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José C. Dañino for the degree of Doctor of Philosophy

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Title: Carbene Rearrangements: Intramolecular Interaction
of a Triple Bond with a Carbene Center

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The tosylhydrazones of 2-heptanone, 4,4-dimethyl-2-heptanone, 6-heptyn-2-one and 4,4-dimethyl-6-heptyn-2-one were synthesized and decomposed under a variety of reaction conditions: dry lithium and sodium salt pyrolyses, sodium methoxide thermolyses in diglyme and photolyses of the lithium salt in tetrahydrofuran. The saturated analogues 2-heptanone tosylhydrazone and its 4,4-dimethyl isomer afforded the alkenes arising from β-hydrogen insertion. It was determined that product distribution in the dry salt pyrolyses of 2-heptanone tosylhydrazone was different for the lithium and the sodium salts. However, the product distribution of the dry sodium salt was very similar to product distribution obtained on thermolysis in diglyme with sodium methoxide. This difference was explained by a reaction of lithium bromide (present as an impurity in all the lithium salts) with the intermediate diazo compound to afford an organolithium intermediate that behaves in a somewhat different fashion than the free carbene. The unsaturated

analogues were found to produce a cyclic product in addition
to the expected acyclic alkenes arising from β-hydrogen
insertion. By comparison of the acyclic alkene distri-
bution obtained in the saturated analogues with those in the
unsaturated analogues, it was concluded that at least some
cyclization was occurring via addition of the diazo moiety
to the triple bond. It was determined that the organo-
lithium intermediate resulting from lithium bromide cat-
alyzed decomposition of the diazo compound was incapable of
cyclization. Alkene distribution upon pyrolyses of the lith-
ium salt of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone at differ-
ent temperatures provides evidence for cyclization to be occur-
ring by a carbenic pathway in competition with the diazo
pathway.

Dry salt pyrolyses of 3,5,5-trimethyl-2-cyclohexenone
tosylhydrazone showed that 1-carbena-3,5,5-trimethyl-2-
cyclohexene does not open up to the acyclic carbene 2-
carbena-4,4-dimethyl-6-hexyne.

Direct photolysis of 1-diazo-5-hexyn-2-one afforded
only the ketene arising from a Wolff rearrangement which
was allowed to react with methanol to afford methyl 5-
hexynoate before isolation. Sensitized photolysis afforded
only the product arising from hydrogen abstraction by the
triplet carbene: 5-hexyn-2-one. No cyclization products
were detected under these reaction conditions.

Carbene Rearrangements:
Intramolecular Interaction of a Triple Bond
With a Carbene Center

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Dean of Graduate School

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Typed by Carolyn Barney for _José C. Dañino_

To Dian, Ruth and Cucho
for their love and encouragement

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CARBENE REARRANGEMENTS:
INTRAMOLECULAR INTERACTION OF A TRIPLE BOND
WITH A CARBENE CENTER

CHAPTER 1. INTRODUCTION

I. General Introduction

The concept of a carbene as a reaction intermediate is
indeed an old one. There are several reports about it in
the nineteenth century literature. In 1862 the German chem-
ist Geuther[1] proposed dichlorocarbene as an intermediate in
the basic hydrolysis of chloroform. In 1897 Nef[2] proposed
the presence of divalent carbon species (carbenes) as inter-
mediates in some organic reactions. Unfortunately these
reports were largely ignored when they first appeared. It
was not until the middle of this century that the existence
of carbenes was experimentally proven and accepted by the
chemical community.

A good portion of the groundwork for carbene chemistry
was laid down by Staudinger and coworkers at the beginning
of this century. They embarked on an extensive and system-
atic study of diazo compounds and, to a smaller extent,
ketenes; both types of compounds are now known to be carbene
precursors. One of the main objectives of their research
was to generate stable diarylmethylenes (i.e., carbenes) by
loss of nitrogen from the corresponding diazo compounds.[3]
They were not able to generate any carbenes stable enough to
exist at room temperature. One of their accomplishments was
to determine the correct structure of diazo compounds.[4]

Diazo compounds[5] were thought to have the structure de-
cribed by the Curtius formula:

$$\begin{array}{c} R' \\ \diagdown \\ C \diagup \diagdown \\ R \diagup \end{array} \begin{array}{c} N \\ \| \\ N \end{array}$$

which in modern nomenclature is called a diazirine. Results
of work done by his research group[6] and by Darapsky[7] led
Staudinger to correctly conclude that the structure of diazo
compounds is the one depicted by the Angeli-Thiele formula:

$$\begin{array}{c} R' \\ \diagdown \\ C = N = N \\ \diagup \\ R \end{array}$$

Another of their accomplishments, although it was not real-
ized at the time, was the discovery of the first carbene
rearrangement[8]:

$$\phi_2 C = C = O \xrightarrow{\Delta}$$

Despite the fact that they were unable to generate any
stable carbenes from either diazo compounds or ketenes[9],
Staudinger and coworkers did not realize that they had
indeed been successful in generating carbenes but the inter-
mediates reacted further to yield stable products.

It wasn't until 1950 that Hine[10] provided the first
experimental evidence for the existence of a carbene, di-
chlorocarbene, as an intermediate in the basic hydrolysis
of chloroform. Further work by Hine and his research group,
mainly on kinetics of the basic hydrolysis of chloroform and
similar haloforms, provided additional evidence for dichlor-
ocarbene and other dihalocarbenes. Shortly thereafter,

Döering and Hoffmann[12] provided the first structural evidence for dichlorocarbene by trapping it with an olefin:

$CHCl_3$ + t-BuOK + [cyclohexene] ⟶ [bicyclic product with Cl Cl]
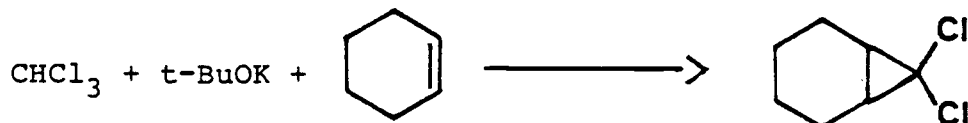
They showed that addition of dichlorocarbene and dibromocarbene to olefins is quite general and that diiodocarbene exhibits analogous behavior.

In 1951 Döering and Knox[13] introduced the term carbene in a paper presented at the National Meeting of the American Chemical Society. The term carbene was defined by the authors as an intermediate containing a carbon atom with two unshared electrons and two covalent bonds. Their report dealt with the reactions of carbethoxy carbene with saturated hydrocarbons to yield products arising from the carbene inserting into carbon-hydrogen bonds. It was noted that, unlike free radicals, the carbethoxy carbene does not exhibit a large preference for a tertiary over a secondary hydrogen. This lack of selectivity between tertiary, secondary and primary hydrogens is also observed in the reactions of methylene with saturated hydrocarbons[14] and ethers.[15]

In 1952 Bamford and Stevens[16] reported a new way of generating carbenes by decomposing tosylhydrazones of ketones and aldehydes. The tosylhydrazone was decomposed by heating in a solution of sodium in ethylene glycol.

In 1956 Skell and Garner[17] discovered that the additions

of dibromocarbene to olefins were stereospecific as shown by the following experiments:

$$\text{(alkene)} + CHBr_3 + t\text{-BuOK} \longrightarrow \text{(dibromocyclopropane)} \quad 80\%$$

$$\text{(alkene)} + CHBr_3 + t\text{BuOK} \longrightarrow \text{(dibromocyclopropane)} \quad 68\%$$
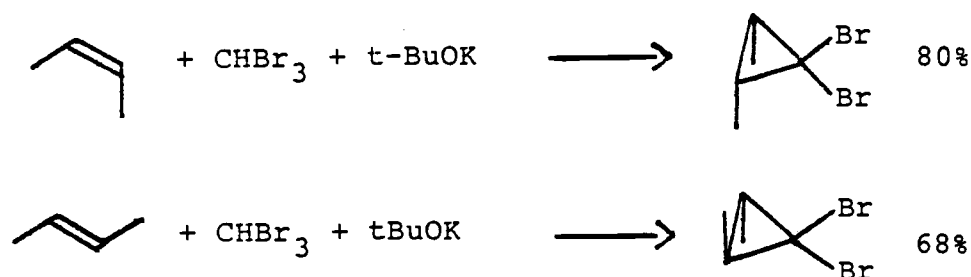
The results of stereospecific additions of dibromocarbene to olefins were confirmed by Döering and La Flamme.[18] The authors also reported the stereospecifity of methylene additions to alkenes. Basing his hypothesis on the evidence of stereospecificity of dibromocarbene additions to olefins, Skell[19] proposed that the structure of the intermediate is a planar one with the carbon exhibiting sp^2 hybridization. The carbon atom utilizes two of the sp^2 hybrid orbitals to bond to the bromine atoms and the third sp^2 orbital contains the unshared electron pair. The species contains an empty p orbital which is perpendicular to the plane of sp^2 orbitals. Thus the structure of singlet dibromocarbene can be represented by the following diagram:

$$C \begin{cases} Br \\ Br \end{cases}$$
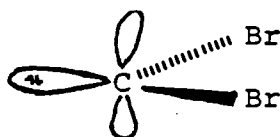
The relative reactivities and selectivities of dibromocarbene[20] and carbethoxycarbene[21] additions to olefins were measured. Similar reactivities were observed for both car-

benes but dibromocarbene has a higher degree of selectivity than carbethoxycarbene. This indicates that dibromocarbene has a larger amount of resonance stabilization than carbethoxycarbene. These results were considered to be consistent with the formulation of singlet carbenes as sp^2 hybridized species with a vacant p orbital that leads to carbonium ion activity.[21] Further results consistent with this view of the structure of carbenes were provided by Döering and Knox.[22] The authors studied the ability of methylene, carbethoxycarbene and dicarbethoxycarbene to discriminate between tertiary, secondary and primary hydrogens in the insertion reaction. The order of preference is tertiary over secondary over primary hydrogen; with dicarbethoxycarbene displaying the largest selectivity, carbethoxycarbene intermediate and methylene hardly any at all. The reactivity was found to be inversely related to selectivity, with methylene being the most reactive and dicarbethoxycarbene the least reactive. Selectivity was explained by polar structures in the transition state.

$$R_3C\!\!+ \quad \diagdown H$$
$$\underset{X}{\diagup}\overset{}{\underset{}{C}}\diagdown CO_2Et$$

x = H or CO_2Et
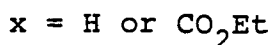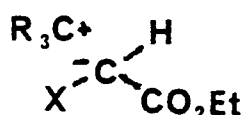
The stability of carbonium ions accounts for the order of hydrogen reactivity since tertiary hydrogen affords tertiary carbonium ion, secondary hydrogen affords secondary carbonium ion and primary hydrogen affords primary carbonium

ion. Reactivity was explained by resonance stabilization in the carbethoxy substituted carbenes which would raise the activation energy relative to methylene.

Several important contributions appeared in 1959. Döering and Prinzbach[23] demonstrated that insertion of methylene into a carbon-hydrogen bond occurs in one step, since the following experiment:

$$Me_2 \; C = \overset{*}{C}H_2 + CH_2N_2 \longrightarrow Et{-}\underset{Me}{\overset{|}{C}} = \overset{*}{C}H_2$$

$$C* = {}^{14}C$$
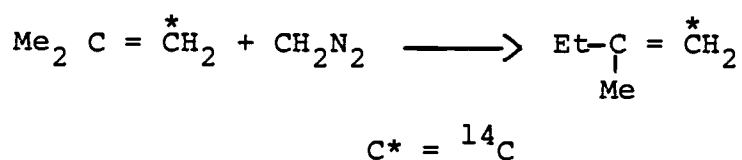
shows very little scrambling of the labelled carbon. Simmons and Smith[24] discovered in that same year the reaction that bears their name and which is a very important synthetic tool in the preparation of cyclopropanes. The reaction involves the stereospecific conversion of an olefin to a cyclopropane with diiodomethane and a zinc-copper couple. It was also found[25] that the methylene transfer reaction has electronic requirements similar to those of other carbenes; however, unlike other carbenes, the reaction exhibited a large steric effect. This result and results from other studies[26] led the authors to conclude that the intermediates generated from diazomethane and in the Simmons-Smith reaction, although similar, are not identical.

Also in 1959 Skell and Woodworth[27] reported a chemical test to determine the spin state of methylene. It was found that methylene added stereospecifically to cis and trans-2-

butene in the gas and liquid phase to yield the correspond-
ing cyclopropanes plus small amounts of carbon-hydrogen
insertion products. The authors argued that stereospecific
addition of methylene to an alkene indicates that the car-
bene is in the singlet state. Non-stereospecific addition
indicates that the carbene is in the triplet state. The
basis for their argument was that singlet methylene can
insert stereospecifically into the alkene since the elec-
trons are all paired. The addition of triplet methylene to
the olefin cannot happen in one step because the electrons
of methylene are unpaired. Triplet methylene adds to an
olefin to form a diradical which undergoes intersystem
crossing and then closes to the cyclopropane. However,
before undergoing intersystem crossing, the diradical may
undergo carbon to carbon bond rotations in such a way that
the addition is not stereospecific. This can be represented
schematically by considering the addition of methylene to
cis-2-butene:

Stereospecific addition (singlet carbene):

$$CH_2\uparrow\downarrow \; + \quad \text{(cis-2-butene)} \quad \longrightarrow \quad \text{(cyclopropane)}$$
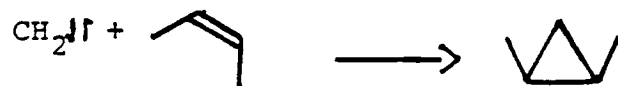
Non-stereospecific addition (triplet carbene):

CH₂⁝⁝ +
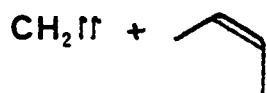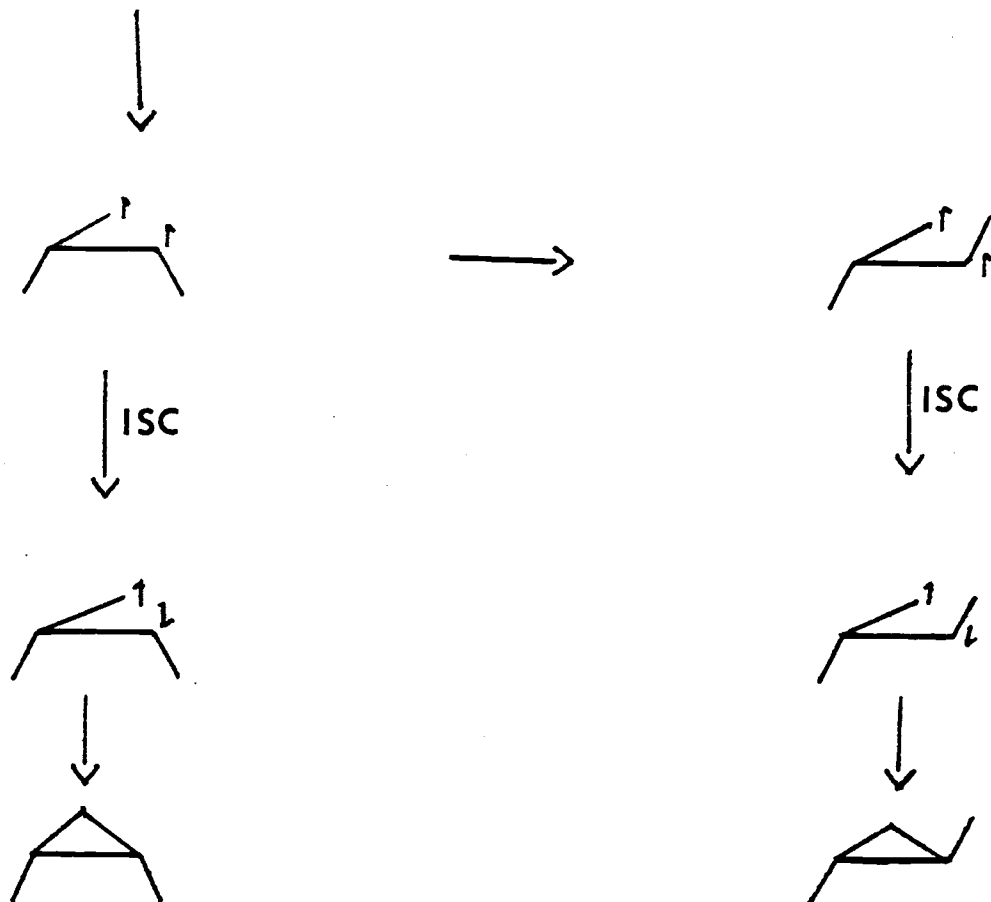
In 1961 Herzberg[28] provided the first physical evidence for the existence of singlet and triplet carbenes by observing the electronic spectra of the two states of methylene.

The above reports are the most salient ones of the early work on carbene chemistry. Since the concept of the carbene as a reactive intermediate was firmly established and accepted by the chemical community, research in this area has been quite extensive during the last 20 years. Although the systematic study of carbenes is not very old,

a considerable amount of information is available. The remainder of this discussion will be devoted to summarizing those aspects of carbene chemistry that are pertinent to this study.

There are two categories of carbenes: carbenoids and free carbenes. Carbenoids[29] are intermediates that qualitatively resemble carbenes in their reactions and are considered to be complexed to a metal. An example of a carbenoid is the intermediate generated in the Simmons-Smith reaction. Carbenoids will not be included in this discussion. Free carbenes are described by Döering and Knox's definition[13] as intermediates that have two covalent bonds and two unshared electrons.

As has been mentioned before, there are two states in which a carbene can exist: the triplet and the singlet. In the singlet carbene both electrons are paired and in the triplet they are unpaired. Because of this difference in electron arrangements, the structures[30] of the two carbene states are different and can be generalized by the following two models. Singlet carbene has an approximately sp^2 hybridization; two of the hybrid orbitals are used for bonding and the third one contains the unshared electron pair leaving an empty p orbital. The angle is thus close to the sp^2 angle of 120°. The triplet carbene approximates sp hybridization and uses the orbitals for bonding, and each unshared electron occupies an unhybridized p orbital. The angle

approximates the sp angle of 180°, although there are some

exceptions. The angle of the singlet is always smaller than

the angle of the triplet. The exact structure of any given

carbene depends on the nature of the substituents directly

attached to the carbene carbon and on the stereochemical and

electronic constraints that their substituents impose on

the intermediate (for example, ring size and resonance

effects). From the absorption spectra, Herzberg and Johns[28]

determined that singlet methylene has a bond angle of 102°

and a carbon-hydrogen bond length of 1.12 Å while triplet

methylene was determined to be a linear or almost linear

species with a carbon-hydrogen bond length of 1.07 Å.

Skell and coworkers[31] confirmed the linear or almost linear

structure of triplet methylene by measuring its absorption

spectrum at 4°K. But a different conclusion was arrived at

by Wasserman and coworkers[32] when they studied the ESR

spectra of triplet methylene, deuteriomethylene and dideu-

teriomethylene at 4.2°K. An angle of 136° was assigned to

triplet methylene. An experiment[33] in which the hyperfine

interaction of ^{13}C was measured in $^{13}CD_2$ yielded an angle

of 137° for the triplet species. Furthermore, in a later

report, Herzberg and Johns[34] retracted their original

assignment of a linear structure for triplet methylene. It

was explained that due to some erroneous assumptions in the

original work, the data from the absorption spectra did not

allow a distinction to be made between a bent or a linear

structure. The corrected calculation yielded an angle of 136°. Thus the generally accepted geometry for triplet methylene is a bent structure with an angle of 136-7°. From the ESR spectra[35] the geometry of triplet diphenylcarbene was determined to be approximately 150° and that of triplet phenylcarbene about 155°. Also from ESR spectra, the angle has been determined as 180° for the following triplet carbenes: cyanocarbene,[36] dicyanocarbene,[37] ethynylcarbene[36] and propynylcarbene.[36] From the ultraviolet spectra,[38] singlet difluorocarbene was determined to have a fluorine-carbon-fluorine angle of 104.9° and a carbon-fluorine bond length of 1.30 Å. Analysis of the infrared spectra of singlet dichlorocarbene[39] recorded at 15°K yielded chlorine-carbon-chlorine angle of 100 ±9°. The ultraviolet spectra of singlet chlorocarbene[40] provided a chlorine-carbon-hydrogen bond angle of about 103°, a carbon-hydrogen bond length of 1.12 Å and a carbon-chlorine bond length of 1.69 Å. The ground state for a variety of carbenes has been determined from spectroscopic and other data. In general, if carbon or hydrogen are attached to the carbene carbon, the ground state is a triplet.[41] If a halogen atom is directly attached to the carbene carbon, then the ground state is the singlet.[41]

The spectroscopic evidence discussed above shows unequivocally that there are two distinct carbene states: singlet and triplet. The two states differ not only in

their hybridization, geometry and spins of the unshared electrons but in their chemistry as well. Less than 20 years ago there was some debate about this last point, but the evidence has proved that singlet and triplet carbenes do have an intrinsic difference in chemical reactivity. One example already discussed, the Skell rule, is stereo-specific addition to olefins of singlet carbene whereas the triplet addition is non-stereospecific. Other examples will be discussed later on. In general, the chemistry of singlet carbenes, due to the empty p orbital, resembles the chemistry of carbonium ions while triplet carbene chemistry resembles free radical chemistry.

Carbenes are short-lived intermediates that have to be generated from a suitable precursor and then react further to yield stable products. To understand carbene chemistry, it is important to provide a background discussion on generation and reactions of carbenes emphasizing those aspects pertinent to this study. Furthermore, α-ketocarbenes will be discussed in a separate section because of their somewhat different chemistry.

II. Formation of Carbenes

There are quite a few methods for the generation of carbenes, although some of them are not very general. The following methods are the most commonly employed.

A. Decomposition of diazo compounds

This is probably the oldest method of generating

carbenes. It was used quite extensively by Staudinger and coworkers. There are two general methods of preparing the diazo compounds:

a) Basic decomposition of compounds of the type

$$RR'CHN \overset{NO}{\diagdown}-X \longrightarrow RR'C = N_2$$

where X = $CONH_2$, CO_2Et, COMe, $CO\phi$, $\underset{\underset{NH}{||}}{C}NHNO_2$, Ts.

All of the above compounds[42] have been used in the preparation of the synthetically important reagent diazomethane. The newer reagents (N-methyl-N-nitroso-N'-nitroguanidine and N-methyl-N-nitroso-p-toluenesulfonamide) have the advantage of providing a higher yield of diazomethane and having a lower toxicity. But for higher homologues, the yields of diazo compound fall off, and in these cases the N-alkyl-N-nitrosourethane method is preferred.

b) Oxidation of hydrazones.

This method is quite convenient since the hydrazones are readily available by reaction of hydrazine with the corresponding carbonyl compound. The method has been used very successfully with the hydrazones of aromatic carbonyl compounds and aliphatic ketones. The oxidation is usually carried out with yellow mercury (II) oxide although there are some reports that silver (I) oxide has been utilized.[43] However, in the synthesis of 2-diazopropane it has been reported that silver (I) oxide[44] affords a lower yield than

mercury (II) oxide.[45]

The corresponding carbenes are obtained from the diazo compounds by thermolysis[46] or photolysis[47] either neat or in solution. The carbenes generated by photolysis have been found to be less selective in their reactions than the same carbene generated thermally.

It is well known that diazomethane is not only explosive but also highly toxic. Other diazo compounds are also toxic and most of them are unstable and can be handled only in dilute solutions. Furthermore, almost all of the precursors to diazo compounds through method A are also toxic. Because of this and also due to the fact that the Bamford-Stevens reaction generally furnishes the same carbene by a safer and more convenient experimental procedure, this method has been rarely used in the last decade.

B. Decomposition of tosylhydrazones

This method of producing carbenes was discovered by Bamford and Stevens[16] in 1952. At present it is the most common method of generating alkyl and aryl carbenes. This method is very convenient since the tosylhydrazones (p-toluenesulfonylhydrazones) are readily available by reaction of the appropriate aldehyde or ketone with tosylhydrazine in refluxing ethanol. The product is usually a stable solid that crystallizes out of solution. Furthermore, generation of the carbene from the tosylhydrazone is experimentally straightforward. The original procedure consisted of heating the tosylhydrazone in a solution of sodium in 1,2-

ethanediol. It was subsequently discovered that in the
presence of protic species a cationic pathway competed with
the carbenic pathway. Powell and Whiting[48] studied the
kinetics of decomposition of the tosyl and mesylhydrazones
of camphor and cyclohexanone. It was known that diazo com-
pounds were intermediates in the decomposition of at least
some tosylhydrazones. The kinetic data showed that the
mesyl and tosylhydrazones decomposed to the diazo compound
by loss of the sulfinate anion in the rate determining step.
The decomposition of camphor tosylhydrazone was shown to
yield not only camphene (C) as believed by Bamford and
Stevens[16] but also tricyclene (B).

A   B   C
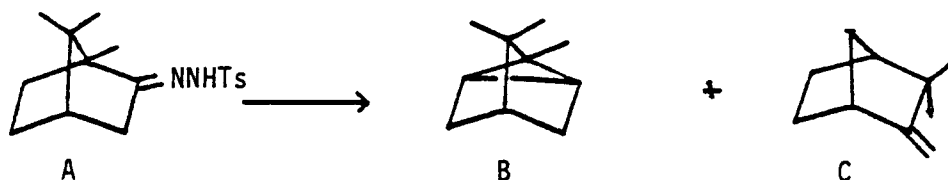
Furthermore it was discovered that the ratio of B:C varied
with the solvent used. With hydroxylic solvents, tricyclene
was the minor product (12-46%). In acetamide tricyclene was
the major product (99%). These results were explained by a
competition between a carbenic and a cationic pathway. In
hydroxylic solvents the diazocamphor can decompose to the
diazonium ion which will rearrange, either directly or via
the carbonium ion, to camphene. In acetamide the diazo com-
pound decomposes almost exclusively to carbene which then
yields tricyclene. Experimental evidence was presented to
support their hypothesis. Diazocamphane affords B and C

when heated in a solution of sodium in ethoxyethanol and
decomposes spontaneously to C in ether solution. In a later
report it was shown that diazocamphane yielded mostly cam-
phene in the polar protic solvents 1,1,1-trifluoroethanol.[49]

The mechanism proposed by Powell and Whiting for the
decomposition of camphor tosylhydrazone was confirmed and
expanded by Shapiro, Duncan and Clopton.[50] Camphor tosyl-
hydrazone was decomposed in dimethylformamide, diglyme and
decalin with either sodium hydride or sodium methoxide. It
was found that the ratio of B/C depended not only on the
solvent used but on the amount of base utilized. Larger
amounts of tricyclene (B) are favored by using the least
polar solvent and an excess of base. More important, it was
found that when camphor tosylhydrazone was decomposed with
sodium methoxide in diglyme containing deuterium oxide, the
tricyclene produced incorporated deuterium. The amount of
deuterium incorporated by tricyclene was dependent on the
number of equivalents of sodium methoxide per equivalent of
tosylhydrazone:

Equivalents of NaoMe	$B-d_1$	B/C
0.75	64%	35/65
2.00	25%	57/43
4.00	8%	92/8
10.00	6%	99.7/0.3

The data indicate that tricyclene is formed by both the
carbenic and ionic pathways and the proportion depends upon
the number of equivalents of base present. The results can

be summarized by the following scheme:
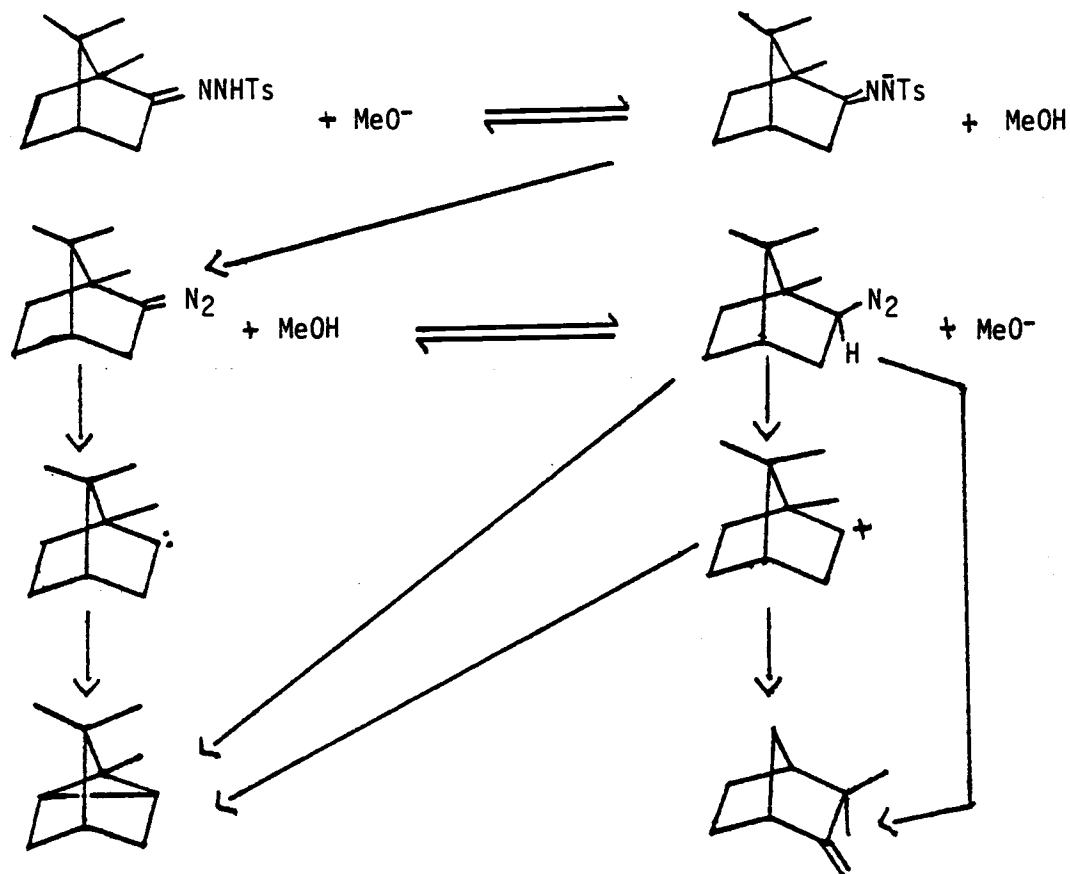
The above results indicate that to ensure a carbenic pathway the reaction should be carried out in an aprotic solvent with an excess of base. The Bamford-Stevens reaction is usually carried out by refluxing the tosylhydrazone dissolved in diglyme with 2-5 equivalents of sodium methoxide. There are two variations that have developed of the Bamford-Stevens reaction. The first one consists of isolating the dry sodium or lithium salt of the tosylhydrazone and heating it under a vacuum.[51] The second variation consists of forming the lithium or sodium salt of the

tosylhydrazone in a suitable solvent and then photolyzing it.[52]

C. <u>Decomposition of diazirines</u>

It was previously mentioned that until the beginning of this century it was thought that diazo compounds had a cyclic structure as postulated by Curtius. Staudinger[5, 6] and Darapsky[7] were the first ones that provided chemical evidence for the correct structure of diazo compounds. The controversy continued until in 1935 Boersch[53] provided electron diffraction data that proved conclusively that diazomethane had a linear and not a cyclic structure. However, it was only in 1960 that the first successful attempts at synthesizing a diazirine were reported independently by Paulsen[54] and Schmitz and Ohme.[55] There are three general methods for the synthesis of diazirines. The first two methods yield a diaziridine which is then oxidized to the corresponding diazirine with either mercury (II) oxide,[54] alkaline permanganate solution[54] or silver (I) oxide.[55] The method employed for the synthesis of a given diazirine depends on the substituents R and R' of the diazirine:

$$\begin{array}{c} R \diagdown \\ \diagdown C \diagup^{\displaystyle N}_{\displaystyle \diagdown N} \| \\ R' \diagup \end{array}$$
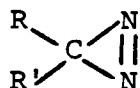
a) R and R' are aryl or alkyl groups. The method of Schmitz[55] is employed where chloramine is allowed to react with the ketone to afford the diaziridine. Alternatively, the method of Paulsen and Huck[56] may be employed.

Ammonia is chlorinated in the gas phase, diluted with nitrogen and the mixture is passed through the ketone to yield the desired diaziridine.

b) R is an aryl or alkyl group, R' is H. The method of Schmitz[55] is used as described above except that an excess of aldehyde is employed followed by aqueous work-up. If an alkaline permanganate workup is substituted for the aqueous one, the diazirine may be obtained directly in yields of 70-90%.[57]

c) R is alkyl or aryl, R' is Br or Cl. The method of Graham[58] is employed. The corresponding nitrile is first converted to an amidine and then allowed to react with either sodium hypochlorite or sodium hypobromite in dimethyl sulfoxide to yield the diazirine.

The carbene can be obtained by either photolysis[59] or thermolysis[60] of the diazirene. There is experimental evidence that photolysis of diazirene produces diazomethane.[61]

In contrast to diazo compounds, diazirenes are quite stable compounds at room temperature and remarkably stable to acids and bases. Diazirenes offer a safer and more convenient alternative to diazo compounds as carbene precursors.

D. Decompositions of organomercury compounds

In 1962, Seyferth and coworkers[62] reported the formation of dibromocarbene and dichlorocarbene by decomposition of phenyltribromomethyl mercury and phenyltrichloromethyl mercury in refluxing benzene. The carbenes add to

cyclohexene to yield the corresponding cyclopropane deriv-
atives in high yield.

The phenyltrihalomethyl mercury compounds decompose in
a concerted step to phenylhalomercury and dihalocarbene.
The alternative mechanism would involve the prior formation
of trihalomethyl anion which would decompose in a second
step to dihalocarbene and halide anion. This mechanism was
disproved when it was shown that dichlorocarbene generated
from organomercury compounds[63] afforded different products
than the same carbene generated from sodium trichloroacetate
and bromodichloromethane (both of these compounds are known
to afford the carbene via the trihalomethyl anion[64]) in
reactions with cyclohexene and vinyl acetate. Dihalocarbenes
generated from organomercury compounds are free carbenes.
This conclusion is based on the selectivity of olefin addi-
tion displayed by dichlorocarbene generated from different
precursors and from the absence of a steric effect to
addition.[63]

The temperature of decomposition of the phenyltrihalo-
methyl mercury compounds can be lowered by the addition of
sodium iodide.[65] In this case the mechanism is changed.
Iodide performs a nucleophilic attack on mercury to displace
the trihalomethyl anion which decomposes further to the
halide ion plus dihalocarbene. This mechanism was experi-
mentally confirmed in the case of phenyltrichloromethyl
mercury[67] by the isolation of chloroform in the presence of

hydrogen donors and by affording the same product distri-
bution as sodium trichloroacetate when reacted with vinyl
acetate.

Halocarbenes generated from organomercury compounds
are very useful for synthetic and mechanistic purposes.
Cyclopropane derivatives are formed in high yield even with
base sensitive olefins and electron deficient olefins which
do not react with other halocarbene precursors. Organo-
mercury compounds provide the best method to study halo-
carbenes since they are formed under mild conditions and the
byproducts of the precursor do not lead to side reactions.
The obvious limitation of this method is that the carbene
generated contains at least one halogen atom.

E. Decomposition of haloforms

As previously mentioned, the first chemical evi-
dence for the existence of carbenes was provided by Hine and
coworkers[10] in a study of the base catalyzed hydrolysis of
chloroform. The following mechanism was proposed:

$$CHCl_3 + OH^- \rightleftharpoons CCl_3^- + H_2O \quad \text{fast}$$

$$CCl_3^- \rightleftharpoons :CCl_2 + Cl^- \quad \text{slow}$$

$$:CCl_2 + H_2O \xrightarrow{OH^-} CO + HCO_2^- \quad \text{fast}$$
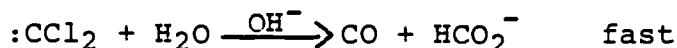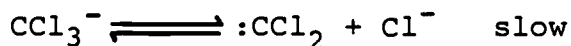
The experimental evidence provided in support of their
mechanism was based on kinetic data. Employing deuterio-
chloroform it was demonstrated that the first step was rapid
and reversible. Addition of sodium fluoride, perchlorate or
nitrite in concentrations of up to 0.16N increases the rate

of hydrolysis, the increase in rate being dependent solely
on the concentration of the added salt and not upon the
identity of the anion. The effect on the rate of hydrolysis
by this group of salts was attributed to an increase in
ionic strength of the medium. In contrast, addition of
sodium chloride, bromide or iodide decreases the initial
rate of reaction. Furthermore, in the case of bromide or
iodide addition the rate of reaction increases with time
whereas in the case of chloride the rate of hydrolysis
remains the same until the reaction goes to completion. The
retarding effect on the rate of reaction by the second group
of salts was attributed to a shift to the left in the rate
determining step (the second step). Reversal of the second
step by added bromide or iodide produces bromodichloromethyl
and iododichloromethyl anion respectively.

$$Br^- + :\ddot{C}Cl_2 \longrightarrow Br\ddot{C}Cl_2^-$$
$$I^- + :\ddot{C}Cl_2 \longrightarrow I\ddot{C}l_2^-$$
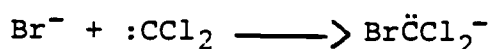
Both of these anions decompose to dichlorocarbene much faster
than trichloromethyl anion. At the beginning of the reaction
the only species affording dichlorocarbene is the trichloro-
methyl anion, but as the reaction proceeds the concentration
of bromodichloromethyl or iododichloromethyl increases. Since
these species are more reactive than trichloromethyl anion,
the rate increases as the reaction proceeds. Reversal of
the second step by added chloride does not change the iden-
tity of the trihalomethyl anion and the rate of hydrolysis

remains constant throughout the reaction. A linear relation-
ship between the decrease in rate caused by the addition of
sodium chloride, bromide or iodide and the Swain-Scott nucleo-
philic constant of the halide ion provides further support
for the proposed mechanism. Additional evidence was provided
by Döering and Hoffman[12] who were able to trap dichloro and
dibromocarbene by allowing them to react with cyclohexene and
isolating the corresponding 7,7-dihalonorcarane.

The conditions for generating halocarbenes in aprotic
solvents require a strong base (e.g. potassium t-butoxide,
sodium methoxide, potassium isopropoxide) which precludes the
presence of base sensitive compounds. Two methods have been
devised to circumvent this problem. The first one[68] involves
utilizing ethylene oxide and catalytic amounts of tetra-
ethylammonium bromide. This method operates according to the
following scheme:

$$Et_4N^+Br^- + \triangle O \longrightarrow Br \diagdown O^-$$

$$Br \diagdown O^- + HCX_3 \longrightarrow Br \diagdown OH + CX_3^-$$

$$CX_3^- \longrightarrow :CX_2 + X^-$$

$$X + \triangle O \longrightarrow X \diagdown O^-$$
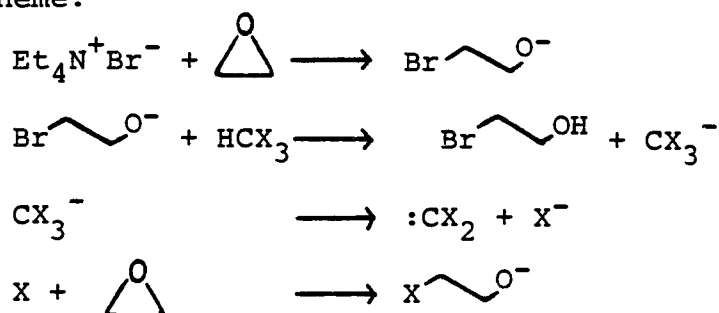
The main drawback of this method is that it requires high
temperatures. The second method[69] involves the usage of
phase transfer catalysts. It has been used quite extensively
in the synthesis of cyclopropane derivatives due to the
simplicity of the experimental procedure and the high yields

of product obtained. Since the trihalomethyl anion is still
the immediate precursor of the carbene, Michael addition to
activated olefins will compete with cyclopropanation. The
only way to avoid this problem is by generating the carbene
from the corresponding organomercury compound.

Almost all of the possible combinations of dihalocar-
benes have been generated by the haloform method.[10, 11]
The limitation of this method is that the carbene generated
has to contain two halogen atoms attached to the carbene
carbon. This method fails in generating monohalocarbenes.

III. Reactions of Carbenes

After a carbene has been formed it will very rapidly
react in such a way as to satisfy the tetravalency of carbon.
The two most common ways of doing this are to insert into a
carbon-hydrogen bond or to add to a carbon-carbon double or
triple bond. Insertions into the bonds of hydrogen to other
elements and carbene reactions with heteroatoms are known
but will not be discussed.

A. Insertion into carbon hydrogen bonds

The methylene insertion reaction was discovered by
Meerwein and coworkers.[70] Diazomethane was photolitically
decomposed in ethyl ether. Propyl ethyl ether and iso-propyl
ethyl ether were obtained as products in a ratio of 1.37:1.00.
The authors did not realize that it was a carbene reaction.
Döering and coworkers[14] found that methylene inserts into
the carbon-hydrogen bonds of the hydrocarbons pentane, 2,3-

dimethylbutane and cyclohexane. The products obtained corresponded to insertion into every possible carbon-hydrogen bond and the product distribution was very nearly a statistical one. Meerwein's original experiments with diazomethane in ethyl ether were reinvestigated by Döering and coworkers[15] utilizing vpc to increase the accuracy of the results. It was found that methylene inserted into the carbon-hydrogen bonds of ethyl ether and also tetra-hydrofuran to yield a ratio of products very close to the statistical ratio. In general, singlet carbenes are more reactive than triplet ones and also less selective.

There has been some controversy in the past with regards to the mechanism of the insertion reaction. The experimental evidence points to a one-step insertion in the case of singlet carbenes and a two-step abstraction-recombination for triplet carbenes. Döering and Prinzbach[23] studied the insertion of methylene into the allylic hydrogen of 1-^{14}C-2- methylpropene. In the liquid phase, less than 1% scrambling of the label was observed whereas in the vapor phase 8% scrambling was detected. Further evidence for the direct insertion mechanism of singlet carbenes is the retention of configuration in the reactions of methylene, carbomethoxycarbene and dichlorocarbene. Methylene inserts with retention of configuration into the axial hydrogen of paraldehyde[71] (all methyl groups in the equatorial position). Carbomethoxycarbene[72] has been shown to insert into the

asymetric carbon-hydrogen bond of (-)methyl 2-methoxypro-
pionate with complete retention of configuration. Likewise,
dichlorocarbene[73] insertion into the benzylic hydrogen of
(+)-2-phenylbutane was shown to occur with retention of
configuration. There is one report in the literature that
describes a methylene insertion with inversion of config-
uration. The decomposition of diazomethane in the presence
of E-1,2-diacetoxycyclopentane[74] was reported to yield
Z-1,2-diacetoxy-1-methylcyclopentane, although in the initial
report[75] the reaction was described to proceed with retention
of configuration. The abstraction-recombination mechanism
for triplet carbenes was invoked to explain the products in
the reaction of methylene with propane.[76] Triplet methylene
abstracts a hydrogen atom from propane to yield methyl,
propyl and isopropyl radicals. The radicals then combine
with each other to form the observed products: ethane,
2-methylpropane, butane, 2,3-dimethylbutane, 2-methylpentane
and hexane. It has been shown recently through ^{19}F CIDNP
studies that triplet diphenylmethylene inserts into the
benzylic hydrogen of 1-methylhexyl 1-fluoro-1-phenylacetate
with complete loss of stereochemistry.[77] Fairly recently
some additional evidence was presented to support the single
step reaction of singlet carbene and the radical abstraction-
recombination of triplet carbene.[78] CIDNP experiments of
methylene insertion into the benzylic hydrogens of toluene
were performed. A CIDNP signal was observed when triplet

methylene reacted with toluene but no signal was observed in the case of singlet methylene.

In carbenes that have β or γ hydrogens, the carbon-hydrogen bond insertion that predominates is an intramolecular one that yields alkenes and cyclopropenes respectively. In general, the β hydrogen shift occurs faster than γ insertion. In the case of isopropyl carbene the β shift is 12 times faster than γ insertion and about 13 times in the case of ethyl carbene.[79] The relative yields of cyclopropane compared to alkene increases with branching at the β-carbon. β-Alkoxy substituents diminish the relative yield of cyclopropane. The following examples illustrate these points:[79,80]
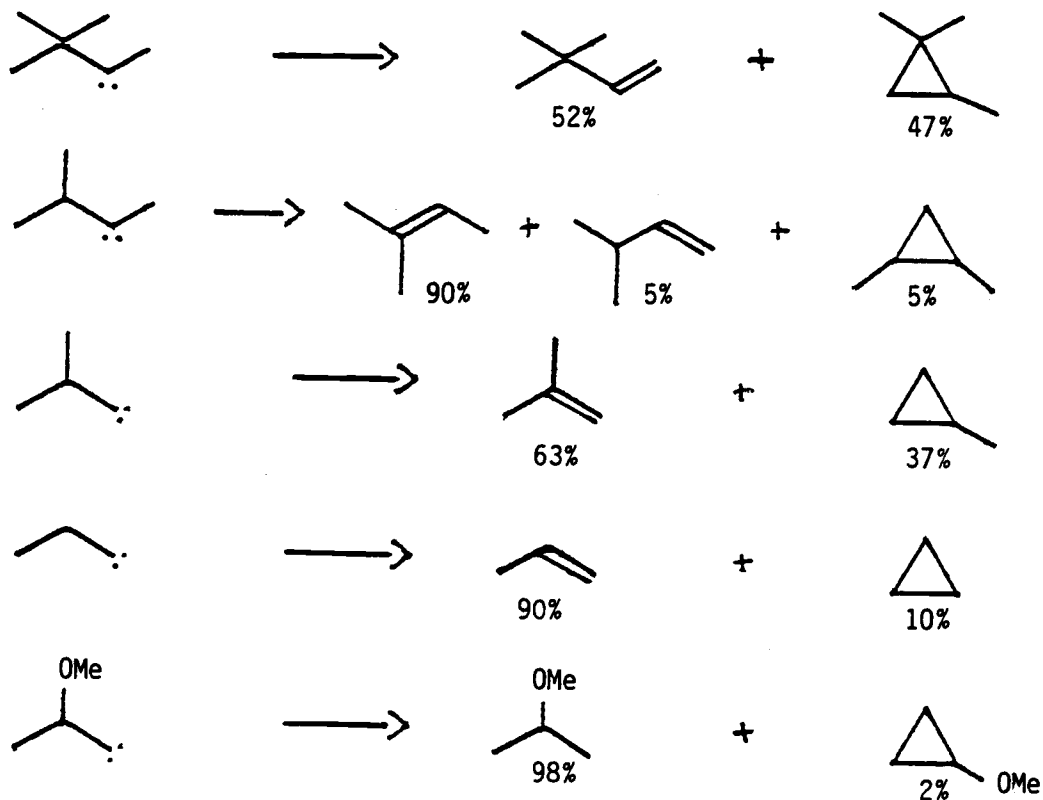
It has been determined by Kirmse[81] that in the formation
of cyclopropanes there is a small preference for secondary
over tertiary hydrogen insertion and for trans over cis
cyclopropane. These preferences are not constant and are
hard to interpret because steric effects play an important
role in insertions. The effects of γ substituents on cyclo-
propane formation have been determined by studying the
following reaction:[82]

x = φ-, CH$_3$-, CH$_2$ = CH-, CH$_3$O-, Me$_2$N-, Cl-
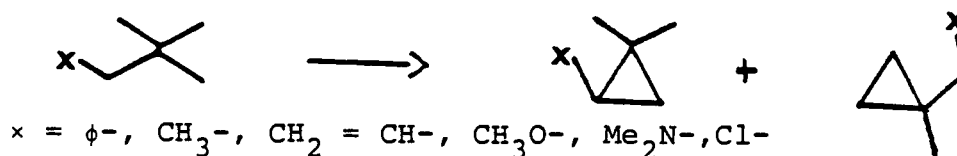
All the above substituents make the insertion reaction
harder. The data has been interpreted as indicative of the
importance of the inductive effect of × in the γ insertion
reaction while the resonance effects are negligible.

In contrast to the γ insertion, the β insertion into
tertiary hydrogen is greatly favored over insertion into
primary hydrogen and insertion into secondary hydrogen is
also favored over insertion into primary hydrogen. Further-
more, in cases where it is possible, the trans isomer is
preferred over the cis isomer. This is illustrated by the
following examples:

a   5%   28%   67%

b ⟶ 45% + 16.8% + 78.8%

a ⟶ 5.1% 89.7%
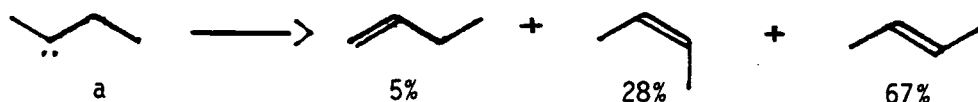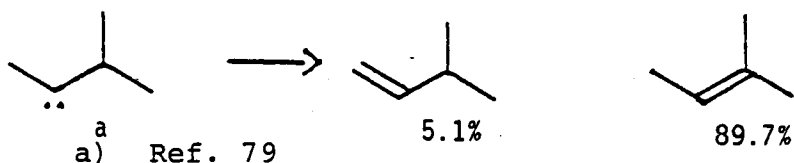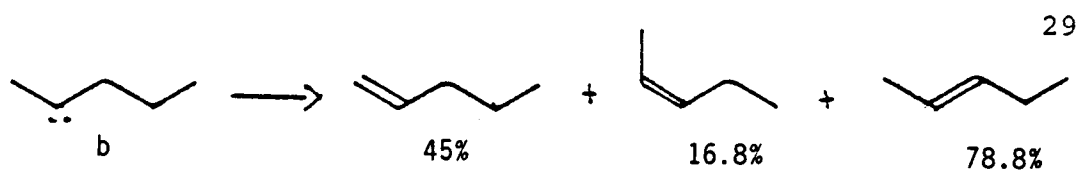
a) Ref. 79

b) Ref. 83

The introduction of the substituents methoxy and hydroxy shifts the selectivity of the β insertion towards the carbon bearing the substituent. Also in the cases of methoxy and carbethoxy, the cis isomer predominates over the trans.

MeO a ⟶ OMe 61% + MeO 23% + MeO 5% + MeO 11%

OH ⟶ [OH] ⟶ H O

EtO$_2$C CO$_2$Et ⟶ EtO$_2$C CO$_2$Et 3% + EtO$_2$C 97% CO$_2$Et
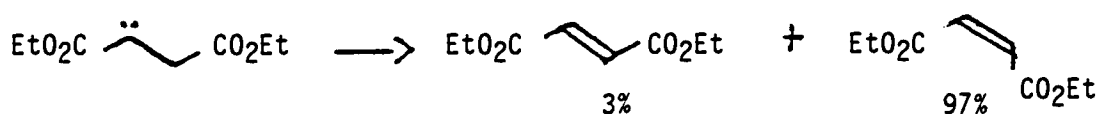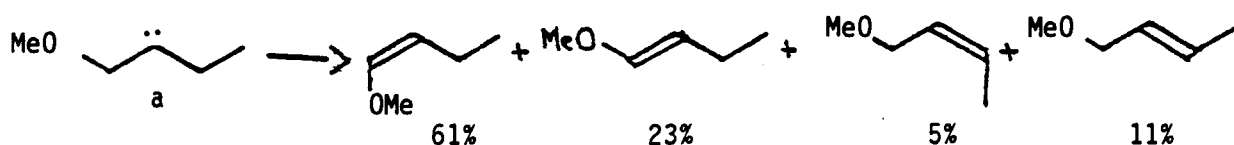
a) Ref. 84

b) Ref. 85

c) Ref. 83

The experimental evidence, although not very substantial, seems to indicate that insertion occurs only in the singlet

carbene and not in the triplet state. In a study of the decomposition 2-phenyldiazoethane in the presence of 2-butene, it was found[86] that the cyclopropane product was formed in a stereospecific fashion. Styrene was also formed by a hydride migration mechanism. Since only singlet carbene was detected, the authors indicated that a hydride migration occurs in the singlet carbene. In another report,[87] the photochemical decomposition of 1-phenyldiazoethane afforded as the only products styrene and acetophenone. When the reaction was photosensitized with benzophenone, the amount of styrene decreased while the amount of acetophenone increased. In the presence of cis-2-butene the following was observed:

% Products
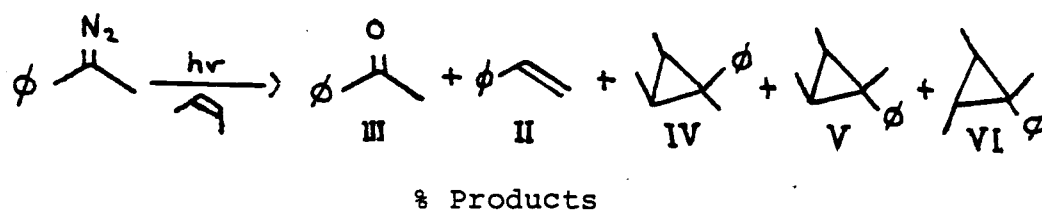
$[\phi_2C=O]$	II	III	IV+V+VI	VI/IV+V
0	6.0	2.3	6.9	4/96
0.36	3.7	20.2	7.1	8/92
1.33	1.7	45.9	6.0	15/85

The direct photolysis yields styrene, acetophenone and cyclopropanes. The cyclopropanes are generated in an almost stereospecific manner. When the reaction is photosensitized two effects become evident. The first one is that cyclopropane formation loses stereospecificity and the second one

is that styrene formation is reduced while acetophenone
formation is increased. All of this evidence supports the
contention that hydrogen migration occurs only in the singlet
carbene.

The photochemical decomposition of methyl diazopro-
pionate in isobutylene also provides evidence for the inter-
mediacy of singlet carbenes in the β insertion.[88] The direct
decomposition afforded the β insertion product methyl acrylate
in 14% whereas the cyclopropane was obtained in only 4%.
Sensitization of the reaction with benzophenone yielded only
3% of methyl acrylate and 72% of the cyclopropane.

    B.   <u>Additions to carbon-carbon double and triple</u>

        <u>bonds</u>

The addition of carbenes to unsaturated linkages was
discovered by Döering and Hoffman.[12] Dibromocarbene and
dichlorocarbene were generated in the presence of olefins
and the corresponding cyclopropanes were obtained. It was
recognized very early by Skell and Woodworth[19] that carbene
additions to appropiate olefins could be used as a tool to
determine the multiplicity (singlet or triplet) of the
carbene. The Skell rule states that if addition to the
alkene (2-butene and 4-methyl-2-pentene have been used exten-
sively) is stereospecific, the carbene is in a singlet state.
If the opposite is observed, that is that addition is non-
stereospecific, then the carbene is in the triplet state.
In the past there has been some opposition to the use of

Skell's rule. One of the problems is that completely non-stereospecific additions (that is equal ratios of cis:trans cyclopropenes from either the cis or the trans olefin) of triplet carbenes are the exception rather than the rule.[89] There have been reports by Hoffman[90] and Dewar[91] that show the rule has a theoretical foundation. Despite the opposition, the usage of the rule has been quite successful in practice and has provided some insights into the chemistry of carbenes.[92]

Another aspect of carbene additions to double bonds, namely their selectivity between different olefins, has also yielded information about carbenes. Early work indicated that dibromocarbene and dichlorocarbene were electrophilic since their olefin-discriminating abilities were similar to those of the electrophilic reagents bromine and peracetic acid.[20] The earlier work has been corroborated by quantitative studies. Dichlorocarbene[93] added to substituted styrenes with a ρ value of -0.619 and correlated with σ^+. The same carbene[94] adds to substituted α-methyl styrenes with a ρ value of -0.378 and correlation with σ^+. Cycloheptatrienylidene[95] and 2,3-diphenyl-2-cyclopropen-1-ylidene[96] behave as nucleophilic species since they only add to electron-poor alkenes. The nucleophilicity of cycloheptatrienylidene was measured by means of a Hammett study.[97] The carbene added to substituted styrenes with a ρ value of +1.05 and a correlation with σ. This was the first example of a carbene

exhibiting a positive ρ value. Recently some evidence has
been provided that implicates the allene 1,2,4,6-cyclohepta-
tetraene in reactions thought to proceed only through cyclo-
heptatrienylidene. This will be discussed further in the
section dealing with carbene to carbene rearrangements.

Intramolecular additions to double bonds have not been
observed very often because β and γ insertions occur much
faster unless the double bond is held in close proximity to
the carbene center. If the double bond is close to the
carbene center due to its position in the chain or to the
geometric structure of the molecule, internal cycloaddition
is observed. Some examples are the following:
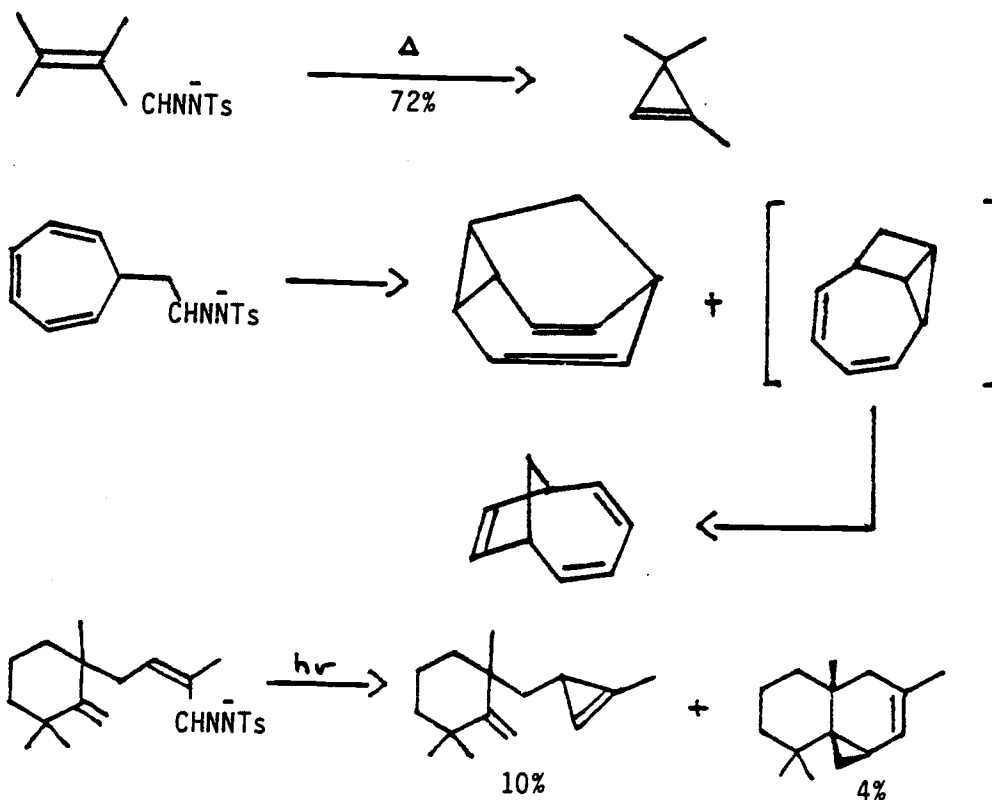
Kirmse[46b] has studied a variety of carbenes where the intramolecular addition to a double bond would yield a cyclopropane ring fused to four, five and six membered rings. The yield of products resulting from intramolecular cycloaddition was very poor in all cases under a variety of conditions. Some examples are the following:
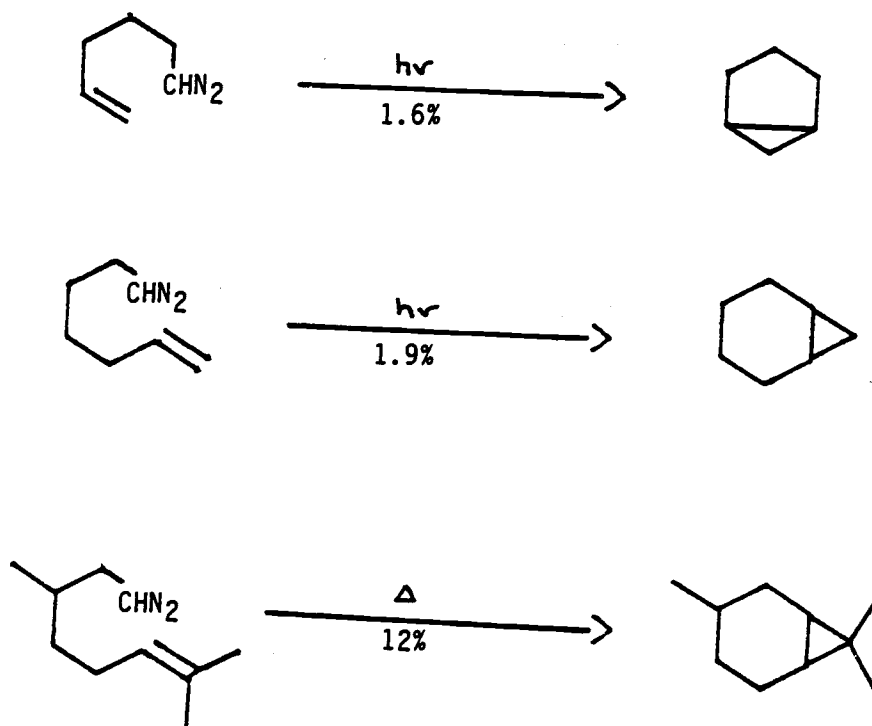
The compounds that did not give any cycloaddition products were 1-carbena-4-pentene and 1-carbena-2,2-dimethyl-4-pentene. Unfortunately the above cyclizations cannot be definitively ascribed to the carbene. It is well known that diazo compounds react with olefins to form pyrazolines. Furthermore, in two of the above cyclizations, a pyrazoline

was isolated.
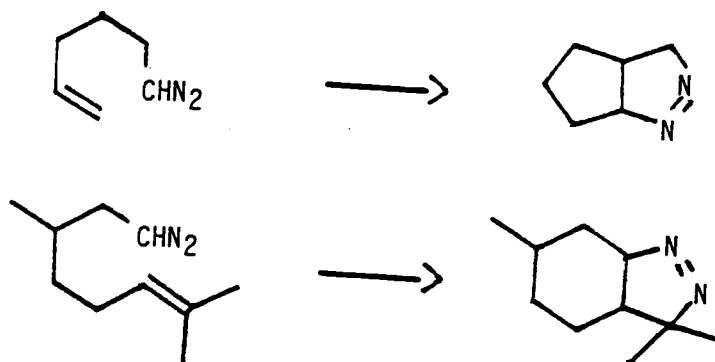
The authors noted that the role of the pyrazoline in the final products could not be determined.

Further studies on similar cycloadditions have shed some light on the problem of diazo versus carbene addition. Kondo and Ojima[101] reported that when a sulfur atom was part of the chain, cyclization occurred in very high yield.

Δ 68.5%

hv 87.5%

In the case of the next higher homologue, thermolysis afford the pyrazoline while photolysis produced the thio-bicyclo compound which was also obtained upon photolysis of the pyrazoline.
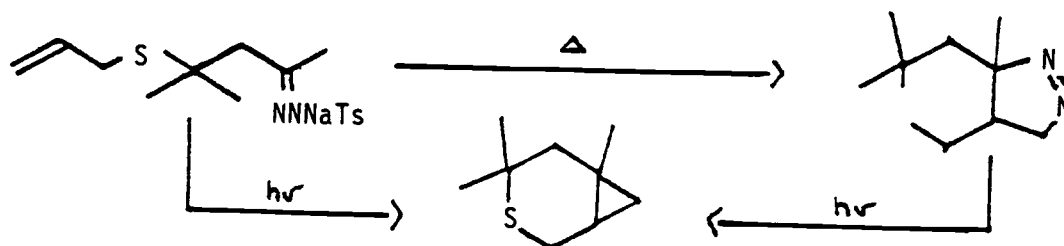
It was claimed[102] that cyclization was caused by dipolar addition of the diazo moiety to the double bond. Photolysis at low temperature of compound I produced only a β insertion product and no cyclized compounds. This can be represented by the following scheme:
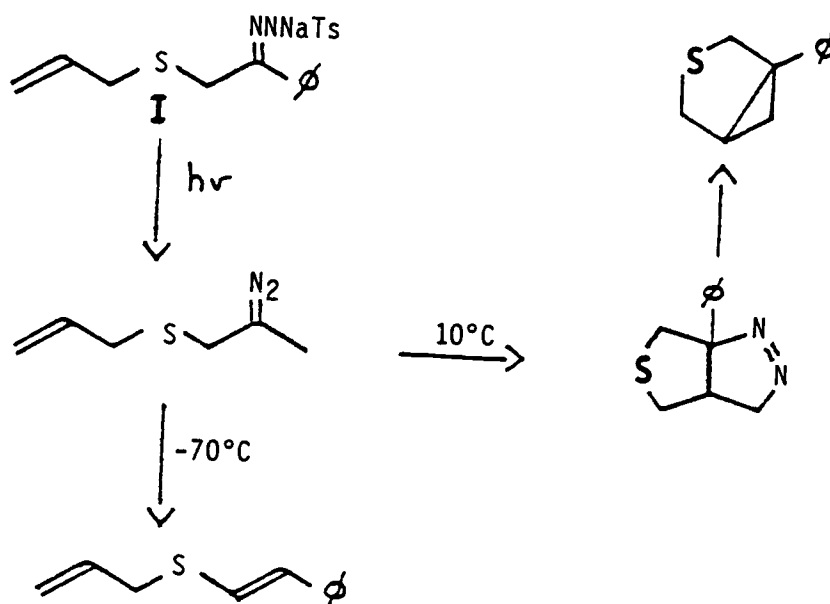
More recently a similar conclusion was arrived at by Padwa and Ku.[103] Thermolysis of the sodium salt of o-allylbenzaldehyde tosylhydrazone (A) yielded the 2-pyrazoline B:
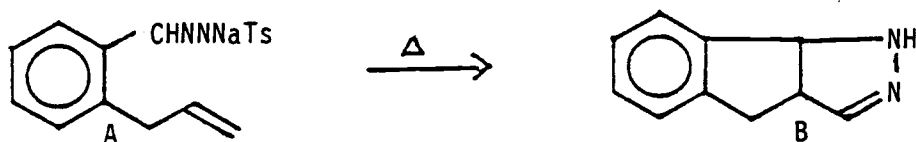
whereas photolysis of A yielded the tricyclic compound C:
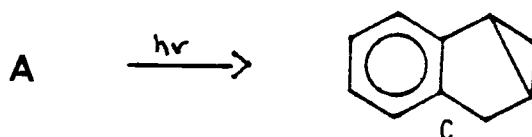
The mechanism postulated was formation of the diazo

compound which would add to the double bond to form a 1-
pyrazoline D which upon further photolysis would yield
compound C or isomerize to the 2-pyrazoline B in the pres-
ence of base. This can be represented by the following
scheme:
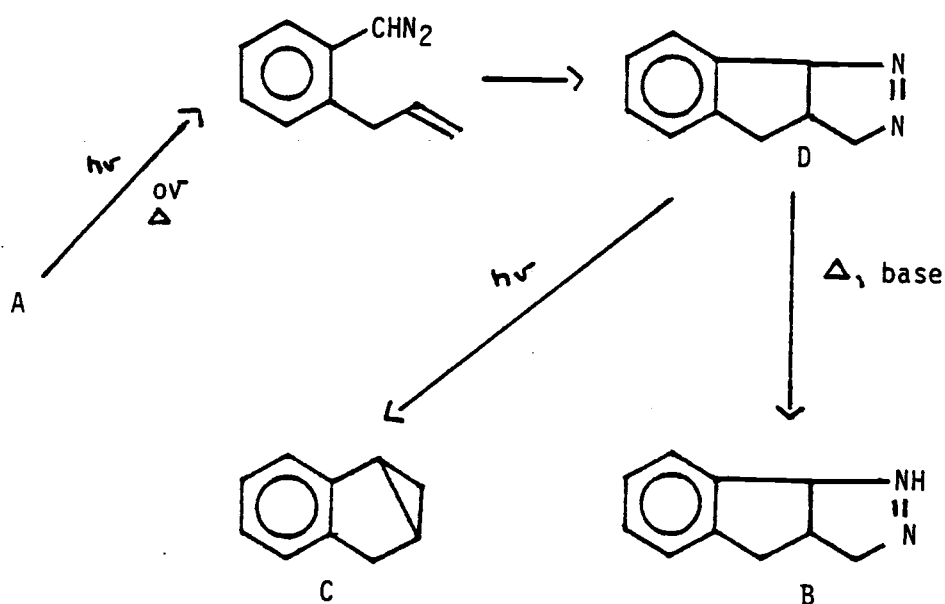
That the 1-pyrazoline D was indeed an intermediate was
demonstrated by independently synthesizing it by two different
methods:
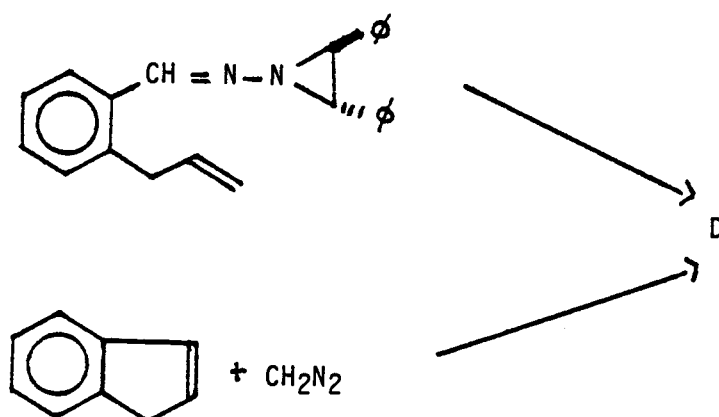
Thermolysis of the 1-pyrazoline D at 100°C in the presence of base yielded the isomeric 2-pyrazoline B. Thermolysis in the absence of base or photolysis of D yields compound C.

The experimental evidence presented for the above cyclizations proves that the diazo addition to the internal double bond provides a pathway to product. The carbene mechanism cannot be ruled out and it is likely that it operates in competition with the diazo addition mechanism.

Carbenes also add to triple bonds and aromatic systems. These reactions take place less readily than additions to double bonds. Diazomethane photolysis in the presence of dialkylacetylenes yields cyclopropenes. Photolysis in 2-butyne-dimethyl ether afforded 1,2-dimethylcyclopropene in 17% yield.[104] Photolysis in 4-octyne yielded 1,2-dipropyl-cyclopropene in 23% yield,[105] but photolysis in the presence of acetylene yielded only allene and propyne.[106] None of the expected cyclopropene could be isolated nor detected spectroscopically, even at 4°K.[107]

Substituted carbenes also add to alkynes. The following are some examples:

ϕ_2CN_2 + $CH_3C \equiv CCH_3$ $\xrightarrow[73\%]{h\nu}$ [cyclopropene structure with two ϕ groups]   Ref. 108

but:

ϕ_2CN_2 + $R-C \equiv CH$ $\longrightarrow$ [indene-type structure with ϕ and R groups]   Ref. 109

R = CH_3, t-Bu
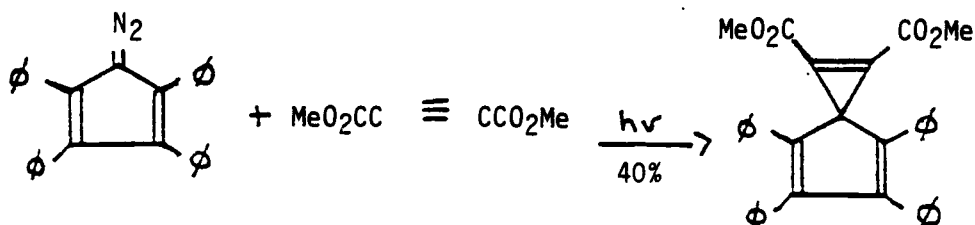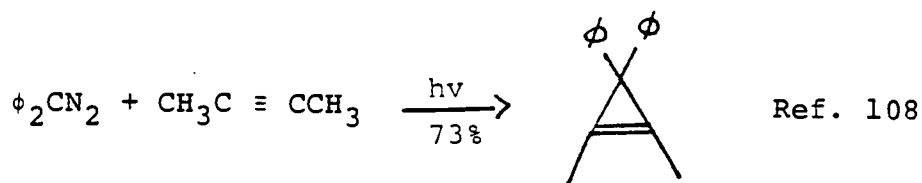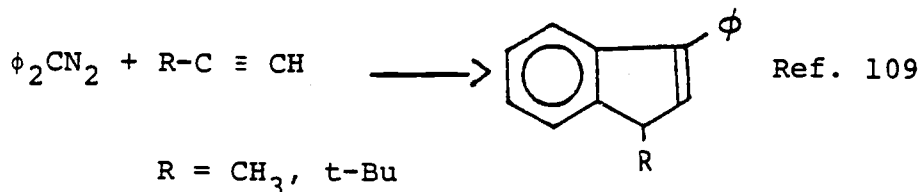
Cyclopropenes are also generated by addition of dihalo-carbenes to alkynes. This reaction is synthetically important because cyclopropenones are isolated upon hydrolysis of the dihalocyclopropenes. Some examples are the following:

$\phi C \equiv C\phi$ + $:CBr_2$ $\longrightarrow$ [dibromocyclopropene with two ϕ groups] $\xrightarrow{H_2O}$ [cyclopropenone with two ϕ groups]   Ref. 110

$\phi C \equiv C\phi$ + $:CCl_2$ $\longrightarrow$ [dichlorocyclopropene with two ϕ groups] $\xrightarrow{H_2O}$ Ref. 111
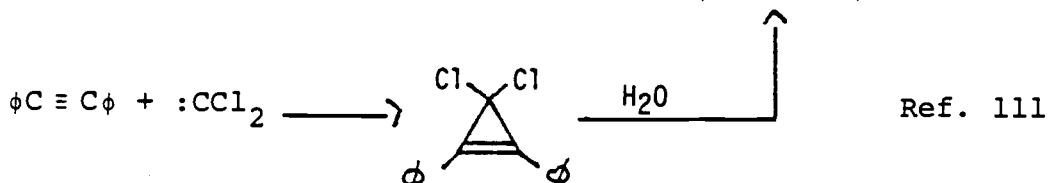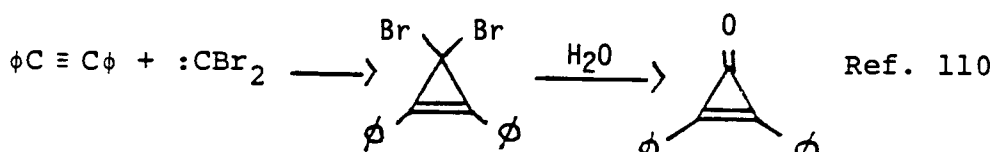
The best yields are obtained when the dihalocarbene is generated from the organomercury precursor.

Carbenes can add to benzene and other aromatic compounds to yield norcaradienes or cycloheptatrienes or a mixture of both. The two products are isomers that equilibrate even at low temperature. The position of the equilibrium depends on the carbene added and the aromatic compound. The reaction is facilitated by electron-releasing groups attached to the aromatic ring, especially alkoxy groups. Some examples are

the following:
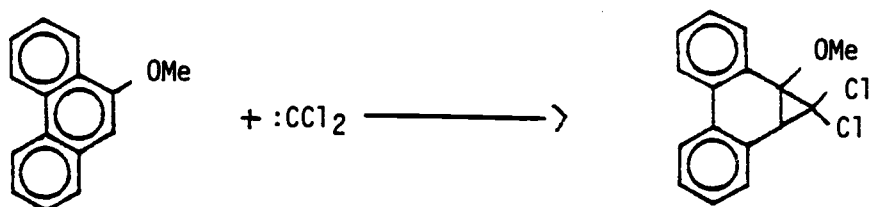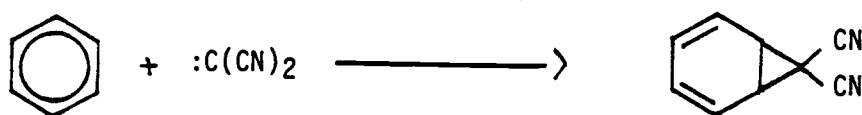
C. Carbene rearrangements

The chemistry of singlet carbenes has been likened to carbonium ions because both species have a vacant p orbital. Thus a very common reaction of both carbenes and carbonium ions yields an olefin. In the case of the carbonium ion a proton is expelled, whereas in the carbene a hydride ion migrates in what is termed a β hydrogen insertion reaction.

Another well-known reaction of carbonium ions is the rearrangement reaction.[116] Rearrangements in carbonium ion

chemistry are quite common. In contrast, carbene rearrange-
ments are less ubiquitous. For our purposes, we shall define
a carbene rearrangement as a reaction in which the carbon
skeleton of the carbene is altered as it goes to products.
Furthermore, the topic will be subdivided into four cate-
gories: (1) 1,2-shifts, (2) fragmentations, (3) stabilized
carbene rearrangements, and (4) carbene to carbene rearrange-
ments.

1. 1,2-Shifts

Together with fragmentations, 1,2 shifts are the most
common type of carbene rearrangement. The rearrangement
involves migration of a β-group × to the carbene center and
concomitant formation of a double bond:

$$-\ddot{C}-\overset{\overset{\displaystyle \times}{|}}{\underset{|}{C}}- \longrightarrow \overset{\times}{\underset{}{\diagdown}}C = C\diagup$$
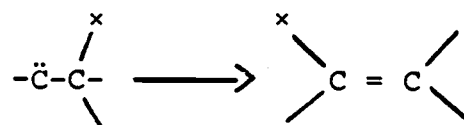
where × can be alkyl, aryl, RO, RS, Cl and F.

Kirmse[84] studied the possibility of alkoxy migration
in a number of carbenes. It was found that alkoxy migrates
to a very small extent but it does accelerate β-hydrogen
insertion. It was found that in β,β-dialkoxy substituted
compounds there is a significant amount of alkoxy migration:

| | hν | 1% | 33% |
| | Δ | 5% | 21% |

$(EtO)_2CHCHN_2 \longrightarrow$ EtO⌒OEt + EtO⌒OEt + EtO₂C=CEtO₂

$h\nu$ 47%   19%

Δ 29%   3%
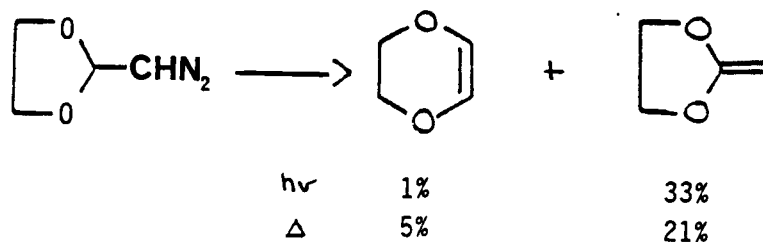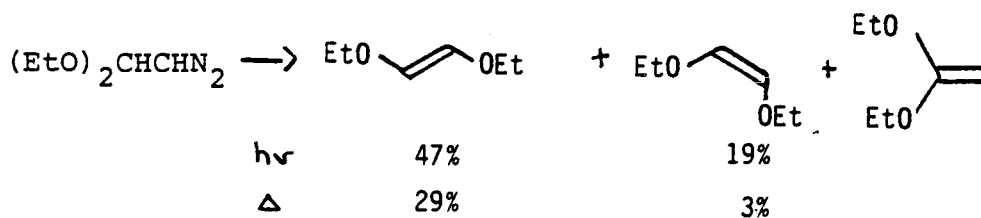
There is at least one example in the literature where an alkoxy migration was found to occur in preference to an alkyl migration.[117]
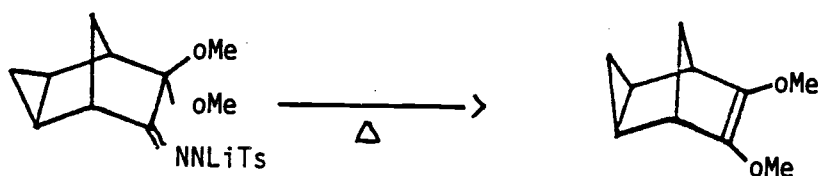
A series of compounds
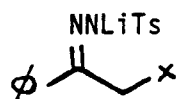
x = OMe, NMe$_2$, SMe or Sϕ

was decomposed and the products analyzed in order to compare the relative efficiences of O, N and S in carbene migrations.[118] In the cases of methoxy and dimethyl amino, the only products found were the cis and trans alkenes formed by β hydrogen insertion. In contrast, the thiomethoxy substituted compound yielded 85-91% rearranged product and the thiophenoxy analogue yielded 92-100% rearranged product. Furthermore, in the following cyclic compounds sulfur migration occurred in preference to methyl migration:

R = H or ϕ
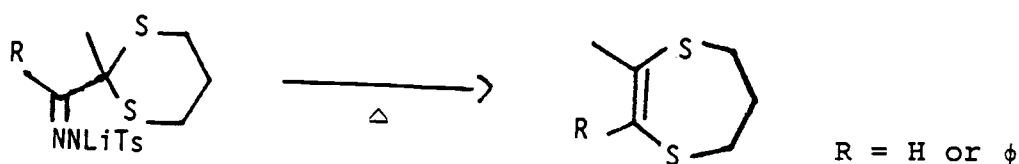
It was pointed out that heteroatom efficiency in migrations
to carbene centers parallels the efficiency in neighboring
group participation.

The ability of sulfur and the inability of oxygen to
participate in 1,2 migrations was confirmed recently in the
following cyclic compounds:[119]
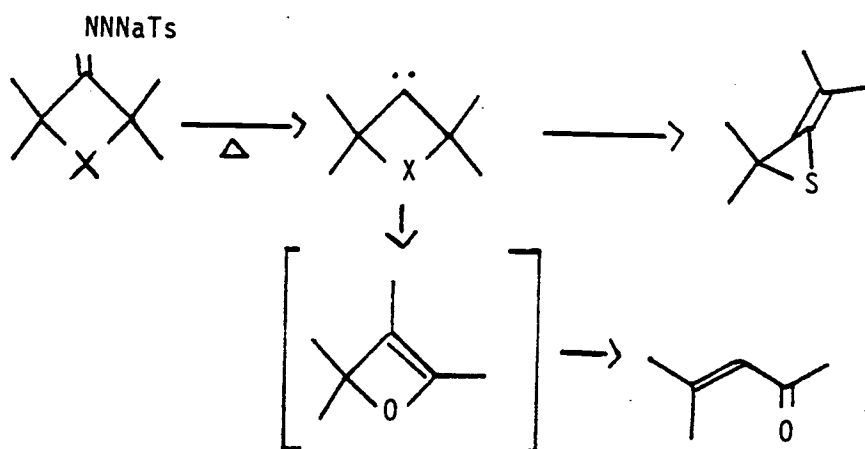
The authors implicated an ylid in the case of sulfur:
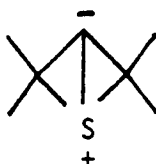
although no experimental evidence was presented. There is
no information in the literature as to the nature of these
heteroatom migrations and thus it is not known whether the
ylids play a role or the transformation is a concerted one.

There are several examples known of fluorine migration
and one involving chlorine migration. The example of
chlorine migration[120] indicates that it occurs much faster
than fluorine migration:

$$CFCl_2\ddot{C}F \longrightarrow CFCl = CFCl = CCl_2 = CF_2$$

$$\qquad\qquad\qquad\qquad 80\% \qquad\qquad 7\%$$
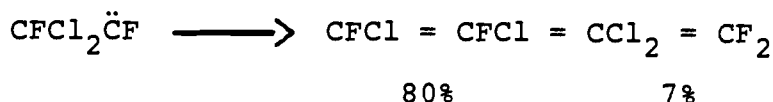
The product distribution is not an accurate measure of chlorine vs. fluorine migratory aptitudes because there is the possibility that part or all of the minor product comes directly from the carbene precursor.

Fluorine migration has been observed in fluoro difluoroaminocarbene,[121] bistrifluoromethylcarbene[122] and trifluoromethylcarbene.[123] In polyfluoro carbenes, fluorine migration does not occur all the time. Trifluoromethyl carbene, if generated in the presence of alkanes, will give the carbonhydrogen insertion product rather than trifluoroethylene.[124] If the carbene has a possibility for a β hydrogen insertion, no fluorine migration occurs.[125]

$$CF_3CF_2CF_2CN_2CH_3 \xrightarrow[92\%]{hv} CF_3CF_2CF_2CH = CH_2$$
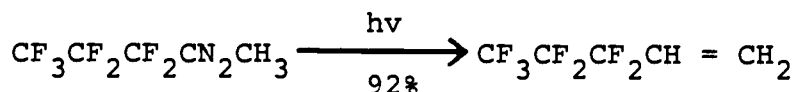
Fluoroalkyl groups migrate faster than fluorine as exemplified by the following reactions:

$$CHF_2CF_2CHN_2 \xrightarrow{hv} CF_2 = CH-CHF_2 \qquad\qquad \text{Ref. 125}$$

$$C_2F_5CF_2CHN_2 \xrightarrow{hv} C_2F_5CH = CF_2$$
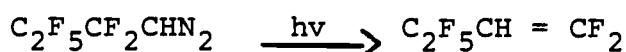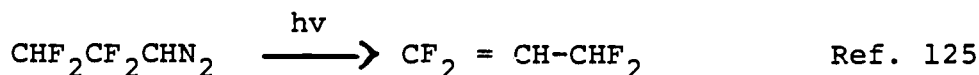
The above examples indicate that both difluoromethyl and perfluoroethyl migrate in preference to fluorine.

Usually alkyl shifts are not observed in most acyclic alkyl and dialkyl carbenes, since their chemistry is dominated by β and γ hydrogen insertions to yield alkenes and

cyclopropanes respectively. Methyl shifts in acyclic car-
benes are known in systems generated by photolysis of diazo-
rines or diazo compounds. Thermolysis of the corresponding
diazirine or diazo compound yields little, if any, methyl
shift. The following are some examples:[126]

Precursor:
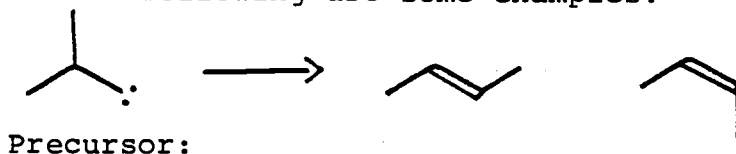
Diazo, hv	5.5%	4%
" , Δ	-	-
Diazirine, hv	9.3%	7.7%
" , Δ	0.5%	0.3%

Precursor:
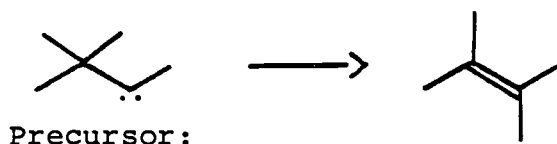
Diazirine, hv	10.4%
" , Δ	0.3%
Tosylhydrazone, NaOMe, Δ	Trace

Precursor:
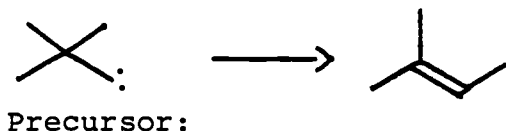
Diazirine, hv	49%
" , Δ	8%
Tosylhydrazone, NaOMe, Δ	7%

From the above data, it can be seen that methyl migra-
tion occurs to a considerable extent only in the case of the
photochemically generated t-butyl carbene. This indicates
that, in photochemically generated carbenes, methyl migration
effectively competes with γ hydrogen insertion but not with
β hydrogen insertion.

Migrations are favored by aryl substituents. The

following products have been observed to arise from neophyl
carbene:[127]

ϕ_2-C(CH$_3$)$_2$-CHN$_2$ $\xrightarrow{60°C}$ ϕ—CH$_2$—C(CH$_3$)=CH$_2$ 51% + CH$_3$—CH=C(CH$_3$)—ϕ 9% + cyclopropane 40%
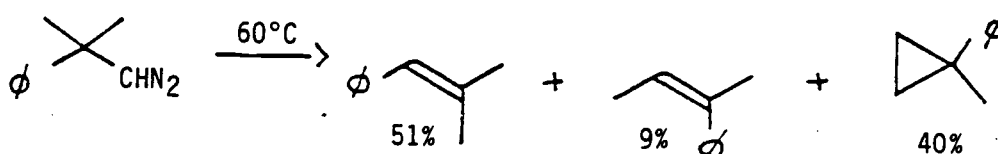
From the product distribution, the ratio of phenyl to methyl
migration is about 5.7. The authors contrasted this value with
carbonium ion value of 3,000-300. The ratio of phenyl migra-
tion to γ hydrogen insertion was calculated to be about 1:2,
indicating that the two processes are competitive.

The migratory aptitudes of substituted phenyl groups
have been studied in two similar series of compounds. The
first series of compounds studied was the tosylhydrazones of
triarylacetaldehyde.[128]

ϕ_2-C-CH = NNHTS $\xrightarrow[\Delta]{NaNH_2}$ ϕ—C(ϕ)=CH—Ar + Ar—C(ϕ)=CH—ϕ (H)

x = p-MeO, m-MeO, p-Me, p-CL and p-NO$_2$
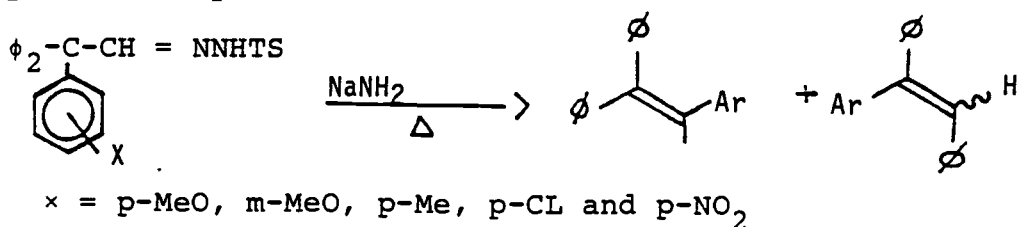
The migratory aptitude had a linear correlation with σ^+ and
yielded a ρ value of -0.28. The second series of compounds
studied was the tosylhydrazones of 2-aryl-2-methyl-1-phenyl-
1-propanones.[129] No products of methyl migration were
detected.

ϕ—C(CH$_3$)$_2$—C(ϕ)=NNNaTs $\longrightarrow$ ϕ—C(CH$_3$)=C(CH$_3$)—ϕ + cyclopropane

X   x = H, p-Me or M-Cl
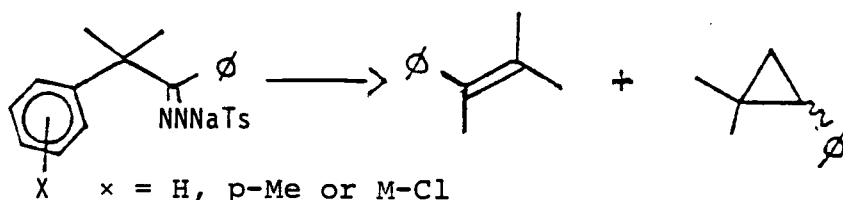
Again, the aryl migratory aptitudes correlated in a linear
fashion with σ^+ and had a ρ value of -0.68. From the ρ
values it is evident that in both series of compounds elect-
ron donating substituents in the phenyl group expedite the
migration and that there is a small amount of negative
charge development at the carbene center.

The stereochemistry of phenyl migration has been invest-
igated by utilizing a stereochemically rigid t-butylcyclo-
hexane system.[130]

NNNaTs $\xrightarrow{\Delta}$ 77.1% + 21.6% + 1.3%

NNNaTs $\xrightarrow{\Delta}$ 41.3% + 6.5%
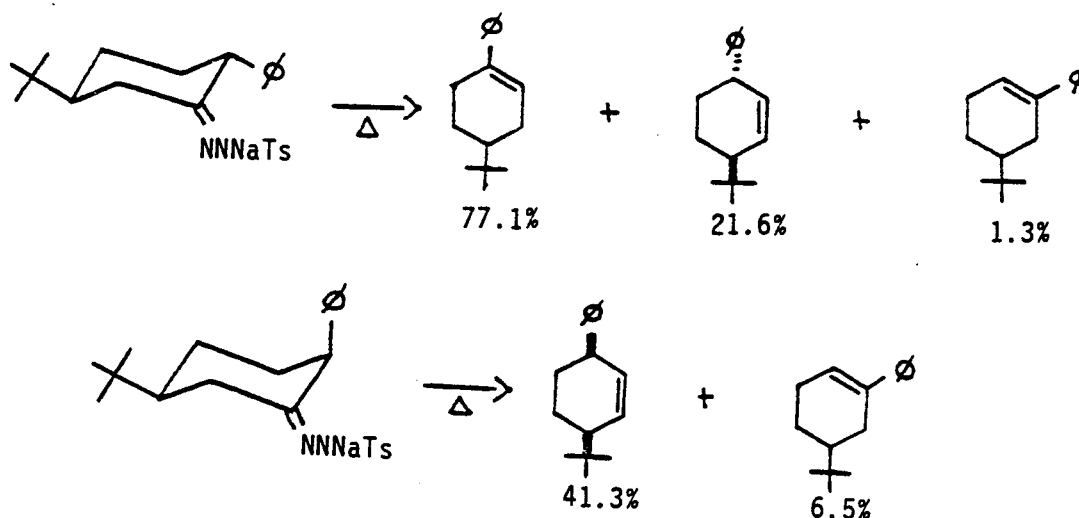
In both reactions the main product(s) is(are) due to a β
hydrogen insertion, thus indicating that phenyl migration
does not compete effectively with it. The amount of phenyl
migration is dependent on whether the phenyl is in the axial
or the equatorial position. The data indicate very clearly
that the steric requirements for phenyl migration are better
met when the substituent is in the axial position, thus
giving an axial to equatorial ratio of 5:1. Also, when the
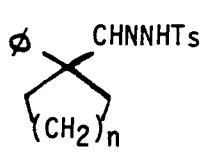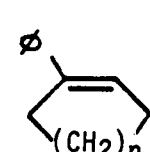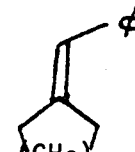
phenyl group is in the axial position we obtain a lower ratio of β hydrogen insertion to migration than when the substituent is in the equatorial position. In other words, phenyl migration competes more favorably with α hydrogen insertion when the substituent is conformationally locked in the axial position.

Alkyl migrations are favored by cyclic systems. The following are examples in which an alkyl migration yields a ring expanded product.[131-3]
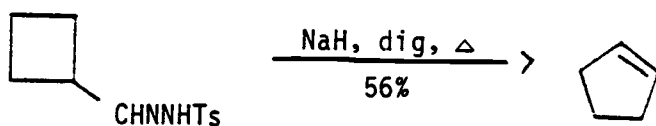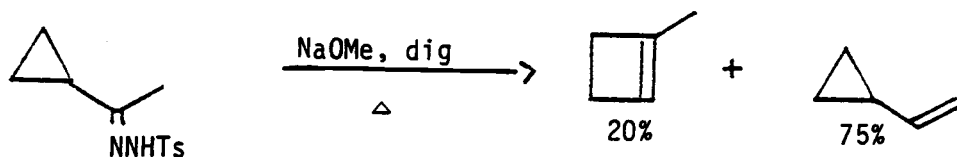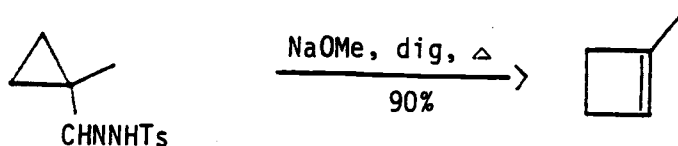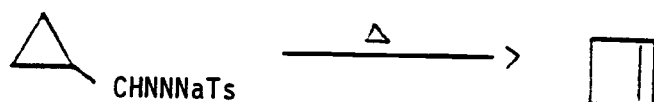
Higher cycloalkyl carbenes do not ring expand. But if a phenyl substituent is placed in the 1 position of the ring, phenyl migration and ring expansion are the only products. The following are some examples:[134]

	ϕ—CHNNHTs on ring with $(CH_2)_n$	ϕ on ring with $(CH_2)_n$	ϕ substituted ring with $(CH_2)_n$
n = 0		100%	-
1		92%	8%
2		80%	20%
3		59%	41%
4		57%	43%

Thus migratory ability is dependent on ring size. When the ring size is smaller than a six-membered one, phenyl migration does not effectively compete with alkyl migration (20% or less). In six- and seven-membered rings, phenyl migration is comparable to alkyl migration (about 6:4).

In the rearrangements of cyclopropylidenes, discovered by W. M. Jones and coworkers, it was found that 1-diazo-2,2-diphenylcyclopropane rearranged to 1,1-diphenyl-1,2-propadiene in 94% yield.[135] It was also learned that the carbene derived from the diazo compound could be trapped by reaction with an alkene to yield a spiropentene.[135,136] The carbene addition to cis and trans-2-butene is stereospecific indicating that the carbene reacts in its singlet state. Furthermore, competitive addition of the carbene to alkene pairs indicated that it is an electrophilic carbene that shows a strong steric effect in its addition reaction.

Some early experimental evidence seemed to indicate that carbene and diazo compounds were both precursors to the allene but further work demonstrated that only the carbene is the precursor to the allene.[137] This reaction is very useful because optically active allenes can be synthesized from optically active trans - 2,3 - disubstituted 1-diazocyclopropanes.[138]

The rearrangement of cyclobutylidene was discovered by Friedman and Shechter.[139] The sodium methoxide-catalyzed decomposition of cyclobutanone tosylhydrazone afforded methylenecyclopropane (80%) and cyclobutene (20%). The rearrangement is susceptible to substituents. Several groups have attempted to synthesize the following cyclopropane:

OCOEt
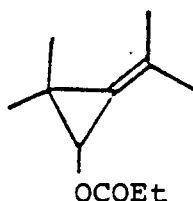
due to the fact that this structure was erroneously assigned to the cockroach sex attactranct. The strategy employed for this synthesis was a ring contraction of the tosylhydrazone of 2,2,4,4-tetramethyl-3-oxo-cyclobutyl propanoate. Pyrolysis or thermolysis of the above-mentioned tosylhydrazone afforded very complex mixtures from which the desired cyclopropyl derivative could not be isolated.[140] It was ascertained[140a] that the parent ketone did undergo the rearrangement.

NNNaTs $\xrightarrow{\Delta}$
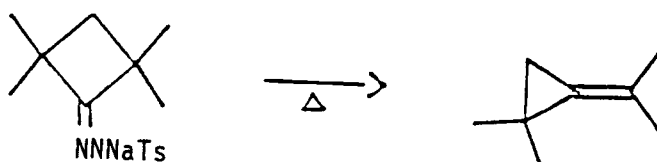
The usage of a tetrahydropyranyl group instead of the pro-
panoyl group was unsuccessful in accomplishing the desired
rearrangement.[141] Instead a small amount of a γ hydrogen
insertion product was isolated.
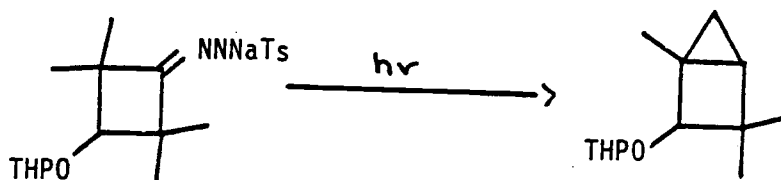
Thus the data seems to suggest that the rearrangement is
sensitive to electronic effects and that electronegative sub-
stituents in the ring do not allow the rearrangement to occur.

Rearrangement of cyclopropyl carbene seems to be more
effective than cyclobutene ring contraction as demonstrated
by the following reaction.[142]
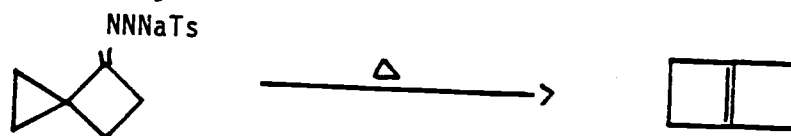
Alkyl migrations are also known for bicyclo and tricyclic
carbenes. In these systems the migratory aptitude depends not
only on the size of the ring but on the position of the carbene
center. The following are some examples:

but

and

Ref. 145
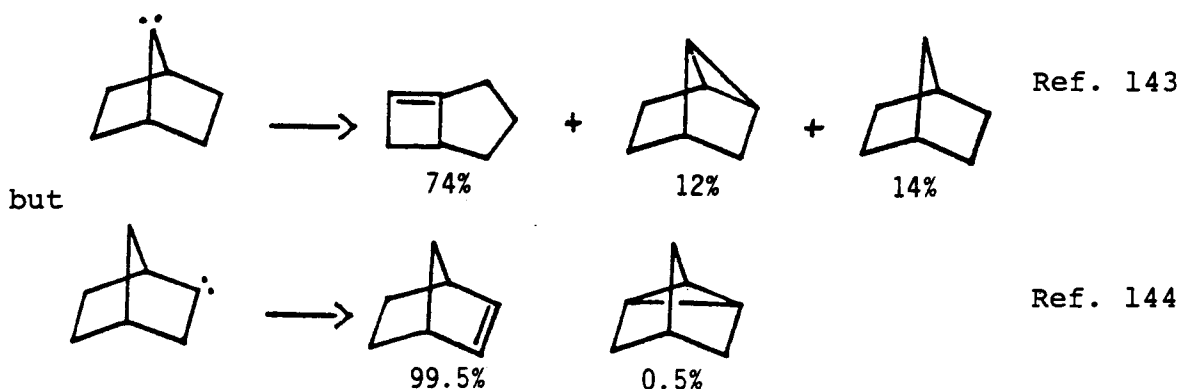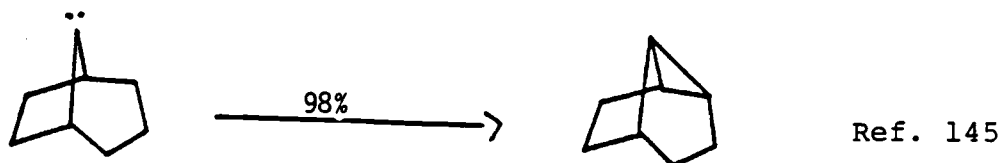
An example of migration in a tricyclic carbene is the following:[146]
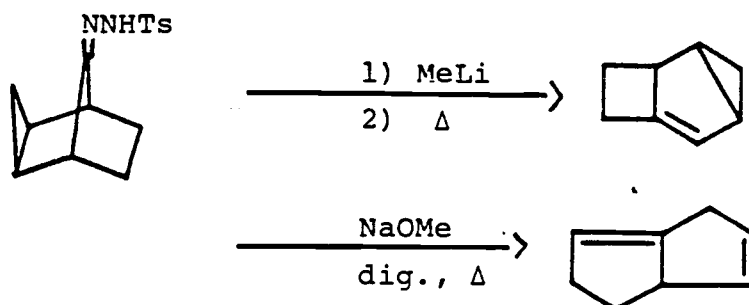
It seems that the multiplicity of the carbene plays a role in 1,2-migrations. The ratio of phenyl to methyl migration in 1-diazo-2-methyl-2-phenyl-propane has been measured under a variety of conditions.[147] The products obtained are due to methyl migration and γ-hydrogen insertion. Under conditions that favor formation of the triplet carbene (photosensitization or bromobenzene as a solvent), the yield of methyl migration and γ-hydrogen insertion products is reduced whereas the yield of phenyl migration products stays about the same as compared to singlet carbene reaction yields. In other words, the phenyl to methyl migration ratio increases in going from singlet to triplet carbene. This result is reasonable in view of the fact that β-hydrogen insertion seems to occur only in the singlet carbene and that only aryl and not alkyl groups do 1,2-migrations in free radicals.[148]

A related rearrangement is the 1,4-alkyl migration in
4,4-dimethylcyclohexadienylidene. This carbene, when gene-
rated in the gas phase, affords 16% p-xylene and 27% tol-
uene.[149] The mechanism is essentially an intermolecular
process where the carbene disproportionates to p-tolyl and
methyl radicals which then recombine to yield only p-xylene.
The mechanism was proven by generating 4,4-dimethyl- and
4,4-diethylcyclohexadienylidene at the same time and analyz-
ing the products formed. Besides toluene and ethylbenzene,
the rearranged products p-xylene, p-diethylbenzene and p-
ethyltoluene were found in close to statistical ratio. The
reaction is synthetically useful since it has been used in the
production of 6 and 7 -paracyclophane.

n = 4,5

B. Fragmentations

Carbene fragmentations usually occur in bicyclic or poly-
cyclic ring systems containing cyclopropyl rings. The products
contain a triple bond, although in some cases allenes are also
formed. One of the first fragmentations of a carbene was ob-
served when the tosylhydrazone of tricyclanone was pyrolyzed:[150]
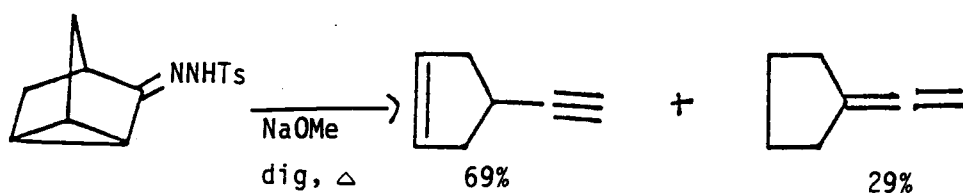
It was determined that the allene was formed by isomerization of the alkyne. The sodium salt of tricyclanone tosylhydrazone was prepared and isolated. It was then dissolved in diglyme and pyrolyzed at 160° to afford the alkyne, 3-ethynyl-1-cyclopentene (42%), as the sole product. Photolysis of the sodium salt of tricyclanone tosylhydrazone did not yield fragmentation products.[150, 151]

Another carbene fragmentation was discovered by Freeman and Kuper in the [3.1.0] bicyclo system.[152] In an effort to determine whether cyclopropane rings were able to interact with non-adjacent carbenes centers, the following tosylhydrazones were decomposed and their chemistry compared.
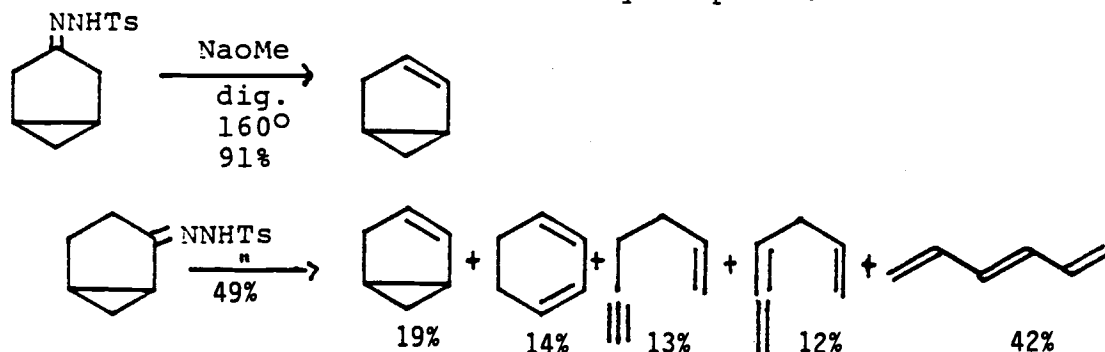
It was determined that 1-hexen-5-yne rearranged under the reaction conditions to the allene and the conjugated triene. Furthermore, when the preformed sodium salt was pyrolyzed in the absence of sodium methoxide, the following products were obtained:
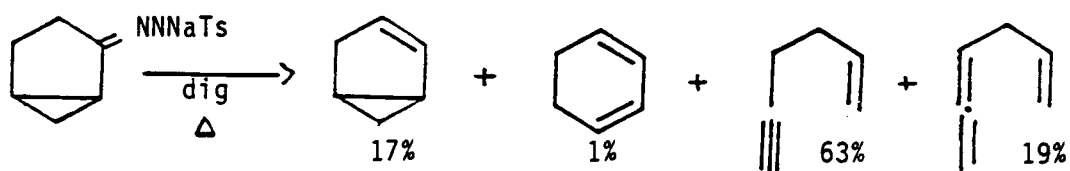
These results were later confirmed in similar bycyclic systems.[153]
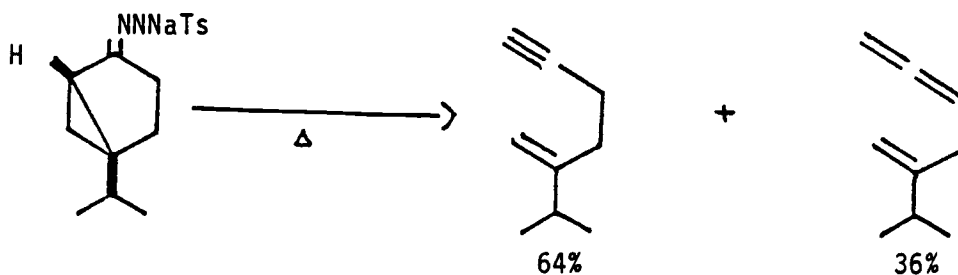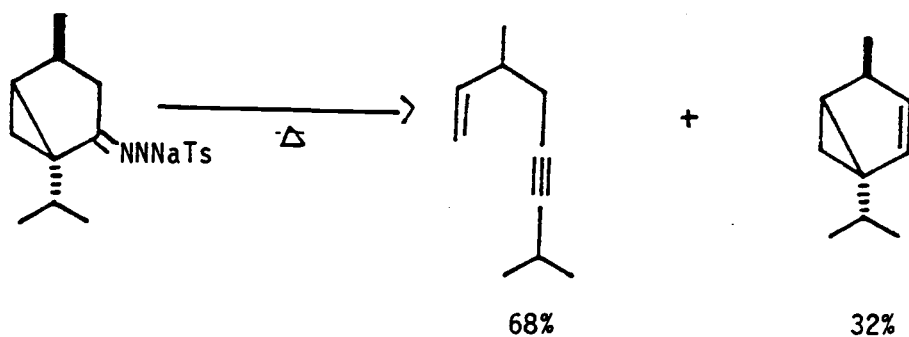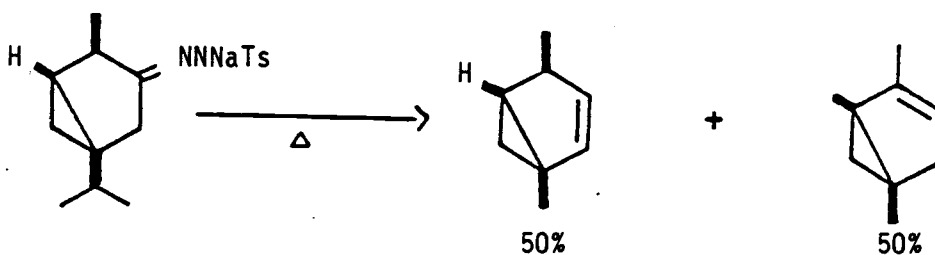
Similar results to the unsubstituted system were observed,

since location of the carbene center next to the cyclopropane led to fragmentation while more remote location led only to β-hydrogen insertion. The same results were observed with a higher homologue, the bicyclo [4.1.0] system.
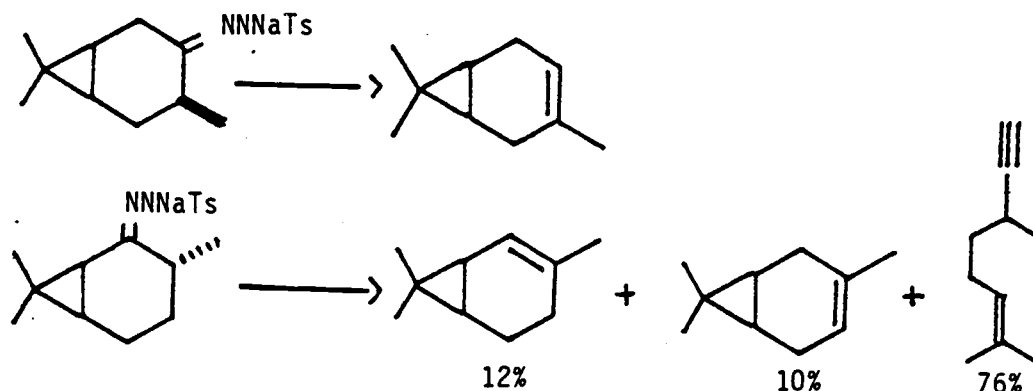
The authors noted that amount of allene formed seemed to be related to relative stabilities of allene and alkyne. Thus we see allene formation in the cases where the alkyne is monosubstituted but none in the case where the alkyne is disubstituted.

The size of the ring fused to the cyclopropane has an effect on whether the fragmentation or the β-hydrogen insertion will be the dominating process.[154]
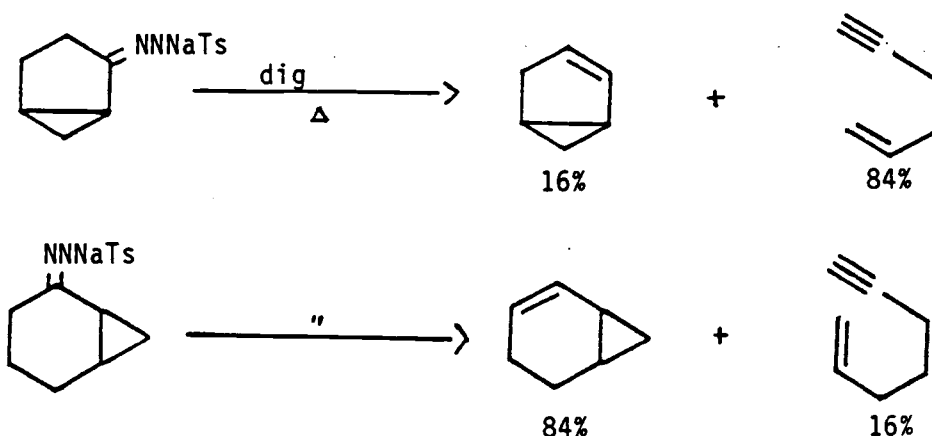
Thus, fragmentation is favored in the smaller system whereas β-hydrogen insertion is favored in the larger bicylo [4.1.0] system. The reaction is also sensitive to substituents in the cyclopropane ring, as demonstrated by the following examples:
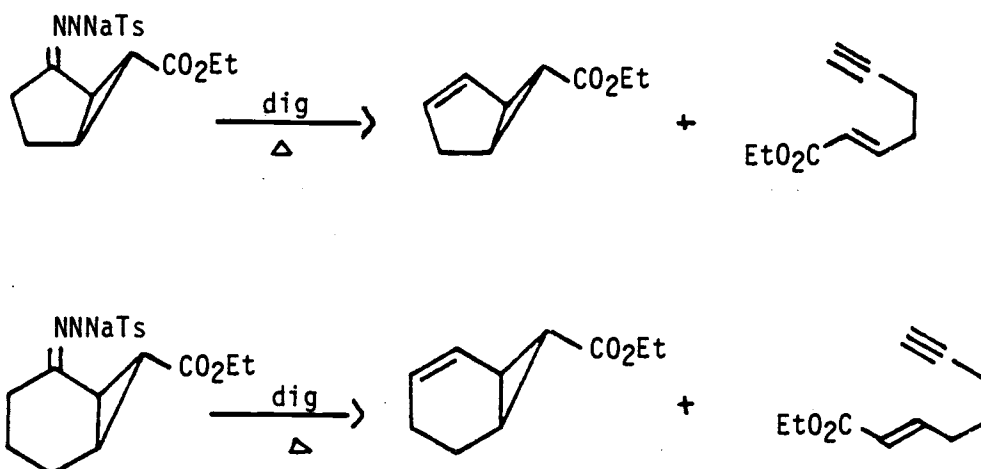
The carbethoxy substituent thus inverts the reaction characteristics making β-hydrogen insertion more favored by the smaller [3.1.0] bicyclic system and fragmentation favored almost as much as β-hydrogen insertion in the larger bicyclo [4.1.0] system. Furthermore, the product distribution is temperature-dependent only when the carboethoxy substituent is present. Lowering the temperature lowers the amount of fragmentation relative to β insertion. It has also been found that the fragmentation is stereospecific, since the isomers with the carboethoxy substituent in the endo position yield the cis alken-ynes.[155]
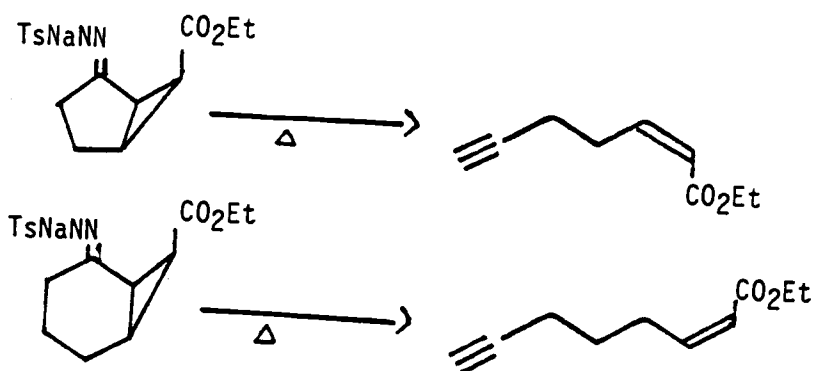
The fragmentation has also been observed in cases where the cyclopropane ring is part of strained tricyclic system or where two or more cyclopropane rings are fused onto a five-, six- or seven-membered ring. The following reactions are some examples:

Ref. 156

Ref. 157

Ref. 158

Ref. 159
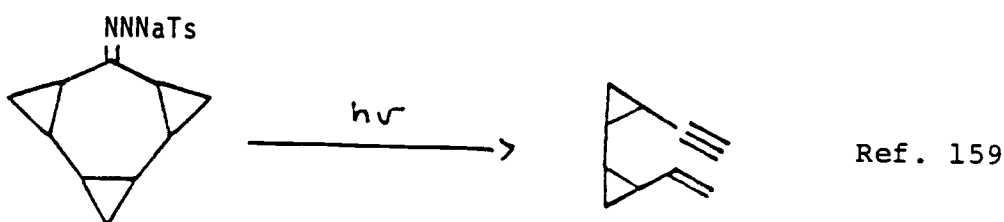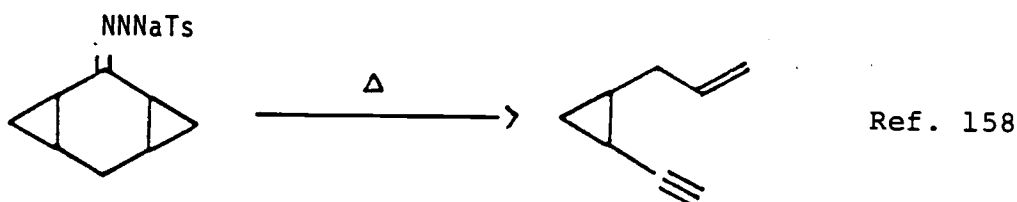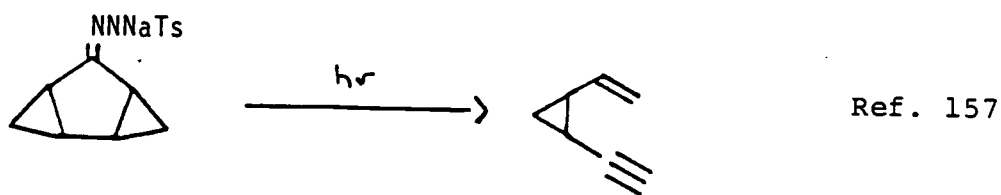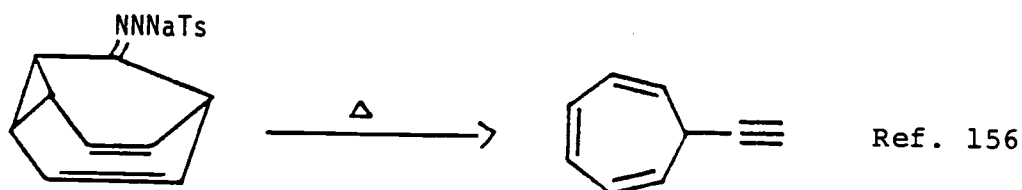
There is also a group of heterocyclic carbenes that frag-
ment to products containing a triple bond. These carbenes do
not contain a cyclopropane ring. The reaction was discovered
by Shechter and co-workers when they found that furyl carbene
fragmented to yield an alkyne.[160]
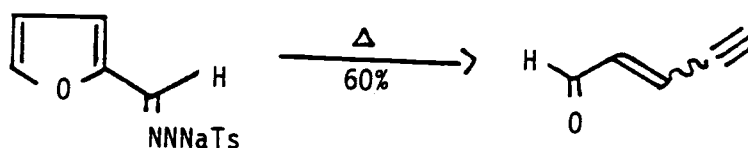
The reaction is quite general and several substituted
compounds were found to yield fragmentation products.

R	Me	H	H	Cl
X	H	Ø	E+	H
% Yield	43	43	47	21
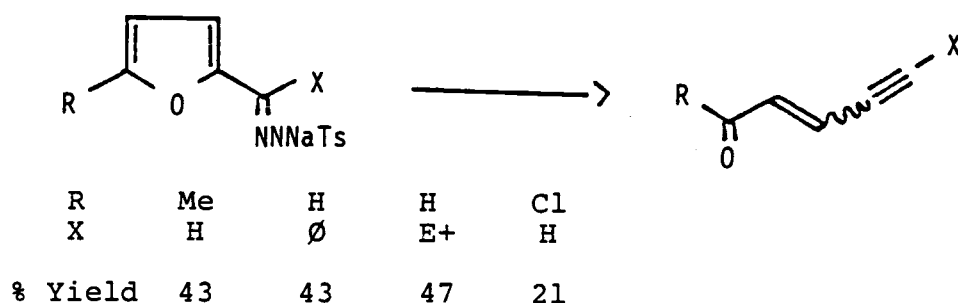
It was also found that related thiophenes also cleaved to yield
acetylenic thioketones or thioaldehydes which polymerized under
the reaction's conditions.

For fragmentation to occur, the carbene carbon has to be
attached at the α position of the furan ring. If the carbene
carbon is attached at the β position of the furan ring, only
products of carbon-hydrogen insertion or addition to double
bonds will be observed.[161]
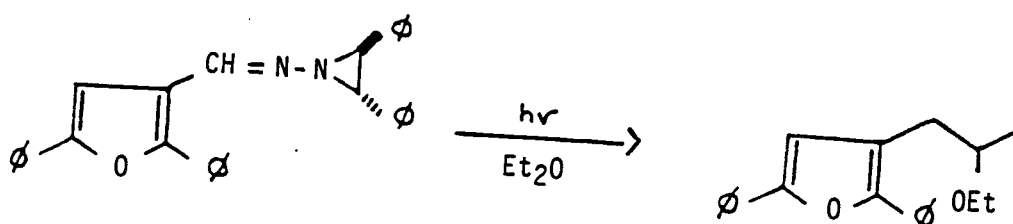
However, a fragmentation was observed when a nitrogen was introduced into the furan ring.
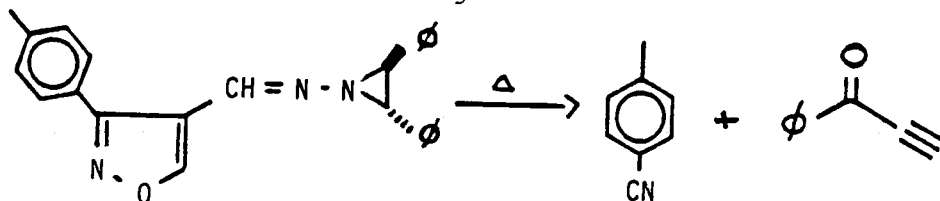
3. <u>Rearrangements of Stabilized Carbenes</u>

Stabilized carbonium ions, also called non-classical carbonium ions, are a well-known and quite extensively studied area of carbonium ions.[162] The subject is still somewhat controversial and Herbert C. Brown is the main opponent of non-classical ions.[163] The nonclassical carbonium ion has some parallel in carbene chemistry. There is a substantial number of carbenes whose reactions have been explained in terms of a stabilized or nonclassical carbene.

In 1968, Gleiter and Hoffmann[164] published a report in which they indicated that extended Hückel molecular orbital calculations indicated that the following carbenes should exist as stabilized (nonclassical) carbenes in their singlet states:
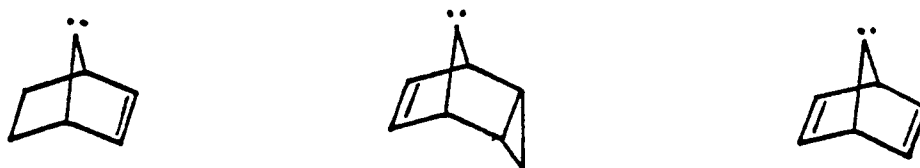
The calculations indicated that the carbene carbon should be tilted to the double bond by about 20°. In the second example, the inclination should be towards the cyclopropane ring since its stabilizing power is larger than a double bond.

Not long after that, Moss and Whittle[165] reported on the

chemistry of 7-norbornanylidene (see page 51). The major

product was derived from an alkyl shift (74%) with a consid-

erable amount (12%) of the insertion product. In contrast,

the chemistry of 7-carbena-2-norbornene[166] is quite different.

The major products are the ones produced by 1,2-alkyl shifts

of either the ethano or the etheno bridge. The insertion pro-

duct was very minor (1%).
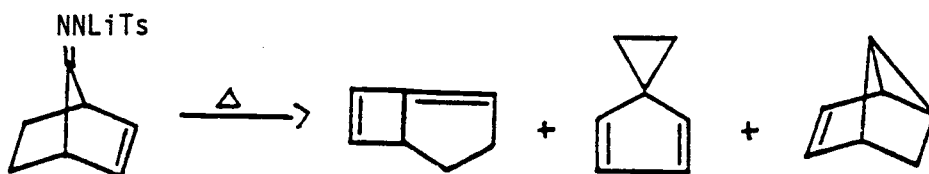
The results were explained in terms of a nonclassical
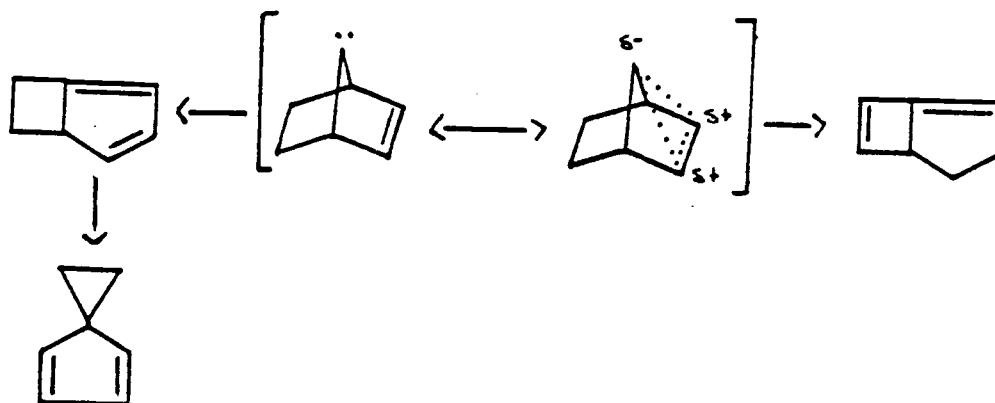
carbene:

The two carbenes also differ in their abilities to react

with olefins to yield cyclopropanes.[167]
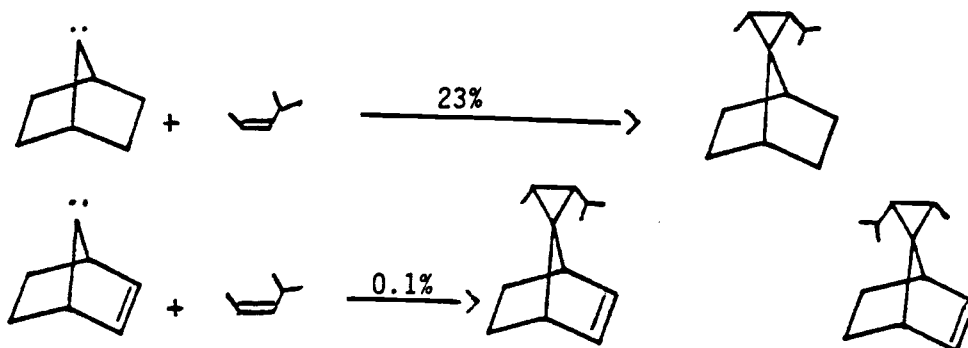
The fact that the second carbene is very inefficient (compared to the first one) in its reaction with the olefin was presented by the authors as evidence in favor of a nonclassical carbene.

Some further evidence for a stabilized carbene in the norbornene system was provided by a study of the following systems:[168]
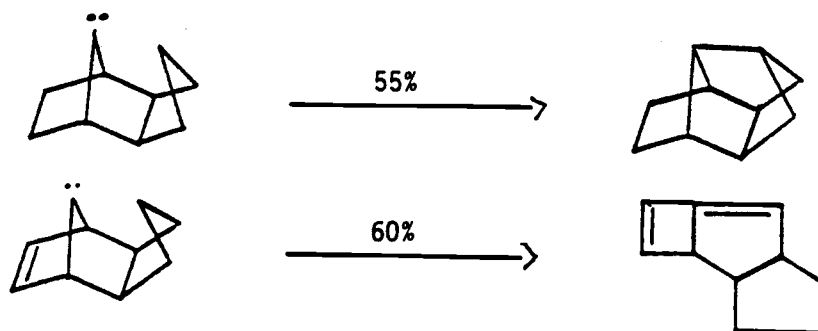
The authors argued that the second carbene gives no products of carbon-hydrogen insertion (as the first carbene does) because it is stabilized by the double bond.

The interaction of the cyclopropane ring with the carbene center analogous to the interaction of the double bond, has also been investigated. Pyrolysis of the following tosyl-hydrazones yield carbenes whose chemistry is quite different.[169]
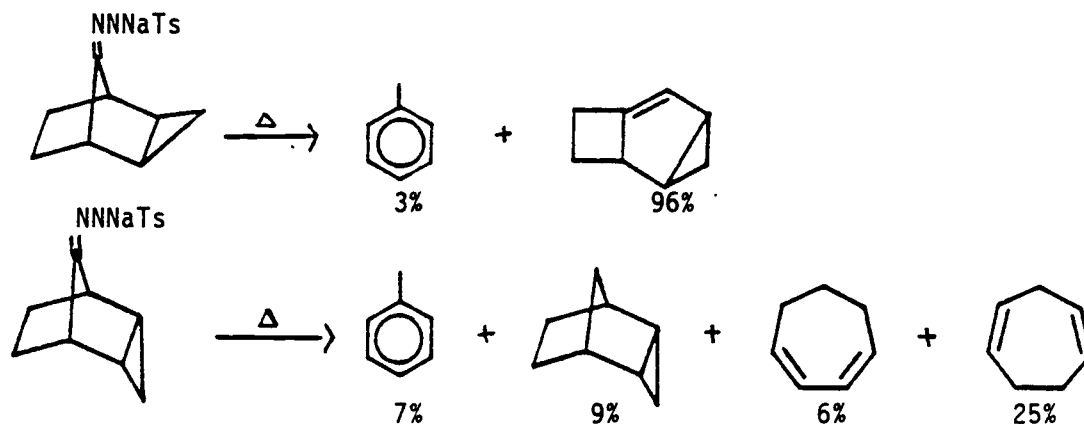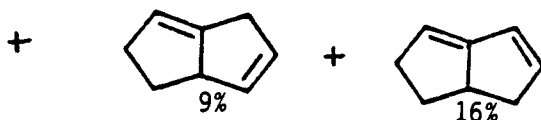
In the first carbene, the cyclopropane ring is in the exo
position and thus cannot participate in the stabilization of
the carbene center due to steric reasons. Thus the major
product arises by a 1,2 alkyl shift of the etheno bridge. The
second carbene has the cyclopropane in the endo position and
thus stabilization of the carbene center is sterically access-
ible. The authors explain the formation of products by the
following scheme:
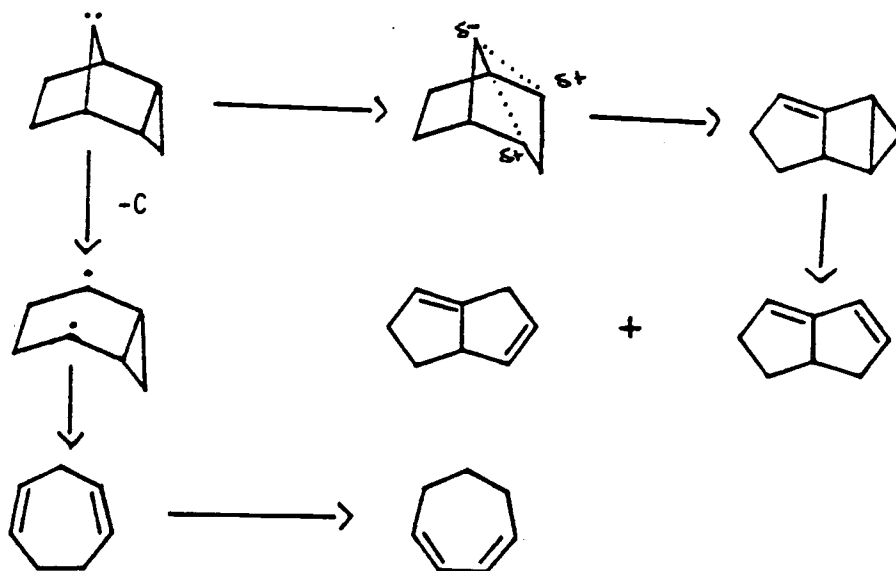
The unsaturated isomer has also been investigated in an
effort to determine whether the strongest interaction would be
with the cyclopropane ring or the double bond.[170]
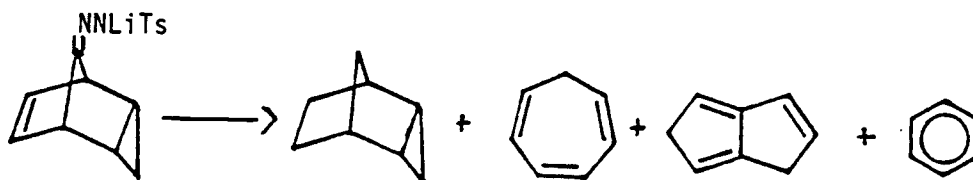
The bicyclic triene product was formed by the mechanism shown below.
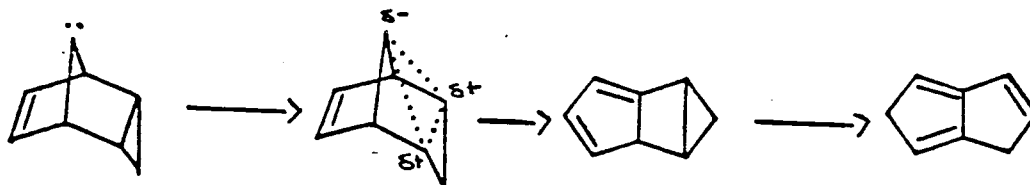
Thus the cyclopropyl ring provides the stabilization of the carbene center to the exclusion of the double bond. This is in accord with the calculations of Hoffmann and Gleiter and what is observed in carbonium ions.[164]

It has been reported that a carbene rearrangement very likely involves the stabilized 7-carbenanorbornene.[171]
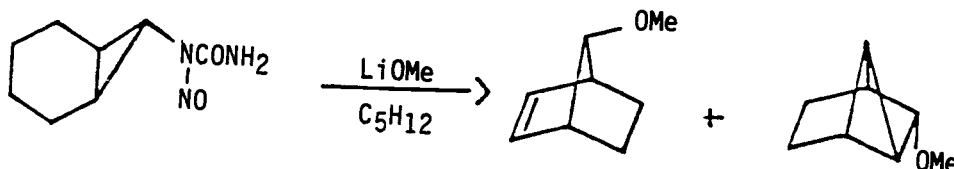
The mechanism proposed is one that involves rearrangement of the cyclopropylidene to 7-carbenanorbornene which reacts with methanol of neutralization to yield a nonclassical carbonium ion which then affords the observed methyl ethers.
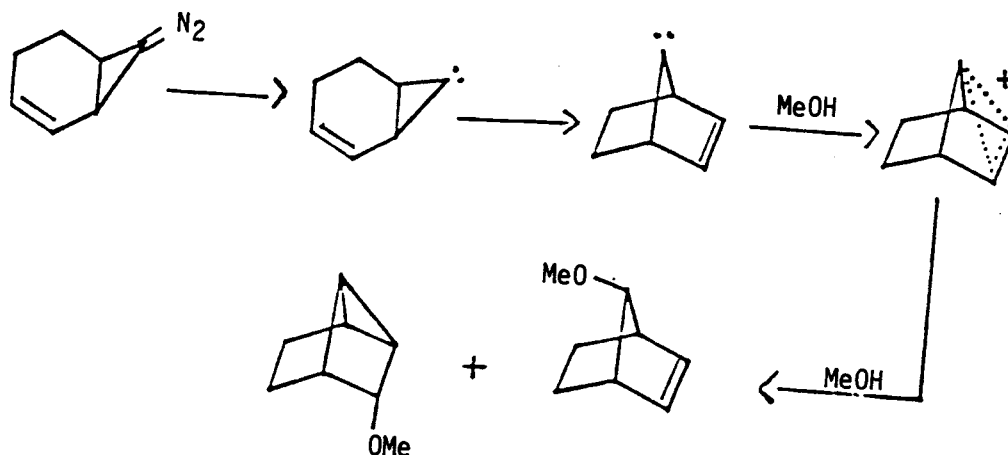
That it is indeed the carbene and not the carbonium ion that rearranges to the norbornane skeleton was demonstrated by the fact that nitrous acid deamination of the corresponding amine hydrochloride did not afford any rearranged product.
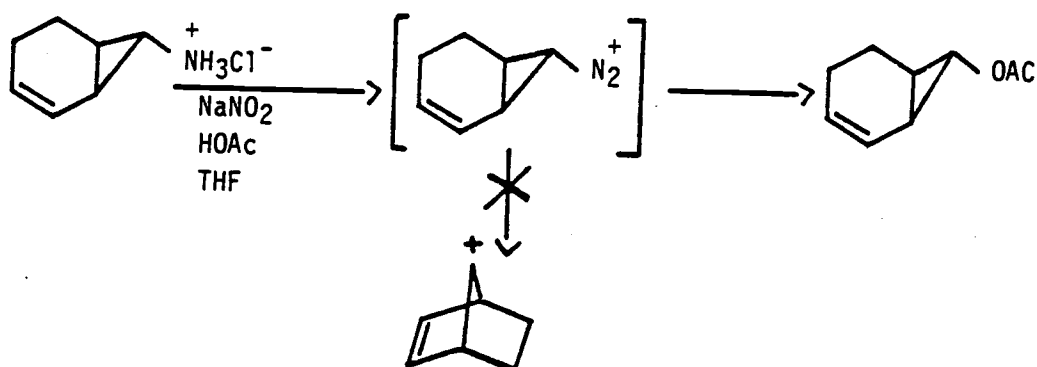
Stabilized carbenes have also been involved in bicyclic systems other than the norbornane system. The following system is one where the stabilized carbene reacts in a markedly different manner than the unstabilized one.[172]
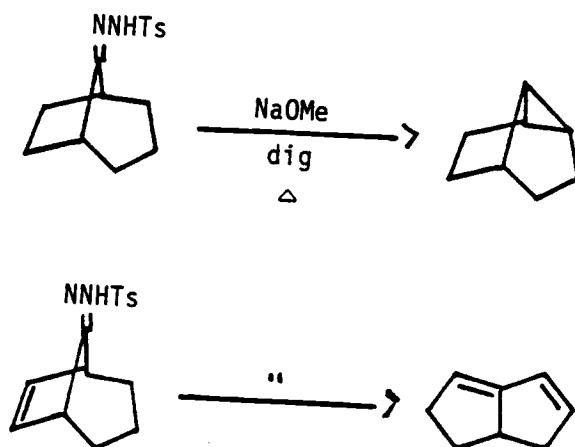
In the next example,[173] although the reactions of the stabilized carbene and its saturated analogue are different,

the contrast is not as striking as the last example.
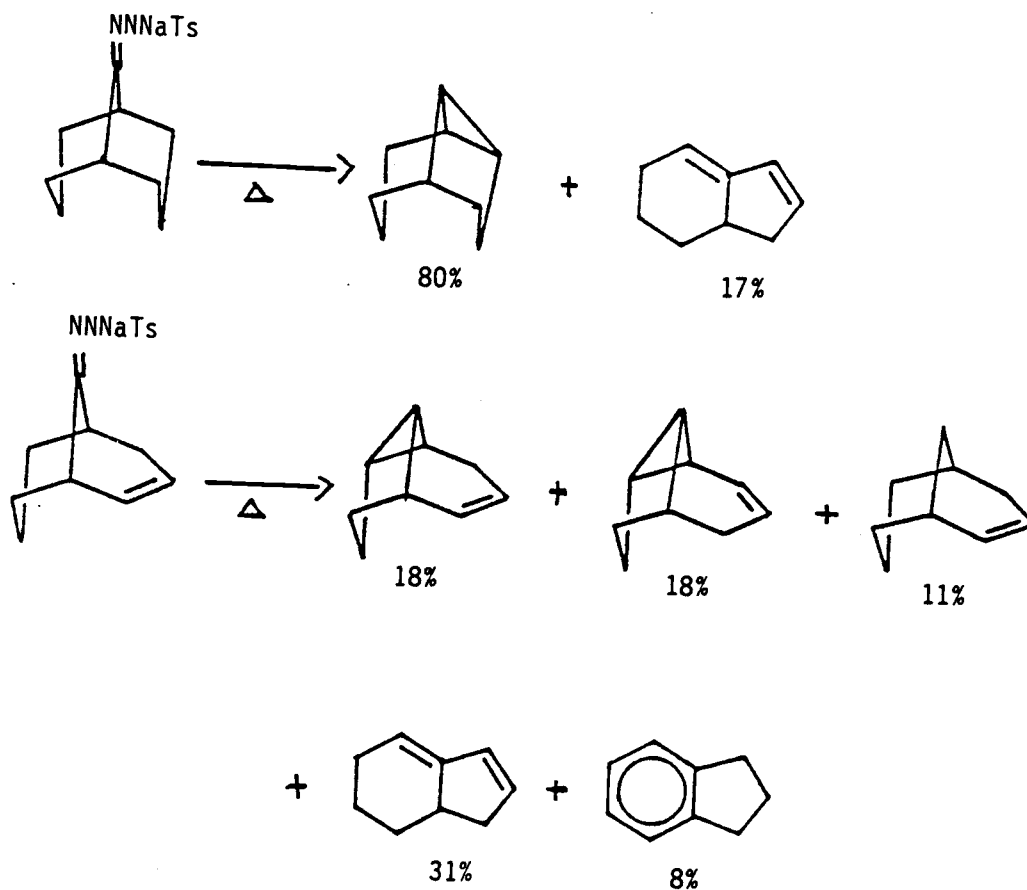
Although the chemistry of the saturated counterparts has not been studied, the following carbenes have been suggested as possibly being nonclassical.[174]
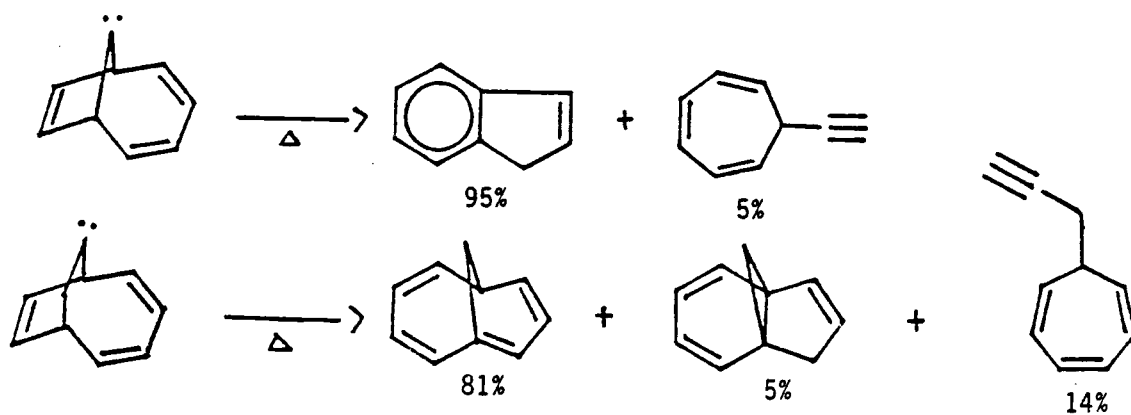
It is interesting to note that none of the β-hydrogen
insertion product
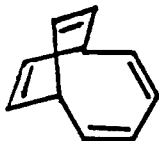
was formed in the thermal reaction, although substantial
amounts were produced in the photochemical reaction.

Recently some evidence has been presented that indicates
that cyclopropyl and cyclobutyl adjacent to carbene centers
tend to stabilize that carbene, at least in cases where the
other group attached to the carbene center is a chlorine atom.
It has been determined that isopropylchlorocarbene is very
reluctant to add to alkenes, preferring to undergo a tertiary
β-hydrogen insertion to yield 1-chloro-2-methylpro
pene.[175] In contrast cyclopropylchlorocarbene adds very
readily to alkenes.[176] It has been determined that cyclo-
propylchlorocarbene addition to cis-butene is stereospecific
thus indicating a singlet state for the carbene. It has also
been determined that cyclopropylchlorocarbene adds to isobutylene
albeit in low yield (10%). Cyclobutylchlorocarbene has also
been found to add efficiently to alkenes.[177]

It should be pointed out that, as in carbonium ion chem-
istry, not everybody agrees with the concept of a nonclassical
carbene. W. M. Jones is one that is somewhat skeptical about
stabilized carbenes, although he agrees that some facts about
the chemistry of these carbenes is explained by a special
stabilization.[178]

    4. Carbene to Carbene Rearrangements

    This is an area that has been extensively studied and

there is a considerable number of examples known. Almost all

of the examples of carbene to carbene rearrangements involve

aromatic carbenes. The first rearrangement of the type was

discovered by Staudinger and coworkers[8] when they found that

pyrolysis of diphenyl ketene afforded fluorene. The authors

did not realize that this was a carbene rearrangement and thus

the mechanism of this reaction was not known for many years.

It was not until 1969 that the mechanism began to be

unravelled when it was reported[179] that the same product,

heptafulvalene, was obtained upon pyrolysis of the sodium salts

of tropone tosylhydrazone and benzaldehyde tosylhydrazone.
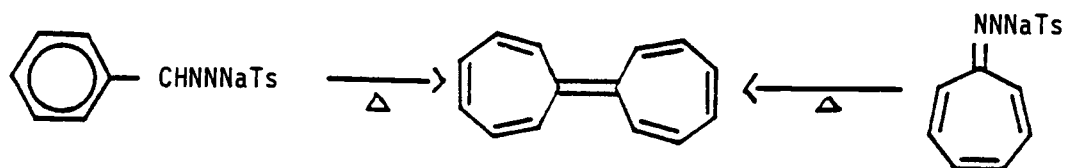
The mechanism proposed involved the rearrangement of phenyl-

carbene to cycloheptatrienylidene via a cyclopropene.
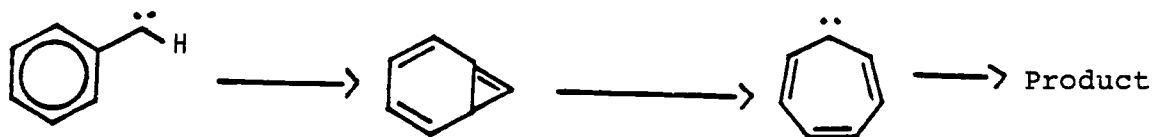
It was indicated that the product heptafulvalene could have

also arisen from dimerization of the cyclopropene or from the

alkene 1,2,4,6-cycloheptatriene formed by an α-hydrogen inser-

tion of cycloheptatrienylidene.
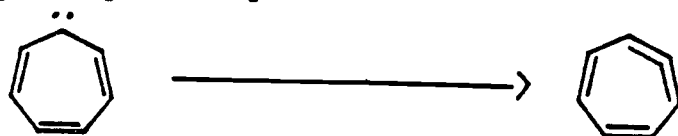
The allene intermediate was dismissed as a possible inter-

mediate. The authors felt that due to steric hindrance

the allene 1,2,4,6-cycloheptatriene could not exist but was rather a resonance form of cycloheptatrienylidene.

The results of W. M. Jones were confirmed and expanded by Wentrup and Wilczek.[180] It was found that phenylcarbene and cycloheptatrienylidene interconvert at 300°C in the gas phase. Furthermore, at higher temperatures (900°C), phenyl carbene but not cycloheptatrienylidene ring contracts to yield fulvenallene. The ring contraction
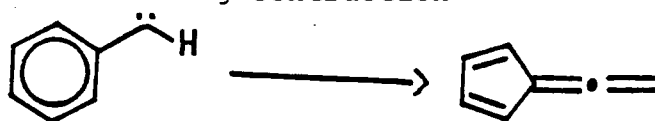
of phenylcarbene to fulvenallene was also observed by Kent, Hedaya and coworkers.[181] These authors found that the yield of fulvenallene was temperature dependent, the highest amounts observed at 900 and 1000°C while only a trace was observed at 600°C.

Wentrup and Wilczek[180] and Myers, Joines and W. M. Jones[182] showed the reaction of diphenyl carbene to yield fluorene involves a carbene to carbene rearrangement. From the position of the methyl(s) in the product fluorene, it was possible to determine that the initially formed carbene ring expanded to form a substituted cycloheptatrienylidene which ring-contracted to form a substituted biphenylcarbene which inserted into a carbon-hydrogen bond to afford the product (see following page).

It was also discovered that if the carbene had an internal trap, no dimerization occurred.[183] Pyrolysis of either iso-meric (ortho, para or meta) tolyldiazomethane afforded benzo-

R = H Ref. 196
R = Me Ref. 198
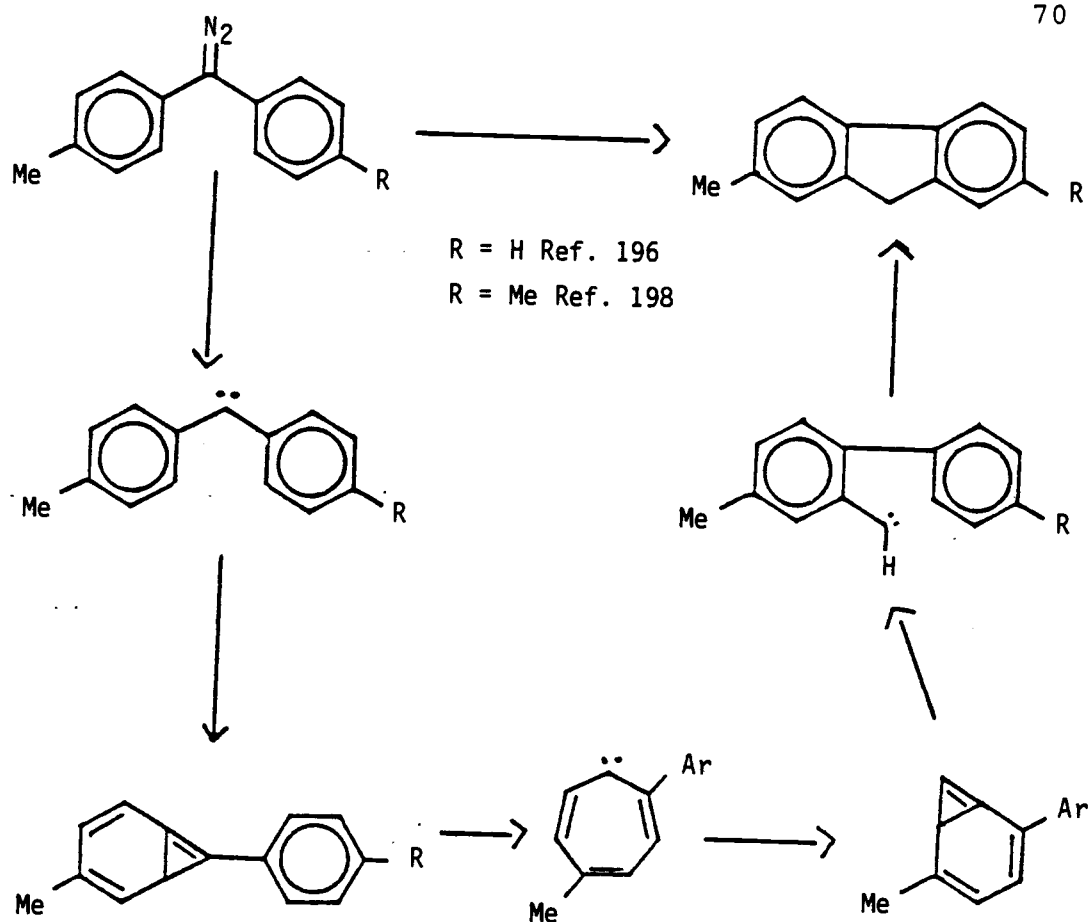
cyclobuitene and styrene. The reaction was explained by a
carbene to carbene rearrangement.

o,p   0.8   :   1.0
m   2.8   :   1.0
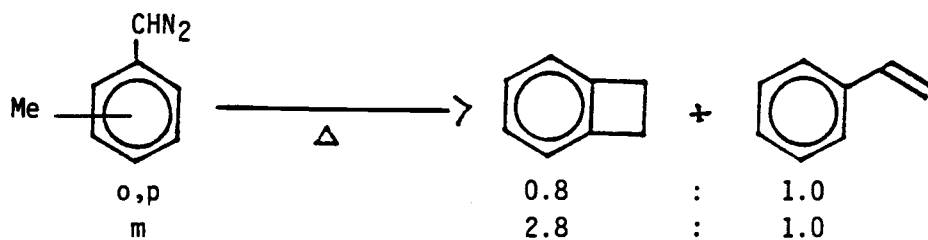
The mechanism, illustrated for the meta isomer, is the
following:
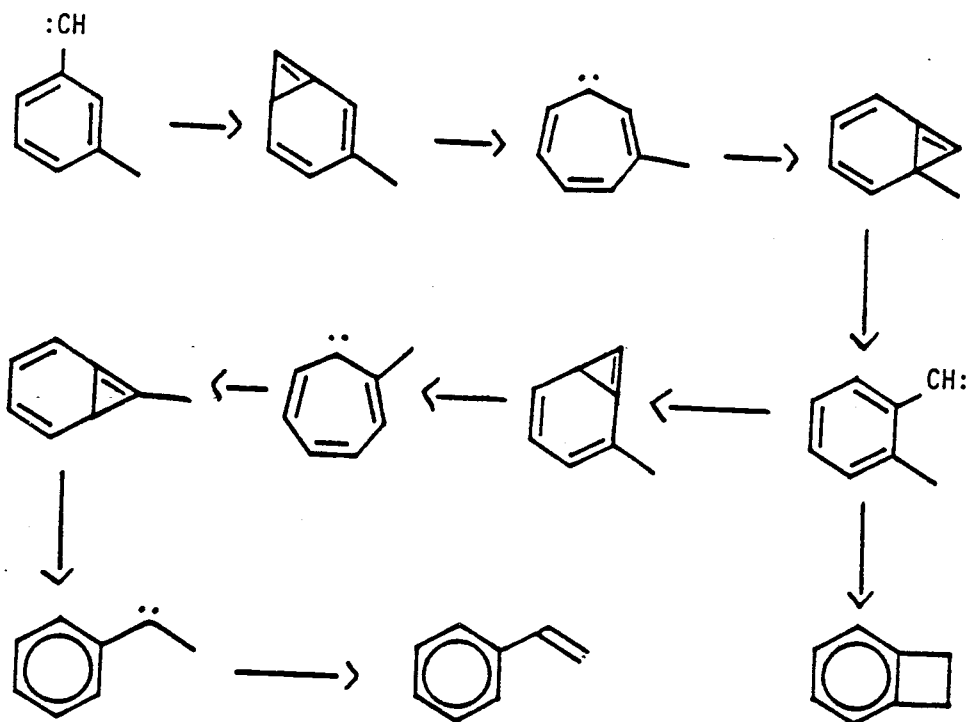
Further evidence was presented for the above mechanism by some labeling studies of Hedaya and Kent[184] and by Shechter and coworkers.[185] Hedaya and Kent utilized p-tolyldiazomethane labeled with carbon-13, whereas Shechter employed o-tolyldiazomethane labeled with deuterium.
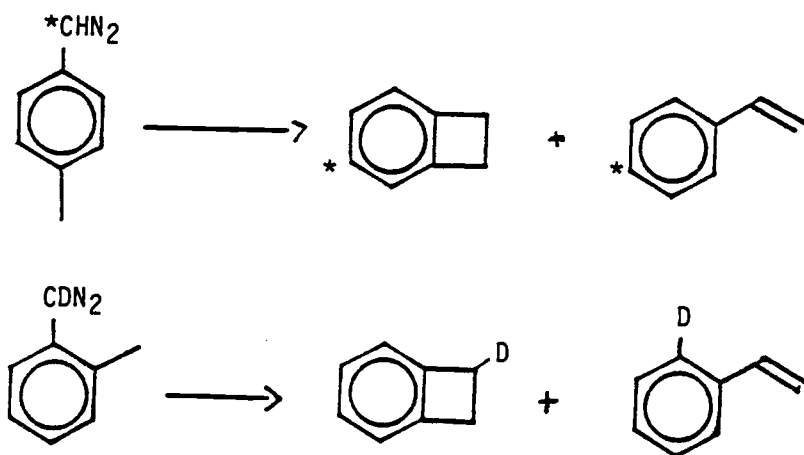
The intermediacy of the cyclopropene in the phenylcarbene-cycloheptatrienylidene rearrangement was demonstrated by W. M. Jones and Coburn[186] who were able to trap it with cyclopentadiene and furan.

X = O, CH_2
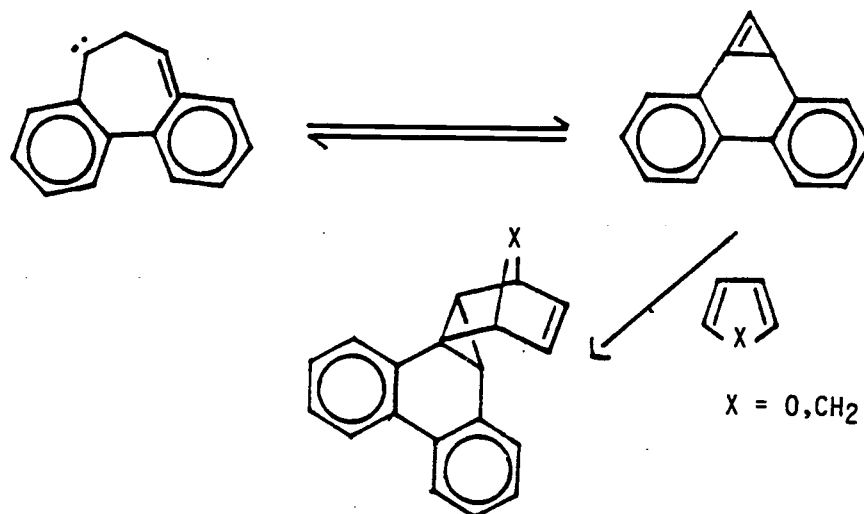
The above reaction is an example of the rearrangement in solution. The first examples of the phenylcarbene-cycloheptatrienylidenes were all in the gas phase at high temperature. W. M. Jones and coworkers[187] showed that the rearrangement also occurs in solution.

The rearrangement in solution of cycloheptatrienylidene has not been accomplished, the only product obtained is the dimer heptafulvalene.[188] Rearrangement is observed in cases where dimerization is disfavored, as in the case where substituents are placed in the 2 and 7 positions of the tropone ring. The following reaction is an example of this technique:
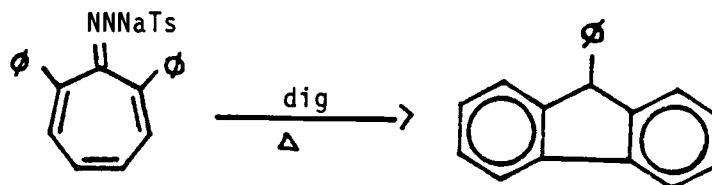
It was mentioned previously that the allene 1,2,4,6-cycloheptatriene was dismissed as an intermediate. Recently there have been some reports that implicate the cyclic allene. A theoretical study by Öhrn, Jones and coworkers[189] employing semiempirical INDO calculations indicate that the non-planar 1,2,4,6-cycloheptatetraene structure is more stable than cycloheptatrienylidene. The same conclusion was reached by Dewar and Landman[190] who employed MINDO/3 calculations. W. M. Jones and Mayor[191] indicated that back in 1970 it was reported by Untch[192] that dehydrochlorination of 1-, 2- or 3-chloro-1,3,5-cycloheptatriene yielded an intermediate that had the same properties as the intermediate generated from the sodium salt of tropone tosylhydrazone. In analogy to other eliminations, the alkene 1,2,4,6-cycloheptatriene is very likely the first intermediate formed in the dehydrochlorination of the chlorocycloheptatrienes.
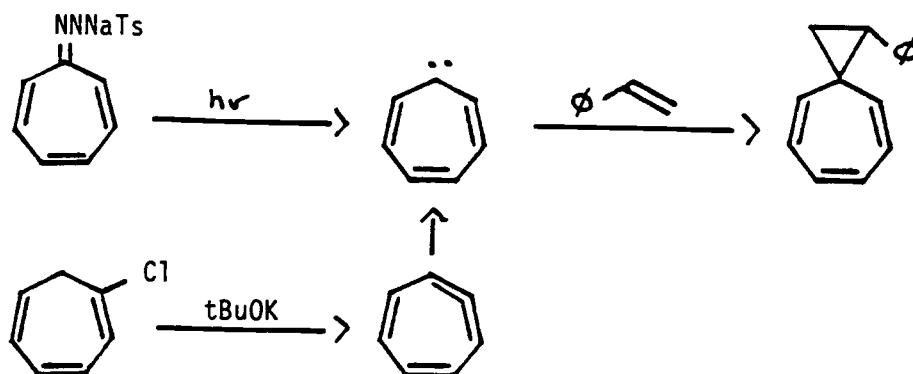
Since the expected addition of an alkene to styrene would be a cyclobutane:
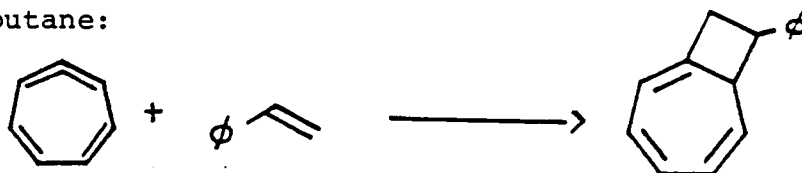
and not the cyclopropane, this fact suggests that the allene either converts entirely to cycloheptatrienylidene or that there is an equilibrium between the two species. To probe further into the carbene-allene problem, 1,2-benzo-5-bromo-1,3,5-cycloheptatriene was synthesized and treated with potassium tert-butoxide in tetrahydrofuran.[191] In this compound, the carbene can be formed directly:
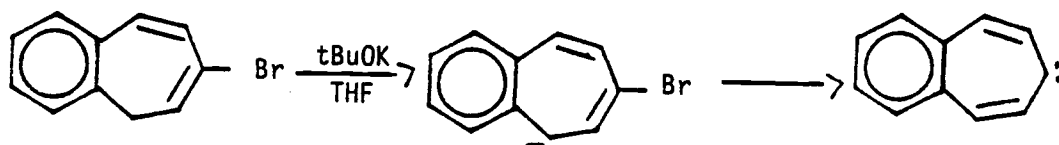
but formation of the allene would require disruption of aromaticity in the benzene ring:

Treatment of the bromo compound for one week with potassium tert-butoxide afforded only starting material. In contrast, the isomeric chloro and the related methyl bromo compounds did react to afford products derived from an allene.[193]
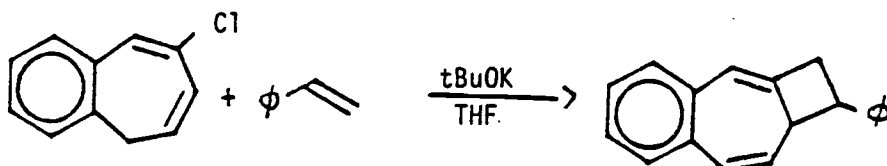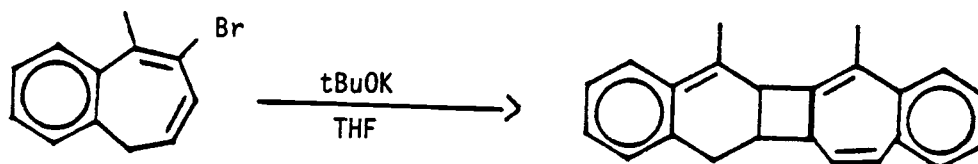
The above two compounds can dehydrohalogenate to the alkene without disrupting the aromatic ring. Thus the first intermediate generated in these compounds is the allene which can then rearrange to the carbene. The carbene can then add to alkenes to yield cyclopropanes or it can rearrange to a phenylcarbene. An example of this last possibility has been provided recently by Jones and Mayor.[194]
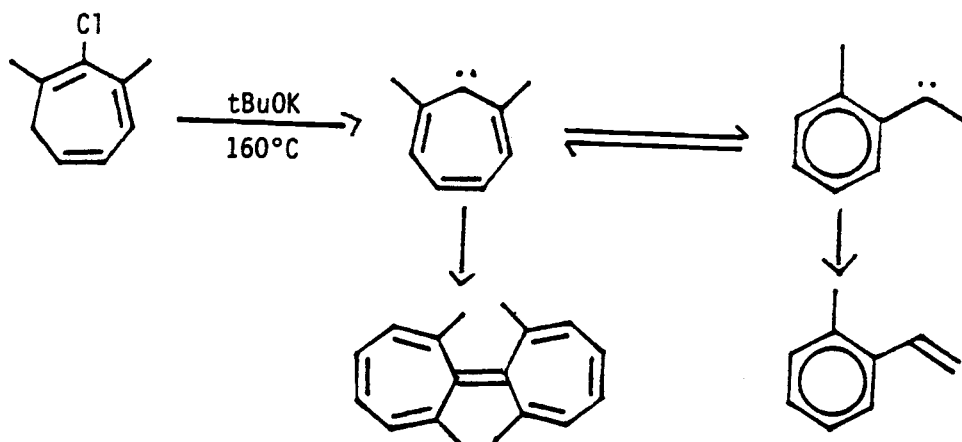
The data indicate that the allene 1,2,4,6-cycloheptatetraene can be formed and that it can isomerize to the carbene. The data, however, do not allow one to completely describe the phenyl carbene to cycloheptatrienylidene rearrangement. There is little doubt that the first step involves formation of the cyclopropene but it is not known whether the cyclopropene compound opens up to the allene or to cycloheptatrienylidene.
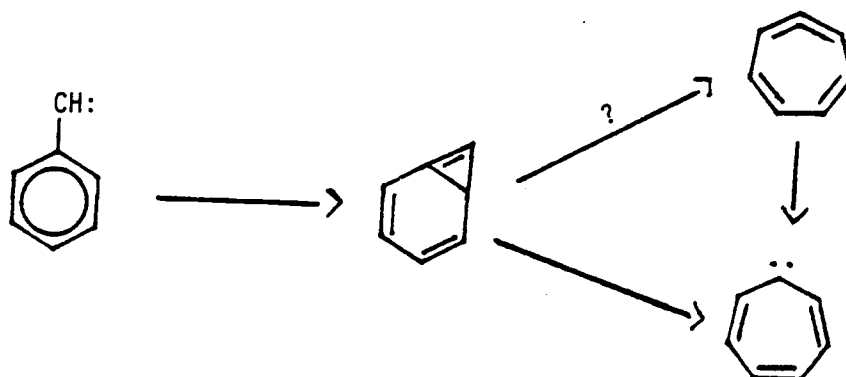
Examples of carbene to carbene rearrangements aside from the phenylcarbene to cycloheptatrienylidene rearrangement are very scarce. The first example concerns the contrasting behavior of two isomeric carbenes in solution containing the 7-carbenanorbornane skeleton.[195]
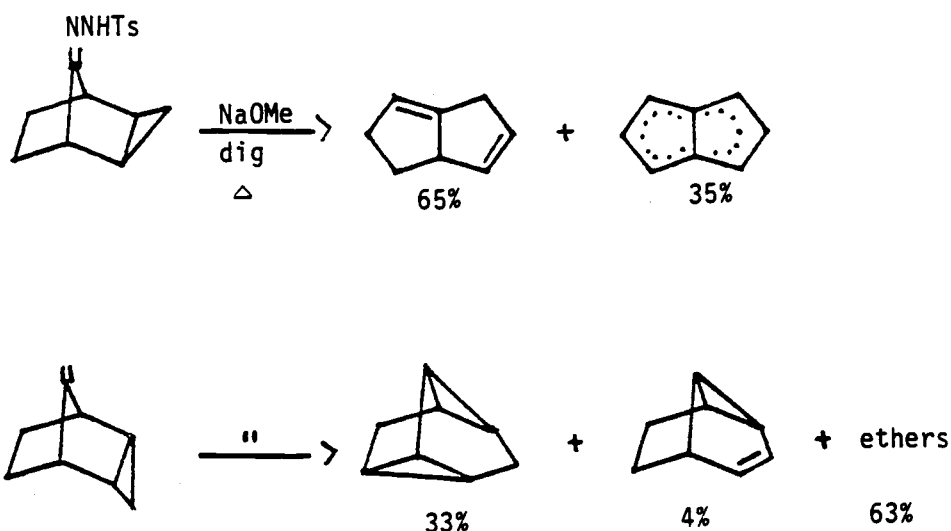
In the first example, where the cyclopropane is in the exo position, the products are rationalized as arising from a 1,2-alkyl shift of the ethano bridge and rupture of the cyclopropane ring. The products of the second example were accounted for by a carbene to carbene rearrangement after a

very detailed study of the reaction that involved deuterium
labeling. The first step was to reduce the yield of methyl-
ethers produced by a carbonium ion reaction. Two approaches
were employed which yielded the same product distribution.

NNRTs

a) R=H,NaH
dig, △

b) R=D,NaOMe
dig, △

81%   +   10%   + ethers

9%
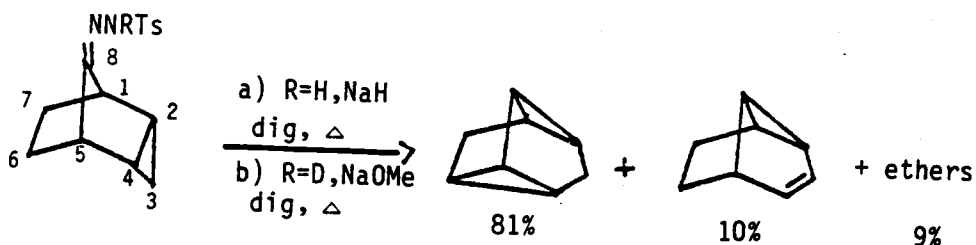
A reasonable mechanism to propose according to the authors
was to envision a migration of the exo hydrogen on C-6 to the
carbene center, bonding of the carbene center to C-2, rupture
of the C-2 to C-4 bond, and bonding between C-4 and C-6. This
process could occur in a concerted intramolecular fashion
since it is a symmetry allowed σ_a^2 + ω_a^2 + ω_a^0 hydrogen shift
or in an intermolecular process.

To test this hypothesis, the dideutered analogue was syn-
thesized and decomposed.

NNHTs

81%   +   10%
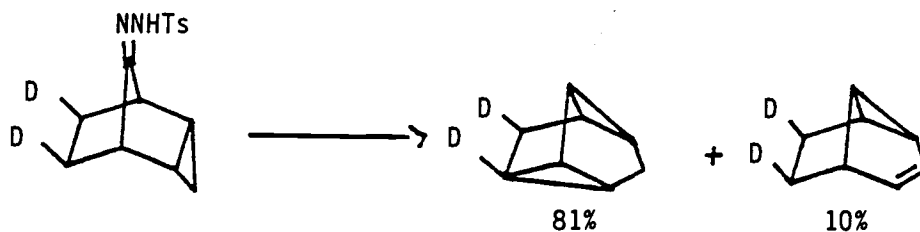
The product ratio was the same as the one for the undeuterated compound indicating that there is no isotope effect. Mass spectral analysis of the products indicated almost no deuterium (less than 3%) was lost on either product. This fact rules out the intermolecular process. Nmr analysis of the products seemed to indicate that no deuterium had migrated during the course of the reaction, but the analysis was complicated by the C_{2v} symmetry of the major product. To circumvent this problem, a less symmetric tosylhydrazone was prepared and decomposed.
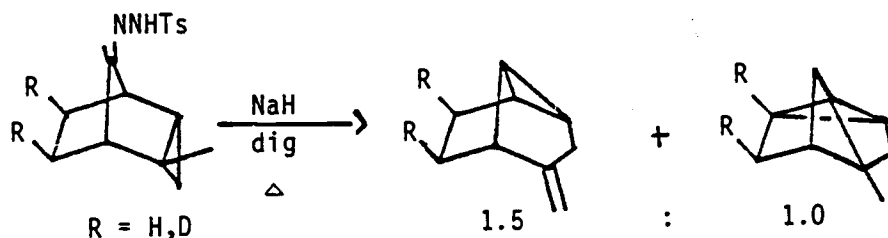
The products obtained are analogous to the ones obtained in the compound without the methyl group. To test the mechanism of the exo-hydrogen migration, the 6,7 exo, exo-dideuterio analogue was also synthesized and decomposed. Mass spectral analysis of the products indicated that less than 4% deuterium was lost. Nmr analysis of the minor product indicated unequivocally that no deuterium migration had occurred. This result can be explained by a carbene to carbene rearrangement:
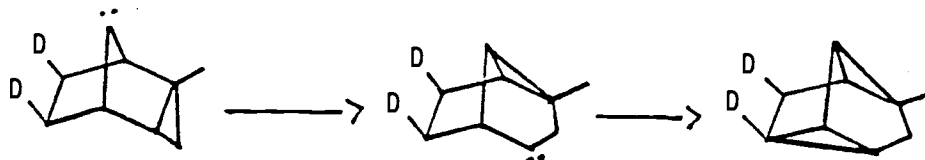
If this mechanism were operating, it would require the loss

of hydrogen at C-4 and gain of hydrogen at the carbene center.

To test this hypothesis the following mono and trideuterated

tosylhydrazones were studied.
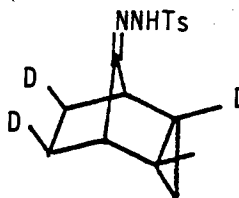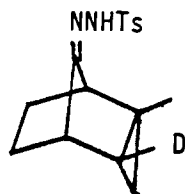
Mass spectral and nmr analysis of the tetracyclic product

obtained on decomposition of the above tosylhydrazones in-

dicates a total loss of deuterium at C-4 and the gain of some

of that deuterium at the carbene center. This provides quite

compelling evidence for the carbene to carbene rearrangement

referred to above. The authors postulated a nonclassical,

stabilized carbene to explain the different behavior evi-

denced by changing the cyclopropane ring from the endo to the

exo position. It should be noted that Murahashi and co-

workers[169] have studied the behavior of the same carbenes

(see the preceding section on nonclassical carbenes) and

found them to yield different products.

The second example involves the rearrangement of 7-

carbena-2-norcarene to 7-carbenanorbornene[171] and has already

been discussed in the section dealing with nonclassical car-

benes.

The third and last example involves a rearrangement similar to the second example. The vinylcyclopropylidene to 3-cyclopentenylidene rearrangement is a common and well-known rearrangement of carbenoids.[196] But the only known case of this rearrangement for a free carbene is the second example. An attempt was made to see if 2-vinylcylobutyl-idene would rearrange to 3-cyclohexenylidene in the gas phase but the main product obtained was the ring contracted methylene-cyclopropane.[197]
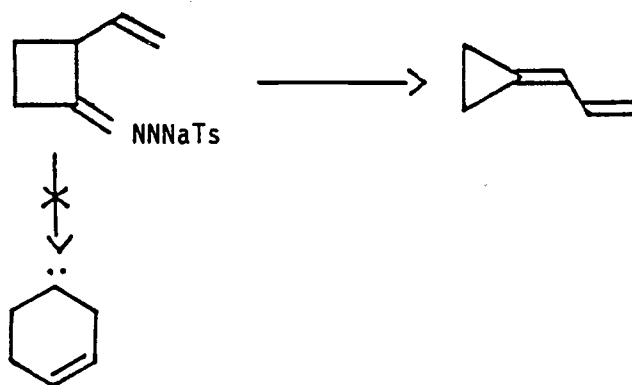
It has been found recently that a strained bicyclic compound that contained the 2-vinylcyclobutylidene moiety did undergo the rearrangement.[198]
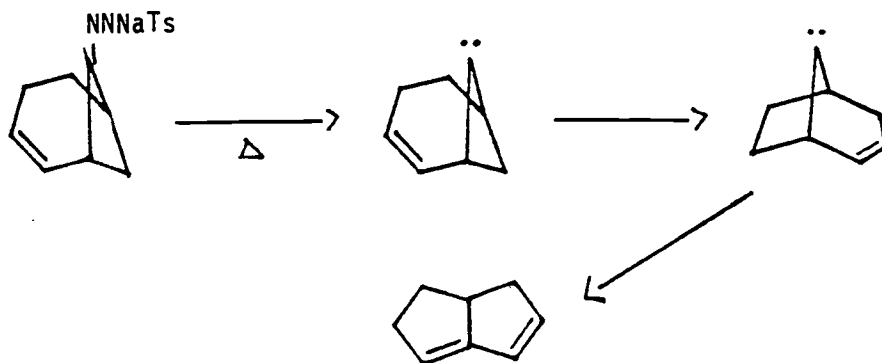
The rearranged carbene 8-carbenabicyclo [3.2.1]-2-octene
has also been discussed in the section of nonclassical car-
benes and affords the bicyclooctadiene in 97% yield.[172]

IV. α-Ketocarbenes

The main difference between alkylcarbenes and α-keto-
carbenes is that the latter undergo the Wolff rearrangement
in addition to the other reactions that alkyl carbenes under-
go. The Wolff rearrangement is a very well-known reaction
and is the basis for the Arndt-Eistert synthesis whereby a
carboxylic acid is converted to its next higher homolog.

α-Ketocarbenes are generated by thermolysis or photolysis
of the corresponding diazoketone. Due to the presence of the
extra carbonyl, the syntheses of the diazoketones are some-
what different than diazoalkenes. Also diazoketones are more
stable than diazoalkanes.

A. Synthesis of Diazoketones

1. Reaction of an acid chloride with diazomethane

This method of generating diazoketones has been used
quite extensively, especially in the Arndt-Eistert synthe-
sis.[199] In this procedure, an ether solution of the acid
chloride is added to an excess (2 equivalents or more) of
diazomethane in ether at 0°C. Addition of triethylamine
renders the excess of diazomethane unnecessary.[200] It has
been reported that dichloromethane can be used as a solvent
instead of ether.[201] The following reactions take place:[199]

$$R-\overset{\overset{\displaystyle O}{\parallel}}{C}-Cl + CH_2N_2 \longrightarrow R-\overset{\overset{\displaystyle O}{\parallel}}{C}-CHN_2 + HCl$$

$$HCl + CH_2N_2 \longrightarrow CH_3Cl + N_2$$

$$HCl + RCOCHN_2 \longrightarrow RCOCH_2Cl + N_2$$
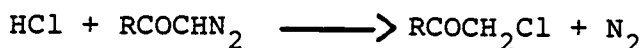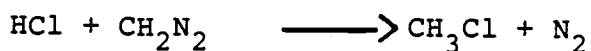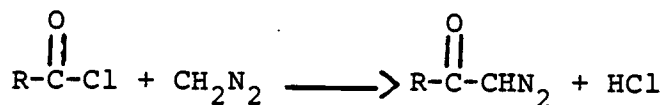
Thus to insure a good yield of diazoketone it is imperative to neutralize the hydrochloric acid generated in the first step with either excess diazomethane or triethylamine, the addition of acid chloride to the diazomethane has to be slow and at a low temperature. The reaction seems to be quite general and occurs under fairly mild conditions. A large number of compounds are known to undergo the reaction.[199] Some examples are the following:[202,203]
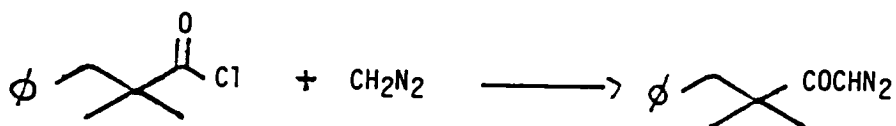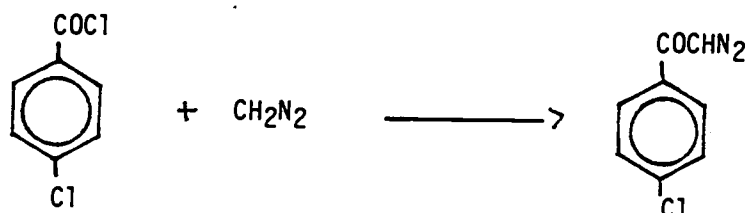
The reaction has been applied to some substituted heterocyclic systems.[204,205]
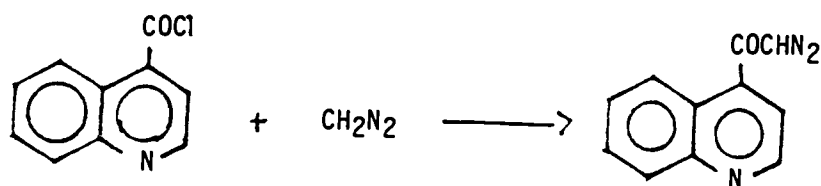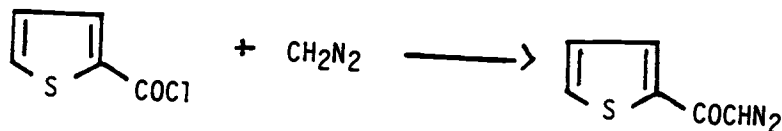
The reaction is very mild and proceeds in the presence of a lactone or a cyclopropane ring adjacent to the acid chloride function.[206,207]
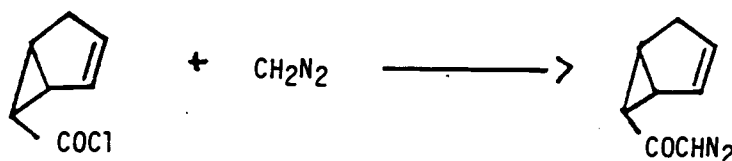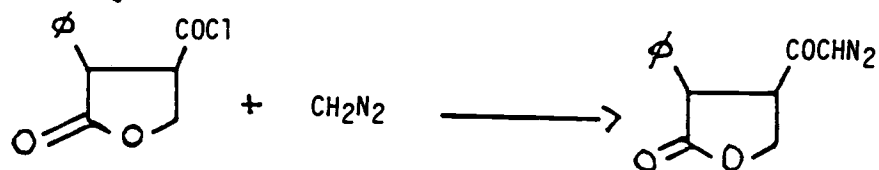
The reaction also proceeds in the presence of double bonds. In the case of α,β-unsaturated acid chloride diazo-ketopyrazolines can be formed if the reaction is allowed to proceed for longer periods of time.[208]

R = H,Me
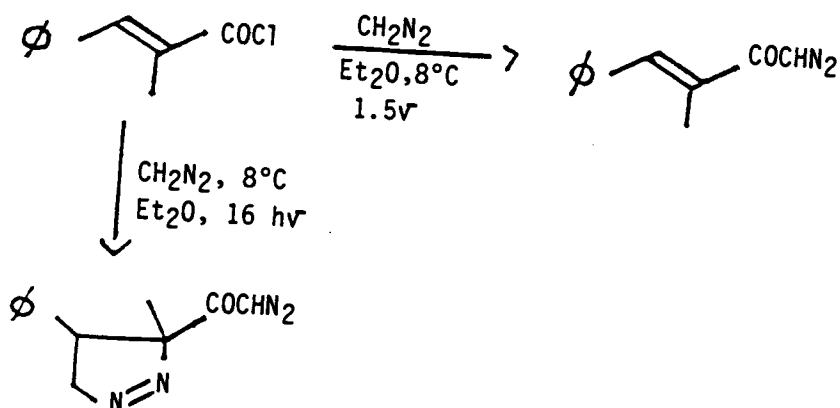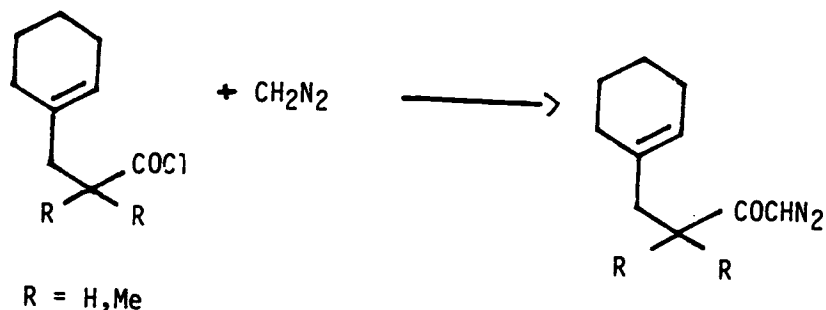
The reaction seems to be subject to steric interferences. The following acid chlorides have been reported as not affording the diazoketone:[199]
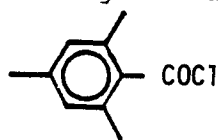
Several variations have been developed for the reaction. Instead of using the acid chloride, one can use the anhydride. In some cases, as for example in the preparation of trifluoro-diazoacetone,[209] this method is preferred to the acid chloride one. Another variation is to use higher homologues of diazomethane and react them with the acid chloride. In these cases, an excess of the diazoalkane has to be avoided because the resulting diazoketone reacts further with the diazo-alkane.[209] In these cases, addition of one equivalent of triethylamine leads to good yields of diazoketones.[210]
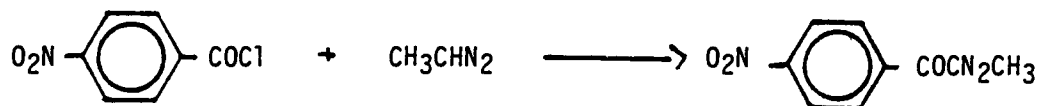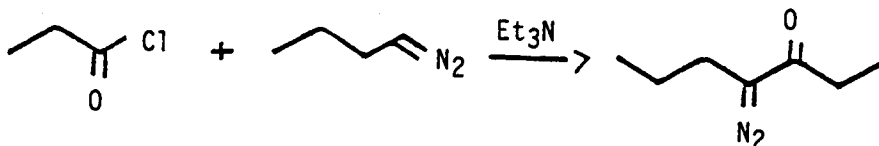
Although the reaction of an acid chloride or an acid anhydride with a diazoalkene is quite general, its main limitation is the inherent one of not being able to generate cyclic diazoketones.

2. Oxidation of Ketohydrazones

This is the oldest way of preparing diazoketones and parallels the synthesis of diazoalkanes from the corresponding hydrazone. The first report of this method is the one from Curtius.[212] The reaction seems to be quite general and not as susceptible to steric hindrance as the Arndt-Eistert method. The Curtius reaction not only affords 2,4,6-trimethylbenzoyldiazomethane in very good yield but it also affords the much more sterically hindered compound 2,4,6-triisopropylbenzoyldiazomethane in excellent yield.[213]
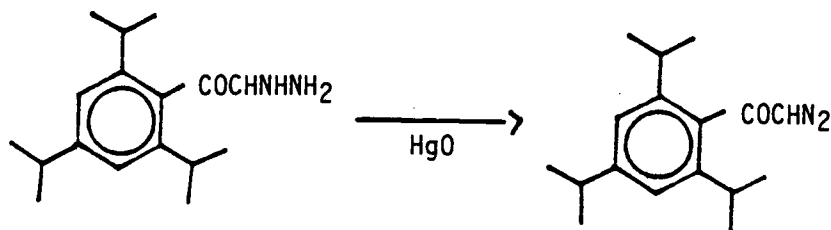
As with the Arndt-Eistert synthesis there are some

examples known that have a heterocyclic ring as part of the molecule.[214] In contrast to the Arndt-Eistert method, the Curtius reaction is applicable to synthesis of cyclic diazo-ketones.[215]
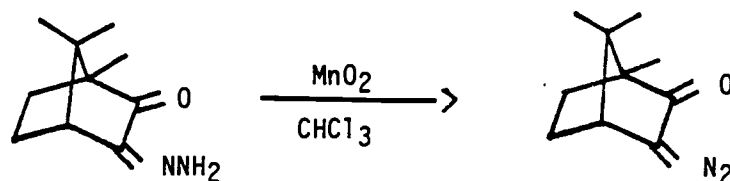
The usual oxidant has been yellow mercury (II) oxide[212-14] and silver (I) oxide.[216] Recently several variations have been introduced. Newman and Arkell reported very good results with mercury (II) trifluoroacetate in triethylamine.[217]
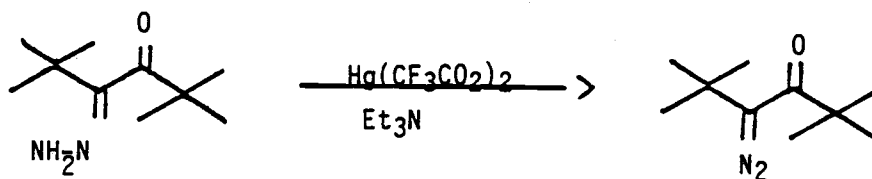
Two further methods for the oxidation of ketohydrazones were reported by Morrison, Danishefsky and Yates:[215] oxidation with calcium hypochlorite in basic methanolic solution and oxidation with activated manganese (IV) oxide in chloroform solution. In all the cases compared, the second method was superior to the first one. Furthermore, the manganese (IV) oxide was compared to the mercury (II) oxide method in one case and found superior.
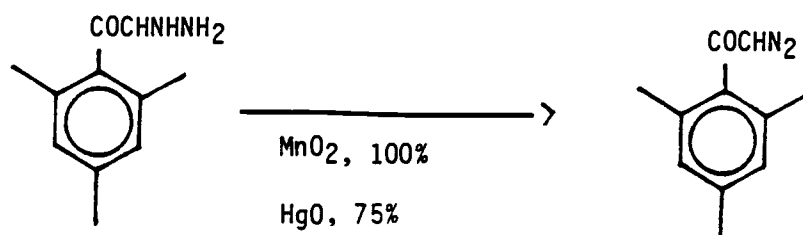
3. Chloramine Oxidation of Ketoximes

This reaction was discovered by Forster[218] in 1915.

The synthesis of diazocamphor and azibenzyl were described

in the first report of the chloramine reaction.
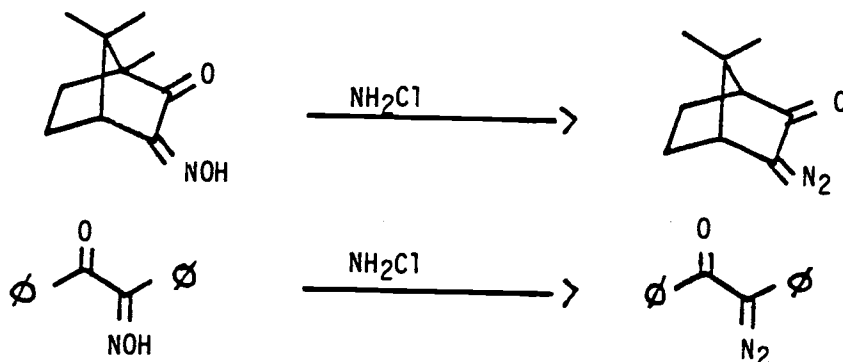
The reaction lay dormant until it was resurrected in the

fifties by Horner, Kirmse, Cava, Meinwald and Gassman[219]

among others. The reaction was applied to the syntheses

of some fused cyclobutenes.
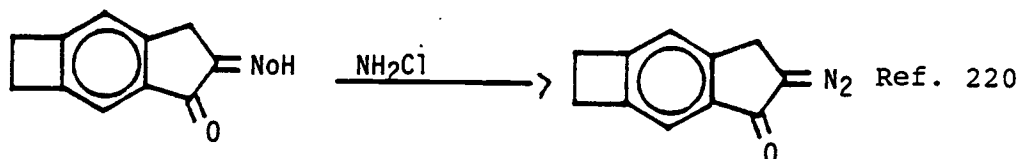
An improvement in the yield of diazoketone was reported

upon substitution of chloramine by amino-0-sulfonic acid.

The ketoximes are generally prepared from the corresponding

ketones by reaction with an alkylnitrite (generally iso-

amylnitrite).

4. Decomposition of α-Ketotosylhydrazones

Cava and coworkers[219c] developed a method whereby a

ketotosylhydrazone is decomposed in aqueous sodium hydroxide

solution to afford the diazoketone in good yield. The

ketotosylhydrazones are prepared by reacting the diketones with tosylhydrazine in methanol or some other solvents.

The reaction has been used mostly to generate cyclic diazoketones although there are a few examples of acyclic ones. There are some examples in which the reaction does not afford the desired product.[221]
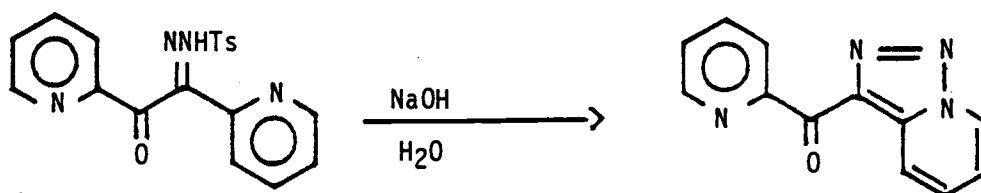
An interesting application of this reaction has been the synthesis of diazoketones from benzoquinones.[222] These compounds are interesting because their structure is between a diazoketone and a diazonium zwitterion due to resonance interactions. It has been found that these compounds do undergo the Wolff rearrangement.[223]

An example of the complementarity of this method to the chloramine one was provided by Cava and coworkers.[219c]
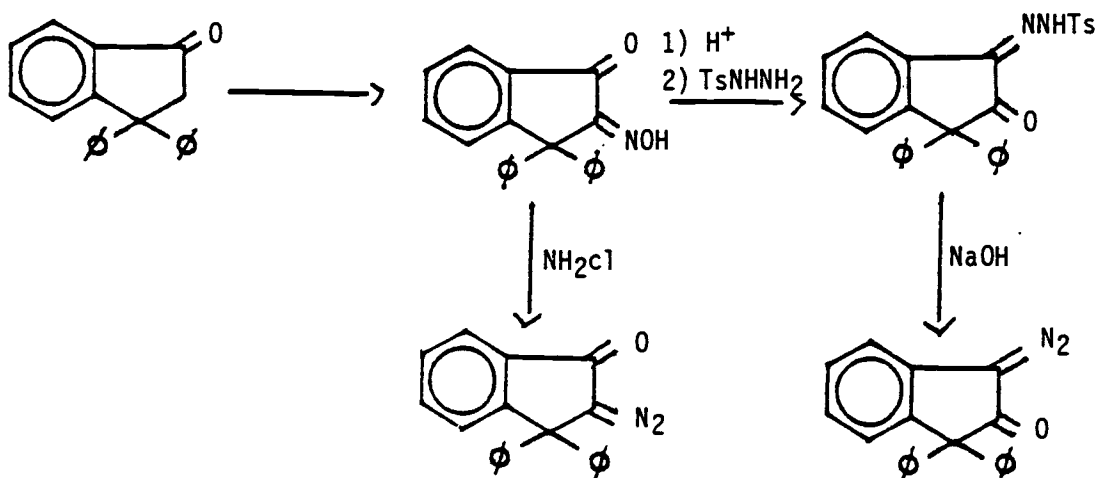
The last three methods (oxidation of ketohydrazones, chloramine reaction with ketoximes and decomposition of keto-tosylhydrazones) have the advantage over the Arndt-Eistert reaction that they can be applied to the synthesis of cyclic diazoketones. Their main disadvantage is one of regiochemistry since the three of them start with α-diketones. In cases where the two substituents are similar, a mixture of products may result. This is a problem that has not been examined closely in the literature and few examples are available.

5. Decomposition of Nitroso Compounds

This method is a very old one and is similar to the one used for the syntheses of diazoalkanes. It was first used by Schiff[224] to prepare diazocamphor and by Angel[225] to prepare diazoacetophenone among other compounds.

This method has not been employed very much. One possible reason is that the yields are not very high and in many cases the diazo compound cannot be isolated. The following examples show two cases where the diazo compound was not isolated.[226]
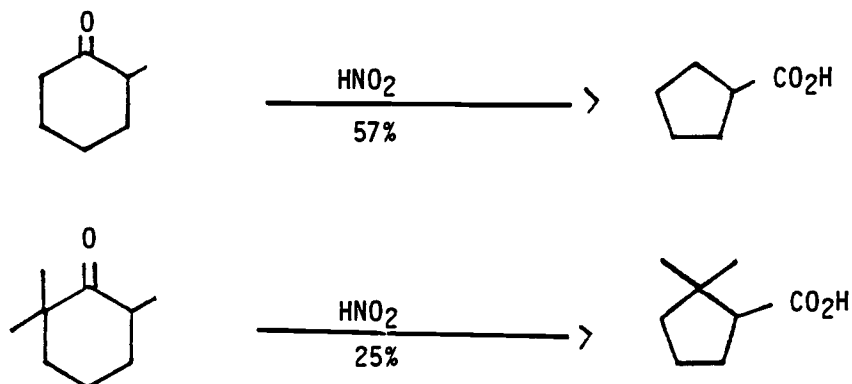
That this method is potentially quite useful was demon-strated by Hauser and Sieg[227] who introduced the diazo sub-stituent into the complex skeleton of a penicillin derivative.

$$\xrightarrow[\text{Me}_2\text{CO/H}_2\text{O}]{\text{NaNO}_2}$$
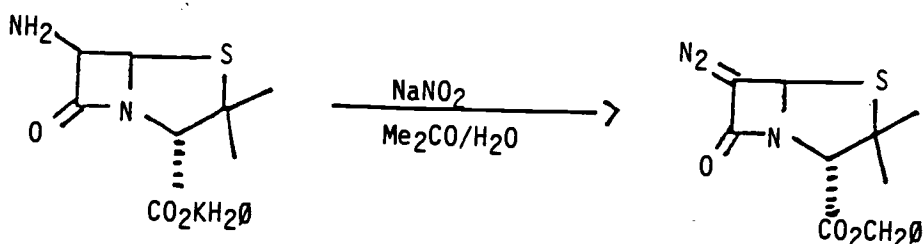
In 1957, Franzen[228] introduced a modification that improved the yield considerably. The modification consisted of acylating the amine to the amide.

$$\xrightarrow[\text{2) NaOMe}]{\text{1) N}_2\text{O}_3}$$

$$\xrightarrow{\text{"}}$$
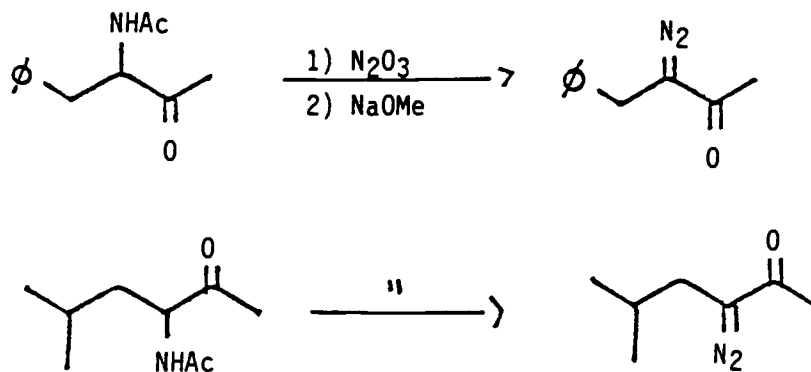
The nitrosation of the amide and decomposition method has been employed to synthesize azibenzil with a carbon-13 label on the carbonyl group.[229]

$$\xrightarrow[\text{2) NaOMe}]{\text{1) N}_2\text{O}_3}$$
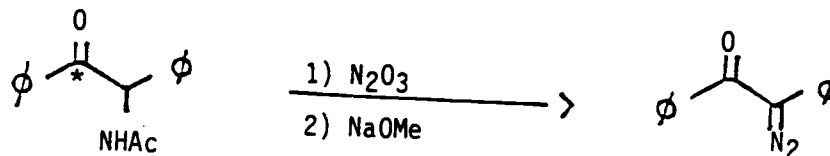
6. Diazo Group Transfer

This method of synthesis has been widely applied only

recently although some studies have been reported in the early literature.[230] The method was applied by Döering and De Puy[231] to the synthesis of diazocyclopentadiene. Several years later Regitz[232] and Hendrickson[233] reported the synthesis of several diazo compounds in good yield.

The method consists of reacting an activited methylene group with an azide (usually tosyl azide since it is readily available, stable and easy to handle). Some examples are the following:[234]
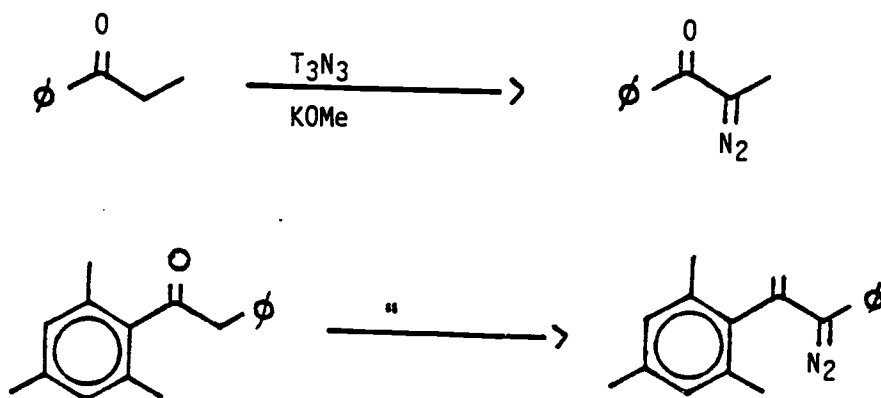
In the case of methylene groups activated by only the adjacent carbonyl, the reaction fails. To circumvent this problem a formyl group is attached via a Claisen condensation.
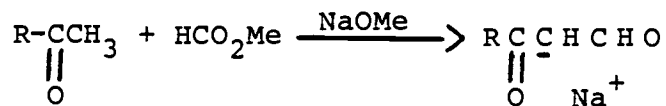
Now the methylene group is sufficiently activated to react with tosylazide. Aqueous work-up removes the activating group[233,235] and affords the diazoketone.

$$\underset{\underset{O}{\parallel}}{R \, C} \, \overset{-}{C}H \, CHO \; Na^+ \xrightarrow{\quad TsN_3 \quad} \underset{\underset{O}{\parallel}}{R - C} \, C\,H\,N_2$$
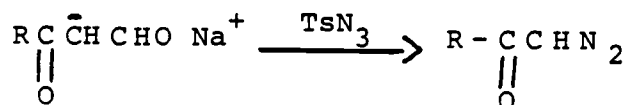
R	Yield
$p\text{-}BrC_6H_4$	78%
$p\text{-}NO_2C_6H_4$	58%
i-Pr	52%
t-Bu	83%

The reaction works very well in the synthesis of cyclic diazoketones. The homologous series from 2-diazocyclopenta-none to 2-diazocycloundecanone has been synthesized in yields ranging from 57-98%.[236] This method has been used also to generate the bicyclic compound diazocamphor[233] and some α,β-unsaturated diazoketones.[237]
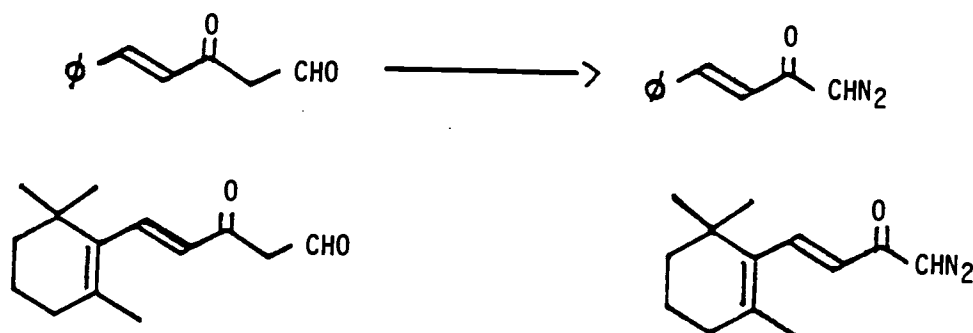
Arnold and coworkers[238] were able to obtain diazoalde-hydes by employing formylenamines.

$$\underset{}{\emptyset \, N\,H\,C\,H} = \overset{\overset{\displaystyle R}{\mid}}{C} - C\,H\,O \xrightarrow{\quad TsN_3 \quad} \underset{\underset{N_2}{\parallel}}{R - C} - C\,H\,O$$
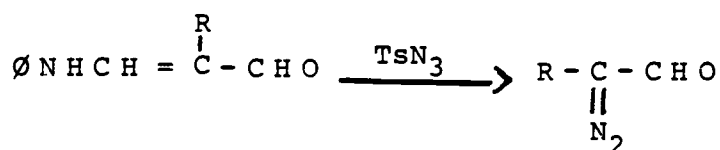
R	Yield
Me	68%
Et	77%
Pr	76%

B. The Wolff Rearrangement

As was mentioned before, a characteristic reaction of ketocarbenes is the Wolff rearrangement. This reaction is not observed in alkyl carbenes. The Wolff rearrangement consists of the migration of an alkyl group to yield a ketene.

$$R - \underset{\underset{N_2}{\|}}{C} - \underset{\underset{O}{\|}}{C} - R' \quad \xrightarrow[\text{or } \Delta]{h\nu} \quad R - \overset{..}{C} - \underset{\underset{O}{\|}}{C} - R' \longrightarrow \underset{R'}{\overset{R}{>}} C = C = O$$
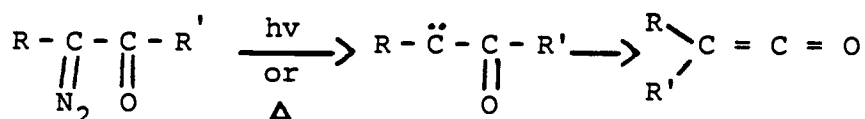
Generally the ketene is not isolated but rather reacted further with either water to yield an acid, an alcohol to yield an ester or ammonia to yield an amide. The reaction was discovered by Wolff in 1902.[239] Although the reaction has been known for a long time, the mechanism has not been completely elucidated.

Huggett and coworkers[240] synthesized diazoacetophenone labelled with carbon-13 on the carbonyl position. The labelled compound was subjected to Arndt-Eistert conditions to afford phenylacetic acid without any migration of the label.

$$\emptyset \overset{O}{\underset{*}{\overset{\|}{C}}} C H N_2 \longrightarrow \emptyset C H_2 \overset{*}{C} O_2 H \xrightarrow{[o]} \emptyset C O_2 H + C O_2$$
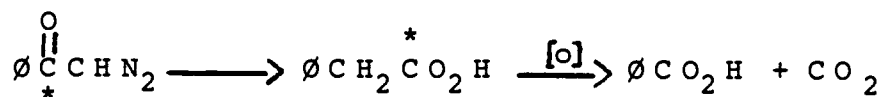
Later on Franzen[241] obtained similar results with 2-diazo-1,2-diphenylethanone labelled with carbon-14 in the carbonyl position.
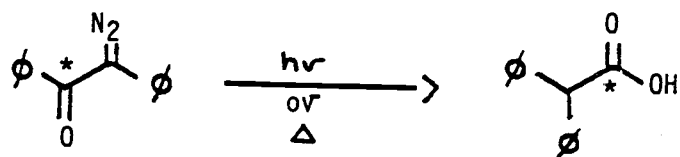
These experiments indicated that a ketene but not oxi-
rene was an intermediate in the Wolff rearrangement. The
intermediacy of ketenes had previously been demonstrated by
Schroeter[242] by isolation of diphenyl-ketene in the decomp-
osition of 2-diazo-1,2-diphenylethanone.

Wolff[239] had suggested that the mechanism of the reac-
tion involved ejection of a nitrogen molecule from the diazo-
ketone to afford a ketocarbene which then underwent alkyl
migration to give the ketene. This was the mechanism that
was accepted although no real experimental evidence existed
to implicate the intermediacy of the ketocarbene.[243]

It was not until 1968 that a ketocarbene was spectro-
scopically observed.[244] Low-temperature photolysis of 2-
diazo-1,2-diphneyl-2-ethanone afforded the corresponding
ketocarbene in its triplet state as determined by its epr
spectrum.

0 - 12%   74 - 80%   0 - 12%
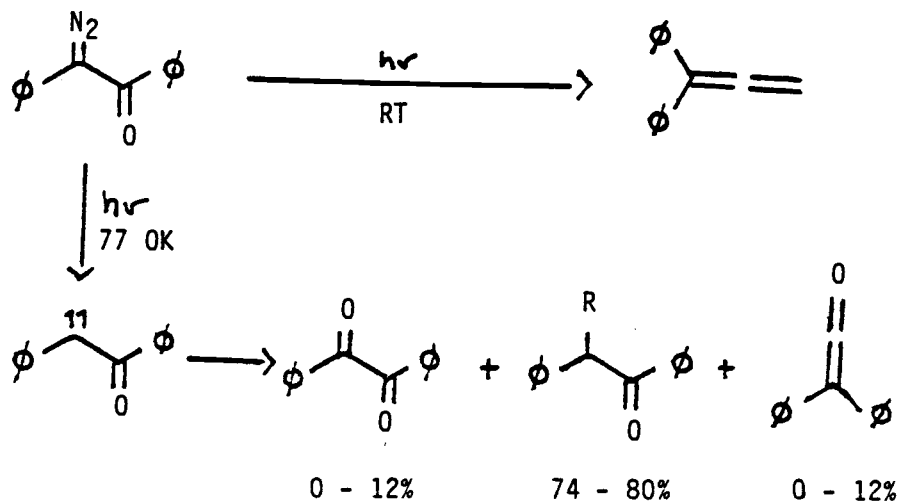
The fact that only a maximum of 12% of ketene was obtained
indicated that triplet carbene was very inefficient in the
Wolff rearrangement and may not even undergo it at all since
it is possible that some singlet carbene may be generated by
intersystem crossing. This experiment, however, did not prove
that the ketocarbene in its singlet state was the precursor
of the Wolff rearrangement since an equally valid alternative
possibility is a concerted step.

The fact that the triplet ketocarbene does not undergo
the Wolff rearrangement had been postulated earlier by Padwa
and Layton[245] to explain the results of the photolytic decom-
position of diazoacetophenone in different alcohols.

$$\phi\overset{O}{\overset{\|}{C}}CHN_2 \xrightarrow[ROH]{h\nu} \phi CH_2CO_2R + \phi\overset{O}{\overset{\|}{C}}CH_3$$

$$A \qquad B$$

ROH	MeOH	EtOH	iPrOH
A/B , hν direct	>300	5.9	2.5
A/B , hν sens.	7.3	1.1	<0.003
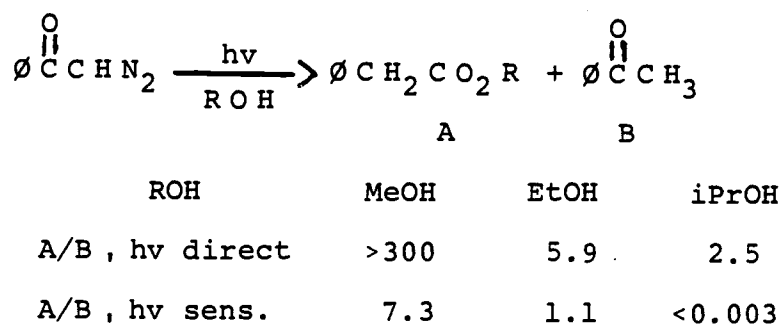
The results were explained by assuming that the diazoketone
has hydrogen bonded to the solvent. Direct irradiation affords
the singlet carbene which undergoes the Wolff rearrangement.
As the acidity of the alcohol is diminished, intersystem cross-
ing to the triplet increases and a larger amount of acetophenone
is formed. The sensitized reaction yields the triplet carbene
which undergoes radical reactions. Hydrogen abstraction from
methanol and ethanol are endothermic, thus intersystem crossing
to the singlet and subsequent formation of the ester compete

very effectively with formation of acetophenone. In the case
of 2-propanol hydrogen abstraction is exothermic, thus it is
favored over intersystem crossing and formation of the ester
is not competitive.

M. Jones and Ando[246] also determined that triplet carbene
does not undergo the Wolff rearrangement. Direct photolysis
of 2-diazocyclohexanone in 2-butene afforded only the product
of Wolff rearrangement whereas sensitized photolysis affords
cyclopropane products formed in a non-stereospecific manner.
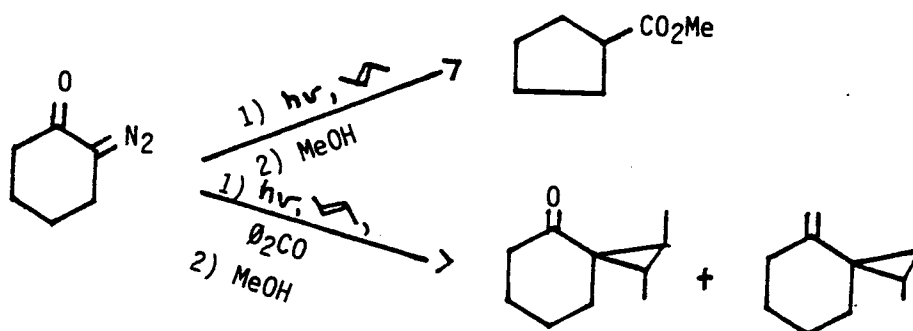
Strausz and coworkers[247] provided experimental evidence
that an oxirene was formed in the gas phase photolysis of 3-
diazo-2-butanone and 1-diazo-2-propanone by using carbonyl-
labelled reactants.

In an effort to understand better the factors affecting
the Wolff rearrangement, Strausz and Frater[248] repeated
Franzen's experiment with 2-diazo-1,2-diphenylethanone and
were able to determine that oxirene particpates to the extent
of 54% in cyclopentene and 46% in dioxane/water.
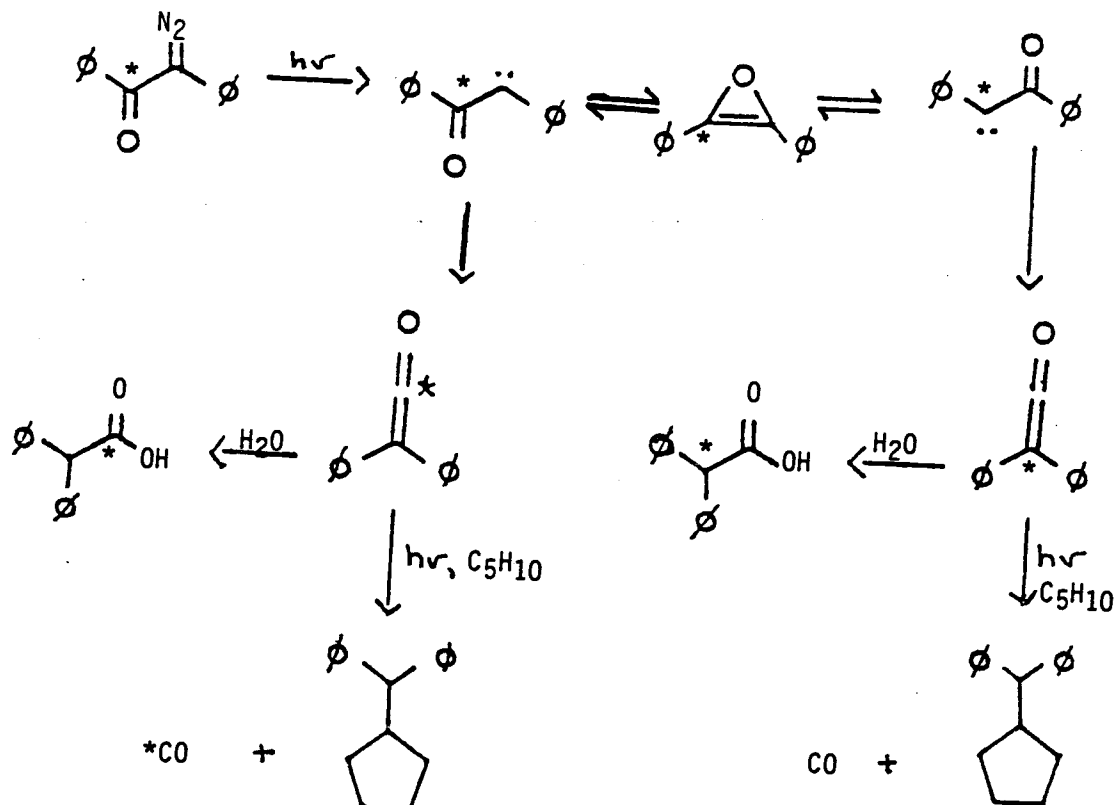
Contrary to the photochemical reaction, the thermal Wolff rearrangement of 2-diazo-1,2-diphenylethanone does not involve oxirene. Also the amount of oxirene participation in the photochemical reaction is somewhat dependent on the wavelenth of excitation.[249] Zeller and coworkers[250] also repeated Franzen's experiment and obtained similar results to those obtained by Strauzs.

Matlin and Sammes[251] showed that there was a significant amount of oxirene participation in the photolysis of 3-diazoheptanone. These results were confirmed by Cormier[252] and coworkers who also improved the yield of the reaction by carefully controlling the irradiation time.
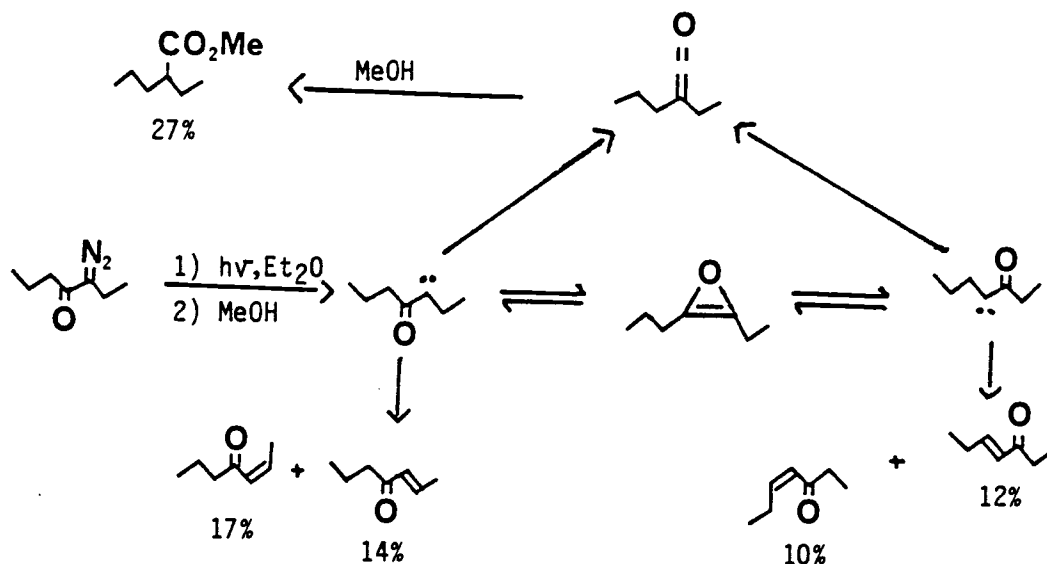
It was determined[251] that sensitized photolysis did not afford any oxirene intermediate.

It was not until very recently that the first experimental evidence was provided that indicated that the ketocarbene was the direct precursor of the Wolff rearrangement.[253] Photolysis of diazoacetophenone at 8°K in an argon matrix afforded the ketene as the sole product. The same reaction carried out in the presence of oxygen afforded a ketone as the sole product. The formation of the ketone is explained by formation of a ketocarbene which is trapped by oxygen and rearranges to the ketone. In the absence of oxygen the ketocarbene undergoes the Wolff rearrangement.

hν, Ar
8°K

hν, Ar/O₂
8°K
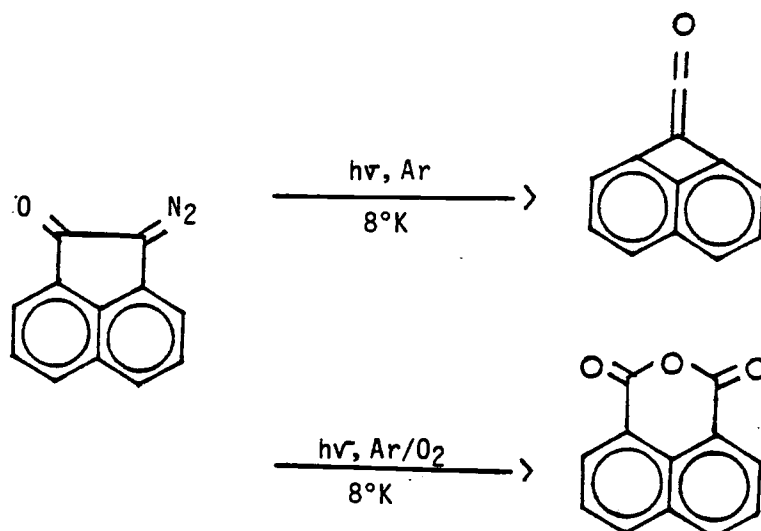
This should be contrasted with a report from Roth and Man-
ion[254] in which it was concluded by means of CIDNP information
that the Wolff rearrangement of diazoacetone did not involve
the carbene (singlet nor triplet).

One factor that has begun to receive some attention
recently is the effect of conformation on the Wolff rearrange-
ment. In 1966, Kaplan and Meloy[255] published a study of the
conformation of diazoketones as determined by nmr. It was
found that alkyldiazoketones existed in a predominantly s-Z con-
formation.
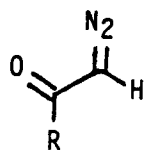
s-Z   s-E
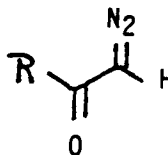
R = Me, Et, T-Bu, ØCH₂, EtO, MeO, Ø

The authors suggested that conformation may play an important
role in the Wolff rearrangement.

It was not until 1979 that the first experimental evi-
dence was provided pointing to the importance of conformation
in the Wolff rearrangement.[256] Photolysis or thermolysis of
4-diazo-2,2,5,5-tetramethyl-3-hexanone, a compound which was
shown by nmr to exist mainly in an s-E conformation, did not
undergo the Wolff rearrangement. In contrast, photolysis or
thermolysis of 2-diazo-3,3,6,6-tetramethylcyclohexanone, a
compound which is locked in an s-Z conformation, afforded
mainly the Wolff rearrangement.

| hv, CCl$_4$ | 78% | 17% |
| , CCl$_2$ = CCl$_2$ | 81% | 16% |

| hv, CCl$_4$ | 96% | 4% |
| , CCl$_4$ | 85% | 15% |
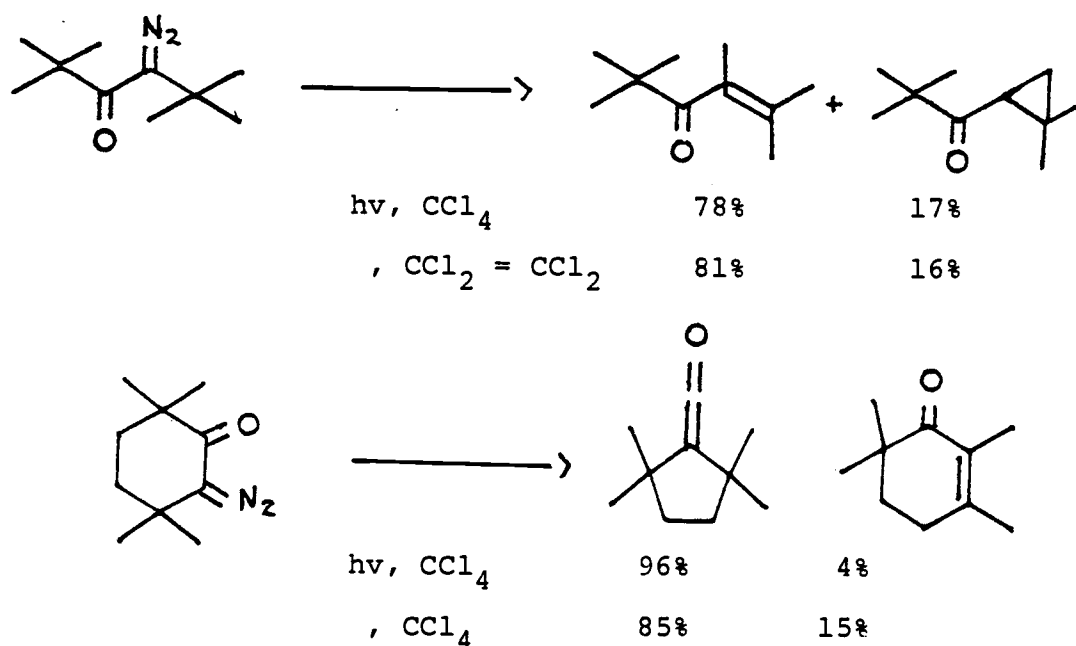
Similar results were obtained by Tomioka and coworkers.[257]
Photolysis of 1-diazo-3-phenylacetone and 1-diazo-3,3-dimethyl-
butanone afforded the Wolff rearrangement product. Both com-
pounds were determined to exist mainly in an s-Z conforma-
tion.[255]
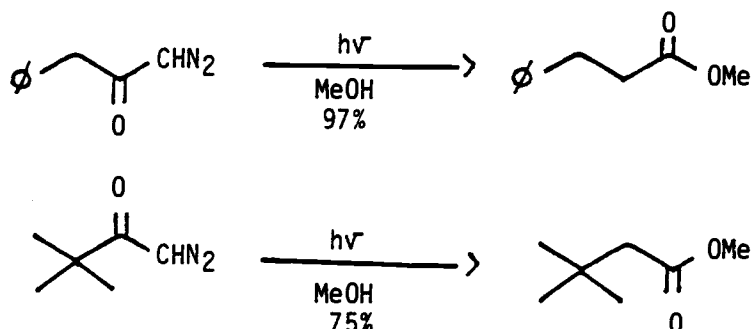
In contrast, photolysis of ethyl 2-diazo-3-hydroxybutanoate
afforded ethyl acetoacetate as the only product. The result
can be explained by assuming that this compound's preferred
conformation is an s-E due to hydrogen bonding.
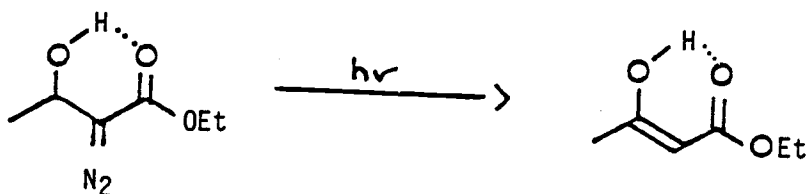
Furthermore, it is postulated that the Wolff rearrangement
occurs directly from the excited singlet s-Z diazoketone
conformer and not through the ketocarbene. This conclusion
is in agreement with the data provided by Roth and Mannion[254]
on the photodecomposition (both direct and sensitized) of
diazoacetone.

C. Carbene Reactions of Ketocarbenes

Once formed the ketocarbene can undergo the reactions
discussed in the section on alkyl carbenes: β and γ hydrogen
insertions to yield enones and cyclopropyl ketones, addition
to unsaturated bonds and alkyl migrations. Some examples of
these reactions have been provided in the section dealing with

the Wolff rearrangement (β and γ hydrogen insertion and a methyl migration).

Ketocarbenes add to double bonds in intra- and inter-molecular reactions. Catalysis by copper salts completely suppresses the Wolff rearrangement and enhances addition, probably by formation of a carbenoid. The catalyzed reaction is a very important one and has been utilized quite extensively in the synthesis of theoretically important molecules and natural products.[258] Most of the work on additions has been done under carbenoid conditions. Some examples of un-catalyzed additions are the following:

Ref. 207

Ref. 275
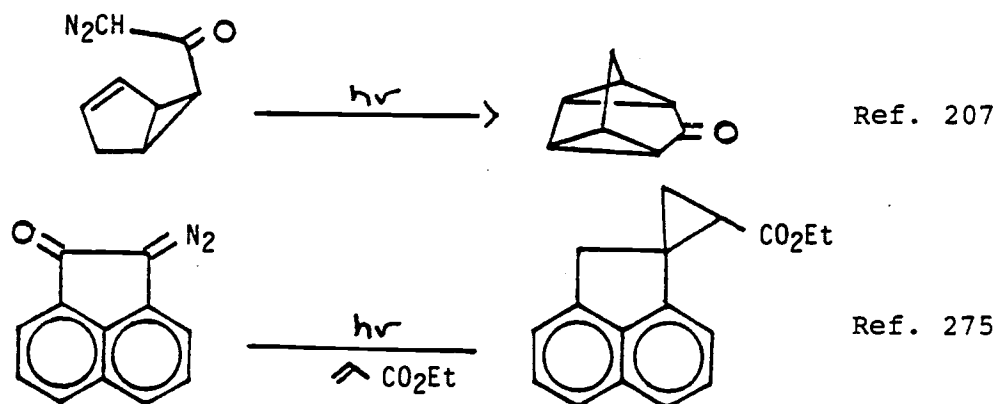
Additions to alkynes are also known although fewer examples than addition to alkenes are known. As with alkenes, addition is enhanced by copper salt catalysis. In some cases, the pyrazole is isolated instead of the cyclopropene.

RESEARCH OBJECTIVES

It is clear from the background discussion that the area of carbene rearrangements has not been thoroughly studied. For this reason our research group has been engaged in studying this aspect of carbene chemistry.

An area of carbene rearrangements that had received no attention in the literature, at least up to the time this research project was commenced, is the intramolecular interaction of a triple bond with a carbene center. It was of interest to us to determine whether an equilibrium could be established between an acyclic carbene containing a triple bond and a rearranged cyclic carbene. The system we decided to study was the following:

(The rearrangement may be a direct one or it may go through an intermediate containing a cyclopropene.)

One problem that was envisioned with the acyclic system is that β-insertion is so facile and rapid that it may not give time to the carbene to undergo the rearrangement. To circumvent this problem, it was decided to also study the following system:
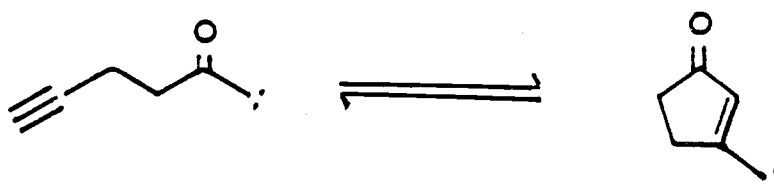
CHAPTER 2.   RESULTS AND DISCUSSION

   I.   General

   The goal of our investigation was to determine whether or

not an acyclic carbene system containing a triple bond would

be capable of existing in an equilibrium with a rearranged

cyclic carbene.   A thorough study of the system should include

generation of the expected carbenes on both sides of the equi-

librium.   It was decided to start the study of this problem

by first generating the acyclic carbene.   The original carbene

that we had intended to study was 1-carbena-5-hexyne, but it

was found that two other related carbene systems were synthet-

ically easier to obtain.   Thus the tosylhydrazone precursors

to 2-carbena-4,4-dimethyl-6-heptyne and 2-carbena-6-heptyne

were synthesized.   Our first experiment was the generation of

2-carbena-4,4-dimethyl-6-heptyne by pyrolysis of the corres-

ponding tosylhydrazone lithium salt.
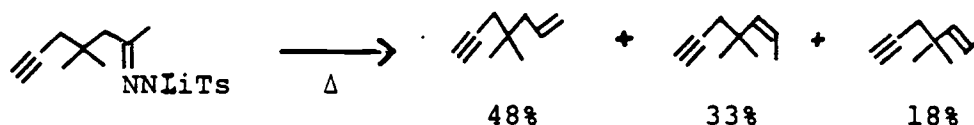
   Our hopes of obtaining a cyclic product arising through

the interaction of the carbene center with the triple bond

were not realized.   Instead the carbene afforded the expected

three isomeric alkenes arising from β-insertion.   The intrig-

ing aspect of this reaction is the product distribution.

Although this is an area that has received very little atten-

tion in the literature, the examples in Table I lead one to

expect the trans isomer as the major alkene product, both in

the gas phase and in solution.

Table I

diazirene, 160°, gas phase   3.3%   29.7%   67.0%

TH, dig., Δ   5%   28%   67%

Ref. 60

diazirene, 160°, gas   68.8%   31.2%

TH, dig., Δ   71.0%   29.0%

Ref. 60

diazirene, 160°, gas   3.1%   96.9%

TH, dig., Δ   5.4%   94.6%

Ref. 60

TH, dig., Δ   4.5%   16.8%   78.8%

Ref. 83

TH, dig., Δ   0.4%   99.6%

Ref. 83

One possible explanation for the anomalous product distribution is that although no cyclic carbene is formed, there is however an interaction between the carbene center and the triple bond that imposes conformational restrictions on the

carbene. These conformational restrictions would then cause the carbene to afford isomeric alkenes in a ratio different than the saturated carbene. Unfortunately, the literature did not provide us with suitable models that would allow us to estimate the product distribution in the saturated carbenes. For this reason it was decided to study the 2-carbenaheptane and the 2-carbena-4,4-dimethylheptane systems.

II. <u>The Saturated Analogues: 2-carbenaheptane and 2-carbena-4,4-dimethylheptane</u>

The carbenes were generated from the tosylhydrazones. The syntheses of 2-heptanone tosylhydrazone and 4,4-dimethyl-2-heptanone tosylhydrazone are outlined on scheme I. The syntheses of 4,4-dimethyl-6-heptyn-2-one is described in part III.

The tosylhydrazones were decomposed thermally in solution and as the dry salt, photolytically in solution. The products observed in these decompositions were the expected alkenes and in some cases the corresponding ketone. Product analysis was carried out by vpc. Product identification from the decompositions of 4,4-dimethyl-2-heptanone tosylhydrazone was done by preparative vpc and spectral identification of each collected peak. In the case of 2-heptanone tosylhydrazone decompositions, it was possible to collect by preparative vpc and identify by spectroscopic means the major products trans-2-heptene and 2-heptanone. The other two products, 1-heptene and cis-2-heptene, were identified by comparison of retention times with those of independently synthesized samples. The syntheses of

1-heptene and cis-2-heptene are depicted in scheme II.

Scheme I
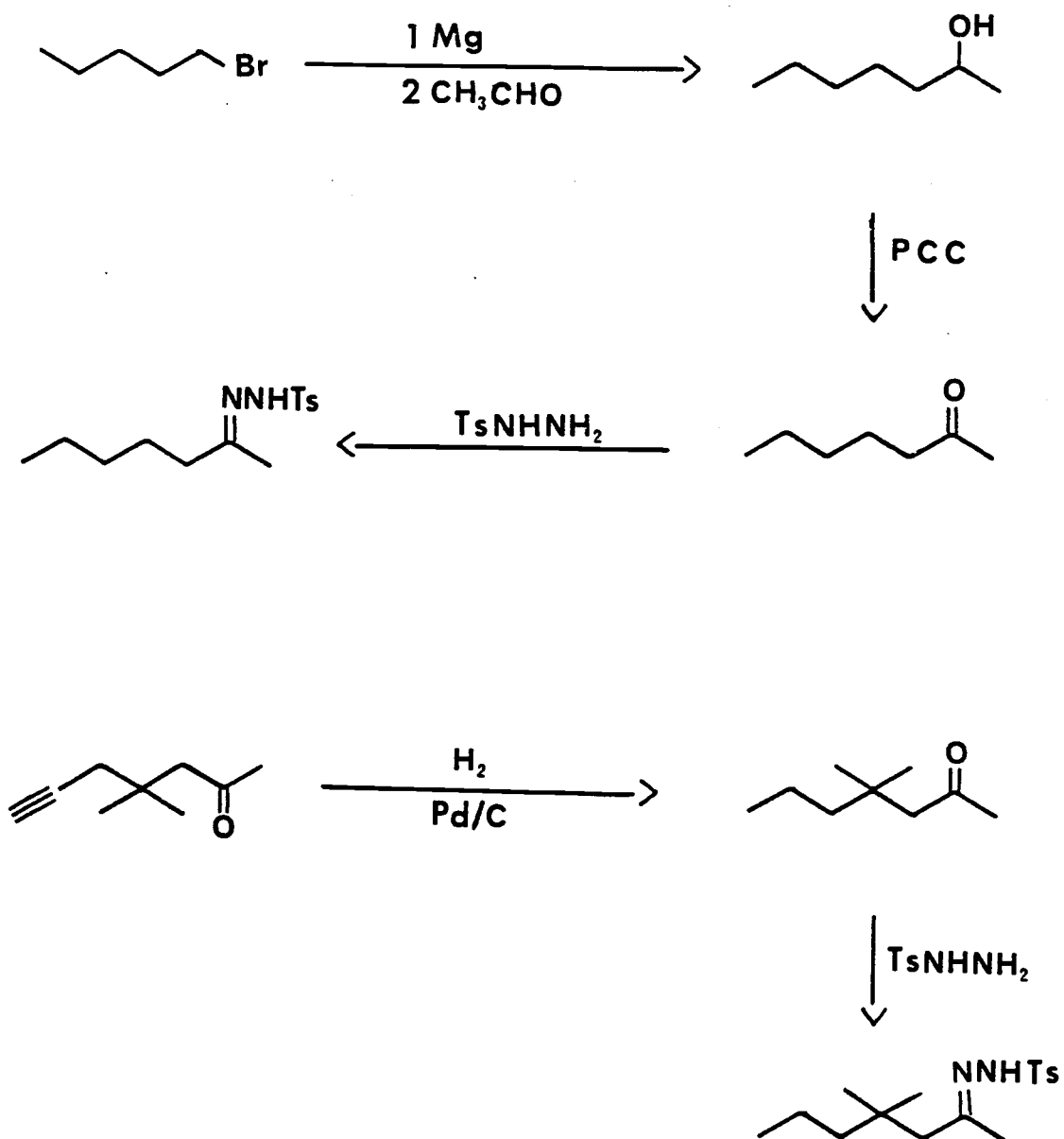
Scheme II
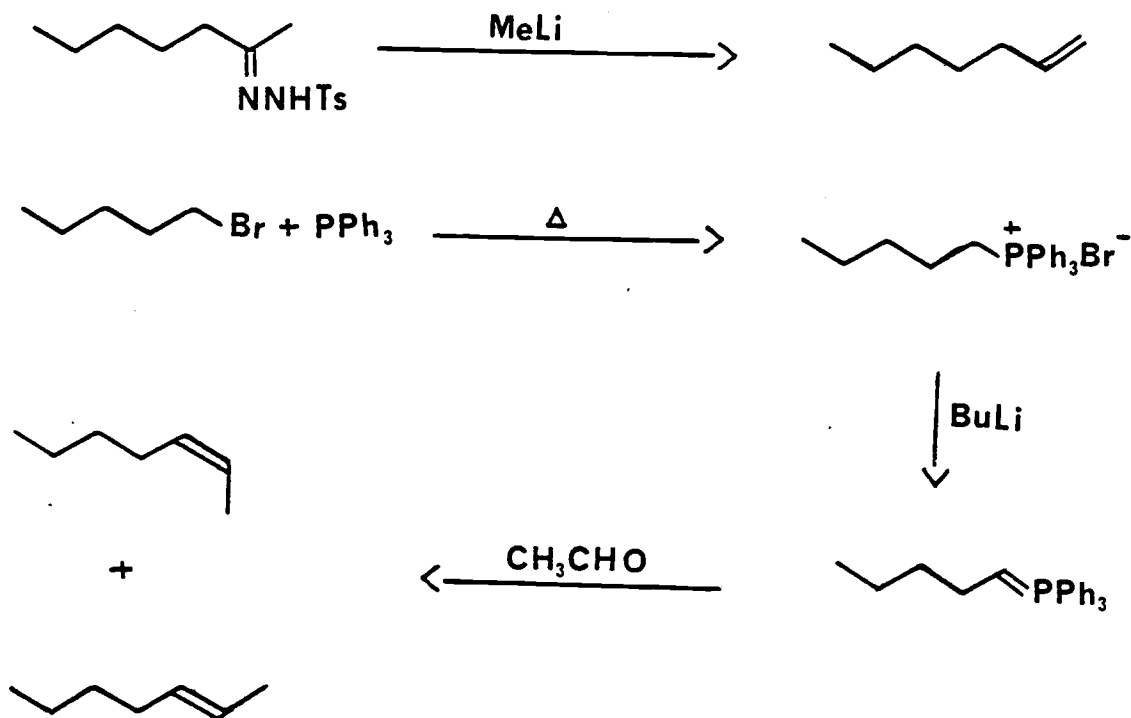
The alkene distributions obtained from the decompositions of 2-heptanone tosylhydrazone and 4,4-dimethyl-2-heptanone tosylhydrazone under different conditions are summarized in Table II.

The data in Table II provides us the following information. The carbenes generated photolytically are less selective than the corresponding thermally generated carbene. This effect has been previously observed in carbenes generated from the diazirine and was explained on the basis of a hot radical effect.[60] An alternative explanation would be a photochemical isomerization of the initially formed alkene and thus the

Table II

Dry Salt

Li, 150°C		4.1%	31.3%	64.6%
Li, 200°C		3.5%	26.6%	69.9%
	Average	3.9%	29.7%	66.4%
Na, 1.0 eq., 150°C		6.4%	16.0%	77.6%
Na, 1.6 eq., 150°C		3.3%	15.5%	81.2%
	Average	4.8%	15.8%	79.4%

Solution

NaOMe, dig., Δ	1.4%	15.8%	82.8%

Photolysis

Li, THF	24.2%	27.9%	47.9%

Dry Salt

Li, 165°C	7.0%	11.8%	81.2%

Solution

NaoMe, dig., Δ	1.6%	trace	98.4%

Photolysis

Li, THF	27.5%	26.3%	46.2%

resultant alkene distribution would be a result of a photo-
chemical equilibration process. To test for photochemical
isomerization, a mixture of 98.4% trans-4,4-dimethyl-2-heptene
and 1.6% of 4,4-dimethyl-1-heptene in tetrahydrofuran was
photolyzed under identical conditions as the tosylhydrazone
lithium salts. After work-up, vpc analysis indicated that the
recovered mixture consisted of 99.1% of the trans isomer and
0.9% of the 1-alkene. Thus it was proven that photochemical
isomerization of the alkenes is not an explanation for the
higher lack of selectivity of the photochemically generated
carbene. A common assumption seems to be that product distri-
bution from carbene reactions are temperature insensitive.
However, there are no data available in the literature to sub-
stantiate this assumption. Pyrolysis of the lithium salt of
2-heptanone tosylhydrazone at 150°C and 200°C afford identical
product distribution and provides experimental evidence in
support of the aforementioned assumption. An interesting
aspect in the chemistry of 2-carbenaheptane is that the product
distribution obtained from the lithium salt is different than
the one obtained from the solution reaction. This result is
contrary to what has been observed in other carbene systems.
It is known that lithium bromide will react with a diazoalkene
to afford an organolithium intermediate which will react fur-
ther.[262] It was claimed that the products from the organolithium
intermediate and the corresponding carbene are identical. If
this were the case for 2-carbena-heptane, then the difference

in product distribution in the gas phase and in solution would
be due to a solvent effect. However, some examples that will
be discussed in the next section indicated that the organo-
lithium intermediate and the carbene do not afford identical
product distributions. Therefore, it was decided to study the
behavior of the free carbene in the gas phase. This was accom-
plished by generating the carbene from the dry tosylhydrazone
sodium salt which was prepared by allowing the tosylhydrazone
to react with sodium methoxide in methanol. Experiments with
other tosylhydrazones seemed to indicate that a small excess
of sodium methoxide increased the relative amount of the 1-
alkene. To test for this possibility, the tosylhydrazone was
allowed to react with 1.0 and 1.6 equivalents of base and the
product distributions compared. The data indicate that an
excess of base has no effect on the alkene composition. Fur-
thermore, the product composition obtained from pyrolysis
of the sodium salt is identical to the one obtained·in
solution, proving that there is not a solvent effect and that
the carbene and the organolithium intermediate do not afford
identical product distributions.

The product distributions of the free 2-carbenaheptane
are numerically identical to the ones obtained from 2-carbena-
pentane generated in solution.[83] In the sterically bulkier
analogue, 2-carbena-4,4-dimethylheptane, the difference in
product distribution of the gas phase and solution reactions
is more dramatic. As is the case with 2-carbena heptane, the

free carbene (generated only in solution) is more selective than the organolithium intermediate, as evidenced by the amount of cis-2-alkene formed. However, the sterically bulkier analogue is much more selective than the 2-carbenaheptane system as indicated by a drop of the cis isomer from 29.7% (2-heptene) to 11.8% (4,4-dimethyl-2-heptene) for the organolithium intermediate and from 15.8% to a trace for the free carbene. This drop in relative amount of cis-2-alkene in going from the 2-carbenaheptane to the 2-carbena-4,4-dimethylheptane can be ascribed to an increase in steric interaction between the t-hexyl group and methyl group (as compared to butyl and methyl) in the transition state leading to cis-4,4-dimethyl-2-heptene. The ratio of trans to cis 4,4-dimethyl-2-heptene obtained from the free carbene in solution is consistent with trans/cis ratio of 99.6/0.4 obtained in the similar carbena-2,2-dimethylpentane system generated under identical conditions.[83]

III. <u>The 2-carbena-6-heptyne and the 2-carbena-4,4-dimethyl-6-heptyne systems</u>

As in the case of the saturated analogues, the title carbenes were generated from the corresponding tosylhydrazones. The syntheses of 6-heptyn-2-one tosylhydrazone and 4,4-dimethyl-6-heptyn-2-one tosylhydrazone are depicted in scheme III. The cyclic ketone 3,5,5-trimethyl-2-cyclohexenone was available commercially, whereas the less substituted one, 3-methyl-2-cyclohexenone, was synthesized via a Robinson annelation.

Scheme III
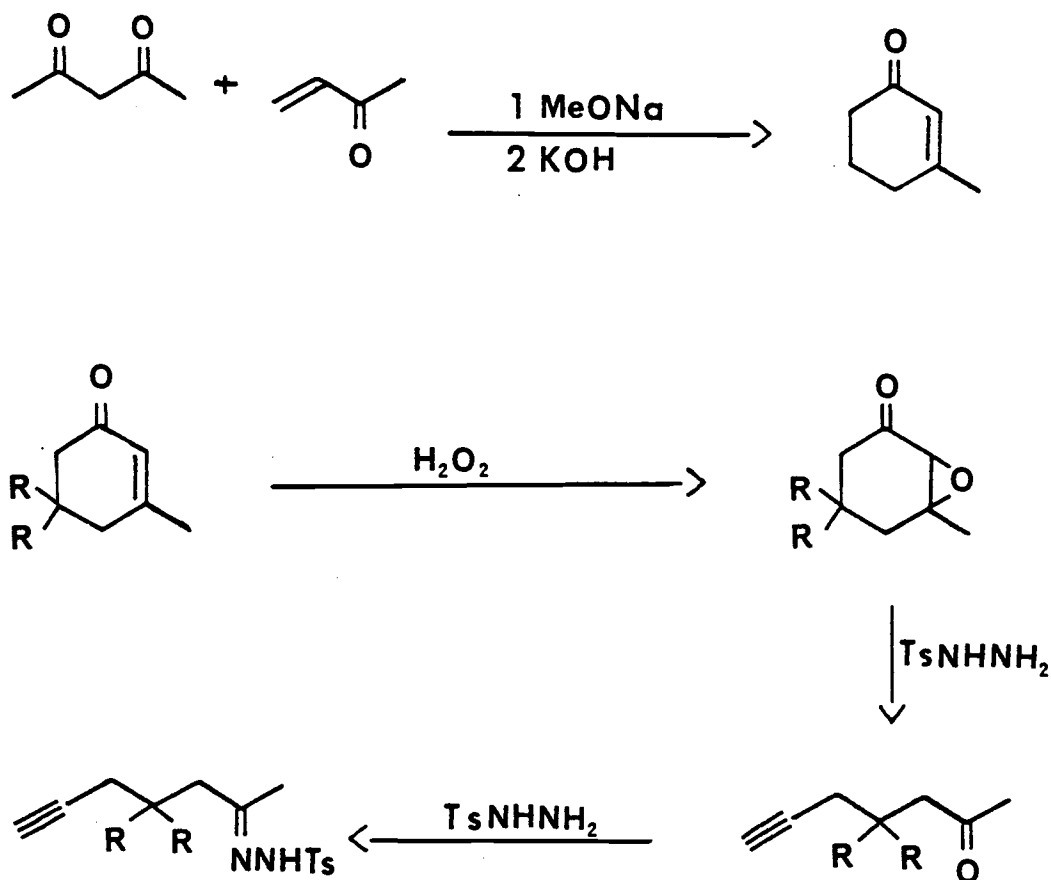
a) R = H
b) R = Me

As has been mentioned previously, generation of 2-carbena-4,4 dimethyl-6-heptyne in the gas phase afforded the three isomeric alkenes arising from β-hydrogen insertion. The relative amounts of these alkenes are quite different than the ones obtained from the saturated analogue 2-carbena-4,4-dimethyl-heptane (compare Tables II and III). Our original theory to account for this unexpected product distribution was an inter-

action between the carbene center and the triple bond. This
interaction would then impose conformational restrictions on
the carbene which are absent in the saturated analogue. This
theory was subsequently proven wrong when it was demonstrated
that the anomalous isomer distribution was caused by using
less than one equivalent of methyl lithium (see Table III).
It is known that protic solvents react with the diazo inter-
mediate to afford products from a diazonium and/or carbonium
ion. In aprotic solvents the tosylhydrazone itself is a source
of protons.[50,52b] The intermediate generated from reaction of
a diazoalkone and a proton is much less selective than the
corresponding carbene as is demonstrated by the following ex-
ample.[83]

NNHTs

	31.9%	29.6%	38.5%
EG	31.9%	29.6%	38.5%
Dig.	4.5%	16.8%	78.8%
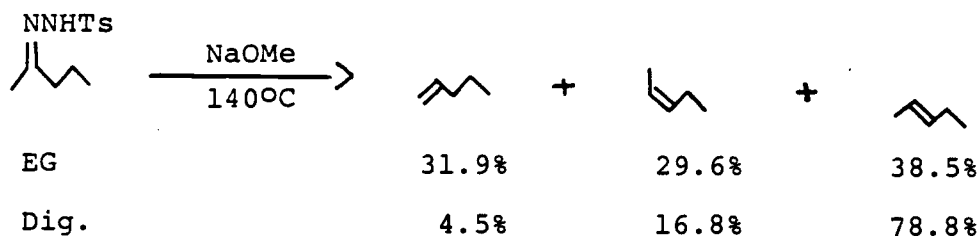
Therefore the explanation for the anomalous product distri-
bution observed in the dry salt pyrolysis of 4,4-dimethyl-6-
heptyn-2-one tosylhydrazone that reacted with less than one equiv-
alent of methyl lithium is that a diazonium and/or carbonium
ion pathway is operating exclusively or in competition with
the carbenic pathway. The interesting aspect is that there
are no reports in the literature reporting observation of
proton donation by unreacted tosylhydrazone in dry salt py-
rolyses.

Table III

1) MeLi
2) Δ

44.0%   37.9%   18.1%

T	eq. MeLi			
a 140°C	1.0 c	44.0%	37.9%	18.1%
190°C	0.8	48.0%	33.0%	18.0%
b 200°C	0.7	38.1%	38.9%	22.4%
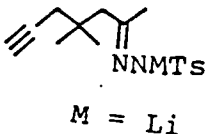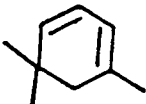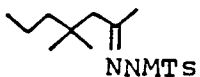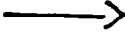
a) Product contained 6.8% of cyclic isomer.

b) Product contained 16.2% of cyclic isomer.

c) Methyl lithium titer used suspected of being in error

   (likely that less than 1.0 eq. was used)

The product composition of the vacuum pyrolyses of lithium salts of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone were found to vary with temperature (see Table IV). It was later established that the largest variation (which occurred with products arising from β insertion) was due to the presence of unreacted tosylhydrazone. In the reactions where one equivalent of base was used (organolithium pathway) the only variation observed was in the amounts of 1,5,5-trimethyl-1,3-cyclohexadiene.

The data in Table IV indicate that while the percentage of the cyclic product increases with increasing temperature, the relative composition of the alkenes remains constant. Furthermore, the composition of the alkenes compares very favorably with those obtained in the saturated analogue. It has been shown in the case of the lithium salt of 2-heptanone

tosylhydrazone that the alkene distribution derived from the organolithium intermediate is temperature invariant, at least in the temperature range studied (150-200°C). The fact that the amount of 1,5,5-trimethyl-1,3-cyclohexadiene increases with increasing temperature indicates that a portion of this product is not produced by the organolithium intermediate.

Table IV

T				
150°C	16.6%	9.8%	3.4%	70.2%
	-	11.8%	4.1%	84.2%
166°C	21.7%	6.7%	2.7%	68.8%
	-	8.6%	3.5%	87.9%
200°C	23.2%	8.5%	3.2%	65.1%
	-	11.1%	4.2%	84.8%
200°C	28.1%	8.8%	4.3%	58.8%
	-	12.3%	6.0%	81.7%
Average		10.9%	4.5%	84.6%

M = Li	166°C	-	7.0%	11.8%	81.2%

The products obtained in pyrolysis of the dry lithium salt of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone were identified by spectroscopic identification after they were isolated by preparative vpc. In addition, 1,5,5-trimethyl-1,3-cyclohexadiene was independently synthesized as shown in scheme IV and its structure ascertained by nmr.

Scheme IV
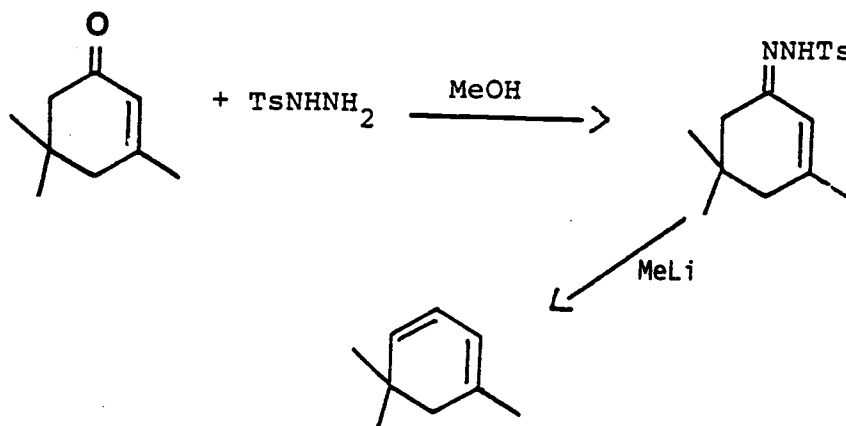
The pyrolysis of the lithium salt of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone fulfilled our goal of obtaining a cyclic product from an acyclic carbene precursor. Unfortunately, this does not prove that the cyclization occurs at the carbene stage. There are four possible stages in which cyclization may occur:

a) tosylhydrazone stage

b) tosylhydrazone lithium salt stage

c) diazo compound stage

d) carbene stage.

It was shown that cyclization does not occur during stage

a or b. The spectral data of the tosylhydrazones of 4,4-dimethyl-6-heptyn-2-one and 3,5,5-trimethyl-2-cyclohexenone proved that cyclization did not occur in the preparation of the tosylhydrazone. That cyclization did not occur in the synthesis of the lithium salt was shown by the following experiments. The lithium salts of the tosylhydrazones of 4,4-dimethyl-6-heptyn-2-one and 3,5,5-trimethyl-2-cyclohexenone were prepared and dried in the usual manner. The dry salt was then dissolved in water and the aqueous solution was then acidified to precipitate the tosylhydrazone which was recovered in yields of 90% or better. The spectra of the recovered tosylhydrazone were identical to the ones from starting material. The aqueous solutions were extracted with pentane. Vpc analysis of the pentane solution indicated the absence of other products.

The cyclization therefore has to occur at the carbene or the diazo stage. There is direct evidence that the diazo group may add to an intramolecular double bond to form a cyclic product. The role of the related carbene in these cyclizations has not been determined but it is possible that it may be operating in competition with diazo cyclization. For a fuller discussion of this point refer to section IIIb in Chapter I. The only example of cyclization involving a triple bond appeared in the literature in 1975 in a report by W. M. Jones and J. P. Mykytka.[260] Pyrolysis of the sodium salt of tosylhydrazone A in benzene affords pyrazole B. However, photolysis of the same

salt at -110°C in dimethyl ether affords
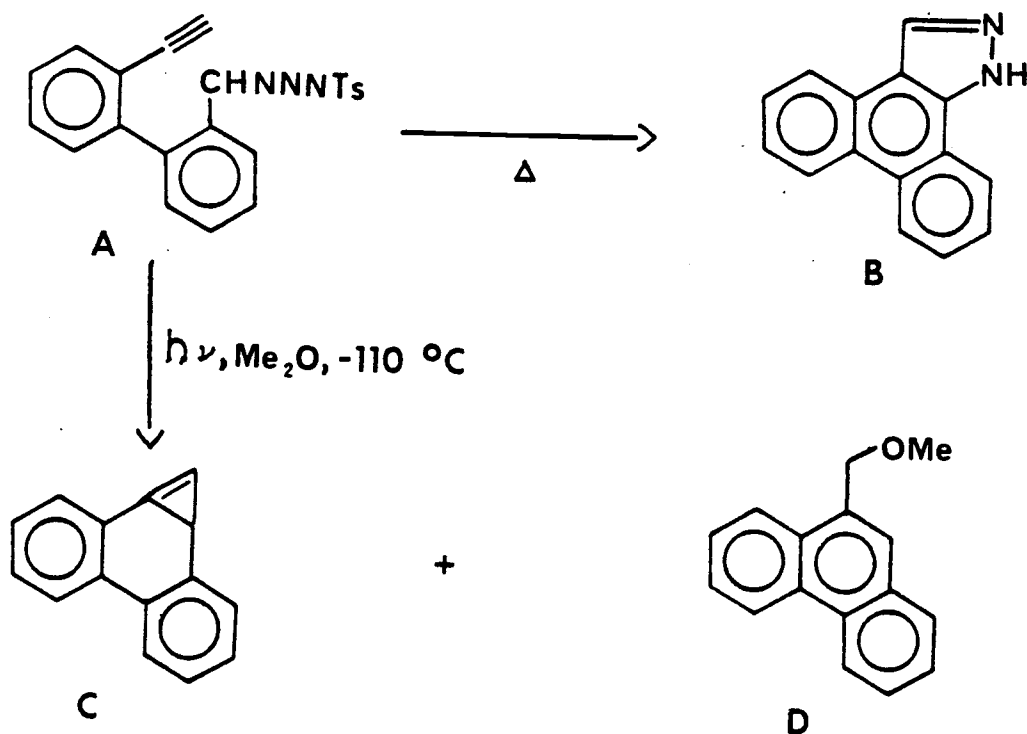
cyclopropene C and methyl ether D. It was determined that the diazo compound generated from A partitioned itself into carbene E and pyrazole F. The carbene E reacted with the triple bond to afford cyclopropene C. The pyrazole reacted further to generate an isomeric carbene G which reacted with solvent to afford product D. It was shown that carbenes E and G did not interconvert at -110°C. (See following page)

The mechanism for the possible formation of 1,5,5-trimethylcyclohexadiene in the pyrolysis of the lithium salt of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone via the carbene and the diazo compound is depicted in Scheme V.
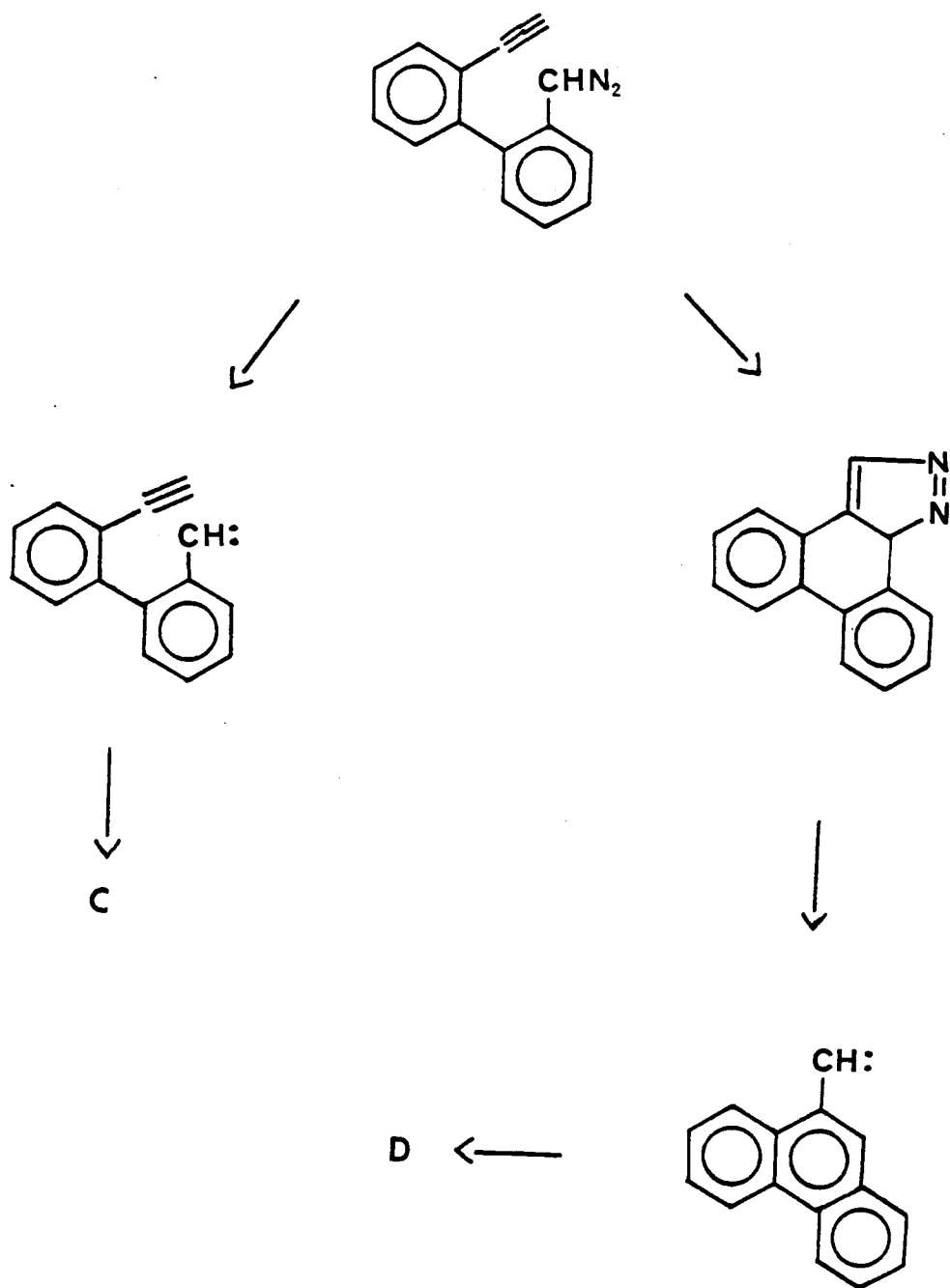
Scheme V
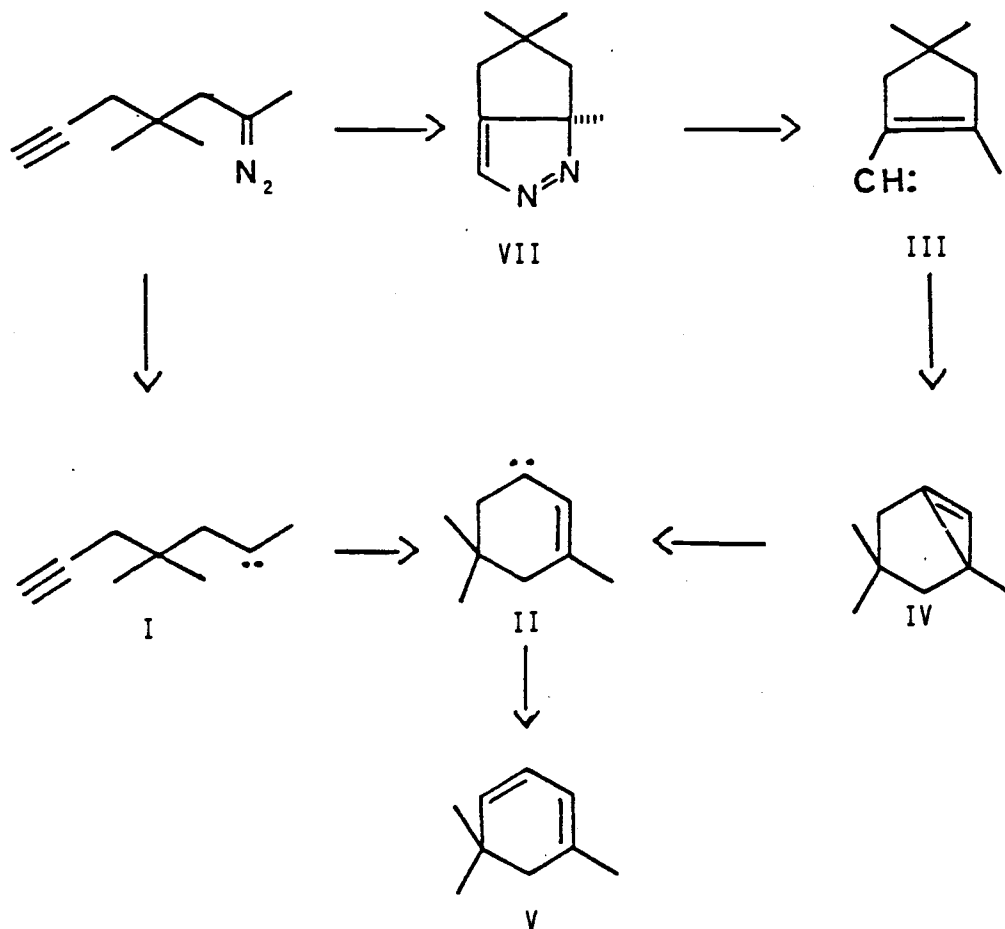
It is possible that carbene I rearranges to carbene II via the cyclopropene IV and that carbene III rearranges directly to carbene II. A recent report[261] on the intramolecular cycloaddition of alyldiazomethane suggests that there is another pathway for the cyclization of diazo-4,4-dimethyl-1-heptyne:
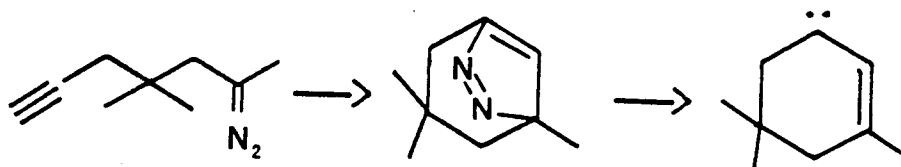
This pathway to cyclization should be less likely than the
one proposed on scheme V due to the fact that formation of A
should be difficult since this intermediate violates Bredt's
rule.

Having established that cyclization does occur in the
2-carbena-4,4-dimethyl-6-heptyne (I) system and/or its diazo
precursor, it was decided to probe this system further. Our
original interest was to determine whether an equilibrium
existed between an acyclic carbene and its cyclic counterpart.
To test this hypothesis in the carbene I system, the carbene
II was generated independently by pyrolysis of the lithium
salt of 3,5,5-trimethyl-2-cyclohexenone tosylhydrazone. If
carbenes I and II are in equilibrium, either directly or via
the cyclopropene intermediate, then direct generation of car-
bene II should produce the products arising from β insertion
in carbene I (4,4-dimethyl-1-hepten-6-yne and cis- and trans-
4,4-dimethyl-5-hepten-1-yne). The results of the pyrolyses
of the lithium salt of 3,5,5-trimethyl-2-cyclohexenone tosyl-
hydrazone are summarized in Table V. The products of the de-
compositions were identified by analysis of spectral data of
samples obtained by preparative vpc. The product mixture was
analyzed by vpc for the presence of 4,4-dimethyl-1-hepten-6-
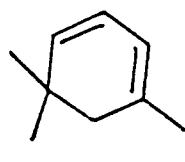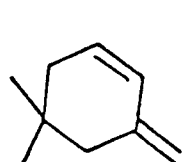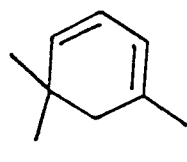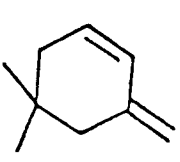
yne, cis- and trans-4,4-dimethyl-5-hepten-1-yne but none was detected. This indicates that carbene II therefore does not revert to carbene I and that if cyclization in the 2-carbena-4,4-dimethyl-6-heptyne system occurs from a rearrangement of carbene I to carbene II, this rearrangement is an irreversible one. However, these experiments do not rule out either the carbene or the diazo pathways for cyclization. They only tell us of the nonexistence of the equilibrium between carbenes I and II.

Table V

NNLiTs

150 °C

+

95.2%   4.8%
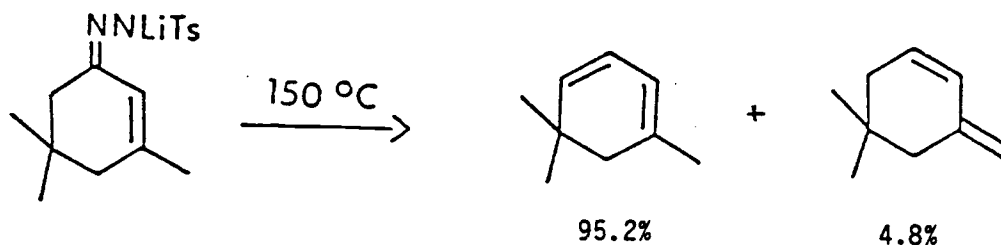
The pyrolysis of the lithium salt of 3,5,5-trimethyl-2-cyclohexenone tosylhydrazone presents an interesting aspect: the formation of the unexpected product 5,5-dimethyl-1-methylene-2-cyclohexene (VI). A possible explanation would be that V isomerizes to VI thermally or catalyzed by the lithium cation. To test for this possibility, mixtures of V and VI were heated at 150°C in pyrex ampoules neat and in the presence of lithium bromide or lithium p-toluenesulfinate. The proportions of V and VI before and after the heating were determined by vpc and are presented in Table VI.

Table VI

	V	VI	Additive	V	VI
	95.6%	4.4%	none	96.0%	4.0%
	94.0%	6.0%	none	93.2%	6.8%
	94.0%	6.0%	Li Br	94.1%	5.9%
	98.2%	1.8%	Li Br	98.2%	1.8%
	94.6%	5.4%	Li Ts	94.5%	5.5%
	94.3%	5.7%	Li Ts	93.6%	6.4%

The data in Table VI indicate that both products V and VI are stable to the reaction conditions and that V is not a precursor for the formation of VI. There are two possible pathways for formation of VI. The first one would be a [1,4] sigmatropic shift of a hydrogen atom in carbene II. This would be an interesting result since there are no reports in the literature of a [1,4] hydrogen shift in a carbene. The second alternative pathway would be a metal cation effect for which there is precedent in the literature. In a study of the decomposition of camphor tosylhydrazone in the presence of base, Shapiro and coworkers[50] have reported that the ratio of tricyclene B (formed by a free carbene mechanism) to camphene C (formed by a cationic mechanism) depended upon the identity of the cation associated with the base. As discussed in Chapter I, Section III-2, the ratio of B/C depends upon the number of equivalents of base employed. Table VI provides data on

the ratio of B/C with varying amounts of sodium and lithium
hydrides.

Table VII

Equivalents NaH	0.75	1.0	1.25	1.50
% tricyclene	47	61	100	100

Equivalents LiH		1.0	2.0	10.0
% tricyclene		40	45	83

As can be seen from the data in Table VII, even with 10 equiv-
alents of lithium hydride there is a 17% yield of camphene.
The formation of camphene was explained as arising from an
intermediate formed by a Lewis acid interaction of the lithium
cation and diazocamphor. This intermediate is similar in be-
havior to the cation formed by the interaction of diazocamphor
and a proton, both affording camphene C as the major product.
The sodium cation has no effect on the B/C ratio. This was
demonstrated by decomposing camphor tosylhydrazone with 0.5
equivalents of sodium methoxide in the presence of varying
amounts of sodium acetate.

Although the literature data on cation effect applies
only to tosylhydrazone decompositions in solution, it was
decided to test whether this effect can also occur in dry salt
pyrolyses. This was accomplished by preparing the sodium salt
of 3,5,5- trimethyl-2-cyclohexenone tosylhydrazone, pyrolyzing
it at 150°C and analyzing the product composition by vpc. The
results are presented in Table VIII.

Table VIII

	Eq. NaOMe	Eq. LiBr	V	VI
a)	1.2	-	94.8%	5.2%
b)	1.0	-	96.7%	3.3%
c)	1.2	-	97.7%	2.3%
d)	1.0	1.0	98.2%	1.8%
e)	1.0	3.0	94.6%	5.4%
f)	1.0	6.0	94.3%	5.7%

In runs b through f, the dry sodium salt was dissolved in THF and then redried to remove occluded MeOH. All runs were done in duplicate (see Experimental).

The results from run a are identical to the ones obtained from the lithium salt and would lead us to conclude that VI is formed by a [1,4] hydrogen shift in carbene II. However, there are two other possible explanations to account for the formation of VI. The first one is that small amounts of methanol are trapped in the salt which react with the intermediate diazo compound to provide a cationic pathway. The second one is that the excess sodium methoxide abstracts an allylic methyl hydrogen:

NNNaTs → $N_2^- Na^+$ + MeOH → Na^+

$^-$OMe

$\downarrow$ MeOH

VI + NaOMe
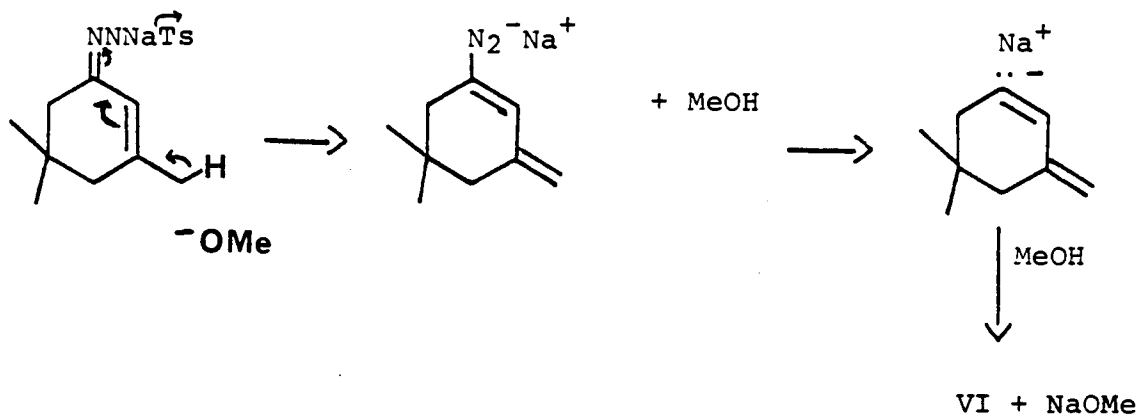
This second alternative is ruled out by run c, where the ex-
clusion of methanol leads to a smaller yield of VI. If sodium
methoxide excess were indeed responsible for the formation of
VI, then runs a and c should have given the same product dist-
ribution. Although the drop in the amount of VI formed is
small in going from run a to b to c, the effect is a real
and reproducible one and suggests that product
VI formed in the sodium salt pyrolyses is due to presence of
methanol. The 1% difference in the amount of VI formed in
run b (3.3%) compared to run c (2.3%) can be explained by
referring to the following equilibrium:

N_2 + MeOH $\rightleftharpoons$ H N_2^+ + MeO$^-$
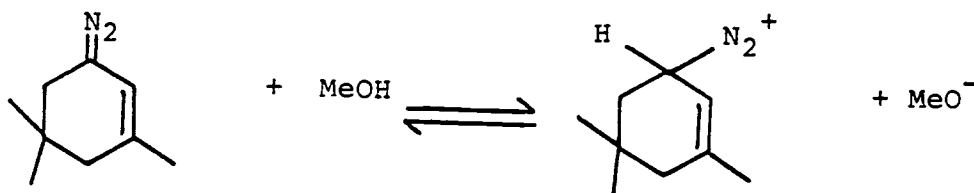
The excess sodium methoxide in run c shifts the equil-
ibrium to the left and thus less cationic product (i.e., VI)
is formed in run c as compared to run b where no excess meth-
oxide ion is present. That a small amount of VI is formed

suggests that not all of the methanol has been excluded.

Having thus determined that carbene II affords only
diene V, we now need to determine the precursor of VI in the
pyrolysis of the lithium salt of 3,5,5-trimethyl-2-cyclohex-
enone tosylhydrazone. It was mentioned above that possibly
a lithium cation effect was responsible for the formation of
VI. Furthermore, it has been already shown that the lithium
and sodium salts of 2-heptanone tosylhydrazone afford slightly
different alkene distributions. To test for this hypothesis,
the sodium salt of 3,5,5-trimethyl-2-cyclohexenone tosyl-
hydrazone was decomposed in the presence of varying amounts
of lithium bromide as shown in Table VIII. Run d in which
only 1.0 equivalent of lithium bromide was employed demon-
strates that this amount has no effect on product distribu-
tion. However, runs e and f indicate that larger amounts of
lithium bromide (3.0 and 6.0 equivalents are equally effec-
tive) produce compound VI in the same amount as the one ob-
served in the pyrolysis of the lithium salt. This strong-
ly suggests that lithium bromide, which was present in the
methyl lithium employed for lithium salt generation, is
responsible for the formation of VI. A likely mechanism for
the formation of byproduct VI is shown in scheme VI.
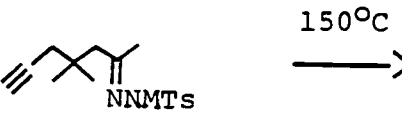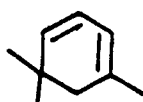
It has been shown that the presence of lithium bromide
has an effect on the product compositions obtained upon
pyrolyses of the salts of 2-heptanone tosylhydrazone and
3,5,5-trimethyl-2-cyclohexenone tosylhydrazone. Thus it is

Scheme VI
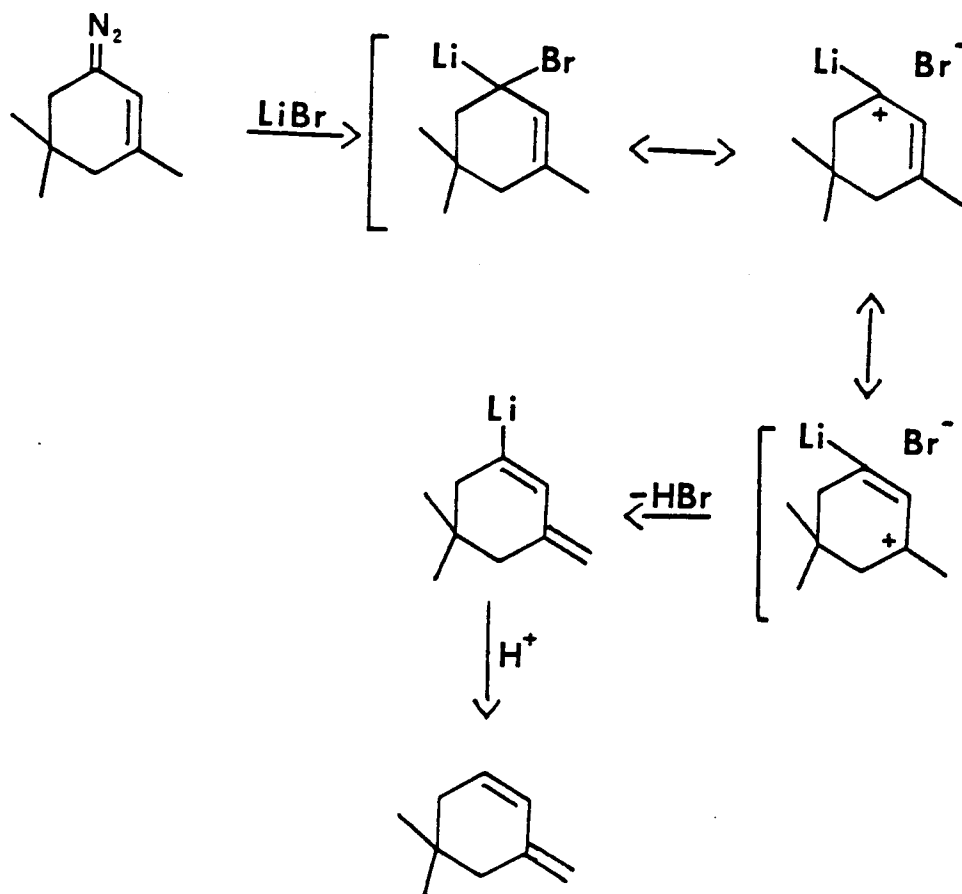
very likely that lithium bromide also has an effect on the
product distribution obtained from the pyrolysis of the
lithium salt of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone.
To ascertain what this effect of lithium bromide is and what
information it provides about the cyclization, the sodium
salt of the above-mentioned tosylhydrazone was prepared and
then pyrolyzed at 150°C. The results are presented in Table IX.

Table IX

M = Na , 1.2 eq. NaOMe	74.6%	8.2%	1.6%	15.5%
		32.4%	6.4%	61.3%
M = Na , 1.0 eq. NaOMe	72.0%	8.7%	2.3%	17.0%
		31.1%	8.2%	60.7%
M = Na,1.0 eq. NaOMe 3.0 eq. LiBr	34.6%	13.2%	5.2%	47.2%
	-	20.1%	7.9%	72.0%
M = Li,1.0 eq. LiBr	16.6%	9.8%	3.4%	70.2%
	-	11.8%	4.1%	84.2%

There are two major differences between the product distributions of the lithium and sodium salts as is evident from Table IX. The first one is that cyclization occurs to a larger extent in the case of the sodium salt (73%) as compared to the lithium salt (17%). The second one is that the sodium salt affords an unusually high amount of the 1-alkene. It was at first thought that this increase in 1-alkene was due to the excess of sodium methoxide; however, repeating the experiment with only 1.0 equivalent of sodium methoxide afforded the same product distribution as the pyrolysis with a 20% excess of base (see Table IX). This result is in agreement with the one obtained with the sodium salt of 2-heptanone tosylhydrazone, where an excess of 60% of sodium methoxide caused no change in the distribution of alkenes.

It has been demonstrated that lithium bromide in the pyrolyses of metal salts of 2-heptanone tosylhydrazone and

3,5,5-trimethyl-2-cyclohexenone tosylhydrazone reacts with
the diazo intermediate to afford an organolithium compound
which affords somewhat different products and product dist-
ribution than the free carbene. That this is indeed the case
for 4,4-dimethyl-6-heptyn-2-one tosylhydrazone is shown by
the third entry in Table IX where the sodium salt is decom-
posed in the presence of 3.0 equivalents of lithium bromide.
It should be pointed out that the sodium salt plus lithium
bromide pyrolysis does not afford the same product distri-
bution as the lithium salt. This is perhaps due to a diff-
erence in crystal structure of the salts caused by the pres-
ence of sodium bromide. Thus the reason for the lower amount
of cyclization in the case of the lithium salt and the sodium
salt plus lithium bromide is that lithium bromide reacts with
the diazo compound to form an organolithium intermediate
which yields only the alkenes and no cyclization product.
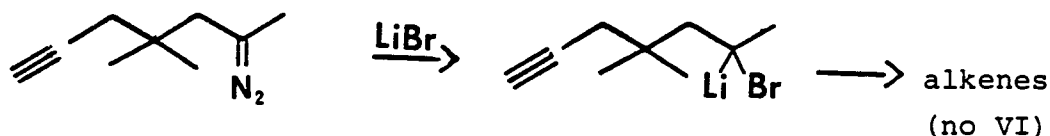
The larger amount of cyclized product in the case of the
sodium salt is due to either cyclization via the diazo com-
pound or due to the free carbene which should be formed more
abundantly in the absence of lithium bromide. Unfortunately,
we do not have the data for the gas phase pyrolysis of the
sodium salt of 4,4-dimethyl-2-heptanone tosylhydrazone for

direct comparison; however, we do have the data for the
reaction in solution (see Table II). In the case of 2-hepta-
none tosylhydrazone, the product distributions of the reaction
in solution and the gas phase pyrolysis of the sodium salt are
identical. Therefore, assuming that the product distributions
in solution and in the gas phase of the sodium salt of 4,4-
dimethyl-2-heptanone tosylhydrazone are similar, one has to
conclude that in the case of the pyrolysis of the sodium salt
there is another intermediate besides the free carbene which
gives rise to the alkenes. A very reasonable intermediate
would be compound VII which is formed by addition of the diazo
moiety to the triple bond. This suggests that in the case of
the sodium salt most, but not necessarily all, of the cycli-
zation occurs at the diazo stage to afford the intermediate
VII which can yield cyclized product V and the acyclic alkenes.
The data in Table IV on the pyrolysis of the lithium salt can
be explained in the following manner. Lithium bromide reacts
with the diazo compound to afford the organolithium inter-
mediate which yields the alkenes directly or dissociates
into the free carbene plus lithium bromide. The free carbene
will then cyclize to give V and undergo a β-insertion to
yield the alkenes. The fact that the alkene distributions in
the pyrolyses of the lithium tosylhydrazone salts of 4,4-
dimethyl-2-heptanone and 4,4-dimethyl-6-heptyn-2-one are very
close argues in favor of the above-described mechanism. It
has been shown (see Table II) that the organolithium inter-

mediate is sterically more demanding than the corresponding free carbene. It would be reasonable to expect that an increase in temperature would increase the amount of organolithium reagent dissociating to free carbene and thus increase the yield of cyclic product V. An alternative explanation is that a larger amount of diazo compound goes into the gas phase without reacting with lithium bromide to afford cyclization mostly via the diazo compound. The decrease of 5% in the amount of cis-2-heptene (see Table II) upon incrementing the reaction temperature from 150 to 200°C is evidence (however, not conclusive due to the small percentage) in favor of both explanations. The fact that the product distribution of acyclic alkenes in the lithium salt pyrolyses of the saturated and unsaturated 4,4-dimethylheptyl systems are somewhat different shows that cyclization occurs also via the diazo pathway. Therefore at 150°C, carbene cyclization occurs only to an extent lower than 17% of total product formation in the lithium salt case.
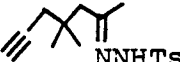
To obtain further information about the cyclization mechanism, the tosylhydrazone of 4,4-dimethyl-6-heptyn-2-one was decomposed in solution with excess sodium methoxide and photolyzed after conversion to the lithium salt. The data is presented in Table X.

Decomposition of the tosylhydrazone in solution affords only cyclized product in low yield and a trace of the acyclic alkenes II a-c. The low yield of product is probably due to destruction (perhaps through polymerization) of starting

Table X

 NNHTs ⟶

	V	IIa(1-ene)	IIb(cis)	IIc(trans)
NaOMe, dig, Δ	3.1%	-	-	-
MeLi, THF, hv	61.0%	4.9%	7.3%	26.8%
		12.6%	18.7%	68.7%

material and/or products. Unfortunately, this experiment provides little information pertinent to the cyclization mechanism. The photolysis experiment indicates that cyclic product VI is produced to a much larger extent than pyrolysis of the lithium salt and slightly less than in the pyrolysis of the sodium salt. The alkene distribution indicates a higher selectivity of the unsaturated as compared to the saturated system. The mechanism of the photolytic decomposition of the tosylhydrazone salt is thought to be similar to the pyrolysis one, absorption of a photon of light allows the salt to lose lithium p-toluenesulfinate to afford the diazo compound which subsequently decomposes to the carbene upon absorption of a second photon. However, the details of the mechanism have not been thoroughly studied. Due to the dilution effect and the difference in temperature, very little organolithium formation is expected in the photolytic reaction. The higher selectivity in alkene formation of the unsaturated 4,4-dimethyl-6-heptyn-2-one tosylhydrazone as compared to its saturated analogue in the photolytic decomposition can be accounted for by the following explanation.

Cyclization of the initially formed diazo compound to inter-
mediate VII (see scheme V) occurs faster than loss of nitrogen
to afford carbene I. Absorption of a second photon allows
intermediate VII to form V via the cyclopropene or the alkenes
via ring-opened carbene I as depicted in Scheme VII.

Scheme VII
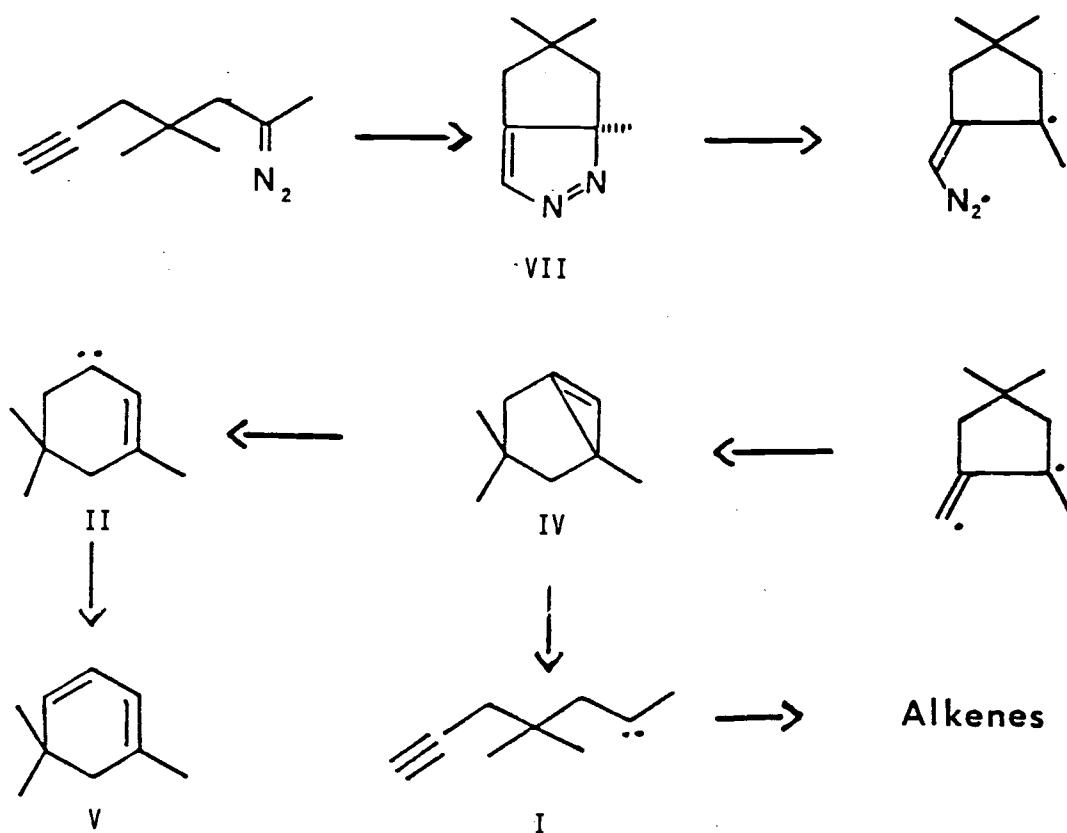
The proposed mechanism for the formation of products via
photolysis is quite similar to the one proposed for the pyrol-
ysis of the sodium salt. This is consistent with the fact
that product distributions are similar in both cases.

The related compound 6-heptyn-2-one tosylhydrazone was
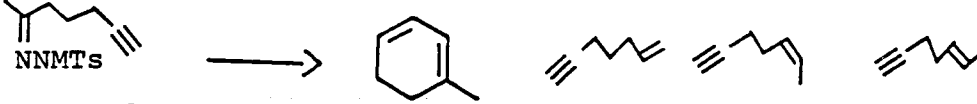
also studied. The lithium salt was thermolyzed as the dry salt and photolyzed in solution; the sodium salt was thermolyzed as the dry salt. However, thermolysis of the tosylhydrazone with excess sodium methoxide in diglyme did not afford any of the expected products. As with the 4,4-dimethyl isomer, the products were the alkenes arising from β-hydrogen insertion and the corresponding cyclic compound 1-methyl-1,3-cyclohexadiene. The identity of the alkenes was determined by preparative vpc and spectral interpretation of each collected peak. The cyclic product was identified by comparison of retention times with that of an authentic sample. The cyclic product was synthesized by a Shapiro reaction on 3-methyl-2-cyclohexenone tosylhydrazone.
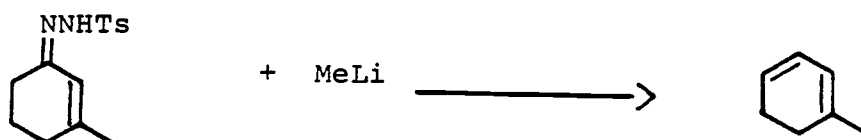
The results of the decompositions of the tosylhydrazone of 6-heptyn-2-one are presented in Table XI. For comparison purposes, the alkene distribution obtained upon reaction of the salt of 2-heptanone tosylhydrazone under identical conditions is included.

The data in Table XI is quite similar to one obtained for the 4,4-dimethyl isomer. For both cases the amount of cyclic product is higher for pyrolysis of the sodium salt than for the lithium salt. The alkene distribution for the pyrolysis of the lithium salt of 6-heptyn-2-one tosylhydrazone is

Table XI

	cyclic			
M = Li, 150°C	4.6%	8.2%	29.5%	57.7%
	–	8.6%	30.9%	60.5%
	*	3.9%	29.7%	66.4%
M = Na, 150°C	49.6%	4.4%	13.5%	32.5%
	–	8.7%	26.8%	64.5%
	*	4.8%	15.8%	79.4%
M = Li, THF, hv	39.5%	15.4%	18.0%	27.1%
	–	25.4%	29.8%	44.8%
	*	24.2%	27.9%	47.9%

*Corresponding alkene distribution obtained upon reaction
  of the lithium or sodium salt of 2-heptanone tosylhydrazone

very close to alkene distribution obtained from the saturated
analogue (2-heptanone tosylhydrazone) while the alkene dist-
ribution from the sodium salt pyrolysis has some significant
differences when compared to the saturated analogue which is
also observed with 4,4-dimethyl-6-heptyn-2-one tosylhydrazone.
An interesting observation is that the 4,4-dimethyl isomer
produces a larger amount of cyclic product in every instance:
16.6% to 4.6% for lithium salt pyrolysis, 72.0% to 49.6% for
the sodium salt pyrolysis and 61.0% to 39.5% for the lithium
salt photolysis. This phenomena, however, is not an unknown
one. On the contrary, it is quite general and is called the
gem dimethyl or the Ingold-Thorpe effect.[263] An example is
the acyloin condensation of diesters to afford nine-membered
hydroxy-keto rings.

R $\diagup$ CO$_2$Me
R $\diagdown$ CO$_2$Me $\longrightarrow$ R, R, O, OH

R = H, 40%

R = Me, 70%
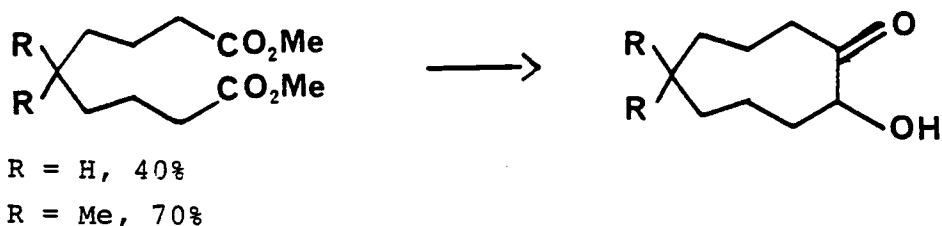
The alkene distribution in the photolytic reaction of the lithium salt of 6-heptyn-2-one tosylhydrazone, unlike its 4,4-dimethyl isomer, is almost identical to the one obtained from its saturated analogue. This can be explained by referring to the fact that cyclization in this system is much less efficient than in the 4,4 dimethyl system. Therefore absorption of a photon by the diazo compound (which will lead to an energy-rich and thus less selective carbene) will compete much more effectively with cyclization.

IV. The 1-Carbena-5-Hexyn-2-One System

The title carbene was generated by photolysis of 1-diazo-5-hexyn-2-one. The diazoketone was prepared from 4-pentynoyl chloride and diazomethane. The acid chloride was prepared from 4-pentynoic acid by reaction with thionyl chloride in benzene. Our first attempt to synthesize 6-heptynoic acid, as described in Scheme VIII, was unsuccessful.

The successful synthesis of 4-pentynoic acid and subsequent steps leading to 1-diazo-5-hexyn-2-one are summarized in Scheme IX.

It was attempted to generate the singlet carbene by direct photolysis of an ether solution of 1-diazo-5-hexyn-2-

Scheme VIII
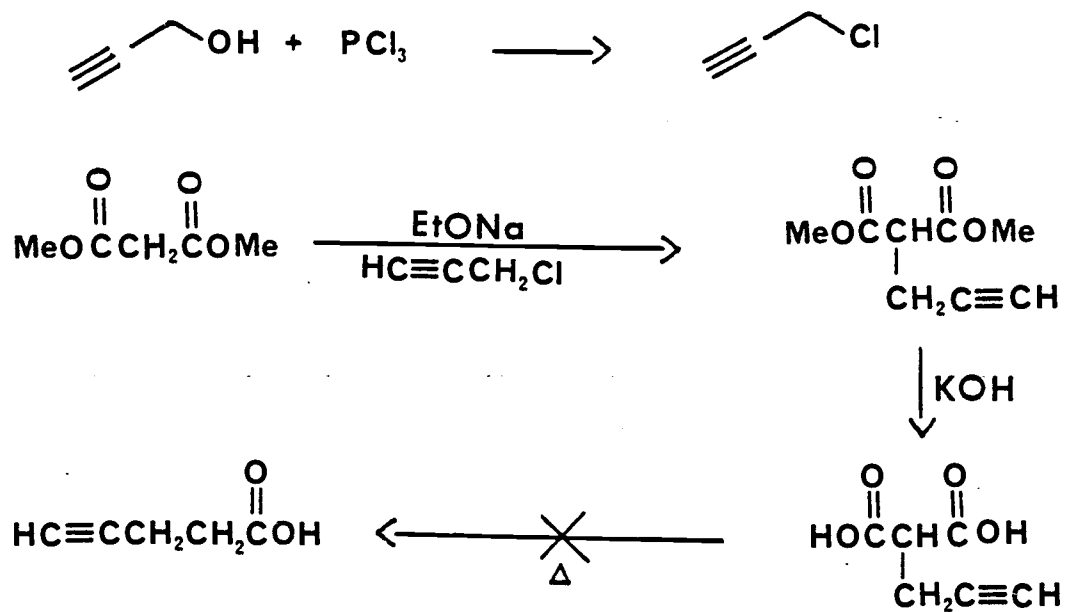
Scheme IX
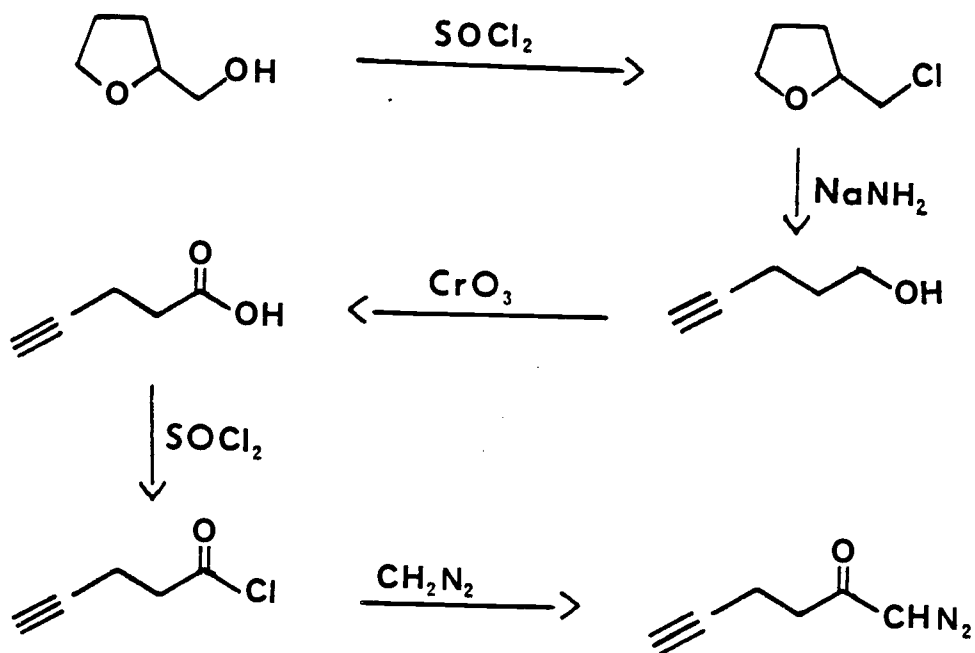
one. The only products observed by vpc were the ketene

formed by a Wolff rearrangement and 1-chloro-5-hexyn-2-one.

However, the ketene proved to be troublesome to handle and it

was converted to more stable ester derivative by allowing it

to react with methanol.
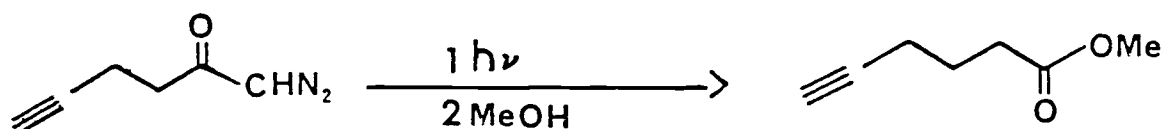
Quantitative vpc indicated that methyl 5-hexynoate was pro-

duced in 17% yield based on diazoketone. The structure of the ester

was determined from its carbon and proton nmr spectra. The

second product, 1-chloro-5-hexyn-2-one, is an impurity that

was formed in the preparation of the diazoketone. This reac-

tion is well documented as has been mentioned in Chapter I,

Section 4Al. The structure of 1-chloro-5-hexyn-2-one was

ascertained from its infrared, proton nmr and mass spectra

and elemental analysis.

As mentioned in the introduction, it is not clear whether

the Wolff rearrangements occur from the excited diazoketone

or from the ketocarbene. In the case of 1-diazo-5-hexyn-2-

one it is not certain, therefore, that the singlet carbene

has been formed since the only observed product was the one

arising from Wolff rearrangement. If the singlet carbene was

indeed formed, the Wolff rearrangement occurs much faster

than any other reaction available to the ketocarbene.

The results of the direct photolysis, namely exclusive

Wolff rearrangement, were not a surprising event. Triplet diazocarbenes do not undergo the Wolff rearrangement and it had been anticipated that generation of triplet 1-carbena-5-hexyn-2-one by sensitized photolysis of the corresponding diazo ketone would have a much better chance for cyclization than the singlet carbene. A plausible mechanism for cyclization is presented in Scheme X. It is quite possible that diradical VIII may rearrange directly to carbene X after spin inversion.

Benzophenone sensitized photolysis of an ether solution of 1-diazo-5-hexyn-2-one afforded only three volatile products. The products were identified by interpretation of their ir, nmr and high resolution mass spectra after each component had been separated from the reaction mixture and collected by preparative vpc. The products obtained were 5-hexyn-2-one (24% yield based on diazoketone), meso-2,3-diethoxy-butane and d,1-2,3-diethoxybutane (92% yield based on 5-hexyn-2-one). The fact that we obtained 5-hexyn-2-one as the sole product coupled with the fact that no Wolff rearrangement occurs in the sensitized photolysis indicates that the triplet ketocarbene has indeed been formed. It is a well-known fact that hydrogens on the carbon next to oxygen in diethyl ether are very susceptible to radical abstractions.[264] Thus with this information a mechanism for this reaction is detailed in Scheme XI.

Scheme X
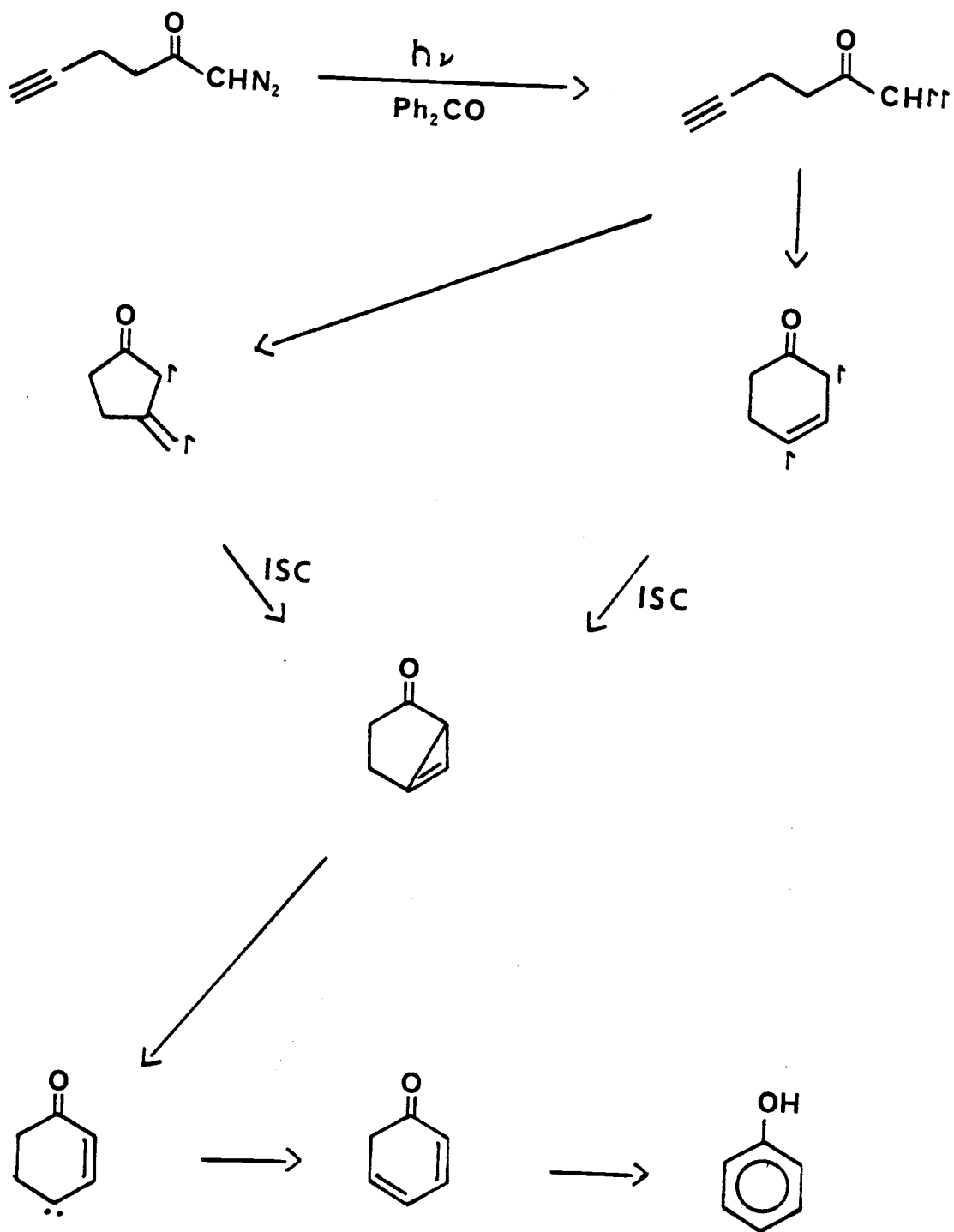
Scheme XI
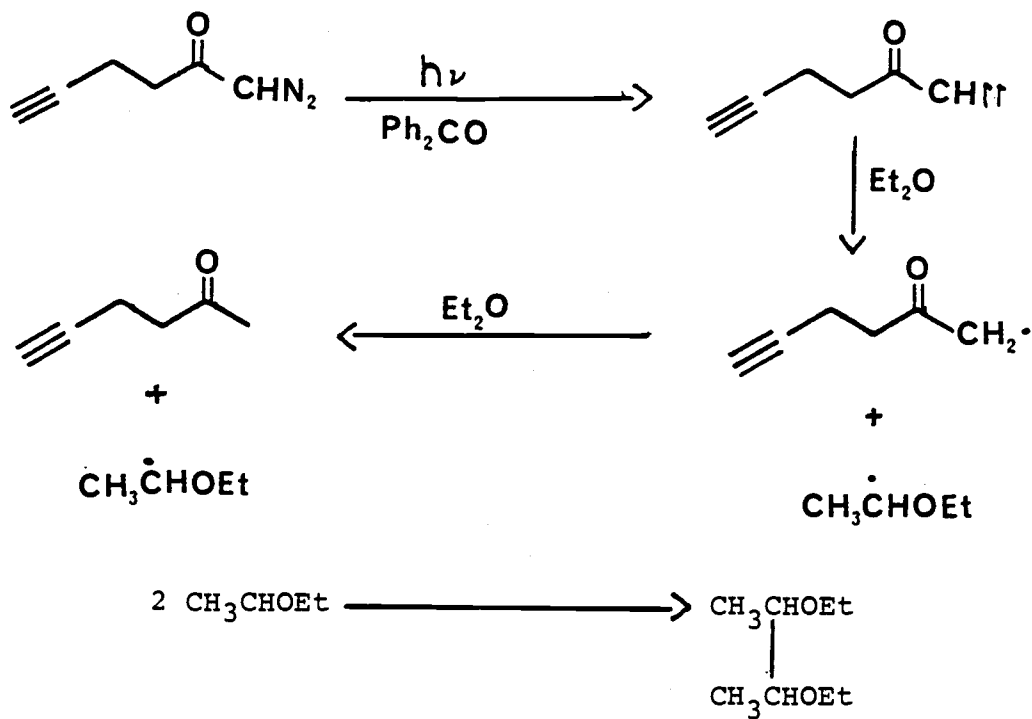
Intramolecular attack of a carbon radical on a triple bond to afford a cyclic product is a known reaction and there are several reports of this reaction in the literature.[265] One example is the following:[266]
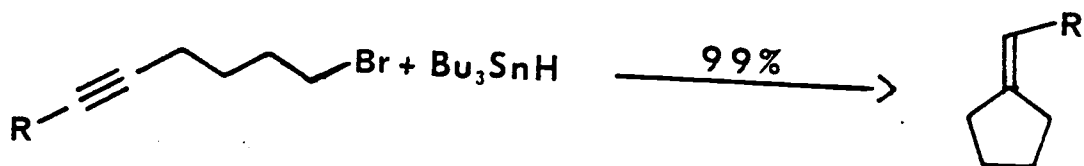
R = Ø, n-C$_5$H$_{11}$

It is thus a reasonable mechanistic possibility that cycliza-
tion may also occur through the radical formed from 1-carbena-
5-hexyn-2-one.
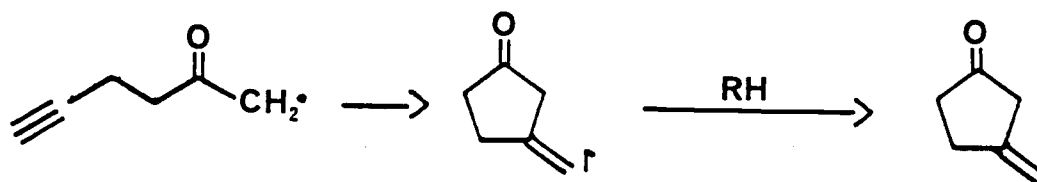
The fact that radical cyclization is not observed either may
be caused by the inability of cyclization to compete with
facile hydrogen abstraction from the solvent. However, other
explanations for the lack of cyclization could be resonance
stabilization of the radical by the carbonyl group and strain
caused by having two sp^2 hybridized carbons in a five-membered
ring. No definite conclusions can be derived because there
is no information available in the literature about 5-hexyn-
2-one-1-yl or structurally similar radicals.

The data on the photolysis of 1-diazo-5-hexyn-2-one indi-
cates that system behaves uninfluenced by the triple bond.
However, it should be pointed out that the 5-hexyn-2-one-1-
yl or a similar radical should be further studied. If this
radical were found to cyclize, this would confirm the possi-
bility that the related carbene may also undergo cyclization
and the sensitized photolysis of 1-diazo-5-hexyn-2-one should
be studied further by changing such parameters as solvent,
sensitizer and irradiation wavelength. Until such work is
done, cyclization in the 1-carbena-5-hexyn-2-one system can
not be ruled out.

V. Conclusions

The conclusions arrived at in this study can be summarized by the following statements.

1. Organolithium carbenoids are formed in the pyrolyses of tosylhydrazone metal salts by reaction of lithium bromide with a diazo intermediate, which afford different alkene product distributions than the corresponding free carbene. It was found that the carbenoid is more sterically demanding than the free carbene and that the alkene product distribution changes very little in the temperature range of 150-200°C. In the case of the tosylhydrazone of 3,5,5-trimethyl-2-cyclohexenone, the carbenoid afforded an isomeric diene in 5% yield in addition to sole product 1,5,5-trimethyl-1,3-cyclohexadiene that is afforded by the free carbene. It has been demonstrated in the case of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone that the corresponding carbenoid will not interact with the triple bond to afford a cyclic product. Since lithium bromide was present in the methyl lithium employed for generating the lithium salts of tosylhydrazones, carbenoid reactions were avoided by generating the sodium salt.

2. It was demonstrated that unreacted tosylhydrazones in the vacuum pyrolyses of tosylhydrazone metal salts will donate a proton to the intermediate diazo compound which reacts further via a cationic rather than via a carbenic pathway.

3. Carbenes generated by photolysis of the tosylhydrazone lithium salts are much less selective than the corresponding

thermally generated carbene.

4. It was proven that 1-carbena-3,5,5-trimethyl-2-cyclo-hexene (II) would not rearrange to the acyclic carbene 2-carbena-4,4-dimethyl-6-heptyne (I) and therefore the carbenes I and II are not in an equilibrium.

5. Thermolysis and photolysis of the tosylhydrazone metal salts of 4,4-dimethyl-6-heptyn-2-one and 6-heptyn-2-one were determined to afford respectively 1,5,5-trimethyl-1,3-cyclo-hexadiene and 1-methyl-1,3-cyclohexadiene plus the alkenes arising from β-insertion. The cyclization products could have been formed at any of the following four stages: (a) tosylhydrazone synthesis; (b) tosylhydrazone metal salt formation; (c) diazo cyclization; and (d) carbene cyclization. Spectral data and regeneration of the original tosylhydrazone by acidification of an aqueous lithium tosylhydrazone solution ruled out possibilities a and b. Alkene distributions from pyrolyses of the sodium salts clearly show that an intermediate other than the carbene is involved, the most likely possibility being an intermediate derived from the diazo compound which can further rearrange to the cyclic diene or open up to afford β-insertion products. The alkene product distribution from the pyrolyses of the lithium salt suggests but does not prove conclusively that carbene cyclization may also be occurring. Some plausible paths leading to cyclic products are shown in Schemes V and VII.

6. Cyclization was more efficient in the 4,4-dimethyl system

than in the isomer without the methyl groups. This was accounted for by the gem-dimethyl effect.

7. The increase in cyclization observed with the increase in temperature in the pyrolysis of the lithium salt of 4,4-dimethyl-6-heptyn-2-one tosylhydrazone was explained as being due to a larger formation of free carbene based on the fact that alkene distribution remained constant. If cyclization had occurred through the diazo compound, an increase in the relative amount of 4,4-dimethyl-6-heptyn-1-ene should have been observed.

8. The data on the photolysis of 1-diazo-5-hexyn-2-one indicated that no cyclization occurred in that system under the conditions studied. The results were inconclusive, however, and the possibility of cyclization under somewhat different conditions cannot be ruled out entirely.

General Methods

Melting points were determined using a Büchi melting
point apparatus and are uncorrected. Boiling points are like-
wise uncorrected. Infrared spectra were recorded on a Perkin-
Elmer 727B infrared spectrophotometer. The infrared spectra
of neat liquids were obtained from a thin film sandwiched
between two sodium chloride plates. The infrared spectra of
solids were obtained from a film deposited on a sodium chlor-
ide plate by allowing a solution of the compound dissolved in
a suitable solvent to evaporate or from a dispersion of the
sample in Nujol oil sandwiched between two sodium chloride
plates. Proton nmr spectra were recorded on either a Varian
Associates EM-360 (60 MHz), HA-100 (100 MHz) or FT-80A (80
MHz) spectrometer. Carbon-13 nmr spectra were obtained on an
FT-80A (20 MHz) spectrometer. Mass spectra were recorded on
a Varian-Matt CH-7 mass spectrometer interfaced to a System
150 computer. High-resolution mass spectra were done by the
University of Oregon Department of Chemistry. Vpc analyses
were carried out on a Hewlett-Packard F&M 700 gas chromato-
graph equipped with a thermal conductivity detector. The
following columns were utilized: (A) 14 ft x 0.25 in aluminum
containing 7% SE-30 on Chromosorb G AW 60/80 mesh; (B) 20 ft
x 0.25 in aluminum containing 20% tricresyl phosphate on
Chromosorb P NAW 60/80 mesh; (C) 20 ft x 0.25 in aluminum con-
taining 5% Carbowax 20M on Chromosorb P NAW 60/80 mesh; (D) 10
ft x 0.25 in aluminum containing 5% Carbowax 20M on Chromosorb

P NAW 60/30 mesh; (E) 6 ft x 0.25 in aluminum containing 8%
SE-30 on Chromosorb W 60/80 mesh.

Product percentage yields calculated from vpc data are
the average of at least three determinations and are uncor-
rected for differences in thermal conductivity among the dif-
ferent components in the mixture. Relative peak areas were
measured with a Hewlett-Packard 3373B Integrator except where
noted. Products are listed in order of increasing retention
times. Elemental analyses were performed by Chemalytics, Inc.,
2230 South Industrial Park Drive, Tempe, Arizona. Diethyl
ether, diglyme and tetrahydrofuran were used shortly after
being distilled from sodium/benzophenone under nitrogen. All
glassware described as dry was placed in an oven heated to
140 °C for at least four hours, assembled while hot under a
stream of nitrogen and allowed to cool before using it.

General Procedure for the Syntheses and Pyrolyses of the
Tosylhydrazone Lithium Salts - In a dry 100-mL round-bottom
flask equipped with a magnetic stirring bar, Claisen adapter,
addition funnel and condenser with gas inlet was dissolved a
carefully weighed amount of the tosylhydrazone in 15 mL of
dry tetrahydrofuran under nitrogen. The funnel was charged
with a solution containing 1 equivalent of methyl lithium in
diethyl ether via a dry syringe. The methyl lithium was added
dropwise to the well-stirred tosylhydrazone solution over a
time period of 10-15 min and stirred for a further 15-30 min
at room temperature. The stirring bar was retrieved, the

solvent was removed in the rotatory evaporator and further
dried by evacuating to 1-3 torr (oil pump) and heating to
65°C (oil bath) for 45-60 min. The flask was then connected
to two dry ice/isopropanol-cooled traps connected in series,
evacuated to 1-3 torr and heated (oil bath) to the desired
temperature for 20-30 min. The volatile products were then
collected from the traps and subjected to vpc analyses.

General Procedure for the Syntheses and Pyrolyses of the
Tosylhydrazone Sodium Salts - In a dry, 100-mL round-bottom
flask equipped with a magnetic stirring bar, Claisen adapter,
glass stopper and gas inlet, was placed 15 mL of absolute
methanol under nitrogen. A carefully weighed amount of
sodium metal was added. After all the metal had reacted,
5.0 mmol of tosylhydrazone was added in one portion and stirred
at room temperature for one hour. The stirring bar was re-
moved and the solution was concentrated in the rotatory
evaporator to about one-third to one-quarter of its original
volume, then 10 mL of tetrahydrofuran was added and the sol-
vent removed in the rotatory evaporator. The process was re-
peated with two more 10-mL portions of tetrahydrofuran. The
dry sodium salt was dried further and pyrolyzed in the same
manner as described for the dry lithium salt.

General Procedure for the Thermal Tosylhydrazone Decompo-
sitions with Sodium Methoxide in Diglyme - In a dry, 100-mL
round-bottom flask equipped with a magnetic stirring bar,
reflux condenser and gas inlet was dissolved 10.0 mmol of

tosylhydrazone in 50 mL of dry diglyme under nitrogen. To the
well-stirred solution was added 2.7 g (50.0 mmol, 5.0 equiv.)
of sodium methoxide in one portion. The solution was heated
at 160 °C for two hours, allowed to cool down to room tempera-
ture, poured into 300 mL of water and extracted with 5 x 20
mL portions of pentane. The combined organic extracts were
washed with 5 x 200 mL portions of water and dried over mag-
nesium sulfate. The pentane solution was concentrated to
about 3-5 mL by distillation through a 20-cm Vigreux column
with a pot temperature of 50-55 °C. The concentrated solution
was used for vpc analyses.

General Procedure for the Photolytic Decomposition of the
Tosylhydrazone Lithium Salts - The lithium salt was prepared
by reacting 2.50 mmol of tosylhydrazone dissolved in 50 mL of
dry THF with a solution containing 2.50 mmol of methyl lithium
in diethyl ether under nitrogen in the same manner as de-
scribed in the general procedure for pyrolyses of lithium
tosylhydrazone salts. The solution was then transferred to a
2.0 x 25.0 cm quartz tube with a small magnetic stirrer and
diluted with 25 mL of tetrahydrofuran to make a solution
0.033 M in the salt. The tube was placed 2-4 cm from a Hanovia
450-watt medium-pressure mercury lamp placed inside a quartz,
water-cooled immersion well equipped with a Pyrex filter. The
reaction tube was connected via a Drierite-filled trap to an
inverted graduated cylinder filled with water to monitor nitro-
gen evolution. After the reaction was over, the solution was

poured into 500 mL of water and extracted with 5 x 25 mL

portions of pentane. The combined organic extracts were

washed with 10 x 200 mL portions of water and dried over mag-

nesium sulfate. The pentane solution was concentrated to

2-5 mL by distillation through a 20-cm Vigreux column with a

pot temperature of 50-55 °C. The residue was analyzed by vpc.

Synthesis of Tosylhydrazine - The procedure reported by L.

Friedman et al.[267] was modified for our purposes. The p-

toluene-sulfonyl chloride was purified by taking a batch of

about 250 g, washing it with 3 x 250 mL portions of water on

a Buchner funnel, drying with suction and recrystallizing

from a 20:1 mixture of 60-80° petroleum ether/benzene. The

yield of purified reactant was 200 g of a pale-brownish solid,

mp 66-68 °C (Lit. mp = 67-68 °C). In a 1-L, three-neck round

bottom flask fitted with a Herschberg stirrer, thermometer

and 250-mL addition funnel was dissolved 200.0 g (1.1 mol) of

purified p-toluenesulfonyl chloride in 350 mL of tetrahydro-

furan. The funnel was charged with 135 mL (2.2 mol) of a 64%

solution of hydrazine in water. The reaction vessel was

cooled to about 10-12 ° with an ice/water bath and the hydra-

zine solution was slowly dripped at such a rate that the

temperature remained between 10 and 15 °C over a time period

of 0.5 hr. The mixture was transferred to a separatory

funnel, the water layer was drawn off and discarded. The

organic layer was placed in a round-bottom flask and the sol-

vent was removed in the rotatory evaporator (the 220 to 250

mL of tetrahydrofuran recovered was recycled and used in further synthesis of tosylhydrazine). The white residue was dissolved in the minimum amount of hot methanol, about 2.5 volumes of water was then added and the flask was then stored in the refrigerator overnight. The crystals that formed were collected by suction filtration, air dried and stored in a vacuum dessicator over Drierite for several days to yield 190 g (93%) of white needles, mp 107-8 °C (lit. mp = 108-10 °C). The IR and 'H NMR spectra matched the ones from an authentic sample.

Synthesis of 4,4-Dimethyl-2-heptanone - In a 500-mL pressure flask was dissolved 11.6 g (0.084 mol) of 4,4-dimethyl-6-heptyn-2-one in 100 mL of methanol. To the solution was added 1.0 g of 10% palladium on charcoal. The reaction flask was attached to a Parr hydrogenation apparatus. The system was flushed three times with hydrogen. The reservoir was filled with 44.5 lbs/sq. in. pressure of hydrogen and the mixture was hydrogenated for 1.25 hr (hydrogen uptake stopped after about 0.5 hr of reaction) whereby the pressure had dropped to 32.0 lbs/sq. in. (hydrogen uptake was about 102% of calculated amount). The catalyst was removed by filtration and the solvent by distillation at atmospheric pressure. The residue was vacuum-distilled to yield 8.8 g (74%) of a clear liquid, bp = 59-61 ° C/12 torr. The product had the following spectral characteristics; IR (neat): 1720 cm^{-1} (carbonyl), 1395 cm^{-1}, 1385 cm^{-1} (doublet) and 1160, 1150

cm^{-1} (gem dimethyl); 'H NMR (20% in $CDCl_3$): distorted triplet at δ0.85 partially overlapped by a singlet at 0.90 (9H, triplet is due to methyl protons of C-7 and singlet is due to gem dimethyl protons), multiplet at δ1.30 (4H, methylene protons on C-5 and C-6), singlet at δ2.15 (3H, methyl protons of C-1) and a singlet at δ2.35 (2H, methylene protons of C-3).

Synthesis of 4,4-Dimethyl-2-heptanone Tosylhydrazone - In a 100-mL round-bottom flask equipped with a magnetic stirring bar and a reflux condenser was dissolved 5.6 g (0.030 mol) of tosylhydrazine in 30 mL of methanol by stirring the mixture in an oil bath heated to 56 °C. After the solid had dissolved, 4.3 g (0.030 mol) of 4,4-dimethyl-2-heptanone was added in one portion. The solution was stirred at 56 °C for 3 hr, transferred to an erlenmeyer flask and water was added until it turned milky. After the solution had cooled down to room temperature it was stored in the refrigerator overnight. The solid that had formed was collected by vacuum filtration and recrystallized from methanol to yield 6.8 g (72%) of white lumpy crystals, mp 78-80 °C. The product exhibited the following spectral characteristics; IR (solid film on sodium chloride plate): 3200 cm^{-1}, strong (amine proton), 1700 cm^{-1}, weak (imine), 1600 and 1500 cm^{-1} (aromatic double bonds), 1395 and 1380 cm^{-1} (gem dimethyl), 1340 and 1170 cm^{-1} (sulfonamide), 810 cm^{-1} (para substituted benzene); 'H NMR (20% $CDCl_3$ solution): singlet at δ0.75 on top of a multiplet δ0.75-1.4 (13 H, the singlet corresponds to the gem dimethyl

protons and the multiplet to the protons on the propyl group

C-5, C-6 and C-7), singlet at δ1.8 (3 H, methyl protons on

C-1), singlet at δ2.15 (2 H, methylene protons at C-3), sing-

let at δ2.45 (3 H, methyl protons on benzene) and a doublet

of doublets at δ7.3 and 7.8 (5 H, protons on benzene ring and

proton on nitrogen buried underneath as evidenced by peak

sharpening upon addition of D_2O).

Anal. Calculated for $C_{16}H_{26}N_2O_2S$: C, 61.90; H, 8.44. Found:

C, 61.94; H, 8.45.

Vacuum Pyrolysis of the Dry Lithium Salt of 4,4-Dimethyl-2-

heptanone Tosylhydrazone - The title salt was prepared in the

manner described in the general procedure by allowing 3.10 g

(10.0 mmol) of tosylhydrazone suspended in 30 mL of dry ethyl

ether to react with 6.0 mL of a 1.67 M methyl lithium solu-

tion. The dry salt was pyrolyzed at 166 °C 0.10 torr to

afford a red oil (turned clear overnight). The oil was ana-

lyzed by vpc on column A at 25 °C and a 60 mL/min flow rate

and found to contain three products. Using heptane as an in-

ternal standard the product composition was determined to be:

4,4-dimethyl-1-heptene, 7.0%; trans-4,4-dimethyl-2-heptene,

81.2% and cis-4,4-dimethyl-2-heptene 11.8%. The yield of

alkenes was 11.3% based on tosylhydrazone.

Thermal Decomposition of 4,4-Dimethyl-2-heptanone Tosylhydra-

zone with Sodium Methoxide in Diglyme - The tosylhydrazone

(3.10 g, 10.0 mmol) was decomposed and worked up as described

in the general procedure. The concentrate was analyzed by

vpc on Column A. By the use of heptane as an internal standard the product was determined to contain: 4,4-dimethyl-1-heptene, 1.6%, trans-4,4-dimethyl-2-heptene, 98.4%, and a trace of cis-4,4-dimethyl-2-heptene. The yield of alkenes was 51% based on tosylhydrazone.

Photolytic Decomposition of the Lithium Salt of 4,4-Dimethyl-2-heptanone Tosylhydrazone - The lithium salt was prepared as described in the general procedure by reacting 0.78 g (2.5 mmol) of tosylhydrazone with 1.5 mL (2.5 mmol) of methyl lithium and photolyzed for 4.0 hours. The solution was worked up and concentrated as described above. The residue was analyzed by vpc on Column A. The product composition was determined to be: 4,4-dimethyl-1-heptene, 27.5%, trans-4,4-dimethyl-2-heptene, 46.2%, and cis-4,4-dimethyl-2-heptene, 26.3%, by using heptane as an internal standard. The yield of alkenes was 12% based on tosylhydrazone.

Stereochemical Integrity of the Alkene Products Derived from the Photochemical Decomposition of the Lithium Salt of 4,4-Dimethyl-2-heptanone Tosylhydrazone - The residue obtained from the decomposition of 4,4-dimethyl-2-heptanone tosylhydrazone with sodium methoxide in diglyme was shown by vpc to consist of 98.4% trans-4,4-dimethyl-2-heptene, 1.6% of 4,4-dimethyl-1-heptene and a trace of cis-4,4-dimethyl-2-heptene. A 172.1 mg aliquot containing 63.4 mg of trans-4,4-dimethyl-2-heptene and 1.0 mg of 4,4-dimethyl-1-heptene was dissolved in 75 mL of dry tetrahydrofuran, photolyzed for 4.0 hr, worked

up and concentrated in the same manner as described for the photolysis of the lithium salt of 4,4-dimethyl-2-heptanone tosylhydrazone. The reconcentrate was analyzed by vpc on Column A. By using heptane as the internal standard the residue was determined to consist of 0.9% 4,4-dimethyl-1-heptene and 99.1% trans-4,4-dimethyl-2-heptene. The recovery of alkenes was 33%.

Identification of Products from the Decomposition of 4,4-Dimethyl-2-heptanone Tosylhydrazone - The product from the thermal decomposition of the title compound showed three peaks upon vpc analysis on Column B at 110 °C and a helium flow rate of 40 mL/min. Spectral data were obtained after isolating each product via preparative vpc. The first peak was identified as solvent (tetrahydrofuran) by comparison of retention times and proton nmr. The second peak was identified as a mixture of 4,4-dimethyl-1-heptene and trans-4,4-dimethyl-2-heptene from its spectral data; IR (neat): 3,050 cm^{-1}, medium (vinyl hydrogen), 1650 cm^{-1}, weak (double bond), doublet at 1390 and 1370 cm^{-1}, medium (gem dimethyl), 990 and 910 cm^{-1}, medium (1-alkene), and 970 cm^{-1}, strong (trans alkene); 'H NMR ($CDCl_3$, microcell): distorted triplet at $\delta 0.85$ (methyl protons on C-7), singlet at $\delta 0.95$ (gem dimethyl), multiplet at $\delta 1.10-1.25$ (methylene protons on carbons 5 and 6), doublet at $\delta 1.65$ (methyl protons on carbon 1) and a multiplet at $\delta 5.25-5.35$ (vinyl protons). That there is a small amount of another product (1-alkene) is indicated by the fact

that some of the peaks are somewhat broadened; one can observe

the following peaks: small doublet at δ1.90 (J ~ 8Hz, methyl-

ene protons next to double bond on carbon 3) and two multi-

plets at δ4.9 and 5.0 and several small peaks between 5.20

and 5.60 (very characteristic of a terminal alkene). The [13]C

NMR spectra (CDCl$_3$, microcell) also indicates the presence of

the above-mentioned compounds. The peaks assigned to 4,4-

dimethyl-1-heptene are: δ17.5 (carbon 6), δ27.1 (carbons of

gem dimethyls), δ33.2 (carbon 4), δ44.8 (carbon 5), δ46.7

(carbon 3), δ116.9 (carbon 1) and δ136.0 (carbon 2). The

following peaks were assigned to trans-4,4-dimethyl-2-heptene:

δ14.92 (carbon 7), δ17.96 (carbon 1), δ18.10 (carbon 6),

δ27.43 (carbons from the gem dimethyls), δ35.9 (carbon 4),

δ45.92 (carbon 5), δ120.12 (carbon 2) and δ141.59 (carbon 3).

The peaks assigned to the 1-alkene were smaller than the ones

from the trans isomer comparing similar carbon atoms. The

peak corresponding to carbon 7 of the 1-alkene was not ob-

served. It could possibly be buried underneath the peak of

carbon 7 of the trans alkene since these two carbons have the

same calculated value for their chemical shift. When a mix-

ture of the trans and 1-alkene was injected on Column A, two

peaks were obtained with the small peak being eluted first.

Attempts to obtain pure samples of each isomer were unsuc-

cessful due to overlapping of the peaks in the course of pre-

parative vpc. That the small peak was indeed the 1-alkene

and the large peak the trans-alkene was confirmed by the

following experiment. The overlapping peaks were collected in two ways. In the first one the whole peak was collected, an infrared spectra was recorded and the ratio of the band at 970 cm^{-1} (trans-alkene) to the band at 990 cm^{-1} was measured. In the second case, only about the latter 60% of the peak (i.e., the collected sample was enriched with the major component) was collected. After recording the infrared spectra, it was found that the ratio of the 970 cm^{-1} band to the 990 cm^{-1} band had increased considerably and thus proved that the major isomer was the trans alkene. The third peak was identified as cis-4,4-dimethyl-2-heptene. IR (neat): 3020 cm^{-1}, strong (vinyl hydrogen), 1660 cm^{-1}, medium (double bond), doublet at 1370 and 1390 cm^{-1}, medium (gem dimethyl) and 710 cm^{-1}, strong (cis double bond), 'H NMR ($CDCl_3$, microcell): distorted triplet at δ 0.90 (3 H, methyl protons on carbon 7), singlet at δ 1.10 (6 H, gem dimethyl protons), multiplet at δ 1.25-1.45 (4 H, methylene protons on carbons 5 and 6), broad doublet at δ 1.70 (3 H, methyl protons, carbon 1) and multiplet at δ 5.20-5.35 (2 H, vinyl protons), ^{13}C NMR ($CDCl_3$, microcell): δ 14.23 (carbon 1), δ 14.99 (carbon 7), δ 18.14 (carbon 6), δ 28.98 (carbons of gem dimethyl), δ 36.59 (carbon 4), δ 46.81 (carbon 5), δ 122.75 (carbon 2) and δ 139.96 (carbon 3). The products of the other reactions were identified by comparison of vpc retention times.

Synthesis of 2,3-Epoxy-3,5,5-Trimethylcyclohexanone - The procedure of Wasson and House[269] was adapted to meet the needs

of this laboratory. In a 1-L 3-neck round-bottom flask
fitted with magnetic stirring, thermometer and 125-mL addition
funnel was dissolved 82.8 g (0.60 mol) of 3,5,5-trimethyl-2-
cyclohexenone in 600 mL of methanol. To the well-stirred
solution was added 173 mL of a 30% hydrogen peroxide solution
in one portion. The funnel was charged with 49.5 mL of a 6 M
solution of sodium hydroxide. The reaction flask was cooled
to 16 °C (Note: reaction does not start if the temperature is
below 15 °C, and if the addition of base is too fast, the
reaction will get out of control) and the sodium hydroxide
solution was dripped in at such a rate that the temperature
was kept between 15 and 20 °C (overall time of addition was
about 1.5 hr). The reaction solution was stirred for 3 hr
keeping the temperature between 25 and 30 °C. It was then
poured into 750 mL of water, allowed to stand at room temper-
ature for four hr and extracted with 4 x 30 mL portions of
ethyl ether. The combined organic extracts were washed with
2 x 400 mL portions of water and dried with magnesium sulfide.
The solvent was removed in the rotatory evaporator and after
distillation 54.8 g (59%) of a clear liquid bp 56-58 °C/2.5
torr (lit. bp 70-73 °C/5 torr) was obtained. The product
showed the following spectral characteristics: IR (neat):
1720 cm^{-1} (carbonyl), 1395 and 1370 cm^{-1} (gem dimethyl), 1250
and 800 cm^{-1} (epoxy); 'H NMR (20% in CDCl$_3$) two singlets at
δ0.9 and δ1.05 (3 H each, gem dimethyl), singlet at δ1.5
(3 H, methyl on C 3), triplet with fine splitting at δ1.8

(2 H, protons on C-4), doublet of doublets at δ 2.1 and δ 2.65 (1 H each, protons on C 6) and a singlet at δ 3.1 (1 H, proton on C 2).

Synthesis of 4,4-Dimethyl-6-heptyn-2-one - The method of Eschenmoser et al.[269] was utilized with modifications. In a 2-L Erlenmeyer flask equipped with a magnetic stirring bar was dissolved 57.1 g (0.274 mole) of tosylhydrazine in 800 mL of a 1:1 dichloromethane/acetic acid solution. In a 1-L Erlenmeyer flask was dissolved 38.4 g (0.274 mole) of 2,3-epoxy-3,5,5-trimethyl-cyclohexanone in 800 mL of a 1:1 solution of dichloromethane/acetic acid. Both flasks were stored in the refrigerator for two hr. The 2-L flask was placed in an ice/water bath and the contents of the 1-L flask were slowly poured in with stirring. The ensuing solution was stirred in the bath for five hr and then stored in the refrigerator for 15 hr. A white precipitate had formed which disappeared upon warming to room temperature. The solution was stirred at room temperature for 24 hr. The solution was divided into two equal portions, each portion was poured into a mixture of 500 mL of ice/water and extracted with 5 x 200 mL portions of ethyl ether. The combined organic extracts were washed with 5 x 200 mL of 10% sodium carbonate, 5 x 200 mL portions of water and dried over magnesium sulfate. After removing the solvent in the rotatory evaporator, the residue was distilled yielding 22.3 g (62%) of a clear liquid, bp 55-60 °C/9 torr (lit. bp 75-80 °C/14 torr). The product

exhibited the following spectral characteristics: IR (neat):

3275 cm^{-1} (ethynyl C-H), 2100 cm^{-1} (triple bond), 1710 cm^{-1}

(carbonyl), 1395, 1385 cm^{-1} (doublet and 1160, 1150 cm^{-1} (gem

dimethyl); 'H NMR (20% in CDCl$_3$): singlet at δ1.1 (6 H, gem

dimethyl), triplet at δ2.0 (1 H, J = 2 Hz, ethynyl proton),

singlet at δ2.15 (3 H, protons on C 1), doublet at δ2.25

(2 H, J = 2 Hz, protons on C 5) and singlet at δ2.5 (2 H,

protons on C 3).

Synthesis of 4,4-Dimethyl-6-heptyn-2-one Tosylhydrazone - In

a 200-mL round-bottom flask equipped with a magnetic stirring

bar and reflux condenser was dissolved 12.7 g (0.0680 mole)

of tosylhydrazine in 100 mL of methanol by stirring the mix-

ture in an oil bath heated to 52 $^{\circ}$C. After all the solid had

dissolved, 9.4 g (0.0680 mole) of 4,4-dimethyl-6-heptyn-2-one

was added in one portion. The solution was stirred at 52 $^{\circ}$C

for 4.5 hr, transferred to a 250-mL Erlenmeyer flask and

stored in the freezer overnight. The crystals that formed

were collected by suction filtration to yield 14.2 g of small

white crystals. A second crop of 2.8 g was obtained by drop-

wise addition of water to the mother liquor until it turned

cloudy, storing the solution in the refrigerator and collect-

ing by suction filtration. A total of 17.0 g (82%), mp 105-

6 $^{\circ}$ of crystalline material was obtained. The product exhib-

ited the following spectral properties; IR (solid film on

sodium chloride plate): 3275 cm^{-1} (ethynyl proton), 3200 cm^{-1}

(amine proton), 2110 cm^{-1} (triple bond), 1640 cm^{-1} (imine),

1600 cm^{-1} (aromatic double bond), 1395 and 1380 cm^{-1} (gem dimethyl), 1340 and 1160 cm^{-1} (sulfonamide), 820 cm^{-1} (para substituted benzene); 'H NMR (20% in CDCl$_3$): singlet at δ 0.9 (6 H, gem dimethyl), singlet at δ 1.85 (3 H, methyl protons), singlet on top of multiplet at δ 1.95 (3 H, methylene protons of C 3 and ethynyl proton) singlet at δ 2.25 (2 H, methylene protons of C 5), singlet at δ 2.45 (3 H, methyl on benzene) and a doublet of doublets at δ 7.30 and δ 7.90 (5 H, aromatic protons and NH proton buried underneath as evidenced by peak sharpening upon addition of D$_2$O).

<u>Anal</u>. calculated for C$_{16}$H$_{22}$N$_2$O$_2$S: C, 62.72; H, 7.24. Found: C, 62.58; H, 6.91.

<u>Vacuum Pyrolyses of the Dry Lithium Salt of 4,4-dimethyl-6-</u>
<u>heptyn-2-one Tosylhydrazone</u> - The title salt was prepared and dried as described in the general procedure by reaction of 1.53 g (5.0 mmol) with 3.6 mL (5.0 mmol) of 1.4 M methyl lithium solution. The salt was then pyrolyzed at different temperatures and analyzed by vpc on Column C at 65 $^\circ$C and a 10 mL/min flow rate of helium employing benzene as an internal standard. The following products were obtained: 1,5,5-tri-methyl-1,3-cyclohexadiene (A), 4,4-dimethyl-1-hepten-6-yne (B), trans-4,4-dimethyl-5-hepten-1-yne (D) and cis-4,4-di-methyl-5-hepten-1-yne. The relative amount of each product and the total yield of products based on tosylhydrazone are shown below for the different reaction temperatures.

T	A	B	C	D	Yield
150 °C	16.6%	9.8%	3.4%	70.2%	16%
166 °C	21.7%	6.7%	2.7%	68.8%	22%
200 °C	23.2%	8.5%	3.2%	65.1%	16%
200 °C	28.1%	8.8%	4.3%	58.8%	12%

Vacuum Pyrolyses of the Dry Lithium Salt of 4,4-Dimethyl-6-heptyn-2-one Tosylhydrazone in the Presence of Unreacted Tosylhydrazone - The salts were prepared in the above-described way but less than 1.0 equivalent of methyl lithium was employed and pyrolyzed at different temperatures. The results of vpc analyses are given below.

T	Eq. MeLi	A	B	C	D
200 °C	0.7	16.2%	31.9%	32.5%	19.2%
190 °C	0.8	-	48.0%	33.0%	18.0%
140 °C	-	6.8%	37.4%	32.2%	15.4%

Vacuum Pyrolyses of the Dry Sodium Salt of 4,4-Dimethyl-6-heptyn-2-one Tosylhydrazone - The salts were prepared and dried as described above using 1.53 g (5.0 mmol) of tosyl-hydrazone and pyrolyzed at 150 °C. Vpc analyses give the following results:

Eq. NaOMe	A	B	C	D	Yield
1.2	75.9%	7.1%	1.1%	15.9%	27%
1.2	73.3%	9.4%	2.2%	15.1%	15%
1.0	69.1%	10.5%	3.4%	17.1%	30%
1.0	74.9%	6.9%	1.2%	17.0%	28%

Vacuum Pyrolyses of the Dry Sodium Salt of 4,4-Dimethyl-6-

heptyn-2-one Tosylhydrazone in the Presence of Lithium Bromide

The salts were prepared and dried in the same manner using

5.0 mmol of tosylhydrazone and 5.0 mmol of sodium as in the

preceding preparation with the exception that after adding

the third portion of tetrahydrofuran, 1.3 g (15.0 mmol, 3.0

eq.) of lithium bromide was added and the drying procedure

was continued without further change. The salts were pyro-

lyzed at 150 °C and analyzed by vpc. The results are given

below.

A	B	C	D	Yield
42.9%	12.2%	6.0%	39.4%	21%
26.3%	14.2%	4.5%	55.1%	23%

Thermal Decomposition of 4,4-Dimethyl-6-heptyn-2-one Tosyl-

hydrazone with Sodium Methoxide in Diglyme - The tosylhydra-

zone (0.92 g, 3.0 mmol) dissolved in 30 mL of dry diglyme was

decomposed with 0.82 g (15.06, 5.0 equiv.) of sodium meth-

oxide as previously described. After work-up, the product

was analyzed by vpc and determined to consist of 1,5,5-tri-

methyl-1,3-cyclohexadiene (3.1%) and a trace of the acyclic

alkenes. The yield was based on tosylhydrazone.

Photolytic Decomposition of the Lithium Salt of 4,4-Dimethyl-

6-heptyn-2-one Tosylhydrazone - The lithium salt was prepared

as previously described and irradiated for 3.0 hr, 40 mL of

nitrogen (ca. 60% of the theoretical amount) was collected.

The residue was analyzed by vpc, the product decomposition

was determined to be: 1,5,5-trimethyl-1,3-cyclohexadiene

(61.0%), cis-4,4-dimethyl-1-heptyn-5-one (7.3%), 4,4-dimethyl-

6-heptyn-1-ene (4.9%) and trans-4,4-dimethyl-1-heptyn-5-ene

(26.8%). The yield of products was 1.3% based on tosyl-

hydrazone.

Chemical Confirmation of the Structure of the Lithium Salt of

4,4-Dimethyl-6-heptyn-2-one Tosylhydrazone - The salt was pre-

pared in the same manner as previously described by reaction

of 0.91 g (3.0 mmol) of tosylhydrazone with 1.7 mL of a 1.75

M solution of methyl lithium (3.0 mmol) under a blanket of

nitrogen. The solution was stirred at room temperature over-

night to allow most of the solvent to evaporate. The dryness

of the salt was insured by heating the flask at 52 °C and 5

torr for 24 hr. The dry salt was treated with 40 mL of water

(all of the solid dissolved). The aqueous solution was acid-

ified with 10 drops (acid to litmus paper) of 3 M sulfuric

acid. The precipitate was collected by suction filtration to

yield 0.80 g of a white, fluffy solid. An 'H NMR of the pro-

duct matched the one of the starting material, 4,4-dimethyl-

6-heptyn-2-one tosylhydrazone. The percent recovery of the

product was 89%.

Identification of Products from the Reactions of 4,4-Dimethyl-

6-heptyn-2-one Tosylhydrazone - The reaction mixture of the

decomposition of the title compound at 166 °C was resolved

into three components on Column D at 70 °C and a helium flow

rate of 50 mL/min. The first peak was identified as 1,5,5-trimethyl-1,3-cyclohexadiene by comparison of its IR, 'H and ^{13}C NMR spectra with those of an independently synthesized sample. The second peak was identified as a mixture of 4,4-dimethyl-1-hepten-6-yne and trans-4,4-dimethyl-5-hepten-1-yne based on IR and NMR spectra. The 'H NMR ($CDCl_3$, micro-cell) exhibited the following peaks: singlet at $\delta 1.0$ (gem dimethyl of 1-alkene), singlet at $\delta 1.10$ (gem dimethyl of trans alkene), doublet at $\delta 1.7$ (methyl on double bond of trans alkene), a triplet on top of another triplet at $\delta 1.9$-2.0 (ethynyl protons of both compounds), multiplet at $\delta 2.05$-2.20 (methylene protons next to triple bond from both compounds plus methylene protons next to double bond on the 1-alkene), multiplet at $\delta 5.0$, broad singlet at $\delta 5.15$ and a multiplet at $\delta 5.6$-6.0 (vinyl protons of 1-alkene) and a narrow multiplet at $\delta 5.45$-5.55 (vinyl protons on trans alkene). The IR (neat) had the following bands: 3300 cm^{-1}, strong (ethynyl hydrogen), 3030 cm^{-1} (vinyl hydrogen), 2125 cm^{-1}, medium (triple bond), 1650 cm^{-1}, weak (double bond), doublet at 1370 and 1390 cm^{-1} (gem dimethyl), 1000 cm^{-1} and 920 cm^{-1}, medium (characteristic band of a terminal vinyl group) and 970 cm^{-1}, strong (characteristic band for a trans alkene). Injection of the reaction mixture into Column C showed one more product: it separated the second peak into two closely spaced ones. An attempt was made to obtain pure samples of each peak to obtain spectral data but the peaks were not resolved upon

injection of larger quantities of materials. The identity of the larger peak as the trans alkene was ascertained by collecting the fused peak and measuring the ratio of the band at 970 cm^{-1} (trans) to the band at 1000 cm^{-1} (1-alkene). Then the ratio was remeasured upon collecting the later ca. 60% of the fused peak (which was enriched in the larger peak which was eluted later). A larger ratio was found. Furthermore, a sample enriched with the larger peak was subjected to ^{13}C NMR (CDCl$_3$, microcell) showing the following peaks: δ14.84 (carbon 7), δ27.28 (gem-dimethyl carbons), δ33.12 (carbon 3), δ35.68 (carbon 4), δ69.59 (carbon 1), δ82.3 (carbon 2), δ121.31 (carbon 6) and δ139.98 (carbon 5) which corresponds to trans-4,4-dimethyl-5-hepten-1-yne. No peaks attributable to the 1-alkene were observed in the carbon nmr.

The last peak from Column E was identified as cis-4,4-dimethyl-5-hepten-1-yne from its spectral data. The 'H NMR (CDCl$_3$, microcell) showed a singlet at δ1.25 (6 H, gem dimethyl), doublet at δ1.75 (3 H, J ≃ 8 Hz, methyl on double bond), triplet at δ1.95 (1 H, J ≃ 2 Hz, ethynyl proton), doublet at δ2.30 (2 H, J ≃ 2Hz, methylene protons next to the triple bond) and a multiplet at δ5.35-5.45 (2 H, vinyl protons). The IR (neat) had the following bands: 3300 cm^{-1}, strong (ethynyl hydrogen), 3010 cm^{-1}, medium (vinyl hydrogen), 2120 cm^{-1}, weak (triple bond), 1650, weak (double bond), doublet at 1370 and 1390 cm^{-1}, medium (gem dimethyl) and 705 cm^{-1} strong (cis double bond). The products from the other

reactions were identified by comparison of their vpc retention times.

Synthesis of 3,5,5-Trimethyl-2-cyclohexenone Tosylhydrazone -
In a 500-mL round-bottom flask, equipped with a magnetic stirring bar and reflux condenser, was dissolved 27.9 g (0.15 mol) of tosylhydrazine in 200 mL of methanol by stirring the mixture in an oil bath heated to 53 °C. After all the solid had dissolved, 20.7 g (0.15 mol) of 3,5,5-trimethyl-2-cyclohexenone dissolved in 30 mL of methanol was added in one portion. The solution was heated with stirring for 5 hr and transferred to an Erlenmeyer flask. Water was added to the warm methanolic solution until it turned cloudy. The flask was scratched with a stirring rod for about 1 min and a solid started to precipitate. The flask was allowed to cool down to room temperature and then stored in the freezer overnight. The solid was collected by suction filtration to yield 41.6 g (90%) of a white powdery solid, mp 134-5 °C. The product had the following spectral characteristics; IR (film on NaCl plate): 3220 cm^{-1}, strong (amine proton), 3025 cm^{-1}, very weak (vinyl protons), 1650 cm^{-1} medium (imine double bond), 1600 cm^{-1}, medium (double bond), 1370 and 1380 cm^{-1}, weak (gem dimethyl), 1340 and 1170 cm^{-1}, strong (sulfonamide) and 820 cm^{-1} (para substituted benzene); 'H NMR (20% in CDCl$_3$): singlets at δ 0.85 and δ 0.95 (6 H, gem dimethyl), 2 broad peaks with some fine splitting at δ 1.75 and δ 1.85 (3 H, methyl on double bond), two broad singlets at δ 1.90 and δ 1.95 (2 H, methylene protons

on C-4), two sharp singlets at δ2.07 and δ2.10 (2 H, methylene protons on C-6), singlet at δ2.4 (3 H, methyl on benzene ring), two multiplets at δ5.90 and δ6.20 (1 H, vinyl proton), two doublets of doublets at δ7.3 and δ7.9 (5 H, aromatic protons) and a broad peak practically buried underneath the δ7.9 doublet (proton on nitrogen, which disappears upon addition of D_2O). The nmr indicates the presence of the two isomers: the syn and the anti.

<u>Anal.</u> calculated for $C_{13}H_{22}N_2O_2S$: C, 62.72; H, 7.24. Found: C,62.57; H, 7.48.

<u>Synthesis of 1,5,5-Trimethyl-1,3-cyclohexadiene</u> - The method of Shapiro[270] was adapted for this preparation. In a 50-mL three-neck round-bottom flask equipped with a magnetic stirring bar, rubber septum, glass stopper and reflux condenser with gas inlet was placed 3.05 g (10.0 mmol) of 3,5,5-trimethyl-2-cyclohexenone tosylhydrazone and 30 mL of dry ethyl ether under nitrogen. To the well-stirred suspension was added 13.7 mL of a 1.75 M solution of methyl lithium (24.0 mmol, 2.4 equiv.) in ethyl ether in two portions (9.0 and 4.7 mL respectively) with a syringe. As addition of methyl lithium proceeded, the solid started to dissolve and the solution turned yellow. After the addition was complete, the solid had completely dissolved and the solution was a deep red. The solution was stirred overnight at room temperature under nitrogen. Several mL of water was added to destroy excess methyl lithium, together with about 15 mL of ether. The

mixture was poured into 30 mL of water and the phases were separated. The aqueous phase was extracted with 3 x 20-mL portions of pentane. The combined organic extracts were washed with 2 x 50-mL portions of water and dried over magnesium sulfate. The pentane solution was concentrated by distillation through a 20-cm Vigreux column and the residue was analyzed by vpc on Column E at 85 °C and a 30 mL/min flow rate of helium. The trace showed the presence of a major component and a small amount of a minor product. The major was collected and it had the following spectral characteristics: IR (neat): 3030 cm^{-1}, medium (vinyl hydrogen), 1650 and 1600 cm^{-1}, weak (conjugated diene), 1360 and 1375 cm^{-1}, medium (gem dimethyl) and 720 cm^{-1} (cis double bond); 'H NMR (20% in CDCl$_3$): singlet at δ1.0 (6 H, gem dimethyl), multiplet at δ1.75 (3 H, methyl on double bond), multiplet at δ2.0 (2 H, methylene protons on C-6), doublet at 5.4 (1 H, J = 10 Hz, vinyl proton on C-4), multiplet at δ5.65 (1 H, vinyl protons on C-2) and a doublet of doublets at δ5.80 (1 H, J$_{34}$ = 10 Hz, J$_{24}$ = 5 Hz, vinyl proton on C-3); ^{13}C NMR (20% in CDCl$_3$): δ23.43 (quartet, methyl carbon on double bond), δ27.95 (quartet, gem dimethyl carbons), δ31.49 (singlet, C-5), δ43.55 (triplet, C-6), δ117.69 (doublet, C-2 or C-3), δ122.81 (doublet, C-3 or C-2), δ134.29 (singlet, C-1) and δ134.45 (doublet, C-4).

NMR Decoupling Experiment on 1,5,5-Trimethyl-1,3-cyclohexadiene - A 20% solution of 1,5,5-trimethyl-1,3-cyclohexadiene

in deuteriochloroform in a 5-mm nmr tube was subjected to the
following decoupling conditions. The multiplet at δ1.75 due
to the protons of the methyl on the double bond was irrad-
iated causing the multiplet at δ5.65 (vinyl proton on C-2) to
sharpen up. No change was observed on the doublet of doublets
at δ5.80 (vinyl proton on C-3) but the doublet at δ5.40 (vinyl
proton on C-4) changed to a doublet of doublets (J = 10, 1.5
Hz). This indicates that the methyl on the double bond is
coupled to the vinyl proton on C-2 but not to vinyl protons on
C-3 and C-4. The new splitting on the signal from the vinyl
proton on C-4 is due to coupling between this proton and the
proton on C-2. This type of coupling is reported to have a
splitting of 1.06 for 1,3-cyclohexadiene. The multiplet at
δ2.0 (methylene protons on C-6) was irradiated causing the
multiplet at δ5.65 (vinyl proton on C-2) to sharpen up. No
change was observed on the signals at δ5.40 and δ5.80 (vinyl
protons on C-3 and C-4). This information indicates that the
vinyl proton on C-2 is coupled to the methylene protons on
C-6. Irradiation of the multiplet at δ5.65 (vinyl proton on
C-2) caused a sharpening of the multiplets at δ1.75 and δ2.0
indicating that the vinyl proton appearing at δ5.65 is coupled
to the methyl protons on C-1 and to the methylene on C-6.
Irradiation of the doublet at δ5.40 caused no change in the
shapes of the multiplets at δ1.75 and δ2.0. These facts con-
firm that the multiplet at δ5.65 is the vinyl proton at C-2.

Vacuum Pyrolyses of the Lithium Salt of the 3,5,5-Trimethyl-2-cyclohexenone Tosylhydrazone - Reaction of 1.53 g (5.0 mmol) of tosylhydrazone with 3.7 mL (5.0 mmol) of methyl lithium solution afforded the lithium salt which was dried and pyrolyzed at 150 $^{\circ}$C in the usual manner. The product was analyzed by vpc on Column D at 85 $^{\circ}$C and a helium flow rate of 30 mL/min. with benzene as an internal standard. The product composition was determined to be 1,5,5-trimethyl-1,3-cyclohexadiene (A) 95.9% and 5,5-dimethyl-1-methylene-2-cyclohexene (B) 4.1%. A second run gave a product composition of 94.5% A and 5.5% B. The yields of products based on tosylhydrazones were 40% for the first and 37% for the second run.

Vacuum Pyrolyses of the Dry Sodium Salt of 3,5,5-Trimethyl-2-cyclohexenone Tosylhydrazone - The dry salt was obtained as previously described employing 1.53 g (5.0 mmol) of tosylhydrazone and pyrolyzed at 150 $^{\circ}$C. Vpc analyses gave the product compositions shown below.

Eq. NaOMe	A	B	Yield
1.2	95.6%	4.4%	24%
1.2	94.0%	6.0%	17%
1.0	96.6%	3.4%	8%
1.0	96.8%	3.2%	14%
1.2	98.2%	1.8%	11%
1.2	97.2%	2.8%	11%

The salt used in the first two runs was not subjected to the tetrahydrofuran/rotatory evaporator treatment.

Vacuum Pyrolyses of the Dry Sodium Salt of 3,5,5-Trimethyl-
2-cyclohexenone Tosylhydrazone in the Presence of Lithium
Bromide - The dry salt was prepared as above employing 1.0 eq.
of sodium with the exception that after the addition of the
third portion of tetrahydrofuran, lithium bromide was added
and drying was continued as described previously. The salt
was pyrolyzed at 150 °C and analyzed by vpc. The product com-
positions obtained are shown below.

Eq. LiBr	A	B	Yield
1.0	98.2%	1.8%	16%
1.0	98.3%	1.7%	21%
3.0	94.6%	5.4%	27%
6.0	94.3%	5.7%	32%

Thermal Stability of 1,5,5-Trimethyl-1,3-cyclohexadiene and
5,5-Dimethyl-1-methylene-2-cyclohexene - Into each of six
heavy-walled ampoules, which had been flushed with argon for
several minutes while being cooled in a dry ice/isopropanol
bath, was placed 0.15-0.20 g of a solution containing known
amounts of the dienes A and B. Two of the tubes contained
1.0 equivalent of lithium bromide and two other tubes con-
tained 0.15 g of solid residue from the pyrolysis of the dry
lithium salt of 3,5,5-trimethyl-2-cyclohexenone tosylhydrazone
(calculated to contain about 0.4 eq. of lithium p-toluene-
sulfinate). The ampoules were sealed, allowed to warm up to
room temperature and heated at 150 °C for 20-30 min. The
ampoules were opened and the contents were analyzed by vpc.

The initial and final compositions are shown below.

Additive	Initial:	A	B	Final:	A	B
none		95.6%	4.4%		96.0%	4.0%
none		94.0%	6.0%		93.2%	6.8%
LiBr		94.0%	6.0%		94.1%	5.9%
LiBr		98.2%	1.8%		98.2%	1.8%
LiTs		94.6%	5.4%		94.5%	5.5%
LiTs		94.3%	5.7%		93.6%	6.4%

Chemical Confirmation of the Structure of the Lithium Salt of

3,5,5-Trimethyl-2-cyclohexenone Tosylhydrazone - A 15.0 mmol

sample of the dry lithium salt was prepared in the usual

manner. A portion of the dry lithium salt (1.7398 g, 5.57

mmol) was dissolved in 50 mL of water and acidified with

several drops of 2 M sulfuric acid (acid to litmus paper).

The precipitate was collected by suction filtration to yield

1.5212 g of a white solid. The nmr of the product matched the

one of 3,5,5-trimethyl-2-cyclohexenone tosylhydrazone. The

amount of product recovered was 89%.

The aqueous phase was extracted with 3 x 10 mL portions

of pentane. The combined pentane extracts were dried with

magnesium sulfate and concentrated by distillation through a

20-cm Vigreux column. The residue was analyzed by vpc. No

peaks corresponding to 1,5,5-trimethyl-1,3-cyclohexadiene nor

5,5-dimethyl-1-methylene-cyclohexadiene were detected.

Identification of Products from the Decomposition of the

Lithium Salt of 3,5,5-Trimethyl-2-cyclohexenone Tosylhydra-

zone - The remainder of the above-prepared salt was pyrolyzed

and the products collected by preparative vpc. The major
compound was identified as 1,5,5-trimethyl-1,3-cyclohexadiene
by comparison of its IR 'H and ^{13}C NMR to those of an inde-
pendently synthesized sample. The minor product was ident-
ified as 5,5-dimethyl-1-methylene-2-cyclohexene based on its
spectral data. The IR (neat) had the following bands: 3075
and 3025 cm^{-1} (vinyl hydrogen), 1650 and 1600 cm^{-1}, medium
(conjugated diene), 1360 and 1375 cm^{-1}, medium (gem dimethyl),
880 cm^{-1}, strong (gem double bond and 720 cm^{-1}, strong (cis
double bond). The 'H NMR (CDCl$_3$, microcell) had the follow-
ing peaks: singlet at δ 0.9 (6 H, gem dimethyl), broad singlet
at δ 1.95 (2 H, methylene protons on C-6), broad singlet at
δ 2.10 (2 H, methylene protons on C-4), broad doublet at δ 4.8
(2 H, exocyclic vinyl protons), multiplet at δ 5.7 (1 H, ole-
finic proton on C-3) and a distorted doublet at δ 6.1 (1 H,
vinyl proton at C-2). The ^{13}C NMR (CDCl$_3$, microcell) had the
following peaks: δ 28.35 (gem dimethyl carbons), δ 29.0
(C-5), δ 39.81 (C-4), δ 44.53 (C-6), δ 111.53 (exocyclic
carbon), δ 139.45 (C-2) and δ 139.61 (C-3). Carbon 1 was not
observed.
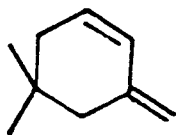
Synthesis of 2-Heptanol - In a 500-mL round-bottom flask
equipped with a Claisen adapter, reflux condenser, addition

funnel, gas inlet and a magnetic stirring bar was placed 8.5

g (0.35 mol) of magnesium turnings under a nitrogen atmos-

phere. The funnel was charged with a solution of 52.9 g (0.35

mol) of 1-bromopentane in 100 mL of dry ethyl ether. About

10 mL of this solution was dripped into the reaction flask

and gently warmed with a warm water bath, but reaction did

not start after refluxing for ca. 10 min. Several drops of

1,2-dibromoethane were added and reaction started immediately.

The reaction mixture was diluted with 25 mL of anhydrous

ethyl ether. The remainder of the alkyl bromide solution was

added at such a rate that a gentle reflux was maintained.

Addition time was 1 hr. The reaction mixture was heated at

reflux for 0.5 hr with a warm water bath. The funnel was

charged with a solution of 16.3 g (0.37 mol) of ethanal in

40 mL of dry ethyl ether. After the reaction mixture had

cooled down to room temperature it was further cooled down to

0 ºC with an ice/water bath and the ethanal solution was

slowly dripped in over a time span of 1.5 hr. The resulting

mixture was stirred for 1 hr at room temperature and then

poured into a mixture consisting of 11 mL of concentrated

sulfuric acid, 100 mL of water and 100 g of ice. After the

ice melted, the phases were separated. The aqueous phase was

extracted with 2 x 50 mL portions of ethyl ether. The com-

bined organic extracts were washed with 2 x 50 mL portions of

10% sodium bicarbonate solution, 3 x 50 mL portions of water

and dried with magnesium sulfate. The solvent was removed in

the rotatory evaporator and the residue was distilled at atmospheric pressure to yield 28.6 g (70%) of a clear liquid, bp 154-157 °C (lit. bp 160 °C). The infrared spectrum matched the one of a known sample.

Synthesis of Pyridinium Chlorochromate - The method of Corey[271] was utilized. In a 250-mL Erlenmeyer flask containing a magnetic stirring bar was dissolved 25.0 g (0.25 mol) of chromium trioxide in 46 mL of 6 M hydrochloric acid with stirring. The solution was cooled to 0 °C with an ice/water bath. A funnel was charged with 19.8 g of pyridine, which was then slowly added into the cold, well-stirred solution over a time period of 0.5 hr. The reaction flask was allowed to stand in the ice/water bath for another 0.5 hr. The orange solid that had formed was collected by suction filtration and dried in a vacuum dessicator to yield 43.7 g (81%). The solid was used without further purification in the next reaction.

Synthesis of 2-Heptanone - The method of Corey and Suggs[271] was adapted for this preparation. In a 500-mL round-bottom flask, fitted with an addition funnel and a magnetic stirring bar, was suspended 32.3 g (0.15 mol) of pyridinium chlorochromate in 200 mL of dichloromethane. The funnel was charged with a solution of 11.6 g (0.10 mol) of 2-heptanol in 20 mL of dichloromethane and slowly added to the well-stirred suspension over a time period of 0.5 hr. The solution was stirred at room temperature for 2.0 hr and 200 mL of dry ethyl ether was added. The liquid was decanted from the black gum. The

gum was washed with 3 x 50 mL of dry ethyl ether. The combined organic extracts were filtered through a funnel containing 2 in. of Florisil. The solvent was removed in the rotatory evaporator and the residue was distilled at atmospheric pressure to yield 9.45 g (83%) of a clear liquid, bp 147-49 ^{o}C (lit. bp 151 ^{o}C). The infrared spectrum matched the one from a known sample.

Synthesis of 2-Heptanone Tosylhydrazone - In a 250-mL round-bottom flask equipped with a reflux condenser and a magnetic stirring bar was dissolved 37.2 g (0.20 mol) of tosylhydrazine in 120 mL of methanol by stirring the mixture in an oil bath preheated to 60 ^{o}C. To the stirred solution was added 22.8 g (0.20 mol) of 2-heptanone in one portion. The solution was heated at 60 ^{o}C for 2.75 hr, allowed to cool to room temperature and treated with water until it turned cloudy. The flask was allowed to stand at room temperature for several hrs. The solid was collected by suction filtration to yield 40.4 g of white, lumpy crystals. The mother liquor was stored in the refrigerator overnight to yield a second crop weighing 8.85 g. A total of 49.3 g (87%) of product was obtained, mp 77-8 ^{o}C. It showed the following spectral characteristics; IR (solid film): 3200 cm^{-1}, strong (NH); 1710 cm^{-1}, weak (C=N); 1330 and 1160 cm^{-1}, strong, (SO$_2$) and 810 cm^{-1} (para substituted benzene); 'H NMR (CDCl$_3$) triplet at δ 0.8 (3 H, terminal methyl), broad multiplet at δ 1.1 to 1.6 (6 H, internal methylenes), singlet at δ 1.83 (3 H, methyl next to

C=N), triplet at δ2.2 (2 H, methylene next to C=N), singlet at δ2.5 (3 H, methyl on benzene ring) and a doublet of doublets at δ7.30 and δ7.90 (5 H, aromatic protons plus the proton on nitrogen buried underneath as evidenced by line sharpening upon addition of D_2O).

Anal. Calculated for $C_{14}H_{22}N_2O_2S$: C, 59.55; H, 7.85. Found: C, 59.54; H, 7.74.

Vacuum Pyrolyses of the Dry Lithium Salt of 2-Heptanone Tosyl-hydrazone - The dry lithium salts were obtained in the usual manner by reaction of 1.42 g (5.0 mmol) of tosylhydrazone with 3.6 mL of 1.4 M (5.0 mmol) of methyl lithium solution. The salts were pyrolyzed and analyzed by vpc on Column B at 55 °C and a 40-mL/min flow rate of helium. Utilizing hexane as an internal standard, the product was determined to consist of 1-heptene (A), trans-2-heptene (C) cis-2-heptene (B) and 2-heptanone. The alkene distribution for each run is shown below. Besides the alkenes, the product of each run contained 20-30% of 2-heptanone.

T	A	B	C	Yield
200 °C	3.5%	26.6%	69.9%	62%
150 °C	3.5%	30.8%	65.7%	57%
150 °C	4.7%	31.8%	63.5%	65%

Vacuum Pyrolyses of the Dry Sodium Salt of 2-Heptanone Tosyl-hydrazone - The dry sodium salts were obtained and pyrolyzed at 150 °C in the manner previously described employing 1.42 g (5.0 mmol) of tosylhydrazone. Vpc analyses indicated that the

product was composed of alkenes A-C; 2-heptanone was not present. The product composition of each run is shown below.

Eq. NaOMe	A	B	C	Yield
1.0	4.0%	14.8%	81.2%	3%
1.0	8.8%	17.3%	73.9%	3%
1.6	1.9%	14.5%	83.6%	5%
1.6	4.6%	16.5%	78.9%	8%

<u>Thermal Decomposition of 2-Heptanone Tosylhydrazone with Sodium Methoxide in Diglyme</u> - The title compound (2.82 g, 10.0 mmol) in dry diglyme was decomposed with 5.10 g (94.3 mmol, 9.4 equiv.) of sodium methoxide as previously described. Vpc analysis indicated that the alkene distribution was 1.4% A, 15.8% B and 82.8% C together with a 16% yield of 2-heptanone. The yield of alkenes was 38% based on tosylhydrazone.

<u>Photolysis of the Lithium Salt of 2-Heptanone Tosylhydrazone</u> - The lithium salt of 1-heptanone tosylhydrazone was irradiated in the manner previously described for 2.5 hr (50 mL of gas were collected). Vpc analysis showed that the alkene composition was 24.2% A, 27.9% B and 47.9% C in a yield of 6%. The product also contained 2% of heptanone.

<u>Identification of Products</u> - The main product, trans-2-heptene was isolated by preparative vpc on Column B. Its IR spectrum matched the one from a known sample. 2-Heptanone was isolated on Column C at 135 $^{\circ}$C. Its IR, ^{1}H and ^{13}C NMR spectra matched the ones obtained on starting material. The identities of 1-heptene and cis-2-heptene were verified by comparing their vpc retention times with the ones of independently synthesized

samples.

Synthesis of 1-Heptene - The method of Shapiro et al.[272] (procedure A) was employed for the preparation of the title compound. Diispropylamine (4.10 g, 40.5 mmol) in 20 mL of tetramethyethylene diamine was allowed to react with 17.1 mL of a 1.4 M solution of methyl lithium (24.0 mmol) in ethyl ether and 2.82 g (10.0 mmol) of 2-heptanone tosylhydrazone. After work-up the solvent was removed by distillation through a 20-cm Vigreux column. The product was collected by preparative vpc on Column B. Its IR spectrum matched the one of a known sample.

Synthesis of Pentyl Triphenylphosphonium Bromide - In a 250-mL round-bottom flask equipped with a reflux condenser and a magnetic stirring bar was dissolved 26.2 g (0.10 mol) of triphenylphosphine in 75 mL of xylene at room temperature. To the well-stirred solution was added 15.3 g (0.10 mol) of 1-bromopentane in one portion. The ensuing solution was heated at reflux for 22 hr and allowed to cool down to room temperature. The precipitate that had formed was collected by suction filtration to yield 35.4 g of crude product. The crude product was purified by dissolving it in dichloromethane and then precipitating with tetrahydrofuran. The flask was stored in the refrigerator for several hrs. The product was collected by suction filtration and stored in a vacuum dessicator over phosphorous pentoxide for several days to yield 30.0 g (73%) of white crystals. The product exhibited the following spec-

tral characteristics; IR (solid film): 3040 cm^{-1}, medium
(aromatic hydrogens), 1590 and 1490 cm^{-1}, medium (aromatic
double bond), 1440, strong and 1000 cm^{-1}, medium (phosphorous
to benzene ring), 760 and 700 cm^{-1} (mono substituted benzene
ring); ^{1}H NMR (20% solution in CDCl$_3$): multiplet at δ 8.0
(15 H, aromatic protons), broad multiplet at δ 3.8 (2 H, pro-
tons on carbon 1 of the pentyl group), multiplet at δ 1.2-1.8
(6 H, methylene protons of carbons 2, 3 and 4 of pentyl
group) and a distorted triplet at δ 0.85 (3 H, methyl protons
of the pentyl group).

Synthesis of cis-2-heptene - The method of Butler and co-
workers[273] was employed for this preparation. Pentyltri-
phenyl phosphonium bromide (13.1 g, 31.7 mmol) in 125 mL of dry
ethyl ether under nitrogen was allowed to react with 19.8 mL
of a 2.4 M solution of butyl lithium (47.6 mmol) in hexane.
The reaction flask was cooled to about 9 °C by means of an
ice/water bath, 2.8 g (63.4 mmol) of ethanal in 60 mL of dry
ether was then added into the reaction flask over a time span
of 2-3 min. The solvent was removed by distillation through
a 20-cm Vigreux column. The concentrated solution was allowed
to stand at room temperature overnight. The liquid residue
was decanted off the precipitate that had formed. An aliquot
containing hexane as an internal standard was analyzed by vpc
on Column B and determined to consist of 35.4% trans-2-heptene
and 64.6% of cis-2-heptene. The yield of alkenes was 24%.
The trans isomer was identified by comparison of its retention

time to that of an authentic sample. The cis isomer was collected by preparative vpc; its IR spectrum matched the one of a known sample.

Synthesis of 6-Acetyl-3-methyl-2-cyclohexenone - The procedure of Lacey[274] with modifications was employed. In a 1-L round-bottom flask equipped with a magnetic stirring bar, Dean-Stark trap and reflux condenser, was dissolved 70.0 g (1.00 mol) of 3-buten-2-one in 120.0 g (1.20 mol) of 2,4-pentanedione. To the well-stirred solution was added 2.50 g (0.046 mol) of sodium methoxide. The solution was heated at reflux for 5 hr after which time 18.6 mL of water had collected in the trap. The solution was allowed to cool to room temperature and 400 mL of ethyl ether was added. The resulting solution was washed with 3 x 50 mL portions of 10% sulfuric acid solution and 2 x 100 mL portions of water. The solvent was removed in the rotatory evaporator and the crude 6-acetyl-3-methyl-2-cyclohexenone obtained was used in the next step without further purification.

Synthesis of 3-Methyl-2-cyclohexenone - The method of Lacey[274] was adapted for this synthesis. In a 1-L round-bottom flask fitted with a magnetic stirring bar and reflux condenser were placed 500 mL of a 10% sodium hydroxide solution and the crude 6-acetyl-3-methyl-2-cyclohexenone. The vigorously stirred mixture was refluxed for 1 hr, allowed to cool to room temperature and extracted with 4 x 200 mL portions of ethyl ether. The combined organic extracts were dried with $MgSO_4$. The

solvent was removed in the rotatory evaporator and the product was isolated by vacuum distillation to yield 61.0 g (55% based on 3-buten-2-one) of a clear liquid, bp 78-81 °C/13 torr (lit bp 79 °C/13 torr). The product had the following spectral characteristics; IR (neat): 3025 cm^{-1} (vinyl hydrogen), 1660 cm^{-1} (conjugated carbonyl), 1620 (conjugated double bond); ^{1}H NMR (10% in CCl_4), singlet (methyl) at $\delta 1.95$ on top of a multiplet (ring protons) $\delta 1.8-2.1$, multiplet at $\delta 2.1-2.35$, singlet (vinyl proton) at $\delta 4.7$ (integration gives a ratio of 9.8 to 1 aliphatic to vinyl protons.

Synthesis of 2,3-Epoxy-3-methylcyclohexanone - The procedure of Eschenmoser et al.[275] was adapted for use in this laboratory. In a 1-L 3-necked round-bottom flask equipped with a thermometer, addition funnel and a magnetic stirring bar was dissolved 51.7 g (0.44 mol) of 3-methyl-2-cyclohexenone in 600 mL of methanol. The funnel was charged with 139.6 g (1.41 mol) of a 30% solution of H_2O_2. The flask was cooled to 2 °C with an ice/water bath and the peroxide solution was slowly dripped into the well-stirred alcoholic solution over a period of 0.75 hr. The temperature rose to 4 °C. The bath was removed and when the temperature reached 5 °C, 8 mL of a 6 M (1.92 g, 0.048 mol) NaOH solution was added in one portion. The temperature started to rise and when it reached 15 °C, the bath was replaced. The temperature rose to 45 °C and started to go down. The solution was stirred for a total of 0.33 hr (temperature was 10 °C). The reaction solution

was poured into a mixture of 500 g of ice and 750 mL of saturated brine solution. The ensuing solution, after the ice had melted, was divided into two equal portions and each one was extracted with 5 x 200 mL portions of CH_2Cl_2. The combined organic extracts were dried over $MgSO_4$. The solvent was removed on the rotatory evaporator and after vacuum distillation 53.0 g (96%) of a clear oil, bp 60-70 °C/10 torr (lit bp 201-2 °C) were obtained. The product had IR (neat): 1720 cm^{-1} (carbonyl), 1260 and 810 cm^{-1} (epoxide), ^1H NMR (20% in $CDCl_3$): singlet at δ 1.45 (3 H, methyl on C 3), complex multiplet at δ 1.7-2.5 (6 H, three adjacent ring methylene groups) and singlet at δ 3.05 (1 H, proton on C 2).

Synthesis of 6-Heptyn-2-one - The procedure of Eschenmoser et al.[276] was employed with modifications. In a 500-mL Erlenmeyer flask was dissolved 14.7 g (0.071 mol, 1.05 equiv.) of tosylhydrazine in 200 mL of a 2:1 dichloromethane/acetic acid solution. In a 250-mL Erlenmeyer flask was dissolved 9.50 g (0.0753 mol, 1.00 equiv.) of 2,3-epoxy-3-methylcyclohexanone in 200 mL of a 2:1 dichloromethane/acetic acid solution. The flasks were cooled by storing in the refrigerator for 1 hr. The contents of the 250-mL flask were poured into the 500-mL flask with swirling. The resulting solution was stored in the refrigerator for 20 hr, a magnetic stirrer was added and the solution was stirred at room temperature for 4 hr. The orange solution was poured into a mixture of 250 g of ice in 250 mL of water. After the ice had melted, the phases were separated

and the aqueous phase was extracted with 3 x 150 mL portions of ethyl ether. The combined organic extracts were washed with 3 x 200 mL portions of a 10% solution of sodium carbonate, 2 x 200 mL of saturated brine solution and dried over $MgSO_4$. The solvent was removed in the rotatory evaporator and the product was vacuum-distilled to yield 3.10 g (38%) of a clear liquid, bp 52-4 ^{o}C/10 torr (lit bp 53 ^{o}C/11 torr). The product had the following spectral characteristics: IR (neat): 3280 cm^{-1} (carbonyl); ^1H NMR (20% in $CDCl_3$): quintet at δ1.75 (2 H, J = 7 Hz), protons on carbon 4), triplet at δ1.95 (1 H, J = 2 Hz, ethynyl proton), singlet at δ2.15 (3 H, methyl protons) partially overlapping a multiplet at δ2.25 (2 H, methylene protons on carbon 5) and a triplet at δ2.6 (2 H, J = 7 Hz, methylene protons on carbon 3). The multiplet at δ2.25 can be discerned as a triplet (J = 7 Hz) further split into doublets (J = 2 Hz).

Synthesis of 6-Heptyn-2-one Tosylhydrazone - In a 100-mL round-bottom flask equipped with a magnetic stirring bar and reflux condenser was dissolved 15.13 g (0.081 mol) of tosylhydrazone in 60 mL of methanol by stirring the mixture in an oil bath heated to 51 ^{o}C. After all the solid had dissolved, 8.95 g (0.081 mol) of 6-heptyn-2-one was added in one portion. The solution was stirred at 51 ^{o}C for 14 hr and then water was added dropwise until the solution turned cloudy. The solution was allowed to cool down to room temperature and then stored in the refrigerator for several hours. The precipitate that

had formed was collected by suction filtration to yield 20.30

g (90%) of white crystals, mp 116-117 °C. The product has the

following spectral characteristics; IR (solid film): 3300

cm^{-1} (ethynyl hydrogen), 3180 cm^{-1} (hydrogen on nitrogen),

1640 cm^{-1} (imine double bond), 1600 cm^{-1} (aromatic double

bond), 1330 and 1160 cm^{-1} (sulfonamide), 800 cm^{-1} (p-substi-

tuted benzene): ^{1}H NMR (20% in CDCl$_3$): doublet of doublets

at δ7.35 and δ7.90 (5 H, aromatic protons on top of NH proton,

peaks sharpen up after addition of D$_2$O), singlet at δ2.5 (3 H,

methyl on benzene ring), triplet at δ2.35 (2 H, J = 7 Hz,

protons on carbon 3), multiplet at δ2.10 (2 H, protons on

C 5), triplet at δ1.95 (1 H, J - 2 Hz), ethynyl proton),

singlet at δ1.80 (3 H, methyl protons of carbon 1) overlapping

with a multiplet at δ1.70 (2 H, J = 7 Hz, methylene protons

on carbon 4).

Anal. Calculated for C$_{14}$H$_{18}$N$_2$O$_2$S: C, 60.41; H, 6.52. Found:

C, 60.70; H, 6.45.

Vacuum Pyrolyses of the Dry Lithium Salt of 6-Heptyn-2-one

Tosylhydrazone - The dry lithium salts were obtained by reac-

tion of 1.39 g of tosylhydrazone with 3.6 mL of a 1.4 M solu-

tion of methyl lithium as described in the general procedure.

The salts were pyrolyzed at 150 °C and analyzed by vpc on

Column B at 75 °C and a 40 mL/min flow rate of helium employ-

ing heptane as the internal standard. The product composition

was determined to be: 8.5% of 1-hepten-6-yne (A), 57.0% of

trans-5-hepten-1-yne (B), 27.7% of cis-5-hepten-1-yne (C) and

6.8% of 1-methyl-1,3-cyclohexadiene (D). A second run had

the following product composition: 7.8% A, 58.4% B, 31.3% C

and 2.5% D. The yields of products were 18 and 13% respect-

ively.

Vacuum Pyrolyses of the Dry Sodium Salt of 6-Heptyn-2-one

Tosylhydrazone - The dry sodium salts were obtained by reac-

tion of 1.39 g (5.0 mmol) of tosylhydrazone with 1.0 eq. of

sodium methoxide generated in situ by addition of 0.115 g

(5.0 mmol) of sodium to 15 mL of methanol as previously

described. The salt was pyrolyzed at 150 °C and analyzed by

vpc. The product composition was determined to be: 5.6% A,

33.7% B, 10.4% C and 50.3% D. A second run was determined to

have the following product composition: 3.2% A, 31.2% B,

16.6% C and 49.0% D. The yields of products were 3 and 4%

respectively.

Photolysis of the Lithium Salt of 6-Heptyn-2-one-Tosylhydra-

zone - The lithium salt was generated employing the experi-

mental procedure earlier described by reacting 0.70 g (2.50

mmol) of tosylhydrazone with 1.5 mL of a 1.67 M solution of

methyl lithium (2.5 mmol). The solution was irradiated for

4.0 hr and 36 mL nitrogen were collected (66% of the theoret-

ical amount). The residue was analyzed by vpc. The product

composition was determined to be: 15.4% A, 27.1% B, 18.0% C

and 39.5% D. The yield of product was 2%.

Identification of Products from the Reactions of 6-Heptyn-2-

one Tosylhydrazone - The products of the vacuum pyrolysis of

the lithium salt of 6-heptyn-2-one tosylhydrazone (generated with 0.8 eq. of methyl lithium) were isolated by preparative vpc and identified by their spectral properties. The first peak was identified as 1-hepten-6-yne. The IR (neat) had the following bands: 3300 cm^{-1}, strong (ethynyl hydrogen), 3060 cm^{-1}, weak (vinyl hydrogen), 2125 cm^{-1}, weak (triple bond), 1650 cm^{-1}, medium (double bond), 995 cm^{-1}, medium and 910 cm^{-1}, strong (characteristic bonds for a terminal olefin). The ^1H NMR ($CDCl_3$, microcell) had the following peaks: multiplet at $\delta 1.6$ (2 H, methylene protons on carbon 4), triplet at $\delta 1.95$ (1 H, ethynyl proton), multiplet at $\delta 2.05-2.4$ (4 H, methylene protons on carbons 3 and 5) and a multiplet at $\delta 5.0$ (2 H) and $\delta 4.8$ (1 H, characteristic pattern of a terminal olefin). The third peak was identified as cis-5-hepten-1-yne based on the following spectral characteristics; IR (neat): 3300 cm^{-1}, strong (ethynyl hydrogen), 3020 cm^{-1}, medium (vinyl hydrogen), 2125 cm^{-1} (triple bond), 1650 cm^{-1}, weak (double bond) and 730 cm^{-1}, strong (characteristic of cis olefin); ^1H NMR ($CDCl_3$, microcell): δ doublet at 1.7 (3 H, methyl protons), broad singlet at $\delta 1.95$ (1 H, ethynyl proton), broad singlet at $\delta 2.25$ (4 H, methylene protons on carbons 3 and 4) and a multiplet at $\delta 5.4-5.6$ (2 H, vinyl protons, characteristic shape of a disubstituted olefin). The second peak was identified as trans-5-hepten-1-yne based on the following spectral characteristics; IR (neat): 3300 cm^{-1}, strong (ethynyl hydrogen), 3040 cm^{-1}, medium (vinyl hydrogen), 2130 cm^{-1}, weak

(triplet bond), 1650 cm^{-1}, weak (double bond) and 965 cm^{-1}, strong (characteristic of a trans olefin); ^{1}H NMR (CDCl$_3$, microcell): doublet at δ1.7 (3 H, methyl protons), broad singlet at δ1.95 (1 H, ethynyl proton), broad singlet at δ2.25 (4 H, methylene protons on carbons 3 and 4) and a multiplet at δ5.4-5.6 (2 H, characteristic of a disubstituted olefin). The fourth product, 1-methyl-1,3-cyclohexadiene, which was not produced in the above reaction, was identified by comparison of its retention time with those of an independently synthesized sample.

Synthesis of 3-Methyl-2-cyclohexenone Tosylhydrazone - In a 100-mL round-bottom flask equipped with a magnetic stirring bar and a reflux condenser was dissolved 9.31 g (0.050 mol) of tosylhydrazine in 30 mL of methanol by heating to 44 $^{\circ}$C (oil bath) for about 10 min. After all the solid had dissolved, 5.51 g (0.050 mol) of 3-methyl-2-cyclohexenone was added in one portion. The solution was heated at 44 $^{\circ}$C for 50 min (it turned dark yellow), allowed to cool down to room temperature and stored in the refrigerator overnight. The precipitate that formed was collected by suction filtration to yield 9.50 g (68%) of a white powder with a slight brownish tinge, mp 144-46 $^{\circ}$C. The product exhibited the following spectral characteristics; IR (solid film): 3200 cm^{-1}, strong (amine hydrogen), 3030 cm^{-1}, weak (vinyl hydrogen), 1650 cm^{-1}, medium (conjugated carbon-nitrogen double bond), 1600 cm^{-1}, medium (conjugated carbon-carbon double bond), 1590 cm^{-1}, shoulder,

and 1490 cm^{-1}, weak (aromatic double bonds), 1330 cm^{-1}, strong and 1170 cm^{-1}, strong (sulfonamide), 820 cm^{-1}, strong (p-substituted benzene); ^{1}H NMR (20% in CDCl$_3$) distorted triplet at δ1.8 (3 H, methyl protons of the carbon attached to carbon 3 of the cyclohexene ring), multiplet from 1.95-2.4 (6 H, methylene protons of carbons 4, 5 and 6 of the cyclohexene ring), singlet at δ2.45 (3 H, methyl protons of the benzylic carbon), broad singlets with fine splitting at δ5.95 and δ6.20 (1 H, vinyl proton, syn and anti isomers), doublet of doublets at δ7.25 and δ7.8 (5 H, aromatic protons with the amine proton buried underneath the doublet at δ7.8 as evidenced by line sharpening upon exchange with D$_2$O).

Anal. Calculated for C$_{14}$H$_{18}$N$_2$O$_2$S: C, 60.41; H, 6.52. Found: C, 60.00; H, 6.28.

Synthesis of 1-Methyl-1,3-cyclohexadiene - The method used for the synthesis of 1,5,5-trimethyl-1,3-cyclohexadiene was employed. A solution of 2.79 g (10.0 mmol) of 3-methyl-2-cyclohexenone tosylhydrazone in 50 mL of dry ether under nitrogen was allowed to react with 13.7 mL of a 1.75 M solution of methyl lithium (24.0 mmol, 2.40 equiv.). The residue obtained after work-up and removal of solvent through a 20-cm Vigreux column was analyzed by vpc on Column C at 80 ^{o}C and a helium flow rate of 50 mL/min. The vpc trace indicated the presence of a major product plus a small amount of an impurity. The major product was obtained by preparative vpc. It had the following spectral properties; IR (neat): 3030 cm^{-1}, strong

(vinyl hydrogen), 1650 cm^{-1}, weak and 1600 cm^{-1} (double bond, characteristic of conjugated diene), 840 cm^{-1} (trisubstituted olefin), 690 cm^{-1} (cis olefin); ^{1}H NMR (20% in $CDCl_3$): broad singlet at δ1.8 (3 H, methyl protons), broad singlet with some fine splitting at δ2.2 (4 H, methylene protons of carbons 5 and 6), broad multiplets at δ5.7 (2 H, vinyl protons) and a broad multiplet at δ5.9 (1 H, vinyl proton), ^{13}C NMR (20% in $CDCl_3$): δ22.80 (methyl carbon attached to double bond), δ23.39 (carbon 5), δ27.98 (carbon 6), δ119.06 (carbon 4), δ122.98 (carbon 2 or 3), δ124.69 (carbon 3 or 2) and δ135.87 (carbon 1).

Synthesis of Tetrahydrofurfuryl Chloride - The procedure employed was the method of Brooks and Snyder.[277] Reaction of 408 g (4.0 mols) of tetrahydrofurfuryl alcohol in 348 g (4.4 mols) of pyridine with 500 g (4.2 mols) of thionyl chloride afforded after vacuum distillation 279 g (58%) of a slightly brown liquid, bp 52-55 °C at 20 torr (lit bp 47-48 °C at 15 torr). A second distillation gave a colorless liquid bp 50-52 °C at 20 torr. The product had the following spectral characteristics; IR (neat): 1070 cm^{-1}, strong (carbon-oxygen stretch) and 740 cm^{-1}, strong (carbon-chlorine stretch); ^{1}H NMR (20% in $CDCl_3$): multiplet at δ1.85 (4 H, methylene protons on carbons 2 and 3 of the ring), multiplet at δ4.5 (2 H, methylene protons on the carbon bearing the chlorine atom) and a multiplet at δ4.9 (3 H, methylene and methine protons on carbons 1 and 4 of the ring).

Synthesis of 4-Pentyn-1-ol - The method of Jones, Eglinton and Whiting[278] was employed. Following their procedure, 401.65 g (3.30 mols) of tetrahydrofurfuryl chloride was reacted to yield 196.0 g (2.33 mols, 71%) of 4-pentyn-1-ol as a clear liquid, bp 76-78 °C at 30 torr (lit bp 70-71 at 29 torr). The product exhibited the following spectral characteristics; IR (neat) 3400 cm^{-1}, broad and strong (hydroxyl), 3320 cm^{-1}, strong (hydrogen attached to sp carbon), 2140 cm^{-1}, medium (triple bond) and 1060 cm^{-1}, strong (carbon-oxygen stretch); nmr (20% solution in deuteriochloroform) triplet at $\delta 1.8$ (1 H, proton on triple bond), multiplet at $\delta 2.0$ (2 H, methylene protons on carbon 2), triplet of doublets at $\delta 2.5$ (2 H, methylene protons adjacent to triple bond), triplet at $\delta 3.9$ (2 H, methylene protons on carbon-bearing hydroxyl group) and a singlet at 4.8 δ (1 H, hydroxyl proton which disappears upon addition of D_2O).

Synthesis of 4-Pentynoic Acid - A chromic acid solution was prepared by dissolving 140.0 g (1.40 mols) of chromium tri-oxide in 200 mL of water in a 1-L Erlenmeyer flask. To this solution was gradually added 122 mL (2.2 mols) of concentra-ted sulfuric acid in small portions and occasional cooling (tap water). After solution had cooled to room temperature, it was diluted with 400 mL of water. In a 500-mL 3-neck round-bottom flask equipped with a Herschberg stirrer, 125-mL addition funnel and thermometer, was dissolved 10.5 g (0.125 mol) of 4-pentyn-1-ol in 250 mL of acetone. The flask

was cooled in an ice/water bath and the funnel was charged
with 110 mL (0.204 mols of CrO_3) of the above-prepared
chromic acid solution. When the temperature of acetone
solution reached 3 $^{\circ}$C, the chromic acid addition was commen-
ced and continued at such a rate that the temperature of the
reaction mixture remained between 10 and 15 $^{\circ}$C. The addition
took about 1 hr. The ice bath was removed and the reaction
mixture was allowed to stir at room temperature overnight.
Several mL of 2-propanol was added (until brownish color dis-
appeared) to destroy excess chromic acid followed by 200 mL
of saturated sodium chloride solution to dissolve the precip-
itated chromium salts. The resulting solution was extracted
with 100 mL of ethyl ether followed by 2 x 50 mL portions of
the same solvent. The combined organic extracts were washed
with 2 x 100 mL portions of saturated sodium chloride solu-
tion and dried over magnesium sulfate. The solvent was re-
moved on the rotatory evaporator to leave behind a brownish
liquid which solidified on standing. Purification by recrys-
tallization from petroleum ether yielded 7.0 g (57%) of white
flakes, mp 51-2 $^{\circ}$C (lit mp 57 $^{\circ}$C). The product had the fol-
lowing spectral characteristics; IR (solid film): 3300 cm^{-1},
sharp, narrow and strong (hydrogen attached to triply bonded
carbon), 2400-3000 cm^{-1}, broad (carboxylic acid, hydrogen
bonded) and 1710 cm^{-1}, strong (carbonyl group); ^{1}H NMR (20%
in $CDCl_3$): triplet at δ 2.05 (1 H, J = 2Hz, proton on triply
bonded carbon), multiplet at δ 2.55 (4 H, methylene protons on

carbons 2 and 3) and singlet at δ11.8 (1 H, hydroxyl proton, disappears upon addition of D_2O).

Synthesis of 4-Pentynoyl Chloride - In a 100-mL round-bottom flask equipped with a magnetic stirring bar, 25 mL addition funnel and gas inlet was dissolved 10.5 g (0.107 mol) of 4-pentynoic acid in 35 mL of dry benzene. The funnel was charged with a solution of 14.0 g (0.118 mol, 1.1 equivalents) of thionyl chloride in 10 mL of dry benzene. The system was flushed with nitrogen for 0.5 hr. The thionyl chloride solution was dripped into the well-stirred reaction flask over a time period of 0.5 hr. The mixture was stirred for 12 hr at room temperature under nitrogen. The solvent and unreacted thionyl chloride were removed by distillation at atmospheric pressure. The product was then obtained by a vacuum distillation that yielded 8.70 g (70%) of a clear liquid, bp 42-44 $^{\circ}$C at 25 torr. The acid chloride showed the following spectral properties; IR (neat): 3320 cm^{-1}, strong (hydrogen on triple bond), 2140 cm^{-1}, weak (triple bond), 1810 cm^{-1}, strong (carbonyl) and 730 cm^{-1} strong (carbon chlorine stretch); ^1H NMR (20% in $CDCl_3$): triplet at δ2.0 (1 H, J = 3 Hz, proton of triple bond), a triplet of doublets (2 H, J = 3 Hz, J^1 = 10 Hz, methylene protons on C-3) and a triplet at δ3.2 (2 H, J = 10 Hz, methylene protons on C-2).

Synthesis of 1-Diazo-5-hexyn-2-one - The method of Arndt[279] was employed to prepare a dilute solution of diazomethane in ethyl ether. The method of Kuper[280] was employed for the preparation of 1-diazo-5-hexyn-2-one. A solution of 2.50 g

(21.5 mmol) of 4-pentynoyl chloride in 10 mL of dry ethyl ether was reacted with the solution containing about 2.8 g (66.7 mmol) of diazomethane at 0 °C. Complete removal of solvent was insured by evacuating the reaction flask to 20 torr for 0.5 hr to leave behind 2.6 g of a yellow oil. No further attempts were made to purify the oil (known to contain 1-chloro-6-hexyn-2-one), which was used right away for the next reaction. The product had the following spectral characteristics; IR (neat): 3300 cm^{-1}, strong (ethynyl hydrogen), 2250 cm^{-1}, medium, shoulder (triple bond), 2150 cm^{-1}, strong (diazo band) and 1640 cm^{-1}; ^{1}H NMR (20% in CDCl$_3$): triplet at δ2.1 (1 H, J = 2 Hz), broad multiplet at δ2.6 (4 H, methylene protons on carbons 3 and 4 and a singlet at δ5.4 (1 H, methine proton on the carbon bearing the diazo group). The ultraviolet spectrum exhibited a λ_{max} at 248 nm with an ϵ value of 10,800 L/mol cm.

Photolysis of 1-Diazo-5-hexyn-2-one - A solution of 1.90 g (15.6 mmol) of 1-diazo-5-hexyn-2-one in 150 mL of dry ethyl ether was degassed by bubbling nitrogen through it for 30 min and then irradiated in a 250-mL photolysis flask with a 450 W high-pressure mercury lamp through a Pyrex filter for 1.5 hr. The reaction solution was stirred with 15 mL of methanol overnight. It was then concentrated to about 8 mL by distilling through a 20 cm Vigreux column (pot temperature of 85 °C). The residue was analyzed by vpc on Column E at 60 °C and a 30 mL/min flow rate of helium. Using nonane as an internal standard, the product was determined to consist of methyl 5-

hexynoate (85%) and l-chloro-5-hexyn-2-one (15%). The yield

of methyl 5-hexynoate was 16.5% based on l-diazo-5-hexyn-2-

one.

<u>Identification of the Products from the Unsensitized Decompo-</u>

<u>sition of l-Diazo-5-hexyn-2-one</u> - The products from the unsen-

sitized photolysis of l-diazo-5-hexyn-2-one were separated and

collected by preparative vpc on Column E. The first peak was

identified as methyl 5-hexynoate. It exhibited the following

spectral characteristics: IR (neat): 3300 cm^{-1}, strong (ethy-

nyl hydrogen), 2100 cm^{-1}, weak (triple bond), 1720 cm^{-1},

strong (carbonyl), 1080 cm^{-1}, medium (carbon to oxygen); ^{1}H

NMR (20% in CDCl$_3$): triplet at δ2.0 (1 H, J = 2 Hz, ethynyl

proton), triplet of doublets at δ2.3 (2 H, J = 2 Hz, J^1 = 10

Hz, methylene protons on carbon 4), multiplet at δ2.1 par-

tially buried under triplet at δ2.0 (2 H, methylene protons

of carbon 3), triplet at δ2.45 (2 H, J^1= 10 Hz, methylene

protons on carbon 2) and a singlet at δ3.7 (3 H, methyl pro-

tons of carbon attached to oxygen). The second peak was iden-

tified as l-chloro-5-hexyn-2-one. It had the following spec-

tral properties; IR (neat): 3300 cm^{-1}, strong (ethynyl hydro-

gen), 2150 cm^{-1}, medium (triple bond), 1750 cm^{-1}, strong

carbonyl), 1240 cm^{-1}, strong (carbon-chlorine bond); MS: 130

(M, Relative intensity = 1.0), 132 (M + 2, RI = 1.2), 105

(RI = 4.8) and 107 (RI = 5.2, $[CH_2CH_2COCH_2Cl]^{+\cdot}$), 95 (RI =

100.0, $[HC{\equiv}CCH_2CH_2COCH_2]^{+\cdot}$), 81 (RI = 29.6, $[HC{\equiv}CCH_2CH_2CO]^{+\cdot}$),

77 (RI = 15.0) and 79 (RI = 10.4, $[COCH_2Cl]^{+\cdot}$).

<u>Anal</u>. Calculated for C_6H_7OCl: C, 55.19; H, 5.40. Found: C, 54.99; H, 5.12.

<u>Benzophenone Sensitized Photolysis of 1-Diazo-5-hexyn-2-one</u>: <u>Absence of Methyl 5-Hexynoate</u> - A solution of 1.80 g (14.7 mmol) of 1-diazo-5-hexyn-2-one and 3.0 g (16.5 mmol) of benzophenone in 175 mL of dry ethyl ether was photolyzed as described above for 4 hr (90 mL of gas, 33% of the theoretical, was evolved). The solution was stirred with 15 mL of methanol overnight. The solution was then concentrated to ca. 10 mL by distilling through a 20-cm Vigreux column (pot temperature of 78 °C). Analysis of the residue by vpc indicated that methyl 5-hexynoate was not a product of this reaction.

<u>Benzophenone Sensitized Photolyses of 1-Diazo-5-hexyn-2-one</u> - A solution of 2.00 g (16.4 mmol) of 1-diazo-5-hexyn-2-one and 3.00 g (16.5 mmol) of benzophenone in 200 mL of dry ethyl ether was photolyzed as described above for 5.0 hr (85 mL of gas was collected, 23% of theoretical). The solution was concentrated by distillation through a 20-cm Vigreux until no more solvent came over. The receiver was changed to a 10-cm tube cooled with a dry ice/2-propanol bath. The system was evacuated to 0.2 torr and 1.62 g of a clear liquid was collected in the trap. The liquid was analyzed by vpc on Column A at 50 °C and a helium flow rate of 30 mL/min and found to consist of 5-hexyn-2-one (18%), 1-chloro-5-hexyn-2-one (12%), 2,3-diethoxy-butane (36%) (either the meso or the d,ℓ dias-

tereomer) and 2,3-diethoxybutane (34%) (either the d,ℓ or the meso diastereomer). The yield of products derived from the diazo compound was 18%.

Identification of Products from the Benzophenone Sensitized Photolysis of 1-Diazo-5-hexyn-2-one - The products of the photolytic decomposition of the title compound, after they were recovered by a vacuum distillation as described in the previous experiment, were separated from the mixture by preparative vpc on Column A and their structures determined from spectral data. The first peak was identified as 5-hexyn-2-one. The ^{1}H NMR (CDCl$_3$, microcell) had the following peaks: triplet at δ1.90 (1 H, J = 2 Hz, ethynyl proton), singlet at δ2.15 (3 H, methyl protons), multiplet at δ2.45 (2 H, methylene protons on carbon 4), triplet at δ2.6 partially buried underneath multiplet at 2.45 (2 H, methylene protons on carbon 3). The ^{13}C NMR (CDCl$_3$, microcell) had the following peaks: δ13.18 (carbon 4), δ29.95 (carbon 1), δ42.39 (carbon 3), δ68.92 (carbon 6), δ78.0 (carbon 5) and δ207.73 (carbon 2).

High resolution mass spectrum. Calculated for C$_6$H$_8$O: 96.058. Found: 96.058.

The second peak was identified as 1-chloro-5-hexyn-2-one by comparison of its infrared spectra with that of product isolated from the unsensitized photolysis of the title compound.

The third peak was identified as 2,3-diethoxybutane (either the meso or the d,ℓ diastereomer, spectral properties

of the two diastereomers are very similar, especially the ^{1}H

NMR which is almost identical). The ^{1}H NMR (CDCl$_3$, microcell):

multiplet at δ1.0-1.25 (12 H, methyl protons) and multiplet

at δ3.25-3.45 (6 H, methylene and methine protons next to

oxygen). The ^{13}C NMR (CDCl$_3$, microcell) has the following

peaks: δ14.64, δ15.29, δ15.33, δ15.70 (methyl carbons), δ64.23,

δ64.45 (methylene carbons next to oxygen), δ77.14 and δ77.98

(methine carbons next to oxygen).

High resolution mass spectrum. Calculated for C$_8$H$_{18}$O$_2$:

146.132. Found: 146.132.

The fourth peak was identified as the other diastereo-

isomer of 2,3-diethoxybutane (no further attempts were made

to differentiate the meso from the d,ℓ pair). The ^{1}H NMR

(CDCl$_3$, microcell) consisted of the following peaks: multi-

plet at δ1.0-1.25 (12 H, methyl protons) and a multiplet at

δ3.3-3.6 (6 H, methylene and methine protons next to oxygen).

The ^{13}C NMR (CDCl$_3$, microcell) exhibited the following peaks:

δ14.90, δ15.04, δ15.60, δ15.72 (methyl carbons), δ64.72,

δ64.83 (methylene carbons), δ77.37 and δ77.53 (methine car-

bons).

High resolution mass spectrum. Calculated for C$_8$H$_{18}$O$_2$:

146.132. Found: 146.131.

Synthesis of α-1-Hydroxydicyclopentadiene - The method of

Woodward and Katz was employed. Commercial selenium dioxide

was purified by sublimation prior to use. Freshly distilled

dicyclopentadiene (186 g, 1.4 mol) in 500 mL of dioxane

containing 20 g of potassium dihydrogen phosphate and 50 mL
of water was allowed to react with 80 g (0.72 mol) of purified
selenium dioxide. After work-up the solvent was removed on
the rotatory evaporator and the residue was vacuum distilled
to yield 92.2 g (44%) of a slightly yellow, waxy oil, bp 76-
80 °C/0.20 torr (lit bp 67 °C/0.1 torr). The product exhib-
ited the following spectral characteristics; IR (neat) 3400-
3300 cm^{-1}, broad strong (hydrogen bonded hydroxyl), 3075 cm^{-1},
medium (vinyl hydrogen) and 1620 cm^{-1}, weak (double bond);
^{1}H NMR (20% in CDCl$_3$): distorted quartet at δ1.5 (2 H, methyl-
ene protons on the bridge carbon), multiplet at δ2.55 (1 H,
exo proton opposite to the hydroxyl group), multiplet at δ2.8
(1 H, exo proton on the side of the hydroxyl group), singlet
at δ3.1 (hydroxyl proton), multiplet at δ3.4 (2 H, bridgehead
protons), singlet with some fine splitting at δ4.1 (1 H,
proton on carbon bearing the hydroxyl group) and a complex
multiplet at δ5.5-6.0 (4 H, vinyl protons).

Synthesis of Dicyclopentadienone - Reaction of α-1-hydroxy-
dicyclopentadiene (40.0 g, 0.267 mol) in 500 mL of acetone
with 170 mL of chromic acid solution using the procedure
employed in the synthesis of 4-pentynoic acid afforded, after
work-up and removal of solvent in the rotatory evaporator,
27.10 g (69%) of a slightly yellow oil which solidified on
standing. The material was used in the next step without
further purification. The product showed the following spec-
tral characteristics; IR (film): 3075 cm^{-1}, weak (vinyl

hydrogen) 1710 cm^{-1}, strong (carbonyl) and 1595 cm^{-1}, medium
(conjugated double bond); ^{1}H NMR (20% in CDCl$_3$): distorted
quartet at δ1.8 (2 H, methylene protons on bridge carbon),
triplet at δ2.8 (1 H, exo proton on side of carbonyl group),
multiplet at δ3.05 (1 H, exo proton on side opposite of car-
bonyl group), broad singlet at δ3.25 (1 H, bridgehead proton
on side opposite of carbonyl group), muliplet at δ3.45 (1 H,
bridgehead proton on the same side as the carbonyl), multi-
plet at δ5.7-6.05 (3 H, vinyl protons) and a doublet of
doublets at δ7.4 (vinyl proton on the β carbon conjugated to
the carbonyl).

Synthesis of Bishomocubyl Ketone - The procedure of Dilling
and Reineke[283] was adapted for this preparation. A 400-mL
photochemical flask equipped with a magnetic stirring bar
was charged with a solution of 27.10 g (0.185 mol) of cyclo-
pentadienone in 350 mL of acetone. The solution was degassed
by bubbling nitrogen through it for 1.25 hr and then photo-
lyzed with a 450-W medium pressure mercury lamp through a
Corex filter for 19.5 hr. The solvent was removed on the
rotatory evaporator to leave behind 27.5 g of a yellow, vis-
cous liquid which solidified upon standing at room temperature.
The product was purified by vacuum sublimation at 110 °C/0.3
torr to yield 12.60 g (47%) of a white powdery solid, mp
114-15 °C. The product exhibited the following spectral
characteristics; IR (Nujol mull): 1780 cm^{-1}, strong (carbonyl);
^{1}H NMR (20% in CDCl$_3$): quartet at δ1.7 (2 H, methylene protons

on bridge carbon), multiplet a δ 2.2 (1 H, methine proton on carbon next to the carbonyl), distorted triplet at δ 2.45 (1 H, methine proton on carbon next to carbonyl) and a broad multiplet at δ 2.8-3.2 (6 H, methine protons).

Synthesis of Bishomocubyl Ketone Tosylhydrazone - In a 50-mL round-bottom flask fitted with a reflux condenser and magnetic stirring was dissolved 1.27 g (6.84 mmol) of tosylhydrazine in 20 mL of methanol by stirring at 56 °C (oil bath) for several min. To the warm solution was added 0.99 g (6.78 mmol) of bishomocubyl ketone in one portion. The solution was stirred at 56 °C for 1 hr, allowed to cool down to room temperature and stored in the refrigerator overnight. The precipitate was collected by suction filtration to yield 1.50 g (70%) of white powdery crystals. The product exhibited the following spectral data; IR (Nujol mull): 3250 cm^{-1}, strong (hydrogen on nitrogen), 1700 cm^{-1}, weak (carbon-nitrogen double bond), 1620 cm^{-1} and 1510 cm^{-1}, moderate, (aromatic double bonds), 1350 cm^{-1} and 1170 cm^{-1}, strong (sulfonamide), 820 cm^{-1}, strong (p-substituted benzene ring); NMR (20% solution in deuteriochloroform) quartet at δ 1.6 (2 H, methylene protons on bridge carbon), singlet at δ 2.5 (3 H, methyl on benzene ring), multiplet at δ 2.7-3.2 (8 H, methine protons), doublets at δ 7.2 and δ 8.0 (4 H, protons on benzene ring) and broad singlet at δ 8.2 (1 H, proton on nitrogen, disappears upon addition of D_2O).

Anal. Calculated for $C_{17}H_{10}N_2O_2S$: C, 64.95; H, 5.45. Found:

C, 64.93; H, 5.61.

Synthesis of 1-Bromocyclohexanecarboxaldehyde - The procedure of E.R.H. Jones et al.[283] was employed to synthesize the title compound by reacting 19.40 g (0.173 mol) of cyclohexanecarboxaldehyde and 12.50 g (0.125 mol) of calcium carbonate in 65 mL of chloroform with 27.64 g (0.173 mol) of bromine dissolved in 50 mL of chloroform. After work-up, the crude product was purified by a vacuum distillation to yield 16.50 g (50%) of a clear liquid, bp 70-72 °C (lit. bp 90-91 °C/20 torr). The product had the following spectral characteristics; IR (neat): 2850 cm^{-1}, medium and 2750 cm^{-1}, weak (aldehydic hydrogen) and 1720 cm^{-1}, strong (carbonyl); ^{1}H NMR (20% in CDCl$_3$): broad multiplet at δ2.4-2.9 (6 H, methylene protons on carbons 3, 4 and 5 of the ring), multiplet at δ3.0-3.2 (4 H, methylene protons on carbons 2 and 6 of the ring) and a singlet at δ9.3 (1 H, aldehydic proton).

Synthesis of 1-Cyclohexenecarboxaldehyde - Commercial N,N-diethylaniline (215 mL) was purified by heating at reflux for 14 hr with 92 mL of acetic anhydride and distilling to afford 115 g of a pale yellow liquid, bp 214-15 °C. The title compound was prepared by the method of E.R.H. Jones and co-workers[283] by heating 16.50 g (0.0863 mol) of 1-bromocyclohexane carboxaldehyde with 35 mL of purified N,N-diethylaniline at 110 °C for 38 hr under nitrogen. After work-up and vacuum distillation, 5.20 g (55%) of a clear liquid was obtained, bp 60-64 °C/9 torr (lit. bp 61-63 °C/10 torr). The

product showed the following spectral data; IR (neat): 3050 cm^{-1}, small shoulder (vinyl hydrogen), 2700 cm^{-1}, medium (aldehyde hydrogen), 1690 cm^{-1} (conjugated carbonyl) and 1650 (conjugated double bond); ^{1}H NMR (20% in CDCl$_3$: multiplet at δ1.6-1.8 (4 H, methylene protons on carbons 4 and 5 of the ring), multiplet at δ2.15-2.45 (4 H, methylene protons on carbons 3 and 6 of the ring), multiplet at δ6.85 (1 H, olefinic proton) and a singlet at δ9.55 (1 H, aldehydic proton).

Synthesis of 1-Cyclohexenecarboxaldehyde Tosylhydrazone - In a 100-mL round-bottom flask equipped with a reflux condenser and a magnetic stirring bar was dissolved 6.17 g (0.0331 mol) of tosylhydrazine in 30 mL of methanol by stirring at 55 °C (oil bath). After all the solid had dissolved, 3.65 g (0.0331 mol) of 1-cyclohexenecarboxaldehyde was added in one portion. The solution was stirred at 55 °C for 0.75 hr, allowed to cool down to room temperature and stored in the freezer overnight. The product was collected by suction filtration to yield 6.40 g (70%) of a white solid. The product exhibited the following spectral characteristics; IR (solid film): 3200 cm^{-1}, medium (amine hydrogen), 3050 cm^{-1}, weak (vinyl hydrogen), 2800 cm^{-1}, medium (aldehydic hydrogen), 1720 cm^{-1}, weak (carbon-nitrogen double bond), 1600 cm^{-1} and 1500 cm^{-1}, medium (aromatic double bonds), 1320 cm^{-1} and 1160 cm^{-1}, strong (sulfonamide) and 810 cm^{-1} (para substituted benzene); ^{1}H NMR (20% in CDCl$_3$): multiplet at δ1.5-1.7 (4 H, methylene protons on carbons 4 and 5 of cyclohexene ring), δ2.1-2.3 (4 H, methylene protons on

carbons 3 and 6 of cyclohexene ring), singlet at $\delta 2.5$ (3 H, methyl protons attached to benzene ring), multiplet at $\delta 6.0$ (1 H, vinyl proton), doublet of doublets at $\delta 7.3$ and 7.85 (4 H, aromatic protons), singlet at $\delta 7.4$ (1 H, proton on carbon doubly bonded to nitrogen) and a broad singlet at $\delta 8.15$ (1 H, amine proton), disappears upon addition of D_2O).

<u>Anal.</u> Calculated for $C_{14}H_{18}N_2O_2S$: C, 60.41; H, 6.52. Found: C, 60.08; H, 6.56.

<u>Synthesis of 1-Acetylcyclohexene Tosylhydrazone</u> - In a 300-mL round-bottom flask equipped with a reflux condenser and a magnetic stirring bar was dissolved 16.72 g (0.0898 mol) of tosylhydrazine in 200 mL of methanol by stirring and heating. To the warm solution was added 11.15 g (0.0898 mol) of 1-acetylcyclohexene[284] in one portion. The solution was heated with stirring at 63 $^{\circ}$C (oil bath) for 1.5 hr. Water was added dropwise to the hot solution until it turned cloudy. The resulting solution was allowed to cool down to room temperature while being vigorously scratched to avoid oiling out of the product. The flask was stored in the freezer overnight. The solid was collected by suction filtration to yield 23.10 g of yellow crystals. The product was recrystallized from methanol yielding 18.6 g (69%) of pale yellow crystals, mp 113-115 $^{\circ}$C. The product exhibited the following spectral properties; IR (Nujol mull): 3050 cm^{-1}, shoulder (vinyl hydrogen), 1700 cm^{-1}, weak (carbon-nitrogen double bond), 1600 cm^{-1} and 1500 cm^{-1}, medium (aromatic double bonds), 1360 cm^{-1}

and 1180 cm^{-1} (sulfonamide) and 810 cm^{-1}, strong (para sub-stituted benzene); ^{1}H NMR (20% CDCl$_3$): multiplet at δ 1.5-1.7 (4 H, methylene protons on carbons 4 and 5 of the ring), singlet at δ 1.95 (3 H, methyl protons of the acetyl group), multiplet at 2.1-2.3 (4 H, methylene protons on carbons 3 and 6 of the ring), singlet at δ 2.5 (3 H, protons on methyl attached to the benzene ring), multiplet at δ 6.2 (1 H, vinyl proton) and a doublet of doublets at δ 7.3 and δ 7.9 (5 H, aromatic protons with the amine proton buried underneath as evidenced by sharpening of the downfield doublet upon addition of D$_2$O. Anal. Calculated for C$_{15}$H$_{20}$N$_2$O$_2$S: C, 61.62; H, 6.90. Found: C, 61.35; H, 6.92.

Synthesis of 1-Cyclopentenecarboxaldehyde Tosylhydrazone - In a 50-mL Erlenmeyer flask equipped with a magnetic stirring bar was dissolved 5.60 g (30.0 mmol) of tosylhydrazine in 30 mL of methanol by heating and stirring. After all of the solid had dissolved, the alcoholic solution was allowed to cool down to room temperature and then 2.85 g (30.0 mmol) of 1-cyclo-pentenecarboxaldehyde[285] was added in one portion. The result-ing solution was stirred at room temperature for 15 min. The precipitate was collected by suction filtration to yield 6.70 g (84%) of white needles. The product exhibited the following spectral features; IR (solid film): 3150 cm^{-1}, strong (amine hydrogen), 3050 cm^{-1}, weak (vinyl hydrogen), 2820 cm^{-1}, medium (hydrogen attached to carbon doubly bonded to nitrogen), 1710 cm^{-1}, weak (carbon to nitrogen double bond), 1630 cm^{-1}, medium

(conjugated double bond), 1320 cm^{-1} and 1160 cm^{-1}, medium
(aromatic double bonds), 1320 cm^{-1} and 1160 cm^{-1}, strong (sul-
fonamide) and 810 cm^{-1}, strong (para substituted benzene); ^{1}H
NMR (20% in CDCl$_3$): distorted quintet at δ1.9 (2 H, methylene
protons of carbon 4 of the ring), singlet at δ2.45 on top of
a multiplet at δ2.35-2.65 (7 H, methyl protons on benzene ring
giving rise to singlet and methylene protons on carbons 3 and
5 of the ring giving rise to the multiplet), multiplet at
δ6.1 (1 H, vinyl proton), doublet of doublets at δ7.3 and
δ7.8 (4 H, aromatic proton), singlet at δ7.65 (1 H, formyl
proton) and a somewhat broad singlet at δ7.95 (1 H, amine
proton which disappears upon the addition of D$_2$O.

Anal. Calculated for C$_{13}$H$_{16}$N$_2$O$_2$S: C, 59.07; H, 6.10. Found:
C, 59.26; H, 6.28.

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APPENDIX

ABBREVIATIONS

dig	diglyme
EG	ethylene glycol
Et	ethyl
Et_2O	diethyl ether
hv	ultraviolet light
Me	methyl
RT	room temperature
THF	tetrahydrofuran
THPO	tetrahydropyranyl
Ts	p-toluenesulfonyl