# THERMOLYSIS OF 2-DIPHENYLMETHYLENEHYDRAZONO-5,5-DIMETHYL-$\Delta^{3}$-1,3,4-OXADIAZOLINE

BY

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Submitted to the Faculty of Graduate Studies through the
Department of Chemistry in Partial Fulfillment
of the Requirement for the Degree of
Master of Science at the
McMaster University

Hamilton, Ontario
1973

## ABSTRACT

The thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in vacuum and in chlorobenzene was studied. In both cases a stable 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt was obtained as the major product. The corresponding imino-oxirane, an isomer of the diazetidinium inner salt, is believed to be a precursor of the above product. Thermolysis of the same oxadiazoline in methanol gave benzophenone methyl carbazate and methyl isopropyl ether, probably involving the initial formation of an isocyanate as an intermediate.

ACKNOWLEDGEMENTS

I wish to express my deepest gratitude to my advisor, Dr. J. Warkentin, for his patient encouragement and expert guidance through this research work; and for his comments, criticism and advice during the writing of this thesis.

I also wish to express my appreciation and thanks to Dr. S. L. Lee for his invaluable assistance in the early stages of research. I am also indebted to Dr. F. R. S. Clark, Mr. J. Platman and Mr. S. R. Korn for their technical assistance. I also owe a great deal to Mr. P. Y. Lau for drawing the figures and to Mr. H. Lui for donating the lead tetra-acetate.

Finally, the author wishes to thank the National Research Council of Canada for financial support.

DEDICATION

TO MY PARENTS

TABLE OF CONTENTS


| | Page |
|---|---|
| TITLE PAGE | i |
| ABSTRACT | ii |
| ACKNOWLEDGEMENTS | iii |
| DEDICATION | iv |
| TABLE OF CONTENTS | v |
| LIST OF FIGURES | viii |
| CHAPTERS | |
| I. HISTORICAL INTRODUCTION | 1 |
| A. General | 1 |
| B. Earlier arguments concerning α-lactams and imino-oxiranes | 10 |
| C. Object | 16 |
| II. RESULTS AND DISCUSSION | 19 |
| III. EXPERIMENTAL | 42 |
| A. General | 42 |
| (i) Outline of experimental section | 42 |
| (ii) Chromatography | 42 |
| (iii) Spectra and others | 43 |
| (iv) Solvents and reagents used in synthesis and reactions | 44 |
| B. Preparation of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline | 46 |
| (i) Preparation of carbohydrazide | 46 |
| (ii) Preparation of benzophenone-4-aminosemicarbazone | 46 |

Page

(iii) Preparation of 1-diphenylmethylene-5-isopropylidene carbohydrazide ..... 46

(iv) Preparation of lead tetraacetate ..... 47

(v) Cyclization of 1-diphenylmethylene-5-isopropylidene carbohydrazide ..... 48

C. Preparation of 2-(p,p'-dichlorodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline ..... 50

(i) Preparation of p,p'-dichlorobenzophenone ..... 50

(ii) Preparation of 1-(p,p'-dichlorobenzophenone)-4-aminosemicarbazone ..... 50

(iii) Preparation of 1-(bis-p-chlorophenyl)methylene-5-isopropylidene carbohydrazide ..... 51

(iv) Cyclization of 1-(bis-p-chlorophenyl)methylene-5-isopropylidene carbohydrazide ..... 51

D. Preparation of 2-(p,p'-dibromodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline ..... 54

(i) Preparation of p,p'-dibromobenzophenone ..... 54

(ii) Preparation of 1-(p,p'-dibromobenzophenone)-4-aminosemicarbazone ..... 55

(iii) Preparation of 1-(bis-p-bromophenyl)methylene-5-isopropylidene carbohydrazide ..... 55

(iv) Cyclization of 1-(bis-p-bromophenyl)methylene-5-isopropylidene carbohydrazide ..... 55

E. Thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in methanol ..... 57

Page

(i) Preparation of benzophenone methyl carbazate ..... 58

(ii) Preparation of methyl isopropyl ether ..... 59

F. Thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in vacuum ..... 60

G. Thermolysis of 2-(p,p'-dichlorodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in vacuum ..... 63

H. Thermolysis of 2-(p,p'-dibromodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in vacuum ..... 64

I. Thermolysis of 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt in methanol ..... 65

J. Synthesis of 2-methoxy-2-methyl-N-(diphenylmethylenimino)-propionamide ..... 66

(i) Preparation of α-methoxy-isobutyric acid ..... 66

(ii) Preparation of methyl-α-methoxy-isobutyrate ..... 67

(iii) Preparation of α-methoxy-isobutyric acid hydrazide ..... 67

(iv) Preparation of 2-methoxy-2-methyl-N-(diphenylmethylen-imino)-propionamide ..... 67

K. Hydrogenation of 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt ..... 68

L. Thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in chlorobenzene ..... 71

M. Thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline in methyl ethyl ketone ..... 72

IV. CONCLUSION ..... 73

BIBLIOGRAPHY ..... 75

LIST OF FIGURES


| Figures | | Page |
|---|---|---|
| I. | Structure of ethylene oxide by X-ray diffraction ..... | 23 |
| II. | Structure of 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt by X-ray diffraction ..... | 34 |
| III. | Apparatus for thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^{3}$-1,3,4-oxadiazoline ..... | 60 |
| IV. | Apparatus for constant pressure hydrogenation ..... | 68 |

CHAPTER I

## HISTORICAL INTRODUCTION

### A. GENERAL

The studies of the thermolysis and photolysis of azo compounds have received much attention since 1949 when Lewis and Matheson[1] discovered that many aliphatic azo compounds are very good sources of free radicals. It has been reported that the thermal or photolytic decomposition of open chain azo alkanes will generally yield radicals and nitrogen[2,3,4] as shown in equation (1).

$$R{-}N{=}N{-}R' \rightarrow \begin{cases} [\,R{-}N{=}N\cdot\,] + \cdot R' \longrightarrow R\cdot + N_2 + \cdot R' \\ R\cdot + N_2 + \cdot R' \end{cases} \qquad (1)$$

Induced polymerisation of olefins in the presence of decomposing azo compounds gives strong evidence for the free radical nature of the reaction[5].

The decomposition is first order[1,6,7] and is nearly independent of the reaction media[1]. The alkyl radicals that are formed may have different stabilities depending on the nature of the species; and rapid recombination to dimers is the usual fate, sometimes accompanied by disproportionation and abstraction of hydrogen

from the environment[8].

It is generally believed that except in special cases, where there are large differences in the stability of the radicals, decomposition of aliphatic azo compounds involves concerted, two-bond cleavages without formation of any intermediate diazoalkyl radicals. Seltzer and Dunne[9,10] have shown that there is a large secondary isotope effect upon α-deuteration of certain symmetrical azo compounds, in which, it has therefore been concluded, both C-N bonds may break simultaneously.

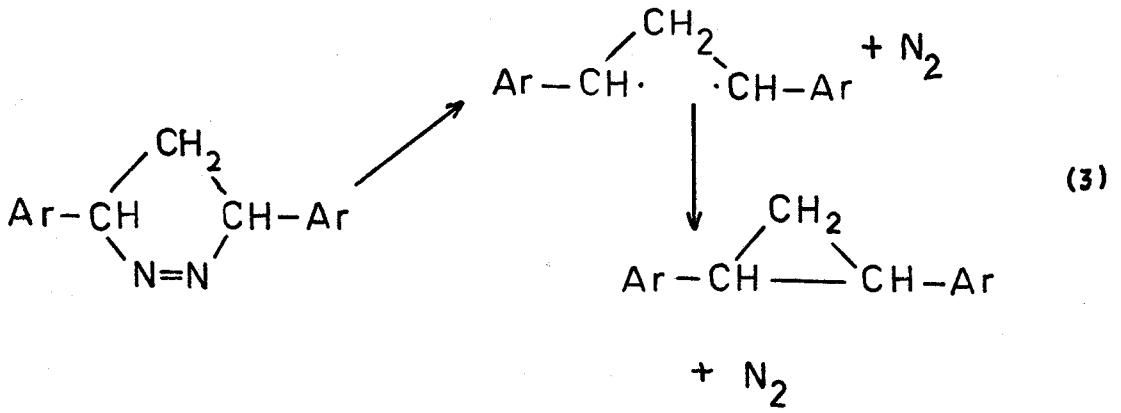
$$R-N=N-R' \longrightarrow R\cdot + N_2 + \cdot R' \qquad (2)$$

Further evidence of the above concerted mechanism has been provided by Overberger from the fact that substituted azoisobutyronitrile derivatives decompose at the same rate whether the racemic or the meso form is used[11].

Crawford[12] and Overberger[13] first investigated the photolytic and thermal decomposition of symmetrical 5-membered cyclic azo compounds and discovered that it involves a biradical process similar to the aliphatic azo compounds as shown in equation (3).

In particular, the thermal decomposition of two compounds, namely; trans-3,5-diphenyl- and trans-3,5-bis(p-chlorophenyl)-1-pyrazoline at 100° in toluene have been studied. Both compounds

decomposed stereospecifically to the corresponding trans-1,2-diarylcyclopropanes. This can be rationalised in terms of the

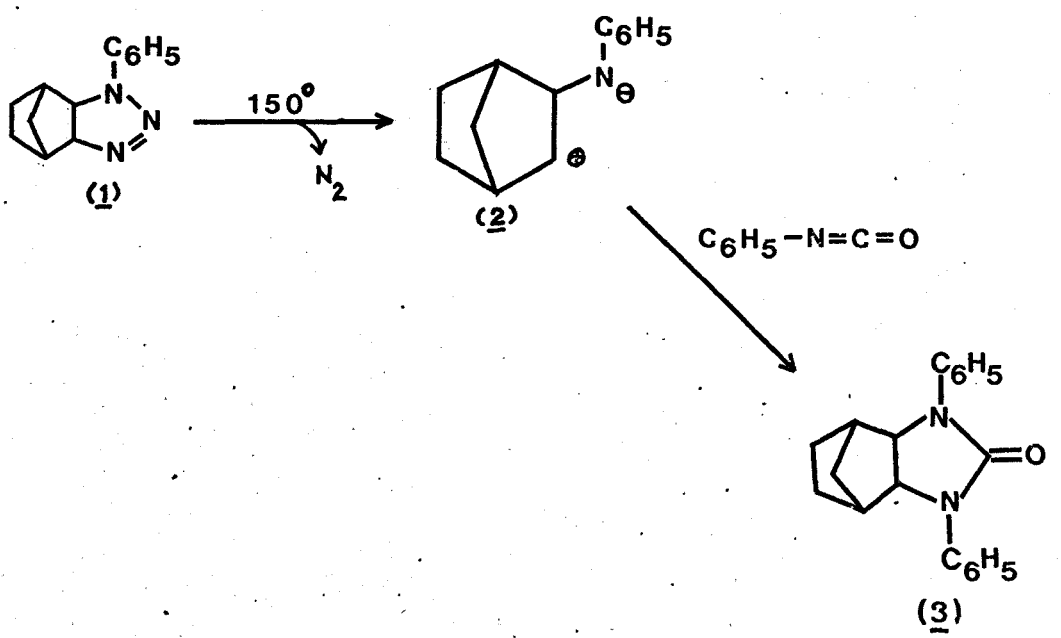


(3)

fast coupling of the intermediate radicals. The close proximity of the two radical moieties and the greater thermodynamic stability of the resulting cyclopropanes could be the sources of the stereospecificity.

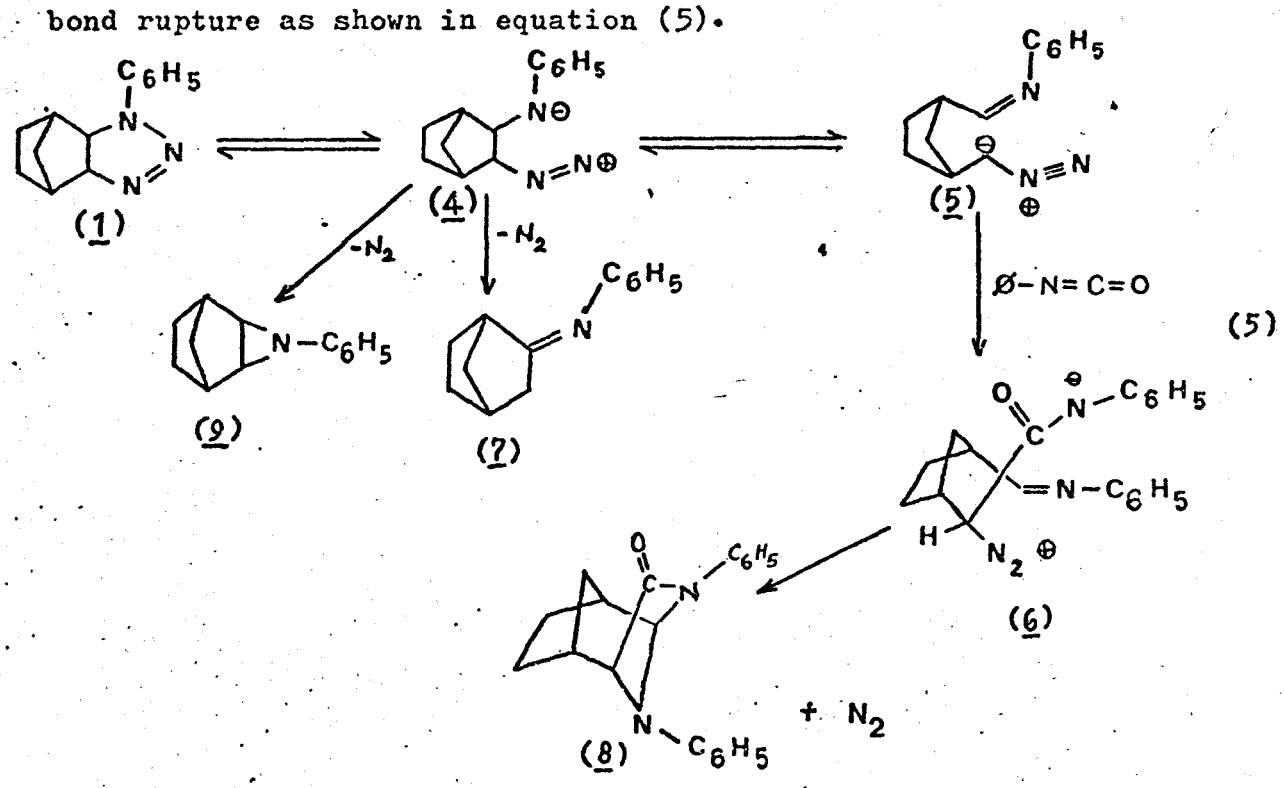
However, thermal decomposition of symmetrical cyclic azo compounds, particularly at higher temperatures generally results in a loss of stereospecificity due to the increase in rate of the rotation around the C - C bonds. This increased rotation is apparently able to compete successfully with the rapid coupling of the biradicals. Thus the photolytic decomposition of trans-3,5-bis(p-methoxyphenyl)-1-pyrazoline gives essentially pure trans-cyclopropane while the thermal decomposition of the same compound at 100° yields 93.3% of trans-1,2-bis(p-methoxyphenyl)-cyclopropane along with a small amount (6.7%) of cis-1,2-bis(p-methoxyphenyl)-cyclopropane.

Unlike open-chain azo compounds, cyclic azo compounds do not always decompose homolytically. Very often, decomposition may go through a dipolar intermediate depending on the electronegativity of the substituents on the carbons adjacent to the azo functions[14,15,16]. This is of particular importance when an heteroatom like oxygen, nitrogen, or sulfur is present on the ring alpha to the ring nitrogen. Huisgen[17] in 1963 performed a series of experiments on the decomposition of several $\Delta^2$-1,2,3-triazolines in the presence of phenyl isocyanate or phenyl isothiocyanate. From the products obtained, it is apparent that the decomposition proceeds through a 1,3-dipolar intermediate and is followed by a 1,3-dipolar cycloaddition. For example, the norbornene phenyl-azide adduct (1) and phenyl isocyanate react at 150° to give nitrogen and a symmetrical urea (3), as shown in equation (4).




(4)

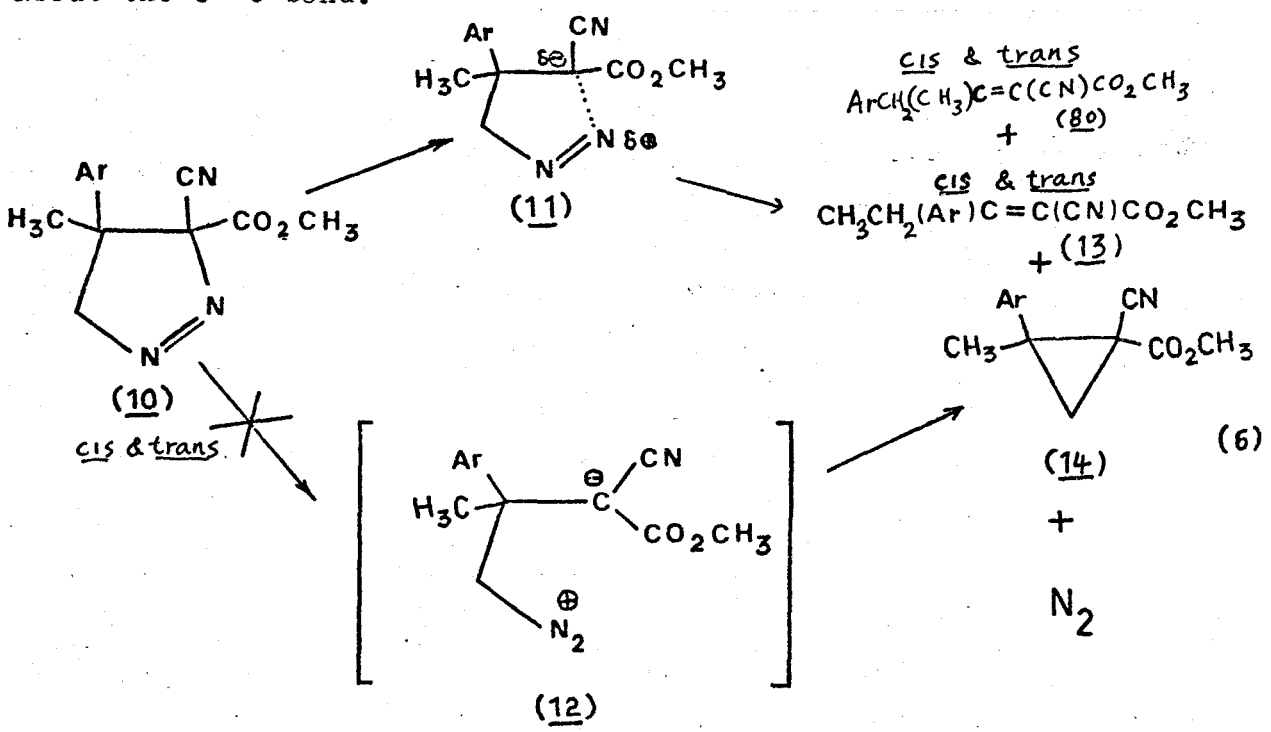
Baldwin[18] in 1965 further investigated the ionic nature of the $\Delta^2$-1,2,3-triazoline decomposition. After careful revision of the work done by Huisgen[17], he found that instead of any urea (3) being formed, the product is actually a 4,10-diphenyl-4,10-diazatricyclo-[4.2.1.$1^{2,5}$]-decan-3-one (8), the structure of which was established spectroscopically and by studying its chemical reactions. To explain the formation of the product (8), he postulated that the triazolines may undergo a stepwise dissociation first with a cleavage of the N - N bond followed by a C - C bond rupture as shown in equation (5).




(5)

Evidence on the pyrolysis of 4-substituted trans-3-cyano-3-carbomethoxy-1-pyrazolines (10)[19], however, revealed that it involves a transition state (11) which is more polar than the

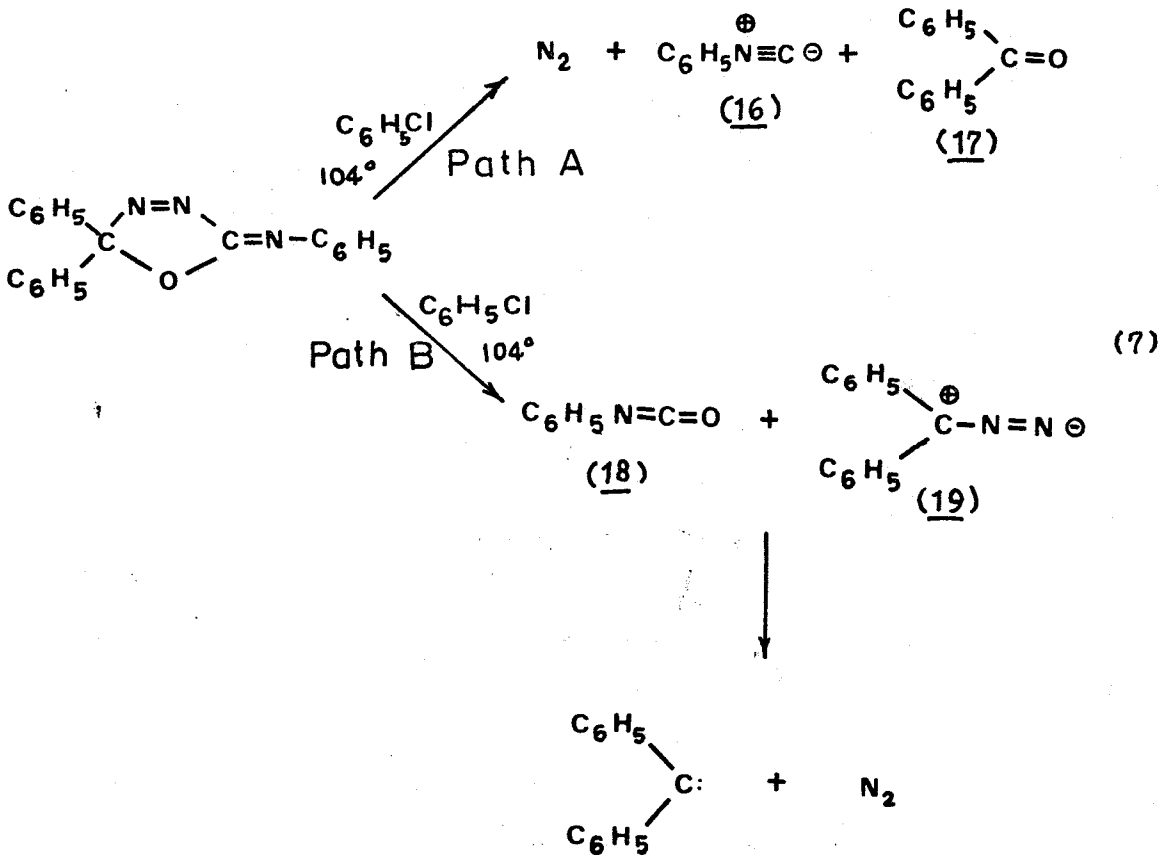
parent pyrazoline (10) but less than that of a zwitterion intermediate (12). Pyrolysis of cis- and trans- (10) gave a mixture of cis- and trans- olefins (80) and (13) resulting from aryl and methyl migration respectively together with a small amount of 2-methyl-2-aryl-1cyano-cyclopropane carboxylates (14). Chemical evidence showed that the nonstereospecific olefins (80) and (13) can be attributed to the cis and trans isomerization of the olefin products rather than to a mechanism involving a zwitterion intermediate (12) which is capable of free rotation about the C - C bond.




(Note: cis and trans denote the relative position of the carbomethoxy group to the aryl group on the adjacent carbon)

The thermal decomposition of $\Delta^3$-1,3,4-oxadiazolines has been studied by West in 1967[20]. Thermolysis of 5,5-diphenyl-2-phenylimino-$\Delta^3$-1,3,4-oxadiazoline (15) at 104° apparently involves two

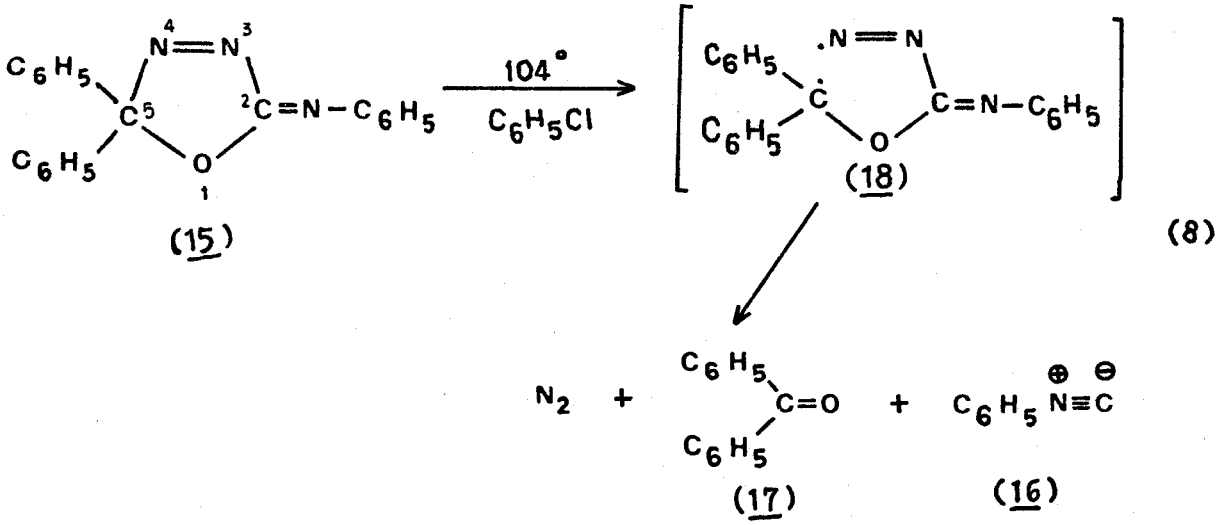
parallel competing processes. One is by direct loss of nitrogen with the formation of phenylisocyanide (16) and benzophenone (17) as the final products; the other is a retro-1,3-dipolar addition involving phenylisocyanate (18) and diphenyldiazomethane (19). Kinetic studies showed that the reaction was unimolecular. Although both pathways A or B showed good agreement with the modified




(7)

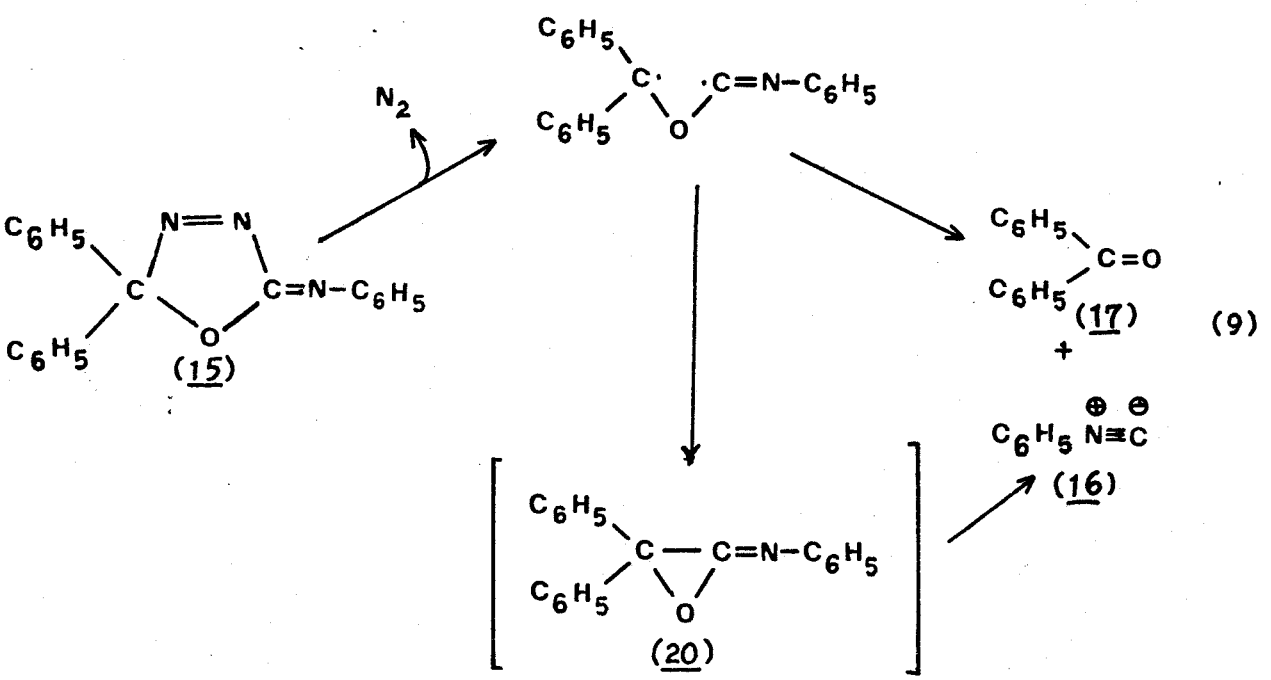
Hammett relationship[21,22], the reverse of pathway B is ruled out since a mixture of diphenyldiazomethane and phenylisocyanate in chlorobenzene at 104° failed to give benzophenone nor phenylisocyanide. Since a heterolytic cleavage is unfavourable in a

relatively non-polar chlorobenzene solvent, the mechanism of reaction A was proposed to be of a homolytic nature in which the $C_5$ - N bond breaking is probably part of the rate determining step.



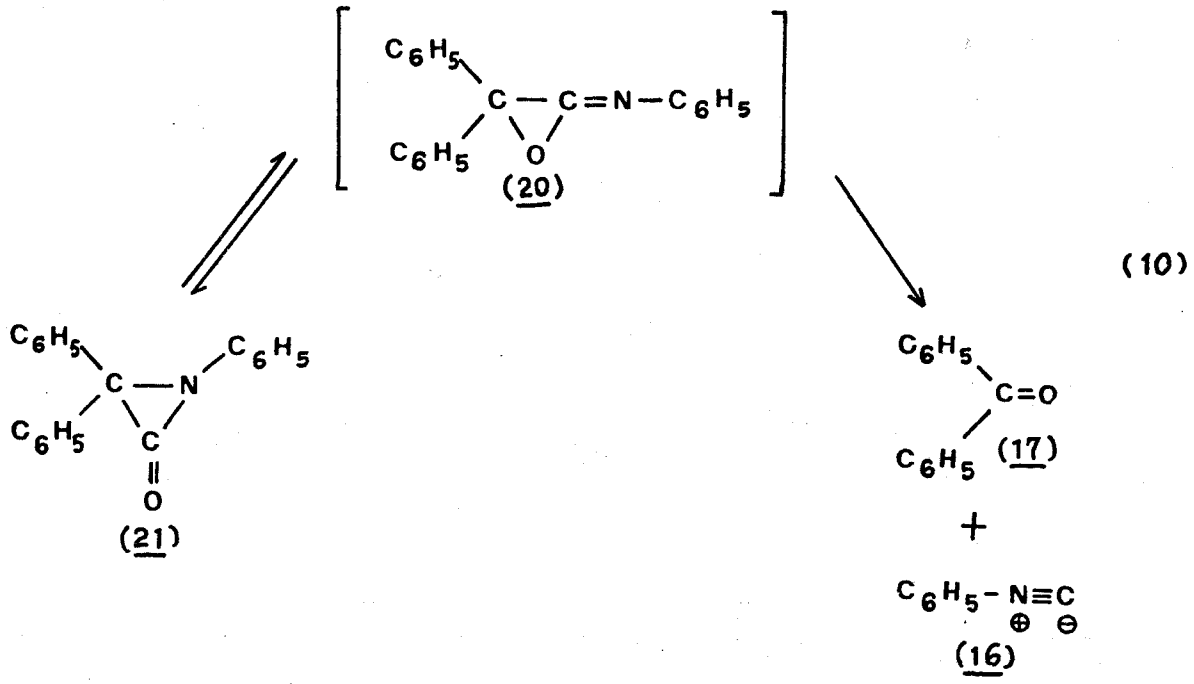

(8)

Alternatively, a concerted process, which is allowed by its orbital symmetry, is also mechanistically possible. An imino-oxirane (20) may be formed in this case since the biradical formed can possibly ring close to give an imino-oxirane structure (20).




(9)

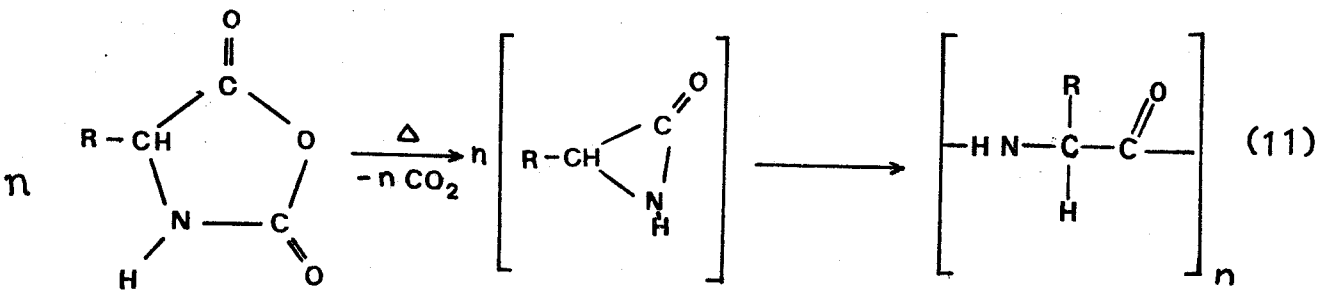
West[20] also proposed the possible existence of an α-lactam system (21) which is an isomer of the imino-oxirane (20). However, the infrared spectrum[23] of the partially decomposed oxadiazoline (15) showed no absorption in the α-lactam carbonyl region (1850 $cm^{-1}$).




(10)

B. EARLIER ARGUMENTS CONCERNING α-LACTAMS AND IMINO-OXIRANES.

Leuchs[24] in 1908 first postulated the existence of α-lactams as intermediates on heating α-amino acid-N-carboxy-anhydrides (22) which rapidly lose carbon dioxide forming polymers (24). The intermediate α-lactams (23), however, were not isolated.



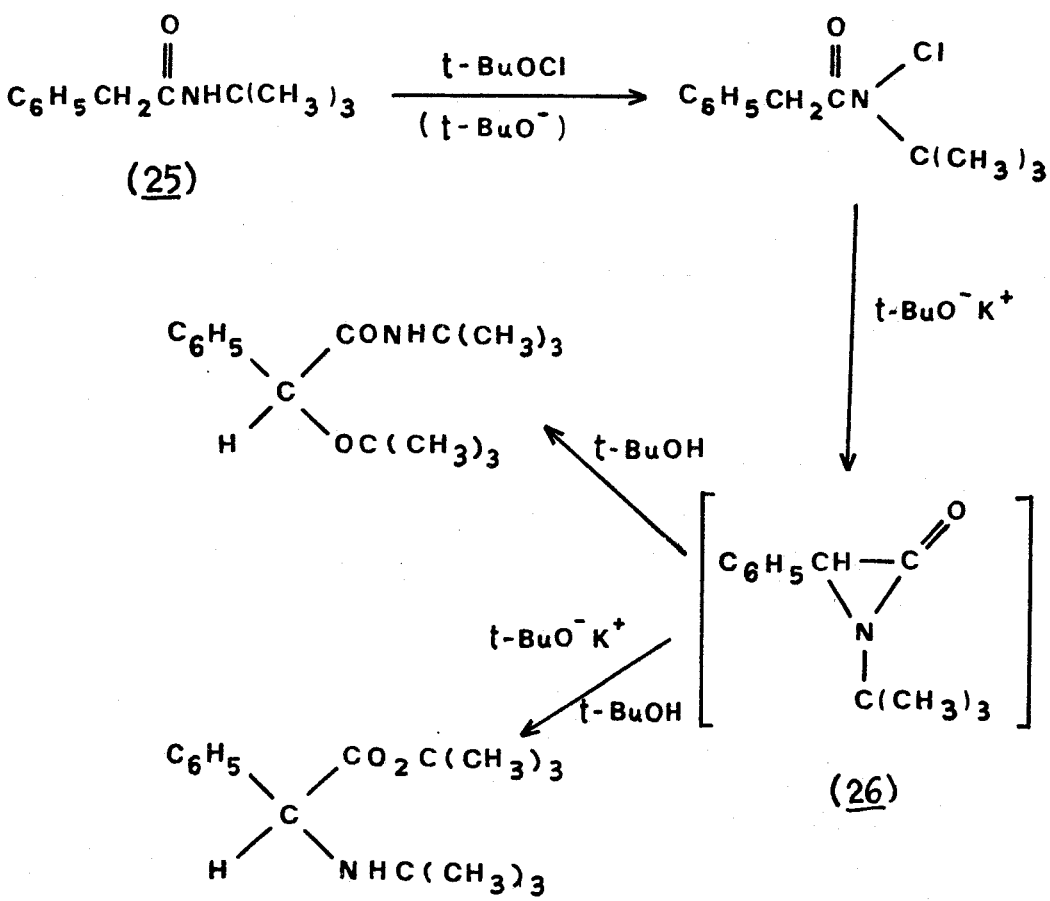

(22) (23) (24)

The existence of α-lactams as intermediates was not substantiated[25] until 1961 when Baumgarten[26] and coworkers first studied the reaction of N-tert-butyl-phenylacetamide (25) with potassium-tert-butoxide and followed the course of the reaction spectroscopically. They observed an intermediate with a carbonyl absorption at 1847 $cm^{-1}$ which is in accordance with the wavelength expected for an α-lactam structure (26)[27].

The discovery of the intermediate α-lactam (26) aroused a series of studies and investigations[28,29]. Baumgarten[28] in 1962 succeeded in synthesising and isolating the same α-lactam (26)

from N-tert-butyl-α-chlorophenylacetamide. The above compound, together with some other known α-lactams, exhibit a carbonyl band in the infrared spectrum at about 1850 $cm^{-1}$.[30]

Reactions of α-lactams, particularly the thermal decomposition, were studied most extensively by Sheehan and his coworkers[31,32,33]. In 1964, Sheehan[33] reported that the reaction of 1-bromo-N-tert-butyl-carboxyamidocyclohexane (27) and potassium butoxide in ether followed by a subsequent heating gave cyclohexanone (30) and t-butyl isocyanide (31) as the major products, together with a small amount of cyclohexene-1-N-t-butylcarboxamide (32).

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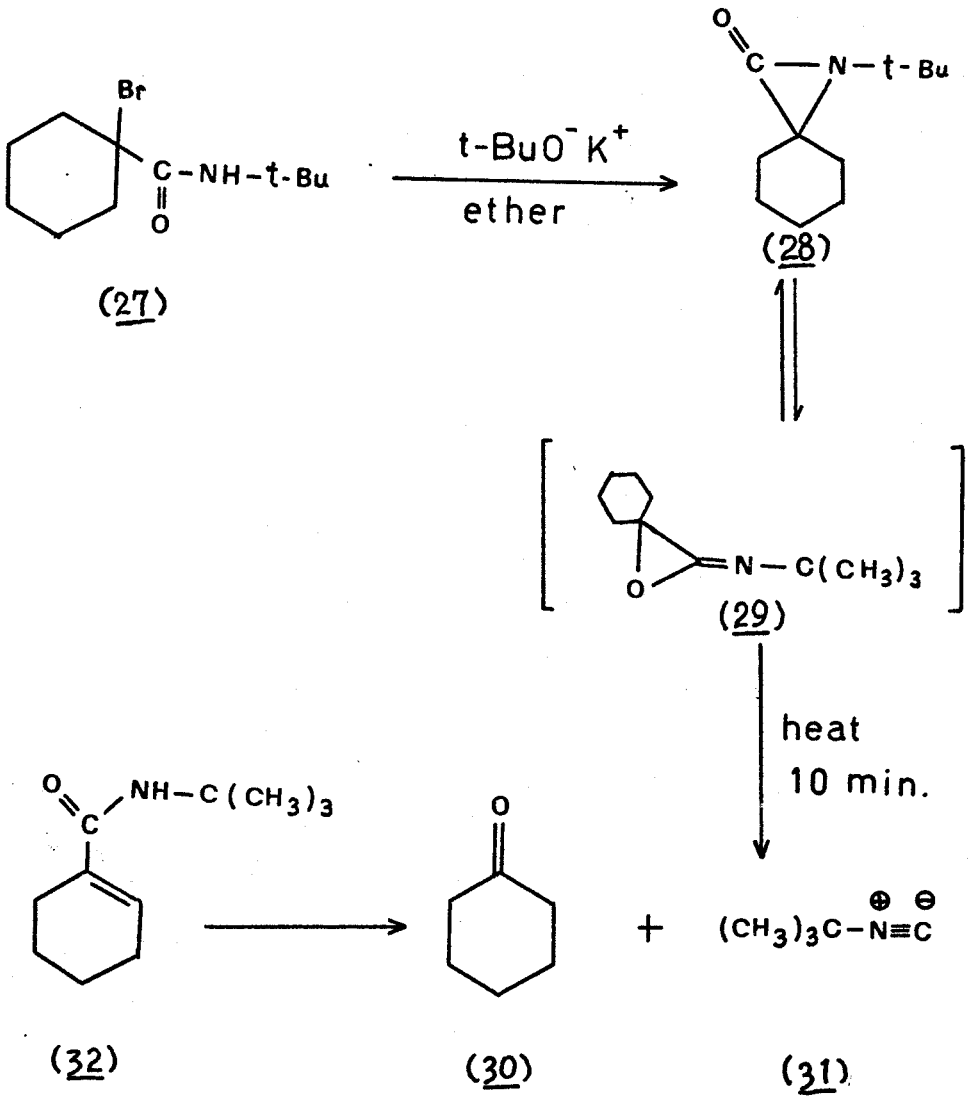
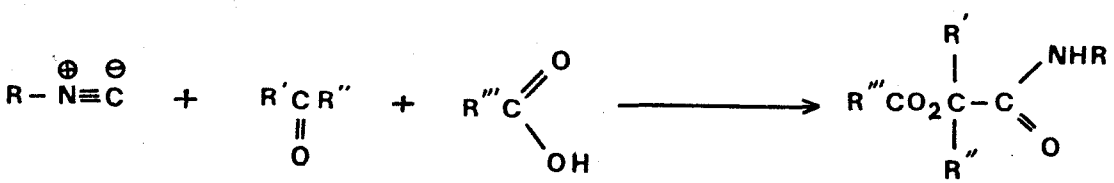



(13)

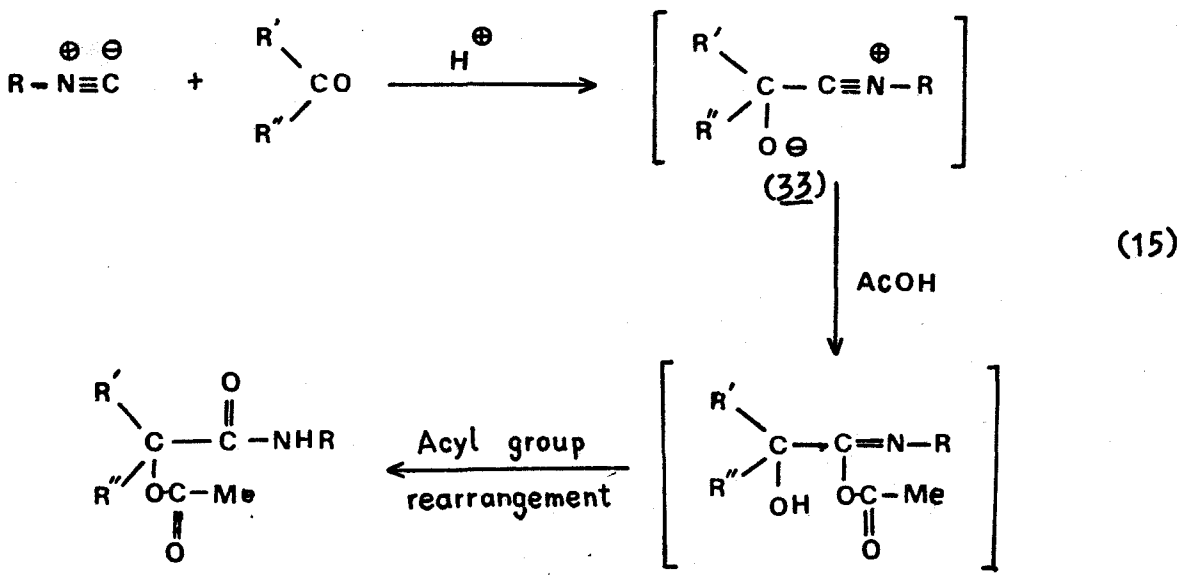
From the products formed, he postulated that the reaction gave a relatively stable α-lactam, 1-t-butyl-3,3-pentamethylene-aziridinone (28), which decomposed sequently on warming, possibly going through an imino-oxirane (29) as intermediate. This postulate, however, as he noted, is not backed up by any experimental facts.

The Passerini reaction[34] has been known since 1921 when Passerini observed that the reaction of a carbonyl compound, isocyanide and carboxylic acid gave the amide of an α-acyloxy acid as shown by equation (14).



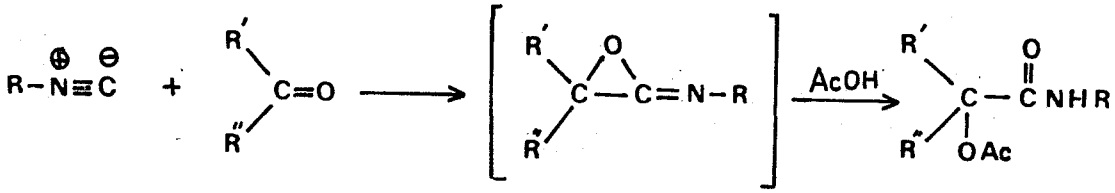
(14)

The above reaction was explained by Ugi and Meyer[35] in terms of a zwitterion intermediate (33), with a subsequent acyl group rearrangement, as shown in the following equation.



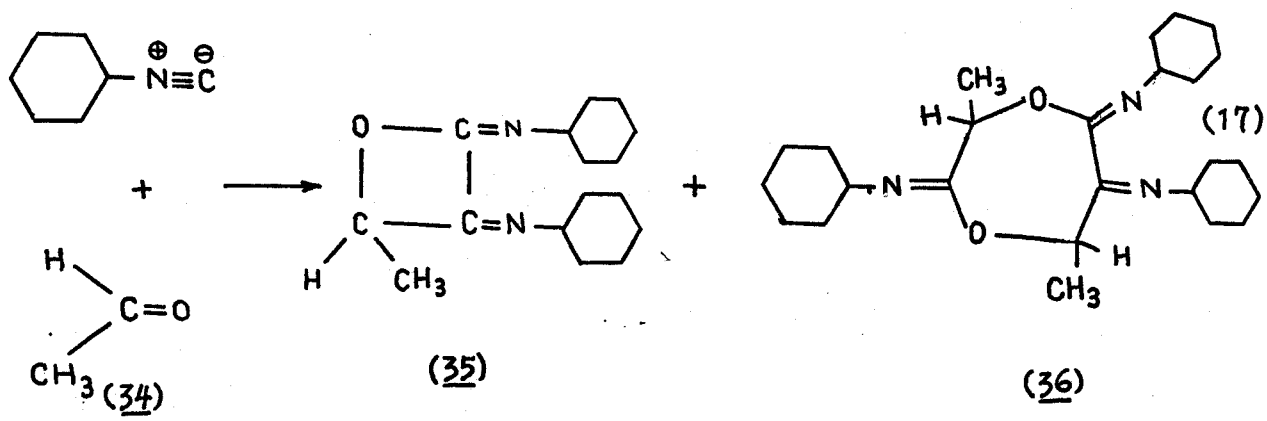

(15)

Taegusa[36] in 1967 proposed that the formation of an imino-oxirane as an intermediate might well account for the product formed in the Passerini reaction.




(16)

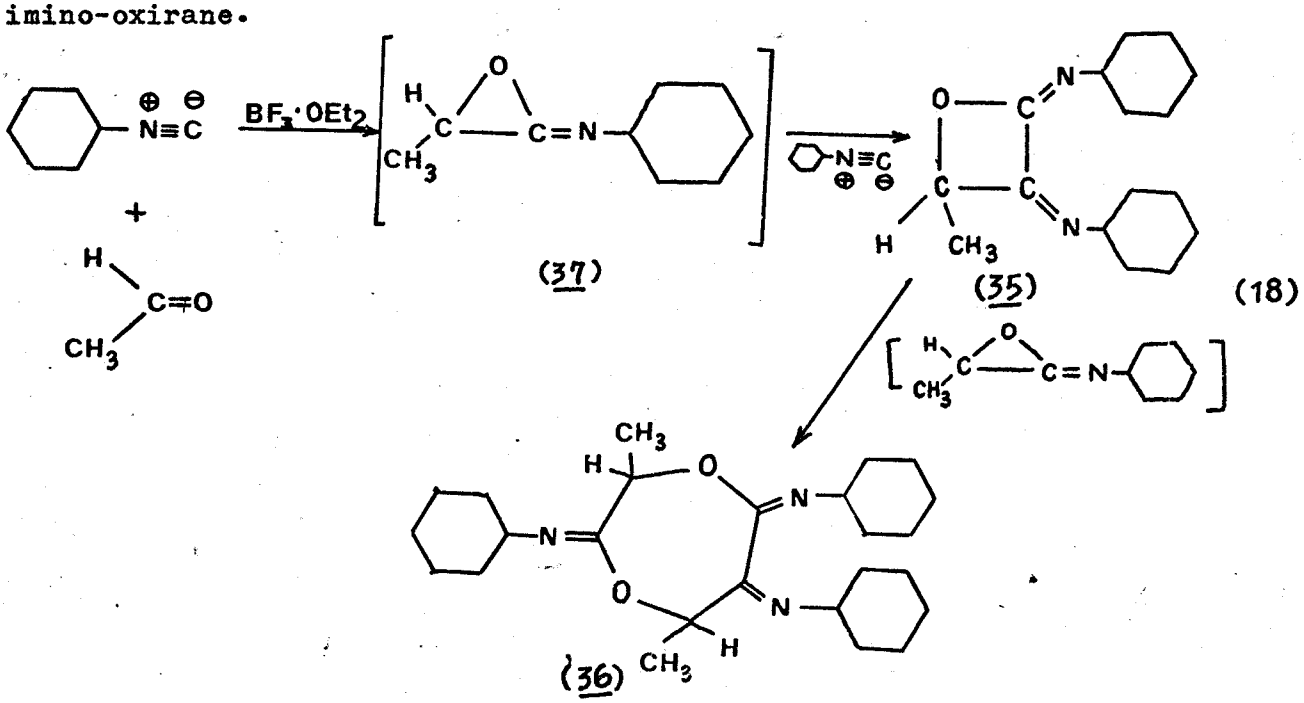
In an attempt to prove this, he studied the reaction of acetyldehyde (34) with cyclohexyl isocyanide in the presence of $BF_3$-etherate at -78°. He found that two cyclic co-oligomers, 2,3-bis(cyclohexylimino)-4-methyl-oxetane (35) and 2,5,6-tris-(cyclohexyl-imino)-3,7-dimethyl-1,4-dioxacycloheptane (36) were obtained as the only products.




(17)

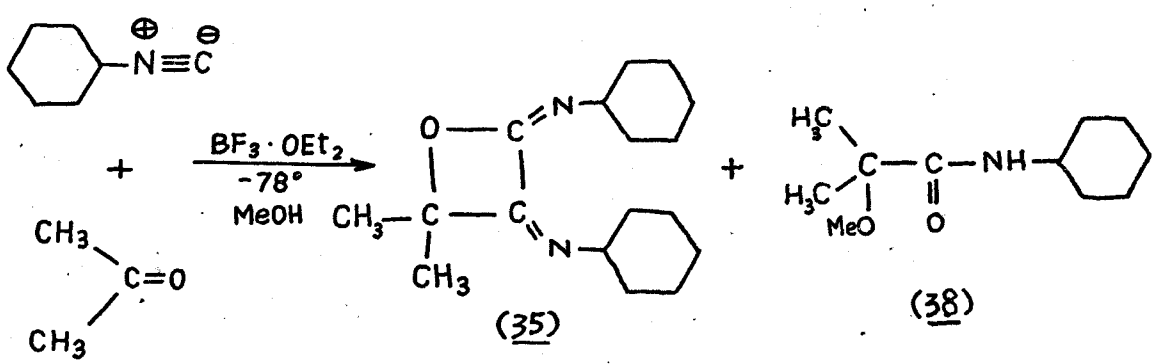
He proposed that the 2,3-bis(cyclohexylimino)-4-methyl-oxetane (35) may be formed by the reaction of the imino-oxirane intermediate (37) with a second molecule of isocyanide while the 2,5,6-tris-

(cyclohexylimino)-3,7-dimethyl-1,4-dioxacycloheptane (36) was formed from the oxetane (35) reacting with another molecule of the imino-oxirane.




(18)

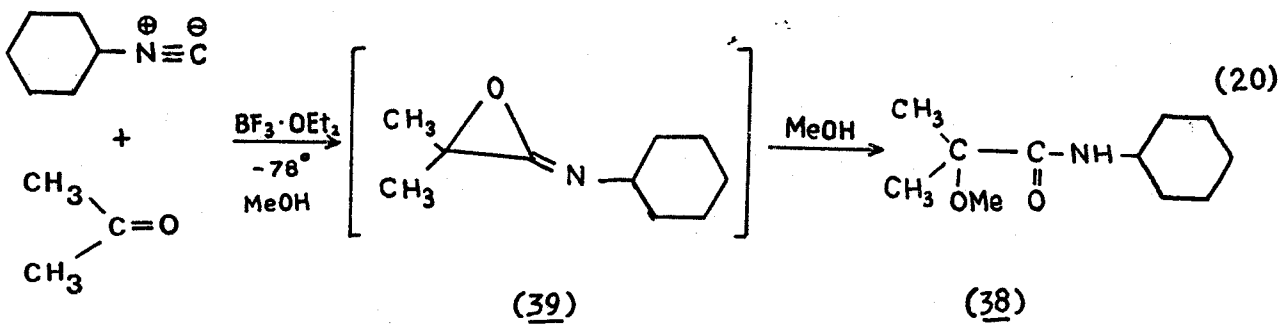
However, on quenching a similar reaction with methanol, he found that the cycloheptane (36) was not formed, instead, another product, 2-methoxy-2-methyl-N-cyclohexyl-propionamide (38) was obtained.




(19)

Although the above reaction can also be rationalised in terms of the formation of the imino-oxirane, as indicated in the

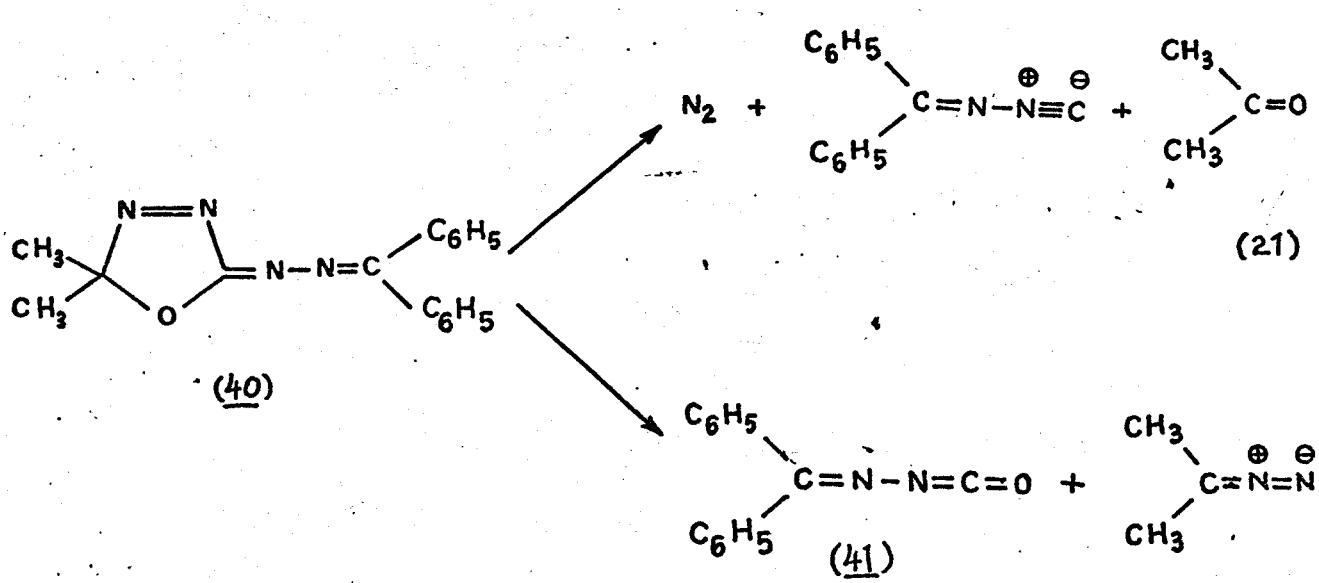
following equation, there is still not quite enough evidence to establish the existence of the imino-oxirane intermediate.



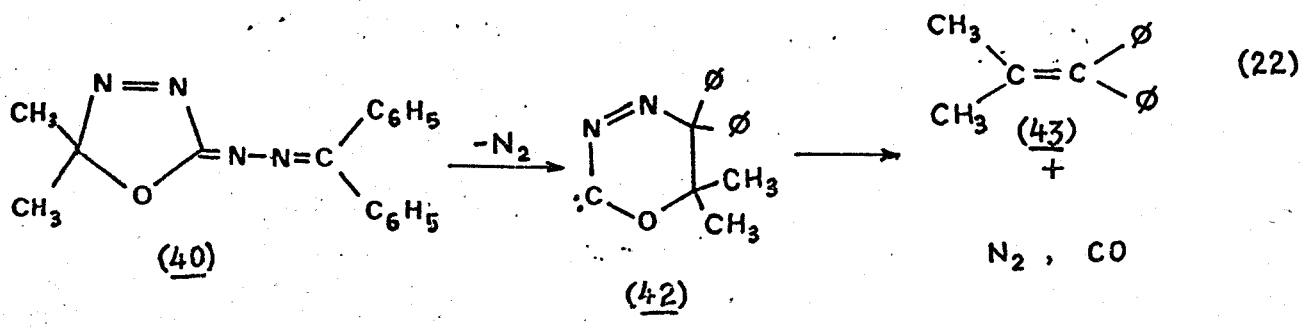

(20)

C. OBJECT

The work presented in this thesis, which is concerned with the thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (40) was undertaken in order to isolate and identify any stable isocyanate (41), which might be formed. Such a product would be the result of decomposition analogous to that of 2-phenylimino-5,5-diphenyl-$\Delta^3$-1,3,4-oxadiazoline (15) as done by West[20] (equation (7)).

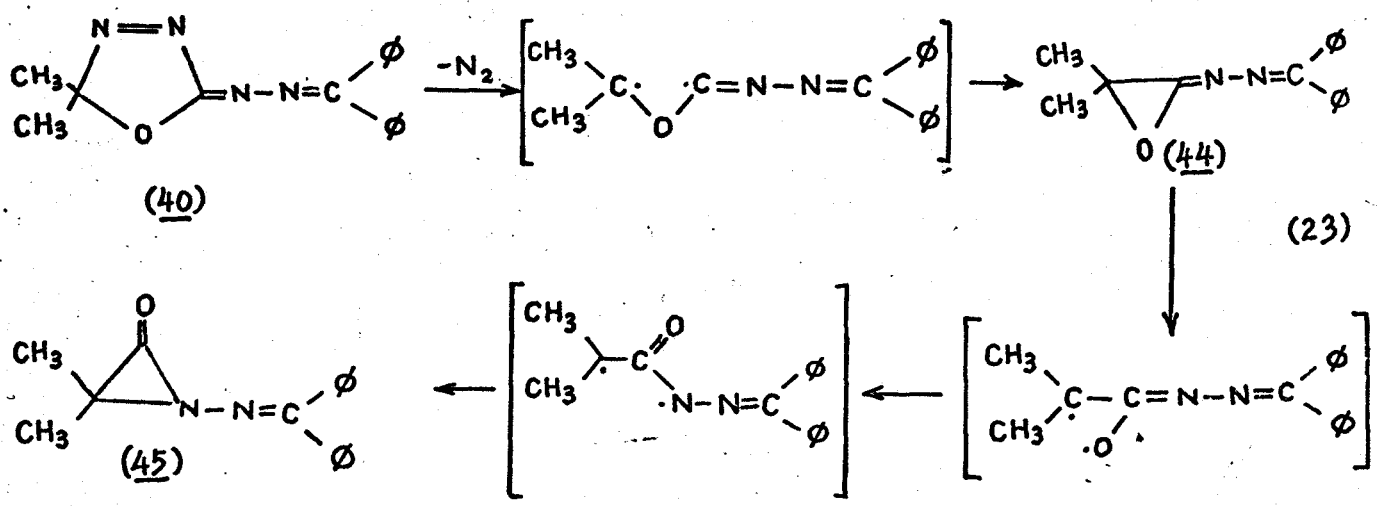



Interest also arose out of the possible formation of other products in the above decomposition. For example, loss of nitrogen with a subsequent ring closure could result in a carbene



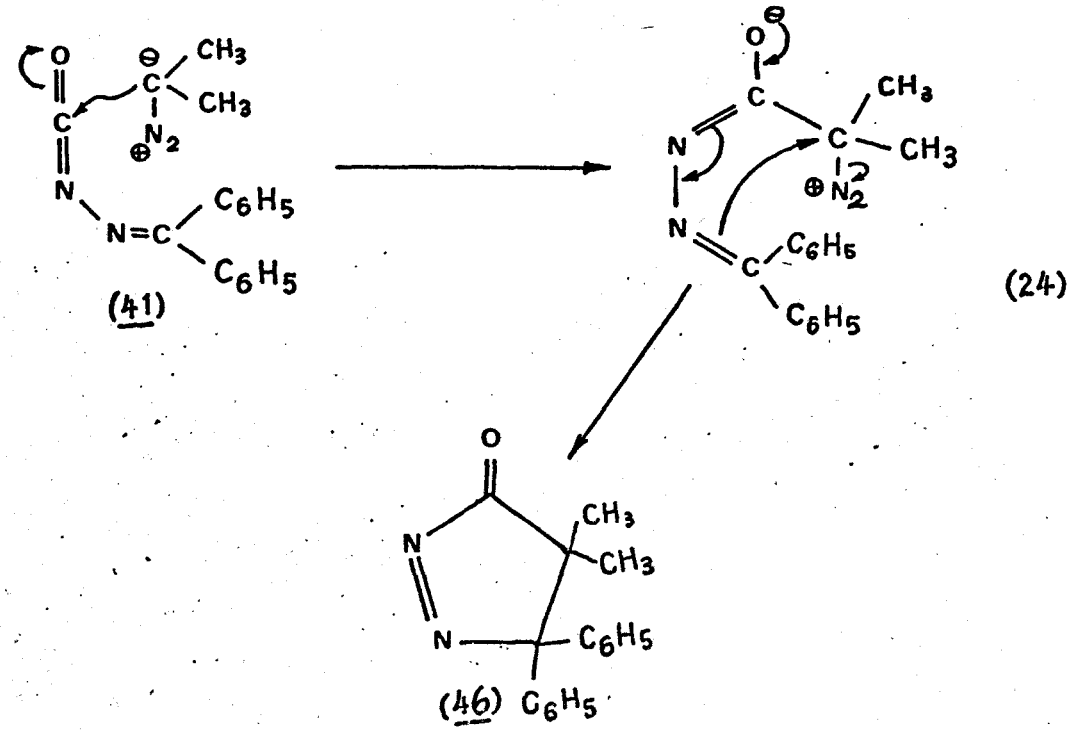
system (42). This, in turn, could lose a molecule of carbon monoxide and nitrogen forming a simple alkene (43).

Homolytic decomposition with loss of nitrogen could either give an imino-oxirane (44) or an α-lactam (45).



(40) (44) (23) (45)

The isocyanate (41) (equation (21)) might react further with the diazomethane forming a diazolinone (46).



(41) (24) (46)

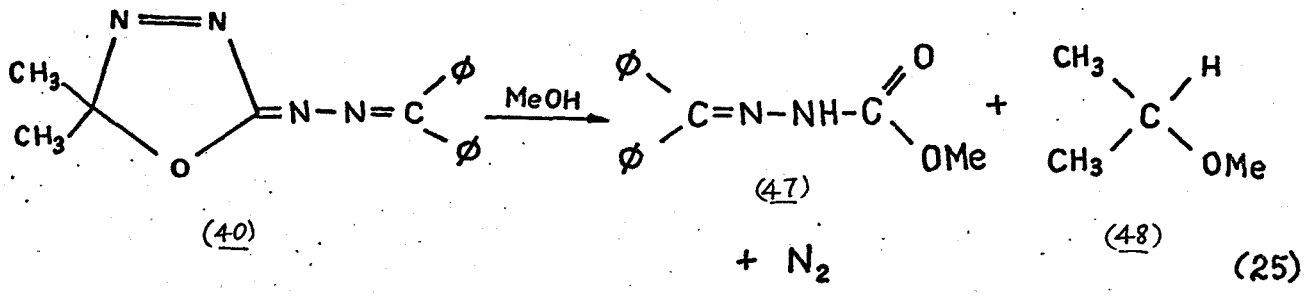
The reaction of the oxadiazoline (40) im methanol and in chlorobenzene has also been studied. Possible mechanisms concerning the decomposition routes are considered.

## CHAPTER II

## RESULTS AND DISCUSSION

The preparation of 2-diphenylmethylenehydrazono-$\Delta^3$-1,3,4-oxadiazoline (40) has been reported previously[23]. Reaction of the oxadiazoline (40) with methanol gave benzophenone methyl carbazate (47) and methyl isopropyl ether (48). Neither isocyanides nor isocyanates were detected.

The crude products of the thermolysis showed two strong ir absorptions at 1625 $cm^{-1}$ and 1655 $cm^{-1}$ and weaker bands at 3360 $cm^{-1}$ and 1010 $cm^{-1}$. The 1010 $cm^{-1}$ band was assigned to methyl isopropyl ether (48). A sample of benzophenone methyl carbazate, which was synthesised independently, also showed a sharp N - H peak at 3360 $cm^{-1}$, with the C = N and C=O absorptions occuring at 1625 $cm^{-1}$ and 1655 $cm^{-1}$ respectively at the expected high intensity.

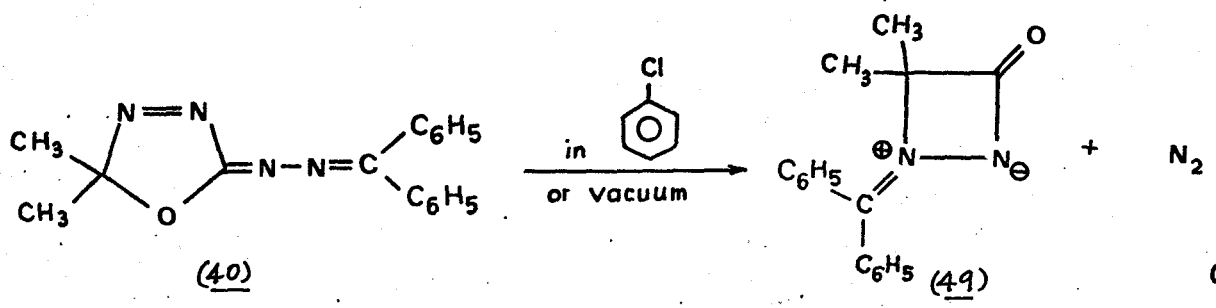



(25)

Thermolysis of neat 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (40) in vacuum at 130° gave a stable 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt

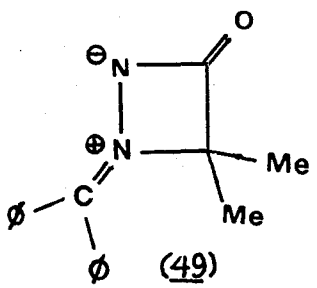
(49) and nitrogen as the final products. The yield was very high; slight amounts of acetone and imino-isocyanate (41), detected only by ir, were present.

Thermolysis of the same oxadiazoline (40) in chlorobenzene, however, gave the stable 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) and nitrogen exclusively. No other side products were detected. This compound, which is basically a β-lactam, showed a characteristic C = O absorption band at 238 nm (log $\epsilon_{max}$ 3.975), and another band at 321 nm (log $\epsilon_{max}$ 4.329). This indicates the introduction of a chromophore relatively different from that of the starting oxadiazoline (40), which showed a $\lambda_{max}$ at 251 nm, with a log $\epsilon_{max}$ equaling 3.980. Molecular weight determination by vaporimetric method showed that it existed as a monomer and microanalysis and mass spectroscopy (m/e 264) confirmed the molecular formula $C_{17}H_{16}N_2O$.

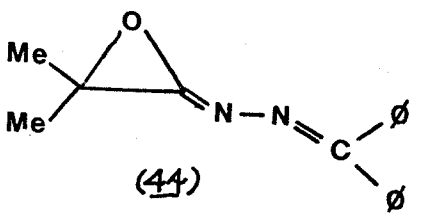



The thermolysis product 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) was a colorless, crystalline

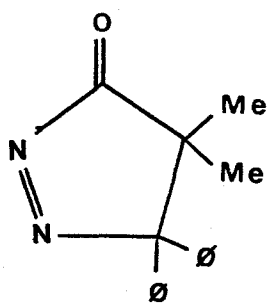
solid with a melting point 171-72.5°. The stability of the compound at this high melting point also suggested the β-lactam structure (49) since imino-oxiranes presumably are very unstable [32,36,37,38]. However, no firm structural assignment could be made with the spectral properties alone since both structures (44) and (49) fitted fairly well the uv, ir and nmr spectra. In addition, several other isomers (50), (51), (52), all of which may formally be derived from the starting oxadiazoline (40) by reasonable mechanistic pathways, had to be considered.



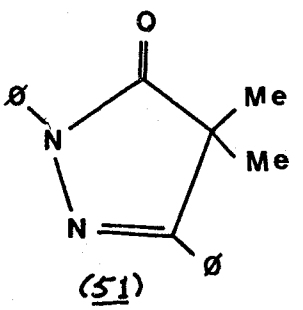

(49)



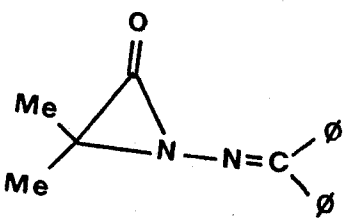

(44)




(50)



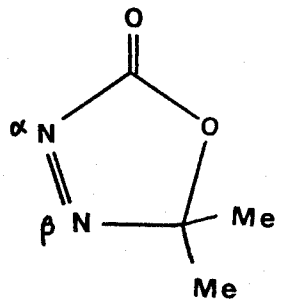

(51)




(52)

The ir spectrum of the thermolysis product showed a strong absorption at 1775 $cm^{-1}$; this was strongly against the α-lactam structure (52) since one would normally expect a strong C = O stretching band at 1850 $cm^{-1}$ for an α-lactam[30]. The strong

absorption band at 1775 $cm^{-1}$, however, was too low for the diazolinone structure (50) based on the fact that the α,β-azo function tends to enhance the carbonyl stretching frequency[39,40]. For example, 5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazolin-2-one (53) showed its carbonyl absorption at 1835 $cm^{-1}$.[39]




$\gamma_{C=O}$ = 1835 $cm^{-1}$

(53)

Structure (51), on the other hand, was not consistent with the chemistry of the product, particularly its hydrogenation to diphenylmethane (described later).

No ir spectrum of imino-oxiranes are available for direct comparison. However, it has been shown by X-ray diffraction[42,43,44] that the epoxide ring function of ethylene oxide has some double bond character. The C - C bond length of the ring carbons measuring 1.47 Å is just intermediate between a normal C - C bond (1.54 Å) and a normal C = C bond (1.33 Å). The H - C - H angle, 116° 15', is also closer to that characteristic of $sp^2$ hybridization (bond angle 120°) than to normal $sp^3$ angles (109° 28').

Basing on the double bond character of the epoxide ring, we would therefore, expect the $C_2 = N$ stretching of the imino-oxirane

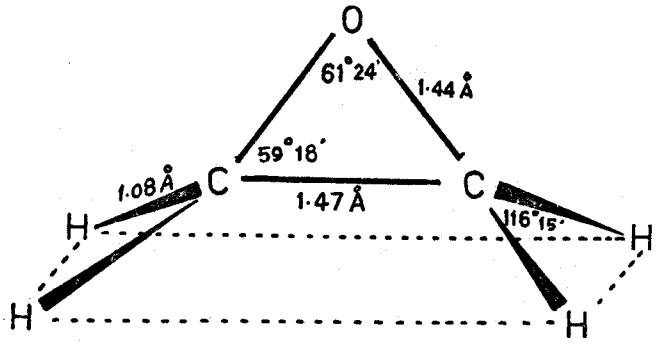
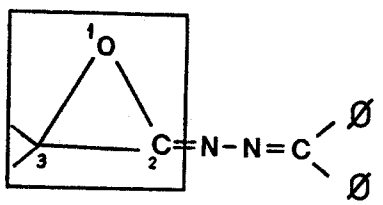
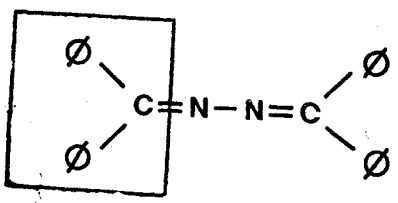



FIG. I : Structure of ethylene oxide by X-ray diffraction.

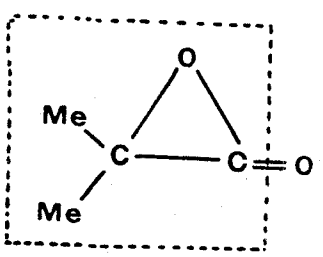
structure (44) to be shifted to a higher wavenumber (such as 1775 $cm^{-1}$) in contrast to the C = N stretching of benzophenone azine (66) which occurs at 1600 $cm^{-1}$; a difference of 175 $cm^{-1}$. That difference is also consistent with the C = O stretching of an α-lactone (54), (1900 $cm^{-1}$)[45] relative to that of a ketone (1705 -




$\gamma_{C_2=N} \Rightarrow 1775\ cm^{-1}$ ?

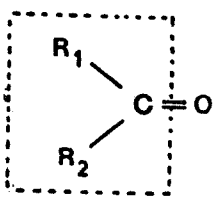



$\gamma_{C=N} \Rightarrow 1600\ cm^{-1}$ } 175 $cm^{-1}$ difference




$\gamma_{C=O} \Rightarrow 1900\ cm^{-1}$

(54)




$\gamma_{C=O} \Rightarrow 1705 - 1725\ cm^{-1}$ } 175 - 195 $cm^{-1}$ difference

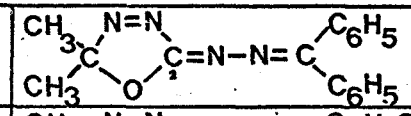
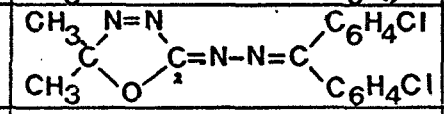
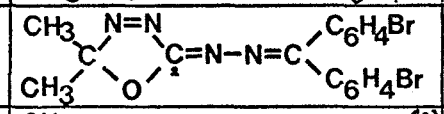
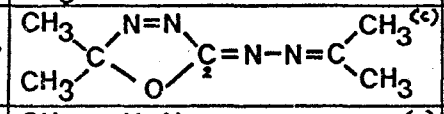
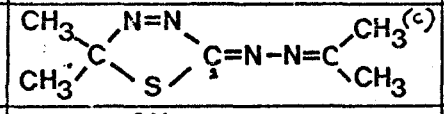
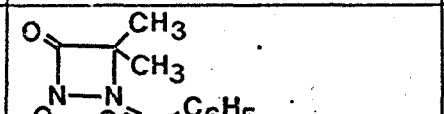
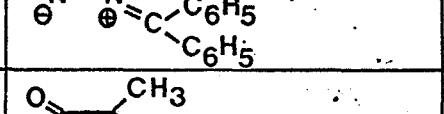
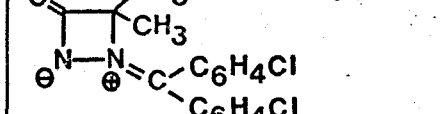
$R_1, R_2$ = alkyl group

1725 $cm^{-1}$). The intensity of the 1775 $cm^{-1}$ absorption is also acceptable in terms of structure (44) since it has been shown that the absorption of many exocyclic C = N bonds are greatly enhanced in intensity[41].

The nmr spectrum ($CDCl_3$) which showed a singlet at 1.47δ (6H) and a multiplet from 7.30δ to 8.13δ (10H) was consistent with both structures (44) and (49), for in both structures the methyl groups are equivalent, since the lone pairs of the nitrogen lie in the same plane determined by the heterocyclic ring.

The uv spectrum of α-lactams and epoxides have received little attention since their ability to delocalize π-electrons is relatively small[49]. However, it should be noted that the wavelength maxima and molar extinction coefficients of the imino-oxirane structure (44) should bear some resemblance to those of the undecomposed oxadiazoline (40). This is supported by the data listed in Table I (see compounds IV and V) in that a change from oxygen to a sulfur function in the cyclic portion changed the absorption maxima and molar extinction coefficients drastically. This shows that oxygen is a rather important factor in affecting the absorption chromophore. Thus, it appears that a change from a five membered ring system to an imino-oxirane structure (44) with the elimination of a nitrogen molecule alone need not introduce too much change in the absorption maxima. However, a $\Delta^3$-

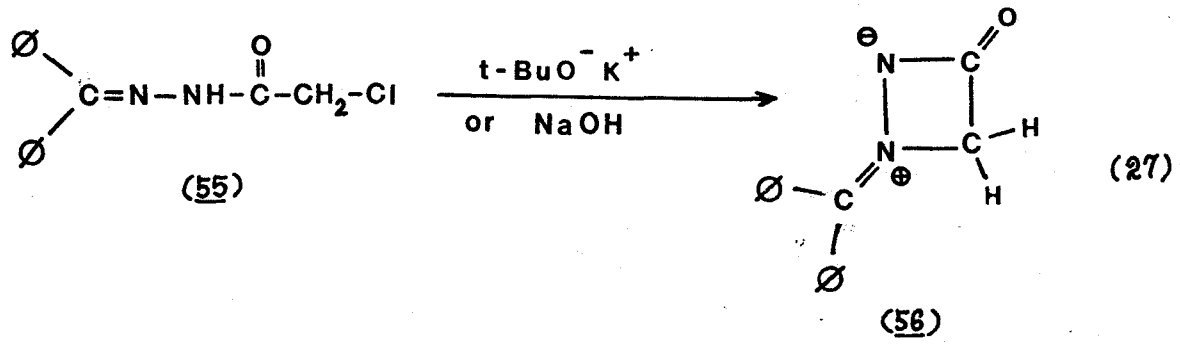
TABLE I: Spectra

| Compound | | I.R., $cm^{-1}$ (a) C=N stretch | C=O stretch | UV, $m\mu$ (b) max | $\log\varepsilon_{max}$ | NMR, ppm (a) |
|---|---|---|---|---|---|---|
| I |  | 1675 | | 251<br>322 | 3.98<br>4.03 | 1.65 s (6H); 7.20-7.80 m (10H) |
| II |  | 1655 | | | | 1.67 s (6H); 7.13-7.73 m (8H) |
| III |  | 1655 | | | | 1.65 s (6H); 6.97-7.58 m (8H) |
| IV |  | 1669 | | 291 | 3.74 | 1.62 s (6H); 2.01 s (3H); 1.95 s (3H) |
| V |  | 1621 | | 210 (d)<br>335 (d) | 3.97 (d)<br>3.67 (d) | 1.83 s (6H); 2.17 s (3H); 2.12 s (3H) |
| VI |  | | 1775 | 238<br>321 | 3.98<br>4.33 | 1.47 s (6H); 7.30-8.13 m (10H) |
| VII |  | | 1775 | 250<br>326 | 4.15<br>4.42 | 1.52 s (6H); 7.32-8.10 m (8H) |
| VIII |  | | 1775 | | | 1.47 s (6H); 7.02-7.77 m (8H) |

(a) $CHCl_3$ or $CCl_4$ as solvent.
(b) In spectroscopically pure absolute ethanol from Consolidated Alcohol Limited.
(c) Data obtained from reference 40.
(d) In hexane.

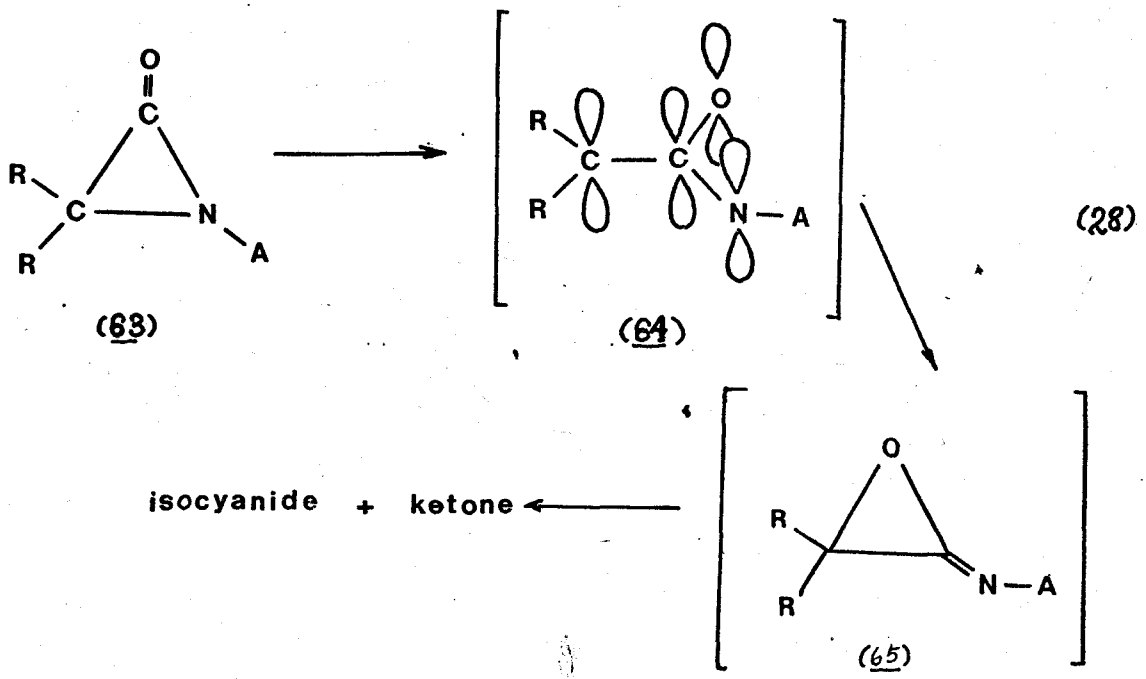
1,3,4-oxadiazoline system is essentially a semicyclic diene with extended conjugation in the cyclic portion; hence, a change in ring size with the elimination of nitrogen should affect the absorption chromophore to at least a small extent.

The thermolysis product, however, showed a more close agreement to the assigned β-lactam structure (49) which showed absorption maxima at 238 nm (log $\epsilon_{max}$ 3.98) and at 321 nm (log $\epsilon_{max}$ 4.33). A similar compound has been synthesised by Greenwald and Taylor[46,47] in 1968 although their synthetic route is quite different and their preparations do not include any ring-disubstituted members. For example, treatment of benzophenone chloracetylhydrazone (55) with sodium hydride or potassium t-butoxide gave a diazetidinone (56) as its cyclization product. This compound showed two strong ir absorption bands in the carbonyl region at 1740 and 1775 $cm^{-1}$. Its uv spectrum (ethanol) also showed a $\lambda_{max}$ at 245 nm (log $\epsilon$ = 4.230) and another one at 325 nm (log $\epsilon$ = 4.421).




(55) (56) (27)

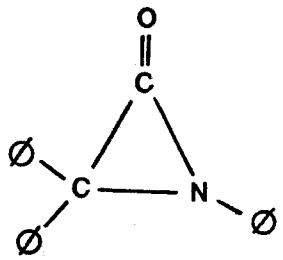
Although the spectral properties of the thermolysis product seemed to fit both (44) and (49), the latter seemed more likely on the basis of the thermal stability of that product. Imino-oxiranes, although required to account for products of α-lactam pyrolysis, have never been isolated. The mechanism for formation of isocyanides and ketones, as proposed by Sheehan[31,37] is formulated in the following equation. It appears that any



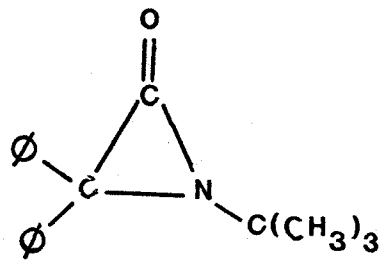

(28)

substituent R which promotes the formation of delocalized transition state (64) will favour the formation of imino-oxirane (65) from the α-lactam (63)[31,37]. Hence the α-lactam structure (57), which consists of three phenyl substituents capable of extending the delocalization and hence promoting the formation of

the delocalized transition state from the localized α-lactam structure is never isolated from reactions in which it is presumably formed while (58) can be isolated at lower temperatures[37].

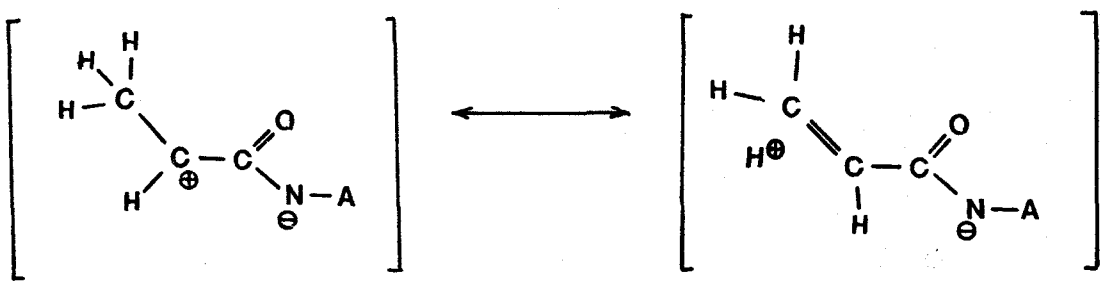


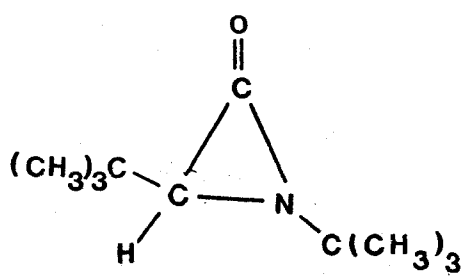
(57)



(58)

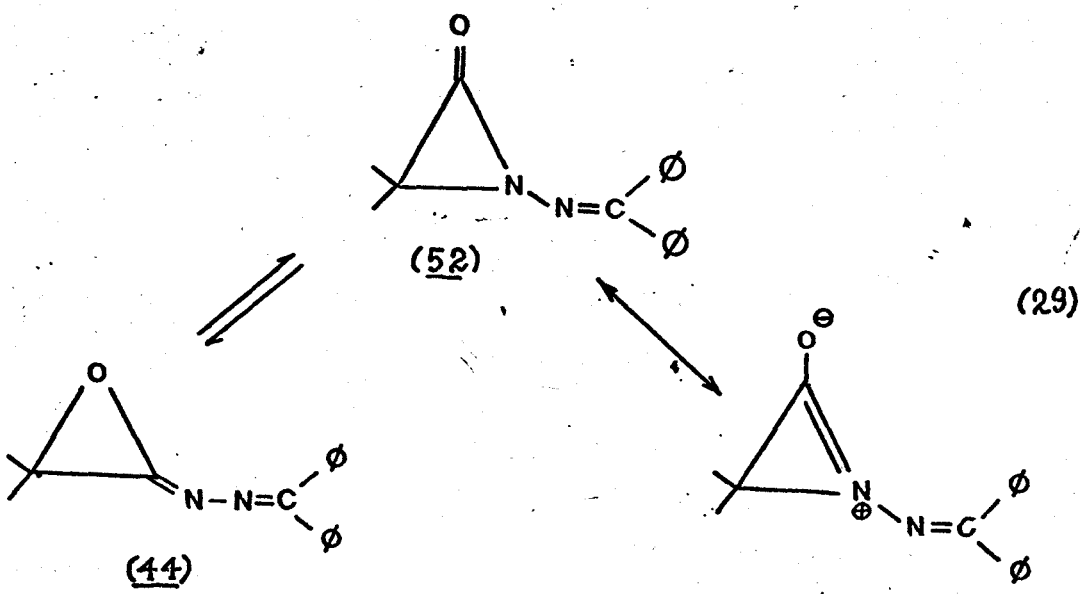
Similarly, when R equals methyl or methylene groups, where delocalization may be achieved only by hyperconjugation, α-lactam stability is relatively high. In the extreme case, when R equals t-butyl, where even hyperconjugation is unimportant, a very stable α-lactam (59) results.





(59)

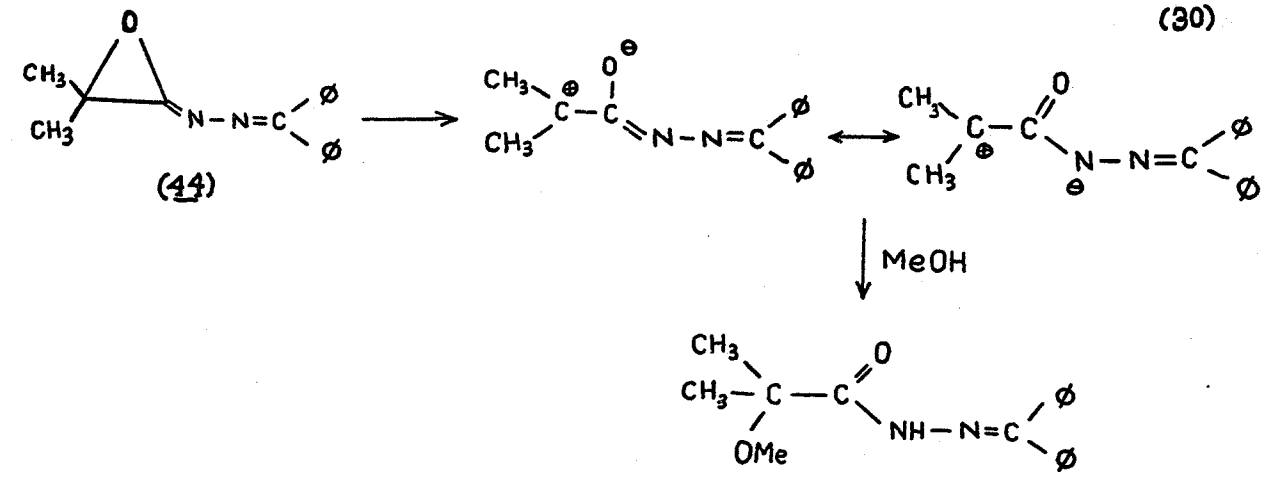
On the other hand, a substituent like $-N=C(C_6H_5)_2$ attached to α-lactam nitrogen might well destabilize it. The normal amide resonance of lactams, shown below, puts charge near that electron-withdrawing substituent. That unfavourable interaction could favour the imino-oxirane isomer at equilibrium. Therefore, (44) could not be firmly ruled out from consideration on the basis of the stability of the product under consideration.




(29)

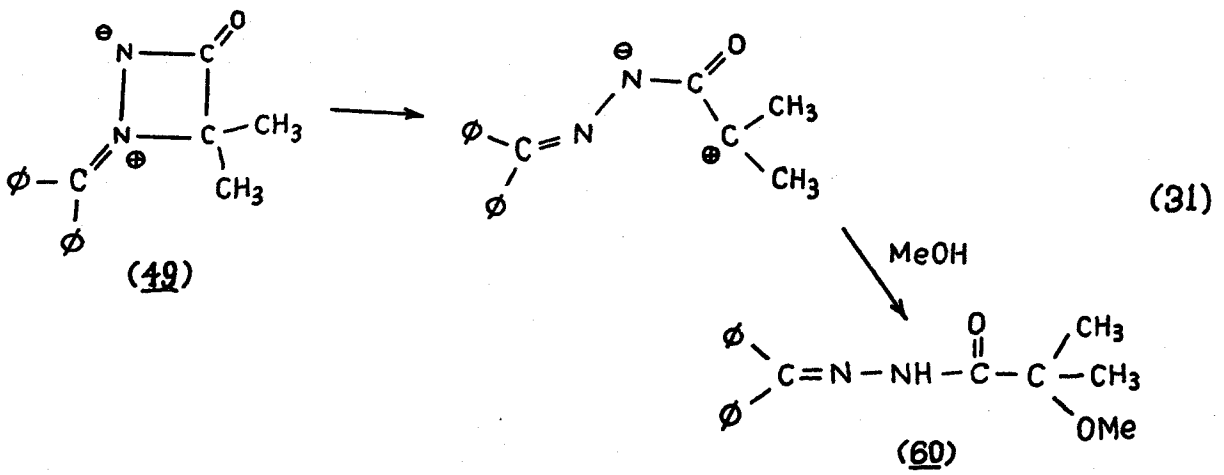
The chemical properties of the pyrolysis product were more informative. For example, the reaction of the above compound in methanol gave a product which is rigorously identified as 2-methoxy-2-methyl-N-(diphenylmethylenimino)-propionamide (60) by comparing its spectra with those of an authentic sample. The result is rather intricating since both structures (44) and (49) can give rise to the same acid amide (60) through two different but similar pathways

as shown in equations (30) and (31).



(30)

(44)

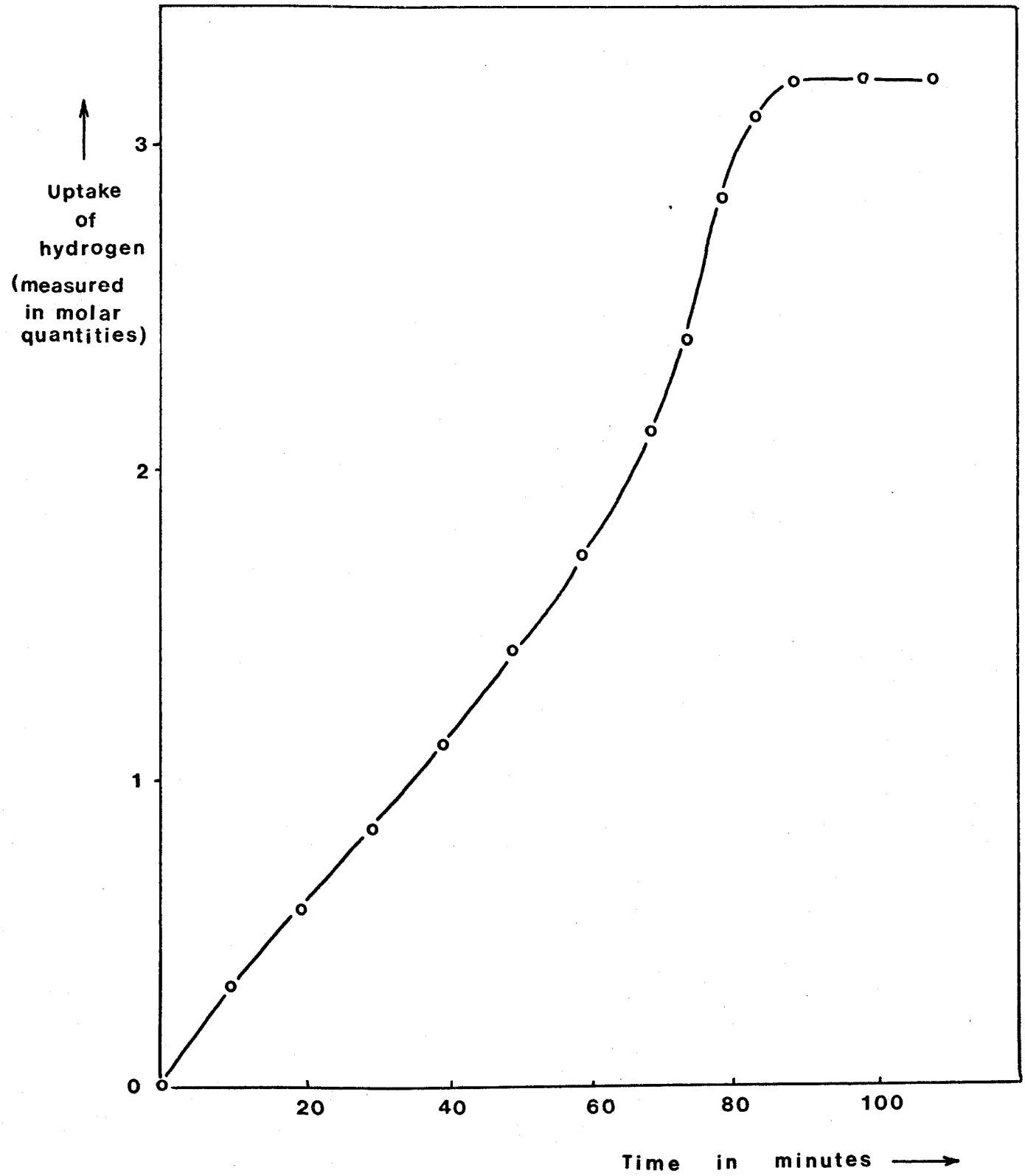


(31)

(49)

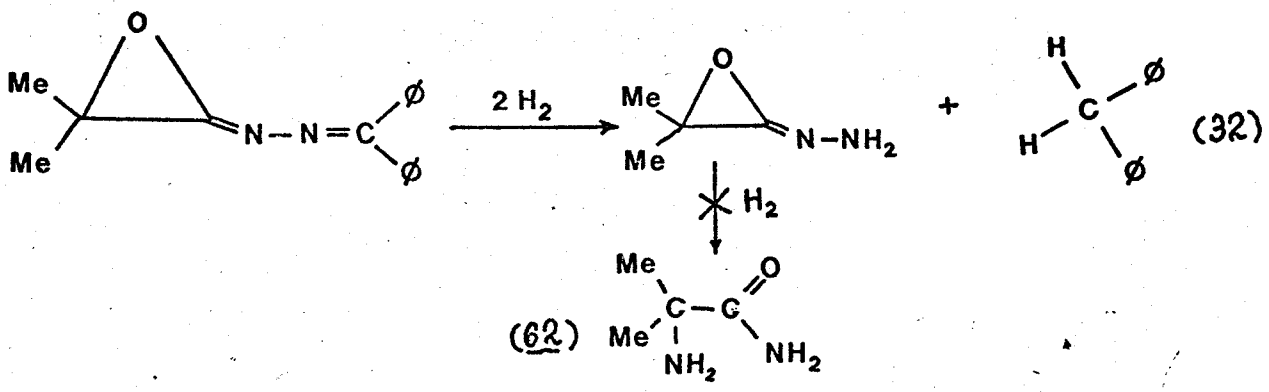
(60)

Hydrogenation of the pyrolysis product in ethanol with 10 % palladium-on-charcoal, however, gave diphenyl methane (61) and 2-amino-2-methyl-propionamide (62) as final products with a total consumption of three moles of hydrogen. The data for a typical run is represented in graph I. The imino-oxirane structure (44), although it can account for the formation of diphenyl methane (61), fails to explain the presence of 2-amino-2-methyl-propionamide (62).

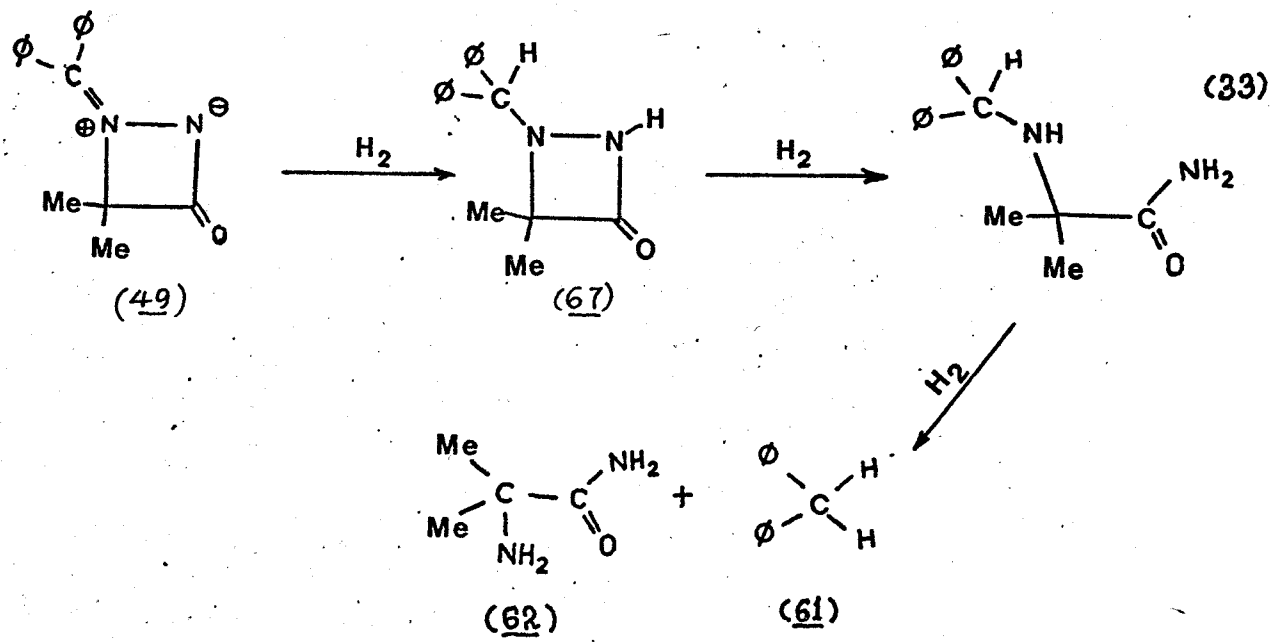



GRAPH I: Graph showing the rate of hydrogenation of 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) in ethanol.

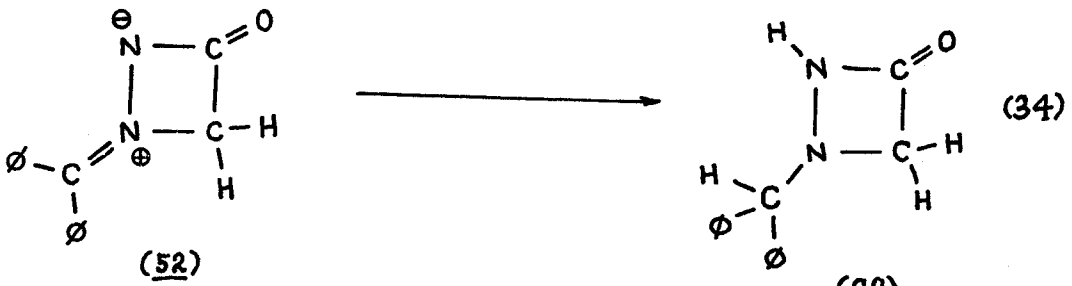
Thus, it appears that the chemical properties of the pyrolysis product can only be accommodated in terms of a β-lactam system (49). The β-lactam (49) probably first acquires a mole of hydrogen forming a dihydro compound (67), which in turn, will take up two moles of hydrogen with a subsequent ring opening and




hydrogenolysis giving diphenyl methane (61) and 2-amino-2-methyl-propionamide (62), equation (33). The abote mechanism is based on the mild reduction of 1-(diphenylmethylene)-3-oxo-1,2-diazetidinium

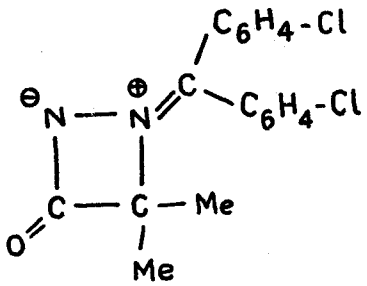


inner salt (52) with sodium borohydride in methanol observed by Taylor in 1968, from which he obtained a dihydro compound (68).[47]



(52) (68) (34)

An X-ray diffraction study of a dichloro-substituted pyrolysis product, i.e. 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (69) was done by Calvo and coworkers in 1972[48]. The results are summarized in Fig. II. The methylene-



(69)

oxo-azetidinium moiety is completely planar with a C(8) - N(15) and a C(18) - O(19) bond length of 1.31 Å and 1.21 Å, respectively. The bond angle of 80.1° at C(16) is relatively small for a $sp^3$

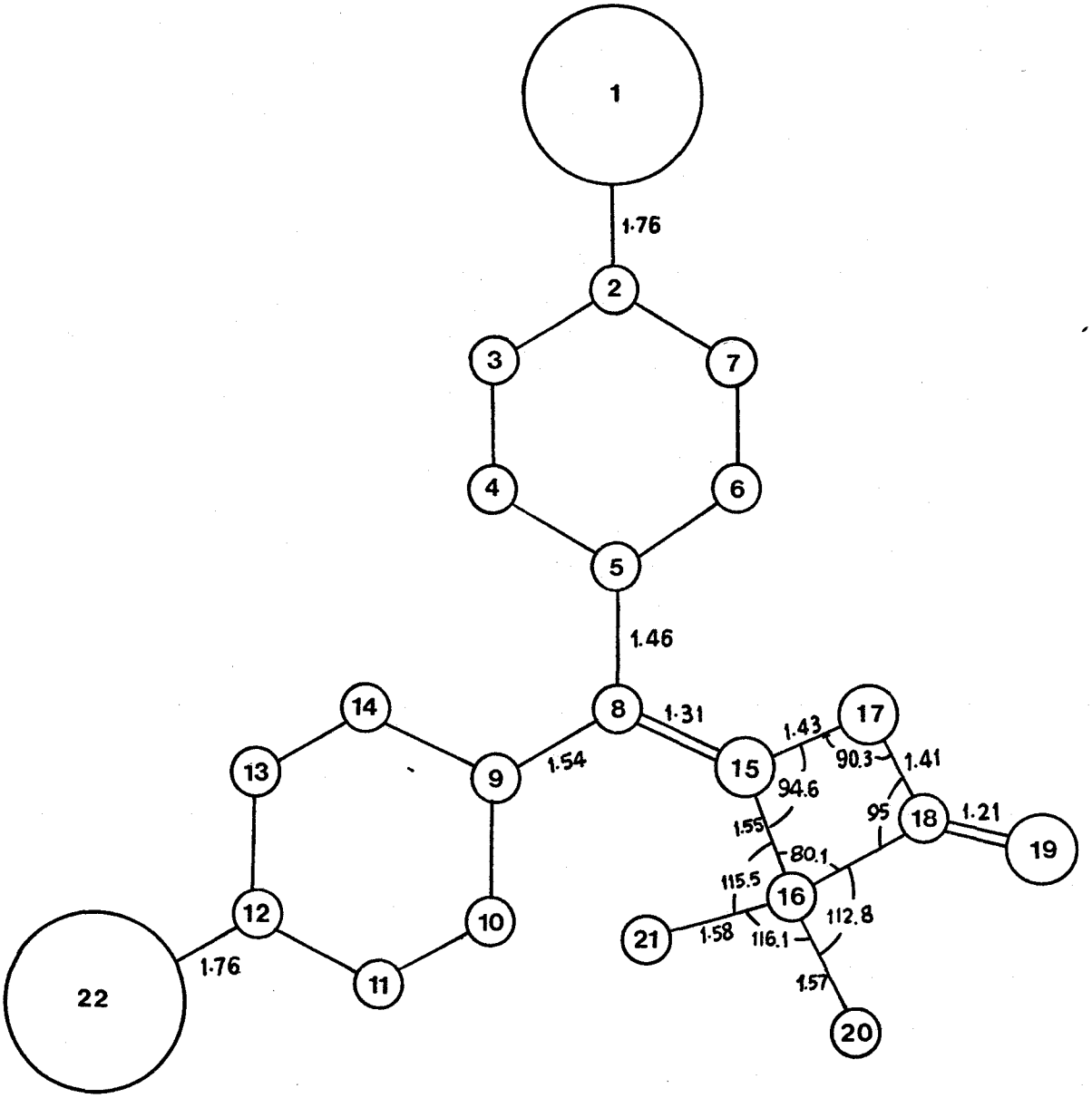
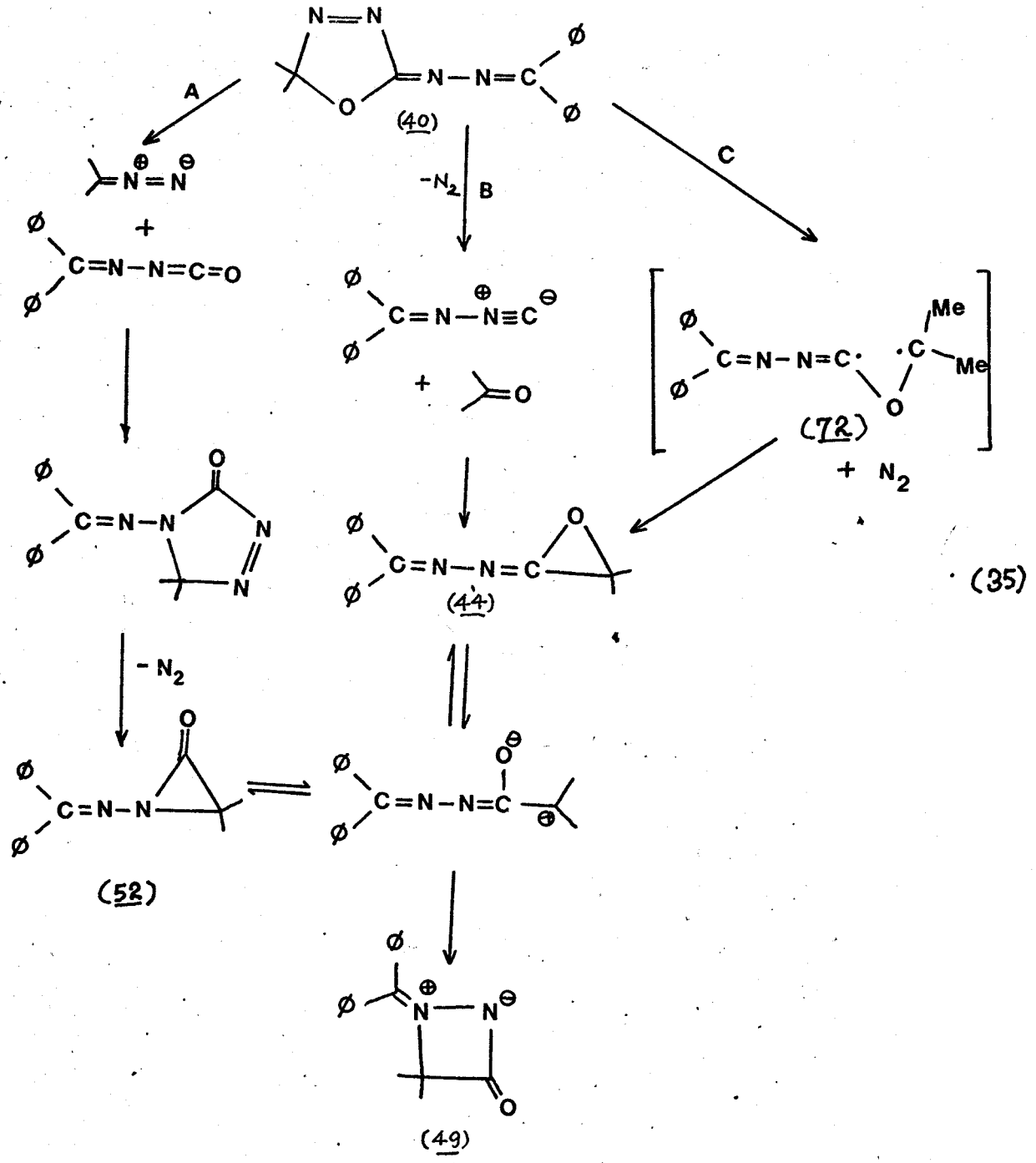



FIG. II : Structure of 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt by X-ray diffraction.[48]

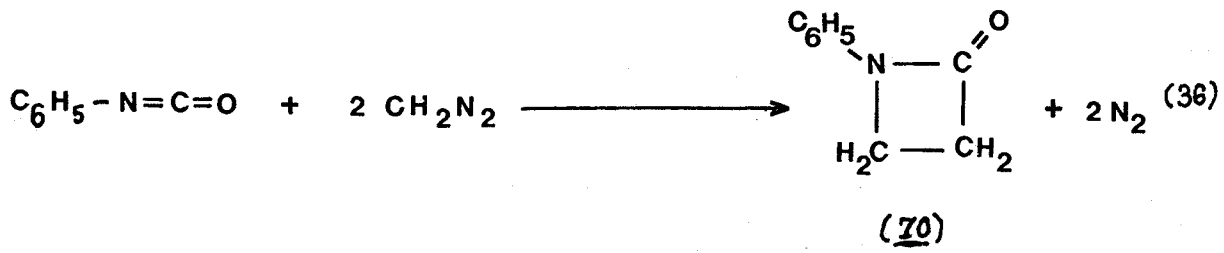
carbon. However, this is to be expected in a highly strained four member ring system where we would normally expect the $sp^2$ carbon (18) and nitrogen (15) to have a greater share of the allowed angles.

The thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (39) in vacuum at 130°, as mentioned on page 19, gave nitrogen and the stable 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) as final products together with a slight amount of acetone and a trace amount of imino-isocyanate which was detected only by infrared spectroscopy. Accordingly, in order to explain the results, three mechanisms are considered, all of which involve the intermediacy of the imino-oxirane (44) and the α-lactam (52). Those intermediates are assumed to be unstable at this high temperature; undergoing subsequent ring opening and closing, giving the aza-β-butyrolactam (49) as the final product, (equation (35)).

The first pathway is not a well known process. It involves the addition of diazomethane onto the N-diphenylmethylenimino-isocyanate (41) which is formed as an initial product. However, it has been shown by Sheehan and Izzo[50] that diazomethane adds to isocyanates in a 2:1 ratio forming a lactam (70) in anaolgy to the formation of cyclobutanone from ketene and diazomethane. The fact that a 2:1 product was not found and the expected short lifetime of $(CH_3)_2C=\overset{+}{N}=\overline{N}$ at 130°, make path A unlikely.

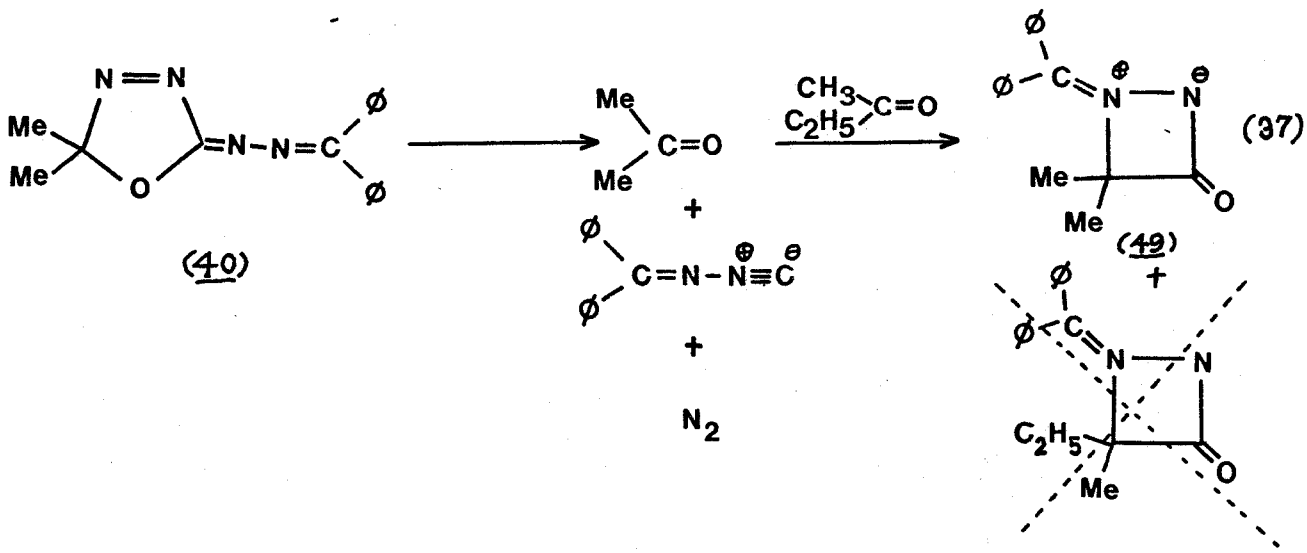


(35)



(70) (36)

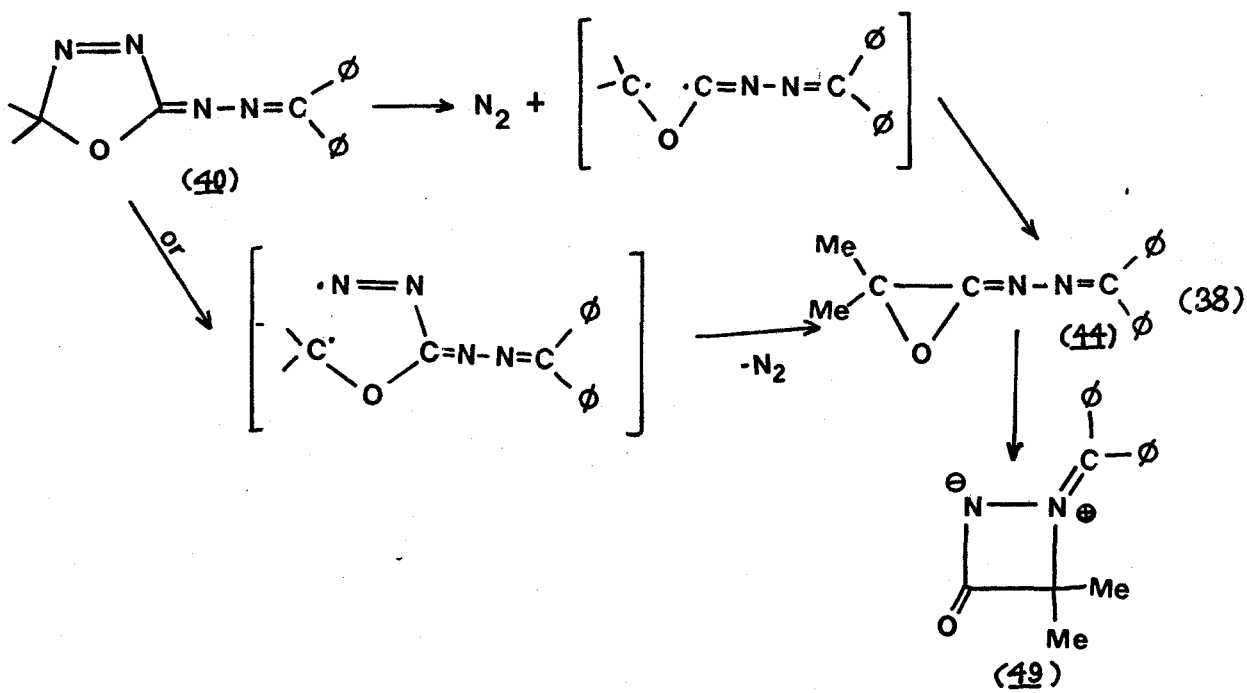
Pathway B, although it can account for the trace amount of acetone detected during the thermolysis process, was disproved experimentally from the fact that the thermolysis of the oxadiazoline (40) in 2-butanone still gave the aza-β-butyrolactam (49) but none of the corresponding compound (71) from capture of butanone. Thus, it appears that pathway C, which involves the biradical



(40) (49) (37)

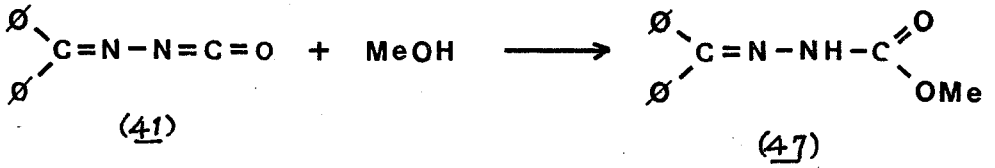
intermediate (72) from a direct loss of a nitrogen molecule is the most probable process. This mechanism is similar to that of West[20], (see page 6) who concluded that the thermolysis of

2-arylimino-5,5-dialkyl-$\Delta^3$-1,3,4-oxadiazolines actually occurs by two competing processes. One is the direct loss of nitrogen and the other is a retro-1,3-dipolar addition involving an isocyanate and a dialkyl-diazomethane. In vacuum or in a relatively non-polar solvent like chlorobenzene, the former decomposition predominates. The biradical formed may recombine rapidly giving an imino-oxirane (44) which subsequently rearranges to give a more stable aza-β-butyrolactam (49).



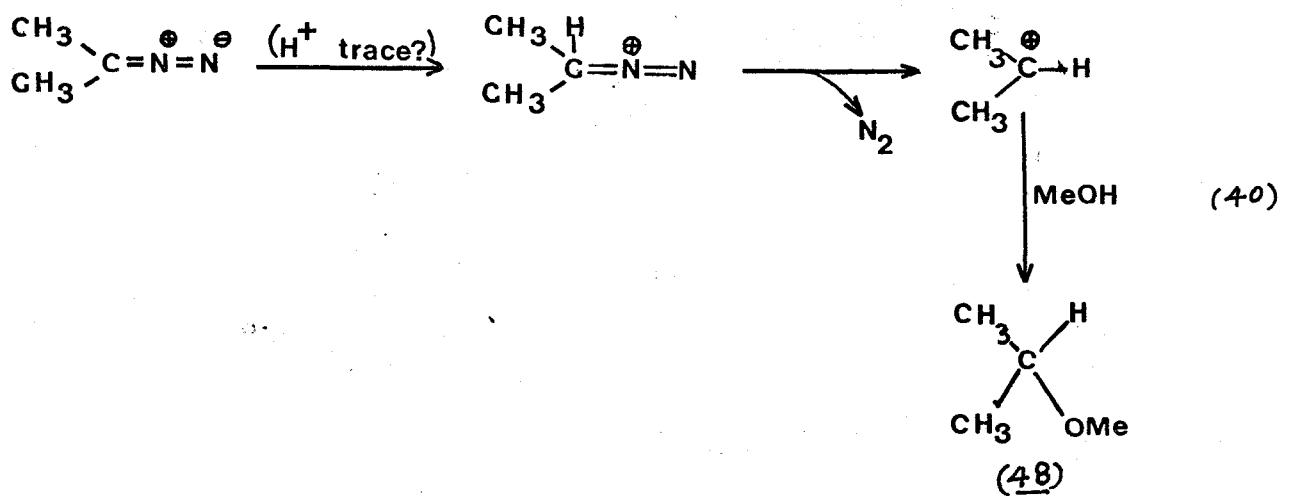

However, in a more polar solvent like methanol, the other pathway, which involves a retro-1,3-dipolar addition mechanism is expected to become more important. Reaction of N-diphenylmethylenimino-isocyanate (41) and methanol gives benzophenone

methyl carbazate (47) as the final product (see page 19).

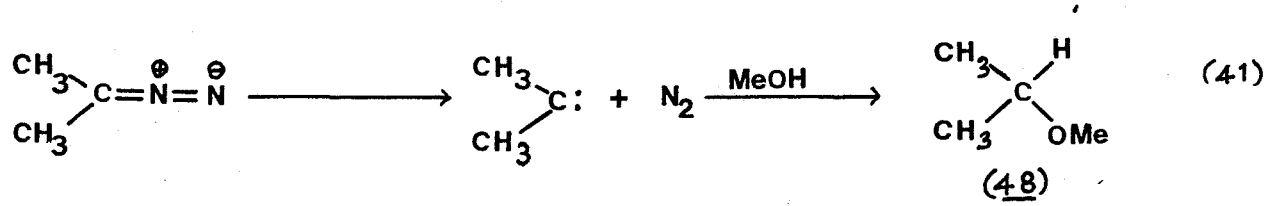


(41) (47) (39)

A further indication that the reaction mechanism in methanol is that of equation (39) was the finding that methyl isopropyl ether (48) was formed. Either a polar reaction involving isopropyl diazonium ion (equation (40)) or a carbene mechanism (equation (41)) could account for that product.

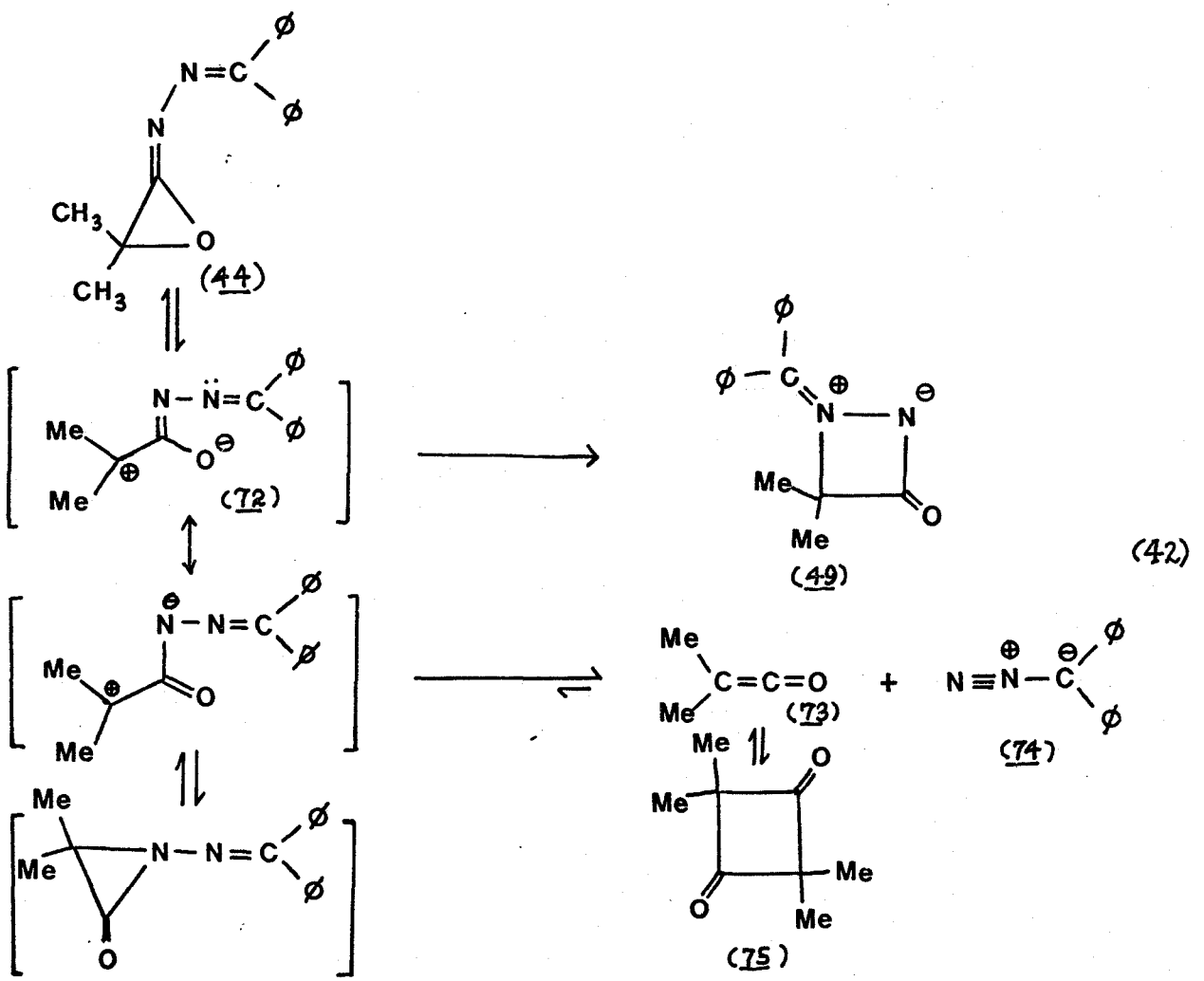


(40) (48)



(41) (48)

A detail concerning rearrangement of imino-oxirane (44) to aza-β-butyrolactam (49) is illustrated in equation (42). The question concerns possible fragmentation of intermediate (or product) to dimethyl ketene and diphenyldiazomethane.




(42)

The intermediate (72) is similar to that involved in polymerization of α-lactones to polyesters[45]. Its fragmentation to dimethyl ketene, during the thermolysis of (40) in vacuum should have been detectable, for some of the ketene should have distilled

to the cold trap where it would have been found as tetramethyl cyclobutanedione (75). The dione could not be detected among the products in the cold trap, suggesting that fragmentation of the zwitterionic intermediate (72) is unimportant relative to cyclization.

# CHAPTER III

# EXPERIMENTAL

## A. GENERAL

(i) Outline of experimental section.-

The experimental section is divided into three parts. The first part consists of the preparation of the $\Delta^3$-1,3,4-oxadiazolines. A modified procedure for the preparation of 2-(p,p'-dichlorodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline is also presented.

The second part is concerned with the thermolysis of the oxadiazolines in vacuum and in solvents. Attempts to identify the products and comparisons of their spectra with authentic samples which were synthesised independently are also described. Detailed experimental procedures are not repeated when these have already been given in cited literature.

A partial study of the possible routes of the decomposition makes up the last part of this section. Detailed procedures in X-ray diffraction studies of the 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (69) will not be described.[48]

(ii) Chromatography.-

Column chromatography was on aluminum oxide, neutral, 0540 (Baker Chemical Co., Phillisburg). Preparative vapor phase chromatography (vpc) was performed on a Varian-Aerograph Model

A90-P3 equipped with a thermal conductivity detector. A helium flow rate of approximately 60 ml/min was used with a 20 % SE30, 60/80 mesh, Chromosorb W column.

(iii) Spectra and others.-

Nuclear magnetic resonance (nmr) spectra were routinely run on a Varian A-60 instrument; carbon tetrachloride or deuterated chloroform was the usual solvent, with tetramethylsilane as internal standard. Chemical shifts are given in parts per million (ppm) downfield from the standard.

Infrared spectra were recorded with a Beckman IR-5 or a Perkin-Elmer Model 337 instrument. In all cases carbon tetrachloride solutions were used.

Ultraviolet (uv) spectra were recorded on a Cary 14 spectrophotometer; spectroscopically pure absolute ethanol from Consolidated Alcohol Limited was the solvent.

Mass spectra were obtained using a Hitachi Perkin-Elmer RMU 6A instrument.

Microanalysis and vaporimetric molecular weight measurements were performed by Geller Laboratories, N.J.,07548. Other analysis were done by Microanalysis Laboratories Limited, Toronto 180, Ontario.

Melting points were determined using a Thomas Hoover 'Unimelt' capillary melting point apparatus and are given uncorrected in Centigrade degrees.

(iv) Solvents and reagents used in synthesis and reactions.-

a). Solvents:

1). chlorobenzene - Fisher Scientific Co., reagent.

2). chloroform - Mallinckrodt Chem. Works Ltd., reagent.

3). ethanol - unless otherwise specified, 99.5 % absolute ethanol was used.

4). methanol - methyl alcohol absolute, Baker and Adamson, reagent.

5). methylene chloride - The McArthur Chemical Co. Ltd., reagent.

6). petroleum ether - Mallinckrodt Chem. Works Ltd., analytical reagent.

b). Reagents:

1). acetic acid - CIL reagent.

2). acetic anhydride - Mallinckrodt analytical reagent.

3). acetone - Mallinckrodt analytical reagent

4). aluminum chloride - Fisher Scientific Co., practical.

5). benzophenone - Fisher Scientific Co., practical.

6). benzoyl chloride - Eastman Chem Corp., practical.

7). 4-bromo-benzoic acid - British Drug Houses Ltd., reagent.

8). calcium chloride anhydrous - Baker and Adamson, reagent.

9). carbon disulfide - Baker and Adamson, reagent.

10). 4,4'-dichlorobenzophenone - Eastman Chem Corp., practical.

11). diethyl carbonate - Baker and Adamson, reagent.

12). dimethyl carbonate - Eastman Chem Corp., practical.

13). hydrazine hydrate (95 %) - Baker and Adamson, reagent.

14). isobutyric acid - Fisher Scientific Co., reagent.

15). lead oxide - Baker and Adamson, reagent.

16). methyl ethyl ketone (2-butanone) - Eastman Chem Corp., reagent.

17). palladium on charcoal (10 %) - Matheson Coleman and Bell.

18). 1,1,1-trichloro-2-methyl-2-propanol - Eastman Chem Corp., practical.

19). sodium bicarbonate - McArthur Chemical Co. Ltd., reagent.

20). sulfuric acid - CIL reagent.

21), thionyl chloride - British Drug House Ltd., reagent.

B. PREPARATION OF 2-DIPHENYLMETHYLENEHYDRAZONO-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE:

(i) Preparation of carbohydrazide.-

The experimental procedure as outlined by West[23] was employed. Since 99 percent hydrazine hydrate gave only a relatively low yield (57 %) of carbohydrazide compared with a 86.5 percent when 85 % hydrazine hydrate was used, 95 % hydrazine hydrate, which was available at the time of the experiment, was diluted to 85 % before use.

A mixture of 67 g (1.99 mol) 95 % hydrazine hydrate in 8 g of water and 45 g (0.42 mol) of diethylcarbonate was refluxed on a steam bath for 48 hours. The resulting solution was evaporated to dryness under reduced pressure. The white solid left was crystallized from 1500 ml of ethanol. Crystals separated in large, white monoclinic forms had a melting point range 154-156° (lit.[51] mp 154°). The yield was 30.7 g (81.2 %).

(ii) Preparation of benzophenone-4-aminosemicarbazone.-

A solution of 7.3 g (0.082 mol) of carbohydrazide and 41 g (0.328 mol) of benzophenone in 100 ml of alcohol and 50 ml water was refluxed for 6 hours. Benzophenone-4-aminosemicarbazone gradually deposited. The crystals were washed with cold alcohol and warm water. Recrystallizing from alcohol gave 15.7 g of glistening, diamond shaped plates (yield 75.2 %) mp 223-224°.

(iii) Preparation of 1-diphenylmethylene-5-isopropylidene

carbohydrazide.-

Benzophenone 4-aminosemicarbazone (12.0 g, 47.2 mmol) and 900 ml acetone was refluxed on a steam bath for 4 hours. The 4-aminosemicarbazone first remain undissolved and then gradually disappeared after two hours. On cooling, white needles of 1-diphenylmethylene-5-isopropylidene carbohydrazide began to separate. The crystals were filtered by suction and were recrystallized from acetone. The yield was 18.6 g (61.8 %), mp 204-206° (lit.[23] mp 200-202°).

(iv) Preparation of lead tetracetate.-

Lead tetracetate can be obtained from Matheson, Coleman and Bell as a reagent. However, it can also be conveniently prepared in the laboratory on a large scale.

A mixture of 500 ml of acetic acid and 335 ml acetic anhydride was heated to 60° in a three necked flask fitted with a mechanical stirrer. Lead oxide (585 g, 0.86 mol) was added in portions of 20g. Fresh additions were made only when the red coloration had mostly disappeared. The temperature was kept constant between 60 to 80° and the solution was cooled with ice after the addition was completed. Large lumps of off-white crystals began to separate. After filtration the crude product was redissolved in hot acetic acid and clarified with decolorizing charcoal (Mallinckrodt Chem. Works Ltd.). The resulting solution was filtered hot. Cooling of the acetic acid solution gave 256 g (67 %, colorless crystals)

of lead tetraacetate.

The above compound can be moistened with acetic anhydride and stored in a screw-capped bottle without hydrolysis. Acetic acid can be removed by washing with petroleum ether. However, in the process of oxidative cyclization of carbonyl compound derivatives, the presence of acetic acid will do no harm to the reaction.

(v) Cyclization of 1-diphenylmethylene-5-isopropylidene carbohydrazide.-

The oxidative cyclization method of carbonyl compound derivatives as done by Warkentin and West[40,52] was employed.

A solution of 23.9 g (53.8 mmol) of lead tetraacetate in 250 ml of methylene chloride was cooled to $0^{\circ}$ in a three necked flask fitted with a mechanical stirrer and a dropping funnel. Nitrogen was bubbled through the solution to purge the vessel during the dropwise addition of the 1-diphenylmethylene-5-isopropylidene carbohydrazide (8.6 g, 29.2 mmol) in 50 ml methylene chloride. Addition was complete after 15 min. The stirring was allowed to continue for another 20 minutes before 40 ml of ice water was added to the mixture. The dark brown slurry was filtered through celite (Johns-Manville Production) and the yellow methylene chloride layer was washed three times with equal volumes of water, once with saturated sodium bicarbonate and thrice more with water before drying with anhydrous magnesium sulfate. The methylene chloride was evaporated under reduced pressure leaving a yellow oil that

solidified immediately on addition of petroleum ether. Crystallization from approximately 1500 ml of petroleum ether gave 6.65 g (78 % yield) of pale yellow, fine, needle-like crystals of oxadiazoline (40), mp 110-112° (no decomposition).

This compound showed a singlet at 1.65$\delta$ (6H), and a multiplet at 7.80-7.20$\delta$ (10H) in its nmr spectrum ($CDCl_3$). Its ir spectrum showed a sharp intense absorption at 1675 $cm^{-1}$ ($CHCl_3$).

C. PREPARATION OF 2-(p,p'-DICHLORODIPHENYLMETHYLENEHYDRAZONO)-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE:

(i) Preparation of p,p'-dichlorobenzophenone.-

p,p'-Dichlorobenzophenone can be obtained from Eastman Chem Corp. as a reagent. It can also be prepared by the Grignard reaction of p-$ClC_6H_4MgCl$ on carbon tetrachloride in tetrahydrofuran solution[53] or by the Friedel-Crafts reaction of carbon tetrachloride and chlorobenzene in the presence of $AlCl_3$[54,23] with a subsequent hydrolysis of the intermediate bis(chlorophenyl)dichloromethanes. The p,p'-dichlorobenzophenone obtained by the latter method had a mp 149-150°.

(ii) Preparation of p,p'-dichlorobenzophenone-4-aminosemicarbazone.-

The reaction of carbohydrazide and p,p'-dichlorobenzophenone, like the corresponding reaction of carbohydrazide and benzophenone, is very sluggish. Pure alcohol dissolves only the p,p'-dichlorobenzophenone but very little carbohydrazide whereas too high a water concentration in alcohol will render dichlorobenzophenone to be insoluble. Only a 7:3 ratio of alcohol to water will allow an optimum concentration of both reagents to make the reaction proceed smoothly.

p,p'-Dichlorobenzophenone (18.5 g, 0.0735 mol, mp 145°) and 13.2 g (0.147 mol) carbohydrazide (mp 155°) was dissolved in 350 ml alcohol and 150 ml water. Acetic acid (1 ml) was added to the

mixture and the solution was refluxed on a steam bath for 40 hours. White crystals began to separate off on cooling. Crystallization from chloroform gave 10.3 g (43.3 % yield) of p,p'-dichlorobenzophenone-4-aminosemicarbazone, mp 197-198°.

The nmr spectrum ($CDCl_3$) showed a multiplet at 7.77-7.23$\delta$ with no other absorptions. Its ir ($CHCl_3$) spectrum showed sharp absorptions at 3350 $cm^{-1}$ and 3448 $cm^{-1}$, and a strong absorption at 1700 $cm^{-1}$.

(iii) Preparation of 1-(bis-p-chlorophenyl)methylene-5-isopropylidene carbohydrazide.-

A solution of 8.3 g (0.0257 mol) of p,p'-dichlorobenzophenone-4-aminosemicarbazone in 600 ml acetone was heated under reflux on a steam bath. The solution turned chalky after 10 minutes. The reaction vessel was heated for another 8 hours before the product, which was insoluble in acetone, was collected as a fine white powder, mp 240° (sharp). The yield was 8.7 g (93.5 %).

The above compound was insoluble in chloroform, acetone and dioxane; slightly soluble in methylene chloride, but moderately soluble in acetic acid.

(iv) Cyclization of 1-(bis-p-chlorophenyl)methylene-5-isopropylidene carbohydrazide.-

The oxidative cyclization procedure was similar to that previously described on page 48. Since 1-(bis-p-chlorophenyl) methylene-5-isopropylidene carbohydrazide was only sparingly

soluble in methylene chloride, a 1:1 mixture of acetic acid and methylene chloride was employed as the solvent. This mixture of solvents will not freeze at 0°.

A solution of 7.0 g (19.3 mmol) of 1-(bis-p-chlorophenyl) methylene-5-isopropylidene carbohydrazide in 70 ml of glacial acetic acid was added over 15 minutes to a solution of 45 g (0.103 mol) of lead tetraacetate in 70 ml of methylene chloride previously cooled to 0°. No precipitation of lead diacetate was observed after 4 hours. The temperature of the reaction vessel was allowed to rise to 25°. Precipitation of lead diacetate began to occur after 30 minutes. The mixture was allowed to react further for 10 hours at 25° before quenching with 70 ml of distilled water. A total volume of 70 ml of methylene chloride was added regularly during the reaction period to compensate for the solvent lost by evaporation. The solution was filtered through celite and the faint yellow methylene chloride layer was washed three times with 70 ml portions of distilled water, once with saturated sodium bicarbonate and then thrice with water before drying with anhydrous magnesium sulfate. Evaporation of the dried methylene chloride solution gave 4.9 g of a yellow solid which was dissolved in 350 ml of low boiling petroleum ether. Cooling of the petroleum ether solution after concentrating to 80 ml gave 4.0 g (57.5 % yield) of 2-(p,p'-dichlorodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (mp 143-45° with decomposition).

The above compound, which is very soluble in methylene chloride, chloroform and chlorobenzene, absorbs in the infrared region ($CHCl_3$) at 1655 $cm^{-1}$. Its nmr spectrum ($CDCl_3$) showed multiplets at 7.13-7.73$\delta$ (8H) and a singlet at 1.67$\delta$ (6H).

D. PREPARATION OF 2-(p,p'-DIBROMO-DIPHENYMETHYLENEHYDRAZONO)-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE:

(i) Preparation of p,p'-dibromobenzophenone.-

p,p'-Dibromobenzophenone can be prepared by Friedel-Crafts acylation reaction[55]. A solution of 29 g (0.144 mol) of 4-bromobenzoic acid and 250 ml (large excess) of thionyl chloride was refluxed over a steam bath for 12 hours. The excess thionyl chloride was vacuum distilled and the white solid left, mostly 4-bromobenzoyl chloride (mp 41°, lit.[56] 42°), was dissolved in 500 ml bromobenzene without further purification. $AlCl_3$ (27 g) was added in small portions at intervals of 20 minutes and stirred rapidly at room temperature. The solution turned green in 15 minutes and eventually darkened to nearly black in color. The reaction was allowed to go on for another half an hour at room temperature before it was heated over a steam bath with vigorous stirring. Fumes of HCl evolved rapidly on heating. After twelve hours, the $AlCl_3$ was destroyed by slowly adding 200 g of ice. The solution gradually turned into a thick white paste with evolution of heat. Benzene (200 ml) was added to extract the products. The organic layer was washed two times with water, twice with sodium bicarbonate and twice more with distilled water. The solution was evaporated to 250 ml under reduced pressure at a temperature of 100°. On cooling, white shinning plates of p,p'-dibromobenzophenone separated. The compound, after washing with petroleum ether, had mp 173° (lit.[60] 175°). The yield was 22.4 g (45.8 %)

(ii) Preparation of 1-(p,p'-dibromobenzophenone)-4-aminosemicarbazone.-

Carbohydrazide (27.5 g, 0.305 mol) and 16 g (0.048 mol) p,p'-dibromobenzophenone was dissolved in a mixture of 1050 ml alcohol and 450 ml water and was refluxed for 12 hours. The mother liquor was concentrated to 500 ml whereupon 20 g of a mixture of 1-(p,p'-dibromobenzophenone)-4-aminosemicarbazone and carbohydrazide separated. Recrystallization from water gave 6.1 g (30.7 % yield) of 1-(p,p'-dibromobenzophenone)-4-aminosemicarbazone, mp 212-14°.

The nmr spectrum ($CDCl_3$) showed multiplets at 7.07-7.80 $\delta$ (8H) and a broad singlet at 3.78 $\delta$ (2H). Its ir ($CHCl_3$) spectrum showed two sharp absorptions at 3340 $cm^{-1}$ and 3440 $cm^{-1}$, and a strong absorption at 1700 $cm^{-1}$.

(iii) Preparation of 1-(bis-p-bromophenyl)methylene-5-isopropylidene carbohydrazide.-

A solution of 6.0 g (1.45 mmol) 1-(p,p'-dibromobenzophenone)-4-aminosemicarbazone in acetone (2500 ml) was refluxed for 24 hours. Evaporation of the solvent to 700 ml yielded 4.0 g of 1-(bis-p-bromophenyl)methylene-5-isopropylidene carbohydrazide on cooling, mp 236° (sharp).

(iv) Cyclization of 1-(bis-p-bromophenyl)methylene-5-isopropylidene carbohydrazide.-

The title compound (4.0 g) in 2000 ml methylene chloride was slowly added to 30 g lead tetraacetate in 50 ml methylene chloride

at room temperature with vigorous stirring. White precipitates of lead diacetate appeared after 5 minutes. The reaction was allowed to go on further for 10 hours before the excess LTA was destroyed by quenching with 500 ml of water. The dark slurry was filtered through celite and the yellow methylene chloride layer was washed thrice with 300 ml of water, once with saturated sodium bicarbonate solution and then thrice with water. The resulting yellow solution, after being dried over anhydrous magnesium sulfate, was evaporated to dryness. Crystallization from petroleum ether gave 3.1 g (77 % yield) of 2-(p,p'-dibromodiphenylmethylenehydrozono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline as yellow needles, mp 173-174° (with decomposition).

The nmr spectrum ($CDCl_3$) showed a singlet at 1.65$\delta$ (6H) and multiplets from 6.97$\delta$ to 7.58$\delta$ (8H). Its ir spectrum showed a strong absorption band at 1655 $cm^{-1}$.

E. THERMOLYSIS OF 2-DIPHENYLMETHYLENEHYDRAZONO-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE:

A light yellow solution of 0.1445 g (0.495 mmol) of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (mp 110-112°) in 3.6 ml methanol was vacuum sealed in a thick walled glass bomb having a total internal volume of approximately 10 c.c. The reaction vessel was immersed in an oil bath previously adjusted to 129-130°. The color of the solution slowly turned to a deep yellow after six hours without any other observable changes.

The partial pressure of the products formed was reduced by cooling the glass bomb with liquid nitrogen before breaking off the seal. The deep yellow solution was transfered to a screw-capped bottle after it was left standing to room temperature. The nmr spectrum (MeOH) of the crude product showed a doublet at 1.03-1.14$\delta$ (methyl isopropyl ether), a singlet at 3.75$\delta$ and a multiplet at 7.30-7.80$\delta$ (benzophenone methyl carbazate). The other peaks of the above compounds were superimposed by the side-bands of the solvent.

The vpc of the crude product was run on a 20% SE 30, 60/80 mesh Chromosorb W column with a helium flow rate of approximately 60 ml/min. at 90°. The peaks occured at the same retention times as those in a chromatogram of an authentic sample of methyl isopropyl ether and acetone. The benzophenone methyl carbazate, which has a melting point of 120-121° [57], remained in the column.

Benzophenone methyl carbazate can be isolated easily from the

crude product as the crystalline solid. The product that was left after thermolysis was evaporated to dryness to get rid of methanol and other volatile materials. The yellow lump of solid left was crystallized from aqueous ethanol to give 72.3 mg (58% yield) of benzophenone methyl carbazate (mp 119-120.5°). Anal. calcd. for $C_{15}H_{14}N_2O_2$: C,70.80; H, 5.52; N, 11.02; O, 12.60. Found: C, 70.91; H, 5.47; N, 10.97.

Isolation of methyl isopropyl ether was not achieved due to the trace amount of that compound formed.

(i) Preparation of benzophenone methyl carbazate.-

Methyl carbazate was prepared by the standard procedure of Diels[57]. The reaction of 7.0 g of dimethyl carbonate and 1.5 equivalents of 64 % hydrazine hydrate in methanol gave, after cooling, filtering, and crystallization from methanol, 4.3 g (61 % yield) of methyl carbazate as a glistening white solid, mp 73-74°, lit.[57] mp 75°.

Methyl carbazate (3.2 g, 0.356 mol) and 7.5 g (0.412 mol) of benzophenone in 50 ml methanol was refluxed for 24 hours. Evaporation of the resulting solution gave a yellow solid which was washed with plenty of petroleum ether. Excess benzophenone, which was very soluble in petroleum ether, was mostly removed. Crystallization from petroleum ether-ether gave 3.7 g (40.9 % yield) of benzophenone methyl carbazate as white crystals.

Its nmr spectrum ($CCl_4$) showed a singlet at 3.75$\delta$ (3H) and

multiplets from 7.20 to 7.77$\delta$ (10H). The ir spectrum showed a sharp N - H absorption at 3360 $cm^{-1}$, and two strong bands at 1625 and 1655 $cm^{-1}$.

(ii) Preparation of methyl isopropyl ether.-

Methyl isopropyl ether was prepared by the method of Wirth[58]. Sodium methylate (8.4 g, 0.156 mol) and 15.0 g (0.122 mol) of 2-bromopropane in 30 ml methanol was refluxed over a steam bath for 3 hours. Sodium bromide slowly deposited as a white solid. Methyl isopropyl ether (3.3 g) containing a small amount of 2-bromopropane was obtained as a colorless distillate collected at a temperature of 60°. Its nmr spectrum, $\delta$ = 3.15-3.65 (1H); $\delta$ = 3.20 (3H) and $\delta$ = 1.03-1.14 (6H), doublet, J = 60 Hz matched that of one component from the thermolysis of (40) in methanol.

F. THERMOLYSIS OF 2-DIPHENYLMETHYLENEHYDRAZONO-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE IN VACUUM:

The thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline was carried out in a pyrex tube (20 mm diameter) which was connected by a delivery tube to a cold trap cooled by liquid nitrogen. The delivery tube had a side arm leading to a vacuum line so that any volatile products that distilled during thermolysis could be collected in the trap. Heat was supplied by a heating coil wrapped externally around the large tube and the

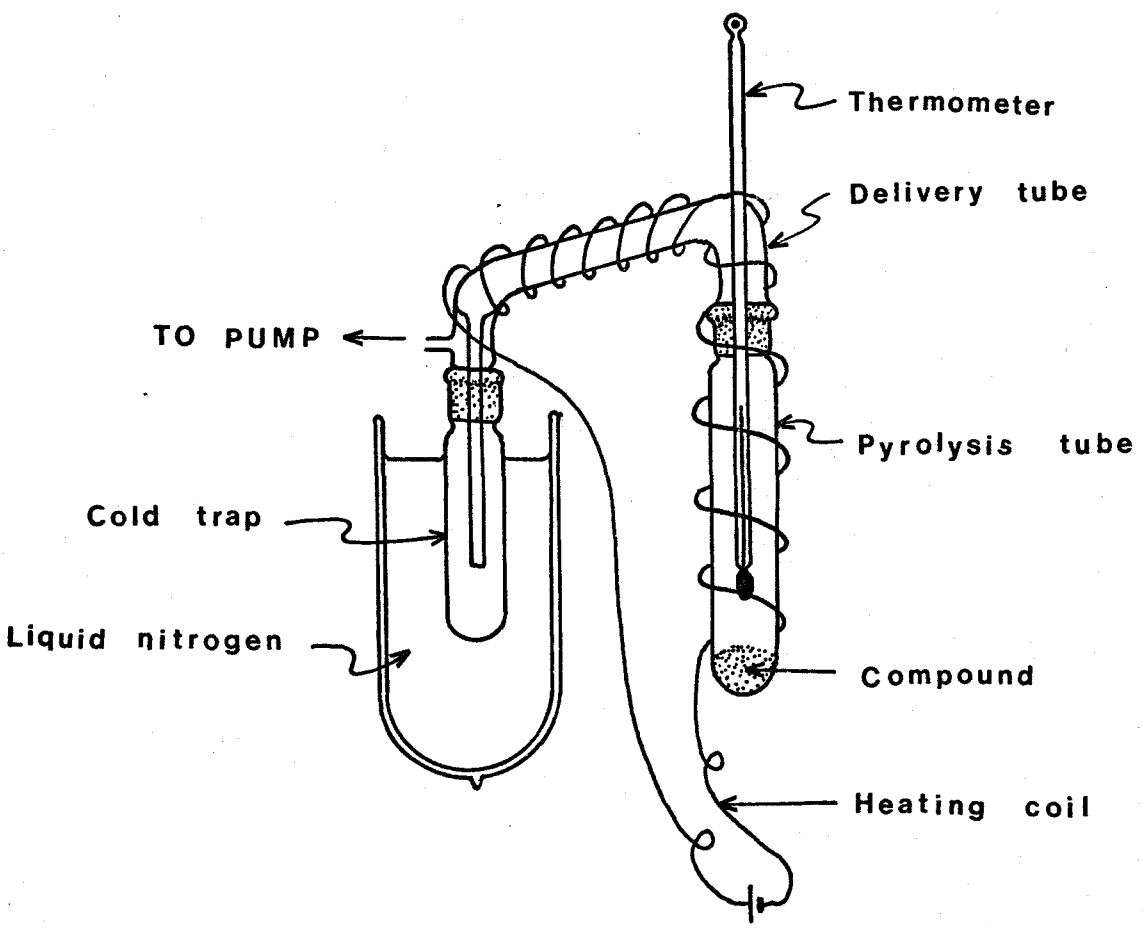



FIG. III : Apparatus for thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl -$\Delta^3$-1,3,4-oxadiazoline.

delivery tube. A thermometer was inserted between the coil and the pyrex tube to register the temperature during the thermolysis (Fig. III). A typical decomposition is described below.

2-Diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (1.85 g) was introduced into the pyrex tube before the apparatus was assembled. The vacuum pump was switched on when heating started. The temperature of the heating coil was adjusted by means of a rheostat which was calibrated to 130° before use. The oxadiazoline started to melt at 110° and it gradually turned darker at 120° as more and more bubbles were formed. A small amount of an orange liquid that distilled over at 130° was collected in the cold trap as a yellow solid. The heating was discontinued after four hours when no more bubbling was observed in the pyrex tube.

The infrared spectrum of the products collected in the cold trap taken immediately after the thermolysis showed no peaks near 2270 $cm^{-1}$ which might indicate the presence of an isocyanate. The nmr and ir spectra, however, indicated that it consisted of the undecomposed oxadiazoline with a small amount of unidentified products.

Thin layer chromatography of the crude products left in the pyrex tube after the pyrolysis showed one major component. Crystallization from carbon tetrachloride gave 0.612 g (33.1 % yield) of faint yellow orthorhombic crystals, mp 171-172.5°.

The mass spectrum of this new compound, which is later identi-

fied as 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49), showed a molecular peak at m/e 264. Its ir spectrum ($CCl_4$) showed a strong absorption at 1775 $cm^{-1}$. The uv spectrum (ethanol) showed a maximum at 238 mμ (log $\epsilon_{max}$ 3.975) and another band at 321 mμ (log $\epsilon_{max}$ 4.329). The $^1H$ nmr spectrum ($CDCl_3$) showed a singlet at 1.47δ (6H) and a multiplet from 8.13 to 7.30δ (10H). Anal. calcd. for $C_{17}H_{16}N_2O$, M. W. 264 : C, 77.27; H, 6.06; N, 10.61. Found: M. W. (vap.) 268; C, 77.22; H, 6.15; N, 10.65.

Thermolysis of the oxadiazoline (40) at higher temperatures (160°) gave essentially the same products as at lower temperatures. However, a trace amount of isocyanate which showed a characteristic peak at 2255 $cm^{-1}$ in ir was detected among the volatile products.

G. THERMOLYSIS OF 2-(p,p'-DICHLORODIPHENYLMETHYLENEHYDRAZONO)-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE IN VACUUM:

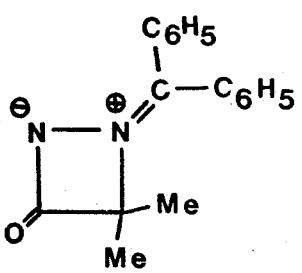
The thermolysis procedure of the above compound in vacuum was similar to that outlined on page 60 except that the temperature was raised to 145°. From 0.804 g (2.22 mmol) of 2-(p,p'-dichlorodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline was obtained a dark brown residue from which 0.267 g (36.2 % yield) of 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (69) was isolated by crystallization from acetone-water, mp 200-201°.

The above compound (69) show a strong absorption at 1775 $cm^{-1}$ in the infrared spectrum. The nmr spectrum ($CDCl_3$) showed a singlet at 1.52$\delta$ (6H) and multiplets from 7.32-8.10$\delta$ (8H). Anal. calcd. for $C_{17}H_{14}N_2OCl_2$, M. W. 333.21 : C, 61.27; H, 4.23; N, 8.41; Cl, 21.27. Found: C, 61.27; H, 4.26; N, 8.46; Cl, 20.98.

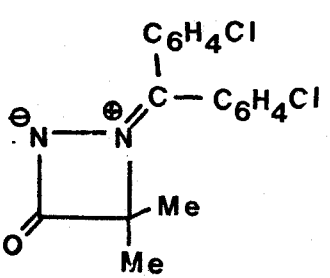
H. THERMOLYSIS OF 2-(p,p'-DIBROMODIPHENYLMETHYLENEHYDRAZONO)-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE IN VACUUM:

The thermolysis procedure of the above compound in vacuum was also similar to that outlined on page 60. The melting point temperature (174°) of the above compound was used. From 0.924 g (2.06 mmol) of 2-(p,p'-dibromodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline was obtained a dark red residue from which 0.341 g (34.7 %) of 1-(p,p'-dibromodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (76) was isolated by crystallization from acetone-water, mp 210-211°.

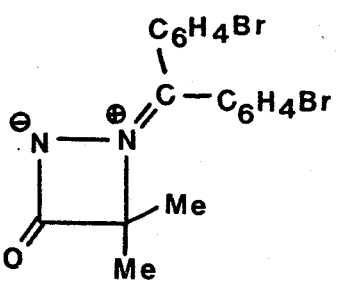
The above compound (76) also showed a strong absorption at 1775 $cm^{-1}$ in the infrared spectrum. The nmr spectrum ($CDCl_3$) showed a singlet at 1.47δ (6H) and multiplets from 7.02 to 7.77δ (8H).




(49)




(69)




(76)

I. THERMOLYSIS OF 1-(DIPHENYLMETHYLENE)-4,4-DIMETHYL-3-OXO-1,2-DIAZETIDINIUM INNER SALT (49) IN METHANOL :

The method employed was similar to the thermolysis of 5,5-dimethyl-2-diphenylmethylenehydrazone-$\Delta^3$-1,3,4-oxadiazoline in methanol as outlined on page 57. A yellow solution of 0.145 g of the $\beta$-aza-butyrolactam (49) in 2.20 ml methanol was vacuum sealed in a thick walled glass tube which was placed in a high pressure bomb containing methanol. The high pressure bomb was heated to 190° for 18 hours. The vapour pressure of the resulting solution, which was now light brown in color, was reduced by freezing the glass tube with liquid nitrogen before breaking off the seal. The excess methanol was removed by evaporating under reduced pressure at 60°. Crystallization from a mixture of petroleum ether and ether gave 0.043 g of a dull yellow powder, mp 125-126°. This compound, which showed a parent peak m/e 296 in its mass spectrum, was unambiguously identified as 2-methoxy-2-methyl-N-(diphenylmethylenimino)-propionamide (60) by comparing its mp, nmr, and ir spectrum with an authentic sample which was synthesised independently.

The nmr spectrum ($CCl_4$) of the above compound showed singlets at 1.30$\delta$(6H) and 2.97$\delta$(3H); multiplets from 7.13 to 7.70$\delta$. Its ir ($CCl_4$) showed an N-H peak at 3345 $cm^{-1}$, and a strong absorption at 1710 $cm^{-1}$. Its uv spectrum (ethanol) showed a maximum at 285 m$\mu$ (log $\varepsilon_{max}$ 4.43). The mass spectrum gave a molecular ion peak at m/e 296.

J. SYNTHESIS OF 2-METHOXY-2-METHYL-N-(DIPHENYLMETHYLENIMINO)-PROPIONAMIDE :

(i). Preparation of α-methoxy-isobutyric acid.-

α-Methoxy-isobutyric acid was prepared by the method of Weizmann[59]. However, fractional distillation of the products at a temperature of 98-99° (20mm) did not yield pure α-methoxy-isobutyric acid. Accordingly, a slight modification was made in the separation process.

To a cold solution of 31.6 g of potassium hydroxide in 17.6 ml of water and 70.5 ml of methyl alcohol contained in a three necked flask fitted with a dropping funnel, a condenser and a mechanical stirrer, a solution of 25.0 g of 1,1,1-trichloro-2-methyl-2-propanol (acetone - chloroform) in 49.5 ml of methanol was slowly added over a period of 5 hours. The violent reaction, which was accompanied by the precipitation of potassium chloride was checked occassionally by cooling with a freezing mixture of acetone and dry ice. The reaction was allowed to go on for forty-five minutes at room temperature and another two hours over a steam bath. The product, together with the potassium chloride formed after the reaction, was poured into 50 ml of ether, and extracted with 100 ml of water. The aqueous layer, which contained potassium chloride and the inorganic salt of the α-methoxy-isobutyric acid, was acidified with sulfuric acid and extracted with ether. Evaporation of the ethereal layer gave 8.0 g (40.8% yield) of α-methoxy-isobutyric acid as a colorless liquid. The nmr spectrum of the above compound (neat) showed singlets at 1.33 δ (6H) and 3.20 δ (3H).

(ii). Preparation of methyl-α-methoxy-isobutyrate [59].-

A solution of 8.0 g of α-methoxy-isobutyric acid in 8.5 ml of methanol and 1.7 ml of concentrated sulfuric acid was refluxed over a steam bath for twelve hours. All the remaining methanol was distilled off at atmospheric pressure after the reaction and the colorless residue was washed two times with double the volume of brine. The ester layer, after separating, was dried over anhydrous calcium chloride; yield 5.6 g (62.5%).

The nmr spectrum (neat) of the above compound showed singlets at 1.33δ(6H), 3.17δ(3H) and 3.67δ(3H).

(iii). Preparation α-methoxy-isobutyric acid hydrazide.-

A mixture of 2.95 g methyl-α-methoxy-isobutyrate and 1.55 g 99% hydrazine hydrate was refluxed over a steam bath for 5 hours. Extraction with ether failed to isolate the product required. Evaporation of the aqueous layer at 80° under reduced pressure gave 1.63 g (52.8% yield) of α-methoxy-isobutyric acid hydrazide as a colorless oil.

(iv). Preparation of 2-methoxy-2-methyl-N-(diphenylmethylenimino)-propionamide.-

α-Methoxy-isobutyrate acid hydrazide (1.63 g) and 4.5 g benzophenone in 20 ml ethanol was refluxed over a steam bath for 17 hours. The ethanol was evaporated off under reduced pressure at 65°. The white solid that was left was washed with 100 ml petroleum ether. Crystallization of the residue in a mixture of ether and petroleum ether gave 0.34 g (10.0% yield) of 2-methoxy-2-methyl-N-(diphenylmethylenimino)-propionamide as a faint yellow solid mp 125-126°. Its nmr spectrum ($CCl_4$) showed singlets at 1.30δ (6H), 2.97δ (3H), and a multiplet from 7.13δ to 7.73δ. Its ir showed an N-H peak at 3345 $cm^{-1}$ and a carbonyl absorption at 1710 $cm^{-1}$.

K. HYDROGENATION OF 1-(DIPHENYLMETHYLENE)-4,4-DIMETHYL-3-OXO-1,2-DIAZETIDINIUM INNER SALT (49) :

The hydrogenation of 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) was carried out in a reaction vessel having an internal volume of 50 ml and bearing a side arm connected to a capillary inlet guarded by a septum for sample injection (see Fig. IV).

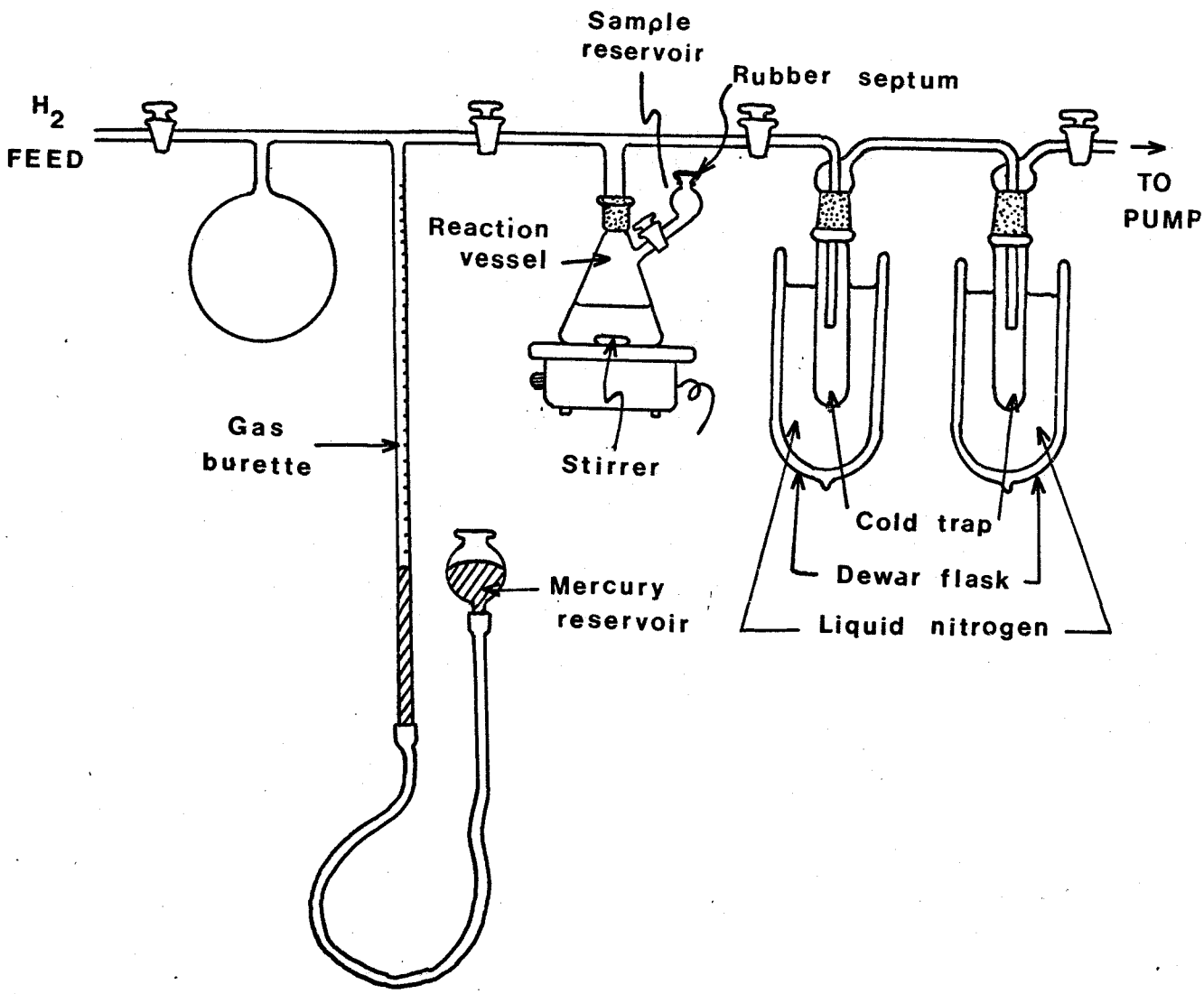



FIG. IV : Apparatus for constant pressure hydrogenation.

Absolute ethanol (30 ml) which was used as the solvent, 0.429 g of 10% palladium-on-charcoal and a stirring bar were first introduced into the reaction vessel before it was assembled to the vacuum line. The amount of hydrogen consumed during the hydrogenation process was measured with a gas burette which was adjusted to constant pressure by a manually adjustable mercury reservoir. The whole system was first flushed with hydrogen by repeatedly pumping and filling it with hydrogen gas. The gas burette was finally adjusted to a convenient reading by carefully regulating the gas inlet and equalizing the pressure simultaneously.

1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) (0.3360 g) was dissolved in the minimum amount of ethanol and was injected into the sample reservoir through the rubber septum by means of a syringe. The sample was then allowed to drain into the rapidly stirring slurry of 10% palladium-on-charcoal in ethanol. Readings were taken by slightly increasing the pressure in the system using the levelling bulb, and taking time and volume when the manometer again indicated one atmosphere. A plot of the burette reading vs. time was plotted at the time of the run and the reaction was stopped as soon as the rate of consumption of hydrogen levelled off.

The hydrogenation experiment was repeated twice. Data obtained were very similar and in all cases, 3.18 to 3.24 moles of hydrogen were used per mole of 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-dizaetidinium inner salt (49). A typical plot of molar hydrogen vs. time is presented in graph I. (see page 31 ).

Ethanol was evaporated from the hydrogenation product under reduced pressure and the residue dissolved in deuterated chloroform. Its nmr spectrum showed singlets at 7.15$\delta$ and 3.96$\delta$ with an integration ratio of 5:1 respectively. That component was unambigiously identified as diphenyl-methane by vpc and by comparing nmr and ir spectra with those of authentic diphenyl-methane. The crude product also showed singlets at 1.31$\delta$ (6H) and at 1.43$\delta$ (2H). Both position and shape of the latter peak, however, varied with concentration and it completely disappeared on shaking the solution with $D_2O$. The latter peak is identified as the amino proton signal of 2-amino-2-methyl-propionamide (62) by comparing with the amino proton signal of t-butylamine (1.23$\delta$)[61] and 2-aminopropan-2-ol (2.17$\delta$)[62]. The amide proton of (62), as compared with the amide proton signal of propionamide (6.42$\delta$)[63], was not observed. The ir spectrum of the 2-amino-2-methyl-propionamide (62) showed a strong band at 1675 $cm^{-1}$ (C = O) with the amine and amide absorption occuring at 3315 $cm^{-1}$ and at 3385 $cm^{-1}$ respectively. 2-Amino-2-methyl-propionamide (62) was separated from diphenylmethane by washing with petroleum ether and subsequently recrystallizing from chloroform-benzene, mp 122-124°.

L. THERMOLYSIS OF 2-DIPHENYLMETHYLENEHYDRAZONO-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE IN CHLOROBENZENE:

The procedure for thermolysis of the above compound in chlorobenzene was essentially the same as that for the thermolysis of the same compound in methanol, as described on page 57. However, contrary to the thermolysis in vacuum, it gave only 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) and nitrogen as final products.

M. THERMOLYSIS OF 2-DIPHENYLMETHYLENEHYDRAZONO-5,5-DIMETHYL-$\Delta^3$-1,3,4-OXADIAZOLINE IN METHYL ETHYL KETONE:

The above compound (0.127 g) in 3.0 ml of methyl ethyl ketone was vacuum sealed in a thick walled glass bomb having a total internal volume of approxiamtely 10 ml. The reaction vessel was immersed in an oil bath previously adjusted to 130°. 1-(Diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) was identified as the only product after four hours heating; yield 0.0787 g.

# CHAPTER IV

## CONCLUSION

The thermolysis of 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (40) was studied in chlorobenzene and in vacuum. The imino-oxirane structure (44), the compound we were most interested in, was not isolated. In both cases, the thermolysis of (40) gave a stable 1-(diphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (49) as the final product. The process is believed to be of a homolytic nature with the initial formation of the imino-oxirane (44) since this is one way that the diazetidinium salt (49) can be formed directly from the parent oxadiazoline (40).

The thermolysis of 2-(p,p'-dichlorodiphenylmethylenehydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline and 2-(p,p'-dibromodiphenylmethylene-hydrazono)-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline, similar to the unsubstituted 2-diphenylmethylenehydrazono-5,5-dimethyl-$\Delta^3$-1,3,4-oxadiazoline (40), gave 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (69) and 1-(p,p'-dibromodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (76) respectively. Although the spectral properties of the above diazetidinium salts (49), (69) and (76) can be accomodated both in terms of the above structures and the corresponding imino-oxiranes, the latter were disproved experimentally from the fact that hydrogenation of (49) gave a 2-methoxy-2-methyl-N-diphenylmethylen-imino)-propionamide (60), which can only be formed from structure (49) through reasonable mechanistic pathways.

The X-ray crystal structure of 1-(p,p'-dichlorodiphenylmethylene)-4,4-dimethyl-3-oxo-1,2-diazetidinium inner salt (69), which confirmed the structure, revealed several interesting features. The heterocyclic ring was completely planar with a C(18)C(16)N(15) bond angle constrained to a small 80.1°. The high melting point of the crystal (49) also supports the assigned zwitterion structure.

In a more polar solvent like methanol, the thermolysis of (40) is believed to be of a heterolytic nature with the initial formation of an isocyanate (41) which eventually reacts with methanol giving a benzophenone methyl carbazate (47).

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