THE REARRANGEMENT OF
CYCLOPROPYL CARBENES

A Thesis submitted to the
University of Southampton
for the degree of
DOCTOR OF PHILOSOPHY

by

Colin Leonard Bird

October, 1969

To my parents

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ABSTRACT

FACULTY OF SCIENCE

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Doctor of Philosophy

THE REARRANGEMENT OF CYCLOPROPYL CARBENES

by Colin Leonard Bird.

This work has been divided into two parts. The first part was concerned with experimental studies on the rearrangement of cyclopropyl carbenes, generated by the decomposition of the p-toluene sulphonyl hydrazones of cyclopropyl aldehydes and ketones at 135 - 140° in an alkaline aprotic medium.

Cyclopropane carboxaldehyde p-toluene sulphonyl hydrazone itself gives rise mainly to cyclobutene. The direction of ring opening has been determined from a study of asymmetrically substituted cyclopropyl carbenes. The substitution pattern in the product cyclobutenes indicated that the least substituted bond of the cyclopropane ring was migrating preferentially during the rearrangement.

Cis-2-methyl cis-3-vinyl cyclopropyl carbene was studied in order to gain some insight into the spin state in which variously substituted cyclopropyl carbenes react. The results indicated that a substantial amount of the reaction was occurring via the triplet state.

Part Two has involved an attempt to simulate the rearrangement theoretically, using the method of CNDO (Complete Neglect of Differential Overlap) for molecular orbital calculations.

Methods were developed for describing the reaction pathway in terms of cartesian coordinates suitable for use with the computer programme for

the CNDO calculations.

The CNDO method was evaluated by determining the barriers to rotation in various cyclopropyl compounds. Reasonably satisfactory values were obtained, so the rearrangement itself was studied. Although the results obtained were not in accord with the experimental observations on the preferred direction of ring-opening, a number of useful points emerged, which assisted in the evaluation of the experimental part.

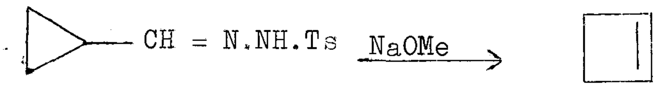
PART I

THE REARRANGEMENT OF CYCLOPROPYL CARBENES

Chapter 1

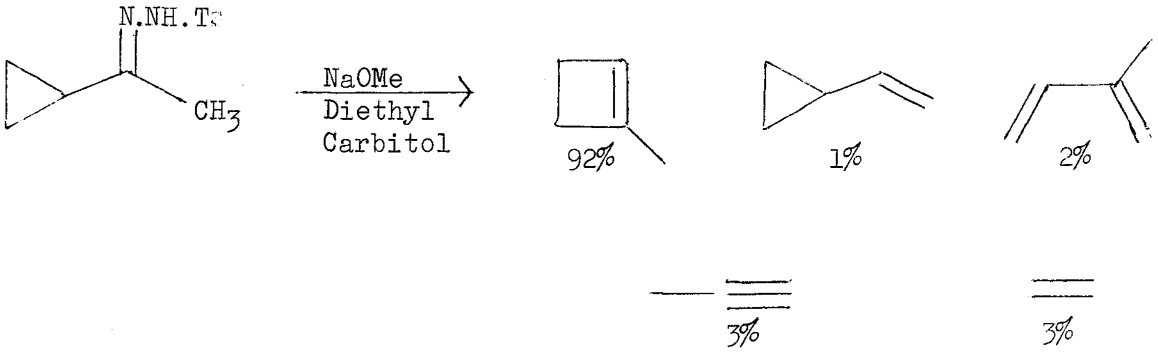
INTRODUCTION

In 1960 Friedman and Shechter reported that the p-toluene sulphonyl (tosyl) hydrazone of cyclopropane carboxaldehyde, on treatment with sodium methoxide at 180°C in an aprotic solvent, gave mainly cyclobutene, by ring expansion.[1]



The yields were 60% in Diethyl Carbitol and 67% in N-methyl-2-pyrrolidone, other products being ethylene (13%, 10%) and acetylene (13%, 10%) by fragmentation and 1,3 butadiene (4·5%, 7%), it not being established whether this was formed directly or by secondary reaction of "excited" cyclobutene. No methylene cyclopropane was detected, although this might have been anticipated by analogy with the 1,2-hydrogen migrations exhibited by aliphatic tosyl hydrazones.[2]

In the same paper Friedman and Shechter reported the decomposition of cyclopropyl methyl ketone tosyl hydrazone, the principal product being 1-methyl cyclobutene.



The decomposition of sulphonyl hydrazones under basic conditions was first reported by Bamford and Stevens,[3] and became known as the Bamford-Stevens reaction. Powell and Whiting[4] have shown that this proceeds via a rate-determining unimolecular elimination of sulphinate anion, leaving a diazo-compound. If the medium contains available protons, this may be assumed to be protonated, and the subsequent reactions to be those of the carbonium ion. In an aprotic medium, however, the diazo-compound can be presumed to lose nitrogen, yielding a carbene intermediate.

Thus cyclopropyl diazomethane is expected to be an intermediate in the decomposition of cyclopropane carboxaldehyde tosyl hydrazone. This diazomethane has been independently synthesised,[5,6,7] as has dicyclopropyl diazomethane.[6,8]

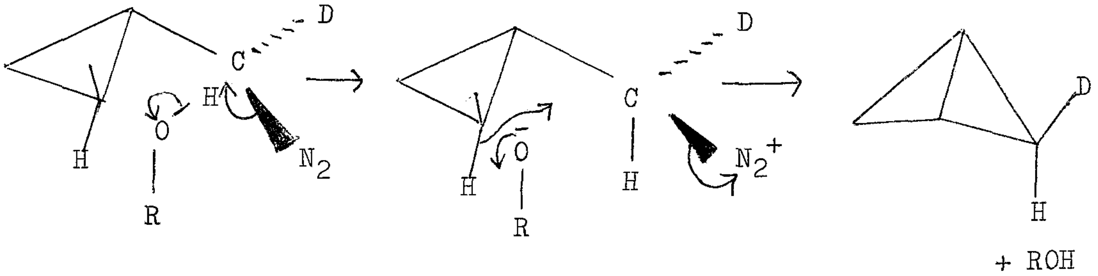
Following a report by Frey and Stevens[9] that the decomposition of cyclopropane carboxaldehyde tosyl hydrazone in fact gave predominantly bicyclo [1.1.0] butane, a considerable amount of effort was devoted to determining the conditions for the formation of bicyclobutane, and the mechanism by which it was formed.[10,11,12,13,14]

It was established that bicyclobutane was formed if the decomposition was carried out with an equivalent or insufficient amount of base in a protic solvent, usually ethylene glycol, although free tosyl hydrazone was considered to be able to act as a proton donor.[10]

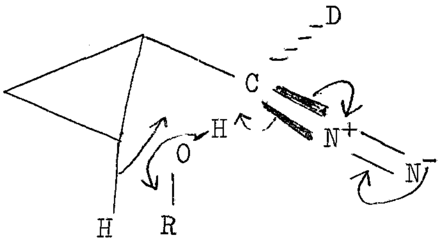
These conditions were believed to favour the intermediacy of a carbonium ion-type intermediate, by analogy with studies on camphor tosyl hydrazone[2,4,15] which gives tricyclene and camphene, the proportion of the latter increasing under increasingly "carbonium ion conditions".

However, deuteration experiments showed considerable stereoselectivity, so it was proposed that an "unusual" carbonium ion, poorly solvated and highly energized, was giving rise to bicyclobutane.[11]

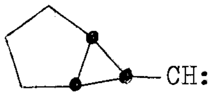
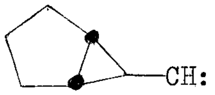
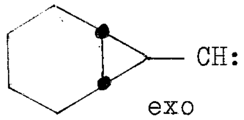
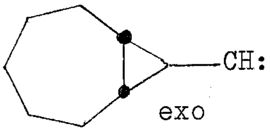
The final mechanism proposed was that of Wiberg and Lavanish[14], involving a proton transfer via a solvent molecule. which was intrinsic to the activated complex.



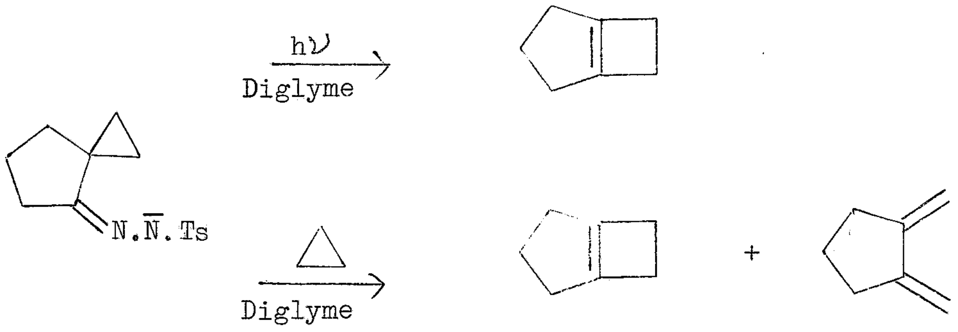
This may be written as a synchronous process:

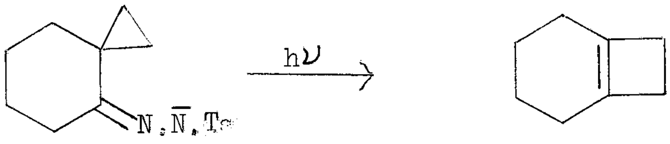


Kirmse and Pook[16] studied some bicyclo [n.1.0] alkyl carbenes (n = 3,4,5) and these were found to yield predominantly cyclobutene products.

Carbene	Products	
	Bicyclo[n.2.0] alkene	Cycloalkene (by fragmentation)
 endo	76%	24%
 exo	69.5%	30.5%
 exo	67%	33%
 exo	72%	28%

These studies were extended to the decomposition of spiro-[2.4]-heptan-4-one and spiro-[2.5]-octan-4-one tosyl hydrazones.[17]



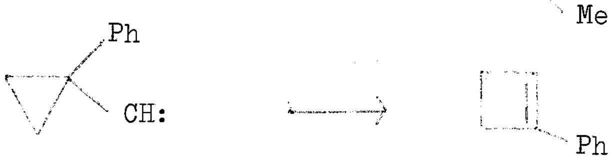


From the absence of spiro-alkene products, it was concluded that the cyclopropyl carbene rearrangement predominates over the intramolecular hydrogen shift. This is observed in other examples of this reaction.

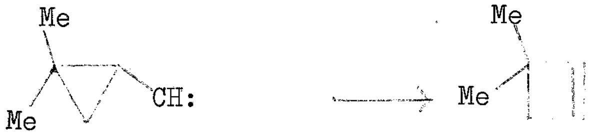
The generality of the ring expansion to cyclobutenes is illustrated by the following examples, which also illustrate the synthetic applicability of the reaction.

(18)

(18)



(10,19)

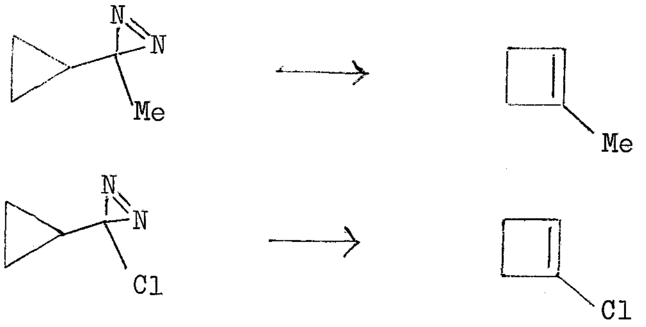


(18)

(20)

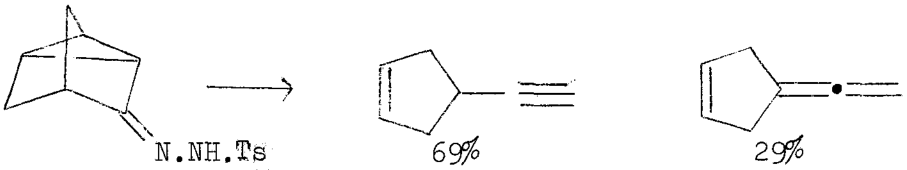
(20)

Bradley has studied the chemistry of 3-cyclopropyl-3-methyl diazirine[21] and 3-cyclopropyl-3-chloro diazirine[22] and these, on pyrolysis, give the respective cyclobutenes as major products.



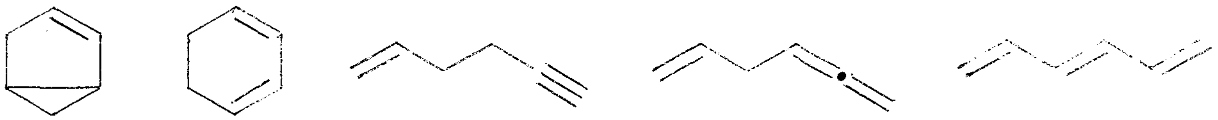
In cases where sufficient steric strain is present to render the cyclobutene an unlikely product, a variety of products are found, usually as a result of fragmentation reactions.

Thus, nortricyclenone tosyl hydrazone gives the acetylene and allene shown below.[23] It was established that the allene was produced from the acetylene by base-catalysed isomerisation under the reaction conditions.



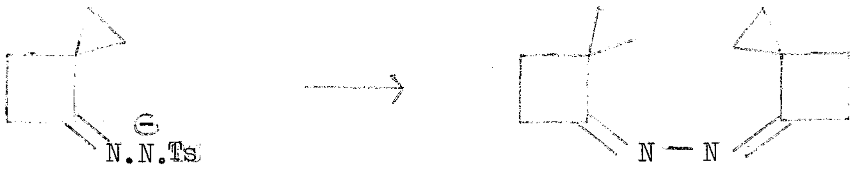
69%   29%

Freeman and Kuper also failed to obtain any cyclobutene product from bicyclo[3.1.0] hexan-2-one tosyl hydrazone,[24] the products being:

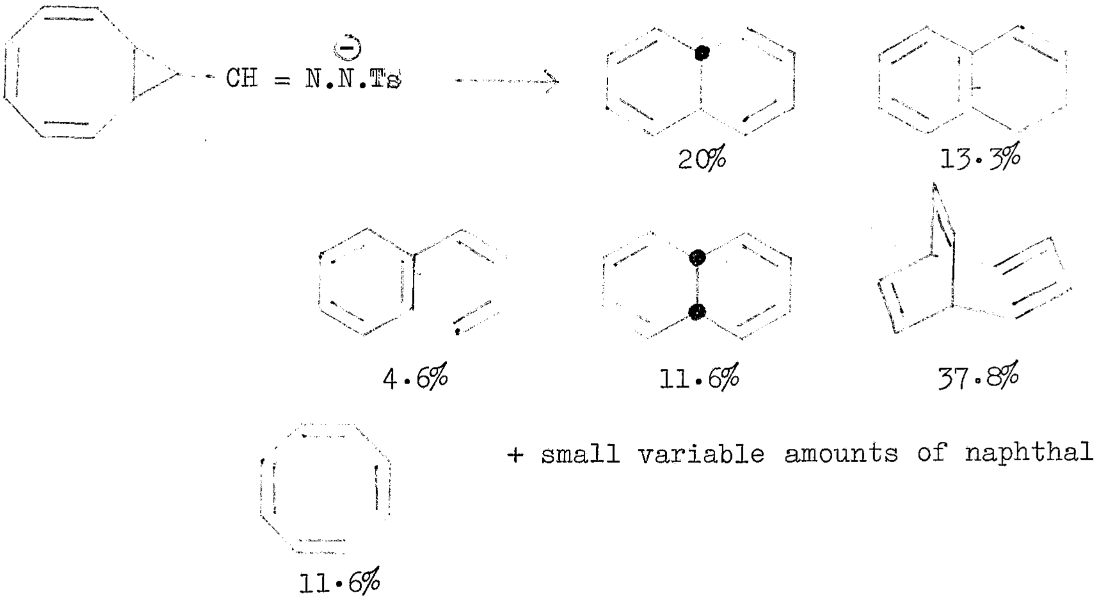


18·6%   14·2%   13·1%   12·3%   41·8%

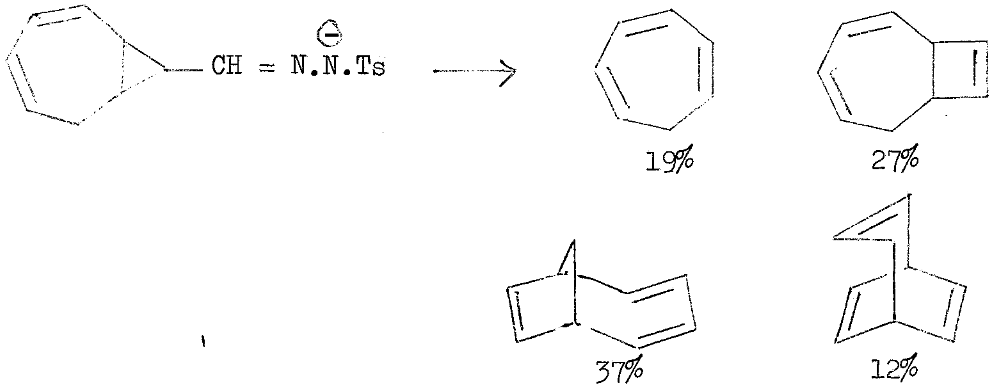
According to Wiberg et al.,[25] Spiro-[2,3]-hexan-4-one tosyl hydrazone gives only azine, a somewhat surprising result.

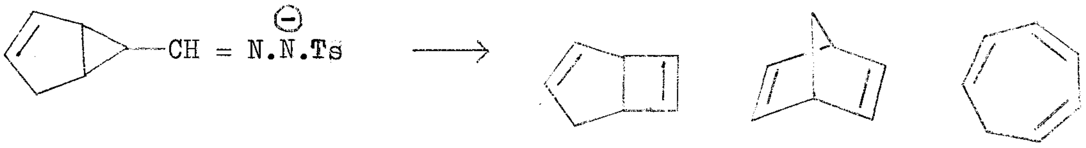


Maitland Jones Jr. et al. have studied a series of compounds in which the cyclopropane ring is substituted by a system of conjugated double bonds, bicyclo[6.1.0]nona-2,4,6-trien-9-yl carbene,[26,28] bicyclo[5.1.0]octa-2,4-dien-8-yl carbene[27,28] and bicyclo[3.1.0]hex-2-en-6-yl carbene.[28] The products from these are indicative of some form of ring-opening, the intermediate presumably being stabilised by the double-bond system.

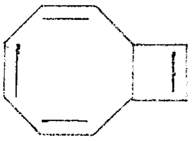


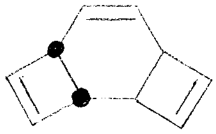
+ small variable amounts of naphthalene.

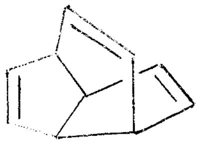


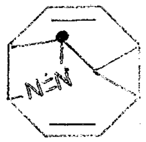


In the first case Jones and Scott[26] failed to isolate any of the cyclobutene derivative, but Masamune [29,30] by photolysing the sodium salt of the tosyl hydrazone at -30°C, and keeping the temperature below 0°C during the work-up, has isolated the cyclobutene (A) and another product, as yet unidentified, the proposed structures being B and C. The endo isomer also yields pyrazoline D.


A

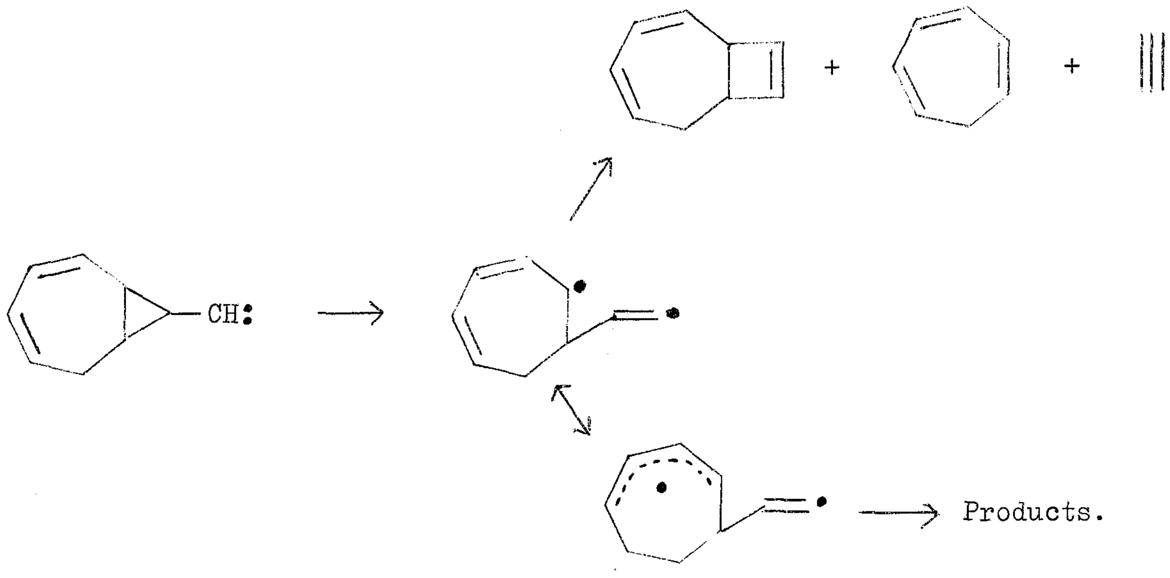

B


C



D

While it is possible to write mechanisms for the transformations observed by Jones et al. without invoking any opening of the cyclopropane ring, their explanation is a convenient one. For example :



The retention or loss of a specific stereochemistry of substitution on the ring should provide evidence about whether ring-opening is involved in the mechanism. In this context Guarino and Wolf have photolysed trans-2,3-dimethyl cyclopropyl diazomethane,[31] and, although no cyclobutene was isolated and identified, examination of the olefin and diene products indicates that the stereochemical integrity of the ring is retained under conditions expected to yield a singlet carbene.

Stereochemical scrambling is observed when inert gas quenching produces substantial quantities of the triplet.

This work followed some earlier studies by Shevlin and Wolf on the photolysis of cyclopropyl diazomethane in the gas phase,[7] from which they obtained mainly fragmentation products, a result similar to that obtained when they reacted cyclopropane with energetic carbon atoms in the gas phase.

This contrasted with earlier work by Engel and Skell,[32] who obtained 65% methylene cyclopropane from the reaction of cyclopropane and carbon atoms simultaneously "condensed" on a cold surface. Commenting on this, Shevlin and Wolf suggested that energetic and spin state differences could account for the variation.

The aim of the present work has been to study cyclopropyl carbenes in which the ring is asymmetrically substituted, making it possible to observe which of the cyclopropane ring bonds is migrating to the carbene centre.[33,34]

Some theoretical calculations, using the method of Complete Neglect of Differential Overlap,[35] have also been undertaken, to examine the possibility of predicting the direction of ring opening theoretically. (Part 2)

The general chemistry of carbenes has been reviewed a number of times, in particular by Kirmse[36] and recently by Moss,[37] an excellent general review.

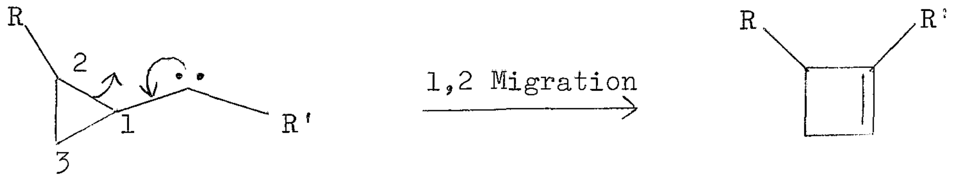
Chapter 2

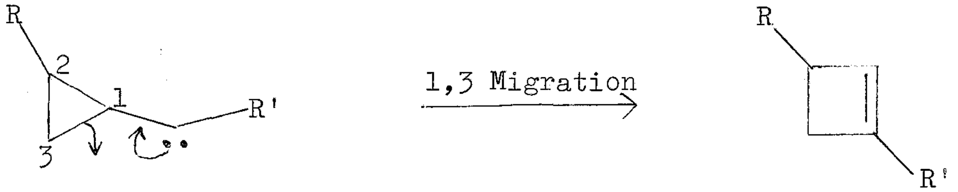
The Rearrangement to Cyclobutenes

For the conversion of cyclopropyl carbene to cyclobutene, a simple 2-electron shift mechanism may be proposed

This may also be written as a radical reaction, but the process remains essentially the same. This remains true if the carbene carbon or the 1-position of the ring are substituted.

However, it is possible to substitute the ring in such a way that the cyclobutene products differ according to whether the 1,2 or the 1,3 bond of the cyclopropane ring migrates.





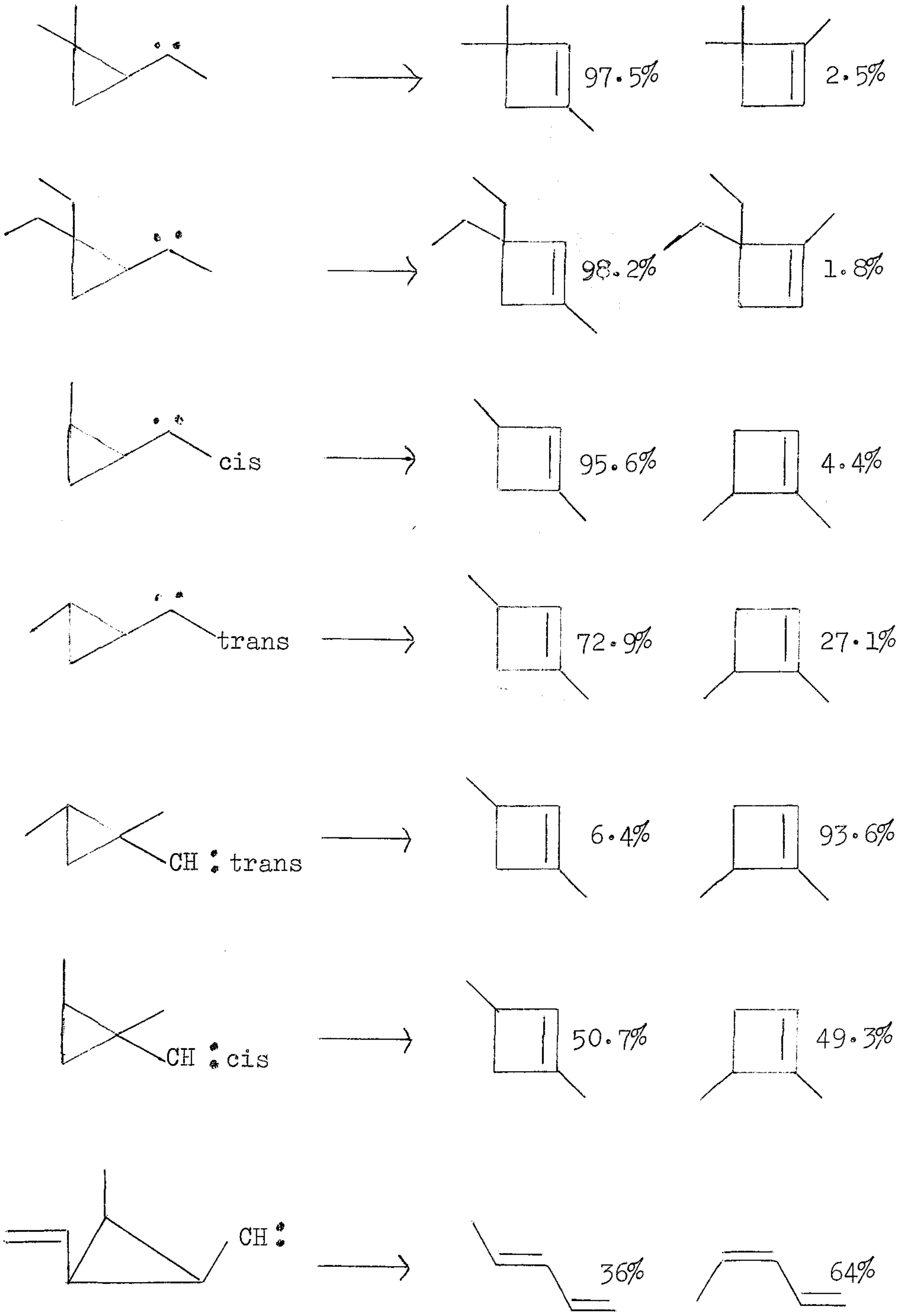
Thus, if R and R' are groups other than hydrogen, it is seen that the two possible pathways generate different products.

If the ring is symmetrically substituted, but in such a way that the substituents have a definite stereochemistry, the retention or loss of this stereochemistry provides evidence about whether the process is synchronous or whether an intermediate of sufficient lifetime to permit bond rotation is formed.

Table I shows the results obtained with variously substituted cyclopropyl carbenes.

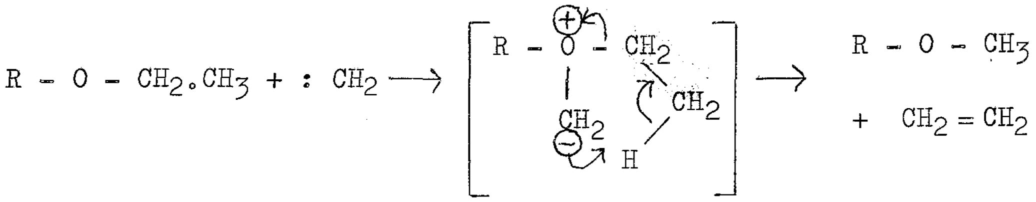
Table I

Relative Yields of Products from Tosyl Hydrazone Decompositions



Carbenes, by their electron-deficient nature, are expected to be electrophilic species. As an example the addition of methylene to olefins may be cited. The π-bond of ethylene is nucleophilic in nature, as seen from the formation of bromonium ions and the participation of the double bond in carbonium ion type solvolyses. Thus the first stage of the methylene addition can be visualised as a polarisation of electrons from the ethylene double bond towards the carbene centre.

An ylid mechanism has been proposed to account for the formation of methyl ethers and olefins from the reaction of methylene with ethers, although the ylid mechanism for the formation of insertion products has been discounted on the basis of carbon-14 labelling.[38]



This mechanism involves electrophilic attack by the carbene on the electron-rich oxygen of the ether.

Thus, if the substituent R on the cyclopropane ring is an alkyl group, these being electron-donating in character, the 1,2 bond will have more available electron density than the 1,3 bond, and the migration of the 1,2 bond is anticipated.

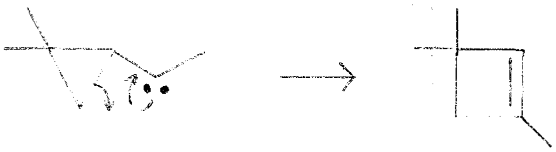
Frey[39], in studies on the pyrolysis of cyclopropanes, has observed that the substitution of a methyl or ethyl group on the ring results in an approximate doubling of the rate of decomposition, and geometrical isomerisation of cis- and trans-1,2-dimethyl cyclopropane is faster than structural isomerisation reactions to yield olefins.

Furthermore, in the structural isomerisation of methyl cyclopropane, the activation energy for the formation of isobutene, which involves breaking the 2,3 bond, is higher than that for the formation of the other butenes, by breaking the 1,2 (1,3) bond.

This points to the fact that alkyl substitution tends to weaken the bond in the cyclopropane ring which is substituted.

Hence, on these grounds, it is anticipated that 2,2-dimethyl cyclopropyl methyl carbene would rearrange preferentially to 1,4,4-trimethyl cyclobutene.

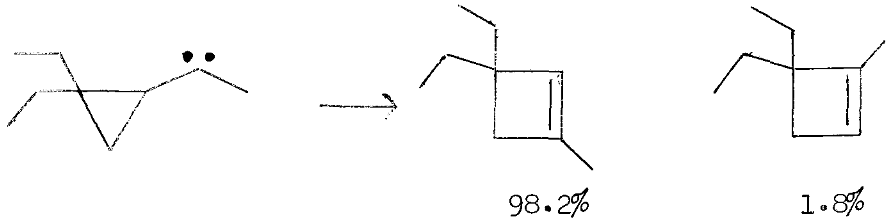
However, only 2.5% of this isomer is found as a product of the decomposition of the tosyl hydrazone, the remaining 97.5% of the cyclobutene products being the 1,3,3 isomer, formed by a 1,3 bond shift in the cyclopropane.



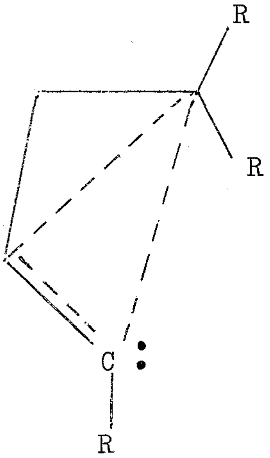
This high selectivity, comparatively unusual in a carbene reaction, is indicative of a factor, or factors, heavily outweighing the electronic effect.

It is envisaged that, during the rearrangement, the carbene centre moves towards the carbon atom to which it is eventually bonded, and towards the migrating bond. Thus it is reasonable to anticipate some steric inhibition to the rearrangement when the ring carbon is substituted, reducing the preference for rearrangement in this direction.

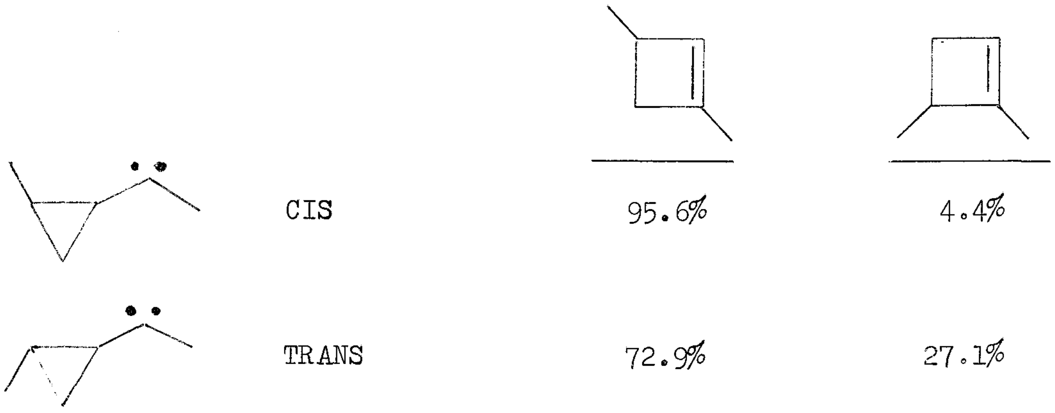
This is supported by the fact that 2,2-diethylcyclopropyl methyl carbene, in which the substituents are larger, gives an even higher proportion of the 1,3,3 substituted cyclobutene.



In these di-substituted cases, no distinction can be made between the effects of the cis- and trans-substituents, but envisaging a transition state of the type below, a cis-substituent on the 2-position would be expected to have a greater effect than that of a trans-substituent, since the carbene centre moves nearer to a cis- than to a trans-substituent.

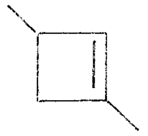
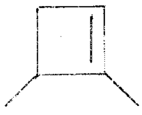


The discrimination in this case is illustrated by cis- and trans-2-methyl cyclopropyl methyl carbenes, shown below



The product distribution from the cis-isomer supports the steric inhibition postulate, but it seems surprising that the steric effect in the trans-case should be sufficient to outweigh the electronic effect to the extent it does. This seems to indicate that a factor, or factors are operating in addition to the steric effect.

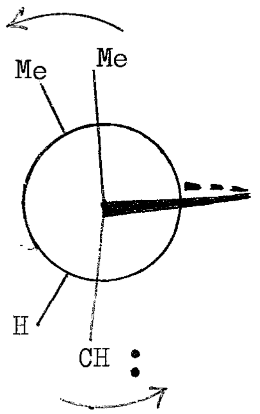
The steric effects can also be observed in the rearrangement of cis- and trans-1,2 dimethyl cyclopropyl carbenes (the prefixes cis- and trans- refer to the two methyl substituents).

			
	TRANS	6.4%	93.6%
	CIS	50.7%	49.3%

In the trans-case, migration of the less-substituted bond yields the 1,4 isomer, the carbene centre moving away from the cis-substituent.

In the cis-case, there is a competing effect in that the eclipsing strain of the two methyl groups is relieved during the rearrangement. This is presumably easier if the more substituted bond migrates.

Thus, looking along the 1,2 bond:



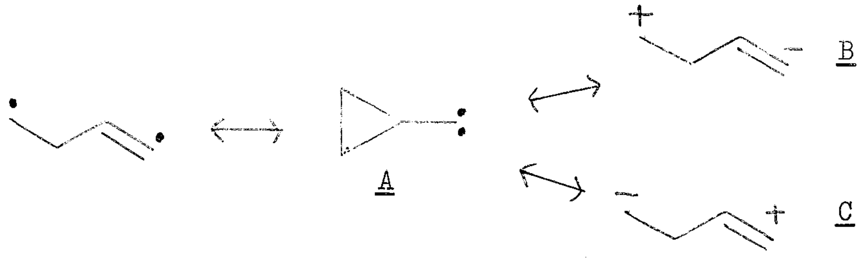
If the carbene centre moves towards the less substituted 1,3 bond (producing 1,4-dimethyl cyclobutene), the rotation about the 1,2 bond forces an increased eclipsing of the methyl groups, resulting in increased strain.

Rotation about the 1,2 bond in the other direction does relieve the eclipsing strain of the methyl groups, but, in swinging the carbene centre towards the more substituted bond, the inhibition to migration in this mode previously observed is encountered.

A balancing of the two opposing inhibiting effects leads in this case to the observed near-equal product ratio.

So far, the directive effects of the alkyl substituents on the ring have been rationalised on steric grounds. Closer examination of electronic effects leads one to consider the possibility of interactions between the ring and the carbene centre producing directive forces additional to the steric forces.

Thus, other canonical forms may be written for cyclopropyl carbene



The bi-radical form can be excluded from consideration for the time being, as this would be expected more from a triplet carbene. The spin-state of the carbene intermediate will be considered in Chapter 3, but it will suffice to say here that the alkyl substituted carbenes are believed to react as singlet species.

The nature of the transition state will depend on the relative importance of the canonical forms A, B and C. In the unlikely event of the three forms being of almost equal importance, that is to say of similar energy as illustrated in Diagram I, the transition state will be effectively non-polar.

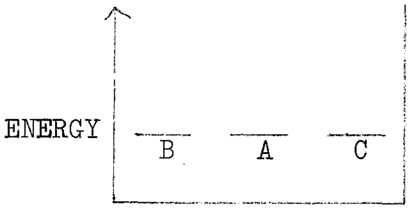


Diagram I

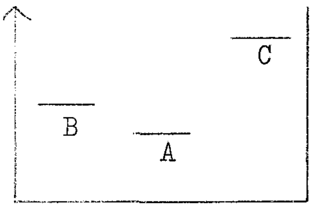


Diagram II

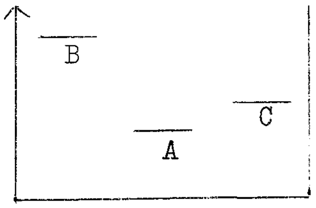
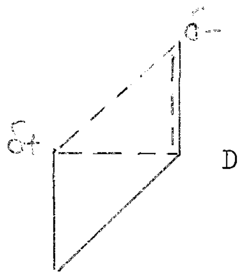
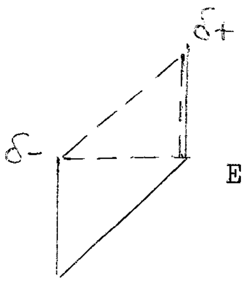


Diagram III



D



E

Diagram II illustrates the case where the predominant contribution is from B, C being of higher energy, so having less effect. If it is assumed that rearrangement takes place in some degree via these polar forms, then this case will lead to a semi-polar transition state of type D.

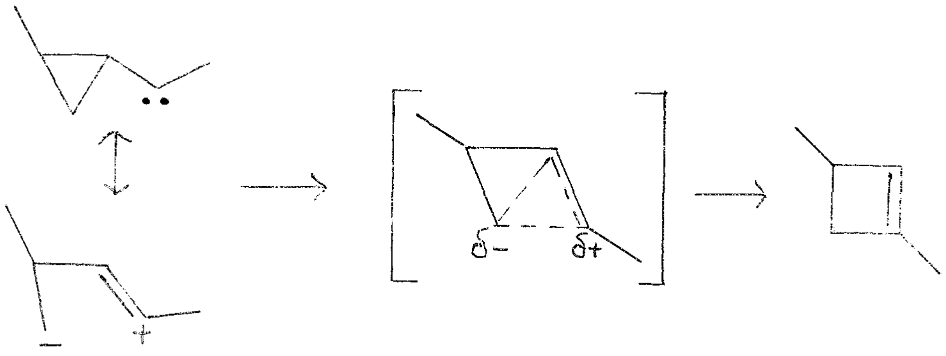
Similarly Diagram III illustrates the case where the predominant contribution is from C, resulting in a transition state of type E.

It is unlikely that these species open and stay open as "zwitterions", but incomplete separation cannot be ruled out, the intermediate resembling an "intimate ion-pair". This, however, would not affect any argument, because only in the case of complete separation is rotation about bonds, and consequent stereochemical scrambling possible.

With a transition state of type D, it is anticipated that alkyl substituents, with their electron-donating character, would have a stabilising effect, leading to preferential migration of the more substituted bond.

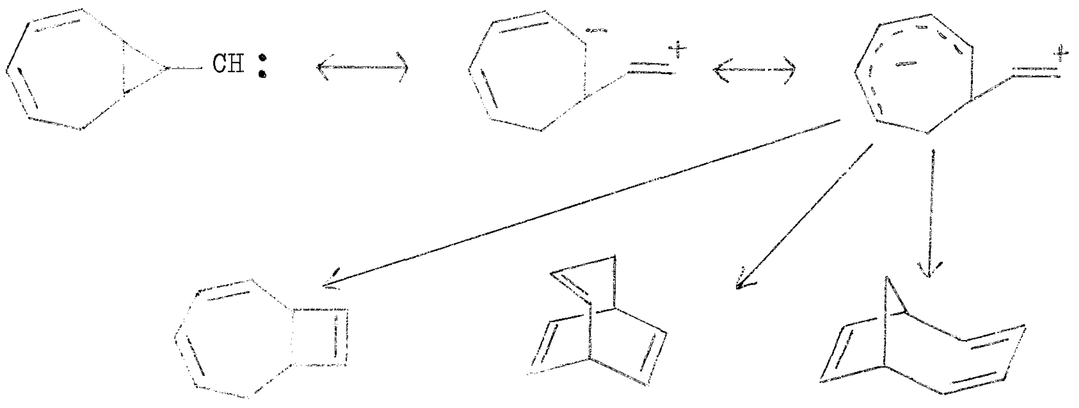
However, with a transition state of type E, the partial negative charge would be destabilised by an alkyl substituent. In this case the partial negative charge would prefer to lie on the unsubstituted carbon of the ring, leading to migration of the least substituted bond, that is, in the observed direction.

Thus, on the basis of this argument, the product ratio for trans-2-methyl cyclopropyl methyl carbene is attributed to the preference of the partial negative charge for the least substituted ring carbon.

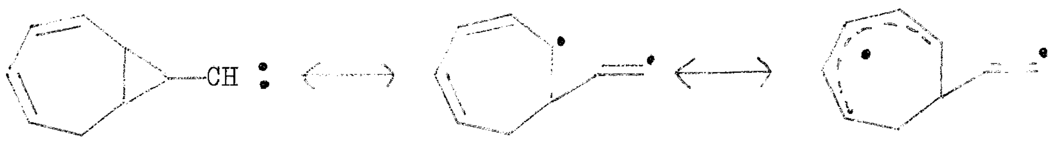


A similar argument is invoked for the case of cis-1,2-dimethyl cyclopropyl carbene, and for the other cases where the steric inhibition effect is reinforced by the electronic effect, this being even greater when the ring is di-alkyl substituted, because of the larger destabilisation of a tertiary partial negative charge as opposed to a secondary one. The greater selectivity of the diethyl cyclopropyl methyl carbene over the dimethyl cyclopropyl methyl carbene is probably a combination of the two effects, although it cannot be determined if one of them predominates.

The results obtained by Maitland Jones Jr. et al.[26-28] with a series of bicyclic cyclopropyl carbenes in which the cyclopropane ring is substituted by unsaturated functions are also susceptible to this type of explanation. Thus:

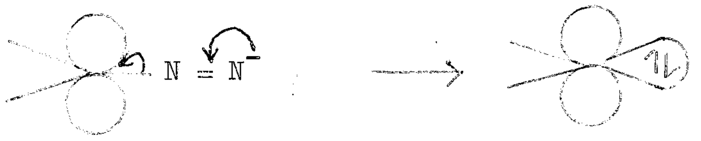


In fact, the intermediate proposed by Maitland Jones Jr. was a bi-radical, the reactions of which would be essentially the same. This is discussed further in Chapter 3.



So far, all the arguments have assumed the intermediacy of a discrete carbene, but it is also possible that this may never exist as such, the reactive intermediate being a "hot" diazo-compound. The rearrangement can then be envisaged as proceeding synchronously with loss of nitrogen.

Two modes of nitrogen loss can be considered in this context

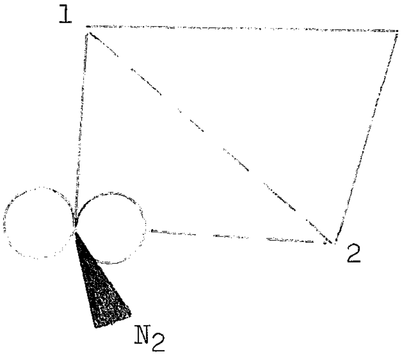


(1)

(2)

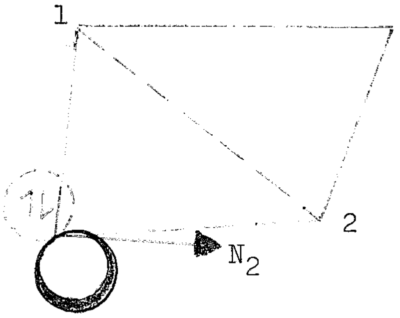
For a synchronous rearrangement, it is assumed that the migrating bond of the cyclopropane ring overlaps with the vacant, or vacated, orbital as the lone-pair, or the lone pair generated by nitrogen loss, commences to form the double bond of the cyclobutene by overlapping with the vacated orbital on carbon 1 of the ring.

Thus, for mode (1) :



The nitrogen leaves from the "side" of the molecule, as the 1,2 bond moves down to overlap with the vacant p-orbital. The lone-pair generated by loss of nitrogen overlaps with the back of the orbital vacated on carbon 1, forming the cyclobutene double bond.

For mode (2)

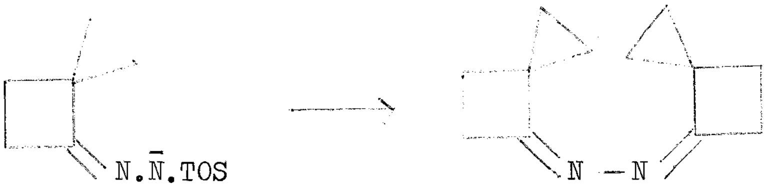


In this case the nitrogen appears to undergo front-side displacement by the migrating 1,2 bond.

If a cis-substituent is present on the 2-carbon, the loss of nitrogen is made more difficult, and indeed a trans-substituent is not without effect in this. This would lead to preferential migration of the less-substituted bond, since the steric inhibition to nitrogen loss is less.

It is not necessary to propose a totally synchronous mechanism, but the time lag between loss of nitrogen and rearrangement must not be long enough to permit vibrational relaxation of the intermediate, distorted carbene resulting from loss of nitrogen. A time lapse of this length would reduce the argument to one around the carbene itself.

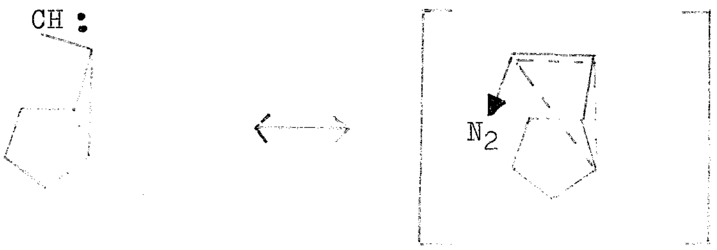
The observation of Wiberg et al.[25] that spiro[2.3]hexan-4-one tosyl hydrazone gives an azine may be argued as providing evidence for this mechanism.



It is extremely difficult to distort this molecule in such a way that overlap of a cyclopropane bond with the vacant orbital generated by the departing nitrogen is synchronous with overlap of the lone pair with the other end of the migrating bond, so that the secondary reaction of the diazo-compound, yielding azine, predominates.

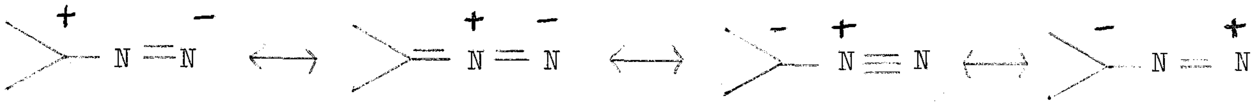
The requisite distortion becomes easier when the size of the larger ring is increased to 5 and 6 carbons, and the rearrangement then proceeds as expected.[17]

In addition to this, in the case of endo-bicyclo[3.1.0] hexyl carbene, Kirmse and Pook[16] obtained a relatively low (30%) yield of hydrocarbon products, compared to the 60-70% yield in the other cases studied. This anomaly might be explained by hindrance of nitrogen loss due to the position of the five-membered ring, although the possibility that the anomaly is false due to inefficient trapping of products cannot be excluded.



It is obviously very difficult to distinguish conclusively on an experimental basis between the two rationalisations proposed. The polar transition state is susceptible to the criticism that transition state D is intuitively more likely than E, although E more conveniently explains the experimental observations.

It is proposed that a compromise between the two possibilities would explain the observed facts. Considering the canonical forms of a diazo-compound, it can be seen



that the carbon atom carries a partial negative charge. If this is delocalised into the cyclopropane ring, the situation leading to a transition state of type E is achieved. Synchronous loss of nitrogen and rearrangement (mode 2) need not be invoked, but the proximity of the nitrogen during the subsequent rearrangement serves to strengthen the argument.

Chapter 3

Fragmentation and Other Reactions

Friedman & Shechter observed 10-13% apiece of ethylene and acetylene from cyclopropyl carbene itself.[1] Mechanisms can be written for this fragmentation involving either 1- or 2-electron shifts in the singlet carbene.

Fragmentation of the triplet carbene would involve an intermediate stage in the radical decomposition, to allow for spin inversion.

Shevlin and Wolf[7] consider that this fragmentation is at least partly governed by spin state, but their conclusions are partly based on energetic carbon atom work, so that the spin states involved may be excited singlets and triplets. However, it can be concluded that the fragmentation occurs to a greater extent when the carbene is generated as an excited species.

Thus the gas phase photolysis of cyclopropyl diazomethane[7] and trans-2,3-dimethyl cyclopropyl diazomethane[37] produces high yields of the respective fragmentation products.

The pyrolysis method used in this work does not lead to accurate analysis for the fragmentation products because condensation of these in the cold trap is not as efficient as for the other, higher-boiling products.

The photolytic procedure, however, involves no appreciable loss of low-boiling products, and in the case of cyclopropyl methyl carbene, generated by photolysis of the lithium salt in diglyme, 9% each of ethylene and methyl acetylene were obtained.

It is difficult to compare this with the 3% obtained by Friedman and Shechter, on pyrolysis of the sodium salt of cyclopropyl methyl ketone tosyl hydrazone at 180°, because it is not known if this result is subject to loss due to inefficient trapping. If this 3% does represent the full yield, then the difference may be attributed to variations in the energy of the species produced by the two routes.

Bradley[21] did not include an analysis of fragmentation products from the decomposition of cyclopropyl methyl diazirine, but it is known that appreciable quantities of these were produced.

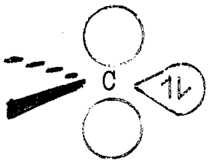
Fragmentation reactions do not give much information about the nature of the intermediate, unless the products of fragmentation can retain or lose any definite stereochemistry present in the starting carbene or tosyl hydrazone. This technique has been used to investigate the spin state in which the cyclopropyl carbene reacts.[31]

The Nature of the Carbene Intermediate

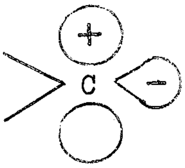
From the flash photolysis of diazomethane Herzberg has demonstrated the existence of two distinct methylene species.[40] One, designated the 'singlet' carbene, had an $\hat{HCH}$ angle of 103° and, in the presence of an inert gas, decayed to a longer-lived, linear species, the 'triplet', which is the ground state.

For a more detailed discussion of the spin-states of carbenes, the two reviews mentioned earlier[36,37] may be read. However, a simplified picture may be considered here:

SINGLET

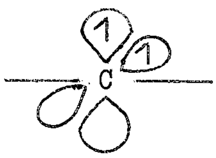


(A)



(B)

TRIPLET



(C)

In the singlet (A) the hybridization at carbon is approximately sp^2, with some compression of the $H\widehat{C}H$ angle from the 'pure' 120° to 103°, probably due partly to mixing of other states and partly to electron-electron repulsions between the bonding and non-bonding electrons in the sp^2 plane, the paired electrons occupying one of the sp^2 orbitals. The $2p_z$ is at right angles to the plane and is vacant. Crudely this situation corresponds to a superimposed carbonium ion and carbanion (B).

In the triplet, the carbon atom is considered to be sp hybridized, with p_y and p_z orbitals, mutually perpendicular with the sp orbitals, having one electron apiece, with spins parallel.

As stated earlier the Bamford-Stevens reaction generates a diazo-compound by unimolecular elimination of sulphinate anion. This diazo-compound is a singlet species, being generated from a singlet tosyl hydrazone anion, and will, on loss of nitrogen, yield a singlet carbene.

The question then arises of whether this carbene reacts as a singlet species, or whether it decays to a triplet before reacting. Moser et al.[41] have observed the e.p.r. spectrum of phenyl carbene, diphenyl carbene and fluorenylidene in 2-methyl tetrahydrofuran glass. However, these species have no ready intramolecular mode of reaction and have the benzene ring(s) available to assist spin inversion to the triplet. The e.p.r. signals are fairly long-lived, indicating an appreciable lifetime for these species under the experimental conditions.

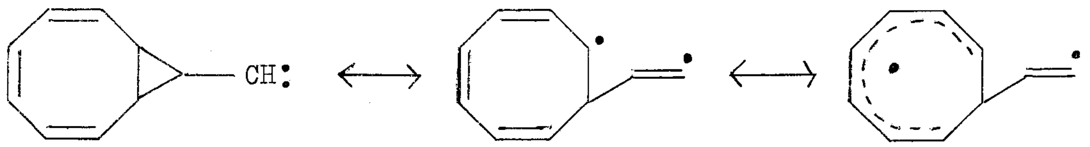
In the absence of a spin-inversion agent such as the benzene ring, it seems likely that the carbene will react before decaying to the triplet, if an intramolecular mode of reaction is available. The reactions of alkyl carbenes are fast, which tends to support the intermediacy of a singlet species.

In an attempt to investigate the spin state of cyclopropyl carbenes, Guarino and Wolf[31] have photolysed trans-2,3-dimethyl cyclopropyl diazomethane in the gas phase. The results from this certainly tend to indicate that the carbene normally reacts as a singlet.

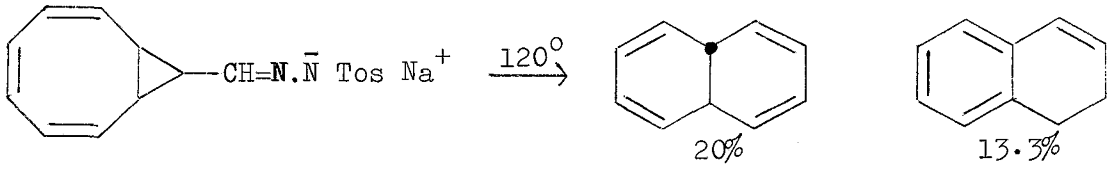
They examined the fragmentation products of this carbene, anticipating that a triplet would fragment to give a triplet olefin, which could undergo rotation about the 'ethylenic' bond, leading to stereochemical scrambling. In the presence of an inert gas, when decay from singlet to triplet would be assisted, 10% and 9% respectively of trans- and cis-butene-2 are found. In the absence of an inert gas, at gas pressures of 11 and 23 torr, less than 2% of cis-butene-2 is found, compared with 43% and 41% trans-butene-2 respectively.

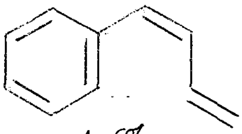
However, the results obtained by Maitland Jones Jr. et al.[26-28] and Masamune[29,30] with the series of bicyclic cyclopropyl carbenes, in which the cyclopropane ring is substituted by unsaturated functions, could well be explained in terms of a triplet species.

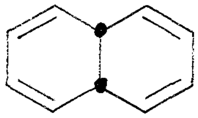
In fact Maitland Jones Jr. has proposed such an intermediate, illustrated below for bicyclo [6.1.0] nona-2,4,6-trien-9-yl carbene.

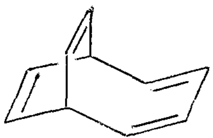


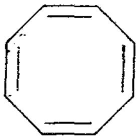
Such an intermediate is supported not only by the nature of the products, which imply a ring-opening process, but also by the insensitivity of the product distribution to whether the carbene centre is exo- or endo.




4.6%

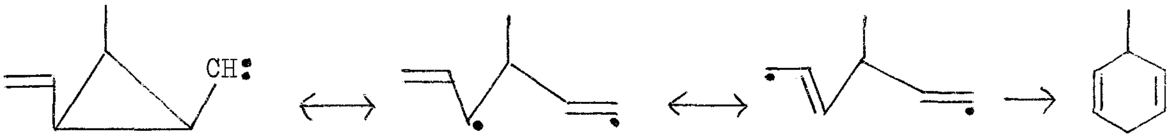

11.6%


37.8%


12.7%

The insensitivity to carbene centre stereochemistry is a good indication that the cyclopropane ring has opened, and that the intermediate is sufficiently long-lived to permit free rotation. Although an ionic intermediate cannot be categorically ruled out, this evidence is only really consistent with a triplet diradical intermediate. This is not too surprising, in view of the probable ability of the conjugated substituent system in the large ring, by analogy with a benzene ring, to permit spin inversion.

In an attempt to correlate this work with that of Guarino and Wolf, cis-2-methyl-cis-3-vinyl cyclopropyl carbene was studied. The major products from this were cis- and trans penta-1,3-dienes in a relative ratio of 64% to 36% respectively, and acetylene. The other products were present in insufficient quantities to permit analysis by available techniques, especially in view of the small amount of total products available. It is anticipated that these minor products would consist of cis- and trans-3-methyl-4-vinyl cyclobutenes, heptatrienes by secondary isomerisation of the cyclobutenes, and 3-methyl cyclohexa-1,4-diene by a reaction analogous to that observed with the bicyclic carbenes.



An authentic sample of 3-methyl cyclohexa-1, 4-diene was available, but none of the minor products had the same v.p.c. retention time as this, so, if it is a product, it is formed in very small quantities.

Only 12·7% of cyclooctatetraene was formed from the bicyclo nonatrienyl carbene, and 19% cycloheptatriene from the bicyclo octadienyl carbene studied by Maitland Jones Jr., these being the analogous fragmentation products to those observed. This discrepancy can probably be explained in terms of an entropy effect, the vinyl group being free to rotate, whereas the conjugated system in the bicyclic cases is held in a favourable orientation for ring closure.

However, since the methyl and vinyl groups are initially cis- to each other, the isolation of both cis- and trans-penta-1,3-dienes is indicative of a fairly long-lived, ring-opened intermediate, probably a triplet.

It would seem, then, that the spin state in which the carbene reacts is dependent on the nature of the substitution on the cyclopropane ring. The presence of a substituent which can stabilise a radical intermediate for a sufficient length of time to permit the spin inversion to the triplet produces stereochemical scrambling in the fragmentation products and reactions involving the carbene centre and the stabilising group.

In the absence of such groups, the reaction of the singlet carbene, yielding cyclobutene products, predominates.

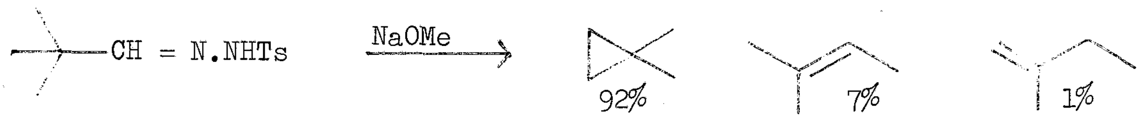
Mention was made earlier of the secondary isomerisation of methyl vinyl cyclobutenes to heptatrienes. There seems little doubt that this, and the more general production of dienes from cyclobutenes is indeed a secondary reaction, that is, that the dienes are not produced directly from the carbene.

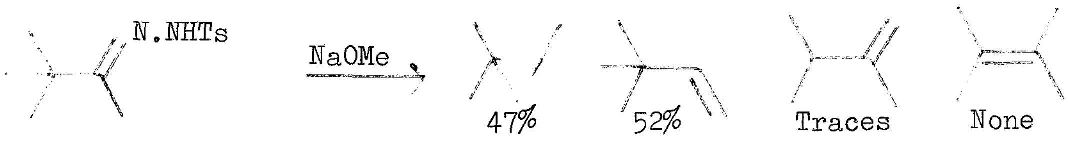
Dienes are always produced in the pyrolysis of the sodium salts of cyclopropyl aldehyde and ketone tosyl hydrazones, in amounts which seem to vary with the severity of the conditions. Hence, no serious attempt was made to analyse for these, although when this was done, the relative amounts corresponded within experimental error to those obtained for the cyclobutenes.

Kirmse and Pook[16], when studying the pyrolysis of the sodium salts of the tosyl hydrazones of bicyclo[3.1.0]hexane-6-aldehyde, bicyclo[4.1.0]heptan-7-aldehyde and bicyclo[5.1.0]octan-8-aldehyde, observed no diene products. Since the cyclobutene products from these carbenes have the 5,6 or 7-membered ring fused cis-, conrotatory opening according to the Woodward-Hoffmann rules[42] would produce a trans-double bond in the ring, an unfavourable situation, so it is not too surprising that secondary diene products are not observed.

In the pyrolysis of the sodium salt of cyclopropyl methyl ketone tosyl hydrazone, Friedman and Shechter[1] observed 2% isoprene. When the lithium salt was photolysed at room temperature, isoprene was observed only in trace quantities ($\sim 2 \times 10^{-4}\%$). Another diene, cis-penta-1,3-diene was observed, but this is believed to arise by another process, and will be considered later, but, with the exception of this special case, the evidence is overwhelmingly in favour of the dienes being secondary products.

Alkyl carbenes in general react by 1,2-, and to some extent 1,3 hydrogen migration, producing olefins and cyclopropanes.[2] The ring expansion reaction of cyclopropyl carbenes to cyclobutenes involves essentially the migration of a carbon-carbon bond, a reaction which does not occur easily in alkyl and dialkyl carbenes. Carbenes of the neopentyl type are, to a certain extent, exceptions to this.[2]





In view of all this, it seems somewhat surprising that no methylene cyclopropane is obtained from cyclopropyl carbene, and only 1% vinyl cyclopropane from cyclopropyl methyl carbene[1], these being the products anticipated from a 1,2-hydrogen shift.

Kirmse and Pook[17] commented on the absence of spiro-alkene products from spiro[2·4]heptan-4-one and spiro[2·5]octan-4-one tosyl hydrazones, concluding that the cyclopropyl carbene-cyclobutene rearrangement was much faster than the hydride shift.

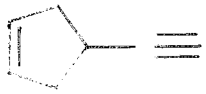
Cyclobutylidene also undergoes predominantly a carbon bond migration, yielding methylene cyclopropane (79-80%), although in this case some cyclobutene (18-20%) is formed by way of the more usual hydride shift.[1]

That the cyclopropyl carbene-cyclobutene rearrangement is so much preferred over the hydride shift may be taken as good indication that there is reasonable interaction between the cyclopropane ring and the carbene centre, probably of the type envisaged in Chapter 2.

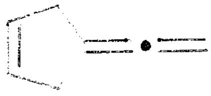
Some cyclopropyl carbenes react anomalously, such as the spiro[2.3]hexan-4-carbene cited in Chapter 2 (although in the absence of experimental detail the magnitude of the anomaly is at least dubious!).

The fragmentation of nortricyclenone tosyl hydrazone observed by Cristol and Harrington[23] is readily explained in terms of the extremely strained nature of the would-be cyclobutene (A). In view of this, it is not surprising that the carbene fragments to the acetylene (B), the allene (C) being established by experiment as a secondary product, produced by base-catalysed isomerisation.

(A)

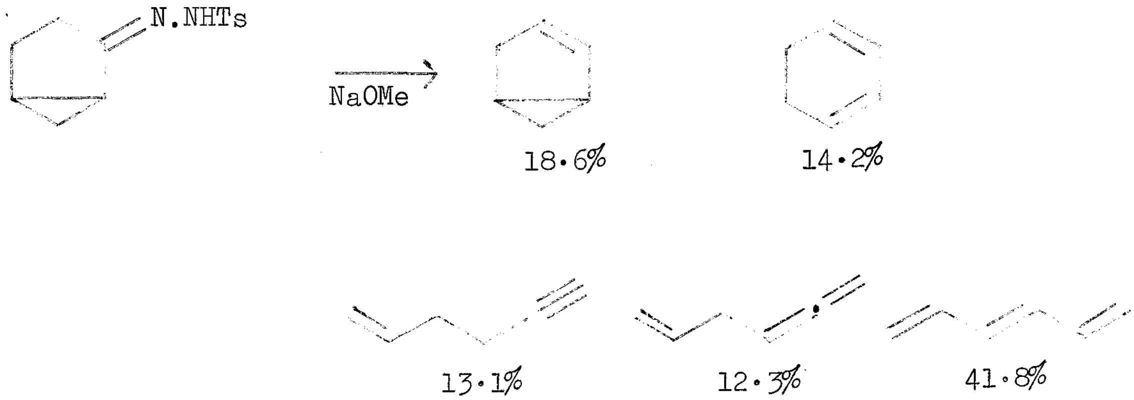


(B)



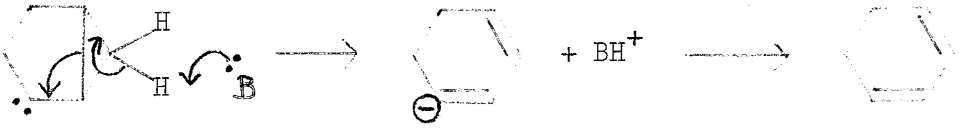
(C)

The products from the decomposition of bicyclo[3.1.0]hexan-1-one tosyl hydrazone[24], as shown below, can be readily explained in terms of known reactions, with the exception of the cyclohexa-1,3-diene.



The absence of a cyclobutene is again explicable in terms of the strained nature of this, should it be formed; the bicyclo[3.1.0]hex-2-ene is produced by hydride shift and the linear products by fragmentation and subsequent secondary reaction of the acetylene.

The mechanism for the formation of the cyclohexadiene proposed by Freeman and Kuper is shown below



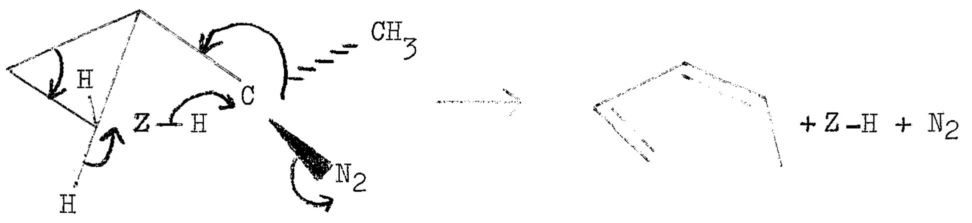
Commenting on this, they suggest that electron drain from the ring encourages attack on the hydrogen on carbon 6, and say that, although the reaction is represented as a 2-step one, it may have some concerted character (with loss of nitrogen), but argue against an intramolecular hydride shift on the grounds that the amount of cyclohexadiene is dependent on the concentration of NaOMe.

Before this is considered further, the case of the anomalous diene produced from cyclopropyl methyl carbene can be introduced, since the two reactions would appear to be related.

When the lithium salt was photolysed, 8·8% cis-1,3-pentadiene was formed. However, there was reason to suppose the lithium salt to be contaminated with free tosyl hydrazone, so the lithium salt was photolysed in the presence of added free tosyl hydrazone, when the percentage of cis-pentadiene increased to 36·5%. This reaction is not peculiar to the photolysis, because cis-pentadiene was obtained in 17·6% yield when the tosyl hydrazone was pyrolyzed with 0·5 equivalent sodium hydride. (The percentages are relative yields of C5 hydrocarbons, the fragmentation products being ignored for this purpose.)

No trans-penta-1,3-diene was observed from these decompositions, which is a very surprising result, implying that the intermediate is reacting in a stereospecific manner.

It is proposed that cis-pentadiene is produced via a transition state similar to that yielding bicyclobutane from cyclopropyl carbene.

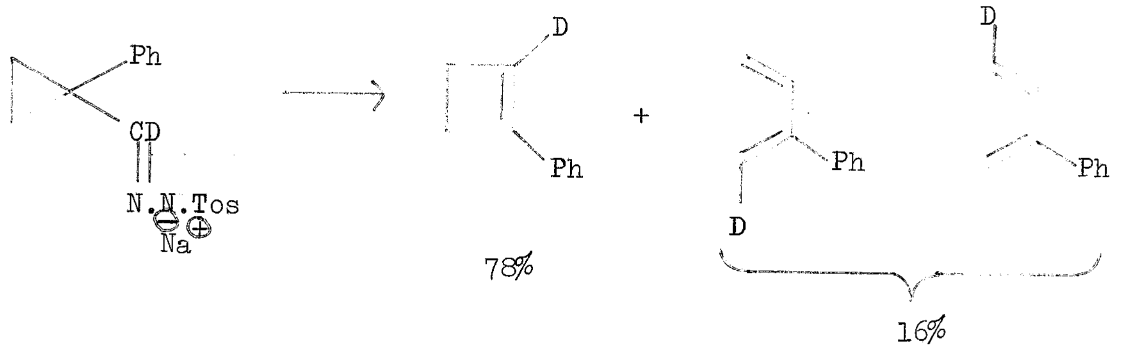


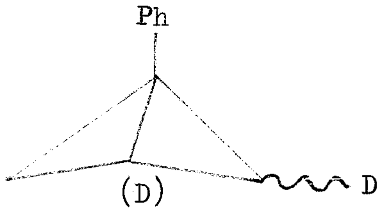
It is necessary to propose that a rotation about the carbene centre occurs in such a way as to leave the methyl group cis-. Why, or how, this rotation occurs, is not at this stage apparent, but the selectivity in the diene product certainly indicates a "tight" transition state, and probably a synchronous process.

This argument is not satisfactory for the bicyclo[3.1.0]hex-2-yl carbene because a rotation such as that proposed above is not possible due to the rigid nature of the molecule. A two-step mechanism, analogous to that proposed, may well be operating in this case.

An alternative possibility, that the cyclohexadiene is produced from hexa-1,3,5-triene (a secondary product) would appear to be eliminated by the fact that Freeman and Kuper did not observe cyclohexadiene in their studies on the secondary isomerisation of the product hex-1-en-5-yne.

Smith et al.[10], studying deuterated 1-phenyl cyclopropyl carbene, observed diene products which they attributed to the isomerisation of a bicyclobutane (D).





It is possible that these dienes are produced by a process analogous to that observed above, although by analogy with cyclopropyl methyl carbene, the deuterium would be expected in a cis-environment to the other double bond in the diene molecule.

It is apparent that this secondary reaction warrants further study.

PART II

CNDO CALCULATIONS

Chapter 4

Introduction, CNDO Calculations

The CNDO (complete neglect of differential overlap) molecular orbital method was originally developed by Pople et al.[35a,b], and is referred to as CNDO/1. The subsequent modification, CNDO/2, developed by Pople and Segal[35c] is essentially the method used in these calculations, with modifications as discussed below in connection with the computer programme.

The CNDO method, and other all-valence-electron semiempirical self-consistent field calculations, have been reviewed recently by Jaffé.[76]

Clark has used the CNDO method for a study of the cyclopropyl-allyl transformation[48] and found the results encouraging although more realistic values were obtained using an 'ab initio' type treatment with Gaussian type orbitals.[77]

Fischer and Kollmar[78] have used CNDO/2 to study reactions such as hydrogenations, isomerizations, rotation barriers and condensations for simple hydrocarbons.

These examples constitute the only attempts to date to use CNDO for studying reaction mechanisms. Other uses of CNDO, and its limitations are discussed by Jaffe[76] and Fischer and Kollmar.[78]

The Computer Programme*:

Input data for this is as shown below:

Number of atoms.
Number of orbitals.
Number of electrons.
Number of orbitals on each atom.

---

* The author is indebted to Dr. J.W. Emsley and Dr.R.A. Storey for the computer programme and assistance with the calculations.

Coordinates (xyz) specifying the position of each atom.
Core charge on each of the atoms (Z_H,Z_C).

In addition to this numerical parameters are input which permit selection of alternatives built into the programme.

The orbital energies and wave-functions were found to be unchanging after 15 iterations.

One centre core and repulsion integrals were estimated from spectroscopic data as described by Clark[79], the parameterisation being that of Sichel and Whitehead.[80] Two centre repulsion integrals were calculated from the one centre integrals using the refined Mataga procedure.[81,82] The programme contains the option of using the original Mataga procedure[83], but this was only used once. The two centre core integrals were calculated from the relevant valence state ionization potentials and overlap integrals and the Mulliken-Wolfsberg-Helmholtz equation.[84] The overlap integrals were calculated using Slater orbitals with orbital exponents obtained using Slater's rules as modified by Burns.[85]

This enables the electronic energy of the system to be calculated. Allowing for the approximations inherent in the method, the value obtained for the electronic energy is as good as the parameterisation permits.

The aim of these calculations is to obtain a value for the total energy of the system, as the sum of electronic and nuclear energies. The calculation of the nuclear energies presents something of a problem in that they cannot accurately be determined directly as the repulsion of two nuclei, since these are shielded by the electrons.

Considering two nuclei sufficiently close that the electron shielding is not important, the nuclear repulsion energy can be calculated on the basis of the interaction between point charges located on the nuclei.

However, for nuclei sufficiently far apart to be considered as atoms, the nuclear repulsion energy should be the same as the corresponding electron repulsion energy, thus enabling the nuclear energy to be approximated from the electron-repulsion integrals.

Discussing this, Clark[48] advocates the use of the latter method when determining total energies and finds it to give better results for the cyclopropyl-allyl cation transformation. Thus, this method was used in these calculations.

The output from the programme is as follows:

Eigenvalues and Eigenvectors
Charge density-bond order matrix
Atom charges
Electronic Energy
Nuclear Energy
Total Energy.

Chapter 5

Calculation of Coordinates

The computer programme for the CNDO calculations requires a description of all atomic positions, input in the form of 3-dimensional cartesian coordinates, the basic unit of distance in these being the Ångstrom.

Basic bond distances and angles were derived from Tables of Interatomic Distances[44], and occasionally directly from the literature.

Using these values, the atomic coordinates for known molecules were calculated to six places of decimals, using "Jean", the ICT on-line, remote access, computer console.

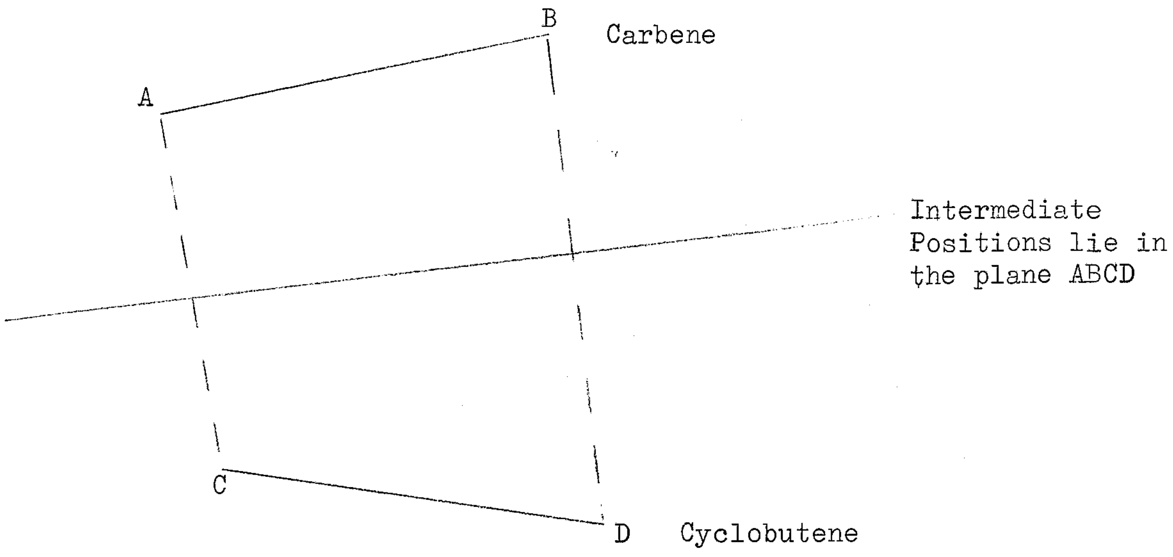
Trigonometric functions are thus evaluated by a mathematical series, avoiding round-off errors in consulting standard tables. The accuracy is necessary on account of the iterative nature of the CNDO calculations, during which round-off errors present as a result of inaccurate coordinates might be magnified into significant errors in the energy.

For the studies on the rearrangement itself, fifteen positions intermediate between the carbene and the cyclobutene were taken, the coordinates for these being computed from the coordinates of the initial and final positions.

Two approaches were tried for this, and these will be described and then illustrated in the context of the actual calculation of coordinates.

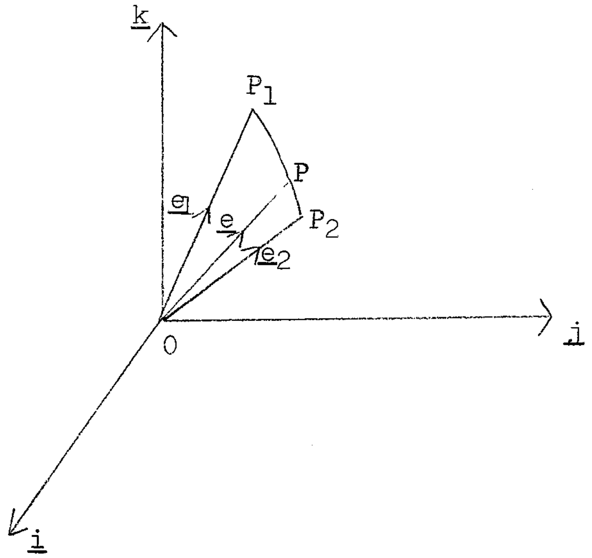
Plane Method

If two lines are taken to represent two bonds, one corresponding to the initial position in space (carbene) and the other to the final position in space (cyclobutene), one mode of movement for the bond is in the plane between the two extreme positions.



Mathematical Treatment

Consider the two lines OP_1 and OP_2. OP is any line in the plane OP_1P_2. Calculation of the direction cosines of this line enables the coordinates of any point along the line to be calculated.



OP_1 has direction cosines l_1, m_1, n_1

$\underline{e}_1$ is a unit vector along OP_1

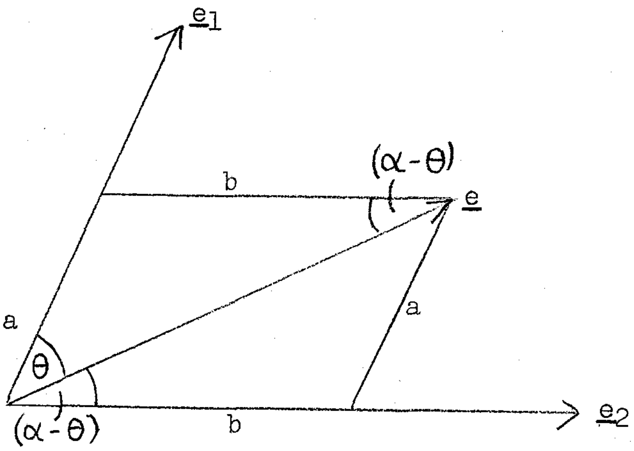
i.e. $\underline{e}_1 = l_1\underline{i} + m_1\underline{j} + n_1\underline{k}$

Similarly for OP_2 (direction cosines l_2, m_2, n_2)

$$\underline{e}_2 = l_2\underline{i} + m_2\underline{j} + n_2\underline{k}$$

Similarly for OP (direction cosines l,m,n)

$$\underline{e} = l\underline{i} + m\underline{j} + n\underline{k}$$



Since $\underline{e}$ lies in the plane of $\underline{e}_1$ and $\underline{e}_2$ it can be expressed, by the parallelogram law for vectors, as

$$\underline{e} = a\underline{e}_1 + b\underline{e}_2$$

And, from the parallelogram:

$$\frac{b}{\sin\theta} = \frac{a}{\sin(\alpha-\theta)} = \lambda$$

where α is the angle between $\underline{e}_1$ and $\underline{e}_2$, and θ is the angle between $\underline{e}_1$ and $\underline{e}$, being a measure of the amount by which OP has moved between OP_1 and OP_2.

Thus, if λ is a constant,

$$a = \lambda \sin(\alpha-\theta)$$

$$b = \lambda \sin\theta$$

Now, when $\theta = 0$, $a = 1$ and $b = 0$

and, when $\theta = \alpha$, $a = 0$ and $b = 1$

so $\lambda = \dfrac{1}{\sin\alpha}$

Hence $\underline{e} = \frac{1}{\sin\alpha} (\sin(\alpha - \theta).\,\underline{e}_1 + \sin\theta.\,\underline{e}_2)$

Expressing the vectors in terms of direction cosines:

$$l\underline{i} + m\underline{j} + n\underline{k} = \frac{1}{\sin\alpha} (\sin(\alpha-\theta).\,\left[l_1\underline{i} + m_1\underline{j} + n_1\underline{k}\right] + \sin\theta.\,\left[l_2\underline{i} + m_2\underline{j} + n_2\underline{k}\right])$$

Thus, the direction cosines of a line lying in the plane OP_1P_2, making an angle θ with OP_1, are:

$$l = \frac{1}{\sin\alpha} (\sin(\alpha-\theta).\,l_1 + \sin\theta.\,l_2) \qquad (1)$$

$$m = \frac{1}{\sin\alpha} (\sin(\alpha-\theta).\,m_1 + \sin\theta.\,m_2) \qquad (2)$$

$$n = \frac{1}{\sin\alpha} (\sin(\alpha-\theta).\,n_1 + \sin\theta.\,n_2) \qquad (3)$$

General Application to the System

Consider a bond in the initial state, that is, the carbene, between an atom having coordinates $(a_1b_1c_1)$ and an atom having coordinates $(x_1y_1z_1)$, and similarly for the final state, the cyclobutene, the respective coordinates being $(a_2b_2c_2)$ and $(x_2y_2z_2)$.

The intermediate bond will have coordinates at each end of (abc) - these being known for every position - and (xyz) - these to be determined.

The direction cosines of the initial and final positions are calculated as below. This automatically refers the two lines to a common origin in space.

$l_1 = (x_1 - a_1)/d_1$ $\qquad l_2 = (x_2 - a_2)/d_2$

$m_1 = (y_1 - b_1)/d_1$ $\qquad m_2 = (y_2 - b_2)/d_2$

$n_1 = (z_1 - c_1)/d_1$ $\qquad n_2 = (z_2 - c_2)/d_2$

Where d_1 and d_2 are the lengths of the initial and final bonds respectively.

The angle α between the two lines can be calculated from the standard expression:

$$\cos\alpha = l_1 l_2 + m_1 m_2 + n_1 n_2$$

The angle θ is determined as an incremented function of α, so, for fifteen intermediate positions, θ takes on successive values of I /16, where I goes from 1 to 15 inclusively, coordinates being computed for each value of I.

Similarly, if d_1 and d_2 are different, the change in length is determined as a function of the incremental number I. Thus, d, the length of the bond in any intermediate position, is given by:

$$d = d_1 + (d_2 - d_1)\ I/16.$$

Using equations (1), (2) and (3), the direction cosines - and from these the required coordinates - can be calculated using the general expressions.

$$x = ld + a$$

$$y = md + b$$

$$z = nd + c$$

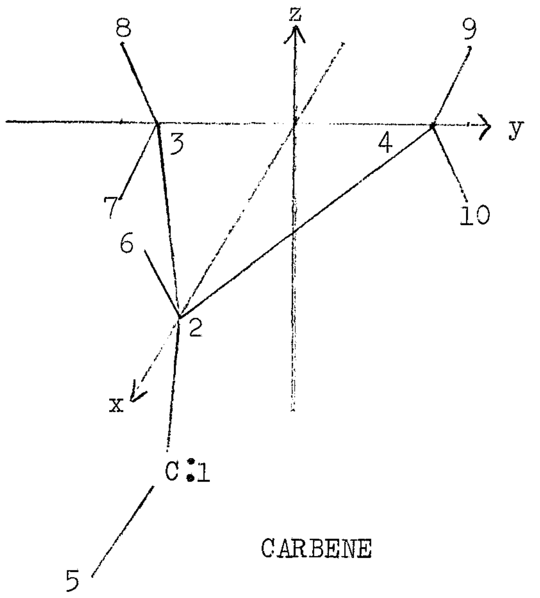
Writing this in full gives the expression for the coordinates of any atom in an intermediate position as determined by the incremental number I.

$$x = \frac{d}{\sin\alpha}\left(\sin(\alpha - \theta).\ l_1 + \sin\theta.\ l_2\right) + a \qquad (4)$$

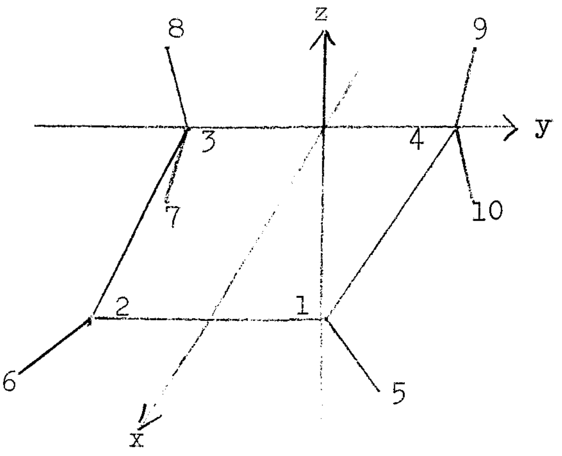
$$y = \frac{d}{\sin\alpha}\left(\sin(\alpha - \theta).\ m_1 + \sin\theta.\ m_2\right) + b \qquad (5)$$

$$z = \frac{d}{\sin\alpha}\left(\sin(\alpha - \theta).\ n_1 + \sin\theta.\ n_2\right) + c \qquad (6)$$

Specific Application to the System



CARBENE



CYCLOBUTENE

The starting point in the calculation of intermediate coordinates was the position of atom 4. Since the molecules are symmetrically arranged on the coordinate axes, atom 3 has numerically the same coordinates as atom 4, the sign of the y-coordinate being reversed.

The coordinates for position 4 are:

Carbene	(0, 0·76, 0)
Cyclobutene	(0, 0·77, 0)

Intermediate positions were taken to have coordinates:

$$(0,\ 0{\cdot}76 + 0{\cdot}01 \times I/16,\ 0)$$

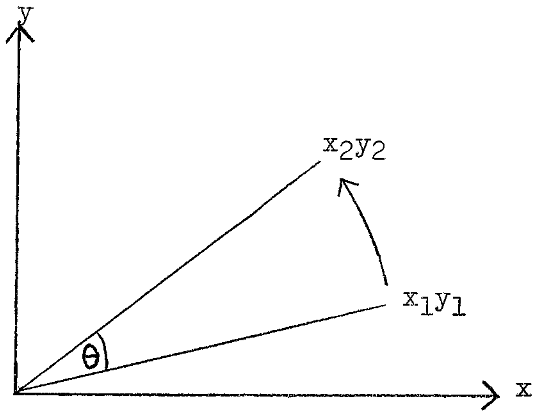
Using these values for position 4 as the values (abc) in equations (4), (5) and (6), intermediate coordinates for positions 9 and 10 were calculated. These give the coordinates for positions 7 and 8 by symmetry.

Coordinates for position 2 were calculated from those for position 3, those for positions 6 and 1 from the calculated coordinates for position 2, and similarly those for position 5 from the calculated coordinates for position 1.

Rotation Method

In this method a line of the correct length (corresponding to the known bond length) is set up along one of the cartesian axes, and by successive rotations about two axes is 'moved' into the final required position. The standard mathematical formula is used in this calculation.

Thus, consider a rotation about the z-axis, that is, in the xy plane, from (x_1y_1) to (x_2y_2).



If θ is the angle of rotation

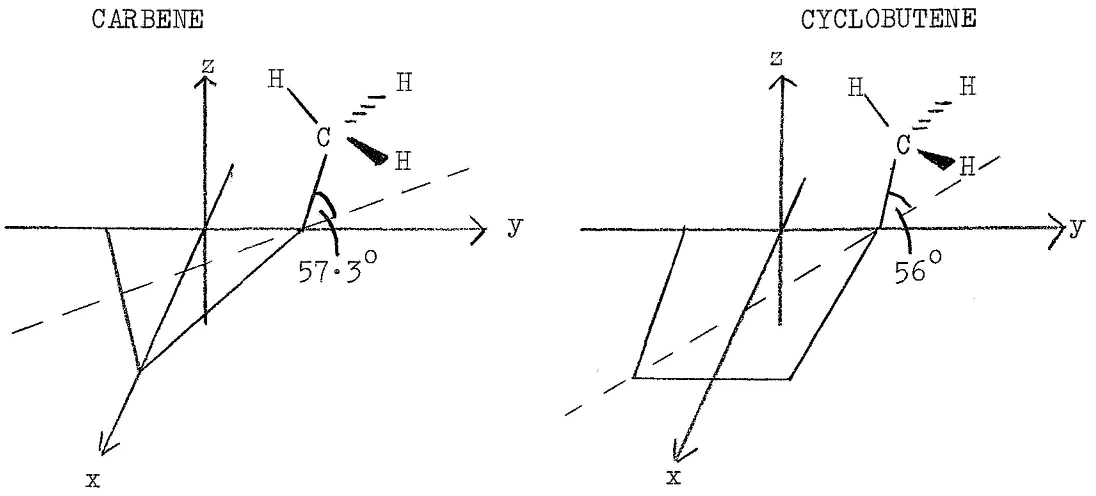
$$x_2 = x_1\cos\theta - y_1\sin\theta$$

$$y_2 = x_1\sin\theta + y_1\cos\theta$$

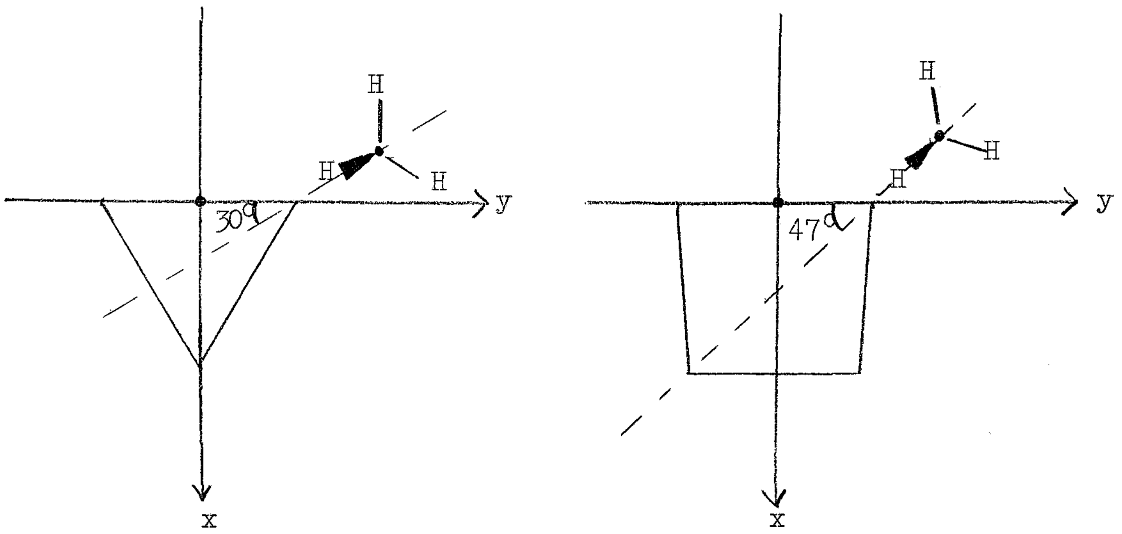
The plane method cannot be used for a methyl group, since this method would not maintain the inter-hydrogen distances at a constant value. Since distances between points remain invariant during a rotation about an axis, the rotation method was used for methyl groups. The carbon-carbon bond (between the methyl carbon and the carbon atom to which the methyl is bonded) was set up along the axis.

This method is best illustrated by two actual examples.

(i) Methyl Group on Ring Carbon



In plan

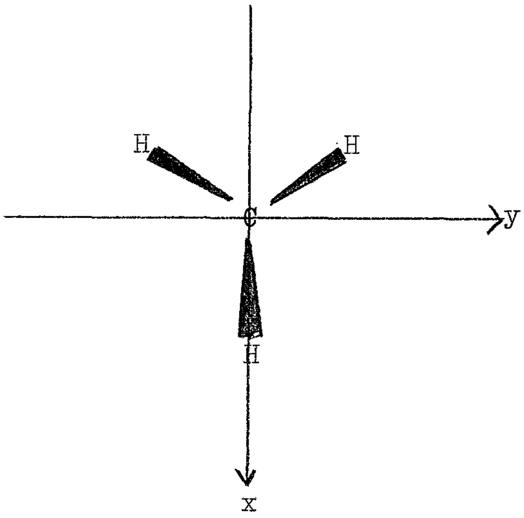


Thus in the carbene and cyclobutene, the carbon-carbon bond makes angles of 57·3° and 56° respectively with the xy plane, that is, a line in this plane which bisects the ring in each case.

Consequently, this carbon-carbon bond makes angles of 32·7° and 34° respectively with the z-axis.

The line bisecting the cyclopropane ring in the carbene is at 60° to the x-axis, and that bisecting the cyclobutene ring is at 43° to the x-axis.

The methyl group was set up with the carbon-carbon bond lying along the z-axis, and that carbon-hydrogen bond which eventually points in towards the ring lying in the xz plane on the positive x-axis. Thus, looking down the z-axis, the initial situation is as shown below.



Successive rotations on this generate a methyl group "attached" to the origin. In order to get it in position on the relevant carbon, having coordinates (0, 0·76 + 0·01 x I/16, 0), the y-coordinates have the value of (0·76 + 0·01 x I/16) added to (or subtracted from) them for the particular value of I.

Rotation by $32{\cdot}7^{\circ}$ about the y-axis, followed by rotation through 60° about the z-axis, and addition of 0·76 to the y-coordinates generates a methyl group on atom 4 of the carbene.

Similarly, successive rotations of 34° about the y-axis and 43° about the z-axis, with addition of 0·77 to the y-coordinates generates a methyl group on atom 4 of the cyclobutene.

Thus, incrementing between these values, intermediate positions can be generated.

1st rotation - about y-axis:

$$\theta = 32.7 + 1.3 \times I/16$$

2nd rotation - about z-axis:

$$\phi = 60.0 - 17.0 \times I/16$$

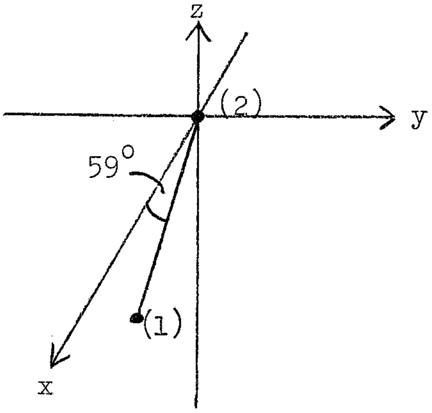
y-coordinates:

Add $0.76 + 0.01 \times I/16$

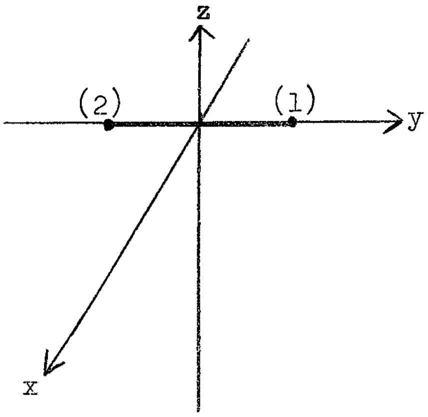
(ii) <u>Carbene Carbon and Hydrogen attached thereto</u>

<u>CARBON</u>

CARBENE



CYCLOBUTENE



The bond changes in length from 1.51Å in the carbene to 1.34Å in the cyclobutene, so this was incremented during the rotations, according to the expression:

$$l = 1.51 - 0.17 \times I/16$$

where l is the length.

This bond makes an angle of 59° with the x-axis in the carbene and 90° in the cyclobutene, and moves from the xz plane to the xy plane, that is, through 90°. Thus a bond of length 1 set up along the x-axis and taken through the two rotations by angles given in the equations below generates the intermediate coordinates.

1st rotation - about y-axis:

$$\theta = 59 + 31 \times I/16$$

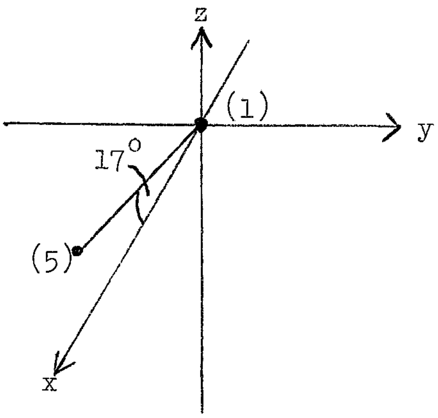
2nd rotation - about x-axis

$$\phi = 90 \times I/16$$

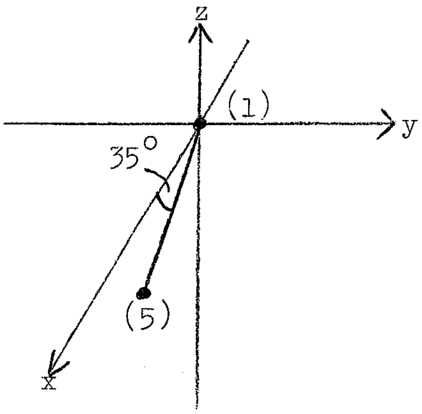
Since position 2 is taken as origin, addition of the coordinates for this position generates the real coordinates of position 1.

HYDROGEN

CARBENE



CYCLOBUTENE



The two rotations in this case are:

1st rotation - about y-axis:

$$\theta = -17 + 52 \times I/16$$

2nd rotation - about x-axis:

$$\phi = 90 \times I/16$$

The coordinates of position 1 are added on to these to yield real coordinates for position 5.

Both of these methods constitute approximations, corresponding to pathways across the energy surface, which do not necessarily correspond to the real situation.

However, the two sets of intermediate coordinates do give essentially similar results, as will be seen later, which does suggest that no serious anomalies are present in this area of the energy surface.

Nevertheless, it is accepted that large errors may be inherent in the above approaches, but short of selecting coordinates by intuition (which is probably even more arbitrary) it was felt that these methods of incrementation between the initial and final positions offered a reasonably acceptable approach to the problem.

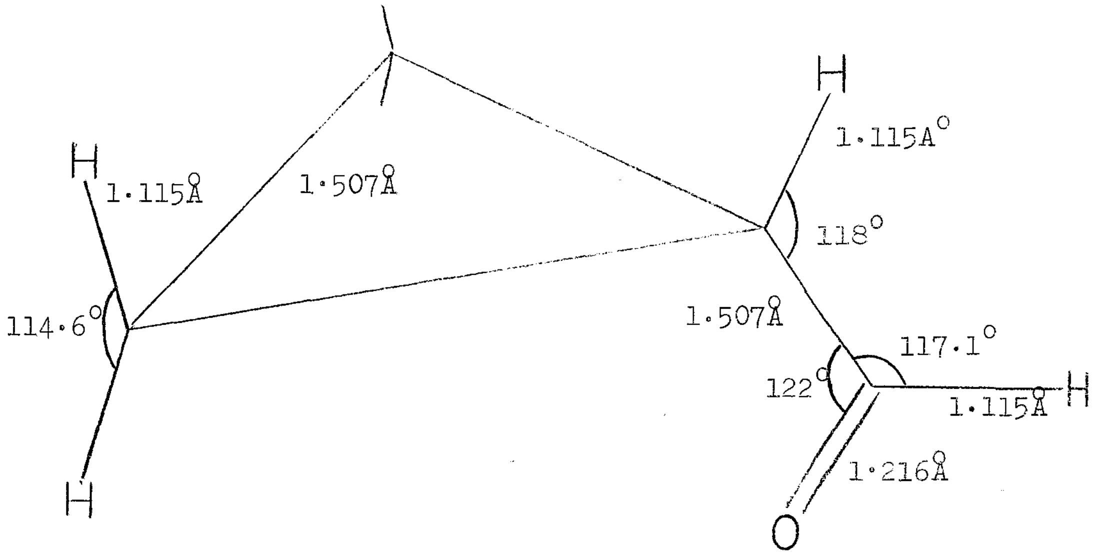
Chapter 6

Rotational Barriers in Cyclopropyl Compounds

These studies were undertaken in order to evaluate the method of CNDO, and the computer programme; when applied to the type of molecule whose rearrangement was to be studied. In the case of cyclopropane carboxaldehyde, experimental values were available with which the calculated results could be compared. The carbenes were studied in order to see if the calculated energies were reasonable and of the right order.

CYCLOPROPANE CARBOXALDEHYDE

By virtue of the fact that Bartell and Guillory[45] had studied the rotational isomerism of this compound by electron diffraction, cyclopropane carboxaldehyde was selected as the first molecule to be examined. The bond lengths and angles quoted by Bartell and Guillory, as shown below, were used in the calculation of the coordinate positions of the atoms. In addition the value of 114·6° was taken for the $\hat{HCH}$ angle on the cyclopropane ring, this being the value in cyclopropyl chloride, as determined by microwave spectroscopy.[44]

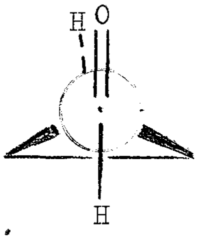


The nuclear charge on the carbon atoms (Z_c) was taken as 4·0, and 3 positions were considered, as described below and illustrated by Newman diagrams.(looking along the bond between the ring and the carbonyl carbon).

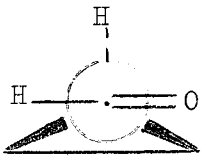
TRANS: With the carbon-oxygen bond trans- to the cyclopropane ring, and the plane of the aldehyde group bisecting the ring.

90° ROTATION: With the aldehyde group as a whole rotated through 90°, so that the plane of this and that of the ring were at 121° to each other.

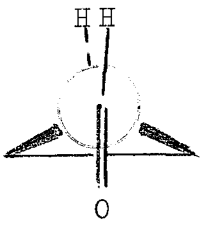
CIS: With the carbon-oxygen bond cis- to the cyclopropane ring, and the plane of the aldehyde group bisecting the ring.



Trans



90° Rotation



Cis

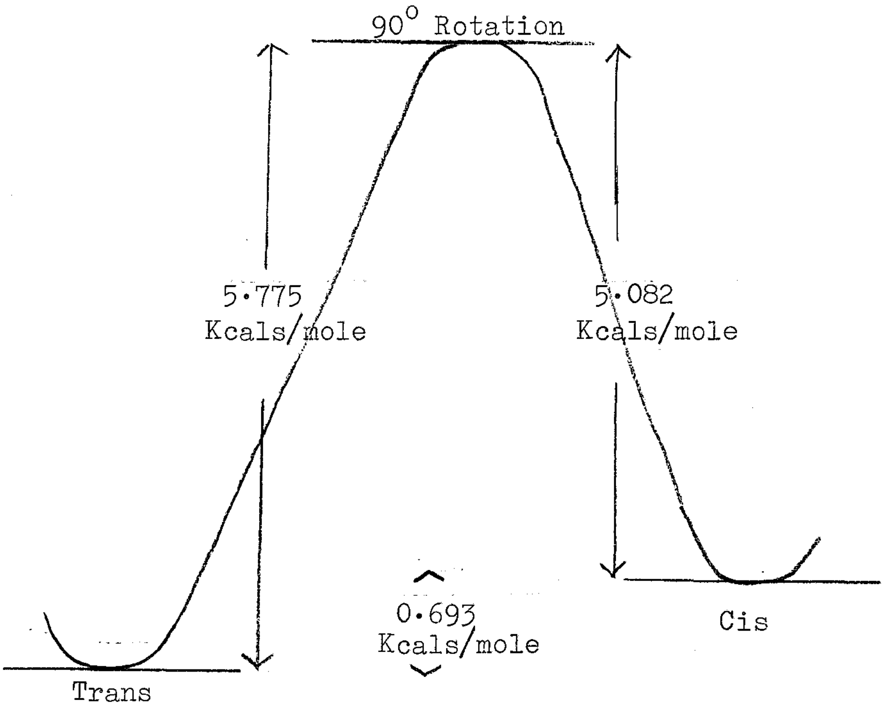
Total energies for these three positions were computed, and the results are shown below

Trans: - 1094·73 e.v.

90° Rotation: - 1094·48 e.v.

Cis: - 1094·70 e.v.

From these values an energy profile can be sketched.

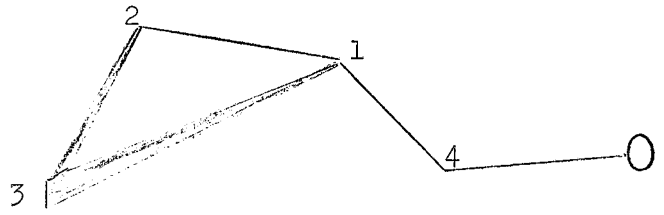


Bartell and Guillory found the equilibrium mixture to contain 45 ± 10% of the trans-conformer, and 55 ± 10% of the cis-conformer. They estimated the barrier to rotation at something in excess of 2·5 Kcals/mole. The experimental equilibrium corresponds to an energy difference between the two conformers of about 0·12 Kcals/mole.

While agreement between theory and experiment is not absolute, the calculated energies are certainly of the right order. Small variations in bond angles and distances would almost certainly improve the correspondence of theory and experiment, although this approach is apt to become somewhat arbitrary. However, the results are certainly encouraging to further studies using this method.

Hoffmann, in a private communication to Bartell and Guillory, had already predicted for cyclopropane carboxaldehyde a substantial two-fold barrier, with a nominal difference in energy between the two forms.

Further interesting information was derived from the charge density data. The following table shows the charges on the atoms - labelled as in the diagram - for each of the three positions.



(In the '90^{o} rotation' position, the oxygen atom is on the same side of the molecule as carbon atom 2.)

	C1	C2	C3	C4	O
TRANS:	4·024	4·037	4·037	3·570	6·465
90^{o} ROTATION:	4·037	4·031	4·056	3·565	6·441
CIS:	4·034	4·023	4·023	3·567	6·473

The total charge density on the three ring carbon atoms is:

TRANS:	12·098
90^{o} ROTATION:	12·124
CIS:	12·080

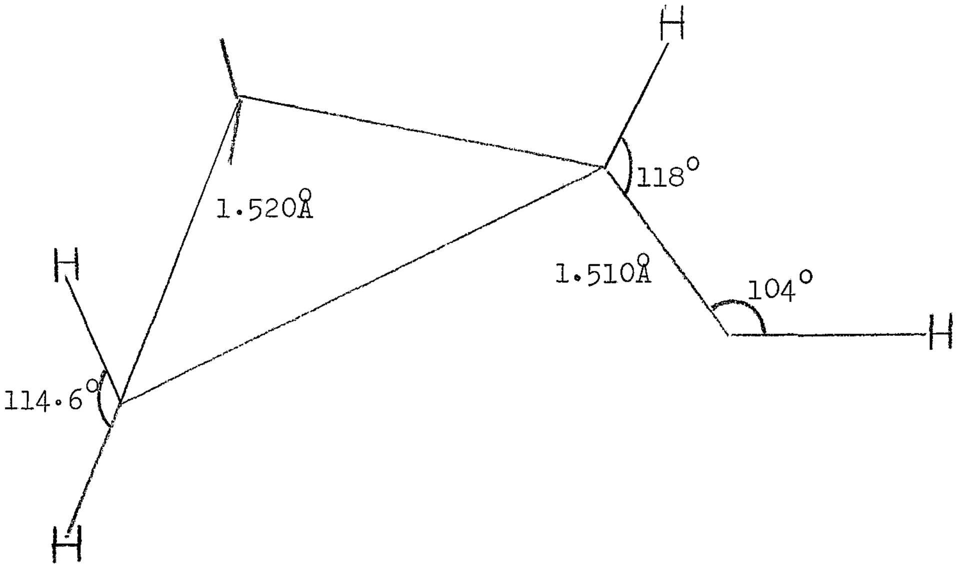
In the '90^{o} Rotation' case, the higher charge density is indicative of a reduction in electron release to the carbonyl group, relative to the 'trans' and 'cis' cases.

The cis-conformer has a lower charge density than the trans- because the position of the oxygen under the ring allows greater electron withdrawal through space, in addition to that through the bonds.

This loss of charge to the carbonyl group can be attributed to a conjugative effect between the ring and the carbonyl group, the effect being greater when the plane of the π-orbital on the carbonyl group and the plane of the ring intersect in a line at right angles to the plane of the aldehyde function, that is, in the cis- and trans-conformers. This can also be seen in the charge on the oxygen atom, which is higher in the 'conjugating' cis- and trans- cases.

CYCLOPROPYL CARBENE

Bond angles and distances were taken as in the diagram below:



All C–H bond lengths are 1·086Å.

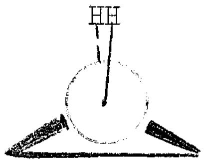
Herzberg reported a bond angle of 102–103° for singlet methylene.[40] This value has subsequently been refined to 102·4°.[46,47] A slightly increased value, 104°, was taken to allow for widening of the angle due to the presence of a substituent on the carbene.

Three positions were considered, as for cyclopropane carboxaldehyde. These are described below and illustrated by Newman diagrams (looking along the bond between the ring and the carbene carbon).

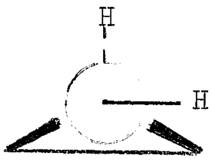
TRANS: With the carbon-hydrogen bond trans- to the cyclopropane ring. The plane formed by the two bonds to the carbene bisects the ring.

90° ROTATION: With the carbon-hydrogen bond rotated through 90°, so that the plane formed by the two bonds to the carbene and that of the ring are at 121° to each other.

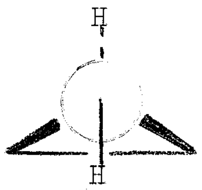
CIS: With the carbon-hydrogen bond cis- to the cyclopropane ring. The plane formed by the two bonds to the carbene bisects the ring.



Trans



90^{o}Rotation



Cis

Energies were calculated for these three positions, using values of both 4·0 and 4·1 for Z_c. It had been observed before[48] that better results were obtained with $Z_c = 4{\cdot}1$, the justification being compensation for the inefficient shielding of the nucleus by the carbon 1s electrons. As can be seen from Table II below, this observation was repeated in this case, the values of the energy differences being lower for $Z_c = 4{\cdot}1$.

Table I.

Absolute Energies of Cyclopropyl Carbene Conformers (ev)

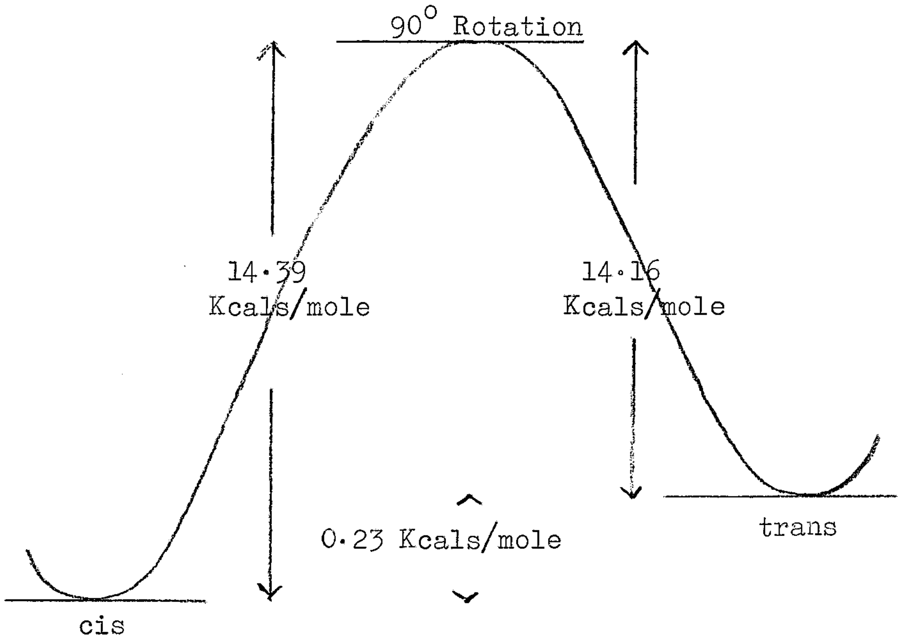
	$Z_c = 4{\cdot}0$	$Z_c = 4{\cdot}1$
CIS:	- 736·148	- 752·147
90^{o} ROTATION:	- 735·473	- 751·524
TRANS:	- 736·128	- 752·137

Table II

Energy Differences (Kcals/mole)

	$Z_c = 4{\cdot}0$	$Z_c = 4{\cdot}1$
Cis- more stable than trans- by:	0·46	0·23
Barrier Cis- to trans- :	15·59	14·39
Barrier trans- to cis- :	15·13	14·16

This is represented below as an energy profile for $Z_C = 4{\cdot}1$.



As with cyclopropane carboxaldehyde, the charge densities on the various atoms, numbered as in the diagram, indicate some conjugative interaction in the cis- and trans- cases.

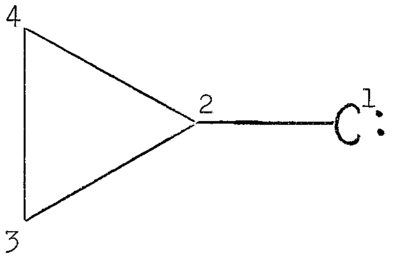
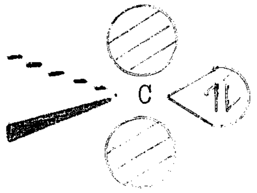


Table III

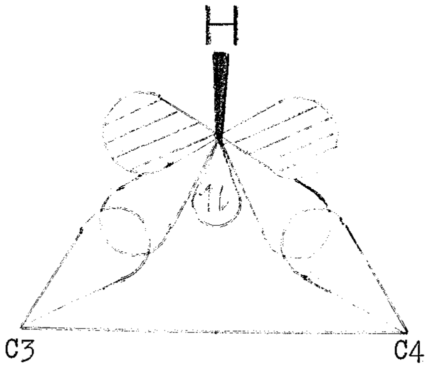
Charge Densities on Carbon Atoms for $Z_C = 4{\cdot}1$

	C1	C2	C3	C4
CIS:	4·223	3·988	4·049	4·049
90° ROTATION:	4·145	4·016	4·092	4·096
TRANS:	4·238	3·985	4·045	4·045

A singlet carbene, as conventionally represented below (A) would, in the cis- and trans- conformers, have the vacant 2p orbital lying in the plane at 121° to the plane of the ring, and overlap between the cyclopropane ring orbitals and this vacant orbital can afford conjugative stabilisation to the carbene. This can be visualised by looking along the C1C2 bond as in diagram (B) below.



(A)



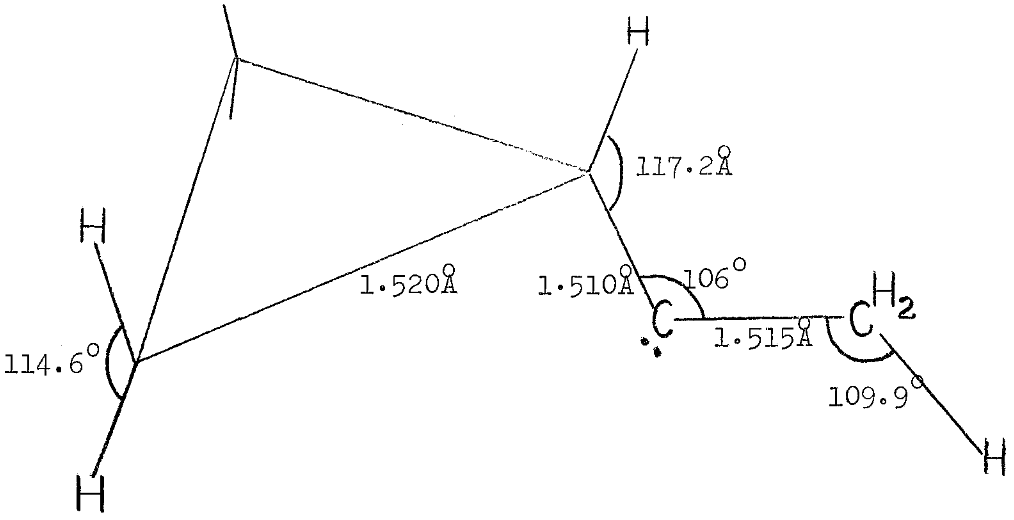
(B)

Implicit in this picture of the stabilisation of the vacant p-orbital is the fact that the filled sp^2 orbital lies at right angles to this, so that the trans- conformer (shown above) has the lone-pair "eclipsed" with the ring. Electron repulsion interactions between the lone-pair and the bonding pairs of the ring bonds, and possibly those of the C-H bonds in a cis-environment to the lone-pair could account for the lesser stability of the trans-conformer with respect to the cis- . That is to say, the lone-pair appears 'bigger' than a hydrogen atom.

The energy barrier is in line with that calculated by Hoffmann[49] for a 'classical' cyclopropyl carbinyl cation, which he predicts to have a strong 2-fold barrier (8.9 Kcals/mole). The preferred orientation of this was found to be with the CH_2^+ and the tertiary hydrogen on the ring in the same plane. This places the vacant orbital in the same relation to the ring as that observed above for the carbene.

CYCLOPROPYL METHYL CARBENE

Bond angles and distances were taken as in the diagram below:



All C–H bond lengths are 1·086Å

These values are taken partly from the standard tables and partly from a paper by Bartell et al.[50], concerned with electron diffraction studies on cyclopropyl methyl ketone.

In this work they found the equilibrium mixture to consist of 80 ± 15% cis-like conformers and 20 ± 15% trans-like conformers (the prefixes refer to the relative environment of the cyclopropane ring and the carbonyl group). They also suggested a barrier to rotation in excess of 2·5 Kcals/mole, as with cyclopropane carboxaldehyde.

The value of the carbene angle was taken as 106°, to allow for widening due to the two substituents, by analogy with the considerations for cyclopropyl carbene.

In this case ten positions were considered in order to examine possible steric interactions of the methyl group. Starting with the conformer having the methyl group cis- to the cyclopropane ring, the methyl group was rotated successively by 20° about the ring-carbene bond until it had been rotated through 180°, this situation corresponding to the trans-conformer. Table IV shows the energies calculated for these various positions and Table V the energy differences between energy maxima and minima.

Table IV

Calculated Energies

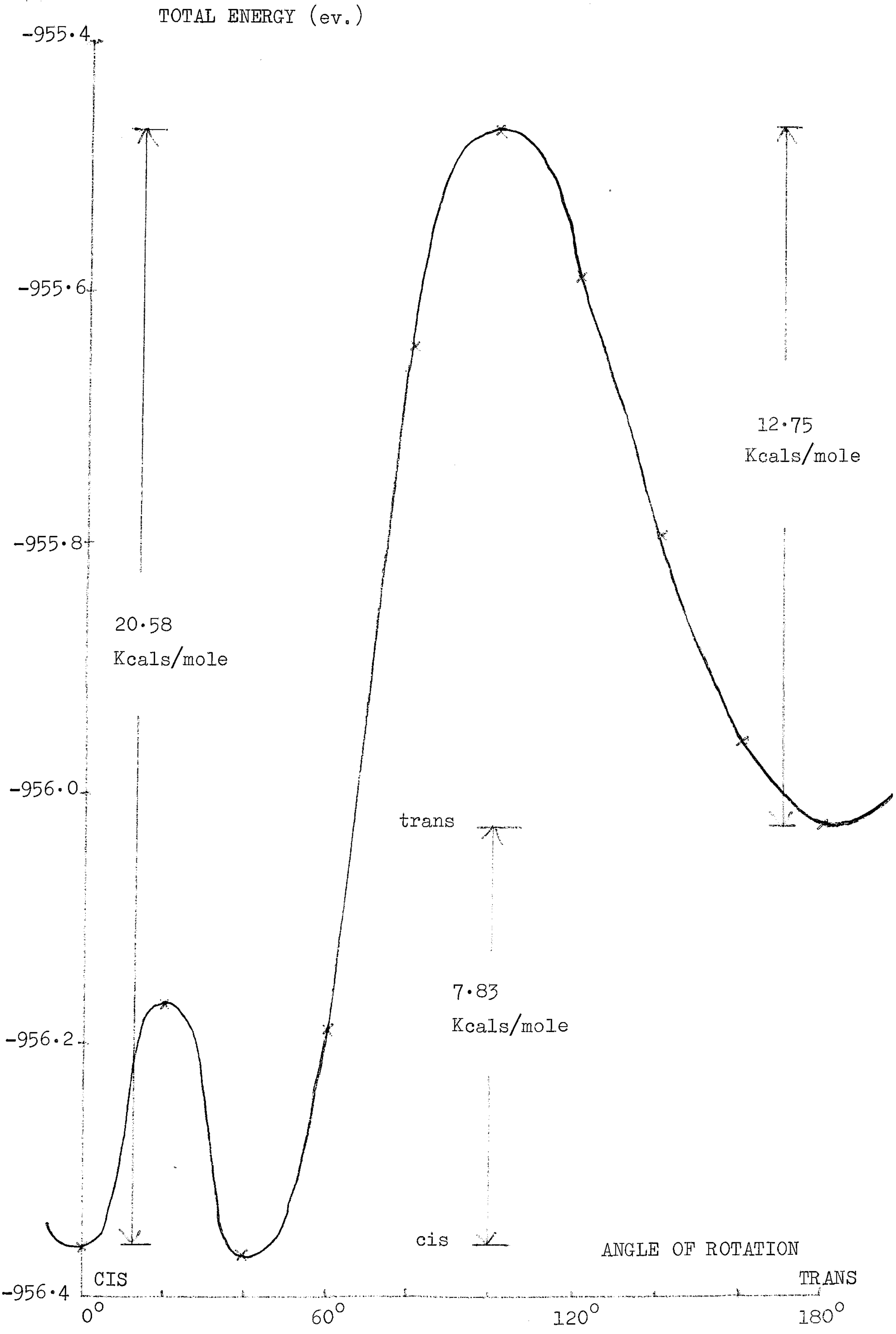
Angle of Rotation	Energy (ev)
0° (cis-)	- 956·362
20°	- 956·168
40°	- 956·367
60°	- 956·187
80°	- 955·643
100°	- 955·471
120°	- 955·587
140°	- 955·794
160°	- 955·958
180° (trans-)	- 956·023

Table V

Energy Differences (Kcals/mole)

Cis- more stable than trans- by:	7·83
Barrier, cis- to '100° rotation':	20·58
Barrier, trans- to '100° rotation':	12·75

The energy profile is shown on page 62.


TOTAL ENERGY (ev.)
-955·4
-955·6
-955·8
-956·0
-956·2
-956·4
20·58
Kcals/mole
12·75
Kcals/mole
trans
7·83
Kcals/mole
cis
ANGLE OF ROTATION
CIS
TRANS
0°
60°
120°
180°

The energy differences in this case seem to be somewhat more exaggerated by comparison with the previous examples, although this may partly be explained by steric effects. Steric effects would explain the small hump (4.5 Kcals/mole) observed at 20° rotation, when the methyl group would have moved into a position of interaction with the hydrogen atoms on the ring.

Rotation of the methyl group about the carbene-methyl bond (superimposed on the other rotation) was not considered because of the complexity involved. Variations due to this might be expected to have some effect on the values of the energy, but these are not anticipated to be large.

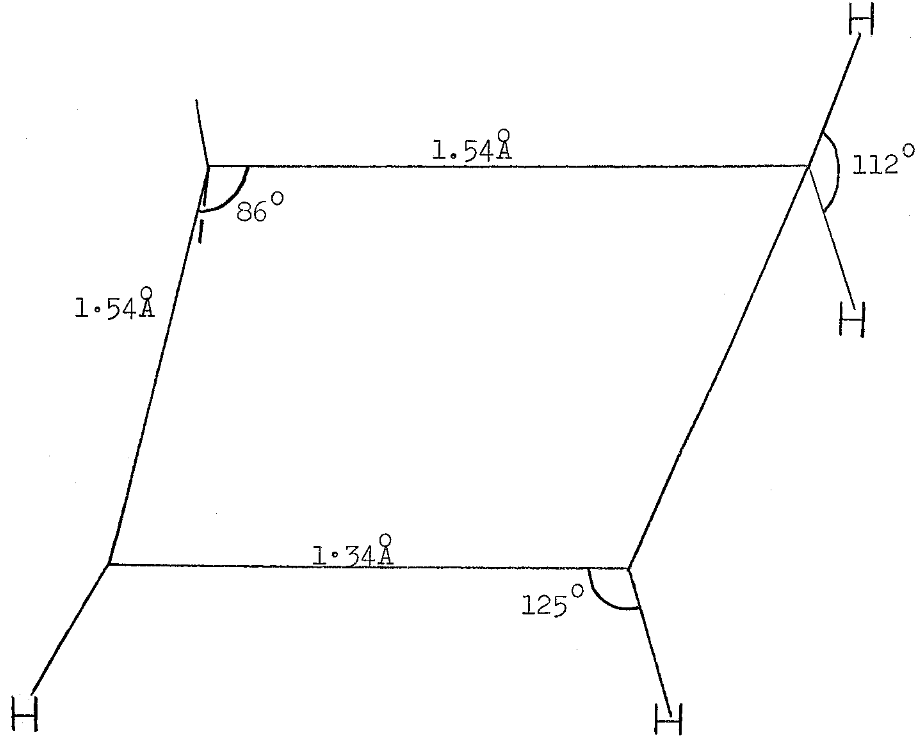
The comparatively high stability of the cis-conformer relative to the trans- is surprising, there being no obvious reason why this should be so - in fact one might expect the trans- to be more stable, since the methyl group is larger than a hydrogen atom. This should overcome the electronic repulsion of the lone-pair observed in cyclopropyl carbene, giving the methyl group a preference for being in a trans-environment to the cyclopropane ring. At this stage no adequate explanation can be advanced as to why these calculations make the cis-conformer more stable.

Chapter 7

Studies on the Rearrangements of Cyclopropyl Carbenes to Cyclobutenes

PARAMETERS:

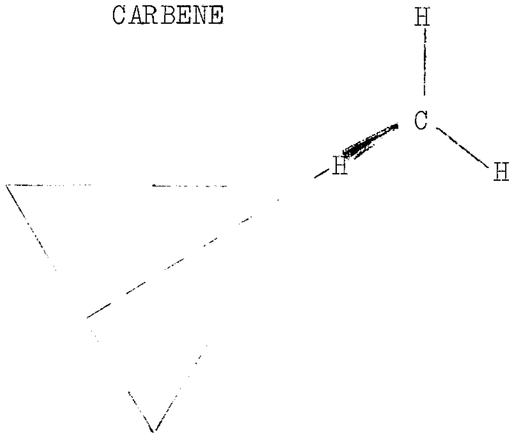
Bond angles and distances for cyclopropyl carbenes and cyclopropyl methyl carbenes were taken as for the studies on rotation barriers. The cyclobutene parameters were as shown below:



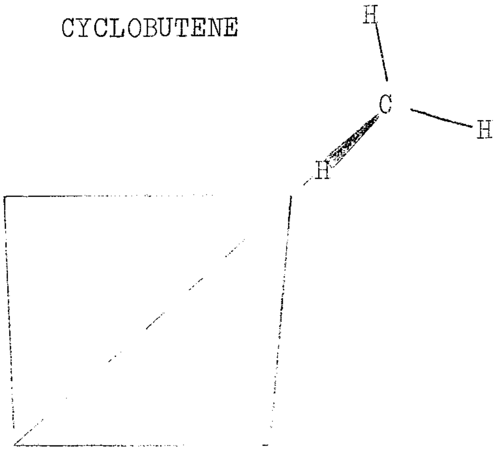
All C–H bond lengths are 1·086 Å.

In cases of substitution of the ring by a methyl group, the carbon–carbon bond distance was taken as 1·54Å, and was assumed to have the same angles relative to the ring as would a carbon–hydrogen bond. C–H distances in the methyl group were taken as 1·086Å, and the $\widehat{HCH}$ angle as 109°. The equilibrium position of the methyl group was taken to be as shown in the diagrams below.

CARBENE



CYCLOBUTENE

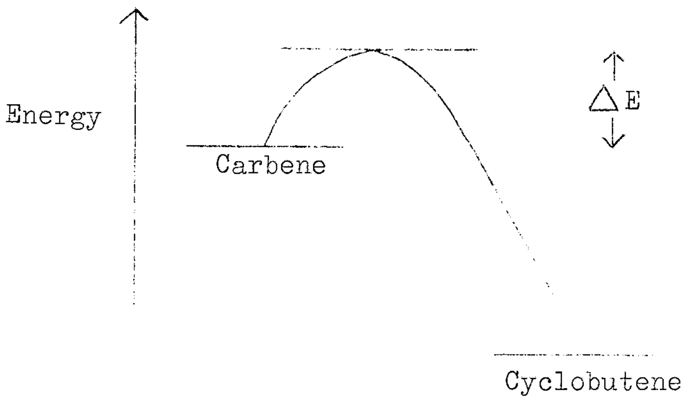


The effect of varying this position will be considered later.

Positions intermediate between the carbene and cyclobutene were determined either by the plane or rotation methods, described in Chapter 5. The particular method used will be specified in the text.

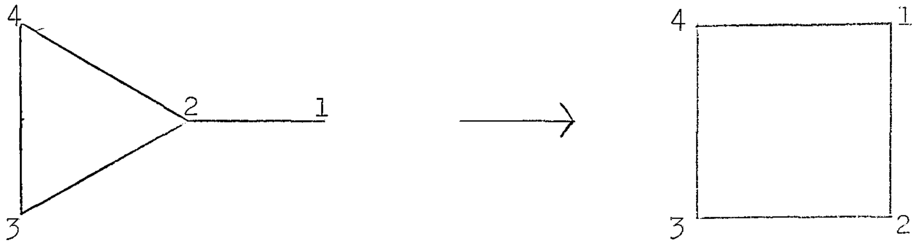
TREATMENT OF RESULTS:

In each case a value for the total energy was obtained for each set of input coordinates. This enabled a plot to be made, of energy against what may be called the incremental number. The latter corresponds to the parameter used to determine the intermediate position in the calculation of the coordinates. Thus the carbene has I=0, the 15 intermediate positions have I values from 1 to 15, and the final position, the cyclobutene, has I=16. The appearance of the plots is as shown in the diagram below.



A value for the calculated activation energy (ΔE) was obtained from the difference in energy between the carbene and the top of the energy curve.

The plot which was in fact used was that of energy and distance between the atoms forming the new bonds.



This plot, which does not affect the value of ΔE, offers a physical picture, in the sense that the distance between carbon atoms 1 and 4 is a measure of the degree of orbital overlap between the two atoms. The C1C4 distances for the two methods of determining the intermediate coordinates are shown in Table I.

Table I

C1C4 Distances

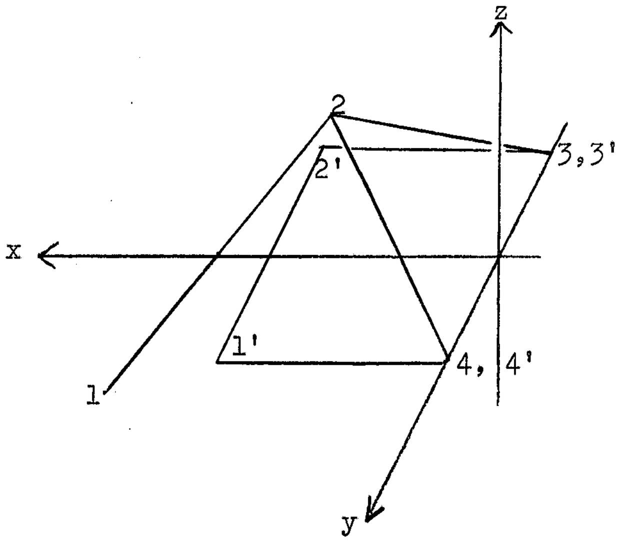
Incremental Number	Plane Method	Rotation Method
0	2·5764	2·5764
1	2·5344	2·5660
2	2·4862	2·5477
3	2·4321	2·5213
4	2·3724	2·4867
5	2·3075	2·4437
6	2·2380	2·3924
7	2·1645	2·3331
8	2·0880	2·2659
9	2·0094	2·1915
10	1·9302	2·1102
11	1·8516	2·0229
12	1·7756	1·9306
13	1.7041	1·8343
14	1·6393	1·7357
15	1·5836	1·6367
16	1·5400	1·5400

CYCLOPROPYL CARBENE TO CYCLOBUTENE:

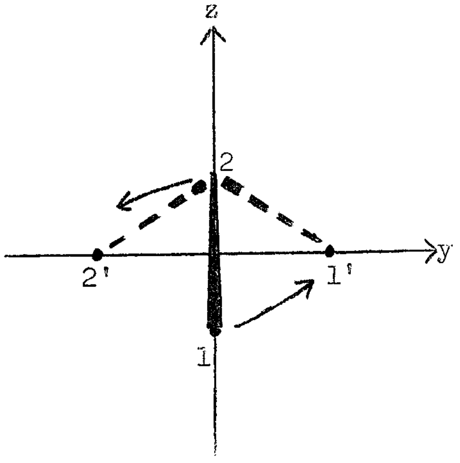
This calculation was performed four times, under varying conditions, leading to progressive reductions in the value obtained for the activation energy.

Initially the situation was considered in which the two carbon atoms eventually forming the double bond of the cyclobutene move approximately the same distance.

Looking along the y-axis



Looking along the x-axis



Thus, in the carbene, C2 and C1 are equidistant from the xy plane. The 'plane method' was used for the calculation of the intermediate coördinates.

Since the cis-conformer of cyclopropyl carbene had been shown to be slightly more stable than the trans-, the first two calculations were conducted with the hydrogen on the carbene in the cis-position. The activation energies obtained were:

$Z_C = 4{\cdot}0$ $\quad E = 45{\cdot}74$ Kcals/mole

$Z_C = 4{\cdot}1$ $\quad E = 44{\cdot}72$ Kcals/mole

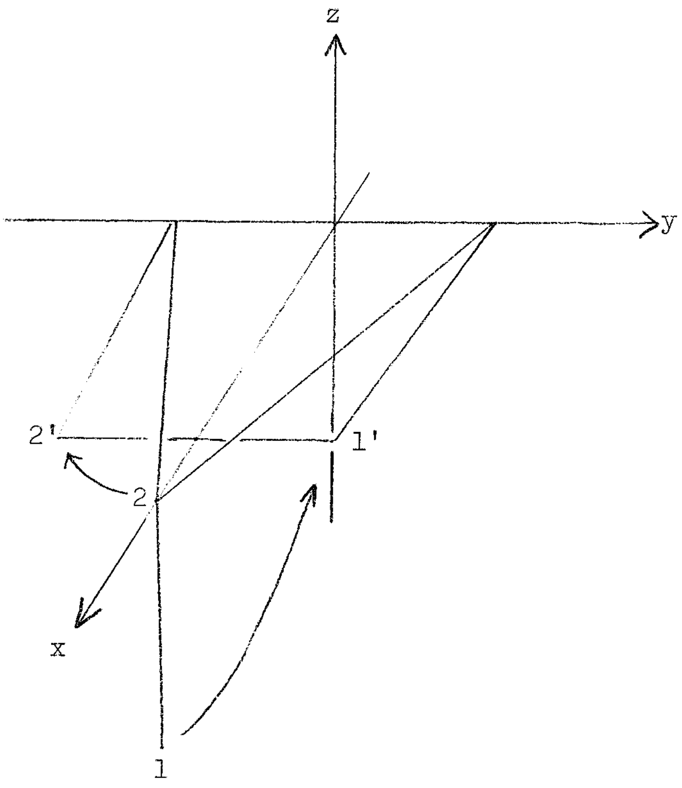
These values are obviously too large for what is a fast and facile reaction, but CNDO is a semi-empirical method and cannot be expected to give extremely accurate values. The fact that the calculated energies are of the right order of magnitude is a hopeful sign.

Intuitively, one expects that the lower the calculated activation energy, the better approximation it is to the real energy, so that a value of 4·1 for Z_c gives a better energy, albeit by a small amount. This is anticipated from the earlier comments on this subject, and all the remaining calculations were performed using a value of 4·1 for the nuclear charge on the carbon atoms.

Since the energy barrier between the cis- and the trans-conformers is reasonably small, interconversion might be expected, so the calculation was performed starting with the trans-conformer, other variables being the same. The activation energy, at 44·47 Kcals/mole, was smaller than that obtained with the cis-conformer.

This is not surprising, since interactions with the ring and ring substituents are minimised in the trans-case, so the remaining calculations were performed with the carbene substituent in a trans-environment to the ring, in order to minimise such interactions, particularly in the case of a methyl substituted carbene.

For the final run, the rotation method was employed for computing intermediate coordinates, with the additional factor that the plane of the cyclopropane ring in the starting carbene was superimposed on that of the cyclobutene. The motion of the atoms is shown in the following diagram.



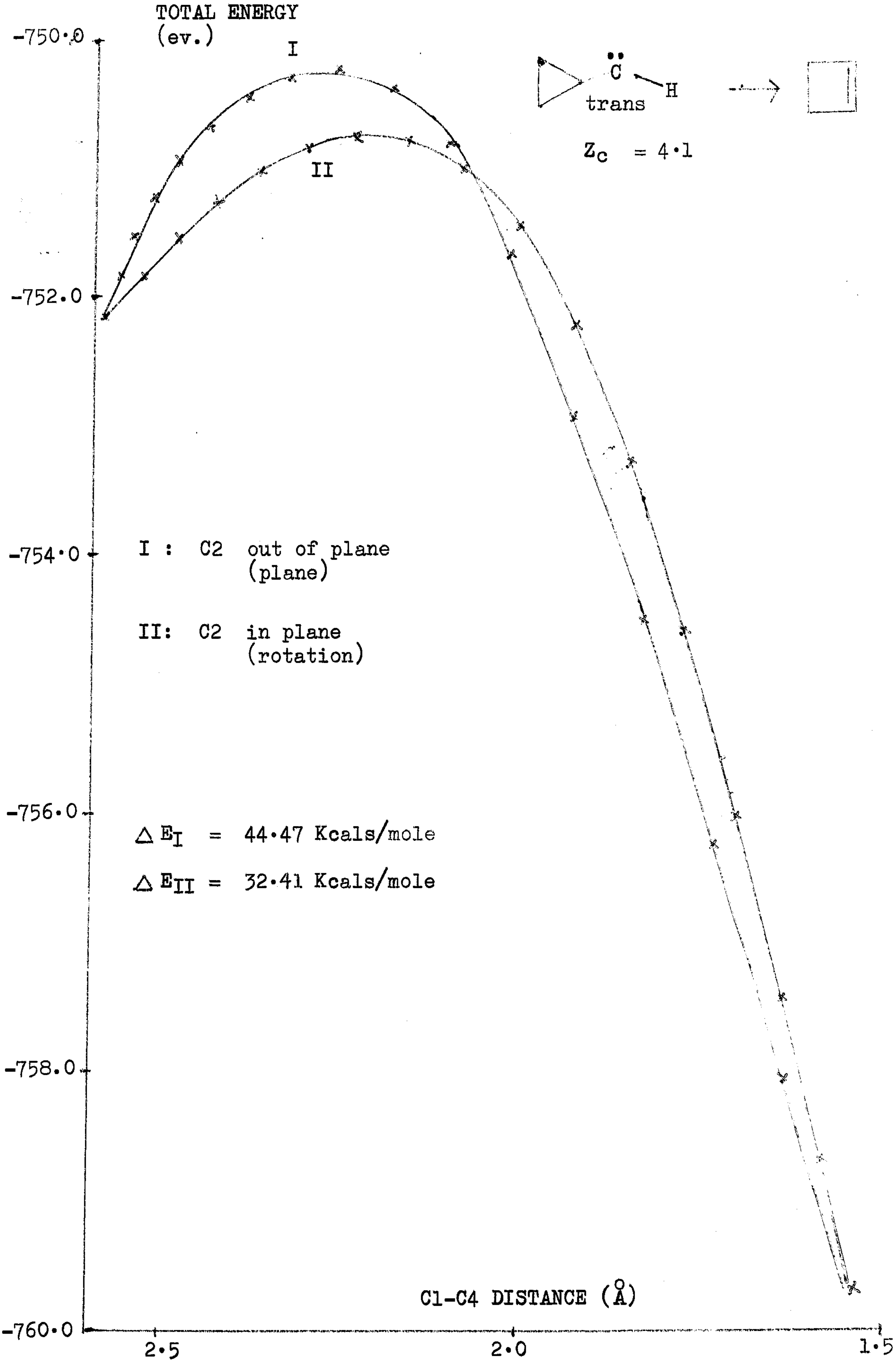
This calculation gave the lowest activation energy, 32·41 Kcals/mole, an observation consistent with the Principle of Least Motion[51], which states that:

> "Those reactions will be favoured that involve the least change in atomic position and electronic configuration."

The motion of the atoms is less with this method than when the plane of the starting cyclopropane ring is out of the plane of the final cyclobutene.

Although two variables appear to have been altered for this calculation, it will be seen later, in the case where the ring is substituted by a methyl group, that the difference between the plane and rotation methods for the calculation of intermediate coordinates is minimal. Thus, the only effective change is that in the relative planes of the initial and final positions. A comparison between the latter two calculations can be made on the energy plot below (Figure I), and Table II gives a summary of the

Figure I


TOTAL ENERGY
(ev.)
-750·0
-752·0
-754·0
-756·0
-758·0
-760·0
I
II
C
H
trans
Z_C = 4·1
I : C2 out of plane
(plane)
II: C2 in plane
(rotation)
ΔE_I = 44·47 Kcals/mole
ΔE_{II} = 32·41 Kcals/mole
C1-C4 DISTANCE (Å)
2·5
2·0
1·5

four calculations.

Table II

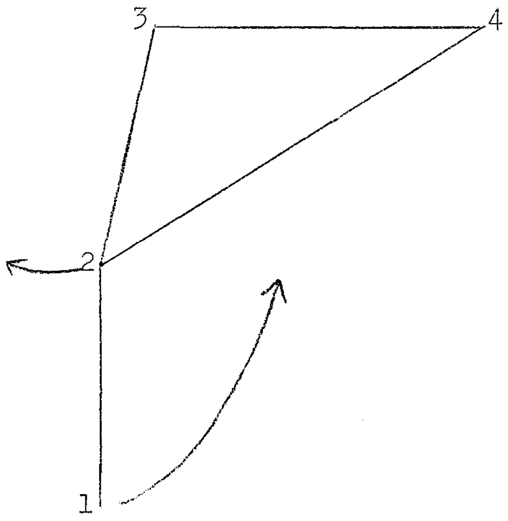
Comparison of Calculations on Cyclopropyl Carbene

CONFORMER	cis	cis	trans	trans
Z_c	4.0	4.1	4.1	4.1
METHOD FOR INTERMEDIATE COORDINATES	Plane	Plane	Plane	Rotation
RELATIVE PLANE	Out	Out	Out	In
CALCULATED ΔE (Kcals/mole)	45.74	44.72	44.47	32.41

During the rearrangement, a decrease occurs in the charge on C4, the atom to which the carbene carbon is eventually bonded. This can be interpreted in terms of the migration of the C4C2 bond into the vacant p-orbital on the carbene, a factor which is significant in comparing theoretical and experimental results.

3- and 4-METHYL CYCLOPROPYL CARBENES:

In both cases the motion of carbon atoms 1 and 2 is the same, as shown below, the distinction being provided by whether the methyl group is on carbon atom 3 or 4.



When the methyl group lies on C3 the rearrangement is towards the least substituted bond, and when it lies on C4 the rearrangement is towards the more substituted bond.

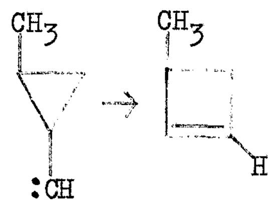
For this calculation the starting cyclopropane ring was taken to lie in the same plane as that of the final cyclobutene, Z_c was taken as 4·1, and the hydrogen substituent on the carbene was in the trans-conformation.

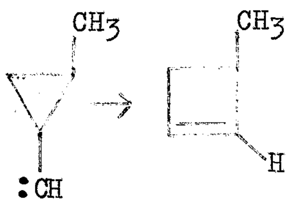
The intermediate coordinates for the ring methyl substituent and the hydrogen substituents on C3 and C4 were computed by the rotation method. This is necessary for the methyl group, as explained in Chapter 5. Consistency was maintained for the hydrogen substituents on these ring positions.

The intermediate coordinates of C1, C2 and hydrogen substituents thereon were computed by both plane and rotation methods, and the activation energies calculated for the two possible directions of rearrangement are shown in Table III.

Table III

Calculated Activation Energies (Kcals/mole)





Method for Intermediate Coordinates	3-METHYL	4-METHYL	
	ΔE	ΔE	$\Delta(\Delta E)$
Plane	33·84	29·73	4·11
Rotation	33·91	29·94	3·97

The calculated energies of activation are virtually independent of the method of computing the intermediate coordinates, although the position of the energy maximum, in relation to the C1C4 distance, is somewhat different. The rotation method generates a smoother curve, as can be seen in Figure II, which is a comparison of the energy plots obtained by the two methods, for the rearrangement of the 4-methyl carbene.

Figures III and IV show the comparative energy plots for the rearrangement of 3- and 4-methyl cyclopropyl carbenes, by the plane and rotation methods respectively.

The similarity in the results obtained by the two methods indicates that the area covered on the energy surface is relatively flat. While it is not possible to be conclusive, this is some indication that the pathways followed are an energy minimum, and that the motions described are realistic. Of course, it is quite possible that the true pathway lies on yet another energy minimum.

The energies are not as low as might be hoped for, but this is almost certainly inherent in a method and an approach which both contain approximations.

In both cases a strong preference is shown for the rearrangement towards the more substituted carbon atom of the ring, that is, when the methyl substituent is on carbon atom 4. This will be discussed in the next section, on 3- and 4-methyl cyclopropyl methyl carbenes, for which the theoretical results may be compared with experimental observations.

3- and 4-METHYL CYCLOPROPYL METHYL CARBENES:

The motion of carbon atoms 1 and 2 is as for the previous case, the distinction again being provided by whether the ring methyl substituent is on carbon atom 3 or 4. Intermediate coordinates were calculated by the

Figure II

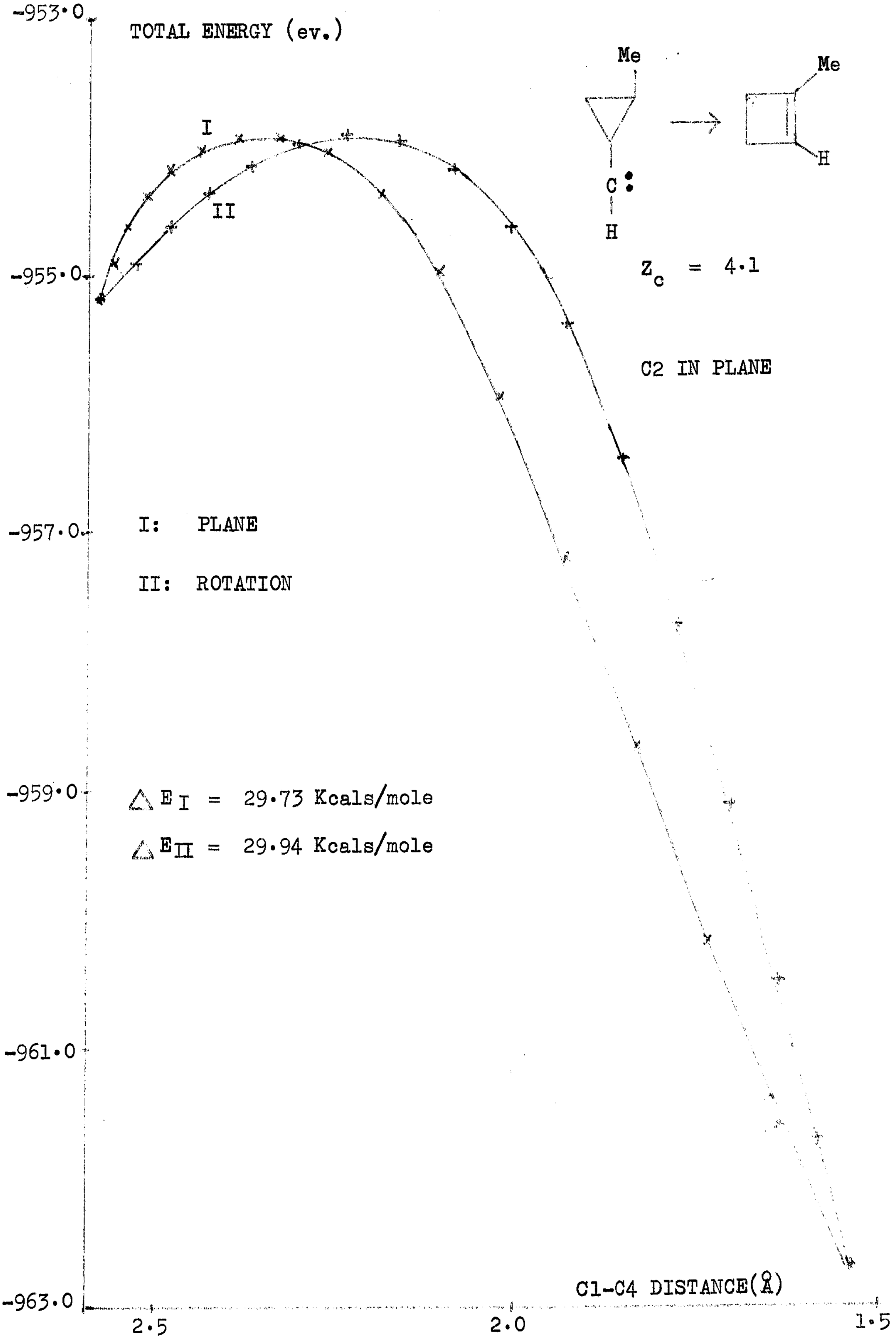

TOTAL ENERGY (ev.)
-953·0
-955·0
-957·0
-959·0
-961·0
-963·0
I
II
Me
Me
C
H
H
Z_c = 4·1
C2 IN PLANE
I: PLANE
II: ROTATION
ΔE_I = 29·73 Kcals/mole
ΔE_{II} = 29·94 Kcals/mole
C1–C4 DISTANCE(Å)
2·5
2·0
1·5

Figure III

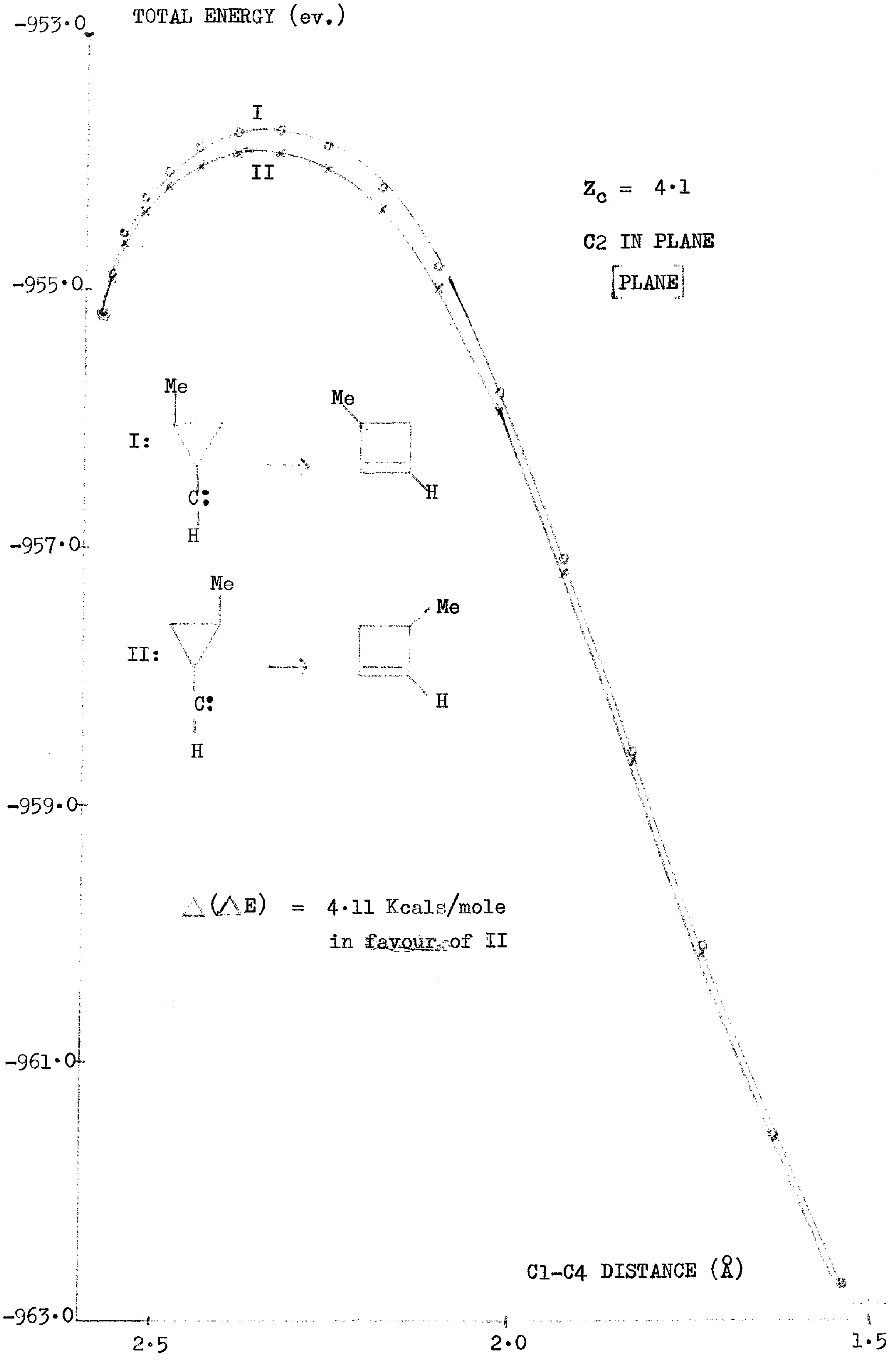
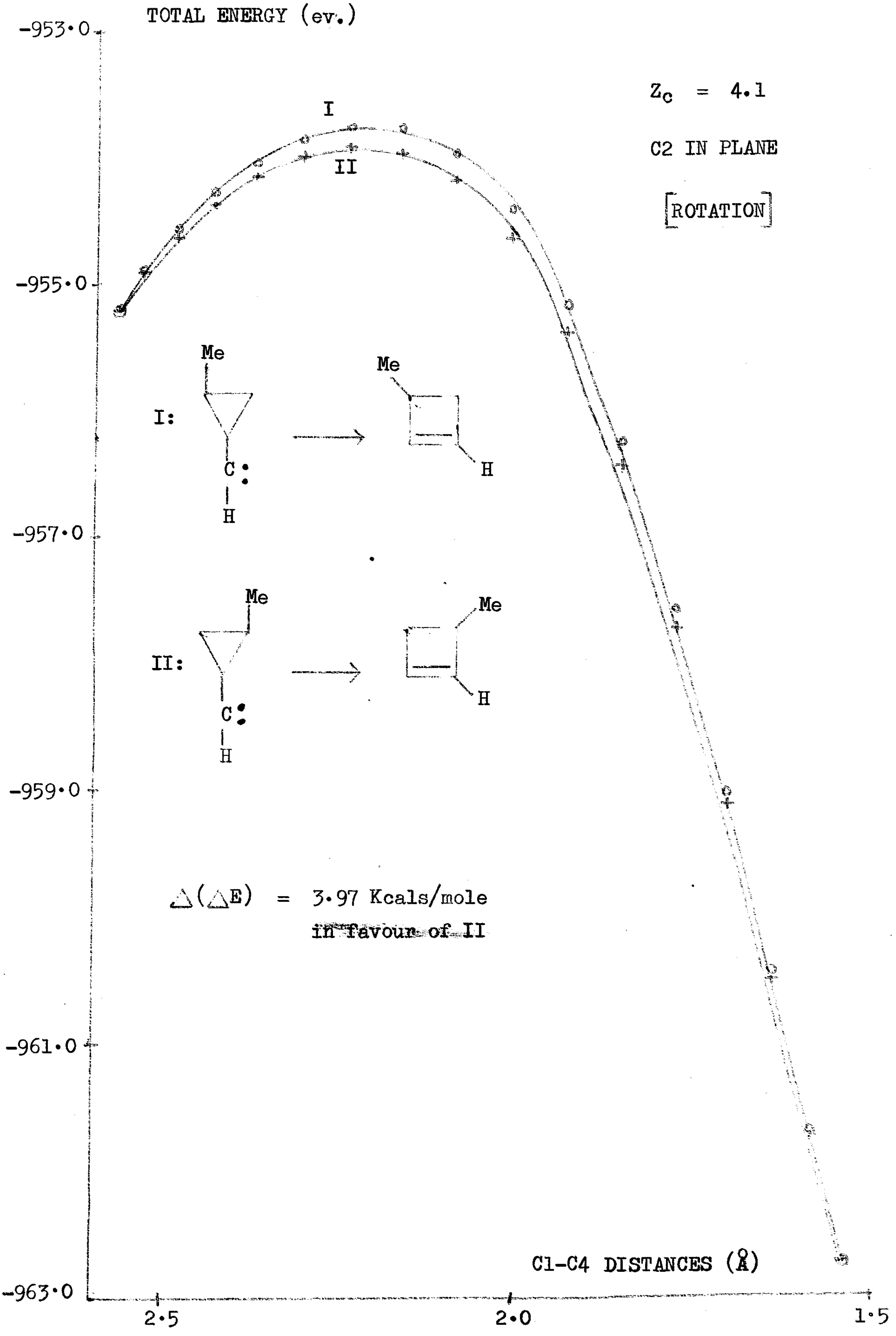

TOTAL ENERGY (ev.)
-953·0
-955·0
-957·0
-959·0
-961·0
-963·0
I
II
Z_c = 4·1
C2 IN PLANE
[PLANE]
I:
Me
C:
H
Me
H
II:
Me
C:
H
Me
H
Δ(ΔE) = 4·11 Kcals/mole
in favour of II
C1-C4 DISTANCE (Å)
2·5
2·0
1·5

Figure IV



Z_c = 4.1

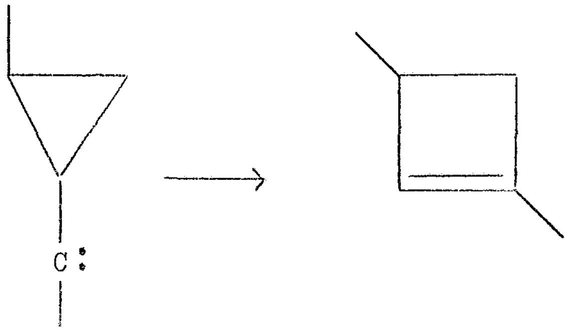
C2 IN PLANE

[ROTATION]

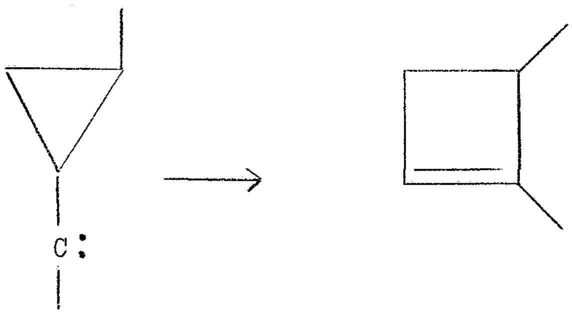
$\Delta(\Delta E)$ = 3·97 Kcals/mole
in favour of II

rotation method, it not being practicable to use the plane method in this case, on account of the methyl group on the carbene. This methyl group is in a trans-environment to the cyclopropane ring.

The comparative energy plot is shown in Figure V, and the individual activation energies are shown below:



ΔE = 44·81 Kcals/mole



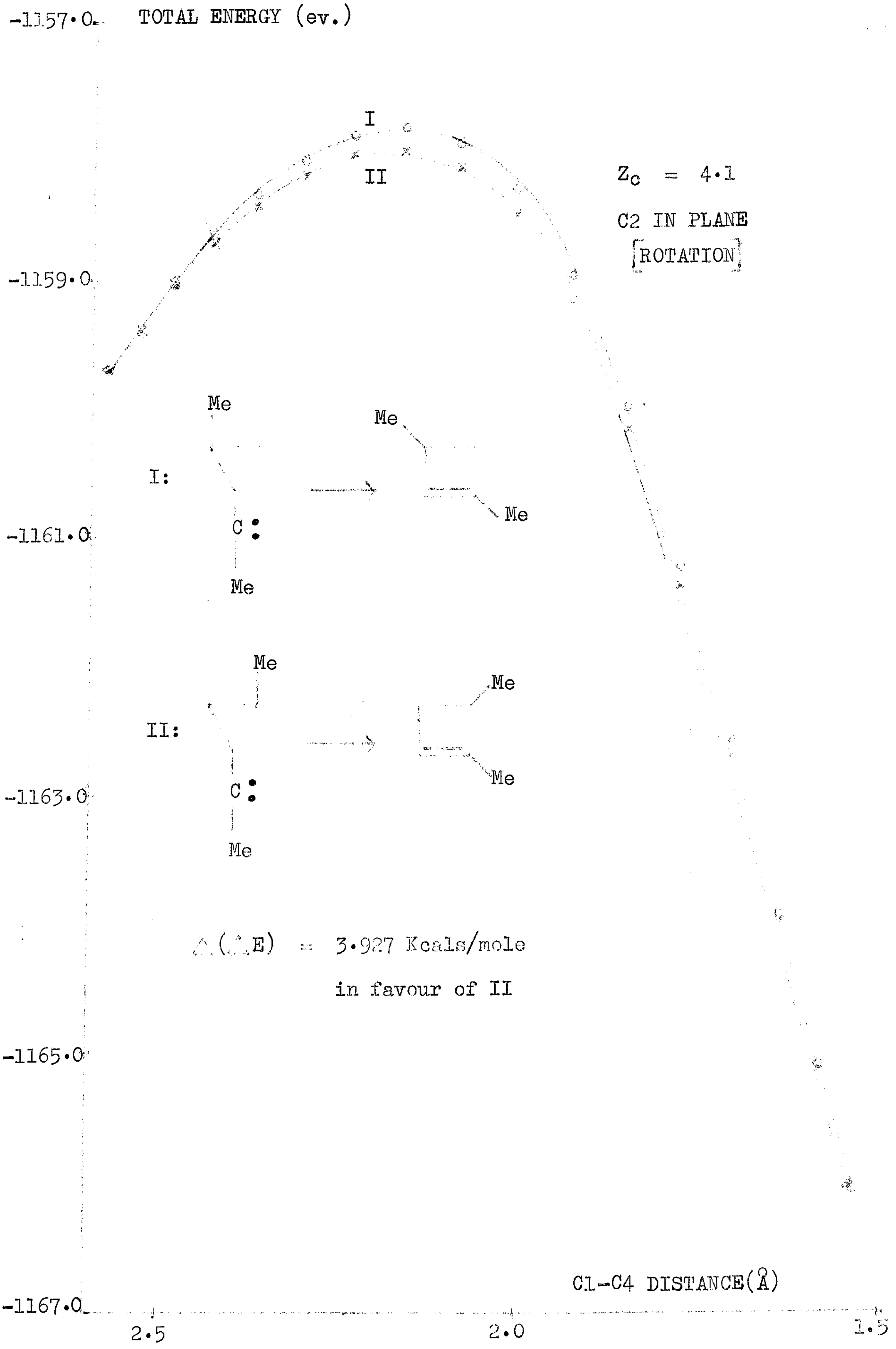
ΔE = 40·89 Kcals/mole

This result is in accord with the naive electronic picture of this system in predicting the direction of rearrangement to be towards the more substituted carbon atom.

Certainly the observation that the charge density on carbon atom 4 goes through a minimum during the process, and the consequent explanation of migration into the vacant p-orbital of the carbene, leads to the conclusion that a methyl substituent on the carbon towards which the carbene is moving should favour that rearrangement over the one in the other direction.

However, this conclusion does not agree with the experimental observations, which suggests that a factor, or factors, influencing the rearrangement have not been taken into account.

Figure V



Z_c = 4·1

C2 IN PLANE

[ROTATION]

$\Delta(\Delta E)$ = 3·927 Kcals/mole

in favour of II

It was suggested in Chapter 2 that steric repulsions were responsible for at least part of the tendency to migrate in the direction of the least substituted carbon atom.

In order to test the possibility that the nuclear repulsions were not sufficiently taken into account, the points at the top of the energy plot for 3- and 4-methyl cyclopropyl carbene were re-calculated using a different method of scaling the nuclear repulsion matrix (Mataga). The result was a difference in activation energies for the two pathways of 3·81 Kcals/mole, still favouring the rearrangement of the 4-methyl cyclopropyl carbene.

Comparing this with the original result of 3·97 Kcals/mole, obtained using the 'Refined Mataga' method of scaling the repulsion matrix, there has been little significant change, which suggests that steric effects are not the major cause of the discrepancy between calculated and experimental observations.

The calculations yield a value for the activation energy, whereas the relative rates for the two processes are measured by determining the product distribution of the cyclobutenes. By the Arrhenius equation (1) the kinetic rate is affected by two factors, the pre-exponential or 'A' factor, and the activation energy

$$K = A.\exp(-\Delta E/RT) \qquad (1)$$

According to the thermodynamic formulation of the theory of reaction rates[52], the 'A' factor is a function of the entropy of activation, as shown in equation (2)

$$A = eKT/h.\ \exp(\Delta S^*/R)$$

Considering the possibility that the cyclobutene product distribution arises by virtue of the pre-exponential factors influencing the rates for the two pathways in the opposite direction to the energies of activation, it was decided to look for effects on the entropies of activation.

The hypothesis proposed was that, when the carbene centre was moving towards carbon atom 4, the positive charge on that carbon would be stabilised by the methyl group. Hyperconjugative interaction between the methyl group and the partial positive charge could then result in restricted rotation of the methyl group, leading to a loss of entropy when the rearrangement proceeded towards carbon 4, relative to rearrangement in the other direction.

In order to test this the methyl group was rotated through angles of 30° and 60°, in order to remove the carbon-hydrogen bonds from 'hyperconjugating' positions. The energy was computed for the point of maximum energy on the respective energy plots. The results are shown in Tables IV and V.

Table IV

Absolute Energies for Rotation of the Ring Methyl Group at the point of Maximum Energy, I=6.(ev.)

	0°(Standard)	30°	60°
4-methyl	- 953·910	- 953·894	- 953·183
3-methyl	- 953·738	- 953·710	- 952·917
Difference	0·172	0·184	0·266

Table V

Energy Differences produced by the Rotation of the Ring Methyl Group. (ev.)

	ΔE $(0 - 30^{\circ})$	ΔE $(0 - 60^{\circ})$
4-methyl	0·016	0·727
3-methyl	0·028	0·821

It is apparent that the energy increase produced by rotating the methyl group is slightly greater for the 3-methyl case, which, although surprising in itself, tends to nullify arguments based on hyperconjugative effects on the entropies of activation. The greater effect shown for the 3-methyl case is probably due to the general levelling of charge densities throughout the molecule.

However, this result could also indicate that the reaction pathways generated by the methods of determining the intermediate coordinates are in fact incorrect, and spurious electronic effects have been introduced.

Since the approach to the problem involved a number of approximations, the failure of these calculations to give a result in accord with experimental observation cannot be altogether too surprising. This particular problem may be too complex to afford a satisfactory theoretical treatment by currently available methods, but nevertheless it seems hopeful that calculations using the CNDO method can be usefully employed for a semi-qualitative treatment of simple organic reactions.

However, some useful pointers have emerged which will be discussed, in the context of the experimental observations, in the next Chapter (8).

Chapter 8

Discussion

In Chapter 2 the rearrangement was seen to commence with the carbene centre 'swinging' towards the carbon atom to which it becomes bonded. This is essentially the picture which emerges from the calculated coordinates at the point of energy maximum, represented diagrammatically in Figure I. (Figure II shows the numbering of the carbon atoms as used in the calculations.)

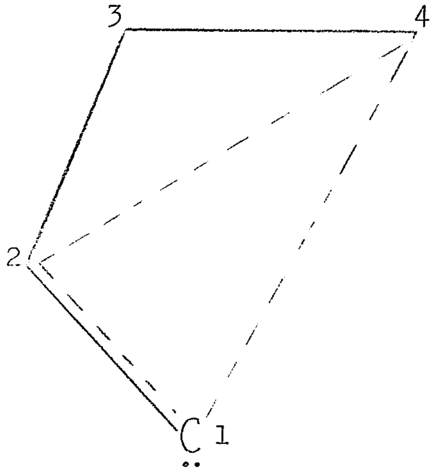


Figure I

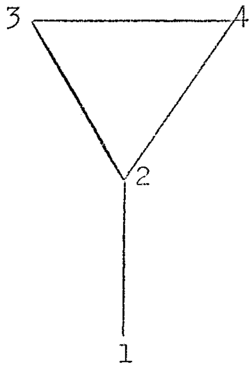


Figure II

The C1C4 distance in the theoretical transition state is somewhat larger than might have been expected from the qualitative picture - the rotation method gives a distance of 2.238Å for the point of energy maximum. This serves to illustrate that the gain in energy from the commencement of bonding between C1 and C4 is effective at fairly large distances.

If the bending-back of the C1C2 bond were accentuated, this gain in energy should be more rapid, possibly leading to a lower activation energy, but it is difficult to visualise an approach to this situation which does not involve the arbitrary choice of coordinates.

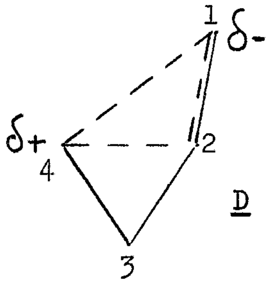
STERIC EFFECTS:

A model of the transition state was made using the coordinates generated by the rotation method, for the point of energy maximum. Examining this, the carbene centre is found to be some 2.0–2.5Å from the carbon atom of a methyl group on C4 in a cis-relationship to the carbene centre. If the methyl group is in a trans-relationship, however, the distance involved is something in excess of 3.5Å.

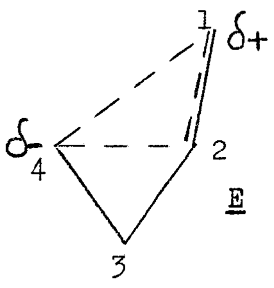
Qualitatively, steric inhibition to rearrangement is understandable for a cis-substituent, but the separation involved for a trans-substituent seems rather larger than would explain the observed cyclobutene product ratio. This conclusion is biased to a certain extent by the assumption, based on the simple electronic picture, that a methyl group favours rearrangement towards the bond on which it is substituted, so that this has to be overcome by any steric effects.

ELECTRONIC EFFECTS:

In Chapter 2 the possibility of transition states having partial positive or negative charges on the ring carbon atoms (D,E) was discussed:



D



E

During the simulated rearrangement, the charge density on C4 passes through a minimum, so the theoretical transition state corresponds with D.

Interaction between the relatively electron rich cyclopropane ring and the electron-deficient carbene would lead to a polarisation of the charges as in D, so that intuitively this is the more likely transition state.

However, the experimental observations seem to be more consistent with E, which suggests that the electronic effects are more subtle than would be at first supposed.

It was concluded earlier that the calculations were based on a somewhat naive picture, and that a factor, or factors influencing the rearrangement had not been taken into account. The possibilities arising from this will now be considered.

The starting point in the theoretical treatment of the rearrangement is a ground state singlet carbene, or a close approximation thereto, which is then required to pass over an energy barrier of 30 or 40 Kcals/mole.

This value is too large in the context of the evident speed of the reaction, but assuming it has the right order of magnitude, there exists the possibility that the carbene, at the time of its generation, is receiving a boost of energy which carries it over the energy hump.

The Bamford-Stevens reaction generates a diazo-compound and this, on decomposition, yields the carbene. The loss of nitrogen, and consequent formation of a strong $N \equiv N$ triplet bond, could provide a considerable energy boost. Two possibilities emerge from this - the generation of an excited carbene, or synchronous rearrangement of the decomposing diazo-compound.

If a free excited carbene is generated, its upper vibrational energy levels will almost certainly be significantly populated. For this to be an important factor, the carbene has to rearrange before coming to thermal equilibrium with the environment. To treat this system theoretically, an analysis of the vibrational levels of the carbene would be necessary, but this would probably involve approximations. A distorted carbene could well have steric repulsions not envisaged in the simple picture of the system, so this suggestion should be considered when attempting to explain the experimental observations.

Synchronous rearrangement of the decomposing diazo-compound was discussed in Chapter 2. With regard to a theoretical approach to this question, considerable problems would be encountered, because of uncertainty about the exact position of the nitrogen molecule, and indeed its mode of loss from the "carbene centre". To attempt to take this into consideration in the calculations would involve a lot of guesswork, and any results obtained would be somewhat arbitrary.

Drawing conclusions about the synchronous rearrangement, based on the calculations as performed, is a little dangerous because the whole system would be modified by the presence of the nitrogen molecule.

Nevertheless, it is not unreasonable to propose that the cyclopropane ring bond would still migrate into the vacant, or vacated, orbital on the "carbene centre". Conclusions based on this are affected by the extent to which the nitrogen molecule has departed. That is to say, is one dealing with a displacement of nitrogen, or migration towards a "carbene centre" effectively "solvated" by a nitrogen molecule?

If this nitrogen molecule produces a situation in which charge is effectively back-donated into the ring, the generation of a partial positive charge, as observed in the calculations, could be overcome. This affords the situation which was suggested as an explanation at the end of Chapter 2, and which is believed to provide the best rationalisation of the experimental observations.

Chapter 9

Experimental

Infrared spectra (IR) were measured on a Unicam SP200 or SP200G spectrophotometer, as liquid films unless otherwise stated.

Proton magnetic resonance spectra (NMR) were run on a Varian A60, or Varian HA100, instrument, as stated in the text. Tetramethylsilane was used as internal reference, unless otherwise stated.

Vapour phase chromatography (VPC) was performed with a Perkin-Elmer model F11 Gas Chromatograph.

An Aerograph A700 Gas Chromatograph was used for preparative VPC.

VPC columns used are tabulated below, with the labels used in the text.

A	2 metre Carbowax 20M (Phase Separations Ltd.), 15% on Chromosorb 'P'.
B	2 metre Polypropylene Glycol, Perkin-Elmer standard column, code number DE 115.
C	2 metre bis-1,2-(2-cyanoethoxy) propane, 20% on Chromosorb 'P'.
D	4 metre bis-1,2-(2-cyanoethoxy) propane, 20% on Chromosorb 'P'.
E	2½ metre Silicone Oil (Hopkin & Williams), 15% on Chromosorb 'P'.
F	10ft. bis-1,3-(2-cyanoethoxy) propane, 15% on Chromosorb 'P'. (For A700)
G	10ft. Carbowax 20M (Phase Separations Ltd.), 15% on Chromosorb 'P'. (For A700)

All melting points (MP) are uncorrected.

Cyclopropyl methyl ketone

This was prepared according to the method of Cannon et al.[53]

2-acetylbutyrolactone (ex Koch-Light) was treated with conc. HCl to convert it to 5-chloropentanone-2 (Crude yield: 66.9%, IR 1705 cm^{-1})

The chloro-ketone was cyclised with aqueous NaOH.

BP 109 - 112.5°C (Lit.110 - 112°C)

Overall Yield: 67.5%

IR 3100 cm^{-1}, 1690 cm^{-1}, 1035 cm^{-1}

VPC (Column A, 70°C, N_2 20psi.) indicates the compound to be 99.9% pure.

Cis-2-methyl cyclopropyl methyl ketone

4-chloro-3-methylbutyronitrile was prepared by the method of Applequist and Peterson.[54]

Anhydrous HBr (Matheson lecture bottle) was added to methallyl chloride (ex BDH) in the presence of benzoyl peroxide, the system being irradiated with a 500-watt tungsten lamp (Phillips "Photolita" PF218E/43), yielding 1-bromo-3-chloro-2-methylpropane in 79% yield.

BP 75-76°C (50mm.)

(Lit. 79-80°C (60mm.)[54], 49°C (15 mm.)[55])

The chloro-bromide was treated with KCN in aqueous ethanol to yield the nitrile in 53.7% yield (based on the chloro-bromide consumed).

BP 90-91° (20mm.)

(Lit. 83-85.5°C (15mm.)[54], 82-83°C (16mm.)[56])

IR 2250 cm^{-1}, 732 cm^{-1}, 689 cm^{-1}.

2-methyl cyclopropane carbonitrile was prepared by ring-closure of the chloro-nitrile with sodamide[57], according to the method of Cloke et al.[56]

The crude ethereal extract was evaporated down and the residue analysed by VPC (Column B, 82°C, N_2 25psi. and 58°C, N_2 20psi.). The solution contained 0·36g. nitrile per ml. of ether, the isomers being present in roughly equal proportions. The identification was by comparison with an authentic sample generously provided by D.C. Neckers, prepared according to reference (58).

<u>IR</u> 2245 cm^{-1}, no peaks below 750 cm^{-1}

Ketone:

The crude ethereal solution of the nitriles was reacted with MeMgBr in ether by the usual method. The dried ethereal extract of the ketone was evaporated down using a 30 cm. fractionating column packed with glass helices, and a total reflux head. The residue was purified, and separated from the trans-isomer, by preparative VPC (Column F, 80°C, H_2 40psi.), yielding 0·59g. cis-2-methyl cyclopropyl methyl ketone.

<u>VPC</u> (Column C, 80°C, N_2 20psi.) indicates the presence of less than 1% of the trans-isomer as the only significant impurity.

<u>IR</u> 3080 cm^{-1}, 1695 cm^{-1}, 1115 cm^{-1}

<u>NMR</u> (60 MHz) (micro-sample, external TMS)

8·05 τ	Singlet	4 protons
8·1 τ	Multiplet	
8·7τ - 9·7τ	Singlet and 2 multiplets	6 protons

The spectrum is similar to that observed by Roberts et al.[59], the differences being attributable to the fact that this was run as a micro-sample.

A sample of ketone was pyrolyzed under vacuum for 4 hours at 170°C and 1 hour at 190°C; VPC (Column C, 80°C, N_2 20psi.) showed 15-20%

formation of hex-5-en-2-one (allyl acetone) by comparison with an authentic sample (ex. Koch-Light). This is in accord with the observations of Roberts et al.[59] on the pyrolysis of the cis-ketone.

Trans-2-methyl cyclopropyl methyl ketone

A sample of the trans-ketone (2·27g.) was obtained as a by-product in the synthesis of the cis-isomer. This was identical with that obtained by the method of Julia et al.[60]

5-Acetoxy-4-methyl pentanone-2 was obtained by heating methallyl acetate and acetaldehyde together in an autoclave in the presence of benzoyl peroxide.

IR 1705 cm^{-1}, 1725 cm^{-1}.

This acetoxy-ketone was mixed with conc.HCl and the product, 5-chloro-4-methyl pentanone-2, was steam distilled out.

IR 1712 cm^{-1}

The trans-ketone was obtained by heating the chloro-ketone with aqueous sodium hydroxide and steam distilling out the product.

VPC (Column C, 80°C, N_2 20psi.) indicates the presence of 1-2% of cis-isomer as the only significant impurity.

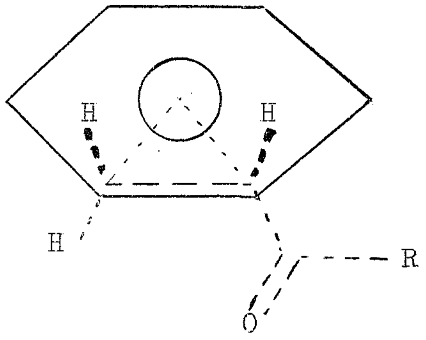
IR 3080 cm^{-1}, 1695 cm^{-1}, 1320 cm^{-1}.

NMR (60 MHz)

$CDCl_3$	7·8τ	Singlet	3 protons
	8·15 - 9·05τ	Complex	6 protons
	9·1 - 9·5τ	Complex	1 proton
CCl_4	7·87τ	Singlet	3 protons
	8·1 - 9·1τ	Complex	6 protons
		Contains singlet	(8·87τ) 3 protons
	9·25 - 9·6τ	Complex	1 proton

Benzene	8.15τ	Singlet	3 protons
	$8.5 - 9.0\tau$	Complex	3 protons
	$9.05 - 9.25\tau$	Doublet	3 protons
		Evidence of further splitting	
	$9.5 - 9.75\tau$	Complex	1 proton
Pyridine	7.9τ	Singlet	3 protons
	$8.2 - 9.15\tau$	Complex	6 protons
	$9.25 - 9.6\tau$	Complex	1 proton
Micro-sample (external TMS)	8.13τ	Singlet	3 protons
	$8.35 - 8.7\tau$	Complex	1 proton
	$8.85 - 9.3\tau$	Complex	5 protons
		Contains singlet (9.15τ), 3 protons	
	$9.45 - 9.75\tau$	Complex	1 proton

The solvent shifts observed can be interpreted in terms of the model proposed by Boykin et al.[61], shown below:



The protons on the side of the ring opposite the carbonyl group lie in the shielding region of the complexed benzene molecule, whereas protons on the same side of the ring as the carbonyl group lie in the very slight shielding or deshielding region of the complexed benzene molecule depending upon the rotamer distribution of the carbonyl group. When compared to $CDCl_3$, the signals for protons in the shielding region of benzene are moved upfield, whereas the signals of the protons not in the shielding region of the complexed molecule remain unchanged or moved slightly downfield.

Thus, on this basis, the upfield shift of the signal for the ring methyl when going from CCl_4 (8·87τ) to benzene (9·05 - 9·25τ) can be taken as confirmation of the trans-stereochemistry of this ketone. The shift is in agreement with the observation by Seyden-Penne et al.[62] of an upfield shift of 16 Hz for this ketone.

Earlier work on solvent shifts in the NMR of cyclopropane derivatives can be found in references 63-66. This includes studies on downfield shifts in pyridine.[64,65] An attempt to investigate such an effect in this case was unsuccessful because the signal for the ring methyl was not distinct.

Pyrolysis of a sample of the trans-ketone under the same conditions as the cis-ketone produced no detectable allyl acetone.

Cis- and trans-1,2-dimethyl cyclopropane carboxaldehyde*

A mixture of angelic, tiglic and α-ethyl acrylic acids was prepared according to Young et al.[67]

2-Hydroxy-2-methylbutyronitrile (ethyl methyl ketone cyanhydrin) was prepared by the action of aqueous sodium bisulphite on a mixture of ethyl methyl ketone and sodium cyanide in aqueous solution. The crude cyanhydrin was decanted off and used as crude material in the hydrolysis to 2-hydroxy-2-methylbutyric acid by heating overnight with conc. HCl under reflux.

BP   115-118°C (15mm.)   (Lit. 115°C (12mm.))

IR   1710-1740 cm^{-1} (broad)

No nitrile absorption.

The unsaturated acids were obtained by slowly heating the hydroxy-acid (3 - $3\frac{1}{2}$ hours) to 186-192°C, when a distillate came over, which separated into two phases in the receiver. This distillate was extracted with petroleum ether (bp 40-60°C), dried and distilled.

BP   88-90°C.

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* The prefixes 'cis-' and 'trans-' refer to the relative stereochemistry of the methyl groups, as used in Chapter 2 with reference to the carbenes.

Methyl Esters:

The mixture of unsaturated acids was converted to the methyl esters according to the procedure described in reference 68, by treatment with dimethyl sulphate and potassium carbonate in acetone (Analar).

BP 116-142°C (Bulk 128-130°C)
Yield 90%
IR 1715 cm^{-1}, 1652 cm^{-1} (shoulder 1630-1635 cm^{-1})
VPC (Column A, 93°C, N_2 20psi.) shows three peaks, with only minor impurities. If the esters are eluted in order of boiling points, the predominant product is methyl angelate.

Cis- and trans-2-methyl but-2-en-1-ol:

These were prepared by the action of lithium aluminium hydride on the mixture of methyl esters. After work-up with 10% aqueous NaOH and water, the ethereal extract was dried over anhydrous potassium carbonate, the ether distilled off and the residue distilled.

BP 135-142°C.
Yield 72%
IR 3400 cm^{-1}, 1660 cm^{-1} (weak)
VPC (Column B, 90°C, N_2 20psi.) showed three peaks, with traces of the esters remaining. The third product is 2-ethyl prop-2-en-1-ol.

Cis- and trans-1,2-dimethyl cyclopropane methanol:

These were prepared from the unsaturated alcohols by the Simmons-Smith procedure according to Le Goff.[69]

On evaporating down the dried ethereal extract and analysing the residue by VPC (Column B, 90·5°C, N_2 20psi.), this was found still to contain some unsaturated alcohols.

An ethereal solution of the product was shaken with 0.5% aqueous potassium permanganate until VPC (as above) showed virtually all the unsaturated alcohols to have gone.

The cyclopropyl alcohols were then separated and purified by preparative VPC (Column G, 90°C, H_2 25psi.).

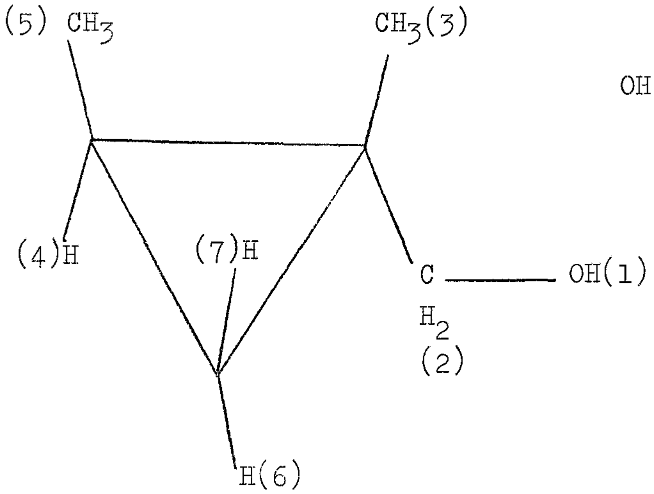
Cis-1,2-dimethyl cyclopropane methanol:

<u>VPC</u> (as above) indicates this to be greater than 95% pure.

<u>IR</u> 3400 cm^{-1}, 1270 cm^{-1}

<u>NMR</u> (100MHz) micro-sample, external TMS.

6.58τ	Singlet		2 protons (2)
8.75τ	Singlet		3 protons (3)
8.815τ	Doublet	6Hz	3 protons (5)
9.1 - 9.5τ	Multiplet		2 protons (4,6)
10.015τ	Triplet	4Hz	1 proton (7)



OH(1) not evident

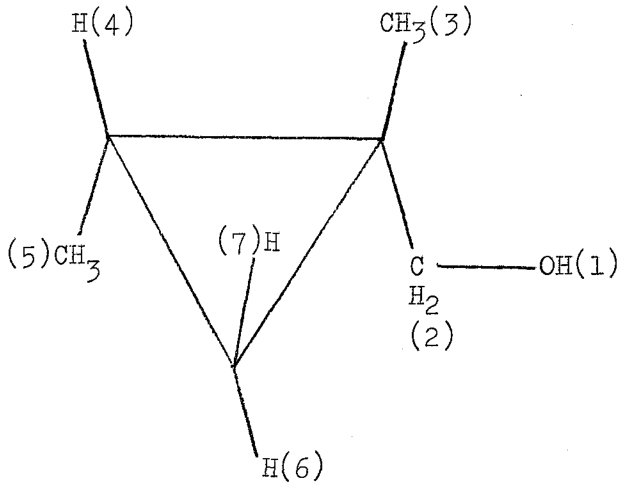
Trans-1,2-dimethyl cyclopropane methanol:

<u>VPC</u> (as above) indicates about 95% purity

<u>IR</u> 3450 cm^{-1}, 1290 cm^{-1}

<u>NMR</u> (100MHz) micro-sample, external TMS

5·33τ	Singlet(broad)		1 proton (1)
6·51τ	Quartet	11·3 Hz	2 protons(2)
8.88τ	Singlet		3 protons(3)
8.89τ	Doublet	6Hz	3 protons(5)
9·31τ	Multiplet		1 proton (4)
9·56τ	Quartet	4,4·5Hz	1 proton (6)
9·93τ	Quartet	9·5,4·5Hz	1 proton (7)



Oxidation of Alcohols to the Corresponding Aldehydes:

This was effected by the procedure of Meinwald et al.[70] using Jones' reagent in a two-phase system with acetone.

Cis-1,2-dimethyl cyclopropane carboxaldehyde

Following the oxidation of the alcohol, the petroleum ether (bp. $40-60^{\circ}C$) extract was dried and evaporated down.

VPC (Column A, $81^{\circ}C$, N_2 20psi.) indicated some contamination by petroleum ether and minimal contamination by acetone. Otherwise the residue was considered pure enough for making the tosyl hydrazone.

IR 3100 cm^{-1}, 2750 cm^{-1}, 1695 cm^{-1}, 1260 cm^{-1}, 1040 cm^{-1}

Trans-1,2-dimethyl cyclopropane carboxaldehyde

This was worked up as for the cis-isomer, and was found by VPC (as above) to be identical with a sample previously prepared from tiglaldehyde, by lithium aluminium hydride reduction, Simmons-Smith cyclopropanation and Jones' oxidation.

IR 3100 cm^{-1}, 2750 cm^{-1}, 1695 cm^{-1}, 1240 cm^{-1}, 1040 cm^{-1}.

2,2 Dimethyl cyclopropyl methyl ketone

This was prepared by the action of methyl magnesium bromide on 2,2-dimethyl cyclopropane carbonitrile.

The nitrile was made by the method of Nelson et al.[71], by heating the ditosylate of 2,2 dimethyl propane-1,3-diol (neopentyl glycol, ex. Koch-Light) with KCN in ethylene glycol.

Ketone:

BP	130-132°C
IR	1690 cm^{-1}
	Trace of nitrile remains (2250 cm^{-1})
NMR	(60MHz)

$CDCl_3$	7.8τ	Singlet	3 protons
	8.8τ	Singlet	3 protons
	8.92τ	Singlet	3 protons
	8.0 - 8.3τ	Multiplet	2 protons
	8.95- 9.4τ	Multiplet	1 proton

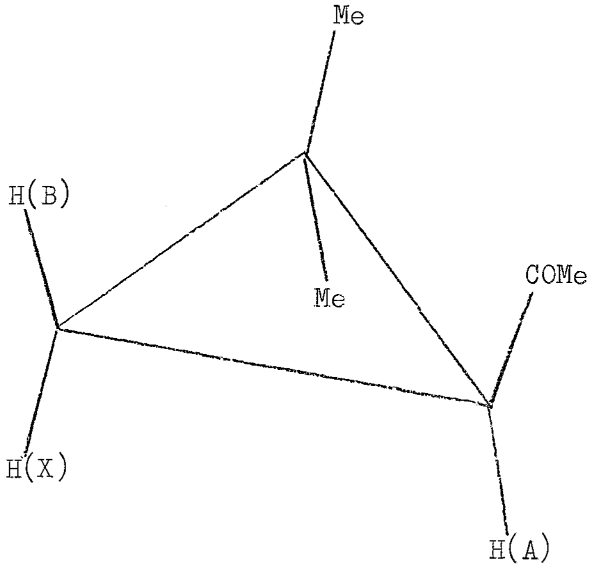
This agrees with the spectrum as reported by Agami and Prevost.[72]

Benzene	8.07τ	Singlet	3 protons
	8.15 - 8.95τ	Multiplet	2 protons
	8.93τ	Singlet	3 protons
	9.02τ	Singlet	3 protons
	9.25 - 9.65τ	Multiplet	1 proton

Pyridine	7·85τ	Singlet	3 protons
	7·9 - 8·85τ	Multiplet	2 protons
	8·91τ	Singlet	3 protons
	8·94τ	Singlet	3 protons
	9·05 - 9·5τ	Multiplet	1 proton

Solvent shift effects as discussed previously can be seen also in this case. Seyden-Penne et al.[62] reported shifts from CCl_4 to benzene of +13Hz for the ring methyl trans- to the acetyl group, and -2Hz for the ring methyl cis- to the acetyl group.

The spectrum ($CDCl_3$) was analysed as an ABX system with the assistance of Dr. M.J. Bulman of this Department, as shown in the diagram below.



$\Delta\nu_{AB}$ = 22·2Hz

J_{AB} = +5·5Hz

J_{AX} = +7·55Hz

J_{BX} = -3·65Hz

2,2-Diethyl cyclopropyl methyl ketone

This was prepared by essentially the same method as used for the dimethyl ketone.

The 2,2-diethyl propane-1,3-diol was obtained by lithium aluminium hydride reduction of diethyl diethyl malonate (ex BDH). After evaporating down the dried ethereal extract, and pumping for a short time on a water pump, IR showed no absorption at 1730 cm^{-1} corresponding to the ester, so the diol was used without further purification for making the di-tosylate.

Ketone:

VPC (Column E, 160°C, N_2 20 psi. and Column A, 140°C, N_2 20psi.) indicates the presence of 3 compounds, one being the nitrile.

IR 1690 cm^{-1}

1703 cm^{-1} (shoulder) implying ketonic impurity

2250 cm^{-1}: nitrile.

The ketone was purified by preparative VPC (Column G, 138°C, H_2 25 psi.)

(The third impurity was found by IR, NMR and Mass Spectrometry to be 5-ethylhept-5-en-2-one, probably produced by thermal rearrangement of diethyl cyclopropyl methyl ketone during distillation.)

IR 3050 cm^{-1}, 1690 cm^{-1}, 1020 cm^{-1}

NMR (100MHz) CCl_4

7·4τ	Singlet	3 protons
7·7 - 9·3τ	Complex	12 protons

The theoretical integration ratio is 3:13.

Cis-2-methyl-cis-3-vinyl cyclopropane carboxaldehyde

Ethyl cis-2-methyl-cis-3-vinyl cyclopropane carboxylate was prepared by the addition of ethyl diazo-acetate to cis-penta-1,3-diene in the presence of anhydrous $CuSO_4$.

Piperylene (ex. Ralph Emanuel) was analysed by VPC (Column D, Room temperature, N_2 20psi.) and found to contain 61% of the trans-isomer, 39% of the cis-isomer and a trace of cyclopentene.

The trans-isomer reacts faster with maleic anhydride in the Diels-Alder reaction, so this was used as a basis for the purification of the cis-isomer.

Maleic anhydride was purified by sublimation.

In a typical experiment, maleic anhydride (110·1g. - 5% excess on the amount calculated for reaction with the trans-component in the diene mixture) was placed in a 1 ℓ. round-bottomed flask with the piperylene (119·0g). The flask was fitted with a large condenser and drying tube and the mixture was stirred magnetically. After slight warming with a hot-air blower, the reaction proceeded vigorously by itself.

When reaction had ceased, and the mixture was cool, the excess hydrocarbon was distilled out under vacuum, using a dry-ice/acetone condenser.

<u>VPC</u> (Column D, Room temperature, N_2 20psi.) showed the composition of the distillate to be:

cyclopentene	2·1%
trans-penta-1,3-diene	3·6%
cis-penta-1,3-diene	94·3%

Ethyl diazo-acetate was prepared on a $^2/_5$ molar scale according to the procedure described by Searle[73], and was used as the crude product after removal of the dichloromethane.

In a 500 ml. 3-necked flask, fitted with a pressure-equalizing dropping funnel and an ice-water condenser, was placed about 2g. of anhydrous $CuSO_4$ and 250 ml. of cis-penta-1,3-diene. This was stirred magnetically, and heated toreflux on a water-bath. When the diene was at reflux, the crude ethyl diazo-acetate, diluted with its volume of cis-penta-1,3 diene, was run in over $\frac{1}{2}$ hr. The solution was maintained at reflux for 2 hrs.,when the reaction was complete.

The excess diene was distilled off, and the dark-brown residue was filtered to remove $CuSO_4$, washing with a little dry ether. The ether was removed on a rotary evaporator, and the esters distilled into a cold trap (dry-ice/alcohol) using a high vacuum (0·05 torr). This removes polymeric material. The distillate was slightly yellow in colour.

Yield: 36.0g. (58·4%)

IR shows a broad carbonyl band ~ 1715 cm^{-1}

VPC (Column A, 140°C, N_2 20psi.) shows 5 products

(Column E, 130°C, N_2 20psi.) shows 6 products.

This mixture of esters was reduced with lithium aluminium hydride by heating under reflux for 3¼ hours. The crude yield, after removal of the ether, and some of the ethanol, was 20g.

VPC (Column A, 130°C, N_2 20psi.) shows three major peaks, one having a shoulder. These correspond to the four possible mono-addition products of ethyl diazo-acetate and cis-penta-1,3-diene.

It was also concluded that about half the ethanol produced in the reduction had co-distilled with the ether, and that very little of the esters remained.

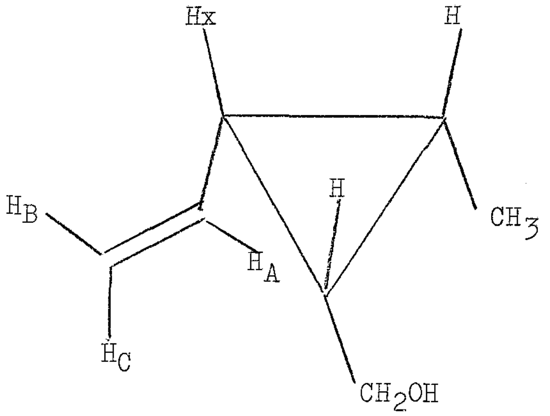
In one preparation, these alcohols were purified, inasmuch as was possible, by preparative VPC (Column G, 130°C, H_2 25psi.). They were collected as two fractions.

The first was tentatively identified as cis-2-methyl-cis-3-vinyl cyclopropane methanol by NMR. The second fraction was a mixture of cis- and trans-2-(1-propenyl)cyclopropane methanol, probably contaminated by trans-2-methyl-trans-2-vinyl cyclopropane methanol. From the relative proportions, it is apparent that, in the presence of $CuSO_4$, ethyl diazo-acetate adds preferentially to the least substituted double bond in the diene, a rather surprising observation.

NMR of first fraction (60MHz) CCl_4

4·1 - 5·2 τ	Complex	3 protons
5·64 τ	Singlet	1 proton
6.57 τ	Doublet 7cps.	2 protons
7·6τ - 9·6τ	Complex	6 protons
	Contains singlet (9·67τ)	3 protons

Part of the spectrum was roughly analysed as below:



$J_{AX} \sim$	7Hz	A:	4·53 τ
$J_{AB} \sim$	17Hz	B:	4·89 τ
$J_{AC} \sim$	9·5Hz	C:	5·02 τ
$J_{BC} \sim$	3Hz		

The mixture of alcohols was oxidised to a mixture of the corresponding aldehydes by the procedure of Meinwald et al.[70], using Jones' reagent in a two-phase system with acetone. Allowance was made for the presence of ethanol in the crude product from the reduction.

Cis-2-methyl-cis-3-vinyl cyclopropane carboxaldehyde was purified and separated from the other isomers by preparative VPC (Column G, 120°C, H_2 25psi.).

Yield: 0·89g. (this was low due to polymerization in the trap used for the preparative VPC)

IR 3075 cm^{-1}, 2725 cm^{-1}, 1690 cm^{-1}, 1645 cm^{-1}, 1010 cm^{-1}, 920 cm^{-1}.

VPC (Column A, 122°C, N_2 20psi.) showed the aldehyde to be pure, except for the presence of a minor impurity ($\sim$ 2%) eluted just before the aldehyde.

NMR (60MHz) CCl_4

- 0·1τ(10·1δ)	Doublet	4·0Hz	1 proton
4·0 - 5·05τ	Complex		3 protons
7·5 - 8·5τ	Complex		3 protons
8·67τ	Doublet	5·5Hz	3 protons

The basis for the assignment of a cis-stereochemistry is as follows:

(i) The stereochemistry of the diene is expected to be retained in the reaction with ethyl diazo-acetate.

(ii) If the $CuSO_4$ complexes with the diene as well as with the ethyl diazo-acetate, the transition state is intuitively expected to have the vinyl and carboethoxy substituents in a cis-relationship to each other.

(iii) The peaks in the vinyl region, and the methyl group absorption, are shifted downfield in the NMR of the aldehyde, as compared to the NMR of the alcohol. This can be explained in terms of deshielding of these protons by the carbonyl group of the aldehyde.

Should this assignment be incorrect, it is not expected that any significant effect on the decomposition of the tosyl hydrazone would be observed.

Preparation and Decomposition of Tosyl Hydrazones

PREPARATION:

The theoretical quantity of p-toluene sulphon-hydrazide was dissolved in the minimum volume of boiling methanol (Analar). This solution was cooled under a water tap until the contents of the flask solidified, when the ketone or aldehyde was added, rinsing the container with a small amount of methanol. The mixture was warmed gently until all the hydrazide was again in solution, and then allowed to stand until the tosyl hydrazone crystallized out.

If crystallization did not occur, the methanol was removed at room temperature using a rotary evaporator. The residual oil was taken up in ether, dried over anhydrous $CaCl_2$ to remove water and methanol. After filtering, the ether was removed at room temperature using a rotary evaporator. The residual oil was pumped down using a rotary pump for 1-2 hours, and was used as the oil in the decomposition.

Tosyl hydrazones were recrystallized from methanol (AR), one recrystallization being found sufficient, and the melting points (when solid) are recorded in the table below (Table I).

IR (Nujol mull). All tosyl hydrazones had absorptions in the following regions.

3200 - 3300 cm^{-1}	N-H
1640 - 1645 cm^{-1}	C=N
$\sim$ 1600 cm^{-1}	Aromatic
1370 - 1380 cm^{-1}	SO_2
1160 - 1170 cm^{-1}	SO_2

Table I

METHYL KETONE	TOSYL HYDRAZONE MP
Cyclopropyl	120 - 121°C
Cis-2-methyl cyclopropyl	139.3 - 140.9°C
Trans-2-methyl cyclopropyl	117.7 - 118.4°C
2,2-Dimethyl cyclopropyl	118.5 - 119.5°C
2,2-Diethyl cyclopropyl	133 - 134°C
CYCLOPROPANE CARBOXALDEHYDE	
Cis-1,2-dimethyl	
Trans-1,2-dimethyl	All oils
Cis-2-methyl-cis-3-vinyl	

DECOMPOSITION (PYROLYSIS)

Some decompositions were effected with sodium methoxide as base. Most of these have been repeated using sodium hydride (50% dispersion in mineral oil), the product ratios being unaltered by this change. The yield of hydrocarbon products is, however, substantially increased. The mineral oil does not affect the decomposition or analysis, so was not removed before use.

Diglyme was purified by heating under reflux with sodium for 1-2 hours in an atmosphere of nitrogen, and distilling from sodium under nitrogen. A substantial early fraction is rejected, since the diglyme contains benzene (u.v.).

A 100 ml 3-neck round-bottomed flask is fitted with thermometer, positioned to dip into the solution, a pressure-equalized dropping funnel with nitrogen inlet and a side-arm, initially connected to a drying-tube (silica-gel). The flask is placed in an oil-bath on a magnetic stirrer/hot-plate.

The flask is flushed with nitrogen and 3 molar equivalents of sodium hydride (sodium methoxide) are put in, and covered with diglyme, purified as above. Stirring and heating are commenced and the contents of the flask heated to 140°C, passing nitrogen all the time.

A cold-trap, containing glass wool, and previously evacuated for 1 hour on the vacuum line, is cooled in a solid CO_2/Methylated Spirits slush bath. This is connected to the side-arm of the flask, and then a solution of the tosyl hydrazone in diglyme (10-15 mls.) is dripped in from the funnel at such a rate as to maintain the temperature between 135°C and 140°C.

When all the tosyl hydrazone solution has been added, nitrogen is passed for 1 hr., maintaining the temperature between 135°C and 140°C.

The contents of the cold trap are transferred on a conventional vacuum line system fitted with Viton A diaphragm valves to a trap containing a little distilled water. The contents of this trap are allowed to come to room temperature, and the trap agitated to get the diglyme into aqueous solution. The hydrocarbon-layer lays on top. This trap is again frozen down, and allowed to warm up, and the hydrocarbons distilled into another trap, leaving behind the aqueous layer as ice.

Decomposition (Photolysis)

This was performed on pre-formed salts, made as below:

Lithium Salt

The calculated quantity of Butyl Lithium (11·85% in Petrol) was added with a syringe to a suspension of the tosyl hydrazone in dry ether. The solid was filtered, washed well with dry ether and dried under vacuum.

Sodium Salt

The calculated quantity of Sodium Hydride (50% suspension in Mineral Oil)was just covered with dry ether. A solution or suspension of the tosyl hydrazone in dry ether was added and the mixture warmed on a water bath until reaction commenced. When evolution of hydrogen had subsided the ether was boiled for a few mins., cooled, and the gelatinous solid washed well with dry ether and dried under vacuum.

Decomposition

0·5 - 1·0g. salt (Lithium,Sodium) was put in a Pyrex test tube with a ground glass joint. 10-15 mls dry diglyme were added and the tube sealed off with a tap, fitted with ground glass joints for fitting to the tube and connecting to the vacuum line. The salt passed into solution, which solution was degassed on the vacuum line, and the tube closed off under vacuum.

This solution was then irradiated for 6-7 hrs with a 125 watt medium pressure mercury lamp, the whole being cooled with water. A white solid separated to the bottom of the tube during the photolysis.

The solution was again degassed on the vacuum line, and distilled over into a trap containing a little water, until 1-2 mls diglyme had distilled, it being presumed that by this time all the reaction products would have been transferred. Work-up is then as for the pyrolysis procedure.

The hydrocarbon layer was then analysed by VPC (Columns C or D, Room temperature, N_2 10psi.). Peak integration was effected by a Ball and Disc Integrator. In one case the accuracy of this was checked by a comparison with a Kent "Chromalog" Digital Integrator, the two methods giving essentially the same analysis.

Note: The product ratio reported in Chapter 2 for the decomposition of trans-2-methyl cyclopropyl methyl ketone tosyl hydrazone differs slightly from that given in reference 33. This is due to improved analytical technique.

Identification of Cyclobutenes

1,3-Dimethyl cyclobutene:
1,4-Dimethyl cyclobutene:

These were identified by comparison with authentic samples prepared by R.F. Skinner according to reference 74.

1,3,3-Trimethyl cyclobutene:
1,4,4-Trimethyl cyclobutene:

A sample of the cyclobutene products from 2,2-dimethyl cyclopropyl methyl carbene was pyrolyzed at 220°C for 2 hrs. under vacuum, and the major diene product, 2,4-dimethyl penta-1,3-diene(produced from 1,3,3-trimethyl cyclobutene) was identified with an authentic sample prepared as below.

Mesityl oxide, on treatment with methyl magnesium bromide, afforded 2,4-dimethylpent-3-en-2-ol, which, on dehydration, gave the required diene. Confirmation of the structure of this diene is obtained by pyrolysis at 300°C, when the product is the same diene.

The reaction of isopropyl magnesium bromide and methyl vinyl ketone, with subsequent dehydration, afforded as one product 3,4-dimethylpenta-1,3-diene, which had the same elution time as the minor diene product from the pyrolysis, this diene being the anticipated result of thermal decomposition of 1,4,4-trimethyl cyclobutene.

3,3-Diethyl-1-methyl cyclobutene

This was identified by NMR (60MHz,micro-sample, external TMS) on the hydrocarbon reaction products.

4·55τ	Quartet	J = 1·5Hz	(J_{AB})	1 proton (A)
8·3τ	Quartet	J = 1·5Hz	(J_{AB}, J_{BC})	3 protons (B)
8·7τ	Quartet	J = 1·5Hz	(J_{BC})	2 protons (C)
8·86τ	Quartet	J = 6·8Hz	(J_{DE})	4 protons (D)*
9·5τ	Triplet	J 6·8Hz	(J_{DE})	6 protons (E)*

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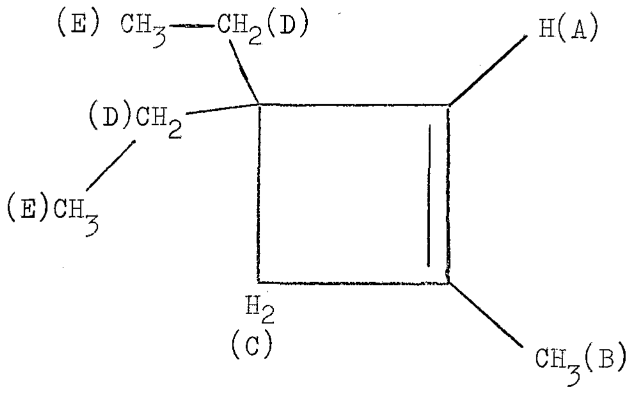
* The two ethyl groups are non-equivalent by about 1·5Hz.



Thus, the major product is 3,3-diethyl-1-methyl cyclobutene.

The minor product, 4,4-diethyl-1-methyl cyclobutene, was intuitively identified by analogy with the trimethyl cyclobutenes, on the assumption that the order of elution of the two products in each case is the same for the same VPC column.

Liquid phases for VPC columns (C,D and F)

a) bis-1,2-(2-cyanoethoxy)propane
b) bis-1,3-(2-cyanoethoxy)propane

These were prepared by the method of Bruson & Riener.[75] Acrylonitrile was condensed with propane-1,2-diol, or propane-1,3-diol, in the presence of a catalytic amount of sodium methoxide.

a) BP 150-151°C (1 mm.) (Lit. 165°C(2 mm.)[75])

IR 2960 cm^{-1}, 2260 cm^{-1}, 1120-1130 cm^{-1} (broad)

NMR (60MHz) $CDCl_3$

6·1 - 6·6 τ	Multiplet	7 protons
7·2 - 7·55 τ	Two superimposed triplets J = 6·5Hz Separation = 2Hz	4 protons
8.8 τ	Doublet J = 6·5Hz	3 protons

b) BP 150-152°C (0·4 mm.) (Lit. 165°C(1 mm.)[75])

IR 2260 cm^{-1}, 1120 cm^{-1} (broad)

NMR (60MHz) $CDCl_3$

6·2 - 6·55 τ	Multiplet		8 protons
7·25- 7·5 τ	Triplet	J = 6·5Hz	4 protons
7·95- 8·3 τ	Quintet	J = 6·0Hz	2 protons.

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