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NAME OF SUPERVISOR/*NOM DU DIRECTEUR DE THÈSE* Dr. J. Warkentin

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CARBONYL YLIDES AND CARBENES FROM Δ^3-1,3,4-OXADIAZOLINES

BY

© MICHEL BEKHAZI, B.Sc., M.Sc.

A THESIS

Submitted to the Faculty of Graduate Studies
in Partial Fulfillment of the Requirements
for the Degree
Doctor of Philosophy

McMaster University
December 1981

CARBONYL YLIDES AND CARBENES FROM Δ^3-1,3,4-OXADIAZOLINES

TO MY MOTHER

AND

IN THE MEMORY OF MY FATHER

Relever un defi, vouloir le gagner sont les deux facteurs essentiels du succés. Si mon succés est le résultat d'efforts continus, il est aussi celui de ceux qui ont gagé sur ma victoire.

MERCI

DOCTOR OF PHILOSOPHY

McMASTER UNIVERSITY

Hamilton, Ontario

TITLE: Carbonyl Ylides and Carbenes from Δ^3-1,3,4-Oxadiazolines

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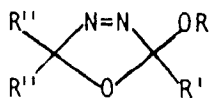
ABSTRACT

A series of new, substituted Δ^3-1,3,4-oxadiazolines were synthesized by oxidation of the corresponding hydrazones, either electrochemically or with lead tetraacetate. 2-Methoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline 1 ($R=R'=R''=CH_3$), when thermolyzed in CD_3OD, gave products of trapping of a



A

carbonyl ylide In CCl_4 or C_6H_6, which are not efficient trapping solvents the ylide underwent fragmentation into carbenes and carbonyl compounds.

As a check that the same intermediate was involved in both solvents 2-methoxy-2-(p-substituted)phenyl-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines were thermolyzed in CCl_4 and in CD_3OD. A Hammett correlation with σ^- was observed in both solvents, with similar slopes. Furthermore, changes in substituents at C_5 also affected the rate of thermolysis of the oxadiazolines. These results led us to conclude that, oxadiazolines of type A thermolyze with concerted loss of nitrogen to give rise to carbonyl ylide intermediates.

Attempts to trap the intermediates (ylide and carbenes) from the thermolysis of the oxadiazolines were successful. Some olefins and carbonyl compounds can trap both intermediates.

The reaction of a carbene with a carbonyl compound to form a carbonyl ylide is the reverse of the ylide fragmentation mentioned above. Such reversibility was proved for one of the carbenes when it was found that thermolysis of 1 ($R=R'=R''=CH_3$) in acetone-d_6 gave propene-d_6 as one of the products.

Thermolysis of 2-methoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline in CCl_4 gave acetone and methoxymethyl carbene (43%) as well as methyl acetate and dimethyl carbene (54%). The 5,5-dicyclopropyl analogue thermolyzed in benzene to a carbonyl ylide which fragmented nearly cleanly to methyl acetate and dicyclopropyl carbene (>90%). In CCl_4 chlorinated products, derived from the reaction of dicyclopropylcarbene with CCl_4, were obtained.

Finally, thermolysis of 2-acetoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline in CCl_4 afforded 1-acetoxyethyl-2-propenyl-ether (>90%) derived from a 1,4-hydrogen shift in the ylide. The 5,5-dicyclopropyl analogue gave only 20% of the analogous 1,4-shift product and the major pathway involved a fragmentation of the ylide to give a rare acyloxycarbene, $CH_3\ddot{C}OAc$.

ACKNOWLEDGEMENTS

I would like to thank my uncle, Antoine N. Békhazi, for being a second father to me. It is through him that I was able to continue my post-secondary education and eventually had the privilege of attending graduate school in the wonderful country of Canada. The faith he had in me helped in overcoming a number of obstacles throughout my life. Je voudrais aussi te remercier pour l'aide que tu as porté à ma mère et à mes soeurs.

Grateful acknowledgements are due to McMaster University for its financial support in the form of scholarships and teaching assistantship duties.

I express my gratitude to Dr. J.C. Scaiano, for running the laser-flash-photolysis experiments, and to Messrs Brian Sayer, Ian Thompson, Fadjar Ramelan and Frank Puzzuoli for their contribution to the spectroscopic portion of this thesis.

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The whole Chemistry Department has had a great influence on the outcome of this work in the form of constructive discussions especially Dr. Peter J. Smith, Dr. Ronald F. Childs and the members on my committee Dr. Jack J. McCullough and Dr. Michael J. McGlinchey.

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Debbie Jewell and Diane Keus , I cannot express in words what you meant to me but one thing is sure your presence and your help were major contributors to my success, thank you.

Finally, I would like to thank Ms. Linda Palmer for bearing through my writing while typing this thesis.

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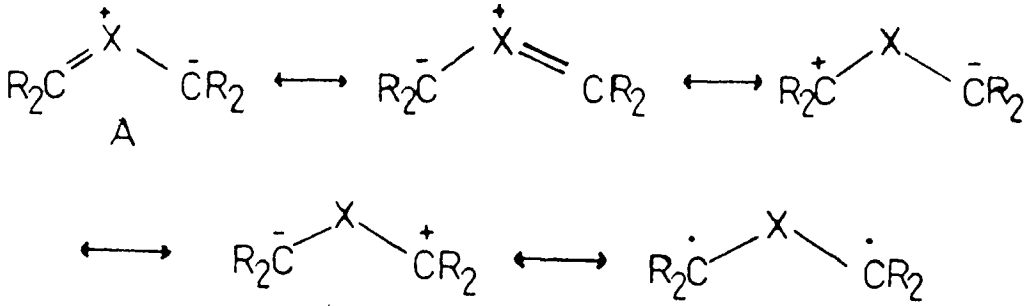
INTRODUCTION

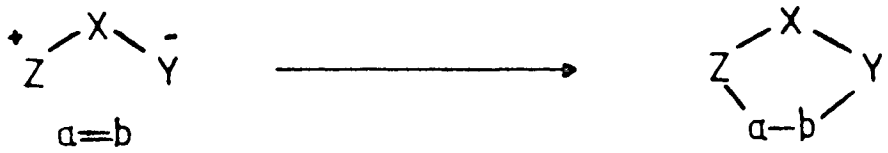
I.1 CARBONYL YLIDES

I.1.1 1,3-DIPOLES[1]

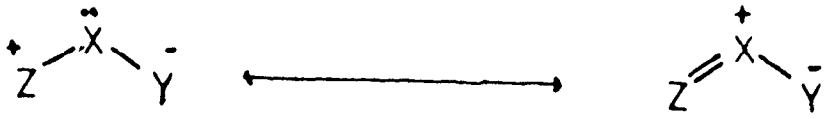
Interest in molecules of the type $R_2C\ X\ CR_2$, where X is a heteroatom, was revived about fifteen years ago. Huisgen[2], recognized that molecules like (A) would exist, and would be 1,3-dipolar species (X = NR, O,S). If X = NR, the molecule is an azomethine; if X = O then it is a carbonyl ylide, and for X = S then it is a thiocarbonyl ylide.[1]



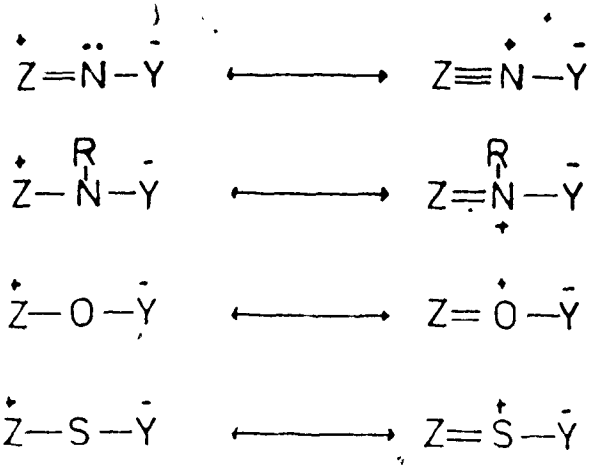
A 1,3-dipole may be defined as a system Z-X-Y, where Z carries a formal positive charge and Y carries a formal negative charge. Such a 1,3-dipole can add to a multiple bond system a=b, called a dipolarophile, to form a five-membered ring.



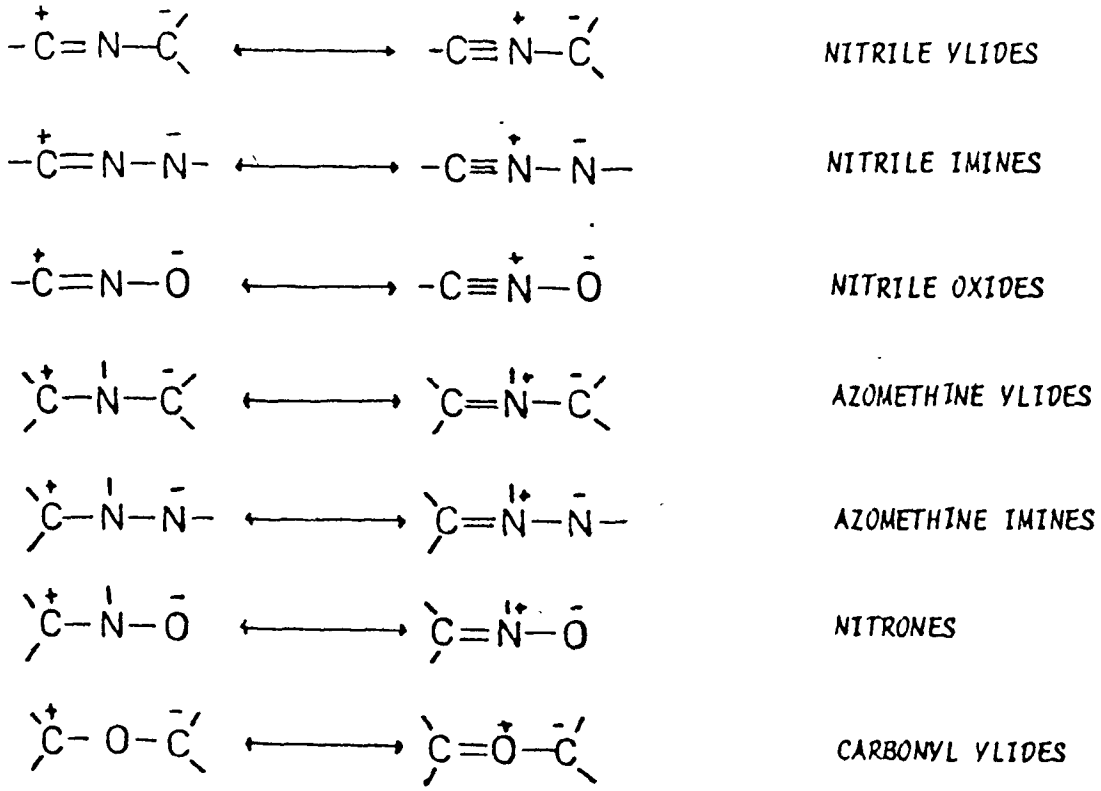
Compounds in which Z is an electron-deficient carbon, nitrogen, or oxygen atom are usually short-lived.[3,4] If X has a lone pair, stabilization of the system is made possible through resonance, by forming a double bond. Compounds of that sort are called "betaines."

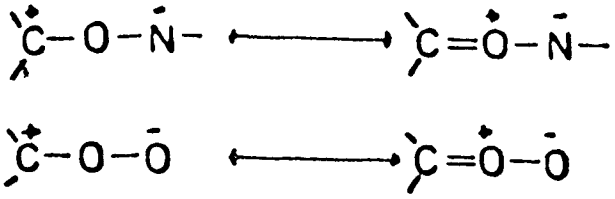


"Betaines", can be referred to as octet-stabilized 1,3-dipoles.



Some examples of 1,3-dipoles and their common names are listed below:





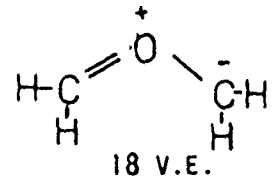
CARBONYL IMINES

CARBONYL OXIDES

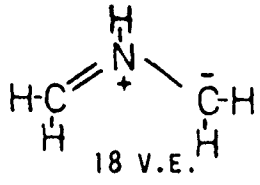
In the following discussion we will concentrate on carbonyl ylides; their generation, their electronical properties, and their reactions.

I.1.2 - *STRUCTURAL AND ELECTRONIC PROPERTIES*

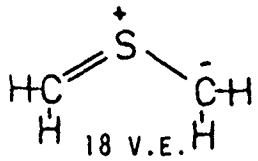
Walsh's[5] rules and newer rationalizations of these rules,[6,7] allow one to predict the geometry of small molecules in the ground state. For example, H-X-H are linear if there are four or less valence electrons (V.E.), and bent if more V.E. are present (H-O-H, 8 V.E., bent). H-X-Y are linear with 10 or less valence electrons, and bent with more (H-C≡N, 10 V.E., linear; CH_3OH, 14 V.E., bent). Z-X-Y are linear if they contain 16 valence electrons or less, and bent if they contain more (CO_2, 16 V.E., linear; SO_2, 18 V.E., bent). Molecules with three separated ligands on a central atom X are planar if they contain 6 V.E. or less for XH_3, 12 V.E. or less for AXH_2, 18 V.E. or less for ABXH, and 24 V.E. or less for ABCX; if these numbers are exceeded the molecule becomes pyramidal (NH_3, 8 V.E., bent; $(CH_3)_3C^+$, 24 V.E., planar). On the basis of those predictions carbonyl ylides (> 16 V.E.) are not linear species. The following examples show different ylides and their predicted geometries.



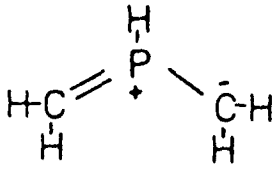
non-linear



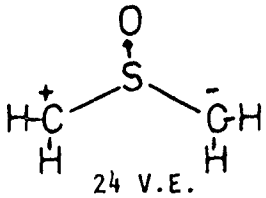
planar



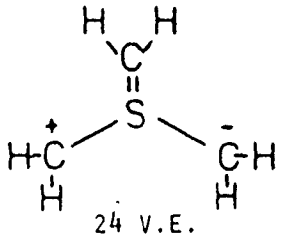
non-linear



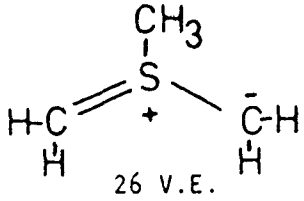
planar



Planar

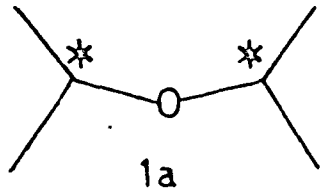


Planar

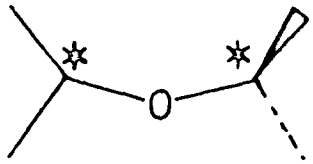


Pyramidal

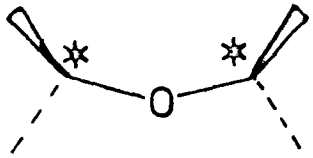
Carbonyl ylides can adopt three different geometries:[8] a fully planar geometry, 0°, 0° (1a) and non-planar 0°, 90° (1b) and 90°, 90° geometries (1c).



1a

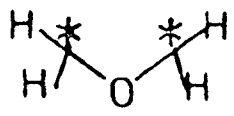


1b



1c

The parent carbonyl ylide (2) is predicted[8] to be a planar species which will rapidly invert about oxygen but only slowly rotate about the partial CO double bonds.



2

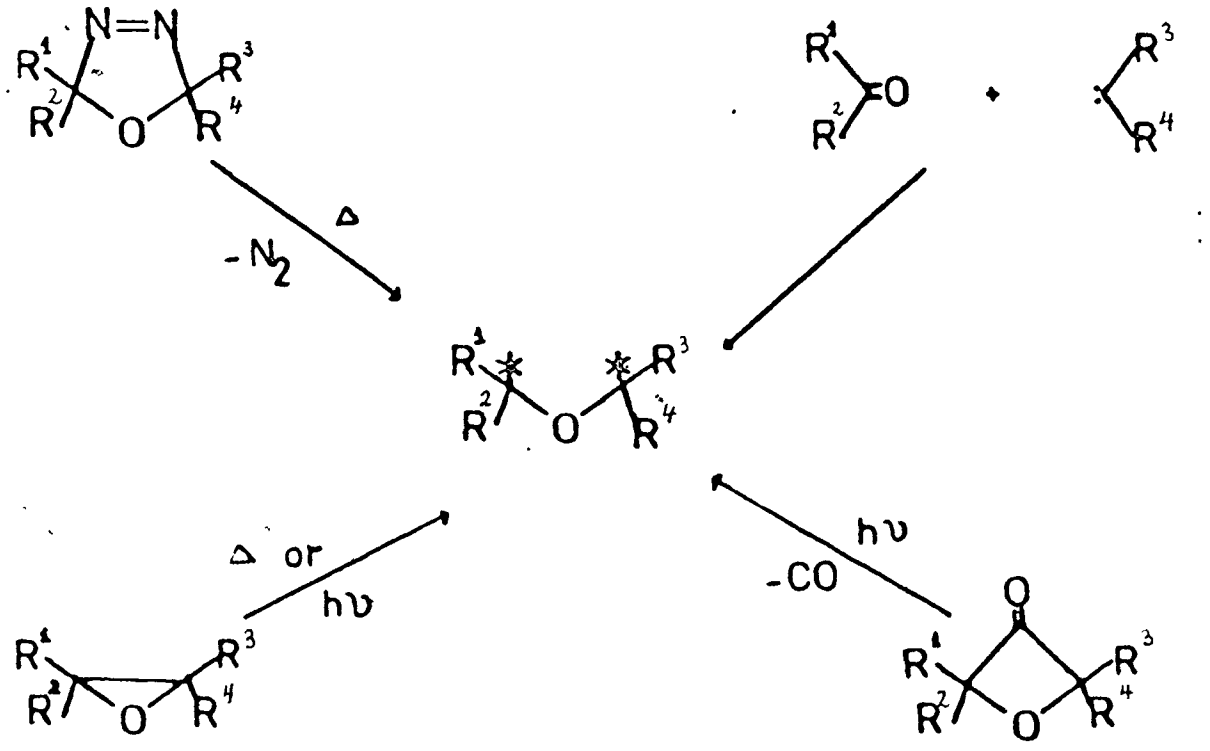
Stabilization of carbonyl ylide (2) is enhanced by electron donating substituents on one side and electron withdrawing substituents on the other.[8] A single cyano group was found[8] to be far more effective than a single amino group

at stabilizing the carbonyl ylide (-16 and -5 Kcal/mole respectively). A second cyano group placed on the same carbon as the first has a slightly larger stabilizing effect than when placed on the remote carbon (-28 and -25 Kcal/mole respectively). The effect of placing two cyano groups and two amino groups on opposite ends of the ylide is an enormous stabilization[8] (-76 Kcal/mole).

Rotation around the C-O bond becomes easy as donors or acceptors are added until, in the 1,1-diamino-3,3-dicyanocarbonyl ylide, the 0°, 90° species is more stable than the 0°, 0° planar species.[8]

I.1.3 - *SOURCES OF CARBONYL YLIDES*

Carbonyl ylides can be generated in several ways:[4] (i) through thermolysis or photolysis of monocyclic and polycyclic oxiranes, (ii) by carbene addition to the carbonyl group of an aldehyde or a ketone, (iii) by thermolysis of Δ^3-1,3,4-oxadiazolines, (iv) through chelotropic extrusion of carbon monoxide from oxetanes. (Scheme 1).

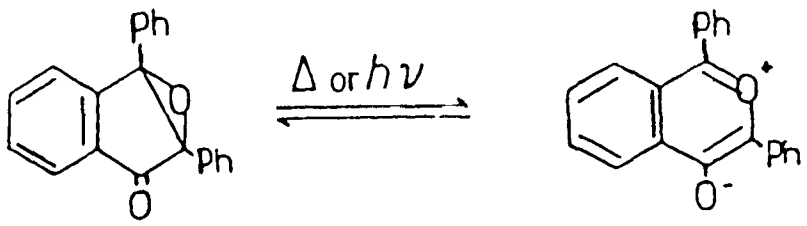


SCHEME 1

I.1.3.1 *FROM OXIRANES*

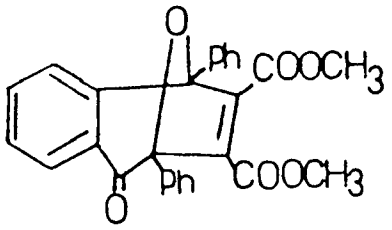
The first unambiguous[1] demonstration of the existence of carbonyl ylides came in 1962 with the discovery of the photochemical tautomerism of an indenone oxide system.[9] 2,3-Diphenyl indenone oxide (3), upon strong heating or when exposed to diffuse daylight turned red, and the red colour faded upon cooling or standing in the dark.[10] The system was thoroughly investigated. Upon U.V. irradiation at 2600-3900°A a new sharp peak in the I.R. appeared at cm^{-1} 1780, suggesting a C=O enolate-like linkage, with weaker peaks at cm^{-1} 1252 on bleaching the solution with visible light the original spectrum was restored. This result provided strong evidence that the red species was photochemically reconverted to the indenone oxide (3). Under these conditions, an equilibrium between 2,3-diphenylindenone oxide (3) and the red benzopyrytium oxide (4) exists, eq 1.

[1]



3 4

The dipolar species (4) was rapidly destroyed when photolysis occurred in the presence of dipolarophiles. Irradiation of indenone oxide (3) in dimethyl acetylenedicarboxylate, and in norbornadiene did not show any sign of a red coloured intermediate. The reactions afforded (5) and (6) respectively.



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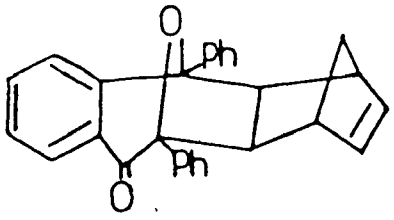
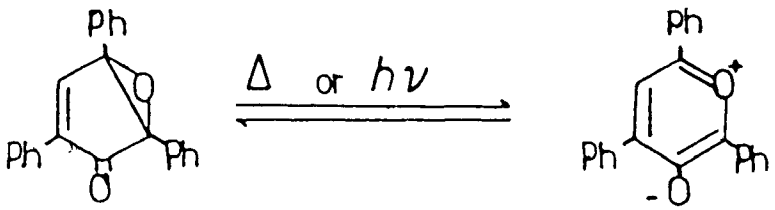


6

Another system, similar to (3) was investigated[11]. Upon thermolysis or photolysis of epoxyketone (7) an equilibrium with carbonyl ylide (8) was established (eq 2).

[2]

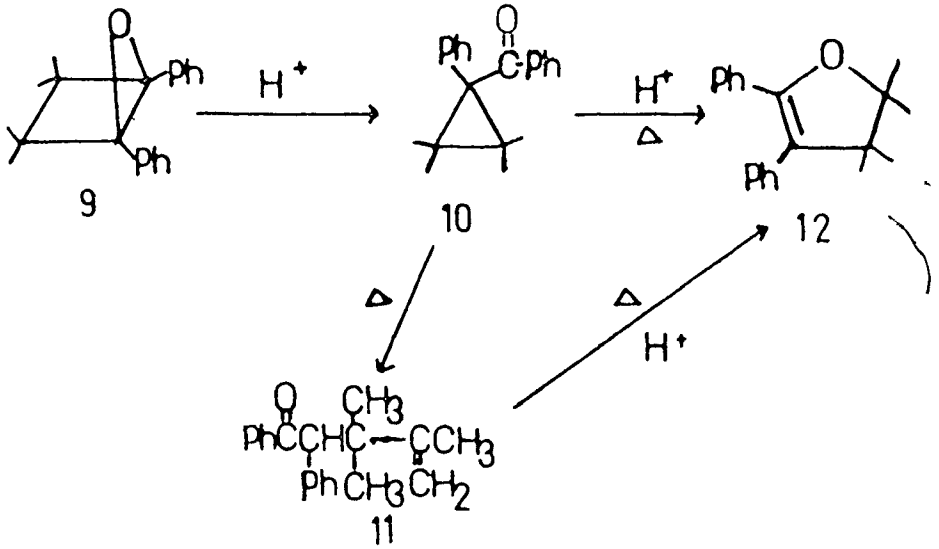


7 8

The ring opening of 3 or 7 must be disrotatory to prevent the formation of a trans-double bond. The dipolar intermediates 4 and 8 acquire a certain stability because the thermal ring closure back to starting material is allowed only from a con-rotatory motion.[1] Finally, the ring-opening of indenone oxides may under the proper conditions be accomplished by means of a nonallowed thermal process.[12]

Photolysis and thermolysis of 5-oxabicyclo[2.1.0]pentane (9) has been reported.[13] Epoxide (9) was stable, however traces of acid catalyzed its rearrangement to cyclopropylketone (10). Thermal rearrangement of 10 yielded olefin 11, which upon treatment with acid, yielded dihydrofuran (12), eq 3.

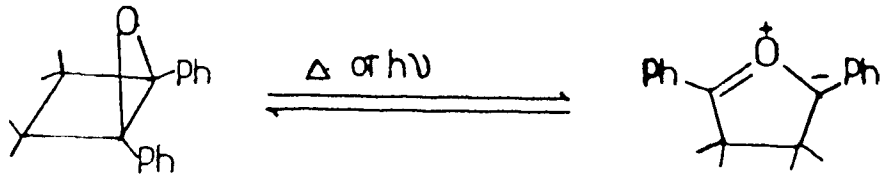
[3]



9 10 12 11

A solution of (9) in benzene or diglyme gave a highly coloured intermediate, when heated at 100°C or when irradiated (2537 A°) at room temperature. The colour disappeared from the irradiated solution with first order kinetics and from the heated solution upon cooling. The solution of 9 in benzene became coloured upon irradiation, with little loss of 9, suggesting a carbonyl ylide intermediate (13) in equilibrium with 9, eq. 4.

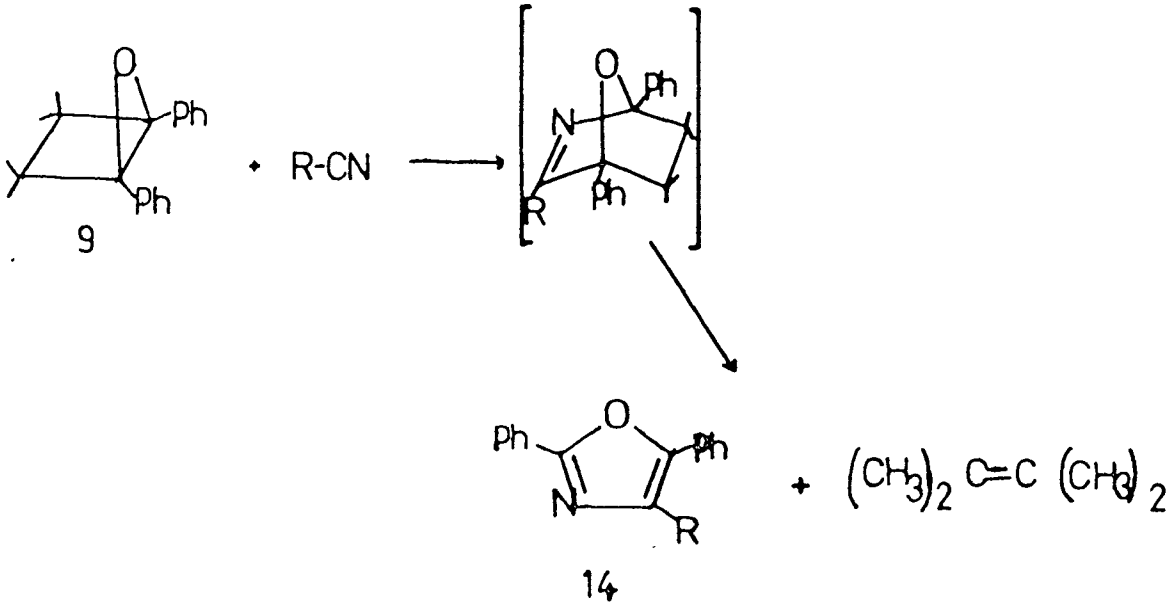
[4]



9 13

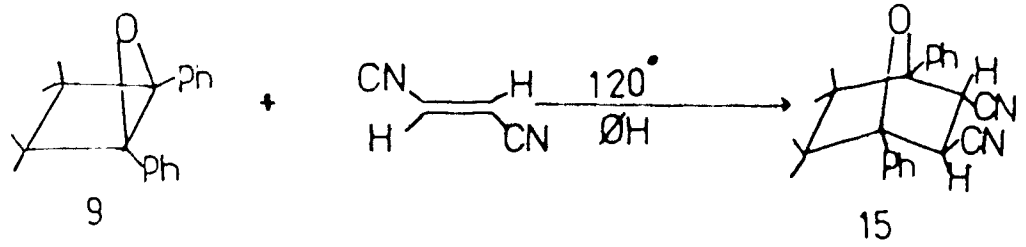
When (9) was heated at 120°C, in cyanobenzene, no colour was produced. After 50 hours the oxide had disappeared with the formation of triphenyloxazole (14) and tetramethylethylene, eq 5. Thermolysis of (9) in the presence of the isomeric 1,2-dicyanoethylene gave (15) and (16,17) respectively, eq 6,7.

[5]



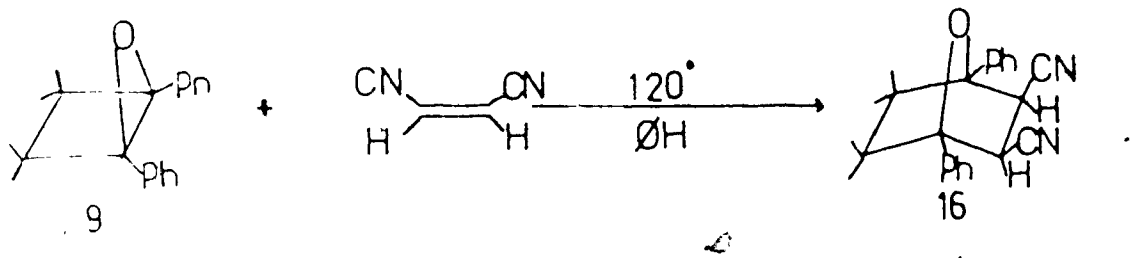
9 14

[6]



9 15

[7]



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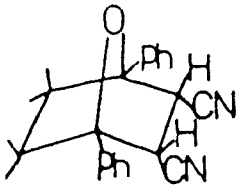


17

I.1.3.2 *FROM REACTION OF CARBENES WITH CARBONYL COMPOUNDS*

A different and less exploited route to carbonyl ylides is the addition of a carbene or a carbinoid to the oxygen of a carbonyl compound.[1] Carbenes can react with compounds containing atoms with unshared electron pairs to form ylides,[14,15] and such ylides are intermediates in many carbene reactions.[16-20] Ylides of nitrogen,[21-26] sulfur[27-33] halogens[34-38] and other elements[15] form as a result of carbene interaction with a non-bonding pair of electrons on the heteroatom of the nucleophilic component,[34,39-41] eq 8.

[8] 

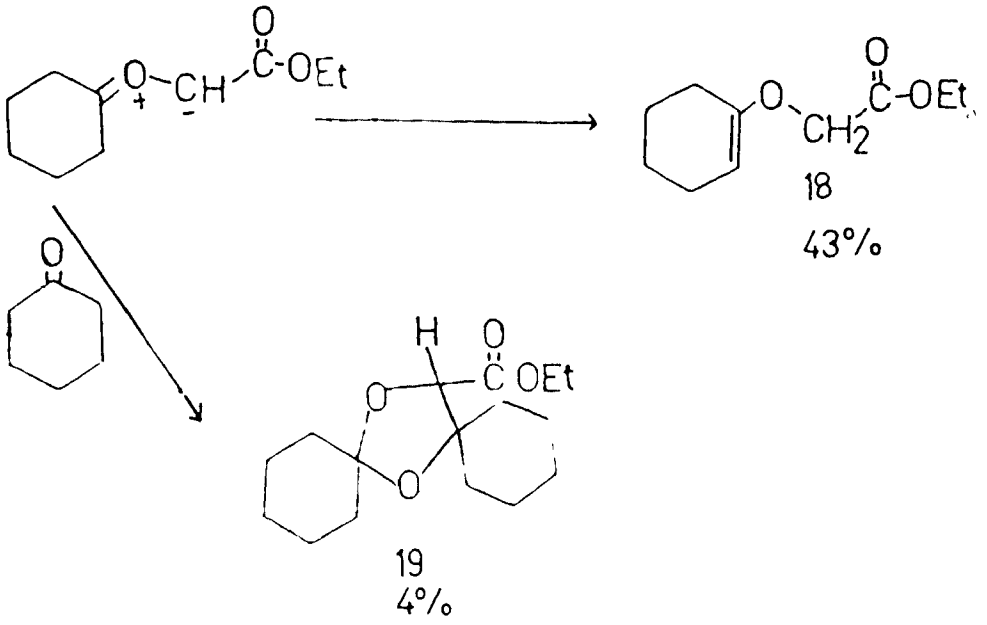
Stable ylides were only obtained from carbenes with electron-withdrawing substituents. The formation of ylides from carbene addition to heteroatoms has been well documented in a number of papers[15,29,42-45] and monographs.[14,28,46,47]

The spin multiplicity of the carbenes[15] responsible for the formation of the ylides was determined from photochemical data. Direct photolysis of diazomalonic esters in dimethylsulfide gave stable sulfonium ylides,[28,29] in high yields. Since singlet biscarbomethoxy carbene is generated under these conditions[48] (90-92%), the authors[28,29] initially concluded that ylide formation only occurs from singlet carbenes. It was later found that ylides were also formed upon sensitized (Ph_2CO) photolysis of diazocarbonyl compounds.[30,31] A detailed investigation of this process led to the hypothesis that a triplet carbene goes to its singlet state prior to the formation of the ylide.[30] The reality of such intersystem crossing was established during the study of carbomethoxy carbene, acetyl carbene, and other carbenes, using the CIDNP method.[49,50]

During the sensitized photolysis of various diazo compounds in allyl sulfides, allyl halides, allyl ethers,[51] allyl alcohols,[52] and vinyl sulfides,[53] the ratio of yields of ylide reaction products to cyclopropanes decreased sharply, in comparison with irradiation without sensitizer. These data confirmed the singlet electronic state of carbenes responsible for the formation of ylides.[15]

The decomposition of ethyl diazoacetate in cyclohexanone in the presence of a copper catalyst was found[54] to form enol ether (18) and cycloadduct (19), eq 9.

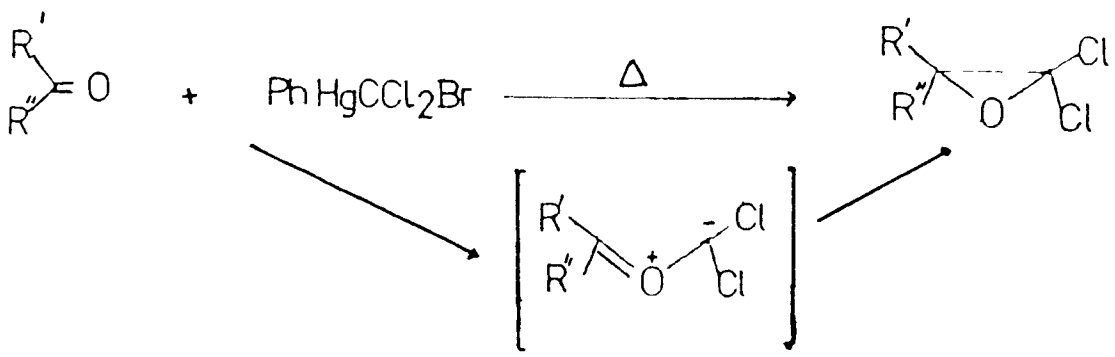
[9]



The proposed[55] carbonyl ylide intermediate can undergo a 1,4-hydrogen shift to give 18 or it can react with another mole of ketone to give 19.

Dihalocarbenes, generated from the thermolysis of phenyltrihalomethylmercury precursors, add to carbonyl groups bearing highly electronegative substituents.[56-58] The epoxide produced in the reaction was believed to be formed from the cyclization of a carbonyl ylide,[59] eq 10.

[10]



However,[60] reactions of $PhHgCX_2Y$ with substrates containing lone-pair substituents might proceed via nucleophilic attack of the heteroatom on the phenyl (trihalomethyl) mercury reagent. Such reactions might go through a direct transfer of $:CX_2$ from the organomercury reagent to the substrate; free carbenes would not necessarily be involved in such cases.[59,61-64]

Thermolysis of benzaldehyde with mercurial (20) in benzene at 75-80°C gives 21, CO, and other products,[65] eq 11. Product 21 was believed to be derived from

[11] $$\underset{20}{PhHgCCl_2Br} + PhCHO \xrightarrow{\Delta} CO + \underset{21}{PhCHCl_2} + \text{Other Products}$$

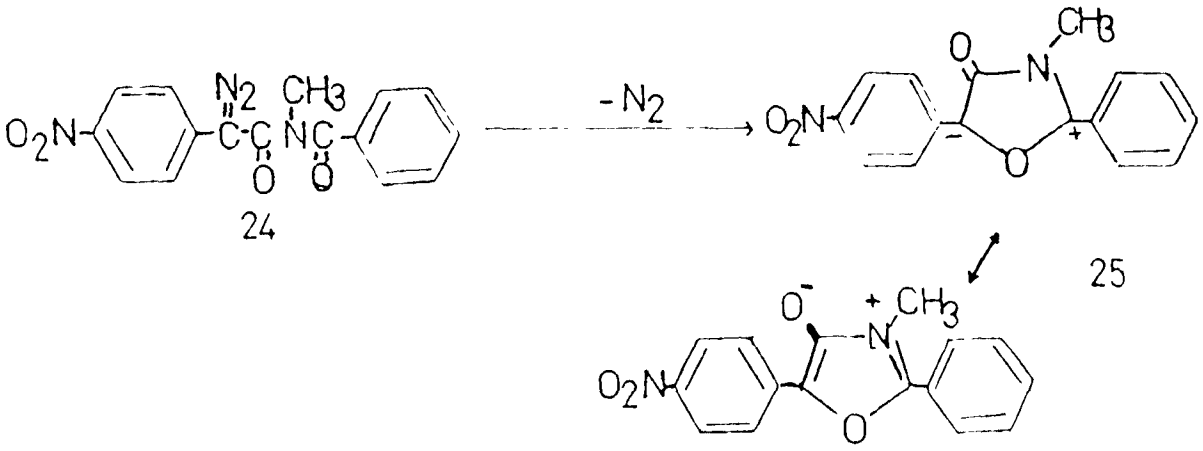
carbene 22 based on previous work which established the ease with which alkoxyhalocarbenes lose carbon monoxide.[66] Because the occurrence of 22 was difficult to envisage except from carbonyl ylide 23, the intermediacy of the 1,3-dipole was strongly suggested, eq 12.

[12] $$PhHgCCl_2Br + PhCHO \xrightarrow{\Delta} \underset{23}{\text{Ph, H, O}^{+}, -Cl, Cl}$$

$$\underset{22}{PhCH(Cl)-O-\ddot{C}-Cl} \xrightarrow{-CO} \underset{21}{PhCHCl_2}$$

Hamagushi and Ibata[67] reported the first synthesis of a stable carbonyl ylide generated by an intramolecular carbene-carbonyl reaction. Thermolysis of diazocompounds 24 in the presence of $Cu(acac)_2$ afforded a red solid identified as 2-phenyl-5 (p-nitrophenyl)-anhydro-4-hydroxy-1,3-oxazolium hydroxide (25). The product was stable, in the crystalline state, in the air for several weeks, eq 13.

[13]

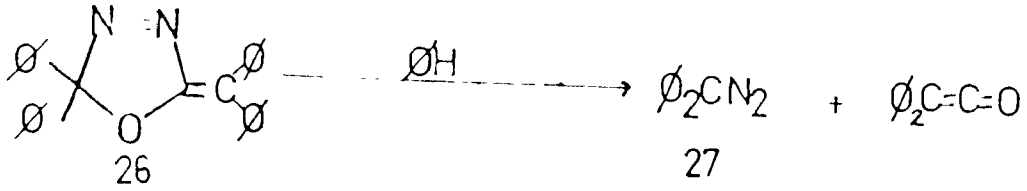


The formation of 25 was explained[67] in terms of the intramolecular attack of the carbene generated by the thermolysis of the diazoalkane (24), on the carbonyl oxygen.

I.1.3.3. *FROM OXADIAZOLINES*

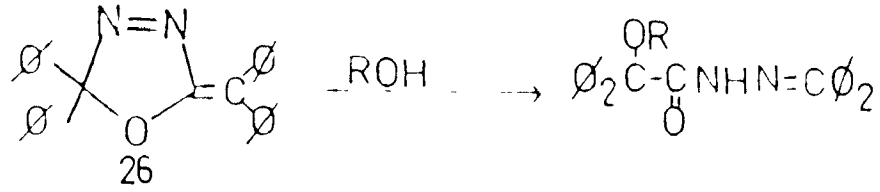
Like diazoalkanes, Δ^3-1,3,4-oxadiazolines can be decomposed thermally and photochemically. It was found[68] that photolysis of oxadiazoline 26 in benzene yielded diphenyldiazomethane and diphenylketone 27 (eq 14). When hydroxylic solvents were used, addition products were obtained, eq 15.

[14]



26 27

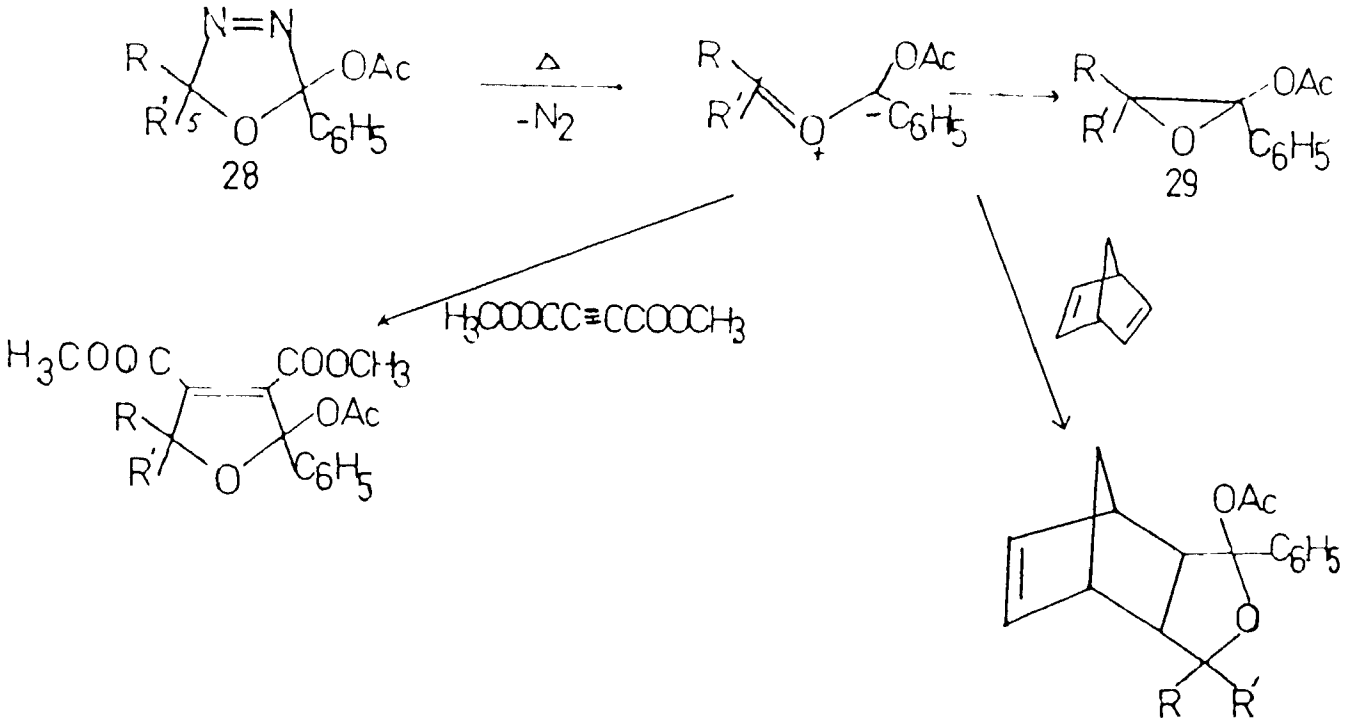
[15]



26

Hoffmann[69] found that 2-acetoxyoxadiazolines 28 thermolyzed to give epoxyacetates 29, via a trappable intermediate. A carbonyl ylide intermediate was proposed, and trapping experiments using norbornadiene and dimethylacetylenedicarboxylate succeeded, eq 16.

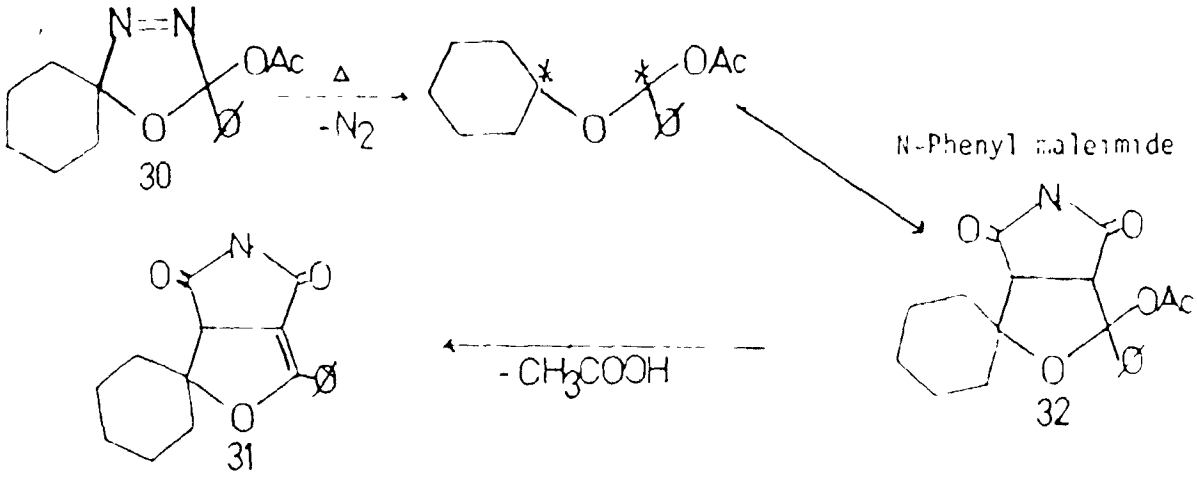
[16]



28 29

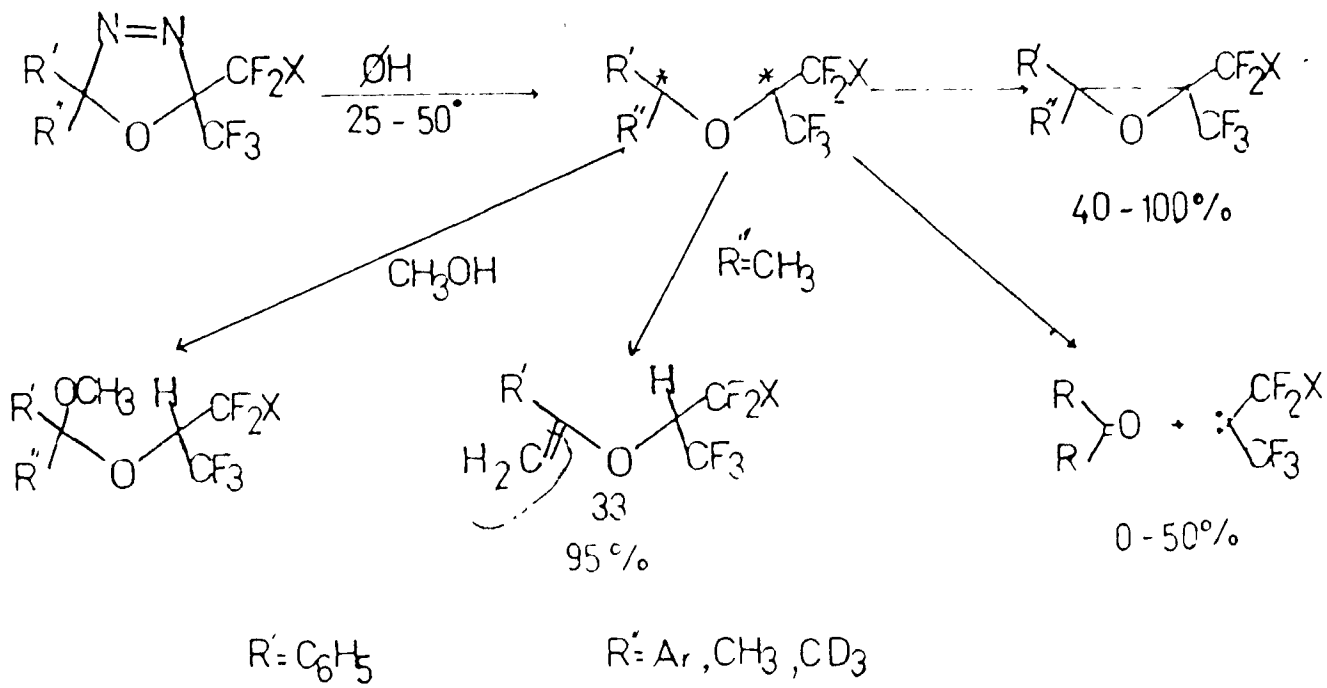
Rajagopalan[70] attempted to identify the intermediate from the thermal decomposition of phenyl - and acetoxy - substituted Δ^3-1,3,4-oxadiazolines. 2-Acetyl-5,5-pentamethylene-2-phenyl-Δ^3-1,3,4-oxadiazoline(30) was thermolyzed with N-phenylmaleimide in anhydrous benzene. Product 31 was identified and it was deduced that 31 was derived from an elimination of a mole of acetic acid from the adduct (32), eq 17.

[17]



Diazoalkanes are known to add to carbonyl compounds.[71] Bartlett[72] found that aromatic diazocompounds readily react with perfluoroacetones to give Δ^3-1,3,4-oxadiazolines, via cycloaddition. Thermolysis of the oxadiazolines goes through a carbonyl ylide intermediate to give epoxides, ketones, enols, and products of intermolecular reactions of the intermediate with traps, eq 18. Enolether (33) was derived from a known[73] 1,4-hydrogen shift in the intermediate ylide.

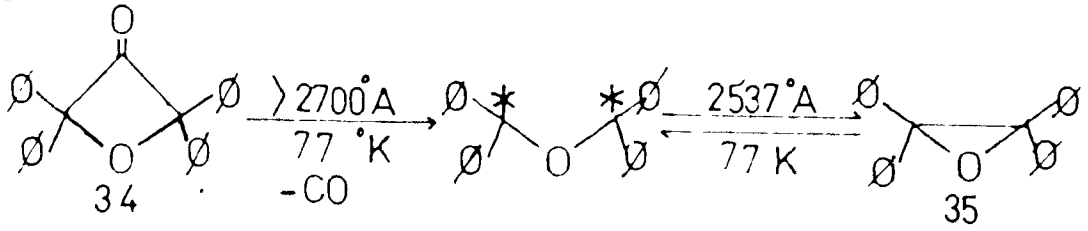
[18]



I.1.3.4. *FROM OXETANES*

Oxetanes are suitable sources of carbonyl ylide intermediates.[4] Griffin[74] showed that at λ = 360 nm, 2,2,4,4-tetraphenyl-3-oxetanone (34) may be photodecarbonylated under conditions where the oxirane (35) is photostable eq 19. The colored intermediate was identical to the one formed from the photolysis of 35 at a different wavelength. The carbonyl ylide was generated from a carbon monoxide extrusion in 34 and from a C-C bond scission in 35.

[19]

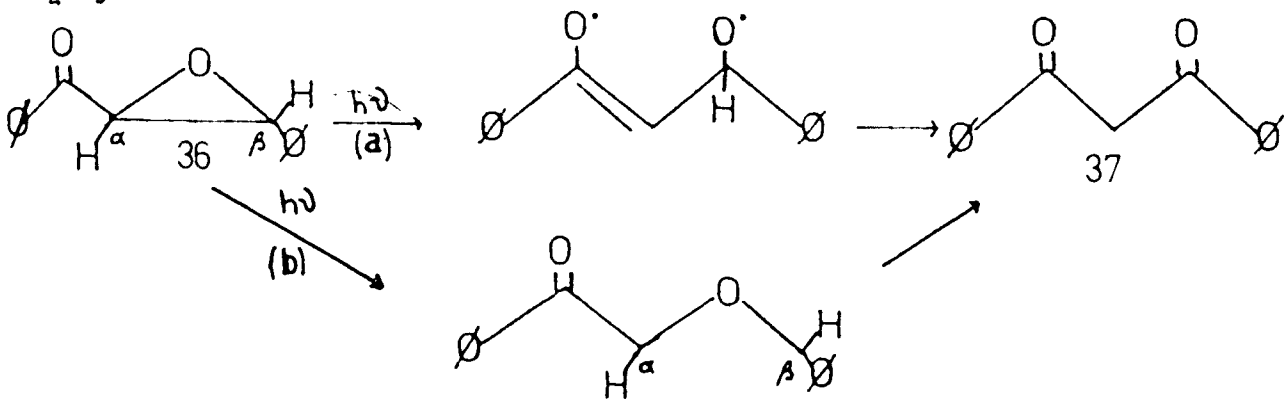


I.1.4-*REACTIONS OF CARBONYL YLIDES*

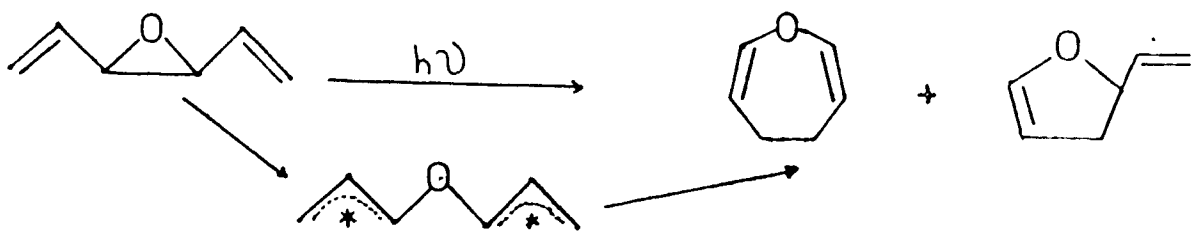
I.1.4.1: *INTRAMOLECULAR NON-DISSOCIATIVE REACTIONS*

Irradiation of trans-chalcone oxide 36 in acetonitrile leads to the formation of dibenzoylmethane 37 as a major product eq 20. Formation of 37 was first assumed[75] to arise from a C-O bond cleavage in the oxirane, followed by a 1,2-hydrogen shift of the β-hydrogen to the α-position (path a). It was later shown that a carbonyl ylide was formed via a C-C bond cleavage[76] (path b), prior to the formation of 37.

[20]

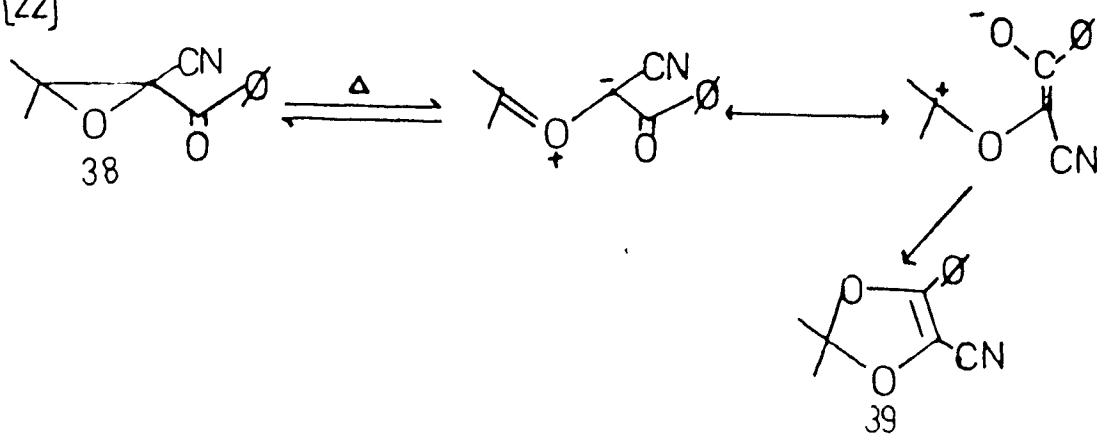


[21]



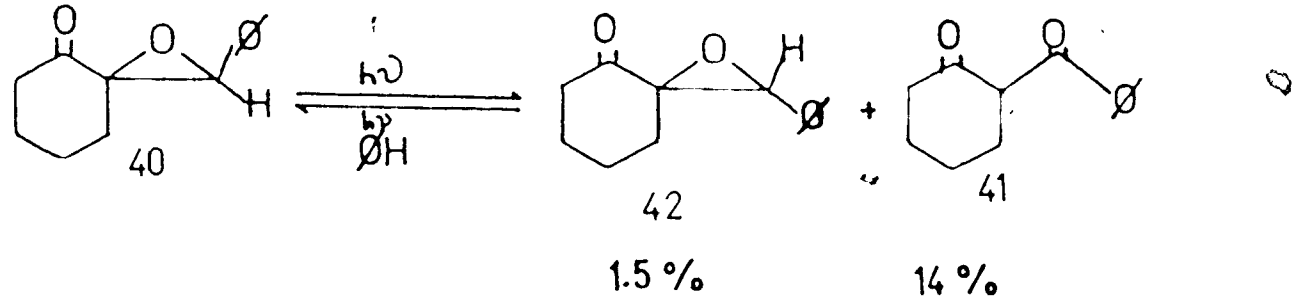
Even though epoxides which are α, α-disubstituted with two electron-withdrawing groups have been shown[1] to give trappable carbonyl ylides, the one derived from 38 was not trapped by dipolarophiles. Compound 39 was the major product,[77] eq 22.

[22]

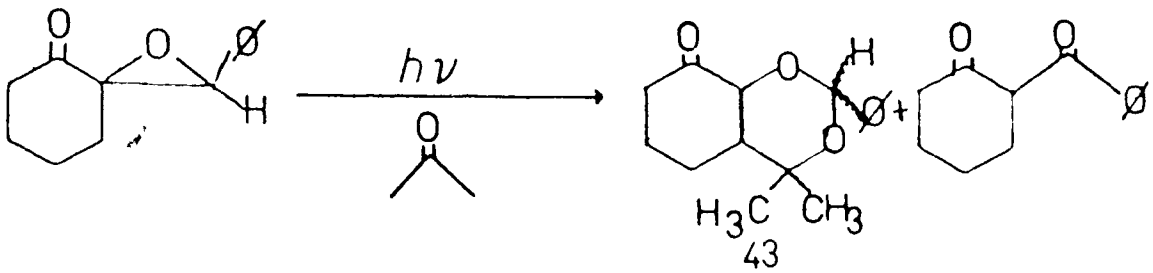


Similarly, Muzart and Pete[78] found that epoxide 40, upon photolysis in benzene, gave diketone 41 and small amounts of a product of isomerization (42), (eq 23). In the presence of acetone the intermediate was trapped by the solvent to give 43, with a small amount of diketone 41 (eq 24).

[23]

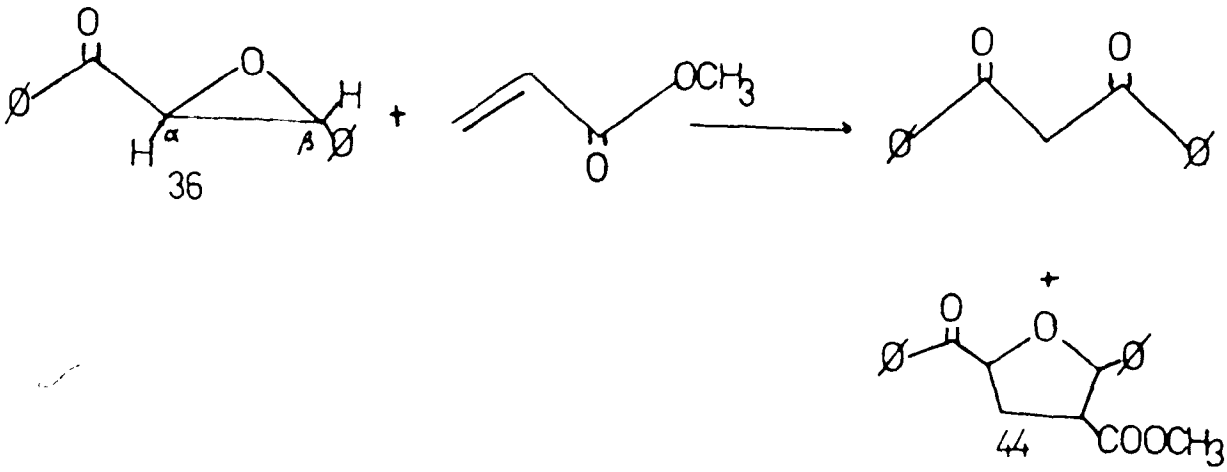


[24]

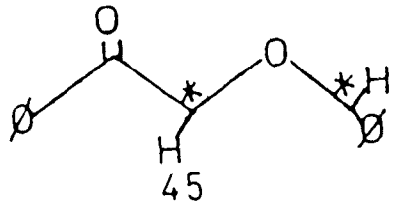


Lee[79] studied the irradiation of trans-chalcone oxides 36. When 36 was photolyzed in methyl acrylate a substituted tetrahydrofuran 44 was formed in addition to the expected[75] dibenzoylmethane, eq 25.

[25]



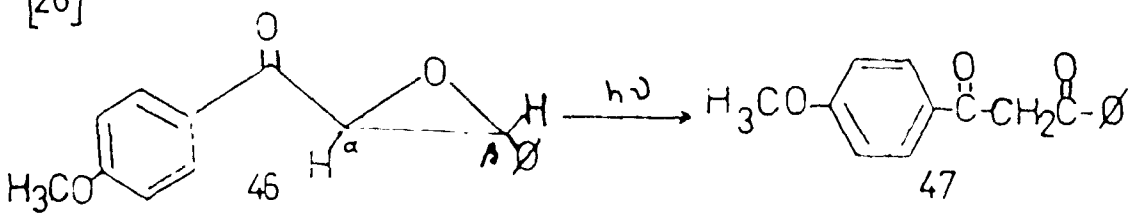
The configuration of the tetrahydrofuran adduct (44) suggested that at least 83% of the intermediate carbonyl ylide was formed by disrotatory cleavage of the C_1-C_2 bond, producing a trans-ylide (45).



The data also suggested that both C-O and C_α-C_β bond cleavages occured from a triplet excited state of 36.

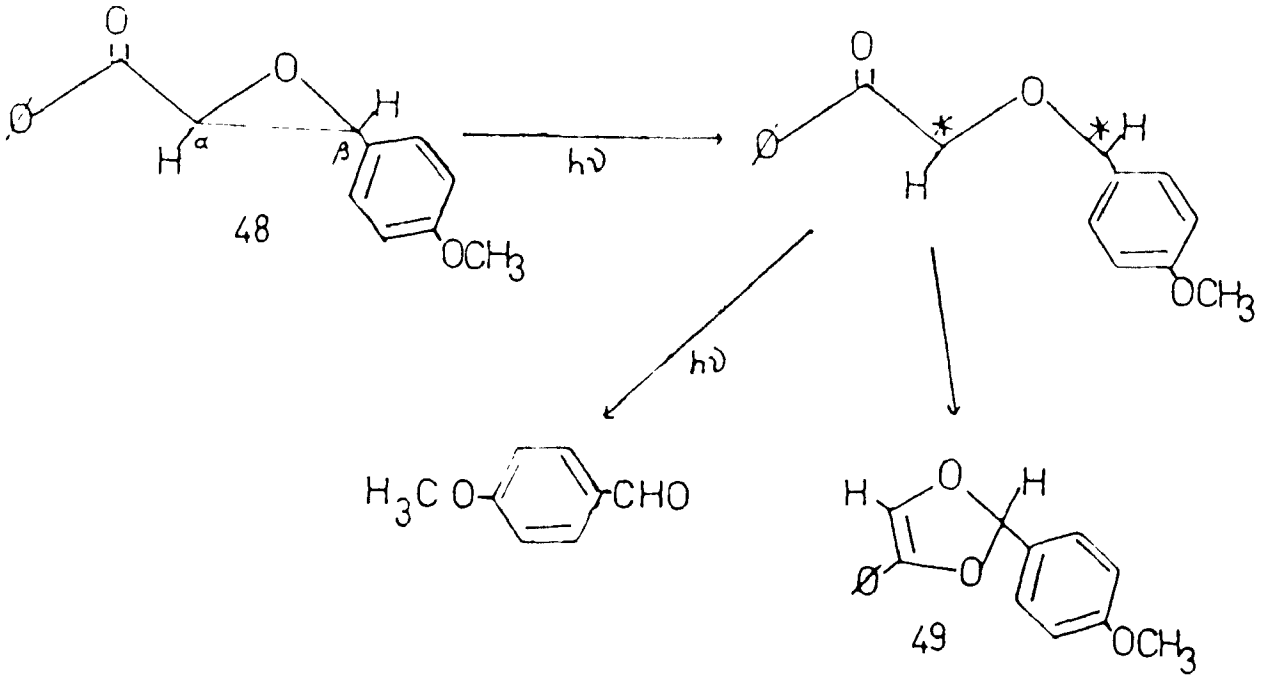
Photolysis of p-methoxychalcone oxide (46), in acetonitrile, cleanly formed 1-(4-methoxyphenyl)-3-phenyl-propanedione (47). Photolysis in methylacrylate decreased the efficiency of the production of the dione, and no tetrahydrofuran adduct was found, eq 26. Photolysis of 46 occured via C-O bond cleavage only.

[26]



When the isomeric chalcone oxide 48 was irradiated, 2-(4-methoxyphenyl)-4-phenyl-1,3-dioxole (49) was formed rapidly with small amounts of anisaldehyde (eq 27). This result pointed to a C_α-C_β bond cleavage leading to a carbonyl ylide, stabilized by the p-methoxyphenyl group. The reactive intermediate can undergo ring closure leading to 48 or it can suffer photodegradation to anisaldehyde.

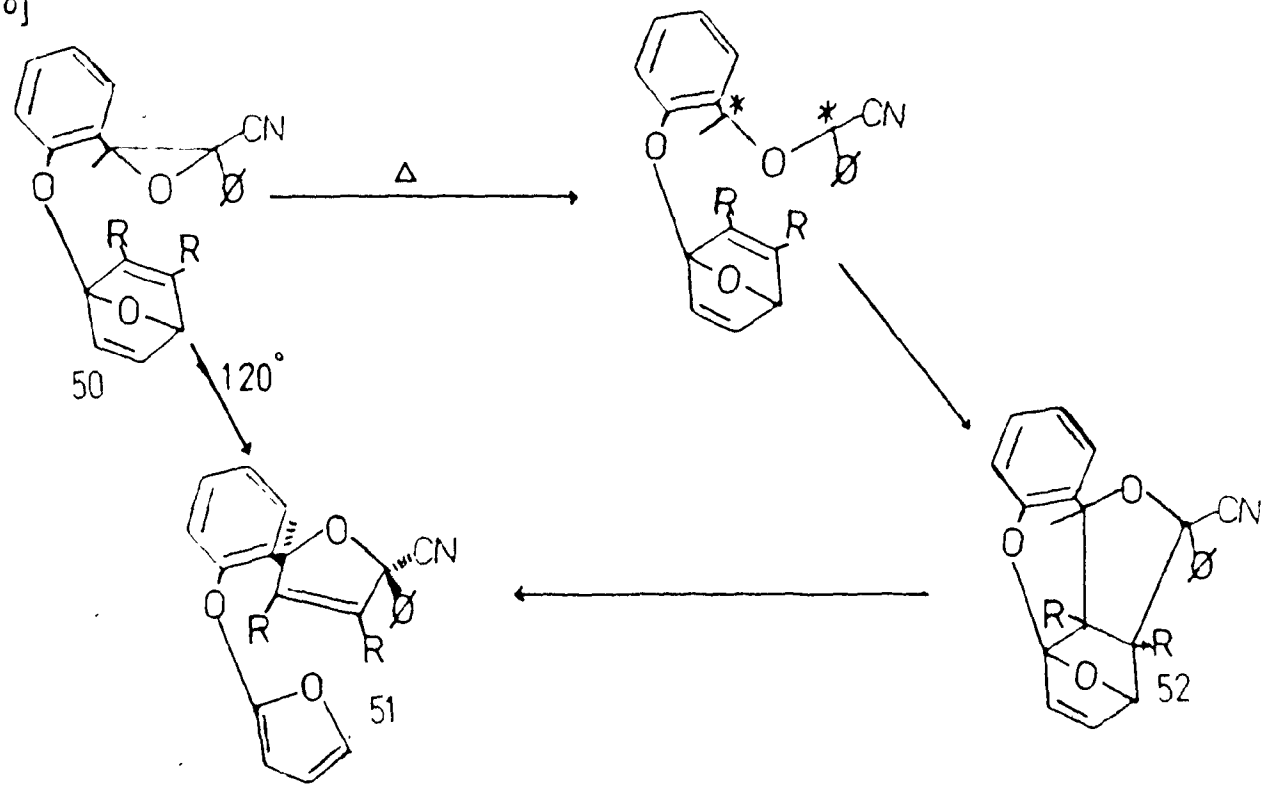
[27]



These results show the importance of substituent effects in controlling C-O vs C-C bond cleavage.

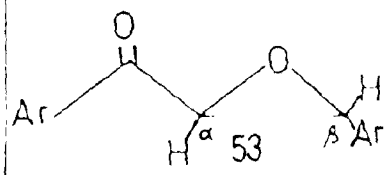
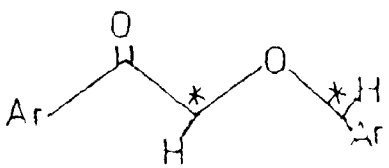
Very recently, thermolysis of epoxide 50 was reported[80] to give cleanly 2,5 dihydrofuran derivative 51. The mechanism involved a ring opening of epoxide 50 followed by an intramolecular cycloaddition reaction giving 52. Compound 52 undergoes rapid cycloreversion leading to 51, eq 28.

[28]



In the presence of dimethylacetylenedicarboxylate, bimolecular cycloaddition did not compete with the intramolecular reaction.

Pete[81] succeeded in detecting carbonyl ylides, generated from α-epoxyketones, from their absorbtion spectra at low temperatures. When photolyzed at 77°K, epoxyketone 53 gave rise to a colored intermediate giving structureless visible spectra. Characterization was made from the maximum absorbtion.

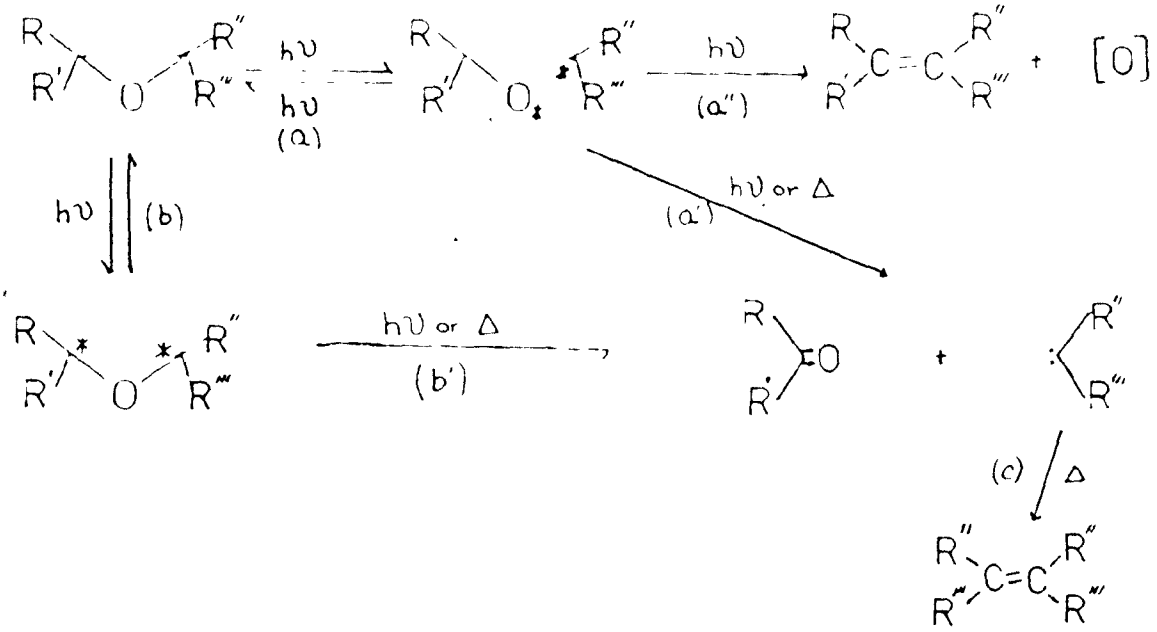
	Emitting excited state	
1	π π^*	585 nm (navy blue)
2	π π^*	560 nm (blue)
3	π π^*	575 nm (blue)

	Ar'	Ar''
1-	C_6H_5	α-Naphthyl
2-	C_6H_5	β-Naphthyl
3-	β-Naphthyl	β-Naphthyl

The colored intermediates were stable for four hours in the dark at 77°K. An increase in the temperature or irradiation with visible light rapidly bleached the sample.

I.1.4.2. FRAGMENTATIONS (DISSOCIATIVE REACTIONS)

Photolysis or pyrolysis of three membered rings frequently yields products from fragmentation of 1,3-diradical or 1,3-dipolar intermediates.[82-84] Low temperature photolysis of aryl oxiranes in rigid glass gave products according to the following scheme[85-87]

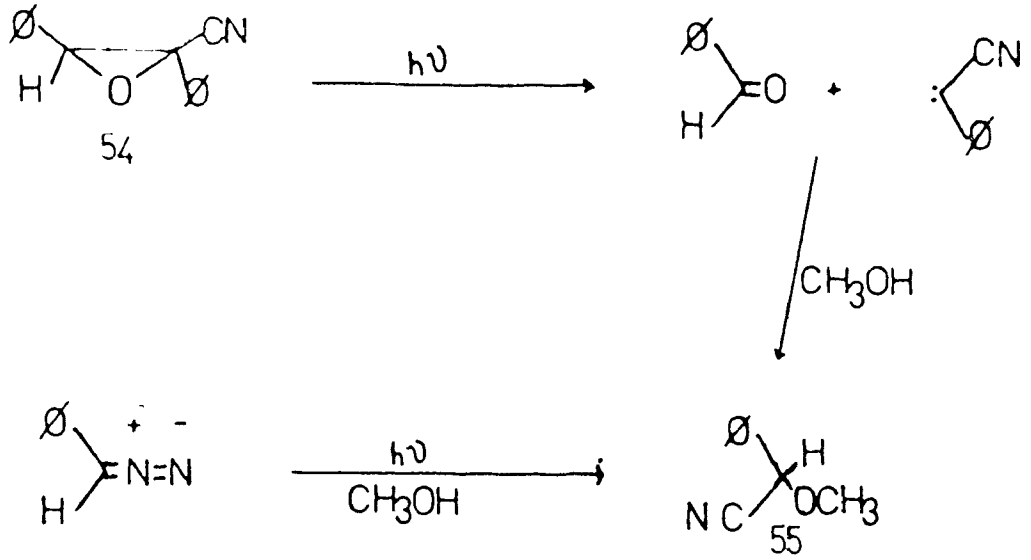


SCHEME 2

The 1st process (a or b) involves the formation of the colored carbonyl ylide intermediate. The second step involves a recyclization to oxirane (a or b) or the fragmentation to a carbene and a carbonyl compound (a' or b'). Alkenes are accounted for by an intramolecular heteroatom extrusion process (a'') or from a carbene dimerization (c). Evidence[88] showed that the colored intermediate was most likely a carbonyl ylide.

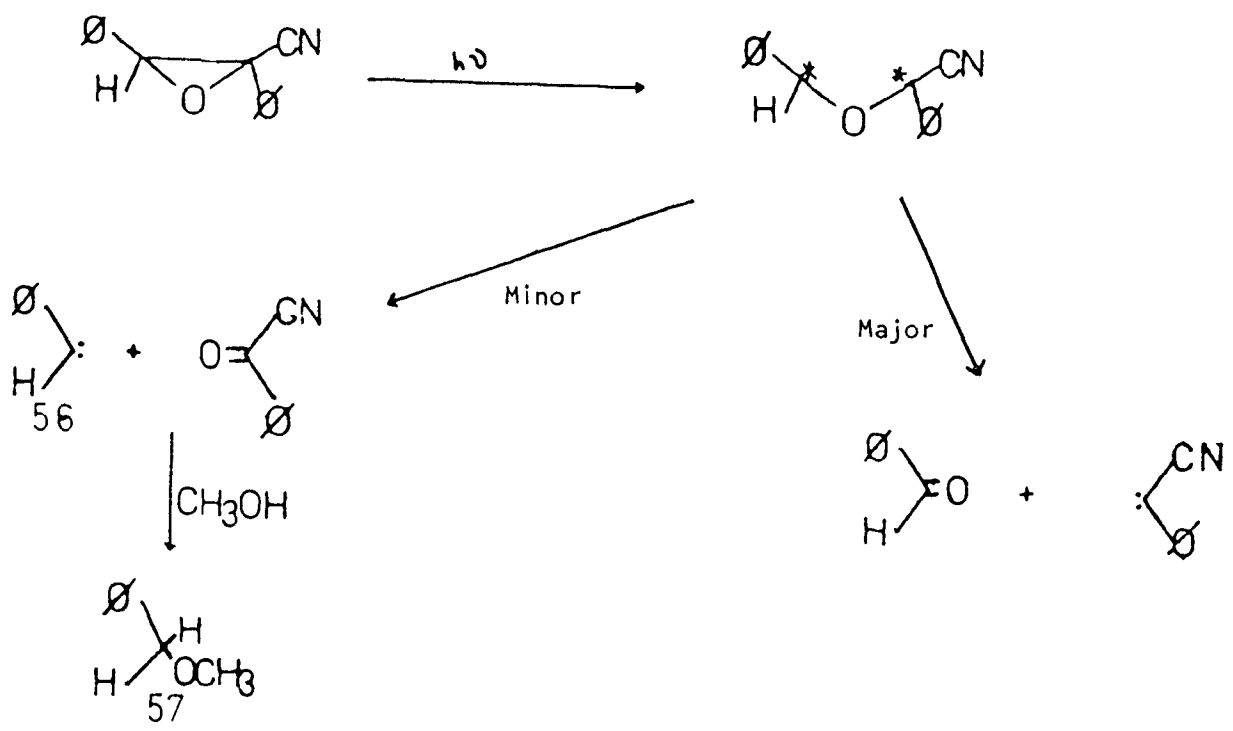
Phenyl substituted oxiranes were found to be precursors to substituted aryl carbenes.[89] When irradiated in methanol, trans-2,3-diphenyl-2-cyano-oxirane (54) gave rise to α-methoxyphenylacetonitrile (55), benzaldehyde, and other products. It was suspected that cyanophenyl methylene was the precursor to the ether. This was confirmed by carrying out a separate experiment, which involved the irradiation of diazophenylacetonitrile in methanol. As a result, ether 55 was produced, eq 29.

[29]



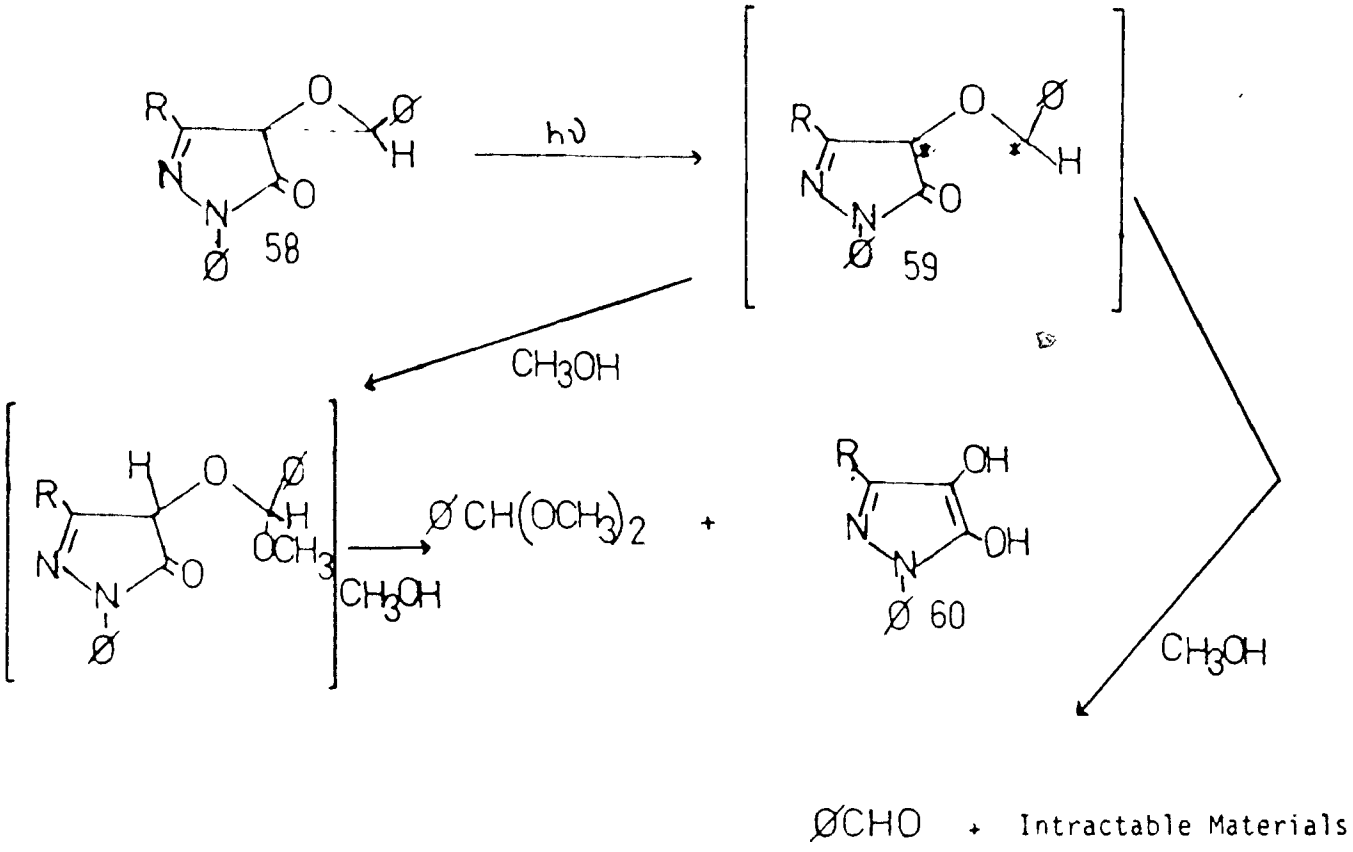
It would be logical to expect the fragmentation to occur both ways, giving phenylmethylene (56) and cyanophenyl methylene. The yield of benzylmethylether (57), derived from the insertion of carbene 56 into methanol, was less than 5%. This meant that the fragmentation occured mostly in one direction, eq 30.

[30]



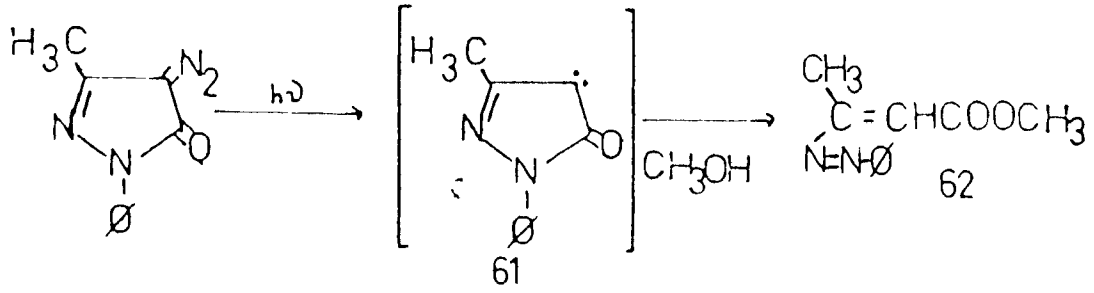
It was predicted[90] that the photochemical ring opening of oxiranes 58 would give heterocyclic carbenes. Photolysis of 58 in a non-protic solvent gave benzaldehyde and intractable products. In the presence of methanol, 60 was isolated. The products were explained on the basis of Scheme 3.

Generation of oxopyrazoline carbene 61 from the diazoalkane in the presence of methanol gave azoester 62, eq 31 The absence of 62 in the photolysis of 58 in methanol led[90] to the conclusion that the photochemical fragmentation of carbonyl ylides 59 does not occur in protic solvents, because of the efficiency with which methanol intercepts that intermediate.


58
59
60
CH3OH
CH3OH
CH3OH
ØCH(OCH3)2
+
ØCHO + Intractable Materials

SCHEME 3

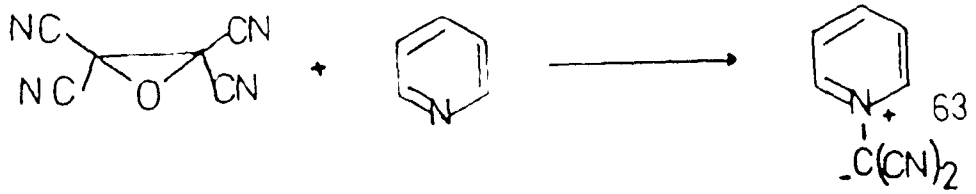
[31]


61
CH3OH
62

I.1.4.3. *INTERMOLECULAR REACTIONS*

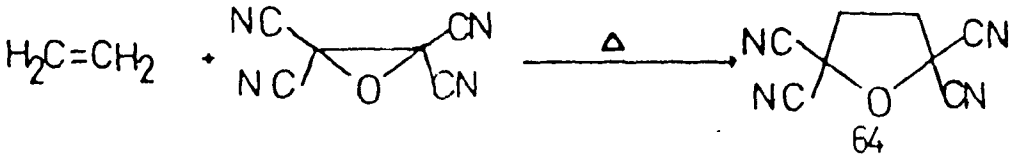
The best known carbonyl ylide is probably the one derived from the thermolysis of tetracyanoethyleneoxide (TCNEO)[91]. The ease with which TCNEO undergoes nucleophilic attack is derived from the strong electron-withdrawing character of the cyano groups. In the presence of iodide ion, TCNEO affords cyanogen iodide and tricyanovinyl alcoholate.[92] With pyridine, ylide 63 is obtained, eq 32.

[32]



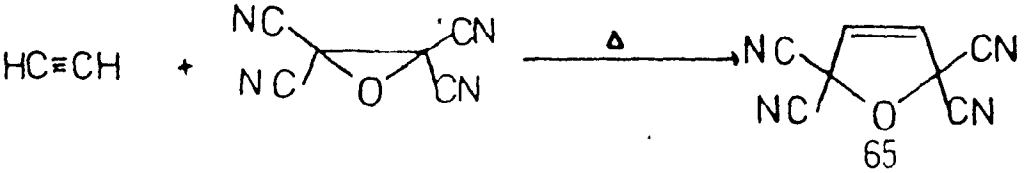
When thermolyzed in an alkene, TCNEO undergoes a cycloaddition reaction with the olefin.[93] Epoxides usually undergo acid catalyzed ring opening involving a C-O bond cleavage, but TCNEO adds to olefins by cleavage of the C-C bond. For example, ethylene and TCNEO condense smoothly to give 2,2,5,5-tetracyanotetrahydrofuran (64), eq 33. The reaction of TCNEO with acetylene gives 2,2,5,5-

[33]



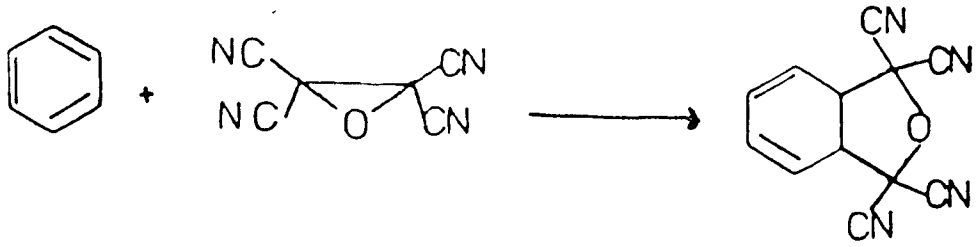
tetracyanodihydrofuran (65), eq 34. TCNEO also adds to aromatic systems

[34]



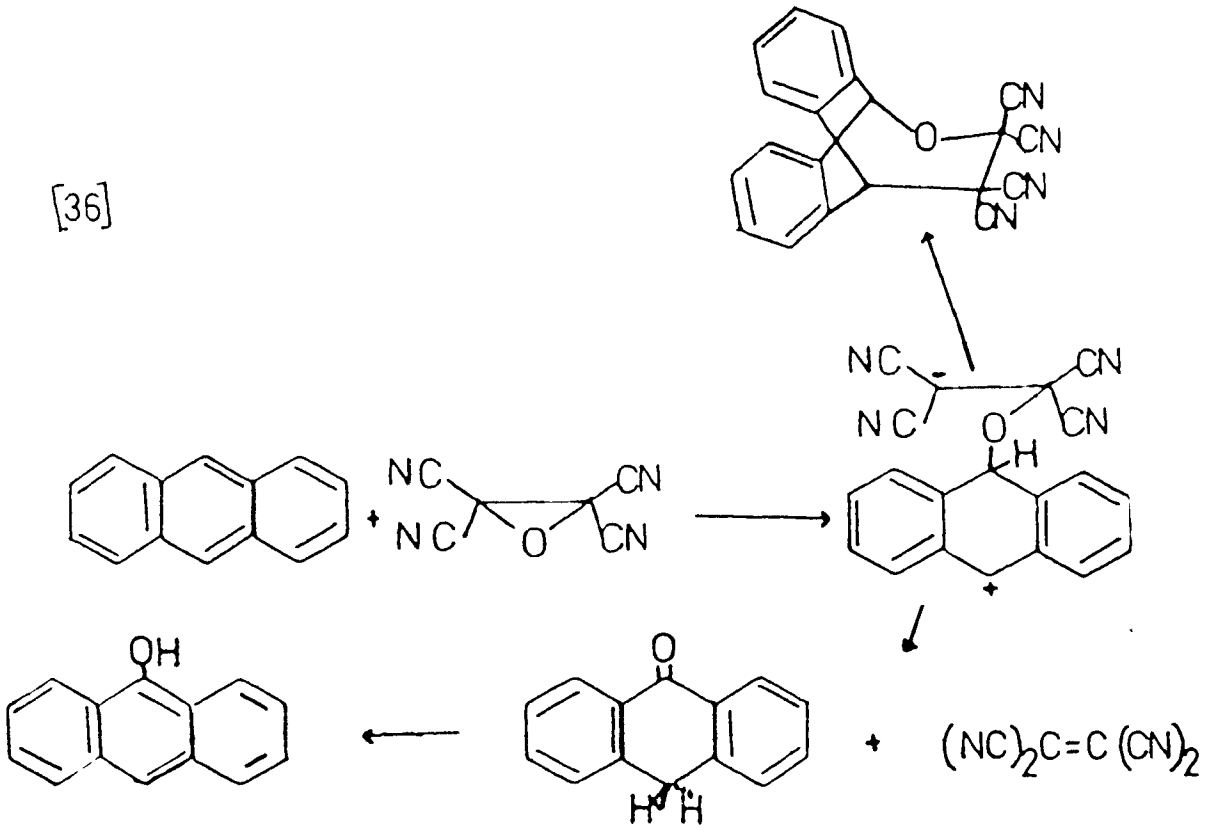
as demonstrated by its reactions with benzene. With aromatics of greater

[35]



nucleophilicity, oxygen transfer may occur,[94] eq 36.

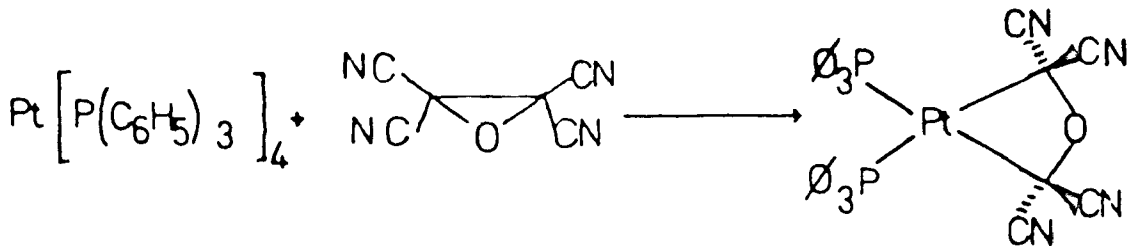
[36]



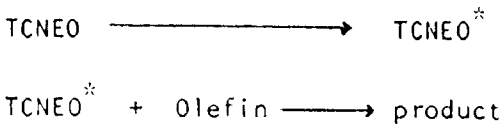
Examination of three separate cis-trans pairs of olefins, 2-butene, stilbene, and 1,2-dichloroethylene, showed that the addition of TCNEO to dipolarophiles was stereospecific.[93]

The carbonyl ylide from TCNEO was also trapped as a metal complex,[95] eq 37.

[37]



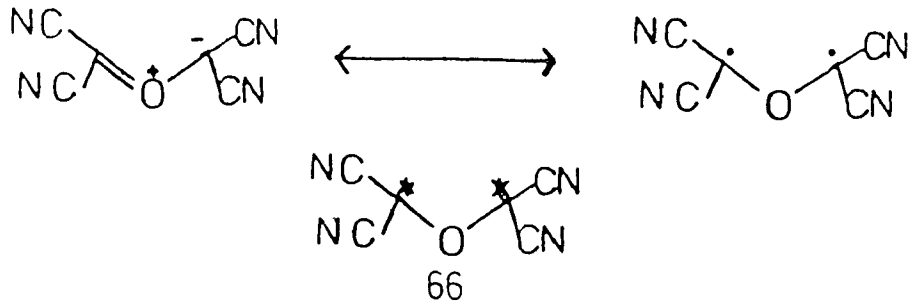
Kinetic studies of the thermolysis of TCNEO showed[96] that the reaction mechanism can be represented by the reaction sequence below, scheme 4.



Scheme 4

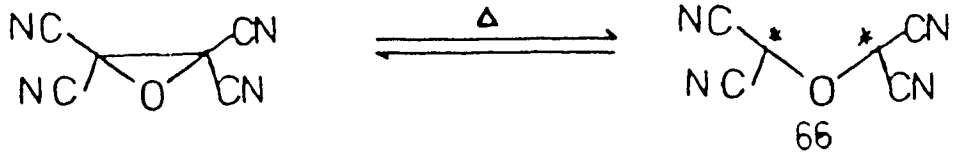
The authors[96] viewed TCNEO* as a hybrid of biradical and zwitterionic canonical forms, generally represented as (66), eq 38.

[38]



The hybrid was believed to add to the olefin by a concerted or near-concerted cyclic process.

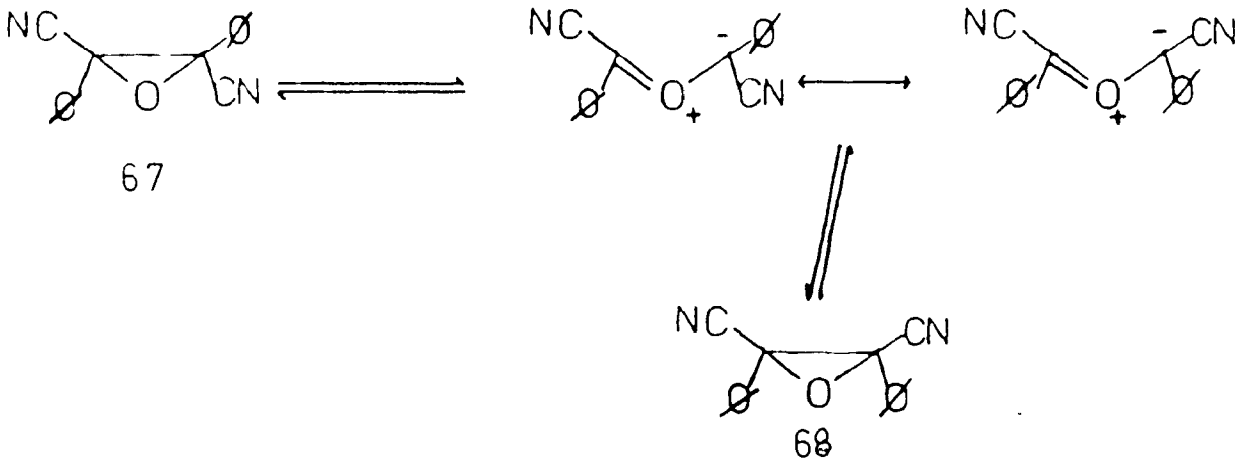
When heated to about 100°C TCNEO was found[96] to be in equilibrium with a low concentration of carbonyl ylide 66, eq 39.



66

Furthermore, trans-2,3-dicyano-2,3-diphenyloxirane[97,98] (67) was found to isomerize, via a carbonyl ylide intermediate, to the cis isomer 68 when heated at 100°C in dioxan, eq 40.

[40]

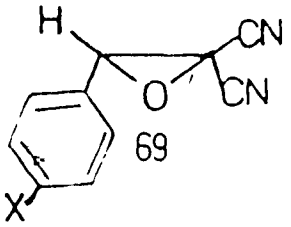


67

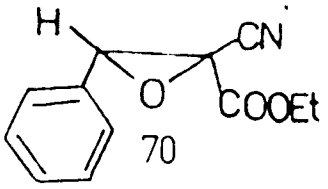
68

The structure of the products from the addition of epoxide 67 to acetylenic and to olefinic dipolarophiles confirmed[99] C-C bond fission.

In order to check the thermal ring opening[100] of 69 and 70, imines 71 were used as traps. The addition of the intermediate from the thermolysis of 69 and 70 to 71 afforded 72 and 73 in over 60% yields.

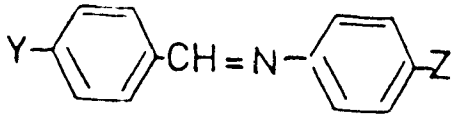


69



70

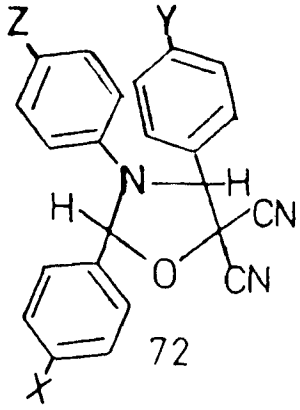
X= H, Cl, OCH_3, NO_2



71

Y= H, OCH_3, NO_2, Cl

Z= H, OCH_3, NO_2



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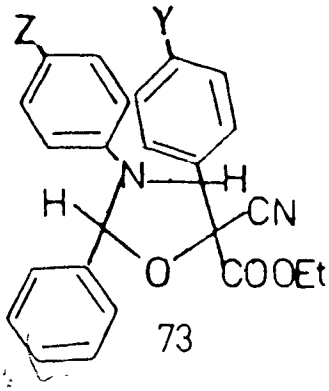


73

The proposed mechanism involved a carbonyl ylide intermediate. Support for that structure came from the observation that the dependence of epoxide 69 reactivity on para substituent (X)[101,102] followed the order: OCH_3 >> Cl ~ H >> NO_2. This result confirmed the ionic character of the intermediate.[103,104]

I.2. CARBENES

I.2.1. INTRODUCTION

Carbenes are neutral, divalent carbon intermediates in which a carbon atom has two covalent bonds, and two non-bonding orbitals containing two electrons. If the two electrons are spin-paired the carbene is a singlet; if the spins are parallel the carbene is a triplet.[105] A triplet carbene often reacts as a diradical.[20]

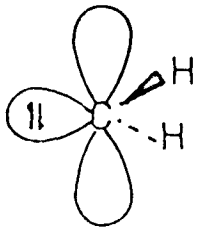
Singlet carbenes are electron deficient, like carbonium ions, while possessing a non-bonding pair like that of carbanions. Electrophilic or nucleophilic character of singlet carbenes depends on the ability of adjacent groups to withdraw electrons from or supply electrons to the carbene carbon.[20]

I.2.2. ELECTRONIC CONFIGURATION OF CARBENES

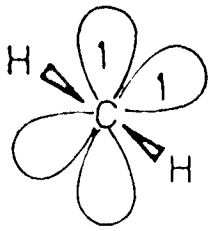
A great deal of attention has been focused on the nature of the electronic configuration of carbenes.[106] If the difference[107] between the energies of the non-bonding molecular orbitals is greater than the energy required to bring a pair of electrons together in a single molecular orbital, then both electrons will occupy the lower-energy non-bonding molecular orbital. Their spins must be paired, giving rise to a singlet electronic state. If, however, the difference in molecular orbital energies is less than the increase in electron-electron repulsion energy from non-bonding electrons when they are brought together in the same spatial orbital, then the non-bonding electrons will occupy different orbitals. Hund's

rule tells us that two electrons occupying different orbitals achieve minimum energy when their spin functions are the same, and thus such a carbene is in a triplet electronic state. A number of articles and reviews have covered the problem extensively. [106-109]

Singlet carbenes [50] are substantially bent (e.g. $^1CH_2$(74) $\theta = 102°$), [110] whereas triplet carbenes are closer to linearity although normally still bent (e.g. $^3CH_2$ (75), $\theta = 136°$) [111].



74



75

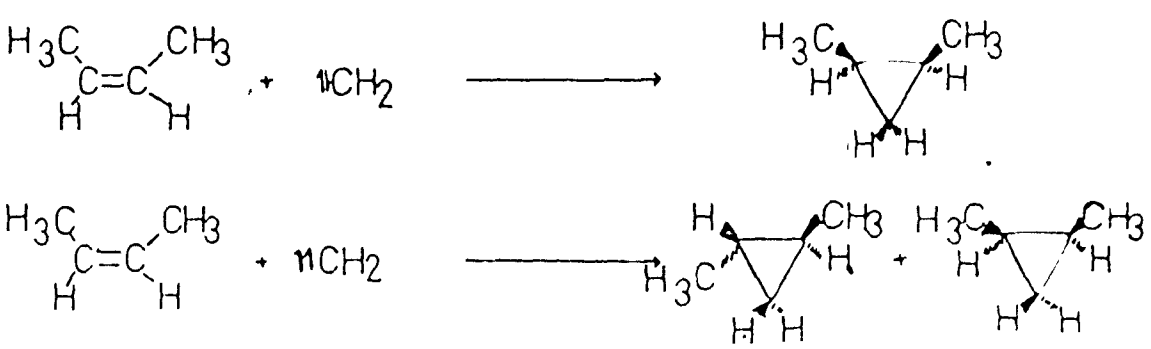
The spin multiplicity of carbenes can be assigned by spectroscopic techniques,[50,115,116] by Chemical evidence, and by theoretical calculations.[112-114]

I.2.2.1 FROM THEORETICAL CALCULATIONS

Theoretical calculations showed that as a general rule the singlet carbene appears to be the ground state for acyclic carbenes, [112] HCX and XCX, whenever X has a lone pair π-donor atom bonded directly to C (i.e., when X=OR, F, NR_2). Electronegativity of the substituent is an important, [113] perhaps decisive, factor in determining the multiplicity of the ground state of substituted acyclic carbenes. Electronegative substituents (e.g. F) favor a singlet ground state, whereas electropositive substituents favor a triplet ground state (e.g. Li). Results of very recent studies by Houk [114] give more complete predictions, including the singlet-triplet energy gap.

I.2.2.2 *FROM CHEMICAL EVIDENCE*

The spin mutiplicity of carbenes had been, for a long time, inferred from chemical evidence.[50] Skell[117-119] argued that singlet carbenes undergo concerted stereospecific addition to olefins and that the corresponding triplet carbene may add non-stereospecifically, eq 41.

[41] 

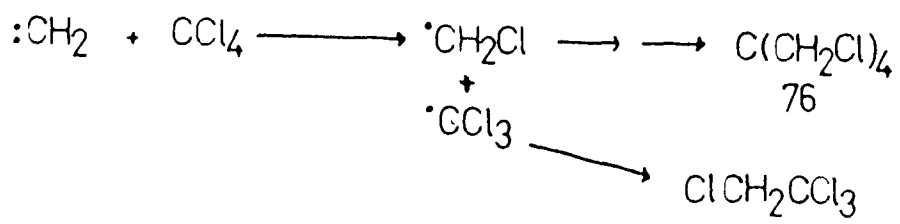
Doering and co-workers[120] demonstrated that insertion into a C-H bond with retention of configuration is typical of singlet carbenes, whereas insertion with loss of optical purity is typical of triplet carbenes. Nevertheless, the application of the above mentioned chemical criteria for assigning spin multiplicities to reacting carbenes is not completely satisfactory.[50]

I.2.2.3 *FROM SPECTROSCOPIC TECHNIQUES*

Molecular spectroscopy has been used to identify singlet and triplet carbenes generated by flash-photolysis of dilute gaseous systems and to determine the structures of these species.[115] ESR spectroscopy is a powerful technique for studying carbenes with triplet ground states at low temperature in inert matrices.[116]

Urry and Eiszner[121] found that, when generated in CCl_4, methylene afforded pentaerythrithyl tetrachloride (76), the formation of which requires four moles of diazomethane per mole of CCl_4. The formation of 76 was explained with a ten step radical chain mechanism, eq 42.

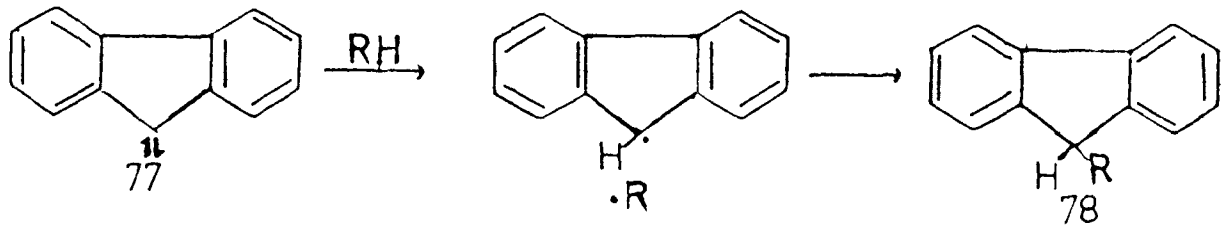
[42]



Roth[122] carried out the reaction in the probe of an NMR spectrometer and observed CIDNP signals of several minor products, most prominently that of 1, 1,1,2-tetrachloroethane. The observed signal directions indicated that singlet methylene was involved in the abstraction reaction that led to the polarized products, and that it initiated the free-radical chain reaction leading to the tetrachloride 76. He concluded that chlorine abstraction was a major reaction of singlet methylenes.[50]

Finally, very recently, Wong, Griller, and Scalano[123] observed, by laser flash photolysis, the reaction of fluorenylidene 77 with alkanes . They concluded that the singlet carbene abstracts a hydrogen from alkanes , in a first step, prior to the formation of product 78, eq 43.

[43]



I.2.3. *REACTIONS AND REACTIVITIES OF CARBENES .*

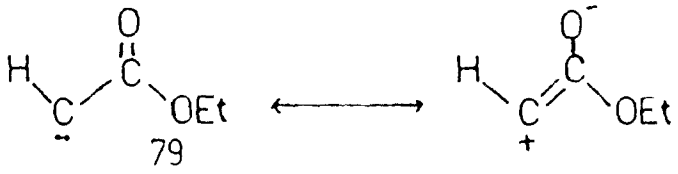
I.2.3.1. *ELECTRONIC EFFECTS IN THE CARBENE*

Although substituents have a great influence on nucleophilicity and electrophilicity of carbenes, most singlet carbenes behave as electrophiles.[124-130] A

quarter of a century ago Doering and Hoffmann[131] reported that dichlorocarbene and dibromocarbene add to simple alkenes generating cyclopropanes. Efforts were made to characterize carbenic addition reactions experimentally and theoretically. Skell[132] and Doering[133] carried out relative reactivity measurements. Two alkenes were allowed to compete for an insufficiency of carbene. From the product mole ratio of the corresponding cyclopropanes, corrected for the initial mole ratio of alkenes, the relative reactivity toward the alkene pair was calculated CBr_2[132] and CCl_2[133] were found to be electrophilic toward simple alkenes.

Resonance effects, in singlet carbenes, can operate in one of two ways both of which result in a net stabilization of the intermediate, relative to methylene. When one of the substituents is an electron-withdrawing group, stabilization results from conjugation, eq 44.

[44]



79

Carbethoxy carbene (79) is more electrophilic than methylene.[34] Lone pair substituents can act as electron-donating groups, stabilizing the divalent carbon through conjugation (eq 45), and making the carbene more nucleophilic than methylene. Relative

[45]

reactivities of m- and -p-substituted phenyl carbenes have been found[134] to be: m-Cl>p-Cl>p-CH_3>p-OCH_3.

Some[4] unifying concepts emerge upon examining the literature. An order of increasing electrophilicities of carbenes has been developed by Harrison[135] $:CF_2 > :CHF > :CH_2$ and $:CF_2 > :CCl_2 > :CBr_2 > :Cl_2 > :CH_2$. More strongly electron-donating substituents increase the nucleophilic character of the carbene and thus raise the activation energy for electrophilic addition to olefins.[16]

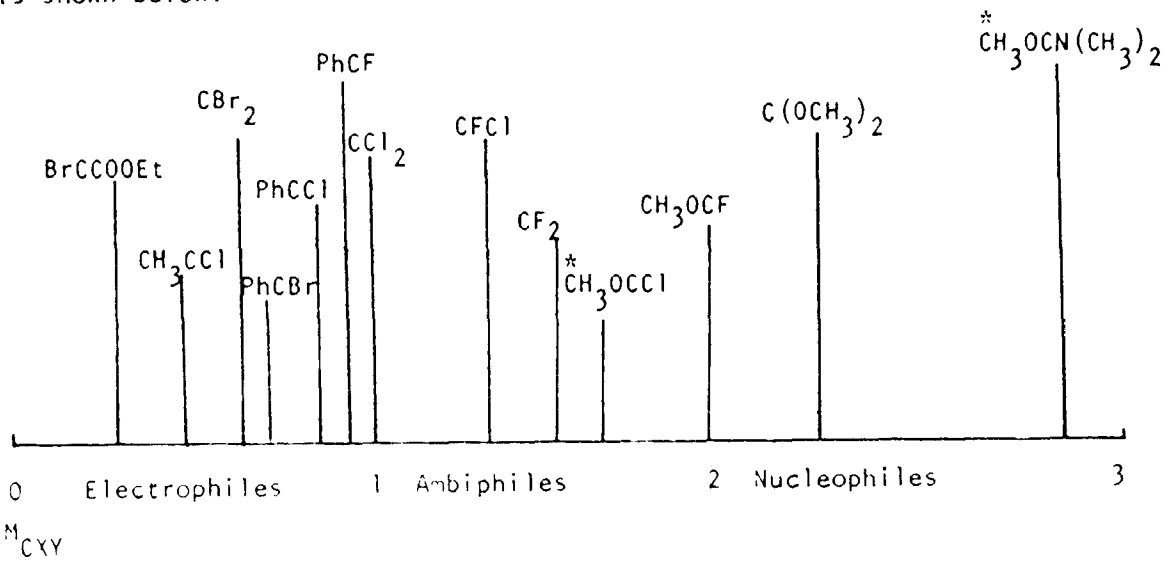
Increasing[4] carbene selectivity is generally encountered with increasing substitution of methylene hydrogen atoms by halogens, carbalkoxyl, aryl, and alkyl groups. Generally the greatest enhancement is achieved when methylene is disubstituted.[16] An order of reagent selectivity toward addition to olefins has been developed by Skell and Cholod[136] $CH_2 < :CBr_2 < Me_2C=C=C: < :CCl_2 < :CF_2$. Skell also interpreted this as the order of decreasing electrophilicities of these singlet carbenes.

A formula[128] was developed allowing predictions of the nucleophilicity and electrophilicity of carbenes. Only singlet carbenes were considered. The following conventions were adopted;[137] a standard set of alkene substrates ($Me_2C=CMe_2$, $Me_2C=CHMe$, $Me_2C=CH_2$, cis-MeCH=CHMe, and trans-MeCH=CHMe), with $Me_2C=CMe_2$ as the reference alkene (ko=1.00), and a standard carbene, CCl_2, were used. Relative reactivities were measured for CXY (X and Y substituents on the carbene) and for CCl_2 at 25°C. The "Carbene Selectivity Index", M_{CXY}, was defined as the least-squares slope of log $(\frac{ki}{ko})_{CXY}$ vs log $(\frac{ki}{ko})_{CCl_2}$. Multiple linear regression analysis[138] of the dependence of M_{CXY} (obs.) on σ^+_R an σ_I, afforded the dual substituent parameter correlation (eq 46) in which $\Sigma_{X,Y}$ represents the sum of the appropriate σ constants[138] for the substituents of the carbene CXY.[139]

[46]

$$M_{CXY} = -1.10 \sum_{X,Y} \sigma^+_R + 0.53 \sum_{X,Y} \sigma_I - 0.31$$

A "carbene selectivity spectrum", towards olefins, in which carbenes are positioned according to experimental or calculated M_{CXY} values was developed and is shown below.[140]



' = Calculated.

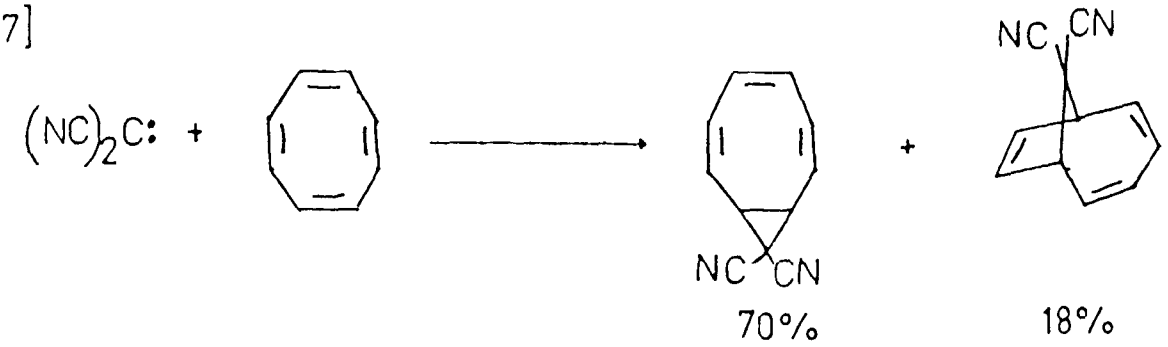
I.2.3.2. *ELECTRONIC EFFECTS IN THE OLEFIN*

Since most carbenes are electrophiles, the addition to olefins would be facilitated by electron-donating groups on the double bond.

Aryl substituents (styrenes) have a slight accelerating influence on the addition of carbenes, which proceeds more rapidly than the corresponding addition to cyclohexene.[141,142] In contrast, fluorine substitution on the olefin has a decelerating effect on the carbene addition reaction..[143-146] Similar deactivating effects have been found when 1-carbalkoxyl[147] and 1-acetyl[148] were substituents on the olefin.

The rates of addition of singlet and triplet carbenes to monoolefins are often comparable, although a rate preference for addition by the singlet species is sometimes observed. However, when the olefin is a diene there is a marked preference for the triplet species over the corresponding singlet species. Stepwise addition of the triplet affords a diradical intermediate stabilized via resonance.[4,129,149-152] The addition of triplet carbenes to dienes affords mostly[153] 1,2 addition products, eq 47.

[47]



I.2.3.3. *STERIC EFFECTS IN THE CARBENE AND THE OLEFIN*

Steric hindrance would be expected to be more important for carbenoid addition to olefins than for carbenes. For carbenoids there is a greater degree of olefin bonding to the divalent carbon in the transition state than for a free carbene.[154] Furthermore, the steric bulk of carbenoids can be enhanced through solvation effects in polar solvents[129] and/or by proximity of the metal atom or the ligands around the metal in a three-centre addition site in the transition state.[155]

The reaction of triplet diphenylcarbene with olefins has been investigated.[156] Diphenyl carbene (triplet) is known to react with olefins in the normal addition way, and also by radical hydrogen abstraction and radical recombination (process known as "abstraction-recombination" instead of "insertion"[4,129,157-159]). Jones[156]

demonstrated that the preference of one path over the other depends on steric factors presented by substituents in the olefin. The competing abstraction-recombination process, observed some years ago for reactions of diphenylcarbene with 2-butene,[160-162] is unusual in that other triplet carbenes do not generally undergo this reaction with olefins. Jones,[156] study demonstrated that the abstraction-recombination reaction is not an inherent feature of the reactivity of triplet diphenylcarbene, but instead it depends as well upon the nature of the olefin with which the carbene reacts.[156]

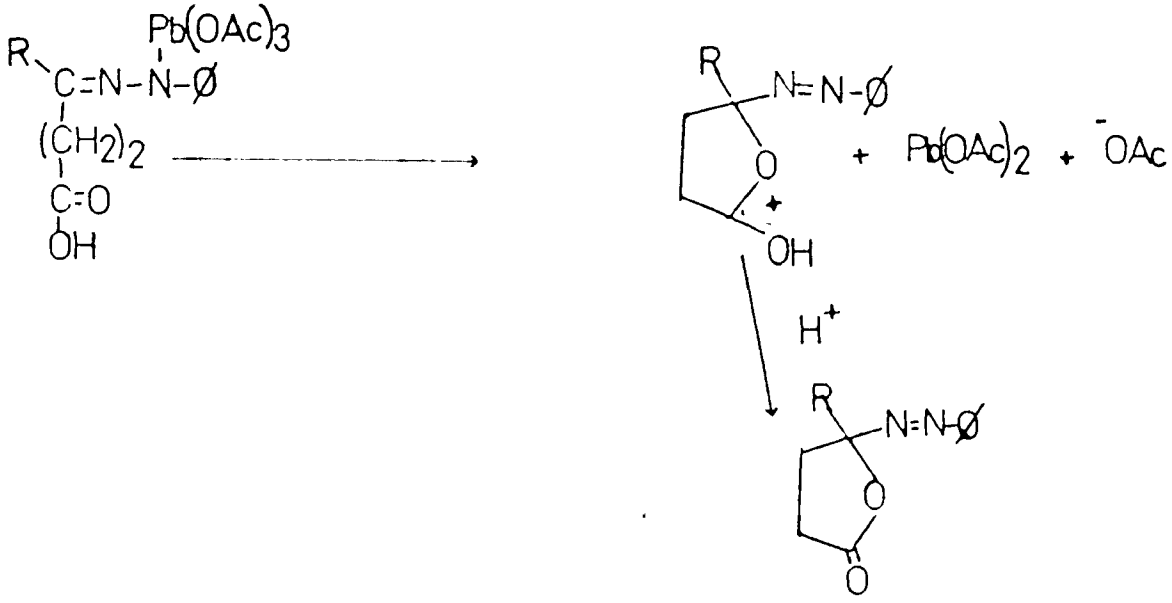
I.3 CHEMICAL AND ELECTROCHEMICAL OXIDATIONS

I.3.1. CHEMICAL OXIDATIONS

The first reported[163] use of lead tetraacetate (LTA) was made by Dimroth in 1923, in the oxidation of malonic esters and aryl substituted methanes to acetoxy derivatives. Concurrently, Criegee[164] studied the conversion of olefins to di-acetoxy compounds, and the use of LTA to cleave 1,2-diols.[165] LTA is a versatile reagent which reacts with sugars,[166] sterols,[167] oximes,[168] semicarbazones,[169,170] hydrazones,[171] azines,[172] and many other nitrogen compounds.[173] Its versatility and its synthetic utility have been reviewed extensively.[174,175]

When a suitable cyclization site occurs in the ketone substituents of the ketone hydrazones, at the 4th or 5th atom from the methine carbon, a cyclic product is obtained upon oxidation with LTA.[176] A probable mechanism for the cyclization is a nucleophilic attack by the carbonyl oxygen on the sp^2 carbon of an organolead intermediate, eq 48.

[48]

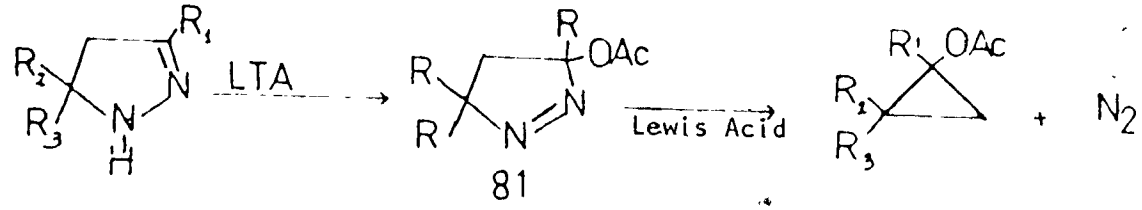


In the case of 80 the C,C double bond is not nucleophilic enough to cause cyclization analogous to that which occurs with a carbonyl group, eq 49.

[49]

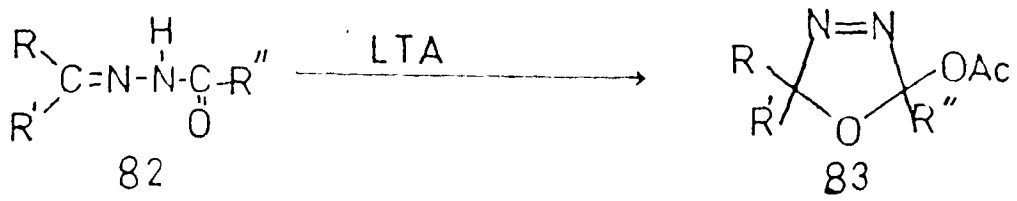
Freeman[177,178] used LTA oxidation to generate azoacetates 81 that were used to synthesize substituted cyclopropanes, eq 50.

[50]



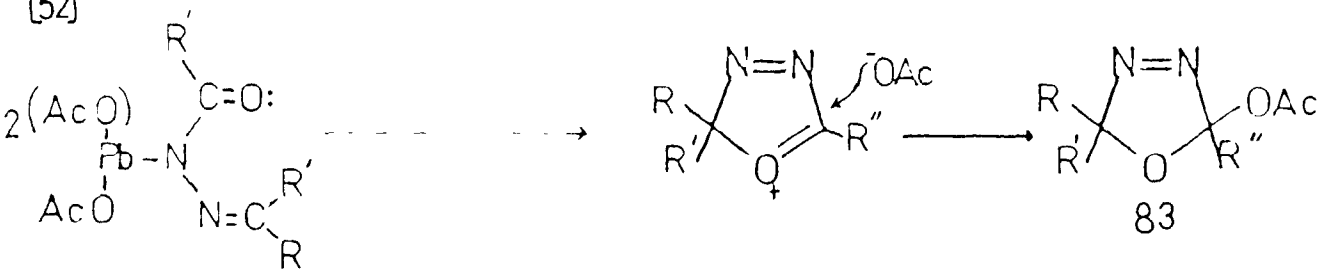
Hoffmann[179-181] first reported that ketone-carbonyl hydrazones of type 82 readily cyclize upon treatment with LTA to Δ^3-1,3,4-oxadiazolines 83, eq 51.

[51]



He envisaged an ionic mechanism for the formation of 83 involving a loss of acetate ion from azoacetate, followed by attack on the resulting carbocation by the carbonyl carbon. Norman[182] also reported this cyclization, but proposed a polar mechanism that does not involve an azoacetate intermediate, eq 52.

[52]



I.3.2. *ELECTROCHEMICAL OXIDATIONS*

I.3.2.1. *INTRODUCTION*

The fundamentals[196] of electrolysis were first proposed by Faraday in 1834 and applied to organic synthesis in 1854. Electrochemical synthesis reached a peak in the 1920's and, because of a lack of equipment for further advances, was abandoned until the early 1950's. With the growth of electronics a new interest has appeared giving a new life to electrochemical synthesis.[197]

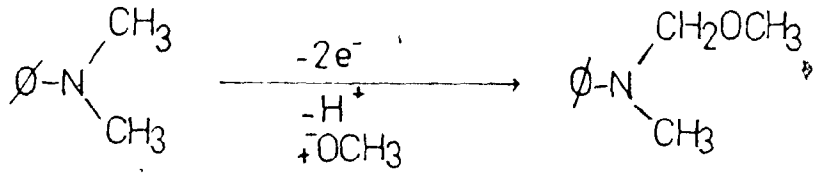
Electrolysis starts with an electron transfer to form a reactive species. This reactive intermediate goes on to yield a number of products.[198] A lot of material has been covered in the literature[198-200] on electrochemical cells, solvents, and solvent supporting electrolytes.

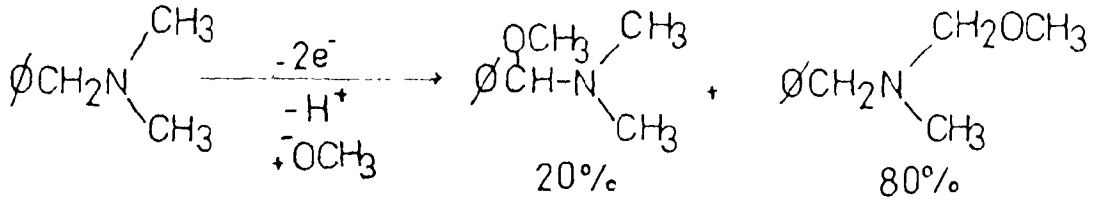
A brief survey of anodic substitution reactions will be presented, in this section, covering C-O[198] C-N,[198] C-C[101] and C-F[202] bond formations.

I.3.2.2. *ANODIC OXIDATIONS*

a - C-O bond formations

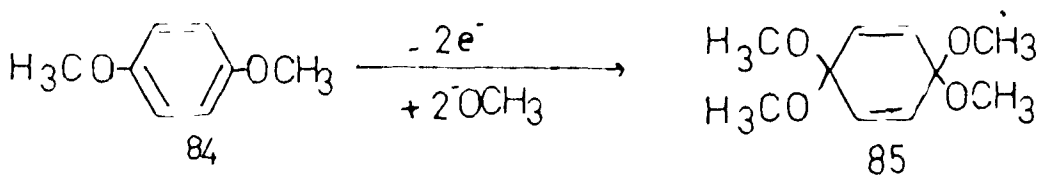
The main example of C-O bond formation is anodic alkoxylation.[198] Anodic alkoxylation can be performed in either strongly basic systems, such as alcohol/alkoxide, or in neutral ones, e.g. alcohol/tetraalkylammonium tetrafluoroborate.[203-204] Substrates like N,N-dimethylaniline[205] and N,N-dimethylbenzylamine[206,207] are methoxylated in 90 and 60% yield respectively, eqs 53, 54.

[53] 

[54] 

Anodic reactions of the methoxylation type often permit unusual reaction pathways due to the fact that carbocations are generated in strongly basic media. The Wheland intermediate can be trapped to give the anodic addition product from an aromatic derivative. As an example 1,4-dimethoxybenzene (84) is oxidized in the presence of methoxide ions to form diketal (85) in high yields, eq 55.[208,209]

[55]



84 85

88%

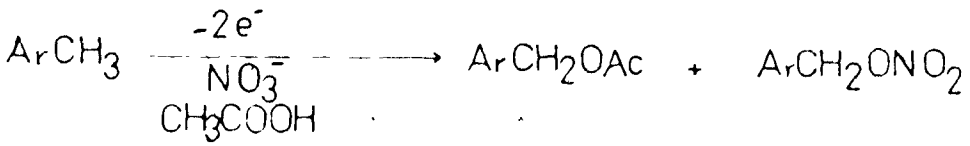
Synthetically useful intermediates can be prepared from anodic additions, as shown from the anodic 1,4-bisalkoxylation that furans undergo with high yields,[210] eq 56.

[56]

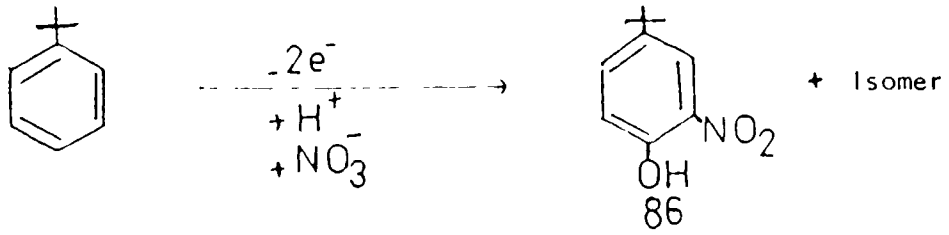
b - C-N bond formation

Anodic nitration is an example of C-N bond formation. Nitration competes with acetoxylation during anodic oxidation of alkylarenes in acetic acid/ammonium nitrate[211-214] eq 57. From alkyl arenes only α-nitrates are formed. If no α-

[57]

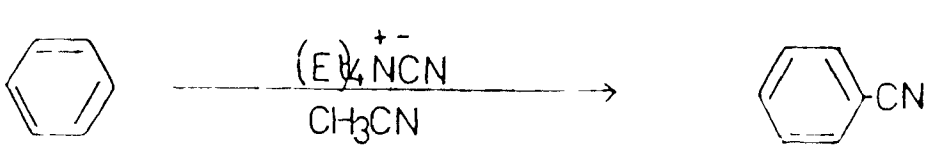


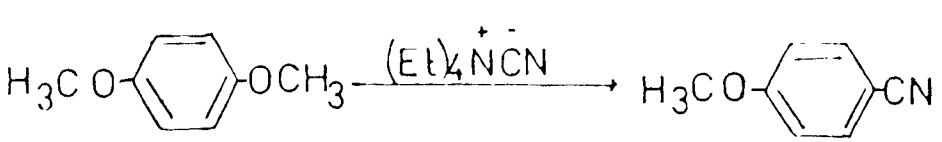
position is available, o-nitrophenols are produced in low yields (eq 58). Phenol (86) is probably formed by rearrangement of nitrates[194].

[58] 

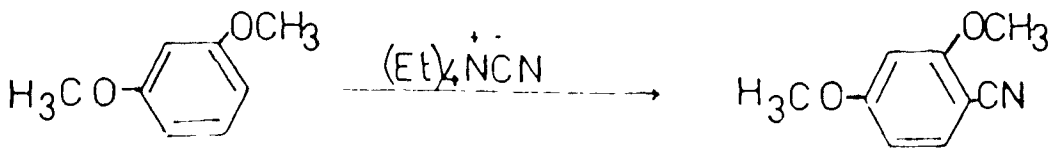
c - C-C bond formation

An example of C-C bond formation is the anodic cyanation. Two types of aromatic cyanation[215] reactions were observed from electrolysis of acetonitrile solutions of tetraethylammonium cyanide containing aromatic substrates. One type was the replacement of aromatic hydrogen in orientations typical of electrophilic aromatic substitution reactions. With di - and trimethoxy benzenes, direct replacement of a methoxy group occurred only when methoxy groups were situated in ortho and para positions. With anisole or meta-oriented methoxy groups reaction of type one occurred,[201] eqs 59-61.

[59] 

[60] 

[61]



d - C-F bond formation

The electrochemical method of fluorination consists of electrolyzing a liquid hydrogen fluoride solution containing appropriate starting compounds, dissolved or dispersed, at a voltage lower than 8 volts. Voltages between 4.5 and 6 volts are used and are insufficient to liberate fluorine gas but sufficient to cause the generation of fluorinated compounds at the anode.[202]

Organic gases (CH_4, C_2H_6, C_3H_8) which are not very soluble in hydrogen fluoride can be fluorinated electrochemically in the presence of a conductivity additive (potassium or sodium fluoride) to yield highly fluorinated products in the following current efficiencies, eqs 62,63.[202, 216-219]

[62]

$$CH_4 \longrightarrow CF_4\,(8.1\%)\,,\ CHF_3\,(11\%)\,,\ CH_2F_2\,,\ CH_3F$$

[63]

$$C_2H_6 \longrightarrow C_2F_6\,(16\%)\,,\ C_2HF_5\,(5.3\%)\,,\ C_2H_2F_4\,(42\%)\,,\ CF_4\,(0.3\%)$$

Electrochemical fluorination of hydrocarbons occurs usually with poor yields; n-octane was converted into perfluoro-n-octane in 11% yield,[220-223] n-hexane gave C_6F_{14} in 22% yield and methylcyclohexane gave C_7F_{14} in 16% yield.[202] Partially fluorinated hydrocarbons are more soluble in hydrogen fluoride than their non fluorinated counterparts.[219] As a result, the yields of fluorinated products are

much higher. Thus 2,2-difluorooctane, respectively, gave the perfluoro compounds in 80%, 62%, 62% and 40% yields.[202]

Finally some examples of electrochemical fluorination of organic molecules are shown in eqs 64-67.

[64] $CH_3CH_2CH \xrightarrow[HF]{-2e^-} CF_3COONa$ [224] 30%

[65] $O(CH_2)_3CH_2 \xrightarrow[HF]{-2e^-} O(CF_2)_3CF_2$ [202] 42 %

[66] $CH_3\overset{O}{\overset{\|}{C}}F \xrightarrow[HF]{-2e^-} CF_3\overset{O}{\overset{\|}{C}}F$ [202] 75-85 %

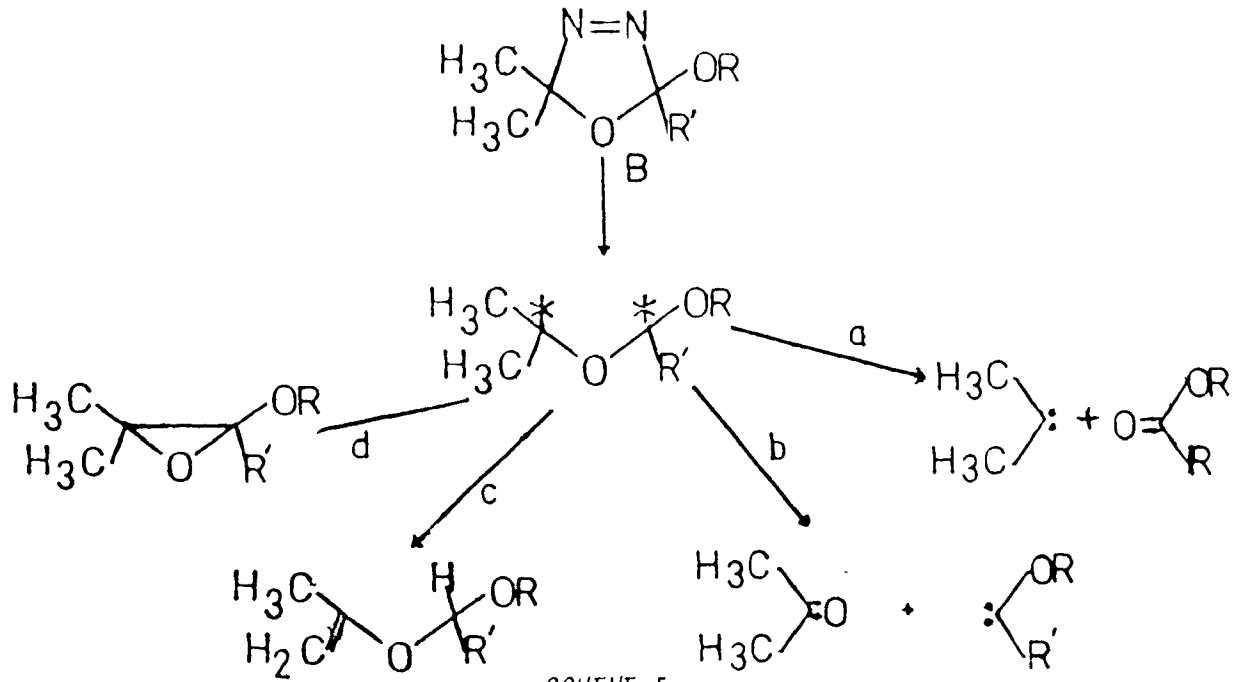
[67] $(CH_3)_2S \longrightarrow CF_3SF_5$ (57%) $+ (CF_3)_2SF_4$ (5.3 %) [205]

RESULTS AND DISCUSSION

RD. 1 OVERVIEW

As shown in the introduction (p. 5 sec I.3.3) carbonyl ylides can be generated from the thermolysis or photolysis of Δ^3-1,3,4-oxadiazolines. In order to propose a mechanism for such a reaction, a search for potential intermediates as well as an identification of the products have to be carried out.

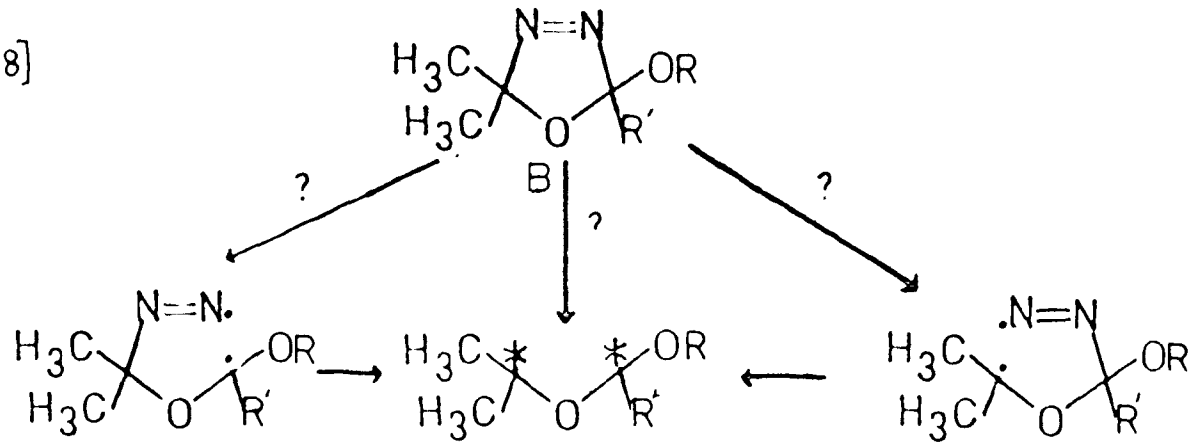
Scheme 5 depicts the various possible pathways in the thermolysis of oxadiazoline B. One of our objectives was to determine how the loss of nitrogen occurs, from the oxadiazoline, in order to get to the carbonyl ylide intermediate,



SCHEME 5

eq 68. Once generated the ylide (scheme 5) can fragment into carbenes and carbonyl compounds (a and b), can undergo a 1,4-hydrogen shift to give an ether (c), and can cyclize to an epoxide (d). Because of the interest in carbenes and in their

[68]

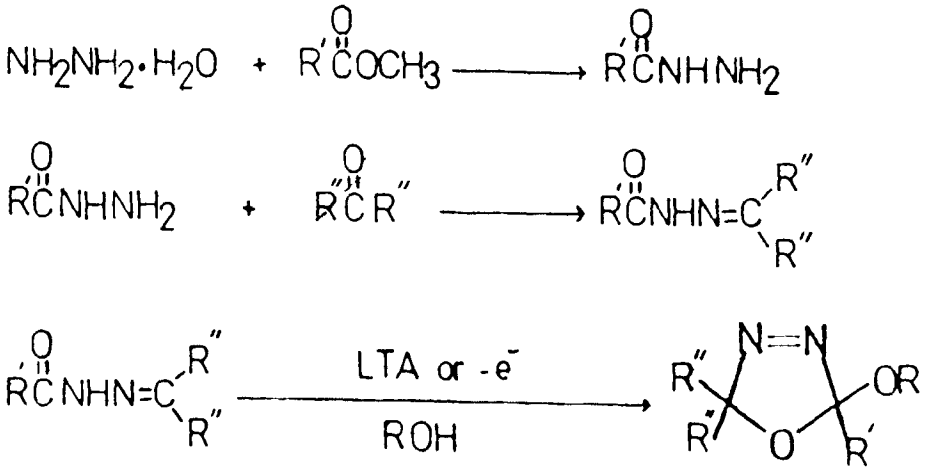


reactions, oxadiazolines are an attractive source of those transient species. The fact that ylides, under our conditions, cannot give carbenoids, makes the conclusions about inherent properties of carbenes more reliable. In an attempt to favour one path (scheme 5) over the others, substituents in oxadiazoline B were changed.

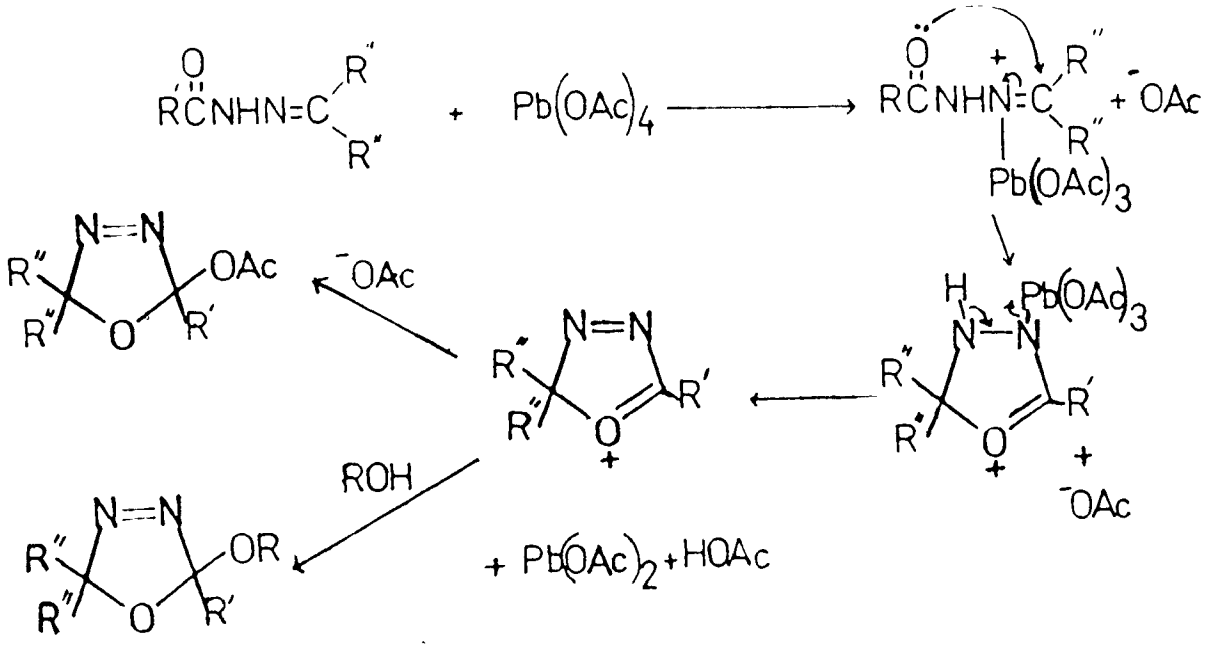
RD. 2 *SYNTHESIS OF OXADIAZOLINES*

The oxadiazolines were synthesized from the reaction of hydrazine hydrate with the appropriate ester to give the corresponding hydrazides. The reaction of the hydrazides with a ketone gave the hydrazones which were oxidized (LTA or electrochemically) to the corresponding oxadiazolines, eq 69.

[69]

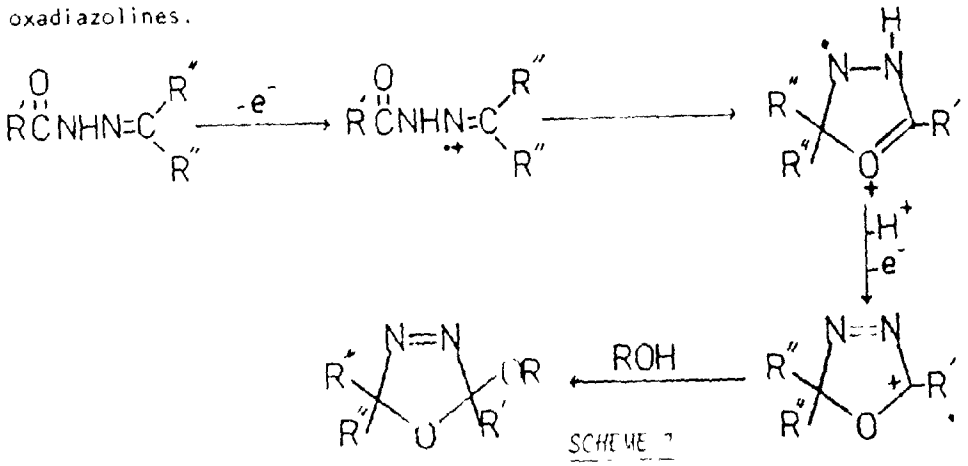


A mechanism for the oxidation of ketone hydrazones must take into account the work done by several workers on LTA oxidations (p 41 sec. I.3.1). A big similarity is found between the oxidation of benzoyl hydrazones to 2-acetoxy-Δ^3-1,3,4-oxadiazolines, reported by Hoffmann[179-181] and by Norman[182], and the work reported here. Different polar mechanisms have been suggested by each worker. The mechanism by Norman (p 42) seems very attractive. Following an intramolecularly promoted decomposition of the hydrazone - lead complex, the resulting cation is attacked by an acetate ion leading to oxadiazoline 83 (p 42). Norman assigned the oxonium ion mechanism on the evidence that, in methanol, a methoxy group rather than an acetoxy group was incorporated into oxadiazoline 83. In addition to Norman's mechanism, an alternative mechanism can be proposed, scheme 6



SCHEME 6

Scheme 7 depicts a possible mechanism for the electrochemical synthesis of oxadiazolines.

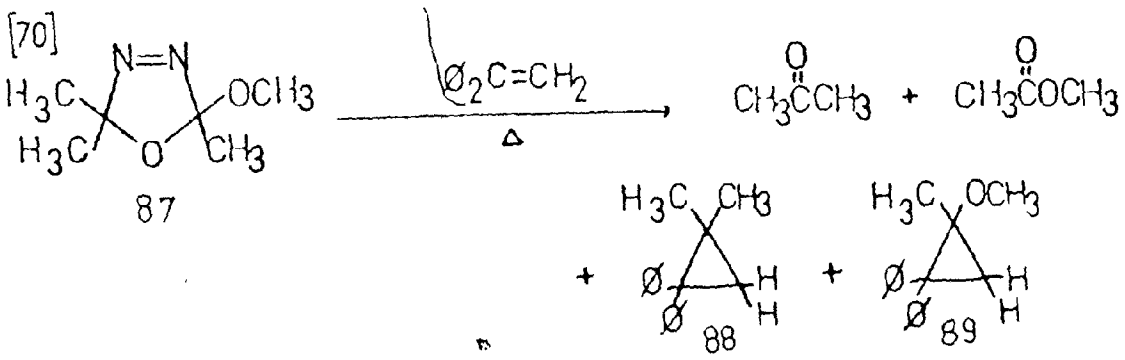


SCHEME 7

RD. 3 EFFECT OF SOLVENT CHANGES ON THE THERMAL DECOMPOSITION OF 2-METHOXY-2,5,5-TRIMETHYL-Δ^3-1,3,4-OXADIAZOLINE.

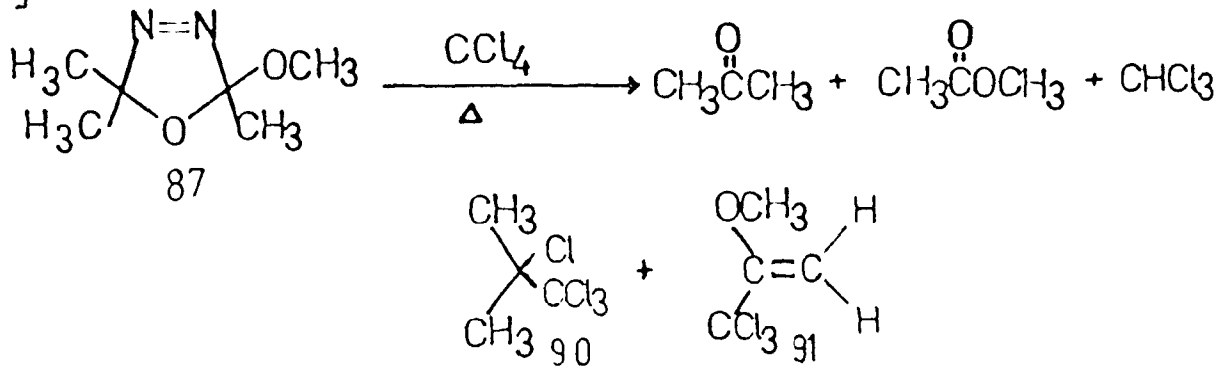
RD. 3.1 THERMOLYSIS IN 1,1-DIPHENYLETHYLENE AND IN CCl_4

Thermolysis[185,225] of methoxyoxadiazoline 87 in 1,1-diphenylethylene gave acetone, methyl acetate, 2,2-dimethyl-1,1-diphenylcyclopropane (88), (^{1}H NMR(CCl_4/TMS) δ,1.12 (S,2H), 1.25 (S,6H), 7.20 (m, 10H)), and 1-methoxy-1-methyl-2,2-diphenylcyclopropane (89), (^{1}H NMR (CCl_4/TMS) δ, 1.16 (m, 4H), 1.25 (d, J=9.0 Hz, 1H), 3.10 (S, 3H), 7.30 (m, 10H)); mass spectrum: m/z = 238 (M^+). Those products were readily explained in terms of dimethyl and methoxymethyl carbene intermediates, eq 70.

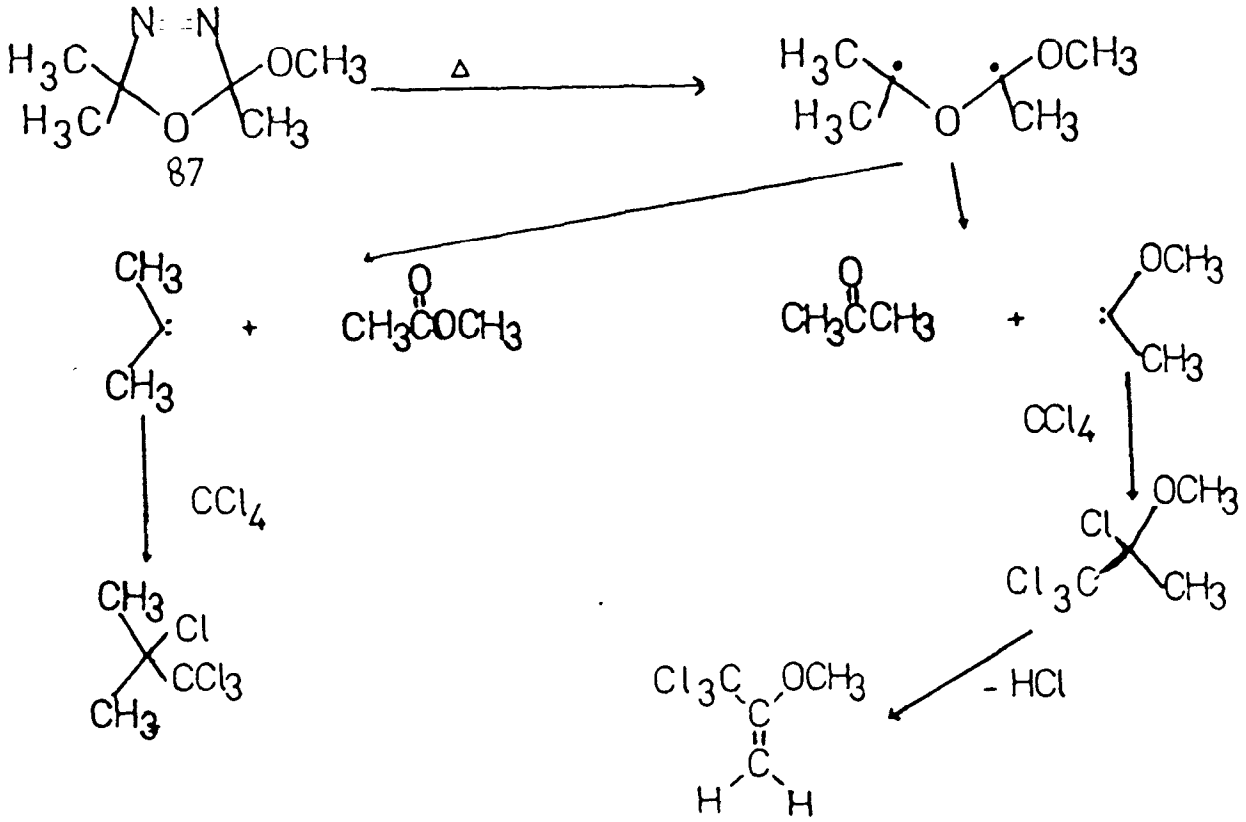


Thermolysis of 87, in CCl_4, followed first order kinetics ($k^{79.5°C}=1.4 \times 10^{-5}$ sec^{-1}, Fig. RD.1), and gave acetone, methyl acetate, chloroform, and chlorinated products 90 and 91. Those results provided further support for carbenic intermediates, eq 71.

[71]



The experimental evidence led to the proposed mechanism, scheme 8.



SCHEME 8

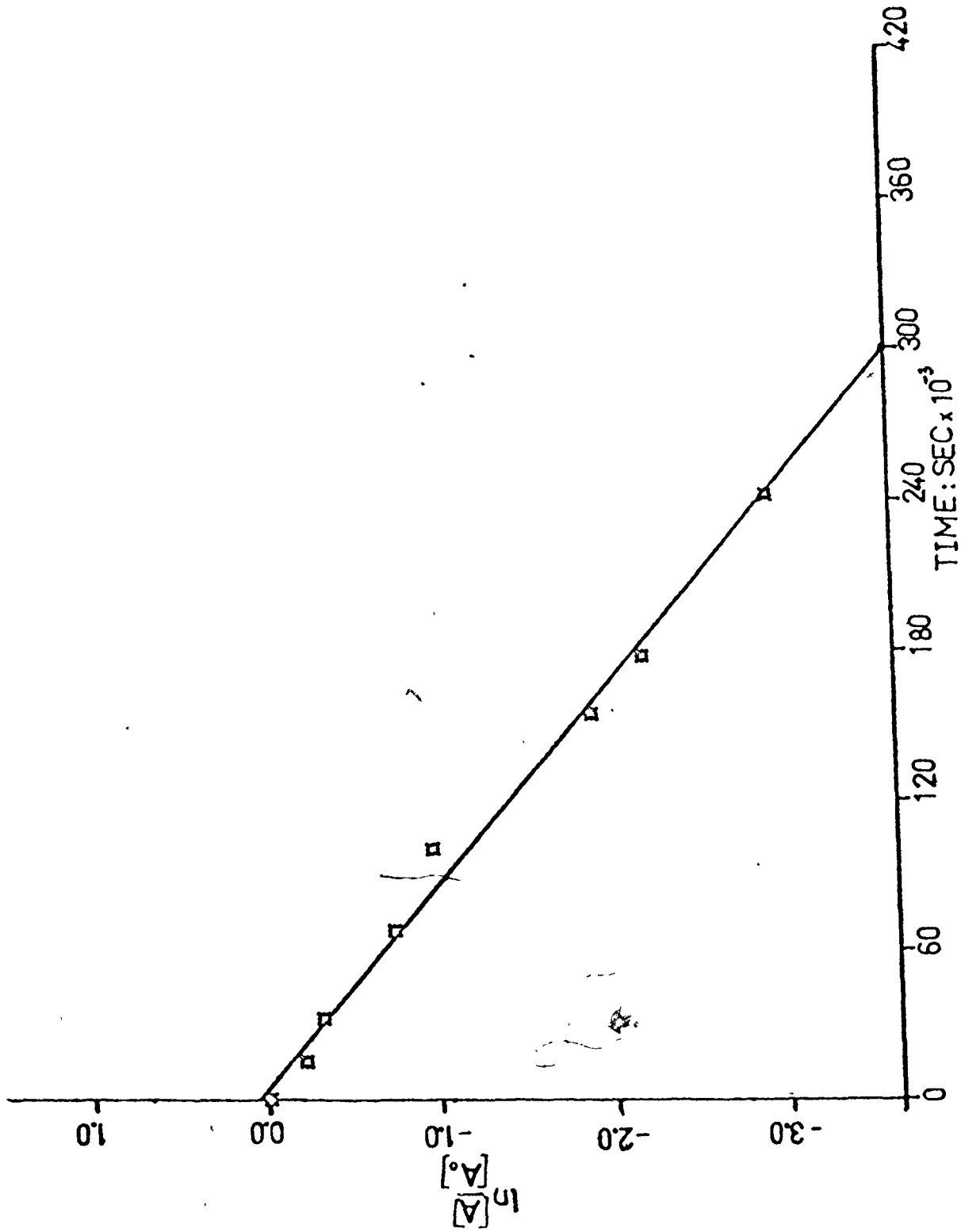


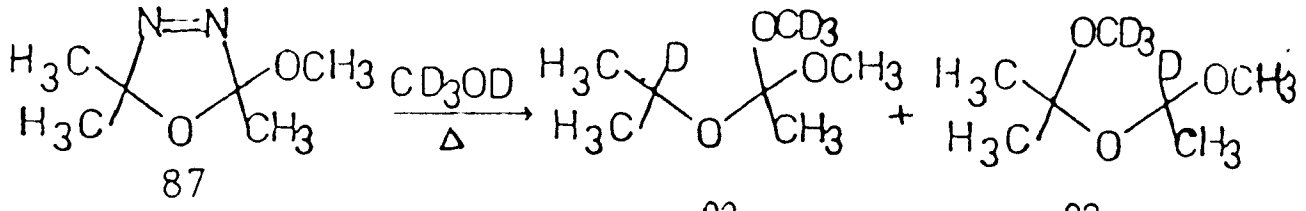
FIG R D. 1 FIRST ORDER THERMOLYSIS OF 87 IN CCl_4 AT 79.5 ± 0.2°C

RD. 3.2 THERMOLYSIS IN CD_3OD AND IN CH_3OH

a - CD_3OD

Thermolysis of 87, in CD_3OD, followed first order kinetics ($k^{79.5°C} = 5.3 \times 10^{-6}$ sec^{-1}, fig RD 2) and afforded[225] ketals 92 and 93, eq 72.

[72]



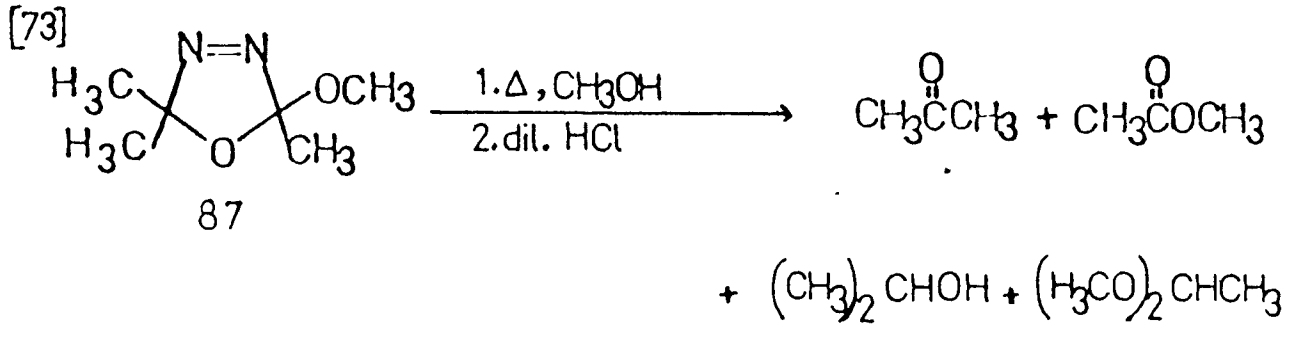
87 92 93

Compounds 92 and 93 were not separated, but their structures could be inferred from the ^1H NMR spectrum of the mixture. Thus, a singlet at δ 1.19 was assigned to the ketal gem-dimethyl groups of 93 and a multiplet at δ 1.15 ($^3J_{HD}$=1.2Hz) was assigned to the deuterium coupled acetal methyl group of 93. Similarly, a multiplet at δ 1.00 ($^3J_{HD}$=1.2Hz) and a singlet at δ 1.92 were assigned to the gem-dimethyl and the orthoester methyl groups, respectively, of 92. Integrals of the above-mentioned signals corresponded to a product ratio of 1:2, and that ratio was used to assign the methoxy singlets at δ 3.26 and δ 3.56 to 92 and 93, respectively. The yields of 92 and 93 were found to be 69% and 29%, respectively.

b - CH_3OH

In an evacuated sealed tube, oxadiazoline 87 was thermolyzed at 79.5°C, in methanol. At the end of the reaction, the tube was opened and dilute HCl was added. The main products are shown in eq 73.

[73]



87

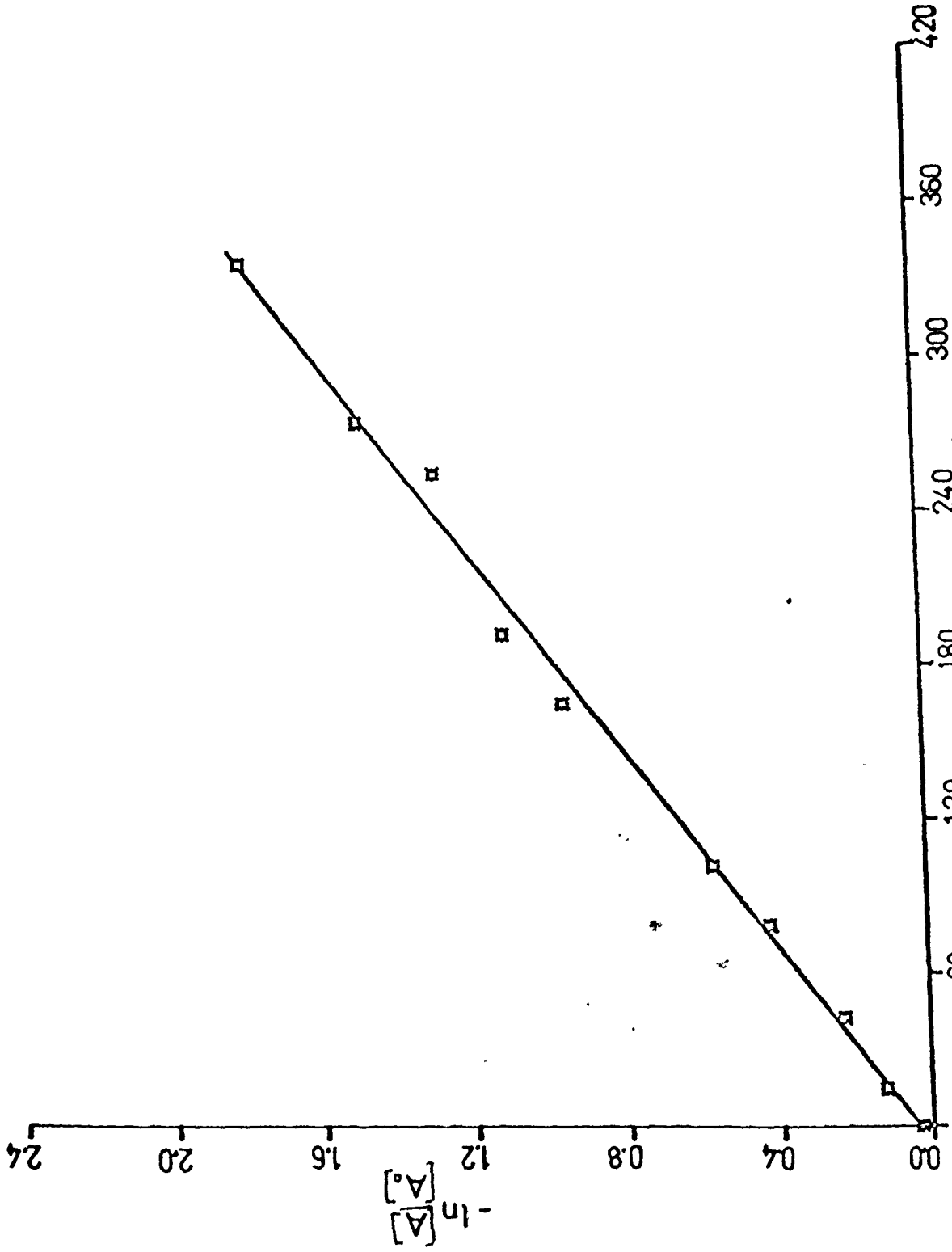


FIG RD 2. FIRST ORDER THERMOLYSIS OF 87 IN CD_3OD AT 79.5 ± 0.2°C

Support for the structures of the products came from GC analysis and NMR spectra.

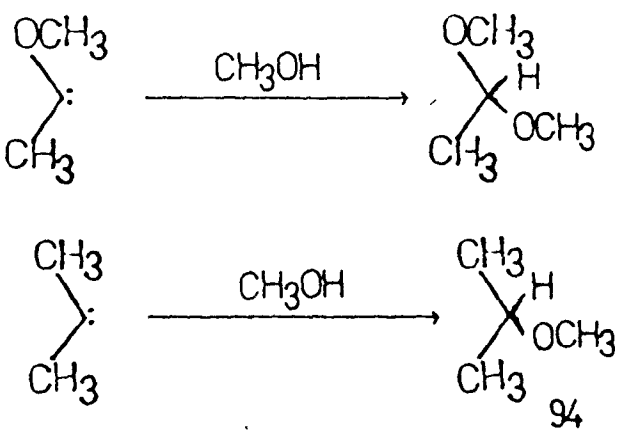
^{1}H NMR (δ,CD_3OD, TMS): 2.11(s),CH_3COCH_3; 2.01 (s,3H) and 3.61 (s,3H), CH_3COOCH_3; 1.07 (d,6H, J=6.0 Hz) and 3.89 (sep, 1H, J=6.0 Hz), $(CH_3)_2CHOH$; 1.26 (d, 3H, J=5.5 Hz), 3.29 (s,6H), and 4.51 (q, 1H, J=5.5 Hz), $(CH_3O)_2CHCH_3$.

Isopropyl alcohol was further identified by comparing the FT-IR spectrum of a component of the reaction products (separated by GC) to that of authentic sample. IR (gas phase, cm^{-1}): 3361, 2978, 2893, 1463, 1378, 1237, 1146, and 1089.

c - Proposed mechanism

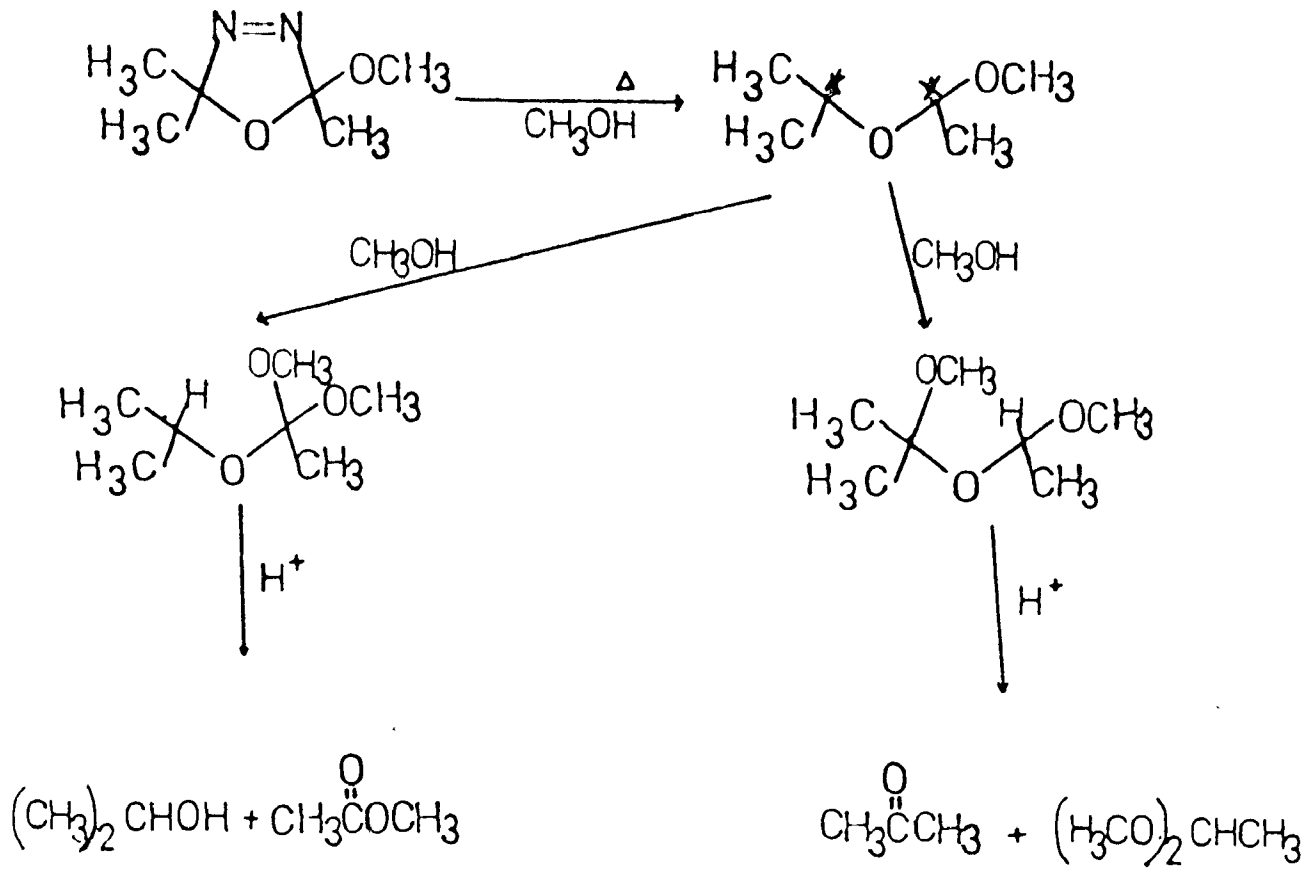
The proposed mechanism for the thermolysis of oxadiazoline 87 in CCl_4 involves a 1,3-diradical (carbonyl ylide) which fragments to give methoxymethyl and dimethyl carbenes (scheme 8, p 52). If that were the case in methanol also, the carbenes would further react with the solvent by a known[227-234] O-H insertion to give the products shown in eq 74

[74]



94

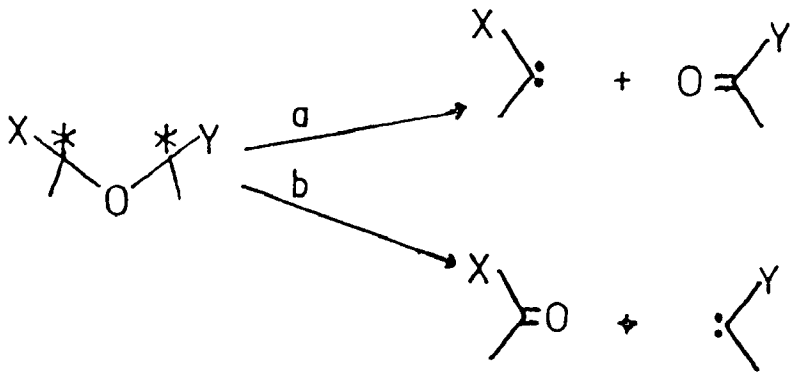
The absence of acetone and methylacetate from the reaction in CD_3OD coupled with the absence of isopropylmethylether (94) from the reaction in CH_3OH indicated that no fragmentation occured and that the carbonyl ylide intermediate was trapped by the solvent, scheme 9.



SCHEME 9

Houk, Griffin, and co-workers[8], published results of theoretical studies of structures and reactions of substituted carbonyl ylides. One of the questions addressed in that paper concerns their fragmentation, eq 75

[75]



The authors' conclusions about fragmentation, based on their studies and on the literature, included the following:

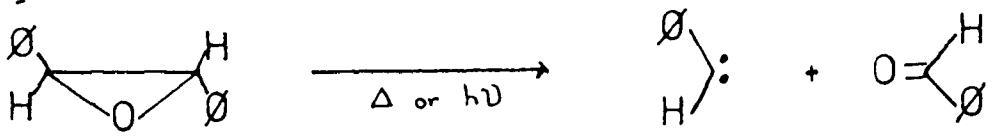
i) Fragmentation of carbonyl ylide (X=Y=H) is endothermic by about 38Kcal/mole

ii) One amino substituent ($X=NH_2$) decreases the thermodynamic barrier to fragmentation in either sense and path a, leading to aminocarbene may actually be exothermic.

iii) Thermal fragmentation of a carbonyl ylide from a coplanar ground state (0°, 0° comformation) is a disallowed process.

Experimental evidence for thermal fragmentation of carbonyl ylides is meager. One unambiguous example is the observation that a photolysis-warm-up procedure produces more fragmentation products from aryloxiranes than does photolysis alone,[88] eq 76. The amount of fragmentation produced by this procedure was estimated to be 20-25 times more than that originally produced by photolysis alone.

[76]



In the thermolysis of methoxyoxadiazoline 87, the only direct evidence for the formation of a carbonyl ylide pertains to methanol solvent. It is very likely that the same intermediate is formed in CCl_4. The similar magnitudes of the first order rate constants ($k^{79.5}_{CD_3OD} = 5.3 \times 10^{-6}$ sec^{-1}, $k^{79.5}_{CCl_4} = 1.4 \times 10^{-5}$ sec^{-1}) would have to be fortuitous if different mechanisms were in operation. It is now well known that a small decrease in rate constant, for the thermolysis of a cis-azocompound, occurs as solvent polarity is increased.[235]

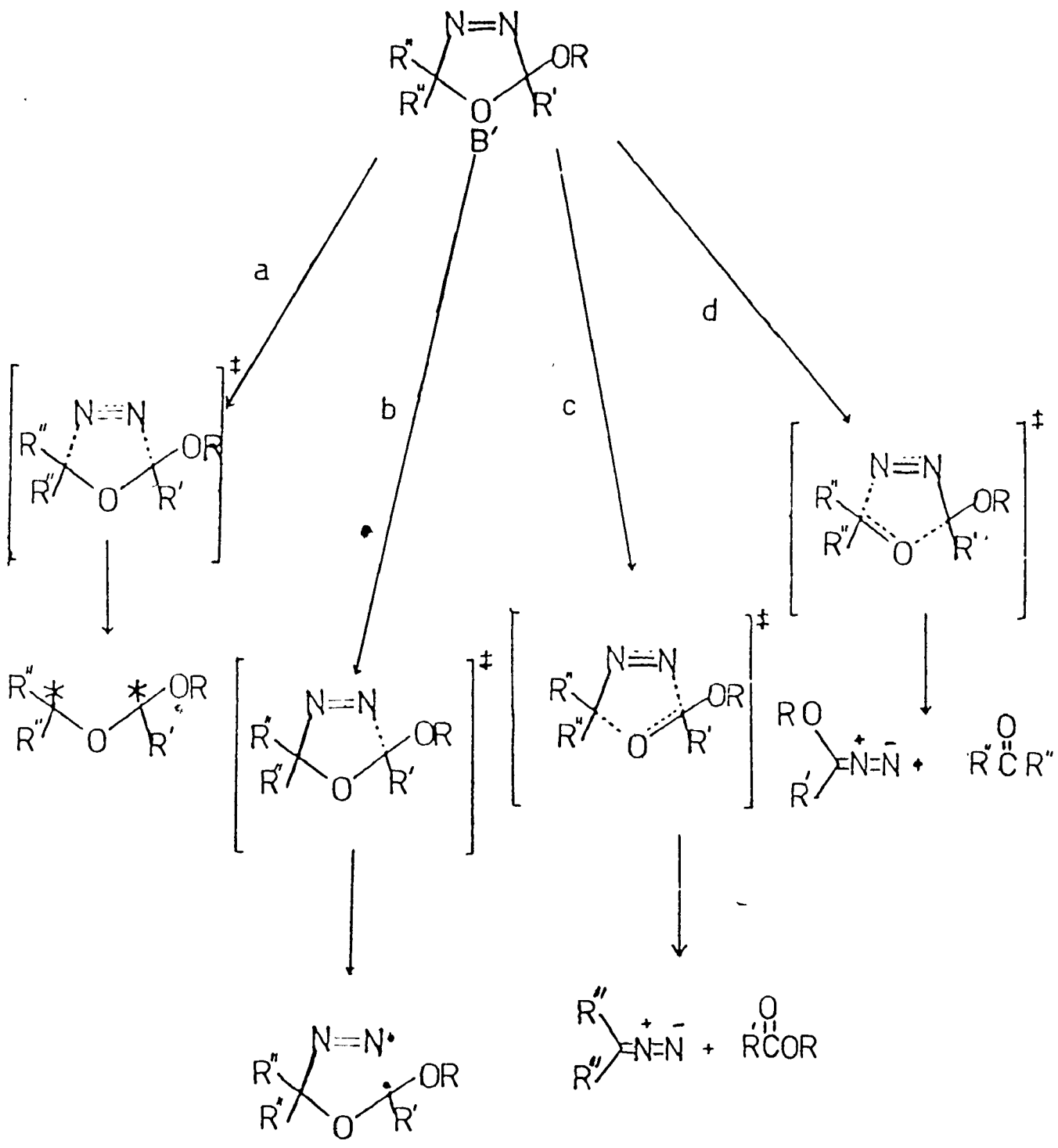
In order for the ylide intermediate to fragment thermally to carbenes and carbonyl compounds, it must either have a non-planar ground state[8] or else a non-planar state must be readily accessible from a planar ground state. Calculations[8] indicate that a donor substituent reduces the barriers to rotation of a 0°, 0° conformation to a 0°, 90° conformation. It is interesting that there is apparently little preference for one fragmentation over the other (CCl_4 results). The theory[8] for amino-substituted carbonyl ylide predicts that the 0°, 90° conformation would have the shorter bond between amino-substituted carbon and carbonyl oxygen, and fragmentation would give mostly aminocarbene. This feature is presumably offset, in the present case, by the greater stabilization that the donor substituent affords to a carbene as compared to a carbonyl compound.

RD 4 SUBSTITUENT EFFECTS ON THE RATES OF THERMOLYSIS OF OXADIAZOLINES

RD 4.1 HAMMETT PLOT

Scheme 10 depicts the various possibilities of bond rupture and bond formation occuring in the transition state for the thermolysis of oxadiazoline B. In the case where R=R'=R''=CH_3, thermolysis in methanol goes via a carbonyl ylide intermediate which could be generated through a concerted or non-concerted loss of nitrogen (path a or b). Thermolysis of the same oxadiazoline in CCl_4 gives carbenes which could arise from diazoalkanes generated from concerted or non-concerted C-N and C-O bond ruptures (paths c and d).

In order to determine if the same intermediate is involved in both solvents, 2-methoxy-2-(p-substituted phenyl)-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines(C) were synthesized and thermolyzed in CCl_4 and CD_3OD at 49.2°C. The following results were obtained (tables RD.1 and RD.2, figs RD.3 and RD.4).



SCHEME 10

TABLE RD.1. FIRST ORDER KINETIC DATA OF THE THERMOLYSIS OF C AT 49.2 ± 0.2°C IN CCl_4

R	S	k x $10^5 sec^{-1}$	t1/2 min	Correlation Coefficient C.C
OCH_3 1	CCl_4	2.57	447	0.9986
CH_3 2	CCl_4	3.68	313	0.9991
H 3	CCl_4	5.00	230	0.9994
Cl 4	CCl_4	7.56	152	0.9988
CF_3 5	CCl_4	10.40	112	0.9987
NO_2 6	CCl_4	39.50	30	0.9984

TABLE RD.2. FIRST ORDER KINETIC DATA OF THE THERMOLYSIS OF C AT 49.2° ± 0.2° IN CD_3OD

R	S	k x $10^5 sec^{-1}$	t1/2 min	C.C.
OCH_3 1	CD_3OD	1.57	736	0.9987
CH_3 2	CD_3OD	2.05	560	0.9996
H 3	CD_3OD	3.16	365	0.9981
Cl 4	CD_3OD	4.76	242	0.9950
CF_3 5	CD_3OD	9.68	119	0.9990
NO_2 6	CD_3OD	38.30	30	0.9983

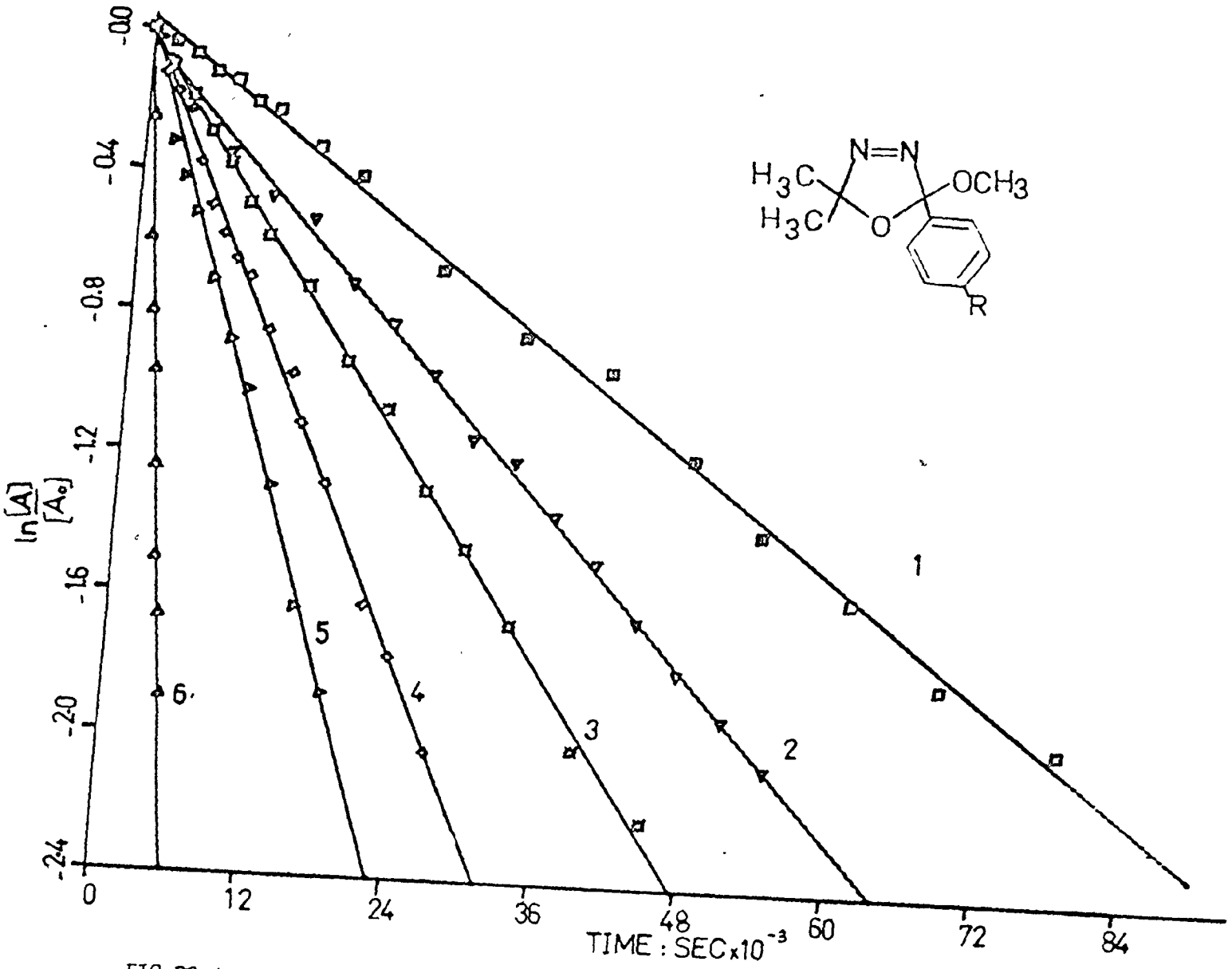


FIG RD.4. FIRST ORDER PLOTS OF KINETICS OF OXADIAZOLINE THERMOLYSIS AT 49.2 ± 0.2°C, IN CCl_4 (TABLE RD.2)

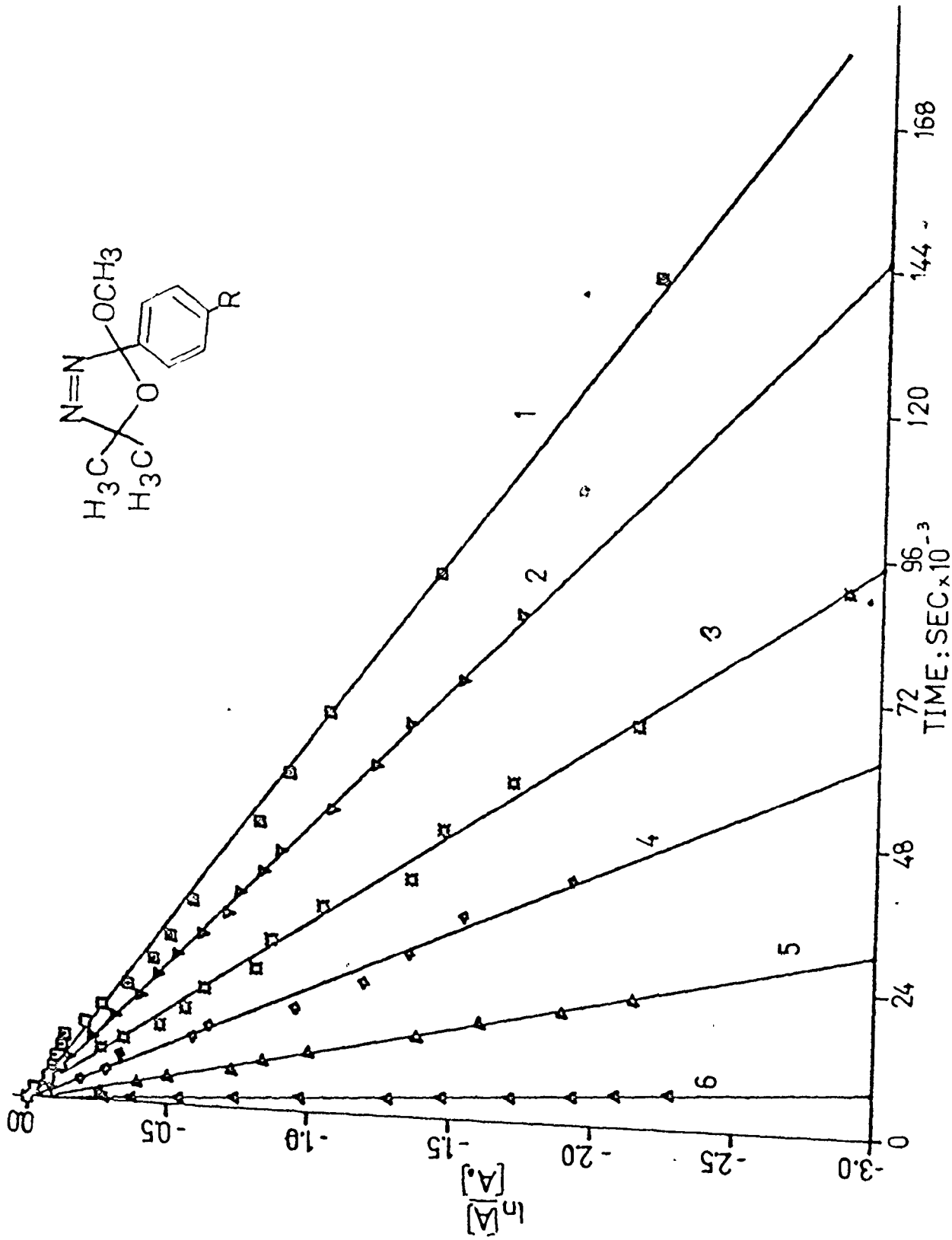
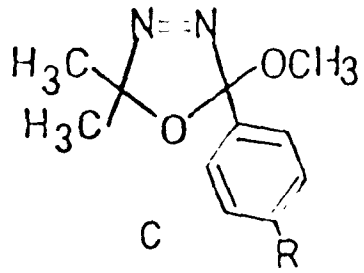


FIG RD.3. FIRST ORDER PLOTS OF KINETICS OF OXADIAZOLINE THERMOLYSIS AT 49.2 ± 0.2°C, in CCl_4 (TABLE RD.1)



The rate of decomposition of the methoxyoxadiazolines was enhanced by electron-withdrawing substituents on the benzene ring. A linear Hammett Plot was obtained with $\rho_{CCl_4} = 0.76$ and $\rho_{CD_3OD} = 0.94$ against σ^- (tables RD.3 and RD.4, fig RD.5).

TABLE RD.3. HAMMETT PLOT DATA (CCl_4)

p-R	$k_R \times 10^5$	k_R/k_H	$\log \frac{k_R}{k_H}$	σ_p^-
OCH_3	2.6	0.52	-0.28	-0.20
CH_3	3.7	0.74	-0.13	-0.17
H	5.0	1.0	0	0
Cl	7.6	1.5	0.18	0.23
CF_3	10.4	2.1	0.32	0.54
NO_2	39.5	7.9	0.90	1.24

$\rho = 0.76$

C.C = 0.9912

TABLE RD.4. HAMMETT PLOT DATA (CD_3OD)

p-R	$k_R \times 10^5$	kR/k_H	$\log \frac{kR}{k_H}$	σ_p^-
OCH_3	1.6	0.50	-0.30	-0.20
CH_3	2.0	0.63	-0.20	-0.17
H	3.2	1.0	0	0
Cl	4.8	1.5	0.18	0.23
CF_3	9.7	3.0	0.48	0.54
NO_2	38.3	12.0	1.1	1.24

$\rho = +0.94$

C.C. = 0.973

The small ρ values ($\rho_{CCl_4} = 0.76$, $\rho_{CD_3OD} = 0.94$) indicate some development of negative charge at C_2 in the transition state. It is noteworthy[236] that even when the ρ values are low, the reactivity of the p-nitrooxadiazoline is better correlated with σ^- than with σ. Because the thermolysis of the oxaziazolines follows a Hammett correlation, in both solvents, with similar ρ values, the intermediate must be the same.

2. MECHANISM OF NITROGEN LOSS

In order to check whether the N_4-C_5 bond is also broken in the rate determining step, several other oxadiazolines were synthesized and were thermolyzed in CCl_4 and CD_3OD. The kinetic results are shown below.

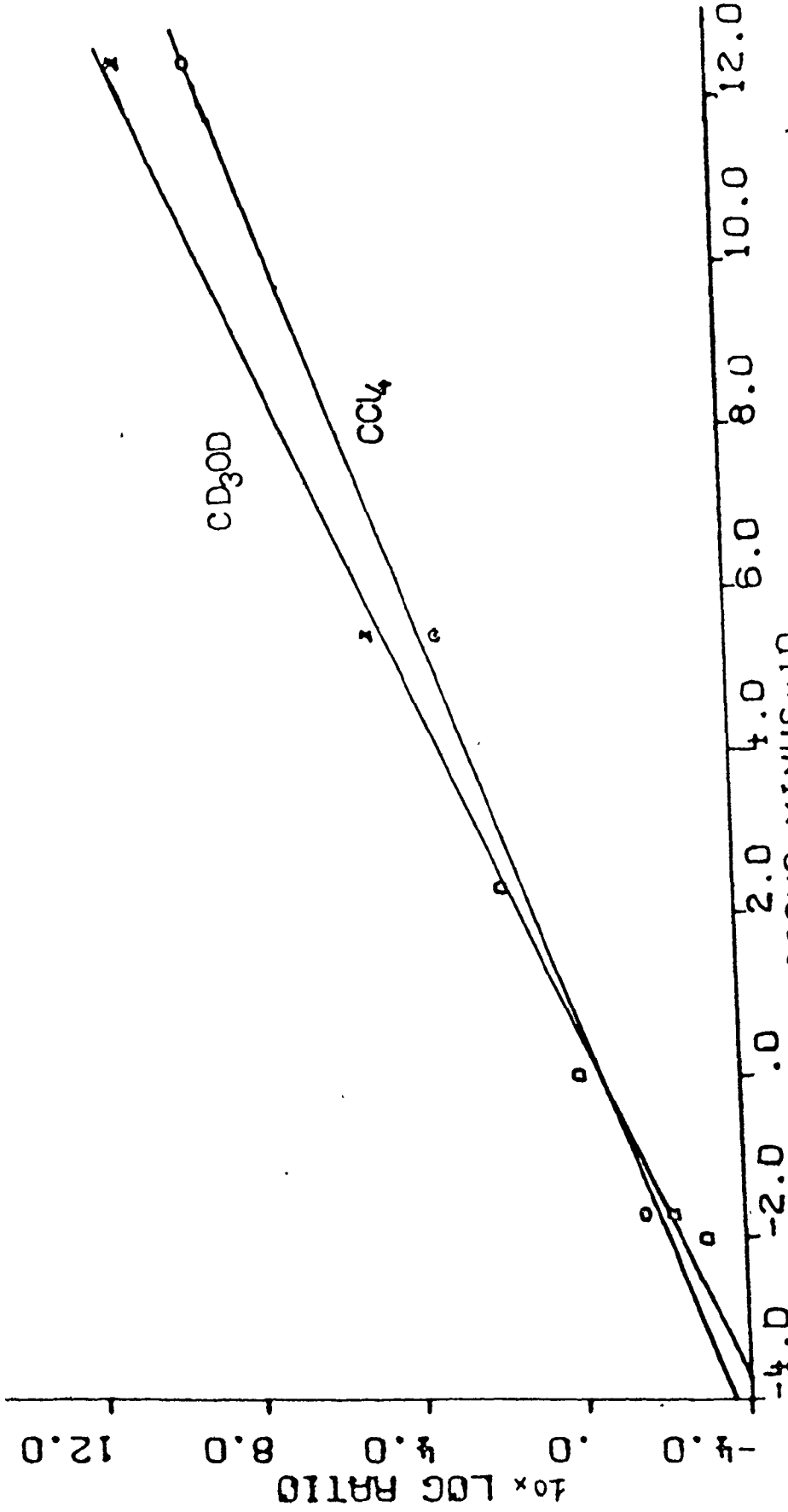
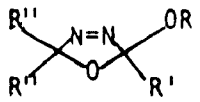


FIG RD.5. HAMMET PLOT FOR DECOMPOSITION OF 2-ARYL-2-METHOXY OXADIAZOLINES, C

TABLE RD.5. FIRST ORDER KINETICS FOR THE THERMOLYSIS OF 

R	R'	R''	k x 10^{+5} sec^{-1}	t1/2min	C.C.	T°C	[S]
CH_3	CH_3	CH_3	1.4	780	0.9969	79.5	CCl_4
t-Butyl	CH_3	CH_3	34.7	55	0.9996	79.5	CCl_4
CH_3	C_6H_5	CH_3	5.0	230	0.9994	49.2	CCl_4
CH_3	CH_3	cyclo-propyl	14.1	81	0.9965	79.5	CCl_4
CH_3	CH_3	CH_3	0.5	2220	0.9973	79.5	CD_3OD
t-Butyl	CH_3	CH_3	13.0	85	0.9994	79.5	CD_3OD
CH_3	C_6H_5	CH_3	3.2	365	0.9981	49.2	CD_3OD
CH_3	CH_3	Cyclo-propyl	6.3	183	0.9979	79.5	CD_3OD

With methoxyoxadiazoline 87 ($R=R'=R''=CH_3$) as the parent molecule, the following conclusions can be drawn:

i) By changing R' from CH_3 to phenyl, the rate of thermolysis of the oxadiazoline was drastically enhanced in both solvents. With R'=phenyl, the rate is 4 and 6 times faster at 49.2°C than with $R'=CH_3$ at 79.5°C, in CCl_4 and in CD_3OD respectively.

ii) Changing the substituent at C_2 from methoxy to t-butoxy enhances the rate by 25 and 26 times in CCl_4 and in CD_3OD respectively. This could be due to steric acceleration by bulky t-butyl group.

Substituent changes at C_2 and C_5 affected the rate of thermolysis of oxadiazoline 87. Furthermore, an attempt, by Dr. P.J. Smith, to synthesize 2-methoxy-2,5,5-triphenyl-Δ^3-1,3,4-oxadiazoline (R=CH_3, R'=R''=C_6H_5) failed in the sense that the oxadiazoline was decomposing upon work-up at 10°C. From those results one can conclude that at the rate determining step, both C_2-N and C_5-N bond scissions are involved.

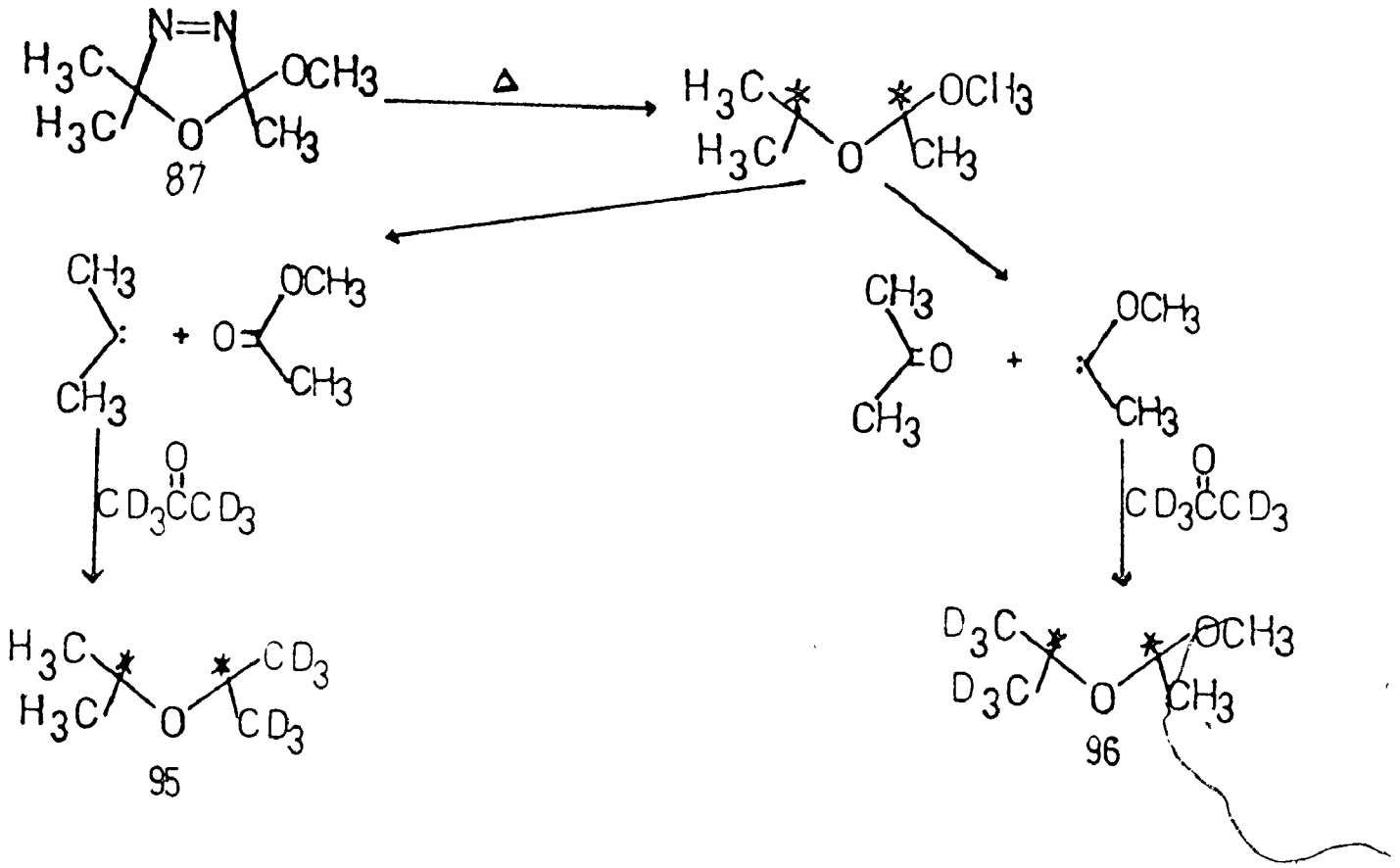
The products from the thermolysis of methoxyoxadiazoline 87, in CD_3OD, were those of trapping of a carbonyl ylide. Thus routes c and d (scheme 10) which do not give rise to a carbonyl ylide intermediate can be ruled out.

Route b, which involves a C_2-N bond scission, is ruled out because of the effects of substituent changes, at C_2 and C_5 (scheme 10), on the rate of thermolysis of the oxadiazolines.

Route a (Scheme 10) leads to a carbonyl ylide which depending on the substituents and the solvent, undergoes fragmentation, trapping, cyclization, and/or an intramolecular 1,4-hydrogen shift.

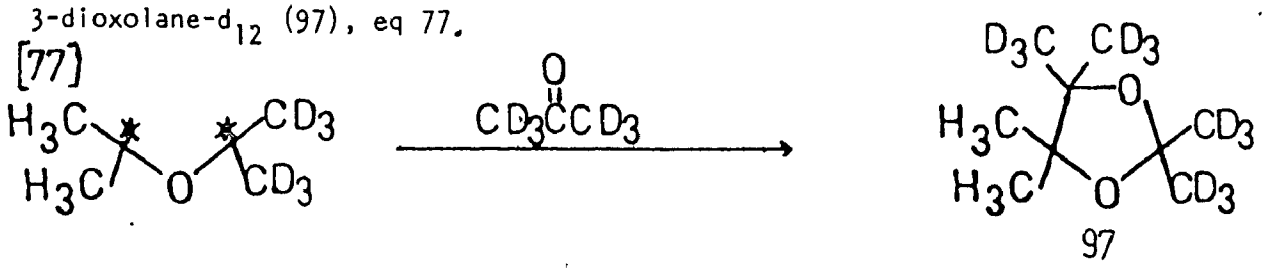
RD.5. REVERSIBILITY OF THE FRAGMENTATION OF THE CARBONYL YLIDE

Carbenes are known[15] to react with ketones to form carbonyl ylides. The carbenes formed in the thermolysis of 2-methoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline (87) in acetone-d_6, would be expected to react with the solvent to form carbonyl ylides, 95 and 96, according to the following scheme.

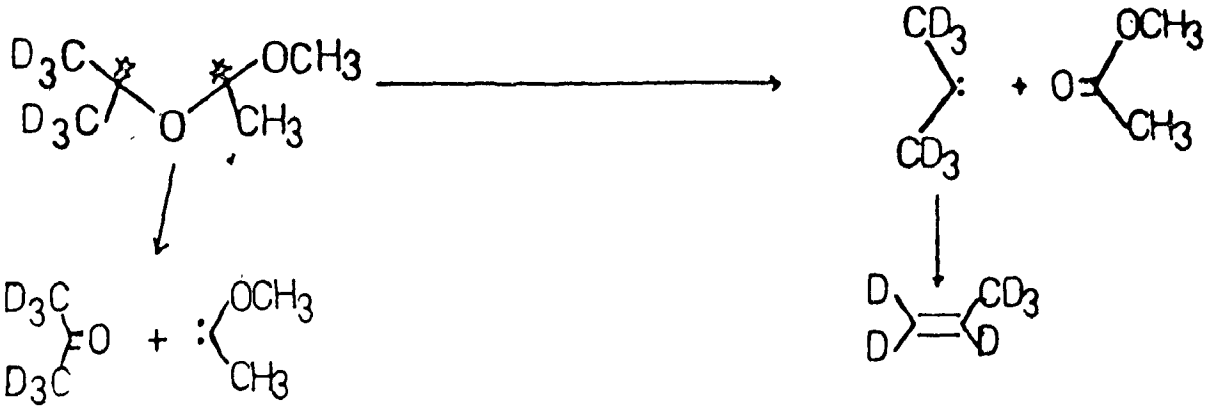


SCHEME 11

Carbonyl ylide 95 is known[237] to add to acetone-d_6 to give hexamethyl-1,3-dioxolane-d_{12} (97), eq 77.



Carbonyl ylide 96 would be expected to fragment in the same fashion as its non-deuterated counterpart (87a) to give propene-d_6, scheme 12.

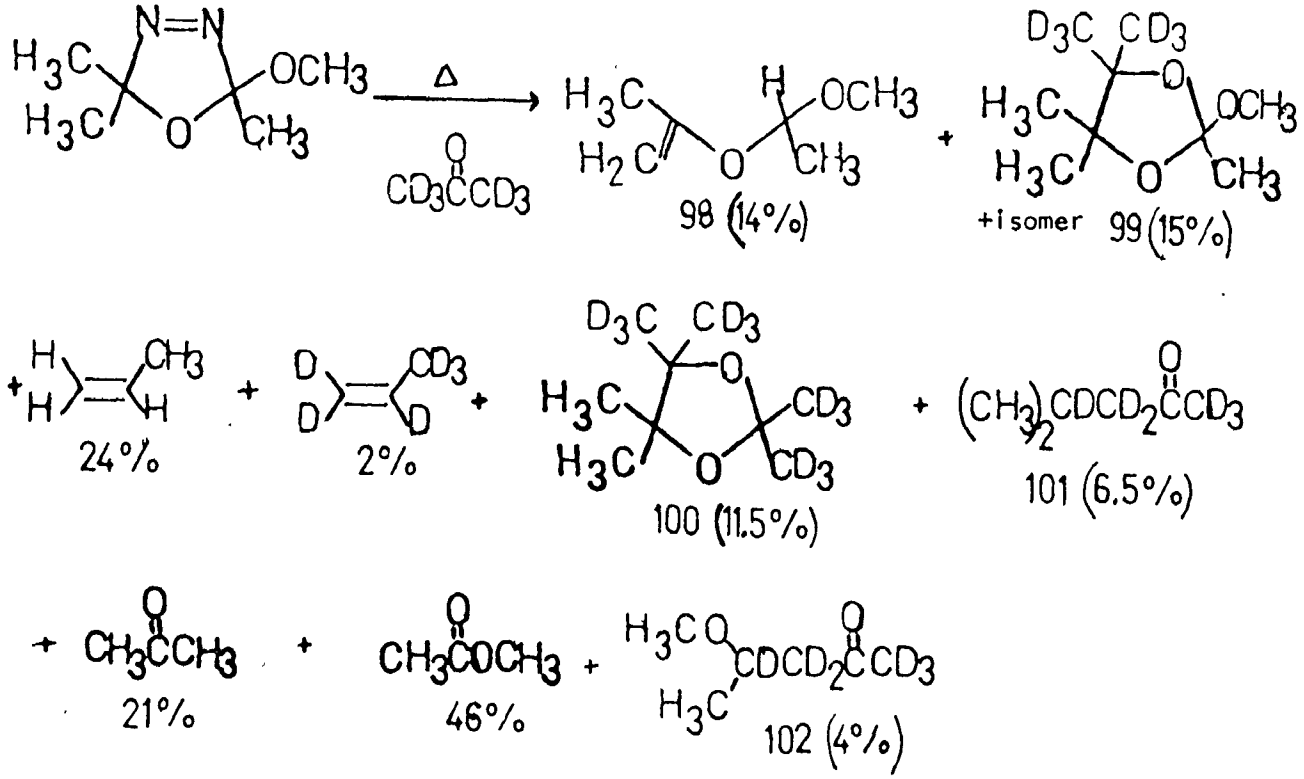


SCHEME 12

RD.5. 1. IDENTIFICATION OF PRODUCTS

Methoxyoxadiazoline (87), upon thermolysis in acetone-d_6, afforded the products shown in eq 78.

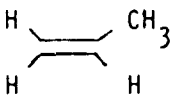
[78]

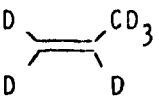


a - *IDENTIFICATION OF PROPENE -d_6*

A solution of authentic propene in CCl_4 was injected into a 10% FFAP column heated at 40°C (flow rate 25ml/min), and the FT-IR spectrum of the olefin was recorded. Propene was the first eluent. The first eluent, from the injection of the mixture of products of the reaction under the same conditions (into the same column), had an FT-IR spectrum which contained the same bands as that of authentic propene, plus additional bands at cm^{-1} 2295, 2264 and 2217, due to C-D stretching in propene-d_6 (calculated values: cm^{-1} 2283, 2252 and 2205).

The ^1H NMR spectrum of an authentic solution of propene in CCl_4 was identical to that of the product from the reaction The proton and deuterium NMR spectra were run on a 400MHz NMR spectrometer and the chemical shifts of propene and propene-d_6 (acetone-d_6 solution) are reported below:





δ	1.69	1.73
	4.91	4.89
	4.99	5.06
	5.78	5.71

Furthermore, propene, from the reaction, was converted to 1,2-dibromopropane by adding a Br_2/CCl_4 solution to the reaction mixture. The bromoalkane was collected from a 20% DEGS column heated at 140°C (flow rate 40ml/min). The retention time, 17 min. under those conditions, corresponded to that of authentic 1,2-dibromopropane. Mass spectra of both samples were recorded and the following results were obtained:

Authentic 1,2-dibromopropane

	m/z	
$^{+}CH_2\underset{\underset{Br}{|}}{C}HCH_3$	121	123
$^{+}CH_2\text{-}CH{=}CH_2$	41	

1,2-dibromoalkane from reaction

	m/z	
$^{+}CH_2\underset{\underset{Br}{|}}{C}HCH_3$	121	123
$^{+}CH_2CH{=}CH_2$	41	
$^{+}CD_2\underset{\underset{Br}{|}}{C}DCD_3$	127	129
$^{+}CD_2CD{=}CD_2$	46	

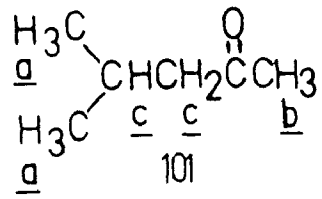
From the peak intensities of the allyl cations (m/z 46, 41), the ratio of propene-d_6 to propene was found to be 8%.

b. *IDENTIFICATION OF OTHER PRODUCTS*

Thermolysis of oxadiazoline 87 was carried out in acetone-d_6 and in acetone. The two product mixtures will be referred to as (i) and (ii) respectively. ^1H NMR spectra were obtained for components of (ii) except for acetone which spectrum was run for the component from (i). Mass spectra were obtained for the component from (i). The mixture of products from both reactions was first separated by bulb to bulb distillation into a volatile and a non-volatile fraction, then the fractions were injected into a GC column.

VOLATILE FRACTION

Both volatile fractions contained acetone, methylacetate, enolether 98 and ketones 101 and 102 (p. 70). Acetone and methyl acetate were identified by comparing their 'H NMR spectra to those of authentic samples. From the 'H NMR[238] spectrum and the mass spectrum[239] of the material eluted third (after acetone and methyl acetate) it was possible to assign the 4-methyl-2-pentanone structure (101) unambiguously.



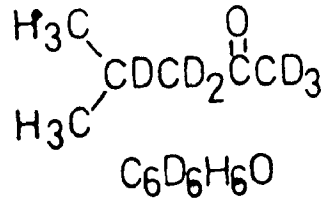
'H NMR Spectrum

$CDCl_3$ (7.27 ppm)

a - 0.93 (d,6H, J=7.5Hz)

b - 2.01 (s,3H)

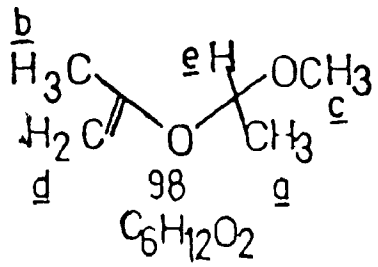
c - 1.87-2.40 (m,3H)



Mass Spectrum

Fragment$^+$	m/z
$C_6D_6H_6O$	106
$C_5D_6H_3O$	91
$C_5D_3H_6O$	88
$C_4D_3H_4O$	74
$C_3D_2H_4O$	60

The fourth product to elute had an 'H NMR spectrum consistent[185] with that expected of enol-ether 98. Irradiation at 1.39δ ((a) protons)) caused the quartet at 5.11δ to collapse to a singlet.



'H NMR Spectrum

$CDCl_3$ (7.27 ppm)

a - 1.39 (d,3H, J=5.4 Hz)

b - 1.84 (s,3H)

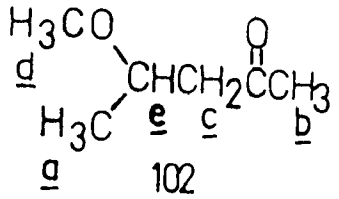
c - 3.36 (s,3H)

d - 3.96 (s,2H)

e - 5.11 (q,1H, J=5.4 Hz).

(M^+=116)

The last fraction to elute was identified from its ^{1}H NMR spectrum[240] and its mass spectrum as 4-methoxy-2-pentanone (102).



102

^{1}H NMR Spectrum

$CDCl_3$ (7.27 ppm)

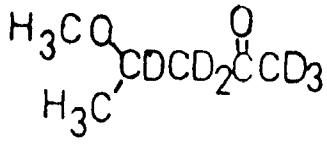
a - 1.11 (d,3H, J=6.0H)

b - 2.03 (s,3H)

c - 2.35-2.46 (m,2H)

d - 3.16 (s,3H)

e - 3.55-3.70 (m,1H)



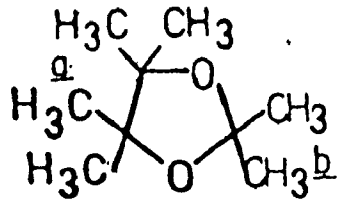
$C_6D_6H_6O_2$

Mass Spectrum

Fragment$^+$	m/z
$C_6D_6H_6O_2$	122
$C_5D_6H_3O_2$	107
$C_5D_3H_6O_2$	104
$C_4D_3H_6O$	76

NON-VOLATILE FRACTIONS

The first eluent had an ^{1}H NMR spectrum consistent[237] with that of hexamethyl-1,3-dioxolane, and a mass spectrum consistent[237] with that of hexamethyl-1,3.-dioxolane-d_{12}.

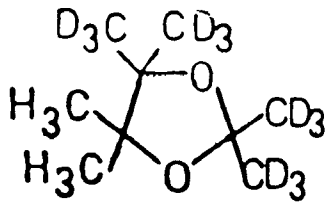


^{1}H NMR Spectrum

$CDCl_3$ (7.27 ppm)

a - 1.25 (s,12H)

b - 1.44 (s,6H)

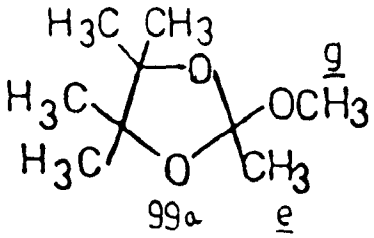


$C_9D_{12}H_6O_2$

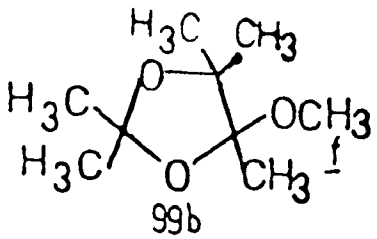
Mass Spectrum

Fragment$^+$	m/z
$C_8D_{12}H_3O_2$	155
$C_8D_9H_6O_2$	152
C_5D_9O	94
$C_5D_6H_3O$	91

The last fraction to elute was methoxy dioxolane (99). The two isomers (99a and 99b) eluted with the same retention time.



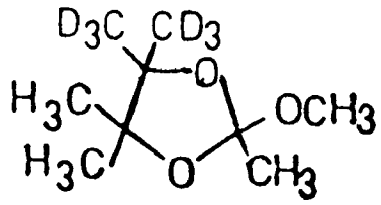
99a



99b

The 'H NMR spectrum of the products showed two methoxy peaks at δ 3.30 and δ 3.35. They were tentatively assigned to f and g, respectively. The relative integrations of those peaks was 99a/99b=1/2. A singlet at δ 1.87 with the same integration as g was assigned to e. The other peaks were at δ 1.25 (s,6H), 1.28 (s,6H), 1.31 (s,6H), and 1.43 (s,9H), where the integrations are relative to the sum of the methoxy integrals=6H.

The mass spectrum of the mixture 99 is given below.

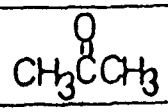
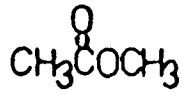
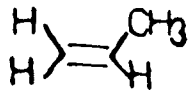
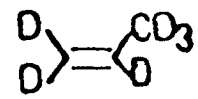
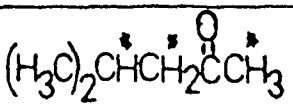
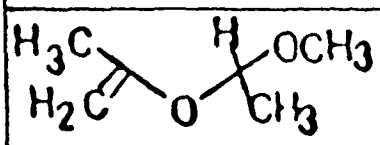
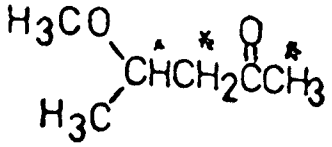
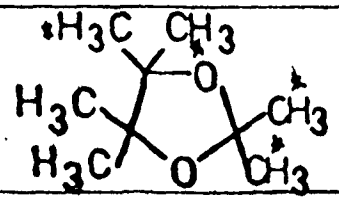
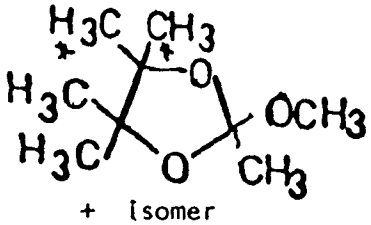


$C_9D_6H_{12}O_3$ + Isomer

Fragment$^+$	m/z (%)
$C_8D_6H_9O_3$	165(58)
$C_8D_6H_9O_2$	149(24)
$C_6D_6H_5O$	105(92)
$C_5D_6H_3O$	91(100)

All the results from the thermolysis of oxadiazoline 87 are tabulated in table RD.6.

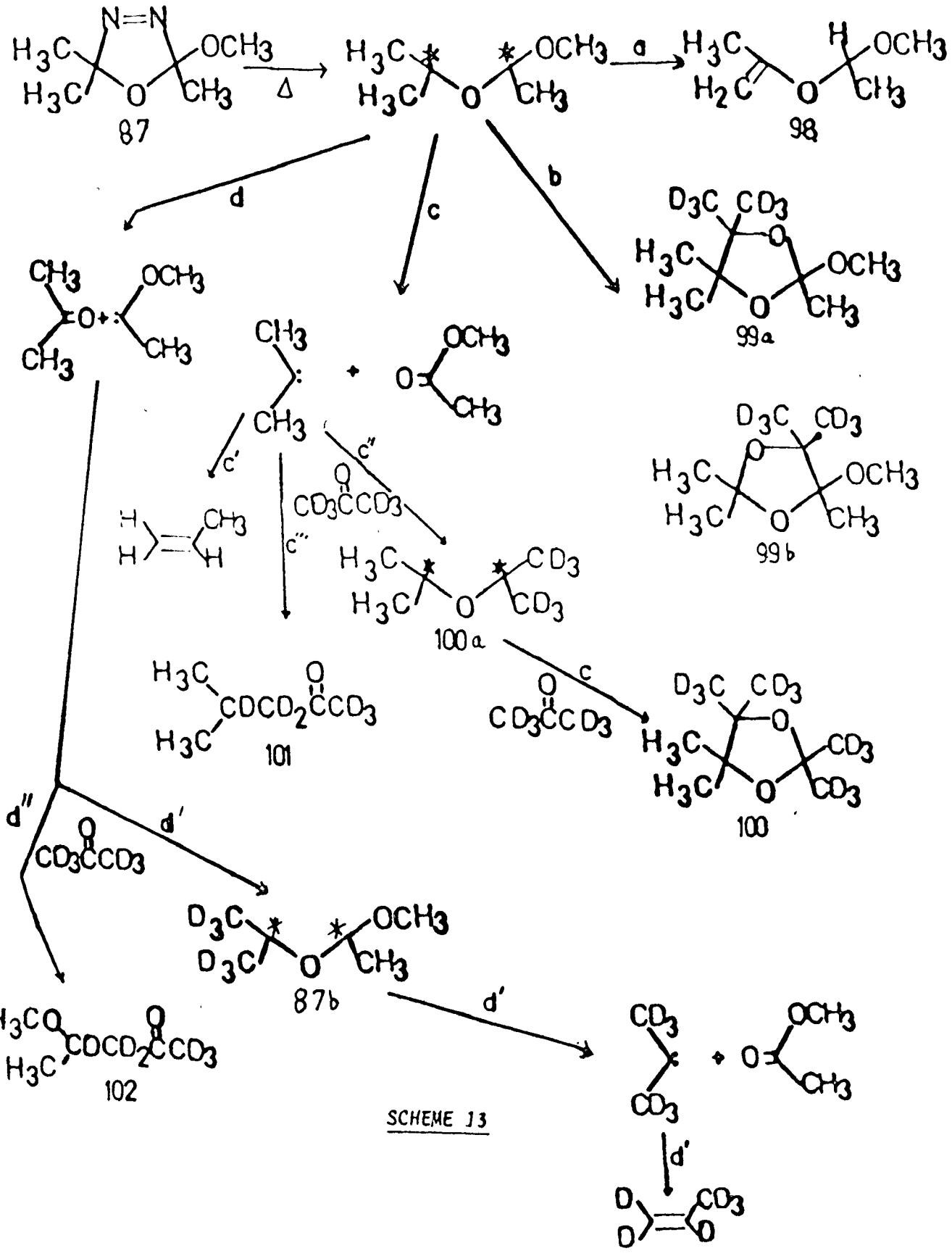
Table RD.6 Products of thermolysis of oxadiazoline 87 in acetone-d_6

Sample	Yield %	H'NMR (ppm)	Mass spec. (Highest mass)
	21	2.17(s)	-
	46	2.06(s,3H) 3.67(s,3H)	-
	24	1.69(d,d,3H) 4.91(m,1H) 4.99(m,1H) 5.78(m,1H)	-
	2	1.73 4.89 5.06 5.71	-
	6.5	0.93(d,6H, J=7.5Hz) 2.01(s,3H) 1.87-2.40(m,3H)	106 (MW)
	14	1.39(d,3H, J=5.4Hz) 1.84(s,3H) 3.36(s,3H) 3.96(s,2H) 5.11(q,1H, J=5.4Hz)	116 (MW)
	4	1.11(d,3H, J=6.0Hz) 2.03(s,3H) 2.35-2.46(m,2H) 3.16(s,3H) 3.55-3.70(m,1H)	122 (MW)
	11.5	1.25(s,12H) 1.44(s,6H)	155 (MW-CH_3)
 + Isomer	15	1.25(s,6H) 1.28(s,6H) 1.31(s,6H) 1.43(s,9H) 1.87(s,3H) 3.30(s,3H) 3.35(s,3H)	165 (MW-CH_3)

* = D *instead of* H *for Mass Spec.*

RD. 5.3 PROPOSED MECHANISM

The mechanism proposed to rationalize the products obtained from thermolysis of 87 in acetone-d_6 is shown below as scheme 13.



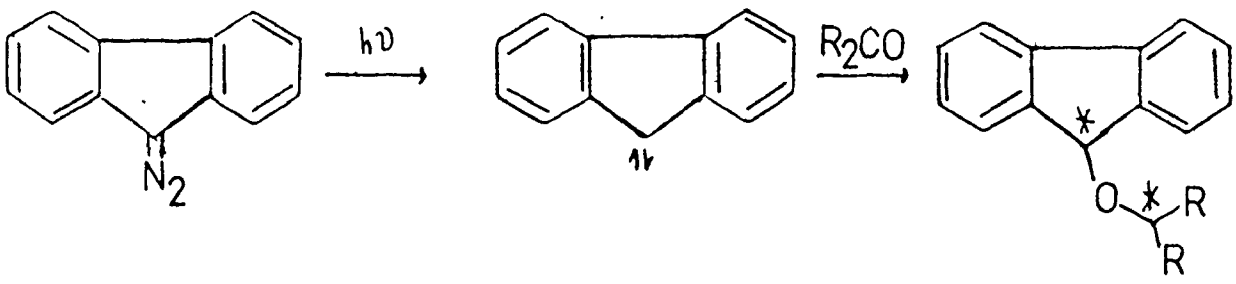
SCHEME 13

As shown in scheme 13, once generated the carbonyl ylide can suffer a 1,4-hydrogen shift to yield enol-ether 98 (path a). The same intermediate can be intercepted by the solvent to form dioxolanes 99 a and b (path b). Fragmentation of the ylide produced dimethyl carbene and methyl acetate through path c, and methoxymethyl carbene and acetone through path d. Dimethyl carbene can undergo a 1,2-hydrogen shift (c') to give propene, can add to acetone-d_6 to generate ylide (100a) which is intercepted by the solvent to form dioxolane 100 (c'') and can insert into the C-D bond of acetone-d_6 to form ketone 101 (c'''). Methoxy methyl carbene can add to the solvent to generate ylide (87b) which fragments to give the precursor of propene-d_6, dimethylcarbene-d_6. Alternatively, methoxymethyl carbene can insert into the C-D bond of the solvent (d'') to give ketone 101. A low yield of propene-d_6 (2%) can be rationalized in terms of what should be expected given the various competition reactions in their known yields (eq 78, p70 and scheme 13). 67% of the ylide fragments and dimethylcarbene (46%), of which 24% ($\sim$ 1/2) goes to propene, is produced in the process. Methoxymethyl carbene (21%) inserts into the C-D bond of acetone-d_6 (4%) or adds to the oxygen (17%) to form an ylide. Fragmentation of the ylide can produce a maximum of 5.5% propene-d_6.

Thermolysis of oxadiazoline 87 in acetone-d_6 goes via a carbonyl ylide. Unlike methanol, acetone-d_6 intercepted only 15% of the ylide. One of the competing reactions of the intermediate is a known[72] intramolecular 1,4-hydrogen shift.

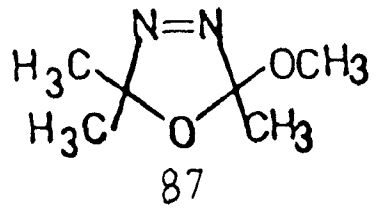
The other competing process is the fragmentation to carbenes and carbonyl compounds. Because ylides can only be formed from the reaction of singlet carbenes with heteroatoms,[15] dimethyl and methoxymethyl carbenes are adding to acetone-d_6 in their singlet state. Examination of the literature[65,67] reveals that carbonyl ylides are obtained from the reaction of $PhHgCX_2Br$ and R_2CN_2 (Cu catalyst) with ketones. It is not clear if carbenes or carbenoids are involved in the processes. The fragmentation of the carbonyl ylide generated from the thermolysis of oxadiazoline 87 must give rise to free carbenes and the results show that such carbenes can add to acetone-d_6 to generate new ylides. The only other example of such a reaction, to our knowledge is very recent unpublished work by P.C. Wong, D. Griller, and J.C. Scaiano[241] in which singlet fluorenylidene adds to ketones to generate carbonyl ylides, eq 78a.

[78a]

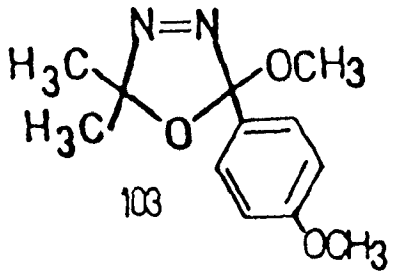


RD.6. TRAPPING EXPERIMENTS

Carbonyl ylides are known to react with alkenes and alkynes by cycloaddition. Since the evidence presented thus far suggested that we are dealing with ylide intermediates, it was decided to use the cycloaddition reaction as a probe for their presence. Two different oxadiazolines (87 and 103) were thermolyzed in several traps, and the results of those experiments are described in this section.



87



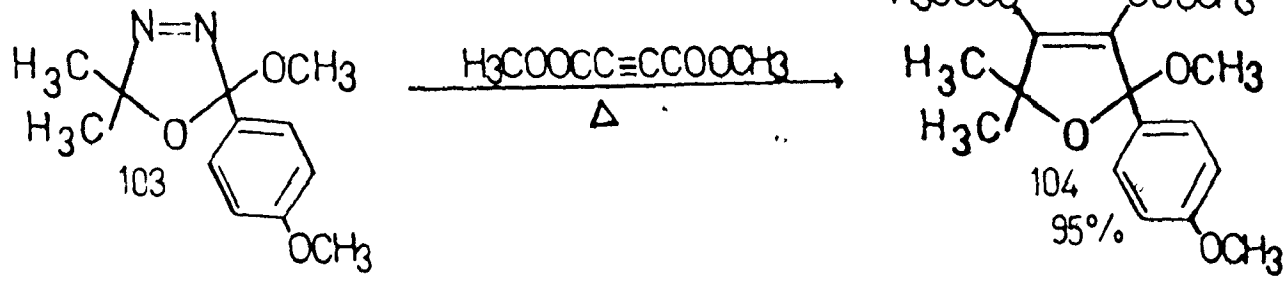
103

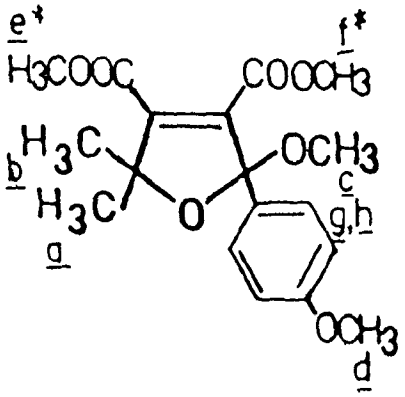
RD 6.1 THERMOLYSIS OF 103 IN VARIOUS YLIDE TRAPS

a - DIMETHYLACETYLENE DICARBOXYLATE (DAD)

Thermolysis of methoxyoxadiazoline 103 in DAD gave over 95% of a product the spectral data of which are best interpreted in terms of structure 104 (eq 79).

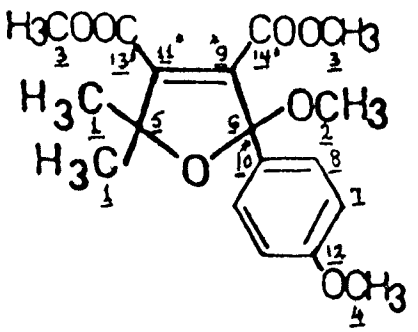
[79]





^{1}H NMR ($CDCl_3$-7.27 ppm)

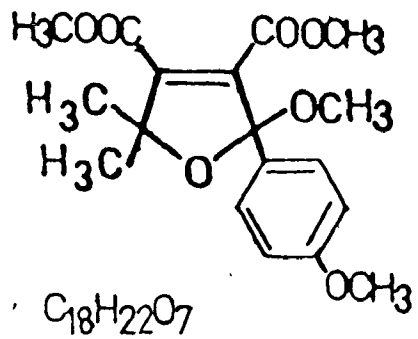
a - 1.66 (s,3H)
b - 1.68 (s,3H)
c - 3.32 (s,3H)
d - 3.71 (s,3H)
*e - 3.80 (s,3H)
*f - 3.82 (s,3H)
g - 6.89 (d,2H, J=9.0Hz)
h - 7.41 (d,2H, J=9.0Hz)



* = Tentative assignments

^{13}C NMR ($CDCl_3$-77.27 ppm)

1 - 26.95	8 - 128.23
2 - 50.96	9 - 130.72
3 - 52.16	10 - 138.62
4 - 55.08	11 - 142.49
5 - 87.10	12 - 159.88
6 -111.28	13 - 162.73
7 -113.40	14 - 163.09



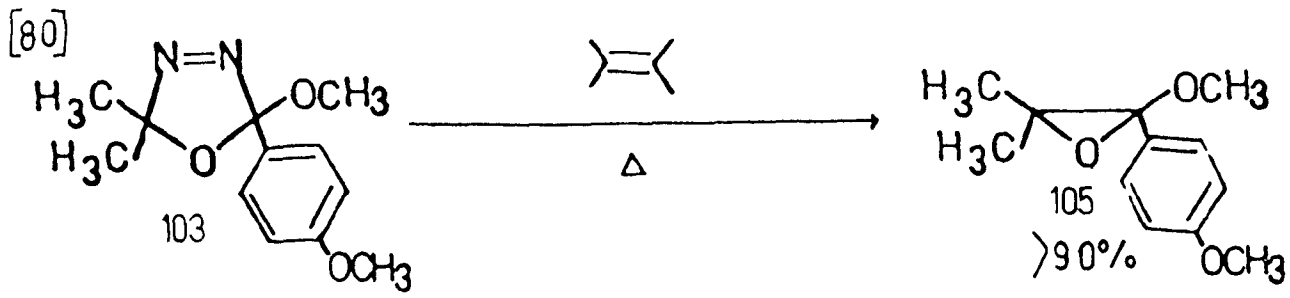
$C_{18}H_{22}O_7$
(MW=350)

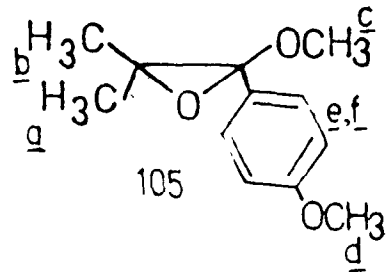
Mass Spectrum

Fragment$^+$	M/Z	%
$C_{17}H_{19}O_6$	319	100
$C_{15}H_{16}O_4$	260	25
$C_{14}H_{13}O_4$	245	18
$C_8H_7O_2$	135	42
C_7H_7O	107	12
C_6H_5	77	5

b - *VARIOUS OLEFINS*

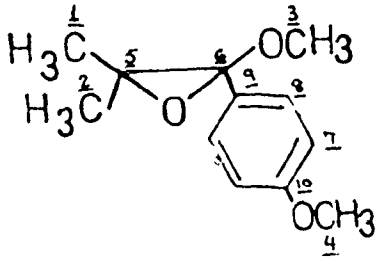
Thermolysis of oxadiazoline 103 in tetramethylethylene, in tetrachloroethylene, and in ethylvinylether afforded over 90% of 105 (eq 80). The spectral data are well interpreted in terms of the structure of epoxide 105.





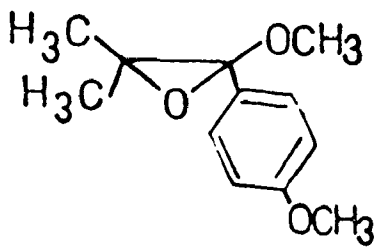
^{1}H NMR ($CDCl_3$-7.27 ppm)

a - 1.02 (s,3H)
b - 1.54 (s,3H)
c - 3.21 (s,3H)
d - 3.84 (s,3H)
e - 6.93 (d,2H, J=9.0Hz)
f - 7.37 (d,2H, J=9.0Hz)



^{13}C NMR ($CDCl_3$-77.27 ppm)

1 - 20.05	6 - 100.05
2 - 20.30	7 - 113.81
3 - 52.50	8 - 129.52
4 - 55.35	9 - 131.86
5 - 67.33	10 - 160.14



$C_{12}H_{16}O_3$

Mass Spectrum

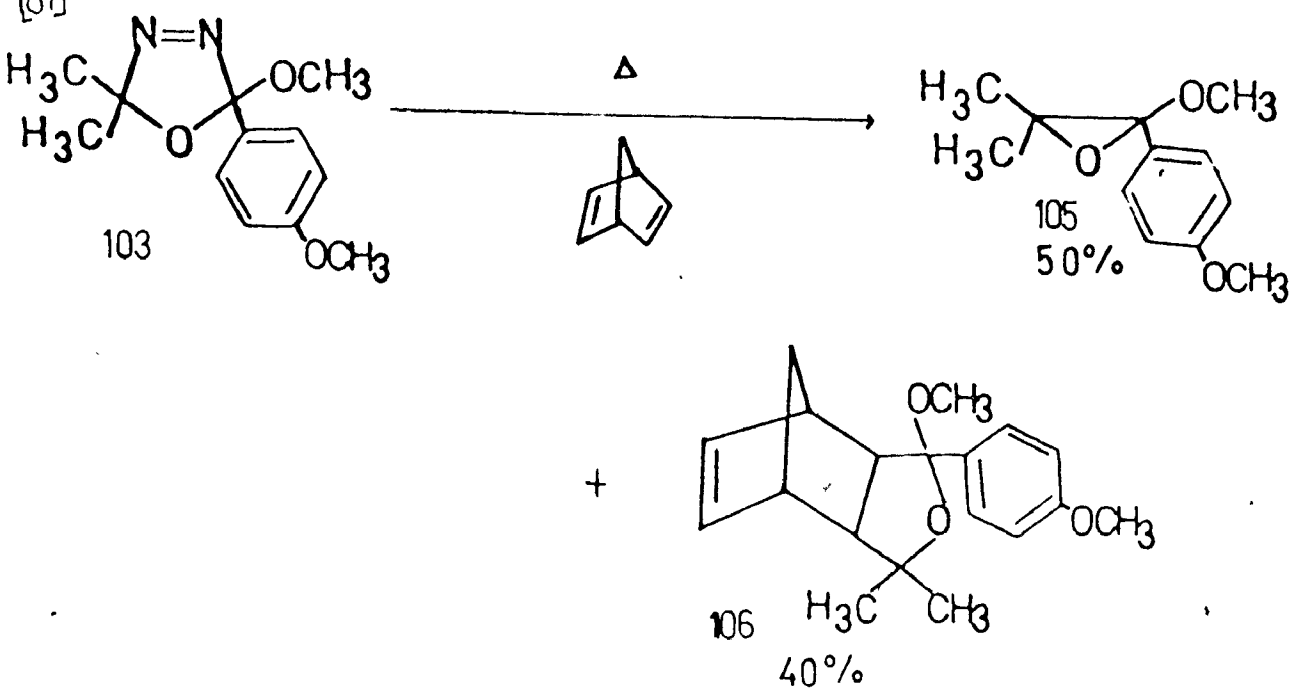
Fragment$^+$	m/z	(%)
$C_{12}H_{16}O_3$	208	(6)
$C_9H_{11}O_3$	151	(100)
$C_{11}H_{13}O_3$	193	(4)
$C_{11}H_{13}O_2$	177	(2)
$C_8H_7O_2$	135	(56)
C_7H_7O	107	(4)
C_6H_5	77	(9)

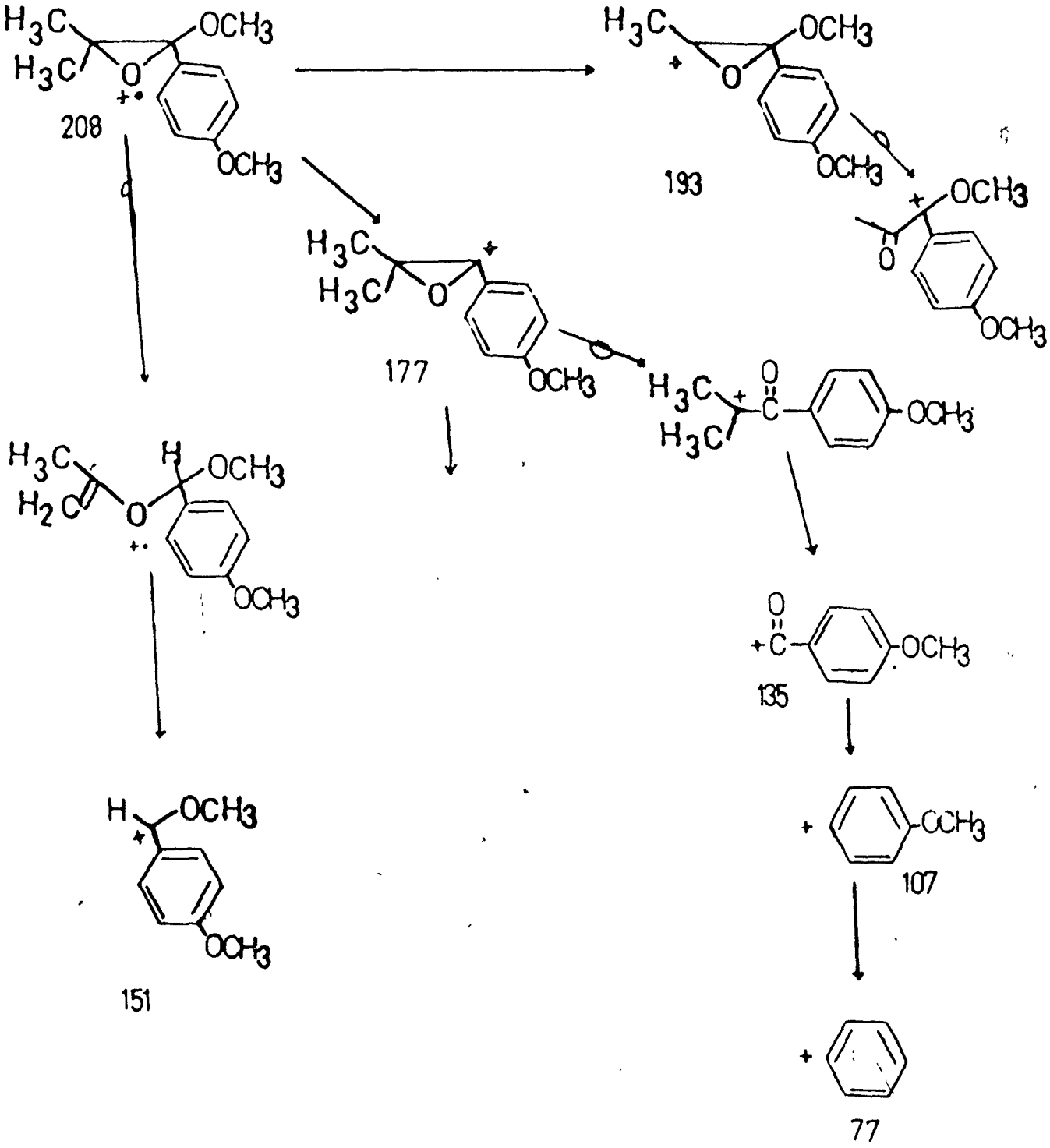
Scheme 14 depicts a possible fragmentation mechanism in the mass spectrum of epoxide 105.

c - *NORBORNADIENE*

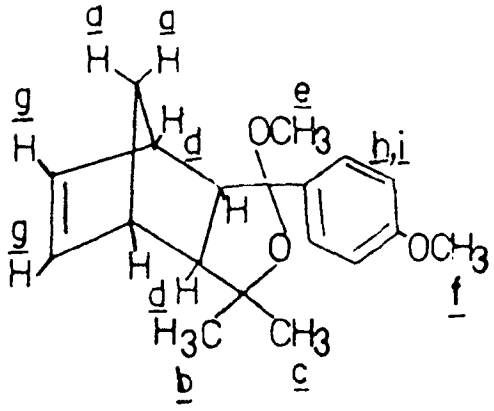
Thermolysis of oxadiazoline 103 in norbornadiene afforded epoxide 105 and cycloadduct 106 (eq 81). The spectra from which structure 106 was deduced are the following.

[81]





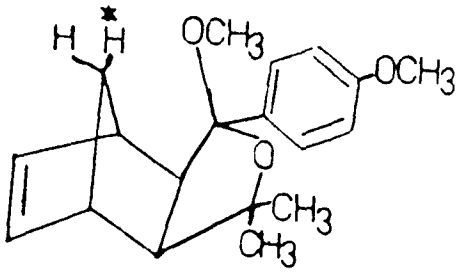
SCHEME 14



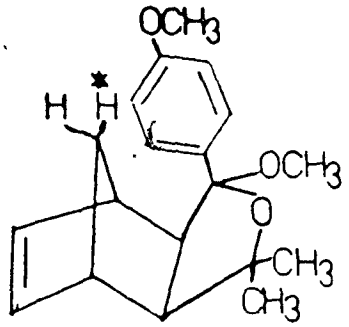
'H NMR ($CDCl_3$-7.27 ppm)

a - 0.95-1.02 (m,1H)
b - 1.38 (s,3H)
c - 1.51 (s,3H)
d - 1.80-2.88 (m,5H)
e - 2.91 (s,3H)
f - 3.82 (s,3H)
g - 6.08 (b-s,2H)
h - 6.78 (d,2H, J=9.0Hz)
i - 7.36 (d,2H, J=9.0Hz)

Norbornadiene normally forms exo-Diels-Alder addition products, two of which 106a and 106b are possible in this case.[242] Adduct 106a is probably the

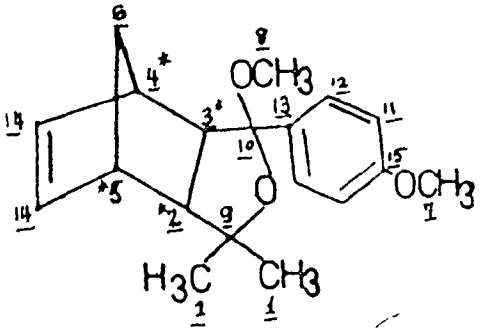


106a



106b

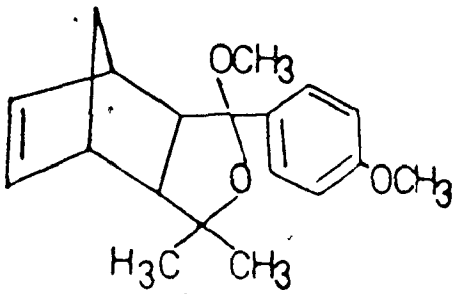
major one because of steric hindrance in 106b. Furthermore, if 106b was the major one, the chemical shift of H* would be at higher field.[11,243]



^{13}C NMR ($CDCl_3$-77.27)

1 - 23.93	9 - 82.02
*2 - 31.60	10 -109.43
*3 - 42.63	11 -113.15
*4 - 43.51	12 -128.57
*5 - 44.17	13 -131.86
6 - 48.70	14 -139.24
7 - 55.13	15 -159.05
8 - 60.10	

* = Tentative assignments.[244]



106

$C_{19}H_{24}O_3$

(MW=300)

Mass Spectrum

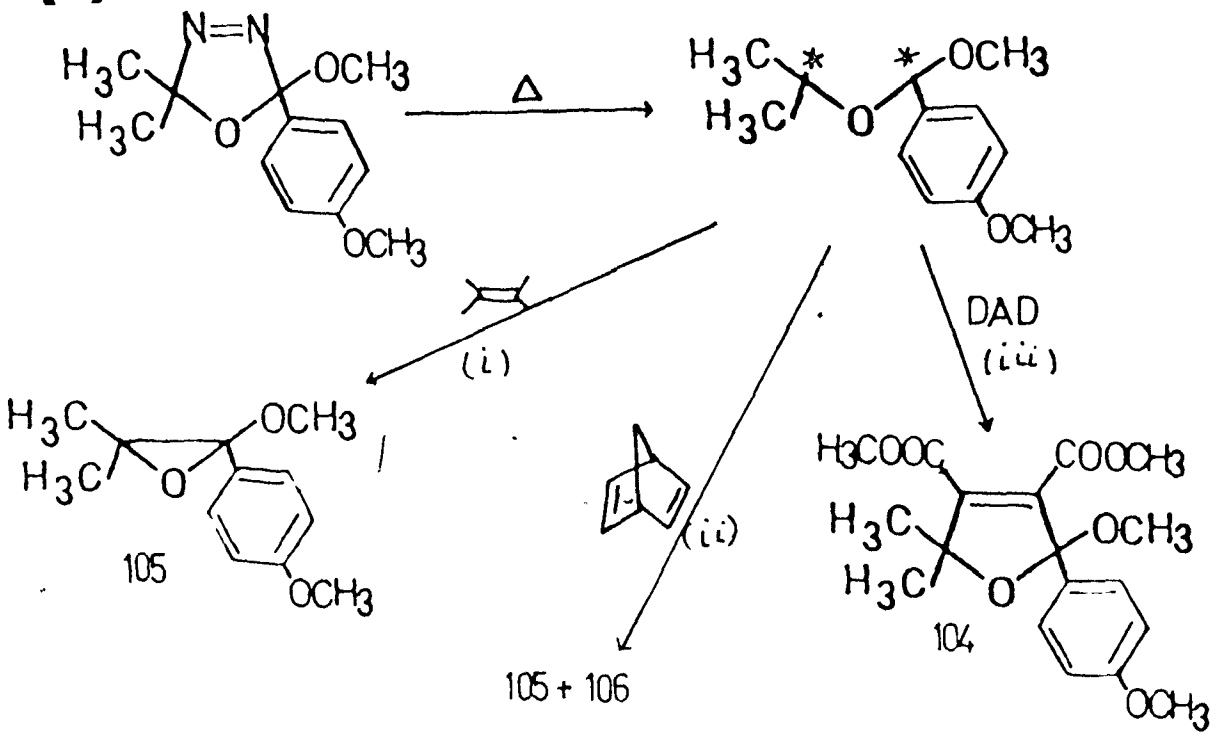
Fragment$^+$	m/z	(%)
$C_{18}H_{21}O_2$	269	(35)
$C_{13}H_{15}O_2$	203	(100)
$C_8H_7O_2$	135	(72)
C_7H_7O	107	(8)
C_6H_5	77	(20)

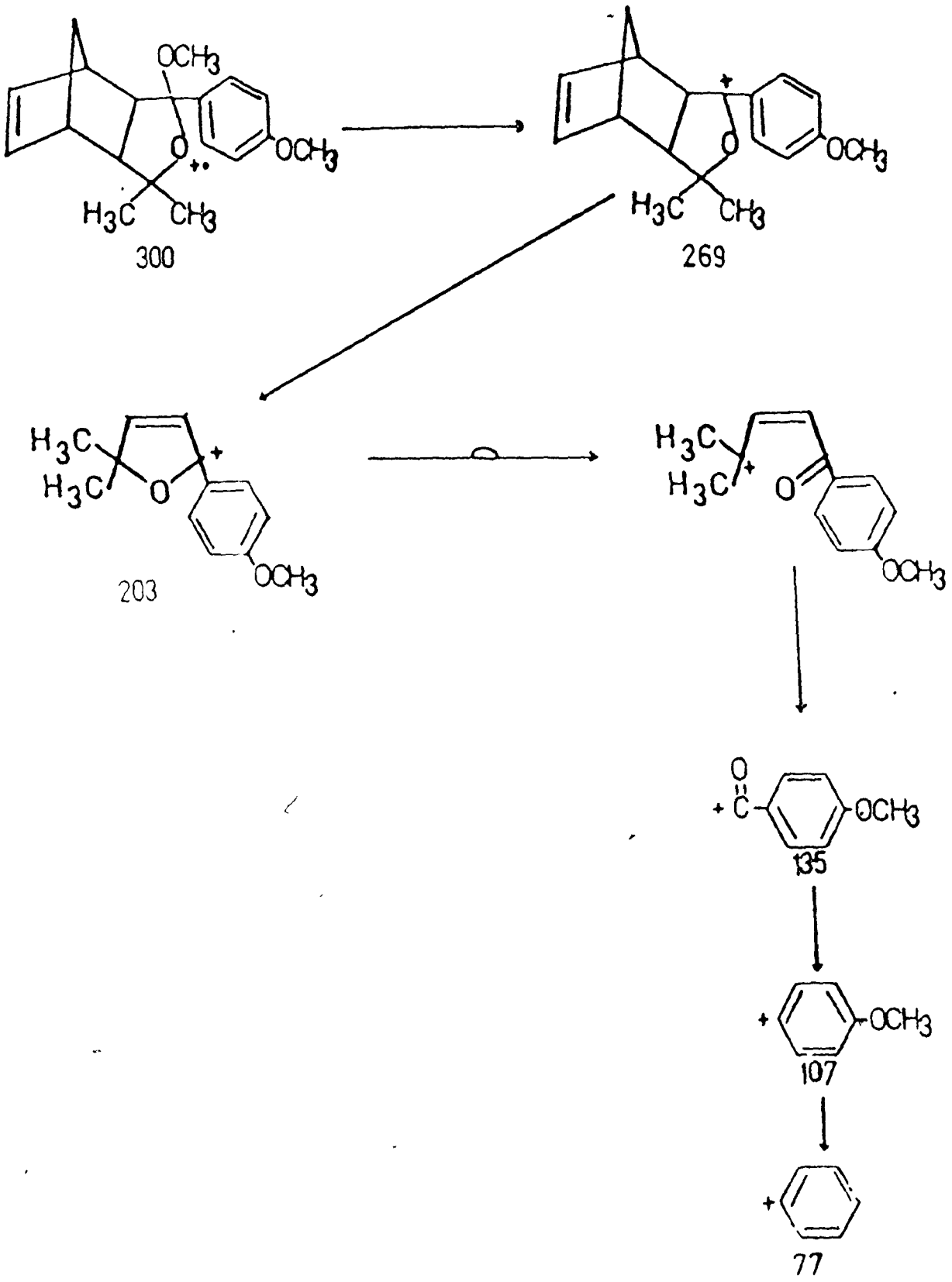
Scheme 15 depicts a possible fragmentation pattern in the mass spectrum of 106.

d - *DISCUSSION*

The different products from the thermolysis of oxadiazoline 103 in different dipolarophiles are shown in equation 82.

[82]





SCHEME 15

Two competitive processes occur in carbonyl ylide (103a), a cyclization leading to epoxide 105 (i and ii) and a 1,3-dipolar addition to the dipolarphile (ii and iii). In various olefins, cyclization to epoxide is the major pathway(i). Norbornadiene, being a more reactive olefin, intercepts ∿ 40% of the ylide, whereas, dimethylacetylenedicarboxylate, known for its reactivity in 1,3-dipolar cycloaddition, competes efficiently with cyclization to the extent where only cycloadduct 104 is produced.

Those reactions established the existence of a carbonyl ylide intermediate in an indirect method. (from the structure of the final products). Dr. J.C. Scaiano (N.R.C. Ottawa, Canada) generated the carbonyl ylide intermediate by laser-flash-photolysis. From following the decay of the intermediate by UV, he was able to get the rate of cyclization ($k^{31°C}_{Cycl.} \simeq 1.3 \times 10^6\ s^{-1}$ (in benzene)) and the rate of trapping by DAD ($k^{31°C}_{DAD} \simeq 1.0 \times 10^9\ M^{-1}s^{-1}$ (in CH_3CN)). Assuming that there is no solvent dependence, one can calculate that at a DAD concentration of 1.3×10^{-3} M 50% of the carbonyl ylide can be trapped at 31°C. On the other hand, an estimate of $k^{80°C}$ (norbornadiene) can be made. Since k_{cycl} at 80°C should not be more than 2^5 times k_{cycl} at 31°C (factor of 2 for 10°C); hence, $k^{80°C}_{cycl} \lesssim 32 \times 1.3 \times 10^6\ sec^{-1} \lesssim 41.6 \times 10^6\ sec^{-1}$. Since neat diene (9.3M) trapped about 4/9 of the ylide then:

$$4[41.6 \times 10^6]\ [Ylide] = 5\ k^{80°C}_{diene}\ [Ylide]\ [Diene]$$

$$k^{80°C}_{diene} = 3.6 \times 10^6\ M^{-1}\ s^{-1}$$

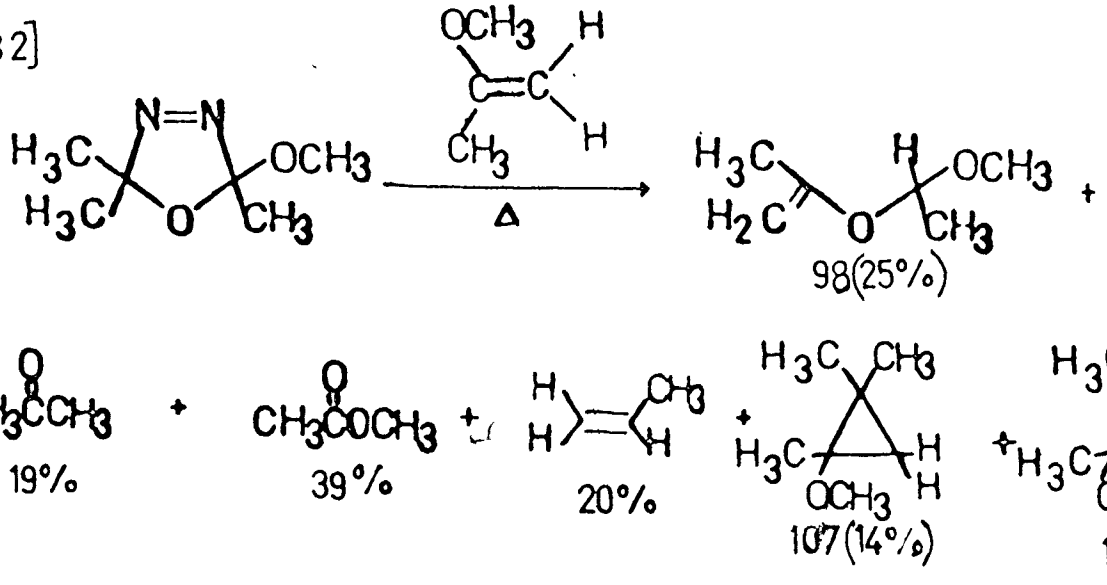
Finally, oxygen trapped the carbonyl ylide very efficiently ($k \simeq 2.0 \times 10^9\ M^{-1}\ s^{-1}$ (in benzene)), hence, exclusion of O_2 is mandatory for clean trapping of the ylide by dipolarophiles.

RD. 2. THERMOLYSIS OF 87 IN VARIOUS OLEFINS AND IN DAD

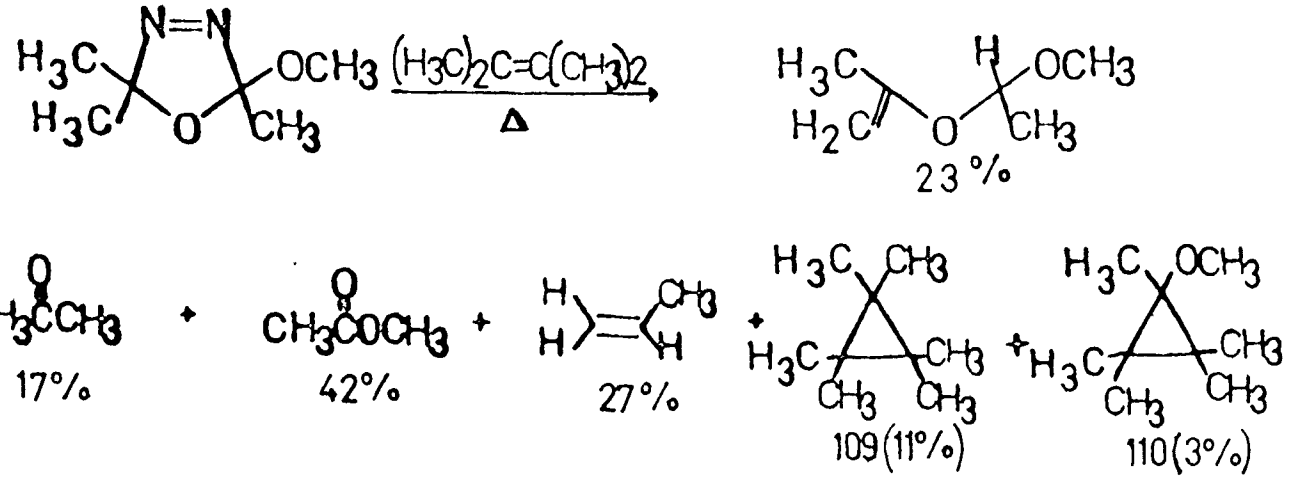
a - 2-METHOXY-PROPENE AND TETRAMETHYLETHYLENE

Thermolysis of oxadiazoline 87 in 2-methoxy-propene and in tetramethylethylene afforded the products shown in eqs 82 and 83 respectively.

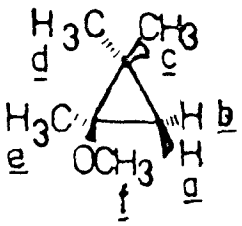
[82]



[83]



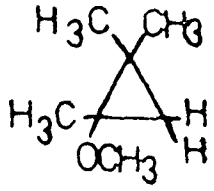
Acetone, methyl acetate, propene and enol-ether 98 were identified by comparing their ^{1}H NMR spectra to those of known samples. The ^{1}H NMR spectra and mass spectra of each of the cyclopropanes are in good accord with structures 107, 108, 109, and 110, respectively.



107

^{1}H NMR ($CDCl_3$-7.27 ppm)

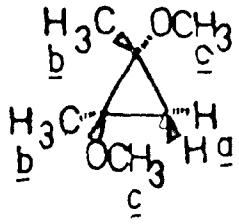
a - 0.13 (d,1H, J=4.9Hz)
b - 0.49 (d,1H, J=4.9Hz)
c - 1.07 (s,3H)
d - 1.18 (s,3H)
e - 1.36 (s,3H)
f - 3.27 (s,3H)



$C_7H_{14}O$

Mass Spectrum

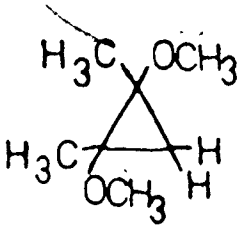
Fragment$^+$	m/z	(%)
$C_7H_{14}O$	114	(3)
$C_6H_{11}O$	99	(100)
C_6H_{11}	83	(4)
C_5H_7	67	(24)



^{1}H NMR ($CDCl_3$-7.27 ppm)

a - 0.54 (s,2H)
b - 1.43 (s,6H)
c - 3.27 (s,6H)

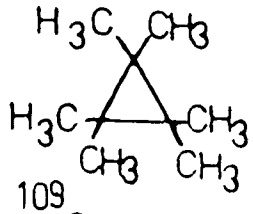
Because the two methylene hydrogens are equivalent, the product collected from the G.C. was the trans-product.



$C_7H_{14}O_2$

Mass Spectrum

Fragment$^+$	m/z	(%)
$C_7H_{14}O_2$	130	(1)
$C_6H_{11}O_2$	115	(100)
$C_6H_{11}O$	99	(22)
C_5H_7O	83	(10)
C_5H_7	67	(13)
C_4H_3	51	(4)



109

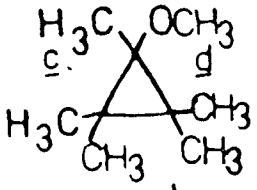
C_9H_{18}

'H NMR ($CDCl_3$-7.27)

0.96 (Lit[245] 0.94-CCl_4)

Mass Spectrum

Fragment$^+$	m/z	(%)
C_9H_{18}	126	(15)
C_8H_{15}	111	(100)
C_6H_9	69	(29)



110 a,b

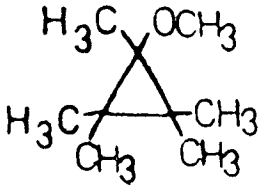
'H NMR ($CDCl_3$-7.27)

a - 1.09 (s,6H)

b - 1.21 (s,6H)

c - 1.41 (s,3H)

d - 3.23 (s,3H)



$C_9H_{18}O$

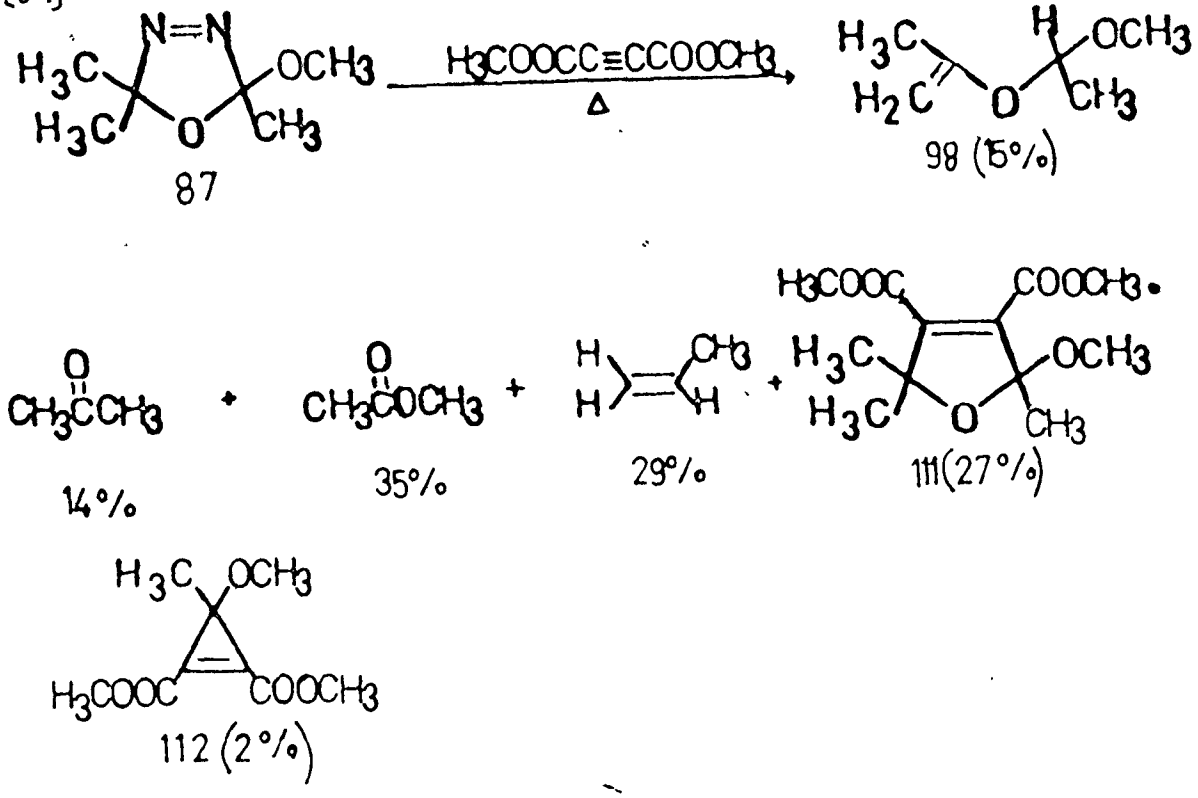
Mass Spectrum

Fragment$^+$	m/z	(%)
$C_9H_{18}O$	142	(2)
$C_8H_{15}O$	127	(100)
C_8H_{15}	111	(13)
C_7H_{11}	95	(23)
C_6H_9	69	(7)

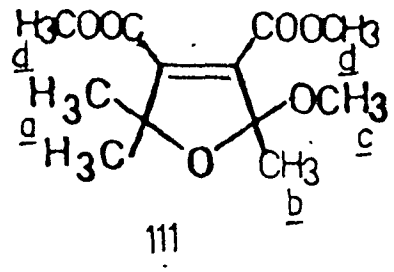
b - *DIMETHYLACETYLENEDICARBOXYLATE (DAD)*

Thermolysis of methoxy oxadiazoline 87 in DAD afforded the products shown in eq 84.

[84]



The following spectral data are best explained in terms of the structure of 111 and a compound tentatively identified as 112.



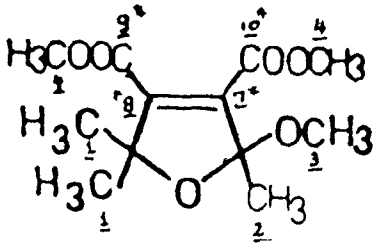
^{1}H NMR ($CDCl_3$-7.27 ppm)

a - 1.48 (s,6H)

b - 1.64 (s,3H)

c - 3.27 (s,3H)

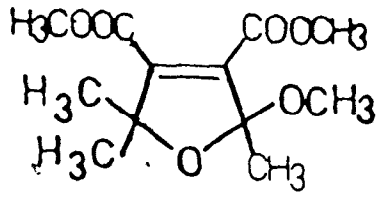
d - 3.83 (s,6H)



III

^{13}C NMR ($CDCl_3$-77.27 ppm)

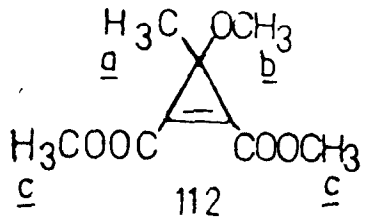
1 - 26.02	6 - 109.39
2 - 26.60	7 - 133.64
3 - 51.24	8 - 141.24
4 - 53.80	9 - 161.06
5 - 83.12	10 - 162.88



$C_{12}H_{18}O_6$

Mass Spectrum

Fragment$^+$	m/z	(%)
$C_{11}H_{15}O_6$	243	(18)
$C_{11}H_{15}O_5$	227	(18)
$C_8H_9O_4$	169	(100)
$C_7H_9O_4$	157	(70)
$C_5H_3O_3$	111	(38)
$C_6H_5O_2$	109	(7)



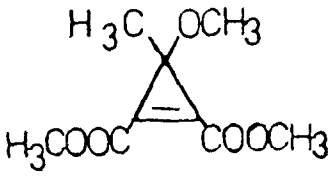
112

^1H NMR ($CDCl_3$-7.27 ppm)

a - 1.30 (s,3H)

b - 3.71 (s,3H)

c - 3.86 (s,6H)



$C_9H_{12}O_5$

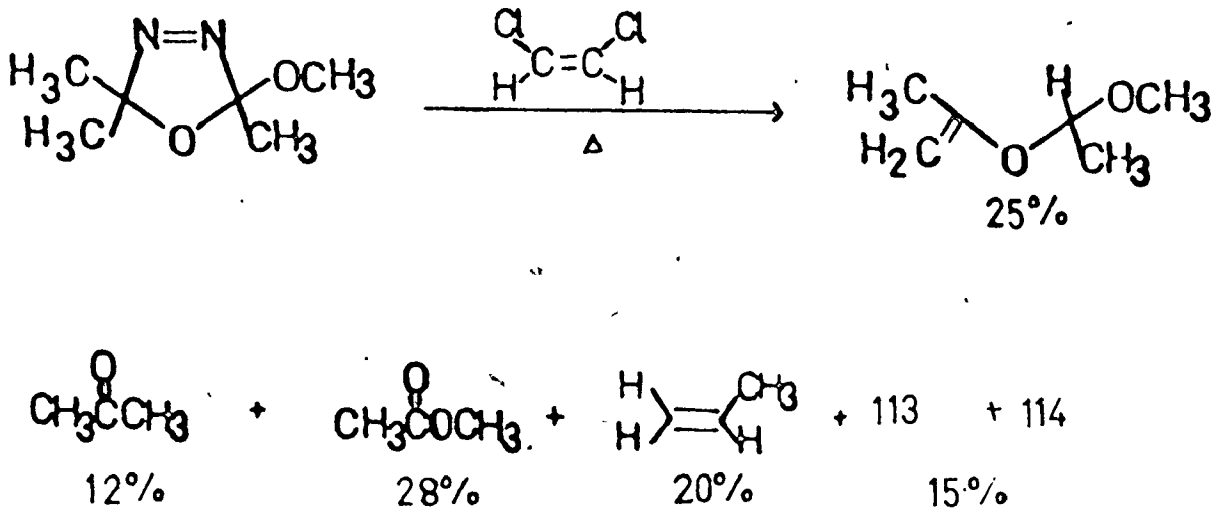
Mass Spectrum

Fragment$^+$	m/z	(%)
$C_8H_9O_5$	185	(16)
$C_8H_9O_4$	169	(24)
$C_5H_3O_3$	111	(100)
$C_4H_3O_2$	83	(12)
$C_2H_3O_2$	59	(80)

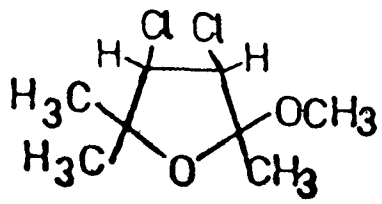
c - *CIS-1,2-DICHLOROETHYLENE*

Thermolysis of methoxy oxadiazoline 87 in cis-1,2-dichloroethylene afforded the products shown in eq 85.

[85]



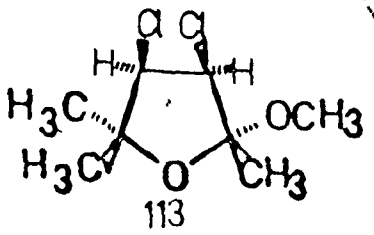
Products 113 and 114 gave the same mass spectrum.



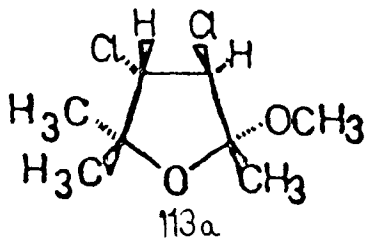
$C_8H_{14}Cl_2O_2$

Fragment	m/z	(%)
$C_7H_{11}Cl_2O_2$	197,199	(10,6)
$C_7H_{11}Cl_2O$	181,183	(40,28)
$C_7H_{10}Cl\ O_2$	161,163	(36,13)
$C_7H_{10}Cl\ O$	145,147	(32,10)
$C_5H_8Cl\ O$	119,121	(100,35)
$C_4H_4Cl\ O$	103,105	(78,24)
$C_4H_3\ O$	67	(39)

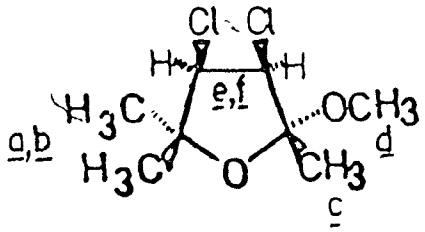
The ^{1}H NMR of 113 contained two doublets at δ 4.33 and δ 4.75 with a coupling constant of 4.9 Hz. From the two possible structures 113a is ruled out because the trans protons should[246] have a coupling constant of over 10 Hz, whereas a coupling constant of 4-8 Hz is due to cis coupling.



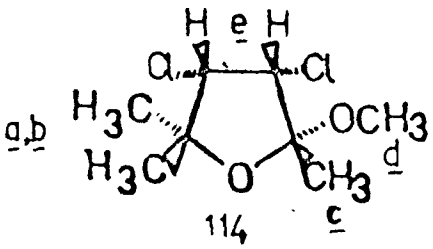
113



113a



^{1}H NMR ($CDCl_3$-7.27 ppm)
a - 1.39 (s,3H)
b - 1.42 (s,3H)
c - 1.54 (s,3H)
d - 3.30 (s,3H)
e - 4.33 (d,1H, J=4.9Hz)
f - 4.75 (d,1H, J=4.9Hz)



114

^{1}H NMR ($CDCl_3$-7.27 ppm)
a - 1.38 (s,3H)
b - 1.46 (s,3H)
c - 1.50 (s,3H)
d - 3.31 (s,3H)
e - 4.30 (s,2H)

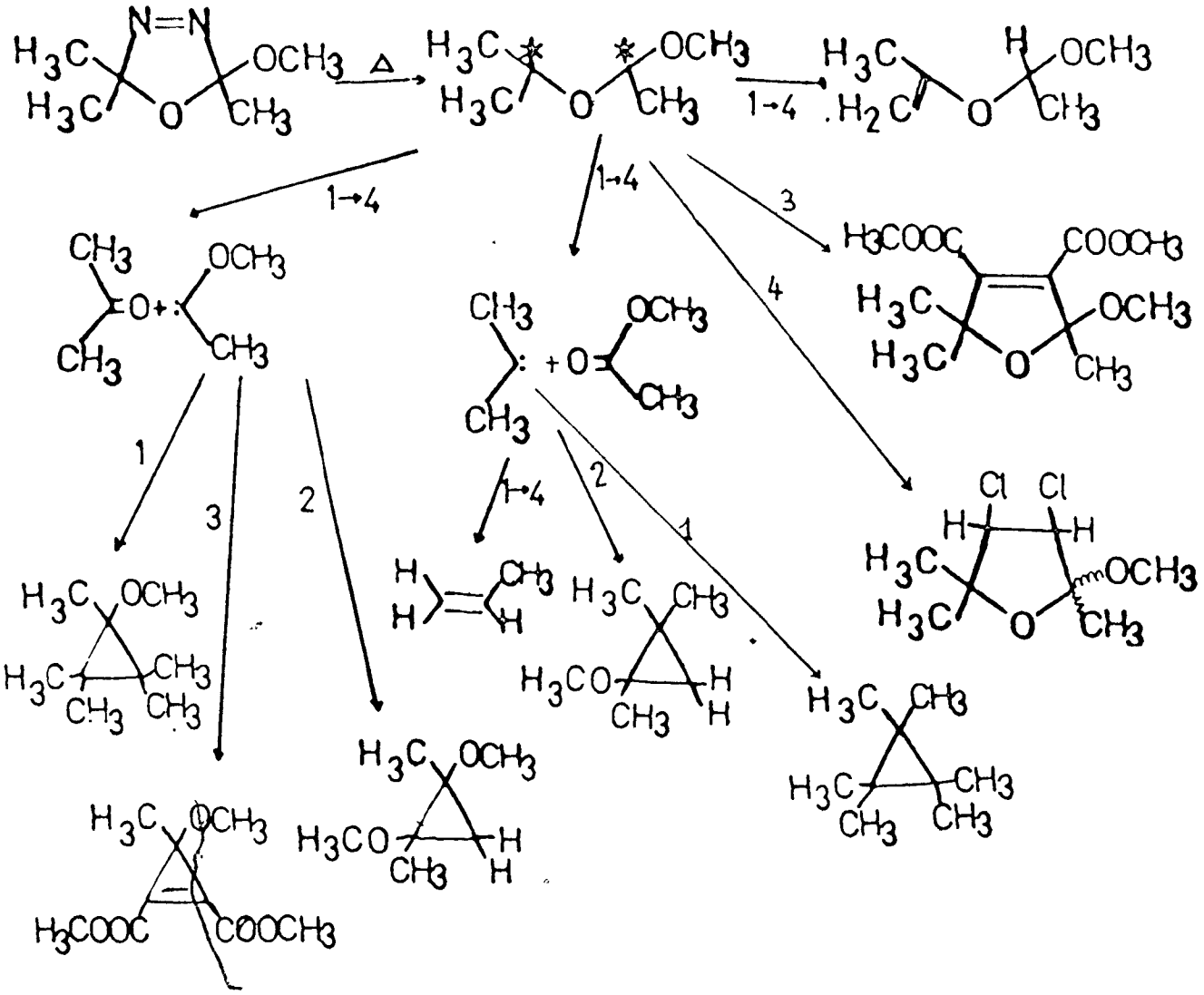
Thus, cycloaddition reaction of the carbonyl ylide, generated from the thermolysis of oxadiazoline 87, and cis-1,2-dichloroethylene produces two isomeric cycloadducts. Because of the cis structure of 113 and the evidence from Huisgen's[247] work, that the 1,3-dipolar addition is a concerted process, the structure of 114

seems reasonable. The fact that the two protons (e) show as a singlet (δ 4.30) would mean that they are accidentally in identical magnetic environments.

d - *DISCUSSION*

Equation 86 summarizes the trapping experiments in part RD. 6.2. (See below for identities of solvents).

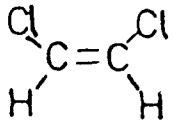
[86]



1- $(H_3C)_2C=C(CH_3)_2$

2- $H_2C=C(OCH_3)CH_3$

3- $H_3COOCC\equiv CCOOCH_3$

4- 

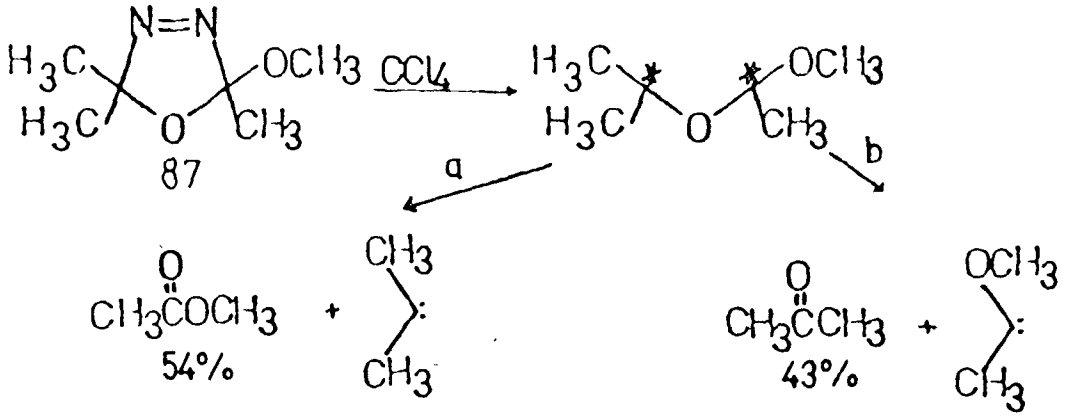
Thermolysis of oxadiazoline 87 generates a carbonyl ylide and carbenes. Alkyl and electron-donating substituents on the olefin decrease the rate of cycloaddition to 1,3-dipolar species whereas electron-withdrawing substituents have an opposite effect, they increase the rate of addition.[248,249] These generalizations are supported with the observations that tetramethylethylene and 2-methoxy-propene do not react with carbonyl ylide 87a, whereas cis-1,2-dichloroethylene and DAD do.

The carbenes generated in the process are electrophilic.[140] In order for their reaction with olefins to be efficient, the double bond should be nucleophilic. In cis-1,2-dichloroethylene the double bond is electrophilic because of the electron-withdrawing substituents hence, no cyclopropanes were found. Presumably the carbenes undergo a 1,2-hydrogen shift more rapidly than they add to dichloroethylene.

RD. 7. THERMOLYSIS OF 5,5-DICYCLOPROPYL-2-METHOXY-2-METHYL-Δ^3-1,3,4-OXADIAZOLINE

When oxadiazoline 87 was thermolyzed in CCl_4, at 80°C, the fragmentation of the carbonyl ylide produced methylacetate (54%) and acetone (43%)[185,226], eq 87. The yields of dimethyl and methoxymethyl carbenes would be 54% and 43% respectively.

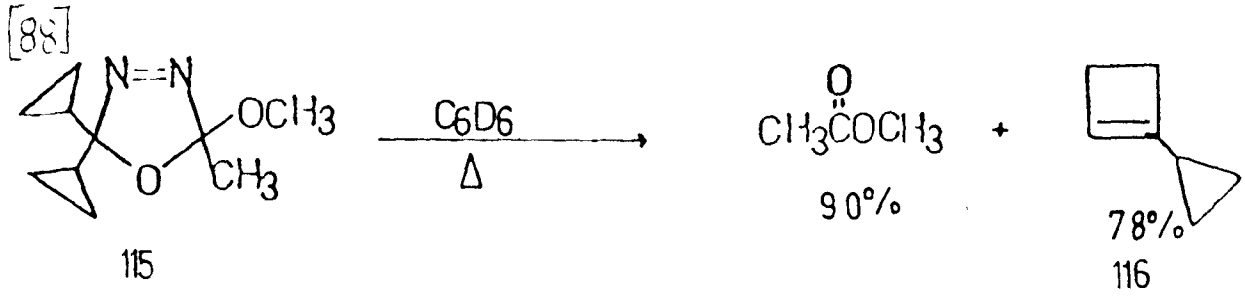
[87]



Thus, the fragmentation occurs in both possible ways in nearly 1:1 ratio. An attempt was made to favour one ylide fragmentation path over the other by changing the substituents at C_5 from methyl to cyclopropyl.

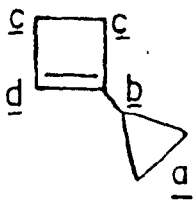
RD.7.1 *THERMOLYSIS IN BENZENE-d_6*

The main products from the thermolysis of 5,5-dicyclopropyl-2-methoxy-2-methyl-Δ^3--1,3,4-oxadiazoline (115), at 79.5°C in benzene-d_6, were methylacetate (90%) and 1-cyclopropyl-cyclobutene (116, 78%), eq 88.



115 116

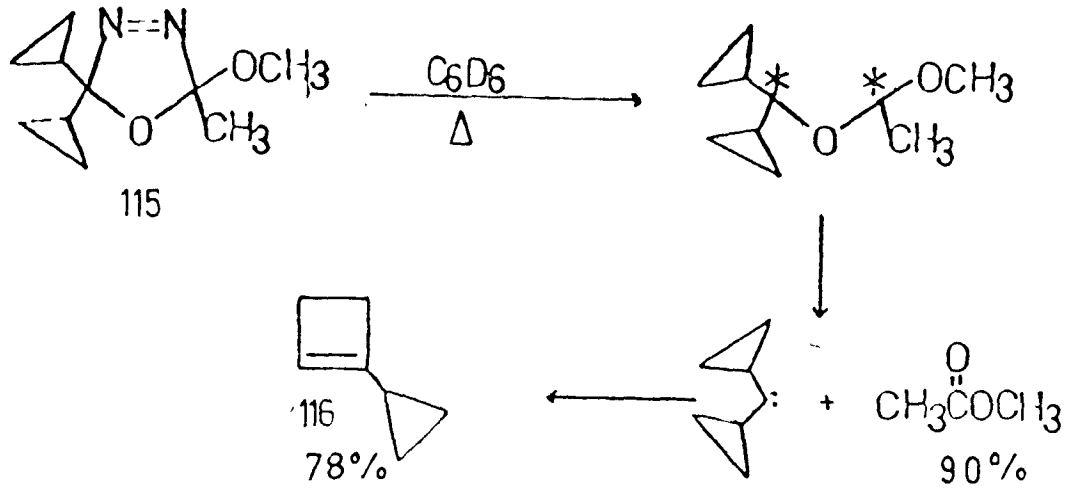
Methyl acetate was identified by comparing its ^{1}H NMR and its IR spectra to those of an authentic sample. 1-Cyclopropyl-cyclobutene had a ^{1}H NMR spectrum identical to a published[250] spectrum.



^{1}H NMR ($CDCl_3$-7.27 ppm)
a - 0.27-0.75 (m,4H)
b - 1.10-1.43 (m,1H)
c - 2.20 (s,4H)
d - 5.51 (s,1H)

The production of methyl acetate, from the thermolysis of 115, is consistent with the fragmentation of the carbonyl ylide via path a (eq 87). The carbene generated in the process is dicyclopropyl carbene. Cyclopropyl substituted meth-

ylenes are known[250-252] to rearrange to give cyclobutenes; in this case, 1-cyclopropyl-cyclobutene (116).



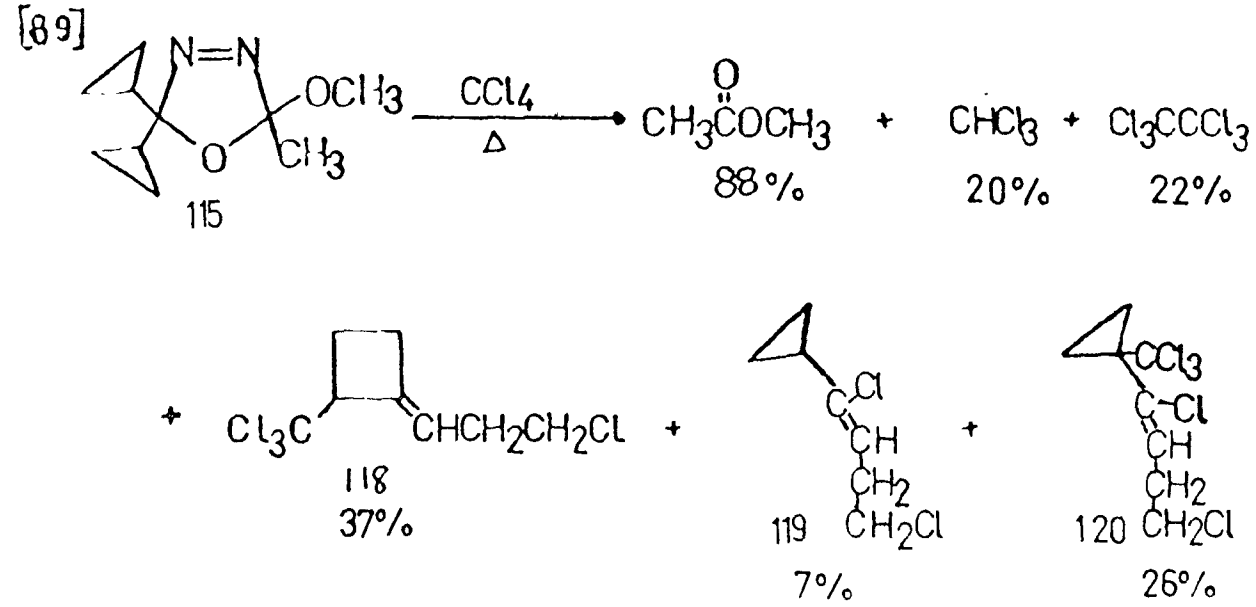
SCHEME 16

RD. 7.2. THERMOLYSIS IN CCl_4

a - IDENTIFICATION OF PRODUCTS

The main products of thermolysis of oxadiazoline 115 in CCl_4, at 79.5°C were products of fragmentation of a carbonyl ylide, eq 89.

[89]



Separation of the mixture was done by bulb to bulb distillation. The low-boiling fraction contained methyl acetate and chloroform which were identified by comparing their respective ^{1}H NMR spectra to those of authentic samples.

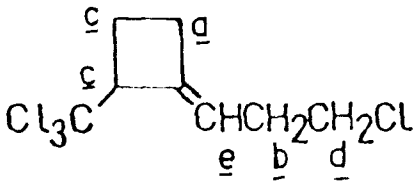
The residue consisted of four major products which were separated by GC. Their structures were deduced from their respective ^{1}H NMR and mass spectra.

(i) *MASS SPECTRUM OF CCl_3CCl_3 (117)* $Cl_3C\,CCl_3$

C_2Cl_6

Fragment$^+$	m/z (%) Theoretical ratio
C_2Cl_5	199(58), 201(97), 203(60), 205(22), 207(4) 16 . 27 : 18 : 6 . 1
C_2Cl_4	164(32), 166(39), 168(20), 170(4) 7.5 : 9 : 4.5 : 1
CCl_3	117(100), 119(98), 121(35), 123(4) 27 : 27 : 9 : 1
CCl_2	82(19), 84(12) 3 : 2

(ii) *PRODUCT* 118



^{1}H NMR ($CDCl_3$-7.27 ppm)

a - 2.50-3.10 (m,2H)

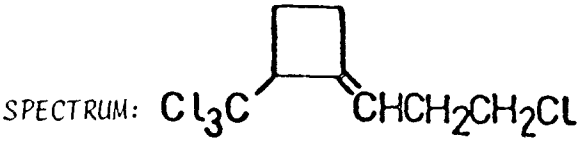
b - 2.78 (q,2H, J=8.0Hz)

c - 3.40-3.80 (m,3H)

d - 3.54 (t,2H, J=8.0Hz)

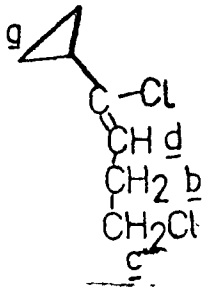
e - 5.81 (t,1H, J=8.0Hz)

Irradiation of the (e) hydrogen made the signal from (b) hydrogens a triplet. When the (b) hydrogens were irradiated the (e) and (d) signals became singlets. Finally, the irradiation of the (d) hydrogens changed the (b) signals to a doublet.

MASS SPECTRUM:  $(C_8H_{10}Cl_4)$

Fragment$^+$	m/z (%) Theoretical ratio
$C_8H_{10}Cl_4$	246(29), 248(39), 250(19), 252(4) 7 : 9 : 4.5 : 1
$C_8H_{10}Cl_3$	211(44), 213(47), 215(14), 217(2) 27 : 27 : 9 : 1
C_8HgCl_2	175(49), 177(30), 179(5) 9 : 6 : 1
C_8H_8Cl	139(100), 141(34) 3 : 1
$C_7H_8Cl_3$	197(4), 199(4), 201(1) 3 : 3 : 1
$C_7H_7Cl_2$	161(17), 163(12) 9 : 6
C_7H_6Cl	125(27), 127(9) 3 : 1

(iii) *PRODUCT 119*



^{1}H NMR ($CDCl_3$-7.27 ppm)

a - 0.60 - 1.20 (m,5H)

b - 2.65 (q,2H, J=7.0Hz)

c - 3.55 (t,2H, J=7.0Hz)

d - 5.74 (t,1H, J=7.0Hz)

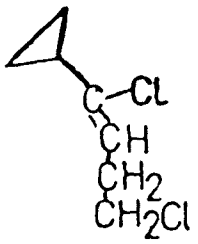
* ≡ irradiation of

b* d and c became singlets

c* b became a doublet

d* b became a triplet

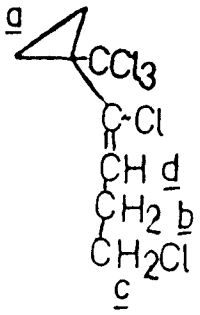
Mass spectrum:



($C_7H_{10}Cl_2$)

Fragment$^+$	m/z (%) Theoretical ration
$C_7H_{10}Cl_2$	164(19), 166(12), 168(2) 9 : 6 : 1
C_6H_8Cl	115(92), 117(30) 3 : 1
$C_7H_{10}Cl$	129(10), 131(3) 3 : 1
C_6H_7	79(100)

(iv) PRODUCT 120



^{1}H NMR ($CDCl_3$-7.27 ppm)

a - 0.95 - 1.24 (m,4H)

b - 2.52 (q,2H, J=8.0Hz)

c - 3.57 (t,2H, J=8.0Hz)

d - 5.82 (t,1H, J=8.0Hz)

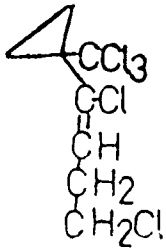
* irradiation of

*d b became a triplet

*c b became a doublet

*b d and c became singlets

Mass Spectrum:

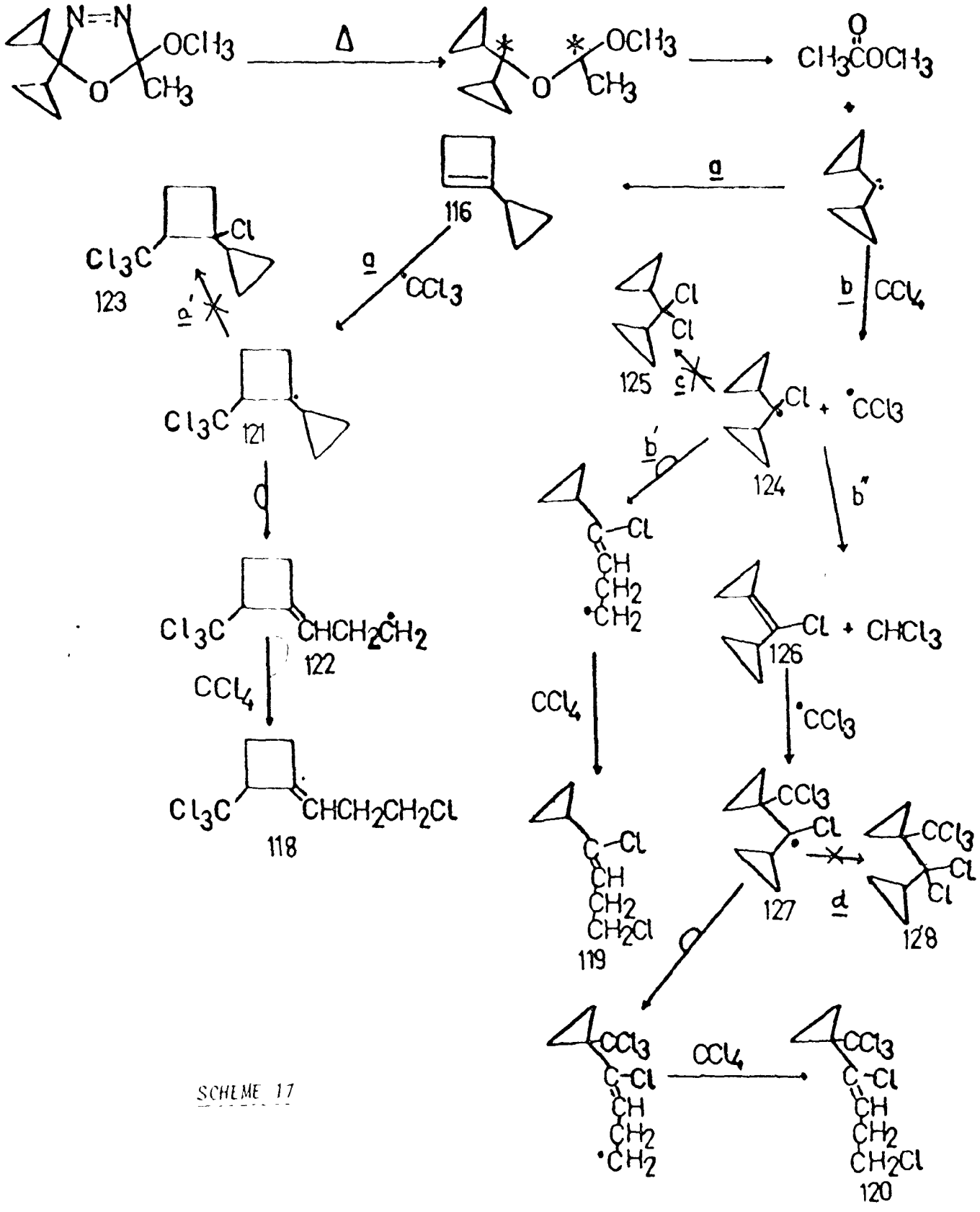


($C_8H_9Cl_5$)

Fragment$^+$	m/z (%) Theoretical ratio
$C_8H_9Cl_5$	280(49), 282(80), 284(50), 286(18), 288(3) 16 : 27 : 18 : 6 : 1
$C_8H_9Cl_4$	245(45), 247(56), 249(29), 251(6) 7.5 : 9 : 4.5 : 1
C_8H_8Cl	209(41), 211(40), 213(17), 215(2) 27 : 27 : 9 : 1
$C_8H_7Cl_2$	173(82), 175(54), 177(9) 9 : 6 : 1
C_8H_7Cl	137(27), 139(9) 3 : 1
$C_7H_7Cl_4$	231(23), 233(29), 235(15), 237(3) 7.5 : 9 : 4.5 : 1
$C_7H_6Cl_3$	195(61), 197(61), 199(21), 201(2) 27 : 27 : 9 : 1
$C_7H_5Cl_2$	159(100), 161(62), 163(10) 9 : 6 : 1

b. PROPOSED MECHANISM

Scheme 17 depicts the probable mechanism for the thermolysis of oxadiazoline 115 in CCl_4.



SCHEME 17

The mechanism as proposed, involves a fragmentation of the carbonyl ylide to give methyl acetate and dicyclopropylcarbene. The rearrangement[251] of the carbene (a) yields 1-cyclopropyl-cyclobutene (116). Addition of $\dot{C}Cl_3$ to the alkene gives radical 121 which either abstract a chlorine from CCl_4 (a') or rearranges to 122 which gives 118 by chlorine abstraction from CCl_4. The rate constant for ring opening of cyclopropylmethyl radicals () is about 10^8 sec^{-1} at 25°C.[253] The rate constant for abstraction from CCl_4 is about 0.5×10^5 $M^{-1}sec^{-1}$ and $2.0 \times 10^1 M^{-1}sec^{-1}$ for t-butyl radicals and methyl radicals respectively (27°C)[254]. These numbers make it possible to predict the ratio of concentrations of 122 to 123. Therefore, it is not surprising to find that only

$$\frac{[122]}{[123]} = \frac{10^8[R\cdot]}{0.5 \times 10^5[R\cdot][CCl_4]} \simeq \frac{10^8}{0.5 \times 10^5[10M]} \simeq 2 \times 10^2$$

122 is produced in the reaction. Dicyclopropyl carbene can abstract a chlorine (b) from CCl_4 to give 124 which rearranges prior to the abstraction of another chlorine (from CCl_4) to give 119. Trichloromethyl radicals can first abstract a hydrogen from 124 to give chloroform and olefin 126, then add to 126 to give 127. Radical 127 rearranges prior to reacting with the solvent to give 120. Using the same argument, as for path a', paths c and d which lead to 125 and 128 respectively, are ruled out. Finally, hexachloroethane is generated from the coupling of trichloromethyl radicals.

Oxadiazoline 115, upon thermolysis, gives rise to a carbonyl ylide which, unlike ylide 87a, fragments mostly in one direction to give methylacetate and dicyclopropyl carbene. Changing the substituents at C_5 from methyl to cyclopropyl appears to have selectively changed the fragmentation pattern of the ylide, making ester formation, in this case, the major pathway (90%).

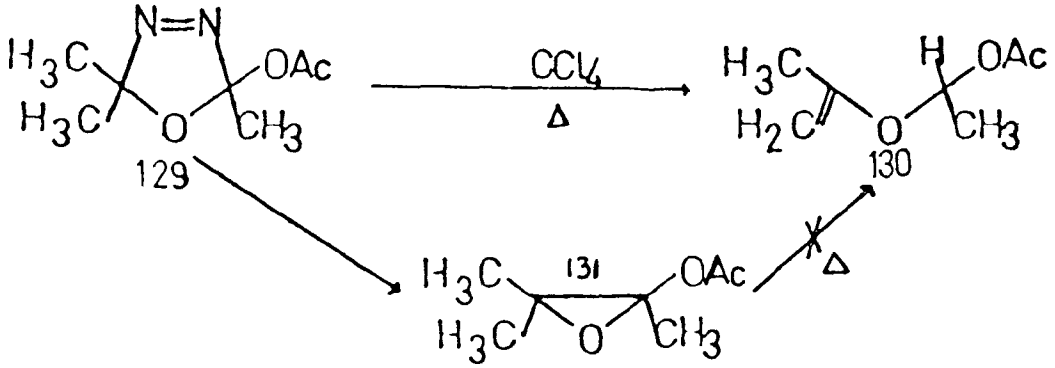
As outlined from the work done by Roth[49,50] (p 10), chlorine abstraction is a fast reaction of singlet carbenes. When generated in its triplet ground state, in CCl_4, carbomethoxy carbene ($:CHCOOCH_3$) reacted with the solvent in its singlet state.[255] It should be safe to assume that dicyclopropyl carbene which is generated in its singlet state, from the fragmentation of the carbonyl ylide, abstracts a chlorine as a singlet. Furthermore, because chloroform, 119, and 120 are formed from the thermolysis, the carbene cannot be inserting, in a concerted way into the C-Cl bond of CCl_4 This insertion would have given 1,1,1,2-tetrachloro-2,2-dicyclopropylethane which was not found.

RD. 8. INTRAMOLECULAR 1,4-HYDROGEN SHIFT

The carbonyl ylide generated from the thermolysis of oxadiazoline 87 gives, in various solvents, around 20% of enol ether 98, derived from a 1,4-hydrogen shift in the ylide.

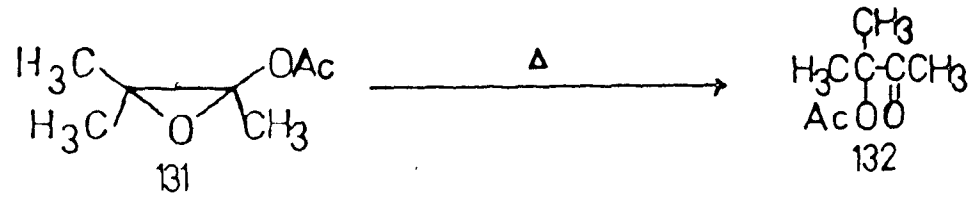
Thermolysis[183,184] of acetoxyoxadiazoline 129, in CCl_4, gave 1-acetoxyethyl-2-propenyl ether 130 (>90%), equ. 90.

[90]



The production of the enol-ether (130) from a thermal opening of 131 was ruled out by the finding that, when thermolyzed, epoxide 131 gives ketone 132, equ. 91.

[91]



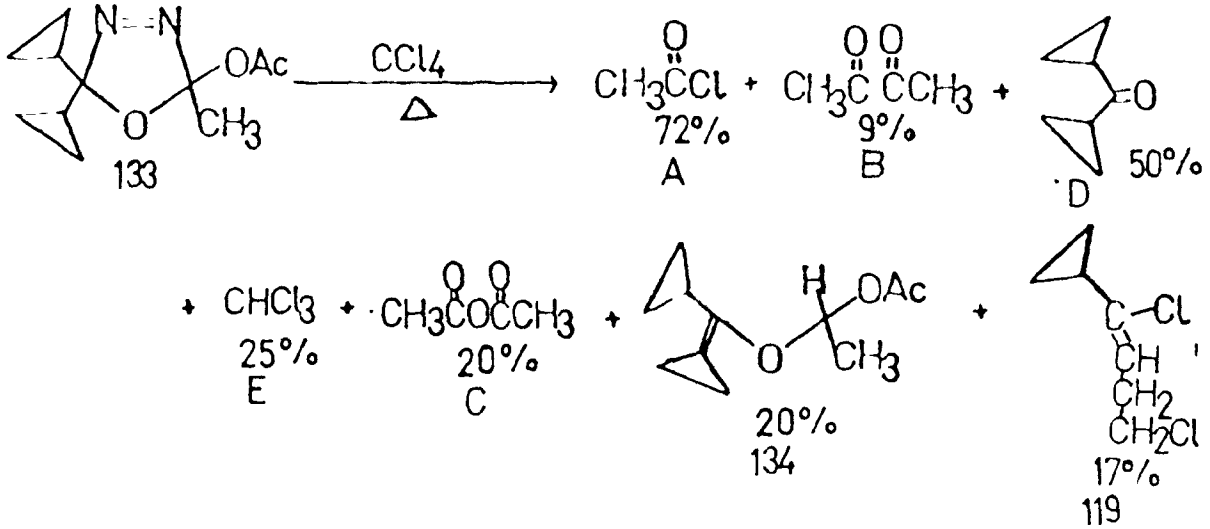
131 132

By changing the substituents at C_5 from CH_3 to cyclopropyl it would be expected that the 1,4-hydrogen shift would be less favoured, because of the strain involved in making a cyclopropylidene.

RD. 8.1. *THERMOLYSIS OF OXADIAZOLINE 133*

2-Acetoxy-5,5-dicyclopropyl-2-methyl-Δ^3-1,3,4-oxadiazoline (133) thermolyzed in CCl_4, at 79.5°C, with first order kinetics ($k = 8.0 \times 10^{-5} sec^{-1}$, C.C. = 0.9993, t 1/2 = 144 min). The main products of the reaction are shown in eq. 92.

[92]



Infrared spectra of authentic A through D were obtained (CCl_4 solutions). The carbonyl stretching frequencies were found to be: cm^{-1} 1812(A), 1724(B), 1838 and 1770(C), and 1693(D). The IR spectrum of the volatile fraction of the reaction products showed five carbonyl absorptions at cm^{-1}: 1838, 1812, 1724, and 1693. Authentic samples were added one at a time to the volatile fraction and each IR spectrum showed an increase in intensity of the corresponding carbonyl band.

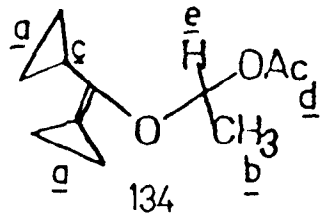
When injected through a GC column, the products in the volatile fraction had the same retention times as those of authentic samples.

TABLE RD. 6. SPECTRAL DATA OF THE VOLATILE PRODUCTS FROM THE THERMOLYSIS OF 129 IN CCl_4

Sample	Yield %	^{1}H NMR	^{1}H NMR*
CH_3CCl (O)	72	2.67	2.64
CH_3CCCH_3 (O,O)	9	2.27	2.27
CH_3COCCH_3 (O,O)	22	2.17	2.17
	50	0.70-1.03(m,8H) 1.70-2.10(m,2H)	0.70-1.06(m,8H) 1.73-2.10(m,2H)
$CHCl_3$	25	7.30	7.30

*Authentic samples

The second volatile fraction contained a product the structure of which was deduced to be 134. The model compound for 134 was enol-ether 130[183].



'H NMR ($CDCl_3$-7.27 ppm)

a - 0.83-1.35 (m,8H)

b - 1.43 (d,3H, J=6.0Hz)

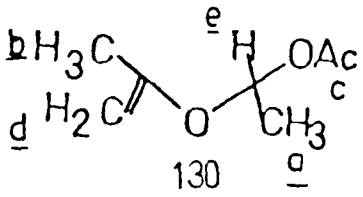
c - 1.88-2.25 (m,1H)

d - 2.03 (s,3H)

e - 6.71 (q,1H, J=6.0Hz)

IR (C=O)cm^{-1} $CDCl_3$ solution. 1742?

Mass spec m/z 196 (M^+)



'H NMR ($CDCl_4$/TMS)

a - 1.50 (d,3H, J=6.0Hz)

b - 1.85 (d,3H, J=1.0Hz)

c - 2.08 (s,3H)

d - 4.05 (m,2H, J_1=4.0Hz, J_2=1.0Hz)

e - 6.40 (q,1H, J=6.0Hz)

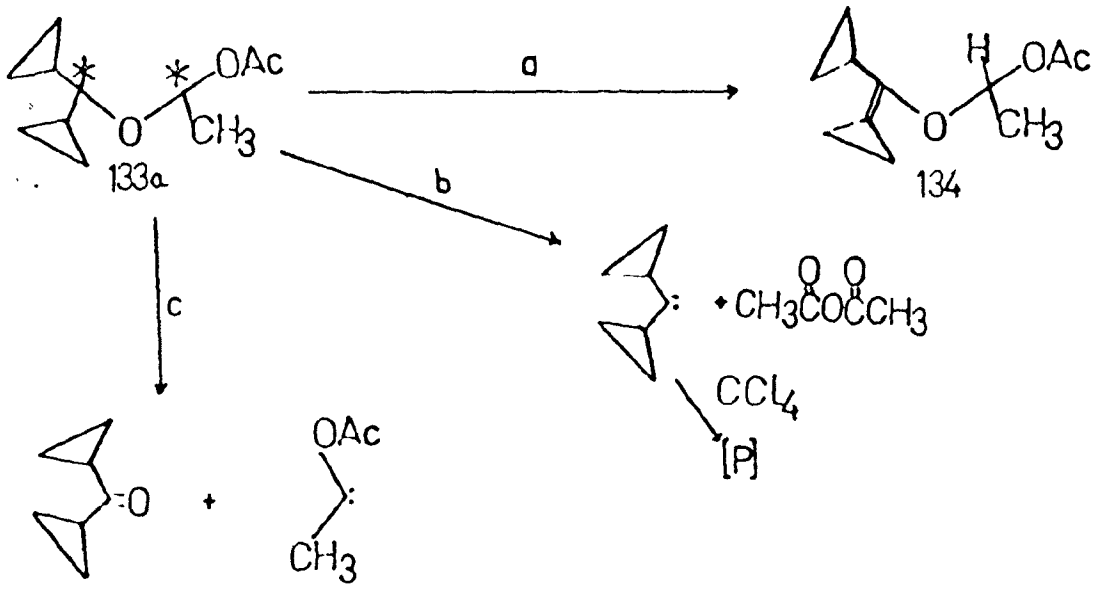
Irradiation of the protons at δ 1.43 in 134 collapsed the quartet at δ 6.71 to a singlet and irradiation at δ 6.71 turned the doublet at δ 1.43 into a singlet.

Finally, the residue contained product 119.(p 107)

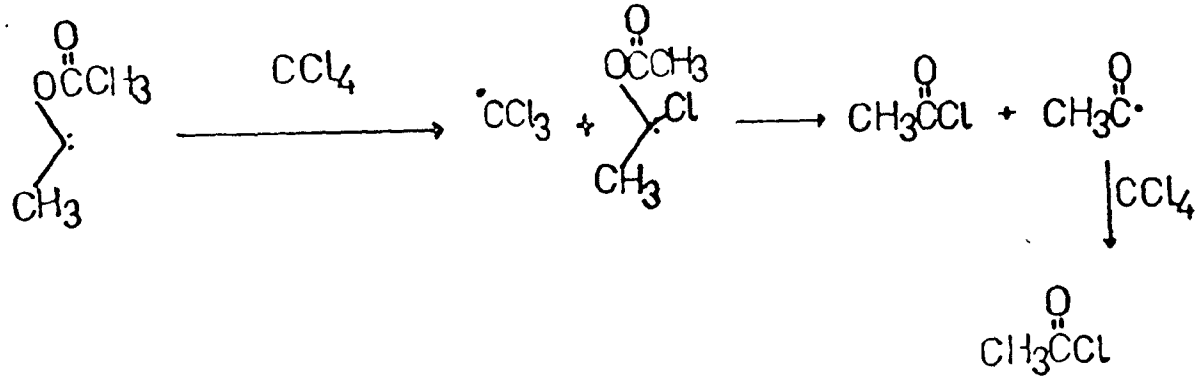
RD. 8.2 *PROPOSED MECHANISM*

Scheme 18 depicts the probable mechanism of the fragmentation of carbonyl ylide 133a.

Acetoxyoxadiazoline 133 (p 10) gives rise, upon thermolysis, to carbonyl ylide 133a. The ylide can undergo an intramolecular 1,4-hydrogen shift to give 134 (path a). Fragmentation of the ylide gives acetic anhydride and dicyclopropylcarbene (path b), and dicyclopropyl ketone and acetoxymethyl carbene (path c). Acyloxy carbenes are known[256-258] to rearrange to 1,2-diketones, which explains the production of biacetyl. Acyloxycarbene 135 can also react instead with CCl_4 as shown by the following scheme (19).

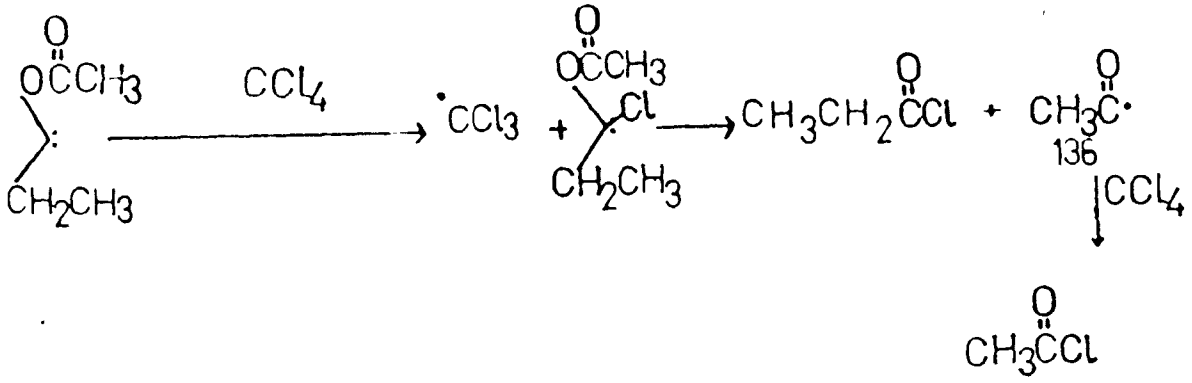


SCHEME 18



SCHEME 19

In order to check this proposal, 2-acetoxy-5,5-dicyclopropyl-2-ethyl-Δ^3-1,3,4-oxadiazoline was thermolyzed at 79.5°C, in CCl_4 and the volatile fraction was analyzed. The ^1H NMR spectrum showed a quartet centered at δ 2.92, a singlet at δ 2.67 and a triplet centered at δ 1.23. The ^1H NMR spectrum of a mixture of authentic acetyl and propionyl chloride showed a singlet at δ 1.23, a quartet and a triplet centered respectively at δ 2.96 and 1.23. When injected through a GC column, the products of the reaction had the same retention times as those of authentic acetyl and propionyl chlorides. The FT-IR (vapour phase) spectra of the products and those of authentic samples were identical (C=O, cm^{-1} 1801 and 1805 respectively).



SCHEME 20

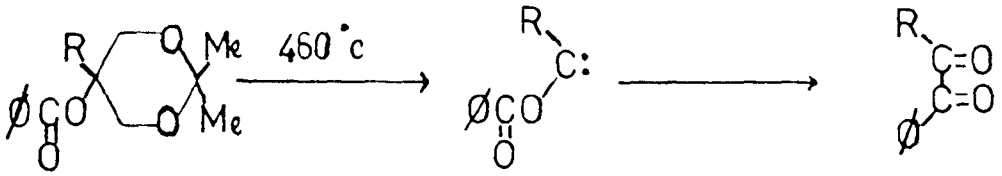
This result confirmed the proposed scheme (19) which involves a chlorine abstraction by the carbene, followed by a radical fragmentation which gives acetyl chloride and acyl radical 136. The radical then can abstract a chlorine from CCl_4 to give another mole of acetyl chloride.

Changing the substituents at C_5 from methyl to cyclopropyl caused the new carbonyl ylide to behave differently than the one generated from 129. Thermolylis of 133 gave 20% 1,4-hydrogen shift product instead of 90% for 129 because cyclopropyl hydrogen abstraction would increase an already large angle strain.

Oxadiazoline 133 is a precursor of an acyloxy carbene. These carbenes are very little known[256,257] and being able to generate them, under mild conditions, would be a nice way to study them and elucidate their chemistry.

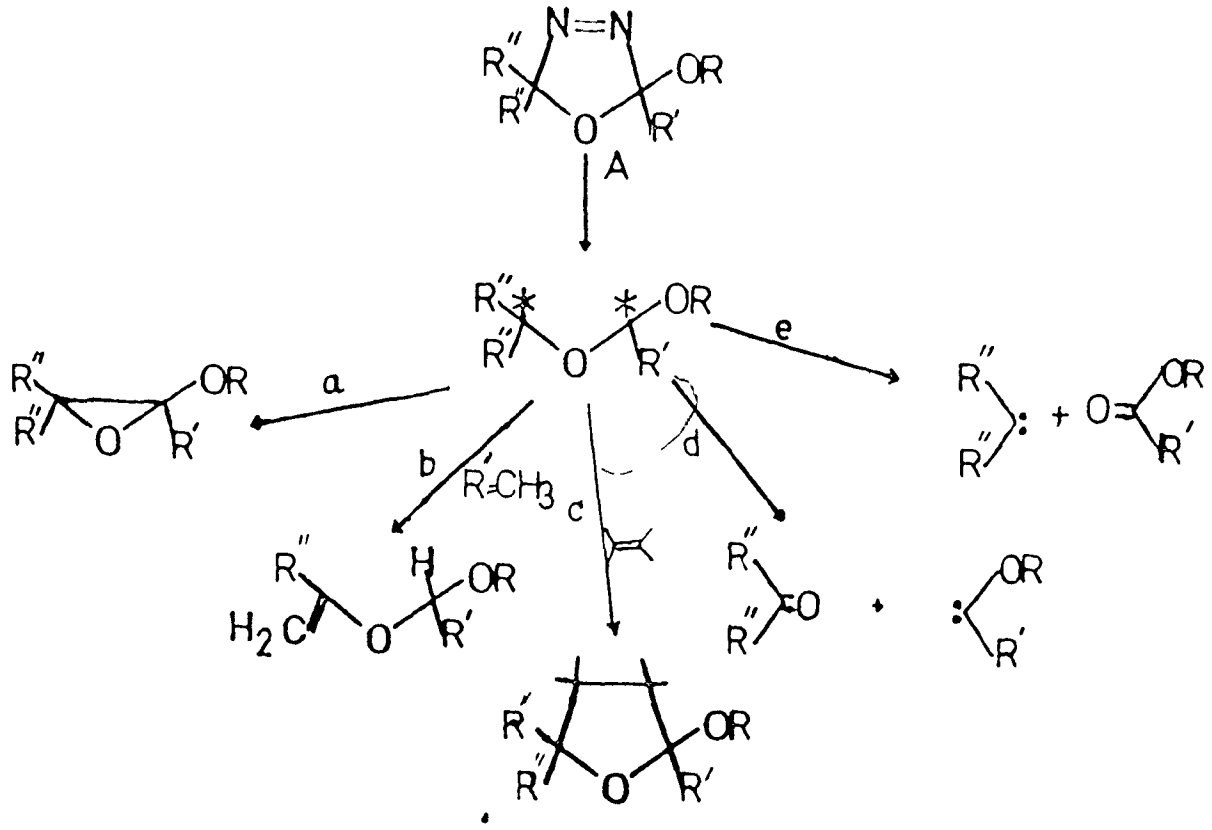
R.F.C. Brown et. al.,[256,257] proposed the intermediacy of acyloxy carbenes to explain the formation of 1,2-diketones, eq 93. They did not observe any direct reaction of the carbenes, namely, addition to double bonds, dimerization, or

[93]



insertion into C-H bonds. They assumed that the rearrangement involves a carbene rather than some earlier transient species.[256,257] Thermolysis of oxadiazoline 133 gives rise to acetoxymethyl carbene which rearranges to biacetyl. Unlike the thermolysis of 138, the reaction of 133 is in the liquid phase which explains the lower yield of rearrangement product. Furthermore, the production of acetyl chloride and propionyl chloride from the thermolysis of 2-acetoxy-5,5-dicyclopropyl-2-ethyl-Δ^3-1,3,4-oxadiazoline in CCl_4 can hardly be explained without involving a carbene intermediate.

RD. 9. SUMMARY



Upon thermolysis, oxadiazolines of type A lose nitrogen in a concerted process. The carbonyl ylide generated in the process can, depending on the substituent, cyclize to give an epoxide (R'=p-$OCH_3C_6H_4$), undergo a 1,4-hydrogen shift (R'=R''=CH_3, R=$\overset{O}{\overset{\|}{C}}CH_3$), be intercepted by a dipolarophile, and fragment into carbenes and carbonyl compounds.

The fragmentation can occur in two directions (d and e). By making R'' = cyclopropyl, fragmentation via path d was favoured to over 90%.

In the case of acetoxyoxadiazolines, with R''=cyclopropyl, the 1,4-hydrogen shift was reduced to 20% (as compared to 90% with R''=CH_3), thus giving rise to a practically unknown new type of carbenes: acyloxy carbenes.

Because of the source of the carbenes,(fragmentation of a carbonyl ylide), there is no confusion about their identity. They must be free carbenes, not carbenoids. The acetone-d_6 reaction confirmed that free carbenes add to ketones to form carbonyl ylides.

Finally, singlet carbenes do not insert into C-Cl bonds but they abstract a chlorine, as a first step, to generate a pair of radicals from which the final products are formed.

EXPERIMENTAL

E.1 INSTRUMENTAL

The spectrometers used to record proton magnetic resonance (pmr) spectra were Varian's T-60 and EM-390, and Bruker's WP-80 and WM-400. Tetramethylsilane (TMS) was used as an internal standard unless otherwise specified. Carbon-13 spectra were taken on a Bruker WP-80 instrument, and internal standards are specified in each case. Deuterium spectra were recorded on a Bruker WM-400 instrument with acetone-d6 as internal reference. Fluorene spectra were taken on a Bruker WH-90 instrument with $CFCl_3$ as internal reference. The chemical shifts are reported in δ values (ppm), followed in brackets by the multiplicity symbol (s = singlet, d = doublet, t = triplet, q = quartet, se = septet, m = multiplet), the relative proton integral, and the coupling constant when appropriate.

Infrared (IR) spectra (CCl_4 solutions unless otherwise specified) were obtained on a Perkin-Elmer model 283 spectrophotometer, using 0.1 mm NaCl cells. Only the major bands (transmittance) are reported.

Gas phase FT-IR spectra were obtained from a Nicolet, model 799, Fourier transform infrared spectrophotometer equipped with a Varian Aerograph model 920 gas chromatograph, with a thermal conductivity detector and model 485 integrator. Preparative gas chromatography (GC) was performed on a Varian Aerograph model A90-P3 instrument.

Mass spectra (MS) were recorded on a VG 7070 mass spectrometer (VG Micromass, Altrincham, UK.). Samples were introduced via a direct insertion probe system or through a Varian Aerograph model 920 GC via a jet separator. The spectra were acquired and processed with the VG 2035 data system.

Melting points were determined on a Thomas Hoover capillary melting point apparatus, and are not corrected.

The laser flash photolysis experiments were conducted by Dr. J.C. Scaiano at NRC, Ottawa. The equipment and the experimental procedures have been discussed elsewhere.[259] Briefly, light pulses (8 ns, 338.1 nm, 1-10 mJ) were obtained from a Molectron UV-24 nitrogen laser and were used to photolyze the sample. Transient intermediates were detected using a sample monitoring system capable of micro - to nanosecond time resolution.[260] All of the laser flash photolysis experiments were carried out using deoxygenated solutions.

The direct current (DC) source used in the electrochemical oxidation of hydrazones was a Fisher, model 40, controlled-potential electroanalyzer. Voltages from 0 - 10 volts can be provided. Controlled potential oxidations can be performed up to 3 volts. The electrochemical cell was a screw cap bottle (500 ml) fitted with two platinum electrodes (fig. E1). The reaction vessel was mounted on a "Thermoelectrics" stirrer-cooler unit, model SK.12.

Bulb to bulb distillations were performed using a "T" joint attached to the vacuum line, a round-bottomed flask and a receiver tube (fig. E2).

The purity of the oxadiazolines was checked by spotting the compounds on thin layer plates (basic alumina) and eluting with three or more different solvents.

Yields of products of thermolysis of oxadiadiazolines were calculated from pmr peak heights and from GC peaks, by the cut and weigh method, or from pmr integrals.

In all kinetic runs where CCl_4 was used as solvent it was washed with $NaHCO_3$ solution and dried over Na_2CO_3 prior to use

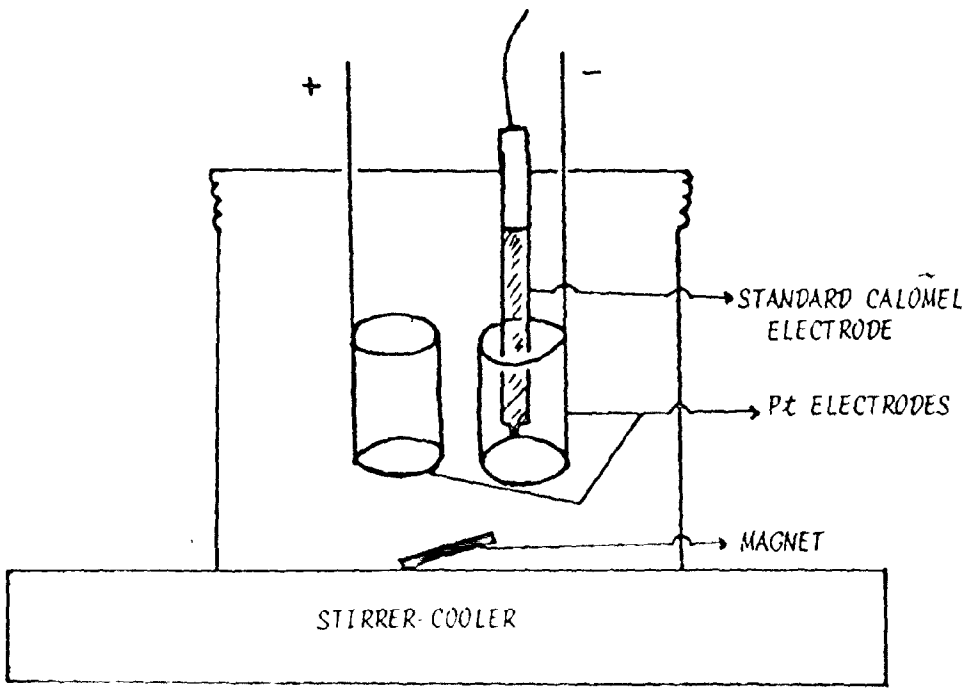


FIG E.1 ELECTROCHEMICAL CELL

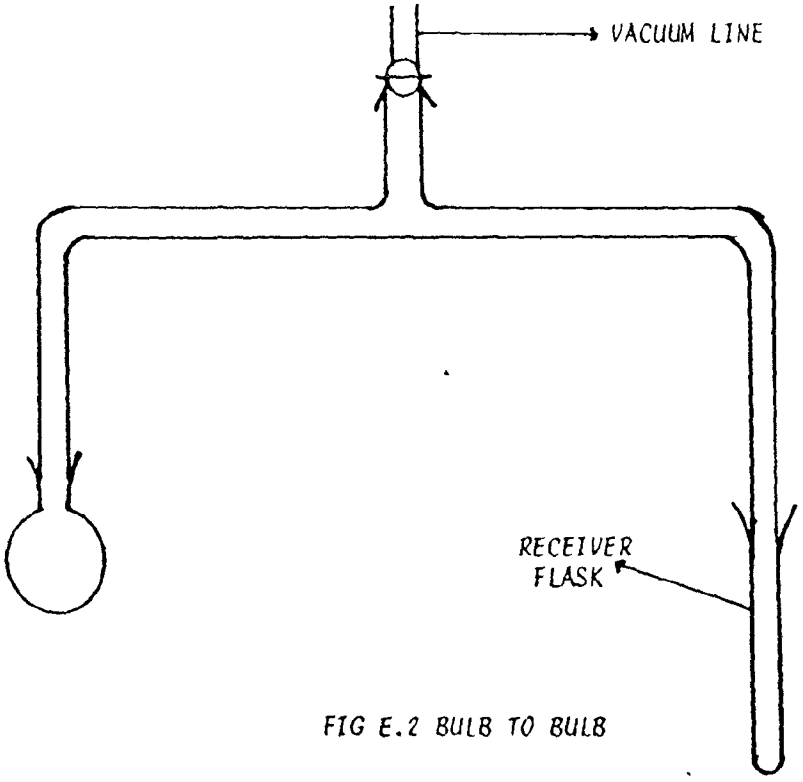


FIG E.2 BULB TO BULB

The chemicals used came from Aldrich, J.T. Baker, Matheson, Fisher, or BDH unless otherwise indicated. Chemicals were purified prior to use, wherever appropriate

E.2 SYNTHESIS

1. SYNTHESIS OF LEAD TETRAACETATE (L.T.A.)

The method used was that of Fieser.[261] Acetic acid (1200 ml) and acetic anhydride (800 ml) were mixed in a three litre, three-necked, round-bottomed flask, fitted with a mechanical stirrer and a thermometer. The mixture was heated to 55°C and stirred vigorously. Red lead oxide (1400 g) was added in portions of 15-20 g over a period of five hours. A fresh addition was made only after the orange colour due to the preceding portion had almost disappeared. The temperature was maintained between 55° and 60°C. At the end of the additions, the reaction mixture was cooled to room temperature and the thick slurry was filtered, washed with cold acetic acid, and recrystallized from hot acetic acid (700 g, 77% yield). Lead tetraacetate was stored in a nitrogen-filled glove bag.

2. SYNTHESIS OF HYDRAZONES ($RCNHN{=}C\begin{matrix}R''\\R''\end{matrix}$, O)

a. ACETONE-N-ACETYL HYDRAZONE

The procedure of Allen and Bell[262] was followed, except for minor modifications. Hydrazine hydrate (100 g, 99%), was added to a solution of ethyl-acetate (150 ml) in ethanol (150 ml, 95%) in a three-necked, round-bottomed flask. The mixture was refluxed for 48 hours, after which ethanol was evaporated with a rotatory evaporator leaving behind the hydrazide and residual hydrazine. The hydrazide was recovered from vacuum distillation (10 Torr, fraction

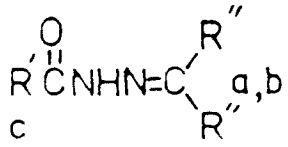
collected between 120° and 130°C), while heating the condensor with steam, to prevent solidification of the product. Recrystallization from ethanol gave acethydrazide of satisfactory purity; m.p.: 65° - 66°C (lit.[263]: 66° - 67°C, 108 g, 75% yield); ^{1}H NMR ($CDCl_3$ solution), δ1 90(S); IR($CDCl_3$ solution): 3452, 3328, 3200, 1679, 1632, 1370, 1000.

The hydrazide (36 g, 0.48 mole) was dissolved in acetone (80 ml), and the solution was left stirring for two hours. Removal of the unreacted ketone with a rotatory evaporator afforded crude acetone-N-acetyl hydrazone, which was then recrystallized from ethanol, (51 g, 93% yield). Spectral data are reported in Table E1

b SYNTHESIS OF OTHER HYDRAZONES

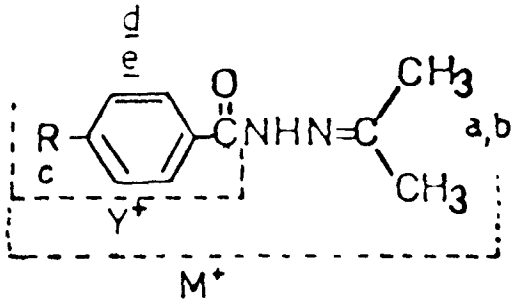
Dicyclopropylketone-N-acetyl hydrazone (R'=CH_3, R''=cyclopropyl) and dicyclopropyl ketone-N-propionyl hydrazone (R'=CH_3CH_2, R''=cyclopropyl) were synthesized by the same procedure as in (a). Recrystallization of the crude products from ethanol-water gave materials with the spectral data listed in Table E1.

The reaction of p-substituted methyl benzoates with hydrazine hydrate afforded the corresponding p-substituted benzoyl hydrazides. The addition of acetone to the hydrazides gave the corresponding acetone-N-(p-substituted) benzoyl hydrazones, which were recrystallized from ethanol. The synthetic procedure described in (a) was followed except for the purification of the hydrazide. Excess hydrazine and ethanol were removed by distillation and acetone was added to the crude solid left behind. Spectral data of benzoyl hydrazones are listed in Table E2.



SAMPLE	YIELD %	M.P. °C (lit.)	^{1}H NMR $CDCl_3$-T.M.S. J(Hz)	IR cm^{-1}	ANALYSIS
R'=R''=CH_3	93	139-140 (139-140)[264]	a=1.87(s,3H) b=1.97(s,3H) c=2.20(s,3H)	3200,3091,2948 1687,1400,1369 1340,1250,1134 1042,1011, 865	-
R'=CH_3 R''=cyclopropyl	82	114-115	a=.50-1.00(m,8H) b=1.13-1.60(m,2H) c=2.20(s,3H)	3362,3020,1670 1448,1376,1330 1250,1225,1176 1038,1024	$C_9H_{14}N_2O$ calculated / found C:65.03 / 65.00 H: 8.50 / 8.39 N·16.85 / 16.98
R'=CH_3CH_2 a' R''=cyclopropyl	74	109-110	a=0.36-0.97(m,8H) a'=0.93(t,3H,J=7.5) b=1.15-1.63(m,2H) c=2.48(q,2H,J=7.5)	3360,3020,2988 2950,1677,1436 1378,1270,1220 1072,1028, 909	-

TABLE E.1 ACYL HYDRAZONES OF KETONES

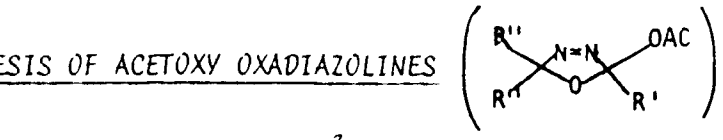


R MW	YIELD %	M.P. °C (lit)	M.S. m/z	^{1}H NMR (PPM) $CHCl_3$-T.M.S. J(Hz)	IR cm^{-1}	ANALYSIS
H 176	85	143-144 (145)[265]	176 M^+ 105 Y^+	a=1.97(s,3H) b=2.08(s,3H) c,d,e=7.30-7.96(m,5H)	3410,3358,3072,3004 2925,1688,1608,1510 1410,1372,1280,1263 1145,1076, 912	-
OCH_3 206	78	135-136	206 M^+ 135 Y^+	a=1.93(s,3H) b=2.03(s,3H) c=3.77(s,3H) d=6.83(d,2H,J=9.0) e=7.73(d,2H,J=9 0)	3408,3358,2998,2850 1684,1615,1499,1445 1370,1254,1148,1032 911, 842	$C_{11}H_{14}N_2O_2$ calculated / found C 64.06 / 63.91 H. 6.84 / 6.76 N:13.58 / 13.29
CH_3 190	80	138-139	190 M^+ 119 Y^+	a=1.93(s,3H) b=2.06(s,3H) c=2.50(s,3H) d=7.08(d,2H,J=8.0) e=7.58(d,2H,J=8.0)	3405,3360,3002,2930 1686,1618,1520,1430 1372,1254,1145,1044 913, 830	$C_{11}H_{14}N_2O$ calculated / found C:69.45 / 69.56 H: 7.42 / 7.44 N:14.72 / 14.88

..... continued

R MW	YIELD %	M.P. °C (lit)	M.S. m/z	^{1}H NMR (PPM) $CHCl_3$=T.M.S. J(Hz)	IR cm^{-1}	ANALYSIS
Cl 210	74	186-187 (188)[266]	210 M^+ 139 Y^+	a=1.95(s,3H) b=2.04(s,3H) d=7.34(d,2H,J=9.0) e=7.72(d,2H,J=9.0)	3045,3358,3000,2922 1692,1602,1512,1485 1431,1372,1292,1276 1145,1039, 909, 845	-
CF_3 244	87	191-192	244 M^+ 173 Y^+	a=1.96(s,3H) b=2.10(s,3H) d=7.66(d,2H,J=8.5) e=7.96(d,2H,J=8.5) ^{19}F NMR:64.66(s)	3405,3359,3010,1698 1683,1652,1626,1587 1520,1502,1430,1374 1330,1279,1262,1174 1135,1118,1099,1070	$C_{11}H_{13}FN_2O$ calculated / found C:54.11 / 54.16 H: 4.54 / 4.60 N:11.47 / 11.75 F:23.34 / 23.57
NO_2 221	54	162-163 (165)[267]	221 M^+ 150 Y^+	a=2.07(s,3H) b=2.17(bs,3H) d=7.99(d,2H,J=9.0) e=8.29(d,2H,J=9.0)	3412,3350,3000,1694 1608,1530,1352,1204 1050, 869, 856	-

TABLE E.3 ACETOXY OXADIAZOLINES

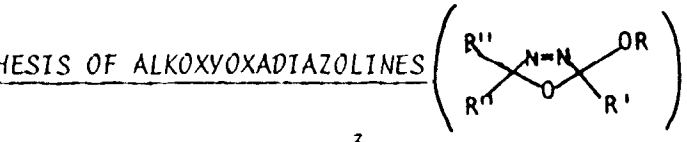
3. SYNTHESIS OF ACETOXY OXADIAZOLINES 

a. 2-ACETOXY-2,5,5-TRIMETHYL-Δ^3-1,3,4-OXADIAZOLINE (R=R'=CH_3)

Acetone-N-acetyl hydrazone (11.4 g, 0.10 mole) was dissolved in a solution of L.T.A. (50.0 g, 0.11 mole) in CH_2Cl_2 (100 ml). The solution was left stirring at 0°C until the colour generated by the compounds upon dissolving in dichlomethane, was discharged. The solution was then filtered by suction through a bed of Celite, and the solvent was evaporated with a rotatory evaporator. The remaining liquid was mixed with 5% $NaHCO_3$ and the aqueous solution was extracted with CH_2Cl_2. The organic fraction was dried over $CaCl_2$, and evaporation of the solvent, with a rotatory evaporator, afforded the crude oxadiazoline, which was purified by bulb to bulb distillation (10^{-2} Torr, room temperature, 14.0 g, 85% yield). Spectral data are listed in table E3.

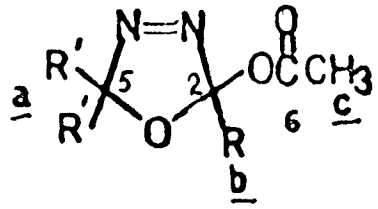
b. OTHER OXADIAZOLINES

2-Acetoxy-5,5-dicyclopropyl-2-methyl and 2-acetoxy-5,5-dicyclopropyl-2-ethyl-Δ^3-1,3,4-oxadiazolines were synthesized from the corresponding hydrazones and were purified by the procedure described above. Spectral data are shown in Table E3.

4. SYNTHESIS OF ALKOXYOXADIAZOLINES 

a. 2-METHOXY-2,5,5-TRIMETHYL-Δ^3-1,3,4-OXADIAZOLINE

Lead tetraacetate (44.3 g, 0.10 mole) was dissolved in absolute methanol (300 ml), giving a yellow solution. Acetone-N-acetylhydrazone (11.4 g, 0.10 mole) was added to the stirred solution and the temperature was maintained at 0°C. The discharge of the colour was taken as evidence for the completion of



SAMPLE	YIELD %	^{1}H NMR ppm, J(Hz)	^{13}C NMR (PPM) $CDCl_3$, -20°C	IR cm^{-1}
$R=CH_3$ $R'=CH_3$	85	a=1.60(s,6H) b=1.92(s,3H) c=2.11(s,3H)	22.17 22.96 24.56 24.87 124.26(C_5) 129.74(C_2) 168.55(C_6)	2995,2940,1760,1460 1385,1370,1225,1130 1110,1010, 985, 920
$R=CH_3$ R'=cyclopropyl	85	a=0.30-1.60(m,10H) b=1.93(s,3H) c=2.03(s,3H)	1.34 1.56 2.08 16.25 22.10 128.21(C_5) 129.74(C_2) 168.33(C_6)	3104,3012,2952,1768 1445,1403,1370,1209 1115,1052,1010, 942 930
a' $R=CH_2CH_3$ R'=chclopropyl	80	a=0.30-1.53(m,10H) a'=1.04(t,3H,J=7.5) c=2.01(s,3H) b=2.40(q,2H,J=7.5)	1.56 1.78 2.00 16.33 22.03 27.94 127.91(C_5) 131.86(C_2) 168.25(C_6)	3105,3012,2952,1768 1465,1405,1370,1205 1112,1068,1010, 918

TABLE E.3 ACETOXY OXADIAZOLINES

the oxidation. At the end of the reaction, KOH pellets (10.0 g) were added to the mixture to hydrolyse the acetoxyoxadiazoline biproduct, and the solution was left stirring for 2 hours at 0°C. The solvent was then evaporated with a rotatory evaporator and water was added. The aqueous solution was extracted with CH_2Cl_2. The organic layer was washed with water several times, and dried over $CaCl_2$. Evaporation of the solvent followed by bulb to bulb distillation (10^{-2} Torr, room temperature) afforded pure methoxyoxadiazoline (8.5 g, 60% yield). Mass spec. Cl/NH_3 162 (M^+). Other spectral data can be found in Table E4.

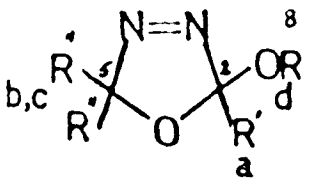
b. *OTHER OXADIAZOLINES*

2-Methoxy-5,5 dicyclopropyl-2-methyl-Δ^3-1,3,4-oxadiazoline (R=R'=CH_3, R''=cyclopropyl), was prepared and purified by the procedure described above. Spectral data are found in Table E4.

2-t-Butoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline (R=t-butyl, R'=R''=CH_3) was synthesized and purified by the same procedures in t-butanol. Spectral data are found in Table E4.

2-Methoxy-2-p-substituted phenyl-Δ^3-1,3,4-oxadiazolines (R=R''=CH_3, R'= (p-X-C_6H_4)) were also synthesized by the method described above. The crude products were purified using a cooled (water)column, packed with basic alumina, which was eluted with a 5% ether in hexane solution. The oxadiazolines eluted first.

In the case of 2-methoxy-2-p-nitrophenyl-Δ^3-1,3,4-oxadiazoline, evaporation of the dichloromethane extract afforded a yellow solid, which was washed with petroleum ether and stored in the freezer.



SAMPLE	YIELD %	^{1}H NMR ppm, J(Hz)	^{13}C NMR(PPM) $CDCl_3$-T.M.S. J(Hz), -20°C	IR cm^{-1}
$R=R'=R''=CH_3$	60	a=1.43(s,3H) b=1.55(s,6H) d=3.06(s,3H)	23.42 24.05 25.17 50.41(C_8) 119.92(C_5) 133.73(C_2)	2918,2892,2837,1558 1459,1370,1192,1116 1050, 990, 890, 850 598, 550
$R=CH_2CH_3$ a' $R'=R''=CH_3$	87	a'=1.15(t,3H,J=7.0) a=1.42(s,3H) b=1.54(s,6H) d=3.19(q,2H,J=7.0)	15.08 24.22 25.31 58.86(C_8) 119.82(C_5) 133.47(C_2)	-
$R=(CH_3)_3C$ $R'=R''=CH_3$	55	d=1.29(s,9H) a=1.42(s,3H) b=1.53(s,3H) c=1.62(s,3H)	24.92 25.14 25.58 30.84 77.20(C_8) 120.26(C_5) 132.48(C_2)	2998,2990,2940,1458 1380,1200,1172,1149 1009, 985, 899, 884
$R=R'=CH_3$ R''=cyclopropyl	71	b,c=0.17-1.47(m,10H) a=1.60(s,3H) d=3.27(s,3H)	1.13 1.34 2.37 16.47 55.96(C_8) 124.33(C_5) 132.23(C_2)	3098,3020,2950,2839 1468,1379,1200,1170 1156,1057,1049, 888 850

TABLE E.4 ALKYL-ALKOXY OXADIAZOLINES

All spectral data of the p-substituted phenyl oxadiazolines are found in Tables E5 and E6.

5. *ELECTROCHEMICAL OXIDATION OF HYDRAZONES*

a. *SYNTHESIS OF OXADIAZOLINES*

$R=CH_3$

Acetone-N-acetyl hydrazone (11.4 g, 0.10 mole) was dissolved in methanol (300 ml). Ammonium perchlorate (5.0 g) was added to the solution, which was electrolyzed for 7 days at a constant anode potential of 1.0 volt against a standard calomel electrode. The temperature was maintained between 5° and 10°C. At the end of the electrolysis period the solvent was evaporated. Carbon tetrachloride (10 ml), which only dissolves the oxadiazoline, was added to the residue, and the mixture was filtered. Evaporation of CCl_4 afforded the oxadiazoline which was purified by bulb to bulb distillation (10^{-2} Torr, room temperature, 7.5 g, 90% yield based on 60% conversion).

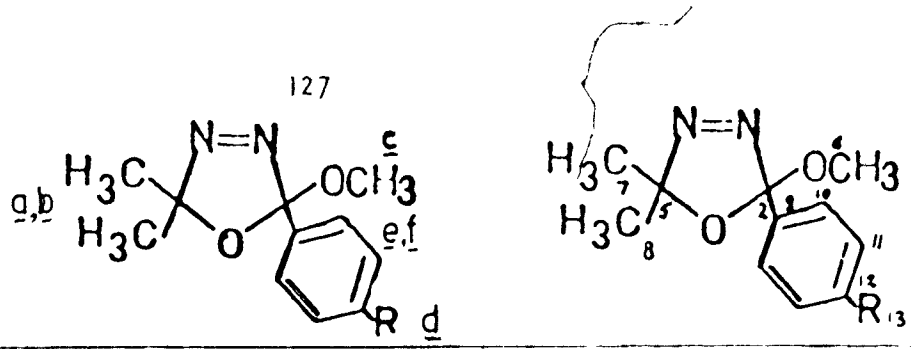
Chloroform (20 ml), which dissolves the hydrazone, was added to the solid from the filtration. The mixture was filtered and chloroform was evaporated on a rotatory evaporator, leaving behind crude unreacted hydrazone (4.5 g, 40%). Spectral data are found in Table E4.

$R=CH_2CH_3$

The analogous procedure was followed, but with ethanol solvent instead of methanol. The ethoxyoxadiazoline was purified by bulb to bulb distillation (10^{-2} Torr, 87% yield, 55% conversion). Spectral data are found in Table E4.

b. *SYNTHESIS OF METHYLPHENYLAZODIPHENYLMETHYL ETHER*

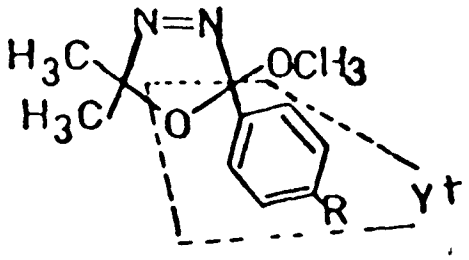
Benzophenone-N-phenylhydrazone (2.7 g, 1.0×10^{-2} mole) was dissolved in



R MW	YIELD %	^{1}H NMR ppm, J(Hz)	^{13}C NMR (PPM) $CDCl_3$-T.M.S. -20°C
H 206	47	a=1.43(s,3H) b=1.60(s,3H) c=3.13(s,3H) d,e,f=7.14-7.70(m,5H)	24.13(C7) 129.71(C12) 24.50(C8) 133.29(C2) 50.96(C6) 135.70(C9) 122.17(C5) 126.78(C10) 128.54(C11)
OCH_3 236	59	a=1.40(s,3H) b=1.56(s,3H) c=3.06(s,3H) d=3.67(s,3H) e=6.73(d,2H,J=9.5) f=7.43(d,2H,J=9.5)	24.06(C7) 121.81(C5) 24.50(C8) 128.24(C10) 50.74(C6) 133.22(C2) 55.28(C13) 160.24(C12) 113.69(C11) 127.81(C9)
CH_3 220	55	a=1.40(s,3H) b=1.56(s,3H) d=2.30(s,3H) c=3.08(s,3H) e=7.10(d,2H,J=8.0) f=7.50(d,2H,J=8.0)	24.35(C13) 126.80(C10) 24.20(C7) 129.27(C11) 24.57(C8) 132.85(C2*) 50.89(C6) 133.84(C9*) 122.03(C5) 139.72(C12)
Cl 240	55	a=1.41(s,3H) b=1.60(s,3H) c=3.10(s,3H) e=7.27(d,2H,J=8.5) f=7.55(d,2H,J=8.5)	24.05(C7) 128.61(C11) 24.35(C8) 132.63(C2) 50.82(C6) 134.17(C9) 122.32(C5) 139.72(C12) 128.17(C10)
CF_3 274	54	a=1.43(s,3H) b=1.61(s,3H) c=3.10(s,3H) e,f=7.26-7.83(m,4H) ^{19}F NMR 62.66(s)	24.34(C7) 127.43(C10) 24.56(C8) 132.69(C2) 51.10(C6) 139.64(C9) 122.97(C5) 125.61(C11)
NO_2 251	29	a=1.43(s,3H) b=1.67(s,3H) c=3.14(s,3H) e=7.58(d,2H,J=8.0) f=8.03(d,2H,J=8.0)	24.35(C7) 128.03(C10) 24.38(C8) 132.19(C2) 51.11(C6) 142.50(C9) 123.70(C5) 148.35(C12) 123.78(C11)

*Tentative assignments

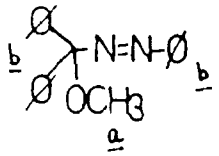
TABLE E.5 ARYL-ALKOXY OXADIAZOLINES



R MW	IR cm^{-1}	M.S. $^{+}$m/z;EI
H 206	2990,2837,1452,1380,1367 1315,1278,1233,1205,1178 1111,1082,1025, 976, 915 902	$136(C_6H_5COOCH_3)^+$ $105(Y)^+$ $77(C\text{-}CO)^+$
OCH_3 236	2998,2939,2838,1612,1509 1452,1382,1368,1312,1238 1208,1197,1108,1054,1036 975, 922, 905	$135(Y)^+$ $107(Y\text{-}CO)^+$
CH_3 220	2990,2938,2837,1615,1510 1458,1437,1380,1365,1310 1276,1232,1208,1196,1178 1107,1065,1021, 902	$150(pCH_3C_6H_5COOCH_3)^+$ $119(Y)^+$ $91(Y\text{-}CO)^+$
Cl 240	2995,2938,2838,1600,1460 1435,1382,1365,1278,1231 1205,1196,1171,1112,1089 1064,1012, 902	$139,141(Y)^+$ $111,113(Y\text{-}CO)^+$
CF_3 274	2992,2938,2835,1621,1467 1434,1381,1365,1323,1278 1230,1207,1195,1168,1132 1113,1105,1022,1013, 903 835	$173(Y)^+$ $145(Y\text{-}CO)^+$
NO_2 251	2995,2930,2857,1607,1525 1464,1435,1382,1368,1351 1276,1235,1195,1115,1074 1076, 915, 907	$150(Y)^+$ $104(Y\text{-}NO_2)^+$ $76(Y\text{-}NO_2\text{-}CO)^+$

TABLE E.6 ARYL-ALKOXY OXADIAZOLINES

methanol (300 ml). Ammonium perchlorate (5.0 g) was added to the solution which was then electrolyzed for 24 hours in the dark at a constant anode potential of 1.0 volt against a standard calomel electrode. The solvent was then evaporated, water was added, and the aqueous solution was extracted with CH_2Cl_2. The organic fraction was then dried over $CaCl_2$ and the solvent was evaporated. The crude azoether was recrystallized from petroleum ether (2.3 g, 90% yield, based on 85% conversion).



^{1}H NMR. δ 3.34 (s,3H), δ 7.11 - 7.88 (m,15H)

IR: 3097, 3017, 3045, 2845, 1975, 1960, 1602, 1529, 1495, 1452, 1310, 1210, 1180, 1096, 1005, 907, 695, 685, 647.

E.3 CHEMISTRY OF 2-METHOXY-2,5,5-TRIMETHYL-Δ^3-1,3,4-OXADIAZOLINE

1. THERMOLYSIS

Methoxyoxadiazoline (20 mg, 1.4×10^{-4} mole), methanol-d4 (0.5 ml) and benzene (1 drop), were mixed together 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} Torr). The thermolysis was carried out in a constant temperature oil bath, maintained at 79.5 ± 0.2°C, for 8 days. At the end of the reaction, the products were not separated, but their structures were deduced from the pmr spectrum of the mixture. The yields were calculated from the integrals of the ^{1}H NMR peaks, by using benzene as internal standard to normalize the integrals. Spectral data can be found in Table E7.

Another thermolysis was carried out with the methoxyoxadiazoline (20 mg,

1.4×10^{-4} mole) in methanol (0.5 ml), in a sealed tube for 7 days. At the end of the reaction, aqueous HCl (3 drops) was added to the solution. Acetone, acetaldehyde dimethyl acetal, isopropyl alcohol, and methyl acetate were separated and collected form gas chromatography columns (a 15% SE-30 and a 10% FFAP heated at 40°C, flow rate 14 ml/min.). Addition of authentic samples one at a time showed an increase in the corresponding peak on the GC trace.

E.4 *KINETIC STUDIES*

The oxadiazolines (20 mg) and CH_2Cl_2 (3 drops) were dissolved in the solvent (0.5 ml, CD_3OD or CCl_4). The solutions were transferred to NMR tubes which were put through three freeze-pump-thaw cycles (vacuum line pressure 10^{-2} Torr), prior to sealing.

In the case of the aryl substituted oxadiazolines, thermolysis was performed in a controlled temperature oil bath, at 49.2 $\pm$ 0.2°C. In the case of the alkyl substituted oxadiazolines the temperature was 79.5 $\pm$ 0.2°C. The reactions were monitored by following the decrease in the integrals of the methoxy signals (methoxyoxadiazolines) or acetoxy signals (acetoxyoxadiazolines), in the ^1H NMR spectrum.

For the aryl substituted oxadiazolines, the reaction was stopped by cooling the tube at liquid nitrogen temperature, prior to running the spectrum at the probe temperature (35°C).

In all cases, the time outside the bath was not counted, and the reactions were followed to, at least, 80% of completion. All the kinetic runs were done at least twice and the average rates are tabulated in Tables RD1 through RD5.

TABLE E.7. PRODUCTS OF THERMOLYSIS OF 87 IN CD_3OD

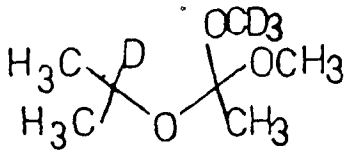
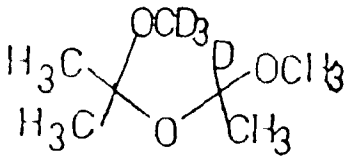
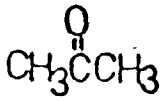
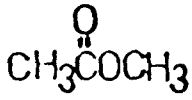
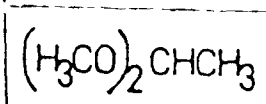
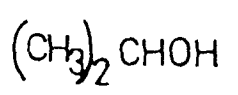
PRODUCT	YIELD %	^1H NMR(ppm) CD_3OD-T.M.S.
	69	a=1.00(t,6H,J=1.2Hz) b=1.92(s,3H) c=3.26(s,3H)
	29	a=1.15(t,3H,J=1.2Hz) b=1.19(s,6H) c=3.56(s,3H)

TABLE E.8. HYDROLYSIS OF THE PRODUCTS OF THERMOLYSIS OF 87 IN CH_3OH

PRODUCT	^1H NMR(ppm) CH_3OH-T.M.S.	FT-IR GAS-PHASE
	2.11(s)	-
	a=2.01(s,3H) b=3.61(s,3H)	-
	a=1.26(d,3H,J=5.5Hz) b=3.29(s,6H) c=4.51(q,1H,J=5.5Hz)	-
	a=1.07(d,6H,J=6.0Hz) b=3.89(sep,1H,J=6.0Hz)	3361,2978,2893 1463,1378,1237 1146,1089

E.5 CHEMISTRY OF 2-METHOXY-2,5,5-TRIMETHYL-Δ^3-1,3,4-OXADIAZOLINE IN ACETONE -d6

1. THERMOLYSIS IN ACETONE -d6

The methoxyoxadiazoline (100 mg, 7.0×10^{-4} mole) was dissolved in acetone -d6 (3.0 ml) in a thick-walled tube. Heating was carried out, for 8 days at 79.5°C, At the end of which the tube was cooled at liquid nitrogen temperature and opened.

2. IDENTIFICATION OF PROPENE -d6

The reaction mixture was distilled by bulb to bulb (10^{-2} Torr) distillation and the distillate was injected on a 5% FFAP column heated at 40°C (flow rate 10 ml/min). The FT-IR spectrum of the first eluted compound contained the same bands as those of authentic propene with additional C-D bands at cm^{-1} 2295, 2264, and 2217. The ^1H NMR spectrum of authentic propene was identical to the one of the first eluted compound and the ^2H NMR spectrum showed peaks identical in chemical shifts to the ones in the ^1H NMR spectrum of propene.

The olefin was converted to the dibromoalkane, by adding a bromine/CCl_4 solution to the mixture of products. Purification of 1,2-dibromopropane was done by preparative GC using a 20% DEGS column, heated at 140°C (flow rate 40 ml/min). All spectral data are tabulated in table RD6. (p 76)

3. IDENTIFICATION OF OTHER REACTION PRODUCTS

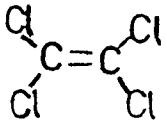
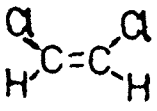
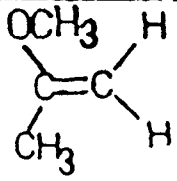
The product mixture from the thermolysis was distilled, bulb to bulb (10^{-2} Torr), at room temperature. The distillate and the residue were injected through a 3% OV-17 column heated at 35°C for 5 minutes, followed by 1°/min rise up to final temperatures of 100°C (volatile) and 200°C (non-volatile). Mass spectra of each eluent were obtained (GC-MS). The distillate and the residue were

injected on a larger scale (30 µl) on a 10% OV-17 column heated at 35°C for 5 minutes (flow rate 30 ml/min), after which the temperature was raised manually. The different products were collected and ^{1}H FT-NMR spectra were obtained. All spectral data are tabulated in Table RD6 (p 76).

E.6 TRAPPING EXPERIMENTS

Table E.9 lists the traps used, the boiling range at which they were distilled, and their ^{1}H NMR data.

TABLE E.9 TRAPS USED IN TRAPPING EXPERIMENTS

SAMPLE	BOILING RANGE °C	^{1}H NMR CCl_4-T.M.S.
$H_3COOCC{\equiv}CCOOCH_3$	105-107(20Torr)	3.78
	88-90	1.94(m,2H) 3.53(m,2H) 6.71(m,4H)
	119-122	-
$(H_3C)_2C{=}C(CH_3)_2$	71-73	1.62
	58-61	6.38
	34-36	1.74(s,3H) 3.47(s,3H) 3.73(s,2H)

The oxadiazoline was dissolved in the freshly distilled trap in a tube, and the tube was sealed under vacuum (10^{-2}Torr). Heating of 2-methoxy-2-(o-methoxy-

phenyl)-5,5-trimethyl-Δ^3-1,3,4-oxadiazoline (a,b,c) and 2-methoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline (d,e,f) were carried out at 80°C for 24 hours and 7 days respectively. At the end of this time the mixture of products was distilled by bulb to bulb distillation (10^{-2}Torr).

a. *DIMETHYLACETYLENEDICARBOXYLATE (DAD)*

The volatile fraction from the bulb to bulb transfer contained DAD. The residue was chromatographed on a column packed with basic alumina using a 20% ether in CCl_4 solution. Two fractions were collected and identified. The first fraction contained DAD and the second fraction contained cycloadduct 104 (p 135)

b. *VARIOUS DIPOLAROPHILES*

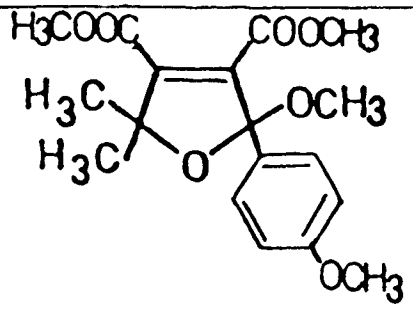
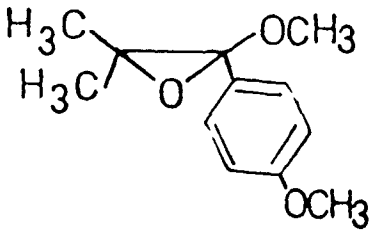
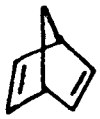
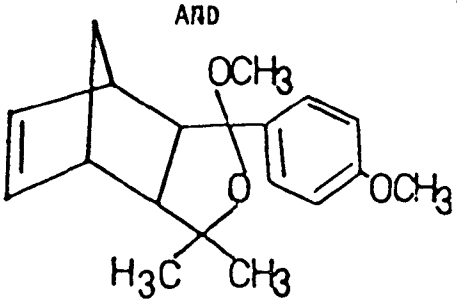
The volatile fractions contained the traps (tetramethylethylene, tetrachloroethylene and ethylvinylether). The residue was chromatographed on 2 mm thick silica plates and eluted with a 5% ether in CCl_4 solution. The mobile band which contained the epoxide (p 135) was extracted with CH_2Cl_2.

c. *NORBORNADIENE*

The volatile fraction contained norbornadiene and the residue a mixture of the epoxide and the norbornadiene adduct (p 135). The two products were separated by preparative thin layer chromatography (as in b) and the plates showed two mobile bands. The first band contained the epoxide and the second band the norbornadiene adduct.

The yields from the trapping experiments (a-c) are shown in Table E10, and the spectral data can be found in section RD6. (p 79).

TABLE E.10 THERMOLYSIS OF OXADIAZOLINE 103(p79)IN TRAPS

TRAP	PRODUCT	YIELD %
DAD		95
		90
	AND 	50 AND 40

d. 2-METHOXY-PROPENE AND TETRAMETHYLETHYLENE

The mixtures of products from both reactions were separated from any polymeric materials by bulb to bulb distillation (10^{-2} Torr, 80°C). The distillates were injected into a 3% OV-17 column heated at 40°C for 5 min., followed by 3°/min rise in temperature up to a final temperature of 120°C. Mass spectra of the different eluents were recorded (GC-MS). The same mixtures were injected into a 10% OV-17 column and the temperature was raised manually (40°C - 120°C, flow rate 35 ml/min) and the different products were collected. ^{1}H NMR spectra and mass spectra are reported in Sec RD 6.2 (p89).

e. DAD

The volatile fraction collected from bulb to bulb distillation (10^{-2} Torr, 50°C contained) acetone, methyl acetate, propene and enol-ether 98 (p137), which were identified by MS and ^{1}H NMR as in d.

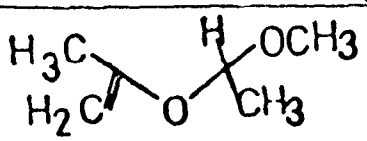
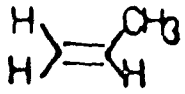
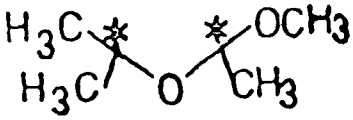
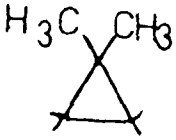
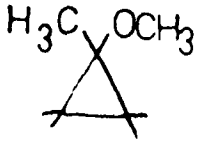
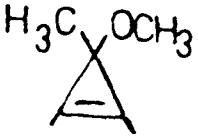
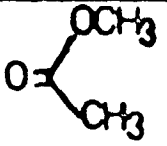
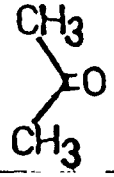
The residue was injected through a 10% OV-17 column heated at 120°C (flow rate 40 ml/mn) and contained dihydrofuran 111 and cyclopropene 112 (p 92).

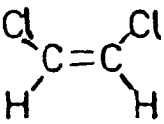
f. CIS-1,2-DICHLOROETHYLENE

The volatile fraction from bulb to bulb distillation (10^{-2} Torr, 50°C) contained acetone, methyl acetate, propene, enol-ether 98 (p 137) and cis-1,2-dichloroethylene. These products were isolated and identified as in part d. The residue contained 113 and 114 (p 94) which were isolated (10% OV-17 column heated at 100°C, flow rate 35 ml/min) and were identified as in d.

All the yields from trapping experiments (d→f) are tabulated in Table EII and the spectral data can be found in section RD6.(p 79).

TABLE E.11 THERMOLYSIS OF OXADIAZOLINE 87(p79) IN TRAPS

PRODUCT \ TRAP	1	2	3	4
	25	23	25	15
	20	27	20	29
	-	-	20	27
	14	11	-	-
	6	3	-	-
	-	-	-	2
	39	42	28	35
	19	17	12	14

1-$H_2C{=}C(OCH_3)CH_3$, 2-$(H_3C)_2C{=}C(CH_3)_2$, 3-  , 4-DAD

E.7 CHEMISTRY OF 2-METHOXY-5,5-DICYCLOPROPYL-2-METHYL-Δ^3-1,3,4-OXADIAZOLINE

1. THERMOLYSIS IN C_6D_6

The methoxy oxadiazoline (20 mg, 1.0×10^{-4} mole) was dissolved in C_6D_6 (0.5 ml) in a medium-walled NMR tube. The solution was frozen, pumped, and thawed three times, and the tube was sealed. The thermolysis was done at 79.5°C, in a controlled temperature oil bath. After 48 hours the tube was opened and the products were separated by bulb to bulb distillation (10^{-2} Torr).

The volatile fraction (distillate), contained methyl acetate and 1-cyclopropylcyclobutene. The ester was identified by comparing its ^1H NMR and IR spectra to those of an authentic sample. The olefin's ^1H NMR spectrum was identical to the published one.[250] Spectral data and yields can be found in section RD.7.1.(p 98).

2. THERMOLYSIS IN CCl_4

The methoxyoxadiazoline (100 mg, 5.0×10^{-4} mole) was dissolved in CCl_4 (5.0 ml) in a thick-walled tube. The same procedure, as before, was followed for sealing the tube. After three days at 79.5°C, the tube was cooled at liquid nitrogen temperature and opened. The mixture was separated by bulb to bulb distillation (10^{-2} Torr). The distillate contained methyl acetate and chloroform. Methyl acetate was identified by comparing its NMR and IR spectra to those of an authentic sample. Chloroform was identified from its NMR spectrum.

The residue was separated on preparative thin layer chromatography plates (Silica gel, 60F-254, 2 mm thick) which were eluted with CH_2Cl_2, and the first band (fastest) was then extracted with dichloromethane. The solvent was evap-

orated with a rotatory evaporator, and the residual mixture was injected into a 15% carbowax column (70°C for 5 min, 1°/min raise up to a final temperature of 200°C, flow rate 25 ml/min.). Mass spectra of the different products were obtained on the fly with the GC/MS instrument. The different fractions were also collected to obtain ^{1}H NMR spectra. All the yields and the spectral data can be found in section RD7.2. (p 99).

E.8 CHEMISTRY OF 2-ACETOXY-5,5-DICYCLOPROPYL-2-METHYL-Δ^3-1,3,4 OXADIAZOLINE

1. THERMOLYSIS IN CCl_4

The acetoxy oxadiazoline (100 mg, 4.5×10^{-4} mole) in CCl_4 (5.0 ml) was degassed (10^{-2} Torr) and sealed into a thick walled tube.

After three days at 79.5°C, the tube was cooled at liquid nitrogen temperature, and opened. The products were separated by bulb to bulb distillation (10^{-2} Torr) and the first distillate was collected by cooling the receiver flask at liquid nitrogen temperature, while the other end was at room temperature. This fraction will be referred to as the first fraction. The second fraction was the one collected from warming the pot to 60°C, at 10^{-2} Torr.

The first fraction contained acetyl chloride, biacetyl, acetic anhydride, dicyclopropyl ketone, and chloroform. The carbonyl stretching frequencies in the IR spectrum of the reaction products matched those of authentic samples. Addition of authentic samples, one at a time, to the reaction products mixture showed an increase in the corresponding carbonyl intensity.

A 10% OV-17 column, (40°C, 25 ml/min), was used to separate and isolate the different products whose ^{1}H NMR spectra matched those of authentic samples.

The second fraction was separated by preparative thin layer chromatography. Silica plates (60F-254, 2 mm thick) were eluted with 20% ether in CCl_4. The

first band (fastest) contained dicyclopropyl ketone, and the second band contained 1-acetoxyethyl cyclopropylidenecyclopropylmethyl ether.

The residue was worked up as in part E.5.2, and contained 119 (p 99) and other chlorinated products. All yields and spectral data can be found in section RD.8.1. (p 107).

2. *IDENTIFICATION OF PROPIONYL CHLORIDE*

2-Acetoxy-5,5-dicyclopropyl-2-ethyl-Δ^3-1,3,4-oxadiazoline (100 mg, 4.4×10^{-4} mole) was thermolyzed in CCl_4 (5.0 ml), in a sealed thick-walled tube, at 79.5°C. After 3 days the mixture of products was separated by bulb to bulb distillation (10^{-2} Torr), and the volatile fraction was analyzed. The ^1H NMR spectrum of the acid chlorides, from the reaction, matched that of authentic acetyl and propionyl chloride (authentic propionyl chloride was prepared by reaction of thionyl chloride with propionic acid). Authentic acid chlorides were injected on a 5% SE-30 solumn heated at 40°C (flow rate 25 ml/min) and their FT-IR spectra and their GC retention times were the same as those of the products from the reaction. All spectral data can be found in section RD.8.2. (p 109).

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