THERMAL REARRANGEMENTS OF 3H-PYRAZOLES, 4H-PYRAZOLEs, AND CYCLOPENTADIENES

By

ELIZABETH ANNE JEFFERSON, B.Sc.

A Thesis
Submitted to the School of Graduate Studies
in Partial Fulfillment of the Requirements
for the Degree
Doctor of Philosophy
McMaster University
(August, 1992)

© Copyright by Elizabeth Anne Jefferson, August 1992
THERMAL REARRANGEMENTS OF 3H-PYRAZOLES
DOCTOR OF PHILOSOPHY (1992)  
(Chemistry)  
MCMASTER UNIVERSITY  
Hamilton, Ontario

TITLE:  
Thermal Rearrangements of $3H$-Pyrazoles.  
$4H$-Pyrazoles, and Cyclopentadienes.

AUTHOR:  
Elizabeth Anne Jefferson, B.Sc. (McMaster University)

SUPERVISOR:  
Professor John Warkentin

NUMBER OF PAGES:  
xv, 204
Abstract

3H-Pyrazoles generally undergo thermal rearrangement by concerted [1,5]-sigmatropic migrations. It has been discovered that 3H-pyrazoles 111a-e undergo thermal rearrangement by an alternative mechanism. A stepwise, ion-pair, mechanism operates in these rearrangements in benzene/toluene, chloroform, and methanol solvents. This mechanism operates because the R substituents can form relatively stable cations. Large rate enhancements for these rearrangements combined with ion-pair trapping by methanol support this mechanism.

\[
\begin{align*}
\text{111a-e} & \quad \text{E=CO}_2\text{CH}_3 \\
\end{align*}
\]

(a: R=CHPh\textsubscript{2}; b: R=CH\textsubscript{2}OMe; c: R=CM\textsubscript{3}; d: R=1-adamantyl; e: R=p-CH\textsubscript{2}C\textsubscript{6}H\textsubscript{4}OMe)

Since 3H-pyrazoles 111b and 111e rearrange to afford 4H-pyrazoles 120b and 120e, respectively, the thermal rearrangements of these more stable isomers were investigated. Ion-pair trapping experiments with methanol suggest that these 4H-pyrazoles also rearrange by a stepwise mechanism and that different ion-pair intermediates are formed from these 4H-pyrazoles compared to the isomeric 3H-pyrazoles.
The sensitivity of the stepwise mechanism to the stabilization of the pyrazole nucleus was explored in the study of the thermal rearrangements of 128b-e. Based on cation trapping experiments with methanol it appears that 3H-pyrazoles 128b-e rearrange by a stepwise mechanism in methanol, but with "tighter" ion pair intermediates. A concerted mechanism, with some charge separation, seems to operate in the thermal rearrangement of 128f.

The generality of rearrangement by a stepwise mechanism was explored by studying the thermal rearrangements of cyclopentadienes 148a-e. Cyclopentadienes 148a-d undergo stepwise rearrangement in methanol solvent, based on ion-pair trapping experiments, while cyclopentadiene 148e rearranges by concerted [1,5]-sigmatropic migrations of carbomethoxy.

This work has shown that thermal rearrangements, where a concerted sigmatropic mechanism can in theory operate, do not necessarily proceed by this mechanism. Furthermore, transition states for such rearrangements seem to run from those with little or no charge separation, through transition states with increasing charge separation, to the two-step, ion-pair extreme.
b: R=CH₂OMe
c: R=CMe₃
d: R=1-adamantyl
e: R=p-CH₂C₆H₄OMe
f: R=CH₂C₆H₅

a: R=CHPh₂
b: R=CH₂OMe
c: R=1-adamantyl
d: R=p-CH₂C₆H₄OMe
e: R=CH₂C₆H₅
Acknowledgements

I am grateful to Professor John Warkentin, my research supervisor, for his kindness, guidance, optimism, and inspiration throughout the course of this work.

The financial support from McMaster University, in terms of Departmental Scholarships and Teaching Assistantships, was much appreciated.

I am deeply indebted to my spouse, Jeff Kay, for his never ending moral support, encouragement, patience, and understanding.

Sincere thanks goes to Dr. Don Hughes, Mr. Brian Sayer, Mr. Ian Thompson, and Mr. George Timmins, from the McMaster NMR facility, for assistance in the operation of the NMR spectrometers.

I also express gratitude to Dr. Richard Smith, Mr. F. Ramelan, and Ms. Carol Kingsmill, from the Mass Spectrometry facility, for several mass spectrometric determinations.

Much thanks goes to my supervisory committee, Professors Nick Werstiuk and William Leigh, for their research advice and comments.

I express thanks to my coworkers, over the past 4 years in ABB 358, for helpful research tips, technical assistance, and their friendship. I especially thank David Pole for proof-reading this thesis and making several helpful suggestions.
# Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSTRACT</td>
<td>iii</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>vi</td>
</tr>
<tr>
<td>TABLE OF CONTENTS</td>
<td>vii</td>
</tr>
<tr>
<td>LIST OF TABLES</td>
<td>xiii</td>
</tr>
</tbody>
</table>

## CHAPTER 1 - Introduction

1.1 [1,5]-Sigmatropic Rearrangements in Cyclopentadienes

  1.1.1 Sigmatropic rearrangements                                      1
  1.1.2 Migration of hydrogen/deuterium in cyclopentadienes             6
  1.1.3 Migration of alkyl substituents in cyclopentadienes             12
  1.1.4 Migration of carbon-based functional groups in cyclopentadienes 17
  1.1.5 Migration of arylazo in cyclopentadienes                         20
  1.1.6 Summary of [1,5]-sigmatropic migrations in cyclopentadienes     22
1.2 3H-Pyrazoles

1.2.1 General

1.2.2 Synthesis of 3H-pyrazoles from alkynes and diazo compounds

1.2.3 Synthesis of 3H-pyrazoles from alkenes and diazo compounds

1.2.4 Photochemical loss of nitrogen from 3H-pyrazoles

1.2.5 Thermal rearrangement of 3H-pyrazoles

1.2.6 Studies on the mechanism of 3H-pyrazole rearrangement

1.2.7 Migratory aptitude of substituents in 3H-pyrazole rearrangements

1.3 Nucleophilic Aliphatic Substitution Reactions

Involving Ion-Pair Intermediates

1.3.1 General

1.3.2 Substrate stability

1.3.3 Leaving group ability

CHAPTER 2 - Studies of the Thermal Rearrangements of Dimethyl 3-Alkyl-3-methyl-3H-pyrazole-4,5-dicarboxylates

2.0 Objective

2.1 Synthesis of oxadiazolines 114a-e
2.2 Synthesis of $3H$-pyrazoles 111a-e
2.3 Rearrangement of $3H$-pyrazoles in benzene-$d_6$ solvent
2.4 Mechanism of rearrangement of $3H$-pyrazoles 111a-e in benzene
2.5 Rearrangement of $3H$-pyrazoles in chloroform
2.6 Rearrangement of $3H$-pyrazoles 111a-e in methanol
2.7 Rearrangement of $3H$-pyrazole 111f in methanol
2.8 Rearrangement of $4H$-pyrazoles 120b and 120e
2.9 Different ion pairs from isomeric $3H$-pyrazoles and $4H$-pyrazoles
2.10 Structural determination of $1H$-pyrazoles and $4H$-pyrazoles
2.11 Conclusion
2.12 Synthetic applications

CHAPTER 3 - Studies of the Thermal Rearrangements of Methyl

3-Alkyl-3-methyl-$3H$-pyrazole-5-carboxylates

3.0 Objective
3.1 Photolysis of oxadiazolines 114a-f in the presence of methyl propionate
3.2 Synthesis of cyclopropenes 135c-f
3.3 Synthesis of $3H$-pyrazoles 128c-f: Modified preparative procedure
3.4 Rearrangement of $3H$-pyrazoles 128b-f in benzene-$d_6$
3.5 Structural determination of pyrazole rearrangement products
3.6 Rearrangement of 128b in dichloromethane
3.7 Rearrangement of $3H$-pyrazoles 128c-f in acetone-$d_6$ 109

3.8 Rearrangement of $3H$-pyrazoles 128c-f in methanol or methanol-$d_4$ 112

3.9 Conclusion 115

3.10 Synthetic applications 117

CHAPTER 4 - Thermal Rearrangements of 5-Alkyl-1,2,3,4,5-

pentakis(methoxycarbonyl)cyclopentadienes 119

4.0 Objective 119

4.1 Synthesis of cyclopentadienes 148a-f 123

4.2 Heating cyclopentadienes 148a and 148b in the NMR probe 125

4.3 Rearrangement of 148a-d in methanol 128

4.4 Rearrangement of 144e and 144f in methanol-$d_4$ 131

4.5 Conclusion 132

CHAPTER 5 - Experimental

5.0 General 136

5.1 Preparation of 2-acetylhydrazones of ketones (113a-e) 137

5.2 Preparation of 5-alkyl-2-methoxy-2,5-dimethyl-$\Delta^3$-1,3,4-
oxadiazolines (114a-e) 139

5.3 Rearrangement of $3H$-pyrazoles 111a-e in benzene-$d_6$ 141

5.4 Modified preparative procedure for the observation of $3H$-pyrazoles 111c-e 145
5.5 Determination of \( k_{\text{obs}} \) for the rearrangement of 3\( H \)-pyrazoles 111c-e 146

5.6 Synthesis of 3\( H \)-pyrazole 111f 147

5.7 Rearrangement of 3\( H \)-pyrazoles 111a-e in chloroform 148

5.8 Rearrangement of 3\( H \)-pyrazoles 111a-e in methanol 151

5.9 Rearrangement of 3\( H \)-pyrazole 111f in methanol 153

5.10 Thermal rearrangements of 4\( H \)-pyrazoles 120b and 120e in benzene-\( d_6 \) 154

5.11 Thermal rearrangements of 4\( H \)-pyrazoles 120b and 120e in methanol/methanol-\( d_6 \) 156

5.12 Preparation of 3\( H \)-pyrazoles 128c-f 157

5.13 Synthesis of cyclopropenes 134c-f 158

5.14 Rearrangement of 3\( H \)-pyrazoles 128b-f in benzene-\( d_6 \) 160

5.15 Determination of \( k_{\text{obs}} \) for the rearrangement of 3\( H \)-pyrazoles 128c-f in benzene-\( d_6 \) 165

5.16 Rearrangement of 128b in dichloromethane 166

5.17 Rearrangement of 3\( H \)-pyrazoles 128c-f in acetone-\( d_6 \) 167

5.18 Determination of \( k_{\text{obs}} \) for the rearrangement of 3\( H \)-pyrazoles 128c-f in acetone-\( d_6 \) 169

5.19 Rearrangement of 3\( H \)-pyrazoles 128b-f in methanol 169
5.20  Synthesis of cyclopentadienes 148a-f  173
5.21  Rearrangement of 148a-f in methanol or methanol-d₄  176

Appendix I  Observed rate constant data  181
Appendix II  Calculation of maximum value for k₄ that would not give
detectible line broadening  187
Appendix III  Infrared Spectra  188

References  192
# List of Tables

1. Selection rules for [1,5]-sigmatropic migrations .......................... 5
2. Kinetic data for compounds 27-31 ........................................ 16
3. Activation parameters for the rearrangement 43a-d $\rightarrow$ 44a-d .... 20
4. Activation parameters for the rearrangement of arylazo groups in compounds 46c-f ........................................ 21
5. Isomerization of 88 to 90 and 91 at 65 °C .................................. 37
6. Rearrangement of 94a-e at 120 °C ......................................... 40
7. Solvolysis rates of alkyl bromides, $R^1R^2R^3CBr$, in EtOH at 55 °C 45
8. Solvolysis rates of arylmethyl chlorides, $R^1R^2R^3CCl$, and tert-butyl chloride in 80% EtOH at 50 °C ........................................ 46
9. Relative reaction rates for some common leaving groups in $S_N1$ reactions ......................................................... 50
10. $^1$H and selected $^{13}$C NMR chemical shifts for 3H-pyrazoles 111c-e 58
11. Products and product yields from the thermal rearrangements of 111a-e at ambient temperature in benzene-$d_6$ ......................... 60
12. Products and product yields from the thermal rearrangements of 111a-e at ambient temperature in chloroform .......................... 67

xiii
13. Products and product yields from the thermal rearrangements of 111a-e at ambient temperature in methanol

14. Products and product yields from thermal rearrangements of 120b and 120e

15. Selected $^{13}$C NMR chemical shifts of 1$H$-pyrazoles 118a-f

16. Selected $^{13}$C NMR chemical shifts of 1$H$-pyrazoles 119a-e

17. $^1H$ NMR and selected $^{13}$C NMR chemical shifts for 4$H$-pyrazoles

18. $^1H$ NMR and selected $^{13}$C NMR chemical shifts for cyclopropenes 134c-f

19. $^1H$ NMR and selected $^{13}$C NMR chemical shifts for 3$H$-pyrazoles 128c-f

20. Products and product yields from the thermal rearrangements of 128b-f in benzene-$d_6$

21. Selected $^{13}$C NMR chemical shifts of 132b-e

22. Selected $^{13}$C NMR chemical shifts of 131b-f

23. Products and product yields from the thermal rearrangements of 128b-f in benzene-$d_6$

24. Products and product yields from the thermal rearrangements of 128b-f in benzene-$d_6$

25. $^1H$ NMR chemical shifts of cyclopentadienes 148a-f

26. Selected $^{13}$C NMR chemical shifts for 148a-f

27. Determination of $k_{obs}$ for 111e in C$_6$D$_6$ at 20 °C

28. Determination of $k_{obs}$ for 111c in C$_6$D$_6$ with 2.5 equivalents of triethylendiamine at 35 °C
29. Determination of $k_{obs}$ for 111d in C$_6$D$_6$ at 35 °C
30. Determination of $k_{obs}$ for 120b in C$_6$D$_6$ at 90 °C
31. Determination of $k_{obs}$ for 120e in C$_6$D$_6$ at 120 °C
32. Determination of $k_{obs}$ for 128c in C$_6$D$_6$ at 90 °C
33. Determination of $k_{obs}$ for 128c in acetone-$d_6$ at 90 °C
34. Determination of $k_{obs}$ for 128c in CD$_3$OD at 50 °C
35. Determination of $k_{obs}$ for 128d in C$_6$D$_6$ at 90 °C
36. Determination of $k_{obs}$ for 128d in acetone-$d_6$ at 90 °C
37. Determination of $k_{obs}$ for 128e in C$_6$D$_6$ at 60 °C
38. Determination of $k_{obs}$ for 128e in C$_6$D$_6$ at 60 °C
39. Determination of $k_{obs}$ for 128e in acetone-$d_6$ at 60 °C
40. Determination of $k_{obs}$ for 128f in C$_6$D$_6$ at 90 °C
41. Determination of $k_{obs}$ for 128f in acetone-$d_6$ at 90 °C
42. Determination of $k_{obs}$ for 148b in CD$_3$OD at 40 °C
43. Determination of $k_{obs}$ for 148c in CD$_3$OD at 50 °C
44. Determination of $k_{obs}$ for 148d in CD$_3$OD at 100 °C
CHAPTER 1

Introduction

1.1 [1,5]-Sigmatropic Rearrangements in Cyclopentadienes

1.1.1 Sigmatropic rearrangements (general)

Reactions in which more than one bond is broken or formed can be divided into two classes. The first is one in which all the bond forming and breaking processes occur simultaneously so that a one-step transformation of reactants to products occurs without the intervention of an intermediate. Such reactions are called concerted since the bond changes occur in concert, at the same time, at more than one centre. The second broad class of reactions is one in which the bond forming and breaking processes occur consecutively so that one or more intermediates is involved. These intermediates may be stable molecules capable of isolation, or they may be reactive species of only transient existence (i.e. ion pairs or radical pairs). When the intermediates are unstable the process is normally considered one reaction which proceeds in a stepwise manner.

Sigmatropic rearrangements belong to a category of concerted reactions called pericyclic reactions. Other reactions falling in the pericyclic category include cycloaddition, electrocyclic, cheletropic, and group transfer processes. Pericyclic reactions are characterized by bonding changes which take place through the reorganization of
electron pairs within a closed loop of interacting orbitals. In order for a reaction to be classified as pericyclic, the bonds breaking and forming must do so simultaneously rather than in two or more steps. Not all bonding changes necessarily have to take place to the same extent at all stages along the reaction coordinate. It is possible for bond formation or cleavage at one site to run substantially ahead of bond formation or cleavage at another. Bond formation and breakage in a pericyclic reaction is therefore simultaneous, but not necessarily synchronous. The application of the fundamental principles of orbital symmetry theory, introduced by Woodward and Hoffmann\textsuperscript{1} and since developed considerably by them\textsuperscript{2-4} and others,\textsuperscript{5-15} has provided much insight into these reactions.

Sigmatropic reactions are concerted, uncatalysed bond migrations involving a transition state in which an atom or group is simultaneously joined to both termini of a $\pi$-electron system. Woodward and Hoffmann have given the name *sigmatropic rearrangements* to such reactions; the adjective "*sigmatropic*" indicating movement of a sigma bond. Several reviews have been published on sigmatropic reactions.\textsuperscript{16-21}

A formal system of nomenclature is widely used for classifying sigmatropic rearrangements. This is characterized by square brackets containing two numbers; the first number is the position of the migration origin, the second number is the position of the migration terminus. For example, in a [1,j]-sigmatropic shift of hydrogen between the ends of a polyene, one end of the migrating $\sigma$ bond remains fixed while the other end moves to the next atom or to a more remote position at the end of an adjacent $\pi$ system (Scheme 1). The orbital on C-1 eventually becomes an sp\textsuperscript{2}-hybridized bonding orbital of the polyene while that on C-j becomes an sp\textsuperscript{3}-hybridized bonding orbital.
There are two stereochemically distinct ways in which overlap can take place in the transition state for a migrating hydrogen (atomic orbital representation, Figure 1). The spherically symmetrical hydrogen orbital can maintain contact at all times with the same face of the $\pi$ system (suprafacial overlap) or move from one face of the $\pi$ system to the other as the reaction takes place (antarafacial overlap). This requirement makes antarafacial [1,3]-hydrogen migration very difficult because transfer of hydrogen to the opposite face of the $\pi$ system is required.

![Scheme 1]

**Scheme 1**

![suprafacial overlap](image1)

![antarafacial overlap](image2)

**Figure 1**
If the migrating group is capable of undergoing stereochemical inversion, then four distinct possibilities exist; both suprafacial or antarafacial routes exist, each of which occur with retention or inversion of configuration at the migrating centre. As an illustrative example of the former, Figure 2 demonstrates possible routes for suprafacial [1,3]-alkyl migration. The use of the front face of the alkyl bonding orbital gives a transition state with no sign inversion while the use of the back face of the alkyl bonding orbital gives a transition state with a sign inversion. The stereochemical consequences of the two processes are distinct because the former process leads to retention of configuration of the migrating group while the latter process leads to inversion of configuration of the migrating group.

Figure 2
Selection rules for thermally allowed sigmatropic rearrangements can be derived by application of the Hückel-Möbius approach (Table 1). This approach considers that sigmatropic migration must occur via aromatic transition states. Möbius transition states are aromatic for \(4n\) π electrons, with one sign inversion in the cycle, while Hückel transition states are aromatic for \((4n+2)\) π electrons, with no sign inversions. A [1,3]-alkyl migration involving 4 π electrons can occur antarafacially via a Möbius transition state, while a [1,5]-sigmatropic hydrogen migration involving 6 π electrons can occur suprafacially via a Hückel transition state.

[1,5]-Sigmatropic rearrangement is also possible in cyclic systems as well as acyclic systems. In the following sections (1.1.2-1.1.6), [1,5]-sigmatropic rearrangements of some cyclopentadienes are discussed.

Table 1. Selection rules for thermal [1,j] sigmatropic migrations.

<table>
<thead>
<tr>
<th>Number of electrons</th>
<th>System Type</th>
<th>(j)</th>
<th>Allowed Migration</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Möbius</td>
<td>3</td>
<td>antarafacial-retention suprafacial-inversion</td>
</tr>
<tr>
<td>6</td>
<td>Hückel</td>
<td>5</td>
<td>antarafacial-inversion suprafacial-retention</td>
</tr>
<tr>
<td>(4n)</td>
<td>Möbius</td>
<td>((4n-1))</td>
<td>antarafacial-retention suprafacial-inversion</td>
</tr>
<tr>
<td>(4n+2)</td>
<td>Hückel</td>
<td>((4n+1))</td>
<td>antarafacial-inversion suprafacial-retention</td>
</tr>
</tbody>
</table>
1.1.2 Migration of hydrogen/deuterium in cyclopentadienes

In the early chemical literature, a number of anomalies were reported during the synthesis of substituted cyclopentadienes where the distribution of double bonds in the product cyclopentadiene was inconsistent with what was expected, based on a synthetic plan (Scheme 2). Decarboxylation of 2,4-diphenylcyclopentadiene-1-carboxylic acid (1) gave 1,4-diphenylcyclopentadiene (2), instead of the expected 1,3-compound.\textsuperscript{22} The dehydration of 1-phenylcyclopent-2-en-1-ol (3) yielded 1-phenylcyclopentadiene (4), instead of 2-phenylcyclopentadiene.\textsuperscript{23} Furthermore, the dehydration of 2,3,4-trimethylcyclopent-2-ene-1-ol (5) led to 1,2,3-trimethylcyclopentadiene (6) instead of the 1,2,5-substituted compound.\textsuperscript{24} The authors either did not attempt to explain these anomalies or explained them by the irreversible isomerization of the initial substituted cyclopentadiene to the energetically more favourable isomer. The majority of these authors were convinced that the endocyclic double bonds in the cyclopentadiene ring were fixed.

The [1,5]-hydrogen shift was discovered in 1961 by Mironov and coworkers.\textsuperscript{25} Direct interconversions of isomeric cyclopentadienes by [1,5]-hydrogen migrations were observed in 5-deuterocyclopentadiene (7), synthesized by treating cyclopentadienylmagnesium bromide with deuterium oxide at -5 °C.\textsuperscript{26,27} In the course of 1 hour at 60 °C, cyclopentadiene 7 was converted into a mixture of equal amounts of 7, 8, and 9. The measurement of the infrared spectra at successive time intervals during the attainment of this equilibrium showed that the deuterocyclopentadienes isomerize in the following sequence $7 \rightleftharpoons 8 \rightleftharpoons 9$.\textsuperscript{28} A [1,5]-deuterium migration in cyclopentadiene 7 is
degenerate. It was suggested that bridged proton-cyclopentadienyl anions were probably transition states in the transformation of isomers (Figure 3).

Scheme 2
In 1964 Roth synthesized 1,2,3,4,5-pentadeuterocyclopentadiene (10) and established that when the cyclopentadiene was heated to 45-65 °C it underwent rearrangement by [1,5]-deuterium migration. The hydrogen atoms were distributed uniformly among the 1-, 2-, and 5-positions of the cyclopentadiene ring. A [1,5]-hydrogen migration in 10 is degenerate. The kinetic parameters for the isomerization of (10)→(11) were determined to be log A = 12.11, ΔH° = 23.6 kcal/mol, and ΔS° = -3.3 eu.
Mironov and coworkers were the first to study the rearrangement of 5-methylcyclopentadiene (12). They established that at 25 °C in the liquid and gas phases 5-methylcyclopentadiene (12) isomerizes to 1-substituted cyclopentadiene 13. The reaction is virtually complete after 3 hours in the liquid phase and after 4 hours in the gas phase; 2-methylcyclopentadiene (14) is then formed only in insignificant amounts (<5%). It was noted that the concentration of isomer 12 decreases by a factor of two after equal time intervals (reaction half-life is constant). Cyclopentadiene 13 rearranges more slowly and after 2-3 days at 25 °C it is transformed into a mixture of approximately equal amounts of 13 and 14 containing <3% of isomer 12. Distillation of cyclopentadienes 12, 13, or 14 at atmospheric pressure led to the formation of the same mixture of cyclopentadienes 13 and 14. It was concluded that the interconversions of the isomeric cyclopentadienes take place by a [1,5]-sigmatropic migration of hydrogen from the C-5 position in the cyclopentadiene ring to a neighbouring carbon atom.

McLean and Haynes also studied the thermal rearrangement of methylcyclopentadiene 12 by using 1H NMR techniques. The first order rate constant for hydrogen migration in 12 was $k_{30}^{°}C = 62.0 \times 10^{-5} \text{ s}^{-1}$. Kinetic parameters were also determined ($\Delta H^i = 20.4 \text{ kcal/mol and } \Delta S^i = -10 \text{ eu}$) for the rearrangement of 12 to 13.
McLean and Haynes also suggested the presence of a polar transition state involving a bridged proton-cyclopentadienyl anion for this concerted reaction. The failure of the authors to observe deuterium incorporation during rearrangements carried out in the presence of D₂O was taken as evidence that separated ions were not formed during rearrangement. In 5-substituted cyclopentadienes, the [1,5]-hydrogen shift takes place at a rate much higher than in their isomers with a free methylene group.⁴¹,⁴²

Insight into the structure of the transition state for the concerted [1,5]-hydrogen migration in cyclopentadienes was provided by a study on deuterium isotope effects by McLean and coworkers.⁴³ They compared the kinetic parameters for the conversion of 5-methylpentadeuterocyclopentadiene (Scheme 3) into the 1-isomer (ΔHᵣ = 21.7 kcal/mol, ΔSᵣ = -6.2 eu) with the corresponding values for 5-methylcyclopentadiene (ΔHᵣ = 19.3 kcal/mol, ΔSᵣ = -10.8 eu) and calculated the kinetic isotope effect (k_H/k_D = 6 at 27 °C). The measured k_H/k_D represents the product of the primary kinetic isotope effect and the secondary effect generated by the four D atoms attached to the double bonds, although it was suggested that the latter hardly constituted 10% of the quoted value. Therefore, it was suggested that the primary kinetic isotope effect of the [1,5]-hydrogen shift exceeded the value which might have been expected from the difference between the dissociation energies of the C-D and C-H bonds. It was concluded that, in the transition state, the migrating hydrogen (deuterium) atom is equidistant from the initial (C-5) and final (C-1) migration centres. Furthermore, the high negative entropy of activation for the reaction is suggestive of a rigorously ordered transition state.
The accumulation of alkyl groups in the cyclopentadiene ring lowers the rate of reaction. McLean and Haynes studied the rearrangement of 15 and found $k_{\text{obsd}} = 5.5 \times 10^{-5} \text{ s}^{-1}$ (30 °C) for the rate of hydrogen migration from C-5 to C-4 in neat 15. Its activation parameters are $\Delta H^\ddagger = 22.5 \text{ kcal/mol}$ and $\Delta S^\ddagger = -4 \text{ eu.}$

Breslow and coworkers studied the effect of C-5 halogen substitution on [1,5]-hydrogen migration in cyclopentadiene 17 ($X = \text{Cl, Br, I}$). Halogen substitution slows down the rate of hydrogen migration compared to the parent hydrocarbon (ie. $X = \text{D}$) even though it stabilizes the reaction product. 5-Deuterocyclopentadiene was reported to equilibrate to an equal mixture of the three isomers in 1 hour at 60 °C, however, Breslow found that 17 ($X = \text{Cl}$) required 2 hours at 75 °C to reach equilibrium containing only the 1- and 2- isomers. Furthermore, cyclopentadiene 17 ($X = \text{Br}$) required 2 hours at 100 °C to reach equilibrium, while 17 ($X = \text{I}$) was not completely equilibrated after 6 hours at 100 °C. Breslow rationalized this rate retardation by stating that a local
positive charge on carbon must be involved in the transition state for 1,5-sigmatropic rearrangement. This suggestion is contrary to both Mironov and McLean who proposed a bridged proton-cyclopentadienyl anion transition state was involved.\textsuperscript{27,31} The mechanism of this rate retardation for 1,5-hydrogen migration from the C-5 position carrying a halogen substituent is obscure and still open to reinterpretation.

1.1.3 Migration of alkyl substituents in cyclopentadienes

1,5-Sigmatropic migrations in cyclopentadienes are not limited to having hydrogen as the migrating group. Cyclopentadienes can also undergo 1,5-alkyl migrations. For example, irreversible thermal isomerization of 1,5,5-trimethylcyclopentadiene (18) to 1,2,3-trimethylcyclopentadiene (19) leads to an equilibrium mixture of substituted trimethylcyclopentadienes (19, 20, and 21) in which isomer 20 predominates. The following kinetic parameters were obtained for the isomerization of 18 to 20: $\Delta H^\ddagger = 40.3$ kcal/mol and $\Delta S^\ddagger = -1$ eu (350-400 °C), according to the data of de Haan and Kloosterziel\textsuperscript{36,37} and $\Delta H^\ddagger = 43.8$ kcal/mol and $\Delta S^\ddagger = 0.7$ eu (328-430 °C), according to the data of Herndon and Manion.\textsuperscript{38,39}
The mechanism of rearrangement involves an initial slow [1,5]-methyl migration followed by rapid [1,5]-hydrogen migrations which eventually leads to a preponderance of the more stable trimethylcyclopentadiene 20. The enthalpy of activation is approximately 20 kcal/mol higher than that for a similar [1,5]-hydrogen migration.\textsuperscript{33} McLean and Findlay found similar activation parameters for [1,5]-methyl migration in 5,5-dimethylcyclopentadiene\textsuperscript{40} and Mironov and coworkers established that [1,5]-methyl migration was indeed reversible in a series of studies of di-, tri-, and tetramethylcyclopentadienes.\textsuperscript{41-44}

The thermal rearrangement of a 5,5-disubstituted cyclopentadiene in which the [1,5]-alkyl shift does not lead to the elimination of geminal substitution was also investigated. 1,2,4,5,5-Pentamethylcyclopentadiene (22) is converted at 400-500 °C (contact time approximately 8 seconds) into 1,2,3,4,5-pentamethylcyclopentadiene (24) via intermediate 23.\textsuperscript{45} The first and rate-determining stage is the reversible isomerization of 22 \(\leftrightarrow\) 23 by [1,5]-methyl shifts. The second irreversible stage (23 \(\rightarrow\) 24) leads to a cyclopentadiene in which [1,5]-hydrogen migration is degenerate.
Kloosterziel and coworkers established the stereospecificity of alkyl migration in the rearrangements of cis- and trans-6,9-dimethylspiro[4.4]nona-1,3-diene (25a and 25b). Compound 26a was obtained from the rearrangement of 25a while compound 26b was obtained from the rearrangement of 25b. The migration of alkyl occurred via a suprafacial pathway with retention of configuration at the migrating carbon.\textsuperscript{46,47}

\[
\begin{align*}
\text{25} & \quad \text{26} \\
(a: R^1=R^2=\text{CH}_3, R^3=\text{H}; \ b: R^1=R^3=\text{CH}_3, R^2=\text{H})
\end{align*}
\]

Evidence in support of a polar transition state in cyclopentadiene [1,5]-alkyl shifts comes from a study of the thermolysis of phenyl-, cyano-, and methoxy-substituted spiro[4.4]nona-1,3-dienes.\textsuperscript{48} Carpenter and Reploge studied the kinetics of rearrangement of compounds 27-31 (Scheme 4) and some of their results are summarized in Table 2.

The suggestion of partial charge development in the transition state for alkyl migration was made because both $\Delta H^\ddagger$ and $\Delta S^\ddagger$ were reduced when the solvent was changed from isooctane to isopropyl alcohol (entries 1, 2, 7, and 8). The cyano group reduces $\Delta H^\ddagger$ by 2.4 kcal/mol in isooctane and 4.3 kcal/mol in isopropyl alcohol. This substituent effect was not attributed to steric, conjugating, or radical stabilizing properties of a cyano group since a phenyl substituent at the same location had virtually no effect on $\Delta H^\ddagger$ (entry 4). The effect of the cyano group was attributed to its electron-withdrawing properties.
Scheme 4
Table 2. Kinetic data for compounds 27-31.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>Temp. Range (°C)</th>
<th>Solvent</th>
<th>ΔH° (kcal/mol)</th>
<th>ΔS° (cal)</th>
<th>k_rel (150 °C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>27→32</td>
<td>141-196</td>
<td>isoctane</td>
<td>32.0 ± 0.2</td>
<td>-5.1 ± 0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>27→32</td>
<td>136-175</td>
<td>isopropyl alcohol</td>
<td>30.9 ± 0.6</td>
<td>-6.7 ± 1.3</td>
<td>1.7</td>
</tr>
<tr>
<td>3</td>
<td>28→33</td>
<td>146-185</td>
<td>isoctane</td>
<td>35.4 ± 1.1</td>
<td>-0.4 ± 2.6</td>
<td>0.2</td>
</tr>
<tr>
<td>4</td>
<td>28→34</td>
<td>146-185</td>
<td>isoctane</td>
<td>32.6 ± 0.6</td>
<td>-4.3 ± 1.3</td>
<td>0.7</td>
</tr>
<tr>
<td>5</td>
<td>29→35</td>
<td>146-185</td>
<td>isoctane</td>
<td>32.4 ± 0.5</td>
<td>-4.8 ± 1.0</td>
<td>0.7</td>
</tr>
<tr>
<td>6</td>
<td>29→36</td>
<td>146-185</td>
<td>isoctane</td>
<td>34.4 ± 0.6</td>
<td>-0.3 ± 1.2</td>
<td>0.6</td>
</tr>
<tr>
<td>7</td>
<td>30→37</td>
<td>120-160</td>
<td>isoctane</td>
<td>29.6 ± 0.2</td>
<td>-5.7 ± 0.5</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>30→37</td>
<td>106-146</td>
<td>isopropyl alcohol</td>
<td>26.6 ± 0.2</td>
<td>-9.9 ± 0.4</td>
<td>55</td>
</tr>
<tr>
<td>9</td>
<td>31→38</td>
<td>160-200</td>
<td>isoctane</td>
<td>32.8 ± 0.4</td>
<td>-4.8 ± 0.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Compounds 28 and 29, containing phenyl on the cyclopentadiene ring, exhibited both regiochemistries for [1,5]-shifts, while compounds 30 and 31 gave only one product. The suggestion was that the regioselectivities observed with compounds 30 and 31 are of electronic origin rather than steric. The charge distribution in bicyclo[3.1.0]hexatriene was calculated by the Hückel molecular orbital model and was like that of an allyl anion fused to a cyclopropenium ion (Figure 4). Therefore, C-2 and C-4 carry the largest negative charges, C-3 the smallest negative charge, and C-1, C-5, and C-6 carry positive charges. Figure 5 shows possible transition states for the thermal rearrangements of 30 and 31.

![Figure 4](image-url)
In the rearrangement of 30, the two possible regiochemistries correspond to placing the acceptor substituent at C-1 or C-2 of the transition state model, Figure 4. One would expect C-2 to be preferred as was observed. For compound 31 the choice is between C-2 and C-3 and since 31 bears a π-donor substituent, one would expect the site of smaller negative charge, i.e., C-3, to be preferred and this regioselectivity was observed.

1.1.4 Migration of carbon-based functional groups in cyclopentadienes

Carbon-based functional groups are also capable of [1,5]-sigmatropic migration in cyclopentadienes. The migration of the following substituents from C-5 of a cyclopentadiene are considered: Ph, CHO, and COOME.

An example of a [1,5]-phenyl migration in a cyclopentadiene ring was described by Youssef and Ogliaruso. Reﬂuxing a solution of 1,2,3,4,5-pentaphenylcyclopentadienol (39) in diphenyl ether produced 40 from a slow [1,5]-phenyl
migration which was followed by tautomerization to the keto form (41). Activation parameters were determined (173-200 °C) to be $\Delta H^\ddagger = 35.3$ kcal/mol and $\Delta S^\ddagger = -7.5$ eu.

![Diagram showing the reaction between structures 39 and 41](image)

[1,5]-Sigmatropic formyl migration in 5-formyl-1,2,3,4,5-pentamethylcyclopenta-1,3-diene (42) is rapid at 25 °C ($k_{\text{ion}} = 90$ s$^{-1}$). Line shape analysis of $^1$H NMR spectra obtained between -20 and +70 °C revealed that migration is associated with an activation enthalpy of $13.2 \pm 0.3$ kcal/mol and an activation entropy of $-5.1 \pm -0.2$ eu.

![Diagram showing structure 42](image)

1,5-Alkyl shifts in cyclopentadienes commonly require temperatures above 330 °C and proceed with $\Delta H^\ddagger > 43$ kcal/mol. The easy migration of the formyl group compared to alkyl groups was attributed to secondary orbital interactions between the vacant $\pi^*$-orbital of the formyl group and the HOMO of the diene (Figure 6).
Carbomethoxy is also a very good migrating group. Hoffmann and coworkers studied the [1,5]-carbomethoxy shift in some 5-R-pentakis(methoxycarbonyl) cyclopentadienes. At 100-150 °C, the transformation 43 → 44 takes place, while at higher temperatures, ( > 160 °C), transformation 44 → 45 occurs as well. Activation parameters for the isomerization of 43a-d to 44a-d in dichlorobenzene are presented in Table 3.

\[
\begin{align*}
43a-d & \rightleftharpoons 44a-d \\
E=\text{CO}_2\text{CH}_3 \\
(a: \text{R}=\text{Me}; \ b: \text{R}=\text{CH}_2\text{CH}_3; \ c: \text{R}=\text{CH(Me)}_2; \ d: \text{R}=\text{Cl})
\end{align*}
\]
Table 3. Activation parameters for the rearrangement 43a-d → 44a-d.

<table>
<thead>
<tr>
<th></th>
<th>Temp. Range (°C)</th>
<th>ΔG‡ (kcal/mol)</th>
<th>ΔH‡ (kcal/mol)</th>
<th>ΔS‡ (eu)</th>
</tr>
</thead>
<tbody>
<tr>
<td>43a, R=Me</td>
<td>104.4-144.8</td>
<td>30.2 ± 0.2</td>
<td>26.9 ± 1.0</td>
<td>-8.6 ± 3.5</td>
</tr>
<tr>
<td>43b, R=CH₂CH₃</td>
<td>99.1-128.9</td>
<td>30.4 ± 0.2</td>
<td>29.3 ± 0.5</td>
<td>-3.4 ± 3.0</td>
</tr>
<tr>
<td>43c, R=CH(Me)₂</td>
<td>99.1-128.9</td>
<td>30.0 ± 0.2</td>
<td>30.6 ± 0.7</td>
<td>+1.2 ± 2.1</td>
</tr>
<tr>
<td>43d, R=Cl</td>
<td>150.2-190.2</td>
<td>31.7 ± 0.2</td>
<td>27.3 ± 1.8</td>
<td>-10.3 ± 4.6</td>
</tr>
</tbody>
</table>

1.1.5 Migration of arylazo in cyclopentadienes

Mikhailov and coworkers investigated the rearrangement of cyclopentadienes 46a-f. In the ¹H NMR spectra of 46c-f in benzonitrile solution, the signal for the protons of the carbomethoxy groups at 30 °C appear in the form of a singlet. With a decrease in the temperature of the solution, this peak is broadened and at -35 °C (for compounds 46c-f) it splits into a triplet with intensity ratios of 2 : 2 : 1. Such spectral behaviour was attributed to the exchange of the positions of the arylazo group in the cyclopentadiene ring, which takes place through the reversible formation of ion pair 47 from covalent substrate 46.
(a: X=OMe; b: X=Me; c: X=H; d: X=I; e: X=Cl; f: X=Br)

For compounds 46a and 46b, the migration of arylazo around the cyclopentadiene ring takes place very rapidly on the $^1$H NMR time scale. Even in solutions at -50 to -70 °C the signal for the protons of the carbomethoxy groups is in the form of a narrow singlet. Table 4 gives the rate constants and activation parameters for the migration of the arylazo groups in 46c-f. Electron-withdrawing substituents at the ortho position of the aryl group retard the exchange process because they destabilize the intermediate diazonium cation.

**Table 4. Activation parameters for the rearrangement of arylazo groups in compounds 46c-f.**

<table>
<thead>
<tr>
<th>Compound</th>
<th>X</th>
<th>$k_{298}$ ($\times 10^2 \text{s}^{-1}$)</th>
<th>$\Delta H^\ddagger$ (kcal/mol)</th>
<th>$\Delta S^\ddagger$ (\text{cal mol}^{-1} \text{K}^{-1})</th>
<th>$\Delta G^\ddagger$ (kcal/mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>46c</td>
<td>H</td>
<td>8.9</td>
<td>11.1 ± 0.4</td>
<td>-7.7 ± 0.6</td>
<td>13.4</td>
</tr>
<tr>
<td>46d</td>
<td>I</td>
<td>6.3</td>
<td>14.2 ± 0.2</td>
<td>+2.1 ± 0.3</td>
<td>13.6</td>
</tr>
<tr>
<td>46e</td>
<td>Cl</td>
<td>5.4</td>
<td>11.3 ± 0.2</td>
<td>-8.2 ± 0.3</td>
<td>13.7</td>
</tr>
<tr>
<td>46f</td>
<td>Br</td>
<td>4.6</td>
<td>11.7 ± 0.4</td>
<td>-7.0 ± 0.7</td>
<td>13.8</td>
</tr>
</tbody>
</table>
1.1.6 Summary of [1,5]-sigmatropic migrations in cyclopentadienes

Generally, the migration of a C-5 substituent in a cyclopentadiene ring occurs by a suprafacial [1,5]-sigmatropic migration. This process has been shown by means of numerous experimental\textsuperscript{16-21} and theoretical studies\textsuperscript{33,48,57,58,59} to occur in a concerted manner.

The nature of the transition state is an interesting feature of these rearrangements. The idea of a proton-cyclopentadienyl anion transition state for [1,5]-hydrogen migration in cyclopentadiene, originally suggested by Mironov and coworkers in 1963,\textsuperscript{37} was also suggested by both Houk\textsuperscript{57} and Carpenter\textsuperscript{48} in independent theoretical studies. The nature of the transition state, however, is dependent on both the structure of the cyclopentadiene and the migrating group. The transition state for concerted migrations seems to vary from one highly ordered, with no charge separation, to one with some degree of charge separation. However, the mechanism for rearrangement of some arylazo 1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes is stepwise, involving a cyclopentadienyl anion and a diazonium cation\textsuperscript{56}. Therefore, it seems that when both the potential cation portion (migrating group) and anion portion of a cyclopentadiene are well stabilized then rearrangement occurs via a stepwise process.

The factors governing the migratory aptitude of substituents in [1,5]-sigmatropic shifts is not well understood. It is clear from various studies that the migratory aptitude of some substituents at C-5 of a cyclopentadiene are the following, in decreasing order: \(\text{CHO} > \text{H} > \text{D} > \text{COOMe} > \text{C}_6\text{H}_5 > \text{Me}\). Ground state strain or bond strength of the shifting \(\sigma\)-bond are factors contributing to some migration tendencies. Furthermore, it appears that secondary orbital interactions between an empty \(\pi^*\)-orbital of some migrating
groups and an occupied molecular orbital of the array of atoms in the cyclopentadiene ring is another contributing factor.

Heterocyclic cyclopentadiene-like systems such as 3\textit{H}-pyrazoles are also prone to [1,5]-sigmatropic rearrangement. The next portion of this introduction (1.2) is a discussion of several aspects of 3\textit{H}-pyrazole chemistry.

1.2 3\textit{H}-Pyrazoles

1.2.1 General

A 3\textit{H}-pyrazole (48) is a cyclopentadiene-like ring system containing two nitrogen atoms in a 1,2-relationship. The 3\textit{H}, 4\textit{H}, and 1\textit{H} prefixes denote the position of the tetrahedral carbon atom in the ring. Isomeric with 3\textit{H}-pyrazoles are 4\textit{H}-pyrazoles (49) and 1\textit{H}-pyrazoles (50). A 4\textit{H}-pyrazole has the tetrahedral carbon centre at the fourth atom in the ring while a 1\textit{H}-pyrazole carries a substituent on a nitrogen atom. The 4\textit{H}-pyrazole is more stable than the 3\textit{H}-pyrazole because of the two relatively strong carbon-nitrogen double bonds, while the most stable pyrazole isomer is the 1\textit{H}-pyrazole because of its aromatic sextet of \pi electrons. The 1-nitrogen atom of 50 contributes its electron pair to the formation of the aromatic sextet.
An excellent review of 3H-pyrazole chemistry was published in 1983 by Sammes and Katritzky. Some discussion of the chemistry of 3H-pyrazoles is also included in other reviews and books on heterocyclic chemistry.

3H-Pyrazoles, like their cyclonentadiene analogues, are also prone to thermal rearrangement. The study of these thermal rearrangements has been of interest to many physical organic chemists. 3H-Pyrazoles undergo thermal rearrangement and frequently afford 1H-pyrazole isomers. Therefore, 3H-pyrazoles can provide a synthetic route to 1H-pyrazoles. The synthesis of 1H-pyrazoles has been of interest because the aromatic pyrazole nucleus was found to be associated with various biological activities; numerous pyrazole patents have been assigned. As examples of useful 1H-pyrazoles, 1H-pyrazole 51 was found useful for fruit abscission while 1H-pyrazole 52 provides excellent herbicidal activity in corn. Other uses of 1H-pyrazoles are as fungicides, pesticides, antibacterials, hypnotics, and textile dyes.
Further interest in 3H-pyrazoles arises from their photolysis, which leads to cyclopropanes via nitrogen elimination. Therefore, 3H-pyrazoles can provide a convenient synthetic route to cyclopropanes. For example, Franck-Neumann and coworkers synthesized 3H-pyrazole 53 which provided a route, via cyclopropene 54, to the cis-disubstituted gem-dimethyl cyclopropane ester 55, a direct precursor of a class of insecticides called pyrethroids (Scheme 5).72

![Scheme 5](image)

2.2.2 Synthesis of 3H-pyrazoles from alkynes and diazo compounds

The most popular method for the synthesis of 3H-pyrazoles involves a 1,3-dipolar cycloaddition between a diazo compound and an alkyne. This is a convenient, one-step synthesis for a variety of 3H-pyrazoles.

For over a century, the reaction between alkynes and diazomethane or monosubstituted diazomethanes has been known to yield 1H-pyrazoles.73 According to Scheme 6, a 1,3-dipolar cycloaddition between a monosubstituted diazo compound (R^1 = H) yields an unstable 3H-pyrazole (56) which undergoes a hydrogen migration to give the 1H-pyrazole (57). When a disubstituted diazomethane is used (R^1, R^2 \neq H), 56 can be
isolated, although it could still rearrange under the reaction conditions. When an
unsymmetric disubstituted alkyne is used 2 regioisomers (58 and 59) may be isolated.

\[ \text{Scheme 6} \]

The most common diazoalkanes used in the synthesis of 3H-pyrazoles have been
diphenylidiazomethane and 2-diazopropane. Some other examples include the following:
1-phenylidazoethane,74,75 methyl 4-diazo-4-phenylbutanoate,76 hexafluoro-2-diazopropane,77
diaryldiazomethanes,74 diazocyclopentadienes and -indenes,78-81 \( \alpha \)-diazo ketones
(acyclic82-85 and cyclic83,86-88), and \( \alpha \)-diazoesters.76,82,84,89,90

The most common alkyne used in cycloaddition reactions with diazo compounds
for the synthesis of 3H-pyrazoles is dimethyl acetylenedicarboxylate. Some examples of
other alkynes that have been used successfully include the following: ethyne,91,92
mono-93-95 and dialkylethynes,96 trifluoromethylethynes,77,78 phenylethynyl,74,76,78,79,86,87,97-99 diphenylethynyl,76,100 1-diethylaminopropyne,80,85,90 propynal,74,101 phenylpropynal,74 mono-84,95,96,102-104 and diacyl alkenes,80,84,104,105 propynoic esters,74,78,79,84,91,98,103,106-110 3-alkyl-105,110 and 3-phenylpropynoic esters,98,105,106,109,111-113 propynonitrile,84,105,114 and dicyanoethynyl.78,79,105,114

The mechanism of the reaction between an alkyne and a diazo compound is a thermally allowed, concerted, 1,3-dipolar cycloaddition process. It is generally controlled by the interaction between the highest occupied molecular orbital (HOMO) of the dipole (diazalkane) and the lowest unoccupied molecular orbital (LUMO) of the dipolarophile (alkyne).18 The smaller the energy difference between the HOMO of the dipole and the LUMO of the dipolarophile, the faster the rate of the reaction.115 Electron-withdrawing substituents R1,R2 and R3,R4 decrease the energy of the HOMO and LUMO, respectively, while electron-donating substituents R1,R2 and R3,R4 increase the energy of the HOMO and LUMO, respectively. For example, the relative rates for the cycloaddition of phenylethyne, methyl propynoate, and dimethyl acetylenedicarboxylate to diphenyldiazomethane at 40 °C are, respectively, 1 : 900 : 8200.98 Increasing the electron-withdrawing power of substituents R3 and R4 decreases the alkyne LUMO energy leading to a smaller energy separation between the HOMO and LUMO.

In extreme cases of strong electron-withdrawing R1 and R2, and electron-donating R3 and R4, the cycloaddition occurs via overlap of the diazoalkane LUMO with the alkyne HOMO. An example of this type of cycloaddition is the reaction of dimethyl diazomalonate with 1-diethylaminopropyne.85
Diazocompounds, which are important precursors of 3H-pyrazoles, have been prepared, for example, by the oxidation of the appropriate hydrazones or base-promoted cleavage of tosylhydrazones.\(^{116,117}\) Although a number of diazo compounds have been synthesized by these or other methods, very few dialkyl diazomethanes (\(R^1R^2CN_2\)) have been utilized. 2-Diazopropane, for example, is purified by codistillation with ether and used as a solution in ether.\(^{118}\) Higher molecular weight diazoalkanes presumably are difficult to obtain because of the problem of purifying them safely.

Recently, Warkentin and coworkers reported that 2-alkoxy-2,5,5-trialkyl-\(\Delta^3\)-1,3,4-oxadiazolines can serve as convenient sources of diazoalkanes.\(^{119}\) They reported that the photolysis of 2-alkoxy-2,5,5-trialkyl-\(\Delta^3\)-1,3,4-oxadiazolines (60a-f) at 300 nm in a Rayonet apparatus led to fragmentation to diazoalkanes 61a-f and ester 62 in high yield (Scheme 7). It was proposed that the oxadiazolines 60a-f decompose via diazenyl diradicals 63a-f.

![Chemical structure](image)

**Scheme 7**

- a: \(R^1=R^2=R^3=\text{CH}_3\)
- b: \(R^1=R^3=\text{CH}_3, R^2=\text{C}_2\text{H}_5\)
- c: \(R^1=R^2=\text{C}_2\text{H}_5, R^3=\text{CH}_3\)
- d: \(R^1=\text{CH}(\text{CH}_3)_2, R^2=R^3=\text{CH}_3\)
- e: \(R^1 R^2=(\text{CH}_2)_3, R^3=\text{CH}_3\)
- f: \(R^1 R^2=(\text{CH}_2)_5, R^3=\text{CH}_3\)
These oxadiazolines were particularly useful for the in situ 1,3-dipolar cycloaddition reactions of diazoalkanes with dimethyl acetylenedicarboxylate, which afforded 3H-pyrazoles. Photolysis of 60a-f at 300 nm in benzene containing dimethyl acetylenedicarboxylate for a 5 hour period gave 3H-pyrazoles 64a-f (56-67% yields). Since the diazoalkanes were trapped as they were being generated, bimolecular conversion of diazoalkanes to azine was minimized. Therefore, this method can provide access to a variety of 3H-pyrazoles of general structure 64, bearing different alkyl substituents at C-3.

\[ \begin{align*}
60a-f \\
(E=\text{CO}_{2}\text{CH}_3)
\end{align*} \]

a: \( R^1=R^2=R^3=\text{CH}_3 \)
b: \( R^1=R^3=\text{CH}_3, R^2=\text{C}_2\text{H}_5 \)
c: \( R^1=R^2=\text{C}_2\text{H}_5, R^3=\text{CH}_3 \)
d: \( R^1=\text{CH(CH}_3)\text{)}_2, R^2=R^3=\text{CH}_3 \)
e: \( R^1 R^2=(\text{CH}_2)\text{)}_4, R^3=\text{CH}_3 \)
f: \( R^1 R^2=(\text{CH}_2)\text{)}_5, R^2=\text{CH}_3 \)
1.2.3 Synthesis of 3H-pyrazoles from alkenes and diazo compounds

3H-Pyrazoles can also be synthesized indirectly by a 1,3-dipolar cycloaddition between an alkene and a diazo compound to afford a cycloadduct, which in some cases can be transformed into a 3H-pyrazole by a subsequent reaction. A few examples illustrating this methodology are discussed below.

α-Diazo carbonyl compounds can undergo 1,3-dipolar cycloadditions with enamines. This provides a synthetic route to some 3H-pyrazoles. Cycloaddition between enamine 65 and methyl diazoacetate in boiling chloroform gave a high yield of 66 which was almost quantitatively converted to 67 by chromatography on silica.\textsuperscript{120}

\[
\begin{align*}
\text{55} & \xrightarrow{\text{N}_2\text{CHCO}_2\text{Me}} \text{65} \\
\text{N-N} & \text{CO}_2\text{Me} \quad \text{SiO}_2 \\
\text{N-N} & \text{CO}_2\text{Me}
\end{align*}
\]

Diazoalkanes can also undergo 1,3-dipolar cycloadditions with cyclopropenes. Cycloaddition of thiieren\textsubscript{2} dioxide 68 to 2-diazopropane gives bicyclic adduct 69 which spontaneously extrudes sulfur dioxide to afford 3H-pyrazole 70 in a 72% yield.\textsuperscript{121}

\[
\begin{align*}
\text{68} & \xrightarrow{\text{N}_2\text{C(Me)}_2} \text{69} \\
\text{C}_6\text{H}_5 & \text{N-N} \quad -\text{SO}_2 \\
\text{C}_6\text{H}_5 & \text{C}_6\text{H}_5 \\
\text{C}_6\text{H}_5 & \text{C}_6\text{H}_5 \\
\end{align*}
\]
Adduct 71, from furan and dimethyl acetylendicarboxylate forms a transient intermediate (72) from reaction with 2-diazopropane. This intermediate spontaneously extrudes furan yielding, quantitatively, 3H-pyrazole 73.\textsuperscript{122}

3H-Pyrazoles can also be synthesized by the oxidation of some Α2-pyrazolines. The cycloaddition of 2-diazopropane to disubstituted alkenes affords the Α2-pyrazolines (74a-f), which can be oxidized with manganese dioxide to yield 3H-pyrazoles 75a-f. The ease of oxidation, however, is strongly dependent on substituents R\textsuperscript{1} and R\textsuperscript{2} of 74.\textsuperscript{123}

a: R\textsuperscript{1}=R\textsuperscript{2}=CN
b: R\textsuperscript{1}=NO\textsubscript{2}, R\textsuperscript{2}=C\textsubscript{6}H\textsubscript{5}
c: R\textsuperscript{1}=NO\textsubscript{2}, R\textsuperscript{2}=CN
d: R\textsuperscript{1}=CO\textsubscript{2}CH\textsubscript{3}, R\textsuperscript{2}=CN
e: R\textsuperscript{1}=CN, R\textsuperscript{2}=CO\textsubscript{2}CH\textsubscript{3}
f: R\textsuperscript{1}=COCH\textsubscript{3}, R\textsuperscript{2}=CN
1.2.4 Photochemical loss of nitrogen from 3H-pyrazoles

The photolysis of 3H-pyrazoles at the wavelength of the ring n→π* transition, results in loss of nitrogen and the formation of a cyclopropene. This is a well known preparative method for the synthesis of cyclopropenes.\textsuperscript{100,109-111,124-131} For example, Warkentin and coworkers synthesized cyclopropenes 77a-e from the photolysis of 3H-pyrazoles 76a-e.\textsuperscript{119}

\[
\begin{align*}
\text{N} & \quad \text{N} \\
\text{E} & \quad \text{E} \\
\text{R}^1 & \quad \text{R}^2
\end{align*}
\]
(E=CO\textsubscript{2}Me)

76a-e

\[
\begin{align*}
\text{R}^1 & \quad \text{R}^2 & \quad \text{E} \\
\text{E} & \quad \text{E} & \quad \text{R}^1 \\
\quad & \quad & 300 \text{nm} \\
\quad & \quad & \text{-N}_2
\end{align*}
\]

(58-70%)

77a-e

a: R\textsuperscript{1}=R\textsuperscript{2}=CH\textsubscript{3}  
b: R\textsuperscript{1}=CH\textsubscript{3}, R\textsuperscript{2}=C\textsubscript{2}H\textsubscript{5}  
c: R\textsuperscript{1}=R\textsuperscript{2}=C\textsubscript{2}H\textsubscript{5}  
d: R\textsuperscript{1}=CH(CH\textsubscript{3})\textsubscript{2}, R\textsuperscript{2}=CH\textsubscript{3}  
e: R\textsuperscript{1}=cyclopropyl, R\textsuperscript{2}=CH\textsubscript{3}

A general mechanism for cyclopropene formation is shown in Scheme 8. The first step involves ring opening of 3H-pyrazole 78 to vinyldiazo compound 79. The vinyldiazo compound 79 is formed from absorption of UV light at the wavelength of the pyrazole ring n→π* transition.
Scheme 8

The confirmation that the diazo compound was a true intermediate was verified by a number of observations. First, a red colour was formed during an induction period prior to nitrogen evolution. Second, in one reaction only 10% of the cyclopropene had been formed when all of the 3H-pyrazole had disappeared. Third, the use of filters to give a narrow band of UV light (320-380 nm) resulted in formation of the diazo compound but suppression of the cyclopropene. Finally, in some cases the vinyldiazo compound has been isolated.

The second step in the mechanism is the formation of vinylcarbene 80 from the vinyldiazo compound by the absorption of light at longer wavelength ( >380 nm). The existence of the carbene intermediate was demonstrated by the formation of dimers and by trapping with active alkenes. The intermediate carbene (80) can also react intramolecularly by insertion into the double bond to give a cyclopropene (81, Step III).
1.2.5 Thermal rearrangement of 3H-pyrazoles

The thermal migration of a substituent from the tetrahedral carbon atom (C-3) of a 3H-pyrazole to another ring carbon or nitrogen atom is referred to as a van Alphen-Hütte rearrangement because of the early work of both van Alphen\textsuperscript{106,139} in 1943 and Hütte in 1960.\textsuperscript{74} A general representation of these rearrangements is Scheme 9. The formation of the product pyrazoles has been accommodated in terms of competitive, suprafacial [1,5]-shifts by a substituent at C-3.\textsuperscript{140} A [1,5] anti-clockwise migration of R\textsuperscript{1} in 82 affords the 1H-pyrazole (83) while a [1,5] clockwise migration of R\textsuperscript{1} in 82 affords the 4H-pyrazole (84).

- \[ \text{82} \rightarrow \text{83} \text{ and/or } \text{84} \]

\textbf{Scheme 9}

1.2.6 Studies on the mechanism of 3H-pyrazole rearrangement

Leigh and Arnold carried out a kinetic study on the rearrangement of 3H-pyrazoles 85a-c in diphenyl ether solution at 190 °C (Scheme 10).\textsuperscript{141} They concluded that these 3H-pyrazole rearrangements were concerted in nature. The products of rearrangement, 86 and 87, were formed in a 10 : 1 ratio. Arrhenius parameters were E\textsubscript{a} = 34.2 ± 0.7 kcal
mol\(^{-1}\) and \(\Delta S^\ddagger = -5.6 \pm 1.6\) eu for 85a \(\rightarrow\) 86a and \(E_a = 35.6 \pm 1.1\) kcal mol\(^{-1}\) and 
\(\Delta S^\ddagger = -7.0 \pm 2.3\) eu for 85a \(\rightarrow\) 87a. The thermodynamically more stable product was the 
aromatic 1H-pyrazole 87. The 4H-pyrazole 86 was stable at 190 °C so the product ratio 
reflects the relative rates of the two competitive [1,5]-methyl migrations. Therefore, 
product formation is controlled by kinetic factors. The fact that the 4H-pyrazole isomer 
(86) is favoured was rationalized in the following manner. Suprafacial migration of 
methyl from C-3 to N-2 makes N-2 tetrahedral, therefore, conformational and electronic 
reorganization must occur before aromatic stabilization can develop. Thus, it was 
suggested that, in the absence of aromatic stabilization, the bonding arrangement in the 
4H-pyrazole, with two relatively strong carbon-nitrogen double bonds, is more stable than 
that in the 1H-pyrazole. The observation of only one of the two possible isomeric N- 
substituted pyrazole products is consistent with a concerted [1,3]-sigmatropic 
rearrangement. A Hammet plot [\(\log(k_w/k_u)\) vs. \(\sigma_p\)] gave a straight line with a slope of 
+ 0.33 for \(\rho\). Leigh and Arnold suggested that this small positive \(\rho\) value is consistent 
with a concerted reaction. However, it may also suggest a small amount of negative 
charge development in the pyrazole ring at the transition state for rearrangement.
Schies and Stalder studied the thermal rearrangement of 3H-pyrazole 88 at 65 °C (Scheme 11). The carbomethoxy substituent migrates to both C-4 and N-2. Migration to carbon generates intermediate 4H-pyrazole 89 which undergoes further rearrangement to 1H-pyrazole 90. Migration of the carbomethoxy substituent to nitrogen yields 1H-pyrazole 91. Activation parameters for the conversion of 88 to 90 and 91 were determined as the following: $E_a = 24.0 \pm 0.4$ kcal/mol and $\log A = 11.8 \pm 0.4$. A kinetic study revealed the influence of solvent polarity on the rate and direction of this rearrangement (Table 5). The overall first order rate constants for the formation of 90 and 91 from 88 showed a small but significant solvent effect. Zwitterionic structures such as 92 or 93 were excluded as distinct reaction intermediates.
Scheme 11

Table 5. Isomerization of 88 to 90 and 91 at 65 °C.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>$E_T^*$</th>
<th>$k_{obs}$ (x10^4 s⁻¹)</th>
<th>Products 90:91</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCl₄</td>
<td>32.5</td>
<td>1.09</td>
<td>20:80</td>
</tr>
<tr>
<td>dioxane</td>
<td>36.0</td>
<td>1.36</td>
<td>22:78</td>
</tr>
<tr>
<td>C₆H₅Cl</td>
<td>37.5</td>
<td>1.70</td>
<td>28:72</td>
</tr>
<tr>
<td>C₆H₅CN</td>
<td>42.0</td>
<td>2.57</td>
<td>39:61</td>
</tr>
<tr>
<td>t-butyl alcohol</td>
<td>43.9</td>
<td>3.19</td>
<td>44:56</td>
</tr>
<tr>
<td>DMSO</td>
<td>45.0</td>
<td>3.09</td>
<td>46:54</td>
</tr>
</tbody>
</table>

*Solvent Polarity Parameter.
1.2.7 Migratory aptitude of substituents in $3H$-pyrazole rearrangements

Schiess and Stalder studied the migration tendencies of some substituents toward sigmatropic rearrangement in $3H$-pyrazoles 94a-e (Scheme 12). Migration of methyl and phenyl in 94a and 94c, respectively, occur exclusively to the adjacent carbon atom giving $1H$-pyrazoles 96a and 96c, respectively. $4H$-Pyrazoles 95a and 95c are intermediates in these rearrangements. $3H$-Pyrazole 94b rearranges to give 97 as well as 96b since the migration of methyl is competitive with the migration of ethyl. The benzyl group in 94d and the carbomethoxy group in 94e migrate to both C-4 and N-2. Table 6 summarizes the results of the kinetic study.

The migration tendency of the R substituents is the following, in increasing order: methyl < ethyl < benzyl < phenyl < carbomethoxy. The second order interaction of the empty $\pi^*$-orbital of a migrating group with an occupied molecular orbital of the array of atoms in the heterocyclic ring contributes to the higher migratory aptitude of some substituents. Presumably, the importance of this interaction decreases the higher the energy of the $\pi^*$-level in the migrating group. Alkyl groups which lack a $\pi^*$-orbital have low migratory aptitudes. Furthermore, the differences in the migration tendencies between methyl, ethyl, and benzyl show that there must be additional factors such as
ground state strain or bond strength of the shifting σ-bond which contribute to the migration tendency of a substituent in [1,5]-sigmatropic migrations.\textsuperscript{143}
Table 6. Rearrangement of 94a-e at 120 °C.

<table>
<thead>
<tr>
<th>94</th>
<th>Products (%)</th>
<th>Ea (kcal/mol)</th>
<th>( k_{obs} ) (s⁻¹)</th>
<th>( k_{rel} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>96</td>
<td>97</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>94a, c</td>
<td>R=CH₃</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>94b, c</td>
<td>R=C₆H₅</td>
<td>94</td>
<td>6</td>
<td>-</td>
</tr>
<tr>
<td>94c, d</td>
<td>R=C₆H₅</td>
<td>100</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>94d, d</td>
<td>R=CH₂-C₆H₅</td>
<td>67</td>
<td>-</td>
<td>33</td>
</tr>
<tr>
<td>94e, c</td>
<td>R=CO₂CH₃</td>
<td>31</td>
<td>-</td>
<td>69</td>
</tr>
</tbody>
</table>

<sup>a</sup> Overall first order rate constants for the disappearance of 94.
<sup>b</sup> Relative rates for the migration of R to carbon (94→96).
<sup>c</sup> In tert-butyl alcohol.
<sup>d</sup> In DMSO.
<sup>e</sup> Corrected for by a statistical factor of 2.

Franck-Neumann and coworkers discovered that 3H-pyrazoles 99a-c undergo spontaneous rearrangement at ambient temperature, under the conditions of their formation, to yield 1H-pyrazoles 100a-c (Scheme 13). ⁸²,⁸⁴ Therefore, the following substituents have high migratory aptitudes: acetyl, carbomethoxy, and cyano. The rearrangements were mechanistically described as concerted [1,5]-sigmatropic rearrangements.

(a: R¹=CH₃, R²=COCH₃, b: R¹=CH₃, R²=CO₂CH₃, c: R¹=CH(CH₃)₂, R²=CN)

Scheme 13
Warkentin and coworkers recently investigated the thermal rearrangement of 3H-pyrazole 101 in benzene-$d_6$ at 160 °C (Scheme 14). 3H-Pyrazole 101 underwent rearrangement by sequential [1,5]-sigmatropic shifts. 1H-Pyrazoles 102 and 104 were formed in a 1 : 2 ratio, respectively. 1H-Pyrazole 102 was formed from a [1,5]-anti-clockwise migration of ethyl to nitrogen (ethyl has a higher migratory aptitude than methyl). An initial [1,5]-shift of ethyl to carbon afforded the intermediate 4H-pyrazole 103 which was unstable at 160 °C. A [1,5]-anti-clockwise migration of carbomethoxy to the carbon bearing the methyl substituent, followed by another [1,5]-anticlockwise migration of carbomethoxy to nitrogen gave 1H-pyrazole 104. This study demonstrates how the migratory aptitude of each substituent on the tetrahedral carbon of a pyrazole dictates the type of products formed from thermal rearrangement.

Scheme 14
1.3 Nucleophilic Aliphatic Substitution Reactions

involving Ion-Pair Intermediates

1.3.1 Nucleophilic aliphatic substitution reactions (general)

A nucleophilic substitution reaction converts a nucleophile and a substrate into a product and a leaving group (Equation 1). These reactions are classically treated in terms of $S_{N}2$ (Equation 2) and $S_{N}1$ (Equation 3) mechanisms which were developed by Hughes and Ingold.$^{147,148}$

\[
\text{Nucleophile} + \text{R-X} \rightarrow \text{Nucleophile-R} + \text{X} \quad (1)
\]

\[
\begin{align*}
\text{Y} + \text{R-X} & \rightarrow [\text{Y} \cdots \text{R} \cdots \text{X}]^+ \rightarrow \text{R-Y} + \text{X} \\
\text{R-X} & \xrightarrow{\text{slow}} \text{R}^+ + \text{X}, \text{ followed by } \text{R}^+ + \text{Y} \xrightarrow{\text{fast}} \text{R-Y} \quad (2)
\end{align*}
\]

An $S_{N}2$ reaction is bimolecular and the rate is first order both in the nucleophile and in the substrate concentration, while an $S_{N}1$ reaction is unimolecular and the rate depends on the concentration of the substrate and is independent of the concentration of the nucleophile. The first, effectively reversible, step is followed by fast reaction of the resulting carbocation with a nucleophile. An $S_{N}2$ reaction is a direct, one-step displacement with no intermediate while an $S_{N}1$ reaction is stepwise. There are several reviews on nucleophilic aliphatic substitution reactions.$^{149-158}$
In the 1950's, Weinstein showed convincingly that the $S_N1$ mechanism was more complex than had been first postulated by Hughes and Ingold.\textsuperscript{159,160} Weinstein obtained evidence that ionization takes place in several stages and he distinguished between "intimate ion pairs" (II) and "solvent-separated ion pairs" (III) as two distinct types of discrete intermediates before the stage of a free carbocation is reached (Scheme 15).

\[
\begin{align*}
R-X & \underset{k_1}{\overset{k_2}{\rightleftharpoons}} R^+X^- \quad \overset{k_2}{\rightleftharpoons} \quad R^+ \quad \underset{k_3}{\overset{k_3}{\rightleftharpoons}} \quad R^+ + X^- \\
I & \quad \quad II & \quad \quad III & \quad \quad IV
\end{align*}
\]

Scheme 15

The Weinstein Ion-Pair Model provides the simplest treatment of nucleophilic aliphatic substitution reactions consistent with the available experimental evidence. An $S_N1$ reaction can be seen as one in which the rate-limiting step is unimolecular formation of II, III, or IV (ie. $k_1$, $k_2$, or $k_3$) followed by fast reaction with a nucleophile. Several factors influence whether I, II, III, or IV will be involved in a particular reaction. An increase in carbocation or leaving group stability promotes reaction through a more dissociated intermediate. An increase in solvent ionizing power also promotes dissociation, but an increase in nucleophilicity has the opposite effect, promoting reaction at an earlier, less dissociated, stage. Classical $S_N1$ reactions are even more complex than the Weinstein ion pair model suggests. For example, there is a continuum between $S_N1$ and $S_N2$ reaction mechanisms. Furthermore, the solvent may provide nucleophilic assistance to ionization.
A new system of nomenclature for describing nucleophilic substitution reactions has been recently recommended by IUPAC\textsuperscript{161,162} and is useful since the Ingold nomenclature has become "overburdened with non-systematic modification for 30 years."\textsuperscript{153}

The formation of a new bond during the transformation of one molecular structure to another is symbolized by "A" (association or attachment), while the bond breaking components are symbolized by "D" (dissociation or detachment). When the changes take place in separate reaction steps, they are separated by a "+". A symbol "*" is used instead of a "+" to designate an intermediate which is of such a short lifetime that it reacts in a step faster than diffusion but slower than a molecular vibration. A subscript "N" is used to designate bond formation to a nucleophile or bond cleavage with loss of a nucleofuge (leaving group). A concerted nucleophilic substitution can then be described as "D\textsubscript{N}A\textsubscript{N}". A stepwise nucleophilic substitution reaction where an intermediate can diffuse through the solvent can be described as "D\textsubscript{N}+A\textsubscript{N}" ("classical S\textsubscript{N}1"). "D\textsubscript{N}A\textsubscript{N}" describes a stepwise nucleophilic substitution reaction involving an ion-pair intermediate which is not diffusionally equilibrated with the bulk of the solvent (contact or solvent-separated ion pair).

The following discussion focuses on some rates of S\textsubscript{N}1 solvolyses (D\textsubscript{N}+A\textsubscript{N} and/or D\textsubscript{N}A\textsubscript{N}). Two factors which affect the rate of ionization include substrate stability and leaving group ability.
1.3.2 Substrate stability

Reaction by an $S_{N1}$ ($D_N+A_N$ and/or $D_N^{*}A_N$) mechanism commonly occurs for tertiary alkyl halides and resonance stabilized secondary alkyl halides, in polar solvents. Changes in substrate structure effect the rate of ionization in such a reaction. The rates of ionization of alkyl halides depend on the stabilities of the corresponding cations. The effect of an alkyl group, compared to hydrogen, when bonded to an $sp^2$ cationic centre is inductively electron-donating and stabilization by hyperconjugation is very important. The effects of $\alpha$-methyl substitution on the rates of solvolysis of some simple alkyl compounds are shown in Table 7. \(^{164,165}\) \textit{tert}-Butyl bromide solvolyzes approximately 320 times faster than methyl bromide in marked contrast to its relative unreactivity in $S_{N2}$ ($A_ND_N$) reactions. Schleyer and coworkers estimated that for $S_{N1}$ reactions ($D_N+A_N$ or $D_N^{*}A_N$) with no assistance to ionization by nucleophiles, the substitution of $H$ by $CH_3$ on the reacting carbon in 2-adamantyl solvolysis accelerates the rate by a factor of $10^5$.\(^{166}\)

<table>
<thead>
<tr>
<th>$R^1$</th>
<th>$R^2$</th>
<th>$R^3$</th>
<th>Relative Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>H</td>
<td>H</td>
<td>1.00</td>
</tr>
<tr>
<td>$CH_3$</td>
<td>H</td>
<td>H</td>
<td>0.38</td>
</tr>
<tr>
<td>$CH_3$</td>
<td>$CH_3$</td>
<td>H</td>
<td>0.28</td>
</tr>
<tr>
<td>$CH_3$</td>
<td>$CH_3$</td>
<td>$CH_3$</td>
<td>320</td>
</tr>
</tbody>
</table>

Table 7. Solvolysis rates of alkyl bromides, $R^1R^2R^3CBr$, in EtOH at 55 °C.

An aryl group attached to the $\alpha$-carbon atom assists a reaction occurring by the $S_{N1}$ ($D_N+A_N$ and/or $D_N^{*}A_N$) mechanism by allowing the developing positive charge to be distributed over the conjugated system 105. In Table 8 the effects of $\alpha$-substitution on
the reacting carbon are compared.\textsuperscript{167-170} tert-Butyl chloride solvolyzes approximately 83 times faster than benzyl chloride, while tert-butyl chloride and α-phenylethyl chloride are alike in reactivities. A rough approximation is that a phenyl group is as effective in stabilizing a carbocation as are two methyl groups.

\begin{table}

\begin{tabular}{|c|c|c|c|}
\hline
$R^1$ & $R^2$ & $R^3$ & Relative Rates \\
\hline
CH$_3$ & CH$_3$ & CH$_3$ & 1.00 \\
C$_6$H$_5$ & H & H & 0.01 \\
C$_6$H$_5$ & CH$_3$ & H & 0.90 \\
C$_6$H$_5$ & C$_6$H$_5$ & H & 1300 \\
\hline
\end{tabular}

\end{table}

The effect of a methoxy group in the para position of a benzyl halide is striking. In 67\% aqueous acetone solvent, para-methoxybenzyl chloride solvolyzes approximately $10^3$ times faster than benzyl chloride.\textsuperscript{171} The para-methoxybenzyl cation is resonance stabilized because the oxygen atom can accept a considerable fraction of the positive charge via resonance, as illustrated with 106. Furthermore, a Hammet plot [log ($k_w/k_h$) vs. $\sigma^+$] for the solvoysis of cumyl chlorides 107 in 90\% aqueous acetone at 25 °C gave a $\rho$ value of -4.54.\textsuperscript{172}
When atoms with unshared electron pairs are bonded to the reaction centre in an
$S_N1$ ($D_NA_N^*$, and/or $D_NA_N$) reaction, two effects must be considered: the inductive effect
which is usually electron-withdrawing, and the electron-donating conjugative effect (108).

For more basic atoms, O, N, S, conjugation is dominant as the following relative solvolysis
rate shows. For example, in ethanol, methyl chloromethyl ether solvolyzes approximately
$10^{13}$ times faster than $n$-propyl chloride.$^{173}$ The intermediate in the solvolysis of methyl
chloromethyl ether should be regarded more as oxonium ion 109 rather than a carbonium
ion.
The first order rate constant for the solvolysis of tert-butyl bromide \( (k^{25\,^\circ\text{C}} = 3.58 \times 10^{-4}\, \text{s}^{-1}) \) is approximately \( 10^3 \) times greater than the first order rate constant for the solvolysis of 1-adamantyl bromide \( (k^{25\,^\circ\text{C}} = 5.10 \times 10^{-7}\, \text{s}^{-1}) \) in 80% aqueous ethanol solution but only 3 times faster in the nonnucleophilic solvent mixture of 97% hexafluoroisopropyl alcohol/water.\(^{174-176}\) It was suggested by Bentley and coworkers that tert-butyl chloride most likely undergoes assisted ionization in nucleophilic solvents (i.e. the nucleophile attacks a carbocation-leaving group ion-pair). Bentley and coworkers found that the equilibrium for anion exchange between 1-adamantyl and tert-butyl cations favours the 1-adamantyl cation in both the gas phase and in solution.\(^{174}\) They suggested that the extra \( \beta \)-and \( \gamma \)-carbons provide sufficient stabilization (i.e. C-C hyperconjugation) to overcome angle strain effects as an sp\(^3\)-hybridized positively charged carbon in the comparatively rigid 1-adamantyl framework is formed. Since \( S_N1 \) solvolysis rates parallel carbocation stabilities, the rates of solvolysis of tert-butyl halides should be lower than those for 1-adamantyl halides. It was predicted that in less nucleophilic solvents, 1-adamantyl halides should solvolyze faster than tert-butyl halides.\(^{174}\) It has been suggested, however, that the solvent effect in tert-butyl halide solvolysis is not due to nucleophilic assistance to substitution but to electrophilic assistance to ionization.\(^{172}\)

1.3.3 Leaving group ability

The leaving group can determine reactivity in nucleophilic substitution. Leaving groups which depart with the bonding electron pair are termed "nucleofuges".\(^{178}\) Nucleofugality, the tendency of an atom or group to depart with the bonding electron pair
has been little studied as available data on most reactions cover only restricted ranges of leaving groups and in many systems the leaving groups are conjugate bases of strong acids. The rate of the reaction will reflect nucleofugality only if the leaving group is involved in the rate determining step as in $S_{N}1$ reactions ($D_{N}A_{N}$ and/or $D_{N}A_{N}$). It is a misconception that nucleofugality depends simply upon the $pK_{a}$ ($H_{2}O$) of the conjugate acid of the leaving group.\textsuperscript{178} The analogy of basicity toward proton and basicity toward carbon fails for leaving groups of different types (ie. sulfonates vs. halides). For a reaction in solution, cleavage of a bond to a leaving group must involve the C-X bond strength [$D(C-X)$], the ability of X to accept the electron pair of the C-X bond as reflected in the electron affinity of X, and the solvation energy of the leaving group.\textsuperscript{179} Transfer of charge to the leaving group is also assisted by resonance delocalization in the leaving group.

Some relative reaction rates for some common leaving groups are given in Table 9.\textsuperscript{159,180-182} As the electron-withdrawing ability of X increases the rate increases and the sulfonates are much better leaving groups than the halogens.
Table 9. Relative reaction rates for some common leaving groups in $S_\text{n}1$ reactions.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Leaving Group</th>
<th>Relative Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OSO$_2$CF$_3$</td>
<td>$2.5 \times 10^{14}$</td>
</tr>
<tr>
<td>2</td>
<td>OSO$_2$C$_6$H$_4$-p-Br</td>
<td>$7.5 \times 10^9$</td>
</tr>
<tr>
<td>3</td>
<td>OSO$_2$C$_6$H$_4$-p-Me</td>
<td>$2.5 \times 10^9$</td>
</tr>
<tr>
<td>4</td>
<td>Br$^b$</td>
<td>$5.0 \times 10^5$</td>
</tr>
<tr>
<td>5</td>
<td>Cl$^{b,e}$</td>
<td>$1.3 \times 10^4$</td>
</tr>
<tr>
<td>6</td>
<td>OCOC$_6$H$_4$-p-NO$_2$</td>
<td>1.0</td>
</tr>
</tbody>
</table>

$^a$Relative rates are approximate because they are not independent of substrate structure.

$^b$Comparisons are for bridgehead solvolysis.

$^c$Entry 2 is compared with entry 3 for 3-anisyl-2-butyl.

$^d$Entry 6 is compared with entry 5 for benzhydryl.

$^e$Data obtained by extrapolation.
CHAPTER 2

Studies of the Thermal Rearrangements of Dimethyl
3-Alkyl-3-methyl-3H-pyrazole-4,5-dicarboxylates

2.0 Objective

3H-Pyrazoles generally undergo thermal rearrangement by competitive [1,5]-
sigmatropic shifts of a substituent from the tetrahedral carbon centre. An example of a 3H-pyrazole which undergoes "typical" [1,5]-
sigmatropic rearrangement is given in Scheme 16. 3-Ethyl-3-methyl-3H-pyrazole-4,5-dicarboxylic acid dimethyl
ester (101) rearranges at 160 °C to give 102 (33%) and 104 (67%). A [1,5]-ethyl
migration to nitrogen forms 102 while a [1,5]-ethyl migration to carbon forms
intermediate 103, which undergoes two consecutive anti-clockwise [1,5]-carbomethoxy
migrations to give 104. It became of interest to investigate the thermal rearrangement of a series of similar
3H-pyrazoles, but ones which may undergo thermal rearrangement by an alternative
mechanism. The objective was to study the thermal rearrangement of dimethyl 3-alkyl-3-
methyl-3H-pyrazole-4,5-dicarboxylates (111a-e) bearing alkyl substituents at C-3 which
are relatively stable in cationic form. The R substituents (benzhydryl, methoxymethyl,
tert-butyl, 1-adamantyl, and para-methoxybenzyl) were chosen because they form cations
in nucleophilic aliphatic substitution reactions of R-X (X = halide).\textsuperscript{150,153} One could determine whether the rearrangement of 3H-pyrazoles 111a-e takes place by a concerted or a stepwise, ion-pair mechanism. Non-concerted [1,5]-sigmatropic rearrangements of 3H-pyrazoles are unknown. A preliminary report of the research in this chapter was communicated in 1990,\textsuperscript{183} and subsequently a full paper has been published in the \textit{Journal of the American Chemical Society} in 1992.\textsuperscript{184}

![Scheme 16](image_url)

(a: R=CHPh$_2$; b: R=CH$_2$OMe; c: R=C(M$_5$)$_3$; d: R=1-adamantyl; e: R=p-CH$_2$C$_6$H$_4$OMe)
The methodology utilized for the synthesis of 3H-pyrazoles 111a-e was developed by Warkentin and coworkers in 1989.\textsuperscript{119} Photochemical reaction of Δ\textsuperscript{1}-1,3,4-oxadiazolines generates diazoalkanes which can readily react with dimethyl acetylenedicarboxylate via 1,3-dipolar cycloadditions to afford the target 3H-pyrazoles. The synthesis of the appropriate oxadiazolines was required.

2.1 Synthesis of 5-alkyl-2-methoxy-2,5-dimethyl-Δ\textsuperscript{1}-1,3,4-oxadiazolines

The first step in the synthesis of oxadiazolines 114a-e involved the condensation of ketones 112a-e with acetic hydrazide to afford acetyl hydrazones 113a-e (Scheme 17). The acetyl hydrazones were characterized by \textsuperscript{1}H and \textsuperscript{13}C NMR spectroscopy as well as high resolution mass spectroscopy. Although the synthesis of acetyl hydrazone 113c was previously reported,\textsuperscript{119} the preparative procedure was modified in this work. The second step in the synthesis of the oxadiazolines involved the oxidative cyclization of 113a-e with lead tetraacetate in methanol solvent to afford oxadiazolines 114a-e. The synthesis of other oxadiazolines by this preparative method has been reported,\textsuperscript{119,146,185-188} and the synthesis of oxadiazoline 114c was previously reported.\textsuperscript{119} The oxadiazolines 114a, 114b, 114d, and 114e are new compounds, which were characterized by both \textsuperscript{1}H and \textsuperscript{13}C NMR spectroscopy as well as high resolution mass spectrometry. A mixture of cis and trans isomers was obtained for oxadiazolines 114 and those percentages are reported in Chapter 5 (Experimental).
Scheme 17

The proposed mechanism of oxidation of 113 with lead tetraacetate (Scheme 18) is not firmly established, but it provides a qualitative understanding of the cyclization process. An intermediate organolead species (115) is formed having a nitrogen-lead bond. This intermediate then cyclizes by an internal nucleophilic substitution. The lone pair of electrons on the carbonyl oxygen attack the carbon-nitrogen double bond to form intermediate carbocation 116, which subsequently undergoes nucleophilic attack by methanol solvent to give oxadiazoline 114.

(a: R=CHPh₂; b: R=CH₂OMe; c: R=C(Me)₃; d: R=1-adamantyl; e: R=p-CH₂C₆H₄OMe)
Scheme 18
2.2 Synthesis of 3H-pyrazoles

Solutions of 5-alkyl-2-methoxy-2,5-dimethyl-Δ^2-1,3,4-oxadiazolines 114a-e in benzene containing dimethyl acetylenedicarboxylate were each photolyzed at 300 nm for 6 hours in a Rayonet apparatus. The oxadiazolines 114a-e underwent C-N bond cleavage and subsequent fragmentation to afford diazoalkanes 117a-e and methyl acetate. The intermediate diazoalkanes (117a-e) rapidly underwent 1,3-dipolar cycloadditions to dimethyl acetylenedicarboxylate to give solutions of unstable 3H-pyrazoles 111a-e (Scheme 19). It was surprising that these 3H-pyrazoles rearranged in the media in which they were generated considering that 3H-pyrazole 101 requires a temperature of 160 °C for thermal rearrangement.\textsuperscript{146}

![Chemical structure](image.png)

(a: R=CHPh₂; b: R=CH₂OMe; c: R=C(Me)₃; d: R=1-adamantyl; e: R=p-CH₂C₆H₄OMe)

Scheme 19
By working quickly at low temperatures, it was possible to observe 3H-pyrazoles \textbf{111c} and \textbf{111d} by both $^1$H and $^{13}$C NMR spectroscopy while 3H-pyrazole \textbf{111e} could only be observed by $^1$H NMR spectroscopy in a solution with its rearrangement products. The diazoalkanes (\textbf{117c-e}) were generated at -73 °C in toluene and dimethyl acetylenedicarboxylate was added with the Rayonet bulbs switched off. The mixtures were warmed quickly to room temperature to allow the $^1$H addition reactions to proceed, and the toluene and volatiles were evaporated with a stream of dry N$_2$. Each residue was dissolved in benzene-$d_6$ and its NMR spectrum was acquired immediately. In Table 10, the $^1$H NMR data and selected $^{13}$C NMR chemical shifts have been tabulated for these 3H-pyrazoles. Some of the $^{13}$C NMR chemical shifts were assigned by comparison to chemical shift assignments made by others for other 3H-pyrazoles.$^{100}$

3H-Pyrazoles \textbf{111a} and \textbf{111b} rearranged too rapidly to be observed by $^1$H NMR spectroscopy. Even when they were generated by the photolysis of \textbf{114a} and \textbf{114b}, respectively, in solutions of toluene-$d_6$ at -73 °C followed by the addition of dimethyl acetylenedicarboxylate with the Rayonet bulbs switched off, quick warming to room temperature for $^1$H NMR spectroscopy showed only products resulting from the rearrangements of \textbf{111a} and \textbf{111b}. 
**Table 10.**

<table>
<thead>
<tr>
<th>3H-Pyrazole, 111</th>
<th>1H NMR (200 MHz)</th>
<th>13C NMR (50 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>111c, R=C(Me)₃</strong></td>
<td>3.40 (s, 3 H, CO₂Me), 3.38 (s, 3 H, CO₂Me), 1.32 (s, 3 H, Me), 0.87 (s, 9 H, C(Me)₃)</td>
<td>107.63 (C-3), 156.37 (C-4), 145.19 (C-5), 16.32 (C-6), 165.52 (C-7), 160.67 (C-8), 52.40 (C-9), 52.06 (C-10).</td>
</tr>
<tr>
<td><strong>111d, R=1-adamantyl</strong></td>
<td>3.45 (s, 3 H, CO₂Me), 3.43 (s, 3 H CO₂Me), 1.87-1.45 (m, 15 H), 1.37 (s, 3 H, Me).</td>
<td>108.20 (C-3), 156.30 (C-4), 145.25 (C-5), 15.04 (C-6), 165.68 (C-7), 160.75 (C-8), 52.36 (C-9), 52.04 (C-10).</td>
</tr>
<tr>
<td><strong>111e</strong>, R=p-CH₂C₆H₄OMe</td>
<td>6.99 (d, 2 H, J = 8.5 Hz), 6.57 (d, 2 H, J = 8.5 Hz), 3.44 (d, 1 H, J = -13.6 Hz), 3.35 (s, 3 H, CO₂Me), 3.26 (s, 3 H, CO₂Me), 3.15 (s, 3 H, OMe), 3.04 (d, 1 H, J = -13.6 Hz), 1.30 (s, 3 H, Me).</td>
<td></td>
</tr>
</tbody>
</table>

* C-7 and C-8 may be reversed. C-9 and C-10 may be reversed.

* The 1H NMR spectrum was obtained from solutions containing 118e (25%), 120e (10%), and 111e (65%). The 13C NMR spectrum of 111e could not be determined from this solution.
2.3 Rearrangement of 3H-pyrazoles 111a-e in benzene-d₆/toluene solvent

Table 11 reveals the products from rearrangement of 3H-pyrazoles 111a-e in benzene-d₆ solvent. Rearrangement of 3H-pyrazole 111a gave two 1H-pyrazoles, 118a (91%) and 119a (9%). 3H-Pyrazole 111b rearranged to give 118b (77%) and 120b (23%), a 4H-pyrazole. The 4H-pyrazole could not be isolated as it was unstable under the conditions of centrifugal chromatography (silica gel) but its ¹H NMR spectrum could be obtained from the ¹H NMR spectrum of the mixture following photolysis. Centrifugal chromatography (silica gel) of the photolysis residue gave 118b (66%) and 121 (19%). The identification of 121, a known 1H-pyrazole, was confirmed by comparing both its ¹H NMR spectrum and its melting point with those reported in the literature.⁸³

Unlike 3H-pyrazoles 111a and 111b, 3H-pyrazoles 111c-e could be observed by ¹H NMR spectroscopy. Therefore, the observed rate constants for rearrangement of these 3H-pyrazoles could be determined by integration of their respective ¹H NMR spectra over time.

Observation of both the ¹H and ¹³C NMR spectra of the photolysis mixture revealed that 111c was formed in a quantitative yield. The rearrangement of 3H-pyrazole 111c in benzene-d₆ was not cleanly first-order, but a good fit to first order kinetics resulted from the addition of 2.5 equivalents of triethylene diamine. Successive integration of the ¹H NMR spectrum over time gave an observed rate constant of (6.2 ± 0.2) x 10⁻⁵ s⁻¹ at 35 °C. 3H-Pyrazole 111c rearranged in benzene-d₆ to give 118c (39%), 121 (61%), and isobutene (60%). The ratio of products formed in the presence of triethylene diamine were very similar. The presence of isobutene was confirmed by a ¹H
Table 11. Products and product yields\(^a\) from the thermal rearrangements of 111a-e at ambient temperature in benzene-\(d_6\).

\[
\begin{align*}
\text{R} & \quad \text{111} & \quad \text{118} & \quad \text{119} & \quad \text{120} & \quad \text{121} & \quad \text{+ other} \\
\text{R} & \quad \text{111a,} & 91 & 9 & \text{nil} & \text{nil} \\
\text{R} & \quad \text{111b,} & 77 & \text{nil} & 23 & \text{nil} \\
\text{R} & \quad \text{111c,} & 39 & \text{nil} & \text{nil} & 61 \quad \text{(isobutene)} \\
\text{R} & \quad \text{111d,} & 63^d & \text{nil} & \text{nil} & \text{nil} \\
\text{R} & \quad \text{111e,} & 64 & \text{nil} & 36 & \text{nil} \\
\end{align*}
\]

\(^a\) At the level of detection afforded by \(^1\)H NMR spectroscopy, the products listed were the only products from rearrangement and yield numbers (\%) reflect complete materials balance prior to opening of a tube, unless otherwise indicated.

\(^b\) \(k = (6.2 \pm 0.2) \times 10^{-5} \text{ s}^{-1}\) at 35 °C.

\(^c\) \(k = (5.6 \pm 0.2) \times 10^{-3} \text{ s}^{-1}\) at 35 °C.

\(^d\) Yield of isolated product. The rearrangement appeared to go in quantitative yield.

\(^e\) \(k = (9.8 \pm 0.4) \times 10^{-5} \text{ s}^{-1}\) at 20 °C.
NMR spectroscopy decoupling experiment on the reaction mixture after the rearrangement of \textbf{111c} (sealed nmr tube). Irradiation of the multiplet at 4.74 ppm (CH$_2$) caused the collapse of the triplet at 1.60 ppm (2 CH$_3$).

\textit{3H}-Pyrazole \textbf{111d} was prepared as a solution in benzene-$d_6$ and observation of the $^1$H and $^{13}$C NMR spectra of the photolysis mixture revealed that \textbf{111d} was formed in a quantitative yield. The observed rate constant for the increase in concentration of rearrangement product \textbf{118d} at 35 °C was $(5.6 \pm 0.2) \times 10^{-5}$ s$^{-1}$. \textit{3H}-Pyrazole \textbf{111d} rearranged to afford only \textbf{118d}.

The $^1$H NMR spectrum of \textbf{111e} was obtained from a solution containing \textbf{118e} (10%), \textbf{120e} (10%), and \textbf{111e} (65%) in benzene-$d_6$. It was not possible to assign the $^{13}$C NMR signals of \textbf{111e} from the spectrum in that solution. The observed rate constant for the disappearance of \textbf{111e} at 20 °C was $(9.80 \pm 0.4) \times 10^{-5}$ s$^{-1}$. \textit{3H}-Pyrazole \textbf{111e} rearranged in benzene-$d_6$ to give \textbf{118e} (64%) and \textbf{120e} (36%). \textit{4H}-Pyrazole \textbf{120e} could be isolated by centrifugal chromatography (silica gel) and it was relatively stable.

\subsection*{2.4 Mechanism of rearrangement of 3H-pyrazoles 111a-e in benzene}

From observed rate constants for the rearrangement of 3H-pyrazoles in benzene-$d_6$, the order of rate constants was established as \textbf{111a} and \textbf{111b} > \textbf{111e} > \textbf{111c} = \textbf{111d}. Rate constants for the fast rearrangements of 3H-pyrazoles \textbf{111a} and \textbf{111b} were not determined. The relative rates of rearrangement of 3H-pyrazoles \textbf{111e}, \textbf{111c}, and \textbf{111d} were approximately 4.9, 1.1, and 1.0, respectively. A 2.8-fold increase in the rate of rearrangement of \textbf{111e} compared to \textbf{111c} was assumed for the 15 °C temperature.
difference between which these observed rate constants were determined. The five $3H$-pyrazoles rearrange with large rate enhancements (approximately $10^4$ for the slowest) compared to $3H$-pyrazole 101 ($R = CH_2CH_3$) which is known to rearrange at 160 °C, presumably by consecutive [1,5]-sigmatropic migrations.\textsuperscript{146} The presence of isobutene as a product in the rearrangement of $3H$-pyrazole 111c suggests the presence of a tert-butyl cation intermediate, which subsequently undergoes proton loss. The large rate enhancements for rearrangement of 111a-e, in addition to the fact that 111c gave isobutene and 121 as fragmentation products, suggest that these $3H$-pyrazoles undergo thermal rearrangement by an alternative mechanism.

The major rearrangement product of the $3H$-pyrazoles (except 111c) in benzene-$d_6$ was $1H$-pyrazole 118. It is interesting that the rearrangement of $3H$-pyrazoles 111b and 111e gave the $4H$-pyrazole as the minor product. This observation is contrary to the reported rearrangements of other $3H$-pyrazoles which rearrange by concerted alkyl migrations from C-3 of the $3H$-pyrazoles. These include the rearrangement of 4,5-diaryl-3,3-dimethyl-$3H$-pyrazoles,\textsuperscript{141} 3-alkyl-3,5-dimethyl-$3H$-pyrazoles (where alkyl = methyl, ethyl, or benzyl),\textsuperscript{143} and dimethyl 3-alkyl-3-methyl-$3H$-pyrazole-4,5-dicarboxylates (where alkyl = methyl, ethyl).\textsuperscript{146} Those rearrangements primarily give the kinetic product initially, the corresponding $4H$-pyrazole, rather than the thermodynamically more stable aromatic counterpart, by what are believed to be concerted [1,5]-sigmatropic rearrangements. Since $3H$-pyrazoles 111b and 111e do not afford the $4H$-pyrazole as the major rearrangement product, this suggests that a different mechanism may be operating
in the thermal rearrangement of the 3H-pyrazoles.

A stepwise mechanism involving a discrete ion-pair intermediate (an alkyl cation and a pyrazole anion) is proposed for the rearrangement of 3H-pyrazoles 111a-e in benzene solvent (Scheme 20). The first step is reversible covalent bond cleavage to an ion pair. The second step is collapse of the ion pair to afford more stable pyrazole isomers.

![Scheme 20]

A radical-pair mechanism seems less likely since the rate determining homolysis of para-substituted dibenzylmercury (122) into a radical pair is enhanced only 1.1-fold for $X = \text{CH}_3$ and 3.4-fold for $X = \text{OCH}_3$ compared to 122, where $X = \text{H}$.\(^{191}\) Therefore, if radical pairs were intermediates in the thermal rearrangement of 111a-e, large rate enhancements for rearrangement would not be observed.

$$\text{p-}X\text{C}_6\text{H}_4\text{CH}_2\text{HgCH}_2\text{C}_6\text{H}_4\text{p-X} \longrightarrow \text{p-}X\text{C}_6\text{H}_4\text{CH}_2 \cdot + \cdot \text{HgCH}_2\text{C}_6\text{H}_4\text{p-X}$$

122

Furthermore, the rearrangement of 3H-pyrazoles 111c-e were observed by $^1\text{H}$ NMR spectroscopy and CIDNP (Chemically Induced Dynamic Nuclear Polarization) was not observed. Although the absence of a CIDNP spectrum is not compelling evidence for the absence of radical pair chemistry, a free radical mechanism is incompatible with the overall evidence.
Scheme 21 shows, in mechanistic terms, the potential products that can be expected from rearrangement of 3H-pyrazole 111 by a stepwise mechanism involving ion-pair formation. An ion-pair intermediate could return to starting material or suffer collapse in four alternative ways (path a). Collapse on either nitrogen atom of the pyrazole anion gives two stable aromatic 1H-pyrazoles (118 and 119). Collapse of the cation to the carbon nearest to the migration origin yields a 4H-pyrazole (120). This is a more stable pyrazole isomer compared to 111 because of its two relatively strong carbon-nitrogen double bonds. Collapse of the cation to the carbon furthest from the migration origin gives another 3H-pyrazole (123). If the cation has a β-hydrogen, proton transfer could generate 121 plus alkene (path b).

The products obtained from the rearrangement of 3H-pyrazoles 111a-e in benzene-
d6, can be rationalized in terms of an ion-pair mechanism for rearrangement. In these rearrangements, the major product from collapse of an intermediate ion pair is 1H-pyrazole 118. For the rearrangement of 3H-pyrazole 111c, loss of a proton from the tert-butyl cation of the ion pair competes with collapse of the ion pair. One would expect collapse of a free carbocation and free pyrazole anion to give the two most stable pyrazoles (118 and 119) in roughly equal amounts. Therefore, it appears that relatively tight ion pairs are formed because only the 1H-pyrazole, with one exception, resulting from collapse of the cation to the nitrogen nearest to its migration origin is observed.

Only in the rearrangement of 3H-pyrazoles 111b and 111e were 4H-pyrazoles (120) detected as minor products. These were formed from migration of the cation to the nearest carbon centre. Since the other 3H-pyrazoles (111a, 111c, and 111d) have larger
migrating groups, steric hindrance with the carbomethoxy group appears to be an important product determining factor. Either the 4H-pyrazoles are not formed during these rearrangements or they undergo further rearrangement to a 1H-pyrazole. In addition, only the rearrangement of 111a led to a mixture of two 1H-pyrazoles. This observation is compatible with an ion-pair mechanism involving rather "tight" ion pairs. The benzhydryl substituent of 111a forms the most stable cation and therefore is likely to become more separated from the anion during its longer lifetime and therefore, collapse of the cation to the distal nitrogen atom occurs to give 119a.

Therefore, by analysis of product distributions, it seems that the rearrangement of 3H-pyrazoles 111a-e led to rather tight ion-pair intermediates in benzene-\(d_6\). The polarity of the rearrangement solvent was increased in an attempt to promote ion-pair separations. This could give rise to a mixture of two stable, aromatic 1H-pyrazoles from the rearrangements of 111a-e.

2.5 Rearrangement of 3H-pyrazoles 111a-e in chloroform or chloroform-\(d\)

Table 12 shows the products from the rearrangement of 3H-pyrazoles 111a-e in chloroform solvent. 3H-Pyrazole 111a rearranged in chloroform solvent to give isomeric 1H-pyrazoles, 118a (73%) and 119a (27%). Since the percentage of 119a increased from 9% to 27% as a result of moving from benzene-\(d_6\) to chloroform solvent this suggests an increase in ion-pair separations.
Table 12. Products and product yields* from the thermal rearrangements of 111a-e at ambient temperature in chloroform.

![Chemical structures]

<table>
<thead>
<tr>
<th>Compound</th>
<th>118</th>
<th>119</th>
<th>120</th>
<th>121</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>111a, R=CHPh₂</td>
<td>73</td>
<td>27</td>
<td>nil</td>
<td>nil</td>
<td></td>
</tr>
<tr>
<td>111b, R=CH₂OMe</td>
<td>72</td>
<td>28</td>
<td>nil</td>
<td>nil</td>
<td></td>
</tr>
<tr>
<td>111c, R=C(Me)₃</td>
<td>28</td>
<td>5</td>
<td>nil</td>
<td>67</td>
<td>55 isobutene</td>
</tr>
<tr>
<td>111d, R=1-adamantyl</td>
<td>69</td>
<td>31</td>
<td>nil</td>
<td>nil</td>
<td></td>
</tr>
<tr>
<td>111e, R=p-CH₂C₆H₄OMe</td>
<td>56</td>
<td>11</td>
<td>32</td>
<td>nil</td>
<td></td>
</tr>
</tbody>
</table>

* At the level of detection afforded by ¹H NMR spectroscopy, the products listed were the only products from rearrangement and yield numbers (%) reflect complete materials balance prior to opening of a tube.

b Reaction solvent was CDCl₃.
An increase in ion-pair separation causes an increased probability of ion-pair collapse at a site far from the migration origin. The rearrangement of 3H-pyrazoles 111b-e in chloroform led to a higher percentage of 1H-pyrazole 119, suggesting that ion pairs from the rearrangement of 111b-e are more separated in chloroform than in benzene. However, since the two 1H-pyrazoles are not formed in roughly equal amounts in all cases, this suggests that the ion pairs are still rather tight and probably not solvent-separated.

The clean chemistry of 111a-e in chloroform is easily rationalized in terms of the ion-pair mechanism, whereas radical pair chemistry in CHCl₃ would be expected to lead to some RH and to the formation of RD from reactions run in CDCl₃. There was no evidence for these products.

2.6 Rearrangement of 3H-pyrazoles 111a-e in methanol or methanol-d₄

The 3H-pyrazoles 111a-e were generated in a nucleophilic solvent, in an effort to trap the ion-pair intermediates. If successful, this would provide strong evidence in support of an ion-pair mechanism for the rearrangement of 3H-pyrazoles 111a-e.

Table 13 lists the products from the rearrangement of 3H-pyrazoles 111a-e in methanol or methanol-d₄. Interception of the cationic migrating group with methanol competed with ion-pair collapse to 1H-pyrazole (118 and/or 119). 3H-Pyrazoles 111b and 111c, both of which afforded a volatile methyl ether, were generated in deuterated solvent in order to determine the percentage of the methyl ether product conveniently by ¹H NMR spectroscopy.
Rearrangement of 3H-pyrazole 111a in methanol gave 118a (26%), 119a (22%), 121 (52%), and 124a (52%). Similarly, 3H-pyrazole 111b rearranged in methanol-d₄ to give 118b (25%), 121 (as the D analogue, 75%), and 124b (dimethoxymethane-d₄, 61%). Rearrangement of 3H-pyrazole 111c in methanol-d₄, gave 118c (20%), 121 (a mixture of H and D analogues, 80%), 124c (tert-butyl methyl ether-d₃, 72%), and isobutene (5%). 3H-Pyrazole 111d gave 118d (54%), 119d (17%), 121(29%), and 124d (23%) from rearrangement in methanol. Likewise, 3H-pyrazole 111e gave 118e (45%), 119e (4%), 121 (51%), and 124e (47%) from rearrangement in methanol.

The presence of dimethoxymethane-d₃, and tert-butyl methyl ether-d₃, from reaction of 111b and 111c in methanol-d₄ was confirmed by gas chromatography and ¹H NMR spectroscopy in spiking experiments with authentic samples of the non-deuterated analogues. The deuterated ethers, 124b and 124c, had ¹H NMR chemical shifts and gas chromatography retention times identical to those of non-deuterated analogues. The presence of benzhydryl methyl ether was confirmed by comparing spectroscopic data with those in the literature while 1-adamantyl methyl ether and p-methoxybenzyl methyl ether were confirmed by comparing spectroscopic data with those of samples prepared by another route.

The chemistry of 3H-pyrazoles 111a-e in methanol provides powerful evidence that rearrangement occurs by an ion-pair mechanism. For 3H-pyrazoles 111a-e, interception of R⁺ with methanol competed with ion-pair collapse to give 1H-pyrazoles.
Table 13. Products and product yields* from the thermal rearrangements of 111a-e in methanol or methanol-\textit{d}_4 at ambient temperature.

<table>
<thead>
<tr>
<th></th>
<th>111a, R=CHPh₂</th>
<th>111b, R=CH₂OME</th>
<th>111c, R=C(Me)₃</th>
<th>111d, R=1-adamantyl</th>
<th>111e, R=p-CH₂C₆H₄OME</th>
<th>+ ROCH₃ (124)</th>
<th>+ other</th>
</tr>
</thead>
<tbody>
<tr>
<td>111</td>
<td>26</td>
<td>22</td>
<td>52</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>111b</td>
<td>25</td>
<td>nil</td>
<td>75</td>
<td>61\textsuperscript{d}</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>111c</td>
<td>20</td>
<td>nil</td>
<td>80\textsuperscript{e}</td>
<td>72\textsuperscript{d}</td>
<td>5 isobutene</td>
<td></td>
<td></td>
</tr>
<tr>
<td>111d</td>
<td>54</td>
<td>17</td>
<td>29</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>111e</td>
<td>45</td>
<td>4</td>
<td>51</td>
<td>47</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\* At the level of detection afforded by \textsuperscript{1}H NMR spectroscopy, the products listed were the only products from rearrangement and yield numbers (%) reflect complete materials balance prior to opening of a tube.

\textsuperscript{b} D analogue.

\textsuperscript{c} Mixture of H and D analogues.

\textsuperscript{d} ROCD₃ from reaction in CD₃OD.
2.7 Rearrangement of 3-benzyl-3-methyl-3\(H\)-pyrazole-4,5-dicarboxylic acid dimethyl ester

Since \(3H\)-pyrazole 111e presumably rearranges by a stepwise mechanism it was of interest to study the rearrangement of \(3H\)-pyrazole 111f (R = benzyl) to determine if the para-methoxy substituent of 111e is necessary for stepwise rearrangement. The para-methoxy substituent enhances the stabilization of the cation portion of the ion-pair intermediate formed from the rearrangement of 111e.

\(3H\)-Pyrazole 111f was synthesized by a modification of the preparative procedure used for the synthesis of \(3H\)-pyrazoles 111a-e (see Experimental). Unlike 111a-e, this \(3H\)-pyrazole was stable to the conditions of its purification by centrifugal chromatography (silica gel). \(3H\)-Pyrazole 111f was refluxed in neat methanol and after 0.5 hours, had rearranged to afford \(4H\)-pyrazole 120f (58%) and 1\(H\)-pyrazole 118f (42%) (Scheme 22). Benzyl methyl ether was not detected.

![Scheme 22](image)

Like other concerted \(3H\)-pyrazole rearrangements,\(^{141,143,146}\) 111f affored the \(4H\)-pyrazole as the major product. Therefore, it appears that 111f rearranges by a concerted mechanism rather than a stepwise mechanism, involving an ion-pair intermediate since a potential benzyl cation intermediate was not intercepted in methanol. This observation
was not too surprising considering that in 67% aqueous acetone, para-methoxybenzyl chloride solvolyzes approximately $10^3$ times faster than benzyl chloride.\textsuperscript{171}

2.8 Rearrangement of $4H$-pyrazoles 120b and 120e

The rearrangement of $3H$-pyrazoles 111b and 111e afforded $4H$-pyrazoles as rearrangement products, providing one with the opportunity to study the rearrangements of these more stable pyrazole isomers. Thermal rearrangements of $4H$-pyrazoles have received considerably less attention than the thermal rearrangements of $3H$-pyrazoles, in general.\textsuperscript{195} The temperatures necessary for $3H$-pyrazole rearrangement sometimes provokes rearrangement of a $4H$-pyrazole product.\textsuperscript{143,146}

Inspection of Table 14 reveals the products formed from the rearrangement of $4H$-pyrazoles, 120b and 120e, in benzene-$d_6$ and methanol or methanol-$d_4$ solvents. As mentioned above, $4H$-pyrazole 120b could not be isolated. It was obtained as a solution, after the rearrangement of 111b in benzene-$d_6$ solvent, which gave 118b (77\%) and 120b (23\%). The observed rate constant for the disappearance of 120b at 90 °C from this reaction mixture was $(1.10 \pm 0.05) \times 10^{-4} \text{ s}^{-1}$. After the thermal rearrangement of 120b, the mixture consisted of 118b (90\%) and 119b (10\%). Therefore, 120b rearranges to give compounds 118b and 119b in the ratio 1.3 : 1.0.

$4H$-Pyrazole 120e could be isolated and its rearrangement in benzene-$d_6$ was followed by $^1\text{H}$ NMR spectroscopy. The increase in the concentrations of the rearrangement products 118e and 119e gave an observed rate constant of $(1.45 \pm 0.08) \times 10^{-4} \text{ s}^{-1}$ at 130 °C. The products 118e and 119e were in the ratio 1.4 : 1.0.
Table 14. Product and product yields\(^a\) from thermal rearrangements of 120\(\text{b}\) and 120\(\text{e}\).

<table>
<thead>
<tr>
<th>Solvent</th>
<th>(\text{R} = \text{CH}_2\text{OMe})(^{bc})</th>
<th>57</th>
<th>43</th>
<th>118</th>
<th>119</th>
<th>121</th>
<th>+ other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene-(d_6)</td>
<td>(\text{R} = \text{p-CH}_2\text{C}_6\text{H}_4\text{OMe}_2)(^d)</td>
<td>58</td>
<td>42</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methanol</td>
<td>(\text{R} = \text{CH}_2\text{OMe})(^{cef})</td>
<td>nil</td>
<td>nil</td>
<td>100</td>
<td></td>
<td></td>
<td>100 ROCD(_3)</td>
</tr>
<tr>
<td></td>
<td>(\text{R} = \text{p-CH}_2\text{C}_6\text{H}_4\text{OMe})(^e)</td>
<td>nil</td>
<td>nil</td>
<td>100</td>
<td></td>
<td></td>
<td>100 ROCH(_3)</td>
</tr>
</tbody>
</table>

\(^a\) At the level of detection afforded by \(^1\text{H}\) NMR spectroscopy, the products listed were the only products and the yield numbers (\%) were determined by \(^1\text{H}\) NMR spectroscopy.

\(^b\) Rearrangement at 90 °C with \(k = (1.10 \pm 0.05) \times 10^{-4}\) s\(^{-1}\).

\(^c\) Rearrangement of 120\(\text{b}\) from solutions containing 120\(\text{b}\) (23\%) and 118\(\text{b}\) (77\%).

\(^d\) Rearrangement at 130 °C with \(k = (1.45 \pm 0.08) \times 10^{-4}\) s\(^{-1}\).

\(^e\) Rearrangement at ambient temperature.

\(^f\) Rearrangement in CD\(_3\)OD.
4H-Pyrazoles are more stable than their 3H-pyrazole counterparts due to the presence of two relatively strong C=N double bonds, and consequently they have a higher barrier to ion-pair formation. 4H-Pyrazole 120b could not be isolated without decomposition while 120e could be isolated by centrifugal chromatography. The faster observed rate of rearrangement of 120b (R = CH₂O Ме) compared to 120e (R = p-CH₂C₆H₄O Ме) is a reflection of the relative stabilities of the different intermediate cations.

Both 120b and 120e rearrange to give the isomeric 1H-pyrazoles (118 and 119) in about the same ratio (118 : 119 = 1.3-1.4 : 1.0). It would be expected that ion-pair formation from a 4H-pyrazole would lead to two isomeric 1H-pyrazoles in approximately the same ratio because the cation would have a similar probability of collapsing on each nitrogen site, given that the migration origin is equidistant from those nitrogen atoms and that ion-pair collapse in benzene can not have a substantial activation energy.

Further evidence that rearrangement takes place by a mechanism other than a concerted one arises from the fact that carbomethoxy migration does not occur from C-4 of the 4H-pyrazoles. It is known that a carbomethoxy substituent has a higher migratory aptitude than both benzyl and ethyl substituents in [1,5]-sigmatropic migrations from C-3 in 3H-pyrazoles.¹⁴³,¹⁴⁶

The rearrangement of 4H-pyrazoles 120b and 120e in methanol solvent could provide evidence for a stepwise mechanism if the intermediate cations of the ion pairs could be trapped. The 4H-pyrazoles, 120b and 120e, were dissolved in methanol-d₄, and methanol, respectively, to determine if the migrating groups could be trapped as cations.
The photolysis mixture from the generation of 3H-pyrazole 111b in benzene-$d_6$ and its subsequent rearrangement to 118b (79%) and 120b (21%), was freed from volatile and the residue was dissolved in methanol-$d_4$. The $^1$H NMR spectrum, taken immediately revealed 118b (79%), 121 (21%), and dimethoxymethane-$d_3$ (21%) indicating that 4H-pyrazole 120b had dissociated to give exclusively methanolysis products. Similarly, 4H-pyrazole 120e was dissolved in methanol solvent and after ten minutes, the solvent was removed in vacuo and the residue was dissolved in CDCl$_3$. The $^1$H NMR spectrum, taken immediately, revealed that p-methoxybenzyl methyl ether (100%) and 121 (100%) had been formed (Table 14). Therefore, it appears these 4H-pyrazoles rearrange by a stepwise mechanism, in both benzene and methanol solvents.

2.9 Different ion pairs from isomeric 3H-pyrazoles and 4H-pyrazoles

It was found that both 4H-pyrazole 120b and 120e undergo methanolysis at room temperature and that virtually all the migrating cation is intercepted by methanol solvent in each case (Table 14). The rearrangement of 3H-pyrazoles 111b and 111e gave 61% and 47% of the appropriate methyl ethers, respectively (Table 13).

The fact that, in methanol, a larger percentage of the migrating group is trapped by solvent if it originates from a 4H-pyrazole than if it originates from the isomeric 3H-pyrazole suggests that these isomeric pyrazoles lead to different ion pairs! Since those ion pairs must be identical once they have become well separated, the suggestion is that the ones from the 4H-pyrazoles are more solvent-separated than the ones from the 3H-pyrazoles or that the former become solvent-separated out the latter do not.
The different fates of isomeric $3H$-pyrazoles and $4H$-pyrazoles in methanol could also be explained in terms of competing stepwise and concerted mechanisms for the former. A common ion-pair mechanism seems more likely, with differentiation arising out of small differences between the ion-pair geometries (memory effects or different degrees of separation) rather than an accidental matching of the activation free energies for concerted and stepwise mechanisms.

2.10 Structural determination of $1H$-pyrazoles and $4H$-pyrazoles

The $1H$ NMR and $13C$ NMR spectra were taken for all pyrazole rearrangement products from $3H$-pyrazoles 111a-f and their mass spectrometric molecular masses were determined. The key spectral features which were important in distinguishing between the isomeric pyrazoles are discussed below.

The $1H$-pyrazoles 118 and 119 can be easily differentiated from the isomeric $3H$-pyrazoles 111 by $1H$ NMR spectroscopy. The methyl singlet of a $1R,5$-methyl-$1H$-pyrazole-3,4-dicarboxylic acid dimethyl ester or a $1R,3$-methyl-$1H$-pyrazole-4,5-dicarboxylic acid dimethyl ester is shifted approximately 1 ppm downfield compared to the methyl singlet of an isomeric $3R,3$-methyl-$3H$-pyrazole-4,5-dicarboxylic acid dimethyl ester. The carbomethoxy singlets for both $1H$-pyrazole 118 and 119 are also shifted downfield in their $1H$ NMR spectra by approximately 0.4 to 0.6 ppm compared to the isomeric $3H$-pyrazole 111. Furthermore, the signal from the proton/s attached to the nitrogen bearing carbon of the R group of $1H$-pyrazoles 118 and 119 is also downfield compared to the corresponding signal for the $3H$-pyrazole isomer. In particular, when R
contains a methylene group, the methylene protons are diastereotopic (AB spin system, doublet of doublets) in the $^1$H NMR spectrum of the $3H$-pyrazole (ie. 111e) while the methylene protons appear in the form of a singlet in the spectra of the isomeric $1H$-pyrazoles. For example, the methylene protons of 118b, 118e, 119b, and 119e appear in the form of a singlet in their respective $^1$H NMR spectra.

Differentiating between a pair of isomeric $1H$-pyrazoles by $^1$H NMR spectroscopy is difficult. W. Holzer showed recently that the $^1$H NOE (Nuclear Overhauser Effect) is a versatile tool for spectral and structural assignment in various N-substituted pyrazoles. Indeed, it was found that a $^1$H NOE experiment was useful in distinguishing between $1H$-pyrazoles 118b and 119b. Irradiation of the N-methylene resonance ($5.43$ ppm) in compound 118b led to an enhancement of both the singlet at $3.33$ ppm (OCH$_3$) and the singlet at $2.57$ ppm (CH$_3$). Since an NOE is observed on the C-methyl signal this is consistent with adjacent methoxymethyl and methyl groups in the 1- and 5- positions of the pyrazole moiety. Irradiation of the N-methylene resonance ($5.47$ ppm) in compound 119b leads to an enhancement of only the singlet at $3.29$ ppm (OCH$_3$). This is consistent with the methoxymethyl and methyl groups in the 1- and 3- positions of the pyrazole moiety. The results of this experiment distinguish 118b from 119b and therefore the $^{13}$C NMR spectra could be assigned to the appropriate $1H$-pyrazoles.
1H-Pyrazoles 118 can also be differentiated from isomeric 1H-pyrazoles 119 by 13C NMR. Table 15 contains selected 13C NMR chemical shifts for 118a-f while Table 16 contains selected 13C NMR chemical shifts for 119a-e. The C-3 and C-5 chemical shifts were useful for distinguishing between the isomeric 1H-pyrazoles. The C-3 chemical shifts of 118a-f appear in the region of 142.47-144.55 ppm while the C-5 chemical shifts arise at higher field, from 140.82-143.50 ppm. The C-3 chemical shifts of 119a-e appear in the region of 135.59-137.17 ppm while the C-5 chemical shifts of 119a-e arise in the region of 148.39-149.98 ppm. The 13C chemical shifts were assigned by comparison with the chemical shift assignments made by others, for other 1H-pyrazoles.197

The isomeric 1H-pyrazoles can also be set apart based on their different polarities. For example, when separating a product solution containing both isomeric 1H-pyrazoles by centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate), 1H-pyrazole 119 elutes before 1H-pyrazole 118.

The 1H NMR and selected 13C NMR chemical shifts of 4H-pyrazoles 120e and 120f are located in Table 17. The sp3-hybridized carbon (C-4) resonates at 76.31 ppm for 120e while it resonates at 76.16 ppm for 120f. This particular high field chemical shift is useful for distinguishing 4H-pyrazoles from their 1H-pyrazole isomers. The 13C chemical shifts were assigned by comparison to the chemical shift assignments made by others for other 4H-pyrazoles.199 The 4H-pyrazoles 120b and 120e contain methylene protons which are diastereotopic and appear in the form of a doublet of doublets in their
Table 15.

Selected $^{13}$C NMR (50 MHz) chemical shifts (ppm) for 1H-pyrazoles 118a-i in CDCl$_3$.

<table>
<thead>
<tr>
<th>118</th>
<th>C-3</th>
<th>C-4</th>
<th>C-5</th>
<th>C-8</th>
<th>C-6, C-7 *</th>
<th>C-9, C-10 b</th>
</tr>
</thead>
<tbody>
<tr>
<td>118a</td>
<td>144.00</td>
<td>112.31</td>
<td>143.50</td>
<td>11.00</td>
<td>163.21, 163.53</td>
<td>51.67, 52.35</td>
</tr>
<tr>
<td>118b</td>
<td>144.55</td>
<td>113.50</td>
<td>143.36</td>
<td>10.33</td>
<td>163.23, 163.66</td>
<td>51.74, 52.83</td>
</tr>
<tr>
<td>118c</td>
<td>142.47</td>
<td>113.91</td>
<td>140.82</td>
<td>13.15</td>
<td>163.43, 164.04</td>
<td>51.65, 52.31</td>
</tr>
<tr>
<td>118d</td>
<td>142.53</td>
<td>113.99</td>
<td>141.06</td>
<td>13.48</td>
<td>163.46, 164.20</td>
<td>51.66, 52.30</td>
</tr>
<tr>
<td>118e</td>
<td>143.46</td>
<td>112.83</td>
<td>142.77</td>
<td>10.76</td>
<td>162.66, 163.34</td>
<td>51.61, 52.36</td>
</tr>
<tr>
<td>118f</td>
<td>143.79</td>
<td>113.01</td>
<td>142.97</td>
<td>10.85</td>
<td>162.68, 163.43</td>
<td>51.76, 52.52</td>
</tr>
</tbody>
</table>

* C-6 and C-7 may be reversed.

b C-9 and C-10 may be reversed.
Table 16.

Selected $^{13}$C NMR (50 MHz) chemical shifts (ppm) of 1H-pyrazoles 119a-e in CDCl$_3$.

<table>
<thead>
<tr>
<th>119</th>
<th>C-3</th>
<th>C-4</th>
<th>C-5</th>
<th>C-6</th>
<th>C-7,</th>
<th>C-9,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>C-8$^a$</td>
<td>C-10$^b$</td>
</tr>
<tr>
<td>119a</td>
<td>137.15</td>
<td>112.93</td>
<td>149.98</td>
<td>13.50</td>
<td>161.46,</td>
<td>51.61,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>163.50</td>
<td>52.92</td>
</tr>
<tr>
<td>119b</td>
<td>135.96</td>
<td>114.27</td>
<td>149.70</td>
<td>12.99</td>
<td>160.48,</td>
<td>51.56,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>163.05</td>
<td>52.83</td>
</tr>
<tr>
<td>119c</td>
<td>137.17</td>
<td>111.37</td>
<td>148.40</td>
<td>13.55</td>
<td>163.34,</td>
<td>51.39,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>164.19</td>
<td>53.22</td>
</tr>
<tr>
<td>119d</td>
<td>136.90</td>
<td>111.12</td>
<td>148.39</td>
<td>13.60</td>
<td>164.33,</td>
<td>51.34,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>164.39</td>
<td>53.24</td>
</tr>
<tr>
<td>119e</td>
<td>135.59</td>
<td>113.38</td>
<td>149.70</td>
<td>13.25</td>
<td>161.12,</td>
<td>51.63,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>163.40</td>
<td>52.85</td>
</tr>
</tbody>
</table>

$^a$ C-7 and C-8 may be reversed.

$^b$ C-9 and C-10 may be reversed.
Table 17.

<table>
<thead>
<tr>
<th>4H-Pyrazole, 120</th>
<th>$^1$H NMR (200 MHz)</th>
<th>$^{13}$C NMR$^{d,e}$ (50 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>120b, *a,b</td>
<td>4.28 (d, 1 H, J = -9.3 Hz), 3.92 (d, 1 H, J = -9.3 Hz), 3.38 (s, 3 H, CO$_2$Me), 3.09 (s, 3 H, CO$_2$Me), 2.76 (s, 3 H, Me).</td>
<td></td>
</tr>
<tr>
<td>R=CH$_2$OMe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120e, *c</td>
<td>6.69 (d, 2 H, J = 8.7 Hz), 6.81 (d, 2 H, J = 8.7 Hz), 3.97 (s, 3 H, CO$_2$Me), 3.71 (s, 6 H, OMe + CO$_2$Me), 3.80 (d, 1 H, J = -14 Hz), 3.45 (d, 1 H, J = -14 Hz), 2.38 (s, 3 H, Me).</td>
<td>176.52 (C-3), 76.31 (C-4), 166.69 (C-5), 165.27 (C-6), 160.61 (C-7), 13.76 (C-8), 53.65 (C-9), 53.09 (C-10).</td>
</tr>
<tr>
<td>R=p-CH$_2$C$_6$H$_4$OMe</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120f, *c</td>
<td>6.88-7.27 (m, 5 H, C$_6$H$_5$), 3.97 (s, 3 H, CO$_2$Me), 3.88 (d, 1 H, J = -14 Hz), 3.72 (s, 3 H, CO$_2$Me), 3.50 (d, 1 H, J = -14 Hz), 2.39 (s, 3 H, Me).</td>
<td>176.32 (C-3), 76.16 (C-4), 166.63 (C-5), 165.36 (C-6), 160.71 (C-7), 13.80 (C-8), 53.72 (C-9), 53.10 (C-10)</td>
</tr>
<tr>
<td>R=CH$_2$C$_6$H$_5$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Solvent is C$_6$D$_6$.
* The $^1$H NMR spectrum was obtained from solutions containing 118b (77%) and 120b (23%). The $^{13}$C NMR spectrum of 120b could not be determined from this solution.
* Solvent is CDCl$_3$.
* C-6 and C-7 may be reversed.
* C-9 and C-10 may be reversed.
1H NMR spectra while their isomeric 1H-pyrazoles have 1H NMR spectra in which those methylene protons appear in the form of a singlet.

2.11 Conclusion

The 3H-pyrazoles 111a-e undergo rearrangement by a stepwise mechanism in benzene, chloroform, and methanol solvents. A summary of the evidence which supports this statement follows. First, in benzene-d₆ solvent, the 3H-pyrazoles 111a-e rearrange with large rate enhancements (approximately 10⁶ for the slowest) compared to the rearrangement of 3H-pyrazole 101 (R = CH₂CH₃). Second, the 4H-pyrazole is not the major product from the rearrangement of 111b and 111e in benzene-d₆ solvent, contrary to the products of those 3H-pyrazoles which rearrange by a concerted mechanism. Third, isobutene is formed, presumably from a tert-butyl cation intermediate, in the rearrangement of 3H-pyrazole 111c in all three solvents. In addition, the clean chemistry for the rearrangement of the 3H-pyrazoles in chloroform solvent disputes a radical-pair mechanism. Finally, methanol solvent intercepts the migrating groups during the rearrangement of the 3H-pyrazoles, diverting them to 121 and the appropriate methyl ethers.

The 4H-pyrazoles 120b and 120e also rearrange by a stepwise, ion-pair mechanism, at least in methanol solvent because the migrating groups were completely intercepted. It appears that these 4H-pyrazoles also rearrange by the two-step mechanism
in benzene-$d_6$, at the higher temperatures required, because roughly equal amounts of isomeric 1H-pyrazoles (118 and 119) were formed.

These rearrangements can be described mechanistically as "formal" [1,5]-sigmatropic rearrangements because some of the products of rearrangement are those that could have arisen by [1,5]-sigmatropic migrations. Reports of such "formal" [1,5]-sigmatropic rearrangements are very rare in the literature.\textsuperscript{56} These rearrangements represent part of a mechanistic continuum which runs from concerted, with very little charge separation, through transition structures with increasing separation of charge, to the two-step, ion-pair extreme.

Cycloaddition reactions, like sigmatropic reactions, belong to the pericyclic category of reactions. There are several examples of cycloaddition reactions which are known to occur by a stepwise mechanism rather than by a concerted process, either synchronous or asynchronous.\textsuperscript{198} One type of cycloaddition reaction which has received much attention in the literature is the Diels Alder reaction, a $2\pi + 4\pi$ cycloaddition process; stepwise Diels Alder reactions have recently been discovered.\textsuperscript{199-202} The work in this chapter is unique because "formal" [1,5]-sigmatropic rearrangements of both 3H-pyrazoles and 4H-pyrazoles have never been reported and "formal" [1,5]-sigmatropic rearrangements of cyclopentadienes are rare.\textsuperscript{56}

2.12 Synthetic applications

3H-Pyrazoles 111a-e are all new compounds, as are the pyrazole rearrangement products, except for 1H-pyrazole 121. The 1H-pyrazoles 118a, 118b, 118d, and 118e can
be made in good yields from the rearrangement of the appropriate 3H-pyrazoles at room temperature (Table 11). The one-pot synthesis of these 1H-pyrazoles from the appropriate oxadiazolines and dimethyl acetylenedicarboxylate is both convenient and mild. These new 1H-pyrazoles might have some use as pesticides or herbicides since the 1H-pyrazole nucleus has been found to be biologically active.\textsuperscript{61,64}

The rearrangement of 3H-pyrazole 111c in methanol gave a high yield of 1H-pyrazole 121. This rearrangement could be useful for the mild synthesis of other NH-pyrazoles by simply modifying the substituents at C-3, C-4, and C-5 (Scheme 23). Other alkyl substituents could be located at C-3 (ie. \( R = \text{CH}_2\text{CH}_3, \text{CH} \) \( \text{CH}_3 \) \( \text{CH}_2 \)) of 3H-pyrazole 125 by the synthesis of the appropriate oxadiazoline 114g. Use of a different alkyne in the 1,3-dipolar cycloaddition reaction with the diazo compound would give other substituents at C-4 and C-5 (ie. \( X = \text{CN}, \text{COCH}_3, \text{COPh}, \text{and CF}_3 \)) of the 3H-pyrazole. Rearrangement of 3H-pyrazole 125 should give NH-pyrazole 126 as the major product. The minor pyrazole product would be 1H-pyrazole 127. Isobutene and tert-butyl methyl ether would also be reaction products, but they could easily be removed during the rotary evaporation of the reaction solvent. Centrifugal chromatography would only be necessary for the separation of NH-pyrazole 126 from 1H-pyrazole 127. Therefore, the stepwise rearrangement of 3H-pyrazole 111c could provide a convenient route to other NH-pyrazoles (126) which may be useful as precursors of both pesticides and herbicides.
\[
\begin{align*}
&(\text{CH}_3)_2COCH_3 + \equiv N + \equiv CH \quad \rightarrow \quad \text{126 (major)} \quad \text{(major)} \\
&(\text{CH}_3)_2C = N(X) + \text{CH}_3OH \quad \rightarrow \quad \text{127 (minor)} \quad \text{(minor)}
\end{align*}
\]
CHAPTER 3

Studies of the Thermal Rearrangements of Methyl 3-alkyl-3-methyl-?Y-pyrazole-5-carboxylates

3.0 Objective

It was discovered that 3H-pyrazoles 111a-e undergo thermal rearrangement by a stepwise mechanism involving ion-pair intermediates (Scheme 24). This mechanism for rearrangement appears to operate because the migrating group is relatively stable as a cation and the counterion is a stabilized, aromatic, pyrazole anion derivative. These "formal" [1,5]-sigmatropic rearrangements were discussed in detail in Chapter 2.

![Scheme 24](image)

(a: R=CHPh2; b: R=CH2OMe; c: R=C(Me)3; d: R=1-adamantyl; e: R=p-CH2C6H4OMe)

It was of interest to investigate the thermal rearrangement of another series of 3H-pyrazoles (128a-e) and determine whether thermal rearrangement takes place by a
concerted or a stepwise mechanism (Scheme 25). The potential pyrazole anion intermediate bears only one carbomethoxy substituent, which renders it less stable than the pyrazole anion formed in the rearrangement of 3H-pyrazoles 111a-e. The R substituents were again chosen as CHPh2, CH3OMe, C(Me)3, 1-adamantyl, and p-CH2C6H4OMe because they readily dissociate as cations in solvolysis reactions of R-X (X = halogen).150,153 It is known that R+ must be a relatively stable cation for stepwise rearrangement, but the sensitivity of the stepwise mechanism to the stabilization of the pyrazole nucleus has not been explored.

(E=CO2Me)

(a: R=CHPh2; b: R=CH2OMe; c: R=C(Me)3; d: R=1-adamantyl; e: R=p-CH2C6H4OMe)

Scheme 25

The thermal rearrangement of 3H-pyrazole 128f (where R = CH2C6H4) would also be investigated in order to compare it to the thermal rearrangements of 3H-pyrazoles 128a-e. Presumably, 3H-pyrazole 128f would rearrange by a concerted mechanism, involving [1,5]-sigmatropic benzyl shifts, since 3H-pyrazole 111f (where R = CH2C6H4) appears to rearrange by this mechanism. Methanol did not get involved in the chemistry of the rearrangement of 111f, which implies that ion pairs are not formed.
The thermal rearrangements of some 3\(H\)-pyrazoles, similar in structure to 3\(H\)-pyrazoles 128a-f, were previously investigated. It is important to review this work briefly because of its relationship to the work described in this chapter. Franck-Neumann and Dietrich-Buchecker studied the thermal rearrangement of 3\(H\)-pyrazole 128g (\(R = \text{Me}\), a substituent which cannot form a relatively stable cation) and found that during 3 hours at 180 \(^{\circ}\)C rearrangement afforded only 1\(H\)-pyrazole 131g (Scheme 26).\(^{84}\) The product 131g was accounted for in terms of an initial [1,5]-sigmatropic migration of methyl to C-4, generating intermediate 4\(H\)-pyrazole 130g, which underwent further rearrangement by a hydrogen migration to nitrogen.

\[
\begin{array}{c}
\text{H}_3\text{C} \\
\begin{array}{c}
\text{N} \\
\begin{array}{c}
\text{N} \\
\text{E} \\
\end{array}
\end{array}
\begin{array}{c}
\text{R} \\
\begin{array}{c}
\text{H} \\
\end{array}
\end{array}
\end{array}
\xrightarrow{180 \, ^{\circ}\text{C}}
\begin{array}{c}
\text{CH}_3 \\
\begin{array}{c}
\text{N} \\
\begin{array}{c}
\text{N} \\
\text{E} \\
\end{array}
\end{array}
\begin{array}{c}
\text{R} \\
\begin{array}{c}
\text{H} \\
\end{array}
\end{array}
\end{array}
\]

Scheme 26

\[
\begin{array}{c}
\text{CH}_3 \\
\begin{array}{c}
\text{N} \\
\begin{array}{c}
\text{N} \\
\text{E} \\
\end{array}
\end{array}
\begin{array}{c}
\text{R} \\
\begin{array}{c}
\text{H} \\
\end{array}
\end{array}
\end{array}
\]

(R=Me, E=CO\(_2\)Me)

Franck-Neumann and Dietrich-Buchecker also studied the thermal rearrangement of 3\(H\)-pyrazoles 128h (\(R = \text{CO}_2\text{Me}\)) and 128i (\(R = \text{COMe}\)) and found that, at room temperature, the acyl group migrated competitively to both carbon and nitrogen by [1,5]-sigmatropic shifts (Scheme 27).\(^{84}\) Carbomethoxy and acyl groups are known to have high migratory aptitudes in [1,5]-sigmatropic rearrangements.\(^{51-55}\) Rearrangement of 3\(H\)-pyrazole 128h gave 131h (58\%) and 132h (42\%) while 3\(H\)-pyrazole 128i gave 131i (95\%) and 132i (5\%).
Scheme 27

The sense of rearrangement of 3H-pyrazoles 128a-f could be determined by the ratio of pyrazole rearrangement products. Clearly, the percentage of 1H-pyrazole 132 would reflect the percentage of migration of R to nitrogen. Similarly, the percentage of 1H-pyrazole 131 should reflect the percentage of migration of R to C-4, since the 4H-pyrazole 130 should undergo further rearrangement by hydrogen migration to nitrogen. Even substituents with high migratory aptitudes in sigmatropic rearrangements (i.e. COOMe, COMe) cannot compete with the fast hydrogen migration in 4H-pyrazole 130. It is known that the rearrangement of 3H-pyrazole 133a gives 1H-pyrazole 133b.\textsuperscript{203} By analogy, if 4H-pyrazole 130b (R = CH₂OMe) were formed, rearrangement should afford 1H-pyrazole 131b.
3.1 Photolysis of oxadiazolines 114a-f in the presence of methyl propiolate

The method chosen for the synthesis of 3H-pyrazoles 128a-f was similar to that utilized for the synthesis of 3H-pyrazoles 111a-e. It involves diazoalkane generation from the photolysis of oxadiazolines, followed by *in situ* trapping of these diazoalkanes with methyl propiolate. The 1,3-dipolar cycloaddition was found to be regiospecific with several other diazo compounds. The synthesis of oxadiazolines 114a-f, which are precursors of diazoalkanes 117a-f, was described in Chapter 2. The oxadiazolines (114a-f) were irradiated at 300 nm at ambient temperature in benzene-\(d_6\) solution in the presence of methyl propiolate (Scheme 28). Only 3H-pyrazoles 128c-f could be detected by this method. However, 3H-pyrazoles 128c-f could not be isolated in very good yields because nitrogen extrusion from the 3H-pyrazoles occurred, giving cyclopropenes 134c-f, even when oxadiazolines 114c-f were still present in solution (path a). For example, after 1 hour of photolysis, 54% of oxadiazoline 114c was depleted and the solution consisted of cyclopropene 134c (28%) and 3H-pyrazole 128c (72%). Furthermore, after 4 hours of photolysis, when 87% of oxadiazoline 114c was depleted, the photolysis solution consisted of 134c (43%) and 128c (57%). Likewise, after 1 hour of photolysis, when 87% of oxadiazoline 114d was depleted, the photolysis solution consisted of 134d (41%)
and 128d (59%). The preparative procedure for the synthesis of 3H-pyrazoles 128c-f had to be modified in order to obtain improved yields.

Scheme 28
3H-Pyrazoles 128 are generally more photolabile than 3H-pyrazoles 111 when exposed to 300 nm irradiation because the wavelength of their n-π* absorption is blue-shifted closer to 300 nm. For example, the n→π* transition for methyl 3,3-dimethyl-3H-pyrazole-5-carboxylate is at 349 nm (MeOH) while the n→π* transition for dimethyl 3,3-dimethyl-3H-pyrazole-4,5-dicarboxylate is at 358 nm (MeOH).¹⁰⁹

Neither 3H-pyrazole 128b nor cyclopropene 134b was observed, following the photolysis of 114b, and only rearrangement products could be detected (Scheme 28, path b). The rearrangement products of this 3H-pyrazole are discussed in Section 3.4.

There were no products resulting from the cycloaddition of diazoalkane 117a to methyl propiolate, according to ¹H NMR spectroscopy. Even when the photolysis of oxadiazoline 114a was carried out in neat methyl propiolate, no products resulting from the cycloaddition of diazoalkane 117a to methyl propiolate could be detected. Presumably this cycloaddition reaction is too slow at room temperature.

3.2 Synthesis of cyclopropenes 134c-f

If the solutions from the irradiation of oxadiazolines 114c-f in the presence of methyl propiolate were photolyzed until the extrusion of nitrogen from 3H-pyrazoles 128c-f was complete, good yields (52-63%) of cyclopropenes 134c-f could be obtained. This one-pot synthesis provides a convenient route to cyclopropenes of general structure 134.

Cyclopropenes 134c-f were identified on the basis of their ¹H and ¹³C NMR spectra as well as their mass spectrometric masses. The ¹H NMR data and selected ¹³C
NMR chemical shifts for these cyclopropenes are tabulated in Table 18. In the $^1$H NMR spectra of cyclopropenes 134c-f, the vinyl proton signal arises in the region of 7.83-7.92 ppm while the methyl signal arises in the region of 1.14-1.30 ppm. In the $^{13}$C NMR spectra of these cyclopropenes, the C-1 signal is located in the region of 124.76-125.97 ppm, the C-2 signal is located in the region of 131.21-131.69 ppm, and the C-3 signal is located in the region of 29.43-36.22 ppm. The C-1 signal was differentiated from the C-2 signal on the basis of a $^{13}$C NMR spin sort experiment with compound 134c.

3.3 Synthesis of 3H-pyrazoles 128c-f: Modified preparative procedure

3H-Pyrazoles 128c-f were synthesized by a modified preparative procedure in an effort to obtain these compounds in good yields. The photolysis of the 3H-pyrazoles, to cyclopropenes, had to be avoided.

The oxadiazolines 114c-f were photolyzed at 300 nm in toluene solvent for 6 hours at -73 °C (Scheme 29). This generated pink solutions of 117c-f at -73 °C. Methyl propiolate was added to those photolysis solutions with the Rayonet bulbs switched off, and then the solutions were allowed to warm to room temperature. This procedure prevented exposure of the 3H-pyrazoles to the 300 nm irradiation and because of the low temperature, suppressed the formation of azines. The 3H-pyrazoles 128c-f were isolated in good yields (43-65%) and were found to be stable compounds at room temperature.
Table 18.

<table>
<thead>
<tr>
<th>Cyclopropene 134</th>
<th>$^1$H NMR (200 MHz)</th>
<th>$^{13}$C NMR (50 Mhz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>134c, R=C(Me)$_3$</td>
<td>7.88 (s, 1 H, CH), 3.77 (s, 3 H, CO$_2$Me), 1.18 (s, 3 H, Me), 0.82 (s, 9 H, CMe$_3$).</td>
<td>125.49 (C-1), 131.65 (C-2), 35.08 (C-3), 162.27 (C-4), 52.05 (C-5), 21.23 (C-6).</td>
</tr>
<tr>
<td>134d, R=1-adamantyl</td>
<td>7.92 (s, 1 H, CH), 3.80 (s, 3 H, CO$_2$Me), 1.93 (bs, 3 H, CH), 1.52-1.72 (m, 6 H, CH$_2$), 1.39-1.41 (m, 6 H, CH$_2$), 1.14 (s, 3 H, Me).</td>
<td>125.49 (C-1), 131.21 (C-2), 36.22 (C-3), 162.46(C-4), 52.04 (C-5), 20.03 (C-6).</td>
</tr>
<tr>
<td>134e, R=p-CH$_2$C$_6$H$_4$OMe</td>
<td>7.83 (s, 1 H, CH), 7.01 (d, 2 H, CH, J = 8.5 Hz), 6.80 (d, 2 H, CH, J = 8.5 Hz), 3.80 (s, 3 H, CO$_2$Me), 3.78 (s, 3 H, OMe), 2.86 (s, 2H, CH$_2$), 1...9 (s, 3 H, Me).</td>
<td>125.72 (C-1), 131.69 (C-2), 29.65 (C-3), 161.82 (C-4), 52.05 (C-5), 25.19 (C-6).</td>
</tr>
<tr>
<td>134f, R=CH$_2$C$_6$H$_5$</td>
<td>7.84 (s, 3 H, CH), 7.26-7.08 (m, 5 H, Ph), 3.80 (s, 3 H, CO$_2$Me), 2.92 (s, 2 H, CH$_2$), 1.30 (s, 3 H, Me).</td>
<td>125.97 (C-1), 131.65 (C-2), 29.43 (C-3), 161.76(C-4), 52.04 (C-5), 25.23 (C-6).</td>
</tr>
</tbody>
</table>
Scheme 29

3H-Pyrazoles 128c-f were identified on the basis of their $^1$H and $^{13}$C NMR spectra as well as their mass spectrometric masses. The $^1$H NMR data and selected $^{13}$C NMR chemical shifts of these 3H-pyrazoles are tabulated in Table 19. In the $^1$H NMR spectra of 3H-pyrazoles 128c-f, the vinyl proton signal arises in the region of 7.66-7.77 ppm, while the methyl signal arises in the region of 1.33-1.47 ppm. In the $^{13}$C NMR spectra of these 3H-pyrazoles, the C-3 signal is located in the region of 98.96-105.60, the C-4 signal is located in the region of 152.86-154.47 ppm, and the C-5 signal is located in the region of 147.01-147.66 ppm. The C-4 signal was differentiated from the C-5 signal on the basis of $^{13}$C NMR spin sort experiments with compounds 128c and 128d.
Table 19.

<table>
<thead>
<tr>
<th>3H-Pyrazole, 128</th>
<th>1H NMR (200 MHz)</th>
<th>13C NMR (50 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>128c, R=C(Me)₃</td>
<td>7.77 (s, 1 H, CH), 3.99 (s, 3 H, CO₂Me), 1.38 (s, 3 H, Me), 1.06 (s, 9 H, CMe₃).</td>
<td>105.08 (C-3), 153.37 (C-4), 147.02 (C-5), 15.06 (C-6), 161.38 (C-7), 52.38 (C-8).</td>
</tr>
<tr>
<td>128d, R=1-adamantyl</td>
<td>7.77 (s, 1 H, CH), 3.98 (s, 3 H, CO₂Me), 1.99 (bs, 3 H, CH), 1.68 (bs, 12 H, CH₂), 1.33 (s, 3 H, Me).</td>
<td>105.60 (C-3), 154.47 (C-4), 147.01 (C-5), 13.73 (C-6), 161.39 (C-7), 52.33 (C-8).</td>
</tr>
<tr>
<td>128e, R=p-CH₂C₆H₄OMe</td>
<td>7.66 (s, 1 H, CH), 7.00 (d, 2 H, CH, J = 8.2 Hz), 6.78 (d, 2 H, CH, J = 8.2 Hz), 3.94 (s, 3 H, CO₂Me), 3.77 (s, 3 H, OMe), 3.29 (d, 1 H, J= - 14 Hz), 3.07 (d, 1 H, J= - 14 Hz), 1.46 (s, 3 H, Me).</td>
<td>99.30 (C-3), 153.11 (C-4), 147.66 (C-5), 18.01 (C-6), 161.09 (C-7), 52.40 (C-8).</td>
</tr>
<tr>
<td>128f, R=CH₂C₆H₅</td>
<td>7.66 (s, 3 H, CH), 7.26-7.07 (m, 5 H, Ph), 3.93 (s, 3 H, CO₂Me), 3.34 (d, 1 H, J= -13 Hz), 3.10 (d, 1 H, J= -13 Hz), 1.47 (s, 3 H, Me).</td>
<td>98.96 (C-3), 152.86 (C-4), 147.60 (C-5), 18.03 (C-6), 161.00 (C-7), 52.34 (C-8).</td>
</tr>
</tbody>
</table>
3.4 Rearrangements of $3H$-pyrazoles 128b-f in benzene-$d_6$ solvent

The thermal rearrangements of $3H$-pyrazoles 128c-f were investigated in benzene-$d_6$ solvent. As mentioned above, $3H$-pyrazole 128b rearranged in benzene-$d_6$ solvent in the medium in which it was generated.

Table 20 reveals the products of the rearrangements of $3H$-pyrazoles 128b-f in benzene-$d_6$ solvent. The rearrangements led to very clean product solutions and the numbers reported are percentages determined by $^1H$ NMR spectroscopy.

$3H$-Pyrazole 128b rearranged in the medium in which it was generated to give 131b (52%) and 132b (48%). Presumably, $1H$-pyrazole 131b was formed by a hydrogen migration in unstable $4H$-pyrazole 130b (where R = CH$_2$OMe). Migration of the methoxymethyl substituent to both N-2 and C-4 had occurred in roughly equal amounts. Since the rearrangement of $3H$-pyrazole 128b is fast at room temperature, it is reasonable to assume an ion-pair mechanism is operating in this rearrangement, especially since $3H$-pyrazole 128g (R = CH$_3$) requires a temperature of 180 °C for thermal rearrangement. Furthermore, 128g affords only 131g from thermal rearrangement.

Unlike $3H$-pyrazole 128b, $3H$-pyrazole 128c was stable at room temperature. The overall rate constant for the decrease in concentration of $3H$-pyrazole 128c in benzene-$d_6$ solvent at 90 °C is (1.06 ± .03) x $10^4$ s$^{-1}$. A fragmentation reaction of 128c gave 136 (55%) and isobutene (55%). The presence of 136 and isobutene suggests that a pyrazole anion and a tert-butyl cation are reaction intermediates. The presence of isobutene was confirmed by a $^1H$ NMR spectroscopy decoupling experiment on the thermolysis mixture.
Table 20. Products and product yields* from the thermal rearrangements of 128b-f in benzene-$d_6$

<table>
<thead>
<tr>
<th></th>
<th>128b, b R=CH$_2$OMe</th>
<th>128c, c R=C(Me)$_3$</th>
<th>128d, d R=1-adamantyl</th>
<th>128e, e R=p-CH$_3$C$_6$H$_4$OMe</th>
<th>128f, f R=CH$_2$C$_6$H$_5$</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>52</td>
<td>28</td>
<td>72</td>
<td>78</td>
<td>100</td>
</tr>
<tr>
<td>Y</td>
<td>48</td>
<td>15</td>
<td>28</td>
<td>22</td>
<td>nil</td>
</tr>
<tr>
<td>Y2</td>
<td>nil</td>
<td>2</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Y3</td>
<td>nil</td>
<td>55</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Y4</td>
<td>nil</td>
<td>55</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
</tbody>
</table>

* At the level of detection afforded by $^1$H NMR spectroscopy, the products listed were the only products from rearrangement and the yield numbers (%) reflect materials balance prior to opening of a tube.

b Rearrangement at ambient temperature.

c Rearrangement at 90 °C with $k = (1.06 \pm 0.03) \times 10^{-4}$ s$^{-1}$.

d Rearrangement at 90 °C with $k = (1.10 \pm 0.09) \times 10^{-4}$ s$^{-1}$.

e Rearrangement at 60 °C with $k = (3.6 \pm 0.2) \times 10^{-4}$ s$^{-1}$.

f Rearrangement at 90 °C with $k = (2.8 \pm 0.1) \times 10^{-4}$ s$^{-1}$. 
(sealed nmr tube). Irradiation of the multiplet at 4.74 ppm (CH$_3$) caused the collapse of the triplet at 1.60 ppm (2 CH$_3$). 1H-Pyrazole 132c (15%), from migration of tert-butyl to nitrogen and 1H-pyrazoles 131c (28%) and 135c (2%) from migration of tert-butyl to carbon were also products in the rearrangement of 128c.

3H-Pyrazole 128d underwent thermal rearrangement at 90 °C with an observed rate constant of (1.10 ± 0.09) x 10$^{-4}$ s$^{-1}$, which is similar to the observed rate constant for the rearrangement of 3H-pyrazole 128c. Rearrangement of 128d afforded 131d (72%) and 132d (28%).

3H-Pyrazole 128e rearranged faster than both 128c and 128d with an observed rate constant of (3.6 ± 0.2) x 10$^{-4}$ s$^{-1}$ (average of 2 runs) at 60 °C. The products of rearrangement of 128e were 131e (78%) and 132e (22%).

The thermal rearrangement of 128f afforded only 131f; the benzyl substituent had migrated only to C-4 in 3H-pyrazole 128f. In contrast, the rearrangements of 128b-e gave a mixture of 1H-pyrazoles 131 and 132; the result of R substituent migration to both C-4 and N-2. The observed rate constant for rearrangement of 128f at 90 °C is (2.8 ± 0.1) x 10$^{-4}$ s$^{-1}$.

It appears that 3H-pyrazoles 128b and 128c rearrange in benzene-$d_6$ solvent by a stepwise mechanism, involving the formation of ion pairs. 3H-Pyrazole 128b (R = CH$_2$OMe) rearranges with a rate enhancement of at least 10$^5$, while 3H-pyrazole 128c rearranges with a rate enhancement of approximately 10$^3$, compared to the rearrangement of 128g (R = Me). Furthermore, 3H-pyrazole 128c affords both 136 and isobutene as products of thermal reaction which is suggestive of an ion-pair intermediate.
Whether or not 3H-pyrazoles 128d-f undergo rearrangement by a stepwise or a concerted mechanism is ambiguous. The approximate relative order of rates of rearrangement of 3H-pyrazoles 128c-f are the following: 128c (1.0), 128d (1.0), 128f (2.6), and 128e (27). All these 3H-pyrazoles rearrange with large rate enhancements compared to the thermal rearrangement of 128g, where a concerted mechanism for rearrangement is assumed. Furthermore, with the exception of 128f, these thermal rearrangements afford rearrangement products from migration of R to both C-4 and N-2. In contrast, the thermal rearrangement of 128g affords only 131g from migration of methyl to C-4.

It is informative that 3H-pyrazole 128e (R = p-CH₂C₆H₄OMe) rearranges approximately 10 times faster than 3H-pyrazole 128f (R = CH₂C₆H₅), assuming a 2-fold increase in the observed rate for every 10 °C increase in temperature. The rate enhancement for 128e, compared to 128f suggests development of some positive charge in the migrating group at the transition state for thermal rearrangement. 3H-Pyrazole 128f may rearrange either by a stepwise or a concerted mechanism involving some degree of charge separation.

The thermal rearrangement of a 3H-pyrazole analogue of 128f, was previously investigated. Schiess and Stalder studied the thermal rearrangement of 3H-pyrazole 137, similar in structure to 3H-pyrazole 128f except that a methyl substituent replaces the carbomethoxy substituent at C-5.¹⁴³ Rearrangement of 137 occurred at 120 °C in DMSO solvent, with an overall first order rate constant of 3.05 x 10⁻⁴ s⁻¹. Thermal rearrangement
afforded only 138 from initial migration of benzyl to C-4 followed by hydrogen migration to nitrogen.

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CH}_2\text{C}_6\text{H}_5 \\
\text{N} & \quad \text{N} \\
\text{I37} & \quad \text{H} \\
\text{CH}_3 & \quad \text{H} \\
\text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_2\text{C}_6\text{H}_5
\end{align*}
\]

\[
\begin{align*}
\text{DMSO} & \quad 120 \degree \text{C} \\
\text{N} & \quad \text{N} \\
\text{I38} & \quad \text{CH}_3 \\
\text{CH}_3 & \quad \text{CH}_2\text{C}_6\text{H}_5
\end{align*}
\]

3\(H\)-Pyrazole 128f rearranges at least 9 times faster than 3\(H\)-pyrazole 137, assuming a factor of 2 per 10 °C for the temperature difference and an additional rate factor for the solvents (\(\text{C}_6\text{D}_6\) for 128f, DMSO for 137). The carbomethoxy substituent at C-5 of 128f is rate enhancing compared to the methyl group at C-5 of 3\(H\)-pyrazole 137. This suggests that there is some negative charge developed within the pyrazole nucleus at the transition state for the rearrangement of 128f. The carbomethoxy substituent is stabilizing toward negative charge development in the pyrazole nucleus compared to the methyl substituent. It seems that 3\(H\)-pyrazole 128f rearranges by a concerted mechanism with some charge separation at the transition state for rearrangement. 3\(H\)-Pyrazole 128f, like 3\(H\)-pyrazole 137, afforded only the rearrangement product from initial migration of benzyl to C-4.

It is unclear clear whether 3\(H\)-pyrazoles 128d and 128e rearrange by a concerted or a stepwise mechanism in spite of their large rate enhancements for rearrangement.
compared to 128g. However, because they afford two rearrangement products (131 and 132), unlike the thermal rearrangement of 128g, this may suggest that they rearrange by a non-concerted mechanism.

3.5 Structural determination of pyrazole rearrangement products

The pyrazole products from the thermal rearrangements of 128b-f were all new compounds, except for 1H-pyrazole 136. 1H-Pyrazoles 132b-e and 1H-pyrazoles 131b-f were identified on the basis of their \(^1\)H and \(^{13}\)C NMR spectra as well as their mass spectrometric masses.

In the \(^1\)H NMR spectra of 1H-pyrazoles 132c-e, the vinyl proton appears in the region of 6.54-6.63 ppm, the carbomethoxy singlet appears in the region of 3.86-3.92 ppm, and the methyl singlet appears in the region of 2.12-2.51 ppm.

A \(^1\)H NOE experiment on compound 132b confirmed that the methoxymethyl substituent was located on N-1 in a 1,5-relationship with the methyl substituent. Irradiation of the methyl singlet at 2.38 ppm caused enhancement of both the CH\(_2\) singlet at 5.45 ppm and the vinyl proton singlet at 6.63 ppm.
The similarities of the $^{13}$C NMR spectra of 132c-e to the $^{13}$C NMR spectrum of 132b confirm that the R substituents of 132b-e are also in a 1,5-relationship with the methyl substituent. Selected $^{13}$C NMR chemical shifts for compounds 132b-e are tabulated in Table 21. Some of the $^{13}$C NMR chemical shifts were assigned by comparison with $^{13}$C NMR chemical shift assignments made by others for similar 1H-pyrazoles. The C-3 chemical shifts appear in the region of 139.42-140.88 ppm, the C-4 chemical shifts appear in the region of 108.94-111.27 ppm, and the C-5 chemical shifts appear in the region of 139.99-142.66 ppm.

1H-Pyrazoles 131b-f are solids, unlike 1H-pyrazoles 132b-e which are oils. In the $^1$H NMR spectra of these compounds, the carbomethoxy singlet appears in the region of 3.85-3.92 ppm and the methyl singlet appears in the region of 2.21-2.47 ppm. Only for compounds 131d and 131f, was a broad NH singlet observed in their $^1$H NMR spectra (4.5-5.1 ppm). Selected $^{13}$C NMR chemical shifts for 1H-pyrazoles 131b-f are located in Table 22. Some of the $^{13}$C NMR chemical shifts were assigned by comparison with chemical shift assignments made by others, for similar 1H-pyrazoles. The C-3 chemical shifts appear in the region of 130.03-139.91 ppm, the C-4 chemical shifts appear in the region of 114.50-129.12 ppm, and the C-5 chemical shifts arise in the region of 137.23-144.31 ppm.

The structure of compound 135c was assigned because of the close similarity of its $^1$H NMR spectrum to the $^1$H NMR spectrum of 131c. Furthermore, 135c eluted just before 131c in centrifugal chromatography (silica gel). As mentioned in Chapter 2, compound 119 is less polar than compound 118.
Table 21.

Selected $^{13}$C NMR chemical shifts of 132b-e in CDCl$_3$.

<table>
<thead>
<tr>
<th></th>
<th>C-3</th>
<th>C-4</th>
<th>C-5</th>
<th>C-6</th>
<th>C-7</th>
<th>C-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>132b</td>
<td>140.88</td>
<td>109.23</td>
<td>142.36</td>
<td>162.85</td>
<td>51.97</td>
<td>10.69</td>
</tr>
<tr>
<td>132c</td>
<td>139.42</td>
<td>111.27</td>
<td>139.99</td>
<td>163.24</td>
<td>51.76</td>
<td>14.65</td>
</tr>
<tr>
<td>132d</td>
<td>139.50</td>
<td>111.26</td>
<td>140.16</td>
<td>163.30</td>
<td>51.80</td>
<td>15.00</td>
</tr>
<tr>
<td>132e</td>
<td>139.95</td>
<td>108.94</td>
<td>142.03</td>
<td>163.03</td>
<td>51.91</td>
<td>11.29</td>
</tr>
</tbody>
</table>
Table 22.

Selected $^{13}\text{C}$ NMR chemical shifts of 131b-f in CDCl$_3$.

<table>
<thead>
<tr>
<th>131</th>
<th>C-3</th>
<th>C-4</th>
<th>C-5</th>
<th>C-6</th>
<th>C-7</th>
<th>C-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>131b</td>
<td>137.95</td>
<td>117.88</td>
<td>144.31</td>
<td>161.93</td>
<td>10.39</td>
<td>51.92</td>
</tr>
<tr>
<td>131c</td>
<td>139.91</td>
<td>129.12</td>
<td>142.49</td>
<td>163.01</td>
<td>14.16</td>
<td>51.92</td>
</tr>
<tr>
<td>131d</td>
<td>130.03</td>
<td>114.50</td>
<td>137.23</td>
<td>162.71</td>
<td>15.37</td>
<td>52.05</td>
</tr>
<tr>
<td>131e</td>
<td>136.75</td>
<td>120.91</td>
<td>143.21</td>
<td>162.21</td>
<td>10.50</td>
<td>51.63</td>
</tr>
<tr>
<td>131f</td>
<td>136.91</td>
<td>120.45</td>
<td>143.31</td>
<td>162.22</td>
<td>10.48</td>
<td>51.61</td>
</tr>
</tbody>
</table>
3.6 Rearrangement of 128b in dichloromethane

The rearrangement of 3H-pyrazole 128b in dichloromethane was investigated. This solvent should increase ion-pair separations and give pyrazole products resulting from collapse of a more separated ion-pair intermediate.

Oxadiazoline 114b and methyl propiolate were dissolved in dichloromethane (base washed and distilled) and irradiated at 300 nm for 6 hours. 3H-Pyrazole 128b rearranged in the medium in which it was generated to give several interesting rearrangement products. Scheme 30 gives the percentages of those products (by 1H NMR spectroscopy) as well as a proposed mechanistic outline for their formation. 3H-Pyrazole 128b dissociates to ion-pair 129b in dichloromethane. The methoxymethyl cation then collapses on both nitrogen atoms of the pyrazole anion to give 132b (24%) and 139b (8%). The methoxymethyl cation also collapses on carbon, adjacent to the migration origin, to afford unstable 4H-pyrazole 130b. Fast migration of hydrogen to nitrogen in this pyrazole to nitrogen affords 1H-pyrazole 131b (50%). The other products are 140b and 136. Alkylation of 131b with the cation of ion-pair intermediate 129b results in proton loss and the formation of 140b (11%). Protonation of the anion of ion-pair 129b gives rise to compound 136. The formation of 139b, 136, and 140b supports a stepwise mechanism involving an ion-pair intermediate in the rearrangement of 3H-pyrazole 128b.
Scheme 30
The structures of compounds 139b and 140b were assigned on the basis of $^1$H and $^{13}$C NMR spectroscopy as well as their mass spectrometric molecular masses. $^1$H NMR NOE experiments were very useful in determining the structures of compounds 139b and 140b. Irradiation of the methyl singlet at 2.30 ppm of 139b gave enhancement only at 6.70 ppm (vinyl proton). This experiment confirms that the methoxymethyl substituent is not in a 1,5-relationship with the methyl substituent. As mentioned above, for compound 132b, irradiation of the methyl singlet at 2.38 ppm caused enhancement of both the CH$_2$ singlet of methoxymethyl at 5.45 ppm and the CH singlet at 6.63 ppm (methoxymethyl and methyl substituents are in a 1,5-relationship).

$^1$H NOE experiments were crucial in determining the structure of compound 140b. Irradiation of the N-methylene singlet of 140b showed enhancement only at 3.32 ppm (N-CH$_2$OCH$_3$). This experiment confirms that the methoxymethyl substituent is not in a 1,5-relationship with the methyl substituent. Furthermore, irradiation of the C-methylene singlet at 4.55 ppm showed enhancement of both the singlet at 3.35 ppm (C-CH$_2$OCH$_3$) and the singlet at 2.34 ppm (CH$_3$). This experiment demonstrates that the methoxymethyl substituent on carbon is in a 3,4-relationship with the methyl substituent.
3.7 Rearrangement of 3H-pyrazoles 128c-f in acetone-\text{d}_6

The rearrangements of 3H-pyrazoles 128c-f in acetone-\text{d}_6 were also investigated. Since the observed rate constants for the rearrangement of these 3H-pyrazoles could be determined, it was possible to quantitate the effect of a change of solvent polarity (benzene-\text{d}_6 to acetone-\text{d}_6) on the observed rates of rearrangement.

Table 23 gives the products from the rearrangement of 3H-pyrazoles 128c-f in acetone-\text{d}_6 solvent. The percentage yields were determined by $^1$H NMR spectroscopy after the rearrangement of these 3H-pyrazoles was complete.

3H-Pyrazole 128c rearranged in acetone-\text{d}_6 at 90 °C with an observed rate constant of $9.7 \pm 0.3 \times 10^{-5}$ s$^{-1}$, which is similar to its observed rate constant of $1.06 \pm 0.03 \times 10^{-4}$ s$^{-1}$ in benzene-\text{d}_6. This is very unusual for a rearrangement which presumably proceeds via an ion-pair intermediate. The move to a more polar solvent should increase the rate of rearrangement. The products of rearrangement in acetone-\text{d}_6 were 131c (38%), 135c (7%), 132e (15%), 136 (41%), and isobutene (34%). The ratio of rates of migration of tert-butyl to C-4 and N-2 was 3 : 1. The reaction products 136 and isobutene suggest the presence of a tert-butyl cation and pyrazole anion intermediate.

The rearrangement of 128d also proceeded with similar rate constants in both acetone-\text{d}_6 [$k = (8.9 \pm 0.4) \times 10^{-5}$ s$^{-1}$] and benzene-\text{d}_6 [$k = (1.1 \pm 0.1) \times 10^{-4}$ s$^{-1}$] solvents. The products of rearrangement in acetone-\text{d}_6 were 131d (72%) and 132d (28%). The ratio of migration rates of 1-adamantyl to C-4 and N-2 was approximately 3 : 1.
Table 23. Products and product yields* from the thermal rearrangements of 128b-f in acetone-\textit{d}_6

<table>
<thead>
<tr>
<th>128e,\textsuperscript{b}</th>
<th>128d,\textsuperscript{c}</th>
<th>128e,\textsuperscript{d}</th>
<th>128f,\textsuperscript{e}</th>
</tr>
</thead>
<tbody>
<tr>
<td>R=C(\textit{Me})\textsubscript{3}</td>
<td>R=1-adamantyl</td>
<td>R=p-\textit{CH}_2\textit{C}_6\textit{H}_4\textit{OMe}</td>
<td>R=\textit{CH}_2\textit{C}_6\textit{H}_5</td>
</tr>
<tr>
<td>38</td>
<td>72</td>
<td>91</td>
<td>100</td>
</tr>
<tr>
<td>15</td>
<td>28</td>
<td>9</td>
<td>nil</td>
</tr>
<tr>
<td>7</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>41</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>isobutene,</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>34</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\* At the level of detection afforded by \textsuperscript{1}H NMR spectroscopy, the products listed were the only products from rearrangement and the yield numbers (%) reflect materials balance prior to opening of a tube.

\textsuperscript{b} Rearrangement at 90 °C with \( k = (9.7 \pm 0.3) \times 10^{-5} \text{ s}^{-1} \).

\textsuperscript{c} Rearrangement at 90 °C with \( k = (8.9 \pm 0.4) \times 10^{-5} \text{ s}^{-1} \).

\textsuperscript{d} Rearrangement at 60 °C with \( k = (2.1 \pm 0.1) \times 10^{-4} \text{ s}^{-1} \).

\textsuperscript{e} Rearrangement at 90 °C with \( k = (2.80 \pm .05) \times 10^{-4} \text{ s}^{-1} \).
The observed rate of rearrangement of 128e in acetone-\(d_6\) [\(k = (2.1 \pm 0.1) \times 10^{-4} \text{ s}^{-1}\)] was less than its observed rate of rearrangement in benzene-\(d_6\) [\(k = (3.6 \pm 0.2) \times 10^{-4} \text{ s}^{-1}\)]. The products of rearrangement in acetone-\(d_6\) were 131e (91%) and 132e (9%) from which the ratio of rates of migration of p-methoxybenzyl to C-4 and N-2 was approximately 10 : 1.0.

3H-Pyrazole 128f rearranged in acetone-\(d_6\) [\(k = (2.80 \pm 0.05) \times 10^{-4} \text{ s}^{-1}\)] with essentially the same rate constant as it did in benzene-\(d_6\) solvent. Once again, the only rearrangement product was 131f. If the rearrangement of 3H-pyrazole 128f was concerted in nature, a change in solvent polarity should not effect the rate of rearrangement; this was observed.

The similar rates of rearrangement of 3H-pyrazoles 128c-e in benzene-\(d_6\) and acetone-\(d_6\) solvents seems to conflict with an ion-pair mechanism for rearrangement. First, 3H-pyrazole 128c fragments to give isobutene and 136 as products in both solvents, which suggests the presence of an ion-pair intermediate. However, moving to a more polar solvent does not increase the rate of rearrangement of 128c as would be expected. Second, 3H-pyrazole 128e (\(R = p-\text{CH}_2\text{C}_6\text{H}_4\text{OMe}\)) rearranges approximately 10 times faster than 3\(\text{\textit{rl}}\)-pyrazole 128f (\(R = \text{CH}_2\text{C}_6\text{H}_5\)); this substituent effect on the rate of rearrangement suggests some degree of positive charge development on R in the transition state for migration of the p-methoxybenzyl substituent. Therefore, moving to a more polar solvent should increase the rate of rearrangement of 128e. Unfortunately, a comparison of the rates of solvolysis of RX (X = halide) in benzene and acetone solvents is not available.
3.8 Rearrangement of 3H-pyrazoles 128b-f in methanol or methanol-d₄

In an effort to trap any intermediate ion pairs in the rearrangements of 128b-f, the rearrangements were carried out in methanol solvent. Perhaps this hydrogen-bonding solvent would give rise to rate enhancements for the rearrangement of 3H-pyrazoles 128c-f.

Table 24 reveals the products from the rearrangement of 3H-pyrazoles 128b-f in methanol or methanol-d₄ solvents. The percentages reported were determined by ¹H NMR spectroscopy, following the complete rearrangement of 128b-f.

3H-Pyrazole 128b rearranged at ambient temperature in methanol-d₄ solvent in the medium in which it was generated. Rearrangement gave 131b (53%), from migration of the methoxymethyl cation to carbon and 132b (21%), from migration of the methoxymethyl cation to nitrogen. 1H-Pyrazole 136 (D analogue, 26%) and 141 (dimethoxymethane-d₅, 26%) are also products. Dimethoxymethane-d₅ was confirmed by ¹H NMR spectroscopy and gas chromatography spiking experiments with an authentic sample of the non-deuterated analogue. Trapping of an ion-pair intermediate provides strong evidence that 3H-pyrazole 128b rearranges by a stepwise mechanism. A smaller portion of the cation intermediate was intercepted from 128b (26%) compared to 111b (75%), which suggests that the ion-pair intermediate from 128b is "tighter" than the ion-pair intermediate from 111b.
Table 24. Products and product yields\(^a\) from the thermal rearrangements of 128b-f in methanol.

<table>
<thead>
<tr>
<th></th>
<th>128b,(\text{b}^\text{a})</th>
<th>131</th>
<th>132</th>
<th>135</th>
<th>136</th>
<th>ROCH(_3)</th>
<th>+ other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R=CH(_3)OMe</td>
<td>53</td>
<td>21</td>
<td>nil</td>
<td>26(^e)</td>
<td>26(^d)</td>
<td></td>
</tr>
<tr>
<td>128c,(\text{c}^\text{a})</td>
<td>R=C(Me)(_3)</td>
<td>18</td>
<td>16</td>
<td>6</td>
<td>60(^f)</td>
<td>31(^d)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>R=1-adamantyl</td>
<td>81</td>
<td>19</td>
<td>nil</td>
<td>trace amount</td>
<td>trace amount</td>
<td></td>
</tr>
<tr>
<td>128d,(\text{d}^\text{a})</td>
<td>R=p-CH(_2)CH(_2)OMe</td>
<td>75</td>
<td>25</td>
<td>nil</td>
<td>trace amount</td>
<td>trace amount</td>
<td></td>
</tr>
<tr>
<td>128e,(\text{e}^\text{a})</td>
<td>R=CH(_2)C(_2)H(_3)</td>
<td>100</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td>nil</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) At the level of detection afforded by \(^1\)H NMR spectroscopy, the products listed were the only products from rearrangement and the yield numbers (% ) reflect materials balance prior to opening of a tube.

\(^b\) Rearrangement at ambient temperature.

\(^c\) D analogue.

\(^d\) CD\(_3\)OR, from rearrangement in CD\(_3\)OD at ambient temperature.

\(^e\) Rearrangement at 90 °C.

\(^f\) Mixture of H and D analogues.

\(^g\) Rearrangement in methanol at 65 °C.
Likewise, an ion-pair intermediate from 3H-pyrazole 128c was intercepted by methanol-$d_4$. After 3H-pyrazole 128c was heated at 90 °C for 20 minutes, $^1$H NMR spectroscopy revealed that thermal rearrangement was complete. tert-Butyl methyl ether-$d_4$ (141c) was present in a 31% yield. The presence of this compound was confirmed by $^1$H NMR spectroscopy and gas chromatography spiking experiments with an authentic sample of the non-deuterated analogue. Other products included 136 (a mixture of H and D analogues, 60%), 131c (18%), 132c (16%), 135e (6%), and isobutene (27%). The products force the conclusion that an intermediate ion pair was generated during the rearrangement of 128c in methanol-$d_4$.

In another experiment, the observed rate constant $[(4.7 \pm 0.1) \times 10^{-4} \text{ s}^{-1}]$ was determined for the rearrangement of 128c in methanol-$d_4$ at 50 °C. The observed rate constant for rearrangement of 128c is approximately 80 times greater in methanol-$d_4$, compared to acetone-$d_6$. This rate enhancement was estimated by assuming a factor of 2 per 10 °C for the temperature difference.

Thermal rearrangement of both 128d and 128e afforded only trace amounts of 136 and 141, after refluxing in methanol solvent for 0.5 hours. The presence of these compounds was confirmed by $^1$H NMR and gas chromatography spiking experiments with compounds prepared by another route.$^{193,194}$ 3H-Pyrazole 128d afforded 131d (81%) and 132 (19%) from rearrangement in methanol solvent while 128e afforded 131e (75%) and 132e (25%). Since rearrangement is complete after 0.5 hours at 65 °C there is a rearrangement rate enhancement for both these 3H-pyrazoles compared to their rearrangements in benzene-$d_6$ or acetone-$d_6$. Presumably, an ion-pair mechanism operates
in these rearrangements, but the ion-pairs in these cases are very "tight" and do not become solvent-separated.

$3H$-Pyrazole 128f rearranged completely, after refluxing in methanol for 0.5 hours, to afford only 131f. Benzyl methyl ether and 136 could not be detected. Since rearrangement was complete after only 0.5 hours at 65 °C, there is also a rate enhancement (at least 41-fold) in this solvent of higher polarity. Presumably, $3H$-pyrazole 128f rearranges by a concerted mechanism with some charge separation.

3.9 Conclusion.

It appears that $3H$-pyrazoles 128b-e rearrange by a stepwise mechanism in methanol solvent since a portion of an ion-pair intermediate was intercepted. However, it seems that the ion pairs from these $3H$-pyrazoles are very "tight" since a smaller portion of the ion-pair intermediate was intercepted than from the analogous $3H$-pyrazoles (111b-e). This is reasonable because the intermediate pyrazole anion derived from $3H$-pyrazoles 128b-e is less stable than the anion derived from $3H$-pyrazoles 111b-e (Scheme 24). The large rate enhancements for the rearrangements of $3H$-pyrazoles 128b-e in methanol compared to benzene also provides support for a stepwise mechanism for rearrangement in methanol solvent.

$3H$-Pyrazole 128b rearranges by a stepwise mechanism in both benzene and dichloromethane because of the large rate enhancements for these rearrangements compared to $3H$-pyrazole 128f ($R = \text{CH}_3$). Furthermore, in dichloromethane solvent 128b affords some products (136, 139b, and 140b) which could not have arisen from a
concerted mechanism for rearrangement. 3H-Pyrazole 128c appears to rearrange by a stepwise mechanism in both benzene-$d_6$ and acetone-$d_6$ because isobutene and 136 were reaction products. For 3H-pyrazoles 128d and 128e it is unclear whether their rearrangements in benzene-$d_6$ and acetone-$d_6$ solvents are concerted, with some charge separation, or stepwise. It seems that 3H-pyrazole 128f rearranges by "normal" [1,5]-sigmatropic shifts of benzyl in benzene-$d_6$, acetone-$d_6$, and methanol solvents. Its rearrangement in methanol seems to involve some charge separation because of the rate enhancement observed in this solvent of higher polarity even though there was no evidence, from trapping, that an ion-pair intermediate is involved.

The observed rate constants for the thermal rearrangements of 128c-e can be compared to the observed rate constants for the thermal rearrangements of 111c-e (Chapter 2) in benzene-$d_6$. The following rate enhancements were estimated by assuming a 2-fold increase in the rate constant for every 10 °C increase in temperature. There is a 27-fold increase in the rate of rearrangement of 111c ($k = 6.2 \times 10^{-3} \text{ s}^{-1}$, 35 °C) compared to 128c ($k = 1.06 \times 10^{-4} \text{ s}^{-1}$, 90 °C), a 23-fold increase in the rate of rearrangement of 111d ($k = 5.6 \times 10^{-5} \text{ s}^{-1}$, 35 °C) compared to 128d ($k = 1.1 \times 10^{-4} \text{ s}^{-1}$, 90 °C), and a 4-fold increase in the rate of rearrangement of 111e ($k = 9.80 \times 10^{-5} \text{ s}^{-1}$, 20 °C) compared to 128e ($k = 3.6 \times 10^{-4} \text{ s}^{-1}$, 60 °C). Therefore, replacing a carbomethoxy group by a hydrogen atom at C-4 of 3H-pyrazole 111 reduces the overall rate of rearrangement. However, the rate reduction is more pronounced for migrating groups which are less stable in cationic form (i.e. R = C(Me)$_3$ and R = 1-adamantyl).

A continuum exists in [1,5]-sigmatropic rearrangements which runs from concerted
with very little charge separation, through transition structures with increasing charge separation, to the two-step, ion-pair extreme. This is reflected in the results in this chapter. The rearrangement of 3H-pyrazole 128f seems to fall in the concerted category with some degree of charge separation. 3H-Pyrazoles 128d and 128e seem to be "borderline" between concerted with considerable charge separation and ion pair. At the other extreme, the rearrangement of 3H-pyrazoles 128b and 128c appear to proceed by a stepwise, ion-pair mechanism.

3.10 Synthetic applications

This work has shown that good yields of 1H-pyrazoles 131d, 131e, and 131f, can be obtained by a convenient synthetic route. This synthetic methodology could provide access to other 1H-pyrazoles of general structure 143 with a variety of alkyl substituents at C-4 and C-5 (Scheme 31). New oxadiazolines 114 would provide diazoalkanes with different R¹ and R² substituents. A 1,3-dipolar cycloaddition of 117 to methyl propiolate generates 3H-pyrazole 142 with different substituents at the tetrahedral carbon centre (ie. R¹ = R² = CH₂CH₃ or CH(CH₃)₂). Thermal rearrangement of this 3H-pyrazole gives a 1H-pyrazole with new substituents at C-4 and C-5 of 143. If 3H-pyrazole 142 contained substituents where R¹R² = (CH₂)₄ or R¹R² = (CH₂)₅ bicyclic compounds such as 144 and 145 could be synthesized. The synthesis of these new compounds could be useful, since the pyrazole nucleus has been found to be biologically active.⁶¹,⁶⁴
Scheme 31

(a: R^1=R^2=CH_2CH_3; b: R^1=R^2=CH(CH_3)_2; c: R^1R^2=(CH_2)_4; d: R^1R^2=(CH_2)_5)
CHAPTER 4

Thermal Rearrangements of 5-Alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes

4.0. Objective

The discovery that some 3H-pyrazoles, as well as some 4H-pyrazoles, undergo thermal rearrangement by a stepwise mechanism involving the formation of intermediate ion pairs (Chapters 2 and 3) raised a question about the generality of rearrangement by such a mechanism. It became of interest to determine if any non-heterocyclic analogues of 3H-pyrazoles, some cyclopentadiene derivatives, were also capable of thermal rearrangement via a stepwise mechanism.

Cyclopentadienes generally undergo thermal rearrangement by [1,5]-sigmatropic migrations of a substituent from the tetrahedral carbon centre of the cyclopentadiene ring, but in 1984 Mikhailov and coworkers discovered that 5-aryloazo-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes 146a-f undergo thermal rearrangements via ion-pair intermediates (Scheme 32).56

In the 1H NMR spectra of 146a-d in benzonitrile solution, the signals for the protons of the methoxycarbonyl groups appear in the form of a singlet at 30 °C. With a decrease in temperature of the solution this peak broadens, and at -35 °C splits into
a triplet with intensity ratios of 2 : 2 : 1. Such spectral behaviour was attributed to the exchange of the positions of the arylazo groups in the cyclopentadiene rings, which takes place by reversible formation of ion-pair intermediates 147a-d from covalent substrates 146a-d. For compounds 146e and 146f the migration of arylazo around the cyclopentadiene ring takes place very rapidly on the $^1$H NMR time scale, and even in solutions at -50 to -70 °C, the signal for the protons of the methoxycarbonyl groups is in the form of a narrow singlet. The degenerate rearrangement of these cyclopentadienes can be viewed as "formal" [1,5]-sigmatropic rearrangements because the products of rearrangement are the same as those from concerted [1,5]-sigmatropic migrations of the arylazo groups.

\begin{align*}
146a-f \ (E=CO_2CH_3) & \quad \Leftrightarrow \quad 147a-f \\
& \quad \text{(a: } X=H; \ b: X=I; \ c: X=Cl; \ d: X=Br; \ e: X=OMe; \ f: X=Me) 
\end{align*}

Scheme 32
Presumably, stepwise rearrangements of 146a-f take place because the arylazo groups form relatively stable cations and the cyclopentadiene anions are stabilized by electron-withdrawing carbomethoxy substituents. Electron-donating substituents in the ortho position of the arylazo ring were found to enhance the rate of rearrangement; a result of increased stabilization of the cation intermediate.

The thermal rearrangements of several 5-alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes were investigated by Hoffmann and coworkers.52,54,55 An example of a "typical" rearrangement of a 5-alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadiene (Scheme 33) comes from their studies of 148f (R=Me).56 Between 105 and 145 °C in 1,2-dichlorobenzene, an equilibrium is set up between 148f and 149f by [1,5]-sigmatropic carbomethoxy shifts. The cyclopentadienes 148f and 149f were obtained in an equimolar ratio and could not be individually isolated by chromatography techniques. At a higher temperature (160 °C), 148f (34%), 149f (29%), and 150f (37%) were obtained in solution. Therefore, at the higher temperature, another [1,5]-sigmatropic carbomethoxy migration in 149f generates 150f.

It follows from Hoffmann's investigations that 5-alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes generally rearrange by [1,5]-sigmatropic carbomethoxy migrations. The carbomethoxy substituent is known to have a high migratory aptitude in [1,5]-sigmatropic rearrangements,51-56 but a low migratory aptitude in carbocation rearrangements.183,184 Hoffmann and coworkers did not investigate the thermal rearrangements of any 5-alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)
cyclopentadienes bearing alkyl substituents at C-5 that are relatively stable in cationic form.

\[
\begin{align*}
148f \quad (R=\text{Me})
\quad E=\text{CO}_2\text{Me} \\
150f \\
159f
\end{align*}
\]

**Scheme 33**

It became of interest to investigate the thermal rearrangements of 148a-e (Scheme 34) to determine if dissociation to ion-pairs 151a-e occurs during rearrangement (path a) or if rearrangement occurs by concerted [1,5]-sigmatropic migrations of the carboxy substituents (path b). The alkyl substituents chosen were CHPh₂, CH₂OMe, 1-adamantyl, p-CH₂C₆H₄OMe, and CH₂C₆H₅ because they readily form cations in solvolysis reactions of R-X (X = halogen). If 148a-e undergo thermal rearrangement by successive migrations of K (path a), then the 5 carboxy substituents of 148a-e would appear in the form of a singlet in the ¹H NMR spectra. Rate constants and activation parameters for these degenerate rearrangements could be determined by ¹H NMR spectroscopy, based on line shape analysis at various temperatures.
Scheme 34

4.1 Synthesis of 5-alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes 148a-f

Compounds 148a-e were prepared by a modification of a procedure used for the synthesis of 5-ethyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadiene.\textsuperscript{54} Compound 148f was also synthesized so that spectral data could be obtained for its rearrangement products 149f and 150f. If cyclopentadienes 148a-e rearrange by [1,5]-carbomethoxy migrations, the rearrangement products could be identified by comparing their spectral data to those of 149f and 150f.

Cyclopentadienes 148a-f were synthesized (Scheme 35) by first mixing pentakis(methoxycarbonyl)cyclopentadiene with Ag\textsubscript{2}O in benzene solution to generate ion-pair 152. Second, the anion of 153 was alkylated with the appropriate alkyl halide. The
percentage yields of 148a-f were not optimized. Cyclopentadiene 148f had been previously prepared by others.\textsuperscript{54,55,205}

\[
\begin{align*}
152 & \quad (E=\text{CO}_2\text{Me}) \\
153 & \\
148 & \quad (R=\text{Me})
\end{align*}
\]

a: $R=\text{CH(Ph)}_2$

b: $R=\text{CH}_2\text{OMe}$

c: $R=1\text{-adamantyl}$

d: $R=p\text{-CH}_2\text{C}_6\text{H}_4\text{OMe}$

e: $R=\text{CH}_2\text{C}_6\text{H}_5$

f: $R=\text{Me}$

Scheme 35

Cyclopentadienes 148a-f are stable compounds at ambient temperature in CDCl$_3$ solution and do not undergo rearrangement according to their $^1$H NMR spectra. Furthermore, compounds 148a-d do not undergo rearrangement in benzonitrile solvent according to their $^1$H NMR spectra. The compounds were identified on the basis of their $^1$H and $^{13}$C NMR spectra as well as their mass spectrometric masses. The $^1$H NMR spectra of cyclopentadienes 148a-f are reported in Table 25. A total of 3 carbomethoxy singlets, in a 2 : 2 : 1 integrated intensity ratio, are observed in the $^1$H NMR spectra of compounds 148a-d and compound 148f. For cyclopentadiene 148e, the $\text{CH}_2$ singlet appears at the same chemical shift as one of the carbomethoxy proton singlets.
Selected $^{13}$C NMR chemical shifts for compounds 148a-f are reported in Table 26. The C-1 and C-4 chemical shifts appear in the range of 141.78-144.86 ppm while the C-2 and C-3 chemical shifts appear in the range of 139.65-142.67 ppm. Furthermore, the C-5 chemical shift of cyclopentadienes 148a-f appears in the range of 63.60-71.84 ppm. Some of the $^{13}$C NMR chemical shifts were assigned on the basis of the $^{13}$C NMR chemical shift assignments made for 1,3-cyclopentadiene.$^{206}$

4.2 Heating cyclopentadienes 148a and 148b in the NMR probe

If cyclopentadienes 148a-e undergo thermal rearrangement by migration of their respective R groups, these degenerate rearrangements could be observed by $^1$H NMR spectroscopy. Cyclopentadienes 148a and 148b were heated in the NMR probe in an effort to observe any potential rearrangement. These cyclopentadienes contain R substituents which, in cationic form, are the most stable ones in the series of cyclopentadienes 148a-e.

Compounds 148a and 148b were warmed in the NMR probe to 80 °C in toluene-$d_6$ solvent. At this temperature, 3 carbomethoxy singlets were observed in the $^1$H NMR spectra of both 148a and 148b. Furthermore, there was no broadening of the carbomethoxy singlets in these $^1$H NMR spectra at 80 °C. Therefore, rearrangement was not observable by $^1$H NMR spectroscopy at this temperature.
<table>
<thead>
<tr>
<th>148</th>
<th>(^{1}H) NMR (200 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>148a, R=CHPh₂</td>
<td>7.35-7.17 (m, 10 H, 2 Ph), 5.60 (s, 1 H, CH), 3.81 (s, 6 H, 2 COOMe), 3.63 (s, 3 H, COOMe), 3.36 (s, 6 H, COOMe).</td>
</tr>
<tr>
<td>148b, R=CH₂OMe</td>
<td>4.23 (s, 2 H, CH₂), 3.88 (s, 6 H, COOMe), 3.83 (s, 6 H, 2 COOMe), 3.68 (s, 3 H, COOMe), 3.26 (s, 3 H, OMe).</td>
</tr>
<tr>
<td>148c, R=1-adamantyl</td>
<td>3.86 (s, 6 H, 2 COOMe), 3.81 (s, 6 H, 2 COOMe), 3.64 (s, 3 H, COOMe), 1.95 (bs, 3 H, CH), 1.88 (bs, 6 H, 3 CH₂), 1.65 (bs, 6 H, 3 CH₂).</td>
</tr>
<tr>
<td>148d, R=p-CH₂C₆H₄OMe</td>
<td>6.92 (d, J= 8.7 Hz, 2 H, CH₃b), 6.69 (d, J = 8.7 Hz, 2 H, CH₃a), 3.87 (s, 6 H, 2 COOMe), 3.77 (s, 6 H, 2 COOMe), 3.74 (s, 3 H, COOMe), 3.71 (s, 2 H, CH₂), 3.69 (s, 3 H, OMe).</td>
</tr>
<tr>
<td>148e, R=CH₂C₆H₅</td>
<td>7.19-7.00 (m, 5 H, Ph), 3.87 (s, 6 H, 2 COOMe), 3.76 (s, 8 H, 2 COOMe + CH₂), 3.70 (s, 3 H, COOMe).</td>
</tr>
<tr>
<td>148f, R=Me</td>
<td>3.88 (s, 6 H, 2 COOMe), 3.83 (s, 6 H, 2 COOMe), 3.66 (s, 3 H, COOMe), 1.69 (s, 3 H, Me).</td>
</tr>
</tbody>
</table>
Table 26.

Selected $^{13}$C NMR chemical shifts for 148a-f in CDCl$_3$ (50 MHz).

<table>
<thead>
<tr>
<th>148</th>
<th>C$<em>{11}$, C$</em>{15}$</th>
<th>C$<em>{2}$, C$</em>{3}$</th>
<th>C$_{5}$</th>
<th>C$<em>{6}$, C$</em>{9}$</th>
<th>C$<em>{7}$, C$</em>{8}$</th>
<th>C$_{10}$</th>
<th>C$<em>{11}$, C$</em>{14}$</th>
<th>C$<em>{12}$, C$</em>{13}$</th>
<th>C$_{15}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>148a, R=CHPh$_2$</td>
<td>143.76</td>
<td>142.67</td>
<td>71.45</td>
<td>162.66</td>
<td>161.48</td>
<td>166.70</td>
<td>52.65</td>
<td>52.80</td>
<td>52.80</td>
</tr>
<tr>
<td>148b, R=CH$_2$OMe</td>
<td>141.78</td>
<td>141.67</td>
<td>71.84</td>
<td>162.55</td>
<td>161.92</td>
<td>165.76</td>
<td>55.72</td>
<td>52.56</td>
<td>53.21</td>
</tr>
<tr>
<td>148c, R=1-adamantyl</td>
<td>144.51</td>
<td>140.70</td>
<td>74.77</td>
<td>165.31</td>
<td>162.61</td>
<td>165.65</td>
<td>52.60</td>
<td>52.46</td>
<td>52.21</td>
</tr>
<tr>
<td>148d, R=p-CH$_2$C$_6$H$_5$OMe</td>
<td>142.87</td>
<td>141.70</td>
<td>68.48</td>
<td>162.34</td>
<td>162.11</td>
<td>167.33</td>
<td>52.66</td>
<td>52.66</td>
<td>53.30</td>
</tr>
<tr>
<td>148e, R=CH$_3$C$_6$H$_5$</td>
<td>142.70</td>
<td>141.82</td>
<td>68.13</td>
<td>162.30</td>
<td>162.06</td>
<td>176.29</td>
<td>52.69</td>
<td>52.67</td>
<td>53.35</td>
</tr>
<tr>
<td>148f, R=Me</td>
<td>144.86</td>
<td>139.65</td>
<td>63.50</td>
<td>162.62</td>
<td>161.82</td>
<td>167.40</td>
<td>52.75</td>
<td>52.59</td>
<td>53.24</td>
</tr>
</tbody>
</table>

* C$_{6}$,C$_{9}$ and C$_{7}$,C$_{8}$ may be reversed.

$^b$ C$_{11}$,C$_{14}$ and C$_{12}$,C$_{13}$ may be reversed.
The polarity of the solvent was increased to see if this would give observable rearrangement of 148b at an elevated temperature in the NMR probe. Cyclopentadiene 148b was heated to 75 °C in nitromethane-\textit{d}_4 solvent and at this temperature, three sharp carbomethoxy singlets were once again observed. Rearrangement in this solvent of higher polarity was still unobservable by \textit{\textsuperscript{1}}H NMR spectroscopy.

The maximum value for the observed constant for rearrangement that would not result in detectible line broadening is in the range of 3.1 - 4.7 s\textsuperscript{-1} (Appendix II contains the calculation of this value).\textsuperscript{297} Therefore, it seems that the rates of rearrangement of both 148a and 148b are too slow on the NMR time scale for detection.

4.3 Rearrangement of 148a-d in methanol

It was then decided to look at the reactions of cyclopentadienes 148a-e in methanol since this solvent could intercept any ion pairs that are formed during the migrations of R in cyclopentadienes 148a-e.

Cyclopentadiene 148a (R = CHPh\textsubscript{2}) was dissolved in methanol-\textit{d}_4 and after 3 minutes at room temperature, \textit{\textsuperscript{1}}H NMR spectroscopy revealed 148a (49%), 152 (51%), and 154f (D analogue, 51%) according to Scheme 36. The rate constant for the overall disappearance of 148a was estimated as 4 x 10\textsuperscript{3} s\textsuperscript{-1}, assuming first order kinetics. In another experiment, cyclopentadiene 148a was dissolved in methanol and after 20 minutes at room temperature, it had been converted to benzhydryl methyl ether and 152 in
quantitative yield. The identity of the methyl ether was confirmed by comparison of its spectroscopic data with those reported in the literature. This cyclopentadiene must have dissociated to an ion-pair intermediate, a cyclopentadiene anion derivative and a benzhydryl cation, which was subsequently trapped by methanol. It could not be determined if ion-pair collapse occurred in competition with ion-pair capture by methanol. Ion-pair collapse of 151a is actually overall degenerate rearrangement of 148a by a stepwise mechanism rather than by a concerted mechanism.

![Chemical Structure Diagram]

(a: R=CH(Ph)₂; b: R=CH₂OMe; c: R=1-adamantyl; d: R=p-CH₂C₆H₄OMe)

Scheme 36

Cyclopentadiene 148b (R = CH₂OMe) dissociates in methanol-₄ at 40 °C with an observed rate constant of \((6.2 \pm 0.3) \times 10^4 \text{ s}^{-1}\). After 2 hours at 40 °C, \(^1\text{H NMR spectroscopy revealed: dimethoxymethane-}₄\) (100%) and 152 (D-analogue, 100%). Dimethoxymethane-₄ was confirmed by \(^1\text{H NMR and gas chromatography spiking experiments with an authentic sample of dimethoxymethane. As in 148a, an ion-pair intermediate must have been formed and intercepted. The fact that 148a dissociates faster than 148b is a reflection of the stability of the intermediate cations of the ion-pairs;
benzhydryl cation being more stable than methoxymethyl cation. Cyclopentadiene 148a dissociates approximately 18 times faster than cyclopentadiene 148b, assuming a 2.8-fold increase in the observed rate constant for the 15 °C temperature difference.

Cyclopentadiene 148c (R = 1 adamantyl) also dissociates to an ion-pair intermediate in methanol solvent. The observed rate constant for the decrease in concentration of 148c in methanol-d₄ at 50 °C was (5.2 ± 0.2) x 10⁻⁴ s⁻¹. After 2 hours at 65 °C in methanol, 148c was quantitatively converted to 152 and 1-adamantyl methyl ether. The 1-adamantyl methyl ether was confirmed by comparison of its spectroscopic data to those of a sample prepared by another route.¹⁹³ Cyclopentadiene 148b dissociates in methanol-d₄ approximately twice as fast as cyclopentadiene 148c, assuming a 2-fold increase in the observed rate constant for the 10 °C temperature difference.

Cyclopentadiene 148d dissociates at 100 °C in methanol-d₄ with an observed rate constant of (3.14 ± 0.08) x 10⁻⁴. After 4 hours in methanol at 100 °C, it was converted to 154d (100%) and 152 (100%). The identity of the methyl ether was confirmed by comparison of its spectroscopic data to those of a sample prepared by another route.¹⁹⁴ Cyclopentadiene 148c dissociates in methanol-d₄ approximately 19 times faster than 148d, assuming a 2-fold increase in the observed rate constant for every 10 °C increase in temperature.

It is clear that cyclopentadienes 148a-d form ion pairs in methanol solvent which are subsequently intercepted by that solvent to give the appropriate methyl ethers (154) and cyclopentadiene 152 (Scheme 36). It is very unlikely that methanol reacts with cyclopentadienes 148a-d by a bimolecular nucleophilic substitution reaction at C-5
because for 148c especially, backside attack of a nucleophile is not possible due to the "bulkiness" of the 1-adamantyl substituent. The approximate relative rates for dissociation of these cyclopentadienes in methanol solvent are as follows: 148a (76), 148b (38), 148c (19), and 148d (1.0).

4.4 Rearrangement of 144e and 144f in methanol-\(d_4\)

The rearrangement of cyclopentadiene 148f (R = Me) had been studied previously,\textsuperscript{52,54,55} however, it was decided to reexamine the rearrangement of 148f in order to obtain spectral data on its rearrangement products to aid in the identification of the rearrangement products from 148e. Cyclopentadiene 148f was dissolved in methanol-\(d_4\) and heated in a sealed nmr tube at 140 °C for 35 minutes. \(^1\)H NMR spectroscopy revealed 148f (62%) and 149f (38%) according to Scheme 37. This cyclopentadiene rearranges by [1,5]-sigmatropic carbomethoxy shifts at this temperature. Cyclopentadienes 148f and 149f could not be separated, but their \(^1\)H and \(^{13}\)C NMR spectra could be obtained from this solution.

\[148f \text{ (R=Me)} \quad \leftrightarrow \quad 149f\]

Scheme 37
Cyclopentadiene 148e (R = CH₂C₆H₅) was dissolved in methanol-d₄ and heated in a sealed nmr tube at 140 °C for 3 hours. ¹H NMR spectroscopy of the solution revealed 148e (63%), 149e (29%), and 150e (8%) according to Scheme 38. This mixture of cyclopentadiene isomers could not be separated by centrifugal chromatography and compounds 149e and 150e were identified on the basis of ¹H NMR spectroscopy. It follows from the structures of the products that cyclopentadiene 148e undergoes thermal rearrangement by [1,5]-sigmatropic carbomethoxy migrations. Presumably, the benzyl substituent is not stable enough as a cation to dissociate heterolytically from covalent 148e in methanol solvent. Therefore, the para-methoxy substituent of 148d (R = p-CH₂C₆H₄OMe) is essential for ion-pair formation.

![Diagram](attachment:image.png)

Scheme 38

4.5 Conclusion

From the evidence presented above, it is clear that cyclopentadienes 148a-d dissociate in methanol solvent to give ion pairs. Presumably, collapse of the ion pairs to covalent 148a-d competes with solvent interception of these ion pairs. It has thus been
shown that cyclopentadienes with carbon-based alkyl groups can undergo stepwise rearrangement.

Unfortunately, these degenerate rearrangements could not be observed by $^1$H NMR spectroscopy. Cyclopentadienes 146a-f undergo faster stepwise rearrangement than 148a-d since rearrangements of the former in benzonitrile solution could be observed by $^1$H NMR spectroscopy while rearrangements of the latter could not. Therefore, the arylazo cations of 146a-f must be more stable than the alkyl-based cations formed from 148a-d.

The order of ease of dissociation of cyclopentadienes 148a-d in methanol-$d_4$ was established as 148a ($R = CHPh_2$) > 148b ($R = CH_2OMe$) > 148c ($R = 1$-adamantyl) > 148d ($R = p$-CH$_2$C$_6$H$_4$OMe). For 3$H$-pyrazoles 128, the order of rearrangement (methanol-$d_4$) was established as 128b ($R = CH_2OMe$) > 128e ($R = p$-CH$_2$C$_6$H$_4$OMe) > 128d ($R = 1$-adamantyl). The reactivity order (1-adamantyl < p-CH$_2$C$_6$H$_4$OMe) in the pyrazole series is reversed in the cyclopentadiene series. Steric hindrance in the ground state as well as cation stability presumably govern the rate of rearrangement of both the cyclopentadienes and the 3$H$-pyrazoles. It appears, however, that rate acceleration due to steric hindrance in the ground state of 148c may be the critical factor leading to a faster rate of dissociation of 148c compared to 148d. Steric acceleration is probably less important in the rates of rearrangement of 3$H$-pyrazoles 128d and 128e because of reduced steric crowding at C-3 in 128. A more frequent collapse of the ion pair from 148d (ion-pair return) compared to collapse of the ion pair from 148c (a factor where steric crowding could also play a role) could also lead to the overall faster rate of dissociation of 148c.
Cyclopentadienes 148a-d are stable compounds in CDCl₃ according to ¹H NMR spectroscopy at ambient temperature while the 3H-pyrazoles 111a, 111b, 111d, and 111e are not stable compounds in CDCl₃ at ambient temperature. 3H-Pyrazoles 111 undergo thermal rearrangements via ion-pair intermediates (Scheme 39). Therefore, this suggests that anion 155 is more stable than anion 156. The 5 carbethoxy substituents must be less stabilizing towards a cyclopentadiene anion than the combination of two ring nitrogen atoms, 2 carbethoxy substituents, and a destabilizing methyl substituent. Perhaps, the intermediate anion formed from the dissociation of 148a-d is less planar than the pyrazole anion formed from the thermal rearrangement of 111 since the carbethoxy substituents are presumably twisted out of plane in 156 to avoid steric congestion.

The rearrangement of cyclopentadiene 148e (R = CH₂C₆H₅) does not belong in the same mechanistic category as the rearrangements of cyclopentadienes 148a-d, which presumably rearrange by a stepwise mechanism. Cyclopentadiene 148e appears to rearrange by a concerted mechanism involving [1,5]-sigmatropic carbethoxy migrations. The benzyl substituent must not be sufficiently stable in cationic form for heterolytic cleavage in 148e.
(E=CO₂Me)

(a: R=CH₃Ph; b: R=CH₂OMe; d: R=1-adamantyl; e: R=p-CH₂C₆H₄OMe)

Scheme 39
CHAPTER 5

Experimental

5.0 General

Melting points were determined on a Thomas Hoover capillary melting point apparatus. Centrifugal chromatography was performed with silica gel (Merck Kieselgel 60 PF$_{254}$) coated plates (2-mm or 4-mm thick) spinning in a Chromatotron Model 7924T apparatus. Analytical thin-layer chromatography was performed with silica gel plates (E. Merck, D-Plastikfolien, Kieselgel 60 F$_{254}$). Proton nuclear magnetic resonance ($^1$H NMR) data were obtained on Varian EM-390, Bruker AC-200, Bruker WM-250, or Bruker AM-500 spectrometers. Chemical shifts are reported in delta (δ) units [parts per million (ppm)] downfield from tetramethylsilane, relative to the singlet at 7.24 ppm for chloroform in chloroform-$d_4$ or relative to the singlet at 7.15 ppm for benzene-$d_5$ in benzene-$d_6$. Splitting patterns are designated as: s, singlet; d, doublet; t, triplet; m, multiplet; bs, broad singlet. Coupling constants are reported in hertz (Hz). Carbon-13 nuclear magnetic resonance ($^{13}$C NMR) spectra were obtained at 50 MHz on a Bruker AC-200 or at 125 MHz on a Bruker AM-500 spectrometer and are reported in ppm relative to the centre line of a triplet at 77.0 ppm for samples run in chloroform-$d_4$ or a triplet at 128.0 for samples run in benzene-$d_6$. High resolution EI spectra were recorded
on a VG ZAB-E double focussing mass spectrometer. Samples were run at 70 eV, source
temperature 200 °C, resolution 5000. Samples were introduced by direct insertion probe.
Photolyses employed a Rayonet photochemical reactor fitted with 300 nm lamps. The
infrared spectra of a selected group of compounds are reported in Appendix III.

5.1 Preparation of 2-acetylhydrazones of ketones, (113).

The following ketones were purchased from Aldrich Chemical Co. and were used
as supplied: 1,1-diphenylacetone, methoxyacetone, pinacolone, 1-adamantyl methyl
ketone, 4-methoxyphenylacetone and phenylacetone. Compounds 113a, 113c, and 113d
were prepared by refluxing equimolar amounts of acetyl hydrazine and the appropriate
ketone in ethanol for 24 hours with 5 mol % of acetic acid. After the mixture was cooled
to room temperature, crystals formed. For the preparation of 113b and 113e, solutions of
equimolar amounts of acetyl hydrazine and the appropriate ketone in benzene were
refluxed until all the water was removed (Dean-Stark trap, 1 h for 113b and 4 h for
113e). The preparation of 111f was previously reported.188

1-Acetyl-2-(1,1-diphenyl-2-propylidene)hydrazine, (113a): 73% yield; mp 158-
159° C (EtOH); 1H NMR (90 MHz, CDCl₃) δ 8.82 (bs, 1 H, NH), 7.45-7.18 (m, 10 H,
2 Ph), 5.02 (s, 1 H), 2.08 (s, 3 H, Ac), 1.87 (s, 3 H, Me); 13C NMR (50 MHz, CDCl₃) δ
174.02, 151.73, 140.33 (2), 129.04 (4), 128.33 (4), 126.77 (2), 59.92, 20.34, 15.41; MS
m/z (M⁺) for C₁₇H₁₄N₂O calcd 266.1419, found 266.1403.
1-Acetyl-2-(1-methoxy-2-propylidene)hydrazine, (113b): 74% yield; mp 82-84 °C (EtOH); \(^1\)H NMR (90 MHz, CDCl\(_3\)) \(\delta\) 8.62 (bs, 1 H, NH), 4.00 (s, 2 H), 3.37 (s, 3 H, OMe), 2.28 (s, 3 H, Ac), 1.88 (s, 3 H, Me); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 174.15, 149.25, 75.97, 57.99, 20.28, 12.56; MS (Cl, CH\(_4\)) m/z (M+H)\(^+\) for \(\text{C}_5\text{H}_{12}\text{N}_2\text{O}_2\+\text{H}\) calcd 145.0977, found 145.0979.

1-Acetyl-2-(3,3-dimethyl-2-butyldiene)hydrazine, (113c): 75% yield; mp 82-83 °C (EtOH); (lit.\(^\text{119}\) mp 80-82 °C); The \(^1\)H NMR spectrum was reported.\(^\text{119}\) \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 174.01, 157.47, 38.52, 27.45 (3), 20.42, 11.12.

1-Acetyl-2-[1-(1-adamanthyl)-1-ethyldenejhydrazine, (113d): 75% yield; mp 169-170 °C (EtOH); \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 8.50 (bs, 1 H, NH), 2.27 (s, 3 H, Ac), 2.05 (bs, 3 H, CH), 1.74 (bs, 15 H, Me + 6 CH\(_2\)) \(^{13}\)C NMR (50 MHz,CDCl\(_3\)) \(\delta\) 173.84, 157.38, 40.35, 39.77, 39.45 (2), 36.88, 36.75 (2), 28.36, 28.19 (2), 20.43, 10.05; MS m/z (M\(^+\)) for \(\text{C}_{14}\text{H}_{22}\text{N}_2\text{O}\) calcd 234.1732, found 234.1736.

1-Acetyl-2-[1-(4-methoxyphenyl)-2-propylidenejhydrazine, (113e): 90% yield; mp 122-124°C (EtOAc); \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 8.76 (bs, 1 H, NH), 7.19 (d, 2 H, J = 7.9 Hz), 6.85 (d, 2 H, J = 7.9 Hz), 3.79 (s, 3 H, OMe), 3.48 (s, 2 H), 2.28 (s, 3 H, Ac), 1.75 (s, 3 H, Me); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 173.79, 158.29, 151.45, 129.71 (2), 128.73, 113.78 (2), 54.96, 44.29, 20.27, 14.53; MS m/z (M\(^+\)) for \(\text{C}_{12}\text{H}_{16}\text{N}_2\text{O}_2\) calcd 220.1212, found 220.1207.
5.2 Preparation of 5-alkyl-2-methoxy-2,5-dimethyl-\(\Delta^3\)-1,3,4-oxadiazolines, (114).

These compounds were obtained by a procedure similar to those described previously.\(^{119,188}\) However, a few modifications were made and therefore the complete procedure for their synthesis is reported here. To a yellow solution of lead tetraacetate (16.5 mmol) in absolute methanol (65 mL) at \(-10^\circ\)C was added the acetyl hydrazone 113 (15.0 mmol). The solution was stirred during the addition and thereafter. After 1 h, if the yellow colour had not been discharged, the cold bath was removed. After the yellow colour was eventually discharged, the reaction flask was once again cooled to \(-10^\circ\)C and potassium hydroxide (pellets, 16.5 mmol, dissolved in 10 mL of absolute methanol) was added to the reaction flask to destroy the acetoxy-oxadiazoline coproduct. The solution was allowed to warm to room temperature slowly and the reaction mixture was left stirring overnight. Most of the solvent was removed in vacuo, water was added to the residue, and the aqueous solution was extracted with CH\(_2\)Cl\(_2\). The organic layer was washed once with water before it was dried over magnesium sulfate. The solution was filtered and the solvent was removed in vacuo. The residue was purified by centrifugal chromatography (silica gel, 19:1 hexane/ethyl acetate). The synthesis and spectral data of oxadiazoline 114f were previously reported.\(^{188}\)

2-Methoxy-2,5-dimethyl-5-(1,1-di phenylmethyl)-\(\Delta^3\)-1,3,4-oxadiazoline, (114a): 63% yield; > 98% trans (by \(^1\)H NMR); \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 7.47-7.14 (m, 10 H, 2 Ph) 4.74 (s, 1 H, CH), 3.21 (s, 3 H, OMe), 1.53 (s, 3 H, Me), 0.80 (s, 3 H, Me); \(^13\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 138.63, 138.53, 133.83, 130.07 (4), 128.32 (2), 127.98 (2),
126.97, 126.91, 124.57, 59.46, 50.89, 23.78, 19.78; MS m/z (M+ - N₂) for C₁₆H₂₀O₂ calc'd 268.1463, found 268.1452.

2-Methoxy-5-methoxymethyl-2,5-dimethyl-Δ³-1,3,4-oxadiazoline, (114b): 45% yield; cis : trans ratio = 1.0 : 5.0; ¹H NMR of trans isomer (500 MHz, CDCl₃) δ 3.78 (d, 1 H, J = -10.8 Hz), 3.55 (d, 1 H, J = -10.8 Hz), 3.33 (s, 3 H, CH₂OMe), 3.12 (s, 3 H, OMe), 1.72 (s, 3 H, Me), 1.56 (s, 3 H, Me); ¹H NMR of cis isomer (500 MHz, CDCl₃) δ 3.72 (d, 1 H, J = -10.8 Hz), 3.69 (d, 1 H, J = -10.8 Hz), 3.41 (s, 3 H, CH₂OMe), 3.23 (s, 3 H, OMe), 1.63 (s, 3 H, Me), 1.45 (s, 3 H, Me); ¹³C NMR of trans isomer (50 MHz, CDCl₃) δ 134.82, 121.28, 74.80, 59.39, 50.26, 22.38, 19.38; ¹³C NMR of cis isomer (50 MHz, CDCl₃) δ 133.72, 120.42, 74.92, 59.52, 50.61, 23.52, 20.32; MS m/z (M+ - OMe) for C₁₂H₁₄N₂O₂ calc'd 143.0821, found 143.0804.

2-Methoxy-2,5-dimethyl-5-(2,2-dimethylethyl)-Δ³-1,3,4-oxadiazoline, (114c): 70% yield; The ¹H NMR spectrum was reported previously.¹¹⁹ ¹³C NMR (50 MHz, CDCl₃) δ 131.05, 127.77, 50.80, 37.36, 25.31 (3), 19.17, 19.09.

5-(1-Adamantyl)-2-methoxy-2,5-dimethyl-Δ³-1,3,4-oxadiazoline, (114d): 81% yield; mp 54-57 °C; > 94% trans (by ¹H NMR, 90 MHz);¹H NMR (200 MHz, CDCl₃) δ 3.37 (s, 3 H, OMe), 2.09-1.48 (m, 15 H), 1.77 (s, 3 H, Me), 1.37 (s, 3 H, Me). ¹³C NMR (50 MHz, CDCl₃) δ 130.76, 127.62, 50.86, 39.11, 36.74 (3), 36.65 (3), 28.16 (3), 9.15, 18.03; MS m/z (M+ - OMe) for C₁₄H₂₁N₂O calc'd 233.1654, found 233.1645.
2-Methoxy-5-(4-methoxybenzyl)-2,5-dimethyl-Δ3-1,3,4-oxadiazoline, (114e): 73% yield; cis : trans ratio = 1.0 : 2.7; 1H NMR of trans isomer (500 MHz, CDCl3) δ 7.07 (d, 2 H, J = 8.7 Hz), 6.80 (d, 2 H, J = 8.7 Hz), 3.77 (s, 3 H, C₆H₄OMe), 3.12 (s, 3 H, OMe), 3.18 (d, 1 H, J = -14.2 Hz), 3.04 (d, 1 H, J = -14.2 Hz), 1.56 (s, 3 H, Me), 1.21 (s, 3 H, Me); 1H NMR of cis isomer (500 MHz, CDCl3) δ 7.22 (d, 2 H, J = 8.7 Hz), 6.85 (d, 2 H, J = 8.7 Hz), 3.79 (s, 3 H, C₆H₄OMe), 3.23 (s, 1 H, J = -14.2 Hz), 3.13 (s, 3 H, OMe), 2.98 (d, 1 H, J = -14.2 Hz), 1.62 (s, 3 H, Me), 1.33 (s, 3 H, Me). Composite integrals for overlapping peaks were satisfactory. 13C NMR of trans isomer (50 MHz, CDCl3) δ 158.54, 133.85, 131.51 (2), 126.28, 122.10, 113.30 (2), 54.87, 50.28, 43.28, 22.48, 21.79; 13C NMR of cis isomer (50 MHz, CDCl3) δ 158.54 (overlaps with trans isomer), 133.35, 131.23 (2), 126.62, 121.38, 113.52 (2), 54.87 (overlaps with trans isomer), 50.40, 42.57, 23.16, 22.12; MS m/z (M⁺-N₂) for C₁₂H₁₈O₃ calcd 222.1256, found 222.1269.

5.3 Rearrangement of 3H-pyrazoles 111a-e in benzene-d₆

General method. Oxadiazoline 114 (0.25 mmol) and dimethyl acetylenedicarboxylate (DMAD) (0.30 mmol) in C₆D₆ (0.5 mL) were irradiated at room temperature with 300 nm light (Rayonet apparatus) for 6 h. A 1H NMR spectrum was taken of the photolysis solution to determine the percentages of reaction products.

Rearrangement of 111a. The percentages of 118a and 119a determined by 1H NMR spectroscopy (200 MHz) after photolysis of 114a were 91 and 9, respectively. The
volatiles were removed in vacuo and centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) gave 118a (51%) and 119a (8%).

5-Methyl-(1,1-diphenylmethyl)-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (118a): $^1$H NMR (200 MHz, CDCl$_3$) δ 7.34-7.17 (m, 10 H, 2 Ph), 6.71 (s, 1 H), 3.87 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 2.45 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 163.53, 163.21, 144.00, 143.50, 137.81 (2), 128.61 (4), 128.39 (4), 128.17 (2), 112.31, 67.00, 52.35, 51.67, 11.00; MS m/z (M$^+$) for C$_{21}$H$_{20}$N$_2$O$_4$ calcd 364.1423, found 364.1438.

3-Methyl-(1,1-diphenylmethyl)-1H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (119a): $^1$H NMR (200 MHz, CDCl$_3$) δ 7.32-7.16 (m, 10 H, 2 Ph) 6.95 (s, 1H), 3.79 (s, 3H, COOMe), 3.78 (s, 3H, COOMe), 2.38 (s, 3H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 161.50, 161.46, 149.98, 138.46 (2), 137.15, 128.66 (4), 128.42 (4), 128.06 (2), 112.93, 67.53, 52.92, 51.61, 13.50; MS m/z (M$^+$) for C$_{21}$H$_{20}$N$_2$O$_4$ calcd 364.1423, found 364.1413.

Rearrangement of 111b. The percentages of 118b and 120b determined by $^1$H NMR spectroscopy (200 MHz) after the photolysis of 114b were 77 and 23, respectively. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 118b (66%) and 121 (19%). The spectroscopic data for 121 were identical to those previously reported.$^{192}$ 4H-Pyrazole 120b could not be isolated without decomposition.
1-Methoxymethyl-5-methyl-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (118b):

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.43 (s, 2 H), 3.93 (s, 3 H, COOMe), 3.85 (s, 3 H, COOMe), 3.33 (s, 3 H, OMe), 2.57 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 163.23, 162.66, 144.55, 143.36, 113.50, 80.53, 56.80, 52.83, 51.74, 10.33; MS m/z (M$^+$) for C$_{10}$H$_{14}$N$_2$O$_3$ calcd 242.0903, found 242.0888.

In a $^1$H NOE experiment, irradiation of the N-methylene resonance (5.43 ppm) led to an enhancement of both the singlet at 3.33 ppm (OMe) and the singlet at 2.57 ppm (Me).

4-Methoxymethyl-5-methyl-4H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (120b):

$^1$H NMR (200 MHz, C$_6$D$_6$) $\delta$ 4.28 (d, 1 H, $J = -9.3$ Hz), 3.92 (d, 1 H, $J = -9.3$ Hz), 3.38 (s, 3 H, COOMe), 3.09 (s, 3 H, COOMe), 2.76 (s, 3 H, OMe), 1.97 (s, 3 H, Me).

**Rearrangement of 111c.** The percentages of 118c, 121, and isobutene determined by $^1$H NMR spectroscopy (90 MHz, sealed tube) were 39, 61, and 60, respectively. The solvent was removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 2:1 hexane/ethyl acetate) to give 118c (24%) and 121 (38%).

1-(tert-Butyl)-5-methyl-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (118c): $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 3.91 (s, 3 H, COOMe), 3.83 (s, 3 H, COOMe), 2.65 (s, 3 H, Me), 1.67 (s, 9 H, C(Me)$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 164.04, 163.43, 142.47, 140.82,
113.91, 61.87, 52.31, 51.65, 29.75, 13.15; MS m/z (M+) for C_{12}H_{18}N_{2}O_{4} calcd 254.1267, found 254.1266.

Rearrangement of 111d. The rearrangement of 111d appeared to go in quantitative yield by observation of the ¹H NMR (200 MHz) spectrum. Centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) gave ¹8d (63%).

1-(1-Adamantyl)-5-methyl-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (118d):
mp 141-143 ºC; ¹H NMR (200 MHz, CDCl₃) δ 3.90 (s, 3 H, OMe), 3.83 (s, 3 H, OMe), 2.69 (s, 3 H, Me), 2.31 (bs, 6 H, 3 CH₂), 2.24 (bs, 3 H, 3 CH₃), 1.75 (bs, 6 H, 3 CH₂); ¹³C NMR (50 MHz, CDCl₃) δ 164.20, 163.46, 142.53, 141.06, 113.99, 63.24, 52.30, 51.66, 41.66 (3), 35.89 (3), 29.79 (3), 13.48; MS m/z (M+) for C_{18}H_{24}N_{2}O_{4} calcd 332.1736, found 332.1739.

Rearrangement of 111e. The percentages of 118e and 120e determined by ¹H NMR spectroscopy (200 MHz) were 64 and 36, respectively. The volatiles were removed in vacuo and centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) gave 118e (37%) and 120e (17%).

1-(4-Methoxybenzyl)-5-methyl-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (118e): ¹H NMR (200 MHz, CDCl₃) δ 7.09 (d, 2 H, CH, J = 8.4 Hz) 6.84 (d, 2 H, CH, J = 8.4 Hz), 5.29 (s, 2 H, CH₂), 3.94 (s, 3 H, COOMe), 3.83 (s, 3 H, COOMe), 3.78 (s,
3 H, OMe), 2.40 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 163.34, 162.66, 159.40, 143.46, 142.77, 128.32 (2), 126.88, 114.22 (2), 112.83, 55.18, 53.52, 52.36, 51.61, 10.76; MS m/z (M$^+$) for C$_{16}$H$_{18}$N$_2$O$_5$ calcd 318.1216, found 318.1217.

4-(4-Methoxybenzyl)-5-methyl-4$H$-pyrazole-3,4-dicarboxylic acid dimethyl ester, (120e): $^1$H NMR (200 MHz, CDCl$_3$) δ 6.81 (d, 2 H, CH, $J = 8.7$ Hz), 6.69 (d, 2 H, CH, $J = 8.7$ Hz), 3.97 (s, 3 H, COOMe), 3.80 (d, 1 H, CH, $J = -14$ Hz), 3.71 (s, 3 H, COOMe), 3.71 (s, 3 H, OMe), 3.45 (d, 1 H, CH, $J = -14$ Hz), 2.38 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 176.52, 166.69, 165.27, 160.61, 159.08, 129.39 (2), 124.29, 114.86, 113.93 (2), 55.07, 53.65, 53.09, 36.77, 13.76; MS m/z (M$^+$) for C$_{16}$H$_{18}$N$_2$O$_5$ calcd 318.1216, found 318.1233.

5.4 Modified preparative procedure for the observation of 3$H$-pyrazoles 111c-e.

Oxadiazoline 114 (0.25 mmol) in toluene (0.5 mL) was irradiated at approximately -73 °C with 300 nm light (Rayonet apparatus) for 7 h. At -73 °C with the Rayonet bulbs switched off, DMAD (0.30 mmol) in 0.1 mL of toluene was added to the photolysis mixture. The mixture was warmed to room temperature and the toluene and volatiles were evaporated at low temperature, with a stream of dry nitrogen gas. NMR spectral data were recorded immediately in benzene-$d_6$. 3$H$-Pyrazoles 111a and 111b could not be observed by $^1$H NMR spectroscopy, as the rearrangement of these 3$H$-pyrazoles had already taken place.
3-(tert-Butyl)-3-methyl-3H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (111c): quantitative yield; $^1$H NMR (200 MHz, C$_6$D$_6$) δ 3.40 (s, 3 H, COOMe), 3.38 (s, 3 H, COOMe), 1.32 (s, 3 H, Me), 0.87 (s, 9 i, C(Me)$_3$); $^{13}$C NMR (50 MHz, C$_6$D$_6$) δ 165.52, 160.67, 156.37, 145.19, 107.63, 52.40, 52.06, 37.94, 26.20, 16.32.

3-(1-Adamantyl)-3-methyl-3H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (111d): quantitative yield; $^1$H NMR (200 MHz, C$_6$D$_6$) δ 3.45 (s, 3 H, COOMe), 3.43 (s, 3 H, COOMe), 1.87-1.45 (m, 15 H), 1.37 (s, 3 H, Me); $^{13}$C NMR (50 MHz, C$_6$D$_6$) δ 165.68, 160.75, 156.30, 145.25, 108.20, 52.36, 52.04, 41.38, 37.98 (3), 36.73 (3), 29.06 (3), 15.04.

3-(4-Methoxybenzyl)-3-methyl-3H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (111e): $^1$H NMR (200 MHz, C$_6$D$_6$) δ 6.99 (d, 2 H, J = 8.5 Hz), 6.57 (d, 2 H, J = 8.5 Hz), 3.44 (d, 1 H, J = -13.6 Hz) 3.35 (s, 3 H, COOMe), 3.26 (s, 3 H, COOMe), 3.15 (s, 3 H, OMe), 3.04 (d, 1 H, J = -13.6 Hz), 1.30 (s, 3 H, Me). Since 3H-pyrazole 111e is unstable at room temperature, the $^1$H NMR spectrum was obtained from solutions containing 118e (25%), 120e (10%), and 111e (65%).

5.5 Determination of $k_{obs}$ for the rearrangement of 3H-pyrazoles 111c-e.

3H-Pyrazole 111c, 111d, and 111e in benzene-$d_6$ solvent were generated by the method outlined above. To the solution containing 111c, triethylenediamine (2.5 equivalents) was added. Progress of the rearrangements of the 3H-pyrazoles was monitored by $^1$H NMR spectroscopy at 250 MHz. Concentration vs. time data (14 or
more points) were obtained for the rearrangements of 111c and 111e to at least two half lives by normalizing the integrated intensity of the methyl singlet of toluene (internal standard) against the integrated intensity of the methyl singlet for each of the 3H-pyrazoles. Concentration vs. time data (8 points) were obtained for the rearrangement of 111d to two half lives by normalizing the integrated intensity of the methyl singlet of residual DMAD against the increasing integrated intensity of the methyl singlet of 1H-pyrazole 118d at 2.42 ppm. The resultant plots of ln((A-x)/A) vs t gave the following observed rate constants: \( k^{35 \, ^\circ \text{C}}(111c) = (6.2 \pm 0.2) \times 10^{-5} \, \text{s}^{-1} \) (correlation coefficient = 0.9941), \( k^{35 \, ^\circ \text{C}}(111d) = (5.6 \pm 0.2) \times 10^{-5} \, \text{s}^{-1} \) (correlation coefficient = 0.9912), \( k^{20 \, ^\circ \text{C}}(111e) = (9.8 \pm 0.4) \times 10^{-5} \, \text{s}^{-1} \) (correlation coefficient = 0.9953). The data for these plots are tabulated in Appendix I.

5.6 Synthesis of 3H-pyrazole 111f.

Oxadiazoline 114e (0.25 mmol) in toluene (0.5 mL) was irradiated at approximately -73 °C with 300 nm light (Rayonet apparatus) for 7 hours. At -73 °C with the Rayonet bulbs switched off, dimethyl acetylenedicarboxylate (0.30 mmol) in 0.1 mL of toluene was added to the pi.−olysis mixture. The mixture was warmed to room temperature and the toluene and volatiles were evaporated with a stream of dry nitrogen. The residue was purified by centrifugal chromatography (silica gel, 7:3 hexanes/ethyl acetate) to give 111f (51%).
3-Benzyl-3-methyl-3H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (111f): $^1$H NMR (200 MHz, CDCl$_3$) δ 7.18-7.05 (m, 5 H, Ph), 3.90 (s, 6 H, 2 COOMe), 3.67 (d, 1 H, J = -14 Hz), 3.28 (d, 1 H, J = -14 Hz), 1.64 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 162.62, 160.50, 151.06, 146.48, 133.67, 129.62 (2), 127.94 (2), 127.24, 101.02, 52.82, 52.78, 41.57, 19.17; MS m/z (M$^+$) for C$_{15}$H$_{16}$N$_2$O$_4$ calcld 288.1110, found 288.1121.

5.7 Rearrangement of 3H-pyrazoles 111a-e in chloroform

**General method.** Oxadiazoline 114 (0.25 mmol) and DMAD (0.30 mmol) in 0.5 mL of CHCl$_3$ (114c was irradiated in CDCl$_3$) were irradiated at room temperature with 300 nm light (Rayonet apparatus) for 6 h. The volatiles from the photolysis mixture were removed in vacuo (except photolysis solution containing the rearrangement products from 111c) and the residues were each dissolved in CDCl$_3$.

**Rearrangement of 111a.** The percentages of 118a and 119a by $^1$H NMR spectroscopy (90 MHz) were 73 and 27, respectively. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) to give 118a (50%) and 119a (19%).

**Rearrangement of 111b.** The percentages of 118b and 119b by $^1$H NMR spectroscopy (200 MHz) were 72 and 28 respectively. The volatiles were removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate)
to give 118b (56%) and 119b (27%).

1-Methoxymethyl-3-methyl-1H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (119b):

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.47 (s, 2 H), 3.92 (s, 3 H, COOMe), 3.81 (s, 3 H, COOMe), 3.29 (s, 3 H, OMe), 2.40 (s, 3 H, Me) $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 163.05, 160.48, 149.70, 135.96, 114.27, 80.84, 56.82, 52.83, 51.56, 12.99; MS $m/z$ (M$^+$) for C$_{10}$H$_{14}$N$_2$O$_3$ calcd 242.0903, found 242.0898.

In a $^1$H NOE experiment, irradiation of the N-methylene singlet at 5.47 ppm led to an enhancement of the singlet at 3.29 ppm (OMe).

Rearrangement of 111c. The percentages determined by $^1$H NMR spectroscopy (200 MHz, sealed nmr tube) of 118c, 121, 119c, and isobutenone were 28, 67, 5, and 55, respectively. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 2:1 hexane/ethyl acetate) to give 118c (20%), 121 (47%), and 119c (4%).

1-(tert-Butyl)-3-methyl-1H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (119c): $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 3.95 (s, 3 H, COOMe), 3.79 (s, 3 H, COOMe), 2.42(s, 3 H, Me), 1.59 (s, 9 H, C(Me)$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 164.19, 163.34, 148.40, 137.17, 111.37, 62.11, 53.22, 51.39, 29.57 (3), 13.55; MS $m/z$ (M$^+$) for C$_{12}$H$_{18}$N$_2$O$_4$ calcd 254.1267, found 254.1269.
Rearrangement of 111d. The percentages of 118d and 119d determined by \(^1\)H NMR spectroscopy (200 MHz) were 69 and 31, respectively. The volatiles were removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) to give 118d (40%) and 119d (19%).

1-(1-Adamantyl)-3-methyl-1H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (119d):
\(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 3.95 (s, 3 H, COOMe), 3.79 (s, 3 H, COOMe), 2.41 (s, 3 H, Me), 2.21 (bs, 9 H), 1.72 (bs, 6 H); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 164.33, 163.39, 148.39, 136.90, 111.12, 63.01, 53.24, 51.34, 41.93 (3), 35.85 (3), 29.74 (3), 13.60; MS \(m/z\) (M\(^+\)) for C\(_{18}\)H\(_{24}\)N\(_2\)O\(_4\) calcd 332.1736, found 332.1739.

Rearrangement of 111e. The percentages of 118e, 120e, and 119e determined by \(^1\)H NMR spectroscopy (200 MHz) were 56, 32, and 11, respectively. The volatiles were removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 118e (37%), 120e (7%), and 119e (7%).

1-(4-Methoxybenzyl)-3-methyl-1H-pyrazole-4,5-dicarboxylic acid dimethyl ester, (119e): \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 7.17 (d, 2 H, \(J = 8.7\) Hz), 6.83 (d, 2 H, \(J = 8.7\) Hz), 2.34 (s, 2 H, CH\(_2\)), 3.85 (s, 3 H, COOMe), 3.81 (s, 3 H, COOMe), 3.78 (s, 3 H, OMe), 2.41 (s, 3 H, Me); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta\) 163.40, 161.12, 159.40, 149.70, 135.59, 130.31, 129.16 (2), 127.79, 114.00 (2), 55.22, 54.29, 52.85, 51.63, 13.25; MS \(m/z\) (M\(^+\)) for C\(_{16}\)H\(_{18}\)N\(_2\)O\(_5\) calcd 318.1216, found 318.1225.
5.8 Rearrangement of 3H-pyrazoles 111a-e in methanol.

**General method.** Oxadiazoline 114 (0.25 mmol) and DMAD (0.30 mmol) in CD$_3$OD or CH$_3$OH (0.5 mL) were irradiated at ambient temperature with 300 nm light (Rayonet apparatus) for 6 hours.

**Rearrangement of 111a in CH$_3$OH.** The volatiles were removed in vacuo and the residue was dissolved in CDCl$_3$. The percentages of 118a, 119a, 121, and benzhydryl methyl ether by $^1$H NMR spectroscopy (200 MHz, CDCl$_3$) were 26, 22, 52, and 52, respectively. The solvent was removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) to give 118a (19%), 119a (17%), 121 (38%), and benzhydryl methyl ether (40%). The spectroscopic data for benzhydryl methyl ether were identical to those previously reported.$^{192}$

**Rearrangement of 111b in CD$_3$OD.** The percentages of 118b, 121 (the D analogue), and dimethoxymethane-$d_3$ were 25, 75, and 61, respectively by $^1$H NMR spectroscopy (200 MHz). Bulb to bulb distillation (0.01 mm Hg) separated the volatiles from the pyrazoles. The presence of dimethoxymethane-$d_3$ in the volatiles was confirmed by gas chromatography and $^1$H NMR spectroscopy spiking experiments with a sample of dimethoxymethane. The residue from bulb to bulb distillation was separated by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 118b (18%) and 121 (D analogue) (58%).
Rearrangement of 111c in CD$_2$OD. The percentages of 118c, 121 (a mixture of H and D analogues), isobutene, and tert-butyl methyl ether were 20, 80, 5, and 72, respectively by $^1$H NMR spectroscopy (90 MHz). Bulb to bulb distillation (0.01 mm Hg) separated the volatiles from the pyrazoles. The presence of tert-butyl methyl ether-d$_3$ in the volatiles was confirmed by gas chromatography and $^1$H NMR spiking experiments with a sample of tert-butyl methyl ether. The residue was separated by centrifugal chromatography (silica gel, 2:1 hexane/ethyl acetate) to give 118c (14%) and 121 (56%).

Rearrangement of 111d in CH$_3$OH. The volatiles were removed in vacuo and the residue was dissolved in CDCl$_3$. The percentages of 118d, 119d, 121, and 1-adamantyl methyl ether determined by $^1$H NMR spectroscopy (200 MHz) were 54, 17, 29, and 23, respectively. The volatiles were removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) to give 118d (34%), 119d (17%), 121 (27%), and 1-adamantyl methyl ether (16%). The spectral data for 1-adamantyl methyl ether were identical to those of a sample prepared by another route.\textsuperscript{193}

Rearrangement of 111e in CH$_3$OH. The volatiles were removed in vacuo and the residue dissolved in CDCl$_3$. The percentages of 118e, 119e, 121, and p-methoxybenzyl methyl ether were determined to be 45, 4, 51, and 47 by $^1$H NMR spectroscopy (200 MHz). The solvent was removed in vacuo and the residue separated by centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) to give 118e (38%), 119e (2%), 121 (51%), and p-methoxybenzyl methyl ether (45%). The spectral data for p-methoxybenzyl
methyl ether were identical to those of a sample prepared by another route.\textsuperscript{194}

3\textit{H}-Pyrazole 111e was also generated in CH\textsubscript{3}OH in the absence of 300 nm irradiation. Oxadiazoline 114e (0.25 mmol) in CH\textsubscript{3}OH (0.5 mL) was irradiated at -73 °C with 300 nm light for 7 h. The Rayonet bulbs were switched off and DMAD (0.6 mmol) in 0.1 mL of CH\textsubscript{3}OH was added to the photolysis mixture at -73 °C. The solution was then warmed quickly to ambient temperature and the volatiles were removed in vacuo. The residue was dissolved in CDCl\textsubscript{3} and the percentages of 118e, 119e, 121, and p-methoxybenzyl methyl ether, by \textsuperscript{1}H NMR spectroscopy (200 MHz) were 56, 12, 32, and 28, respectively.

5.9 Rearrangement of 111f in methanol.

3\textit{H}-pyrazole 111f (0.123 g, 0.428 mmol) was dissolved in 8 mL of methanol and refluxed for 15 minutes. Thin layer chromatography revealed that 3\textit{H}-pyrazole 111f was no longer present. The solvent was removed in vacuo and the residue was dissolved in CDCl\textsubscript{3}. The \textsuperscript{1}H NMR spectrum (200 MHz, CDCl\textsubscript{3}) revealed 118f (42\%) and 120f (58\%). The CDCl\textsubscript{3} was removed in vacuo and the residue was separated by centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) to give 120f (45\%) and 118f (32\%).

4-Benzyl-5-methyl-4\textit{H}-pyrazole-3,4-dicarboxylic acid dimethyl ester (120f): mp 136-138 °C; \textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{3}) \(\delta\) 7.20-6.88 (m, 5 H, Ph), 3.97 (s, 3 H, COOMe), 3.85 (d, 1 H, \(J = -14\) Hz), 3.72 (s, 3 H, COOMe), 3.50 (d, 1 H, \(J = -14\) Hz), 2.39 (s, 3 H, Me); \textsuperscript{13}C (50 MHz, CDCl\textsubscript{3}) \(\delta\) 176.32, 166.63, 165.36, 160.71, 132.57, 128.65 (2),
128.38 (2), 127.96, 76.16, 53.72, 53.10, 37.41, 13.80; MS m/z (M⁺) for C₁₅H₁₆N₂O₄ calc'd 288.1110, found 288.1110.

1-Benzyl-5-methyl-1H-pyrazole-3,4-dicarboxylic acid dimethyl ester, (118f): ¹H NMR (200 MHz, CDCl₃) δ 7.34-7.10 (m, 5 H, Ph), 5.36 (s, 2 H, CH₂), 3.95 (s, 3 H, COOMe), 3.84 (s, 3 H, COOMe), 2.39 (s, 3 H, Me); ¹³C NMR (50 MHz, CDCl₃) δ 163.43, 162.68, 143.79, 142.97, 134.90, 128.97 (2), 128.22, 126.86 (2), 140.1, 54.94, 52.52, 51.76, 10.85; MS m/z (M⁺) for C₁₅H₁₆N₂O₄ calc'd 288.1110, found 288.1119.

5.10 Thermal rearrangements of 4H-pyrazoles 120b and 120c in benzene-d₆.

Rearrangement of 120b. Oxadiazoline 114b (0.25 mmol) and DMAD (0.30 mmol) were dissolved in C₆D₆ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in an nmr tube. Irradiation at room temperature with 300 nm light (Rayonet apparatus) for 6 h gave rearrangement products 118b (77%) and 120b (23%). The tube was then heated at 90 °C and progress of the rearrangement of 120b was monitored by ¹H NMR spectroscopy at 200 MHz. Concentration vs. time data (10 points) were obtained by normalizing the integrated intensity of the methyl singlet of methyl acetate (generated as a by-product in the photolysis of 114b) against the integrated intensity of the methyl singlet of 120b for two half lives. The resultant plot of ln [(A-x)/A] vs. t yielded an observed rate constant (1.10 ± 0.05 x 10⁻⁴ s⁻¹, correlation coefficient = 0.9905) for the decrease in concentration of 111b. After the rearrangement of 111b was complete, the
solution consisted of 118b (90%) and 119b (10%). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) to give 118b (75%) and 119b (6%).

**Rearrangement of 120e.** Compound 120e (0.072 g, 0.226 mmol) and methyl acetate (0.113 mmol, internal standard) were dissolved in C₆D₆ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was then heated at 130 °C and progress of the rearrangement of 120e was monitored by ¹H NMR spectroscopy (200 MHz). Concentration vs. time data were obtained by normalizing the integrated intensity of the methyl singlet of methyl acetate against the sum of the integrated intensity of the CH₂ singlets of the two 1H-pyrazole rearrangement products (118e and 119e) for two half-lives. The resultant plot of ln [(A-x)/A] vs. t yielded an observed rate constant (1.45 ± 0.08 x 10⁻⁴ s⁻¹, correlation coefficient = 0.9939) for the increase in concentration of the two 1H-pyrazoles. After the thermal rearrangement of 120e was complete, the mixture consisted of 118e (58%) and 119e (42%). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 118e (50%) and 119e (35%).
5.11 Thermal rearrangements of 4H-pyrazoles 120b and 120e in methanol/methanol-d₄.

Rearrangement of 120b. The volatiles from the photolysis mixture, after generation of 3H-pyrazole 111b in C₆D₆ (79% of 118b and 21% of 120b), were removed and the residue was dissolved in CD₃OD. A ¹H NMR spectrum was taken immediately and it revealed 118b (79%), 121 (21%), and dimethoxymethane-d₃ (21%). Bulb to bulb distillation (0.01 mm Hg) separated the volatiles from the pyrazoles. The presence of dimethoxymethane-d₃ in the volatiles was confirmed by gas chromatography and ¹H NMR spectroscopy spiking experiments with an authentic sample of dimethoxymethane. The residue from bulb to bulb distillation was separated by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 118b (65%) and 121 (D analogue) (16%).

Rearrangement of 120e. Compound 120e (0.06 g, 0.189 mmol) was dissolved in methanol for ten minutes. The methanol was then removed in vacuo and the residue was dissolved in CDCl₃ and a ¹H NMR spectrum was taken. ¹H NMR spectroscopy revealed a quantitative yield of 121 and p-methoxybenzyl methyl ether. The CDCl₃ was removed and the residue was separated by centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) to give 121 (76%) and p-methoxybenzyl methyl ether (80%).
5.12 Preparation of 3-alkyl-3-methyl-3H-pyrazole-5-carboxylic acid methyl esters (128c-f).

**General.** The oxadiazolines 114b-f (0.25 mmol) were dissolved in toluene (0.5 mL) and irradiated at -73 °C with 300 nm light (Rayonet apparatus) for 7 hours. At -73 °C, with the Rayonet bulbs switched off, methyl propiolate (0.50 mmol in 0.1 mL of toluene) was added to the photolysis mixtures. The mixtures were warmed to room temperature and the volatiles were removed in vacuo and the residues dissolved in hexane. The solid 3H-pyrazoles were filtered and washed with hexane.

3-Methyl-3-(tert)-butyl-3H-pyrazole-5-carboxylic acid methyl ester, (128c): 43% yield, mp 55-58 °C; 
\[ ^1H \text{ NMR (200 MHz, CDCl}_3 \] \( \delta \) 7.77 (s, 1 H, CH), 3.99 (s, 3 H, COOMe), 1.38 (s, 3 H, Me), 1.06 (s, 9 H, C(Me)_2); 
\[ ^{13}C \text{ NMR spin sort (50 MHz, CDCl}_3 \] \( \delta \) 161.38 (+ve), 154.37 (-ve), 147.02 (+ve), 105.08 (+ve), 52.38 (-ve), 37.45 (+ve), 26.77 (3, -ve), 15.06 (-ve); MS m/z (M⁺) for C_{10}H_{16}N_{2}O_{2} calc 196.1212, found 196.1211.

3-(1-Adamantyl)-3-methyl-3H-pyrazole-5-carboxylic acid methyl ester, (128d): 52% yield, mp 120-121 °C; 
\[ ^1H \text{ NMR (200 MHz, CDCl}_3 \] \( \delta \) 7.77 (s, 1 H, CH), 3.98 (s, 3 H, COOMe), 1.99 (bs, 3 H, CH), 1.68 (bs, 12 H, CH₂), 1.33 (s, 3 H, Me); 
\[ ^{13}C \text{ NMR spin sort (50 MHz, CDCl}_3 \] \( \delta \) 161.39 (+ve), 154.47 (-ve), 147.01 (+ve), 105.60 (+ve), 52.33 (-ve), 40.60 (+ve), 38.59 (3, +ve), 36.68 (3, +ve), 28.72 (3, -ve), 13.73 (-ve). MS m/z (M⁺) for C_{16}H_{22}N_{2}O_{2} calc 274.1681, found 274.1690.
3-(4-Methoxybenzyl)-3-methyl-3H-pyrazole-5-carboxylic acid methyl ester, (128c): 45% yield, mp 127-130 °C; \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 7.66 (s, 1 H, CH), 7.00 (d, 2 H, \(J = 8.2\) Hz), 6.78 (d, 2 H, \(J = 8.2\) Hz), 3.94 (s, 3 H, COOMe), 3.77 (s, 3 H, OMe), 3.29 (d, 1 H, CH, \(J = -13.7\) Hz), 3.07 (d, 1 H, CH, \(J = -13.7\) Hz), 1.46 (s, 3 H, Me); \(^{13}\)C NMR (200 MHz, CDCl\(_3\)) \(\delta\) 161.09, 158.65, 153.11, 147.66, 130.70 (2), 129.07, 113.66, 99.30, 55.14, 52.40, 40.45, 28.09, 18.01; MS \(m/z\) (M\(^+\)) for C\(_{13}\)H\(_{16}\)N\(_2\)O\(_3\) calcld 260.1161, found 260.1155.

3-Benzyl-3-methyl-3H-pyrazole-5-carboxylic acid methyl ester, (128f): 65% yield, mp 114-116 °C; \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta\) 7.66 (s, 1 H, CH), 7.26-7.07 (m, 5 H, Ph). 3.93 (s, 3 H, COOMe), 3.34 (d, 1 H, \(J = -13.4\) Hz), 3.10 (d, 1 H, \(J = -13.4\) Hz), 1.47 (s, 3 H, Me); \(^{13}\)C NMR (200 MHz, CDCl\(_3\)) \(\delta\) 161.00, 152.86, 147.60, 134.72, 129.60 (2), 128.25 (2), 127.17, 98.96, 52.34, 41.12, 18.03; MS \(m/z\) (M\(^+\)) for C\(_{13}\)H\(_{14}\)N\(_2\)O\(_2\) calcld 230.1055, fc and 230.1065.

5.13 Synthesis of 3-alkyl-1-methoxycarbonyl-3-methylcyclopropenes (134c-f):

**General.** Oxadiazolines 114 (0.25 mmol) in 0.5 mL of benzene-\(d_6\) containing methyl propiolate (0.30 mmol) were photolyzed (t = 16 hours for 114c, t = 7 hours for 114d, t = 12 hours for 114e and 114f) until loss of nitrogen from 3\(H\)-pyrazoles 128c-f was complete and only cyclopropenes 134c-f could be observed by \(^1\)H NMR spectroscopy.
These $^1$H NMR spectra revealed quantitative yields of cyclopropenes. The cyclopropenes were isolated by centrifugal chromatography (silica gel, 98:2 hexane/ethyl acetate).

3-(tert-Butyl)-1-methoxycarbonyl-3-methylcyclopropene, (134c): 60% yield, $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 7.88 (s, 1 H, CH), 3.77 (s, 3 H, COOMe), 1.18 (s, 3 H, Me), 0.82 (s, 9 H, Me$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 162.27, 131.65, 125.49, 52.02, 36.54, 35.08, 28.68 (3), 21.23; MS m/z (M$^+$) for C$_{10}$H$_{16}$O$_2$ calcd 168.1150, found 168.1152.

3-(1-Adamantyl)-1-methoxycarbonyl-3-methylcyclopropene, (134d): 55% yield, $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 7.92 (s, 1 H, CH), 3.80 (s, 3 H, COOMe), 1.93 (bs, 3 H, CH), 1.52-1.72 (m, 6 H, CH$_2$), 1.39-1.41 (m, 6 H, CH$_2$), 1.14 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 162.46, 131.21, 124.76, 52.04, 41.07 (3), 36.96 (3), 36.69, 36.22, 28.77 (3), 20.03; MS m/z (M$^+$) for C$_{16}$H$_{22}$O$_2$ calcd 246.1620, found 246.1617.

3-(4-Methoxybenzyl)-1-methoxycarbonyl-3-methylcyclopropene, (134e): 52% yield, $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 7.83 (s, 1 H, CH), 7.01 (d, 2 H, J = 8.5 Hz), 6.80 (d, 2 H, J = 8.5 Hz), 3.80 (s, 3 H, OMe), 3.78 (s, 3 H, OMe), 2.86 (s, 2 H, CH$_2$), 1.29 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 161.82, 157.88, 131.76, 131.69, 130.23 (2), 125.72, 113.64 (2), 55.18, 52.05, 44.92, 29.65, 25.19; MS m/z (M$^+$) for C$_{14}$H$_{16}$O$_3$ calcd 232.1099, found 232.1096.
3-Benzyl-1-methoxycarbonyl-3-methylcylopropene, (134f): 63% yield, $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 7.84 (s, 1 H, CH), 7.08-7.26 (m, 5 H, Ph), 3.80 (s, 3 H, COOMe), 2.92 (s, 2 H, CH$_2$), 1.30 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 161.74, 139.56, 131.64, 129.30 (2), 128.22 (2), 125.96, 52.03, 45.86, 29.41, 25.22; MS $m/z$ (M$^+$) for C$_{13}$H$_{14}$O$_2$ calcd 202.0994, found 202.0984.

5.14 Rearrangement of 3H-pyrazoles 128b-f in benzene-$d_6$.

Rearrangement of 128b. Oxadiazoline 114b (0.25 mmol) and methyl propiolate (0.50 mmol) in C$_6$D$_6$ (0.5 mL) were irradiated at room temperature with 300 nm light (Rayonet apparatus) for 6 hours. A 1.1:1:0 ratio of 131b:132b was indicated by $^1$H NMR spectroscopy (200 MHz, C$_6$D$_6$). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131b (28%) and 132b (31%).

1-Methoxymethyl-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (132b): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.63 (s, 1 H, CH), 5.45 (s, 2 H, CH$_2$), 3.92 (s, 3 H, COOMe), 3.32 (s, 3 H, OMe), 2.38 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 162.85, 142.66, 140.88, 109.23, 80.33, 56.40, 51.97, 10.69; MS $m/z$ (M$^+$) for C$_{8}$H$_{12}$N$_{2}$O$_{3}$ calcd 184.0848, found 184.0843.

In a $^1$H NOE experiment, irradiation of the methyl singlet at 2.38 ppm caused enhancement at both 5.45 ppm (CH$_2$) and 6.63 ppm (vinyl proton).
4-Methoxymethyl-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (131b): mp 85-88 °C. ¹H NMR (200 MHz, CDCl₃) δ 4.62 (s, 2 H, CH₂), 3.92 (s, 3 H, COOMe), 3.37 (s, 3 H, OMe), 2.36 (s, 3 H, Me); ¹³C NMR (50 MHz, CDCl₃) δ 161.93, 144.31, 137.95, 117.88, 63.41, 57.88, 51.92, 10.39; MS m/z (M⁺) for C₉H₁₂N₂O₃ calc 184.0848, found 184.0841.

Rearrangement of 128c. 3H-Pyrrole 128c (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C₆D₆ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was heated at 90 °C for 15 hours. The percentages of 131c, 132c, 135c, 136, and isobutene by ¹H NMR spectroscopy (200 MHz) were 28, 15, 2, 55, and 25, respectively. The presence of isobutene was confirmed by a ¹H NMR decoupling experiment on the reaction mixture following the rearrangement of 128c. Irradiation of the multiplet at 4.74 ppm (CH₃) caused collapse of the triplet at 1.60 ppm (2 Me). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131c (19%), 132c (7%), 135c (1%), and 136 (42%).

4-(tert-Butyl)-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (131c): mp 145-148 °C. ¹H NMR (200 MHz, CDCl₃) δ 3.88 (s, 3 H, OMe), 2.42 (s, 3 H, Me), 1.42 (s, 9 H, C(Me)₃); ¹³C NMR (50 MHz, CDCl₃) δ 163.01, 142.49, 139.91, 129.12, 51.92, 31.49, 31.12 (3), 14.16; MS m/z (M⁺) for C₁₀H₁₆N₂O₃ calc 196.1211, found 196.1197.
1-(tert-Butyl)-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (132c): $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 6.58 (s, 1 H, CH), 3.89 (s, 3 H, COOMe), 2.47 (s, 3 H, Me), 1.67 (s, 9 H, C(Me)$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 163.24, 139.99, 139.42, 111.27, 61.12, 51.76, 29.82 (3), 14.65; MS $m/z$ (M$^+$) for C$_{16}$H$_{16}$N$_2$O$_3$ calcd 196.1211, found 196.1212.

4-(tert-Butyl)-3-methyl-1H-pyrazole-5-carboxylic acid methyl ester, (135c): $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 3.90 (s, 3 H, COOMe), 2.41 (s, 3 H, Me), 1.39 (s, 9 H, C(Me)$_3$); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 162.12, 154.00, 137.11, 116.81, 51.66, 31.08, 29.16, 10.13; MS $m/z$ (M$^+$) for C$_{16}$H$_{16}$N$_2$O$_3$ calcd 196.1211, found 196.1204.

5-Methyl-1H-pyrazole-3-carboxylic acid methyl ester, (136):$^{204}$ mp 74-76 °C; $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 6.57 (s, 1 H, CH), 3.89 (s, 3 H, OMe), 2.38 (s, 3 H, Me); $^{13}$C NMR (50.32, CDCl$_3$) $\delta$ 162.51, 132.61, 141.77, 107.19, 51.78, 11.22; MS $m/z$ (M$^+$) for C$_6$H$_5$N$_2$O$_2$ calcd 140.0586, found 140.0570.

**Rearrangement of 128d.** 3H-Pyrazole 128d (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C$_6$D$_6$ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a NMR tube. The tube was heated at 90 °C for 14 hours. The percentages of 131d and 132d by $^1$H NMR spectroscopy (200 MHz) were 72 and 28. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131d (55%) and 132d (18%).
4-(1-Adamantyl)-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (131d): mp 239-241 °C (sublimes) \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta 4.50\) (s, 1 H, NH), 3.90 (s, 3 H, COOMe), 2.46 (s, 3 H, Me), 2.14 (bs, 6 H, CH\(_2\)), 2.03 (bs, 3H, CH), 1.76 (bs, 6 H, CH\(_2\)); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta 162.71, 137.23, 130.03, 114.50, 52.05, 41.76\) (3), 36.67 (3), 34.14, 28.87 (3), 15.37; MS \(m/z\) (M\(^+\)) for C\(_{16}\)H\(_{22}\)N\(_2\)O\(_2\) calcd 274.1681, found 274.1688.

!-(1-Adamantyl)-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (132d): \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta 6.57\) (s, 1 H, CH), 3.89 (s, 3 H, COOMe), 2.51 (s, 3 H, Me), 2.32 (bs, 6 H, CH\(_2\)), 2.23 (bs, 3 H, CH), 1.75 (bs, 6 H, CH\(_2\)); \(^{13}\)C NMR (50 MHz, CDCl\(_3\)) \(\delta 163.30, 140.16, 139.50, 112.26, 62.28, 51.80, 41.64\) (3), 36.08 (3), 29.71 (3), 15.00; MS \(m/z\) (M\(^+\)) for C\(_{16}\)H\(_{22}\)N\(_2\)O\(_2\) calcd 274.1681, found 274.1685.

Rearrangement of 128e. 3H-pyrazole 128e (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in C\(_6\)D\(_6\) (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a NMR tube. The tube was heated at 60 °C for 5 hours. The percentages of 131e and 132e by \(^1\)H NMR spectroscopy (200 MHz) were 78 and 22. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 70:30 hexane/ethyl acetate) to give 131e (60%) and 132e (15%).

4-(4-Methoxybenzyl)-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (131e): mp 129-131 °C; \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta 7.07\) (d, 2 H, CH, \(J = 8.6\) Hz, 6.78 (d, 2 H,
CH, $J = 8.6$ Hz), 4.03 (s, 2 H, CH$_2$), 3.85 (s, 3 H, COOMe), 3.76 (s, 3 H, OMe), 2.21 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 162.21, 157.68, 143.21, 136.75, 132.46, 129.05 (2), 120.91, 113.62 (2), 55.16, 51.63, 28.12, 10.50; MS m/z (M$^+$) for C$_{14}$H$_{16}$N$_2$O$_3$ calcd 260.1161, found 260.1164.

1-(4-Methoxybenzyl)-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (I32e):

$^1$H NMR (200 MHz, CDCl$_3$) δ 7.01 (d, 2 H, CH, $J = 8.8$ Hz), 6.77 (d, 2 H, CH, $J = 8.8$ Hz), 6.54 (s, 1 H, CH), 5.24 (s, 2 H, CH$_2$), 3.86 (s, 3 H, COOMe), 3.71 (s, 3 H, OMe), 2.12 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 163.01, 159.24, 142.03, 128.26 (2), 127.78, 114.14 (2), 108.94, 55.23, 53.63, 51.91, 11.29; MS m/z (M$^+$) for C$_{16}$H$_{16}$N$_2$O$_3$ calcd 260.1161, found 260.1149.

Rearrangement of 128f. 3H-Pyrazole 128f (0.200 mmol) and phenoxy-2-propanonc (0.100 mmol, internal standard) were dissolved in C$_6$D$_6$ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was heated at 90 °C for 6 hours. 1H-Pyrazole 131f appeared to be formed in quantitative yield by $^1$H NMR spectroscopy (200 MHz). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 60:40 hexane/ethyl acetate) to give 131f (81%).

4-Benzyl-5-methyl-1H-pyrazole-3-carboxylic acid methyl ester, (131f): mp 102-104 °C;

$^1$H NMR (200 MHz, CDCl$_3$) δ 7.17-7.36 (m, 5 H, Ph), 5.10 (s, 1 H, NH), 4.11 (s, 2 H, CH$_2$), 3.88 (s, 3 H, COOMe), 2.21 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 162.22,
143.31, 140.34, 136.91, 128.24, 128.15 (2), 125.84 (2), 120.45, 51.61, 29.05, 10.48; MS
m/z (M⁺) for C₁₅H₁₄N₂O₂ calcd 230.1055, found 230.1062.

5.15 Determination of kₐₙs for the rearrangement of 3H-pyrazoles 128c-f
in benzene-d₆.

3H-Pyrazole 128 (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal
standard) were dissolved in C₆D₆ (0.5 mL), degassed (three freeze-pump-thaw cycles), and
sealed in a nmr tube. The tube was heated at 90 °C for 128c, 128d, and 128f and at 60
°C for 128e, and progress of the rearrangement of 128 was monitored by ¹H NMR
spectroscopy (200 MHz). Concentration vs. time data were obtained by normalizing the
integrated intensity of the CH₂ singlet of phenoxy-2-propanone against the integrated
intensity of the methyl singlet of 3H-pyrazole 128. The decrease in concentration of 128
was monitored to at least 2 half lifes. The resultant plots of ln [(A-x)/A] vs t gave the
following observed rate constants:

k₀⁰°C (128c) = (1.06 ± .03) x 10⁻⁴ s⁻¹ (correlation coefficient = 0.9975)
k₀⁰°C (128d) = (1.10 ± .09) x 10⁻⁴ s⁻¹ (correlation coefficient = 0.9850)
k₀⁰°C (128e) = (3.8 ± 0.1) x 10⁻⁴ s⁻¹ (correlation coefficient = 0.9952)
k₀⁰°C (128e) = (3.3 ± 0.2) x 10⁻⁴ s⁻¹ (correlation coefficient = 0.9898)
k₀³°C (128f) = (2.8 ± 0.1) x 10⁻⁴ s⁻¹ (correlation coefficient = 0.9955)
5.16 Rearrangement of 128b in dichloromethane.

Oxadiazoline 114b (0.92 mmol) and methyl propiolate (1.21 mmol) were dissolved in CH₂Cl₂ (0.5 mL, base washed with NaHCO₃ and distilled) and irradiated at room temperature with 300 nm light (Rayonet apparatus) for 6 hours. The volatiles were removed in vacuo and the residue was dissolved in CDCl₃ and the percentages of products determined by ¹H NMR spectroscopy were 131b (50), 132b (24), 136 (7), 139b (8), and 140b (11). The residue was purified by centrifugal chromatography (silica gel, 2:1 diethyl ether/hexanes) to give 131b (32%), 132b (18%), 136 (4%), 139b (5%), and 140b (7%).

1-Methoxymethyl-3-methyl-1H-pyrazole-5-carboxylic acid methyl ester, (139b): ¹H NMR (500 MHz, CDCl₃) δ 6.69 (s, 1 H, CH), 5.75 (s, 2 H, CH₂), 3.88 (s, 3 H, COOMe), 3.35 (s, 3 H, OMe), 2.30 (s, 3 H, Me); ¹³C NMR (50 MHz, CDCl₃) δ 159.95, 148.30, 133.09, 112.20, 80.52, 56.75, 51.99, 13.34; MS (Cl, CH₄) m/z (M⁺) for C₇H₁₂N₂O₃-H calcd 183.0770, found 183.0759.

In a ¹H NOE experiment, irradiation of the methyl singlet at 2.30 ppm caused enhancement at 6.69 ppm (vinyl proton).

1,4-bis(Methoxymethyl)-3-methyl-1H-pyrazole-5-carboxylic acid methyl ester, (140b): ¹H NMR (500 MHz, CDCl₃) δ 5.72 (s, 2 H, N-CH₂), 4.55 (s, 2 H, C-CH₂), 3.95 (s, 3 H, COOMe), 3.35 (s, 3 H, C-CH₂OMe), 3.32 (s, 3 H, N-CH₂OMe), 2.32 (s, 3 H, Me); ¹³C NMR (50 MHz, CDCl₃) δ 160.22, 148.96, 130.98, 121.78, 81.23, 64.06, 57.94, 56.77,
52.08, 11.77; MS (Cl, CH₄) m/z (M⁺) for C₁₉H₂₆N₂O₄ calc'd 228.1110, found 228.1096.

In a ¹H NOE experiment, irradiation of the methyl singlet at 2.32 ppm caused enhancement of the singlet at 4.55 ppm (C-CH₃), while irradiation of the methylene singlet at 5.72 caused enhancement of the singlet at 3.32 (N-CH₂OCH₃). Furthermore, irradiation of the methylene singlet at 4.55 caused enhancement of the singlet at 3.35 ppm (C-CH₂OCH₃).

5.17 Rearrangements of 3H-pyrazoles 128c-f in acetone-d₆.

Rearrangement of 128c. 3H-Pyrazole 128c (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d₆ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a NMR tube. The tube was heated at 90 °C for 16 hours. The percentages of 131c, 132c, 135c, 136, and isobutene by ¹H NMR spectroscopy (200 MHz) were 38, 15, 7, 41, and 34, respectively. The presence of isobutene was confirmed by a ¹H NMR decoupling experiment on the reaction mixture following the rearrangement of 128c. Irradiation of the multiplet at 4.74 ppm (CH₂) caused collapse of the triplet at 1.60 ppm (2 Me). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131c (24%), 132c (8%), 135c (3%), and 136 (32%).

Rearrangement of 128d. 3H-Pyrazole 128d (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-d₆ (0.5 mL), degassed (three...
freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was heated at 90 °C for 16 hours. The percentages of 131d and 132d by 1H NMR spectroscopy (200 MHz) were 72 and 28, respectively. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131d (58%) and 132d (21%).

**Rearrangement of 128e.** 3H-Pyrazole 128e (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-\(d_6\) (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was heated at 60 °C for 6 hours. The percentages of 131e and 132e by 1H NMR spectroscopy (200 MHz) were 90 and 9, respectively. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 70:30 hexane/ethyl acetate) to give 131e (80%) and 132e (5%).

**Rearrangement of 128f.** 3H-Pyrazole 128f (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-\(d_6\) (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was heated at 90 °C for 6 hours. 1H-pyrazole 131f appeared to be formed in quantitative yield by 1H NMR spectroscopy (200 MHz). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 60:40 hexane/ethyl acetate) to give 131f (84%).
5.18 Determination of \( k_{\text{obs}} \) for the rearrangement of \( 3H \)-pyrazoles 128c-f in acetone-\( d_6 \).

\( 3H \)-pyrazole 128 (0.200 mmol) and phenoxy-2-propanone (0.100 mmol, internal standard) were dissolved in acetone-\( d_6 \) (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a nmr tube. The tube was heated at 90 °C for 128c, 128d, and 128f and at 60 °C for 128e, and progress of the rearrangement of 128 was monitored by \(^1\)H NMR spectroscopy (200 MHz). Concentration vs. time data were obtained by normalizing the integrated intensity of the \( \text{CH}_2 \) singlet of phenoxy-2-propanone against the integrated intensity of the methyl singlet of \( 3H \)-pyrazole 128. The decrease in concentration of 128 was monitored to at least 2 half lives. The resultant plots of

\[
\ln \left\{ \frac{(A-x)}{A} \right\} \text{ vs } t \text{ gave the following observed rate constants :}
\]

\[
k^{90}c(128c) = (9.7 \pm 0.3) \times 10^{-5} \text{ s}^{-1} \text{ (correlation coefficient = 0.9954)}
\]

\[
k^{90}c(128d) = (8.9 \pm 0.4) \times 10^{-5} \text{ s}^{-1} \text{ (correlation coefficient = 0.9924)}
\]

\[
k^{60}c(128e) = (2.1 \pm 0.1) \times 10^{-4} \text{ s}^{-1} \text{ (correlation coefficient = 0.9990)}
\]

\[
k^{90}c(128f) = (2.80 \pm 0.05) \times 10^{-4} \text{ s}^{-1} \text{ (correlation coefficient = 0.9988)}
\]

5.19 Rearrangement of \( 3H \)-pyrazoles 128b-f in methanol.

**Rearrangement of 128b.** Oxadiazoline 114b (0.25 mmol) and methyl propiolate (0.50 mmol) were dissolved in methanol-\( d_4 \) (0.5 mL) and irradiated at room temperature with 300 nm light (Rayonet apparatus) for 6 hours. The percentages by \(^1\)H NMR (200 MHz,
CD$_2$OD) of 131b, 132b, 136, and dimethoxymethane-$d_3$ were 53%, 21%, 26% and 26%, respectively. Bulb to bulb distillation at 0.01 mm Hg separated the volatiles from the pyrazoles. Dimethoxymethane-$d_3$ was confirmed by $^1$H NMR and gas chromatography spiking experiments with an authentic sample of dimethoxymethane. The residue was separated by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131b (48%), 132 (16%), and 136 (24%).

**Rearrangement of 128c.** 3H-Pyrazole 128c (0.200 mmol) was dissolved in C$_6$D$_6$ (0.5 mL), degassed (three freeze-pump-thaw cycles), and sealed in a NMR tube. The tube was heated at 90 °C for 20 minutes. The percentages of 131c, 132c, 135c, 136, tert-butyl methyl ether-$d_3$, and isobutene by $^1$H NMR spectroscopy (200 MHz) were 18, 16, 6, 60, 31, and 27, respectively. The presence of isobutene was confirmed by a $^1$H NMR decoupling experiment on the reaction mixture following the rearrangement of 128c. Irradiation of the multiplet at 4.74 ppm (CH$_2$) caused collapse of the triplet at 1.60 ppm (2 Me). Bulb to bulb distillation at 0.01 mm Hg separated the volatiles from the pyrazoles. tert-Butyl methyl ether-$d_3$ was confirmed by $^1$H NMR and gas chromatography spiking experiments. The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131c (11%), 132c (12%), 135c (4%), and 136 (55%).

In another experiment 3H-pyrazole 128c (20 mg, 0.102 mmol) and 2-phenoxy-2-propanone (7.7 mg, 0.05 mg, internal standard) were dissolved in methanol-$d_4$. The tube was heated at 50 °C for 1 hour and the progress of the rearrangement of 128c was
monitored by $^1$H NMR spectroscopy. Concentration vs. time data were obtained by normalizing the integrated intensity of the CH$_2$ singlet of phenoxy-2-propanone against the integrated intensity of the methyl singlet of 3H-pyrazole 128c. The decrease in concentration of 128c was monitored for 2.4 half lifes. The resultant plot of ln [(A-x)/A] vs t with 5 data points gave a rate constant of 4.7 ± 0.1 x 10$^{-4}$ s$^{-1}$ (correlation coefficient = 0.9993).

**Rearrangement of 128d.** 3H-Pyrazole 128d (0.200 mmol) was dissolved in methanol (5 mL) and refluxed for 0.5 hours. The percentages of 131d and 132d by $^1$H NMR spectroscopy (200 MHz) were 81 and 19. Only trace amounts of 136 and 1-adamantyl methyl ether were detected by gas chromatography and $^1$H NMR spectroscopy. The volatiles were removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 1:1 hexane/ethyl acetate) to give 131d (70%) and 132d (13%).

In another experiment 128d (0.100 mmol) and phenoxy-2-propanone (0.05 mmol, internal standard) were dissolved in methanol-d$_4$ and heated at 50 °C for 30 minutes. $^1$H NMR spectroscopy revealed 128d (7%), 131d (76%), and 132d (17%).

**Rearrangement of 128e.** 3H-Pyrazole 128e (0.200 mmol) was dissolved in methanol (5 mL) and the solution was refluxed for 0.5 hours. The percentages of 131e and 132e by $^1$H NMR spectroscopy (200 MHz) were 75 and 25, respectively. Only trace amounts of 136 and p-methoxybenzyl methyl ether were detected by gas chromatography and $^1$H NMR spectroscopy. The volatiles were removed in vacuo and the residue was purified.
by centrifugal chromatography (silica gel, 70:30 hexane/ethyl acetate) to give \textbf{131e} (63\%) and \textbf{132e} (16\%).

In another experiment, \textbf{128e} (0.100 mmol) and phenoxy-2-propanone (0.05 mmol, internal standard) were dissolved in 0.5 mL of methanol-$d_4$. After 9 minutes at ambient temperature, $^1$H NMR spectroscopy (200 MHz) revealed \textbf{128e} (8\%), \textbf{131e} (65\%), and \textbf{132e} (27\%). After 15 minutes at ambient temperature the solution consisted of \textbf{131e} (81\%) and \textbf{132e} (19\%).

**Rearrangement of 128f.** $3H$-Pyrazole \textbf{128f} (0.200 mmol) was dissolved in methanol (5 mL) and refluxed for 0.5 hours. The solution was not homogeneous. $1H$-Pyrazole \textbf{131f} appeared to be formed in quantitative yield by $^1$H NMR spectroscopy (200 MHz). The volatiles were removed in vacuo and the residue was purified by centrifugal chromatography (silica gel, 60:40 hexane/ethyl acetate) to give \textbf{131f} (86\%).

In another experiment, \textbf{128f} (0.100 mmol) and phenoxy-2-propanone (0.05 mmol, internal standard) in 0.5 mL of methanol-$d_4$ were placed in an nmr tube. Initially the solution was not homogeneous. However, the solution was homogeneous after 1.6 hours at 40 °C and it contained \textbf{128f} (42\%) and \textbf{131f} (58\%). The solution was then heated at 50 °C for 30 minutes after which it contained \textbf{128f} (21\%) and \textbf{131f} (79\%).
5.20 Synthesis of 5-Alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes

(148a-f):

General. The syntheses of 5-alkyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadienes were adapted from a procedure for the synthesis of 5-ethyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadiene.54 Pentakis(methoxycarbonyl)cyclopentadiene (0.50 g, 1.43 mmol), Ag₂O (0.16 g, 0.73 mmol), and benzene (9 mL) were stirred for 2 hours at room temperature. The halide (2.38 mmol) was then added and the mixture was stirred for 2 hours. The solution was filtered and most of the benzene was removed by rotary evaporation. Crude product solutions of 148a and 148b were subjected to centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate). For crude product solutions of 148c and 148d, CH₂Cl₂ was added and the solution was washed three times with 10% NaHCO₃. The CH₂Cl₂ layer was dried with MgSO₄ and filtered. The CH₂Cl₂ was removed by rotary evaporation and the residues were subjected to centrifugal chromatography (silica gel, 7:3 hexane/ethyl acetate) except in the cases of 148e and 148f, which were recrystallized from methanol. The isolated percentage yields of 148a-f were not optimized. Pentakis(methoxycarbonyl)cyclopentadiene, silver (I) oxide, and the following halides were purchased from Aldrich Chemical Co. and used as supplied: bromodiphenylmethane (for 148a), chloromethyl methyl ether (for 148b), 1-bromoadamantane (for 148c), 4-methoxybenzyl chloride (for 148d), benzyl bromide (for 148e), and iodoethane (for 148f).
1,2,3,4,5-pentakis(Methoxycarbonyl)-5-(1,1-diphenylmethyl)cyclopentadiene, (148a): 25% yield; mp 108-110 °C; 1H NMR (200 MHz, CDCl₃) δ 7.35-7.17 (m, 10 H, 2 Ph), 5.60 (s, 1 H, CH), 3.81 (s, 6 H, 2 COOME), 3.63 (s, 3 H, COOME), 3.36 (s, 6 H, COOME); 13C NMR (50 MHz, CDCl₃) δ 166.70, 162.66 (2), 161.48 (2), 143.76 (2), 142.67 (2), 139.12 (2), 129.27 (4), 128.00 (4), 127.11 (2), 71.45, 53.30, 52.80, 52.65 (2), 52.06 (2); MS m/z (M⁺) for C₂₈H₂₆O₁₀ calcd 522.1526 found, 522.1514.

1,2,3,4,5-pentakis(Methoxycarbonyl)-5-methoxymethylcyclopentadiene, (148b): 39% yield; mp 119-120 °C; 1H NMR (200 MHz, CDCl₃) δ 4.23 (s, 2 H, CH₂), 3.88 (s, 6 H, 2 COOME), 3.83 (s, 6 H, 2 COOME), 3.68 (s, 3 H, COOME), 3.26 (s, 3 H, OMe); 13C NMR (50 MHz, CDCl₃) δ 165.76, 162.55 (2), 161.92 (2), 141.78 (2), 141.67 (2), 71.84, 68.71, 59.87, 53.21, 52.72 (2), 52.56 (2); m/z (M⁺) for C₁₇H₂₀O₁₁ calcd 400.1006, found 400.0995.

5-(1-Adamantyl)-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadiene, (148c): 22% yield; mp 124-125°C; 1H NMR (200 MHz, CDCl₃) δ 3.86 (s, 6 H, 2 COOME), 3.81 (s, 6 H, 2 COOME), 3.64 (s, 3 H, COOME), 1.95 (bs, 3 H, CH), 1.88 (bs, 6 H, 3 CH₂), 1.65 (bs, 6 H, 3 CH₂); 13C NMR (50 MHz, CDCl₃) δ 165.65, 163.31 (2), 162.61 (2), 144.51 (2), 140.70 (2), 74.77, 52.60 (2), 52.46 (2), 52.21, 42.55, 38.09 (3), 36.35 (3), 28.94 (3); MS m/z (M⁺) for C₂₅H₃₀O₁₀·H calcd 489.1761 found 489.1756.
1,2,3,4,5-pentakis(Methoxycarbonyl)-5-(4-methoxybenzyl)cyclopentadiene, (148d): 31% yield; mp 88.5-89.5 °C; $^1$H NMR (200 MHz, CDCl$_3$) δ 6.92 (d, $J = 8.7$ Hz, 2 H, CH$_{ortho}$), 6.69 (d, $J = 8.7$ Hz, 2 H, CH$_{meta}$), 3.87 (s, 6 H, 2 COOMe), 3.77 (s, 6 H, 2 COOMe), 3.74 (s, 3 H, COOMe), 3.71 (s, 2 H, CH$_2$), 3.69 (s, 3 H, OMe); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 167.33, 162.34 (2), 162.11 (2), 158.60, 142.87 (2), 141.70 (2), 130.19 (2), 125.45, 113.18 (2), 68.48, 55.06, 53.30, 52.66 (4), 37.26; $m/z$ (M$^+$) for C$_{23}$H$_{24}$O$_{11}$ calcd 476.1319, found 476.1296.

5-Benzyl-1,2,3,4,5-pentakis(methoxycarbonyl)cyclopentadiene, (148e): 45% yield; mp 116-117 °C; $^1$H NMR (200 MHz, CDCl$_3$) δ 7.19-7.00 (m, 5H, Ph), 3.87 (s, 6 H, 2 COOMe), 3.76 (s, 8 H, 2 COOMe, CH$_2$), 3.70 (s, 3 H, COOMe); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 176.29, 162.30 (2), 162.06 (2), 142.70 (2), 141.82 (2), 133.40, 129.09 (2), 127.81 (2), 127.28, 68.13, 53.35, 52.69 (2), 52.67 (2), 38.01; MS $m/z$ (M$^+$) for C$_{22}$H$_{22}$O$_{10}$ calcd 446.1213, found 446.1218.

1,2,3,4,5-pentakis(Methoxycarbonyl)-5-ethylcyclopentadiene, (148f): 50% yield; mp 99-100 °C (lit. 101-102 °C); $^{2}$H NMR (200 MHz, CDCl$_3$) δ 3.88 (s, 6 H, 2 COOMe), 3.83 (s, 6 H, 2 COOMe), 3.66 (s, 3 H, COOMe), 1.69 (s, 3 H, Me); $^{13}$C NMR (50 MHz, CDCl$_3$) δ 167.40, 162.62 (2), 161.82 (2), 144.86 (2), 139.65 (2), 65.60, 53.24, 52.75 (2), 52.59 (2), 17.35.
5.21 Rearrangement of 148a-f in methanol or methanol-d₄.

Rearrangement of 148a in methanol-d₄. Cyclopentadiene 143a (0.0124 g, 0.0240 mmol) and toluene (2.52 µL, internal standard) were dissolved in 0.5 mL of methanol-d₄. After 3 minutes at ambient temperature ¹H NMR spectroscopy (200 MHz) revealed 148a (49%), 152 (D analogue, 51%), and 154f (D analogue, 51%). After 20 minutes at ambient temperature, ¹H NMR spectroscopy (200 MHz) revealed 152 (D analogue, 100%) and 154a (D, analogue 100%). In another experiment, cyclopentadiene 148a (0.200 g, 0.038 mmol) was dissolved in methanol (1.0 mL) for 20 minutes. The volatiles were removed in vacuo and the residue was dissolved in CDCl₃. ¹H NMR spectroscopy revealed 152 (100%) and benzhydryl methyl ether (100%). The CDCl₃ was removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) to give 152 (77%) and 154f (82%). Compound 154f was confirmed by the comparison of its spectroscopic data to those reported in the literature for benzhydryl methyl ether.¹⁹²

Rearrangement of 148b in methanol-d₄. Cyclopentadiene 148b (0.0076 g, 0.0189 mmol) and toluene (2.00 µL, internal standard) were dissolved in methanol-d₄ and placed in an nmr tube. The tube was then heated at 40 °C and the rate of disappearance of 148b was monitored by ¹H NMR spectroscopy (200 MHz). Concentration vs. time data (7 points) were obtained by normalizing the integrated intensity of the methyl singlet of toluene against the integrated intensity of the CH₂ singlet of 148b for 2 half lifetimes. The resultant plot of ln((A-x)/A) vs. t yielded an observed rate constant of
(5.2 ± 0.3) x 10^{-4} \text{s}^{-1} \text{(correlation coefficient = 0.9934)} \text{for the decrease in concentration of 148b. After 2 hours at 40 °C,} ^{1}\text{H NMR spectroscopy (200 MHz) revealed 154b (D analogue, 100%) and 152 (D analogue, 100%). Bulb to bulb distillation (0.01 mm Hg) separated the volatiles from 152. The presence of dimethoxymethane-}d_{3} \text{in the volatiles was confirmed by gas chromatography and} ^{1}\text{H NMR spectroscopy spiking experiments with an authentic sample of dimethoxymethane.}

**Rearrangement of 148c in methanol and methanol-}d_{4}.** Cyclopentadiene 148c (0.0085 g, 0.0174 mmol) and toluene (1.75 μL, internal standard) were dissolved in methanol-}d_{4} \text{(0.5 mL) and placed in a nmr tube. The tube was then heated at 50 °C and the rate of disappearance of 148c was monitored by} ^{1}\text{H NMR spectroscopy (200 MHz). Concentration vs. time data (6 points) were obtained by normalizing the integrated intensity of the methyl singlet of toluene against the integrated intensity of the COOMe singlet of 148c at 3.5 ppm for 2.6 half lifes. The resultant plot of ln\{(A-x)/A\} vs. t yielded an observed rate constant of (5.2 ± 0.2) x 10^{-4} \text{s}^{-1} \text{(correlation coefficient = 0.9966)} \text{for the decrease in concentration of 148c. After 3 hours at 50 °C the solution consisted of 152 (D analogue, 100%) and 154c (D analogue, 100%). In another experiment, cyclopentadiene 148c (0.0100 g, 0.0205 mmol) was dissolved in 0.5 mL of methanol. After 2 hours at 65 °C, the solvent was removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 4:1 hexane/ethyl acetate) to give 152 (67%) and 1-adamantyl methyl ether (73%). The spectral data for 1-adamantyl methyl ether were identical to those of a sample prepared by another route.}^{193}
Rearrangement of 148d in methanol. Cyclopentadiene 148d (0.0104 g, 0.0219 mmol) and toluene (1.75 μL, internal standard) were dissolved in methanol-d₄ (0.5 mL) and placed in a nmr tube. The tube was then heated at 100 °C and the rate of disappearance of 148d was monitored by ¹H NMR spectroscopy (200 MHz). Concentration vs. time data (9 points) were obtained by normalizing the integrated intensity of the methyl singlet of toluene against the integrated intensity of the COOMe singlet of 148d at 3.77 ppm for 2.5 half lives. The resultant plot of ln((A-x)/A) vs. t yielded an observed rate constant of (3.14 ± 0.03) x 10⁻⁴ s⁻¹ (correlation coefficient = 0.9980) for the decrease in concentration of 148d. After 4 hours at 50 °C the solution consisted of 152 (D analogue, 100%) and 154d (D analogue, 100%). In another experiment, cyclopentadiene 148d (0.0200 g, 0.0420 mmol) was dissolved in methanol (1.0 mL) and sealed in a tube. The tube was heated at 100 °C for 4 hours. The solvent was removed in vacuo and the residue dissolved in chloroform-d. ¹H NMR spectroscopy revealed 152 (100%) and 154d (100%). The solvent was removed in vacuo and the residue was subjected to centrifugal chromatography (silica gel, 3:2 hexane/ethyl acetate) to give 152 (71%) and 154d (82%). The spectral data for p-methoxybenzyl methyl ether were identical to those of a sample prepared by another route.⁹₄

Rearrangement of 148e in methanol-d₄. Cyclopentadiene 148e (0.030 g, 0.063 mmol) was dissolved in methanol-d₄ (0.5 mL). The solution was then degassed (three freeze-pump-thaw cycles), and sealed in an nmr tube. The tube was heated at 140 °C for 3 hours after which ¹H NMR spectroscopy (200 MHz) revealed 148e (63%), 149e (29%),
and 150e (8%). The carbomethoxy and methylene signals from the $^1$H NMR spectra of 149e and 150e could be identified in that solution. This mixture of isomers could not be separated by column chromatography.

4-Benzyl-1,2,3,5,5-pentakis(methoxycarbonyl)cyclopentadiene, (149e): $^1$H NMR (200 MHz, CDCl$_3$) δ 4.37 (s, 2 H, CH$_2$), 3.95 (s, 3 H, COOMe), 3.83 (s, 3 H, COOMe), 3.74 (s, 3 H, COOMe), 3.36 (s, 6 H, 2 COOMe).

3-Benzyl-1,2,4,5,5-pentakis(methoxycarbonyl)cyclopentadiene, (150e): $^1$H NMR (200 MHz, CDCl$_3$) δ 4.24 (s, 2 H, CH$_2$), 3.38 (s, 3 H, COOMe), 3.79 (s, 6 H, 2 COOMe), 3.77 (s, 3 H, COOMe), 3.51 (s, 3 H, COOMe).

Rearrangement of 148f in methanol-$d_4$. Cyclopentadiene 148f (0.0262 g, 0.0707 mmol) was dissolved in methanol-$d_4$ (0.5 mL). The solution was then degassed (three freeze-pump-thaw cycles), and sealed in an nmr tube. The tube was heated at 140 ºC for 35 minutes and $^1$H NMR spectroscopy (90 MHz) revealed 148f (62%) and 149g (38%). After the nmr tube was heated for an additional period of 1 hour and 25 minutes, $^1$H NMR spectroscopy (200 MHz) revealed 148f (60%) and 149f (40%). After the nmr tube was heated at 140 ºC for an additional 1 hour period, $^1$H NMR (200 MHz) spectroscopy revealed 148f (57%) and 149f (43%). These two isomers could not be separated by centrifugal chromatography. The volatiles were removed in vacuo and the residue dissolved in chloroform-$d$. Signals corresponding to the $^1$H NMR and $^{13}$C NMR spectra
of 149f could be identified from this solution.

1,2,3,5,5-pentakis(Methoxycarbonyl)-4-methylcyclopentadiene, (149f): $^1$H NMR (200 MHz, CDCl$_3$) $\delta$ 3.93 (s, 3 H, COOME), 3.82 (s, 3 H, COOME), 3.78 (s, 3 H, COOME), 3.75 (s, 6 H, 2 COOME), 2.42 (s, 3 H, Me). $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 164.77, 164.11 (2), 161.90, 161.38, 158.47, 147.55, 132.08, 131.55, 74.51, 53.68 (2), 52.67 (overlap with isomer assumed), 52.28 (2), 14.58.
APPENDIX I

Observed Rate Constant Data

Plot of the first order rate of disappearance of 111e in C₆D₆ at 20 °C (sample plot).

\[ k_{\text{obs}} = (9.8 \pm 0.4) \times 10^{-5} \text{ s}^{-1} \]
Table 27. Determination of \( k_{\text{obs}} \) for \textbf{111e} in \( \text{C}_6\text{D}_6 \) at \( 30^\circ \text{C} \).

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln{(A-x)/A} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>605</td>
<td>-0.061</td>
</tr>
<tr>
<td>1278</td>
<td>-0.121</td>
</tr>
<tr>
<td>1984</td>
<td>-0.248</td>
</tr>
<tr>
<td>2904</td>
<td>-0.279</td>
</tr>
<tr>
<td>3893</td>
<td>-0.412</td>
</tr>
<tr>
<td>4746</td>
<td>-0.467</td>
</tr>
<tr>
<td>5699</td>
<td>-0.574</td>
</tr>
<tr>
<td>6608</td>
<td>-0.657</td>
</tr>
</tbody>
</table>

Slope \( (m) = (-9.8 \pm 0.4) \times 10^{-5} \text{s}^{-1} \)
Correlation Coefficient \( (R) = 0.9953 \)

Table 28. Determination of \( k_{\text{obs}} \) for \textbf{111c} in \( \text{C}_6\text{D}_6 \) with 2.5 equivalents of triethylenediamine at \( 35^\circ \text{C} \).

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln{(A-x)/A} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>987</td>
<td>0</td>
</tr>
<tr>
<td>1920</td>
<td>-0.069</td>
</tr>
<tr>
<td>5950</td>
<td>-0.246</td>
</tr>
<tr>
<td>7082</td>
<td>-0.280</td>
</tr>
<tr>
<td>8205</td>
<td>-0.374</td>
</tr>
<tr>
<td>9489</td>
<td>-0.465</td>
</tr>
<tr>
<td>10749</td>
<td>-0.562</td>
</tr>
<tr>
<td>11970</td>
<td>-0.562</td>
</tr>
<tr>
<td>13320</td>
<td>-0.667</td>
</tr>
<tr>
<td>14752</td>
<td>-0.752</td>
</tr>
<tr>
<td>16194</td>
<td>-0.836</td>
</tr>
<tr>
<td>18542</td>
<td>-1.050</td>
</tr>
<tr>
<td>21007</td>
<td>-1.200</td>
</tr>
<tr>
<td>24005</td>
<td>-1.451</td>
</tr>
</tbody>
</table>

\( m = (-6.2 \pm 0.2) \times 10^{-5} \text{s}^{-1} \)
\( R = 0.9941 \)

Table 29. Determination of \( k_{\text{obs}} \) for \textbf{111d} in \( \text{C}_6\text{D}_6 \) at \( 35^\circ \text{C} \).

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln{(A-x)/A} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>5173</td>
<td>1.377</td>
</tr>
<tr>
<td>5941</td>
<td>1.422</td>
</tr>
<tr>
<td>6563</td>
<td>1.448</td>
</tr>
<tr>
<td>7771</td>
<td>1.542</td>
</tr>
<tr>
<td>8988</td>
<td>1.591</td>
</tr>
<tr>
<td>9641</td>
<td>1.576</td>
</tr>
<tr>
<td>10644</td>
<td>1.728</td>
</tr>
<tr>
<td>11576</td>
<td>1.781</td>
</tr>
<tr>
<td>12730</td>
<td>1.833</td>
</tr>
<tr>
<td>13808</td>
<td>1.907</td>
</tr>
<tr>
<td>15013</td>
<td>1.960</td>
</tr>
<tr>
<td>16346</td>
<td>1.981</td>
</tr>
<tr>
<td>17572</td>
<td>2.100</td>
</tr>
<tr>
<td>18865</td>
<td>2.167</td>
</tr>
<tr>
<td>20045</td>
<td>2.166</td>
</tr>
</tbody>
</table>

\( m = (5.6 \pm 0.2) \times 10^{-5} \text{s}^{-1} \)
\( R = 0.9912 \)
Table 30. Determination of $k_{obs}$ for 120b in C$_6$D$_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1171</td>
<td>0</td>
</tr>
<tr>
<td>2034</td>
<td>-0.205</td>
</tr>
<tr>
<td>2835</td>
<td>-0.244</td>
</tr>
<tr>
<td>4635</td>
<td>-0.290</td>
</tr>
<tr>
<td>5559</td>
<td>-0.375</td>
</tr>
<tr>
<td>7667</td>
<td>-0.683</td>
</tr>
<tr>
<td>8900</td>
<td>-0.786</td>
</tr>
<tr>
<td>11934</td>
<td>-1.264</td>
</tr>
<tr>
<td>13219</td>
<td>-1.299</td>
</tr>
<tr>
<td>14900</td>
<td>-1.550</td>
</tr>
</tbody>
</table>

$m = (-1.10 \pm 0.05) \times 10^4$ s$^{-1}$
$R = 0.9905$

Table 31. Determination of $k_{obs}$ for 120e in C$_6$D$_6$ at 130 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>2755</td>
<td>1.511</td>
</tr>
<tr>
<td>3369</td>
<td>1.578</td>
</tr>
<tr>
<td>3985</td>
<td>1.668</td>
</tr>
<tr>
<td>4581</td>
<td>1.771</td>
</tr>
<tr>
<td>5172</td>
<td>1.891</td>
</tr>
<tr>
<td>6380</td>
<td>2.011</td>
</tr>
</tbody>
</table>

$m = (1.45 \pm 0.08) \times 10^4$ s$^{-1}$
$R = 0.9939$

Table 32. Determination of $k_{obs}$ for 128c in C$_6$D$_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1796</td>
<td>-0.113</td>
</tr>
<tr>
<td>3599</td>
<td>-0.276</td>
</tr>
<tr>
<td>5298</td>
<td>-0.474</td>
</tr>
<tr>
<td>6904</td>
<td>-0.625</td>
</tr>
<tr>
<td>8642</td>
<td>-0.788</td>
</tr>
<tr>
<td>10142</td>
<td>-0.890</td>
</tr>
<tr>
<td>11774</td>
<td>-1.248</td>
</tr>
<tr>
<td>13462</td>
<td>-1.382</td>
</tr>
<tr>
<td>15242</td>
<td>-1.555</td>
</tr>
</tbody>
</table>

$m = (-1.06 \pm 0.03) \times 10^4$ s$^{-1}$
$R = 0.9975$

Table 33. Determination of $k_{obs}$ for 128c in acetone-d$_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>608</td>
<td>-0.061</td>
</tr>
<tr>
<td>845</td>
<td>-0.205</td>
</tr>
<tr>
<td>909</td>
<td>-0.220</td>
</tr>
<tr>
<td>1476</td>
<td>-0.362</td>
</tr>
<tr>
<td>3212</td>
<td>-0.391</td>
</tr>
<tr>
<td>5055</td>
<td>-0.581</td>
</tr>
<tr>
<td>6899</td>
<td>-0.799</td>
</tr>
<tr>
<td>8707</td>
<td>-0.922</td>
</tr>
<tr>
<td>11071</td>
<td>-1.141</td>
</tr>
<tr>
<td>13035</td>
<td>-1.310</td>
</tr>
<tr>
<td>16027</td>
<td>-1.684</td>
</tr>
<tr>
<td>18097</td>
<td>-1.834</td>
</tr>
</tbody>
</table>

$m = (-9.7 \pm 0.3) \times 10^5$s$^{-1}$
$R = 0.9954$
Table 34. Determination of $k_{obs}$ for 128c in CD$_3$OD at 50 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln((A-x)/A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>911</td>
<td>-0.368</td>
</tr>
<tr>
<td>1805</td>
<td>-0.793</td>
</tr>
<tr>
<td>2757</td>
<td>-1.280</td>
</tr>
<tr>
<td>3580</td>
<td>-1.648</td>
</tr>
</tbody>
</table>

$m = (-4.7 \pm 0.1) \times 10^{-4} \text{ s}^{-1}$
$R = 0.9993$

Table 35. Determination of $k_{obs}$ for 128d in C$_6$D$_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln((A-x)/A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>975</td>
<td>-0.116</td>
</tr>
<tr>
<td>3463</td>
<td>-0.270</td>
</tr>
<tr>
<td>4393</td>
<td>-0.567</td>
</tr>
<tr>
<td>7388</td>
<td>-0.898</td>
</tr>
<tr>
<td>10001</td>
<td>-1.203</td>
</tr>
<tr>
<td>12602</td>
<td>-1.279</td>
</tr>
</tbody>
</table>

$m = (-1.10 \pm 0.09) \times 10^{-4} \text{ s}^{-1}$
$R = 0.9850$

Table 36. Determination of $k_{obs}$ for 128d in acetone-$d_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln((A-x)/A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>608</td>
<td>0</td>
</tr>
<tr>
<td>1453</td>
<td>-0.172</td>
</tr>
<tr>
<td>2362</td>
<td>-0.218</td>
</tr>
<tr>
<td>3838</td>
<td>-0.385</td>
</tr>
<tr>
<td>5574</td>
<td>-0.490</td>
</tr>
<tr>
<td>7417</td>
<td>-0.795</td>
</tr>
<tr>
<td>9261</td>
<td>-0.890</td>
</tr>
<tr>
<td>11069</td>
<td>-0.944</td>
</tr>
<tr>
<td>13433</td>
<td>-1.097</td>
</tr>
<tr>
<td>20459</td>
<td>-1.889</td>
</tr>
</tbody>
</table>

$m = (-8.9 \pm 0.4) \times 10^{-5} \text{ s}^{-1}$
$R = 0.9924$

Table 37. Determination of $k_{obs}$ for 128e in C$_6$D$_6$ at 60 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln((A-x)/A)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>922</td>
<td>-0.116</td>
</tr>
<tr>
<td>2019</td>
<td>-0.355</td>
</tr>
<tr>
<td>2998</td>
<td>-0.710</td>
</tr>
<tr>
<td>4021</td>
<td>-0.957</td>
</tr>
<tr>
<td>4957</td>
<td>-1.360</td>
</tr>
<tr>
<td>5958</td>
<td>-1.688</td>
</tr>
<tr>
<td>6964</td>
<td>-2.166</td>
</tr>
<tr>
<td>7939</td>
<td>-2.601</td>
</tr>
</tbody>
</table>

$m = (-3.3 \pm 0.2) \times 10^{-4} \text{ s}^{-1}$
$R = 0.9898$
### Table 38. Determination of $k_{\text{obs}}$ for 128e in C$_6$D$_6$ at 60 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln((A-x)/A) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>601</td>
<td>-0.160</td>
</tr>
<tr>
<td>1205</td>
<td>-0.352</td>
</tr>
<tr>
<td>2057</td>
<td>-0.632</td>
</tr>
<tr>
<td>2823</td>
<td>-0.825</td>
</tr>
<tr>
<td>3470</td>
<td>-1.239</td>
</tr>
<tr>
<td>3986</td>
<td>-1.439</td>
</tr>
<tr>
<td>4521</td>
<td>-1.633</td>
</tr>
<tr>
<td>5066</td>
<td>-1.789</td>
</tr>
<tr>
<td>5638</td>
<td>-2.135</td>
</tr>
</tbody>
</table>

\[ m = (-3.8 \pm 0.1) \times 10^{-4} \text{ s}^{-1} \]

\[ R = 0.9952 \]

### Table 39. Determination of $k_{\text{obs}}$ for 128e in acetone-$d_6$ at 60 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln((A-x)/A) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>465</td>
<td>-0.018</td>
</tr>
<tr>
<td>1096</td>
<td>-0.169</td>
</tr>
<tr>
<td>1771</td>
<td>-0.237</td>
</tr>
<tr>
<td>2704</td>
<td>-0.420</td>
</tr>
<tr>
<td>4497</td>
<td>-0.826</td>
</tr>
<tr>
<td>5361</td>
<td>-1.065</td>
</tr>
<tr>
<td>6376</td>
<td>-1.402</td>
</tr>
<tr>
<td>7403</td>
<td>-1.354</td>
</tr>
</tbody>
</table>

\[ m = (-2.1 \pm 0.1) \times 10^{-4} \text{ s}^{-1} \]

\[ R = 0.9990 \]

### Table 40. Determination of $k_{\text{obs}}$ for 128f in C$_6$D$_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln((A-x)/A) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>975</td>
<td>0</td>
</tr>
<tr>
<td>3463</td>
<td>-0.558</td>
</tr>
<tr>
<td>4461</td>
<td>-0.752</td>
</tr>
<tr>
<td>5484</td>
<td>-1.130</td>
</tr>
<tr>
<td>6420</td>
<td>-1.418</td>
</tr>
<tr>
<td>7421</td>
<td>-1.797</td>
</tr>
<tr>
<td>8427</td>
<td>-2.037</td>
</tr>
<tr>
<td>9402</td>
<td>-2.294</td>
</tr>
</tbody>
</table>

\[ m = (-2.8 \pm 0.1) \times 10^{-4} \text{ s}^{-1} \]

\[ R = 0.9955 \]

### Table 41. Determination of $k_{\text{obs}}$ for 128f in acetone-$d_6$ at 90 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>( \ln((A-x)/A) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>608</td>
<td>0</td>
</tr>
<tr>
<td>1453</td>
<td>-0.134</td>
</tr>
<tr>
<td>2362</td>
<td>-0.441</td>
</tr>
<tr>
<td>3285</td>
<td>-0.641</td>
</tr>
<tr>
<td>4205</td>
<td>-0.962</td>
</tr>
<tr>
<td>5063</td>
<td>-1.187</td>
</tr>
<tr>
<td>5694</td>
<td>-1.378</td>
</tr>
<tr>
<td>6334</td>
<td>-1.537</td>
</tr>
<tr>
<td>6996</td>
<td>-1.714</td>
</tr>
<tr>
<td>7759</td>
<td>-1.980</td>
</tr>
</tbody>
</table>

\[ m = (-2.80 \pm 0.05) \times 10^{-4} \text{ s}^{-1} \]

\[ R = 0.9988 \]
### Table 42. Determination of $k_{obs}$ for 148b in CD$_2$OD at 40 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>271</td>
<td>-0.142</td>
</tr>
<tr>
<td>549</td>
<td>-0.286</td>
</tr>
<tr>
<td>831</td>
<td>-0.400</td>
</tr>
<tr>
<td>1462</td>
<td>-0.760</td>
</tr>
<tr>
<td>1805</td>
<td>-1.110</td>
</tr>
<tr>
<td>2199</td>
<td>-1.360</td>
</tr>
</tbody>
</table>

$m = (-6.2 \pm 0.3) \times 10^{-4} \text{ s}^{-1}$

$R = 0.9935$

### Table 43. Determination of $k_{obs}$ for 148c in CD$_2$OD at 50 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1162</td>
<td>-0.627</td>
</tr>
<tr>
<td>2002</td>
<td>-1.068</td>
</tr>
<tr>
<td>2634</td>
<td>-1.346</td>
</tr>
<tr>
<td>3053</td>
<td>-1.681</td>
</tr>
<tr>
<td>3443</td>
<td>-1.720</td>
</tr>
</tbody>
</table>

$m = (-5.2 \pm 0.2) \times 10^{-4} \text{ s}^{-1}$

$R = 0.9966$

### Table 44. Determination of $k_{obs}$ for 148d in CD$_2$OD at 100 °C.

<table>
<thead>
<tr>
<th>Time (sec)</th>
<th>Ln{(A-x)/A}</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>600</td>
<td>-0.072</td>
</tr>
<tr>
<td>1307</td>
<td>-0.315</td>
</tr>
<tr>
<td>2019</td>
<td>-0.545</td>
</tr>
<tr>
<td>2621</td>
<td>-0.733</td>
</tr>
<tr>
<td>3346</td>
<td>-1.026</td>
</tr>
<tr>
<td>4043</td>
<td>-1.184</td>
</tr>
<tr>
<td>4766</td>
<td>-1.448</td>
</tr>
<tr>
<td>5427</td>
<td>-1.631</td>
</tr>
</tbody>
</table>

$m = (-3.14 \pm 0.08) \times 10^{-4} \text{ s}^{-1}$

$R = 0.9980$
APPENDIX II

Calculation of the maximum value for \( k_r \) that would not give detectible Line Broadening

The width of a relevant NMR line has a broadening contribution, at half height \((\Delta \nu_{1/2})\) as follows:

\[
\Delta \nu_{1/2} = (\tau_A \pi)^{-1} \quad (\tau_A = \text{the lifetime of a nucleus in environment A})
\]

Therefore,

\[
\Delta \nu_{1/2} = k_r / \pi \quad (k_r = \text{rate of rearrangement})
\]

For detectible line broadening:

\[
k_r > (\Delta \nu_{1/2}) \pi
\]

Since,

\[
1.0 \text{ Hz} < \Delta \nu_{1/2} < 1.5 \text{ Hz}
\]

Then,

\[
k_r > 3.1 - 4.7 \text{ s}^{-1}
\]
APPENDIX III

Infrared Spectra

General Experimental: Infrared (IR) spectra were recorded on a Bio-Rad FTS-40 spectrometer and are reported as $\lambda_{\text{max}}$ in cm$^{-1}$. IR spectra were measured in CCl$_4$ on NaCl plates and absorptions are reported as weak (w), medium (m), or strong (s).

**113b:** IR ν (N-H) 3194 (w), (N-H) 3108 (w), 2990 (w), 2929 (w), 2823 (w), 1717 (m), 1679 (s), 1637 (w), 1457 (w), 1373 (m), 1337 (w), 1326 (w), 1261 (w), 1194 (w), 1103 (m) cm$^{-1}$.

**113d:** IR ν (N-H) 3195 (w), 2927 (s), 2908 (s), 2851 (m), 1735 (w), 1710 (m), 1676 (s), 1654 (w), 1452 (w), 1417 (w), 1377 (w) 1314 (w), 1242 (w), 1128 (w), 993 (w), 909 (m) cm$^{-1}$.

**114b:** IR ν 2997 (m), 2943 (m), 2889 (m), 2834 (m), 2817 (w), 2738 (w), 1574 (w), 1468 (m), 1454 (m), 1376 (m), 1303 (w), 1275 (w), 1233 (s), 1206 (s), 1196 (s), 1157 (s), 1121 (s), 1062 (s), 992 (m), 911 (s), 871 (w), 857 (w) cm$^{-1}$.
114e: IR v 3001 (w), 2943 (w), 2913 (w), 2836 (w), 1614 (m), 1515 (s), 1464 (w), 1442 (w), 1376 (m), 1322 (w), 1303 (w), 1251 (s), 1188 (m), 1181 (m), 1152 (s), 1060 (m), 1041 (m), 969 (w), 909 (m), 833 (w) cm$^{-1}$.

118a: IR v 2952 (w), (C=O) 1745 (m), (C=O) 1720 (m), 1556 (w), 1307 (w), 1238 (w), 1216 (m), 1174 (w), 1085 (w) cm$^{-1}$.

119a: IR v 3033 (w), 2952 (w), 2841 (m), (C=O) 1723 (s), 1544 (m), 1495 (w), 1450 (m), 1304 (m), 1239 (s), 1193 (w), 1107 (s), 1068 (m), 1014 (w), 960 (w), 822 (w), 700 (m) cm$^{-1}$.

119d: IR v 2913 (s), 2854 (m), (C=O) 1723 (s), 1485 (w), 1450 (m), 1420 (w), 1353 (w), 1308 (w), 1241 (s), 1205 (s), 1108 (m), 1035 (w), 1023 (m), 950 (w), 701 (w), 625 (w) cm$^{-1}$.

134c: IR v 2965 (s), 2872 (w), 2843 (w), 1762 (s), (C=C) 1736 (s), (C=O) 1699 (s), 1473 (w), 1436 (m), 1365 (w), 1292 (w), 1253 (m), 1232 (s), 1171 (w) cm$^{-1}$.

134d: IR v 2909 (s), 2852 (s), (C=C) 1732 (s), (C=O) 1701 (m), 1450 (m), 1437 (m), 1363 (w), 1310 (w), 1251 (m), 1203 (m), 1167 (m), 1034 (w), 909 (m) cm$^{-1}$.
128c: IR v 2970 (s), 2956 (m), 1752 (s), (C=O) 1730 (s), (C=C-N=N) 1621 (m), 1458 (m), 1435 (m), 1370 (m), 1266 (s), 1219 (m), 1197 (w), 1114 (m), 1076 (m), 1056 (m), 982 (m), 925 (w), 668 (w), 551 (w) cm⁻¹.

128f: IR v 3112 (w), 1752 (m), (C=O) 1732 (s), (C=C-N=N) 1609 (w), 1454 (m), 1304 (w), 1271 (s), 1073 (w), 1046 (w), 702 (w), 625 (w) cm⁻¹.

131b: IR v (N-H) 3455 (m), (N-H) 3197 (w), 2960 (m), 2823 (w), (C=O) 1723 (s), 1463 (m), 1440 (m), 1304 (m), 1261 (s), 1245 (w), 1196 (m), 1096 (s), 1015 (s), 957 (w) cm⁻¹.

131c: IR v (N-H) 3465 (m), (N-H) 3196 (w), 2987 (w), 2955 (m), 2918 (w), 2872 (w), (C=O) 1742 (s), 1444 (m), 1361 (m), 1266 (m), 1216 (m), 1201 (m), 1169 (m), 1106 (w), 1032 (m) cm⁻¹.

132c: IR v 2984 (m), 2952 (m), 1742 (m), (C=O) 1722 (s), 1448 (m), 1351 (w), 1270 (w), 1224 (s), 1170 (m), 1110 (m), 1032 (w), 1020 (w), 951 (w) cm⁻¹.

132e: IR v 3001 (w), 2954 (m), 2912 (w), 2837 (w), 1743 (m), (C=O) 1723 (s), 1614 (m), 1587 (w), 1515 (s), 1459 (m), 1424 (m), 1382 (w), 1295 (w), 1250 (s), 1227 (s), 1177 (m), 1040 (m), 1023 (m), 951 (w), 909 (m), 827 (w) cm⁻¹.
139b: IR ν 2996 (w), 2952 (m), 2932 (m), 2855 (w), (C=O) 1733 (s), 1456 (m), 1256 (s), 1194 (w), 1153 (w), 1109 (w), 1086 (m), 1005 (w), 921 (w) cm\(^{-1}\).

135c: IR ν (N-H) 3467 (w), 2960 (m), 2929 (m), 2860 (w), (C=O) 1737 (s), 1717 (m), 1458 (w), 1374 (w), 1259 (w), 1230 (m), 1019 (w), 909 (s) cm\(^{-1}\).

148e: IR ν 3033 (w), 2953 (m), 2846 (w), (C=O) 1748 (s), (C=C) 1625 (w), 1455 (m), 1436 (s), 1344 (m), 1287 (m), 1254 (s), 1222 (s), 1180 (m), 1145 (w), 1132 (w), 1067 (w), 999 (m), 702 (m) cm\(^{-1}\).

148b: IR ν 3029 (w), 2953 (w), 2828 (w), (C=O) 1747 (s), (C=C) 1627 (w), 1436 (m), 1344 (w), 1247 (m), 1211 (m), 1171 (w), 1118 (w), 981 (w), 937 (w), 625 (w), 474 (w) cm\(^{-1}\).
REFERENCES


