MECHANISM OF PYROLYSIS OF
3,3,4,5-TETRASUBSTITUTED 1-PYRAZOLINES

BY

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ABSTRACT

A series of tetrasubstituted 1-pyrazolines uniquely substituted at all three carbon centers has been prepared and decomposed thermally. The 1-pyrazolines in which three of the substituents occupy a pseudo equatorial position and the remaining substituent occupies a pseudo axial position give as the major product the cyclopropane with retention of configuration. On the other hand, the 1-pyrazolines in which two substituents are pseudo equatorial and two are pseudo axial give a random distribution of cyclopropanes. Evidence is presented that the former set of pyrazolines have a larger degree of folding between the two planes defined by C-3, C-4, C-5 and C-5, N-1, N-2, C-3. This suggests that the larger the degree of folding in the pyrazoline molecule the more stereospecificity there is. Two mechanisms are proposed to account for the cyclopropane formed with retention of configuration - one involving a concerted mechanism and the other involving an intermediate resembling a pyramidal diradical.

In the case of one pair of C-5 isomeric pyrazolines, the pyrazoline in which three substituents are pseudo equatorial and one is pseudo axial gave 99% cyclopropane products whereas the C-5 isomer in which there are two substituents both equatorial and axial gave 67% olefin products. This supports the mechanism involving concerted migration of the hydrogen at C-4 that is trans to the leaving nitrogen.
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I. INTRODUCTION

Pyrolysis of 1-Pyrazolines

(a) 3-Acetyl and 3-Carbomethoxy-1-Pyrazolines

von Auwers and Konig (1,2) studied the stereochemistry of the preparation of cyclopropanes by the addition of diazomethane to double bonds activated by electron-withdrawing groups, followed by thermal decomposition of the resulting pyrazolines. They concluded that when the intermediate pyrazolines are 1-pyrazolines, the cyclopropanes formed retain the geometry of the initial olefins. Other studies by Jones (3-5) on 2-pyrazolines were based on the assumption that 1-pyrazolines decompose with retention of geometry. However, major errors in the analytical results of von Auwers and Konig have been demonstrated by McGreer and co-workers (6,7). In later work by Jones and Tai (8,9), they conclude that at best the reaction is partially stereospecific with respect to the three and four positions of the pyrazoline.

Rinehart and Van Auken (10,11) prepared and studied both the thermal and photolytic decompositions of the two isomeric pyrazolines, cis- and trans-3,5-dimethyl-3-carbomethoxy-1-pyrazolines (1 and 2). Pyrolysis of the stereochemically pure pyrazolines 1 and 2 gave four products including two cyclopropanes, indicating the reaction gives products of mixed stereochemistry, although a slight degree of stereo-
selectivity is noted. The results were explained by the ionic mechanism as shown in Figure 1.

Figure 1 - Ionic mechanism for the pyrolysis of 3,4-dimethyl-3-carbomethoxy-1-pyrazolines.
The C-3 N-2 bond is first broken to give the ionic species 7 in which there is competition between rotation and loss of nitrogen. It is expected that loss of nitrogen (step b) is faster than rotation, and thus the resonance forms 8 and 9 would cyclize immediately upon formation (step c), resulting in some stereoselectivity. Besides losing nitrogen (step b), the ionic species 7 can also possibly give displacement of the diazonium group by backside attack of the C-3 carbanion (step d). With larger groups present, any of these routes would predict an increase in stereoselectivity as a result of more hindered rotation. Similarly, stereoselectivity should be reduced when the pyrazoline is modified in such a way as to increase the stability, and hence the life-time, of the intermediates involved. The possibility that the pyrazolines themselves isomerize (reverse of step a) was ruled out since after partial pyrolysis none of the other isomeric pyrazoline could be detected.

McGreer and co-workers (7,12,13) have investigated the pyrolysis of 3-methyl-3-carbomethoxy-1-pyrazoline (10) and the two isomeric pyrazolines, cis- and trans-3,5-dimethyl-3-carbomethoxy-1-pyrazolines (11 and 12). Pyrolysis of the three pyrazolines 10, 11, and 12 gave the following product distributions.

\begin{align*}
\text{10} & \quad 65 \\
\text{11} & \quad 15 \\
\text{12} & \quad 15 \\
\text{13} & \quad 15 \\
\text{14} & \quad 5 \\
\text{15} & \quad 65 \\
\text{16} & \quad 15 \\
\end{align*}
There are two important features from this data. First of all, the α,β and β,γ-unsaturated esters are formed essentially stereospecifically; that is, the olefin 18 from the pyrazoline 11, and the olefin 17 from the pyrazoline 12. An explanation is possible assuming hydrogen migration is concerted with nitrogen elimination, and assuming that the pyrazolines 11 and 12 exist entirely in the conformations as shown in Figure 2. The results then suggest that the hydrogens designated as H₂, which are trans to the leaving nitrogen, are migrating in the olefin-forming reaction.

The second feature from the data is the cyclopropane-forming reaction in which the cis-pyrazoline 11 gives predominantly the trans-cyclopropane 4, and the cyclopropane 5 with the methyls cis is the predominant cyclopropane from the trans-pyrazoline 12. Thus the cyclopropane-forming reaction is not stereoselective and requires inversion either at C-3 or C-5. The transition state may involve a diradical 9 or a dipolar structure 7 (Figure 1) but McGreer and
Figure 2 - Olefin formation from preferred conformations of 3,5-dimethyl-3-carbomethoxy-1-pyrazolines.

co-workers favour a concerted process. The effect of solvent has been to raise the proportion of the olefins in the product as the dielectric constant of the solvent is raised and this suggests that the cyclopropane products are formed through a slightly different transition state and presumably less polar than the olefins. To obtain inversion by a concerted process two extremes for nitrogen expulsion are considered. One is loss of nitrogen in the C-3, C-4 and C-5 plane, accompanied by formation of two p-orbitals at C-3 and C-5 which would bond to give product of retained configuration. The other is loss of nitrogen perpendicular to the C-3, C-4 and C-5 plane giving two p-orbitals at C-3 and C-5 parallel to each other. However, the groups at C-3 and C-5 would
be sufficiently close to each other to cause unequal stretching of the C-N bonds in the transition state, which would permit a twisting of the molecule and eventually lead to inversion at one center.

McGreer et al. (14) have also studied the pyrolysis of the three pyrazolines, 3-methyl-3-acetyl-1-pyrazoline (20) and cis- and trans-3,5-dimethyl-3-acetyl-1-pyrazoline (21 and 22). Pyrolysis of the pyrazoline 20 gave five products including 2,3-dimethyl-4,5-dihydrofuran (27), and pyrolysis of the pyrazolines 21 and 22 gave six products including 2,3,5-trimethyl-4,5-dihydrofuran (33).

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<th>30</th>
<th>31</th>
<th>32</th>
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<tr>
<td>N≡N</td>
<td>16</td>
<td>24</td>
<td>35</td>
<td>0</td>
<td>2</td>
<td>23</td>
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<tr>
<td></td>
<td>61</td>
<td>17</td>
<td>0</td>
<td>18</td>
<td>4</td>
<td>0</td>
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\[ \begin{array}{cccccc}
COCH_3 & \text{N} & \text{N} & \text{COCH}_3 & \text{COCH}_3 & \text{COCH}_3 \\
23 & 65 & 14 & 14 & 4 & 3 \\
20 & & & & & \\
\end{array} \]

\[ \begin{array}{cccccc}
COCH_3 & \text{N} & \text{N} & \text{COCH}_3 & \text{COCH}_3 & \text{COCH}_3 \\
28 & 16 & 24 & 35 & 0 & 2 \\
21 & & & & & \\
\end{array} \]

\[ \begin{array}{cccccc}
COCH_3 & \text{N} & \text{N} & \text{COCH}_3 & \text{COCH}_3 & \text{COCH}_3 \\
29 & 24 & 35 & 0 & 2 & 23 \\
22 & & & & & \\
\end{array} \]
The formation of the dihydrofuran derivatives is explained assuming an intermediate 34 (Figure 3) is formed with negative charge.

![Figure 3 - Intermediate in dihydrofuran formation.](image)

built up on C-3 of the pyrazoline. As this negative charge is delocalized into the carbonyl oxygen, the oxygen will be able to participate in a ring closure reaction. The fact that the dihydrofuran derivative 33 is formed exclusively from the pyrazoline 21 shows that steric factors present play an important roll. Assuming that the pyrazolines 21 and 22 exist entirely in the conformations as shown in Figure 4, then it can

![Figure 4 - Preferred conformations of 3,5-dimethyl-3-acetyl-1-pyrazolines.](image)

be seen that in 21 the oxygen is in a more favourable position for ring closure. The amount of dihydrofuran is also influenced by the reaction medium. The percentage of the dihydrofuran isomer is highest in a non-polar solvent.

There is also an interesting correlation between the cis- and
trans-3,5-dimethyl-3-acetyl-1-pyrazolines (21 and 22) and the cis- and trans-3,5-dimethyl-3-carbomethoxy-1-pyrazolines (11 and 12). The two trans-pyrazolines 22 and 12 give almost identical product distribution ratios (cis-cyclopropane:trans-cyclopropane:olefin) of 60:15:25 and 61:17:22 respectively. For the cis-pyrazolines, the product distribution ratios (cis-cyclopropane:trans-cyclopropane:olefin) are 18:48:34 for the 3-carbomethoxy pyrazoline 11 and 16:24:37 plus 23% dihydrofuran for the 3-acetyl pyrazoline 21. If the dihydrofuran portion is added onto the trans-cyclopropane, the ratio becomes 16:47:37 for the pyrazoline 21, which is close to the ratio observed for the corresponding trans-3-carbomethoxy-pyrazoline 12. This suggests that the dihydrofuran product is being formed at the expense of the trans-cyclopropane during the pyrolysis of the cis-pyrazoline 21.

McGreer and Wu (15) demonstrated stereospecific olefin formation by preparing and pyrolyzing the two isomeric pyrazolines, cis- and trans-3-methyl-4-ethyl-3-carbomethoxy-1-pyrazolines (35 and 36). Each pyrazoline gave stereospecifically a different α,β-unsaturated ester. This stereospecificity can be related to the structure of the pyrazoline through the requirement that loss of nitrogen must be from the side of the pyrazoline that is trans to the migrating hydrogen at C-4.

The product distribution shows the same general trends as the corresponding 4-methyl pyrazolines 1 and 2. Pyrazolines 35 and 36 do however show a greater proportion of cyclopropane product, and at the same time a greater tendency towards stereospecific formation of the cyclopropanes. The mechanism based on concerted migration of hydrogen
from C-4 to C-5 trans to the leaving nitrogen can be applied in this case. The transition states 42 and 43 may be anticipated for the pyrazolines 35 and 36 as in Figure 5.

Figure 5 - Transition states of the olefin forming reaction for cis- and trans-3-methyl-4-ethyl-1-pyrazolines.

Another example that illustrates the concerted type olefin formation is the cis,trans- and cis,cis-3,4,5-trimethyl-3-carbomethoxy-1-pyrazolines (44 and 45). On the basis of the proposed olefin forming
reaction, the $\alpha,\beta$-unsaturated esters expected from the pyrolysis of the pyrazolines 44 and 45 will be the same in both cases.

\[
\begin{align*}
\text{CO}_2\text{CH}_3 & \quad 46 & \quad 47 & \quad 48 & \quad 49 \\
\text{CO}_2\text{CH}_3 & \quad 61 & \quad 32 & \quad 0 & \quad 6
\end{align*}
\]

McGreer and Masters (16) have determined the kinetics and product distribution for the pyrolysis of 3-methyl-3-carbomethoxy-1-pyrazoline (10) and its 4,4-$d_2$ and 5,5-$d_2$ analogues 50 and 51 in tetralin, n-butyl phthalate, nitrobenzene and foramide. The kinetic isotope effects $k_H/k_D$ for the 5,5-$d_2$ pyrazoline 51 of 1.22 and for the 4,4-$d_2$ pyrazoline 50 of 1.36 are consistent with a mechanism involving migration of the C-4 hydrogen concerted with loss of nitrogen.
Using the scheme in Figure 6, the kinetic isotope effect can be divided into a contribution from the olefin forming reaction and a

Figure 6 - Kinetic scheme for the 3-methyl-3-carbethoxy-1-pyrazolines.
contribution from the cyclopropane forming reaction by making use of
the product distributions. For the pyrazoline 10 and its 4,4-d_2
analogue 50:

\[
\frac{k_H}{k_D} = \frac{k_{OH} + k_{cH}}{k_{OD} + k_{cD}} = 1.36
\]

\[
\frac{k_{oH}}{k_{cH}} = \frac{31.1}{68.9} \quad \text{and} \quad \frac{k_{oD}}{k_{cD}} = \frac{21.8}{78.2}
\]

Thus

\[
\frac{k_{oH}}{k_{oD}} = 1.94 \quad \text{and} \quad \frac{k_{cH}}{k_{cD}} = 1.20
\]

For the pyrazoline 10 and its 5,5-d_2 analogue 51:

\[
\frac{k_H}{k_D} = \frac{k_{OH} + k_{cH}}{k_{OD} + k_{cD}} = 1.22
\]

\[
\frac{k_{oH}}{k_{cH}} = \frac{33.2}{66.8} \quad \text{and} \quad \frac{k_{oD}}{k_{cD}} = \frac{36.2}{63.8}
\]

Thus

\[
\frac{k_{oH}}{k_{oD}} = 1.12 \quad \text{and} \quad \frac{k_{cH}}{k_{cD}} = 1.28
\]
A primary isotope effect for the hydrogen on C-4 is expected with a magnitude of 1.41 to 2.36, based on studies by Sester and Rabinovitch (17a) and Blacks (17b) for the cyclopropane to olefin isomerization. The isotope effect in the cyclopropane to propylene reaction has been attributed to a primary effect associated with the breaking of the migrating C-D bond. For the cyclopropane forming reaction the isotope effect of 1.20 may be attributed to a secondary isotope effect related to the change of hybridization from $sp^3$ towards $sp^2$ found in cyclopropane.

The kinetic isotope effect of 1.22 found for the 5,5-$d_2$ pyrazoline $51$ was divided into 1.12 and 1.28 for the olefin and cyclopropane forming reaction respectively. This provides evidence that the C-5 N-1 bond is breaking in the transition state in the olefin forming reaction. This also provides evidence that there is a change of hybridization at C-5 and the C-5 N-1 bond is breaking in the transition state of the cyclopropane forming reaction. This secondary isotope effect is in line with that found by Seltzer and co-workers (17a-c) for azoalkanes. Further mention will be made of deuterium isotope effects in the discussion of deuterated alkyl pyrazolines (19-23).

(b) 3,5-Diaryl-1-Pyrazolines

Overberger and co-workers (25-28) have prepared a series of 3,5-diaryl-1-pyrazolines and determined the product ratios and rates of thermal decomposition.

The kinetic studies on the 3,5-diaryl-1-pyrazolines indicated that electronic contributions had little effect since the rates and
activation energies for the **trans**-pyrazolines 52, 53 and 55 were essentially the same.

Electron spin resonance studies of the photolytic decomposition of pyrazoline 52 indicated the presence of a free radical. This suggested a mechanism involving a free radical as illustrated in the scheme in Figure 7.

(c) **3-Cyano-3-Carbomethoxy-1-Pyrazolines**

A structure such as the ionic species 7 in Figure 1 suggests that positive charge is built up at C-5 of the pyrazoline system in the transition state. If this is the case, rearrangements characteristic
Figure 7 - Radical mechanism for 3,5-diaryl-1-pyrazolines.

of carbonium ions should be possible for the pyrazoline system. McGreer et al. (29) have prepared a number of 4,4-dialkyl-3-cyano-3-carbomethoxy-1-pyrazolines.
The results obtained from the pyrolysis of the pyrazolines 56, 57 and 58 are consistent with the development of a positive charge at C-5 of the pyrazoline system. In addition, preliminary studies on the rate of pyrolysis were carried out in a variety of solvents. The results suggest a transition state which is more polar than the starting material.

Hamelin and Carrie (30 a-e) and McGreer and Wigfield (31) have prepared a number of 3-cyano-3-carboethoxy (or 3-carbomethoxy)-4-alkyl-4-aryl-1-pyrazolines and studied the pyrolysis reaction. Typical product distributions at 70° in nitrobenzene are shown.
The cis-pyrazolines 69 and 72 (carbomethoxy and aryl cis) gave predominately the olefin from aryl migration, whereas the trans-pyrazolines 67, 70 and 71 gave predominately the olefin from methyl migration. A kinetic study was also carried out for the pyrolysis reaction and the value of the secondary deuterium kinetic isotope effect of $k_H/k_D = 1.03$ suggests that at the transition state there is little progress in the bond breaking of the C-5 N-1 bond. This result differs considerably from the result obtained by McGreer and Masters (16) who obtained an isotope effect of $k_H/k_D = 1.22$ for 3-methyl-3-carbomethoxy-5,5-d$_2$-1-
It was also found that there is negligible effect on the rate on going from p-methoxyphenyl to phenyl to p-nitrophenyl. This suggests that migration of the aryl group and any resulting participation has also progressed to a negligible degree in the transition state. This again differs from the 4,4-d$_2$-1-pyrazoline 50 in which it was found that the C-4 hydrogen was involved in considerable participation in the transition state.

Another interesting piece of information obtained from the same study is the entropy of activation values. The negative values are not consistent with those found by McGreer and Masters (16) although they are consistent with additional constraint in the degrees of freedom of the transition state compared to the starting material which is observed in reactions occurring via ionic transition states in polar media.

Another fact drawn out by solvent effects is that the change of rate in tetralin to nitrobenzene to formamide was found to be 1:34:3.4 x 10$^3$. Such a change of rate can be attributed to a transition state more polar than the starting material. Considering all the results together (the 5,5-d$_2$ isotope effect, aryl groups on rates, entropy of activation, solvent effect on rates) the transition state 73 may be represented as in Figure 8.

![Figure 8 - Transition state for the pyrolysis of 3-cyano-3-carbomethoxy-4-alkyl-4-aryl-1-pyrazolines.](image)
(d) Alkyl Substituted-1-Pyrazolines

Crawford and co-workers (19a-c) have prepared and studied the kinetics of a series of alkyl substituted 1-pyrazolines. First order kinetics were observed to greater than 95% completion and the rate was found to be independent of pressure. As the number of methyl groups are increased on the pyrazoline, the activation energies show a continuous decrease from 42.4 Kcal/mole for 74 to 37.7 Kcal/mole for pyrazoline 82. The decrease per methyl group of approximately one Kcal/mole may be due to an increase in ground state energies. The entropy of activation varies from 11.2 eu for 74 to 4.6 eu for pyrazoline 82, as is expected if the transition state more closely resembles the starting materials on proceeding from pyrazoline 74 to 82.

<table>
<thead>
<tr>
<th></th>
<th>74</th>
<th>75</th>
<th>76</th>
<th>79</th>
<th>80</th>
<th>81</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclopropane</td>
<td></td>
<td>89.2</td>
<td>93.3</td>
<td>52.3</td>
<td>72.6</td>
<td>99.36</td>
</tr>
<tr>
<td>olefin</td>
<td>10.8</td>
<td>6.7</td>
<td>47.7</td>
<td>cis</td>
<td>cis</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.7</td>
<td>2.0</td>
<td></td>
</tr>
<tr>
<td>cyclopropane</td>
<td>33.2</td>
<td>72.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>olefin</td>
<td>cis</td>
<td>cis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.7</td>
<td>2.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
In the same work, the C-4 deuterated pyrazoline 84 was prepared. A kinetic isotope effect of $k_H/k_D = 1.07$ was observed. Following the proposed reaction sequence in Figure 9 the isotope effect for the olefin forming reaction may be calculated.

Assuming $k_{cH}/k_{cD} = 1.0$

From product distributions $k_{oH}/k_{cH} = 47.7/52.3$

$k_{OD}/k_{cD} = 34.0/66.0$

Then $\frac{k_{oH}}{k_{OD}} = 1.80$
The value of 1.80 is close to the value observed for the isomerization of deuterated cyclopropanes (17a,b). The alternative approach of assuming that the olefin and cyclopropane come from different paths gives rise to the kinetic scheme outlined in Figure 10:

![Kinetic Scheme](image)

**Figure 10** - Alternative kinetic scheme for pyrolysis of alkyl substituted 1-pyrazolines.

\[
\frac{k_H}{k_D} = \frac{k_{\text{OH}} + k_{\text{CH}}}{k_{\text{OD}} + k_{\text{CD}}} = 1.07
\]

\[
\frac{k_{\text{OH}}}{k_{\text{CH}}} = \frac{47.7}{52.3} \quad \text{and} \quad \frac{k_{\text{OD}}}{k_{\text{CD}}} = \frac{34.0}{66.0}
\]
Then \[ \frac{k_{OH}}{k_{OD}} = 1.50 \quad \text{and} \quad \frac{k_{CH}}{k_{CD}} = 0.84 \]

The value of 0.84 implies that substitution of deuterium at C-4 increases the rate of cyclopropane by 19%, thus indicating such a scheme (Figure 10) is highly improbable. It was therefore concluded that a common nitrogen-free intermediate is formed after the rate determining step.

Further evidence for a nitrogen-free intermediate is furnished by Crawford and Cameron (21) by the pyrolysis of 3-vinyl-1-pyrazoline (85) and 3-vinyl-5,5-d_2-1-pyrazoline (86). Because the energy of activation was 10.2 kcal/mole less than the parent 1-pyrazoline, this suggested that in the rate determining transition state, complete delocalization involving the vinyl group is attained and thus the C-3 N-2 bond is almost completely broken. The secondary isotope effect of \( k_H/k_D = 1.21 \) is in agreement with the expected value (18a-c). The conclusion is that both carbon-nitrogen bonds are breaking in the rate determining transition state as represented in Figure 11, with the C-3 N-2 bond rupture far in advance of the C-5 N-1 bond.

**Figure 11** - Rate determining transition state for 3-vinyl-1-pyrazoline.
On the basis of the results obtained from deuterium isotope effects, the nitrogen-free intermediate was thought of as a \( \pi \)-cyclopropane. Comparison of the results from pyrazolines 79 and 80, cis- and trans-3,5-dimethyl-1-pyrazolines respectively, indicates that the two terminal carbons of the intermediate are not free of each other (or the lifetime of the intermediate is short) so that equilibrium may be reached. If an equilibrium could be reached, then the products from both pyrazolines 79 and 80 would be identical. One possibility, to explain why the two terminal carbons are not free, is in terms of \( \pi\pi - \pi\pi \) bonding as in species 87. The conversion of a 1-pyrazoline into a nitrogen-free intermediate with an antisymmetric singlet trimethylene structure 88 may also be considered. Such a structure as 88 is especially desirable since the immediate consequence of this species is that conrotation would be preferred to give the inverted stereochemistry, which is in agreement with experimental results obtained from the pyrolysis of several 3,5-disubstituted-1-pyrazolines (11,13,14).

Crawford and Erikson (22) have studied the thermolysis of cis- and trans-4-deuterio-3-methyl-1-pyrazolines (89 and 90), resulting in

![Figure 12 - \( \pi \)-Cyclopropane intermediates.](image-url)
further evidence for a nitrogen-free intermediate such as the antisymmetric trimethylene singlet 88. The advantage of pyrazoline 89 and 90 is that the same trimethylene structure 91 will result from both pyrazolines and thus should give identical product ratios independent of the initial stereochemistry.

<table>
<thead>
<tr>
<th></th>
<th>cyclopropane</th>
<th>cis-2-butene</th>
<th>trans-1-butene</th>
<th>1-butene</th>
</tr>
</thead>
<tbody>
<tr>
<td>89</td>
<td>D</td>
<td>D</td>
<td>D</td>
<td>D</td>
</tr>
<tr>
<td>N≡N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>95.1</td>
<td>1.4</td>
<td>1.0</td>
<td>2.5</td>
</tr>
<tr>
<td>50:50</td>
<td>78:22</td>
<td>72:28</td>
<td></td>
<td>63:37</td>
</tr>
<tr>
<td>90</td>
<td>D</td>
<td></td>
<td></td>
<td>D</td>
</tr>
<tr>
<td>N≡N</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>94.7</td>
<td>1.5</td>
<td>1.1</td>
<td>2.7</td>
</tr>
<tr>
<td>50:50</td>
<td>75:25</td>
<td>63:37</td>
<td></td>
<td>65:35</td>
</tr>
</tbody>
</table>

The results are quite consistent with the proposal of an intermediate free of nitrogen, in that the product distributions are nearly the same for both 89 and 90 and the ratio of hydrogen:deuterium migration for the olefins is nearly equal for both pyrazolines. The results also do not allow for the possibility of a concerted migration of only the hydrogen transoid to the departing nitrogen as shown by the intermediate 91a and 91b in Figure 13. If a transoid mechanism were operating, only trans-2-butene 92, in which the hydrogen migrated, would
Figure 13 - Concerted transition state for olefin forming reaction for cis- and trans-4-deuterio-3-methyl-1-pyrazolines.

result. Similarly, only cis-2-butene 93 in which deuterium migrated would result.

Further studies by Crawford and Ali (23) have given results consistent with the nitrogen-free intermediate proposed as species 88, an antisymmetric trimethylene singlet. They prepared and studied the pyrolysis of cis- and trans-3,4-dimethyl-1-pyrazolines (94 and 95) and their 5,5-d$_2$ analogues 96 and 97. Isotope effects of 1.19 and 1.21 were found for the cis and trans-pyrazolines 94 and 95.
respectively, implying that the C-5 N-1 bond is breaking in the rate determining transition state. That the product distributions from 94 and 95 are different can be explained by use of two discrete intermediates 98 and 99 (Figure 14), both being produced from each pyrazoline but in different ratios depending on the relative populations of the two conformations. The results are also indicative of non-stereospecific olefin formation as already shown by use of cis- and trans-4-deutério-3-methyl-1-pyrazoline (23). For a transoid elimination of nitrogen, the olefins 100 and 101 in Figure 15 would be the expected products. However, it was found that only 4% of 100 was formed from 96 and only

\[
\begin{array}{cccc}
46.0 & 21.8 & 16.3 & 15.8
\end{array}
\]
Figure 15 - Transition states and olefins expected on the basis of concerted mechanism for pyrolysis of cis- and trans-3,4-dimethyl-5,5-d$_2$-1-pyrazolines.

6% of 101 from pyrazoline 97. This can be explained by the scheme in Figure 14, assuming that the major intermediate from the cis-pyrazoline 94 is 99, and the major intermediate from the trans-pyrazoline 95 is 98. It is suggested that the second methyl group at C-4 leads to steric crowding in the rate determining transition state.

Al-Sader and Crawford (24) have studied the product ratios and rates of a series of deuterated 1-pyrazolines. Isotope effects at both C-4 and C-5 were determined for both the olefin and cyclopropane forming reaction. The C-4 isotope effect is larger than expected, but hyperconjugative interactions may be giving rise to the enhanced $\beta$-deuterium isotope effects in the rate determining step.

<table>
<thead>
<tr>
<th></th>
<th>cyclopropane</th>
<th>propylene</th>
<th>$k_H/k_D$</th>
</tr>
</thead>
<tbody>
<tr>
<td>74</td>
<td>88.43</td>
<td>11.57</td>
<td>1.00</td>
</tr>
</tbody>
</table>
It was found that the ratio of CD₂H-CH=CH₂ and CD=CH-CH₃ from the pyrolysis of pyrazoline ¹⁰² was 52:48, giving an inverse intramolecular isotope effect of $k_{H}^{0} / k_{D}^{0} = 0.92$. The value of 0.92 is consistent with the increase in olefin going from ¹⁰² to ¹⁰³. The inverse isotope effect is explained by the change in hybridization on going from $sp^{2}$ to $sp^{3}$.
Figure 16 - Kinetic scheme for 3,3-d$_2$- and 3,3,5,5-d$_4$-1-pyrazolines.

Assuming $\frac{k_{074}}{k_{0102}} = 1.0$

From the product distributions -

$$\frac{2k_{074}}{k_{C77}} = \frac{11.57}{88.43}$$

$$\frac{k_{0102} + k_{0102}}{k_{C102}} = \frac{12.01}{87.99}$$

Then $\frac{k_{C74}}{k_{C102}} = 1.00$
Similarly, by assuming
\[
\frac{k_D^{0102}}{k_D^{0103}} = 1.00
\]

Then
\[
\frac{k^{C102}}{k^{C103}} = 1.01
\]

The values of \(k^{C74}/k^{C102} = 1.00\) and \(k^{C102}/k^{C103} = 1.01\) suggest that there is little or no change in the C-H or C-D force constants of the terminal methylene groups to cyclopropane and propylene.

A scheme may also be drawn out for the C-4 deuterated pyrazolines as shown in Figure 17.

\[\text{Figure 17 - Kinetic scheme for 4-d}_1\text{- and 4,4-d}_2\text{-1-pyrazolines.}\]

From the propylene arrived from pyrazoline 104, the ratio of \(\text{CH}_2=CD-\text{CH}_3\) to \(\text{CH}_2=\text{CH-CH}_2\text{D}\) was 2:1, giving an isotope effect of \(k_H^{0104}/k_D^{0104} = 1.50\).

Assuming
\[
\frac{k_H^{074}}{k_H^{0104}} = 1.01
\]
From the product distributions -

\[
\frac{k_{C74}^{11}}{k_{C74}^{074}} = \frac{11.57}{88.43}
\]

\[
\frac{k_{C104}^{0104} + k_{D}}{k_{C104}^{104}} = \frac{10.79}{89.21}
\]

Then

\[
\frac{k_{C74}}{k_{C104}} = 1.13
\]

Similarly, by assuming

\[
\frac{k_{0104}}{k_{0105}} = 1.01
\]

Then

\[
\frac{k_{C104}}{k_{C105}} = 1.13
\]

Thus deuterium substitution at the C-4 position of the pyrazoline molecule slows down the rate at which the intermediate cyclizes to cyclopropane. This is what is expected on going from sp\(^3\) to sp\(^2\) hybridization, keeping in mind that the C-H bonds in cyclopropane closely resemble sp\(^2\) hybridization.

In summary, the isotope effects for the deuterated 1-pyrazoline derivatives are:

For 3-d\(_2\) deuterium substitution \(\frac{k_{H}^{0}}{k_{D}^{0}} = 0.92\)

\[\frac{k_{C}^{C}}{k_{D}^{C}} = 1.00\]
For $^{4}$-d$_{1}$ deuterium substitution $k^{0}_{H}/k^{0}_{D} = 1.50$

$k^{C}_{H}/k^{C}_{D} = 1.13$

Recently, Crawford and Mishra (32) have prepared (3R:5R)-(+) -trans-3,5-dimethyl-1-pyrazoline (106). On thermolysis, pyrazoline 106 gave 25.6% of trans-1,2-dimethyl cyclopropane (108a and 108b) of 23% optical purity having the S:S configuration (108b), thus indicating an excess of double inversion. If the trimethylene species 107 (Figure 19) were the intermediate, then a racemic mixture of 108 should result. In order to account for the 23% optical purity, use is made of a pyramidal diradical intermediate proposed by Allred and Smith (33). In their system, using exo- and endo-5-methoxy-2,3-diazobicyclo[2.2.1]-2-heptene (109 and 110), they have attributed inversion to the formation of structurally inverted pyramidal diradicals 113 and 114 (Figure 18). The inversion was considered to be a consequence of recoil from energy
released by C-N bond breaking. Ring closure before complete equilibration accounts for the excess of the product of inverted structure.

Figure 18 - Pyramidal diradical mechanism for decomposition of exo- and endo-5-methoxy-2,3-diazabicyclo[2.2.1]-2-heptene.
Thus Crawford and Mishra suggest that the scheme that best fits the data utilizes the pyramidal diradical. This scheme will rationalize the excess of double inversion found for the trans-cyclopropane. The racemic trans-cyclopropane, the cis-cyclopropane and olefins are believed to arise from a trimethylene intermediate. The data thus far cannot distinguish if the trimethylene intermediate is formed from the pyrazoline or from the pyramidal diradical structure or from both. Neither can the data tell if the pyramidal diradical is equilibrating.

The first example of a bicyclic system in which the major product is the one that results from double inversion was reported by Roth and Martin (34). The pyrazoline exo-5,6-dideuterio-2,3-diazobicyclo-[2.2.1]-2-heptene (115) gave a 3:1 mixture of trans- and cis-2,3-dideuterio-bicyclo[2.1.0]pentane (116 and 117). The predominant product was attributed to concerted elimination of nitrogen with accompanying back-side p-orbital overlap in the transition state (Figure 19).
This introduction has treated two main aspects in the pyrolysis of 1-pyrazolines - one the olefin forming reaction, and the other the cyclopropane forming reaction. In the case of alkyl substituted 1-pyrazolines (part (d) of "introduction"), there is considerable evidence for a trimethylene intermediate, both for olefin and cyclopropane formation. In the case of 3-acetyl and 3-carbomethoxy pyrazolines (part (a) of "introduction"), a transoid mechanism in which the substituent at C-4 of the pyrazoline migrates with concerted loss of nitrogen has been well established. However, there is very little known about the mechanism of formation of cyclopropane derivatives from 3-acetyl or 3-carbomethoxy pyrazolines.

It is the purpose of this research to further investigate the formation of cyclopropane derivatives by the preparation and pyrolysis of a series of 3-methyl-3-acetyl-1-pyrazolines uniquely substituted at all three carbon centers. It was also anticipated that the same series of pyrazolines would give results that would emphasize the importance of the conformation of the starting 1-pyrazoline in the olefin forming reaction.
II. RESULTS AND DISCUSSION

Preparation and Product Distributions

The 1-pyrazolines prepared for the present work are listed in Table I. The pyrazolines were prepared by the addition of either diazoethane or phenyldiazomethane to the appropriate \( \alpha,\beta \)-unsaturated ketone.

TABLE I

3,3,4,5-Tetrasubstituted-1-Pyrazolines

\[
\text{1-Pyrazoline} \quad R_2 \quad R_3 \quad R_4 \quad R_5
\]

<table>
<thead>
<tr>
<th>1-Pyrazoline</th>
<th>( R_2 )</th>
<th>( R_3 )</th>
<th>( R_4 )</th>
<th>( R_5 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>118</td>
<td>H</td>
<td>( \text{CH}_3 )</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>H</td>
</tr>
<tr>
<td>119</td>
<td>H</td>
<td>( \text{CH}_3 )</td>
<td>H</td>
<td>( \text{C}_6\text{H}_5 )</td>
</tr>
<tr>
<td>120</td>
<td>( \text{CH}_3 )</td>
<td>H</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>H</td>
</tr>
<tr>
<td>121</td>
<td>( \text{CH}_3 )</td>
<td>H</td>
<td>H</td>
<td>( \text{C}_6\text{H}_5 )</td>
</tr>
<tr>
<td>122</td>
<td>H</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>( \text{CH}_3 )</td>
<td>H</td>
</tr>
<tr>
<td>123</td>
<td>H</td>
<td>( \text{C}_6\text{H}_5 )</td>
<td>H</td>
<td>( \text{CH}_3 )</td>
</tr>
</tbody>
</table>
Addition of phenyldiazomethane to 3-methyl-3-pentene-2-one, (E)-
(24) gave the pyrazolines 118 and 119 in about a 2:1 ratio respectively.
Purification by column chromatography gave a mixture of the two C-5
isomeric pyrazolines as a clear colourless liquid. The pyrazolines
could not be crystallized.

\[ \text{COCH}_3 + \text{C}_6\text{H}_5\text{CHN}_2 \rightarrow \text{COCH}_3 \]

24  118  119

It was not possible to separate the isomeric pyrazolines in order
to obtain pure samples of each, either by t.l.c. or by column chromatography. However, the pyrazoline 118 was enriched to 85% and the pyra-
zoline 119 to 62% by successive column chromatography. The purpose
of separating the pyrazolines was to establish the product distributions
from the pyrolysis of each. An indirect second method became available
to determine the products of pyrolysis from pyrazoline 118, as it was
discovered that when a mixture of the two pyrazolines in ether solution
was kept at room temperature over several weeks only 118 pyrolyzed.
Investigation of the decomposition products by column chromatography
revealed that none of the cyclopropane 127 was present. Thus cyclo-
propane 127 must occur exclusively from pyrazoline 119 and the
decomposition products must therefore be representative of pyrazoline
118. Evidence that the pyrazoline 118 was decomposing exclusively at
room temperature in ether solution is the fact that the starting ratio
of 118:119 was about 2:1 respectively and after several weeks the ratio approached 1:3 respectively. It is assumed that the difference of product distributions is negligible for pyrazoline 118 in ether solution compared to neat pyrolysis.

The product distribution for 118 is that for the ether solution at room temperature. The product distribution for 100% 119 is calculated using the neat pyrolysis of a 25:75 ratio of 118:119 respectively and then correcting to 100% 119 using the results for the decomposition of 118 in ether solution. Five products were identified, three cyclopropanes and two α,β-unsaturated ketones, and the product distributions are given in Table II. There were two minor products that

![Reaction diagram]

remained unidentified. It is possible that the unidentified products were the dihydrofuran derivatives 130 expected from pyrazoline 119. Formation of dihydrofuran products was shown to be characteristic of 3-acetyl-1-pyrazolines (14). In one of the conformations possible for pyrazoline 119, the acetyl group would be in a favourable position for ring closure to occur.
The peaks attributed to the α,β-unsaturated ketones had the same retention times as 128 and 129 obtained by the independent synthesis and were isolated in about 10% purity along with 90% of the cyclopropane 127. The 10% portion was determined to be a mixture of the two olefins 128 and 129 on the basis of the characteristic benzylic hydrogen absorptions in the n.m.r. spectrum. Only 129 is expected from the pyrolysis of 118 or 119 (15) and the low yield of 128 and 129 makes the significance of this result uncertain. It may be that thermal isomerization on the v.p.c. column has taken place as considerable overlap of the two peaks occurred, characteristic of such isomerization.

Addition of phenyl diazomethane to 3-methyl-3-pentene-2-one, (Z)- (25) gave the pyrazolines 120 and 121 in about a 2:1 ratio respectively. Purification by column chromatography gave a mixture of the two C-5 isomeric pyrazolines as a white solid.
As in the case of the two pyrazolines 118 and 119, it was not possible to separate the isomeric pyrazolines completely, either by t.l.c. or column chromatography. However, it was possible to enrich 120 to 80% and 121 to 50% by column chromatography. It was also possible to separate partially the two pyrazolines by slow recrystallization from ether-petroleum ether, with subsequent separation of the crystals according to size. Samples enriched to 95% 120 and 75% 121 were thus obtained. The product distributions for 120 and 121 are calculated using the product distributions from their enriched samples.

Four products were obtained, three isomeric cyclopropanes and one \(\alpha,\beta\)-unsaturated ketone, and the calculated distributions are given in Table II. Two minor products were not identified although it is possible that the formation of the dihydrofuran derivative 130 took place, resulting from ring closure of the pyrazoline 120 (14). The olefin 128 was identified solely on the basis of comparison of retention
times with authentic samples of 128 and 129. Only 128 is expected if a transoid concerted elimination of nitrogen (15) takes place. The other unidentified product was present in less than one percent. The possibility that this unidentified product was the cyclopropane 133 was excluded on the grounds that when a sample containing this product was heated at 220° for 2 hours this same product did not rearrange to the \( \gamma,\delta \)-isomers 134 and 135, as would be expected in the case of an acetyl group cis to a methyl group in a cyclopropane derivative (35). The peak in the v.p.c. assigned as the \( \alpha,\beta \)-unsaturated ketone 128 also remained unchanged on heating to 220° for 2 hours.

![Chemical structures](image)

To further exclude cyclopropane 133 as a product, a sample containing both pyrazolines 120 and 121 was decomposed at 120-30° and the n.m.r. of the resulting products was run. Characteristic peaks in the n.m.r. expected for the C-3 methyl and acetyl methyl of cyclopropane 133 (Table V) were not observed. Also absent were any peaks attributed to the \( \gamma,\delta \)-isomers possible from the pyrolysis of 133.

Addition of diazoethane to 3-methyl-4-phenyl-3-butene-2-one, (E)-(132) gave the pyrazolines 122 and 123 in a ratio of 90:10 respectively. After three treatments of the olefin with the diazo compound, the crude product was triturated with petroleum ether to yield white crystals.
TABLE II

Pyrolysis Products for 3-Acetyl-3',4'-dimethyl-5-(and 5')-phenyl-1-
apyrazolines (118 and 119) and 3'-Acetyl-3',4-dimethyl-5-(and 5')-phenyl-
1-pyrazolines (120 and 121).

<table>
<thead>
<tr>
<th>1-Pyrazoline</th>
<th>Δ 125</th>
<th>Δ 126</th>
<th>α,β-E 128 and 129</th>
<th>Δ 127</th>
</tr>
</thead>
<tbody>
<tr>
<td>118</td>
<td>1</td>
<td>98</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>119</td>
<td>13</td>
<td>25</td>
<td>21(7:14)</td>
<td>41</td>
</tr>
<tr>
<td>120</td>
<td>91</td>
<td>6</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>121</td>
<td>26</td>
<td>22</td>
<td>7</td>
<td>45</td>
</tr>
</tbody>
</table>

1 Geometrical assignment was not made.

Recrystallization from ether-petroleum ether yielded the pure pyrazoline 122. The mother liquor, now consisting of about a 50:50 mixture of

\[
\text{C}_6\text{H}_5\text{COCH}_3 + \text{CH}_3\text{CH}_2\text{NH}_2 \rightarrow \text{C}_6\text{H}_5\text{COCH}_3 + \text{C}_6\text{H}_5\text{COCH}_3
\]

132 122 123

122 and 123, was seeded with pure crystals of 122 and left for one week. On removing the additional crystals of 122, the mother liquor was fractionated by column chromatography. Product data for the pyrolysis of fractions containing 122 and 123 in the ratios of 28:72, 32:68 and
respectively were determined. The data from the 28:72 sample with the data from pure 122 permitted calculations of the product composition from 123 given in Table III.

![Chemical structures](image)

**TABLE III**

Pyrolysis Products for 3-Acetyl-3',5- (and 3',5')-dimethyl-4'-phenyl-1-pyrazolines (122 and 123)

<table>
<thead>
<tr>
<th>1-Pyrazoline</th>
<th>(\alpha,\beta-E)</th>
<th>(\beta,\gamma-E)</th>
<th>(\alpha,\beta-Z)</th>
<th>(\beta,\gamma-Z)</th>
<th>(\Delta)</th>
<th>(\Delta)</th>
<th>(\Delta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>122</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>79</td>
<td>trace</td>
<td>1</td>
</tr>
<tr>
<td>123</td>
<td>28</td>
<td>37(^1)</td>
<td>2</td>
<td>0</td>
<td>21</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

\(^1\) Geometrical assignment based on transoidal elimination (15).
**TABLE IV**

N.m.r. Data for 3,3,4,5-Tetrasubstituted-1-pyrazolines

<table>
<thead>
<tr>
<th>Pyrazoline (^2)</th>
<th>CO(\text{CH}_3)</th>
<th>C-3 methyl</th>
<th>H-4</th>
<th>H-5</th>
<th>C-4 or (J_{H_4-H_5})</th>
<th>C-5 methyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\text{C}_6\text{H}_5)</td>
<td>(\text{COCH}_3) (\text{N}) (\text{N}) (\text{C}_6\text{H}_5)</td>
<td>7.58</td>
<td>8.82</td>
<td>8.08</td>
<td>5.32</td>
<td>8.97</td>
</tr>
<tr>
<td>(\text{C}_6\text{H}_5)</td>
<td>(\text{COCH}_3) (\text{N}) (\text{N}) (\text{C}_6\text{H}_5)</td>
<td>7.76</td>
<td>8.52</td>
<td>7.29</td>
<td>4.63</td>
<td>9.65</td>
</tr>
<tr>
<td>(\text{C}_6\text{H}_5)</td>
<td>(\text{COCH}_3) (\text{N}) (\text{N}) (\text{C}_6\text{H}_5)</td>
<td>7.96</td>
<td>8.31</td>
<td>8.4</td>
<td>5.10</td>
<td>9.03</td>
</tr>
<tr>
<td>(\text{C}_6\text{H}_5)</td>
<td>(\text{COCH}_3) (\text{N}) (\text{N}) (\text{C}_6\text{H}_5)</td>
<td>7.58</td>
<td>8.68</td>
<td>7.7</td>
<td>4.69</td>
<td>9.82</td>
</tr>
<tr>
<td>(\text{C}_6\text{H}_5)</td>
<td>(\text{COCH}_3) (\text{N}) (\text{N}) (\text{C}_6\text{H}_5)</td>
<td>7.52</td>
<td>8.93</td>
<td>6.78</td>
<td>5.18</td>
<td>8.48</td>
</tr>
</tbody>
</table>
Six products were identified and one, consisting of about 1% of the total was not. Three of the products were isomeric cyclopropanes, and the remaining products were α,β- and β,γ-unsaturated ketones. No evidence for the β,γ-unsaturated olefin 3-methyl-4-phenyl-4-hexene-2-one, (Z)-(139) was found.

**Identification of Pyrazolines**

The assignment to the 1-pyrazolines isomeric at C-5 was made primarily on the basis of n.m.r. and the pertinent data is given in Table IV. In the five membered pyrazoline ring the anisotropy of the -N=N- double bond affects the substituents at C-3, C-4, and C-5 unequally. When the pyrazoline is in one of its conformations, the pseudo axial positions are in a shielding zone and thus the chemical shifts of substituents in these positions are shifted upfield; whereas

<table>
<thead>
<tr>
<th>Pyrazoline</th>
<th>COCH$_3$</th>
<th>C-3 methyl</th>
<th>H-4</th>
<th>H-5</th>
<th>C-4 or C-5 methyl</th>
<th>J$_{H_4-H_5}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.75</td>
<td>8.50</td>
<td>6.27</td>
<td>5.91</td>
<td>8.56</td>
<td>7.0</td>
</tr>
</tbody>
</table>

1 Chemical shift values in τ units.
2 Drawn in preferred conformation.
3 Hz units.
the pseudo equatorial positions are in a deshielding zone and thus the chemical shifts are lowered in value.

For example, consider the two isomeric pyrazolines, cis- and trans-3,5-dimethyl-3-acetyl-1-pyrazolines (21 and 22) which are drawn in their preferred conformation in Figure 20. The C-3 methyl of the trans-pyrazoline 22 is expected to be at higher field than the C-3 methyl of the cis-pyrazoline 21. In other words, the C-3 methyl of the trans-pyrazoline is expected to spend more time in the shielding zone of the -N=N- group than the C-3 methyl of the cis-pyrazoline. A similar argument holds for the acetyl groups at C-3 (14).

For the series of pyrazolines prepared in this work it is necessary to differentiate between pairs of compounds isomeric at C-5, for example, pyrazolines 118 and 119. The conformation for pyrazoline 118 in which three groups are in the pseudo equatorial position is expected to be the preferred conformation; whereas pyrazoline 119 will have its two conformations more equally populated, since each isomer has two substituents in both the pseudo equatorial and pseudo axial positions (13-15). Hence the C-3 methyl, C-4 hydrogen and C-5 hydrogen of 118 are expected to be at higher field than the same three groups in

\[
\begin{align*}
\text{cis-21} & \quad \text{trans-22} \\
\begin{array}{c}
\text{COCH}_3 \\
\text{N} \\
\end{array} & \quad \begin{array}{c}
\text{COCH}_3 \\
\text{N} \\
\end{array} \\
7.65 \tau & \quad 8.40 \tau \\
8.83 \tau & \quad 7.78 \tau
\end{align*}
\]
Figure 21 - Conformational preferences of 5-(and 5')-phenyl-3',4'-dimethyl-3-acetyl-1-pyrazolines (118 and 119).

pyrazoline 119. Likewise, the acetyl group and the C-4 methyl are expected to be at lower field in pyrazoline 118. A similar argument holds for the relative chemical shifts of the substituents in pyrazolines 120 and 121 (Table IV).

The corresponding substituents for pyrazolines 122 and 123 - acetyl methyl, C-3 methyl, C-5 methyl, C-4 hydrogen - have chemical shifts which are consistent with the above rationalization. However, the C-5 hydrogens of pyrazolines 122 and 123 have the opposite relative chemical shifts from what is expected. The chemical shift of the C-5 hydrogen of 123 is at 3.91 ppm or 0.73 ppm higher than the chemical shift of the C-5 hydrogen of 122 at 5.18 ppm. Since the C-5 hydrogen of 123 is expected to be at least 0.3 ppm lower and not 0.73 ppm higher than the C-5 hydrogen of 122, then either the C-5 hydrogen of 122 is deshielded by about 1.2 ppm or the C-5 hydrogen of 123 is shielded by about 1.2 ppm - presumably due to the effect of the phenyl group at C-4.

An explanation for the position of the C-5 hydrogen chemical shifts is not evident. It is difficult to determine which of the two
C-5 hydrogens has the normal chemical shift, since comparisons with other 3-acetyl-1-pyrazolines (Figure 22) tend to suggest that the C-5 hydrogen of 122 is much lower than expected and the C-5 hydrogen of 123 is slightly higher than expected. On this basis, it appears that the

![Diagram showing preferred conformations and H-5 chemical shift values of some 3-methyl-3-acetyl-1-pyrazolines.](image)

Figure 22 - Preferred conformations and H-5 chemical shift values of some 3-methyl-3-acetyl-1-pyrazolines.

phenyl group at C-4 is deshielding the hydrogen which is cis at C-5 in the pyrazoline 122.

Other valuable information which aids in the assignments to the C-5 isomeric 1-pyrazolines is the magnitude of the vicinal coupling constant, which is dependent on the dihedral angle (13), similar to ethane derivatives (36). Overberger et al. (27) have prepared cis- and trans-3,5-bis(p-methoxyphenyl)-1-pyrazolines (54 and 53). The cis-pyrazoline has a vicinal trans-(a,a)-coupling of 11.5 Hz compared to the vicinal cis coupling for the trans-pyrazoline of about 8.0 Hz. Similar
coupling constants are observed for the C-5 isomeric 1-pyrazolines (Table IV) in which the pyrazolines 118, 120 and 122 display larger couplings than the respective pyrazolines 119, 121 and 123.

Physical data that are consistent with the assignments to the 1-pyrazolines are the $R_f$ values. The $R_f$ values of the three pyrazolines 118, 120 and 122 are less than their C-5 isomeric counterparts 119, 121 and 123 respectively. The product distributions also support the structural assignments in that the pyrazolines 118, 120 and 122 give as the major product from pyrolysis the cyclopropane resulting from retention of configuration, whereas the pyrazolines 119, 121 and 123 give a more random distribution of products.

Identification of Cyclopropanes

There are four possible cyclopropane products and these are presented in Table V. Identification is based on three aspects: the relative positions of the chemical shifts, the H-2 H-3 coupling constants, and the thermal rearrangement of cis-1-acetyl-3-methyl-cyclopropane derivatives to γ,δ-unsaturated ketones.

The relative positions of the chemical shifts of the 1-methyl and 1-acetyl groups provide important information in determining the stereochemistry between C-1 and C-2.¹ It is expected that the substituent, in this case either acetyl or methyl, cis to the phenyl group will be more shielded, relative to the group when it is trans. It is found that in cyclopropanes 125 and 127 the acetyl resonances are at 7.81 and 7.79 $\tau$ respectively, well within the normal range of 7.4-7.9 $\tau$.

¹ C-2 is always taken as the carbon bearing the phenyl group.
TABLE V

N.m.r. Data¹ for 1,1,2,3-Tetrasubstituted Cyclopropanes

<table>
<thead>
<tr>
<th>Cyclopropane</th>
<th>COCH&lt;sub&gt;3&lt;/sub&gt;</th>
<th>C&lt;sub&gt;1&lt;/sub&gt;-CH&lt;sub&gt;3&lt;/sub&gt;</th>
<th>C&lt;sub&gt;2&lt;/sub&gt;-H</th>
<th>C&lt;sub&gt;3&lt;/sub&gt;-H</th>
<th>C&lt;sub&gt;3&lt;/sub&gt;-CH&lt;sub&gt;3&lt;/sub&gt;</th>
<th>J&lt;sub&gt;H&lt;sub&gt;2&lt;/sub&gt;-H&lt;sub&gt;3&lt;/sub&gt;&lt;/sub&gt; (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>8.20</td>
<td>8.51</td>
<td>7.99</td>
<td>7.66</td>
<td>8.76</td>
<td>7.0</td>
</tr>
<tr>
<td>COCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>7.79</td>
<td>8.88</td>
<td>7.19</td>
<td>8.2</td>
<td>8.95</td>
<td>9.8</td>
</tr>
<tr>
<td>C&lt;sub&gt;6&lt;/sub&gt;H&lt;sub&gt;5&lt;/sub&gt;</td>
<td>7.81</td>
<td>8.92</td>
<td>7.15</td>
<td>8.6</td>
<td>8.88</td>
<td>6.4</td>
</tr>
<tr>
<td>COCH&lt;sub&gt;3&lt;/sub&gt;</td>
<td>8.2&lt;sup&gt;2&lt;/sup&gt;</td>
<td>8.5&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

¹ Chemical shift values in τ units.
2 Approximate expected values.

The respective C-1 methyls of 125 and 127 appear at 8.92 and 8.87 τ. However, in the case of cyclopropane 126, the acetyl resonance is shifted by about 0.4 ppm to higher field at 8.20 τ and the C-1 methyl is about 0.4 ppm lower at 8.51 τ. Thus the phenyl group significantly shields the acetyl group and must be cis in cyclopropane 126.

Roberts et al. (37) have studied the absolute magnitudes of the n.m.r. coupling constants for several cyclopropane derivatives and
have found that in general $J_{\text{cis}} > J_{\text{trans}} > J_{\text{gem}}$. In particular, values of $J_{\text{cis}}$ were found to be in the range of 8.0 - 11.2 Hz and $J_{\text{trans}}$ in the range of 5.2 - 7.0 Hz. For the cyclopropanes 125 and 126, the $H_2$-$H_3$ coupling constants of 6.4 and 7.0 Hz respectively are consistent with trans coupling. For the remaining cyclopropane 127, the coupling of 9.8 Hz is attributed to cis coupling. The H-2 H-3 coupling constant establishes the stereochemistry between C-2 and C-3.

The third check used in the identification of the cyclopropanes was the expectation that the cyclopropanes, in which the acetyl and C-3 methyl are cis, would rearrange thermally to the $\gamma,\delta$-unsaturated ketones (35). Thus on heating cyclopropane 123 at 227° for 3.5 hours, complete rearrangement took place to the erythro- and threo-$\gamma,\delta$-unsaturated ketones 134 and 135 in a ratio of 2:1 respectively. Identification of the erythro- and threo-isomers was based on the fact that the substituent - methyl or acetyl - which is cis to the phenyl group in the most stable conformation will be shielded (38). Neither cyclopropane 126 or 127 rearranged under similar reaction conditions.

- Figure 23 - Thermal rearrangement of 1-acetyl-1',3-dimethyl-2'-phenyl-cyclopropane.
Thus there are three pieces of evidence, all of which are internally consistent and providing an unambiguous assignment to the three isomeric cyclopropanes 125, 126 and 127.

**Identification of Olefins**

The thermal decomposition of pyrazoline 123 gave 3-methyl-4-phenyl-3-hexene-2-one, (E)- (136) and 3-methyl-4-phenyl-4-hexene-2-one, (E)- (137) in 28 and 37% respectively. The corresponding Z isomer of 136, that is, 3-methyl-4-phenyl-3-hexene-2-one, (Z)- (138) was detected in about 2%. The corresponding Z- 139 isomer of 137 was not detected at all (Table III).

According to the transoid nitrogen elimination (15), the α,β- and β,γ-unsaturated ketones 136 and 137 are expected to be the major olefins from the pyrolysis of pyrazoline 123. Since the v.p.c. retention times of the olefins from the pyrolysis of 123 are almost identical, it was necessary to isolate them together. Peaks in the n.m.r. are clearly resolved for 136 and 137. However, several smaller peaks, possibly due to the olefin 138 and other impurities were also present in the n.m.r. In order to confirm the structure of the α,β-unsaturated ketone 136 and the presence of 138, a mixture of the α,β-unsaturated olefins 136 and 138 were synthesized for comparison.

A modified Wittig (39), using propiophenone and trimethyl α-phosphonopropionate gave methyl-2-methyl-3-phenyl-2-pentenoate, (E)- (140) and (Z)- (141) in a 1:2 ratio respectively. Hydrolysis of the esters gave the corresponding acids 142 and 143 in about a 1:2 ratio respectively. Subsequent reaction of the acids with methyl lithium (40) yielded a mixture of the olefins 136 and 138 in a ratio of 1:9.
Assignment of structures to the α,β-unsaturated ketones 136 and 138 is made by comparison of the acetyl and C-3 methyl resonances in the n.m.r. The E- 136 isomer gives a normal acetyl peak at 7.95 τ whereas the Z- 138 isomer, with the acetyl and phenyl cis, has the acetyl peak shifted upfield by about 0.5 ppm to 8.51 τ. A similar shift of the C-3 methyl due to the phenyl group is observed (Figure 25).

Figure 24 - Reaction sequence in preparation of 3-methyl-4-phenyl-3-hexene-2-one, (E)- (136) and, (Z)- (138).

Figure 25 - 3-Methyl-4-phenyl-3-hexene-2-one, (E)- (136) and (Z)- (138) assignments by n.m.r.
Authentic samples of 137 and 139 were not available for comparison and therefore assignment of structure 137 is based entirely on the transoid nitrogen elimination mechanism (15). Such a mechanism would predict that the C-5 methyl and phenyl groups are cis, as they are in the starting pyrazoline 123. The major $\alpha,\beta$-unsaturated ketone product is consistent with the transoid elimination mechanism.

The thermal decomposition of pyrazolines 121 and 119 gave the $\alpha,\beta$-unsaturated ketones 3-methyl-4-benzyl-3-pentene-2-one, (E)- (128) and (Z)- (129). The expected $\beta,\gamma$-unsaturated ketones were not detected. Identification of the two ketones 128 and 129 was based on the presence of benzylic hydrogen absorptions in the n.m.r. and by comparison of retention times with those obtained from an authentic mixture.

A modified Wittig (39), using phenyl acetone and trimethyl $\alpha$-phosphonopropionate gave methyl 3-methyl-3-benzyl-2-butenoate, (E)- (144) and (Z)- (145). Conversion of the esters to the corresponding acids 146 and 147 and subsequent reaction of the acids with methyl lithium (40) gave the two ketones 128 and 129 in a 1:2 ratio respectively. Fifty percent of the reaction product was one of the $\beta,\gamma$-unsaturated ketone isomers.

It was not possible to determine the stereochemistry of the isomeric 3-methyl-4-benzyl-3-pentene-2-ones (E)- (136) and (Z)- (138) by using the chemical shifts of the benzylic hydrogens. Normally the C-5 hydrogens of an $\alpha,\beta$-unsaturated ketone that are cis to the acetyl group are at lower field in the n.m.r.; however, there are at least two exceptions. One is the ketones 3-methyl-3-pentene-2-one (E)- (24)
Figure 26 - Reaction sequence for preparation of 3-methyl-4-benzyl-3-pentene-2-one, (E)- (128) and (Z)- (129), and (Z)- (25) in which the C-5 hydrogens resonate at 8.18 and 8.19 respectively (14). The other is two ketones from this work, 3-methyl-4-phenyl-3-pentene-2-one (E)- (136) and (Z)- (138), with both the C-5 and C-6 hydrogens of the E isomer appearing at higher field than the corresponding peaks of the Z isomer.

Discussion

(a) Olefin Formation

Part (a) of the discussion will be concerned with olefin formation from the pyrolysis of 1-pyrazolines. The main feature concerning the olefin forming reaction from the pyrolysis of the tetrasubstituted 1-pyrazolines in this work is that pyrazoline 122 gives only cyclopropane products, whereas the C-5 isomeric pyrazoline 123 gives 67 percent α,β- and β,γ-unsaturated ketones and 33 percent cyclopropane products (Table III). This result demonstrates the dependence of the olefin
forming reactions on the conformation of the starting 1-pyrazoline and supports the mechanism involving concerted loss of nitrogen from the side of the pyrazoline that is trans to the migrating hydrogen at C-4 (13-15). That olefin formation resulted from pyrazoline 123 and not from pyrazoline 122 depends on the fact that pyrazidine 122 must populate entirely the conformation in which three groups (acetyl, C-5 methyl, phenyl) occupy pseudo equatorial positions and the remaining group (C-3 methyl) occupies a pseudo axial position; whereas pyrazoline 123 populates both conformations (Figure 27).

Figure 27 - Preferred conformations of 3-acetyl-3',5-(and 3',5')-4-phenyl-1-pyrazolines (122 and 123).
That pyrazoline 122 occupies only one conformation and that pyrazoline 123 occupies both conformations is derived from n.m.r. studies. It has been established by McGreer and co-workers (13-15) that a substituent at C-4 or C-5 prefers to occupy a pseudo equatorial position. It is therefore expected that pyrazoline 122 prefers the conformation with three of its substituents pseudo equatorial and one pseudo axial. Pyrazoline 123 is expected to occupy more equally both conformations, with the conformation avoiding the 3,5-diaxial (methyl and methyl) interaction being the major contributor (Figure 27). Thus the pyrazoline 123 should more readily yield olefin products.

Additional evidence for conformational preference based on n.m.r. is obtained from chemical shift values, in particular, the C-3 and acetyl methyl resonances (Table VI). Representative values for a pyrazoline that occupies both conformations equally are obtained from 3-methyl-3-acetyl-1-pyrazoline (20). That both conformations of pyrazoline 20 are equally populated is based on two factors. One is that the C-5 hydrogens have identical chemical shift values and the other is that the two isomeric α,β-unsaturated ketones are formed equally (14).

Chemical shift values of pyrazolines that occupy only one conformation may be obtained from cis- and trans-3,5-dimethyl-3-acetyl-1-pyrazolines (21 and 22). It appears that the conformational preference of a 3-methyl-3-acetyl-1-pyrazoline may be decided upon either by the position of the C-3 and acetyl methyl resonances or by the difference between the two values (Table VI). Thus the C-3 and acetyl methyl chemical shifts of 21 and 22 should give an indication of values expected for other C-3 methyl and C-3 acetyl 1-pyrazolines that have
TABLE VI

N.m.r. Data for Determination of Conformational Preferences of 3-Methyl-3-acetyl-1-pyrazolines

<table>
<thead>
<tr>
<th>Pyrazoline (^1)</th>
<th>3-methyl((\tau))</th>
<th>acetyl</th>
<th>methyl((\tau))</th>
<th>(\Delta) (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>122</td>
<td>(8.93^2)</td>
<td>7.52^2</td>
<td>1.41</td>
<td></td>
</tr>
<tr>
<td>118</td>
<td>8.82</td>
<td>7.58</td>
<td>1.24</td>
<td></td>
</tr>
<tr>
<td>121</td>
<td>8.68</td>
<td>7.58</td>
<td>1.10</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>8.63</td>
<td>7.65</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>8.57</td>
<td>7.73</td>
<td>0.84</td>
<td></td>
</tr>
</tbody>
</table>
TABLE VI (Continued)

| Pyrazoline\(^1\) | 3-methyl(\(\tau\)) acetyl methyl(\(\tau\))  \(\Delta\)(ppm) |
|-----------------|--------------------------|--------------------------|
|                 | 8.52 | 7.76 | 0.76 |
| 119             | 8.50\(^2\) | 7.75\(^2\) | 0.75 |
| 123             | 8.40 | 7.78 | 0.62 |
| 21              | 8.31 | 7.96 | 0.35 |

1 Drawn in preferred conformation.

2 Influenced by C-4 phenyl group.
a preference for one conformation over the other (Table VI). That pyrazolines 21 and 22 occupy only one conformation is based on the stereospecific formation of an $\alpha,\beta$-unsaturated ketone from each. The values of the C-3 methyl resonance at 8.49 $\tau$ and the C-3 acetyl methyl at 7.75 $\tau$ for pyrazoline 123 fall between the respective values for pyrazolines 20 and 21, indicating population of both conformations, with the one in which the two methyls are pseudo equatorial being preferred. On the other hand the values of the C-3 and acetyl methyl resonances for pyrazoline 122 are more extreme than expected on comparison to pyrazoline 22. This not only indicates a strong preference for one conformation but also may indicate a larger degree of folding in pyrazoline 122 compared to 22. This latter point will be dealt with in more detail in part (b) of the discussion, concerning the formation of cyclopropanes from 1-pyrazolines.

The point being made from the comparison of the products from the C-5 isomeric pyrazolines 122 and 123 is that the C-4 hydrogen must be pseudo equatorial before it can migrate either to C-3 or C-5. Since pyrazoline 122 exists in only one conformation (Figure 27), the C-4 hydrogen is always pseudo axial and thus is never in a favourable position to migrate trans to the leaving nitrogen. However, pyrazoline 123, occupying both conformations, now has a C-4 hydrogen pseudo equatorial in one of the conformations. It is through this conformation that the formation of 67 percent olefin takes place.

(b) Cyclopropane Formation

Part (b) of the discussion will be concerned with cyclopropane formation from the pyrolysis of 1-pyrazolines. Stereochemical aspects
of cyclopropane formation have been studied by McGreer and co-workers (12-15) for both 3,4- and 3,5-dialkyl-3-acetyl-(and 3-carbomethoxy)-1-pyrazolines (Table VIII). Other studies have been made on 3,5-diaryl-1-pyrazolines by Overberger and co-workers (25-28), and on 3,4- and 3,5-disubstituted-1-pyrazolines by Crawford and co-workers (19a-c,22,23,32) (Table IX). It is the purpose of the present study to extend the understanding of cyclopropane formation by studying the pyrolysis of pyrazolines uniquely substituted at all three carbon centers.

The most significant feature in the pyrolysis of the 1-pyrazolines in this work (Table VII) is the fact that the pyrazolines 118, 120 and 122 - in which three of the substituents are pseudo equatorial and the other pseudo axial - give the cyclopropane resulting from retention at both C-3 and C-5 as the major product; whereas the pyrazolines 119, 121 and 123 - in which two of the substituents are pseudo equatorial and the other two pseudo axial - give a random distribution of cyclopropanes. In the latter case, the major product may or may not be the cyclopropane resulting from retention at both C-3 and C-5.

This result suggests that there is a distinct difference between the two sets of pyrazolines - on one hand 118, 120 and 122 - and on the other hand 119, 121 and 123. It is the former set of pyrazolines that appear to be abnormal since other 3,5-disubstituted 1-pyrazolines with an electron withdrawing group at C-3 give as the major cyclopropane the one resulting from inversion at either C-3 or C-5 (13,14). Typical examples from Table VIII and cis- and trans-3,5-dimethyl-3-acetyl-1-pyrazolines (21 and 22).

The most obvious differences - using pyrazolines 122 and 123 as an
### TABLE VII

Cyclopropane Products\(^\dagger\) from 3,3,4,5-Tetrasubstituted-1-pyrazolines

<table>
<thead>
<tr>
<th>1-Pyrazoline</th>
<th>125</th>
<th>126</th>
<th>127</th>
<th>133</th>
</tr>
</thead>
<tbody>
<tr>
<td>[\text{C}_6\text{H}_5\text{COCH}_3]</td>
<td>[\text{C}_6\text{H}_5\text{COCH}_3]</td>
<td>[\text{C}_6\text{H}_5\text{COCH}_3]</td>
<td>[\text{C}_6\text{H}_5\text{COCH}_3]</td>
<td>[\text{C}_6\text{H}_5\text{COCH}_3]</td>
</tr>
</tbody>
</table>

\[\text{Inversion requirements follow cyclopropane percentages: } i3 - \text{ inversion at C-3}; i5 - \text{ inversion at C-5}; i3,5 - \text{ inversion at C-3 and C-5.}\]
TABLE VIII

Distribution of Cyclopropane Products for Pyrazolines with Electron Withdrawning Groups at C-3

<table>
<thead>
<tr>
<th>Pyrazoline</th>
<th>cis-Δ</th>
<th>trans-Δ</th>
<th>other</th>
<th>ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>(11)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td>(11)</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td></td>
<td></td>
<td>(13)</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td></td>
<td></td>
<td>(13)</td>
</tr>
<tr>
<td>21</td>
<td></td>
<td></td>
<td></td>
<td>(14)</td>
</tr>
<tr>
<td>22</td>
<td></td>
<td></td>
<td></td>
<td>(14)</td>
</tr>
<tr>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td>(15)</td>
</tr>
<tr>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td>(15)</td>
</tr>
<tr>
<td>146</td>
<td>29.6</td>
<td>0.13</td>
<td>70.4</td>
<td>(31)</td>
</tr>
</tbody>
</table>
### TABLE IX

Distribution of Cyclopropane Products for 3,5-Diaryl-1-pyrazolines and Alkyl Substituted 1-Pyrazolines

<table>
<thead>
<tr>
<th>Pyrazoline</th>
<th>cis-Δ</th>
<th>trans-Δ</th>
<th>Other</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>52 ( \text{C}_6\text{H}_5 ) \text{N} ( \text{C}_6\text{H}_5 )</td>
<td>11(_{13}) or 5</td>
<td>89</td>
<td>0</td>
<td>(28)</td>
</tr>
<tr>
<td>p-anisyl ( \text{N} ) p-anisyl</td>
<td>6.7(_{13}) or 5</td>
<td>93.0</td>
<td>0</td>
<td>(28)</td>
</tr>
<tr>
<td>p-anisyl ( \text{N} ) p-anisyl</td>
<td>43.0</td>
<td>57.0(_{13}) or 5</td>
<td>0</td>
<td>(28)</td>
</tr>
<tr>
<td>Cl-C(_2\text{H}_4) ( \text{N} ) Cl ( \text{C}_6\text{H}_4)-Cl</td>
<td>0(_{13}) or 5</td>
<td>100</td>
<td>0</td>
<td>(28)</td>
</tr>
<tr>
<td>79</td>
<td>33.2</td>
<td>66.1(_{13}) or 5</td>
<td>0.7</td>
<td>(19)</td>
</tr>
<tr>
<td>80</td>
<td>72.6(_{13}) or 5</td>
<td>25.4</td>
<td>2.0</td>
<td>(19)</td>
</tr>
<tr>
<td>89</td>
<td>50</td>
<td>50(_{13})</td>
<td>4.9</td>
<td>(22)</td>
</tr>
<tr>
<td>90</td>
<td>50(_{13})</td>
<td>50</td>
<td>5.3</td>
<td>(22)</td>
</tr>
<tr>
<td>94</td>
<td>45.4</td>
<td>33.0(_{13})</td>
<td>21.6</td>
<td>(23)</td>
</tr>
<tr>
<td>95</td>
<td>46.0(_{13})</td>
<td>21.8</td>
<td>22.2</td>
<td>(23)</td>
</tr>
</tbody>
</table>
example - is that pyrazoline 122 exists in only one conformation, whereas pyrazoline 123 occupies both conformations. This point concerning conformational preferences of 122 and 123 has been discussed previously in part (a) of the discussion.

The explanation chosen to explain the fact that from pyrazolines 118, 120 and 122 the major cyclopropane is the one in which retention is observed at both C-3 and C-5, whereas pyrazoline 119, 121, and 123 give a random selection of cyclopropanes does not depend on the obvious difference between conformational populations. Instead, it is proposed that it is the difference between the degree of folding in the pyrazoline molecule, where the degree of folding is defined as the angle between the plane of atoms C-3, C-4, C-5 and the plane of atoms C-3, N-2, N-1, C-5.

McGreer et al (13) have estimated the cis-dihedral angle and the trans-(a,a)-dihedral angle to be about 25° and 145° respectively for cis- and trans-3,5-dimethyl-1-pyrazolines (11 and 12). This estimation was based on the observed coupling constants of about 8.0 Hz for both the cis- and trans-(a,a)-coupling. The calculated dihedral angles of 25° and 145° gives a folding of about 25° between the two planes in the pyrazolines 11 and 12. Assuming that the trans-(a,a)-coupling constant increases as the axial-axial dihedral angle increases (36), then the pyrazolines 118, 120 and 122 have a larger degree of folding than usual. The H-4 H-3 trans-coupling observed are 10.4, 9.8 and 8.4 Hz respectively.

It is possible that this larger degree of folding in the pyrazoline ring system accounts for the major product from pyrazolines 118, 120 and
122 being the cyclopropane formed with retention at both C-3 and C-5. If the axial-axial coupling constant is proportional to the degree of folding then it is expected that the folding decreases from pyrazolines 118 to 120 to 122 with trans-couplings of 10.4, 9.8, and 8.4 Hz respectively. This order also correlates with the degree of stereospecificity of 98 to 91 to 79 percent for pyrazolines 118, 120 and 122 respectively. The stereospecificity refers to the percentage of the cyclopropane formed with the same configuration as the starting pyrazoline.

Another indication of the degree of folding is obtained from the chemical shift values of the C-3 and acetyl methyl resonances, or their difference, in the n.m.r. (Table VI). However, the resonances of the respective groups for pyrazolines 118, 120 and 122 have more extreme values than expected on comparison to cis- and trans-3,5-dimethyl-3-acetyl-1-pyrazolines (21 and 22) which occupy only one conformation (14) (Figure 4). The more extreme values in the n.m.r. spectrum can be attributed to increased folding of the pyrazoline molecule. Increased folding places the substituents at C-3 (or C-5) in a more intense shielding (equatorial) or deshielding (axial) zone of the -N=N- double bond.

On the basis of the preceding explanation of the results, two mechanisms are proposed to account for the large degree of retention in the formation of cyclopropanes from pyrazolines 118, 120 and 122. One mechanism is that as the pyrazoline is expelling nitrogen, there is at the same time some overlap of the potential bonding orbitals between
C-3 and C-5 and thus a cyclopropane with retention of configuration is formed in a concerted process (Figure 28). How much bonding there is between the C-3 and C-5 positions of the pyrazoline in the transition state is dependent on the degree of folding in the starting pyrazoline molecule.

Figure 28 - Concerted mechanism for formation of cyclopropanes with retention of configuration.

An alternative explanation, which allows for an intermediate, utilizes the formation of a pyramidal diradical (Figure 29) as described by Allred and Smith (33) (Figure 18). However, the pyramidal diradical is not "inverted" at C-3 and C-5, where inversion was a consequence of recoil from the energy released by the C-N bond breaking (33), but is formed merely from the expulsion of nitrogen without recoil (Figure 29). Upon the formation of this pyramidal diradical, immediate ring closure results in a cyclopropane with retention at C-3 and C-5.

It may be that a true pyramidal diradical is not produced but that the

Figure 29 - Pyramidal diradical mechanism for formation of cyclopropanes with retention of configuration.
back lobes have some development. This would give an intermediate between the pyramidal diradical and a trimethylene species where the p-orbitals are fully developed. The more the intermediate resembles a pyramidal diradical, the more cyclopropane with retention of configuration. Thus the larger the degree of folding in the pyrazoline molecule the more the intermediate will resemble the pyramidal diradical. Exactly why a greater folding in the pyrazoline molecule should allow for greater overlap of the developing bond between C-3 and C-5 (mechanism 1) or should make the intermediate resemble more strongly a pyramidal diradical (mechanism 2) is not understood.

Thus a mechanism involving either a concerted process or an intermediate resembling a pyramidal diradical is proposed to play an important part in the formation of cyclopropanes in which retention of configuration is observed. The degree to which a pyrazoline gives a cyclopropane with retention of configuration appears dependent on the degree of folding in the pyrazoline molecule. In a pyrazoline such as 118, the degree of folding is large and pyrolysis gives 98 percent of the cyclopropane 126 resulting from retention at C-3 and C-5. In pyrazolines such as cis- and trans-3,5-dimethyl-3-acetyl-1-pyrazoline (21 and 22) and the analogous 3-carbomethoxy-1-pyrazolines 10 and 11, the cyclopropane with the same stereochemistry as the starting pyrazoline varies from 15 to 18 percent (Table VIII). This is consistent with the lesser degree of folding in pyrazolines 10, 11, 21 and 22 as indicated by n.m.r. However, the degree of folding may be to such a lesser degree in pyrazolines 10, 11, 21 and 22 compared to 118, 120 and 122 that the cyclopropanes with retention of stereochemistry may not be formed
at all through either of the above two mechanisms but rather through some alternative route.

Another feature of the results is that cyclopropane 133 was never observed as a product of pyrolysis from any of the six pyrazolines in this study (Table VII). It was anticipated that pyrazoline 121 would give to some extent cyclopropane 133, since the pyrazoline and cyclopropane have the same stereochemistry about the carbon atoms. Such was the case with the analogous pyrazolines 119 and 123 as cyclopropanes with retention of configuration were formed from both pyrazolines.

The chemical shift values (Table VI) of the acetyl and C-3 methyls of pyrazoline 121 indicate that the molecule occupies entirely the conformation in which the C-3 acetyl group and the C-5 phenyl group are pseudo equatorial; whereas the n.m.r. of the analogous pyrazolines 119 and 123 indicates that both conformations are occupied, with the conformation most highly populated being the one in which the 3,5-diaxial interaction is avoided. This suggests that for 3,5-diaxial interactions, phenyl and acetyl (pyrazoline 121) is much greater than either phenyl and methyl (pyrazoline 119) or methyl and methyl (pyrazoline 123). Such a severe interaction of a phenyl and acetyl may also be indicative of an equally severe interaction in the transition state. However, such an interaction between an acetyl and phenyl group cannot be the main factor which explains the lack of formation of cyclopropane 133 since cyclopropane 126, with a phenyl and acetyl cis, is formed substantially from each of the pyrazolines 119, 121, and 123. The additional factor must therefore be due to the presence of the C-4 methyl group which is cis to both the acetyl group at C-3 and the methyl group at C-5 in the
starting pyrazoline 121, and which gives rise to steric crowding in
the transition state.

Before continuing on to the next point concerning double
inversion at C-3 and C-5, it is first necessary to comment briefly on
the formation of bicyclo[2.1.0]pentane derivatives from the correspond­
ing 2,3-diazobicyclo[2.2.1]-2-heptene (33,34). Allred and Smith (33)
have proposed an inverted pyramidal diradical formed from the consequences
of recoil from energy released by C-N bond breaking. Ring closure before
complete equilibration accounts for the excess of the product of inverted
structure (Figure 18). However, the product of inverted structure may
also be rationalized using the second mechanism (Figure 29) from this
work involving an intermediate resembling a pyramidal diradical, which
accounted for the large degree of retention in the formation of
cyclopropane products from pyrazolines 118, 120 and 122 (Table VII).
Expulsion of nitrogen from the bicyclic pyrazoline without recoil and
double inversion would result in an intermediate (Figure 30) resembling
a pyramidal diradical in which the back lobes are partially developed.
The distinct difference between the intermediates from 118, 120 and 122

Figure 30 - Intermediate resembling a pyramidal diradical species in
pyrolysis of endo-5-methoxy-2,3-diazabicyclo[2.2.1]-2-heptene.
and the intermediate from 109 and 110 is that in the former case the larger front lobes are pointing towards each other; however, in the latter case the strain of the five membered ring results in the back lobes pointing towards each other. Taking into consideration the bonding in bicyclo[2.1.0]pentane (46), the back lobes are in a favourable geometric position to bond as opposed to the front lobes. Allred and Smith (33) have suggested that the pyramidal diradical in their case can equilibrate, although not entirely, before ring closure occurs. However, in the second mechanism in this work the intermediate resembling a pyramidal diradical ring closes immediately upon formation.

Similar work by Roth and Martin (34) has indicated predominance of double inversion in the pyrolysis of exo-5,6-dideuterio-2,3-diazobicyclo-[2.2.1]-2-heptene (115) (Figure 19). Their proposed mechanism involving concerted elimination of nitrogen with accompanying backside p-orbital overlap in the transition state seems equally improbable from a geometrical point of view since the developing backside p-orbitals are directed away from each other.

The feature in the present study concerning double inversion is the substantial contribution of the cyclopropane in which inversion has taken place at both C-3 and C-5 of the starting pyrazolines 119, 121 and 123 (Table VII). There are several mechanisms which can explain double inversion, two of which have been mentioned in the preceding two paragraphs. As pointed out, the use of an "inverted" pyramidal diradical by Allred and Smith (33) is not necessary from the point of view that an intermediate resembling a pyramidal diradical can equally explain the predominance of the double inverted product. The other mechanism by Roth and Martin (34) seemed unlikely from a
Thus a third mechanism may be required to explain the considerable amount of double inverted cyclopropane product formed from the pyrolysis of the 1-pyrazolines 119, 121 and 123. One such mechanism would involve a trimethylene intermediate, in which a symmetrical trimethylene on disrotation, would give cyclopropanes with retention or inversion at both C-3 and C-5. However, to this date there is no conclusive evidence that a trimethylene intermediate participates in the pyrolysis of 1-pyrazolines with an electron withdrawing group at C-3, although the existence of a trimethylene intermediate is quite well established in the pyrolysis of alkyl substituted 1-pyrazolines (19-24,32).

As pointed out in part (a) of the Introduction, very little is known about the formation of cyclopropane derivatives from the pyrolysis of 1-pyrazolines that have an electron-withdrawing group, such as acetyl or carbomethoxy, at the C-3 position. A concerted mechanism (Figure 28) or a mechanism involving an intermediate resembling a pyramidal diradical (Figure 29) has been proposed to account for the formation of cyclopropanes that have the same stereochemistry as the starting pyrazoline. However, additional experimental data are required in order to further the understanding of cyclopropanes formed by an inversion at either C-3 or C-5 or by a double inversion at C-3 and C-5.
III. EXPERIMENTAL

General Statement

Melting points (m.p.) and boiling points (b.p.) are uncorrected.

Infrared (i.r.)-spectra were recorded on a Perkin-Elmer model 137 spectrophotometer. All spectra were measured as a liquid film using sodium chloride plates.

The 60 MHz nuclear magnetic resonance (n.m.r.) spectra were recorded on either a Varian Associates Model A-60 spectrometer or a Jelco Model C-60 spectrometer by Miss P. Watson. The 100 MHz nuclear magnetic resonance spectra were recorded on a Varian Associates Model HR-100 spectrometer by Mr. R. Burton. The spectra were run as solutions either in carbon tetrachloride or deuteriochloroform (Merck, Sharp and Dohm) with Tetramethylsilane as the internal reference.

The vapour-phase chromatography (v.p.c.) units used were an Aerograph Model A-90-P and an Aerograph Model A-90-P3. All columns used were 10' x 1/4" unless otherwise indicated.

The elemental microanalyses were performed by Mr. P. Borda.

Petroleum ether refers to the fraction boiling between 30-60°.

N-Nitroso-N-ethyl Urea

N-Nitroso-N-ethyl urea was prepared according to the procedure given by Chiu (41).
Diazoethane

Diazoethane was prepared from N-nitroso-N-ethyl urea according to the procedure given by Chiu (41).

Benzaldehyde Hydrazone

A procedure similar to that of Curtius (42) was used in the preparation of benzaldehyde hydrazone. Into a 250 ml round bottom flask equipped with a mechanical stirrer was placed 1.5 g of barium oxide and 50 g (1.0 mole) of hydrazine hydrate. Over a period of one hr 95 g (0.90 mole) of freshly distilled benzaldehyde (Analar) was added. The reaction mixture was stirred vigourously at 100° for 6 hr. Before completion of the reaction a considerable amount of solid was formed, but during the course of the reaction the solution again became clear. The reaction mixture was cooled, diluted with ether, and filtered. The ether layer was dried with sodium sulphate and concentrated with a rotatory evaporator. The crude reaction product was distilled under vacuum to yield 90 g (0.74 mole) of a clear pale yellow liquid: yield 82%; b.p. 138-40° (14 mm); n.m.r. 4.08 τ (broad singlet) nitrogen protons, 2.43 τ (singlet) benzylic hydrogen, 2.40 and 2.74 τ (multiplets with areas of 2 and 3 respectively) $A_2B_3$ system of aromatic hydrogens.

Phenyl Diazomethane

A procedure similar to Standinger (43), with yellow mercuric oxide (AC) as the oxidant, was used in the preparation of phenyl diazomethane. Into a 250 ml Erlenmeyer was placed 12 g (0.1 mole) of benzaldehyde hydrazone, 70 ml of petroleum ether and 1 ml of saturated potassium hydroxide alcoholic (ethanol) solution. The flask was placed in an
ice-water bath and over a period of 20 min 21.6 g (0.1 mole) of mercuric oxide was added to the magnetically stirred solution. The mixture was allowed to stir for an additional 10 min and the decanted petroleum ether layer was filtered. The resulting red solution was made up to 100 ml with petroleum ether and used immediately. The preparation was carried out in a fume hood. Based on the reaction with 0.1 molar quantities of methyl isopropenyl ketone, methylmethacrylate, and methacrylonitrile, the yield of phenyl diazomethane varied between 50 and 65%.

3-Methyl-3-pentene-2-one, (Z)- (25)

Irradiation of 12 g (0.12 mole) of 3-methyl-3-pentene-2-one, (E)- (24) (Aldrich) in 100 ml of ether for 16 hr in a silica tube using a Hanovia 450 W lamp (2537 Å) resulted in approximately 25% conversion to the desired Z isomer 25 as determined by v.p.c. (didecyl phthalate, 138°, 120 ml per min). The retention times for the Z and E isomers were 8.6 and 11.0 min respectively (lit. (14): b.p. 124° and 147° respectively). The ether was removed and a simple distillation gave a fraction boiling between 131-136° which consisted of a 50:50 mixture of the Z and E isomers. The 50:50 mixture was then fractionally distilled using a Nester and Faust stainless steel spinning-band apparatus. The fraction between 124-30° was collected and consisted of a 90:10 ratio of the Z and E isomers respectively. Since the spinning-band distillation failed to purify the Z isomer sufficiently, 1.8 g (0.18 mole) was collected using the v.p.c. resulting in greater than 95% purity.
3-Methyl-4-phenyl-3-butene-2-one, \( (E) \) - (132)

The olefin \( 132 \) was prepared according to the procedure of Noyce (44). Into a 500 ml round bottom flask was placed 106 g (1.0 mole) of benzaldehyde and 72 g (1.0 mole) of methyl ethyl ketone together with 3 ml of concentrated sulphuric acid and 100 ml of acetic acid. The mixture was stirred at 75-85° for 3 hr. The reaction was monitored by v.p.c. (SE 30, 210°, 120 ml per min).

The reaction mixture was poured onto 650 g of ice and water and extracted with ether. The ether was extracted with saturated sodium chloride solution, 10\% sodium carbonate, and again with saturated sodium chloride. The solution was dried over sodium sulphate, concentrated using a rotatory evaporator, and vacuum distilled to collect the fraction between 100-105° at 0.5 mm. The product was recrystallized from ether-petroleum ether (1:1) to give white crystals: yield 23\%; m.p. 37-40°; n.m.r. 7.97 \( \tau \) (doublet \( J = 1.5 \) Hz) C-3 methyl, 7.60 \( \tau \) (singlet) acetyl methyl, 2.54 \( \tau \) (multiplet) vinyl hydrogen, 2.65 \( \tau \) (singlet) aromatic hydrogens.

3-Acetyl-3',4'-dimethyl-5-phenyl-1-pyrazoline\(^1\) (118) and 3-Acetyl-3',4'-dimethyl-5'-phenyl-1-pyrazoline (119)

(a) Preparation and Enrichment

To an ether solution of 9.8 g (0.1 mole) of 3-methyl-3-pentene-2-one, \( (E) \) - (124) was added phenyl diazomethane (from 12 g (0.1 mole) of benzaldehyde hydrazone). The solution was left at -5° for 10 days. Pyrazoline formation was indicated by use of n.m.r. The ratio of the

\(^1\) See Appendix for nomenclature
two pyrazolines 119 and 118 was estimated in the crude reaction mixture as 1:2 respectively. The pyrazolines 118 and 119 were stored as a solution in ether-petroleum ether at -5°.

Column chromatography (silica gel, ether-petroleum ether, 5:95 to 10:90) on the crude reaction mixture gave two main fractions, the second of which yielded together the pure pyrazolines 118 and 119 as clear colourless liquids. By determining the ratio of the pyrazolines in successive fractions, it was found that the pyrazoline 119 had the larger R_f value.

For the pyrazoline 118: n.m.r. 8.82 and 7.58 τ (singlets) C-3 and acetyl methyls respectively, 8.97 τ (doublet J = 7.0 Hz) C-4 methyl, 5.32 τ (doublet J = 10.4 Hz) C-5 hydrogen, 8.08 τ (multiplet) C-4 hydrogen, 2.7 τ (multiplet) aromatic hydrogens.

For the pyrazoline 119: n.m.r. 8.52 and 7.76 τ (singlets) C-3 and acetyl methyl respectively, 9.65 τ (doublet J = 7.5 Hz) C-4 methyl, 4.63 τ (doublet J = 8.5 Hz) C-5 hydrogen, 7.29 τ (multiplet) C-4 hydrogen, 2.7 τ (multiplet) aromatic hydrogens.

Anal. Calcd. for C_{13}H_{16}ON_2 (as a mixture of 118 and 119): C, 72.19; H, 7.46; N, 12.95. Found: C, 72.29; H, 7.36; N, 13.11.

It was not possible to obtain pure samples of 100% 118 or 100% 119 by t.l.c. or by column chromatography. However, the pyrazoline 118 was enriched to 85% and the pyrazoline 119 to 62% by successive columns. A second method was used to enrich the pyrazoline 118. Although the preferential decomposition of one pyrazoline over the other was unsuccessful at 55°, it was discovered that over a period of several weeks slow decomposition of the pyrazoline 118 took place.
at room temperature, thus enriching $^{119}$. Using column chromatography as described previously it was possible to determine the decomposition products from 100% $^{118}$ from the first fraction, and the decomposition products from a mixture of $^{118}$ and $^{119}$ in the ratio 25:75 respectively from the second fraction. Evidence that $^{118}$ decomposed exclusively at room temperature in ether-petroleum ether solution resulted from the fact that the first fraction from column chromatography contained none of the cyclopropane $^{127}$. Thus the cyclopropane $^{127}$ must occur exclusively from the decomposition of the other pyrazoline $^{119}$.

(b) Pyrolysis and Product Identification

The pyrolysis of the pyrazolines $^{118}$ and $^{119}$ was carried out either as a neat sample at 100-120° or as a neat sample pyrolyzed in the injector of the v.p.c. The v.p.c. (FFAP, 218°, 120 ml per min) showed 6 peaks A, B, C, D, E, and F with retention times 8.6, 12.2, 13.6, 16.4, 17.6, and 20.0 min respectively.

Peak A was not isolated or identified as it was present in only trace amounts.

Peak B was isolated and identified as a mixture of the cyclopropane $^{125}$ and the rearranged $\gamma,\delta$-isomers $^{134}$ and $^{135}$ on the basis of n.m.r.

Peak C was isolated and identified as the compound 1-acetyl-1',3'-dimethyl-2-phenyl cyclopropane ($^{126}$): i.r. 1695 cm$^{-1}$ (carbonyl stretching frequency); n.m.r 8.20 and 8.51 $\tau$ (singlets) acetyl and C-1 methyls respectively, 8.76 $\tau$ (doublet $J = 6.2$ Hz) C-3 methyl, 7.99 $\tau$ (doublet $J = 7.0$ Hz) C-2 hydrogen, 7.66 $\tau$ (multiplet of approximately 5 lines) C-3 hydrogen, 2.8 $\tau$ (broadened singlet) aromatic hydrogens.
Peaks D and E were not isolated in pure form since they were not present in large amounts and since their retention times were close to that of the major peak F. Partial separation gave an approximate D and E to F ratio of 10:90 respectively. By comparison of the benzylic hydrogens in the n.m.r. and retention times with authentic samples, peaks D and E were assigned the structures 3-methyl-4-benzyl-3-pentene-2-one, (E)- (128) and, (Z)- (129). Although only one of these olefins is expected (13,15) from the pyrazolines 118 and 119, it is possible that the olefins readily isomerize thermally on the v.p.c. column. Considerable overlapping of the two peaks D and E was observed. Evidence for both olefins being present lies in the fact that the n.m.r. displays two broad singlets for the benzylic hydrogens in the appropriate region. Additional evidence is that the peaks D and E have similar retention times as the authentic samples that were synthesized.

Peak F was isolated and identified as the compound 1-acetyl-1',3'-dimethyl-2'-phenyl cyclopropane (127): i.r. 1690 cm\(^{-1}\) (carbonyl stretching frequency); n.m.r. (100 MHz) 7.79 and 8.88 \(\tau\) (singlets) acetyl and C-1 methyls respectively, 8.95 \(\tau\) (doublet \(J = 6.4\) Hz) C-3 methyl, 7.19 \(\tau\) (doublet \(J = 9.8\) Hz) C-2 hydrogen, 8.2 \(\tau\) (multiplet) C-3 hydrogen, 2.9 \(\tau\) (broadened singlet) aromatic hydrogens. Anal. Calcd. for C\(_{13}\)H\(_{16}\)O: C, 82.93; H, 8.57. Found: C, 82.89; H, 8.75.
(c) **Product Distribution**

**TABLE X**

Distribution\(^1\) of Products for the Pyrolysis\(^2\) of Different Ratios of the Pyrazolines \(^{118}\) and \(^{119}\)

<table>
<thead>
<tr>
<th>Ratio of (^{118}:^{119})</th>
<th>125</th>
<th>126</th>
<th>129</th>
<th>127</th>
</tr>
</thead>
<tbody>
<tr>
<td>100:0(^4)</td>
<td>1</td>
<td>98</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>85:15(^5)</td>
<td>2</td>
<td>91</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>74:26(^5)</td>
<td>2</td>
<td>86</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>51:49(^5)</td>
<td>6</td>
<td>66</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>38:62(^5)</td>
<td>8</td>
<td>54</td>
<td>13</td>
<td>25</td>
</tr>
<tr>
<td>25:75(^4)</td>
<td>10</td>
<td>43</td>
<td>16</td>
<td>31</td>
</tr>
<tr>
<td>0:100(^6)</td>
<td>13</td>
<td>25</td>
<td>21</td>
<td>41</td>
</tr>
</tbody>
</table>

1. Average of three runs by v.p.c.
2. Distribution of products from neat and v.p.c. Pyrolysis are identical.
3. Average of three integrations of C-5 hydrogens.
4. Preferential decomposition of pyrazolines \(^{118}\) and \(^{119}\) at r.t.
5. Successive fractionating by column chromatography.
6. Correction to 100% using results of preferential decomposition results.
3'-Acetyl-3,4'-dimethyl-5-phenyl-1-pyrazoline (120) and 3'-Acetyl-3,4'-dimethyl-5'-phenyl-1-pyrazoline (121)

(a) **Preparation and Enrichment**

To an ether solution of 1.8 g (0.18 mole) of 3-methyl-3-pentene-2-one, (Z)- (25) was added phenyl diazomethane (from 3.2 g (0.27 mole) of benzaldehyde hydrazone). The solution was left at -5° for 2 weeks. Pyrazoline formation was indicated by use of n.m.r. The ratio of the two pyrazolines 121 and 120 was estimated in the crude reaction mixture as 1:2 respectively. The pyrazolines 120 and 121 were stored as a solution in ether-petroleum ether at -5°.

Column chromatography (silica gel, ether-petroleum ether, 5:95 to 10:90) on the crude reaction mixture gave two main fractions, the second of which yielded together the pure pyrazolines 120 and 121 as white solids. By determining the ratio of the pyrazolines in successive fraction, it was determined that the pyrazoline 121 had the larger $K_f$ value.

For the pyrazoline 120: n.m.r. 8.31 and 7.96 $\tau$ (singlets) C-3 and acetyl methyl respectively, 9.03 $\tau$ (doublet $J = 6.8$ Hz) C-4 methyl, 5.10 $\tau$ (doublet $J = 9.8$ Hz) C-5 hydrogen, 8.4 $\tau$ (multiplet C-4 hydrogen, 2.7 $\tau$ (singlet) aromatic hydrogens.

For the pyrazoline 121: n.m.r. 8.68 and 7.58 $\tau$ (singlets) C-3 and acetyl methyl respectively, 9.82 $\tau$ (doublet $J = 7.4$ Hz) C-4 methyl, 4.69 $\tau$ (doublet $J = 7.5$ Hz) C-5 hydrogen, 7.7 $\tau$ (multiplet C-4 hydrogen, 2.7 $\tau$ (singlet) aromatic hydrogens. Anal. Calcd. for C$_{13}$H$_{16}$ON$_2$ (as a mixture of 120 and 121): C, 72.19; H, 7.46; N, 12.95. Found: C, 72.40; H, 7.40; N, 12.70.
As in the case of the pyrazolines 118 and 119, it was not possible to obtain pure samples of the pyrazolines 120 and 121 by t.l.c. or by column chromatography. However, pyrazoline 120 could be enriched to 80% and pyrazoline 121 to 50% by one run using column chromatography. As a result of combining several fractions obtained from column chromatography and recrystallizing for microanalysis it was discovered that two different types of crystals slowly developed. The pyrazolines were recrystallized from ether-petroleum ether (10:90) and left at -5° for two weeks. By separating the crystals according to size, samples enriched to 95% and 75% in 120 and 121 respectively were obtained.

(b) Pyrolysis and Product Identification

The pyrolysis of pyrazolines 120 and 121 was carried out neat at 130-140°. The products of pyrolysis were analyzed using the v.p.c. (FFAP, 218°, 120 ml per min) which showed 6 peaks, A, B, C, D, E, and F with retention times 8.4, 12.2, 13.6, 16.4, 18.6 and 20.0 min respectively.

Peak A was not isolated and identified as it was present in only trace amounts.

Peak B was isolated and identified as a mixture of the cyclopropane 125 and the rearranged γ,δ-isomers 134 and 135 on the basis of n.m.r.

Peak C was isolated as a mixture with peak B and identified as the cyclopropane 126 on the basis of n.m.r. and comparison of retention times.

Peak D was present in only small amounts and therefore could not be isolated. Its retention time does however, fall into the same
region as one of the two α,β-unsaturated ketones 128 and 129. Because of the small amount of peak D present it was difficult to tell if isomerization, as suggested in the section dealing with the two ketones 128 and 129 from the pyrolysis of the pyrazolines 118 and 119, was occurring. More important is the fact that on heating the products of pyrolysis at 220° for 2 hours, the peak D did not decrease in size. Thus peak D could not be the cyclopropane 133 which under these conditions would rearrange to the γ,δ-olefins 134 and 135.

Peak E was also present in very small amounts and therefore was not isolated or identified.

Peak F was isolated and identified as the cyclopropane 127 on the basis of n.m.r. and retention times.

(c) Product Distribution

TABLE XI

Distribution of Products for the Pyrolysis of Different Ratios of the Pyrazolines 120 and 121

<table>
<thead>
<tr>
<th>Ratio of 120:121</th>
<th>125</th>
<th>126</th>
<th>128</th>
<th>127</th>
</tr>
</thead>
<tbody>
<tr>
<td>25:75</td>
<td>42</td>
<td>18</td>
<td>5</td>
<td>35</td>
</tr>
<tr>
<td>58:42</td>
<td>65</td>
<td>12</td>
<td>1</td>
<td>22</td>
</tr>
<tr>
<td>95:5</td>
<td>88</td>
<td>7</td>
<td>trace</td>
<td>5</td>
</tr>
<tr>
<td>100:0&lt;sup&gt;3&lt;/sup&gt;</td>
<td>91</td>
<td>6</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>0:100&lt;sup&gt;2&lt;/sup&gt;</td>
<td>26</td>
<td>22</td>
<td>7</td>
<td>45</td>
</tr>
</tbody>
</table>

1 Average of three runs by v.p.c.

2 Integration of n.m.r. spectra.

3 Correction to 100% using 25:75 and 95:5 ratios of 120 and 121 respectively.
3-Acetyl-3',5-dimethyl-4'-phenyl-1-pyrazoline (122) and 3-Acetyl-3',5'-
dimethyl-4'-phenyl-1-pyrazoline (123)

(a) Preparation and Enrichment

To an ether solution of 11.2 g (0.07 mole) of 3-methyl-4-phenyl-3-
butene-2-one, (E)- (132) was added diazoethane (from 23.4 g (0.20 mole)
of N-nitroso-N-ethyl urea). The solution was left for one week at -5°
and became clear and colourless. Pyrazoline formation was indicated
by use of n.m.r. The ratio of the two pyrazolines 122 and 123 was
estimated in the crude reaction mixture as 90:10 respectively. The
first treatment of the olefin 132 with diazoethane resulted in about
35% formation of pyrazoline products. The olefin 132 was then treated
twice more with diazoethane with a one week interval between the
second and third treatment. The pyrazolines 122 and 123 were stored
as a solution in ether-petroleum ether at -5°.

Two weeks after the third treatment the solvent was removed with
a rotatory evaporator. The crude reaction product was triturated with
petroleum ether to give white crystals. Recrystallization from
petroleum ether-ether (95:5) yielded the pure pyrazoline 122 as a
white solid: m.p. 65-68° dec 107°; n.m.r. 8.93 and 7.52 τ (singlets)
C-3 and acetyl methyls respectively, 8.48 τ (doublet J = 7.0 Hz) C-5
methyl, 6.78 τ (doublet J = 8.4 Hz) C-4 hydrogen, 5.18 τ (multiplet) C-5
hydrogen, 2.8 τ (multiplet) aromatic hydrogens. Anal. Calcd. for
C_{13}H_{16}O_N_2: C, 72.19; H, 7.46; N, 12.95. Found: C, 71.96; H, 7.61;
N, 12.95.

The mother liquor from the above recrystallization was approximated
by n.m.r. as a 50:50 mixture of the two pyrazolines. The solvent was
removed from the mother liquor and then diluted with 10 ml of petroleum ether-ether (95:5) and seeded with pure crystals of the pyrazoline 122. The solution was left for one week at -5°, after which it was observed that not only additional crystals of 122 were present but also a liquid, presumably the pyrazoline 123. After the removal of the solid white crystals, the mother liquor was then fractionated by column chromatography (silica gel, petroleum ether-ether, 95:5 to 90:10). Three fractions were used for the product distribution study. The ratio of the two pyrazolines 123 and 122 in the three fractions, as determined by the integration of the two acetyl peaks, was 72:28, 68:32, and 64:36 respectively. By considering successive fractions, it was found that the pyrazoline 123 had the larger $R_f$ value. It was not possible to crystallize any of the fractions and thus the pyrazoline 123 must be a liquid.

For the pyrazoline 123: n.m.r. 8.50 and 7.75 $\tau$ (singlets) C-3 and acetyl methyls respectively, 8.56 $\tau$ (doublet $J = 7.0$ Hz) C-5 methyl, 6.27 $\tau$ (doublet $J = 7.0$ Hz) C-4 hydrogen, 5.9 $\tau$ (multiplet) C-5 hydrogen, 2.8 $\tau$ (multiplet) aromatic hydrogens; no microanalysis was performed on the mixture of the two pyrazolines 122 and 123.

(b) Pyrolysis and Product Identification

The pyrazolines 122 and 123 were decomposed neat at 140-145°. The product distribution was determined by v.p.c. (FFAP, 208°, 120 ml per min) which showed five peaks A, B, C, D, and E with retention times 12.2, 13.4, 14.0, 21.0, and 23.5 min respectively.

Peak A was isolated and found to consist of two major products (>95%). The first compound identified was 3-methyl-4-phenyl-3-hexene-
2-one, (E)- (136): i.r. 1685 cm\(^{-1}\) (carbonyl stretching frequency); n.m.r. (100 MHz) 7.93 \(\tau\) (singlet) acetyl methyl, 8.35 \(\tau\) (multiplet showing long range coupling) alpha methyl, 9.11 \(\tau\) (triplet \(J = 7.3\) Hz) C-6 hydrogens, 7.60 \(\tau\) (quartet showing long range coupling \(J = 7.3\) Hz) C-5 hydrogens, 2.8 \(\tau\) (multiplet) aromatic hydrogens. The second compound was identified as 3-methyl-4-phenyl-4-hexene-2-one, (E)- (137): i.r. 1715 cm\(^{-1}\); n.m.r. (100 MHz) 7.78 \(\tau\) (singlet) acetyl methyl, 8.88 \(\tau\) and 8.45 \(\tau\) (doublets \(J = 7.0\) Hz) C-3 and C-5 methyl respectively, 6.65 \(\tau\) (quartet \(J = 7.0\) Hz) C-5 hydrogen, 4.43 \(\tau\) (quartet \(J = 7.0\) Hz) vinyl hydrogen, 4.43 \(\tau\) (quartet \(J = 7.0\) Hz) vinyl hydrogen, 2.8 \(\tau\) (multiplet) aromatic hydrogens. The n.m.r. of peak A also indicated the presence of the other \(\alpha,\beta\)-unsaturated ketone 3-methyl-4-phenyl-3-hexene-2-one, (Z)- (138). Peaks in the n.m.r. (100 MHz) assigned to the olefin 138 by comparison with an authentic sample were: 8.10 \(\tau\) (singlet) acetyl methyl, 8.50 \(\tau\) (singlet) alpha methyl, 9.07 \(\tau\) (triplet \(J = 7.5\) Hz). It was not possible to conclude if any of the remaining extraneous peaks in the n.m.r. were due to the other \(\beta,\gamma\)-isomer 3-methyl-4-phenyl-4-hexene-2-one, (Z)- (139) since an authentic sample was not available for comparison. Anal. Calcd. for \(\text{C}_{15}\text{H}_{16}\text{O}\) (peak A): C, 82.93; H, 8.57. Found: C, 83.10; H, 8.71.

Peaks B and C were isolated and identified together. Peak B was assigned as having consisted of the cyclopropane 125 and the rearranged \(\gamma,\delta\)-olefins 134 and 135. Peak C was assigned as having consisted of the cyclopropane 125 on the basis of retention times and characteristic peaks in the n.m.r.: 8.32 and 8.55 \(\tau\) (singlets) C-1 and acetyl methyls respectively. The peak B was collected by v.p.c. for i.r.,
n.m.r. and microanalysis. For the compound 1-acetyl-1',3-dimethyl-2'-phenyl cyclopropane \(125\): \(\text{i.r. } 1690 \text{ cm}^{-1}\) (carbonyl stretching frequency); n.m.r. (100 MHz) 8.92 and 7.81 \(\tau\) (singlets) C-1 and acetyl methyls respectively, 8.88 \(\tau\) (doublet \(J = 6.4 \text{ Hz}\)) C-3 methyl, 7.15 \(\tau\) (doublet \(J = 6.4 \text{ Hz}\)) C-2 hydrogen, 8.6 \(\tau\) (multiplet) C-3 hydrogen, 2.9 \(\tau\) (singlet) aromatic hydrogens. Anal. Calcd. for \(\text{C}_{12}\text{H}_{16}\) (mixture of \(125, 134\) and 135): C, 82.93; H, 8.57. Found: C, 82.83; H, 8.78.

Peak D was not isolated as it was present in only a small quantity. It was identified as cyclopropane 126 only on the basis of its retention time.

Peak E was isolated and identified as the cyclopropane 127. Its retention time and n.m.r. were identical to the same cyclopropane isolated from the decomposition of the pyrazolines 119, 120 and 121.

(c) Product Distribution

TABLE XII

Distribution\(^1\) of Products for the Pyrolysis of Different Ratios of the Pyrazolines \(122\) and \(123\)

<table>
<thead>
<tr>
<th>Ratio(^2) of (122:123)</th>
<th>olefins</th>
<th>(125)</th>
<th>(126)</th>
<th>unid.</th>
<th>(127)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>79</td>
<td>trace</td>
<td>1</td>
<td>20</td>
</tr>
<tr>
<td>100:0(^3)</td>
<td>45</td>
<td>41</td>
<td>2</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>36:64</td>
<td>46</td>
<td>39</td>
<td>3</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td>32:68</td>
<td>48</td>
<td>37</td>
<td>4</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>28:72</td>
<td>67</td>
<td>21</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
</tbody>
</table>

\(^1\) Average of three runs by v.p.c.

\(^2\) Average of three integrations of acetyl hydrogens.

\(^3\) From pure Pyrazoline 122.

\(^4\) Corrected to 100\% using 100:0 and 28:72 ratios of 122 and 123 respectively.
Rearrangement of 1-acetyl-1',3-dimethyl-2'-phenyl to erythro- and threo-3-methyl-4-phenyl-5-hexene-2-one (134 and 135)

Four 50 mg samples of the cyclopropane 125 already containing some of the γ,δ-olefins were sealed in pyrex tubes (2 mm diam) and placed in a furnace maintained at 227° for 3.5 hours. The v.p.c. (DC 550, 210°, 120 ml per min) indicated that the cyclopropane 125 had completely rearranged to the γ,δ-olefins 134 and 135. The ratio of the threo 135 to erythro 134 isomer was estimated by n.m.r. at 2:1. It was not possible to separate the two γ,δ-isomers by v.p.c. The rearranged products could however be collected as a mixture on the v.p.c. as a clear colourless liquid: i.r. 1723 cm⁻¹ (carbonyl stretching frequency); n.m.r. (100 MHz) 7.95 and 8.25 τ (singlets) acetyl methyls of 135 and 134 respectively, 9.16 and 8.92 τ (doublets J = 6.9 Hz) C-3 methyls of 135 and 134 respectively, 6.60 τ (triplet J = 9.0 Hz) C-5 hydrogens, 7.17 τ (multiplet of 8 lines) C-3 hydrogens, 4.12 τ (complex multiplet 40 Hz wide of area one) and 5.03 τ (complex multiplet 32 Hz wide of area two) vinyl hydrogens. Anal. Calcd. for C₁₃H₁₆O: C, 82.93; H, 8.57. Found: C, 8.71; H, 8.75. Assignment of acetyl methyls and the C-3 methyls was made on the basis that the function, in this case methyl or acetyl, that is cis to the phenyl group will be shielded (38) in the most stable conformation.

Trimethyl α-phosphonopropionate

Trimethyl α-phosphonopropionate was prepared according to the procedure given by Kinstle (39). The resulting reaction mixture was distilled to give a 31% yield of product boiling between 93-100° at 0.3 mm.
Methyl 3-methyl-3-benzyl-2-butenoate, (E)- (144) and Methyl 3-methyl-3-benzyl-2-butenoate, (Z)- (145)

The procedure according to Kinstle (39) was used. To a slurry of 4.32 g (0.18 mole) of sodium hydride (Ventron) in 200 ml of dry 1,2-dimethoxyethane maintained at 15° was added dropwise in one hour 35.3 g (0.18 mole) of trimethyl α-phosphonopropionate. After the addition, the grey solution was stirred for one hr at room temperature and for 5 min at 35°. The solution was cooled to 15° and 24.1 g (0.18 mole) of freshly distilled phenyl acetone (Eastman) was added dropwise in 20 min with rapid stirring. The mixture was warmed to room temperature and stirred vigorously for 15 min and then 20 min at 65°. Ice (300 g) was added with stirring. The mixture was extracted with five 100 ml portions of ether. The combined ether extracts were washed with two 100 ml portions of water to remove the glyme. The ether layer was dried over sodium sulphate and the ether was removed to give 20.8 g (54%) of crude product. The v.p.c. (Ap J, 222°, 120 ml per min) showed at least three products A, B, and C with retention times 18.6, 19.6 and 21.1 min with A and B overlapping considerably. The n.m.r. indicated the presence of both α,β- and β,γ-isomers in approximately a 70:30 ratio respectively. For the α,β- 144 and 145 and β,γ-unsaturated esters: i.r. 1715-1740 cm⁻¹ (overlapping carbonyl stretching frequencies); n.m.r. 8.68 τ (doublet J = 7.2 Hz) C-2 β,γ-methyl, 8.0-8.4τ(multiplets) vinyl methyls, 6.80 τ (quartet J = 7.2 Hz) C-2 β,γ-hydrogen, 6.54 τ (broad singlet) α,β-benzylic hydrogens, 6.3-6.4 τ carbomethoxy methyls, 3.65 τ (broad singlet) β,γ-vinyl hydrogen, 2.8-2.9 τ aromatic hydrogens. Anal. Calcd. for C₁₃H₁₆O₂
(mixture of peaks A, B, and C): C, 76.43; H, 7.90. Found: C, 76.20; H, 8.10.

3-Methyl-4-benzyl-3-pentene-2-one, (E) - (128) and 3-Methyl-4-benzyl-3-pentene-2-one, (Z) - (129)

The general procedure according to Vogel (45) was used in the conversion of the esters 144 and 145 to their corresponding acids 146 and 147. In a 100 ml flask was refluxed 6 g of the crude esters 144 and 145 in 50 ml of 20% sodium hydroxide for 2.2 hours. The crude reaction mixture was cooled and extracted twice with ether and then acidified with hydrogen chloride. The resulting solution was extracted twice with ether which was dried with magnesium sulphate. Removing the ether gave 2.1 g of a white solid containing the crude acids 146 and 147.

The conversion of the acids to the corresponding methyl ketones was done according to the procedure of DePuy (40). Into a 50 ml 3 necked round bottom flask equipped with a condenser, mechanical stirrer, and nitrogen was placed 2.1 g (0.011 mole) of the crude acids 146 and 147 and 25 ml of anhydrous ether. Methyl lithium in ether (0.022 mole) was added dropwise. After the addition, saturated ammonium chloride was added dropwise to destroy the excess methyl lithium. Two clear layers resulted and the ether layer was separated and washed with a saturated ammonium chloride solution, twice with water, and dried over magnesium sulphate. The ether was removed to yield 1.0 g of crude ketone. Bulb to bulb distillation yielded 0.8 g (0.004 mole). The yield from the acids was 38% and from phenyl acetone was 8%. The yield
of the acids from phenyl ketone was 20%.

The v.p.c. (FFAP, 218°, 120 ml per min) showed three main peaks A, B, and C with retention times of approximately 15.8, 16.3, and 17.6 min and with an area ratio of 3:1:2 respectively. Peaks A and B overlapped considerably. The α,β to β,γ ratio in the crude reaction mixture was estimated at 50:50 by n.m.r. Thus peak A was assigned as the β,γ-isomer and peaks B and C as the α,β-unsaturated ketones 128 and 129. The peaks B and C have the same retention times as peaks D and E from the pyrolysis of pyrazolines 118 and 119.

For the α,β-unsaturated ketones 128 and 129: i.r. 1680 and 1685 cm⁻¹ (overlapping carbonyl stretching frequencies); n.m.r. (100 MHz) 7.81 and 7.82 τ (singlets) acetyl methyls, 8.25 and 8.26 τ (singlets) C-3 methyls, 6.54 and 6.59 τ (broad singlets of areas 1:2 respectively) benzylic hydrogens.

For the β,γ-unsaturated ketone: i.r. 1710 cm⁻¹ (carbonyl stretching frequency); n.m.r. (100 MHz) 7.91 τ (singlet) acetyl methyl, 8.80 τ (doublet J = 6.9 Hz) C-3 methyl, 6.77 τ (quartet J = 6.9 Hz) C-3 hydrogen, 3.58 τ (broad singlet) vinyl hydrogen.

Multiplets at 8.08, 8.14 and 8.41 τ were assigned to the two β-methyls of the α,β-isomers and to the α-methyl of the β,γ-isomers.

Anal. Calcd. for C₁₃H₁₆O (mixture of peaks A, B, and C): C, 82.93; H, 8.57. Found: C, 82.51; H, 8.66.

Methyl-2-methyl-3-phenyl-2-pentenoate, (E)- (140) and Methyl-2-methyl-3-phenyl-2-pentenoate, (Z)- (141)

The procedure according to Kinstle (39) was used as previously described for the preparation of the esters 144 and 145. A bulb to bulb
distillation of the crude reaction product gave a clear colourless liquid whose v.p.c. (FFAP 212°, 120 ml per min) showed one peak with retention time 10.7 minutes. The n.m.r. indicated that the peak consisted of the two expected α,β-unsaturated esters 140 and 141 in a 2:1 ratio respectively.

For the esters 140 and 141: i.r. 1725 and 1735 cm\(^{-1}\) (overlapping carbonyl stretching frequencies); n.m.r. 6.29 and 6.77 τ (singlets) carbomethoxy methyls respectively, 8.32 and 8.00 τ (singlets) alpha methyls respectively, 9.05 τ (triplet J = 3.8 Hz) C-5 hydrogens, 6.5-6.6 τ (overlapping quartets) C-4 hydrogens, 2.9 τ aromatic hydrogens. Anal. Calcd. for C\(_{15}\)H\(_{16}\)O: C, 76.43; H, 7.90. Found: C, 76.02; H, 7.91.

3-Methyl-4-phenyl-3-hexene-2-one, (E)- (136) and 3-Methyl-4-phenyl-3-hexene-2-one, (Z)- (138)

A procedure, similar to the conversion of the methyl esters 144 and 145 to their corresponding acids 146 and 147, was used except that it was necessary to reflux the reaction mixture for 24 hours. The n.m.r. indicated a 72:28 mixture of the acids with the E isomer predominating. For the acids 142 and 143: n.m.r. 7.96 and 8.30 τ (singlets) alpha methyls, 9.06 τ (triplet J = 3.8 Hz) C-5 hydrogens, 7.26 and 7.52 τ (quartets) C-4 hydrogens, -0.95 τ (broad singlet) acid proton.

The conversion of the acids 142 and 143, derived from the methyl esters 140 and 141, was carried out according to the procedure of DePuy (40) and is similar to that described for the preparation of the ketones 128 and 129. The yield of 136 and 138 from their corresponding acids was 8.0%, and from propiophenone 0.6%. The yield of the acids
from propiophenone was 7.5%.

The v.p.c. (FFAP 215°, 120 ml per min) showed as the major product two overlapping peaks A and B with retention times 9.0 and 9.4 minutes. The n.m.r. indicated that the two ketones 138 and 136 were present in a ratio of 90:10 although the initial corresponding acids were in a ratio of 72:28 respectively.

For the ketones 136 and 138: i.r. 1680-90 cm\(^{-1}\) (overlapping carbonyl stretching frequencies); n.m.r. (100 MHz) 7.95 and 8.51 \(\tau\) (singlets) acetyl methyls respectively, 8.34 and 8.10 \(\tau\) (multiplets alpha methyls respectively, 9.00 and 9.10\(\tau\)(triplets \(J = 7.4\) Hz) C-6 hydrogens, 7.53 \(\tau\) (quartet \(J = 7.4\) Hz) C-5 hydrogens of 138. Anal. Calcd. for \(C_{13}H_{16}O\): C, 82.93; H, 8.57. Found: C, 83.05; H, 8.58.
BIBLIOGRAPHY


Nomencature

The main purpose of the following system of nomenclature is to unambiguously assign the stereochemistry about the three carbon skeleton of cyclopropanes and 1-pyrazolines that are uniquely substituted at all three carbon centers. A "prime" used as a superscript on the carbon number indicates substituents on one side of the ring system whereas the lack of a superscript indicates substituents on the other side.

For example, pyrazoline 118 becomes 3-acetyl-3',4'-dimethyl-5-phenyl-1-pyrazoline and the C-5 isomer 119 becomes 3-acetyl-3',4'-dimethyl-5'-phenyl-1-pyrazoline. Cyclopropane 126 is called 1-acetyl-1',3'-dimethyl-2-phenyl cyclopropane.