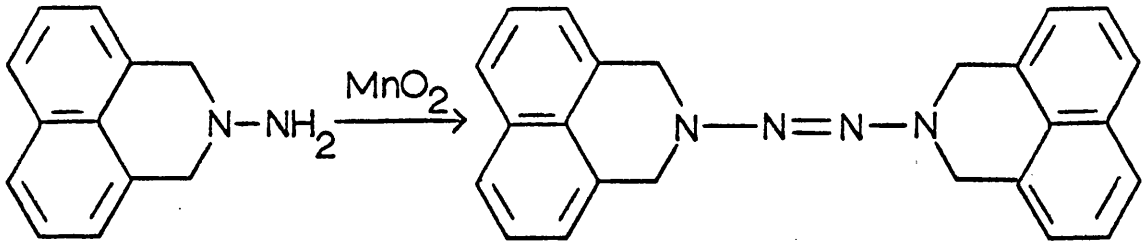
N-Aminonaphthalimide

This N-amino compound (170) was conveniently prepared in high yield (90%) from 1,8-naphthalic anhydride and hydrazine hydrate by a one step process.

Oxidation of (170) with L.T.A. gave naphthalimide (171) as the only isolable product. This may be taken in contrast to the oxidation of the reduced form (172) with manganese dioxide, which gave only the tetrazene (173).[196] The comparison may be dubious in view of the different oxidants used, but it is felt that L.T.A. and (172) would still give the tetrazene (173) by analogy with 1,1-dibenzylhydrazine.[190]



(170) (171)



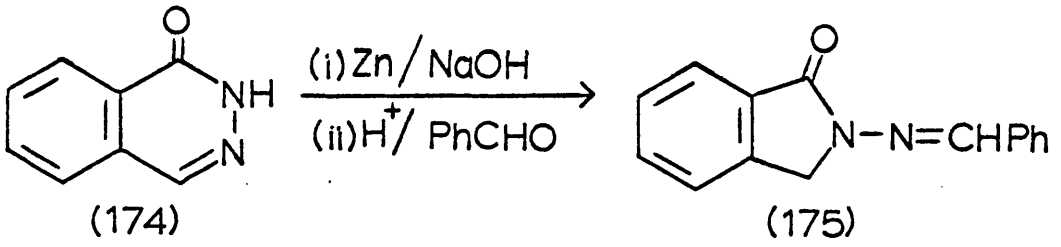
(172) (173)

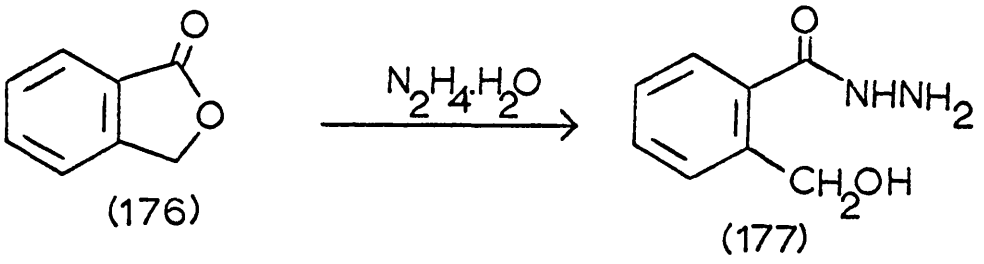
N-Aminophthalimidine

This compound, hitherto unknown, might be expected to show similarities to either N-aminophthalimide or N-aminoisolindoline on oxidation, or even to N-aminooxindole, of which it is an isomer.

There was one report[152] of the isolation of the benzylidene derivative (175) of the N-amino compound (179) from a rather curious reaction. Reduction of phthalazone (174) with zinc and sodium hydroxide followed by acidification and shaking with benzaldehyde, afforded the benzylidene derivative (175). The latter reaction is similar[150] to the condensation of phthalhydrazide (161) with aldehydes to give derivatives of N-amino-phthalimide. Repetition of the original work,[152] but omitting the acidification and benzaldehyde treatment stage, and substituting instead a chloroform extraction, afforded trace amounts of a brown oil which by

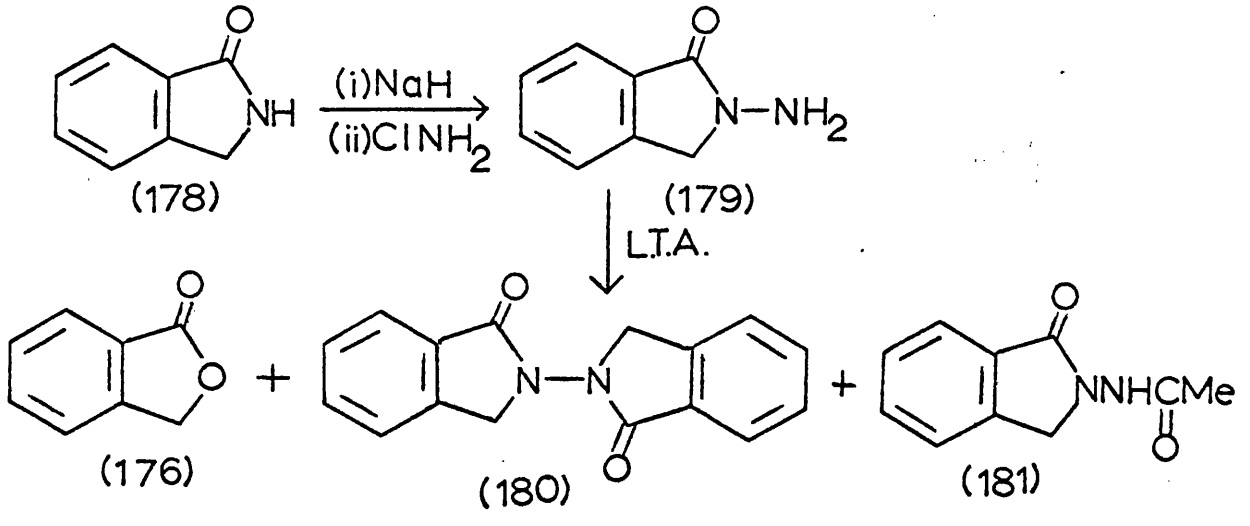
I.R. spectra comparison consisted mainly of impure N-aminophthalimidine (179) (prepared later).





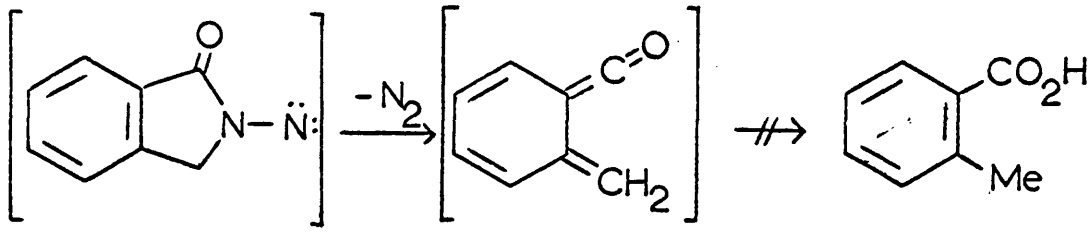
Several approaches to the synthesis of N-aminophthalimidine were attempted. Treatment of phthalide (176) with hydrazine hydrate under a variety of conditions afforded only o-hydroxymethylbenzhydrazide-(177).[197]

Attempted amination of phthalimidine (178) (prepared by an improvement of the literature method[198]) with either H.O.S. or hydrazine hydrate, gave a quantitative recovery of phthalimidine. However chloramine did aminate phthalimidine to give the N-amino compound (179). The yield of the N-amino compound varied with the scale of the reaction. The properties of the benzylidene derivative (175) were in accord with those reported earlier.[152]



Upon oxidation with L.T.A., (179) gave neither phthalimidine (178) nor phthalazone (174) as might have been expected by analogy with N-aminophthalimide and N-aminooxindole respectively. Instead there was a very vigorous gas evolution. The major products isolated by chromatography were biphthalimidine (180) and N-acetylaminophthalimidine (181), plus a trace of phthalide (176). These products however, only accounted for about 25% of the material used and do not explain the vigorous evolution of gas (N_2?). On the other hand Carpino[195] only accounted for 26% of his starting material, N-aminoisoindoline, but the product had lost nitrogen!

The products isolated in our oxidation, (176), (180) and (181) might be expected as minor products by analogy with N-aminophthalimide. It may be speculated that the major reaction pathway involves the keten (182) which might be expected to give some o-toluic acid, or even o-methyl toluate in the presence of methanol. However neither was isolated.



(182)

N-Aminocarbazole

This was prepared by an improvement of the literature method[155] by reduction of the N-nitroso compound with lithium aluminium hydride.

Upon oxidation with L.T.A. it gave the very insoluble tetrazene (121), of unknown configuration. The reported preparation[155] of (121) was not reproducible. An extra step had to be incorporated. The initial

precipitate had to be washed with water to remove the large amount of lead diacetate.

$$\underset{(120)}{Cz-NH_2} \xrightarrow{L.T.A.} \underset{(121)}{Cz-N=N-Cz}$$

(Cz = N-carbazolyl)

Oxidation of N-Amino compounds in the presence of Olefins

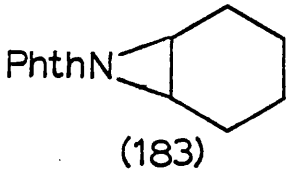
Following the work of Atkinson and Rees[39,40] we initially extended their oxidation of 3-aminobenzoxazolin-2(3H)-one route to N-aminophthalimide, 3-amino-2-methyl-4-quinazolone[188] and 1-amino-2-quinolone.[188]

(a) By far the most extensive work in this thesis has been conducted with N-aminophthalimide (148), primarily because of its ease of synthesis.

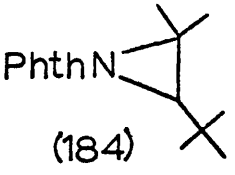
It was found that oxidation of (148) in the presence of nucleophilic olefins such as cyclohexene and the but-2-enes, commonly used as carbene traps, gave the corresponding aziridines in fair to excellent yield.

The majority of the early work was conducted using a vast excess of the olefin in dichloromethane, followed by chromatographic work up. It was subsequently shown that the optimum amount of olefin was ca. 5 mol.. The use of larger amounts did not improve the yield, but the use of smaller amounts resulted in a corresponding decrease in the yield of aziridine.

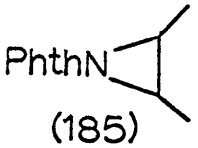
When a chromatographic work up was employed, the retention time had to be kept to a minimum otherwise considerable losses occurred. When 7-phthalimido-7-azabicyclo[4,1,0]heptane (183) was adsorbed on a deactivated alumina column and eluted after 2 hr. only 20% was recovered. On the other hand the yield of 2-t-butyl-3,3-dimethyl-1-phthalimido-aziridine (184) was the same (61%) whether column chromatography was employed or not. This may be attributable to the stabilising influence of the t-butyl group on the three membered ring.[199a]



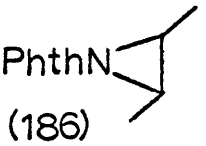
(183)



(184)



(185)



(186)

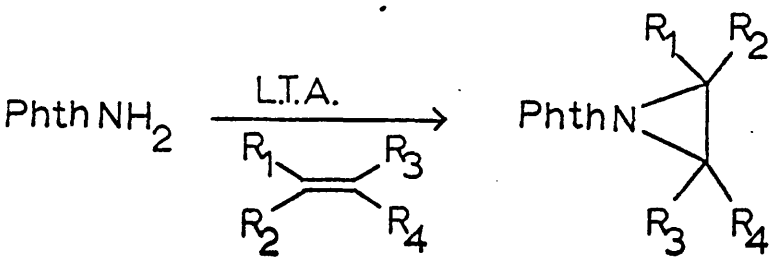
Whenever the yield of aziridine was low, phthalimide was the other product isolated. Most of this phthalimide could be removed by washing with 1% aqueous sodium hydroxide. Recrystallisation of the residue generally afforded the pure aziridine.

The additions to cis- and trans-but-2-ene to give (185) and (186) respectively were at least 95% stereoselective by examination of the N.M.R. spectra of the reaction mixtures. The yield of aziridine (185) was half that of (186) under identical conditions. It is unlikely that this is due to the stability of the resultant aziridine, since Dreiding[192] has found that the aziridine (185) is considerably more stable than (186). This may perhaps indicate an unfavourable reaction for the nitrene to undergo addition to cis-olefins, deamination being preferred; (cf. diethyl maleate and cis-1,2-dichloroethylene discussed later).

The stereospecific additions would tend to indicate that the nitrene is reacting in its singlet state, which may even be its ground state. This could achieve some stability by electron delocalisation of the type mentioned earlier. If indeed this delocalised form were contributing to the stability of the nitrene, then a consequence should be an increase in nucleophilicity of the intermediate.

We sought evidence for this by studying the addition to 'electron deficient' olefins. The corresponding aziridines were obtained just as readily as from the more usual olefins, and in some cases, more so. Esters of acrylic, methacrylic, crotonic and fumaric acids gave good yields of aziridines as did mesityl oxide and some halogenated olefins.

Table (2) shows the aziridines (187) obtained from N-aminophthalimide and olefins.



(187)

Several olefins, notably butadiene, cis-1,2-dichloroethylene, 1,1-dichloroethylene, acrylonitrile, acrylic acid and methacrylic acid failed unexpectedly to give aziridines.

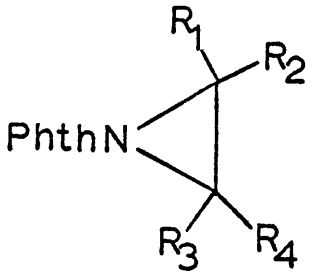
The failure with butadiene may be a consequence of the lability of the possible adduct, a 2-vinylaziridine.[39,40] Campbell[200] also failed to obtain an adduct with butadiene.

The failure with cis-1,2-dichloroethylene was completely unexpected since the trans-isomer and 1,2,2 trichloroethylene (which possesses two cis-chlorine atoms) both added well. A similar result was subsequently noted[188] with 3-amino-2-methyl-4-quinazolone and cis-1,2-dichloroethylene.

When diethyl maleate was used as the olefin, none of the expected aziridine was isolated; instead a small amount of the trans-aziridine was obtained. This could either be due to isomerisation of the aziridine during work up or to preferential addition of the nitrene to a small amount of fumarate present in the maleate. The latter explanation is the more likely especially when taken in conjunction with the results obtained for cis-but-2-ene and cis-1,2-dichloroethylene. Experiments have indicated that carbene addition[201] and 1,3-dipolar addition[202] to dimethyl fumarate is at least 100 times faster than to dimethyl maleate. Crowding of the transition state may be important.

The absence of any maleate adduct in our case would tend to suggest that deamination proceeds faster than addition.

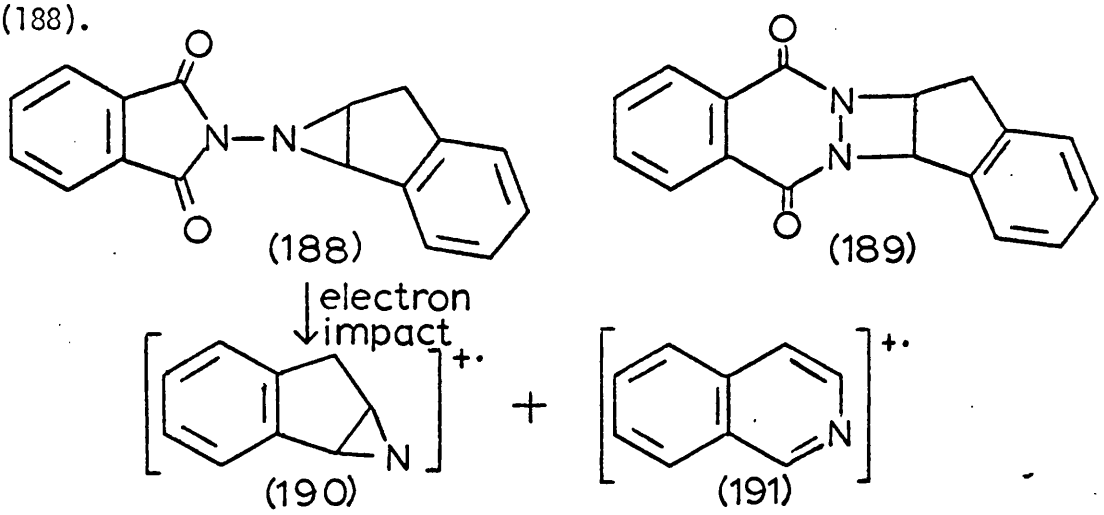
Table 2 Phthalimidoaziridines



R_1	R_2	R_3	R_4	Yield %
Me	H	Me	H	19
Me	H	H	Me	36
CMe_3	H	Me	Me	61
Ph	H	H	H	42
$R_1, R_3 = [CH_2]_4$	H		H	40
R_1, R_2 = o-CH_2 - C_6H_4	H		H	18
COMe	H	Me	Me	88
CO_2Me	H	Me	Me	75
CO_2R^*	H	H	H	65-90
CO_2R^*	Me	H	H	70-100
CO_2R^*	H	H	Me	75-90
CO_2Et	H	H	CO_2Et	20
OCOMe	H	H	H	85
Cl	H	H	Cl	60
Cl	Cl	H	Cl	90
Br	H	H	H	48
Cl	Me	Me	Cl	29

R* = Me, Et, i-Pr, t-Bu.

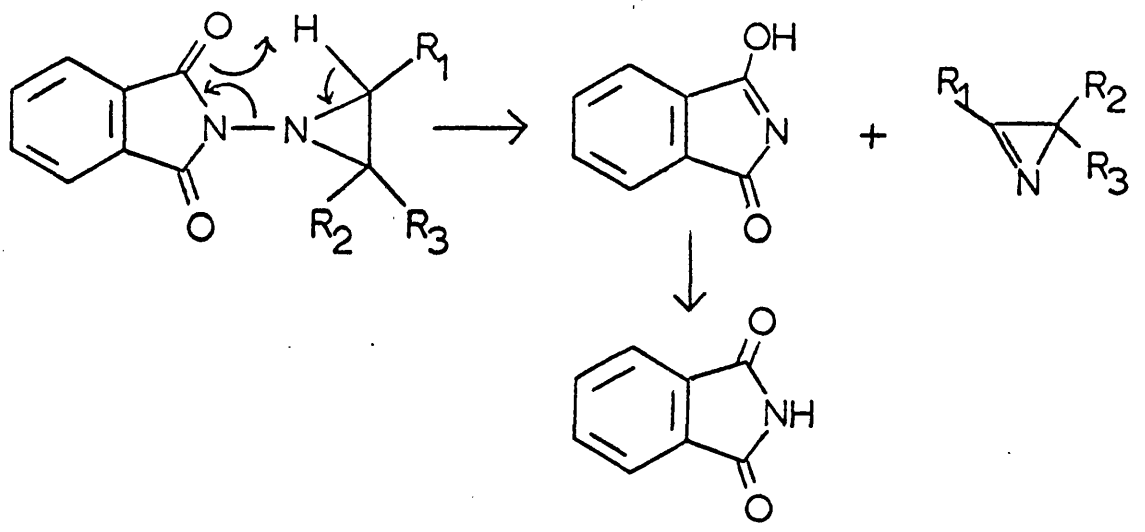
The addition of N-phthalimido nitrene to indene to give aziridine (188) (yellow needles m.p. 189°) may be compared with the oxidation of phthalhydrazide (161) by L.T.A. in the presence of indene,[203] to give the 1:1 adduct (189) (colourless crystals m.p. 256-258°). The latter was independently synthesised for purposes of comparison and possessed a markedly different I.R. spectrum, but a very similar N.M.R. spectrum to (188).



It is interesting to note also that the mass spectral breakdown pattern of (188) shows very large peaks at m/e 130 and 129 which are consistent with the aziridinium ion (190) and isoquinoline (191).[180]

The scission of the labile N-N bond under electron impact in most aziridines studied, to give the aziridinium ion, is one of the major modes of fragmentation. A similar observation[41] has been made for 1-methoxy-aziridines involving N-O bond scission.

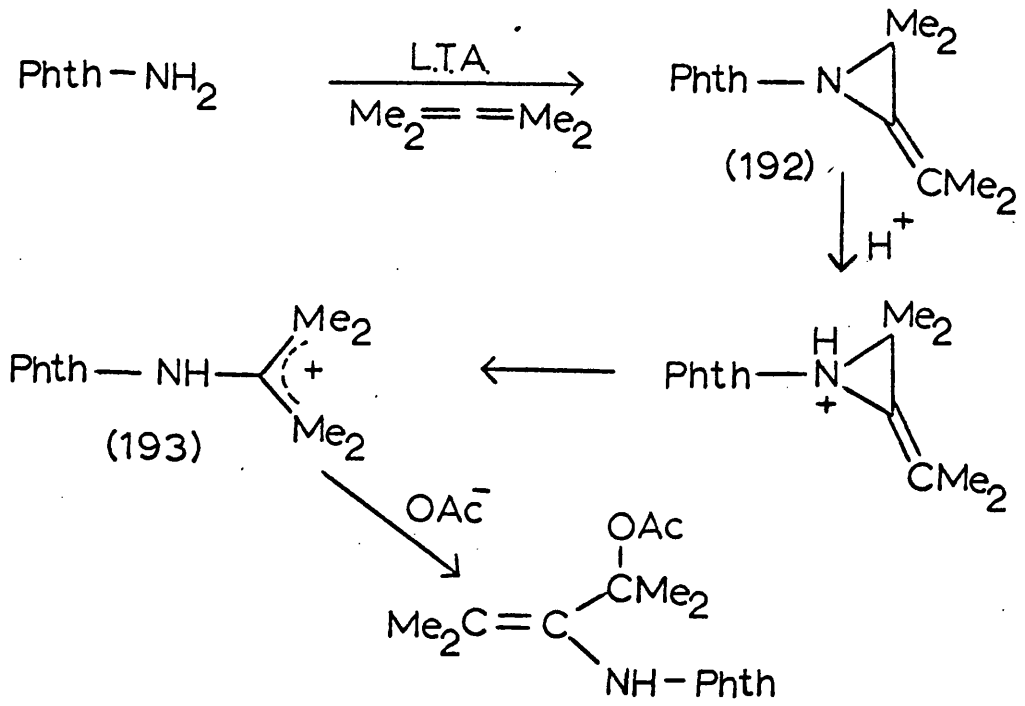
Also present in the mass spectrum of (188), and all aziridines studied, is a large peak for phthalimide at m/e 147. This may occur via 1,5-hydrogen shifts as shown. This mechanism is similar to that proposed by Dreiding[192] for oxidative deamination, and receives further support from the fact that 1,4-bisphthaloyltetrazene (151) exhibits a peak at m/e = 146 for the phthalimido radical and not at m/e = 147.



The aziridine derived from vinyl acetate exhibited remarkable stability compared with the other reported 2-acetoxyaziridines.[21] It could be obtained in a pure state without chromatography and could even be recrystallised from ethanol without change. Its mass spectrum was unique for the aziridines studied. It did not show a peak for the aziridinium ion but showed instead that the major fragmentation involved loss of keten.

Other workers have extended the addition of N-phthalimido nitrene to cyclooctatetraene,[204] a dichlorocyclobutene,[205] trans-stilbene,[206] 1,3-cyclohexadiene,[192] bicyclo[2,2,1]heptadiene,[192] and cis- and trans-4-methylpent-2-ene[207] to give the corresponding aziridines.

When this general aziridine synthesis was extended to tetramethylallene, the ring opened compound (194) was obtained. The reaction is considered as initially giving the exo isopropylidene aziridine (192) which undergoes protonation on the aziridine ring nitrogen with subsequent ring opening to give the tertiary carbonium ion (193). The final step is the attack by acetate ion to give the product (194), a secondary enamine.

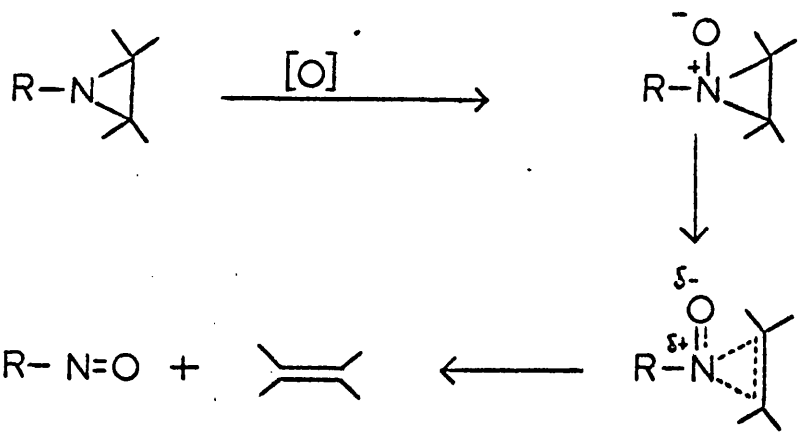


(194)

(b) The oxidation of N-aminonaphthalimide in the presence of olefins was briefly studied. Cyclohexene and methyl methacrylate gave the corresponding aziridines in good yields as highly crystalline solids.

(c) Aziridine syntheses with 3-aminobenzoxazolin-2(3H)-one were extended to the acrylate, methacrylate and crotonate esters, partly as an extension of the characterisation of the intermediate nitrenoid species and partly in connection with the N.M.R. investigation discussed later.

(d) Only very low yields of aziridines were obtained with 2-methylbut-2-ene and styrene when the procedure was extended to N-aminocarbazole. No aziridine could be isolated from N-aminophthalimidine and cyclohexene. The oxidation of both N-amino compounds in the presence of olefins led to the isolation of the corresponding N-nitroso heterocyclics in variable yields. The latter compounds probably arise from further oxidation of the intermediate aziridines as outlined.



This scheme has been proposed[208] for the stereospecific deaminations of some N-alkylaziridines by m-chloroperbenzoic acid.

The extent of the above sequence of reactions would depend upon the ease of oxidation of the aziridines. The sequence carbazolyl > phthalimidinyl > phthalimido aziridines appears reasonable in terms of the nucleophilicities of the aziridine nitrogen atoms involved. The stability of the final N-nitroso compounds may also be important. Both those isolated are quite stable at room temperature and are well documented. On the other hand, N-nitrosophthalimide appears to possess only a transitory existence,[209] decomposing in the air to oxides of nitrogen and phthalimide. Perhaps some of the phthalimide isolated during oxidations in the presence of olefins could originate from this source.

No N-nitroso carbazole could be detected from the oxidation of the N-amino compound alone with 1 mol. and 2 mol. of L.T.A..

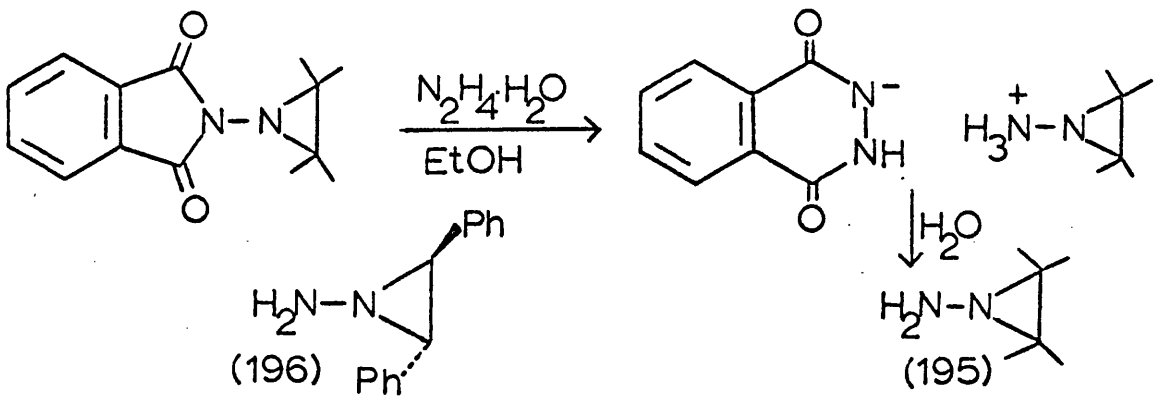
Oxidation of N-aminophthalimidine in the presence of cyclohexene did not profoundly alter the yields of biphthalimidine and N-acetylamino-phthalimidine isolated. Again the major visible reaction was the vigorous evolution of gas, but no compounds could be isolated which accounted for such a loss of nitrogen.

In view of the types of N-amino compounds that can be oxidised in the presence of olefins to give aziridines, here and elsewhere,[188,210,211] a broad general statement may be tentatively made. 'Those N-amino compounds which give primarily the deaminated species on oxidation are most likely to give aziridines when oxidised in the presence of olefins.'

A simple efficient method to remove the lactam or imide residue from the aziridine would have greatly improved the utility of the aziridine synthesis. Two approaches were considered, hydrogenolysis and hydrazinolysis.

7-Phthalimido-7-azabicyclo[4,1,0]heptane (183) appeared to take up the theoretical amount of hydrogen over 4 days. However since the majority of the starting material was recovered unchanged and the volume of hydrogen was small, the apparent uptake is attributable to slow diffusion of hydrogen out of the apparatus.

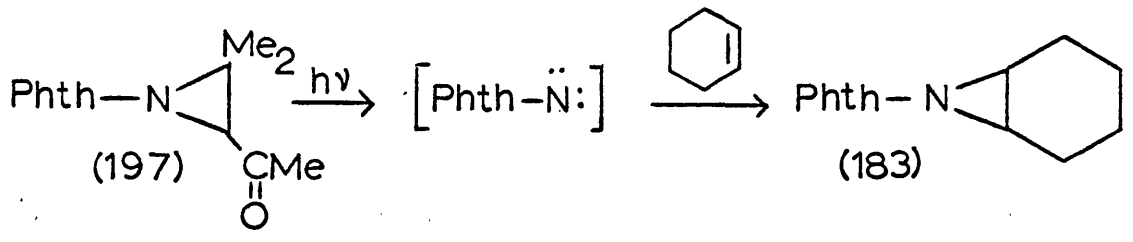
A more attractive means of reduction is hydrazinolysis which is the final step in the Gabriel synthesis of primary amines.[212] The final product would be an N-aminoaziridine (195). When 2-t-butyl-2,2-dimethyl-1-phthalimidoaziridine (184) was subjected to hydrazinolysis, phthalhydrazide and N-aminophthalimide were the only identifiable products isolated. A gas (di-imide?) was also evolved.



Carpino[206] has met with more success with hydrazinolysis and was able to isolate the N-aminoaziridine (196) from the aziridine derived from N-aminophthalimide and trans-stilbene.

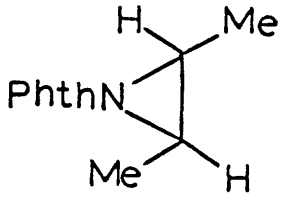
Consequently it appears that isolation of the resultant N-amino-aziridine is possible if suitable conditions are chosen, such as low temperature hydrazinolysis. The resultant N-aminoaziridines are thermally labile, reverting to the olefin and a gas (di-imide?) upon warming.

It was found that the photolysis of the aziridine (197), derived from mesityl oxide, gave the aziridine (183) in the presence of cyclo-hexene. The aziridine (183) was stable to further photolysis in the presence of 2,4,4-trimethylpent-2-ene. This reaction has been extended[207] and it has been shown that the lability of the aziridine to photolysis depends upon the presence of an unsaturated group (e.g. ester or benzene ring) in the 2-position of the aziridine ring. (The U.V. spectra of aziridines studied are not very characteristic and exhibit mainly end absorption). The reaction has been found to be stereospecific and is thought to proceed via the amino-nitrene. Phenylnitrene has been shown to be generated during the photolysis of certain N-phenyloxaziridines.[213]

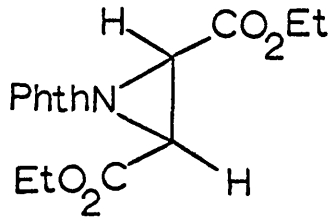


N.M.R. Spectra of Aziridines

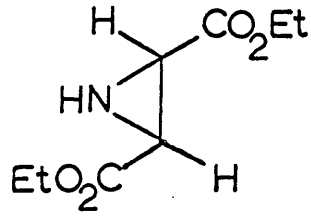
Many of the aziridines prepared had temperature dependent spectra, frequently showing the presence of invertomers below about 130°. The reasons for slow nitrogen inversion have been expounded in the Introduction, Pt.(2).



(186)



(198)



(199)

The room temperature spectrum (CCl_4 solution) of aziridine (186) showed non-equivalence of the methyl groups and the aziridine ring protons. The methyl groups consisted of two doublets separated by 6 c.p.s. and the aziridine ring protons essentially as two overlapping quartets separated by 12 c.p.s..

Similarly the aziridine (198) exhibited (CCl_4 solution) non-equivalence of the ester protons and aziridine ring protons. The methyl groups of the esters consisted of two overlapping triplets separated by 5 c.p.s. and the methylene protons as two overlapping quartets separated by 8 c.p.s.. The aziridine ring protons appeared as two doublets separated by 19 c.p.s..

The latter example may be compared with the parent aziridine (199) which is reported[214] as having equivalent ester groups and ring protons in its N.M.R. spectrum. This is attributable to rapid inversion of the nitrogen.

The spectra observed for the two phthalimido aziridines (186) and (198) are consistent with slow nitrogen inversion. It is emphasised that the terms 'slow' and 'rapid' are used with respect to the N.M.R. timescale.

Atkinson[86] noted that the aziridine (62) derived from 3-amino-benzoxazolin-2(3H)-one and trans-but-2-ene, an analogue of (186), exhibited non-equivalence of the methyl groups and aziridine ring protons at room temperature. However, coalescence of the methyl groups was obtained upon running the spectrum at ca. 150° and higher.

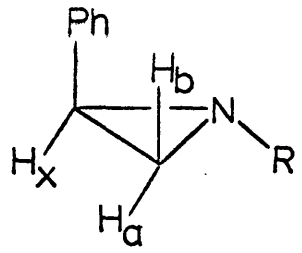
The coalescence temperature for the phthalimido aziridine (186) was not obtained, but the separate signals for the ester protons of (198) coalesced (in o-dichlorobenzene solution) to a single triplet and quartet at 120° and higher. The aziridine ring protons of (198) gradually broadened as the temperature was raised and by ca. 150° had practically disappeared into the base line. At even higher temperatures they would be expected to reappear as a singlet at the mean position of the original two doublets. Upon cooling, the original spectrum was obtained.

The assignment of peaks in the N.M.R. spectra of the N-aminoaziridines studied, follows from an accumulation of observations. Briefly, aziridine ring protons are deshielded when cis to the N-heterocyclic substituent and appear at lower field. This has been attributed[86] to the deshielding effects of the aromatic ring and the carbonyl group of the N-heterocyclic substituent. On the other hand, aziridine ring alkyl groups or ring ester groups are shielded when cis to the N-substituent, and appear at higher field. As anticipated, the shielding of, say, a methyl group of an ethyl ester [cf. (198)] is less than that of the adjacent methylene.

By far the largest shielding - deshielding effects are experienced by the aziridine ring protons, separated in some cases by up to 90 c.p.s..

The above assignment of peaks to aziridine ring protons is contrary to those of the N-alkyl (except t-butyl) aziridines,[52] where the magnetically anisotropic N-alkyl C-N bond shields the cis protons.

That our assignments are correct may be demonstrated by comparing the N-substituted styrenimines (200a and b) with (200c-e).



(200)

(a) R = phthalimido

(b) R = carbazolyl

(c) R = Me (ref. 215)

(d) R = t-Bu (ref. 52)

(e) R = NH_2, Cl (ref. 216)

In styrenimines (200a and b) and (200d and e) the proton H_b is shifted to higher field and the proton H_a to lower field than in the methyl, ethyl and i-propyl N-substituted styrenimines (CCl_4 solutions). Consequently H_b is the high field proton. The cause of the shifts in the styrenimine (200d) has been attributed[52] to a 'dispersion-induced deshielding and shielding effect' caused by the sterically demanding t-butyl group.

Upon studying the effect of temperature on the N.M.R. spectrum of the phthalimido styrenimine (200a) in a o-dichlorobenzene solution, it was found that the signal of the proton H_b broadened at ca. 110° and that the H_a and H_x signals gradually separated from the proximity of the H_b signal [cf. Fig.(1)].

It has been demonstrated[217] that benzene solvates an aziridine molecule on the opposite side to the lone-pair of electrons on the nitrogen atom. The result is an upfield shift of the protons trans to the lone-pair with respect to say carbon tetrachloride. It is anticipated that o-dichlorobenzene will have the same effect. Consequently the separation of the signals in our case (200a) is due to the gradual downfield shift of the H_a and H_x signals, with increasing temperature, as solvation decreases.

The broadening of the H_b signal is due to incomplete averaging out of the N^{14}-C-H coupling by quadrupolar relaxation of the nitrogen nucleus.

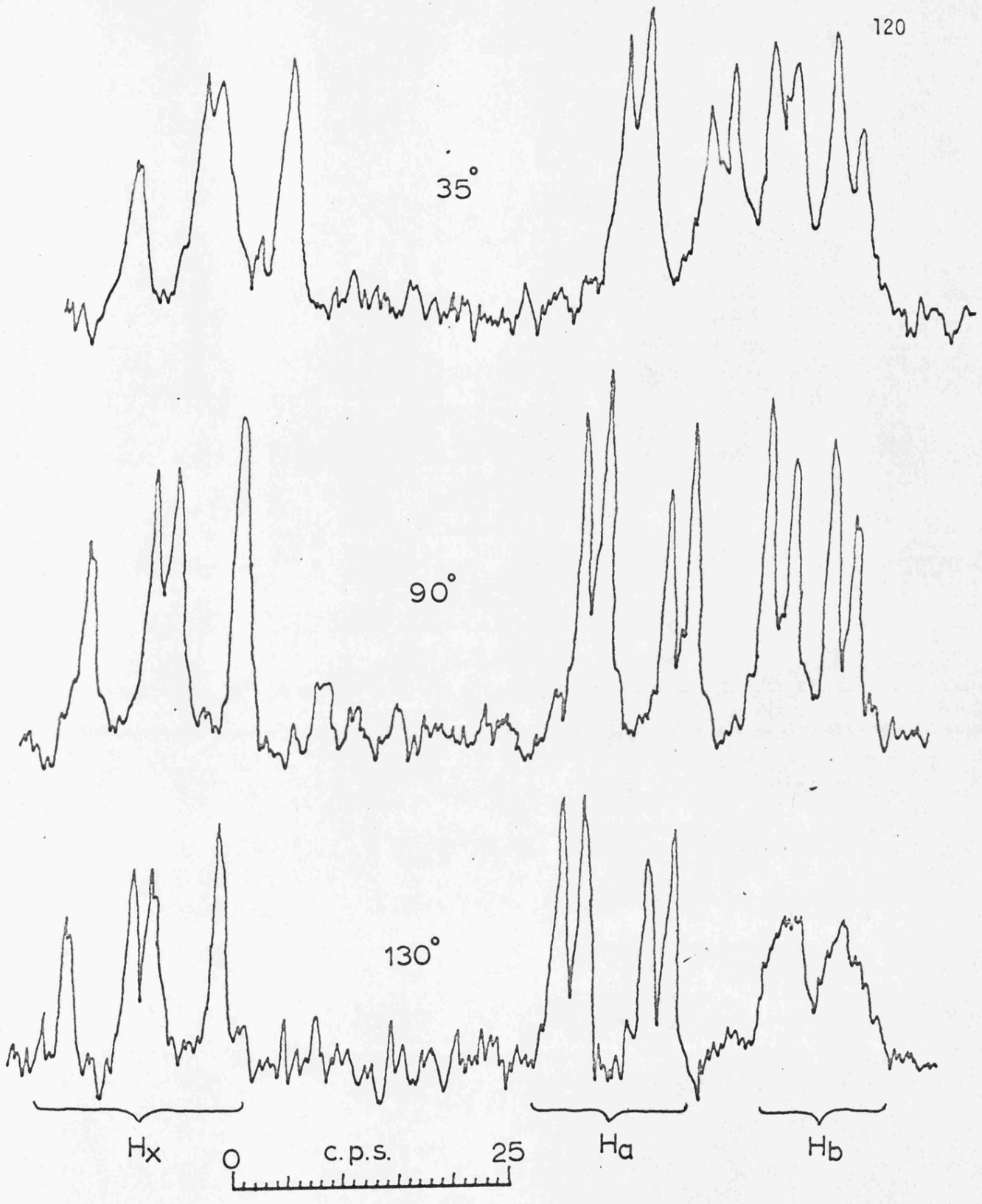
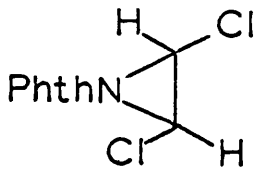


Fig.(1) Aziridine ring proton spectra of 2-phenyl-1-phthalimidoaziridine in o-dichlorobenzene.

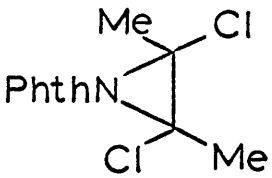
At low temperatures the N^{14}-C-H coupling is averaged by the rapid relaxation of the N^{14} nucleus. However as the temperature is increased then the relaxation time becomes sufficiently small, finally reaching a critical value when broadening ensues. Only the protons cis to the nitrogen lone-pair are affected. Room temperature broadening of H_b has been observed with styrenimines (200c and e). It has been suggested[215,216] that this broadening offers an excellent indication of the conformation of the molecule. Our observation is in harmony with this proposal.

The magnitudes of the vicinal and germinal coupling constants[199b,218] for our aziridines: J cis 7-9 c.p.s., J trans 4-5 c.p.s., and J gem 1-3 c.p.s., also support our assignments.

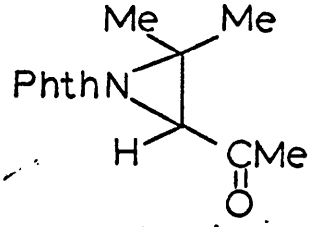
The room temperature spectra of aziridines (201) and (202) showed equivalent aziridine ring protons and ring methyl groups respectively.



(201)



(202)



(197)

Similarly (197) exhibited a single peak for the geminal methyl groups (all $CDCl_3$ solutions). The latter may be taken in contrast to the corresponding quinazolone aziridine[207] which shows two signals for the geminal methyl groups separated by 9 c.p.s..

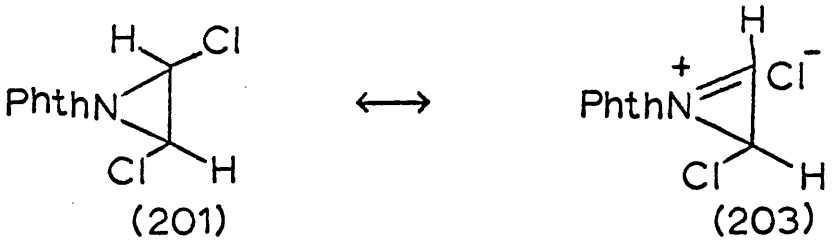
The coincidence of peaks for the three phthalimido aziridines above would tend to suggest equivalence of the nuclei i.e. that nitrogen inversion was rapid.

To test this, each aziridine in turn, was cooled to -60° and spectra obtained. The most striking spectra were obtained with the trans-2,3-

dichloroaziridine (201), shown in Fig.(2). At -50° and below, the singlet at room temperature was resolved into two doublets separated by 60 c.p.s. about the mean position of the room temperature singlet. Spectra were obtained at various temperatures down to -60° and the coalescence temperature found to be ca. -10°. This corresponds to a $\Delta G^{\ddagger}$ for inversion at -10° of about 14 kc.mole.$^{-1}$ The abnormally low coupling constant J trans = 2.0 c.p.s. is in accord with the prediction[218] that aziridine ring substituents of increasing electronegativity tend to decrease all the coupling constants. This is thought to be due to the amount of π character of the ring and the hybridisation of the carbon atom involved, by analogy with the corresponding epoxide and cyclopropane systems.[219]

The increase in the rate of inversion for the aziridine (201) is thought to be partly attributable to the inductive effect of the chlorine atoms reducing the electron density of the aziridine nitrogen lone pair, thus accelerating the rate of inversion.

The large difference (130°) in the coalescence temperatures of the dichloroaziridine (201) and the diethyl fumarate derived aziridine (198) cannot satisfactorily be explained in terms of inductive or conjugative effects. We believe that an important contributing form of the aziridine (201) is the resonance form (203). This would greatly enhance the attainment of a planar transition state. Further evidence for this species is presented in the rearrangements of halogenoaziridines.



(201) (203)

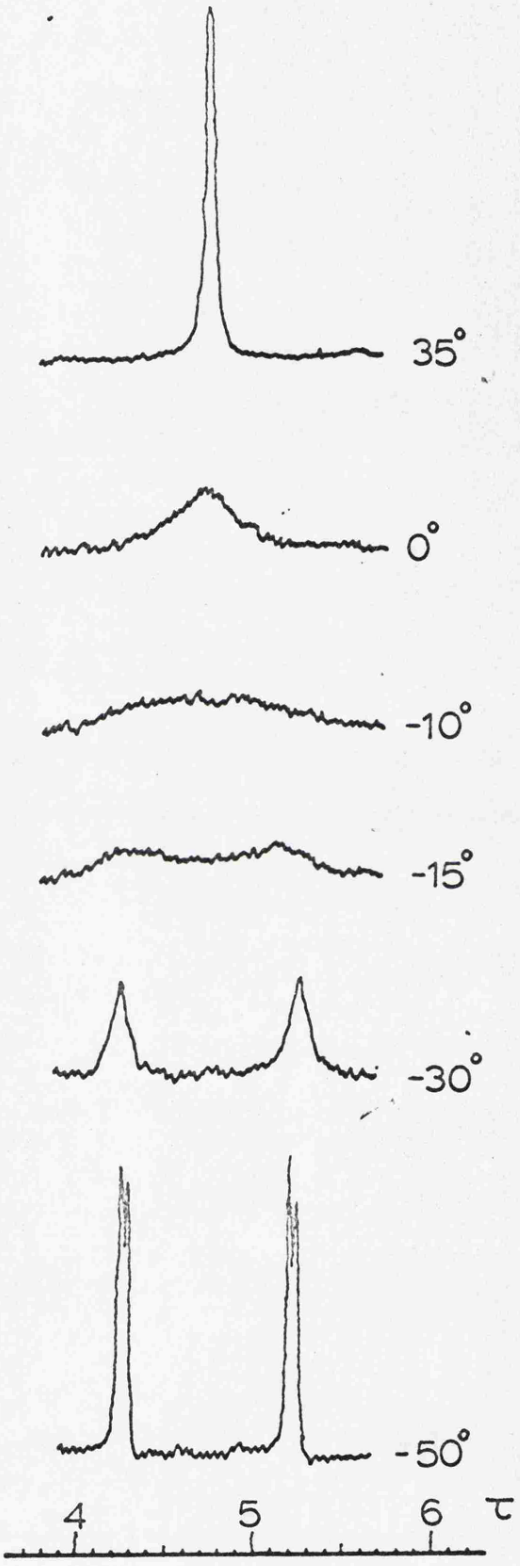


Fig.(2) Aziridine ring proton spectra of trans-2,3-dichloro-1-phthalimidoaziridine in $CDCl_3$.

It was anticipated that the coalescence temperature for the trans-2,3-dichloro-2,3-dimethylaziridine (202) would be lower than that for (201) because the methyl groups should stabilise the ionic resonance form. When the -60° N.M.R. spectrum (60 Mc.) of aziridine (202) was obtained, there was no separation of the coincident methyl signals. Only slight broadening occurred. This could be attributable to one or both of two factors:

(i) that inversion is rapid and $T_c < 60°$

(ii) the chemical shift difference of the methyl groups is small.

It is anticipated that (i) is the more likely but (ii) cannot completely be ruled out.

In the -60° N.M.R. spectrum of the mesityl oxide derived aziridine (197), the singlet for the geminal methyl groups at room temperature was partly resolved into two broad signals separated by 4 c.p.s.. In view of the reasons (i) and (ii) put forward earlier, and the observed spectrum of the quinazolone-derived aziridine, it is not thought that inversion of (197) is rapid at room temperature, instead merely that the chemical shift difference of the geminal methyl groups is small. The difference is slightly increased at lower temperature.

The N.M.R. spectra of N-substituted heterocyclic aziridines such as the styrenimines (200) and the aziridine (184) substituted in the 2-position with a t-butyl group, show the presence of single invertomers. This is due to the large free energy difference between the invertomers. The preferred invertomer is the one with the bulky group trans to the N-substituent.

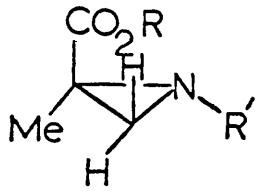
Following the observation that phthalimido nitrene added well to the esters of acrylic, methacrylic and crotonic acids to give the corresponding aziridines, it was noted that all the N.M.R. spectra showed

the presence of invertomers in varying ratios. A study was undertaken in conjunction with R.S. Atkinson and D.C. Horwell in an attempt to understand the factors which determined the invertomer ratios. My study was concerned with the benzoxazolinyl and phthalimido aziridines. The results of all workers have been used in the following discussion, but details have been concentrated on the phthalimido and benzoxazolinyl aziridines.

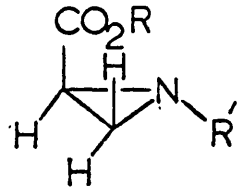
Aziridines (204-207, a-d) were conveniently prepared from the methacrylate esters. As mentioned earlier, the anisotropic effects of the N-substituents enhance the separation of the corresponding signals in the two invertomers and facilitate integration. The N.M.R. spectra of aziridines (204 and 205, a-d) are given in Table (3) with signals for invertomers with ester cis (A) and trans (B) to the heterocycle given separately.

The assignments of peaks for the methacrylate derived aziridines in Table (3) follows from an examination of the aziridines derived from the acrylate esters (204e and h, 205e-h) given in Table (4). Even in these cases two invertomers are visible for the ester protons.

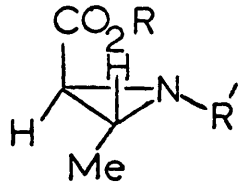
If the reasonable assumption is made for the acrylate derived aziridines that the major invertomer is the one with the ester and N-substituent trans (B), then the excellent correlation of chemical shift of the ester groups in acrylate and methacrylate derived aziridines [see Figs. (3) and (4) and Tables (3) and (4)] supports our assignments in the latter.



(a) R = Me
(b) Et
(c) iPr
(d) tBu

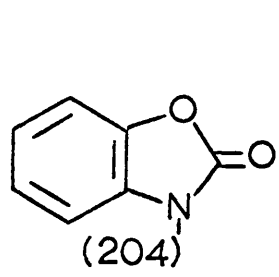


(e) R = Me
(f) Et
(g) iPr
(h) tBu

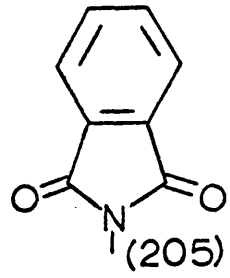


(j) R = Me
(k) Et
(l) iPr
(m) tBu

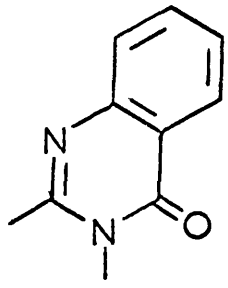
R′ =



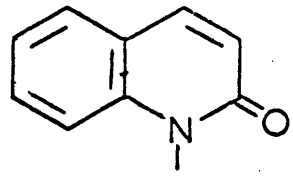
(204)



(205)



(206)



(207)

The following conclusions may be drawn.

(i) Aziridine ring methyl groups are shielded when cis to the N-substituent. The magnitude of the shielding varies in the order carbostyril (207) > quinazolone (206) > benzoxazolinone (204) > phthalimido (205). Along with the shielding of the cis aziridine ring methyl group goes a smaller deshielding of the trans aziridine ring methyl group.

(ii) All protons of ester alkyl groups are shielded when cis to the N-substituent.

(iii) Aziridine ring protons are deshielded when cis to the N-substituent, particularly in (A) where the ester group is also cis, since an ester group has a deshielding effect upon the cis hydrogen.

The isopropyl esters in the acrylate and methacrylate derived aziridines show non-equivalence of the methyl groups only in the invertomer (A) where the heterocycle and ester are cis. These methyls are non-equivalent because of the nitrogen and carbon centres of asymmetry. However it is thought that the more congested environment and the proximity of the heterocycle will cause greater non-equivalence in (A) than (B).[76]

The aziridine ring protons in the invertomers (B) with the heterocycle and ester trans, (205 and 207, a-d) appear as a single peak in the room temperature spectra, whereas the corresponding invertomer signals in aziridines (204 and 206, a-d) consist of two close doublets. However upon cooling to -60°, aziridine (205a) exhibited two doublets (J = 2 c.p.s.) separated by 6 c.p.s. about the mean position of the original singlet. This separation could be due to one or both of two factors:

(i) at room temperature the chemical shift difference of the two protons is small

(ii) changes in rotamer populations (discussed in detail later) upon cooling, remove the coincidental identity of chemical shift.

It would appear that (ii) is more favourable in view of the slow rate of inversion at room temperature.

In all the benzoxazolinyl-methacrylate ester aziridines (204a-d) the doublet due to the aziridine ring proton trans to the N-substituent in the invertomer (B) was broadened considerably [cf. Fig.(3)] presumably by N^{14}-C-H coupling.[215,216]

Table 3 N.M.R. data of methacrylate derived aziridines [τ ($CDCl_3$)]

	A: ester and heterocycle (R) cis				B: ester and heterocycle (R) trans				
	H cis to R	H trans to R	CO_2R'	Me	H cis to R	H trans to R	CO_2R'	Me	aromatic H
a	6.05, d, J2	7.31, d, J2	6.49	8.28	6.24, d, J2	6.93, d, J2	6.15	8.47	2.85, 2.82 (2 lines)
b	6.02, d, J2	7.33, d, J2	9.03, t, J7 6.07, q, J7	8.30	6.30, d, J2	6.95, d, J2	8.65, t, J7 5.70, t, J7	8.49	2.92, 2.86 (2 lines)
(204)									
c	5.97, d, J2	7.36, d, J2	9.05, 9.08, 2d, J6.5 5.28, h, J6.5	8.33	6.32, d, J2	6.98, d, J2	8.68, d, J6 4.88, h, J6	8.52	2.94, 2.88 (2 lines)
d	5.94, d, J2	7.38, d, J2	8.88	8.34	6.33, d, J2	7.00, d, J2	8.45	8.53	2.90, 2.84 (2 lines)
a	6.58, d, J2	7.31, d, J2	6.32	8.31	6.91	6.91	6.16	8.46	2.4 - 2.2, m
b	6.56, d, J2	7.34, d, J2	8.84, t, J7 5.93, q, J7	8.32	6.93	6.93	8.68, t, J7 5.73, q, J7	8.47	2.4 - 2.2, m
(205)									
c	6.55, d, J2	7.36, d, J2	8.89, 8.85, 2d, J6 5.14, h, J6	8.33	6.95	6.95	8.69, d, J7 4.88, h, J6	8.48	2.4 - 2.2, m
d	6.56, d, J2	7.39, d, J2	8.67	8.37	6.98	6.98	8.47	8.53	2.4 - 2.2, m

Table 4 N.M.R. data [τ ($CDCl_3$)] for acrylate derived aziridines

		A	B					
		ester cis to heterocycle (R)	ester trans to heterocycle (R)					
		CO_2R'	CO_2R'	H cis to R	H trans to R	H gem to CO_2R'	aromatic H	invertomer ratio (A/B)
(204)	e	6.42	6.17	6.66, dd, J8 x 1	7.22, dd, J4.5 x 1	6.40, dd, J8 x 4.5	3.0 - 2.7, m	1:14
	h	8.81	8.44	6.75, d, J7.5	7.28, d, J4.5	6.57, dd, J7.5 x 4.5	3.0 - 2.7, m	1:8.8
(205)	e	6.30	6.15	7.17, dd, J7 x 1.5	7.18, dd, J6 x1.5	6.79, dd, J7 x 6	2.3 - 2.2, m	1:5.8
	f	8.78, t, J7.5 5.87, q, J7.5	8.66, t, J7.5 5.70, q, J7.5	7.16, dd, J6 x 1.5	7.18, dd, J6 x 1.5	6.81, dd, J6 x 6	2.3 - 2.2, m	1:4.8
	g	uncertain	8.69, 8.64, 2d, J6.5 4.86, h, J6.5	7.15, dd, J7 x 1.5	7.18, dd, J5 x 1.5	6.80, dd, J7 x 5	2.3 - 2.2, m	uncertain
	h	8.62	8.44	7.25, d, J8	7.22, d, J4.5	6.90, dd, J8 x 4.5	2.3 - 2.2, m	1:3.3

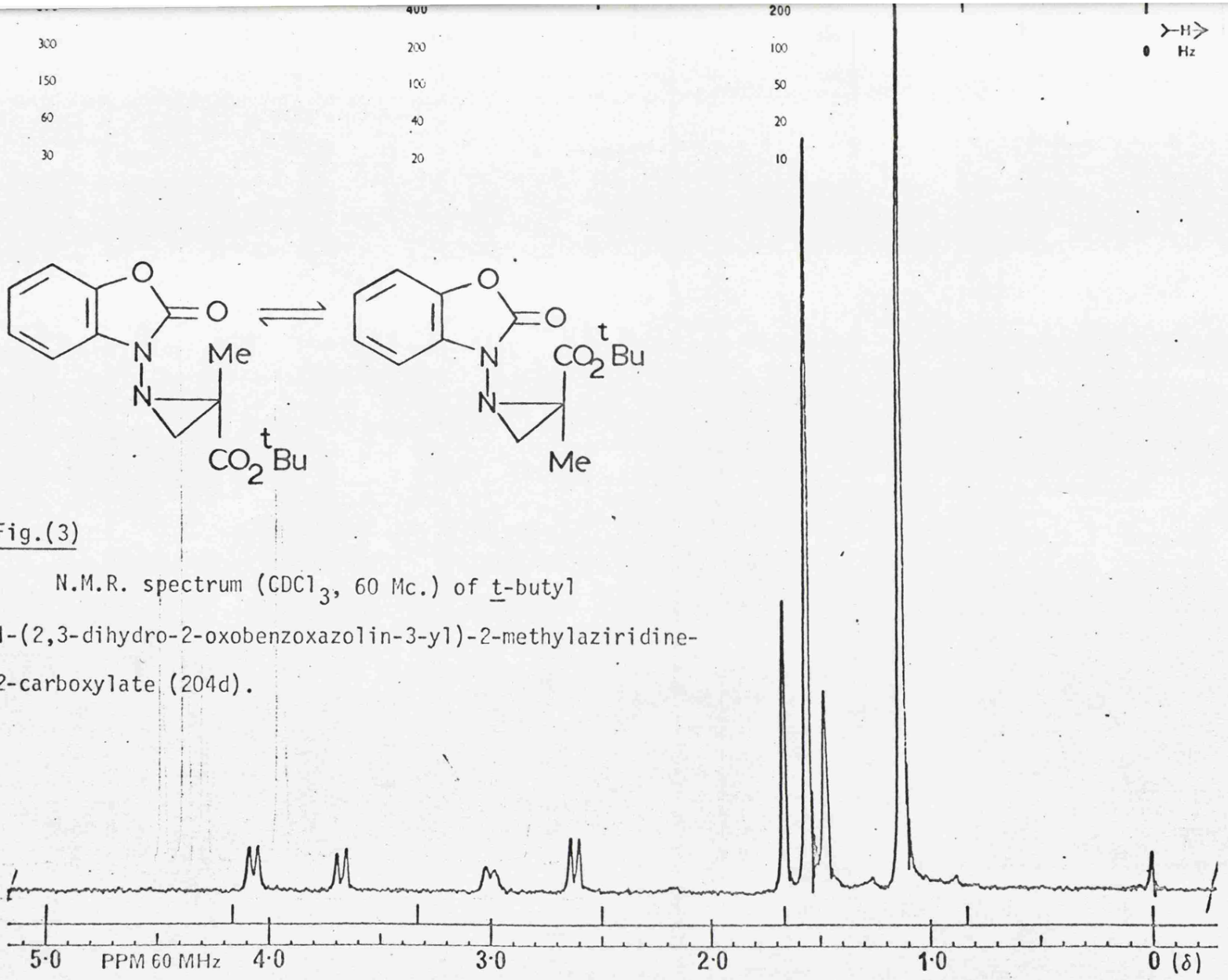


Fig.(3)

N.M.R. spectrum ($CDCl_3$, 60 Mc.) of t-butyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)-2-methylaziridine-2-carboxylate (204d).

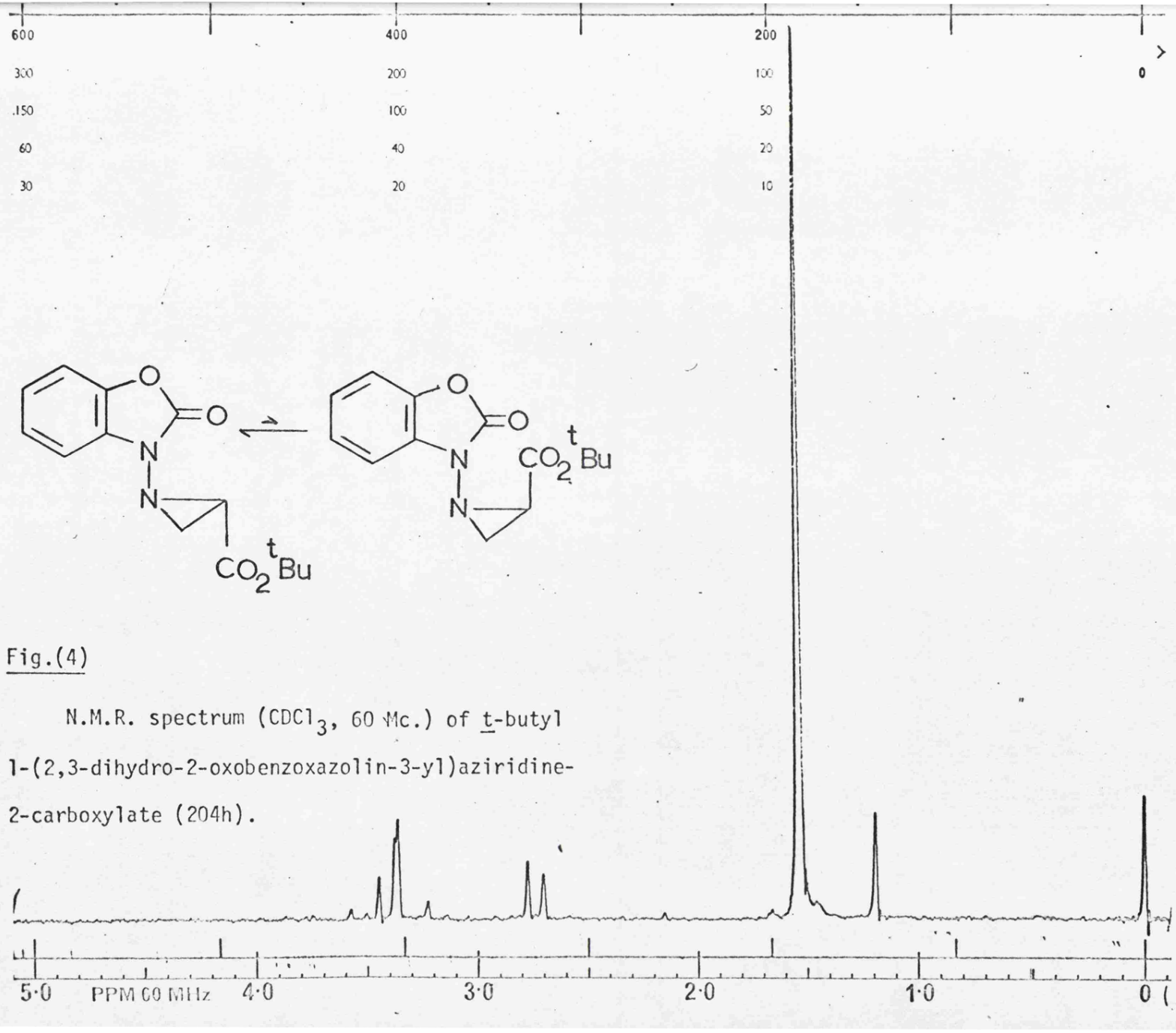
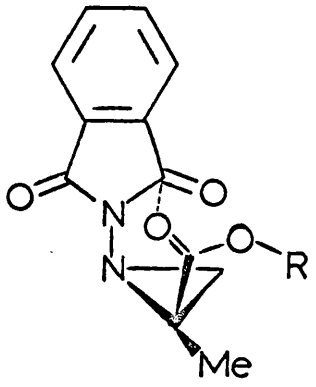


Fig.(4)

N.M.R. spectrum ($CDCl_3$, 60 Mc.) of t-butyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)aziridine-2-carboxylate (204h).

Examination of the invertomer ratios by integration comparisons of various peaks in Tables (3) and (4) shown in Tables (5) and (4) leads to a surprising conclusion. As the size of the ester alkyl group is increased from methyl to t-butyl, then the proportion of the invertomer with the ester cis to the heterocycle (A:B) increases by about two fold in both the acrylate and methacrylate derived aziridines. On purely steric grounds, the reverse might be expected. Conformational free energy values for the corresponding groups in cyclohexane chemistry are scarce,[220] but the limited values do express the same trend.

A possible explanation of this trend in our case is a dipolar attraction between the ester carbonyl oxygen atom and the electrophilic carbon atom(s) of the lactam or imide carbonyl(s) as shown.



As R increases in bulk, those rotamers about the aziridine ring-ester bond will be favoured where R and the N-substituent are furthest apart. The ester carbonyl oxygen would then assume a position, which on a time average basis is closer to the lactam or imide carbonyl carbon.

There is also a statistical effect to be considered. The phthalimido residue (205) contains two equivalent electrophilic centres with which the dipolar attraction is favoured. Similarly the quinazolone (206) possesses corresponding (less) electrophilic centres. On the other hand the carbostyril (207) possesses only one (less) electrophilic centre.

In the benzoxazolinone case (204) the electrophilic centre is expected to be the least electrophilic of all because of the mesomeric effect of the ring oxygen atom.

Table (5)

Ratio of ester cis/trans (A/B) to heterocycle for methacrylate-derived aziridines in Table (3)

	a	b	c	d
(204)	0.7	0.9	1.1	1.5
(205)	1.8	2.2	2.8	3.5
(206)	2.1	2.4	2.9	3.3
(207)	1.9	2.2	2.5	3.2

Some support of this explanation comes from an examination of the invertomer ratios of the t-butyl esters [Table (5)] of the four N-substituents. These values are found to be in accord with the expected electrophilicities of the two carbon atoms involved. The t-butyl ester invertomer ratio is most likely to reflect the electrophilicities if the explanation offered is correct. Further support comes from a study of the invertomer ratios in the benzimidazolylaziridines[188] which lack the lactam carbonyl.

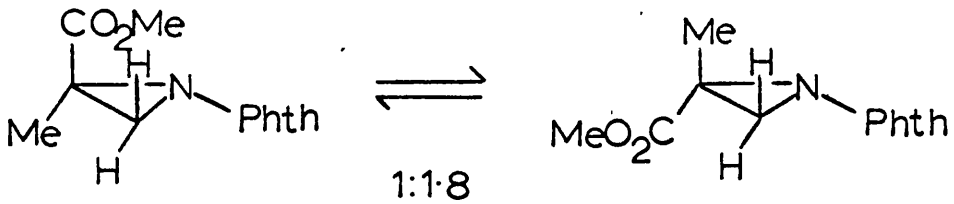
The crotonate derived aziridines (204 j and m, 205j-m) were also studied [Table (6)]. Adopting the same shielding-deshielding relationship, it is apparent again that the preference for the cis configuration of the N-substituent and ester becomes greater as the size of the latter is increased. A notable difference however is the magnitude of the invertomer ratios for methacrylate and crotonate derived aziridines.

Table 6 N.M.R. data [τ ($CDCl_3$)] for crotonate derived aziridines

	A			B				
	ester cis to heterocycle (R)			ester trans to heterocycle (R)				
	H gem to ester	CO_2R'	Me	H gem to Me	CO_2R'	Me	aromatic H	Invertomer Ratio ($A/_B$)
(204) j	6.96, d, J5	6.44	8.38, d, J5	6.4 - 6.0, m	6.18	8.57, d, J5	3.1 - 2.8, m	1.7:1
m	7.10, d, J5	8.83	8.54, d, J5	6.3 - 6.0, m	8.48	8.61, d, J5.5	3.0 - 2.8, m	ca. 4:1
j	6.95, d, J5.5	6.31	8.48, d, J5.5	6.7 - 6.5, m	6.15	8.56, d, J5.5	2.3 - 2.1, m	4:1
k	7.01, d, J5	8.81, t, J7.5 5.90, q, J7.5	8.52, d, J5.5	6.78, q, J5	8.69, t, J7.5 5.73, q, J7.5	8.59, d, J5.5	2.4 - 2.2, m	ca. 5.5:1
(205) l	7.02, d, J5	8.82, 8.78, 2d, J6 5.07, h, J6	8.50, d, J6	6.8 - 6.4, m	uncertain	uncertain	2.4 - 2.1, m	uncertain
m	7.06, d, J5	8.63	8.50, d, J5.5	6.66, q, J5.5	8.45	uncertain	2.3 - 2.2, m	ca. 7:1

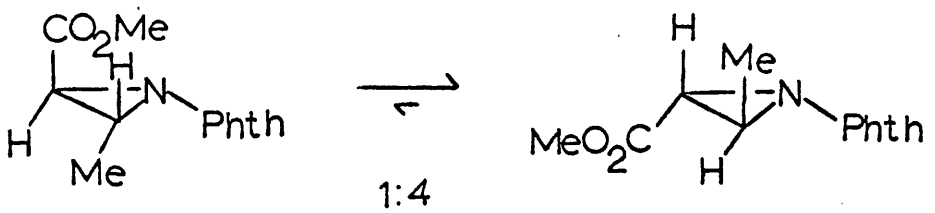
A second possible explanation of the trend would be an increasing repulsion between the lone-pair on the aziridine ring nitrogen and the ester as the size of the latter is increased. The only evidence we have against this is the observed invertomer ratios reflecting the electrophilic character of the heterocyclic carbon atoms involved. No such trend would be expected if lone-pair interactions were of overwhelming importance.

It is interesting to consider quantitatively the equilibrium between invertomers of aziridines (205a) and (205j) for which the invertomer ratios have been determined as 1:1.8 and 1:4 respectively. Using the relationship that $\Delta G = -RT \ln k$, these values correspond to free energy differences of 0.36 kc.mole.$^{-1}$ and 0.85 kc.mole.$^{-1}$ respectively. It may be fortuitous that the former value of 0.36 kc.mole.$^{-1}$ corresponds very closely to a value of 0.43 kc.mole.$^{-1}$ computed using conformational free energies (1.7 kc.mole.$^{-1}$ and 1.27 kc.mole.$^{-1}$) derived in cyclohexanes for methyl and methoxycarbonyl groups respectively.[220] For this comparison the additivity of 'aziridine conformational free energy values' has been assumed.



1:1·8

(205a)



1:4

(205j)

If all the values (7 in all) of invertomer ratios for the methyl crotonate and methyl methacrylate-derived aziridines are calculated independently and an average taken, then this gives the remarkable figure of 0.43 kc.mole.$^{-1}$, the same as that derived for cyclohexanes!

If a similar approach is applied to the corresponding methyl acrylate-derived aziridines (204-207, e) then the 'aziridine conformational free energy value ($-\Delta G$)' for a methoxycarbonyl group is 1.4 kc.mole.$^{-1}$, compared to 1.27 kc.mole.$^{-1}$ for cyclohexanes.[220] As before, the carbostyril and quinazolone N-substituted aziridines best reflect this value.

It is stressed that it is in the methyl esters where the dipolar attractive forces are least and the comparison with cyclohexane conformational analysis may be made.

The invertomer ratio of t-butyl 1-(2,3-dihydro-2-oxobenzoxazolin-3-yl)-aziridine-2-carboxylate (204h) was determined in different solvents [Table (7)] by R.S. Atkinson, but was found to be relatively insensitive to solvent changes.

Table (7)

Solvent	Invertomer Ratio
$CDCl_3$	1:8.8
CCl_4	1:8.1
CD_3CO_2D	1:7.3
pyridine	1:9.0
benzene	1:7.6

Similarly the invertomer ratio of the phthalimido-methyl methacrylate derived aziridine (205a) was found to be only fractionally affected at -60°. The invertomer with the ester and phthalimido cis (A) was very slightly more favoured at -60° than at room temperature.

The separate peaks for the two invertomer ester methyl groups of aziridine (205e) derived from methyl acrylate and N-aminophthalimide, coalesced at ca. 130° in o-dichlorobenzene. Similarly the analogous methyl methacrylate derived aziridine (205a) showed coalescence of the ester methyls and ring methyls separately at ca. 110°.

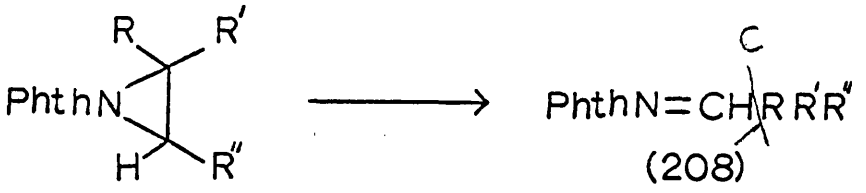
It is suggested that invertomer ratios in suitably designed aziridines offer a quantitative way for comparing interactions between substituents, steric or otherwise.

A number of N-phenyl substituted aziridines similar to (204-207, a-d) have been synthesised[221] which show no evidence of invertomers at room temperature; the phenyl group is known[53] to increase the rate of inversion.

In view of the coalescence temperatures (110-150°) obtained for the N-aminoaziridines studied by our group, it is unlikely that Brois[87] will achieve his objective of separating invertomers of N-aminoaziridines. It is felt that the lone-pair repulsions between the aziridine ring nitrogen and the adjacent nitrogen, coupled with the insufficient electronegativity of the adjacent nitrogen atom are not sufficient to allow the separation of invertomers at room temperature. More success may be achieved with N-methoxyaziridines.[41]

The Rearrangement of Halogenoaziridines

The aziridines derived from trans-1,2-dichloroethylene and 1,2,2-trichloroethylene with N-aminophthalimide were found to deteriorate quite rapidly at room temperature and in the dark. When heated for a short time just above their melting points, they were converted smoothly and in high yield to the ring opened hydrazone structures (208). When N-aminophthalimide was oxidised in the presence of trans-1,2-dibromoethylene the hydrazone (208d) was obtained directly, without detection of the corresponding aziridine. The trichloromethyl derivative (208b) was independently synthesised from chloral and N-aminophthalimide. Only the chlorine atom on the less substituted carbon atom of the trichloroethylene derived aziridine migrated, i.e. the reaction proceded in one direction only.



(208)

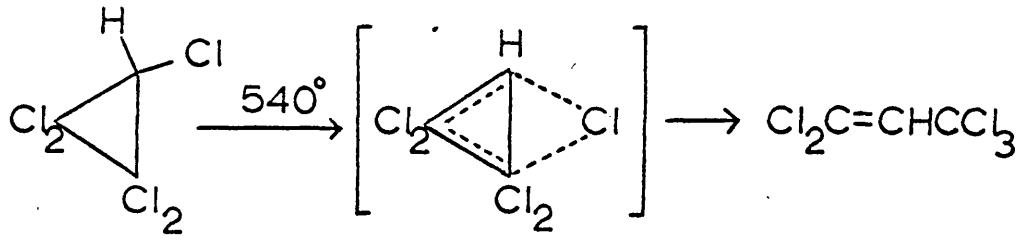
(a) R = R″ = Cl, R′ = H

(b) R = R′ = R″ = Cl

(c) R = Br, R′ = R″ = H

(d) R = R″ = Br, R′ = H

Analogous rearrangements have been observed with polyhalogenocyclopropanes,[222] but at much higher temperatures. Again the chlorine atom on the less substituted carbon atom of the cyclopropane (209) was the one to migrate, to give only the substituted ethylene (210).



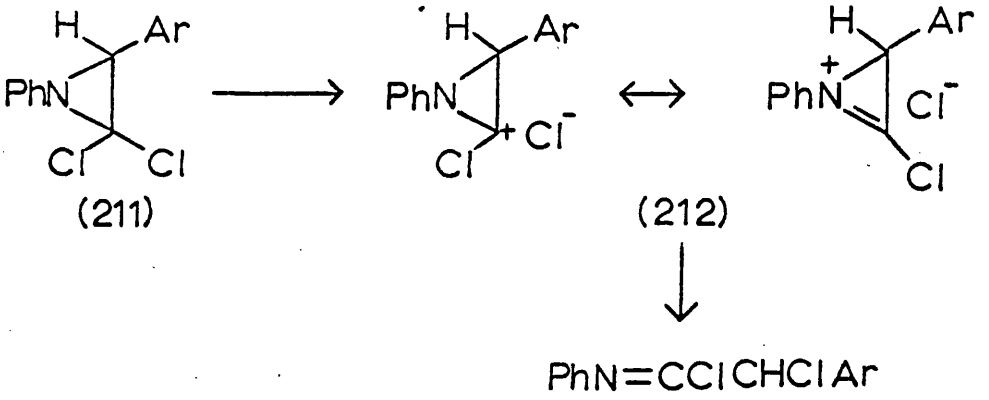
(209) (210)

The rearrangements of halogenocyclopropanes fused to small and medium sized rings[223,224] go at much lower temperatures (150-200°). These rearrangements have been interpreted as involving initial heterolytic cleavage to give halide ion and an allylic carbonium ion, in accord with the predictions of Woodward and Hoffmann.[225,226] The rate of rearrangement should depend upon the ease of heterolysis of the carbon-halogen bond.

The rearrangement of halogen-substituted three membered heterocyclic rings proceeds faster than the corresponding cyclopropanes. Indeed, attempts to prepare 2-halogenoepoxides of 1-halogeno substituted olefins have often resulted in the isolation of the rearranged product, a 2-halogenocarbonyl compound.[227-230]

A similar rearrangement has been observed with an episulphide.[231]

There is one isolated example[232,233] of a rearrangement of a 2-chloroaziridine (211) similar to that observed by us. Radiochemical data, with external chlorine-36, indicated that the reaction was predominantly intramolecular; kinetic data showed it to be first order in aziridine. These observations coupled with more sophisticated kinetic measurements were interpreted as involving a non-exchanging ion-pair (212), in which a C-Cl bond has been broken heterolytically and the resultant ring positive charge was stabilised as shown.

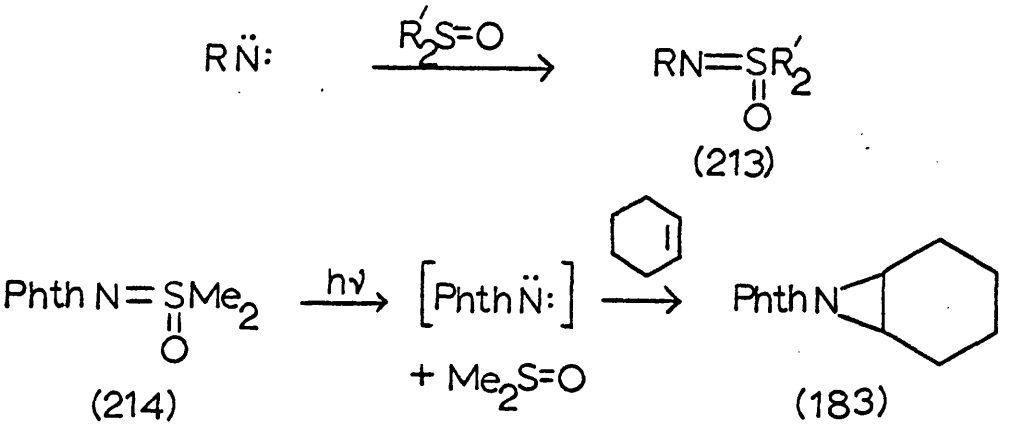


Similarly the retention of optical activity[229] in an analogous 2-chloroepoxide to 2-chloroketone rearrangement, supported an ion-pair mechanism.[228]

Some support that this type of mechanism is operative in our rearrangements comes from the interpretation of the chloroaziridine N.M.R. spectra discussed earlier. The low barrier to nitrogen inversion observed, indicates that the planar transition state is easily achieved. This would be enhanced by ionic resonance structures of the forms (203) and (212). We conclude that the rearrangement observed by us involves the same type of ion-pair mechanism. The lone-pair on the hetero-atom facilitates cleavage of the carbon-halogen bond.

Oxidation of the N-Amino Compounds in the presence of Sulphoxides

Sulphoxides have been found to be efficient traps for nitrenes,[31,234-237] the products of the reaction being the corresponding sulphoximines (213).



We have found that dimethyl sulphoxide is indeed a very good trap (probably the best tried) for the amino-nitrenes derived from the oxidation of the N-amino compounds. N-Aminophthalimide, N-aminonaphthalimide and 3-aminobenzoxazolin-2(3H)-one all gave high yields of the corresponding sulphoximines when oxidised with L.T.A. in dimethyl sulphoxide.

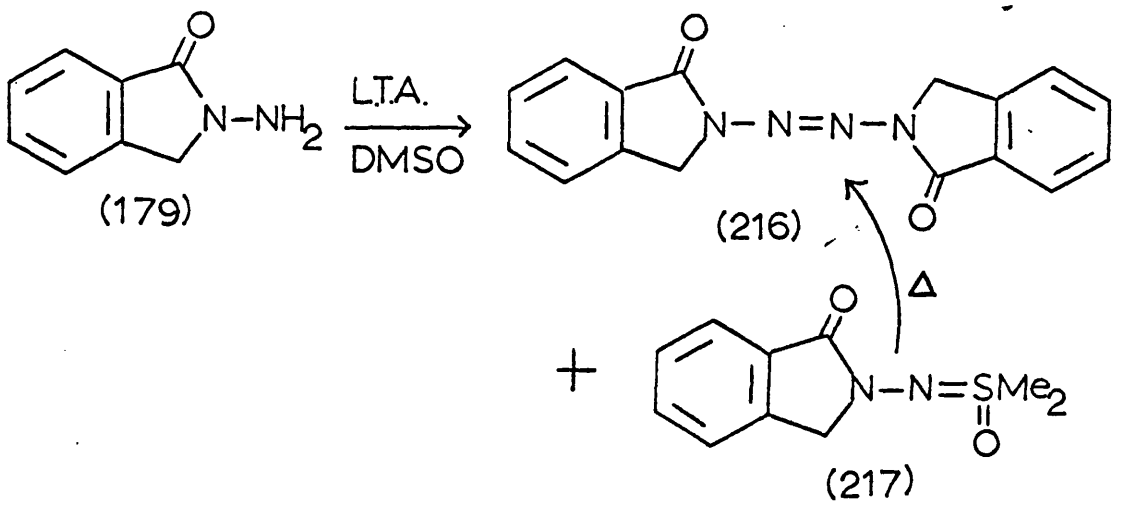
It was found that the photolysis of sulphoximine (214) in acetonitrile containing cyclohexene gave the corresponding aziridine (183). The only likely common intermediate in this reaction and the photolysis of the mesityl oxide derived aziridine (197) and the oxidation of the N-amino compounds, is the amino-nitrene.

It is suggested that the photolysis of sulphoximines is not a general way of generating nitrenes, since it has been found that certain sulphonyl sulphoximines (215) give aryl radicals upon photolysis.[238]

$$ArSO_2N = \overset{O}{\overset{\|}{S}}Me_2 \xrightarrow{h\nu} Ar.$$

(215)

The oxidation of N-aminophthalimidine (179) by L.T.A. in dimethyl sulphoxide was rather curious. Gas evolution was completely arrested. When the solution was poured into water then extracted with chloroform, and the extracts washed with water, the very insoluble tetrazene (216) was obtained directly with no trace of the sulphoximine (217). However if the original reaction mixture was poured directly into chloroform or dichloromethane, then washed with water, the soluble sulphoximine (217) was isolated together with smaller amounts of the tetrazene.

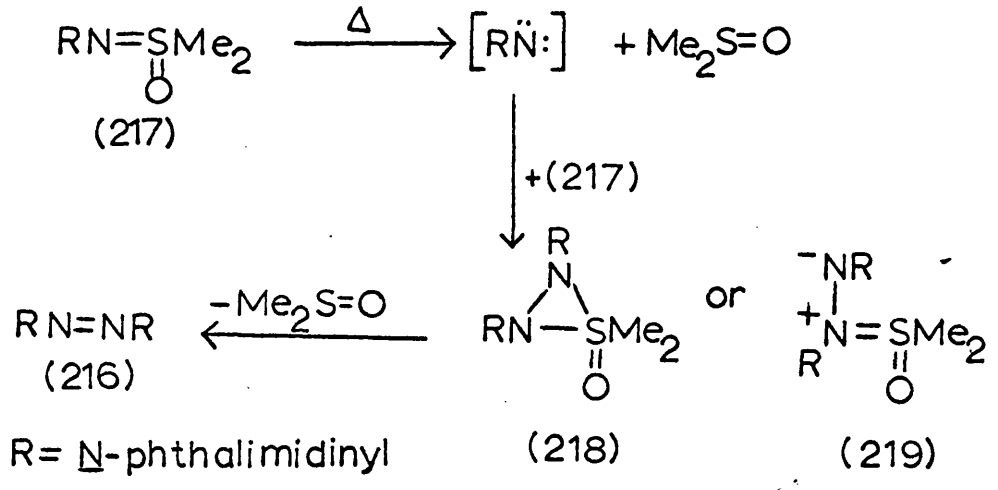


(179) (216) (217)

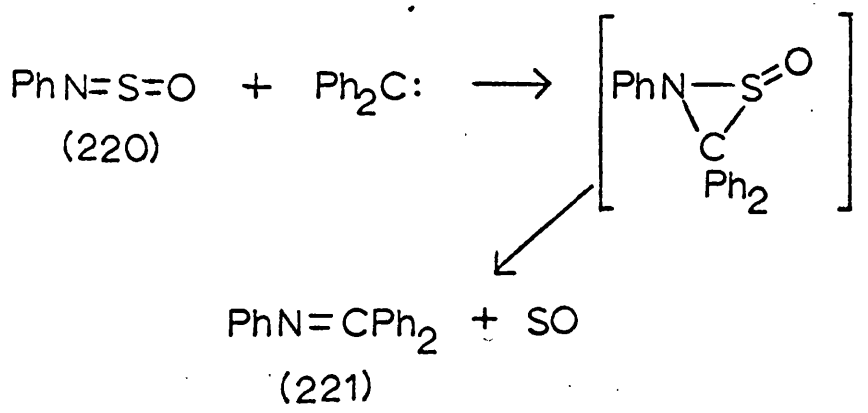
The sulphoximine (217) proved to be extremely labile and was converted to the tetrazene upon recrystallisation from ethanol. Evidence for the structure of the sulphoximine consisted of the following. Its I.R. spectrum showed strong peaks at ca. 1200 and 1040 $cm.^{-1}$ indicative of the N = S = O system. The N.M.R. spectrum ($CDCl_3$) showed a six proton singlet at τ 6.76 characteristic of the dimethylsulphoximine moiety,

besides the other usual phthalimidino peaks. The mass spectrum showed no parent peak (the parent peak of other sulphoximines was very small), but a base peak at m/e 78 for D.M.S.O.. This again is characteristic of the other sulphoximines studied. The remainder of the spectrum was due to the phthalimidino moiety.

The tetrazene was not isolated from the oxidation of the N-amino compound alone in dichloromethane. It showed remarkable thermal stability with a m.p. > 320°.



The conversion of the sulphoximine to the tetrazene may proceed as outlined. It is considered that the initially produced nitrene may add to the N = S bond of the sulphoximine to give the three membered ring (218) which readily fragments to give the tetrazene (216) and D.M.S.O.; or the nitrene could add to the sulphoximine to give the open structure (219) which could fragment before collapsing to (218).



A similar mechanism involving a three membered ring has been proposed[239] to account for the formation of N-diphenylmethyleneaniline (221) from the photolysis of N-sulphinylaniline (220) in the presence of diphenylcarbene.

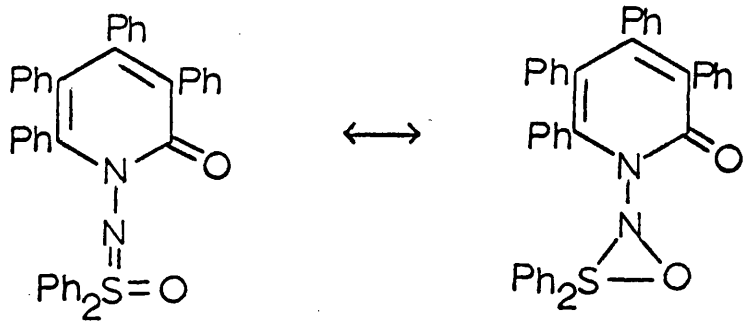
Mixed azobenzenes have been obtained from the reaction of substituted phenyl azides with N-sulphinylaniline,[159] presumably via a similar mechanism.

$$X-C_6H_4N_3 + PhN=S=O \xrightarrow{\Delta} X-C_6H_4-N=N-Ph$$

Oxidation of N-aminocarbazole by L.T.A. in dimethyl sulphoxide gave an uncharacterisable black solid, which may have consisted of some very impure tetrazene. This black colouration is typical of all N-aminocarbazole oxidations and considerably hampers isolation of pure compounds. During chromatography, the eluant acquires a deep purple colour when ca. 10% ether in petroleum has been reached. It is not removable by digestion with charcoal.

All dimethylsulphoximines studied had the characteristic S = O peak in the I.R. spectrum at ca. 1040 $cm.^{-1}$, present also in D.M.S.O.. However it was noted[210] that this was absent in the I.R. spectrum of the diphenyl-

sulphoximine (222). This was attributed to the oxathioaziridine structure (223). However at that time I.R. spectral data was scarce for sulphoximines.



(222) (223)

A study of this phenomenon was undertaken in conjunction with D.C. Horwell[188] to seek more evidence for the oxathioaziridine structure.

The methylphenylsulphoximine and diphenylsulphoximine of N-amino-phthalimide were prepared and their I.R. spectra observed as nujol mulls and chloroform solutions.

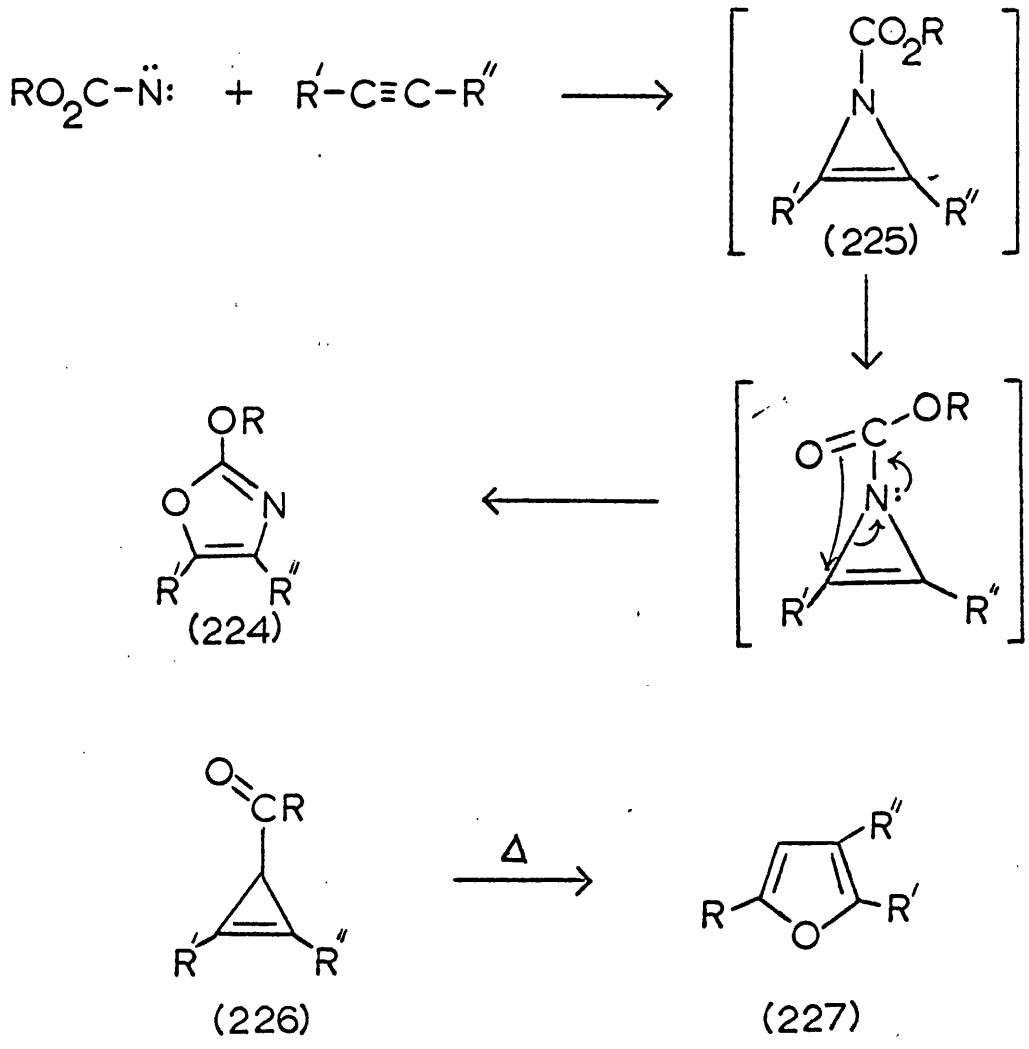
It was found that the S = O peak in the parent sulphoxides with phenyl substituents was shifted from ca. 1040 $cm.^{-1}$ to ca. 1090 $cm.^{-1}$ in the corresponding sulphoximines. Indeed N-sulphinylaniline shows no marked absorption in the region 1000-1100 $cm.^{-1}$. By far the most characteristic and intense peak of all sulphoximines studied was that in the region 1190-1230 $cm.^{-1}$. As the result of a thorough investigation,[240] this absorption is attributable to the N = S = O group.

Consequently there is negligible evidence for the existence of the oxathioaziridine species.

Oxidation of N-Aminophthalimide in the presence of Acetylenes

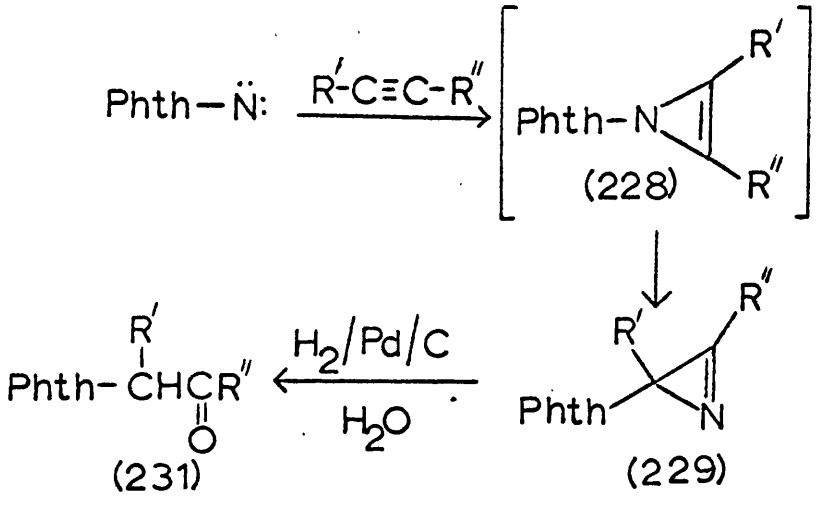
One logical extension of the addition of our nitrenes to olefins was to study the reaction with acetylenes, as an obvious route to 1H-azirines.

So far the addition of acyl nitrenes to acetylenes has led to products other than azirines, such as oxazoles, by supposed 1,3-dipolar addition.[24, 241, 242] The formation of oxazoles (224) need not necessarily involve 1,3-dipolar addition, but could involve the intermediate 1H-azirine (225) which rearranges as shown. This mechanism looks more attractive when compared to the analogous acylcyclopropene (226) to furan (227) rearrangement.[243,244]



Nitrene itself has been added to acetylene at 4°K in a solid argon matrix.[34] Spectroscopic evidence pointed to the formation of ketenimine.

Phthalimido nitrene, generated from the oxidation of the N-amino compound with L.T.A., was found to add to the terminal and dialkyl acetylenes shown.



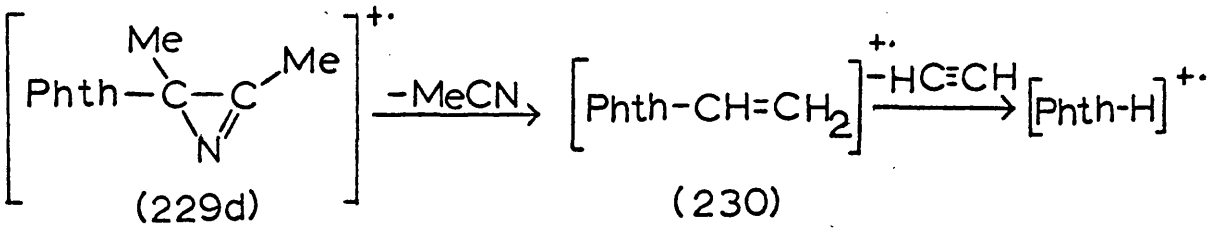
	R'	R''
a	H	Me
b	H	Pr
c	H	Bu
d	Me	Me
e	Et	Et

The product (in low yield) was not the 1H-azirine (228) but the 2H-azirine (229). This was readily determined by the adducts from but-2-yne and hex-3-yne, which exhibited non-equivalence of the methyl groups and ethyl groups respectively in their N.M.R. spectra. The latter spectrum showed non-equivalence of the protons in both methylene groups. The greater non-equivalence (12 c.p.s.) was exhibited by the methylene protons attached directly to the centre of asymmetry, C-2 of the azirine ring. The non-equivalence of the methylene protons attached to C-3 of the ring was 2.5 c.p.s., in accord with their position relative to the asymmetric centre. Similarly the N.M.R. spectrum of the azirine (229b), substituted in the 3-position with an n-propyl group showed non-equivalence (2.5 c.p.s.) of the methylene protons attached directly to C-3. Hassner and Fowler[122] never noticed this phenomenom in similarly substituted azirines.

Formally two 2H-azirines are possible from the monoalkyl acetylenes, but one of them would be unsubstituted in the 3-position and susceptible to polymerisation.[122] Indeed those azirines isolated from the monoalkyl acetylenes were those with the alkyl group in the 3-position of the azirine ring. The other isomer probably polymerised.

The C = N vibration of 2H-azirines should occur at ca. 1740 $cm.^{-1}$; however this is not a very strong absorption[101] and would be masked in our cases by the phthalimido carbonyl absorption.

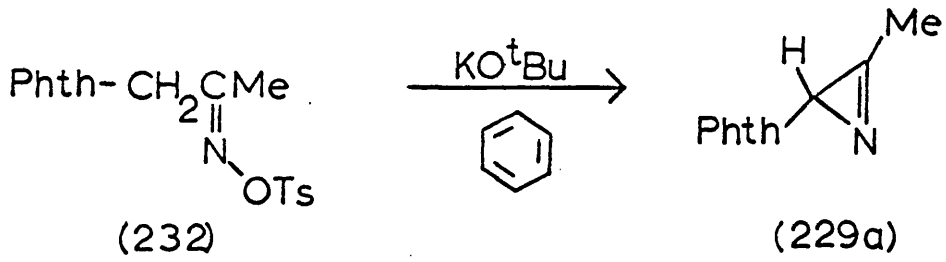
Mass spectral breakdown patterns of the 2H-azirines studied were very indicative of structure. For example the but-2-yne derived azirine (229d) showed a parent peak at m/e 214 followed by successive peaks at m/e 173 and m/e 147. These represent losses of 41 mass units, suggested as MeCN to give N-vinylphthalimide (230), and subsequently 26 mass units to give phthalimide, by loss of acetylene.



(229d) (230)

Further structural evidence was provided by the quantitative conversion of the azirine (229b) to the ketone (231) by catalytic hydrogenation in moist ethyl acetate [cf. ref. (101)]. The ketone was independently synthesised from potassium phthalimide and 1-bromopentan-2-one. Lithium aluminium hydride reduction of the azirines was complex, and no identifiable products were isolated [cf. ref. (101)].

The structure of azirine (229a) was confirmed by an independent synthesis from the oxime toluene-p-sulphonate (232) and potassium t-butoxide in boiling benzene, by a Neber type reaction.



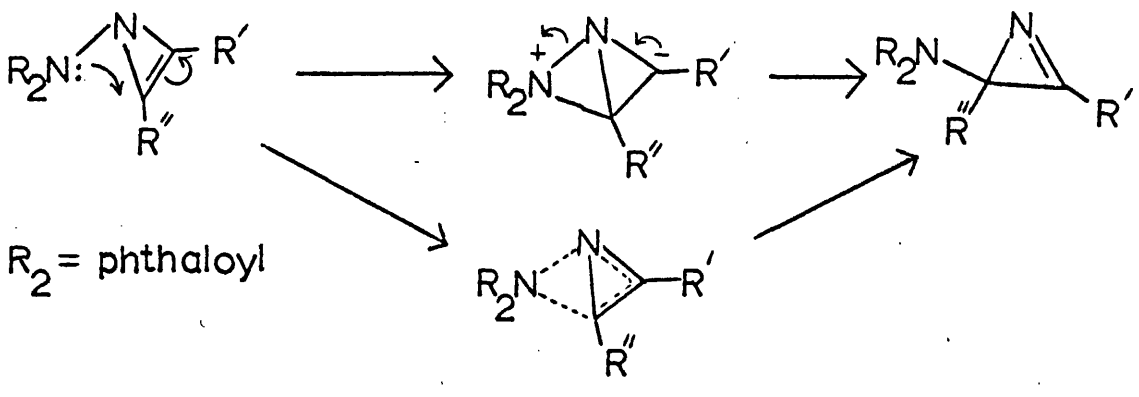
(232) (229a)

We believe that 1H-azirines (228) are first formed in the addition of phthalimido nitrene to acetylenes but rearrange very rapidly to the 2H-isomers.

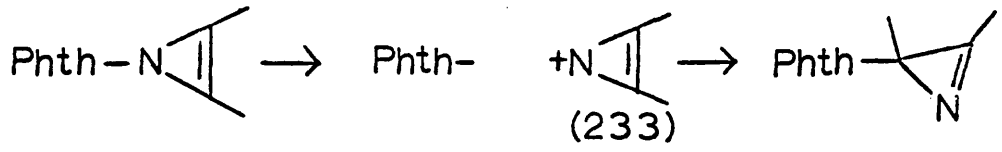
The 1H-azirine could exist as a cyclic, planar 4π electron system isoelectronic with the cyclopropenyl anion, and could be destabilised by electron delocalisation; that is, it would be anti-aromatic.[245,246]

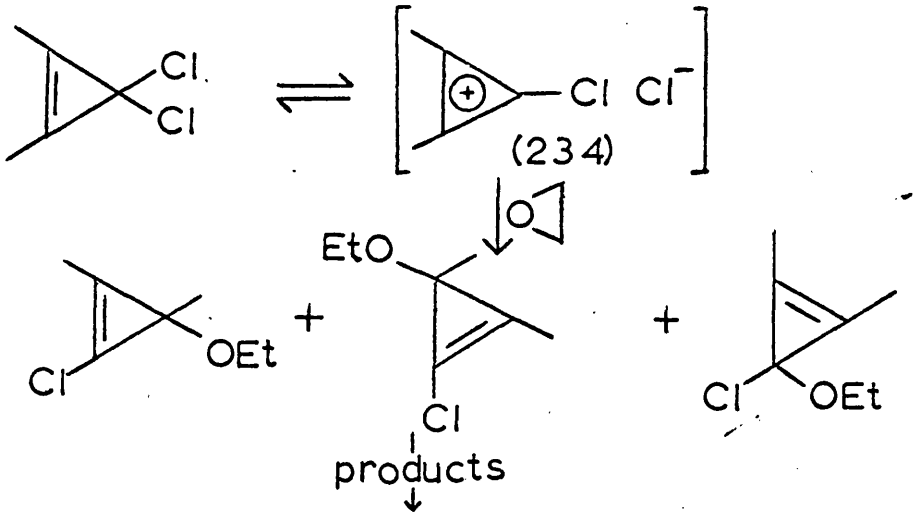
In the 2H-azirine the nitrogen lone-pair is in an sp^2 orbital orthogonal to the $p\pi$ orbital of the C = N bond. It is no longer anti-aromatic but is non-aromatic.

The mechanism of the rearrangement is still uncertain but several can be suggested. It could involve a stepwise zwitterionic mechanism or a possible [1,3] sigmatropic shift type mechanism as shown. Neither can be excluded in the absence of any conflicting evidence.

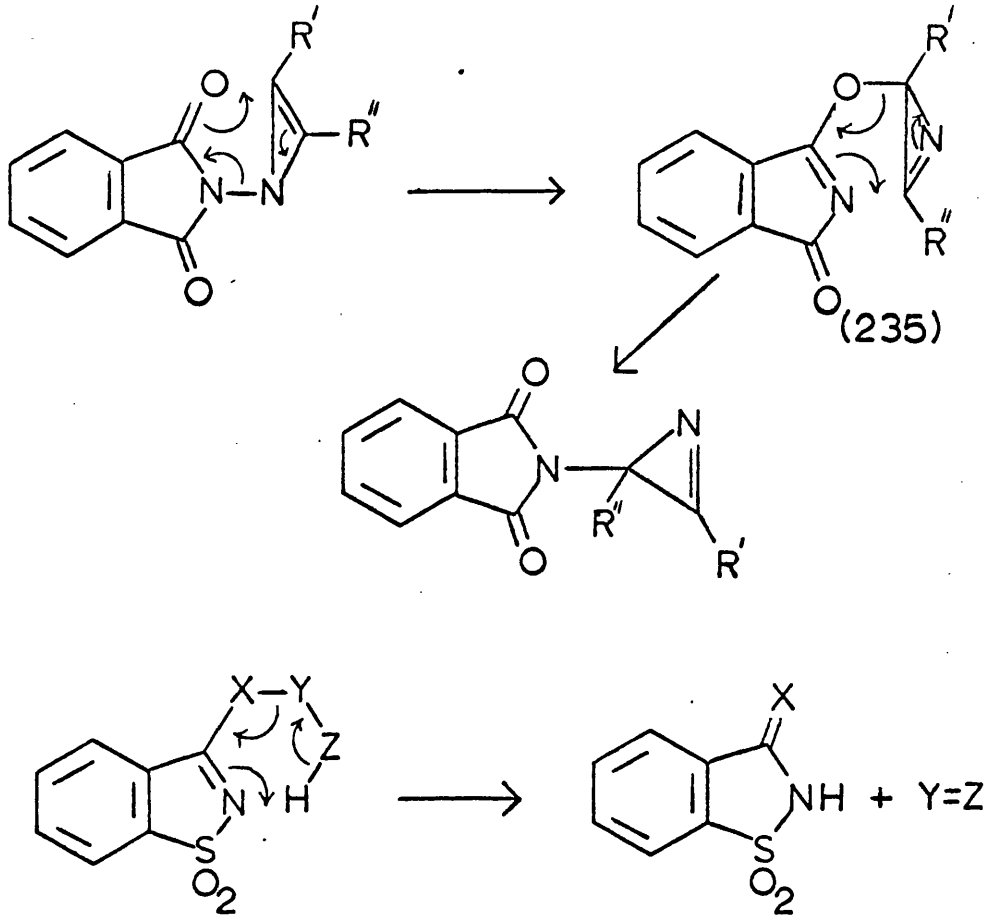


Perhaps a more attractive mechanism is one involving heterolytic fission of the N-N bond to give the phthalimido anion and the nitrenium ion (233). The latter should be aromatic. No confirmatory evidence has been provided, but a similarly related species, a cyclopropenyl cation (234) has been proposed[247-249] as an intermediate in the reactions of 3,3-dichlorocyclopropenes.





The most attractive mechanism is one involving two [3,3] shifts or Claisen type rearrangements via the O-azirine (235). This is quite similar to the mechanism of oxidative deamination via the tetrazane as proposed by Dreiding.[192] Rearrangements similar to the second [3,3] shift suggested above are known[250] to proceed very readily, with elimination, in the pseudosaccharin series, as shown.



Preliminary experiments[251] indicate that O-allyl pseudophthalimide will rearrange to N-allylphthalimide.

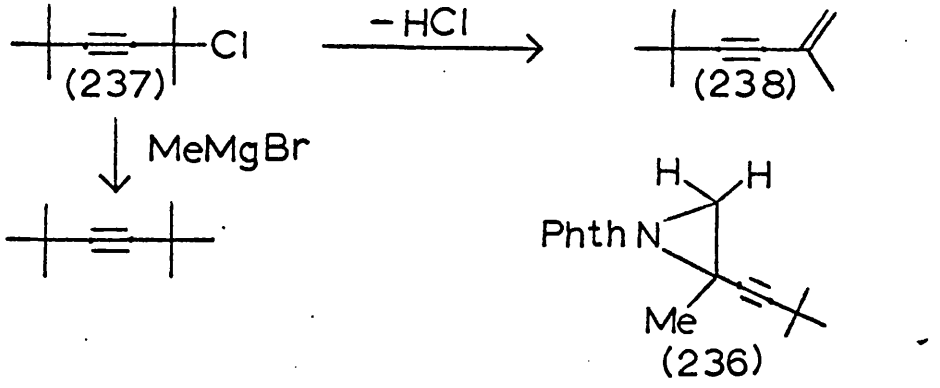
Consequently the azirine rearrangement via the Claisen type mechanism is perhaps the most likely.

Azirines could not be isolated from the following acetylenes: (i) Phenylacetylene (ii) Diphenylacetylene (iii) t-Butylacetylene (iv) Di-t-butylacetylene (v) Di-n-hexylacetylene (vi) 1,4-Dimethoxybut-2-yne (vii) 1,4-Dichlorobut-2-yne (viii) Dimethyl acetylenedicarboxylate (ix) methyl tetrolate (x) 1-(N,N-Diethylamino)prop-1-yne.

Phthalimide (60-80%) was the major product isolated, except in the case of yneamine (x) which was preferentially attacked by L.T.A..

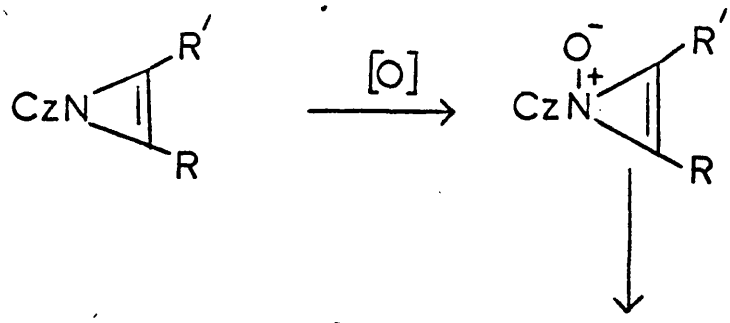
Di-t-butylacetylene reacted rather anomalously. The product isolated was in fact an aziridine (236). This was shown to be formed from an impurity (238) in the acetylene. The last step in the synthesis of

di-t-butylacetylene involves the addition of MeMgBr to the t-alkyl chloride (237). The latter compound can easily eliminate HCl under the conditions, to give the eneyne (238). The olefinic double bond of the latter reacted preferentially with the nitrene to give the aziridine (236). The impurity (238) could not be completely removed even after several fractionations with a spinning band column. It was also just detectable in the N.M.R. spectrum.



Before spinning band fractionation about 15% of the impurity was present. This was the material first used in the experimental section. After fractionation the impurity was reduced to 1-2%, although the nitrene still preferred to react with the double bond rather than the triple bond, since no azirines could be isolated.

The oxidation of N-aminocarbazole by L.T.A. in the presence of hex-3-yne produced no isolable azirine. Instead N-nitrosocarbazole (18%) and carbazole (33%) were isolated. The formation of the nitroso compound also occurred in the presence of olefins as mentioned earlier. If the source of the nitroso compound in the olefin case was indeed from the aziridine N-oxide decomposition, then a similar mechanism could operate perhaps even more favourably with acetylenes.



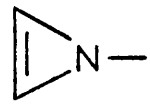
[Cz = N-carbazolyl] $CzN{=}O + R'{-}C{\equiv}C{-}R$

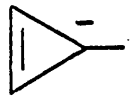
The 1H-azirine first formed would receive stabilisation by N-oxide formation as shown. The lone pair on the nitrogen would be delocalised in forming the N-O bond. Consequently the ring system is no longer anti-aromatic,but is non-aromatic. Disproportionation of the N-oxide would result in the nitroso compound and the acetylene. These observations indicate that the initial nitrenoid-acetylene complex probably has a finite existence.

If a similar pathway were operative in the phthalimido system, then this would account for the low yields of 2H-azirines and high yields of phthalimide.

Other Attempts to generate the 1H-Azirine system

The 1H-azirine system (239) would be isoelectronic with the cyclopropenyl anion (240), possessing 4π electrons. According to quantum mechanical calculations, systems with $4n\pi$ electrons should have anti-aromatic character and be destabilised by electron delocalisation.


(239)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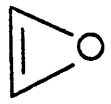
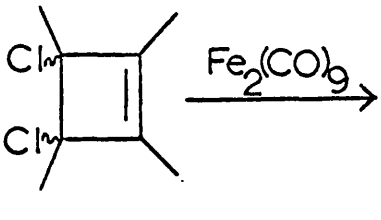
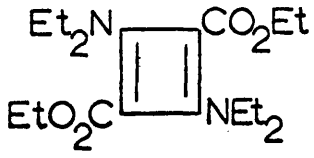

(241)


(242)


(243)



(244)



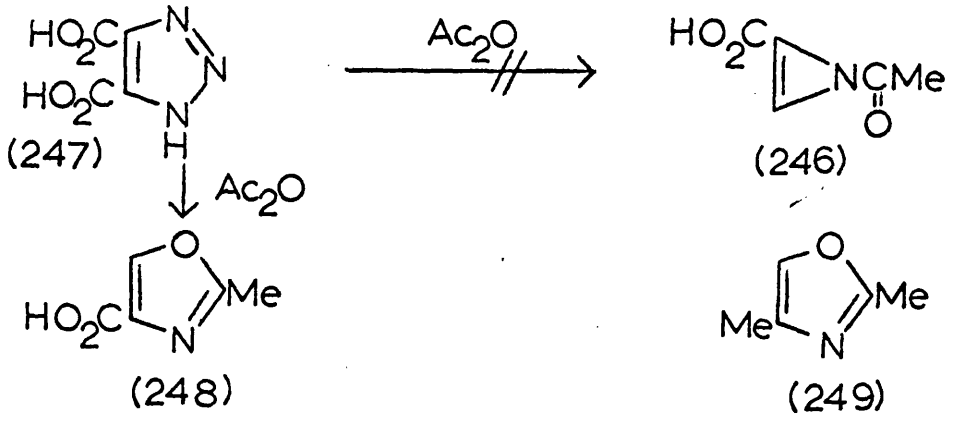
(245)

Other heterocyclic anologues are oxirine (241) and thiirine (242). These have been suggested as intermediates during the photochemical gas-phase Wolff rearrangement[252] and peracid oxidation of acetylenes,[253] and in the gas-phase addition of sulphur atoms to acetylenes and photolysis of 1,2,3-thiadiazoles.[254]

Much attention has been focused on the cyclobutadiene (243) 4π electron system.[255] The chemistry of (243) indicates that it is a highly reactive species. Numerous approaches have been made to the system. Some of the most successful have been the dehalogenation of dichloro-cyclobutenes by metal carbonyls. The resultant cyclobutadiene is 'trapped' as a metal carbonyl complex e.g. (244).[256]

So far only one uncomplexed cyclobutadiene has been synthesised (245).[257] This has been achieved with the aid of electron withdrawing and donating groups as shown.

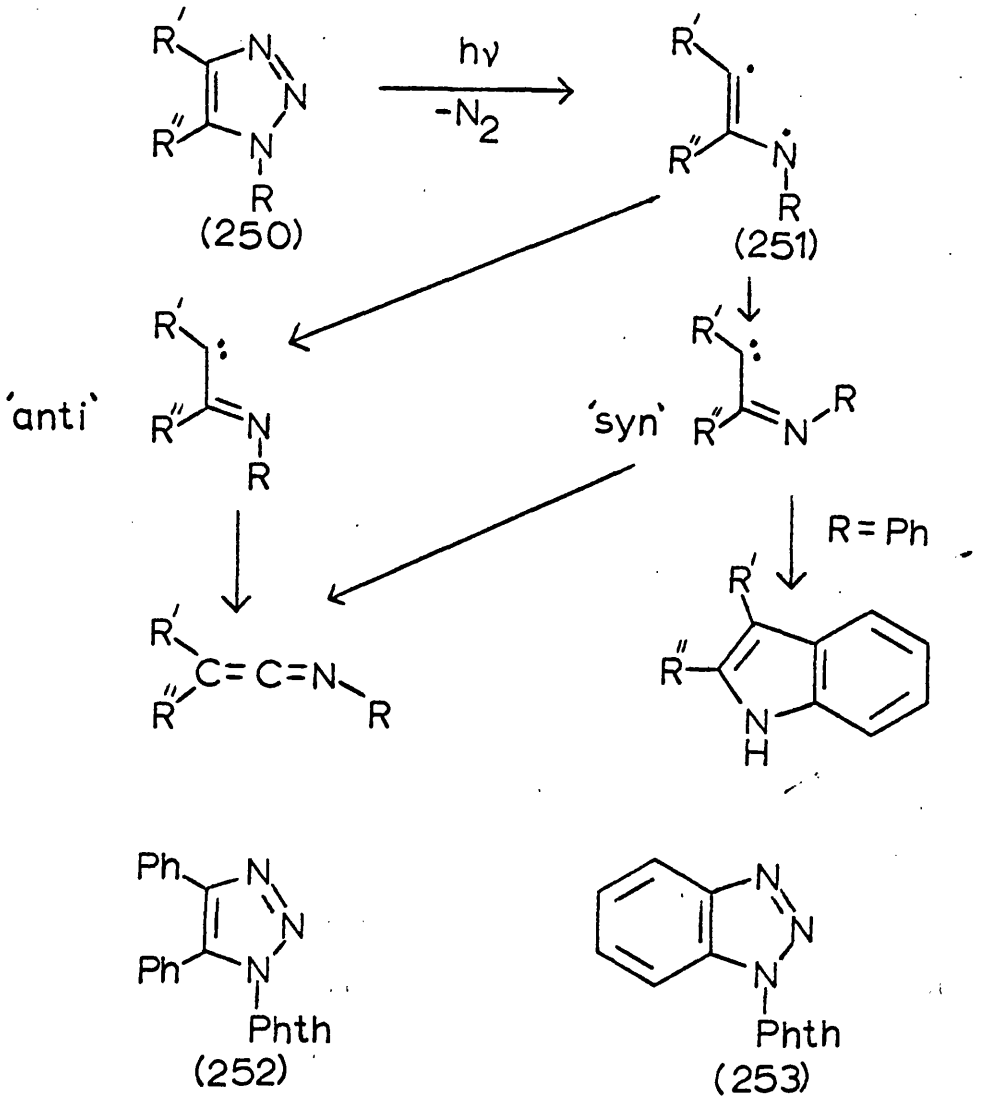
The suggested high energy, anti-aromatic character of the 1H-azirine could explain why there was only one report[170] in the literature of its existence. 1-Acetyl-1H-azirine-2-carboxylic acid (246) was reported[170] as a product from the reaction of 1H-1,2,3-triazole-4,5-dicarboxylic acid (247) with acetic anhydride. We repeated this reaction and found that the m.p. (183-4°) of the product was in accord with that of the isomeric oxazole (248). Similarly the I.R. spectrum indicated the oxazole structure by analogy with I.R. spectra of other oxazoles.[258] The spectra of (248) and (249) were identical below 1100 cm.$^{-1}$, and the peaks at ca. 3150 cm.$^{-1}$, characteristic of oxazoles,[258] were also present.



Attempted dehydrohalogenation of certain 2-chloroaziridines was unsuccessful[259] in producing the 1H-azirine. In fact prior to this work it had been noted[260] that monochloroaziridines underwent nucleophilic displacement rather than elimination, with base.

Several workers[261-263] have studied the photolysis and thermolysis of 1H-1,2,3-triazole derivatives (250) in the hope of detecting the 1H-azirine. The diradical produced (251) prefers to rearrange as shown

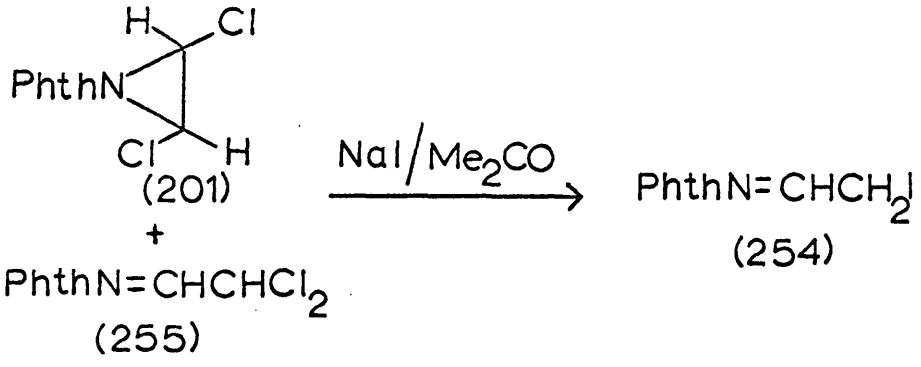
rather than close to generate the 1H-azirine system. Preliminary studies indicate that the 1-phthalimido triazoles (252) and (253) do not even lose nitrogen upon photolysis. Work is in progress to determine the nature of the products.



We chose to concentrate our efforts on dehalogenation reactions of 2,3-dichloroaziridines, and were encouraged by the results obtained in generating cyclobutadiene in this manner.

In the absence of any 'traps' we expected that the 1H-azirine would rearrange to the 2H-isomer, and the latter was actually sought.

The simplest approach was to use sodium iodide in acetone as the reagent. The trans-2,3-dichloroaziridine (201) very rapidly gave the hydrazone (254), as did the aziridine rearrangement product (255). It is inferred that the reagent catalyses the rearrangement and that the reductive substitution takes place with (255).



Most of the exploratory work was conducted with the aziridine (201) mainly because it was easily made. The results may have been misleading since the 1H-azirine or subsequent 2H-azirine that would have been produced, would almost certainly have been unstable because of lack of substituents.[122]

A more versatile dehalogenating reagent is sodium naphthalene.[264] When applied to our system it did in fact react with the aziridine (201) but no products were obtained. The intense green colour of the reagent was immediately discharged and a red one developed. This could be interpreted as a transference of the radical anion to the benzene ring of the phthalimido substituent. It was observed also that the reagent reacted faster with the rearrangement product (255). Again the reagent may have catalysed the rearrangement. Since no products at all could be isolated or even indicated by t.l.c., we attempted to intercept the possible intermediate with furan and cyclopentadiene. Both were unsuccessful. Had the rearrangement product (255) been the sole species

undergoing dechlorination then the ketimine (256) might have been expected as the product. This no doubt would have polymerised or reacted further, but a possible degradation product is phthalimide. This was never detected.

$$\underset{(255)}{\text{Phth - N = CH - CHCl}_2} \xrightarrow{-2Cl} \underset{(256)}{\text{Phth - N = C = CH}_2}$$

Since we were unable to isolate the 2H-azirine from the previous reactions or trap out the 1H-azirine, we sought more specific dehalogenating reagents which could themselves trap out the reactive intermediate. By analogy with cyclobutadiene chemistry the reagents of choice were the transition metal carbonyls. The easiest to handle is di-iron enneacarbonyl, prepared from the photolysis of iron pentacarbonyl in glacial acetic acid as golden yellow flakes, decomposing at 100-120° and practically insoluble in all organic solvents. Exploratory studies indicated that the aziridine (201) was indeed dehalogenated but no products or complexes could be detected.

We sought a 2,3-dichloroaziridine with substituents in the other 2,3-positions. Aziridine (202) was chosen partly because a specimen of the possible resultant 2H-azirine had previously been prepared by us from but-2-yne and N-aminophthalimide. In order to prepare (202), trans-2,3-dichlorobut-2-ene (257) was required. However trans-dichloro olefins have received little attention in the past, and in view of the synthetic difficulties encountered, it is not surprising. The required olefin was obtained in low yield after several steps from 1,3-dichlorobut-2-ene (258).

$MeCCl=CHCH_2Cl + Cl_2 \longrightarrow CH_2ClCCl_2CHClCH_2Cl + CH_2=CClCHClCH_2Cl$

(258)

$+ MeCCl_2CHClCH_2Cl$

KOH

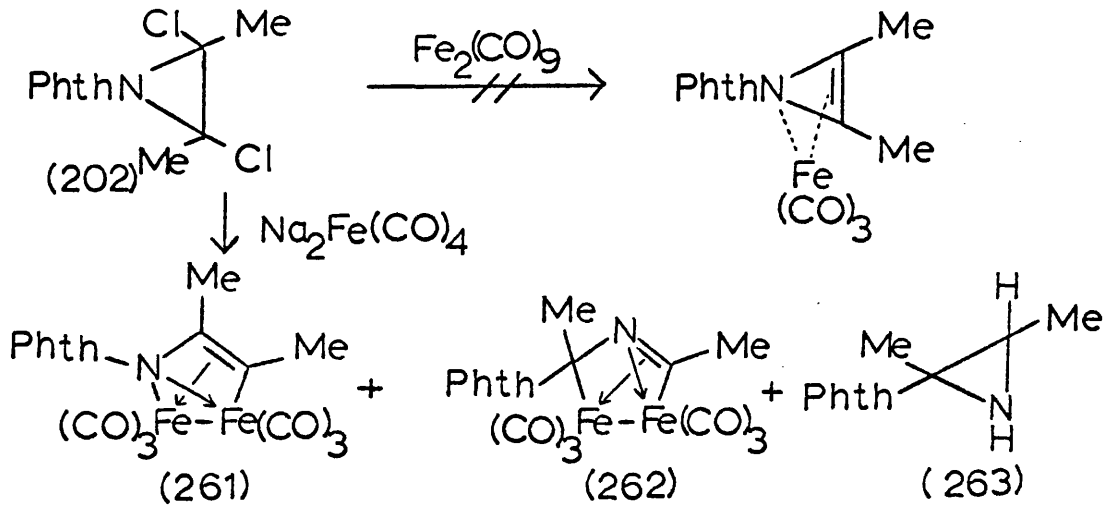
$MeCCl_2CCl=CH_2$

$+$ $\xrightarrow{LiAlH_4}$ $MeCCl=CClMe$

$MeCCl=CClCH_2Cl$ (257)

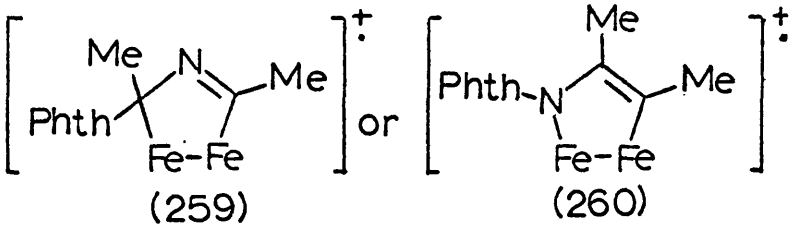
It was vitally important that the latter compound should be of the highest purity otherwise the first stage of the synthesis, chlorination, proceeded in very low yield. Oxidation of N-aminophthalimide in the presence of trans-2,3-dichlorobut-2-ene produced the aziridine (202) in relatively low yield (29%). Consequently reactions conducted with this aziridine were very carefully chosen.

It was hoped that di-iron enneacarbonyl would dechlorinate the aziridine (202) and then complex the 1H-azirine, in an analogous manner to the cyclobutadiene (244). However the aziridine and the reagent did not react in benzene or T.H.F.; the di-iron enneacarbonyl merely decomposed rapidly to iron pentacarbonyl, tri-iron dodecacarbonyl and carbon monoxide.



(261) (262) (263)

A perhaps more versatile metal carbonyl reagent is disodium iron tetracarbonyl,[265] prepared from iron pentacarbonyl and sodium borohydride. Exploratory studies with aziridine (201) indicated that this reagent was effective at dechlorination, as shown by the detection of sodium chloride. Consequently the substituted aziridine (202) was treated with this reagent. Two separate iron carbonyl complexes were isolated in extremely low yield after two applications of prep. t.l.c.. There was sufficient quantity of each to enable only I.R., mass spectral and m.p. determinations to be made. The complexes appeared to decompose during chromatography. The minor, faster running component was obtained in a pure state, m.p. 147° dec.. Its I.R. spectrum showed only terminal carbonyls (1950-2041 $cm.^{-1}$) and no bridging carbonyls (< 1900 $cm.^{-1}$). The characteristic peaks for the phthalimido carbonyl system [1799 (w) and 1746 (s) $cm.^{-1}$] were also present, plus a strong peak at 1706 $cm.^{-1}$, probably due to a C = C or C = N in the complex. The mass spectrum showed m/e = 494 for the parent ion, followed by six successive losses of 28 mass units (6-CO) to give m/e = 326 corresponding possibly to the fragment (259) or (260). Successive mass losses of 41, 26 and 112 are attributable to MeCN, HC≡CH and 2Fe. The losses of 41 and 26 mass units are supported by metastable peaks.



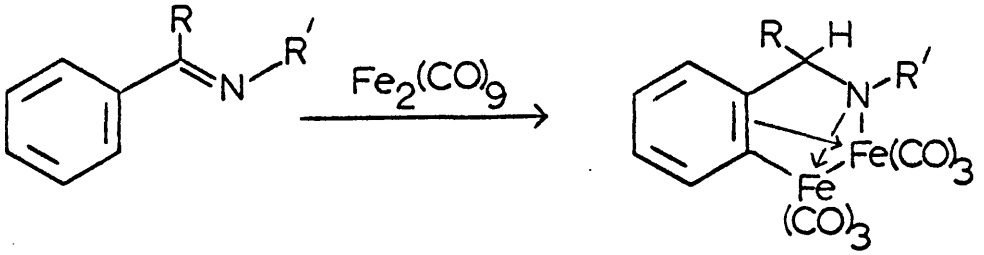
(259) (260)

A similar breakdown pattern has been reported in the previous section for the 2H-azirine (229d) derived from but-2-yne. The above data are consistent with structures (261) and (262), both conforming to the 'inert gas rule'.

The slower running, minor component could not be obtained pure. It was always contaminated with colourless sublimable flakes. The I.R. spectrum of the complex shows it to be very similar to that of the first one isolated. The metal carbonyls present are solely terminal (1976-2074 $cm.^{-1}$). In addition to the characteristic phthalimido pattern of peaks, there is also a broad peak at 3185 $cm.^{-1}$, suggestive of an N-H group. The complex was extremely thermally labile decomposing at ca. 85°. The mass spectrum obtained is almost certainly that of the colourless flake impurity since this sublimed from the probe and the resultant spectrum did not show the presence of metal carbonyls even at operating temperatures below the m.p.. Bearing in mind the N-H group in the I.R. spectrum, the mass spectrum could conceivably fit for the aziridine (263) i.e. the reduced 2H-azirine. The parent ion shows m/e = 216 with subsequent peaks at m/e = 201 and 187. These could correspond to losses of CH_3- and $-CH_2$- respectively; m/e = 147 corresponds to phthalimide. The spurious peak at m/e = 162 could correspond to either N-aminophthalimide or a protonated form of N-methylphthalimide.

Structural evidence for the labile iron carbonyl complex rests solely on I.R. spectra comparison with the other complex isolated. Since the first complex isolated could be either of (261) or (262), it is suggested that the latter complex isolated could also be (261) or (262).

Similar complexes (264) have been isolated from Schiff bases,[266,267] which also exhibited similar mass spectral fragmentation[266] to that of our complex.



(264)

The question remains unanswered whether the complexes isolated are derived from the dichloroaziridine (202) or its thermal rearrangement product. The structure proposed for complex (262) contains an N-phthalimido carbon bond, whereas the starting aziridine contained an N-N bond. It is conceivable that the formation of this complex involves dechlorination of the aziridine to give the 1H-azirine which rearranges to the 2H-isomer, but is complexed during or after the rearrangement. The same reasoning cannot apply unambiguously to the formation of the suggested complex (261) since this could equally be formed from the rearranged dichloroaziridine. Consequently the reagent again could be catalysing the chloroaziridine rearrangement.

Both complexes (261) and (262) are dimeric in iron, whereas the reagent was only monomeric. This tends to suggest that the 1H-azirine does not want to be complexed in an analogous manner to cyclobutadiene by iron tricarbonyl, and that there is little hope of obtaining a 1H-azirine complex with the ring intact.

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ABSTRACT

The work presented in this thesis concerns the oxidation of N-amino compounds and the interception of the reactive intermediates, the postulated amino-nitrenes.

The Introduction has been divided into three parts concerning (1) the synthesis of aziridines from nitrenes and olefins (2) nitrogen inversion as studied by N.M.R. spectroscopy (3) synthetic approaches to 2H-azirines.

The preparation of one new N-amino compound, N-aminophthalimidine is reported and the oxidations of that compound and of N-aminophthalimide, N-aminonaphthalimide, 3-aminobenzoxazolin-2(3H)-one and N-aminocarbazole are reported. The oxidation of the N-amino compounds alone leads to a variety of products, a major one frequently being the deaminated compound. The mechanism of oxidative deamination is discussed and an intermediate in the reaction, a tetrazane, has been isolated.

Oxidations in the presence of olefins and sulphoxides generally give aziridines and sulphoximines.

The N.M.R. spectra of most aziridines studied showed the presence of invertomers at room temperature. The implications of slow nitrogen inversion as a tool for conformational analysis are discussed.

Several chloro- and bromo-substituted aziridines were found to undergo a facile thermal rearrangement with ring opening to give hydrazones.

Sulphoximines and certain aziridines substituted in the 2-position with an unsaturated group were shown to produce the amino-nitrenes upon photolysis.

When N-aminophthalimide was oxidised in the presence of acetylenes, 2H-azirines and not 1H-azirines were isolated. The mechanism of this novel rearrangement is discussed, and other attempted syntheses of the 1H-azirine system are reported.