INFORMATION TO USERS

This was produced from a copy of a document sent to us for microfilming. While the most advanced technological means to photograph and reproduce this document have been used, the quality is heavily dependent upon the quality of the material submitted.

The following explanation of techniques is provided to help you understand markings or notations which may appear on this reproduction.

1. The sign or "target" for pages apparently lacking from the document photographed is "Missing Page(s)". If it was possible to obtain the missing page(s) or section, they are spliced into the film along with adjacent pages. This may have necessitated cutting through an image and duplicating adjacent pages to assure you of complete continuity.

2. When an image on the film is obliterated with a round black mark it is an indication that the film inspector noticed either blurred copy because of movement during exposure, or duplicate copy. Unless we meant to delete copyrighted materials that should not have been filmed, you will find a good image of the page in the adjacent frame.

3. When a map, drawing or chart, etc., is part of the material being photographed the photographer has followed a definite method in "sectioning" the material. It is customary to begin filming at the upper left hand corner of a large sheet and to continue from left to right in equal sections with small overlaps. If necessary, sectioning is continued again—beginning below the first row and continuing on until complete.

4. For any illustrations that cannot be reproduced satisfactorily by xerography, photographic prints can be purchased at additional cost and tipped into your xerographic copy. Requests can be made to our Dissertations Customer Services Department.

5. Some pages in any document may have indistinct print. In all cases we have filmed the best available copy.
EVANGELISTA, RAMON ACANTILADO
IMINUM ION FORMATION AND DEUTERIUM EXCHANGE
BY ACETONE IN THE PRESENCE OF SECONDARY
AMINES AND ANALOGOUS HYDRAZINE AND
HYDROXILAMINE DERIVATIVES.

THE OHIO STATE UNIVERSITY, PH.D., 1978
IMINIUM ION FORMATION AND DEUTERIUM EXCHANGE BY ACETONE
IN THE PRESENCE OF SECONDARY AMINES AND ANALOGOUS
HYDRAZINE AND HYDROXYLAMINE DERIVATIVES

DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate
School of The Ohio State University

By
Ramon A. Evangelista, B.S.

* * * * *

The Ohio State University
1978

Reading Committee:
Professor Jack Hine
Professor Miles Chedekel
Professor Robert Cuellette

Approved By

Advisor
Department of Chemistry
To my parents
ACKNOWLEDGMENTS

I would like to thank my adviser, Professor Jack Hine, for his valuable suggestions and guidance during the entire course of this research and for his pleasant disposition in our discussions of the problems involved in this study.

I would also like to thank my laboratory colleagues for their help in the experiments, especially Larry Green for the instructions on the operations of the stopped-flow spectrophotometer, Robert Flachskam for instructions on deuteration experiments, and William Sacks and James Zeigler for instructions on calculations and computer programming.

I would also like to express my sincere gratitude to Miss Gina Arzaga for her encouragement, friendship, and companionship which helped make my non-chemistry life more fruitful.
VITA

June 21, 1952 ................................... Born - Manila, Philippines

1973 .............................................. B.S., University of the
Philippines, Quezon City, Philippines

1973-1974 ....................................... Laboratory Instructor, Department
of Chemistry, University of the
Philippines

1974-1975 ....................................... Teaching Associate, Department of
Chemistry, The Ohio State Univ.,
Columbus, Ohio 43210

1975-1978 ....................................... Research Associate, Department of
Chemistry, The Ohio State
University, Columbus, Ohio 43210

Major Field: Physical Organic Chemistry
# TABLE OF CONTENTS

## ACKNOWLEDGMENTS

Page iii

## VITA

Page iv

## LIST OF TABLES

Page viii

## LIST OF FIGURES

Page xi

## Chapter

### I. INTRODUCTION

Page 1

### II. EXPERIMENTAL

Page 10

#### A. Chemicals

Page 10

#### B. Instrumentation

Page 13

#### C. Synthetic Procedures

Page 17

1. Synthesis of 2-Dimethylaminomethylpyrrolidine
2. Synthesis of Pyrazolidine
3. Synthesis of Isoxazolidine
4. Synthesis of Iminium Salts

#### D. Determination of Dissociation Constants of
Ammonium Ions

Page 35

#### E. Detection of Reaction Between Acetone and
Pyrazolidinium Ions by pH Measurements

Page 36

#### F. NMR Study of Iminium Ion Formation

Page 37

#### G. UV Study of Iminium Ion Formation

Page 38

#### H. Determination of Equilibrium Constants for Iminium
Ion Formation by Measurements of UV Equilibrium
Absorbances

Page 40

#### I. Determination of Equilibrium Constants for Iminium
Ion Formation by NMR

Page 43

1. Reaction Between Acetone-$d_6$ and
$O,N$-Dimethylhydroxylammonium Ions

Page 44
CONTENTS (CONT'D)

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Reaction Between Acetone-(d_6) and 1,2-Dimethylhydrazinium Ions</td>
<td>45</td>
</tr>
<tr>
<td>J. Kinetics of Iminium Ion Formation and Hydrolysis</td>
<td>46</td>
</tr>
<tr>
<td>1. Acetone - Hydroxylamine - 2-Dimethylaminomethylpyrrolidine Kinetics</td>
<td>46</td>
</tr>
<tr>
<td>2. N-Isopropylidenehydrazolinium Ion Hydrolysis</td>
<td>47</td>
</tr>
<tr>
<td>3. Acetone - Pyrazolidinium Ion Reaction</td>
<td>49</td>
</tr>
<tr>
<td>4. N-Isopropylideneisoxazolidinium Ion Hydrolysis</td>
<td>50</td>
</tr>
<tr>
<td>K. Deuterium Exchange Kinetics</td>
<td>51</td>
</tr>
</tbody>
</table>

III. RESULTS

<p>| A. pK's of Protonated Amines                                          | 55   |
| B. Acetone - Hydroxylamine - 2-Dimethylaminomethylpyrrolidine Kinetics| 61   |
| C. Evidences for Iminium Ion Formation Between Acetone and the Salts of Pyrazolidine, Isoxazolidine, (O,N)-Dimethylhydroxylamine and 1,2-Dimethylhydrazine | 75   |
| 1. Acetone and Pyrazolidinium Ions                                    | 75   |
| 2. Acetone and Isoxazolidinium Ions                                   | 82   |
| 3. Acetone and (O,N)-Dimethylhydroxylammonium Ions                  | 95   |
| 4. Acetone and (1,2)-Dimethylhydrazinium Ions                       | 105  |
| D. Hydrolysis of N-Isopropylidenehydrazolinium Ion                   | 116  |
| E. Acetone - Pyrazolidinium Ion Reaction                              | 124  |
| F. Determination of Equilibrium Constants for Iminium Ion Formation by Measurement of UV Equilibrium Absorbances | 131  |
| 1. Acetone and Isoxazolidinium Ions                                   | 131  |
| 2. Acetone and (O,N)-Dimethylhydroxylammonium Ions                  | 134  |
| 3. Acetone and (1,2)-Dimethylhydrazinium Ions                       | 139  |
| G. Determination of Equilibrium Constants for Iminium Ion Formation by NMR. | 141  |
| 1. Acetone-(d_6) - (O,N)-Dimethylhydroxylammonium Ion Reaction     | 141  |</p>
<table>
<thead>
<tr>
<th>CONTENTS (CONT'D)</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. Acetone - 1,2-Dimethylhydrazinium Ion Reaction</td>
<td>151</td>
</tr>
<tr>
<td>H. Hydrolysis of N-Isopropyldeneisoaxazolidinium Ion</td>
<td>159</td>
</tr>
<tr>
<td>I. Dedeteration of Acetone-d_{6} in the Presence of Pyrrolidine and 3-Dimethylaminopropionitrile</td>
<td>173</td>
</tr>
<tr>
<td>J. Dedeteration of Acetone-d_{6} in the Presence of Pyridine, Pyrrolidine and Dimethylamine</td>
<td>181</td>
</tr>
<tr>
<td>K. Dedeteration of Acetone-d_{6} in the Presence of Pyridine, Pyrazolidine and 1,2-Dimethylhydrazine</td>
<td>185</td>
</tr>
<tr>
<td>L. Dedeteration of Acetone-d_{6} in the Presence of Pyridine, Isoxazolidine and O,N-Dimethylhydroxylamine</td>
<td>189</td>
</tr>
<tr>
<td>IV. DISCUSSION</td>
<td>198</td>
</tr>
<tr>
<td>A. Acetone - Hydroxylamine - 2-Dimethylaminomethylpyrrolidine Kinetics</td>
<td>198</td>
</tr>
<tr>
<td>B. Iminium Ion Formation With Pyrazolidinium, Isoxazolidinium, O,N-Dimethylhydroxylammonium and 1,2-Dimethylhydrazinium Ions</td>
<td>207</td>
</tr>
<tr>
<td>C. Dedeteration of Acetone-d_{6} in the Presence of Pyrrolidine and Dimethylamine</td>
<td>218</td>
</tr>
<tr>
<td>D. Dedeteration of Acetone-d_{6} in the Presence of Pyrazolidine, Isoxazolidine, O,N-Dimethylhydroxyamine and 1,2-Dimethylhydrazine</td>
<td>220</td>
</tr>
<tr>
<td>V. CONCLUSIONS</td>
<td>228</td>
</tr>
<tr>
<td>VI. SUGGESTIONS FOR FUTURE RESEARCH</td>
<td>230</td>
</tr>
<tr>
<td>APPENDIX</td>
<td>237</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>260</td>
</tr>
<tr>
<td>Table</td>
<td>Page</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>1. Results of Determination of Dissociation Constants of Protonated Amines</td>
<td>58</td>
</tr>
<tr>
<td>2. pK's of Ammonium Ions</td>
<td>60</td>
</tr>
<tr>
<td>3. Results of Acetone - Hydroxylamine-2-Dimethylaminomethylpyrroolidine Kinetics</td>
<td>63</td>
</tr>
<tr>
<td>4. pH's of Solutions Resulting from Injection of Acetone into Pyrazolidine Buffer</td>
<td>75</td>
</tr>
<tr>
<td>5. Absorbances at Different Times After Injection of Acetone into 1,2-Dimethylhydrazinium Ion Solutions</td>
<td>112</td>
</tr>
<tr>
<td>6. Equilibrium Absorbances of Solutions Resulting from Injection of N-Isopropylidene-1,2-dimethylhydrazinium Perchlorate Solution into 0.1 M Formate Buffer</td>
<td>115</td>
</tr>
<tr>
<td>7. Results of Kinetic Study of Hydrolysis of N-Isopropylidene-pyrazolidinium Ions</td>
<td>117</td>
</tr>
<tr>
<td>8. Catalytic Constants for the Hydrolysis of N-Isopropylidene-pyrazolidinium Ions</td>
<td>123</td>
</tr>
<tr>
<td>9. Results of Kinetic Study of Iminium Ion Formation Between Acetone and Pyrazolidinium Ions</td>
<td>126</td>
</tr>
<tr>
<td>10. Absorbances of Aqueous Acetone Solutions at 275 nm</td>
<td>131</td>
</tr>
<tr>
<td>11. Equilibrium Absorbances at 275 nm of Acetone-Isoxazolidinium Bromide Solutions</td>
<td>132</td>
</tr>
<tr>
<td>12. Equilibrium Absorbances at 275 nm of Acetone-O,N-Dimethylhydroxylamine Hydrochloride Solutions</td>
<td>136</td>
</tr>
<tr>
<td>13. Absorbances of Aqueous Acetone Solutions at 240 nm</td>
<td>139</td>
</tr>
<tr>
<td>14. Extrapolated Equilibrium Absorbances at 240 nm of Acetone-1,2-Dimethylhydrazinium Ion Solutions</td>
<td>140</td>
</tr>
</tbody>
</table>
TABLES (CONT'D)

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>15.</td>
<td>Integration Values in the NMR Spectra of O,N-Dimethylhydroxylammonium Ions in D$_2$O</td>
<td>143</td>
</tr>
<tr>
<td>16.</td>
<td>Integration Values in the NMR Spectra of Acetone-d$_8$ O,N-Dimethylhydroxylammonium Ion Solutions</td>
<td>145</td>
</tr>
<tr>
<td>17.</td>
<td>Equilibrium Constants for Iminium Ion Formation Between Acetone-d$_8$ and O,N-Dimethylhydroxylammonium Ions at Different Concentrations of D$_2$O.</td>
<td>148</td>
</tr>
<tr>
<td>18.</td>
<td>Equilibrium Constants for Iminium Ion Formation Between Acetone and O,N-Dimethylhydroxylammonium Ions Extrapolated to Dilute Aqueous Solutions.</td>
<td>149</td>
</tr>
<tr>
<td>19.</td>
<td>Integration Values in the NMR Spectra of 1,2-Dimethylhydrazinium Ions in D$_2$O</td>
<td>152</td>
</tr>
<tr>
<td>20.</td>
<td>Integration Values in the NMR Spectra of Acetone-d$_8$-1,2-Dimethylhydrazinium Ion Solutions</td>
<td>153</td>
</tr>
<tr>
<td>21.</td>
<td>Equilibrium Constants for Iminium Ion Formation Between Acetone-d$_8$ and 1,2-Dimethylhydrazinium Ions at Different Concentrations of D$_2$O.</td>
<td>156</td>
</tr>
<tr>
<td>22.</td>
<td>Equilibrium Constants at 35$^\circ$ for Iminium Ion Formation Between Acetone-d$_8$ and 1,2-Dimethylhydrazinium Ions Extrapolated to Dilute Aqueous Solution</td>
<td>157</td>
</tr>
<tr>
<td>23.</td>
<td>Rates of Hydrolysis of N-Isopropylideneisoxazolidinium Ion at Different pH's</td>
<td>161</td>
</tr>
<tr>
<td>24.</td>
<td>Results of Dedeuteration Experiments with Acetone-d$_8$ in the Presence of Pyrrolidine and 3-Dimethylaminopropionitrile</td>
<td>177</td>
</tr>
<tr>
<td>25.</td>
<td>Results of Dedeuteration Experiments with Acetone-d$_8$ in the Presence of Pyridine, Pyrrolidine, and Dimethylamine</td>
<td>182</td>
</tr>
<tr>
<td>26.</td>
<td>Results of Dedeuteration of Acetone-d$_8$ in the Presence of Pyridine, Pyrazolidine, and 1,2-Dimethylhydrazine.</td>
<td>186</td>
</tr>
</tbody>
</table>
## TABLES (CONT'D)

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>27.</td>
<td>Results of Dedeuteration of Acetone-$d_3$ in the Presence of Pyridine, Isoxazolidine, and O,N-Dimethylhydroxylamine</td>
<td>190</td>
</tr>
<tr>
<td>28.</td>
<td>Equilibrium Concentrations in Dedeuteration of Acetone-$d_3$ in the Presence of Pyridine, Isoxazolidine and O,N-Dimethylhydroxylamine</td>
<td>194</td>
</tr>
<tr>
<td>29.</td>
<td>Equilibrium and Kinetic Constants for Iminium Ion Formation and Deuterium Exchange by Acetone in the Presence of Secondary Ammonium Ions</td>
<td>222</td>
</tr>
</tbody>
</table>
## LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Set-up for Transfer of Acetone-Chloroform Mixture Into Mass Spec Bulbs</td>
<td>54</td>
</tr>
<tr>
<td>2.</td>
<td>Rate Constant for 2-Dimethylaminomethylpyrrolidine Catalyzed Oximation of Acetone vs. Hydroxylamine Concentration at pH 9.95</td>
<td>66</td>
</tr>
<tr>
<td>3.</td>
<td>Rate Constant for 2-Dimethylaminomethylpyrrolidine-Catalyzed Oximation of Acetone vs. Hydroxylamine Concentration at pH 8.90</td>
<td>67</td>
</tr>
<tr>
<td>4.</td>
<td>60 MHz PMR Spectrum of Pyrazolidinium Perchlorate in D$_2$O</td>
<td>78</td>
</tr>
<tr>
<td>5.</td>
<td>60 MHz PMR Spectrum of 6:1 (mole/mole) Acetone-d$_3$-Pyrazolidinium Perchlorate in D$_2$O</td>
<td>79</td>
</tr>
<tr>
<td>6.</td>
<td>60 MHz PMR Spectrum of N-Isopropylideneperazolidinium Perchlorate in DMF-d$_7$</td>
<td>80</td>
</tr>
<tr>
<td>7.</td>
<td>60 MHz PMR Spectrum of Isoxazolidinium Bromide in D$_2$O</td>
<td>83</td>
</tr>
<tr>
<td>8.</td>
<td>60 MHz PMR Spectrum of Acetone-d$_3$-Isoxazolidinium Bromide Solution in D$_2$O</td>
<td>84</td>
</tr>
<tr>
<td>9.</td>
<td>60 MHz PMR Spectrum of Acetone-d$_3$-Isoxazolidinium Bromide Solution in D$_2$O-DMSO-d$_3$</td>
<td>85</td>
</tr>
<tr>
<td>10.</td>
<td>60 MHz PMR Spectrum of Acetone-d$_3$-Isoxazolidinium Bromide in D$_2$O, 2$1/2$ Hours After Mixing</td>
<td>86</td>
</tr>
<tr>
<td>11.</td>
<td>60 MHz PMR Spectrum of Acetone-d$_3$-Isoxazolidinium Bromide in D$_2$O-DMSO-d$_3$, 48 Hours After Mixing</td>
<td>87</td>
</tr>
<tr>
<td>12.</td>
<td>60 MHz PMR Spectrum of N-Isopropylideneisoxazolidinium Perchlorate in CD$_3$CN</td>
<td>88</td>
</tr>
<tr>
<td>13.</td>
<td>60 MHz PMR Spectrum of O,N-Dimethylhydroxylamine Hydrochloride in D$_2$O</td>
<td>94</td>
</tr>
<tr>
<td>Figure</td>
<td>FIGURES (CONT'D)</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>---------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>14</td>
<td>60 MHz PMR Spectrum of Acetone-$d_6$-$O,N$-Dimethylhydroxylamine Hydrochloride Solution in D$_2$O</td>
<td>96</td>
</tr>
<tr>
<td>15</td>
<td>60 MHz PMR Spectrum of Acetone-$O,N$-Dimethylhydroxylamine Hydrochloride Solution in D$_2$O</td>
<td>97</td>
</tr>
<tr>
<td>16</td>
<td>60 MHz PMR Spectrum of $\text{N-Isopropylidene}$-$O,N$-Dimethylhydroxylammonium Perchlorate in DMSO-$d_6$</td>
<td>98</td>
</tr>
<tr>
<td>17</td>
<td>60 MHz PMR Spectrum of Solution of $\text{N-Isopropylidene}$-$O,N$-Dimethylhydroxylammonium Perchlorate in DMSO-$d_6$ After Addition of D$_2$O</td>
<td>99</td>
</tr>
<tr>
<td>18</td>
<td>60 MHz PMR Spectrum of 1,2-Dimethylhydrazine Hydrochloride in D$_2$O</td>
<td>104</td>
</tr>
<tr>
<td>19</td>
<td>60 MHz PMR Spectrum of Acetone-$d_6$-1,2-Dimethylhydrazine Hydrochloride Solution in D$_2$O</td>
<td>105</td>
</tr>
<tr>
<td>20</td>
<td>60 MHz PMR Spectrum of Acetone-1,2-Dimethylhydrazine Hydrochloride in D$_2$O</td>
<td>106</td>
</tr>
<tr>
<td>21</td>
<td>60 MHz PMR Spectrum of $\text{N-Isopropylidene}$-1,2-dimethylhydrazinium Perchlorate in CD$_3$CN</td>
<td>107</td>
</tr>
<tr>
<td>22</td>
<td>60 MHz PMR Spectrum of $\text{N-Isopropylidene}$-1,2-dimethylhydrazinium Perchlorate in CD$_3$CN After Addition of D$_2$O</td>
<td>108</td>
</tr>
<tr>
<td>23</td>
<td>Log of Rate Constant for $\text{N-Isopropylidene}$pyrazolidinium Ion Hydrolysis Extrapolated to Zero Buffer Concentration vs. pH</td>
<td>122</td>
</tr>
<tr>
<td>24</td>
<td>Brønsted Plot for Hydrolysis of $\text{N-Isopropylidene}$pyrazolidinium Ion</td>
<td>125</td>
</tr>
<tr>
<td>25</td>
<td>Equilibrium Absorbance of Acetone-Isoxazolidinium Bromide Mixtures vs. Amine Salt Concentration</td>
<td>135</td>
</tr>
<tr>
<td>26</td>
<td>Equilibrium Absorbance of Acetone-$O,N$-Hydroxylamine Hydrochloride Mixture vs. Amine Salt Concentration</td>
<td>138</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-------------</td>
<td>------</td>
</tr>
<tr>
<td>27.</td>
<td>Extrapolated Equilibrium Absorbance of Acetone-1,2-Dimethylhydrazine Hydrochloride vs. Amine Salt Concentration.</td>
<td>142</td>
</tr>
<tr>
<td>28.</td>
<td>Equilibrium Constant for Iminium Ion Formation Between Acetone and O,N-Dimethylhydroxylammonium Ions vs. Mole Fraction of D$_2$O</td>
<td>150</td>
</tr>
<tr>
<td>29.</td>
<td>Log of Equilibrium Constant for Iminium Ion Formation Between Acetone and 1,2-Dimethylhydrazinium Ions vs. Mole Fraction of D$_2$O</td>
<td>158</td>
</tr>
<tr>
<td>30.</td>
<td>Rate Constant for N-Isopropylideneisoazolidinium Ion Hydrolysis vs. pH</td>
<td>167</td>
</tr>
<tr>
<td>31.</td>
<td>Brønsted Plot for Hydrolysis of N-Isopropylideneisoazolidinium Ion</td>
<td>172</td>
</tr>
<tr>
<td>32.</td>
<td>Log of Iminium Ion Formation Rate Constant for Secondary Amines vs. pK of Ammonium Ions</td>
<td>203</td>
</tr>
<tr>
<td>33.</td>
<td>Transition State for Dehydration of Carbinolamine Formed from Acetone and the Tertiary Monoprotonated Form of DMAMP</td>
<td>204</td>
</tr>
<tr>
<td>34.</td>
<td>Newman Projection of Transition State for the Dehydration of Carbinolamine Formed from Acetone and the Tertiary Monoprotonated Form of DMAMP</td>
<td>206</td>
</tr>
<tr>
<td>35.</td>
<td>Log $k_{II}$ vs. pK of Secondary Ammonium Ions</td>
<td>225</td>
</tr>
</tbody>
</table>
CHAPTER I. INTRODUCTION

Imines and iminium ions have been studied extensively in recent years because of their role as intermediates in numerous enzymatic and non-enzymatic reactions. Examples of enzymes which utilize the formation of Schiff bases in binding with their carbonyl substrates are acetoacetate decarboxylase, $^1$ 2-keto-3-deoxy-L-arabonate dehydratase, $^2$ D-4-deoxy-5-oxoglucarate hydrolase (decarboxylating), $^3$ and dehydroquinate hydrolase. $^4$ It has been shown in all these cases that the carbonyl substrate becomes bound to a lysine residue in the enzyme. This was done by treatment of the enzyme in the presence of its substrate with sodium borohydride, which reduces the imine to an amine, hydrolysis of the protein and isolation of the lysine substituted at the $\epsilon$-position. The mechanism of action of aldolases $^5,^6,^7$ and transaldolases $^8,^9$ has also been proposed to involve Schiff base formation with lysine residues. However, in these cases, it is not the substrate which becomes attached to the lysine residue after reduction with borohydride and hydrolysis, but the product in the case of aldolases and the intermediate product, for example, dihydroxyacetone, in the case of transaldolases.

Many non-enzymatic reactions whose mechanisms require the carbonyl compound to pass through an enol or enolate ion intermediate
are catalyzed by primary or secondary amines. Some of these reactions are non-enzymatic analogues of the reactions catalyzed by the above-mentioned enzymes. Examples of these reactions are the α-deuterium exchange of aldehydes and ketones,\textsuperscript{10,11,12} halogenation,\textsuperscript{13} dehydration of β-hydroxy aldehydes and ketones,\textsuperscript{14} decarboxylation of β-keto- and α-nitro-carboxylic acids,\textsuperscript{15} aldol condensation,\textsuperscript{16} dealdolization,\textsuperscript{17} Michael addition,\textsuperscript{18} and Knoevenagel reaction.\textsuperscript{19,20}

In these reactions, the carbonyl compound condenses with the primary or secondary amine to form the iminium ion which gets converted to an enamine instead of the enol or enolate as in the case of the uncatalyzed reaction.

\[ \overset{\text{O}}{\overset{\text{R}_{2}NH}{\rightleftharpoons}} \overset{\text{NR}_{2}^{+}}{\text{H}} + \overset{\text{OH}^{-}}{\text{H}} \quad (1) \]

\[ \overset{\text{NR}_{2}^{+}}{\text{H}} + \overset{\text{B}^{+}}{\overset{\text{B}^{-}}{\text{B}: \rightleftharpoons \overset{\text{NR}_{2}}{\text{B}} + \overset{\text{BH}^{+}}{\text{H}} \quad (2) \]

The activation energy barrier for enolization is replaced by two barriers of lower energy - one for iminium ion formation and the other for enamine formation. If enolization is the rate-determining step in the uncatalyzed reaction, one of these two will be rate-limiting in the amine-catalyzed reaction depending on the relative heights of the two barriers. The loss of the α-hydrogen from the iminium ion is much faster than that from the carbonyl compound
because the positively-charged nitrogen acts as an electron sink to accept the negative charge created at the α-carbon. In the case of the uncatalyzed reaction in near neutral or acidic medium, the catalyst is the proton but because of the very low pK of the conjugate acids of simple aliphatic carbonyl compounds (~ -7), only a very small amount of the carbonyl compound gets protonated. With primary amines as catalyst, the carbonyl oxygen is replaced by an imino nitrogen. The Schiff base itself is even less reactive than the carbonyl compound but it is easily protonated to form the very reactive iminium ion. The Schiff base is generally only about two or three pK units less basic than the parent amine. In the case of nucleophilic reactions towards carbonyl compounds, because of the positive charge of the imino group, the carbon atom which was originally the carbonyl carbon becomes more susceptible to nucleophilic attack, for example by hydroxylamine in the case of oxime formation and by an enol or enolate ion to form a carbon-carbon bond in the case of aldol condensation.

Iminium ions also play an important role in reactions like the well-known Mannich reaction and aminonitrile formation. In these reactions, the amine does not act as a catalyst but ends up as part of the product. The iminium ion intermediates undergo nucleophilic attack at the electron-deficient carbon to form a substituted amine.
Intensive work has been done by Hine regarding iminium ion formation between primary amines and acetone. This carbonyl compound was chosen because it offers no complication of cis-trans isomerism, unlike in the case of isobutyaldehyde. In that study, it has been shown that the primary-tertiary diamines with two or three carbon atoms between the nitrogen atoms form iminium ions at pH's where there are significant amounts of the mono-protonated form much faster than that predicted by a plot of the logarithm of the rate constant for iminium ion formation against the pK's of the ammonium ions (which are measures of the basicities of the amines). The increased rate has been attributed to internal general acid catalysis by the protonated tertiary amino group in the dehydration of the initially formed carbinolamine, which is usually the rate-determining step in iminium ion formation in near neutral or basic medium.

Scheme I

\[ \text{H}_2\text{N} + \text{CH}_3\text{CH}_2\text{CH}_2\text{NH}^{+}\text{CH}_3 \rightarrow \text{H}_2\text{O} + \text{CH}_3\text{CH}_2\text{CH}_2\text{N}^{+}\text{CH}_3 \]
By the same method of trapping with hydroxylamine, iminium ion formation with secondary amines has been studied. It has been found that as in the case of primary amines, the rate of iminium ion formation increases with increasing basicity of the amine. However, there is an important difference in iminium ion formation between the two classes of amines studied. The primary amines used were of the type $\text{RCH}_2\text{NH}_2$ so that hydrogen is always on one side of the imino double bond and the differences in the $\text{RCH}_2$ group on the other side cause differences in rate primarily by polar effects. With secondary amines, it was found that the rate of reaction is very much dependent on whether the amine is cyclic or acyclic and on the ring size if it is cyclic. If a correction taken from the solvolysis of the tertiary alkyl chlorides is introduced, the logarithms of the corrected iminium ion formation rate constants become a linear function of the pK of the ammonium ions and the resulting line is lower but nearly parallel to that of the primary amines.

The question now remains whether the iminium ion formation with secondary amines is capable of being catalyzed by an internal general acid such as a tertiary ammonio group just like the case of primary-tertiary diamines with two or three carbon atoms between the nitrogens. To this end, iminium ion formation with 2-dimethylamino-methylpyrrolidine (DMAMP) with acetone was studied. Since the equilibrium constant for this reaction is expected to be small such
that no change in concentrations will be observed when acetone and the amine are mixed together, it was decided that the reaction be studied by trapping the iminium ions with hydroxylamine as in the case of the previous work.

Another question that arises is whether secondary amines are capable of catalyzing the α-deuterium exchange of acetone just like primary amines are. Previous work on dedeuteration of isobutyraldehyde-2-\textsuperscript{3}H\textsubscript{5} in the presence of morpholine, piperazine and dimethylamine resulted in no detection of catalysis of the deuterium exchange via iminium ions. This was attributed to steric hindrance between the isopropyl group of isobutyraldehyde and the alkyl groups from the secondary amine. With acetone, the isopropyl group is replaced by a methyl group. Although the hydrogen is replaced by a methyl on the other side of the imino double bond, the steric interaction between the groups across the double bond should be considerably smaller in this system. Thus, there is a possibility that catalysis via iminium ions may be observed. The experimental approach to this problem is to study the deuterium exchange of acetone-\textsubscript{d\textsubscript{5}} with the protons from the solvent in the presence of a tertiary amine which is capable of removing deuterons by simple base catalysis and with a secondary
amine capable of forming iminium ions with acetone-$d_6$. The kinetic studies should be performed at pH regions where no significant amount of free secondary amine is present because the rates of simple base-catalyzed removal of deuterium by secondary amines are not known and where there are significant amounts of tertiary amines which can remove the deuterium from both acetone-$d_6$ and the deuterated iminium ion. Because of the values of their dissociation constants of their conjugate acids, pyrrolidine (PYR) and 3-dimethylaminopropionitrile (DPN) were chosen.

\[
\begin{align*}
\text{(PYR)} & \quad \text{(DPN)} \\
& \quad (\text{CH}_3)_2\text{N}-\text{CH}_2\text{CH}_2\text{C} \equiv \text{N}
\end{align*}
\]

One very intriguing question is whether the $\alpha$-effect is operative for iminium ion formation with secondary amines. The $\alpha$-effect is a positive deviation from the Brønsted plot for nucleophilic reactions, which is a plot of the logarithms of rate constant versus the $pK$'s of the conjugate acids of the nucleophiles, which are measures of their basicities. The $\alpha$-effect generalization was first made by Edwards$^{31}$ and the name $\alpha$-effect comes from the fact that all these nucleophiles with increased reaction rates have atoms containing one or more unshared pairs of electrons beside the nucleophilic atom.
The term α-nucleophile includes hydroperoxy ions, hypochlorite ions, hydrazines and hydroxylamines. It is now believed that the α-effect is due to one or a combination of factors such as ground state destabilization of the nucleophile, transition state destabilization, solvent effects and product stability and that the enhanced rates could not be all attributed to just one explanation which can be applied generally for all α-nucleophiles.

One thing to be expected from iminium ion formation with amines containing atoms with an unshared pair of electrons beside the nitrogen is that the product will be stabilized relative to iminium ions formed from ordinary amines. In other words, the equilibrium constants for iminium ion formation with these amines will be larger than that for ordinary amines. The carbon-nitrogen double bond will be stabilized in the same manner as carbon-carbon double bonds are stabilized by alkoxy or amino groups. In a way, this will be a significant step towards finding an effective catalyst for deuterium exchange because the concentration of the more reactive species (the iminium ion) will be increased and consequently the rate of reaction. However, the use of a compound with an NH₂ group should be avoided because, if oxygen or another nitrogen is chosen as the atom containing the unshared pair of electrons, the resulting reaction will be oxime or hydrazone formation, a reaction whose equilibrium constant is expected to be so large that almost all of the carbonyl compound will be tied up as the hydrazone or oxime (for example, the
equilibrium constant for the formation of the oxime from acetone and hydroxylamine is \(4.65 \times 10^5 \text{ M}^{-1}\).\(^{29}\) If this happens, it could not be considered catalysis by the amine in the real sense of the word.

The first compound chosen for this study is pyrazolidine (PYRZN). This is expected to be an unhindered catalyst because the alkyl groups flanking the nitrogen are pulled back and because the iminium ion will be stabilized two ways: a) by conjugation of the imino double bond with the unshared pair of electrons of the neighboring nitrogen atom, and b) by the five-membered ring effect, a generalization made by Brown, Brewster, and Schechter\(^{34}\) regarding formation or retention of a double bond exo to a five-membered ring. The study was then extended to isoxazolidine (ISOX), 0,N-dimethylohydroxylamine (ONHX) and 1,2-dimethylhydrazine (DMHZ).

\[
\begin{align*}
\text{PYRZN} & : & \text{ISOX} & : & \text{ONHX} & : & \text{DMHZ} \\
\text{H} & & \text{H} & & \text{CH}_3\text{NHOCCH}_3 & & \text{CH}_3\text{NHNHCCH}_3 \\
\text{NH} & & \text{O} & & & & \\
\end{align*}
\]

The question of whether these amines can catalyze any of the reactions which involve enol or enolate ion intermediates was dealt with by attempting to use these amines as catalysts for dedeuteration, which is the simplest of the reactions mentioned.
A. Chemicals

Reagents and Starting Materials

The following compounds were used without prior purification:

- Glacial acetic acid (Mallinckrodt)
- Acetohydroxamic acid (Polysciences Inc.)
- Acetone-\( d_6 \) (Aldrich, 99.5\% isotopic purity)
- Benzenesulfonyl chloride (Matheson, Coleman and Bell)
- Benzoyl chloride (J.T. Baker)
- Cacodylic acid (Fisher)
- 1,3-dibromopropane (Aldrich)
- N,N'-dicyclohexylcarbodiimide (Aldrich)
- Anhydrous dimethylamine (Eastman)
- L-Glutamic acid (Sigma Chemical Corp.)
- Hydrazine hydrate (Eastman)
- Hydrogen bromide gas (Matheson)
- Hydrogen chloride gas (Matheson)
- Isobutyryl chloride (Eastman)
- Lithium aluminum hydride (Alfa)
- Oxalic acid (J.T. Baker)
- Potassium metal (J.T. Baker)
- Potassium carbonate (Mallinkrodt)
- L-2-pyrrolidone-5-carboxylic acid (Aldrich)
- Silver nitrate (Mallinkrodt)
- Sodium metal (J.T. Baker)
- Sodium borate decahydrate (J.T. Baker)
- Sodium chloride (Mallinkrodt)
- Sodium perchlorate monohydrate (G. Frederick Smith)

Acetone (Matheson, Coleman and Bell) was found to have no detectable impurities by GC using Carbowax-KOH column (Column temperature = 110°).

Dichlorofluorescein indicator solution for Fajans titration of chloride was prepared by J. Wilson.
Sodium formate (J.T. Baker) was dried overnight at 60° in the vacuum oven.

Hydroxylamine hydrochloride (Aldrich) was recrystallized from methanol containing a small amount of concentrated hydrochloric acid. M.p. - 155-156°.

Thionyl chloride (Matheson, Coleman and Bell) was purified according to the method of Fieser. Fifty milliliters of the unpurified liquid was mixed with 10 ml of quinoline and distilled through a glass bead column. The distillate was then mixed with raw linseed oil and fractionated through the same column.

Amines and Amine Salts

3-Dimethylaminopropionitrile (Eastman) was distilled through a stainless steel Heli-pack column at 5 mm Hg. The fraction used for kinetic studies had 99.1% purity determined by GC using Carbowax-KOH column (column temperature = 175°).

1,2-Dimethylhydrazine dihydrochloride (Aldrich) was recrystallized from absolute ethanol with a very small amount of concentrated hydrochloric acid. M.p. in open air - 120-125°. M.p. in sealed tube = 173-176° (Lit. m.p. - 165-167°). Its NMR spectrum does not show any impurity and the chloride concentration of its aqueous solution determined by Fajans titration agreed with the expected value within 1.5%.

O,N-Dimethylhydroxylamine hydrochloride (Aldrich) was recrystallized from 1:1 methanol-isopropanol mixture. The needles melted at 116-118° (lit. m.p. = 115-117°).
Pyrrolidine (Aldrich) was distilled under nitrogen through the Nester-Faust Spinning Band Column at 85°. The distilled liquid had no impurities which are detectable by GC using Carbowax-KOH column (column temperature = 90°).

Pyridine (Fisher) was found to have no detectable impurities by GC using Carbowax-KOH column (column temperature = 120°).

**NMR Solvents**

The following NMR solvents were used without prior purification: acetonitrile-d₃ (Aldrich, 99% isotopic purity); N,N-dimethylformamide-d₇ (Merck, 99.5% isotopic purity); and deuterium oxide (Aldrich, 99.8% isotopic purity).

**Solvents**

The following solvents were used without prior purification: carbon tetrachloride (VWR Scientific); chloroform (J.T. Baker); absolute ethanol (Gold Shield); 95% ethanol (Gold Shield); ether (Matheson, Coleman, and Bell); ethyl acetate (Mallinckrodt).

Acetonitrile (Fisher) was dried with Molecular Sieves Type 3A and was distilled under nitrogen.

N,N-Dimethylformamide (Fisher) was dried over Molecular Sieves Type 4A.

Tetrahydrofuran (Matheson, Coleman, And Bell) was stirred for several hours with calcium hydride and was distilled under nitrogen.
Double-distilled water was obtained from The Ohio State University Laboratory Stores. Prior to kinetic and equilibrium studies, it was boiled for about 15 minutes to remove dissolved gases and then allowed to cool down under nitrogen.

**Standard Solutions**

Standard solutions of hydrochloric acid, sodium hydroxide, and perchloric acid were obtained from The Ohio State University Reagent Store.

**Standard Buffer Solutions**

Beckman 14848 Buffer (pH 7.389 at 35°) and Fisher B-79 Buffer (pH 4.02 at 35°) were used to standardize the pH meter. The buffer powders were dissolved in nitrogen saturated double-distilled water in proportions specified by the manufacturers. The solutions were stored under nitrogen when not in use.

**B. Instrumentation**

**Constant Temperature Bath**

The sample and reference cell compartments of the Cary 1605 UV-visible spectrophotometer were maintained at 35.0 ± 0.1° by a circulating water-ethylene glycol bath manufactured by Cole-Parmer Instrument and Equipment Company. The deuterium exchange kinetics and pH measurements were done in a Sargent S-84805 thermostatic water bath equilibrated at 35.0 ± 0.1°. The solutions for stopped-flow measurements were kept at 35.0 ± 0.1° by a circulating water bath controlled by a Quick-Set Thermo-Regulator manufactured by HB Instrument Co.
Calculations

The linear and non-linear least squares analyses were performed using the Hewlett-Packard 9830A Calculator which is interfaced with the Hewlett-Packard 9866A Printer. All programs were written in augmented BASIC language.

Data Acquisition

Time-voltage data pairs were transferred from the Cary 1605 recorder or the Durrum Stopped-Flow Spectrophotometer to the Nicolet Digital Oscilloscope Model 1090 connected to the Hewlett-Packard 9830A Calculator via the Nicolet Calculator Interface Model 191 A.

Elemental Analysis

Elemental analyses of ammonium and iminium salts were performed by the Scandinavian Microanalytical Laboratory in Herlev, Denmark.

Gas Liquid Chromatography

The purities of liquids used in this study were determined with the F and M Dual Column Temperature Programmed Gas Chromatography Model 720 with a filament conductivity detector, using either a Carbowax 20M or Carbowax-KOH column (length = 6 ft, diameter = 1/4 in) on Chromosorb P at a helium gas flow rate of 50 cc/min.

Infrared Spectra

Infrared spectra were recorded with the Perkin-Elmer Grating Infrared Spectrophotometer Model 337.
Mass Spectra

Mass spectra were taken by Mr. R. Weisenberger using the AEI Model MS-902 Mass Spectrometer. The peaks were recorded on photographic paper and the heights were measured with a magnifying glass and a ruler.

Melting Point Determination

Melting points were measured using an assembly composed of a Kofler Micro Hot Stage and the Thermopan Microscope. The melting point of 1,2-dimethylhydrazine dihydrochloride was taken in a sealed tube using the Hoover Capillary Melting Point Apparatus.

Proton Magnetic Resonance Measurements

The PMR spectra were recorded with the Varian A60A or the Varian EM 360L NMR Spectrometer locked on the tetramethysilane signal. The PMR spectra of 2-dimethylaminomethylpyrrolidine were taken at the Institute of Polymer Science in Akron, Ohio, using the HR-300 Spectrometer.

pH Measurements

The pH of buffer solutions were determined by the Radiometer pH Meter Model 26 and the Radiometer GK 2301 Combination Electrode.

pK Determinations

Determination of the dissociation constants of the ammonium ions used in this study were performed by addition of hydrochloric acid or sodium hydroxide titrant into amine or amine salt solution,
respectively, in a titration cell immersed in the constant
temperature bath. During titration, the titration cell rests on a
platform which holds the pH electrode, the buret tip, a thermometer,
a tube from a nitrogen tank, and a stirrer. The titrant was added
either from a 10-ml glass buret or from the Radiometer Auto-Burette
Type ABU 1 b with a capacity of 25 ml.

**Plotting**

Plotting of data points and calculated functions were made with
the Hewlett-Packard Calculator Plotter interfaced with the Hewlett-
Packard Calculator 9830A.

**Stopped-Flow Measurements**

Stopped-flow kinetic measurements were performed using the Durrum
D-150 stopped-flow spectrophotometer with a Beckman Hydrogen Lamp
Power Supply. The solutions in the drive syringes were allowed at
least 20 minutes to reach the desired equilibrium temperature before
kinetic measurements were made.

**Ultraviolet Measurements**

All ultraviolet spectra and kinetic and equilibrium measurements
were made with the Cary Recording Spectrophotometer Model 1605. The
solutions were placed in Beckman quartz cells (1mm, 1 cm, or 10 cm)
and allowed to temperature-equilibrate to $35.0 \pm 0.1^\circ$ before measure-
ments were made. Spectra were recorded on the chart paper while
kinetic data were displayed on the Nicolet Digital Oscilloscope Model
1090, transferred to the memory of the HP Calculator and stored in
cassette tapes.
Vacuum Evaporation

Evaporation of volatile liquids at low pressure was carried out using the Buchi Rotovap Vacuum Evaporator connected to the house vacuum which produces a pressure of about 20 mm Hg.

Vacuum Control

Maintenance of a constant low pressure during distillation was accomplished using a Cartesian Diver manufactured by Cole-Parmer Instrument and Equipment Company.

Weighing

All weighings were done on a Mettler Type B5 H26 single pan balance with an accuracy of 0.1 mg.

C. Synthetic Procedures

1. Synthesis of 2-Dimethylaminomethylpyrrolidine

The synthesis of 2-dimethylaminomethylpyrrolidine was attempted via the following scheme.

\[
\text{Scheme II}
\]

\[
\text{O} \quad \text{N} \quad \text{C} \quad \text{OH} \quad + \quad (\text{CH}_3)_2\text{NH} \quad \rightarrow \quad \text{O} \quad \text{N} \quad \text{C} \quad \text{N} \quad \text{CH}_3 \quad \text{CH}_3 \quad \quad \text{[H]} \quad \rightarrow \\
\text{H} \quad \text{N} \quad \text{CH}_2 \quad \text{N} \quad \text{CH}_3 \quad \text{CH}_3
\]
a. **Attempts at Synthesis of N,N-Dimethyl-5-oxo-pyrrolidine-carboxamide from L-2-pyrrolidone-5-carboxylic Acid**

L-2-Pyrrolidone-5-carboxylic acid (25.8 g, 0.2 mole) was added to 500 ml of dichloromethane and the mixture was stirred while being cooled in an ice bath. Anhydrous dimethylamine (10.8 g, 0.22 mole) was added to the mixture from a cooled flask. While stirring at 0°, 45 g (0.22 mole) of N,N'-dicyclohexylcarbodiimide was added. The mixture was allowed to stir overnight at room temperature. A white precipitate thought to be dicyclohexylurea was filtered off. The solvent was evaporated using the Rotovap until the mixture turned into a thick syrup. Ethyl acetate was added to recrystallize the product. Part of the solid dissolved in ethyl acetate. After drying, the solid melted at 232-233° which agrees with the melting point of dicyclohexylurea. The solid which dissolved and crystallized from ethyl acetate melted at 190-203°. The desired product which has a melting point of 115-117° was not obtained.

The synthesis of the desired amide was again attempted by treating dimethylamine with the acid chloride of L-2-pyrrolidone-5-carboxylic acid. One gram of the acid was mixed with 5.0 ml of purified thionyl chloride. The mixture quickly turned into a black liquid. This liquid was added dropwise to an ice cold solution of dimethylamine in water but no precipitate was obtained. The final mixture remained a black liquid.

The synthesis of the desired amide was then attempted by treating dimethylamine with the mixed anhydride of L-2-pyrrolidone-5-carboxylic acid and benzenesulfonyl chloride. The acid (6.0 g) was
dissolved in 10 ml of pyridine. While stirring in an ice bath, 3.0 ml of benzenesulfonyl chloride was added slowly. The mixture quickly turned black. Addition of 1.6 ml of dimethylamine in a flask cooled with ice did not produce any change.

b. Synthesis of N,N-dimethyl-5-oxo-pyrrolidinecarboxamide
from Glutamic Acid

The procedure of Angier and Smith was followed in carrying out the following synthetic scheme.

Scheme III

L-Glutamic acid (200 g, 1.36 mole) was slurried through 600 ml of absolute ethanol. Dry hydrogen chloride gas was bubbled through the mixture for three hours. Two hundred milliliters more of absolute ethanol were added. The mixture remained a suspension at this point. The mixture was then refluxed for one hour over a steam bath during which all the solids dissolved. Ethanol was then removed by vacuum evaporation. Just before complete dryness, 100 ml of water was added to dissolve the solid residue. The mixture was cooled to 15°C and,
with vigorous stirring, concentrated ammonia solution was added until the pH reached 9.5 as seen by pH paper. Three 100 ml portions of ether were used to extract the product. After evaporation of the ether by vacuum, 191 g of yellow liquid was obtained, corresponding to 68% yield of diethyl-L-glutamate.

For the conversion of diethylglutamate to the desired amide, 191 g of the unpurified ester was mixed with 200 g of anhydrous dimethylamine in a thick-walled bottle kept cold in an ice bath. The bottle was sealed while cold with a rubber stopper secured firmly by copper wires. The mixture was allowed to stand at room temperature for four weeks. The stopper was then removed while the bottle was kept cold with ice. The bottle was left unstoppered at room temperature, allowing some of the excess dimethylamine to escape. The remaining excess amine was removed using the Rotovap. This caused the residue to become a thick viscous liquid which quickly turned to a hard yellow solid after being seeded with a few crystals of sodium chloride. The solid was distilled without a condenser over an oil bath at 0.06 mm Hg using a diffusion pump. The major fraction distilled at 205-210°. The adapter leading to the collecting flask was wrapped with heating tape to prevent the compound from solidifying before it reaches the collecting flask. The distilled yellow solid was recrystallized from hot ethyl acetate. The NMR of the solid in DMSO-d$_6$ was consistent with the structure of the desired compound.
NMR Spectrum

\[ \delta 7.5 \text{ (broad singlet, 1 proton)} - N-H; \delta 4.5 \text{ (broad triplet, 1 proton)} - H-C-C-N(Me)_2; \delta 2.9 \text{ and } \delta 2.8 \text{ (singlets, 6 protons)} - C-N(CH_3)_2; \delta 1.80-2.5 \text{ (multiplet, 4 protons)} - \\
\text{methylenes.} \]

c) Reduction of \(N,N\)-dimethyl-5-oxopyrrolidinecarboxamide

\[
\begin{align*}
\text{H} & \quad \text{O} & \quad \text{C} & \quad \text{N} & \quad \text{CH}_3 \\
\text{O} & \quad \text{N} & \quad \text{C} & \quad \text{N} & \quad \text{CH}_3 \\
\text{LiAlH}_4 & \quad \text{THF} & \quad \text{H} & \quad \text{N} & \quad \text{CH}_2 - \text{N} & \quad \text{CH}_3 \\
\end{align*}
\]

The procedure by Saito, Kikugawa, and Yamada\(^{38}\) for proline dimethylamide was followed. \(N,N\)-dimethyl-5-oxopyrrolidinecarboxamide (47 g) was added slowly to a suspension of 14.3 g of lithium aluminum hydride in 700 ml of tetrahydrofuran in a three-necked flask immersed in an ice bath. The mixture was then refluxed with stirring under nitrogen for 18 hours. After cooling to room temperature the mixture was cooled in an ice bath and 16 ml of 15% aqueous sodium hydroxide solution and 35 ml of water were added successively. Two hundred-forty ml of tetrahydrofuran was added and the mixture was refluxed for half an hour to destroy the excess lithium aluminum hydride. The mixture was filtered and the filtrate was dried over anhydrous potassium carbonate. The liquid was distilled at 80 mm Hg. Four fractions were taken and the major fraction, weighing 9.6 g was collected at 100-105°. The GC of this fraction taken with a Carbowax-KOH column showed that 75% of it is a compound believed to be the desired product. The liquid was redistilled at 80 mm Hg and the fraction boiling at 105-110°
was collected. The GC of this fraction showed a purity of 99.9% with two impurities of shorter retention times. 8.2 g of this liquid were obtained, corresponding to 21% yield based on the amide.

IR, NMR and mass spectroscopy were used to identify the compound.

IR: 3250 cm⁻¹ (broad) - N-H stretch; 2750-2950 cm⁻¹ - C-H stretches; 1420 cm⁻¹ (sharp) - C-N-H bending; no carbonyl peak.

Mass spectrum: \( m/e = 128 \) - parent peak
\[ m/e = 55 \text{ (more intense than 128 peak)} - CH₂-N(CH₃)₂⁺ \]
\[ m/e = 70 \text{ (more intense than 128 peak)} - \]

300 MHz NMR in D₂O:

![Chemical Structure Image]

162 Hz (multiplet, 1 proton) - one of d protons; 292 Hz (multiplet, 2 protons) - one of d and one of e protons; 344 Hz (multiplet, 1 proton) - one of e protons; 440 Hz (singlet, 6 protons) - a protons; 492 Hz (doublet of doublets, 2 protons) - b protons; 604 Hz (multiplet, 1 proton) - one of f protons; 638 Hz (multiplet, 1 proton) one of f protons; 720 Hz (quintet, 1 proton) - c proton.

This assignment was confirmed by decoupling experiments. When the signal at 720 Hz was irradiated at its frequency, the peak at
492 Hz becomes a singlet and the peak at 126 became a broadened quartet. When the signal at 162 Hz was irradiated, the peaks at 292 Hz, 344 Hz, and 720 Hz became simpler and broader. When the signal at 492 was irradiated, the peak at 720 Hz became a triplet. Irradiation at 344 Hz caused the peaks at 604 Hz and 720 Hz to become symmetric doublets.

The synthesis was repeated with 19.2 g of amide, 6.0 g of lithium aluminum hydride, and 500 ml of tetrahydrofuran. The liquid (4.7 g) was obtained with 98.3% purity by GC with 0.4% being tetrahydrofuran. The yield was 30% based on the amide.

Attempts to prepare the dihydrochloride and dihydrobromide did not succeed because the solids obtained by bubbling hydrogen chloride or hydrogen bromide gas into ether solutions of the amine remained wet even after overnight standing in the vacuum oven at 50°.

2. Synthesis of Pyrazolidine

a. Synthesis of Pyrazolidine from 1,3-Dibromopropane and Hydrazine

\[
\text{NH}_2\text{NH}_2 + \text{Br(CH}_2\text{)}_3\text{Br} \rightarrow \text{KOH} \rightarrow \text{NH}_2\text{NH}(\text{CH}_2\text{)}_3\text{NH} \tag{4}
\]

The procedure of Buhle, Moore and Wiselogle\textsuperscript{38} was followed. In a three-necked flask provided with a mechanical stirrer were placed 600 ml of 95% ethanol and 3.0 moles of hydrazine. While the solution
is refluxing under nitrogen, 150 ml of 1,3-dibromopropane was added dropwise from an addition funnel. The refluxing was continued for half an hour. The mixture was allowed to cool to room temperature and was then kept in the freezer for several hours. A large amount of solid, believed to be hydrazine monohydrobromide was filtered off. Potassium hydroxide pellets (40 g) was added to the filtrate while stirring. The precipitated potassium chloride was then removed by filtration. Ethanol was removed from the filtrate by distillation under nitrogen using a Vigreux column. The remaining liquid was distilled at 60 mm Hg and the fraction boiling from 32° to 55° was collected. The pressure was then reduced to 20 mm Hg and the fraction boiling from 25° to 88° was collected. The two fractions were combined and the resulting liquid was fractionated at 26 mm Hg using the Nester-Faust Spinning Band Column. Eleven fractions were collected because the temperature at which the liquid distilled kept rising. The major fractions were those boiling from 45-50°, 58-65°, and 75-85°.

The GC of the fraction collected at 58-65° taken using a Carbowax-KOH column showed that it consists of 89% of the most abundant component which is suspected to be pyrazolidine. One hundred forty milligrams of this liquid was dissolved in 2.5 ml of absolute ethanol. The resulting solution was mixed with 12.5 ml of 0.5 M oxalic acid in absolute ethanol. A white precipitate was formed. After filtration and drying, it melted at 118-120° (lit. m.p. = 114-
The liquid (0.5 ml) was mixed with 1.7 g of benzoyl chloride. Aqueous sodium hydroxide solution (20%) was added to neutralize the acid formed. A white solid precipitated out. After recrystallization from ethanol, this solid melted at 146-147°C (lit. m.p. for dibenzoylpyrazolidine = 146-147°C). The preparation of pyrazolidinium hydrochloride and hydrobromide was attempted by treating the 89% liquid in ether with either hydrogen chloride or hydrogen bromide gas. After evaporation of ether, the solids were obtained wet. Taking the melting points of the solids was not possible because of their hygroscopicity.

In another attempt at the synthesis using the same amounts, 13 fractions were collected by distillation through the spinning band column at 26 mm Hg. Five of the fractions contained pyrazolidine ranging from 56 to 76%. These five fractions were combined and the resulting liquid was redistilled through a short Vigreux column at 26 mm Hg. Eight fractions were collected. The five higher boiling fractions contained pyrazolidine ranging from 35 to 88%. Because of the very close boiling points of the several compounds present in each fraction, they could not be separated from each other. The NMR of a portion of the 88% fraction in D₂O showed a triplet at δ3.0 (-CH₂-N-N-CH₂) and a quartet at δ1.8 (C-CH₂-C).

The 88% fraction was mixed with its equivalent amount of 1.0 M perchloric acid at Dry Ice temperatures behind a safety shield. Tetrahydrofuran was added and the mixture was allowed to reach room
temperature. The liquids were removed by vacuum without heating. The solid residue was collected and recrystallized four times from absolute ethanol under nitrogen. The solid, believed to be pyrazolidinium perchlorate, melted at 182-183°. NMR in D$_2$O: $\delta$4.7 (singlet, 2 protons) - H$_2$O; $\delta$3.3 (triplet, $J$ = 7 Hz, 4 protons) - CH$_2$-N-N-CH$_2$; $\delta$2.1 (quintet, $J$ = 7 Hz, 2 protons) - C-CH$_2$-C.

Elemental analysis: Found (\%) - C, 20.89; H, 5.38; Cl, 20.49
Calc'd from C$_3$H$_6$N$_2$ClO$_4$ C, 20.88; H, 5.26; Cl, 20.54

After three weeks, the solid showed a much lower melting point indicating decomposition.

Due to the fact that pyrazolidine could not be separated from the several other compounds present in the collected fractions, another synthetic method was tried.

b. Synthesis of Pyrazolidine from $N,N'$-Diisobutylhydrazine and 1,3-Dibromopropane

Scheme IV

\[
\begin{align*}
\text{NH}_2\text{NH}_2 + 2(\text{CH}_3)_2\text{CHCOCl} & \rightarrow (\text{CH}_3)_2\text{CH}-\text{C}-\text{NH} \quad \text{HN} \\
& \quad 1) \text{HCl} \rightarrow (\text{CH}_3)_2\text{CH}-\text{C}-\text{N} \\
& \quad 2) \text{NaOH} \rightarrow \text{Br}(\text{CH}_2)_3\text{Br}
\end{align*}
\]
The procedure of Stetter and Spangenberg for the above synthetic scheme was followed.

**N,N'-Diisobutyrylhydrazine**

Isobutyryl chloride (69.4 g) was added dropwise to a solution of 20.4 g of 80% hydrazine hydrate and 45 g of potassium carbonate in 250 ml of water. The hydrazide precipitated in white clumps. The solid was washed with cold water and then dried in the vacuum oven at 50°. The solid melted at 242-245° but started subliming at around 150°. Yield was 47% based on isobutyryl chloride.

**N,N'-Diisobutyrylpyrazolidine**

N,N'-Diisobutyrylhydrazine (26.1 g) was slurried with vigorous stirring in 77 ml of absolute ethanol. To this was added dropwise potassium ethoxide solution made by dissolving 6.5 g of potassium metal in 60 ml of absolute ethanol. Most of the solid dissolved when the addition was completed. The alcohol was removed by vacuum and the solid residue was dissolved in 125 ml of dry N,N-dimethylformamide. To the resulting solution, 15.6 g of 1,3-dibromopropane was added dropwise while stirring and refluxing in a three-nicked flask. Potassium bromide and diisobutyrylhydrazine were removed by suction filtration. The filtrate was distilled at 0.5 mm Hg and the fraction distilling at 105-110° was collected. The yield is 71% based on 1,3-dibromopropane. The liquid obtained was 93% pure as seen by GC. Redistillation increased the purity to 97.3%.
**Pyrazolidine**

N,N'-Diisobutylpyrazolidine (9.4 g) was allowed to reflux with 25 ml of concentrated hydrochloric acid with stirring for 10 hrs. A water-insoluble layer remained on top, so 15 ml more of concentrated hydrochloric acid were added. All the liquids were removed by vacuum (0.5 mm Hg) over a water bath. The thick semi-solid residue was allowed to reflux with 6 g of potassium hydroxide in 30 ml of ethanol. The potassium chloride formed was filtered off and washed with ethanol. The combined filtrate and washings were distilled at 25 mm Hg through a glass helices column. After the ethanol boiled off, pyrazolidine was collected at 52-55°. The GC showed that 60% of the liquid is pyrazolidine. The liquid (0.3 ml) was reacted with 4.5 ml of 1.0 M aqueous perchloric acid at dry ice temperature with a small amount of tetrahydrofuran. All the liquids were removed at 0.5 mm Hg over a water bath at 45° behind a safety shield. The solid residue was dissolved at room temperature under nitrogen in a THF-ethanol mixture and was allowed to crystallize in the freezer. The melting point of pyrazolidinium perchlorate after two recrystallizations was 181-185°.

3. **Synthesis of Isoxazolidine**

Following the procedure of H. King but using acetohydroxamic acid instead of N-hydroxyurethane, isoxazolidine was obtained in extremely low yield, so another method was tried.
The reaction analogous to that used for the preparation of pyrazolidine was carried out.

$$\text{H}_2\text{NOH} \cdot \text{HCl} + \text{Br(CH}_2_3\text{Br} \xrightarrow{\text{base \ EtOH}} \text{H}$$

(5)

Hydroxylamine hydrochloride (11.4 g), 33.1 g of 1,3-dibromo-propane and 250 ml of 95% ethanol were mixed together in a 500 ml three-necked flask with a mechanical stirrer with a reflux condenser. To this mixture, heated to 65° with stirring under nitrogen, was added dropwise over a period of 45 minutes, a potassium hydroxide-in-ethanol solution (30.4 g of potassium hydroxide pellets in 150 ml of 95% ethanol). The mixture was heated and stirred for 1½ hours more and then was cooled to room temperature. The liquid portion of the reaction mixture contained a very small amount of unreacted 1,3-dibromopropane as seen by GC.

The mixture was filtered to remove potassium chloride and potassium bromide. Ethanol was removed from the filtrate using the Rotovap. The remaining liquid was distilled at 2.5 mm Hg, heating the distillation flask to dryness, with the collecting flask immersed in a Dry Ice-isopropanol bath. The distillate was fractionated at 36 mm Hg through a short Vigreux column. Four fractions were collected. The two higher boiling fractions, one collected at 42-60° and the other at 64-72° were combined. A small portion of the resulting liquid was dissolved in ether and mixed with a saturated solution of hydrogen
chloride gas in ether. After removal of the ether by vacuum, the solid residue was recrystallized in absolute ethanol-THF mixture.

The isoxazolidine hydrochloride needles melted at 124°-125° (lit. m.p. = 124°-125°). The hydrobromide was prepared exactly the same way but using hydrogen bromide instead of hydrogen chloride gas. After recrystallization in ethanol-tetrahydrofuran mixture, the plates melted at 109°-111° (no lit. value). The NMR of the two salts in D₂O are identical. δ4.8 (singlet, 2 protons) - H₂O; δ4.3 (triplet, J = 7 Hz, 2 protons) - C-CH₂-O; δ3.7 (triplet, J = 7 Hz, 2 protons) - CH₂-N⁺; δ2.5 (quintet, J = 7 Hz, 2 protons) - C-CH₂-C. Because the hydrochloride is more hygroscopic than the hydrobromide, the latter was used for the kinetic and equilibrium studies. Elemental analysis of isoxazolidinium bromide: Found (%) - C, 23.43; H, 5.24; N, 8.98; Br, 51.09; Calc'd for C₃H₇NOBr - C, 23.40; H, 5.24; N, 9.09; Br, 51.89.

The synthesis was repeated using sodium ethoxide, prepared by dissolving sodium metal in absolute ethanol, as base instead of potassium hydroxide. The yield of isoxazolidinium bromide based on 1,3-dibromopropane was 30%.

4. Synthesis of Iminium Salts

The method of Leonard and Paukstelis of direct reaction between amine perchlorate salt and carbonyl compound was employed. In all cases, the handling and recrystallization of the perchlorate salts were done behind a safety shield as a precautionary measure
against explosion. The purified solids were always handled under
nitrogen except during weighing.

a. \textit{N}-Isopropylidene.pyrazolidinium Perchlorate

Acetone (3.7 ml) was mixed with 0.5 ml of 10 M aqueous solution
of pyrazolidinium perchlorate. After an hour, 5 ml of tetrahydrofuran
was added and the mixture was kept in the freezer. After several
hours, \textit{N}-isopropylidene.pyrazolidinium perchlorate crystallized as
needles. M.p. after recrystallization in 1:1 ethanol-tetrahydrofuran
mixture = 139-140°. The yield is about 70% based on pyrazolidinium
perchlorate.

NMR in DMSO-\textsubscript{d6}: 87.2 (broad singlet, 1 proton) - H-N-N\textsuperscript{+}=C; 84.2
(triplet with broad peaks, J=7 Hz, 2 protons) - CH\textsubscript{2}-N\textsuperscript{+}=C; 83.35
(triplet, J=7 Hz, 2 protons) - CH\textsubscript{2}-NH-N\textsuperscript{+}=C; 82.3 (singlet, 6 protons) -
N\textsuperscript{+}=C(CH\textsubscript{3})\textsubscript{2}; 82.2 (quintet, 7 Hz, 2 protons) - C-CH\textsubscript{2}-C.

NMR in DMF-\textsubscript{d7}: 87.4 (broad singlet, 1 proton) - HN-N\textsuperscript{+}=C; 84.1 (broad
triplet, J=7, 2 protons) - CH\textsubscript{2}-N\textsuperscript{+}=C; 83.3 (triplet, J=7 Hz, 2
protons) - C-CH\textsubscript{2}-NH; 82.3 (two very close singlets, 6 protons) -
N\textsuperscript{+}=C(CH\textsubscript{3})\textsubscript{2}; 82.2 (quintet, J=7 Hz, 2 protons) - C-CH\textsubscript{2}-C.

NMR in CD\textsubscript{3}CN: 86.0 (broad singlet, 1 proton) - HN-N\textsuperscript{+}=C; 84.25 (broad
triplet, J=7 Hz, 2 protons) - CH\textsubscript{2}-N\textsuperscript{+}=C; 83.2 (triplet, J=7 Hz, 2
protons) - CH\textsubscript{2}-N-N\textsuperscript{+}=C; 82.05 (two very close singlets, 6 protons) -
N\textsuperscript{+}=C(CH\textsubscript{3})\textsubscript{2}; 82.0 (quintet, J=7 Hz, 2 protons) - C-CH\textsubscript{2}-C.

Elemental analysis: Found (\%) - C, 54.03; H, 6.20; N, 13.16; Cl, 16.70;
Calc'd for C\textsubscript{6}H\textsubscript{13}N\textsubscript{2}ClO\textsubscript{4}: C, 33.89; H, 6.16; N, 13.17; Cl, 16.67.
b. N-Isopropylideneisoxazolidinium Perchlorate

After unsuccessful attempts to prepare N-isopropylideneisoxazolidinium bromide and fluoroborate, the preparation of the perchlorate salt was done. A mixture of ethanol and isoxazolidine was obtained in the synthesis of the latter (p. 25). The amount of isoxazolidine in the mixture was determined by titration with standard hydrochloric acid solution using 2,4-dinitrophenol as indicator. The color of the solution being titrated changed from yellow to colorless when the end point was reached. The titration results showed that 58.8% of the solution was isoxazolidine. The solution (2.5 ml) was allowed to react with 3.35 ml of 6.0 M perchloric acid. Ten ml of tetrahydrofuran was added and the mixture was subjected to low pressure (0.03 mm Hg) to remove the volatile liquids. However, the residue remained liquid. The NMR spectrum of this liquid in D$_2$O showed the presence of isoxazolidinium ion and ethanol. Ten ml of acetone was added to this liquid residue and one hour was allowed for the reaction to occur. After removal of excess acetone and water at low pressure, a wet solid was obtained. This solid was dissolved in minimum amount of 1:1 acetone-THF mixture over a water bath at 45°. The mixture was kept in the freezer until the product crystallized out. The yield based on isoxazolidine is 52%; m.p. - 99-100°.

NMR in DMSO-$d_6$:  δ4.5 (triplet, $J=6.5$, 2 protons) - CH$_2$-O-N$^+=$C;  
δ4.3 (triplet, $J=6.5$ Hz, 2 protons) - CH$_2$-N$^+=$C;  δ2.5 (quintet, $J=7$ Hz, 2 protons) - C-CH$_2$-C;  δ2.4 (singlet, 6 protons) - N$^+=$C(CH$_3$)$_2$. 
NMR in CD₃CN:  δ4.3 (triplet, J = 7 Hz, 2 protons) - CH₂-O-N⁺=C; δ4.05 (triplet, J = 7 Hz, 2 protons) - CH₂-N⁺=C; δ2.35 (quintet, J = 7 Hz, 2 protons) - CH₂-C; δ2.1 (two very close singlets, 6 protons) - N⁺=C(CH₃)₂.

Elemental Analysis: Found (%) - C, 33.99; H, 5.84; N, 6.58; Cl, 16.68. Calc'd for C₆H₁₂NO₄O₄:  C, 33.74; H, 5.66; N, 6.53; Cl, 16.60.

c. N-Isopropylidene-0,N-Dimethylhydroxylammonium Perchlorate

0,N-Dimethylhydroxylamine hydrochloride (0.97 g) was dissolved in 2.85 ml of 3.5 M sodium hydroxide. The free amine was extracted with two 25-ml portions of ether. About 20 ml of tetrahydrofuran was added to make the mixture miscible with water. Perchloric acid (1.065 M, 1.65 ml) was added to the mixture. Removal of all the liquids was attempted by warming the mixture at 45° at 0.5 mm Hg. A slightly yellowish viscous liquid remained. Acetone (20 ml) was added and 30 minutes were allowed for the reaction. About 50 ml of tetrahydrofuran was added but no solid appeared. All the liquids were removed by vacuum leaving a white solid behind. The solid was recrystallized from 2:1 tetrahydrofuran-acetone in the same manner as N-isopropylideneisoxazolidinium perchlorate. M.p. = 186-188°. Yield was 65% based on 0,N-dimethylhydroxylamine hydrochloride.

NMR in DMSO-d₆:  δ3.95 (singlet, 3 protons) - CH₃-O-N⁺=C; δ3.75 (broad singlet, 3 protons) - CH₃-N⁺=C; δ2.45 (singlet, 6 protons) - N⁺=C(CH₃)₂.

NMR in CD₃CN:  δ4.75 (singlet, 3 protons) - CH₃-O-N⁺=C; δ3.5 (broad singlet, 3 protons) - CH₃-N⁺=C; δ2.25 (three very close singlets, 6 protons) - N⁺=C(CH₃)₂.
Elemental analysis: Found (%) - C, 29.86; H, 6.11; N, 6.90; Cl, 17.69. Calc'd for C₅H₁₂NCIO₄: C, 29.79; H, 6.00; N, 6.95; Cl, 17.58.

d. N-Isopropylidene-1,2-dimethylhydrazinium Perchlorate

1,2-Dimethylhydrazine dihydrochloride (2.4 g) was added to a mixture of 3.0 g of sodium hydroxide pellets in about 15 ml of methanol while being stirred in an ice bath. All the liquids were then distilled under nitrogen by heating the flask to 150° and allowed to collect in a flask with about 20 ml of water. Perchloric acid (6.0 M) solution was added dropwise to the amine-methanol-water mixture while the pH was being measured. All the theoretical amount of perchloric acid was used and the pH of the solution decreased to 3.1.

The mixture was subjected to 0.5 mm Hg pressure over a water bath at 45°. A viscous liquid remained in the flask. To this 20 ml of acetone was added and one hour was allowed for the reaction to occur. Tetrahydrofuran was added but no solid precipitated out. All the liquids were removed by vacuum, leaving behind a white solid. This solid was recrystallized three times in 1:3 acetone-tetrahydrofuran mixture in the same manner as N-isopropylideneisoxazolidinium perchlorate. M.p. = 150-153°. Yield was 41% based on 1,2-dimethylhydrazine dihydrochloride.

NMR in DMSO-d₆: 66.6 (broad peak, 1 proton) - H-N-N⁺C; 83.6 (singlet, 3 protons) - CH₃-N⁺C; 82.65 (doublet, J = 7 Hz, 3 protons) -
CH₃-NH-N⁺=C; δ2.5 (singlet, 3 protons) - one of (CH₃)₂C=N⁺; δ2.4 (singlet, 3 protons) - one of (CH₃)₂C=N⁺.

NMR in CD₃CN: δ5.3 (broad quartet, J = 6 Hz, 1 proton) - HN-N⁺=C;
δ3.45 (broad singlet, 3 protons) - CH₃-N⁺=C; δ2.5 (doublet, J = 6 Hz, 3 protons) - CH₃-NH-N⁺=C; δ2.35 (singlet, 3 protons) - one of (CH₃)₂C=N⁺; δ2.20 (singlet, 3 protons) - one of (CH₃)₂C=N⁺.

Elemental analysis: Found (%): C, 30.05; H, 6.66; N, 14.05; Cl, 17.45.
Calc'd for C₅H₁₃N₂ClO₄: C, 29.94; H, 6.53; N, 13.96; Cl, 17.67.

D. Determination of Dissociation Constants of Ammonium Ions

Determination of the pK's of the protonated amines, which are measures of the basicities of the amines used in this study, was performed by measuring the pH while titrating a dilute solution of the amine or amine salt with standard hydrochloric acid or sodium hydroxide solution, respectively. Preparation and pipetting of solutions were performed under a large inverted funnel whose stem is connected to a Tygon tube leading to a nitrogen tank. Accurately measured volumes of the amine solutions were placed in Radiometer titration cells which were then immersed in the 35° bath and allowed to attain temperature equilibration for 30 minutes. The titration cells were then placed in the titration apparatus described in the instrumentation section. The previously standardized pH electrode was then immersed in the solution to be titrated. The titrant solution was delivered either from the
Autoburette via a capillary tube manufactured by Radiometer Corporation
or from a 10 ml glass buret with graduations equal to 0.02 ml whose tip
was held 2 inches above the solution to be titrated. The titrant
reservoir of the Autoburette was sealed with a rubber stopper with a
hole fitted with an Ascarite tube. The stirrer was turned on while
adding increments of the titrant solution which were about 0.2 ml for
the 10 ml buret and about 0.4 ml for the Autoburette and turned off
while the pH was being read.

E. Detection of Reaction Between Acetone and Pyrazolidinium Ions by
pH Measurements

Acetone (0.20 ml) was injected into 5.0 ml of solution consisting
of 0.160 M pyrazolidinium ions, 0.040 M free pyrazolidine and 0.100 M
sodium chloride to make the initial acetone concentration equal to
0.52 M. The expected pH calculated from the pK of pyrazolidinium ions
was 6.80. The pH electrode was immersed in the solution a few seconds
after injection of acetone. The pH drifted gradually upwards and
settled at 7.395.

Three 5.00 ml portions of a buffer solution consisting of 0.030 M
free pyrazolidine, 0.0120 M pyrazolidinium ions and 0.15 M sodium
chloride were placed in separate stoppered test tubes and equilibrated
at 35°. Varying amounts of acetone were injected into the solutions to
produce different initial concentrations of acetone and the tubes were
immediately shaken. The pH electrode was quickly immersed into the
test tubes and the pH of the solutions were recorded at different
times after injection. The solutions were kept stoppered under
nitrogen and immersed in the 35° bath between pH readings.

F. NMR Study of Iminium Ion Formation

A 5-mm NMR tube containing about 0.4 ml of a relatively concen-
trated (0.5 to 1 M) solution of the protonated amine (pyrazolidinium,
isoazolidinium, 0,N-dimethylhydroxylammonium, or 1,2-dimethylhydra-
zinium ion) in D₂O was prepared and sealed under nitrogen. In the
case of the first three amines, the amine salt (perchlorate, chloride
or bromide) was placed in the NMR tube and D₂O was injected. In the
case of 1,2-dimethylhydrazinium ions, a weighed amount of 1,2-
dimethylhydrazine dihydrochloride was placed in an NMR tube and an
equivalent amount of sodium deuterioxide in D₂O was added. This would
produce an equivalent amount of sodium chloride. The sodium deuter-
oxide solution was prepared by dissolving cut pieces of sodium metal,
previously dipped in ether and allowed to dry in air for about 15
seconds, into a flask of stirred D₂O. The solution was standardized
by adding an accurately measured aliquot into a known amount of
hydrochloric acid and then back-titrating the excess hydrochloric acid
with standard sodium hydroxide solution.

The NMR spectra of the solutions were taken with the Varian A60A
with the offset zeroed with a tube containing tetramethylsilane in
in CDCl₃ and the sweep width set at 500 cps. Acetone or acetone-d₆ (0.2 or 0.3 ml) was then injected and the spectrum of the resulting solution was taken at different times. In some cases, additional portions of acetone or acetone-d₆ were added to the same NMR tube and the spectrum was taken afterwards.

For the investigation of the hydrolysis of an iminium ion, the NMR spectrum of an approximately 1 M solution of the iminium perchlorate salt in DMSO-d₆ or CD₃CN was recorded. Deuterium oxide (0.1-0.3 ml) was added to the NMR tube and the spectrum was taken at different times after injection. Tetramethylsilane in CDCl₃ was used as external standard.

G. UV Study of Iminium Ion Formation

The UV spectrum of a solution was taken by allowing the wavelength to decrease automatically from 350 to 200 nm. A continuous graph of absorbance against the wavelength was obtained on the chart paper. The solution was usually contained in a 1-cm quartz cell which was kept in the 35°C thermostated cell compartment of the Cary 1605 for about 20 minutes before scanning is started. The volume of the solution is 3.00 ml measured by pipetting from a volumetric flask. The reference cell contains 3.00 ml of water or an amine solution identical to that in the sample cell if it is desired that the absorbance due to the amine be cancelled. The amine solution was prepared in a volumetric flask and kept under nitrogen at all times.
The spectrum of acetone was taken by injecting a concentrated aqueous acetone solution using a microliter syringe into water in the sample cell and then scanning from 350 to 200 nm. To investigate the spectral changes involved in a reaction between acetone and protonated amine a concentrated solution of acetone was injected into 3.00 ml of 0.05 to 0.01 M amine salt solution and the spectrum of the resulting solution was taken at different times after injection.

Sometimes, it was necessary to investigate the reaction at different times at a constant wavelength. The recorder was zeroed at one wavelength with amine salt solution in the sample cell and water as reference or with amine solution in both sample and reference cells. Acetone was injected and the recorder chart was allowed to roll at a constant speed. The horizontal distance which the pen has traveled on the chart measures the time that has elapsed since the time of injection. The pen moves either up or down, depending on the absorbances of the products and reactants, and thus a curve is obtained on the chart.

To investigate the hydrolysis of an iminium ion, a concentrated solution of the iminium perchlorate salt in acetonitrile is injected using a microliter syringe into water or hydrochloric acid solution in the UV cell. Acetonitrile was chosen because this solvent does not have any absorbance from 350 to 225 nm. N,N-Dimethylformamide and dimethylsulfoxide, which can also dissolve the iminium perchlorate salt, have large absorbances at 235 nm and shorter wavelengths. The spectrum
and changes in absorbances at different times at a constant wavelength were recorded in the same manner as the iminium ion formation reaction.

H. Determination of Equilibrium Constant for Iminium Ion Formation

By Measurements of UV Equilibrium Absorbances

This method was employed for the determination of the equilibrium constants for the reactions between acetone and three different protonated amines - isoxazolidine, O,N-dimethylhydroxylamine and 1,2-dimethylhydrazine. A constant amount of acetone was injected into solutions of varying concentrations of protonated amine. The extent of reaction was measured by recording the equilibrium UV absorbances. Prior to injection of acetone, the protonated amine solution has been allowed to equilibrate at 35° for 20 minutes and the spectrophotometer has been zeroed with the same protonated amine solution in the reference cell.

For isoxazolidinium and O,N-dimethylhydroxylammonium ions, the wavelength at which the measurements were made was 275 nm where absorption by the free or protonated amine would not cause any complication. The extinction coefficient of acetone at this wavelength was first determined. Accurately measured volumes of a 2.000 M acetone solution were injected using a microliter syringe into 3.00 ml of water in the sample cell with water being used to zero the instrument before each injection. The absorbance was then recorded.
For the acetone-isoxazolidinium ion reaction, a stock solution of isoxazolidinium bromide was prepared. Since the salt is hygroscopic, and may have absorbed water during weighing, the exact concentration of the solution was determined by titrating portions of it with standard sodium hydroxide solution to the pink phenolphthalein end point. Quite surprisingly, the concentration based on the titration results was exactly equal to the concentration calculated from the weight of solute and volume of solution - 1.005 M.

Accurately measured volumes of this solution were pipetted into 10.00 ml volumetric flask. One milliliter of 1.0041 M hydrochloric acid was added to each flask and the solution was diluted to mark. Three-ml portions of the resulting solutions were placed in the 1-cm UV cells. Twenty-five microliters of 3.599 M acetone solution was injected into the protonated amine solution to produce an initial acetone concentration of 0.02974 M. The absorbance was recorded after it has ceased to decrease which was about 30 minutes after injection.

For the acetone-0,N-dimethylhydroxylammonium ion reaction, a solution of 0,N-dimethylhydroxylamine hydrochloride whose concentration was 1.000 M was prepared. Titrations of portions of this with a standard sodium hydroxide solution gave a concentration of 0.9942 M. From this, 10.00-ml solutions of varying concentrations were prepared. After temperature equilibration, 30 microliters of 2.000 M acetone solution was injected into 3.00-ml solutions in the UV cells to produce
an initial acetone concentration of 0.01980 M. No change in absorbance was observed as time progressed, indicating that equilibrium was attained immediately after injection.

In the case of 1,2-dimethylhydrazinium ions, the absorbance after acetone is injected into many times its molar amount of the monoprotonated amine never levels off to an equilibrium value because of a slower second reaction. The equilibrium absorbances for the faster reaction, which is believed to be iminium ion formation, were extrapolated by taking points along the initial portions of the time-absorbance curve and feeding the time-absorbance data pairs into program 2 (Appendix) written by Dr. William Sachs which calculates $A_1$, $A_2$, and $k$ by a nonlinear least squares treatment of the following equation.

$$Y = A_1e^{-kt} + A_2$$ (6)

The time-absorbance data pairs were taken immediately after injection until that portion of the curve where there is only 0.005 or less increase in absorbance.

First, the extinction coefficient of acetone at 240 nm was determined in the same manner as the measurement of extinction coefficient at 275 nm. A solution of 1,2-dimethylhydrazine dihydrochloride was prepared whose concentration based on weight of solute and volume of solution is 0.5047 M. Since the salt is hygroscopic, the exact concentration of the solution was determined by titrating
portions of it with standard silver nitrate solution by the Fajans method. The concentration based on the titration results was 0.5070 M. Accurately measured volumes of this solution were pipetted into 10.00 ml flasks. Amounts of sodium hydroxide solution equivalent to the amount of dihydrochloride in each flask were added to produce the monoprotonated amine. Sodium chloride was added to bring the ionic strength to 0.3 M. The solutions were diluted with water to the mark. Three ml portions were placed in the UV cells. After temperature equilibration, 15.00 microliters of 3.00 M acetone solution was injected into the UV cell and immediately after, the absorbance started rising to produce a curve which looks like that of a first-order reaction.

I. Determination of Equilibrium Constants for Iminium Ion Formation by NMR

This method was employed for the determination of equilibrium constants for the reaction between acetone and 2,N-dimethylhydroxylammonium ion and between acetone and 1,2-dimethylhydrazinium ion. All NMR spectra for this study were taken with the Varian EM 360L NMR Spectrometer. The integration values were read from a digital readout which was installed by The Ohio State University Electronics Shop. Acetone-\text{d}_6 instead of light acetone was used to avoid large spinning side bands. The temperature of the sample probe during the measurements was 33°. Five millimeter (external diameter) NMR tubes were used.
Preparation of protonated amine solutions and injection of acetone-\textsubscript{d\textsubscript{6}} into the NMR tubes were done under nitrogen. Integration of each spectrum was done at least three times.

1. Reaction Between Acetone-\textsubscript{d\textsubscript{6}} and O,N-Dimethylhydroxylammonium Ions

The concentration of the before addition and after reaction with acetone-\textsubscript{d\textsubscript{6}} were measured by recording the integration values relative to a compound whose concentration does not change with time. In this case the compound chosen was methanol. Solutions of O,N-dimethylhydroxylamine hydrochloride with methanol in D\textsubscript{2}O with exactly known concentrations were prepared. The concentration of the protonated amine was not checked by Fajans titration since it was seen before that the titration gives the expected results within experimental error. The CH\textsubscript{3}-O-N=\textsubscript{+}C peak and the CH\textsubscript{3}-N=\textsubscript{+}C peak of the iminium ion were too close to the CH\textsubscript{3}-O-N=\textsubscript{+} peak of the unreacted amine for accurate integration. The water peak could not be used as an internal standard because appreciable exchange of protons between water and acetone-\textsubscript{d\textsubscript{6}} has taken place during the time allowed for iminium ion formation (about 10 minutes) as seen from the formation of a small multiplet at \textdelta2.1 due to acetone-\textsubscript{d\textsubscript{5}}. The NMR tubes were weighed before and after addition of the O,N-dimethylhydroxylamine hydrochloride-methanol-D\textsubscript{2}O solutions and before and after each of the four additions of acetone-\textsubscript{d\textsubscript{6}} into each NMR tube. The CH\textsubscript{3}-N=\textsubscript{+}O peak of the unreacted
protonated amine and the CH\textsubscript{3}-O peak of methanol at 63.3 were integrated before and after injection of each portion of acetone-d\textsubscript{6} into the tube.

2. Reaction Between Acetone-d\textsubscript{6} and 1,2-Dimethylhydrazinium Ions

Solutions of 1,2-dimethylhydrazine dihydrochloride and equivalent amounts of sodium deuteroxide in D\textsubscript{2}O were prepared in 2.00 ml volumetric flasks to produce CH\textsubscript{3}ND\textsubscript{5}NDCH\textsubscript{3}\textsuperscript{+} solutions of known concentration. Accurately measured volumes of the resulting solutions were placed in previously weighed NMR tubes and the tubes were weighed afterwards. The NMR spectrum of the solution in each tube was taken and the water peak at 64.7 and the CH\textsubscript{3}-N peak at 62.8 were integrated. Accurately measured volumes of acetone-d\textsubscript{6} were injected into each tube and the formation of the CH\textsubscript{3}-N\textsuperscript{+}=C peak of the iminium ion was observed. This peak was integrated relative to the water peak. There was no change in the size of the peak five minutes and one hour after injection indicating that equilibrium is attained before the spectrum is taken. Also, the appearance of a multiplet at 62.1 due to acetone-d\textsubscript{6} was not observed indicating that no appreciable exchange has taken place during the time allowed for iminium ion formation (about 10 minutes) and, therefore, water could be used as internal standard to measure the CH\textsubscript{3}-N\textsuperscript{+}=C peak. Then, another portion of acetone-d\textsubscript{6} was injected and the spectrum was again taken. The tube was weighed before and after addition of the CH\textsubscript{3}ND\textsubscript{5}NDCH\textsubscript{3}\textsuperscript{+} solution and before and after each injection of acetone-d\textsubscript{6}.
J. Kinetics of Iminium Ion Formation and Hydrolysis

The preparation, handling and storage of all the solutions used in this study were done under nitrogen.

1. Acetone-Hydroxylamine-2-Dimethylaminomethylpyrrolidine Kinetics

Stock solutions of 1 M hydroxylamine hydrochloride, 0.5 M 2-dimethylaminomethylpyrrolidine, 1 M NaCl and 1 M acetone were prepared quantitatively. Accurately measured volumes of the first three stock solutions plus either standard sodium hydroxide or hydrochloric acid solution were pipetted into 10.00 ml volumetric flask to produce buffer solutions with pH's within one pH unit of the pK₁ of the diamine. The hydrochloric acid or sodium hydroxide solution was used to protonate some of the free amine or to deprotonate some of the ammonium ions to bring about the desired protonation ratio. At these pH's the concentration of the diprotonated amine is considered negligible, so the resulting solutions were buffered only by the free and mono-protonated amine. Because of the low pK of its ammonium ion, hydroxylamine is considered essentially completely unprotonated in these solutions. Three 3.00-ml portions of these buffer solutions were placed in the 1-cm UV cells. Two of these were used to react with acetone to obtain the rate constants for duplicate kinetic runs while the remaining one was placed in the reference cell to cancel out absorbances due to hydroxylamine, diamine or impurities. After temperature equilibration, the UV cell was taken out and 30.00 micro-liters of the 1 M acetone solution was injected. The cell was
immediately capped, shaken and placed back into the cell compartment. As soon as the slit is opened, the absorbance due to acetone is seen to decrease as time progresses. The time-absorbance data pairs were stored in a cassette tape as described in the instrumentation section. The two 3.00-ml portions of the buffer solution spent for kinetics were combined and placed in a stoppered test tube. The pH of the solution was taken while the test tube was immersed in the 35° water bath.

2. N-Isopropylidenepyrazolidinium Ion Hydrolysis

A 0.05 M solution of N-isopropylidenepyrazolidinium perchlorate in acetonitrile was prepared. To initiate the reaction, small portions of this solution were injected using microliter syringes into buffer solutions previously equilibrated at 35°. In all cases 3.00-ml of buffer solutions in 1.00-cm quartz cells were used. In some cases, 6.00 microliters of the iminium ion solution were injected to produce an initial iminium ion concentration of 1.0 x 10^-4 M which produces an initial absorbance of about 0.5. In other cases, 10.00 microliters of the iminium ion solution were injected to produce an initial iminium ion concentration of 1.7 x 10^-4 M which produces an initial absorbance of about 0.8. The same buffer solution was used to zero the instrument before injection. Two or three duplicate kinetic runs were made for each buffer solution. At the end of the reaction, the absorbance decreased to about 0.01. Thus, the absorbance of the products at 235nm
was negligible compared to the initial absorbance of the iminium ion.

One molar stock solutions of sodium formate, acetic acid, cacodylic acid and N-methylmorpholine were prepared. The acetic acid solution was prepared from glacial acetic acid and was standardized by titrating portions of it with standard sodium hydroxide solution using phenolphthalein as indicator. The 25.00 ml buffer solutions were prepared from these stock solutions by adding hydrochloric acid or sodium hydroxide solution to bring about the desired protonation ratios. Sodium chloride was added to fill up the ionic strength to 0.5 M. Borate-buffered solutions were prepared from solid sodium borate decahydrate and either hydrochloric acid or sodium hydroxide added to vary the buffer ratio. The pH of the solutions spent for kinetics were measured as before. The following shows the pH range studied for each buffer and the total buffer concentration used.

<table>
<thead>
<tr>
<th>pH range</th>
<th>Buffer</th>
<th>Total conc. used (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.7 - 1.95</td>
<td>hydrochloric acid</td>
<td>0.05, 0.048, 0.1, 0.24</td>
</tr>
<tr>
<td>2.5</td>
<td>formate</td>
<td>0.05, 0.1, 0.3</td>
</tr>
<tr>
<td>3.5 - 4.8</td>
<td>acetate</td>
<td>0.05, 0.1, 0.3</td>
</tr>
<tr>
<td>5.6 - 6.4</td>
<td>cacodylate</td>
<td>0.05, 0.1, 0.2, 0.3, 0.4</td>
</tr>
<tr>
<td>7.4 - 8.2</td>
<td>N-methylmorpholine</td>
<td>0.05, 0.1, 0.3</td>
</tr>
<tr>
<td>8.2 - 9.0</td>
<td>borate</td>
<td>0.05, 0.1, 0.2</td>
</tr>
</tbody>
</table>

The time-absorbance data pairs were read from the chart which rolled out of the spectrophotometer recorder. Twenty points equally
spaced with respect to absorbance were taken for the calculation of each rate constant. The reaction is a first order one so the data were fed into the Sachs program (Appendix) to calculate the rate constant.

3. Acetone-Pyrazolidinium Ion Reaction

The kinetics of this reaction was studied by monitoring the formation of the iminium ion at its 235 nm maximum absorbance. To initiate the reaction, acetone was injected into many times its molar amount of pyrazolidinium ion with acetic acid-acetate buffer if the desired pH is more than one unit from the pK of pyrazolidinium ion. The same buffer solution was in the reference cell to zero the instrument before injection.

Two types of cells were used - 0.1 and 1-cm cells. The following shows the initial concentrations of acetone, total pyrazolidine concentration and the type of cell used:

5 x 10^{-3} M acetone injected into 0.1 M pyrazolidine + 0.1 M total buffer (formate or acetate) in 0.5 ml solution - 0.1 cm cells

6.66 x 10^{-4} M acetone injected into 0.1 M pyrazolidine + 0.1 M buffer in 3.00 ml solution - 1.0 cm cells.

2 x 10^{-4} M acetone injected into 0.05 M pyrazolidine + 0.1 M buffer in 3.00 ml solution - 1.0 cm cells.

The solutions were prepared in the same manner as the solutions used in the hydrolysis reaction except that solid pyrazolidinium
perchlorate was weighed in the volumetric flask and then the other components of the buffer such as sodium formate or acetic acid, hydrochloric acid or sodium hydroxide and sodium chloride were added and water was added to fill to the mark.

Immediately after injection of acetone, the absorbance started rising and leveled off as the reaction approached equilibrium. In some cases, the time-absorbance data pairs were generated in the oscilloscope and in others, the data were read from the chart paper. The Sachs program was used to analyze the data.

4. **N-Isopropylideneisoxazolidinium Ion Hydrolysis**

The reaction was initiated by injecting 32.00 microliters of a 0.8782 M solution of N-isopropylideneisoxazolidinium perchlorate in CH₃CN into 28.00 ml of aqueous buffer solution in a 10-cm cylindrical quartz cell. Immediately after injection, the increase in absorbance due to acetone formation was monitored at 275 nm with the same buffer solution in the reference cell so that absorbances due to the buffer components would cancel. Thirty time-absorbance data pairs were taken to calculate each first order rate constant using the Sachs program.

Hydrochloric acid was used to maintain the pH of the solution below 2; formic acid-formate was used for pH 2.5 to 3.5; acetic acid-acetate from pH 3 to 5.5; and cacodylic acid-cacodylate from 5.5 to 7.5. These buffer solutions were prepared from 1 M stock solutions.
in the same manner as those used for the N-isopropyldenepyrazolidinium ion hydrolysis. The pH's were taken using the solutions spent for kinetics.

K. Deuterium Exchange Kinetics

The solutions used for studying kinetics of deuterium exchange of acetone-d$_3$ were prepared, handled and stored under nitrogen at all times. For each kinetic run, a buffer solution of the secondary or tertiary amine or a mixture of secondary and tertiary amines is prepared from the free amines or amine salts. The expected pH of the solution was always within one pH unit of the pK of at least one of the ammonium ions present in the solution. Hydrochloric acid or sodium hydroxide solution was added to bring about the desired protonation ratio. Sodium chloride was used to bring the ionic strength to 0.3 M. Usually ten 5.00-ml or 2.00 ml portions of the amine buffer solution were pipetted into glass ampoules which were then sealed with rubber septums. Nine of these ampoules were immersed in the 35° bath up to their necks for about 30 minutes before the reaction is started. The remaining one contains the "zero time" sample for the kinetic run. To initiate the reaction, 0.20 ml or 0.080 ml of acetone-d$_3$ was injected into each 5.00-ml or 2.00 ml amine solution, respectively. The ampoule is quickly shaken and placed back into the bath. This would produce an initial acetone-d$_3$ concentration of 0.52 M. The samples were then taken for reaction quenching at different times so that
different extent of reaction would be observed. A sample is taken for quenching when it is estimated that 10% decrease in the acetone-\(d_6\) content has taken place since the last sample was quenched. The 10th and last sample of the kinetic run usually contains only between 5 and 10% of the initial acetone-\(d_6\) content. For the "zero time" sample, the reaction was quenched immediately after injection of acetone-\(d_6\).

To quench the reaction in one sample, the ampoule was taken out of the bath and an amount of 3 M perchloric acid just enough to protonate all the free amine or with a little excess is injected into the sample. Then, 0.50 ml or 0.20 ml of chloroform is injected into the 5.00 ml or 2.00 ml solution, respectively. The ampoule is quickly shaken to extract the acetone of different deuterium content into the chloroform layer. After the two layers stratify, the neck of the ampoule is broken off and a clean syringe is used to transfer the chloroform layer into a 5 ml flask containing three or four pieces of Drierite. The flask is sealed with a greased stopper and kept in the freezer until the transfer of the acetone-chloroform mixture into the mass spec bulbs.

For pH measurement, 5.00 ml of the amine buffer solution is placed in a stoppered test tube. After temperature equilibration at 35°, the pH was measured before and after addition of 0.20 ml of light acetone.
The transfer of the chloroform-acetone mixture into the mass spec bulbs is performed after all the samples have been quenched. The mass spec bulbs are 50-ml Pyrex flasks with narrow necks fitted with ground glass stopcocks. Prior to transfer, the mass spec bulbs are cleaned thoroughly with carbon tetrachloride in the hood to remove grease used in the previous kinetic run. After drying, the mass spec bulb stopcocks are greased with Apiezon N. The bulbs are then evacuated by pairs using a T-shaped tube called the yoke. While in vacuum, the bulbs are heated with a Bunsen burner to remove traces of moisture. The bulb stoppers are then closed and the bulbs are removed from the yoke and allowed to cool down to room temperature.

To transfer the chloroform-acetone solution into the mass spec bulb, the 5-ml flask containing the solution with Drierite is attached to one end of the yoke (Figure 1) and the previously evacuated mass spec bulb is attached to the other end with stopcock A closed. The 5-ml flask is then immersed in a Dry Ice-isopropanol bath for 30 seconds. This causes some of the contents of the flask to freeze but the more important effect is the lowering of the vapor pressure of acetone and chloroform in the flask. Stopcock A is then opened. As air enters the vacuum pump, it produces a gurgling sound which gradually diminishes as vacuum is restored. Stopcock B is then opened and stopcock A is closed. The Dry Ice-isopropanol bath is transferred to cool down the mass spec bulb and the 5-ml flask is
Figure 1. Set-up for transfer of acetone-chloroform mixture into mass spec bulbs.

wrapped in a warmed towel. After about 20 seconds, droplets of liquid are seen on the inner walls of the mass spec bulb. Stopcock B is then closed and the mass spec bulb is removed from the yoke and stored in the freezer until mass spectral analysis.
CHAPTER III. RESULTS

A. pK's of Protonated Amines

The computer programs used to calculate the dissociation constants for the ammonium ions from the titrant volume pH data pairs were written by J. Zeigler. One program which was used to calculate the pK of 1,2-dimethylhydrazinium ion was written by Dr. J. Hine. These programs are presented in the Appendix. These programs calculate the pK's of the ammonium ions at zero ionic strength from the observed pH (defined as $-\log a_+^-$), the ionic strength and the logarithm of the ratios of the concentrations of the unprotonated amine [Am] and the monoprotonated amine [Am$^+$] or the monoprotonated and the diprotonated amine [Am$H^+$]. The dissociation constants are defined in equations 7 and 8.

$$K_1 = \frac{a_+^+[Am]}{[AmH^+]Y_{AmH^+}} \quad (7)$$

$$K_2 = \frac{a_+^+[AmH^+]Y_{AmH^+}}{[AmH^+H^+]Y_{AmH^+H^+}} \quad (8)$$

The activity coefficients $\gamma$'s were calculated from the Davies equation.

$$\log \gamma_\pm = -0.5192\mu(\frac{\sqrt{\mu}}{1+\sqrt{\mu}} - 0.2\mu) \quad (9)$$
where \( Z \) is the charge of the ion and \( \mu \) is the mean ionic strength.

In the case of 1,2-dimethylhydrazine, since the dihydrochloride was titrated with a standard sodium hydroxide solution, it was first attempted to calculate \( pK_1 \) and \( pK_2 \). However, the calculation could not converge to give values of the two \( pK \)'s. It appeared that it was about to converge to a value of \( 5 \times 10^{-8} \) for \( K_1 \) but \( K_2 \) varied from 0.1 to 5 as a result of several iterations. The calculation was allowed to go through 30 iterations but it did not give consistent values for \( K_2 \). The reason for this is the fact that the equilibrium constant for the dissociation of the diprotonated to monoprotonated amine and a proton is so large that pH could not be considered a reliable measure of acidity in the acidity range where the diprotonated amine exists. An acidity function based on the dissociation of a similar diprotonated amine should be used. (The value of \( pK_2 \) was estimated by Jencks and co-workers\(^{46} \) to be equal to -2.5 from \( \sigma^p \) correlations.) However, since \( K_1 \) is the value which is being sought and since \( K_2 \) is expected to be very large, it was thought that the solution of the amine dihydrochloride in water could be considered a mixture of the monoprotonated amine and an equivalent amount of hydrochloric acid. Thus, a volume of the sodium hydroxide solution for half neutralization can be calculated. This is the amount of sodium hydroxide required to convert the diprotonated amine to the monoprotonated amine. Then, the titration can be considered to be a
determination of a pK of a monoprotonated amine. The volume of the solution to be titrated fed into the program which calculates $K_1$ for monoprotonated monoamines is the sum of the volume before the titrant is added and the volume of sodium hydroxide required for half neutralization and the initial concentration of monoprotonated amine and sodium chloride in the titrant solution were adjusted accordingly. The results of the titrations are shown in Table 1.

Table 2 shows the values chosen as the pK's of the ammonium ions used in this study. The values are the averages of the negative logarithms of the dissociation constants in Table 1. The results are compared with the corresponding values at 25°.

With regard to the secondary amines with atoms containing lone pairs of electrons beside the nitrogen, it is seen that these amines are about three to six orders of magnitude less basic than ordinary secondary amines. This is because of the strong electron-withdrawing effect of the atom beside the nitrogen. It can also be seen that the experimental values obtained at 35° are consistently lower than the corresponding literature values at 25° by about 0.3 to 0.4 pK units. The hydroxylamine derivatives are much less basic than the hydrazines owing to the higher electronegativity of oxygen and statistical difference in the number of basic nitrogens in the free amine. However, it is not clear why the expected result that five-membered cyclic amines are more basic than acyclic ones (pyrrolidine is three
<table>
<thead>
<tr>
<th>Amine</th>
<th>Conc. of Titrant (M)</th>
<th>Initial [Am] (M)</th>
<th>Calc'd [Am]₀ (M)</th>
<th>K₁</th>
<th>K₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMAMP</td>
<td>0.1009 HCl</td>
<td>0.02080</td>
<td>0.02015</td>
<td>$(1.43 \pm 0.02) \times 10^{-10}$</td>
<td>$(1.76 \pm 0.04) \times 10^{-8}$</td>
</tr>
<tr>
<td></td>
<td>0.1009</td>
<td>0.02080</td>
<td>0.02080</td>
<td>$(1.40 \pm 0.02) \times 10^{-10}$</td>
<td>$(1.73 \pm 0.04) \times 10^{-8}$</td>
</tr>
<tr>
<td></td>
<td>0.1009</td>
<td>0.02080</td>
<td>0.02019</td>
<td>$(1.46 \pm 0.05) \times 10^{-10}$</td>
<td>$(1.80 \pm 0.05) \times 10^{-8}$</td>
</tr>
<tr>
<td>DMAMP</td>
<td>0.04036</td>
<td>0.01364</td>
<td>0.01366</td>
<td>$(1.49 \pm 0.02) \times 10^{-10}$</td>
<td>$(1.68 \pm 0.04) \times 10^{-8}$</td>
</tr>
<tr>
<td></td>
<td>0.04036</td>
<td>0.01364</td>
<td>0.01384</td>
<td>$(1.52 \pm 0.02) \times 10^{-10}$</td>
<td>$(1.69 \pm 0.04) \times 10^{-8}$</td>
</tr>
<tr>
<td></td>
<td>0.04036</td>
<td>0.01364</td>
<td>0.01353</td>
<td>$(1.67 \pm 0.02) \times 10^{-10}$</td>
<td>$(1.75 \pm 0.06) \times 10^{-8}$</td>
</tr>
<tr>
<td>PYRZNH⁺</td>
<td>0.04723 NaOH</td>
<td>0.03976</td>
<td>0.04165</td>
<td>$(5.60 \pm 0.02) \times 10^{-8}$</td>
<td></td>
</tr>
<tr>
<td>ClO₄⁻</td>
<td>0.04723</td>
<td>0.03976</td>
<td>0.04269</td>
<td>$(5.55 \pm 0.03) \times 10^{-8}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.03778 NaOH</td>
<td>0.02906</td>
<td>0.03194</td>
<td>$(5.53 \pm 0.03) \times 10^{-8}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1490 NaOH</td>
<td>0.09994b</td>
<td>0.1021</td>
<td>$(5.62 \pm 0.02) \times 10^{-8}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1490</td>
<td>0.09994b</td>
<td>0.1028</td>
<td>$(5.61 \pm 0.02) \times 10^{-8}$</td>
<td></td>
</tr>
<tr>
<td>ISOXH⁺</td>
<td>0.1011 NaOH</td>
<td>0.1001</td>
<td>0.1106</td>
<td>$(1.86 \pm 0.02) \times 10^{-5}$</td>
<td></td>
</tr>
<tr>
<td>Br⁻</td>
<td>0.1011</td>
<td>0.1001</td>
<td>0.1124</td>
<td>$(1.66 \pm 0.02) \times 10^{-5}$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.1011</td>
<td>0.1001</td>
<td>0.1102</td>
<td>$(1.91 \pm 0.02) \times 10^{-5}$</td>
<td></td>
</tr>
<tr>
<td>OHHX⁺</td>
<td>0.09994 NaOH</td>
<td>0.09994c</td>
<td>0.1163</td>
<td>$(3.43 \pm 0.04) \times 10^{-5}$</td>
<td></td>
</tr>
<tr>
<td>Cl⁻</td>
<td>0.09994</td>
<td>0.09994c</td>
<td>0.1169</td>
<td>$(3.38 \pm 0.04) \times 10^{-5}$</td>
<td></td>
</tr>
</tbody>
</table>
Table 1 (continued)

<table>
<thead>
<tr>
<th>Amine&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Conc.</th>
<th>Initial</th>
<th>Calc'd</th>
<th>$K_1$</th>
<th>$K_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMHZH&lt;sup&gt;++&lt;/sup&gt;</td>
<td>0.09994</td>
<td>0.09994&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.1198</td>
<td>(3.10 ± 0.04) x 10&lt;sup&gt;-5&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>2Cl&lt;sup&gt;−&lt;/sup&gt;</td>
<td>0.1814</td>
<td>NaOH</td>
<td>0.04773&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.03789</td>
<td>(4.62 ± 0.11) x 10&lt;sup&gt;-8&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>0.1814</td>
<td></td>
<td>0.04773&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.03809</td>
<td>(4.79 ± 0.08) x 10&lt;sup&gt;-8&lt;/sup&gt;</td>
</tr>
<tr>
<td>DMHZH&lt;sup&gt;++&lt;/sup&gt;</td>
<td>0.1814</td>
<td>NaOH</td>
<td>0.04773&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.03898</td>
<td>(5.11 ± 0.08) x 10&lt;sup&gt;-8&lt;/sup&gt;</td>
</tr>
<tr>
<td>2Cl&lt;sup&gt;−&lt;/sup&gt;</td>
<td>0.1814</td>
<td></td>
<td>0.04773&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.03963</td>
<td>(4.95 ± 0.07) x 10&lt;sup&gt;-8&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>0.1814</td>
<td></td>
<td>0.04773&lt;sup&gt;e&lt;/sup&gt;</td>
<td>0.04007</td>
<td>(4.84 ± 0.11) x 10&lt;sup&gt;-8&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>DMAMP = 2-dimethylaminomethylpyrrolidine; PYRZN = pyrazolidine; ISOX = isoxazolidine; ONHX = O,N-dimethylhydroxylamine; DMHZ = dimethylhydrazine.

<sup>b</sup>Both titrant and titrand solutions contain 0.10 M NaCl and 0.10 M NaClO<sub>4</sub> initially to investigate effect of inert salts on the dissociation constants.

<sup>c</sup>This is the concentration calculated from the results of Fajans titration with AgNO<sub>3</sub>. The concentration calculated from the weight of solute and volume of solution is 0.09999 M.

<sup>d</sup>Concentration from Fajans titration. Concentration from amounts of solute and solvent is 0.04848 M.

<sup>e</sup>Same as d but using program written by Dr. J. Hine.
### TABLE 2
**pK's of Ammonium Ions in Water at 35°**

<table>
<thead>
<tr>
<th>Amine</th>
<th>pK₁ at 35°</th>
<th>pK₂ at 35°</th>
<th>pK₁ at 25°</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMAMP</td>
<td>9.82</td>
<td>5.77</td>
<td>no lit. value</td>
</tr>
<tr>
<td>PYRZN</td>
<td>7.25</td>
<td>--</td>
<td>7.60ᵇ</td>
</tr>
<tr>
<td>ISOX</td>
<td>4.73</td>
<td>--</td>
<td>5.05ᵇ</td>
</tr>
<tr>
<td>ONHX</td>
<td>4.48</td>
<td>--</td>
<td>4.75ᵇ, 4.88ᶜ</td>
</tr>
<tr>
<td>DMHZ</td>
<td>7.32</td>
<td>--</td>
<td>7.52ᵇ, 7.69ᶜ</td>
</tr>
</tbody>
</table>

ᵃDMAMP = 2-dimethylaminomethylpyrrolidine; PYRZN = pyrazolidine; ISOX = isoxazolidine; ONHX = O,N-dimethylhydroxylamine; DMHZ = 1,2-dimethylhydrazine.

ᵇRef. 45. Experimental details not given.

ᶜRef. 46. By titration at 1.0 M ionic strength.

Times more basic than dimethylamine) is observed with the hydroxylamines and not with the hydrazines. It could be that the pK₁ of 1,2-dimethylhydrazinium ion is off from the correct value by a few hundredths due to the assumption that after addition of half of the required volume of sodium hydroxide solution for neutralization, only the monoprotonated amine exist in solution.
B. Acetone - 2-Dimethylaminomethylpyrrolidine - Hydroxylamine

Kinetics

In these reactions, it is assumed that the diamine behaves like ordinary secondary amines whose equilibrium constants for iminium ion formation with acetone are so small that there is no detectable change in the acetone concentration when the iminium ions are formed. Thus, the diamine merely acts as a catalyst for oxime formation.

Since the initial concentration of hydroxylamine is three to twelve times that of acetone and since the reactions were carried out to a point where the hydroxylamine concentration does not decrease by more than 16%, the reaction is considered to be pseudo-first order in acetone. Thus, the reaction should obey the rate law expressed in equation (10).

\[
[Ac] = [Ac]_0 e^{-k_{obs}t}
\]  

(10)

In terms of absorbances, since only the absorbance of acetone is being observed, the rate of change is expressed in equation (11). The extinction coefficient of the oxime at this wavelength is too small to measure.  

\[
Abs = \varepsilon_{Ac} [Ac]_0 e^{-k_{obs}t}
\]  

(11)

Twelve to forty time absorbance data pairs were fed into a program written by Dr. W. Sachs (program 2 (Appendix)) which calculates the parameters \(A_1, A_2\) and \(k\) by a nonlinear least squares analysis of equation (6).
In this case, $Y$ is the observed absorbance at time $t$. At $t = 0$, $Y$ should be $A_1 + A_2$ which is the initial absorbance of acetone. At the end of the reaction, $Y$ becomes $A_2$ which is expected to be zero or a very small number since acetone gets used up completely at equilibrium (the equilibrium constant for oxime formation at $35^\circ$ is $4.65 \times 10^{5} M^{-1}$). The results in Table 3 show that the calculated absorbances at $t = 0$ agree with the expected value (0.155) within 12%. It can also be seen that the differences between rate constants for duplicate runs are largest for the cases where there is only 3 to 1 concentration ratio between hydroxylamine and acetone, the largest being 30%. The relative standard deviation from first-order behavior calculated from the differences between the observed and the calculated absorbances were also largest in these cases, as large as 16%. If the 3:1 hydroxylamine-acetone kinetic runs were not included, the deviations between the rate constants for duplicate runs would not have exceeded 10% and the relative standard deviation from the first-order rate law would not have exceeded 4%. Thus, it appeared that the kinetic runs where there is only 3:1 ratio of hydroxylamine to acetone concentration are not as reliable as the others.

In Cholod and Chess' work on iminium ion formation between acetone and primary amines, it was determined that in most cases, the iminium ions are quantitatively captured by hydroxylamine to form
### Table 3

**Results of Acetone-Hydroxylamine-2-Dimethylaminomethylpyrrolidine Kinetics**

<table>
<thead>
<tr>
<th>pH&lt;sub&gt;obs&lt;/sub&gt;</th>
<th>[Hx]&lt;sub&gt;0&lt;/sub&gt;</th>
<th>Total [DMAMP]</th>
<th>HCl or NaOH added</th>
<th>Ionic strength</th>
<th>k&lt;sub&gt;obs&lt;/sub&gt; x 10&lt;sup&gt;3&lt;/sup&gt;</th>
<th>[Hx]&lt;sub&gt;ave&lt;/sub&gt;</th>
<th>A&lt;sub&gt;1&lt;/sub&gt; + A&lt;sub&gt;2&lt;/sub&gt;</th>
<th>A&lt;sub&gt;2&lt;/sub&gt;</th>
<th>% change in [Ac]</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.94</td>
<td>0.0496</td>
<td>0.0995</td>
<td>0</td>
<td>0.298</td>
<td>4.44 ± 0.05</td>
<td>0.0460</td>
<td>0.172</td>
<td>0.027</td>
<td>73.6</td>
</tr>
<tr>
<td>9.94</td>
<td>0.0496</td>
<td>0.0995</td>
<td>0</td>
<td>0.298</td>
<td>4.67 ± 0.10</td>
<td>0.0459</td>
<td>0.154</td>
<td>0.013</td>
<td>74.9</td>
</tr>
<tr>
<td>9.99</td>
<td>0.0794</td>
<td>0.0995</td>
<td>0.0299 NaOH</td>
<td>0.297</td>
<td>5.82 ± 0.04</td>
<td>0.0750</td>
<td>0.147</td>
<td>0.001</td>
<td>89.1</td>
</tr>
<tr>
<td>9.99</td>
<td>0.0794</td>
<td>0.0995</td>
<td>0.0299 NaOH</td>
<td>0.297</td>
<td>5.66 ± 0.06</td>
<td>0.0751</td>
<td>0.155</td>
<td>0.005</td>
<td>87.2</td>
</tr>
<tr>
<td>9.94</td>
<td>0.0298</td>
<td>0.0995</td>
<td>0.0198 HCl</td>
<td>0.297</td>
<td>3.62 ± 0.30</td>
<td>0.0274</td>
<td>0.155</td>
<td>0.016</td>
<td>47.7</td>
</tr>
<tr>
<td>9.94</td>
<td>0.0298</td>
<td>0.0995</td>
<td>0.0198 HCl</td>
<td>0.297</td>
<td>2.68 ± 0.44</td>
<td>0.0275</td>
<td>0.158</td>
<td>-0.021</td>
<td>47.2</td>
</tr>
<tr>
<td>9.97</td>
<td>0.119</td>
<td>0.0995</td>
<td>0.0692 NaOH</td>
<td>0.295</td>
<td>7.22 ± 0.07</td>
<td>0.115</td>
<td>0.147</td>
<td>0.015</td>
<td>84.0</td>
</tr>
<tr>
<td>9.97</td>
<td>0.119</td>
<td>0.0995</td>
<td>0.0692 NaOH</td>
<td>0.295</td>
<td>7.07 ± 0.07</td>
<td>0.115</td>
<td>0.150</td>
<td>0.015</td>
<td>85.8</td>
</tr>
<tr>
<td>9.99</td>
<td>0.0992</td>
<td>0.101</td>
<td>0.0496 NaOH</td>
<td>0.297</td>
<td>6.53 ± 0.05</td>
<td>0.0948</td>
<td>0.149</td>
<td>0.00727</td>
<td>88.2</td>
</tr>
<tr>
<td>9.97</td>
<td>0.0597</td>
<td>0.101</td>
<td>0.00989 HCl</td>
<td>0.297</td>
<td>4.36 ± 0.16</td>
<td>0.0567</td>
<td>0.149</td>
<td>0.010</td>
<td>59.7</td>
</tr>
<tr>
<td>9.95</td>
<td>0.0496</td>
<td>0.0990</td>
<td>0</td>
<td>0.298</td>
<td>4.13 ± 0.12</td>
<td>0.0459</td>
<td>0.15</td>
<td>-0.015</td>
<td>76.3</td>
</tr>
<tr>
<td>9.95</td>
<td>0.0496</td>
<td>0.0990</td>
<td>0</td>
<td>0.298</td>
<td>4.54 ± 0.05</td>
<td>0.0459</td>
<td>0.151</td>
<td>-0.002</td>
<td>74.8</td>
</tr>
<tr>
<td>8.93</td>
<td>0.0892</td>
<td>0.0990</td>
<td>0</td>
<td>0.297</td>
<td>5.77 ± 0.03</td>
<td>0.0848</td>
<td>0.159</td>
<td>0.010</td>
<td>88.2</td>
</tr>
<tr>
<td>8.895</td>
<td>0.0496</td>
<td>0.0990</td>
<td>0.0396 HCl</td>
<td>0.297</td>
<td>4.42 ± 0.05</td>
<td>0.0458</td>
<td>0.145</td>
<td>0.000</td>
<td>75.7</td>
</tr>
<tr>
<td>8.895</td>
<td>0.0496</td>
<td>0.0990</td>
<td>0.0396 HCl</td>
<td>0.297</td>
<td>4.27 ± 0.03</td>
<td>0.0459</td>
<td>0.150</td>
<td>0.000</td>
<td>75.0</td>
</tr>
<tr>
<td>8.875</td>
<td>0.119</td>
<td>0.0990</td>
<td>0.0297 NaOH</td>
<td>0.297</td>
<td>6.24 ± 0.03</td>
<td>0.114</td>
<td>0.144</td>
<td>0.001</td>
<td>90.4</td>
</tr>
<tr>
<td>8.89</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0.0281 NaOH</td>
<td>0.258</td>
<td>4.01 ± 0.15</td>
<td>0.0275</td>
<td>0.155</td>
<td>0.020</td>
<td>44.6</td>
</tr>
<tr>
<td>8.89</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0.0281 NaOH</td>
<td>0.258</td>
<td>3.83 ± 0.16</td>
<td>0.0274</td>
<td>0.152</td>
<td>0.012</td>
<td>45.5</td>
</tr>
<tr>
<td>pH&lt;sub&gt;obs&lt;/sub&gt;</td>
<td>[Hx]&lt;sub&gt;0&lt;/sub&gt;</td>
<td>[DMAMP]</td>
<td>HCl or NaOH</td>
<td>Ionic strength</td>
<td>k&lt;sub&gt;obs&lt;/sub&gt; x 10&lt;sup&gt;3&lt;/sup&gt;</td>
<td>[Hx]&lt;sub&gt;ave&lt;/sub&gt;</td>
<td>A&lt;sub&gt;1&lt;/sub&gt; + A&lt;sub&gt;2&lt;/sub&gt;</td>
<td>A&lt;sub&gt;2&lt;/sub&gt;</td>
<td>% change in [Ac]</td>
</tr>
<tr>
<td>--------------</td>
<td>--------------</td>
<td>----------</td>
<td>-----------</td>
<td>----------------</td>
<td>-----------------</td>
<td>------------</td>
<td>----------------</td>
<td>------</td>
<td>---------------</td>
</tr>
<tr>
<td>8.785</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0.0281 NaOH</td>
<td>0.238</td>
<td>3.14 ± 0.14</td>
<td>0.0274</td>
<td>0.151</td>
<td>-0.008</td>
<td>44.1</td>
</tr>
<tr>
<td>8.785</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0.0281 NaOH</td>
<td>0.238</td>
<td>4.16 ± 0.15</td>
<td>0.0275</td>
<td>0.154</td>
<td>0.021</td>
<td>44.5</td>
</tr>
<tr>
<td>8.62</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0.0595 NaOH</td>
<td>0.297</td>
<td>3.81 ± 0.17</td>
<td>0.0274</td>
<td>0.153</td>
<td>0.010</td>
<td>45.9</td>
</tr>
<tr>
<td>8.62</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0.0595 NaOH</td>
<td>0.297</td>
<td>3.57 ± 0.10</td>
<td>0.0272</td>
<td>0.155</td>
<td>0.005</td>
<td>49.2</td>
</tr>
<tr>
<td>8.46</td>
<td>0.119</td>
<td>0.0990</td>
<td>0.0196 NaOH</td>
<td>0.297</td>
<td>6.95 ± 0.03</td>
<td>0.114</td>
<td>0.135</td>
<td>-0.011</td>
<td>97.8</td>
</tr>
<tr>
<td>8.46</td>
<td>0.119</td>
<td>0.0990</td>
<td>0.0196 NaOH</td>
<td>0.297</td>
<td>7.01 ± 0.04</td>
<td>0.114</td>
<td>0.146</td>
<td>-0.000</td>
<td>93.0</td>
</tr>
<tr>
<td>9.43</td>
<td>0.0793</td>
<td>0.0990</td>
<td>0</td>
<td>0.297</td>
<td>4.84 ± 0.05</td>
<td>0.0747</td>
<td>0.149</td>
<td>0.000</td>
<td>84.0</td>
</tr>
<tr>
<td>9.43</td>
<td>0.793</td>
<td>0.0990</td>
<td>0</td>
<td>0.297</td>
<td>4.87 ± 0.03</td>
<td>0.0751</td>
<td>0.149</td>
<td>0.001</td>
<td>91.9</td>
</tr>
<tr>
<td>10.3</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0</td>
<td>0.248</td>
<td>3.79 ± 0.02</td>
<td>0.0273</td>
<td>0.160</td>
<td>0.015</td>
<td>47.9</td>
</tr>
<tr>
<td>10.3</td>
<td>0.0297</td>
<td>0.0990</td>
<td>0</td>
<td>0.248</td>
<td>3.75 ± 0.25</td>
<td>0.0274</td>
<td>0.153</td>
<td>0.013</td>
<td>46.3</td>
</tr>
<tr>
<td>10.64</td>
<td>0.0793</td>
<td>0.0990</td>
<td>0.0627 NaOH</td>
<td>0.297</td>
<td>9.98 ± 0.09</td>
<td>0.0748</td>
<td>0.141</td>
<td>0.010</td>
<td>90.9</td>
</tr>
<tr>
<td>9.95</td>
<td>0.0297</td>
<td>0.198</td>
<td>0.0694 HCl</td>
<td>0.297</td>
<td>4.28 ± 0.46</td>
<td>0.0275</td>
<td>0.151</td>
<td>-0.034</td>
<td>43.8</td>
</tr>
<tr>
<td>9.95</td>
<td>0.0297</td>
<td>0.198</td>
<td>0.0684 HCl</td>
<td>0.297</td>
<td>5.02 ± 0.17</td>
<td>0.0275</td>
<td>0.150</td>
<td>-0.013</td>
<td>43.8</td>
</tr>
<tr>
<td>9.955</td>
<td>0.0793</td>
<td>0.198</td>
<td>0.0198 HCl</td>
<td>0.297</td>
<td>9.46 ± 0.04</td>
<td>0.0746</td>
<td>0.149</td>
<td>0.003</td>
<td>95.8</td>
</tr>
<tr>
<td>9.955</td>
<td>0.0793</td>
<td>0.198</td>
<td>0.0198 HCl</td>
<td>0.297</td>
<td>9.02 ± 0.05</td>
<td>0.0745</td>
<td>0.147</td>
<td>-0.000</td>
<td>96.9</td>
</tr>
<tr>
<td>9.955</td>
<td>0.119</td>
<td>0.198</td>
<td>0.0198 NaOH</td>
<td>0.297</td>
<td>10.8 ± 0.07</td>
<td>0.115</td>
<td>0.148</td>
<td>0.003</td>
<td>86.0</td>
</tr>
<tr>
<td>9.955</td>
<td>0.119</td>
<td>0.198</td>
<td>0.0198 NaOH</td>
<td>0.297</td>
<td>10.4 ± 0.05</td>
<td>0.115</td>
<td>0.144</td>
<td>0.003</td>
<td>85.2</td>
</tr>
</tbody>
</table>
the oxime. In other words, the hydrolysis of the iminium ions back to acetone and amine is so slow that it could be neglected. The first-order rate constant for iminium ion formation $k_{im}$ could then be determined from equation (12) where $k_{ox}$ is the second order rate

$$k_{im} = k_{obs} - k_{ox} [Hx]$$ (12)

constant for the "background reaction" (oximation in the absence of amines). However, with 2-dimethylaminomethylpyrrolidine it is not certain whether complete capture of the iminium ions is occurring. Thus, in these experiments, the hydroxylamine concentration was varied from 0.05 to 0.12 M at constant catalyst concentration and constant protonation ratio to determine the minimum concentration of hydroxylamine required for complete capture of iminium ions. The plots of $k_{obs}$ vs hydroxylamine concentration for solutions buffered near pH 8.89 and pH 9.95 are shown in Figures 2 and 3. If the intermediate iminium ions are quantitatively captured, equation (12) will be obeyed which means that $k_{obs}$ will be a linear function of $[Hx]$ with slope $k_{ox}$ and intercept $k_{im}$. The line determined by equation (12) should be parallel to the line $k_{obs} = k_{ox} [Hx]$ which is the rate constant for the background reaction and the vertical distance between the two lines will be $k_{im}$, the first order rate constant for the iminium ion formation. However, it is clear that the experimental points do not follow a straight line. The line below the experimental points represents the rate constant for the
Fig. 2. First Order Rate Constant for 2-Dimethylaminomethylpyrrolidine-catalyzed Oximation of Acetone vs. Hydroxylamine Concentration at pH \( \text{average} \) 9.95 in Water at 35°
Fig. 3. First Order Rate Constant for 2-Dimethylaminomethylpyrrolidine-catalyzed Oximation of Acetone vs. Hydroxylamine Concentration at pH_{average} 8.90 in Water at 35°
"background reaction" at the average of the pH's of the kinetic runs in question. The distance of the points from the line increases as the hydroxylamine concentration is increased which means that the fraction of iminium ions which gets captured by the hydroxylamine increases as [Hx] becomes larger. These results indicate that equation (12) could not be employed to calculate the iminium ion formation rate constant.

The reaction is believed to proceed via the following scheme which breaks up iminium ion formation into an uncatalyzed and an acid-catalyzed pathway. From the principle of microscopic reversibility, the hydrolysis of the iminium ion has to proceed via attack of water and hydroxide ions. In addition, a hydroxide-catalyzed attack of hydroxylamine on the iminium ion was included because this appears to have some contribution to the rate in previous work with secondary amines, although its reality was doubtful.

\[ R_2NH + \xrightarrow{=} 0 \rightleftharpoons NR_2 + OH^- \]  
\[ R_2NH_2 + \xrightarrow{=} 0 \rightleftharpoons NR_2 + H_2O \]  
\[ NR_2 + NH_2OH + OH^- \xrightarrow{k''} NOH + HNR_2 + H_2O \]  
\[ 0 + NH_2OH \xrightarrow{k_{ox}} NOH \]

The rate law for the formation of the oxime following this scheme is equation (17).
\[
\frac{d[\text{ox}]}{dt} = k_0 [\text{NR}_2^+][\text{NH}_2\text{OH}] + k_{o'} [\text{OH}^-][\text{NH}_2\text{OH}][\text{N}_4\text{H}_2^+] + k_{\text{ox}} [\text{OH}^-][\text{NH}_2\text{OH}] + k_2 [\text{NH}_2\text{OH}][\text{OH}^-]
\]

\[(17)\]

A steady-state treatment can be performed on the intermediate iminium ions.

\[
\frac{d[\text{NR}_2^+]}{dt} = k_{\text{im}} [\text{R}_2\text{NH}] + k_{\text{imh}} [\text{R}_2\text{NH}_2^+] - k_d' + k_2 [\text{NH}_2\text{OH}][\text{OH}^-]
\]

\[(18)\]

The steady-state concentration of the iminium ion can then be expressed in terms of the measurable concentrations of the other species.

\[
[\text{NR}_2^+] = \frac{(k_{\text{im}} [\text{R}_2\text{NH}] + k_{\text{imh}} [\text{R}_2\text{NH}_2^+])[\text{OH}^-]}{k_d'[\text{OH}^-] + k_d'[\text{NH}_2\text{OH}][\text{OH}^-] + k_o[\text{NH}_2\text{OH}][\text{OH}^-]}
\]

\[(19)\]

The rate constants \(k_d\) and \(k_d'\) are not independent of each other.

\[
\frac{k_{\text{im}}/k_d}{k_{\text{imh}}/k_d'} = \frac{[\text{NR}_2^+][\text{OH}^-]/[\text{R}_2\text{NH}][\text{OH}^-]}{[\text{NR}_2^+][\text{R}_2\text{NH}^+][\text{OH}^-]} = \frac{[\text{OH}^-][\text{R}_2\text{NH}_2^+]}{[\text{R}_2\text{NH}]}\]

\[(20)\]

\[
\frac{k_{\text{im}}/k_d}{k_{\text{imh}}/k_d'} = K_w \gamma^2
\]

\[(21)\]

where \(K_w\) is the autoprotolysis constant for water equal to \(10^{-13.68}\) at \(35^\circ\), \(K_{\text{R}_2\text{NH}_2^+}\) is the dissociation constant for the monoprotonated amine equal to \(10^{-9.82}\) and \(\gamma\) is the activity coefficient calculated from the Davies equation.
Thus equation (17) becomes equation (23).

\[
\text{d}[O_x] \quad = \quad \frac{(k_{im} [R_2NH] + k_{imh} [R_2NH_2^+])([NH_2OH] + k'_o[NH_2OH][OH^-])}{k_{d} [OH^-] + \frac{k_{d} k_{im} K v^2}{k_{im} R_2NH_2^+} + k_o[NH_2OH] + k'_o[NH_2OH][OH^-]}
\]

\[+ k_{ox} [NH_2OH][OH^-] \]

If both the numerator and denominator of the first term on the right side of eq. (23) are divided by \( k_o \), the first order rate constant for the disappearance of acetone can be expressed as in eq. (24).

\[
k_{obs} = \frac{(k_{im} [R_2NH] + k_{imh} [R_2NH_2^+]) [NH_2OH](1 + [OH^-]z)}{y([OH^-] + k_{imh} c/k_{im}) + [NH_2OH](1 + [OH^-]z)} + k_{ox} [NH_2OH]
\]

where \( y = k_d/k_o \), \( z = k'_o/k_o \) and \( c = K_{w} v^2/[R_2NH_2^+] \).

A nonlinear least squares analysis was performed on eq. (24) using the method of Hamilton\(^{49}\) and using the \( k_{obs} \) from the 35 kinetic runs with weighting equal to \( 1/(k_{obs})^2 \) and \( k_{im}, k_{imh}, y \) and \( z \) as the disposable parameters. Program 3 (Appendix) was written to do the nonlinear least squares calculations. The second order rate constant for uncatalyzed oximation, \( k_{ox} \), was determined from previous work.\(^{29}\)
The hydronium ion concentration, \([H^+]\), and the hydroxide ion concentration, \([OH^-]\), were calculated from the observed pH using equation (26) and equation (27), respectively.

\[
[H^+] = 10^{-pH \cdot \log \gamma}
\]

(26)

\[
[OH^-] = 10^{-13.68 + pH \cdot \log \gamma}
\]

(27)

For the value of \([\text{NH}_2\text{OH}]\), the average hydroxylamine concentration during the reaction was used. This value did not differ from the initial hydroxylamine concentration by more than 8%. The free amine and the protonated amine concentrations were calculated from the total amine concentration, the observed pH and the activity coefficient.

The results of the analysis are shown in the following.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calc'd Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>(k_{\text{im}})</td>
<td>0.0327 M(^{-1})s(^{-1})</td>
<td>0.0121 M(^{-1})s(^{-1})</td>
</tr>
<tr>
<td>(k_{\text{imh}})</td>
<td>0.0660 M(^{-1})s(^{-1})</td>
<td>7.14 x 10(^{-3}) M(^{-1})s(^{-1})</td>
</tr>
<tr>
<td>(k_d/k_o)</td>
<td>46.4</td>
<td>14.9</td>
</tr>
<tr>
<td>(k'_o/k_o)</td>
<td>912 M(^{-1})</td>
<td>927 M(^{-1})</td>
</tr>
</tbody>
</table>

Standard deviation of analysis = 0.0945

The standard deviation of analysis is the square root of the sum of the squares of the deviation between the observed and calculated rate constants divided by the number of rate constant.
minus the number of parameters. There were 9 kinetic runs showing more than 10% relative deviation from the calculated rate constants, all of them with 3 to 1 hydroxylamine to acetone concentration ratio. The largest relative deviation was 26%. It can be seen that the calculated value of the parameter $k'_{\text{o}}/k_{\text{o}}$ is not reliable because the standard deviation is even larger than the parameter itself. This means that it is uncertain whether or not the hydroxide-catalyzed attack of hydroxylamine on the iminium ion is real. If this value is set equal to zero, in other words, if hydroxide-catalyzed attack of hydroxylamine is considered non-existent, $k_{\text{obs}}$ can be expressed as in equation (28).

$$k_{\text{obs}} = \frac{(k_{\text{im}}[R_\text{ONH}] + k_{\text{imh}}[R_\text{ONH}^+])[NH_\text{OH}]}{y([NH_\text{OH}] + (k_{\text{im}}/k_{\text{imh}})c) + [NH_\text{OH}] } + k_{\text{ox}}[NH_\text{OH}]$$ (28)

A nonlinear least squares analysis was performed on the above equation using the results of the same 35 kinetic runs with weighting equal to $1/(k_{\text{obs}})^2$. The results of the analysis are shown below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calc'd Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{\text{im}}$</td>
<td>0.0423 M$^{-1}$s$^{-1}$</td>
<td>7.88 x 10$^{-3}$ M$^{-1}$s$^{-1}$</td>
</tr>
<tr>
<td>$k_{\text{imh}}$</td>
<td>0.0605 M$^{-1}$s$^{-1}$</td>
<td>4.30 x 10$^{-3}$ M$^{-1}$s$^{-1}$</td>
</tr>
<tr>
<td>$k_{d}/k_{\text{o}}$</td>
<td>51.5</td>
<td>13.5</td>
</tr>
</tbody>
</table>

Standard deviation of analysis = 0.0964
Nine kinetic runs had more than 10% relative deviation between the observed and calculated rate constants, all of them with 3 to 1 hydroxylamine to acetone concentration ratio. Since there was only a very small change in the standard deviation of analysis in going from a four to a three-parameter equation, it is still uncertain whether the hydroxide-catalyzed attack of hydroxylamine on the iminium ion is significant.

Since it is believed that the kinetic runs with 3 to 1 hydroxylamine to acetone concentration ratio were less reliable than the others, the results of four kinetic runs with more than 15% relative deviation between the observed and calculated rate constants in the two previous analyses were not included, reducing the number of kinetic runs to 31. A nonlinear least squares analysis on eq. (24) was performed using these 31 runs. The results are shown below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calc'd Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{im}$</td>
<td>0.0201 M$^{-1}$s$^{-1}$</td>
<td>4.79 x 10$^{-3}$ M$^{-2}$s$^{-1}$</td>
</tr>
<tr>
<td>$k_{inh}$</td>
<td>0.0620 M$^{-1}$s$^{-1}$</td>
<td>2.83 x 10$^{-3}$ M$^{-1}$s$^{-1}$</td>
</tr>
<tr>
<td>$k_d/k_o$</td>
<td>23.6</td>
<td>4.53</td>
</tr>
<tr>
<td>$k_o/k_o'$</td>
<td>3982 M$^{-1}$</td>
<td>1834 M$^{-1}$</td>
</tr>
</tbody>
</table>

Standard deviation of analysis = 0.0481

The standard deviation of analysis was reduced to half its value using 35 kinetic runs and the relative deviation between the observed and calculated rate constants was only 8.6%. However, the standard
deviation of the parameter $k'_o/k_o$ is about half of the value of the parameter itself, so an analysis on eq. (28) was performed using the 31 kinetic runs. The results are shown below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calc'd Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{im}$</td>
<td>$0.0378 \text{ M}^{-1}\text{s}^{-1}$</td>
<td>$3.44 \times 10^{-3} \text{ M}^{-1}\text{s}^{-1}$</td>
</tr>
<tr>
<td>$k_{imh}$</td>
<td>$0.0525 \text{ M}^{-1}\text{s}^{-1}$</td>
<td>$2.01 \times 10^{-3} \text{ M}^{-1}\text{s}^{-1}$</td>
</tr>
<tr>
<td>$k_d/k_o$</td>
<td>28.0</td>
<td>5.02</td>
</tr>
</tbody>
</table>

Standard deviation of analysis = 0.0558

The standard deviation of analysis was only slightly larger than that of the 31-run 4-parameter analysis. The largest deviation between the observed and calculated rate constants was 11.3%. Since the agreement became worse in going from a four- to a three-parameter analysis, the results of the four-parameter analysis were accepted as the more reliable values of $k_{im}$ and $k_{imh}$. On the other hand, since there was only a small difference between the standard deviations of analyses, it is still uncertain whether the hydroxide-catalyzed attack of hydroxylamine on the iminium ion is real. It is not an unlikely possibility that the calculated value for $k'_o/k_o$ is just a number with no physical significance that makes the analysis better.
C. Evidence for Iminium Ion Formation Between Acetone and Salts of Pyrazolidine, Isoxazolidine, O,N-Dimethylhydroxylamine and 1,2-Dimethylhydrazine

1. Acetone and Pyrazolidinium Ions

a. pH Changes

The following table shows the results of the pH measurements on solutions produced by injecting different amounts of acetone into 5.00 ml of buffer solution consisting of 0.03 M free pyrazolidine, 0.12 M pyrazolidinium ions and 0.15 M sodium chloride.

<table>
<thead>
<tr>
<th>Time</th>
<th>Buffer Soln. Without Ac</th>
<th>Buffer Soln. + 0.06 M Ac</th>
<th>Buffer Soln. + 0.12 M Ac</th>
<th>Buffer soln. + 0.24 M Ac</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.755</td>
<td>6.830</td>
<td>6.900</td>
<td>7.040</td>
</tr>
<tr>
<td>75 min.</td>
<td>6.750</td>
<td>6.860</td>
<td>6.960</td>
<td>7.130</td>
</tr>
<tr>
<td>3 hrs</td>
<td>6.730</td>
<td>6.830</td>
<td>6.930</td>
<td>7.110</td>
</tr>
</tbody>
</table>

Injection of acetone solution into an amine buffer solution which does not react with it causes a slight decrease in pH. It has been seen in solutions used for dedeuteration experiments that
injection of an amount of acetone to produce 0.52 M into tertiary amine buffers causes an increase of about 0.04 to 0.06 pH units. Since the amounts of acetone injected above are much smaller than this, the change in pH to be expected due to change in polarity of the medium should be less than 0.04 to 0.06. However, the increases in pH seen in Table 4 are much larger than this. The most likely explanation for the above results is that acetone reacts with pyrazolidinium ions to form iminium ions.

\[
(CH_3)_2C=O + H_2N+ \xrightleftharpoons{} (CH_3)_2C=N+ + H_2O \quad (29)
\]

This reaction causes a decrease in the concentration of pyrazolidinium ions by shifting the equilibrium in eq. (30) to the left. This

\[
\xrightleftharpoons{} \quad (30)
\]

causes a decrease in the concentration of hydronium ions corresponding to the observed increase in pH 75 minutes after injection.

It appears that the reaction has occurred to a large extent at "0 time" as seen in the large differences between the pH's of the solutions with and without acetone at that time. This is because acetone was injected into all three solutions before the pH's were measured which takes about a minute for each solution.
The small decrease (0.02 to 0.03 units) in pH from 75 minutes to 3 hours after injection observed in all solutions even with the one without acetone may be due to a drift in the calibration of the pH meter or decomposition due to air oxidation of one of the components of the buffer.

b. NMR

The NMR spectrum of a 0.5 M solution of pyrazolidinium perchlorate in H₂O shows the large water peak at δ 4.7, a 2-proton quintet at δ2.25 (C-CH₃-C), and a 4-proton triplet centered at δ3.5 (CH₃-N). Spectra taken immediately after and 35 minutes after injection of 0.18 ml of acetone into the tube showed gradual changes. Thirty-five minutes after injection, the spectrum indicates complete conversion of pyrazolidinium ions to N-isopropylidenepyrazolidinium ions - large water peak at δ4.7; singlet at δ3.45 (CH₃-N⁺-C); quintet at δ3.35 (CH₃-C-N⁺-C); singlet with fine splitting at δ2.35 ((CH₃)₂C=N⁺); and a singlet at δ2.15 due to unreacted acetone.

To eliminate large spinning side bands, the same was done using D₂O as solvent and replacing acetone with acetone-d₆. The NMR spectrum of pyrazolidinium perchlorate in D₂O (Figure 4) consists of a singlet at δ4.7 (H₂O); a 4-proton triplet at δ3.4; and a 2-proton quintet at δ3.4 (C-CH₃-C). Between the time of injection and one hour and 20 minutes after, the spectra showed changes. More acetone-d₆ was injected into the tube to bring the acetone-d₆ pyrazolidinium ion ratio to 6:1. The spectrum thereafter (Figure 5) showed complete
Fig. 4. 60 MHz FMR Spectrum of Pyrazolidinium Perchlorate in D$_2$O.
Fig. 5. 60 MHz FNR Spectrum of a Solution of 6:1 (mole/mole) Acetone-$_2$-Pyrazolidinium Perchlorate in $D_2O$. 

6.0 5.0 4.0 3.0 2.0 1.0
Fig. 6. 60 MHz PMR Spectrum of N-Isopropylidinepyrazolidinium Perchlorate in DMF-d$_7$.
conversion of the protonated amine to \( N \)-isopropylidenehyrazolidinium ion - singlet at \( 84.6 \) (HgO); a 2-proton triplet at \( 84.1 \) (C-CH\(_2\)-N\(^+\)=C); a 2-proton triplet at \( 83.45 \) (C-CH\(_2\)-N-N\(^+\)=C) and a 2-proton quintet at \( 82.3 \) (C-CH\(_2\)-C-N\(^+\)=C). The spectra described are shown with the spectrum of N-isopropylidenehyrazolidinium perchlorate in CD\(_3\)CN (Figure 6) for comparison.

c. UV

The spectrum of a 0.0506 M pyrazolidinium perchlorate solution in water using 1-cm cells showed a maximum at 225 nm with an absorbance of 0.382 at that wavelength. Acetone solution (0.05 ml, 1 M) was injected into this solution to produce an initial acetone concentration of 0.01 M. The maximum at 225 nm disappeared and was replaced by a steep climb from 300 to 270 nm. The maximum would lie between 260 and 210 nm but could not be seen because it was off scale.

Using 1-mm cells, the spectrum of a 0.03 M solution of the amine salt in water showed a maximum at 260 nm (abs. - 0.0034) and a higher maximum at 228 nm (abs. - 0.022). An amount of acetone was injected into the solution to produce an initial acetone concentration of 0.03 M. Between the time of injection and one hour after, the spectrum showed gradual changes. One hour after, the spectrum showed a large peak with a maximum at 235 nm and an absorbance of 2.9 at that wavelength. There was no absorption from 300 to 350 nm.

With the wavelength set at 235 nm, acetone was injected into a pH 9.64 solution containing 0.1 M pyrazolidine buffered by trimethylamine and into a pH 11.8 solution containing 0.1 M pyrazolidine and
0.17 M sodium hydroxide. No reaction was observed. The absorbance after 40 minutes remained the same as the absorbance immediately after injection.

These experiments show that there is indeed a reaction between acetone and pyrazolidinium ions and that the product has an absorption maximum at 235 nm with an extinction coefficient at that wavelength which is much greater than any of the reactants.

2. Acetone and Isoxazolidinium Ions.
   a. NMR

The NMR spectrum of a 1.0 M isoxazolidinium bromide in D$_2$O (Figure 7) consisted of: a 2-proton singlet at $\delta$4.8 (H$_2$O), a 2-proton triplet at $\delta$4.35 (CH$_2$-O); a 2-proton triplet at $\delta$3.70 (CH$_2$-N$^+$); and a 2-proton triplet at $\delta$2.60 (C-CH$_2$-C). Acetone-$d_3$ (0.20 ml) was injected into the solution. Spectra taken 5 minutes to 60 minutes after injection showed gradual changes. The spectrum 60 minutes after injection (Figure 8) showed peaks which agree with the structure of the iminium ion - 2-proton triplet at $\delta$4.5 (CH$_2$-O-N$^+$=C); a 2-proton triplet at $\delta$4.3 (CH$_2$-N$^+$=C); a singlet at $\delta$4.25 (H$_2$O); a quintet at $\delta$2.55 (C-CH$_2$-C); and a small multiplet at $\delta$2.0 due to acetone-$d_5$.

The spectrum taken 1$\frac{1}{2}$ days and 3 days after injection showed no further changes.

Four days after injection, 0.30 ml of DMSO-$d_6$ was added to the solution to cause the water peak to shift by a solvent effect to
Fig. 7. 60 MHz FMR Spectrum of Isoxazolidinium Bromide in D₂O.
Fig. 8. 60 MHz NMR Spectrum of a Solution Resulting from Injection of 0.20 ml Acetone-$d_6$ into 1.0 M Ioxazolidinium Bromide in D$_2$O.
Fig. 9. 60 MHz PMR Spectrum of a Solution of 0.20 ml of Acetone-\textsubscript{d\textsubscript{6}} Isoxazolidinium Bromide and 0.30 ml of DMSO-\textsubscript{d\textsubscript{6}} in D\textsubscript{2}O.
Fig. 10. 60 MHz PFR Spectrum of a Solution Resulting from Injection of Acetone in 1 M Isoxazolidinium Bromide in D$_2$O, 2$^{1/2}$ hrs. After Injection of Acetone.
Fig. 11. 60 MHz PMR Spectrum of a Solution Resulting from Injection of Acetone into Isoxazolidinium Bromide in $D_2O$, 48 hours after injection of Acetone; 0.30 ml of DMSO-$d_6$ added.
Fig. 12. 60 MHz FMR Spectrum of N-Isopropylideneisoxazolidinium Perchlorate in CD$_3$CN.
reveal the peaks overlapping with it. The spectrum thereafter (Figure 9) consisted of: a 2-proton triplet at δ4.55 (CH₂-O-N⁺=C); a 2-proton triplet at δ4.35 (CH₂-N⁺=C); a singlet at δ4.25 (H₂O); a 2-proton quintet at δ2.60 (C-CH₂-C); and a small multiplet at δ2.05 due to acetone-d₅.

Spectra were also taken after injection of light acetone replacing acetone-d₃ into a 1 M solution of isoxazolidinium bromide in D₂O. Two and a half hours after injection, the spectrum (Figure 10) consisted of: a 2-proton triplet at δ4.66 (CH₂-0-N⁺=C); a 2-proton broadened triplet at δ4.44 (CH₂-N⁺=C); a singlet at δ4.66 (H₂O); a 2-proton quintet at δ2.65 (C-CH₂-C); a peak which appears to be finely split into a triplet (J = 1) at δ2.45 ((CH₃)₂C=N⁺); and a large singlet at δ2.2 due to unreacted acetone.

Forty-eight hours after injection of acetone, 0.30 ml of DMSO-d₆ was added to cause the signals to shift by a solvent effect. The spectrum (Figure 11) then consisted of: a 2-proton triplet at δ4.67 (CH₂-O-N⁺=C); a 2-proton broadened triplet at δ4.44 (CH₂-N⁺=C); a singlet at δ4.56 (H₂O); a 2-proton quintet at δ2.70 (C-CH₂-C); a peak which appears to be split into a triplet (J = 1) at δ2.50 (N⁺=C(CH₃)₂); and a singlet at δ2.2 due to unreacted acetone.

b. UV

The UV spectrum of a 0.01 M aqueous acetone solution in a 1-cm cell with water as reference showed negligible absorbances from 350 to
310 nm, a steady rise from 310 to 265 nm, a maximum at 265 nm with an absorbance of 0.16 and a sharp rise at wavelengths shorter than 220 nm, going off scale at about 210 nm.

The spectrum of a 0.1 M aqueous isoxazolidinium bromide solution with water as reference consisted of very small absorbances from 350 to 245 nm and a sharp rise at shorter wavelengths, going off scale at 235 nm. Injection of acetone into a 0.1 M isoxazolidinium bromide to produce an initial acetone concentration of 0.01 M and scanning with water as reference produced a spectrum consisting of very small absorbances from 350 to 310 nm, a steady rise from 310 to 265 nm, a maximum at 265 nm with an absorbance of 0.14 at that wavelength, a slight decrease from 263 to 245 nm, and a sharp rise from 245 to 240 nm where the absorbance goes off scale.

With 0.08 M isoxazolidinium bromide solution in both reference and sample cells, scanning produced a spectrum with negligible absorbances from 350 to 230 nm. At shorter wavelengths, the absorbance rises sharply and goes off scale at 225 nm. This means that between 350 and 230 nm, the absorbance of the amine salt is cancelled by placing the same solution in the reference and sample cells.

Injection of acetone solution into 0.08 M isoxazolidinium bromide with the same amine salt solution in the reference cell and scanning immediately after injection produced a spectrum consisting of very small absorbances from 350 to 310 nm, a steady increase from 310 to 265 nm, a maximum at 265 nm with an absorbance of 0.126, a slight
decrease from 265 to 255 nm, and a sharp rise at shorter wavelengths going off scale at 245 nm.

With the wavelength set at 275 nm, acetone solution was injected into 0.08 M isoxazolidinium bromide to produce an initial acetone concentration of 0.01 M. Recording the absorbance as time progressed immediately after injection produced a curve which looks like that of a first order reaction starting at an absorbance of 0.14 at 16 seconds after injection and levelling to 0.106 at 330 seconds after injection.

The spectrum of a solution of 0.1 M isoxazolidinium bromide and 0.1 M hydrochloric acid using water as reference showed very small absorbances from 550 to 245 nm and a sharp rise at shorter wavelengths going off scale at 230 nm. If the same solution is placed in both reference and sample cells, the spectrum showed negligible absorbances from 550 to 230 nm and a sharp rise at shorter wavelengths going off scale at 225 nm.

Injection of acetone into a solution of 0.1 M isoxazolidinium bromide and 0.1 M with the same solution as reference produced a spectrum consisting of negligible absorbances from 350 to 310 nm, a steady rise from 310 to 265 nm, a maximum at 265 nm with an absorbance of 0.117, a slight decrease from 265 to 255 nm, and a sharp rise at shorter wavelengths going off scale at 245 nm.

With the wavelength set at 275 nm, acetone was injected into a solution 0.1 M in isoxazolidinium bromide and 0.1 M in hydrochloric acid to produce an initial acetone concentration of 0.01 M.
Recording the absorbance as time progresses immediately after injection produced a curve which looks like that of a first order reaction starting at 0.136 at 17 seconds after injection and levelling to an equilibrium absorbance of 0.096 at 310 seconds after.

Injection of acetone into a buffer solution consisting of 0.09 M free and 0.01 M protonated isoxazolidine to produce an initial acetone concentration of 0.01 M produced a spectrum consisting of very small absorbances from 350 to 310 nm, a steady rise from 310 to 265 nm, a maximum at 265 nm where it had an absorbance of 0.175, a slight decrease from 265 to 245 nm, and a sharp rise at shorter wavelengths going off scale at 240 nm.

With the wavelength set at 275 nm, acetone was injected into a buffer solution consisting of 0.09 M free and 0.01 M protonated isoxazolidine with the same solution as the reference to produce an original acetone concentration of 0.01 M. Immediately after injection, the mixture had an absorbance of 0.154. The absorbance decreased slightly to an equilibrium value of 0.148 at 315 seconds after injection.

To study the hydrolysis of the iminium ion, 30 microliters of 1 M N-isopropylideneisoxazolidinium perchlorate in dry acetonitrile was injected into 3 ml of 1 M hydrochloric acid solution to produce an initial iminium ion concentration of 0.01 M. Spectra taken with the same hydrochloric acid solution in the reference cell showed increasing absorbance as time progresses with a maximum at 265 nm which is also
the $\lambda_{\text{max}}$ for acetone. The system appeared to have reached equilibrium after about 1000 seconds. The spectrum at this time showed a gradual rise from 300 nm to a maximum at 265 nm where it has an absorbance of 0.18, a decrease to a minimum of 240 nm with an absorbance of 0.12 and a sharp climb at lower wavelengths going off scale at 225 nm.

The following conclusions can be drawn from the preceding results: a) acetone and isoxazolidinium ions react to form N-isopropylideneiso-oxazolidinium ions (eq. 31);

$$\text{(CH}_3\text{)}_2\text{CO} + \text{H}_2\text{N}^+\text{O} \rightarrow \text{(CH}_3\text{)}_2\text{C}^=\text{N}^+\text{O} + \text{H}_2\text{O}$$ (31)

as shown from the decrease in absorbance of acetone when injected into a solution of the protonated amine; b) the iminium ion has little or no absorbance at wavelengths greater than 250 nm as seen from the fact that the spectrum of the acetone-oxazolidinium ion mixture has the same shape as that of the acetone from 350 to 250 nm except that the absorbance of the former is lower; and c) N-isopropylideneoxazolidinium perchlorate undergoes hydrolysis at a measurable rate to give acetone and the protonated amine.

3. Acetone and O,N-Dimethylhydroxylammonium Ions

a. NMR

The NMR spectrum of O,N-dimethylhydroxylamine hydrochloride in D$_2$O (Figure 13) consisted of the following peaks: a singlet at 84.8 (H$_2$O), a 3 proton singlet at 83.90 (CH$_3$-O-), and a 3-proton singlet.
Fig. 13. 60 MHz PMR Spectrum of O,N-Dimethylhydroxylamine Hydrochloride in D_2O.
at δ2.00 (CH₃-N⁺). Acetone-d₆ (0.20 ml) was injected into the solution under nitrogen and the tube was quickly shaken. Thirty minutes after injection, the spectrum of the resulting solution consisted of: a singlet at δ4.50 (H₂O), a small singlet at δ3.95 (CH₃-O-N=C); a singlet at δ3.80 (CH₃-0, unreacted amine), a small singlet at δ3.75 (CH₂-N=C), a singlet at δ2.90 (CH₃-N⁺, unreacted amine), and a small multiplet at δ2.05 due to the acetone-d₆.

Another 0.20 ml of acetone-d₆ was injected into the same NMR tube to convert more of the amine to product. Five and a half hours after the first injection and 1 ½ hours after the second, the spectrum (Figure 14) consisted of a singlet at δ4.35 (H₂O), a small singlet at δ3.85 (CH₃-O-N=C), a singlet at δ3.70 (CH₃-0, unreacted amine), a small singlet at δ3.65 (CH₂-N⁺=C), a singlet at δ2.80 (CH₃-N⁺, unreacted amine) and a small multiplet at δ1.90 due to acetone-d₆.

Light acetone (0.3 ml) was injected into an NMR tube containing O₂N-dimethylhydroxylamine hydrochloride in 0.40 ml D₂O. One hour and 20 minutes after injection, the spectrum (Figure 15) consisted of a singlet at δ4.55 (H₂O), a small singlet at δ3.9 (CH₃-O-N⁺=C), a singlet at δ3.75 (CH₃-0, unreacted amine), two very close singlets at δ2.45 ((CH₃)₂C=N⁺) and a very large singlet at δ2.1 due to unreacted acetone.

The NMR spectrum of N-isopropylidene-O₂N-dimethylhydroxylammonium perchlorate in DMSO-d₆ (Figure 16) consisted of a 3-proton singlet at δ3.95 (CH₃-O-N⁺=C), a 3-proton broadened singlet at δ3.75 (CH₃-N⁺=C)
Fig. 14. 60 MHz FMR Spectrum of a Solution Resulting from Injection of Acetone-$d_6$ into $\text{O}_2\text{N}_2$-Dimethylhydroxylamine Hydrochloride in $\text{D}_2\text{O}$. 
Fig. 15. 60 MHz PFR Spectrum of a Solution Resulting from Injection of 0.30 ml Acetone into $\text{O}_2\text{N}_2$-Dimethylhydroxylamine Hydrochloride in $\text{D}_2\text{O}$. 
Fig. 16. 60 MHz PMR Spectrum of $N$-Isopropylidene-$Q,N$-dimethylhydroxylammonium Perchlorate in DMSO-$d_6$. 
Fig. 17. 60 MHz FMR Spectrum of a Solution Resulting from Injection of D₂O into N-Isopropylidene-0,N-dimethylhydroxylammonium Perchlorate in DMSO-d₆.
and a broad singlet at $\delta 2.45 \ (\text{CH}_3)_2\text{C}=\text{N}^+$. Deuterium oxide (0.15 ml) was injected into the NMR tube. The spectrum (Figure 17) of the resulting solution five minutes after injection showed only peaks due to deuteronated amine and acetone-singlet at $\delta 3.80 \ (\text{CH}_3-\text{O})$, singlet at $\delta 2.85 \ (\text{CH}_3-\text{N}^+)$ and a singlet at $\delta 2.10 \ (\text{acetone})$.

These results clearly show that acetone and $\text{O}_2\text{N}$-dimethylhydroxylammonium ions react to form $\text{N}$-isopropylidene-$\text{O}_2\text{N}$-dimethylhydroxylammonium ions (Eq. 31) and that the equilibrium constant for this reaction is smaller than that between acetone and pyrazolidinium or

$$\text{CH}_3\text{CO} + \text{CH}_3\text{NH}_2^+ \text{OCH}_3 \rightarrow (\text{CH}_3)_2\text{C}=\text{N}^+ + \text{H}_2\text{O} \quad (32)$$

isoxazolidinium ions. The latter conclusion was deduced from the fact that even after addition of a large amount of acetone, most of the ammonium ions remained unreacted and from the fact that addition of a relatively small amount of $\text{D}_2\text{O}$ caused complete conversion of the iminium ion into acetone and deuteronated amine.

b. UV

The UV spectrum of a 0.2 M $\text{O}_2\text{N}$-dimethylhydroxylamine hydrochloride solution in a 1-cm cell using water as reference showed small (<0.05) absorbances from 350 to 240 nm. At shorter wavelengths, the absorbance rises sharply and goes off scale at 210 nm. An amount of acetone solution was injected to produce an initial acetone concentration of 0.02 M. Immediately after injection, the spectrum of the
resulting solution showed negligible absorbances from 350 to 315 nm, a steady rise from 315 to a maximum at 265 nm where it had an absorbance of 0.31, a gradual drop from 265 to 225 nm, a maximum at 225 nm with an absorbance of 0.155, and a sharp rise at shorter wavelengths going off scale at 215 nm. The spectrum did not show any further change up to 30 minutes after injection. It appears that just like the acetone-isoxazolidinium ion reaction, the product has little, if any absorption at wavelengths greater than 240 nm. Also, it appears that equilibrium is attained immediately after injection because no change was observed in the spectrum as time progressed.

To observe the hydrolysis of the iminium ion, 30 microliters of 1.0 M N-isopropylidene-O,N-dimethylhydroxylammonium perchlorate in dry acetonitrile was injected into 3 ml of 1.0 M hydrochloric acid to produce an initial iminium ion concentration of 0.01 M. The spectrum of the resulting solution taken 5 minutes after injection using the same hydrochloric acid solution as reference showed small absorbances (< 0.05) from 350 to 300 nm, a steady rise from 315 to a maximum at 265 nm where it has an absorbance of 0.176, a gradual decrease from 265 to a minimum at 237 nm where it has an absorbance of 0.10 and a sharp rise at shorter wavelengths going off scale at 215 nm. From 300 to 240 nm the resulting spectrum looks very much like that of acetone. In fact, at this wavelength range, it is almost superimposable with the spectrum of 0.01 M acetone in hydrochloric acid. Below 237 nm, the absorbance rises sharply as the wavelength is
decreased while that of acetone does not rise again until 210 nm. The difference is due to the absorbance of the amine, either free or protonated.

With the wavelength set at 275 nm, 30 microliters of 1.0 M iminium perchlorate solution in acetonitrile were injected into 3.0 ml of 1.0 M hydrochloric acid solution. The absorbance as a function of time was recorded immediately after injection with the same hydrochloric acid solution as reference. The graph showed a slight decrease in absorbance from 0.16 at 18 seconds, to 0.152 at 198 seconds and levelling to an equilibrium value of 0.148 at about 550 seconds after injection. The same amount of the iminium perchlorate in acetonitrile solution was injected into 3.0 ml of water. The spectrum 7 minutes after injection, taken with water as reference, showed small absorbances (< 0.05) from 350 to 300 nm, a gradual rise from 300 to a maximum at 265 nm where it had an absorbance of 0.178, a gradual drop to a maximum at 233 nm with an absorbance of 0.0725, and a sharp rise at shorter wavelengths, going off scale at 215 nm. The same amount of the iminium ion perchlorate was again injected into 3 ml of water. With the wavelength set at 275 nm, the absorbance as a function of time was recorded with water as reference. The graph showed a slight decrease in absorbance from 0.165 at 14 seconds to 0.154 at 104 seconds and levelling to an equilibrium value of 0.152 around 200 seconds after injection.
At 275 nm, 0.01 M acetone solution should have an absorbance of 0.155, calculated from its extinction coefficient of 15.5 cm$^{-1}$M$^{-1}$ (p. 131). Solutions resulting from injection of the same amount of iminium ion into water or hydrochloric acid solution had absorbances very near this value immediately after injection. Thus, the preceding results indicate that the hydrolysis of the iminium ion to give acetone and the protonated amine occurs at a rate which cannot be measured by conventional methods. The slight (8%) decrease in absorbance which occurs at a measurable rate is unexplained owing to the fact that the NMR results in DMSO-$d_6$ shows only one reaction occurring - the hydrolysis of the iminium ion.

4. Acetone and 1,2-Dimethylhydrazinium Ions

a. NMR

A solution of 1,2-dimethylhydrazinium ions in D$_2$O, prepared by addition of an equivalent amount of sodium deuterioxide in D$_2$O solution to 1,2-dimethylhydrazine dihydrochloride (Figure 18) showed only two peaks - singlet at $\delta_{4.75}$ (H$_2$O) and a singlet at $\delta_{2.85}$ (CH$_3$-N$^+$). Acetone-$d_6$ (0.20 ml) was injected into the solution. One and a half hours after injection, the NMR spectrum of the resulting solution indicates conversion of some of the protonated amine to $N$-isopropylidene-1,2-dimethylhydrazinium ions - singlet at $\delta_{4.6}$ (H$_2$O), small singlet at $\delta_{3.70}$ (CH$_3$-N$^+$=C) and a singlet at $\delta_{2.70}$ (CH$_3$-CN), unreacted amine). Three days after injection of acetone-$d_6$ the NMR spectrum (Figure 19) shows a slightly bigger iminium ion peak and a
Fig. 18. 60 MHz PMR Spectrum of 1,2-Dimethylhydrazine Hydrochloride in D$_2$O.
Fig. 19. 60 MHz PMR Spectrum of a Solution Resulting from Injection of Acetone-d$_6$ into 1,2-Dimethylhydrazine Hydrochloride in D$_2$O; 3 Days after Injection.
Fig. 20. 60 MHz FMR Spectrum of a Solution Resulting from Injection of Acetone into 1,2-Dimethylhydrazine Hydrochloride in D$_2$O; 3 Days after Injection.
Fig. 21. 60 MHz PMR Spectrum of \( \text{H-Isopropylidene-1,2-dimethylhydrazinium Perchlorate} \) in \( \text{CD}_3\text{CN} \).
Fig. 22. 60 MHz EPR Spectrum of a Solution Resulting from Injection of 0.15 ml of D₂O into N-Isopropyldene-1,2-dimethylhydrazinium Perchlorate in CD₃CN; Five Minutes after Injection.
multiply at 62.1 due to acetone-d2. The CH3-N-N⁺=C peak is hidden under the larger 62.7 peak which is due to the unreacted ammonium ion. This is confirmed by the integration values.

The spectrum of a solution produced by injection of light acetone into 1,2-dimethylhydrazinium ion in D2O two hours after injection consisted of a singlet at 64.55 (H2O), a singlet at 62.70 (CH3-N, unreacted amine) and a large singlet at 62.1 (unreacted acetone). Three days after injection of acetone (Figure 20), the spectrum showed evidences of formation of the iminium ion - large singlet at 64.60 (H2O), small broadened singlet at 63.60 (CH3-N⁺=C), small singlet at 62.80 (CH3-N-N⁺=C), singlet at 62.70 (unreacted amine), large peak at 62.1 (exchanged acetone). The (CH3)2C=N⁺ peak is believed to be hidden under the very large acetone peak.

The spectrum of N-isopropylidene-1,2-dimethylhydrazinium perchlorate in CD3CN (Figure 21) consists of a 1-proton broadened quartet at 65.3 (HN-N⁺=C), a 3-proton broadened singlet at 65.45 (CH3-N⁺=C), a 3-proton doublet at 62.5 (CH3-NH-N⁺=C), a singlet at 62.85 (one of (CH3)2C=N⁺), a singlet at 62.70 (one of (CH3)2C=N⁺) and a small multiplet at 61.75 due to acetonitrile-d2. Five minutes after injection of 0.15 ml of D2O into the NMR tube (Figure 22), the spectrum indicates hydrolysis of the iminium ion to form acetone and deuteronated amine - a small broad peak at 63.85 (H2O), a small broad singlet at 63.5 (CH3-N-N⁺=C), a small singlet at 62.35 (one of (CH3)2C=N⁺), a small singlet at 62.25 (one of (CH3)2C=N⁺), a large
singlet at 82.55 (CH$_3$-N, deuteronated amine) and a large singlet at 81.95 (acetone). Fifteen minutes after injection of D$_2$O, the peaks at 82.25, 82.35, and 83.5 have decreased to about half their sizes 5 minutes after injection. Two days after, the same three peaks have decreased further to 1/4 their sizes 5 minutes after injection.

These results clearly show that acetone and 1,2-dimethylhydrazinium ions react to form N-isopropylidene-1,2-dimethylhydrazinium ions (equation 33) with an equilibrium constant much smaller than

$$\text{(CH}_3\text{)}_2\text{CO} + \text{CH}_3\text{NH}_2^+\text{NHCH}_3 \rightarrow \text{(CH}_3\text{)}_2\text{C}=\text{N}^+\text{NHCH}_3 \text{CH}_3 + \text{H}_2\text{O} \quad (33)$$

that between acetone and pyrazolidinium or isoxazolidinium ions and that the reaction is directly observable. The iminium ion hydrolyzes back to acetone and the protonated amine at a slow measurable rate which is unexpected based on the results of hydrolysis of N-isopropylidene-$\text{O,N}$-dimethylhydroxylammonium ions whose rate is too fast to measure.

b. UV

The spectrum of a 0.10 M 1,2-dimethylhydrazinium ions prepared by mixing equivalent amounts of the dihydrochloride and sodium hydroxide showed small absorbances ($< 0.05$) from 300 to 250 nm and a sharp rise at shorter wavelengths going off scale at 225 nm. With the same monoprotonated amine solution in both reference and sample cells, the absorbances from 300 to 230 cancel out and at shorter wavelengths,
the slit width is exceeded. Acetone solution was then injected into the solution to produce an initial acetone concentration of 0.01 M. Immediately after injection, the spectrum showed a steady rise from 350 nm to a maximum at 265 nm where it has an absorbance of 0.199 and a decrease at shorter wavelengths until the slit width is exceeded at 225 nm. About 5 minutes after injection, the absorbance increased slightly to 0.202 at the maximum. That part of the spectrum at wavelengths longer than 265 nm is almost superimposable on that of the same concentration of acetone, but at shorter wavelengths the absorbance of the acetone-amine salt mixture is higher. It appeared that the reaction can be best monitored at 240 nm where the absorbance of 0.01 M acetone solution is only half of the absorbance produced when 0.01 M acetone is allowed to react with 0.1 M mono-protonated amine.

With the wavelength set at 240 nm and the instrument zeroed with the same monoprotonated amine solution in both the sample and reference cells, the absorbance was recorded as a function of time after acetone was injected into amine salt solutions of different concentrations. The results are presented in Table 5.

The results indicate that there is more than one reaction occurring after acetone is injected into the monoprotonated amine solution. This was concluded from the fact that the absorbance does not level off to an equilibrium value at a time when it is expected to do so judging from its initial rate of increase. From the NMR
### TABLE 5

**ABSORBANCES AT DIFFERENT TIMES AFTER INJECTION OF ACETONE INTO 1,2-DIMETHYLDRAZINIUM ION SOLUTIONS**

<table>
<thead>
<tr>
<th></th>
<th>CH₃NH₂NHCH₃⁺ = 0.01 M</th>
<th>CH₃NH₂NHCH₃⁺ = 0.15 M</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>time (s)</td>
<td>absorbance</td>
</tr>
<tr>
<td>CH₂(NH₂)₂CO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>time (s) absorbance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>0.260</td>
<td>14</td>
</tr>
<tr>
<td>104</td>
<td>0.344</td>
<td>104</td>
</tr>
<tr>
<td>194</td>
<td>0.360</td>
<td>194</td>
</tr>
<tr>
<td>284</td>
<td>0.366</td>
<td>284</td>
</tr>
<tr>
<td>374</td>
<td>0.370</td>
<td>374</td>
</tr>
<tr>
<td>554</td>
<td>0.375</td>
<td>554</td>
</tr>
<tr>
<td>914</td>
<td>0.378</td>
<td>914</td>
</tr>
<tr>
<td>1364</td>
<td>0.380</td>
<td>1364</td>
</tr>
<tr>
<td>1994</td>
<td>0.385</td>
<td>1994</td>
</tr>
<tr>
<td>2714</td>
<td>0.392</td>
<td>2804</td>
</tr>
</tbody>
</table>

|                  | CH₃NH₂NHCH₃⁺ = 0.20 M | CH₃NH₂NHCH₃⁺ = 0.25 M |
|                  | (CH₂)₂CO               | (CH₂)₂CO               |
|                  | time (s) absorbance    | time (s) absorbance    |
| 14               | 0.310                  | 16                     | 0.310                  |
| 104              | 0.410                  | 106                    | 0.423                  |
| 194              | 0.528                  | 196                    | 0.571                  |
| 284              | 0.539                  | 286                    | 0.583                  |
| 374              | 0.541                  | 5 hrs                  | 1.12                   |
| 554              | 0.545                  | 5 hrs                  | 1.12                   |
| 914              | 0.551                  | + 1000 s               | 1.14                   |
| 1364             | 0.553                  |                         |                        |
| 1994             | 0.553                  |                         |                        |
| 2444             | 0.553                  |                         |                        |

---

*The 1000 seconds was measured accurately while the 5 hrs was not.*
results, the reaction which occurs at shorter periods of time is iminium ion formation. The NMR spectra do not show evidence for a second, slower reaction. Thus, it was thought that this second slower reaction produces a compound which is formed in insignificant amounts but whose extinction coefficient at 240 nm is very large.

To study the hydrolysis of the iminium ion, 10 microliters of a 1.064 M N-isopropylidene-1,2-dimethylhydrazinium perchlorate solution in acetonitrile was injected into 3 mL of water to produce an initial iminium ion concentration of 0.00353 M. The spectrum of the resulting solution, taken with water as reference, showed small (< 0.05) absorbances from 350 to 320 nm, a steady climb to a maximum at 265 nm with an absorbance of 1.12 at that wavelength, a decrease to a minimum of 0.20 at 222 nm, and another rise at lower wavelengths until the slit width limit is exceeded.

With the wavelength set at 275 nm, 10 microliters of the 1.064 M iminium perchlorate salt in acetonitrile were injected into 3 mL of water. The graph of absorbance as a function of time showed a decrease much like that of a first order reaction with an absorbance of 1.29 at 78 seconds after injection and levelling to an equilibrium value of 1.17 at around 250 seconds after injection.

Ten microliters of 1.064 M iminium perchlorate solution in acetonitrile was injected into 3 mL of 0.0999 M hydrochloric acid to produce an initial iminium ion concentration of 0.00353 M. The spectrum of the resulting solution showed small absorbances (<0.05)
from 350 to 320 nm, a steady rise from 320 to a maximum at 265 nm with an absorbance of 0.99 at that wavelength, a decrease to a minimum of 0.204 at 222 nm, and a climb at lower wavelengths until the slit width limit is exceeded.

With the wavelength set at 275 nm, the iminium perchlorate solution was injected into 3 ml of 0.0999 M hydrochloric acid to produce an initial iminium ion concentration of 0.00353 M. The absorbance decreased from 1.44 at 18.5 seconds after injection to an equilibrium value of 0.946 at around 300 seconds after injection.

Different amounts of the iminium perchlorate in acetonitrile solution were injected into 3 ml of 0.1 M formate buffer (half-protonated) to produce different initial concentrations of the iminium ion. Formate buffer was chosen to ensure that the hydrolysis would yield only acetone and the monoprotonated amine. The absorbances levelled to their equilibrium absorbances after about 5 minutes. The same formate buffer solution was used as reference. The results are shown in Table 6.

The results indicate that at equilibrium other compounds are present besides acetone and 1,2-dimethylhydrazinium ions. This may be due to some decomposition of the iminium perchlorate solution which produces unidentified compounds with very strong absorbances. This was concluded from the fact that the same solution kept two days longer produced higher equilibrium absorbances. This decomposition occurred despite storage of the solution under nitrogen at all
<table>
<thead>
<tr>
<th>Vol. of 1.064 M Im⁺ ClO₄⁻ in CH₃CN injected into 3.00 mls of formate buffer (microliters)</th>
<th>Initial Iminium Ion Conc. (M)</th>
<th>Equilibrium Absorbance</th>
<th>Absorbance of Acetone Equal to Initial Im⁺ Conc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.00</td>
<td>7.09 x 10⁻⁴</td>
<td>0.286</td>
<td>0.0110</td>
</tr>
<tr>
<td>3.00</td>
<td>1.06 x 10⁻³</td>
<td>0.400</td>
<td>0.0164</td>
</tr>
<tr>
<td>5.00</td>
<td>1.77 x 10⁻³</td>
<td>0.645</td>
<td>0.0274</td>
</tr>
<tr>
<td>8.00</td>
<td>2.84 x 10⁻³</td>
<td>1.10</td>
<td>0.0440</td>
</tr>
<tr>
<td>10.00</td>
<td>3.53 x 10⁻³</td>
<td>1.34</td>
<td>0.0547</td>
</tr>
<tr>
<td>11.00</td>
<td>3.89 x 10⁻³</td>
<td>1.98</td>
<td>0.0603</td>
</tr>
<tr>
<td>12.00</td>
<td>4.24 x 10⁻³</td>
<td>1.64</td>
<td>0.0657</td>
</tr>
<tr>
<td>14.00</td>
<td>4.94 x 10⁻³</td>
<td>2.58</td>
<td>0.0766</td>
</tr>
<tr>
<td>15.00</td>
<td>5.29 x 10⁻³</td>
<td>2.14</td>
<td>0.0820</td>
</tr>
</tbody>
</table>

*The iminium perchlorate solution in CH₃CN was kept two days longer than in the other cases.*
times. It is believed that this process is the same as that which produces large absorbances at a slower rate than iminium ion formation observed when acetone is added to a solution of 1,2-dimethyl-hydrazinium ions. Because of this, a kinetic study of the hydrolysis of the iminium ion was not undertaken.

D. Hydrolysis of N-Isopropylidenehyrazolidinium Ion

Table 7 shows the observed first order rate constants ($k_{obs}$) for solutions of different pH's and total buffer concentrations for the hydrolysis of the iminium ion to acetone and amine (eq. 34), measured

$$(\text{CH}_3)_2C=NN + H_2O \leftrightarrow (\text{CH}_3)_2CO + \text{H}_2N^+ \quad \text{eq. (34)}$$

by monitoring the disappearance of the iminium ion at its maximum at 235 nm. The rate constants were calculated from time-absorbance data pairs by a non-linear least squares analysis of eq. (5). The calculated parameters $A_1 + A_2$, which should be the absorbance at $t = 0$, and $A_2$, which should be the absorbance at $t = \infty$, are also shown. The averages of the rate constants for duplicate runs ($k_{ave}'s$) weighted according to the standard deviations of the $k_{obs}'s$ were calculated from eq. (35). The $k_{ave}'s$ for duplicate runs did not differ from each other by more than 3%.

$$k_{ave} = \frac{\sum_{i=1}^{k_{obs}} k_{obs,i}}{\sum_{i=1}^{k_{obs}} \text{Std. Dev.}_i} \quad \text{eq. (35)}$$
TABLE 7
RESULTS OF KINETIC STUDY OF HYDROLYSIS OF N-ISOPROPYLDENEFYRAZOLIDINUM ION IN AQUEOUS SOLUTION AT 35°

<table>
<thead>
<tr>
<th>pH</th>
<th>Buffer</th>
<th>Buffer Ratio</th>
<th>Ionic Strength</th>
<th>A1 + A2</th>
<th>A2</th>
<th>k_{obs} (s^{-1})</th>
<th>k_{ave} (s^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.700</td>
<td>0.300</td>
<td>0.300</td>
<td>0.849</td>
<td>0.008</td>
<td>248 + 2</td>
<td>2.57 x 10^{-2}</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.836</td>
<td>0.010</td>
<td>263 + 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.838</td>
<td>0.010</td>
<td>251 + 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.08</td>
<td>0.300</td>
<td>0.542</td>
<td>0.054</td>
<td>117 + 1</td>
<td>1.17 x 10^{-3}</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.552</td>
<td>0.006</td>
<td>117 + 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.38</td>
<td>0.300</td>
<td>0.543</td>
<td>0.012</td>
<td>64.8 + 0.1</td>
<td>6.46 x 10^{-3}</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.547</td>
<td>0.009</td>
<td>64.5 ± 0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.55</td>
<td>0.300</td>
<td>0.558</td>
<td>0.004</td>
<td>42.3 ± 0.2</td>
<td>4.21 x 10^{-3}</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.550</td>
<td>0.002</td>
<td>42.3 ± 0.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.908</td>
<td>0.004</td>
<td>41.8 ± 0.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.915</td>
<td>0.300</td>
<td>0.542</td>
<td>0.047</td>
<td>25.9 ± 0.8</td>
<td>2.52 x 10^{-3}</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.554</td>
<td>0.026</td>
<td>25.0 ± 0.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.52</td>
<td>0.1000</td>
<td>0.0901</td>
<td>9.11</td>
<td>0.300</td>
<td>0.554</td>
<td>0.002</td>
<td>10.4 ± 0.1</td>
</tr>
<tr>
<td>formate</td>
<td>0.00989</td>
<td>0.300</td>
<td>0.554</td>
<td>0.001</td>
<td>10.4 ± 0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.2723</td>
<td>9.85</td>
<td>0.300</td>
<td>0.536</td>
<td>0.016</td>
<td>10.6 ± 0.1</td>
<td>1.06 x 10^{-3}</td>
</tr>
<tr>
<td></td>
<td>0.02770</td>
<td>0.300</td>
<td>0.552</td>
<td>-0.001</td>
<td>10.6 ± 0.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.555</td>
<td>0.003</td>
<td>10.5 ± 0.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.53</td>
<td>0.09994</td>
<td>0.09189</td>
<td>11.4</td>
<td>0.300</td>
<td>0.542</td>
<td>0.003</td>
<td>6.93 ± 0.06</td>
</tr>
<tr>
<td>acetate</td>
<td>0.00805</td>
<td>0.300</td>
<td>0.549</td>
<td>0.007</td>
<td>6.95 ± 0.07</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 7 (continued)

<table>
<thead>
<tr>
<th>pH&lt;sub&gt;obs&lt;/sub&gt;</th>
<th>[Buffer]&lt;sub&gt;t&lt;/sub&gt; (M)</th>
<th>Buffer Ratio</th>
<th>Ionic Strength</th>
<th>A&lt;sub&gt;1&lt;/sub&gt; + A&lt;sub&gt;2&lt;/sub&gt;</th>
<th>A&lt;sub&gt;2&lt;/sub&gt;</th>
<th>10&lt;sup&gt;4&lt;/sup&gt;k&lt;sub&gt;obs&lt;/sub&gt;</th>
<th>k&lt;sub&gt;ave&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.51</td>
<td>0.3000 acetate</td>
<td>0.2762</td>
<td>0.300</td>
<td>0.550</td>
<td>0.012</td>
<td>7.30 ± 0.10</td>
<td>7.34 x 10&lt;sup&gt;-4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.02584</td>
<td>0.553</td>
<td>0.004</td>
<td></td>
<td>7.37 ± 0.09</td>
<td></td>
</tr>
<tr>
<td>4.78</td>
<td>0.04967 acetate</td>
<td>0.01887</td>
<td>0.300</td>
<td>0.551</td>
<td>0.028</td>
<td>7.35 ± 0.45</td>
<td>7.14 x 10&lt;sup&gt;-4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0508</td>
<td>0.548</td>
<td>0.012</td>
<td></td>
<td>7.13 ± 0.04</td>
<td></td>
</tr>
<tr>
<td>4.76</td>
<td>0.09934 acetate</td>
<td>0.03874</td>
<td>0.299</td>
<td>0.914</td>
<td>0.005</td>
<td>8.08 ± 0.20</td>
<td>8.08 x 10&lt;sup&gt;-4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.06060</td>
<td>0.561</td>
<td>0.013</td>
<td></td>
<td>8.08 ± 0.06</td>
<td></td>
</tr>
<tr>
<td>4.785</td>
<td>0.3000 acetate</td>
<td>0.1172</td>
<td>0.299</td>
<td>0.550</td>
<td>-0.027</td>
<td>10.4 ± 0.1</td>
<td>1.06 x 10&lt;sup&gt;-3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1828</td>
<td>0.534</td>
<td>-0.029</td>
<td></td>
<td>10.7 ± 0.1</td>
<td></td>
</tr>
<tr>
<td>6.41</td>
<td>0.1000 cacodylate</td>
<td>0.03543</td>
<td>0.301</td>
<td>0.901</td>
<td>0.014</td>
<td>15.4 ± 0.1</td>
<td>1.54 x 10&lt;sup&gt;-3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0646</td>
<td>0.550</td>
<td>0.013</td>
<td></td>
<td>15.5 ± 0.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.540</td>
<td>0.007</td>
<td></td>
<td>15.6 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>6.44</td>
<td>0.3000 cacodylate</td>
<td>0.1073</td>
<td>0.301</td>
<td>0.578</td>
<td>0.010</td>
<td>30.7 ± 0.2</td>
<td>3.07 x 10&lt;sup&gt;-3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.1927</td>
<td>0.560</td>
<td>0.011</td>
<td></td>
<td>30.6 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>7.36</td>
<td>0.1001 N-methyl-</td>
<td>0.05406</td>
<td>0.300</td>
<td>0.534</td>
<td>0.010</td>
<td>26.7 ± 0.2</td>
<td>2.65 x 10&lt;sup&gt;-3&lt;/sup&gt;</td>
</tr>
<tr>
<td>morpholine</td>
<td></td>
<td>0.04594</td>
<td>0.526</td>
<td>0.000</td>
<td></td>
<td>26.2 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>7.365</td>
<td>0.3003 N-methyl-</td>
<td>0.1622</td>
<td>0.300</td>
<td>0.567</td>
<td>0.023</td>
<td>29.5 ± 0.1</td>
<td>2.93 x 10&lt;sup&gt;-3&lt;/sup&gt;</td>
</tr>
<tr>
<td>morpholine</td>
<td></td>
<td>0.1361</td>
<td>0.529</td>
<td>0.016</td>
<td></td>
<td>28.6 ± 0.2</td>
<td></td>
</tr>
<tr>
<td>7.81</td>
<td>0.1001 N-methyl-</td>
<td>0.03044</td>
<td>0.300</td>
<td>0.529</td>
<td>0.014</td>
<td>60.7 ± 0.3</td>
<td>6.14 x 10&lt;sup&gt;-3&lt;/sup&gt;</td>
</tr>
<tr>
<td>morpholine</td>
<td></td>
<td>0.0697</td>
<td>0.551</td>
<td>0.018</td>
<td></td>
<td>62.3 ± 0.3</td>
<td></td>
</tr>
<tr>
<td>pH_{obs}</td>
<td>[Buffer]_t^{(M)}</td>
<td>Buffer ratio</td>
<td>Ionic Strength</td>
<td>(A_1 + A_2)</td>
<td>(A_2)</td>
<td>(10^2 k_{obs})</td>
<td>(k_{ave})</td>
</tr>
<tr>
<td>----------</td>
<td>-----------------</td>
<td>---------------</td>
<td>----------------</td>
<td>----------------</td>
<td>---------</td>
<td>---------------------</td>
<td>--------</td>
</tr>
<tr>
<td>7.815</td>
<td>0.3003</td>
<td>0.0921 = 0.442</td>
<td>0.300</td>
<td>0.521</td>
<td>0.009</td>
<td>62.6 ± 0.5</td>
<td>6.31 x 10^{-3}</td>
</tr>
<tr>
<td></td>
<td>N-methyl-Morpholine</td>
<td>0.2082</td>
<td></td>
<td>0.527</td>
<td>0.010</td>
<td>65.5 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>8.205</td>
<td>0.1001</td>
<td>0.01482 = 0.174</td>
<td>0.298</td>
<td>0.539</td>
<td>0.018</td>
<td>151 ± 2</td>
<td>1.42 x 10^{-2}</td>
</tr>
<tr>
<td></td>
<td>N-methyl-Morpholine</td>
<td>0.06528</td>
<td></td>
<td>0.523</td>
<td>0.030</td>
<td>140 ± 1</td>
<td></td>
</tr>
<tr>
<td>8.22</td>
<td>0.3003</td>
<td>0.04405 = 0.172</td>
<td>0.299</td>
<td>0.532</td>
<td>0.010</td>
<td>174 ± 1</td>
<td>1.47 x 10^{-2}</td>
</tr>
<tr>
<td></td>
<td>N-methyl-Morpholine</td>
<td>0.2562</td>
<td></td>
<td>0.525</td>
<td>0.009</td>
<td>145 ± 1</td>
<td></td>
</tr>
<tr>
<td>9.01</td>
<td>0.1052</td>
<td>0.0516 = 1.00</td>
<td>0.302</td>
<td>1.19</td>
<td>0.018</td>
<td>1160 ± 80</td>
<td>1.16 x 10^{-1}</td>
</tr>
<tr>
<td></td>
<td>borate</td>
<td>0.0516</td>
<td></td>
<td>1.52</td>
<td>0.030</td>
<td>1250 ± 30</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.45</td>
<td>0.027</td>
<td>1200 ± 20</td>
<td></td>
</tr>
<tr>
<td>8.91</td>
<td>0.0499</td>
<td>0.0249 = 1.00</td>
<td>0.301</td>
<td>0.716</td>
<td>0.024</td>
<td>710 ± 8</td>
<td>7.04 x 10^{-2}</td>
</tr>
<tr>
<td></td>
<td>borate</td>
<td>0.0249</td>
<td></td>
<td>0.859</td>
<td>0.028</td>
<td>697 ± 6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.919</td>
<td>0.026</td>
<td>713 ± 9</td>
<td></td>
</tr>
<tr>
<td>3.205</td>
<td>0.04998</td>
<td>0.05584 = 2.46</td>
<td>0.300</td>
<td>0.517</td>
<td>0.026</td>
<td>7.56 ± 0.18</td>
<td>7.31 x 10^{-4}</td>
</tr>
<tr>
<td></td>
<td>formate</td>
<td>0.01858</td>
<td></td>
<td>0.537</td>
<td>0.005</td>
<td>7.18 ± 0.13</td>
<td></td>
</tr>
<tr>
<td>3.10</td>
<td>0.09996</td>
<td>0.07299 = 2.59</td>
<td>0.300</td>
<td>0.524</td>
<td>0.010</td>
<td>7.76 ± 0.09</td>
<td>7.62 x 10^{-4}</td>
</tr>
<tr>
<td></td>
<td>formate</td>
<td>0.02787</td>
<td></td>
<td>0.522</td>
<td>0.009</td>
<td>7.55 ± 0.07</td>
<td></td>
</tr>
<tr>
<td>3.10</td>
<td>0.2999</td>
<td>0.2155 = 2.55</td>
<td>0.300</td>
<td>0.542</td>
<td>0.008</td>
<td>8.48 ± 0.07</td>
<td>8.40 x 10^{-4}</td>
</tr>
<tr>
<td></td>
<td>formate</td>
<td>0.0844</td>
<td></td>
<td>0.524</td>
<td>0.005</td>
<td>8.24 ± 0.10</td>
<td></td>
</tr>
<tr>
<td>5.575</td>
<td>0.1000</td>
<td>0.07787 = 3.52</td>
<td>0.300</td>
<td>0.525</td>
<td>0.029</td>
<td>9.04 ± 0.06</td>
<td>9.06 x 10^{-4}</td>
</tr>
<tr>
<td></td>
<td>cacodylate</td>
<td>0.02235</td>
<td></td>
<td>0.563</td>
<td>0.043</td>
<td>9.32 ± 0.28</td>
<td></td>
</tr>
<tr>
<td>5.575</td>
<td>0.5000</td>
<td>0.2335 = 3.51</td>
<td>0.300</td>
<td>0.530</td>
<td>0.031</td>
<td>14.8 ± 0.2</td>
<td>1.47 x 10^{-3}</td>
</tr>
</tbody>
</table>
Table 7 (continued)

<table>
<thead>
<tr>
<th>pH</th>
<th>Buffer</th>
<th>Buffer Ratio</th>
<th>Ionic Strength</th>
<th>A1 + A2</th>
<th>A2</th>
<th>10^4 k_{obs}</th>
<th>k_{ave}</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.59</td>
<td>0.5000</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>cacodylate</td>
<td>0.3900 0.1100</td>
<td>= 3.55</td>
<td>0.300</td>
<td>0.525</td>
<td>0.030</td>
<td>20.2 ± 0.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.98 x 10^{-3}</td>
</tr>
<tr>
<td>6.39</td>
<td>0.05000</td>
<td>0.01820 0.03198</td>
<td>= 0.563</td>
<td>0.300</td>
<td>0.557</td>
<td>0.029</td>
<td>11.7 ± 0.1</td>
</tr>
<tr>
<td></td>
<td>cacodylate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.18 x 10^{-3}</td>
</tr>
<tr>
<td>6.425</td>
<td>0.2000</td>
<td>0.07206 0.1279</td>
<td>= 0.563</td>
<td>0.300</td>
<td>0.589</td>
<td>0.064</td>
<td>22.5 ± 0.3</td>
</tr>
<tr>
<td></td>
<td>cacodylate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.26 x 10^{-3}</td>
</tr>
<tr>
<td>6.475</td>
<td>0.4000</td>
<td>0.1429 0.2571</td>
<td>= 0.556</td>
<td>0.301</td>
<td>0.553</td>
<td>0.021</td>
<td>39.6 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>cacodylate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.92 x 10^{-3}</td>
</tr>
<tr>
<td>7.395</td>
<td>0.05005</td>
<td>0.02723 0.02282</td>
<td>= 1.19</td>
<td>0.299</td>
<td>0.545</td>
<td>0.036</td>
<td>26.3 ± 0.2</td>
</tr>
<tr>
<td></td>
<td>N-methyl-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.60 x 10^{-3}</td>
</tr>
<tr>
<td></td>
<td>morpholine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.815</td>
<td>0.05005</td>
<td>0.01522 0.03983</td>
<td>= 0.382</td>
<td>0.299</td>
<td>0.550</td>
<td>0.043</td>
<td>59.1 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>N-methyl-</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.94 x 10^{-3}</td>
</tr>
<tr>
<td></td>
<td>morpholine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8.165</td>
<td>0.04988</td>
<td>0.04160 0.00828</td>
<td>= 5.02</td>
<td>0.301</td>
<td>0.562</td>
<td>0.038</td>
<td>122 ± 1</td>
</tr>
<tr>
<td></td>
<td>borate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.26 x 10^{-2}</td>
</tr>
<tr>
<td>8.12</td>
<td>0.1000</td>
<td>0.08330 0.01668</td>
<td>= 4.99</td>
<td>0.300</td>
<td>0.532</td>
<td>0.036</td>
<td>125 ± 1</td>
</tr>
<tr>
<td></td>
<td>borate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.22 x 10^{-2}</td>
</tr>
<tr>
<td>7.97</td>
<td>0.2003</td>
<td>0.1666 0.05337</td>
<td>= 4.99</td>
<td>0.300</td>
<td>0.539</td>
<td>0.037</td>
<td>106 ± 1</td>
</tr>
<tr>
<td></td>
<td>borate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.07 x 10^{-2}</td>
</tr>
</tbody>
</table>
When the rate constants for reactions at the same buffer ratio were plotted against the total buffer concentration, straight lines were obtained indicating either general acid- or base-catalysis. It appeared that the latter is more likely because the slope of the line is greater when the ratio $[A^-]/[HA]$ is higher. These lines were extrapolated to zero buffer concentration and the intercepts were taken as the rate constants for the reaction if there were no general acid-or base-catalysis, that is, if the only catalysts for the reaction were protons and hydroxide ions. The log of these extrapolated rate constants were plotted against pH and the points seem to follow a tub-shaped curve. These 13 extrapolated rate constants were treated in a nonlinear least squares analysis of eq. (36) in a program

$$\log k_{\text{extrapolated}} = \log (k_w + k_h[H^+] + k_{oh}[OH^-])$$

written by J. Zeigler. The analysis resulted in values of 6.48 x $10^{-4}s^{-1}$, 0.0935 $M^{-1}s^{-1}$ and 27.7 $M^{-1}s^{-1}$ for $k_w$, $k_h$ and $k_{oh}$, respectively, with standard deviations of 2.4%, 2.7% and 2.8%. A plot of $\log k_{\text{extrapolated}}$ against pH is shown in Figure 23.

To obtain the catalytic constants for all the general acids and bases, the 36 rate constants were treated in a 13-parameter linear least squares analysis of eq. (37), minimizing the sum of the squares of the fractional deviations. The resulting $k_a$'s for formic acid,

$$k_{\text{obs}} = k_w + \sum a_i[H_{B_i}] + \sum b_i[B_i]$$

(37)
Fig. 23. Log of Rate Constant for the Hydrolysis of N-Isopropylidenehyrazolidinium Ions in Water at 35°C Extrapolated to Zero Buffer Concentration vs. pH
N-methylmorpholinium ion and boric acid were small negative numbers and that for acetic acid was as large as its standard deviation. The constant for cacodylate ion was 25 times the value for cacodylic acid. It is evident from these results that general acid catalysis is negligible. Thus, the $k_a$'s were all set equal to zero and the rate constants were treated in an 8-parameter linear least squares analysis (Program 4) which includes only catalysis by hydroxide, hydronium and the general bases and an uncatalyzed term which is a first order rate constant. The calculated rate constants and their standard deviations are shown in Table 8.

### TABLE 8

**CATALYTIC CONSTANTS FOR THE HYDROLYSIS OF N-ISOPROPYLDENE-PYRAZOLIDINIUM ION IN WATER AT 35°**

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$k \left( M^{-1} s^{-1} \right)$</th>
<th>Std. Dev. ( (M^{-1} s^{-1}) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCO$_2^-$</td>
<td>$12 \times 10^{-4}$</td>
<td>$7 \times 10^{-4}$</td>
</tr>
<tr>
<td>CH$_3$CO$_2^-$</td>
<td>$24 \times 10^{-4}$</td>
<td>$4 \times 10^{-4}$</td>
</tr>
<tr>
<td>(CH$_3$)$_2$AsO$_2^-$</td>
<td>$114 \times 10^{-4}$</td>
<td>$5 \times 10^{-4}$</td>
</tr>
<tr>
<td>Pyrazolidine</td>
<td>$102 \times 10^{-4}$</td>
<td>$43 \times 10^{-4}$</td>
</tr>
<tr>
<td>N-methylmorpholine</td>
<td>$25 \times 10^{-4}$</td>
<td>$12 \times 10^{-4}$</td>
</tr>
<tr>
<td>Borate ion</td>
<td>$1470 \times 10^{-4}$</td>
<td>$380 \times 10^{-4}$</td>
</tr>
<tr>
<td>OH$^-$</td>
<td>2740</td>
<td>84</td>
</tr>
<tr>
<td>H$^+$</td>
<td>$935 \times 10^{-4}$</td>
<td>$27 \times 10^{-4}$</td>
</tr>
<tr>
<td>None</td>
<td>$6.4 \times 10^{-4}$</td>
<td>$0.2 \times 10^{-4}$</td>
</tr>
</tbody>
</table>

*This value was obtained from study of the kinetics of iminium ion formation.

b. This refers to $k_w$ whose dimensions are $s^{-1}$. 
The rates of the reaction in solutions more acidic or more basic than the ones used to obtain the rate constants in Table 7 are too fast to measure. For example, injection of the iminium ion solution into a solution of pH 11.8 produced the expected equilibrium absorbance immediately after injection and no change was observed afterwards.

The log of the catalytic constants for the general bases were plotted against the pK's of their conjugate acids. The points for the four oxy-bases - formate, acetate, cacodylate and borate - form a good straight line (Figure 24) with a slope equal to 0.386 and an intercept equal to -4.4. The point for N-methylmorpholine and pyrazolidine lies 0.31 and 0.36 log units, respectively, below the line at their pK's. This is not unusual because the Brønsted relationship is known to be obeyed only for structurally related bases. Nevertheless, it is still somewhat surprising that the point for borate catalysis should not show any deviation from the line formed by the other oxy-bases because it is known that borate buffers cause problems due to polymerization and the fact that boric acid undergo ionization predominantly by addition of hydroxide ions, rather than by the loss of a proton.

E. Acetone - Pyrazolidinium Ion Reaction

The results of the kinetic study are shown in Table 9. For the reaction described in eq. (37), since the initial concentration of pyrazolidinium ions is at least 20 times that of acetone, the
Fig. 24. Log of General Base Catalysis Constant for the Hydrolysis of N-Isopropylidenehyrazolidinium Ions in Water at 35° vs. pK of the Conjugate Acids of General Bases
### Table 9

**RESULTS OF KINETIC STUDY OF IMINUM ION FORMATION BETWEEN ACETONE AND PYRAZOLIDINUM IONS**

<table>
<thead>
<tr>
<th>pH$_{obs}$</th>
<th>[Am]$_t$ (M)</th>
<th>[Ac]$_o$ x 10$^3$</th>
<th>Buffer$_t$ (M)</th>
<th>Ionic Strength (M)</th>
<th>Cell Thickness (cm)</th>
<th>A$_2$</th>
<th>$k_{obs}$ (s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.765</td>
<td>0.100</td>
<td>4.95</td>
<td>0.200 HCL</td>
<td>0.300</td>
<td>0.1</td>
<td>1.39</td>
<td>2.45 x 10$^{-2}$</td>
</tr>
<tr>
<td>0.765</td>
<td>0.100</td>
<td>4.95</td>
<td>0.200 HCL</td>
<td>0.300</td>
<td>0.1</td>
<td>1.34</td>
<td>2.26 x 10$^{-2}$</td>
</tr>
<tr>
<td>1.04</td>
<td>0.103</td>
<td>0.666</td>
<td>0.100 HCL</td>
<td>0.303</td>
<td>1.0</td>
<td>1.73</td>
<td>3.55 x 10$^{-2}$</td>
</tr>
<tr>
<td>1.04</td>
<td>0.103</td>
<td>0.666</td>
<td>0.100 HCL</td>
<td>0.303</td>
<td>1.0</td>
<td>1.72</td>
<td>2.27 x 10$^{-2}$</td>
</tr>
<tr>
<td>1.04</td>
<td>0.199</td>
<td>0.666</td>
<td>0.100 HCL</td>
<td>0.299</td>
<td>1.0</td>
<td>2.10</td>
<td>3.17 x 10$^{-2}$</td>
</tr>
<tr>
<td>1.04</td>
<td>0.199</td>
<td>0.666</td>
<td>0.100 HCL</td>
<td>0.299</td>
<td>1.0</td>
<td>1.77</td>
<td>3.17 x 10$^{-2}$</td>
</tr>
<tr>
<td>1.53</td>
<td>0.101</td>
<td>4.95</td>
<td>0.0315 HCL</td>
<td>0.302</td>
<td>0.1</td>
<td>1.23</td>
<td>7.97 x 10$^{-3}$</td>
</tr>
<tr>
<td>1.53</td>
<td>0.101</td>
<td>4.95</td>
<td>0.0315 HCL</td>
<td>0.302</td>
<td>0.1</td>
<td>1.26</td>
<td>7.99 x 10$^{-3}$</td>
</tr>
<tr>
<td>1.87</td>
<td>0.102</td>
<td>0.666</td>
<td>0.0142 HCL</td>
<td>0.301</td>
<td>1.0</td>
<td>1.69</td>
<td>4.45 x 10$^{-3}$</td>
</tr>
<tr>
<td>1.87</td>
<td>0.102</td>
<td>0.666</td>
<td>0.0142 HCL</td>
<td>0.301</td>
<td>1.0</td>
<td>1.78</td>
<td>4.21 x 10$^{-3}$</td>
</tr>
<tr>
<td>3.55</td>
<td>0.0997</td>
<td>4.95</td>
<td>0.100 acetate</td>
<td>0.132</td>
<td>0.1</td>
<td>1.21</td>
<td>6.2 x 10$^{-3}$</td>
</tr>
<tr>
<td>3.55</td>
<td>0.0997</td>
<td>4.95</td>
<td>0.100 acetate</td>
<td>0.132</td>
<td>0.1</td>
<td>1.21</td>
<td>1.63 x 10$^{-3}$</td>
</tr>
<tr>
<td>3.55</td>
<td>0.0997</td>
<td>4.95</td>
<td>0.100 acetate</td>
<td>0.132</td>
<td>0.1</td>
<td>1.23</td>
<td>1.65 x 10$^{-3}$</td>
</tr>
<tr>
<td>3.51</td>
<td>0.0754</td>
<td>0.666</td>
<td>0.298 acetate</td>
<td>0.272</td>
<td>1.0</td>
<td>1.43</td>
<td>1.51 x 10$^{-3}$</td>
</tr>
<tr>
<td>4.805</td>
<td>0.100</td>
<td>4.95</td>
<td>0.150 acetate</td>
<td>0.250</td>
<td>0.1</td>
<td>0.991</td>
<td>3.59 x 10$^{-3}$</td>
</tr>
<tr>
<td>4.805</td>
<td>0.100</td>
<td>4.95</td>
<td>0.150 acetate</td>
<td>0.250</td>
<td>0.1</td>
<td>1.18</td>
<td>3.48 x 10$^{-3}$</td>
</tr>
<tr>
<td>6.37</td>
<td>0.100</td>
<td>4.95</td>
<td>0.300</td>
<td>0.1</td>
<td>1.16</td>
<td>2.13</td>
<td>10$^{-3}$</td>
</tr>
</tbody>
</table>
Table 9 (continued)

<table>
<thead>
<tr>
<th>pH\textsuperscript{obs}</th>
<th>[Am]\textsubscript{t}</th>
<th>[Ac]\textsubscript{0} x 10\textsuperscript{3}</th>
<th>Ionic Strength</th>
<th>Cell Thickness</th>
<th>A\textsubscript{2}</th>
<th>k\textsubscript{obs}</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.37</td>
<td>0.100</td>
<td>4.95</td>
<td>0.300</td>
<td>0.1</td>
<td>1.17</td>
<td>2.22 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>6.37</td>
<td>0.100</td>
<td>4.95</td>
<td>0.300</td>
<td>0.1</td>
<td>1.17</td>
<td>2.22 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>7.365</td>
<td>0.0992</td>
<td>4.95</td>
<td>0.299</td>
<td>0.1</td>
<td>0.774</td>
<td>4.53 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>7.365</td>
<td>0.0992</td>
<td>4.95</td>
<td>0.299</td>
<td>0.1</td>
<td>0.804</td>
<td>4.37 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>7.365</td>
<td>0.0992</td>
<td>4.95</td>
<td>0.299</td>
<td>0.1</td>
<td>0.771</td>
<td>4.30 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>7.92</td>
<td>0.0990</td>
<td>0.666</td>
<td>0.329</td>
<td>1.0</td>
<td>0.626</td>
<td>9.17 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>7.92</td>
<td>0.0990</td>
<td>0.666</td>
<td>0.329</td>
<td>1.0</td>
<td>0.646</td>
<td>8.13 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>8.56</td>
<td>0.0991</td>
<td>0.666</td>
<td>0.299</td>
<td>1.0</td>
<td>0.109</td>
<td>3.66 x 10\textsuperscript{-2}</td>
</tr>
<tr>
<td>8.56</td>
<td>0.0991</td>
<td>0.666</td>
<td>0.299</td>
<td>1.0</td>
<td>0.109</td>
<td>3.62 x 10\textsuperscript{-2}</td>
</tr>
<tr>
<td>0.640</td>
<td>0.0495</td>
<td>0.201</td>
<td>0.285 HCl</td>
<td>0.333</td>
<td>1.0</td>
<td>0.345 \textsuperscript{a} \textsuperscript{b}</td>
</tr>
<tr>
<td>0.640</td>
<td>0.0495</td>
<td>0.201</td>
<td>0.285 HCl</td>
<td>0.333</td>
<td>1.0</td>
<td>0.338 \textsuperscript{a} \textsuperscript{b}</td>
</tr>
<tr>
<td>4.74</td>
<td>0.0505</td>
<td>0.201</td>
<td>0.0993 acetate</td>
<td>0.300</td>
<td>1.0</td>
<td>0.327 \textsuperscript{a} \textsuperscript{b}</td>
</tr>
<tr>
<td>4.74</td>
<td>0.0505</td>
<td>0.201</td>
<td>0.0993 acetate</td>
<td>0.300</td>
<td>1.0</td>
<td>0.336 \textsuperscript{a} \textsuperscript{b}</td>
</tr>
<tr>
<td>6.30</td>
<td>0.0505</td>
<td>0.201</td>
<td>0.300</td>
<td>1.0</td>
<td>0.323</td>
<td>1.54 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>6.30</td>
<td>0.0505</td>
<td>0.201</td>
<td>0.300</td>
<td>1.0</td>
<td>0.316</td>
<td>1.54 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>8.06</td>
<td>0.0504</td>
<td>0.201</td>
<td>0.300</td>
<td>1.0</td>
<td>0.0801</td>
<td>9.73 x 10\textsuperscript{-3}</td>
</tr>
<tr>
<td>8.06</td>
<td>0.0504</td>
<td>0.201</td>
<td>0.300</td>
<td>1.0</td>
<td>0.0826</td>
<td>1.02 x 10\textsuperscript{-2}</td>
</tr>
</tbody>
</table>

\textsuperscript{a} In water at 35°
pyrazolidinium ion concentration \([\text{AmH}^+]\) is assumed to remain constant throughout the reaction. Because of the position of equilibrium, acetone does not get used up completely at any time during the reaction.

\[
\text{Ac} + \text{AmH}^+ \xrightarrow{k_f \to k_h} \text{Im}^+ + \text{H}_2\text{O} \tag{38}
\]

The rate of formation of the iminium ion is expressed in eq. (39).

\[
\frac{d[\text{Im}^+]}{dt} = k_f [\text{Ac}][\text{AmH}^+] - k_h [\text{Im}^+] \tag{39}
\]

The integrated rate law for this differential equation, assuming \([\text{Im}^+] = [\text{Ac}]_0 - [\text{Ac}]\) is equation (40).

\[
[\text{Im}^+] = \frac{k_f [\text{AmH}^+][\text{Ac}]_0}{k_f [\text{AmH}^+] + k_h} e^{-(k_f [\text{AmH}^+] + k_h)t} + [\text{Ac}]_0 - \frac{k_h [\text{Ac}]_0}{k_f [\text{AmH}^+] + k_h} \tag{40}
\]

This means that the \(k_{\text{obs}}\) calculated by the Sachs program (eq. 6) is the sum of the pseudo-first order rate constant for iminium ion formation and the first order rate constant for hydrolysis.

\[
k_{\text{obs}} = k_f [\text{AmH}^+] + k_h \tag{41}
\]

The equilibrium constant for iminium ion formation, defined in eq. (42), is also equal to \(k_f / k_h\). The observed first order rate constant

\[
K = \frac{[\text{Im}^+]_{\text{eq}}}{[\text{AmH}^+]_{\text{eq}} [\text{Ac}]_{\text{eq}}} \tag{42}
\]
$k_{\text{obs}}$ can then be expressed as a function of the hydrolysis rate constant and the equilibrium constant.

$$\text{obs} = k_k \text{[AmH}^+) + k_h$$

(43)

The pyrazolidinium ion concentration can be expressed as a function of the total amine concentration and the hydronium ion concentration.

$$\text{[AmH}^+) = \frac{[\text{Am}]_t[H^+]}{K_{\text{AmH}^+} + [H^+]$$

(44)

In eq. (44) $K_{\text{AmH}^+}$ is the dissociation constant for pyrazolidinium ions, equal to $10^{-7.25}$ at $35^\circ$. Combination of eq. (43) and eq. (44) results in eq. (45).

$$k_{\text{obs}} = \frac{k[\text{Am}]_t[H^+]}{K_{\text{AmH}^+} + [H^+] + k_h$$

(45)

However, it was thought that, since free pyrazolidine is a base, it should be capable of catalyzing both iminium ion formation and hydrolysis. Since the forward reaction (acetone + pyrazolidinium ions) occurred in the presence of large amounts of pyrazolidine, especially in the pH range 6.4 - 8.5, a term $k_{\text{PYRZN}}$ should be added to $k_h$ to account for the contribution of general base catalysis by free pyrazolidine on the rate of hydrolysis. Thus eq. (46) should be more appropriate than eq. (45).
A nonlinear least squares analysis was performed on eq. (46) using the 29 observed rate constants in Table 9 with weighting equal to $1/(k_{\text{obs}})^2$. The value of $k_h$ for a given pH was calculated from eq. 36 determined from a kinetic study of the hydrolysis of the iminium ion. The analysis gave a value of $9.33 \, \text{M}^{-1}$ for $K$ and $0.011 \, \text{M}^{-1}$ for $k_{\text{pyrzn}}$ with standard deviations of $6.1\%$ and $3.8\%$, respectively. This general base catalytic constant was included in the Brønsted plot in Figure 24.

In the hydrolysis reaction, the values $A_1 + A_2$ in Table 7, calculated from the Sachs program, should be the absorbance of the iminium ion at $t=0$. These values divided by the initial concentration of the injected $N$-isopropylidenehydrazolium ion, give the extinction coefficient of the ion at 235 nm. The average of 25 kinetic runs was $5.45 \times 10^3 \, \text{M}^{-1}\text{cm}^{-1}$. From the results of the iminium ion formation kinetics (Table 9), the value of $A_2$ which should be the absorbances at equilibrium and the concentrations of the iminium ion at equilibrium, calculated from the equilibrium constant ($9.33 \, \text{M}^{-1}$) should give the extinction coefficient of the ion at 235 nm. The average from 31 kinetic runs was $5.26 \times 10^3 \, \text{M}^{-1}\text{cm}^{-1}$.

$$k_{\text{obs}} = \frac{K [A_m]_t [H^+]}{K_{AmH^+} + [H^+]} + 1 \left( k_h + k_{\text{pyrzn}}[^{\text{PYRZN}}] \right)$$

(46)
F. Determination of Equilibrium Constants for Iminium Ion Formation by Measurement of UV Equilibrium Absorbances

1. Acetone and Isoxazolidinium Ions

Table 10 shows the absorbances at 275 nm of solutions of acetone of different concentrations. The plot of absorbance against concentration gives an excellent straight line with intercept equal to 0.0024 and slope equal to 15.5 which is the extinction coefficient of acetone at 275 nm with dimensions of $M^{-1}cm^{-1}$.

<table>
<thead>
<tr>
<th>[Ac] (M)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.00995</td>
<td>0.156</td>
</tr>
<tr>
<td>0.0198</td>
<td>0.306</td>
</tr>
<tr>
<td>0.328</td>
<td>0.513</td>
</tr>
<tr>
<td>0.0456</td>
<td>0.712</td>
</tr>
<tr>
<td>0.0645</td>
<td>0.998</td>
</tr>
</tbody>
</table>

Table 11 shows the equilibrium absorbances of solutions resulting from injection of a constant amount of acetone into solutions of isoxazolidinium bromide of varying concentrations.

Since the absorbance of the protonated amine at 275 nm is very low, and since the same amine solution was placed in both the
<table>
<thead>
<tr>
<th>Initial Conc. of Isoxazolidinium Ions (M)</th>
<th>Equilibrium Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0299</td>
<td>0.366</td>
</tr>
<tr>
<td>0.0299</td>
<td>0.366</td>
</tr>
<tr>
<td>0.0498</td>
<td>0.338</td>
</tr>
<tr>
<td>0.0498</td>
<td>0.334</td>
</tr>
<tr>
<td>0.0748</td>
<td>0.290</td>
</tr>
<tr>
<td>0.0748</td>
<td>0.295</td>
</tr>
<tr>
<td>0.0997</td>
<td>0.270</td>
</tr>
<tr>
<td>0.0997</td>
<td>0.266</td>
</tr>
<tr>
<td>0.150</td>
<td>0.218</td>
</tr>
<tr>
<td>0.150</td>
<td>0.215</td>
</tr>
<tr>
<td>0.199</td>
<td>0.185</td>
</tr>
<tr>
<td>0.199</td>
<td>0.180</td>
</tr>
<tr>
<td>0.249</td>
<td>0.158</td>
</tr>
<tr>
<td>0.249</td>
<td>0.156</td>
</tr>
<tr>
<td>0.299</td>
<td>0.141</td>
</tr>
<tr>
<td>0.399</td>
<td>0.109</td>
</tr>
<tr>
<td>0.399</td>
<td>0.106</td>
</tr>
<tr>
<td>0.498</td>
<td>0.0895</td>
</tr>
<tr>
<td>0.498</td>
<td>0.0905</td>
</tr>
</tbody>
</table>
reference and sample cells, the change in absorbance due to decrease in the amine concentration can be considered negligible. Thus, the absorbance at equilibrium is due only to acetone and the iminium ion.

\[ \text{Abs} = [\text{Ac}]_{\text{eq}} e_{\text{Ac}} + [\text{Im}^+]_{\text{eq}} e_{\text{Im}} \quad (47) \]

\[ \text{Abs} = [\text{Ac}]_{\text{eq}} e_{\text{Ac}} + ([\text{Ac}]_0 - [\text{Ac}]_{\text{eq}}) e_{\text{Im}} \quad (48) \]

The equilibrium constant for iminium ion formation \( K \) is defined as follows.

\[ K = \frac{[\text{Im}]_{\text{eq}}}{[\text{Ac}]_{\text{eq}}[\text{AmH}^+]_{\text{eq}}} = \frac{[\text{Ac}]_0 - [\text{Ac}]_{\text{eq}}}{([\text{AmH}^+]_0 - [\text{Ac}]_0 + [\text{Ac}]_{\text{eq}}) [\text{Ac}]_{\text{eq}}} \quad (49) \]

The concentration of acetone at equilibrium can be expressed in terms of the equilibrium constant.

\[ [\text{Ac}]_{\text{eq}} = \frac{-(K[\text{AmH}^+]_0 - K[\text{Ac}]_0 + 1) \pm \sqrt{(K[\text{AmH}^+]_0 - K[\text{Ac}]_0 + 1)^2 + 4K[\text{Ac}]_0}}{2K} \quad (50) \]

Only the negative sign on the square root would give physically plausible results. Combining eqs. (48) and (50), an equation is obtained which expresses the equilibrium absorbance as a function of the initial protonated amine concentration \([\text{AmH}^+]_0\), the equilibrium constant \( K \), the initial acetone concentration \([\text{Ac}]_0\), the extinction coefficient of the iminium ion \( e_{\text{Im}} \) and the extinction coefficient of acetone at 275 nm.
Abs = $[\text{Ac}]_0 \varepsilon_{\text{Im}} - \frac{(\varepsilon_{\text{Ac}} - \varepsilon_{\text{Im}})(K[A\text{mH}^+]_0 - K[\text{Ac}]_0 + 1)}{2K}$

\[ + \frac{(\varepsilon_{\text{Ac}} - \varepsilon_{\text{Im}})(\sqrt{(K[A\text{mH}^+]_0 - K[\text{Ac}]_0 + 1)^2 + 4[\text{Ac}]_0})}{2K} \] (51)

In eq. (51), only $K$ and $\varepsilon_{\text{Im}}$ are unknown. A nonlinear least squares analysis was performed on the 19 experimentally determined values of Abs with unit weighting using Program 6a (Appendix). The analysis gave fairly good results with no more than 4% difference between observed and calculated equilibrium absorbances. The calculated values, together with their standard deviations are shown below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K$</td>
<td>8.96 M$^{-1}$</td>
<td>0.364 M$^{-1}$</td>
</tr>
<tr>
<td>$\varepsilon_{\text{Im}}$</td>
<td>0.217 M$^{-1}$cm$^{-1}$</td>
<td>0.215 M$^{-1}$cm$^{-1}$</td>
</tr>
</tbody>
</table>

The experimental points and the calculated function is shown in Figure 25.

As suspected, the extinction coefficient of the iminium ion at 275 nm is very small compared to that of acetone. Because of its small magnitude, it could not be accurately determined, as seen from the large standard deviation.

2. Acetone and $O,N$-Dimethylhydroxylammonium Ions

Table 12 shows the equilibrium absorbances of solutions resulting from injection of a constant amount of acetone into
Fig. 25. Equilibrium Absorbance of Solution Resulting from Injection of Acetone to Produce 0.0297 M Initial Acetone Concentration into Isoxazolidinium Bromide Solution vs. the Initial Concentration of the Amine Salt
TABLE 12

EQUILIBRIUM ABSORBANCES AT 275 nm OF SOLUTIONS RESULTING FROM
ADDITION OF A CONSTANT AMOUNT OF ACETONE INTO O,N-DIMETHYL-
HYDROXYLAMINE HYDROCHLORIDE SOLUTIONS AT 35\degree C

\[ [\text{Ac}]_0 = 0.01980 \text{ M} \]

<table>
<thead>
<tr>
<th>([\text{ONHX}^+]_0)</th>
<th>Equilibrium Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.09844</td>
<td>0.304</td>
</tr>
<tr>
<td>0.09844</td>
<td>0.304</td>
</tr>
<tr>
<td>0.1969</td>
<td>0.302</td>
</tr>
<tr>
<td>0.1969</td>
<td>0.302</td>
</tr>
<tr>
<td>0.2953</td>
<td>0.298</td>
</tr>
<tr>
<td>0.3937</td>
<td>0.295</td>
</tr>
<tr>
<td>0.3937</td>
<td>0.296</td>
</tr>
<tr>
<td>0.4922</td>
<td>0.292</td>
</tr>
<tr>
<td>0.4922</td>
<td>0.294</td>
</tr>
<tr>
<td>0.5906</td>
<td>0.288</td>
</tr>
<tr>
<td>0.5906</td>
<td>0.291</td>
</tr>
<tr>
<td>0.7854</td>
<td>0.282</td>
</tr>
<tr>
<td>0.7854</td>
<td>0.281</td>
</tr>
<tr>
<td>0.9818</td>
<td>0.270</td>
</tr>
<tr>
<td>0.9818</td>
<td>0.270</td>
</tr>
</tbody>
</table>
0,N-hydroxylammonium ion solutions of varying concentrations. The values in this table were treated in a nonlinear least squares analysis of eq. (51). The analysis resulted in the following values.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>K</td>
<td>-0.387 M⁻¹</td>
<td>0.0345 M⁻¹</td>
</tr>
<tr>
<td>ε_{Im}</td>
<td>18.5 M⁻¹cm⁻¹</td>
<td>0.402 M⁻¹cm⁻¹</td>
</tr>
</tbody>
</table>

The analysis resulted in a physically impossible value for the equilibrium constant. Thus, it was then assumed that the iminium ion, N-isopropylidene-0,N-dimethylhydroxylammonium ion, has zero absorbance at 275 nm. This is not a poor assumption since the similar N-isopropylideneisoxazolidinium ion has an extinction coefficient of only 0.217 M⁻¹cm⁻¹ with a standard deviation of 0.215 M⁻¹cm⁻¹ compared to 15.5 M⁻¹cm⁻¹ for acetone at that wavelength. Setting the ε_{Im} equal to zero in eq. (51) results in eq. (52).

\[
\text{Abs} = \frac{(K[\text{AmH}^+]_0 - K[\text{Ac}]_0 + 1) - \sqrt{(K[\text{AmH}^+]_0 - K[\text{Ac}]_0 + 1)^2 + 4K[\text{Ac}]_0}}{2K}
\]

A nonlinear least squares analysis of eq. 52 was performed using the values in Table 12 with unit weighting using program 6b (Appendix). The analysis gave a value of 0.117 M⁻¹ for K with a standard deviation of 0.0052 M⁻¹. The plot of the equilibrium absorbance against the initial ammonium ion concentration is shown in Figure 26. The differences between the observed and calculated equilibrium absorbance did not exceed 2%.
Fig. 26. Equilibrium Absorbance of Solution Resulting from Injection of Acetone to Produce 0.0198 M Initial Acetone Concentration into O,N-Dimethylhydroxylammonium Chloride Solution vs. the Initial Concentration of the Amine Salt
3. Acetone and 1,2-Dimethylhydrazinium Ions

The absorbances at 240 nm of aqueous acetone solution of different concentrations are shown in Table 13. The plot of absorbance against the concentration gave an excellent straight line with an intercept equal to 0.00124 and slope equal to 7.36 which is the extinction coefficient of acetone at 240 nm with units of \( \text{M}^{-1}\text{cm}^{-1} \).

**TABLE 13**

**ABSORBANCES OF AQUEOUS ACETONE SOLUTIONS AT 240 nm**

<table>
<thead>
<tr>
<th>[Ac]</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.004990</td>
<td>0.03580</td>
</tr>
<tr>
<td>0.009970</td>
<td>0.07540</td>
</tr>
<tr>
<td>0.01493</td>
<td>0.1134</td>
</tr>
<tr>
<td>0.01990</td>
<td>0.1495</td>
</tr>
<tr>
<td>0.02479</td>
<td>0.1810</td>
</tr>
</tbody>
</table>

Table 14 shows the extrapolated initial and equilibrium absorbances, \( A_1 + A_2 \) and \( A_2 \), respectively, of solutions resulting from injection of acetone into 1,2-dimethylhydrazinium ion solutions of varying concentrations. The parameters \( A_1 \) and \( A_2 \) were calculated from the Sachs equation (eq. 6) using Program 2 (Appendix) and the points from the time - absorbance curves.


### Table 14

Extrapolated absorbances at 240 nm of solutions resulting from injection of a constant amount of acetone into 1,2-dimethylhydrazinium ion solutions of varying concentrations

\[
[\text{Ac}]_0 = 0.01473 \text{ M}
\]

<table>
<thead>
<tr>
<th>([\text{Am}^+\text{H}^+]_0) (M)</th>
<th>(A_2) Extrapolated Eq. Abs.</th>
<th>(A_1 + A_2) Extrapolated Initial Abs.</th>
<th>(10^3 k_{\text{obs}}) (s(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1005</td>
<td>0.2351</td>
<td>0.1300</td>
<td>7.02 ± 0.25</td>
</tr>
<tr>
<td>0.1003</td>
<td>0.2356</td>
<td>0.1256</td>
<td>6.57 ± 0.30</td>
</tr>
<tr>
<td>0.1117</td>
<td>0.2990</td>
<td>0.1324</td>
<td>5.58 ± 0.17</td>
</tr>
<tr>
<td>0.1117</td>
<td>0.2935</td>
<td>0.1361</td>
<td>5.27 ± 0.12</td>
</tr>
<tr>
<td>0.1270</td>
<td>0.3355</td>
<td>0.1140</td>
<td>5.48 ± 0.08</td>
</tr>
<tr>
<td>0.1270</td>
<td>0.3418</td>
<td>0.1281</td>
<td>5.37 ± 0.11</td>
</tr>
<tr>
<td>0.1675</td>
<td>0.4067</td>
<td>0.1399</td>
<td>6.33 ± 0.06</td>
</tr>
<tr>
<td>0.1675</td>
<td>0.4067</td>
<td>0.1384</td>
<td>5.88 ± 0.06</td>
</tr>
<tr>
<td>0.1981</td>
<td>0.4849</td>
<td>0.0909</td>
<td>6.65 ± 0.13</td>
</tr>
<tr>
<td>0.1981</td>
<td>0.4850</td>
<td>0.0878</td>
<td>6.38 ± 0.11</td>
</tr>
<tr>
<td>0.2489</td>
<td>0.5288</td>
<td>0.0794</td>
<td>7.30 ± 0.10</td>
</tr>
<tr>
<td>0.2489</td>
<td>0.5251</td>
<td>0.0896</td>
<td>7.65 ± 0.09</td>
</tr>
<tr>
<td>0.2944</td>
<td>0.5545</td>
<td>0.1361</td>
<td>8.48 ± 0.07</td>
</tr>
<tr>
<td>0.2944</td>
<td>0.5500</td>
<td>0.1376</td>
<td>8.77 ± 0.06</td>
</tr>
</tbody>
</table>
The values in Table 14 were treated in a nonlinear least squares analysis of eq. (50) using Program 6c (Appendix). The calculated parameters and their standard deviations are shown below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K$</td>
<td>0.758 M$^{-1}$</td>
<td>0.594 M$^{-1}$</td>
</tr>
<tr>
<td>$\varepsilon_{Im}$</td>
<td>182 M$^{-1}$cm$^{-1}$</td>
<td>108 M$^{-1}$cm$^{-1}$</td>
</tr>
</tbody>
</table>

A plot of the extrapolated equilibrium absorbances against the initial 1,2-dimethylhydrazinium ion concentration (Figure 27) shows that the experimental points appear to follow a line of greater curvature than the calculated function and this is reflected in the very large standard deviations of the calculated parameters. It was thought that the equilibrium constant was too small to be accurately measured by this method. Thus, it was decided that measurement of the equilibrium constant by NMR be attempted. The observed first order rate constants in Table 14 do not increase proportionately to the AmH$^+$ concentration. This is most probably due to the fact that the reaction rate is very much dependent on pH, which was not controlled in the unbuffered solutions.

G. Determination of Equilibrium Constants for Iminium Ion Formation by NMR

1. Acetone-$d_3$ - O,N-Dimethylhydroxylammonium Ion Reaction

Table 15 shows the integration values for the methyl peaks of the protonated amine, $I_{CH_3-N^+}$, and that for the methyl peak of
Fig. 27. Extrapolated Equilibrium Absorbance of Solution Resulting from Injection of Acetone to Produce 0.01473 M Initial Acetone Concentration vs. the Initial Concentration of 1,2-Dimethylhydrazinium Ions
<table>
<thead>
<tr>
<th>Table 15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Integration Values in the NMR Spectra of O,N-Dimethylhydroxylammonium Ion in D$_2$O</strong></td>
</tr>
</tbody>
</table>

**Before Injection of Acetone-d$_6$**

<table>
<thead>
<tr>
<th></th>
<th>[AmH$^+\text{]}$ before Ac Injection</th>
<th>Vol. of [AmH$^+\text{]}$ soln before Ac injection</th>
<th>Wt. of [AmH$^+\text{]}$ soln before Ac injection</th>
<th>$I_{\text{CH}_3\text{OH}}$</th>
<th>$I_{\text{CH}_3\text{-N}^+}$</th>
<th>[CH$_3$OH] before Ac injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>NMR tube I</td>
<td>1.49</td>
<td>0.40</td>
<td>0.4441</td>
<td>569</td>
<td>1021</td>
<td>0.830</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>551</td>
<td>1031</td>
<td>0.796</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>554</td>
<td>1034</td>
<td>0.798</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>547</td>
<td>1056</td>
<td>0.787</td>
</tr>
<tr>
<td>NMR tube II</td>
<td>1.49</td>
<td>0.40</td>
<td>0.4438</td>
<td>578</td>
<td>1052</td>
<td>0.818</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>570</td>
<td>1058</td>
<td>0.803</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>568</td>
<td>1054</td>
<td>0.803</td>
</tr>
</tbody>
</table>
methanol, \( I_{\text{CH}_3\text{OH}} \) before injection of acetone-\( \text{d}_6 \) into NMR tubes containing \( O,N \)-dimethylhydroxylamine hydrochloride in \( D_2O \).

Table 16 shows the integration values for the methanol peak, \( I_{\text{CH}_3\text{OH}} \), and the \( \text{CH}_2-N^+ -O \) peak of the unreacted ammonium ion, \( I_{\text{CH}_3-N^+} \), and the equilibrium unreacted ammonium ion concentrations which were calculated in the following manner.

\[
[AmH^+]_{eq} = \frac{(I_{\text{CH}_3-N^+}) ([\text{CH}_3\text{OH}]_{\text{before Ac injection}})(\text{Vol. before Ac inj.})}{(I_{\text{CH}_3\text{OH}})(\text{Vol. after Ac injection})}
\]  

The average \([\text{CH}_3\text{OH}]\) before injection of acetone-\( \text{d}_6 \) into each NMR tube was used in the calculation. Additivity of volumes was assumed with regards to the mixing of acetone-\( \text{d}_6 \) and the AmH\(^+ \) solution.

From the results of Table 16, dimensionless equilibrium constants were calculated.

\[
K_{\text{dimensionless}} = \frac{[\text{Im}^+]_{eq} [D_2O]}{[AmH^+]_{eq} [Ac-\text{d}_6]_{eq}}
\]

These dimensionless equilibrium constants were divided by 55 M to make them comparable to those obtained from the UV results. Due to the fact that large amounts of acetone were added to produce enough iminium ions, these measurements were not considered to be taken in dilute aqueous solutions. Thus, the changes in concentration of \( D_2O \) had to be considered. The concentration of \( D_2O \) was calculated in
<table>
<thead>
<tr>
<th>Vol. of Ac injected (ml)</th>
<th>Wt. of Ac injected (g)</th>
<th>Vol. of soln. after Ac injection (ml)</th>
<th>$I_{\text{CH}_3\text{OH}}$</th>
<th>$I_{\text{CH}_3-N^+}$</th>
<th>$[\text{AmH}^+]_{\text{eq}}$ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NMR tube I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.050</td>
<td>0.04146</td>
<td>0.45</td>
<td>624</td>
<td>986</td>
<td>1.13</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>607</td>
<td>1001</td>
<td>1.18</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>594</td>
<td>975</td>
<td>1.17</td>
</tr>
<tr>
<td>0.10</td>
<td>0.0844</td>
<td>0.50</td>
<td>469</td>
<td>690</td>
<td>0.945</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>477</td>
<td>689</td>
<td>0.927</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>459</td>
<td>692</td>
<td>0.967</td>
</tr>
<tr>
<td>0.15</td>
<td>0.1273</td>
<td>0.55</td>
<td>429</td>
<td>540</td>
<td>0.755</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>429</td>
<td>575</td>
<td>0.783</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>416</td>
<td>572</td>
<td>0.803</td>
</tr>
<tr>
<td>0.27</td>
<td>0.2206</td>
<td>0.67</td>
<td>338</td>
<td>458</td>
<td>0.649</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>341</td>
<td>451</td>
<td>0.634</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>345</td>
<td>442</td>
<td>0.641</td>
</tr>
<tr>
<td><strong>NMR tube II</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.030</td>
<td>0.0252</td>
<td>0.43</td>
<td>525</td>
<td>903</td>
<td>1.29</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>514</td>
<td>898</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>530</td>
<td>896</td>
<td>1.27</td>
</tr>
<tr>
<td>0.08</td>
<td>0.0681</td>
<td>0.48</td>
<td>487</td>
<td>778</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>489</td>
<td>777</td>
<td>1.07</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>500</td>
<td>794</td>
<td>1.07</td>
</tr>
<tr>
<td>0.18</td>
<td>0.1552</td>
<td>0.58</td>
<td>428</td>
<td>587</td>
<td>0.764</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>418</td>
<td>587</td>
<td>0.782</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>414</td>
<td>584</td>
<td>0.786</td>
</tr>
</tbody>
</table>
Table 16 (continued)

<table>
<thead>
<tr>
<th>Vol. of Ac injected (ml)</th>
<th>Wt. of Ac injected (g)</th>
<th>Vol. of soln. after Ac injection (ml)</th>
<th>I$_{CH_3OH}$</th>
<th>I$_{CH_3-N^+}$</th>
<th>[AmH$^+$]$_{eq}$ (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.33</td>
<td>0.2858</td>
<td>0.73</td>
<td>355</td>
<td>491</td>
<td>0.613</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>354</td>
<td>482</td>
<td>0.603</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>357</td>
<td>482</td>
<td>0.598</td>
</tr>
</tbody>
</table>
three different ways - molarity of D$_2$O ([D$_2$O]), mole fraction of D$_2$O ($\chi_{D_2O}$), and percentage weight of D$_2$O (% D$_2$O). The weight of D$_2$O is the weight of the amine hydrochloride solution in the NMR tube before injection of acetone-$d_6$ minus the weight of the dissolved salt. Table 17 shows the calculated equilibrium constants in $M^{-1}$ and the different expressions of the concentration of D$_2$O.

Since the equilibrium constant is seen to increase monotonically as the amount of acetone increases, extrapolation to dilute aqueous solution, that is, 55 M H$_2$O or $\chi_{D_2O} = 1$ or 100 % D$_2$O, seems possible. This was done by plotting $K$ or log $K$ as a function of different expressions of D$_2$O concentration or their logarithms and finding out which one of these plots best fits a straight line whose equation will be used to calculate the equilibrium constant in pure water. Table 18 shows the different functions plotted, the slopes and intercepts of the least squares line from the experimental points, the $R^2$ measures of fit calculated using the Hewlett-Packard Plotter Pack program, the square roots of the sums of the squares of the deviations between the observed and calculated $K$'s and the $K$'s extrapolated to dilute aqueous solution. There is no obvious reason why $K$ or log $K$ should be linear function of any of the expressions of D$_2$O but it was thought that the best straight line would give the best estimate of $K$ in dilute aqueous solution.

The plot of $K$ vs $\chi_{D_2O}$ which best fits a straight line is shown in Figure 28. The equilibrium constant extrapolated to dilute
TABLE 17
EQUILIBRIUM CONSTANTS AT 35° FOR IMINIUM ION FORMATION BETWEEN ACETONE-\(d_6\) AND O,N-DIMETHYLHYDROXYLAMMONIUM IONS AT DIFFERENT CONCENTRATIONS OF D\(_2\)O

<table>
<thead>
<tr>
<th>([\text{AmH}^+]_0)</th>
<th>([\text{Ac-d}_6]_0)</th>
<th>([\text{D}_2\text{O}])</th>
<th>([\text{Im}^+]_{eq})</th>
<th>(K , (\text{M}^{-1}))</th>
<th>(\chi_{\text{D}_2\text{O}})</th>
<th>% (\text{D}_2\text{O})</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.32</td>
<td>1.44</td>
<td>42.8</td>
<td>0.160</td>
<td>0.083</td>
<td>0.924</td>
<td>77.4</td>
</tr>
<tr>
<td>1.19</td>
<td>2.63</td>
<td>38.5</td>
<td>0.244</td>
<td>0.075</td>
<td>0.894</td>
<td>71.1</td>
</tr>
<tr>
<td>1.08</td>
<td>3.61</td>
<td>35.0</td>
<td>0.287</td>
<td>0.069</td>
<td>0.866</td>
<td>65.8</td>
</tr>
<tr>
<td>0.889</td>
<td>5.13</td>
<td>28.8</td>
<td>0.257</td>
<td>0.044</td>
<td>0.812</td>
<td>56.5</td>
</tr>
<tr>
<td>1.39</td>
<td>0.914</td>
<td>44.8</td>
<td>0.110</td>
<td>0.087</td>
<td>0.935</td>
<td>80.0</td>
</tr>
<tr>
<td>1.24</td>
<td>2.21</td>
<td>40.1</td>
<td>0.170</td>
<td>0.057</td>
<td>0.905</td>
<td>73.3</td>
</tr>
<tr>
<td>1.03</td>
<td>4.17</td>
<td>33.2</td>
<td>0.253</td>
<td>0.050</td>
<td>0.848</td>
<td>62.7</td>
</tr>
<tr>
<td>0.816</td>
<td>6.11</td>
<td>26.4</td>
<td>0.211</td>
<td>0.028</td>
<td>0.778</td>
<td>51.4</td>
</tr>
</tbody>
</table>
### TABLE 18
EQUILIBRIUM CONSTANTS AT 35° FOR IMINUM ION FORMATION BETWEEN ACETONE-$d_3$ AND $O_2N$-DIMETHYLHYDROXYLAMMONIUM IONS EXTRAPOLATED TO DILUTE AQUEOUS SOLUTIONS

<table>
<thead>
<tr>
<th>Function Plotted</th>
<th>$R^2$</th>
<th>Std. Dev. of Analysis</th>
<th>Slope</th>
<th>Intercept</th>
<th>K Extrapolated to Pure Water (M$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K$ vs. $x_{D_2O}$</td>
<td>0.970</td>
<td>$4.19 \times 10^{-3}$</td>
<td>0.376</td>
<td>-0.264</td>
<td>0.11</td>
</tr>
<tr>
<td>$K$ vs. $% D_2O$</td>
<td>0.957</td>
<td>$4.99 \times 10^{-3}$</td>
<td>2.05</td>
<td>-0.0736</td>
<td>0.13</td>
</tr>
<tr>
<td>$K$ vs. $[D_2O]$</td>
<td>0.942</td>
<td>$5.81 \times 10^{-3}$</td>
<td>3.11</td>
<td>-0.0488</td>
<td>0.12</td>
</tr>
<tr>
<td>log $K$ vs. $x_{D_2O}$</td>
<td>0.938</td>
<td>0.0488</td>
<td>3.01</td>
<td>-3.84</td>
<td>0.15</td>
</tr>
<tr>
<td>log $K$ vs. log $D_2O$</td>
<td>0.919</td>
<td>0.0560</td>
<td>2.01</td>
<td>-4.34</td>
<td>0.14</td>
</tr>
<tr>
<td>log $K$ vs. $% D_2O$</td>
<td>0.908</td>
<td>0.0595</td>
<td>0.0162</td>
<td>-2.31</td>
<td>0.20</td>
</tr>
<tr>
<td>log $K$ vs. $[D_2O]$</td>
<td>0.881</td>
<td>0.0675</td>
<td>0.0245</td>
<td>-2.11</td>
<td>0.17</td>
</tr>
</tbody>
</table>
Fig. 28. Equilibrium Constant for Iminium Ion Formation Between Acetone-$d_6$ and $\text{O}_2\text{N}$-Dimethylammonium Ion at $33^\circ$ vs. Mole Fraction of $\text{D}_2\text{O}$.
aqueous solution from this plot (0.11 M⁻¹) agrees extremely well with that obtained from UV equilibrium absorbances using light acetone (0.117 M⁻¹). If both UV and NMR results are correct, then the isotope effect in iminium ion formation in going from acetone to acetone-d₅ is not significant, which is the assumption made for all the dedeuteration experiments in this study.

2. Acetone-d₅ and 1,2-Dimethylhydrazinium Ions

Table 19 shows the integration values of the CH₃-N peak of the monoprotonated amine (I₁CH₃) and those for water protons (I₁H₂O) before injection of acetone-d₅. From these values and the concentration of the monoprotonated amine which is accurately known, the concentration of water protons can be calculated.

\[
[H₂O protons] \text{ before Ac injection} = \frac{([AmH⁺]\text{before injection}) (I₁H₂O)}{I₁CH₃} \quad (6)
\]

(55)

Table 20 shows the integration values for the water peak and the integration values of the CH₃-N⁺=C peak of the iminium ion, I₁CH₃-N⁺=C, and the equilibrium iminium ion concentration which was calculated in the following manner.

\[
[Im⁺]_{eq} = \frac{(I₁CH₃-N⁺=C)([H₂O protons] \text{ before Ac injection})}{(I₁H₂O') (3 protons)} \times \frac{(Vol. \text{ before Ac injection})}{(Vol. \text{ after Ac injection})} \quad (56)
\]
**TABLE 19**

INTEGRATION VALUES IN THE NMR SPECTRA OF 1,2-DIMETHYLHYDRAZINIUM ION IN D$_2$O BEFORE INJECTION OF ACETONE-d$_6$

<table>
<thead>
<tr>
<th>NMR tube</th>
<th>[AmH$^+$] before Ac injection</th>
<th>Vol. of AmH$^+$ soln. before Ac injection</th>
<th>Wt. of AmH$^+$ soln. before Ac injection</th>
<th>I$_{H_2O}$</th>
<th>I$_{CH_3}$</th>
<th>[H$_2$O protons] before Ac injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.50 M</td>
<td>0.40 ml</td>
<td>0.4652 g</td>
<td>691</td>
<td>1010</td>
<td>6.16 M</td>
</tr>
<tr>
<td>II</td>
<td>1.50 M</td>
<td>0.33 ml</td>
<td>0.3809 g</td>
<td>754</td>
<td>1012</td>
<td>6.71 M</td>
</tr>
<tr>
<td>III</td>
<td>1.56 M</td>
<td>0.40 ml</td>
<td>0.4729 g</td>
<td>795</td>
<td>1090</td>
<td>6.83 M</td>
</tr>
<tr>
<td>IV</td>
<td>1.56 M</td>
<td>0.40 ml</td>
<td>0.4669 g</td>
<td>771</td>
<td>1008</td>
<td>7.16 M</td>
</tr>
<tr>
<td></td>
<td>Vol. of Ac-d$_5$ injected</td>
<td>Wt. of Ac-d$_5$ injected</td>
<td>Vol. of soln. after injection</td>
<td>I$_{H_2O}$</td>
<td>I$_{CH_3-N^+}$</td>
<td>[Im$^+$]$_{eq}$ (M)</td>
</tr>
<tr>
<td>----------------</td>
<td>---------------------------</td>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>------------</td>
<td>--------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>NMR tube I</td>
<td>0.20 ml</td>
<td>0.1709 g</td>
<td>0.60 ml</td>
<td>1236</td>
<td>119</td>
<td>0.134</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1205</td>
<td>149</td>
<td>0.171</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1241</td>
<td>130</td>
<td>0.145</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1236</td>
<td>130</td>
<td>0.142</td>
</tr>
<tr>
<td></td>
<td>0.40 ml</td>
<td>0.3430 g</td>
<td>0.80 ml</td>
<td>903</td>
<td>85</td>
<td>0.0979</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>918</td>
<td>100</td>
<td>0.113</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>905</td>
<td>77</td>
<td>0.0885</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>894</td>
<td>97</td>
<td>0.113</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>929</td>
<td>91</td>
<td>0.102</td>
</tr>
<tr>
<td>NMR tube II</td>
<td>0.10 ml</td>
<td>0.0802 g</td>
<td>0.43 ml</td>
<td>1397</td>
<td>98</td>
<td>0.120</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1399</td>
<td>101</td>
<td>0.124</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1430</td>
<td>101</td>
<td>0.121</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1416</td>
<td>99</td>
<td>0.120</td>
</tr>
<tr>
<td></td>
<td>0.35 ml</td>
<td>0.2947 g</td>
<td>0.68 ml</td>
<td>857</td>
<td>88</td>
<td>0.111</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>856</td>
<td>89</td>
<td>0.113</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>847</td>
<td>87</td>
<td>0.111</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>840</td>
<td>83</td>
<td>0.107</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>847</td>
<td>87</td>
<td>0.111</td>
</tr>
<tr>
<td>NMR tube III</td>
<td>0.050 ml</td>
<td>0.0392 g</td>
<td>0.45 ml</td>
<td>1719</td>
<td>60</td>
<td>0.0691</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1710</td>
<td>57</td>
<td>0.0660</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1715</td>
<td>58</td>
<td>0.0669</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1702</td>
<td>60</td>
<td>0.0698</td>
</tr>
<tr>
<td></td>
<td>Vol. of Ac-d₆ injected</td>
<td>Wt. of Ac-d₆ injected</td>
<td>Vol. of soln after injection</td>
<td>I₃H₂O</td>
<td>I₃CH₃-N⁺=C</td>
<td>[Im⁺]eq</td>
</tr>
<tr>
<td>------------------</td>
<td>------------------------</td>
<td>----------------------</td>
<td>-----------------------------</td>
<td>-------</td>
<td>-----------</td>
<td>---------</td>
</tr>
<tr>
<td>NMR tube III</td>
<td>0.080 ml</td>
<td>0.0645 g</td>
<td>0.48 ml</td>
<td>1704</td>
<td>92</td>
<td>0.100</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1673</td>
<td>77</td>
<td>0.0854</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1661</td>
<td>90</td>
<td>0.101</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1652</td>
<td>91</td>
<td>0.102</td>
</tr>
<tr>
<td></td>
<td>0.28 ml</td>
<td>0.2353 g</td>
<td>0.68 ml</td>
<td>1169</td>
<td>101</td>
<td>0.113</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1167</td>
<td>89</td>
<td>0.0999</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1178</td>
<td>106</td>
<td>0.118</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1177</td>
<td>107</td>
<td>0.119</td>
</tr>
<tr>
<td>NMR tube IV</td>
<td>0.030 ml</td>
<td>0.0248 g</td>
<td>0.43 ml</td>
<td>1652</td>
<td>42</td>
<td>0.0564</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1668</td>
<td>40</td>
<td>0.0532</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1662</td>
<td>40</td>
<td>0.0534</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1641</td>
<td>40</td>
<td>0.0540</td>
</tr>
<tr>
<td></td>
<td>0.13 ml</td>
<td>0.1099 g</td>
<td>0.53 ml</td>
<td>1431</td>
<td>100</td>
<td>0.126</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1419</td>
<td>100</td>
<td>0.127</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1411</td>
<td>96</td>
<td>0.122</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1394</td>
<td>100</td>
<td>0.126</td>
</tr>
</tbody>
</table>
The average [H$_2$O protons] before injection of acetone-$d_3$ for each NMR tube was used in the calculation of the equilibrium iminium ion concentration. From the value in Table 20, dimensionless equilibrium constants were calculated.

$$K_{\text{dimensionless}} = \frac{[\text{Im}^+]_{\text{eq}}[\text{D}_2\text{O}]}{([\text{AmH}^+]_0 - [\text{Im}^+]_{\text{eq}})([\text{Ac}-d_3]_0 - [\text{Im}^+]_{\text{eq}})}$$  (57)

These dimensionless equilibrium constants were divided by 55 M. To determine the effect of changes in polarity due to the large amounts of acetone-$d_3$ added, the concentration of D$_2$O was calculated in three different ways as before. Table 21 shows the equilibrium constants at different D$_2$O concentrations.

Extrapolation to dilute aqueous solution was done as in the case of O,N-dimethylhydroxylammonium ions. Table 22 shows the equilibrium constants extrapolated to pure water and the different functions plotted in making the extrapolation. The plot which best fits a straight line, log $K$ vs. $x_{D_2O}$, is shown in Figure 29. The equilibrium constant extrapolated to pure water using this plot, 0.057 M$^{-1}$, was accepted as the equilibrium constant in dilute aqueous solution for iminium ion formation between acetone-$d_3$ and 1,2-dimethylhydrazinium ions. Three other plots give extrapolated equilibrium constants within 10% of this value and these provide additional reliability to the method of extrapolation.
## TABLE 21

EQUILIBRIUM CONSTANTS AT 33 ° FOR IMINIIUM ION FORMATION BETWEEN ACETONE-\(d_5\) AND 1,2-DIMETHYLHYDRAZINUM IONS AT DIFFERENT CONCENTRATIONS OF D\(_2\)O

<table>
<thead>
<tr>
<th>([\text{AmH}^+]_0)</th>
<th>([\text{Ac-d}_5]_0)</th>
<th>([D_2O])</th>
<th>([\text{Im}^+]_\text{eq})</th>
<th>(K (M^{-1}))</th>
<th>(X_{D_2O})</th>
<th>% (D_2O)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.00</td>
<td>4.44</td>
<td>31.0</td>
<td>0.142</td>
<td>0.022</td>
<td>0.827</td>
<td>58.5</td>
</tr>
<tr>
<td>0.750</td>
<td>6.69</td>
<td>23.2</td>
<td>0.106</td>
<td>0.011</td>
<td>0.739</td>
<td>46.1</td>
</tr>
<tr>
<td>1.15</td>
<td>2.91</td>
<td>35.3</td>
<td>0.121</td>
<td>0.027</td>
<td>0.874</td>
<td>66.0</td>
</tr>
<tr>
<td>0.728</td>
<td>6.76</td>
<td>22.3</td>
<td>0.111</td>
<td>0.011</td>
<td>0.731</td>
<td>45.0</td>
</tr>
<tr>
<td>1.39</td>
<td>1.36</td>
<td>41.7</td>
<td>0.0680</td>
<td>0.030</td>
<td>0.913</td>
<td>73.5</td>
</tr>
<tr>
<td>1.30</td>
<td>2.10</td>
<td>39.1</td>
<td>0.0971</td>
<td>0.029</td>
<td>0.895</td>
<td>70.0</td>
</tr>
<tr>
<td>0.918</td>
<td>5.40</td>
<td>27.2</td>
<td>0.112</td>
<td>0.014</td>
<td>0.739</td>
<td>53.1</td>
</tr>
<tr>
<td>1.45</td>
<td>0.899</td>
<td>43.0</td>
<td>0.0542</td>
<td>0.036</td>
<td>0.919</td>
<td>75.3</td>
</tr>
<tr>
<td>1.18</td>
<td>3.23</td>
<td>34.9</td>
<td>0.126</td>
<td>0.025</td>
<td>0.862</td>
<td>64.2</td>
</tr>
</tbody>
</table>
**TABLE 22**

EQUILIBRIUM CONSTANTS AT 35° FOR IMINIMUM ION FORMATION BETWEEN ACETONE-\(d_6\) AND 1,2-DIMETHYHYDRAZINUM IONS EXTRAPOLATED TO DILUTE AQUEOUS SOLUTION

<table>
<thead>
<tr>
<th>Function Plotted</th>
<th>(R^2)</th>
<th>Std. Dev. of Analysis</th>
<th>Slope</th>
<th>Intercept</th>
<th>K extrapolated to pure water (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>log (K) vs (X_{D_2O})</td>
<td>0.974</td>
<td>0.0336</td>
<td>2.71</td>
<td>-3.95</td>
<td>0.057</td>
</tr>
<tr>
<td>log (K) vs log ([D_2O])</td>
<td>0.971</td>
<td>0.0357</td>
<td>1.83</td>
<td>-4.44</td>
<td>0.056</td>
</tr>
<tr>
<td>(K) vs (% D_2O)</td>
<td>0.969</td>
<td>0.00168</td>
<td>7.81</td>
<td>-0.0251</td>
<td>0.053</td>
</tr>
<tr>
<td>log (K) vs (% D_2O)</td>
<td>0.967</td>
<td>0.0380</td>
<td>0.0170</td>
<td>-2.72</td>
<td>0.095</td>
</tr>
<tr>
<td>(K) vs ([D_2O])</td>
<td>0.964</td>
<td>0.00182</td>
<td>1.15</td>
<td>-0.0155</td>
<td>0.050</td>
</tr>
<tr>
<td>(k) vs (X_{D_2O})</td>
<td>0.956</td>
<td>0.00202</td>
<td>0.123</td>
<td>-0.0804</td>
<td>0.042</td>
</tr>
<tr>
<td>log (K) vs ([D_2O])</td>
<td>0.954</td>
<td>0.0461</td>
<td>0.0251</td>
<td>-2.51</td>
<td>0.074</td>
</tr>
</tbody>
</table>

457
Fig. 29. Log of Equilibrium Constant for Iminium Ion Formation Between Acetone-$d_6$ and 1,2-Dimethylhydrazinium Ion at 33° vs. Mole Fraction of D$_2$O.
It should be pointed out that in these experiments and also in the case of $0.0N$-dimethylhydroxylammonium ions, acetone-$d_8$ was injected into the same NMR tube two or three times causing dilution of the ammonium salt. Thus, it is not only the acetone concentration which was varied in the experiments but also the ammonium salt concentration and it is possible that changes in both could affect the equilibrium constant. However, there was no obvious correlation between the deviation of the points from the line in Figures 28 and 29 and the salt concentration.

H. Hydrolysis of N-Isopropylideneisoxazolidinium Ion

A kinetic study of the reaction between acetone and isoxazolidinium ions at different pH's (0.8-5.2) by monitoring the UV absorbance of acetone at 275 nm indicated that the reaction is quite too fast to measure. At its fastest rate, the reaction has proceeded to 40% completion before the first time-absorbance point can be recorded. Because of its rapid rate, the differences between rate constants for duplicate runs were as high as 20%. This rapid rate may be due to the fact that the observed first order rate constant for the disappearance of acetone when reacting with excess isoxazolidinium ions is the sum of the pseudo-first order rate constant for the forward reaction (iminium ion formation) and the first order rate constant for hydrolysis.49

When the iminium ion formation reaction was studied by stopped-flow measurements under similar conditions, there was an
unexplained decrease in transmittance after reaching a maximum when
the reaction was allowed to proceed at pH's where there are significant
amounts of free isoxazolidine (pH > 4.9). The reaction at lower pH's
behaved normally, showing only a steady increase in transmittance
and levelling off to an equilibrium value corresponding to the loss
of acetone as it reacts to form iminium ions.

Because of the above problems, it was decided that the reverse
reaction - the hydrolysis of the iminium ion - be studied. Ten cm
cells were used so that accurate absorbances could be recorded from
the relatively low concentration of acetone which results from the
hydrolysis. If the initial concentration of the iminium salts were
made larger in order to obtain larger absorbances in 1-cm cells, the
reaction could not be considered a simple first order one because
towards the end, the reverse reaction which is second order (first
order in protonated amine and first order in acetone) would cause
complications. The integrated equation for a reversible reaction,
first order forward and second order reverse, is so complicated that
it was avoided. The initial concentration of iminium ion used
(1 x 10^{-3} M) would result in 99.1% hydrolysis, as calculated from
the equilibrium constant of 8.96 M^{-1}. If the initial concentration
were increased 10 times so that 1-cm cells could be used, only 92%
hydrolysis would be attained at equilibrium.

Table 25 shows the first order rate constants obtained at
different pH's for the hydrolysis of N-isopropylideneisoxazolidinium
<table>
<thead>
<tr>
<th>pH_{obs}</th>
<th>Buffer Components</th>
<th>Ionic Strength (M)</th>
<th>k_{obs} \times 10^2 (s^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.630</td>
<td>0.3012 M HCl</td>
<td>0.3012</td>
<td>0.952</td>
</tr>
<tr>
<td>0.920</td>
<td>0.1426 M HCl</td>
<td>0.3006</td>
<td>0.957</td>
</tr>
<tr>
<td>1.42</td>
<td>0.04498 M HCl</td>
<td>0.3000</td>
<td>0.977</td>
</tr>
<tr>
<td>1.90</td>
<td>0.01426 M HCl</td>
<td>0.3000</td>
<td>1.02</td>
</tr>
<tr>
<td>2.69</td>
<td>0.08891 M formic acid, 0.01109 M formate</td>
<td>0.3000</td>
<td>1.33</td>
</tr>
<tr>
<td>2.62</td>
<td>0.2667 M formic acid, 0.03338 M formate</td>
<td>0.3001</td>
<td>1.34</td>
</tr>
<tr>
<td>3.24</td>
<td>0.0668 M formic acid, 0.03332 M formate</td>
<td>0.3000</td>
<td>1.54</td>
</tr>
<tr>
<td>3.22</td>
<td>0.2002 M formic acid, 0.09986 M formate</td>
<td>0.3001</td>
<td>1.90</td>
</tr>
<tr>
<td>3.98</td>
<td>0.07856 M acetic acid, 0.1999 M acetate</td>
<td>0.3000</td>
<td>1.71</td>
</tr>
<tr>
<td>3.98</td>
<td>0.2351 M acetic acid, 0.05604 M acetate</td>
<td>0.3000</td>
<td>1.92</td>
</tr>
<tr>
<td>4.59</td>
<td>0.04831 M acetic acid, 0.05004 M acetate</td>
<td>0.2996</td>
<td>1.97</td>
</tr>
<tr>
<td>4.61</td>
<td>0.1314 M acetic acid, 0.1361 M acetate</td>
<td>0.3001</td>
<td>2.12</td>
</tr>
<tr>
<td>5.22</td>
<td>0.01829 M acetic acid, 0.08006 M acetate</td>
<td>0.3001</td>
<td>1.98</td>
</tr>
<tr>
<td>5.27</td>
<td>0.05483 M acetic acid, 0.2402 M acetate</td>
<td>0.3002</td>
<td>2.35</td>
</tr>
<tr>
<td>5.82</td>
<td>0.06578 M cacodylic acid, 0.03222 M cacodylate</td>
<td>0.3004</td>
<td>2.09</td>
</tr>
<tr>
<td>5.78</td>
<td>0.1667 M cacodylic acid, 0.08329 M cacodylate</td>
<td>0.2999</td>
<td>2.30</td>
</tr>
<tr>
<td>6.48</td>
<td>0.03275 M cacodylic acid, 0.0625 M cacodylate</td>
<td>0.3008</td>
<td>2.08</td>
</tr>
</tbody>
</table>
Table 23 (continued)

<table>
<thead>
<tr>
<th>$pH_{obs}$</th>
<th>Buffer Components</th>
<th>Ionic Strength</th>
<th>$k_{obs} \times 10^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>6.52</td>
<td>0.09986 M cacodylic acid, 0.2001 M cacodylate</td>
<td>0.3001</td>
<td>2.69</td>
</tr>
<tr>
<td>7.24</td>
<td>0.00910 M cacodylic acid, 0.09090 M cacodylate</td>
<td>0.2989</td>
<td>2.02</td>
</tr>
<tr>
<td>7.36</td>
<td>0.02731 M cacodylic acid, 0.2727 M cacodylate</td>
<td>0.2999</td>
<td>3.33</td>
</tr>
</tbody>
</table>
ion calculated from the Sachs equation (eq. 6) using Program 2 (Appendix). These rate constants are the averages of two or three rate constants for duplicate runs weighted according to their standard deviations (eq. 34). The results of duplicate runs did not differ from each other by more than 15%.

At higher pH's, in solutions buffered by borate, the rate constants could not be accurately determined because of the rapid rate of reaction. A plot of log $k_{obs}$ vs. pH shows that the rate is fairly pH independent in the very acidic region (pH < 1.5), rising slightly from pH 2.5 to 4.5 and levelling off to another pH independent region from pH 4.5 to 7.4. From this trend, the following mechanism was proposed. This mechanism involves rate-controlling proton transfer by the carbinolamine (C) to form a zwitterion (Z) and a rate-controlling proton removal from the protonated carbinolamine ($CH^+$) to form the same zwitterion which dissociates to the amine and acetone in a fast step. The last step is considered to be a fast one so

$$H_2O + (CH_3)_2C=NH^+\quad Im^+ \overset{k_5}{\underset{k_5}{\rightleftharpoons}} (CH_3)_2C-NH^+\quad CH^+ \quad OH$$

$$\overset{k_4}{\underset{k_4}{\rightleftharpoons}} (CH_3)_2C-N\quad O\quad OH \quad C$$

$$\overset{k_3}{\underset{k_3}{\rightleftharpoons}} (CH_3)_2C-NH\quad O\quad OH \quad Z$$
\[ (\text{CH}_3)_2C\text{N} \xrightleftharpoons[k_2]{k_{-2}} \text{CH}_3\text{NH}^+ \]  \quad (61)

\[ (\text{CH}_3)_2C\text{NH}^+ \xrightleftharpoons[k_1]{k_{-1}} \text{CH}_3\text{CO} + \text{HN} \]  \quad (62)

\( k_{-1} > k_3[\text{H}^+] \) or \( k_2 \). Thus, the rate depends upon the concentration of the carbinolamine intermediates.

\[
\text{rate} = k_{-3} \left[ \text{CH}^+ \right] + k_{-2} \left[ \text{C} \right]
\]  \quad (63)

If a steady-state treatment is performed on the intermediate carbinolamine, both free and protonated, eq. (64) is obtained.

\[
k_{-5} \left[ \text{Im}^+ \right] = k_{-3} \left[ \text{CH}^+ \right] + k_{-2} \left[ \text{C} \right] + k_5 \left[ \text{CH}^+ \right]
\]  \quad (64)

The protonation of the carbinolamine is considered to be a rapid equilibrium.

\[
\left[ \text{C} \right] = K_4 \left[ \text{CH}^+ \right] / \left[ \text{H}^+ \right]
\]  \quad (65)

Combining eq. (64) and eq. (65), the following is obtained.

\[
k_{-5} \left[ \text{Im}^+ \right] = \frac{(k_{-3} + k_5)[\text{H}^+][\text{CH}^+] + k_{-2}K_4[\text{CH}^+]}{[\text{H}^+]} \]  \quad (66)

An equation is then derived expressing the concentration of the intermediate protonated carbinolamine in terms of measureable concentrations.
\[
[\text{CH}^+] = \frac{k_{-5}[\text{Im}^+][\text{H}^+]}{(k_5 + k_{-3})[\text{H}^+] + k_{-2}K_4}
\]

(67)

The rate expression in eq. (65) now becomes eq. (68).

\[
\text{rate} = \frac{(k_{-3}[\text{H}^+] + k_{-2}K_4)[\text{CH}^+]}{(k_5 + k_{-3})[\text{H}^+] + k_{-2}K_4}
\]

(68)

Combination of eqs. (67) and (68) produces eq. (69).

\[
\text{rate} = (k_{-3}[\text{H}^+] + k_{-2}K_4) \frac{k_{-5}[\text{Im}^+]}{(k_5 + k_{-3})[\text{H}^+] + k_{-2}K_4}
\]

(69)

The first order rate constant is now expressed as a function of acidity in eq. (70).

\[
k_{\text{obs}} = \frac{k_{-5}[\text{H}^+] + k_{-2}K_4k_{-5}/k_{-3}}{(1+k_5/k_{-3})[\text{H}^+] + k_{-2}K_4/k_{-3}}
\]

(70)

In very acidic solutions, \(k_{-5}[\text{H}^+]\) and \((1+k_5/k_{-3})[\text{H}^+]\) become very large compared to \(k_{-2}K_4/k_{-3}\) and the equation is reduced to a pH-independent one which represents the rate below pH 2.

\[
k_{\text{obs}} = \frac{k_{-3}}{1 + k_5/k_{-3}}
\]

(71)

At pH's greater than 4.5, \([\text{H}^+]\) becomes very small and the rate again becomes pH-independent.

\[
k_{\text{obs}} = k_{-5}
\]

(72)
Equation (69) disregards the contribution of general base catalysis to the rate of hydrolysis. To determine the rate constant without general base catalysis, the rate constants were assumed to be linear functions of the total buffer concentration and the Y-intercepts of the lines are the extrapolated rate constants at zero buffer concentration. A nonlinear least squares analysis was performed on eq. (70) using the rate constants extrapolated to zero buffer concentration with weighting equal to 1/(k_{obs})^2. These rate constants and the average pH of the two solutions with different total buffer concentration but with the same protonation ratio were fed into Program 6a (Appendix) which treats k_{-5}, k_{-2}K_{4}/k_{-3} and k_{5}/k_{-3} as the disposable parameters. The analysis gave values of 0.0181 s^{-1}, 2.19 x 10^{-3} M and 0.905 for k_{-5}, k_{-2}K_{4}/k_{-3} and k_{5}/k_{-3}, respectively, with standard deviations of 3.0%, 36% and 8.9%. A plot of k_{obs} against pH with the calculated function is shown in Figure 30. It can be seen that there was fairly good agreement between the observed and calculated rate constants, the difference not being greater than 11%.

To obtain more accurate results, all the rate constants should be included in the analysis and the contribution due to general base catalysis should be included in the rate equation. In the proposed mechanism, two steps are likely to be general base catalyzed - the attack of water on the iminium ion to form the protonated carbinolamine whose rate is governed by k_{-5} and the removal of the proton.
Fig. 30. First Order Rate Constant for the Hydrolysis of N-Isopropylidinesisoxazolidinium Ion at 35°C Extrapolated to Zero Buffer Concentration vs. pH.
from the oxygen of the protonated carbinolamine to form the zwitterion whose rate is governed by $k_3$. Since $k_5$ predominates in the pH region buffered by acetate and cacodylate, it was decided that general base catalysis terms be added only to $k_5$. Addition of similar terms to $k_3$ would produce a very complicated equation with several disposable parameters. Thus, a six-parameter nonlinear least squares analysis was performed on eq. (73) where $k_5 = k_5/k_5$, $k_{5f}$, $k_{5a}$, and $k_{5c}$ are the second order rate constants for general base catalysis by

$$
\frac{k_{obs}}{[H^+]} = \frac{(k_{5f} + k_{5a}[F^-] + k_{5c}[C^-])([H^+] + k_{2}K_4/k_{-3})}{k_5k_{-3}}
$$

(73)

formate, acetate and cacodylate ions, respectively, on the attack of water on the iminium ion and $[F^-], [A^-]$ and $[C^-]$ are the concentrations of formate, acetate and cacodylate ions. The sum of the squares of the fractional deviations was minimized. It can be noticed that eq. (73) is the same as eq. (70) except that general base catalysis terms were added to $k_5$. All the rate constants in Table 13 were fed into Program 7 (Appendix) which carried out the calculation. The concentrations of general bases were calculated from the observed pH and the total buffer concentration. In eq. (74), $[B]$ is the concentration of the general base which may be formate, acetate or

$$
[B] = \frac{\text{total buffer conc.}}{1 + 10^{(pK-pH+\log \gamma)}}
$$

(74)
 cacodylate ions and pK is the negative logarithm of the dissociation constant of the conjugate acid of the general base and γ is the activity coefficient calculated from the Davies equation.

The analysis resulted in the following calculated parameters and their standard deviations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>k₅</td>
<td>0.0185 s⁻¹</td>
<td>4.90 x 10⁻⁴ s⁻¹</td>
</tr>
<tr>
<td>k₅f</td>
<td>0.0553 M⁻¹s⁻¹</td>
<td>0.0204 M⁻¹ s⁻¹</td>
</tr>
<tr>
<td>k₅a</td>
<td>0.0212 M⁻¹s⁻¹</td>
<td>4.52 x 10⁻³M⁻¹s⁻¹</td>
</tr>
<tr>
<td>k₅c</td>
<td>0.0432 M⁻¹s⁻¹</td>
<td>5.92 x 10⁻³M⁻¹s⁻¹</td>
</tr>
<tr>
<td>k⁻₂K₄/k₃</td>
<td>3.21 x 10⁻³ M</td>
<td>8.42 x 10⁻⁴ M</td>
</tr>
<tr>
<td>K₅k⁻₅</td>
<td>0.0192 s⁻¹</td>
<td>1.03 x 10⁻³ s⁻¹</td>
</tr>
</tbody>
</table>

It can be seen that the calculated values for k₅ and k⁻₂K₄/k₃ are in fair agreement with the values obtained by analysis of eq. (70). Also, the value 0.0192 s⁻¹ for K₅k⁻₅ is very close to the value obtained by dividing k₅(0.0181 s⁻¹) by K₅/k₃ (0.905) which are the values obtained by analysis of eq. (70) using rate constants extrapolated to zero buffer concentration. The relative magnitudes of the general base catalysis constants for acetate and cacodylate appear to be in agreement with their basicities but that for formate, which is a weaker base than either of the two, is higher than both values. A very likely explanation for this is that formate is acting as a general base catalyst not only on the attack of water on the iminium
ion but also on the removal of proton from the oxygen of the protonated carbinolamine to form the zwitterion which is the step predominating at the rising part of the curve. In other words, this is an example of the fairly common deviation from a linear free energy relationship due to a change in mechanism. Also, the value for general base catalysis constant for formate may not be as reliable as the other parameters because it has the highest relative standard deviation (37\%).

An investigation of the reliability of $k_{-5f}$ was attempted. A plot of log of the general base catalysis constants against the pK's of the conjugate acids of the bases was constructed. The line passing through the points for acetate and cacodylate has a slope of 0.198 and a Y-intercept of -2.62. At its pK value, the point for formate lies about 0.6 log units above the line. If general base catalysis by formate on the attack of water on the iminium ion were proportional to its basicity, that is, if the point for formate were to lie on the Brønsted line determined by points for acetate and cacodylate, $k_{-5f}$ would have a value of 0.0135 M$^{-1}$s$^{-1}$. Thus eq. (73) was altered such that the value for $k_{-5f}$ was set equal to 0.0135 to give rise to eq. (75).

$$k_{obs} = \frac{(k_{-5} + 0.0135[F^-] + k_{-5a}[A^-] + k_{-5c}[C^-])([H^+] + k_{-2}K_4/k_{-3})}{[H^+]} \left(\frac{k_{-5} + 0.0135[F^-] + k_{-5a}[A^-] + k_{-5c}[C^-]}{K_Sk_{-3}}\right) + k_{-2}K_4/k_{-3}$$ (75)
A five-parameter nonlinear least squares analysis on eq. (75) was performed using all the rate constants in Table 23. The analysis resulted in the following values.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_5$</td>
<td>0.0185 s$^{-1}$</td>
<td>5.43 x 10$^{-4}$ s$^{-1}$</td>
</tr>
<tr>
<td>$k_{5a}$</td>
<td>0.0202 M$^{-1}$s$^{-1}$</td>
<td>5.17 x 10$^{-3}$ M$^{-1}$s$^{-1}$</td>
</tr>
<tr>
<td>$k_{5c}$</td>
<td>0.0426 M$^{-1}$s$^{-1}$</td>
<td>6.77 x 10$^{-3}$ M$^{-1}$s$^{-1}$</td>
</tr>
<tr>
<td>$k_2K_4/k_3$</td>
<td>4.72 x 10$^{-3}$ M</td>
<td>1.09 x 10$^{-3}$ M</td>
</tr>
<tr>
<td>$K_5k_3$</td>
<td>0.0185 s$^{-1}$</td>
<td>1.13 x 10$^{-3}$ s$^{-1}$</td>
</tr>
</tbody>
</table>

The relative standard deviations for all the parameters became larger as a result of the new analysis. The effect is largest on $k_2K_4/k_3$ which is expected because this parameter involves the reactions which predominate at the pH region buffered by formate. However, the values for all the other parameters, except for $k_2K_4/k_3$, are fairly close to the values obtained from analysis of eq. (73). This indicates that the deviation of the point for formate catalysis from the Brönsted line may be due to the unreliability with which the parameter was calculated instead of the possibility that the reaction follows a mechanism different from that proposed in eqs. (58) through (62). Thus, the values obtained from the nonlinear analysis of eq. (73) were considered acceptable.
Fig. 31. Log of the General Base Catalysis Constant for the Hydrolysis of N-Isopropylideneisoaxazolidinium Ion at 35°C vs. the pK of the Conjugate Acid of the General Base Catalyst.
I. Dedeuteration of Acetone-$d_6$ in the Presence of Pyrrolidine and 3-Dimethylaminopropionitrile

In labelling the kinetic samples, the letter E is placed before the abbreviation(s) of the amine or amines used in the kinetic run. The first digit represents the number of times kinetic runs have been done using the amine(s). The next two digits which can range from 01 to 10 represent the number of that sample on that particular kinetic run. For example, E-DPN-FYR-300 is the label for the third kinetic run using 3-dimethylaminopropionitrile and pyrrolidine. The samples in that kinetic run will have the labels E-DPN-FYR-301 to E-DPN-FYR-310.

The outputs from mass spectral analyses are strips of photographic paper, one for each kinetic sample. The heights of the peaks with m/e values from 58 to 64 corresponding to acetone-$d_0$ to acetone-$d_6$ were measured. The height of the peak at m/e = 65 was also measured to correct for the amount of $^{18}C$ and $^{13}C$ isotopes. The measured heights were fed into a program written by Dr. R. Flachskam which calculates the corrected heights of the parent peaks for the $d_6$, $d_5$, $d_4$, $d_3$, $d_2$, $d_1$ and $d_0$ forms of acetone by assuming normal abundances of $^{18}C$ and $^{13}C$ in each fraction which are 1.11% and 0.20%, respectively, of the total carbons and oxygens. It then calculates the fraction of acetone of different deuterium content by eq. (76), neglecting isotope effects on fragmentation.

\[ f_6 = \frac{h_{64}}{\left( \sum_{i=58}^{64} h_i \right)} \]  

(76)
In eq. (76), \( f_e \) is the fraction of acetone which is hexa-deuterated, \( h_{d4} \) is the corrected peak height at \( m/e = 64 \) (that is, the height that would have been obtained at \( m/e = 64 \) if \(^{12}C\) and \(^{16}O\) were the only isotopes of carbon and oxygen present), and \( h_i \) is the corrected peak height at \( m/e = i \).

In this study, acetone-\( d_3 \) was allowed to undergo exchange of its deuteriums with protons from the solvent. This results in consecutive dedeuterations.

\[
d_6 \overset{k_6}{\longrightarrow} d_5 \overset{k_5}{\longrightarrow} d_4 \overset{k_4}{\longrightarrow} \text{etc}
\]  

(77)

In all cases, the loss of the \( d_6 \) species is a first order reaction.

\[
f_e = (f_{e0}) e^{-kt}
\]  

(78)

In the presence of secondary amines, acetone forms iminium ions, which can either hydrolyze to form acetone and the amine or dedeuterate to form the \( d_5 \) iminium ion. The latter can hydrolyze to form the amine and acetone-\( d_5 \) or it can undergo another dedeuteration to form the \( d_4 \) iminium ion. The dedeuteration of acetone without passing through the iminium ion intermediates proceeds concurrently with these processes. This reaction, whose rate constant is equal to \( k_p \) in the following scheme is brought about by the solvent and catalysis such as hydronium and hydroxide ions and the free amines. The same catalysts can also cause dedeuteration of the iminium ions. Scheme V is similar to that presented in earlier work.\(^{12}\)
In Scheme V, secondary deuterium isotope effects are neglected such that the rates of iminium ion formation by acetone-\(d_4\) and acetone-\(d_5\) are considered equal and that acetone-\(d_5\) undergoes deuteriation at exactly \(5/6\) the rate at which acetone-\(d_4\) does. For the step governed by \(k_p\), acetone has to pass through an enol or enolate ion intermediate which then accepts a proton from the solvent to form the acetone species of lower deuterium content. In the step governed by \(k_e\), a base has to remove the deuteron from the iminium ion to transform it to an enamine. The deuterated base exchanges the deuteron with protons from the solvent. The protonated base then provides the proton to convert the enamine to the iminium ion-\(d_5\).

\[
\begin{align*}
\text{CD}_3\text{C}-\text{CD}_3 + B & \rightleftharpoons \text{CD}_3\text{C}^+\text{CD}_2 + \text{BD}^+ \\
\text{BD}^+ + \text{H}_2\text{O} & \rightarrow \text{BH}^+ + \text{DOH} \\
\text{BH}^+ + \text{CD}_3\text{C}^=\text{CD}_2 & \rightleftharpoons \text{CD}_3\text{C}-\text{CD}_2\text{H} + B
\end{align*}
\]

\(175\)
According to Scheme V, if a steady-state assumption is made for the intermediate iminium ions, the first order rate constant for the loss of acetone-\(d_6\) may be expressed in equation (82), where \(r\) is a ratio of rate constants \(k_e/k_i\). Also, from Scheme V, an expression for the formation of acetone-\(d_6\) may be derived.

\[
k_{-6} = k + \frac{k_{im}r}{1+r} \quad (82)
\]

\[
\frac{df_5}{dt} = k_p f_e - (5/6)k_p f_5 + k_{im} (\frac{r}{1+r}) \frac{1}{1+(5/6)r} f_e - k_{im} \frac{5r/6}{1+5r/6} \quad (83)
\]

Integration results in eq. (84) where \(q\) is defined in eq. (85).

\[
f_5 = (6f_6)\circ + (f_5)\circ e^{-(1-q/6)k_6t} - 6f_6\circ e^{-k_6t} \quad (84)
\]

\[
q = \frac{5r(k_p/k_6) + 6}{5r + 6} \quad (85)
\]

If acetone-\(d_6\) is dedeuterated via the pathway which does not involve iminium ions (\(k_6 - k_p\)) or if the iminium ions hydrolyze much faster than they can undergo exchange (\(r \ll 1\)), \(q\) will be equal to 1.00. The program which calculates the first order rate constant for the disappearance of acetone-\(d_6\) (Program 9, Appendix) was written by Dr. J. Hine and also calculates the value of \(q\) by a nonlinear least squares analysis of eq. (78) and eq. (84) given the values of time, \(f_6\) and \(f_5\) for the different samples in a kinetic run.

Table 24 shows the results of the dedeuteration experiments with acetone-\(d_6\) in the presence of pyrrolidine (PYR) and
表格 24

在水中的完成的去甲基化实验结果

<table>
<thead>
<tr>
<th>Kinetic Run #</th>
<th>$pH_{obs}$</th>
<th>$[DPN]_t$</th>
<th>$[PYR]_t$</th>
<th>Ionic Strength (M)</th>
<th>$10^5 k_e (s^{-1})$</th>
<th>$q$</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-DPN-PYR-200</td>
<td>7.08</td>
<td>0.2009</td>
<td>0.1997</td>
<td>0.2898</td>
<td>9.80 ± 0.23</td>
<td>0.471 ± 0.023</td>
</tr>
<tr>
<td>E-DPN-PYR-300</td>
<td>6.325</td>
<td>0.2007</td>
<td>0.1998</td>
<td>0.3605</td>
<td>2.17 ± 0.17</td>
<td>0.413 ± 0.034</td>
</tr>
<tr>
<td>E-DPN-PYR-400</td>
<td>8.045</td>
<td>0.2008</td>
<td>0.2019</td>
<td>0.2156</td>
<td>32.1 ± 1.6</td>
<td>0.662 ± 0.050</td>
</tr>
<tr>
<td>E-DPN-PYR-500</td>
<td>6.40</td>
<td>0.2009</td>
<td>0.2007</td>
<td>0.3610</td>
<td>2.43 ± 0.15</td>
<td>0.457 ± 0.062</td>
</tr>
<tr>
<td>E-DPN-PYR-600</td>
<td>7.92</td>
<td>0.2012</td>
<td>0.2016</td>
<td>0.2156</td>
<td>35.1 ± 0.18</td>
<td>0.604 ± 0.050</td>
</tr>
<tr>
<td>E-DPN-PYR-700</td>
<td>7.075</td>
<td>0.2005</td>
<td>0.1997</td>
<td>0.2898</td>
<td>8.92 ± 0.29</td>
<td>0.430 ± 0.032</td>
</tr>
</tbody>
</table>
3-dimethylaminopropionitrile (DPN) at pH's buffered by the latter amine and where the former is essentially completely protonated. The source of ions in these experiments is hydrochloric acid which was added to protonate essentially all the PYR and a significant fraction of the DPN.

Since the DPN is the base present in largest amount, it is assumed to be mainly responsible for the deuteration of the iminium ion.

\[ k_e = k_n[DPN] \] (86)

If it is assumed that there is no acid catalyzed iminium ion formation between acetone and pyrrolidine, the balanced equation for the reaction governed by \( k_{im} \) is eq. (87).

\[
\begin{align*}
(CD_3)_2C=O + HN & \rightleftharpoons (CD_3)_2C=N^+ + OH^- \\
\end{align*}
\] (87)

The principle of microscopic reversibility states that the hydrolysis of the iminium ion is brought about solely by attack of hydroxide ions.

\[ k_d = k_r[OH^-] \] (88)

Thus, the ratio of rate constants \( r = k_e/k_d \) can be expressed in eq. (89).

\[ r = \frac{k_n[DPN]}{k_r[OH^-]} \] (89)

A combination of the equations for the dissociation of protonated DPN and the self-ionization of water results in eq. (90) where
\( K_{DPNH^+} \) is the dissociation constant for protonated DPN equal to 10^{-6.89} at 35^\circ C and \( K_w \) is the autoprotolysis constant of water, equal to 10^{-13.68} at 35^\circ C.47

\[
\frac{[DPN]}{[OH^-]} = \frac{[DPNH^+]K_{DPNH^+}}{K_w}
\]  

(90)

Thus eq. (89) becomes eq. (91).

\[
r = \frac{k_nK_{DPNH^+}[DPNH^+]}{k_pK_w}
\]  

(91)

The \( k_{im} \) in Scheme V can be expressed as a product of a second order rate constant, \( k_B \) and the free pyrrolidine concentration, assuming there is no acid-catalyzed iminium ion formation.

\[
k_{im} = k_B[PYR]
\]  

(92)

Combining eqs. (82), (91), and (92) results in eq. (93) where

\[
u = \frac{k_nK_{DPNH^+}}{k_pK_w}
\]

\[
k_a = k_p + k_B[PYR] \frac{u[DPNH^+]}{1 + u[DPNH^+]}
\]  

(93)

A nonlinear least squares analysis was performed on eq. (93) by feeding the results in Table 24 into Program 10 (Appendix) with weighting equal to \( 1/(k_a)^2 \). The sum of the rate constants for
dedeuteration of acetone by the two bases present in significant amounts, hydroxide ions and free DPN is \( k_p \). From previous work, \( k_{OH} \) is equal to \( 6.5 \times 10^{-2} \text{ M}^{-1}\text{s}^{-1} \) and \( k_{DPN} \) is equal to \( 2.41 \times 10^{-4} \text{ M}^{-1}\text{s}^{-1} \).

\[
\frac{k}{p} = k_{OH}[OH^-] + k_{DPN}[DPN] \tag{94}
\]

The concentrations of free pyrrolidine and DPNH\(^+\) were calculated from the total amine concentrations and the observed pH's.

\[
[\text{Am}] = \frac{[\text{Am}]_t}{1 + 10^{(pK - pH_{obs} - \log \gamma)}} \tag{95}
\]

\[
[\text{AmH}^+] = \frac{[\text{Am}]_t}{1 + 10^{(pH_{obs} - \log \gamma - pK)}} \tag{96}
\]

The least squares analysis resulted in values of 34.4 and 5.09 \text{ M}^{-1}\text{s}^{-1} for \( u \) and \( k_p \), respectively, with standard deviations of 19\% and 9\%. The analysis gave fairly good results with no more than 12\% relative deviation between the observed and calculated \( k_e \)'s. The calculation of the value of \( u \) introduces the possibility of calculating \( q \) by another method besides that from \( k_e \) values using eq. (84) whose results are listed in Table 24. Since \( r = u[\text{DPNH}^+] \), eq. (85) can now be expressed as eq. (97). The \( q \) values resulting from this equation did not differ by more than 13\% from the \( q \) values calculated from \( f_5 \) values using eq. (84).

\[
q = \frac{5u[\text{DPNH}^+](k_p/k_e) + 6}{5u[\text{DPNH}^+] + 6} \tag{97}
\]
J. Dedeuteration of Acetone-$d_6$ in the Presence of Pyridine, Pyrrolidine and Dimethylamine

The solutions used for these reactions are buffered by 0.4 M total pyridine which is half-protonated. Thus, the secondary amines - pyrrolidine and dimethylamine - are essentially completely protonated in these solutions. The results of the dedeuteration studies are presented in Table 25. It can be seen that 0.1 M pyrrolidinium ions increase the rate of dedeuteration of acetone-$d_6$ in 1:1 pyridine buffers by 5-fold while the same amount of dimethylammonium ions increase the rate by only 12%.

The value $r$, equal to $k_e/k_d$, the ratio of the rate constant for exchange and the rate constant for hydrolysis of the iminium ion, can be calculated by a rearrangement of eq. (85).

$$ r = \frac{6 k_e (1-q)}{5 \left( k_e q - k_p \right) } \quad \text{(98)} $$

The rate constant for simple base-catalyzed removal of the deuterium from acetone-$d_6$, $k_p$, is simply the $k_e$ for the kinetic run without the secondary amines. Using the average of the $k_e$'s from the two duplicate runs and the average $k_p$, eq. (98) gives $r$ values of 0.890 for the pyrrolidinium ion-catalyzed reaction and 9.1 for the dimethylammonium ion-catalyzed reaction. This means that with pyrrolidine, the iminium ion has about equal chances of undergoing
TABLE 25

RESULTS OF DEDEUTERATION EXPERIMENTS WITH ACETONE-\text{d}_2 IN THE PRESENCE OF PYRIDINE, PYRROLIDINE AND DIMETHYLAMINE IN WATER AT 35°K

<table>
<thead>
<tr>
<th>Kinetic Run #</th>
<th>$pH_{\text{obs}}$</th>
<th>$[\text{PYRDN}]_t$</th>
<th>[sec-amine]</th>
<th>$10^7 k_3$ (s$^{-1}$)</th>
<th>$q$</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-PYRDN-200</td>
<td>5.09</td>
<td>0.3856</td>
<td>none</td>
<td>5.08 ± 0.09</td>
<td>0.942 ± 0.019</td>
</tr>
<tr>
<td>E-PYRDN-300</td>
<td>5.06</td>
<td>0.3854</td>
<td>none</td>
<td>5.04 ± 0.30</td>
<td>0.879 ± 0.061</td>
</tr>
<tr>
<td>E-PYRDN-PYR-200</td>
<td>5.06</td>
<td>0.3847</td>
<td>0.1000</td>
<td>26.5 ± 0.5</td>
<td>0.654 ± 0.046</td>
</tr>
<tr>
<td>E-PYRDN-PYR-300</td>
<td>5.04</td>
<td>0.3866</td>
<td>0.09637</td>
<td>25.2 ± 0.6</td>
<td>0.662 ± 0.0254</td>
</tr>
<tr>
<td>E-PYRDN-DMA-200</td>
<td>5.06</td>
<td>0.3849</td>
<td>0.0956</td>
<td>5.65 ± 0.12</td>
<td>0.910 ± 0.023</td>
</tr>
<tr>
<td>E-PYRDN-DMA-300</td>
<td>5.055</td>
<td>0.3856</td>
<td>0.0957</td>
<td>5.67 ± 0.10</td>
<td>0.093 ± 0.018</td>
</tr>
</tbody>
</table>
exchange and hydrolysis back to ketone and amine. The calculated
r value for the dimethylammonium ion-catalyzed reaction cannot be
relied upon as a basis for which step is rate-controlling - iminium
ion formation or exchange. This is because, in the denominator of
eq. (98), two values which are within experimental uncertainties of
each other are being subtracted, $k_{eq}$ and $k_p$. The calculated r value
of 9.1 indicates that the iminium ions undergo exchange most of the
time and only occasionally hydrolyzes back to ketone and amine. This
means that, if such an r value is correct, acetone-$d_3$ can be
transformed to acetone-$d_4$ or another acetone species with less
deuteriums without passing through acetone-$d_5$. However, an
examination of the percentages of the various acetone species at
different times during the reaction does not show a clear tendency
for tri-, di-, and mono-protonated acetone to appear earlier in the
reaction compared to the results of dedeuteration with pyridine alone.
This failure to show such a tendency may be due to r not being large
enough or to only a very small fraction of the total reaction being
due to catalysis via iminium ions or a combination of the two.
Solving for $k_{im}$ from eq. (99) which is a rearrangement of eq. (82)
gives values of $4.40 \times 10^{-8} s^{-1}$ and $6.64 \times 10^{-8} s^{-1}$ for the PYR- and

$$
k_{im} = \frac{(k_{eq} - k_p)(1+r)}{r}
$$

(99)

DMA-catalyzed reactions, respectively. If it is assumed that there
is contribution by acid catalysis in iminium ion formation, then the
first order rate constant for iminium ion formation, $k_{im}$, will be a sum of two terms (eq. 100). The values of $k_{em}$ for light acetone have been determined previously - $0.0504 \text{ M}^{-1}\text{s}^{-1}$ for DMA and $4.25 \text{ M}^{-1}\text{s}^{-1}$ for PYR. Using the values of the free amine and protonated amine concentrations calculated from eqs. (95) and (96), $k_{amn}$ was found to be equal to $4.18 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ for pyrrolidine and $5.62 \times 10^{-7} \text{ M}^{-1}\text{s}^{-1}$ for dimethylamine. These values are the second order rate constants for acid-catalyzed iminium ion formation. From these values, it can be calculated that, under the experimental conditions, $94\%$ of the iminium ion formation between acetone-$d_8$ and pyrrolidine is acid-catalyzed while for dimethylamine, the corresponding value is $81\%$.

If there were no acid catalysis in iminium ion formation, the second term in eq. (100) should be zero. The value of $k_{im}$ calculated with this assumption can be used in eq. (101) which is a rearrangement of eq. (82) to calculate $r$. This resulted in negative values of $r$ for both amines.

$$r = \frac{k_{e} - k_{p}}{k_{im} - k_{e} + k_{p}}$$

(101)

This negative value arose from the fact that $k_{im}$ is smaller than $k_{e} - k_{p}$. Only if catalysis by the protonated amine is included will make $r$ positive and physically plausible. Thus, acid-catalyzed
iminium ion formation between acetone and the two amines at this pH region is real.

K. Dedeutration of Acetone-$d_3$ in the Presence of Pyridine, Pyrazolidine and 1,2-Dimethylhydrazine

The results of dedeuteration experiments in the presence of pyridine and either pyrazolidine or 1,2-dimethylhydrazine are presented in Table 26. The solutions used for this study are buffered by 0.4 M total pyridine which is half-protonated. The secondary amine catalysts are essentially completely protonated at this pH region. Comparison of the results in Table 26 with those of Table 25 shows that 0.1 M pyrazolidinium ions increase the rate of dedeuteration of acetone-$d_3$ in 1:1 pyridine buffers by 55-fold while 1,2-dimethylhydrazinimum ions increase the rate only 11-fold. Since it has been established that iminium ion formation occurs between acetone and the protonated amine, the reaction should follow Scheme VI.

\[
\text{Scheme VI}
\]

\[
\begin{align*}
\text{CD}_3\text{COCD}_3 + H_2N^+ & \rightleftharpoons K \text{CD}_3\text{C}-\text{CD}_3 + H_2O \\
\text{CD}_3\text{COCD}_2H + H_2N^+ & \rightleftharpoons K \text{CD}_3\text{C}-\text{CD}_2H + H_2O \\
\text{acetone-}d_4 & \rightleftharpoons \text{imininium ion-}d_4
\end{align*}
\]
<table>
<thead>
<tr>
<th>Kinetic Run #</th>
<th>$pH_{\text{obs}}$</th>
<th>[PYRDN]</th>
<th>[sec-amine]</th>
<th>$10^6 k_e$ (s$^{-1}$)</th>
<th>$q$</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-PYRDN-PYRZN-200</td>
<td>5.09</td>
<td>0.3892</td>
<td>0.0962</td>
<td>$28.1 \pm 0.8$</td>
<td>$0.916 \pm 0.034$</td>
</tr>
<tr>
<td>E-PYRDN-PYRZN-300</td>
<td>5.02</td>
<td>0.3852</td>
<td>0.0963</td>
<td>$28.0 \pm 0.6$</td>
<td>$0.918 \pm 0.025$</td>
</tr>
<tr>
<td>E-PYRDN-DHZ-200</td>
<td>5.06</td>
<td>0.3825</td>
<td>0.09619</td>
<td>$5.76 \pm 0.06$</td>
<td>$0.963 \pm 0.011$</td>
</tr>
<tr>
<td>E-PYRDN-DHZ-300</td>
<td>5.06</td>
<td>0.3846</td>
<td>0.09668</td>
<td>$5.71 \pm 0.08$</td>
<td>$0.959 \pm 0.013$</td>
</tr>
</tbody>
</table>
The two deuteromethyl groups in the iminium ion-\(^{\text{d6}}\) are nonequivalent. The abstraction of deuteron from one side is likely to be preferred over that from the other side. However, this nonequivalence is not expected to cause any complications because iminium ion formation occurs as a fast equilibrium compared to dedeuteration such that there will also be rapid interconversion of the two iminium ion-\(^{\text{d6}}\) geometric isomers.

Besides the uncatalyzed, hydronium ion, hydroxide ion-, and pyridine-catalyzed enolization of acetone, there is also attack of pyridine to remove the deuterons from the initially formed iminium ion. The formation of the latter is fast compared to dedeuteration, as seen from NMR results. The removal of deuterons from the iminium ion by water and hydroxide ions is being neglected based on previous results on isobutyraldehyde-2-\(^{\text{d}}\) exchange in the presence of methylammonium ions and various buffers.\(^{52}\) In that work, it was estimated that hydroxide ion is at best \(1.4 \times 10^4\) times more effective than pyridine and pyridine is \(6 \times 10^4\) times more effective than water in dedeuterating the \(N\)-methyliminium ion of isobutyraldehyde. Under the conditions of the experiments in this study, the pyridine concentration is \(5 \times 10^8\) times greater than the hydroxide ion concentration and that of water is 270 times greater than that of pyridine. If the relative abilities of these bases to dedeuterate the \(N\)-methyliminium ion of isobutyraldehyde are similar to those abilities to dedeuterate \(N\)-isopropylidenepyrazolidinium and
1 8 8

N-isopropylidene-1,2-dimethylhydrazinium ions, under the conditions of the experiments, dedeuteration of the iminium ions by pyridine should be more than 10^5 times faster than dedeuteration by hydroxide and more than 200 times faster than dedeuteration by water. Thus, the terms due to these processes were not included in the rate equation.

The terms due to dedeuteration of acetone-d₈ and the iminium ion by free secondary amine were also not included because only less than half of a percent of the secondary amines exists in the unprotonated form which means that the concentration of free pyridine is more than 400 times the concentration of free secondary amine. 3,4-Lutidine, which has about the same basicity as PYRZN and DMDE, is only about twice as effective as pyridine in dedeuterating the N-methyliuminium ion of isobutyraldehyde. Clearly, such a slight increase in the ability to dedeuterate the iminium ion due to increase in basicity is not enough to offset the very large difference in concentration between pyridine and the secondary amines. The first order rate constant for the disappearance of acetone-d₈, k₈, is then expressed in eq. (102).

\[ k_8 = k_w + k_h [H^+] + k_{OH^-} + k_{\text{PYRZN}} + k_{\text{II}} [\text{AmH}^+] [\text{PYRZN}] \] (102)

Previous work on monofunctional catalysis of acetone-d₈ exchange reported values of 4.40 x 10^{-10}s^{-1}, 1.45 x 10^{-5} M^{-1}s^{-1}, and 6.5 x 10^{-2} M^{-1}s^{-1} for k_w', k_h', and k_{OH}', respectively. In the case
of the deuteration with pyridine without secondary amines, only
the first four terms on the right side of eq. (102) make
significant contribution to the rate. From those kinetic runs
(E-PYRDN-200 and 300), the value of \( k_{\text{PYRDN}} \) is calculated to be \( 2.62 \times 10^{-6} \text{ M}^{-1}\text{s}^{-1} \). In eq. (102) the \( k_a \)'s are the experimentally
determined values. Thus, only \( k_{\text{II}} \) remains unknown. From the
results in Table 26, \( k_{\text{II}} \) for PYRZN was calculated to be equal to
\( 7.65 \times 10^{-3} \text{ M}^2\text{s}^{-1} \) and \( k_{\text{II}} \) for DMHZ was calculated to be equal to
\( 2.92 \times 10^{-4} \text{ M}^2\text{s}^{-1} \).

L. Dedeuteration of Acetone-\( \delta_6 \) in the Presence of Pyridine,
Isoxazolidine and \( \text{O}_2\text{N-DMH} \)

The experimental results for deuteration of acetone-\( \delta_6 \) in
the presence of pyridine and either ISOX or DMHZ or the secondary
amine alone are presented in Table 27. In these experiments, unlike
in the PYRZN and DMHZ cases, there are significant amounts of free
secondary amine at the pH's studied. Thus, at equilibrium, four
amine species exist - free secondary amine and its salt and
pyridine and pyridinium ions. The amount of free secondary amine
has to be considered because it is also capable of acting as a base
to remove the \( \alpha \)-deuterons from acetone-\( \delta_6 \) and from the iminium
ions. Immediately after injection of acetone-\( \delta_6 \), the pH of the
solution changes because of the fact that iminium ions are being
formed and the equilibrium between the free amines and their salts
<table>
<thead>
<tr>
<th>Kinetic Run #</th>
<th>$pH_{obs}$</th>
<th>$[\text{PYRDN}]_t$</th>
<th>$[\text{sec-amine}]_t$</th>
<th>$\text{HCl or NaOH added}$</th>
<th>$10^6 k_0 \text{ (s}^{-1})$</th>
<th>$q$</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-PYRDN-ISOX-300</td>
<td>5.00</td>
<td>0.3868</td>
<td>0.09653</td>
<td>0.1931 M HCl</td>
<td>13.3 ± 0.2</td>
<td>0.981 ± 0.019</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-400</td>
<td>5.56</td>
<td>0.3913</td>
<td>0.1936</td>
<td>0</td>
<td>39.5 ± 0.8</td>
<td>0.994 ± 0.021</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-800</td>
<td>5.25</td>
<td>0.3855</td>
<td>0.09653</td>
<td>0.1448 M HCl</td>
<td>14.4 ± 0.4</td>
<td>0.985 ± 0.027</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-900</td>
<td>5.12</td>
<td>0.3844</td>
<td>0.1937</td>
<td>0.1448 M HCl</td>
<td>32.5 ± 0.6</td>
<td>0.969 ± 0.019</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-1000</td>
<td>5.23</td>
<td>0.3809</td>
<td>0.1922</td>
<td>0.09627 M HCl</td>
<td>34.0 ± 0.6</td>
<td>0.985 ± 0.019</td>
</tr>
<tr>
<td>E-ISOX-300</td>
<td>5.00</td>
<td>0</td>
<td>0.1922</td>
<td>0.04805 M NaOH</td>
<td>8.23 ± 0.19</td>
<td>0.967 ± 0.022</td>
</tr>
<tr>
<td>E-ISOX-400</td>
<td>5.86</td>
<td>0</td>
<td>0.1866</td>
<td>0.1276 M NaOH</td>
<td>9.83 ± 0.30</td>
<td>0.985 ± 0.030</td>
</tr>
<tr>
<td>E-PYRDN-ONHX-300</td>
<td>5.28</td>
<td>0.3856</td>
<td>0.1912</td>
<td>0</td>
<td>66.1 ± 0.3</td>
<td>1.01 ± 0.031</td>
</tr>
<tr>
<td>E-PYRDN-ONHX-400</td>
<td>5.03</td>
<td>0.3846</td>
<td>0.2868</td>
<td>0</td>
<td>146 ± 3</td>
<td>0.995 ± 0.020</td>
</tr>
<tr>
<td>E-ONHX-300</td>
<td>4.11</td>
<td>0</td>
<td>0.1912</td>
<td>0.04805 M NaOH</td>
<td>23.1 ± 0.3</td>
<td>0.980 ± 0.017</td>
</tr>
<tr>
<td>E-ONHX-500</td>
<td>4.95</td>
<td>0</td>
<td>0.2860</td>
<td>0.1922 M NaOH</td>
<td>60.8 ± 2</td>
<td>0.988 ± 0.022</td>
</tr>
</tbody>
</table>

**TABLE 27**

RESULTS OF DEDEUTERATION OF ACETONE-$d_6$ IN THE PRESENCE OF PYRIDINE, ISOXAZOLIDINE AND $O,N$-DIMETHYLHYDROXYLAMINE
are disturbed. The observed pH's listed in Table 27 are the pH's measured after about 20 minutes, long after equilibrium has been established. This pH change is more pronounced in the solutions with ISOX than those with ONHX because of the much greater equilibrium constant for iminium ion between acetone and ISOH$^+$ than between acetone and ONHXH$^+$. The calculation of the equilibrium concentrations of all the species in solution would not be simple because of the several competing equilibria.

The two amines are in equilibrium with their protonated forms.

$$\text{PYRDNH}^+ \xrightleftharpoons{K_{\text{PYRDNH}^+}} \text{PYRDN} + H^+$$  \hspace{1cm} \text{(103)}

$$\text{AmH}^+ \xrightleftharpoons{K_{\text{AmH}^+}} \text{Am} + H^+$$  \hspace{1cm} \text{(104)}

Combining these two equilibria results in eq. (105)

$$\frac{[\text{PYRDNH}^+][\text{Am}]}{[\text{PYRDN}][\text{AmH}^+]} = \frac{K_{\text{AmH}^+}}{K_{\text{PYRDNH}^+}}$$  \hspace{1cm} \text{(105)}

The value of the pK for pyridine (5.11)$^{53}$ was used to calculate $\frac{K_{\text{AmH}^+}}{K_{\text{PYRDNH}^+}}$. The sum of the equilibrium concentrations of free and protonated pyridine is equal to the total pyridine concentration which is known.

$$[\text{PYRDN}] + [\text{PYRDNH}^+] = [\text{PYRDN}]_t$$  \hspace{1cm} \text{(106)}

The sum of the equilibrium concentrations of acetone and the iminium ion is equal to 0.52 M.
\[ [\text{Ac}] + [\text{Im}^+] = 0.52 \] 

(107)

The sum of the equilibrium concentrations of the free and protonated secondary amine and that of the iminium ion is equal to the total amine concentration which is known.

\[
[\text{Am}] + [\text{AmH}^+] + [\text{Im}^+] = [\text{Am}]_t
\]

(108)

The sum of the concentrations of the positive ions is equal to the sum of the concentrations of the negative ions.

\[
[\text{PYRDNH}^+] + [\text{AmH}^+] + [\text{Im}^+] = [\text{Cl}^-] + [\text{Br}^-] - [\text{Na}^+]
\]

(109)

The iminium ion exists in equilibrium with acetone and the protonated secondary amines. The equilibrium constant for iminium ion formation, \( K \), has been determined to be equal to 8.96 \( M^{-1} \) and 0.117 \( M^{-1} \) for ISOXH\(^+\) and ONHXH\(^+\), respectively.

\[
\frac{[\text{Im}^+]}{[\text{Ac}][\text{AmH}^+]} = K
\]

(110)

Combination of eqs. (105) to (110) leads to eq. (111) which is reduced to only one unknown - \([\text{AmH}^+]\).

\[
\frac{(K_{\text{AmH}^+}/K_{\text{PYRDNH}})[\text{PYRDN}]_t - I + [\text{AmH}^+] + A)[\text{AmH}^+]}{I - [\text{AmH}^+] - A} + [\text{AmH}^+] + A - [\text{Am}]_t = 0
\]

(111)

In eq. (111), \( A = \frac{0.52 \times K[\text{AmH}^+]}{1 + K[\text{AmH}^+]} \) and \( I = [\text{Cl}^-] + [\text{Br}^-] - [\text{Na}^+] \). The value of \([\text{AmH}^+]\) for each kinetic run was calculated from eq. (111).
using the Hewlett-Packard Math Pack. The remaining five unknowns, 
[Am], [PYRDN], [PYRDNH⁺], [Im⁺], and [Ac] were calculated from one 
or a combination of eqs. (105) through (110). The calculated 
equilibrium concentrations are listed in Table 28.

It is seen from Table 28 in the ISOX cases 11 to 22% of the 
total amount of acetone is tied up as the iminium ion while for the 
ONHX cases the corresponding values are from 0.3 to 1.5%.

The dedeuteration process follows the reactions in Scheme VI 
plus some additional ones. These are the removal of the deuteron 
by the free secondary amine from the initially formed iminium ion and 
from acetone itself and spontaneous or non-catalyzed dedeuteration 
of the iminium ion. If the catalytic terms due to those reactions 
are added to eq. (102), eq. (112) is obtained.

\[
k_\circ = k_w + k_h [H^+] + k_{oh} [OH^-] + k_{pyrdn} [PYRDN] + k_{am} [Am] + k_I [AmH⁺]
\]
\[
+ k_{II} [AmH⁺][PYRDN] + k_{III} [AmH⁺][Am]
\]

(112)

A linear least squares analysis for each secondary amine on 
eq. (112) was performed using the results in Table 27 and the 
calculated equilibrium concentrations in Table 28, minimizing the 
sum of the squares of the fractional deviations between the 
observed and calculated k_\circ's. For the ISOX cases, doing the analysis 
on all seven kinetic runs resulted in poor agreement between the 
observed and calculated rate constants for the first, second, and
<table>
<thead>
<tr>
<th>Kinetic Run #</th>
<th>[Am]</th>
<th>[AmH⁺]</th>
<th>[PYRDN]</th>
<th>[PYRDNH⁺]</th>
<th>[Im⁺]</th>
<th>[Ac]</th>
</tr>
</thead>
<tbody>
<tr>
<td>E-PYRDN-ISOX-300</td>
<td>0.02557</td>
<td>0.01385</td>
<td>0.1682</td>
<td>0.2186</td>
<td>0.05741</td>
<td>0.4626</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-400</td>
<td>0.1077</td>
<td>0.01704</td>
<td>0.2836</td>
<td>0.1077</td>
<td>0.06887</td>
<td>0.4511</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-800</td>
<td>0.03358</td>
<td>0.01216</td>
<td>0.2051</td>
<td>0.1784</td>
<td>0.05109</td>
<td>0.4689</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-900</td>
<td>0.05983</td>
<td>0.02837</td>
<td>0.1798</td>
<td>0.2046</td>
<td>0.1054</td>
<td>0.4146</td>
</tr>
<tr>
<td>E-PYRDN-ISOX-1000</td>
<td>0.07354</td>
<td>0.02464</td>
<td>0.2112</td>
<td>0.1697</td>
<td>0.09402</td>
<td>0.4260</td>
</tr>
<tr>
<td>E-ISOX-300</td>
<td>0.0480</td>
<td>0.03105</td>
<td>0    0</td>
<td>0.1132</td>
<td>0.4086</td>
<td></td>
</tr>
<tr>
<td>E-ISOX-400</td>
<td>0.1276</td>
<td>0.01150</td>
<td>0    0</td>
<td>0.04770</td>
<td>0.4723</td>
<td></td>
</tr>
<tr>
<td>E-PYRDN-ONHX-300</td>
<td>0.1620</td>
<td>0.02752</td>
<td>0.2236</td>
<td>0.1620</td>
<td>0.00160</td>
<td>0.5180</td>
</tr>
<tr>
<td>E-PYRDN-ONHX-400</td>
<td>0.2170</td>
<td>0.06854</td>
<td>0.1676</td>
<td>0.2170</td>
<td>0.00398</td>
<td>0.5160</td>
</tr>
<tr>
<td>E-ONHX-300</td>
<td>0.04805</td>
<td>0.1352</td>
<td>0    0</td>
<td>0.00795</td>
<td>0.5120</td>
<td></td>
</tr>
<tr>
<td>E-ONHX-500</td>
<td>0.1922</td>
<td>0.08848</td>
<td>0    0</td>
<td>0.00532</td>
<td>0.5150</td>
<td></td>
</tr>
</tbody>
</table>
third runs (35%, 19%, and 30% deviations, respectively). The results of one or two kinetic runs were systematically discarded and the analysis was done on the resulting combinations. The best result was given by the analysis wherein the second (E-PYRDN-ISOX-400) and the third (E-PYRDN-ISOX-800) runs were discarded. The calculated parameters resulting from this analysis are shown below. The largest deviation between the observed and calculated $k_a$'s was only 0.26%.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{Am}$</td>
<td>$2.74 \times 10^{-3} \text{M}^{-1}\text{s}^{-1}$</td>
<td>$1.13 \times 10^{-6} \text{M}^{-1}\text{s}^{-1}$</td>
</tr>
<tr>
<td>$k_I$</td>
<td>$1.93 \times 10^{-5} \text{M}^{-1}\text{s}^{-1}$</td>
<td>$4.69 \times 10^{-6} \text{M}^{-1}\text{s}^{-1}$</td>
</tr>
<tr>
<td>$k_{II}$</td>
<td>$4.46 \times 10^{-3} \text{M}^{2}\text{s}^{-1}$</td>
<td>$1.41 \times 10^{-5} \text{M}^{2}\text{s}^{-1}$</td>
</tr>
<tr>
<td>$k_{III}$</td>
<td>$4.26 \times 10^{-3} \text{M}^{2}\text{s}^{-1}$</td>
<td>$1.30 \times 10^{-4} \text{M}^{2}\text{s}^{-1}$</td>
</tr>
</tbody>
</table>

At first, it might be thought that the failure of the results of all the kinetic runs to give a good least squares analysis is due to the non-applicability of the steady-state assumption for this system. In other words, equilibrium in iminium ion formation might not have been established prior to deuteriation such that the two processes occur concurrently at comparable rates. A lower limit for the first order rate constant for iminium ion formation between acetone-$d_6$ and isoxazolidinium ions at equilibrium can be obtained by multiplying the rate constant for hydrolysis calculated from eq. (73), the equilibrium constant for iminium ion formation which
is 8.96 M⁻¹, and the equilibrium concentration of isoxazolidinium ions shown in Table 28. The value that will be obtained is a lower limit because free pyridine and free isoxazolidine act as general bases in iminium ion formation but their contributions to the rate are unknown. It turns out that these lower limits for the rate constants for iminium ion formation are 70 to 650 times greater than the corresponding k_eq's which means that the assumption that iminium ion formation occurs as a rapid equilibrium prior to deuterization is valid. Thus, the non-applicability of the steady-state assumption would not heal the discarded runs.

For the ONHX cases, the analysis resulted in negative values for k_Am and k_I. When either one of the k_Am [Am] and k_I [AmH⁺] terms were omitted, the analysis on the remaining three parameters resulted in small negative values for k_Am or k_I. This means that the removal of the deuterium from the iminium ion by pyridine or free ONHX is much faster than the deuterization of acetone by free ONHX and uncatalyzed deuterization of the iminium ion that the rate for the latter two processes could not be measured. Thus, the k_Am [Am] and k_I [AmH⁺] terms were omitted and the analysis was performed with only two disposable parameters - k_II and k_III. The calculated values are shown below. The agreement between the observed and calculated values was a very good one with no more than 2.3% relative deviation.
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Calculated Value</th>
<th>Std. Dev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{II}$</td>
<td>$8.26 \times 10^{-3} \ \text{M}^{-2}\text{s}^{-1}$</td>
<td>$1.83 \times 10^{-4} \ \text{M}^{-2}\text{s}^{-1}$</td>
</tr>
<tr>
<td>$k_{III}$</td>
<td>$3.57 \times 10^{-3} \ \text{M}^{-2}\text{s}^{-1}$</td>
<td>$5.30 \times 10^{-5} \ \text{M}^{-2}\text{s}^{-1}$</td>
</tr>
</tbody>
</table>
A. Acetone - Hydroxylamine - 2-Dimethylaminomethylpyrrolidine Kinetics

In Hine, Cholod, and Chess's work, the logarithms of the rate constants for iminium ion formation between acetone and various primary monoamines and primary tertiary diamines were plotted against the pK's of the ammonium ions which are measures of the basicities of the amines. A satisfactory straight line with a positive slope was obtained for simple monoamines. The points for the tertiary mono-protonated form of trans-2-dimethylaminomethylcyclopentylamine and the tertiary monoprotonated 3-dimethylaminopropylamine were found to be about 2 and 3 log units, respectively, above the line. The explanation given for the abnormally rapid rate of iminium ion formation with these amines is that the protonated tertiary amino group is acting as an internal general acid catalyst for the dehydration of the intermediate carbinolamine. To find out whether the same process is occurring with 2-dimethylaminomethylpyrrolidine, the basicity of the tertiary amino group has to be estimated.

The pK's of the protonated diamine, 9.82 and 5.77, are defined as follows.

\[
K_1 = \frac{[H^+][Am]}{[AmH^+]} = 10^{-9.82}
\]

(113)
The concentration of the monoprotonated amine, \([A_{diH'}]\), is the sum of the concentrations of the secondary monoprotonated amine \([HST^+]\) and the tertiary monoprotonated amine \([HTS^+]\). Thus, the equation for the dissociation of the monoprotonated amine becomes eq. (115).

\[
K_2 = \frac{[H^+][AmH^+]}{[AmH_2^{++}]} \quad (114)
\]

It can be seen that each term on the right side of eq. (115) is a reciprocal of the "microscopic" dissociation constant for the monoprotonated amines. Thus eq. (115) is equivalent to eq. (116).

\[
\frac{1}{K_1} = \frac{[H^+][ST]}{[HST^+] + [HTS^+]} \quad (115)
\]

\[
\frac{1}{K_1} = \frac{1}{K_{HST^+}} + \frac{1}{K_{STH^+}} \quad (116)
\]

The values of \(K_{HST^+}\) and \(K_{STH^+}\) are not known but they can be estimated. This can be done by considering the compound as pyrrolidine with a dimethylaminomethyl group on the \(\beta\) position or as \(N,N\)-dimethylbutylamine with a secondary amino group on the \(\beta\) position. A nitrogen on the position of the amine is expected to reduce the basicity relative to the unsubstituted compound. Thus a basicity reduction factor \(\beta\) is defined as follows where \(K_{PYR^+}\) and \(K_{BuNHMe_2^+}\) are the dissociation constants for pyrrolidinium and

\[
K_{HST^+} = K_{PYR^+}^\beta \quad (117)
\]

\[
K_{HTS^+} = K_{BuNHMe_2^+}^\beta \quad (118)
\]
\(N,N\text{-dimethylbutylammonium ions, which are equal to} 10^{-9.80} \text{ and} 10^{-9.80} \text{ at } 35^\circ\text{C}, \text{ respectively.}^{29,12}\) If it is assumed that the two \(\beta\)'s are equal, then, there are three equations and three unknowns. Combination of these three equations give the following values.

\[
\begin{align*}
\beta &= 19.1 \\
K_{\text{HST}^+} &= 1.59 \times 10^{-10} \\
K_{\text{HTS}^+} &= 5.03 \times 10^{-9}
\end{align*}
\]

The ratio \(K_{\text{STH}^+}/K_{\text{HST}^+}\) is equal to 19.1. This means that at equilibrium 95\% of the monoprotonated amine is secondary nitrogen-protonated and 5\% is tertiary protonated. These values appear to be reasonable considering the fact that secondary amino groups are more basic than primary amino groups which are 1.6 to 3.7 times as basic as tertiary amino groups in \(\omega\)-dimethylaminoalkylamines.\(^{54}\)

The dissociation constants of the diprotonated amine are measures of the basicities of the monoprotonated amines and these values should be determined and used in the Brønsted relationship. The dissociation constant for the removal of the proton from the secondary amino group of the diprotonated amine \(K_{\text{HTS}^{++}}\) and the dissociation constant for the removal of the proton from the tertiary amino group \(K_{\text{HST}^{++}}\) can be calculated.

\[
K_{\text{HST}^{++}} = \frac{[\text{H}^+][\text{STH}^+]}{[\text{HST}^{++}]} = \left(10^{-5.77}(1/20.1) = 8.45 \times 10^{-8}\right) (119)
\]

\[
K_{\text{HTS}^{++}} = \frac{[\text{H}^+][\text{HTS}^+]}{[\text{HTS}^{++}]} = \left(10^{-5.77}(1/20.1) = 8.45 \times 10^{-8}\right) (119)
\]
Thus $K_{HSTH^{++}}$ is equal to 7.07 and $pK_{HSTH^{++}}$ is equal to 5.79.

Next, the catalytic constants for each species have to be determined. The kinetic results gave a value of $0.0620 \text{ M}^{-1}\text{s}^{-1}$ for $k_{imh}$ which is the second order rate constant for acid-catalyzed iminium ion formation regardless of the site of protonation. The rate of this reaction is the sum of catalysis by two species.

$$k_{imh}[AmH^+] = k_{STH^+}[STH^+] + k_{HST^+}[HST^+]$$  \hspace{1cm} (121)

The second term on the right side of the above equation is believed to be insignificant because studies on iminium ion formation with pyrrolidine, morpholine and dimethylamine\textsuperscript{28} showed the absence of proton catalysis at pH's buffered by the amines and the results of deuterium experiments with acetone-$d_5$ in the presence of pyrrolidine at pH's near 7 indicate that acid-catalyzed iminium ion formation contributes negligibly (p. 219). Thus, acid-catalyzed iminium ion formation with DMAMP is attributed only to the tertiary monoprotonated form of the diamine and the second order catalytic constant for this reaction can be calculated as follows.

$$k_{STH^+} = \frac{k_{imh}[AmH^+]}{STH^+}$$  \hspace{1cm} (122)

The above equation gives a value of $1.25 \text{ M}^{-1}\text{s}^{-1}$ for $k_{STH^+}$. 

\[
K_{HSTH^{++}} = \frac{[H^+][HST^+]}{[HSTH^{++}]} = (10^{-5.77})(19.1/20.1) = 1.61 \times 10^{-8}
\]  \hspace{1cm} (120)
In the work on secondary amines, the log of the second order rate constants for iminium ion formation were plotted against the pK of the amines - pyrrolidine, dimethylamine and morpholine. After corrections were made for the "five-membered ring effect" for pyrrolidine and the "six-membered ring effect" for morpholine, a straight line is obtained passing through the three points with a slope of 0.54 and an intercept of -6.96. The second order catalytic constant for iminium ion formation between acetone and free DMAMP ($k_{im}$) is $0.0201 \text{ M}^{-1}\text{s}^{-1}$. The point for this value (9.82, log 0.0201) lies very close to the line. The estimated point for iminium ion formation between acetone and the tertiary monoprotonated diamine (7.07, log 1.25) lies 3.2 log units above the line. This means that the tertiary monoprotonated form of 2-dimethylaminomethylpyrrolidine forms iminium ions with acetone at a rate which is about 1500 times faster than that expected from its basicity.

The fact that the point for the free amine lies almost exactly on the line is largely a coincidence. Forming the imino double bond exocyclic to the five-membered ring should increase the iminium ion formation by about the same amount as that for pyrrolidine (about 1.6 log units above the line). On the other hand, the presence of the dimethylaminomethyl group on the 2-position should destabilize the iminium ion relative to that of pyrrolidine due to steric effect. The fact that the two effects seem to cancel each other is indeed remarkable.
Fig. 32. Log of Iminium Ion Formation Rate Constant vs. pK of Protonated Secondary Amines. Rate for pyrrolidine was corrected for the five-membered ring effect. Rate for morpholine was corrected for the six-membered ring effect.
Although the same double bond stabilization and steric requirements are expected for the tertiary monoprotonated form of the diamine as the free form, the point for the former still lies 3.2 log units above the corrected Brønsted line. The most likely explanation for this tremendous rate acceleration is internal general acid catalysis by the protonated tertiary amino group on the dehydration of the intermediate carbinolamine, the transition state of which is shown in Figure 33.

Figure 33. Transition state for dehydration of carbinolamine formed from acetone and the tertiary monoprotonated form of DMAMP.

There have been previous reports of internal catalysis in the formation or hydrolysis of imines or iminium ions. Bruice and coworkers suggested that intramolecular general acid catalysis by phenolic hydroxyl in the dehydration of the carbinolamine is a possible mechanism in the formation of imines by 3-hydroxypyridine-4-aldehyde, but Hine stated that the magnitude of the rate
acceleration compared to pyridine-4-aldehyde is small enough to be explained by polar effects. The hydrolysis of the similar N-salicylidene-2-aminopropane has been studied\(^{56}\) and the workers eliminated the possibility of internal catalysis by the ortho hydroxy group because the rate of hydrolysis is in the same order of magnitude as that of \(\text{o-methoxy-}N\)-benzylidene-2-aminopropane. Internal catalysis by the ortho hydroxy group in the dehydration of the carbinolamine has also been suggested as an explanation for the rapid rate of hydrolysis of \(N\)-salicylideneaniline in basic medium. Fife and Hutchins\(^{57}\) have studied the hydrolysis of 2-(substituted phenyl)-\(N,\text{N}\)-dimethyl-1,3-imidazolidines and suggested intramolecular general base catalysis by an amino group in the attack of water to form the carbinolamine from the iminium ion, which is an intermediate in the hydrolysis. The proposed transition state is very similar to that shown in Figure 37, the only difference is that it is approached from the iminium ion side. Kayser and Pollack\(^{58}\) proposed internal general base catalysis by the carboxylate group as an explanation for the abnormally rapid rate of hydrolysis of Schiff bases derived from glycine or aspartic acid and cyclohexene-1-carboxaldehyde, the transition state of which is also similar to that in Figure 35 and also approached from the iminium ion side. Another work has shown that decrease in solvent polarity has a synergistic effect with this internal general base catalysis.\(^{59}\)
The work which inspired this study is that by Hine, Cholod and Chess with primary amines and primary-tertiary diamines. The monoprotonated form of 2-dimethylaminoethylamine was found to exhibit the largest deviation from the line produced by plotting log of the rate constant for iminium ion formation against the pK's of simple primary amines. This amine, which has two carbon atoms between the two amino groups as in the case of DMAMP, is 1000-fold too reactive to fall on the line. If the estimation of the pK of DMAMP is correct, then the tertiary-protonated form of DMAMP is even more reactive towards iminium ion formation than the tertiary-protonated form of 2-dimethylaminoethylamine relative to the members of their respective family of amines. The reason may be that in the dehydration of the carbinolamine, in the case of the former, there is restricted rotation around the bond between the nitrogen which will become the imino nitrogen and the 2-carbon because this bond is part of the ring system. The Newman projection of the transition state is shown in Figure 34.

Figure 34. Newman projection of the transition state of the dehydration of carbinolamine formed between acetone and the tertiary monoprotonated form of 2-dimethylamino- methylpyrrolidine.
B. Iminium Ion Formation with Pyrazolidinium, Isoxazolidinium,  
_0_2N-Dimethylhydroxylammonium and 1,2-Dimethylhydrazinium Ions

The NMR and UV results show convincingly that iminium ions are formed when acetone is allowed to react with the protonated forms of the amines having atoms containing unshared pairs of electrons beside the nitrogen. This is something remarkable because it has always been known that equilibrium constants for iminium ion formation are so small that in aqueous solutions, no change can be observed when acetone is allowed to react with ordinary amines or amine salts. The fact that the reaction is between acetone and the protonated amine caused surprise at first but previous work with primary amines with polar substituents\(^{51}\) has shown that the lower the basicity of an amine, the earlier acid catalysis will make its contribution in going from basic to acidic pH regions. The ammonium ions used in this study have pK's \(4\) to \(7\) units lower than simple aliphatic amines.

There are only very few instances wherein a carbonyl compound has been allowed to react with an N-alkylated hydroxylamine or hydrazine derivative. One reaction which is very similar to that found in this study is the formation of nitrone hydrochlorides from ketones and N-methylhydroxylamine hydrochloride.\(^{60}\) The nitrone hydrochlorides of acetone, cyclopentanone, acetophenone and benzophenone have been prepared this way (eq. 125). The products are
\[ 
\begin{align*}
\text{C} &= 0 + \text{HONH}_2^+\text{CH}_3 \text{Cl}^- \quad \rightarrow \quad \text{C} = \text{N}^{\text{OH}}_0 \text{CH}_3 \text{Cl}^- + \text{H}_2\text{O} \quad (123)
\end{align*}
\]

Hygroscopic crystalline compounds which are instantly hydrolyzed by action of water. \(\text{O,N-Disubstituted hydroxylamines have been found to react with aldehydes to form carbinolamines which are unusual in that they are distillable.}\)

\[
\begin{align*}
\text{RCHO} + \text{R'}\text{NHOR} & \quad \rightarrow \quad \text{R'}\text{-N-OR} \\
\text{R-CH-OH} & \quad (124)
\end{align*}
\]

\[
\begin{align*}
\text{RCHO} + 2 \text{R'}\text{NHOR} & \quad \rightarrow \quad \text{R'}\text{-N-CHR-}\text{N}-\text{OR'} \\
\text{OR} & \quad (125)
\end{align*}
\]

Phenylhydroxylamine and acetone form a dimeric product (eq. 126) which most probably results from an aldol-type condensation of a nitrone intermediate.

\[
\begin{align*}
(\text{CH}_3)_2\text{C}=\text{O} + \phi\text{NOH} & \quad \rightarrow \quad \left[ (\text{CH}_3)_2\text{C}=\text{N}^+\phi \right] \rightarrow (\text{CH}_3)_2\text{C}-\phi\text{C}-\text{CH}_2-\text{C}-\text{CH}_3 \\
\phi\text{NOH} & \quad (126)
\end{align*}
\]

Gem-dihydrazines are formed from dialkylhydrazines and formaldehyde.

\[
\begin{align*}
2(\text{CH}_3)_2\text{N-NICl}_3 + \text{CH}_2\text{O} & \quad \rightarrow \quad (\text{CH}_3)_2\text{N-N-CH}_2-\text{N-N(Ch)}_3 \\
\text{CH}_3 & \quad \text{CH}_3 \\
\end{align*}
\]

None of the above reactions occurred in aqueous solution.

The equilibrium constant \(K'\) for the reaction between acetone and the free amines to form iminium ions and hydroxide ion (eq. 128) is not independent of the experimentally determined equilibrium...
constant $K$ for the reaction between acetone and the protonated amines to form the same iminium ions and water ($9.33 \text{ M}^{-1}$, $8.96 \text{ M}^{-1}$, $0.117 \text{ M}^{-1}$ and $0.057 \text{ M}^{-1}$ for PYRZNH$^+$, ISOXH$^+$, ONHXH$^+$, and DMHZH$^+$, respectively). The relationship between the two rate constants (eq. 129) involves $K_{\text{AmNH}^+}$ the dissociation constant of the ammonium ion and $K_w$ the autoprotolysis constant of water. Eq. 129 gives $K'$ values of $3.47 \times 10^{-6}$, $1.01 \times 10^{-8}$, $7.38 \times 10^{-11}$, and $2.49 \times 10^{-6}$ for PYRZN, ISOX, ONHX, and DMHZ, respectively. These values reveal why no change is observed when acetone is allowed to react with any of these amines at pH's where essentially only the free amine exists.

With regard to the relative magnitude of the equilibrium constants for iminium ion formation between acetone and the four ammonium ions, it is clear that the five-membered ring effect is operative in this process. The fact that equilibrium constants for PYRZNH$^+$ and ISOXH$^+$ are almost 100 times greater than those for ONHXH$^+$ and DMHZH$^+$ is in accord with the generalization that five-membered rings stabilize double bonds exo to them relative to acyclic double bonds.

The fact that the expectation that a nitrogen atom would stabilize a double bond attached to it better than an oxygen atom
is followed for the five-membered ring cases (PYRZNH⁺ and ISOXH⁺) but reversed in the acyclic cases (ONHXH⁺ and DMHZH⁺) is puzzling. Apparently, the -NHCH₃ group occupies more space than the -OCH₃ group and this produces steric interaction with the methyl cis to it across the imino double bond. In the five membered ring iminium ions, the analogous groups are pulled back as part of the ring and, thus, the greater double bond stabilizing ability of nitrogen wins out.

The NMR spectra reveal some interesting facts. The spectra of the iminium perchlorates in different solvents show that the two methyls attached to the imino carbon, (CH₃)₂C=N⁺, whose signals are usually between 62.0 and 62.5 may or may not be magnetically equivalent depending on the iminium ion and the solvent. All the salts show nonequivalence of the two methyls in CD₃CN and D₂O. The iminium ion derived from acetone and PYRZNH⁺ has nonequivalent methyls in DMF-d₇. In DMSO-d₆, the NMR spectra of the iminium salts from PYRZNH⁺, ISOXH⁺, and ONHXH⁺ show only one signal for these methyls. This is most probably due to interaction between the nucleophilic oxygen of this solvent and the electron-deficient imino carbon which causes rotation around the C-N bond which is faster than the NMR time scale. The iminium salt from DMHZH⁺ is unique in that the nonequivalence of the two methyls is retained in DMSO-d₆. This may be an indication that the C-N bond in this ion
has a greater double bond character than the imino double bond of the other salts. This may be due to smaller extent of conjugation with the neighboring nitrogen which may be an explanation of the unexpectedly small equilibrium constant for the formation of this ion compared to the others. This non-equivalence of the two methys could also be due to steric hindrance to attack by the nucleophilic oxygen of DMSO-d₅ because of the apparent greater steric bulk of the CH₃NH- group compared with the CH₃O- group, as mentioned before. This ion is also unusual in that the separation of signals due to the (CH₃)₂C=N⁺ peaks is much larger (7 Hz) than that for the other salts in CD₃CN (about 1-2 Hz). This may be due to the steric interaction of the (CH₃)₂C=N⁺ methys with the CH₃NH- group and the other methyl across the double bond, making the two (CH₃)₂C=N⁺ methys very chemically different. This interaction is expected to be less with the iminium ion derived from PYRZNH⁺ because the corresponding groups are pulled back by the five-membered ring.

Considerable amounts of NMR data exist in the literature about iminium ions. Bohme and Viehe have compiled a tremendous amount of information on these species. They have listed barriers of rotation around the C=N⁺ bond which were measured by observing the coalescence of NMR signals. From their data, the conclusion was made that simple unconjugated iminium salts have a high barrier of rotation (70-90 Kcal/mole) which cannot be measured by NMR. If
conjugation exists, the barrier of rotation becomes lower. For example, conjugation with a carbon-carbon double bond reduces the barrier to 30 to 35 Kcal/mole. Martin et al.\textsuperscript{64} have done a H\textsuperscript{1} and C\textsuperscript{13} structural and dynamic study of various substituted iminium ions of the type (CH\textsubscript{3})\textsubscript{2}N\textsuperscript{+}=CXY and found that rotation around the C-N bond is generally slow with respect to the NMR time scale and that the greater the electron-donating ability of X and Y, the lower will be the barrier for rotation. Some information has been published regarding NMR data on iminium salts related to the ones used in this study. Bauer, et al.\textsuperscript{65} reported that the four N(CH\textsubscript{3})\textsubscript{2} methyls in 2-methoxy-1,1,2,3,3-pentamethylguanidine perchlorate (I) in D\textsubscript{2}O are equivalent and that restricted rotation is not observed. Saito and coworkers\textsuperscript{65} observed that the \(\alpha\)-methylene protons of cyclohexanone oxime monohydrochloride (II) in CHCl\textsubscript{3} solution gives only one NMR peak. On the other hand, Olah and Kiovsky\textsuperscript{67} observed that the methyl peaks of protonated acetoxime (III) in FSO\textsubscript{3}H-SbF\textsubscript{5}-SO\textsubscript{2} solution are two separate signals. The fact that some workers observed nonequivalence while others did not seems to imply that the barrier for rotation about the C-N bond is easily affected by changes in the atoms or groups attached to the imino nitrogen. Martin et al.\textsuperscript{63} also reported that the counterion is linked through an ion-pair to the iminocyl carbon atom. In this study, the non-nucleophilic perchlorate ion was used, but the solvent DMSO-\textsubscript{d\textsubscript{6}} contains a nucleophilic oxygen which can interact in the same manner. Thus, the observed
coalescence of the \((\text{CH}_3)_2\text{C}=\text{N}^+\) signals when the iminium salts are dissolved in DMSO-\text{d}_5 is not very surprising.

\[
\begin{align*}
\text{I} & \quad \text{II} & \quad \text{III} \\
\text{CH}_3
\end{align*}
\]

With regard to the mechanism of hydrolysis of \(\text{N}\)-isopropylidene-pyrazolidinium ion, the observed non-catalyzed, general base-catalyzed, hydronium ion-catalyzed and hydroxide ion-catalyzed terms may be rationalized in the mechanism described in eq. (130) through eq. 133.

Non-catalyzed reaction:

\[
(\text{CH}_3)_2\text{C}=\text{N}^+ + \text{H}_2\text{O} \xleftrightarrow{\text{slow}} (\text{CH}_3)_2\text{C}^+ + \text{H}_2\text{O} \xleftrightarrow{\text{fast}} (\text{CH}_3)_2\text{C} = \text{NH}^+ + \text{H}_2\text{O} 
\]

(130)

General base-catalyzed reaction:

\[
(\text{CH}_3)_2\text{C}=\text{N}^+ + \text{H-O-H} \cdots \text{B} \xleftrightarrow{\text{slow}} (\text{CH}_3)_2\text{C}^+ + \text{H}_2\text{O} \xleftrightarrow{\text{fast}} (\text{CH}_3)_2\text{C} = \text{NH}^+ + \text{H}_2\text{O} 
\]

(131)
Hydronium ion-catalyzed reaction:

\[
(CH_3)_2C=N^+ + H^+ \rightleftharpoons (CH_3)_2C=N^+ + H_2O, \text{ slow} \quad (152)
\]

\[
(\text{fast}) \quad (CH_3)_2C-NH_2^+ \rightleftharpoons (CH_3)_2CO + HN^+ + H^+
\]

"Hydroxide ion-catalyzed" reaction:

\[
(CH_3)_2C=N^+ + \text{OH}^- \rightleftharpoons (CH_3)_2C-N\text{OH}^- \quad (135)
\]

\[
(\text{fast}) \quad (CH_3)_2CO + HN^+ + \text{OH}^-
\]

In all of the above reactions, the rate-determining step is attack of water or hydroxide ion on the iminium ion to form the carbinolamine. Alternatively, it might be thought that water or hydroxide ion attacks the iminium ion in a fast step prior to rate-determining breakdown of the carbinolamine to acetone and the amine. This may also give rise to the observed hydronium-, hydroxide-, and general base-catalysis as shown in eqs. (134) through (137).

Non-catalyzed reaction:

\[
(CH_3)_2C=N^+ + H_2O \xleftrightarrow{\text{fast}} (CH_3)_2C-NH_2^+ \xleftrightarrow{\text{slow}} (CH_3)_2CO + HN^+ + \text{OH}^-
\]

\[
(\text{CH}_3)_2C=O + H_2N^+ + \text{NH}
\]
General base-catalyzed reaction:

\[
(\text{CH}_3)_2C=\text{N}^+ + H_2O \xrightleftharpoons{\text{fast}} (\text{CH}_3)_2C-\text{NH}^+ \xrightarrow{\text{slow}} (\text{CH}_3)_2C=\text{O} + \text{HN}^+ + \text{BH}^+
\]

(135)

Hydronium ion-catalyzed reaction:

\[
(\text{CH}_3)_2C=\text{N}^+ + H_2O \xrightleftharpoons{\text{fast}} (\text{CH}_3)_2C-\text{NH}^+ \xrightarrow{\text{H}^+, \text{fast}} (\text{CH}_3)_2C=\text{O} + \text{H}_2\text{N}^+ + \text{NH}^+ + \text{OH}^-
\]

(136)

Hydroxide-catalyzed reaction:

\[
(\text{CH}_3)_2C=\text{N}^+ + H_2O \xrightleftharpoons{\text{fast}} (\text{CH}_3)_2C-\text{NH}^+ \xrightarrow{\text{slow}} (\text{CH}_3)_2C=\text{O} + \text{HN}^+ + \text{H}_2\text{O}
\]

(137)

The difference between the two mechanisms may be detected by comparing the amount of catalysis produced by hydroxide with those of the other general bases. When the point for hydroxide catalysis is
included in the Bronsted plot in Figure 24, it lies 1.85 log units above the line formed by the other oxy-bases. Equation (137) shows the hydroxide ion acting as a general base in the breakdown of the carbinolamine into acetone and the amine in the same manner as the other general bases in eq. (135). The positive deviation of hydroxide ion from the line indicates that it catalyzes the reaction by a mechanism different from catalysis by the other bases. The most likely mechanism is rate-controlling attack of the hydroxide ion on the iminium ion. Just as hydroxide ion attack is rate-controlling, attack by water should be likewise, which means that the mechanism expressed in eqs. (130) through (133) is the more plausible one. This is consistent with previous findings that, except in very acidic solutions, attack of water or hydroxide on the iminium ion is the rate-determining step in imine hydrolysis. 22b,27

Another evidence which favors rate-determining attack of hydroxide on the iminium ion to form the carbinolamine is the shape of the pH profile in Figure 23. The right limb of the plot is a straight line with a slope of unity, which indicates direct attack of hydroxide ion on the substrate in a rate-determining step. The left limb is a straight line of slope minus one which suggests complete protonation prior to the rate-determining step.

The protonated iminium ion appears very unstable due to the two positive charges right next to each other but it seems to be the only explanation for the observed hydronium ion catalysis.
The fact that such hydronium ion-catalyzed term is not observed in the hydrolysis of $N$-isopropylideneisoxazolidinium ion supports the idea that the protonation occurs on the nitrogen adjacent to the $C=\text{N}^+$ bond. The mechanism proposed for this reaction (eqs. 58 through eq. 62) is similar to that proposed by Pollack$^{57,68}$ for hydrolysis of Schiff bases derived from cyclohexene-1-carboxaldehyde and that by Jencks and Sayer$^{69,70}$ in their analysis of Schiff base formation but the pH profiles for these reactions are different from that found in this study because their imines have to be protonated first before water attacks.

For the $N$-isopropylideneisoxazolidinium ion hydrolysis beyond pH 7.5, the rate again starts to increase with increasing pH but the rate constants could not be measured accurately in this pH region because of the very rapid reaction. This is most probably due to rate-controlling attack of hydroxide on the iminium ion. Thus, if the rate constants could be measured, the rate-pH profile in this pH region is expected to be similar to the right limb of the rate-pH profile for the $N$-isopropylidene-2-pyrazolidinium ion hydrolysis.

The rate constant for uncatalyzed iminium ion formation between acetone and pyrazolidine (reaction between acetone and free amine to give iminium ion and hydroxide) can be calculated and compared with the other secondary amines. This rate constant is obtained by multiplying the second-order rate constant for attack of hydroxide
on the iminium ion \((2740 \text{ M}^{-1} \text{s}^{-1} \text{ from Table 8})\) and the equilibrium constant for the reaction between acetone and free pyrazolidine to give iminium ion and hydroxide, calculated from eq. \((129) \ (3.47 \times 10^{-6})\). The resulting value \((9.50 \times 10^{-3} \text{ M}^{-1} \text{s}^{-1})\) should be divided by two to take account of symmetry (two equivalent nitrogens compared to only one for ordinary amines) while the dissociation constant for pyrazolidinium ions should be multiplied by two. The log of the resulting symmetry-corrected rate constant and symmetry-corrected pK of pyrazolidinium ions determines a point which lies 0.90 log unit above the line in Figure 32. The point for pyrrolidine lies 1.62 log units above the line and this enhanced rate of iminium ion formation was attributed to the "five-membered ring effect". The explanation which can be offered for this is that the \(\alpha\)-effect is not operative in uncatalyzed iminium ion formation and that, although pyrazolidine is a five-membered ring, its geometry may differ from the pyrrolidine ring such that the latter can stabilize a double bond exo to it to a greater extent.

C. Dedepuration of Acetone-\(d_6\) in the Presence of Pyrrolidine and Dimethylamine

The calculated value for \(k_B\) \((5.09 \text{ M}^{-1} \text{s}^{-1})\) which is the second order rate constant for iminium ion formation between acetone-\(d_3\) and pyrrolidine in solutions buffered by 3-dimethylaminopropionitrile agrees reasonably well with that obtained by Dempsey \((4.25 \text{ M}^{-1} \text{s}^{-1})\)\(^{29}\)
which was determined by an entirely different method - by pyrrolidine catalyzed oximation of light acetone. The 16% relative deviation between the two values could very well be due to the difference in the rates of iminium ion formation between acetone and acetone-$d_6$, in other words, secondary deuterium isotope effect (acetone-$d_6$ is more reactive towards oxime formation and towards iminium ion formation with diamines. The average $k_D/k_H$ is 1.2). This suggests that the acid-catalyzed iminium ion formation is not significant at this pH range ($6.3 - 8.0$). A more careful examination of the results confirms that this is indeed the case. Equation (93) does not take into account proton catalysis in iminium ion formation. Thus, it is expected that, if such proton catalysis is significant, the observed $k_e$'s obtained from the more acidic solutions would be higher than the $k_e$'s calculated by least squares analysis of the function. However, such a trend is not evident. Values of $k_{im}$ can be calculated from eq. (99) using the $k_e$ and $k_p$ values in Table 24 and the $r$ value calculated from eq. (98). These $k_{im}$ values were all lower than the $k_{im}$ values calculated from eq. (100) using a value of $k_{am}$ equal to $4.25 \text{ M}^{-1}\text{s}^{-1}$ obtained from amine-catalyzed oximation of light acetone and a value of $k_{amH}$ equal to $4.18 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ obtained from pyrrolidine-catalyzed deuteration of acetone-$d_6$ in pyridine buffer, except in two cases (the kinetic run at pH 7.08 where the difference is 16% and that at 7.92 where the difference is 14%). This means that although pyrrolidine is about 99.99%
protonated under these conditions, the iminium ion is still formed from acetone and free pyrrolidine just as Dempsey observed in more basic solutions. In pyridine-buffered solutions (pH ~ 5), however, iminium ion formation with pyrrolidine and dimethylamine occurs mostly via acid-catalyzed pathway. This suggests that there is a break in the pH profile (log of rate constant vs. pH) for iminium ion formation between acetone and these amines at around pH 6. Acid catalysis in iminium ion formation has been seen before in the case of iminium ion formation between isobutyraldehyde and primary amines with polar substituents\textsuperscript{51} and in primary ammonium ion-catalyzed isobutyraldehyde-2-d exchange in pyridine buffers.\textsuperscript{52} The q values and the calculated r values suggest that the iminium ion formation with pyrrolidine is partly rate controlling in the deuteration process while with dimethylamine no similar conclusion can be made because only a very small fraction of the total rate is due to deuteration via iminium ions.

D. Dedeuteration of Acetone-d\textsubscript{6} in the Presence of Pyrazolidine, Isoxazolidine, O,N-Dimethylhydroxylamine, and 1,2-Dimethylhydrazine

In these experiments, k\textsubscript{0}, the first order rate constant for the disappearance of acetone-d\textsubscript{6} was treated as the sum of rates of deuterium exchange due to uncatalyzed, hydronium ion- and hydroxide ion-catalyzed enolization of acetone and attack of free amines on
both acetone and the iminium ion. Among these contributions, the most important is the removal of deuterons from the iminium ion by pyridine, the rate of which is equal to $k_{II} [\text{AmH}^+] [\text{PYRDN}]$ in eqs. (102) and (112). This term contributes 98% to the total rate of dedeuteration to the PYRDN-PYRZN kinetic runs, 55 to 78% in the PYRDN-ISOX runs, 62 to 77% in the PYRDN-ONHX runs, and 91% in the PYRDN-DMHZ runs. This term constitutes the major pathway for the dedeuteration because the iminium ion is much more reactive than acetone and pyridine is the base present in largest concentration.

The relative effectiveness of the four different $\alpha$-ammonium ions as catalysts for dedeuteration by pyridine can be seen in the values of $k_{II}$ in the summary of the dedeuteration results in the presence of secondary amines in Table 29. The $k_{II}$ value is a true measure of catalysis in dedeuteration. It can then be concluded that in solutions where the amines exist predominantly in the protonated form, the order of decreasing effectiveness as catalysts for the dedeuteration of acetone-$d_8$ by pyridine is ONHX$^+$ > ISOX$^+$ > DMHZ$^+$. However, the hydrazine derivatives have an advantage over the hydroxylamine derivatives in that they are more basic so that they can exist as ammonium ions and, as such, effective catalysts over a wider pH range.

In order that the results of dedeuteration in the presence of the four $\alpha$-ammonium ions can be compared with those of pyrrolidine
TABLE 29

EQUILIBRIUM AND KINETIC CONSTANTS FOR IMINUM ION FORMATION AND DEUTERIUM EXCHANGE BY
ACETONE IN THE PRESENCE OF SECONDARY AMMONIUM IONS\textsuperscript{a}

<table>
<thead>
<tr>
<th>Ammonium Ion\textsuperscript{b}</th>
<th>pK</th>
<th>K for $\text{C}^+=\text{N}$ formation (M$^{-1}$)</th>
<th>$10^6 \text{k}_{II}$ (M$^{-2}$ s$^{-1}$)</th>
<th>rate of dedeuteration of Im$^+$ by pyridine relative to Ac-$d_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>PYRH$^+$</td>
<td>10.99</td>
<td>---</td>
<td>55</td>
<td>---</td>
</tr>
<tr>
<td>DMAH$^+$</td>
<td>10.49</td>
<td>---</td>
<td>1.6</td>
<td>---</td>
</tr>
<tr>
<td>PYRZNH$^+$</td>
<td>7.25</td>
<td>9.33</td>
<td>7510</td>
<td>307</td>
</tr>
<tr>
<td>ISOXH$^+$</td>
<td>4.73</td>
<td>8.96</td>
<td>4460</td>
<td>190</td>
</tr>
<tr>
<td>ONHXH$^+$</td>
<td>4.48</td>
<td>0.117</td>
<td>8260</td>
<td>27000</td>
</tr>
<tr>
<td>DMHZH$^+$</td>
<td>7.32</td>
<td>0.057</td>
<td>292</td>
<td>1950</td>
</tr>
</tbody>
</table>

\textsuperscript{a}In water at 35°

\textsuperscript{b}PYRH$^+$ = pyrrolidinium ion, DMAH$^+$ = dimethylammonium ion, PYRZNH$^+$ = pyrazolidinium ion, ISOXH$^+$ = isoxazolidinium ion, ONHXH$^+$ = O,N-dimethylhydroxylammonium ion, DMHZN$^+$ = 1,2-dimethylhydrazinium ion.
and dimethylamine, $k^\text{II}_p$ values for the latter two were calculated from eq. (138) where $k_p$ is the $k_\text{p}$ in the presence of pyridine alone.

$$k^\text{II} = \frac{k_\text{p}}{[\text{PYRDN}][R_2\text{NH}_2]} \quad (138)$$

These values were also included in Table 29. Because the values of $k_\text{p}$ and $k^\text{II}_p$ are so close to each other for dimethylamine and because of the experimental uncertainties involved, the $k^\text{II}_p$ value for this amine calculated from eq. (138) can only be regarded as a rough upper limit.

The relative rates of dedeuteration of the four iminium ions-$d_\text{g}$ and acetone by pyridine can also be calculated from the $k^\text{II}_p[\text{AmH}^+][\text{PYRDN}]$ term and from the results of the kinetic runs without secondary amine catalyst. The rate of disappearance of acetone-$d_\text{g}$ by removal of deuterons by pyridine is equal to $2.62 \times 10^{-6} [\text{Ac-}d_\text{g}] [\text{PYRDN}]$. This was derived from the average $k_\text{p}$'s for the runs E-PYRDN-200 and E-PYRDN-300. The rate of disappearance of acetone-$d_\text{g}$ via removal of deuterons from the iminium ion by pyridine is equal to $k^\text{II}_p[\text{Ac-}d_\text{g}] [\text{AmH}^+][\text{PYRDN}]$ which is also equal to $(k^\text{II}_p/K) [\text{Im}^+] [\text{PYRDN}]$ where $K$ is the equilibrium constant for the iminium ion formation in $M^{-1}$. The $k^\text{II}_p/K$ value for PYRZN is $8.20 \times 10^{-4} M^{-1}s^{-1}$; $4.98 \times 10^{-4} M^{-1}s^{-1}$ for ISOX; $7.06 \times 10^{-2} M^{-1}s^{-1}$ for ONHX; and $5.09 \times 10^{-3} M^{-1}s^{-1}$ for DMHZ. These values can be directly compared with $2.62 \times 10^{-8} M^{-1}s^{-1}$ which is the second
order rate constant for the dedeuteration of acetone-\(d_3\) by pyridine and the ratio shows how much faster the iminium ion undergoes dedeuteration by pyridine compared to acetone-\(d_3\). For the PYRZN the ratio is 307; 190 for ISOX; 27000 for ONHX; and 1950 for DMHZ. A number related to this is the rate of enolization of the protonated ketimine of acetone calculated by Bender\(^{13}\) to be \(10^6\) times faster than that of acetone. The \(N\)-methyliminium ion of isobutyraldehyde was calculated by Hine\(^{11}\) to donate its \(\alpha\)-deuteron to water \(10^3\) times as rapidly as the aldehyde does. Methylamine removes the deuterons from the \(N\)-methyliminium ion of acetone \(10^{4.6}\) times faster than from acetone. Methylamine also removes the deuterons from the \(N\)-methyliminium ion of isobutyraldehyde-2-\(d\) about \(10^3\) times faster than from the aldehyde itself. Thus, the number obtained by Bender appears to be too high compared to those found by Hine and those found in this study.

A plot of \(\log k_{II}\) vs. the \(pK\) of the ammonium ions is shown in Figure 35. The points for the three acyclic ammonium ions, \(O,N\)-dimethylhydroxylammonium, 1,2-dimethylhydrazinium and dimethylammonium ions form a good straight line with a slope of \(-0.62\). The point for two of the five-membered ring ammonium ions, pyrazolidinium and pyrrolidinium ions, determine a line which is higher than that for the acyclic ammonium ions with a slope of \(-0.56\) but the point for isoxazolidinium ion lies even below the line for the acyclic
Fig. 35. Log $k_{II}$ for the Dedeuteration of Acetone-$_d_6$ in Pyrydine Buffers in the Presence of Secondary Ammonium Ions vs. $pK$ of the Ammonium Ions
ammonium ions. The dedeuteration of isobutyraldehyde-2-\textsubscript{d} in pyridine buffers is catalyzed by primary ammonium ions and the slope of the corresponding log rate constant-pK plot is -0.40.\textsuperscript{52} The negative slopes in all these cases show that the more acidic the ammonium ion, the greater is the rate of dedeuteration. In other words, the rate is increased by electron withdrawing groups attached to the nitrogen. The explanation given for this is that the positive charge on the nitrogen is decreased in going from the reactant (the ammonium ion), where it has a full positive charge, to the transition state, where it has only a partial positive charge as shown below.

\[
\begin{array}{c}
R & \delta^+ \text{C} & \text{CD}_3 \\
R & \text{N} & \text{CD}_2 \cdot \cdot \cdot \text{D} \cdot \cdot \cdot \text{NC}_5 \text{H}_5 \delta^+
\end{array}
\]

The fact that the line determined by two of the three five-membered ring ammonium ions lies above the line for the acyclic ammonium ions may be due to the "five-membered ring effect". No satisfactory explanation could be given for why the point for isoxazolidinium ion lies even below the line for the acyclic amines. One reason may be that the rate is very much dependent on the conformations of both the ammonium ions and the iminium ions, which are unknown in these cases.

There is no reason why the slope of the log \( k_{II} \)-pK plot should be equal to that found from isobutyraldehyde-2-\textsubscript{d} and secondary amines, but if lines of slope -0.4 are drawn passing through the
points for pyrrolidinium and dimethylammonium ions, the points for
the α-ammonium ions, except that of isoxazolidinium ion, will lie
above these lines. If such treatment were valid, the enhanced
reactivity of the α-ammonium ions may be considered an α-effect in
dedeuteration.

Regarding the relative magnitudes of the rates of dedeuteration
of the iminium ion by pyridine compared to that of acetone, it
appears that the five-membered ring effect is again operative in this
process. The rate of dedeuteration is directly related to the
conversion of the iminium ion to the enamine (eq. 79). In this
reaction, the C=N^+ double bond, which is exo to the five-membered
ring in the PYRZN and ISOX cases, is being replaced by a single bond.
This explains why the iminium ions from the acyclic amines undergo
dedeuteration much faster than those from the cyclic ones. However,
no satisfactory explanation could be made for the fact that in the
five-membered ring cases, the nitrogen-substituted iminium ion
undergoes dedeuteration faster than the oxygen analogue while the
reverse is true for the acyclic iminium ions.
CHAPTER V. CONCLUSIONS

The oximation studies in the presence of 2-dimethylaminomethylpyrrolidine show that internal acid catalysis by the protonated dimethylamino group in the dehydration of the intermediate carbinolamine is possible with secondary amines just as it is with primary-tertiary diamines with two or three carbon atoms between the nitrogen atoms.

This study has also shown that acetone forms iminium ions with pyrazolidinium, isoxazolidinium, O,N-dimethylhydroxylammonium and 1,2-dimethylhydrazinium ions with equilibrium constants large enough such that the reactions can be directly observed by NMR or UV measurements. The kinetics of hydrolysis of N-isopropylidenepyrazolidinium ion showed catalysis by hydronium ions, hydroxide ions and general bases and involves rate-determining attack of water and hydroxide ions on the iminium ion to form the carbinolamine. The hydrolysis of the N-isopropylideneisoxazolidinium ion is also general base-catalyzed but involves rate controlling formation of a zwitterion from the carbinolamine or protonated carbinolamine. The formation of iminium ions between acetone and O,N-dimethylhydroxylammonium ions is too fast to measure while that between acetone and 1,2-dimethylhydrazinium ions proceeds concurrently with a slower unidentified reaction which produces strong absorbances in UV but not observed in NMR.
Dedetermination studies with acetone-\(d_3\) in the presence of pyrroloidine show that secondary amines can also catalyze deuterium exchange of acetone via iminium ion formation which is partly rate-limiting with this particular amine. Pyrazolidinium, isoxazolidinium, \(\text{O}_2\text{N}-\text{dimethylhydroxylammonium}\) and \(1,2\text{-dimethylhydrazinium}\) ions are all very effective catalysts for deuterium exchange because of their large equilibrium constants for iminium ion formation with acetone. With these ions, iminium ion formation occurs as a fast equilibrium prior to deuterium removal.
CHAPTER IV. SUGGESTIONS FOR FURTHER RESEARCH

The findings revealed by this study may open the way for some experiments which could yield interesting results, but first the causes of the anomalies which arose in this study should be investigated because they too may lead to the discovery of previously unknown reactions. The first one which should be investigated is the reaction between acetone and 1,2-dimethylhydrozinium ions. Addition of acetone to a solution of 1,2-dimethylhydrazinium ions results in iminium ion formation, as seen by NMR, but UV measurements revealed the occurrence of a slower reaction which produces very strong absorbances. When the reverse reaction, the hydrolysis of the iminium ion, is observed, it was seen that the equilibrium absorbances are much higher than would be expected if acetone and 1,2-dimethylhydrazinium ions were the only absorbing species, in spite of the fact that this iminium ion should hydrolyze to a greater extent at equilibrium than the other iminium ions. The possibility of air-oxidation should be investigated. The reaction should be studied under conditions where there is a more strict exclusion of air as in a dry box and with the use of air-tight UV cells. Doing the experiment under a blanket of nitrogen did not seem to suffice. If it were found that air oxidation is not responsible for the slower increase in
absorbance, the possibility of side reactions such as an aldol-type condensation of acetone with the iminium ion. Another possibility is that the enamine may have been formed in amounts large enough to cause the observed absorbance. A very sensitive NMR spectrometer has to be used to prove the structure of these compounds, if indeed they are formed.

Another unexplained observation is the slight (~ 8%) decrease in absorbance which occurred after injection of N-isopropylidene-0,N-dimethylhydroxylammonium ion-in-acetonitrile solution into water or hydrochloric acid solution. The hydrolysis appears to be instantaneous because immediately after injection, the absorbance already has the value expected if acetone were the only species absorbing. It has been shown that the iminium ion has negligible absorbance at this wavelength (275 nm). Thus, the reason cannot be enamine formation or aldol condensation involving the iminium ion because the latter appears to be completely hydrolyzed before the absorbance decrease is observed. One possibility is that the absorbance immediately after injection may be due mostly to acetone but the amine may have a very small contribution. After hydrolysis, the amine may be undergoing air oxidation, causing the small absorbance decrease. This possibility can be investigated by studying the hydrolysis under strictly air-free conditions.

The mechanism which was proposed for the hydrolysis of N-isopropylidenepyrazolidinium ion involves rate-controlling attack of
water or hydroxide ion on the iminium ion to form the carbinolamine which rapidly decomposes to acetone and the amine. This was favored over a rate-controlling breakdown of the carbinolamine to acetone and the amine based on the position of hydroxide ion on the Brønsted plot. Stopped-flow studies on the reverse reaction (iminium ion formation from acetone and pyrazolidinium ions) may yield more convincing evidence. The mixing of acetone and pyrazolidinium ions causes a steady increase in absorbance due to the formation of the iminium ion. By observing the very early stages of this reaction in the stopped-flow spectrophotometer, the absorbance can be extrapolated to \( t = 0 \). If the extrapolated absorbance is less than that expected from the absorbances of acetone and the amine, this means that the reactants are consumed in a reaction whose rate is too fast to measure even with stopped-flow techniques. This reaction may be carbinolamine formation and its equilibrium constant may also be determined, assuming that the carbinolamine has negligible absorbances at the wavelength at which iminium ion formation is being studied. If such is observed, it means that the rate-controlling step in iminium ion formation is dehydration of the carbinolamine and, from the principle of microscopic reversibility, that in the hydrolysis reaction is the attack of water or hydroxide to form the carbinolamine. This technique has been previously employed to measure the equilibrium constant for carbinolamine formation in oximation and in isobutyraldehyde methylimine formation.\textsuperscript{29}

\textsuperscript{29}
This study has shown that, with the use of ammonium ion with atoms containing an unshared pair of electrons beside the nitrogen, iminium ion formation occurs as a fast equilibrium compared to dedeuteration. In other words, the first of the two barriers for amine-catalyzed enolization is lowered with the use of these amines. The next step then in the search for more effective dedeuteration catalyst is to lower the energy barrier for enamine formation or the removal of deuterons from the iminium ion. This can conceivably be done by having the amino group, which will form the iminium ion, and the basic moiety, which will remove the deuterons, in the same molecule. One must, therefore, choose a compound which, at a certain pH, will give rise to significant amounts of the species in which the nitrogen α to the atom with the unshared pair is protonated and the basic group is unprotonated. The basic group has to be of smaller or comparable basicity to a hydrazine or hydroxylamine. The carboxylate group fits this description but it has been shown that, compared to other bases of similar basicity, carboxylates are poor catalysts for dedeuteration. The best candidate is a pyridine base. Therefore, the dedeuteration catalyst should be a pyridine-substituted hydrazine. The suggested experiment is the study of the deuterium exchange by acetone-\textsuperscript{\text{2}}H in water in the presence of \textit{N}-2-picoly\textit{N},N\textsuperscript{\prime}-dimethylhydrazine (IV) or \textit{N}-2-picoly\textit{pyrazolidine (V}). The hydrazine derivatives were preferred over the hydroxylamine derivatives because of their
basicity, allowing greater protonation of the secondary nitrogen without protonating the pyridine nitrogen to a large extent. If these will form iminium ions with acetone with equilibrium constants comparable with those of pyrazolidinium and 1,2-dimethylhydrazinium ions, and if the pyridine nitrogen is favorably geometrically oriented to remove the α-deuterions of the iminium ion, these or one of these may just be the best bifunctional catalyst \( \text{D}_{\text{12}} \) for dedeuteration of acetone.

The relative values of the equilibrium constants for iminium ion formation may be explained by conformational changes in going from the protonated amine to the iminium ion. To investigate such a possibility, iminium ion formation between acetone and six-membered ring protonated α-amines was studied and the results compared with those found with the four α-amines in this study. The expected order of rate and equilibrium constants for iminium ion formation with simple secondary amines is five-membered > acyclic > six-membered.
Thus, it is possible that the equilibrium constant for the formation of six-membered iminium ions are so small that the reaction cannot be observed. However, it is also possible that the unshared electron pair in the α-amines may affect the conformation of both the amine salt and the iminium ion in an unexpected manner. Thus, the reaction between acetone and the protonated forms of hexahydropyridazine (VI) and tetrahydro-1,2-oxazine (VII) should be investigated.

\[
\begin{align*}
\text{VI} & \\
\text{VII} & 
\end{align*}
\]

Finally, it would be interesting to determine the catalytic ability of these amines in reactions which involve enolization such as dealdolization or decarboxylation of a β-keto acid. To ensure that catalysis via iminium ions will occur, it is suggested that the reaction to be studied should be one in which enolization is the rate-controlling step. For example, Westheimer and Cohen have found that the rate-controlling step in the dealdolization of diacetone alcohol is the second of the three equations written below. If the

\[
\begin{align*}
\text{OH} & \\
\text{(CH}_3\text{)}_2\text{C-CH}_2\text{COCH}_3 + \text{OH} & \xrightarrow{\text{fast}} (\text{CH}_3\text{)}_2\text{C-CH}_2\text{COCH}_3 + \text{H}_2\text{O} \\
\text{(CH}_3\text{)}_2\text{C-CH}_2\text{COCH}_3 & \xrightarrow{\text{slow}} \text{CH}_3\text{COCH}_3 + \text{CH}_2\text{COCH}_3 \\
\text{CH}_2\text{O-CH}_3 + \text{H}_2\text{O} & \xrightarrow{\text{fast}} \text{CH}_3\text{COCH}_3 + \text{OH} 
\end{align*}
\]
reaction is carried out in the presence of pyrazolidine around pH 6, it is predicted that such a step will be accelerated because the negative charge will be accepted by the positive imino group resulting in the formation of the enamine instead of the enolate. The decarboxylation of α,α-dimethylacetoacetic acid also involves enolate ion formation in the rate-determining step. It is also predicted that this reaction will be catalyzed by pyrazolidine when carried out at around pH 6 because most of the pyrazolidine will be in the protonated form resulting in a large extent of iminium ion formation and the carboxylate group will be unprotonated which is a requirement for the decarboxylation. The breakdown of the intermediate is shown below. Thus, catalysis by the protonated forms of these α-amines may provide large rate acceleration in near neutral medium.

![Diagram of the intermediate](image-url)
PLEASE NOTE:

Appendix contains computer print-out.
Filmed as received.

UNIVERSITY MICROFILMS INTERNATIONAL
APPENDIX
Program 1. Preparation for Calculation of \( pK' \)'s of Protonated Amines.
Written by J. Zeigler

```plaintext
10 DIM CS(30,3),DS(3,3),EC(30,3),FC(1,13),HC(4,11),HC(30,3),IC(3,3)
20 DIM NS(1,1),OE(1,13),PE(1,11),RE(1,11),SE(1,11),TE(1,11),WS(30,13),Ye(4,30)
30 DIM TF(40),AI(5),JA(13),CA(30),DA(5),MS(50)
40 FD=5
50 PI=3
60 P=2
70 P=3
80 P=4
90 WHY=(-12.68)
100 X=0
110 DISP "TITLE:"
120 INPUT TA
130 DISP "'MONO' OR 'DI' - AMINE?"
140 INPUT BA
150 IF BA="MONO" THEN 180
160 IF BA="DI" THEN 150
170 GOTO 120
180 DISP "IS THE 'BI' - AMINE PROTONATED?"
190 INPUT BA
200 IF BA="YES" THEN 210
210 IF BA="NO" THEN 230
220 GOTO 180
230 BA=0
240 DIS="UN"
250 DISP "CONC. OF STD. HCL SOL'N?"
260 INPUT A
270 GOTO 60
280 DISP "IS THE 'DI'-AMINE DI-PROTONATED?"
290 INPUT BA
300 IF BA="YES" THEN 310
310 IF BA="NO" THEN 370
320 IF BA="YES" THEN 340
330 GOTO 290
340 BA=2
350 DIS=\"DI\"
360 GOTO 390
370 DIS=\"MONO"
380 BA=1
390 DISP "CONC. OF STD. NAOH SOL'N?"
400 INPUT A
410 DISP "TOLERANCE?"
420 INPUT A
430 DISP "VOL. (L) OF TITRANT SOL'N?"
440 INPUT V
450 DISP "INITIAL CONC. HCI SOLUTION?"
460 INPUT S
470 DISP "# OF DATA PAIRS <<31>"
480 INPUT H
490 REDIM CI(1,2),CH(1,3),LC(1,2),HC(13,11),IC(30,13),Ye(4,30)
500 DISP "IS DATA ON TAPE?"
510 INPUT RA
520 IF RA="YES" THEN 530
530 IF RA="NO" THEN 550
540 GOTO 500
550 FPRINT "I X(I) PH(I)"
560 FOR I = 1 TO N
570 DISP "X("I")",PFH("I")"
580 INPUT CI(I),CH(I-1),LC(I+1),HC(I+1)
590 WRITE (15,600),CI(I),CH(I-1),LC(I+1),HC(I+1)
600 FOR F = 5 TO 1
610 NEXT I
620 DISP "APE THERE ANY CORRECTIONS?"
630 INPUT RA
640 IF RA="NO" THEN 740
650 IF RA="YES" THEN 670
660 GOTO 620
670 FPRINT "CORRECTION"
680 DISP "LINE NUMBER?"
690 INPUT L
700 Disp "X("L")",PFH("L")"
710 INPUT CI(L),CH(L),LC(L-1),HC(L-1)
720 WRITE (15,600),CI(L),CH(L-1),LC(L-1),HC(L-1)
730 GOTO 620
740 DISP "FILE NUMBER FOR DATA STORAGE?"
750 INPUT F
```
Program 1a. Calculation of $pK$ of Monoprotonated Monoamines.

650 PRINT "FED I N"
651 PRINT "REDI M"
652 PRINT "D I S P ' I N P U T P R I N T P R I N T P R I N T P R I N T M I = 2 FOR I = 2 TO N 660 M I I = (I - 2) TO N 661 IF I = 2 THEN 664 662 IF ABS(MI1) < ABS(M11) THEN 664 663 M I = 1 664 NEXT I 665 M I I = M I 1 666 FOR I = 1 TO N 667 Y[I] = Y[I] + (Y[I] - Y[I - 1]) * (G[I] - 0.5) / (G[I] + 0.5) + U + Y[I - 1] 668 NEXT I 669 FOR I = 1 TO N 670 IF Y[I] > Y[I - 1] THEN 671 671 NEXT I 672 STOP
961 \[ U = 0.5(U + (T_{C1,1} + V)/(C1,1 + V) + (C1,1 + V)/G1,1) \]

970 \[ G1,1 = 10^3(U + (0.5(U + (1 + U^0.5)^{-0.2}U)) \]

980 \[ H1,1 = (V + (T_{C1,1} + V)/(C1,1 + V) + (10^3 - V)/(C1,1 + V)) \]

990 \[ H2,1 = (H1,1 - (W + (10^3 - V)/(C1,1 + V)) - (10^3 - V)/(C1,1 + V)) \]

1000 \[ H3,1 = (V + (10^3 - V)/(C1,1 + V) + (C1,1 + V)/G1,1) \]

1010 \[ G1,1 = 1 + V \]

1020 \[ G2,1 = G1,1 + V \]

1030 \[ G2,2 = 3^2 \]

1040 \[ G2,1 = (C1,1 - (10^3 - V)/(C1,1 + V) + (10^3 - V)/(C1,1 + V)) \]

1050 \[ G3,2 = (V + (10^3 - V)/(C1,1 + V) + (C1,1 + V)/G1,1) \]

1060 \[ G3,3 = (V + (10^3 - V)/(C1,1 + V) + (C1,1 + V)/G1,1) \]

1070 \[ G3,3 = (V + (10^3 - V)/(C1,1 + V) + (C1,1 + V)/G1,1) \]

1080 \[ MAT = U] \]

1090 \[ MAT = 0 \]

1100 \[ MAT = 1 \]

1110 \[ MAT = 2 \]

1120 \[ FOR I = 1 TO 3 \]

1130 \[ IF A83(0CK,1]/YC,13 > THEN \]

1140 \[ NEXT K \]

1150 \[ GOTO 1190 \]

1160 \[ GOTO 1190 \]

1170 \[ GOTO 1190 \]

1180 \[ GOTO 1190 \]

1190 \[ GOTO 1190 \]

1200 \[ GOTO 1190 \]

1210 \[ GOTO 1190 \]

1220 \[ GOTO 1190 \]

1230 \[ GOTO 1190 \]

1240 \[ GOTO 1190 \]

1250 \[ MAT = TPH(J) \]

1260 \[ FOR I = 1 TO N \]

1270 \[ MAT = inhibitor \]

1280 \[ MAT = inhibitor \]

1290 \[ NEXT I \]

1300 \[ MAT = inhibitor \]

1310 \[ MAT = inhibitor \]

1320 \[ MAT = inhibitor \]

1330 \[ MAT = inhibitor \]

1340 \[ MAT = inhibitor \]

1350 \[ MAT = inhibitor \]

1360 \[ MAT = inhibitor \]

1370 \[ PRINT \]

1380 \[ PRINT \]

1390 \[ PRINT \]

1400 \[ PRINT \]

1410 \[ PRINT \]

1420 \[ PRINT \]

1430 \[ PRINT \]

1440 \[ PRINT \]

1450 \[ PRINT \]

1460 \[ PRINT \]

1470 \[ PRINT \]

1480 \[ PRINT \]

1490 \[ PRINT \]

1500 \[ PRINT \]

1510 \[ PRINT \]

1520 \[ PRINT \]

1530 \[ PRINT \]

1540 \[ PRINT \]

1550 \[ PRINT \]

1560 \[ PRINT \]

1570 \[ END \]
241

Program 1b ,

10

20
3
4
5
6

0
0
0
0

70

8 0
9 0

R
R
D
I
P
P
P
P
P

100
110

120
1
1
1
1
1
1
1

3
4
5
6
7
8
9

0
0
0
0
0
0
0

200
210

220
2
2
2
2
2
2
2
3
3
3
3
3
3
3
3
3
3
4
4
4
4
4
4
4
4

3
4
5
6
7
8
9
0
1
2
3
4
5
6
7
8
9
0
1
2
3
4
5
6
7

0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0

4
5
5
5
5
5
5
5
5
5
5
6
6
6
6
6
6
6
6
6
6
7
7
7
7
7
7

9
0
1
2
3
4
5
6
7
8
9
0
1
2
3
4
5
6
7
8
9
0
1
2
3
4
5

0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0
0

480

C a lc u la tio n o f jK 's o f U nprotonated D iam ines,

E I U M
E D I M
" C U E 3 9 E 9 C O N C
0 ' A M . T :', t.H l , K 8 2 " !
I S P
TC 1 - n - T C 2 . 1 ] , T C
1 ]
N P U T
R I N T
A T
' I N I T I A L
C U E S 3
I N I T I A L
T O T A L
A M
R I N T
A T
' I N I T I A L
G U E 3 3
K A l
= " ! T C 2 . - 1 1
R I N T
' I N I T I A L
C U E 3 3
A T
K A 2
= " ; T C 3 , 1 ]
R I N T
R I N T
F O R
1 = 2
TO. N
T H E N
1 4 0
I F
CC I , 1 ]« C C I- ■ 1 1 1 !
AC I ]= A C I - l 3
G O T O
1 5 0
AC I 3 = ( C C I , 2 ' 3 - C C I- - 1 , 2 ] ) / ( C C I , 1 3 -C C 1 - 1 , 1 ]
N E X T
I
AC 1 3 = A C 2 3
M 2 = 0
F O R
1 = 1
T O
N
YC I , 1 ]= C C 1 . 2 3
D = ( C C I . 1 3 + 'Y)^'::TC 2 , 1 3 *T C 3 . 1 3 + T C 3 , 1 3 * 1 0 K YC I , 2 3 = a C 1 , 1 ]*'v' + T C 2 , 1 3 ' T C 3 , 1 3 ' / D
Y C 1 , 3 3 = ■:T C 1 , 1 3 ^ ' v ' - T C 3 . 1 3 . ^ 1 O t ( - ' V C 1 , 1 3 ) ) / D
YC 1 . 4 3 = (T C 1 , 1 3 ^ ' v ' ^ ( 1 0 t i - V C I . 1 3 ' ) t 2 ; 'D

U"(2*V*S:' /(CC I.,
u=0. 5 * ( U + ( C C 1 . 1

1 3 +' v ' ) + 1 0 t < - Y C 1 . 1 3 > + V C
3 » A . ' / ( C C 1 , 1 3 + '/) )
5 1 3 9 ( ( LIT 0 . 5 ) / ( 1 + U T 0 . 5 )
I 3T2:,

1

,3

. R C
C U ,

1 ) 4 3 , D C 4 , 1 ] , 9 C
1 ] , L C l . , N ]

I N E

C O N C .

= " i T C l i

1 , 3 ] , K C 3 , N 1

1 3

)

Y C

1 , 1

3 + 4 » V C

3 ) + ( 1 0 K - Y C

1

,4

3 + N * 1

01 Y C

1 , 1

3 ) > t 2 >

1 , 1 3

GC I 3 = 1 0 1 ( - 0 .
) - 0 , 2 * U ) >
UC I , 1 3 = 1 / ( A C
N E X T
I
F O R
1 = 1
T O
N
F O R
3 = 1
T O
5
U = ( 2 ^ 3 ' V ) / ' V + CC I , 1 3 ) + ( 1 0 T ( - V C I . 1 3 ) ) / G C I 3 + Y C 1 , 3 3
+
l O T< Y C 1 , 1 3 ) ) / G C
U = U + 0 . 5 * ( ( C C I , 1 3 ^ A ' / ( C C 1 . 1 3 + T ':'+ 4-Y C 1 , 4 3 )
C C I 3 = 1 0 1 ( - 0 . 5 1 3 9 - ( ( ( U T O . 5 ' ( 1 -» ( U T 0 . 5 n ) - 0 . 2 * U ) )
HC 1 , 1 3 = ( ( T C 1 , 1 3 T - ' ; ' / ( C C I , 1 3 + V
) - Y C 1 . 2 3 -V C 1 , 3 3 -V C 1 , 4 3
H t 2 » 1 3 = ( 1 0 t >:-VC I , 1 3 ) " G C I 3 + YC 1 , 3 3 - N / ( ( 1 0 T ( - Y C I , 1 3 , ' ) * G C I 3 )
H C 2 , 1 3 = H C 2 , 1 3 - ( C C I , 1 3 „ A ) . ( C C 1 , 1 3 + '','' ' + 2 T Y C 1 , 4 3
H C 3 , 1 3= ( ( V C I , 2 3 * 1 0 T ( - ' t ' C I, 1 3 ) ' / (Y C I , 3 3 . r C C I 3 t T C 2 , 1 3 ' ) - l
H C 4 , 1 3 = ( ( Y C I , 3 3 - , : 1 0 t ( - V C I,
(V C 1 , 4 3 * ( G C I 3 t 3 ) ( ^ T C 3 , 1 3 ) > - l
P C 1 , 1 3 = P C 2 . 2 3 = (!C 3 . 4 3 = P C 4 ,' 2 3 = 0
PC 1 , 2 3 = p [ 1 , 3 3=C)C 1 , 4 3 = - l
PC 2 , 3 3 = 1
PC 2 , 4 3 = 2
PC 2 , 1 3 = - ( ' . L 0 G ( 1 0 ) '/ C C I 3 ) , c '
1 0 t '- V C 1 . 1 3 ) + N * 1 0 T Y C 1 , 1 3 )
P C 3 , 1 3 = - ' " L 0 G ( 1 0 ) .'^'I'C 1 . 2 3 - 1 0 1 ' : - Y C I .
1 3 : ' ) / ( Y C 1 , 3
3*G C I 3 ( ( T C 2 , 1 3)
P C 3 , 2 3 = ' . 1 0 1 ' . . - Y C 1 . 1 3 ) ) . . ' I'C 1 . 3 3 „ G C I 3 - T C 2 . 1 3 ' '
P C 3 , 3 3 = - ( Y C I . 2 3 - ( 1 0 T ( - Y C 1 . 1 3 ) ) / ( ( Y C I , 3 3 1 2 ) * G C I 3 ,^ T C 2 . 1 3)
PC 4 , 1 3 = - ' ( L 0 G ( 1 0 ) ' t V C 1 . 3 3 - 1 0 T ' ' - ' , C 1 . 1 3 ) ) / ( Y C 1 , 4 3-»( GC I 3 1 3 ) * T C 3 . 1 3 )
P C 4 , 3 3 = ( 1 0 t ( - Y C 1 , 1 3 ) . . '. ( Y C 1 , 4 3 - ' G C I 3 T 3 ) - T C 3 , 1 3 )
P C 4 , 4 3 = - ( V C I . 3 3 * 1 0 T ( - V C I , 1 3 ) ) " . ( Y C I , 4 3 T 2 ) * ( G C I 3 t 3 ) * T C 3 , 1 3 )
M A T
P = IN'.''(P)
M A T
0 = P * H
YC I , 1 3 = Y C 1 , 1 3 - O C 1 , 1 3
3 -O C 2 , 1 3
Y C I , 2 3 = V C I ,
YC I , 3 3 = VC I ,
3 -O C 3 ' 1 3
Y C 1 , 4 3 = Y C I . 4 3 -O C 4 ' 1 3
4
F O R
K = 1
TO
I F
A 8 3 ( 0 C K , 1 3 /V C I , K 3 ) . > T
T H E N
6 0 0
N E X T
K
G O T O
6 1 0

13 '.

N E
EC
PC
PC
P C
PC
PC
PC
PC
PC
M A
JC
JC
JC

X
I
1
1
3
4
1
1
1
1
T
1
1
1

T
, 1
, 2
, 1
, 2
, 3
, 1
, 2 '
, 3
, 4
S
, 1
, 2
, 3

J
3
3
3
3
3
3

= CC I ,
=PC 1,
= ' Y / ' ''.
= -'Xi'C
= -'. YC
= - P C 1
3 = - 0 C 1
3 =- P [ 1
3 = - 0 C 1
= R » P
3 = 3C 1 ,
3 = £C 1 ,
3 = 3C 1 ,

LC 1 , I 3 = EC I ,
N E X T
I

2 3 -Y C
3
+
1
I
,
,
,
,

3 =
CC
, 2
, 3
1 3
2 3
3 3
4 3

P C
I ,
3 3 r

1 , 1 3
2 , 1 3 = R C 2 . 2 3 = P C 2 , 3 3 = P C 3 , 1 3 = P C 3 , 3 3=F'C 4 , 1 3 = R C 4 , 2
1 3.'
, 1 0 t ( - V C
I . 1 3 ) ) / ( Y C I , 3 3 i ^ G C I 3 * ( T C 2 , 13 1 2 ) )
i 0 t ( . - Y C
I , 1 3 ) : ' / ( Y C 1 , 4 3* ( GC I
3 1 3 ) * - < TC 3 , 1 3 1 2 ) )

1 3
2 3
3 3
1 3 + l'JC 1 , 1 3
.

.

.

.

3 = 0

I 3


Program 2. Non-linear Least Squares Calculation of $A_1$, $A_2$ and $k$ in eq. 6.

Written by Dr. W. Sachs.
260 IF N2 = 3 AND N4 = 0 THEN 280
270 GOTO 310
280 DISP "ILLEGAL FILE, TRY AGAIN"
290 WAIT 6000
300 GOTO 240
310 LOAD DATA N2,Z
311 FOR I=1 TO 30
312 Y(I)=X(I)2
313 Ti(I)=X(I)
314 NEXT I
315 N5=30
320 GOTO 420
330 DISP "DATA TO BE KEIED INP"1
340 INPUT N2
350 IF N2=0 THEN 430
360 DISP "NUMBER OF POINTS"1
370 INPUT N2
380 FOR I=1 TO N2
390 DISP "<Y(I),Ti(I)> = "1
400 INPUT X(I),Ti(I)
410 NEXT I
420 GOTO 460
430 DISP "THERE IS NO DATA, TRY AGAIN"
440 WAIT 5000
450 GOTO 150
460 MAT L=EXP[5]
470 GOTO M1 OF 500,510,540
480 PRINT "MODEL: Y = A1*EXP(-K1*T)"
490 N5=2
500 GOTO 560
510 PRINT "MODEL: Y = A1*EXP(-K1*T) + A2"
520 N5=3
530 GOTO 560
550 N5=5
560 WRITE (.15,570)
570 FORMAT /,
580 N3=0
590 DISP "ANY CONSTANT PARAMETERS?"1
600 INPUT N2
610 IF N2=0 THEN 1040
620 DISP "A1 CONSTANT?"1
630 INPUT N2
640 IF N2=0 THEN 700
650 L11=1
660 N3=N3+1
670 DISP "A1 = "1
680 INPUT A1
690 PRINT "A1, CONSTANT AT"1A11
700 DISP "K1 CONSTANT?"1
710 INPUT N2
720 IF N2=0 THEN 730
730 L22=1
740 N3=N3+1
750 DISP "K1 = "1
760 INPUT K1
770 PRINT "K1, CONSTANT AT"1A22
780 GOTO M1 OF 1040,750,790
790 DISP "A2 CONSTANT?"1
800 INPUT N2
810 IF N2=0 THEN 870
820 DISP "A2 = "1
830 INPUT A2
840 PRINT "A2, CONSTANT AT"1A33
850 L33=1
860 N3=N3+1
870 GOTO M1 OF 1040,850,880
880 DISP "K2 CONSTANT?"1
890 INPUT N2
900 IF N2=0 THEN 960
910 L44=1
920 N3=N3+1
930 DISP "K2 = "1
940 INPUT K4
950 PRINT "K2, CONSTANT AT"1A44
THEM I310
COHTFINTS
IMPUTE M2
IF N2 = 0 THEN 1040
L3 = N2 + 1
DISP "A3 CONSTANT?":
I30 INPUT AC5
130 PRINT "A3 CONSTANT AT"; AC5
140 M2 = M5
150 M3 = M2 - M3
160 MAT E=CEP(N2)
170 DISP "LINEAR CONSTRAINTS?":
180 INPUT M5
190 IF M5=0 OR M1=1 THEN 210
200 DISP "NUMBER OF CONSTRAINTS":
I110 INPUT M5
I120 REDIM X[M5]
1130 MAT F=CEP(N5,5)
1140 FOR I=1 TO M5
I150 J2=0
I160 DISP "X(<"; I; ") =": J
1170 INPUT X(I,J)
1180 FOR J=1 TO M2 STEP 2
1190 J2=J2+1
1200 DISP "X(<"; J2; ") =": J
1210 INPUT PC(J,1)
1220 NEXT J
1230 NEXT I
1240 PRINT
I250 PRINT "CONSTRAINT EQUATIONS"
1270 FOR I=1 TO M5
1280 WRITE (15,1430)PC(I,1); PC(I,3); PC(I,5); X(I)
1290 NEXT I
1300 GOSUB 3420
1310 PRINT
I320 IF M4=0 THEN 1420
1330 PRINT "THE CONSTRAINTS: INCLUDING THOSE IMPLIED BY"
1340 PRINT "HOLDING PARAMETERS CONSTANT: ARE REDUNDANT."
1350 PRINT "IS OF RANK LESS THAN INS1. TRY AGAIN."
1360 MAT A=CEP(5)
1370 MAT L=CEP(5)
1380 N5=0
I390 WRITE (15,1400)
1400 FORMAT /,,/
1410 GOTO 470
1420 DISP "HSTART=1: (O=NO; HSTART=YES)"
1430 FORMAT E12.4,*E12.4,*E12.4,*E12.4,*E12.4,*E12.4
1450 INPUT M5
1460 IF M5=0 THEN 1480
1470 N1=N5
1480 DISP "WEIGHTING = 1/Y(I)+2 ?":
1490 INPUT M5
1500 MAT W=CON(1,2)
1510 IF M5=0 THEN 1570
1520 PRINT "WEIGHTING = 1/Y(I)+2"
1530 FOR I=N1 TO N2
1540 WE(I)=WE(I)+Y(I)
1550 NEXT I
1560 GOTO 1580
1570 PRINT "UNIT WEIGHTING"
1580 GOSUB 2590
1590 WRITE (15,1600)AC11,AC21,AC31,AC41,AC51
1600 FORMAT /"STARTING VALUES")/SE12.3
1610 N2=0
1620 IF N2=0 THEN 2190
1630 MAT H=CEP(H3-H3)
1640 MAT F=CEP(5,5)
1650 MAT G=CEP(5,5)
1660 I=H5 = 1
1670 FOR I=N1 TO N2
1680 DC(I)=E(I)-P-AC(2)+T(I)
1690 DC(I)=DC(I)-DC(I)
1700 E(I)=S(I)
1710 IF L1=0 THEN 1720
1720 EC(I)=EC(I)+AC(I)-DC(I)
1730 GOTO M1 OF 1550,1740,1780
1740 DC3=1
1750 IF L3=0 THEN 1850
1760 E3=E3-AC(3)
1770 GOTO 1050
1780 DC3=E3-AC(4)+T(I)
1790 DC3=DC3+T(I)+DC3
1800 DC5=1
Program 3. Non-linear Least Squares Calculation of $k_{im}$, $k_{inh}$, $y$ and $z$ in eq. 24.
Program 4. Linear Least Squares Calculation of \( k_w \), \( k_h \), \( k_{oh} \) and \( k_b \)'s in eq. 37.

```
10 REM THIS PROGRAM CALCULATES SECOND ORDER RATE CONSTANTS FOR CATALYSIS BY
20 REM HYDROXIDE, HYDROXYLIDE, FORMATE, ACETATE, CACO3, BORATE, HYDROGEN, AND
30 REM FOR THE HYDROLYSIS OF N-Iso-PROPYLIDINE/ACIDOLILLUM PERCHLORATE BY
40 REM A LINEAR LEAST SQUARES METHOD MINIMIZING THE SUM OF THE SQUARES OF THE
45 REM FRACTIONAL DEVIATIONS
50 DIM F(36),X(36),Y(36),Z(36),W(36),T(36),V(36)
60 DIM U(36)
70 DISP "HOW MANY SOLUTIONS?"
80 INPUT N
90 REM DATA REVIEW
100 REM "FILE # FOR DATA ARRAY:"
110 DISP 90
120 INPUT 0
130 LOAD DATA 0:0
140 G0=.5190:(50.0<0.0<0.0<0.0)
150 FOR I=1 TO N
160 A(I)=1:V(I)=0
170 C(I)=1:G(I)=0:1.7
180 R(I)=1:W(I)=0
190 REM \( 3 \times 10^1 \) \( 1 \times 0 \)
200 REM \( 2 \times 0 \) \( 1 \times 0 \)
210 REM \( 3 \times 0 \) \( 1 \times 0 \)
220 REM \( 4 \times 0 \) \( 0 \times 0 \)
230 REM \( 5 \times 0 \) \( 4 \times 0 \)
240 REM \( 6 \times 0 \) \( 3 \times 0 \)
250 REM \( 7 \times 0 \) \( 4 \times 0 \)
260 REM \( 8 \times 0 \) \( 0 \times 0 \)
270 REM \( 9 \times 0 \) \( 7 \times 0 \)
280 REM \( 0 \times 0 \) \( 0 \times 0 \)
290 REM \( 1 \times 0 \) \( 1 \times 0 \)
300 REM \( 2 \times 0 \) \( 2 \times 0 \)
310 REM \( 3 \times 0 \) \( 3 \times 0 \)
320 REM \( 4 \times 0 \) \( 4 \times 0 \)
330 REM \( 5 \times 0 \) \( 5 \times 0 \)
340 REM \( 6 \times 0 \) \( 6 \times 0 \)
350 REM \( 7 \times 0 \) \( 7 \times 0 \)
360 REM \( 8 \times 0 \) \( 8 \times 0 \)
370 REM \( 9 \times 0 \) \( 9 \times 0 \)
380 REM \( 0 \times 0 \) \( 0 \times 0 \)
390 REM \( 1 \times 0 \) \( 1 \times 0 \)
400 REM \( 2 \times 0 \) \( 2 \times 0 \)
410 REM \( 3 \times 0 \) \( 3 \times 0 \)
420 REM \( 4 \times 0 \) \( 4 \times 0 \)
430 REM \( 5 \times 0 \) \( 5 \times 0 \)
440 REM \( 6 \times 0 \) \( 6 \times 0 \)
450 REM \( 7 \times 0 \) \( 7 \times 0 \)
460 REM \( 8 \times 0 \) \( 8 \times 0 \)
470 REM \( 9 \times 0 \) \( 9 \times 0 \)
480 REM \( 0 \times 0 \) \( 0 \times 0 \)
```

Program 5. Non-Linear Least Squares Calculation of $K$ and $k_{pyrdn}$ in Eq. 46.
Written by J. Zeigler.

The user has to make adjustments such that the number of functions in lines 820 through 910 is equal to the number of unknown parameters and define the function to be analyzed in line 1490 and the differential equations, the Jacobian matrix in lines 1500 through 1590.

5 REM GENERALIZED LINEAR & NON-LINEAR LEAST SQUARES PROGRAM
10 DIM H[100,100];T[10,10];L[10,10];J[10,10];I[10,10];M[10,10];N[10,10];P[10,10];Q[10,10];R[10,10];S[10,10];T[10,10];U[10,10];V[10,10];W[10,10];X[10,10];Y[10,10];Z[10,10]
20 DIM K[100];P[100];Q[100];R[100];S[100];T[100];U[100];V[100];W[100];X[100];Y[100];Z[100]
30 DISP "TITLE";
40 INPUT T
50 DISP "NUMBER OF OBSERVATIONS";
60 INPUT N
70 DISP "NUMBER OF PARAMETERS";
80 INPUT P
90 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
100 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
110 DISP "HEIGHT MATRIX (YES OR NO)";
120 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
130 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
140 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
150 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
160 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
170 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
180 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
190 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
200 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
210 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
220 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
230 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
240 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
250 REM IN I[1];J[1];K[1];L[1];M[1];N[1];O[1];P[1];Q[1];R[1];S[1];T[1];U[1];V[1];W[1];X[1];Y[1];Z[1]
260 INPUT L.X.Y
270 G: = L.X
280 G: = Y
290 WRITE (15.200) L.X; G:; o: L: : 2
300 GOTO 220
310 DISP "DATA FILE NUMBER" = 1
320 INPUT F1
330 IF D1="YES" THEN 360
340 STORE DATA F1+0
350 GOTO 370
360 LOAD DATA F1+0
370 MAT T = ZER0(F, 11)
380 GOSUB 1400
390 FOR I=1 TO N
400 EI; J = MAT[I; 2]
410 NEXT I
420 IF W= "NO" THEN 470
430 FOR I=1 TO N
440 WC I = 1 / OC I; 2
450 NEXT I
460 GOTO 500
470 FOR I=1 TO N
480 HC I = 1
490 NEXT I
500 DISP "IS THE FUNCTION LINEAR"
510 INPUT LF
520 IF LF="YES" THEN 590
530 FOR I=1 TO P
540 DISP "INITIAL GUESS AT PARAMETER"= III
550 INPUT TI(1; 1)
560 NEXT I
570 DISP "TOLERANCE"
580 PRINT TC I
590 PRINT T T
600 PRINT LF
610 IF LF="YES" THEN 550
620 PRINT "NON-LINEAR FUNCTION"
630 PRINT "TOLERANCE = " IT
640 GOTO 660
650 PRINT "LINEAR FUNCTION"
660 IF W="YES" THEN 690
670 PRINT "UN-WEIGHTED ANALYSIS"
680 GOTO 710
690 WRITE (15.700) 9: 8: 9: 5: 9: 0
700 WRITE (15.700) 9: 8: 9: 5: 9: 0
710 WRITE (15.700) 9: 8: 9: 5: 9: 0
720 FORMAT F5.0; " OBSERVATIONS"
730 WRITE (15.740) F
740 FORMAT F5.0; " PARAMETERS"
750 PRINT "DATA FROM FILE #" = F1
760 IF LF="YES" THEN 600
770 FOR I=1 TO N
780 EI; J = E(I; 1) = FN(I; C)
790 NEXT I
800 PRINT LF
810 FOR I=1 TO N
820 J(I; 1) = FNR (0; (I; 1))
830 J(I; 2) = FNE (0; (I; 1))
840 J(I; 3) = FNE (0; (I; 1))
850 J(I; 4) = FNE (0; (I; 1))
860 J(I; 5) = FNE (0; (I; 1))
870 J(I; 6) = FNE (0; (I; 1))
880 J(I; 7) = FNE (0; (I; 1))
890 J(I; 8) = FNE (0; (I; 1))
900 J(I; 9) = FNE (0; (I; 1))
910 J(I; 10) = FNE (0; (I; 1))
920 NEXT I
930 FOR I=1 TO N
940 FOR J=1 TO P
950 K(J; 1) = J(I; 1) - W(I; 1)
960 NEXT J
970 NEXT I
980 MAT L = + L
990 MAT L = RN(L)
1000 MAT M = - E
1010 MAT M = + M
1020 MAT T= T+ D
1030 FOR I=1 TO N
1040 NEXT I
Program 6a. Function analyzed and differential equations for the Jacobian matrix in Eq. 51 for Ac - ISOXH\textsuperscript{+} reaction.
1490 DEF FN0(X)
1492 A=X+T[1,1]-0.01473*T[1,1]+1
1494 B=(X+T[1,1]-0.01473*T[1,1]+1)*T[1,1]+3*0.152+0.01473*T[1,1]
1496 C=0.01473*T[2,1]+(X+T[1,1]+3)*R*SORB/(2+T[1,1])
1498 RETURN C
1500 DEF FN0(X)
1502 A=X+T[1,1]-0.01473*T[1,1]+1
1504 B=(X+T[1,1]-0.01473*T[1,1]+1)*T[1,1]+3*0.152+0.01473*T[1,1]
1506 C=0.01473*R*SORB/(2+T[1,1]+A+(X-0.152)+0.02946*T[1,1])
1508 D=2+S*SORB+T[1,1]+2
1509 E=0-D
1510 RETURN E
1510 DEF FN0(X)
1512 A=X+T[1,1]-0.01473*T[1,1]+1
1514 B=(X+T[1,1]-0.01473*T[1,1]+1)*T[1,1]+3*0.152+0.01473*T[1,1]
1516 C=0.01473*R*SORB/(2+T[1,1])
1518 RETURN C

Program 6d. Function Analyzed and Differential Equation for the Jacobian Matrix in Eq. 70.

1490 DEF FN0(X)
1492 A=T[1,1]+10*(-X+0.152)+T[1,1]-T[2,1]
1494 B=(X+T[3,1]+13*(-X+0.152)+T[1,1]
1496 C=A*B
1498 RETURN C
1500 DEF FN0(X)
1502 A=1+0*(-X+0.152)+T[2,1]+(10*(-X+0.152)+T[2,1])
1504 B=(X+T[3,1]+10*(-X+0.152)+T[2,1])
1506 C=10*(A+B)*C
1508 RETURN C
1510 DEF FN0(X)
1512 A=1+0*(-X+0.152)+T[2,1]+(10*(-X+0.152)+T[2,1])
1514 C=10*(A+B)*C
1516 O=A+B*C
1518 RETURN O
1520 DEF FN0(X)
1522 A=-1*(-X+0.152)+T[1,1]+T[2,1]+10*(-X+0.152)
1524 B=(X+T[3,1]+10*(-X+0.152)+T[2,1])
1526 O=A+B*C
1528 RETURN O
1600 STOP
Program 7. Non-linear Least Squares Calculation of $k_{-5}$, $k_{-5r}$, $k_{fa}$, $k_{-5o}$, $k_{-2}4/k_{-3}$, and $K$ in Eq. 73.

10 REM THIS PROGRAM CALCULATES FOR N-ISOPROPYLDIETHYLAMMONIUM ION HYDRO-
20 REM LYSIS BASED ON THE MECHANISM WHICH INVOLVES GENERAL BASE CATALYZED
30 REM ATTACH OF WATER ON THE INITIUM ION AND RATE-DETERMINING PROTON TRANS-
40 REM PEP TO CONVERT THE CARBONATE OR PROTONATED CARBONATE INTO THE
50 REM Zwitterion
60 DIM RL(1:20),R(1:20),E(1:20),S(1:20),R(1:20),G(1:20),L(1:20)
70 DIM RL(1:20),R(1:20),E(1:20),S(1:20),R(1:20),G(1:20),L(1:20)
80 REM "HOWNY PUNS?"
90 INPUT H
100 REDIM FLU([H+6],[H+6],[H+6],[H+6],[H+6],[H+6],[H+6],[H+6])
110 REDIM M([H+6])
120 INPUT "FILE # FOR DATA ARRAY"
130 INPUT V
140 FOR I=1 TO N
150 IF Abs(XC(I))<0.2 THEN 220
160 NEXT I
170 FOR I=1 TO N
180 M(I)=SQRT([1+SQRT(1+6)])/2
190 NEXT I
200 FOR I=1 TO N
210 M(I)=M(I)/2
220 NEXT I
230 FOR I=1 TO N
240 XC(I)=XC(I)/2
250 NEXT I
260 NEXT I
270 FOR I=1 TO N
280 XC(I)=XC(I)/2
290 NEXT I
300 FOR I=1 TO N
310 XC(I)=XC(I)/2
320 NEXT I
330 FOR I=1 TO N
340 XC(I)=XC(I)/2
350 NEXT I
360 FOR I=1 TO N
370 XC(I)=XC(I)/2
380 NEXT I
390 FOR I=1 TO N
400 XC(I)=XC(I)/2
410 NEXT I
420 FOR I=1 TO N
430 XC(I)=XC(I)/2
440 NEXT I
450 FOR I=1 TO N
460 XC(I)=XC(I)/2
470 NEXT I
480 FOR I=1 TO N
490 XC(I)=XC(I)/2
500 NEXT I
510 FOR I=1 TO N
520 XC(I)=XC(I)/2
530 NEXT I
540 FOR I=1 TO N
550 XC(I)=XC(I)/2
560 NEXT I
570 PRINT "I=(-5)=""0(I)":""STD DE=""R(1)"
580 PRINT "I=(-5) FOMATE=""R(1)":""STD DE=""R(2)"
590 PRINT "I=(-5) ACETATE=""R(1)":""STD DE=""R(3)"
600 PRINT "I=(-5) CACODYLATE=""R(1)":""STD DE=""R(4)"

---

10 REM THIS PROGRAM CALCULATES FOR N-ISOPROPYLDIETHYLAMMONIUM ION HYDRO-
20 REM LYSIS BASED ON THE MECHANISM WHICH INVOLVES GENERAL BASE CATALYZED
30 REM ATTACH OF WATER ON THE INITIUM ION AND RATE-DETERMINING PROTON TRANS-
40 REM PEP TO CONVERT THE CARBONATE OR PROTONATED CARBONATE INTO THE
50 REM Zwitterion
60 DIM RL(1:20),R(1:20),E(1:20),S(1:20),R(1:20),G(1:20),L(1:20)
70 DIM RL(1:20),R(1:20),E(1:20),S(1:20),R(1:20),G(1:20),L(1:20)
80 REM "HOWNY PUNS?"
90 INPUT H
100 REDIM FLU([H+6],[H+6],[H+6],[H+6],[H+6],[H+6],[H+6],[H+6])
110 REDIM M([H+6])
120 INPUT "FILE # FOR DATA ARRAY"
130 INPUT V
140 FOR I=1 TO N
150 IF Abs(XC(I))<0.2 THEN 220
160 NEXT I
170 FOR I=1 TO N
180 M(I)=SQRT([1+SQRT(1+6)])/2
190 NEXT I
200 FOR I=1 TO N
210 M(I)=M(I)/2
220 NEXT I
230 FOR I=1 TO N
240 XC(I)=XC(I)/2
250 NEXT I
260 NEXT I
270 FOR I=1 TO N
280 XC(I)=XC(I)/2
290 NEXT I
300 FOR I=1 TO N
310 XC(I)=XC(I)/2
320 NEXT I
330 FOR I=1 TO N
340 XC(I)=XC(I)/2
350 NEXT I
360 FOR I=1 TO N
370 XC(I)=XC(I)/2
380 NEXT I
390 FOR I=1 TO N
400 XC(I)=XC(I)/2
410 NEXT I
420 FOR I=1 TO N
430 XC(I)=XC(I)/2
440 NEXT I
450 FOR I=1 TO N
460 XC(I)=XC(I)/2
470 NEXT I
480 FOR I=1 TO N
490 XC(I)=XC(I)/2
500 NEXT I
510 FOR I=1 TO N
520 XC(I)=XC(I)/2
530 NEXT I
540 FOR I=1 TO N
550 XC(I)=XC(I)/2
560 NEXT I
570 PRINT "I=(-5)=""0(I)":""STD DE=""R(1)"
580 PRINT "I=(-5) FOMATE=""R(1)":""STD DE=""R(2)"
590 PRINT "I=(-5) ACETATE=""R(1)":""STD DE=""R(3)"
600 PRINT "I=(-5) CACODYLATE=""R(1)":""STD DE=""R(4)"
Program 8. Calculation of Fractions of Acetone of Different Deuterium Content Using Eq. 76.
Written by Dr. R. Flachskam.

10 REM
20 REM CORRECTION OF MASS SPEC PEAK HEIGHTS OF DEUTERATED ACETONE
30 REM FOR C-13 AND O-18, PARENT PEAKS 52 THROUGH 64 ARE CORRECTED.
40 REM THIS PROGRAM IS WRITTEN IN BASIC FOR HP-9330A COMPUTER.
50 REM
60 REM CORRECTION FACTORS:
70 REM C-13 3 CARBON ATOMS = 1.11% = 3.33%
80 REM 0-13 1 OXYGEN ATOM = 0.20%
90 REM SOURCE - K. BIEHAN, MASS SPECTROMETRY, P. 60
100 REM
110 REM FOR EACH SAMPLE TYPE:
120 REM (1) SAMPLE NUMBER
130 REM (2) PEAK HEIGHTS FROM M/E 58 TO 65 SEPARATED BY COMMAS
140 REM
150 REM PROGRAM CONVERTED FROM FORTRAN IV TO BASIC BY R.L.FLACHSKAM 5-9-75
160 WRITE (15,170) OF ACETONE-D FOR C-13 AND O-18
170 FORMAT "CORRECTION OF MASS SPEC PEAK HEIGHTS"
180 PRINT 190 PRINT
200 DIM A(60),B(65),C(65),D(65),E(65)
210 MAT A=EPE
220 MAT B=EPE
230 MAT C=EPE
240 MAT D=EPE
250 MAT E=EPE
260 MAT F=EPE
270 DIS "SAMPLE NUMBER"
280 INPUT A
290 PRINT "SAMPLE NUMBER \"IATI"
300 DIS "PEAK HTS FROM M/E 58 TO 65"!
310 INPUT A(00),A(01),A(02),A(03),A(04),A(05),A(06),A(07),A(08),A(09),A(10),A(11)
320 FOR I=58 TO 65
330 I=I+1
340 L=L+2
350 A(I)=0.0000+0.0002+0.0002+0.0002
360 B(I)=A(I)+A(I)
370 C(I)=A(I)+A(I)
380 D(I)=A(I)+A(I)
390 NEXT I
400 S=0
Program 9. Non-linear Least Squares Calculation of $k_6$ in Eq. 78
and $q$ in Eq. 84.

Written by Dr. J. Hine
Program 10. Non-linear Least Squares Calculation of $k_B$ and $u$ in Eq. 93.

```plaintext
10 REM NON-LINEARP LEAST SQUARES CALCULATION FOR $k_B$ OF PYRrolidine,
20 REM $u$ AND $u$ FOR THE DECARTERATION OF ACETONE $D_e$
30 DIM D(10,3),F(20,3),M(20,3),C(20,3),E(20,3),R(10,5)
40 DIM X(20,3),Y(20,3),Z(10,5)
50 DISP "NUMBER OF RUNS":1
60 INPUT N
70 RE DIM M(10,3),F(20,3),M(20,3),C(20,3),E(20,3),R(10,5)
80 REM DIM X(20,3),Y(20,3),Z(10,5),T(10,5),U(10,5),H(20,3),R(20,3)
90 REM DIM S(10,5),M(10,5)
100 INPUT NI
110 LOAD DATA N,NI
120 FOR I=1 TO N
130 E[I,5]=10(I-10)-0.59<-SQR(E[I,5]+SQR(E[I,5])-0.2*E[I,5])
140 E[I,3]=E[I,2]-10(I-10)-10.994(<10(I-10)-10.994)
150 E[I,2]=E[I,3]-10(I-10)-10.995(<10(I-10)-10.995)
160 E[I,1]=E[I,4]-10(I-10)-10.996(<10(I-10)-10.996)
170 NEXT I
180 FOR J=1 TO N
190 P[J,1]=1/(E[J]+1)12
200 P[J,2]=P[J,1]*P[J,2]
210 P[J,3]=P[J,2]*P[J,3]
220 P[J,4]=P[J,3]*P[J,4]
230 P[J,5]=P[J,4]*P[J,5]
240 FOR K=1 TO N
250 FOR L=1 TO N
260 GOTO 240
270 NEXT L
280 NEXT K
```

The text contains a program for non-linear least squares calculation, but the full details of the program's structure and variables are not provided in the image.
Program 11. Linear Least Squares Calculation of $k_{nm}$, $k_1$, $k_II$, and $k_{III}$ in Eq. 112.
200 MAT E=TPN(A)
205 MAT E=B+n
210 MAT C=E+H
215 MAT G=C+B
220 MAT X=G+F
225 MAT T=A*X
230 MAT V=F-T
235 MAT U=TPN(V)
240 MAT L=U+W
245 MAT P=L*V
250 MAT M=(Y(J)+C)
255 MAT M=(1/(N-4))*M
260 FOR I=1 TO 4
265 MAT M=SOR(X(J),I)
270 NEXT I
275 PRINT
280 PRINT "FOR 1=1 TO 4"
285 PRINT "M=SOR(X(J),I)"
290 NEXT I
295 PRINT
300 PRINT "FOR I=1 TO 4"
305 PRINT "M=SOR(X(J),I)"
310 PRINT "NEXT I"
315 PRINT
320 PRINT "FOR I=1 TO 4"
325 PRINT "M=SOR(X(J),I)"
330 PRINT "NEXT I"
335 PRINT
340 PRINT "FOR I=1 TO 4"
345 PRINT "M=SOR(X(J),I)"
350 PRINT "NEXT I"
355 PRINT
360 PRINT "FOR I=1 TO 4"
365 PRINT "M=SOR(X(J),I)"
370 PRINT "NEXT I"
375 PRINT
380 PRINT "FOR I=1 TO 4"
385 PRINT "M=SOR(X(J),I)"
390 PRINT "NEXT I"
395 PRINT
400 PRINT
405 PRINT "FOR I=1 TO 4"
410 PRINT "M=SOR(X(J),I)"
415 PRINT "NEXT I"
420 PRINT
425 PRINT "FOR I=1 TO 4"
430 PRINT "M=SOR(X(J),I)"
435 PRINT "NEXT I"
440 PRINT
445 PRINT "FOR I=1 TO 4"
450 PRINT "M=SOR(X(J),I)"
455 PRINT "NEXT I"
460 PRINT
465 PRINT "FOR I=1 TO 4"
470 PRINT "M=SOR(X(J),I)"
475 PRINT "NEXT I"
480 PRINT
485 PRINT "FOR I=1 TO 4"
490 PRINT "M=SOR(X(J),I)"
495 PRINT "NEXT I"
500 PRINT
505 PRINT "FOR I=1 TO 4"
510 PRINT "M=SOR(X(J),I)"
515 PRINT "NEXT I"
520 PRINT
525 PRINT "FOR I=1 TO 4"
530 PRINT "M=SOR(X(J),I)"
535 PRINT "NEXT I"
540 PRINT
545 PRINT "FOR I=1 TO 4"
550 PRINT "M=SOR(X(J),I)"
555 PRINT "NEXT I"
560 PRINT
565 PRINT "FOR I=1 TO 4"
570 PRINT "M=SOR(X(J),I)"
575 PRINT "NEXT I"
580 PRINT
585 PRINT "FOR I=1 TO 4"
590 PRINT "M=SOR(X(J),I)"
595 PRINT "NEXT I"
600 Y=0
605 FOR I=1 TO N
610 X(I)=Y(I)+2
615 PRINT "FOR I=1 TO N"
620 PRINT "X(I)=Y(I)+2"
625 PRINT "NEXT I"
630 PRINT
635 PRINT "END"
REFERENCES


260


   c) p. 170 (d) p. 180 (e) p. 472. (f) pp. 116-118.


