Spiro Oxadiazolines –

Source of Cyclic Dioxa Carbenes

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by

BESY JOSE

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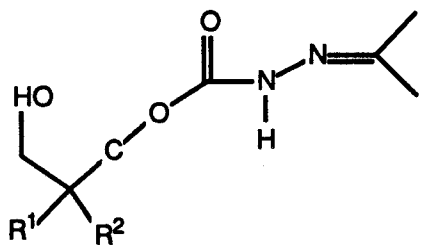
Abstract

It is known that alkoxyoxadiazolines undergo thermal decomposition to form carbenes via an ylide intermediate. This project involved the preparation and subsequent thermolysis of spirooxadiazolines of type 4.

Spiro oxadiazoline (4) was prepared by oxidation of (3) with lead tetraacetate in dichloromethane. The first order rate constant for the thermolysis of 4b in benzene at 111°C is determined. The primary thermolysis products were found to be acetone, nitrogen and the cyclic dioxacarbene (5). Formation of (5) was confirmed by various trapping experiments.



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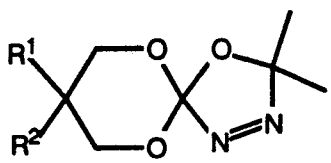

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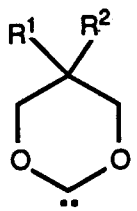

5

a, $R^1 = R^2 = H$
b, $R^1 = R^2 = Me$

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(Chemistry)

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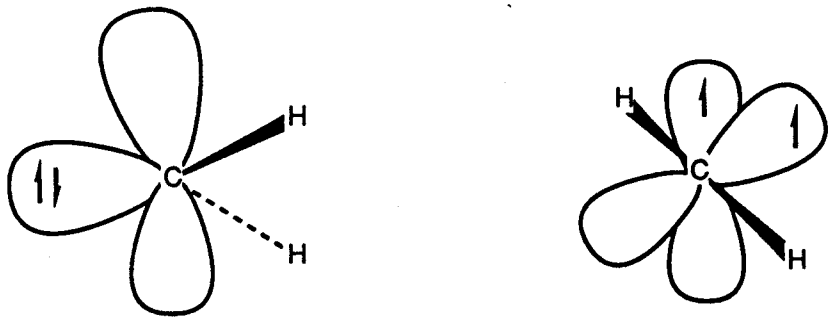
1. Introduction

The role of carbenes in chemistry is a well advanced field of research over the past few years. There is scarcely an active organic chemist who has not turned his attention in one way or another to carbene chemistry. Synthetic use of carbenes for the formation of cyclopropanes[1] and bridged or multicyclic compounds has received intense attention. Furthermore, much research is still being carried out to explore the mechanisms of carbene reactions.[2,3]

Generation of carbenes from the thermolysis of Δ^3-1,3,4-oxadiazolines is now well established.[4] Therefore, this introduction will deal primarily with some aspects of oxadiazoline and carbene chemistry. More attention will be given to the use of oxadiazolines as precursors for carbenes than to other methods for generation of carbenes.

1.1 Carbenes

Carbenes are neutral, bivalent carbon intermediates in which the carbon atom has two covalent bonds and two non-bonding orbitals containing two electrons. If the two electrons are spin-paired the carbene is a singlet; if the spins are parallel, the carbene is a triplet.[5] The non-bonding molecular orbitals determine the nature of the carbene. If the two non-bonding orbitals are degenerate, Hund's rule indicates that the non-bonding electrons be assigned to different orbitals. The resulting carbene is a triplet.[5] However, if the orbitals have different energies, the electrons will occupy the lower energy orbital forming a (spin-paired) singlet carbene.



Singlet Triplet

A triplet carbene often reacts as a diradical.[6] Singlet carbenes may behave as electrophiles or nucleophiles, depending on the substituents.[7,8]

Singlet carbenes have a "vacant orbital" like carbonium ions, while possessing a non-bonding pair like that of carbanions. Triplet carbenes are approximately sp-hybridized and the non-bonding electrons are contained in mutually orthogonal p-orbitals. The formation of singlet vs. triplet carbene is dependent only on the mode of preparation. Thus, the carbene may initially be formed in either state, regardless of the more stable form.

Carbenes with NR_2, SR or OR substituents behave like nucleophiles in contrast to the electrophilic behaviour of many divalent carbon intermediates.[7]

1.2 Generation of Carbenes

According to the mechanism of formation, the generation of carbenes can be classified as:

A. Generation via α-elimination

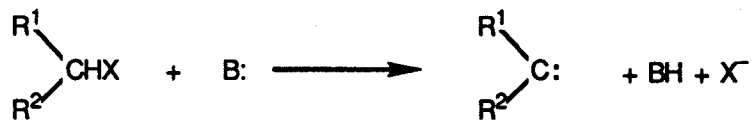
B. Generation via N_2 loss from diazo compounds

C. Generation via other methods.

A. Generation via α-Elimination

a) Halides

α-Elimination of hydrogen halide in the presence of strong base provided one of the best methods of generating carbenes,[7,9] eq. [1].

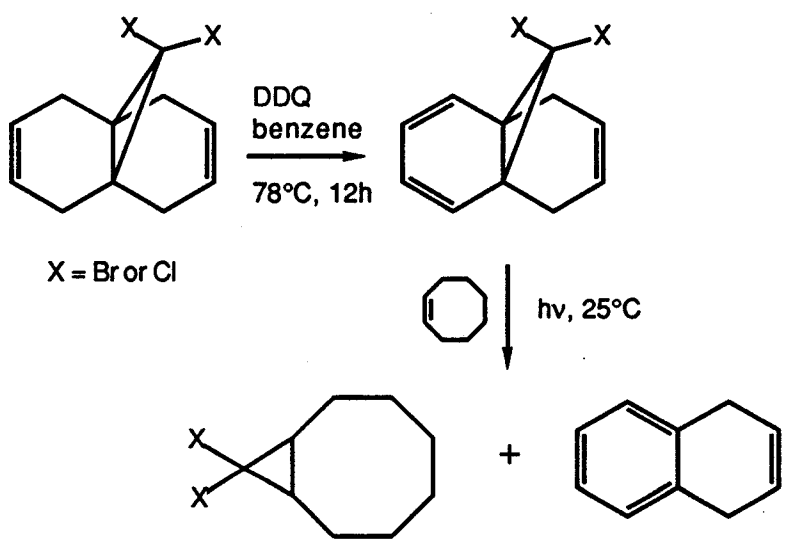


[1]

Dichlorocarbene :CCl_2 was first prepared by Hine using chloroform as the precursor,[10] eq. [2].

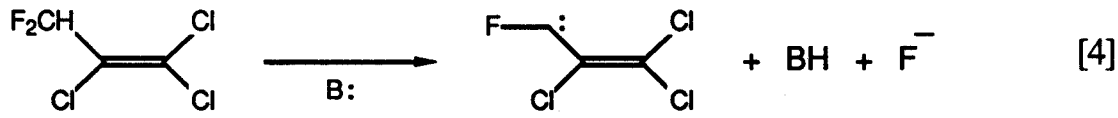
[2]

Photolysis of propellanes provided an efficient photochemical source of :CCl_2 and :CBr_2 and the latter was trapped with cyclooctene,[11] eq. [3].



[3].

A number of oligohalopropenes react with sterically hindered bases to form halo(halovinyl) carbenes by α-elimination,[12] eq. [4]. Preparation of

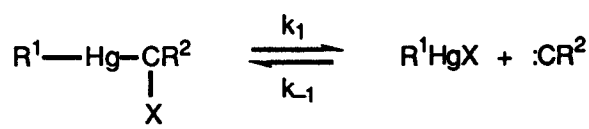


[4]

chlorocarbene from methylene chloride and formation of arylcarbenes from benzyl halides provided other routes for carbenes.[8] The use of the α-elimination method is limited to precursors without β-hydrogen since alkene formation via E2 elimination is a competitive process.

b) α-Halomercury Compounds

A variety of carbenes can be generated by the thermolysis of α-halomercury compounds. Kinetic studies of the thermolysis indicates that the decomposition is reversible and first order in mercurial, suggesting the mechanism of the reaction,[13] eq. [5].

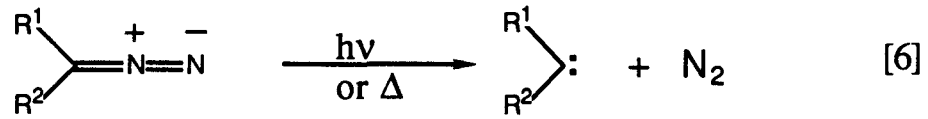


[5]

B. Generation via Diazo Compounds

a) From Diazoalkanes:

Carbenes can be generated by the pyrolysis or photolysis of diazoalkanes,[6,7,14,15,16] eq. [6].



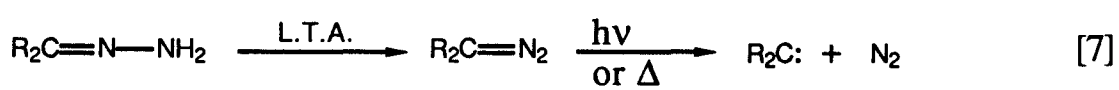
[6]

The first suggestion that the decomposition of diazomethane might involve methylene, $:CH_2$, as an intermediate was made by Nef at the end of the last century. The photolysis of diazo compounds both in the gas phase and in solution, initiates a methylene transfer.[17] The photochemical decomposition may be used to generate either triplet or singlet carbenes selectively. Direct photolysis leads to the formation of singlet carbenes while photosensitized decomposition affords triplet carbenes. Photosensitizers are often in the form of aromatic ketones.[8]

Diazoalkanes can be generated from hydrazones, toluene p-sulfonyl hydrazones, Δ^3-1,3,4-oxadiazolines and other compounds. They are extremely toxic and unstable compounds. As a result, they are best generated *in situ* rather than isolated. Thus the use of diazoalkanes in routine synthesis is limited.

b) From Hydrazones

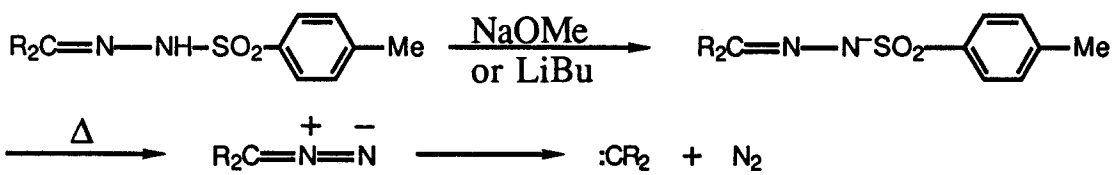
Oxidation of hydrazones under mild conditions using lead tetraacetate(L.T.A.) yields diazoalkanes,[18] which can be decomposed directly to carbenes, eq. [7].



[7]

c) From Tosylhydrazones

The reactions of NaOMe or LiBu with toluene p-sulfonyl hydrazones followed by thermolysis[19] or photolysis[20] of the salts yield carbenes, eq. [8].

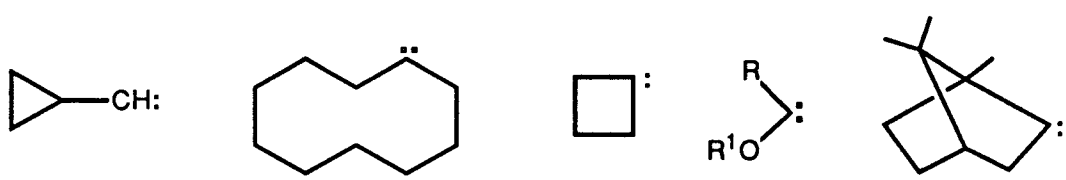


[8]

Decomposition of a tosyl azo compound at room temperature under neutral or basic conditions generates the unsaturated carbene $R_2C{=}C{:}$,[21] eq. [9].

[9]

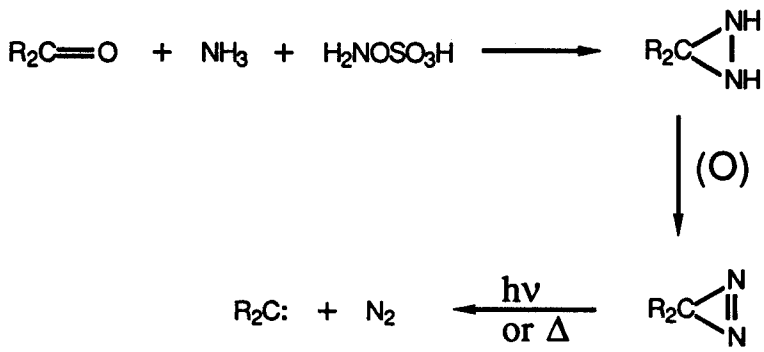
Among the wide ranges of carbenes generated by this method are



d) From Diazirines

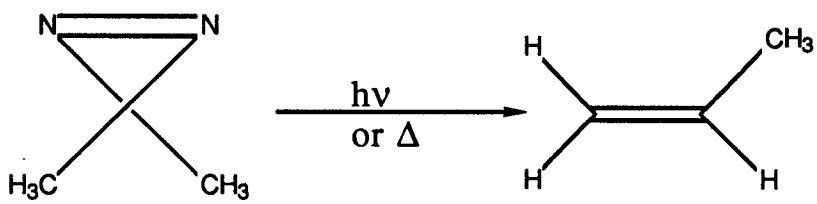
The photolysis of diazirine is an excellent procedure for generating carbenes, since the diazirine tends to be less hazardous than the isomeric diazoalkane. Diazirines can be synthesized by oxidation of diaziridines which, in

turn, are prepared from ammonia, hydroxylamine o-sulfoninc acid and a ketone,[22] eq. [10].



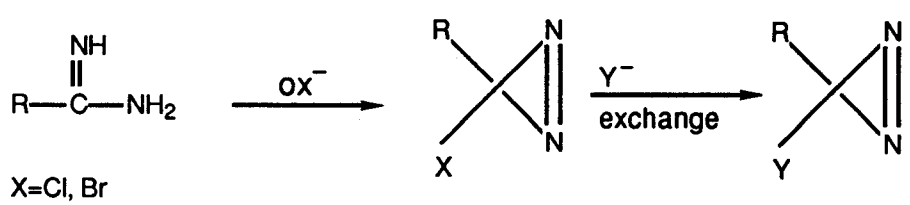
[10]

In the case of dimethyl diazirine, both photolysis[23] and thermolysis[24] in the gas phase yield propene as a major product, eq. [11].



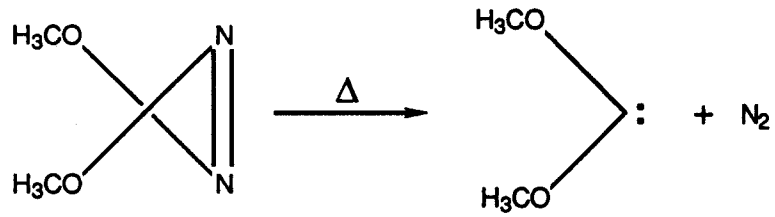
[11]

Nowadays, diazirines are of great importance because of their tolerance for heteroatomic substituents. The diazirine exchange reaction (eq. [12]) reported by Moss[3b] indicates the potential for a wide spectrum of carbenes from diazirines,[25,26,27,28] eq. [12].



[12]

The generation of dimethoxycarbene via 3,3-dimethoxydiazirine opened the window for the first spectroscopic study of a nucleophilic carbene,[25] eq. [13].



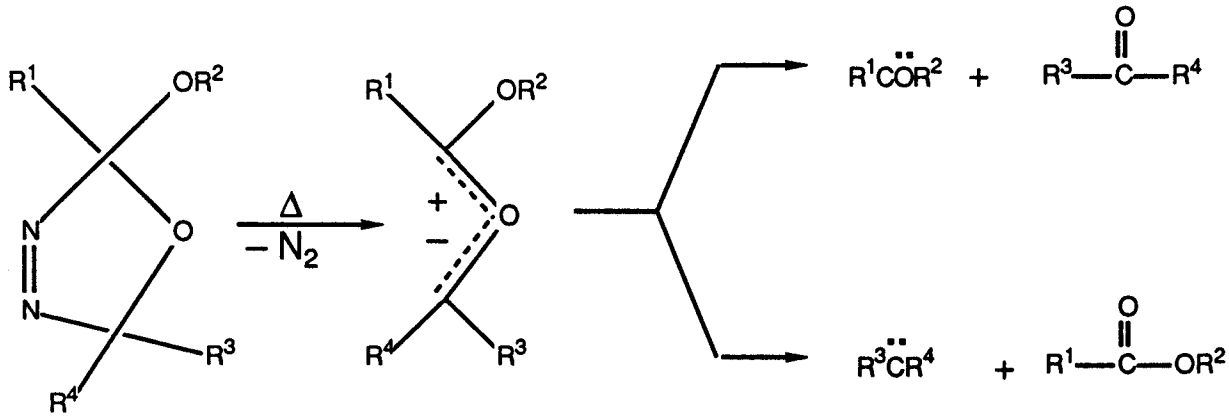
[13]

Both diazirines and diazoalkanes[8] are useful to a limited extent as their preparation is difficult and they are potentially explosive.

e) From Oxadiazolines

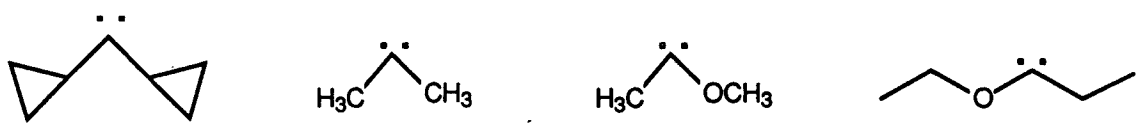
The facile generation of carbenes from stable precursors is necessary if carbenes are to be useful for routine synthesis. The relative stability and ease of preparation of oxadiazolines make them ideal carbene precursors.

Thermolysis of an alkoxy oxadiazoline affords a carbene via a carbonyl ylide intermediate. Warkentin and co-workers[29] have shown that the ylide intermediate fragments in two directions, forming two sets of corresponding carbonyl compounds as shown in Scheme 1.



Scheme 1

One of the advantages of this oxadiazoline precursor is that there is no ambiguity about whether the carbene is a free species or a metal-complexed carbene (a carbenoid).[4] Furthermore, the presence a of five-membered ring avoids the ring strain associated with diazirine. Therefore, oxadiazolines have increased stability over diazirines. Various carbenes generated from oxadiazolines include:[30]

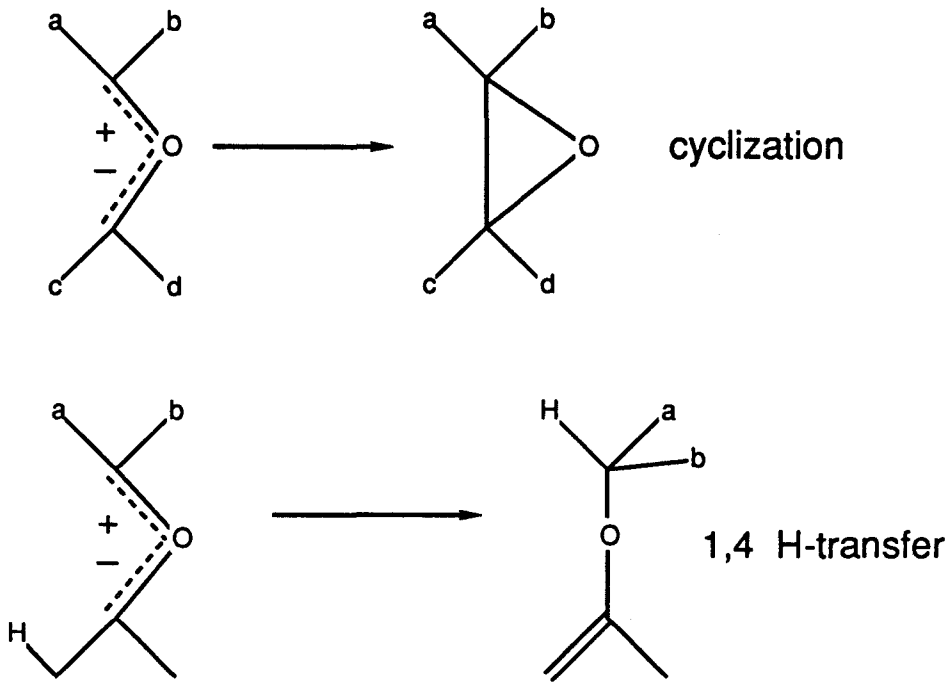


Limitations of the Method:

There are two main limitations to the use of oxadiazolines as carbene precursors.

i)The two-directional fragmentation of the ylide as seen in Scheme 1 limits the selective generation of a specific carbene.

ii)Intramolecular reactions of ylides[31] summarized in Scheme 2 may prevent carbene formation.



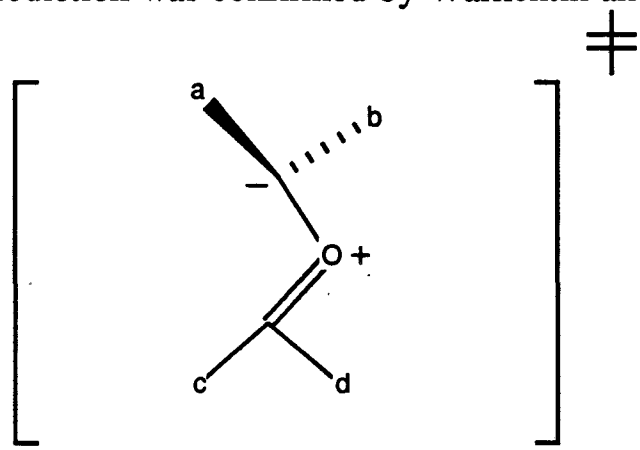
Scheme 2

Thus for carbene-forming reactions of oxadiazolines to be synthetically useful, fast unidirectional fragmentation of the ylide intermediate is necessary.

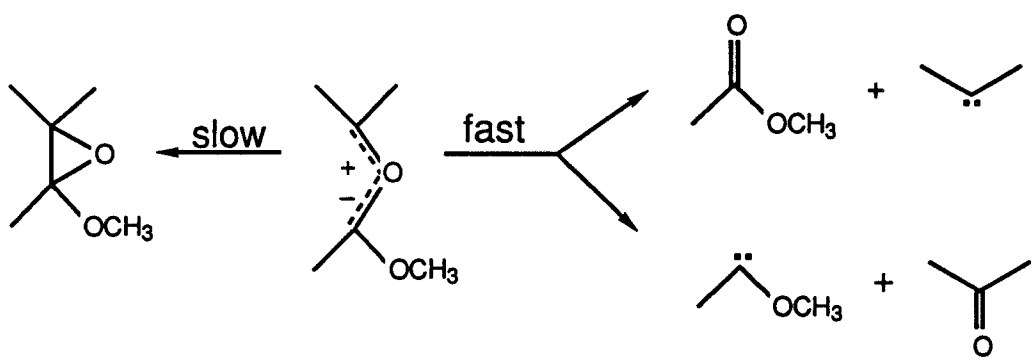
Theoretical studies by Houk[31] of fragmentation of substituted carbonyl ylides, provide a solution to these limitations. The conclusions of their work were as follows:

1)Fragmentation of carbonyl ylides occurs via a non-planar transition state (0°, 90°-conformation)

Donor substituents (OR, NR_2) reduce the barrier to rotation from the ground state (0°, 0°-conformation) to the transition state (0-90°) for fragmentation. This prediction was confirmed by Warkentin and co-workers,[32]



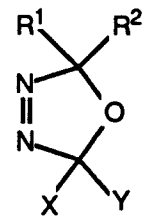
by their observation that methoxy-substituted ylides fragment to carbenes more rapidly than they close to oxiranes, as shown in Scheme 3.



Scheme 3

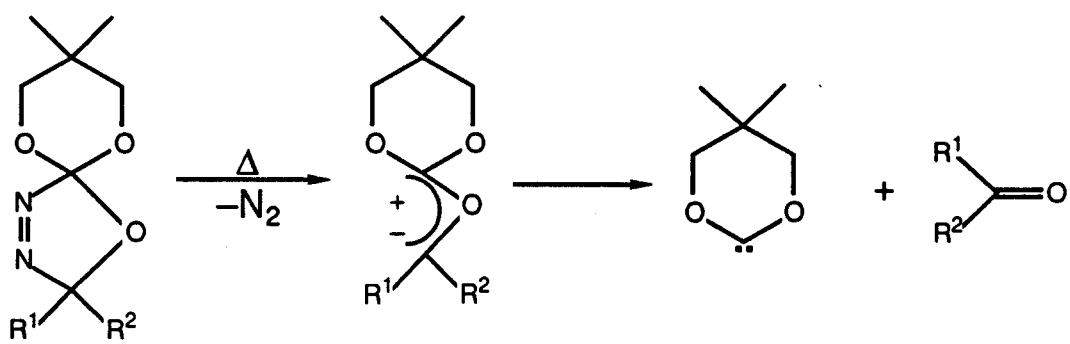
2)Carbonyl ylides usually fragment to give the most stable carbene, e.g. for an amino substituted carbonyl ylide, the transition state has the longer bond between the amino substituted carbon and carbonyl oxygen (longer than the other C–O bond), resulting in fragmentation to form the more stable amino carbene.

From Houk's conclusions, oxadiazoline 1, with $R_1 = R_2$ = alkyl and X, Y = electron-donating, would be a good precursor for the carbene, $X\ddot{C}Y$.



I

The choice of substituents for a relatively stable carbene $X\ddot{C}Y$ is limited.The most reasonable substituents are X = Y = OMe, X = OMe, Y = NH_2, and X = Y = NH_2. Thus to study the chemistry and stability of cyclic dioxacarbene from a spiro oxadiazoline II will be an interesting subject, (Scheme 4). Thermolysis of II would potentially provide a carbonyl ylide which would undergo fast one-directional fragmentation to form only one set of carbene products as in Scheme 4.



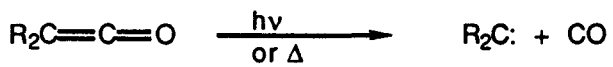
II

Scheme 4

C. Other Methods of Carbene Generation

i)from Ketenes:

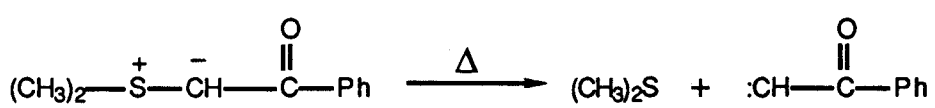
Substituted ketenes can generate carbenes by thermolysis[33] or photolysis[7] with loss of CO in the process, eq. [14]. That route is not a good one, because ketenes tend to polymerize under the same conditions needed to generate carbenes.[5]



[14]

ii)From ylides:

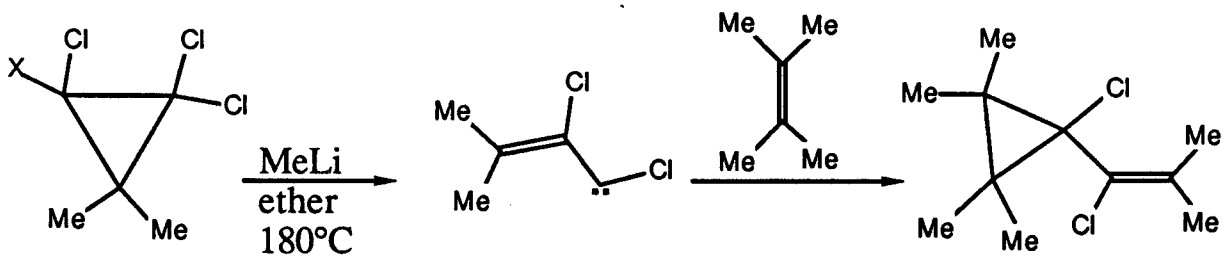
Carbenes can be generated from the thermolysis or photolysis of sulphur,[34] phosphorous[35,36] or nitrogen[37] ylides. Equation [15] gives an example of thermolysis of a sulphur ylide; and the carbene is generated by heterolytic cleavage of the sulphur-carbon bond.



[15]

iii)From cyclopropanes:

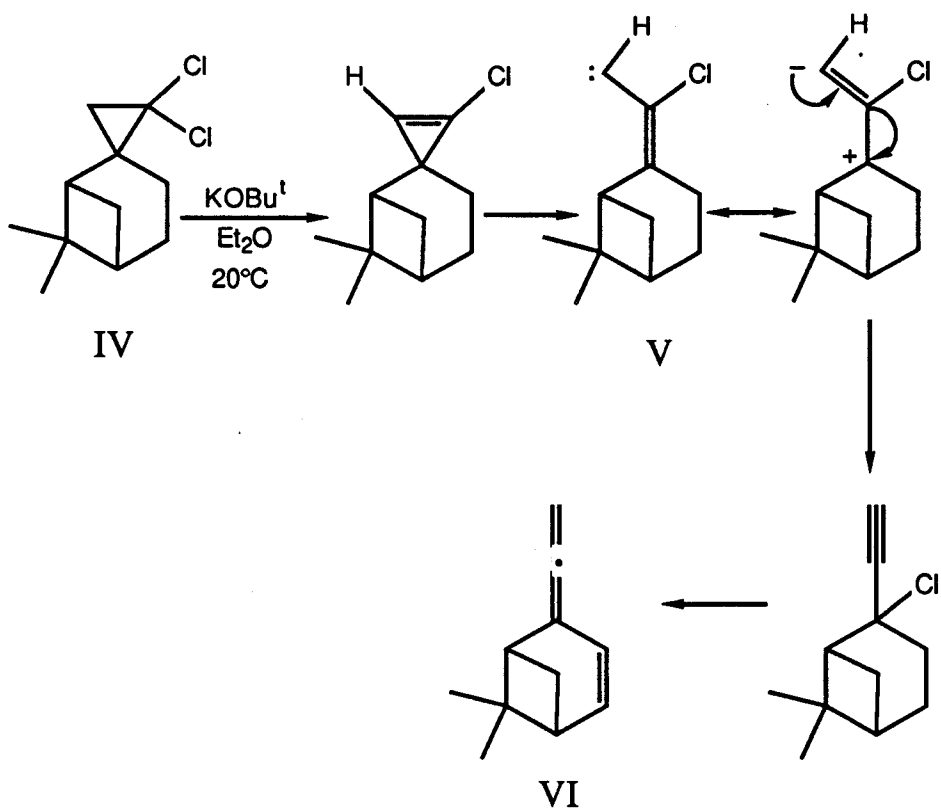
Reactions of III (X = H, Cl, Br) with MeLi in ether in the presence of alkenes leads to cyclopropanes; through an intermediate carbene,[38] eq. [16].



III

[16]

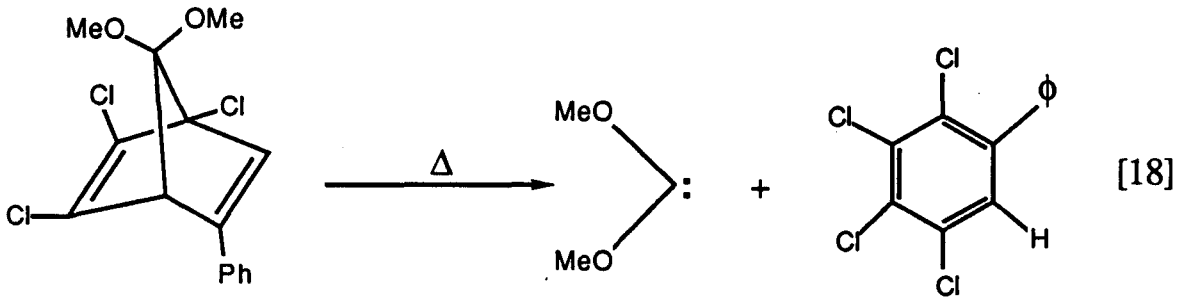
Similarly the reaction of β-pinene adduct(IV) with KOBu^t–Et_2O at 20°C leads to a product(VI)(41%). The mechanism may involve ring opening of an intermediate chlorocyclopropane to give the vinyl carbene(V)[38], eq. [17].



IV V VI

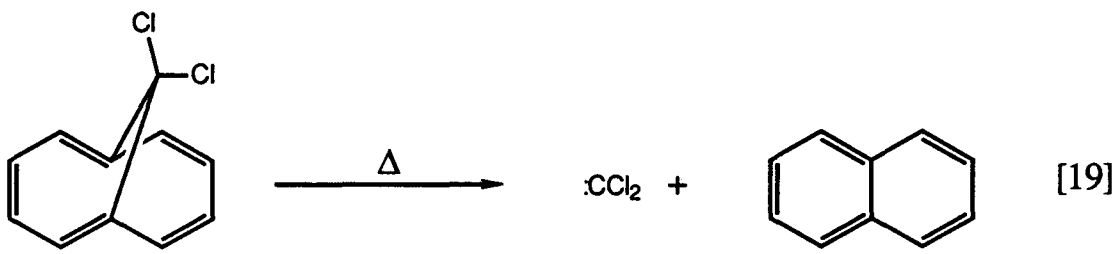
[17]

Dimethoxy carbene[39] and dichlorocarbene[40] can be generated from the thermolysis of VIIa and VIIb respectively, eqs. [18] and [19].



[18]

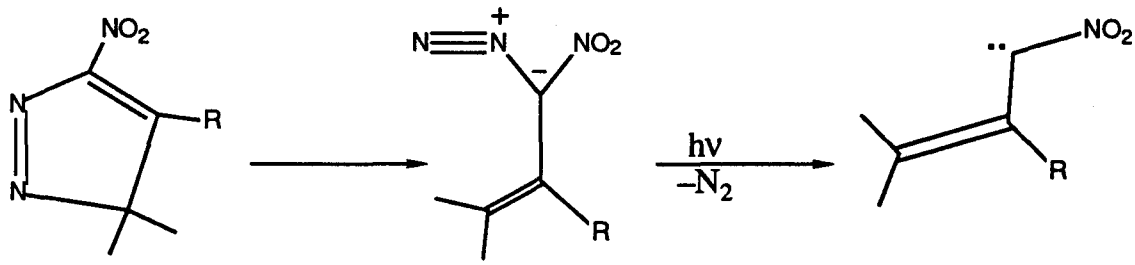
VIIa



[19]

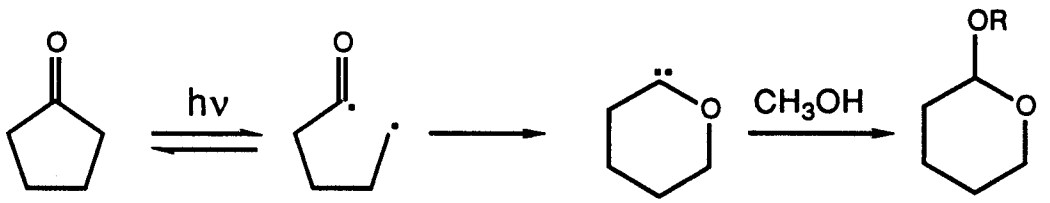
VIIb

Nitrovinyl carbenes are generated by the photolysis of 3H-pyrazoles,[41] eq. [20], and oxacarbenes can be generated from cyclopentanones by a non-concerted photolysis in presence of methanol,[42] eq. [21].



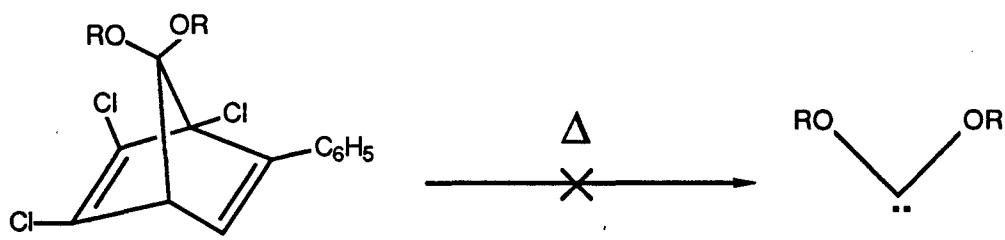
[20]

R = C_6H_5, CN



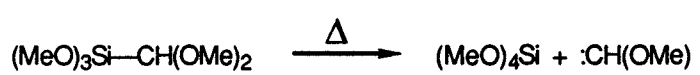
[21]

Attempts to generate cyclic oxacarbenes from the pyrolysis of norbornadienone ketals failed,[43] eq. [22]. Dimethoxymethyl trimethoxy silane on thermolysis generated methoxy carbene[44], eq. [23].



[22]

R = $CH_2C(CH_3)_2CH_2$



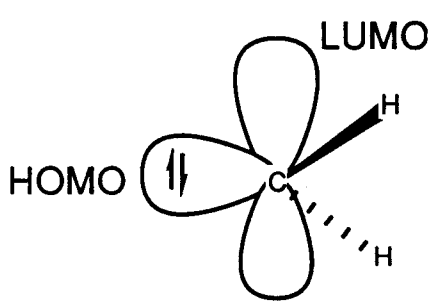
[23]

1.3 Reactions of Carbenes

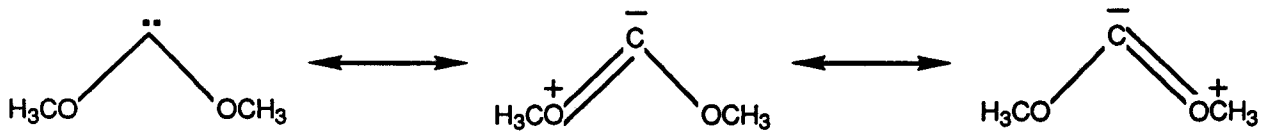
Carbene Stability and Reactivity

Since singlet carbenes are usually predominant in carbene chemistry, the discussion will be focussed mainly on them. Although substituents have a great influence on nucleophilicity and electrophilicity of carbenes, most singlet carbenes behave as electrophiles.[45,46,47] It became an exhausting task for many organic chemists to make sense and order out of carbenic reactivity.[7,48] It is quite clear that substituted carbenes are less reactive and more discriminating than methylene(:CH_2). The most stable carbenes also exhibit the greatest selectivity in their reactions.[35] One way to measure carbenic selectivity or "philicity" is addition reactions of carbenes with alkenes.[35,49,50]

The stability of carbenes may be rationalized by examination of the energies of the HOMO and LUMO carbene orbitals.[50] Electron withdrawing substituents on the carbene lower E_{LUMO} and consequently decrease the selectivity while increasing the electrophilicity of the carbene, e.g. :CCl_2, :CF_2, MeĊF, MeĊCN, etc.



Electron-donating substituents raise the energy of the LUMO by donation of electron density and the resulting carbene exhibits increased stability and selectivity, e.g. dimethoxy carbene(DMC) is so strongly stabilized by resonance that LUMO is no longer a p-orbital at the carbenic carbon.[1,3b]



DMC

An order of increasing electrophilicities of carbenes has been developed by Harrison:[51]

$:CF_2 > :CHF > :CH_2$ and $:CF_2 > :CCl_2 > :CBr_2 > :Cl_2 > :CH_2$.

Reactions:

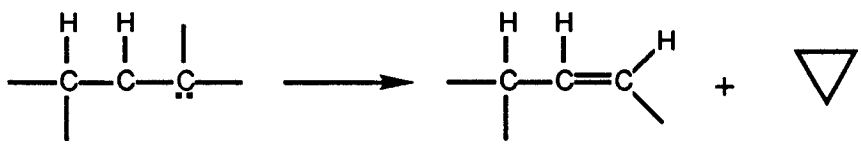
The chemical behaviour of a carbene depends on its electronic state. As we mentioned earlier, the state in which carbene is produced depends on the method of generation. The two general reactions of carbene are insertion and addition.

[A] Insertion and Hydrogen Abstraction:

Triplet carbenes behave as free radicals: hydrogen abstraction, addition to carbon-carbon double bonds and coupling of derived radicals are typical reactions. Laser flash photolysis has been used to obtain rate constants for some of these processes.[14]

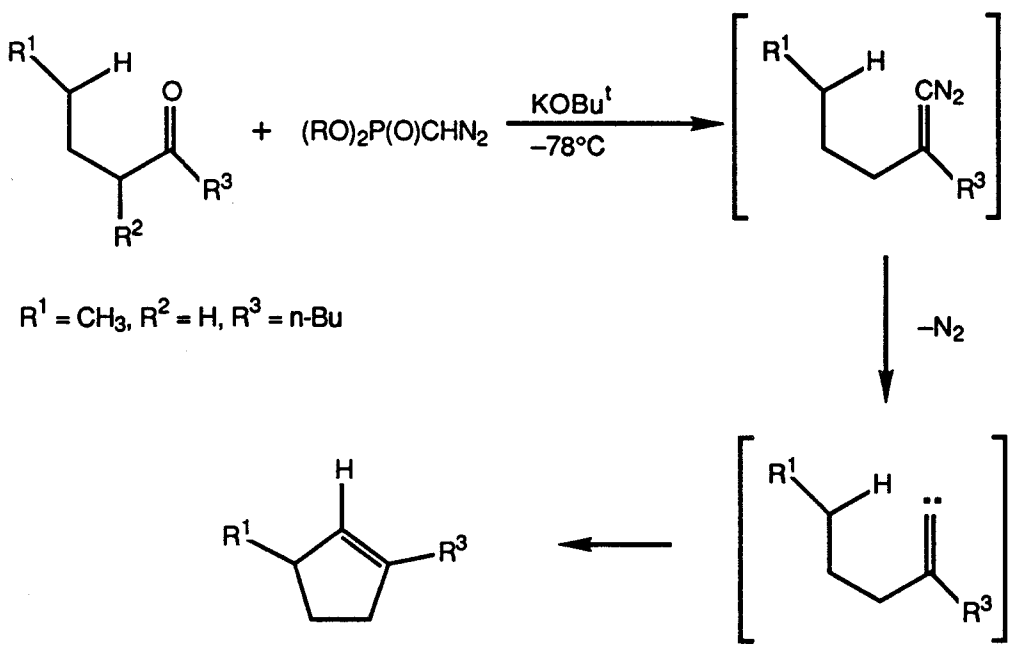
Singlet carbenes also add to double bonds, but the stereochemical consequences are different for the singlet and triplet. Singlet carbenes also show a unique reaction called insertion. Depending on the substituents, intramolecular or intermolecular insertion or addition can occur.

Alkyl and dialkyl carbenes react predominantly by insertion of the divalent carbon into β and γ C-H bonds, yielding olefins and cyclopropanes,[7,52] eq. [24].



[24]

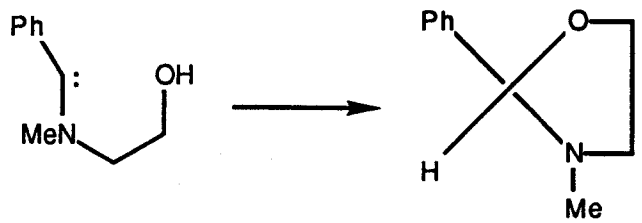
Cyclopentenes can be formed in reasonable yield by intramolecular insertion of alkylidene carbenes,[53] eq. [25].



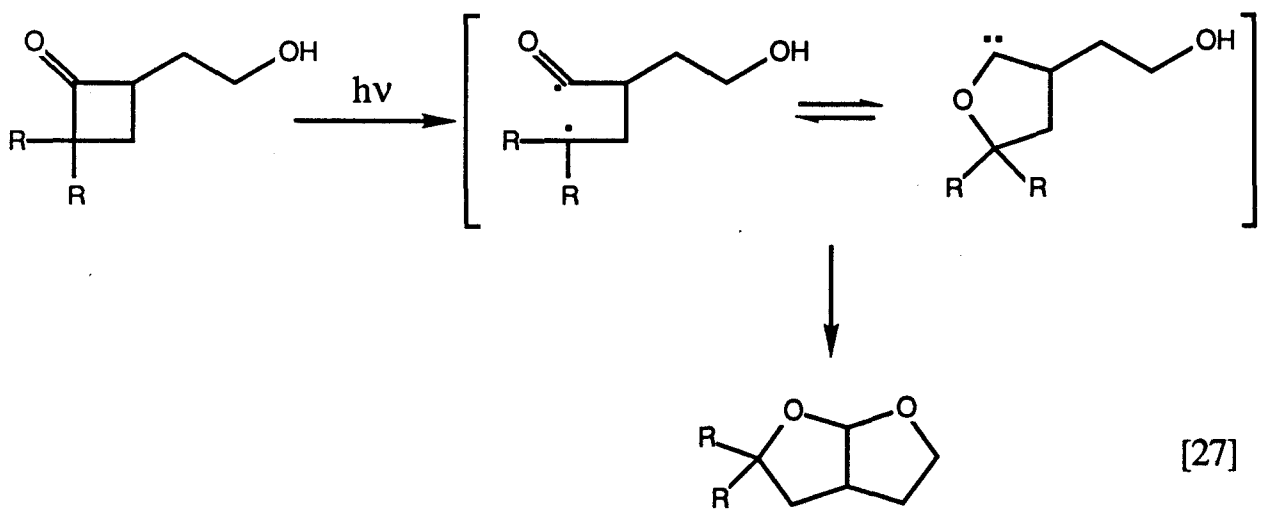
$R^1 = CH_3$, $R^2 = H$, R^3 = n-Bu

[25]

Amino(phenyl) carbenes form five-membered rings by intramolecular insertion into O-H or N-H bonds,[28] eq. [26]. Photochemical ring expansion of cyclic ketones to oxacarbenes has found synthetic application in cases involving intramolecular insertion of carbenes into O-H bonds,[54] eq. [27].

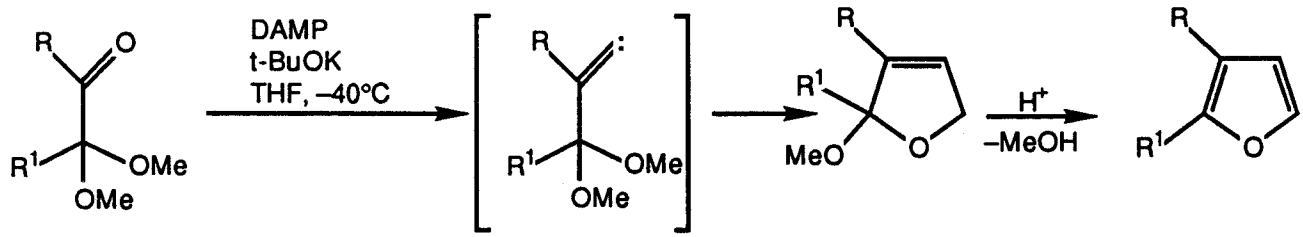


[26]



[27]

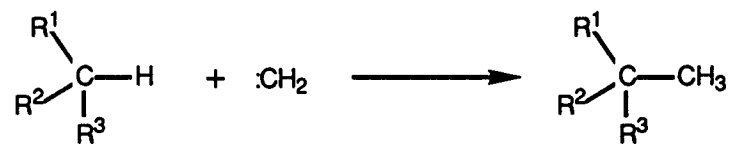
The reaction of α,α-dimethoxy ketones with diethyl diazomethyl phosphates(DAMP) provides a recent synthesis of furan by insertion of carbene,[55] eq. [28].



R = R^1 = (–CH$_2$–)$_4$, (–CH$_2$–)$_3$
R = Bu, R^1 = H
R = Ph, R^1 = H

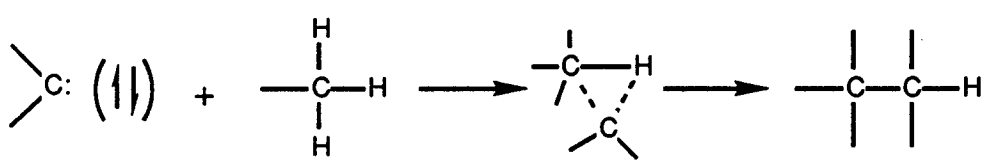
[28]

ii) Intermolecular Insertion:



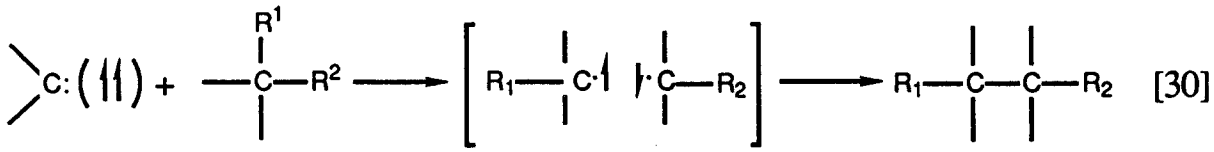
Two different mechanisms can be explained for the methylene insertion into a double bond: 1) concerted, and 2) non-concerted.

1) The concerted mechanism for a singlet carbene will involve a three-centre transition state,[56] eq. [29].

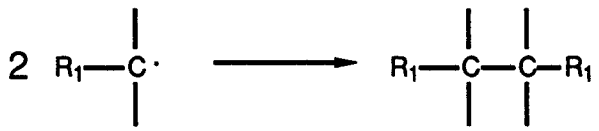


[29]

2) Radical pair formation occurs in the non-concerted mechanism where the radical pair undergoes efficient combination because of a contribution from an ionic state,[57] eqs. [30], [31] and [32].



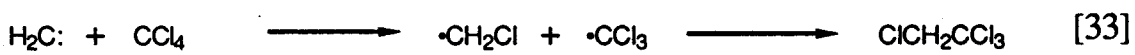
[30]



[31]

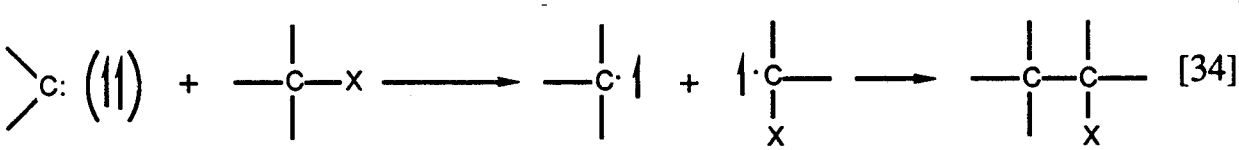
[32]

Although a concerted insertion mechanism can occur for monohaloalkanes, it is not common in the case of polyhaloalkanes due to steric reasons. In the latter case, a halogen abstraction is followed by a radical coupling reaction,[58] eq. [33].



[33]

A non-concerted mechanism is also proposed for triplet carbenes,[7] eq. [34].

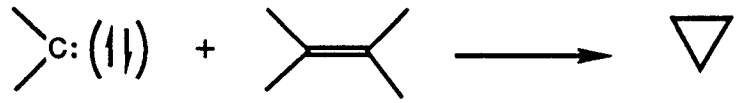


[34]

[B] Addition Reactions

A second characteristic reaction of carbenes is addition to alkenes to yield cyclopropanes.[59] Singlet carbenes might react as either nucleophiles or electrophiles, and triplets may be expected to behave like free radicals. The

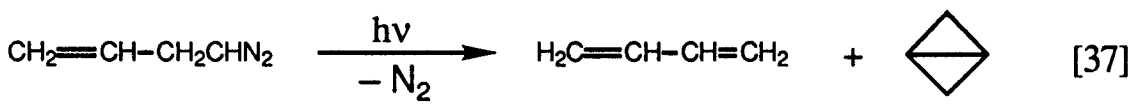
former add in a concerted process, while the latter add in a non-concerted manner, eqs. [35] and [36].



[35]

[36]

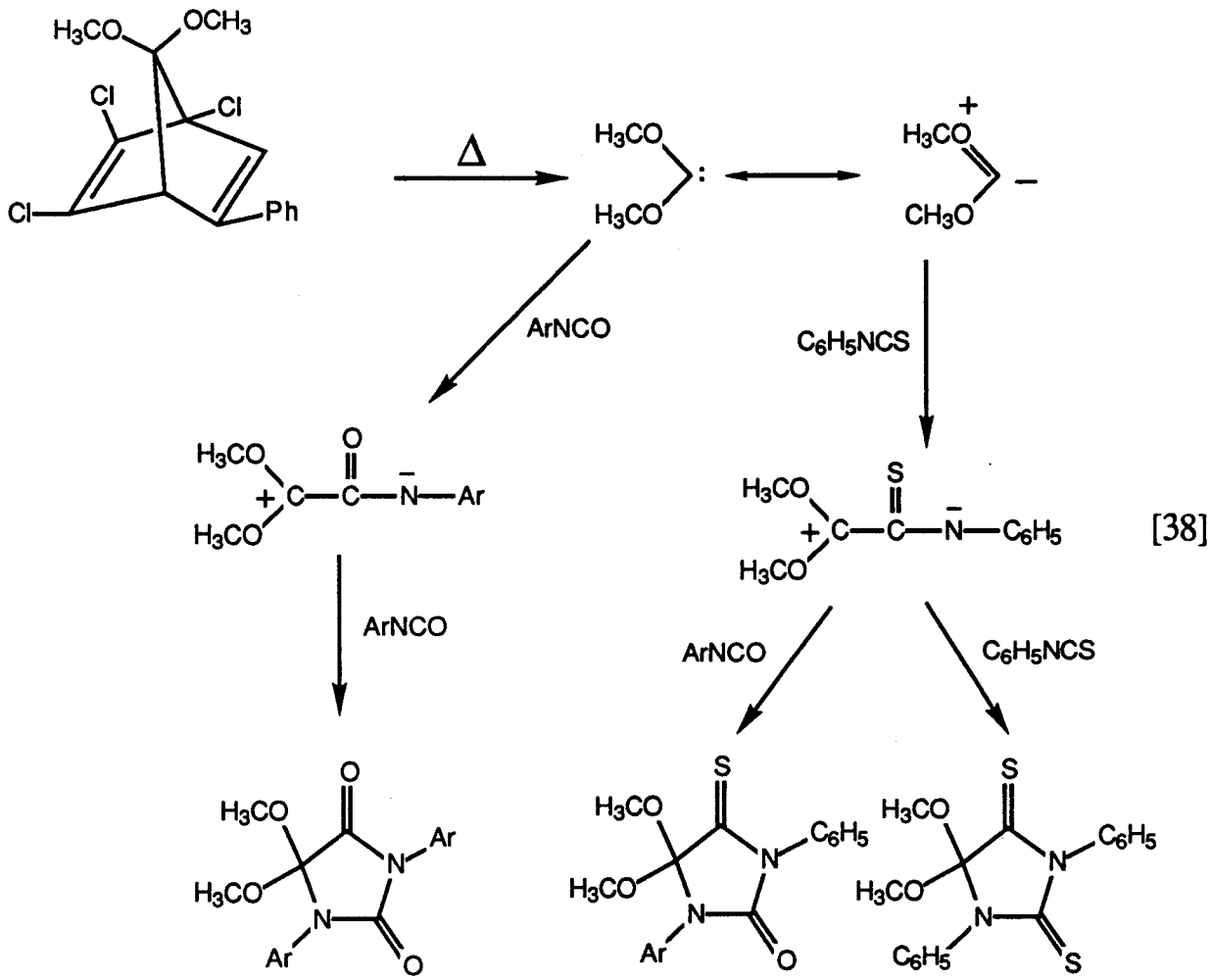
An allylic carbene gives a mixture of intramolecular C-H insertion and intramolecular addition to the double bond,[60] eq. [37].



[37]

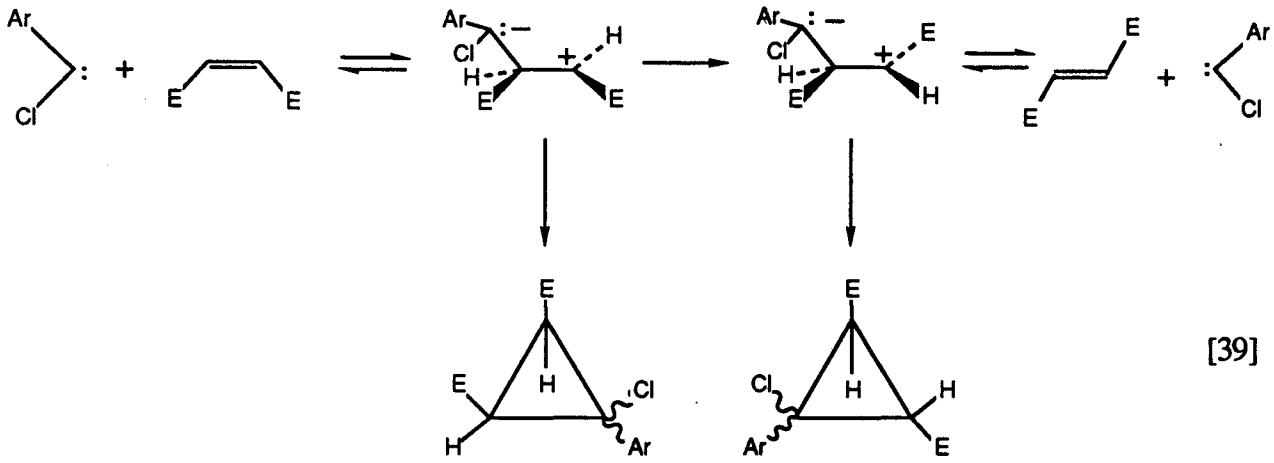
Intermolecular Addition

In the case of dimethoxy carbene, addition to aryl isocyanates with phenyl isothiocyanate as reference compound gave a positive ρ-value of +2.0±0.5. Hoffmann[61] interpreted this positive ρ-value as evidence of the nucleophilic character of the carbene, eq. [38].



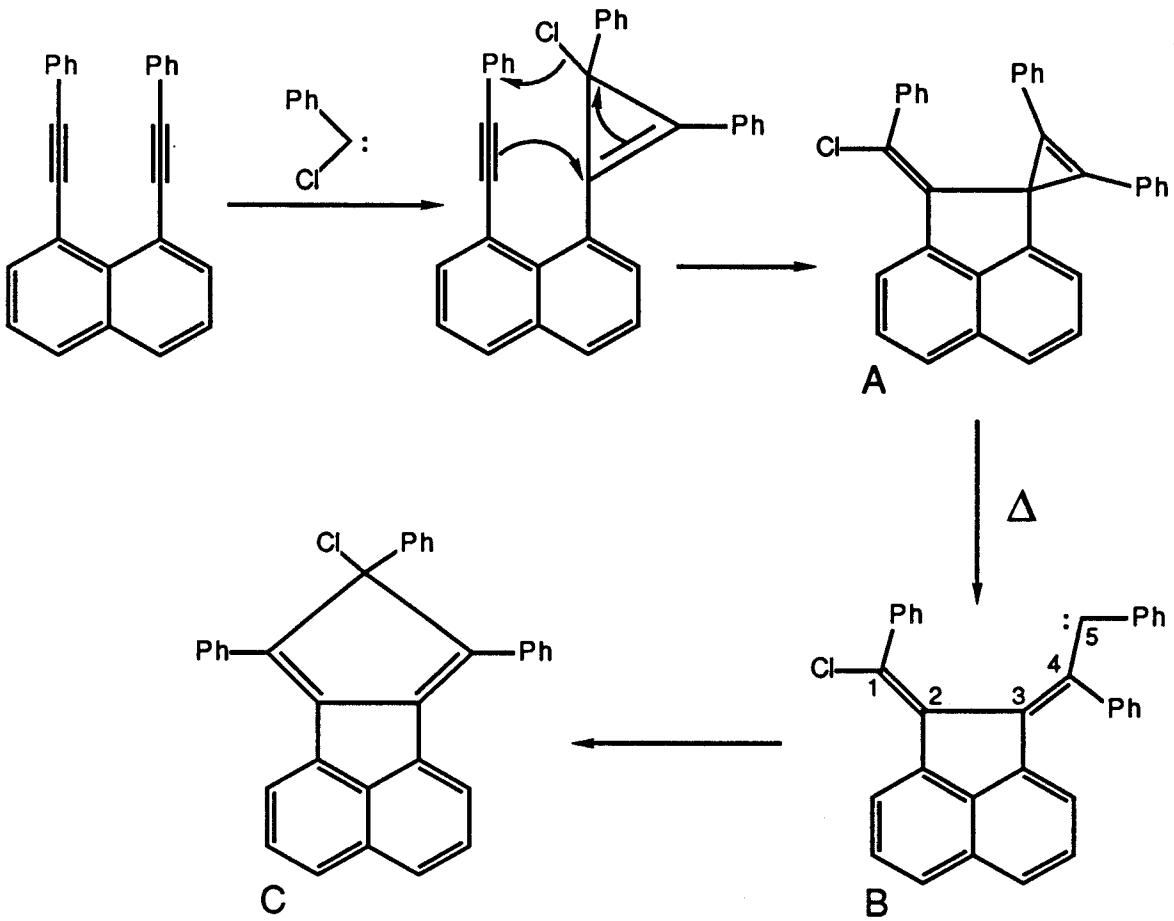
[38]

Non-concerted addition of arylchloro carbenes to diethyl maleate accompanied by isomerization of maleate to fumarate, is consistent with an intermediate carbene-alkene dipolar adduct,[62] eq. [39].



[39]

Addition of phenylchlorocarbene to 1,8-bis(phenylethynyl)naphthalene is followed by an ene-type reaction of the initial cyclopropene to give A. Upon heating, this ring opens to carbene B which undergoes electrocyclization followed by a 1,5-chlorine shift to give C,[63] eq. [40].



[40]

1.4 Oxidation of Hydrazones

a) Use of Lead Tetraacetate(L.T.A)

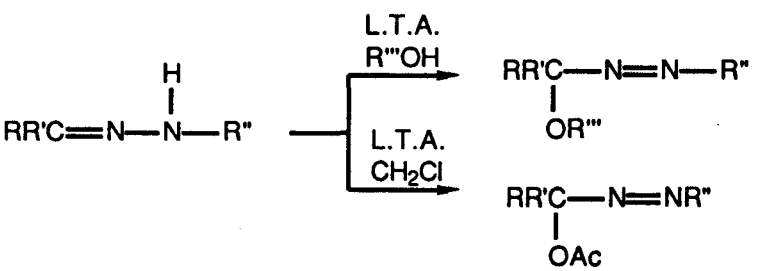
The use of L.T.A. as an oxidizing agent was first reported by Dimorth in 1923, when L.T.A. was used to oxidize malonic esters and aryl substituted methanes to acetoxy derivatives.[64]

L.T.A. is a versatile reagent which reacts with sugars[65], sterols[66], oximes[67], semicarbazones,[68] hydrazones[69], azines[70], and many other organic nitrogen

compounds.[71] Its versatility and synthetic utility have been reviewed extensively.[72,73] Here more attention will be given to the use of L.T.A. in the oxidation of hydrazones.

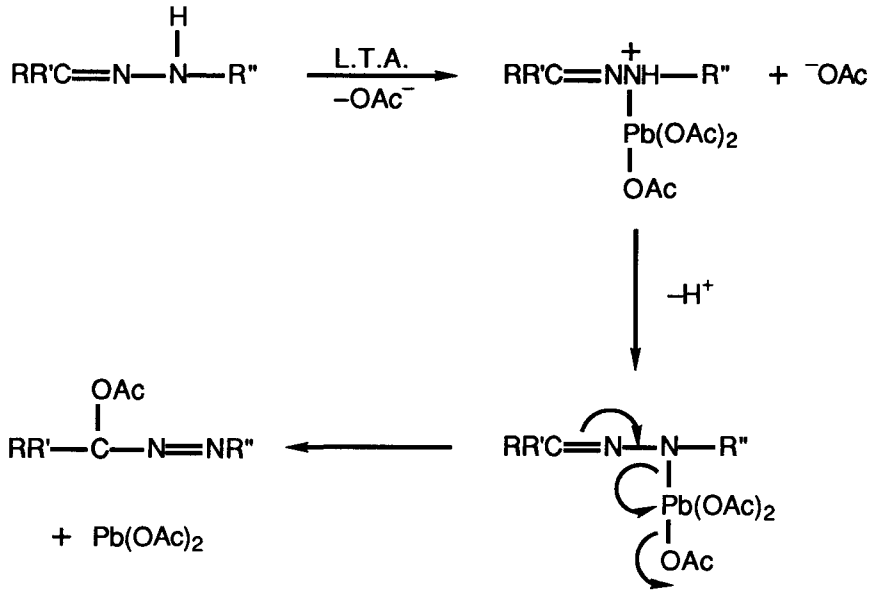
Reactions of L.T.A. with Hydrazones

Aldehyde hydrazones form acyl hydrazones[74] upon treatment with L.T.A., whereas ketohydrazones yield, in general, azoacetates in dichloromethane and azoethers in alcoholic medium, eq. [41].



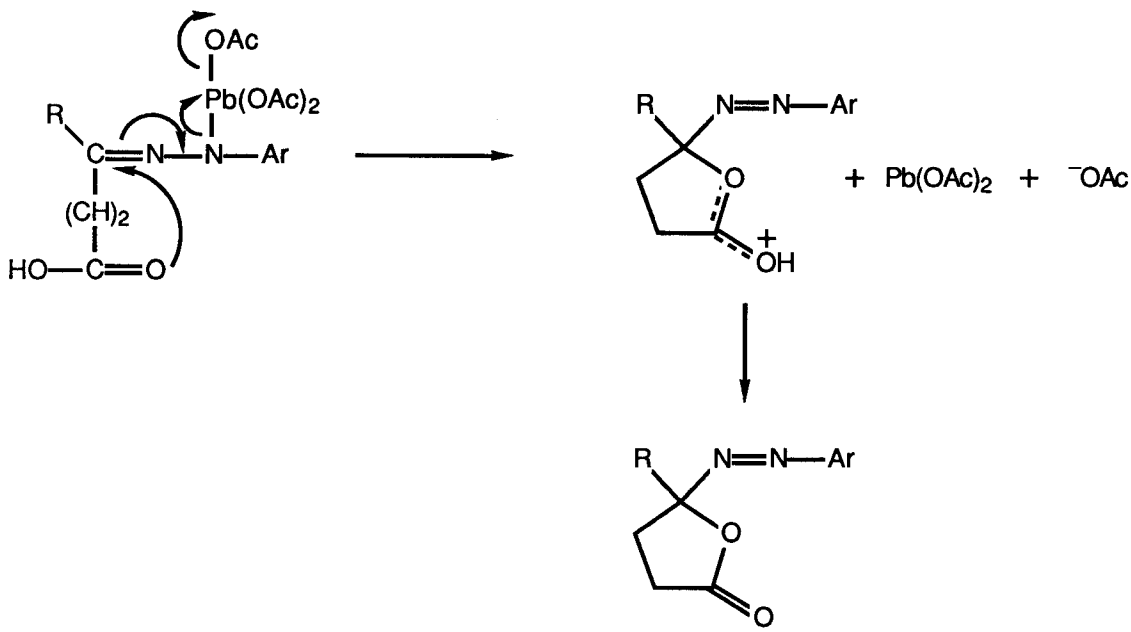
[41]

The mechanism proposed for the reaction of L.T.A. with aldehyde hydrazones was a radical one.[8,75] Although Gibbs and co-workers did some reactions with oximes and observed radicals by E.S.R. spectroscopy, there is no evidence for such intermediates in the oxidation of ketohydrazones. A polar mechanism is suggested because of the increased rate of reaction[76] relative to the reaction of aldehyde hydrazones with L.T.A., eq. [42].



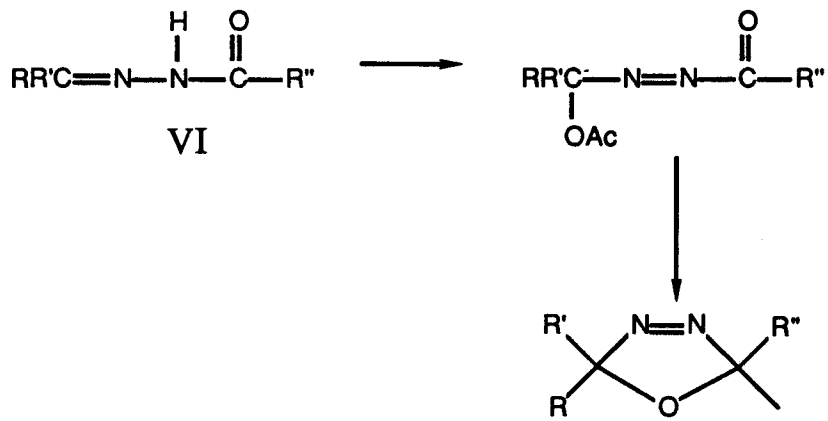
[42]

A cyclic product is obtained when a suitable cyclization site exists in the ketone substituents of ketohydrazones.[77] The proposed mechanism is as in eq. [43].



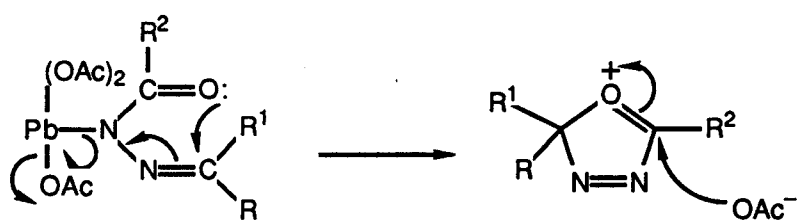
[43]

Hoffman[78] first reported that ketone carbonyl hydrazones of type VI readily cyclize upon treatment with L.T.A. to form Δ^3-1,3,4-oxadiazolines(VII) as in eq. [44].



[44]

He proposed an ionic mechanism for the formation of VII, involving the loss of an acetate ion from azoacetate (Eq. [44]) followed by attack on the resulting carbocation by the carbonyl oxygen. Norman has also reported this cyclization.[79] He proposed a polar mechanism, eq. [45].

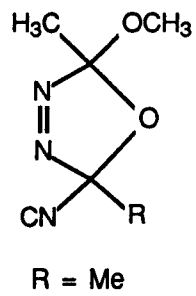


[45]

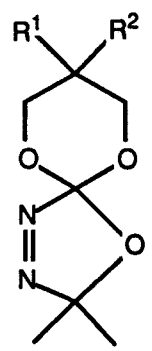
They found that thermolysis of Δ^3-1,3,4-oxadiazolines formed epoxides by the loss of nitrogen.

1.5 Purpose

The purpose of this work was to synthesize oxadiazolines which would act as selective precursors of cyano carbenes or of cyclic dioxacarbenes. For those purposes, the target molecules were compounds such as the 2-methoxy-5-cyano-Δ^3-1,3,4-oxadiazoline and spiro oxadiazolines of type 4, below. The cyano compound compound was expected to form a carbonyl ylide with both methoxy and cyano substituents. That ylide would be useful if it could be trapped by 1,3-dipolar cycloaddition. On the other hand, if it fragmented rapidly, it could form $CH_3\ddot{C}CN$. Spiro oxadiazolines 4 would, it was hoped, undergo thermolysis to form carbonylylides that would fragment cleanly to cyclic dioxacarbenes.



R = Me

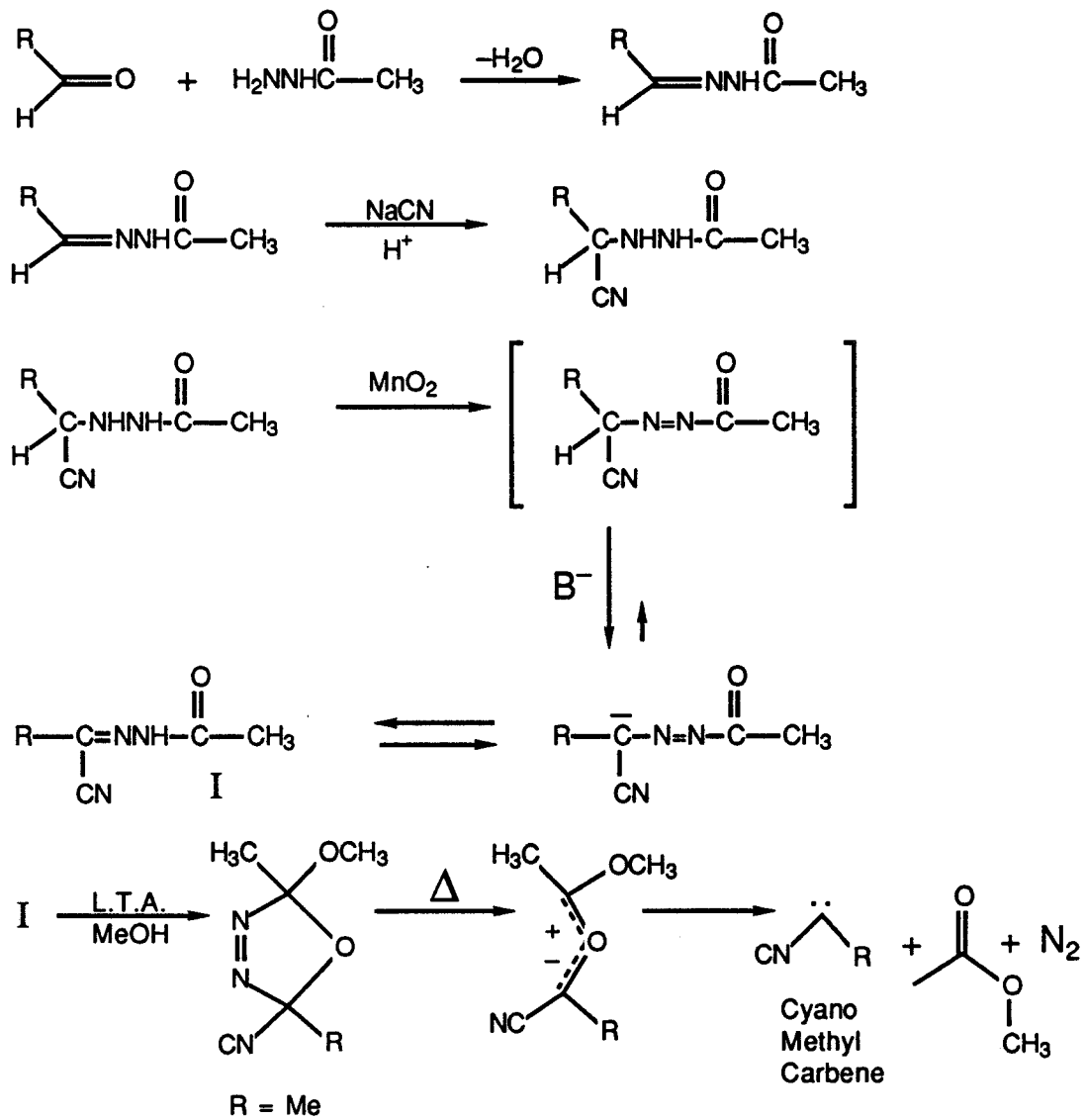


4a, $R^1 = R^2 = H$

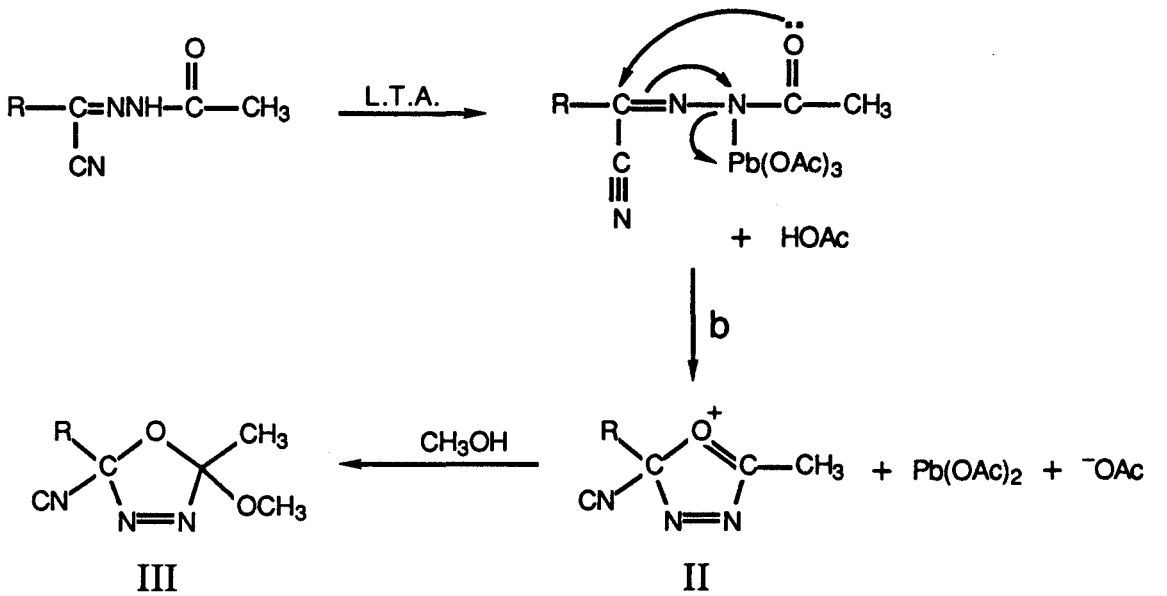
4b, $R^1 = R^2 = Me$

2. Results and Discussion

The initial attempt was to synthesize an oxadiazoline that would give the cyanomethyl carbene via the carbonylylide on thermolysis. The approach for the synthesis of that oxadiazoline was as follows:



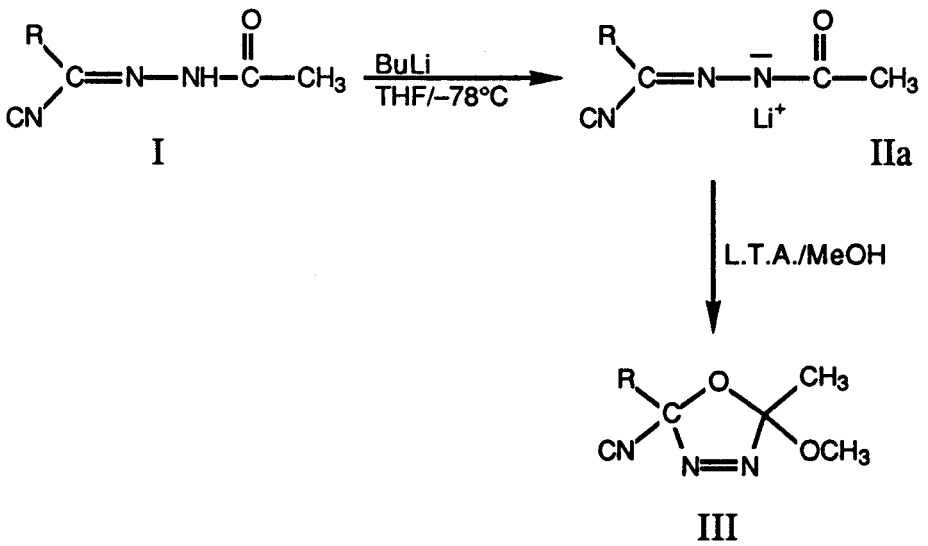
A mechanism for L.T.A. oxidation of ketone hydrazones was proposed by Gladstone and Norman.[79] The first step involves the formation of a bond between the nitrogen of the NH group and lead. Decomposition of the lead-nitrogen complex is intramolecularly assisted by the carbonyl oxygen and yields a cation which in the presence of methanol gives the oxadiazoline



Scheme 5

The formation of the intermediate II was presumably very hard because of the presence of the strong electron-withdrawing cyano group inhibiting the cyclization step b. Attempts to synthesize the oxadiazoline III by various other methods also failed.

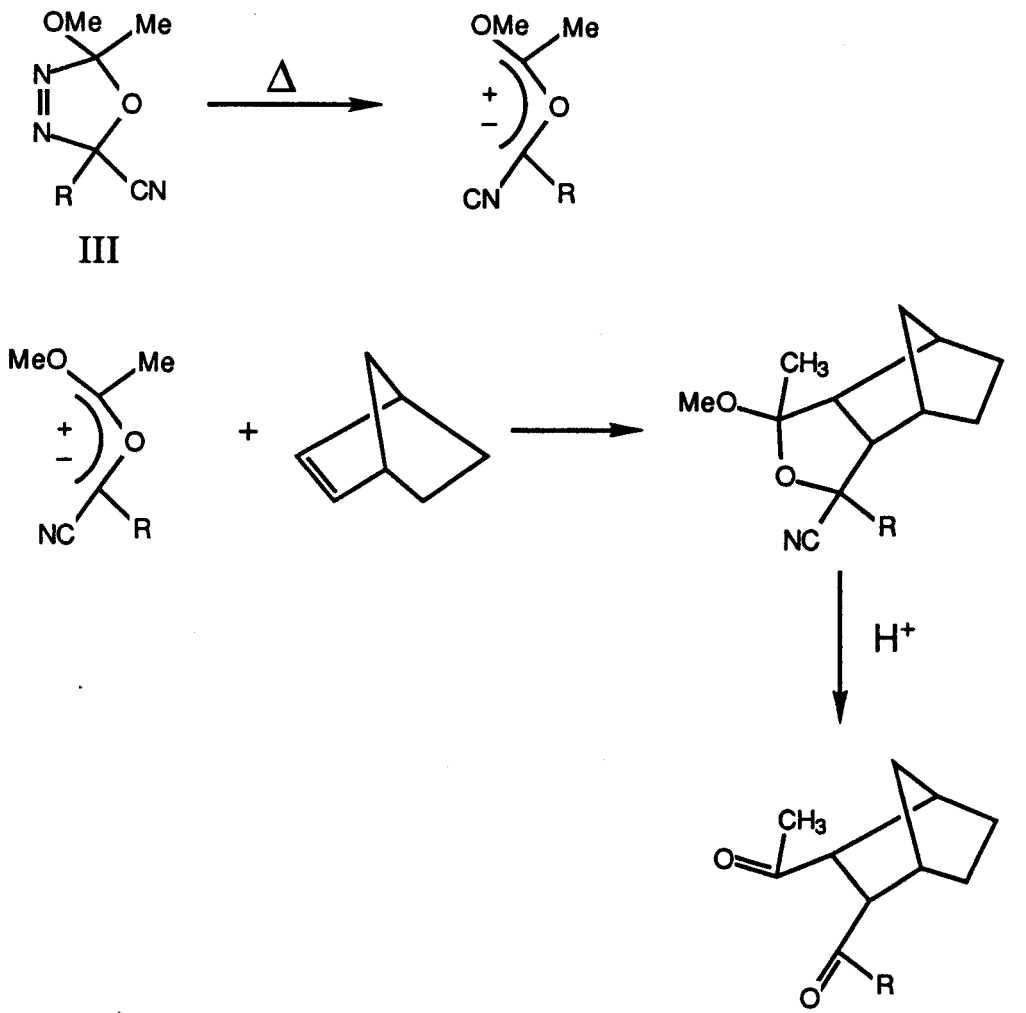
In one method, the lithium salt was prepared to increase reactivity toward L.T.A., as outlined below.



III

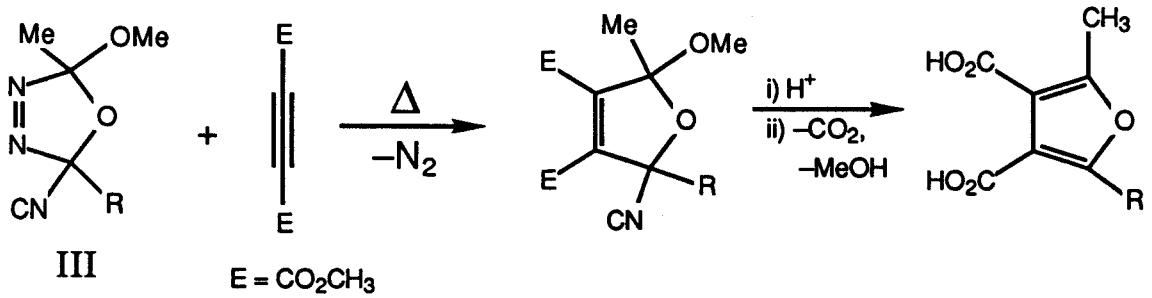
Although the anion IIa was prepared, it also failed to cyclize to the oxadiazoline III.

The main purpose of synthesizing the above oxadiazoline III was to generate the ylide, to be useful for a general 1,4-diketone synthesis as shown in Scheme 6 below:

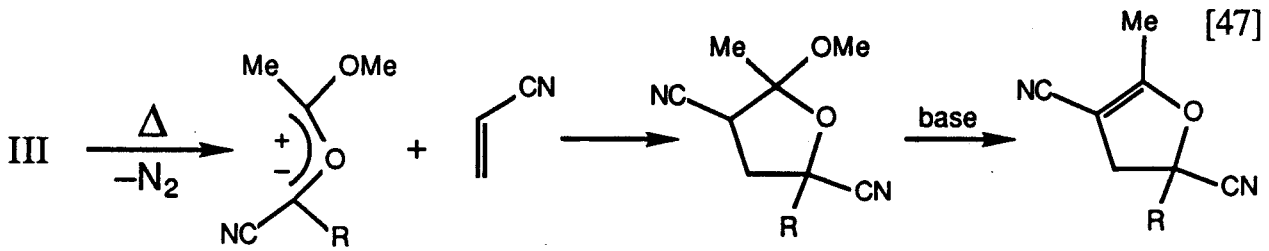


Scheme 6

Other trapping experiments of the ylide from III should give rise to various new compounds, such as the furan (eq. [46]) or dihydrofuran (eq. [47]), as shown below:



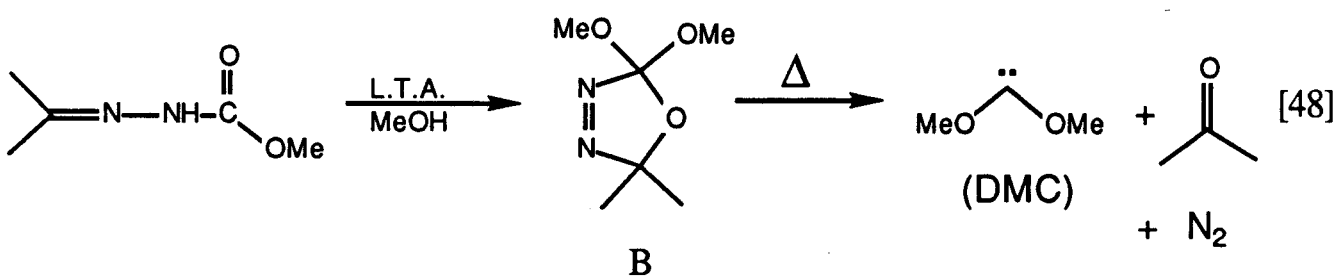
[46]



[47]

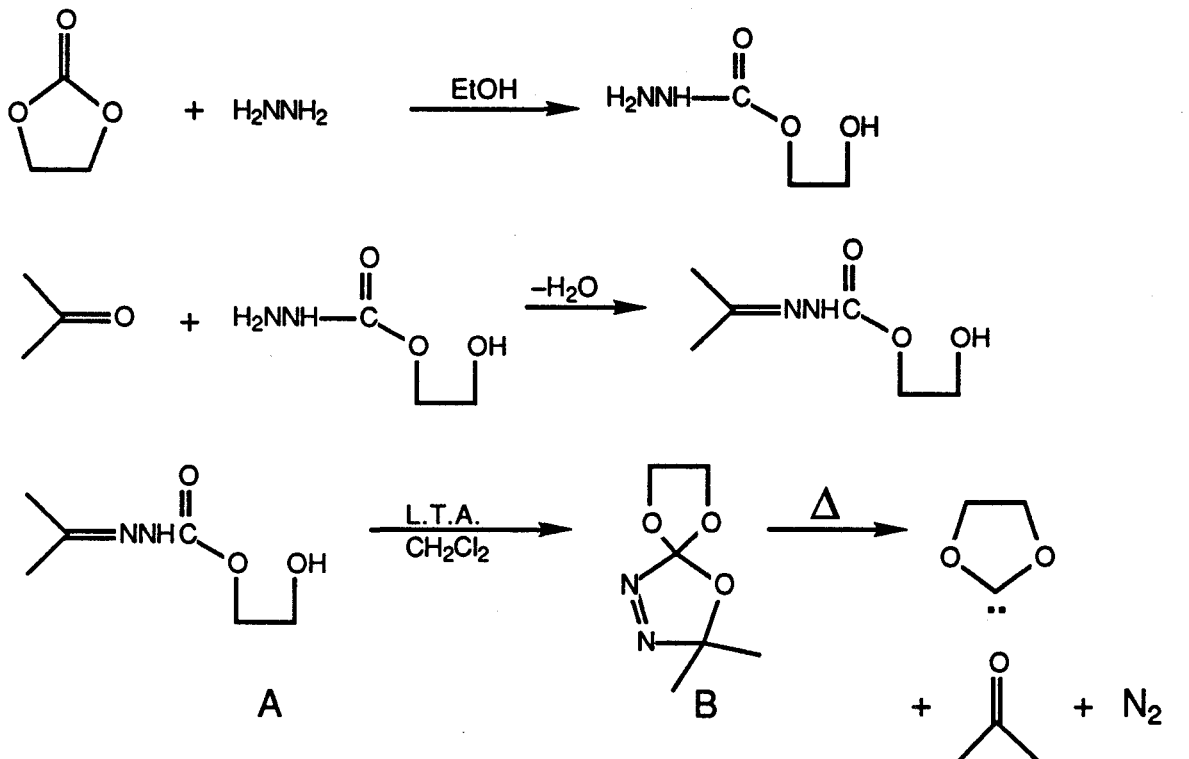
2.1 Synthesis of Spiro Oxadiazolines

Failure to synthesize the oxadiazoline III led to a search for others that could serve as sources of carbenes. During this time Tadey[80] and Warkentin generated dimethoxy carbene(DMC) from 2,2-dimethoxy 5,5-dimethyl-Δ^3-1,3,4-oxadiazoline as shown below, eq. [48].



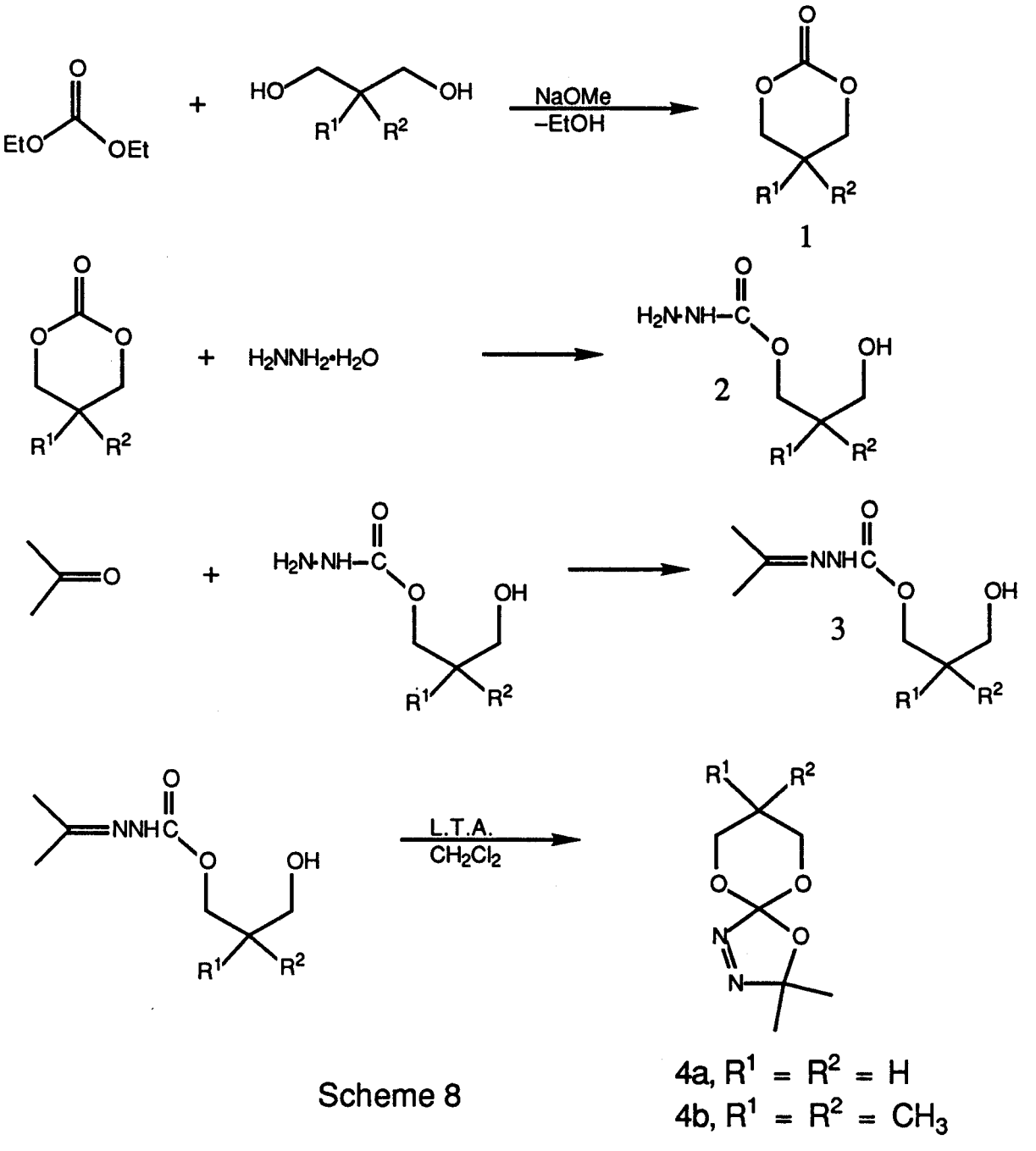
[48]

Various thermolysis and trapping experiments by Moss and co-workers showed that DMC is an archetypal nucleophilic carbene. After the generation of dimethoxycarbene, an attempt to generate a cyclic dioxacarbene from a spiro oxadiazoline was a success, according to Scheme 7.



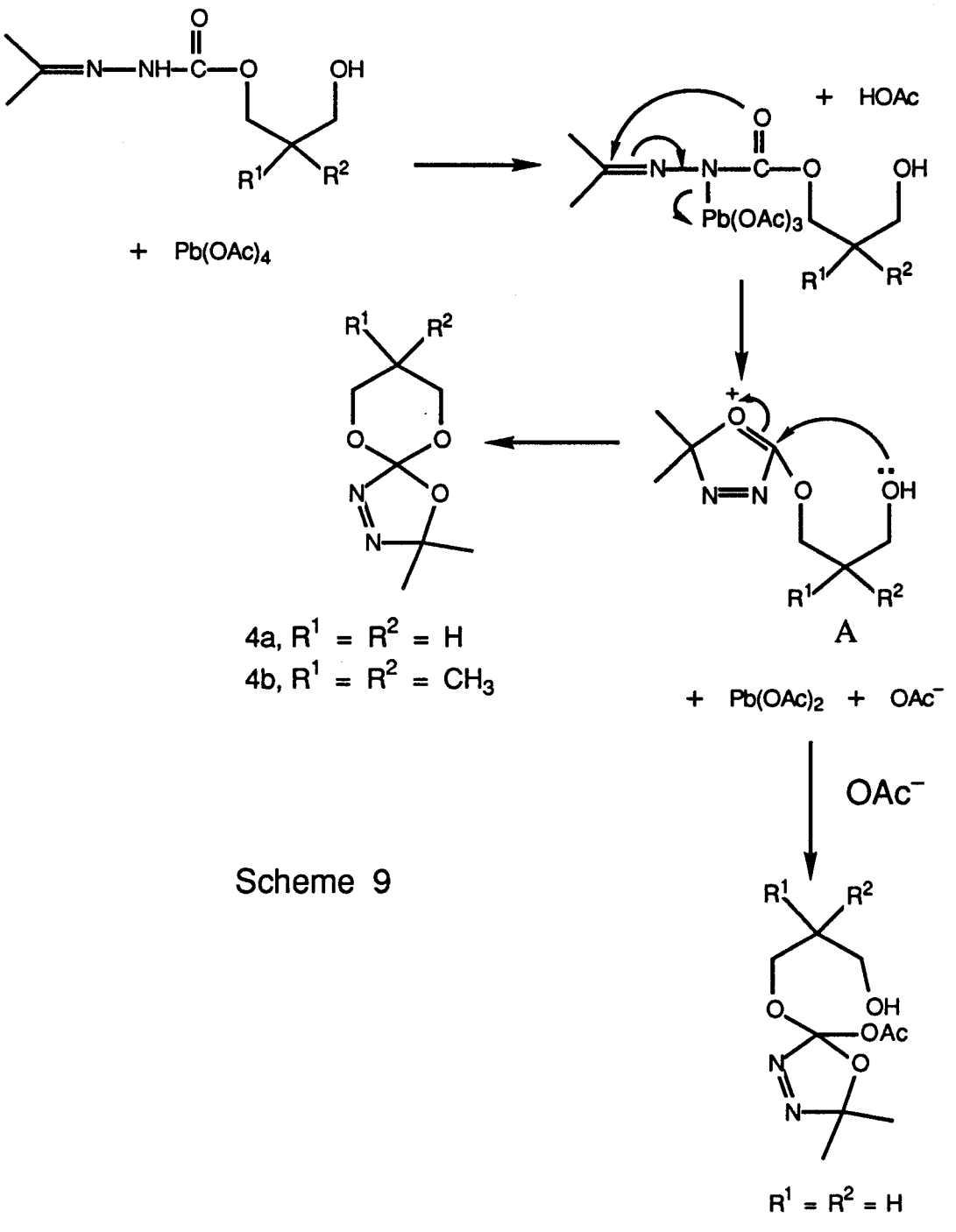
Scheme 7

Although synthesis of the spiro oxadiazoline B was successful, the yield of the product was very low (10%). This was attributed to the ring strain associated with intramolecular cyclization of A to spiro oxadiazoline B. Therefore synthesis of larger-ring oxadiazolines was approached according to Scheme 8:



Scheme 8

The expected mechanism for the L.T.A. oxidation can be written as follows, (Scheme 9)



Scheme 9

The first step involves the formation of a bond between nitrogen of the NH group and lead. Decomposition of the lead-nitrogen complex followed by the

intramolecular ring closure of A yields the spiro oxadiazoline 4. Intramolecular cyclization competes with attack of acetate ion in the last step, and the yield of 4a($R^1 = R^2 = H$) was only 75%. But in the case of 4b($R^1 = R^2 = Me$), the actual yield was 90%, pointing to the fact that the presence of two Me groups in the six-membered ring (as in A) make it easy for intramolecular cyclization.[81]

Evidence for the formation of the spiro oxadiazoline was obtained from both NMR and mass spectroscopic analysis. In the MS, 4 showed the highest m/z values corresponding to M-28 when run in the ei mode. That is, the oxadiazoline fragments and loses nitrogen during the analysis.

2.2 Thermolysis in Benzene

2.2.1 Rate Constant Calculations

Thermolysis of 4b at 111°C in d_6-benzene was carried out in an evacuated NMR tube. The decomposition was followed using toluene as an internal standard for integration. A plot of the *ln*(integral 4b/integral toluene) versus time(see Fig. 1) indicates first-order kinetics($K_{111°C} = 1.82\times10^{-5}\ s^{-1}$). These results indicate that the rate of thermolysis is similar to the rate constant for dimethoxy oxadiazoline. (The rate constant for dimethoxy oxadiazoline, B in eq. [48] was $K_{100°C} = 1.19\times10^{-5}\ s^{-1}$).

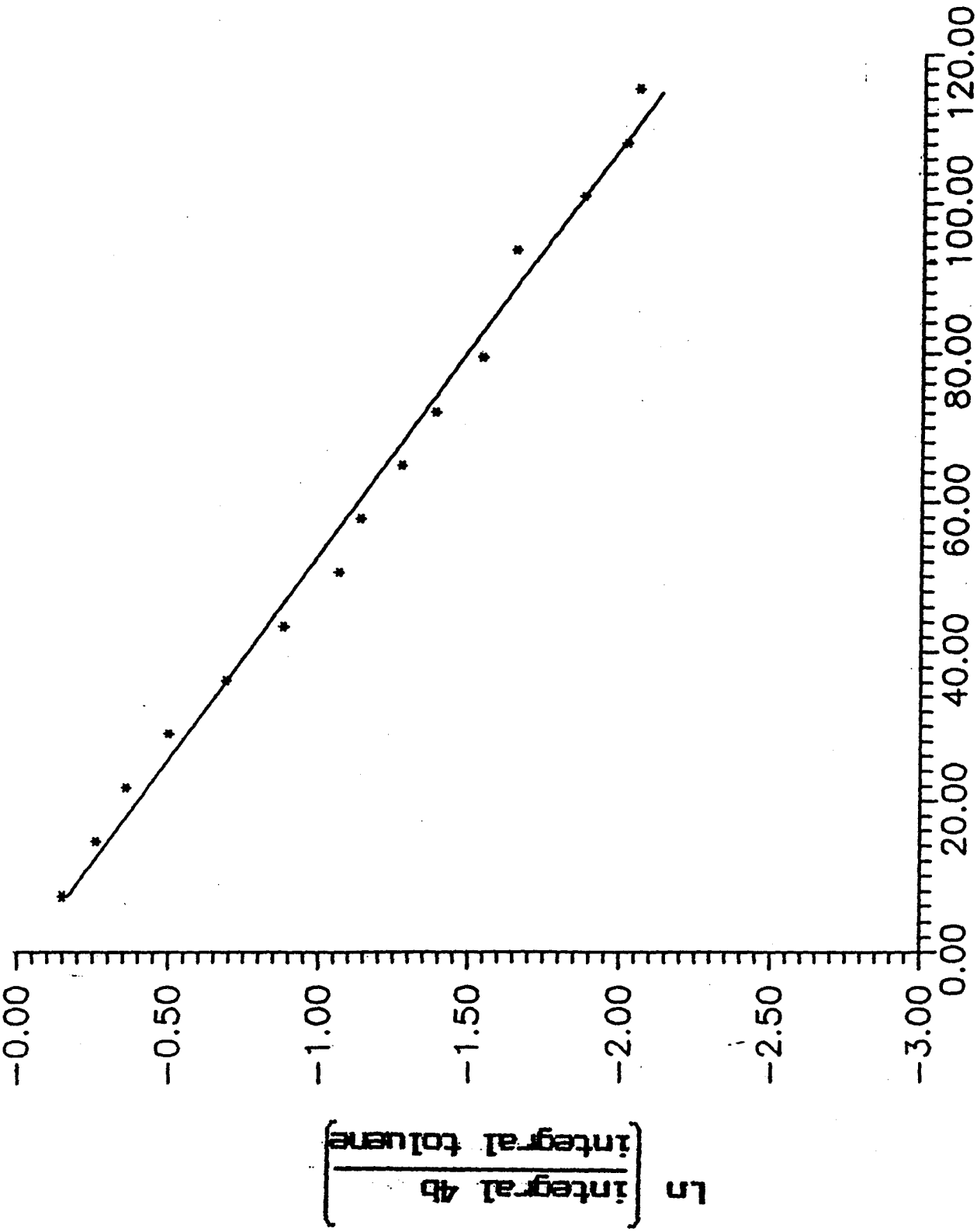
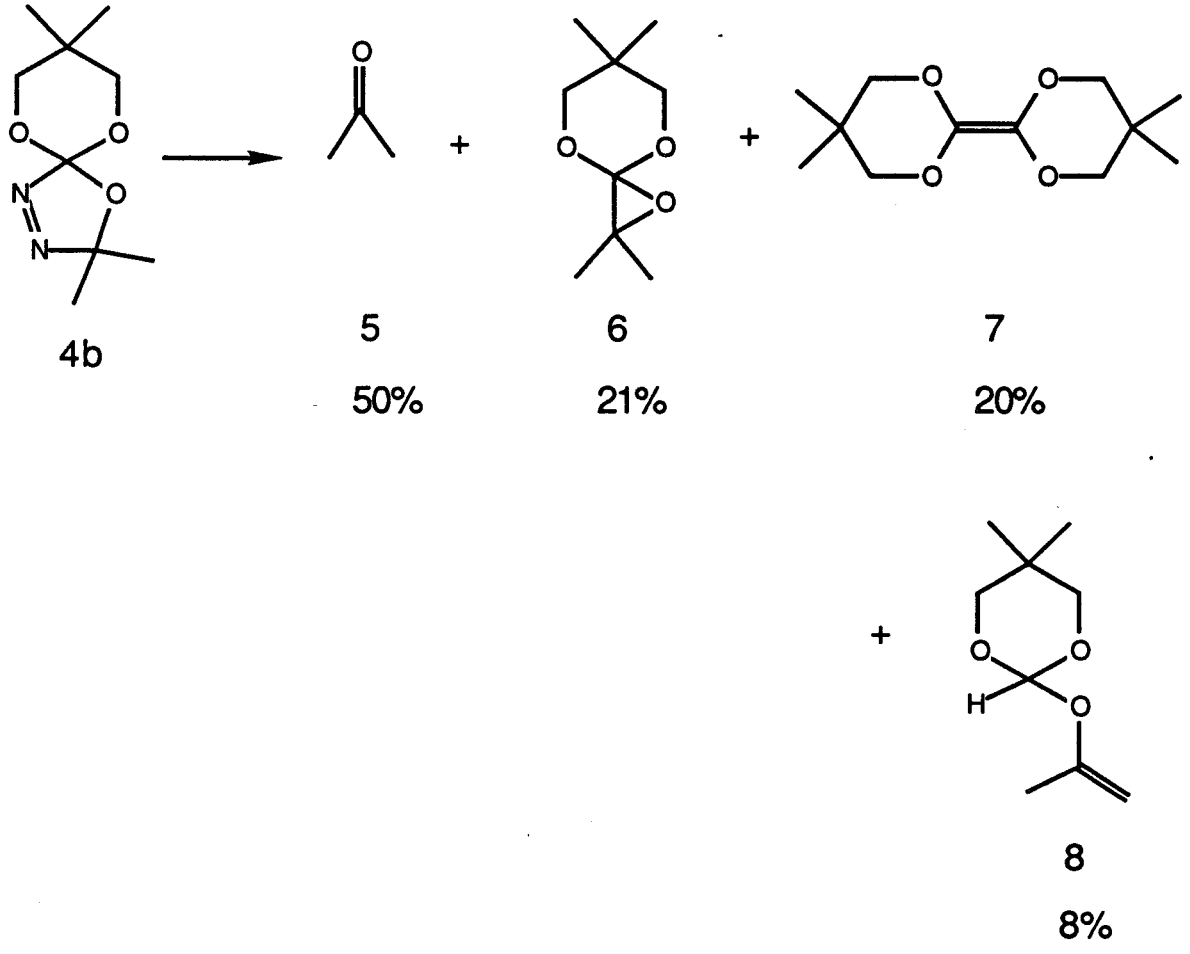


Figure 1: First Order Plot for Thermolysis of 4b.

Products of Thermolysis of 4b in Benzene

Thermolysis of 4b in benzene affords the following products, eq. [49].

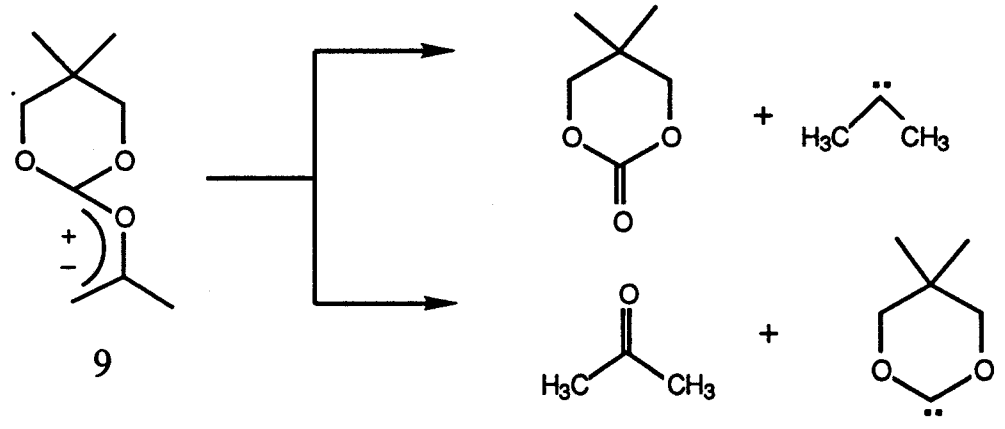


[49]

Product yields were determined by averaging ^1H NMR integrals. The evidence for the presence of these products was obtained by GC/MS analysis. The following peaks were the important ones obtained in the mass spectrum (ei mode). Spectral data for the products are given in the experimental section.

m/e	M^+
229	$(C_{12}H_{21}O_4)^+$
115	$(C_6H_{11}O_2)^+$
173	$(C_9H_{17}O_3)^+$

The results from GC/MS analysis gave no evidence for two-directional fragmentation, eq. [50]. That is, there was no indication for the formation of cyclic carbonate and dimethyl carbene when GC data of an authentic sample of carbonate was compared with that of the thermolysis products.

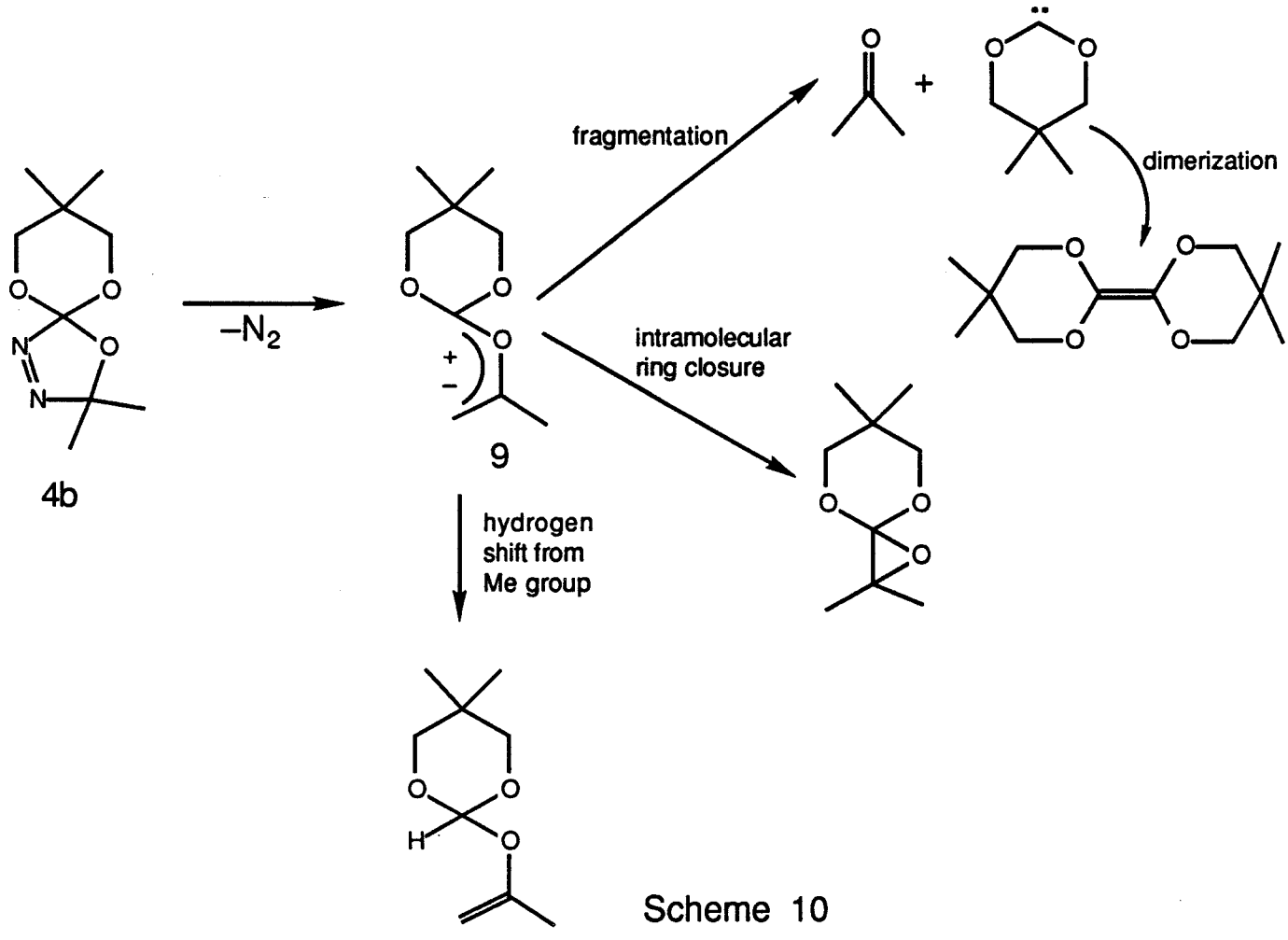


9

[50]

Thus the products that were obtained support the claim made earlier, as in Schemes 2 and 4.

1. Fragmentation of ylide 9 was the favoured process.
2. Fragmentation of 9 occurred in one sense to produce cyclic dioxacarbene. A mechanism that can account for the products obtained from the thermolysis is shown in Scheme 10:



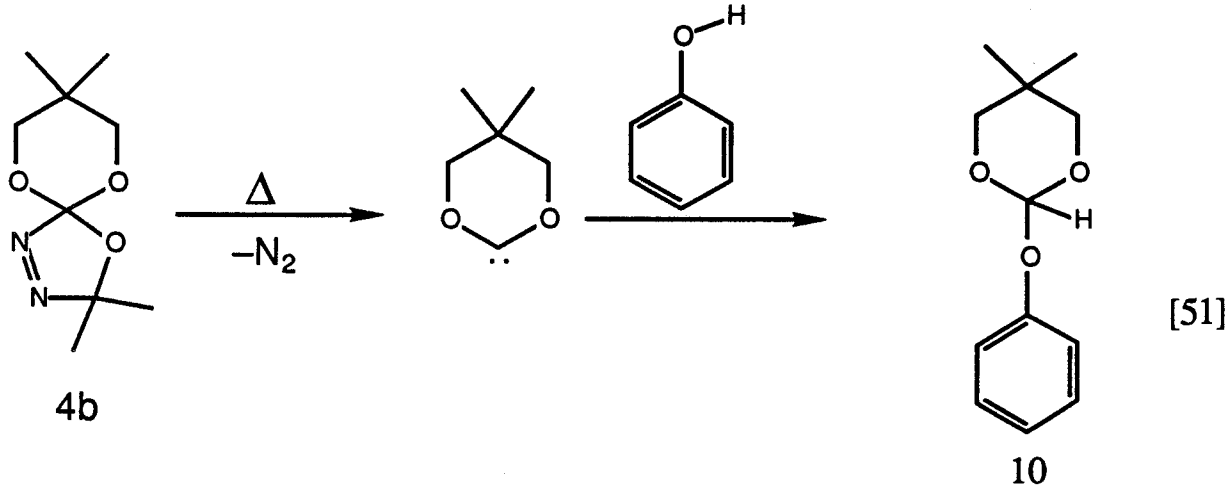
Scheme 10

2.3 Trapping Experiments

The insertion of a carbene with a variety of C-X bonds and addition to multiple bonds is well-documented.[7,8] In view of these facts, the reaction of cyclic dioxacarbene with phenol, carbon tetrachloride, chloroform, DMAD, and phenyl acetylene were carried out to gain insight into insertion reactions of a cyclic dioxacarbene. It should be noted that most of the trapping experiments were qualitative rather than quantitative.

2.3.1 Thermolysis in Phenol

Thermolysis of 4b in phenol would be expected to give the product shown in eq. [51].



4b

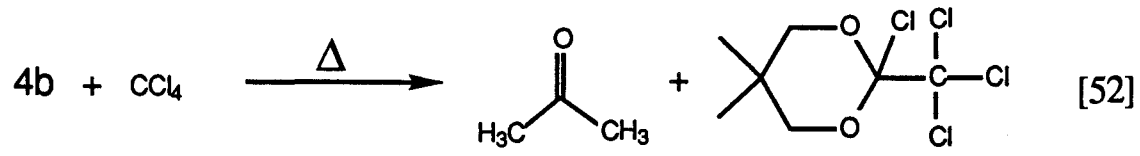
10

[51]

Dioxacarbene inserts into the -OH bond of phenol to form an orthoester 10, according to the above equation. Although GC/MS analysis of the crude mixture after thermolysis provided evidence for the formation of 10, an attempt to separate 10 out of the mixture failed. This may be due to the presence of excess phenol(acidic) which causes the hydrolysis of orthoester 10.

2.3.2 Thermolysis in Carbon Tetrachloride

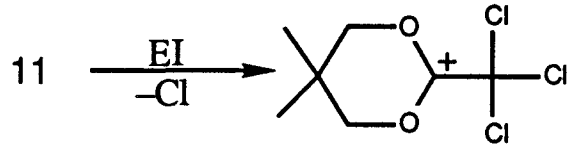
Thermolysis of spiro oxadiazoline 4b gave major products as shown in eq. [52].



[52]

11

Evidence for the formation of 11 was based on GC/MS analysis. The parent peaks at m/e=231, 233, 235 can be rationalized by loss of Cl from 11 to form the cation 12.



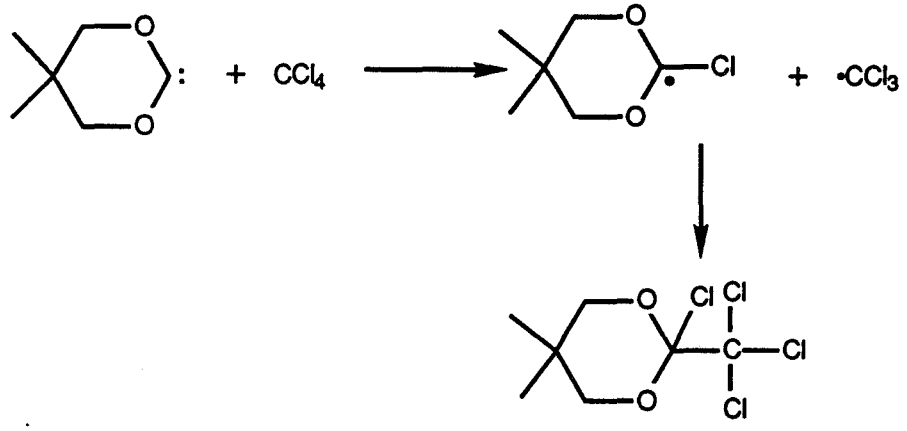
12

Furthermore, the intensity ratios of the peaks indicate the presence of three chlorine atoms.

	$(^{35}Cl)_3$	$(^{35}Cl_2)^{37}Cl$	$^{35}Cl(^{37}Cl_2)$
m/z	231	233	235
ratio	1	1	0.3

The formation of 11 may be rationalized by an intermolecular insertion of cyclic dioxacarbene into the C-Cl bond of CCl_4. Two mechanisms for the insertion may be proposed. Singlet carbenes can insert into C-X bonds via a one step concerted process.[7] Conversely, a two step process proposed by Warkentin[32], for the reaction of an acyloxy carbene with CCl_4 can account for

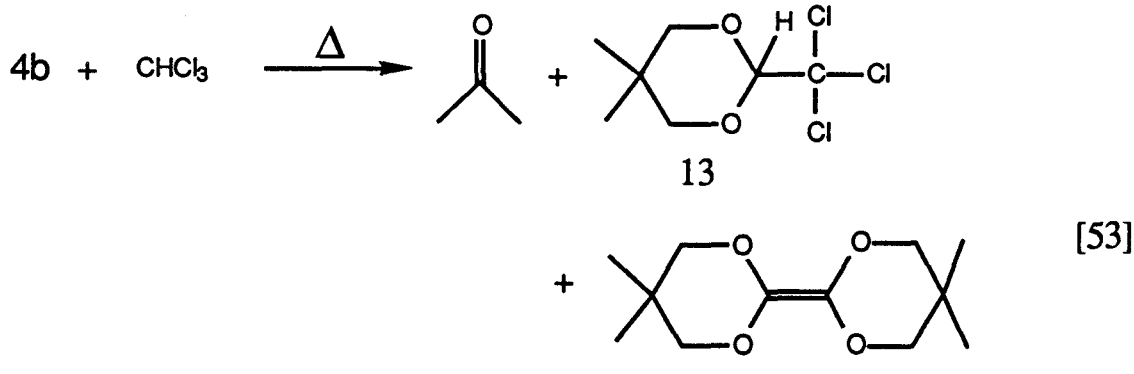
the products formed here. The stepwise insertion involves first abstraction of chlorine by the carbene (to form radical intermediates) followed by recombination of the radicals to form the product in Scheme 11.



Scheme 11

2.3.3 Thermolysis in Chloroform

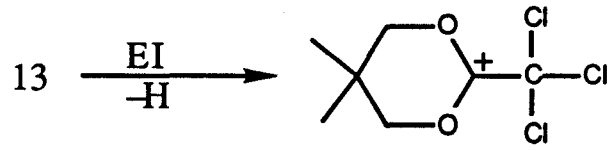
Analysis of the products from the thermolysis of oxadiazoline 4b in chloroform, using GC/MS, indicated the formation of an insertion (C-H insertion) product together with the dimer of the carbene.



13

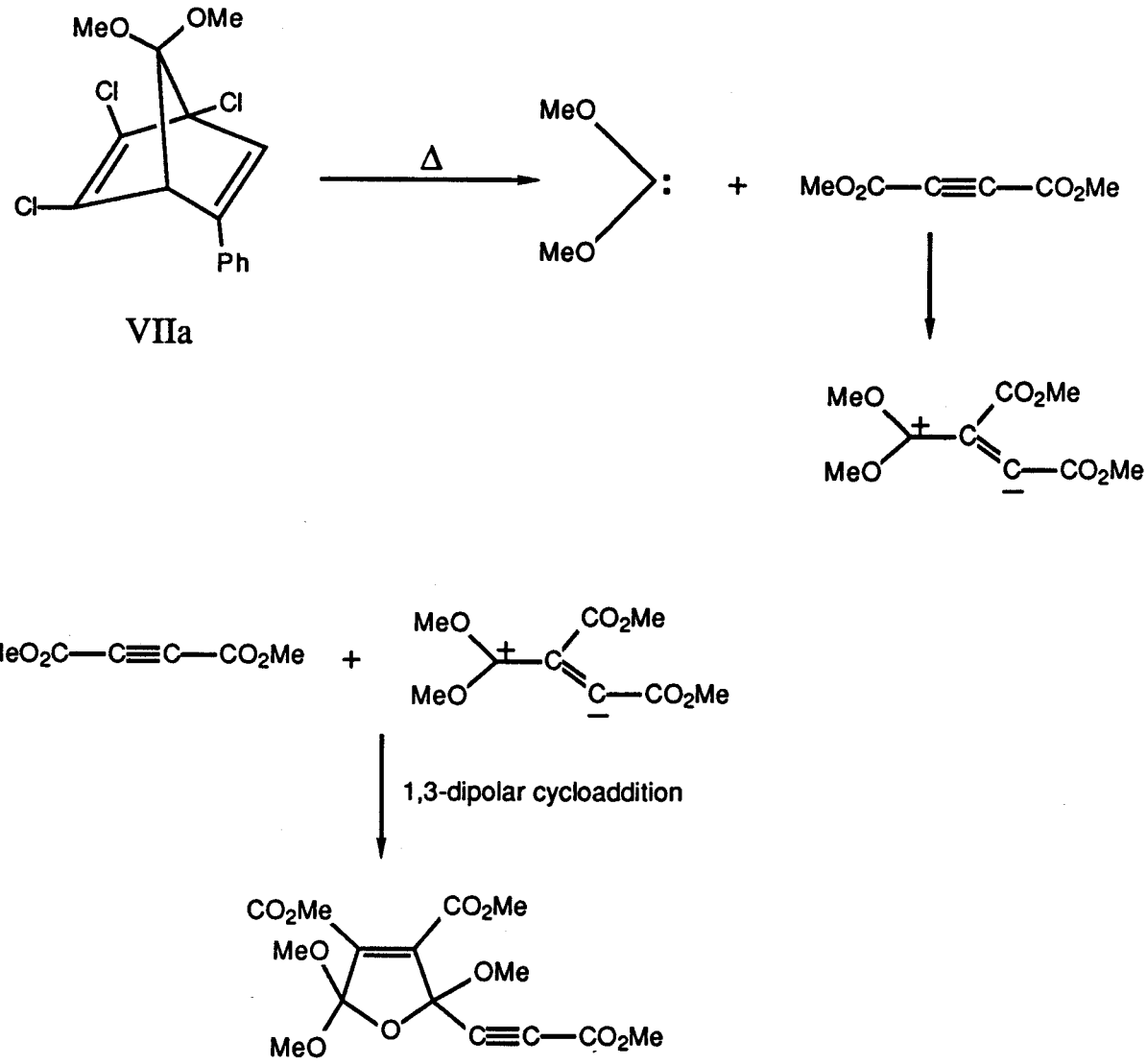
[53]

Evidence for 13 came from GC/MS analysis. The structure 13 was proposed because of observation of peaks at m/z = 231, 233 and 235 (in the ratio 1:1:0.3)



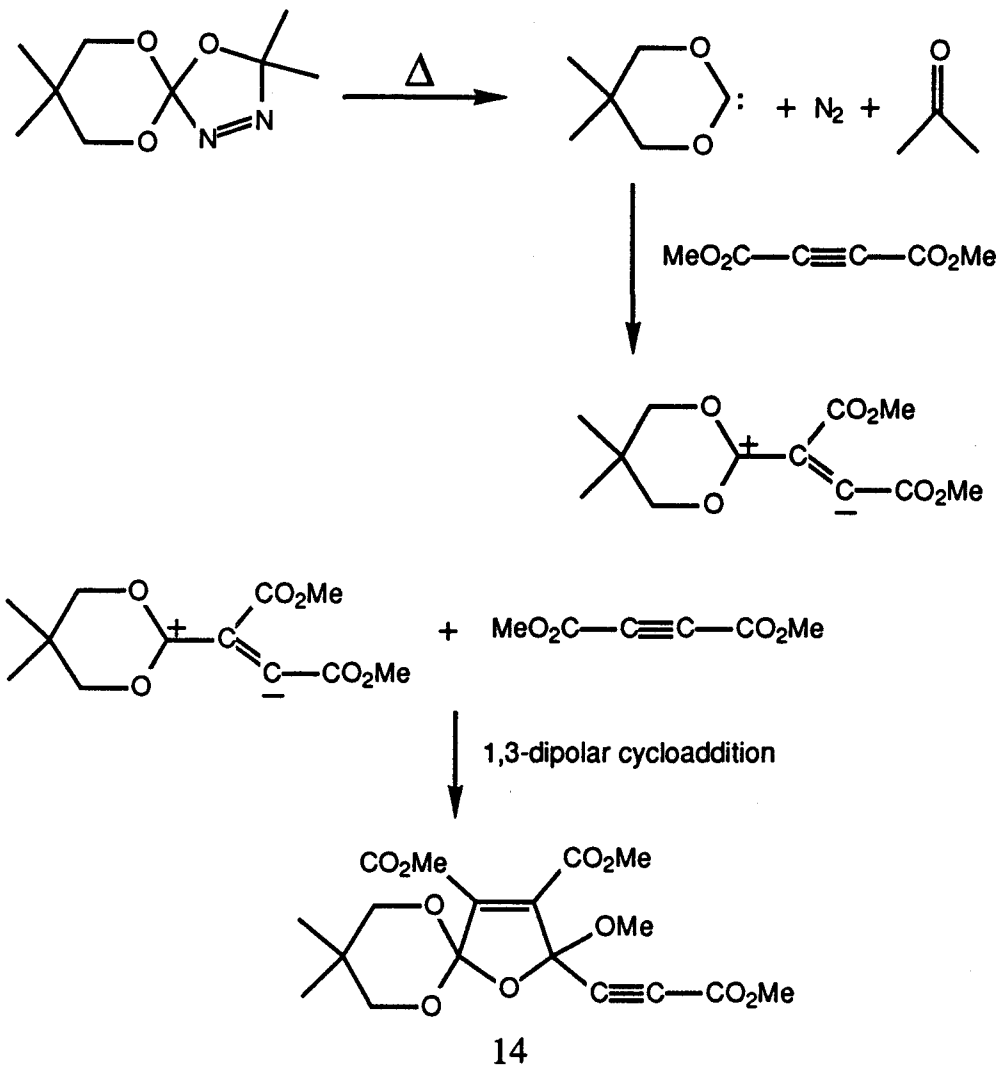
2.3.4 Thermolysis with Dimethyl Acetylene Dicarboxylate (DMAD)

Thermolysis of spiro oxadiazoline 4b with DMAD showed formation of a cyclic adduct 14 involving two steps. The reaction can be explained by the nucleophilic addition of cyclic dioxacarbene to DMAD followed by a 1,3-dipolar cycloaddition between the carbene adduct and another molecule of DMAD (Scheme 13). In addition to product (14), some other adducts were formed, but not identified. R.W. Hoffmann and co-workers synthesized a compound similar to 14 as shown below(Scheme 12)[82]



VIIa

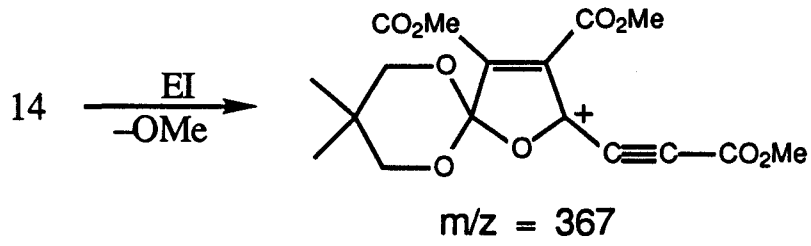
Scheme 12



14

Scheme 13

Evidence for the formation of 14 came from GC/MS analysis. The parent peak at m/z = 367 may be formed from 14 by the loss of one methoxy group.

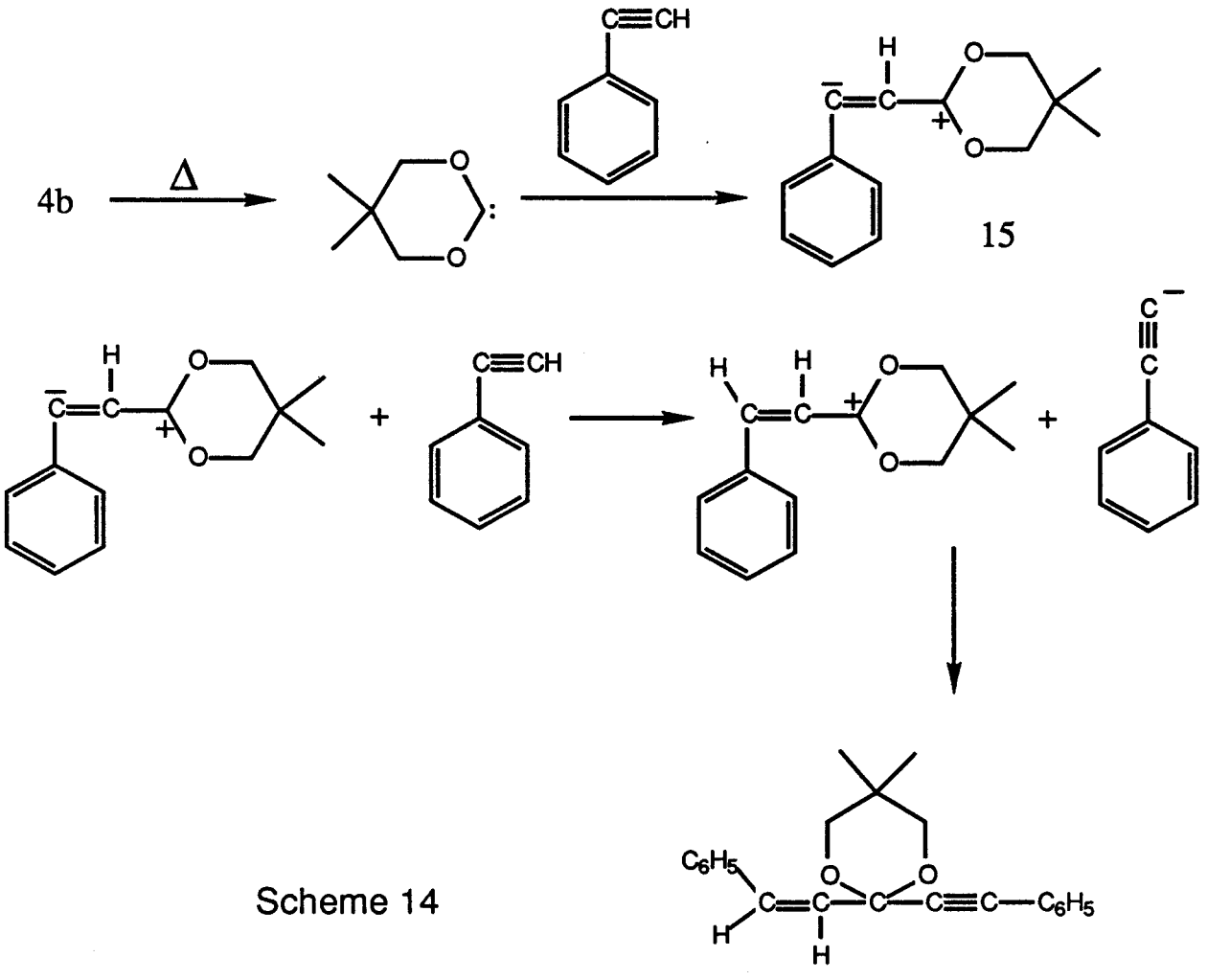


m/z = 367

The structure of 14 was confirmed by ^{1}H nmr spectroscopy after separation from the crude thermolysis mixture by centrifugal chromatography (see experimental section).

2.3.5 Thermolysis with Phenyl Acetylene

Thermolysis of spiro oxadiazoline 4b with phenyl acetylene afforded the product 17 according to Scheme 14[82]:



Scheme 14

17

Formation of 17 was supported by GC/MS analysis which gave a peak at m/e = 319 (M+1).

3. Structure Elucidation of Spiro Oxadiazoline 4b

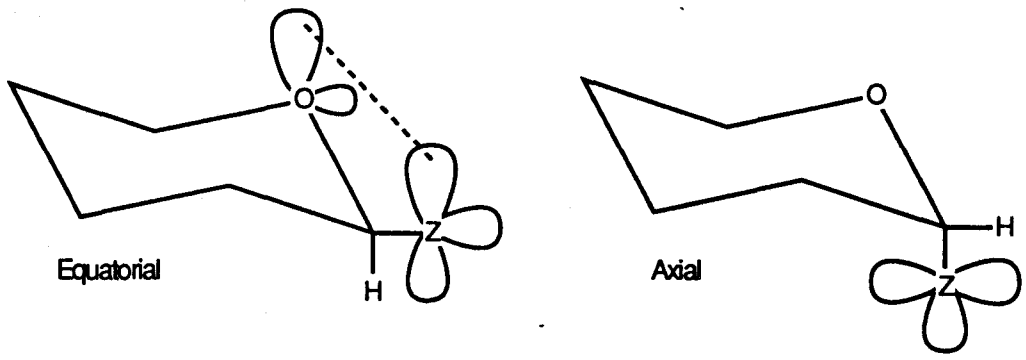
X-ray crystallographic analysis of the spiro oxadiazoline 4b gave the structure with bond lengths as shown in Figure 2 (Page 56).

The crystal and molecular structure of the spiro oxadiazoline 4b has been determined at 193K. Crystals are orthorhombic, of space group P_{cmn}, with a=6.288(1)Å, b=9.452(2)Å, c=17.762(4)Å, v=1055.7(4)Å^3, D_c=1.26gcm^3; for z=4 and R_1=0.0449(R_2=0.0459) for 739 reflections.

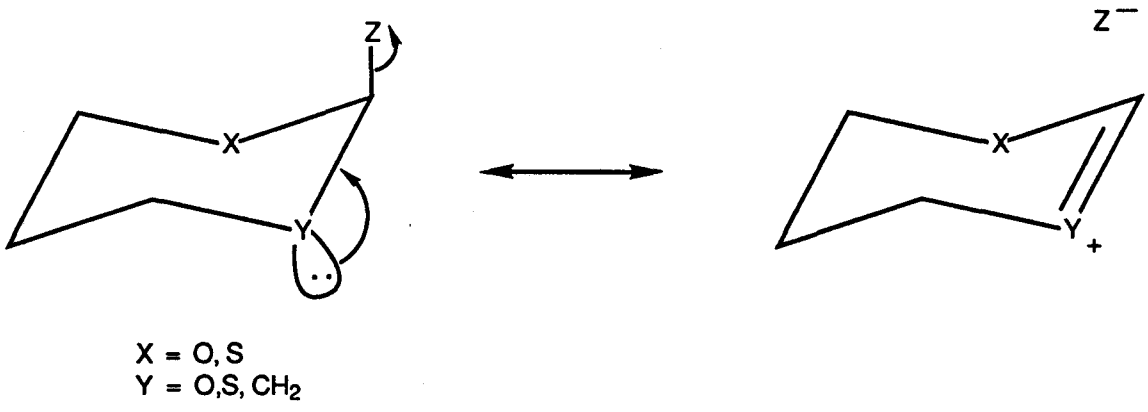
3.1 Conformational Analysis of Spiro Oxadiazoline, 4b

The tendency of electronegative substituents to assume the axial rather than the equatorial orientation at the anomeric centre of sugars, known as the "Anomeric Effect", has been observed in many other heterocyclic systems. The most striking effects are observed when one or both of the heteroatoms in six-membered ring systems is oxygen, and relate to the conformation about the C—O bond, which in turn has remarkable effects on the structure and reactivity of compounds like tetrahydropyrans, glucosides, aldopyranosides and 1,3-dioxanes. Nevertheless, and despite the appearance of several reviews,[83a] the exact nature of the phenomenon is not well understood.

A simple example of the anomeric effect is that in aldopyranosides, the cause of which was once thought to be the interaction between lone pairs of the ring oxygen and those of the substituent at carbon α to the ring oxygen. This interaction is less for the axial than for the equatorial conformer as shown below:



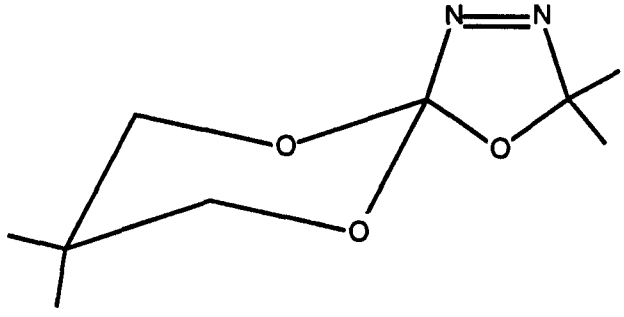
In addition to the above dipole-dipole interactions, stereoelectronic factors also play a major role in the anomeric effect as observed in various 2-substituted tetrahydropyrans,[83b] 1,3-dioxanes[83c] and 1,3-dithianes.[83d] Structural and theoretical studies showed that there is a stereoelectronic preference for that conformation in which the best donor lone pair or bond is antiperiplanar to the best acceptor bond, as shown below:



Here in the X—C—Z or Y—C—Z segment, double bond/no bond resonance structures can be written for axial conformers, where a lone pair of electrons on sulphur or oxygen is antiperiplanar(app) to the C—Z bond. It is a general trend that strongly electron-withdrawing or electronegative substituents lower the σ*

molecular orbital level, and increase the overlap with the donor orbitals. This n-σ^* stabilization has been supported by calculations of conformational energies for axial and equatorial isomers of various ring systems. It was found that in general, the anomeric effect varies inversely with the dielectric constant of the medium.

From the X-ray crystallographic study of the spiro oxadiazoline 4b, it was found that the azo function prefers the axial position (see Fig. 2, p. 56) which is comparable to the conformations of 2,2-disubstituted 1,3-dioxanes. It was found that the anomeric effect increases with increasing electronegativity and follows the order F > O > N > C. In the case of N, the effect depends on the substituents at the nitrogen centre. The anomeric effect was found to be more effective for the more electronegative sp and sp^2-hybridized nitrogen groups, which are also those with the greatest charge density on nitrogen.[83a] Since the azo function is more electronegative than an alkoxy group, its preference for the axial position is quite reasonable as shown:



4b

In order to gain insight into the above phenomenon, ^{15}N n.O.e. experiments were conducted in an attempt to determine the conformation of 4b in solution ($CDCl_3$). With the azo group axial, N-4 of the oxadiazoline ring is close

to axial hyrogens of the 1,3-dioxane ring and therefore a ^{15}N n.O.e. enhancement between those atoms might be observable. With the azo group equatorial, the distance is much too large for an Overhauser effect. Although the ^{15}N spectrum of spiro oxadiazoline 4b was acquired (δ $CDCl_3$, 70.05ppm and 90.02ppm, Ref. nitromethane), the Overhauser experiment failed because of the low intensity of ^{15}N signals. The synthesis of ^{15}N-enriched spiro oxadiazolines of type 4b might provide information about the axial preference of the azo function of 4b in solution.

The procedure for the X-ray crystallography and solution of structure are described in the experimental section.

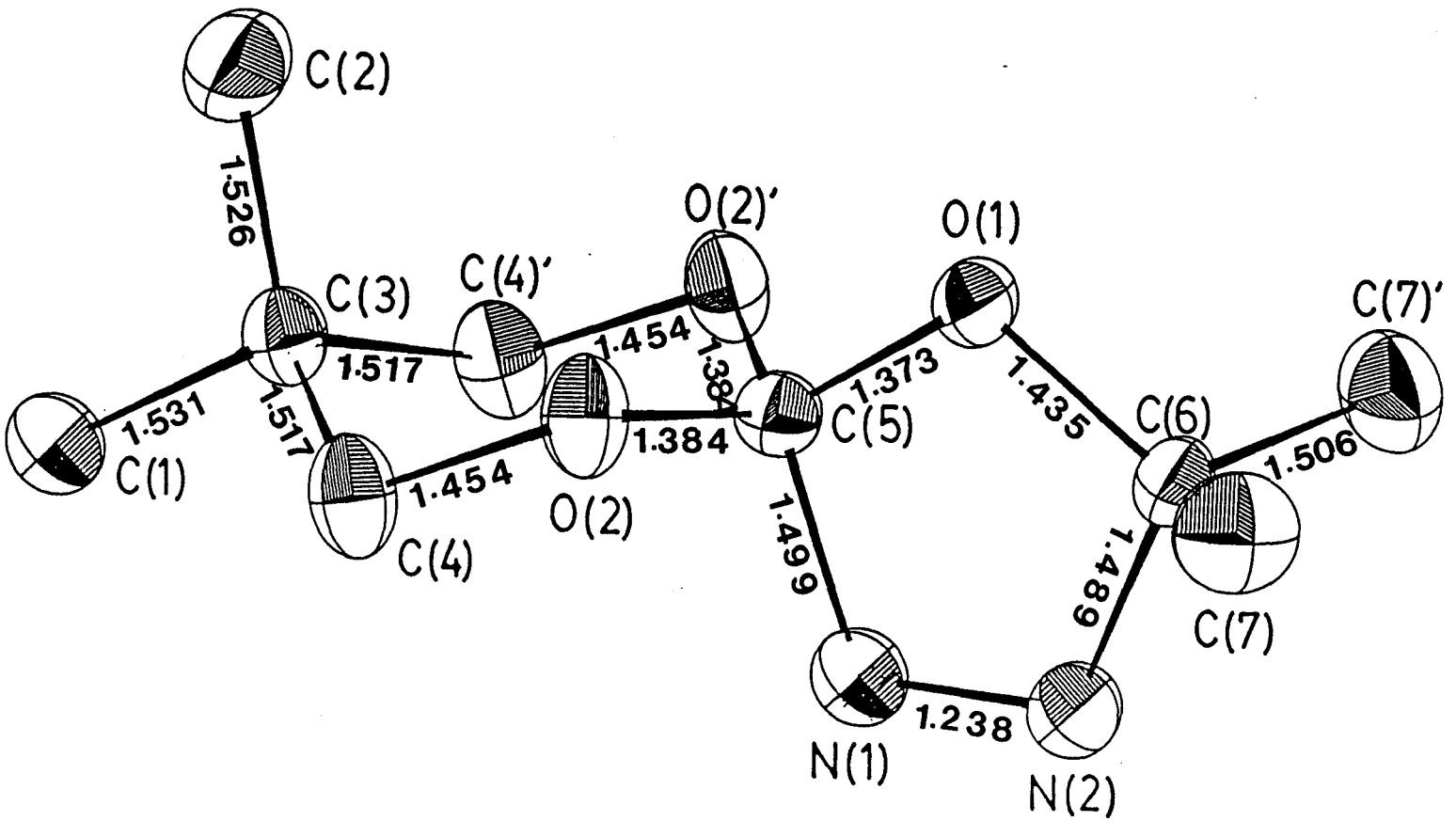
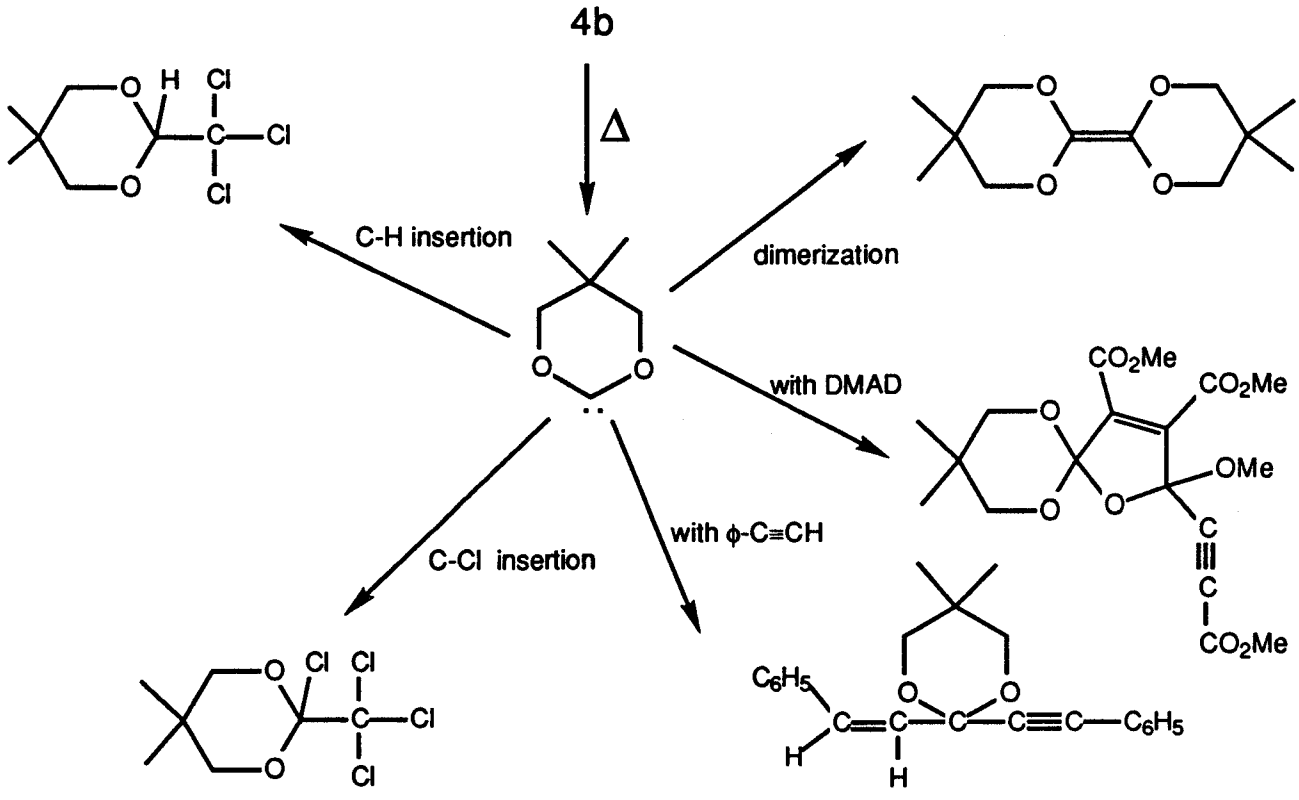

C(2)
1.526
C(3)
C(4)'
O(2)'
O(1)
C(7)'
1.517
1.454
1.384
1.373
1.435
1.506
1.531
1.517
1.384
C(5)
C(6)
C(1)
1.454
O(2)
1.499
1.489
C(4)
C(7)
1.238
N(1)
N(2)

Figure 2

4. Summary

Thermolysis of spiro oxadiazoline 4b yields cyclic dioxacarbenes(CDC) via one-directional fragmentation of an ylide intermediate.

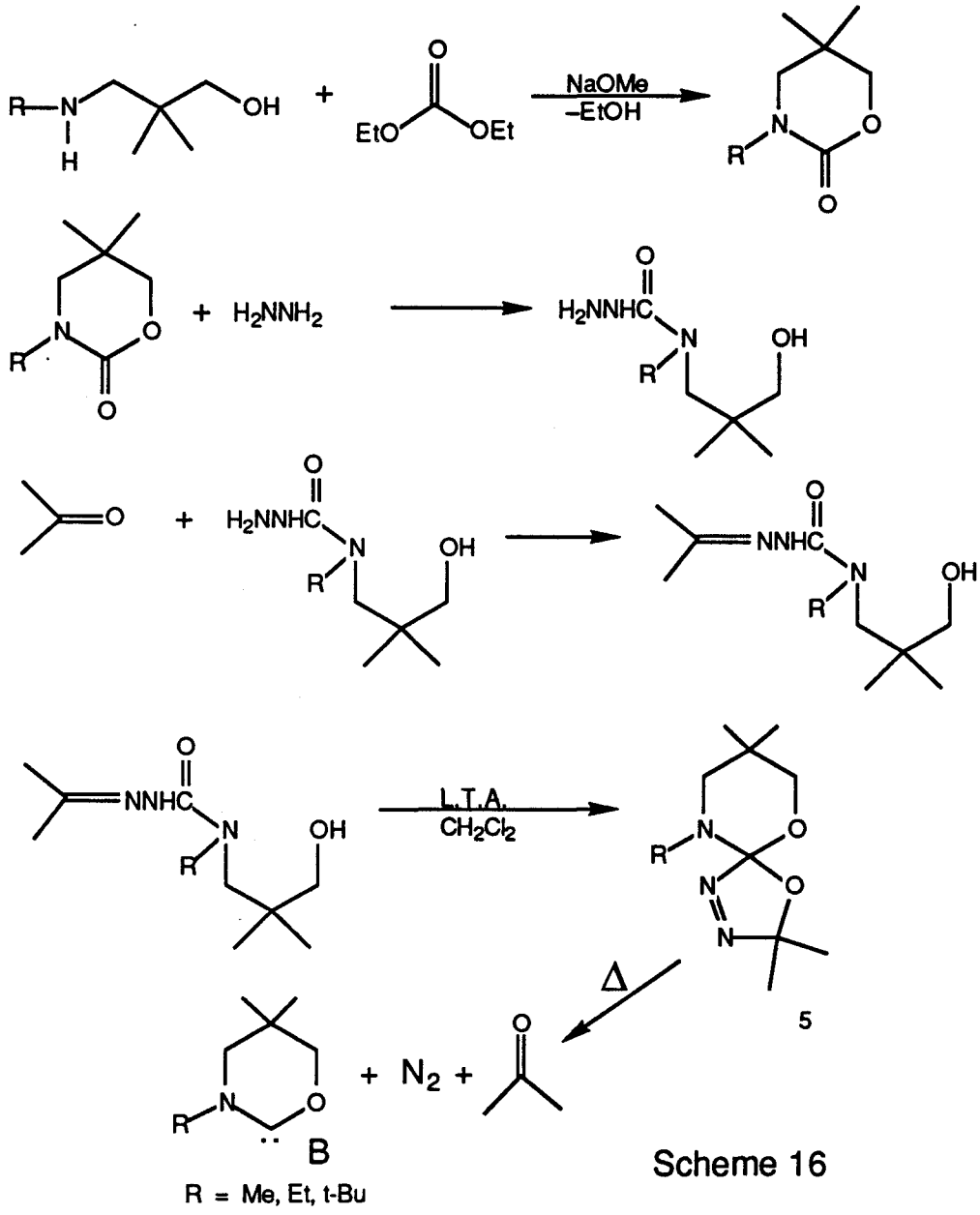
A cyclic dioxacarbene undergoes synthetically useful reactions (Scheme 15), by insertion into C-H or C-Cl bonds and also by reaction with various dipolarophiles like DMAD and phenyl acetylene.



Scheme 15

5. Future Work

1. Synthesis of spiro oxadiazolines of type 4 generating cyclic dioxacarbenes can lead to the generation of more stable and useful imino-oxo carbenes like B, from spiro oxadiazolines of type 5, according to Scheme 16:



Scheme 16

6. Experimental

6.1 Instrumental

The proton and ^{13}C NMR spectra were obtained from the Varian Em390(^{1}H NMR) and Bruker AM500(^{1}H NMR and ^{13}C NMR) spectrometers. The solvents used for NMR were chloroform-D, benzene and D_6-DMSO.

The infra-red spectra (IR) were obtained on the Perkin-Elmer Model 283 Spectrometer, using $CDCl_3$ as the solvent. The Raman spectra were obtained on a SPEX spectrometer equipped with an Argon Innova 90 laser.

Gas chromatograms for routine analysis were obtained on the Varian 490 Vista series chromatograph employing a DB-5 capillary column. The VG70-70F chromatograph/spectrometer was used for GC/MS analysis. Centrifugal chromatography was carried out on silica (Merck Kieselgel 60 PF_{254}) coated plates spinning in a chomatotron model 179247 apparatus.

A Thomas Hoover capillary melting point apparatus was used for melting point determinations.

6.2 X-Ray Crystallography

The procedure for the crystallographic study was developed by Dr. Chris Frampton, McMaster University, Hamilton, Ontario.

Crystals of spiro oxadiazoline 4b were grown from EtOH/water. Large transparent block-shaped crystals were examined under a polarizing microscope for homogeneity. A small well-formed crystal, 0.15×0.25×0.25mm, was cut

from a block and sealed in a Lindemann capillary. Unit cell parameters at 193K were obtained from a least squares fit of ψ, ϕ and 2θ for 15 reflections in the range ($19.0 < 2\theta < 24.4°$) recorded on a Nicolet P3 diffractometer with the use of graphite monochromated Mo K_α radiation; (λ=0.71069Å at 22°C). Intensity data were also recorded on a Nicolet P3 diffractometer at 193K with the use of an ω-2θ scan for 1722 reflections in the quadrant $h, k, \pm l$, with $2\theta \leq 45°$C. The methods of selection of scan rates and initial data treatment have been described.[84,85] Corrections for Lorentz-polarization effects were applied to all reflections. Two standard reflections (2,0,7; 75% and 0,5,4; 1.83%) monitored every 48 reflections showed no sign of crystal decomposition or instrument instability. Symmetry-equivalent data were averaged (R_{int}=0.0160) to give 739 unique reflections. A summary of full crystal data is given in Table SI.

Solution of Structure:

The structure was solved by direct methods based on 171 reflections with $|E| > 1.2$ and 50 sets of starting phases with the use of the program SHELXS-86.[86] Full-matrix least squares refinement of the co-ordinates of all the non-hydrogen atoms followed by a three-dimensional electron density synthesis revealed the positional parameters for all of the hydrogen atoms. The temperature factors of the non-hydrogen atoms, which were previously isotropic, were made anisotropic and further cycles of refinement using full-matrix least squares minimizing $\Sigma w(|F_o| - |F_c|)^2$ was terminated when the maximum shift/error reached 0.004. Corrections for secondary extinction were not necessary. Throughout the refinement, scattering curves were taken from reference 86[87]. All calculations were performed on a VAX 8650 computer.

Programs used were: XTAL[88], data reduction; SHELXS-86[86], structure solution; SHELXS-76[89], structure refinement; MOLGEOM[90], molecular geometry; and SNOOPI[91], diagrams. Final atomic positional parameters are given in Table SII, selected bond lengths and bond angles are given in Table SIII. Tables SIV-SVII list the least squares mean planes and dihedral/torsional angles, hydrogen atom positional parameters, bond lengths and bond angles involving hydrogen atoms, and anisotropic temperature factors are given at the end of the experimental section.

6.3 Synthesis Reactions

6.3.1 Synthesis of Trimethylene Carbonate, 1a

A mixture of 60.8g (0.8 mole) of trimethylene glycol, 114g (20% excess) of diethyl carbonate and 1.5-1.8g of dry sodium methoxide was placed in a flask equipped with a 36-inch Vigreux column.[81,92] The mixture was heated (the external temperature was 150-160°C) and the ethanol formed in the course of the reaction was distilled off at 77-84°C. After two hours, at which time the internal temperature reached 130°C, excess of diethyl carbonate was removed by distillation at reduced pressure. The residue was taken up in benzene, washed with water, dried and the solvent removed. Distillation at reduced pressure (1mm Hg) yielded 42g(64%) of 1a: bp 123°C at 1mm, mp 47-48°C. White, pure crystals melting at 50-51°C were obtained either after sublimation *in vacuo* or by recrystallization from benzene-ligroin.

^{1}H NMR(90 MHz, δ, $CDCl_3$), 2.13(p, 2H), 4.47(t, J=5.8 Hz, 4H).

6.3.2 Synthesis of Neopentylene Carbonate, 1b

A mixture of 83.32g(0.8 mole) of 2,2-dimethyl 1,3-propanediol, 114g of diethyl carbonate (20% excess) and 1.5-1.8g of dry sodium methoxide was placed in a flask equipped with a 36-inch Vigreux column and the procedure for synthesis of 1a was followed. Distillation at reduced pressure after removing the solvent yielded 90g(86%) of 1b; bp 122°C at 2mm Hg and mp 107°C. White crystals melting at 110°C were obtained either after sublimation *in vacuo* or by recrystallization from benzene-ligroin.

^{1}H NMR(δ, $CDCl_3$), 0.97(s, 6H), 4.00(m, 4H)

6.3.3 Synthesis of (3-Hydroxyprop-1-yl)hydrazino Carboxylate, 2a

The procedure of Allen and Bell was followed, except for minor modifications.[93] Hydrazine hydrate(20.28g, 0.4 mole) was added over a period of half an hour to a mixture of trimethylene carbonate (40.8g, 0.4 mole) and ethanol (100mL/95%) in a 1-litre round bottom flask. After refluxing the mixture for 48 hours, the solvent was evaporated, and 2a was obtained as a white solid. Recrystallization from ethanol yielded white crystals with mp 52-53°C; yield = 85%.

^{1}H NMR(90 MHz, δ, D_6-DMSO), 1.69(p, J=6.6Hz, 2H), 3.47(t, J=6.6Hz, 2H), 4.02(t, J=6.6Hz, 2H), 7.95(broad, NH), 3.08(NH_2 & OH).

6.3.4 Synthesis of (2,2-Dimethyl,-3-hydroxyprop-1-yl)hydrazino Carboxylate, 2b

Hydrazine hydrate (10.14g, 0.2 mole) was added to a mixture of neopentylene carbonate 1b (26g, 0.2 mole) in ethanol (80mL, 95%) and refluxed for 48 hours. A white solid (2b) was obtained after the solvent was evaporated. Recrystallization from ethanol/water yielded crystals of 2b, melting at 115°C; yield = 90%.

^{1}H NMR(90 MHz, δ, $CDCl_3$), 0.97(s, 6H), 3.34(s, 2H), 4.00(s, 2H), 6.5(broad, NH), 2.93(NH_2 & OH).

6.3.5 Synthesis of 1-(3-Hydroxyprop-1-oxycarbonyl)-2-(2-propylidene)hydrazine, 3a

(3-Hydroxy prop-1-yl)hydrazino carboxylate 2a (26.8g, 0.2 mole) was dissolved in 50ml benzene and acetone (23.2g, 0.4 mole). This mixture was then refluxed using a Dean-Stark trap and the excess acetone was evaporated on a rotary evaporator. The product 3a(viscous liquid) obtained was of satisfactory purity, determined by NMR spectroscopy.

^{1}H NMR(90 MHz, δ, $CDCl_3$), 1.93(p, J=6.0Hz, 2H), 1.90(s, 3H), 2.03(s, 3H), 3.72(t, J=6.0Hz, 2H), 4.35(t, J=6.0Hz, 2H), 8.4(b, NH), 3.72(b, OH).

IR($CDCl_3$), cm^{-1}, 640, 935, 1080, 1425, 1650, 3575, 3625.

6.3.6 Synthesis of 1-(2,2-Dimethyl, 3-hydroxyprop-1-oxycarbonyl)-2-(2-propylidene)hydrazine, 3b

40.4g(0.25 mole) of (2,2-dimethyl 3-hydroxy prop 1-yl) hydrazinocarboxylate was dissolved in acetone(23.2g, 0.4 mole). Sodium sulphate was added to the mixture to remove water formed during the reaction. The mixture was left stirring for twelve hours, and the excess of acetone was evaporated on a rotary evaporator. The product obtained(3b, viscous liquid) was of satisfactory purity, determined by NMR spectroscopy.

^{1}H NMR(δ, $CDCl_3$), 0.97(s, 6H), 1.90(s, 3H), 2.08(s, 3H), 3.37(s, 2H), 4.07(s, 2H), 3.85(sharp, OH), 7.88(b, NH)

IR, cm^{-1}, 620, 960, 1050, 1350, 1650, 3000, 3500, 3625.

6.3.7 Synthesis of 3,4-diaza-2,2-dimethyl-1,6,10-trioxa spiro[4,5]dec-3-ene, Spiro Oxadiazoline 4a

3a(26.37g, 0.152 mole) and lead tetraacetate(56.45g, 0.152 mole) were dissolved in 500mL of dichloromethane. The mixture was stirred at room temperature for about 4 days, until the heavy yellow colour was changed to a light yellow colour. The $Pb(OAc)_2$ formed was filtered off and the solvent was evaporated on a rotary evaporator. The residue was washed with very cold 10% sodium bicarbonate solution in small portions and extracted with CH_2Cl_2 and dried. Solid spiro oxadiazoline 4a was obtained after evaporation of the solvent. Pure spiro oxadiazoline was separated out after recrystallization from petroleum ether, mp 57-58°C, yield = 75%.

^{1}H NMR(500 MHz, δ, $CDCl_3$), δ:1.86(m, ^2J=13.6Hz, $^3J_{ea}$=$^3J_{ee}$=3.9Hz, 1H, H_{8e}), δ:2.17(m, ^2J=13.6Hz, $^3J_{aa}$=11.0Hz, $^3J_{ae}$=3.9Hz, 1H, H_{8a}); δ:4.21(m, ^2J=13.1Hz, $^3J_{ee}$=$^3J_{ea}$=3.9Hz, 2H, H_{7e} and H_{9e}), δ:4.57(m, ^2J=13.1Hz, $^3J_{ae}$=3.9Hz, $^3J_{aa}$=11.0Hz, 2H, H_{7a} and H_{9a}). (See Table I for more spectral data).

6.3.8 Synthesis of 3,4 diaza-2,2,8,8-tetramethyl-1,6,10-trioxa spiro[4,5]dec-3-ene, Spiro Oxadiazoline 4b

Lead tetraacetate(41.67g, 0.094 mole) was dissolved in 150mL of dichloromethane. A solution of 3b(19g, 0.094mole) in 100mL of CH_2Cl_2 was added drop by drop to the stirring solution of L.T.A. over a period of one hour. The mixture was stirred until the heavy yellow colour was changed to light yellow. The $Pb(OAc)_2$ formed was filtered off, and the solvent was evaporated on a rotary evaporator. The residue was washed with very cold 10% sodium bicarbonate solution in small portions, extracted with dichloromethane and dried. White needle-shaped crystals were formed from the solution and were filtered. Pure spiro oxadiazoline 4b was obtained after recrystallization from EtOH/water. mp, 117-118°C, yield = 90%. See Table 1 for spectral data.

6.4 Thermolysis Reactions

6.4.1 Thermolysis in Benzene

Spiro oxadiazoline 4b (10mg) and benzene (1mL) were mixed together and transferred to an NMR tube. The sample was degassed by means of three freeze-

pump-thaw cycles, using liquid nitrogen temperature at a vacuum line pressure of 10^{-2} mm Hg before sealing.

Thermolysis was performed in a refluxing toluene bath at 111±0.5°C. The reaction was monitored by ^{1}H NMR spectroscopy by following the decrease in intensity of the methyl signals of 4b at 2-hour intervals. The time outside the bath was not counted.

^{1}H NMR (δ, $CDCl_3$) data for the products of thermolysis (eq. [49]):

6, 0.98(s, 3H), 1.21(s, 3H), 1.46(s, 6H), 3.52(d, 2H), 4.07(d, 2H).

7, 0.945(s, 6H), 0.95(s,6H), 3.74(d, 4H), 4.04(d, 4H).

8, 0.79(s,3H), 0.95(s, 3H), 1.45(s, 3H), 3.33(d, 2H), 3.36(d, 2H), 4.09(s, 2H), 4.94(s, 1H).

6.4.2 Thermolysis in the Presence of Phenol

Spiro oxadiazoline 4b (10mg, 5×10^{-5} mole) and phenol (9.4mg, 1×10^{-4} mole) were dissolved in benzene and transferred to an NMR tube. The tube was then sealed under vacuum (10^{-2} mm Hg) after several freeze-pump-thaw cycles. The mixture was thermolysed for 5 days at 100°C and analysed by GC/MS using DB-5 capillary column.

MS, (ei mode), m/z (fragment, %): 208($C_5H_{16}O_3$, 5), 115($C_6H_{11}O_2$, 100), 103(C_6H_6O, 50).

6.4.3 Thermolysis in Carbon Tetrachloride and Chloroform

Oxadiazoline 4b (10mg) was dissolved in CCl_4 (1mL) and transferred to an NMR tube which was sealed under high vacuum. The thermal decomposition was

carried out at 100°C for 5 days and products were analyzed by GC/MS using a DB-5 column. The thermolysis in $CHCl_3$ was performed in the same manner.

In CCl_4; ms, (ei mode), m/z (fragment, %): 231($C_7H_{10}O_2Cl_3$, 20), 131($C_6H_{11}O_3$, 30), 69(C_5H_9, 100).

In $CHCl_3$; ms, (ei mode), m/z (fragment, %): 231($C_7H_{10}O_2Cl_3$, 25), 131($C_6H_{11}O_3$, 35), 83($CHCl_2$, 20).

6.4.4 Thermolysis with DMAD

Spiro oxadiazoline 4b (20mg, 0.0001 mole) and DMAD (28mg, 0.0002 mole) were dissolved in benzene (1.5mL) and transferred into an NMR tube which was sealed under high vacuum. The thermolysis was carried out at 100°C for 5 days. Both the solvent and excess DMAD were evaporated off and the residue was analysed by GC/MS. The product (14) was separated by centrifugal chromatography(chromatotron).

^1H NMR (δ, $CDCl_3$) data for product (14), 0.82(s, 3H), 1.24(s, 3H), 3,46(s, 3H), 3,79(s, 3H), 3.86(s, 3H), 3.87(s, 3H), 3,57(d, J=8.7Hz, 2H), 4.03(d, J=8.7Hz, 2H).

6.4.5 Thermolysis with Phenylacetylene

10mg (5×10^{-5} mole) of oxadiazoline 4b and 10.2mg of phenylacetylene were dissolved in benzene and transferred to an NMR tube which was sealed under vacuum. The thermolysis was carried out at 130°C for 5 days. Benzene was evaporated off and the mixture was analysed by GC/MS using a DB-5 column.

MS, (ei mode), m/z (fragment, %): 319($C_{22}H_{22}O_2$+H, 2), 115($C_6H_{10}O_2$+H, 20), 103(C_8H_7, 100).

Table I Spectral Data for Spiro Oxadiazolines 4a and 4b

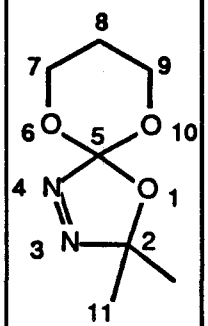
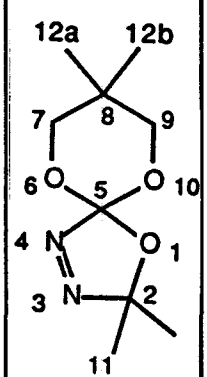
Sample	Yield	MP °C	^{1}H NMR	^{13}C NMR	I.R. cm^{-1}	Raman
 4a	75%	57-58	(90 MHz, $CDCl_3$) 1.53(s,6H) 1.86(m,1H) 2.16(m,1H) 4.20(m,2H) 4.57(m,2H)	133.59(C5) 119.71(C2) 64.63(C9) 24.48(C11) 23.77(C8)	1070 1140 1252 1360 1460 2980 3000	680 710 770 1135 1460 1580 2050 2400 2980 3000
 4b	90%	117-118	0.98(s,3H) 1.22(s,3H) 1.52(s,6H) 3.73(d,2H) 4.25(d,2H) 500MHz ^{1}H nmr 0.99(s,3H) 1.21(s,3H) 1.52(s,6H) 3.73 and 3.75(d,2H) 4.22 and 4.24(d,2H) J=11.1 Hz	133.52(C5) 119.75(C2) 74.89(C9) 29.71(C8) 24.52(C11) 22.53(C12a) 21.73(C12b)	800 1140 1252 1360 1460 2980 3140	610 700 770 800 1252 1580 1460 2980 3000

Table SI. Full Crystal Data for *Spiro*-Oxadiazoline.

Formula	$C_9H_{16}N_2O_3$
f.w.	200.24
Crystal Shape; size, mm	Block; 0.15×0.25×0.25
System	Orthorhombic
Systematic absences	$0kl$, $l \neq 2n$; $hk0$, $h + k \neq 2n$; $h00$, $h \neq 2n$; $00l$, $l \neq 2n$
Space Group	P *cmn* No–62
a, Å	6.288(1)
b, Å	9.452(2)
c, Å	17.769(4)
V, Å^3	1055.7(4)
Z	4
Dc, g cm^{-3}	1.26
F(000)	432
Diffractometer	Nicolet P3
Temperature	193K
Radiation	MoKα λ=0.71069Å
μ(MoKα), cm^{-1}	0.59
No. of reflections used in cell dtn.	15, (19.0° < 2θ < 24.4°)
Standard reflections (esd %)	2,0,7 (1.75) 0,5,4 (1.83)
Data collected	$h, k, \pm l$
Maximum 2θ reflections collected	45°

Table SI. Cont'd.

No. of reflections collected	1722
No. of independent reflections	739
R_{int}[b]	0.0160
Final Shift/error max. (ave.)	0.004 (0.001)
No. of variables	110
Final R_1, R_2[c]	0.0449, 0.0459
Weighting Scheme	$\omega=(\sigma^2F+0.000491F^2)^{-1}$
Error in observation of unit weight[d]	1.6324
Highest peak, eÅ^{-3}; location	0.23; 0.007,0.750,0.594
Lowest peak, eÅ^{-3}	–0.22

[a]Special setting of P*nma*.

[b]$R_{int}=(\Sigma(N\Sigma(\omega(<F>-F)^2))/\Sigma(N-1)\Sigma\omega F_o^2)^{\frac{1}{2}}$.

[c]$R_1=\Sigma|\,|F_o|-|F_c|\,|/\Sigma|F_o|$; $R_2=(\Sigma\omega(|F_o|-|F_c|)^2/\Sigma\omega F_o^2)^{\frac{1}{2}}$.

[d]$S=(\Sigma\omega(|F_o|-|F_c|)^2/(m-n))^{\frac{1}{2}}$ m=No. of reflections, n=No. of variables.

Table SII. Positional parameters ($\times 10^4$) and $U_{eq}(Å^2)$ ($\times 10^4$) for *Spiro*-Oxadiazoline with standard errors in parentheses.

Atom	x	y	z	$U_{eq}(Å^2)$
C(1)	–5434(5)	7500	6980(2)	312
C(2)	–1564(6)	7500	6638(2)	463
C(3)	–3158(5)	7500	7286(2)	264
C(4)	–2855(4)	6220(2)	7790(1)	315
C(5)	–417(5)	7500	8564(2)	244
C(6)	1742(5)	7500	9595(1)	244
C(7)	2800(5)	6169(3)	9872(2)	419
O(1)	1673(3)	7500	8787(1)	307
O(2)	–794(2)	6273(1)	8161(1)	301
N(1)	–1718(4)	7500	9271(1)	307
N(2)	–524(4)	7500	9825(1)	306

$U_{eq} = \frac{1}{3}(U_{11} + U_{22} + U_{33})$

Table SIII. Selected bond lengths (Å) and bond angles (°) for *Spiro*-Oxadiazoline with estimated standard deviations in parentheses.

C(1)–C(3)	1.531(4)	O(1)–C(5)	1.373(3)
C(2)–C(3)	1.526(5)	C(5)–N(1)	1.499(4)
C(3)–C(4)	1.517(3)	N(1)–N(2)	1.238(3)
C(3)–C(4)'	1.517(3)	N(2)–C(6)	1.482(4)
C(4)–O(2)	1.454(3)	C(6)–O(1)	1.435(3)
C(4)'–O(2)'	1.454(3)	C(6)–C(7)	1.506(3)
O(2)–C(5)	1.384(2)	C(6)–C(7)'	1.506(3)
O(2)'–C(5)	1.384(2)		

C(1)–C(3)–C(2)	110.3(3)	O(1)–C(5)–N(1)	106.3(2)
C(1)–C(3)–C(4)	109.1(2)	C(5)–N(1)–N(2)	109.6(2)
C(2)–C(3)–C(4)	111.3(2)	N(1)–N(2)–C(6)	111.3(2)
C(4)–C(3)–C(4)'	105.8(2)	N(2)–C(6)–O(1)	104.3(2)
C(3)–C(4)–O(2)	110.6(2)	C(7)–C(6)–N(2)	109.5(2)
C(4)–O(2)–C(5)	114.5(2)	C(7)–C(6)–O(1)	109.9(2)
O(2)–C(5)–O(2)'	114.0(2)	C(7)–C(6)–C(7)'	113.4(3)
O(2)–C(5)–O(1)	108.3(1)	C(5)–O(1)–C(6)	108.5(2)
O(2)–C(5)–N(1)	109.9(1)		

Symmetry Operator for atoms designated with primes, x, 1.5–y, z.

Table SIV. Least-squares mean planes, (Å), dihedral and torsional angles, (°), for *Spiro*-Oxadiazoline.

Plane 1.

N(1),0.000(3)*;N(2),0.000(3)*;O(1),0.000(3)*;C(5),0.000(3)*;C(6),0.000(4)*
C(4),–1.209(5);O(2),–1.160(3);C(7),–1.258(4).

Plane 2.

C(1),0.000(5)*;C(2),0.000(6)*;C(3),0.000(4)*.

Plane 3.

C(4),0.000(3)*;C(3),0.000(4)*;C(4)',0.000(3)*.

Plane 4.

C(4),0.000(3)*;C(4)',0.000(3)*;O(2),0.000(2)*;O(2)',0.000(2)*.

Plane 5.

C(5),0.000(4)*;O(2),0.000(2)*;O(2)',0.000(2)*.

Plane 6.

C(7),0.000(4)*;C(6),0.000(4)*;C(7)',0.000(4)*.

Plane 7.

C(5),0.331(3)*;O(2)',–0.077(2)*;C(4)',0.225(3)*;C(3),–0.352(4)*;C(4),0.225(3)*
O(2),–0.077(2)*.

Equations of best planes (in Å, orthogonal axes).

Planes 1,2.	0.0000x + 1.0000y + 0.0000z = 7.0890
Plane 3.	–0.9781x + 0.0000y + 0.2082z = 4.6368
Plane 4.	–0.4534x + 0.0000y + 0.8913z = 13.1462
Plane 5.	–0.9493x + 0.0000y + 0.3143z = 5.0300
Plane 6.	–0.5946x + 0.0000y + 0.8040z = 13.0512
Plane 7.	–0.6284x + 0.0000y + 0.7779z = 11.6658

Table SIV. Cont'd.

Dihedral Angles.

Plane 1.–Plane 2.	0.0(3)	Plane 3.–Plane 4.	51.0(2)
Plane 1.–Plane 3.	90.0(1)	Plane 3.–Plane 5.	6.3(3)
Plane 1.–Plane 4.	90.0(1)	Plane 3.–Plane 6.	41.5(3)
Plane 1.–Plane 5.	90.0(1)	Plane 3.–Plane 7.	39.0(2)
Plane 1.–Plane 6.	90.0(1)	Plane 4.–Plane 5.	44.7(2)
Plane 1.–Plane 7.	90.0(1)	Plane 4.–Plane 6.	9.5(3)
Plane 2.–Plane 3.	90.0(1)	Plane 4.–Plane 7.	12.0(1)
Plane 2.–Plane 4.	90.0(2)	Plane 5.–Plane 6.	35.2(3)
Plane 2.–Plane 5.	90.0(1)	Plane 5.–Plane 7.	32.7(2)
Plane 2.–Plane 6.	90.0(2)	Plane 6.–Plane 7.	2.5(3)
Plane 2.–Plane 7.	90.0(2)		

Torsional Angles.

C(1)–C(3)–C(4)–O(2)	6.7	C(4)–O(2)–C(5)–N(1)	73.2
C(2)–C(3)–C(4)–O(2)	64.8	O(2)–C(5)–N(1)–N(2)	116.9
C(3)–C(4)–O(2)–C(5)	55.0	O(2)–C(5)–O(1)–C(6)	62.0
C(4)–O(2)–C(5)–O(1)	8.8	C(5)–O(1)–C(6)–C(7)	117.3

Table SV. Hydrogen positional parameters ($\times 10^4$) for *Spiro*-Oxadiazoline.

Atom	x	y	z
H(11)	–5675	6657	6652
H(12)	–6426	7500	7358
H(21)	–1813	6666	6323
H(22)	–13	7500	6817
H(41)	–3996	6129	8172
H(42)	–2782	5363	7513
H(71)	2722	6158	10439
H(72)	2064	5353	9659
H(73)	4287	6123	9706

Table SVI. Bond lengths (Å) and bond angles (°) involving hydrogen atoms for *Spiro*-Oxadiazoline.

C(1)–H(11)	0.997	C(4)–H(41)'	0.992
C(1)–H(11)'	0.997	C(4)–H(42)'	0.948
C(1)–H(12)	0.916	C(7)–H(71)	1.009
C(2)–H(21)	0.980	C(7)–H(72)	0.975
C(2)–H(21)'	0.980	C(7)–H(73)	0.981
C(2)–H(22)	1.025	C(7)'–H(71)'	1.009
C(4)–H(41)	0.992	C(7)'–H(72)'	0.975
C(4)–H(42)	0.948	C(7)'–H(73)'	0.981

C(3)–C(1)–H(11)	110.4	C(3)–C(4)–H(41)	112.5
C(3)–C(1)–H(11)'	110.4	C(3)–C(4)–H(42)	112.4
C(3)–C(1)–H(12)	112.1	O(2)–C(4)–H(41)	109.7
H(11)–C(1)–H(12)	108.9	O(2)–C(4)–H(42)	102.8
H(12)–C(1)–H(11)'	108.9	H(41)–C(4)–H(42)	108.4
H(11)–C(1)–H(11)'	105.9	C(6)–C(7)–H(71)	108.2
C(3)–C(2)–H(21)	109.0	C(6)–C(7)–H(72)	109.0
C(3)–C(2)–H(21)'	109.0	C(6)–C(7)–H(73)	111.1
C(3)–C(2)–H(22)	113.0	H(71)–C(7)–H(72)	110.9
H(21)–C(2)–H(22)	109.2	H(71)–C(7)–H(73)	110.2
H(22)–C(2)–H(21)'	109.2	H(72)–C(7)–H(73)	107.6
H(21)–C(2)–H(21)'	107.2		

Symmetry Operator for atoms designated with primes, x, 1.5–y, z.

Table SVII. Anisotropic temperature factors ($\times 10^4$) for *Spiro*-Oxadiazoline with standard errors in parentheses.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C(1)	25(2)	36(2)	32(2)	0	–1(2)	0
C(2)	34(2)	75(3)	30(2)	0	–2(2)	0
C(3)	24(2)	29(2)	27(2)	0	–4(1)	0
C(4)	33(1)	24(1)	37(1)	–3(1)	–11(1)	2(1)
C(5)	22(2)	29(2)	23(2)	0	2(1)	0
C(6)	26(2)	30(2)	18(2)	0	–2(1)	0
C(7)	42(2)	39(2)	44(2)	–9(1)	–2(1)	–8(1)
O(1)	19(1)	52(1)	22(1)	0	–2(1)	0
O(2)	33(1)	26(1)	33(1)	–4(1)	–11(1)	6(1)
N(1)	23(2)	39(2)	30(2)	0	–1(1)	0
N(2)	28(2)	38(2)	26(2)	0	0(1)	0

Anisotropic temperature factors are of the form:

$$\exp[-2\pi^2(h^2\mathbf{a}^{*2}U_{11}+k^2\mathbf{b}^{*2}U_{22}+\ell^2\mathbf{c}^{*2}U_{33}+2hk\mathbf{a}^*\mathbf{b}^*U_{12}+2h\ell\mathbf{a}^*\mathbf{c}^*U_{13}+2k\ell\mathbf{b}^*\mathbf{c}^*U_{23})]$$

where $\mathbf{a}^*$, $\mathbf{b}^*$ and $\mathbf{c}^*$ are the reciprocal lattice vectors.

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