SYNTHESIS AND THERMOLYSIS OF 2,2-DIOXY-5,5-DIMETHYL-Δ^3-1,3,4-OXADIAZOLINES: DIOXYCARBENES AND THEIR REACTIONS

By

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SYNTHESIS AND THERMOLYSIS OF Δ^3-1,3,4-OXADIAZOLINES

To my husband Mohamed

and

my daughter Walaa

DOCTOR OF PHILOSOPHY (1996) McMASTER UNIVERSITY

(Chemistry) Hamilton, Ontario

TITLE: Synthesis and thermolysis of 2,2-dioxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines: Dioxycarbenes and their reactions

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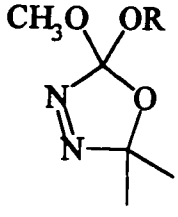
ABSTRACT

Oxadiazolines (I-III), which are novel thermal sources of dioxycarbenes, were synthesized by the exchange method using the acetoxy analogue. The thermal fragmentation of 2,2-dialkoxy oxadiazolines was established to be unidirectional. At 100 °C, oxadiazolines (I) decomposed forming nitrogen, acetone, and alkoxymethoxycarbenes as deduced from the identification of the carbene dimers MeO(OR)C=C(OR)OMe.

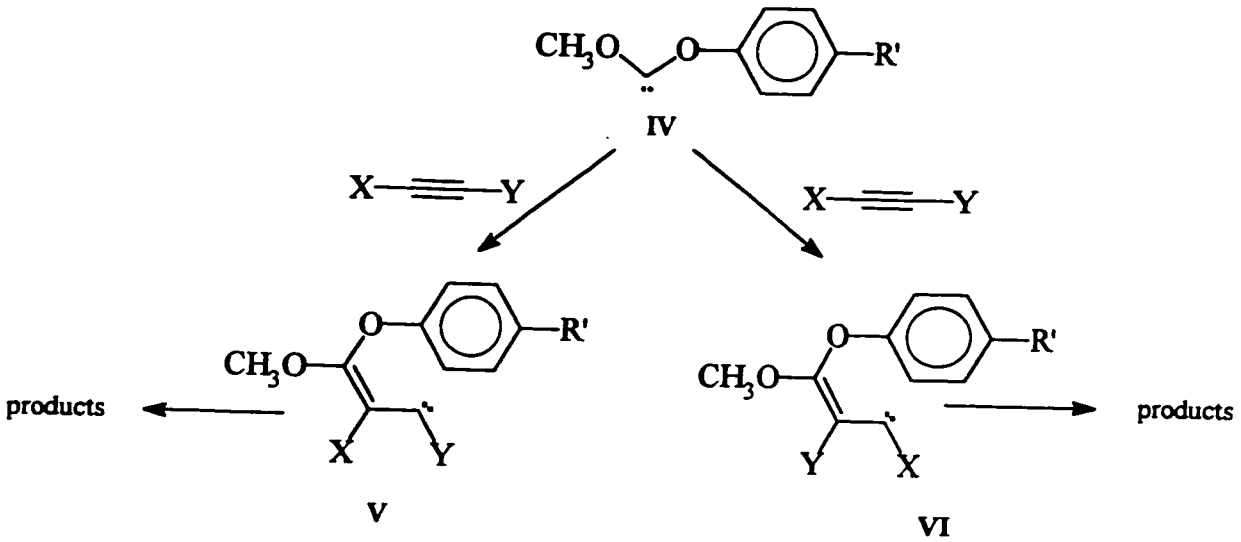


I R= alkyl
II R= aryl
III R= benzyl

On the other hand, thermolysis of the aryloxymethoxy oxadiazolines (II) was a multidirectional fragmentation process, with the aryloxymethoxycarbene formation as the major course. A competitive fragmentation afforded the methyl aryl carbonate and diazopropane.

The thermal chemistry of the benzyloxymethoxy oxadiazolines (III) is similar to that of the aryloxymethoxy analogue (II). The oxadiazoline (III) loses N_2 thermally, and also produces acetone and the benzyloxymethoxycarbene *via* the carbonyl ylide. In addition, the carbene rearranges producing the corresponding ester *via* 1,2-benzyl group migration to the carbene centre. This rearrangement is a substituent dependent process which is enhanced by electron donating groups.

The intermolecular reactions of aryloxymethoxycarbene (IV) with alkynes resulted in a regioselective generation of a 3,3-dioxyvinylcarbene (V or VI). This carbene can either undergo an intramolecular nucleophilic aromatic substitution and / or further reaction with the alkyne. The reaction pathway of (V or VI) is strongly dependent on the nature of the substituent (R').



Finally, the aryloxymethoxycarbenes were trapped inter- and intramolecularly *via* OH insertion reactions.

ACKNOWLEDGEMENTS

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INTRODUCTION

Carbenes are divalent carbon intermediates with two nonbonding electrons on one carbon atom. They are regarded as short lived and highly reactive and they play a prominent role in the broad field of reactive intermediates[1].

There are clear indications of carbene intermediates sprinkled through the early literature. The route leading to the recognition of the true character of carbenes as reactive intermediates included the work of H. Staudinger[2c] (1912), H. Meerwein[2e] (1942), J. Hine[2f] (1950) and W. E. Doering[2g] (1956) who was the first to use the name "carbene".

Detailed information on carbenes has not been available in the early years, but with the development of improved analytical tools, a better understanding of the mechanisms of carbene reactions became possible. Since the chemistry of carbenes is so rich and diverse, the interest of many researchers in these species has been growing.

1.1 Electronic structure of substituted carbenes:

The most intriguing feature of carbene chemistry is the electronic configuration of the divalent species. Carbenes can exist in two spin multipilicities. In a singlet configuration (1c) the two nonbonding electrons are paired in an orbital approximating sp^2 character, whereas the fourth orbital, a π-orbital, is empty. In a triplet configuration (1b), the two nonbonding

electrons are unpaired, occuping two different orbitals with substantial p-character (Figure 1).

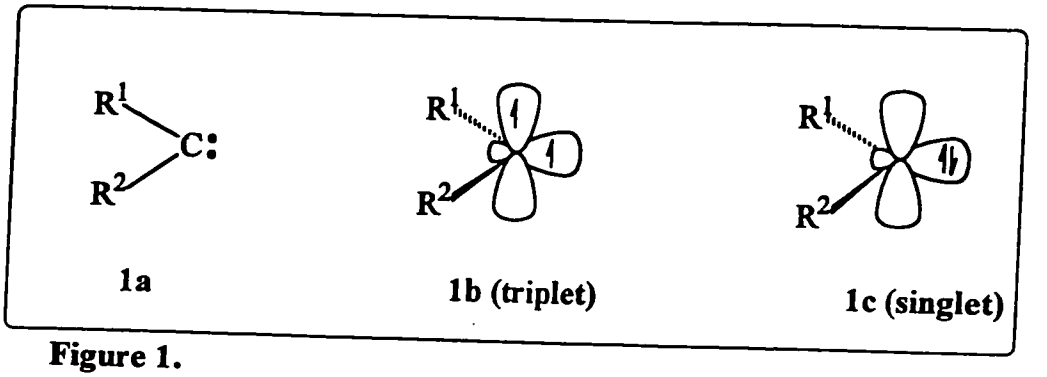


Figure 1.

Whether the ground state of a substituted carbene XCY is singlet or triplet is determined by the substituents X and Y. Generally, the singlet state is stabilized by substituents donating $p\pi$ lone pairs to the empty carbon $p\pi$ orbital. A knowledge of the ground spin state, the singlet-triplet splitting (ΔE_{ST}), and other effects of a particular substituent on carbene properties is of great importance in understanding the chemistry of carbenes. Singlets react either as electrophiles, nucleophiles, or ambiphiles and both concerted and stepwise processes are possible. Triplets behave like radicals and reactions are stepwise.

According to Houk, *et al.*[4], there is a remarkable correlation between the magnitude of the singlet-triplet gap and the π-donor or π-acceptor character of the substituent . A relatively high-lying π-orbital of a donor substituent will mix with the carbene $\pi(p)$ orbital. The singlet will be stabilized more than the triplet due to stabilization of 2 π-electrons **(2a)**, while the triplet carbene stabilization is less due to a counteracting effect of one π-electron **(2b)** (Figure 2).

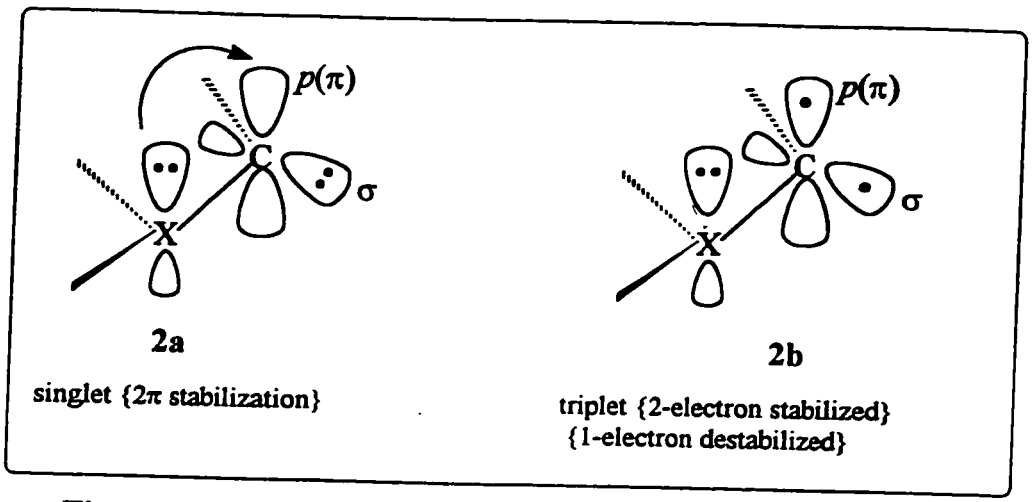


Figure 2.

On the other hand, the influence of π-acceptors depends on the geometry of the carbene. If the carbene geometry is like that shown in Figure (3) i.e. the acceptors π^*-orbital is parallel to the carbene $p(\pi)$ orbital, then the acceptor can only stabilize the triplet (3a). Putting the π^*-orbital perpendicular to the carbene $p(\pi)$ orbital (parallel to the carbene σ orbital) permits greater stabilization of the singlet (4b) than the triplet (4a) (Figure 4).

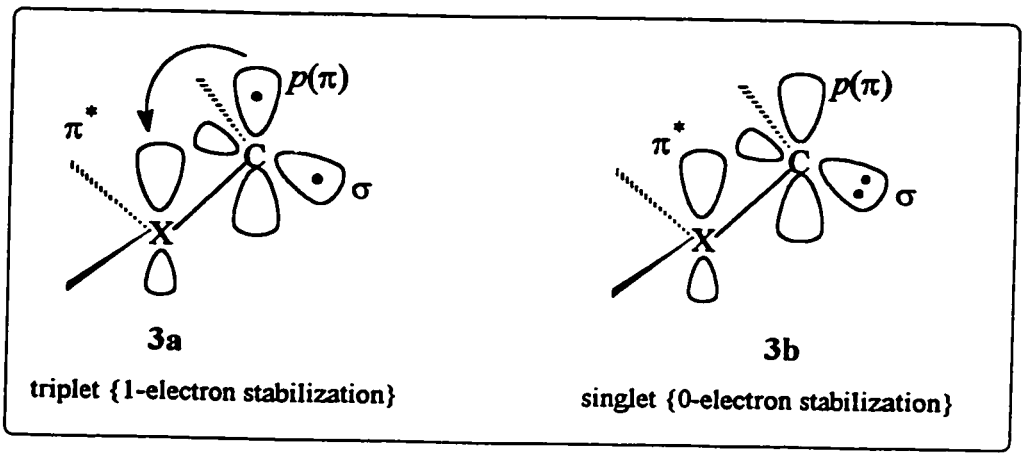


Figure 3.

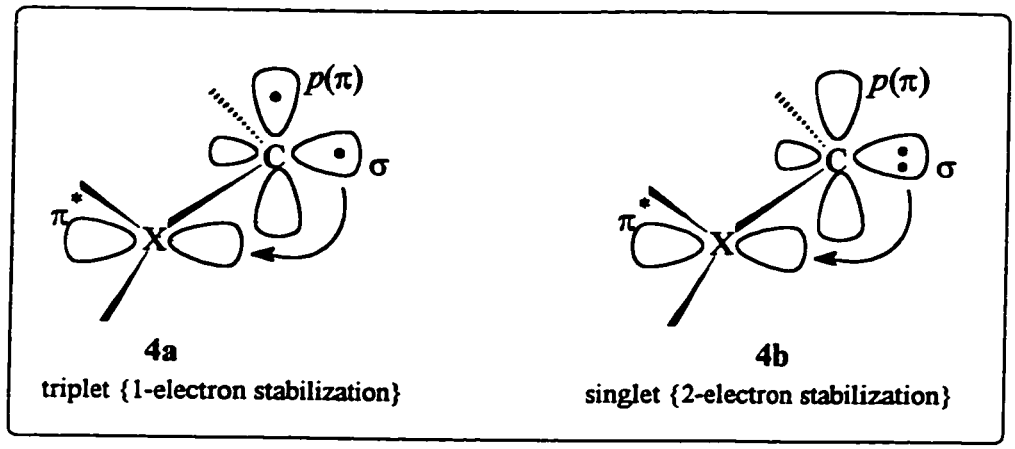


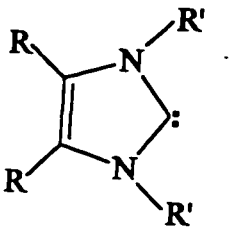
Figure 4.

Recently, much work has focused on the study of the magnitude of the energy gap between the triplet and the singlet states. Of particular interest are substituted carbenes with electronegative groups where π-donation stabilizes the singlet state relative to the triplet state[4a,b]. Many dioxy- and diaminocarbenes are calculated to be nucleophilic singlets with a large singlet triplet gap.[5,6]

Most carbenes are highly reactive, short lived species that can only be generated *in situ*. In 1991 Arduengo and coworkers reported[7a-c] the isolation of the first stable crystalline carbene. The 1,3-di(1-adamantyl) imadazol-2-ylidene **5a** proved to be the prototype for a whole family of stable divalent carbon compounds including some without significant steric crowding **5(b,c)**. The remarkably stable carbenes have been fully characterized using X-ray and spectroscopic methods.

According to Arduengo,[7a,c] the stability of these highly nucleophilic carbenes is due to a complete lack of electrophilic reactivity (reactions originating from the p-orbital), which in turn results from the electron density above and below the molecular plane of the carbene

due to nitrogen lone pair of electrons. As a result, a nucleophile approaching from above or below the carbene plane will not react with the formally vacant p-orbital due to electron-electron repulsion. Also, the carbene dimerization process, which involves attack by the σ-orbital of one carbene onto the p-orbital of another carbene, is totally suppressed due to the absence of the electrophilic reactivity in the carbenes (**5**).



5a R=H, R'=1-Ad
b R=R'=Me
c R=H, R'=Ar

1.2. Generation of Carbenes:

1.2.1. Dioxycarbenes:

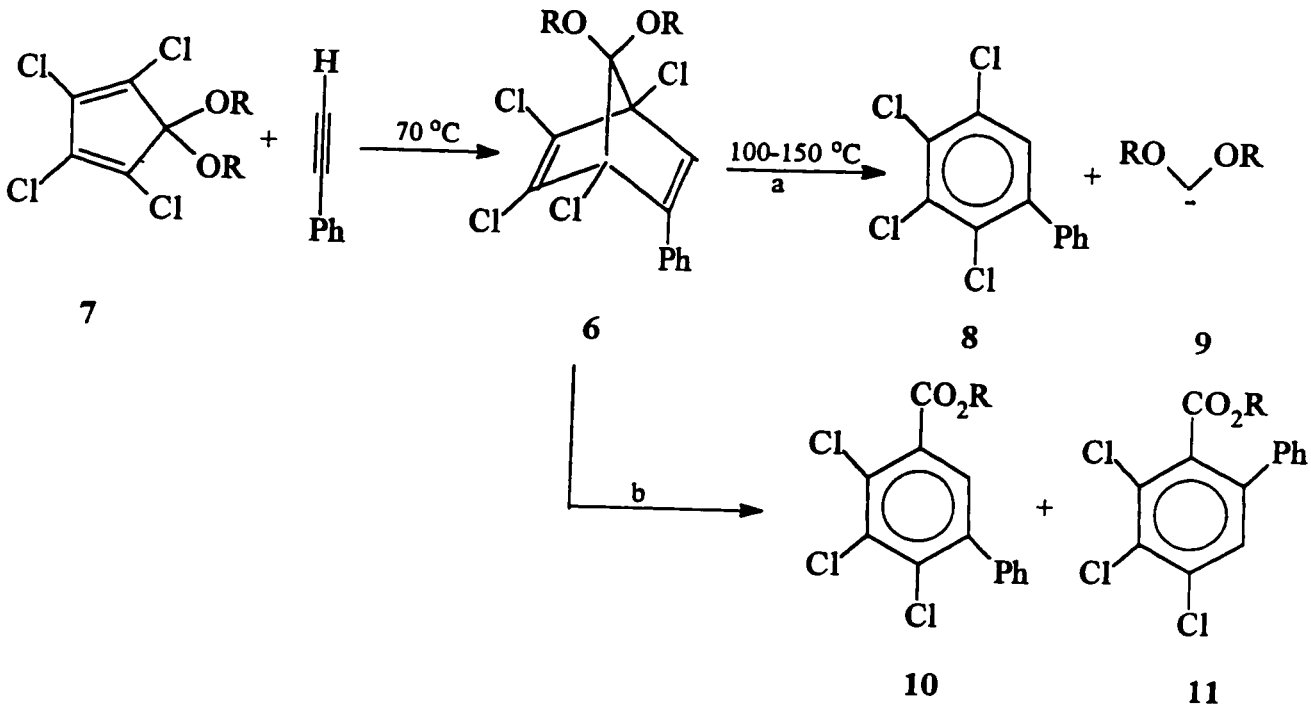
Dioxycarbenes have generated much interest over the past few years, as they are potential carbonyl group equivalents in organic synthesis. Conventional carbenes can be generated by a variety of methods; however, there are only a few well established precursors of dioxycarbenes.[8a-g]

1.2.1.1. Norbornadienone Ketals:

This method of carbene generation was developed by R. W. Hoffmann[9a-d] and D. M. Lemal[9e,f] in the early 1960's. The required norbornadienone ketals (**6**) which were prepared by Diels-Alder addition (150 °C) of tetrachlorocyclopentadienone ketals (**7**) to phenylacetylene (Scheme 1) can then undergo thermal cycloelimination to form carbenes. This

method is used to generate various dioxycarbenes.

This method has a few limitations. First, only symmetric carbenes have been generated effectively, persumably because unsymmetric cyclopentadienone ketals (7) are difficult to synthesize. Second, the thermal decomposition of (6) also yields the high molecular mass biphenyl side product (8) which can be difficult to remove. Pathway (b) can also compete with (a) forming side products 10 and 11. Consequently, the side products from thermolysis can interfere with the isolation of products from reactions of (9).



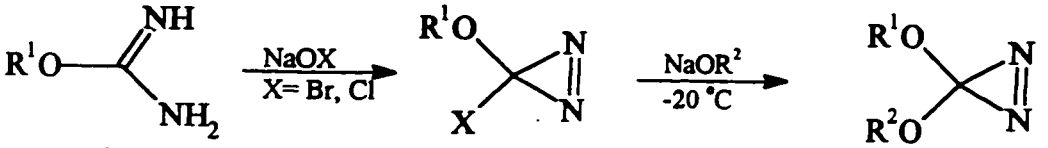
Scheme 1

$+ CH_3Cl$

It has also been shown by Hoffmann, *et al.* that $(MeO)_3CH$ eliminates CH_3OH (145 °C), forming $(CH_3O)_2C$: which can be trapped by ArNCO.[10a] Similarly, dimethylamino(methoxy)carbene is generated by pyrolytic elimination of methanol from amide acetals at 80 °C.[10b]

1.2.1.2. Diazirines:

Diazirines, cyclic isomers of diazoalkanes, have assumed central importance in carbene chemistry due to their tolerance of heteroatom substituents. The halodiazirines **13(a-c)**, which are prepared by Graham oxidation of the corresponding amidines **12(a-c)**, react with external nucleophiles ($^{-}OR^2$) to form dioxydiazirines **14(a-d)**.[11a-c]

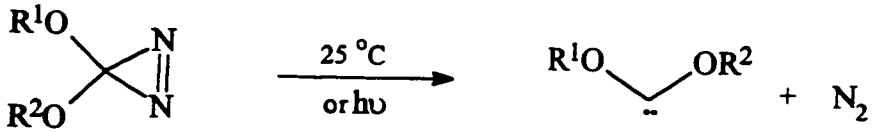


12 a: $R^1 = CH_3$
b: $R^1 = Ph$
c: $R^1 = CH_2CF_3$,

13(a-c)

14a $R^1 = R^2 = CH_3$
b $R^1 = Ph$, $R^2 = CH_3$
c $R^1 = R^2 = CH_2CF_3$
d $R^1 = CH_3$, $R^2 = CH_2CF_3$

The photochemical decomposition of the dioxydiazirines **14(a-d)** is used to generate dialkoxy and alkoxyaryloxycarbenes.[11a-c] This method has an advantage, as the carbenes can be generated photochemically as well as thermally at low temperatures. The relatively short half life of the diazirines (except for **14c**) produced can be a major drawback. In addition to the short half lives of most dioxydiazirines, they are reported to explode under certain conditions. As a result, they cannot be isolated and can only be obtained at high dilution in hydrocarbon solvents (e.g. pentane).



14a $R^1 = R^2 = CH_3$ ($\tau_{1/2}$= 21 min.)
b $R^1 = Ph$, $R^2 = CH_3$ ($\tau_{1/2}$= 64 min.)
c $R^1 = R^2 = CH_2CF_3$ ($\tau_{1/2}$= 5 hrs.)
d $R^1 = CH_3$, $R^2 = CH_2CF_3$ ($\tau_{1/2}$= 94 min.)

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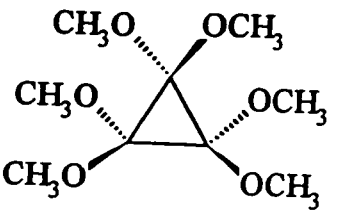
A thermolytic [1+2] cycloreversion of hexamethoxycyclopropane has also been reported. The persubstituted cyclopropane (16) is known to extrude dimethoxycarbene upon pyrolysis at 200 °C.[12] This high temperature required for the thermolysis of (16) rules out its use as a dimethoxycarbene precusor because of the instability of many carbene traps at such high temperature.



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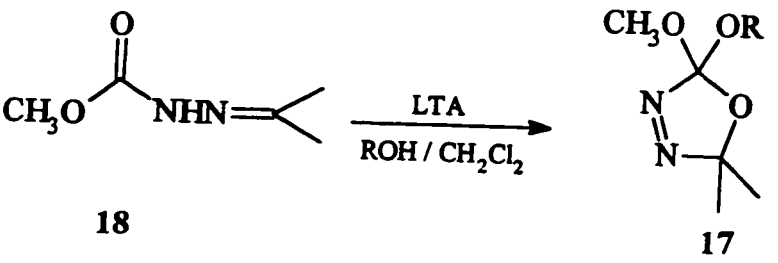
1.2.1.3. 2,2-Dialkoxy-Δ^3-1,3,4-oxadiazolines:

The dioxy oxadiazolines display a number of advantages over norbornadienone ketals and dioxydiazirines. They can serve as a convenient source of dioxycarbenes as they have the advantage of being readily accessible, shelf stable liquids at room temperature unlike the diazirines which are relatively unstable. In contrast to norbornadienone ketals, which produce the non-volatile byproduct 8 and the side-products 10 and 11 upon generation of dioxycarbenes, the thermolysis of dioxy oxadiazolines give dioxycarbenes quite cleanly, with acetone and nitrogen as byproducts.

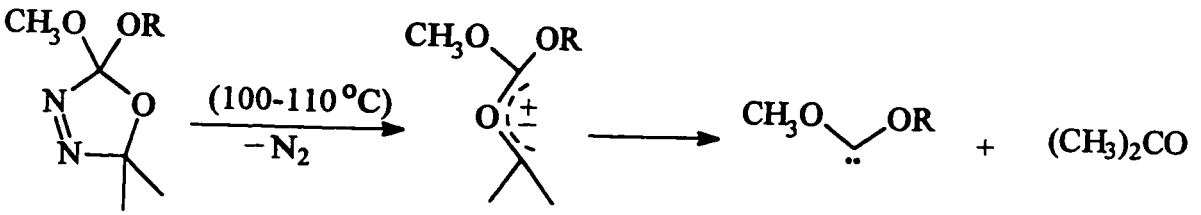
Generally, 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines (17) are prepared by oxidative cyclization of the hydrazone (18) ($(CH_3)_2C{=}NNHCO_2CH_3$) with lead tetraacetate ($Pb(OAc)_4$) in alcohol (ROH), or in CH_2Cl_2 containing ROH.[13]



18 17

Similarly, the electrocyclic oxidation technique was used by Chiba, *et al.*[14] to induce the intramolecular cyclization of the carbonyl hydrazones to the corresponding 2-methoxy-Δ^3-1,3,4-oxadiazolines. Recently, Yang, *et al.*[15] reported the use of iodobenzene diacetate ($C_6H_5I(O_2CCH_3)_2$) in the conversion of N-acyl hydrazones to the 2-alkoxy-Δ^3-1,3,4-oxadiazolines.

Carbene generation by thermal extrusion of N_2 and $(CH_3)_2CO$ from 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines **17(a-c)** was reported by Warkentin, *et al.*[13] The 2-alkoxy-2-methoxy-Δ^3-1,3,4-oxadiazolines undergo thermal decomposition at 100-110 °C. Dialkoxycarbenes are generated via carbonyl ylide intermediates **19(a-c)**. It has been shown that those ylides with two alkoxy substituents on the same carbon atom can readily undergo a uni-directional fragmentation (Scheme 2).



17 19 20

17a: R= CH_3; **b:** R= CH_2CH_3; **c:** R= $CH_2CH_2C{\equiv}CH$

Scheme 2

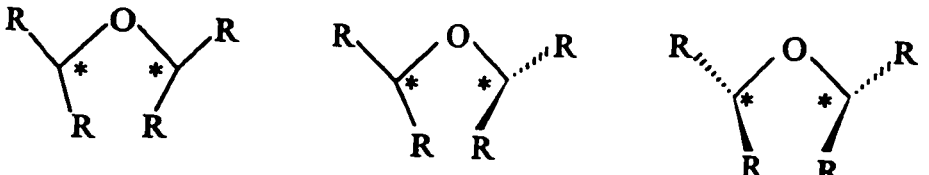
The observed first order rate constants for the decomposition of the alkoxy oxadiazolines are: k(100 °C)= 1.19 x 10^{-5} s^{-1} for **17a**, and k(110 °C)= 4.7 x 10^{-5} s^{-1} for **17c**. The corresponding half lives of the dialkoxy oxadiazolines are $\tau_{1/2}$ (in benzene)= 16.1 hrs (100 °C) for **17a**, and 4.1 hrs (110 °C) for **17c**. The formation of **20a** is also possible by pyrolysis of **17a** under conditions of very low vapour pressure mass spectrometry.[16] Békhazi[17a], found that the 2-methoxy-2-methyl-Δ^3-1,3,4-oxadiazolines decompose with similar kinetics at a slightly lower temperature k(80 °C)= 1.4 x 10^{-5} s^{-1}.

i. Thermolysis to carbonyl ylides and carbenes:

The formation of the ylides from the thermal decomposition of a 2-alkoxy-Δ^3-1,3,4-oxadiazoline is now well established.[17a-d] Warkentin, *et al.* were able to trap the ylide generated from 2-methoxy-2-methyl-Δ^3-1,3,4-oxadiazoline with methanol-d_4, thus providing direct evidence for the intermediacy of a carbonyl ylide.[17b] The intermediacy of analogous ylides from 2,2-dialkoxy oxadiazolines has been generally assumed but there is a theoretical paper by W.B. Smith claiming that such ylides may not be true intermediates.[17e]

ii. Carbonyl ylides: structure and reactions

Carbonyl ylides can adopt many geometries; however, normally 1,3-dipoles are at their

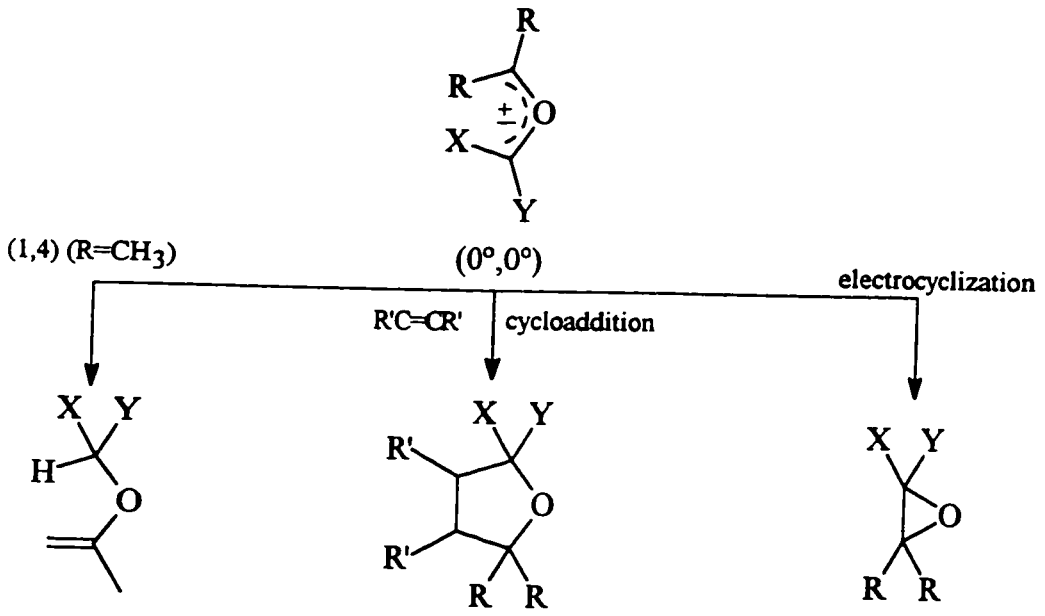


21(0°,0°) **22(0°,90°)** **23(90°,90°)**

(*) stands for the diradical and dipolar character of the carbonyl ylides

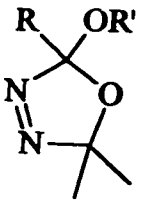
energy minimum when they are planar (0°,0°-conformation), a geometry that maximizes π-bonding.[18a-c]

The (0°,0°) ylide can undergo characteristic reactions that include [1,3]-dipolar cycloadditions, electrocyclic ring closures, and [1,4]-H migrations[17a] (Scheme 3).



Scheme 3

Some substituent effects on the carbonyl ylide reactions have been studied experimentally by Warkentin, *et al.*[17c] It was observed that a phenyl group at one end of the carbonyl ylide considerably reduced the rate of fragmentation. Instead the carbonyl ylide from **24a** cyclizes to the oxirane with estimated rate constant of k(31 °C)= 1.3×10^6 s^{-1} and, in the presence of a dipolarophile, cycloaddition occurs with estimated rate constants of 1×10^5 $M^{-1}s^{-1}$ and 1×10^9 $M^{-1}s^{-1}$ to norbornadiene and to dimethyl acetylenedicarboxylate, respectively.[17c] In the case of the ylide from **24b**, fragmentation to the carbonyl compound and the carbene is the major process. Also upon thermolysis of **24c**, an acyloxycarbene is generated.



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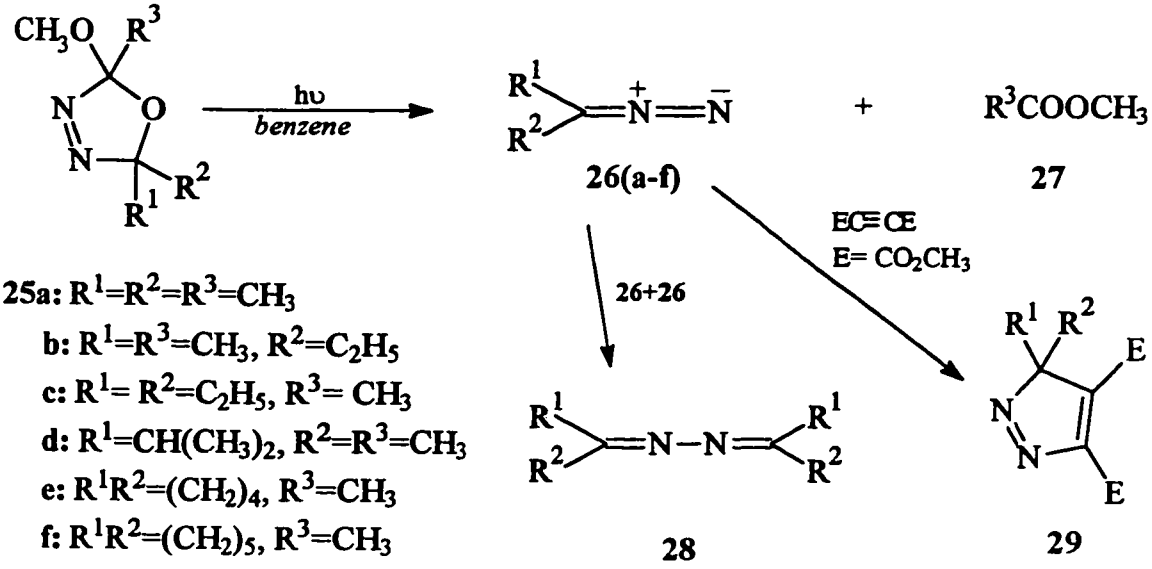
24a: R= Ar; R'= CH_3
b: R=R= CH_3
c: R= CH_3; R'= O=CCH_3

Warkentin *et al.*[19] reported that the photolysis of the 2-alkoxy-2,5,5-trialkyl oxadiazolines **25(a-f)** led to the fragmentation to diazoalkanes **26(a-f)** and ester **27** in high yield. The diazoalkanes **26(a-f)** undergo intermolecular reaction giving rise to azine or they can be trapped by 1,3-dipolarophiles to afford cycloadducts (Scheme 4). The diazoalkanes generated from the oxadiazoline fragmentations react with dimethyl acetylenedicarboxylate to afford 3H-pyrazoles (**29**). In the absence of trapping agents, azines **28(a-f)** are formed as products of bimolecular conversion of the diazoalkanes **26(a-f)**.



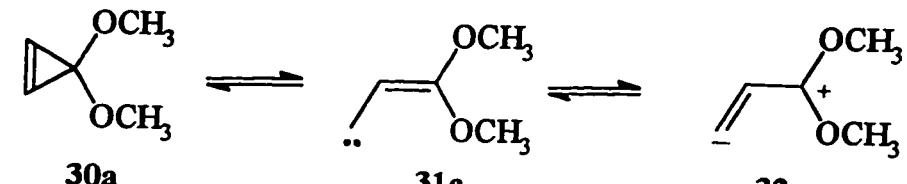
25a: R^1=R^2=R^3=CH_3
b: R^1=R^3=CH_3, R^2=C_2H_5
c: R^1= R^2=C_2H_5, R^3= CH_3
d: R^1=$CH(CH_3)_2$, R^2=R^3=CH_3
e: R^1R^2=$(CH_2)_4$, R^3=CH_3
f: R^1R^2=$(CH_2)_5$, R^3=CH_3

Scheme 4

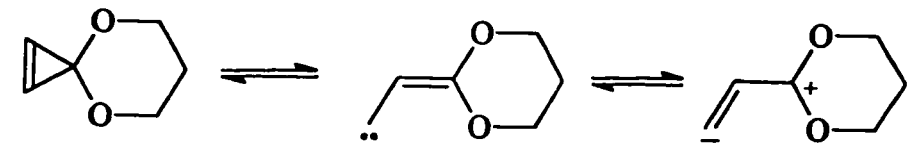
1.2.2. Vinylcarbenes:

In the literature, there are numerous examples of cyclopropene / vinylcarbene interconversion. Cyclopropenes have been shown to open thermally in the gas phase (160-190 °C) to provide vinylcarbenes. The reversibility of this reaction has been demonstrated first by Bergman, *et al.*[20] in the pyrolysis reaction of optically active 1,3-diethyl cyclopropene.

The cyclopropenone ketals **30(a,b)** were first recorded[21] in 1972 and since then have been studied for several synthetic purposes. Studies by Boger, *et al.*[22a-i] revealed that the cyclopropenone ketals **30(a,b)** can generate 3,3-dioxyvinylcarbenes **31(a,b)** via the thermal ring opening at 70-100 °C. Cyclopropenone ketal **30b** undergoes the same reactions as **30a** but has the advantage of being considerably more stable. Cyclopropenone ketal **30b** can be stored for few months at -20 °C without significant decomposition. As a result, **30b** was widely used in the study of the 3,3-dioxyvinylcarbene reactions. The 3,3-dioxyvinylcarbene **(31)** is known to undergo cycloaddition reactions with electron deficient olefins to provide a number of interesting cycloadducts.[22a]



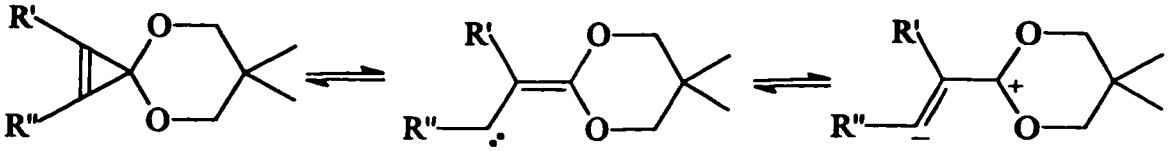
30a **31a** **32a**



30b **31b** **32b**

In 1989, Nakamura, *et al.* reported a key discovery that functionalized cyclopropenes can be synthesized by alkylation of metalated cyclopropenone acetals (CPA) (**33** R'=H,

R"=M).[23a,b] With the availability of these CPA derivatives bearing substituents of diverse electronic character,[23a-d] the issue of regioselectivity of ring cleavage was introduced.[23c-f]



33a R'=R"=H
b R'=H, R"=CH_2CH_3
c R'=H, R"=Ph
d R'=Ph, R"=CO_2-*i*-Pr

34 **35**

1.3. Reactions of dioxycarbenes:

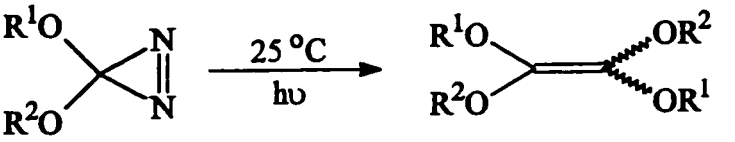
Among the characteristic reactions of singlet carbenes are dimerization, insertion into a single bond such as C-H, C-O, O-H, addition to unsaturated bonds and carbene rearrangement.[1] The mechanisms involving reactions of carbenes with several types of substrates can be established by making use of isotope labelling and product stereochemistry.

1.3.1. Intermolecular Reactions:

i. Dimerization:

The dimerization of singlet carbenes is believed to involve the attack of the occupied in plane σ-lone pair of one singlet carbene center on the out of plane vacant *p*-orbital of a second carbene.[24] The formation of dioxycarbene dimers has been well established.[25] Moss, *et al.*[11a-d] reported that the photochemical decomposition of **14a** in pentane (372 nm) leads to the carbene dimer **36a** as the sole product. Similarly, **36b** is formed (81% yield) by the decomposition of **14b** , with E:Z ratio of 1.0. On the other hand, **36(c,d)** are isolated in low

yields due to their high volatility and instability.



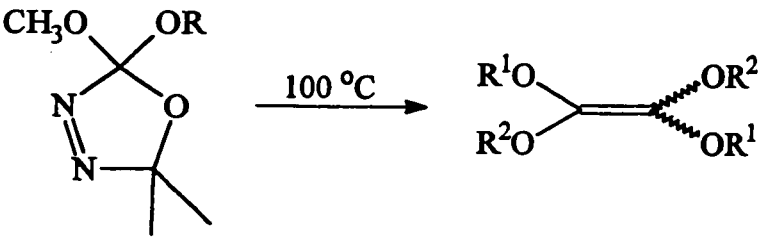
14a $R^1 = R^2 = CH_3$ **36(a-d)**

b $R^1 = Ph$, $R^2 = CH_3$

c $R^1 = R^2 = CH_2CF_3$

d $R^1 = CH_3$, $R^2 = CH_2CF_3$

Also, Warkentin, *et al.*[13] showed that thermolysis of **17(a,b)** afforded the corresponding tetraalkoxy ethylene(s) as major products with 88 and 73% yields of **37(a,b)** respectively. Dimerization of the ethoxymethoxycarbene occurred with little or no discrimination within experimental error, with E:Z ratio equal 1.0.



17a: $R = CH_3$, **b:**CH_2CH_3 **37(a,b)**

ii. Addition to multiple bonds:

a. [1+2] Cycloaddition :

Doering described methylene as "the most indiscriminate reagent known in organic chemistry".[26] Substituted carbenes are less reactive and more discriminating than methylene in carbene / alkene reactions.[27] In order to systematize the reactivity order of substituted

carbenes, Moss has introduced the concept of "carbene selectivity index",[11a,28] m_{CXY} (eq.1).

$$\log(k_i/k_o)_{CXY} = m_{CXY} \log(k_i/k_o)_{CCl_2} \qquad (1)$$

In the left hand side of equation 1, k_i are the rate constants for addition of the carbene under investigation, (:CXY) to the six di, tri, and tetra methyl ethenes which are a standard set of alkenes, and k_o is the rate constant for its reaction with $(CH_3)_2C{=}CH_2$. The logarithms are plotted versus similar measurements for $:CCl_2$ and the slope is the selectivity index m_{CXY}. Moreover, the dependence of m_{CXY} on the X- and Y-substituents is correlated to σ_R^+ and σ_I (eq.2).[11a]

$$m_{CXY} = -1.10\Sigma_{X,Y}\sigma_R^+ + 0.53\Sigma_{X,Y}\sigma_I - 0.31 \qquad (2)$$

The categorizing ability of equation 2 is conveniently displayed in Figure 5, where experimental and calculated m_{CXY}'s are included in a "carbene selectivity spectrum".[11a] The calculated (m_{CXY}) of (MeO)PhOC: was 2.11, only slightly lower than that calculated for $(MeO)_2C$: (2.22) and clearly in the region of the selectivity spectrum associated with nucleophilic carbenes.

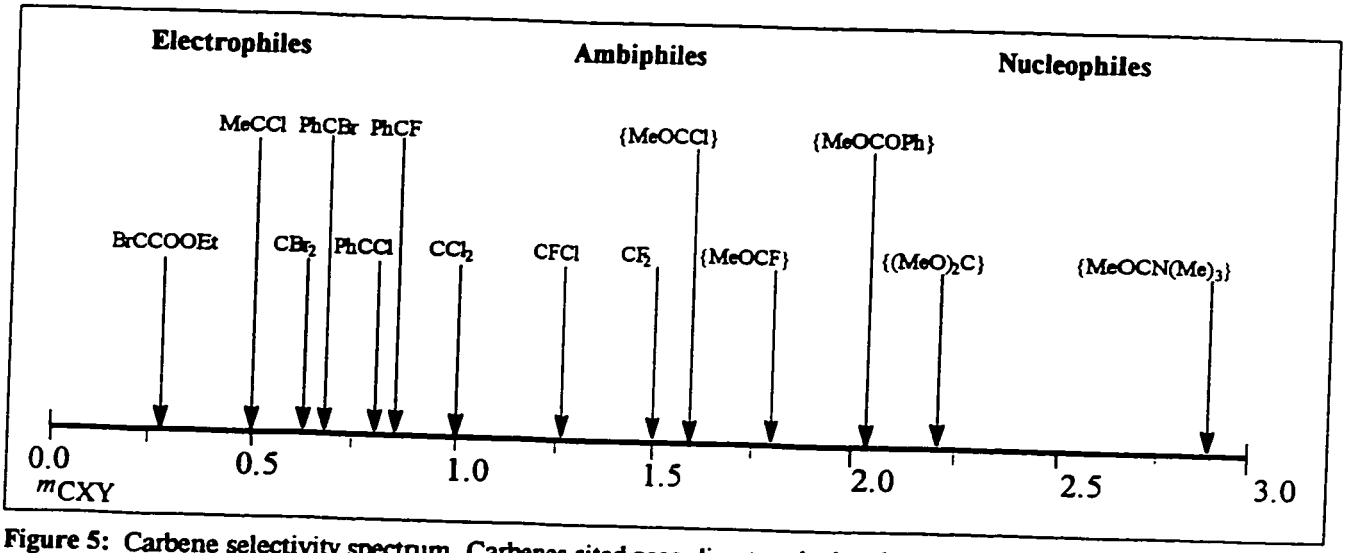
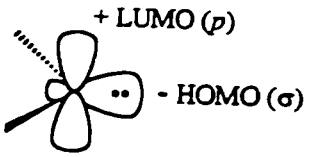


Figure 5: Carbene selectivity spectrum. Carbenes sited according to calculated m_{CXY} appear in brackets.

Mechanism of the [1+2] cycloaddition:



38

Moss reported the FMO approach as a general method to rationalize carbenic philicity. The addition of a carbene (38) to an alkene involves simultaneous interactions of the vacant carbenic *p*-orbital (LUMO) with the filled alkene π orbital (HOMO) and of the filled carbenic σ orbital (HOMO) with the vacant alkene π* orbital (LUMO).[28a,29] Although a singlet carbene is inherently both an electrophile and a nucleophile; the differential energies Δϵ determine the orbital interactions (Fig.6) i.e. $LUMO_{carbene}$ / $HOMO_{alkene}$ or $HOMO_{carbene}$ / $LUMO_{alkene}$ FMO analysis permits rapid characterization of the carbene philicity towards an alkene by estimating the differential orbital energies.

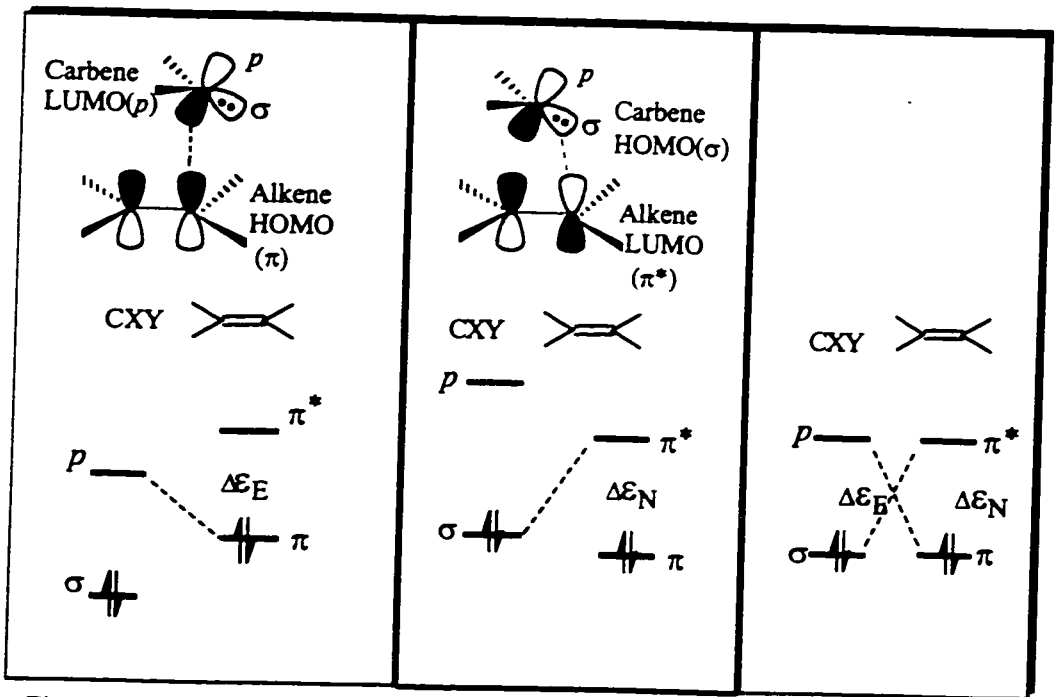


Figure 6a. $\Delta\varepsilon_{Electrophilic}$ Figure 6b. $\Delta\varepsilon_{Nucleophilic}$ Figure 6c. $\Delta\varepsilon_E=\Delta\varepsilon_N$

If a given carbene interacts with an alkene so that $LUMO_{carbene}$- $HOMO_{alkene}$ is smaller than $LUMO_{alkene}$- $HOMO_{carbene}$, then that carbene is considered electrophilic (Fig 6a). On the other hand, if $LUMO_{alkene}$- $HOMO_{carbene}$ is smaller than $LUMO_{carbene}$- $HOMO_{alkene}$ then that carbene is considered nucleophilic (Fig 6b). An ambiphilic carbene would exihibit a crossing of differential orbital energies (Fig 6c).

In all these cases, the stabilization of a cycloaddition transition state (TS) depends on the differential interaction energies. Placing basic unshared electrons on an atom next to the carbene center will raise the carbene LUMO (*p*-orbital); the reaction is slower and more selective. If the adjacent lone pair is basic enough, the dominant interaction will become carbene HOMO with alkene LUMO (Figure 6b); the carbene is now nucleophilic.

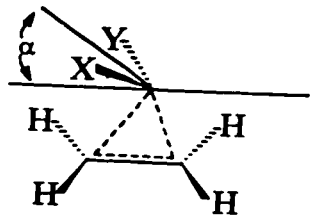


Figure 7

Rondan and Houk[30] (using STO-3G basis set) calculated the angle of tilt of the CXY plane with respect to the original ethene plane at the addition transition state. For pure electrophilic approach, α would be 0° (Figure 7), while a pure nucleophilic approach would have $\alpha = 90°$. In fact, α is 36° for CCl_2 and increases smoothly to 58° for $C(OH)_2$.

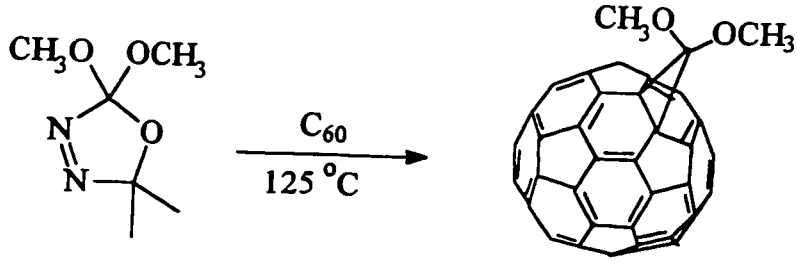
Cyclopropane formation:

Dimethoxycarbene (DMC) is characterized with (m_{CXY}) value 2.2, which is clearly in the region of the selectivity spectrum associated with nucleophilic carbenes. The nucleophilic

carbenes usually react faster with electron deficient alkenes, whereas electrophilic carbenes react faster with electron rich alkenes.[11b,28a,32,33] The absolute rate constant for the reaction of dimethoxycarbene with chloroacrylonitrile was found to be k_{abs}= 5.0 x 10^5 $M^{-1}s^{-1}$, while with acrylonitrile a much slower rate was observed, k_{abs}~10^3 $M^{-1}s^{-1}$.[31a,b]

On the other hand, the calculated m_{CXY} for methoxyphenoxycarbene is 2.11, only slightly lower than that calculated for DMC. Competition experiments for additions of thermally generated (25 °C) MeO(OPh)C: to equimolar binary mixtures of Me_2C=CMe_2, CH_2=CHCN, CH_2=CClCN give a substrate reactivity order of 1: 28: 870 respectively.[11c] In addition, bis-trifluoroethoxycarbene $(CF_3CH_2O)_2C$: and trifluoroethoxymethoxy carbene $CF_3CH_2O(CH_3O)C$: are reported to be nucleophilic and qualitatively similar to their $(MeO)_2C$: analogue. $(TFE)_2C$: and TFE(MeO)C: each add to acrylonitrile and methyl acrylate affording the corresponding cyclopropanes.[11b]

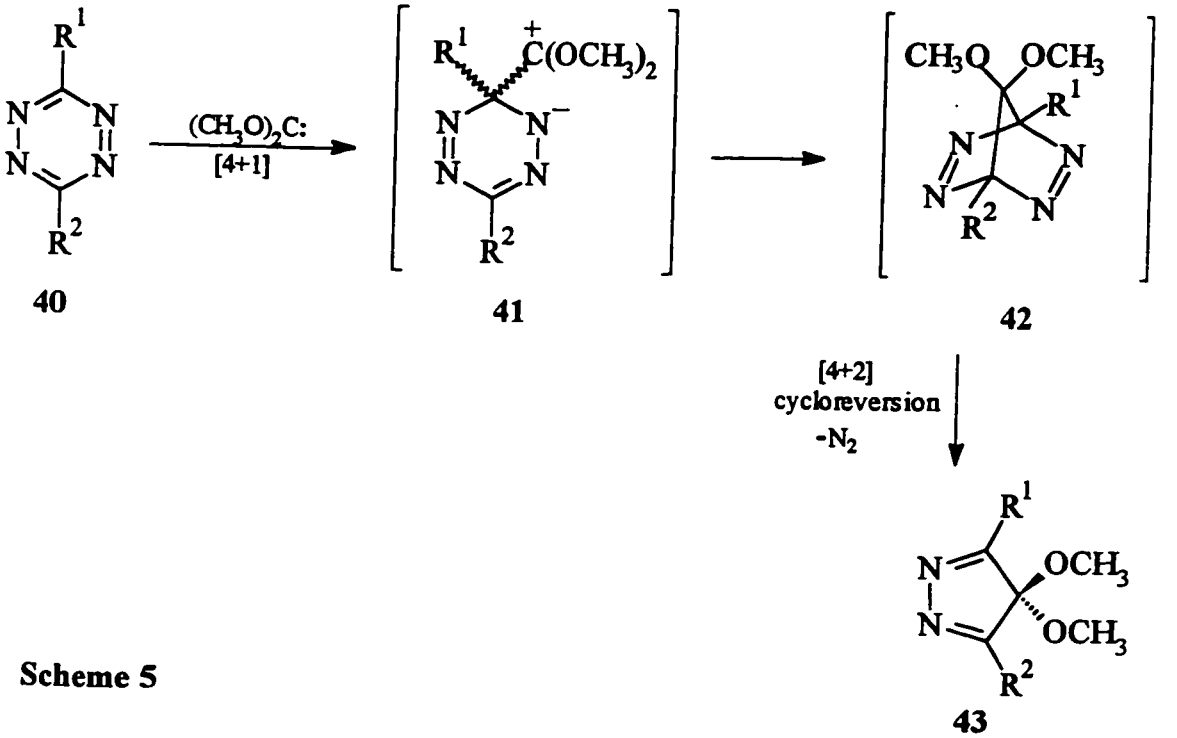
Recently, the functionalization of buckminster fullerene (C_{60}) with dimethoxycarbene **17a**, giving dimethoxymethanofullerene (**39**), has been reported.[34,35] The electron withdrawing nature of C_{60} makes it ideal for [1+2] cycloaddition with nucleophilic carbenes and provides a valuable route to 1,2-addition products.



17a **39**

b. [1+4] cycloadditions:

Singlet carbenes may react with polyenes to give 1,4 cycloaddition products. Dimethoxycarbene is reported to be trapped by 1,2,4,5-tetrazines (40) via [1+4] cycloaddition (Scheme 5). The isopyrazole (4H-pyrazole) 43 is formed in a two step reaction sequence through the [1+4] cycloadduct (42) (a high strained intermediate) which eliminates nitrogen by subsequent [4+2] cycloreversion.[36,37]



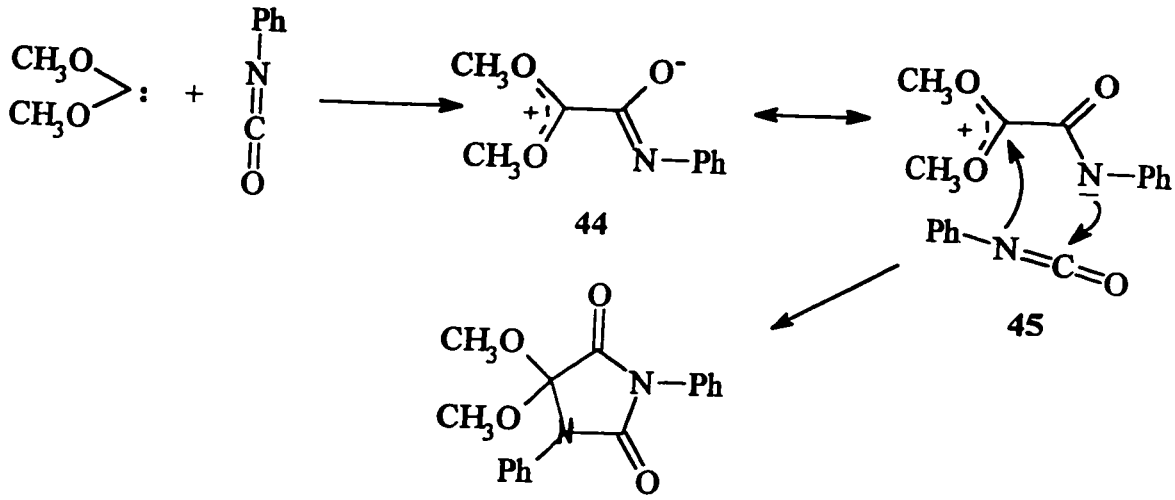
40 41 42 43

Scheme 5

c. Reactions of cumulenes:

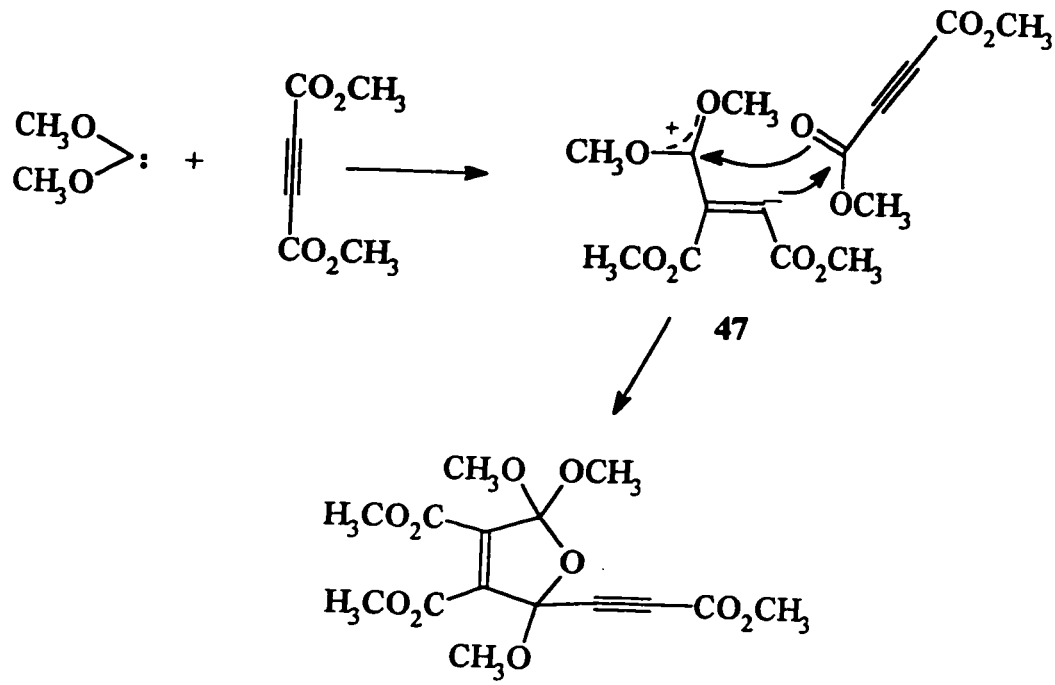
Dialkoxycarbenes are known to add to electrophilic multiple bond systems to form 1,3 dipoles, which in turn can add to a second molecule of the multiple bond system via [3+2] cycloaddition forming five membered rings.[33b,9b,38] Hoffmann, *et al*[33b,38] reported the addition of dimethoxycarbene to phenyl isocyanate to afford 4,4-dimethoxyhydantoin (46), a product

containing two units of phenyl isocyanate and one unit of carbene (2:1 adduct). The formation of (46) was proposed to arise from addition of the carbene to phenyl isocyanate to yield a 1,3-dipolar intermediate (45) which undergoes a regioselective addition with another equivalent of phenyl isocyanate to yield 46 (Scheme 6).



Scheme 6

Similarly, a reaction of dimethoxycarbene with dimethyl acetylenedicarboxylate affords the substituted dihydrofuran (48). The overall 1:2 stoichiometry for this reaction has been reported by Hoffmann, *et al.*[9b,10a] The proposed mechanism for (48) proceeds with initial addition of the carbene to the triple bond of DMAD to form a 1,3-dipole intermediate (47). Subsequently, the 1,3-dipole reacts with another equivalent of DMAD by addition across the C=O bond to yield (48) (Scheme 7).



Scheme 7

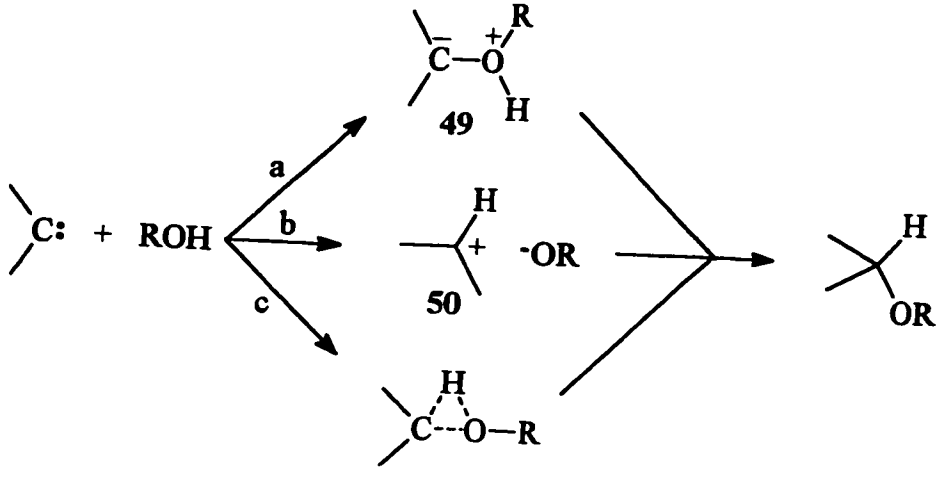
iii. OH Insertion reactions:

The reaction of carbenes with hydroxylic substrates to give ethers have been studied extensively.[1] In the case of singlet carbenes, several mechanisms have been considered (Scheme 8).[39,40]

a. Electrophilic attack on an oxygen lone pair with the formation of an ylide (49), with subsequent proton transfer from O to C (path a).

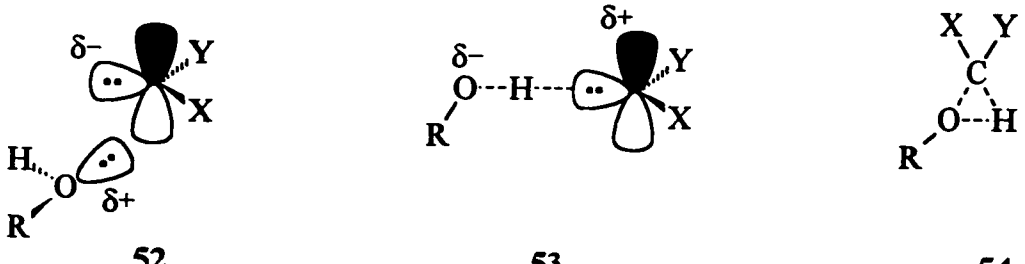
b. Carbene protonation followed by rapid collapse of the carbocation / alkoxide ion pair (path b).

c. Direct three center O-H insertion (path c).



Scheme 8

Predominantly electrophilic carbenes with reactivity centered in the vacant *p*-orbital react with the nucleophile (RO-H) *via* an ylide type, carbene LUMO (p) / alcohol HOMO (O-2p) interaction (**52**). On the other hand, highly stabilized nucleophilic carbenes such as $(MeO)_2C$: where the reactivity is dominated by the lone pair, react via a proton transfer mechanism (**53**). Between the transition states **52** and **53**, there is a three center transition state **54** for concerted insertion.[40]



The formation of trialkyl orthoformates *via* reaction of carbenes with alcohols (ROH) has been reported.[11b,13,40,24] Moss *et al.*[40] measured the kinetics of the OH insertion of dimethoxycarbene. The decay of DMC as a function of [methanol] in pentane at 20 °C was measured by laser flash photolysis. A relatively large kinetic isotope effect (KIE) of 3.3 ± 0.5

was observed for the insertion of $(MeO)_2C$: into MeOH(D), suggestive of substantial O-H to carbene proton transfer during the reaction (53).[40] Also, the pseudo-first order rate constants for decay of $(MeO)_2C$: in 1M solutions of alcohol in CH_3CN were determined, which reflects the carbene's reactivity as a function of the alcohol's acidity (Table 1).[39]

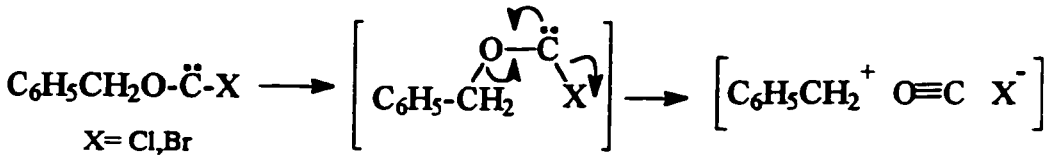
Table 1. Pseudo-first-order rate constants for reaction of dimethoxycarbene with 1M hydroxylic substrates in CH_3CN solution at 20 °C.

substrate	pK_a	k_ψ, s^{-1} {$(MeO)_2C$:}
CH_3CH_2OH	15.90	$3.2\pm0.9 \times 10^4$
CH_3OH	15.54	$8.8\pm0.9 \times 10^4$
$ClCH_2CH_2OH$	14.31	$9.1\pm1.0 \times 10^5$
FCH_2CH_2OH	14.20	$2.3\pm0.2 \times 10^6$
F_3CCH_2OH	12.37	$6.3\pm0.9 \times 10^7$
$(F_3C)_2CHOH$	9.30	$6.7\pm0.7 \times 10^8$
CH_3COOH	4.76	$2.4\pm0.4 \times 10^9$

1.3.2. Intramolecular Reactions:

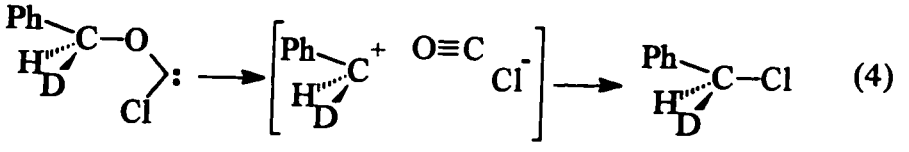
i. Carbene fragmentation:

Intramolecular fragmentation of alkoxyhalocarbenes appears to be rather general.[40a-c] Benzyloxyhalocarbenes (55), undergo the fragmentation with the formation of carbon monoxide and the benzyl cation / halide ion pair (57). The efficiency of the carbene (55) fragmentation depends on the identities of R and X (Eq. 3). The relatively stable benzyl cation permits the carbene fragmentation to compete with more usual intermolecular reactions that lead to carbene capture. The fragmentation process depends on the nature of the leaving group (X). The benzyloxychloro (or bromo) carbenes (55) fragment rapidly rather than being captured by carbene traps. On the other hand, benzyloxyfluorocarbene, $PhCH_2O(F)C$: resists fragmentation and adds to alkenes instead.[41c]



55 56 57 (3)

According to Moss *et al.*[41b,42] the intrafragmentation of (55) is an S_Ni mechanism involving a four center transition state (56) which leads to the formation of the ion pair (57). The observation of high retention of configuration in the deuterium labelling experiment,[41b,c] (Eq. 4) is consistant with the idea that the ion pairs are formed from cis (58) configured precursor carbene. These fragment so as to leave the Cl^- counter ion in appropiate relative geometry for recombination with retention with $PhCHD^+$ cation (59).

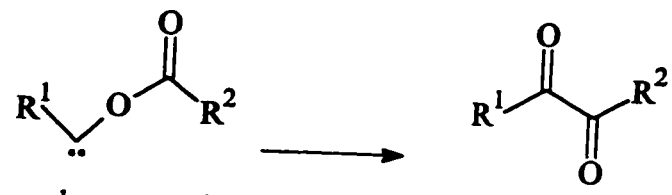


58 59 60 (4)

ii. Carbene rearrangement:

Acyloxycarbenes **61(a-e)** are little known intermediates, with only few examples having been reported to date.[17d,43] In a nucleophilic carbene, a 1,2-acyl shift is not easily accessible because an electron donating substituent stabilizes the carbene center. In few cases, the formation of diketones (62) via acyl migration in the acyloxycarbene intermediate is observed (Eq.5). The rearrangement of carbene **55c** to biacetyl is considered to be strong evidence for the formation of an acyloxycarbene in the thermolysis of 2-acetoxy-2,5,5-trialkyl-Δ^3-1,3,4-oxadiazoline.[17d] Recently, Moss *et al.*[43b] reported that acetoxyphenylcarbene

61e undergoes acyl migration to form 3-phenyl-2,3-propanedione 62e. The rate constant for this acyloxycarbene rearrangement was found to be k_{re} (60 °C) = (1.3±0.2) x 10^5 s^{-1} with conversion yield >90%.



(5)

61 a: $R^1 = CH_3$, $R^2 = C_6H_5$
b: $R^1 = R^2 = C_6H_5$
c: $R^1 = R^2 = CH_3$
d: $R^1 = CH_2CH_3$, $R^2 = CH_3$
e: $R^1 = C_6H_5$, $R^2 = CH_3$

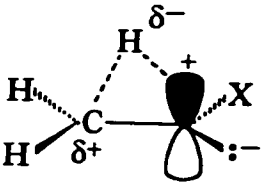
62

iii. C-H Insertion:

Insertion of the carbene into an adjacent C-H bond, known as 1,2-hydrogen migration, leads to alkenes (Eq. 6).[1b,c] These rearrangements take place from the singlet carbenes. The 1,2-H rate constant can be adjusted or tuned by appropriate selection of the substituent, X, in carbene (63). The hydride migrates to the vacant carbenic LUMO (p-orbital) of the singlet carbene in the transition state (65). Electron donation by X decreases the vacancy (electrophilicity) of p, and increases the activation energy, which in turn slows the hydride shift. Theoretical calculations have deduced energy barriers to this rearrangement for CH_3-C-X as a function of the increasing electron donating ability of X. The 1,2-H activation energies ranged from E_a= 0.6 kcal.mol^{-1} (X=H) to E_a= 27 kcal.mol^{-1} (X=*trans*-OMe).[44a]

$$RCH_2\text{-}\ddot{C}\text{-}X \xrightarrow{\text{1,2-H shift}} RCH{=}CHX \qquad (6)$$

63 64

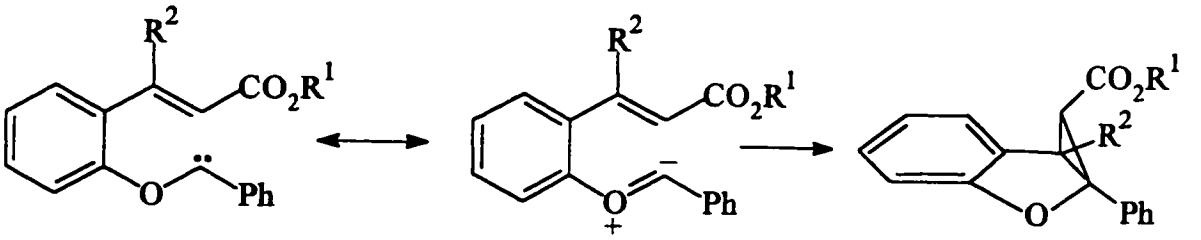


65

Although 1,2-H migration of alkoxy(alkyl)carbenes is turned off relative to other carbenic reactions, it has been reported that it can be restored by a combination of electronic tuning and thermal activation.[44b] Thermally activated hydride shifts were observed with (phenoxymethyl)methoxycarbene $PhOCH_2(CH_3O)C$: and (phenoxymethyl) trifluoroethoxycarbene $PhOCH_2(CF_3CH_2O)C$:, where appropriate substituents were introduced at both the migration origin and the migration terminus.

iv. Reactions with alkenes:

Little is known about intramolecular cycloadditions of nucleophilic carbenes. Similar to intermolecular [1+2] cycloadditions, the intramolecular process should form two new rings, one of which is a cyclopropane. Vasella, *et al.*[45] reported the addition of alkoxycarbenes (66) to electron deficient alkenes intramolecularly, leading to the formation of fused cyclopropanes (67).

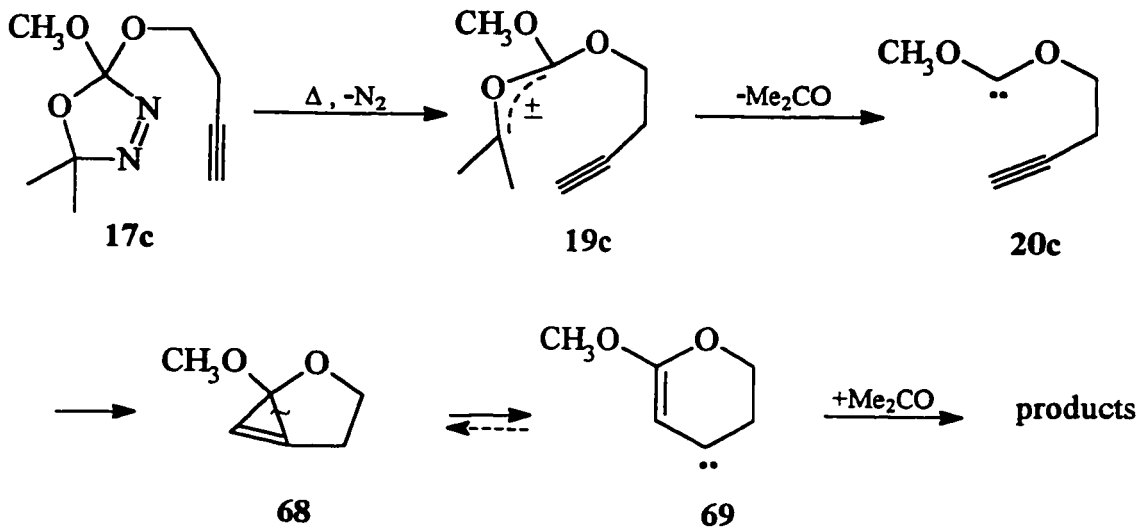


66a 66b 67

v. Reactions with alkynes:

Nucleophilic carbenes are known by their low reactivity towards unactivated CC multiple bonds.[11b,28a,39] Intramolecular addition of dialkoxycarbenes to unactivated triple bonds was reported by Warkentin *et al.*[46] (Scheme 9). The 2,2-dialkoxy-Δ^3-1,3,4-oxadiazoline (**17c**) was prepared to investigate the intramolecular reactions of the triple bond with the dialkoxy carbene.

The first step involves the thermal fragmentation of the oxadiazoline (**17c**) to N_2 and the carbonyl ylide (**19c**). The ylide fragmentation to butynoxymethoxycarbene (**20c**) and acetone is based on the chemistry of the dimethoxy analogue. The carbene reaction probably afforded a cyclopropene intermediate (**68**) via intramolecular cycloaddition, which in turn was converted to vinylcarbene (**69**).[22,23]



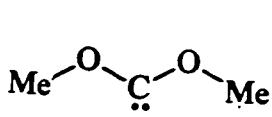
17c **19c** **20c**

68 **69**

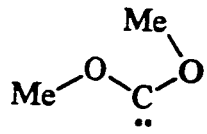
Scheme 9

1.4. *ab initio* Calculations of dioxycarbenes:

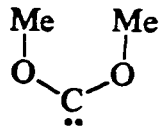
The Gaussian 86 programs were employed in the *ab initio* calculations on dimethoxycarbene using a 6-31G* basis set, where singlet conformers 70(a-c) were geometrically optimized.[11b] At low temperature, 70a and 70b should coexist but all *cis* 70c is at a higher relative energy. The high-lying LUMO (and HOMO) energies calculated for DMC are responsible for its nucleophilicity. The excited singlet states (for DMC) corresponding to HOMO → LUMO excitation were calculated to be 109 kcal/mol for 70b, and 104 kcal/mol for 70a above the corresponding ground states, while the lowest triplet states for 70a and 70b were calculated to be 76.3 and 76.7 kcal/mol above their respective ground states.



70a



70b

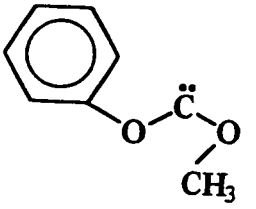


70c

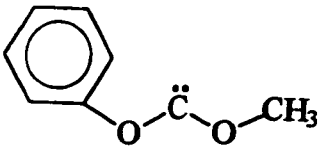
	70a	70b	70c
ε_{LU}(eV)	4.34	4.49	4.35
ε_{HO}(eV)	-10.62	-10.38	-9.64
E_{rel}(kcal/mol)	0.00	1.56	21.34

Similarly, *ab initio* calculations were carried out on MeO(PhO)C: by using standard sets.[11b] Low energy conformers 71(a-c) were revealed by calculations. With oxacarbenes, strong interaction between oxygen lone pair electrons and the singlet carbene vacant 2p orbital generates significant double bond character in the carbenic C-O bonds. The orbital energies associated with filled carbenic σ-orbitals (HOMO) and vacant p-orbitals (LUMO)

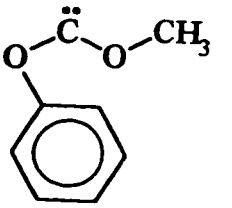
of 71(a-c) are quite similar to the calculated orbital energies of $(MeO)_2C$: so that the nucleophilicity of MeO(PhO)C: is again understandable.



71a



71b



71c

	71a	71b	71c
ε_{LU}(eV)	3.35	3.33	4.29
ε_{HO}(eV)	-10.49	-10.78	-10.64
E_{rel}(kcal/mol)	0.00	1.27	2.18

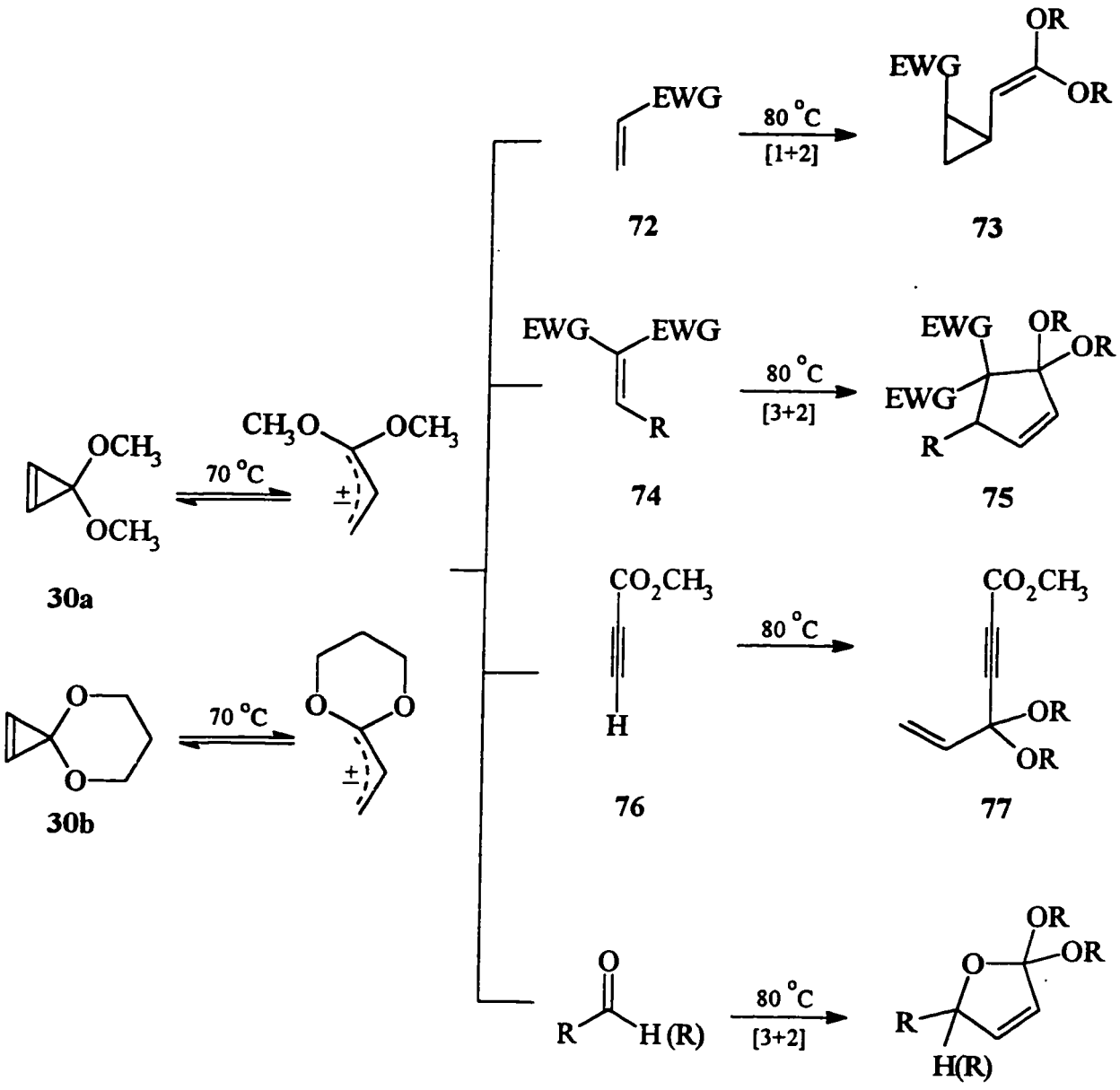
1.5. Reactions of vinylcarbenes:

The preparation and selected reactions of the cyclopropenone ketals were reported in the early 1970's and it is only in recent years that detailed investigations on the scope, mechanism and synthetic utility of their thermal reactions have been conducted.[22(a-j)] The successful observation of the intermolecular cycloaddition reactions of the π-delocalized singlet vinylcarbenes generated from **30(a,b)** were reported by Boger *et al.* In the presence of suitable electron deficient π-substrates intermolecular cycloaddition reactions of the π-delocalized singlet vinylcarbenes are observed to be competitive with reclosure to the cyclopropenone ketal. The thermal reactions of the cyclopropenone ketals **30(a,b)** include (Scheme 10):

1. [1+2] cycloadditions to provide ketene acetals with an observable *endo* effect.
2. [3+2] cycloadditions to provide functionalized cyclopentenes.

3. Reactions with alkynes.

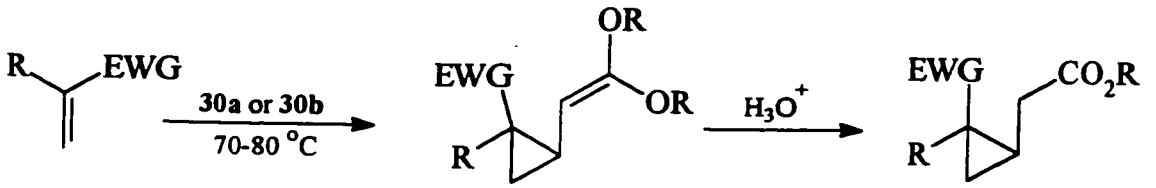
4. [3+2] reactions with selected carbon-oxygen double bonds.



Scheme 10

1.5.1. [1+2] Cycloadditions reactions of vinylcarbenes (cyclopropane formation):

Reactions of **30(a,b)** with electron deficient olefins bearing a single electron withdrawing substituent leads to the capture of the 3,3-dioxyvinylcarbene *via* [1+2] cycloaddition forming cyclopropane ketene acetal cycloadducts **(81)** (Eq. 7).[22c,e] A subsequent hydrolysis of the cyclopropane ketene acetal cycloadducts **(81)** gives the corresponding cyclopropane esters **(82)** which can be isolated by chromatography.

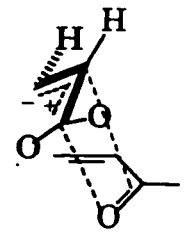


(7)

80 **81** **82**

EWG= CO_2CH_3, CN, $CO_2CH_2CH_3$
R= H, CH_3, Ph

An *endo* effect is operative in the [1+2] concerted cycloaddition reactions that provide predominantly the thermodynamically less stable *cis* isomer of the cyclopropane ketene acetals. This *endo* effect is derived from a stabilizing interaction of the substrate's electron withdrawing substituent and the allylic cation component of the π-delocalized vinylcarbene present in the transition state (Figure 8).[22a]

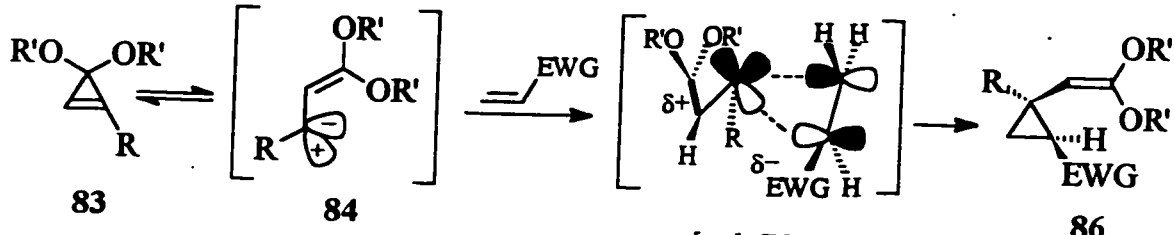


(the carbonyl group is EWG of eq. 7)

Figure 8

The regiochemistry of the substituted cyclopropene **(83)** ring cleavage and the stereochemistry of the [1+2] cycloaddition have been examined by Nakamura, *et al.* For all

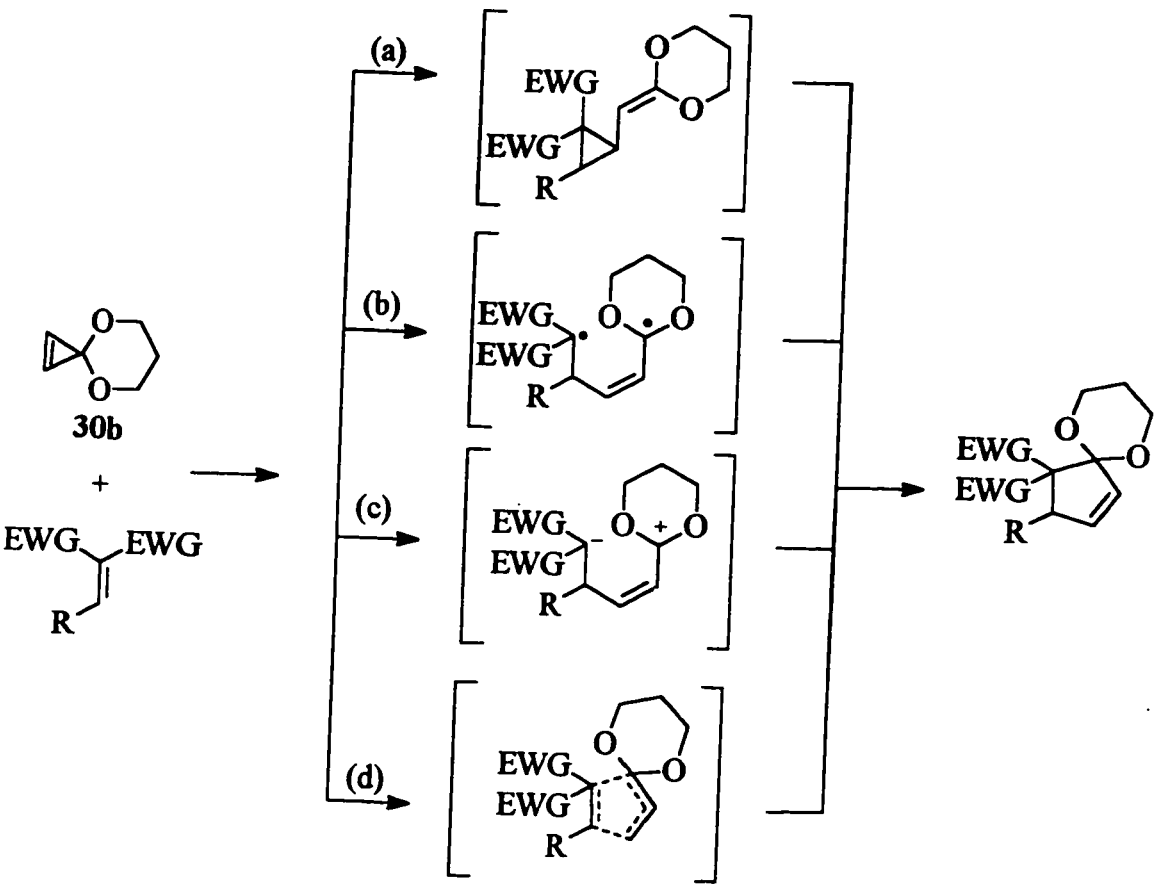
cases examined, the reactions of the substituted cyclopropanes proceeded with high selectivity via the *endo* transition state (85) to give predominantly the *cis* stereoisomer (86).[23e,f,47]



R'= $(CH_2)_3$, CH_3
R= Et, Ph, $Si(CH_3)_3$
EWG= CO_2CH_3, CN

1.5.2. [3+2] Cycloaddition reactions of π-delocalized singlet vinylcarbenes (cyclopentene formation):

The reactions of the thermally generated π-delocalized singlet vinylcarbenes with electron deficient olefins possessing two geminal electron withdrawing substituents provide cyclopentenone ketals via [3+2] cycloadditions. According to Boger *et.al.*[22b,e,j] a number of possible mechanistic pathways may be envisioned for this reaction (Scheme 11). These include: a) initial formation of the cyclopropane ketene acetal (as shown previously in equation 7) by a [1+2] cycloaddition followed by a biradical or zwitterionic vinylcyclopropane rearrangement; b) a stepwise addition-cyclization via a biradical intermediate; c) a stepwise addition-cyclization via a zwitterionic intermediate; d) a concerted [3+2] cycloaddition of the π-delocalized vinylcarbene with the alkene.



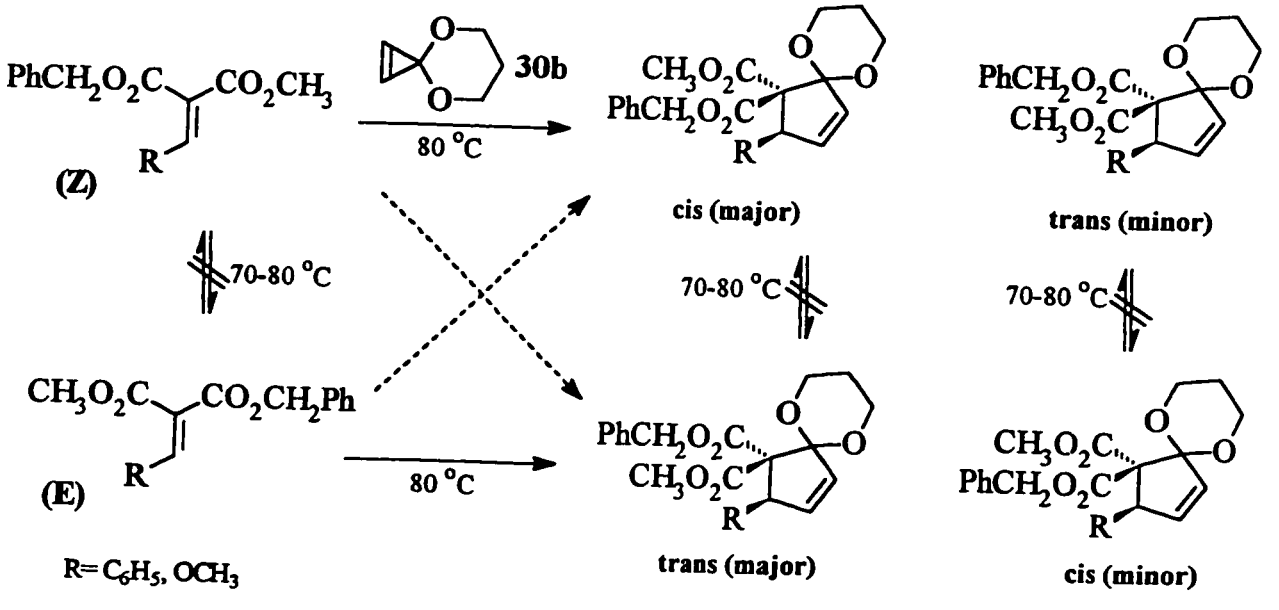
Scheme 11

In carefully detailed experiments the proposed [1+2] cycloadduct (cyclopropane ketene acetal) was not detected in a reaction of thermally generated 3,3-dioxyvinylcarbene with electron deficient olefins possessing two geminal electron withdrawing substituents. This observation rules out the prospect of initial [1+2] cycloaddition followed by biradical or zwitterionic vinyl cyclopropane rearrangement. Therefore pathway (a) was eliminated based on these results.

The [3+2] cycloadditions proceed equally well in the presence of free radical initiators as well as in the presence of radical traps. This lack of inhibition of the [3+2] cycloaddition by the radical traps rules out the progress of the reaction via a biradical intermediate.[22j] As a

result pathway (b) can be eliminated as a mechanistic possibility. The independance of the [3+2] cycloaddition reaction of the solvent polarity excluded a reaction mechanism via a zwitterionic intermediate. Therefore pathway (c) is also ruled out.

If a concerted pathway is operative, the [3+2] cycloaddition should proceed with complete retention of the substrate olefin geometry. In a [3+2] cycloaddition of E and Z isomeric alkenes, containing two different geminal electron withdrawing groups, a partial loss of the substrate olefin geometry was observed (Scheme 12). The conformational stabilities of the E and Z alkenes as well as that of the products were tested under the reaction conditions to confirm that the loss of the alkene geometry occurred during the cycloaddition reactions. This loss of the alkene geometry clearly rules out a completely concerted mechanism (d).

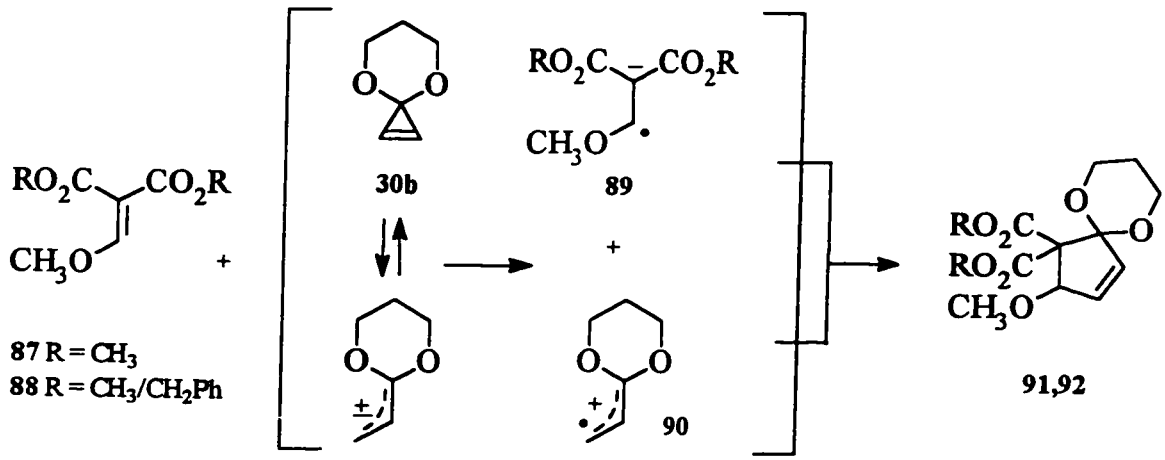


Scheme 12

An alternative single electron transfer / anion-radical and cation-radical combination mechanism was proposed by Boger *et al.*[22j] This mechanism involves the thermal generation

of a π-delocalized singlet carbene followed by a single-electron transfer (charge tranfer) from the nucleophilic π-delocalized singlet vinylcarbene to the electron deficient substrate with the generation of the π-delocalized radical cation (90) and stabilized substrate radical anion (89). A subsquent radical anion / radical cation combination would follow (Scheme 13).

This mechanism is operative only for electron deficient olefins bearing two geminal electron withdrawing substituents that possess the capabilities for preferential stabilization of a radical anion intermediate (89). This proposed mechanism is consistent with the experimental observation of solvent independency. Also, this pathway would be expected to display a partial loss of the alkene geometry.



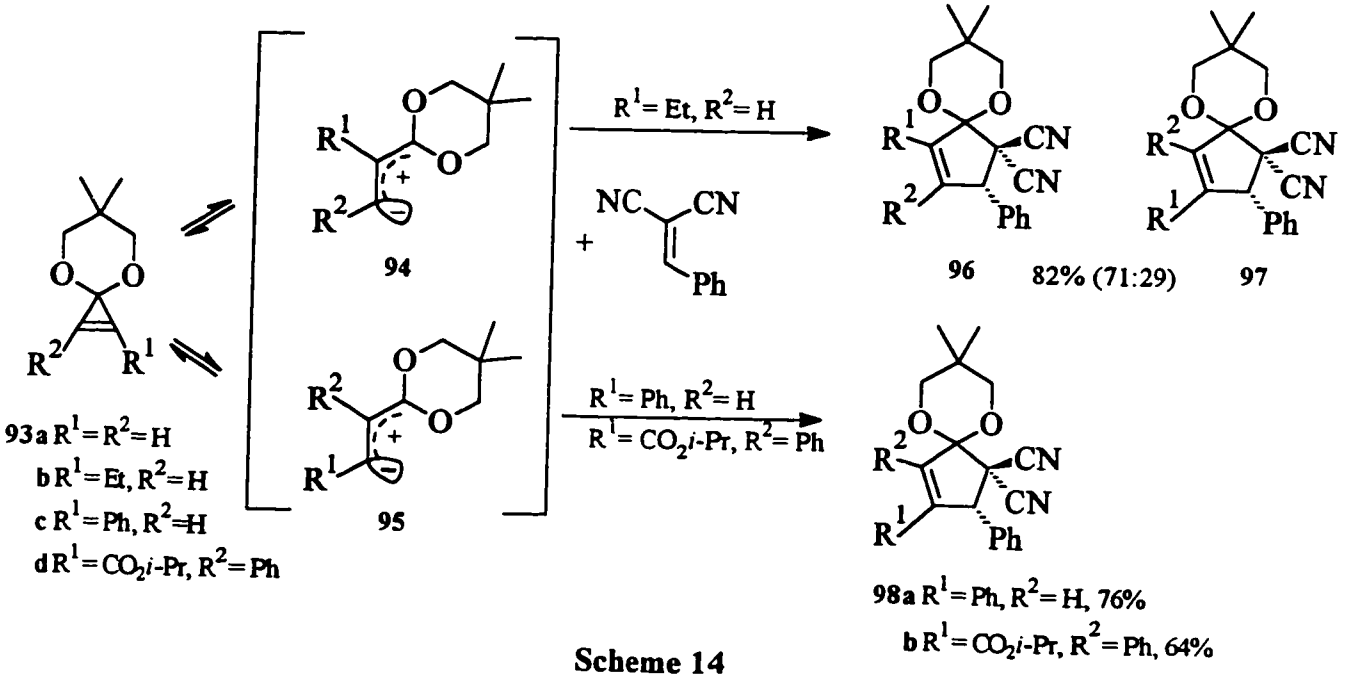
Scheme 13

Regiochemistry of [3+2] cycloaddition:

The thermal [3+2] cycloaddition of substituted cyclopropenone ketals **93(b,c,d)** to an electron deficient olefin is more complex than that of the parent compound **93a** (Scheme 14).[23c,f] Substituents on the cyclopropenyl double bond create an issue of regioselectivity of the C-C σ-bond cleavage (i.e. the formation of **94** or **95**). The [3+2] cycloaddition reaction

of 93b with benzylidenemalononitrile gave a 71:29 mixture of the cycloadducts 96 and 97, wherein the major product was due to the cycloaddition of the internally substituted carbene 94. This result is in direct contrast to the [1+2] cycloaddtion reaction of 93b with acrylonitrile, which led to the exclusive capture of only the terminally substituted 3,3-dioxyvinylcarbene 95b, therefore indicating a significant mechanistic difference between the [1+2] and the [3+2] cycloaddition reactions.

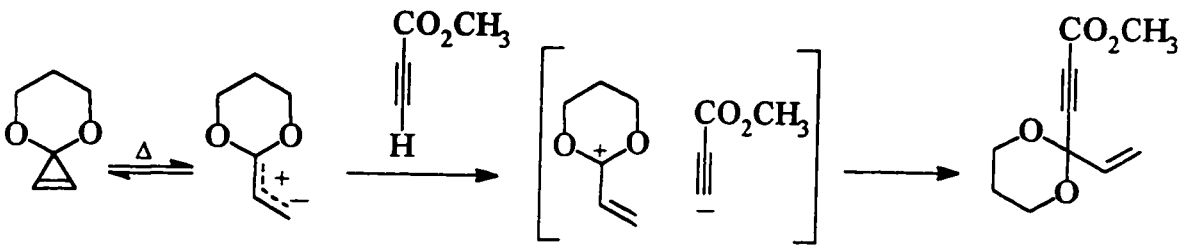
Although only moderate regioselectivity was observed for the above [3+2] cycloaddition, the phenyl and isopropyl ester cyclopropenone ketals 93c and 93d displayed excellent regioselectivity and gave a single regioisomer. In the latter two cases, the cycloadducts 98a and 98b are derived from exclusive trapping of the terminally substituted vinylcarbene (95). This is attributed to the anion stabilizing groups (R^1= Ph, CO_2i-Pr) which demonstrate an overwhelming control over regioselectivity in the ring opening of the cyclopropenone ketals 93c and 93d.[23c]



Scheme 14

1.5.3. Reactions with alkynes:

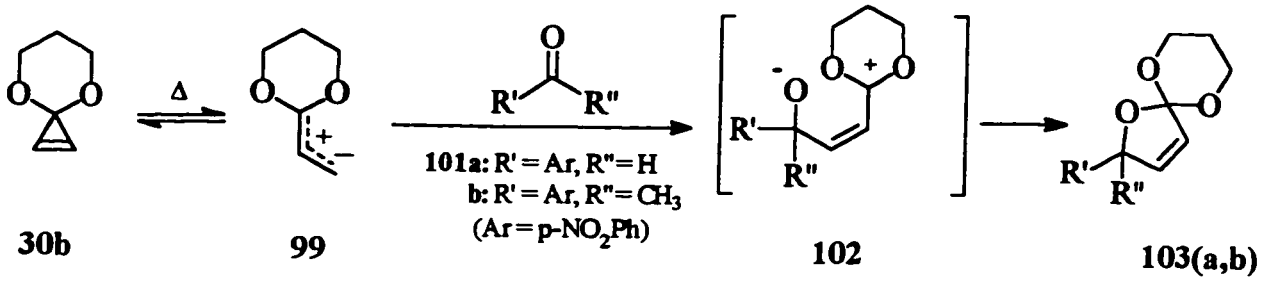
Given the ease with which electron deficient olefins react with cyclopropenone ketals to provide cyclopentenone ketals, their reactions with electron deficient alkynes was explored.[22e] Methyl propiolate was found to participate in a thermal reaction with **30b** providing the keto alkyne product (**100**). This product is derived from the protonation of the vinyl-anion moiety of the π-delocalized vinylcarbene with the acidic alkyne proton, followed by ion pair collapse. On the other hand, dimethyl acetylenedicarboxylate failed to participate in thermal reactions with the vinylcarbene derived from **30b**.



30b **99** **100**

1.5.4. Reactions with carbonyl compounds:

The reaction of cyclopropenone ketal **30b** with carbonyl compounds proceeds *via* the thermal generation and subsequent [3+2] cycloaddition of the π-delocalized vinylcarbene.[22e,h] *p*-Nitrobenzaldehyde and *p*-nitroacetophenone reacted with the thermally generated vinylcarbene **99** to form the butenolide orthoester [3+2] cycloadducts **103(a,b)** (Scheme 15). A number of mechanisms can be envisioned for the observed carbonyl [3+2] cycloadduct. Among these possible pathways is nucleophilic attack by the vinylcarbene onto the electron deficient carbonyl carbon followed by collapse of the zwitterion intermediate.[22h]



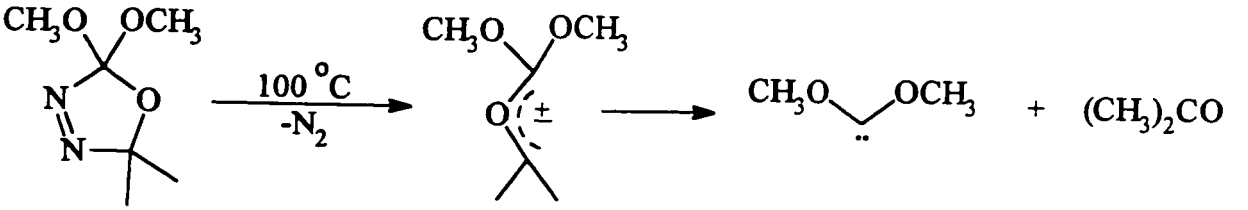
Scheme 15

Chapter 2

RESULTS AND DISCUSSION

2.1. Objectives:

2,2-Dimethoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**17a**) is a readily accessible, shelf stable compound that can serve as a convenient source of dimethoxycarbene (**20a**).[13] The thermolysis of (**17a**) at 100 °C in benzene forms N_2 and a carbonyl ylide (**19a**) which yields acetone and dimethoxycarbene (**20a**).



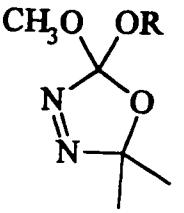
17a **19a** **20a**

The first objective of this work was to expand this promising first result to synthesize interesting new unsymmetric 2,2-dialkoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines and study their thermal chemistry.

The new 2,2-dialkoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines were prepared by oxidation of various hydrazones using lead tetraacetate (LTA) in the presence of an alcohol. This method was limited because only oxidation insensitive hydroxy compounds can be used in the preparation of these oxadiazolines. Phenoxy substituted oxadiazolines cannot be prepared by this route since phenols can be oxidized easily by reagents such as LTA. Therefore, our second objective was to develop a general synthetic approach to 2,2-dioxy-

5,5-dimethyl-Δ^3-1,3,4-oxadiazolines to overcome the problem of oxidizing the oxidation sensitive starting materials. The 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline was utilized as a precursor in the exchange method to prepare 2,2-dioxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines that cannot be prepared by the LTA oxidation method.

The third objective was to compare the thermal chemistry of the dialkoxy oxadiazoline (104) to the alkoxyaryloxy (105) and alkoxybenzyloxy (106) analogues. The thermal fragmentation of the dialkoxy oxadiazoline (104) was established to be essentially unidirectional. On the other hand the thermolysis of (105) and (106) was a multidirectional fragmentation with the carbene formation as the major course.



104 R= alkyl
105 R= aryl
106 R= benzyl

Finally, the fourth objective was to study the inter- and intramolecular reactions of the alkoxyaryloxycarbenes.

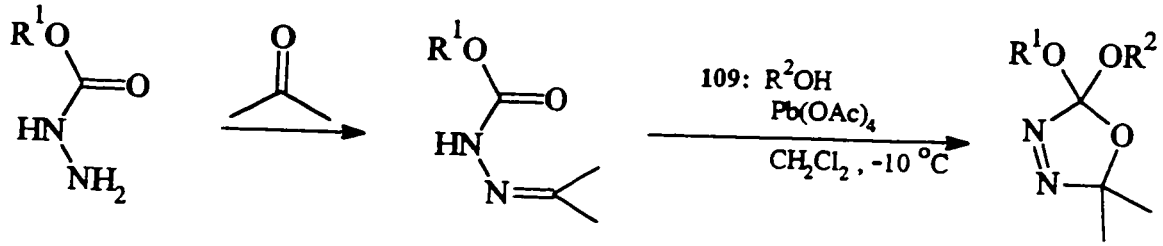
Preliminary reports of the research in this chapter, dealing with the synthesis of the 2,2-dioxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines, were communicated in 1992 and 1994 in *The Journal of the American Chemical Society*.[13,48]

2.2. Synthesis of 2-alkoxy-2-methoxy-Δ^3-1,3,4-oxadiazolines by LTA oxidation:

The first objective of this research involved the synthesis of a series of unsymmetric 2,2-dialkoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines. The methodology utilized for the synthesis

of the methoxy-Δ^3-1,3,4-oxadiazolines is well established.[49] The initial step in the synthesis of the oxadiazolines involved the condensation of alkoxycarbonyl hydrazines (107) with acetone to afford the corresponding alkoxycarbonyl hydrazones (108) which were characterized by ^1H, ^{13}C NMR spectroscopies and high resolution mass spectrometry.

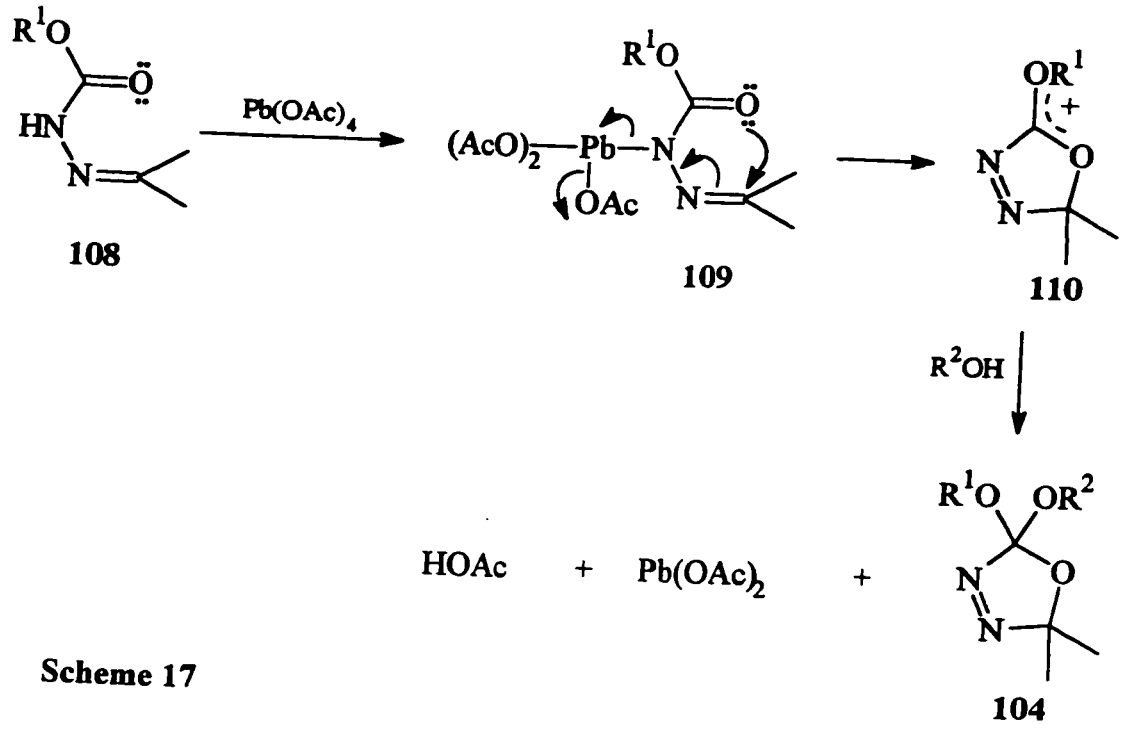
The second step was the oxidative cyclization of 108(a-d) with lead tetraacetate in the alcohols 109(a,b) or in methylene chloride containing the alcohols 109(c,d) (Scheme 16).



104 a: $R^1 = CH_2CH_3$, $R^2 = CH_3$, b: $R^1 = C(CH_3)_3$, $R^2 = CH_3$,
c: $R^1 = CH_3$, $R^2 = CH(CH_3)_2$, d: $R^1 = CH_3$, $R^2 = CH_2CH_2CH_3$

Scheme 16

A mechanism for lead tetraacetate oxidation of (108) was proposed[17,49,50] as shown in Scheme 17. The first step involves complexation of lead to the nitrogen forming an organolead intermediate (109) which then cyclizes by an internal nucleophilic attack of the carbonyl oxygen. The elimination of lead(II) to form the stabilized cyclic cation (110) is followed by an alcohol attack to yield the dialkoxy oxadiazoline (104).



108 109 110 104

Scheme 17

The purification of the crude oxadiazolines was carried out using centrifugal chromatography. All the purified oxadiazolines were clear liquids, with the yields listed in Table 2. The 2,2-dialkoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines **104(a-d)** were identified on the basis of ^{1}H and ^{13}C NMR spectroscopy as well as mass spectrometry. The peaks in ^{1}H and ^{13}C NMR spectra agreed well with those found in the 2,2-dimethoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline **(17a)**.[13] In the low resolution mass spectra molecular ions were not observed for the 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines **104(a-d)**. Most of the electron ionization mass spectra showed peaks corresponding to the loss of the alkoxy groups (m/z= 129 (M^+-OR^2)). The loss of the alkoxy group, rather than N_2, seems to be a characteristic fragmentation of the dialkoxy oxadiazolines.[13] All the dialkoxy oxadiazolines studied showed $[M+1]^+$ peaks in the low resolution chemical ionization mass spectra (LRCIMS).

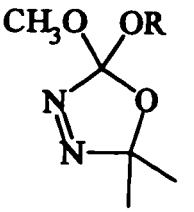


Table 2. Yields of the purified dialkoxy oxadiazolines using the LTA oxidation method

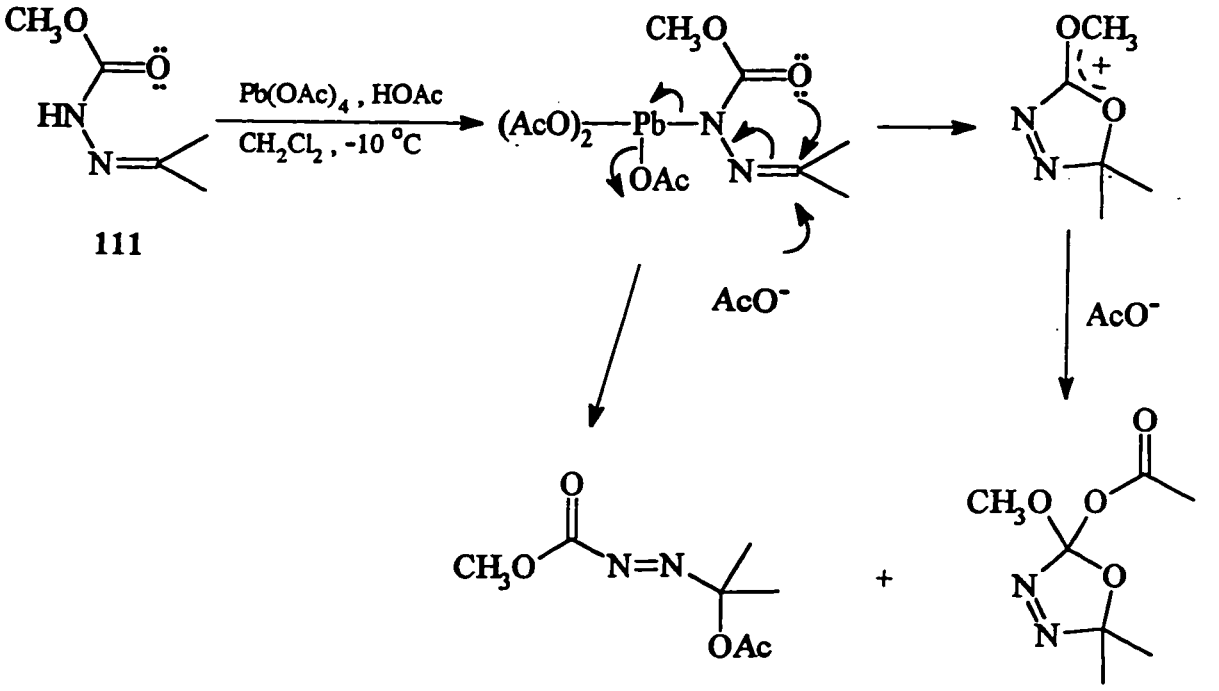
Oxadiazoline	**104a** R= CH_2CH_3	**104b** R= $C(CH_3)_3$	**104c** R= $CH(CH_3)_2$	**104d** R= $CH_2CH_2CH_3$
% yield	65	50	50	17

2.3. Synthesis of 2-acetoxy-2-methoxy-Δ^3-1,3,4-oxadiazoline:

Although dialkoxy oxadiazolines 104(a-d) are available by LTA oxidation of (108), there are limitations to this preparation method. In certain cases, the yields of the oxadiazoline are rather low. Also, in many cases, the oxidation does not proceed cleanly, as a result, purification by chromatography is required to obtain pure oxadiazoline. In addition, this method allows only alcohols that are oxidation resistant to be used. As a result, 2,2-dioxy-oxadiazolines with oxidation sensitive functionality (e.g. R^2 = Ph) are not easily synthesized via this route. In order to overcome these problems, a general new approach[48] to 2,2-dioxy-oxadiazolines (104,105,106) from 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (112) was followed. The latter is formed by oxidation of the (methoxycarbonyl) hydrazone of acetone (111) with LTA in dichloromethane (Scheme 18).

The oxidation afforded a mixture of 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (112) and the acyclic byproduct (113) in a ratio of 75 : 25; combined yield of

90%. Partial separation of **112** from **113** is possible by slow bulb to bulb distillation under vacuum, but this process is not necessary for the preparation of pure **104-106**. Instead, the mixture can be stored in the refrigerator for later use after extraction of the CH_2Cl_2 solution with aqueous $NaHCO_3$, drying the organic layer, and evaporation of the solvent.[48]



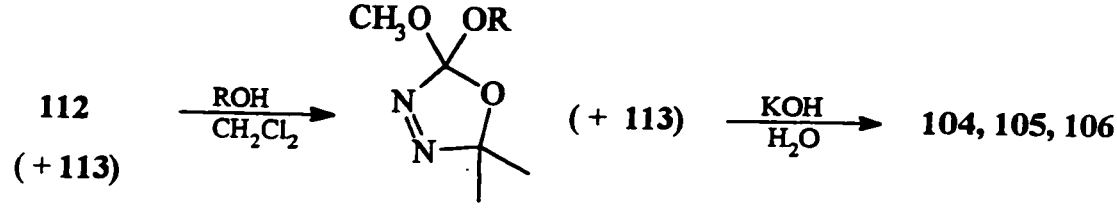
111

Scheme 18 **113** **112**

2.4. Synthesis of 2,2-dioxy-Δ^3-1,3,4-oxadiazolines via an exchange method:

Treatment of the unseparated reaction products **112** and **113** in CH_2Cl_2 containing acetic acid with the appropriate alcohol or phenol results in the conversion of **112** to **104, 105** or **106** (Scheme 19). This exchange can be monitored by NMR and is usually complete within 48 hrs when carried out in refluxing CH_2Cl_2. Once the reaction is completed, selective hydrolysis of **113** with aqueous base yields the pure oxadiazolines (**104, 105 or 106**).Table

3 lists the 2,2-dioxy oxadiazolines (104,105,106) that were prepared in yields ranging from 61 to 94% for the substitution step.[48] The substitution reaction that converts 112 to 104, 105 or 106 is probably an S_N1 reaction similar to the S_N reaction that converts 3-alkoxy-3-halo-1,2-diazirines to 2,2-dialkoxy diazirines.[11a]

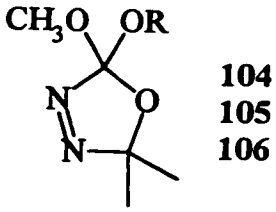


104, 105, 106

R = alkyl, aryl, benzyl

Scheme 19

This method is convenient for preparation of a wide variety of oxadiazolines. It is especially good for those nucleophilic capturing agents (e.g. phenols) that are not stable towards oxidizing agents. The 2-aryloxy-2-methoxy oxadiazolines **105** became available for the first time and the carbenes derived from these oxadiazolines undergo some interesting chemistry.



104
105
106

Table 3: 2,2-Dioxyoxadiazolines (104,105,106) from 112

104 R	yield (%)[a]	105 R	yield (%)[a]	106 R	yield (%)[a]
a CH_2CH_3	90	a C_6H_4-*p*-OCH_3	68	a $CH_2C_6H_4$-*p*-OCH_3	77
b $C(CH_3)_3$	67	b C_6H_4-*p*-CH_3	65	b $CH_2C_6H_4$-*p*-CH_3	60
c $CH(CH_3)_2$	74	c C_6H_5	61	c $CH_2C_6H_5$	89
d $CH_2CH_2CH_3$	92	d C_6H_4-*p*-Cl	68	d $CH_2C_6H_4$-*p*-Cl	90
		e C_6H_4-*p*-CF_3	58	e $CH_2C_6H_4$-*p*-CF_3	88
		f C_6H_4-*p*-CN	67	f $CH_2C_6H_4$-*p*-NO_2	64
		g C_6H_4-*p*-NO_2	62		

[a] Yields of isolated product for the exchange step.

2.5. Thermolysis of 2,2-dialkoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines:

The structures of 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines **104(a-d)** were established by ^1H and ^{13}C NMR spectroscopy. The ^1H NMR data and selected ^{13}C NMR chemical shifts for these 2,2-dialkoxy oxadiazolines are in Table 4. In the ^1H NMR spectra of the dialkoxy oxadiazolines **104(a-d)**, the methoxy singlets appear in the region of 3.26-3.46 ppm while the C-5 methyl signals appear in the region 1.23-1.56 ppm. In the ^{13}C NMR spectra of these dialkoxy oxadiazolines, the C-2 chemical shifts appear in the region 137.0-137.9 ppm, and the C-5 chemical shifts appear in the region of 118.3-118.6 ppm.

The 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines **104(a-d)** proved to be stable at room temperature, but they decompose in benzene solution at 100 °C (sealed tube). The disappearance of the C-5 methyl signals and their replacement with the acetone signal was

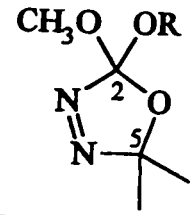


Table 4: Selected ^{1}H NMR and ^{13}C NMR chemical shifts (ppm) for **104(a-d)** in $CDCl_3$

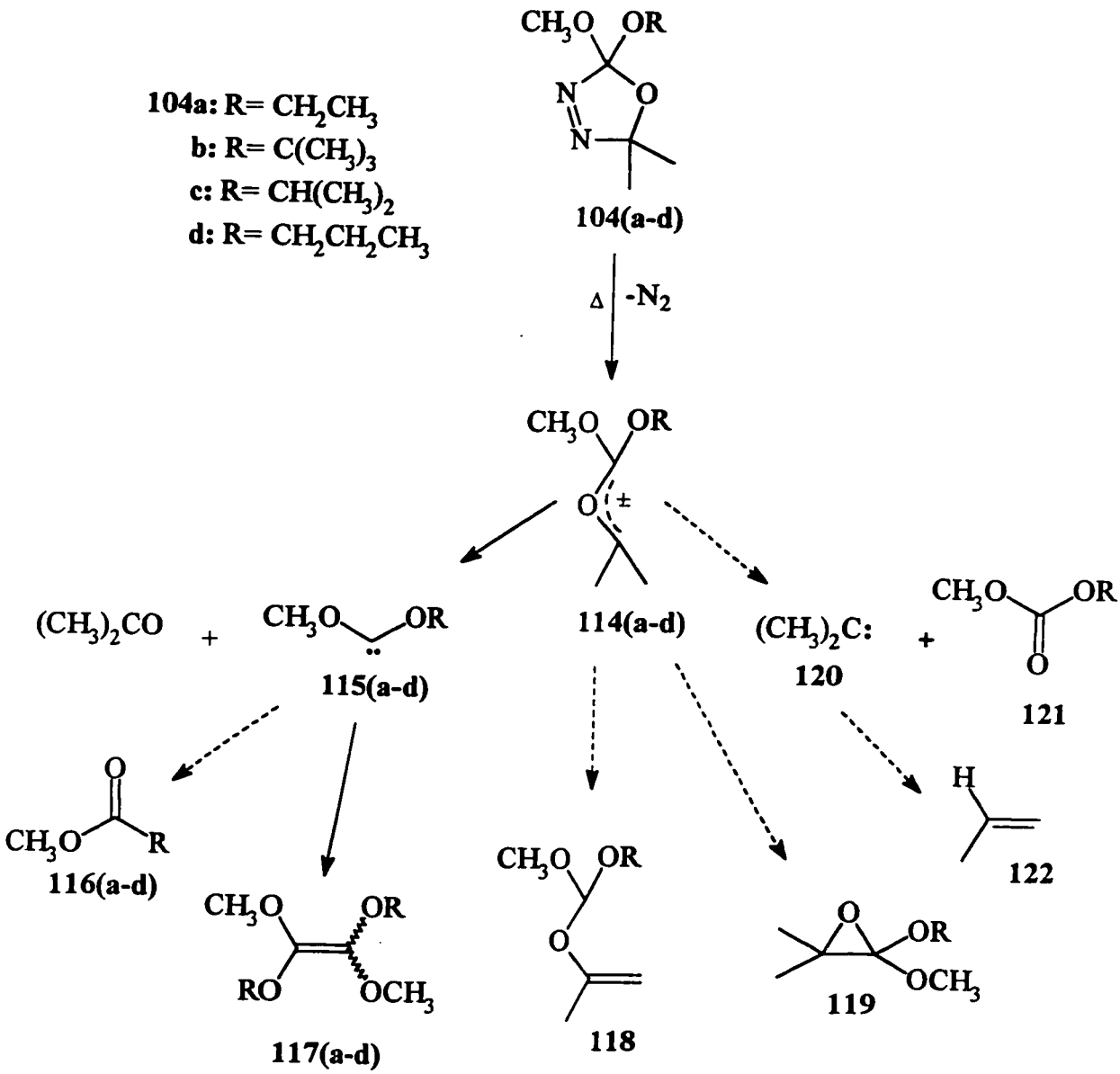
Oxadiazolines, **104**	^{1}H NMR (200 MHz)	^{13}C NMR (50 MHz)
104a R= CH_2CH_3	3.26 (s, 3H, OCH_3), 1.26 (s, 3H, CH_3), 1.25 (s, 3H, (CH_3).	137.9 (C-2), 118.6 (C-5), 51.6 (OCH_3), 23.9 (CH_3), 23.8 (CH_3).
104b R= $C(CH_3)_3$	3.32 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.51 (s, 3H, CH_3).	137.4 (C-2), 118.3 (C-5), 51.4 (OCH_3), 24.0 (CH_3), 23.7 (CH_3).
104c R= $CH(CH_3)_2$	3.41 (s, 3H, OCH_3), 1.26 (s, 3H, CH_3), 1.23 (s, 3H, CH_3).	137.2 (C-2), 118.3 (C-5), 51.5 (OCH_3), 23.4 (CH_3), 23.3 (CH_3).
104d R= $CH_2CH_2CH_3$	3.46 (s, 3H, OCH_3), 1.54 (s, 3H, CH_3), 1.54 (s, 3H, CH_3).	137.0 (C-2), 118.6 (C-5), 51.6 (OCH_3), 23.9 (CH_3), 23.9 (CH_3).

obvious from ^{1}H NMR spectroscopy. The overall mechanism of thermal decomposition of Δ^3-1,3,4-oxadiazolines bearing a heteroatom at C-2 is quite well established.[9,13,19,50]

The first step is a concerted irreversible 1,3-dipolar cycloreversion forming N_2 and the carbonyl ylide **114**. On the basis of analogy, **114** might be expected to undergo a 1,4-H shift to **118**[50b,c], electrocyclization to oxirane **119**[17c], and fragmentation to carbonyl compound and carbene.[17,50] (Scheme 20).

Compound **118**, which should be stable under the reaction conditions, was not detectable by ^{1}H NMR spectroscopy. The oxirane **119** was also not observed. The carbonate **121** was not obtained either, nor was there any evidence by ^{1}H NMR spectroscopy for the formation of propene (**122**) the expected product from fast rearrangement of dimethylcarbene **120**.[17a] On the other hand, the high yield of acetone implies that **114** fragments rapidly, and essentially unidirectionally, to dialkoxycarbene **115** and acetone.

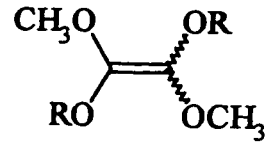
The esters **116(a-d)**, which might have been formed via carbene rearrangement, were not observed by comparison with authentic samples using ^{1}H NMR spectroscopy. Further evidence for the formation of the dialkoxycarbene intermediates **115(a-d)** came from the observation of the (E) and (Z) tetraalkoxy ethylenes, **117(a-d)**, expected from bimolecular reaction of **115(a-d)**.


104a: R= CH2CH3
b: R= C(CH3)3
c: R= CH(CH3)2
d: R= CH2CH2CH3
104(a-d)
Δ -N2
114(a-d)
(CH3)2CO
115(a-d)
(CH3)2C:
120
121
116(a-d)
117(a-d)
118
119
122

Scheme 20

The carbene dimers **117(a-d)** were not separated but their structures could be inferred from ^{1}H and ^{13}C NMR spectroscopy. The two methoxy singlets at $\delta \sim 3.4$ were assigned to the E and Z dimers while the integrals from the ^{1}H NMR spectra of the isomer mixture corresponded to their ratio (Table 5). These geometric isomers were assigned on the basis of the expectation that the major isomer would have the E configuration. As shown in Table 5, dimerization of ethoxymethoxycarbene **115a** occurred with little or no discrimination; within experimental error the E:Z ratio was 1.0. This is due to the fact that the ethyl substituent is relatively small, as a result there is no preferential formation of E- or Z-isomer.

Table 5: Ratios and yields of alkoxymethoxycarbene dimers from the thermolysis of **104(a-d)**.



Oxadiazoline **104**	% of dimer **117(a-d)**	dimer ratio[a] Z : E	OCH_3 (δ ppm) E	OCH_3 (δ ppm) Z	% Me_2CO
a: CH_2CH_3	70	1 : 1	3.44	3.43	81
b: $C(CH_3)_3$	71	1 : 4	3.25	3.22	61
c: $CH(CH_3)_2$	33	1 : 1.3	3.47	3.43	77
d: $CH_2CH_2CH_3$	53	1 : 1	3.45	3.36	79

a. By ^{1}H NMR in benzene-d_6

For the n-propyl substituent, the n-propyl chain can provide structure flexibility to adopt the least interaction geometries between the adjacent n-propoxy substituents in the Z orientation. As a result there is also no preferential formation of E- or Z-isomer.

In the case of *t*-butoxy dimers **117b** an E orientation preference was observed. This is due to the fact that adjacent *t*-butoxy substituents will experience some interaction if they

are in the Z orientation, therefore favoring E orientation slightly more. The relatively low percentage of **117c**, compared to **117(a,b)** is not well understood, further reactions of **115c** may be responsible in part.

2.6. Rate constants for thermolysis of 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines:

In order to study the use of oxadiazolines as dialkoxy carbenes precursors, the substituent effects on the rate of thermolysis were investigated. Table 6 shows the effect of the substituent (R) on the thermolysis rate constants of dialkoxy oxadiazolines **104(a-d)** to form carbonyl ylides **114(a-d)** (see Appendix II for data).

The oxadiazoline **104(a-d)** decompositions were carried out in sealed NMR tubes immersed in a constant temperature oil bath at 100 °C. The tubes were removed periodically and chilled quickly to room temperature for integration of the ^{1}H NMR spectra. The decay of the methyl group singlets at C-5 of the oxadiazoline and the growth of the acetone methyl signal at δ= 1.55, relative to the internal benzene reference signal at δ= 7.15 was convenient for monitoring the thermolysis progress. The thermolysis reactions were followed to 75% or more of completion. A plot of ln ([oxadiazoline]$_t$ / [oxadiazoline]$_o$) versus time gave a straight line, which indicates that the oxadiazolines decay by first order kinetics (Table 6). Even at high conversions, there was no evidence for consumption of acetone by ^{1}H NMR spectroscopy.

Taking dimethoxy oxadiazoline (entry1) as reference[13] (relative rate=1.0) is convenient because all the other oxadiazolines **104(a-d)** decompose faster. It is clear that the substituents effect in this case is steric. The rate of decomposition of **104a** did not differ much from that

of dimethoxy oxadiazoline previously determined[13] (entry 1). However, changing the substituent at C-2 from OCH_2CH_3 to $OC(CH_3)_3$ enhanced the rate of decomposition by a factor of ≈7.

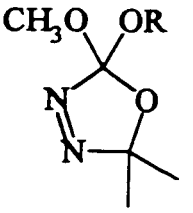
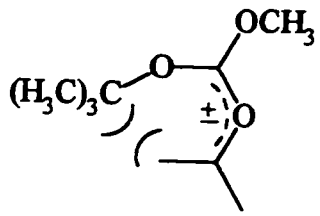


Table 6: Substituent effect on the rate of decomposition of dialkoxy oxadiazolines **104(a-d)**. (*thermolysis in* C_6D_6) at 100 °C

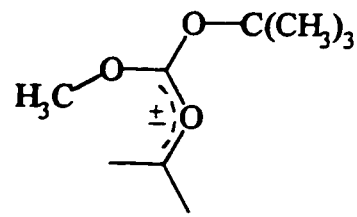
Entry	R (104)	k^a (10^{-5} s^{-1})	$t_{1/2}{}^b$	$k_{rel}{}^c$	correlation coefficient[e]
1	CH_3	1.19	16.17[d]	1.00	0.9500
2	a: CH_2CH_3	1.58	12.18	1.32	0.9558
3	b: $C(CH_3)_3$	8.23	2.34	6.92	0.9412
4	c: $CH(CH_3)_2$	2.49	7.73	2.09	0.9758
5	d: $CH_2CH_2CH_3$	1.74	11.06	1.46	0.9361

a. Rate constant of thermolysis at 100 °C (sec^{-1})
b. Half life (hrs)
c. Relative rate constants
d. ref. 13
e. correlation coefficient of ln ($[104]_t$) / ($[104]_0$) vs. time

The steric acceleration by the bulky $OC(CH_3)_3$ group is responsible for the high reactivity of **104b**. The *t*-butoxy group permits a relatively facile cycloreversion of the oxadiazoline to the exo ylide. In all planar geometry, the endo ylide has a large interaction between $C(CH_3)_3$ and CH_3. As a result the *endo* ylide has to be twisted in order to reduce this interaction, whereas an *exo* ylide can relieve this interaction between the CH_3 and the large t-butoxy group. Similarly, it was observed that the rate of decomposition of **104c** is faster than that of **104a** but slower that of than **104b**.



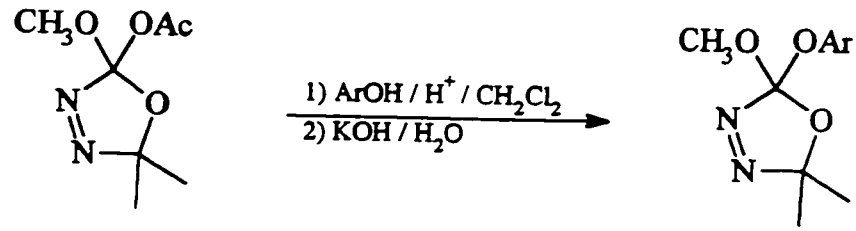
(0°,0°)
endo ylide



(0°,0°)
exo ylide

2.7. Thermolysis of 2-alkoxy-2-aryloxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines:

The exchange method mentioned previously was used to prepare a series of substituted 2-alkoxy-2-aryloxy oxadiazolines **105(a-g)** prepared by reacting the crude acetoxy oxadiazoline **(112+113)** with the corresponding phenols (two fold excess) in acid catalyzed reactions. After completion of the reaction, the crude product mixture with excess ArOH and **113** (remained unreacted after the exchange) was treated with dilute base. After extraction and evaporation of the volatiles, the oxadiazolines **105(a-g)** were obtained in good yields and sufficient purity as judged by ^{1}H NMR spectroscopy.



112 **105(a-g)**

The 2-alkoxy-2-aryloxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines **105(a-g)** were identified on the basis of ^{1}H and ^{13}C NMR spectroscopy as well as mass spectrometry. The selected ^{1}H and ^{13}C NMR chemical shifts for these alkoxyaryloxy oxadiazolines are in Table 7.

The ^{1}H and ^{13}C NMR chemical shifts of the alkoxyaryloxy oxadiazolines **105(a-g)** are comparable to those of the dialkoxy analogues **104(a-d)**. In the ^{1}H NMR spectra of **105(a-g)**, the methoxy singlets appear in the region of 3.53-3.62 ppm while the C-5 methyl signals appear in the region 1.20-1.84 ppm. In the ^{13}C NMR spectra of these alkoxyaryloxy oxadiazolines, the C-2 chemical shifts appear in the region 134.3-136.8 ppm, and the C-5 chemical shifts appear in the region of 120.1-120.8 ppm, confirming the presence of the oxadiazoline ring.

In the low resolution mass spectra molecular ions were not observed for the 2-alkoxy-2-aryloxy-Δ^{3}-1,3,4-oxadiazolines **105(a-g)**. The electron impact ionization mass spectra showed peaks corresponding to the loss of the methoxy groups (M^{+}-OCH_3) and not the M^{+}-N_2 peaks, which seems to be a characteristic fragmentation pattern of all alkoxyaryloxy oxadiazolines, as well as dialkoxy oxadiazolines. All the alkoxyaryloxy oxadiazolines studied showed the highest intensity peaks corresponding to m/z = 129 (M^{+}-OAr).

A mechanism that can account for the products obtained from the thermolysis of **105(a-g)** in benzene-d_6 is shown in Scheme 21 where the identity of those products was confirmed by ^{1}H and ^{13}C NMR spectroscopy. For the totally thermolyzed oxadiazolines, the percentage yields were determined after normalization of the peak integrals against that of the toluene methyl signal which was used as an internal standard (Table 8).

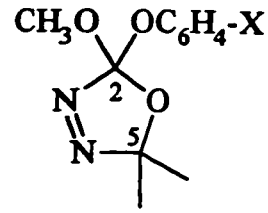


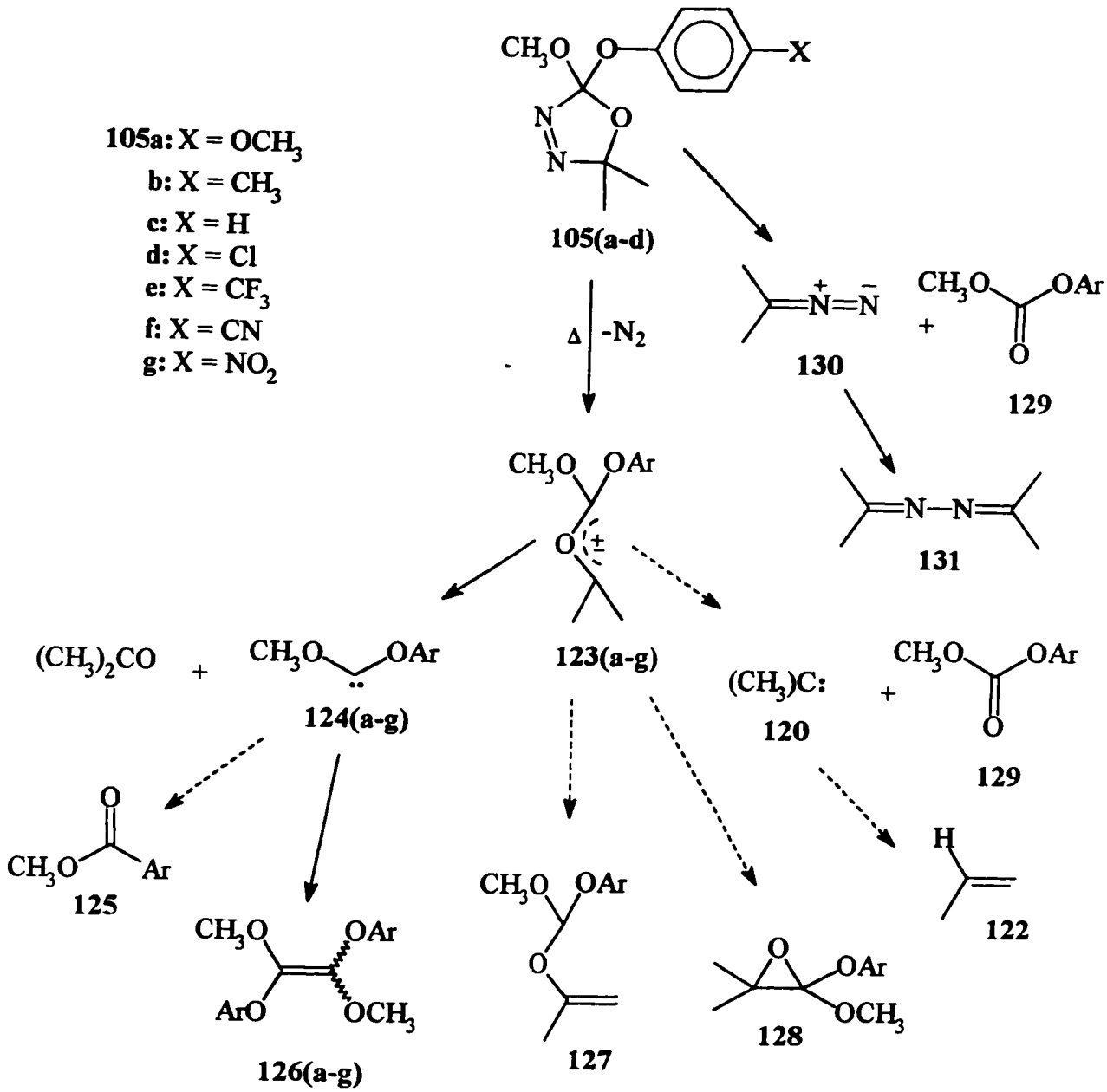
Table 7: Selected ^{1}H NMR and ^{13}C NMR chemical shifts (ppm) for 105(a-g) in $CDCl_3$

Oxadiazolines, 105	^{1}H NMR (200 MHz)	^{13}C NMR (50 MHz)
105a X = *p*-OCH_3	3.62 (s, 3H, OCH_3), 1.52 (s, 3H, CH_3), 1.20 (s, 3H, CH_3).	136.8 (C-2), 120.1 (C-5), 52.3 (OCH_3), 24.1 (CH_3), 23.3 (CH_3).
105b X = *p*-CH_3	3.60 (s, 3H, OCH_3), 1.55 (s, 3H, CH_3), 1.26 (s, 3H, CH_3).	134.2 (C-2), 120.4 (C-5), 52.5 (OCH_3), 23.6 (CH_3), 20.7 (CH_3).
105c X = *p*-H	3.61 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.27 (s, 3H, CH_3).	136.4 (C-2), 120.2 (C-5), 52.1 (OCH_3), 23.8 (CH_3), 23.2 (CH_3).
105d X = *p*-Cl	3.57 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.34 (s, 3H, CH_3),	136.4 (C-2), 120.8 (C-5), 52.5 (OCH_3), 24.1 (CH_3), 23.8 (CH_3).
105e X = *p*-CF_3	3.55 (s, 3H, OCH_3), 1.62 (s, 3H, CH_3), 1.42 (s, 3H, CH_3).	135.0 (C-2), 120.5 (C-5), 52.6 (OCH_3), 24.0 (CH_3), 23.9 (CH_3).
105f X = *p*-CN	3.53 (s, 3H, OCH_3), 1.84 (s, 3H, CH_3), 1.46 (s, 3H, CH_3).	135.7 (C-2), 121.4 (C-5), 52.4 (OCH_3), 23.8 (CH_3), 23.7 (CH_3).
105g X = *p*-NO_2	3.53 (s, 3H, OCH_3), 1.65 (s, 3H, CH_3), 1.49 (s, 3H, CH_3),	134.3 (C-2), 120.3 (C-5), 51.1 (OCH_3), 22.5 (CH_3), 22.3 (CH_3).

All seven oxadiazolines **105(a-g)** fragmented thermally to N_2, acetone, and carbene MeO(ArO)C:, **124(a-g)**, as deduced from the identification of MeO(ArO)C=C(OAr)OMe **126(a-g)** as major products in the absence of carbene trapping agents. The dimers isolated using centrifugal chromatography were readily recognized from the ^1H and ^{13}C NMR spectra as well as their mass spectra. The selected ^1H and ^{13}C NMR chemical shifts are in Table 9. The ^1H NMR spectral data of **126c** are in agreement with those reported earlier.[11c] In the ^{13}C NMR spectra, the vinylic signals of **126(a-g)** occur near $\delta = 138$ ppm in comparison with those of **117(a-d)** near $\delta = 141$ ppm.

The low resolution mass spectra of all the alkoxyaryloxy dimers **126(a-g)** showed the highest intensity peaks corresponding to the molecular ions m/z = M^+. In the electron impact ionization mass spectra peaks corresponding to the loss of the methyl groups M^+-CH_3 were observed which seem to be a characteristic fragmentation pattern of all alkoxyaryloxycarbene dimers. The CI mass spectra for all these compounds revealed the [M^++1] peaks to be the base peaks. High resolution mass spectrometric molecular weights could be obtained for **126(a-g)**, because of the recognizable molecular ion peak. The percentage yields and the isomer ratios of the dimers **126(a-g)** are given in Table 8. Although there is a preferential formation of the E-isomer, the p-substituents appear to have a minor effect on the stereochemistry of dimerization.

Neither oxirane **128** nor 1,4-H migration product **127** were observed in the total thermolysis products. Also, the esters **125**, expected from aryl migration, could not be detected by comparison with authentic samples using GC.


105a: X = OCH3
b: X = CH3
c: X = H
d: X = Cl
e: X = CF3
f: X = CN
g: X = NO2
105(a-d)
Δ -N2
130
129
131
123(a-g)
(CH3)2CO
124(a-g)
(CH3)C:
120
125
126(a-g)
127
128
122

Scheme 21

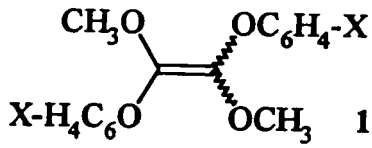
It was recognized that the thermal fragmentation of the alkoxyaryloxy oxadiazolines **105(a-g)** might occur in a multidirectional sense. A competitive fragmentation of **105(a-g)** afforded acetone azine **131** which is known to be generated *via* a bimolecular conversion of the 2-diazopropane **130**. The presence of acetone azine **131** was based on the following observations: i) Two singlets (δ= 1.79 and 1.81) in the ^{1}H NMR spectrum which could not be due to signals of other products. ii) Those chemical shifts corresponded to ^{1}H chemical shifts of an authentic acetone azine sample.

Additional evidence for the multi-fragmentation of the oxadiazolines **105(a-g)** came from the observation of the methyl aryl carbonates **129**, which were formed in yields comparable to that of **131** within experimental error (Table 8). The absence of propene **122**, from the fast rearrangement of dimethyl carbene **120**, rules out the possibilty of formation of the carbonate **129** via the fragmentation of carbonyl ylide **(123)** (Scheme 21).

Table 8: Products ratios and yields from the thermolysis of oxadiazolines **105(a-g)** in C_6D_6

Oxadiazoline **105**	dimer **126**(%)	dimer ratio Z : E	azine **131** (%)	$ArOCO_2CH_3$ **129** (%)	$(CH_3)_2CO$ (%)
a C_6H_4-*p*-OCH_3	57	1 : 1.46	21	16	55
b C_6H_4-*p*-CH_3	60	1 : 1.32	14	16	60
c C_6H_5	46	1 : 1.37	15	19	54
d C_6H_4-*p*-Cl	56	1 : 1.30	19	19	48
e C_6H_4-*p*-CF_3	57	1 : 1.24	15	18	52
f C_6H_4-*p*-CN	46	1 : 1.46	20	16	55
g C_6H_4-*p*-NO_2	52	1 : 1.45	16	17	57

Table 9: Selected ^{1}H and ^{13}C NMR chemical shifts (ppm) for 126(a-g) in $CDCl_3$

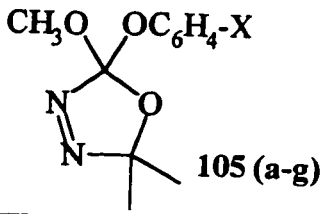


126 (a-g)

Carbene dimers, **126**	^{1}H NMR (200 MHz)	^{13}C NMR (50 MHz)
126a X= *p*-OCH_3	3.64 (s, 3H, OCH_3) 3.56 (s, 3H, OCH_3)	138.4 (C=C), 58.0 (OCH_3), 57.8 (OCH_3).
126b X= *p*-CH_3	3.63 (s, 3H, OCH_3) 3.52 (s, 3H, OCH_3)	138.1 (C=C), 57.8 (OCH_3), 57.6 (OCH_3).
126c X= *p*-H	3.67 (s, 3H, OCH_3) 3.54 (s, 3H, OCH_3)	138.2 (C=C), 58.1 (OVH_3), 57.9 (OCH_3).
126d X= *p*-Cl	3.67 (s, 3H, OCH_3) 3.53 (s, 3H, OCH_3)	138.2 (C=C), 58.1 (OCH_3), 57.9 (OCH_3).
126e X= *p*-CF_3	3.71 (s, 3H, OCH_3) 3.57 (s, 3H, OCH_3)	138.2 (C=C), 58.4 (OCH_3), 58.2 (OCH_3).
126f X= *p*-CN	3.73 (s, 3H, OCH_3) 3.57 (s, 3H, OCH_3)	138.1 (C=C), 58.7 (OCH_3), 58.4 (OCH_3).
126g X= *p*-NO_2	3.77 (s, 3H, OCH_3) 3.61 (s, 3H, OCH_3)	138.1 (C=C), 58.8 (OCH_3), 58.4 (OCH_3).

2.8. Rate constants for thermolysis of 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazolines:

The unimolecular fragmentation of the oxadiazolines **105(a-g)** was followed by ^1H NMR spectroscopy using peak areas which were normalized to that of an internal standard (toluene δ= 2.19 ppm). Compounds **105(a-g)** decomposed in C_6D_6 at 100 °C with first order kinetics, with correlation coefficients typically better than 0.980. Rate constants are correlated with the Hammett substituent constant (σ) with ρ(100 °C)= 0.21. The effects of p-substituents in the aryloxy group at C-2 on the rate constant of thermolysis of **105(a-g)** at 100 °C are indicated in Table 10 (see Appendix II for data).



105 (a-g)

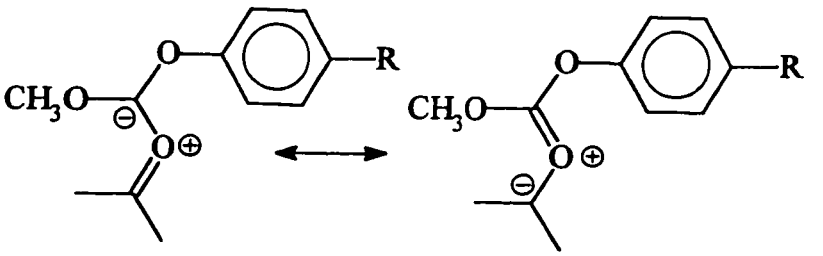
Table 10: Substituent effects on the rate of decomposition of aryloxymethoxy oxadiazolines **105(a-g)** (in C_6D_6 at 100 °C)

Oxadiazoline **105** X	k^a (10^{-5} s^{-1})	$t_{1/2}{}^b$	$k_X/k_H{}^c$	$\log(k_X/k_H)$	$\sigma_X{}^d$	correlation coefficient[e]
a: *p*-OCH_3	1.63	11.81	0.831	-0.080	-0.27	0.9920
b: *p*-CH_3	1.80	10.69	0.918	-0.037	-0.17	0.9880
c: *p*-H	1.96	9.82	1.000	0.000	0.00	0.9849
d: *p*-Cl	2.04	9.43	1.040	0.017	0.23	0.9832
e: *p*-CF_3	2.38	8.09	1.214	0.084	0.54	0.9974
f: *p*-CN	2.64	7.57	1.346	0.129	0.63	0.9403
g: *p*-NO_2	2.93	6.57	1.494	0.174	0.78	0.9976

a. Rate constant of thermolysis at 100 °C
b. Half life (hrs)
c. Relative rate constants k (**105**-X) / k (**105**-H)
d. Hammett substituent contants (σ_{para})
e. Correlation coefficient of ln ($[\mathbf{105}]_t$) / ($[\mathbf{105}]_o$) vs time

The 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazolines **105(a-g)** probably fragment via a concerted loss of nitrogen to form the carbonyl ylides **123(a-g)** followed by fragmentation to acetone and the alkoxyaryloxycarbenes **124(a-g)**. The presence of aryloxy group at C-2 leads to an enhancement of the thermolysis rate constants of **105(a-g)** in comparison with those values determined for the 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines **104(a-d)**

The enhancement of the thermolysis rate constant by electron withdrawing groups indicates that C-2 becomes more electron rich as the oxadiazolines **105(a-g)** pass from the ground state to the transition state. That is a result that would be expected from a mechanism involving an ylide like transition state, as the following dipolar ylide structures suggest. The relatively small ρ value (0.21) would suggest that little negative charge has developed at C-2.



2.9. Addition reactions of alkoxyaryloxycarbenes:

2.9.1. Reactions with Alkynes:

A. Dimethyl acetylenedicarboxylate (DMAD):

Oxadiazolines **105(a-g)** are convenient precusors of the alkoxyaryloxycarbenes **124(a-g)** which can be generated by thermolysis at 100 °C. The numerous products from the thermal fragmentation of **105(a-g)** in benzene are well characterized, but the greater interest is in

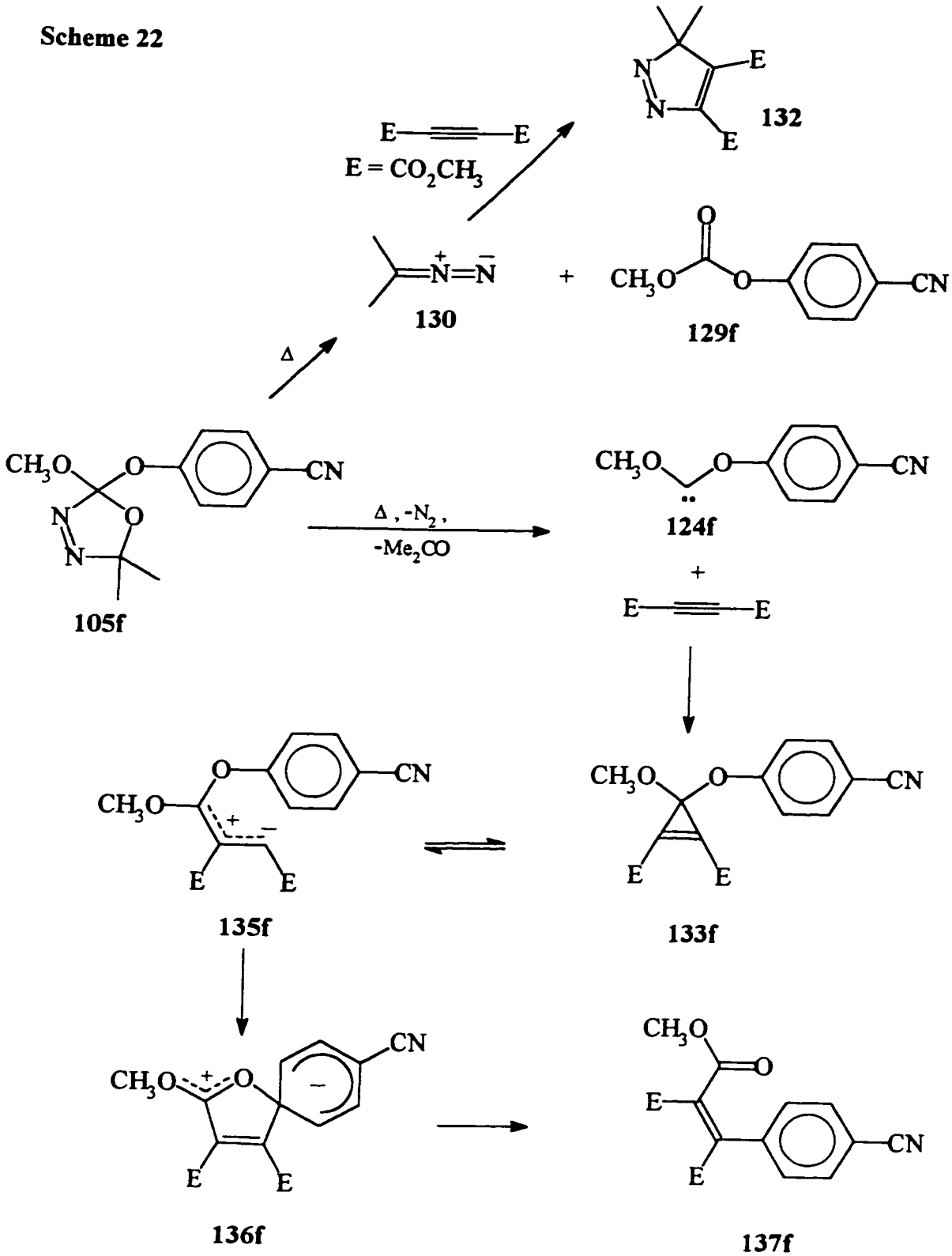
trapping the carbenes **124(a-g)** by cycloaddition.

The thermolysis of **105f** at 100 °C in benzene (sealed tube) in the presence of dimethyl acetylenedicarboxylate did not afford the cyclopropenone ketal **133f** as a final product. Instead, the major product obtained was **137f**, which is an isomer of the cyclopropene **133f**. The alkene **137f**, which was isolated in 45% yield, was characterized by means of IR spectroscopy, ^{1}H NMR spectroscopy ^{13}C NMR spectroscopy, and high resolution mass spectrometry.

The ^{1}H NMR spectrum had three different methoxy singlets (δ(ppm)= 3.87, 3.85, 3.64) excluding the possibility of symmetric cyclopropene **133f**. The infrared showed sharp (C=O) absorptions at 1748 cm^{-1} and 1723 cm^{-1}, and an alkene band at 1640 cm^{-1}. In addition, ^{13}C NMR spectroscopy showed vinylic signals at δ= 128.3 and 144.6 as well as ester signals at δ= 162.8, 163.8 and 165.9 ppm.

The formation of the substituted alkene **137f** can be rationalized as shown in Scheme 22. The possible route to **137f** is by a two step mechanism which involves the initial formation of a π-delocalized 3,3-dioxyvinylcarbene **135f**, followed by intramolecular aromatic substitution. The vinylcarbene **(135f)** may be formed either directly via nucleophilic attack of the dioxycarbene **124f** onto one of the carbon atoms of DMAD, or via a concerted [1+2] cycloaddition between the carbene and DMAD followed by thermal ring opening of the resulting cyclopropene **133f** as shown in Scheme 22. The reversibility of this step has been reported by Boger *et al.*[22] The alkoxyaryloxyvinylcarbene **135f** from **133f** is analogous to 3,3-dioxyvinylcarbenes **31(a,b)** generated by thermolysis of cyclopropenone ketals **30(a,b)**.

Scheme 22

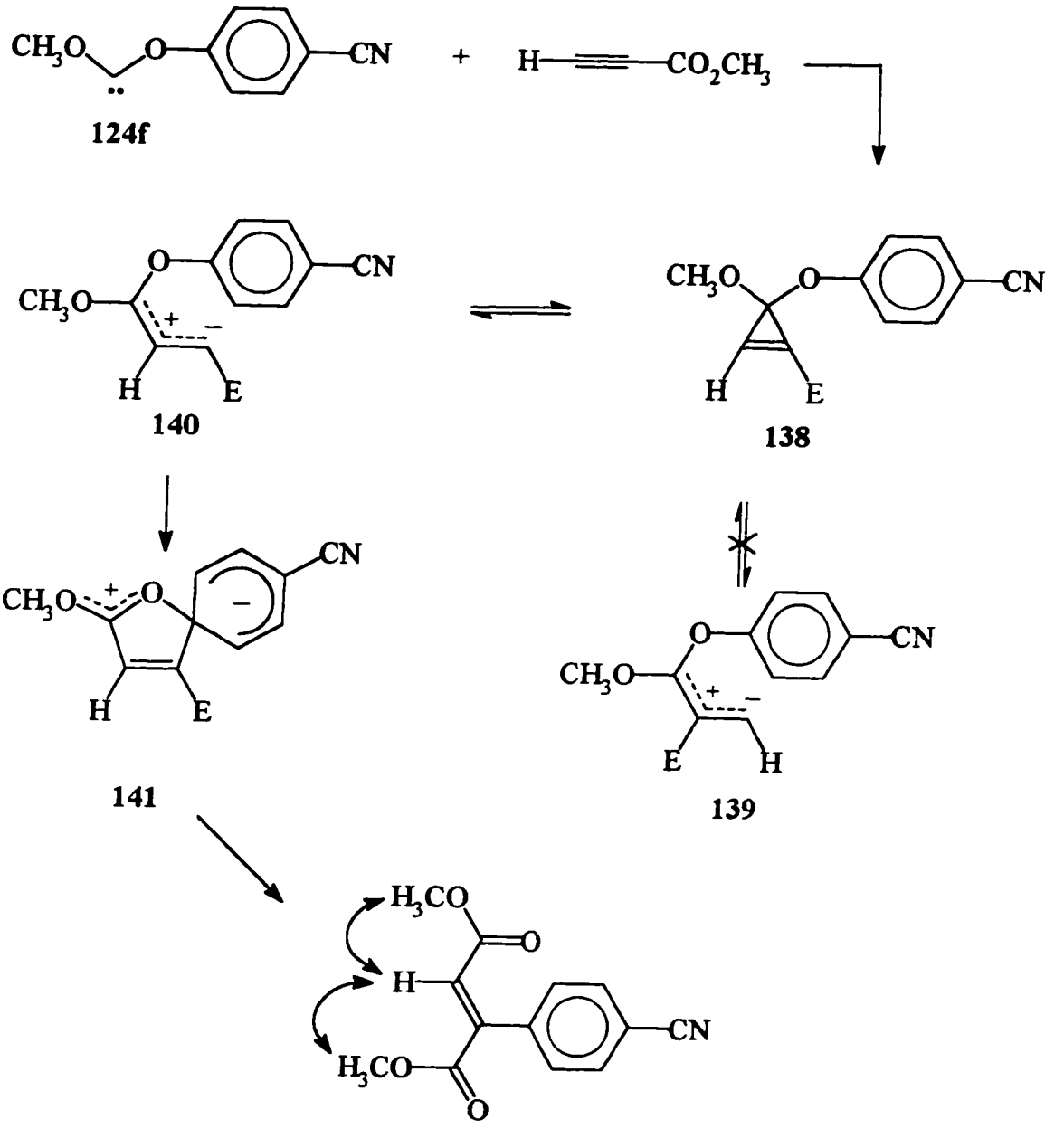

E—≡—E
E = CO2CH3
132
130
+
129f
Δ
105f
Δ , -N2 ,
-Me2CO
124f
+
E—≡—E
135f
133f
136f
137f

The alkoxyaryloxyvinylcarbene **135f** undergoes an intramolecular aromatic substitution which probably occurs through the dipole intermediate **136f**. This phenolic deoxygenation process seems to be enhanced by the presence of the p-substituted (CN) electron withdrawing group.

The diazopropane **130** generated from the competitive fragmentation of the oxadiazoline **105f** (Scheme 22) was trapped as it was being generated. The diazopropane **130** reacted with dimethyl acetylenedicarboxylate through 1,3-dipolar cycloaddition affording the 3-H pyrazole **132**. The ^{1}H and ^{13}C NMR data of **132** were compared to the literature values.[19]

B. Methyl propiolate:

Similar to the thermolysis of **105f** in the presence of DMAD, the thermolysis of the oxadiazoline **105f** (benzene sealed tube) in the presence of methyl propiolate also led to the formation of the alkene product **142** which was isolated in 35% yield. The formation of this alkene **142** is attributed to initial formation of a π-delocalized vinylcarbene **140** as observed in the reaction of **124f** with DMAD. The π-delocalized vinylcarbene **140** can be formed by either regioselective nucleophilic attack of the carbene onto one of the alkyne carbons or via regioselective ring opening the cyclopropeneone ketal intermediate **138** as shown in Scheme 23. In the literature, Nakamura *et al.*[23] reported that anion stablizing groups such as esters demonstrate an overwhelming control over regioselectivity in the formation of the vinylcarbene intermediates.



Scheme 23

The intermediate **140** is nucleophilic enough to react *via* intramolecular nucleophilic aromatic substitution through the dipole intermediate **141** which collapses to **142**. The ^1H NMR spectrum of the crude thermolysis products as well as that of isolated **142** indicated the formation of a single regioisomer (Scheme 23).

The alkene **142** was characterized by means of ^1H NMR spectroscopy, ^{13}C NMR spectroscopy, and high resolution mass spectrometry. The ^1H NMR spectrum showed a vinyl proton signal at $\delta = 7.08$ and two ester singlets at $\delta = 3.60$ and 3.78. The ^{13}C NMR spectra showed two C=C signals at 129.9 and 142.8 which are comparable with those of **137f**.

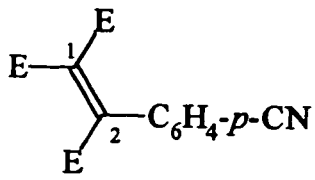
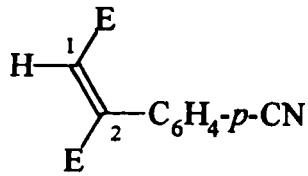
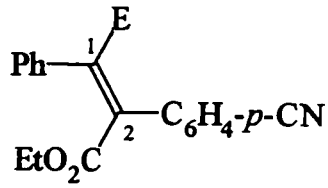
A ^1H NOE experiment on the alkene **142** confirmed that the ester substituents are trans. Irradiation of the vinyl (CH) proton singlet at 7.08 ppm caused an enhancement of both the singlet at 3.78 ppm (OCH_3) and the singlet at 3.60 ppm (OCH_3). In addition the irradiation of the OCH_3 singlet at 3.60 ppm in **132** led to an enhancement of only the (CH) proton singlet at 7.08 ppm. The results of this NOE experiment are consistent with the mechanism proposed earlier (Scheme 23).

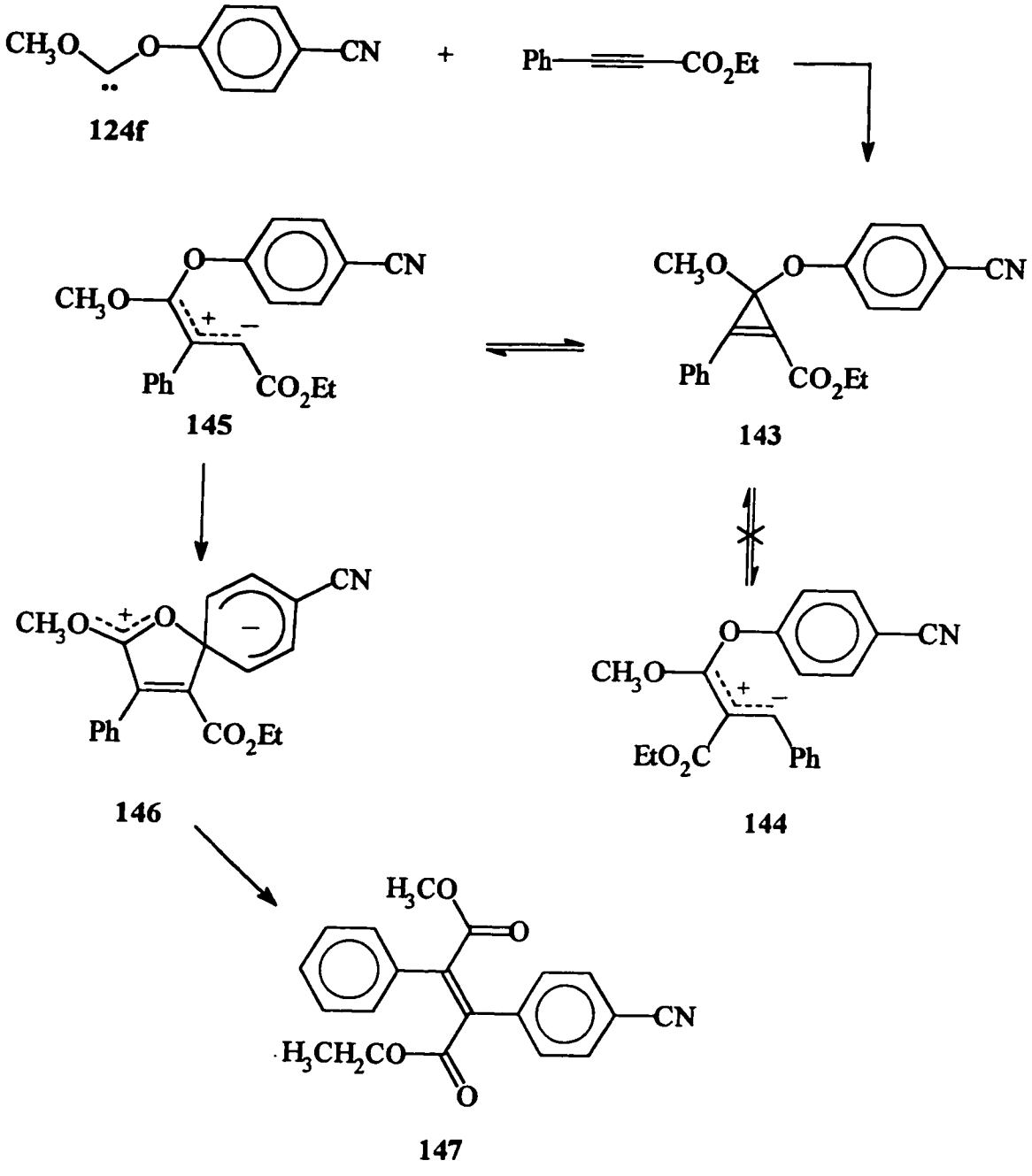
C. Ethyl phenyl propiolate:

Similarly, thermolysis of the oxadiazoline **105f** in ethyl phenyl propiolate afforded the unsymmetric alkene **147** in 43% yield (Scheme 24). The isolated alkene **147** was characterized by ^1H NMR spectroscopy, ^{13}C NMR spectroscopy, and high resolution mass spectrometry. The structure was confirmed by comparing the ^{13}C NMR data of **147** with those of **137f** and **142** (Table 11).

The formation of this alkene **147** is attributed to initial formation of a π-delocalized vinylcarbene **145** as observed in the reaction of **124f** with DMAD. The π-delocalized vinylcarbene **145** can be formed by either regioselective nucleophilic attack of the carbene onto one of the alkyne carbons or via regioselective ring opening the cyclopropeneone ketal intermediate **143** as shown in Scheme 24. The preferential formation of **145** over **144** is due to the stabilizing effect of the ester group. The intramolecular aromatic substitution of **145** leads to the formation of unsymmetric alkene **147** through the dipole intermediate **146** (Scheme 24). Analogous aryl transfer mechanism was reported by Scherowsky, *et al.*[51]

Table 11: ^{13}C NMR for C-1 and C-2 in alkenes **137f**, **142** and **147**.

	 **137f**	 **142**	 **147**
C-1 (δ)	128.3	129.9	139.1
C-2 (δ)	144.6	142.8	141.9

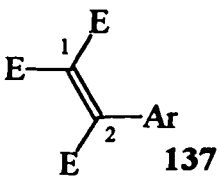


Scheme 24

2.9.2. Substitutent effects on reactions of alkoxyaryloxycarbenes with alkynes:

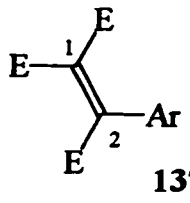
The reaction of oxadiazoline **105f** with DMAD to form substituted alkene **137f** is already presented. The purpose of the following work was to investigate whether the electron withdrawing group is required for the formation of **137** via the dipolar intermediate **136**. In order to test this assumption, a series of five p-substituted oxadiazolines **105(a,c,e,f,g)** were reacted with DMAD under the same conditions (see Experimental). For oxadiazoline **105(c,e,f,g)** the substituted alkenes **137(c,e,f,g)** were obtained (Scheme 25). The structures fit the ^{1}H NMR data by the presence of three non-equivalent methoxy groups (Table 12).

Table 12: Selected ^{1}H NMR data for alkenes **137(c, e, f, g)**.

 **137**	%yield	OCH_3	OCH_3	OCH_3
137c: Ar = C_6H_5	7	3.85	3.83	3.62
137e: Ar = C_6H_4-*p*-CF_3	40	3.86	3.83	3.64
137f: Ar = C_6H_4-*p*-CN	45	3.87	3.86	3.64
137g: Ar = C_6H_4-*p*-NO_2	43	3.88	3.86	3.64

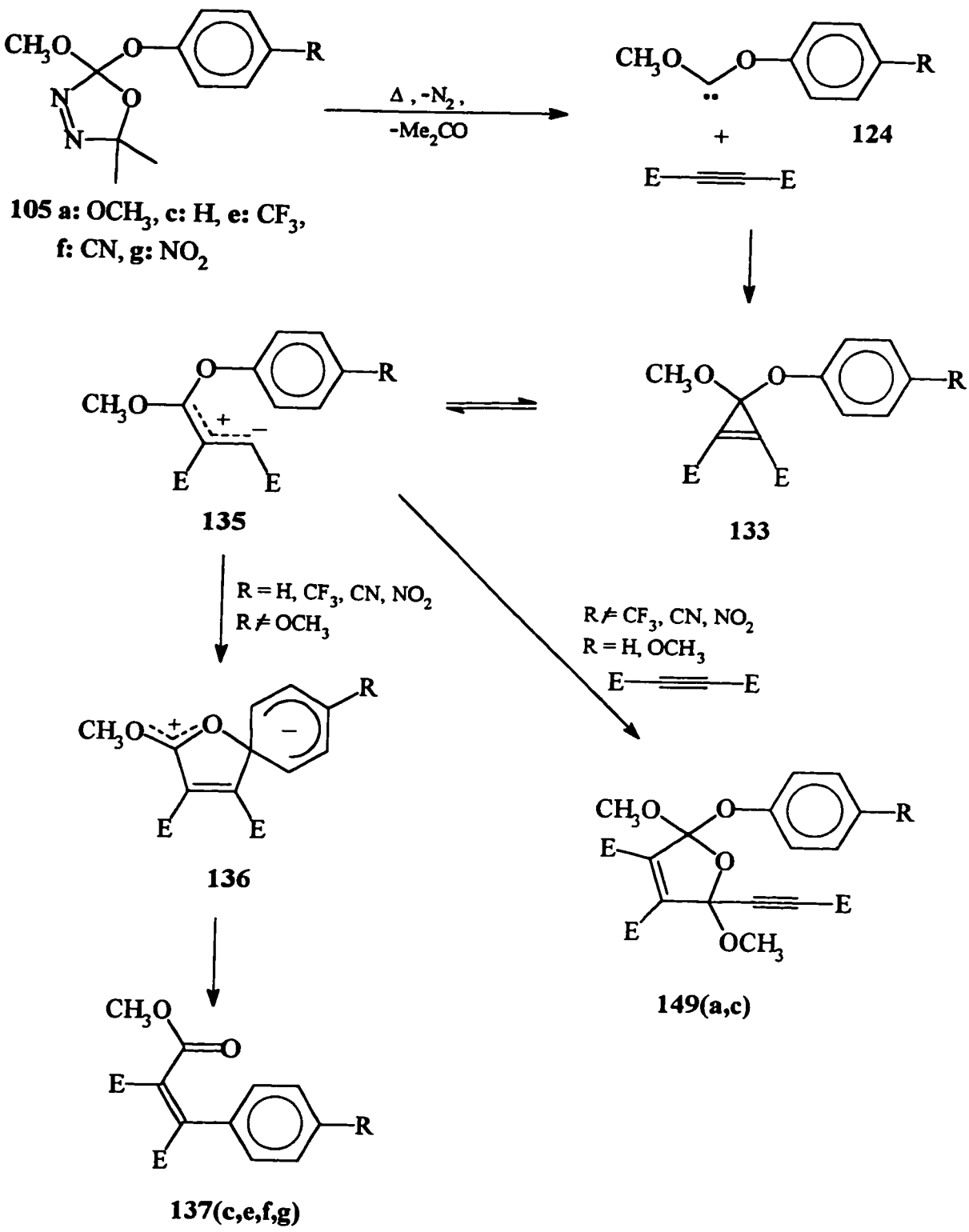
Also, the ^{13}C NMR spectra showed vinylic signals in all the alkenes at δ= 126-129 and 143-145 ppm for C-1 and C-2, respectively (Table 13). High resolution mass spectrometry was obtainable for all structures and in addition the chemical ionization mass spectra showed (M^++1) peaks.

Table 13: Selected ^{13}C NMR data for alkenes **137c, e, f, g**

 137	^{13}C NMR (50.32 MHz, $CDCl_3$= 77.00 ppm)							
	C=O	C=O	C=O	C-1	C-2	OCH_3	OCH_3	OCH_3
c: Ar = C_6H_5	165.0	164.0	163.0	126.7	143.0	52.9	52.7	52.5
e: Ar = C_6H_4-*p*-CF_3	166.3	164.1	162.8	128.7	145.0	53.2	52.9	52.6
f: Ar = C_6H_4-*p*-CN	165.9	163.8	162.8	128.3	144.6	53.3	53.2	52.9
g: Ar = C_6H_4-*p*-NO_2	165.5	163.4	162.6	129.8	144.3	53.0	52.9	52.6

The fact that **137c** was obtained in 7% yield in comparison with the yields of **137(e,f,g)** (Table 12) indicates that the absence of an electron withdrawing group retarded the intramolecular substitution process. Apparently, the vinyl carbene **135** reacted with a second molecule of DMAD to afford 1:2 cycloadduct **149c** (Scheme 25).

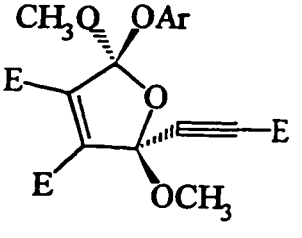
In a reaction of oxadiazoline **105a** with DMAD under the same reaction conditions, only **149a** was formed and there was no evidence of **137a** in the crude products mixture. This proves that the ability to stabilize the anionic charge in the dipolar intermediate **136** by electron withdrawing groups increases the likelihood for the formation of the substituted alkene **137**. On the other hand, electron donating groups (e.g. OMe) inhibit the intramolecular aromatic substitution step, and totally suppress the alkene formation, thus leading the reaction to a different pathway (Scheme 25).

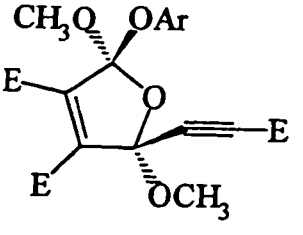

105 a: OCH3, c: H, e: CF3,
f: CN, g: NO2
Δ, -N2,
-Me2CO
124
135
133
R = H, CF3, CN, NO2
R ≠ OCH3
R ≠ CF3, CN, NO2
R = H, OCH3
136
149(a,c)
137(c,e,f,g)

Scheme 25

The analogue from the reaction of methoxyphenoxycarbene **124c** with DMAD has been reported for the case of dimethoxycarbene.[9b,10a] A possible route to **149** involves the formation of a π-delocalized vinylcarbene **135** followed by a [3+2] cycloaddition of **135** with the C=O bond of another molecule of DMAD (Scheme 25). The structures **149(a,c)** were confirmed by ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy, and high resolution mass spectrometry.

The cycloadduct **149a** was formed as a diastereomeric mixture of **149a'** and **149a"** (ratio 1:1) which were isolated by chromatography in a combined yield of 45%. Similarly, the cycloadduct **149c** was formed in as a diastereomeric mixture of **149c'** and **149c"** (ratio 1:1.3) which were isolated by chromatography in a combined yield of 38%.

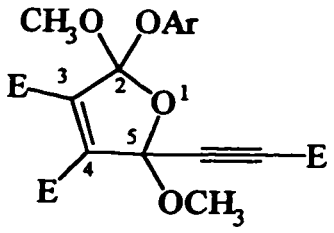




Ar= C_6H_4-*p*-OCH_3	**149a'**	**149a"**	ratio (1:1)
Ar= C_6H_5	**149c'**	**149c"**	ratio (1:1.3)

The ^{13}C NMR spectra confirmed the presence of two stereogenic centers, at C-2 and C-5 in both cycloadducts **149a** and **149c** while C-3 and C-4 signals come at the same value of δ in each diastereomer (Table 14). The major diastereomer in the cycloadduct **149c** is probably **149c"**.

Table 14: Selected ^{13}C NMR data for **149a, 149c**

	^{13}C NMR (50.32 MHz, $CDCl_3$ = 77.00 ppm)			
	C-2	C-3	C-4	C-5
149a Ar= C_6H_4-*p*-OCH_3	123.0	140.0	136.3	100.5
	122.6	140.0	136.3	100.2
149c Ar= C_6H_5	123.1	140.2	136.7	101.0
	122.8	140.2	136.7	100.6

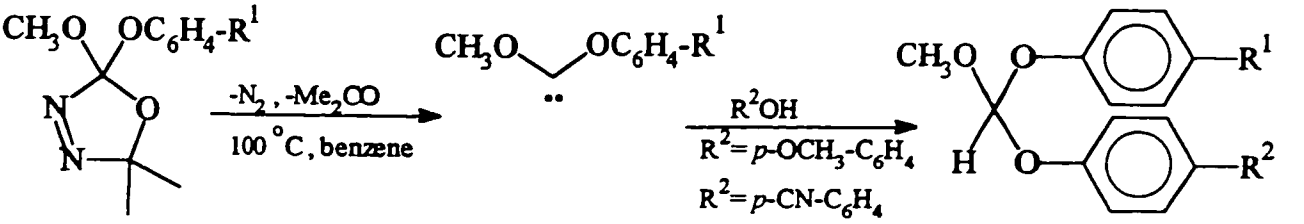
The high resolution mass was obtained for the (M^+-OPh) fragment of **149c** due to the absence of the molecular ion in the EI spectrum. On the other hand, the presence of a methoxyaryl group in **149a** stabilized the molecular ion for high resolution mass determination.

2.10. Insertion reactions of 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazolines:

2.10.1. Intermolecular insertions:

In order to prove further that the thermal decomposition of the 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazolines **105(a-g)** indeed gave alkoxyaryloxycarbenes **124(a-g)** some oxadiazolines were thermolyzed in the presence of phenols in order to trap these carbenes. The thermolysis of the oxadiazolines **105(a,c,f)** in benzene in the presence of *para* substituted phenol produced the methoxy diaryloxy formates (**150, 151, 152**) which are formed by OH insertion of the carbenes into the phenols. The mechanism of this OH insertion is persumably first protonation of the carbene to form a cation and then collapse with aryloxy anion to form

the product.



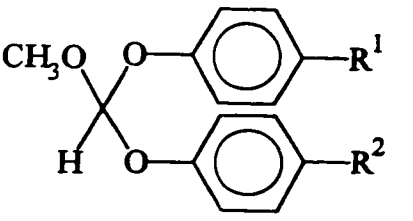
105a: $R^1 = p\text{-}OCH_3$
e: $R^1 = p\text{-}H$
f: $R^1 = p\text{-}CN$

150 $R^1 = R^2 = OCH_3$
151 $R^1 = H$, $R^2 = CN$
152 $R^1 = R^2 = CN$

These thermolyses were quite clean and the purification could be achieved by removing excess phenols by extracting the crude mixture with dilute base. The yields shown in Table 15 are isolated yields of the ortho esters purified by centrifugal chromatography.

The ^1H and ^{13}C NMR chemical shifts of **150-152** are in Table 15. The ^1H NMR spectra are those expected of orthoesters. Singlets at $\delta = 5.95$, 6.18 or 6.35 ppm, corresponding to CH and singlets at $\delta = 3.56$, 3.57 or 3.58 ppm corresponding to OCH_3 were obtained.

Table 15: Selected ^1H and ^{13}C NMR data of orthoesters **150, 151, 152**

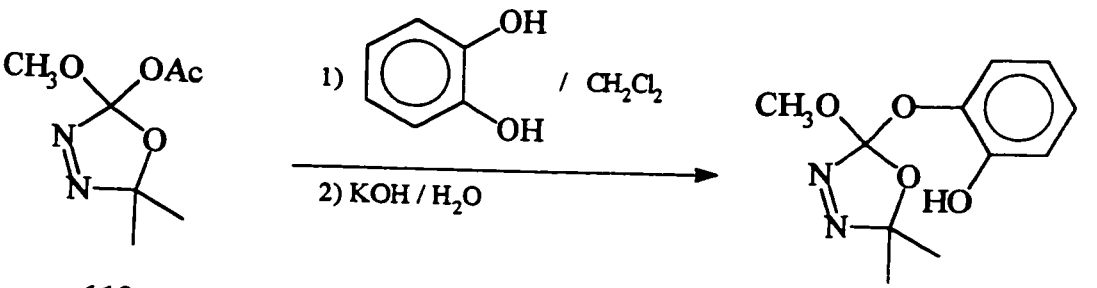
	^1H NMR		^{13}C NMR	
	%yield	CH	OCH_3	CH	OCH_3
150 $R^1 = R^2 = OCH_3$	43	5.95	3.56	155.4	50.6
151 $R^1 = H$, $R^2 = CN$	42	6.18	3.57	154.3	50.4
152 $R^1 = R^2 = CN$	45	6.35	3.58	156.8	51.0

The ^{13}C spectra showed the CH and OCH_3 chemical shifts at δ ~155 and ~50 respectively. While **150** and **151** showed a molecular ion M^+, the high resolution mass spectrometry of **152** was done on the (M^+-OCH_3) fragment due to the absence of the molecular ion in the spectrum.

2.10.2. Intramolecular insertions:

The alkoxyaryloxycarbenes are efficiently trapped intermolecularly using phenols. The following logical step was to test the possibility of trapping the alkoxyaryloxycarbenes intramolecularly. The 2-methoxy-2-(2-hydroxy)phenoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**153**) was prepared in order to investigate whether the carbene **156** resulting from thermolysis of **153** would undergo an intramolecular OH insertion.

Treatment of the crude 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (3.6 mmol of oxadiazoline) in CH_2Cl_2 with catechol (3.6 mmol) results in the conversion of **112** to **153**. The purification of **153** was carried out rapidly by selective hydrolysis of **113** using 0.9 mmol KOH to avoid the formation of the phenoxide salt of **153**.

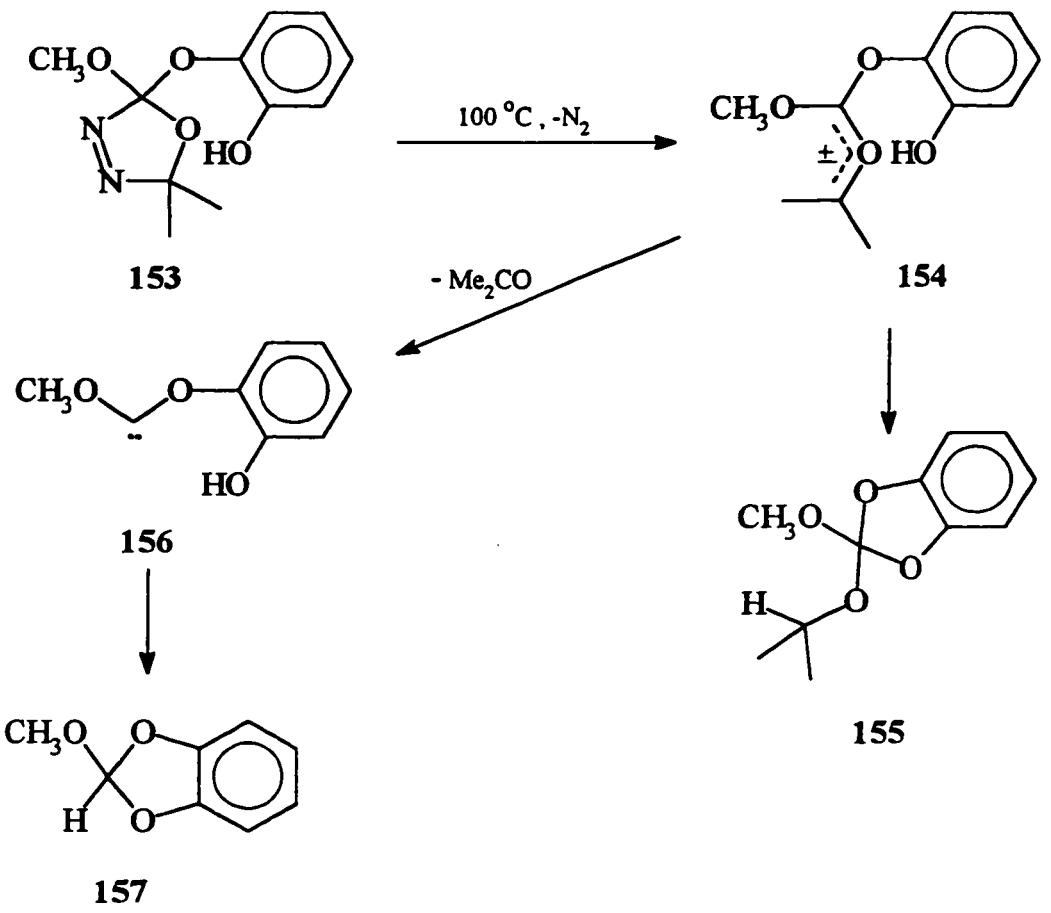


112 **153**

The 2-methoxy-2-(2-hydroxy)phenoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**153**) was obtained in 62% yield. The ^{1}H NMR spectrum was comparable to that of the previously synthesized 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazoline **105**. Also ^{13}C NMR spectrum showed C-2 and C-5 at δ= 137.1 and 120.0, respectively indicating the presence of the oxadiazoline ring.

Thermolysis of (**153**) in benzene at 100 °C gave two products (Scheme 26). The first product **155**, which was stable enough to survive the reaction conditions, was isolated in 24% yield. This product, which is a result of the carbonyl ylide entrapment, is probably formed *via* hydroxyl attack on C-2 of the ylide followed by a proton transfer to C-5. The ^{1}H NMR spectrum had a methoxy singlet at δ= 3.88 ppm and a septet at δ= 4.53 corresponding to $(CH_3)_2\underline{C}\underline{H}$. The CI spectrum confirmed the structure by showing a signal at m/z = 228 for the $(M+NH_4)^+$ ion.

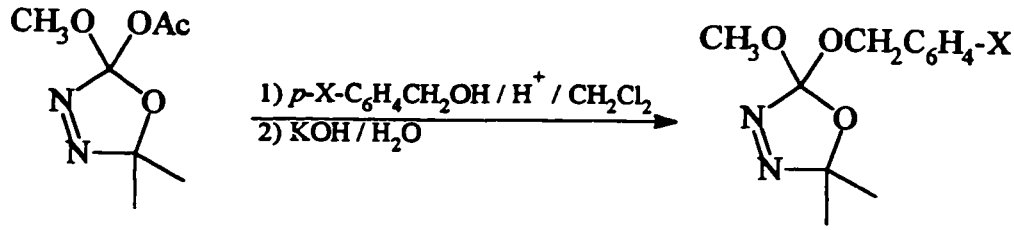
The second product **157** (22%) was formed via an intramolecular insertion reaction between the thermally generated carbene **156** and the ortho hydroxyl group. The ^{1}H NMR spectrum showed a singlet at δ= 6.21 ppm corresponding to CH and a singlet at δ= 3.60 corresponding to the methoxy group. Moreover, the ^{13}C NMR spectra confirmed the structure by showing the CH and OCH_3 chemical shifts at δ= 153.7 and 51.0 ppm.



Scheme 26

2.11. Thermolysis of 2-alkoxy-2-benzyloxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines:

After studing the thermal chemistry of the dialkoxy oxadiazolines **104(a-d)** and the alkoxyaryloxy oxadiazolines **105(a-g)**, it was of interest to extend the scope of this work by studying the thermal chemistry of the alkoxybenzyloxy oxadiazolines **106(a-f)**. The 2-alkoxy-2-benzyloxy-Δ^3-1,3,4-oxadiazolines **106(a-f)** were prepared by reacting the crude acetoxymethoxy oxadiazoline **112** with the corresponding benzyl alcohols in CH_2Cl_2. The by-product **113** in the crude oxadiazoline **112**, which remained unreacted after the exchange, was selectively hydrolyzed by treating the solution with dilute base.

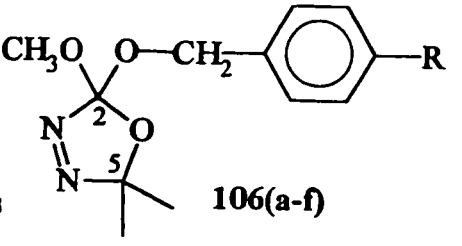


112 **106(a-f)**

The ^{1}H NMR spectra of the new oxadiazolines **106(a-f)** were comparable to those of the aryloxy analogues **105(a-g)** with methoxy signal at δ~ 3.48 and methyl peaks at δ~ 1.55 and 1.58 (Table 16). Also, the ^{1}H NMR spectra showed two doublets at δ ~4.8 and 4.7 ppm, due to the diastereotopic benzylic methylene groups of the oxadiazolines **106(a-f)**.

The ^{13}C NMR spectra showed the characteristic C-2 and C-5 signals at δ= ~136 and ~118 ppm, respectively, indicating the presence of the oxadiazoline ring. In addition a peak corresponding to the benzylic carbon at ~66 ppm was observed (Table 16). The mass spectra showed the highest m/z values corresponding to the benzylic cation $(CH_2\text{-}C_6H_4\text{-}X)^+$ when run in the EI mode.

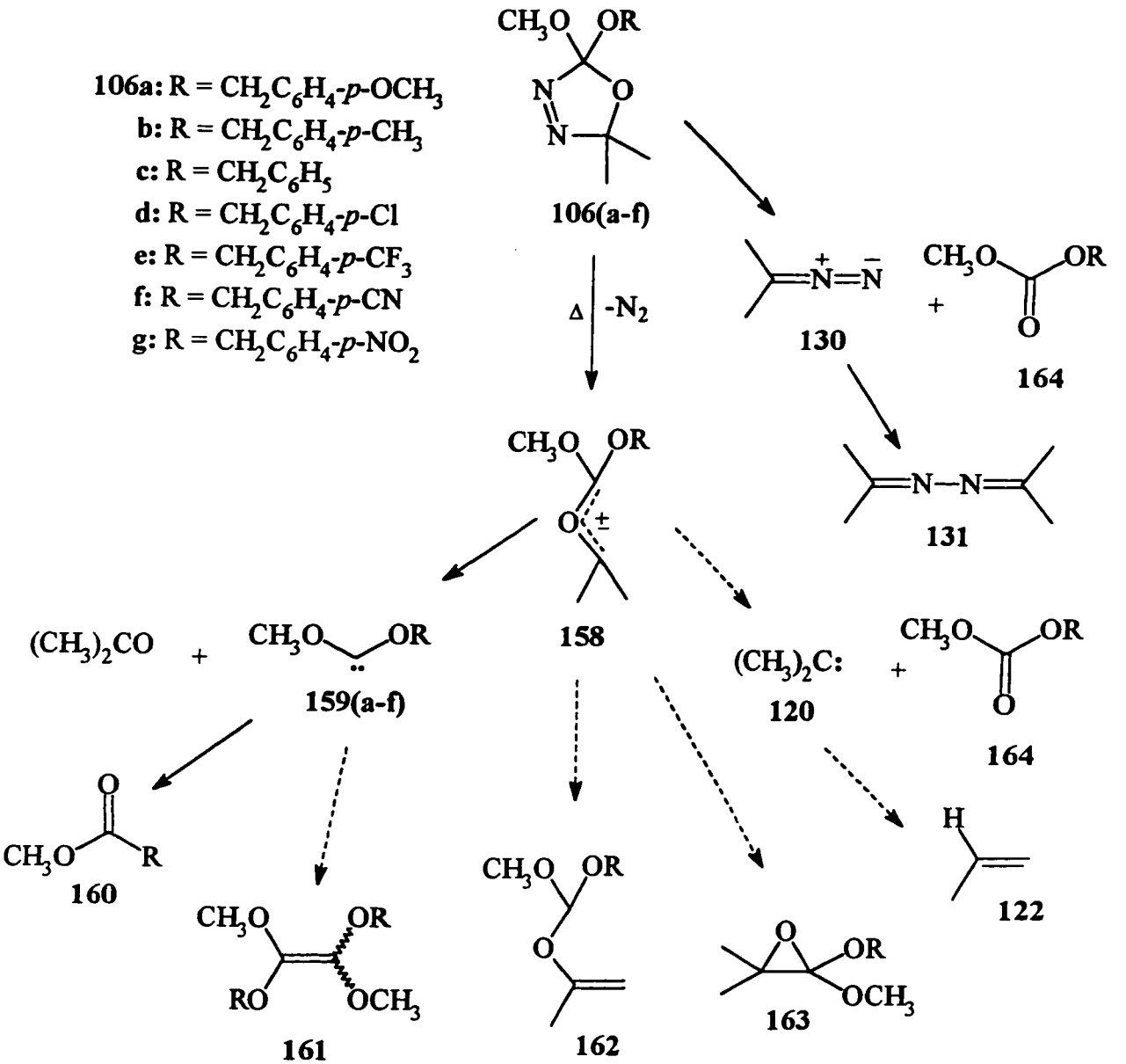
Thermolysis of the oxadiazolines **106** in benzene at 100 °C took the course outlined in Scheme 27. The mechanism involves the cycloreversion of the oxadiazoline **106** to N_2 and the carbonyl ylide **158** which doesn't undergo any of the known ylide reactions except unidirectional fragmentation to form acetone and $MeO(ArCH_2O)C:$, carbene **159**.



106(a-f)

Table 16: Selected ^{1}H NMR and ^{13}C NMR chemical shifts (ppm) for oxadiazolines106(a-f) in $CDCl_3$

Oxadiazoline	^{1}H NMR (200 MHz)	^{13}C NMR (50 MHz)
106a R= OCH_3	4.74 (s, 1H, CH), 4.66 (s, 1H, CH), 3.48 (s, 3H, OCH_3), 1.58 (s, 3H, CH_3), 1.55 (s, 3H, CH_3)	136.9 (C-2), 119.2 (C-5), 66.4 (OCH_2), 51.9 (OCH_3), 24.1 (CH_3), 23.9 (CH_3).
106b R= CH_3	4.79 (s, 1H, CH), 4.69 (s, 1H, CH), 3.48 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.54 (s, 3H, CH_3)	137.6 (C-2), 119.4 (C-5), 66.6 (OCH_2), 52.0 (OCH_3), 24.0 (CH_3), 21.1 (CH_3).
106c R= H	4.81 (s, 1H, CH), 4.78 (s, 1H, CH), 3.50 (s, 3H, OCH_3), 1.58 (s, 3H, CH_3), 1.55 (s, 3H, CH_3)	136.9 (C-2), 119.3 (C-5), 66.7 (OCH_2), 52.0 (OCH_3), 24.1 (CH_3), 24.1 (CH_3).
106d R= Cl	4.81 (s, 1H, CH), 4.72 (s, 1H, CH), 3.47 (s, 3H, OCH_3), 1.58 (s, 3H, CH_3), 1.53 (s, 3H, CH_3)	137.6 (C-2), 119.4 (C-5), 65.9 (OCH_2), 51.9 (OCH_3), 24.1 (CH_3), 24.0 (CH_3).
106e R= CF_3	4.93 (s, 1H, CH), 4.83 (s, 1H, CH), 3.48 (s, 3H, OCH_3), 1.59 (s, 3H, CH_3), 1.54 (s, 3H, CH_3)	136.9 (C-2), 119.6 (C-5), 65.9 (OCH_2), 52.0 (OCH_3), 24.2 (CH_3), 23.9 (CH_3).
106f R= NO_2	4.95 (s, 1H, CH), 4.93 (s, 1H, CH), 3.47 (s, 3H, OCH_3), 1.58 (s, 3H, CH_3), 1.55 (s, 3H, CH_3)	136.8 (C-2), 119.8 (C-5), 65.5 (OCH_2), 52.0 (OCH_3), 24.2 (CH_3), 23.9 (CH_3).


106a: R = CH2C6H4-p-OCH3
b: R = CH2C6H4-p-CH3
c: R = CH2C6H5
d: R = CH2C6H4-p-Cl
e: R = CH2C6H4-p-CF3
f: R = CH2C6H4-p-CN
g: R = CH2C6H4-p-NO2
106(a-f)
Δ -N2
130
164
131
158
(CH3)2CO
159(a-f)
(CH3)2C:
120
164
160
161
162
163
122

Scheme 27

The formation of the carbene dimer is usually taken as diagnostic of carbene generation; however in this case there was no evidence of the formation of the carbene dimer **161**. Instead, the evidence of the intermediacy of the carbene **159** came from the observation of the product **160** which resulted from the 1,2-migration of the benzyl group to the carbene centre (Table 17). The rearrangement products **160(a,c,e,f)** were isolated by chromatography and identified using ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy as well as mass spectrometry. Also, ^{1}H and ^{13}C chemical shifts of **160(a,c)** corresponded to those of authentic samples. The ^{1}H NMR spectra of **160(a,c,e,f)** showed the OCH_3 signal at δ ~ 3.67-3.72 ppm and the CH_2 peak at δ ~ 3.55-3.75 ppm (Table 18). Further evidence for the formation of **160(a,c,e,f)** came from their ^{13}C NMR spectra. These spectra contained the CH_2 peak at δ ~ 40.7 ppm which is characteristic of phenyl acetic acid derivatives.

Table 17: Products yields (%) from the thermolysis of oxadiazolines **106(a-f)** in C_6D_6

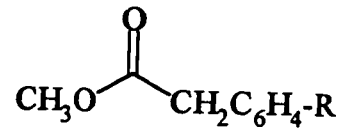
R **106**	CH_3O_2CR **160**	CH_3OCO_2R **164**	azine **131**	Me_2CO
a: $CH_2C_6H_4$-*p*-OCH_3	35	25	8	53
b: $CH_2C_6H_4$-*p*-CH_3	25	21	9	49
c: $CH_2C_6H_5$	20	20	13	45
d: $CH_2C_6H_4$-*p*-Cl	21	26	10	47
e: $CH_2C_6H_4$-*p*-CF_3	20	25	11	52
f: $CH_2C_6H_4$-*p*-NO_2	19	23	8	51

It seems that the benzyl migration process is somewhat sensitive to the p-substituents in the carbene **162**. The percentage yield of **160** (Table 17) can be used as a measure of the ease of formation of these phenyl acetic acid derivatives. It is observed that *p*-OCH_3 enhances

the formation of **160a**, in comparison with the *p*-CF_3 and *p*-NO_2 which reduce the yields of **160e** and **160f**. Probably the benzyl group is migrating with some cationic character which is stabilized by electron donating groups such as OCH_3.

There is no direct precedence for the benzyl migration of the benzyloxymethoxycarbenes. In the literature, benzyloxyhalocarbenes[40,41] are reported to fragment rather than forming benzyl migration products. Although the electronic distribution of the benzyloxyhalocarbene is different from that of the carbene **160**, there is evidence of the formation of the benzylic cation in the fragmentation process. This benzylic cation formation is consistent with the partial cationic charge in the 1,2 migration process in this study.

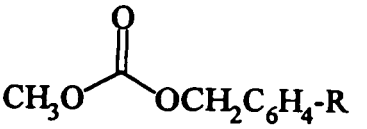
Table 18: Selected ^1H and ^{13}C NMR chemical shifts (ppm) for **160(a,c,e,f)** in $CDCl_3$



R	OCH_3	CH_2	OCH_3	CH_2
a: *p*-OCH_3	3.67	3.55	51.8	40.1
c: *p*-H	3.66	3.60	51.9	40.8
e: *p*-CF_3	3.70	3.68	51.9	40.7
f: *p*-NO_2	3.75	3.72	52.3	40.7

As in case of the alkoxyaryloxy oxadiazolines **105(a-g)**, acetone azine **131** and the benzyl methyl carbonates **164** were found among the thermolysis products. Those originate from the competitive fragmentation of the oxadiazolines **106(a-f)** (Scheme 22). The benzyl methyl carbonates **164(a,c,e,f)** were isolated. The ^1H NMR showed OCH_3 at ~3.76 and CH_2 at ~5.21 ppm. Also the ^{13}C NMR showed OCH_3, CH_2, C=O at ~54.6, 69.4, and 155 ppm, respectively (Table 19).

Table 19: Selected ^{1}H and ^{13}C NMR chemical shifts (ppm) for 164(a,c,e,f) in $CDCl_3$



R	OCH_3	OCH_2	OCH_3	OCH_2	C=O
a: *p*-OCH_3	3.76	5.08	54.6	69.4	155.6
c: *p*-H	3.76	5.14	54.5	69.3	155.4
e: *p*-CF_3	3.81	5.21	54.9	68.4	155.5
f: *p*-NO_2	3.83	5.26	55.1	67.8	155.3

2.12. Rate constants for thermolysis of 2-alkoxy-2-benyloxy-Δ^3-1,3,4-oxadiazolines:

The unimolecular fragmentation of the oxadiazolines **106(a-f)** was followed by ^{1}H NMR spectroscopy using peak areas which were normalized to that of an internal standard (toluene, δ= 2.19 ppm). Compounds **106(a-f)** decomposed in C_6D_6 at 100 °C with first order kinetics, with correlation coefficients typically better than 0.980. Rate constants are correlated with the Hammett substituent constant (σ) with ρ(100 °C)= 0.12. The effects of p-substituents in the benzyloxy group at C-2 on the rate constant of thermolysis of **106(a-f)** at 100 °C are indicated in Table 19 (see Appendix II for data).

The results indicate that changes in the p-substituents of the oxadiazoline **106** have little effect on the rate of decomposition. The small value of ρ(0.12) is attributed to the remote position of the substituents (i.e. not interacting conjugatively with the benzyloxy oxygen). However, the general effect of going from p-OCH_3 to p-NO_2 is to increase the rate of deomposition of the benzyloxymethoxy oxadiazolines **106(a-f)**. This observation is consistent with the fact that electron withdrawing groups stabilize the anion at the C-2 of the

carbonyl ylide **158** better than electron donating groups, thereby favoring the decomposition of the oxadiazoline to the ylide.

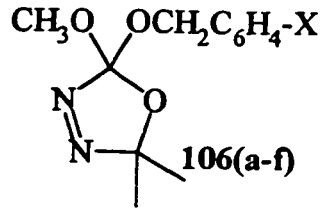


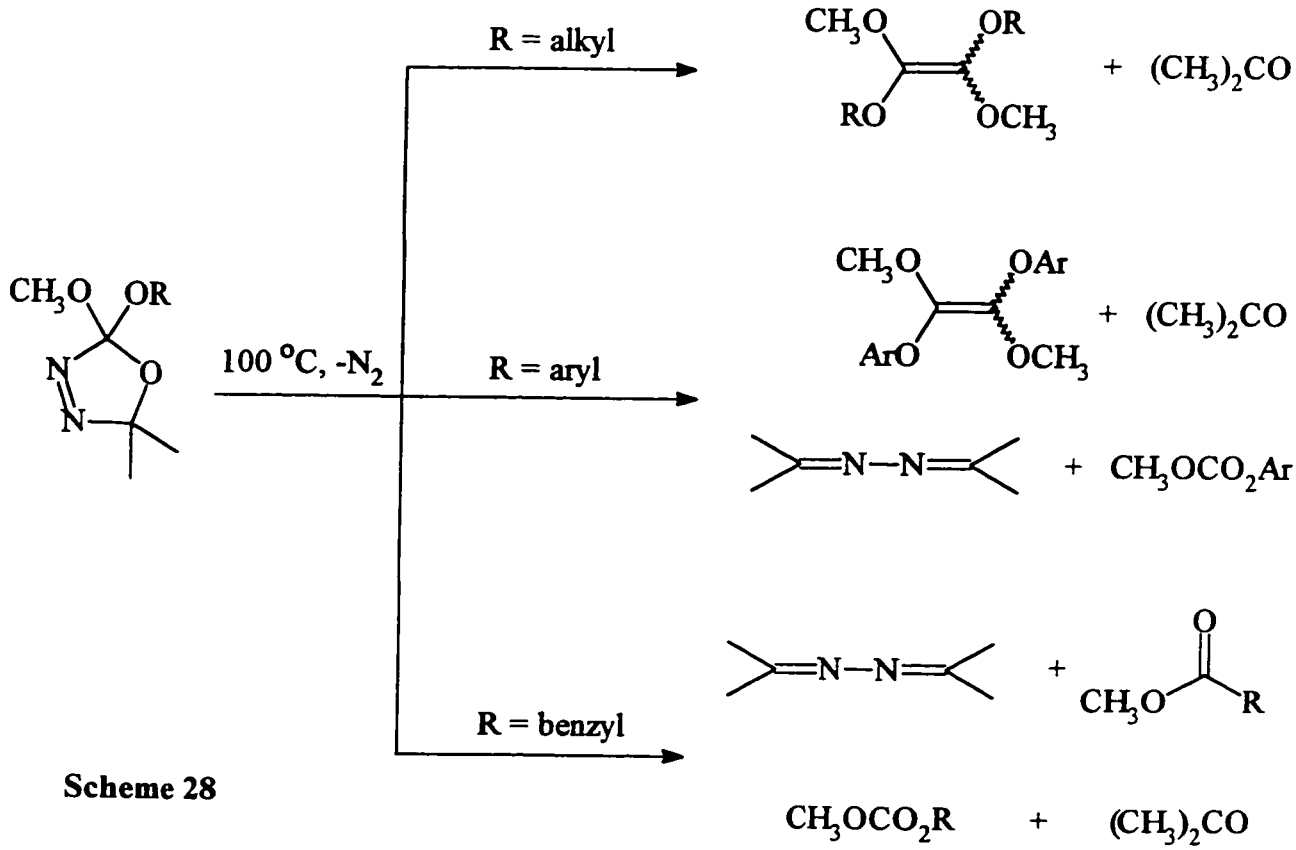
Table 20: Substituent effects on the rate of decomposition of benzyloxymethoxy oxadiazolines **106(a-f)** (in C_6D_6 at 100 °C)

Oxadiazoline **106** X	k^a (10^{-5} s^{-1})	$t_{1/2}{}^b$	$k_X/k_H{}^c$	$\log(k_X/k_H)$	$\sigma_X{}^d$	correlation coefficient[e]
a: *p*-OCH_3	2.09	9.21	0.889	-0.051	-0.27	0.9930
b: *p*-CH_3	2.11	9.08	0.902	-0.044	-0.17	0.9738
c: *p*-H	2.35	8.19	1.000	0.000	0.00	0.9903
d: *p*-Cl	2.55	7.55	1.085	0.035	0.23	0.9870
e: *p*-CF_3	2.62	7.35	1.115	0.047	0.54	0.9848
f: *p*-NO_2	2.83	6.80	1.109	0.045	0.78	0.9802

a. Rate constant of thermolysis at 100 °C
b. Half life (hrs)
c. Relative rate constants k (**106**-X) / k (**106**-H)
d. Hammett substituent contants (σ_{para})
e. Correlation coefficient of ln ($[\mathbf{106}]_t$) / ($[\mathbf{106}]_o$) vs time

2.13 Conclusion:

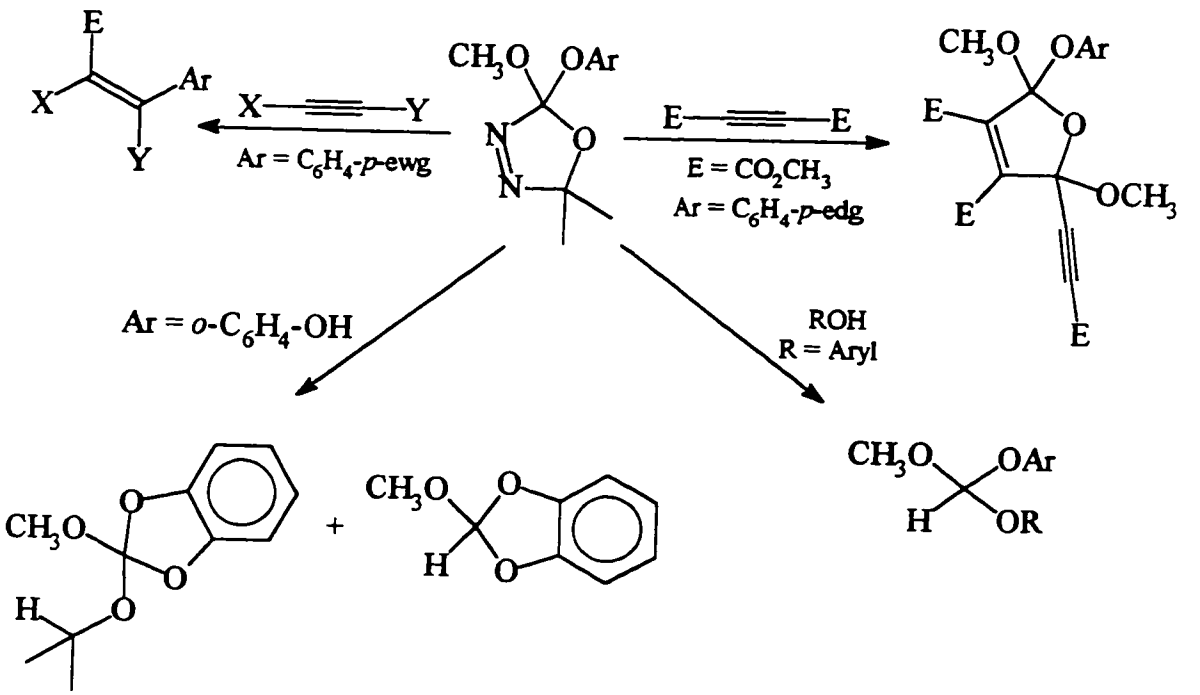
It can be concluded that while the 2,2-dialkoxy, 2-alkoxy-2-aryloxy and 2-alkoxy-2-benzyloxy-Δ^3-1,3,4-oxadiazolines are structurally similar their thermolysis chemistry is different. The 2,2-dioxy-Δ^3-1,3,4-oxadiazolines are very stable at room temperature, but at 100°C they fragment to dialkoxy, alkoxyaryloxy and alkoxybenzyloxycarbenes, respectively. The thermal fragmentation of the 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines (104) is established to be unidirectional. On the other hand, the thermolyses of the 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazolines (105) and the 2-alkoxy-2-benzyloxy-Δ^3-1,3,4-oxadiazolines (106) are multidirectional with the carbene formation as the major course (Scheme 28).



Scheme 28

The reaction of the alkoxyaryloxycarbenes with alkynes led to the formation of substituted alkenes. The mechanism of this process indicates the formation of a vinylcarbene intermediate followed by intramolecular aromatic substitution. In addition the alkoxyaryloxycarbenes were trapped inter- and intramolecularly *via* insertion reactions (Scheme 29).

In summary, the 2,2-dioxy-Δ^3-1,3,4-oxadiazolines have been synthesized in good yields and they have proven to be good sources of dioxycarbenes. The exchange method proved to be a suitable synthetic route for new oxadiazolines that could not be synthesized by the lead tetraacetate oxidation method.



Scheme 29

CHAPTER 3

EXPERIMENTAL

3.1. General:

Melting points were determined on a Thomas Hoover capillary melting point apparatus.

Nuclear magnetic resonance (NMR) spectra were recorded on Bruker AM-200, Bruker AM-300, or Bruker AM-500 spectrometers with a 5mm dual frequency ^{1}H-^{13}C probe. The proton spectra were acquired at 200.13 MHz on the AM-200, 300.13 MHz on the AM-300, and 500.14 MHz on the AM-500. $CDCl_3$ was used as a solvent, unless otherwise noted. The internal standard was TMS or the residual CH signal in $CDCl_3$. Chemical shifts were reported in delta (δ) units (ppm) downfield from TMS. The multiplicity patterns are : s= singlet, d= doublet, t= triplet, m= multiplet, bs= broad singlet. The coupling constants are reported in Hertz (Hz).

^{13}C NMR spectra were acquired at 125.76 MHz on the AM-500, or at 75.46 MHz on the AM-300, or at 50.32 MHz on the AM-200. The peaks are reported in ppm referenced to the 77.00 ppm peak of $CDCl_3$. Chemical shifts are reported in δ values (ppm) followed by the carbon type.

Analytical thin layer chromatography (TLC) was conducted by using plastic-backed, Merck Kieselgel 60 F_{254}, 0.2 mm silica plates. Preparative chromatographic separations was carried out using centrifugal chromatography on silica (Merck Kiesegel 60 PF_{254}) coated

plates, 2 mm thick, spinning in a Chromatotron model 17924T apparatus. Compounds were visualized by means of UV light (254 nm).

Infrared spectra (IR) were recorded on a Bio-Rad FTS-40 spectrometer and are reported in wavenumbers (cm^{-1}).

Low resolution EI and CI mass spectra (LRMS) were obtained using a VG Analytical ZAB-E double focusing mass spectrometer. Typical experimental conditions were as follows: electron energy= 70 eV, source temperature= 200 °C. Samples were introduced by direct insertion probe with pressure= 2×10^{-6} mbar for EI and 4×10^{-5} mbar for CI.

Gas chromatographic analysis were done on a Varian VISTA 6000 instrument equipped with an off column flash injector and a flame ionization detector (FID) at 300 °C. GC/MS determinations were obtained using a Hewlett Packard MSD.

Chromatography solvents (EtOAc, hexanes) were distilled before use.

3.2. Synthesis of 2-alkoxycarbonyl hydrazones of acetone (108):

The following alkoxycarbonyl hydrazines were purchased from Aldrich Chemical Co. and were used as supplied: Methyl hydrazino carboxylate (methoxycarbonyl hydrazine, methyl carbazate), ethyl carbazate, *tert*-butyl carbazate. The hydrazones were prepared by refluxing of the alkoxycarbonyl hydrazines **107(a-c)** (0.04 mol) in acetone (0.2 mol) for two hours. Magnesium sulphate ($MgSO_4$) was added as drying agent to remove the water produced in the reaction. The products were recovered after filtration of the reaction mixture, followed by evaporation of the acetone. The hydrazones were obtained in satisfactory purity and recrystallization was not required.

1-Ethoxy-carbonyl-2-(2-propylidene) hydrazone (108a):

White solid, 83% yield, mp 64 - 65 °C; (lit.[52] mp 74-75 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.47 (bs, 1H, NH), 4.26 (m, ^3J = 7.1 Hz, 2H, OCH_2), 2.08 (s, 3H, CH_3), 1.86 (s, 3H, CH_3), 1.32 (t, ^3J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.2 (C=O), 150.8 ($\underline{C}(CH_3)_2$, 61.5 ($\underline{C}H_2$), 25.1 ($\underline{C}H_3$), 16.0 ($\underline{C}H_3$), 14.4 ($CH_2\underline{C}H_3$). MS (EI) m/z: 130 (100%), 129 (10%), 99 (10%), 85 (20%), 72 (12%), 56 (12%). MS (CI, NH_3) m/z: 162 ($(M+NH_4)^+$, 5%), 145 (M^++H, 100%).

1-*tert*-Butoxy-carbonyl-2-(2-propylidene) hydrazone (108b):

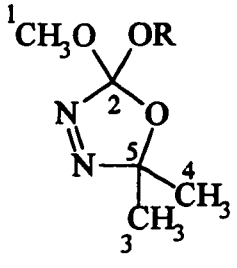
White solid[53], 80% yield, mp 81 - 83 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.40 (bs, 1H, NH), 2.07 (s, 3H, CH_3), 1.84 (s, 3H, CH_3), 1.51 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 152.9 (C=O), 149.8 ($\underline{C}(CH_3)_2$, 80.8 ($\underline{C}(CH_3)_3$, 25.3 (CH_3), 22.2 ($C(\underline{C}H_3)_3$, 15.9 (CH_3). MS (EI) m/z: 172 (M^+, 3%), 99 (M^+-$OC(CH_3)_3$, 25%), 57 (100%). MS (CI, NH_3) m/z: 190 ($(M+NH_4)^+$, trace), 173 (M^++H, 20%), 117 (100%), 73 (15%), 52 (10%). MS (HR) m/z: calculated for $C_8H_{16}N_2O_2$ 172.1212; found 172.1219.

1-Methoxy-carbonyl-2-(2-propylidene) hydrazone (108c):

White solid, 89% yield, mp 84 - 86 °C; (lit.[54] mp 90-92 °C) ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.62 (bs, 1H, NH), 3.83 (s, 3H, OCH_3), 2.05 (s, 3H, CH_3), 1.84 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.8 (C=O), 151.0 ($\underline{C}(CH_3)_2$, 52.7 ($O\underline{C}H_3$), 25.1 ($\underline{C}H_3$), 16.1 ($\underline{C}H_3$). MS (EI) m/z: 130 (M^+, 100%), 115 (M^+-CH_3, 45%), 83 (47%), 71 (45%), 56 (41%). MS (CI, NH_3) m/z: 148 ($(M+NH_4)^+$, 2%), 131 (M^++H, 100%). MS (HR) m/z: calculated for $C_5H_{10}N_2O_2$ 130.0742, found 130.0749.

3.3. Synthesis of 2-alkoxy-2-methoxy-Δ^3-1,3,4-oxadiazoline (LTA procedure):

The general procedure[13] was followed for the oxidation of the hydrazones 108(a-c) with the corresponding absolute alcohol or a mixture of CH_2Cl_2 containing the alcohol. Solid lead tetraacetate, $Pb(OAc)_4$ (0.04 mol) was slowly added to an ice cooled solution of the hydrazone (0.038 mol) and 125 ml of the alcohol and/or methylene chloride. The solution was stirred during the addition of the lead tetraacetate, and the stirring continued overnight. The precipitate of lead(II) salt that was formed was filtered off. The organic layer was neutralized using 10% $NaHCO_3$, then washed once with water before it was dried over magnesium sulphate. The solution was filtered and the solvent was removed in vacuo. The crude oxadiazolines were purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent. The following arbitrary numbering system is used in describing spectra.



104(a-d)

2-Ethoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (104a):

Oil, 65% yield (LTA oxidation method); 90% yield (exchange method); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.71 (q, ^3J = 7.1 Hz, 1H, OCH_2), 3.68 (q, ^3J = 7.1 Hz, 1H, OCH_2), 3.26 (s, 3H, OCH_3), 1.26 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.03 (t, ^3J = 7.1 Hz, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 137.9 (C2), 118.6 (C5), 60.5 ($\underline{C}H_2$), 51.6 (C1), 23.9 (C3 or C4),

23.8 (C4 or C3), 15.2 ($CH_2\underline{C}H_3$). MS (EI) m/z: 146 (M^+-N_2, 18%), 125 (24%), 105 (100%), 77 (44%) (molecular ion not observed). MS (CI, NH_3) m/z: 175 (M^++H, 8%), 105 (17%), 80 (100%).

2-Methoxy-2-*tert*-butoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (104b):

Oil, 50% yield (LTA oxidation method); 67% yield (exchange method); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.32 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.51 (s, 3H, CH_3), 1.41 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 137.4 (C2), 118.3 (C5), 78.8 ($\underline{C}(CH_3)_3$), 51.4 (C1), 29.9 ($C(\underline{C}H_3)_3$), 24.0 (C3 or C4), 23.7 (C4 or C3). MS (EI) m/z: 185 (12%), 172 (22%), 145 (M^+-$C(CH_3)_3$, 42%), 129 (M^+-$OC(CH_3)_3$, 85%), 116 (100%), 99 (19%) (molecular ion not observed). MS (CI, NH_3) m/z: 203 (M^++H, trace), 173 (M^++H-N_2, 57%), 134 (10%), 127 (40%), 98 (28%), 73 (14%).

2-Isopropoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (104c):

Oil, 50% yield (LTA oxidation method); 74% yield (exchange method); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.23 (m, 1H, OCH), 3.41 (s, 3H, OCH_3), 1.54 (d, 6H, $C(CH_3)_2$), 1.26 (s, 3H, CH_3), 1.23 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 137.2 (C2), 118.3 (C5), 68.3 ($\underline{C}H$), 51.5 (C1), 23.9 ($CH(\underline{C}H_3)_2$), 23.4 (C3 or C4), 23.3 (C4 or C3). MS (EI) m/z: 160 (M^+-N_2, 3%), 129 (160-OCH_3, 23%), 118 (160-$C(CH_3)_2$, 12%), 101 (7%), 77 (25%), 73 (50%), 59 ($OCH(CH_3)_2^+$, 100%), 43 (51%) (molecular ion not observed). MS (CI, NH_3) m/z: 189 (M^++H, 20%), 164 (85%), 159 (M^++H-OCH_3, 25%), 150 (24%), 136 (100%), 120 (30%), 103 (15%), 88 (27%), 77 (24%), 58 (38%).

2-Methoxy-2-propoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (104d):

Oil, 17% yield (LTA oxidation method); 92% yield (exchange method); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.66 (m, ^3J = 6.6 Hz, 2H, OCH_2), 3.46 (s, 3H, OCH_3), 1.62 (m, ^3J = 6.6 & 7.3 Hz, 2H, CH_2), 1.54 (s, 6H, $C(CH_3)_2$), 0.93 (t, ^3J = 7.3 Hz, 3H, CH_3). Total integral of 1.62 & 1.54 peaks was satisfactory. ^{13}C NMR (50 MHz, $CDCl_3$) δ: 137.0 (C2), 118.6 (C5), 60.1 ($O\underline{C}H_2$), 51.6 (C1), 22.6 ($\underline{C}H_2$), 23.9 (C3,C4), 10.2 ($\underline{C}H_3$). MS (EI) m/z: 185 (15%), 167 (10%), 149 (43%), 129 (M^+-$OCH_2CH_2CH_3$, 30%), 112 (15%), 97 (28%), 81 (49%), 69 (100%), 57 (65%) (molecular ion not observed). MS (CI, NH_3) m/z: 206 ($(M+NH_4)^+$, 13%), 189 (M^++H, 16%), 157 (42%), 136 (100%), 129 (35%), 119 (20%), 101 (38%), 73 (20%), 60 (59%).

3.4. Synthesis of 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (112):

The general[48] procedure was followed for the oxidation of 1-methoxycarbonyl-2-(2-propylidene) hydrazone (**108c**) with $Pb(OAc)_4$ and HOAc. To an ice cooled solution of the carbomethoxy hydrazone of acetone (**108c**) (5.3 gm, 41 mmol) and acetic acid (1 ml) in CH_2Cl_2, solid lead tetraacetate (19 gm, 43 mmol) was added. The mixture was stirred during addition of LTA and stirring was continued overnight while allowing the mixture to warm to room temperature. Pb(II) salts were then vacuum filtered and the organic layer was neutralized using 10% $NaHCO_3$. After extraction and drying over anhydrous magnesium sulfate, the excess solvent was evaporated. The oxadiazoline **112** was obtained in 55-60%, combined with 30% of an acyclic byproduct **113**. Partial separation of **112** from **113** is possible by bulb to bulb distillation under vacuum, but this proccess is not necessary for subsquent reactions.

2-Acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (112):

Oil, 55-60% yield; ^{1}H NMR (200 MHz, $CDCl_3$)[48] δ: 3.56 (s, 3H, OCH_3), 2.12 (s, 3H, $OC(O)CH_3$), 1.64 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 166.4 (C=O), 134.0 (C2), 122.3 (C5), 52.6 ($O\underline{C}H_3$), 24.2 ($\underline{C}H_3$), 21.7 ($\underline{C}H_3$), 19.7 ($C(O)\underline{C}H_3$). MS (EI) m/z: 129 (M^+-$OC(O)CH_3$), 117, 73, 59, 43 (100%), (molecular ion not observed). MS (CI, NH_3) m/z: 206 $(M+NH_4)^+$, 189 (M^++H).

Methyl-2,3-diaza-4-methyl-4-acetoxypent-2-enoate (113):

Oil, 30% yield, ^{1}H NMR (200 MHz, $CDCl_3$)[48] δ: 3.98 (s, 3H, CO_2CH_3), 2.11 (s, 3H, $OC(O)CH_3$), 1.62 (s, 6H, $C(CH_3)_2$). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 169.1 ($\underline{C}(O)CH_3$), 161.8 ($\underline{C}O_2CH_3$), 101.7 ($\underline{C}(CH_3)_2$), 54.8 ($CO_2\underline{C}H_3$), 24.2 (CH_3), 21.7 (CH_3). MS (EI) m/z: 129 (M^+-O_2CCH_3, 101, 73, 59, 43(100%), (molecular ion not observed). MS (CI, NH_3) m/z: 206 $(M+NH_4)^+$.

3.5. Exchange method of synthesis: Preparation of 2,2-dioxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines (104, 105, 106):

To an acidic CH_2Cl_2 solution (1.0 ml acetic acid in 25 ml CH_2Cl_2) containing **112** and **113** (3.58 mmol of **112**); alcohol or phenol (7.16 mmol) was added. The reaction solution was refluxed for 24 hrs or more until completion of the reaction. After allowing the mixture to cool, excess solvent was evaporated by means of a rotary evaporator. 5% KOH was added and the heterogeneous mixture was stirred for 1 hr. The aqueous mixture was extracted using CH_2Cl_2 and dried over magnesium sulfate. Evaporation of the solvent left the oxadiazolines

(104, 105, 106) which were analytically pure by ^1H NMR.

3.6. Thermolysis of 2-alkoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (104):

The 2-alkoxy-2-methoxy-Δ^3-1,3,4-oxadiazolines **104(a-d)** were dissolved in C_6D_6 (0.5 mL) containing (1 μl) C_6H_6 in a medium-walled NMR tube. After three cycles of degassing, at liquid nitrogen temperature, and thawing at room temperature, the tube was sealed under vacuum (10^{-2} mm of Hg). The thermolysis was carried out in a constant temperature oil bath 100±0.1°C, for 72 hours. At the end of the reaction, the yields of the thermolysis products were determined by NMR spectroscopy. The thermolysis products were analyzed using GC/Ms.

1,2-Dimethoxy-1,2-diethoxy ethene (117a):

70% yield[13]; cis : trans ratio (1 : 1) by GC/MS and NMR; ^1H NMR (500 MHz, C_6D_6) δ: 3.76 (q, 2H, ^3J = 7.1 Hz, OCH_2), 3.74 (q, 2H, ^3J = 7.1 Hz, OCH_2), 3.44 (s, 3H, OCH_3), 3.43 (s, 3H, OCH_3), 1.13 (t, 6H, ^3J = 7.1 Hz, CH_3). ^{13}C NMR (125.76 MHz, C_6D_6) δ: 140.88 (C=C), 140.76 (C=C), 65.87 (OCH_2), 57.60 (OCH_3), 57.44 (OCH_3), 15.14 (CH_3), 14.17(CH_3). MS (GCMS, EI) m/z: 176 (M^+, 19%), 147 (M^+-OCH_3, 26%), 119 (89%), 59 (CH_3CO, 100%), 47 (CH_3O_2, 82%).

1,2-Dimethoxy-1,2-di-*tert*-butoxy ethene (117b):

71% yield; cis : trans ratio (1 : 4) by NMR; ^1H NMR (500 MHz, C_6D_6) δ: 3.25 (s, 3H, OCH_3), 3.22 (s, 3H, OCH_3), 1.65 (s, 9H, $C(CH_3)_3$), 1.64 (s, 9H, $C(CH_3)_3$); (total integrals

were in satisfactory ratio). ^{13}C NMR (125.76 MHz, C_6D_6) δ: 141.93 (C=C), 49.92 (OCH_3), 49.80 (OCH_3), 24.02 ($C(CH_3)_3$).

1,2 Dimethoxy-1,2-di-*iso*-propoxy ethene (117c):

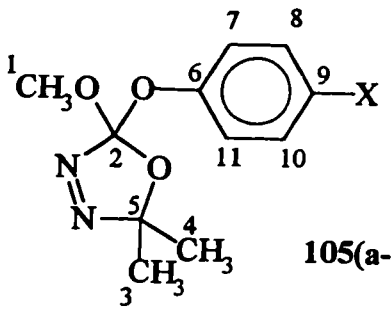
53% yield; cis : trans ratio (1 : 1.3) by NMR; ^1H NMR (500 MHz, C_6D_6) δ: 4.32-4.15 (m, 2H, OCH), 3.47 (s, 3H, OCH_3), 3.43 (s, 3H, OCH_3). ^{13}C NMR (125.76 MHz, C_6D_6) δ: 140.5 (C=C), 140.1 (C=C), 71.9 (CH), 71.4 (CH), 57.5 (OCH_3), 57.1 (OCH_3), 22.4 (CH_3), 22.2 (CH_3). MS (GCMS, EI) m/z: 204 (M^+, 3%), 161 (M^+-$CH(CH_3)_2$, 7%), 119 (161-$C(CH_3)_2$, 100%), 59 (100%), 47 (100%).

3.7. Rate constants of thermolysis of 2,2-dialkoxy-Δ^3-1,3,4-oxadiazolines:

2,2-Dialkoxy-Δ^3-1,3,4-oxadiazoline **104** (~0.1 mmol.) was dissolved in 0.5 mL C_6D_6 and 2 μL C_6H_6 (internal standard) in a medium walled NMR tube. After three cycles of degassing, at liquid nitrogen temperature, and thawing to room temperature, the tube was sealed under vacuum. The thermolysis was carried out in a constant temperature oil bath, at 100 ± 0.1°C. The tube was removed from time to time and chilled to room temperature with water. The methyl signals from **104** against the benzene signal afforded values of the concentration of the remaining oxadiazoline. The decomposition was followed through three half lives. The time outside the oil bath was not counted and time in the bath was not corrected for the warm up period for insertion of the samples at room temperature. The integrals of the disappearing methyl signals were measured and normalized against the benzene integral. The resultant plot of ln {(A-x) / A} vs. t in all thermolyses yielded a straight

line corresponding to standard first order plots.

3.8. Synthesis of 2-aryloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines 105(a-g): To a mixture of the 2-acetoxy-2-methoxy-Δ^3-1,3,4-oxadiazoline (112) and acylic product (113) (0.90 g, 3.58 mmol of oxadiazoline) in CH_2Cl_2 (35 mL) was added a p-substituted phenol (7.16 mmol) and acetic acid (1.0 mL). The resulting solution was refluxed for 72 hours. After cooling the reaction mixture, the excess solvent was evaporated by means of a rotary evaporator. KOH pellets were added and the heterogeneous mixture was stirred rapidly; after 1 hour, 50 mL. of water was added the mixture was stirred for 10 minutes. The organic layer was separated and dried over $MgSO_4$. Evaporation of the solvent left the oxadiazolines 105(a-g) which were analytically pure by ^1H NMR.



105(a-g)

2-Methoxy-2(4-methoxyphenoxy)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105a): Oil, 68% yield; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.08 (d, 2H, Ar, ^3J = 9.1 Hz), 6.80 (d, 2H, Ar, ^3J = 9.1 Hz), 3.76 (s, 3H, OCH_3 of Ar), 3.62 (s, 3H, OCH_3), 1.52 (s, 3H, CH_3), 1.20 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 156.6 (C9), 145.1 (C6), 136.8 (C2), 123.2 (C7,C11), 120.1 (C5), 113.9 (C8,C10), 55.3 ($O\underline{C}H_3$ of Ar), 52.3 (C1), 24.1 (C3 or C4), 23.3 (C4 or C3). MS (EI) m/z: 221 (M^+-OCH_3, 27%), 205 (42%), 149 (100%), 135

(COC_6H_4OMe, 33%), 129 (M^+-$CH_3OC_6H_4$, 58%), 123 (OC_6H_4OMe, 45%), 95 (15%), 73 (44%), 56 (29%) (molecular ion not observed). MS (CI, NH_3) m/z: 221 (8%), 200 (17%), 167 (38%), 149 (39%), 129 (100%), 124 ($CH_3OC_6H_4O$+H, 11%), 58 (10%).

2-Methoxy-2(4-methylphenoxy)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105b):

Oil, 65% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.07 (s, 4H, Ar), 3.60 (s, 3H, OCH_3), 2.30 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 1.26 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 149.55 (C6), 134.15 (C2), 129.60 (C8,C10), 121.61 (C7,C11), 120.35 (C5), 52.51 (C1), 24.20 (C3 or C4), 23.58 (C4 or C3), 20.71 ($\underline{C}H_3$). MS (EI) m/z: 205 (M^+-OCH_3, 9%), 199 (29%), 176 (18%), 149 (72%), 129 (M^+-$OC_6H_4CH_3$, 88%), 119 ($COC_6H_4CH_3$, 100%), 107 ($OC_6H_4CH_3$, 39%), 91 (58%), 73 (55%), 56 (24%), 42 (47%) (molecular ion not observed). MS (CI, NH_3) m/z: 254 ($(M+NH_4)^+$, 10%), 205 (5%), 184 (42%), 129 (100%), 58 (28%).

2-Methoxy-2-phenoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105c):

Oil, 61% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.12 - 7.33 (m, 5H, C_6H_5), 3.61 (s, 3H, OCH_3), 1.56 (s, 3H, CH_3), 1.27 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 151.7 (C6), 136.4 (C2), 128.7 (C8,C10), 124.2 (C9), 121.3 (C7,C11), 120.2 (C5), 52.1 (C1), 23.8 (C3 or C4), 23.2 (C4 or C3). MS (EI) m/z: 191 (M^+-OCH_3, 12%), 179 (M^+-N_2-CH_3, 17%), 153 (12%), 129 (M^+-PhO, 100%), 105 (PhCO, 74%), 94 (12%), 77 (60%) (molecular ion not observed). MS (CI, NH_3) m/z: 240 ($(M+NH_4)^+$, 5%), 191 (3%), 170 (24%), 129 (100%), 58 (19%).

2(4-Chlorophenoxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105d):

Oil, 68% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.25 (d, 2H, Ar, ^3J = 7.1 Hz), 7.13 (d, 2H, Ar, ^3J = 7.1 Hz), 3.57 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.34 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 150.55 (C6), 136.4 (C2), 129.74 (C9), 129.16 (C8,C10), 122.74 (C7,C11), 120.79 (C5), 52.53 (C1), 24.10 (C3 or C4), 23.77 (C4 or C3). MS (EI) m/z: 225 (M^+-OCH_3, 7%), 213 (M^+-N_2-CH_3, 11%), 169 (32%), 153 (22%), 139 (55%), 129 (M^+-OC_6H_4Cl, 100%), 111 (C_6H_4Cl, 30%), 99 (40%), 84 (39%), 73 (49%), 59 (24%), 42 (50%) (molecular ion not observed). MS (CI, NH_3) m/z: 276 ($(M+NH_4)^+$, 33%), 274 ($(M+NH_4)^+$, 100%), 225 (45%), 204 (60%), 186 (17%), 171 (95%).

2-Methoxy-2(4-trifluoromethylphenoxy)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105e):

Oil, 58% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.57 (d, 2H, Ar, ^3J = 8.7 Hz), 7.34 (d, 2H, Ar, ^3J = 8.7 Hz), 3.55 (s, 3H, OCH_3), 1.62 (s, 3H, CH_3), 1.42 (s, 3H, CH_3). ^{19}F NMR ($CDCl_3$ vs $CFCl_3$) δ: -62.2 (s, CF_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 158.25 (C6), 135.00 (C2), 126.60 (C8,C10), 120.53 (C7,C11), 120.15 (C5), 52.59 (C1), 24.03 (C3 or C4), 23.94 (C4 or C3). (Carbons coupled to fluorine were not observed). MS (EI) m/z: 265 (16%), 209 (14%), 162 (80%), 121 (100%), 92 (26%) (molecular ion not observed). MS (CI, NH_3) m/z: 205 (10%), 129 (100%).

2(4-Cyanophenoxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105f):

Oil, 67% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.62 (d, 2H, Ar, ^3J = 8.8 Hz), 7.35 (d, 2H, Ar, ^3J = 8.8 Hz), 3.53 (s, 3H, OCH_3), 1.84 (s, 3H, CH_3), 1.46 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.46 (C6), 135.76 (C2), 133.42 (C8,C10), 121.39 (C5), 120.48 (C7,C11),

118.38 (CN), 107.17 (C9), 52.38 (C1), 23.80 (C3 or C4), 23.72 (C4 or C3). MS (EI) m/z: 216 (M^+-OCH_3, 5%), 160 (22%), 129 (M^+-C_6H_4CN, 100%), 102 (C_6H_4CN, 9%), 73 (28%), 56 (12%) (molecular ion not observed). MS (CI, NH_3) m/z: 265 ($(M+NH_4)^+$, 15%), 248 (M^++H, 13%), 162 (M^++H-2CH_3, 10%), 129 (100%), 73 (11%), 58 (32%).

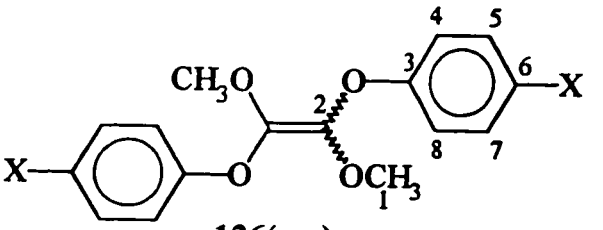
2(4-Nitrophenoxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (105g):

Oil, 62% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.21 (d, 2H, Ar, ^3J = 9.2 Hz), 7.39 (d, 2H, Ar, ^3J = 9.2 Hz), 3.53 (s, 3H, OCH_3), 1.65 (s, 3H, CH_3), 1.49 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.75 (C6), 142.24 (C8,C10), 134.34 (C2), 123.72 (C7,C11), 120.26 (C5), 118.37 (C9), 51.05 (C1), 22.49 (C3 or C4), 22.31(C4 or C3). MS (EI) m/z: 236 (M^+-OCH_3, 4%), 180 (19%), 150 (22%), 129 (M^+-$OC_6H_4NO_2$, 100%), 122 ($OC_6H_4NO_2$, 14%), 108 (9%), 92 (10%), 73 (12%), 59 (11%) (molecular ion not obsreved). MS (CI, NH_3) m/z: 285 ($(M+NH_4)^+$, 14%), 182 (30%), 152 (32%), 129 (100%), 110 (31%), 60 (19%).

3.9. Thermolysis of 2-aryloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines (105a-g):

A solution of 2-aryloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline **105** (1.0 mmol) in 30 mL of dry benzene was prepared. The solution was placed in a 50 mL thick walled glass tube. After three cycles of degassing at liquid nitrogen temperature, and thawing at room temperature, the tube was sealed under vacuum (10^{-2} mm of Hg). The thermolysis was carried out in a constant temperature oil bath 100±0.1°C, for 96 hours. At the end of the oxadiazoline thermolysis the tube was cooled to room temperature, opened and the solvent was evaporated

by means of a rotary evaporator. The residue was then purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.



126(a-g)

1,2-Di(4-methoxyphenoxy)-1,2-dimethoxy ethene (126a):

white solid, 57% yield; cis : trans ratio (1 : 1.46) by NMR; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.95 (d, 2H, Ar, ^3J = 9.1 Hz), 6.87 (d, 2H, Ar, ^3J = 9.1 Hz), 6.74 (d, 2H, Ar, ^3J = 9.1 Hz), 6.65 (d, 2H, Ar, ^3J = 9.1 Hz), 3.64 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3), 3.56 (s, 3H, OCH_3 of Ar), 3.36 (s, 3H, OCH_3 of Ar). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.1 (C6), 149.9 (C3), 149.7 (C3), 138.4 (C2), 116.9 (C4,C8), 116.7 (C4,C8), 114.5 (C5,C7), 114.3 (C5,C7), 58.0 (C1), 57.8 (C1), 55.4 (OCH_3 of Ar). MS (EI) m/z: 332 (M^+, 100%), 317 (M^+-CH_3, 53%), 289 (80%), 225 (25%), 193 (20%), 167 (85%), 123 (93%), 77 (C_6H_5, 45%), 59 (15%). MS (CI, NH_3) m/z: 333 ((M^++H), 100%), 289 (10%), 225 (10%), 167 (40%). MS (HR) m/z: calculated for $C_{18}H_{20}O_6$ 332.1260, found 332.1264.

1,2-Di(4-methylphenoxy)-1,2-dimethoxy ethene (126b):

white solid, 60% yield; cis : trans ratio (1 : 1.32) by NMR; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.08 (d, 2H, Ar, ^3J = 8.8 Hz), 7.04 (d, 2H, Ar, ^3J = 8.8 Hz), 7.01 (d, 2H, Ar, ^3J = 8.8 Hz), 6.92 (d, 2H, Ar, ^3J = 8.8 Hz), 3.63 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 2.24 (s, 3H, CH_3

of Ar), 2.21 (s, 3H, CH_3 of Ar). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.1 (C3), 154.0 (C3), 138.1 (C2), 131.8 (C6), 131.7 (C6), 129.7 (C5,C7), 129.6 (C5,C7), 115.6 (C4,C8), 115.5 (C4,C8), 57.8 (C1), 57.6 (C1), 20.2 (CH_3). MS (EI) m/z: 300 (M^+, 100%), 257 (62%), 209 (69%), 177 (17%), 151 (80%), 107 (20%), 91 (61%), 65 (22%). MS (CI, NH_3) m/z: 301 ((M^++H), 100%), 285 (20%), 257 (15%), 209 (40%), 193 (12%), 151 (100%), 108 (10%). MS (HR) m/z: calculated for $C_{18}H_{20}O_4$ 300.1362, found 300.1375.

1,2-Diphenoxy-1,2-dimethoxy ethene (126c):

white solid[11c], 46% yield; cis : trans ratio (1 : 1.37) by NMR; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.32-7.01 (m, 5H, C_6H_5), 3.67 (s, 3H, OCH_3), 3.54 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 156.1 (C3), 155.8 (C3), 138.2 (C2), 129.4 (C5,C7), 129.3 (C5,C7), 122.9 (C6), 122.6 (C6), 115.9 (C4,C8), 115.7 (C4,C8), 58.1 (C1), 57.9 (C1). MS (EI) m/z: 272 (M^+, 25%), 257 (M^+-CH_3, 30%), 229 (37%), 185 (30%), 137 (32%), 105 (12%), 77 (C_6H_5, 100%), 51 (22%). MS (CI, NH_3) m/z: 273 ((M^++H), 100%), 257 (10%), 229 (9%), 195 (20%), 137 (23%). MS (HR) m/z: calculated for $C_{16}H_{16}O_4$ 272.1049, found 272.1044.

1,2-Di(4-chlorophenoxy)-1,2-dimethoxy ethene (126d):

white solid, 56% yield; cis : trans ratio (1 : 1.30) by NMR; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.27 (d, 2H, Ar, ^3J = 9.0 Hz), 7.20 (d, 2H, Ar, ^3J = 9.0 Hz), 7.09 (d, 2H, Ar, ^3J = 9.0 Hz), 6.94 (d, 2H, Ar, ^3J = 9.0 Hz), 3.67 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.9 (C3), 154.6 (C3), 138.1 (C2), 129.3 (C4,C8), 129.2 (C4,C8), 127.7 (C6), 127.6 (C6), 117.1 (C5,C7), 58.1 (C1), 57.9 (C1). MS (EI) m/z: 342 (M^+, 70%), 340 (M^+,

100%), 327 (M^+-CH_3, 26%), 325 (M^+-CH_3, 45%), 297 (42%), 229 (50%), 171 (26%), 75 (20%), 59 (30%). MS (CI, NH_3) m/z: 343 ((M^++H), 62%), 341 ((M^++H), 100%), 229 (19%), 171 (23%), 118 (9%). MS (HR) m/z: calculated for $C_{16}H_{14}Cl_2O_4$ 340.0269, found 340.0275.

2,2-Di(4-trifluoromethylphenoxy)-1,2-dimethoxy ethene (126e):

white solid, 57% yield; cis : trans ratio (1 : 1.24) by NMR; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.63 (d, 2H, Ar, ^3J = 8.0 Hz), 7.57 (d, 2H, Ar, ^3J = 8.0 Hz), 7.10 (d, 2H, Ar, ^3J = 8.0 Hz), 7.09 (d, 2H, Ar, ^3J = 8.0 Hz), 3.71 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3). ^{19}F NMR ($CDCl_3$ vs $CFCl_3$) δ: -62.2 (s, CF_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.5 (C3), 138.2 (C2), 128.2 (q, C6), 126.9 (q, CF_3), 126.8 (q, CF_3), 120.1 (C4,C8), 117.2 (C5,C7), 58.4 (C1), 58.2 (C1). ($^1J_{CF}$ and $^2J_{CF}$ can't be calculated due to overlap of peaks). MS (EI) m/z: 408 (M^+, 50%), 393 (M^+-CH_3, 29%), 365 (22%), 335 (10%), 263 (90%), 205 (100%), 145 (28%). MS (CI, NH_3) m/z: 409 ((M^++H), 15%), 263 (25%), 205 (100%), 118 (25%), 60 (83%). MS (HR) m/z: calculated for $C_{18}H_{14}F_6O_4$ 408.0796, found 408.0796.

1,2-Di(4-cyanophenoxy)-1,2-dimethoxy ethene (126f):

white solid, 46% yield; cis : trans ratio (1 : 1.46) by NMR; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.59 (d, 2H, Ar, ^3J = 8.9 Hz), 7.07 (d, 2H, Ar, ^3J = 8.9 Hz), 7.67 (d, 2H, Ar, ^3J = 8.9 Hz), 7.14 (d, 2H, Ar, ^3J = 8.9 Hz), 3.73 (s, 3H, OCH_3), 3.57 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 159.2 (C3), 158.9 (C3), 138.1 (C2), 134.0 (C5,C7), 118.5 (CN), 116.6 (C4,C8), 106.7 (C6), 58.7 (C1), 58.4 (C1). MS (EI) m/z: 322 (M^+, 55%), 307 (M^+-CH_3, 79%), 279 (100%), 249 (11%), 235 (10%), 220 (35%), 204 (9%), 192 (35%). MS (CI, NH_3) m/z: 340 ($(M+NH_4)^+$, 100%). MS (HR) m/z: calculated for $C_{18}H_{14}N_2O_4$ 322.0954, found 322.0950.

1,2-Di(4-nitrophenoxy)-1,2-dimethoxy ethene (126g):

white solid, 52% yield; cis : trans ratio (1 : 1.45) by NMR; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.27 (d, 2H, Ar, ^3J = 9.2 Hz), 8.20 (d, 2H, Ar, ^3J = 9.2 Hz), 7.39 (d, 2H, Ar, ^3J = 9.2 Hz), 7.12 (d, 2H, Ar, ^3J = 9.2 Hz), 3.77 (s, 3H, OCH_3), 3.61 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 160.7 (C3), 160.3 (C3), 143.2 (C6), 138.1 (C2), 125.7 (C5,C7), 116.0 (C4,C8), 58.8 (C1), 58.4 (C1). MS (EI) m/z: 362 (M^+, 53%), 347 (M^+-CH_3, 100%), 331 (11%), 319 (29%), 240 (31%), 182 (100%), 122 (8%), 75 (7%). MS (CI, NH_3) m/z: 380 ($(M+NH_4)^+$, 100%), 294 (15%), 182 (25%), 133 (25%). MS (HR) m/z: calculated for $C_{16}H_{14}N_2O_8$ 362.0750, found 362.0751.

4-Cyanophenyl methyl carbonate (129f):

white solid, 16% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.70 (d, 2H, Ar, ^3J = 8.7 Hz), 7.33 (d, 2H, Ar, ^3J = 8.7 Hz), 3.94 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.1 (Ar), 153.1(C=O), 133.7 (Ar), 122.0 (Ar), 120.6 (CN), 118.0 (Ar), 55.7 (OCH_3). MS (EI) m/z: 177 (M^+, 39%), 133 (100%), 118 (22%), 103 (50%), 90 (91%), 84 (80%), 59 (75%). MS (CI, NH_3) m/z: 195 ($(M+NH_4)^+$, 100%), 129 (47%). MS (HR) m/z: calculated for $C_9H_7NO_3$ 177.0425, found 177.0429.

3.10. Rate constants of thermolysis of 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazolines:

A 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazoline **105** (~0.1 mmol.) was dissolved in 0.5 mL C_6D_6 and 2 μL $CH_3C_6H_5$ (internal standard) in a medium walled NMR tube. After three cycles of degassing, at liquid nitrogen temperature, and thawing to room temperature, the

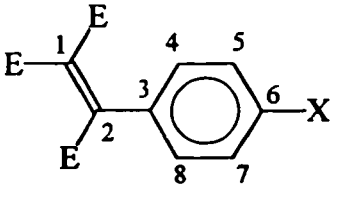
tube was sealed under vacuum. The thermolysis was carried out in a constant temperature oil bath, at 100 ± 0.1°C. The tube was removed from time to time and chilled to room temperature with water. The methyl signals from **105** against the toluene methyl signal afforded values of the concentration of the remaining oxadiazoline. The decomposition was followed through three half lives. The time outside the oil bath was not counted and time in the bath was not corrected for the warm up period for insertion of the samples at room temperature. The integral of the disappearing methyl signals were measured and normalized against the toluene methyl integral. The resultant plot of ln {(A-x) / A} vs. t in all thermolyses yielded a straight line corresponding to standard first order plots.

3.11. Addition reactions of alkoxyaryloxycarbenes:

3.11.1. Reactions with alkynes:

A. Dimethyl acetylenedicarboxylate (DMAD):

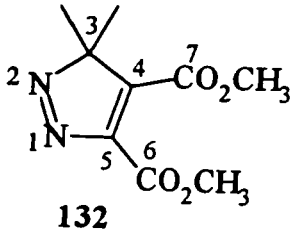
The oxadiazoline **106f** (0.50 mmol), DMAD (0.90 mmol) and benzene (30 mL) were sealed into a thick walled glass tube. Thermolysis was carried out in constant oil bath at 100±0.1°C, for 30 hours. At the end of the reaction, the excess solvent was evaporated by means of a rotary evaporator and the crude thermolysis products were purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.



137f

2-(4-Cyanophenyl)-1,1,2-tri(methoxycarbonyl) ethene (137f):

yellow oil; 45% yield; IR (film) υ 2240 cm^{-1} (C≡N), 1748, 1723 cm^{-1} (C=O), 1649 cm^{-1} (C=C); ^1H NMR (200 MHz, $CDCl_3$) δ: 7.70 (d, 2H, Ar, ^3J = 8.6 Hz), 7.49 (d, 2H, Ar, ^3J = 8.6 Hz), 3.87 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 165.94 (C=O), 163.88 (C=O), 162.81 (C=O), 144.6 (C2), 137.34 (C3), 134.08 (C5,C7), 128.38 (C1), 128.32 (C4,C8), 117.94 (C≡N), 113.65 (C6), 53.29 (OCH_3), 53.23 (OCH_3), 52.91 (OCH_3). MS (EI) m/z: 303 (M^+, 50%), 272 (M^+-OCH_3, 85%), 244 (M^+-OCH_3-C=O, 95%), 216 (M^+-CO_2Me-CO 15%), 200 (M^+-CO_2Me-CO_2, 50%), 176 (20%), 154 (100%), 127 (15%), 84 (20%), 59 (29%). MS (CI, NH_3) m/z: 321 ($(M+NH_4)^+$, 100%). MS (HR) m/z: Calculated for $C_{15}H_{13}NO_6$ 303.0743, found 303.0746.



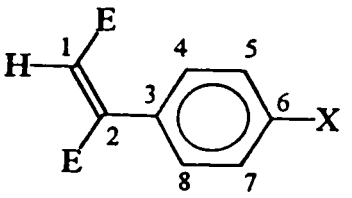
132

3,3-Dimethyl-3H-pyrazole-4,5-dicarboxylic acid dimethyl ester (132):

15% yield; IR (film) υ 1731 cm^{-1} (C=O), 1641 cm^{-1} (C=C), 1571 cm^{-1} (N=N); ^1H NMR (200 MHz, $CDCl_3$) δ: 4.00 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 1.58 (s, 6H, $C(CH_3)_2$). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 162.96 (C7), 160.81(C6), 153.62 (C4), 144.84 (C5), 97.41 (C3), 52.99 (2xOCH_3), 20.09 ($(CH_3)_2$). MS (EI) m/z: 212 (M^+, trace), 183 (12%), 169 (9%), 154 (55%), 141 (40%), 125 (38%), 109 (30%), 97 (45%), 84 (100%). MS (CI, NH_3) m/z: 213 (M^++H, 100%), 199 (M^++H-N, 25%), 185 (M^++H-N_2, 10%).

B. Methyl propiolate:

The oxadiazoline **106f** (0.50 mmol), methyl propiolate (0.90 mmol) and benzene (30 mL) were mixed in a thick walled glass tube. Thermolysis was carried out in constant oil bath at 100±0.1 °C, for 30 hours. At the end of the reaction, the excess solvent was evaporated by means of a rotary evaporator and the crude thermolysis products were purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.



142

1-(4-Cyanophenyl)-1,2-di(methoxycarbonyl) ethene (142):

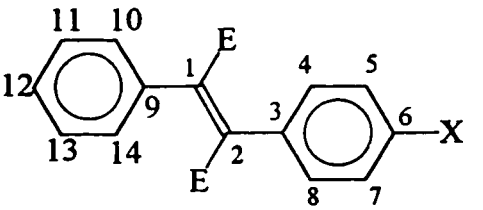
yellow oil; 35% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.68 (d, 2H, Ar, ^3J = 8.4 Hz), 7.34 (d, 2H, Ar, ^3J = 8.4 Hz), 7.08 (s, 1H, CH), 3.78 (s, 3H, OCH_3), 3.60 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 165.58 (C=O), 164.81 (C=O), 142.88 (C2), 138.65 (C3), 131.57 (C5,C7), 129.99 (C1), 129.63 (C4,C8), 118.51 (C≡N), 112.42 (C6), 53.18 (OCH_3), 52.09 (OCH_3). MS (EI) m/z: 245 (M^+, 80%), 230 (M^+-CH_3, 10%), 214 (M^+-OCH_3, 78%), 186 (M^+-CO_2CH_3, 100%), 162 (27%), 127 (55%), 84 (65%). MS (CI, NH_3) m/z: 263 ($(M+NH_4)^+$, 100%). MS (HR) m/z: Calculated for $C_{13}H_{11}NO_4$ 245.0688, found 245.0687.

In a ^{1}H NOE experiment, irradiation of the vinyl (CH) singlet at 7.08 ppm caused an enhancement of both the singlet at 3.78 ppm (OCH_3) and the singlet at 3.60 ppm (OCH_3). In addition the irradiation of the OCH_3 singlet at 3.60 ppm led to an enhancement of only the

(C<u>H</u>) proton singlet at 7.08 ppm.

C. Ethyl phenyl propiolate:

The substituted alkene **(147)** was synthesized following the above procedure. The oxadiazoline **106f** (0.50 mmol), methyl propiolate (0.90 mmol) and benzene (30 mL) were mixed in a thick walled glass tube. Thermolysis was carried out in constant oil bath at 100±0.1°C, for 30 hours. At the end of the reaction, the excess solvent was evaporated by means of a rotary evaporator and the crude thermolysis products were purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.



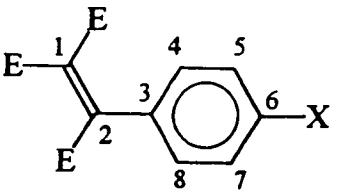
147

1-Methoxycarbonyl-1-phenyl-2-ethoxycarbonyl-2(4-cyanophenyl) ethene (147): white solid; mp 77 - 78 °C; 43% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.71 - 7.00 (m, 9H, Ar), 3.99 (q, 2H, CH_2, ^3J = 7.1 Hz), 3.92 (s, 3H, OCH_3), 0.92 (t, 3H, CH_3, ^3J = 7.1Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 167.4 (<u>C</u>=O), 166.7 (<u>C</u>=O), 141.9 (C2), 139.1 (C1), 133.5 (C12), 131.9 (C5,C7), 129.7 (C3), 128.7 (C11,C13), 128.2 (C4,C8), 127.8 (C10,C14), 122.5 (C9), 118.1 (<u>C</u>≡N), 112.3 (C6), 61.5 (CH_2), 52.2 (O<u>C</u>H_3), 13.3 (CH_2<u>C</u>H_3). MS (EI) m/z: 335 (M^+, 100%), 307 (45%), 262 (52%), 203 (90%), 177 (35%), 105 (54%), 84 (80%), 59 (56%). MS (CI, NH_3) m/z: 353 ($(M+NH_4)^+$, 100%), 287 (38%), 259 (95%),

217 (21%), 195 (10%), 137 (10%). MS (HR) m/z: Calculated for $C_{20}H_{17}NO_4$ 335.1157, found 335.1153.

3.11.2. Substituent effects on the reactions of alkoxyaryloxycarbenes with alkynes:

The substituted alkenes **137(c,e,f,g)** were synthesized according to the following procedure. The oxadiazoline **106f** (0.50 mmol), DMAD (0.90 mmol) and benzene (30 mL) were mixed in a thick walled glass tube. Thermolysis was carried out in constant oil bath at 100±0.1°C, for 72 hours. At the end of the reaction, the excess solvent was evaporated by means of a rotary evaporator and the crude thermolysis products were purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.



137(c,e,f)

1,1,2-Tri(methoxycarbonyl)-2-phenyl ethene (137c):

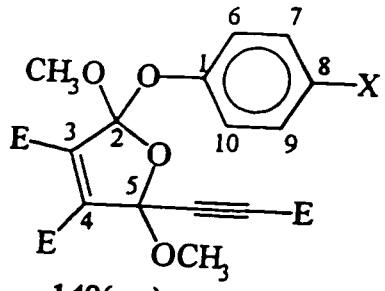
yellow oil; 7% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.37 - 6.90 (m, 5H, Ph), 3.86 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.62 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 165.0 (C=O), 164.0 (C=O), 163.0 (C=O), 143.0 (C2), 132.8 (C3), 129.2 (C4,C8), 127.4 (C5,C7), 126.7 (C1), 123.7 (C6), 52.9 (OCH_3), 52.7 (OCH_3), 52.5 (OCH_3). MS (EI) m/z: 278 (M^+, 52%), 219 (20%), 167 (19%), 77 (C_6H_5, 19%), 48 (100%). MS (CI, NH_3) m/z: 279 ($(M+NH_4)^+$, 100%), 219 (10%). MS (HR) m/z: Calculated for $C_{14}H_{14}O_6$ 278.0790, found 278.0789.

1,1,2-Tri(methoxycarbonyl)-2-(4-trifluoromethylphenyl) ethene (137e):

yellow oil; 40% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.67 (d, 2H, Ar, ^{3}J = 8.4 Hz), 7.52 (d, 2H, Ar, ^{3}J = 8.4 Hz), 3.86 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3). ^{19}F NMR ($CDCl_3$ vs $CFCl_3$) δ: -63.2 (s, CF_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 166.3 (C=O), 164.1 (C=O), 162.8 (C=O), 145.0 (C2), 136.3 (C3), 131.9 (q, C6), 128.7 (C1), 127.9 (C5,C7), 126.4 (C4,C8), 125.5 (q, CF_3), 53.2 (OCH_3), 52.9 (OCH_3), 52.6 (OCH_3). ($^{1}J_{CF}$ and $^{2}J_{CF}$ can't be calculated due to overlap of peaks). MS (EI) m/z: 346 (M^+, 78%), 315 (M^+-OCH_3, 85%), 287 (M^+-CO_2CH_3, 100%), 243 (50%), 219 (22%), 197 (95%), 157 (12%), 115 (9%), 59 (46%). MS (CI, NH_3) m/z: 364 ($(M+NH_4)^+$, 100%), 347 ($(M+H)^+$, 88%), 332 (17%), 267 (10%), 205 (10%), 121 (11%). MS (HR) m/z: Calculated for $C_{15}H_{13}F_3O_6$ 346.0664, found 346.0669.

1,1,2-Tri(methoxycarbonyl)-2-(4-nitrophenyl) ethene (137g):

yellow oil; 43% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.25 (d, 2H, Ar, ^{3}J = 8.8 Hz), 7.55 (d, 2H, Ar, ^{3}J = 8.8 Hz), 3.88 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.64 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 165.54 (C=O), 163.47 (C=O), 162.62 (C=O), 148.18 (C3), 144.3 (C2), 139.03 (C6), 129.84 (C1), 128.64 (C5,C7), 123.48 (C4,C8), 53.04 (OCH_3), 52.96 (OCH_3), 52.66 (OCH_3). MS (EI) m/z: 323 (M^+, 38%), 292 (M^+-OCH_3, 70%), 264 (M^+-CO_2CH_3, 100%), 220 (36%), 196 (15%), 174 (36%), 128 (16%), 59 (42%). MS (CI, NH_3) m/z: 341 ($(M+NH_4)^+$, 100%). MS (HR) m/z: Calculated for $C_{14}H_{13}NO_8$ 323.0641, found 323.0651.



149(a,c)

3,4-Di(methoxycarbonyl)-5-(methoxycarbonylethynyl)-2,5-dimethoxy-2-(4-methoxyphenoxy)-2,5-dihydrofuran (149a):

yellow oil; 45% yield; diastereomer ratio 1 : 1 by NMR; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.13 (d, 2H, Ar, ^3J = 9.1 Hz), 7.11 (d, 2H, Ar, ^3J = 9.1 Hz), 6.82 (d, 4H, Ar, ^3J = 9.1 Hz), 3.94 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.56 (s, 3H, OCH_3), 3.52 (s, 3H, OCH_3), 3.50 (s, 3H, OCH_3), 3.36 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 161.4 (C=O), 159.8 (2xC=O), 156.9 (C=O), 156.7 (C8), 156.5 (C=O), 152.8 (C=O), 145.8(C1), 145.4 (C1), 140.0 (C3), 139.7 (C3), 136.3 (C4), 124.8 (C6,C10), 123.3 (C6,C10), 123.0 (C2), 122.6 (C2), 113.9 (C7,C9), 113.8 (C7,C9), 100.5 (C5), 100.2 (C5), 78.4 (C≡C), 78.2 (C≡C), 55.6 (OCH_3), 55.4 (OCH_3), 55.2 (OCH_3), 53.1 (2xOCH_3), 52.9 (OCH_3), 52.8 (OCH_3), 52.4 (OCH_3), 52.1 (OCH_3), 51.7 (OCH_3), 51.3 (2xOCH_3).

MS (EI) m/z: 450 (M^+, 10%), 387 (11%), 359 (12%), 327 (M^+-$OC_6H_4OCH_3$, 100%), 309 (18%), 249 (62%), 157 (39%), 123 ($OC_6H_4OCH_3$, 100%), 157(10%). MS (CI, NH_3) m/z: 468 ($(M+NH_4)^+$, 7%), 419 (10%), 344 (52%), 327 (95%), 309 (100%), 249 (30%). MS (HR) m/z: Calculated for $C_{21}H_{22}O_{11}$ 450.1162, found 450.1156.

3,4-Di(methoxycarbonyl)-5-(methoxycarbonylethynyl)-2,5-dimethoxy-2-phenoxy-2,5-dihydrofuran (149c):

yellow oil; 38% yield; diastereomer ratio 1 : 1.3 by NMR; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.11 - 7.29 (m, 5H, Ph), 3.87 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 3.56 (s, 3H, CO_2CH_3), 3.55 (s, 3H, CO_2CH_3), 3.33 (s, 3H, CO_2CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 161.50 (C=O), 160.07 (C=O), 153.05 (C=O), 152.32 (C1), 140.24 (C3), 136.79 (C4), 129.13 (C7,C9), 124.77 (C8), 123.18 (C2), 122.82 (C2), 122.29 (C6,C10), 101.02 (C5), 100.63 (C5), 78.51 (C≡C), 78.01 (C≡C), 53.28 (2xOCH_3), 53.23 (2xOCH_3), 53.15 (2xOCH_3), 52.48 (2xOCH_3), 52.17 (2xOCH_3).

MS (EI) m/z: 327 (M^+-OC_6H_5, 100%), 157 (54%), 111 (10%), 77 (C_6H_5, 11%), 59 (13%). MS (CI, NH_3) m/z: 406 ((M^++H)-CH_3), 15%), 389 (9%), 344 (30%), 327 (100%), 312 (13%), 279 (10%), 157 (11%). MS (HR) m/z: Calculated for (M^+-OC_6H_5) $C_{14}H_{15}O_9$ 327.0716, found 327.0713.

3.12. Insertion reactions of alkoxyaryloxycarbenes:

3.12.1 Intermolecular insertions:

The oxadiazoline **106** (0.50 mmol), phenol (0.90 mmol) and benzene (30 mL) were mixed in a thick walled glass tube. Thermolysis was carried out in constant oil bath at 100±0.1°C, for 72 hours. At the end of the reaction, the excess solvent was evaporated by vacuo. The crude thermolysis products were dissolved in CH_2Cl_2 and extracted with 5% $NaHCO_3$. The organic layer was collected and dried over anhydrous magnesium sulfate. After evaporation of the organic layer, the residue was purified by centrifugal chromatography (2mm silica gel plate),

using 9:1 hexanes/ethyl acetate as the eluent.

150: white solid, 43% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.01 (d, 2H, Ar, ^3J = 9.1 Hz), 6.85 (d, 2H, Ar, ^3J = 9.1 Hz), 5.95 (s, 1H, C<u>H</u>), 3.75 (s, 3H, 2xOCH_3 of Ar), 3.56 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.4 (<u>C</u>H), 147.9 (Ar), 119.1 (Ar), 114.4 (Ar), 112.8 (Ar), 53.2 (2xOCH_3 of Ar), 50.6 (O<u>C</u>H_3). MS (EI) m/z: 290 (M^+, 6%), 259 (M^+-OCH_3, 28%), 167 (M^+-$OC_6H_4OCH_3$, 100%). MS (CI, NH_3) m/z: 259 (20%), 167 (100%). MS (HR) m/z: calculated for $C_{16}H_{18}O_5$ 290.1154, found 290.1163.

151: white solid, 42% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.35 - 7.03 (m, 9H, Ar), 6.19 (s, 1H, C<u>H</u>), 3.57 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 154.3 (<u>C</u>H), 130.1 (Ar), 129.5 (Ar), 123.0 (Ar), 120.4 (CN), 118.1 (Ar), 117.6 (Ar), 117.0 (Ar), 116.9 (Ar), 111.3 (Ar), 50.4 (O<u>C</u>H_3). MS (EI) m/z: 255 (M^+, trace%), 230 (M^+-CH_3, 3%), 199 (10%), 137 (M^+-OC_6H_4CN, 100%), 109 (5%), 94 (6%), 77 (C_6H_5, 16%), 51 (3%). MS (CI, NH_3) m/z: 228 ((M^++H-CN, trace%), 199 (9%), 137 (100%), 122 (5%), 77 (3%), 60 (6%). MS (HR) m/z: calculated for $C_{15}H_{13}NO_3$ 255.08959, found 255.08954.

152: white solid, 45% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.64 (d, 2H+2H, Ar, ^3J = 8.8 Hz), 7.16 (d, 2H+2H, Ar, ^3J = 8.8 Hz), 6.35 (s, 1H, C<u>H</u>), 3.58 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 156.85 (<u>C</u>H), 134.00 (Ar), 118.39 (CN), 117.74 (Ar), 109.98 (Ar), 106.73 (Ar), 51.03 (O<u>C</u>H_3). MS (EI) m/z: 249 (M^+-OCH_3, 10%), 162 (M^+-OC_6H_4CN, 100%), 119 (12%), 102 (C_6H_4CN, 20%). MS (CI, NH_3) m/z: 298 (($M+NH_4$)$^+$, 100%), 162

(70%), 137 (9%). MS (HR) m/z: calculated for (M^+-OCH_3); $C_{15}H_9N_2O_2$ 249.0664, found 249.0660.

3.12.2. Intramolecular insertion:

Synthesis of 2-(2-hydroxyphenoxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (153):

To a mixture of the 2-acetoxy-2-methoxy-Δ^3-1,3,4-oxadiazoline **(112)** and acylic product **(113)** (3.60 mmol of oxadiazoline) in CH_2Cl_2 (35 mL) was added catechol (3.60 mmol). The resulting solution was refluxed for 24 hours. After cooling, the reaction mixture was stirred with KOH (0.9 mmol) and 50 mL. of water. The organic layer was separated and dried over $MgSO_4$. Evaporation of the solvent left the oxadiazoline **153** as an oil which was pure by ^1H NMR.

153: 62% yield; ^1H NMR (200 MHz, $CDCl_3$) δ: 6.77-7.14 (m, 4H, Ar), 5.97 (s, 1H, OH), 3.63 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.26 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 148.9 (Ar), 138.4 (Ar), 137.1 (C2), 126.4 (Ar), 123.5 (Ar), 121.1 (Ar), 120.0 (C5), 116.6 (Ar), 52.8 ($O\underline{C}H_3$), 24.9 ($\underline{C}H_3$), 23.3 ($\underline{C}H_3$). MS (EI) m/z: 207 (M^+-OCH_3, 40%), 147 (22%), 73 (28%) (molecular ion not observed). MS (CI, NH_3) m/z: 186 (19%), 129 (10%).

Thermolysis of 2-(2-hydroxyphenoxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (153):

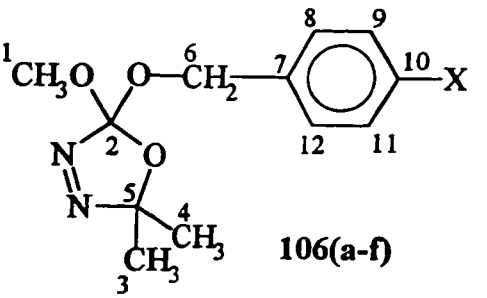
A solution of 2-aryloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline **153** (1.0 mmol) in 25 mL of dry benzene was prepared. The solution was added to 50 mL thick walled glass

tube. The thermolysis was carried out in a constant temperature oil bath 100±0.1°C, for 96 hours. At the end of the oxadiazoline thermolysis the tube was cooled to room temperature, opened and the solvent was evaporated by means of a rotary evaporator. The residue was then purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.

155: oil, 24% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.82 - 7.22 (m, 4H, Ar), 4.53 (septet, 1H, CH, ^3J = 6.1 Hz), 3.88 (s, 3H, OCH_3), 1.34 (s, 3H, CH_3, ^3J = 6.1 Hz), 1.31 (s, 3H, CH_3, ^3J = 6.1 Hz). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 153.83 ($\underline{C}(OCH_3)$), 149.54 (Ar), 141.42 (Ar), 126.85 (Ar), 122.40 (Ar), 120.69 (Ar), 115.53 (Ar), 77.49 ($\underline{C}(CH_3)_2$), 55.35 ($O\underline{C}H_3$), 22.00 ($2x\underline{C}H_3$). MS (EI) m/z: 210 (M^+, 24%), 195 (M^+-CH_3, 10%), 168 (31%), 151 (M^+-$OCH(CH_3)_2$, 11%), 124 (68%), 109 (100%), 81 (32%), 59 ($OCH(CH_3)_2$, 37%). MS (CI, NH_3) m/z: 228 ($(M+NH_4)^+$, 100%), 211 (M^++H, 4%), 195 (15%). MS (HR) m/z: Calculated for $C_{11}H_{17}O_4$ 210.0891, found 210.0877.

157: oil[55,56], 22% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.84 - 7.38 (m, 4H, Ar), 6.21 (s, 1H, CH), 3.60 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 153.7 ($\underline{C}H$), 127.1 (Ar), 124.6 (Ar), 121.1 (Ar), 120.7 (Ar), 51.0 ($O\underline{C}H_3$). MS (EI) m/z: 121 (M^+-OCH_3, 100%), 109 (70%) (molecular ion not observed). MS (CI, NH_3) m/z: 131 (100%), 58 (38%). MS (HR) m/z: Calculated for M^+-OCH_3: $C_7H_5O_2$ 121.0290, found 121.0301.

3.13. Synthesis of 2-benzyloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106): To a mixture of the 2-acetoxy-2-methoxy-Δ^3-1,3,4-oxadiazoline **(112)** and acylic product **(113)** (0.90 g, 3.58 mmol of oxadiazoline) in CH_2Cl_2 (35 mL) was added a p-substituted benzyl alcohol (1.0 mmol) and acetic acid (1.0 mL). The resulting solution was refluxed for 48 hours. After cooling the reaction mixture, the excess solvent was evaporated by vacuo. KOH pellets were added and the heterogeneous mixture was stirred rapidly; after 1 hour, 50 mL. of water was added and the mixture was stirred for 10 minutes. The organic layer was separated and dried over $MgSO_4$. Evaporation of the solvent left the oxadiazolines **106(a-f)** as oils which were pure by ^1H NMR.



106(a-f)

2-Methoxy-2-(4-methoxybenzyloxy)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106a): oil, 77% yield; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.28 (d, 2H, Ar, ^3J = 9 Hz), 6.87 (d, 2H, Ar, ^3J = 9 Hz), 4.74 (d, 1H, CH_2, ^2J = -13 Hz), 4.66 (d, 1H, CH_2, ^2J = -13 Hz), 3.80 (s, 3H, OCH_3 of Ar), 3.48 (s, 3H, OCH_3), 1.57 (s, 3H, CH_3), 1.55 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 159.3 (C10), 136.9 (C2), 129.5 (C8,C12), 119.2 (C5), 113.7 (C9,C11), 66.4 (C6), 55.1 ($O\underline{C}H_3$ of Ar), 51.9 (C1), 24.1 (C3 or C4), 23.9 (C4 or C3). MS (EI) m/z: 196 (10%), 138 (32%), 121 ($(CH_2C_6H_4OCH_3)^+$, 100%), 109 (18%), 84 (18%), 73 (17%) (molecular ion not observed). MS (CI, NH_3) m/z: 267 ($(M^+$+H), 4%),163 (100%), 121 (78%).

163 (100%), 121 (78%).

2-Methoxy-2-(4-methylbenzyloxy)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106b):

oil, 60% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.24 (d, 2H, Ar, ^3J = 7 Hz), 7.14 (d, 2H, Ar, ^3J = 7 Hz), 4.79 (d, 1H, CH_2, ^2J = -11 Hz), 4.69 (d, 1H, CH_2, ^2J = -11 Hz), 3.48 (s, 3H, OCH_3), 2.34 (s, 3H, CH_3 of Ar), 1.57 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 142.6 (C7), 137.6 (C2), 133.6 (C10), 129.0 (C9,C11), 127.9 (C8,C12), 119.4 (C5), 66.6 (C6), 52.0 (C1), 24.0 (C3,C4), 21.1 (CH_3 of Ar). MS (EI) m/z: 105 ($(CH_2C_6H_4CH_3)^+$, 100%), 73 (59%), 59 (10%) (molecular ion not observed). MS (CI, NH_3) m/z: 198 (25%), 147 (43%), 122 ($(OCH_2C_6H_4CH_3)^+$+H, 100%), 73 (18%), 58 (14%).

2-Benzyloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106c):

oil, 89% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.34 - 7.36 (m, 5H, Ph), 4.81 (d, 1H, CH_2, ^2J= -11.4 Hz), 4.78 (d, 1H, CH_2, ^2J = -11.4 Hz), 3.50 (s, 3H, OCH_3), 1.58 (s, 3H, CH_3), 1.55 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 136.99 (C2), 136.73 (C7), 128.36 (C8,C12), 127.75 (C9,C11), 119.35 (C5), 110.97 (C9), 66.70 (C6), 52.01 (C1), 24.10 (C3,C4). MS (EI) m/z: 234 (30%), 201 (21%), 179 (31%), 166 (M^+-N_2-$C(CH_3)_2$, 78%), 150 (MeOCOPh, 62%), 149 (100%) (molecular ion not observed). MS (CI, NH_3) m/z: 207 (40%), 184 (29%), 179 (12%), 108 ($(OCH_2C_6H_5)^+$+H, 100%), 73 (12%).

2-(4-Chlorobenzyloxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106d):

oil, 90% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.33 (d, 2H, Ar, ^3J = 5 Hz), 7.30 (d, 2H, Ar,

^3J = 5 Hz), 4.81 (d, 1H, CH_2, ^2J = -11.8 Hz), 4.72 (d, 1H, CH_2, ^2J = -11.8 Hz), 3.47 (s, 3H, OCH_3), 1.58 (s, 3H, CH_3), 1.53 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 137.6 (C2), 135.3 (C10), 133.7 (C7), 129.0 (C8,C10), 128.5 (C9,C11), 119.4 (C5), 65.9 (C6), 51.9 (C1), 24.1 (C3 or C4), 24.0 (C4 or C3) (molecular ion not observed). MS (EI) m/z: 127 ($(CH_2C_6H_4Cl)^+$, 30%), 125 ($(CH_2C_6H_4Cl)^+$, 100%), 89 (16%), 73 (77%), 59 (10%). MS (CI, NH_3) m/z: 288 ($(M+NH_4)^+$, 86%), 218 (11%), 195 (8%), 167 (5%), 144 ($(OCH_2C_6H_4Cl)^+$+H, 33%), 142 ($(OCH_2C_6H_4Cl)^+$+H, 100%), 125 (25%), 73 (26%), 60 (26%).

2-Methoxy-2-(4-trifluoromethylbenzyloxy)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106e): oil, 88% yield; ^1H NMR (200 MHz, $CDCl_3$) δ: 7.60 (d, 2H, Ar, ^3J = 8.1 Hz), 7.46 (d, 2H, Ar, ^3J = 8.1 Hz), 4.93 (d, 1H, CH_2, ^2J = -8.2 Hz), 4.83 (d, 1H, CH_2, ^2J = -8.2 Hz), 3.48 (s, 3H, OCH_3), 1.59 (s, 3H, CH_3), 1.54 (s, 3H, CH_3). ^{19}F NMR($CDCl_3$ vs $CFCl_3$) δ: -62.5 (s, CF_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 140.95 (C7), 136.93 (C2), 127.61 (C9,C11), 125.37 (C8,C12), 119.66 (C5), 65.90 (C6), 52.05 (C1), 24.20 (C3 or C4), 23.98 (C4 or C3). (Carbons coupled to fluorine were not observed). MS (EI) m/z: 159 ($(CH_2C_6H_4CF_3)^+$, 100%), 140 (10%), 127 (11%), 109 (23%), 84 (12%), 73 (94%), 59 (29%) (molecular ion not observed). MS (CI, NH_3) m/z: 322 ($(M+NH_4)^+$, 6%), 193 (10%), 176 ($(OCH_2C_6H_4CF_3)^+$+H, 100%), 131 (15%), 60 (52%).

2-(4-Nitrobenzyloxy)-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106f): oil, 64% yield; ^1H NMR (200 MHz, $CDCl_3$) δ: 8.21 (d, 2H, Ar, ^3J = 8.7 Hz), 7.52 (d, 2H, Ar, ^3J = 8.7 Hz), 4.95 (d, 1H, CH_2), 4.93 (d, 1H, CH_2), 3.47 (s, 3H, OCH_3), 1.58 (s,3H,CH_3),1.55 (s, 3H, CH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 147.57 (C7), 144.39 (C10), 136.88 (C2),

127.83 (C9,C11), 123.65 (C8,C12), 119.87 (C5), 65.51 (C6), 52.07 (C1), 24.26 (C3 or C4), 23.94 (C4 or C3). MS (EI) m/z: 211 (M^+-$(CH_3)_2CN_2$, 8%), 152 (M^+-$(CH_3)_2CN_2$-CO_2CH_3, 17%), 136 ($OCH_2C_6H_4NO_2$, 40%), 120 ($CH_2C_6H_4NO_2$, 16%), 106 (10%), 84 (31%), 73 (100%) (molecular ion not observed). MS (CI, NH_3) m/z: 299 ($(M+NH_4)^+$, 100%), 282 (M^++H, 8%).

3.14. Thermolysis of 2-benzyloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (106): A solution of 2-benzyloxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline **106** (1.0 mmol) in 30 mL of dry benzene was sealed into a 50 mL thick walled glass tube. The thermolysis was carried out in a constant temperature oil bath 100±0.1°C, for 96 hours. At the end of the oxadiazoline thermolysis the tube was cooled to room temperature, opened and the solvent was evaporated by means of a rotary evaporator. The residue was then purified by centrifugal chromatography (2mm silica gel plate), using 9:1 hexanes/ethyl acetate as the eluent.

4-Methoxyphenyl acetic acid methyl ester (160a):

oil,[57] 35% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.18 (d, 2H, Ar, ^3J = 8.5 Hz), 6.84 (d, 2H, Ar, ^3J = 8.5 Hz), 3.77 (s, 3H, OCH_3 of Ar), 3.67 (s, 3H, OCH_3), 3.55 (s, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 172.2 (C=O), 55.1 (OCH_3 of Ar), 51.8 (OCH_3), 40.1 (CH_2).

Methyl phenyl acetate (160c):

oil, 20% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.25 - 7.35 (m, 5H, Ar), 3.66 (s, 3H, OCH_3), 3.60 (s, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 171.9 (C=O), 51.9 (OCH_3), 40.8 (CH_2).

4-Trifluoromethylphenyl acetic acid methyl ester (160e):

oil, 20% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.58 (d, 2H, Ar, ^{3}J = 8.6 Hz), 7.40 (d, 2H, Ar, ^{3}J = 8.6 Hz), 3.70 (s, 3H, OCH_3), 3.68 (s, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 51.9 (OCH_3), 40.7 (CH_2). ^{19}F NMR ($CDCl_3$ vs $CFCl_3$) δ: -62.5 (s, CF_3). MS (EI) m/z; 159 (($CH_2C_6H_4CF_3$)$^{+}$, 100%), 109 (40%), 91 (11%), 61 (10%). MS (CI, NH_3) m/z: 219 (M^{+}+H, 38%), 176 (($OCH_2C_6H_4CF_3$)$^{+}$+H, 100%).

4-Nitrophenyl acetic acid methyl ester (160f):

19% yield[58]; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.17 (d, 2H, Ar, ^{3}J = 8 Hz), 7.46 (d, 2H, Ar, ^{3}J = 8 Hz), 3.75 (s, 3H, OCH_3), 3.72 (s, 2H, CH_2). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 147.9 (Ar), 145.2 (Ar), 130.2 (Ar), 123.5 (Ar), 52.3 (OCH_3), 40.7 (CH_2). MS (EI) m/z: 195 (M^{+}, 12%), 136 (M^{+}-CO_2CH_3, 72%). MS (CI, NH_3) m/z: 196 (M^{+}+H, 40%). MS (HR) m/z: Calculated for $C_9H_9NO_4$ 195.0574, found 195.0531.

4-Methoxybenzyl methyl carbonate (164a):

25% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.31 (d, 2H, Ar, ^{3}J = 8.6 Hz), 6.87 (d, 2H, Ar, ^{3}J = 8.6 Hz), 5.08 (s, 2H, CH_2), 3.79 (s, 3H, OCH_3 of Ar), 3.76 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.6 (C=O), 69.4 (CH_2), 55.1 (OCH_3 of Ar), 54.6 (OCH_3). MS (EI) m/z: 196 (M^{+}, 15%), 121 (($CH_2C_6H_4OCH_3$)$^{+}$, 100%), 91 (10%), 77 (11%). MS (CI, NH_3) m/z: 138 (10%), 121 (100%). MS (HR) m/z: Calculated for $C_{10}H_{12}O_4$ 196.0736, found 196.0743.

Benzyl methyl carbonate (164c):

20% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.35 - 7.25 (m, 5H, Ar), 5.14 (s, 2H, CH_2), 3.76 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.4 (C=O), 69.3 (CH_2), 54.5 (OCH_3). MS (EI) m/z: 155 (M^+-CH_3, 12%), 107 (M^+-CH_3CO_2, 26%), 91 ($CH_2C_6H_5$, 100%), 65 (29%). MS (CI, NH_3) m/z: 184 ($(M+NH_4)_+$, 100%), 168 (78%), 108 ($(M+H)^+$-CH_3CO_2, 60%), 75 (39%).

Methyl 4-trifluoromethylbenzylcarbonate (164e):

25% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.62 (d, 2H, Ar, ^{3}J = 8 Hz), 7.49 (d, 2H, Ar, ^{3}J = 8.6 Hz), 5.21 (s, 2H, CH_2), 3.81 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.5 (C=O), 68.4 (CH_2), 54.9 (OCH_3). ^{19}F NMR($CDCl_3$ vs $CFCl_3$) δ: -62.7 (s, CF_3). MS (EI) m/z: 234 (M^+, 5%), 219 (M^+-CH_3), 40%), 199 ($(CH_2C_6H_4CF_3)^+$, 100%), 109 (40%), 91 (11%), 61 (10%). MS (CI, NH_3) m/z: 176 (100%).

Methyl 4-nitrobenzyl carbonate (164f):

23% yield; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 8.23 (d, 2H, Ar, ^{3}J = 8.8 Hz), 7.55 (d, 2H, Ar, ^{3}J = 8.8 Hz), 5.26 (s, 2H, CH_2), 3.83 (s, 3H, OCH_3). ^{13}C NMR (50 MHz, $CDCl_3$) δ: 155.3 (C=O), 67.8 (CH_2), 55.1 (OCH_3). MS (EI) m/z: 211 (M^+, 35%), 152 (M^+-CO_2CH_3), 62%). MS (CI, NH_3) m/z: 229 ($(M+NH_4)^+$, 10%), 153 ($(OCH_2C_6H_4NO_2)^+$+H, 20%).

3.15. Rate constants for thermolysis of 2-alkyloxy-2-benzyloxy—Δ^3-1,3,4-oxadiazolines (106):

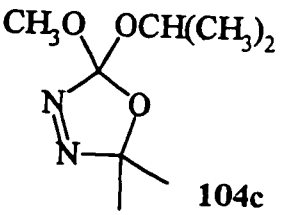
A 2-alkoxy-2-aryloxy-Δ^3-1,3,4-oxadiazoline **106** (~0.1 mmol.) was dissolved in 0.5 mL C_6D_6 and 2 μL CH_3-C_6H_5 (internal standard) in a medium walled NMR tube. After three cycles of degassing, at liquid nitrogen temperature, and thawing to room temperature, the tube was sealed under vacuum. The thermolysis was carried out in a constant temperature oil bath, at 100 ± 0.1 °C. The tube was removed from time to time and chilled to room temperature with water. The integrals of the methyl signals from **106** against those of the toluene methyl signal afforded values of the concentration of the remaining oxadiazoline. The decomposition was followed through three half lives. Time outside the oil bath was not counted and time in the bath was not corrected for the warm up period for insertion of the samples at room temperature. Integrals of the disappearing methyl signals were measured and normalized against the toluene methyl integral. The resultant plot of ln {(A-x) / A} vs. t in all thermolyses yielded a straight line corresponding to standard first order plots.

Appendix I

Inversion recovery pulse sequence (T_1):

For accurate study of the rates of decomposition of the oxadiazolines **(104,104,106)** using ^1H NMR spectroscopy, the inversion recovery experiment (T_1) was performed. T_1 is the time taken by a peak to return to 63% of its intensity (or 0.63 of the thermal equilibrium value) after application of an FID pulse. Usually, $5T_1$ is the time that is required between acquistions of the peak intensities in a kinetic study.[59,60] This is particularly impoartant if the T_1 values for sample and reference peaks are very different. The T_1 values for benzene and for the methyl signal of toluene are large.

The oxadiazoline **104c** serves as an example in the determination of the T_1 value. For determination of the rate constants of decomposition of the oxadiazolines, the data were collected in three blocks with a single scan in each block when benzene was used as an internal standard, and 16 scans in each block when the toluene-methyl signal was used as an internal standard.



104c

Table 21:
Inversion recovery values
T_1 for oxadiazolines and references.

Type of H	OCH_3	CH_3	CH_3	CH	$CH(CH_3)_2$	C_6H_6	CH_3-C_6H_5
T_1 (sec)	7.42	3.73	3.67	12.94	3.18	236.96	13.56
$5T_1$(sec)	37.09	18.65	18.34	64.69	15.91	1184.8 (19.75 min)	67.82 (1.13 min)

Appendix II

Observed Rate Constant Data

Table 22. Determination of the rate constant of thermolysis of **104a** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
32400	-0.2269
46800	-0.6370
61200	-0.8055
75600	-1.2636
90000	-1.3802
100800	-1.4199

Slope (m) = $(-1.58 \pm 0.10) \times 10^{-5}\ s^{-1}$
Correlation Coefficient (R) = 0.9558

Table 23. Determination of the rate constant of thermolysis of **104b** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.5123
10800	-1.6284
25200	-2.7958
43200	-3.5847

Slope (m) = $(-8.23 \pm 0.10) \times 10^{-5}\ s^{-1}$
Correlation Coefficient (R) = 0.9412

Table 24. Determination of the rate constant of thermolysis of **104c** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.1520
10800	-0.3581
25200	-0.8199
43200	-1.3718
57600	-1.4648
72000	-1.7965

Slope (m) = $(-2.49 \pm 0.07) \times 10^{-5}\ s^{-1}$
Correlation Coefficient (R) = 0.9758

Table 25. Determination of the rate constant of thermolysis of **104d** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.4271
25200	-0.8844
43200	-1.0639
72000	-1.5570
86400	-1.6494

Slope (m) = $(-1.74 \pm 0.20) \times 10^{-5}\ s^{-1}$
Correlation Coefficient (R) = 0.9361

Table 26. Determination of the rate constant of thermolysis of **105a** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.0673
25200	-0.5331
39600	-0.8132
54000	-1.0056
70200	-1.2705
84600	-1.3514
100800	-1.7672
115200	-1.9185
129600	-2.1710
Slope (m) = (-1.63 ± 0.05) x 10^{-5} s^{-1}	
Correlation Coefficient (R) = 0.9920	

Table 27. Determination of the rate constant of thermolysis of **105b** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.014
10800	-0.153
18000	-0.278
25200	-0.479
32400	-0.736
39600	-0.554
Slope (m) = (-1.80 ± 0.20) x 10^{-5} s^{-1}	
Correlation Coefficient (R) = 0.9880	

Table 28. Determination of the rate constant of thermolysis of **105c** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.2952
14400	-0.4041
118800	-2.1627
129600	-2.9060
144000	-3.0796
172800	-3.4049
Slope (m) = (-1.96 ± 0.10) x 10^{-5} s^{-1}	
Correlation Coefficient (R) = 0.9849	

Table 29. Determination of the rate constant of thermolysis of **105d** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
10800	-0.121
18000	-0.276
25200	-0.460
32400	-0.639
39600	-0.766
Slope (m) = (-2.04 ± 0.13) x 10^{-5} s^{-1}	
Correlation Coefficient (R) = 0.9832	

Table 30. Determination of the rate constant of thermolysis of **105e** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.112
10800	-0.275
18000	-0.457
25200	-0.651
32400	-0.780
39600	-0.945
Slope (m) = (-2.38 ± 0.20) x 10^{-5} s^{-1} Correlation Coefficient (R) = 0.9974	

Table 31. Determination of the rate constant of thermolysis of **105f** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
25200	-0.093
39600	-1.330
54000	-1.591
100800	-2.814
129600	-3.154
Slope (m) = (-2.64 ± 0.30) x 10^{-5} s^{-1} Correlation Coefficient (R) = 0.9403	

Table 32. Determination of the rate constant of thermolysis of **105g** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
3600	-0.156
10800	-0.309
18000	-0.528
25200	-0.775
32400	-0.963
39600	-1.170
Slope (m) = (-2.93 ± 0.05) x 10^{-5} s^{-1} Correlation Coefficient (R) = 0.9976	

Table 33. Determination of the rate constant of thermolysis of **106a** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
7200	-0.2158
18000	-0.4406
28800	-0.6441
39600	-0.8495
Slope (m) = (-2.09 ± 0.10) x 10^{-5} s^{-1} Correlation Coefficient (R) = 0.9930	

Table 34. Determination of the rate constant of thermolysis of **106b** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
7200	-0.0265
18000	-0.2930
28800	-0.4977
39600	-0.8138
Slope (m) = $(-2.11 \pm 0.2) \times 10^{-5}\ s^{-1}$	
Correlation Coefficient (R) = 0.9738	

Table 35. Determination of the rate constant of thermolysis of **106c** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
7200	-0.1963
18000	-0.5042
28800	-0.6599
39600	-0.9587
Slope (m) = $(-2.35 \pm 0.10) \times 10^{-5}\ s^{-1}$	
Correlation Coefficient (R) = 0.9903	

Table 36. Determination of the rate constant of thermolysis of **106d** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
7200	-0.0697
18000	-0.3583
28800	-0.6756
39600	-0.9759
Slope (m) = $(-2.55 \pm 0.10) \times 10^{-5}\ s^{-1}$	
Correlation Coefficient (R) = 0.9870	

Table 37. Determination of the rate constant of thermolysis of **106e** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
7200	-0.1631
18000	-0.5587
28800	-0.7044
39600	-1.0534
Slope (m) = $(-2.62 \pm 0.10) \times 10^{-5}\ s^{-1}$	
Correlation Coefficient (R) = 0.9848	

Table 38. Determination of the rate constant of thermolysis of **106f** in C_6D_6 at 100 °C

Time (sec)	Ln{(A-x)/A}
0	0
7200	-0.2189
18000	-0.4266
28800	-0.9060
39600	-1.0853
Slope (m) = $(-2.83 \pm 0.20) \times 10^{-5}\ s^{-1}$	
Correlation Coefficient (R) = 0.9802	

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