MECHANISTIC STUDIES IN THE CHEMISTRY OF CARBENES AND NITRENES

A THESIS

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DOCTOR OF PHILOSOPHY

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BY

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CONTENTS

SUMMARY

The broad classes of nitrene reactions are discussed; particular attention is given to the electronic configurations of the species at the moment of reaction.

Evidence is presented that, while generated in the singlet state, carbethoxynitrene undergoes slow intersystem crossing to a triplet ground state. It is shown that, by variation in experimental conditions, reaction of either the metastable singlet or the more stable triplet form may be favoured. Accordingly, when the nitrene is produced in the presence of high concentrations of substrate, it reacts to a significant extent at the 1-position of anthracene and effects stereospecific addition to *cis*- and *trans*-butene-2. At low concentrations of these substrates, however, anthracene is attacked quite selectively at the 9-position and addition to butene-2 is non-stereospecific. Conclusions arising from some aspects of this work are discussed in the light of recent results of McConaghy and Lwowski.[10,11]

As the temperature is raised, increasing proportions of triplet carbethoxynitrene are seen to react, suggesting an energy requirement for the process singlet nitrene → triplet nitrene. The theoretical basis for this conclusion is discussed in detail.

Brief consideration is given to the effect of substituents on reactivity of carbenes. This approach is used to interpret the reactions of carbethoxycarbene and dichlorocarbene with anthracene.

The properties of carbamate-lead(IV) and carbamate-silver complexes are briefly reported in an appendix.

STATEMENT

This thesis contains no material previously submitted for a degree or diploma in any University, and to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference is made in the text.

J.W. REDMOND

ACKNOWLEDGEMENTS

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CHAPTER 1

REACTIONS OF CARBETHOXYNITRENE

1.1. INTRODUCTION

SCOPE AND LIMITATIONS

The chemistry of nitrenes was last reviewed in 1963.[1,2] Although it was then appreciated that the species could exist in singlet or triplet states, it has been shown only recently that some nitrenes can exist in *either* electronic configuration.[10,11,24] By variation in experimental conditions, therefore, it has become possible to alter the products of nitrene reactions. It is proposed here to discuss particularly this recent work because it is in this context that our studies are most relevant.

NOMENCLATURE

The terminology used to denote monovalent nitrogen fragments has been confused and confusing.[1,2] Although not systematic,[1] the term 'nitrene' is becoming increasingly accepted.

GENERATION OF NITRENE INTERMEDIATES

Decomposition (thermal or photochemical) of azides provides the 'normal' route to nitrenes. In this way alkyl-, aryl- and acylnitrenes are available, e.g.

$$n\text{-BuN}_3 \longrightarrow n\text{-BuN} + N_2$$

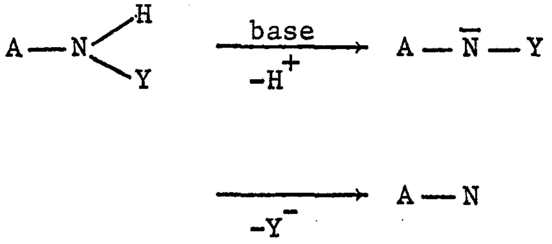
$$\text{PhN}_3 \longrightarrow \text{PhN} + N_2$$

$$EtOCON_3 \longrightarrow EtOCON + N_2$$

$$PhSO_2N_3 \longrightarrow PhSO_2N + N_2$$

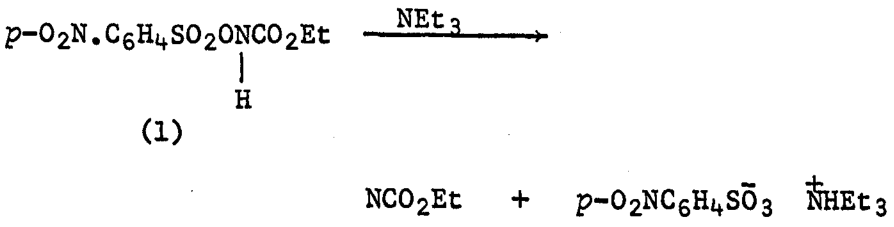
This route has close analogy in the generation of carbenes from diazo compounds.

α-Elimination is also a formally possible source of nitrenes, i.e.



(where Y^- is a 'good' leaving group)

In only one case, however, has it been convincingly shown that a free nitrene intermediate results:[3]

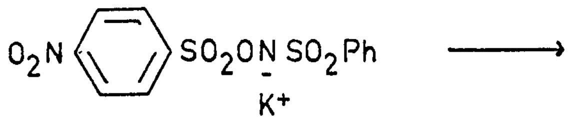


$$p\text{-}O_2N.C_6H_4SO_2O\underset{\overset{|}{H}}{N}CO_2Et \xrightarrow{NEt_3} NCO_2Et + p\text{-}O_2NC_6H_4S\bar{O}_3\ \overset{+}{N}HEt_3$$

(1)

(2)

When allowed to stand in methanol, the salt 3 is converted to products which can arise from phenylsulphonylnitrene (4).[4]



(3)

$PhNHSO_2OMe$ (67%)

$PhSO_2NHOMe$ (2%)

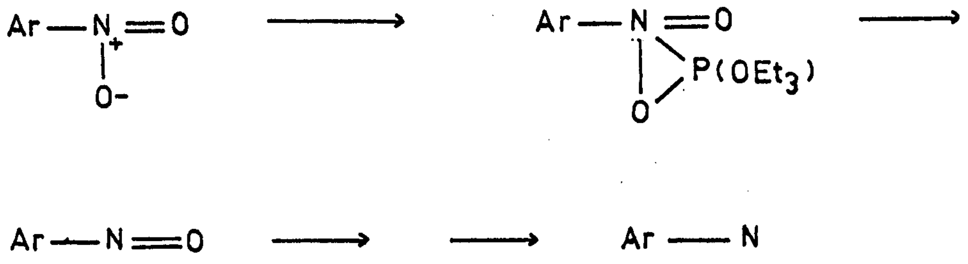
$PhSO_2NH_2$ (4 - 5%)

$PhSO_2N$

(4)

The parent NH may exist as an intermediate in the Raschig hydrazine synthesis, which depends on the treatment of chloramine with strong alkali.[2]

Reductive cyclization of nitro compounds is well documented.[5,6] Smolinsky and Feuer have shown[5] that nitrenes are frequently involved in the triethyl phosphite deoxygenation procedure, i.e.



It seems, however, that ferrous oxalate does not convert nitro compounds to nitrenes.[5,6]

EVIDENCE FOR EXISTENCE OF NITRENES

1. Electron Spin Resonance (e.s.r.) Studies

A triplet nitrene (see below) has non-zero electronic angular momentum and, if prevented from reacting with the medium, can be detected by e.s.r. spectrometry. In this way alkyl-,[8] aryl-,[7] cyano-,[12] arylsulphonyl-,[7] and acylnitrenes[9] have been successfully studied.

2. Kinetic Studies

The thermal decomposition of phenyl, *p*-methoxyphenyl and cyclohexyl azides was studied by Walker and Waters.[13] The reactions were of first order and essentially independent of the media. In the presence of indene, however, decomposition of the aryl azides was much faster due to substrate participation.

Thermolysis of substituted phenyl,[14] biphenyl[14] and triarylmethyl[15] azides shows first-order kinetics which are only slightly dependent on the nature of the substituents. Azidoformate decomposition, too, is unimolecular.[16] First-order kinetics provide good evidence for the intermediacy of free nitrenes.

3. Ultraviolet Spectroscopy

Reiser *et al.*[17] irradiated 2-azidobiphenyl in an inert matrix at 77°K. They recorded the ultraviolet spectrum of the intermediate nitrene which is stable at that temperature and which must be activated before cyclization to carbazole can occur.

ELECTRONIC CHARACTER OF NITRENES

Nitrenes, like carbenes, are electron-deficient. In each case the reactive atom has associated with it only six electrons in the valence shell and therefore formally resembles 'borane' (BH_3), a carbonium ion ($R_3\overset{+}{C}$), oxygen and sulphur atoms and the bromonium ion (Br^+).

Both carbon and nitrogen atoms have four low-energy orbitals available for bonding. In a carbene four electrons are associated with bonding orbitals, leaving two orbitals for occupation by two electrons. If these non-bonding orbitals are degenerate, each will by singly occupied by electrons of parallel spin ('triplet-state' carbene - Fig. 1.1.1 a). If, however, these orbitals differ in energy, occupation of the lower-energy orbital by paired electrons may be energetically favoured (Fig. 1.1.1 b). 'Spin-pairing' will be preferred if the electron-pairing energy (E_{pairing}) is less than $\Delta E_{\text{orbital}}$.

On the other hand, a nitrene nitrogen possesses only two electrons localized in a σ bond. Three non-bonding orbitals are available for occupation by four electrons. The possible electronic states are shown in Fig. 1.1.2 a and b.

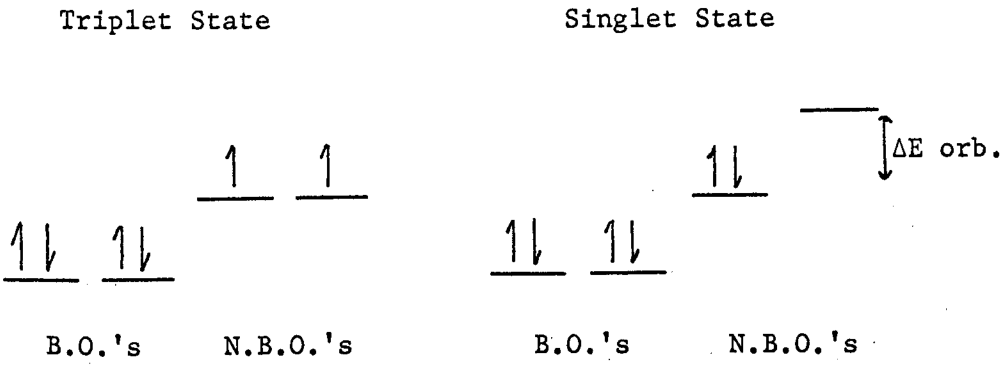


Fig. 1.1.1

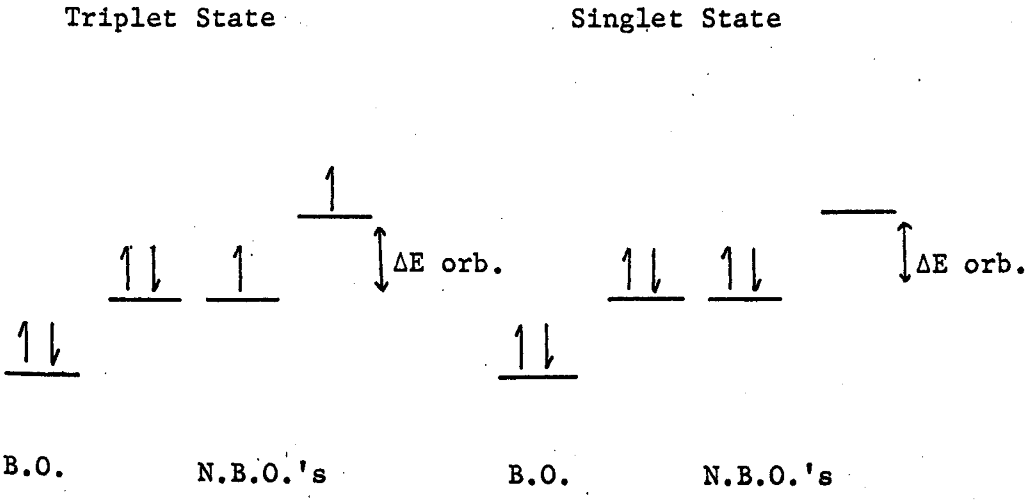


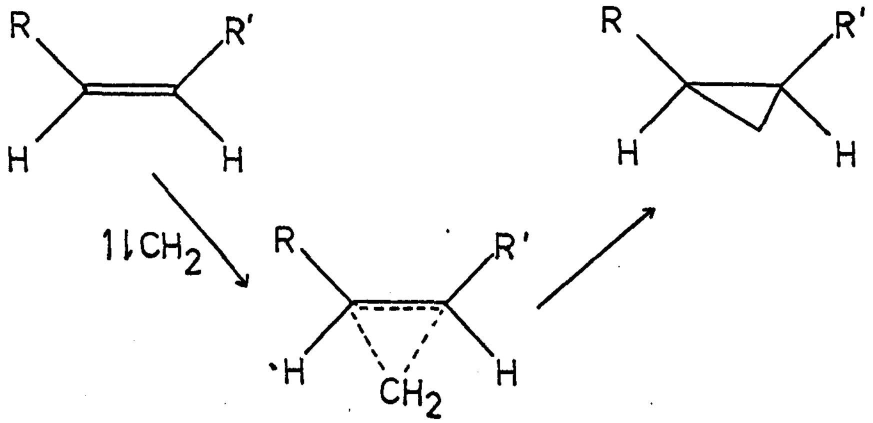
Fig. 1.1.2

As before, the singlet state has lower energy if $E_{\text{pairing}} < \Delta E_{\text{orbital}}$.

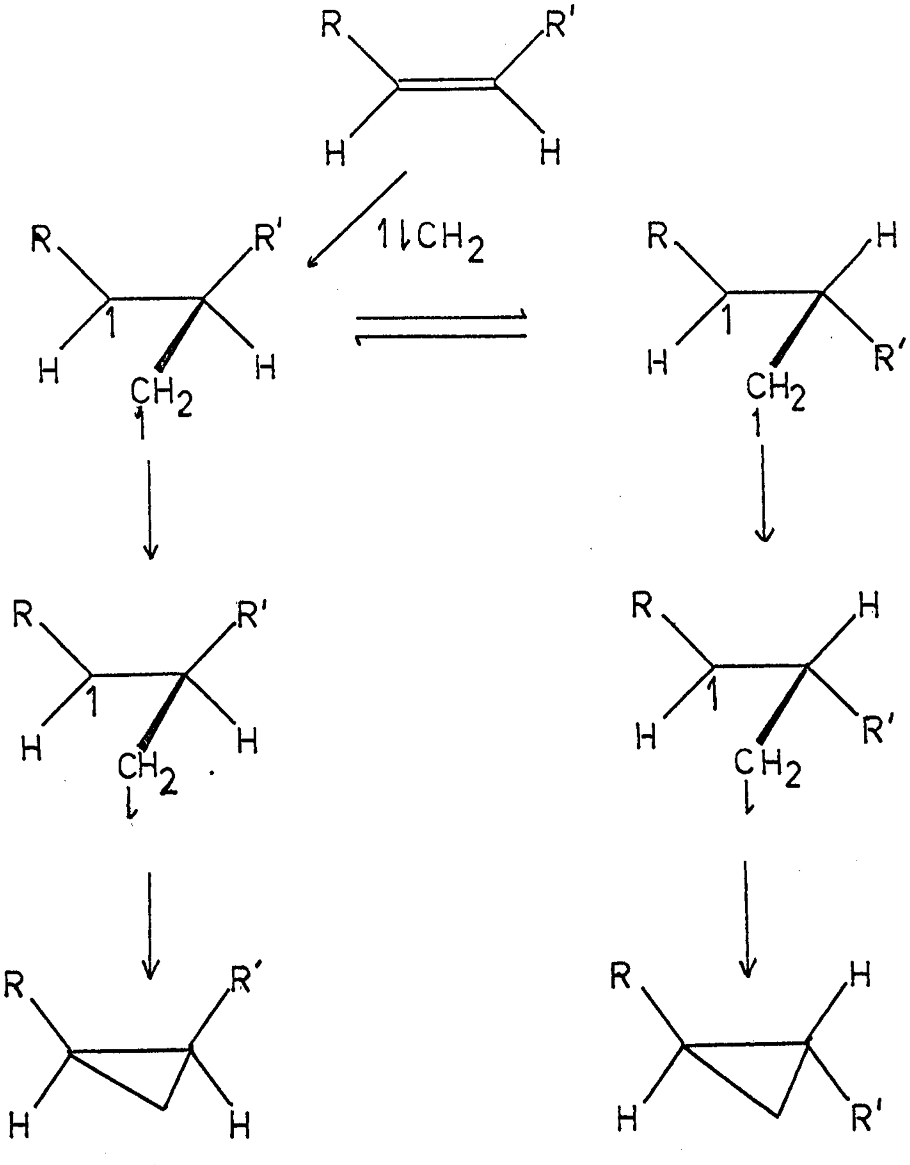
INFLUENCE OF ELECTRONIC CHARACTER ON REACTIVITY

The study of nitrenes is quite recent and because of their formal similarity to carbenes, most of their chemistry has been rationalized in terms of concepts which have become accepted in the carbene field. The two concepts of greatest practical importance are due to Skell:[18,19]

(a) A singlet species adds to a double bond in one concerted process. Configurational relationships in the starting olefin are therefore retained in the product (Scheme 1.1.I).



On the other hand, a triplet carbene or nitrene is believed to add in two steps: a triplet 1,3-diradical is first formed and it is necessary for spin inversion to occur before ring closure can give the stable (singlet) product. Skell has maintained that

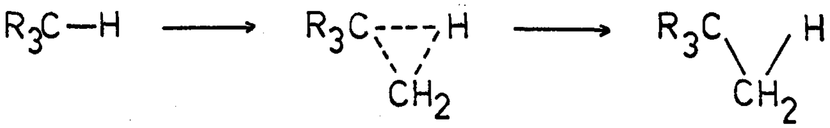

R
R'
H
H
$1\downarrow CH_2$
R
R'
H
1
CH_2
H
1
R
H
H
1
R'
CH_2
1
R
R'
H
1
H
CH_2
R
H
H
1
R'
CH_2
R
R'
H
H
R
H
H
R'

Scheme 1.1.II

rotation about a carbon-carbon single bond should be faster than spin inversion and that therefore the configurational integrity of the olefin should be lost (Scheme 1.1.II).

Although Skell's arguments were based largely on intuition and although his approach has been severely questioned by DeMore and Benson,[20] the above schemes seem to be generally accepted.

(b) A singlet carbene (or nitrene) inserts* into C-H bonds by a single-step process (Scheme 1.1.III).



Scheme 1.1.III

Although Hammond[21] has reported that triplet methylene cannot insert into C-H bonds, a more recent study has shown that the process does occur.[22] Moreover, cyanonitrene, in both singlet and triplet states, inserts into 1,2-dimethylcyclohexane.[24]

It is assumed that insertion into C-H bonds by a triplet nitrene involves initial hydrogen-atom abstraction to form a pair

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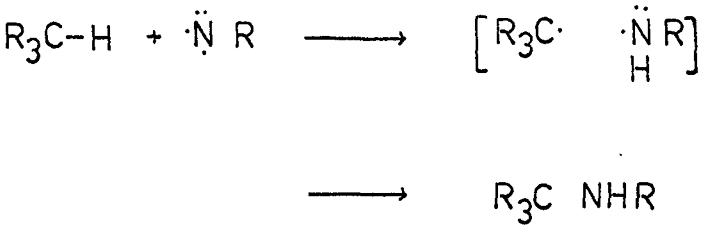
* In this thesis 'insertion' refers to the result of an overall process and carries no mechanistic implications.

of radicals which can then link to form the product[24] (Scheme 1.1.IV).



$$R_3C{-}H + \cdot\ddot{N}R \longrightarrow [R_3C\cdot \quad \cdot\overset{}{\underset{H}{N}}R] \longrightarrow R_3C\,NHR$$

Scheme 1.1.IV

If the intermediate alkyl radical enjoys a sufficient life-time, it can undergo configurational inversion so that any asymmetry, if present in the substrate, may be lost. 'One-step' insertion of a singlet nitrene would achieve 100% retention of configuration.

ELECTRONIC STATES OF NITRENES UNDER REACTION CONDITIONS

Every method of nitrene formation involves detachment of a low-energy 'side fragment' (N_2, $ArSO_3^-$ or Et_3PO_4) from a precursor, P. If the precursor has a singlet electronic configuration, spin conservation requires that fission give two singlet or two triplet fragments (Scheme 1.1.V).

(*a*) $^1P \longrightarrow {}^1$(nitrene) + ^{1}(side fragment)

(*b*) $^1P \longrightarrow {}^3$(nitrene) + ^{3}(side fragment)

Scheme 1.1.V

If the nitrene has lower energy in the singlet state, there is no ambiguity and mode (*a*) will apply; but if the triplet nitrene is more stable, mode (*b*) must be considered. Because the energy separation between ^{1}(side fragment) and ^{3}(side fragment) is likely to be greater than that between ^{1}(nitrene) and ^{3}(nitrene),[24] mode (*a*) will still apply. The metastable singlet nitrene so formed may react as such or convert to the ground state before reacting. It follows, then, that variation of experimental conditions may favour reaction of one or other nitrene form with a substrate and that examination of the products, in the light of Skell's proposals, might allow evaluation of the proportions of these two forms present. (The factors of importance for the process of intersystem crossing between electronic states of different multiplicity will be discussed later.)

If, on the other hand, a nitrene is produced by fission of a triplet-state precursor, one singlet and one triplet fragment will result (Scheme 1.1.VI).

$$(c) \quad {}^3P \longrightarrow {}^3(\text{nitrene}) + {}^1(\text{side fragment})$$

$$(d) \quad {}^3P \longrightarrow {}^1(\text{nitrene}) + {}^3(\text{side fragment})$$

Scheme 1.1.VI

Such decomposition of a triplet species may be achieved by photosensitized photolysis of an azide, giving nitrogen as a side fragment. The formation of triplet nitrogen is highly improbable on energetic grounds[24] and therefore mode (*c*) should apply.

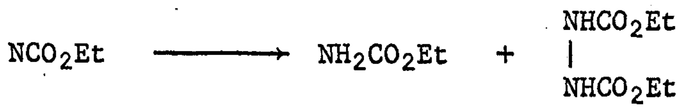
GENERAL REACTION TYPES

Several reaction courses are generally available to nitrenes. These will now be considered with emphasis on the likely electronic configurations of the reacting species.

1. Reactions with Carbon-Hydrogen Bonds

A. *Hydrogen-Atom Abstraction.*

There is no *a priori** reason why a singlet nitrene cannot abstract hydrogen atoms from a substrate.[16] Evidence is accumulating, however, that such behaviour is characteristic of triplet species.[10,16] Some ethyl carbamate (5) and diethyl hydrazinodiformate (6) are produced when carbethoxynitrene (4) reacts with 4-methylpentene-2[10] and cyclic ethers.[25] At low substrate concentrations, the amounts of these products are markedly increased, suggesting their formation from the triplet nitrene (see page 103).



$$\dot{N}CO_2Et \longrightarrow NH_2CO_2Et + \begin{array}{c} NHCO_2Et \\ | \\ NHCO_2Et \end{array}$$

(4) (5) (6)

The general process is, then,

$$R-\dot{\underset{\cdot}{N}}: + H-R' \longrightarrow R-\underset{\cdot}{\ddot{N}}-H + R'\cdot$$

Because spin conservation is observed in this reaction, the triplet nitrene gives rise to a 'triplet pair' of radicals which repel one another rather than couple to form an insertion product.* The amino radical so formed may abstract a further hydrogen atom to give an amino compound, e.g.

$$PhN_3 \xrightarrow[\text{decalin}]{\Delta} PhNH_2 \qquad \text{(ref. 13)}$$

(7) (79%)

$$NH_2CON_3 \xrightarrow[Pr^iOH]{h\nu} NH_2CONH_2 \qquad \text{(ref. 26)}$$

(8) (80%)

Dimerization of the initial amino radical may occur, e.g.

$$ArSO_2ONHCO_2Et \xrightarrow{NEt_3} \begin{array}{c} NHCO_2Et \\ | \\ NHCO_2Et \end{array} \qquad \text{(ref. 10)}$$

(9)

(up to 42%)

(6)

Finally the amino radical may encounter an alkyl radical, with which it forms a 'singlet pair', and link with it to form an insertion product.

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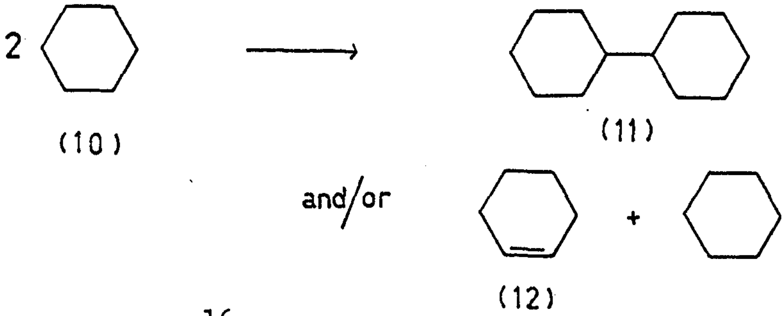
* See detailed discussion on p. 105.

It would be expected that the alkyl radicals which fail to couple in this way would either couple with one another or disproportionate. If, therefore, a triplet nitrene is generated in a medium containing cyclohexane, the cyclohexyl radicals (10) produced should give bicyclohexyl (11) and/or cyclohexene (12).



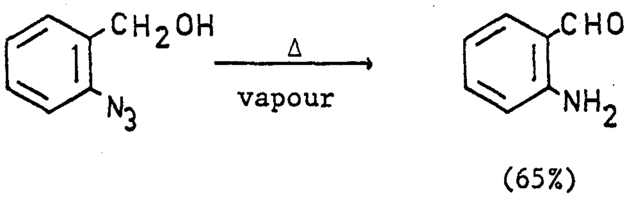
Breslow *et al.*[16] have reported that thermolysis of *n*-octadecyl azidoformate in cyclohexane gives rise to cyclohexene but *no* bicyclohexyl. They suggested that the (triplet) nitrene abstracted two adjacent hydrogen atoms from the *same* cyclohexane molecule, either by a concerted process or by rapid consecutive reactions. If spin conservation is observed and if the radicals of a 'triplet pair' do experience powerful mutual repulsion, it is difficult to understand how either of these processes could occur.

Moreover, Kolbe electrolysis of potassium cyclohexane carboxylate, which gives rise to high local concentrations of cyclohexyl radicals, affords bicyclohexyl in only 14% yield.[27] The efficiency of dimerization is therefore not high and disproportionation must be preferred. This conclusion seems reasonable in the light of present knowledge. Although the behaviour of cyclohexyl radicals has not been described, secondary and tertiary radicals do show a marked tendency to disproportionate.[108]

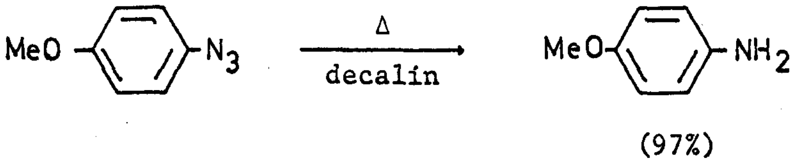
Furthermore, Walker and Waters[13] have observed that decomposition of phenyl azide in cumene produces no α-methylstyrene (by abstraction of adjacent hydrogen atoms), although a 75% yield of aniline resulted.

Many nitrenes efficiently abstract hydrogen atoms from substrates, e.g.

$$\mathrm{N_3CO_2Et} \xrightarrow[\mathrm{EtOH}]{h\nu} \underset{(90\%)}{\mathrm{NH_2CO_2Et}} + \underset{(80\%)}{\mathrm{CH_3CHO}}$$ (ref. 28)



(ref. 29)



(ref. 30)

If hydrogen atom abstraction is achieved by a nitrene generated from a singlet precursor, this can be taken as good evidence of a triplet ground state for the species. In this way, alkoxycarbonylnitrenes,[16,28,31] benzoylnitrene[28,32] and arylnitrenes[13,14] are shown to be ground-state triplets. Failure, however, to isolate products of hydrogen-atom abstraction does not disprove that the ground state has a triplet configuration, e.g. *p*-toluenesulphonylnitrene, which gives rise to an e.s.r. signal, effects little or no hydrogen-atom abstraction from cumene[33] or cyclohexane;[34] nor do other sulphonylnitrenes.[33,34] Reaction of these nitrenes in the singlet state must therefore be more rapid than intersystem crossing to the triplet configuration.

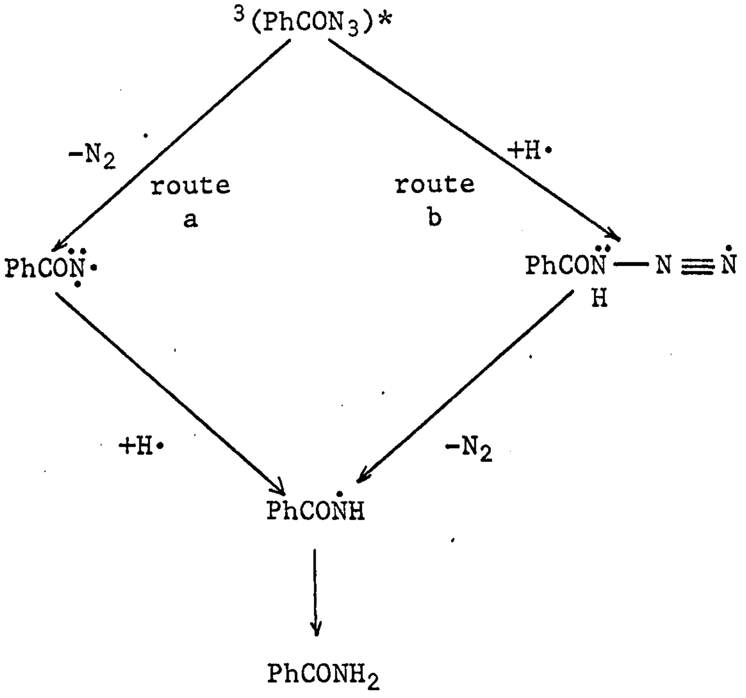
On the other hand, before concluding on the basis of this criterion that a triplet nitrene is present in a system, one must be careful to exclude the possibility of hydrogen-atom abstraction by other species possessing radical character. For instance, benzophenone-sensitized photolysis of benzoyl azide (13) in propanol-2 gives quantitative yields of benzamide (14) and acetone[32] (Scheme 1.1.VII). The triplet azide *may* decompose to the triplet nitrene (route a) or it may first abstract a hydrogen atom from the solvent before splitting off nitrogen (route b). In fact, evidence is available that triplet ethyl azidoformate does *not* decompose to triplet carbethoxynitrene.[11]

$${}^{1}(Ph_2CO) \xrightarrow{h\nu} {}^{1}(Ph_2CO)^*$$

$${}^{1}(Ph_2CO)^* \xrightarrow[\text{crossing}]{\text{intersystem}} {}^{3}(Ph_2CO)^*$$

$${}^{3}(Ph_2CO)^* + {}^{1}(PhCON_3) \longrightarrow {}^{1}(Ph_2CO) + {}^{3}(PhCON_3)^*$$

(13)



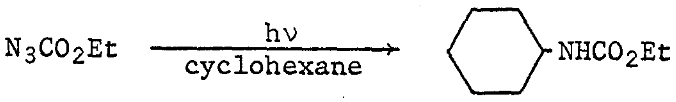
(14)

Scheme 1.1.VII

B. *Insertion into Carbon-Hydrogen Bonds.*

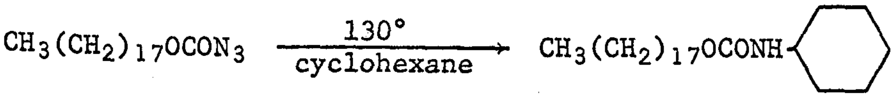
The possible coupling of complementary radicals formed by hydrogen-atom abstraction has already been considered. This behaviour has been observed for triplet cyanonitrene (see below). One-step insertion of singlet nitrenes undoubtedly also occurs.[24,40]

The first example of intermolecular bond insertion by a nitrene was provided by Lwowski and Mattingly;[35]



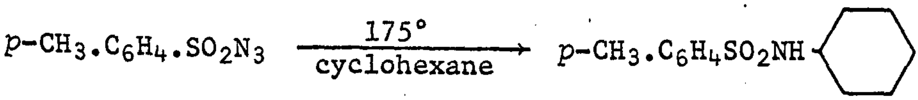
(*ca.* 50%)

More recently, *n*-octadecyloxycarbonylnitrene,[16] alkyl- and arylsulphonylnitrenes[33,34] and phenylnitrene[36] have been shown to possess this property, e.g.



(ref. 16)

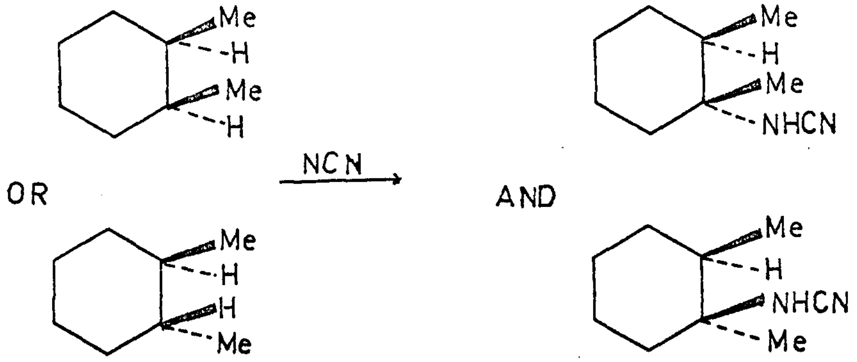
(60%)



(ref. 34)

(*ca.* 60%)

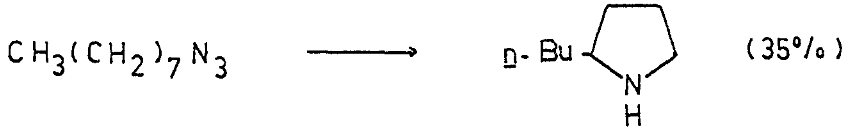
The particularly elegant work of Anastassiou and Simmons[23,24] merits detailed consideration. They studied the insertion of cyanonitrene into the tertiary C-H bonds of *cis*- and *trans*-1,2-dimethylcyclohexane (15 and 16). When neat substrates were employed, almost complete retention of configuration was noted; but when increasing amounts of relatively inert diluents were added, appreciable proportions of 'wrong' products were obtained, in which configurational inversion had taken place at the reacting carbon (Scheme 1.1.VIII).



In the neat substrates, almost all the initially-formed singlet cyanonitrene underwent one-step insertion; but dilution of the substrates allowed sufficient time for intersystem crossing to take place to the triplet ground state. The triplet form inserted by a two-step process and, because configurational inversion could occur in the intermediate *tert*-alkyl radical, the process was no longer stereospecific. An external 'heavy-atom' effect was noted: methylene bromide more efficiently promoted intersystem crossing in cyanonitrene than did methylene chloride.[24]

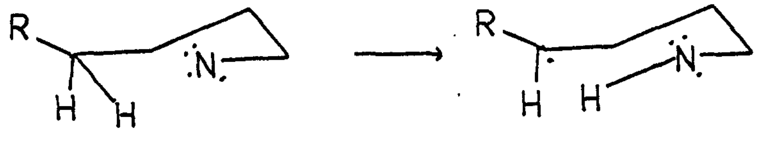
C. *Cyclization.*

Barton and Morgan[37] first reported cyclization of nitrenes in 1962. In studies successfully directed towards synthesis of the alkaloid conessine, they found that thermolysis of *n*-alkyl azides gave pyrrolidines in modest yields, e.g.



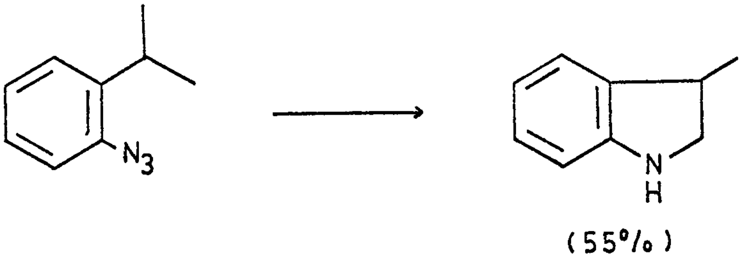
It has been observed more recently, however, that such reactions are highly irreproducible.[38] Primary amines and aldimines, instead, were the main products.

The cyclization process was interpreted in terms of abstraction of a δ-hydrogen atom by the (triplet) nitrene, followed by cyclic linking of the resultant diradical.[37] By analogy to the well-known Hofmann-Freytag-Löffler and Barton reactions, the 'rule of six' was applied to explain why only pyrrolidines, and no piperidines, were formed. The most favourable transition state for hydrogen-atom transfer was considered to be that of a six-membered ring in the chair form,[39] i.e.



Because a triplet nitrene would give rise to a 'triplet radical pair', the radicals would repel one another. Therefore, once spin inversion has occurred, the molecule would *once again* take up a fairly closely-defined conformation before cyclization. This doubly-demanding entropy requirement may explain why the overall process occurs with low efficiency.

Cyclizations of aryl- and acylnitrenes are more satisfactory, e.g.



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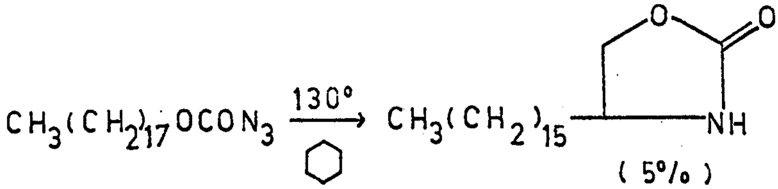
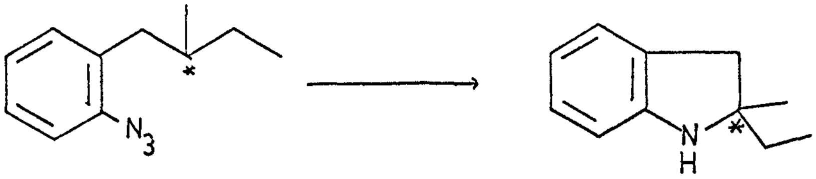


(ref. 16)

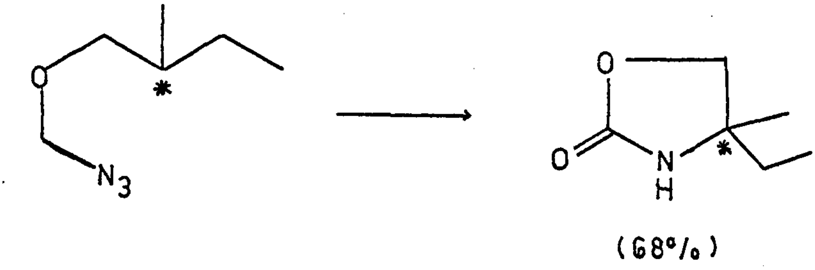
Arylnitrenes have triplet ground states.[7] When the singlet species are generated in hydrocarbon media, amines are produced by hydrogen-atom abstraction while insertion into the C-H bonds of the solvent is not important.[13,14,36] It appears, then, that collision-promoted intersystem crossing is much more rapid than reactions of the singlet species. In the vapour phase, however, the lifetime of the singlet state may be sufficient to allow (one-step) cyclization before intersystem crossing can take place. Smolinsky and Feuer[40] have convincingly shown that such cyclization of a *singlet* arylnitrene can occur:



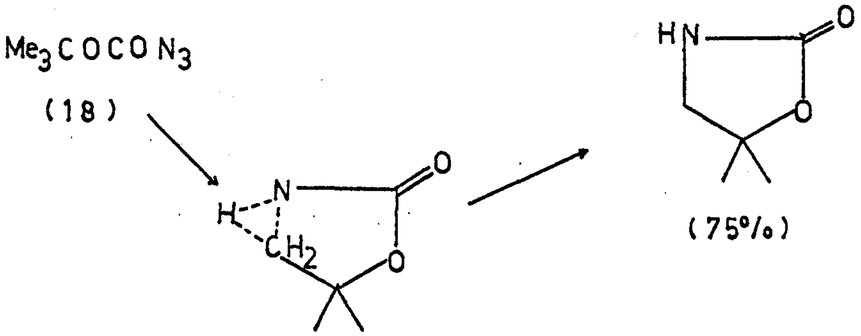
(17)

The nitrene from the azide 17 inserted at the asymmetric centre to give a product of 65% optical purity.[5,40] It is likely, therefore, that much of the product resulted from one-step cyclization of the singlet arylnitrene.

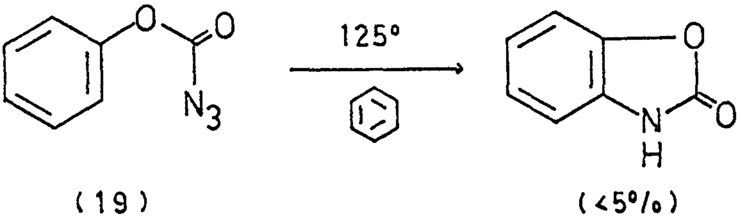
Azidoformates decompose to singlet nitrenes which undergo only slow intersystem crossing to the triplet state.[10,11] It is not surprising, therefore, that cyclization can occur in good yield and with essentially complete stereospecificity,[40,41] i.e.



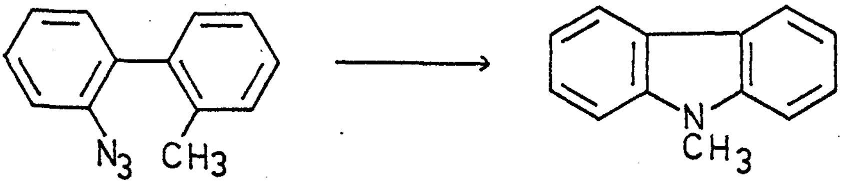
Photolysis of *tert.*-butyl azidoformate (18) in various solvents affords good yields of 5,5-dimethyloxazolidone-2:[28,42]



The lifetime of the metastable singlet nitrene is expected to be long enough for one-step cyclization to occur. Similarly, the nitrene obtained from phenylazidoformate (19) cyclizes into the aromatic ring, but in low yield:[43]

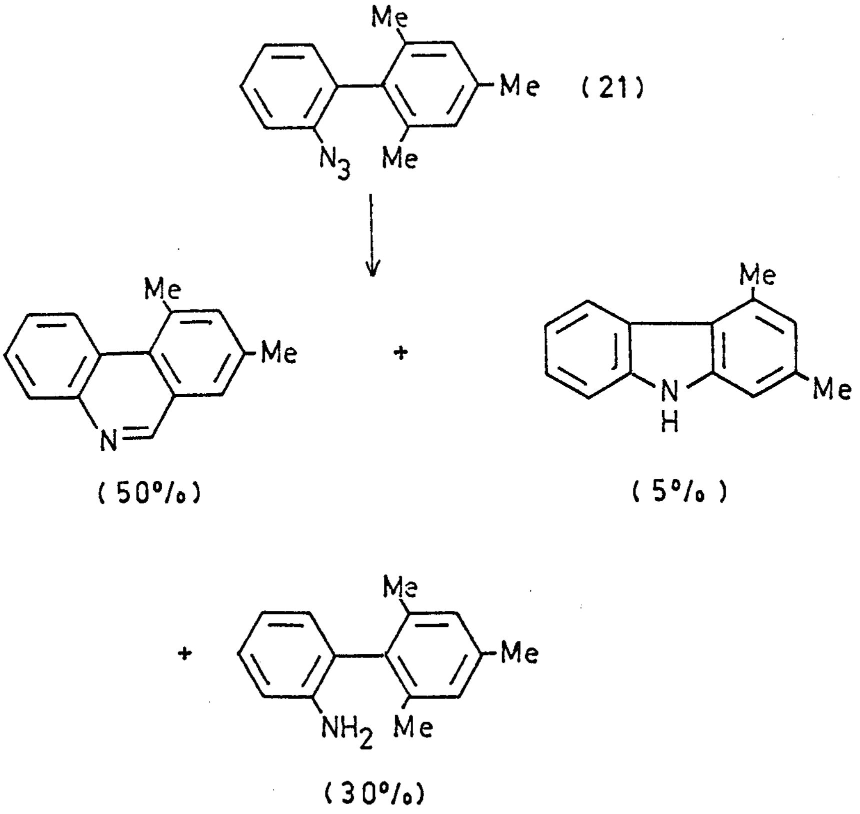


The behaviour of biphenyl-2-nitrenes is hard to rationalize: 2-azido-2'-methylbiphenyl (20), when decomposed in diphenyl ether at 248-250°, affords *N*-methylcarbazole in 91% yield:

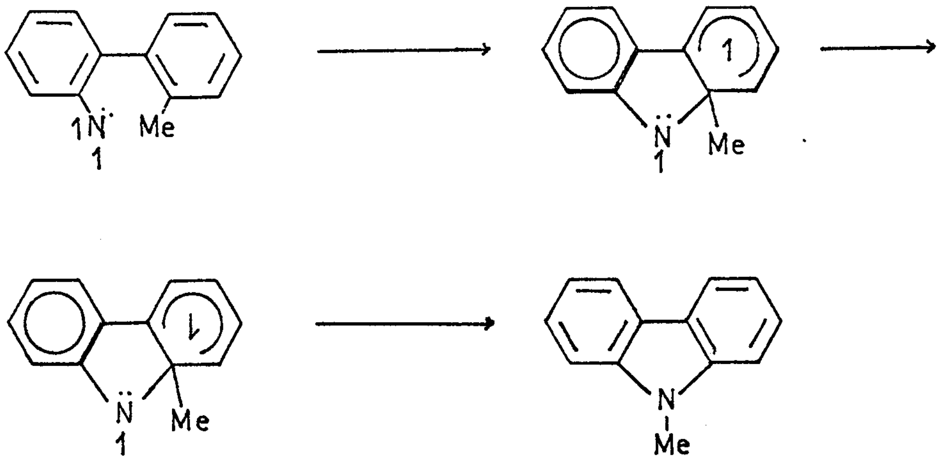


(20)

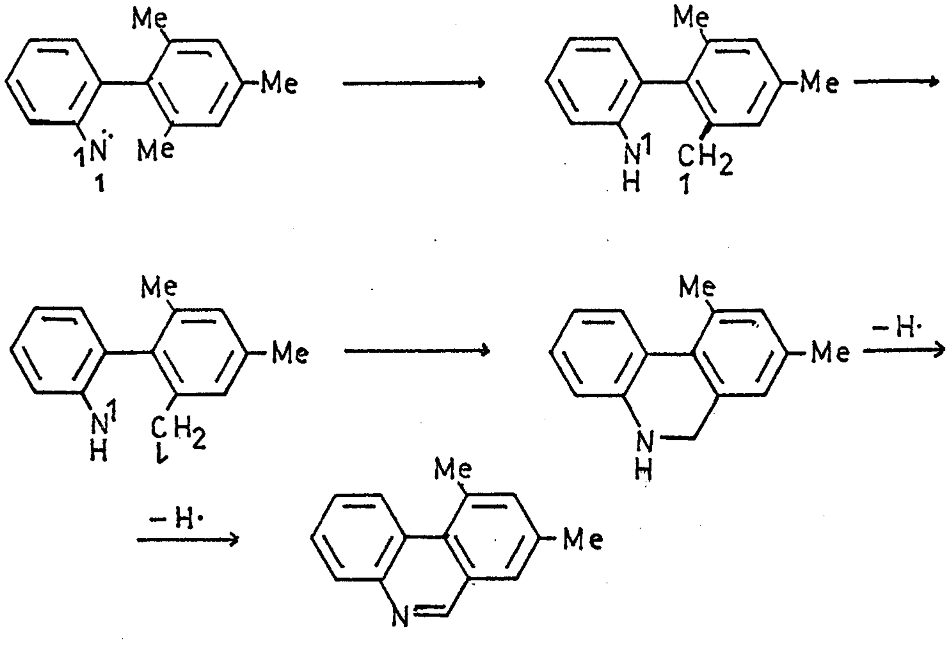
On the other hand, the corresponding trimethylaryl azide 21 is converted mainly to the phenanthridine:



The carbazoles probably result from 'radical' attack of the nitrene on the aromatic system, followed by a 1,2-shift of a methyl group (Scheme 1.1.IX). The phenanthridine is certainly formed *via* the dihydro-compound 22 (Scheme 1.1.X).



Scheme 1.1.IX



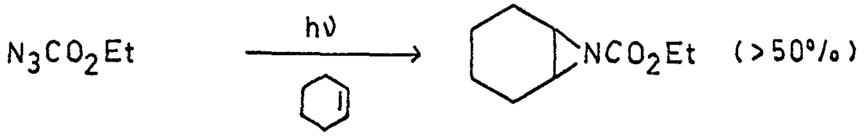
Scheme 1.1.X

The true intermediacy of nitrenes in such cyclizations has been brilliantly illustrated by Reiser, Wagner and Bowes[17] (see p. 4).

2. Reactions with Multiple Bonds

A. *Addition to Carbon-Carbon Double Bonds.*

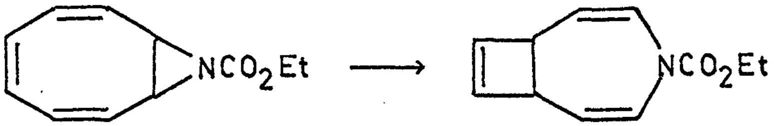
Lwowski and Mattingly were first to report addition of carbethoxynitrene to a double bond:[35,46-48] photolysis of ethyl azidoformate in cyclohexene gave 7-carbethoxy-7-azabicyclo[4,1,0]-heptane (23).



(23)

Addition of carbethoxynitrene to *cis*- and *trans*-butene-2,[50] butadiene[50] and *cis*- and *trans*-4-methylpentene-2[10,11] has also been achieved; but because it is particularly germane to arguments developed in this thesis, detailed discussion will be deferred until later.

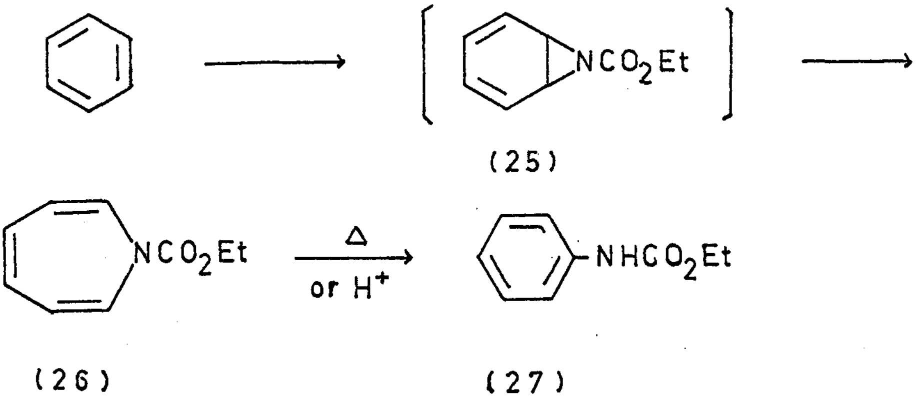
The primary adduct of carbethoxynitrene (24) and cyclooctatetraene rearranges at 50°:[49]



(24)

B. *Reactions with aromatic systems.*

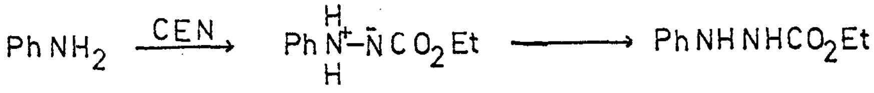
Carbethoxynitrene, produced by thermal[43,51] or photochemical[46,52] decomposition of ethyl azidoformate, or by α-elimination,[48] reacts with benzene to give *N*-carbethoxyazepine (26), perhaps *via* the 7-azanorcaradiene 25.



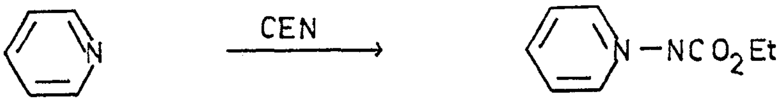
Under the influence of acid, or on heating, this product isomerizes to phenylurethane (27).

Substituted benzenes also react with carbethoxynitrene: toluene,[43,53] xylenes,[53] mesitylene,[53] durene[53] and chlorobenzene[53] are all converted to azepine derivatives. Furthermore, the approximately equal distribution of isomeric products suggests that the reaction is not very susceptible to polar effects.

Anisole, on the other hand, gives only a small yield of (three ?) methoxyazepines with *o*- and *p*-methoxyphenylurethanes (28 and 30) as the main products.[53] It would seem, then, that these products result from nitrene attack at the electron-rich *o*- and *p*-positions of the anisole ring, i.e. that carbethoxynitrene is highly electrophilic. Its reactions with aniline[53] and pyridine[53] are consistent with this view:

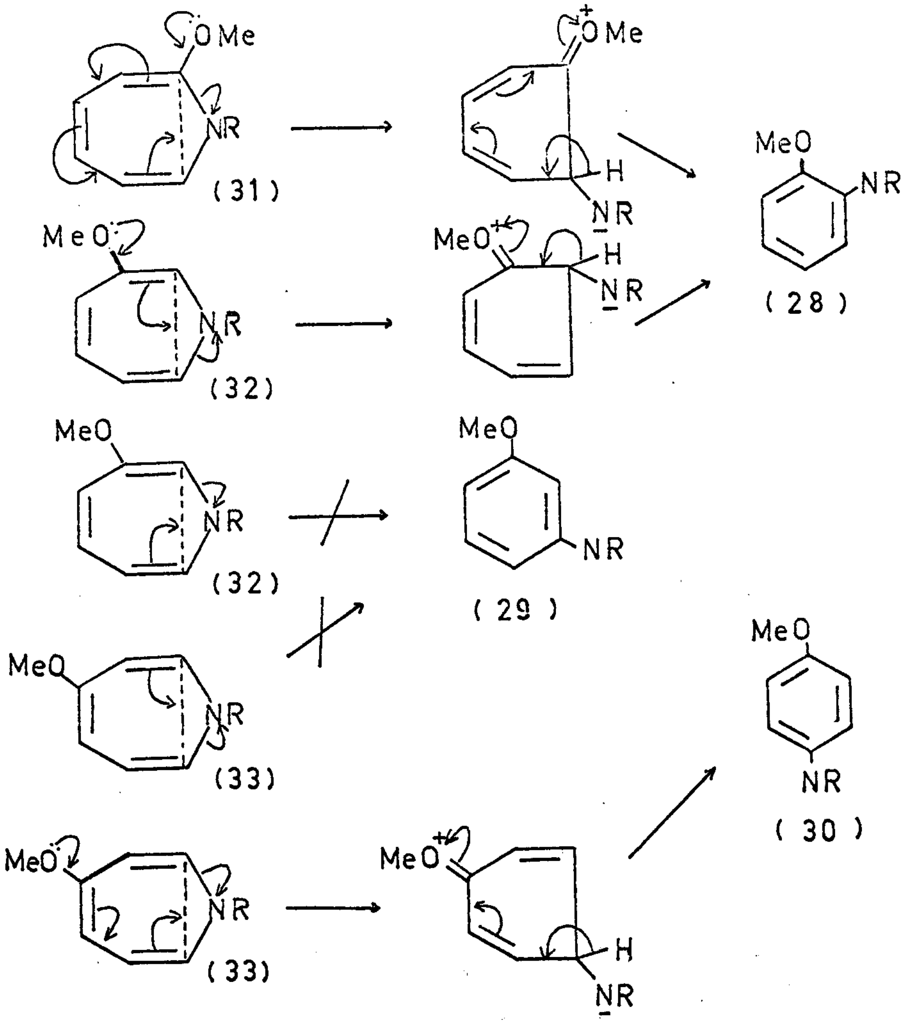


$$PhNH_2 \xrightarrow{CEN} Ph\overset{H}{\underset{H}{N^+}}-\bar{N}CO_2Et \longrightarrow PhNHNHCO_2Et$$



It is possible, however, that 28 and 29 result from rearrangement of approximately equal amounts of the three isomeric *N*-carbethoxymethoxyazepines (31-33) (Scheme 1.1.XI). The methoxyl group can participate in rearrangement of 32 and 33 to 28 and 30 respectively, whereas no assistance can be given to formation of 29. This scheme is consistent with the isomerizations of *N*-cyanoazepines observed by Marsh and Simmons.[54]

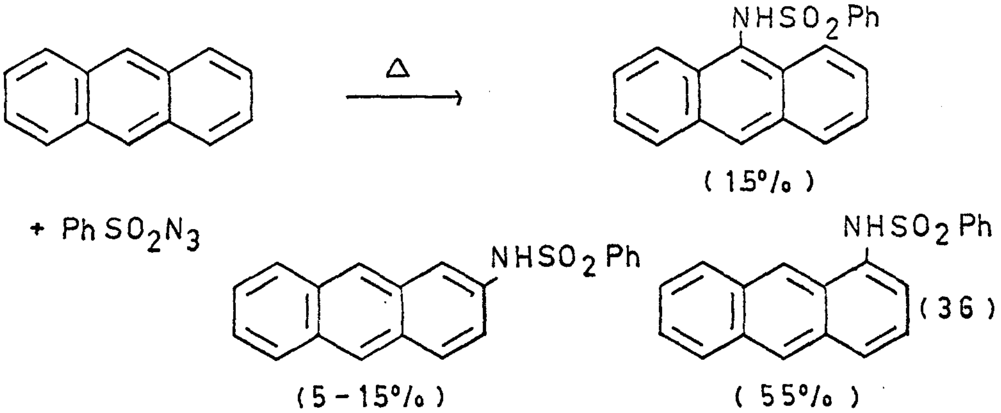
Cyanonitrene also converts benzene derivatives to azepines,[54] i.e.



($R = CO_2Et$)

Scheme 1.1.XI.

Thermolysis of benzenesulphonyl azide in the presence of benzene[33] or anthracene[55] leads to *N*-arylbenzenesulphonamides, e.g.



Tilney-Bassett[55] suggested 'double-bond' attack at the 1,2-bond of anthracene, followed by rearrangement of the primary aziridine adduct, to explain the predominance of 36 in the product mixture.

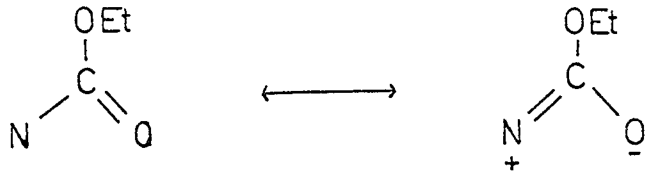
Very recently, Lwowski and Johnson[56] have shown that only *singlet* carbethoxynitrene is able to react with benzene. This electronic requirement may apply also to cyanonitrene and benzenesulphonylnitrene and to alkylnitrenes, which give rise to *N*-alkylanilines in low yield,[37] e.g.

$$n\text{-BuN}_3 \xrightarrow[\text{benzene}]{h\nu} n\text{-BuNHPh}$$

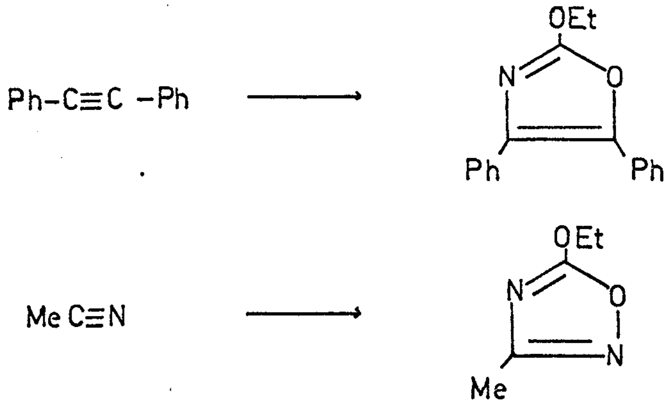
$$(22\%)$$

C. *'Abnormal' Nitrene Addition.*

Singlet carbethoxynitrene is subject to resonance stabilization:



The species therefore exists as a 1,3-dipole and can undergo cycloaddition to alkynes[57] and nitriles,[58] e.g.



Treatment of pyrrole, furan and thiophene with ethyl azidoformate at 130° leads, in all cases, to pyrrole derivatives. Anomalous 1,4-addition of the nitrene has been proposed.[59] Similarly, 1,4-addition of cyanonitrene to cyclooctatetraene has been noted.[108] Whereas the singlet nitrene adds by a concerted process to give a 'normal' adduct, two-step addition of the triplet species leads to some 1,4-adduct.

3. Stabilization by Rearrangement

Decomposition of acyl azides gives rise to acylnitrenes which show a wide variation of abilities to rearrange. Species of types I and II, generated by thermolysis *or* photolysis, readily rearrange to isocyanates: those of types III, IV and V rearrange

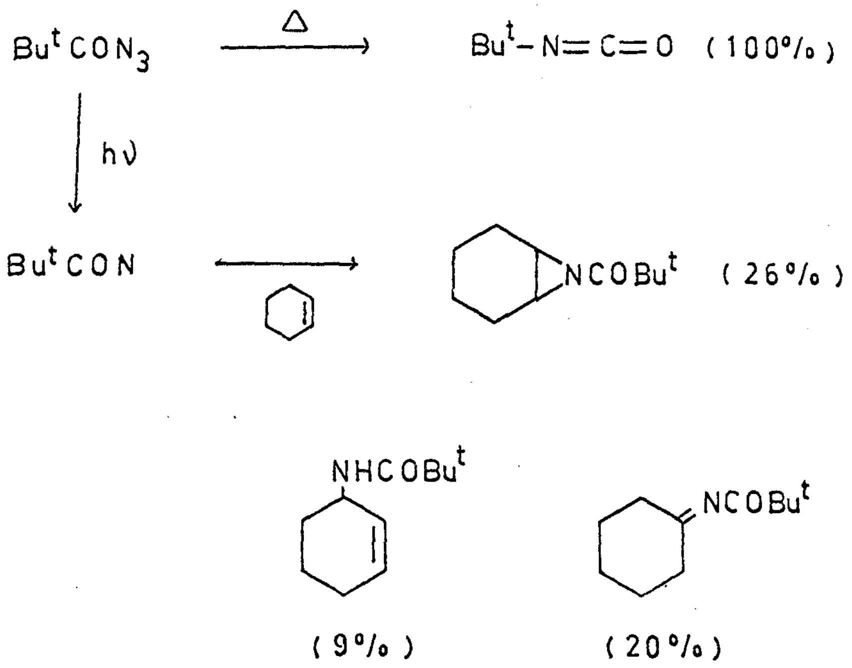
$RCON$	$ArCON$
Type I	Type II

$ROCON$	R_2NCON	$ArSO_2N$
Type III	Type IV	Type V

only when produced by photolysis in a polar medium (methanol). The reason for this difference in properties is not understood; but it seems certain that carbethoxy-,[60] carbamoyl-[60] and benzenesulphonylnitrenes[4] rearrange only when strongly hydrogen-bonded in a protic solvent.

It is not yet possible to assign a particular electronic configuration to the rearranging nitrene. Photosensitized photolysis of an acyl azide *may not* lead to a triplet nitrene; so the quantitative formation of benzamide from benzoyl azide (page 16) must be viewed with reserve. Furthermore, trapping of a singlet nitrene with dimethyl sulphoxide or dimethyl sulphide (page 36) indicates *only* that the singlet species is present at some stage of the reaction sequence.

Pivaloyl azide (37) provides an interesting intermediate example:[61] thermal decomposition affords *tert.*-butyl isocyanate in quantitative yield, while photolysis in hydrocarbons gives a nitrene capable of intermolecular reactions. Lwowski and Tisue[61] concluded that thermolysis of 37 must cause rearrangement concerted with nitrogen elimination, whereas photolysis produces a true nitrene intermediate.



The main course followed by an alkylnitrene involves a 1,2-hydrogen shift with formation of an imine,[37,38] e.g.

$$CH_3CH_2CH_2CH_2N_3 \xrightarrow{h\nu} CH_3CH_2CH_2CH{=}NH$$

70%

Again, the electronic state of the rearranging nitrene is not known.

Decomposition of triarylmethyl azides (38) leads to benzophenone anils:

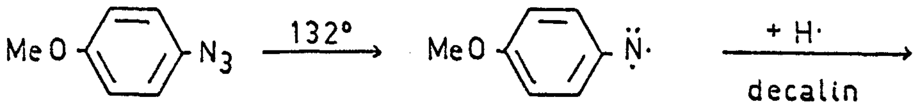
$$\underset{(38)}{Ar_3CN_3} \longrightarrow Ar_2C{=}NAr$$

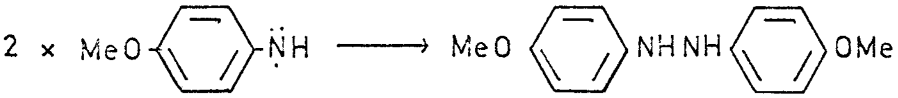
When the process is thermally-induced, nitrogen elimination and rearrangement are concerted;[64] but photolysis (direct[63] and sensitized[62]) leads to free nitrenes. Regardless of its electronic character, introduction of a substituent into one of the aryl groups increases its migratory aptitude, suggesting that the nitrene rearranges when in the triplet (diradical) state.

4. Dimerization

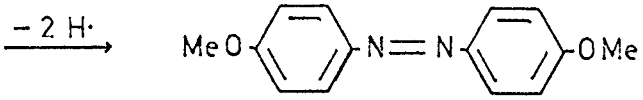
An obvious course for stabilization of a nitrene is dimerization to form an azo compound; and indeed azo compounds *are* formed on decomposition of azides. Formation of these dimers, however, *need* not involve true nitrene dimerization.

Walker and Waters[13] have suggested that 4,4'-dimethoxyazobenzene (39) is formed *via* the hydrazo compound (38):



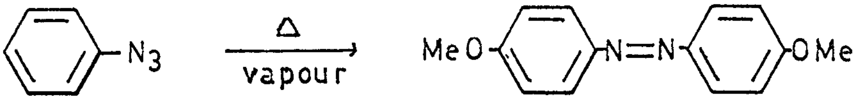


(38)

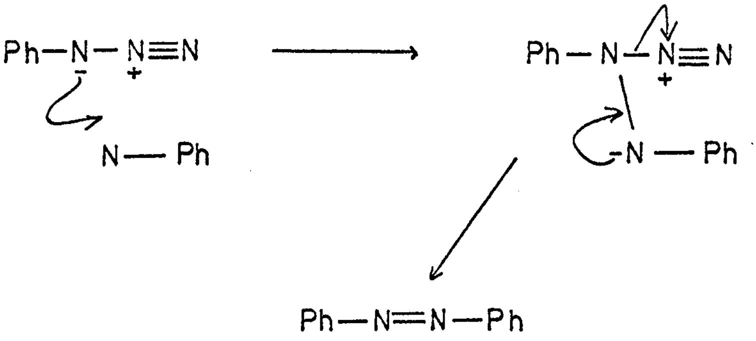


(39)

On the other hand, Smolinsky has prepared azo compounds in high yield by vapour-phase thermolysis of aryl azides[29] (i.e. where no hydrogen atoms are available for abstraction), e.g.



It still cannot be concluded, however, that true dimerization of arylnitrenes has occurred. Attack of a nitrene on an intact azide molecule is possible, e.g.



In fact, such a mechanism has been proposed for the formation of azodicarbonitrile (41) from cyanogen azide[65] (40):

$$\mathrm{NCN} + \mathrm{N_3CN} \xrightarrow[\text{vapour}]{200^\circ} \mathrm{NCN{=}NCN} \qquad (54\%)$$

(40) (41)

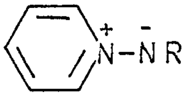
Furthermore, diethyl azodiformate which is produced on photolysis of ethyl azidoformate is not formed by dimerization of carbethoxynitrene.[66,67]

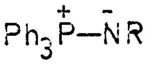
Whatever the precise mechanism involved, the efficiency of formation of azo compounds by solution photolysis of aryl halides varies greatly with the solvent, e.g. *p*-methoxyphenyl azide gave the azo compound in only 18% yield in benzene, whereas use of dimethyl sulphide as solvent raised the yield to 91%.[68]

5. Ylide Formation

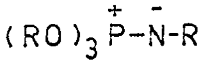
Because a nitrene is electron-deficient, it is able to form a dative-covalent bond with an atom bearing a lone pair. In this way, nitrogen,[53,69] phosphorus[31,65,70] and sulphur[71] ylides, of general formulae 40-44, have been prepared.

These adducts are probably formed from singlet nitrenes, as they require donation of an electron pair into an empty nitrene orbital. Arylnitrenes, therefore, which are either generated in the triplet state or rapidly cross over to this state (high hydrogen-atom abstraction rate; low bond insertion probability),

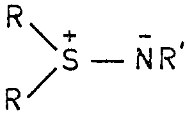

(40)

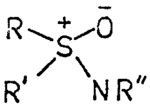

(41)

$Ph_3\overset{+}{P}-\overset{-}{N}R$


(42)

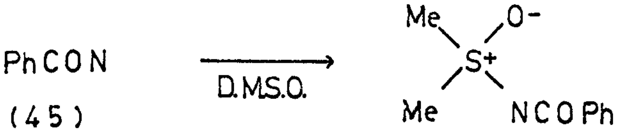
$(RO)_3\overset{+}{P}-\overset{-}{N}-R$


(43)

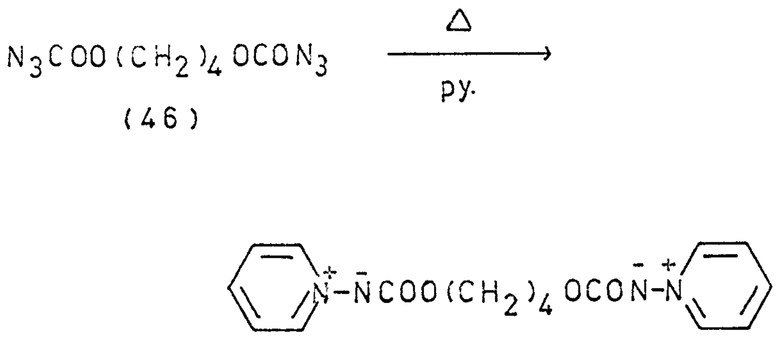

(44)

do not form ylides. In fact, dimethyl sulphide is the best solvent for preparation of azobenzene from phenyl azide.[68]

On the other hand, Horner and Christmann[71] were able to trap benzoylnitrene (45) before rearrangement to phenyl isocyanate.



However, formation of an ylide does not necessarily *prove* the presence of a nitrene. The reaction conditions are important: thermolytic conditions are necessary to decompose tetramethylene 1,4-diazidoformate (46) in pyridine.[31] A nitrene intermediate is therefore involved in the formation of the betaine 47. Ethyl azidoformate, on the other hand, reacts with triphenyl phosphine (48) at room temperature without the intermediacy of a nitrene.



(46)

(47)

$$N_3CO_2Et \quad + \quad Ph_3P \quad \longrightarrow \quad Ph_3P{=}NCO_2Et$$

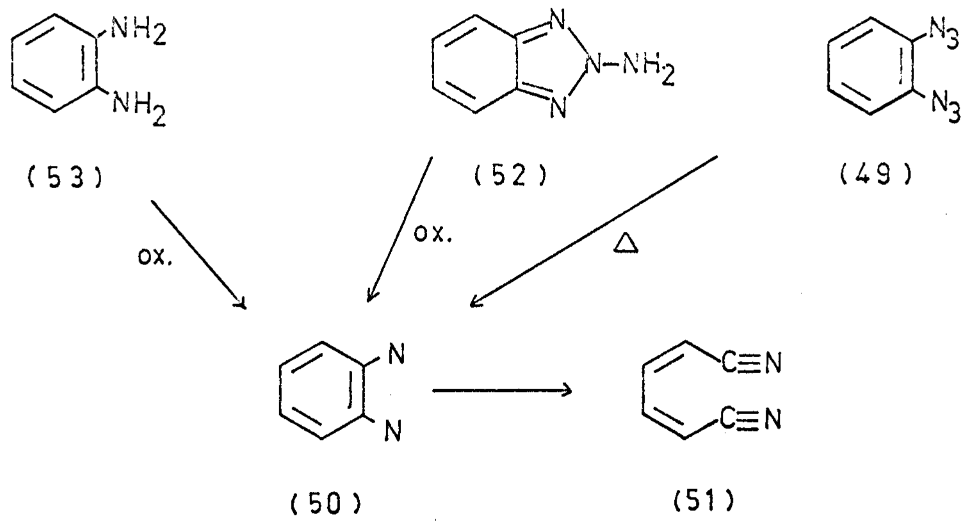
(48)

Similar spontaneous reactions of benzoyl azide[70] and cyanogen azide[65] with phosphorus compounds are known.

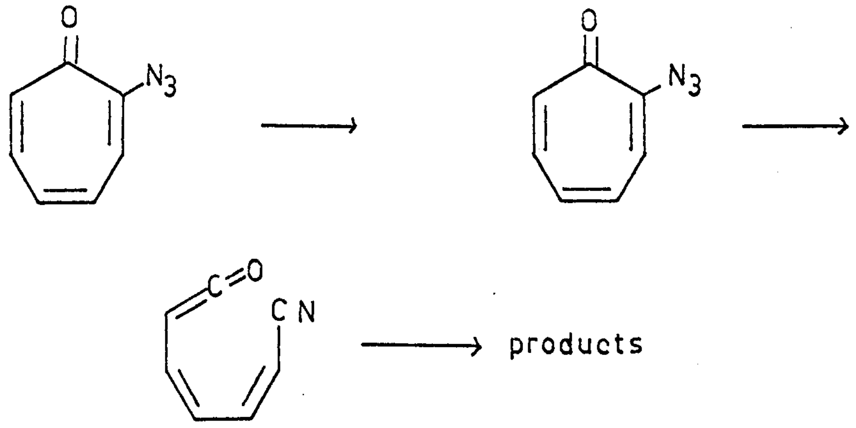
6. α,β-Bond Fission

A more-recently recognized class of nitrene reactions involves fission of a carbon-carbon bond α,β to the nitrene centre. In this way, even an aromatic system can be ruptured.

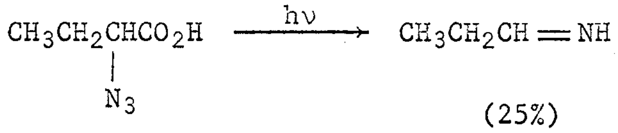
Thermolysis of *o*-diazidobenzene (49) gives rise to the dinitrene 50 which isomerizes to *cis*,*cis*-mucononitrile[72] (51). The same product is available by oxidation of 2-aminobenzotriazole (52)[73] and *o*-phenylenediamine (53).[74]



Decomposition of 2-azidotropone involves similar ring fission:[107]

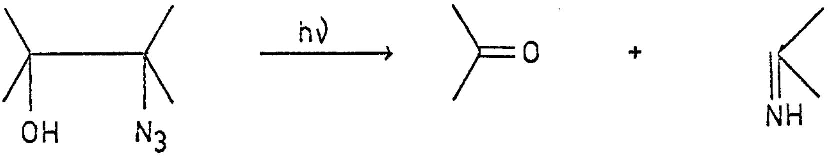


Photolysis of α-azidoacids causes decarboxylation. Low yields of imines result,[38,75] e.g.



$$CH_3CH_2\underset{\underset{N_3}{|}}{C}HCO_2H \xrightarrow{h\nu} \underset{(25\%)}{CH_3CH_2CH{=}NH}$$

α,β-Bond fission has also been achieved by photolysis of a steroidal β-hydroxyazide,[76] i.e.



The process proceeds with only low efficiency.

1.2. REACTION OF CARBETHOXYNITRENE WITH POLYCYCLIC AROMATIC HYDROCARBONS

As discussed earlier, carbethoxynitrene is isoelectronic with carbethoxycarbene. Detailed investigation of the reaction of ethyl diazoacetate with anthracene has confirmed that the *main* product is formed by addition of the carbene moiety across the 1,2-bond of the substrate; but the yield is low and minor amounts of other isomeric products are produced (see Chapter 2). Furthermore, the products of reaction of carbethoxynitrene with benzene derivatives have yet to be shown to result from a single type of reaction.[53] The reaction of carbethoxynitrene with polycyclic aromatic hydrocarbons was therefore studied with a view to gaining some understanding of its character as a 'double-bond' reagent *vis-à-vis* an electrophilic species (or perhaps radical species).

Preliminary attempts to photolyse ethyl azidoformate in the presence of anthracene were unsuccessful: the substrate preferentially absorbs all light below 400 mμ. Accordingly, carbethoxynitrene was generated by thermolysis of the ester at 132°.

Ethyl azidoformate was added dropwise to a solution of excess anthracene in boiling chlorobenzene. Removal of the solvent *in vacuo* and chromatography of the residue on neutral alumina afforded a mixture of the three anthrylurethanes. The 9-isomer predominated, together with less 1-isomer and only a trace of 2-anthrylurethane. The actual yields could not be estimated with any accuracy because extensive decomposition of the products occurred during chromatography. Deactivated alumina (Activity II to IV) and silica gel provided inadequate resolution.

Anthracene derivatives show intense ultraviolet absorption ($\varepsilon \geq 10^5$) in the range 250-270 mμ and so lend themselves to estimation by quantitative thin layer chromatography (Q.T.L.C.). Again, alumina caused extensive decomposition and erratic results; but, provided manipulations were carried out under a yellow safe-light, QTLC on silica gel satisfactorily resolved microgram amounts of anthrylmethane mixtures. The yields were*:

1-anthrylurethane:	30%
2-anthrylurethane:	trace
9-anthrylurethane:	47%

* average of triplicate reactions

Reaction of carbethoxynitrene with phenanthrene was carried out without a solvent: the ester was added dropwise to the stirred hydrocarbon at 125-130°. Chromatography of the mixed products on neutral alumina or silica gel produced ineffective separation. Crystallization of selected fractions, however, gave pure samples of 1- and 9-phenanthrylurethanes and of an isomeric compound, identified as 4-phenanthrylurethane on the basis of its elemental analysis, molecular weight and absorption spectra. 4-Aminophenanthrene and 4-phenanthryl isocyanate were prepared by known routes; but it was not possible to convert them to the corresponding urethane (see Section 1.6).

Estimation of the yields of the main products was carried out using the i.r. spectrum of a carbon disulphide solution of the mixed products. By this means, too, formation of the 2- and 3-isomers was excluded. (The principal infrared absorption maxima of anthryl-, phenanthryl- and pyrenylurethanes are shown in Table 1.2.7.) The total yields were:

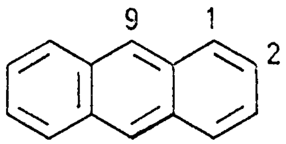
1-phenanthrylurethane:	20%
4-phenanthrylurethane:	1.6% *
9-phenanthrylurethane:	31%

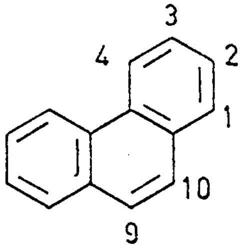
* amount of product isolated after column chromatography.

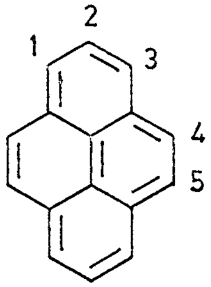
Pyrene, dissolved in boiling chlorobenzene, was treated with ethyl azidoformate. A mixture of 1- and 4-pyrenylurethanes resulted. Although these products were separated by column chromatography followed by fractional crystallization, the yields were more accurately determined using ultraviolet spectroscopy. The yields were:

1-pyrenylurethane:	28%
4-pyrenylurethane:	13%

The absence of characteristic absorption bands in the infrared spectrum of the mixed products confirmed that no 2-isomer was formed in the reaction.







For convenience in discussion, these product distributions are reproduced in Table 1.2.1.

The results clearly indicate that, in reaction with these systems, carbethoxynitrene does not behave as a simple 'double-bond' reagent. Rather, because its order of preference for reactive positions in the substrates closely parallels those shown by the nitronium ion[80,81] and phenyl radical,[78,79,82,83] it would seem that the nitrene possesses electrophilic and/or radical character.

Closer inspection of the *degree* of preference of the nitrene for the most reactive positions is instructive. It is seen that anthracene affords more 1-anthrylurethane than expected. Similarly, phenanthrene and pyrene are more reactive in the 9-

TABLE 1.2.1

THEORETICAL INDICES OF REACTIVITY AND YIELDS OF PRODUCTS FROM REACTIONS OF AROMATIC COMPOUNDS WITH CARBETHOXYNITRENE AND OTHER REAGENTS

Compound	Pos'n	% Yield†			$F_{m.o.}$*	B§
		Urethane	Nitro Compound (80,81)	Phenyl Derivative (78,79,82,83)		
Anthracene	1	38%	-	14%	.459	1.74 (1:2)
	2	∿1%	-	1.6%	.408	1.74 (1:2)
	9	61%	-	84%	.520	1.61 (9:9a)
Phenanthrene	1	38%	25%	31%$^{\phi}$	.450	1.71 (1:2)
	2	nil	7%	8%$^{\phi}$	.402	1.71 (1:2)
	3	nil	23%	8%$^{\phi}$	.408	1.70 (3:4)
	4	∿3%	6%	21%$^{\phi}$	.440	1.70 (3:4)
	9	59%	36%	31%$^{\phi}$	.451	1.77 (9:10)
Pyrene	1	68%	100%	100%	.468	1.67 (1:2)
	2	nil	nil	nil	.393	1.67 (1:2)
	4	32%	nil	nil	.452	1.78 (4:5)

* Free-valence number calculated by the molecular-orbital method.[77]

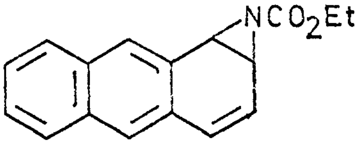
§ Bond order calculated by the molecular orbital method.[77]

† Calculated on the basis of total yield of isomeric urethanes = 100%

ϕ Calculated from previous data.[78,79]

and 4-positions respectively than towards electrophilic and radical reagents. Furthermore, in each case the isomer formed in unexpectedly high yield results from reaction at a position on the bond of highest order.

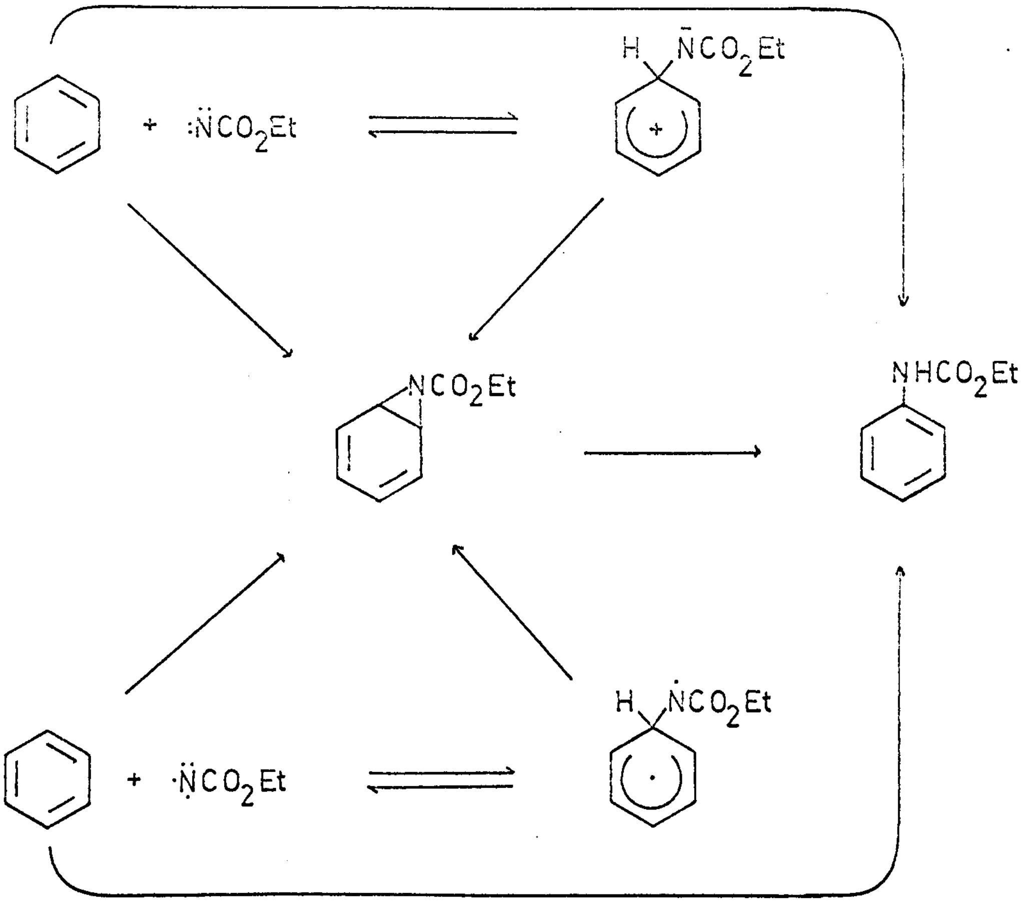
The results suggest that the nitrene species reacts with these substrates in two or more distinct ways: in addition to a process of 'double-bond' attack proceeding *via* a primary aziridine adduct, e.g. (54), direct substitution pathways (electrophilic and radical) may be operating.



(54)

Since the conclusion of this work it has been convincingly argued that carbethoxynitrene is initially generated in the singlet state, but subsequently undergoes intersystem crossing to the triplet form.[10,11,100,106] It is likely that both electronic forms were present during the reactions described above.

The mechanistic routes which may be available to these two species are set out in Scheme 1.2.I. To illustrate the general aromatic substrate, a benzene ring is shown.



Scheme 1.2.I

Three types of pathway are formally available.

(i) Direct insertion into an aromatic C-H bond, leading *directly* to an arylurethane. This reaction is without mechanistic analogy and, in view of other reaction courses available to the nitrene, must be regarded as highly unlikely.

(ii) Direct, one-step, addition to a C-C bond of high order leading to an aziridine which may then rearrange to an arylurethane.

(iii) Electrophilic (or radical) attack on the aromatic π system, proceeding *via* a σ-complex analogous to that involved in electrophilic (or radical) substitution. This intermediate may then rearrange or couple at the *ortho*-position to form the intermediate aziridine.

If either nitrene species is to behave as a true 'double-bond' reagent and react preferentially across bonds of high*est* order, mode (ii) must apply or the first step of (iii) must be readily reversible.

To elucidate which of the above modes do apply, the reaction of the nitrene with anthracene was studied in greater detail: Lwowski *et al.*[10,11,100,106] have shown that, as the concentration of a reactive substrate in an inert medium is decreased, the mean lifetime of the initially generated carbethoxynitrene becomes sufficient to allow intersystem crossing to a species of different spin multiplicity. These workers suggested, particularly on the basis of stereospecificity of addition of the nitrene to 4-methylpent-2-ene (see Section 1.3), that *singlet* carbethoxynitrene is generated from *N*-*p*-nitrobenzenesulphonoxyurethane; but, at low olefin concentrations, much of the nitrene reacts in the triplet state.

Anthracene, in varying concentrations in boiling chlorobenzene (132°), was treated with ethyl azidoformate and the yields estimated by Q.T.L.C. A large excess of anthracene was used; so the substrate concentration was effectively unchanged during reaction.

[Anthracene] (mole %)	Yield % 1-anthryl urethane	Yield % 9-anthryl urethane	9-:1- isomer ratio
0.95	2.6	25.3	9.7
1.10	3.4	26.0	7.7
1.40	5.3	26.4	5.0
1.85	7.3	27.8	3.8
2.80	14.3	26.4	1.86
8.7	30	47	1.57

TABLE 1.2.2

REACTION OF ETHYL AZIDOFORMATE WITH ANTHRACENE IN CHLOROBENZENE AT 132°

It is apparent (Table 1.2.2) that the product composition is strongly dependent on reactant concentration. Furthermore, the 9-:1- isomer ratio at the lowest concentration is closely similar to that reported for free radical substitution. (It is not possible to compare this ratio with that obtained for electrophilic attack on anthracene because a facile addition-elimination occurs across the *meso*-positions.)

It is likely, then, that while both singlet and triplet nitrenes react at high substrate concentrations, the triplet form becomes more important at low concentrations.

When carbethoxynitrene, generated by reaction of *N*-*p*-nitrobenzenesulphonoxyurethane with *N*,*N*-diethylcyclohexylamine, is allowed to react with anthracene, a similar but smaller variation in isomer ratio resulted with change in reactant concentrations (Table 1.2.3).

[Anthracene] (mole %)	Yield % 1-anthryl urethane	Yield % 9-anthryl urethane	9-:1- isomer ratio
0.95	4.8	16.9	3.5
2.80	8.9	17.7	2.0

TABLE 1.2.3

REACTION OF ANTHRACENE WITH CARBETHOXYNITRENE (α-ELIMINATION ROUTE) IN CHLOROBENZENE AT 132°

The presence of *N*,*N*-diethylcyclohexylamine during reaction of ethyl azidoformate with anthracene caused markedly decreased preference for attack at the 9-position (Table 1.2.4). It seems, therefore that the amine acts as a preferential trap for the triplet nitrene.

The reaction of carbethoxynitrene with pyridine, *N*-methylaniline and *N*,*N*-dimethylaniline has been described (see p. Pyridine forms a moderately stable betaine presumably by reaction with the *singlet* nitrene: the other substrates are converted to

Medium	[Anthracene] (mole %)	Yield % 1-anthryl urethane	Yield % 9-anthryl urethane	9-:1- isomer ratio
PhCl/R_3N*	0.95	1.8	3.8	2.1
Cumene	8.7	15.0	17.1	1.1_3
PhCl/py†	8.7	6.3	17.1	2.7
PhCl/olefin§	8.7	9	13	1.4_4

* $[C_6H_{11}N(Et)_2]$ = 0.95 mole %

† [pyridine] = 8.7 mole %

§ [9-undecenoic acid] - 8.7 mole %

<u>TABLE 1.2.4</u>

REACTION OF ETHYL AZIDOFORMATE WITH ANTHRACENE AT 132° IN THE PRESENCE OF ADDITIVES

hydrazine derivatives by 1,2-shifts in the primary betaine adducts. *N,N*-Diethylcyclohexylamine is expected to react in the same way. In this substrate, however, there is also available a tertiary C-H bond α to the nitrogen. Hydrogen-atom abstraction by the triplet species is therefore energetically favourable; and the effect of this amine on the 9-:1- isomer ratio (Table 1.2.4) suggests that this process *does* occur.

When cumene was used a solvent for reaction of ethyl azidoformate with anthracene, the 9-:1- isomer ratio was lowered (Table

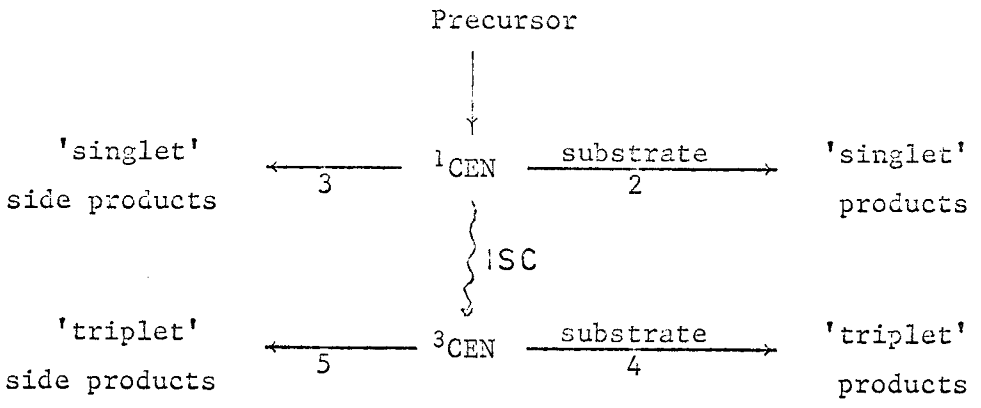
1.2.4). This effect is attributed to preferential removal of *triplet* carbethoxynitrene from the reaction system (see Section 1.5).

Addition of pyridine when chlorobenzene is used as solvent lowers the yields of *both* anthrylurethanes. (This is to be expected if the additive reacts with the *initially* generated nitrene species.) It is not clear, however, why pyridine should increase the preference of the nitrene for attack at the 9-position.

Although addition of an olefin (9-undecenoic acid) to the azidoformate-anthracene reaction mixture caused marked reduction in the overall yields of anthrylurethanes, the 9-:1-isomer ratio was little changed (Table 1.2.4). Anthracene must therefore be much more susceptible than 9-undecenoic acid to attack by *triplet* carbethoxynitrene.

The above results are consistent with the view that carbethoxynitrene is generated in the singlet state, but subsequently crosses over a (lower-energy) triplet form. This triplet form shows a marked preference for attack at the 9-position of anthracene while the singlet species is much less selective (and *may* even react preferentially at the 1-position).

The amount of triplet nitrene present in any reaction system depends on the concentration and reactivity of the substrate. The singlet species undergoes competing reactions, shown in Scheme 1.2.II, where ^{1}CEN and ^{3}CEN represent the singlet and triplet nitrenes respectively.



Scheme 1.2.II

$$\text{Rate of Reaction 1} = k_1\,[^1\text{CEN}]$$

$$\text{Rate of Reaction 2} = k_2\,[^1\text{CEN}][\text{substrate}]$$

$$\therefore \frac{\text{Rate 1}}{\text{Rate 2}} = \frac{k_1}{k_2}\,[\text{substrate}]^{-1}$$

Now *provided* ^{1}CEN and ^{3}CEN are equally susceptible to side reactions, (i.e. $k_3/k_2 = k_5/k_4$),

$$\frac{\text{Rate 1}}{\text{Rate 2}} = \frac{\text{T}}{\text{S}}$$

where T and S represent the amounts of anthrylurethanes formed from triplet and singlet species respectively.

$$\text{i.e.} \quad \frac{\text{T}}{\text{S}} = \frac{k_1}{k_2}\,[\text{substrate}]^{-1}$$

A plot of T/S against $[\text{substrate}]^{-1}$ should then be a straight line, through the origin, of slope k_1/k_2.

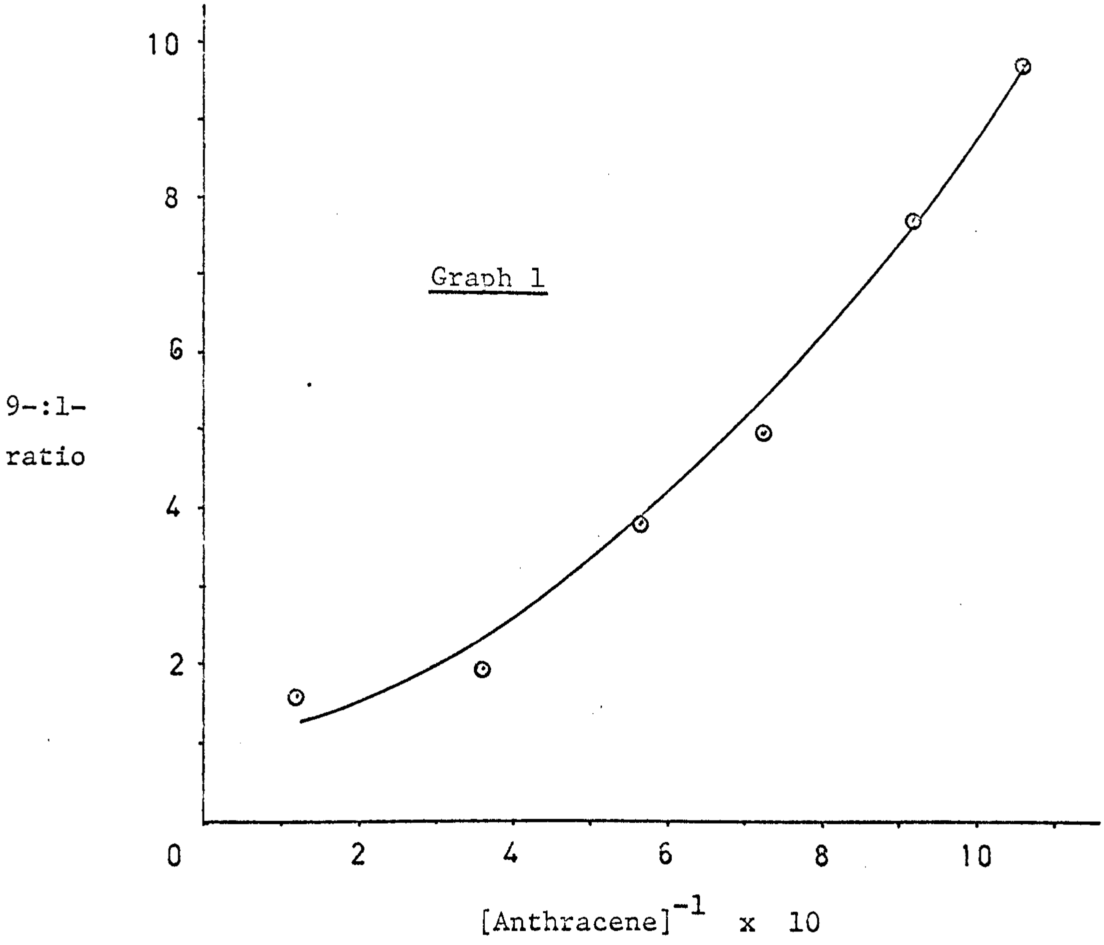
Experimental limitations in the azidoformate/anthracene system prevent successful application of this approach. The insolubility of anthracene in suitable solvents limits [Anthracene] to 8.7 mole %, so that it is not possible to estimate the 9-:1-isomer ratio for [Anthracene] = 100 mole %, i.e. the ratio for predominantly singlet nitrene attack. Furthermore, because yields of anthrylurethanes dropped markedly at [Anthracene] < 0.95 mole %, it is not possible to evaluate the ratio of products as [Anthracene] approaches 0 mole %, i.e. the ratio for triplet nitrene.

From the data obtained, however, it *is* possible to draw some firm conclusions. If it is assumed that the singlet nitrene leads *solely* to 1-anthrylurethane (*via* an aziridine intermediate) and the triplet form yields *only* 9-anthrylurethane, a plot of (9-:1-isomer ratio) against $[\text{Anthracene}]^{-1}$ should be a straight line through the origin. The graph is *not* linear, indicating that the foregoing assumption is not correct. In particular, it is not correct that singlet carbethoxynitrene behaves exclusively as a double bond reagent.

If, then, both singlet and triplet species lead to 9-anthrylurethane, the proportion of this product formed from each species will vary with the substrate concentration. It was expected that the triplet nitrene reacting by a radical process, would show, on reaction with 9-deuterioanthracene, a kinetic isotope effect slightly different from that operating for electrophilic attack

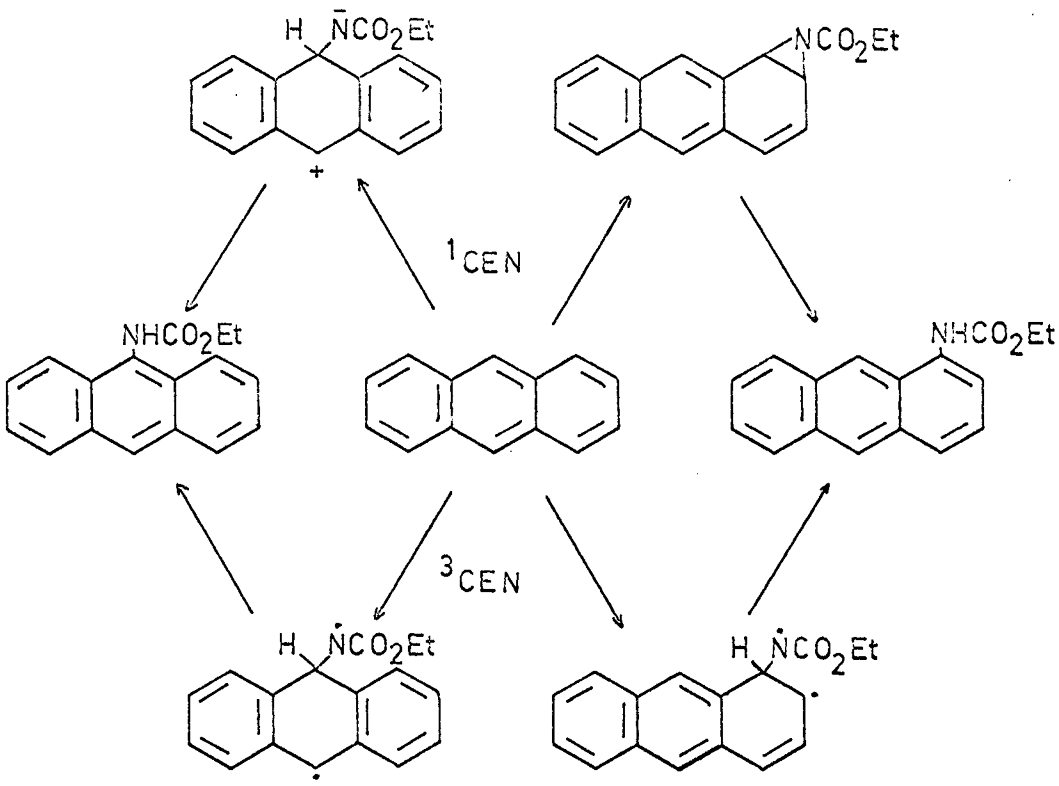
[Anthracene] (mole %)	$[\text{Anthracene}]^{-1} \times 10$	$\frac{9-}{1-}$ ratio
0.95	10.5	9.7
1.10	9.1	7.7
1.40	7.2	5.0
1.85	5.6	3.8
2.80	3.6	1.8_6
8.7	1.2	1.5_7

TABLE 1.2.5



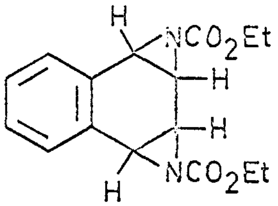
of the singlet form. It seemed, therefore, that the *average* kinetic isotope effect would depend slightly on [Anthracene] But k_H/k_D = 1.5 for [Anthracene] = 0.95 *and* 8.7 mole %. Such a small value definitely excludes direct insertion of the nitrene into the aromatic C-H bond as a route to 9-anthrylurethane but provides no positive evidence of the route(s) operating.

The probable mechanistic pathways are shown in Scheme 1.2.III.

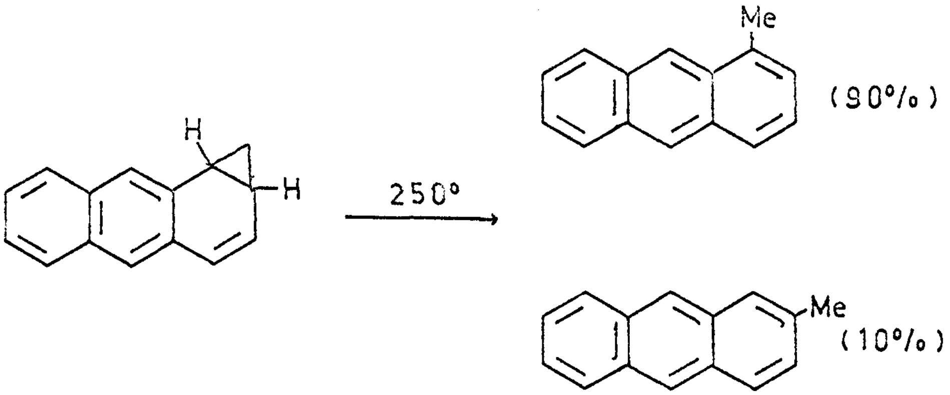


Scheme 1.2.III

Hafner *et al.*[53] have reported that carbethoxynitrene reacts with naphthalene to give 1-naphthylurethane as the sole product. Without comment, they proposed that this product was formed *via* an aziridine intermediate. There is no doubt that the nitrene is capable of such addition to naphthalene: photolysis of a solution of the substrate in ethyl azidoformate affords the diadduct:[84]



If such a primary adduct is formed from carbethoxynitrene and anthracene, it is not clear why it should rearrange almost solely to 1-anthrylurethane, with only a trace of the 2-isomer. An analogy, however, is available:[85] thermal rearrangement of the corresponding cyclopropane affords a large excess of 1-methylanthracene:



As previously pointed out (Scheme 1.2.II), the proportion of triplet carbethoxynitrene reacting with a substrate depends on the relative rates of intersystem crossing (Reaction 1) and reaction of the singlet species with the substrate (Reaction 2). Reaction 2 certainly involves an activation energy and, because Reaction 1 was expected to be relatively temperature-independent, it was expected that the proportion of triplet nitrene would decrease with increase in temperature.

Reactions of anthracene with carbethoxynitrene, generated by α-elimination, were studied at various temperatures. The nitrene precursor decomposes at *ca.* 160°; so the maximum temperature chosen for the study was 147°. The minimum temperature (40°) was dictated by the sparing solubility of anthracene. *N,N*-diethylcyclohexylamine was chosen as the tertiary amine because of its high boiling point (193°).[86] The results of the studies are shown in Table 1.2.6.

In spite of expectations, the proportion of triplet nitrene reacting with anthracene *increases* with increased temperature. It is tempting to conclude that intersystem crossing of singlet carbethoxynitrene to the triplet state involves an activation energy which is greater than the average activation energy for reaction of the singlet form with anthracene.

Temp. (°C)	Solvent	Yield % 1-anthryl urethane	Yield % 9-anthryl urethane	Total Yield anthryl urethane	9-:1- isomer ratio
40	CH_2Cl_2	15.0	17.1	32.1	1.1_4
61	$CHCl_3$	8.9	14.1	23.0	1.5_8
84	$(ClCH_2)_2$	9.2	19.8	29.0	2.1_5
100	PhCl	9.0	19.8	28.8	2.2_0
132	PhCl	4.8	16.9	21.7	3.5_2
147	$(Cl_2CH)_2$	4.2	16.2	20.4	3.9

TABLE 1.2.6

REACTION OF CARBETHOXYNITRENE (α-ELIMINATION ROUTE) WITH ANTHRACENE

[ANTHRACENE] = 0.95 MOLE %

If reactions 3 and 5 (Scheme 1.2.II) are negligible,

$$\frac{\text{Rate 1}}{\text{Rate 2}} = \frac{A_1\, e^{-\frac{E_1}{RT}}}{A_2\, e^{-\frac{E_2}{RT}}} = \frac{A_1}{A_2}\, e^{\frac{-(E_1 - E_2)}{RT}}$$

whence, as before,

$$\frac{[\text{9-Anthrylurethane}]}{[\text{1-Anthrylurethane}]} = \frac{A_1}{A_2}\, e^{\frac{-(E_1 - E_2)}{RT}}$$

$$\text{i.e. } \log_{10}\ (\text{9-:1- ratio}) = \log_{10}\frac{A_1}{A_2} - \frac{(E_1 - E_2)}{4.6}\cdot\frac{1}{T}$$

Plotting of these results gives a good straight line of equation

$$\log_{10}\ (9\text{-}:1\text{- ratio}) = 2.4 - \frac{0.78}{T}$$

Hence $(E_1 - E_2) = 3.6$ kcal/mole.

The physical significance of the activation energy for intersystem crossing will be discussed in detail in Section 1.3.

With increased temperatures, the total yields of anthrylurethanes fell off steadily (Table 1.2.5). It appears that the triplet nitrene is more susceptible than the singlet form to side reactions ($k_5 > k_3$). Therefore, even if it were possible to assess the proportion of anthrylurethanes arising from the triplet nitrene, this value would not truly represent the proportion of triplet species present in the system.

This objection applies also to interpretation of the results of the dilution studies (Table 1.2.2): the total urethane yield varied from 77% (at 8.7 mole % anthracene) to 28% (at 0.95 mole % anthracene). It must be concluded, then, that very little *quantitative* significance can be attached to results obtained from the anthracene/carbethoxynitrene system.

TABLE 1.2.7

PRINCIPAL ABSORPTION MAXIMA (cm^{-1}) IN THE INFRARED SPECTRA (NUJOL MULLS) OF ANTHRYL-, PHENANTHRYL-, AND PYRENYL-URETHANES

Urethane										
1-anthryl	3300m	1690vs		1530m	1240s	1090m		875m		730m
2-anthryl	3400m	1730vs	1630m 1580m	1500m	1225s	1070m		895s		747s
9-anthryl	3300m	1690vs	1530m	1500m	1245s	1050m		887w	842w 837w	
1-phenanthryl	3300s	1695vs	1540s	1495m	1245vs	1090m	1050m		805s	760m 750m
2-phenanthryl	3400s	1700vs	1570m 1540s	1520m	1245vs	1085m		887m	833m 817s	748s
3-phenanthryl	3360s	1695vs	1570m 1545s	1500m	1295m 1245vs	1075s			837s 805m	750m 747m
4-phenanthryl	3450w	1725vs	1530s	1490s	1240m 1210vs	1100m 1090m	1055m		805s	767s 762s
9-phenanthryl	3300s	1690vs	1540s	1490m	1245	1125m 1100w	1055m	890m		770s 740s 725s
1-pyrenyl	3250m	1680vs	1550m	1525m	1255vs	1120m 1080m	1055m		845s	707m
2-pyrenyl	3350m	1690vs	1600m 1540s		1250vs	1090m 1080m		870s	843m 820m	710s
4-pyrenyl	3300m	1680vs	1590w 1535s		1250vs 1215m	1100m	1040m	875m	840m 835m	775m 718s

1.3. REACTION OF CARBETHOXYNITRENE WITH CIS- AND TRANS-BUTENE-2

The mechanistic study of nitrene addition to olefins offers important advantages over its reaction with anthracene:

(i) A much wider range of substrate concentrations is available in a highly inert solvent ('Freon' TF) so that the limiting proportions of *cis*- and *trans*-aziridines, obtained from triplet carbethoxynitrene at infinite dilution, can be estimated with fair accuracy.

(ii) There is little ambiguity as to the sources of the products. It is expected that, in solution, any 'hot' aziridines formed by (one-step) addition of singlet carbethoxynitrene would be very rapidly quenched by collision with solvent molecules. It is unlikely, then, that 'wrong' aziridine could result from reaction of the singlet species. 'Wrong' product therefore must result from reaction of triplet carbethoxynitrene. Furthermore, the proportion of 'wrong' product can be used as a measure of the proportion of this triplet species reacting with an olefin.

If the rate of carbon-carbon bond rotation is comparable with the rate of spin inversion in the diradical intermediate (page 7) some triplet nitrene will provide stereospecific addition. It is possible, however, by mathematical manipulation, to make due allowance for this complication.

(iii) No metastable intermediates, which rearrange to give the observed products, are implicated. In the case of anthracene, several activation energies are involved, both in the initial reaction of the singlet nitrene by various modes and in the rearrangement of the metastable aziridine intermediate. Quite clearly, then, quantitative comparison of the apparent activation energies for intersystem crossing of the singlet nitrene and its reaction with anthracene can have only doubtful significance.

Hafner *et al.*[50] have reported in a brief communication results of reaction of carbomethoxynitrene with *cis*- and *trans*-butene-2. They were unable to resolve the aziridine mixtures produced using vapour phase chromatography (v.p.c.). Alkaline hydrolysis, however, gave a mixture of parent aziridines which were easily separable. Reaction of the nitrene with *cis*-butene-2 gave 13% *trans* isomer while the *trans*-olefin gave 8% *cis* isomer in the aziridine mixtures. Our preliminary studies indicated that, although v.p.c. separation is extremely difficult, accurate and reproducible estimation of the compositions of the *cis*/*trans*-aziridine mixtures was possible under carefully controlled conditions.

Because of the volatility of the butenes, accurate control of compositions of reaction mixtures presented problems. Solutions of each olefin in 'Freon' TF (*ca.* 20% v/v) were used as stock 'concentrates', and their concentrations were checked from time to time by reaction of aliquots with excess bromine (in carbon tetrachloride) and back-titration. All manipulations were carried out using apparatus which had been chilled to -20°. Ethyl azidoformate (0.05 to 0.06 mole equivs.) was added to the diluted olefin solutions which were degassed and sealed in glass tubes under reduced pressure. The tubes were heated in a thermostatically controlled oven or oil bath. Temperature control was better than ±0.5°.

After the reaction, the tubes were cooled to -78°, carefully broken open and allowed to warm to room temperature. When the olefin had evaporated, the solutions, which were in all cases quite colourless, were diluted to a standard volume and analysed by vapour phase chromatography.

Because the reaction mixtures were prepared at low temperatures and the thermolyses carried out at temperatures above the boiling points of the components, detailed calculations are needed to determine olefin concentrations in the liquid phase during reaction. It is necessary, then, to know the densities of *cis*- and *trans*-butene-2 and 'Freon' TF at -20° and the vapour pressures of these components at 80° and 120°.

Density figures for *cis*- and *trans*-butene-2 are available:[87]

			20°		25°	
cis-butene-2	D	=	0.6213	;	0.6154	g./ml.
trans-butene-2	D	=	0.6042	;	0.5984	g./ml.

Hence, in each case,

$$\frac{dD}{dt} = -0.0012 \text{ g./ml./}^{\circ}\text{C}$$

in the range 20-25°. Assuming that this differential is constant from -20° to 25°,

$$\begin{aligned} D \text{ (\textit{cis}-butene-2)} &= 0.621 + (40 \times 0.0012) \\ &= 0.67 \text{ g./ml. at } -20^{\circ} \\ \text{and } D \text{ (\textit{trans}-butene-2)} &= 0.604 + (40 \times 0.0012) \\ &= 0.65 \text{ g./ml. at } -20^{\circ} \end{aligned}$$

The density of 'Freon' TF at -20° has been published.[88] It was assumed that the relative error in volumes delivered by pipettes (at -20°) were constant; and this source of error was therefore ignored.

Vapour pressures of the components at the reaction temperatures were not directly available, but were calculated by the 'Cox Chart' method.[89] The olefins were grouped in Family (3), "Freon' TF in Family (2) and ethyl azidoformate in Family (5). The calculated pressures (in atmospheres) are shown:

Temp.	*cis*-butene-2	*trans*-butene-2	'Freon' TF	ethyl azidoform.
80°	6.90	7.40	2.16	0.13
120°	19.5	20.4	7.40	0.72

A typical calculation will illustrate the general method of correction:

Initial liquid composition:

Et azidoform.			0.050 g.	≡	0.00043 mole
cis-butene-2	0.50 ml	=	0.335 g.	≡	0.00598 mole
'Freon' TF	4.50 ml	=	7.96 g.	≡	0.0424 mole

Hence:

$$N^{L}_{\text{azide}} = 0.009$$

$$N^{L}_{\text{olefin}} = 0.123$$

$$N^{L}_{\text{Freon}} = 0.868,$$

where N^{L} represents the mole fraction of a particular component in the liquid phase.

Composition of vapour:

Because the tube was sealed under vacuum, the total internal pressure is calculated as

$$P = \sum_n N^L_n P^o_n$$

where P^o_n is the vapour pressure of pure nth component at the reaction temperature. i.e. Total Pressure at 80°

$$= (0.009 \times 0.13) + (0.123 \times 6.90) + (0.828 \times 2.16)$$

$$= 2.72 \text{ atmos.}$$

Hence $N^V_{azide} = 0.0004$

$N^V_{olefin} = 0.31$

$N^V_{Freon} = 0.69$

Now the initial volume occupied by the vapour was the total enclosed volume *less* the initial liquid volume. In this case,

Initial vapour volume = (24-5)

= 19 ml.

The process of vaporization tends to decrease the bulk of the liquid; but, on the other hand, heating of the liquid causes expansion. These effects largely cancel and the vapour volume at 80° is therefore assumed to be 19 ml. Hence the masses of components in the vapour phase were:

Et azidoformate: $\left(0.0004 \times \frac{0.019}{22.4} \times \frac{273}{353} \times 115\right)$ g.

~ 0

cis-butene-2: $$\left(0.31 \times \frac{0.019}{22.4} \times \frac{273}{353} \times 56\right) \text{ g.}$$

$$= 0.041 \text{ g.}$$

'Freon' TF: $$\left(0.69 \times \frac{0.019}{22.4} \times \frac{273}{353} \times 187.4\right) \text{ g.}$$

$$= 0.31 \text{ g.}$$

Composition of liquid after vaporization:

Et azidoformate: 0.050 g. $\equiv$ 0.00043 mole

cis-butene-2 : (0.335-0.041) = 0.294 g. $\equiv$ 0.0053 mole

'Freon' TF : (7.96 -0.31) = 7.65 g. $\equiv$ 0.0408 mole

whence N^{L}_{butene} (corr.) = 0.115

The concentration of *cis*-butene-2 therefore dropped from 12.3 mole % to 11.5 mole % under the reaction conditions, i.e. a lowering of 6.5% resulted.

Such a non-differential calculation takes no account of the change in liquid composition *during* vaporization. This, however, introduces an error of only (6.5% of 6.5%) - an error which is not significant. Furthermore, the nitrogen evolved during decomposition of the azidoformate has not been considered. Although the amounts of azide were quite small (0.01 to 0.10 g.), they represented 2 to 20 ml of nitrogen (measured at N.T.P.). This, then, is a much more serious source of error; but at most it causes an uncertainty of *ca.* 2% in the calculated liquid composition.

The foregoing calculation rests on the assumption that Raoult's Law accurately describes the behaviour of the reaction systems. This assumption seems reasonable; the components are non-polar (i.e. interactions are uniform) and the conditions moderate (not above 120° and 10 atmos. pressure). Even if the systems deviate from thermodynamic ideality by 50%, the total error in the estimated olefin concentrations would not exceed 5%.

The experimental results are set out in Tables 1.3.1 to 1.3.4. In all cases the aziridine yields were quite good and v.p.c. indicated that amounts of isomeric by-products did not exceed 3% of the aziridine yields. Furthermore, the yields were strikingly independent of olefin concentration.

The possibility of thermal isomerization of the aziridines has been excluded: heating of a reaction mixture for 24 hr at 120° gave a product mixture virtually identical with that obtained after 4 hr. Moreover, isomerization of butene-2 at this temperature is improbable.

The likely stereochemical consequences of reaction of triplet nitrenes with olefins have been discussed (page 7). The above results are certainly consistent with a scheme which depicts increased participation of triplet carbethoxynitrene (^{3}CEN) at low substrate concentrations, e.g. Scheme 1.3.I.

REACTION OF ETHYL AZIDOFORMATE WITH CIS-BUTENE-2 AT 80°

TABLE 1.3.1

[olefin] initial (mole %)	[olefin] corrected (mole %)	log [olefin] (corr.)	% *trans* aziridine† (x)	% total aziridine yield
27.5	23.7	1.37_5	20.6	70
22.5	18.5	1.26_5	22.5	
	18.7	1.27	22.6	
17.1	14.0	1.15	28.7	
14.4	11.8	1.07_5	27.1	69
9.7	9.0	0.95_5	32.8	
8.8	7.3	0.86_5	36.0	66
5.9	5.2	0.72	39.7	66
3.0	2.6	0.41_5	40.8	
2.1	2.0	0.30	47.1	
0.30	0.28	-0.55	46.9	63

†*cis* + *trans* = 100%

TABLE 1.3.5

log [olefin] (corr.)	[olefin] (corr.)	x (%)	$(\frac{X}{x} - 1)$*
0.9	7.9	34.4	0.37
1.0	10.0	31.7	0.48
1.1	12.6	29.0	0.62
1.2	15.9	26.3	0.79
1.3	20.0	23.7	0.98
1.4	25.1	20.9	1.25
1.5	31.6	18.3	1.57

* X = 47%

REACTION OF ETHYL AZIDOFORMATE WITH TRANS-BUTENE-2 AT 80°

TABLE 1.3.2

[olefin] initial (mole %)	[olefin] corrected (mole %)	log [olefin] (corr.)	% *cis* aziridine† (x)	% total aziridine yield
27.5	24.6	1.39	11.9	68
	23.7	1.37_5	13.6	
22.5	18.2	1.26	14.8	
17.1	14.0	1.14_5	17.3	68
	13.5	1.13	16.3	
14.4	11.8	1.07	20.1	
	11.2	1.05	20.6	
9.7	8.7	0.94	24.4	
5.9	5.2	0.71_5	25.6	
3.0	2.0	0.30	32.2	66
2.1	1.85	0.27	31.2	67
0.30	0.28	-0.55	36.9	64

† *cis* + *trans* = 100%

TABLE 1.3.6

log [olefin] (corr.)	[olefin] (corr.)	x (%)	$(\frac{X}{x} - 1)$*
0.8	6.3	25.1	0.47
0.9	7.9	22.9	0.62
1.0	10.0	20.7	0.79
1.1	12.6	18.5	1.00
1.2	15.9	16.2	1.28
1.3	20.0	13.9	1.66
1.4	25.1	11.6	2.19

* X = 37%

REACTION OF ETHYL AZIDOFORMATE WITH CIS-BUTENE-2 AT 120°

TABLE 1.3.3

[olefin] initial (mole %)	[olefin] corrected (mole %)	log [olefin] (corr.)	% *trans* aziridine† (x)	% total aziridine yield
22.5	18.5	1.26_5	24.0	64
19.8	15.3	1.18_5	29.5	
	17.4	1.24	29.5	
14.0	13.7	1.13_5	30.5	
12.1	11.8	1.07	32.6	64
9.7	9.0	0.95_5	35.1	
7.8	7.2_5	0.86	37.2	
5.2_3	5.0_5	0.70_5	41.4	61
2.5_7	2.5	0.40	43.8	62
1.2	1.0_2	0.01	46.0	
0.6	0.5_5	-0.26	48.7	60

† *cis* + *trans* = 100%

TABLE 1.3.7

log [olefin] (corr.)	[olefin] (corr.)	x (%)	($\frac{X}{x}$ - 1)*
0.90	7.9	36.7	0.33
0.95	8.9	35.5	0.38
1.00	10.0	34.4	0.42
1.05	11.2	33.2	0.48
1.10	12.6	32.1	0.53
1.15	14.1	30.9	0.59
1.20	15.9	29.7	0.65
1.25	17.8	28.5	0.72

* X = 49%

REACTION OF ETHYL AZIDOFORMATE WITH TRANS-BUTENE-2 AT 120°

TABLE 1.3.4

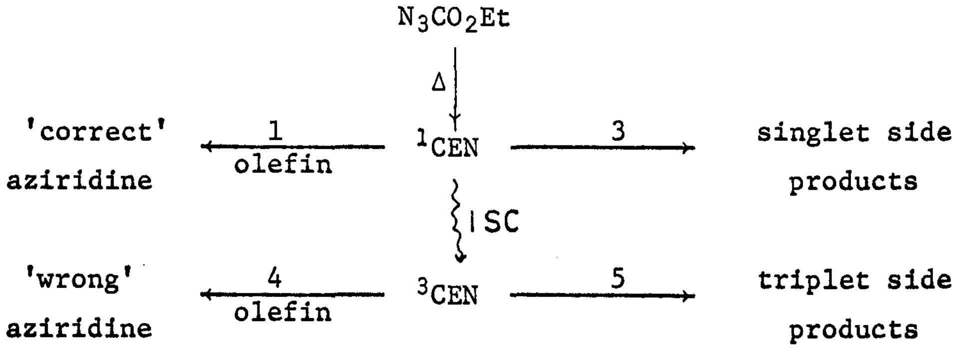
[olefin] initial (mole %)	[olefin] corrected (mole %)	log [olefin] (corr.)	% *cis* aziridine† (x)	% total aziridine yield
27.4	25.6	1.41	19.7	60
24.9	21.4	1.33	22.8	
22.3	20.5	1.31	21.3	59
19.8	17.4	1.24	24.4	
17.1	14.2	1.15	24.8	
12.7	10.9	1.04	28.1	53
1.2	1.0	0.00	36.0	40
0.6	0.5	-0.30	38.8	

† *cis* + *trans* = 100%

TABLE 1.3.8

log [olefin] (corr.)	[olefin] (corr.)	x (%)	$(\frac{X}{x} - 1)$*
1.0	10.0	29.1	0.34
1.1	12.6	26.8	0.45
1.2	15.9	24.5	0.59
1.3	20.0	22.3	0.75
1.4	25.1	20.1	0.94
1.5	31.6	17.8	1.19

* X = 39%



Scheme 1.3.I

Since the aziridines were obtained in good yield, reaction 3 cannot be important; and because yields do not decrease markedly with decrease in [olefin], reaction 5 is not significant. There exists, therefore, a simple competition between reactions 1 and 2. Now:

$$\text{Rate of Reaction 1} = k_1\,[{}^1\text{CEN}][\text{olefin}]$$

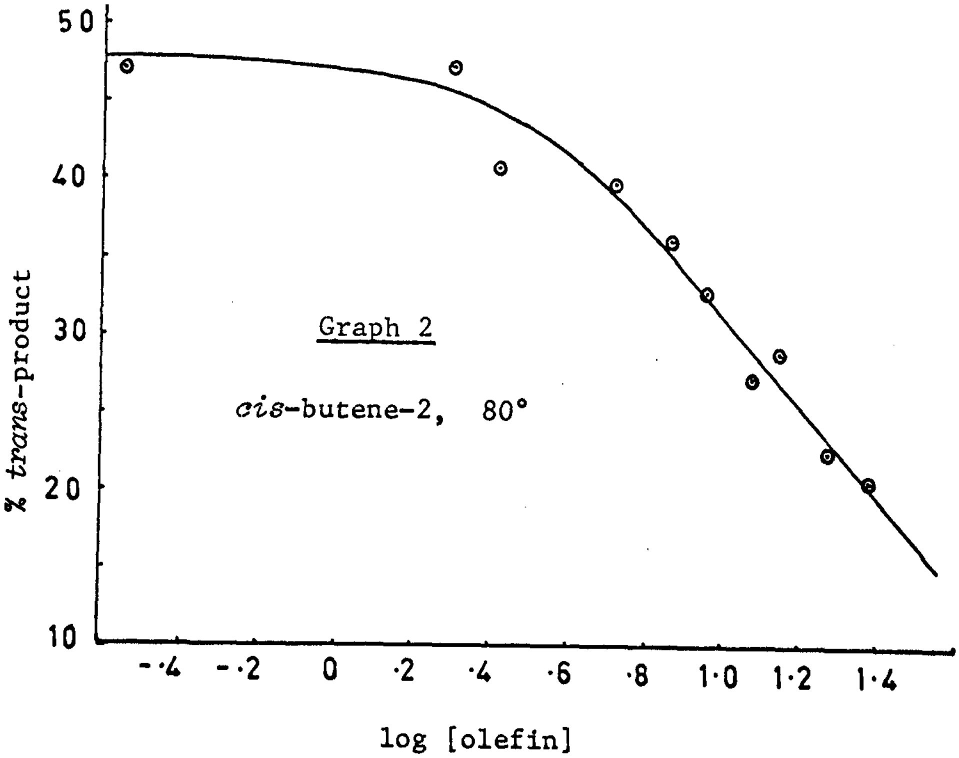
$$\text{Rate of Reaction 2} = k_2\,[{}^1\text{CEN}]$$

and

$$\frac{\text{Rate of Reaction 1}}{\text{Rate of Reaction 2}} = \frac{k_1}{k_2}\,[\text{olefin}]$$

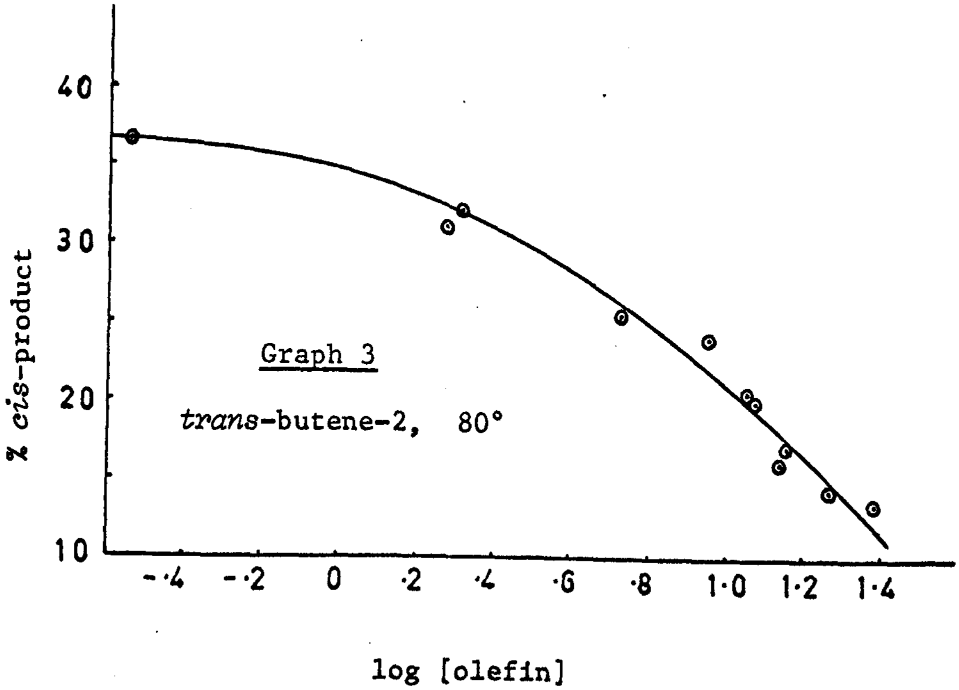
Therefore, it an assessment of the relative rates of Reactions 1 and 2 is possible, the above scheme can be verified quantitatively.

Graphs 2 and 5 show plots of proportions of 'wrong' isomer against log[olefin] rather than against [olefin]. In this way, adequate weight is given to successive dilutions at the low concentration end of the scale. The limiting proportion of



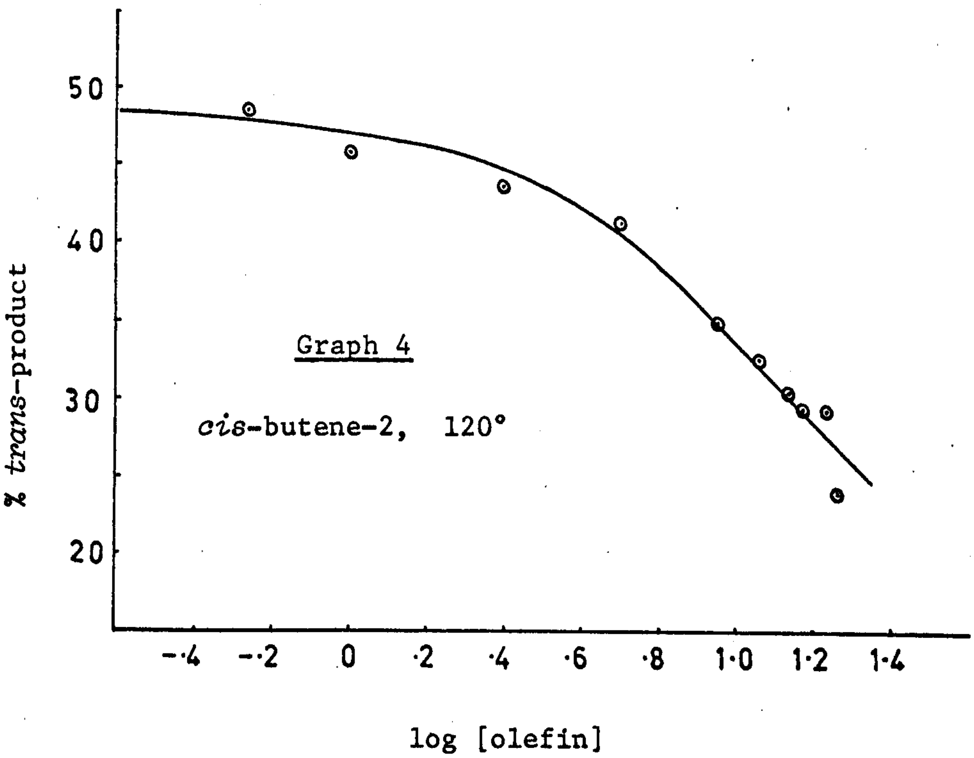
Graph 2

cis-butene-2, 80°



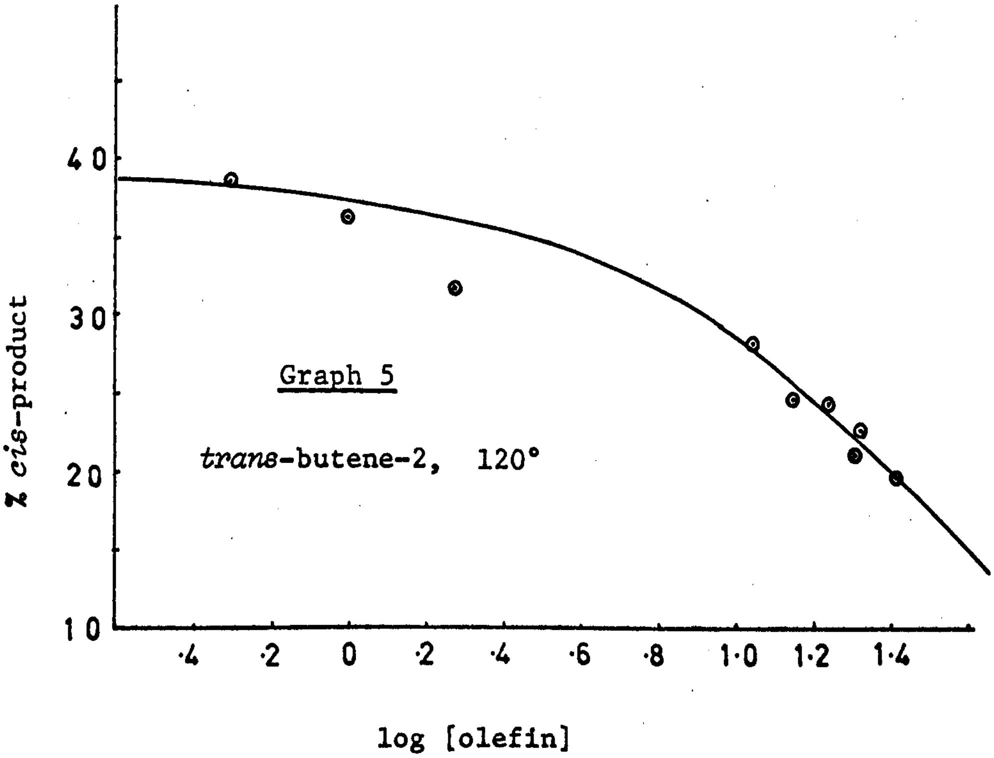
Graph 3

trans-butene-2, 80°



Graph 4

cis-butene-2, 120°



Graph 5

trans-butene-2, 120°

'wrong' isomer can then be estimated with reasonable accuracy.

That each of these graphs has a linear section is probably fortuitous. In order to apply a kinetic treatment, it is absolutely essential that the initially-formed singlet nitrene be in a uniform environment. At olefin concentrations much above 20 mole % there is a fairly high probability that the nitrene will encounter regions where the local substrate concentration is markedly different from the bulk average. Values from this concentration range were therefore not considered for detailed mathematical treatment. On the other hand, as log[olefin] becomes negative, the curve flattens off. It will be seen that values of "% 'wrong' isomer" in this region, when subjected to kinetic treatment, introduce large errors. Neither of these objections, however, applies to values in the linear sections of the graphs.

If x is the percentage of 'wrong' isomer and X its limiting value as [olefin] approaches zero, x/X is the proportion of nitrene which reacts in the triplet state with the substrate.

Then:

$$\frac{\text{Rate of Reaction 1}}{\text{Rate of Reaction 2}} = \frac{1 - \frac{x}{X}}{\frac{x}{X}} = \left(\frac{X}{x} - 1\right)$$

and

$$\left(\frac{X}{x} - 1\right) = \frac{k_1}{k_2}\,[\text{olefin}]$$

Hence a plot of $\{\frac{X}{x} - 1\}$ against [olefin] should give a straight line, of gradient k_1/k_2, passing through the origin.

It is clear that the foregoing mathematical treatment leads to considerable magnification of experimental errors. A graphical averaging procedure was therefore adopted: pairs of values of log[olefin] and % 'wrong' isomer were abstracted from the linear sections of graphs 2 to 5 and the processed values shown in Tables 1.2.5 to 1.2.8. The derived plots show excellent linearity (graphs 6 and 7) and pass through the origin: good evidence for the validity of the above treatment.

The values of k_1/k_2 (mole %) obtained from the slopes of the graphs are:

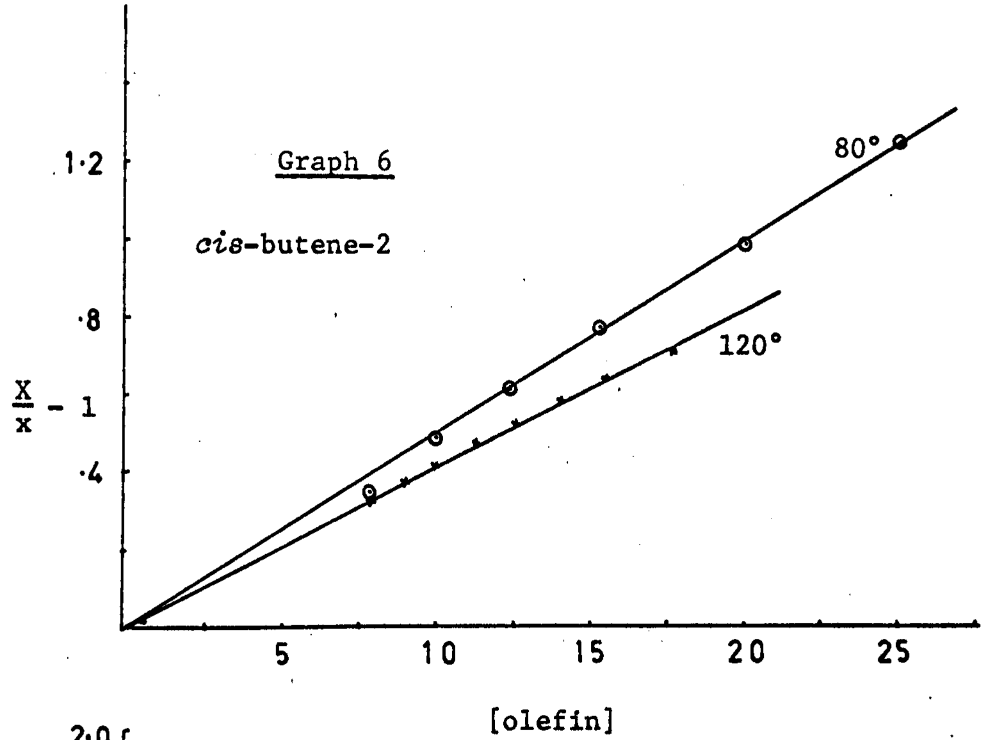
	80°	120°
cis	0.050	0.042
trans	0.080	0.038

Although considerable error is inherent in these values, two firm qualitative conclusions can be drawn:

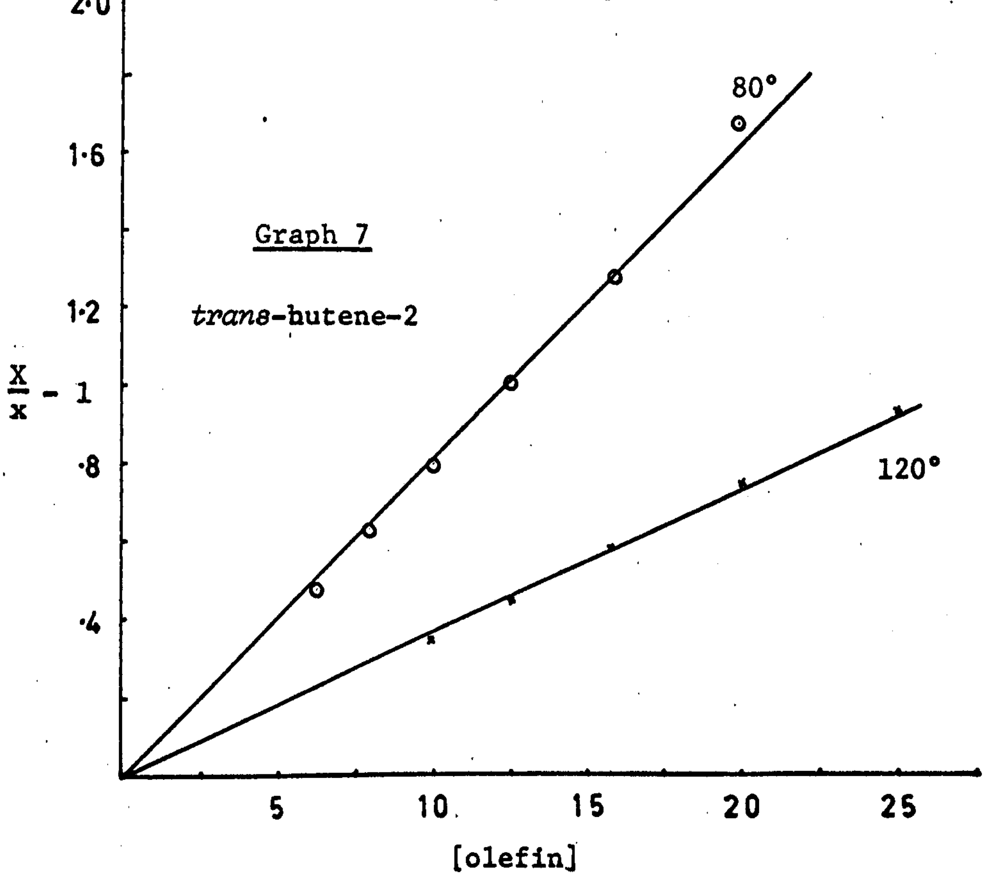
(i) k_1/k_2 (*trans*, 80°) is greater than k_1/k_2 (*cis*, 80°) by a factor of 1.6, i.e. *trans*-butene-2 is 1.6 times more reactive than the *cis*-isomer towards attack by singlet carbethoxynitrene.

(ii) k_1/k_2 (*cis* and *trans*) decreases with rise in temperature.

The significance of these conclusions will be discussed in detail.


Graph 6

cis-butene-2


Graph 7

trans-butene-2

RELATIVE REACTIVITIES OF *CIS*- AND *TRANS*-BUTENE-2

Baird and Dewar[90] have calculated the heat contents of *cis*- and *trans*-1,2-dimethylcyclopropane. The *cis*-isomer is higher in energy by 2.6 kcal/mole and it is likely that the difference in energies between *cis*- and *trans*-*N*-carbethoxy-2,3-dimethylaziridines is very close to this value. On the other hand, *cis*-butene-2 has a standard enthalpy only 1.0 kcal/mole higher than that of the *trans*-isomer.[87b]

There is no doubt that addition of carbethoxynitrene to an olefin is exothermic. Since $H^o_{cis} - H^o_{trans}$ is greater for products than for reactants and since it is reasonable to assume the same general shape for the reaction profiles, it follows that the profiles will gradually diverge (Fig. 1.3.1), i.e. $\Delta H^o_P > \Delta(\Delta E^{\ddagger}) > \Delta H^o_R$. It therefore follows that $\Delta E_{cis} > \Delta E_{trans}$.

Absolute reaction rate theory describes an equilibrium between the reactants and activated complex. Because $\Delta E^{\ddagger}$ (more correctly $\Delta G^{\ddagger}$) determines the position of this equilibrium, and therefore the rate of reaction, it follows that the *trans*-olefin should react more rapidly than the *cis*-isomer.

Few values are available for relative tendencies of *cis*- and *trans*-olefins towards cycloadditions. Our result, however, is in accord with the conclusion of Doering and Henderson[94] that dichlorocarbene adds to *trans*-pentene-2 1.3 times as rapidly as to the *cis*-isomer. On the other hand, McConaghy and Lwowski[10] found

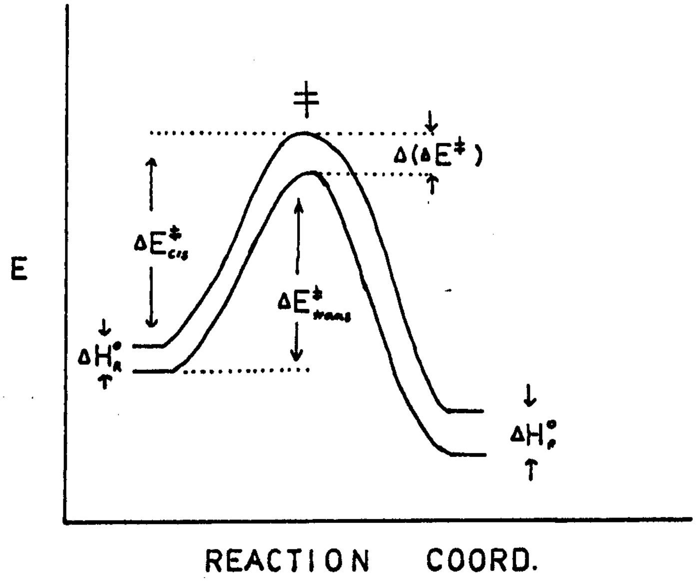


Fig. 1.3.1

that *trans*-4-methylpentene-2 is only 0.7 times as susceptible as the *cis*-olefin to attack by carbethoxynitrene. The reason for this discrepancy is not understood. (Bromine and di*iso*amylborane add to *cis*-butene-2 faster than to the *trans*-olefin.[95] It is not reasonable, however, to compare these examples with cycloadditions in which specific non-bonded interactions are brought into effect.)

VARIATION OF k_1/k_2 WITH TEMPERATURE

If intersystem crossing were temperature-independent, k_1/k_2 would increase with rise in temperature. In fact there is a *decrease* in the ratio, suggesting an energetic requirement for the process ^{1}CEN $\longrightarrow$ ^{3}CEN.

Gouterman[109] has proposed a theoretical model for radiationless transitions. He derived an expression for the ratio of thermally-induced to spontaneous intercombinational transitions:

$$\frac{A_T}{A_S} = [\exp\left(\frac{\hbar w}{kT}\right) - 1]^{-1}$$

This model predicts that intersystem crossing is favoured by an increase in temperature and therefore implies an energetic requirement for the process.

Furthermore, instances of energy requirements for intersystem crossing processes have been reported. Henson and Owen[91] have reported a temperature dependence for primary processes in the photolysis of diphenylacetylene. Internal conversion ($^1D \rightsquigarrow D$) and collision-promoted intersystem crossing ($^1D \rightsquigarrow {}^3D$) show energy requirements and this is reflected in a variation of fluorescence quantum yield with temperature. Furthermore Lim *et al.*[92] have reported that the temperature dependence of the quantum yield of fluorescence of substituted anthracenes is due to an activation energy requirement for the $^1S \rightsquigarrow T$ intersystem crossing. Strachan and Thornton[93] have assumed an activation energy of 1.5 kcal/mole for the process $^1S \rightsquigarrow {}^1T$ in order to explain the results of photolysis of ketene at various temperatures and wavelengths.

THE SIGNIFICANCE OF E_a FOR INTERSYSTEM CROSSING

Fig. 1.3.2 shows some typical lower potential energy curves for a diatomic molecule.[96a] Absorption of a photon causes excitation to an upper (singlet) electronic level (A). The high density of excited states above the lowest excited (S_1) singlet level results in many crossings and near-crossings of potential energy surfaces. The cascade of energy down to S_1 is therefore extremely rapid and, once S_1 is reacted, there follows rapid vibrational relaxation to the lowest vibrational (j = o) sublevel, from which fluorescence ($S_1 \rightsquigarrow S_o$) and radiationless internal conversion ($S_1 \rightsquigarrow S_o$) may proceed. Intersystem crossing to triplet states is subject to spin prohibition and therefore takes place much more slowly than internal conversion. Significant intersystem crossing can therefore proceed only from the j = o level of S_1.

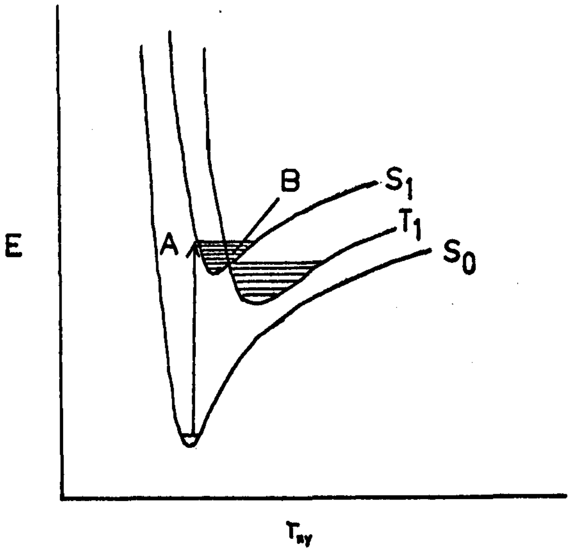


Fig. 1.3.2 (after Turro[96a])

The above simple model qualitatively describes the energy levels of carbethoxynitrene. There is, however, no S_o state; so there is no competition between intersystem crossing ($S_1 \rightsquigarrow T_1$) and internal conversion ($S_1 \rightsquigarrow S_o$) and fluorescence ($S_1 \longrightarrow S_o$). Therefore, although the frequency of intercombinational transition may be low, significant conversion to the triplet state can result.

The rate of intersystem crossing from an electronic state Ψ_r, with vibrational wave function χ_{nr}, to another electronic state Ψ_s, with vibrational wave function χ_{ms}, depends on the perturbation matrix element..[97]

$$\left\langle \Psi_r\chi_{nr} \mid H' \mid \Psi_s\chi_{ms} \right\rangle$$

where H' is the change in the Hamiltonian brought about by a colliding molecule. This matrix element is large only if the vibrational overlap integral $\langle \chi_{nr} \mid \chi_{ms} \rangle$ is large. If χ_{nr} is a low vibrational state and χ_{ms} a high state, this overlap will be small and the frequency of transition therefore low. It follows, then, that transition probability is high only when electronic levels are similar in energy. In such a favourable case, there will generally be a large overlap of the two sets of vibrational functions near the point of intersection of the potential energy surfaces.

Even when these requirements for initial and final states are fulfilled, the molecule must be subjected to a collision which, in promoting the intercombinational process:

(i) transfers to the molecule sufficient thermal energy to raise it to the overlap point B; and

(ii) provides sufficient perturbation to break down electronic spin quantization.

Because vibrational quenching is extremely rapid, intersystem crossing must occur very quickly after the singlet receives thermal energy. Furthermore, once the molecule has entered the T_1 state, it is efficiently reduced to the j = o vibrational level. Then, if there is a large energy gap between the j = o levels of S_1 and T_1, the molecule will be trapped in the triplet state, because insufficient thermal energy is available to return it to S_1.

Turro[96b] has pointed out that a solution may be approximated to a gas at infinite pressure. That is, molecules are in constant collision with their environment. However, the collisions cannot be elastic, but rather there are 'sticky encounters' in which molecules suffer a number of collisions before diffusing apart. As previously mentioned, vibrational quenching is very efficient and a rapid 'ebb' and 'flow' of thermal energy occurs between solute and solvent molecules. The same solvent molecule could then furnish the thermal energy necessary for intersystem crossing and quench the vibrationally-excited triplet so formed as well as provide the necessary perturbing environment.

Presumably this molecular contact must be quite intimate to allow 'mixing' of the external perturbation with the solute states.

In order to achieve such close contact, the energy of the collision must be sufficient to momentarily overcome coulombic and Pauli repulsion forces. This energy is in addition to that which must be *transferred* to the solute molecule.

If strict spin quantization applies, no intercombinational transitions are possible in a molecule. This spin prohibition, however, is relaxed in the presence of external or internal perturbations which increase the amount of spin-orbit coupling. The external effect is produced when a paramagnetic species or a molecule containing a heavy atom collides with another molecule: the internal spin-orbit effect can be brought about by substitution of such a heavy atom into the molecule in question. Although Anastassiou[24] has reported an external heavy atom effect on cyanonitrene, no such effect is discernible with carbethoxynitrene.

[Anthracene] (mole %)	Solvent	9-:1- ratio
0.95	$(CH_2Cl)_2$	2.15
0.95	$(CH_2Br)_2$	2.27

TABLE 1.3.9

REACTION OF CARBETHOXYNITRENE (α-ELIMINATION SOURCE)
WITH ANTHRACENE AT 84°

The brominated solvent should effect a more efficient conversio to the triplet state[96c] and show a greater preference for attack at the 9-position of anthracene (see page 49). In fact the steady increase in the 9-:1- isomer ratio with temperature is strikingly independent of the various solvents used. This absence of external heavy atom effect suggests that carbethoxynitrene is not subject to spin quantization and that, provided collisions of sufficient energy are available, intersystem crossing occurs with fair efficiency.

Furthermore, McConaghy and Lwowski[11] have recently reported that methylene chloride shows no greater tendency than neopentane to promote intersystem crossing in this nitrene species.

ADDITION OF TRIPLET CARBETHOXYNITRENE TO BUTENE-2

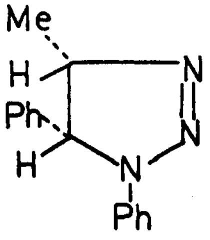
In a detailed discussion of the mechanism of methylene addition to olefins, DeMore and Benson[20] maintain that for *both* singlet and triplet species, the process involves two steps, an initial diradical being formed. They believe that the observed stereospecificity reflects the relative rates of spin inversion, ring closure and carbon-carbon bond rotation. Their calculations predict that cyclization of a singlet diradical is about $10^{0.8}$ times faster than carbon-carbon bond rotation; so singlet methylene should add with predominant retention of stereochemistry. However, spin inversion in the triplet diradical delays cyclization long enough for conformational alteration to occur.

Gaspar and Hammond,[98] on the other hand, conclude that *any* diradical (singlet or triplet) must be a free rotator during the time required to close the ring. It follows that, provided isomerization of 'hot' products does not take place, lack of stereospecificity is proof of the existence of a diradical intermediate. They therefore support the view that singlet methylene adds in a single step. Neither group seems to have considered the possibility of cases where the rates of spin inversion (followed by rapid ring-closure) and bond-rotation are comparable.

Our work indicates that, at high dilution, carbethoxynitrene reacts with *cis*- and *trans*-butene-2 to give different proportions of aziridine products. The intermediate 1,3-diradical has therefore not reached conformational equilibrium. Moreover, McConaghy and Lwowski,[10,11] working with *cis*- and *trans*-4-methylpentene-2, obtained markedly different product distributions at low substrate concentrations. They assumed, however, that these distributions would be identical at infinite dilution.

Scheiner[99] has subjected *cis*- and *trans*-1,5-diphenyl-4-methyltriazolines (54 and 55) to benzophenone-sensitized photolysis (Table 1.3.10).

Conformational equilibrium has not been reached: *cis*- and *trans*-triazolines give slightly different product distributions; and, more importantly, a predominance of the thermodynamically



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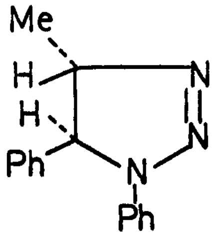

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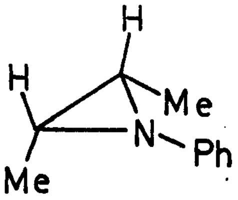

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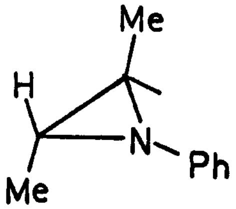

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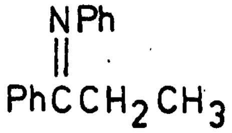


$\mathrm{Ph}\overset{\overset{\mathrm{NPh}}{\|}}{\mathrm{C}}\mathrm{CH_2CH_3}$

(58)

Triazoline	*cis*-aziridine (56) yield %	*trans*-aziridine (57) yield %	Imine (58) yield %
(54)	60	36	4
(55)	54	42	4

TABLE 1.3.10

BENZOPHENONE-SENSITIZED PHOTOLYSIS OF TRIAZOLINES 54 AND 55

less-stable *cis*-aziridine (56) is obtained in each case. Scheiner has briefly commented that this may reflect rate differences in the cyclization process. However, because of non-bonded interactions in the products, the activation energy for cyclization to the *cis*-aziridine should be greater than for the *trans*-aziridine (cf. page 79). Closure to the *cis*-product should then be less favoured; and this, in addition to a preference for a *transoid* diradical should lead to a marked preponderance of the *trans*-product.

1.4. REACTION OF CARBETHOXYNITRENE WITH CIS- AND TRANS-4-METHYLPENTENE-2

Since the completion of work described in Section 1.3, McConaghy and Lwowski[10,11] published detailed analyses of the results of addition of carbethoxynitrene to the isomeric 4-methylpentenes-2. Some of these results had formed part of a preliminary note.[100] Because they have reached some conclusions which, we believe, are surprising, their results will be discussed here at some length.

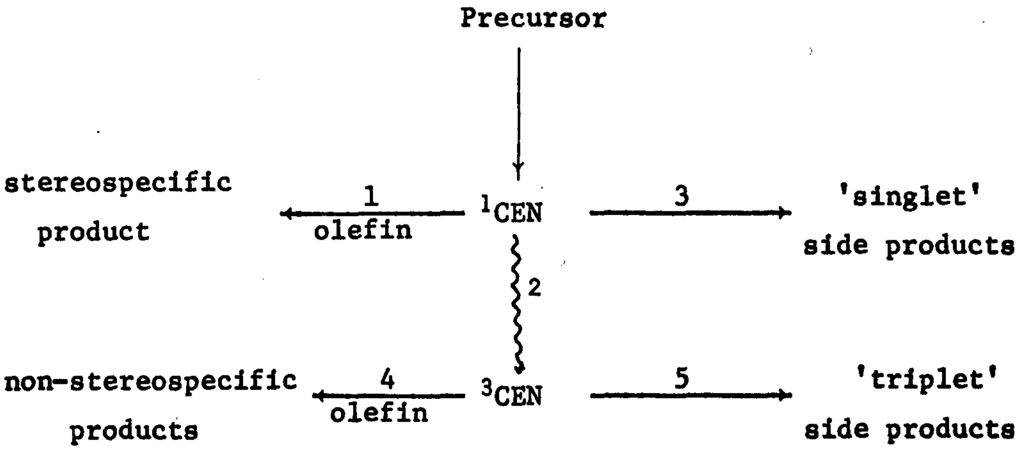
Carbethoxynitrene was generated by reaction of *N*-*p*-nitrobenzenesulphonoxyurethane with triethylamine[10] and by thermolysis[11] and photolysis[11] of ethyl azidoformate. The results are shown in Table 1.4.1.

[olefin] (mole %)	log [olefin]	% *trans*-aziridine		
		α-elim. 35°	thermolysis 100°	photolysis 38°
100	2.00		14	26
33	1.52	7.8	18	28.5
10	1.00	17.5	33	35
5	0.70	26	41	43
3.3	0.52	34	46	
2.5	0.40	37.5		50
1.5	0.17	43	51	54.5
1.00	0.00		54	

TABLE 1.4.1

REACTION OF CARBETHOXYNITRENE WITH *CIS*-4-METHYLPENTENE-2

By a rather indirect series of calculations, these workers concluded that the triplet nitrene, on reaction with *either cis-* or *trans*-olefin, leads to a 20:80 mixture of *cis-* and *trans*-aziridines. On this basis, they estimated the proportion of triplet carbethoxynitrene present at each substrate concentration. Their modified reaction scheme[10] is shown:



Scheme 1.4.I

A steady-state approach yielded the relationship:

$$\frac{T}{S} = \frac{k_2}{k_1}\,[\text{olefin}]^{-1} ,$$

where T represents the amount of aziridine products formed from triplet nitrene and S the amount arising from the singlet form.

Treatment of results obtained from α-elimination experiments (Table 1.4.2) revealed that a plot of T/S against $[\text{olefin}]^{-1}$ was linear only for [olefin] above 3 mole %. Better linearity, however, was obtained when side reactions of the triplet nitrene were considered: k_5/k_4 was taken as 0.015 and T/S plotted against $\{[\text{olefin}] + k_5/k_4\}^{-1}$.

k_5/k_4 is a measure of the proportion of triplet carbethoxynitrene undergoing reactions other than aziridine formation. Because yields of the low-concentration thermolysis reactions are much better than those obtained from α-elimination, the triplet nitrene must react with species present only in the α-elimination system. It is likely, therefore, that these side reactions are bimolecular; so k_5/k_4, being a ratio of second-order rate constants, truly reflects the relative rates of reactions 4 and 5.

The α-elimination experiments show that, as [olefin] decreases from 33 to 1.5 mole %, the absolute yield of aziridines drops from 57 to 24%. This suggests that k_5/k_4 is approximately 1.4 [=(57-24)/24]. The value of the ratio actually chosen was 0.015. It is difficult to understand how such a low value could explain the sharp drop-off in aziridine yields. Moreover, because thermolysis of ethyl azidoformate afforded better aziridine yields at low concentrations, k_5/k_4 (thermolysis) should be lower than before. The value chosen (0.03 to 0.04), however, was *higher*.

Results of photolysis of ethyl azidoformate in solutions of *cis*-4-methylpentene-2 were subjected to the same method of analysis. Assuming $k_5/k_4 = 0.01$, the plot was linear with an intercept of T/S = 0.44. The conclusion was that approximately one-third of the nitrene was produced *initially* in the *triplet* state.

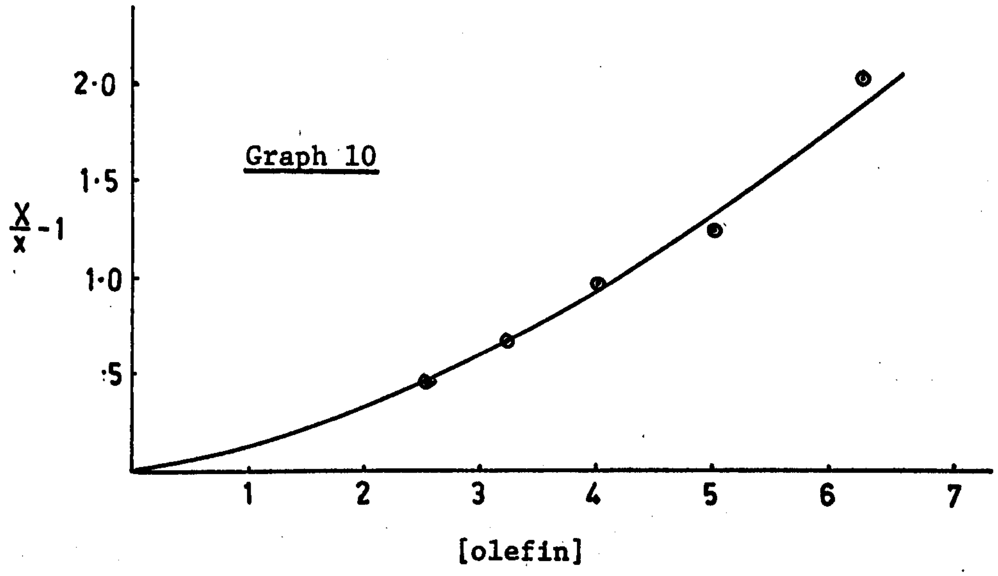
For reasons outlined in Section 1.3, we believe that these workers' basic assumption is incorrect. The composition of the aziridine mixture produced by the triplet nitrene is *not* the same for both *cis*- and *trans*-olefins. The diradical intermediate does *not* reach conformational equilibrium. Moreover, their product distributions (from *cis*-olefin) strongly imply a limiting proportion of *ca.* 55% *trans*-aziridine.

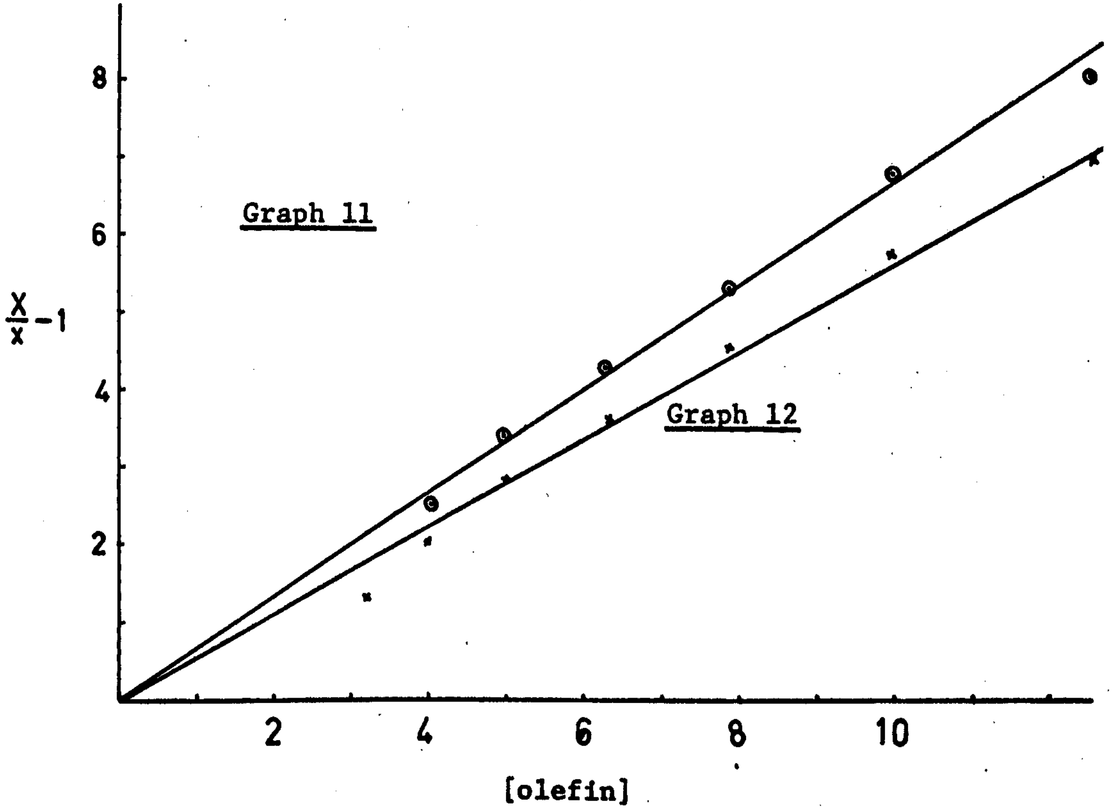
This proportion of 'wrong' isomer was assumed correct and out kinetic analysis (page 77) applied. The results are tabulated and the resultant graphs shown.

log [olefin]	[olefin]	α-elimination		thermolysis		photolysis	
		% trans aziridine	$(\frac{X}{x} - 1)$	% trans aziridine	$(\frac{X}{x} - 1)$	% trans aziridine	$(\frac{X}{x} - 1)$
0.4	2.5	38	0.45				
0.5	3.2	33	0.67	46.5	0.21	48.5	0.13
0.6	4.0	28	0.97	44	0.25	46	0.20
0.7	5.0	23	1.24	41	0.34	43	0.28
0.8	6.3	18	2.05	38.5	0.43	40.5	0.36
0.9	7.9			36	0.53	38	0.45
1.0	10.0			33	0.67	35	0.57
1.1	12.6			30.5	0.80	32.5	0.69

TABLE 1.4.2

REACTION OF CARBETHOXYNITRENE WITH *CIS*-4-METHYLPENTENE-2


Graph 10
$\frac{X}{x}-1$
2·0
1·5
1·0
·5
1
2
3
4
5
6
7
[olefin]


Graph 11
Graph 12
$\frac{X}{x}-1$
8
6
4
2
2
4
6
8
10
[olefin]

Graphs 11 and 12 show excellent linear relationships. Graph 10, however, is distinctly non-linear and requires comment.

McConaghy and Lwowski[10,11] made the steady state assumption that $d[^3CEN]/dt = 0$ and required, therefore, that they give explicit consideration to side reactions of the triplet nitrene. Our approach involves no such formal assumption but does assume that all triplet nitrene reacts to form aziridines. That this is not so is clear from the decrease in aziridine yields as [olefin] is lowered. For this reason detailed kinetic analysis of the α-elimination system seems of little value.

The other workers were concerned to explain why the stereospecificity of addition of carbethoxynitrene to 4-methylpentene-2 is markedly lower in photolysis than α-elimination experiments. As has been pointed out, k_5/k_4 (α-elim.) seems to be *ca.* 1.4. That is, *ca.* 60% of triplet nitrene is being diverted to formation of non-aziridine products. The *cis-/trans*-aziridine ratio therefore does not accurately indicate the singlet/triplet nitrene ratio and the apparent difference in stereospecificity is misleading.

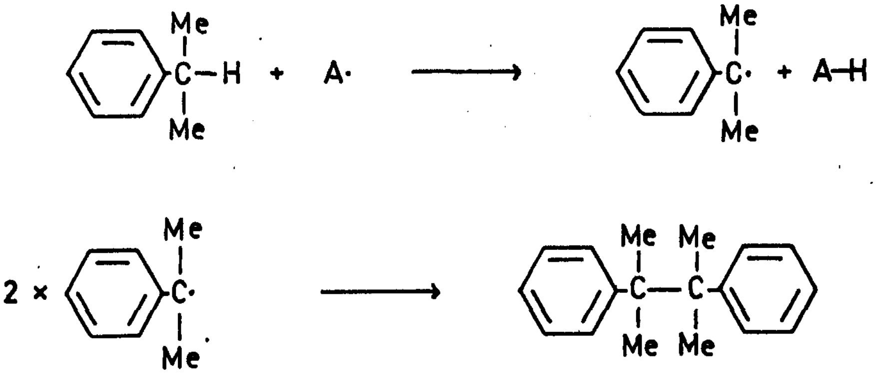
The American workers' conclusion that photolysis of ethylazidoformate gives rise directly to some triplet nitrene would provide an explanation for this difference *if* the difference were real. Our kinetic analysis, however, suggests that the nitrene, as generated, is in no way different from that obtained by α-elimination or photolysis. There are further indications that this partial generation in the triplet state cannot occur (see Section 1.6).

Comparison of the slopes of Graphs 11 and 12 shows that, while $k_1/k_2 = 0.055$ at 38°, the ratio increases to 0.067 at 100°, i.e. the proportion of triplet nitrene operating in a system *decreases* with increased temperature. It seems, therefore, that the activation energy for intersystem crossing is *less* than that required for addition of the singlet nitrene to 4-methylpentene-2. Intersystem crossing, however is energetically *more* demanding than singlet carbethoxynitrene addition to *cis*- and *trans*-butene-2; so *cis*-4-methylpentene-2 must be less susceptible to nitrene addition than either butene-2. This difference in reactivities can be explained in terms of the bulk of the *iso*propyl group of 4-methylpentene-2.

1.5. TRIPLET CARBETHOXYNITRENE

REACTION OF ETHYLAZIDOFORMATE WITH CUMENE

Cumene readily donates hydrogen atoms to suitable free radicals, producing cumyl radicals which dimerize with high efficiency to bicumyl[e.g. 101-104] which can readily be isolated or estimated by vapour phase chromatography (v.p.c.), i.e.



Thermal (*a*) and photochemical (*c*) decomposition of ethyl azidoformate in cumene led to modest yields of bicumyl (Table 1.5.1). V.p.c. revealed an unresolved mixture of other products. These were not studied in detail, but it is likely that they were formed by attack of carbethoxynitrene on the aromatic ring and methyl groups of cumene.

The singlet nitrene is believed incapable of effecting hydrogen abstraction (see p. 12). The active species may be excited (triplet) azide or triplet nitrene, each of which is

Code	Mole % ethyl azidoformate	Solvent	Mode of decomposition	Mole bicumyl per mole of azide
a	1	cumene	Δ, 132°	0.11
b	1	cumene + 10% $(CHCl_2)_2$	Δ, 132°	0.10
c	1	cumene	hν, 120 hr	0.12
d	1	cumene	hν, 120 hr (+ PhCOMe)*	0.37
e	0	cumene	"	0.05

* (moles azide):(moles PhCOMe) = 1:1

TABLE 1.5.1

DECOMPOSITION OF ETHYL AZIDOFORMATE IN CUMENE

expected to display 'radical' reactivity. The close similarity of the yields of bicumyl from thermolysis and photolysis makes the former alternative unlikely; but sensitized photolysis was undertaken in order to study the properties of triplet ethyl azidoformate.

A cumene solution of ethyl azidoformate and sensitizer (each 1 mole %) was irradiated through thick Pyrex walls. Benzophenone (E_T = 68.5 kcal)[105] was ineffective as a sensitizer; but acetophenone (E_T = 73.6 kcal)[105] brought about nitrogen evolution, giving a modest yield of bicumyl (Reaction *d*). Triplet acetophenone is able to abstract some hydrogen atoms from cumene (Reaction *e*), but the yield is much higher in the presence of the azide. The yield, too, is much higher than those obtained on thermal and direct photochemical decomposition of the azide.

Acetophenone-sensitized decomposition of the azide therefore more efficiently produces species which are able to abstract hydrogen atoms. But this evidence still does not permit assignment of this property to triplet azide or triplet nitrene. Further evidence must therefore be considered:

(i) Reaction *d* led to very little attack on the aromatic ring of cumene (as evidenced by v.p.c.).

(ii) Acetophenone-sensitized photolysis of ethyl azidoformate in the presence of naphthalene leads to only trace amounts of 1-naphthylurethane, the major product of reaction of carbethoxynitrene with the hydrocarbon.

(iii) Photosensitized decomposition of the azide in *cis*- and *trans*-butene-2 and *cis*-4-methylpentene-2[11] affords no aziridines.

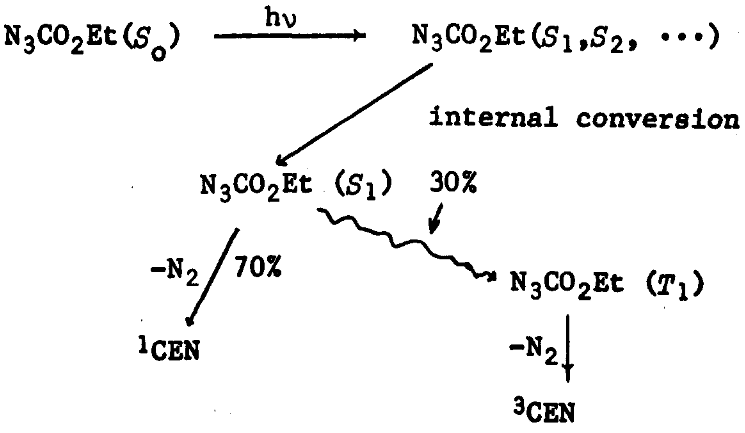
(iv) Acetophenone-induced decomposition of ethyl azidoformate in cyclohexene leads to ethyl carbamate as the main product.[47]

It has recently been reported[56] that only *singlet* carbethoxynitrene reacts with benzene, whereas both singlet and triplet forms add to the double bond of cyclohexene. Results (i) and (ii) therefore exclude the formation of singlet carbethoxynitrene: failure to add to the olefins excludes both singlet and triplet species as intermediates in Reaction *d*. It is likely, then, that triplet acetophenone raises the azide to a triplet state in which it is able to abstract hydrogen atoms but unable to decompose to the triplet nitrene.

On the other hand, thermolysis of ethyl azidoformate *does* produce a species with radical character. This cannot be the triplet azide because spin conservation is strictly observed in thermal reactions at moderate temperatures. It is concluded, then, that there *does* exist a triplet (diradical); nitrene, and because spin conservation requires that the nitrene be formed as a singlet, intersystem crossing to the triplet state must take place.

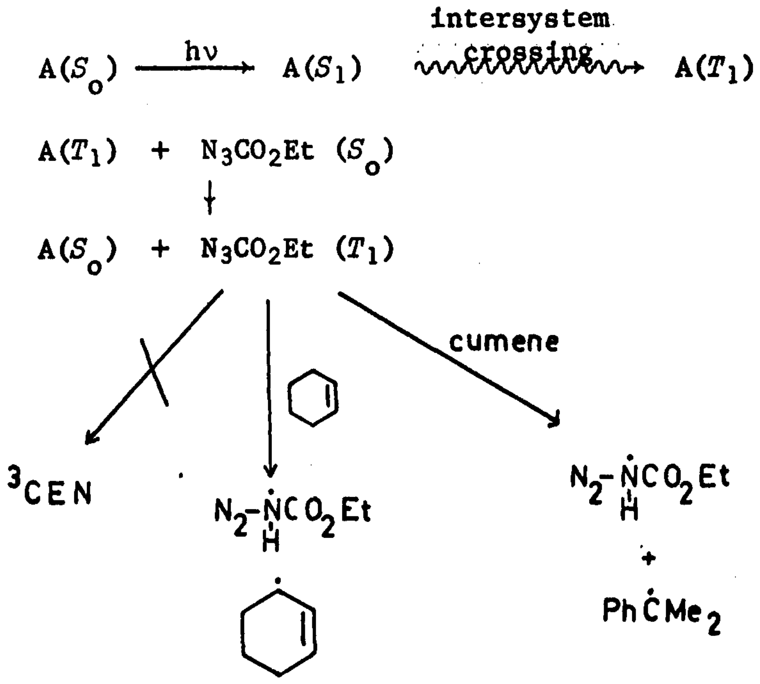
Intersystem crossing is believed to be susceptible to an external 'heavy-atom' effect (see page 85). Addition of an inert halogen compound, however, produced no significant change in bicumyl yield (Reaction *b*).

McConaghy and Lwowski[11] claim that direct photolysis of ethyl azidoformate produces both singlet and triplet nitrenes in the ratio 7:3. For this to occur, the lowest excited singlet (S_1) state must have a sufficient lifetime to allow intersystem crossing to the T_1 state to occur (Scheme 1.5.I).



Scheme 1.5.I

Because intersystem crossing is likely to take place only from S_1, the triplet azide so produced would be T_1 (i.e. in the lowest triplet level). Now, acetophenone seems to possess just enough triplet energy to excite ethyl azidoformate; so it is unlikely that the azide is raised to a triplet level above T_1. (Even if excitation to, say, T_2 did take place, internal conversion to T_1 is expected to be extremely rapid.). This T_1 azide has been shown capable of hydrogen abstraction but incapable of decomposition to triplet carbethoxynitrene and therefore Scheme 1.5.I cannot be correct. Likely pathways for photosensitized decomposition of ethyl azidoformate are shown in Scheme 1.5.II, where A represents the sensitizer.



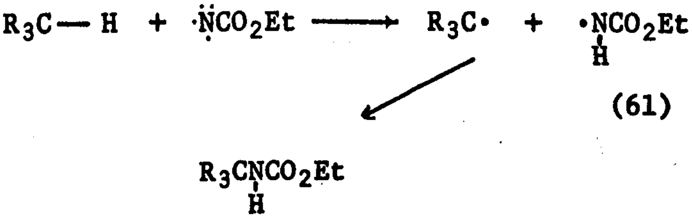
Scheme 1.5.II

THE REACTION OF TRIPLET CARBETHOXYNITRENE WITH CARBON-HYDROGEN BONDS

It has been maintained that, while singlet carbethoxynitrene inserts into aliphatic C-H bonds, the triplet form cannot. This argument was originally presented on the basis of the reactions of triplet methylene.[21] More recently, however, results of competition experiments have been offered as evidence.[56]

Carbethoxynitrene (produced by α-elimination) was allowed to react with equimolar mixtures of benzene and cyclohexane at various concentrations in methylene chloride.[56] At high dilution, the yields of both *N*-carbethoxyazepine and cyclohexylurethane were very low. When a similar competitive experiment was carried out using benzene and cyclohexene, the yields of the azepine dropped more sharply than those of the aziridine (7-carbethoxy-7-azabicyclo[4.1.0]heptane, 59). The conclusion was that, because triplet nitrene is more in evidence at low substrate concentrations, only the singlet form can react with benzene and aliphatic C-H bonds.

At first, this conclusion seems puzzling. An abstraction radical recombination process should be possible:

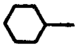
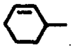


$$R_3C{-}H + \cdot\overset{\cdot}{\underset{\cdot}{N}}CO_2Et \longrightarrow R_3C\cdot + \cdot\underset{H}{N}CO_2Et$$

$$\swarrow$$

$$R_3C\underset{H}{N}CO_2Et$$

(61)

The extent to which such hydrogen abstraction can occur depends on the nett enthalpy change. DH^{o} ($EtO_2CN — H$) = *ca.* 103 kcal/mole while DH^{o} ( H) = *ca.* 95 kcal/mole and DH^{o} ( H) = *ca.* 85 kcal/mole.[109] Hydrogen-atom transfer from aliphatic and allylic methylene groups is therefore exothermic and expected to take place; and transfer from cumene and cyclohexene *does* take place. The formation of bicumyl and 3,3'-bicyclohexenyl, however, suggests that combination of a stabilized hydrocarbon radical with a urethanyl radical is not efficient.

Dilution Studies.

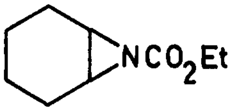
In order to study the effect of an increasing proportion of triplet carbethoxynitrene, ethyl azidoformate was decomposed in solutions of cyclohexane in 'Freon' TF at 80°. The absolute yields of urethane products are shown in Table 1.5.II.

[cyclohexane]* initial (mole %)	[cyclohexane] corrected (mole %)	Yield % $C_6H_{11}NHCO_2Et$	Yield % NH_2CO_2Et
20	21.8	57	11
18	19.6	42	16
16	17.4	43	15
14	15.3	43	12
12	13.1	41	11
8	8.8	36	9
4	4.4	26	<5
2	2.1	19	<2
1	1.0	10	<1

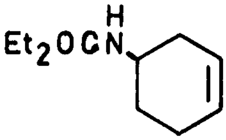
* [ethyl azidoformate] = [cyclohexane]/14

<u>TABLE 1.5.II</u>

Lwowski and Mattingly[47] have studied the photochemical decomposition of ethyl azidoformate in neat cyclohexene. Among other products, 59 and 60 are formed in the ratio 17:1, i.e. one carbon-carbon double bond is 17 times more reactive towards (singlet) carbethoxynitrene than four aliphatic carbon-hydrogen bonds. Therefore the double bond of an olefin is expected to be *approximately* 6 times more reactive than cyclohexane (12 C-H bonds). It follows that cyclohexane, at a concentration of 20 mole %, is equivalent in reactivity to *ca.* 3 mole % of butene-2. But, at this concentration of olefin, over 80% of the nitrene reacts in the triplet state; so the moderate yields of cyclohexylurethane shown in Table 1.5II result largely from reaction of the triplet nitrene.



(59)



(60)

Bond Insertion by Triplet Nitrenes.

When two radicals are separated by an infinite distance, their spins should not be correlated; but there must be a distance of approach within which there is a significant energy difference for radical pairs with parallel and antiparallel spins.[212] If the spins are parallel (i.e. 'singlet pair') an incipient σ-bond exists between the radicals: a 'triplet pair' has incipient antibonding character and must be of higher energy.

Abstraction of a hydrogen atom from an alkane by a triplet nitrene produces a 'triplet' radical pair:

$$\mathrm{R{-}H} \quad + \quad 1\,\overset{1}{\underset{\cdot\cdot}{\mathrm{N}}}\mathrm{CO_2Et} \longrightarrow [\mathrm{R}1 \quad + \quad 1\,\overset{\mathrm{H}}{\mathrm{N}}\mathrm{CO_2Et}]$$

(61)

Quite clearly, unless spin inversion takes place, there can be no bonding between these radicals.

Now, because the alkane and nitrene must be very close for hydrogen transfer to occur, the nascent radical pair must be formed at a point such as A (Fig. 1.5.1), high on the triplet energy profile. It is likely, then, that the strong Pauli repulsion would cause the radicals to burst free of the solvent cage. Each separated radical can then link with a complementary radical, with which it forms a

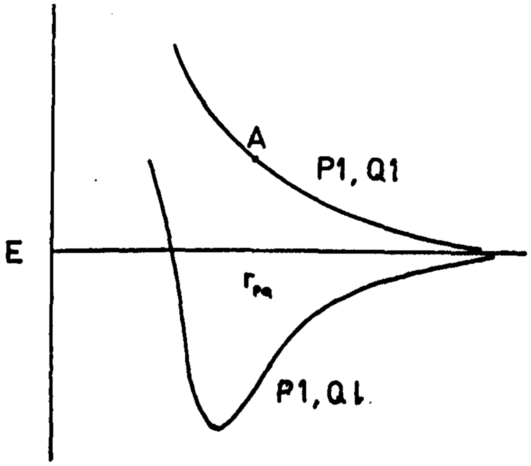


Fig. 1.5.1

'singlet pair', to form the insertion product. The time elapsing before such a favourable encounter depends on the concentrations of the radicals.

The methanyl radical (61) is highly reactive and, unless coupling with a cyclohexyl radical is favoured, will abstract a further hydrogen atom from the medium. Therefore, as the concentrations of the reactants are lowered, side reactions of the urethanyl radical become more important, with a resultant lowering in the efficiency of the insertion process.

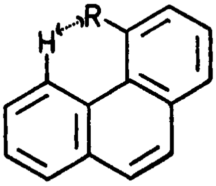
It might have been expected that dilution of the substrate would give an increased yield of ethyl carbamate. In fact yields of both urethanes decrease rapidly at [cyclohexane] below *ca.* 10 mole %. Possibly this is due to increased favourability of side reactions of the triplet nitrene.

1.6. PREPARATION OF REFERENCE COMPOUNDS

REACTION OF ETHYL AZIDOFORMATE WITH AROMATIC HYDROCARBONS

In almost every case, products were identified by comparison (i.r., u.v. spectra) with specimens obtained by treatment of the corresponding arylamines with ethyl chloroformate. 4-Phenanthrylurethane, however, could not be prepared.

A substituent in the 4-position of phenanthrene interacts strongly with the 5-hydrogen (69). Any reaction which tends to increase the bulk of this substituent is therefore energetically unfavourable (ΔH^{o} positive). The activation energy (E_a) is then expected to be high (Fig. 1.6.1).



(69)

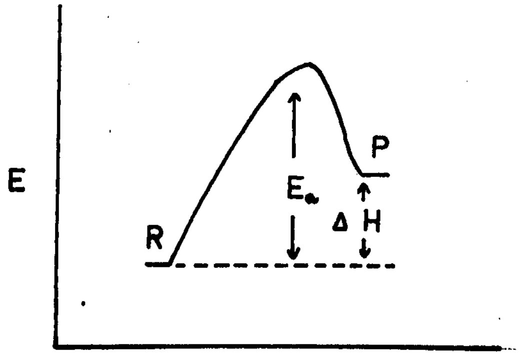


Fig. 1.6.1

For this reason it was not possible to convert 4-phenanthrylamine to the urethane. Moreover, prolonged boiling of 4-phenanthryl isocyanate in ethanol with *p*-toluenesulphonic acid or sodium ethoxide gave only unchanged starting material.

Arylurethanes are very resistant to hydrolysis: none of the authentic samples could be satisfactorily reconverted to the amine. Concentrated hydrochloric acid/acetic acid caused extensive tarring and sodium hydroxide/dimethyl sulphoxide was without effect. For this reason, the suspected 4-phenanthrylurethane could not be related to 4-phenanthrylamine.

REACTION OF ETHYL AZIDOFORMATE WITH BUTENE-2

The preparation of *cis*- and *trans*-1-carbethoxy-2,3-dimethylaziridines from the epimeric butane-2,3-diol acetates is tedious and time-consuming. Decomposition of ethyl azidoformate in *cis*- and *trans*-butenes-2 was therefore carried out on a preparative scale in the hope that the aziridines might be obtained in reasonable isomeric purity. Distillation of the crude products gave the expected compounds heavily contaminated with ethyl carbamate which was readily removed by extraction with water. Careful fractionation of the distillates then gave *cis*-1-carbethoxy-2,3-dimethylaziridine (94% isomeric purity) and *trans*-1-carbethoxy-2,3-dimethylaziridine (91% isomeric purity) as judged by v.p.c.

CHAPTER 2

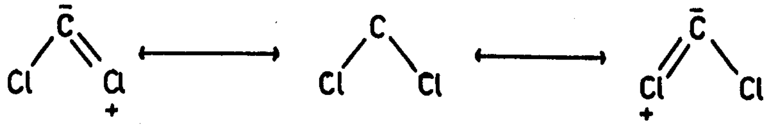
REACTIONS OF CARBENES WITH ANTHRACENE

2.1. THE MODIFICATION OF CARBENE REACTIVITY

In Chapter 1 it was pointed out that a carbene may exist in a singlet or triplet electronic configuration. This review will give brief consideration to the effects of substituents on the relative stabilities and reactivities of the two forms.

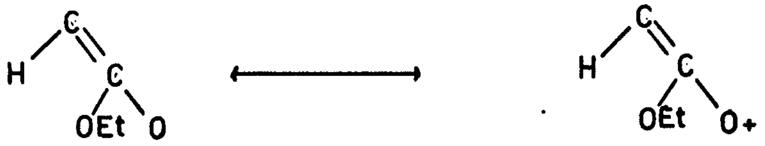
SUBSTITUENT EFFECTS

A singlet carbene is generally considered to be a bent species requiring sp^2 hybridization at the central carbon.[19] Two sp^2 orbitals are engaged in σ-bonds which the third hybrid orbital contains the non-bonding electron pair. The vacant p-orbital confers electophilic character, and therefore, instability, on the species. It follows, then, that the carbene may be stabilized by overlap of this p-orbital with a suitable p- or π-orbital in a substituent. In this way, mesomeric stabilization of halocarbenes is achieved with resultant decrease in electrophilicity, e.g. dichlorocarbene (70).



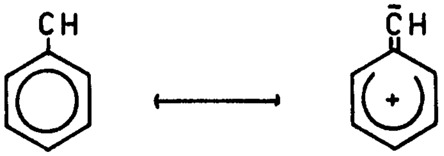
(70)

On the other hand, although possessing the correct symmetry, the π-orbital of a carbonyl group cannot effectively stabilize a singlet carbene, e.g. carbethoxycarbene (71), because the resonance hybrid requires a contribution from the high-energy dipole 72.



(71) (72)

Furthermore, the strong inductive (-I) effect of the ester group serves to destabilize the carbene centre by enhancing its electron deficiency. Singlet arylcarbenes should be subject to some stabilization, e.g.



It is therefore possible to group singlet carbenes according to the influence of substituents on their stability.

Destabilized Singlet Carbenes	Stabilized Singlet Carbenes
$CHCO_2Et$	CHPh
$C(CO_2Et)_2$	CPh_2
$C(CN)_2$	CHCl
$C(CF_3)CN$	CCl_2
$C(CF_3)_2$	

Triplet carbenes can be stabilized by suitably-disposed p- or π-orbitals *regardless* of the electronegative character of the substituent groups, e.g. propargylene (73).[111]

$$H-C-C\equiv C-H \longleftrightarrow H-C\equiv C-C-H$$

(73)

ELECTRONIC CONFIGURATIONS OF GROUND STATES

On the basis of Skell's first hypothesis (page 7), it seems that methylene,[112] dicyanocarbene,[113] diphenylcarbene,[114] phenylcarbene[115] and fluorenylidene[116] have triplet ground states. Dichlorocarbene, on the other hand, is the only carbene *known* to be a ground-state singlet.[117] Nothing is known of the spin multiplicities of the other carbene species.

ELECTRONIC CONFIGURATIONS OF REACTING CARBENES

As discussed on page 10, unless produced by sensitized photolysis, a carbene is generated in the singlet state. If the ground state, too, is a singlet, there is no ambiguity; but if the ground state has a triplet configuration, the species may react as a singlet and/or triplet.

There is, therefore, a competition between reaction of the singlet with the substrate and intersystem crossing to the triplet state.

If the singlet form is destabilized by substitution with electronegative groups, reaction of the singlet may be more favoured than intersystem crossing. On the other hand, diphenylcarbene is stabilized as a singlet even though its ground state has a triplet configuration.[118] In this case reaction with the substrate is slow enough to allow intersystem crossing to compete. Addition to double bonds is therefore non-stereospecific.[114]

GENERAL REACTIONS OF CARBENES

1. *Insertion in Carbon-Hydrogen Bonds.*

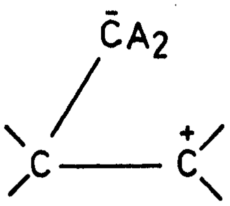
Insertion of a singlet carbene into a C-H bond is considered to be a concerted 'no-mechanism' process (see page 9). This attack on the highly-localized electron cloud of a σ-bond requires that the (singlet) carbene possess marked electrophilic character. Stabilization, therefore, of the species decreases its reactivity and increases the selectivity of bond insertion. In fact, dichlorocarbene is so stabilized as to be incapable of insertion into aliphatic C-H bonds.[122]

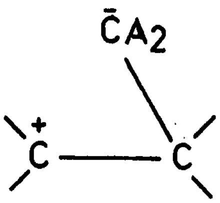
A triplet carbene is capable of hydrogen atom abstraction and an overall insertion process is possible as a result of coupling of a 'singlet pair' of complementary radicals. The process, however, is inherently less efficient than insertion by a singlet species (see page 107). The ease of the initial abstraction is highly dependent on the nett enthalpy change for the process, and therefore the weakest C-H bonds are preferentially attacked.

2. *Addition to Olefins.*

Because a π-electron cloud is much more diffuse and polarizable than electrons in a σ-bond, it is more susceptible to electrophilic attack. For this reason, singlet carbene addition to a double bond occurs more readily than bond insertion.

A singlet carbene is believed to add to an olefin by a concerted process. There is no opportunity for rotation about the C-C bond and therefore the addition is stereospecific (see page 105). It does not seem meaningful to consider two-step addition because the dipolar intermediates (73 and 74) differ from the 'no-mechanism' transition state (75) only in the degree of charge separation.


(73)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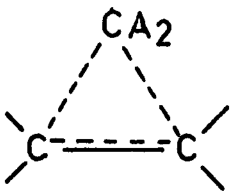

(75)

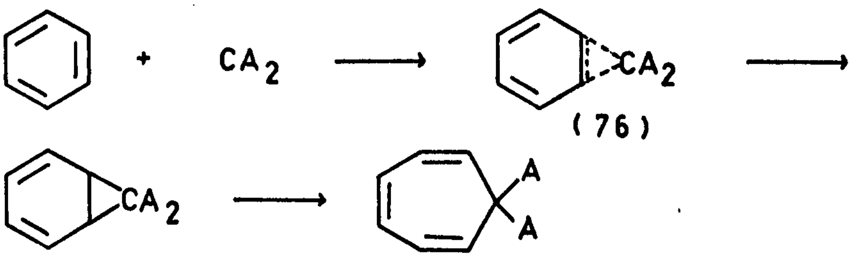
In fact 73 and 74 are contributing forms of the resonance hybrid 75.

The addition of a triplet carbene involves two steps: the triplet diradical initially formed must undergo spin inversion before ring closure can occur.

3. *Reaction with Aromatic Carbon-Carbon Bonds.*

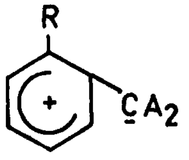
Because the π-electron density at any point in an aromatic hydrocarbon is always less than that in a simple olefin, reaction with a singlet carbene is less favoured. Stabilized singlets therefore add inefficiently or not at all.

By analogy with addition to an olefin, a 'no-mechanism' scheme is proposed, i.e.

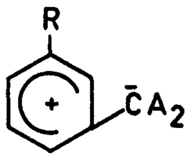


(76)

But in this case the stabilized ionic forms 77 and 78 will contribute more substantially to the transition state 76.



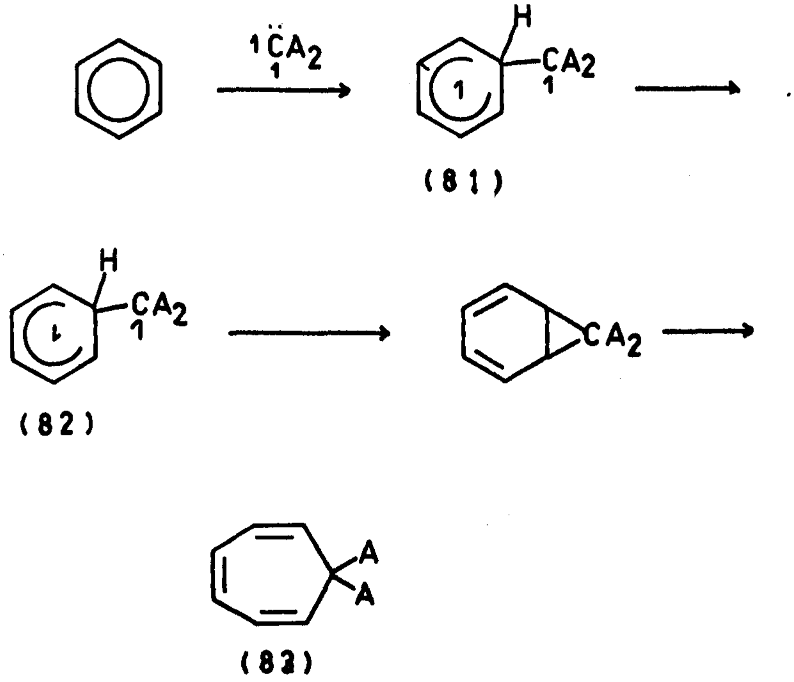
(77, R=H)
(79, R=OMe)



(78, R=H)
(80, R=OMe)

If there is present a substituent which is capable of mesomeric stabilization (+M) of a positive charge in the ring, these canonical forms (e.g., 79 and 80) will differ in energy and therefore contribute unequally to the transition state. In such a case the carbene will approach the C-C bond asymmetrically so that true 'double-bond' attack will not occur.

Reaction of a triplet carbene with an aromatic system *must* occur in two steps. A diradical σ-complex is therefore indicated; but because spin conservation is likely to be observed, this intermediate (81) should have a triplet configuration. Formation of 81 should therefore be energetically unfavourable (due to Pauli destabilization) and rapidly reversible. The rate of intersystem crossing to 82 is not known, but probably it is sufficiently low to provide a substantial impediment to formation of 83. Reaction of a



triplet carbene with an aromatic substrate is therefore expected to be a highly inefficient process.

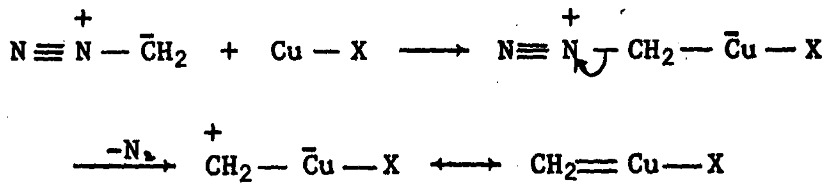
The more important classes of carbenes will now be discussed in terms of the effect of substituents on reactivity and electronic stability. Special attention will be given to reactions with aromatic substrates.

METHYLENE

Photolysis or thermolysis of diazomethane or ketene gives rise to the species in the singlet state; but the ground state is known to have a triplet configuration.[112,123] Methylene, generated in solution, adds stereospecifically to olefins[18,19,124,125] and inserts indiscriminately into the C-H bonds of saturated hydrocarbons.[126] Reaction of the metastable singlet form is therefore indicated.

Methylene, generated by photolysis in either liquid or vapour phase, reacts with benzene to give toluene and cycloheptatriene.[127,128] (It is interesting that earlier workers[129] claimed the isolation of norcaradiene but obtained no toluene.) Nothing is known of the electronic state of the methylene which reacts with the benzene, but the moderate yields of products (*ca.* 40% total) *suggest* the operation of a singlet.

The catalysed decomposition of diazomethane in the presence of aromatic substrates has been extensively studied.[130-137] The most effective catalysts were cuprous chloride, cuprous bromide and cupric chloride. In an early paper, Müller and Fricke[130] proposed that benzene suffers electrophilic attack by an 'inverse ylide' of methylene (84).

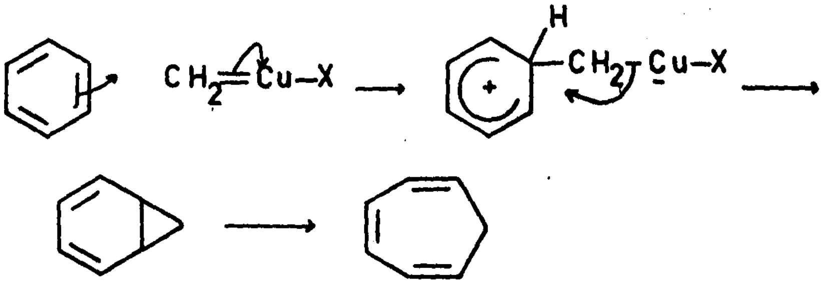


$$\overset{+}{N}\equiv N-\bar{C}H_2 + Cu-X \longrightarrow N\equiv\overset{+}{N}-CH_2-\bar{C}u-X$$

$$\xrightarrow{-N_2} \overset{+}{C}H_2-\bar{C}u-X \longleftrightarrow CH_2=Cu-X$$

(84)

This ylide is stabilized by overlap of the vacant p-orbital of the (trigonal) methylene moiety with a filled dsp^2 copper orbital. The reaction with benzene is depicted in Scheme 2.1.I.



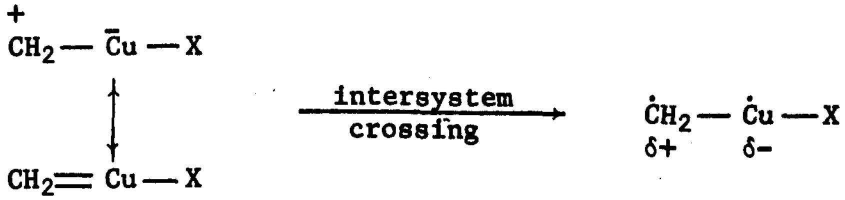
Scheme 2.1.I

Monosubstituted benzene can give rise to three isomeric cycloheptatrienes and *provided* bond isomerisation does not occur, the proportions of these products are an indication of the susceptibility of the bonds to methylene addition. The results obtained with anisole and for alkyl- and halo-substituted benzenes[132] cannot be convincingly explained in terms of electrophilic attack (cf. ref. 138a). Furthermore, competition experiments by Müller *et al.*[139] show little variation in the *absolute* reactivities of substituted benzenes, i.e.

$$\begin{array}{ccccccc} \text{PhOMe} & > & \text{PhMe} & \sim & \text{PhH} & > & \text{PhCl} \\ 1.54 & & 1 & & 1 & & 0.25 \quad \text{(Reactivity)} . \end{array}$$

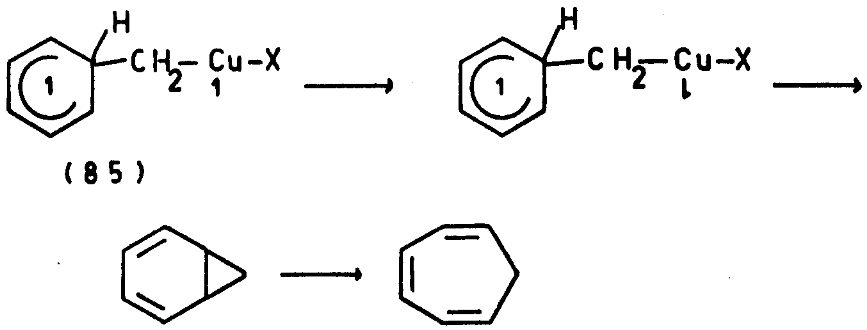
These values are reminiscent of the substrate preferences of the electrophilic *p*-nitrophenyl radical.[140a] Certainly electrophilic attack, producing charge separation in the transition state, is excluded by this result (cf. ref. 138b).

If radical attack does take place, intersystem crossing of the singlet ylide must be more rapid than its reaction with the substrate. Intersystem crossing is 'forbidden' and can take place only when spin quantization is destroyed by spin-orbit coupling. Such spin-orbit coupling is well known in transition metals (e.g. Cu) and therefore intersystem crossing of the methylene ylide may be highly favoured, i.e.



Radical reactivity of the species is therefore not surprising. The electrophilic character may result from slight polarization of the C-Cu bond by the electronegative halogen, X.

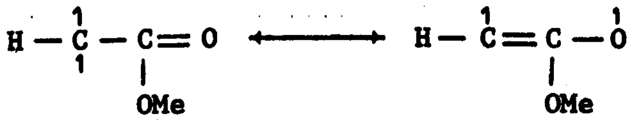
Although it has been argued that the reaction of a triplet carbene with an aromatic substrate is inefficient (page 117), the yields obtained by catalytic decomposition of diazomethane in aromatic solvents are moderate to good. This is probably because of the efficient promotion by copper of intersystem crossing in the diradical σ-complex 85.



(85)

CARBALKOXYCARBENES

Carbomethoxycarbene, in the singlet state, is destabilized by the electron-withdrawing ester group. When generated in neat olefin, the species achieves stereospecific addition,[141] indicating participation of this singlet form. On the other hand, the ester group is able to delocalize an odd electron and therefore stabilize the species in the triplet state, i.e., assuming sp hybridization of the electron-deficient carbon,

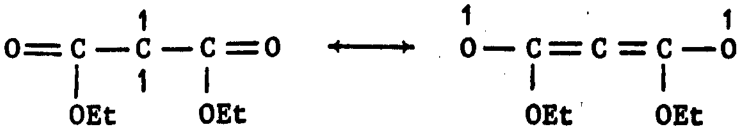


$$H-\overset{1}{\underset{1}{C}}-\underset{\displaystyle OMe}{\underset{|}{C}}=O \longleftrightarrow H-\overset{1}{C}=\underset{\displaystyle OMe}{\underset{|}{C}}-\overset{1}{O}$$

It might be suspected, then, that carbalkoxycarbenes have triplet ground states. Little relevant information is available and studies of the stereospecificity of addition of the carbene at various substrate concentrations therefore merit attention.

Carbethoxycarbene inserts selectively into C-H bonds: the ratio of preference of tertiary and secondary over primary bonds is 3.1:2.3:1.[119] If the species *is* a ground-state triplet this selectivity can be explained in terms of bond energies (page 104).

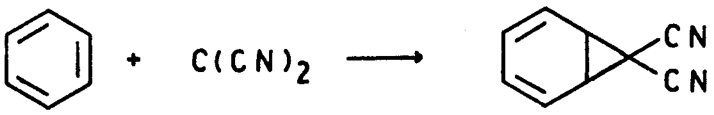
*Bis*carbethoxycarbene is generated as an even more destabilized singlet. It does not, however, react with benzene.[142] This is best explained in terms of extremely rapid intersystem crossing to a highly-stabilized linear triplet form (86) which is unable to react efficiently with benzene.



(86)

DICYANOCARBENE

This species is known to possess a triplet ground state.[12] The metastable singlet form, however, is so destabilized that reaction with substrates can successfully compete with intersystem crossing. Benzene, *p*-xylene and naphthalene therefore afford good yields of adducts,[143] e.g. 87.

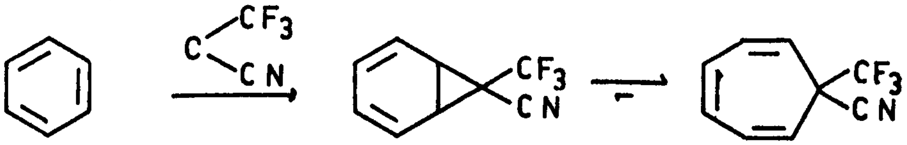


(87)

It is of interest that 87 was the first simple norcaradiene to be isolated.

*BIS*TRIFLUOROMETHYLCARBENE AND CYANOTRIFLUOROMETHYLCARBENE

Both species are generated as highly destabilized singlets which react efficiently with benzene,[144,145] e.g.



The equilibrium 88 $\rightleftharpoons$ 89 is the only known case of norcaradiene cycloheptatriene equilibrium.[145]

ARYLCARBENES

Although phenyl- and diphenylcarbene are stabilized in both singlet and triplet configurations, both species have been shown by e.s.r. studies[118,146] to be ground-state triplets. Accordingly, diphenylcarbene adds non-stereospecifically to olefins;[147] but the small amounts of 'wrong' products obtained when phenyldiazomethane is photolysed in butene-2 solutions[121] suggest that intersystem crossing for this species is quite slow.

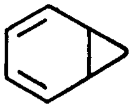
HALOCARBENES

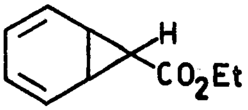
Dichlorocarbene has a singlet ground state[117] and, as such, is highly stabilized. The species adds stereospecifically to olefins[122] but is so feebly electrophilic that aliphatic C-H bonds and benzene are inert towards[122] it. Only highly-activated aromatic systems are attacked by dichlorocarbene, e.g. phenoxide ion (Reimer-Tiemann Reaction) and the indenyl anion.[148]

Chlorocarbene has been less extensively studied. Most reactions reported for it are reactions of an organolithium intermediate.[120] Recently, however, Closs and Coyle have decomposed chlorodiazomethane at -30°.[120,149] The resultant free chlorocarbene inserts into C-H bonds, while the more stabilized dichlorocarbene cannot. Nothing is known of the ground-state configuration of chlorocarbene.

2.2. THE REACTION OF CARBETHOXYCARBENE WITH ANTHRACENE

In 1885 Buchner and Curtius[149] first reported the decomposition of ethyl diazoacetate in an aromatic hydrocarbon (toluene) and further reports followed over a period of almost 40 years.* In all cases the primary products were considered to be derivatives of norcaradiene (90) which displayed varying tendencies to rearrange.


(90)



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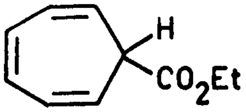

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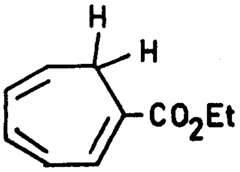

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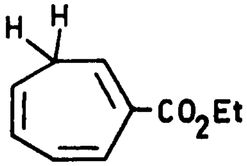

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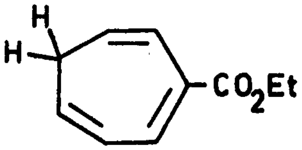

(95)

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* For references to this earlier work, see Ref. 154.

Accordingly, benzene was considered to be converted to the ester 91 which, on alkaline hydrolysis, underwent ring expansion to four isomeric cycloheptatriene acids (92-95).

Alkyl-substituted benzenes gave, in addition to norcaradienes and cycloheptatrienes, derivatives of phenylacetic acid (96) and 2-phenylpropionic acid (97). The reaction was shown to be very

$PhCH_2CO_2H$

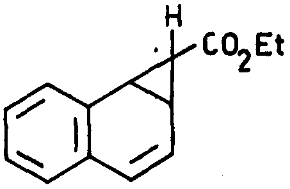
(96)

$PhCH_2CH_2CO_2H$

(97)

sensitive to steric hindrance by substituted groups.[150]

Naphthalene, on the other hand, was converted to 98 which *resists* thermal isomerization to the cycloheptatriene 99.[151,152]



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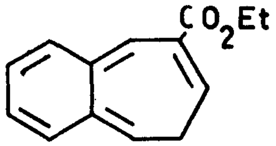
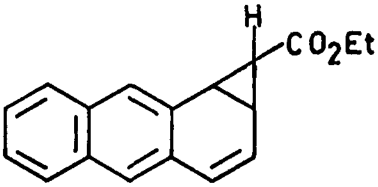


(99)

Addition of the divalent carbon moiety had taken place *only* at the 1,2-bond of the substrate. Moreover, adducts 100-103 were isolated after thermal decomposition of ethyl diazoacetate in the presence of anthracene,[153] phenanthrene,[154] pyrene[153] and 1,2-benzanthracene.[153]

In this respect the reactions of the diazoester paralleled those of ozone and osmium tetroxide. When non-equivalent C-C bonds in an aromatic substrate were available for reaction, these reagents seemed to attack *only* at positions of highest bond order. They therefore behaved as 'double-bond' reagents.[155]



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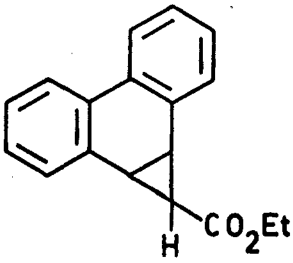

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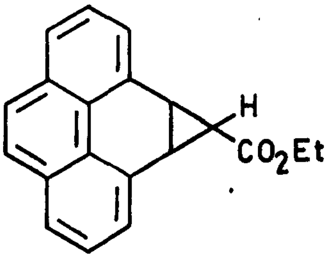

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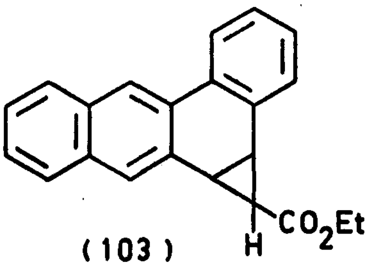


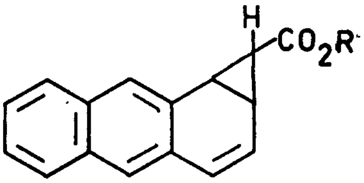
(103)

It has since been realized that thermolysis of diazo compounds gives rise to carbenes which can participate in many different reaction processes. For this reason many reactions of ethyl diazoacetate have been reinvestigated. Simple alkyl- and halo-substituted benzenes are converted to mixtures of cycloheptatriene esters. Steric rather than electronic effects seem to control the orientation of carbene attack;[156,157] and results using dimethylnaphthalenes as substrates demand the same conclusion.[158,159] Furthermore phenanthrene[160,161] and pyrene[153] do not react *solely* at the bonds of highest order. These results cast considerable doubt on the value of diazoacetic ester as a 'double-bond' reagent.

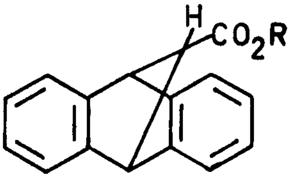
Singlet carbethoxycarbene, being electron-deficient, is able to under take electrophilic attack on the π-electron systems of olefins, acetylenes and aromatic hydrocarbons. It is not clear, however, how this electrophilic activity differs from that of 'normal' electrophilic agents. Specifically, why carbethoxycarbene cannot convert benzene to ethyl phenylacetate is not understood.

Anthracene is extremely susceptible to electrophilic attack at the 9-position whereas 'double-bond' attack at the 1,2-bond is most favoured. It seemed possible, therefore, that any 'normal' electrophilic activity of carbethoxycarbene might lead to products different from that of 'double-bond' attack. For this reason, the reaction of ethyl diazoacetate with anthracene was reinvestigated.

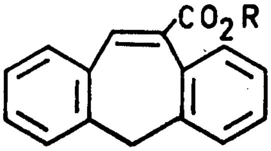
Ethyl diazoacetate was added slowly to a solution of anthracene in decalin.[153] The previously reported product (100)[153] was isolated in yields of 5-10%. On one occasion, however, no 1,2-adduct was obtained; instead trace amounts of 105 were formed. In an effort to isolate larger quantities of 105, a non-hydrolytic work-up was employed. The crude ester mixture, after extraction from unchanged anthracene, was subjected to column chromatography on neutral alumina. In addition to 104, a small quantity of 107 was separated as a sticky semisolid. No 106a was obtained.



(100, R=H)
(104, R=Me)
(104a, R=Et)



(105, R=H)
(106, R=Me)
(106a, R=Et)



(107, R=Et)
(107a, R=Me)

The structures of these products, which were established by nuclear magnetic resonance (n.m.r.) spectrometry (Table 2.2.1), were consistent with the observed infrared and ultraviolet spectra. Furthermore, 106 was found to be identical to an authentic sample (Section 2.4).

These results accord closely with other reports. Catalysed decomposition of diazomethane in the presence of anthracene[136] leads to the adducts 108-110. Moreover, base-induced decomposition of benzaldehyde tosylhydrazone with anthracene[162] affords 111 and 112.

TABLE 2.2.1

(a) Compound 104

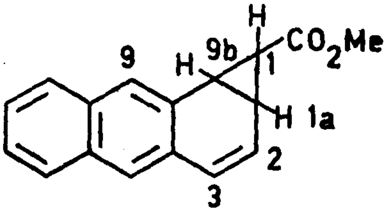
Signal	Proton Count	Position (c/s.)	J (c./s.)	Assignment
triplet	1	63	$J_{1,9_b} = J_{1,1_a} = 3.8$	1-H
multiplet	1	155	$J_{1,1_a} = 3.8$ $J_{1_a,9_b} = 8.8$ $J_{1_a,2} = 4.0$ $J_{1_a,3} = 1.2$	1a-H
doublet of doublets	1	190	$J_{1,9_b} = 3.8$ $J_{1_a,9_b} = 8.8$	9b-H
singlet	3	233	-	ester CH_3
multiplet (AB)	2	384	$J_{1_a,2} = 4.0$ $J_{2,4} = 1.2$ $J_{4,9} = 0.3$	2-H, 3-H
multiplet	6	*ca.* 450	-	aromatics

(b) Compound 106

singlet	3	207	-	ester CH_3
triplet	1	214	$J_{9,11} = J_{10,11} = 1.6$	11-H
doublet	2	283	1.6	9-H, 10-H
multiplet	8	*ca.* 425	-	aromatics

(c) Compound 107

triplet	3	83	8.0	ester CH_3
singlet	2	218	-	5-H_2
quartet	2	260	8.0	ester CH_2
multiplet	8	435	-	aromatics
singlet	1	482	-	11-H



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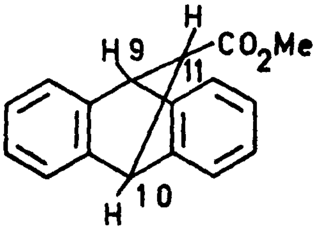

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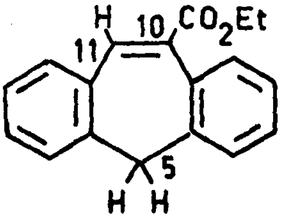

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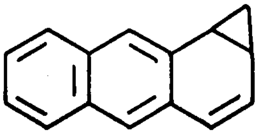

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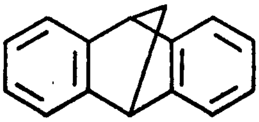

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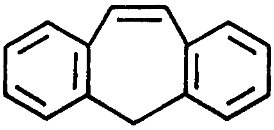

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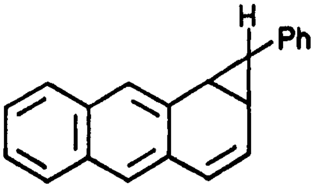

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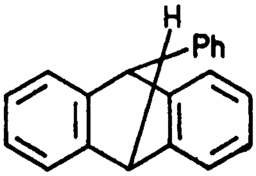


(112)

Comparison of these results, however, is of doubtful advantage. The structure and electronic character of the methylene-cuprous halide complex is not known with certainty; and tosylhydrazones, when treated with base, lead to some cationic species which may react with anthracene.[163]

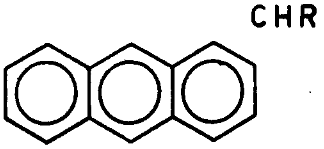
Brown[164] and Badger[155] have used Bond Localization Energy as a criterion to predict sites of 'double-bond' attack in aromatic hydrocarbons. This parameter allows direct comparison of the stabilities of the alternative products of a reaction and, by implication, provides a *relative* measure of the activation energies for the competing reactions. The implication is valid, however, *only* if the reaction profiles have the same general shape and do not cross.[165] It is probably not reasonable to make such an assumption.

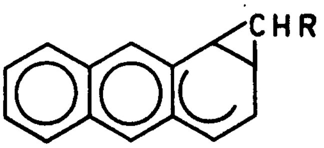
As noted before, 'double-bond' attack on an aromatic substrate involves a hybrid transition state to which two σ-complexes contribute. Various parameters are available for assessment of energies of σ-complexes. For this discussion L_r^+ has been chosen. This Cation Localization Energy is defined[166a] as the π-bonding energy required to isolate two electrons, at position r, from the remainder of the π-network of an aromatic system. The relevant values for anthracene are:[166b,167]

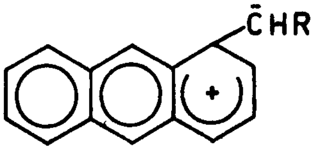
$L_1^+ = -2.25\ \beta$ $\qquad$ $L_9^+ = -2.00\ \beta$

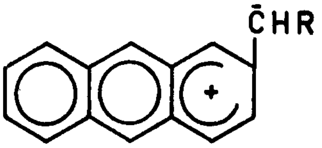
$L_2^+ = -2.46\ \beta$ $\qquad$ $L_{9a}^+ = -3.72\ \beta$

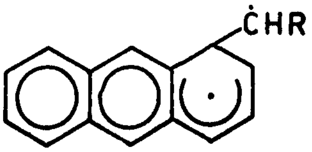
Let us now consider the transition state for attack of a carbene, CHR, at the 1,2-bond of anthracene. The contributing forms are:

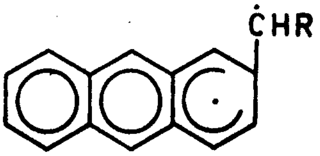

I


II


III


IV


V


VI

The wave function, Ψ, for the transition state is then

$$\Psi = \sum_{n=I}^{VI} C_n \psi_n$$

The energy difference between III and IV or V and VI is given by

$$L_1^+ - L_2^+ = -2.25\,\beta - (-2.46\,\beta)$$

$$= 0.21\,\beta \sim 3\ \text{kcal/mole.}$$[166]

Therefore, because these pairs differ only slightly in energy, each contributes significantly to the transition state ($C_{III} \sim C_{IV}$ and $C_V \sim C_{VI}$), thus lowering its energy. The electrophilic carbene therefore attacks the 1,2-bond fairly symmetrically by a process closely approximating true 'double-bond' attack. The reaction profile is quite featureless (Fig. 2.2.1).

Addition of carbethoxycarbene to the 2,3-bond requires a transition state to which identical σ-complexes contribute. Because L_2^+ is higher than L_1^+, however, the process is less favoured than 1,2-attack. On the other hand, the transition state for addition of the carbene at the 1,9a and 9,9a bonds invokes contributions from σ-complexes which are very different in energy. The reaction therefore requires the intermediacy of a species which closely resembles the more stable σ-complex. In this case, the reaction profile is not featureless but shows a deep shoulder, corresponding to this intermediate, on the forward slope (Fig. 2.2.2). This

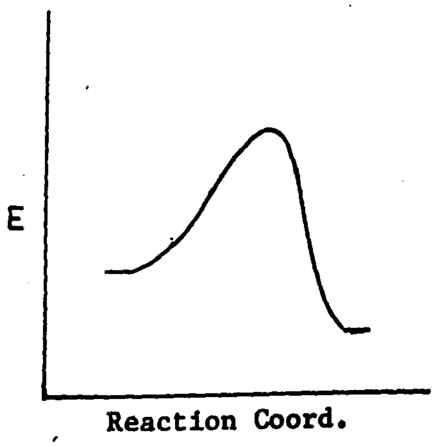


Fig. 2.2.1

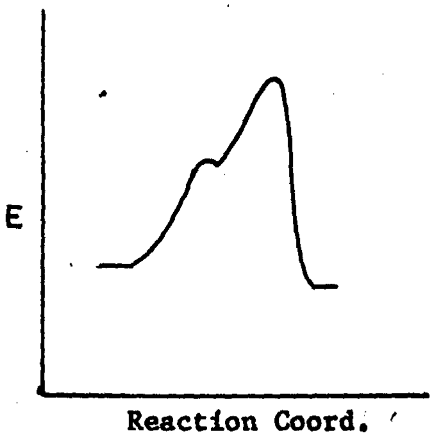
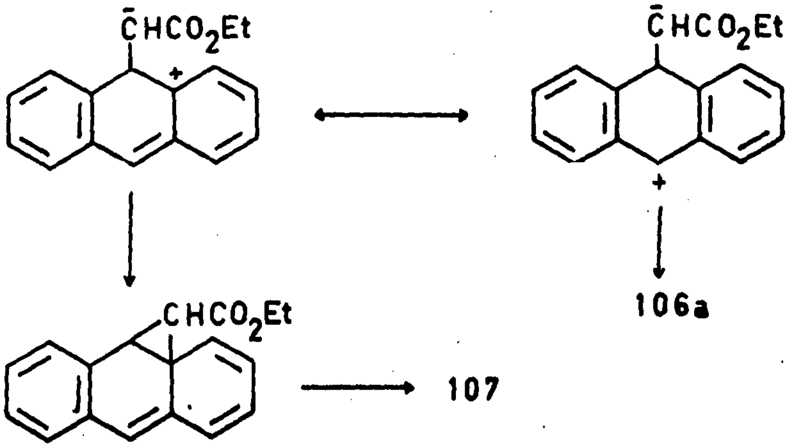


Fig. 2.2.2

intermediate requires additional energy to reach the transition state which, on the basis of product stabilities, is expected to be higher in energy than that for 1,2-addition. The reverse reaction, however, is energetically less demanding and occurs preferentially so the proportion of successful reactions at the 1,9a and 9,9a bonds is very low.

While the 9,10-adduct (105) was isolated by crystallization, only the ring-expanded product (107) was obtained on chromatography. That the ester 106 was not converted to 107a under chromatographic conditions was shown by subjecting an authentic sample to identical treatment. Furthermore, heating of 106 at 160° for 8 hours gave only unchanged starting material; so 107 could not have been produced from 106a under the reaction conditions.

Although 106a and 107 were formed independently, it is possible that they arose from the same intermediate, e.g.



On the other hand, one product *may* be formed from the triplet carbene *via* a diradical intermediate; but it is possible only to speculate on this point.

Since the completion of this work, it has been reported[168] that the 9,10-adduct 106a was formed, in unspecified yield, by catalysed decomposition of ethyl diazoacetate in the presence of anthracene. Although markedly improved yields of 1,2-adduct (100, 29%) were obtained, we were unable to reproduce this result. It is well known, however, that the effectiveness of copper and copper salts as catalysts is very variable and unpredictable.[130]

2.3. THE REACTION OF DICHLOROCARBENE WITH ANTHRACENE

Murray[168] has claimed that dichlorocarbene reacts with anthracene: addition of chloroform to a slurry of potassium *tert*.-butoxide and anthracene in benzene led to a 10% yield of 10-chloro-5-(1,1-dimethylethoxy)-5*H*-dibenzo[*a*.*d*]cycloheptene (113). This report is of considerable interest because there is no other example of the reaction of dichlorocarbene with an aromatic hydrocarbon.

It was proposed that electrophilic attack at the highly-active 9-position of anthracene leads to a dipolar intermediate (114) which undergoes ring closure. The high-energy intermediate then rearranges under the influence of the base present (Scheme 2.3.I). For reasons outlined in Section 2.2, formation of an intermediate such as 114 is improbable. Other methods of generation of dichlorocarbene were therefore investigated in order to gain some understanding of the reaction sequence.

Generation of Dichlorocarbene: Methods

A. $CHCl_3$ — $KOBu^t$.[169]

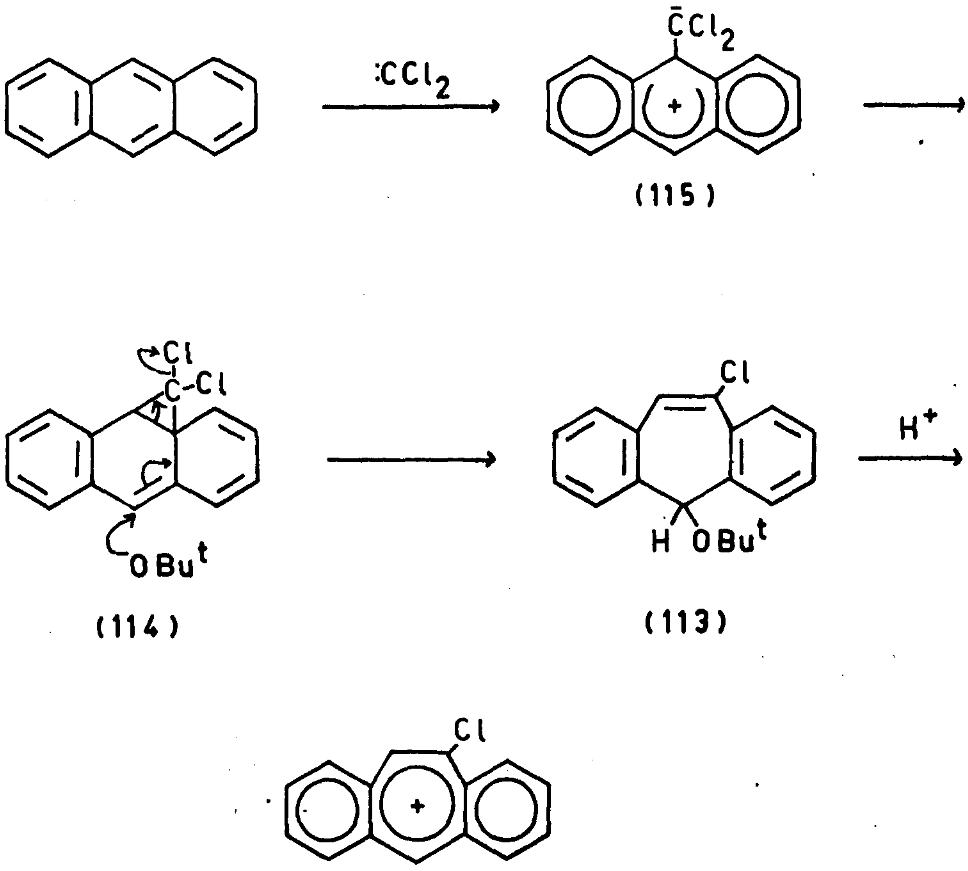
B. CCl_3CO_2Et — NaOMe.[171]

C. CCl_3CO_2Na, heat.[170]

D. CCl_3CO_2Na — $KOBu^t$, heat.

E. $PhHgCCl_3$, heat.[172]

F. $PhHgCCl_3$ — NaI.[173]



(115′)

Scheme 2.3.I

When dissolved in sulphuric acid (92%), 113 is converted to a red cation (115′), providing a sensitive test for the presence of 113 and related compounds. In this way it was shown that Method B led to only *very slight* attack on the substrate while Methods C-F were completely ineffectual.

We considered it *just* possible that the 9,9a-adduct 114 is formed reversibly, i.e.

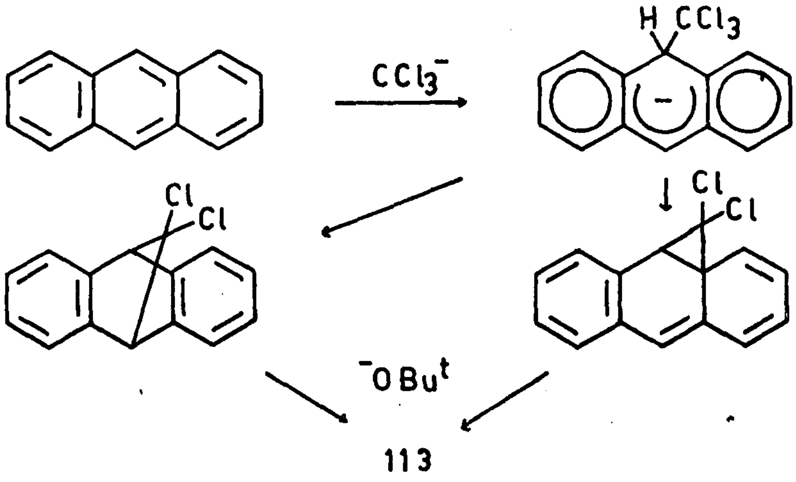
$$\text{Anthracene} \overset{CCl_2}{\rightleftharpoons} 115 \rightleftharpoons 114 \xrightarrow{^{-}OBu^t} 113$$

Scheme 2.3.II

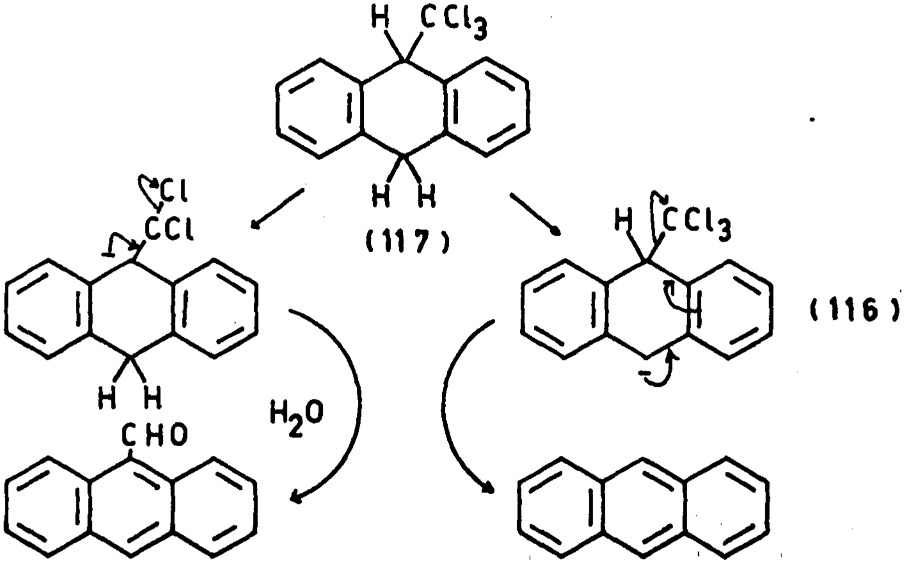
Because of the marked decrease in stability of the π-electron system, 114 should have high energy. The equilibrium 115 $\rightleftharpoons$ 114 should lie heavily towards 115 so that, unless 114 is subject to an alternative non-reversible reaction, there would be little evidence of reaction. However, Method D is without effect. Scheme 2.3.II therefore cannot apply.

Thermal decomposition of phenyltrichloromethylmercury (Method E) produces highly electrophilic dichlorocarbene without the intermediacy of the anion CCl_3^-.[172] If, therefore, anthracene were really converted to 113 through the agency of the carbene, Method E would have given an adduct in better yield. It seems highly unlikely, then, that dichlorocarbene does react with anthracene.

An alternative reaction sequence for formation of 113 is shown in Scheme 2.3.III. (Analogous nucleophilic attack of the dimsyl anion on anthracene is known.[174,175]) To test this hypothesis, 9,10-dihydro-9-trichloromethylanthracene (117) was treated with potassium *tert*.-butoxide in benzene. Anthracene and 9-anthraldehyde were formed (Scheme 2.3.IV). It appears, then, that 116 is not an intermediate in the formation of 113.



Scheme 2.3.III



Scheme 2.3.IV

Therefore, while it seems certain that 113 is not formed through the agency of dichlorocarbene, the details of the reaction process are not yet understood.

2.4. PREPARATION OF REFERENCE COMPOUNDS

METHYL 9,10-DIHYDRO-9,10-METHANOANTHRACENE-11-CARBOXYLATE (124a)

Meinwald and Miller[190] have reported in a brief communication the preparation of the bridged acid 124 from the previously-known diketone 121. We encountered many difficulties in repeating their reaction sequence but subsequently improved the efficiency and reproducibility of almost every step.

Acetate 118.

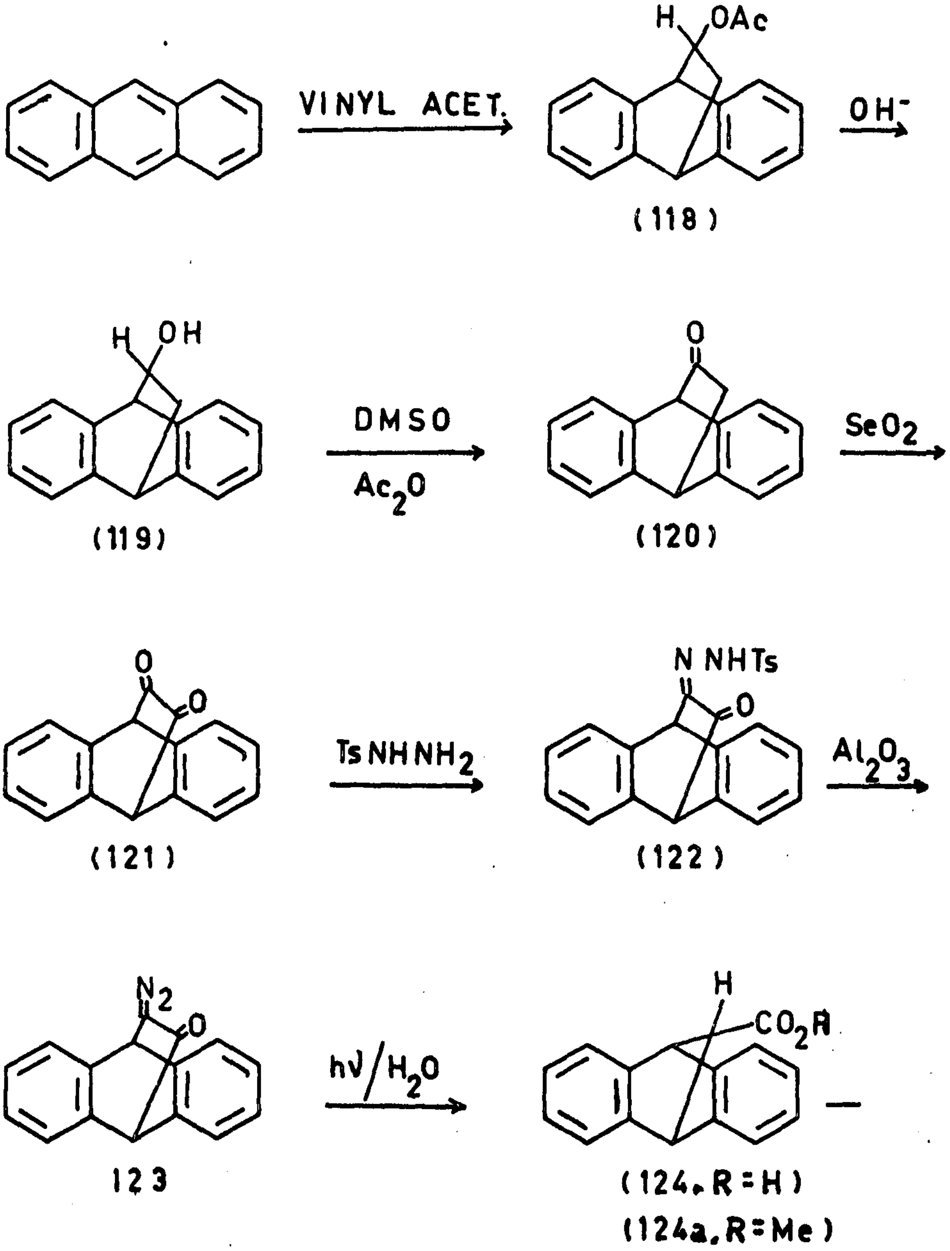
When the addition of vinyl acetate to anthracene according to the procedure of Alder and Rickert,[187] large amounts of dark, sticky polymer resulted, making purification of 118 very difficult. When hydroquinone was added as a chain-inhibitor, however, the reaction proceeded cleanly to give the product in good yield.

Alcohol 119.

Alkaline hydrolysis of the acetate 118 gave the corresponding alcohol in a high state of purity. The transesterification procedure of Wawzonek and Hallum[188] offered no advantages.

Ketone 120.

Oxidation of the alcohol 119 with chromic oxide has been reported;[188] only a crude yield was quoted (81%). Repetition of


VINYL ACET.
H
OAc
(118)
OH⁻
H
OH
(119)
DMSO
Ac_2O
O
(120)
SeO_2
O
O
(121)
$TsNHNH_2$
N NHTs
O
(122)
Al_2O_3
N_2
O
123
hν/H_2O
H
CO_2R
(124, R = H)
(124a, R = Me)

the procedure showed that this product consisted mainly of alcohol 119 and anthraquinone with only traces of the ketone 120. Similar results were noted for the oxidation procedures of Jones[203] and Brown and Garg.[204] It seems, then, that oxidation of ketone 120 occurs more readily than that of the alcohol 119.

Treatment of 119 with dimethyl sulphoxide-acetic anhydride, however, gave, on crystallization from toluene, pure ketone 120. Moreover, evaporation of the mother liquors gave a solid consisting mainly of acetate 118 which could be re-subjected to hydrolysis and oxidation.

Diketone 121.

The reported procedure[189] was followed; but a much higher yield was obtained on crystallization from toluene rather than benzene and carbon tetrachloride.

Diazoketone 123.

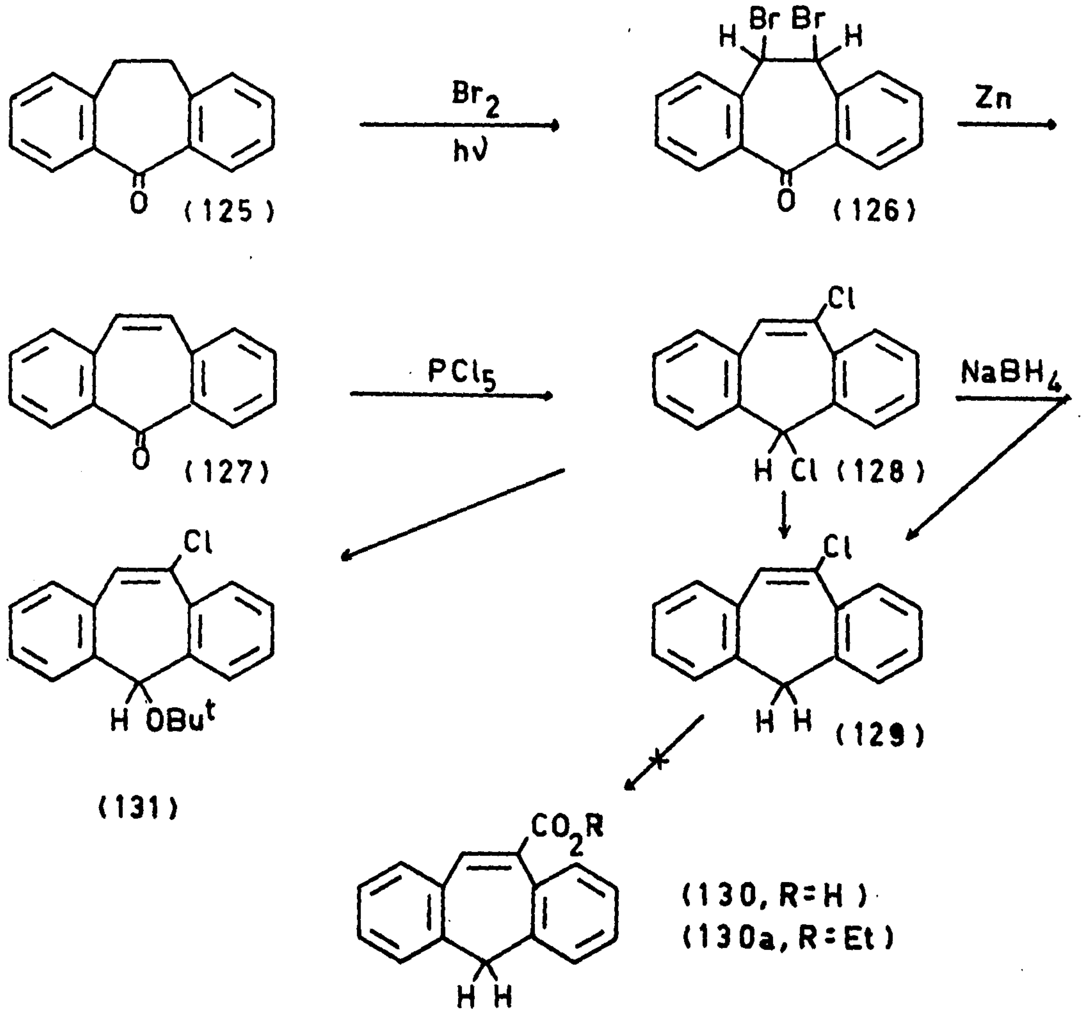
After stirring a suspension of tosylhydrazone 122 in 10% sodium hydroxide solution for 48 hours, the starting material was recovered quantitatively. This is in contrast with a literature report.[190] Efficient reaction was achieved, however, by using aluminium oxide as the basic catalyst.[191]

Carboxylic Acid 124.

The photochemical conversion of 123 to the product 124 is inefficient and unpredictable. While exposure to strong sunlight gave the acid 124 in 15% yield, irradiation by a medium-pressure mercury-quartz lamp produced only dianthracene. Presumably this product is formed by dimerization of anthracene, but there is no evidence as to how the two-carbon bridge is lost from 123.

10-CHLORO-5-(1,1-DIMETHYLETHOXY)-5*H*-DIBENZO[*a*.*d*]-CYCLOHEPTENE (131) and ETHYL 5*H*-DIBENZO[*a*.*d*]CYCLOHEPTENE-10-CARBOXYLATE (130a)

Looker[194] has reported a very elegant synthesis of the key-intermediate 129 from the ketone 127. While this step was readily reproduced, it was found impossible to achieve, in satisfactory yields, the reported single-step conversion of 125 to 127. Treibs and Klinkhammer[193] effected this conversion in 90% yield by irradiation of the molten starting material during the addition of bromine (1 mole equiv.). We, on the other hand, obtained a mixture of the original ketone 125 and the dibromoketone 126. Use of larger amounts of bromine led to good yields (75-80%) of 126. Subsequent debromination using zinc gave the required ketone 127 in excellent yield.



The halogen in the chloride 129 participates in an extended resonance system. It is not surprising, therefore, that it was impossible to metalate the molecule at this position.

CHAPTER 3

EXPERIMENTAL

3.0. PREAMBLE

General.

Melting points were determined using a Kofler hot stage and are uncorrected.

Microanalyses were carried out by the Australian Microanalytical Service, Melbourne.

All organic extracts were dried over magnesium sulphate.

Spectroscopic Apparatus and Techniques.

Infrared spectra were determined with Perkin-Elmer 237 and 337 Grating Spectrophotometers; ultraviolet spectra with a Perkin-Elmer 137UV spectrophotometer.

Nuclear magnetic resonance spectra were recorded by Mr. L. Paltridge with a Varian DP60 spectrometer operated at 60 Mc/s. The solvent was deuterochloroform and chemical shifts were measured relative to tetramethylsilane as internal standard.

Mass spectra were recorded by Mr. D.B. Cobb with a Hitachi-Perkin Elmer RMU-6D Spectrometer fitted with a double-focus attachment.

Materials.

Anthracene, phenanthrene and pyrene were the purest available commercial samples. In each case the melting point and other physical properties were in satisfactory agree ment with previously recorded values.

Ethyl azidoformate was prepared by treatment of ethyl chloroformate with sodium azide.[177] It was not distilled before use.

Ethyl diazoacetate was prepared by the method of Searle.[202]

Sodium methoxide and potassium *tert*.-butoxide were prepared by the same general method. Freshly-cut alkali metal (1 part), alcohol (10 parts) and dry benzene (50 parts) were stirred and boiled under reflux until all the metal had disappeared. A 30 cm. packed fractionating column was then fitted and distillation carried out until pure benzene started to distil over. Removal of the rest of the benzene under reduced pressure gave the alkoxide as a fine white powder.

Sodium trichloroacetate was prepared by neutralizing trichloroacetic acid, dissolved in dry methanol, with sodium methoxide in methanol. The solvent was removed under reduced pressure and the salt dried in a vacuum desiccator.

Chlorobenzene and 1,2-dimethoxyethane were dried over calcium hydride and distilled.

Benzene was dried over calcium chloride, carefully distilled and stored over sodium.

Adsorption chromatography was conducted on Spence alumina type UG1 which had been treated with ethyl acetate, washed and reactivated by heating at 160° overnight; or on Whatman silica gel SG31.

Vapour Phase Chromatography (v.p.c.).

Analyses were carried out using a Perkin-Elmer 800 Gas Chromatograph equipped with a flame-ionization detector. In all cases the (nitrogen) carrier gas flow rate was 60 ml./min. Because all peaks of interest were symmetrical, the areas were calculated as (peak height x width at $\frac{1}{2}$-height) and the results so obtained checked from time to time by the more tedious method of cut—and-weigh. Agreement was always better than ±0.3%. Calibration curves of detector response *vers.* weight of compounds were set up *under the conditions of the analysis*. The columns used were:

Column A: 5% Silicone QF-1 (FS1265) on 60-80 mesh Chromosorb W (acid-washed, DMCS treated) in completely silanized aluminium tubing (10 ft. x 0.25 in.).

Column B: 15% Methyl Silicone Rubber Gum, SE30, on 80-100 mesh Gas Chrom P, in stainless-steel tubing (12 ft. x 0.25 in.).

Column C: 15% UCON-Oil LB-550X, on 80-100 mesh Gas-Chrom P, in aluminium tubing (5 ft. x 0.25 in.).

3.1. WORK CARRIED OUT IN CHAPTER 1

PREPARATION OF REFERENCE COMPOUNDS

Arylamines.

The arylamines required for conversion into ethyl *N*-(aryl)-carbamates were prepared by methods described in the literature. In each case the melting point of the product was in satisfactory agreement with the value previously recorded.

1- and 2-Aminoanthracene were each obtained by reduction of the appropriate aminoanthraquinone with zinc and alkali.[178,179]

9-Aminoanthracene was formed from anthrone when it was heated with aqueous ammonia under pressure.[180]

1- and 4-Aminophenanthrene were prepared from 1-oxo- and 4-oxo-1,2,3,4-tetrahydrophenanthrene respectively.[181]

2- and 3-Aminophenanthrene were each formed in good yield by rearrangement of the oxime of the appropriate acetylphenanthrene.[182]

9-Aminophenanthrene was produced in good yield by treatment of 9-phenanthrol with hot aqueous ammoniacal ammonium sulphite.[183]

1-Aminopyrene was obtained by reduction of 1-nitropyrene.[184]

2-Aminopyrene was prepared by the Curtius rearrangement of pyrene-2-carboxazide.[184]

4-Aminopyrene resulted from treatment of 4-hydroxypyrene with ammoniacal ammonium sulphide.[184]

Ethyl N-*(aryl)carbamates*

The following preparation of ethyl *N*-(1-anthryl)carbamate is illustrative of the general method. A solution of 1-aminoanthracene (0.100 g, 0.42 mmole), ethyl chloroformate (0.063 g, 0.46 mmole), and purified diethylaniline (0.25 g) in ethanol (15 ml) was boiled under reflux for 2 hr and then poured into 1% aqueous hydrochloric acid (50 ml). The precipitate was collected, washed, and crystallized from hexane/chloroform. *Ethyl* N-*(1-anthryl)carbamate* (0.120 g, 88%) was obtained as pale yellow needles, m.p. 144-145° (Found: C, 77.0; H, 5.75; N, 5.1. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%), λ_{max} (log ε) 254 (5.15), 332sh (3.42), 349sh (3.69), 356 sh (3.72), 365 (3.82), 380 mμ (3.76).

The following ethyl *N*-(aryl)carbamates were prepared similarly:

(1) *Ethyl* N-*(2-anthryl)carbamate* (86% yield) as bright yellow plates (from hexane/chloroform), m.p. 217-218° (Found: C, 77.0; H, 5.75; N, 5.1%), λ_{max} (log ε) 261 (4.92), 271 (4.88), 322sh (3.28), 338 (3.51), 355 (3.59), 374 (3.52), 392 mμ (3.39).

(2) *Ethyl* N-*(9-anthryl)carbamate* (87% yield) as cream needles (from hexane/chloroform), m.p. 233.5-234.5° (Found: C, 77.1; H, 5.65; N, 5.0%), λ_{max} (log ε) 249sh (4.98), 254.5 (5.21), 318sh (3.06), 332 (3.45), 347 (3.75), 364.5 (3.92), 383.5 mμ (3.87).

(3) *Ethyl* N-*(1-phenanthryl)carbamate* (92% yield) as plates (from ethanol/water), m.p. 155-156° (lit.[182] m.p. 153.5-154°), λ_{max} (log ε) 256 (4.71), 281sh (4.00), 298 (4.07), 339 (2.72), 355 mμ (2.64).

(4) *Ethyl* N-*(2-phenanthryl)carbamate* (90% yield) as needles (from ethanol/water), m.p. 123-124° (lit.[185] m.p. 125°), λ_{max} (log ε) 264 (4.88), 293 (4.30), 301sh (3.86), 323 (2.70), 339 (2.74), 355 mμ (2.59).

(5) *Ethyl* N-*(9-phenanthryl)carbamate* (90% yield) as needles (from ethanol/water), m.p. 156-158° (lit.[186] m.p. 156-158°), λ_{max} (log ε) 255 (4.71), 276 (4.13), 298 (4.02), 341 (2.61), 357 mμ (2.47).

(6) *Ethyl* N-*(1-pyrenyl)carbamate* (89% yield) as needles (from ethanol/water), m.p. 187-188° (Found: C, 78.85; H, 5.35; N, 4.8. $C_{19}H_{15}NO_2$ requires C, 78.9; H, 5.2; N, 4.8%), λ_{max} (log ε) 235.5sh (4.60), 243 (4.80), 267.5 (4.35), 277.5 (4.54), 313sh (3.95), 329 (4.28), 340 (4.44), 383 mμ (3.17).

(7) *Ethyl* N-*(2-pyrenyl)carbamate* (90% yield) as needles (from ethanol/water), m.p. 173-174.5° (Found: C, 78.5; H, 5.1; N, 5.0%), λ_{max} (log ε) 254 (4.89), 284sh (4.32), 309.5 (3.98), 323 (4.39), 338.5 (4.60), 367 (2.92), 379sh (2.55), 388 mμ (3.02).

(8) *Ethyl* N-*(4-pyrenyl)carbamate* (92% yield) as needles (from ethanol/water), m.p. 227-228.5° (Found: C, 78.9; H, 5.3; N, 5.0), λ_{max} (log ε) 235.5sh (4.58), 242 (4.81), 255sh (4.20), 265sh (4.36), 275 (4.54), 311sh (3.93), 324.5 (4.24), 340 (4.39), 378 mμ (2.78).

The following procedure was used for the preparation of ethyl *N*-(3-phenanthryl)carbamate: 3-aminophenanthrene (0.100 g, 0.42 mmole) and ethyl chloroformate (0.063 g, 0.46 mmole) were dissolved in a mixture of pyridine (1 ml) and benzene (50 ml) and the solution was boiled under reflux for 3 hr. The reaction mixture was then evaporated on the water-bath and the residue was crystallized from aqueous methanol. The required carbamate (93%) formed plates, m.p. 122-123° (lit.[185] m.p. 123°), λ_{max} (log ε) 253sh (4.71), 259 (4.75), 280 (4.25), 298 (4.16), 308 (4.17), 340 (3.04), 357 mμ (3.01).

Numerous attempts to prepare ethyl *N*-(4-phenanthryl)carbamate by reaction of 4-aminophenanthrene with ethyl chloroformate under forcing conditions were unsuccessful; in each case the amine was recovered unchanged. Similarly, 4-phenanthryl isocyanate was unaffected by vigorous treatment with ethanol using either acidic or basic catalysts.

cis- *and* trans-N-*carbethoxy-2,3-dimethylaziridines.*

Ethyl azidoformate (1.0 g) and *cis*- or *trans*-butene-2 were sealed in a Pyrex tube and heated at 80° for 24 hours. Evaporation of excess olefin gave a yellow oil (1.3 g) which was distilled (85-90°/40 mm). Examination by b.p.c. (Columns A and C) showed large amounts of ethyl carbamate to be present.

The distillates (each *ca.* 1.0 g) were dissolved in 'Freon' TF (50 ml) and shaken with water (6 x 100 ml). Evaporation of the dried organic layer gave a colourless oil which, on careful fractionation through a Vigreux column gave either cis-N-*carbethoxy-2,3-dimethylaziridine* (52% yield, 94% isomeric purity), b.p. 82°/40 mm (Found:

C, 58.44; H, 9.44; N, 9.62%) or trans-N-*carbethoxy-2,3-dimethylaziridine* (55% yield, 91% isomeric purity), b.p. 84°/40 mm (Found: C, 58.92; H, 8.88; N, 9.79. $C_7H_{13}NO_2$ requires C, 58.72; H, 9.15; N, 9.78%).

QUANTITATIVE THIN-LAYER CHROMATOGRAPHY

Preparation of Plates.

The adsorbent (Merck alumina G or Kieselgel G) was extracted thrice with boiling methanol (2 parts), then heated at 160° for 4 hr. After trituration with water (2 parts) for 6 min (alumina) or 4.75 min (silica gel) the adsorbent was spread as a 0.5 mm layer on glass plates (6 cm by 18 cm) which were heated at 140° for 12 hr and stored in a desiccator.

Separation of Reaction Products.

A sample (*ca*. 1.3 g) of the crude reaction product was dissolved in freshly distilled chloroform (100 ml). Using a Hamilton gas-chromatographic syringe 10 µl of solution were applied as a spot to the base-line of the chromatography plate, and small separate marker spots were applied close to the edges. The plate was then developed with 20:1 benzene/ethyl acetate (alumina plates) or 10:1 benzene/ethyl acetate (silica gel plates). The *N*-anthrylcarbamic esters proved to be extremely light sensitive; accordingly all manipulations were conducted under a Wratten yellow safelight or in darkness.

Estimation of Reaction Products.

The positions of the required products on the developed plate were determined by observing the marker spots under ultraviolet light while the rest of the plate was protected from exposure with metal foil. Sections (4 cm^2) of the layer containing the spots were separately scraped from the plate and each was extracted with boiling ethanol. The filtered extracts were each made up to 10.0 ml and the amounts of isomeric ethyl *N*-anthrylcarbamates in each solution were determined by measuring the optical density at the appropriate wavelength, i.e. 254 mμ (ε 142,000) for ethyl *N*-(1-anthryl)carbamate; 271 mμ (ε 75,200) for ethyl *N*-(2-anthryl)carbamate; 254.5 mμ (ε 163,000)for ethyl *N*-(9-anthryl)carbamate.

REACTION OF POLYCYCLIC HYDROCARBONS WITH ETHYL AZIDOFORMATE

Anthracene.

Ethyl azidoformate (6.6 g, 0.057 mole) was added dropwise with stirring during 3 hr to a solution of anthracene (10 g, 0.057 mole) in chlorobenzene (60 ml) at 120-125° under nitrogen. The mixture was maintained at 120-125° for a further 1 hr and the solvent was then evaporated under reduced pressure. The residue was digested with boiling methanol (250 ml). Evaporation of the extract afforded a red-brown gum (2.60 g) which was chromatographed on a column (20 cm by 3.4 cm) of neutral alumina, activity III. Elution of the column with 4:1 benzene/ethyl acetate afforded successively: (i) a mixture of ethyl *N*-(1-anthryl)carbamate and ethyl *N*-(2-anthryl)carbamate from which the pure 1-isomer (0.13 g, 1.8%) was obtained by crystallization from ethanol; (ii) ethyl *N*-(9-anthryl)carbamate (0.46 g, 9%); and (iii) a large amount of coloured gum shown in separate experiments to be formed by decomposition of anthrylcarbamates on the column.

A second experiment was conducted with the same quantities of reactants. However, the yields of products were determined by submitting samples of the residue obtained by evaporation of the reaction mixture to thin-layer chromatography (see above). It was found that the products tended to undergo decomposition on alumina plates, but that reproducible results were obtained when silica gel plates were used. On silica gel, when the solvent system 10:1 benzene/ethyl acetate was used ethyl *N*-(1-anthryl)-carbamate had R_F 0.49, the 2-isomer had R_F 0.53 and the 9-isomer had R_F 0.38. The yields of products determined by thin-layer chromatography were ethyl *N*-(1-anthryl)carbamate (30%), ethyl *N*-(2-anthryl)carbamate (*ca.* 1%) and ethyl *N*-(9-anthryl)carbamate (47%).

Phenanthrene.

Ethyl azidoformate (1.1 g, 0.01 mole) was added dropwise with stirring during 3 hr to molten phenanthrene (10.0 g, 0.058 mole) at 125-130° under nitrogen. The temperature was maintained at 125-130° for a further hour, after which time the reaction mixture was cooled, dissolved in hexane, and chromatographed on a column (30 cm by 3.4 cm) of neutral alumina, activity I. Elution of the column first with hexane and later with benzene afforded successively: (i) phenanthrene (8.50 g); (ii) ethyl *N*-(9-phenanthryl)carbamate (0.13 g); (iii) a mixture (1.24 g) of ethyl *N*-(9-phenanthryl)carbamate and ethyl *N*-(1-phenanthryl)carbamate; and (iv) a mixture (0.12 g) of ethyl *N*-(1-phenanthryl)carbamate and an isomeric compound. The chromatographic fraction (iii) was separated into its pure components by fractional crystallization from hexane/chloroform. The amount of each isomer in the mixture was more accurately determined by measuring the optical density of a solution of the mixture in carbon disulphide at 721 and 797 cm^{-1}. The relative amounts of the two components could then be calculated using the appropriate values of extinction coefficient, i.e. ethyl *N*-(1-phenanthryl)carbamate has ε 1.6 at 721 cm^{-1} and ε 33.1 at 797 cm^{-1}, and ethyl *N*-(9-phenanthryl)carbamate has ε 29.8 at 721 cm^{-1} and ε 1.5 at 797 cm^{-1}.

The chromatographic fraction (iv) was separated by fractional crystallization from ethanol and from hexane/chloroform into ethyl *N*-(1-phenanthryl)carbamate (0.07 g) and a less soluble compound tentatively identified as *ethyl* N-*(4-phenanthryl)carbamate* (0.04 g), which formed plates (from aqueous methanol), m.p. 154.5-156° (Found: C, 77.0; H, 5.75; N, 5.2; mol.wt.(Rast), 247. $C_{17}H_{15}NO_2$ requires C, 77.0; H, 5.7; N, 5.3%; mol.wt., 265), λ_{max} (log ε) 255 (4.72), 286sh (4.00), 297 (4.06), 339 (2.72), 355 mμ (2.59). The 4-urethane resisted numerous attempts to convert it into 4-aminophenanthrene by hydrolysis under either basic or acidic conditions.

The absence of characteristic absorption peaks at 1570 and 837 cm^{-1} in the infrared spectrum of the crude product indicated that ethyl *N*-(2-phenanthryl)carbamate and the 3-isomer were not formed in the reaction. The total overall yields of products were ethyl *N*-(1-phenanthryl)carbamate, 0.53 g (20%); ethyl *N*-(4-phenanthryl)-carbamate, 0.04 g (1.6%); ethyl *N*-(9-phenanthryl)carbamate, 0.89 g (31%).

Pyrene.

Ethyl azidoformate (1.40 g, 0.012 mole) was added dropwise with stirring during 3 hr to a boiling solution of pyrene (12.5 g, 0.06 mole) in chlorobenzene (12 ml) under nitrogen. After the addition the solution was refluxed for a further hour and the solvent was then removed by distillation under reduced pressure. The residue was chromatographed on a column (15 cm by 4.3 cm) of neutral alumina, activity III. Elution of the column first with hexane and then with benzene afforded successively pyrene (10.1 g) and a mixture (1.47 g) of ethyl *N*-(1-pyrenyl)carbamate and ethyl *N*-(4-pyrenyl)carbamate, fractional crystallization of which from ethanol afforded the pure 1-isomer. The isomer ratio in the mixture was determined by measuring the optical density of a solution at 383 mμ at which wavelength the 1-isomer has ε 95 and the 3-isomer ε 1495. The calculated yields were ethyl *N*-(4-pyrenyl)carbamate, 0.47 g (13%), and ethyl *N*-(1-pyrenyl)carbamate, 1.00 g (28%). The absence of characteristic absorption bands at 870 and 820 cm^{-1} in the infrared spectrum of the crude product confirmed that the 2-isomer was not formed during the reaction.

MASS SPECTROMETRY

In order to determine the extent of deuteration of anthracene, the mass spectrum of the compound was determined using a low ionizing voltage (10 volts) to eliminate the *M*-1 peak. This procedure simplified calculations and increased the accuracy of the result.[176a] The peak abundances are shown in Table 3.1.I.

TABLE 3.1.I

	$C_{14}H_{10}$	"$C_{14}H_9D$"	
m/e	abundance*	abundance*	corrected abundances*
178	100	13	13
179	16	100	98
180	2	15	15
181	0	2	2

* arbitrary units

$$\frac{[C_{14}H_9D]}{[C_{14}H_9D] + [C_{14}H_{10}]} = \frac{98}{98 + 13} = 0.88$$

The 9-deuterioanthracene was therefore 88% isotopically pure.

The mass spectrum of partially-deuterated 9-anthrylurethane, isolated by thin-layer chromatography, shows a large and variable abundance of the $M + 1$ peak due to ion-molecule collisions. The isocyanate peaks ($M - 46$) were therefore used to calculate the isomeric purity of the compound (Table 3.1.II).

TABLE 3.1.II

m/e	$C_{14}H_9NCO$	$C_{14}H_8D.NCO$	
	abundance*	abundance*	corrected abundance*
218	7	7	7
219	100	100	93
220	18	115	98
221	0	1	1

* arbitrary units

$$\frac{[C_{14}H_9NCO]}{[C_{14}H_8D.NCO]} = \frac{93}{98} = 0.95$$

If k_H^H = rate constant for nitrene attack at the *meso* position of undeuterated anthracene.

k_H^D and k_D^D = rate constants for attack at the undeuterated and deuterated *meso* positions, respectively, of 9-deuterioanthracene.

K_f^D = rate of formation of undeuterated 9-anthrylurethane.

K_f^D = rate of formation of deuterated 9-anthrylurethane.

$$\frac{K_f^H}{K_f^D} = \frac{k_H^H\,[C_{14}H_{10}] + k_D^D\,[C_{14}H_9D]}{k_H^D\,[C_{14}H_9D]}$$

now $k_H^H = 2k_H^D$

and $[C_{14}H_{10}] = \frac{0.12}{0.88}\,[C_{14}H_9D]$

$$\therefore \frac{K_f^H}{K_f^D} = 2 \cdot \frac{0.12}{0.88} + \frac{k_D^D}{k_H^D}$$

$$\text{i.e. } 0.95 = 0.27 + \frac{k_D^D}{k_H^D}$$

$$\text{and } \frac{k_H^D}{k_D^D} = 1.5$$

REACTION OF ALIPHATIC HYDROCARBONS WITH ETHYL AZIDOFORMATE

Reaction of Ethyl Azidoformate with Butene-2.

A stock concentrate of butene-2 in 'Freon' TF was prepared at *ca.* -20°; the olefin concentration was estimated by addition of an aliquot of this solution to excess bromine in carbon tetrachloride. Potassium iodide solution was then added, followed by starch indicator and the iodine estimated by titration against standard sodium thiosulphate solution. The concentrate was stored at below -30°.

Appropriate quantities of concentrate and 'Freon' TF were transferred to a cooled 'Carius' Tube, containing a weighed quantity of ethyl azidoformate, at -20 to -30° which was then flushed by a slow stream of oxygen-free nitrogen. After freezing the contents in liquid nitrogen, the tube was evacuated to *ca.* 40 mm pressure and quickly sealed. The reaction times employed were:

80°: 24 hours
120°: 4.5 hours

After completion of the reaction, the tubes were chilled once again in liquid nitrogen and broken open. When the olefin had evaporated at room temperature, the reaction mixture was diluted to 10 ml and examined by v.p.c. Column A was used with injector at 160°, column at 107° and detector at 120°. Estimations on each solution were carried out in triplicate.

The sensitized photolysis of ethyl azidoformate in the presence of *cis*-butene-2 was carried out in a similar sealed tube. The azide (0.100 g, 0.87 mmole), acetophenone (0.084 g, 0.87 mmole) and *cis*-butene-2 (*ca.* 1.0 g) in 'Freon' TF (5 ml) were irradiated for 18 hours in a 'Rayonet' photochemical reactor using fluorescent lamps with maximum emission at 350 mμ. No aziridines were formed.

Reaction of Ethyl Azidoformate with Cyclohexane.

A stock solution containing 2% ethyl azidoformate and 20% cyclohexane in 'Freon' TF was employed. This concentrate was diluted and sealed into Pyrex tubes as before. After being maintained at 80° for 24 hours, these solutions were subjected to v.p.c. analysis using Column C. Ethyl carbamate was estimated using injector at 150°, column at 125° and detector at 140°; cyclohexylurethane was determined with injector at 180°, column at 160° and detector at 180°.

Reaction of Ethyl Azidoformate with Cumene.

Thermolysis: The solution (100 ml) was added to a flask, fitted with a reflux condenser, which was thoroughly flushed with oxygen-free nitrogen and heated for 4 hours in the vapour of boiling chlorobenzene.

Photolyses: Irradiation by means of a Philips 125W medium-pressure mercury-quartz lamp was carried out in a water-cooled Pyrex apparatus. The lamp was surrounded by a cylindrical water-jacket which was in turn surrounded by a jacket containing the solution.

3.2. WORK REPORTED IN CHAPTER 2

METHYL 9,10-DIHYDRO-9,10-METHANOANTHRACENE-11-CARBOXYLATE (124a)

11-Acetoxy-9,10-ethano-9,10-dihydroanthracene (118).

A modification of the procedure of Alder and Rickert[187] was employed: a solution of anthracene (70 g) and distilled vinyl acetate (140 g, containing 1% hydroquinone) in dry xylene (840 ml) was heated and stirred at 220-230° for 14 hours. Evaporation under reduced pressure gave a semisolid residue which was stirred with hexane and allowed to stand at 0° overnight. The solid product was washed free of most of the sticky polyvinyl acetate with warm methanol (2 x 100 ml) and crystallized from methanol to give a white powder, m.p. 95-6° (lit.[187] 100-101°). The yield was 75.0 g (72%) (lit. yield 41%). Because further purification is tedious, the adduct was used in this state of purity.

11-Hydroxy-9,10-ethano-9,10-dihydroanthracene (119).

Finely ground acetate 118 (60.0 g) was suspended in 10% aqueous sodium hydroxide solution (500 ml), ethanol (100 ml) added and the mixture boiled vigorously under reflux for 4 hours. After cooling, the suspension was diluted with water (600 ml), stirred for 10 min. and filtered to give a cream powder. Crystallization from methanol afforded needles, 47.0 g (95%), m.p. 142-4° (lit.[188] 142-3°).

11-Keto-9,10-ethano-9,10-dihydroanthracene (120).

A solution of the alcohol 119 in dimethyl sulphoxide (525 ml, distilled from calcium hydride) and acetic anhydride (350 ml) was allowed to stand at room temperature for 20 hours. The mixture was then poured into ice-water (2 l.) and stirred vigorously for 2 hours to hydrolyse the acetic anhydride. Decantation of the clear supernatant left a sticky white solid which was dissolved in ether (500 ml) and shaken repeatedly with water and, finally, saturated brine. Evaporation of the ether layer gave a yellowish solid (32.4 g) which, on crystallization from toluene, afforded colourless needles (20.5 g, 59%), m.p. 152-3° (lit.[188] 152.5-153.5°).

11,12-Diketo-9,10-ethano-9,10-dihydroanthracene (121).

Oxidation of the ketone 120 by selenium dioxide was carried out according to the procedure of Vaughan and Yoshimine.[189] A single crystallization from toluene gave the diketone 121 as well-developed yellow prisms, yield 62% (lit.[189] 33%), m.p. 203.5-204° (lit.[189] 199-200.5°).

11,12-Diketo-9,10-ethano-9,10-dihydroanthracene monotosylhydrazone (122).

A solution of *p*-toluenesulphonhydrazide (11.8 g, 0.064 mole) in warm methanol (150 ml) was added slowly (10 min.) to a well-stirred solution of the diketone 121 (15.0 g, 0.064 mole) in hot methanol (400 ml). Stirring was continued for 2 hours and the mixture allowed to stand overnight before filtering. The product, after washing with cold methanol, was obtained as deep-yellow prisms, 21.4 g (83%), m.p. 194-6°, dec. (lit.[190] 195.5-196.5°).

11-Diazo-12-keto-9,10-ethano-9,10-dihydroanthracene (123).

The tosylhydrazone 122 (15.0 g) was dissolved in methylene chloride (600 ml), Spence alumina type UG1 (200 g) added and the mixture stirred slowly for 4 hours.[191] Filtration and washing of the alumina with methylene chloride (4 x 250 ml) gave a bright yellow filtrate, evaporation of which left a deep orange oil which crystallized on scratching. This crude product was digested with boiling hexane (200 ml), leaving an orange-yellow powder, 8.2 g (96%), m.p. 149-151° (lit.[190] 149-151°).

Methyl 9,10-dihydro-9,10-methanoanthracene-11-carboxylate (124a).

(a) Distilled water (25 ml) was added to a solution of the diazoketone 123 (1.00 g) in dioxan (100 ml) and the mixture irradiated for 48 hours by means of a mercury-quartz lamp. Dianthracene (0.11 g) was filtered off and the filtrate evaporated under reduced pressure. A solution in benzene (50 ml) of the gummy residue was shaken with sodium bicarbonate solution; acidification of the aqueous layer afforded no acidic products.

(b) A similar solution of the diazoketone in a Pyrex flask fitted with a gas vent was exposed to strong sunlight for 2 days. On working-up, dianthracene (0.055 g) was isolated in addition to a crude acidic mixture (0.23 g) which was esterified using diazomethane. The ester mixture was chromatographed on silica gel (40 g); elution with ethyl acetate/hexane (1:49) gave the ester 124a, 0.165 g (15%), m.p. 140-143°. Sublimation (78°/0.11 mm) afforded needles, m.p. 149.5-152°.

10-CHLORO-5-(1,1-DIMETHYLETHOXY)-5*H*-DIBENZO[*a.d*]CYCLOHEPTENE (131) and ETHYL 5*H*-DIBENZO[*a.d*]CYCLOHEPTENE-10-CARBOXYLATE (130a)

*10,11-Dihydro-5*H*-dibenzo*[a.d]*cyclohepten-5-one (125).*

This intermediate was readily available by the excellent three-step procedure of Campbell, Ginsig and Schmid.[192]

*10,11-Dibromo-10,11-dihydro-5*H*-dibenzo*[a.d]*cyclohepten-5-one (126).*

The ketone 125 (20.0 g, 0.096 mole) was heated in the vapour of boiling chlorobenzene (132°) while irradiating with an ultraviolet 'sun lamp'. The addition of bromine (40.0 g, 0.25 mole) during 3 hours caused vigorous evolution of hydrogen bromide; an efficient condenser was necessary to prevent excessive loss of bromine. Irradiation was continued for a further 1 hour before the solid product was broken up and washed with chloroform. The yield of dibromide 125 was 27.0 g (77%), m.p. 208-9° (lit.[193] 211°).

5H-Dibenz[a.d]*cyclohepten-5-one (127).*

Acid-washed zinc powder (4.5 g, 0.069 g atom) was added portionwise to a stirred mixture of the dibromide 126 (25.0 g, 0.068 mole) and acetic acid (1 ml) in ether (250 ml). The suspension boiled spontaneously while the dibromide gradually disappeared over 10 min. The turbid ether solution was washed with dilute acid and water and, after drying, gave the ketone 127. Trituration with cold ether (5 ml) afforded colourless needles, 11.0 g (98%), m.p. 88.5-89.5° (lit.[192] 89°).

5,10-Dichloro-5H-dibenzo[a.d]*cycloheptene (128).*

The ketone 127 (10.0 g, 0.049 mole) and phosphorus pentachloride (10.0 g, 0.049 mole) were heated together at 160° for 2 hours.[194] The molten crude product was mixed with acid-washed sand (25 g) and the mixture extracted with hexane in a Sohxlet apparatus. Crystallization from petroleum ether (b.p. 60-80°) gave prisms, 9.5 g (75%), m.p. 119-120° (lit.[194] 118-120°).

10-Chloro-5H-dibenzo[a.d]*cycloheptene (129).*

The dichloride 128 was treated with sodium borohydride according to the procedure of Looker.[194]

10-Chloro-5-(1,1-dimethylethoxy)-5H-dibenzo[a.d]*cycloheptene (113).*

The dichloride 128 (0.200 g) was dissolved in *tert.*-butyl alcohol (10 ml), freshly-cut potassium (*ca.* 0.02 g) added and the mixture stirred overnight. After evaporation of the alcohol under reduced pressure, the residue was dissolved in ether and washed briefly with water. The organic layer gave a white solid which crystallized from hexane/chloroform as white prisms, 0.172 g (75%), m.p. 128.5-129° (lit.[168] 128-9°).

Attempted preparation of 5H-*dibenzo*[a.d]*cycloheptene-10-carboxylic acid (130a).*

(a) The chloride 129 in tetrahydrofuran was boiled with magnesium (2 g equiv.) for 48 hours. The starting material was recovered unchanged.

(b) The chloride 129 in boiling tetrahydrofuran was treated for 16 hours with methylmagnesium bromide (5 mole equiv.). No reaction occurred.

(c) *n*-Butyllithium (5 mole equiv.) was added to the chloride 129 in ether. The mixture was boiled and stirred for 4 hours, during which time a deep olive-green colouration developed. No acidic products, however, were formed when the solution was poured onto 'dry ice'.

9-TRICHLOROMETHYL-9,10-DIHYDROANTHRACENE

2-Bromobenzoic acid was prepared from anthranilic acid by the excellent general method of Vingiello,[195] m.p. 149-150° (lit.[196] 150°).

2-Bromobenzoyl chloride was obtained from the corresponding acid by heating with phosphorus pentachloride (1 mole equiv.) at 140° for $\frac{1}{2}$ hour. The yield was 89%, b.p. 115-117°/10 mm (lit.[197] 158°/49 mm).

2-Bromobenzophenone: The general method of Vingiello[195] gave, in 88% yield, large prisms, m.p. 40° (lit.[198] 42°).

2-Bromodiphenylmethane: Reduction of 2-bromobenzophenone by red phosphorus-hydriodic acid produced well-developed prisms in 83% yield, m.p. 28-29° (no lit. m.p.[199]).

Trichloromethyl-2-benzylphenylcarbinol: Reaction with chloral of the Grignard reagent from 2-bromodiphenylmethane, as described previously,[195] gave a viscous liquid. The yield was 49% (lit. 33%) and b.p. 160-2°/0.3 mm (lit. 170-5°/1 mm).

9-Trichloromethyl-9,10-dihydroanthracene: The above carbinol was treated with phosphorus pentoxide to give colourless needles, m.p. 120-2° (lit.[195] 122-3°).

REACTION OF ANTHRACENE WITH ETHYL DIAZOACETATE

Uncatalysed Reaction.

The procedure of Badger, Cook and Gibb[153] was adopted. Ethyl diazoacetate (9.5 g, 0.083 mole) was added during 4 hours to a stirred solution of anthracene (59 g, 0.33 mole) in decalin (300 ml) at 140-145°. The temperature was then raised to 160° during 1 hour and maintained at this temperature for 1 hour. The cooled solution was filtered and most of the decalin removed in steam. The residue was recombined with the filtered solid and boiled under reflux with 10% ethanolic sodium hydroxide solution (500 ml). After the ethanol and remainder of the decalin were removed, the boiling solution was filtered. Acidification of the filtrate gave a sticky solid from which *1H-cycloprop*[a]*anthracene-1-carboxylic acid (100)* was isolated in 5-10% yield as a white crystalline powder, m.p. 283-5° (darkening from 240°), λ_{max} (log ε), 222 (5.30), 253 (5.73), 259sh (5.62), 270sh (5.37), 287 (5.13), 298 (5.24), 310 (5.20), 336 (4.11), 347 (3.73), 351 mμ (4.06); ν_{max} (nujol), 1650 cm^{-1} (C═O str.). Esterification with ethereal diazomethane gave the *methyl ester 104* as colourless plates (methanol), m.p. 123-4°, λ_{max} (log ε), 222 (5.29), 253 (5.73), 259sh (5.61), 270sh (5.37), 287 (5.11), 298 (5.23), 310 (5.18), 336 (4.05), 347 (3.63), 351 mμ (4.03); ν_{max} (nujol), 1720 cm^{-1} (C═O str.).

Chromatographic Work-up

After the reaction was complete, the decalin was removed under reduced pressure and the residue extracted with hot methanol (1 x 150 ml, 2 x 50 ml). When subjected to chromatography on neutral alumina, activity I, two isomeric esters were eluted with ethyl acetate/benzene

(1/9): *ethyl 1*H-*cycloprop*[a]*anthracene-1-carboxylate (104a)* as colourless plates, m.p. 125-6° (lit.[200] 125-6°); and *ethyl 5*H-*dibenzo*[a.d]*cycloheptene-10-carboxylate (107)* (in 0.1% yield) as a sticky semi-solid, λ_{max} (log ε), 297 mμ (3.40); ν_{max} (nujol), 1700 cm^{-1} (C$=$O str.). Because of the difficulty in handling the compound, only an approximate analysis was possible. (Found: C, *ca.* 79; H, *ca.* 6. $C_{18}H_{16}O_2$ requires C, 81.7; H, 6.1%).

Catalysed Reactions.

Anthracene (39 g, 0.22 mole) was dissolved in chlorobenzene (400 ml) at 100° (water bath). Catalyst (2.0 g) was added and the mixture stirred vigorously at 100° during the addition of ethyl diazoacetate (10.0 g, 0.088 mole). Heating and stirring were continued after addition was complete; then the solvent was removed under reduced pressure. The residue was boiled with methanol (400 ml) for $\frac{1}{2}$ hour, filtered off and washed with cold methanol (2 x 100 ml). After addition of sodium hydroxide (50 g) in water (400 ml), the mixture was boiled under reflux for 4 hours. The cooled solution was filtered and the methanol evaporated. After washing with ether, the aqueous solution was acidified, to give the 1,2-adduct 100. No other aromatic acid could be detected.

Catalyst	Time of addition	Time of stirring after addition	Yield of acid (100)
Copper bronze	30 min	4 hr.	10%
Cuprous bromide	90 min	30 min	5% (v.impure)
Anhydrous copper sulphate	20 min	30 min	29%

REACTION OF ANTHRACENE WITH DICHLOROCARBENE

Method A: Chloroform-Potassium tert.*-butoxide*

A suspension of finely-ground anthracene (10.0 g, 0.056 mole) and potassium *tert.*-butoxide (from potassium, 2.20 g, 0.056 g. atom) in dry benzene (150 ml) was cooled to 5° while chloroform (6.75 g, 0.056 mole) was added during 30 min. After stirring for a further 30 min, the mixture was warmed to *ca.* 40° and filtered quickly through diatomaceous earth. The brown mixture (3.0 g) obtained on evaporation of the filtrate gave, after chromatography on neutral alumina, Activity I (300 g), *10-chloro-5-(1,1-dimethylethoxy)-5*H*-dibenzo*[a.d]*-cycloheptene (113)*, 1.40 g (10%) which was identical with an authentic sample.

Method B: Ethyl Trichloroacetate-Sodium Methoxide

To a suspension of anthracene (5.0 g, 0.028 mole) and sodium methoxide (from sodium, 0.78 g, 0.028 g. atom) in dry benzene (100 ml) at 5°, ethyl trichloroacetate (5.4 g, 0.028 mole) was added during 1 hour. After warming to 40°, the mixture was filtered; evaporation of the filtrate gave a brown solid (1.7 g). Part of this residue was boiled with potassium *tert.*-butoxide in benzene. The product so obtained gave no pink colour with conc. sulphuric acid.

Methods C and D: Decarboxylation of Sodium Trichloroacetate

Anthracene (5.0 g, 0.028 mole), sodium trichloracetate (5.2 g, 0.028 mole) and (Method D) potassium *tert.*-butoxide (from potassium 1.10 g, 0.028 g. atom) in dimethoxyethane (sodium-dried, 50 ml) were boiled under reflux for 22 hours. Treatment with base, then acid, showed no pink colour.

Methods E and F: Decomposition of Phenyltrichloromethylmercury

Anthracene (1.0 g, 5.6 mmole) and phenyltrichloromethylmercury (2.2 g, 5.6 mmole) and (Method F) anhydrous sodium iodide (0.84 g, 5.6 mmole) in dry dimethoxyethane (30 ml) were boiled under reflux for 48 hours or (Method F) 4 hours. The anthracene did not react.

Treatment of 9-trichloromethyl-9,10-dihydroanthracene (117)

The trichlorocompound 117 (2.0 g, 6.8 mmole) and potassium *tert.*-butoxide (from potassium, 1.31 g, 0.034 g. atom) in dry benzene (25 ml) were stirred for 4 hours. After treatment with water, the organic layer gave a residue (1.12 g) which was subjected to chromatography on silica gel (50 g). Elution with hexane gave anthracene, 0.24 g (20%); ether/hexane (1:19) gave 9-anthraldehyde, 0.68 g (50%).

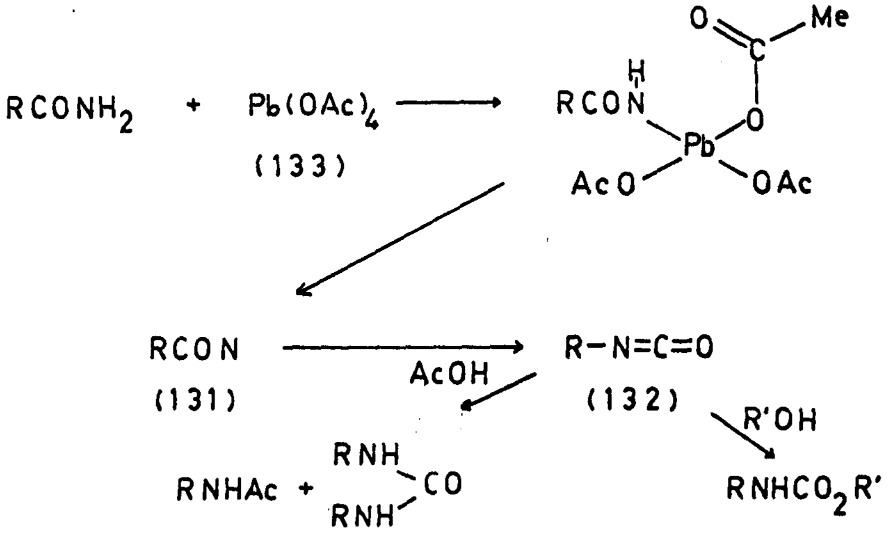
APPENDIX

METAL DERIVATIVES OF CARBAMATES

METAL DERIVATIVES OF CARBAMATES

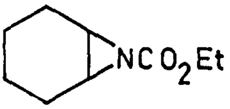
LEAD(IV)-CARBAMATE DERIVATIVES

The reaction of primary amides with lead tetraacetate has been reported.[208-210] The earlier authors[208,209] suggested that the intermediate *iso*cyanate 132 resulted from rearrangement of an acylnitrene 131 (Scheme AI). It seemed possible, therefore, that treatment of a carbamate, $ROCONH_2$, with lead tetraacetate might provide a novel route to a carbalkoxynitrene.

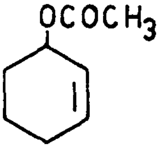


Scheme AI

To a solution of ethyl carbamate in boiling cyclohexene was added lead tetraacetate (133, 1 mole equiv.); the reaction was monitored from time to time by addition to water of a small sample of reaction mixture. A black precipitate of lead dioxide indicated the presence of lead(IV) species. No aziridine (135) resulted from



(135)



(136)

addition of a nitrene to the cyclohexene double bond, but instead the acetate 136 was obtained in moderate yield after a reaction time of 6 hours. This time is comparable to that required in the absence of ethyl carbamate.[211] It seemed possible that reaction of lead tetraacetate with the carbamate was too slow to compete with acetoxylation of the olefin.

It has been noted[209,210] that amides are consumed much more rapidly by lead tetraacetate in alcoholic solvents than in non-polar media. The reaction was therefore repeated using a 1:1 mixture of cyclohexene and methanol as solvent. The reaction was complete in 10 minutes; only a trace amount of acetate 134 was produced, together with formaldehyde as the main product.

Repetition of the reaction in neat methanol and ethane showed that very rapid and efficient oxidation of the solvents was effected. The ethyl carbamate, which serves a catalytic role, was recovered unchanged. In fact, 0.1 mole equiv. of this compound is sufficient to markedly increase the rate of oxidation of the alcohols. Similarly *tert.*-butyl carbamate, which is recovered unchanged after treatment for long periods with lead tetraacetate (133) in non-polar solvents, has a marked catalytic effect on the oxidation of methanol by 133.

The colours of the reaction mixtures are of interest. In alcoholic media, partial or complete ligand exchange occurs with lead tetraacetate; the alkoxylead compounds are highly-coloured.

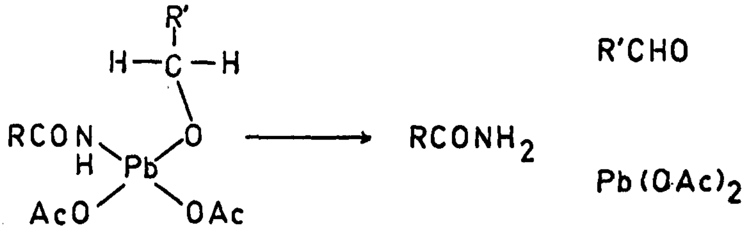
TABLE A1

NH_2CO_2Et (mole equivs.)	L.T.A. (mole equivs.)	Solvent	Initial Colour	Time	Products
1.0	1.0	cyclo hexene	pale brown	6 hr.	acetate 69%
1.0	1.0	MeOH/ cyclo hexene	yellow	10 min	HCHO
1.0	1.0	MeOH	yellow	10 min	HCHO
1.0	1.0	EtOH	red-brown	1 hr	MeCHO 86%
0.1	1.0	EtOH	red-brown	2 hr	MeCHO 82%
1.0	1.0	benzene	transient brown	5 days	no reaction

TABLE A2

$NH_3CO_2Bu^t$ (mole equivs.)	L.T.A. (mole equivs.)	Solvent	Initial Colour	Time	Products
1.0	1.0	benzene	transient deep brown	7 days	no reaction
1.0	1.0	cyclo hexene	pale brown	2 days	no reaction
1.0	1.0	CCl_4	transient deep brown	7 days	no reaction
1.0	1.0	MeOH	deep brown	$5\frac{1}{2}$ min	HCHO

When an alkyl carbamate is added, therefore, there will be present lead complexes with alkoxy, carbamyl and (possibly) acetoxy ligands, e.g. 137. Such a compound can decompose by a cyclic five-membered transition state to an aldehyde (or ketone), carbamate and a lead(II) derivative.



(137)

An acylnitrene is not involved.

On the other hand, addition of 133 to a solution of a carbamate in benzene produces a transient deep colouration which fades to a pale brown. The lead derivative present, probably 138, is stable over long periods at reflux temperatures.

$$\text{ROCONH}—\text{Pb(OAc)}_3$$

(138)

It is clear, therefore, that treatment of alkyl carbamates with lead tetraacetate does not lead to formation of alkoxycarbonylnitrenes.

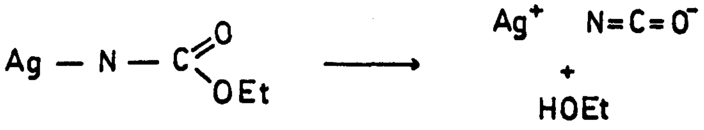
SILVER-CARBAMATE DERIVATIVES

Triplet carbethoxynitrene displays radical-type activity and, in its substitution reactions with anthracene, should behave like the urethanyl radical (140). We therefore studied the thermal decomposition of the silver-carbamate complex (139) in the hope that homolysis of the Ag — N bond might give rise to 140.

$$\mathrm{Ag - NHCO_2Et} \qquad\qquad \mathrm{H\dot{N}CO_2Et}$$

(139) (140)

The silver derivative was prepared by addition of aqueous potassium hydroxide to a solution of ethyl carbamate and silver nitrate in water. The (flocculent) bright-orange precipitate was filtered off and quickly washed with ethanol, then ether. The i.r. spectrum of the freshly-prepared compound showed absorption at 3350 (N — H stretch.) and 1610 cm^{-1} (C = O stretch.) on standing, this compound gradually turned black while an i.r. band at 2200 cm^{-1} became prominent until, after 8 hours at room temperature, it was the only important band. The black compound was identified as silver cyanate by comparison with an authentic sample and is considered to be formed according to Scheme AII.



Scheme AII

This decomposition is very rapid at higher temperatures and is complete within 5 min when carried out in boiling benzene or ethanol.

In order to confirm this proposed mechanism, the silver derivative of cholesteryl carbamate was prepared. Decomposition of this complex gave cholesterol in 76% overall yield. Subsequently it was found unnecessary to isolate the silver derivative and decomposition *in situ* by boiling the reaction mixture gave a markedly improved yield (> 95%) of cholesterol.

Similar *in situ* decomposition of the silver derivatives of *n*-octyl and cinnamyl carbamates gave the corresponding alcohols in 97 and 92% yields, respectively. Phenyl carbamate was converted to an extremely labile complex and warming on a water bath for 5 min gave phenol, 80%, isolated as the tribromo-derivative.

Alkyl and aryl carbamates, which are quite resistant to hydrolysis, can therefore be cleaved under quite mild conditions.

EXPERIMENTAL

PREPARATION OF CARBAMATES

The excellent general procedure of Loev and Kormendy[205] was employed. The preparation of *tert.*-butyl carbamate is typical.

tert.-*Butyl carbamate.*

Trifluoroacetic acid (15.5 ml, 0.21 mole) was added slowly to a stirred mixture of *tert.*-butyl alcohol (7.4 g, 0.1 mole) and sodium cyanate (13.0 g, 0.2 mole) in dry benzene (50 ml). The container was loosely stoppered and the suspension stirred for 3 hours. Water (25 ml) was added and the clear organic layer separated and dried. Evaporation gave a solid residue which was crystallized from hot water to give needles, 7.8 g (67%), m.p. 107.5-108° (lit.[205] 107-108°).

By the same method, the following carbamates were prepared:

n-octyl carbamate, in 92% yield, as waxy plates (ethanol/water), m.p. 66-67° (lit.[206] 67°);

phenyl carbamate, in 57% yield, as prisms, (ethanol/water), m.p. 142.5-143° (lit.[207] 143°);

cinnamyl carbamate, in 82% yield, as prisms, m.p. 120.5-121°. (Found: C, 67.96; H, 5.96; N, 7.99. $C_{10}H_{11}NO_2$ requires C, 67.78; H, 6.26; N, 7.91%).

cholesteryl carbamate, in 70% yield, as waxy prisms, m.p. 202.5-204.5°. (Found: C, 77.97; H, 10.79; N, 3.26. $C_{28}H_{47}NO_2$ requires C, 78.27; H, 11.03; 3.26%).

REACTION OF CARBAMATES WITH LEAD TETRAACETATE

The carbamate was dissolved in boiling solvent (5 ml per g of lead salt) which was stirred magnetically under an atmosphere of dry, oxygen-free nitrogen. Lead tetraacetate (freed from acetic acid in a desiccator containing potassium hydroxide pellets) was added quickly to this solution. When the reaction was completed, anhydrous potassium carbonate was added and the mixture allowed to stand overnight. After filtration through diatomaceous earth, the liquid was carefully evaporated on a steam bath; the residue was dissolved in ether and filtered. The resultant solution was subjected to analysis by v.p.c. using column C. The volatile aldehyde produced during the reaction was swept by the nitrogen stream into a solution of 2,4-dinitrophenylhydrazine in 10% hydrochloric acid. The yield is expressed in terms of the 2,4-dinitrophenylhydrazone produced.

PREPARATION OF SILVER DERIVATIVES

Silver-Cholesteryl Carbamate complex

Cholesteryl carbamate (0.200 g, 0.46 mmole) was dissolved in acetone (20 ml). To this solution silver nitrate (0.080 g, 0.46 mmole) in water (1 ml) was added, followed by potassium hydroxide (0.026 g, 0.46 mmole) in water (1 ml), added dropwise. The yellow flocculent precipitate (0.21 g, 82%) gradually darkened on storage at room temperature; boiling in benzene for 4 hours gave cholesterol (0.115 g, 74%) and silver cyanate. A better yield of cholesterol (95%) was obtained by decomposing the silver derivative *in situ*.

The same general method was used to prepare silver derivatives of ethyl, *n*-octyl, phenyl and cinnamyl carbamates. Each complex was quite unstable and decomposed to give the corresponding hydroxy-compound in high yield.

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REACTION OF LEAD TETRA-ACETATE WITH PRIMARY AMIDES. FORMATION OF ALKYL CARBAMATES.

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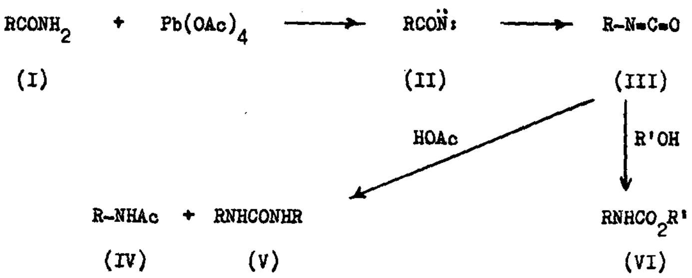
(Received 20 September 1965)

In a previous communication[1] we described the formation of _N_-acetylamines and _N_,_N_'-dialkylureas by interaction of primary amides and lead tetra-acetate in benzene or preferably in acetic acid. Evidence was presented in support of the hypothesis that the reaction proceeds initially to the appropriate isocyanate (III) from which the final products, (IV) and (V), were formed by reaction with acetic acid. It was also suggested that the rearrangement (I ⟶ III) involves the intermediacy of an acylnitrene (II). Independently, the reaction of lead tetra-acetate with primary amides and t-butanol in the presence of triethylamine was studied by Baumgarten and Staklis[2] who showed that t-butyl carbamates (VI, R'=t-Bu) are produced under these conditions. These authors confirmed the initial formation of the isocyanate and they further suggested that the reaction proceeds _via_ a nitrene intermediate.



We also have studied the reaction of lead tetra-acetate with primary amides in the presence of alcohols. The discordance of some of our results with observations of Baumgarten and Staklis[2] prompts us to report them herein. Specifically, we find the reaction to be of much wider application than was previously recognised. Thus it was stated[2] that the reaction fails with compounds containing active methylene groups (phenylacetamide), or olefinic double bonds (cinnamamide) and can not be carried out in methanol or ethanol solvent. However, in our hands the reaction has proceeded smoothly in all these cases.

The results of our experiments are summarised in the accompanying table. The successful formation of alkyl carbamates when the reaction was conducted in alcoholic solvents was observed in experiments 1 to 9. In ethanol and methanol at the reflux temperature the reaction usually proceeds rapidly, and its completion, marked by the disappearance of the yellow colour first formed upon mixing of the reactants occurs in most instances in less than 1 hour. In a typical experiment (1) cyclohexanecarboxamide (1.0 g) and lead tetra-acetate (3.8 g) in methanol (50 ml) were stirred under nitrogen at 55-60°. After 1 hour the mixture was diluted with aqueous sodium carbonate and extracted with ether. Evaporation of the extract afforded methyl N-cyclohexylcarbamate

Table 1

Products from Interaction of Lead Tetra-acetate, Primary Amides and Alcohols

Expt.	Amide (I)	Alcohol[a]	Reaction Time	Yields (%)	
				Carbamate (VI)	Urea (V)
1	R= cyclohexyl	MeOH	30 min	96	nil
2	"	EtOH	60 "	88	"
3	"	t-BuOH	60 "	33	27
4	"	t-BuOH[b]	60 "	49	14
5	24-nor-5β-cholanyl	MeOH[c,d]	3 hr	58	nil[e]
6	" "	MeOH	4 hr	86	"
7	phenyl	"	20 min	62	"
8	p-nitrophenyl	"	30 "	69	"
9	benzyl	"	5 "	67	"
10	phenyl	cholesterol[b,c]	60 "	35	"
11	dec-9-enyl	EtOH[c]	2 hr	51	"
12	3β-acetoxyandrost-5-en-17β-yl	MeOH	10 min	57	"

[a] Unless otherwise stated the alcohol was also used as solvent.

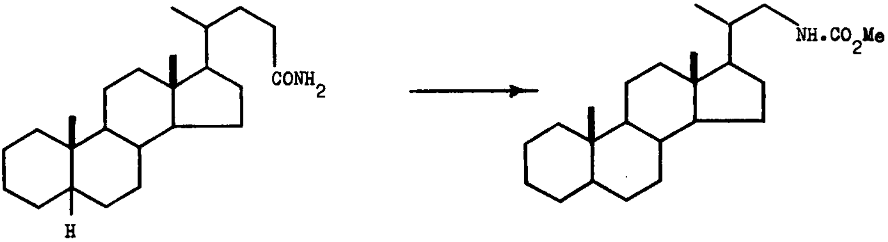
[b] Reaction conducted in the presence of pyridine.

[c] Benzene solvent.

[d] Methanol present as solvent of crystallization.

[e] Products included N-acetyl-24-nor-5β-cholanylamine (29%).

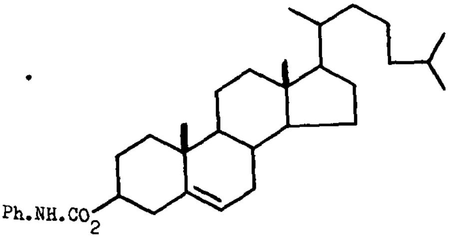
Of special interest, in that it illustrates well the ease of the reaction, is the formation of methyl N-(24-nor-5β-cholanyl)carbamate (VIII) by treatment of cholanamide (VII) with lead tetra-acetate (expt. 5). Although the only methanol available was that present as solvent of crystallization the product consisted mainly of the urethane (VIII), together with a smaller amount of N-acetyl-24-nor-5β-cholanylamine. The latter acetyl compound was the sole product when scrupulously dried amide was treated with lead tetra-acetate in benzene.[2] Conversely, when methanol was employed as solvent for the reaction only the urethane (VIII) was isolated (expt. 6).



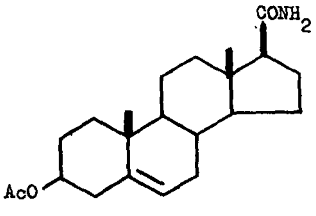
(VII) (VIII)

In accord with previous observations[2] we found that neat t-butanol is not a satisfactory solvent for the preparation of urethanes. Thus, cyclohexanecarboxamide when treated with lead tetra-acetate in t-butanol (expt. 3) afforded comparable amounts of t-butyl N-cyclohexylcarbamate (VI; R=cyclohexyl, R'=t-Bu) and N,N'-dicyclohexylurea. However when the reaction was repeated in the presence of pyridine (expt. 4) the yield of urea was greatly decreased, and that of the urethane proportionately increased.

The successful preparation of cholesteryl N-phenyl carbamate (IX) by interaction of lead tetra-acetate, benzamide, and cholesterol in benzene-pyridine is particularly significant in that it illustrates the applicability of the reaction to the formation of urethanes containing complex alkyl groups. Other examples of the reaction when applied to olefinic starting materials are the preparation of carbamates from 10-undecenamide (expt. 11) and from 3β-acetoxyandrost-5-ene-17β-carboxamide (X) (expt. 12).



(IX)



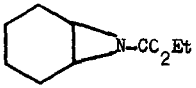
(X)

The reaction also has been successfully applied to a substituted aromatic amide (*p*-nitrobenzamide) and to an amide containing a reactive methylene group (phenylacetamide).

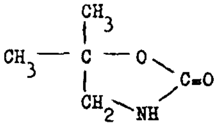
With a view to obtain evidence concerning the intermediacy of acylnitrenes in the reaction we have attempted to apply it to alkyl carbamates (XI) containing an unsubstituted -NH_2 group. Nitrenes potentially capable of formation from this type of precursor undergo rearrangement only with difficulty^4 and thus may be readily detected by their intermolecular reaction with suitable acceptors, e.g. olefins.^{5}

$ROCONH_2$

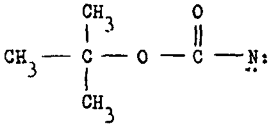
(XI)



(XII)



(XIII)



$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-O-\overset{O}{\overset{\|}{C}}-\ddot{N}:$

(XIV)

However, treatment of ethyl carbamate (XI, R=Et) with lead tetra-acetate in cyclohexene afforded solely 3-cylohexenyl acetate, and the aziridine (XII) known to be formed by addition of carbethoxynitrene to cyclohexene[5] could not be detected. When ethanol was employed as solvent acetaldehyde was formed in high yield and the carbamate was recovered unchanged. It was noted that the oxidation of ethanol by lead tetra-acetate proceeded very much faster in the presence of ethyl carbamate, than in its absence. Methanol was similarly rapidly oxidized by lead tetra-acetate in the presence of ethyl carbamate or t-butyl carbamate (XI, R=t-Bu). The latter compound (XI, R=t-Bu) was recovered unchanged after refluxion with lead tetra-acetate in benzene for one week. There was no evidence for the formation of the cyclic compound (XIII) which is obtained in good yield by an intramolecular insertion process from the appropriate nitrene (XIV) when generated photochemically.[6] The mechanistic implications of these observations will be discussed in detail elsewhere. In summary our conclusions are that the reaction of carbamates with lead tetra-acetate does not lead to nitrenes, and that probably the conversion (I → III) of carboxamides into isocyanates also does not proceed *via* nitrenes but involves a concerted oxidative rearrangement of a tetravalent lead - amide complex.

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