STUDIES OF SOME Δ^3-1,3,4-OXADIAZOLINES AND -OXADIAZOLINONES

THE SYNTHESIS AND THERMAL DECOMPOSITION OF 5,5-DIPHENYL-2-(ARYLIMINO)-Δ^3-1,3,4-OXADIAZOLINES AND 5,5-DIALKYL-Δ^3-1,3,4-OXADIAZOLIN-2-ONES

by

AUDREY M. CAMERON, B.A.

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TITLE: The Synthesis and Thermal Decomposition of 5,5-Diphenyl-2-(Arylimino)-Δ^3-1,3,4-Oxadiazolines and 5,5-Dialkyl-Δ^3-1,3,4-Oxadiazolin-2-ones

AUTHOR: Audrey M. Cameron, B.A. (Saskatchewan)

SUPERVISOR: Dr. J. Warkentin

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SCOPE AND CONTENTS:

The thermal decomposition of 2-(arylimino)-5,5-diphenyl-Δ^3-1,3,4-oxadiazolines, prepared by the oxidation of benzophenone 4-arylsemicarbazones by lead tetra-acetate, was studied. A possible mechanism of the decomposition is discussed in the light of a correlation between the rate constants and substituent constants. The configuration of N,5,5-trisubstituted-2-imino-Δ^3-1,3,4-oxadiazolines was determined. Several new compounds, 5,5-dialkyl-Δ^3-1,3,4-oxadiazolin-2-ones, were prepared by hydrolysis of 5,5-dialkyl-2-(methylimino)-Δ^3-1,3,4-oxadiazolines. A literature survey of the oxidative cyclization of nitrogen-containing carbonyl derivatives, and of the thermal decomposition of cyclic azo compounds is presented.

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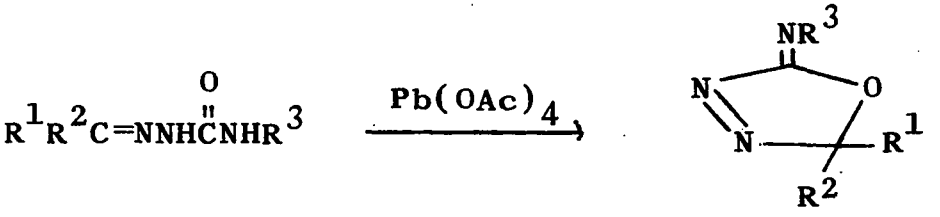
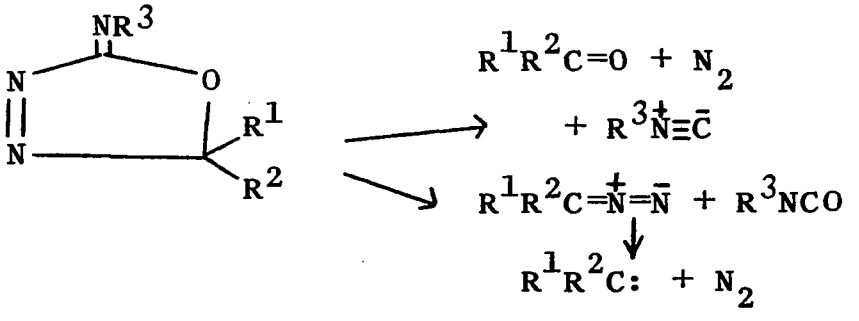
GENERAL INTRODUCTION

West and Warkentin reported that the oxidative cyclization of 4-substituted semicarbazones gave 2-(substituted imino)-Δ^3-1,3,4-oxadiazolines (1). The thermolysis of these heterocycles proceeded by two parallel

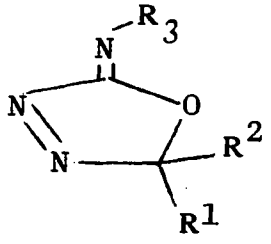


first-order pathways. From the variation in the ratio of the two modes of decomposition with the substituents R^1 and R^2, the authors were able to reach some conclusions about the nature of the transition states involved.

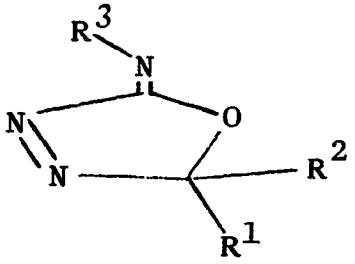


One of the objectives of this study was to gain a better insight into the mechanism of decomposition by studying the effects of changing the exocyclic substituents (R^3) on rates and products of the thermolysis of 5,5-diphenyl-2-(arylimino)-Δ^3-1,3,4-oxadiazolines.

A second objective was to determine the stereochemistry (E or Z) of the oxadiazolines that had been synthesized.



Z



E

A new series of compounds, 5,5-dialkyl-Δ^3-1,3,4-oxadiazolin-2-ones, were discovered to be byproducts from the lead tetra-acetate oxidation of alkanone 4-alkylsemicarbazones. The thermolysis of these compounds was also investigated.

The use of agents other than lead tetra-acetate for the oxidative cyclization of 4-substituted semicarbazones was studied.

HISTORICAL INTRODUCTION

General

This introduction will examine first the scope and applicability of the oxidative cyclization of nitrogen-containing derivatives of carbonyl compounds. Although the use of such a cyclization was restricted in this study to the oxidation of 4-substituted semicarbazones, the background of this preparative method encompasses many other carbonyl derivatives. Indeed, this reaction, employing lead tetra-acetate, manganese dioxide, ferric chloride, as well as other oxidizing agents, has been a valuable synthetic route to many heterocyclic compounds. Reviews of this field may be found in the literature (1b, 1c).

The second part of this introduction will examine the kinetic results previously obtained from the thermolysis of some 2-(phenylimino)-5,5-diaryl-Δ^3-1,3,4-oxadiazolines (1a). In addition, descriptions of the various modes of azo decomposition to be found in the literature are included.

I. Oxidative Cyclization of Carbonyl Derivatives

A. By Lead Tetra-acetate

Benzoyl hydrazones of some selected ketones have been shown to undergo cyclization through the action of lead tetra-acetate in methylene chloride (2,3). At -40°C, the characteristic red-brown colour of the benzoylazo chromophore was produced when the oxidizing agent was added to the hydrazone. When the reaction mixture was warmed to -20°C, the only product isolated was the Δ^3-1,3,4-oxadiazoline (eq. 1).

$$R^1R^2C{=}NNHC(=O)Ph \xrightarrow[-40^\circ C]{LTA} R^1R^2C(OAc)-N{=}N-C(=O)Ph \qquad [1]$$

$$\xrightarrow{-20^\circ C} \text{2-acetoxy-2-phenyl-5,5-}R^1R^2\text{-1,3,4-oxadiazoline}$$

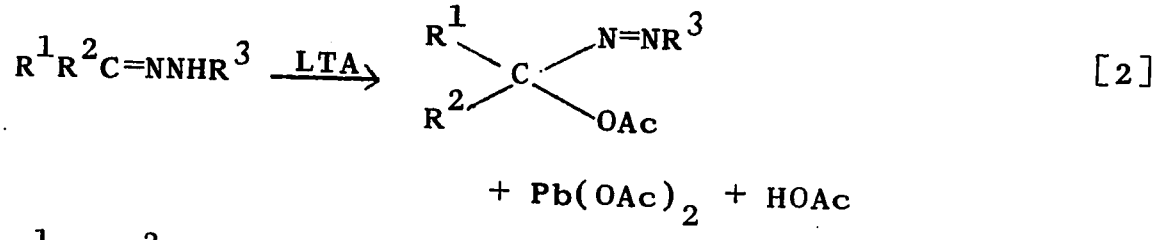
$R^1R^2 = (CH_2)_5$

$R^1 = Ph,\ R^2 = Me$

$R^1 = R^2 = Ph$

The existence of the intermediate "azoacetate" had previously been reported by Iffland (4). When a ketohydrazone was treated with one mole of lead tetra-acetate in methylene chloride, acetic acid, or benzene at 0—10°C,

"azoacetates" were obtained (eq. 2). The yield of this



[2]

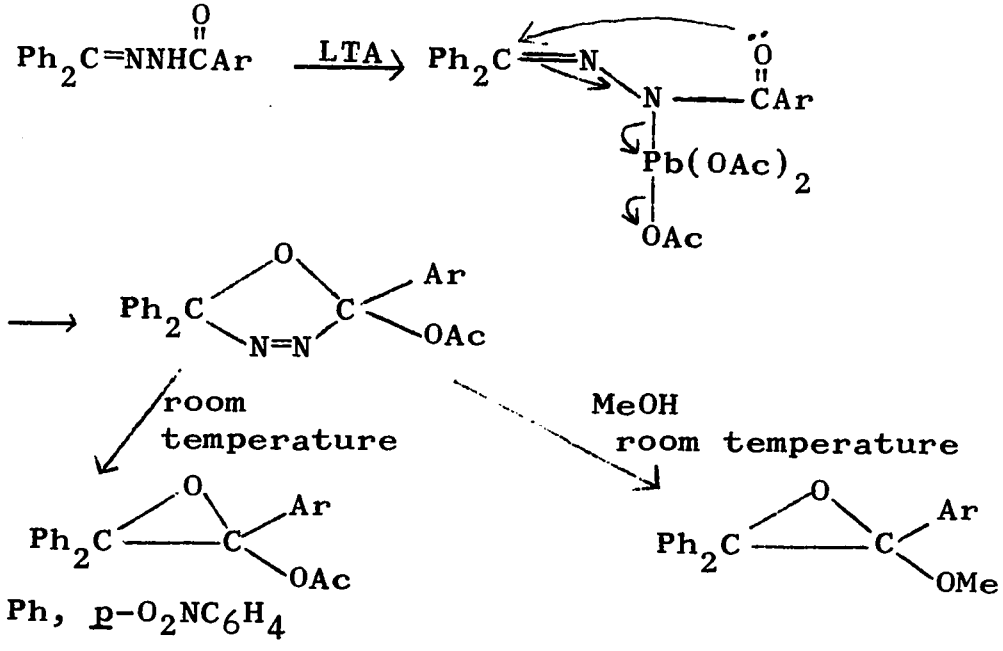
$R^1 = R^2 = Me, Ph$

$R^1R^2 = (CH_2)_5$

$R^3 = Ph, \underline{p}\text{-}BrC_6H_4, \underline{p}\text{-}O_2NC_6H_4, 2,4\text{-}(O_2N)_2C_6H_3, Me$

reaction varied between 65 and 90 percent.

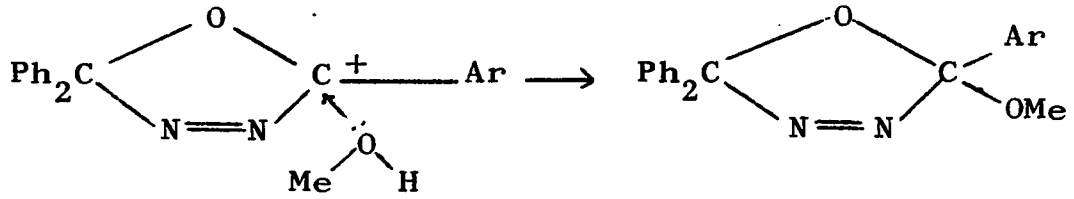
Although Hoffman had proposed an intermediate "azoacetate" to explain the cyclization of the ketohydrazone, Gladstone and Norman suggested that the reaction intermediate actually involved a N-Pb complex (eq. 3). A strong



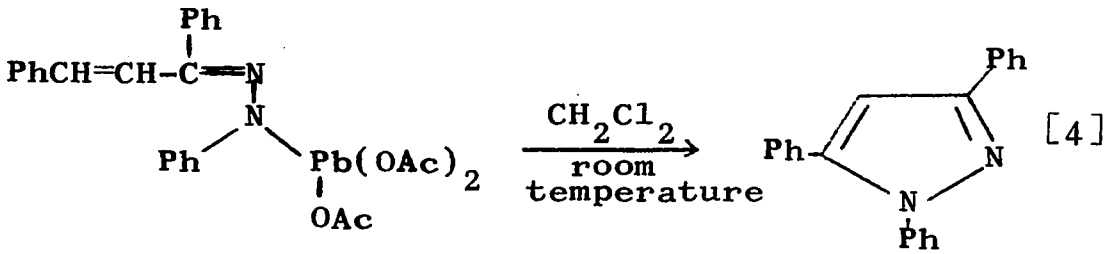
[3]

Ar = Ph, $\underline{p}\text{-}O_2NC_6H_4$

argument in favour of this mechanism, namely, formation of a N-Pb bond, followed by heterolysis of this bond (with assistance from the carbonyl oxygen), was the observation that when the reaction was carried out in methanol, a methoxyepoxide was obtained (5). Although the authors depicted this result by the following mechanism, it must be noted that lead tetra-acetate is known to undergo exchange in hydroxylic solvents.

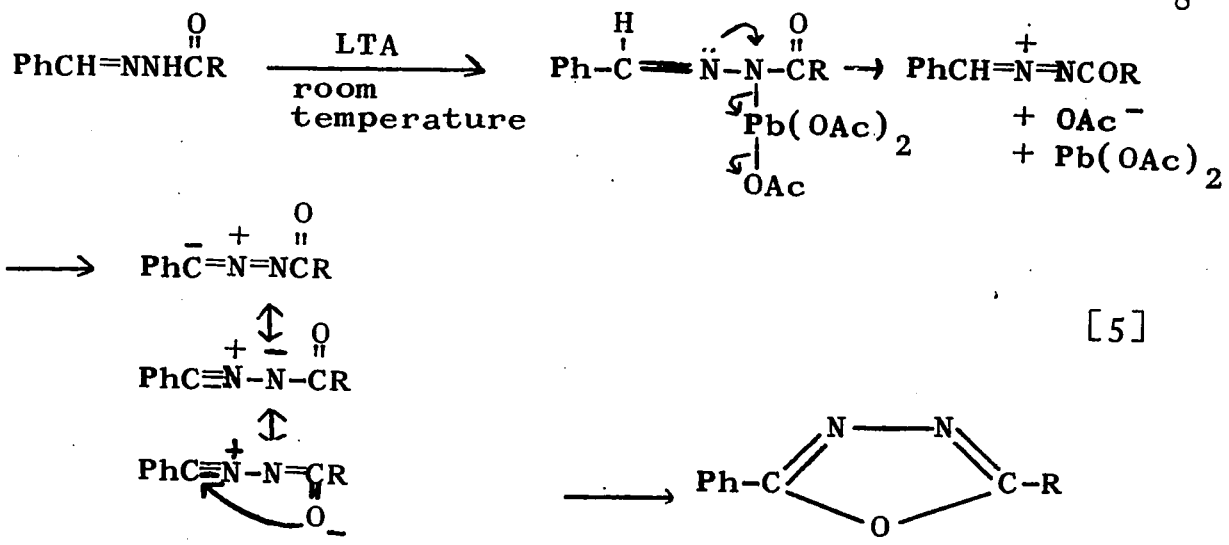


The ring closure of chalcone phenylhydrazone to 1,3,5-triphenylpyrazole was reported by Gladstone and Norman (6). The yield of pyrazole was 74% (eq. 4).



[4]

A high yield synthesis of 1,3,4-oxadiazoles was reported from the reaction of lead tetra-acetate and aldehyde hydrazones (eq. 5) (7). The authors suggested that the reaction involved an intermediate nitrilimine.

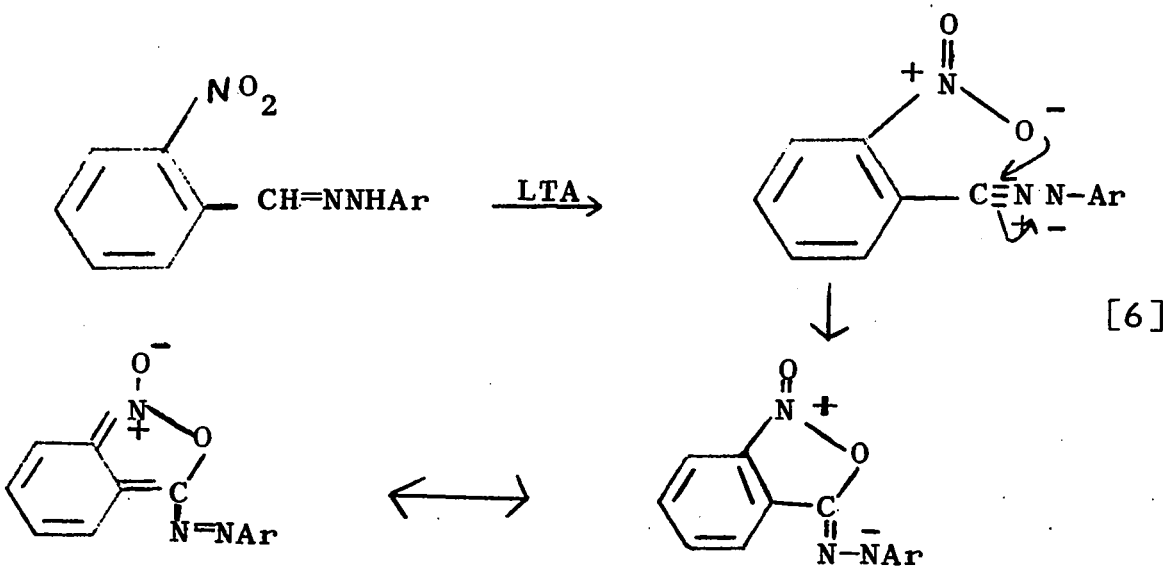


[5]

R = Ph (87% yield)

R = NPh_2 (76% yield)

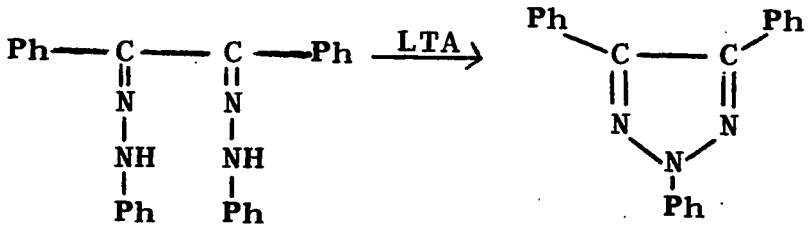
A novel synthesis of 3-aryl-azoanthranil 1-oxides in 76 and 54 percent yields was also attributed to the intermediacy of a nitrilimine (eq. 6) (7).



[6]

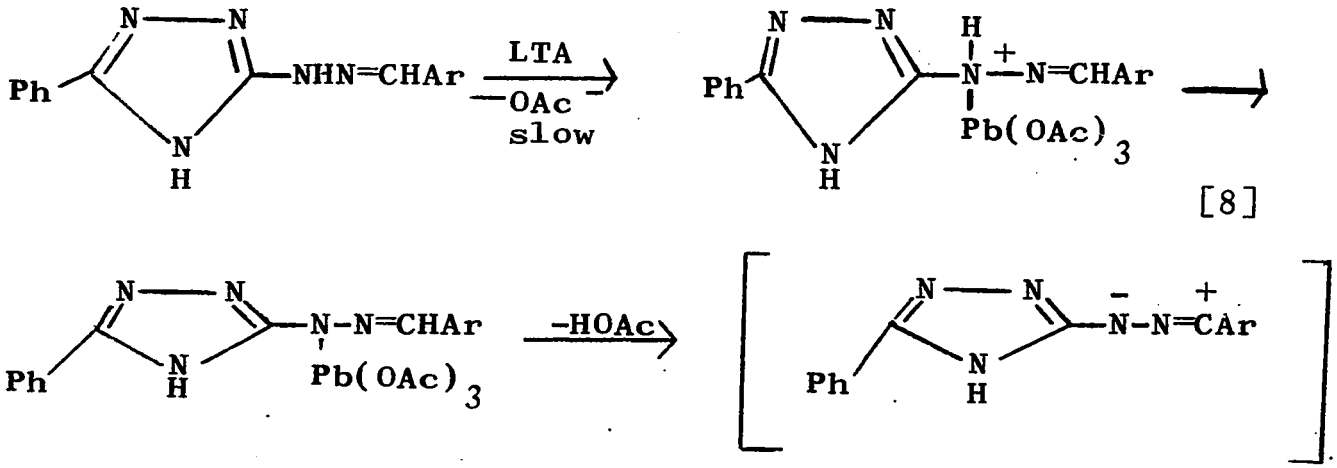
Ar = Ph, p-$O_2NC_6H_4$

The cyclization of a phenyl osazone derivative was reported by Norman to yield 33% of the triazole product (eq. 7) (8).

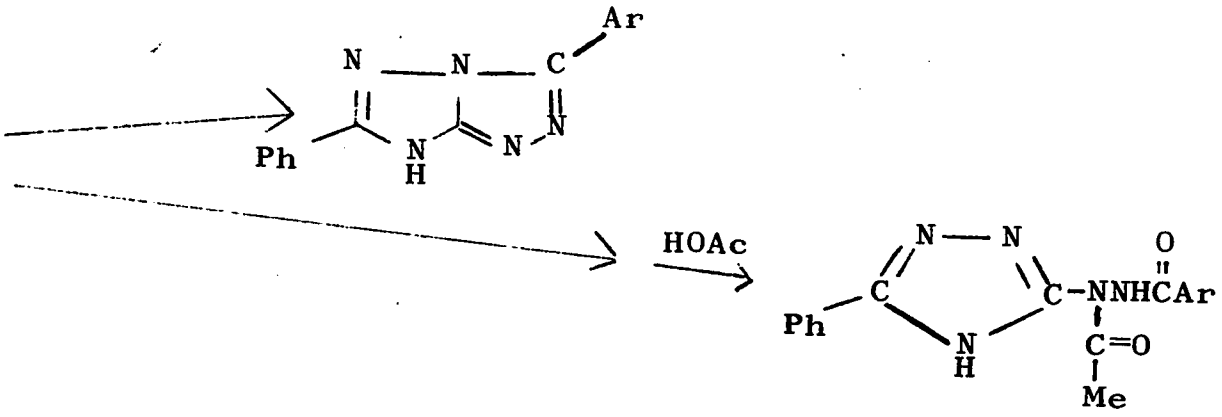


[7]

Another oxidative cyclization which has been represented by a polar mechanism was the reaction of 3-phenyl-1,2,4-triazolylhydrazones with lead tetra-acetate in glacial acetic acid at 35°C (9). Scott found that under these conditions there was competition between oxidative cyclization of the hydrazone to give 3-aryl-6-phenyl-s-triazolo[4,3-b]-s-triazoles, and acetoxylation of the hydrazone to yield N-acetyl hydrazides (eq. 8). By varying

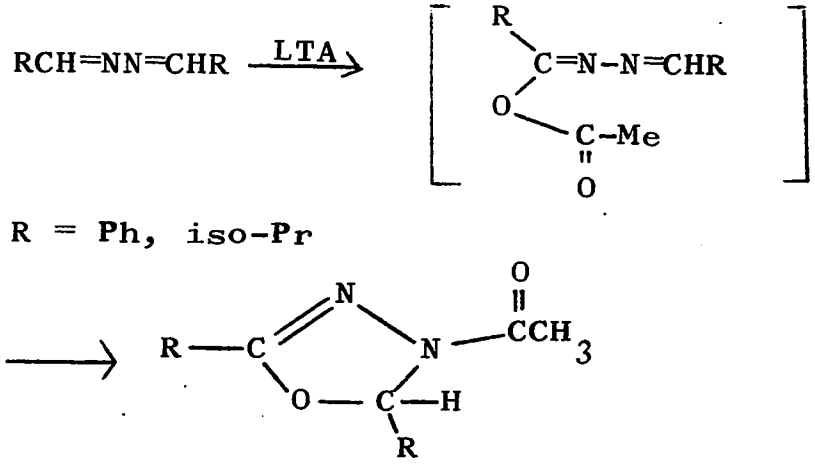


[8]



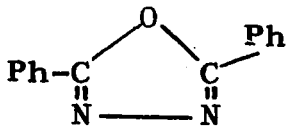
the nature of Ar, Scott obtained a Hammett ρ of -0.60 with r=0.995 for the cyclization reaction. This, he suggested, indicated that the first step of the reaction, the S_N2 displacement on Pb(IV), was the rate-determining step.

The reaction of both aldazines and ketazines with lead tetra-acetate has been the subject of a study by Gillis and LaMontagne (10). While aromatic ketazines failed to react with lead tetra-acetate, aliphatic ketazines gave α,β-unsaturated "azoacetates." The oxidation of aldazines (RCH=NN=CHR, R=alkyl or aryl) yielded 1,3,4-oxadiazoles (eq. 9). In the case of R=Ph, further oxidation of the



[9]

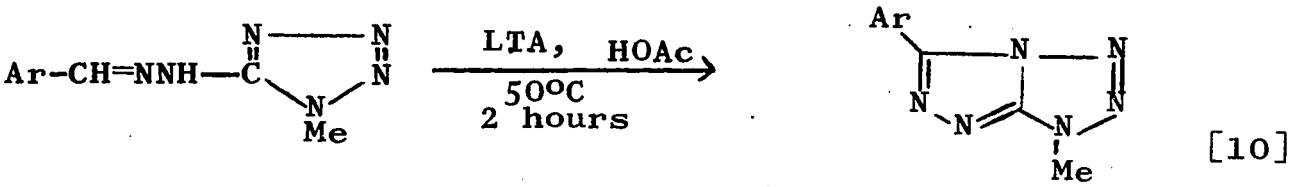
oxadiazole, formed in 35% yield, led to 2,5-diphenyl-1,3,4-oxadiazole (I). When two equivalents of lead tetra-acetate



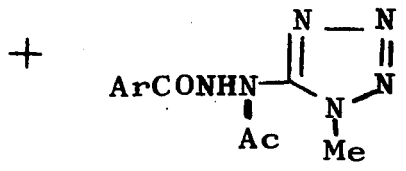
I

were reacted with benzaldehyde azine for two hours at room temperature in benzene, a 90% yield of I was obtained.

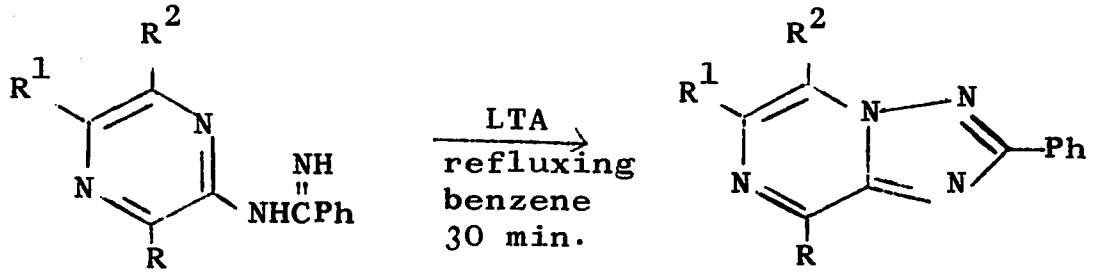
Scott and Butler's study of the reaction of lead tetra-acetate with tetrazolylhydrazone revealed that such reactions may involve a competition between oxidative cyclization and formation of N-acetyl derivatives (11) (eq. 10). The hydrazine derivatives were the major product (37-41% yield) in all cases.



Ar = p-MeC_6H_4, Ph, p-ClC_6H_4 22-26% yield [10]



A similar cyclization to a heterocyclic moiety was observed in the reaction of lead tetra-acetate with N-2-pyrazinylbenzamidines to yield 2-phenyl-s-triazolo-[2,3-a-]pyrazines (12) (eq. 11).



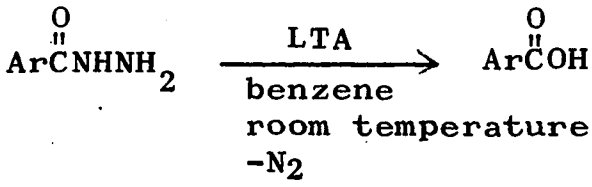
[11]

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

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

$R = H$, $R^1 = R^2 = Ph$

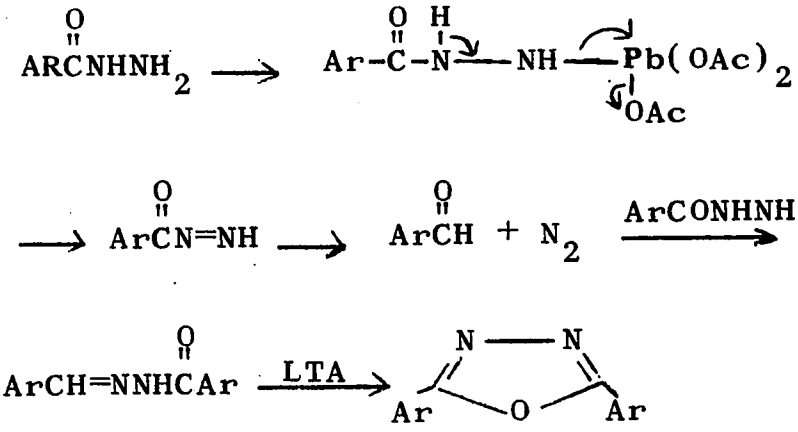
The observation that the oxidation of monoacylhydrazines in a very dilute benzene solution resulted in a small yield of oxadiazole has been reported by Aylward and Norman (13). The major product observed, however, was the aromatic acid (eq. 12). However, if the reaction were



[12]

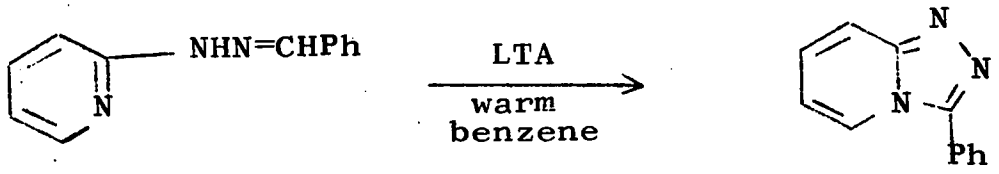
Ar = Ph, p-ClC_6H_4, p-MeC_6H_4, p-$MeOC_6H_4$

executed by adding lead tetra-acetate slowly over six hours to a very dilute solution, oxadiazole was also obtained. The authors attributed this product to the following sequence of steps (eq. 13).



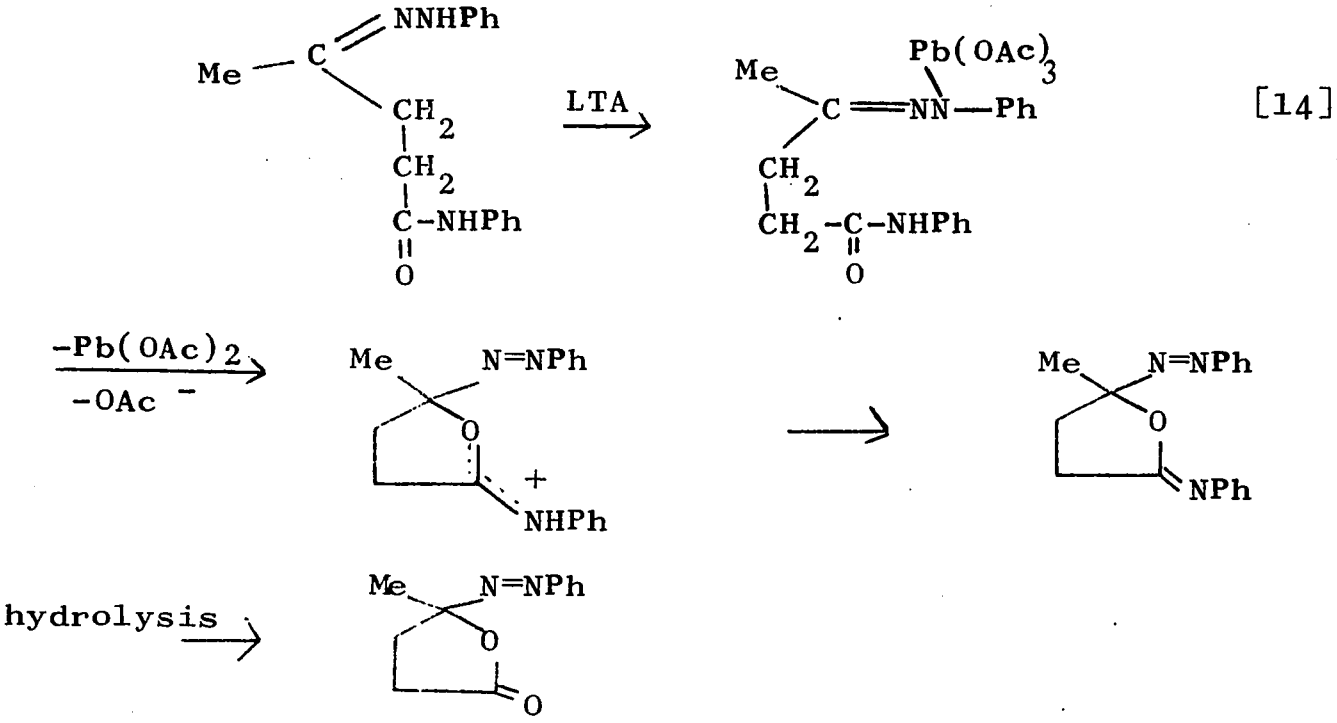
[13]

Yet another cyclization of a heterocyclic hydrazone was demonstrated by Bower and Doyle (14) (eq. 13a). This reaction was also applicable to pyrimidinylhydrazones.



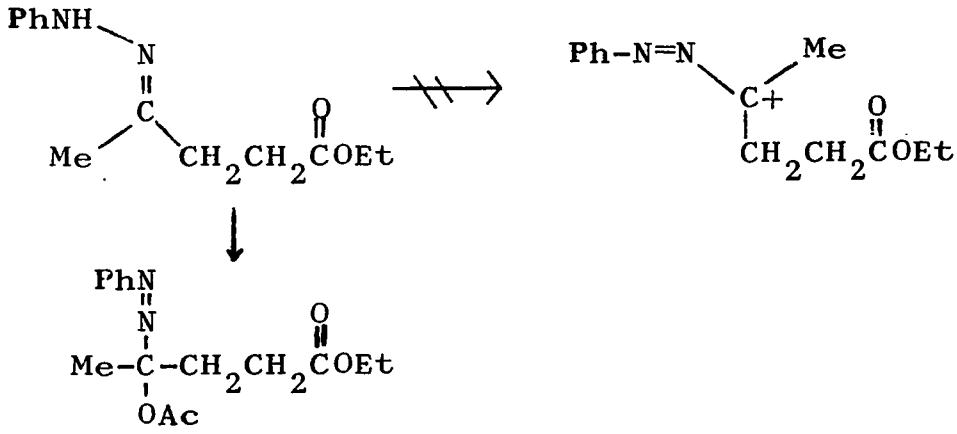
[13a]

The reaction of lead tetra-acetate with the hydrazones of ketoacids and ketoamides may lead to either "azoacetates" or cyclized products. Gubelt and Warkentin found that if a nucleophilic substituent were present at such a position as to produce a 5- or 6-membered ring, "azoacetate" formation was suppressed (15). For example, the arylhydrazones of levulinic acid and levulinanilide gave mainly cyclized product (eq. 14). The authors suggested that oxygen - rather than nitrogen - ring closure



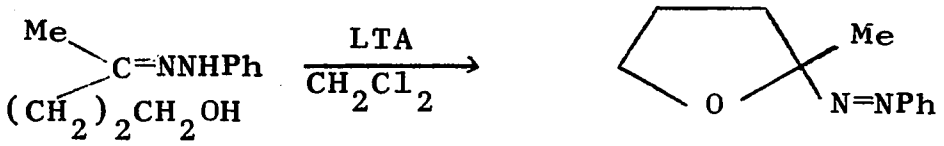
[14]

was preferred because of the greater stability of the intermediate cation when an O-C bond was formed. The fact that the analogous ester of levulinic acid did not undergo cyclization indicated that the reaction was proceeding through the mechanism shown above. If the reaction had involved a cation of the type suggested by Hoffman (2,3), ring closure would be expected to be facile (eq. 15).



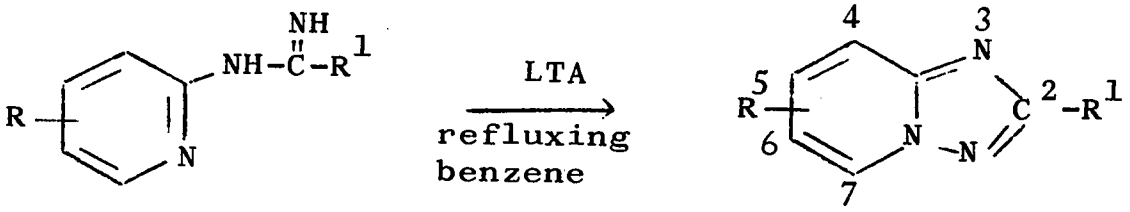
[15]

Oxidative cyclization of an alcoholic analogue resulted in the formation of 2-(phenylazo)-2-methyltetrahydrofuran in 79% yield (eq. 16).



[16]

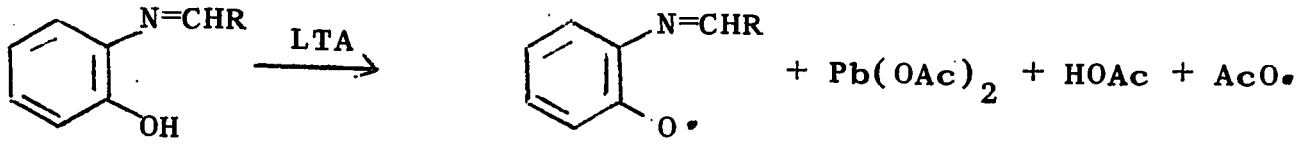
Potts and coworkers suggested a free radical mechanism for the cyclization of some N-(2-pyridyl)alkyl-(or aryl-)amidines to 2-alkyl(aryl)-s-triazolo[1,5-a] pyridines (16) (eq. 17).

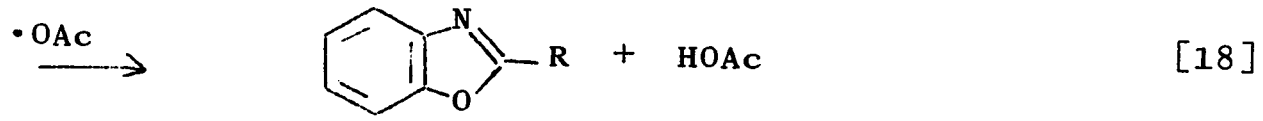


[17]

In product: $R = H, 4\text{-}CH_3, 5\text{-}CH_3, 6\text{-}CH_3, 7\text{-}CH_3,$
$R^1 = Et, Ph, CH_3$

A similar mechanism was suggested by Stephens and Bower for the preparation of some benziminazoles and benzoxazoles from Schiff's bases (17) (eq. 18).

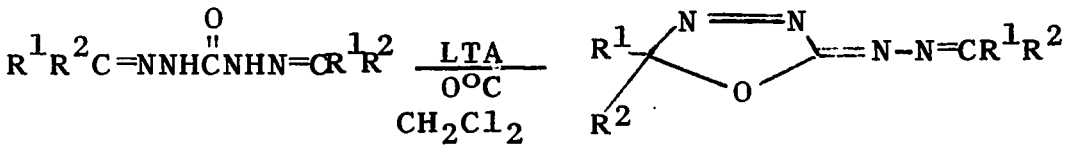




[18]

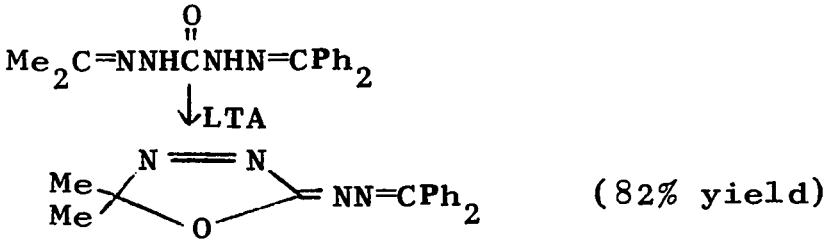
R = p-$NO_2C_6H_4$

The oxidation of carbohydrazones of aliphatic or aryl ketones was studied by West and Warkentin (18,19). The products, 2-(alkylidenehydrazono)-5,5-dialkyl-Δ^3-1,3,4-oxadiazolines, were obtained in yields of 36 to 76%. Aliphatic ketone derivatives were more easily oxidized than those of diaryl ketones (eq. 19). In the case of an



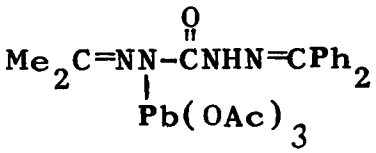
[19]

unsymmetrical carbohydrazone, only one product was formed (19) (eq. 20). The author's rationale for this fact was

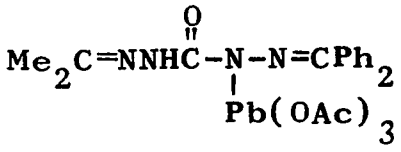


[20]

the faster formation of the intermediate II. Intermediate III, the alternative intermediate, would be disfavoured because of the lower nucleophilicity of the $-NH-N=CPh_2$ group, and also because of higher steric hindrance.

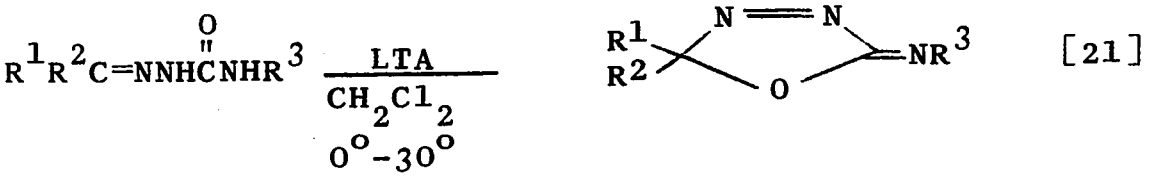


II



III

An analogous O to C closure was found in the oxidative cyclization of 4-substituted semicarbazones (1). The relative reactivities of aliphatic versus diaryl ketone semicarbazones were similar to those found in the previous carbohydrazone reaction (18,19a) (eq. 21).



[21]

$R^1 = R^2 = Me$, $R^3 = CH_2Ph$

$R^1 = R^2 = Me$, $R^3 = Fh$

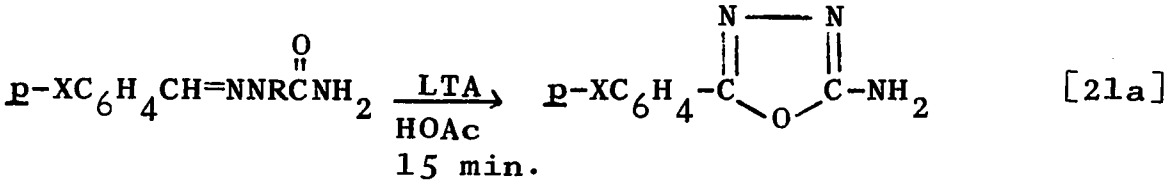
$R^1 = R^2 = R^3 = Ph$

$R^1 = R^2 = \underline{p}\text{-}MeC_6H_4$, $R^3 = Ph$

$R^1 = R^2 = \underline{p}\text{-}ClC_6H_4$, $R^3 = Ph$

$R^1 = R^2 = \underline{p}\text{-}MeOC_6H_4$, $R^3 = Ph$

Aldehydic semicarbazones underwent similar cyclization (19b) (eq. 21a). The authors suggested that the



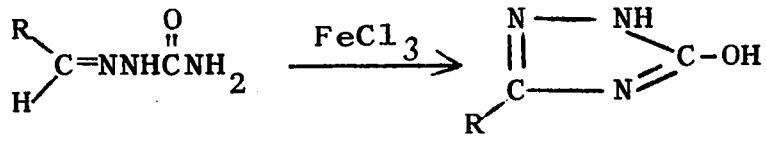
[21a]

X = H, OMe, Me, Cl, Br and R = H.

products were formed <u>via</u> 1,5-dipolar addition of intermediate nitrilimines $ArC^{+}=N-N^{-}-C(=O)NH_2$. To support this claim, they cited the fact that when nitrilimine formation was prevented, (R=Me), no reaction occurred.

B. By Oxidizing Agents Other than Lead Tetra-acetate

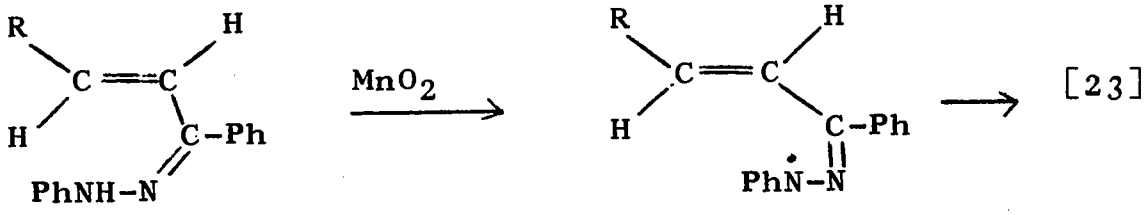
A very early (1900) example of an oxidative cyclization was reported by Young and Witham (20). The ferric chloride oxidation of benzaldehyde semicarbazones to 3-hydroxytriazoles was accomplished in a one hour reaction in alcoholic solution at 125°C (eq. 22).



[22]

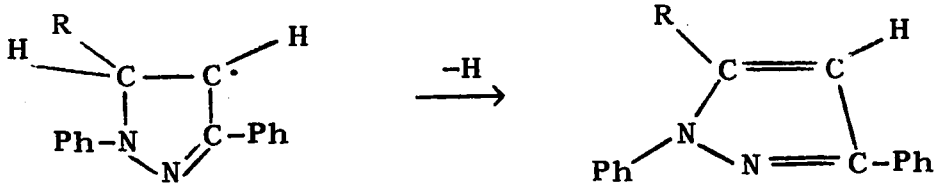
R = Ph, m-$NO_2C_6H_4$, PhCH=CH

Manganese dioxide has been used in the oxidative cyclization of nitrogen-containing compounds. For example, Bhatnagar and George obtained a 73% yield of 1,3,5-triphenylpyrazole from the oxidation of benzalacetophenone phenylhydrazone (21). The reaction, carried out in dry benzene at room temperature for five hours, was presumed to be free radical in nature (eq. 23). They found that

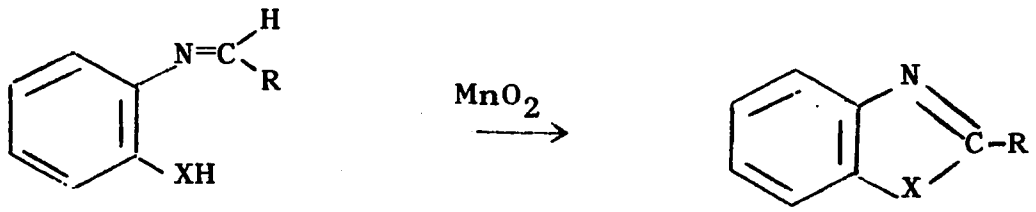


[23]

R = Ph, m-$O_2NC_6H_4$



under similar conditions, o-aminobenzylidene anils and o-hydroxybenzylidene anils also underwent ring closure (eq. 24).



[24]

R = p-$NO_2C_6H_4$, X = NH

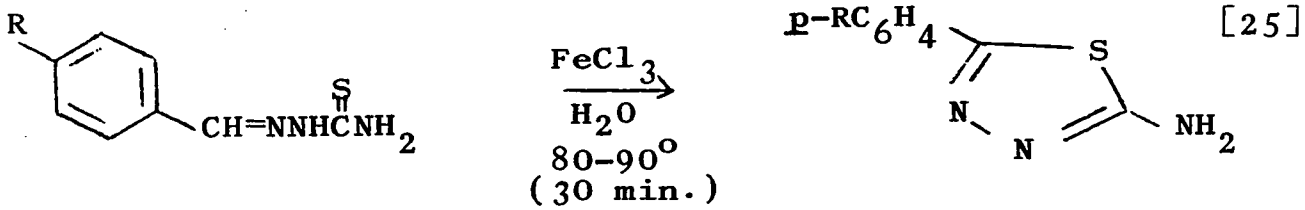
R = m-$NO_2C_6H_4$, X = NH

R = p-$NO_2C_6H_4$, X = O

R = m-$NO_2C_6H_4$, X = O

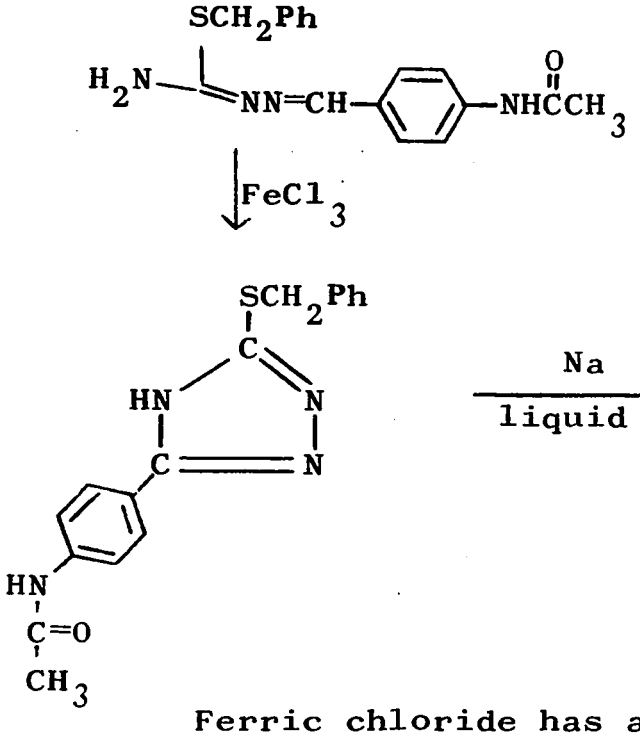
Yields ranged from 15 to 75 percent.

Aldehyde thiosemicarbazones have been reported to give either S to C or N to C closure when reacted with ferric chloride in hydroxylic solvents. Bernstein and coworkers reported the synthesis of 5-substituted-2-amino-1,3,4-thiadiazole derivatives from thiosemicarbazones (22) (eq. 25). However, if the thiocarbonyl function were protected by benzylation, the isomeric heterocycle was produced (23) (eq. 26).



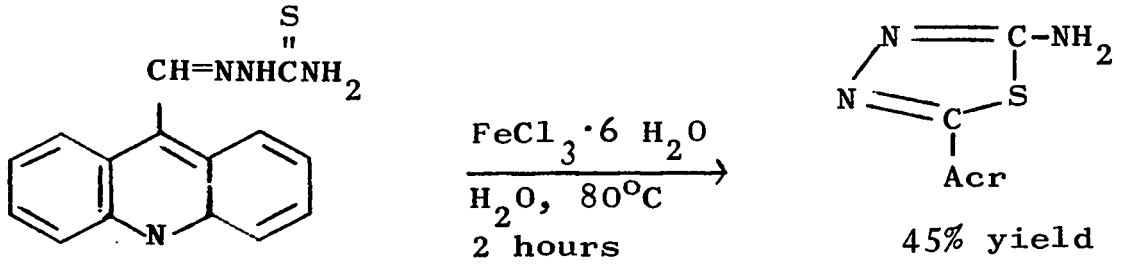
[25]

R = OMe, NH_2



[26]

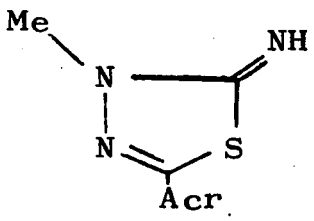
Ferric chloride has also been employed in the cyclization of 9-acridinealdehyde thiosemicarbazone (24) (eq. 27). Similarly, two methyl derivatives of this

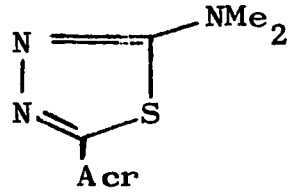


[27]

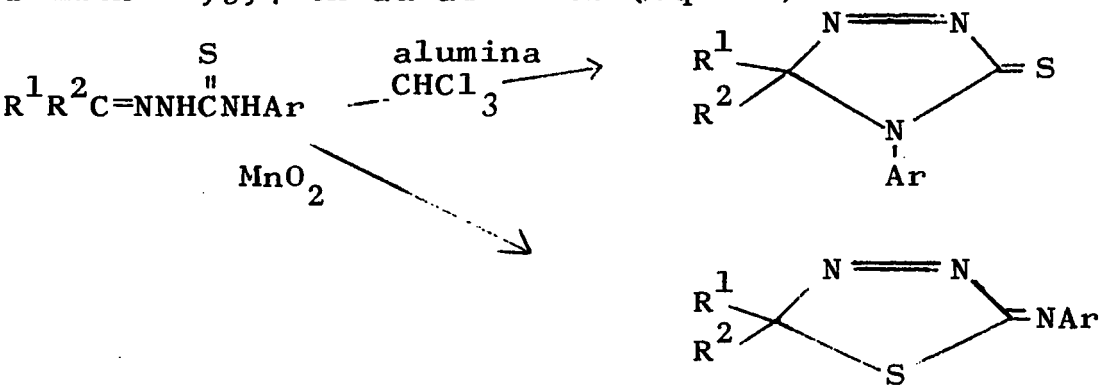
Acr = 9-acridinyl

semicarbazone were oxidized to yield analogous products:



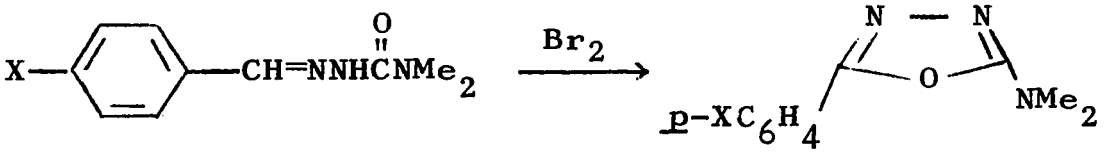


The compounds, 4-arylthiosemicarbazones, have been shown to undergo either S to C or N to C closure, depending upon the reaction conditions used (25). Oxidation in the presence of basic alumina yielded 3-thio-Δ^1-1,2,4-triazolines; oxidation by active manganese dioxide yielded 2-imino-1,3,4-thiadiazolines (eq. 28).



[28]

Bromine, also, has been used as an oxidizing agent for nitrogen-containing compounds. The cyclization of benzaldehyde 4,4-dimethylsemicarbazone was found to yield oxadiazoles (26) (eq. 29).

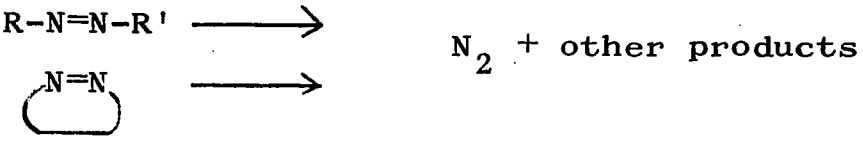


[29]

II. Thermal Decomposition of Cyclic Azo Compounds - Mechanistic Studies

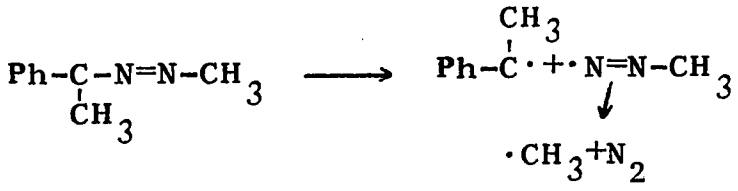
The study by West and Warkentin (1) of the thermolysis of some Δ^3-1,3,4-oxadiazolines, the only study closely related to that presented in this thesis, will be examined in this section. In addition, because of the widespread interest in the thermolysis of both cyclic and noncyclic azo compounds, a brief introduction to this larger field of interest has been included.

The thermolysis of azo compounds leads to the formation of molecular nitrogen through the cleavage of two C-N bonds (27,28).



Depending on the nature of the groups bonded to each nitrogen, this cleavage may range from a fully concerted process to a two step reaction. If the stability of the incipient radicals is similar, the reaction involves simultaneous cleavage of both bonds to yield nitrogen and two radicals.

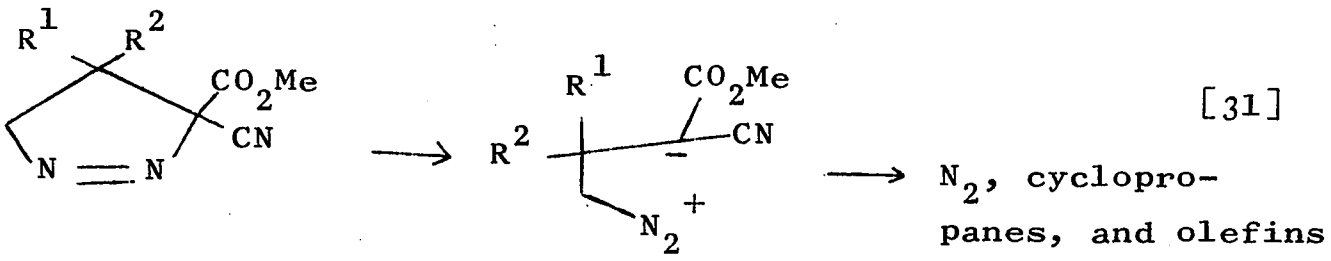
However, if the stability of the two possible radicals (R· and R''·) differ greatly, a two step process is possible. For example, Seltzer and Dunne have concluded from isotopic studies on the thermolysis of α-phenylethylazomethane that the first step of the decomposition is the formation of a short-lived diazo radical (29) (eq. 30).



[30]

Between these two limiting cases lies a spectrum of thermolysis transition states in which both nitrogen-carbon bonds are stretched in the same step, but to unequal degrees (30).

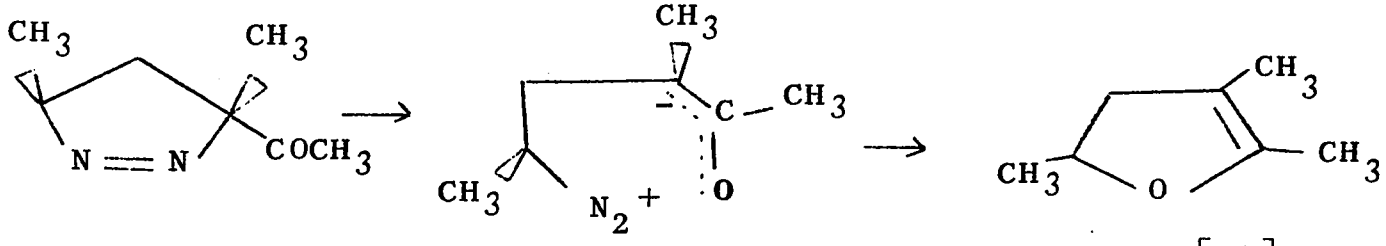
The mechanisms discussed above are homolytic in nature and result in the formation of free radicals. However, if the azo compound contains functional groups capable of stabilizing developing centres of charge, the result may be a heterolytic bond fission. For example, McGreer has studied the thermal decomposition of pyrazolines bearing electronegative substituents (31) (eq. 31).



[31]

He reported that the olefins formed arose from alkyl rearrangements that would be expected only from an intermediate bearing some positive charge at C-5. This fact, together with the observation that the rate of pyrolysis was faster in polar than in nonpolar solvents, suggested an ionic character for the decomposition. An identical, but independent, study by Hamelin and Carrié confirmed these results (32).

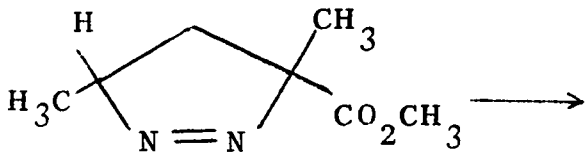
Similarly, thermolysis of <u>cis</u>- and <u>trans</u>-3,5-dimethyl-3-acetyl-Δ^1-pyrazoline gave a complex mixture of cyclopropanes, olefins, and dihydrofurans (33). The <u>cis</u> isomer yielded up to 32% of the latter product, presumably through ring closure of a zwitterionic intermediate (eq. 32). However, the <u>trans</u>



[32]

isomer gave little of this product. This suggested to the authors that some restriction to rotation about the C_3-C_4 bond was present. Hence, there existed partial bonding between N and C_3.

A similar study was made of the thermolysis of cis- and trans-3-carbomethoxy-3,5-dimethyl-1-pyrazoline (34) (eq. 33). The decomposition rate was not enhanced by polar

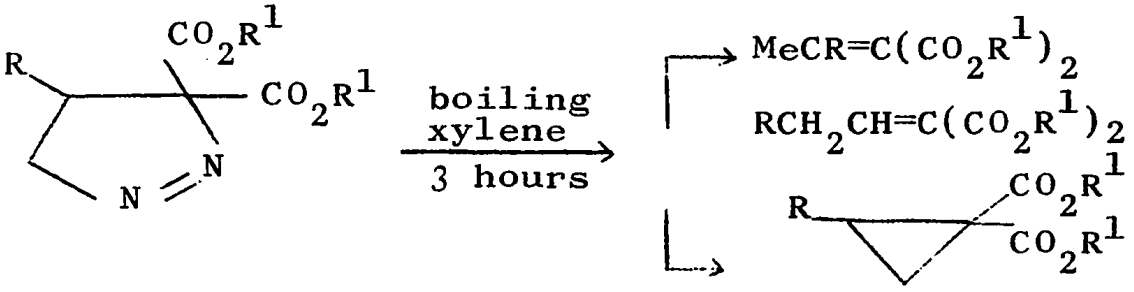


$\longrightarrow$ cyclopropane and olefins [33]

solvents, nor was methyl methacrylate found in the product mixture. Such a product would be expected if a zwitterionic intermediate were operative. However, evidence against completely concerted nitrogen loss was also present: cyclopropane formation was not stereospecific.

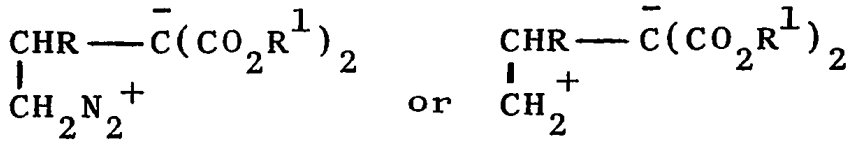
On the basis of these studies, McGreer has postulated a spectrum of transition states for the thermolysis of Δ^1-pyrazolines. These range from fully concerted nitrogen loss to heterolytic bond cleavage to give a zwitterionic intermediate.

Similar conclusions were reached by Danion-Bougot and Carrié from a study of the pyrolysis of some 1-pyrazolines disubstituted at C_3 with electrophilic groups (35). The authors found that such pyrolyses involved migration of either alkyl groups, or of H, from C_4 to C_5 (eq. 34). The

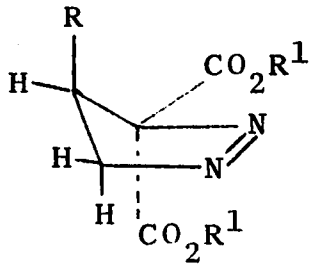


[34]

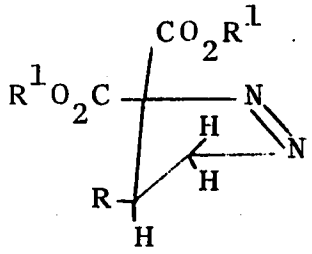
ethylenic products predominated. Such migrations, the authors reasoned, could arise only because of cationic centres:



Assuming the rotation about the C_3-C_4 bond in the intermediates is slow compared to the rate of rearrangement, the authors attributed the ratio of the two possible ethylenic products to the existence of two possible conformations of the starting material.

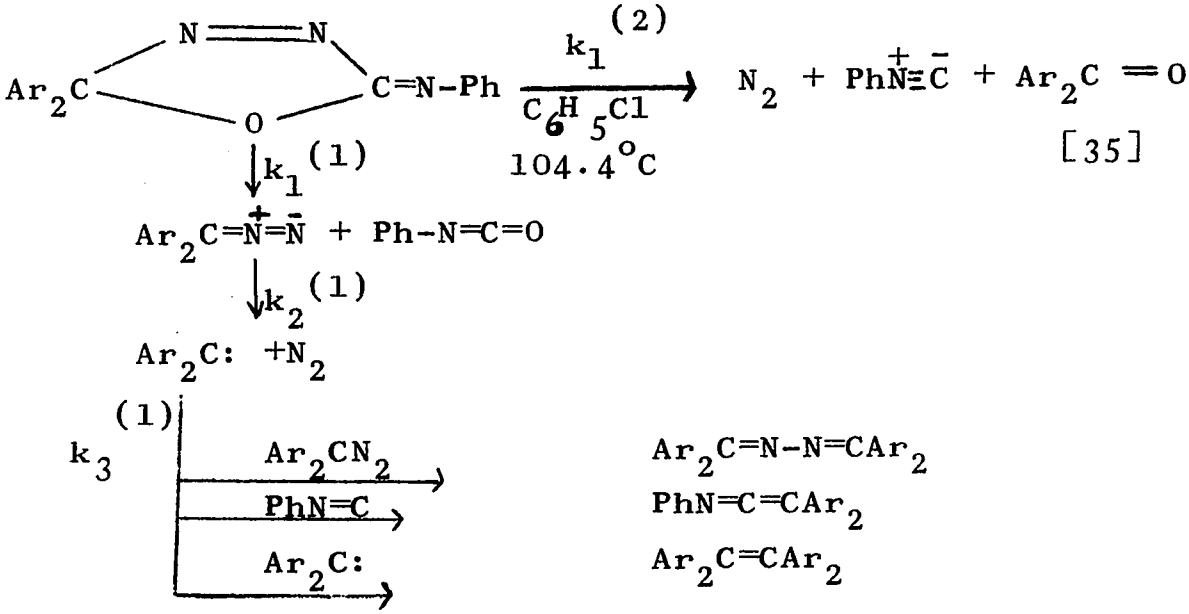


→ product from H migration



→ product from R migration

A series of 5,5-diaryl-2-(phenylimino)-Δ^3-1,3,4-oxadiazolines were the object of a thermolytic study by West and Warkentin (1a). The decomposition followed two parallel first-order processes, as shown below (eq. 35).



[35]

Overall, the theoretical volume of nitrogen per mole of starting material was obtained in gas evolution studies. Part of this nitrogen evolution resulted from a direct loss of nitrogen from the molecule; part resulted from a two step process: a retro-1,3-dipolar addition, followed by decomposition of the resultant diaryldiazomethane. The products other than nitrogen were characterized by their isolation from a partially decomposed sample of oxadiazoline; their melting points and infra-red spectra were then compared with those of authentic materials. In this way, phenyl isocyanate, phenyl isocyanide, benzophenone, and diaryldiazomethane were determined to be decomposition products.

In a sample carried to complete decomposition, benzophenone and phenyl isocyanate were the major products (infra-red study). No diaryldiazomethane was left, although a small amount of phenyl isocyanide remained. In addition, the infra-red spectrum showed a new absorption at 2000 cm^{-1} that was ascribed to the ketenimine $Ar_2C{=}C{=}N{-}Ph$. Attempts to isolate the material were unsuccessful.

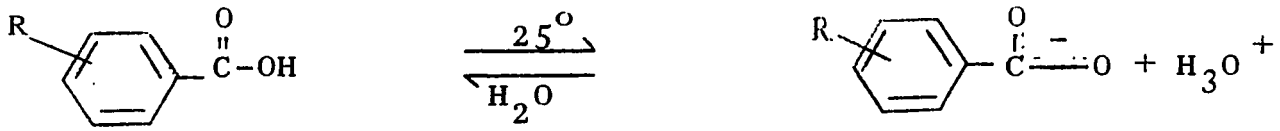
Kinetic analysis of this thermolysis required two approaches: (a) the rate of total nitrogen evolution was

determined in a gas evolution train, and (b) the diazomethane concentration was followed by an infra-red technique. From a rate expression too involved to explain fully here, it was then possible to obtain values for both $k_1^{(2)}$ and $k_1^{(1)}$.

It was noted that changing the nature of the aryl groups attached to C_5 (from electron donating to electron withdrawing) greatly changed the ratio of the two decomposition pathways. That is, increasing the electron density at C-5 increased the rate of one of the first-order pathways, while decreasing the rate of the other.

The Hammett equation, and modifications of it, was used to study this structure-reactivity relationship. Such a free energy relationship has been used frequently to correlate structure and reactivity.

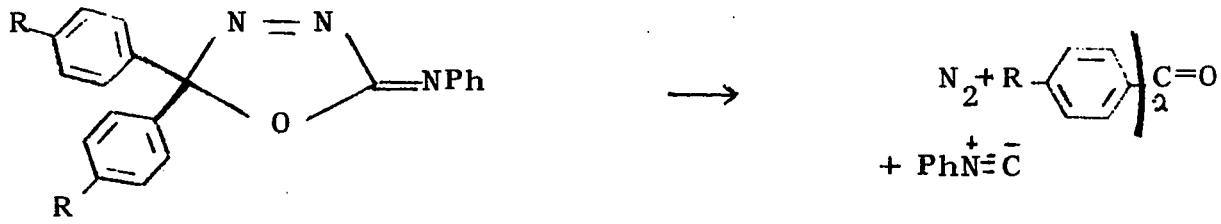
The Hammett equation was first defined on the basis of the ionization of m- or p-substituted and unsubstituted benzoic acids (36):



Then, $\log K/K_o = \rho\sigma$, where K_o is the equilibrium constant of benzoic acid, and K is the equilibrium constant for the

m- or p-substituted acid. Since ρ for this reaction was defined as +1.0, the σ values for electron-withdrawing groups are positive, while σ values for electron-releasing substituents are negative. Rho was called the reaction parameter. If the reaction under study is aided by electron withdrawal, ρ is positive (as in the ionization of benzoic acids). If the absolute value of ρ is greater than 1.0, the reaction under consideration is more sensitive to substituent effects than is the ionization of benzoic acid.

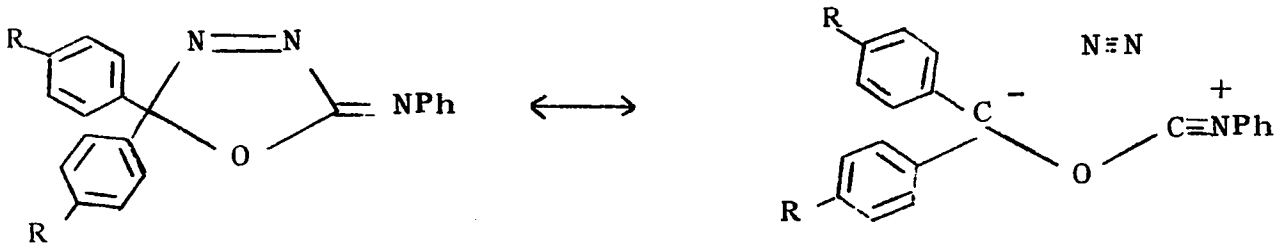
The correlation of the rates of the direct evolution of nitrogen ($k_1^{(2)}$) with 2σ (two R substituents are present) was made for the following series of oxadiazolines:



R = H, p-Cl, p-CH_3

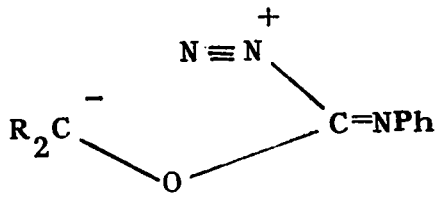
Only three substituted oxadiazolines were available in this case, because, on the one hand, starting material with strongly withdrawing substituents were not accessible, and, on the other, strongly donating substituents completely suppressed the reaction. Nevertheless, a roughly obtained

value of +0.62 indicated that electron-withdrawing substituents enhanced the rate of decomposition slightly. This relatively small effect may perhaps be attributed to weakening of the C-N bonds in the ground state by inductive electron withdrawing:



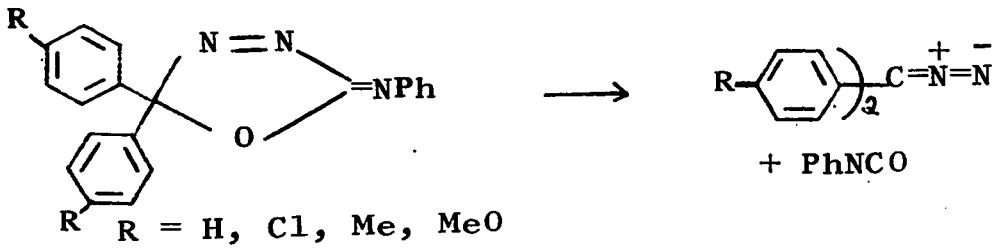
Because the correlation was somewhat tenuous - only three points were used, and these did not give a very good fit to a straight line - the authors felt that no conclusions, other than the fact that the C_5-N bond was breaking in the rate-determining step, could be drawn. The bond breaking was thought to be a homolytic process.

The magnitude of ρ also suggested that there could not be development of a full negative change at C-5. The ρ value for a transition state such as that shown below would be much larger than 0.62.



The only definite conclusion that could be made on the basis of the available evidence was that a C_5-N bond was being broken in the rate-determining step. Thus, whether the mechanism involved cleavage of two azo-carbon bonds or a fully concerted decomposition could not be ascertained.

A similar correlation of structure and rate of decomposition <u>via</u> the retro-1,3-addition reaction was attempted for the following series of oxadiazolines:



R = H, Cl, Me, MeO

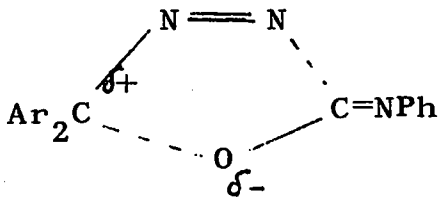
However, a linear relationship could not be obtained between σ and log k/k_o; nor did a linear relationship exist between log k/k_o and σ^+. (The σ^+ constants, obtained by Brown and Okamoto from the solvolysis of substituted <u>tert</u>-cumyl chlorides, have been used successfully in the correlation of rates of reactions involving development

of positive charge at the transition state)(37).

The most satisfying correlation was obtained with the modified Hammett relation of Tsuno and Yukawa (38). When r was set equal to 0.5, the equation

$$\log k/k_o = \rho(\sigma + r\Delta\sigma^+)$$

gave a ρ value of -1.31. This modified Hammett equation is based on the premise that because the degree of resonance delocalization should depend on the amount of charge generated at the transition state, the substituent "constant" should also vary with the reaction. West and Warkentin therefore contended that considerably less positive charge was developed at the decomposition transition state than is developed in solvolysis of cumyl chlorides. Their interpretation of these results is shown below:



No conclusion about the extent of C-N bond breaking could be drawn.

EXPERIMENTAL

Introduction

The experimental section has been divided broadly into two halves: synthesis of several new Δ^3-1,3,4-oxadiazolines and Δ^3-1,3,4-oxadiazolinones, and thermal decomposition of some of these compounds.

I. Synthesis

A. General

The infrared spectra were recorded on Perkin Elmer 521, or Beckman 337 instruments. Ultraviolet and visible spectra were run on a Cary 14 instrument. A Varian A-60 or T-60 was used in N.M.R. studies. Solvents used in obtaining these spectra are mentioned in the appropriate section of the text.

Elemental analyses were performed by Swarzkopf Microanalytical Laboratory, Woodside, N. Y.; Alfred Bernhardt, Mülheim, German; and A. B. Gygli, Toronto, Canada. In a few cases, satisfactory analyses were not obtained; these analyses were regarded as criteria of purity, not of structure.

Melting points were determined on a Thomas-Hoover

capillary melting point apparatus and are uncorrected.

All nuclear magnetic resonance spectra are expressed in parts per million (p.p.m.) from tetramethylsilane (TMS). Infra-red spectra are quoted in reciprocal centimeters. Ultraviolet and visible spectra are described by a number representing λ_{max} in millimicrons, followed by a bracketed number describing log ε.

B. Preparation of 5,5-Dimethyl-2-(arylimino)-Δ^3-1,3,4-oxadiazolines

The synthetic methods used to prepare most of the Δ^3-1,3,4-oxadiazolines in this section have previously been described by West and Warkentin (1). Nevertheless, the first preparation in this section has been dealt with in some detail. The ensuing examples have been dealt with briefly.

(1) Preparation of 5,5-Dimethyl-2-(phenylimino)-Δ^3-1,3,4-oxadiazoline

Acetone semicarbazone was prepared by the usual method from acetone and semicarbazide hydrochloride (Fisher certified reagent) to give a white powder, m.p. 187-188°C [lit. (39) m.p. 187-188°C].

Following the method of Borsche (40), 58 g (0.5

mole) of acetone semicarbazone was reacted with 93 g (1.0 mole) of aniline (Fisher certified reagent) at 146-152°C to yield 28 g (29%) of acetone 4-phenylsemicarbazone, m.p. 154-155°C, after recrystallization from ethanol [lit. (39) m.p. 155-156°C].

This substituted semicarbazone (3.0 g, 0.016 mole) was dissolved in 100 ml of methylene chloride and added dropwise to an ice-cold stirred solution of 10 g (0.022 mole) of lead tetra-acetate (MCB, washed with 30-60°C petroleum ether prior to use) in 200 ml of methylene chloride. During the thirty minute addition, the reaction flask was swept with a slow stream of nitrogen. At the end of this time, the reaction mixture was opaque and yellow.

The reaction was stopped by the addition of 200 ml of water; the mixture was filtered through wet Celite cake to remove lead dioxide. This was followed by three washings each of water, aqueous sodium bicarbonate, and water. After drying over anhydrous sodium sulfate, the methylene chloride was removed on the rotary evaporator. The orange oil was crystallized from chloroform and 30-60°C petroleum ether to yield 2.8 g (96%) of bright yellow crystals, m.p. 125-128°C [lit. (1) m.p. 125-128°C].

(2) Preparation of 5,5-Dimethyl-2-[(p-methoxyphenyl)imino]-Δ^3-1,3,4-oxadiazoline

Acetone semicarbazone (25 g, 0.22 mole) was heated with 40 g (0.33 mole) of p-anisidine (BDH reagent) in 175 ml of bis(2-methoxyethyl) ether at 160°C. After fifteen minutes, the dark brown solution was poured into 600 ml of 10% acetic acid solution. The product, a light tan solid, was recrystallized from ethanol to yield 11.6 g (24%) of shiny tan crystals, m.p. 167-169°C.

NMR($CDCl_3$): 1.90 s (3H), 2.00 s (3H), 3.65 s (3H), 6.8-7.5 m (4H).

IR(KBr disc): 1681 (C=N).

Analysis: Calculated for $C_{11}H_{15}N_3O_2$: C 59.71, H 6.83, N 18.99; Found: C 59.66, H 6.65, N 18.75.

The product (22 g, 0.10 mole) was oxidized at 0°C with lead tetra-acetate (66.5 g, 0.15 mole) yielding 14.4 g (67%) of yellow crystals, m.p. 94-95°C, after recrystallization from 30-60°C petroleum ether.

NMR($CDCl_3$): 1.71 s (6H), 3.95 s (3H), 7.49 q (4H).

IR($CHCl_3$): 1694 (C=N), 1114, 947, 835.

Analysis: Calculated for $C_{11}H_{13}N_3O_2$: C 60.24, H 5.98, N 19.18; Found: C 60.17, H 5.99, N 18.74.

(3) Preparation of 5,5-Dimethyl-2-(p-tolylimino)-Δ^3-1,3,4-oxadiazoline

Acetone semicarbazone (28.8 g, 0.25 mole) was heated at 143°C for 30 minutes with 32.2 g (0.30 mole) of p-toluidine (Eastman Organic) in 300 ml of bis(2-methoxyethyl) ether. The dark solution was poured into 400 ml of 10% acetic acid solution, and the precipitate recrystallized from ethanol-water. Light tan crystals, (11.7 g, 23%) m.p. 174-176°C. were obtained [lit. (41) m.p. 174-175°C].

Lead tetra-acetate (33 g, 0.015 mole) was used to oxidize the semicarbazone prepared as described above (10 g, 0.050 mole). The yield of yellow crystals, after one recrystallization from petroleum ether-chloroform, was 9.6 g (95%), m.p. 97-98.5°C.

NMR(CCl_4): 1.67 s (6H), 2.43 s (3H), 7.44 m (4H).

IR($CHCl_3$): 1697, 1115, 947, 821.

UV(95% ethanol): 226(4.00), 332(3.89).

Analysis: Calculated for $C_{11}H_{13}N_3O$: C 64.99, H 6.45, N 20.69; Found: C 64.72, H 6.52, N 20.42.

(4) Preparation of 5,5-Dimethyl-2-[(p-chlorophenyl)imino]-Δ^3-1,3,4-oxadiazoline

Acetone semicarbazone (28.8 g, 0.25 mole) was stirred with p-chloroaniline (38 g, 0.30 mole) (Eastman Organic) at 160°C in 150 ml of bis(2-methoxyethyl) ether until evolution of ammonia had ceased. The yield of substituted semicarbazone was 7.7 g (14%), m.p. 169-170°C.

NMR($CDCl_3$): 1.95 s (3H), 2.04 s (3H), 7.15-7.6 q (4H), 8.45 s (broad, 1H), 9.2 s (broad, 1H).

IR($CHCl_3$): 1690.

Analysis: Calculated for $C_{10}H_{12}ClN_3O$: C 53.22, H 5.36, Cl 15.71, N 18.62; Found: C 53.13 H 5.65, Cl 15.62, N 18.56.

The oxidation of the substituted semicarbazone with 22.7 g (0.51 mole) of lead tetra-acetate gave 6.0 g (78%) of pale yellow crystals. They were recrystallized from 30-60°C petroleum ether, m.p. 85-86°C.

NMR($CDCl_3$): 1.73 s (6H), 7.62 s (4H).

UV(95% ethanol): 227(4.02), and 325(3.82).

IR($CHCl_3$): 1701, 1115, 948, 826.

Analysis: Calculated for $C_{10}H_{10}ClN_3O$: C 53.70, H 4.51, N 18.79; Found: C 53.73, H 4.45, N 18.53.

(5) Preparation of 5,5-Dimethyl-2-[(p-nitrophenyl)imino]-Δ^3-1,3,4-oxadiazoline

In step one of this three-step synthesis, 4-(p-nitrophenyl)semicarbazide was prepared by a variation of the method of Tsao (42). p-Nitrophenyl isocyanate (Eastman practical) (10 g, 0.061 mole) in 100 ml of toluene was added dropwise to a rapidly stirred solution of anhydrous hydrazine (Matheson, 97%) (3.2 g, 0.10 mole) in 240 ml of toluene. After three hours, an orange-tan precipitate formed. When this solid was filtered, and recrystallized from absolute ethanol, 8.4 g (70%) of the reported product was obtained, m.p. 183-184°C (dec.) (42). The hydrochloride salt was prepared by dissolving the solid in boiling absolute ethanol and adding excess concentrated hydrochloric acid. Upon cooling, 7.8 g of the salt, m.p. 239.5-240.5°C [lit. (42) m.p. 239°C (dec.)] was obtained.

The semicarbazone was prepared by dissolving the salt in a minimum amount of 0.1N hydrochloric acid. Addition of 2.5 ml of acetone in 10 ml of water caused precipitation of a yellow solid. Yield of the unrecrystallized product was 7.0 g (87%), m.p. 236-237°C [lit. (42) m.p. 235°C].

Because the semicarbazone was only slightly soluble

in methylene chloride, the oxidation procedure was modified slightly to include a longer reaction time. A slurry of 7.0 g of the semicarbazone, and 20 g of lead tetra-acetate in 500 ml of methylene chloride was stirred under nitrogen for five hours at ice temperature. At the end of this time, the mixture was lemon yellow. After the customary work-up and recrystallization from petroleum ether-chloroform, 0.6 g (8.5%) of a mixture of two types of crystals was obtained. Both the opaque, pale yellow crystals, and the cylindrical, bright yellow needles had a m.p. of 108-109°C. Their various spectra were identical.

NMR($CDCl_3$): 1.70 s (6H), 7.35-8.30 q (4H).

IR($CHCl_3$): 1693, 1590, 1340.

UV(95% ethanol): 316(4.16), and 220(4.01).

Analysis: Calculated for $C_{10}H_{10}N_4O_3$: C 51.28, H 4.30, N 23.92; Found: C 51.96, H 4.21, N 23.73.

(6) Preparation of 5,5-Dimethyl-2-[(p-bromophenyl)imino]-Δ^3-1,3,4-oxadiazoline

Acetone semicarbazone (23 g, 0.20 mole) was heated at 140-150°C for thirty-five minutes with 50 g (0.29 mole) of p-bromoaniline (Eastern) in 200 ml of bis(2-methoxyethyl)

ether. After work-up and recrystallization from ethanol, 5.5 g (10% yield) of a white solid, m.p. 171-173°C, was obtained [lit. (43) m.p. 174°C].

Acetone 4-(p-bromophenyl)semicarbazone (5.0 g, 0.0054 mole) was oxidized with 12 g of lead tetra-acetate (0.026 mole). Crystallization of the resultant red oil from petroleum ether-chloroform gave 1.1 g (22% yield) of pale yellow crystals, m.p. 101-101.5°C.

NMR($CDCl_3$): 1.62 s (6H), 7.24 q (4H).

UV(95% ethanol): 3250(4.033), 2280(4.223).

IR($CHCl_3$): 1694, 1478, 1110, 946.

Analysis: Calculated for $C_{10}H_{10}BrN_3O$: C 44.80, H 4.13, N 15.68, Br 29.80; Found: C 44.98, H 4.06, N 15.84, Br 30.06.

C. Preparation of 5,5-Diphenyl-2-(arylimino)-Δ^3-1,3,4-oxadiazolines

The first preparation in this series will be described in detail. It may be assumed that unless otherwise indicated, the remaining preparations were similar.

(1) Preparation of 5,5-Diphenyl-2-(p-anisylimino)-Δ^3-1,3,4-oxadiazoline

Benzophenone (55 g, 0.26 mole, Fisher reagent),

sodium acetate trihydrate (49 g, 0.60 mole) and semicarbazide hydrochloride (67 g, 0.60 mole, Fisher reagent) were refluxed in 800 ml of ethanol and 200 ml of water to yield 45 g (72%) of benzophenone semicarbazone, m.p. 163-166°C.

The 4-substituted semicarbazone was prepared by heating and stirring benzophenone semicarbazone (30 g, 0.13 mole) and p-anisidine (Eastman practical, 62 g, 0.50 mole) in 200 ml of bis(2-methoxyethyl) ether. After a thirty-minute reaction at 160°C, the dark solution was cooled and poured into 1500 ml of 10% acetic acid. A dark brown solid (28 g) was obtained. After one recrystallization from absolute ethanol 19 g (42%) of pale yellow crystals, m.p. 164-167°C were obtained.

NMR($CDCl_3$): 3.79 s (3H), 6.8-7.7 m (14H), 8.18 s (1H, broad).

IR(KBr disc.): 1672, 1490, 1120.

Benzophenone 4-(p-anisyl)semicarbazone (4.3 g, 0.012 mole) in 50 ml of methylene chloride was added dropwise to a stirred solution of 10.6 g (0.024 mole) of lead tetra-acetate in 200 ml of the same solvent at 0°C. The solution was stirred for one hour at room temperature. The reaction was quenched by the addition of 200 ml of water,

and the subsequent work-up followed the scheme used for section B. Crystallization of the resultant red oil from petroleum ether-chloroform produced 0.31 g (7.2% yield) of yellow crystals, m.p. 85-87°C (dec.).

NMR(CCl_4): 3.80 s (3H), 6.76-7.60 m (14H).

IR($CHCl_3$): 1680.

(2) Preparation of 5,5-Diphenyl-2-(phenylimino)-Δ^3-1,3,4-oxadiazoline

The procedure followed that described by West and Warkentin (1). The oxidation of 10 g (0.032 mole) of benzophenone 4-phenylsemicarbazone with 21.2 g (0.048 mole) of lead tetra-acetate yielded 1.5 g (15%) of the expected oxadiazoline after two recrystallizations from petroleum ether-chloroform. The melting point of the yellow crystals was 125-127°C (dec.) [lit. (1) m.p. 125-127°C].

(3) Preparation of 5,5-Diphenyl-2-(p-tolylimino)-Δ^3-1,3,4-oxadiazoline

Heating benzophenone semicarbazone (30 g, 0.13 mole) and p-toluidine (Eastman practical, 53 g, 0.5 mole) in 300 ml of bis(2-methoxyethyl) ether gave 22 g (54%) of benzophenone 4-p-tolylsemicarbazone as white crystals, m.p. 187.5-188.5°C.

NMR($CDCl_3$): 2.31 s (3H), 7.0-7.7 m (14H), 8.25 s (1H, broad).

IR(KBr disc.): 1675, 1530, 1107.

The substituted semicarbazone (15 g, 0.046 mole) was oxidized with lead tetra-acetate (30 g, 0.069 mole) in a two and one-half hour reaction at room temperature. Crystallization occurred when the red oil obtained after work-up was taken up in petroleum ether-chloroform. The yield of the oxadiazoline, m.p. 101-103°C, was 32 g (21%).

NMR(CCl_4): 2.35 s (3H), 7.04-7.5 m (14H).

IR(bromobenzene): 1687, 1142.

Analysis: Calculated for $C_{21}H_{17}N_3O$: C 77.04, H 5.23, N 12.84; Found: C 77.14, H 5.35, N 12.88.

(4) Preparation of 5,5-Diphenyl-2-[(p-chlorophenyl)imino]-Δ^3-1,3,4-oxadiazoline

Benzophenone semicarbazone (30 g, 0.125 mole) was reacted with p-chloroaniline (Eastman practical, 64 g, 0.50 mole) in bis(2-methoxyethyl) ether. The yield was 19 g of off-white crystals, m.p. 202-202.5°C.

NMR($CDCl_3$): 7.2-7.78 m (14H), 8.33 s (1H, broad).

IR($CHCl_3$): 1687, 1588, 1507, 1120.

The oxidation of the semicarbazone (12.5 g,

0.036 mole) was accomplished with 24 g (0.054 mole) of lead tetra-acetate in a total volume of 500 ml of methylene chloride. An amount of 1.0 g (8% yield) of yellow crystals of oxadiazoline, m.p. 97-99°C, was obtained.

NMR($CDCl_3$): 7.37 s.

IR(CCl_4): 1696, 1485, 930, 866.

Analysis: Calculated for $C_{20}H_{14}N_3OCl$: C 69.01, H 4.06, N 12.08; Found: C 69.24, H 3.97, N 12.01.

(5) Preparation of 5,5-Diphenyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline

The compound 4-methylsemicarbazide was made according to the method of Vogelsang (44). The reaction of 30 ml of 95% hydrazine (Eastman) with 15 ml of methyl isocyanate (Eastman) produced 17.5 g (99%) of unrecrystallized product m.p. 111-114°C [lit. (46) m.p. 114-116°C].

Benzophenone (9.2 g, 0.050 mole), 4-methylsemicarbazide (5.5 g, 0.062 mole), and a few ml of acetic acid were refluxed in 20 ml of water and 20 ml of ethanol for thirteen hours. Upon cooling, white shiny crystals precipitated out. After one recrystallization from ethanol-water, 6.7 g of

benzophenone 4-methylsemicarbazone, m.p. 151-152°C, was obtained.

NMR($CDCl_3$): 2.91 s (3H), 3.00 s (3H), 6.33 s (1H, broad), 7.15-7.70 m (10H).

IR(CCl_4): 1685, 1507, 1110.

This semicarbazone (5.0 g, 0.020 mole) was oxidized with 17.5 g (0.040 mole) of lead tetra-acetate in a two-hour reaction at room temperature. Attempts to crystallize the pink oil obtained were unsuccessful.. The oil was therefore chromatographed on a 10 cm X 4 cm florisil column with a 3:1 petroleum ether-chloroform solvent. The pink solid obtained was recrystallized twice from petroleum ether to yield 0.3 g (6% yield) of white crystals, m.p. 57-59°C.

NMR($CDCl_3$): 3.41 s (3H), 7.47 s (10H).

IR($CHCl_3$): 1717, 1525, 1425, 928.

Analysis: Calculated for $C_{15}H_{13}N_3O$: C 71.69, H 5.21, N 16.72; Found: C 69.92, H 5.28, N 16.64.

UV(95% ethanol): 250(4.176).

(6) Attempted Preparation of 5,5-Diphenyl 2-[p-nitrophenyl)imino]-Δ^3-1,3,4-oxadiazoline

The compound 4-(p-nitrophenyl)semicarbazide hydrochloride (0.0086 mole, 2.0 g) was refluxed with

benzophenone (1.6 g, 0.0086 mole) and sodium acetate trihydrate (2.3 g, 0.0172 mole) in 80 ml of ethanol and 20 ml of water. An eighteen-hour reflux yielded, after one recrystallization from ethanol, 1.2 g (39% yield) of a pale yellow solid, m.p. 225-228°C.

The first attempt to oxidize benzophenone 4-(p-nitrophenyl)semicarbazone involved a slight modification of the usual procedure because of the low solubility of the semicarbazone in methylene chloride. A slurry of the semicarbazone (4.0 g, 0.011 mole) and lead tetra-acetate (5.6 g, 0.015 mole) in 200 ml of methylene chloride was stirred at room temperature for twenty hours. At the end of this time, no oxadiazoline could be detected.

The second attempt to oxidatively cyclize the semicarbazone employed lead tetra(trifluoroacetate) (45,46). This oxidizing agent (2.5 g, 0.058 mole) was dissolved in 10 ml (0.13 mole) of trifluoroacetic acid which had been dried with a few drops of acetic anhydride. The solution was stirred under nitrogen and cooled in an ice bath. The semicarbazone (1.0 g, 0.028 mole) was added as the dry solid. This caused an immediate darkening of the solution. The reaction was stirred at room temperature for two hours.

The reaction mixture was diluted with methylene chloride. After neutralization of the reaction mixture with 10% sodium hydroxide solution, the methylene chloride layer was worked up by the usual washing procedure. The spectral data of the yellow solid obtained by this process did not coincide with that data anticipated for an oxadiazoline. No further study of this reaction was undertaken.

D. Preparation of 5,5-Dialkyl-2-(alkylimino)-Δ^3-1,3,4-oxadiazolines and 5,5-Dialkyl-Δ^3-1,3,4-oxadiazolinones

(1) Preparation of 5,5-Dimethyl-2-(phenethylimino)-Δ^3-1,3,4-oxadiazoline

Acetone semicarbazone (28.8 g, 0.25 mole) was heated for thirty-five minutes with 2-phenethylamine (61 g, 0.50 mole) at 130-150°C. Vigorous evolution of ammonia occurred. After the usual work-up and recrystallization from water-ethanol, 37.5 g (67% yield) of shiny tan crystals were obtained, m.p. 87-89°C.

NMR($CDCl_3$): 1.85 s (3H), 1.92 s (3H), 2.75-3.75 m (4H), 7.28 s (5H).

IR(CCl_4): 1670, 1242, 1120.

Benzophenone 4-phenethylsemicarbazone (10 g,

0.046 mole) was oxidized with lead tetra-acetate (30 g, 0.068 mole) in 200 ml of methylene chloride. The reaction mixture, after one hour of stirring at room temperature, was worked up to yield 4.5 g of a colourless oil. After

NMR($CDCl_3$): 1.43 s (3H), 2.85-3.84 m (4H), 7.23 s (5H).

IR($CHCl_3$): 1720, 1370, 980.

one month in the refrigerator, a few milligrams of a white crystalline solid, m.p. 130-132°C, was obtained. However, from the spectral data obtained on this compound, it was shown to be bis(phenethyl)urea [lit. (47) m.p. 140-141°C].

NMR($CDCl_3$): 2.68-3.61 m (4H), 7.27 s (5H), 4.4 s (1H, broad).

Mass spectrum: parent ion at m/e = 268.

The oxadiazoline remaining had the same NMR and IR values as given for the mixture. It could not be induced to crystallize.

(2) Preparation of 5,5-Dimethyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline and 5,5-Dimethyl-Δ^3-1,3,4-oxadiazolinone

The compound 4-methylsemicarbazide was prepared as described in part C (5). Unrecrystallized 4-methylsemicarbazide (4.0 g, 0.045 mole) was dissolved in 15 ml of

water and 10 ml of ethanol. A few drops of acetic acid were added to the solution, and, with vigorous stirring, acetone (2.6 g, 0.046 mole) was added in 20 ml of ethanol. After several minutes of stirring, the solution was put on the rotary evaporator until a solid began to precipitate. After recrystallization of the solid from ethanol, 5.1 g (87%) of acetone 4-methylsemicarbazone, m.p. 114-116°C [lit. (44) m.p. 116°C] was obtained.

NMR($CDCl_3$): 1.93 s (3H), 2.81 s (3H), 2.88 s (3H), 6.26 s (2H, broad).

IR(KBr disc.): 1673, 1545, 1117.

Lead tetra-acetate (50 g, 0.11 mole) was used to oxidize 11.5 g (0.089 mole) of the semicarbazone. The procedure followed was similar to that followed for the preparation of other 5,5-dimethyloxādiazolines, with the exception of one point: all wash solutions were used ice-cold to minimize hydrolysis of the product. The yield in this reaction was 6.0 g (55%) of a waxy, yellowish solid. The spectral data suggested that the product was a mixture of two compounds.

NMR(CCl_4): 1.59 s, 1.67 s, 3.13 s; integral ratios were 2:3.5:1, respectively.

IR(CCl_4): 3020, 1835, 1724, 1459, 1378, 936, 874.

The difficulties of separating these two compounds resulted from their similar sublimation pressures, and similar solubilities in petroleum ether-chloroform mixtures. An attempt to use column chromatography to achieve a separation was also unsuccessful. When 0.4 g of the mixture was eluted from a column of 40 g of 20% activated charcoal in Celite, the product (or products) was reduced to acetone 4-methylsemicarbazone. The eluting solvent was 1:1 petroleum ether-methylene chloride.

The separation technique which was found to be most satisfactory was vapor phase chromatography employing a 5' X 1/4" 20% SE-30 column (60/80 DMCS, Chrom W) that had been prepared with Silyl 8 (Pierce Chemical Company) to remove all compounds bearing active H groups. The instrument used was an Aerograph A-90-P. By using collector, detector, and column temperature below 85°C, satisfactory separation was achieved.

The material with the shortest retention time proved to be 5,5-dimethyl-Δ^3-1,3,4-oxidiazolinone. It was an oil at room temperature.

NMR($CDCl_3$): 1.63 s.

IR(CCl_4): 1835.

UV(distilled hexane): 216 nm(3.54), 365(2.51), 373(2.57), 381(2.38).

Analysis: Calculated for $C_4H_6N_2O_2$: C 42.11, H 5.26, N 24.56. Found: C 41.97, H 5.35, N 24.81.

The material with the longer retention time was shown to be 5,5-dimethyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline.

NMR($CDCl_3$): 1.65 s (6H), 3.32 s (3H).

IR(CCl_4): 2590, 1712, 1367, 880, 930.

UV(distilled hexane): 3340(1.45), 2550(2.66).

(3) Preparation of 5-Ethyl-5-methyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline and 5-Ethyl-5-methyl-Δ^3-1,3,4-oxadiazolinone

An aqueous solution of 4-methylsemicarbazide (10 g, 0.11 mole) was reacted with 8.1 g (0.12 mole) of methyl ethyl ketone. The reaction was catalyzed by a few drops of acetic acid. Methyl ethyl ketone 4-methylsemicarbazone, m.p. 58-62°C, was obtained in 52% yield (9.0 g).

The prepared semicarbazone (17 g, 0.12 mole) was oxidized with 56 g (0.13 mole) of lead tetra-acetate to

yield 12 g of product. The infra-red spectrum of the unpurified product suggested strongly that it was a mixture, similar to that found in the previous preparation. The predominant feature of the spectrum was two strong carbonyl-like absorptions at 1837 and 1715 cm^{-1}. The technique used to separate the two components was the same as that used in the preceding preparation.

5-Ethyl-5-methyl-Δ^3-1,3,4-oxadiazolinone:

NMR($CDCl_3$): 1.63 s (3H), 0.80 t (3H), 2.10 q (2H).

IR(CCl_4): 1835, 1105, 939.

UV(distilled hexane): 2160(2.99), 3650(1.99), 3730(2.04), 3810(1.83).

Analysis: Calculated for $C_5H_8N_2O_2$: C 46.87, H 6.30, N 21.89; Found: C 47.01, H 5.99, N 21.69.

5-Ethyl-5-methyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline:

NMR(CCl_4): 3.32 s (3H), 2.02 q (2H), 1.57 s (3H), 0.80 t (3H).

IR(CCl_4): 1713, 1198, 1118, 935.

UV(distilled hexane): 2590(3.56) and weak shoulder at 3370.

Analysis: Calculated for $C_6H_{11}N_3O$: C 51.06, H 7.87, N 29.80. Found: C 52.36, H 8.37, N 29.40.

(4) Oxidative Cyclization of Acetone Semicarbazone

Acetone semicarbazone (2.0 g, 0.17 mole) was reacted with 10 g (0.022 mole) of lead tetra-acetate in methylene chloride. After a half-hour reaction at room temperature, the mixture was worked up by the usual procedure. The yellowish oil (0.7 g) obtained showed a strong infra-red absorption at 1835 cm^{-1}. Both the spectral data and the retention time exhibited by this material in vapour phase chromatography suggested that it was identical to the previously prepared 5,5-dimethyl-Δ^3-1,3,4-oxadiazolinone.

(5) Oxidative Cyclization of Benzophenone Semicarbazone

Benzophenone semicarbazone (50 mg, 0.0021 mole) was oxidized with 1.8 g (0.0040 mole) of lead tetra-acetate in 10 ml of methylene chloride. The pinkish oil obtained after work-up revealed the presence of both diphenyldiazomethane and 5,5-diphenyl-Δ^3-1,3,4-oxadiazolinone. The instability of the latter, even at -20°C, prevented its purification. At this temperature, the oil turned progressively darker red, indicating the formation of diphenyldiazomethane.

E. Alternative Means of Oxidative Cyclization of 4-Substituted Ketone Semicarbazones

Partly as a result of work published in this field (48,49), and partly as a result of the failure to cyclize benzophenone 4-(p-nitrophenyl)semicarbazone, a few preliminary experiments were carried out to find other oxidizing agents which would cyclize ketone 4-aryl(alkyl) semicarbazones.

(1) Oxidative Cyclization of Benzophenone 4-Phenylsemicarbazone Using Active Manganese Dioxide

The active manganese dioxide was prepared by the method of Attenburrow (49). Manganese sulphate tetrahydrate (BDH, Analar, 111 g) in 150 ml of water and 117 ml of 40% w/v sodium hydroxide solution was reacted with 96 g of potassium permanganate (Shawinigan reagent) in 600 ml of water to yield a dark brown solid. This was dried overnight at 110°C and powdered before use.

Benzophenone 4-phenylsemicarbazone (2.0 g, 0.0064 mole) was stirred with 20 g of active manganese dioxide in 150 ml of benzene for 48 hours at room temperature. The mixture was filtered through Celite and evaporated down to an orange oil. Crystallization of the oil from

chloroform-petroleum ether yielded 0.3 g (15%) of yellow crystals. The infra-red spectrum and a mixed melting point with an authentic sample confirmed its identification as 5,5-diphenyl-2-(phenylimino)-Δ^3-1,3,4-oxadiazoline. Starting material was also recovered.

(2) Attempted Oxidative Cyclization of Acetone 4-Phenylsemicarbazone

The semicarbazone (1.0 g, 0.0077 mole) was stirred with 10 g of active manganese dioxide in 75 ml of benzene for 24 hours at room temperature. After filtration through Celite and evaporation, a red oil was obtained. The infra-red spectrum of this oil was similar to that of the expected Δ^3-1,3,4-oxadiazoline. However, the nuclear magnetic resonance trace exhibited only two absorptions: 1.42 (s) and 3.43 (broad, s). The oil was chromatographed on a column of Florisil using 1:5 chloroform-petroleum ether as solvent. The first fraction obtained yielded an orange solid, m.p. 62-63°C, that possessed no methyl functions (NMR). No further investigation of this material was attempted.

(3) Oxidative Cyclization of Acetone 4-Phenyl-semicarbazone by an Oxygen/Basic Alumina System

The semicarbazone (1.2 g, 0.0093 mole) was stirred with 20 g of basic alumina in 25 ml of reagent chloroform at room temperature. After several days, no reaction had taken place. The flask was then tightly stoppered and kept at 40-45°C for 25 days. Periodically, oxygen was bubbled through the mixture. At the end of this time, the mixture was filtered through Celite and evaporated. An infra-red spectrum of the oil obtained indicated that approximately 50% of it was starting material. The oil was crystallized from petroleum ether-carbon tetrachloride to give a first crop of starting material. The second crop (0.2 g) of yellow crystals, m.p. 141-142°C, showed the following characteristics:

Mass spectrum: parent ion at m/e = 191.

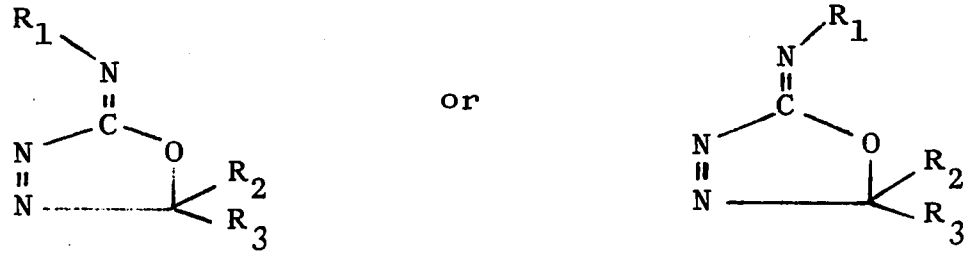
NMR($CDCl_3$): 1.57 s (6H), 7.16 m (5H).

IR(CCl_4): 1760, 1365, 1500.

These values agreed with those found by Landquist for 3,3-dimethyl-4-phenyl-Δ^3-1,2,4-triazolin-5-one (48).

F. Attempted Isomerization of some Δ^3-1,3,4-Oxadiazolines

All available evidence - infra-red and nuclear magnetic resonance spectra, vapour phase chromatography, as in the case of 5,5-dimethyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline, and the X-ray crystallographic study described elsewhere - strongly suggested that the Δ^3-1,3,4-oxadiazolines existed exclusively as one of two possible isomers:



Several attempts were made to prepare both isomeric forms; these were unsuccessful. These attempted isomerizations are described below.

(1) 5,5-Dimethyl-2-(benzylimino)-Δ^3-1,3,4-oxadiazoline was heated at 50°C for two hours with potassium iodide and benzyl chloride in deuterated acetonitrile. Nuclear magnetic resonance spectra, recorded both before and after the attempted isomerization, revealed that only thermal decomposition of the oxadiazoline had occurred.

(2) Dry hydrogen bromide was bubbled through a benzene solution containg 2-(benzylimino)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline. No new products were detected.

(3) The most promising experiment along these lines was the reaction between 2-(p-tolylimino)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline and p-anisidine. The oxadiazoline was reacted with two equivalents of p-anisidine hydrochloride in absolute methanol for two hours at room temperature. At the end of this time, the initially bright yellow solution had darkened. The solution was diluted with carbon tetrachloride, and washed repeatedly with water, then 10% sodium hydroxide solution. At the end of this procedure, a nuclear magnetic resonance spectrum showed that p-anisidine had been removed from the solution, but that much of the p-toluidine remained. The carbon tetrachloride solution was then chromatographed on a column of basic alumina with 1:1 chloroform-petroleum ether. The first fraction recovered from the column was a yellow oil. Nuclear magnetic resonance and infra-red spectra suggested that it was a mixture of the starting oxadiazoline and 2-(p-anisylimino)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline. The oil was crystallized from carbon tetrachloride-petroleum ether to give the latter oxadiazoline as the first crop of

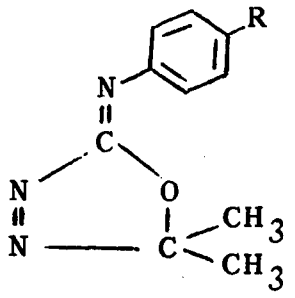
crystals. Spectral analysis and a mixed melting point with an authentic sample conclusively established its identity as the expected oxadiazoline. However, the expected isomerization of both starting material and product apparently did not occur. Further investigation is indicated.

II. Thermal Decomposition Studies of some Δ^3-1,3,4-Oxadiazolines and Oxadiazolinones

This section has been divided into three parts. In part A, the unsuccessful attempt to study the thermolysis of 2-(arylimino)-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines is described. Part B describes the successful study of the thermolysis of 2-(arylimino)-5,5-diphenyl-Δ^3-1,3,4-oxadiazolines. The last section is concerned with product and yield studies on the thermolysis of two oxadiazolinone derivatives.

A. Thermal Decomposition of 2-(Arylimino)-5,5-dimethyl-Δ^3-1,3,4-oxadiazolines

The thermal decomposition of the following series of compounds was studied:



R = H
CH$_3$
OCH$_3$
Cl
NO$_2$

The apparatus and experimental techniques used have been described previously (1), but will be briefly reiterated here. The existence of two parallel decomposition pathways necessitated the measurement of two independent rate constants. These measurements were done by (a) following the pressure change with time in a gas evolution train, and (b) measuring the rate of production of each aryl isocyanate formed in the thermolysis. The latter technique involved sealing aliquots of an oxadiazoline-bromobenzene solution into heavy-walled ampoules, and, at convenient intervals of time, removing a sample from the constant temperature bath (135^{o}C). This was immediately immersed into a dry ice-acetone slush bath. At the end of the kinetic run, each ampoule was opened, and the infra-red spectrum of each sample was scanned through the 2000 to 2500 cm^{-1} region (Perkin Elmer 521). The peak heights of the isocyanate absorptions were translated into the

units of "moles of isocyanate per litre" through the use of a calibration chart. This chart had been prepared by recording infra-red peak heights of standard solutions of each isocyanate. A typical calibration curve is shown.

When it became obvious that aryl isocyanates were not being formed in a first-order process, several attempts were made to discover the identity of the substance which was reacting with the aryl isocyanate being produced. Phenyl isocyanate was heated at 135°C with each of the following compounds: acetone, phenyl isocyanide, 4-methyl-1-pentene (analogous to the propene formed in the thermolysis solutions from dimethyl carbene), and p-tolyl isocyanate. In each case, the conditions used were identical to those used during the thermolysis. None of these substances reacted with phenyl isocyanate. No further study of these thermolyses was undertaken.

B. Thermal Decomposition of 2-(Arylimino)-5,5-diphenyl-Δ^3-1,3,4-oxadiazoline

The thermolysis of the following series of compounds was studied:

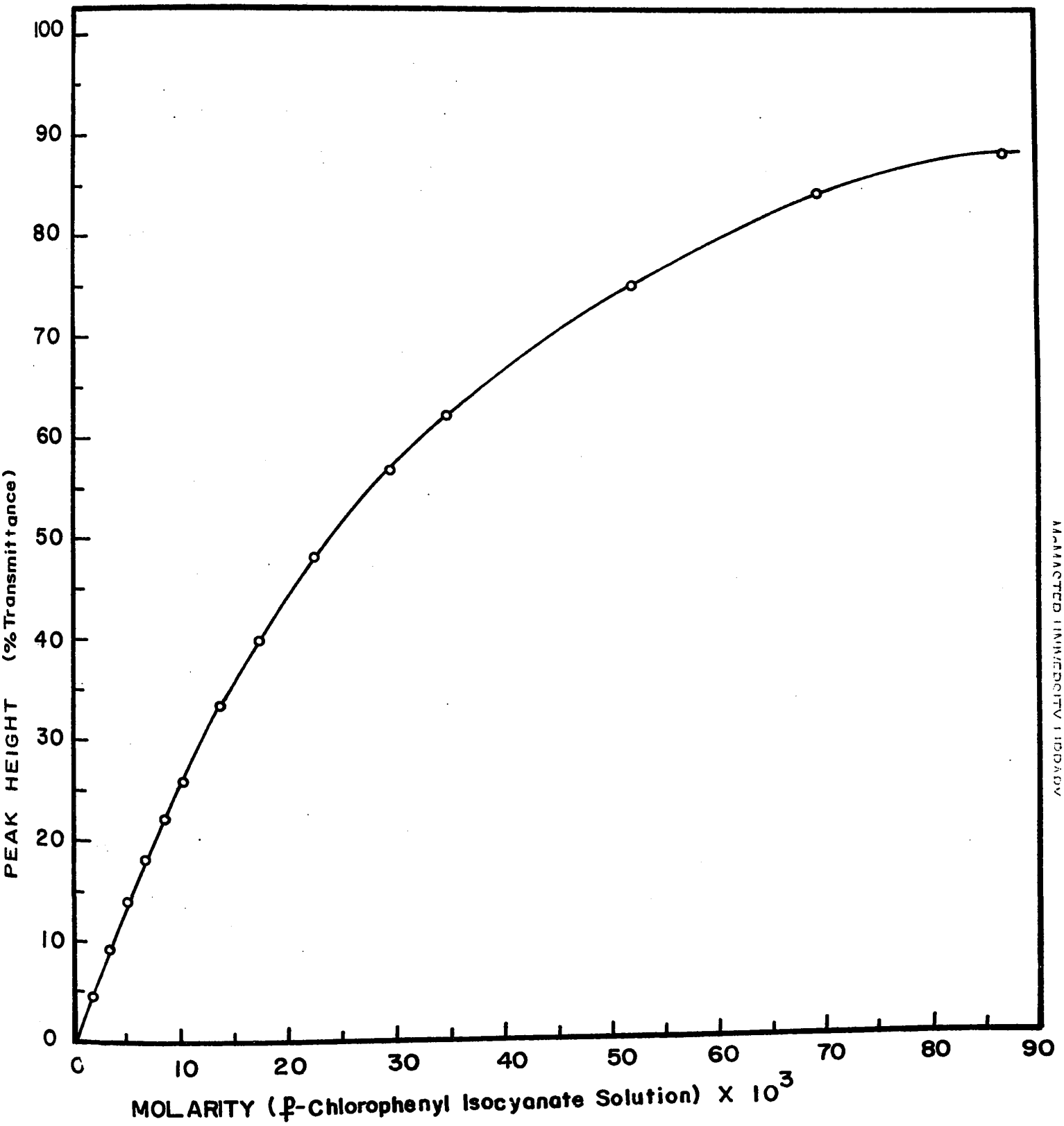


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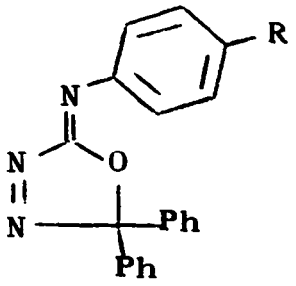
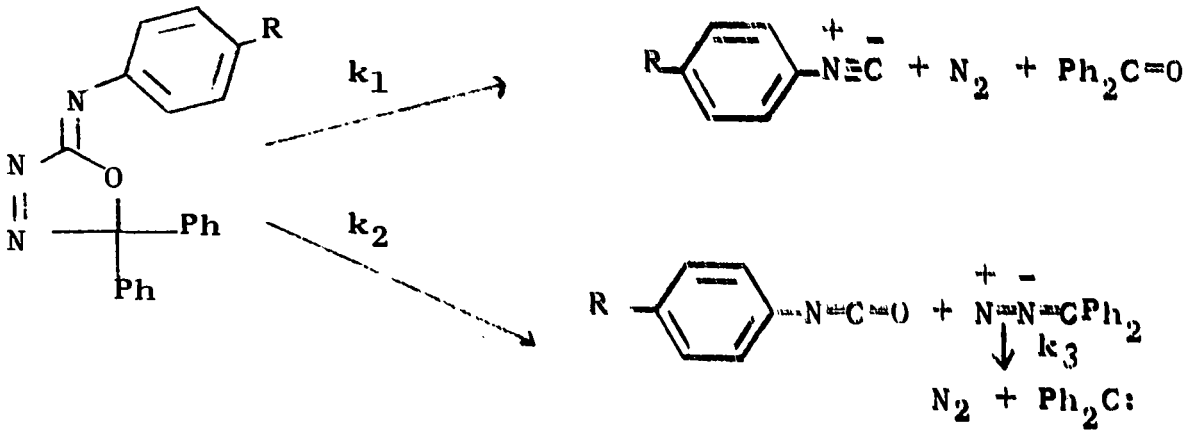
Fig.1 Plot of Absorption Peak Height (2263 cm^{-1}) versus Molarity of p— Chlorophenyl Isocyanate in Bromobenzene



R = H
CH$_3$
OCH$_3$
Cl

The solvent used was chlorobenzene which had been purified by one passage through a 5 cm X 20 cm column of alumina.

Infra-red studies of the partially decomposed oxadiazoline solutions showed these thermolyses to be very similar to those studied by West and Warkentin. The rate



constant k_2 was determined by following the production of aryl isocyanate. The rate constant k_1 was determined by following the production of benzophenone. Both of these measurements used the infra-red technique described in part A of this section.

The solvent used in the thermolyses was thoroughly degassed to prevent the possibility of dissolved oxygen in the solvent reacting with diphenyl carbene to produce benzophenone. This degassing was a two-part process: (a) the bulk solvent, after chromatography, was refluxed under nitrogen for several hours; (b) after the oxadiazoline had been dissolved in the solvent, each sample was degassed three times by freeze-pump-thaw cycles. The sample was then sealed under vacuum.

The constant temperature bath was regulated at 84.9 $^{o}C \pm 0.2^{o}C$ as measured by a National Research Council calibrated thermometer. At intervals, samples were removed from the bath and quickly immersed in dry ice-acetone. At the completion of the experiment, each sample was scanned on the Perkin Elmer 521 using 0.1 mm sodium bromide cells. The peak heights of both the aryl isocyanate (at approximately 2260 cm^{-1}) and of benzophenone (at approximately 1650 cm^{-1}) were recorded.

As well, in an analogous fashion, 2-(p-tolylimino)-5,5-diphenyl-Δ^3-1,3,4-oxadiazoline was decomposed thermally in nitrobenzene (Fisher certified reagent).

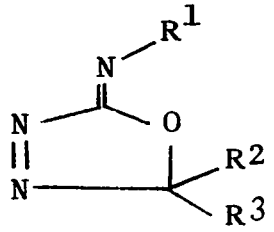
C. Thermal Decomposition of 5,5-Dimethyl-Δ^3-1,3,4-oxadiazolinone, and of 5-Ethyl-5-methyl-Δ^3-1,3,4-oxadiazolinone

Product studies only were undertaken in these thermolyses. Both compounds were thermolyzed in sealed tubes at 100°C. The composition of the products (after complete reaction) were obtained by vapour phase chromatographic techniques and from nuclear magnetic resonance spectra. The gaseous products were examined neither qualitatively nor quantitatively. Thermolyses were performed both neat and in carbon tetrachloride.

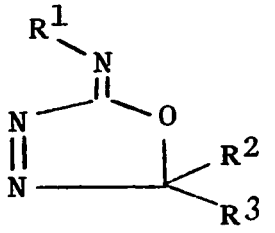
RESULTS AND DISCUSSION

I. Preparation and Stereochemistry of 2-Imino-Δ^3-1,3,4-oxadiazolines

In all cases studied thus far, only one of the two possible isomers of 2-(arylimino) or (alkylimino)-Δ^3-1,3,4-oxadiazolines has been isolated (1).



Z-isomer

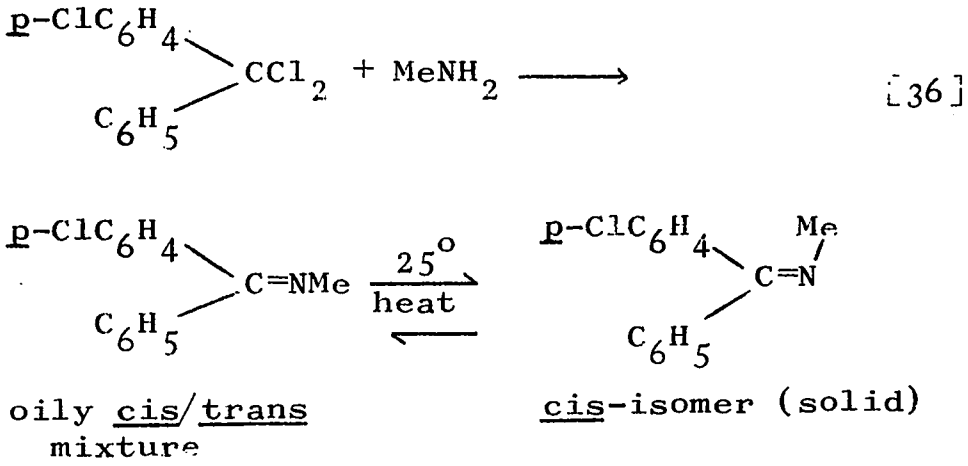


E -isomer

The products isolated from these preparations had sharp melting points, and showed infra-red, ultraviolet, and nuclear magnetic resonance spectra compatible with the existence of only one stereoisomer.

These results were in sharp contrast to previous reports of isomerism in ketimines. For example, in 1962, Curtin and Hausser found that cis-p-chlorobenzophenone methylimine crystallized as the cis isomer, but rearranged to an equilibrium mixture of cis and trans isomers in

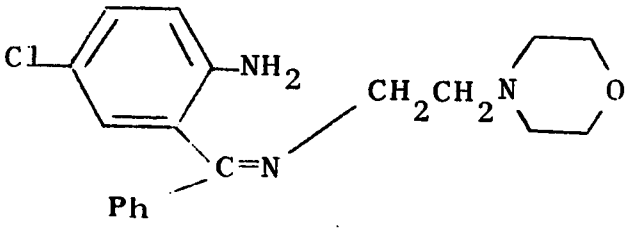
cyclohexane solution (eq. 36) (51). The infra-red spectrum of a freshly prepared sample was different from that of a sample which had been allowed to equilibrate at room temperature for two weeks. Ultraviolet spectra were also used to differentiate between cis and trans isomers, but the nuclear magnetic resonance spectra were identical. Similarly, p-nitrobenzophenone methylimine was obtained as the trans isomer in the solid state, but as an equilibrium mixture in solution (51). Similar results were obtained for aryl-



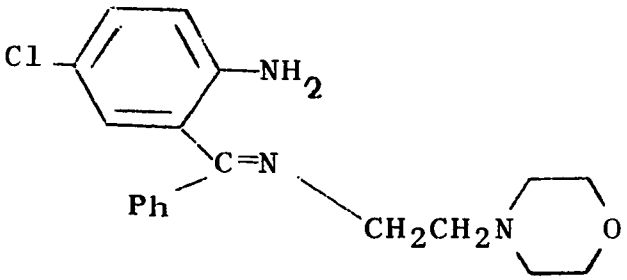
imines of some substituted benzophenones (51). The energies of activation for these isomerizations ranged from 18-20 kcal/mole for 4-nitro-4'-methoxybenzophenone p-tolylimine to 27.1 kcal/mole for p-nitrobenzophenone methylimine.

Two isomers of a morpholinoimine were reported by Bell, Conklin, and Childress (52,53). The two isomers

exhibited different melting points and absorption spectra. They did not equilibrate in solution. IV and V were



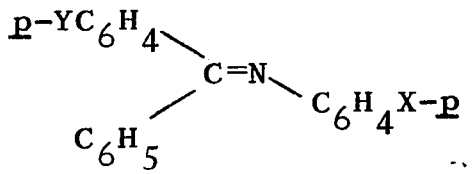
IV



V

separated by fractional crystallization; heating pure V above its melting point resulted in formation of IV.

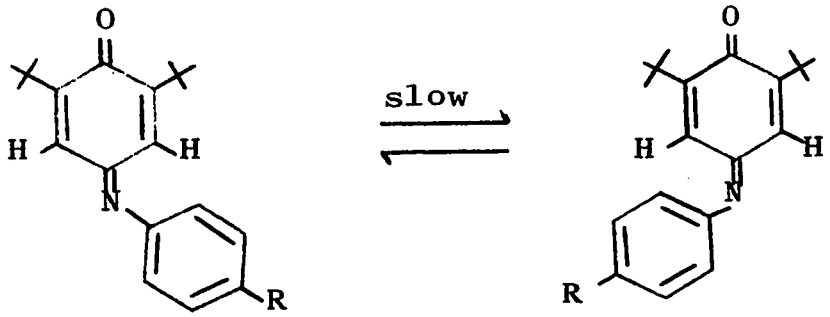
Nuclear magnetic resonance studies by Curtin and McCarty on some benzophenone arylimines revealed two methoxyl proton peaks (of 0.04-0.06 p.p.m. separation) in an equilibrated solution of the isomers (54). Thus the



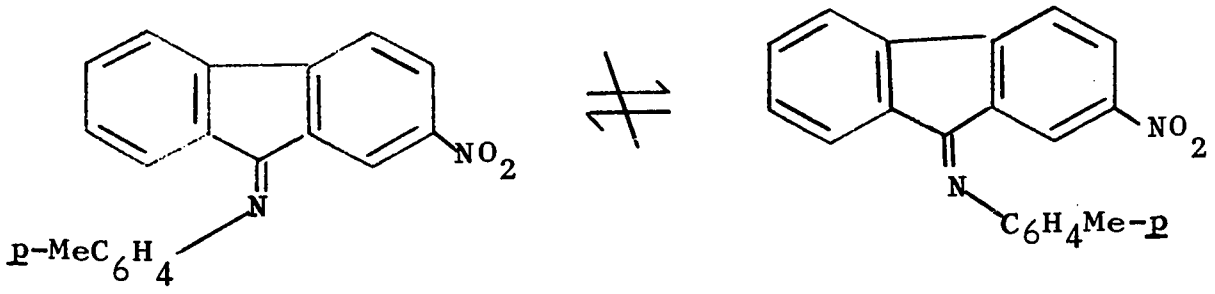
X = Me, Y = OMe
X = NMe_2, Y = OMe
X = Cl, Y = OMe

isomerization of the N-aryl groups was slow on the NMR time scale.

A similar magnetic resonance study by Rieker and Kessler on anils of 2,6-di-tert-butyl-1,4-benzoquinone showed that the tert-butyl resonance appeared as two singlets at τ 8.65 and 8.80 (55).



Another example has been reported of nonequilibrating ketimines. Taylor and Fletcher obtained isomers VI and VII by entirely different preparative methods (56). The structures were assigned on the basis of spectral data.

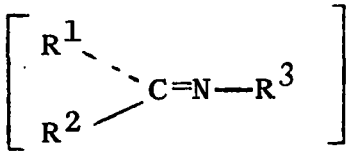


VI VII

[These results have been disputed by Curtin and Hausser (51)].

The configurational stability of the arylimino and alkylimino heterocycles discussed in the present work is not surprising in the light of the thermal instability of these compounds and the probable mechanism of isomerization. The energy of activation for the isomerization of alkylimines or arylimines of benzophenones has been calculated to be approximately 20-25 kcal/mole (51,54). This may be compared to the activation energy of the pyrolysis of iminooxadiazolines (20 kcal/mole) (1). Thus, it is probable that isomerization about the imino nitrogen is a kinetically slower process than the pyrolysis of the molecule.

The most probable mechanism for the uncatalyzed isomerization of ketimines is a lateral shift mechanism in which C, N, and R are colinear in the transition state.



Moreover, it has been observed that the most facile isomerizations are those in which R^3 is a bulky group (e.g., aryl). Presumably, relief of steric strain in the transition state is responsible for this effect. Assuming that the steric crowding in an imino oxadiazoline is less than that in an

analogous benzophenone imine, it is likely that the energy of activation for the isomerization of an iminooxadiazoline is several kcal/mole higher than that for a benzophenone imine. That is, there will be little relief of steric strain as the iminooxadiazoline approaches the linear transition state.

The existence of only one stereoisomer in the 2-iminooxadiazoline preparations raised three questions: (a) which isomer (Z or E) was obtained in the cyclization of semicarbazones? (b) why was the cyclization stereospecific? (c) how may the other isomer be obtained?

An X-ray crystal structure of 2-[(p-bromophenyl)-imino]-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline resolved the question of which isomer had been prepared (Figure 2). Several interesting results were observed among the experimentally determined bond angles and lengths: As was to be expected, the length of the C_5-O bond is considerably greater than that of the C_2-O bond. The relative weakness of the latter bond may be an important factor determining the pyrolysis mechanisms. The magnitude of the interior angles centred at C_2 and at each of the ring nitrogens reveal some strain in the ring system. The imino bond

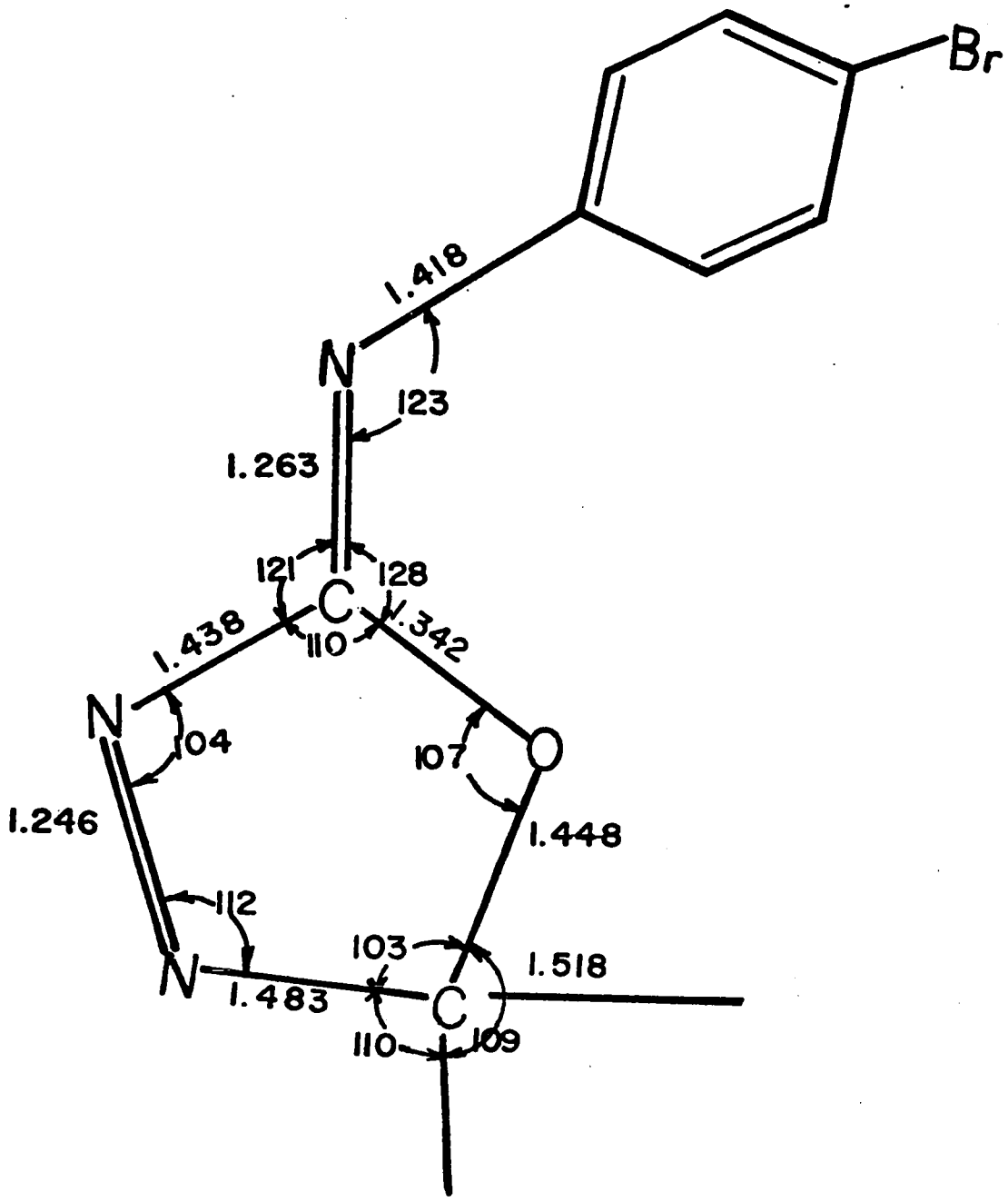
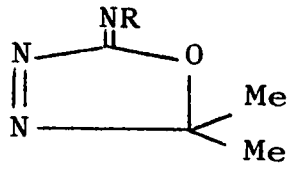


Fig. 2 Z – 5, 5 – Dimethyl – 2 – [(p – Bromophenyl)imino] – Δ^3 – 1, 3, 4 – Oxadiazoline

possesses an unusually high bond order. The shortness of this bond [1.263 Å versus an average of 1.30 Å for non-conjugated C=N bonds or 1.36 Å for azaaromatic compounds (57)] is reflected in its unusually high stretching frequency (58). Layton and coworkers have studied the correlation of carbon-nitrogen bond lengths with their infra-red stretching frequencies. According to this correlation, the imino bond under consideration possesses a considerable degree of triple bond character.

The nuclear magnetic resonance spectra of the phenyl-substituted oxadiazolines shown below also suggested that 2-(substituted-imino)-Δ^3-1,3,4-oxadiazolines have a Z-configuration. Increased shielding of ring methyls with

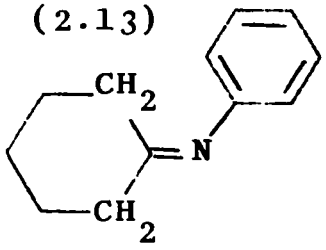


R	Ph	CH_2Ph	CH_2CH_2Ph
δ (ring Me)	1.62	1.54	1.43

increased chain length is most easily explained if the compounds exist in the configuration shown.

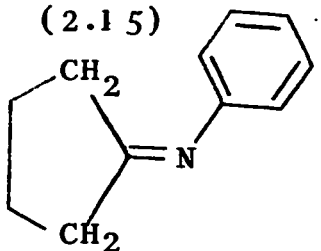
The preceding results may be compared to those found by Saito and Nukada in cyclopentane and cyclohexane imines (57a), for which some chemical shifts (δ) are recorded below. The authors concluded that

(2.13)



(2.41)

(2.15)

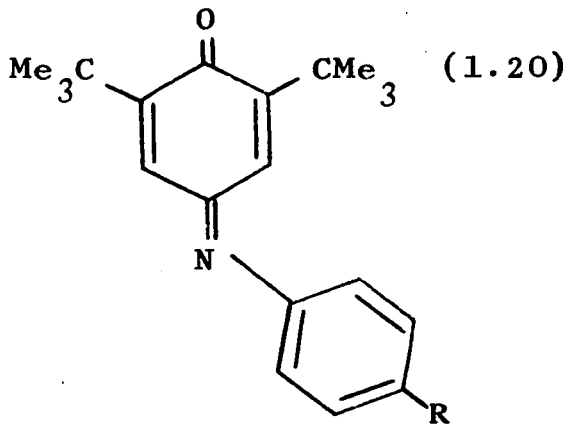


(2.53)

the C=N plane is nearly perpendicular to the phenyl plane and that the differences in the α-methylene proton signals is due to the phenyl ring current.

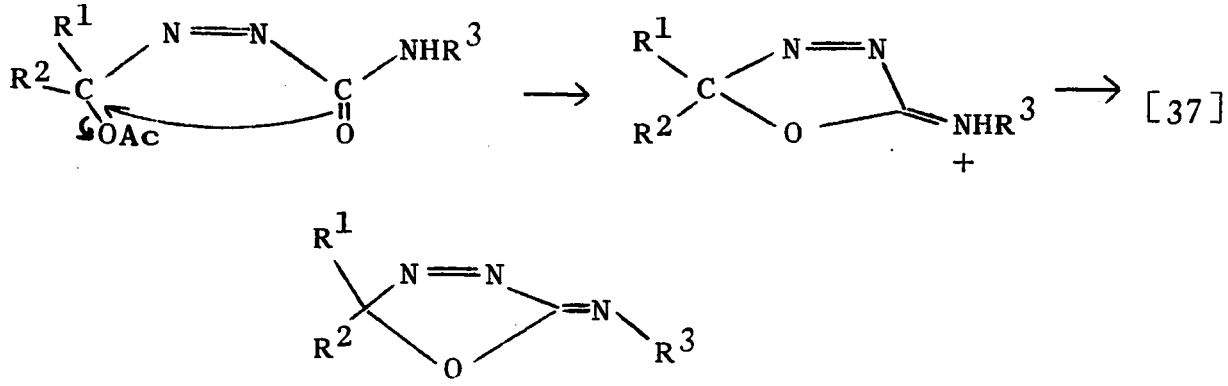
A similar anisotropic effect of a phenylimino group was found by Reiker and Kessler in a study of benzoquinone anils (55). Their conclusions were similar to those reached by Saito and Nukada.

(1.35)



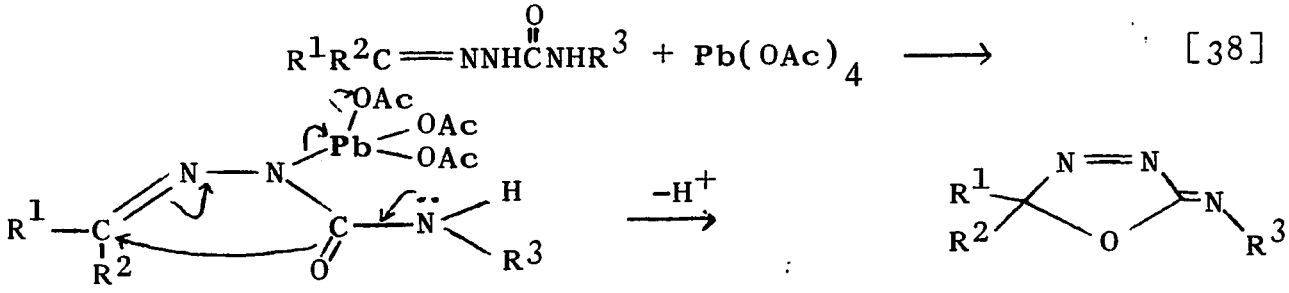
(1.20)

The stereospecificity of the oxidative cyclization reaction may be useful in elucidating its mechanism. For example, a mechanism involving prior formation of an "azoacetate" would not account for the high degree of specificity encountered (eq. 37).



[37]

Such a mechanism has been postulated by Hoffmann for the oxidation of benzoyl hydrazones to 2-acetoxy-Δ^3-1,3,4-oxadiazolines. Both isomers would be expected from such a mechanism. However, a mechanism involving formation of a Pb-N species would be expected to involve large steric requirements (eq. 38). Such steric requirements would force

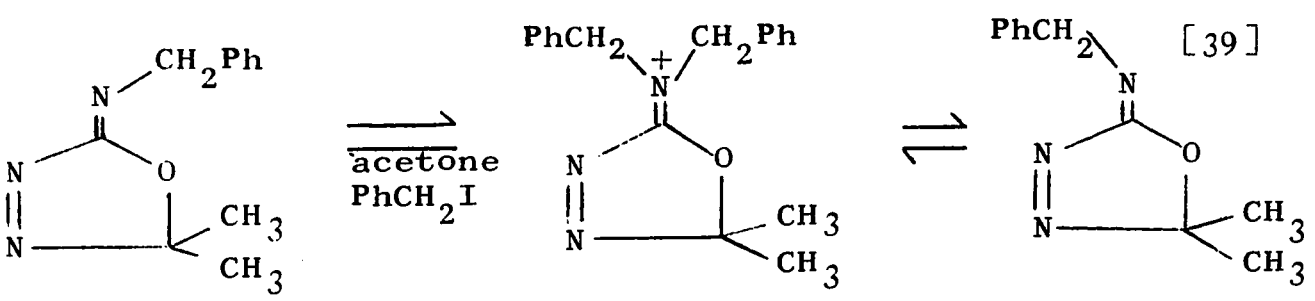


[38]

the R^3 group to a position as distant as possible from the N-Pb bond. This requirement would result in the production of the isomer in which R^3 is <u>syn</u> to the ring oxygen atom. Indeed, it is not even necessary to invoke retention of the N-Pb bond until after ketimine formation. The steric effect of the newly formed $Pb(OAc)_2$ would have

the same consequences on the configuration of the intermediates and product. The steric effect of such leaving groups is well known, especially in the case of S_N1 nucleophilic displacements at saturated carbon atoms.

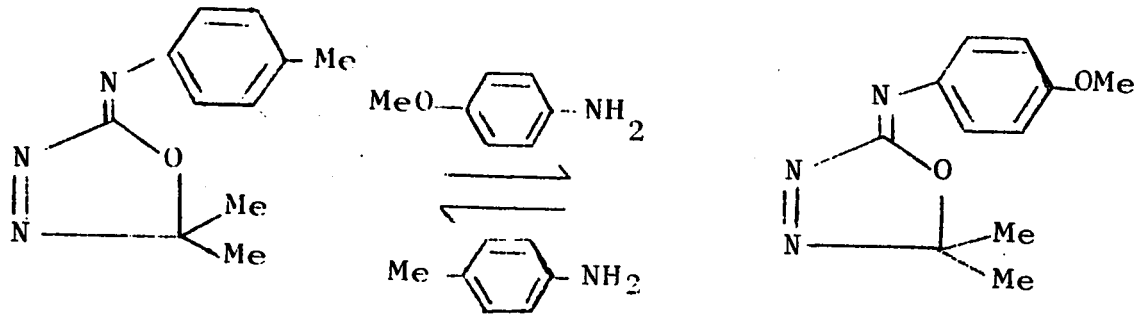
Although no uncatalyzed ketimine isomerization was observed in the iminooxadiazolines, it was hoped that isomerization could be effected through chemical means. Thus, the well-known addition of alkyl halides to Schiff bases was used in an attempt to prepare the quaternary immonium salt (57). It was expected that in the reverse



[39]

reaction, leading to the starting material, both ketimine isomers would appear (eq. 39). That is, because there are no apparent steric barriers to the existence of either isomer, both should exist in an equilibrium mixture. However, all such attempts met with failure.

The most promising result obtained in these investigations was the apparent displacement of an N-(p-tolyl) group by an N-(p-anisyl) group, as is shown in equation 40.

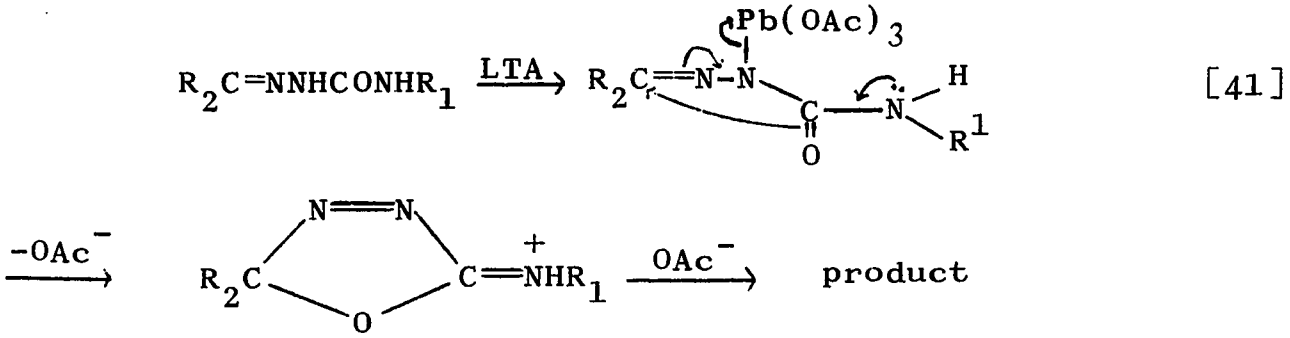


[40]

A study has been made of a similar equilibrium (57). When equilibrium constants for the displacement of substituted benzalanilines by aryl amines were compared, the "relative displacement abilities" of these amines were obtained. The results were given as follows: sulphanilamide 1; p-anisidine, 30-38; aniline, 14-15; m-nitroaniline, 1.15; p-nitroaniline, 0.36. Thus, it would be expected that the formation of the p-methoxyphenyl substituted oxadiazoline in the above equilibrium would be favoured. Although some of this product was obtained, its relative yield was not determined. However, all spectral data obtained on the sample indicated that it consisted of one isomer, having a configuration identical to that of the starting material. The reason for this surprising result is not known, but further work is indicated.

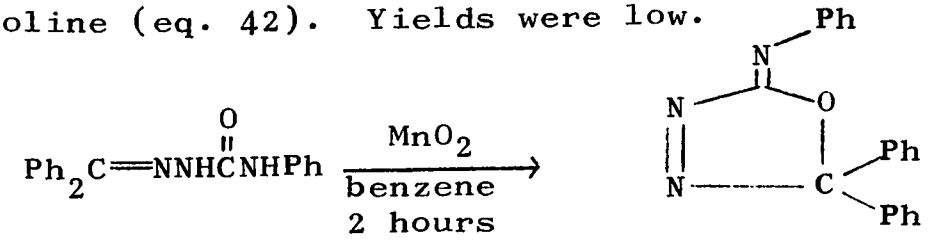
Nevertheless, this transamination may be useful for the preparation of certain Δ^3-1,3,4-oxadiazolines which, until now, have been difficult to synthesize. Thus, it has

been found that cyclization of semicarbazones of the type $R_2C{=}NNHCONHR_1$, where R_1 is a strongly electron-withdrawing substituent (e.g., p-$NO_2C_6H_4$), is difficult to effect. In fact, all attempts to cyclize $Ph_2C{=}NNHCONHC_6H_4NO_2$-p were unsuccessful. A substituent such as p-O_2N-C_6H_4 would sufficiently destabilize the developing cation in the following mechanistic scheme to prevent cyclization (eq. 41).



[41]

Limited success was achieved in finding oxidizing agents other than lead tetra-acetate for the preparation of oxadiazolines. Manganese dioxide was found to cyclize benzophenone 4-phenylsemicarbazone to the corresponding oxadiazoline (eq. 42). Yields were low.

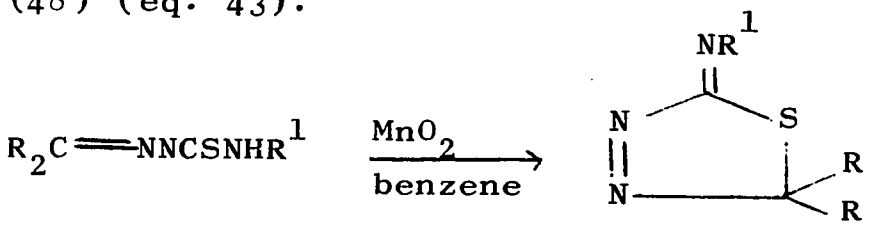


[42]

Repeating the reaction conditions and using acetone

4-phenylsemicarbazone gave only starting material after several hours. Spectral data and a mixed melting point indicated that the configuration of the oxadiazoline obtained by this method was identical to that of oxadiazolines prepared by the lead tetra-acetate method.

This manganese dioxide method may be compared to oxidative cyclization of thiosemicarbazones by the same reagent (48) (eq. 43).



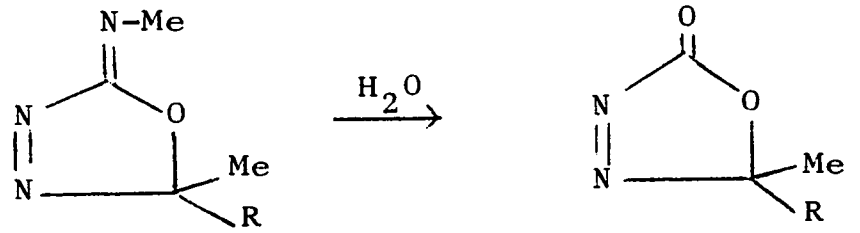
[43]

The author did not propose a mechanism for the reaction; nor did he establish the configuration of the product.

In the same paper, Landquist also reported that thiosemicarbazones were cyclized by atmospheric oxygen in a slurry of basic alumina and chloroform to triazolinethiones (48). It was found during the course of our studies that an analogous reaction occurred with acetone 4-phenylsemicarbazone, although the yield was very low. Therefore, the most feasible route to 3,3-dimethyl-4-phenyl-Δ^3-1,2,4-triazolin-5-one is the desulfurization of the thione analog by mercuric acetate (48).

II. Preparation and Thermolysis of Δ^3-1,3,4-Oxadiazolin-2-ones

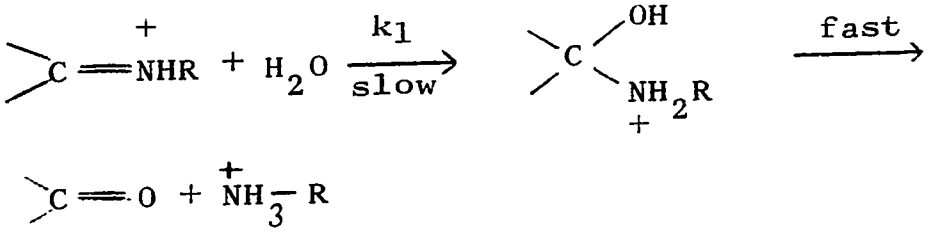
The 5,5-dimethyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline and 5-methyl-5-ethyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline preparations resulted in concurrent formation of oxadiazolinones from the hydrolysis of the oxadiazolines (eq. 44).



[44]

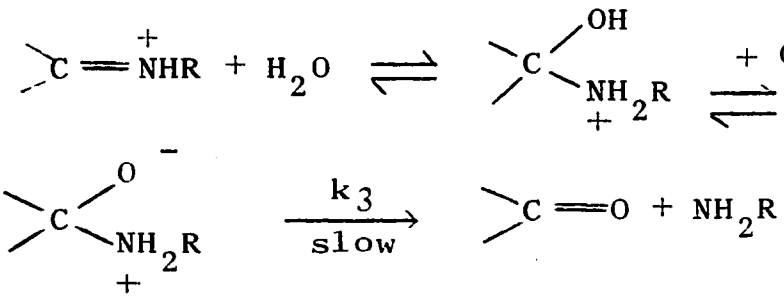
R = Me, Et

Because of the interest in recent years in the hydrolysis of imines, it may be useful to discuss the relative rates of hydrolysis of oxadiazolines (57,60,61). The acid catalyzed hydrolysis of benzylidene-tert-butylamines at 25° exhibits a change in the rate-determining step. From pH 8 to 5, the rate-determining step is the nucleophilic attack by water on the protonated imine (eq. 45).



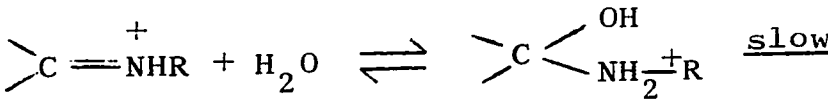
[45]

At still lower pH values, the decomposition of the intermediate carbinolamine becomes rate-determining (eq. 46).



[46]

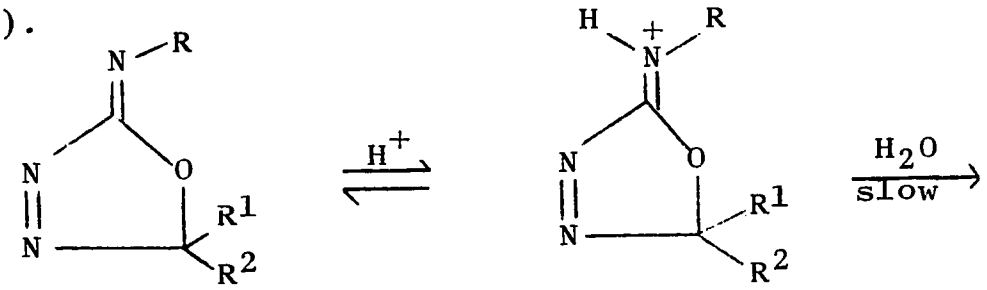
Under the moderately acid conditions present in the work-up of the oxadiazolines, it was noted that only (methylimino)-oxadiazolines, not (arylimino)oxadiazolines, underwent hydrolysis. This observation strongly suggests that the former mechanism is in effect under these conditions. That is, under conditions of complete protonation, phenylimines should experience more facile hydrolysis than alkylimines. Jencks has proposed that, for benzylideneanilines at low pH, a mechanism involving decomposition of the protonated carbinolamine may be operative (eq. 47) (61). The electron-



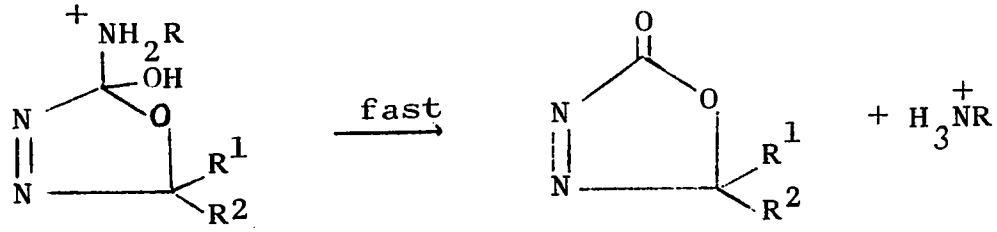
[47]

withdrawing phenyl group on the nitrogen permits amine expulsion with less driving force than in the case of more basic amines. In the case of more basic amines, e.g.,

benzylidene-tert-butylamine, this step requires a prior proton removal from the oxygen atom of the intermediate, in order to obtain sufficient driving force to expel the strongly basic amine. Thus, the most probable mechanism of iminooxadiazoline hydrolysis is initial protonation of the substrate, followed by nucleophilic attack by water (eq. 48).

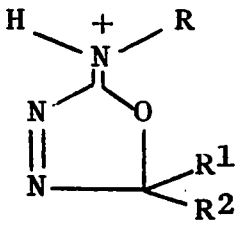


[48]



The slow rate of hydrolysis of arylimines (R = aryl), as compared to the rate of hydrolysis of alkylimines (R = methyl), may be due to electronic factors, or steric factors, or both. The concentration of protonated imine is low when the imino group is a weak base, e.g., =NPh. Thus, the rate will be dependent on the basicity of the imine. As well, steric crowding may affect the reaction

rate in two ways. In the first place, steric factors may render difficult the solvation of the conjugate acid (VIII).



VIII

In the second place, steric crowding may reduce the rate of nucleophilic attack at C-2. The observation that (methylimino)oxadiazolines are readily hydrolyzed, while (benzylimino)oxadiazolines are not, indicates that steric factors are important.

The alternative route to oxadiazolinones - lead tetra-acetate oxidation of $Me_2C{=}NNHCNH_2$ (O) or $Ph_2C{=}NNHCNH_2$ (O) — presumably involves cyclization of the semicarbazone to 2-imino-Δ^3-1,3,4-oxadiazoline, followed by hydrolysis. This route permitted the first synthesis of a phenyl-substituted oxadiazolinone. 5,5-Diphenyl-Δ^3-1,3,4-oxadiazolin-2-one was an exceedingly unstable compound that decomposed at room temperature to diphenyldiazomethane and other unexamined products. This instability accounts for the absence of the compound during the preparation of

5,5-diphenyl-2-(methylimino)-Δ^3-1,3,4-oxadiazoline.

It must be noted that the oxadiazolinones underwent decomposition in water. This reaction occurred under acidic, neutral, or basic conditions. Although it was assumed that the reaction involved ring opening, the products were not fully explored. The addition of 5,5-dimethyl-Δ^3-1,3,4-oxadiazolin-2-one to distilled water resulted in gas evolution and production of acetone and acetone azine. The latter two products were shown to be present by a comparison of the nuclear magnetic resonance spectrum of the products with the spectra of authentic samples. The identity of the gas was not examined. While the decomposition of the above mentioned oxadiazolinone appeared to be complete in a matter of minutes, that of 5-methyl-5-ethyl-Δ^3-1,3,4-oxadiazolinone required several hours for completion.

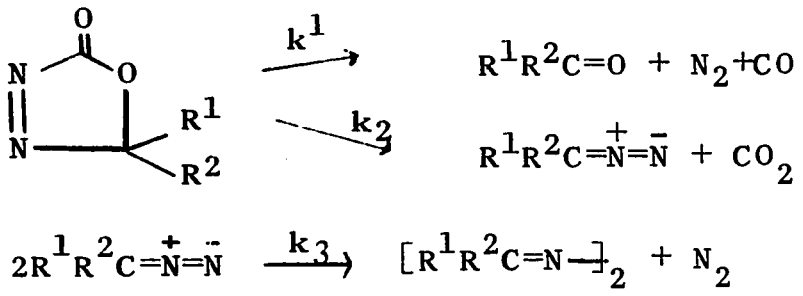
The thermolysis of 5,5-dimethyl-Δ^3-1,3,4-oxadiazolin-2-one was studied both neat and in carbon tetrachloride. The neat thermolysis at 100°C in a sealed glass tube for 20 hours produced 100% acetone azine (by v.p.c. and n.m.r.). A carbon tetrachloride solution, heated at 100°C for 20 hours, gave mainly acetone and some azine. Similarly, neat

thermolysis at 83°C gave 12% azine and 67% acetone, as well as unidentified products. At this temperature, the thermolysis in solution gave about 67% acetone and 22% azine.

5-Methyl-5-ethyl-Δ^3-1,3,4-oxadiazolin-2-one was thermolyzed at 83°C (neat) to give 49% 2-butanone, 40% 2-butanone azine, and 11% unidentified product. In carbon tetrachloride solution it was thermolyzed at the same temperature to give 91% 2-butanone, 8% azine, and 0.8% unidentified product.

In order to determine whether or not the ketones observed in these thermolyses originated from a reaction between air and the azines present, azine samples were heated under the same conditions as described above. No acetone (or 2-butanone) could be detected (by n.m.r. and v.p.c.) in the heated samples.

Subsequent to the completion of these product studies, the kinetics of oxadiazolinone thermolysis were investigated by Lee and Warkentin (62). The thermolysis was found to proceed by two unimolecular processes at 83°C, in methanol or carbon tetrachloride (eq. 49). The production

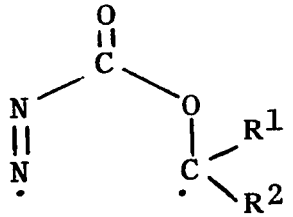


[49]

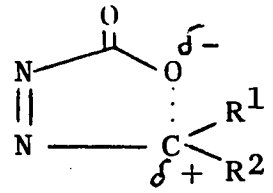
$R^1 = Me,\ R^2 = Et$

$R^1 = R^2 = Me$

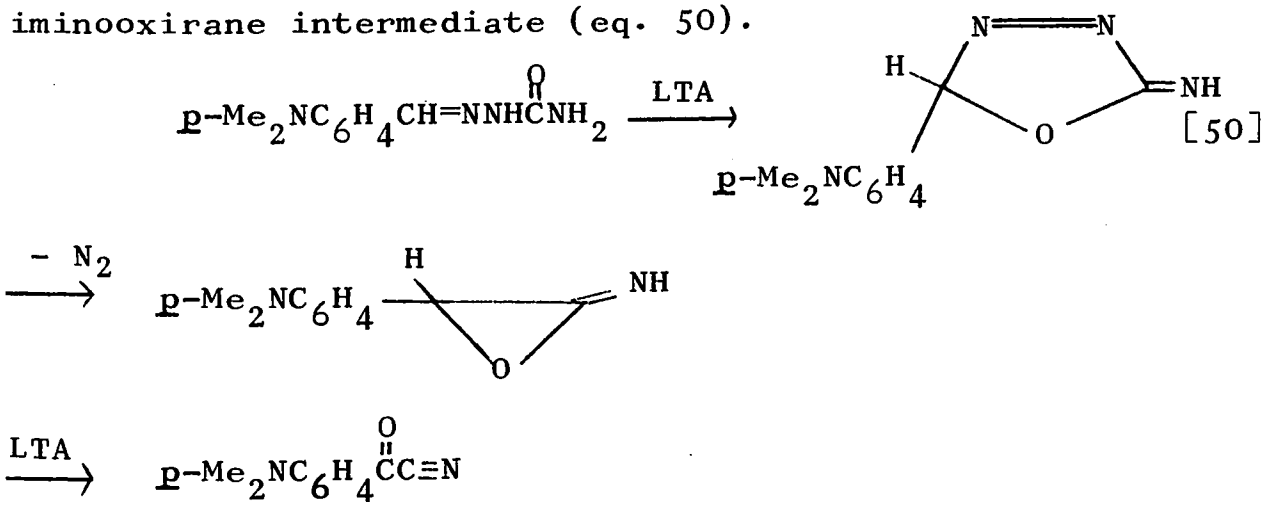
of ketone was thought to involve a diradical-like, rather than a dipolar transition state. Changing the solvent from



carbon tetrachloride to methanol had little effect on the magnitude of k_1. However, alternative processes involving concerted cleavage of 2 or 3 bonds could not be ruled out on the available evidence. In contrast, changing the thermolysis solvent from carbon tetrachloride to methanol caused a 15-fold increase in k_2. Thus, the production of carbon dioxide and diazo compound was judged to involve a more polar transition state. However, once again, the accumulated evidence does not rule out a completely concerted decomposition leading directly to diazoalkane.

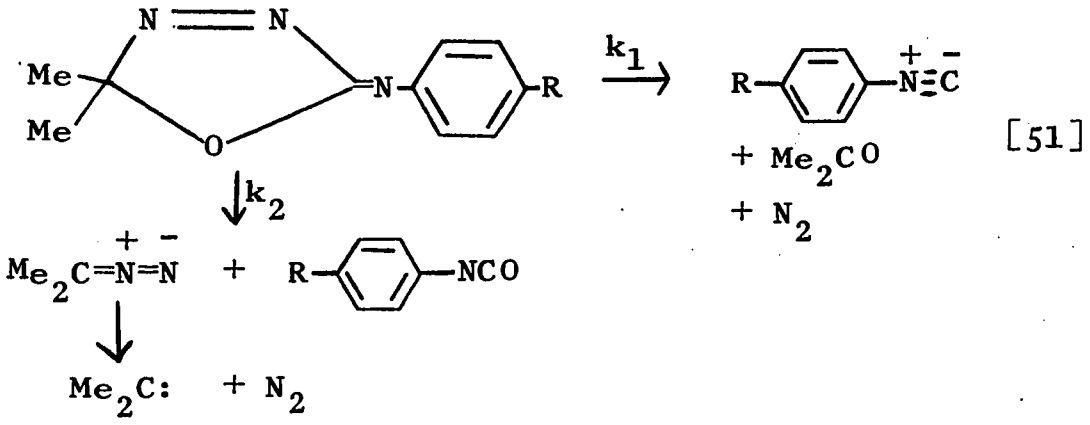


More recently, it was shown that fully concerted decomposition, if it occurs, is not general (63). p-(Dimethylamino)benzaldehyde semicarbazone is oxidized by lead tetra-acetate to the aroyl nitrile; this process is most easily rationalized in terms of a stepwise reaction via an iminooxirane intermediate (eq. 50).



[50]

decomposition of 5,5-diaryl-2-(phenylimino)-Δ^3-1,3,4-oxadiazolines (1). It was thus expected that k_1 and k_2 would be obtainable through measurement (a) of (k_1+k_2) by a gas evolution study; (b) of k_2 by following the increase in isocyanate concentration with time.(eq. 51).



[51]

The diazo intermediate was not stable enough to be detected in the infra-red spectra of partially decomposed samples. Its stability is known to be lower than that of diaryldiazomethanes (50). At the temperatures used in the thermolysis, the rate constant for its decomposition to carbene and nitrogen is much larger than k_2. Also, aryl isocyanides could not be detected in the infra-red spectra. However, the characteristic odour of isocyanide pervaded the decomposed solutions, indicating a low concentration to be present. Presumably, aryl isocyanides were removed from solution by reaction with

dimethylcarbene to form the ketenimine, $Me_2C{=}C{=}NAr$.

Decomposing 5,5-dimethyl-2-(phenylimino)-Δ^3-1,3,4-oxadiazoline in bromobenzene gave a value for (k_1+k_2) of 7.63×10^{-4} sec^{-1} (gas evolution method) (Fig. 3. In this Guggenheim kinetic plot, V=volume of gas evolved after t time, and V'=volume of gas evolved after time $(t+\Delta)$ where Δ =2 half-lives). However, the formation of phenyl isocyanate, as followed by the intensity of the isocyanate absorption at 2256 cm^{-1} in the infra-red, was not first order. Typical results, as shown in Table I, indicate that the isocyanate concentration rose to 23% of the theoretical maximum, then decreased.

Attempts to discover the identity of the compound reacting with the aryl isocyanates were unsuccessful. For example, heating a solution of p-methoxyphenyl isocyanate and acetone in bromobenzene under the same conditions as those used in the thermolyses did not cause a decrease in isocyanate concentration (infra-red). To examine the possibility that an impurity in the solvent reacted with the isocyanate, 5,5-dimethyl-2-(phenylimino)-Δ^3-1,3,4-oxadiazoline was thermolyzed in specially purified bromobenzene. A sample of bromobenzene was washed with sulphuric acid, water, sodium bicarbonate, and finally, water. It

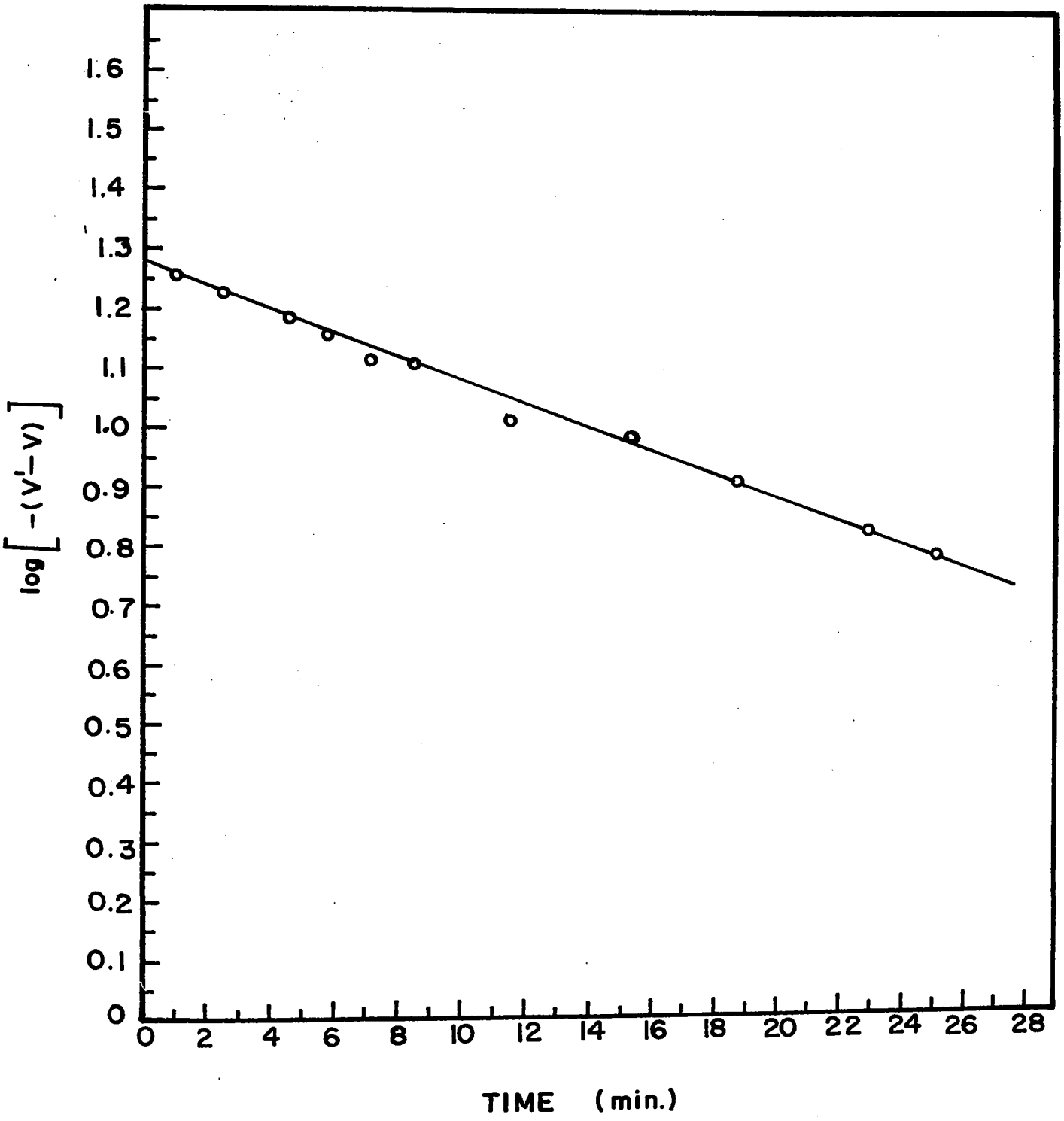


Fig. 3. Total Rate of Decomposition of 5,5 – Dimethyl – 2 – (Phenylimino) – Δ^3 – 1,3,4 – Oxadiazoline at 150° C in Bromobenzene

TABLE I

Decomposition of 5,5-Dimethyl-2-(Phenylimino)-Δ^3-1,3,4-Oxadiazoline at 150°C in Bromobenzene

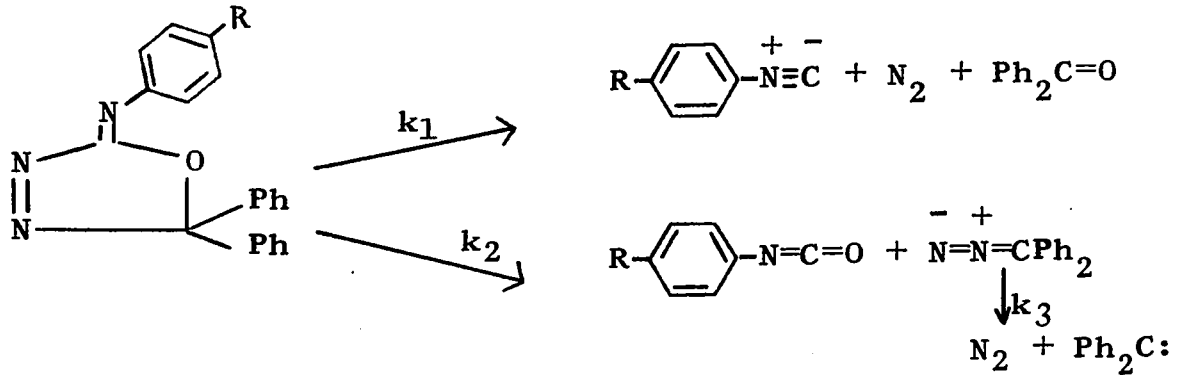
Time (min.)	Peak Height (% T) [a]	Molarity of Isocyanate x 10^3
5	3.8	1.2
10	7.9	2.7
20	13.1	4.6
31	16.6	5.8
40	19.0	6.8
50	21.8	7.9
60	23.6	8.7
72	25.6	9.4
85	26.8	9.9
150	31.6	11.8
180	32.0	12.5
210	32.3	12.7
240	33.6	13.1
270	33.7	13.0
300	33.0	12.8
325	32.3	12.7
1500	16.9	5.9

(a) The height of the peak at 2256 cm^{-1} in the infra-red spectrum.

was dried over calcium chloride and distilled from calcium chloride through a glass helices-packed column. However, the thermolysis data obtained in this solvent were similar to the results previously obtained. Similarly, heating an isocyanate and phenyl isocyanide did not result in a reaction between the two components. One of the products present after thermolysis of the 5,5-dimethyl-Δ^3-1,3,4-oxadiazolines was propene, formed from dimethylcarbene (64). To test the possibility that a reaction between the isocyanate and propene (or other olefin) may have removed isocyanate from solution, an isocyanate and 4-methyl-1-pentene were heated in sealed tubes. As expected, there was no evidence of reaction between those components.

IV. Thermolysis of 5,5-Diphenyl-2-(arylimino)-Δ^3-1,3,4-oxadiazolines

No such problems were encountered in the thermolysis studies of 5,5-diphenyl-2-(arylimino)-Δ^3-1,3,4-oxadiazolines. The two modes of decomposition are reiterated below:



Both modes of decomposition were kinetically first order. The rate constants k_1 and k_2 were obtained by following, respectively, the concentrations of benzophenone and aryl isocyanate by infra-red. Typical results for each are shown in Tables II and III and Figures 4 and 5.

The rates of the reactions were correlated with σ by the Hammett relation. The results are shown in Tables IV and V and Figures 6 and 7. The results obtained were as follows: In chlorobenzene, the Hammett relationship for the formation of isocyanate via a retro-1,3-dipolar addition possessed a ρ value of +1.1. The ρ value for the formation of benzophenone was +1.0.

The effect of solvent polarity on the decomposition of these oxadiazolines was determined. Thus, 5,5-diphenyl-2-(p-tolylimino)-Δ^3-1,3,4-oxadiazoline was decomposed in nitrobenzene. In this solvent, the rate constant (k_2) for the formation of p-tolyl isocyanate was 4.16×10^{-2} min^{-1} (versus 1.89×10^{-2} min^{-1} in chlorobenzene), whereas the rate constant (k_1) for the formation of benzophenone was 1.30×10^{-2} min^{-1} (versus 1.33×10^{-2} min^{-1} in chlorobenzene). The significance of these results will be explained in conjunction with the discussion of possible transition

TABLE II

Kinetics of Benzophenone Production in the Decomposition of 5,5-Diphenyl-2-(p-Tolylimino)-Δ^3-1,3,4-Oxadiazoline at 85°C in Chlorobenzene

Time (min.)	Peak Height [a]	Molarity Benzophenone (M_t) [b]	$M_\infty - M_t$ [c]	log ($M_\infty - M_t$)
0	0.0	0.0	20.8	1.318
5	2.5	4.6	16.2	1.210
10	3.8	5.7	15.1	1.179
15	5.4	7.0	13.8	1.140
20	6.8	8.3	12.5	1.097
26	7.0	8.4	12.4	1.093
30	8.1	9.2	11.6	1.064
40	9.0	10.0	10.8	1.033
50	10.7	11.7	9.1	0.959
60	13.0	14.0	6.8	0.833
90	13.5	15.0	5.8	0.763
120	15.0	16.3	4.5	0.653
180	18.5	20.8	0.0	0.00
240	18.5	20.8	0.0	0.00

(a) The height of the absorption band at 1650 cm^{-1} in the infra-red.

(b) The molarity at time (t) is obtained by referral to a calibration chart.

(c) The final molarity of the solution with respect to benzophenone is called M_∞.

TABLE III

Kinetics of Isocyanate Production in the Decomposition of 5,5-Diphenyl-2-(p-Tolylimino)-Δ^3-1,3,4-Oxadiazoline at 85°C in Chlorobenzene

Time (min.)	Peak Height [a]	Molarity Isocyanate (M_t) [b]	$M_\infty - M_t$ [c]	log ($M_\infty - M_t$)
0	0.0	0.0	20.6	1.314
5	3.4	1.7	18.9	1.276
10	6.8	3.7	16.9	1.228
15	9.8	5.2	15.4	1.118
20	12.5	6.4	14.2	1.152
26	15.8	8.3	12.3	1.090
30	17.8	9.3	11.3	1.053
40	20.5	10.8	9.8	0.991
50	23.8	13.2	7.4	0.869
60	26.7	14.8	5.8	0.763
90	28.8	16.5	4.1	0.613
120	31.5	18.4	2.2	0.342
180	35.0	20.6	0.0	0.000
240	35.6	20.6	0.0	0.000

(a) The height of the absorption band at 2270 cm^{-1} in the infra-red.

(b) The molarity is obtained by referral to a calibration chart.

(c) The final molarity of the solution with respect to isocyanate is called M_∞.

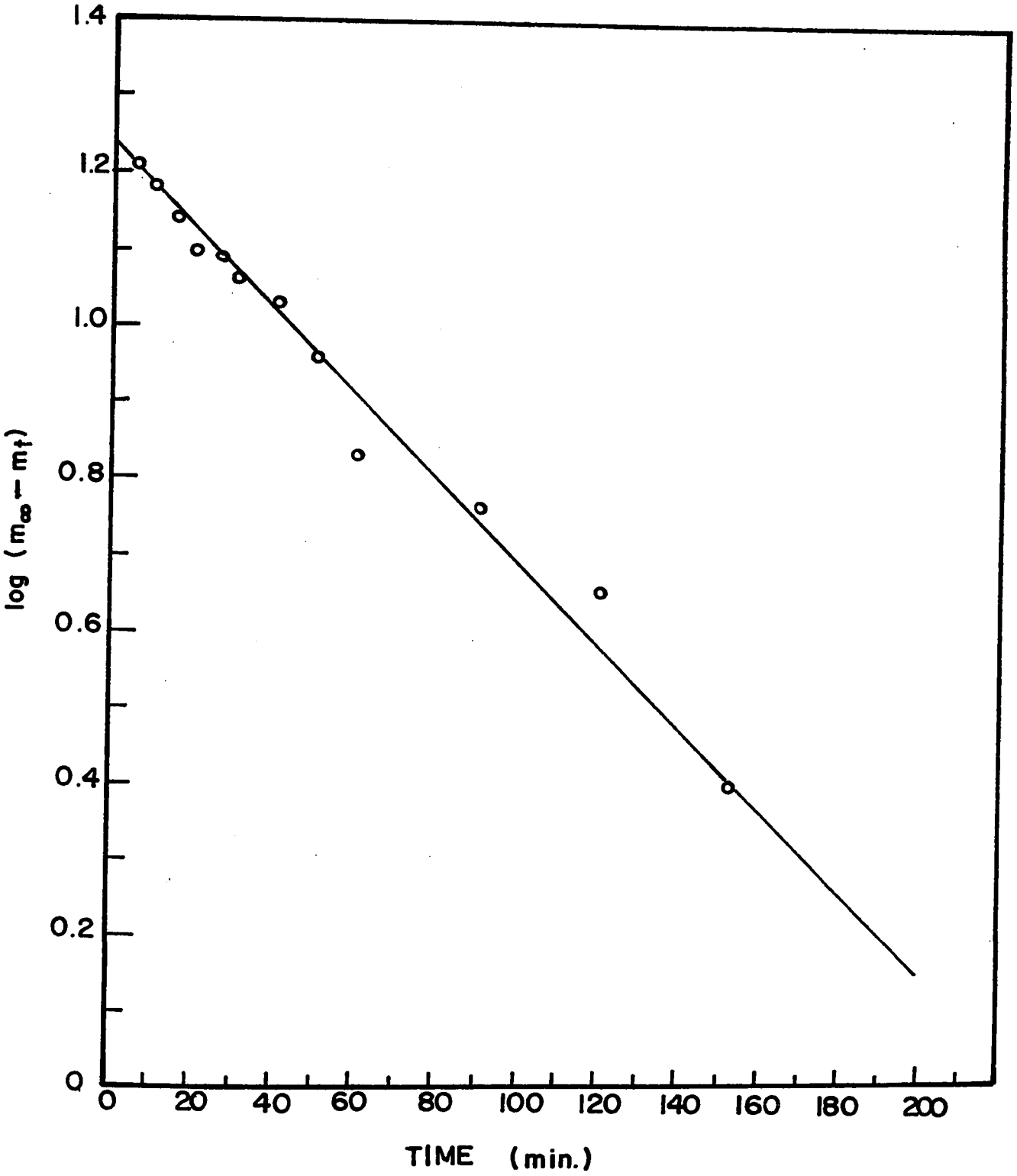


Fig. 4. Rate of Benzophenone Production in the Decomposition of 5, 5-Diphenyl-2-(p-Tolylimino)-Δ^3-1, 3, 4 — Oxadiazoline in Chlorobenzene at 85°C

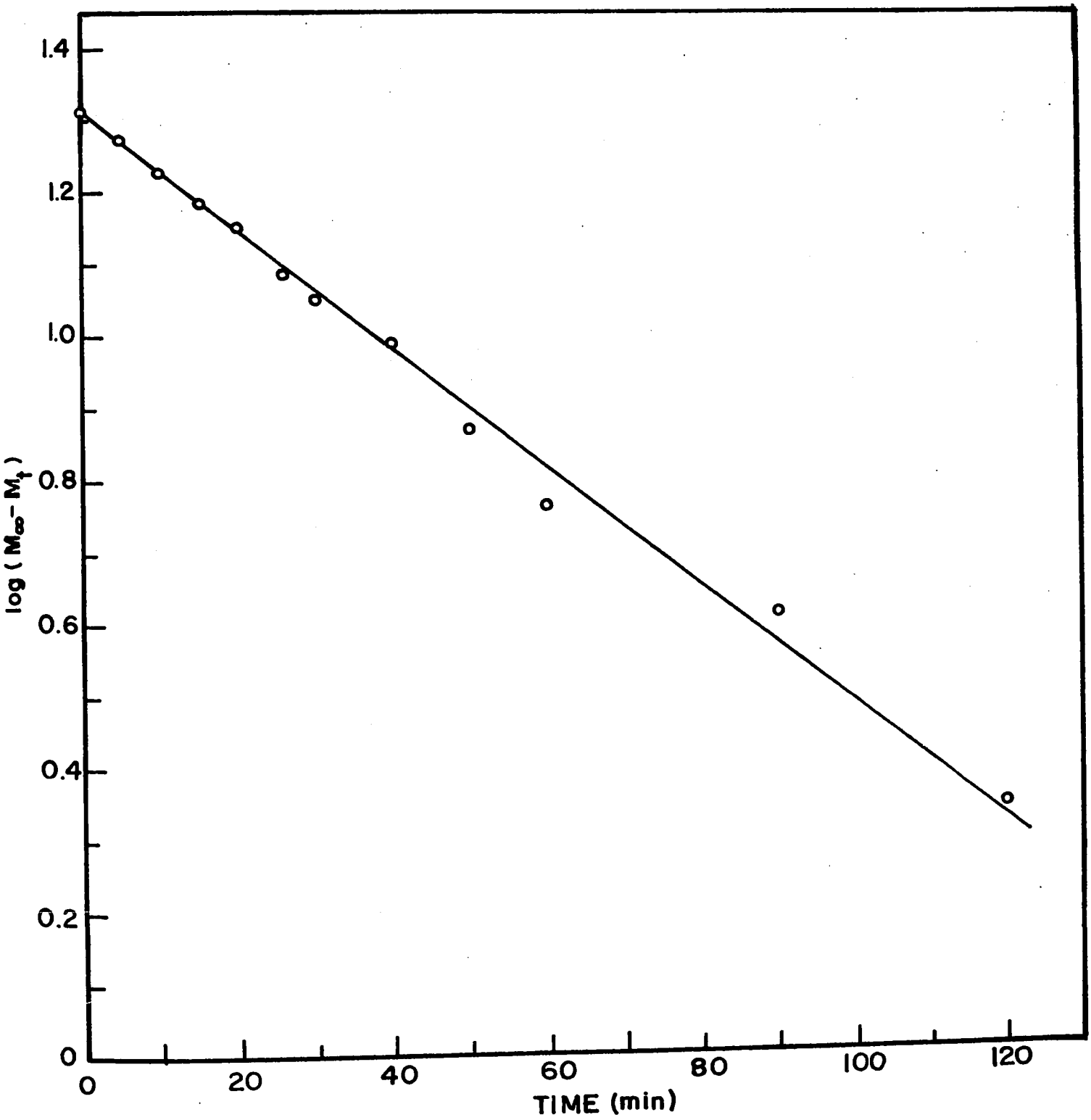


Fig.5 Rate of Isocyanate Production in the Decomposition of 5, 5 — Diphenyl — 2 — (p-Tolylimino) — Δ^3 — 1, 3, 4 —Oxadiazoline in Chlorobenzene at 85° C

TABLE IV

Correlation of Rates of Isocyanate Formation from 5,5-Diphenyl-2-(Arylimino)-Δ^3-1,3,4-Oxadiazolines by the Hammett Relation

Substituent	$k_2 \times 10^2$ min^{-1} [a]	$\log_{10} k_2/k_2^o$ [b]	σ
p-MeO	1.30 ± 0.015	-0.341 ± 0.013	-0.268 ± 0.02
p-Me	1.89 ± 0.015	-0.178 ± 0.007	-0.170 ± 0.02
H	2.85 ± 0.020	0.000 ± 0.006	0.000 ±
p-Cl	5.02 ± 0.25	0.246 ± 0.021	0.227 ± 0.02

(a) The precision of the kinetic results is expressed as an average deviation.

(b) The deviation is obtained from the limiting values of the expressed fraction.

TABLE V

Correlation of Rates of Benzophenone Formation from 5,5-Diphenyl-2-(Arylimino)-Δ^3-1,3,4-Oxadiazolines by the Hammett Relation

Substituent	$k_1 \times 10^2$ [a] min^{-1}	$\log_{10} k_1/k_1^o$ [b]	σ
p-MeO	0.965 ± 0.010	-0.343 ± 0.034	-0.268 ± 0.02
p-Me	1.33 ± 0.070	-0.204 ± 0.050	-0.170 ± 0.02
H	2.13 ± 0.13	0.000 ± 0.053	0.000 ±
p-Cl	3.24 ± 0.20	0.182 ± 0.054	0.227 ± 0.02

(a) The precision of the kinetic results is expressed as an average deviation.

(b) The deviation is obtained from the limiting values of the expressed fraction.

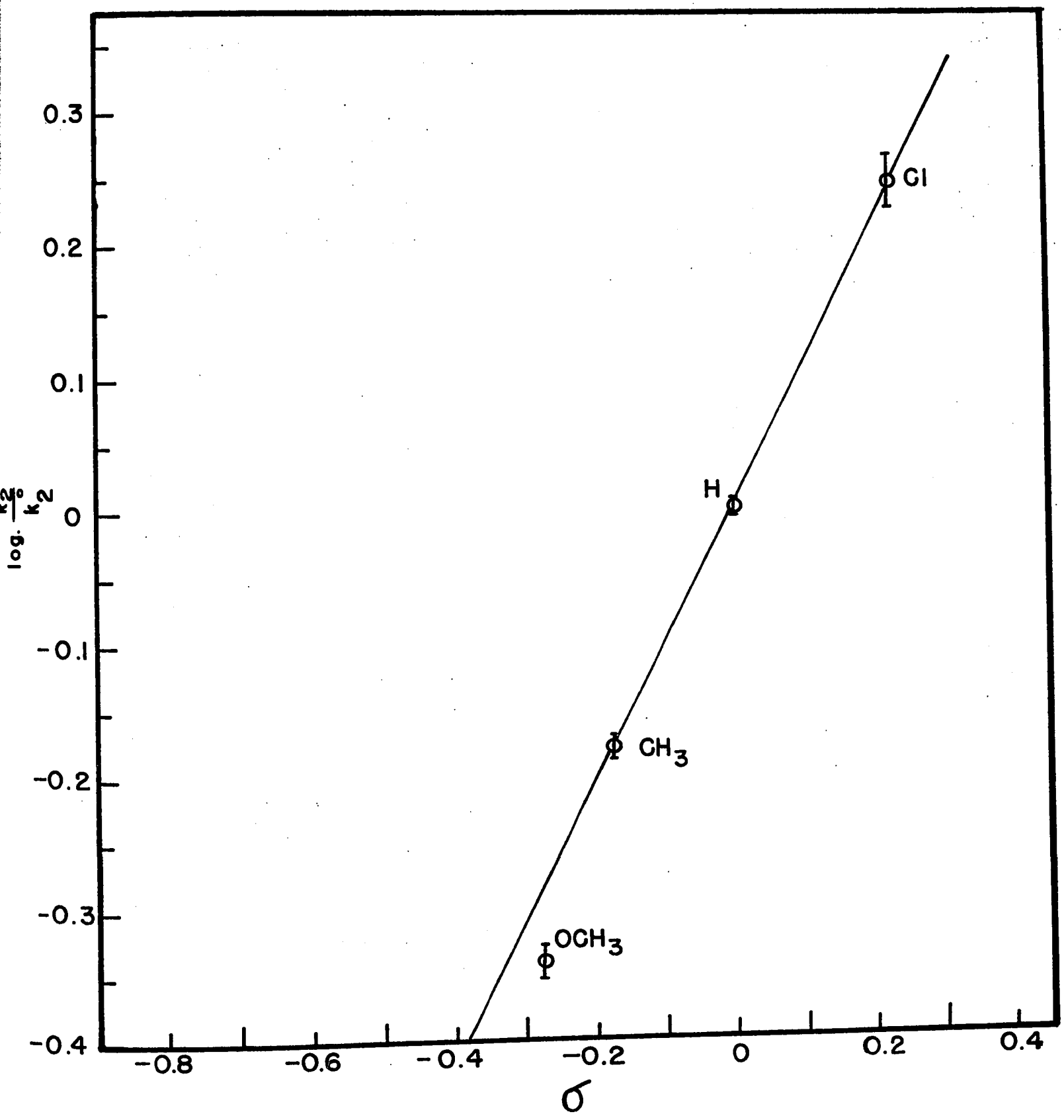


Fig. 6 Correlation of Rates of Aryl Isocyanate Formation by the Hammett Equation using Hammett Substituent Constants (*6*)

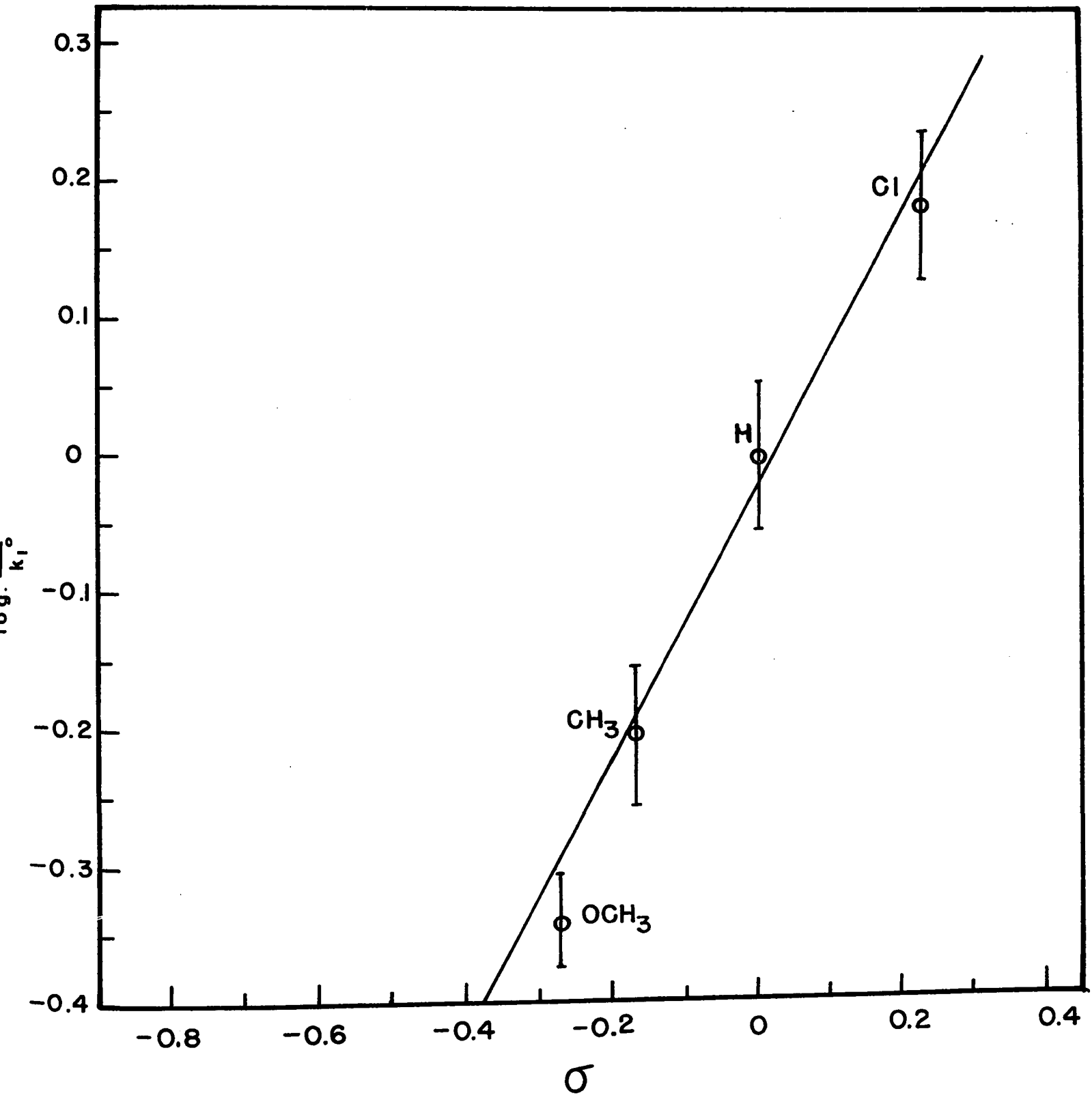
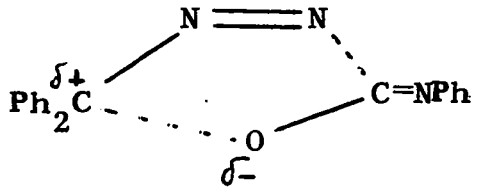


Fig. 7 Correlation of Rates of Benzophenone Formation by the Hammett Equation using the Hammett Substituent Constants (σ)

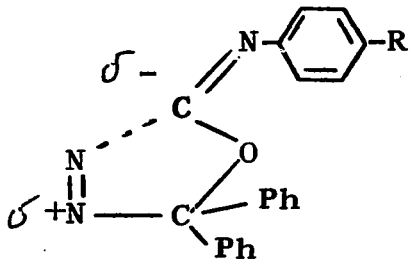
states for the decomposition routes.

West and Warkentin have favoured a transition state for the retro-1,3-dipolar reaction that possessed partial ionic character (1). The extent of the C-N bond breaking



could not be assigned on the basis of their investigations.

The present study confirms this general conclusion. The ρ value of +1.1 indicates that a transition state stabilized by electron withdrawal at exocyclic nitrogen must be involved. However, no direct evidence on the extent of C-N bond breaking was obtained. Thus, transition states similar to the following one cannot be conclusively ruled out. However, the X-ray crystal structure of a typical

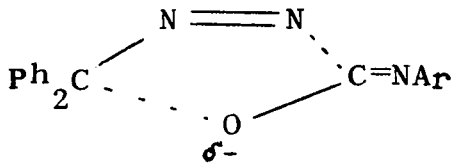


oxadiazoline revealed that the C_5-O bond is long, and, therefore, relatively weak. On the other hand, the C_2-N_3 bond is a short and strong bond.

The Woodward-Hoffmann rules may be used to predict the stereochemical course of an electrocyclic ring closure (or opening) on the basis of the symmetry of the highest occupied molecular orbital of the open-chain reactants (65). By these rules, a concerted $2\pi \rightarrow 2\sigma$ process(or its reverse) is allowed thermally when $m+n = 4q+2$ (m and n are the number of π-electrons in the two open-chain reactants; q is an integer, e.g. 0,1,2,3$\cdots$). In this case, the electrocyclic ring closure being considered is the addition of $Ph_2\overset{+}{C}=\overset{-}{N}=N$ to Ar-N=C=O to give the oxadiazoline. Since this reaction fulfills the criterion of $m+n = 6$, the concerted addition reaction is thermally allowed. That is, both the C-O and the C-N bonds may be partially broken at the transition state. However, it must be borne in mind that, while the Woodward-Hoffmann rules are useful in predicting the "concertedness" of a reaction, they cannot be used to predict the extent to which each bond is broken (or formed) at the transition state. Thus, while these rules may predict that both the C-O and the C-N bonds can be broken in a thermal decomposition, they do not imply that both bonds are necessarily broken to the same extent at the transition state.

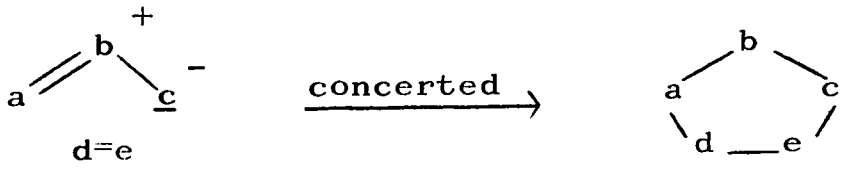
The results of the thermolysis of 5,5-diphenyl-2-(p-tolylimino)-Δ^3-1,3,4-oxadiazoline in a more polar solvent (nitrobenzene) indicated that the transition state for the retro-1,3-dipolar addition was more ionic than the starting material. Thus, the rate of formation of p-tolyl isocyanate was more than doubled in nitrobenzene.

The sum total of the preceding evidence would seem to support the previously suggested transition state. Although, according to the Woodward-Hoffmann rules, both



bonds (C-O and C-N) may be breaking simultaneously, the extent of C-N bond cleavage is most likely small compared to that of C-O bond cleavage.

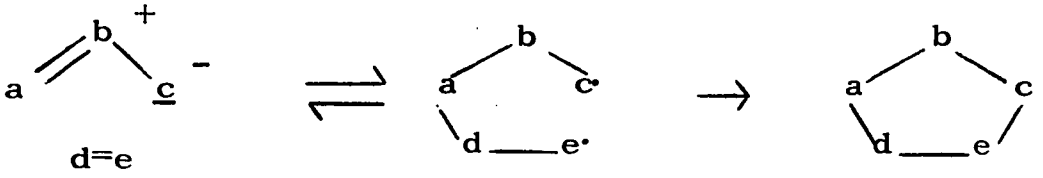
Indeed, there has been some controversy over the mechanism of 1,3-dipolar cycloadditions. Huisgen strongly favours a concerted mechanism (eq. 52) (66,67). The



[52]

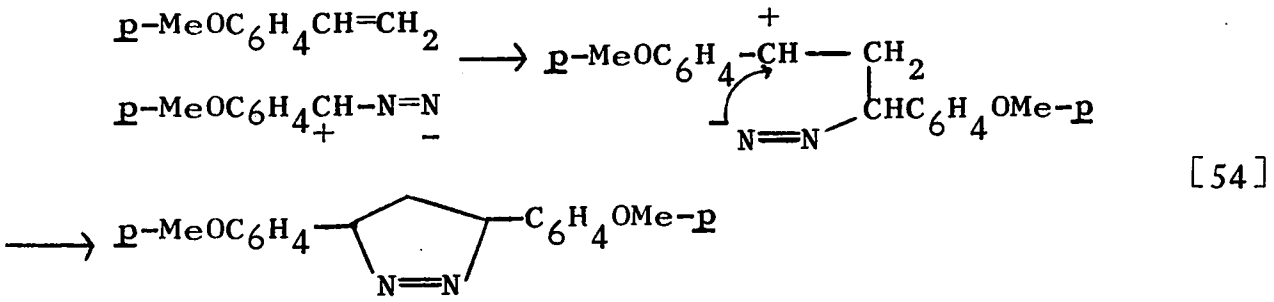
Woodward-Hoffmann rules may be applied to this system to demonstrate that "concertedness" is allowed thermally (68,69). In contrast to this single-step, four-centre

cycloaddition is Firestone's proposed mechanism involving a two-step reaction with a discreet intermediate (70) (eq. 53). Firestone also suggests that the activation



[53]

energies for both advance and retrograde motion along the reaction coordinate from the proposed diradical intermediate must be less than that for rotation about a single bond. Yet another mechanism has been suggested by Overberger (71) (eq. 54). The mechanism shown was used to

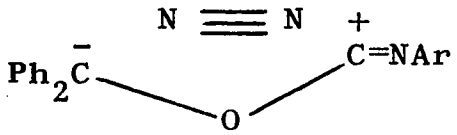


[54]

account for formation of both <u>cis</u> and <u>trans</u> products in the reaction mixture.

When the Hammett relationship was applied to the decomposition pathway involving direct formation of nitrogen, a ρ value of +1.0 was obtained (Figure 7). This indicates that the transition state is stabilized by electron withdrawal at the exocyclic nitrogen.

This result rules out the possibility that the decomposition is a heterolytic process. Hammett correlations of rates with substituent constants for substituents at both the exocyclic nitrogen and at C_5 show rate increases with more strongly electron-withdrawing groups. No heterolytic transition state embodying these two facts can be envisaged. Thus, a transition state such as IX would be expected to have a negative ρ value for a Hammett-



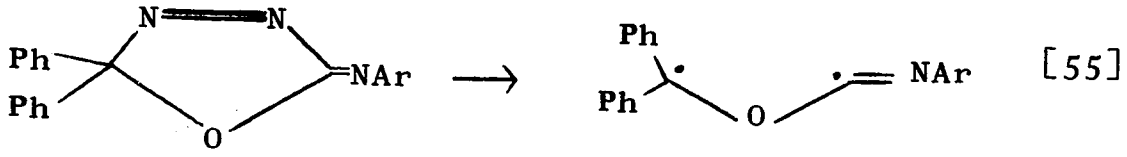
IX

like study of the substituent effect at the imino nitrogen atom.

The absence of a highly polarized transition state was confirmed by the thermolysis rate of 5,5-diphenyl-2-(p-tolylimino)-Δ^3-1,3,4-oxadiazoline in nitrobenzene. The rate constant in this more polar solvent was almost identical to that in chlorobenzene. Since a polarized transition state such as IX would be greatly stabilized in a polar solvent, the rate of decomposition *via* this pathway should be enhanced by changing the reaction medium from chlorobenzene to nitrobenzene. Because such a rate enhancement

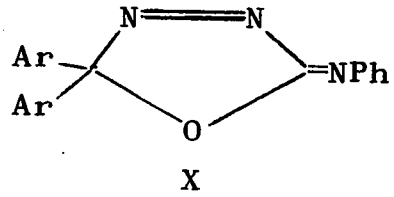
was not found, a heterolytic mechanism must be ruled out.

On the basis of the available evidence, the best interpretation of the results appears to involve a homolytic process (eq. 55). As has been noted, applying a Hammett



[55]

treatment to the corresponding reaction of X did not give



X

a good fit to a straight line (1). Although the authors were reluctant to state that the correlation followed the Hammett equation, it was obvious that the reaction rate was increased slightly by electron-withdrawing substituents.

Two factors may be operative here: ground state effects and radical stabilization. On the one hand, it is known that para substituents generally stabilize the odd electron in a transition state during a homolytic unimolecular decomposition whether the substituents are electron withdrawing or electron donating. Thus, in the formation of triphenylmethyl radicals from hexaphenylethane, both electron-withdrawing and electron-donating substituents

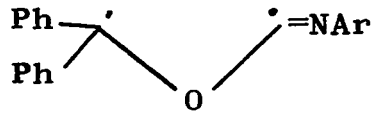
accelerate the rate of reaction (72). Similarly, in equation 55, an odd electron at C_5 would be stabilized by conjugation with the phenyl rings. On the other hand, the effect of electron-withdrawing substituents at C_5 may be explained in terms of a ground state inductive effect. If this effect were the only one present, the correlation would be expected to follow the Hammett equation. For example, in the thermolysis of 4,4'-disubstituted benzoyldimides, the rates were in the order (73):

$$k_{X=Cl} > k_{X=Me} > k_{X=OMe}$$

$$XC_6H_4\overset{O}{\overset{\|}{C}}N{=}N\overset{O}{\overset{\|}{C}}C_6H_4X \longrightarrow 2XC_6H_4\dot{C}O+N_2 \qquad [56]$$

This was attributed to the weakening of the C-N bonds in the ground state by inductive electron withdrawal. Thus, it is seen that consideration of both effects may explain the rather poor fit to the Hammett equation of the study by West and Warkentin (1a, 74).

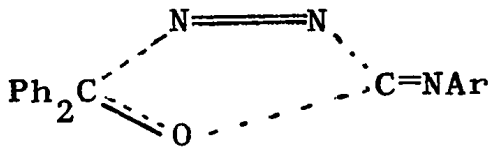
However, in the present study, a radical centre forming at C_2 is not in conjugation with the aryl ring. Thus, changing the nature of the aryl group would have



XI

little effect on the stability of the radical. Under these circumstances, ground state inductive effects would dominate. Thus, electron withdrawal from the C_2-N_3 bond by Ar, as well as by the azo linkage, would serve to weaken this bond. This inductive effect would be expected to follow the Hammett σ constants.

Another possible mechanism for direct formation of nitrogen from the compounds under study is a fully concerted decomposition. The transition state may be envisaged as follows:



The substituent effects in this one-step decomposition would be ground state effects. However, this mechanism does not explain the poor correlation found by West and Warkentin in their kinetic studies.

SUMMARY

Several new 5,5-diphenyl (or dimethyl)-2-[phenyl-(or alkyl-)imino]-Δ^3-1,3,4-oxadiazolines were synthesized and characterized. An X-ray crystal structure of 5,5-dimethyl-2-[(p-bromophenyl)imino]-Δ^3-1,3,4-oxadiazoline revealed that these heterocycles exist in the Z-configuration.

A search for reagents other than lead tetra-acetate which would oxidatively cyclize 4-substituted semicarbazones was partially fruitful. Manganese dioxide gave a low yield of 5,5-diphenyl-2-(phenylimino)-Δ^3-1,3,4-oxadiazoline from benzophenone 4-phenylsemicarbazone.

Two examples of a new heterocyclic system, Δ^3-1,3,4-oxadiazolin-2-ones, were prepared and characterized. Product studies of their thermal decomposition revealed the existence of two pathways of decomposition.

The thermal decomposition of 5,5-diphenyl-2-(arylimino)-Δ^3-1,3,4-oxadiazolines was studied kinetically. As had been reported previously (1), two pathways were operative in the thermolysis.

A study of the effect of para substituents in the arylimino moiety on the thermolysis rates was made. Both pathways were accelerated by electron-withdrawing para substituents; the Hammett ρ value in both cases was approximately 1. In the case of the retro-1,3-dipolar addition to yield aryl isocyanate and diphenyldiazomethane, the ρ value is attributed to a partially ionic transition state. In the case of the direct evolution of nitrogen, the mechanism of decomposition is proposed to be either a completely concerted cleavage or a homolytic decomposition yielding a diradical intermediate. The substituent effects on this mode of decomposition were judged to be ground state effects, primarily.

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