1975


Nafisa Begum Islam
Louisiana State University and Agricultural & Mechanical College

Follow this and additional works at: https://digitalcommons.lsu.edu/gradschool_disstheses

Recommended Citation
https://digitalcommons.lsu.edu/gradschool_disstheses/2795

This Dissertation is brought to you for free and open access by the Graduate School at LSU Digital Commons. It has been accepted for inclusion in LSU Historical Dissertations and Theses by an authorized administrator of LSU Digital Commons. For more information, please contact gradetd@lsu.edu.
INFORMATION TO USERS

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

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

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

2. When an image on the film is obliterated with a large round black mark, it is an indication that the photographer suspected that the copy may have moved during exposure and thus cause a blurred image. You will find a good image of the page in the adjacent frame.

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

4. The majority of users indicate that the textual content is of greatest value, however, a somewhat higher quality reproduction could be made from “photographs” if essential to the understanding of the dissertation. Silver prints of “photographs” may be ordered at additional charge by writing the Order Department, giving the catalog number, title, author and specific pages you wish reproduced.

5. PLEASE NOTE: Some pages may have indistinct print. Filmed as received.

Xerox University Microfilms
300 North Zeeb Road
Ann Arbor, Michigan 48106
ISLAM, Nafisa Begum, 1947-
SYNTHETIC ORGANIC CHEMISTRY: PART I. PREPARATION AND CHARACTERIZATION OF PYRIDYLBENZENES AND RELATED INTERMEDIATES. PART II. SYNTHESIS OF CYCLIC POLYOLEFINS.

The Louisiana State University and Agricultural and Mechanical College, Ph.D., 1975
Chemistry, organic

Xerox University Microfilms, Ann Arbor, Michigan 48106
SYNTHETIC ORGANIC CHEMISTRY:

PART I. PREPARATION AND CHARACTERIZATION OF PYRIDYL BENZENES AND RELATED INTERMEDIATES

PART II. SYNTHESIS OF CYCLIC POLYOLEFINS

A Dissertation

Submitted to the Graduate Faculty of the Louisiana State University and Agricultural and Mechanical College in partial fulfillment of the requirements for the degree of Doctor of Philosophy in

The Department of Chemistry

by

Nafisa B. Islam
B.Sc., Mysore University, 1964
M.Sc., Mysore University, 1966

May, 1975
For

My Parents

And

My Husband, Mir
ACKNOWLEDGEMENT

The author wishes to express her sincere appreciation and deep gratitude to her major professor, Dr. George R. Newkome, for his advice and constant encouragement during the course of this investigation. Appreciation is also extended to Dr. William H. Baddley, Dr. William H. Daly, Dr. Norman S. Bhaaca, and Dr. Lynn K. Runnels, for serving as members of her advisory committee.

The author wishes to thank her husband, Dr. Mir N. Islam for his encouragement and assistance which contributed immeasurably to the completion of this work. Special thanks are extended to her parents for their wholehearted support in her academic endeavors.

The writer also wishes to acknowledge the following people: Mr. Ralph L. Seab, Mr. John R. Martin, and Mrs. Paula B. Moses for technical services.
# TABLE OF CONTENTS

| ACKNOWLEDGEMENT | iii       |
| LIST OF TABLES | ix        |
| LIST OF SCHEMES | x        |
| ABSTRACT | xii       |
| FOREWORD | xiv       |
| PART I. Preparation and Characterization of Pyridylbenzenes and Related Intermediates | 1        |
| I. INTRODUCTION | 2        |
| II. EXPERIMENTAL | 27       |
| A. General Comments | 27       |
| B. Solvents | 29        |
| C. Syntheses | 29        |
| 1. Ethyl 2-pyridylacetate  
Method A | 29        |
| Method B | 30        |
| 2. 2-Pyridylacetonitrile  
Method A | 30        |
| Method B | 31        |
| 3. 1,3-Di(2-pyridyl)acetone  
Method A | 33        |
| Method B | 33        |
| 4. 1-Phenyl-3-(2-pyridyl)propan-2-one | 34        |
| 5. (E)-1-phenyl-2-(2-pyridyl)ethene  
Method A | 34        |
| Method B | 35        |
| 6. Phenyl(2-pyridyl)glyoxal | 35        |
| 7. 1-Phenyl-2-(2-pyridyl)-1,2-dibromoethane | 36        |
| 8. Phenyl(2-pyridyl)acetylene  
Method A | 36        |
<p>| Method B | 37        |</p>
<table>
<thead>
<tr>
<th>No.</th>
<th>Chemical</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.</td>
<td>(E)-1,2-Di(2-pyridyl)ethene.</td>
<td>37</td>
</tr>
<tr>
<td>10.</td>
<td>1,2-Di(2-pyridyl)-1,2-dibromoethane.</td>
<td>37</td>
</tr>
<tr>
<td>11.</td>
<td>Di(2-pyridyl)acetylene</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Method A</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>Method B</td>
<td>38</td>
</tr>
<tr>
<td>12.</td>
<td>(4SR,5SR)-4-Hydroxy-2,5-dimethyl-3,4-diphenyl-2-cyclopenten-1-one.</td>
<td>39</td>
</tr>
<tr>
<td>13.</td>
<td>2,5-Dimethyl-3,4-diphenylcyclopentadienone</td>
<td>39</td>
</tr>
<tr>
<td>14.</td>
<td>(4SR,5SR)-4-Hydroxy-2,5-dimethyl-3,4-di(2-pyridyl)cyclopenten-1-one</td>
<td>39</td>
</tr>
<tr>
<td>15.</td>
<td>3,4-Dihydroxy-2,5-dimethyl-3,4-di(2-pyridyl)cyclopentanone</td>
<td>40</td>
</tr>
<tr>
<td>16.</td>
<td>1,4-Dimethyl-2,3,5,6-tetraphenylbenzene.</td>
<td>40</td>
</tr>
<tr>
<td>17.</td>
<td>(4SR,5SR)-4-Hydroxy-2,5-dicarbomethoxy-3,4-diphenyl-2-cyclopenten-1-one.</td>
<td>41</td>
</tr>
<tr>
<td>18.</td>
<td>2,5-Dicarbomethoxy-3,4-diphenylcyclopentadienone</td>
<td>41</td>
</tr>
<tr>
<td>19.</td>
<td>(4SR,5SR)-4-Hydroxy-2,5-dicarbomethoxy-3,4-di(2-pyridyl)-2-cyclopenten-1-one.</td>
<td>44</td>
</tr>
<tr>
<td>20.</td>
<td>Dimethyl 2,3,5,6-tetraphenyl-1,4-benzenedicarboxylate.</td>
<td>44</td>
</tr>
<tr>
<td>21.</td>
<td>Tetramethyl 5,6-Diphenyl-1,2,3,4-benzenetetra-carboxylate.</td>
<td>44</td>
</tr>
<tr>
<td>22.</td>
<td>Dimethyl 3,4,5,6-tetraphenyl-1,2-benzenedicarboxylate.</td>
<td>45</td>
</tr>
<tr>
<td>23.</td>
<td>Dimethyl 1,4-Dimethyl-5,6-diphenyl-2,3-benzenedicarboxylate.</td>
<td>45</td>
</tr>
<tr>
<td>24.</td>
<td>(4SR,5SR)-4-Hydroxy-2,3,4,5-tetraphenyl-2-cyclopenten-1-one.</td>
<td>45</td>
</tr>
<tr>
<td>25.</td>
<td>(4SR,5SR)-2-Hydroxy-3-(2-pyridyl)-2,4,5-triphenyl-2-cyclopenten-1-one.</td>
<td>46</td>
</tr>
<tr>
<td>26.</td>
<td>(4SR,5SR)-4-Hydroxy-2-(2-pyridyl)-3,4,5-triphenyl-2-cyclopenten-1-one.</td>
<td>46</td>
</tr>
<tr>
<td>PAGE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>27. (4SR,5SR)-4-Hydroxy-2,5-diphenyl-3,4-di(2-pyridyl)-2-cyclopenten-1-one</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>28. (4SR,5SR)-4-Hydroxy-3,4-diphenyl-2,3-di(2-pyridyl)-2-cyclopenten-1-one</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>29. Condensation of Phenyl(2-pyridyl)glyoxal with 1,3-Di(2-pyridyl)acetone</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td>30. Condensation of 2-Pyridil with 1,3-Di(2-pyridyl)acetone</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>31. Condensation of 2-Pyridil with 1-Phenyl-3-(2-pyridyl)propanone</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>32. Condensation of Phenyl(2-pyridyl)glyoxal with 1-Phenyl-3-(2-pyridyl)propanone</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>33. 2,5-Diphenyl-3,4-di(2-pyridyl)cyclopentadienone</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>34. 2,3,4-Triphenyl-5-(2-pyridyl)cyclopentadienone</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>35. 1-(2-Pyridyl)-2,3,4,5,6-pentaphenylbenzene</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>36. 1,2-Di(2-pyridyl)-3,4,5,6-tetraphenylbenzene</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>37. Attempted Synthesis of 1,2-Di(2-pyridyl)-3-phenylpropanol Method A</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Method B</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Method C</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Methods D-G</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>38. Attempted Synthesis of 1,2,3-Tri(2-pyridyl)-2-propanol Methods A-C</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Methods D and E</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>39. Attempted Synthesis of Di(2-pyridyl)cyclopropenone Method A</td>
<td>57</td>
<td></td>
</tr>
<tr>
<td>Methods B-F</td>
<td>58</td>
<td></td>
</tr>
<tr>
<td>40. Attempted Synthesis of Phenyl(2-pyridyl)-cyclopropenone Methods A-F</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>III. RESULTS AND DISCUSSION</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>IV. SUMMARY AND CONCLUSIONS</td>
<td>92</td>
<td></td>
</tr>
<tr>
<td>REFERENCES</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>PART II. Synthesis of Cyclic Polyolefins</td>
<td>PAGE</td>
<td></td>
</tr>
<tr>
<td>------------------------------------------</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>102</td>
<td></td>
</tr>
<tr>
<td>II. EXPERIMENTAL</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>A. General Comments</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>B. Syntheses</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>1. 2-Methylcyclopentane-1,3-dione</td>
<td>127</td>
<td></td>
</tr>
<tr>
<td>2. 2-Methyl-2-(3-oxobutyl)cyclopentane-1,3-dione</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>3. 5,6,7,8-Tetrahydro-8-methylindane-1,5-dione</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>4. (+)-7,7a-Dihydro-1β-hydroxy-7aβ-methyl-5(6H)-indanone</td>
<td>129</td>
<td></td>
</tr>
<tr>
<td>5. 1β-Hydroxy-7aβ-Methyl-Δ³(3a)-1,2,4,5,6,7-hexahydroindene Method A</td>
<td>130</td>
<td></td>
</tr>
<tr>
<td>Method B</td>
<td>132</td>
<td></td>
</tr>
<tr>
<td>6. 1,6-Dioxo-8a-methyl-1,2,3,4,6,7,8,8a-octahydonaphthalene</td>
<td>135</td>
<td></td>
</tr>
<tr>
<td>7. 1-Keto-9-methyl-6-(N-pyrrolidino)-Δ⁴,⁵-octalin</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>8. 2-Phenyl-5a-methyl-4,5,5a,6,7,8-hexahyronaphtho(2,1-b)furan-6-one</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>9. 2-Phenyl-5a-methyl-4,5,5a,6,7,8-hexahydonaphtho(2,1-b)furan-6-ol</td>
<td>136</td>
<td></td>
</tr>
<tr>
<td>10. 2-Phenyl-5a-methyl-6-methanesulfonyl-4,5,5a,6,7,8-hexahydonaphtha(2,1-b)furan</td>
<td>137</td>
<td></td>
</tr>
<tr>
<td>11. Hydroboration of the mesylate derivative Method A</td>
<td>137</td>
<td></td>
</tr>
<tr>
<td>Method B</td>
<td>138</td>
<td></td>
</tr>
<tr>
<td>12. Trans,trans-9-methyl-2-phenyl-6,7,10,11-tetrahydrocyclodeca(b)furan</td>
<td>138</td>
<td></td>
</tr>
<tr>
<td>13. Cope rearrangement of Cyclodecatriene derivative</td>
<td>139</td>
<td></td>
</tr>
<tr>
<td>III. RESULTS AND DISCUSSION</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>IV. SUMMARY AND CONCLUSIONS</td>
<td>151</td>
<td></td>
</tr>
</tbody>
</table>
### LIST OF TABLES

<table>
<thead>
<tr>
<th>TABLE NUMBER</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I.</td>
<td>42</td>
</tr>
<tr>
<td>II.</td>
<td>43</td>
</tr>
<tr>
<td>III.</td>
<td>51</td>
</tr>
<tr>
<td>IV.</td>
<td>52</td>
</tr>
<tr>
<td>V.</td>
<td>53</td>
</tr>
<tr>
<td>VI.</td>
<td>75</td>
</tr>
<tr>
<td>VII.</td>
<td>82</td>
</tr>
<tr>
<td>VIII.</td>
<td>84</td>
</tr>
<tr>
<td>IX.</td>
<td>88</td>
</tr>
</tbody>
</table>

I. Synthesis of 1,4-Dimethyl-2,3,5,6-tetraaryl Heteroarylbenzenes

II. Analyses of 1,4-Dimethyl-2,3,5,6-tetraaryl Heteroarylbenzenes

III. Synthesis of Hexaaryl- and Heteroarylbenzenes

IV. Hexaaryl- and Heteroarylbenzenes

V. Analyses of Hexaaryl- and Heteroarylbenzenes

VI. Tetraaryl- and Heteroaryl Cyclopentenolones

VII. Spectral Data of 1,4-Dimethyl-2,3,5,6-tetraaryl and heteroarylbenzenes

VIII. Hexasubstituted Benzenes

IX. Spectral data of Hexaaryl- and Heteroarylbenzenes
LIST OF SCHEMES

<table>
<thead>
<tr>
<th>SCHEME NUMBER</th>
<th>PAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PART I.</td>
<td></td>
</tr>
<tr>
<td>I. (2-Pyridylacetates)</td>
<td>4</td>
</tr>
<tr>
<td>II. (2-Pyridylacetonitrile)</td>
<td>5</td>
</tr>
<tr>
<td>III. (Boekelheide Rearrangement; 2-Hydroxymethylpyridine)</td>
<td>10</td>
</tr>
<tr>
<td>IV. 2-Picolylketones</td>
<td>10</td>
</tr>
<tr>
<td>V. 2-Picolylketones and t-Carbinols</td>
<td>12</td>
</tr>
<tr>
<td>VI. 1,3-Di(2-pyridyl)acetone</td>
<td>12</td>
</tr>
<tr>
<td>VII. Phenyl(2-pyridyl)glyoxal and Phenyl(2-pyridyl)acetylene</td>
<td>15</td>
</tr>
<tr>
<td>VIII. Di(2-pyridyl)acetylene</td>
<td>17</td>
</tr>
<tr>
<td>IX. Diarylcyclopropenones</td>
<td>19</td>
</tr>
<tr>
<td>X. Diphenylcyclopropenone</td>
<td>20</td>
</tr>
<tr>
<td>XI. Diarylcyclopentenolones</td>
<td>23</td>
</tr>
<tr>
<td>XII. 1,3-Di(2-pyridyl)acetone</td>
<td>61</td>
</tr>
<tr>
<td>XIII. Mechanism of Acylation of 2-Picolyllithium with Esters</td>
<td>65</td>
</tr>
<tr>
<td>XIV. Tetraaryl and Heteroaryl Cyclopentenolones and Cyclopentadienones</td>
<td>74</td>
</tr>
<tr>
<td>XV. Hexaaryl and Heteroarylbzenenes</td>
<td>86</td>
</tr>
<tr>
<td>XVI. Configurational Isomers of Hexa(2-pyridyl)benzene</td>
<td>90</td>
</tr>
<tr>
<td>PART II.</td>
<td></td>
</tr>
<tr>
<td>I. Solvolytic Fragmentation of Decahydroquinolyltosylates</td>
<td>107</td>
</tr>
<tr>
<td>II. Mechanism of Fragmentation of Decahydroquinolyltosylates</td>
<td>108</td>
</tr>
<tr>
<td>III. 6-Methyl-trans-5-cyclodecenone</td>
<td>111</td>
</tr>
<tr>
<td>IV. Trans,trans-1-methyl-1,6-cyclodecadiene</td>
<td>112</td>
</tr>
<tr>
<td>V. Mechanism of Solvolytic Fragmentation of Methane-sulfonyl Boronate</td>
<td>113</td>
</tr>
<tr>
<td>SCHEME NUMBER</td>
<td>DESCRIPTION</td>
</tr>
<tr>
<td>---------------</td>
<td>-------------</td>
</tr>
<tr>
<td>VI.</td>
<td>Trans, trans-1-methyl-1,5-cyclodecadiene</td>
</tr>
<tr>
<td>VII.</td>
<td>Trans, trans-1,7,7-trimethyl-1,5-cyclodecadiene</td>
</tr>
<tr>
<td>VIII.</td>
<td>Mechanism of Formation of trans, trans-1-methyl-1,5-cyclodecadiene</td>
</tr>
<tr>
<td>IX.</td>
<td>6-Methyl-1,5- and 6-Methyl-1,6-cyclodecadiene-3-ones</td>
</tr>
<tr>
<td>X.</td>
<td>1β-Hydroxy-7αβ-methyl-Δ^3(3α)-1,2,4,5,6,7-hexahydroindene (Method A)</td>
</tr>
<tr>
<td>XI.</td>
<td>1β-Hydroxy-7αβ-methyl-Δ^3(3α)-1,2,4,5,6,7-hexahydroindene (Method B)</td>
</tr>
<tr>
<td>XII.</td>
<td>2-Phenyl-5α-methyl-4,5,5α,6,7,8-hexahydronaphtho-(2,1-b)furan-6-ol</td>
</tr>
</tbody>
</table>
ABSTRACT

Tetra-, hexaaryl-, and heteroarylbenzenes were synthesized by Diels-Alder condensation of diaryl- and heteroarylacetylenes and appropriately substituted cyclopentadienones, generated in situ from cyclopentenolones. These substituted benzenes were analytically and spectrally characterized.

Di- and tetraaryl- and heteroarylcyclopentenolones were synthesized from the base catalyzed reaction of appropriate diketone with acetone. The stereochemistry of these compounds was elucidated on the basis of their nmr spectra. It was also shown that there is stereoselective structural preference to form trans isomers.

Synthetic methods were found for efficient preparation of 2-pyridylacetonitrile and 1,3-di(2-pyridyl)acetone by improvement of the reported procedures.

Reactions of 2-picolyllithium or 2-pyridylmagnesium bromide with ethyl benzoate and ethyl 2-pyridinecarboxylate afforded exclusively 2-phenacylpyridine and 2-picolyl pyridylketone, respectively.

Attempts to prepare di(2-pyridyl)cyclopropenone by routes similar to the preparation of the known diphenylcyclopropenone were unsuccessful.

Part II of this Dissertation is concerned with the synthesis of cyclic polyolefins. Synthesis of trans,trans-9-methyl-2-phenyl-6,7,10,11-tetrahydrocyclocloocta[4]furan through solvolytic fragmentation of its bicyclic boronate mesylate precursor was described. The bicyclic alcohols, 1β-hydroxy-7αβ-methyl-Δ3(3α)-1,2,4,5,6,7-hexahydropyndene, and 1β-hydroxy-7αβ-methyl-Δ3a(4)-1,2,3,5,6,7-hexahydropyndene were synthesized with a view
to prepare 1-methyl-1,4- and -1,5-cyclononadienes by similar solvolytic fragmentation of boronate mesylates. But the yield of these alcohols from a ten-step sequence was not sufficient to carry out the subsequent fragmentation reactions.
This Dissertation is comprised of two parts. Part I is concerned with the preparation and characterization of heteroarylbenzenes and related intermediates. Although numerous procedures have been reported for the preparation of arylbenzenes, only a few are applicable to the synthesis of the desired heterocyclic substituted benzenes. Efficient synthetic procedures for the construction of hexa-substituted benzenes, specifically the 2-pyridyl moiety, are described from appropriately substituted cyclopentenolones, which have been structurally elucidated.

Part II of this Dissertation is concerned with the synthesis of cyclic polyolefins. The presence of medium rings, 1,5-cyclodecadienes, in natural products as well as their vital role in the biosynthesis of terpenes and steroids has stimulated considerable interest in developing new synthetic methods. The stereochemically controlled synthetic approach to the cyclo-1,5-diene moiety through the solvolytic fragmentation of bicyclic boronate mesylate was successful when applied to the preparation of trans,trans-9-methyl-2-phenyl-6,7,10,11-tetrahydrocyclodeca[b]furan (127). Synthesis of 1β-hydroxy-7αβ-methyl-Δ^3(3a)-1,2,4,5,6,7-hexahydroindene and 1β-hydroxy-7αβ-methyl-Δ^3a(4)-1,2,3,5,6,7-hexahydroindene, necessary precursors to 1-methyl-1,4- and 1,5-cyclononadienes, respectively, are described; however, limited quantities of these intermediates after the described ten-step sequence did not permit the further fragmentation reactions.
PART I

PREPARATION AND CHARACTERIZATION OF

PYRIDYLBENZENES AND RELATED INTERMEDIATES
INTRODUCTION

The basic properties of pyridine largely arise from the nitrogen "lone pair" electrons in which the strong electron withdrawal caused by the annular nitrogen atom activates the substituents like methyl, hydroxyl, etc. For example, the methyl group reactivity in 2-methylpyridine closely resembles that of o-nitrotoluene (1).  

\[
\begin{align*}
\text{2-Methylpyridine} & \quad \text{O-Nitrotoluene} \\
\end{align*}
\]

2-Pyridylmethyl (2-picolyl) hydrogens are acidic (pKa 5.94) and thus readily abstracted by strong bases. Acidity of α-side chain protons can be further increased by simple preparation of its corresponding pyridinium salt or N-oxide. This type of functionalization has three major drawbacks in synthetic sequences in that; (a) additional synthetic steps lengthen the project; (b) normally these Nderivatives are difficult to remove; and (c) an ortho steric effect may be detrimental in subsequent reactions.  

Alternatively, the acidity of the 2-picolyl hydrogens is enhanced upon replacement of one or more of the α-protons with electron withdrawing substituents, such as; --COOH, --COOR, --CN, and --COR. A brief summary of pertinent side-chain functionalization procedures in simple pyridyl systems is thus necessary.  

Oparina\(^3\) reported that 2-pyridylacetic acid undergoes facile decarboxylation at 50-60°. To circumvent this potential problem, thermally
stable esters were generally utilized to activate the 2-picolyl hydrogens. Oparina's method to prepare alkyl 2-pyridylacetate is shown in Scheme I. 2-Phenacylpyridine (20) was first converted to the oxime 2, which afforded 2-pyridylacetanilide (3) upon subsequent treatment with concentrated mineral acid (Beckmann Rearrangement). Solvolysis of 3 in methanol or ethanol gave the alkyl esters 4 or 5, respectively. Woodward and Kornfeld employed direct carboxylation of 2-picolyllithium (7) with carbon dioxide and esterification of the resultant acid salt afforded ethyl 2-pyridylacetate (5) in 35-40% overall yields. Analogously, Hiltmann, et al., obtained 5 in 25% yield by using 2-picolylsodium; whereas Goldberg and Levine isolated 5 in 44.5% yield by direct carboethoxylation of the 2-picolyllithium (7) via an inverse addition procedure.

The preparation of 2-pyridylacetonitrile (13) (37% overall yield) from 6, afforded a general procedure to many of the key intermediates in the synthesis of numerous substituted pyridines (see Scheme II). Oxidation of 2-picoline (6) by aqueous potassium permanganate afforded acid 9, which upon esterification provided ethyl 2-pyridylcarboxylate (10). Reduction of ester 10 with lithium aluminum hydride
Scheme 1

29 \[ \text{NH}_2\text{OH} \rightarrow 2 \]

3 \[ \text{H}^+ \rightarrow \]

\[ 4 \text{(R=CH}_3\text{)} \]

5 \[ \text{(R=Et)} \]
Scheme II

6 \xrightarrow{\text{KMnO}_4, 83\%} 9

9 \xrightarrow{88\%, \text{EtOH/H}^+} 10

10 \xrightarrow{\text{LAH, 70\%}} 11

11 \xrightarrow{83\%, \text{SOCl}_2} 12

12 \xrightarrow{\text{KCN/EtOH, 79\%}} 13

13 \xrightarrow{\text{NaCN/DMSO, 87\%}}
afforded alcohol 11, 11 which with thionyl chloride gave 2-picolylchloride hydrochloride (12). 12 Potassium cyanide in an aqueous alcoholic medium effected the nucleophilic transformation of 12 to 13; 13 however, improved conversion can be realized by using nucleophilic enhancing solvents such as dimethylsulfoxide. 14

Boekelheide and Linn 15 effected a novel synthesis of 2-hydroxymethylpyridine (11); this procedure retains the name of Boekelheide Rearrangement and is shown in Scheme III. Treatment of 6 with an in situ generated peracid afforded the N-oxide (14). Subsequent thermal rearrangement of 14 in the presence of acetic anhydride afforded mainly 2-pyridylcarbinol acetate (15) and small amounts of 5-acetoxy-2-methylpyridine and 3-acetoxy-2-methylpyridine. 16 Hydrolysis of 15 afforded the desired alcohol 11 in 50% overall yield from 14.

2-Chloromethylpyridine (16), as the free base, can be made from 12 or, better, in one step by similar treatment of 14 with benzene-sulfonyl chloride, followed by thermolysis of the intermediary salt. 17, 18 Mathes and Schuly 19 obtained 65% of 2-chloromethylpyridine (16) along

![Scheme III](image)

with 5% of 2,2-dichloropicoline (17) by direct chlorination of 2-picoline (6) with chlorine. Grundmann, et al., 20 oxidized 2-pyridinecarboxaldehyde

![Equation](image)
hydrazone (18)\textsuperscript{21} with silver oxide and obtained 2-diazomethylpyridine (19), which was converted to 2-chloromethylpyridine (16) upon treatment with ethereal hydrogen chloride

2-PICOLYLKETONES AND ALCOHOLS

2-Picolylketones, classically prepared by Claisen-type of acylation of 2-picolyllithium (7), were initially reported by Bergmann and Rosenthal,\textsuperscript{22} who isolated 2-phenacylpyridine (20) from 2-picolyllithium and benzoyl chloride.

Beets\textsuperscript{23} reported the action of acetic anhydride or ethyl acetate with 2-picolyllithium and obtained two major products, methyl 2-picolylketone (21) and 1,3-bis-(2-pyridyl)-2-methyl-2-propanol (22). Kloppenburg and Wibaut\textsuperscript{24} studied systematically the complex reaction of

\[\text{2-PICOLYLKETONES AND ALCOHOLS}\]

\[\text{2-Picolylketones, classically prepared by Claisen-type of acylation of 2-picolyllithium (7), were initially reported by Bergmann and Rosenthal, who isolated 2-phenacylpyridine (20) from 2-picolyllithium and benzoyl chloride.}\]

\[\text{Beets reported the action of acetic anhydride or ethyl acetate with 2-picolyllithium and obtained two major products, methyl 2-picolylketone (21) and 1,3-bis-(2-pyridyl)-2-methyl-2-propanol (22). Kloppenburg and Wibaut studied systematically the complex reaction of}\]

\[\text{\[\text{2-PICOLYLKETONES AND ALCOHOLS}\]}\]
acetyl and benzoyl chlorides with 2-picolyllithium (7) and found that the product distribution depends to a great extent upon the reaction conditions; (a) rapid addition of excess of acetyl chloride with strong cooling gave only ketone 21; whereas, (b) slow addition resulted in predominant formation of carbinol 22. Similarly, addition of benzoyl chloride to 7 afforded ketone 20 and olefin 23, which resulted from subsequent dehydration of the intermediary alcohol. Treatment of 7 with benzoic anhydride

\[ \text{Fast} \]

\[ \text{Slow} \]

\[ \text{20} (18\%) \]

\[ \text{23} (17\%) \]

gave the phenylketone 20 along with a trace amount of 2-pyridyldibenzoyl-methane (24). 24
Burgess, et al., obtained ketone 20 from 2-picolyllithium (7) and benzonitrile; whereas Wibaut and DeJong isolated the intermediary ketimines under similar conditions from benzonitrile, acetonitrile, and 2-cyanopyridine with 2-picolyllithium (Scheme IV). Weiss and Hauser obtained ketone 20 by direct acetylation of 2-methylpyridine (6) with ethyl benzoate using potassium or sodium amide as the condensing agent. Dornow and Bruncken similarly obtained ketones 20 or 26 from 6 with ethyl benzoate or ethyl 2-pyridinecarboxylate, respectively, and potassium ethoxide as the condensing agent. Gilman and Towlre reacted acetyl chloride with 2-picolyllithium (7) or 2-picolylmagnesium bromide (27) obtaining two major products; ketone 21 and carbinol 22 (Scheme V). Profft, et al., reacted both the aliphatic and aromatic esters with 2-picolylmagnesium bromide and obtained the ketone and carbinol depending upon the concentration of the reactants. Thus 27 formed ketone 26, when equimolecular proportions of ester was used, and carbinol 28 was formed when the amount of organometallic compound was doubled. Goldberg, et al., made a considerable improvement in the 2-picolylketone preparation by using
Scheme III

![Chemical reactions and structures](image)

Scheme IV

![Chemical reactions and structures](image)

20 (R = C₆H₅)
26 (R = 2-C₅H₄N)
methyl esters as acetylation agents. Rapid addition of limited quantities of methyl ester to \( 7 \) afforded the ketone, e.g., with methyl benzoate, ketone \( 20 \) was isolated in 80% yield. In addition to the 2-picolyl ketones, alkyl di-2-picolylcarbinols were isolated as minor products in those experiments in which aliphatic esters were used as the acetylation agent, but only ketones\(^{32} \) were formed with aromatic or heterocyclic acetylation agents. Uhlemann\(^{33} \) similarly obtained 2-picolylbenzyl ketone (29) in 57% yield using methyl phenylacetate.

\[
\begin{align*}
\text{Py}_2 + \text{H}_3\text{COOC} & \xrightarrow{\text{Et}_2\text{O}} \\
\text{2-Picolylketone (29) (57%)}
\end{align*}
\]

1,3-Di(2-pyridyl)acetone (8) was obtained (6%) by acylation of 2-picolyllithium (7) with diethyl carbonate\(^7 \) or ethyl chloroformate.\(^{34} \) Bodalski, et al.,\(^{35} \) made considerable improvement (36-44%) in this synthetic procedure by utilizing either ethyl 2-pyridylacetate or 2-pyridylacetonitrile as depicted in Scheme VI. However, when 2-picolyllithium (7) was replaced by 2-picolylmagnesium bromide, the isolated yield of ketone (8) was reduced considerably.

**DIARYLALKENES**

2-Stilbazole (31) was first obtained\(^{36} \) by condensation of 2-methylpyridine (6) and benzaldehyde in the presence of zinc chloride at 180-230°. The same product was obtained when 2-methylpyridine, water, and benzaldehyde\(^{37} \) in a 4:3:6 ratio were heated in a sealed tube with isolated yields of 57% and 87% using hydrochloric acid\(^{38} \) and acetic
Scheme V

\[
\begin{align*}
\text{PhLi} & \quad \rightarrow \quad \text{Py} \quad \text{CH}_2\text{Li} \\
\text{MgBr}_2 & \quad \rightarrow \quad \text{Py} \quad \text{CH}_3 \\
\text{CH}_3\text{COCl} & \quad \rightarrow \quad \text{Py} \quad \text{CH}_3 \text{C} = \text{O} + \text{Py} \quad \text{CH}_3 \quad \text{OH} \quad \text{Py}
\end{align*}
\]

Scheme VI

\[
\begin{align*}
\text{CO}_2\text{Et} & \quad \rightarrow \quad \text{Py} \quad \text{CH}_3 \text{C} = \text{O} + \text{Py} \quad \text{CH}_3 \quad \text{OH} \quad \text{Py} \\
\text{Li} & \quad \rightarrow \quad \text{Py} \quad \text{CH}_3 \text{C} = \text{N} \quad \text{Py} \\
\text{H}_3\text{O}^+ & \quad \rightarrow \quad \text{Py} \quad \text{CH}_3 \text{C} = \text{N} \quad \text{Py} \quad \text{Li}
\end{align*}
\]
anhydride\textsuperscript{39,40} respectively. Similarly, simple N-derivatives of 2-methylpyridine have been condensed with aromatic aldehydes under very mild conditions. 2-Pyridinium methyl iodide (32) was reacted with aromatic aldehydes in the presence of piperidine affording (40-75\%) the corresponding trans-2-stilbazole methiodides (33).

\[ \text{N}^+ \text{CH}_3 \quad \text{CH}_3 \quad \text{ArCHO} \quad \text{Piperidine} \quad \text{CH}_3\text{OH; } \Delta \quad \text{N}^+ \text{CH}_3 \quad \text{Ar} \]

Ylides (i.e., 34), prepared from 16 and ethylphosphonates,\textsuperscript{41} also have been condensed with aldehydes and ketones,\textsuperscript{42} for example, 34 and benzaldehyde afforded trans-2-stilbazole (31) in 75-87\% yield.\textsuperscript{43}

\[ \text{CHP(OEt)}_2 \quad \text{CHO} \quad \text{C}_6\text{H}_6, \Delta \quad \text{87\%} \quad \text{31} \]

Recently, ylide 36 was prepared, although in low yield, by reaction of two equivalents of methylenetriphenylphosphorane (35) with 2-bromo-pyridine.\textsuperscript{44} In a unique and simple oxidative condensation, 2-hydroxymethylpyridine (11) and 2-methylpyridine-N-oxide (14) were heated over
potassium hydroxide giving (41%) trans-1,2-di-(2-pyridyl)ethene (37). 45

1,2-DIKETONES

1-Phenyl-2-(2-pyridyl)ethene-1,2-dione (40) was first prepared 46 from 2-stilbazole (31) via initial bromination, hydrolysis to diol 39, and oxidation to diketone 40, as outlined in Scheme VII. Although

---

**Scheme VII**

- **35** + 2 CH₂=P(Ph)₃ → **36**
- **11** + **14** (KOH, 165°) → **37**
- **41** + SeO₂ (86%) → **42**
- **31** + SeO₂, 200° → **43 (20%)**
Scheme VII

39 Con. HNO₃ ➔ 40

31 Br₂ ➔ 38

\[ \text{OH}^- \downarrow \]

+ 45 46 K₂CO₃; Cu⁺ DMF ➔ 44
benzil (42) was obtained (86%) by oxidation of stilbene (43) with selenium dioxide. Under similar reaction conditions, 2-stilbazole (31) gave two major products, 1-phenyl-2-(2-pyridyl)ethane-1,2-dione (40) and 2-(2-pyridyl)selenonaphthene (43). Dione 40 was also obtained (59%) by oxidation of 2-phenacyclpyridine (20) with selenium dioxide.

\[
\begin{align*}
\text{20} & \xrightarrow{\text{SeO}_2} \text{40 (59\%)} \\
\end{align*}
\]

**ACETYLENES**

Scheuing and Winterhalden were the first to isolate phenyl-(2-pyridyl)acetylene (44) by treatment of 2-stilbazole dibromide with refluxing ethanolic potassium hydroxide. Acetylene 44 also was conveniently obtained by coupling of phenylacetylene (45) with 2-iodopyridine (46) in the presence of activated copper powder. (Scheme VII).

Di(2-pyridyl)acetylene (47) was obtained from 1,2-di(2-pyridyl)ethene (37) via bromination and dehydrobromination as outlined in Scheme VIII. Yield data were improved by replacing the normal alkali bases with potassium tert-butoxide in refluxing tert-butyl alcohol. Pure acetylene 47 and di(6-methyl-2-pyridyl)acetylene were obtained in improved yields (93% and 95%, respectively) by the procedure of Newkome, et al. Acetylene 47 was also obtained by a convenient new route in
Scheme VIII

\[ \text{Pyridine} \rightarrow \text{O} \quad \text{Br}_2 \rightarrow 89\% \]

\[ \text{KOH; CH}_3\text{OH} \rightarrow \]

\[ [\text{Pyridine} \quad \text{C} = \text{C} \quad \text{Pyridine}] \rightarrow \Delta \quad 90\% \]

\[ \text{DMF} \quad 52\% \]

\[ + \text{H}_3\text{C} - \text{SO}_2\text{NH} \cdot \text{NH}_2 \]
90% yield from 2-pyridil (48), via pyrolysis of 1,1'-dipyrido 2,3,4-triazole (49).

DIARYLCYCLOPROPENONES

Diphenylcyclopropenone (52) was first synthesized by Breslow, et al.,58 through the addition of phenylchlorocarbene to phenylketene dimethyl acetal (50) followed by hydrolysis of the initially formed chlorocyclopropanone ketal (51) as outlined in Scheme IX. This reaction has been employed in the synthesis of various arylphenylcyclopropenones which can utilize an appropriate starting arylidene chloride. However, p-nitrobenzylidene chloride failed to react and the desired products were obtained in very low yields with ortho-substituents. Concurrently with the initial isolation by Breslow, et al., Vol'pin and Kursanov59 synthesized 52 in 20-30% yield by the reaction of diphenylacetylene (53) with dibromocarbene which was generated from bromoform and potassium tert-butoxide. Comparable yields were obtained using alternate carbene sources such as: dichlorocarbene, chloroform and potassium tert-butoxide or phenyl (bromodichloromethyl)mercury and the carbenoid generated from methyl trichloroacetate and sodium methoxide.60,61 The most efficient procedure (Scheme X) for a preparative scale is the elimination of hydrogen bromide from α,α'-dibromodibenyl ketone (54) by a modified Favorskii reaction62 affording 52 in 45% overall yield from dibenzyl ketone.

Ketone 52 was also obtained from the reaction of trichlorocyclopropenium tetrachloroaluminate (55)63 with benzene derivatives via a Friedel-Crafts reaction. This latter procedure to symmetrical diarylcyclopropenone is reported to be general for aromatic hydrocarbons bearing weakly activating groups (alkyl) or weakly deactivating substituents (halogens). However,
Scheme IX

\[
\begin{align*}
\text{C}_6\text{H}_5\text{C} &= \text{C} + \text{ArCHCl}_2 \xrightarrow{\text{KOBu}^+} \text{C}_6\text{H}_5\text{C} = \text{C} \\
\text{C}_6\text{H}_5\text{C} &\equiv \text{C} + \text{KOBu}^+ \\
\text{C}_6\text{H}_5\text{C} = \text{C} + \text{H}_3\text{O}^+ \\
\text{C}_6\text{H}_5\text{C} &\equiv \text{C} + \text{H}_2\text{O} \\
\text{C}_6\text{H}_5\text{C} &\equiv \text{C} + \text{C}_6\text{H}_{14} \\
\text{C}_6\text{H}_5\text{C} &\equiv \text{C} \equiv \text{C} = \text{C}_6\text{H}_5
\end{align*}
\]

50

51

52 (Ar = \text{C}_6\text{H}_5) 80% 

\[\text{Ar} = p-\text{ClC}_6\text{H}_4 (43\%) \]
\[= m-\text{ClC}_6\text{H}_4 (46\%) \]
\[= o-\text{ClC}_6\text{H}_4 (40\%) \]
\[= p-(\text{CH}_3)_2\text{N-C}_6\text{H}_4 (6\%) \]

53

+ 

: \text{C} \text{X}_2 

(X = \text{Cl or Br})
Scheme X

\[ R_1-CH_2-C-CH_2-R_2 \]

\[ \xrightarrow{\text{Br}_2, \text{HOAc}} \]

\[ R_1-\text{CHBr}-C-\text{CHBr}-R_2 \]

54 \( R_1=R_2=C_6H_5 \)

\[ \xrightarrow{\text{Et}_3\text{N}} \]

\[ \begin{array}{c}
\text{H} \\
\text{Br} \\
\text{R}_1 \\
\text{R}_2
\end{array} \]

52 \( R_1=R_2=C_6H_5 \)

\[ \xrightarrow{\text{H}_2\text{O}} \]

\[ \begin{array}{c}
\text{Cl} \\
\text{C}_6\text{H}_5 \\
\text{Cl}
\end{array} \]

\[ \xrightarrow{55} \]

\[ \begin{array}{c}
\text{Cl} \\
\text{C}_6\text{H}_5 \\
\text{Cl}
\end{array} \]

\[ \xrightarrow{\text{2C}_6\text{H}_6} \]

\[ \text{C}_6\text{H}_5\text{C}≡\text{C}-\text{COCH}_3 \]

\[ \xrightarrow{\text{H}_2\text{O}} \]

\[ \text{C}_6\text{H}_5\text{C}≡\text{C}-\text{COCH}_3 + \text{Cl} \]

\[ \xrightarrow{56} \]
with strongly activating substituents, all three halogens were replaced by aryl groups and no cyclopropenone derivatives could be obtained. Recently, 52 was prepared by insertion of phenylchlorocarbene to phenylmethoxyacetylene (56) after hydrolysis. A unique new procedure to substituted cyclopropenones has recently been proposed by Trost, et al, in which bis-diazoketones are photolyzed in methanol to afford the cyclized ketones. Thus, photolysis of 1,3-bis(diazo)-1,3-diphenyl-2-propanone (57) using either monochromatic light at 4360 Å or a visible region photoflood afforded diphenylcyclopropenone (52). Failure to synthesize nitro-

![Chemical structure of 57 and 52]

substituted phenylcyclopropenones via the above procedures led to the direct nitration of 52 as an alternative route. Both mono- and di-

![Chemical structures of 58 and 59]

NanO3 (1 mole)
nitrophenyl cyclopropenones, substituted in the meta-position (58 and 59), have been isolated.\textsuperscript{67}

**CYCLOPENTADIENONES**

The first compound in the series of diarylcyclopentadienones was obtained by Japp and Miller\textsuperscript{68} through condensation of benzil (42) with acetone in the presence of potassium hydroxide (Scheme XI). The intermediary 3,4-diphenyl-4-hydroxy-2-cyclopenten-1-one (60) was first isolated; subsequent dehydration of 60 using various dehydrating agents (e.g., hot dilute sulfuric acid, acetic acid, and sodium acetate, ethanol and sulfuric acid, acetic anhydride and sulfuric acid) gave the dimer 69, which arose \textit{via} a Diels-Alder condensation. Numerous 3,4-diarylcyclopentadienones\textsuperscript{69} have been prepared by condensation of benzil (42), or substituted benzils, with the appropriately substituted 2-propanones in the presence of aqueous and/or alcoholic potassium hydroxide, sodium hydroxide, sodium ethoxide, 10\% tetraethylammonium hydroxide, or benzyltrimethylammonium hydroxide. In some cases, when the aryl substituents possess ortho functionality this condensation could be catalyzed only with Triton B.\textsuperscript{70} The position of equilibrium between monomer 61 and dimer depends upon the nature of the cyclopentadienone substituents; for example, when \( R_1 = R_2 = \text{CH}_3 \), a dissociating dimer was obtained and for aryl and higher alkyl substituents, only monomers were isolated.\textsuperscript{71} A number of tetraphenylcyclopentadienones (tetracyclones) substituted with activating groups, i.e., methoxy, halogens, and methyl, have been prepared.\textsuperscript{70,72} However, all attempts to introduce a nitro substituted benzil \textit{via} this condensation reaction either did not react or afforded intractable tars. Nevertheless, methylsulfonyl group (\textit{CH}_3\textit{SO}_2\textsuperscript{--}) has been successfully introduced
Scheme XI

$$
\text{Ar} \quad \text{CH}_2R_1 \quad \text{base} \quad \text{Ar} \quad \text{CH}_2R_2
$$

42 ($\text{Ar} = \text{C}_6\text{H}_5$)

$$
\begin{bmatrix}
\text{Ar} & \text{R}_1 \\
\text{Ar} & \text{R}_2
\end{bmatrix}
\quad 2
\quad \text{H}_2\text{O}
$$

61 (monomer)

62 ($R = R = \text{H}$)
into 1,3-diphenyl-2-propanone, and reacted with benzil via this condensation. 2-Pyridyl substituted tetracyclone (64) was first prepared by Eistert and Fink from 2,2'-dipyridil (48) and dibenzylketone (63). The intermediary hydroxyalcohol was isolated, and upon reflux in ethylene glycol afforded the diene 64. Recently, 65 was prepared from benzil and 2-picolyl ketone. 75

\[
\begin{align*}
\text{Py} \quad \text{O} + \quad \text{Ph} \quad \text{O} & \rightarrow \quad \text{KOH} \\
\text{Ph} \quad \text{O} & \rightarrow \quad \text{EtOH}
\end{align*}
\]

SUBSTITUTED BENZENES

Although numerous procedures are reported for the preparation of arylbenzenes, only several are applicable to the synthesis of the heterocyclic substituted benzenes.

The Cu(I) oxide promoted arylation of a polynitrobenzene by an iodoarene can be illustrated by the reaction of excess of p-iodoanisole (66), 1,3,5-trinitrobenzene (67), and Cu(I)oxide in quinoline at high temperature affording (16%) the triarylated product 68. Benzene derivatives are obtained by Diels-Alder reactions of 2-pyrones (69) with
acetylenes followed by loss of carbon dioxide from the intermediate adduct. Unsymmetrically substituted acetylenes and 2-pyrones containing unsymmetrically substituted diene fragments reveal varying degrees of stereoselectivity with regard to the direction of addition depending on the positions and types of substituents. The readily available substituted cyclopentadienones condense with diverse acetylenes forming irreversibly the aromatic compounds directly with simultaneous loss of carbon monoxide from the bicyclic intermediate. Thus, hexaphenylbenzene (71) itself was first obtained from condensation of tetracyclone (70) with diphenylacetylene. The trimerization of tolan in non-hydroxylic
solvents using bis(benzonitrile)palladium chloride(I)\textsuperscript{79} also generates 71, as the major product. A few arylbenzenes with 2-pyridyl moiety have also been prepared, but not fully characterized.\textsuperscript{75,80}

\[ 3 \text{Ph} - \text{C} = \text{C} - \text{Ph} \]
\[ + \]
\[ (\text{C}_6\text{H}_5\text{CN})_2\text{PdCl}_2 \]
\[ \text{C}_6\text{H}_6, \text{CHCl}_3 \text{ or } \text{CH}_3\text{COCH}_3 \]
\[ \rightarrow 71 \]
EXPERIMENTAL

General Comments

The reagents used in all syntheses were reagent grade commercial chemicals. Unless otherwise indicated, these chemicals were used without further purification.

All glass apparatus used for Grignard and hydroboration reactions were dried separately in an oven overnight before assembly. After assembly, nitrogen was swept through the system for 15 minutes before the reaction was begun, and a slow stream of nitrogen was maintained throughout the reaction. All reaction mixtures were stirred magnetically unless mentioned otherwise.

Melting points below 300° were obtained with a Thomas Hoover melting point apparatus and are uncorrected. Melting points greater than 300° were obtained by a Dupont-900 Differential Thermal Analyzer (DTA) and were corrected with a thermocouple conversion chart. Boiling points were recorded uncorrected with reduced pressure specified in millimeters (mm) of mercury.

Infrared (ir) spectra were recorded on either a Perkin-Elmer 137 or a Perkin-Elmer 621 grating spectrophotometer.

Ultraviolet (uv) spectra were recorded on a Cary-14 recording spectrophotometer in matched 1 cm quartz cells and were corrected by solvent blank. Absorbance values were reported in wavelength (nm) followed by molar extinction coefficient (ε).

Mass spectrograms were obtained on a Hitachi-Perkin-Elmer RMS-4 mass spectrometer by Mrs. Paula B. Moses of the Louisiana State University.
Chemistry Department technical staff. Conditions were usually 70 eV and 80 μA. A fluorocarbon was used as a counting reference.

Proton nuclear magnetic resonance (nmr) spectra were obtained with a Varian Associates A-60A, Varian Associates HA-100, or a Perkin-Elmer Rl2-B spectrometer. Samples were examined as 10-20% solutions in carbon tetrachloride, deuterochloroform, deuteracetone, deuterodimethylsulfoxide, deuterobenzene, or N,N-dimethylacetonitrile with tetramethylsilane or hexamethyldisilane as reference. All chemical shifts are recorded relative to TMS in parts per million (δ).

Elemental analyses were performed by Mr. Ralph L. Seab of the Louisiana State University Chemistry Department technical staff.

Thin layer chromatography (tlc) was performed on 20 cm glass plates with a standard 0.25 mm coating of silica gel (Brinkmann HF-254+366). Preparative layer chromatography (plc) utilized silica gel thicknesses of either 2 mm (Brinkmann PF-254+366) or 5 mm (Brinkmann PF-254+13% CaSO₄ binder). Column chromatography utilized either silica gel (Baker, 60-200 mesh) or florisil (60-200 mesh). Dry column chromatography utilized nylon tubing and Waters Associates Dry Column Grade, Activity III, absorbents (silica gel and alumina). Absorbent used for preliminary purification was Merck silica gel (150-200 mesh; Baker, C-190N).

Gas phase chromatography (glc) was performed with a Varian Aerograph 90-P using a 3.8"X 10' column packed with 20% SE 30 on 60/80 mesh Chromosorb W.
Solvents

Benzene, ethyl ether, petroleum ether, and toluene were dried over sodium ribbon.

Tetrahydrofuran, 1,2-dimethoxyethane (DME), and bromobenzene were distilled from lithium aluminum hydride and stored over activated molecular sieves (Linde Type 4A).

Dimethylsulfoxide (DMSO), N,N-dimethylformamide, and boron trifluoride-etherate (BF$_3$-Et$_2$O), and hexamethylphosphorictriamide (HMPTA) were distilled from calcium hydride at reduced pressure and stored over activated molecular sieves.

Pyridine and 2-picoline were dried over barium oxide and distilled.

Benzoyl chloride was dried over sodium sulfate and distilled at reduced pressure.

Diglyme was dried over calcium hydride, distilled from lithium aluminum hydride at reduced pressure and stored over sodium borohydride.

Syntheses

Ethyl 2-Pyridylacetate ($\xi$). Method A. $^8$ A suspension of 2-picoline (27 ml, 0.3 mole), diethylcarbonate (121 ml, 1.05 mole), and sodium hydride (43 g, 1.0 mole) in dry 1,2-dimethoxyethane (100 ml) was refluxed for 12 hours. After cooling and carefully pouring into water, the mixture was extracted with ether, dried over anhydrous magnesium sulfate and concentrated in vacuo. Fractional distillation of the residue afforded 10 g (20%) of ethyl 2-pyridylacetate; bp 110-116°
(6 mm) $^{[\text{lit.} 82]}$ bp 122-125° (12 mm)]; nmr (CDCl$_3$) δ 61.23 (-CH$_3$, t, 3H), 3.83 (-CH$_2$CO, s, 2H), 4.17 (-CH$_2$CH$_3$, q, 2H), 7.0-7.8 (pyr-H, m, 3H), 8.45-8.65 (6-pyr-H, m, 1H); ir (neat) 1738 (C=O, ester), 1587, 1160, and 1036 cm$^{-1}$.

Method B. (from 2-Picolyllithium and Diethylcarbonate). $^7$ To an ethereal solution of 2-picolyllithium [0.4 mole; prepared from lithium (0.8 mole), bromobenzene (82.8 g), and 2-picoline (37.2 g)] was added diethyl carbonate (23.6 g, 0.2 mole) in ether (25 ml) with cooling, maintaining the temperature between 20-25°. The mixture was refluxed for 30 minutes, cooled, carefully poured into ice-water, extracted several times with ether, dried over anhydrous magnesium sulfate, and concentrated in vacuo affording a residue which was fractionally distilled affording 12 g (36%) of 5, bp 90-92° (2 mm).

2-Pyridylacetonitrile ($^3$). Method A. To a mixture of lithium aluminum hydride (9.5 g, 0.25 mole) in anhydrous ether (400 ml), ethyl 2-pyridinecarboxylate [30.2 g, 0.2 mole; bp 110-113° (6 mm)] was added dropwise with cooling over 1.5 hours. After the addition was complete, the excess hydride was immediately decomposed by cautiously adding water (25 ml). The precipitate of the hydroxides was filtered, washed with absolute ethanol, and the combined ether and ethanol extracts were concentrated. The residue was dissolved in absolute ethanol (70 ml), anhydrous ether (200 ml) was added, and after 12 hours the mixture was filtered. Concentration and fractional distillation of the residue afforded 153 g (70%) of 2-pyridylmethanol ($^3$); bp 90-92° (5.5 mm) $^{[\text{lit.} 83]}$ bp 103-105° (11mm)]; picrate mp 158-159° (lit. $^7$ mp 158-159°); nmr (CDCl$_3$) δ 4.6 (pyr-CH$_2$-, d, 2H), 5.65 (-OH, m, 1H), 6.98-7.85 (pyr-H, m, 3H), 8.38-8.6 (6-pyr-H, d, 1H).
2-Pyridylmethanol (12.5 g, 0.115 mole) was added to thionyl chloride (41 g, 0.348 mole) at 0° over 1.5 hours. After the addition was complete, the reaction mixture was refluxed for 2.5 hours, cooled, and the excess of thionyl chloride distilled in vacuo. The residue was dissolved in absolute ethanol (10 ml). The solution was heated for 1 hour, cooled for 3 hours, and the precipitate collected and washed with benzene and ether, affording 11.5 g (60%) of 2-chloromethylpyridine hydrochloride: mp 128-129° (lit. mp 128-129°).

A suspension of the above hydrochloride (11.5 g, 0.06 mole) and potassium cyanide (1 g) in 60% ethanol (70 ml) was refluxed for 3 hours, then stirred overnight at 25°. The reaction mixture was poured into a saturated solution of potassium carbonate and extracted with chloroform. The extract was concentrated in vacuo and the residue distilled affording 6.4 g (90%) of 2-pyridylacetonitrile (13): bp 95-97° (1.4 mm) [lit. bp 79-81° (0.4 mm)].

Method B. A mixture of 2-picoline (93.2 g, 1 mole), glacial acetic acid (600 ml), and 30% aqueous hydrogen peroxide (170 ml) was heated for 12 hours at 70-80°. The solution was concentrated in vacuo, water added, and then reconcentrated in vacuo several times to remove traces of acid and hydrogen peroxide. The residue was dissolved in chloroform (500 ml) and shaken with an aqueous paste of potassium carbonate until no further carbon dioxide was evolved. The chloroform layer was separated, dried over anhydrous sodium sulfate, and concentrated in vacuo. Fractional distillation of the residue afforded 90 g (83%) of 2-picoline N-oxide (14): bp 103-104° (9.6 mm) [lit. bp 123-124° (15 mm)]; picrate: mp 125-126° (lit. mp 125-126.5°); nmr (CDCl₃) δ 2.7 (-CH₃, s, 3H), 6.8-7.4 (pyr-H,
To a refluxing solution of 14 (55 g, 0.5 mole) in benzene (400 ml), benzenesulfonyl chloride (88 g, 0.5 mole) in benzene (100 ml) was added over 1 hour. After refluxing for an additional 1.5 hours, the solution was cooled and extracted with 5% hydrochloric acid solution. The aqueous extract was neutralized with solid sodium carbonate and extracted several times with ether. The extract was washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo at room temperature. The residue was dissolved in ethyl acetate and purified by rapid filtration through a short column of silica gel. Removal of the solvent afforded 35 g of a pale yellow oil; nmr spectrum of this oil indicates it to be predominantly (90%) 2-chloromethylpyridine (16): nmr (CDCl₃) δ 4.72 (pyr-CH₂, s, 2H), 7.05-7.95 (pyr-H, m, 3H), 8.5-8.7 (6-pyr-H, m, 1H).

Since this product is known to be unstable, it was immediately dissolved in anhydrous dimethylsulfoxide (125 ml) and added to a mixture of potassium cyanide (25 g, 0.382 mole) in dimethylsulfoxide (125 ml) over one hour while maintaining the temperature between 20-25°C with cooling. After stirring at 25°C overnight, the mixture was poured into water containing a small amount of sodium carbonate and extracted with chloroform. The organic extract was washed with water, dried over anhydrous sodium sulfate, and concentrated in vacuo. Fractional distillation of the residue afforded 25.5 g (80%) of 2-pyridylacetonitrile (13): bp 79-81°C (0.4 mm) [lit.¹³ bp 118-120°C (13 mm)]; nmr (CDCl₃) δ 3.85 (pyr-CH₂, s, 2H), 6.95-7.8 (pyr-H, m, 3H), 8.45 (6-pyr-H, d, 1H); ir (neat) 2220 (C≡N), 1585, 1490, 1470, 1445, 1235, 759, and 694 cm⁻¹.
1,3-Di(2-pyridyl)acetone (8) Method A. To an ethereal solution of 2-picolyllithium (0.36 mole in 300 ml of diethyl ether) was added dropwise ethyl 2-pyridylacetate (20 g, 0.121 mole) at 25°. After stirring overnight, the reaction mixture was refluxed for 1.5 hours, cooled, and poured into 2 N hydrochloric acid solution. The acid layer was neutralized with 40% sodium hydroxide solution and extracted with chloroform. The extract was dried over anhydrous magnesium sulfate, concentrated, and the residue was fractionally distilled affording 8 g (32%) of 1,3-di(2-pyridyl)acetone: bp 182-185° (1.4 mm) [lit. 35 bp 130-135° (0.05 mm)]. Recrystallization from diethyl ether gave pale yellow crystals: mp 80-81° (lit. 35 mp 80-81°); nmr (CCl₄) [60% exists in enol form] δ 3.6 (CH₂ of enol, s, ~1.2 H), 3.95 (CH₂CO, s, ~1.6 H), 5.32 (vinyl-H, s, ~0.6 H), 6.7-7.7 (pyr-H, m, 6 H), 8.1-8.5 (6-pyr-H, m, 2 H); ir (CCl₄) 1720 (C=O, weak), 1640 (C=C, strong), 1460 and 1325 cm⁻¹.

Method B. To an ethereal solution of 2-picolyllithium (0.50 mole, prepared from lithium (7 g), bromobenzene (80 g), and 2-picoline (46.5 g) in anhydrous diethyl ether (400 ml)] was added dropwise a solution of 2-pyridylacetonitrile (20 g, 0.17 mole) in ether (50 ml) at 25° over 1 hour. After stirring overnight, the mixture was refluxed for 1.5 hour, cooled, and poured into 2 N hydrochloric acid solution. The aqueous layer was refluxed for 1.5 hour, cooled, neutralized with 40% sodium hydroxide solution, and extracted with chloroform. The organic extract was dried over anhydrous magnesium sulfate and concentrated in vacuo giving the residual oil, which was fractionally distilled affording 22 g (60%) of 1,3-di(2-pyridyl)acetone (8): bp 115-120° (0.01 mm) [lit. 35 bp 130-135° (0.05 mm)], which solidified on cooling to 0°. Recrystallization from diethyl ether gave pale yellow crystals: mp 80-81°.
1-Phenyl-3-(2-pyridyl)propan-2-one (29). To a solution of 2-picolyllithium [0.5 mole, prepared from lithium (7 g), bromobenzene (85 g), and 2-picoline (46.5 g, 0.5 mole) in anhydrous diethyl ether (400 ml)] was added phenylacetonitrile (20 g, 0.17 mole) in ether (25 ml) dropwise at 25° over 1 hour. After stirring overnight, the mixture was carefully poured into 2 N hydrochloric acid solution. The organic extract was separated and extracted with 2 N hydrochloric acid solution. The combined acidic extracts were refluxed for 1.5 hours, cooled, neutralized with a 40% sodium hydroxide solution, and extracted with chloroform. The organic extract was dried over anhydrous sodium sulfate and concentrated in vacuo affording a residue which was fractionally distilled affording 12 g (33%) of 1-phenyl-3-(2-pyridyl)propan-2-one: bp 167-173° (3.5 mm) [lit.33 bp 140-142° (3 mm)]; nmr (CDCl₃) δ 3.56 (ph-CH₃, enol), 3.79 (ph-CH₂CO), 3.9 (pyr-CH₂CO), 5.2 (vinyl H), 6.6-7.65 (arom-H and -OH), 7.9-8.17 (6-pyr-H, enol), 8.42-8.66 (6-pyr-H) (about 22% exists as enol); ir (neat) 1720 (C=O), 1650 (C=C, enol), 1600, 1470, 1330, 1150, 1060, 1000, 930, 800, 750, and 700 cm⁻¹.

(E)-1-Phenyl-2-(2-pyridyl)ethene (trans-2-stilbazole) (31).

Method A. A mixture of 2-picoline (46.5 g, 0.5 mole), benzaldehyde (76.5 g, 0.7 mole), acetic anhydride (51 g, 0.5 mole), potassium acetate (50 g), and a trace of iodine was refluxed for 40 hours under nitrogen. After cooling, 2 N hydrochloric acid solution (200 ml) was added and the excess benzaldehyde was steam distilled. Upon cooling the residue deposited white crystals of 2-stilbazole hydrochloride and cinnamic acid. This mixture was stirred with 28% ammonium hydroxide solution (50 ml) and filtered affording 57 g (60%) of 2-stilbazole, which was recrystallized from absolute alcohol yielding 40 g (51%) of pure (31): mp 90-91°
Method B.  

A mixture of 2-picoline (113 g, 1.21 mole), benzaldehyde (130 g, 1.225 mole), and acetic anhydride (55 g, 0.535 mole) was refluxed for 40 hours. The excess reagents were removed by distillation in vacuo and the residual oil was fractionally distilled affording 125 g (57%) of 2-stilbazole: bp 120-122° (0.6 mm) [lit. bp 150-160° (3 mm)]. Recrystallization from absolute alcohol afforded colorless crystals: mp 91°.

Phenyl(2-pyridyl)glyoxol (40).  

2-Stilbazole (20 g, 0.11 mole) was heated to 200-210° and held at this temperature while selenium dioxide (20 g) was added in small portions. After the addition, the mixture was held at the same temperature until water ceased to distill. After cooling, the mixture was diluted with methanol (50 ml) and filtered to remove selenium metal. The alcoholic filtrate was diluted with water, neutralized with solid sodium bicarbonate, and extracted with ether. The extract was decolorized and concentrated in vacuo. The residue was fractionally distilled affording two products: (i) phenyl(2-pyridyl)glyoxol (40): bp 128-130° (0.2 mm) [lit. bp 168-173° (1-2 mm)]; 9 g (31%); mp 72-73° (ethanol-petroleum ether A; lit. mp 72-72.5°); nmr (CDCl₃) 67.3-8.3 (arom-H and pyr-H, m, 8H), 8.58 (6-pyr-H, d, 1H); ir (CHCl₃) 1780, 1760, 1675, 1660, 1520, 1510, 1290, 995, and 885 cm⁻¹. 

Anal. Calcd for C₁₃H₉NO₂: C, 73.92; H, 4.29; N, 6.64. Found: C, 73.93; H, 4.13; N, 6.58.

(ii) 2-α-pyridylselenonaphthene: bp 150-152° (0.2 mm); 8 g (20%). Recrystallization from ethanol-petroleum ether A afforded
colorless needle-like crystals: mp 141-142° (lit. mp 137-140°); nmr (CDCl₃) δ 6.95-7.42 (arom-H, m, 4H), 7.49-8.05 (pyr-H and vinyl-H, m, 4H), 8.05 (6-pyr-H, d, 1H); ir (CHCl₃) 1600 (C=C), 1475 and 1440 cm⁻¹.

Anal. Calcd. for C₁₅H₁₂NSe: C, 60.47; H, 3.51; N, 5.39. Found: C, 60.76; H, 3.43; N, 5.35.

1-Phenyl-2-(2-pyridyl)-1,2-dibromoethane.85 A solution of bromine (15.5 g, 0.097 mole) in carbon disulfide (10 ml) was added at 25° to a solution of 2-stilbazole (17.6 g, 0.097 mole) in carbon disulfide. After stirring for 1 hour, the precipitate was filtered, washed with methanol, and recrystallized from benzene affording 20 g (60%) of 1-phenyl-2-(2-pyridyl)-1,2-dibromoethane: mp 185-186° (lit. mp 185-186°) nmr (CDCl₃) δ 5.35-6.05 (CHBr, m, 2H), 7.1-7.9 (arom-H and pyr-H, m, 8H), 8.55-8.9 (6-pyr-H, m, 1H); ir (CDCl₃) 1590, 1450, 1375, 1245, 900, 860, and 720 cm⁻¹.

Anal. Calcd for C₁₃H₁₁NBr: C, 45.76; H, 3.22; N, 4.10. Found: C, 45.84; H, 3.24; N, 4.15.

Phenyl(2-pyridyl)acetylene (44) Method A.85 A mixture of 1-phenyl-2-(2-pyridyl)-1,2-dibromoethane (18.2 g, 0.053 mole) and potassium hydroxide (9 g, 0.161 mole) in absolute ethanol (50 ml) was refluxed for 1.5 hours under nitrogen. The mixture was cooled, filtered, and the filtrate concentrated in vacuo. The residue was dissolved in water, extracted with ether, washed with water, a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, concentrated, and fractionally distilled affording 8.85 g (93%) of phenyl(2-pyridyl)-acetylene: bp 120-122° (0.3 mm) [lit. bp 160-164° (3-4 mm)]; nmr (CDCl₃) δ 6.92-7.7 (arom-H and pyr-H, m, 8H), 8.52 (6-pyr-H, d, 1H); ir (neat) 3400 (C=C), 2350 (C≡C), 1625, 1520, 1480, 1460, 1440, 1320, 1280, 1240, 1150, 980, 910, 710, and 690 cm⁻¹.
Method B. 2-Iodopyridine was prepared by a published method in 35% yield by reaction of 2-bromopyridine with hydroiodic acid.

A mixture of 2-iodopyridine (4.1 g, 0.025 mole), phenylacetylene (3 g, 0.029 mole), activated copper powder (1.9 g), and finely crushed anhydrous potassium carbonate (10.4 g) in dimethylformamide (50 ml) was heated at 140° for 5 hours. After cooling, the reaction mixture was diluted with ether (500 ml) and the residue filtered. The filtrate was washed with 10% ammonium hydroxide solution, water, and extracted with 4 N hydrochloric acid solution. The acidic extract was neutralized with solid potassium hydroxide and extracted with ether. The extract was washed with water, dried over anhydrous potassium carbonate, and concentrated. The residual oil upon fractional distillation in vacuo afforded 3.2 g (88%) of phenyl(2-pyridyl)acetylene (44): bp 102-105° (0.3 mm).

(E)-1,2-Di(2-pyridyl)ethene (37). A mixture of 2-picoline (85 g, 0.914 mole), 2-pyridinecarboxaldehyde (40 g, 0.374 mole), and acetic anhydride (40 g, 0.392 mole) was refluxed for 14 hours. Excess reagents were removed in vacuo and residue was fractionally distilled affording 30 g (38%) of pure olefin [bp 173-178° (1.4 mm)], which upon recrystallization from ethyl acetate afforded pale greenish-yellow needles: mp 118-120° (lit88 mp 118-119°); nmr (CDCl₃) δ 6.95-7.90 (pyr-H, m, 6H), 7.70 (vinyl-H, s, 2H), 8.50-8.75 (6-pyr-H, m, 2H); ir (CHCl₃) 1575, 1555, 1310, 977, 789, and 744 cm⁻¹.

1,2-Di(2-pyridyl)-1,2-dibromoethane. To a solution of (E)-1,2-di(2-pyridyl)ethene (18 g, 0.1 mole) in glacial acetic acid (25 ml), bromine (16 g, 0.1 mole) in acetic acid (8 ml) was added dropwise over 1 hour with external cooling. After stirring for 1 hour at 25°, the crystals were collected, washed with methanol affording 16 g (47%) of the dibromide:
mp 149-150° (lit.\textsuperscript{56} mp 149-150°); nmr (CDCl\textsubscript{3}) \textsuperscript{6} 65.96 (CHBr, s, 2H), 7.10-7.95 (pyr-H, m, 6H), 8.60-8.85 (6-pyr-H, m, 2H); ir (nujol) 1585, 1565, 1145, 993, 788, and 749 cm\textsuperscript{-1}.

Di(2-pyridyl)acetylene (47). Method A.\textsuperscript{56} To a refluxing solution of potassium hydroxide (30 g) in methanol (100 ml) the above dibromide (11 g, 0.032 mole) was added rapidly in small portions. After the addition was complete, the mixture was refluxed for an additional 30 minutes. After cooling, potassium bromide was filtered and the filtrate concentrated to dryness. The residue was dissolved in water and extracted with ether. The extract was washed with a saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated affording the crude acetylene. Recrystallization from petroleum ether A afforded 5.2 g (90%) of (47): mp 69-71° (lit.\textsuperscript{50} mp 69-70°); nmr (CDCl\textsubscript{3}) \textsuperscript{6} 67.1-7.5 (pyr-H, m, 2H), 7.50-7.95 (pyr-H, m, 4H), 8.55-8.75 (6-pyr-H, m, 2H), ir (CHCl\textsubscript{3}), 1575, 1550, 987, 802, and 774 cm\textsuperscript{-1}.

Method B. p-Toluenesulfonylhydrazine was prepared (88%) by a published method\textsuperscript{89} from p-toluenesulfonyl chloride: mp 110° (lit.\textsuperscript{89} mp 110°).

A mixture of 2-pyridil (4.5 g, 0.021 mole) and p-toluenesulfonylhydrazine (8.0 g, 0.043 mole) in dimethylformamide (20 ml) was heated at 100-120° for 6 hours. The mixture was cooled and filtered affording 2.6 g (52%) of 1,1'-dipyridotriazole: mp 254-255° (lit.\textsuperscript{57} 254-255°).

The triazole was heated slowly to its melting point at which point it decomposed evolving nitrogen and sulfur dioxide. After cooling, the residue was dissolved in diethyl ether, decolorized, and concentrated affording 1.6 g (90%) of the crude acetylene. Recrystallization from petroleum ether A gave colorless crystals of the acetylene (47): mp 69-70°.
Condensation of Benzil with 3-Pentanone. A mixture of benzil (2.10 g, 0.01 mole) and 3-pentanone (1 g, 0.011 mole) in absolute ethanol (20 ml) was cooled to 10° and a 24% solution of potassium hydroxide in 95% ethanol (5 ml) was added dropwise with stirring. After an additional 20 hours at room temperature, the crystals were collected, washed with boiling water, then diethyl ether and recrystallized from absolute alcohol affording 2.25 g (80%) of 22 as colorless plates: mp 150° (lit. 150°); nmr (CDCl₃) 6 2.71 (-CH₂ q, J = 7 Hz, 1H), 1.24 (-CH₂CH₃, d, J = 2 Hz, 3H), 2.0 (=C-CH₃, s, 3H), 2.32 (-OH, s, 1H), 7.1-7.5 (arom-H, m, 10H); ir (CHCl₃) 3600, 3400, 1715, 1450, 1325, 1020, 935, and 695 cm⁻¹.

2,5-Dimethyl-3,4-diphenylcyclopentadienone (73). To a suspension of above alcohol (5 g, 0.018 mole) in acetic anhydride (20 ml), concentrated sulfuric acid (10 drops) was added at room temperature. The solid dissolved, the solution turned green, and orange crystals, which formed immediately, were collected, washed with alcohol, dried, and recrystallized from absolute alcohol affording 3.8 g (80%) of the dienone 73 as orange crystals: mp 181-182° (lit. 182°); nmr (acetone-d₆) 6 2.1 (=C-CH₃, s, 6H), 7.2-7.6 (arom-H, m, 10H); ir (CHCl₃) 1765 (C=O), 1675, 1610, 1460, 1375, 1330, 1025, 930, and 700 cm⁻¹.

(4SR,5SR)-4-Hydroxy-2,5-dimethyl-3,4-diphenyl-2-cyclopenten-1-one (74). Condensation of 2-Pyridil with 3-Pentanone. A mixture of 2-pyridil (2.11 g, 0.01 mole) and 3-pentanone (1 g, 0.011 mole) in absolute ethanol (20 ml) was reacted with a 30% solution of potassium hydroxide in 95% ethanol (10 ml) at room temperature. The mixture was stirred for 48 hours and then allowed to stand for another 48 hours. The colorless crystals formed were collected, washed with 95% ethanol, and
4.0 recrystallized from absolute alcohol affording 1.68 g (60%) of alcohol 74: mp 163-164°; nmr (CDCl₃) 61.26 (-CHCH₃, d, J = 7 Hz, 3H), 2.06 (=C-CH₃, s, 3H), 2.14 (-OH, s, 1H), 2.76 (-CH-CH₃, q, J = 7 Hz, 1H), 6.9-7.9 (pyr-H, m, 6H), 8.26-8.6 (6-pyr-H, m, 2H); ir (CHCl₃) 3450 (-OH), 1725 (C=O), 1600, 1475, 1440, 1345, 1025, 990, and 670 cm⁻¹.


3,4-Dihydroxy-2,5-dimethyl-3,4-di(2-pyridyl)cyclopentanone (75). The above reaction mixture, after stirring for 48 hours at room temperature, was poured into water (25 ml) and after 24 hours, the crystals which formed were collected, washed with ethanol and dried, affording 1.5 g (50%) of diol 75: mp 167°; nmr (CDCl₃) 60.95 (CH₃, d, J = 7 Hz, 6H), 2.2 (CH, q, J = 7 Hz, 2H), 7-7.35 (OH, m, 2H), 7.5-8.2 (pyr-H, m, 6H), 8.32 (6-pyr-H, d, 2H); ir (CHCl₃) 3500, 1750, 1600, 1460, 1025, 1010, and 665 cm⁻¹.


1,4-Dimethyl-2,3,5,6-tetraphenylbenzene (76). A mixture of 2,5-dimethyl-3,4-diphenylcyclopentadienone (2.6 g, 0.01 mole) [or 72 (2.7 g, 0.01 mole)] and diphenylacetylene (3.56 g, 0.02 mole) was heated via bunsen burner to 350° until completely melted. A gas is liberated and upon cooling, colorless crystals were deposited which were recrystallized from dimethylformamide affording 2.87 g (70%) of shiny silvery plates: mp (DTA) 362°; nmr [CH₃CON(CH₃)₂] 63.81 (CH₃, s), 6.92-7.15 (arom-H, m); ir (nujol) 1595, 775, 740, and 692 cm⁻¹; uv (1,2-dichloroethane) 238 nm (59,500).
Anal. Calcd for C_{32}H_{24}: C, 93.61; H, 6.38. Found: C, 93.69; H, 6.41.

The other 1,4-dimethyl-2,3,5,6-tetraarylbenzenes (77-80) were prepared by similar method as outlined in Tables I, II, and VII.

(4SR,5SR)-4-Hydroxy-2,5-dicarbomethoxy-3,4-diphenyl-2-cyclopenten-1-one (81). Condensation of Benzil with Dimethyl 1,3-Acetonedicarboxylate. 1,3-Acetonedicarboxylic acid was prepared (70%) by a published method\(^9\) by dehydration of citric acid with fuming sulfuric acid. Dimethyl 1,3-acetonedicarboxylate was prepared (50%) by standard esterification procedures using absolute methyl alcohol, saturated with hydrogen chloride gas: bp 114-116° (10 mm).

Benzil (2.1 g, 0.01 mole) and dimethyl 1,3-acetonedicarboxylate (1.74 g, 0.01 mole) were dissolved in absolute methyl alcohol (20 ml). A 10% solution of tetraethylammonium hydroxide (2 ml) was added dropwise with stirring. The mixture was stirred overnight and the yellow crystals were collected, washed with methyl alcohol, and dried affording 1.8 g (96%) of alcohol 81: mp 146-147° (lit.\(^9\) mp 147-148°); nmr (CDCl\(_3\)) \(\delta3.75\) (–CH\(_3\), s, 6H), \(3.18\) (–OH, s, 1H), \(3.85\) (–H, s, 1H), \(7.33\) (arom–H, m, 10H); ir (CHCl\(_3\)) 3400 (–OH), 1735, 1705, 1610, 1425, and 1330 cm\(^{-1}\).

2,5-Dicarbomethoxy-3,4-diphenylcyclopentadienone (82). To a suspension of the above alcohol (6.0 g, 0.0164 mole) in acetic anhydride (20 ml), concentrated sulfuric acid (10 drops) was added with stirring. The solution turned dark red. After cooling, the resultant orange-red crystals were collected, washed with absolute alcohol, and dried affording 5.2 g (93%) of the dienone (82): mp 175° (lit.\(^9\) mp 173°); nmr (CDCl\(_3\)) \(\delta3.75\) (–CH\(_3\), s, 6H), \(6.8-7.5\) (arom–H, m, 10H); ir (CHCl\(_3\)) 1720, 1610, and 1350 cm\(^{-1}\).
<table>
<thead>
<tr>
<th>Compound</th>
<th>Cyclopentenolone</th>
<th>Acetylene</th>
<th>Reaction Temperature</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>ph ph</td>
<td>ph ph</td>
<td>350°</td>
<td>70</td>
</tr>
<tr>
<td>77</td>
<td>ph ph</td>
<td>ph 2-pyr</td>
<td>275°</td>
<td>50</td>
</tr>
<tr>
<td>78</td>
<td>ph ph</td>
<td>2-pyr 2-pyr</td>
<td>300°</td>
<td>60</td>
</tr>
<tr>
<td>79</td>
<td>2-pyr 2-pyr</td>
<td>ph 2-pyr</td>
<td>225°</td>
<td>40</td>
</tr>
<tr>
<td>80</td>
<td>2-pyr 2-pyr</td>
<td>2-pyr 2-pyr</td>
<td>200°</td>
<td>60</td>
</tr>
</tbody>
</table>
TABLE II
ANALYSES OF 1,4-DIMETHYL-2,3,5,6-TETRAARYLBENZENES

<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>Carbon Calcd</th>
<th>Carbon Found</th>
<th>Hydrogen Calcd</th>
<th>Hydrogen Found</th>
<th>Nitrogen Calcd</th>
<th>Nitrogen Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>76</td>
<td>C\textsubscript{32}H\textsubscript{26}</td>
<td>93.61</td>
<td>93.69</td>
<td>6.38</td>
<td>6.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>77</td>
<td>C\textsubscript{31}H\textsubscript{25}N</td>
<td>90.46</td>
<td>90.10</td>
<td>6.12</td>
<td>6.02</td>
<td>3.40</td>
<td>3.40</td>
</tr>
<tr>
<td>78</td>
<td>C\textsubscript{30}H\textsubscript{24}N\textsubscript{2}</td>
<td>87.33</td>
<td>87.35</td>
<td>5.83</td>
<td>5.76</td>
<td>6.84</td>
<td>6.65</td>
</tr>
<tr>
<td>79</td>
<td>C\textsubscript{29}H\textsubscript{23}N\textsubscript{3}</td>
<td>84.26</td>
<td>84.12</td>
<td>5.57</td>
<td>5.50</td>
<td>10.17</td>
<td>10.05</td>
</tr>
<tr>
<td>80</td>
<td>C\textsubscript{28}H\textsubscript{22}N\textsubscript{4}</td>
<td>81.15</td>
<td>81.01</td>
<td>5.31</td>
<td>5.23</td>
<td>13.52</td>
<td>13.35</td>
</tr>
</tbody>
</table>
Condensation of 2-Pyridil with Dimethyl 1,3-Acetonedicarboxylate. A mixture of 2-pyridil (2.11 g, 0.01 mole) and dimethyl-1,3-acetonedicarboxylate (1.74 g, 0.01 mole) in absolute ethanol (20 ml) was cooled to 10° and a 10% solution of potassium hydroxide (5 ml) was added with stirring. After 20 hours, the crystals were collected and washed with ethanol affording 3.3 g (90%) of alcohol (83): mp 112°; nmr (CDCl₃) δ 3.3 (-OH, s, 1H), 3.75 (COOCH₃, s, 3H), 3.85 (≡C–COOCH₃, s, 3H), 3.95 (-CH, s, 1H), 6.9-7.85 (pyr–H, m, 6H), 8.1-8.45 (6-pyr–H, m, 2H); ir (CHCl₃) 3370 (-OH), 1750, 1710, 1600, 1530, and 1330 cm⁻¹.

Anal. Calcd for C₁₉H₁₆O₆N₆: C, 61.95; H, 4.35; N, 7.61. Found: C, 61.67; H, 4.10; N, 7.45.

Dimethyl 2,3,5,6-Tetraphenyl-1,4-benzenedicarboxylate (84). A mixture of 2,5-dicarbomethoxy-3,4-diphenylcyclopentadienone (3.48 g, 0.01 mole) and diphenylacetylene (4.45 g, 0.025 mole) was heated to ca. 300° using a sand bath. The mixture reacted with strong evolution of gas and crystals formed upon cooling. Trituration with acetone afforded the product which was recrystallized from absolute alcohol affording 3.24 g (65%) of 84: mp (DTA) 307°; nmr (CDCl₃) δ 3.14 (CH₃, s, 6H), 7.11 (arom–H, s, 20H); ir (CHCl₃) 1730, 1440, 1430, 1060, 930, and 670 cm⁻¹; uv (EtOH) 208 nm (85,500).


Tetramethyl 5,6-Diphenyl-1,2,3,4-benzenetetracarboxylate (85). A mixture of 2,5-dicarbomethoxy-3,4-diphenylcyclopentadienone (3.48 g, 0.01 mole) and dimethyl acetylenedicarboxylate (4.26 g, 0.03 mole) in toluene (10 ml) was refluxed for 5 hours. After cooling, petroleum ether...
A (10 ml) was added, affording 2.72 g (50%) of the crystalline tetraester 85: mp (DTA) 223° (lit. mp 223-224°); nmr (CDCl₃) δ 3.45 (CH₃, s, 6H), 3.88 (CH₃, s, 6H), 6.83-7.29 (arom-H, m, 10H); ir (CHCl₃) 1740, 1450, 1350, 1330, 1180, 1100, 930, 710, and 670 cm⁻¹; uv (EtOH) 208 nm (85,000).

Dimethyl 3,4,5,6-Tetraphenyl-1,2-benzenedicarboxylate (86).

Tetraphenylcyclopentadienone (79) was prepared by the standard procedure⁹⁵ from benzil and dibenzylketone: mp 257° (lit. mp 257-258°).

A mixture of 70 (2 g, 5.2 mmole), dimethyl acetylenedicarboxylate (1 ml), and o-dichlorobenzene (10 ml) was refluxed gently until the color changed from purple to pale tan. The solution was cooled to 100° and diluted with 95% ethyl alcohol (15 ml) affording 2.2 g (90%) of the colorless crystals of 84: mp (DTA) 258° (lit. mp 257-258°); nmr (CDCl₃) δ 3.45 (CH₃, s, 6H), 6.51-6.92 (arom-H, m, 10H), 7.07 (arom-H, s, 10H); ir (CHCl₃) 1720, 1430, 1340, 1075, 930, and 670 cm⁻¹; uv (EtOH) 208 nm (85,500).

Dimethyl 1,4-Dimethyl-5,6-diphenyl-2,3-benzenedicarboxylate (87).

A mixture of 73 (5 g, 0.018 mole) and dimethyl 1,3-acetylenedicarboxylate (15.66 g, 0.09 mole) was refluxed for 5 minutes and upon cooling, the resultant crystals were recrystallized from benzene-methanol, affording 5 g (75%) of white crystals of 87: mp 212° (lit. mp 212°); nmr (CDCl₃) δ 2.09 (CH₃, s, 6H), 3.91 (-COOCH₃, s, 6H), 6.30-7.37 (arom-H, m, 10H); ir (CHCl₃) 1710, 1430, 1325, 1100, 1060, 935, and 695 cm⁻¹.

(4SR,5SR)-4-Hydroxy-2,3,4,5-tetraphenyl-2-cyclopenten-1-one (88).

Condensation of Benzil with Dibenzylketone. To a solution of benzil (2.11 g, 0.01 mole) and dibenzylketone (2.10 g, 0.01 mole) in absolute ethanol (20 ml), a 20% solution of potassium hydroxide in 95% ethanol...
(5 ml) was added dropwise with stirring. After 15 minutes, the resultant crystals were collected and recrystallized from absolute ethanol, affording 3.5 g (90%) of alcohol mp 210° (lit. mp 208°); nmr (CDCl₃) δ 4.51 (CHCO, s, 1H), 6.75-7.49 (arom-H and -OH, m, 21H); ir (CHCl₃) 3400 (-OH), 1700 (C=O), 1430, 930, and 695 cm⁻¹.

(4SR,5SR)-4-Hydroxy-3-(2-pyridyl)-2,4,5-triphenyl-2-cyclopenten-1-one (88). Condensation of Phenyl(2-pyridyl)glyoxal with Dibenzylketone.

Similar to the published procedure for preparation of tetracyclone, a mixture of phenyl(2-pyridyl)glyoxal (2.1 g, 0.01 mole) and dibenzylketone (2.10 g, 0.01 mole) in absolute ethanol (20 ml) was heated to reflux and a 24% solution of potassium hydroxide in 95% ethanol (5 ml) was added dropwise with stirring. The reaction mixture changed to dark red. After refluxing for an additional 30 minutes, the mixture was cooled and the pale red crystals collected and recrystallized from absolute ethanol affording 2.43 g (60%) of colorless crystals of 88: mp 139-140°; nmr (CDCl₃) 64.57 (COCH, s, 1H), 6.88-7.58 (arom-H, pyr-H, and OH, m, 19H), 8.32-8.44 (6-pyr-H at C₃, d, 1H); ir (CHCl₃) 3360 (-OH), 1700 (C=O), 1595, 1430, and 930 cm⁻¹.

Anal. Calcd for C₂₈H₂₁N₀: C, 83.37; H, 5.21; N, 3.47. Found: C, 83.21; H, 5.01; N, 3.44.

(4SR,5SR)-4-Hydroxy-2-(2-pyridyl)-3,4,5-triphenyl-2-cyclopenten-1-one (90). Condensation of Benzil with 1'-Pheny1-3-(2-pyridyl)propanone.

Reaction of benzil (2.12 g, 0.01 mole) with 29 (2.7 g, 0.01 mole) by the above procedure afforded 2.35 g (83%) of 90: mp 147-148° (ethyl acetate-petroleum ether B); nmr (CDCl₃) 64.56 (COCH, s, 1H), 6.75-7.62 (arom-H, pyr-H, and -OH, m, 19H), 8.50-8.64 (6-pyr-H, m, 1H); ir (CHCl₃) 3400 (-OH), 1630 (C=O), 1600, 1414, 1160, 1075, 925, and 695 cm⁻¹.
Anal. Calcd for C\textsubscript{28}H\textsubscript{21}NO: C, 83.37; H, 5.21; N, 3.47. Found: C, 83.32; H, 5.19; N, 3.51.

(4SR,5SR)-4-Hydroxy-2,5-diphenyl-3,4-di(2-pyridyl)-2-cyclopenten-1-one (91). Condensation of 2-Pyridil with Dibenzylketone.

Reaction of 2-pyridil (2.12 g, 0.01 mole) with dibenzylketone (2.10 g, 0.01 mole) by above procedure afforded 3.23 g (80%) of 91: mp 188° (lit. mp 178-180°); nmr (CDCl\textsubscript{3}) δ 4.34 (COCH-, s, 1H), 6.55 (-OH, s, 1H), 6.87-7.82 (arom-H and pyr-H, m, 16H), 8.22-8.43 (6-pyr-H, m, 2H); ir (CHCl\textsubscript{3}) 3300 (~OH), 1700 (C=O), 1595, 1465, and 1425 cm\textsuperscript{-1}.

Anal. Calcd for C\textsubscript{27}H\textsubscript{20}N\textsubscript{2}O\textsubscript{2}: C, 80.18; H, 4.98; N, 6.93. Found: C, 80.05; H, 4.85; N, 6.73.

Condensation of Phenyl(2-pyridyl)glyoxol (40) with 1,3-Di(2-pyridyl)acetone (8).

Reaction of 40 (2.1 g, 0.01 mole) with 8 in the presence of base at reflux afforded 2.8 g (70%) of the orange crystalline (4SR,5SR)-4-hydroxy-4-phenyl-2,3,5-tri-(2-pyridyl)-2-cyclopenten-1-one (93) and/or (4SR,5SR)-4-hydroxy-3-phenyl-2,4,5-tri-(2-pyridyl)-2-cyclopenten-1-one (94) which could not be separated: mp 136-137°; nmr
Condensation of 2-Pyridil with 1,3-Di(2-pyridyl)acetone (8).

Reaction of 2-pyridil (2.12 g, 0.01 mole) with 8 (2.12 g, 0.01 mole) by the above method afforded 3.25 g (80%) of a mixture of (4SR,5SR)-4-hydroxy-2,3,4,5-tetra(2-pyridyl)-2-cyclopenten-1-one (95) and (4SR,5RS)-4-hydroxy-2,3,4,5-tetra(2-pyridyl)-2-cyclopenten-1-one (95a) in the ratio of (95:5); mp 147-148° (benzene-ethyl acetate); nmr (CDCl₃) δ 4.68 (COCH, s, ~0.95), 4.82 (COCH, s, ~0.05), 6.65-7.90 (arom-H, pyr-H, and OH, m, 13H), 8.22-8.70 (6-pyr-H, m, 4H); ir (CHCl₃) 3350 (-OH), 1700 (C=O), 1630, 1595, 1475, 1425, 1330, and 1000 cm⁻¹.

Condensation of 2-Pyridil with 1-Phenyl-3-(2-pyridyl)propanone (29). Similar condensation of 2-pyridil (2.12 g, 0.01 mole) with 29 (2.7 g, 0.01 mole) by the above method afforded an inseparable mixture of 3.2 g (80%) of (4SR,5SR)-4-hydroxy-5-phenyl-2,3,4-tri-(2-pyridyl)-2-cyclopenten-1-one (96) and (4SR,5SR)-4-hydroxy-2-phenyl-3,4,5-tri-(2-pyridyl)-2-cyclopenten-1-one (97) in the ratio of (90:10); mp 146-147° (ethanol); nmr (CDCl₃) δ 4.38 (COCH, s, 0.9H), 4.66 (COCH, s, 0.1H), 6.65-7.90 (arom-H, pyr-H, and OH, m, 15H), 8.21-8.32 (6-pyr-H, m, 1H), 8.32-8.43 (6-pyr-H, m, 1H), 8.49-8.60 (6-pyr-H, m, 1H); ir (CHCl₃) 3250 (-OH), 1700 (C=O), 1595, 1475, 1425, 1330, and 1000 cm⁻¹.

Condensation of Phenyl(2-pyridyl)glyoxal (40) with 1-Phenyl-3-(2-pyridyl)propanone (29). Condensation of 40 with 29 in 1:1 molar ratio by the above method afforded 1.2 g (30%) of an inseparable mixture of
(4SR,5SR)-4-hydroxy-3,5-diphenyl-2,4-di-(2-pyridyl)-2-cyclopenten-1-one (98), (4SR,5SR)-4-hydroxy-2,4-diphenyl-3,5-di-(2-pyridyl)-2-cyclopenten-1-one (92), and/or (4SR,5SR)-4-hydroxy-2,3-diphenyl-4,5-di-(2-pyridyl)-2-cyclopenten-1-one (100) in the ratio of (90:10): mp 148-149° (ethanol) nmr (CDCl₃)  64.28 (COCH, s, ~0.9H), 4.82 (COCH, s, ~0.1H), 6.86-7.77 (arom-H, pyr-H, and -OH, m, 17H), 8.40-8.52 (6-pyr-H, m, 1H), 8.61-8.70 (6-pyr-H, m, 1H); ir (CHCl₃) 3310 (–OH), 1700 (C=O), 1495, 1425, and 1360 cm⁻¹.

**Anal.** Calcd for C₂₇H₂₀N₂O₂:  C, 80.18; H, 4.98; N, 6.93. Found: C, 79.96; H, 4.84; N, 6.83.

2,5-Diphenyl-3,4-di(2-pyridyl)cyclopentadienone (64). Alcohol 91 (1 g, 0.0025 mole) in ethylene glycol (5 ml) was refluxed for 10 minutes. After cooling, the product was collected as dark violet crystals. Recrystallization from methanol afforded 620 mg (65%) of dienone 64: mp 200° (lit. 74 mp 200-201°); nmr (CDCl₃) 66.50-8.80 (arom-H and pyr-H, m); ir (KBr) 1720 (C=O), 1585, 1570, 1120, 1090, 995, 825, 795, 760, 755, 715, and 700 cm⁻¹; uv (MeOH) 250 nm (18,950); vis (MeOH) 493 nm (643).**Anal.** Calcd for C₂₇H₁₈N₂O:  C, 83.92; H, 4.70; N, 7.25. Found: C, 83.72; H, 4.55; N, 7.20.

2,3,4-Triphenyl-5-(2-pyridyl)cyclopentadienone (65). Alcohol 90 (1.05 g, 0.0025 mol) was suspended in ethylene-glycol (5 ml) and heated up to 200°. Upon cooling, trituration with methanol formed dark red crystals, which were collected and washed with methanol affording 500 mg (50%) of 65: mp 220-221°; nmr (CDCl₃) 66.8-7.8 (arom-H and pyr-H, m, 18H), 8.42-8.53 (6-pyr-H, m, 1H); ir (nujol) 1685 (C=O), 1290, 795, 740, 710, and 693 cm⁻¹; uv (MeOH) 290 nm (13,100) and 241 (13,900); vis (MeOH) 443 nm (12,940).
Anal. Calcd for C_{28}H_{19}NO: C, 87.25; H, 4.97; N, 3.64. Found: C, 86.99; H, 4.89; N, 3.60.

1-(2-Pyridyl)-2,3,4,5,6-pentaphenylbenzene (101). Similar to the method of Dilthey and Hurtig\(^{78}\) for the preparation of hexaphenylbenzene, a mixture of tetraphenylcyclopentadienone (79) (3.84 g, 0.01 mole) and phenyl(2-pyridyl)acetylene (5.37 g, 0.03 mole) was heated to 300° (using sand bath). Gas was evolved at the elevated temperatures, the purple color began to fade and changed to pale red in about 15 minutes. The solution was cooled to room temperature, triturated with benzene; the crystals were collected and recrystallized from dimethylformamide affording 4.28 g (80%) of 101: mp (DTA) 466°. Spectral data and analytical results are in Tables IX and V, respectively.

1,2-Di(2-pyridyl)-3,4,5,6-tetraphenylbenzene (102). A mixture of 91 (4.0 g, 0.01 mole) and diphenylacetylene (4.45 g, 0.025 mole) was heated to 350° via bunsen burner until completely melted. After cooling, the residue was triturated with benzene and the product recrystallized from dimethylformamide affording 5.09 g (95%) of 102: mp (DTA) 468°. Spectral data and analytical results are in Table IX and V, respectively.

The other hexaarylbenzenes (103-112) are prepared by this condensation procedure from the appropriate tetraarylcyclopentadienones with diarylacetylenes at elevated temperature and all recrystallized from dimethylformamide. The results are outlined in Tables III, IV, V, and IX.

Attempted Synthesis of 1,2-Di(2-pyridyl)-3-phenylpropanol (113). Method A. To a solution of phenyllithium [0.5 mole, prepared from lithium (7 g), and bromobenzene (80 g)] in ether (200 ml) 2-picoline (46.5 g, 0.5 mole) was added over 10 minutes. After refluxing for 30 minutes, the mixture was cooled to 0°, and ethyl benzoate (30 g, 0.2 mole) was
### TABLE III

**SYNTHESES OF HEXAARYLBENZENES**

\[
\text{Ar}_5 = \text{Ar}_6 = \text{ph} \ (53) \\
\text{Ar}_5 = \text{Ar}_6 = 2\text{-pyr} \ (47) \\
\text{Ar}_5 = \text{ph}; \text{Ar}_6 = 2\text{-pyr} \ (44)
\]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cyclopentenolone</th>
<th>Acetylene</th>
<th>Reaction Temp.,°C</th>
<th>% Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>70^a</td>
<td>0.01</td>
<td>44</td>
<td>0.03</td>
</tr>
<tr>
<td>102</td>
<td>91</td>
<td>0.01</td>
<td>53</td>
<td>0.025</td>
</tr>
<tr>
<td>103</td>
<td>96+97</td>
<td>0.01</td>
<td>53</td>
<td>0.03</td>
</tr>
<tr>
<td>104</td>
<td>95</td>
<td>0.01</td>
<td>53</td>
<td>0.025</td>
</tr>
<tr>
<td>105</td>
<td>95</td>
<td>0.01</td>
<td>44</td>
<td>0.03</td>
</tr>
<tr>
<td>106</td>
<td>95</td>
<td>0.01</td>
<td>47</td>
<td>0.025</td>
</tr>
<tr>
<td>107</td>
<td>92</td>
<td>0.01</td>
<td>53</td>
<td>0.03</td>
</tr>
<tr>
<td>108</td>
<td>92</td>
<td>0.01</td>
<td>44</td>
<td>0.03</td>
</tr>
<tr>
<td>109</td>
<td>91</td>
<td>0.01</td>
<td>47</td>
<td>0.02</td>
</tr>
<tr>
<td>110</td>
<td>(98+99+100)</td>
<td>0.01</td>
<td>53</td>
<td>0.03</td>
</tr>
<tr>
<td>111</td>
<td>(98+99+100)</td>
<td>0.01</td>
<td>44</td>
<td>0.025</td>
</tr>
<tr>
<td>112</td>
<td>(98+99+100)</td>
<td>0.01</td>
<td>44</td>
<td>0.02</td>
</tr>
</tbody>
</table>

^a. Dienone starting material.
<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar₁</th>
<th>Ar₂</th>
<th>Ar₃</th>
<th>Ar₄</th>
<th>Ar₅</th>
<th>Ar₆</th>
<th>mp°Cₐ</th>
</tr>
</thead>
<tbody>
<tr>
<td>71</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>465</td>
</tr>
<tr>
<td>101</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>466</td>
</tr>
<tr>
<td>102</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>468</td>
</tr>
<tr>
<td>103</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>473</td>
</tr>
<tr>
<td>104</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>479</td>
</tr>
<tr>
<td>105</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>484</td>
</tr>
<tr>
<td>106</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>486</td>
</tr>
<tr>
<td>107</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>474</td>
</tr>
<tr>
<td>108</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>470</td>
</tr>
<tr>
<td>109</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>479</td>
</tr>
<tr>
<td>110</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>476</td>
</tr>
<tr>
<td>111</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>481</td>
</tr>
<tr>
<td>112</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>479</td>
</tr>
</tbody>
</table>

a. Corrected temperature; by DTA
<table>
<thead>
<tr>
<th>Compound</th>
<th>Formula</th>
<th>Carbon Calcd</th>
<th>Carbon Found</th>
<th>Hydrogen Calcd</th>
<th>Hydrogen Found</th>
<th>Nitrogen Calcd</th>
<th>Nitrogen Found</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>C_{41}H_{29}N</td>
<td>91.96</td>
<td>91.65</td>
<td>5.41</td>
<td>5.53</td>
<td>2.61</td>
<td>2.51</td>
</tr>
<tr>
<td>102</td>
<td>C_{40}H_{28}N_2</td>
<td>89.55</td>
<td>89.24</td>
<td>5.22</td>
<td>5.15</td>
<td>5.22</td>
<td>5.20</td>
</tr>
<tr>
<td>103</td>
<td>C_{39}H_{27}N_3</td>
<td>87.15</td>
<td>87.04</td>
<td>5.03</td>
<td>5.27</td>
<td>7.82</td>
<td>7.43</td>
</tr>
<tr>
<td>104</td>
<td>C_{38}H_{26}N_4</td>
<td>84.75</td>
<td>84.65</td>
<td>4.83</td>
<td>4.63</td>
<td>10.40</td>
<td>10.16</td>
</tr>
<tr>
<td>105</td>
<td>C_{37}H_{25}N_5</td>
<td>82.37</td>
<td>82.07</td>
<td>4.63</td>
<td>4.55</td>
<td>12.91</td>
<td>12.68</td>
</tr>
<tr>
<td>106</td>
<td>C_{36}H_{24}N_6</td>
<td>80.00</td>
<td>79.96</td>
<td>4.50</td>
<td>4.25</td>
<td>15.50</td>
<td>15.48</td>
</tr>
<tr>
<td>107</td>
<td>C_{40}H_{28}N_2</td>
<td>89.55</td>
<td>89.36</td>
<td>5.22</td>
<td>5.11</td>
<td>5.22</td>
<td>5.08</td>
</tr>
<tr>
<td>108</td>
<td>C_{39}H_{27}N_3</td>
<td>87.15</td>
<td>86.93</td>
<td>5.03</td>
<td>4.93</td>
<td>7.82</td>
<td>7.63</td>
</tr>
<tr>
<td>109</td>
<td>C_{38}H_{26}N_4</td>
<td>84.75</td>
<td>84.82</td>
<td>4.83</td>
<td>4.96</td>
<td>10.40</td>
<td>10.25</td>
</tr>
<tr>
<td>110</td>
<td>C_{40}H_{28}N_2</td>
<td>89.55</td>
<td>89.21</td>
<td>5.22</td>
<td>5.16</td>
<td>5.22</td>
<td>5.22</td>
</tr>
<tr>
<td>111</td>
<td>C_{38}H_{26}N_4</td>
<td>84.75</td>
<td>84.48</td>
<td>4.83</td>
<td>4.65</td>
<td>10.40</td>
<td>10.23</td>
</tr>
<tr>
<td>112</td>
<td>C_{39}H_{27}N_3</td>
<td>87.15</td>
<td>86.90</td>
<td>5.03</td>
<td>4.88</td>
<td>7.82</td>
<td>7.76</td>
</tr>
</tbody>
</table>
added controlling the temperature between 0-5°. After stirring overnight, the mixture was refluxed for 1 hour, cooled, and poured into ice-cold 25% ammonium chloride solution (50 ml). The ether layer was separated, and the aqueous layer was extracted several times with ether. The organic extracts were dried over anhydrous sodium sulfate, concentrated, and the residue fractionally distilled affording 30 g (75%) of α-(2-pyridyl)acetophenone (26) bp 135-140° (0.1 mm), which crystallized on standing. Recrystallization from petroleum ether A gave pale yellow needle-like clusters: mp 57-58° (lit.31 mp 57-58°); picrate: mp 179-180° (lit.31 mp 179-180°); nmr (CDCl₃) (keto and enol forms) δ4.43 (pyr-CH₂, s, ~ 1H), 6.04 (vinyl H or OH, s, ~ 0.5H) 6.68-7.70 (arom-H, and -OH or vinyl-H, m, ~ 6.5H), 7.70-8.27 (o-Bz-H and 6-pyr-H, m, ~ 2.5H), 8.42-8.60 (pyr-H, m, ~ 0.5H); ir (CHCl₃) 1700, 1075, 1025, 885, 810, and 695 cm⁻¹.

Method B. To a solution of phenyllithium (0.025 mole) in ether (50 ml), 2-picoline (2.32 g, 0.025 mole) was added and then the solution was refluxed for 30 minutes. After cooling to 0°, α-(2-pyridyl)acetophenone (4.95 g, 0.025 mole) in anhydrous ether (20 ml) was added dropwise, controlling the temperature between 0-5°. Then the mixture was stirred overnight. After the above work-up procedure, only the starting material was isolated.

Method C. (By Grignard reaction).30 To a solution of 2-picolylmagnesium bromide [0.5 mole, prepared from magnesium (6 g), ethylbromide (54.5 g), and 2-picoline (50 g)] in tetrahydrofuran (100 ml), ethyl benzoate (30 g, 0.2 mole) was added dropwise controlling the temperature between 0-5°, followed by stirring overnight. The reaction mixture was poured into ice-cold 25% ammonium chloride solution (50 ml),
extracted with ether, dried over anhydrous magnesium sulfate, concentrated, and the residue fractionally distilled affording 24 g (60%) of \( \alpha-(2\text{-pyridyl})\text{acetophenone} \) \((20)\): bp 155-160\(^{\circ}\). The product solidified upon cooling: mp 57-58\(^{\circ}\) (lit.\(^{31}\) mp 57-58\(^{\circ}\)).

**Method D.** Rerun of the above reaction by Method C using dibutyl-ether instead of tetrahydrofuran as solvent also gave (60%) ketone \((20)\).

**Method E.** To a solution of 2-picolylmagnesium bromide [0.025 mole, prepared from magnesium (0.6 g), ethylbromide (2.7 g), and 2-picoline (23 g)] in tetrahydrofuran (10 ml), \( \alpha-(2\text{-pyridyl})\text{acetophenone} \) (5.0 g, 0.025 mole) was added at 0\(^{\circ}\). After the general work-up, only the starting material was isolated.

**Method F.**\(^{24}\) To a boiling solution of 2-picolyllithium [0.15 mole, prepared from lithium (3.2 g), bromobenzene (34 g), and 2-picoline (14 g)] in diethylether (200 ml), benzoylchloride (17 ml, 0.15 mole) was added dropwise. After stirring overnight at 25\(^{\circ}\), the reaction mixture was poured into ice-cold 40% solution of ammonium chloride (20 ml), extracted with ether, dried, concentrated, and the residue fractionally distilled affording 15 g (50%) of \( \alpha-(2\text{-pyridyl})\text{acetophenone} \) \((20)\): bp 140-150\(^{\circ}\) (0.2 mm).

**Method G.**\(^{26}\) To an ethereal solution of 2-picolyllithium (0.18 mole), a solution of benzonitrile (18 g, 0.18 mole) in ether (20 ml) was added dropwise at 25\(^{\circ}\). After stirring for 2 hours, water (100 ml) was added and then 2 N sulfuric acid (100 ml). The mixture was refluxed for 30 minutes, cooled, and extracted with ether. The extract was dried, concentrated, and the residue fractionally distilled affording 10.5 g (30%) of \( \alpha-(2\text{-pyridyl})\text{acetophenone} \) \((20)\): bp 140-150\(^{\circ}\) (0.2 mm).
Attempted Synthesis of 1,2,3-Tri(2-pyridyl)-2-propanol (28).

Method A. Ethyl 2-pyridinecarboxylate was prepared (53%) by standard esterification using ethanol and sulfuric acid: bp 105-110° (10 mm) [lit.24 bp 240-245° (760 mm)]; nmr (CCl₄) δ.4 (CH₃, t, 3H) 4.4 (-CH₂, q, 2H), 7.35-8.2 (arom-H, m, 3H), 8.7 (6-pyr-H, d, 1H); ir (neat) 1730, 1550, 1480, 1440, 1375, 1300, 1245, 1145, 1135, 1080, 1050, 1025, 990, 750, 710, and 685 cm⁻¹.

To an ethereal solution of 2-picolyllithium (0.25 mole), ethyl 2-pyridinecarboxylate (15 g, 0.1 mole) was added dropwise at 0°. After stirring overnight at 25°, the mixture was refluxed for 1 hour, cooled, and poured into ice-cold 40% solution of ammonium chloride (50 ml). The ether layer was separated and the aqueous layer was extracted with ether. The combined extracts were dried and distilled [bp 175-177° (1.4 mm)] affording 11 g (55%) of α-(2-picoly) 2-pyridylketone: mp 89-90° (lit.24 mp 89-90°); dipicrate mp 153° (lit.24 mp 154-155°); nmr (CDCl₃) (keto and enol forms), 64.7 (vinyl-H or OH, s, ~ 0.5H), 6.79-8.35 (arom-H, pyr-CH₂, OH or vinyl-H, m, ~ 8H), 8.43-8.68 (6-pyr-H, m, ~ 1.5H); ir (CCl₄) 1725 (weak, C=O), 1650 (enol band), 1600, 1590, 1475, 1430, 1380, and 1280 cm⁻¹.

Method B. To an ethereal solution of 2-picolyllithium (0.025 mole) at 0°, a solution of α-(2-picoly) 2-pyridylketone (5 g, 0.025 mole) in ether (10 ml) was added dropwise. The mixture was stirred overnight, and after the general work-up as mentioned above, only the starting material was isolated.

Method C. (Grignard reaction).30 To a solution of 2-picolylmagnesium bromide (0.5 mole) in dibutylether (100 ml), ethyl 2-pyridinecarboxylate (30 g, 0.2 mole) was added dropwise at 0°. After stirring
overnight at 25°, the mixture was poured into ice-cold 40% ammonium chloride solution, extracted with ether, dried, concentrated, and the residue fractionally distilled [bp 149-150° (1.2 mm)] affording 12 g (30%) of ketone (26), which was crystallized from petroleum ether A: mp 89-90° (lit. 24 mp 89-90°).

**Method D.** To a solution of 2-picoly lmagnesium bromide (0.025 mole) in dibutylether (10 ml), a solution of α-(2-picolyl) 2-pyridylketone (5 g, 0.025 mole) was added at 0°. After stirring overnight at 25° the reaction was worked up as described above affording only the starting material.

**Method E.** To an ethereal solution of 2-picolyllithium (0.12 mole) a solution of picolinonitrile (12 g, 0.115 mole) in ether (20 ml) was added at 25°. After stirring for 1 hour, the reaction mixture was cautiously poured into 2 N hydrochloric acid solution. The aqueous layer was separated, refluxed for 1.5 hours, cooled, neutralized, and extracted with ether. The ether extract was dried, concentrated in vacuo, and the residue fractionally distilled [bp 175-177° (1.4 mm)] affording 4.7 g (20%) of ketone 20, which was crystallized from petroleum ether A: mp 89-90° (lit. 26 mp 89-90°).

**Attempted Synthesis of Di(2-pyridyl)cyclopropenone (114).**

**Method A.** To a solution of 1,3-di(2-pyridyl)acetone (2.12 g, 0.01 mole) in glacial acetic acid (10 ml), a solution of bromine (3.2 g, 0.02 mole) in acetic acid (10 ml) was added dropwise at 25°. After the addition was complete, the reaction mixture was stirred for an additional 5 minutes, and then poured into water (25 ml). The solution was decolorized by adding solid sodium sulfite and cooled. Since no precipitate was formed, the mixture was extracted with chloroform and the extract concentrated affording the starting ketone.
Method B. To a stirred solution of 1,3-di(2-pyridyl)acetone (2.12 g, 0.01 mole) in dichloromethane (10 ml), a solution of bromine (3.2 g, 0.02 mole) in dichloromethane (10 ml) and triethylamine (5 ml) in dichloromethane (10 ml), was added simultaneously at 25° with stirring. After an additional 30 minutes the mixture was extracted with 6 N hydrochloric acid solution. This extract was neutralized with solid sodium bicarbonate, extracted with chloroform, and concentrated in vacuo giving the starting ketone.

Method C. Rerun of the reaction by Method B using N-ethyldiisopropylamine instead of triethylamine also gave the unreacted starting material.

Method D. To a mixture of di(2-pyridyl)acetylene (1.63 g, 77 mmole) and potassium tert-butoxide (3.36 g, 300 mmole) in anhydrous hexane (15 ml), dry bromoform (2.53 g, 100 mmole) was added at 0°. After stirring for 30 minutes at 25°, the reaction mixture was poured into water (25 ml), and extracted with benzene. The benzene-hexane solution was washed with water, dried, and concentrated in vacuo affording the initial acetylene.

Method E. A rerun of the reaction by Method D at 25° instead of 0° afforded the starting material.

Method F. To a mixture of di(2-pyridyl)acetylene (1.08 g, 60 mmole) and potassium tert-butoxide (0.54 g, 50 mmole) in dry hexane (10 ml), dry chloroform (0.18 g, 150 mmole) in hexane (2 ml) was added dropwise at 0°. After stirring for 30 minutes at 25°, the reaction mixture was worked up as described in method D giving the starting acetylene.
Attempted synthesis of phenyl (2-pyridyl)cyclopropenone (115) using 29 by methods A-C or by using phenyl(2-pyridyl)acetylene (44) by methods D-F was also unsuccessful.
The major objective of this project is the construction of aryl- and heteroarylbenzenes, specifically the 2-pyridyl substituent, by the Diels-Alder condensation of appropriately substituted cyclopentenolones with diarylacetylenes. Structural elucidation of the various substituted cyclopentenolones is considered; the synthetic aspects have been divided into sections to simplify the presentation.

1. Preparation of Starting Materials

a. Preparation of Aryl- and Heteroarylacetones

The initially designed plan for synthesizing 1,3-di(2-pyridyl)-acetone (8) is depicted in Scheme XII. Ethyl 2-pyridylacetate (5) was initially prepared by the reaction of 2-picoline (6) with sodium hydride and diethyl carbonate, affording 5 in 20% yield. Improved yield (30%) of 5 was obtained by direct carboethoxylation of 2-picollyllithium (7) (prepared from lithium, bromobenzene, and 2-picoline) with diethyl carbonate. Condensation of 5 with 7 afforded ketone 8 in 32% yield. Later, improved yields (60%) of 8 could be realized by reaction of 7 with 2-pyridylacetetonitrile (13), which was obtained in 37% overall yield via a four-step sequence: (1) esterification of acid 2, (2) reduction of ethyl 2-pyridylcarboxylate (10) with lithium aluminum hydride, (3) conversion to the chloride salt 12 by treatment of 11 with thionyl chloride, and (4) subsequent reaction of 12 with potassium cyanide in 60% ethanol (Scheme II). 2-Chloromethylpyridine (16) as the free base was later synthesized more conveniently in a one-step reaction of 2-picoline-N-oxide (14) with
Scheme XII

\[
\text{PhLi} \quad \rightarrow \quad \text{COOEt} \quad \rightarrow \quad \text{NaH, EtOCHO, EtOCHOEt} \quad \rightarrow \quad \text{CHClLi} \quad \rightarrow \quad \text{CN} \quad \rightarrow \quad \text{KCN, DMSO, 20°} \quad \rightarrow \quad \text{C}_6\text{H}_5\text{SO}_2Cl \quad \rightarrow \quad \text{H}_2\text{O}_2, \text{HOAc} \quad \rightarrow \quad \text{16} \quad \rightarrow \quad \text{14} \quad \rightarrow \quad \text{16} \quad \rightarrow \quad \text{14} \quad \rightarrow \quad \text{16}
\]
benzenesulfonfyl chloride in benzene. Improved yield (80%) of 13 was afforded by carrying the reaction of 16 with potassium cyanide in dimethylsulfoxide at 20° with external cooling instead of the reported yield at 40° (34%). Acylation of 7 with 13 was carried out by slight modification of the literature procedure. After a detailed study of the conditions necessary to maximize the yield, it was found that first carrying the reaction overnight at 25° and then refluxing, instead of directly refluxing after mixing the reagents, increased the yield of 8 from 44% to 60%. Ketone 8 was found to exist in carbon tetrachloride solution largely in the enol form, as evidenced by a strong enol band at 1640 cm⁻¹ and only a weak absorption at 1720 cm⁻¹, characteristic of the carbonyl group. Exact equilibrium values were obtained from nmr data, which exhibited singlets at 5.25 and 3.6 for the enol vinylic and methylene hydrogens, respectively. Absorption at 63.86 corresponds to the methylene hydrogens of the keto form. Thus, 8 is in the enol form 8b to the extent of approximately 60%.

3-(2-Pyridyl)-1-phenylpropanone-2 (29) was synthesized in 33%
yield by similar acylation of 7 with phenyl acetonitrile. Ketone 29 exists in about 22% as enol, as evidenced by ir and nmr data. The ir spectrum of 29 exhibited an enol band at 1650 cm\(^{-1}\) as well as a strong absorption at 1720 cm\(^{-1}\), characteristic of the isolated carbonyl group. The nmr spectrum showed absorptions at δ3.56 and 5.25 for the enol methylene and vinyl hydrogens, respectively; whereas, the methylene hydrogens of the keto form appeared as singlets at δ3.79 and 3.90.

Along this line, acylation of 7 was carried out with either ethyl benzoate, benzoyl chloride, or benzonitrile to see if any

\[
\begin{align*}
\text{CHLi} & \quad \text{COOEt} \\
\text{\text{7} \quad \text{\text{113}}} \\
\end{align*}
\]

1,3-di(2-pyridyl)-2-phenyl-2-propanol (113) was formed as a secondary product, along with \(\alpha\)-(2-pyridyl)acetophenone (20). However, in each case, the ketone 20 was isolated exclusively! Similar reaction of 7 with ethyl 2-pyridylcarboxylate or 2-picolinonitrile also afforded only 2-picolyl 2-pyridylketone (26). Acylation of 2-picolylmagnesium bromide
(obtained by the reaction of phenylmagnesium bromide with 2-picoline) with ethyl benzoate and ethyl 2-pyridylcarboxylate also afforded exclusively the ketones 20 and 26, respectively. Attempts to react 20 and 26 with $\mathcal{L}$ or 27 resulted in the isolation of the initial ketones! Thus, it was not possible to prepare the $\mathcal{L}$-carbinols ($28$ and 113) by any of the above methods. Goldberg and Levine\textsuperscript{7} have reported the reaction of $\mathcal{L}$ with numerous esters, both aromatic and aliphatic, and have proposed a mechanism for these acylations, depicted in Scheme XIII. According to
Scheme XIII

\[
\text{Path a: } \quad \text{PyCH}_2\text{Li}^{+} + \text{RCOOR'} \rightarrow \text{PyCH}_2\text{OR'} + \sigma + \text{LiOR'}
\]

\[
\text{Path b: } \quad \text{PyCH}_2\text{Li}^{+} + \text{RCOOR'} \rightarrow \text{PyCH}_2\text{LiOR'} + \text{LiOR'}
\]
those authors, adduct A is the primary acylation product of \( \mathcal{Z} \) with carboxylic acid esters. Reaction of anion \( \mathcal{Z} \) can proceed in two ways: (1) elimination of alcohol resulting in the formation of the enol B (via path a), and (2) nucleophilic substitution by the anion of \( \mathcal{Z} \) forming carbinol C (via path b). The keto-carbinol ratio is strongly influenced by steric factors. Steric hinderance on the \( \beta \)-carbon atom impeded nucleophilic substitution (path b) and thus changes the ratio in favor of ketone. In support of this mechanism, they found that when 2-picolyllithium (7) was acylated with aliphatic esters, mixtures of ketones and carbinols were obtained but with aromatic or heterocyclic esters, only ketones were formed. The data from our experiments substantiate their results, as no carbinols were isolated with either aromatic or heterocyclic esters. Another alternative explanation is that even if \( \text{t-carbinol} \) is formed it may be decomposing rapidly to decrease the crowding around \( \beta \)-carbon by a concerted fragmentation in workup to regenerate the intermediate ketone and 2-picoline.
b. Preparation of Phenyl(2-pyridyl)glyoxal

Oxidation of 2-stilbazole (31) with selenium dioxide afforded phenyl(2-pyridyl)glyoxal (40) in 31% yield, along with 8% of 2-α-pyridylselenonaphthene (43). The nmr spectrum of 43 exhibited a broad multiplet between δ 6.95-8.05 for the aromatic and pyridyl hydrogens, in which the vinylic hydrogen resonance was superimposed. The unique 6-pyridyl hydrogen showed resonance at δ 8.05.

\[ \text{31} \xrightarrow{\text{SeO}_2} \text{40} + \text{43} \]

\[ \begin{array}{c}
\text{N} \\
\text{C} \\
\text{Se} \\
\text{C} \\
\text{N}
\end{array} \]

\[ \begin{array}{c}
\text{N} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{N}
\end{array} \]

\[ \begin{array}{c}
\text{N} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{N}
\end{array} \]

\[ \begin{array}{c}
\text{N} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{N}
\end{array} \]

\[ \begin{array}{c}
\text{N} \\
\text{C} \\
\text{C} \\
\text{C} \\
\text{N}
\end{array} \]

c. Preparation of Aryl- and Heteroarylacetylenes

Phenyl (2-pyridyl)acetylene (44) was synthesized (56%) from 2-stilbazone (31) by: (1) bromination with bromine in carboxodisulfide,

\[ \text{31} \xrightarrow{\text{Br}_2} \text{44} \]

\[ \begin{array}{c}
\text{N} \\
\text{C} \\
\text{Br} \\
\text{H} \\
\text{Br}
\end{array} \]

\[ \text{KOH} \]

\[ \text{EtOH} \]

\[ \text{44} \]

then (2) didehydrobromination by refluxing the intermediate dibromide with ethanolic potassium hydroxide. Acetylene 44 was obtained (88%) by an alternate method via coupling of phenylacetylene (45) with 2-iodopyridine (46) in the presence of copper powder.
Di(2-pyridyl)acetylene (47) was similarly prepared (Scheme VII) from 1,2-di(2-pyridyl)ethene (37) by bromination with bromine in glacial acetic acid to form the dibromide and then didehydrobromination of the dibromide with refluxing ethanolic potassium hydroxide in 43% overall yield. More conveniently, 47 was obtained in 90% yield by pyrolysis of 1,1'-dipyridotriazole (49) which was obtained in 52% yield from the reaction of 2-pyridil (48) with p-toluenesulfonylhydrazine.

2. Attempted Synthesis of Di(2-pyridyl)cyclopropenone and Phenyl(2-pyridyl)cyclopropenone

Attempts were made to synthesize di(2-pyridyl)cyclopropenone (114) and phenyl(2-pyridyl)cyclopropenone (115), in which, the cis configuration of the two aryl groups is rigidly constructed. These compounds should exhibit a marked similarity to the platínocycle 116, whose cobalt complex 117 shows spectacular biological properties.
Similar to the synthesis of diphenylcyclopropenone (52) by Breslow and Posner, the initially designed plan for construction of 114 and 115 would involve the bromination of 8 and 29, respectively, followed by

\[
\begin{align*}
&P\text{y} - \text{C} = \text{C} - \text{Ar} + \text{Br}_2 \rightarrow &\text{Py} - \text{C} = \text{C} - \text{Ar} + 2\text{Br}^- \\
&8(\text{Ar} = 2\text{-Py}) & 114(\text{Ar} = 2\text{-Py}) \\
&29(\text{Ar} = \text{Ph}) & 115(\text{Ar} = \text{Ph})
\end{align*}
\]

didehydrobromination of the resultant dibromide intermediates. Attempts to brominate 8 or 29 with bromine in glacial acetic acid at 25° resulted in the isolation of the starting materials. Bromination of 8 or 29 at 50° resulted in intractable tars. Reactions of either 8 or 29 with simultaneous addition of bromine in glacial acetic acid and triethylamine or N-ethyl-diisopropylamine also returned the starting materials.

Another route was envisioned involving carbene addition to acetylenes 44 or 47. Kursanov and Vol'pin have reported that the reaction of dihalocarbenes with a disubstituted acetylene leads, after hydrolysis, to disubstituted cyclopropenone. Treatment of 47 with

\[
\text{Py} - \text{C} = \text{C} - \text{Ar} + \text{CCl}_2 + \text{Br}_2 \rightarrow \text{N. R.}
\]

44(\text{Ar} = \text{Ph}),
47(\text{Ar} = \text{Py})

dibromocarbene and dichlorocarbene (obtained by reaction of potassium tert-butoxide with bromoform and chloroform, respectively) in hexane at 0° and at 25° resulted in the isolation of the starting material. Similar
attempts to react 44 with dichlorocarbene or dibromocarbene were also fruitless.

3. Preparation of Cyclopentenolones and Cyclopentadienones

Cyclopentenolones, in general, were synthesized by base catalyzed condensation of the appropriate ketone with aryl- or heteroaryl α-diketones. Thus, 72 was obtained by reaction of benzil (42) with 3-pentanone in the presence of ethanolic potassium hydroxide at 25°. Treatment of 72 with acetic anhydride and concentrated sulfuric acid afforded the dienone 73. Similar reaction of 2-pyridil (48) with 3-pentanone afforded 74 in 60% yield. In the presence of excess of water, diol 75 was also isolated, which must have formed by addition of water to the double bond of 74. The ir spectrum of 74 exhibited absorption at 1725 cm\(^{-1}\), characteristic of the conjugated carbonyl group and absorption at 3450 cm\(^{-1}\) confirming the presence of the hydroxyl group. Since
the steric interference of the methyl group with the pyridyl moiety would be far more severe than interference of methyl and hydroxyl groups, the configuration of the product must have the methyl and pyridyl groups in trans orientation. The nmr spectrum of 74 showed absorption for methyl group coupled to the C5 proton as a doublet at δ1.26 (J = 7 Hz) and an allylic methyl group as a singlet at δ2.06. The single proton strongly coupled to the methyl showed absorption at δ2.76 as a quartet (J = 7 Hz). The ir spectrum of 75 exhibited absorptions at 3500 cm⁻¹ for the hydroxyl group and the carbonyl group absorption appeared at 1750 cm⁻¹. The nmr spectrum of 75 showed the methyl proton strongly coupled to the hydrogens at δ0.95 as doublet (J = 7 Hz) and the C2 and C5 protons appeared as a quartet at δ2.2 (J = 7 Hz). The hydroxyl protons, exchangeable with D₂O showed absorption at δ7.17. The relatively narrow chemical shift range (δ7.5-8.2) of the aromatic protons multiplet indicates that the two pyridyl groups have a trans-arrangement. This conclusion is further supported by the presence of the single methyl proton doublet signal at δ0.95 (J = 7 Hz); i.e., the doublets of the secondary methyl groups must coincide, in accord with the all trans structure 75.

Condensation of benzil (42) with dimethyl 1,3-acetonedicarboxylate in the presence of base afforded 81, which upon reaction with acetic anhydride and concentrated sulfuric acid formed dienone 82. The ir
spectrum of 81 exhibited absorptions at 3400 cm\(^{-1}\) for the hydroxyl group and at 1735 cm\(^{-1}\) for the carbonyl group of carbomethoxy group and absorption at 1705 cm\(^{-1}\) corresponding to the conjugated carbonyl group. The nmr spectrum of 81 showed absorption at \(\delta 3.75\) for the methyl protons of the carbomethoxy group and a singlet at \(\delta 3.85\) for the C\(_5\) proton. The hydroxyl hydrogen absorption appeared at \(\delta 3.18\) and was exchangeable in D\(_2\)O. The ir spectrum of 82 had absorptions at 1720 and 1610 cm\(^{-1}\) for the ester carbonyl and the conjugated ring carbonyl, respectively. The nmr spectrum of 82 had a six-proton singlet at \(\delta 3.75\) for the carbomethoxy groups, whereas the aromatic protons appeared between \(\delta 6.8-7.5\). Similar reaction of dimethyl 1,3-acetonedicarboxylate with 2-pyridil (48) in the presence of ethanolic potassium hydroxide gave 83 in 90% yield. The ir spectrum of 83 exhibited absorptions at 3370 cm\(^{-1}\) for the hydroxyl group, 1750 cm\(^{-1}\) for the carbomethoxy groups, and 1710 cm\(^{-1}\) for the conjugated ring carbonyl group. The nmr spectrum showed singlets for the C\(_5\) and C\(_2\) methyl absorptions at \(\delta 3.75\) and 3.85, respectively, and a one-proton singlet at \(\delta 3.95\) for the C\(_5\) hydrogen. The hydroxyl proton absorption appeared at \(\delta 3.3\) and was readily exchanged with D\(_2\)O.

Tetraphenylcyclopentenolone 88 was synthesized by similar condensation of benzil (42) with dibenzylketone (63) in the presence of
ethanolic potassium hydroxide at 25°. Condensation of 2-pyridil (48) with dibenzylketone (63) in the presence of ethanolic potassium hydroxide at 78° afforded 91. All the other cyclopentenolones (89, 90, 92-100) were obtained by a similar condensation reaction of the appropriate α-diketone with a disubstituted acetone (Scheme XIV). The structures of these compounds were determined using nmr spectroscopy. In several of these reactions, mixtures of isomers are possible; but, since the steric interference of the C₄ and C₅ aryl groups would be more severe than the C₅ aryl-hydroxyl group interaction, the isomer with the C₄ and C₅ aryl groups in trans configuration would be favored. In fact, the reaction showed strong stereoselectivity and one isomer was formed either solely or at least predominantly. In cases where mixtures were formed, the isomers were inseparable and behaved as a single, pure compound under all chromatographic (tlc in 20 solvent systems) techniques as well as numerous fractional crystallization (with six different solvent systems) experiments. The presence of isomers was detected from nmr spectral data. (Table VI).
**TABLE VI**

**TETRAARYL- AND HETEROARYL-CYCLOPENTENOLONES**

![Structures of trans and cis isomers]

<table>
<thead>
<tr>
<th>Compound</th>
<th>Ar&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Ar&lt;sup&gt;2&lt;/sup&gt;</th>
<th>Ar&lt;sup&gt;3&lt;/sup&gt;</th>
<th>Ar&lt;sup&gt;4&lt;/sup&gt;</th>
<th>mp, °C (Solvent)</th>
<th>% Yield</th>
<th>% Ratio of Mixture</th>
<th>Nmr, δ (PPM)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Ir&lt;sub&gt;21b&lt;/sub&gt; cm&lt;sup&gt;-1&lt;/sup&gt;</th>
<th>C=O</th>
</tr>
</thead>
<tbody>
<tr>
<td>88</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>210(EtOH)</td>
<td>50</td>
<td>---</td>
<td>4.51</td>
<td>1700</td>
<td></td>
</tr>
<tr>
<td>89</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>139-140(EtOH)</td>
<td>60</td>
<td>---</td>
<td>4.57 8.37</td>
<td>1700</td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>ph</td>
<td>147-148(EtOAc-Pet.ether)</td>
<td>83</td>
<td>---</td>
<td>4.56 8.60</td>
<td>1630</td>
<td></td>
</tr>
<tr>
<td>91</td>
<td>ph</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>188(ØH-EtOH)</td>
<td>80</td>
<td>---</td>
<td>4.34 8.28 8.36</td>
<td>1700</td>
<td></td>
</tr>
<tr>
<td>92</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>2-pyr</td>
<td>170(EtOAc)</td>
<td>80</td>
<td>---</td>
<td>4.73 8.49 8.62</td>
<td>1660</td>
<td></td>
</tr>
<tr>
<td>93</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>136-137(EtOH)</td>
<td>70</td>
<td>---</td>
<td>4.74 c</td>
<td>1725</td>
<td></td>
</tr>
<tr>
<td>94</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>147-148(ØH-EtOAc)</td>
<td>80</td>
<td>95</td>
<td>4.68 8.32 8.42 8.50 8.66</td>
<td>1700(s) 1630(w)</td>
<td></td>
</tr>
<tr>
<td>95</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>147-148(ØH-EtOAc)</td>
<td>80</td>
<td>5</td>
<td>4.82 8.32 8.42 8.50 8.66</td>
<td>1700(s) 1630(w)</td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
<table>
<thead>
<tr>
<th>96</th>
<th>2-pyr</th>
<th>2-pyr</th>
<th>2-pyr</th>
<th>ph</th>
<th>146-147(EtOH)</th>
<th>80</th>
<th>90</th>
<th>4.38</th>
<th>8.26</th>
<th>8.38</th>
<th>8.60</th>
<th>1700</th>
</tr>
</thead>
<tbody>
<tr>
<td>97</td>
<td>ph</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td></td>
<td></td>
<td>10</td>
<td>4.66</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>98</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>148-149(EtOH)</td>
<td>30</td>
<td>90</td>
<td>4.27</td>
<td>8.46</td>
<td></td>
<td></td>
<td>8.66</td>
</tr>
<tr>
<td>99</td>
<td>ph</td>
<td>2-pyr</td>
<td>ph</td>
<td>2-pyr</td>
<td>148-149(EtOH)</td>
<td>30</td>
<td>10</td>
<td>4.82</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>2-pyr</td>
<td>2-pyr</td>
<td>ph</td>
<td>ph</td>
<td>148-149(EtOH)</td>
<td>30</td>
<td>10</td>
<td>4.82</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. In deuteriochloroform, ca 10% wt/vol.

b. In chloroform.

c. Broad overlapping multiplet of 3 hydrogens between 8.24-8.69.
The nmr spectrum of \( \mathcal{88} \) exhibited an absorption as a singlet at \( \delta_{4.51} \) for the \( \text{C}_5 \) benzylic hydrogen, and a broad aromatic region between \( \delta_{6.75}-7.49 \) under which the hydroxyl hydrogen resonance was hidden. The ir spectrum of \( \mathcal{88} \) had absorptions at \( 3400 \text{ cm}^{-1} \) for the hydroxyl group and \( 1700 \text{ cm}^{-1} \) for the conjugated ring carbonyl group. Condensation of \( \mathcal{40} \) with dibenzylketone (63) afforded \( \mathcal{89} \), which is confirmed to be a single isomer as shown from its spectral data. In the nmr spectrum of \( \mathcal{89} \), the benzylic proton is a singlet at \( \delta_{4.57} \) and the 6-pyridyl hydrogen absorption is a typical broad doublet at \( \delta_{8.37} \). The similarity of the chemical shifts between benzylic hydrogen in both \( \mathcal{89} \) and \( \mathcal{88} \) suggest that they are structurally similar and that the product of this condensation has structure \( \mathcal{89} \) (\( \text{Ph-C-C-H} \)) and not \( \mathcal{89a} \) (\( \text{pyr-C-C-H} \)). The ir spectrum of \( \mathcal{89} \) exhibited absorptions at \( 3360 \text{ cm}^{-1} \) for the hydroxyl group and \( 1700 \text{ cm}^{-1} \) for the conjugated ring carbonyl group. Similarly, condensation of benzil (42) with \( \mathcal{29} \) can form either \( \mathcal{90} \) and/or \( \mathcal{90a} \). The nmr spectrum, however, indicated that the product is solely \( \mathcal{90} \) as confirmed by the absorption for the \( \text{C}_5 \) proton at \( \delta_{4.56} \) suggesting it to be a benzylic proton, as in \( \mathcal{88} \) and \( \mathcal{89} \). The \( \text{C}_2 \) 6-pyridyl hydrogen absorption appeared at \( \delta_{8.60} \). The ir spectrum of \( \mathcal{90} \) had absorption at \( 1630 \text{ cm}^{-1} \) characteristic of the unsaturated carbonyl function. Reaction of \( \mathcal{48} \) with dibenzylketone (63) afforded \( \mathcal{91} \) as a single isomer, as indicated by nmr data. The \( \text{C}_5 \) proton
showed a singlet at $\delta 4.34$ and the C$_3$ and C$_4$ 6-pyridyl hydrogens appeared at $\delta 8.28$ and 8.36, respectively. The carbonyl absorption of 91 is seen at 1700 cm$^{-1}$. Reaction of 42 with 8 formed 92 also as a single isomer. In this case, the nmr spectrum showed the C$_5$ proton absorption as a singlet at $\delta 4.73$ and the C$_5$ and C$_2$ 6-pyridyl hydrogens exhibited resonances at $\delta 8.49$ and 8.62, respectively. Reaction of 40 with 8 afforded a product whose nmr spectrum showed the C$_5$ proton absorption at $\delta 4.74$ and the 6-pyridyl protons appeared as broad overlapping three-proton multiplet between $\delta 8.24$-8.69. Therefore, it was not possible to distinguish between structures 93 and 94 or possibly a mixture; fortuitously this mixture afforded a single dienone, 94a. Reaction of 48 with 8 afforded a product whose nmr spectrum showed single proton absorptions at $\delta 4.68$ and 4.82, indicating that this reaction product was a mixture of both the cis (95a) and trans (95) isomers. The proton, shielded by the C$_4$ pyridyl substituent in trans isomer (95) appeared at $\delta 4.68$, whereas the less shielded C$_4$ proton in the cis isomer (95a) appeared at $\delta 4.82$. The C$_3$, C$_4$, C$_5$, and C$_6$ pyridyl protons exhibited absorptions at $\delta 8.32$, 8.42, 8.50, and 8.66, respectively. The nmr integration showed that the product is a mixture of trans and cis isomers in the ratio of 95:5, respectively. Condensation of 48 with 29 afforded a reaction mixture whose nmr spectrum showed single proton absorptions at $\delta 4.38$ and 4.66, indicating that the reaction product was a mixture of 96 ($-C-CH-ph$) and 97 ($C-CH-py$). The benzylic proton of 96 appeared at $\delta 4.38$ and the C$_5$ proton of 97 appeared at $\delta 4.66$. The C$_3$, C$_4$, and C$_2$ 6-pyridyl hydrogens appeared at $\delta 8.26$, 8.38, and 8.60, respectively. The nmr integration showed that the mixture of 96 and 97 is present in the ratio of 90:10, respectively. Condensation of 40 with 29 can theoretically form four products, 98, 99, 100.
and 100a. The nmr spectrum of the product, however, showed absorption for
the single C₅ proton at δ4.27 and 4.82, which indicates the presence of
the isomers 98, along with 99 and/or 100 in the ratio of 90:10, respect-
atively. The C₄ and C₂ 6-pyridyl hydrogens appeared at δ8.46 and 8.66, 
respectively.

From the results of the nmr data of these tetraaryl- and hetero-
arylcyclopentenolones, some generalizations can be drawn about the chemical
shift of the C₅ hydrogen singlet, since its position is so dependent upon
the type of aryl groups at C₄ and C₅ of the five-membered ring. When
there are phenyl groups at both of these positions, the proton singlet
lies in the region δ4.51-4.57. If there is a C₄ 2-pyridyl group and a
C₅ phenyl group, the benzylic proton singlet is shifted to the high field
region between δ4.2-4.40. When there is a C₅ 2-pyridyl group and a C₄
phenyl group, or if there are 2-pyridyl groups at both C₄ and C₅, the
proton absorption lies in the region between δ4.7-4.82. In the last two
cases, the proton absorption lies in the same region probably because of
hydrogen bonding between the C₄ hydroxyl group and the nitrogen of the
C₅ 2-pyridyl group.

In all these compounds, the general order of observed product
preference is as follows:
The position of 6-pyridyl hydrogen absorption also depends, albeit to a lesser extent, upon the position of the pyridyl group on the five-membered ring. If the pyridyl moiety is at C4, its 6-pyridyl hydrogen absorption is in the region between δ8.32-8.53. This position is shifted to δ8.42-8.55 for the C5 pyridyl group. But the 6-pyridyl hydrogen is exhibited at δ8.50-8.73, if the pyridyl group is at C2 and at δ8.2-8.45 for the C3 pyridyl group. The considerable upfield absorption in the last case is due probably to the conjugation of the C3 pyridine group with the α,β-unsaturated ring carbonyl moiety.

Dehydration of the cyclopentenolones does not occur readily under either acidic or basic conditions, since attempted dehydration of these compounds with numerous dehydrating agents (such as, hot dilute sulfuric acid, ethanol and sulfuric acid, acetic anhydride and concentrated sulfuric acid, acetic acid and sodium acetate, p-toluenesulfonic acid in benzene, potassium t-butoxide in t-butyl alcohol, or phosphorous tetraiodide in pyridine) and under various conditions resulted in the isolation of the starting materials. Only compounds 88, 90, and 91 could be dehydrated by heating with ethylene glycol or hexamethy phosphoric triamide (HMPTA) affording the dienones 70, 65, and 64, respectively. All the others are resistant towards dehydration or possibly if elimination did occur, water is re-added across the α,β-unsaturated carbonyl moiety under the standard workup conditions.
4. Preparation of Aryl- and Heteroarylbenzenes

A series of 1,4-dimethyl-2,3,5,6-tetraaryl- and heteroarylbenzenes (76-80) were synthesized by the Diels-Alder condensation of the cyclopentenolones 72 and 74 with the appropriate diarylacetylenes (44, 47, and 53) as depicted in Table I. All these substituted benzenes are colorless, high melting solids with similar electronic spectra (Table VII). The chemical shift for the methyl singlet in all these compounds is practically the same (δ 3.81-3.88). The uv spectra of these compounds showed broad absorption bands showing only one maximum completely without fine structure suggesting that free rotation of the substituents is occurring about the connecting bonds around the ring and that the molecules are non-rigid.102
<table>
<thead>
<tr>
<th>Compound</th>
<th>mp,°(C)</th>
<th>ir, cm⁻¹</th>
<th>uv λ_max nm(ε, x10⁻³)</th>
<th>CH₃(s)</th>
<th>nmr δ (PPM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Arom and Pyr-H(m)</td>
</tr>
<tr>
<td>76</td>
<td>362</td>
<td>1595, 775, 740, and 692</td>
<td>234(59.5)</td>
<td>3.81</td>
<td>6.92-7.15</td>
</tr>
<tr>
<td>77</td>
<td>359</td>
<td>1580, 1555, 975, 745, and 695</td>
<td>231(51.0)</td>
<td>3.82</td>
<td>6.78-7.24</td>
</tr>
<tr>
<td>78</td>
<td>345</td>
<td>1595, 995, 790, 745, and 695</td>
<td>225(35.0)</td>
<td>3.84</td>
<td>6.77-7.14</td>
</tr>
<tr>
<td>79</td>
<td>353</td>
<td>1575, 1550, 1140, 990, 750, &amp; 715</td>
<td>235(48.5)</td>
<td>3.85</td>
<td>6.82-7.18</td>
</tr>
<tr>
<td>80</td>
<td>391</td>
<td>1595, 995, 800, 770, 745, &amp; 735</td>
<td>221(36.0)</td>
<td>3.88</td>
<td>6.84-7.18</td>
</tr>
</tbody>
</table>

a. Corrected temperature; by DTA.

b. In nujol.

c. In 1,2-dichloroethane.

d. In hexachloro-1,3-butadiene at 110° with hexamethyilsilane as reference.
Diels-Alder condensation of \( \text{81} \) with diphenylacetylene \( (53) \) afforded \( \text{84} \) in 65% yield. Similar reaction of \( \text{81} \) with dimethyl acetylenecarboxylate gave \( \text{85} \) in 59% yield. Condensation of \( \text{88} \) with dimethyl acetylenedicarboxylate formed \( \text{86} \), whereas reaction of \( \text{72} \) with dimethyl acetylenedicarboxylate afforded \( \text{87} \) in 75% yield. The spectral data are in Table VIII. One generalization which can be drawn from the nmr spectra of these compounds is that when the substituents (R groups) are hydrogen, as in the case of \( \text{o-terphenyl (118)} \), the protons of ortho
<table>
<thead>
<tr>
<th>Compound</th>
<th>R₁</th>
<th>R₂</th>
<th>R₃</th>
<th>R₄</th>
<th>nmr δ(PPM)ᵃ (arom)</th>
<th>λ uv nm(ex10⁻³)ᵇ</th>
</tr>
</thead>
<tbody>
<tr>
<td>118</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>H</td>
<td>7.11(s,10H), 7.3(s,4H)</td>
<td>232(85.0)</td>
</tr>
<tr>
<td>84</td>
<td>COOCH₃</td>
<td>Ph</td>
<td>Ph</td>
<td>COOCH₃</td>
<td>7.11(s,20H)</td>
<td>203(59.5)</td>
</tr>
<tr>
<td>85</td>
<td>COOCH₃</td>
<td>COOCH₃</td>
<td>COOCH₃</td>
<td>COOCH₃</td>
<td>6.83-7.29(m, 10H)</td>
<td>208(85.0)</td>
</tr>
<tr>
<td>86</td>
<td>Ph</td>
<td>COOCH₃</td>
<td>COOCH₃</td>
<td>Ph</td>
<td>6.51-6.92(m, 10H), 7.07(s, 10H)</td>
<td>208(85.5)</td>
</tr>
<tr>
<td>87</td>
<td>CH₃</td>
<td>COOCH₃</td>
<td>COOCH₃</td>
<td>CH₃</td>
<td>6.30-7.37(m, 10H)</td>
<td>235(65.5)</td>
</tr>
</tbody>
</table>

a. Deuteriochloroform solvent, ca. 10% wt/vol.
b. In absolute ethanol.
phenyl groups appear as a singlet; but if the R groups are either carbomethoxy (85) or methyl and carbomethoxy (87), the ortho phenyl protons appear as a multiplet, as in the nmr spectrum of p-terphenyl. The similarity of the spectra of 85 and 87 with the spectrum of p-terphenyl suggest that there is some degree of conjugation of the substituents with the aromatic central ring. The fine structure of the uv absorption curves of these compounds further suggests that free rotation of the substituents about the connecting bonds is highly restricted and the molecules are rigid.102

Reaction of dimethyl 3,4-di(2-pyridyl)cyclopentenolone 2,5-dicarboxylate (83) with dimethyl acetylenedicarboxylate or with other diarylacetylenes resulted in intractable tars. Many pyridine compounds are known to react with dimethyl acetylenedicarboxylate yielding 1:2 adducts. Pyridine itself gives such adducts, e.g., 119.103 Thus, in retrospect, degradative side reactions, which probably incorporate the pyridyl moieties, are operative.

Diels-Alder condensations of substituted cyclopentadienones, generated in situ from tetraaryl- and heteroarylcyclopentenolones, with diarylacetylenes at high temperatures, by the method of Dilthey and Hurtig,78 resulted in the formation of aryl- and heteroarylbenzenes (Scheme XV). The cyclopentenolones were isolated either as a single
isomer (88-92) or as a mixture of isomers (93-97) both of which, upon dehydration, give a single cyclopentadienone derivative. The mixture of 98, 99, and 100, however, afforded two cyclopentadienones, 99a and 100b upon dehydration in the ratio of 95:5, respectively. (Scheme XIV). Thus, it was possible to prepare hexasubstituted benzenes 71 and 101-109 as pure, single compounds by proper choice of the reactants, where only one geometrical isomer is generated (Table III). Reaction of either diphenylacetylene or di(2-pyridyl)acetylene with the mixture of the intermediate dienone 99a (95%) and 100b (5%) could form predominantly (95%) either 110 or 111, respectively (Scheme XV). After several crystallizations of each from boiling dimethylformamide, both 110 and 111 were isolated analytically pure. Similar condensation of the mixture (99a and 100b) with phenyl(2-pyridyl)acetylene could form 112, along with minor isomers 102 and 103. But, depending upon the polar attraction between the diene and the dienophile, which is an important factor in determining the direction of addition in Diels-Alder reactions, formation of 112 is strongly favored and in fact, after several crystallizations of the reaction product from boiling dimethylformamide, 112 (with constant melting point, higher than those of either 102 or 103) was isolated.

All these hexasubstituted benzenes are colorless, high melting solids, with similar spectra (Table IX). In the uv absorption spectra, all these compounds have absorption maxima between 245-247 nm. The similarity of the electronic spectra of pyridylbenzenes with hexaphenylbenzene (71) suggest that the steric arrangement of the substituents in pyridylbenzenes is similar to that in 71, in which the six phenyl groups are nearly orthogonal to the central benzene nucleus. The
<table>
<thead>
<tr>
<th>Compound</th>
<th>ir, cm⁻¹ᵃ</th>
<th>uv, λnm(ex10⁻³)ᵇ</th>
<th>nmr δ (PPM)ᶜ</th>
</tr>
</thead>
<tbody>
<tr>
<td>71</td>
<td>1450,1350,780, 725 and 692</td>
<td>247(59.0)</td>
<td>6.81-7.11</td>
</tr>
<tr>
<td>101</td>
<td>1580,1550,793, 737, and 698</td>
<td>247(52.0)</td>
<td>6.82-7.15</td>
</tr>
<tr>
<td>102</td>
<td>1580,792,747, 734, and 697</td>
<td>246(62.0)</td>
<td>6.70-7.46</td>
</tr>
<tr>
<td>103</td>
<td>1580,784,731, and 695</td>
<td>245(75.5)</td>
<td>6.76-7.41</td>
</tr>
<tr>
<td>104</td>
<td>1590,800,730, and 692</td>
<td>244(72.5)</td>
<td>6.76-7.64</td>
</tr>
<tr>
<td>105</td>
<td>1575,1530,1145, 990,805,745, 720, and 695</td>
<td>245(62.0)</td>
<td>6.62-7.12</td>
</tr>
<tr>
<td>106</td>
<td>1675,1595,1175, 1150,810,755, and 720</td>
<td>247(58.0)</td>
<td>6.72-7.46</td>
</tr>
<tr>
<td>107</td>
<td>1600,790,740, and 695</td>
<td>244(58.0)</td>
<td>6.80-7.28</td>
</tr>
<tr>
<td>108</td>
<td>1595,1150,800, 735, and 695</td>
<td>246(58.0)</td>
<td>6.68-7.18</td>
</tr>
<tr>
<td>109</td>
<td>1575,1550,800, 745, and 695</td>
<td>245(77.5)</td>
<td>6.74-7.47</td>
</tr>
<tr>
<td>110</td>
<td>1590,790,745, and 695</td>
<td>245(73.0)</td>
<td>6.82-7.26</td>
</tr>
<tr>
<td>111</td>
<td>1580,785,730, and 700</td>
<td>244(60.5)</td>
<td>6.69-7.43</td>
</tr>
<tr>
<td>112</td>
<td>1570,1500,790, 730, and 695</td>
<td>245(62.0)</td>
<td>6.76-7.43</td>
</tr>
</tbody>
</table>

ᵃ. In nujol. ᵃ. In 1,2-dichloroethane. ᵃ. In dimethylacetamide at 110⁰.
absence of absorption at higher wavelength regions also indicates that there is no conjugation of the aryl group with the central ring. These molecules are nonrigid and outer rings oscillate with no appreciable restriction on a rather limited angle interval of approximately 10° from the orthogonal form. The C-C bonds distances in the rings, the C-C bridge distances, and the C-H bond distances should be close to those present in hexaphenylbenzene and the size of nonbonding electrons orbital of nitrogens should be approximately the same as a C-H bond distance. Temperature study on the nmr spectra of these compounds was performed using dimethylacetamide as the solvent. Due to extreme insolubility of these benzenes, the spectra were run from 150° down to 70°. But there was no change in their nmr patterns and at temperatures below 70° the compounds crystallized from solution.

Thus, the evidence indicates that there is a constant melting isomer for each of the hexasubstituted benzenes. However, since complete rotation of the substituents about the connecting bonds is prevented by steric bulk, information concerning substituent rotation is a much more difficult aspect of this project than originally envisioned. For example, hexa(2-pyridyl)benzene (106) has been isolated and spectrally and analytically characterized; however, the question of configurational isomers (106 has eight isomers, Scheme XVI) must be evaluated after assurance that 106 is indeed a single configurational isomer. The possibility that 106 is a composition of isomers cannot be ruled out on either spectral data or synthetic mode of construction. Even if all eight isomers could be separated from reaction product of 106, the only method currently available to differentiate the configurations would be X-ray.
Scheme XVI

106 (uuuuuu) (uuuuud)

(uududd) (uddduu)

(uuuudd) (uuudud)

(dduduu) (dududu)

-.N- depicts pyridine nitrogen up(u) and

---N--- depicts pyridine nitrogen down(d) when observed from top of the central ring.
analysis of each pure isomer. In addition to the eight configurational isomers of 106, one of these isomers (ddu duu) can exist in optically active forms. The other 2-pyridyl substituted benzenes can also have configurational isomers and at present it is not possible to find out whether the products isolated in each case is a single configurational isomer or a composition of isomers.
SUMMARY AND CONCLUSION

Although numerous procedures are reported for the preparation of arylbenzenes, only a few are applicable to the syntheses of the heterocyclic substituted benzenes. Efficient synthetic procedures for the construction of hexasubstituted benzenes, specifically with the 2-pyridyl moiety, are described from the appropriately substituted cyclopentenolones.

Synthetic procedures were found for the efficient preparation of 2-pyridylacetonitrile (13) and 1,3-di(2-pyridyl)acetone (8) by improvement of the reported procedures.\textsuperscript{14,35}

\textit{Di(2-pyridyl)cyclopentenolones (74 and 83)} have been synthesized from base catalyzed condensations of 2-pyridil (48) with 3-pentanone and dimethyl-1,3-acetonedicarboxylate, respectively. Tetraaryl- and heteroarylcyclopentenolones (88-100) have been synthesized by similar base catalyzed condensation of appropriate diketones (40, 42, and 48) with acetones (8, 29, and 63) and their stereochemistry elucidated from their nmr spectra. These compounds were shown to form predominantly one isomer stereoselectively, even through mixtures of isomers are possible. A general trend is drawn about their spectral properties and the observed structural preference is shown.

Hexasubstituted benzenes (76-80, 84, 100-112) have been prepared by Diels-Alder condensations of substituted cyclopentadienones, generated \textit{in situ} from the above cyclopentenolones, with diaryl- and heteroarylacetylenes (44, 47, and 53). These substituted benzenes were analytically and spectrally characterized. The evidence indicates that
the steric arrangements of the substituents in pyridylbenzenes is similar to that in hexaphenylbenzene. These molecules are non-rigid and the peripheral rings oscillate with no appreciable restriction in a rather limited angle interval of approximately $\pm 10^\circ$ from the orthogononal form. But complete rotation of the substituents above the connecting bonds is prevented by steric bulk. However, it is not possible to ascertain whether the product isolated in each case is a single configurational isomer or a composition of geometrical isomers.

Attempted syntheses of di(2-pyridyl)cyclopropenone (114) and phenyl(2-pyridyl)cyclopropenone (115) by routes analogous to the preparation of diphenylcyclopropenone (52) were unsuccessful.

A study was made on the reaction products obtained from the condensation of 2-picolyllithium (7) with ethyl benzoate and ethyl 2-pyridylcarboxylate (5) and in both cases the respective ketones were isolated exclusively. Similar reactions of 2-picolylmagnesium bromide (27) with ethyl benzoate and with 5 also afforded only 20 and 26, respectively.
REFERENCES


PART II

SYNTHESIS OF CYCLIC POLYOLEFINS
INTRODUCTION

From the earliest days of structural organic chemistry, chemists have been intrigued by cyclic molecules. But only in recent years have cyclic compounds containing eight to eleven atoms in the ring (medium rings) been the subject of systematic research. No general synthesis of medium ring carbocycles was available until 1947. All attempts to adopt standard ring closure methods such as the Ruzicka salt pyrolysis (equation i) to the synthesis of medium ring ketones failed completely.

\[
\text{(CH}_2\text{)}_n\text{M}^{++}\text{heat} \rightarrow \text{[CH}_2\text{]}_n\text{C}=\text{O}
\]

fails for \( n = 8-10 \)

Even the Ziegler method (ii) for cyclizing \( \alpha,\omega \)-dinitriles at high dilution, which succeeded admirably in the synthesis of large ring compounds, failed completely when applied to the closure of medium rings.¹

\[
\text{(CH}_2\text{)}_n\text{CN} \rightarrow \text{EtNH}^+\text{Na}^-\text{High Dilution} \rightarrow \text{[CH}_2\text{]}_n\text{C}=\text{NH}
\]

fails for \( n = 7-9 \)

The first successful synthesis of medium rings was reported independently by Prelog² and Stoll³ by application of the acyloin condensation (iii).

\[
\text{(CH}_2\text{)}_n\text{COOEt} \rightarrow \text{Na Xylene} \rightarrow \text{[CH}_2\text{]}_n\text{COOH}
\]

\( n = 7 \) (40%) \( n = 8 \) (65%) \( n = 9 \) (70%)
Corey and Hamanaka\textsuperscript{4} obtained humulene (1), a 1,4,8-cyclodeca-
triene upon treatment of acyclic allylic $\alpha,\omega$-dibromides with nickel
carbonyl (iv). Attempts to synthesize 1,5-cyclodecadiene by this route
led only to 1,2-divinylcyclohexane (2).

\[
\begin{align*}
(\text{CH}_2)_n & \xrightarrow{\text{Ni(CO)}_4} \text{(CH}_2\text{)}_4 \\
\text{(CH}_2\text{)}_n & \xrightarrow{n=2} \text{(iv)}
\end{align*}
\]

By far the greatest success in the synthesis of cyclodecane
derivatives has been achieved through the application of fragmentation
reactions to appropriate bicyclic compounds. Fragmentation of cyclic
1,3-diol monosulfonates has been shown to be of interest in the synthesis
of several medium ring systems. Thus, Wharton, et al.,\textsuperscript{5} synthesized the
5-cyclodecenone \textit{via} the base initiated cleavage of the bicyclic hydroxy-
tosylate (3). Marshall and Scanio\textsuperscript{6} similarly employed a base initiated
fragmentation to convert the bicyclo [5.3.1]undecanyl hydroxytosylate (5)
to the cis-cyclohexenylcarboxaldehyde (8). Likewise, the related bicyclo[5.3.1]undecanyl hydroxytosylate (7) yielded the trans-cyclohexenylmethanol (8) upon treatment with lithium aluminum hydride. Corey, et al. utilized a similar fragmentation reaction to construct the nine-membered ring of caryophyllene (10) and isocaryophyllene (12) through the base initiated cleavage of hydroxytosylates 9 and 11, respectively. The solvolysis is accompanied by isomerization of the ring junction from cis- to trans-configuration. Wharton obtained 1,5-cyclohexadiene derivative 14 from zinc induced fragmentation of dibromide 13.
Corey and Hortmann\textsuperscript{10} described an application of the stereo-specific photofragmentation of a 1,3-cyclohexadiene derivative (15) which yielded the cyclodecatriene (16) upon ultraviolet irradiation. Selective hydrogenation of this intermediate afforded dihydrocostunolide (17), a naturally occurring 1,5-cyclodecadiene.

Grob, et. al,\textsuperscript{11} examined the solvolytic fragmentation of a number of decahydroquinolyl tosylates which proceed \textit{via} azacyclodecadienes as intermediates. Thus, upon treatment with aqueous ethanolic sodium hydroxide, the \textit{trans}, anti isomer (18) generated the \textit{trans}-azacyclodecadiene intermediate (19), the \textit{cis}, syn-decahydroquinolyl tosylate (20) afforded the \textit{cis} isomer (21). The \textit{trans}, syn-decahydroquinolyl tosylate (22), however, gave only substitution and elimination products 23 and 24, with none
of the fragmentation product being formed (Schemes I and II), thus il-
ustrating the importance of stereoelectronic factors to fragmentation
reaction. Tosylates 18 and 20 can both achieve a trans anti-
periplanar conformation which favors concerted fragmentation. The trans,
syn isomer 22, however, cannot attain the favored geometry without
calling upon intrinsically higher energy boat conformers which would
increase the transition state energy for fragmentation relative to that
for the observed substitution and elimination reactions. Hofmann de-
gradation of heterocycles containing a quaternary bridged nitrogen atom
has been found to be a useful technique for preparing medium sized un-
saturated heterocyclic systems. Paquette and Scott\textsuperscript{12} obtained the\textgreek{\alpha},\textgreek{\beta}-
unsaturated lactams 26 and 28 by subjecting the related quaternary

\begin{equation}
\begin{array}{c}
\text{N}^+ \\
\text{CH}_3 \\
\text{25}
\end{array}
\xrightarrow{1) \text{OH}^-} \\
\xrightarrow{2) \Delta}
\begin{array}{c}
\text{N} \\
\text{CH}_3 \\
\text{26}
\end{array}
\end{equation}

\begin{equation}
\begin{array}{c}
\text{N}^+ \\
\text{CH}_3 \\
\text{27}
\end{array}
\xrightarrow{1) \text{OH}^-} \\
\xrightarrow{2) \Delta}
\begin{array}{c}
\text{N} \\
\text{CH}_3 \\
\text{28}
\end{array}
\end{equation}

ammonium iodides 25 and 27 to Hofmann elimination. Similarly,
Aeberli and Houlihan\textsuperscript{13} isolated the medium sized heterocycles 30 and
32 on treatment of 29 and 31 with sodium methoxide-methanol.
Scheme 1

18 \[\text{OH}^-, \text{EtOH} \rightarrow \text{H}_2\text{O} \rightarrow \]

19

20 \[\text{OH}^-, \text{EtOH} \rightarrow \text{H}_2\text{O} \rightarrow \]

21

22 \[\text{OH}^-, \text{EtOH} \rightarrow \text{H}_2\text{O} \rightarrow \]

23 \( R = \text{H, Et} \) + 24
Scheme II

18

20

22

NO FRAGMENTATION
PRODUCT
Imines (Schiff bases) containing a nucleofugal group in the β-position also become fragmentable after addition of a nucleophile. Thus, the 3H-indole derivative \( \sim \) formed the unsaturated nine-membered lactam \( \sim \) on reacting with sodium hydroxide.\(^{14}\)

Mukharji and Das Gupta\(^{15}\) isolated a mixture of \( \alpha, \beta \) and \( \beta, \gamma \) isomers of trimethylcyclodecadienone (36) from the fragmentation of the tosylate of cis 6,6,9-trimethyl-3-oxo-8-hydroxydecalin (35) with potassium \( t \)-butoxide in hot \( t \)-butyl alcohol.
Mesylates have also been used as suitable nucleofugal group for fragmentation reactions. Thus, 1,3-diol monomesylate (38) undergoes facile fragmentation under solvolytic conditions in aqueous pyridine containing acetic acid affording 6-methyl-trans-5-cyclodecenone (39). The requisite mesylate was prepared from the known dione 37 as illustrated in Scheme III. Marshall and Bundy synthesized the trans,trans-1,6-diene (41) from the fragmentation of the methanesulfonate of the boronate (40) which was synthesized according to Scheme IV. The product obtained was a 85:15 mixture of trans,trans-1-methyl-1,6-cyclodecadiene (41) and the tricyclic hydrocarbon (42) in 90% yield based on methanesulfonate. These products must arise via the pathway depicted in Scheme V, wherein both stereoisomeric secondary alkanaboronates adopt the antiperiplanar conformation which favors concerted fragmentation. As indicated, both reacting centers undergo inversion of configuration during the course of this reaction. The necessity of antiperiplanar alignment of the breaking bonds in the boronate fragmentation reaction was demonstrated by the contrasting behavior of the epimeric unsaturated methanesulfonates 43 and 46. Compound 43, upon hydroboration followed by basic treatment, afforded an 85:15 mixture of the trans,trans-1,6-cyclodecadiene (44) and the tricyclic hydrocarbon 45 in 60% yield, whereas under identical conditions the epimer 46 afforded the cis,trans-1,6-cyclodecadiene (47).
Scheme III

\[
\text{37} \xrightarrow{1) \text{LAH}} \text{OBz} \underset{2) \text{BzCl}}{\xrightarrow{}} \text{OBz}
\]

\[
\text{H}_2\text{O}_2, \text{OH}^-
\]

\[
\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O} \\
\text{CH}_3\text{OH}, \text{HOAc}
\]

\[
\text{PtO, EtOH} \\
\text{HOAc}
\]

\[
\text{H}_2\text{O}, \text{OH}^-
\]

\[
\text{MscI,} \\
\text{C}_5\text{H}_5\text{N}
\]

\[
\text{KOBu}^+, \\
\text{Bu}^+\text{OH}
\]

\[
\text{39} \xrightarrow{\text{KOBu}^+, \text{Bu}^+\text{OH}} \text{38}
\]
Scheme IV

\[ \text{37} \xrightarrow{1) \text{LAH}} \xrightarrow{2) \text{Ac}_2\text{O}} \text{RO} \]

\[ \text{R = H, } -\text{COCH}_3 \]

\[ \text{37} \xrightarrow{\text{Li, EtNH}_2} \]

\[ \text{OMs} \xrightarrow{\text{MsCl, C}_5\text{H}_5\text{N}} \]

\[ \text{OMs} \xrightarrow{\text{BH}_3, \text{THF}} \xrightarrow{2) \text{OH}^-} \text{OH} \]

\[ \text{40} \xrightarrow{\text{OH}^-} \text{41} + \text{42} \]
Scheme V

1) BH₃, THF
2) OH⁻
in only 5% yield. The remaining material in this case consisted of boron containing compounds. Both olefins $\mathbf{43}$ and $\mathbf{46}$ should afford cis-linked decalylboranes upon hydroboration. In the former case, a low energy conformation with the optimal trans antiparallel alignment of the breaking bond can readily be attained. However, with the decalylborane $\mathbf{48}$, derived from the unsaturated mesylate $\mathbf{46}$, neither of the two available all-chair conformers $\mathbf{48a}$ and $\mathbf{48b}$ meet these requirements.

Hence, higher energy boat conformers must be invoked for concerted fragmentation to take place.

Decalylboronate systems (49) leading to 1,5-cyclodecadienes could fragment either by internal cleavage or by peripheral cleavage leading to two isomeric products. However, the results indicate that such reactions exhibit a remarkably high preference for internal cleavage.
affording the cyclodecadienes (50a) and the isomeric divinylcyclohexanes (50b) are produced upon pyrolysis of the cyclodecadienes only. Thus, the unsaturated mesylate 56, synthesized as outlined in Scheme VI, afforded a 93:7 mixture of the 1,5-cyclodecadiene (57) and the tricyclic hydrocarbon (42) in 90% yield upon hydroboration followed by basic fragmentation. The isomeric 1,2-divinylcyclohexane (58) was produced upon pyrolysis of 57 at 300°. Likewise, the unsaturated methanesulfonate gave rise to the corresponding 1,5-cyclodecadiene 61 in 60% yield under the aforementioned reaction conditions as illustrated in Scheme VII. Here also, none of the divinyl isomer 62 could be detected, although this material was obtained readily upon pyrolysis of the cyclodecadiene 61. Cyclodecadiene 57 is obtained in unexpectedly high yield because it is formed both from trans (56a) and cis (56b) decalylboronates. Mesylate 56a possesses the ideal antiperiplanar geometry for concerted fragmentation, but the mesylate 56b can easily adopt a boat conformation such as 56c for fragmentation to occur (Scheme VIII).

The directional specificity of decalylboronate cleavage leading to 1,5-cyclodecadienes contrasts sharply with that found by Grob for the analogous decahydroquinolyl tosylate (63) fragmentation which affords only products related to peripheral cleavage (63 → 64) and not
Scheme VI

1) NaBH₄
2) \( \) → \( \)

KOBu\(^+\), Bu\(^+\)OH
HOAc

1) LAH
2) MsCl, C\(_5\)H\(_5\)N

1) Li • NH\(_3\)
2) H\(_3\)O\(^+\)
3) MsCl, C\(_5\)H\(_5\)N

1) BH\(_3\), THF
2) OH\(^-\)

300°
Scheme VII

1) NaBH₄

2) OTOP

C D

37

52

KOBu⁺, Bu⁺OH

CH₃⁻

1) N₂H₂·H₂O, KOH

(HOCH₂CH₂)₂O

2) H₃O⁺

3) MsCl, C₅H₅N

OR

CH₃ CH₃

59 (R=H)

60 (R=Ms)

1) BH₃, THF

2) OH⁻

Δ

CH₃ CH₃

61

62
Scheme VIII

1) BH₃, THF
2) OH⁻

trans 56a + cis 56b

57

56c
internal cleavage (63 → 65). Conceivably, the transition state for the former reaction (with decalylboronates) resembles the reactants while the transition state for the latter (with decahydroquinolyl tosylate) more closely resembles the products. Alternatively, both reactions may proceed with internal cleavage via reactant-like transition states with the product of internal cleavage from the decahydroquinoline system undergoing an exceedingly facile (Cope-type) rearrangement to the observed product. 19

6-Methyl-1,6-cyclodecadiene-3-one (67) and 6-methyl-1,5-cyclodecadiene-3-one (68) are synthesized by a reasonable but more involved route as depicted in Scheme IX, 20 involving fragmentation of the hydroxymesylate derivative 66. Fragmentation of a similar hydroxymesylate 69 with sodium t-butoxide afforded the conjugated cyclodeca-

\[
\begin{align*}
\text{71} & \quad \xrightarrow{\text{LAH}} \quad \text{70} \\
\text{69} & \quad \xrightarrow{\text{NaOBu}^+} \quad \text{70}
\end{align*}
\]

dienone 70, whereas treatment with lithium aluminum hydride resulted in the cis,trans-cyclodecadienol (71). Similarly, treatment of cis-mesylate

\[
\begin{align*}
\text{72} & \quad \xrightarrow{\text{NAH in THF}} \quad \text{73}
\end{align*}
\]
Scheme IX

1. LAH
2. Ac₂O; C₅H₅N
3. HOCH₂CH₂OH

m-ClC₆H₄CO₃H

1. LAH
2. MsCl

KOBu⁺
Bu⁺OH 95%

1. LAH
2. H₂O; H⁺

1. Ac₂O; C₅H₅N
2. Δ (-HOAc)

67 + 68
with sodium hydride in tetrahydrofuran gave the unstable cyclodecane 73, whereas attempted fragmentation of the trans-isomer was unsuccessful.\textsuperscript{22}

Medium ring compounds have also been synthesized by ring enlargement reactions. In suitable constituted molecules, the nucleophytic substitution may accompany a Wagner-Meerwin rearrangement leading to ring expansion. For example, cyclooctylmethylamine (74) afforded a mixture containing cyclononene (75), cyclononanol (76), and cyclooctylcarbinol (77) upon treatment with nitrous acid.\textsuperscript{23}

\begin{align*}
\text{CH}_2\text{NH}_2 \quad \xrightarrow{\text{HNO}_2} \quad \text{CH}_2\text{OH} \\
\text{74} & \quad \text{75} & \quad \text{76} & \quad \text{77}
\end{align*}

The presence of the hydroxyl group at C-1 of the cycloalkylcarbinyl system greatly increases the tendency for ring expansion by the pinacol-type rearrangement. Thus, cyclooctanone (79) and cyclononanone (80) are isolated by treatment of the appropriate hydroxymethylamine (78) with nitrous acid.\textsuperscript{24} Diazolalkanes react with cycloalkanones (81) in the presence of Lewis acids to give good yield of the corresponding ring
$(\text{CH}_2)_n \text{C} = \text{O} + \text{RCHN}_2 \xrightarrow{\text{AlCl}_3/\text{BF}_3} (\text{CH}_2)_n \text{CHR} \text{C} = \text{O}$

$\sim 81$

$C_7 \rightarrow C_8 (82\%)$  $C_{10} \rightarrow C_{11} (57\%)$

$C_8 \rightarrow C_9 (66\%)$  $C_{11} \rightarrow C_{12} (63\%)$

$C_9 \rightarrow C_{10} (72\%)$

expansion products ($82\%)$. Bicyclo[6.1.0] nona-2,4-diene ($83\%)$ upon heating to $160^\circ$ established an equilibrium with 1,4,7-cyclononatriene ($84\%)$;

![Diagram of bicyclo[6.1.0] nona-2,4-diene](image)

whereas, bicyclo[6.1.0] nona-2,5-diene ($85\%)$ undergoes irreversible conversion at $130^\circ$ to 1,5,7-nonatriene ($86\%)$.

![Diagram of bicyclo[6.1.0] nona-2,5-diene](image)

Dibromo-, dichloro-, and exomonobromo-carbene adducts of cycloheptene and cyclooctene ($87\%$ and $89\%$) undergo rapid solvolysis in the presence of silver perchlorate stereospecifically to give high yields of trans-cyclooctene and trans-cyclononene derivatives ($88\%)$ and ($90\%)$,
respectively. Similarly, methanolysis of 9,9-dibromo- or dichlorobicyclo-
[6.1.0]non-4-ene (91) afforded the corresponding trans,cis-cyclononadiene
derivatives (92). In each case, the product obtained was that expected

for the rearrangement involving the concerted transformation of a cyclo-
propyl to an allyl cation with an exo-leaving group. Cis-bicyclo[6.1.0]-
nona-2,4,6-triene (93) on treating with sodium at 0° in a mixture of
hexamethylenephosphordiamine-tetrahydrofuran (19:1) afforded 40-60% yield of cis,cis,cis,cis-cyclonona-1,3,5,7-tetraene (94). Allylic alcohol, on heating, rearranges to the ketone via cleavage to a biradical, resulting in ring expansion by two carbon atoms by a process called the oxy-Cope rearrangement. Bicyclo[5.2.0]nonene (97) rearranges thermally to 1,3-cyclononadiene (98). Similarly, cis-bicyclo[4.3.0]nona-2,4-diene (99) on ultraviolet irradiation rearranges smoothly giving trans,cis,cis-cyclononatriene (100). A novel method available for the expansion of a carbocyclic ring by two carbon atoms under mild conditions involves the condensation of dienamines with dimethyl acetylenedicarboxylate. Thus, 1-dimethylamine-1,3-cyclooctadiene (101), when treated with
the dienophile formed 1,3,5-cyclodecatriene derivative 102 in 49.3% yield by a sequence involving the intermediate formation of a cyclobutenene adduct. Similar treatment of 103 with dimethyl acetylenedicarboxylate afforded the heterocyclic 1,3,5-cyclodecatriene 104 in 51% yield. Cycloalkenes have been synthesized by catalytic dimerization and trimerization of conjugated dienes. Thus, heating butadiene with a benzene solution of nickel acetylacetonate, triphenylphosphine, and diethylaluminum ethoxide afforded a mixture of 1,5-cyclooctadiene and 1,5,9-cyclododecatriene, whereas heating with a mixture of titanium tetra- butoxide, dimethylsulfoxide and an organoaluminum halide (Et₃Al₂Cl₃) yielded 1,5,9-cyclododecatriene with 91.5% selectivity. Similarly, cis,trans-1,5-cyclodecadiene was produced in 95% yield from the cyclocooligomerization of butadiene and ethylene (1:2 - 2:1.5) on heating in
benzene containing nickel acetylacetonate, triethylaluminum, and the organo-phosphorus compound \((O-phC_6H_4)P\).

\[ +HC=CH + \text{Ni-acetylacetonate} + \]
\[ \text{Et}_3\text{Al} + (O-phC_6H_4)P \]
\[ \text{PPh}_3 + \text{Et}_2\text{Al(OEt)} + \]
\[ \text{Ni-acetylacetonate} \]
\[ \text{Ti(OBu)}_4 + \text{Et}_3\text{Al}_2\text{Cl}_3 + (\text{CH}_3)_2\text{SO} \]

1,5-cyclooctadiene +
1,5,9-cyclododecatriene

It is not within the scope of this review to discuss the transannular reactions or the conformation of cycloalkenes. However, general information concerning their reactivity\(^{38}\) and optical activity\(^{39,40,41}\) can be obtained in recent publications.
EXPERIMENTAL

A. General

The analytical techniques employed were the same as those described in Part I (Experimental).

B. Syntheses

2-Methylcyclopentane-1,3-dione (105) was prepared by the method of House and Czuba by the reaction of 2-butanone and acetic anhydride in the presence of 70% perchloric acid catalyst in 26% yield: bp 116-120° (760 mm); nmr (CCl₄) δ 1.48 (C-CH₃, m, 3H), 1.80 (C-CH₃, m, 3H), 2.07 (-OCOCH₃, s, 3H), 4.90 (vinyl-H, q, 1H); ir (neat) 1760 (ester C=O), 1705 (enol C=C), 1425, 1350, 1225, 1175, 1025, 960, 900, 835, and 785 cm⁻¹.

To azeotropically dried nitrobenzene (1 liter), anhydrous aluminum chloride (466 g, 3.5 mole) was added, followed by succinic anhydride (100 g, 1.0 mole) under nitrogen, controlling the temperature between 45-80°. After heating to 110° for 2 hours, the mixture was cooled to 25° and 2-buten-2-ol acetate (171 g, 1.5 mole) was added maintaining the temperature near 25° by external cooling. After stirring for 30 minutes, the reaction mixture was heated to 110° for 2 hours, cooled, and quenched by 1 liter of ice water. After the mixture stood overnight in the refrigerator, a brown precipitate was collected, washed with nitrobenzene, and then with petroleum ether A. The crude dione was decolorized, and recrystallized from hot water affording 80 g (70%) of the colorless dione mp 210-212° (lit. mp 210-212°); nmr (DMSO-d₆) δ 1.5 (-CH₃, s, 3H), 2.37 (ring -CH₂-, s, 4H) 4.55 (-CH, s, 1H).
2-Methyl-2-(3-oxobutyl)cyclopentane-1,3-dione (106). A mixture of 2-methylcyclopentane-1,3-dione (65 g, 0.5 mole), anhydrous methanol (250 ml), freshly distilled methyl vinyl ketone (63 g, 0.9 mole), and potassium hydroxide (3 pellets) was refluxed for 5 hours. After removing the solvent, the residue was treated with water and extracted with chloroform, dried over anhydrous magnesium sulfate, concentrated in vacuo, and fractionally distilled collecting the fraction with bp 108-112° (0.1 mm), which solidified upon cooling. Recrystallization from ethyl acetate afforded 86 g (60%) of the triketone 106: mp 116-118° (lit. mp 117-118°)

nmr (CDCl₃) δ 1.04 (angular CH₃, s, 3H), 2.10 (-COCH₃, s, 3H), 2.80 (ring -CH₂-, s, 4H); ir (CHCl₃) 1750 (C=O), 1705, 1660, 1340, 1230, 1140, 1110, and 870 cm⁻¹.

Upon prolonged heating of the above reaction mixture for 8 hours, two products were obtained: 106 and 4-hydroxy-1,4-dimethylcyclo[3,2,1]-octane-7,8-dione (107): 20 g (15%); mp 165° (lit. mp 164-166°); nmr (CDCl₃) δ 1.08 (angular CH₃, s, 3H), 1.35 (CH₃, s, 3H), 1.12-1.92 (methylene-H and -CH, m, 3H), 2.40-2.82 (methylene-H, and OH, m, 5H); ir (CHCl₃) 3450 (-OH), 1770, 1715, 915, 745, and 715 cm⁻¹; ms (70 eV and 80µA) m/e (relative intensity) 182 (64), 150 (96), 126 (64), 113 (57), 98 (47), 70 (53), 56 (66), and 44 (100).


5,6,7,8-Tetrahydro-8-methylindane-1,5-dione (108). A solution of 2-methyl-2-(3-oxobutyl)cyclopentane-1,3-dione (45 g, 0.155 mole) in benzene (250 ml) was refluxed for 5 hours with p-toluenesulfonic acid (4 g) removing the water with a Dean-Stark trap. After removing the
solvent, the oily residue was dissolved in ethyl acetate and filtered through a short column of florisil. The filtrate was evaporated and the crude product recrystallized from diethyl ether affording 33.5 g (83%) of the pale yellow dione 108: mp 72-73° (lit. mp 72-73°); nmr (CDCl₃) δ1.3 (angular CH₃, s, 3H), 2.1-3.1 (methylene-H, broad m, 10H); 5.98 (vinyl-OH, s, 1H); ir (CHCl₃) 1745 (5-membered ring ketone), 1665 (α,β-unsaturated ketone), 1440, 1350, 1140, 1060, 1010, and 860 cm⁻¹.

(+)-7,7α-Dihydro-αβ-hydroxy-7αβ-methyl-5(6H)-indenone (109). Lithium aluminum tri-t-butoxyhydride was prepared by addition of t-butyralcohol (74 g, 1.00 mole) dropwise to ethereal solution of lithium aluminum hydride (12.13 g, 0.32 mole). Removal of the solvent gave the product in quantitative yield.

A solution of lithium aluminum tri-t-butoxyhydride (93.75 g) in dry tetrahydrofuran (600 ml) was added dropwise to 108 (24.6 g, 0.082 mole) in tetrahydrofuran (300 ml) at 0°. After stirring at 0° for 9 minutes, acetone (50 ml) in ice-water (175 ml) was added carefully and the resulting suspension was neutralized with 2N sulfuric acid. After removing the solvent, the residue was extracted with ethyl acetate and then with ether. The combined organic extract was washed with 10% sodium chloride solution, dried over anhydrous sodium sulfate, decolorized, and the solvents removed in vacuo. A colorless oil crystallized after standing for 8 days affording 22.73 g (91%) of the β-hydroxy alcohol 109; mp 66-67° (lit. mp 66.5-67.5°) nmr (CDCl₃) δ 1.15 (angular CH₃, s, 3H), 3.1 (-OH, s, 1H), 3.8 (CHOH, t, J = ~ 7.5 Hz, 1H), 5.78 (vinyl-H, s, 1H); ir (CHCl₃) 3250-3500 (bonded -OH), 1554 (α,β-unsaturated ketone), 1440, 1420, 1354, 1322, 1270, 1128, 1140, 1086, 1076, 1035, 1025, 1005, 950,
and 870 cm⁻¹; uv (CH₃OH) 240 nm (11500); 2,4-dinitrophenylhydrazone: mp 149° (lit.⁴⁴ mp 149°); semicarbazone: mp 180° (lit.⁴⁴ mp 180°).

1α-Hydroxy-7αβ-Methyl-Δ³(3α)-1,2,4,5,6,7-hexahydroindene (116).

Method A.

a. Tetrahydropyranyl ether 110.⁴⁷ A solution of 109 (15 g, 0.051 mole) in anhydrous tetrahydrofuran (50 ml) was treated with anhydrous dihydropyran (25 ml) and phosphorus oxychloride (12 drops). After stirring at 25° for 20 hours, the reaction mixture was poured into cold 10% sodium bicarbonate solution (50 ml) and extracted with ether. The extract was washed with 10% sodium chloride solution, dried over anhydrous sodium sulfate, and the solvent removed in vacuo. The residual oil was dissolved in anhydrous toluene and evaporated several times affording 18.5 g (98%) of the ether 110 as pale yellow oil: nmr (CCl₄) δ 1.16 (angular CH₃, s, 3H), 4.6 [-CH(O-THP), t, 1H], 5.76 (vinyl-H, s, 1H); ir (CHCl₃) 1665 (α,β-unsaturated ketone), 1135, 1120, 1075, 1030, and 1020 cm⁻¹ (ether bands); uv (CH₃OH) 238 nm (13,475).

b. Deconjugation of 110.⁴⁸ To a five-liter flask equipped with mechanical stirrer, solid potassium t-butoxide (85 g) was added under nitrogen followed by redistilled t-butanol (800 ml). After the solid dissolved, 110 (18 g) in t-butanol (25 ml) was added dropwise. The mixture was agitated at 25° for 2 hours, then 10% acetic acid solution (3 liters) was added as rapidly as possible, followed in 5 minutes, by solid sodium bicarbonate until solution became neutral. Ether extraction gave, upon concentration, 17 g (94%) of 111 as a brown viscous oil, which was a 60:40 mixture of conjugated and deconjugated ethers: nmr (CCl₄) δ 1.2 (angular CH₃, s, 3H), 3.2-4.2 (CHO-, m, 1H), 5.22 [ =C(3)H₃].
m, \( \sim 0.4H \), 5.7\( [ =C(4)H, m, \sim 0.6H] \); ir (CHCl\(_3\)) 1710 (deconjugated ketone), 1660 (\( \alpha,\beta \)-unsaturated ketone), 1140, 1070, 1030, and 975 cm\(^{-1}\).

c. Reduction of 113.\(^{19}\) The above crude ketone (17 g) in anhydrous ether (500 ml) was treated with lithium aluminum hydride (4.25 g), added in small portions at 0-5\(^{\circ}\). After stirring at 25\(^{\circ}\) for 2 hours, a 10% sodium hydroxide solution (10 ml) was carefully added and the mixture stirred overnight. The precipitate was filtered and the solvent was removed in vacuo affording 13.6 g (80%) of 112: nmr (CDCl\(_3\)) \( \delta 1.18 \) (angular CH\(_3\), s, 3H), 3.3-4 (CHO-, t, 1H), 4.9 (-OH, m, 1H), 5.28\( =C(3)H, m, \sim 0.04H\), 5.7\( =C(4)H, s, \sim 0.6H\); ir (CHCl\(_3\)), 3400 (-OH), 1660 (C=C), 1340, 1210, 1125, 1075, 1025, 975, 920, 900, 870, and 860 cm\(^{-1}\).

d. Mesylate.\(^{19}\) The above crude alcoholic mixture (12 g, 0.05 mole) in anhydrous pyridine (50 ml) was cooled to 0\(^{\circ}\), and methanesulfonyl chloride (6 ml) was added dropwise. After stirring at 25\(^{\circ}\) for 5 hours, the reaction mixture was poured into cold 10% sodium hydroxide solution (100 ml) and extracted with hexane. The extract was washed successively with 3% sulfuric acid solution, water, saturated sodium bicarbonate solution, water, and saturated sodium chloride solution. Upon concentration, 5.1 g (33%) of crude methanesulfonate 113 were isolated as a pale yellow oil: nmr (CCl\(_4\)) \( \delta 1.18 \) (angular CH\(_3\), s, 3H), 3.0 (CH\(_3\)-SO\(_2\)-O, s, 3H), 5.15 \( =C(3)H, m, \sim 0.4H\), 5.75\( =C(4)H, s, \sim 0.6H\); ir (CHCl\(_3\)) 1430, 1340, 1250, 1075, 1050, 975, 865, and 820 cm\(^{-1}\).

e. Reduction of 113.\(^{19}\) Lithium ribbon (3 g) was dissolved in 350 ml anhydrous ammonia (distilled through a potassium hydroxide column), followed by dropwise addition of the crude methanesulfonate 113 (5.0 g) in absolute ethanol (20 ml). After stirring for 12 hours, ethanol (25 ml)
was added, followed by solid ammonium chloride (26 g). Ammonia was al-
lowed to evaporate overnight under a slow nitrogen stream. The residue
was dissolved in water, extracted with ether and concentrated affording
3.5 g (71%) of 114 as a pale yellow oil: nmr (CCl₄) δ 1.05 (angular CH₃,
s, 3H), 5.15 [=C(3)H, m, ~ 0.4H], 5.75 [=C(4)H, m, ~ 0.6H]; ir (CHCl₃)
1630, 1440, 1125, 1075, 1025, and 970 cm⁻¹.

f. Hydrolysis of 114.¹⁹ The above ether (3.5 g) in 95%
ethanol (100 ml), concentrated hydrochloric acid (8 ml), and water (20 ml)
was refluxed for 2 hours. After cooling, the mixture was extracted with
ether, washed with water, saturated ammonium sulfate solution, and con-
centrated affording 900 mgs (40%) of a pale yellow oil. Separation
using gas liquid chromatography on 30% SE-30 on 60/80 mesh chromosorb W
gave two products: (i) 1β-hydroxy-7αβ-methyl-Δ³(4)-1,2,3,5,6,7-
hexahydroindene (115); nmr (CCl₄) δ 0.99 (angular CH₃, s, 3H), 5.40
 [=C(4)H, m, 1H], 4.05 [-CHOH, t, J=8 Hz, 1H]; ir (CHCl₃) 3600 (-OH),
1640 (C=O), 1550, 1350, 1180, 960, 910, 880, and 840 cm⁻¹.

Anal. Calcd for C₁₀H₁₆O: C, 78.99; H, 10.53. Found: C,
78.88; H, 10.30.

(ii) 1β-hydroxy-7αβ-methyl-Δ³(3a)-1,2,4,5,6,7-hexahydroindene (116):
mp 67-69°; nmr (CCl₄) δ 0.96 (angular CH₃, s, 3H), 4.0 [-CHOH, t, J=
8 Hz, 1H], 5.12 [=C(3)H, t, 1H]; ir (CHCl₃) 3600 (-OH), 1650 (C=O),
1125, 1075, 1040, 980, and 815 cm⁻¹.

Anal. Calcd for C₁₀H₁₆O: C, 78.99; H, 10.53. Found: C,
78.80; H, 10.27.

Method B.
a. Enol acetate (112) of 108.⁴⁹ A mixture of 5,6,7,8-
tetrahydro-8a-methylindane-1,5-dione (39 g, 0.25 mole), acetyl chloride
(160 ml) and acetic anhydride (160 ml) was refluxed under nitrogen for 6 hours. After removing the solvents in vacuo, the residue was fractionally distilled affording 48 g (92%) of **117**, bp 108-110° (0.2 mm), which was crystallized from ethyl acetate: mp 61-62°; nmr (CDCl₃) δ 1.18 (angular CH₃, s, 3H), 2.09 (CH₃CO, s, 3H), 5.72 [ =C(3)H, t, 1H], 6.03 [ =C(4)H, s, 1H]; ir (CHCl₃), 3005, 1775, 1665, and 1110 cm⁻¹.


b. **Semicarbazone 118 of the Enol Acetate (117).**⁵⁰ The above enol acetate (46.8 g, 0.112 mole) in absolute methanol (230 ml) was warmed to 50° and a solution of semicarbazide hydrochloride (51.10 g) in methanol-water (1:1, 230 ml) was added. After stirring for 0.5 hour, the precipitate was collected, washed with methanol-water mixture affording 36 g (61%) of the semicarbazone **118**: mp 200-202° (d); nmr (DMSO-d₆) δ 1.14 (angular CH₃, s, 3H), 2.1 (CH₃CO, s, 3H), 5.55 [ =C(3)H, m, 1H], 6.0 [ =C(4)H, s, 1H]; ir (nujol) 3500, 3200, 1775, 1710, 1680, 1600, 1250, 1225, 1120, 1090, and 910 cm⁻¹.

**Anal.** Calcd for C₁₁H₁₇N₃O₃: C, 59.31; H, 6.45; N, 15.96. Found: C, 59.01; H, 6.22; N, 15.78.

c. **Reduction of the Semicarbazone 118.**⁵¹,⁵² A mixture of the above semicarbazone (32.7 g, 0.127 mole) in ethanol (675 ml) was added dropwise to a stirred solution of sodium borohydride (78.3 g) in 95% ethanol (3 liters) at 0°. After 45 minutes at 0°, the mixture was stored for two days at -5°, then poured into 10% sodium hydroxide solution and extracted several times with chloroform. Concentration of the extract afforded 7.2 g (26%) of the semicarbazone alcohol **119**: mp 170-172°; nmr (DMSO-d₆) δ 0.82 (angular CH₃, s, 3H), 3.25 (NHCONH₂, m, 3H), 5.60
134

\[ =\text{C}(3)\text{H}, \text{t}, 1\text{H} \]; ir (nujol) 3400, 3125, 1665, 1590, 1370, 1070, and 1025 cm\(^{-1}\).

**Anal.** Calcd for \(C_{11}H_{17}O_{2}N_{3}\): C, 59.19; H, 7.62; N, 18.83. Found: C, 59.22; H, 7.55; N, 18.52.

d. **Hydrolysis of Semicarbazone Alcohol** \(120\) \(^{53}\) A solution of the above semicarbazone alcohol (6.6 g, 0.029 mole) in 2.5 N hydrochloric acid (500 ml) was cooled to 5\(^{\circ}\), then treated dropwise with a 10% sodium nitrite solution (75 ml). After stirring at 5\(^{\circ}\) for 0.5 hour, a 60% solution of urea (75 ml) was added. The resulting solution was neutralized with concentrated sodium bicarbonate solution, extracted with ethyl acetate, and concentrated in vacuo to afford 2.5 g (50%) of the alcohol \(120\) as pale yellow solid: mp 58-60\(^{\circ}\); nmr (acetone-\(d_6\)) \(\delta 1.1\) (angular \(\text{CH}_3\), s, 3H), 4.2 (\(\text{CHOH}\), m, 1H), 5.35 \[ =\text{C}(3)\text{H}, \text{t}, 1\text{H} \]; ir (CHCl\(_3\)) 3400, 1780, 1455, and 1060 cm\(^{-1}\).

**Anal.** Calcd for \(C_{10}H_{14}O_2\): C, 72.28; H, 8.42. Found: C, 71.95; H, 8.25.

e. **Mesylate** \(121\) \(^{52}\) The above alcohol (2.2 g, 0.013 mole) in anhydrous pyridine (25 ml) was treated with dropwise addition of methanesulfonyl chloride (3 ml) at 0\(^{\circ}\). After stirring at 25\(^{\circ}\) for 6 hours, the solution was cooled to 0\(^{\circ}\) and poured into a cold 10% sodium bicarbonate solution (25 ml) and extracted with ether. The extract was washed successively with 3% sulfuric acid solution, water, saturated sodium bicarbonate solution, water, saturated sodium chloride solution, dried over anhydrous sodium sulfate and concentrated in vacuo affording 2.8 g (88%) of mesylate \(121\) as a semisolid: nmr (acetone \(d_6\)) \(\delta 1.2\) (angular \(\text{CH}_3\), s, 3H) 3.07 (\(-\text{OSO}_2\text{CH}_3\), s, 3H), 5.38 \[ =\text{C}(3)\text{H}, \text{t}, 1\text{H} \]; ir (CHCl\(_3\)) 2910, 1670, 1350, 1175, 1000, 960, 910, and 875 cm\(^{-1}\).
f. 1β-Hydroxy-7αβ-methyl-Δ^3(3a) -1,2,4,5,6,7-hexahydroindene (116). The above mesylate \( \text{mesylate} \) (2.45 g, 0.016 mole) in anhydrous ether (25 ml) was treated with lithium aluminum hydride (2 g) at 0°. After stirring overnight at 25°, a 10% sodium hydroxide solution (5 ml) was carefully added, and the product extracted with ether. The extract, after standard work-up procedures, gave a pale yellow solid, which was recrystallized from pentane affording 400 mgs (26%) of the unsaturated alcohol. mp 67-69°; nmr (acetone-\( \text{d}_6 \)) \( \delta \) 0.99 (angular \( \text{CH}_3 \), s, 3H), 4.05 (\( \text{CHOH} \), t, \( J = 8 \) Hz, 1H), 5.14 \( \text{[=CH(3)H]} \), t, 1H); ir \( \text{(CHCl}_3 \text{)} \) 3600 (-OH), 1650 (OC), 1125, 1075, 1040, 980, and 815 cm\(^{-1} \).

Anal. Calcd for \( \text{C}_{10}\text{H}_{16}\text{O} \): C, 78.99; H, 10.53. Found; C, 78.80; H, 10.27.

1,6-Dioxo-8α-methyl-1,2,3,4,6,7,8,8α-Octahydonaphthalene (37). A mixture of 2-methyl-1,3-cyclohexanedione (63.1 g, 0.5 mole), methyl vinyl ketone (52.6 g, 0.75 mole), absolute methanol (250 ml) and potassium hydroxide (3 pellets) was refluxed under nitrogen for 3 hours. After removal of the solvent and excess of methyl vinyl ketone, the residual liquid was refluxed with anhydrous benzene (250 ml) and pyrrolidine (3 ml) removing the water via a Dean-Stark separator. After cooling, the solution was diluted with ether (150 ml), washed with 2% hydrochloric acid solution, water, saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. After concentrating, the residue was distilled collecting the fraction bp 130-140° (0.1 mm), which solidified upon standing at 0°. Recrystallization from ether afforded 45 g (50%) of pure dione. mp 47-48° (lit. \( \text{mp} \) 47-48°); nmr \( \text{(CDCl}_3 \text{)} \) \( \delta \) 1.45 (angular \( \text{CH}_3 \), s, 3H), 1.8-2.9 (methylene \( \text{H} \), m, 10H), 5.85 (vinyl-\( \text{H} \), s, 1H); ir \( \text{(CHCl}_3 \text{)} \) 1715 (C=O), 1650 (C=C), 1330, 1140, 1060, and 865 cm\(^{-1} \).
1-Keto-9-methyl-6-(N-pyrrolidino)-Δ^4,5-octalin (122). A mixture of above dione, \( \Delta \) (46.6 g, 0.262 mole), pyrrolidine (41 g, 0.577 mole), and a crystal of p-toluenesulfonic acid in benzene (650 ml) was refluxed under nitrogen for 18 hours, removing the water via a Dean-Stark separator. The solvent was evaporated, additional benzene added, then evaporated to remove excess pyrrolidine, affording 60 g of the crude dieneamine 122: nmr (CDC\(_3\)) \( \delta \) 1.15 (angular CH\(_3\), s, 3H), 4.25 [C(5)H, s, 1H], 5.18 [C(4)H, t, 1H]; ir (CHC\(_3\)) 1725, 1640, 1620, 1400, 1350, 1225, 950, and 910 cm\(^{-1}\).

Since the product decomposes upon distillation, the crude compound was taken to the next step directly assuming the yield to be quantitative.

2-Phenyl-5a-methyl-4,5,5a,6,7,8-hexahydronaphtho(2,1-b)furan-6-one (123). A mixture of the above dieneamine (23.1 g, 0.1 mole), \( \alpha \)-bromoacetophenone (19.9 g, 0.1 mole) in dry dimethylformamide (50 ml) was refluxed under nitrogen for 20 hours. After cooling, the reaction mixture was diluted with water, refluxed for 1 hour, and the solvents removed in vacuo. The residue was dissolved in benzene-ether-chloroform mixture (1:1:1), washed with water, dried over anhydrous magnesium sulfate, and chromatographed through a florisil column eluting with chloroform. Concentration in vacuo afforded 11 g (40%) of the furan derivative 123 as pale yellow solid: mp 146-147° (lit. mp 147-149°); nmr (CDCl\(_3\)) \( \delta \) 1.25 (angular CH\(_3\), s, 3H), 5.89 [-C(9)H, t, 1H], 6.65 [-C(1)H, s, 1H], 7.1-7.75 (arom-H, m, 5H); ir (CHCl\(_3\)) 1700 (C=O), 930, 760, and 695 cm\(^{-1}\).

Reduction of Furan Derivative 123. An ethanolic mixture of the above furan derivative (5 g, 0.018 mole) and sodium borohydride (5 g) was stirred at 25° for 10 hours. After decomposing the excess of sodium
borohydride with dilute acetic acid, the solvents were removed and the residue was extracted with chloroform. The extract was washed with saturated sodium chloride, dried, and concentrated in vacuo affording 5.2 g (100%) of alcohol 124: mp 126–128°; nmr (CDCl₃) δ 1.04 (angular CH₃, s, 3H), 3.4 (-OH, d, 1H), 3.6 [CH(OH), m, 1H], 5.6[ C(9)H, t, J = 8 Hz, 1H], 6.6 [C(1)H, s, 1H], 7.1–7.8 (arom-H, m, 5H); ir (CHCl₃) 3400 (-OH), 1600, 1440, 1230, 1060, 950, 915, 810, 738, and 694 cm⁻¹.

A suitable elemental analysis for the alcohol 124 could not be obtained.

Mesylate 125 from Alcohol 124. Alcohol, 124 (2.8 g, 0.01 mole) in anhydrous pyridine (10 ml) was cooled to 0° and methanesulfonyl chloride (1 ml) was added dropwise. The solution was allowed to reach 25° over four hours, cooled, and poured into ice-cold 10% sodium bicarbonate solution (25 ml), and extracted with ether. The extract was washed sequentially with 3% sulfuric acid, water, saturated sodium bicarbonate solution, and saturated ammonium sulfate solution. Upon concentration, 3.0 g (83%) of crude mesylate 125 was isolated; nmr (CDCl₃) δ 1.09 (angular CH₃, s, 3H), 2.9 (-OSO₂CH₃, s, 3H), 4.55 (-CHOSO₂-, t, 1H), 5.65 [ C(9)H, m, 1H], 6.60 [ C(1)H, s, 1H], 7.1–7.7 (arom-H, m, 5H); ir (CHCl₃) 1440, 1330, 1225, 1175, 920, and 760 cm⁻¹.

Hydroboration of the Mesylate 125.

Method A. To a 1.0 molar borane solution in tetrahydrofuran (10 ml), the above mesylate 222 (1 g, 28 mmole) in tetrahydrofuran (15 ml) was added dropwise at 0°, with stirring under nitrogen. The mixture was stirred at 0° for 3 hours, then 1 ml of water was cautiously added followed by 10% sodium hydroxide solution (10 ml) maintaining the
temperature below 5°. Extraction with pentane and concentration in vacuo at 25° yielded the starting mesylate.

Rerun of the above described reaction at 25° or at 50° yielded the starting mesylate.

**Method B.** To a mixture of the above mesylate (500 mgs, 14 mmole) and sodium borohydride (2 g, 52 mmol) in diglyme (100 ml) under nitrogen, cooled to 10° in an ice-salt bath, freshly distilled boron trifluoride etherate (10 g, 85 mmole) in diglyme (50 ml) was added dropwise with stirring. After stirring overnight at 25°, the reaction mixture was cooled to 0° and the excess of hydride decomposed by careful addition of water (2 ml). The resulting solution was poured into 30% sodium hydroxide solution (50 ml), and extracted with ether. The extract was washed five times with equal volumes of ice-water to remove diglyme, dried over anhydrous magnesium sulfate and concentrated in vacuo. Trituration of the residue with carbon tetrachloride afforded 250 mgs (43%) of a white powder of the hydroboration product 126: mp 160°; nmr (acetone-d₆) δ 0.85 (angular) CH₃, s, 3H), 3.1 (-OSO₂CH₃, s, 3H) 4.35-4.80 (CHOSO₂, m, 1H), 6.75 (vinyl-H, s, 1H), 7.1-7.8 (arom-H, m, 5H); ir (CHCl₃) 3350 (-OH), 1600 1225, 1310, 1175, 1110, 920, 785, 755, and 695 cm⁻¹.


**Hydroboration and Fragmentation of the Mesylate 125.** The mesylate 125 was hydroborated internally with sodium borohydride and boron trifluoride etherate in diglyme as described above in Method B. After stirring overnight, the reaction mixture was cooled to 0°, water (2 ml), followed by 30% sodium hydroxide solution (50 ml) was added and refluxed for 1.5 hours. After cooling, the mixture was extracted with ether, and
the extract washed with ice-water, dried, and concentrated. The residue was chromatographed on silica gel eluting with cyclohexane-ethyl acetate (1:1) affording 125 mg (35%) of the cyclodecatriene derivative 127: 

\[ \text{mp } 130°; \text{ nmr } (\text{CDCl}_3) \delta 2.05 (\text{=C-CH}_3, \text{s}, 3\text{H}), 2.25-3.0 (\text{allylic-H, m, 8H}), 6.5 \text{ =C(Ph)=CH-}, \text{s}, 1\text{H}, 6.95-7.70 (\text{arom-H, m, 5H}); \text{ ir } (\text{CHCl}_3) 3050 (\text{-CH=CH-}), \text{ 1720, 1660 (C=CH), 1430, 1160, 935 (trans disubstituted C=C), 820, and 695 cm}^{-1}. \]

Anal. Calcd for C_{19}H_{20}O: C, 86.36; H, 7.57. Found: C, 86.21; H, 7.59.

Pyrolysis of Cyclodecatriene Derivative 127. The above cyclodecatriene 127 (100 mg) was heated at 300° in a sublimation tube under a water pump vacuum. After 5 minutes, the mixture was rapidly cooled with ice water and the residue chromatographed (plc, 2 mm, 3 x, 1:1 cyclohexane-ethyl acetate) giving the Cope product 128 in 20% yield: 

\[ \text{mp } 135°; \text{ nmr } (\text{CDCl}_3) \delta 1.25 (\text{angular CH}_3, \text{s}, 3\text{H}), 4.7-5.3 (\text{CH}=\text{CH}_2, \text{m, 6H}), 6.55 [\text{ =C(Ph)=CH-}, \text{s}, 1\text{H}], 7.0-8.1 (\text{arom-H, m, 5H}) \text{ ir } (\text{CHCl}_3) 3000 (\text{C=CH}_2), 1710, 1650, 1610 (\text{C=C}), 1440, 1375, 1175, 1080, 1025, 975 (\text{terminal } =\text{CH}_2), 930 \text{ and 910 } (\text{CH}=\text{CH}_2). \]
RESULTS AND DISCUSSION

The alcohol 1β-hydroxy-7αβ-methyl-Δ^3(3α)-1,2,4,5,6,7-hexahydroindene (116) was required to synthesize 1-methyl-1,4-cyclononadiene through hydroboration and subsequent solvolytic fragmentation of its methanesulfonate. Scheme X outlined the initially designed plan for obtaining the alcohol 116. The starting material, 2-methylcyclopentane-1,3-dione (105), was prepared according to the literature procedure\(^4\) in 70% yield. Michael addition of methyl vinyl ketone to the dione 105 in refluxing methanolic potassium hydroxide solution afforded the triketone 106. Dehydration of the triketone 106 in boiling benzene in the presence of p-toluenesulfonic acid afforded the known racemic bicyclic diketone 108 in 48% overall yield from 105. The ir spectrum of 108 showed absorption at 1745 cm\(^{-1}\) for α,β-unsaturated ketone. The nmr spectrum exhibited a singlet at δ 1.30 for the angular methyl group and the vinylic proton resonance appeared as a singlet at δ 5.98. The 1-keto group of dione 108 was reduced with lithium aluminum tri(t-butoxy)hydride affording alcohol 109 in 91% yield. The ir spectrum of 109 showed broad absorption between 3250-3500 cm\(^{-1}\) for the hydroxyl group and a conjugated carbonyl band at 1665 cm\(^{-1}\). The nmr spectrum exhibited singlets at δ 1.15 for the angular methyl and at 5.78 for the vinylic proton. The C\(_1\)-proton absorption at δ 3.8 as broad triplet (J = 7 Hz) is characteristic of anα- proton resonance,\(^5\) establishing β-configuration of the hydroxyl group. The IUPAC nomenclature\(^6\) for these compounds is given in the Experimental Section.

From this step onwards, the reaction sequence essentially parallels the synthesis of 9β-methyl-Δ^4(10)octalol-1 (55) as outlined in Scheme VI. The hydroxyl group of the unsaturated keto alcohol 109 was protected by converting to the tetrahydropyranyl ether (110)\(^4\) in 98%
Scheme X

1) LiAl(OBu\(^+\))\(_3\)H
2) THP

109 (R = H)
110 (R = THP)

KOH
C\(_2\)H\(_5\)OH

106

1) LAH
2) MsCl, C\(_5\)H\(_5\)N

112 (R = H)
113 (R = Ms)

114

H\(_3\)O\(^+\)

116

111

KOBu\(^+\), Bu\(^+\)OH

105

108
yield. The nmr spectrum of 110 exhibited a singlet at $\delta$ 1.16 for angular methyl and at 5.76 for the vinylic proton at $C_4$. The absorption at 1665 cm$^{-1}$ in the ir spectrum of 110 corresponds to the $\alpha,\beta$-unsaturated ketone. Deconjugation of the ether 110 was carried out by the method of Ringold and Malhotra, who demonstrated that a steroidal $\alpha,\beta$-unsaturated ketone may be deconjugated by irreversible protonation at oxygen atom of the conjugated anion (derived from treatment of the steroid with potassium tert-butoxide in tert-butyl alcohol) to form an enol which tautomerizes in neutral or weakly acidic media to the $\beta,\gamma$-unsaturated ketone. However, when

pyranylether 110 was subjected to this deconjugation procedure, a mixture of isomeric ethers was obtained. The extent of deconjugation was determined by ir and nmr. The ir spectrum has absorptions at 1710 and 1660 cm$^{-1}$ for deconjugated and conjugated ketones, respectively. Nmr analysis of the reaction mixture showed absorption at $\delta$ 5.22 and 5.70 for the vinyl hydrogen of deconjugated and conjugated ketones, respectively. Thus, the composition of the mixture was estimated from nmr integration to be about 40:60 for deconjugated and conjugated isomers which indicates that deconjugation of 110 was not very successful. The model bicyclic compound 9-methyl-14(10)-octaline-3-one underwent 80% deconjugation under the same experimental conditions. Similar deconjugation of the ether 52 by Marshall, et al., resulted in the formation of at least 85% of $\beta,\gamma$-unsaturated ketone (Scheme VI). The difference in reactivity of 110 and

![Diagram](image-url)
is because of the greater stability of an endo-double bond in a cyclo-
hexane ring. Subsequent removal of the 3-keto group by initial reduction
of the mixture with lithium aluminum hydride to alcohol, conversion to mesylate by reaction with methanesulfonyl chloride in pyridine,
and then hydrogenolysis with lithium in liquid ammonia afforded the pyranal ether. Acid hydrolysis of gave the mixture of unsaturated alcohols. Separation of these alcohols using gas liquid chromatography on 30% SE-30
on 60/80 mesh chromsorb W afforded the isomerically pure alcohols, and hydrolysis, resulting in only 3% over-all yield of the desired alcohol from. Further reactions were not carried out due to lack of product.

An alternative method was envisioned for bond migration from
six-membered ring to five-membered ring by first converting to the
3-enol acetate and then removing the double bond of the six-membered ring by reduction. The envisioned reaction pathway is shown in Scheme XI. The α,β-unsaturated dione was converted to its 3-enol acetate in 92% yield by refluxing with acetic anhydride and acetyl chloride. The ir spectrum of has absorptions at 1775 (acetate) and 1665 cm\(^{-1}\) (carbonyl). The nmr spectrum showed singlets at 1.18 and 2.09 for angular methyl and acetoxyl protons, respectively. The vinyl protons at C\(_3\) and C\(_4\) appear at 5.72 and 6.03, respectively. It has been previously shown by Wendler, et al. that when the reduction of a particular ketonic group from a molecule having more than one keto group was not desirable, this keto group could be effectively protected as its
Scheme XI

$\text{AcCl, } \text{Ac}_2\text{O}$

$\text{MsCl, } \text{C}_5\text{H}_5\text{N}$

$\text{NH}_2\text{CONNH}_2\cdot\text{HCl, CH}_3\text{OH, C}_5\text{H}_5\text{N}$
The semicarbazone derivative. The semicarbazone then makes possible the selective reduction of other carbonyl functions with lithium borohydride, after which the protecting ketonic group could be regenerated by removing the semicarbazone group with pyruvic acid. Accordingly, the keto group in the enol acetate 117 was protected by treatment with semicarbazide hydrochloride, to form enol acetate semicarbazide (118) in 61% yield. The nmr spectrum of 118 showed the vinylic protons of C3 and C4 at δ 5.55 and 6.0, respectively. The enol acetate function in 118 was then reduced with sodium borohydride in aqueous ethanol51,52 affording the semicarbazone of the homoallylic alcohol (119) in 26% yield. Repetition of this reaction by changing the solvent system to aqueous methanol or aqueous tetrahydrofuran or by using lithium borohydride or potassium borohydride did not improve the yield. The semicarbazone group in 119 was then removed with pyruvic acid50 (30%) or using nitrous acid53 (50%), the latter permitting the low temperature reversal of the reduced semicarbazone affording the keto alcohol 120. Subsequent conversion of 120 to methanesulfonate (121), and reduction of 121 with lithium aluminum hydride afforded the desired alcohol 116. However, the overall yield of the alcohol 116 from the dione 108 was only about 2%. The maximum percentage of alcohol 116 formation was not sufficient to warrant any further experiments with this system.

A decision was made to investigate a bicyclodecadiene derivative (124) instead. The use of this compound has several advantages over the above one: i) no discrete deconjugation step is involved; ii) fusion of the furan ring automatically deconjugated the α,β-unsaturated system; and iii) there is not an extra carbonyl group to remove. The starting diketone 37 was prepared by the literature procedure54 in 50% yield.
Steroidal C₃-ketones have been shown by Heyl and Herr⁶₀ to condense readily with pyrrolidine to form 3-(N-pyrrolidyl)enamine with the elimination of water. In those polyketonic steroids having α,β-unsaturated carbonyl groups in the C₃-position and other carbonyl groups elsewhere in the molecule, the reaction is selective on the C₃-position leaving the other functional groups unprotected and available for further study. Thus, the dione 37 was reacted with pyrrolidine by refluxing for 18 hours in the presence of p-toluenesulfonic acid catalyst affording the enamine 122⁵⁵ (Scheme XII). The work-up procedure deviated somewhat from the literature method since the enamine 122 is unstable and decomposes easily. Rather than distillation of the crude reaction mixture,⁵⁵ the volatile materials were removed in vacuo and then the residue was immediately taken to the next step. Thus, the crude enamine 122 on reaction with α-bromoacetophenone formed the furan derivative 123 in 40% yield. The more elaborate IUPAC nomenclature for these compounds is given in the Experimental Section. The ir spectrum of 123 has absorption at 1700 cm⁻¹, characteristic of the carbonyl group. Nmr spectrum of 123 showed absorptions at δ 1.25 for the angular methyl and at 5.89 and 6.65 for the vinylic protons at C₉ and C₁, respectively, in agreement with the structure 123. Reduction of 123 with sodium borohydride afforded the alcohol 124 in quantitative yield. The ir spectrum of 124 showed strong absorption at 3400 cm⁻¹ for the hydroxyl group at C₉ and the nmr spectrum exhibited an angular methyl singlet at δ 1.04 and the vinylic hydrogens of C₉ and C₁ at δ 5.60 and 6.60, respectively. The C₆-proton absorption at δ 3.6 as broad triplet (J = 8 Hz) is again characteristic of an α-proton resonance,⁵⁶ establishing the desired β-configuration of the hydroxyl group. This result is substantiated by analogy of reductions
Scheme XII

\[
\begin{align*}
&\text{37} \\
&\xrightarrow{\text{N} - \text{H}_2\text{O}} \\
&\xrightarrow{\text{C}_6\text{H}_5\text{COCH}_2\text{Br}} \text{DMF} \\
&\xrightarrow{\text{LAH}} \\
&\xrightarrow{\text{MsCl}} \text{C}_5\text{H}_5\text{N} \\
\end{align*}
\]
in similar systems.\textsuperscript{18,44} The rest of the reaction sequence essentially parallels the synthesis of trans, trans-1,5-cyclodecadiene (57) from the octaline mesylate (56) by Marshall and Bundy\textsuperscript{18} (Scheme VI). The alcohol 124 was converted to the mesylate 125 in 83\% yield by reacting with methanesulfonyl chloride in pyridine. The nmr spectrum of 125 showed sharp singlets at $\delta$ 1.09 and 2.9 for the angular methyl and methanesulfonyl groups, respectively. The vinylic protons absorptions at C\textsubscript{9} and C\textsubscript{1} appear at $\delta$ 5.65 and 6.60, respectively. Initial attempts to hydroborate 125 were unsuccessful. The reactions were carried with a 1 Molar borane solution in tetrahydrofuran at 0\textdegree, 25\textdegree, and at 50\textdegree, and the starting mesylate was isolated in each case. But internal hydroboration with sodium borohydride and boron trifluoride etherate in diglyme, followed by alkali treatment at 25\textdegree afforded the boronate mesylate 126,\textsuperscript{19} which was identified by elemental analysis and spectral data. The nmr spectrum of 126 confirmed the lack of olefinic proton at C\textsubscript{9} and the remaining olefinic proton absorption appeared at $\delta$ 6.75. The angular methyl and methanesulfonyl groups exhibited singlets at $\delta$ 0.85 and 3.1, respectively. The ir spectrum exhibited strong absorption at 3350 cm\textsuperscript{-1} indicating the presence of hydroxyl group. Treatment of the mesylate 125 with sodium borohydride and boron trifluoride etherate in diglyme, followed by refluxing with 30\% sodium hydroxide for 1.5 hours,
resulted in the thermal fragmentation of the initially formed boronate mesylate affording the 1,3,5-cyclodecatriene derivative (127). This product must arise via the pathway depicted below, wherein the boronate mesylate adopts the anti-periplanar conformation which favors concerted 1,4-fragmentation. The IR spectrum of 127 exhibited absorption at 935 cm\(^{-1}\) indicating the presence of trans disubstituted double bonds. The other absorptions appear at 3050 (CH=CH\(-\)), 1720, and 1660 (C=C). The NMR spectrum displayed a three protons singlet at \(\delta\) 2.05 for the vinylic methyl protons and the vinyl proton at C\(_1\) appeared at \(\delta\) 6.5 as a sharp singlet. The remaining vinyl protons exhibited broad absorption between \(\delta\) 4.65-5.10. Pyrolysis of 127 at 300\(^\circ\) afforded the Cope product 128 which was characterized by its IR and NMR spectra. The absorptions at 975 and 910 cm\(^{-1}\), in the IR spectrum of 128 are characteristic of the =CH\(_2\) groups. The NMR spectrum exhibited a sharp singlet of three protons at \(\delta\) 1.25 for the angular methyl group. The vinyl protons at C\(_6\), C\(_7\), C\(_8\),
C\(_9\) appear as complex absorption between \(\delta 4.7-5.3\). The vinyl proton at C\(_1\) exhibited a sharp singlet at \(\delta 6.55\). Thus the results indicate that solvolytic fragmentation of 126 shows high preference for internal cleavage to form the 1,5,7-cyclodecatriene derivative (127) and the product 128 is formed from Cope rearrangement of 127 and not directly from 126.
SUMMARY AND CONCLUSIONS

Medium ring compounds provide a class of chemically interesting and synthetically challenging structures. The importance of 1,5-cyclooctadienes as natural products and their vital role in the biosynthesis of terpenes and steroids has stimulated the development of new methods for their efficient synthesis. Synthesis of 1,5,7-cyclodecatriene derivative (127) through the solvolytic fragmentation of the boronate mesylate derivative (126) is described.

Mesylate 125 was synthesized from the commercially available 2-methyl-1,3-cyclohexanone by a five-steps sequence synthesis. Although 125 is unreactive towards hydroboration with a borane solution in tetrahydrofuran, it could be easily hydroborated using sodium borohydride and boron trifluoride etherate in diglyme. Solvolytic fragmentation of 126 afforded 127. The fragmentation reaction showed a remarkably high preference for internal cleavage and indicated that the direction specificity of the cleavage was controlled by C-C bond strength, the product arising via cleavage of the more highly substituted C-C bond, a conclusion which has several well documented analogies. Cope product 128 was obtained by pyrolysis of 127.

Alcohols 115 and 116 were prepared by ten-steps sequence with a view to synthesize 1-methyl-1,4- and 1,5-cyclononadienes. But the overall yields were very poor and further reaction was not carried out.
REFERENCES

87, 3996 (1965).
Abstr., 76, 126456t (1972).
Chem. Abstr., 76, 153242z (1972).


VITA

Nafisa Begum is a native of Bangalore, India, where she completed her elementary and secondary education in private school systems. She received her B.Sc., Degree from Mysore University, Bangalore, in 1964, and her M.Sc. Degree in 1966. During 1962 to 1966, she received Government of India Merit Scholarship. She served as Lecturer in Chemistry at Maharani's College, Bangalore, for two years, and in September of 1968, she entered the Graduate School of Louisiana State University in Baton Rouge, where she is now a candidate for the Doctor of Philosophy Degree in Chemistry with a major in Organic Chemistry and a minor in Inorganic Chemistry.

In August of 1970, she was married to Mir N. Islam. She is the mother of a 2½-year-old boy, Najmi.

She is a member of Phi Kappa Phi, Iota Sigma Pi, and Phi Lambda Upsilon.
Candidate: Nafisa B. Islam

Major Field: Chemistry


Approved:

[Signature]
Major Professor and Chairman

[Signature]
Dean of the Graduate School

EXAMINING COMMITTEE:

[Signature]

[Signature]

[Signature]

Date of Examination:

April 18, 1975