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
JELINSKI, Lynn Woodard, 1949-
DISSYMMETRIC 1,3-DIENES SYNTHSES AND
DYNAMIC NMR MEASUREMENTS.

University of Hawaii, Ph.D., 1976
Chemistry, organic

Xerox University Microfilms, Ann Arbor, Michigan 48106
DISSYMMETRIC 1,3-DIENES

SYNTHESES AND DYNAMIC NMR MEASUREMENTS

A DISSERTATION SUBMITTED TO THE GRADUATE DIVISION OF THE
UNIVERSITY OF HAWAII IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

IN CHEMISTRY

AUGUST 1976

By

Lynn W. Jelinski

Dissertation Committee

Edgar F. Kiefer, Chairman
Thomas T. Bopp
Richard J. Guillory
Robert S. H. Liu
Paul J. Scheuer
I am grateful to Professor R. M. Kellogg of the University of Gronigen, The Netherlands, for his generous gift of $\text{trans}$-2,5-di-$\text{tert}$-butyl-3,4-dicarbomethoxy-2,5-dihydrothiophene.
ABSTRACT

Dissymmetric 1,3-Dienes
Syntheses and Dynamic Nmr Measurements

When sufficiently congested, 1,3-dienes are forced to adopt skewed conformations which are chiral. A number of new atropisomeric 1,3-dienes of structural types I, II, III, and IV have been synthesized and their nmr barriers to rotation about the sp² - sp² single bond have been determined by dynamic nmr.

Racemization rates for the 5-membered cyclic compounds I were found to be very sensitive to heteroatom substitution (∆G⁺ ranged from 8.0 kcal/mol for R = O to 15.45 kcal/mol for R = SO₂), whereas the energy barriers for the acyclic analogues II were less dependent upon the nature of R (∆G⁺ = 19.0 kcal/mol for R = CN to 20.9 kcal/mol for R = SAC). This is explained in terms of the bond length and bond angle changes enforced in the cyclic compounds I in comparison to a relatively constant "buttressing effect" present in the acyclic compounds II.

A substantial increase in the free energy of racemization for compounds III could be realized by the addition of nitrogen (diamino or diamido) to the ring system. The low and high temperature dynamical nmr processes observed in compounds III were assigned to nitrogen inversions and ring-flipping, respectively.
Estimates for the free energy barrier to rotation about the $sp^2 - sp^2$ single bond in the dineopentylidene compounds IV were made in the presence of an optically active shift reagent. The $(E,E)$-dineopentylidene system was found to have a $\Delta G^\ddagger$ in excess of 24 kcal/mol, whereas the free energy barrier for the $(E,Z)$-dineopentylidene system was less than 15 kcal/mol.
TABLE OF CONTENTS

ACKNOWLEDGMENTS ........................................ iii

ABSTRACT .................................................. iv

LIST OF TABLES ........................................... xiii

LIST OF ILLUSTRATIONS ................................... xiv

LIST OF STRUCTURES ...................................... xxii

I. INTRODUCTION

A. Formulation of the Problem .......................... 1

B. Historical Background of the Study of Dissymmetric 1,3-Dienes ................................. 2

C. Use of Dynamic Nmr to Determine Free Energies of Racemization ............................ 12

II. EXPERIMENTAL

A. General

1. Instruments ........................................ 17

2. Solvents, Reagents, Materials .................... 18
   a. Purification .................................. 18
   b. Miscellaneous Materials, Reagents, Procedures ... 19

B. Syntheses and Properties of Compounds

1. Acyclic Diisopropylidene Compounds
   a. Ethyl Hydrogen Isopropylidenesuccinate, 25 .... 24
   b. Diethyl Isopropylidenesuccinate, 26 ........ 25
   c. Ethyl Hydrogen Diisopropylidene-succinate, 27 .... 25
   d. 2,3-Diisopropylidene-1,4-butanediol, 28 .... 26
   e. 2,3-Diisopropylidene-1,4-dibromobutane, 29 .... 27
   f. 2,3-Diisopropylidene-1,4-diazipobutane, 30 .... 28
2,3-Diisopropylidene-1,4-diethoxybutane, \( g \)...
2,3-Diisopropylidene-1,4-dicyanobutane, \( h \)...
2,3-Diisopropylidene-1,4-butane-dithiolacetate, \( i \)...
2,3-Diisopropylidene-1,4-butanediacetate, \( j \)...
Diisopropylidenedisuccinic acid, \( k \)...
Dimethyl Diisopropylidenedisuccinate, \( l \)...
3,4-Diisopropylidene-2,5-dimethyl-2,5-hexanediol, \( m \)...

2. Cyclic 5-Membered Ring Diisopropylidene Compounds

a. 3,4-Diisopropylidenetetrahydrothiophene, \( 38 \)...
b. 3,4-Diisopropylidenetetrahydrothiophene-1-oxide, \( 39 \)...
c. 3,4-Diisopropylidenetetrahydrothiophene-1,1-dioxide, \( 40 \)...
d. 3,4-Diisopropylideneden-N-methylpyrrolidine, \( 41 \)...
e. 3,4-Diisopropylideneden-N-benzylpyrrolidine, \( 42 \)...
f. 3,4-Diisopropylidenetetrahydrofuran, \( 43 \)...
g. 3,4-Diisopropylideneden-N,N-dimethylpyrrolidinium bromide, \( 44 \)...
h. 3,4-Diisopropylideneden-1,1-dicarbethoxy-cyclopentane, \( 45 \)...
i. 3,4-Diisopropylideneden-2,2,5,5-tetramethyl-tetrahydrofuran, \( 46 \)...

3. Cyclic 6-Membered Ring Diisopropylidene Compounds

a. 3,4-Diisopropylideneden-1,2-dimethylhexahydropyridazine, \( 47 \)...
b. 3,4-Diisopropylideneden-1,2-dibenzyhexahydropyridazine, \( 48 \)...

Page
\( 29 \)
\( 30 \)
\( 31 \)
\( 31 \)
\( 32 \)
\( 33 \)
\( 33 \)
\( 34 \)
\( 35 \)
\( 36 \)
\( 37 \)
\( 37 \)
\( 38 \)
\( 39 \)
\( 40 \)
\( 41 \)
\( 42 \)
\( 43 \)
c. 3,4-Diisopropylidene-8-phenyl-1,6,8-triazobicyclo[4.3.0]nonane-7,9-dione, 49

4. Dineopentylidene Compounds

a. Trans-2,5-di-tert-butyl-3,4-dicarbomethoxy-2,5-dihydrothiophene-1,1-dioxide, 51
b. Dimethyl (E,Z)-Dineopentylidenesuccinate, 52

46

47

47

48

49

50

50

51

52

53

53

54

54

55

55

56
| h. Ethyl Hydrogen (E)-α-Benzylidene-α'-isopropyldenedesuccinate, 67a | 56 |
| i. Dimethyl (E)-α-Benzylidene-α'-isopropyldenedesuccinate, 68 | 57 |
| j. Dimethyl (Z)-α-Benzylidene-α'-isopropyldenedesuccinate, 69 | 58 |
| k. (E)-3-Benzylidene-4-isopropylidene-2,5-dimethyl-2,5-hexanediol, 70 | 59 |
| l. (E)-3-Benzylidene-4-isopropylidene-2,2,5,5-tetramethyltetrahydrofuran, 71 | 59 |
| m. (Z)-3-Benzylidene-4-isopropylidene-2,5-dimethyl-2,5-hexanediol, 72 | 60 |
| n. (Z)-3-Benzylidene-4-isopropylidene-2,2,5,5-tetramethyltetrahydrofuran, 73 | 61 |
| o. 3-Benzyl-4-isopropenyl-2,2,5,5-tetramethyl-2,5-dihydrofuran, 74 | 61 |
| p. Diisopropyldenedesuccinic anhydride, 75 | 62 |
| q. 2,5-Dimethyl-4-(hydrazinocarbonylhydrochloride)-2,4-hexadiene-3-carboxylic acid, 76 | 63 |
| r. 2,5-Dimethyl-4-(aminocarbonyl)2,4-hexadiene-3-carboxylic acid, 77 | 63 |
| s. 2,5-Dimethyl-4-(N-methyaminocarbonyl)-2,4-hexadiene-3-carboxylic acid, 78 | 64 |
| t. 2,5-Dimethyl-4-(N,N-dimethyaminocarbonyl)-2,4-hexadiene-3-carboxylic acid, 79 | 65 |
| u. 2,3,7,8-Tetraisopropyldened-perhydro-1,4,6,9-tetraketopyridazine [1,2-a]pyridazine, 80 | 66 |
| v. N,N-Bis(3,4-diisopropyldenedesuccinimide), 81 | 67 |
| w. 2,5-Dimethyl-4-carbethoxy-2,4-hexadiene-3-carbonyl chloride, 82 | 69 |
III. RESULTS AND DISCUSSION

A. Syntheses

1. Acyclic Diisopropylidene Compounds

2. Cyclic Five-membered Ring Diisopropylidene Compounds

3. Cyclic Six-membered Ring Diisopropylidene Compounds

4. Dineopentylidene Compounds

5. Miscellaneous 1,3-Dienes

6. Unsuccessful Synthetic Attempts

7. Summary of Syntheses
   a. Generality of the Stobbe Condensation
   b. Tendency for Five-membered Ring Formation
   c. The Dineopentylidene Series of Compounds

B. Dynamic Nmr Results

1. Table of DnMr Results
2. Dynamic Nmr Results for Individual Compounds

a. 3,4-Diisopropylidene-2,2,5,5-tetramethyl-tetrahydrofuran, 46  
   109

b. (E)-Benzylidene-4-isopropylidene-2,2,5,5-tetramethyltetrahydrofuran, 71  
   114

c. 2,3-Diisopropylidene-1,4-butanediol, 28  
   117

d. 2,3-Diisopropylidene-1,4-dibromobutane, 29  
   123

e. 2,3-Diisopropylidene-1,4-dicyanobutane, 32  
   128

f. 2,3-Diisopropylidene-1,4-butane-dithiolacetate, 33  
   129

g. 1,2-Diisopropylidene-3,3,4,4-tetramethyl-cyclobutane, 60  
   130

h. 4,5-Diisopropylidene-1,2-dimethylhexahydropyridazine, 47  
   131

i. 4,5-Diisopropylidene-1,2-dibenzylhexahydropyridazine, 48  
   139

j. 3,4-Diisopropylidenetetrahydrothiophene, 38  
   142

k. 3,4-Diisopropylidenetetrahydrothiophene-1-oxide, 39  
   146

l. 3,4-Diisopropylidenetetrahydrothiophene-1,1-dioxide, 40  
   149

m. 3,4-Diisopropylidene-N-methylpyrrolidine, 41  
   153

n. 3,4-Diisopropylidene-N-benzylpyrrolidine, 42  
   154

o. 3,4-Diisopropylidenetetrahydrofuran, 43  
   155

p. 3,4-Diisopropylidene-1,1-dicarbethoxy-cyclopentane, 45  
   160

q. Dimethyl (E,E)-Dineopentylidenesuccinate, 53  
   165

r. Dimethyl (E,Z)-Dineopentylidenesuccinate, 52  
   166
3. Error Involved in the DnMr Results 167

4. Discussion of Dynamic Nmr Results
   a. Cyclic 1,3-Dienes 170
   b. Acyclic 1,3-Dienes 171

C. Resolution Attempts 173
   1. Metal Complexes
      a. Nickel (II) Complexes 173
      b. Platinum (II) Complex 174
   2. Chiral Reducing Agent 175
   3. Reduction of the Chiral Ester 176
      a. Reaction of the Diene-diol 28 with Phthalic Anhydride 178
      b. Attempts to Functionalize Compound 49 179
   4. Column Chromatography on (-)-TAPA-impregnated Silica Gel 176
   5. Classical Resolution Attempts 178
      a. Reaction of the Diene-diol 28 with Phthalic Anhydride 178
      b. Attempts to Functionalize Compound 49 179
   D. CNDO/2 Calculation for a Model 1,3-Diene System 181
   E. \(^{13}\)C T\(_1\) Measurement for the Diene-diol 28 184

IV. APPENDIX-Spectral Data For Synthetic Products 186

V. LITERATURE CITED 312
## LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(E)/(Z) Product Ratios from the Stobbe Condensation</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>Dynamic Nmr Data</td>
<td>105</td>
</tr>
<tr>
<td>3</td>
<td>Dynamic Nmr Data for Compound 46</td>
<td>113</td>
</tr>
<tr>
<td>4</td>
<td>Dynamic Nmr Data for Compound 28</td>
<td>121</td>
</tr>
<tr>
<td>5</td>
<td>Dynamic Nmr Data for Compound 29</td>
<td>127</td>
</tr>
<tr>
<td>6</td>
<td>Dynamic Nmr Data for Compound 38</td>
<td>145</td>
</tr>
<tr>
<td>7</td>
<td>Dynamic Nmr Data for Compound 40</td>
<td>152</td>
</tr>
<tr>
<td>8</td>
<td>Dynamic Nmr Data for Compound 43</td>
<td>159</td>
</tr>
<tr>
<td>9</td>
<td>Dynamic Nmr Data for Compound 45</td>
<td>164</td>
</tr>
</tbody>
</table>
### LIST OF ILLUSTRATIONS

<table>
<thead>
<tr>
<th>Figure</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The nmr time scale</td>
<td>12</td>
</tr>
<tr>
<td>2</td>
<td>Typical temperature-dependent nmr spectra for the AB region in the coupled AB case</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>Percent transmission curves for Corning filters</td>
<td>23</td>
</tr>
<tr>
<td>4</td>
<td>Experimental and calculated dnmr spectra for compound 46</td>
<td>111</td>
</tr>
<tr>
<td>5</td>
<td>Arrhenius plot for compound 46</td>
<td>112</td>
</tr>
<tr>
<td>6</td>
<td>Experimental and calculated dnmr spectra for compound 28</td>
<td>119</td>
</tr>
<tr>
<td>7</td>
<td>Arrhenius plot for compound 28</td>
<td>120</td>
</tr>
<tr>
<td>8</td>
<td>Nmr spectra of compound 28 in the presence of the chiral shift reagent Eu(tfc)$_3$</td>
<td>122</td>
</tr>
<tr>
<td>9</td>
<td>Experimental and calculated dnmr spectra for compound 29</td>
<td>125</td>
</tr>
<tr>
<td>10</td>
<td>Arrhenius plot for compound 29</td>
<td>126</td>
</tr>
<tr>
<td>11</td>
<td>Experimental dnmr spectra for compound 47</td>
<td>136</td>
</tr>
<tr>
<td>12</td>
<td>Experimental high temperature dnmr spectra for compound 47</td>
<td>138</td>
</tr>
<tr>
<td>13</td>
<td>Experimental low temperature dnmr spectra for compound 48</td>
<td>140</td>
</tr>
<tr>
<td>14</td>
<td>Experimental high temperature dnmr spectra for compound 48</td>
<td>141</td>
</tr>
<tr>
<td>15</td>
<td>Experimental and calculated dnmr spectra for compound 38</td>
<td>143</td>
</tr>
<tr>
<td>16</td>
<td>Arrhenius plot for compound 38</td>
<td>144</td>
</tr>
<tr>
<td>17</td>
<td>Experimental dnmr spectra for compound 39</td>
<td>148</td>
</tr>
<tr>
<td>18</td>
<td>Experimental and calculated dnmr spectra for compound 40</td>
<td>150</td>
</tr>
<tr>
<td>19</td>
<td>Arrhenius plot for compound 40</td>
<td>151</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>20</td>
<td>Experimental and calculated dnmr spectra for compound 43</td>
<td>157</td>
</tr>
<tr>
<td>21</td>
<td>Arrhenius plot for compound 43</td>
<td>158</td>
</tr>
<tr>
<td>22</td>
<td>Experimental and calculated dnmr spectra for compound 45</td>
<td>162</td>
</tr>
<tr>
<td>23</td>
<td>Arrhenius plot for compound 45</td>
<td>163</td>
</tr>
<tr>
<td>24</td>
<td>Results of CNDO/2 calculations for the model diene system 108</td>
<td>183</td>
</tr>
<tr>
<td>25</td>
<td>Spin-lattice relaxation time results for compound 28</td>
<td>185</td>
</tr>
<tr>
<td>A-1</td>
<td>Nmr spectrum of compound 26</td>
<td>187</td>
</tr>
<tr>
<td>A-2</td>
<td>Nmr spectrum of compound 27</td>
<td>188</td>
</tr>
<tr>
<td>A-3</td>
<td>Nmr spectrum of compound 28</td>
<td>189</td>
</tr>
<tr>
<td>A-4</td>
<td>$^{13}$C Nmr spectrum of compound 28</td>
<td>190</td>
</tr>
<tr>
<td>A-5</td>
<td>Ir spectrum of compound 28</td>
<td>191</td>
</tr>
<tr>
<td>A-6</td>
<td>Mass spectrum of compound 28</td>
<td>192</td>
</tr>
<tr>
<td>A-7</td>
<td>Nmr spectrum of compound 29</td>
<td>193</td>
</tr>
<tr>
<td>A-8</td>
<td>Ir spectrum of compound 29</td>
<td>194</td>
</tr>
<tr>
<td>A-9</td>
<td>Mass spectrum of compound 29</td>
<td>195</td>
</tr>
<tr>
<td>A-10</td>
<td>Nmr spectrum of compound 30</td>
<td>196</td>
</tr>
<tr>
<td>A-11</td>
<td>Ir spectrum of compound 30</td>
<td>197</td>
</tr>
<tr>
<td>A-12</td>
<td>Mass spectrum of compound 30</td>
<td>198</td>
</tr>
<tr>
<td>A-13</td>
<td>Nmr spectrum of compound 31</td>
<td>199</td>
</tr>
<tr>
<td>A-14</td>
<td>Nmr spectrum of compound 32</td>
<td>200</td>
</tr>
<tr>
<td>A-15</td>
<td>Ir spectrum of compound 32</td>
<td>201</td>
</tr>
<tr>
<td>A-16</td>
<td>Mass spectrum of compound 32</td>
<td>202</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>A-17</td>
<td>Nmr spectrum of compound 33</td>
<td>203</td>
</tr>
<tr>
<td>A-18</td>
<td>Ir spectrum of compound 33</td>
<td>204</td>
</tr>
<tr>
<td>A-19</td>
<td>Nmr spectrum of compound 34</td>
<td>205</td>
</tr>
<tr>
<td>A-20</td>
<td>Nmr spectrum of compound 35</td>
<td>206</td>
</tr>
<tr>
<td>A-21</td>
<td>Ir spectrum of compound 35</td>
<td>207</td>
</tr>
<tr>
<td>A-22</td>
<td>Nmr spectrum of compound 36</td>
<td>208</td>
</tr>
<tr>
<td>A-23</td>
<td>Nmr spectrum of compound 37</td>
<td>209</td>
</tr>
<tr>
<td>A-24</td>
<td>Ir spectrum of compound 37</td>
<td>210</td>
</tr>
<tr>
<td>A-25</td>
<td>Mass spectrum of compound 37</td>
<td>211</td>
</tr>
<tr>
<td>A-26</td>
<td>Nmr spectrum of compound 38</td>
<td>212</td>
</tr>
<tr>
<td>A-27</td>
<td>Ir spectrum of compound 38</td>
<td>213</td>
</tr>
<tr>
<td>A-28</td>
<td>Mass spectrum of compound 38</td>
<td>214</td>
</tr>
<tr>
<td>A-29</td>
<td>Nmr spectrum of compound 39</td>
<td>215</td>
</tr>
<tr>
<td>A-30</td>
<td>Ir spectrum of compound 39</td>
<td>216</td>
</tr>
<tr>
<td>A-31</td>
<td>Mass spectrum of compound 39</td>
<td>217</td>
</tr>
<tr>
<td>A-32</td>
<td>Nmr spectrum of compound 40</td>
<td>218</td>
</tr>
<tr>
<td>A-33</td>
<td>Ir spectrum of compound 40</td>
<td>219</td>
</tr>
<tr>
<td>A-34</td>
<td>Mass spectrum of compound 40</td>
<td>220</td>
</tr>
<tr>
<td>A-35</td>
<td>Nmr spectrum of compound 41</td>
<td>221</td>
</tr>
<tr>
<td>A-36</td>
<td>Ir spectrum of compound 41</td>
<td>222</td>
</tr>
<tr>
<td>A-37</td>
<td>Mass spectrum of compound 41</td>
<td>223</td>
</tr>
<tr>
<td>A-38</td>
<td>Nmr spectrum of compound 42</td>
<td>224</td>
</tr>
<tr>
<td>A-39</td>
<td>Ir spectrum of compound 42</td>
<td>225</td>
</tr>
<tr>
<td>A-40</td>
<td>Mass spectrum of compound 42</td>
<td>226</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>-------------</td>
<td>------</td>
</tr>
<tr>
<td>A-41</td>
<td>Nmr spectrum of compound 43</td>
<td>227</td>
</tr>
<tr>
<td>A-42</td>
<td>Ir spectrum of compound 43</td>
<td>228</td>
</tr>
<tr>
<td>A-43</td>
<td>Mass spectrum of compound 43</td>
<td>229</td>
</tr>
<tr>
<td>A-44</td>
<td>Nmr spectrum of compound 45</td>
<td>230</td>
</tr>
<tr>
<td>A-45</td>
<td>Ir spectrum of compound 45</td>
<td>231</td>
</tr>
<tr>
<td>A-46</td>
<td>Mass spectrum of compound 45</td>
<td>232</td>
</tr>
<tr>
<td>A-47</td>
<td>Nmr spectrum of compound 46</td>
<td>233</td>
</tr>
<tr>
<td>A-48</td>
<td>Nmr spectrum of the hydrochloride salt of compound 47</td>
<td>234</td>
</tr>
<tr>
<td>A-49</td>
<td>Ir spectrum of the hydrochloride salt of compound 47</td>
<td>235</td>
</tr>
<tr>
<td>A-50</td>
<td>Mass spectrum of the hydrochloride salt of compound 47</td>
<td>236</td>
</tr>
<tr>
<td>A-51</td>
<td>Nmr spectrum of compound 47</td>
<td>237</td>
</tr>
<tr>
<td>A-52</td>
<td>$^{13}$C Nmr spectrum of compound 47</td>
<td>238</td>
</tr>
<tr>
<td>A-53</td>
<td>Nmr spectrum of compound 48</td>
<td>239</td>
</tr>
<tr>
<td>A-54</td>
<td>Ir spectrum of compound 48</td>
<td>240</td>
</tr>
<tr>
<td>A-55</td>
<td>Mass spectrum of compound 48</td>
<td>241</td>
</tr>
<tr>
<td>A-56</td>
<td>Nmr spectrum of compound 49</td>
<td>242</td>
</tr>
<tr>
<td>A-57</td>
<td>Ir spectrum of compound 49</td>
<td>243</td>
</tr>
<tr>
<td>A-58</td>
<td>Nmr spectrum of compound 51</td>
<td>244</td>
</tr>
<tr>
<td>A-59</td>
<td>Ir spectrum of compound 51</td>
<td>245</td>
</tr>
<tr>
<td>A-60</td>
<td>Nmr spectrum of compound 52</td>
<td>246</td>
</tr>
<tr>
<td>A-61</td>
<td>Mass spectrum of compound 52</td>
<td>247</td>
</tr>
<tr>
<td>A-62</td>
<td>Nmr spectrum of compound 53</td>
<td>248</td>
</tr>
<tr>
<td>A-63</td>
<td>Nmr spectrum of compound 54</td>
<td>249</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>A-64</td>
<td>Nmr spectrum of compound 55</td>
<td>250</td>
</tr>
<tr>
<td>A-65</td>
<td>Nmr spectrum of compound 56</td>
<td>251</td>
</tr>
<tr>
<td>A-66</td>
<td>Nmr spectrum of compound 57</td>
<td>252</td>
</tr>
<tr>
<td>A-67</td>
<td>Ir spectrum of compound 57</td>
<td>253</td>
</tr>
<tr>
<td>A-68</td>
<td>Mass spectrum of compound 57</td>
<td>254</td>
</tr>
<tr>
<td>A-69</td>
<td>Nmr spectrum of compound 58</td>
<td>255</td>
</tr>
<tr>
<td>A-70</td>
<td>Mass spectrum of compound 58</td>
<td>256</td>
</tr>
<tr>
<td>A-71</td>
<td>Nmr spectrum of compound 59</td>
<td>257</td>
</tr>
<tr>
<td>A-72</td>
<td>Mass spectrum of compound 59</td>
<td>258</td>
</tr>
<tr>
<td>A-73</td>
<td>Nmr spectrum of compound 62</td>
<td>259</td>
</tr>
<tr>
<td>A-74</td>
<td>Nmr spectrum of compound 64</td>
<td>260</td>
</tr>
<tr>
<td>A-75</td>
<td>Nmr spectrum of compound 65</td>
<td>261</td>
</tr>
<tr>
<td>A-76</td>
<td>Ir spectrum of compound 65</td>
<td>262</td>
</tr>
<tr>
<td>A-77</td>
<td>Nmr spectrum of compound 66</td>
<td>263</td>
</tr>
<tr>
<td>A-78</td>
<td>Ir spectrum of compound 66</td>
<td>264</td>
</tr>
<tr>
<td>A-79</td>
<td>Nmr spectrum of the hydrolysis product of compound 67a</td>
<td>265</td>
</tr>
<tr>
<td>A-80</td>
<td>Ir spectrum of the hydrolysis product of compound 67a</td>
<td>266</td>
</tr>
<tr>
<td>A-81</td>
<td>Nmr spectrum of compound 68</td>
<td>267</td>
</tr>
<tr>
<td>A-82</td>
<td>Nmr spectrum of a mixture of compounds 68 and 69</td>
<td>268</td>
</tr>
<tr>
<td>A-83</td>
<td>Nmr spectrum of compound 70</td>
<td>269</td>
</tr>
<tr>
<td>A-84</td>
<td>Ir spectrum of compound 70</td>
<td>270</td>
</tr>
<tr>
<td>A-85</td>
<td>Nmr spectrum of compound 71</td>
<td>271</td>
</tr>
<tr>
<td>A-86</td>
<td>$^{13}$C Nmr spectrum of compound 71</td>
<td>272</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>--------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>A-87</td>
<td>Ir spectrum of compound 71</td>
<td>273</td>
</tr>
<tr>
<td>A-88</td>
<td>Mass spectrum of compound 71</td>
<td>274</td>
</tr>
<tr>
<td>A-89</td>
<td>Nmr spectrum of compound 73</td>
<td>275</td>
</tr>
<tr>
<td>A-90</td>
<td>Nmr spectrum of compound 74</td>
<td>276</td>
</tr>
<tr>
<td>A-91</td>
<td>Nmr spectrum of compound 75</td>
<td>277</td>
</tr>
<tr>
<td>A-92</td>
<td>Ir spectrum of compound 75</td>
<td>278</td>
</tr>
<tr>
<td>A-93</td>
<td>Nmr spectrum of compound 76</td>
<td>279</td>
</tr>
<tr>
<td>A-94</td>
<td>Ir spectrum of compound 76</td>
<td>280</td>
</tr>
<tr>
<td>A-95</td>
<td>Mass spectrum of compound 76</td>
<td>281</td>
</tr>
<tr>
<td>A-96</td>
<td>Ir spectrum of compound 77</td>
<td>282</td>
</tr>
<tr>
<td>A-97</td>
<td>Mass spectrum of compound 77</td>
<td>283</td>
</tr>
<tr>
<td>A-98</td>
<td>Nmr spectrum of compound 78</td>
<td>284</td>
</tr>
<tr>
<td>A-99</td>
<td>Ir spectrum of compound 78</td>
<td>285</td>
</tr>
<tr>
<td>A-100</td>
<td>Mass spectrum of compound 78</td>
<td>286</td>
</tr>
<tr>
<td>A-101</td>
<td>Nmr spectrum of compound 79</td>
<td>287</td>
</tr>
<tr>
<td>A-102</td>
<td>Ir spectrum of compound 79</td>
<td>288</td>
</tr>
<tr>
<td>A-103</td>
<td>Mass spectrum of compound 79</td>
<td>289</td>
</tr>
<tr>
<td>A-104</td>
<td>Nmr spectrum of compound 80</td>
<td>290</td>
</tr>
<tr>
<td>A-105</td>
<td>Ir spectrum of compound 80</td>
<td>291</td>
</tr>
<tr>
<td>A-106</td>
<td>Mass spectrum of compound 80</td>
<td>292</td>
</tr>
<tr>
<td>A-107</td>
<td>Nmr spectrum of compound 81</td>
<td>293</td>
</tr>
<tr>
<td>A-108</td>
<td>Ir spectrum of compound 81</td>
<td>294</td>
</tr>
<tr>
<td>A-109</td>
<td>Mass spectrum of compound 81</td>
<td>295</td>
</tr>
<tr>
<td>A-110</td>
<td>Nmr spectrum of compound 82</td>
<td>296</td>
</tr>
<tr>
<td>Figure</td>
<td>Description</td>
<td>Page</td>
</tr>
<tr>
<td>----------</td>
<td>------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>A-111</td>
<td>Ir spectrum of compound 82</td>
<td>297</td>
</tr>
<tr>
<td>A-112</td>
<td>Mass spectrum of compound 82</td>
<td>298</td>
</tr>
<tr>
<td>A-113</td>
<td>Nmr spectrum of compound 83</td>
<td>299</td>
</tr>
<tr>
<td>A-114</td>
<td>Ir spectrum of compound 83</td>
<td>300</td>
</tr>
<tr>
<td>A-115</td>
<td>Mass spectrum of compound 83</td>
<td>301</td>
</tr>
<tr>
<td>A-116</td>
<td>Nmr spectrum of compound 84</td>
<td>302</td>
</tr>
<tr>
<td>A-117</td>
<td>Nmr spectrum of a mixture of compounds 86 and 87</td>
<td>303</td>
</tr>
<tr>
<td>A-118</td>
<td>Ir spectrum of a mixture of compounds 86 and 87</td>
<td>304</td>
</tr>
<tr>
<td>A-119</td>
<td>Nmr spectrum of a mixture of compounds 88 and 89</td>
<td>305</td>
</tr>
<tr>
<td>A-120</td>
<td>Ir spectrum of a mixture of compounds 88 and 89</td>
<td>306</td>
</tr>
<tr>
<td>A-121</td>
<td>Nmr spectrum of compound 93</td>
<td>307</td>
</tr>
<tr>
<td>A-122</td>
<td>Ir spectrum of compound 93</td>
<td>308</td>
</tr>
<tr>
<td>A-123</td>
<td>Nmr spectrum of compound 106</td>
<td>309</td>
</tr>
<tr>
<td>A-124</td>
<td>Ir spectrum of compound 106</td>
<td>310</td>
</tr>
<tr>
<td>A-125</td>
<td>Mass spectrum of compound 106</td>
<td>311</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Scheme</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acyclic Diisopropylidene Compounds</td>
<td>81</td>
</tr>
<tr>
<td>2</td>
<td>Cyclic Five-membered Ring Diisopropylidene Compounds</td>
<td>83</td>
</tr>
<tr>
<td>3</td>
<td>Cyclic Six-membered Ring Diisopropylidene Compounds</td>
<td>84</td>
</tr>
<tr>
<td>4</td>
<td>Dineopentylidene Compounds</td>
<td>85</td>
</tr>
<tr>
<td>5</td>
<td>Miscellaneous 1,3-Dienes</td>
<td>86</td>
</tr>
<tr>
<td>6</td>
<td>Miscellaneous 1,3-Dienes</td>
<td>86</td>
</tr>
<tr>
<td>Scheme</td>
<td>Title</td>
<td>Page</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>7</td>
<td>Miscellaneous 1,3-Dienes</td>
<td>87</td>
</tr>
<tr>
<td>8</td>
<td>Miscellaneous 1,3-Dienes</td>
<td>88</td>
</tr>
<tr>
<td>9</td>
<td>Miscellaneous 1,3-Dienes</td>
<td>89</td>
</tr>
<tr>
<td>10</td>
<td>Miscellaneous 1,3-Dienes</td>
<td>90</td>
</tr>
<tr>
<td>11</td>
<td>Unsuccessful Attempts to Obtain Cyclic Seven-membered Ring Compounds</td>
<td>91</td>
</tr>
<tr>
<td>12</td>
<td>Miscellaneous Unsuccessful Synthetic Attempts</td>
<td>93</td>
</tr>
<tr>
<td>13</td>
<td>Mechanism of the Stobbe Condensation</td>
<td>96</td>
</tr>
</tbody>
</table>
LIST OF STRUCTURES

1

2

3

4

5

6

7

8

9
I. INTRODUCTION

A. Formulation of the Problem

Although highly symmetrical chiral molecules such as the allenes, spiranes, and biphenyls have long been regarded with theoretical interest,¹ the dissymmetric 1,3-dienes ¹ and ², which represent a special class of such compounds had until recently, escaped systematic study.

When rotation about the sp² - sp² single bond (C₁ - C₂) is restricted, molecules ¹ and ² become non-superimposable on their mirror images and are thus chiral. Various factors are thought to influence the energy barrier to rotation about the sp² - sp² single bond. Among these are: a) the size of the "inside" diene substituent, R₁; b) the interaction of the "outside" diene substituent, R₂, with other groups on the molecular backbone (e.g. R₃); the size of the ring, in the
case of compound 1; and d) the nature of any heteroatom substituents in the ring of compound 2.

The purposes of this work were to synthesize a series of 1,3-dienes 1 and 2 which could be used to further elucidate the structural and steric factors affecting the racemization process, to determine barriers to racemization by dynamic nmr (dnmr), and to obtain an optically active 1,3-diene suitable for both polarimetric and dnmr rate studies.

B. Historical Background of the Study of Dissymmetric 1,3-Dienes

This section summarizes the work that has been done to date by others who have studied racemization rates for 1,3-dienes. Most of the results cited were published after this work was underway.

Kipping, in 1952, was the first person to call attention to the fact that 1,3-dienes are potentially chiral. He expended a considerable amount of energy trying to prepare an optically active cyclobutane, 3, and in 1957 finally reported on his inability to prepare compound 3 in optically active form.
Meanwhile, in Germany, Goldschmidt et al. had prepared the 1,3-diene $\sim$ and had achieved a classical resolution via its brucine salt.$^4$ A value for $\Delta G^+$ of 22 kcal/mol can be calculated for compound $\sim$ from the polarimetric data that Goldschmidt, et al. give in their paper.

Boer et al., in 1967, were apparently the first researchers to measure a dynamic nmr barrier for a 1,3-diene. They reported an $E_a$ of $18.3 \pm 0.23 \text{ kcal/mol}$ at a coalescence temperature of $87^\circ$ for the stannole derivative, $\sim$. A crystal structure indicated that compound $\sim$ existed in the solid with a diene skew angle of $73^\circ$ from cisoid coplanar.$^5$
A similarly constituted stannole, \( \sim \), has been recently investigated by Rhee and Zuckerman, and was found to have an \( E_a \) of 12.1 kcal/mol at a coalescence temperature of 90°.\(^6\)

Because of the similarity in coalescence temperatures for compounds \( \sim \) and \( \sim \), and because of the large disparity in the reported energies of activation, the latter \( E_a \) value must be considered suspect.

\[ \text{Ph Ph } \]
\[ \text{Ph --O-- Ph } \]
\[ \text{Br-Sn } \]
\[ \text{CH}_3 \text{CH}_3 \]
\[ \sim \]

\[ \text{Ph Ph } \]
\[ \text{Ph --S-- Ph } \]
\[ \text{Br-Sn } \]
\[ \text{Li-Sn Br } \]
\[ (\text{C}_5\text{H}_5)_2 \]
\[ \sim \]

In 1968, DeGroot, Evenhuis, and Wynberg commented briefly on the free energy barrier to racemization of 8.3 kcal/mol that they observed for the seven-membered sulfide, \( \sim \).
The high barrier to enantiomerization observed by Kiefer, Levek, and Bopp for the urazole \( \sim \), and the absence of a measurable racemization barrier for \( \sim \) led to the formulation of this thesis problem.\(^8\)

\[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{N} & \quad \text{N} \\
\text{N} & \quad \text{N} \\
\text{N-Ph} & \\
\text{O} & \quad \text{O}
\end{align*}
\]

While this work was underway, three independent groups of researchers published their findings on the study of racemization barriers for 1,3-dienes.

Bomse and Morton, at Brown University, prepared the acyclic hydrocarbon \( 10 \) by the pyrolysis of 1,2-diisopropylidene-3,3,4,4-tetramethylcyclobutane at 200°. Subsequent partial hydrogenation of \( 10 \) at 25° yielded the symmetrical diene, \( 11 \). A free energy barrier for racemization (\( \Delta G^\ddagger = 25 \text{ kcal/mol} \)) was determined for compound \( 10 \) by dnmr. The barrier for compound \( 11 \) was too high to be measured by dnmr, and was estimated to be 26 kcal/mol.\(^9\)
In a series of communications and papers, Pasto et al. at Notre Dame University reported the direct synthesis of compounds 12 - 15 in optically active form according to the synthetic scheme shown on the following page. \textsuperscript{10a-c}
(±)-(S)-12

Ph
N
N-Ph
N
O
O
H

(+)-(S)-12

(-)-(R)

ClSO₂NCO

(+)-13

CH₃
N
N-Ph
N
O
O
H

(+)-15a X = NSO₂Cl
Y = 0

(+)-15b X = 0
Y = NSO₂Cl

(+)-(S)-14a X = NSO₂Cl
Y = 0

(+)-(S)-14b X = NH
Y = 0

(+)-(S)-14c X = 0
Y = NSO₂Cl
The chiral 1,3-dienes 13 and 15 did not racemize at room temperature during a period of several weeks nor did they racemize at 100° for short periods of time. However, because the diastereotopic methylene protons of compounds 13, 15a, and 15b appeared accidentally equivalent in the proton nmr, determination of the dnmr rates of enantiomerization was not attempted. Similarly, the ambient temperature proton nmr resonances of the diastereotopic methyl groups in compound 16a were accidentally degenerate. Upon lowering the probe temperature, coalescence occurred at -28° and at lower temperatures two singlets were observed for the saturated gem-dimethyl groups. This coalescence phenomenon ( ΔG° = 11.9 kcal/mol) was assigned to N-N bridge inversion and the diene enantiomerization process in compound 16a was assumed to have a much higher free energy of activation (ΔG° > 21 kcal/mol).

In conjunction with this dnmr study, an x-ray structural determination was performed on the similar compound 16b. The dihedral angle between the diene planes was found to be 52.3° and the N-N bridge was non-planar (19.1° skew between the planes of the two rings).
A collaborative effort between Köbrich at the Institut für Organische Chemie der Technischen Universität, Hanover, Germany, and Mannscheck at the Fachbereich Chemie der Universität, Regensburg, Germany, has elucidated some of the steric factors affecting the racemization process in dissymmetric 1,3-dienes. They have also succeeded in the classical resolution of several of these 1,3-dienes.\textsuperscript{11}

In their initial paper in this series, Köbrich et al. established that the interaction of the "outside" substituents X and Y of compound \textsuperscript{17} with the chlorines on the 2 and 3 positions of the diene backbone resulted in high barriers to rotation about the \(sp^2\) - \(sp^2\) single bond.\textsuperscript{11a} This phenomenon was later termed a "buttressing effect."
Köbrich et al. then applied the Stobbe condensation to the synthesis of some 1,3-dienes and studied their dnmr behavior. It was found that there was no signal broadening of the methylene proton nmr resonances of any of the three geometric isomers 18 when observed down to -60°, although the benzyl ester 19 exhibited diastereotopic methylene resonances at ~ -50°.11b

A subsequent paper by Köbrich et al., demonstrated that optically active auxiliary reagents could be used to establish the fact that certain 1,3-dienes are chiral. Compound 20, in the presence of a chiral shift reagent, exhibited diastereomeric association complexes in the nmr at ambient temperature.11c

A partial resolution of compound 21 was achieved by classical means and its polarimetric barrier to racemization was found to be $\Delta G^\ddagger_{20} = 23.7 \pm 0.3$ kcal/mol. This barrier was considered too high to be determined by dnmr.11d

The 1,3-diene 22 was also resolved classically. It proved to be optically stable in solution for several days at room temperature and for 8 hours at 80°.11e

In their final paper in this series, Mannschreck and Köbrich presented the dnmr behavior of a series of thirteen 1,3-dienes, 23, along with arguments that the enantiomerization process probably proceeds through a transoid transition state. Evidence is also presented for the importance of the "buttressing effect."11f
C. Use of Dynamic Nmr to Determine Free Energies of Racemization

In order to obtain internal rotational rate data by nmr spectroscopy, the compound under consideration must undergo a dynamic process at a rate suitable for measurement by nmr, and the dynamic process must be detectable by nmr.

Figure 1, below, shows the $\Delta G$ range and the range in log K that is normally measurable by nmr spectroscopy. It can be seen that the rate constant, K, must therefore be of the magnitude of $10^{-1}$ to $10^{-5}$ sec$^{-1}$ in order for the process to be simultaneously measurable by dnmr and by direct observation (e.g. polarimetry).

\[
\begin{array}{c}
\text{log k} \\
-16.6 \quad -9.3 \quad -1.9 \quad 5.4 \\
\text{direct observation} \\
\text{flash} \\
\text{photolysis} \\
\text{nmr} \\
\end{array}
\]

Figure 1. The nmr time scale.
A compound with a rate constant of the correct order of magnitude for dnmr measurement must also exhibit an observable change in its nmr spectrum in order for the dynamic process to be measured. A careful consideration of the symmetry relationships in compound 24 illustrates this requirement.

When rotation about the sp$^2$ - sp$^2$ single bond is rapid, compound 24 is time-averaged planar, and it then possesses not only a C$_2$ axis, but also a mirror plane of symmetry. In this case, the diastereotopic groups A and B become equivalent and exhibit isochronous chemical shifts in the nmr.$^{13}$

In the case that rotation about the sp$^2$ - sp$^2$ single bond is restricted, the molecule is no longer time-averaged planar and the diastereotopic groups A and B may exhibit different, or anisochronous, chemical shifts. Rate data can be derived from the shapes of the nmr signals in the transition region from rapid exchange to slow exchange.$^{12,14,15}$ Figure 2 illustrates typical dnmr spectra observed for the coupled AB
case. "Coalescence" is defined as the temperature at which the signal for group A and the signal from group B just become indistinguishable.

Figure 2. Typical temperature-dependent nmr spectra for the AB region in the coupled AB case.
Lineshapes can be computer-generated to determine the rate constant, \( k \), if the following parameters are known: the chemical shift difference (\( \Delta \nu \)); the coupling constant (\( J \)); and the lifetime in the absence of exchange (\( T_2 \)).

The activation energy, \( E_a \), can then be determined from the slope of an Arrhenius plot of \( \ln k \) vs. \( 1/T \).

Transition state theory provides the relationship between the rate constant, \( k \), and the transition state parameters \( \Delta S^+ \) and \( \Delta H^+ \):

\[
k = \frac{k_B T}{\tau} e^{\frac{\Delta S^+}{R} - \frac{\Delta H^+}{RT}}
\]  \hspace{1cm} (1)

where \( k \) = the rate constant 
\( \tau \) = the lifetime 
\( k_B \) = the Boltzmann constant 
\( h \) = Planck's constant 
\( T \) = absolute temperature 
\( R \) = the gas constant

Therefore, by dividing equation (1) by the temperature and by taking the natural logarithm of both sides, one obtains an equation for a straight line, from which \( \Delta S^+ \) and \( \Delta H^+ \) can be determined:
\[ \ln \frac{1}{T_c} = \left[ \ln \frac{k_B}{h} + \frac{\Delta S^\ddagger}{R} \right] - \left[ \frac{\Delta H^\ddagger}{R} \right] \frac{1}{T} \]  

intercept \hspace{1cm} \text{slope} \hspace{1cm} (2)

The free energy of activation at the coalescence temperature, \( \Delta G_c^\ddagger \), can then be calculated by subtracting \( T_c \Delta S^\ddagger \) from \( \Delta H^\ddagger \). By complete line-shape analysis one can thus obtain \( \Delta G^\ddagger \), \( \Delta S^\ddagger \), \( \Delta H^\ddagger \), and \( E_a \).

\( \Delta G^\ddagger \) can also be determined by application of equation (3):\(^{16}\)

\[ \Delta G_c^\ddagger = 4.57 T_c \left[ 9.97 + \log_{10} \frac{T_c}{(\Delta \nu_{AB}^2 + 6 J_{AB}^2)^{1/2}} \right] \] \hspace{1cm} (3)

Where \( T_c \) = coalescence temperature, in °K

\( \Delta \nu_{AB} \) = chemical shift difference for the AB system, in Hz

\( J_{AB} \) = the coupling constant between A and B, in Hz.

Although the use of equation (3) for the determination of \( \Delta G_c^\ddagger \) has been the subject of much debate,\(^{17}\) it has proven to be fairly accurate, especially in the uncoupled AB case.
II. EXPERIMENTAL

A. General

1. Instruments

Nmr spectra were recorded on a Varian HA-100, a Varian A-60, or a Varian XL-100 spectrometer. Chemical shifts are recorded in parts per million downfield from internal tetramethylsilane unless otherwise noted. Signal multiplicities are designated as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m).

Infrared spectra were obtained using a Beckman Model IR-10 or a Perkin Elmer Model 467 spectrometer. Bands are recorded in cm\(^{-1}\) and are designated as strong (s), medium (m), weak (w), and broad (br).

Ultraviolet spectra were recorded using a Beckman C III ACTA spectrometer with quartz cells.

Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6D or a Varian MAT 311 high resolution spectrometer operating at 70 eV. Signal intensities are recorded as a percentage of the base peak.

Melting points were determined on a Fisher Johns melting point apparatus or with a Hershberg apparatus and are uncorrected.

Polarimetric measurements were obtained from either an ETL-NPL Automatic Polarimeter (Type 143 A) or a Kern-Aarau manual polarimeter using a sodium vapor lamp and are recorded
designating the concentration as grams of substrate per 100 ml of solvent.

2. Solvents, Reagents, Materials

a. Purification

The following methods were used for purification of various solvents and reagents when dry and/or pure reagents were required. Unless otherwise noted, all other solvents and reagents employed were of Reagent Grade or better, and were used without further purification.

Acetone was distilled from calcium sulfate or Analytical Reagent Grade acetone was used without further purification.

Acetonitrile was distilled from phosphorus pentoxide or Analytical Reagent Grade material was used without further purification.

Benzene was distilled azeotropically and then distilled from NaAlH₂(0CH₂CH₂OCH₃)₂, (Red-al, Aldrich Chemical Co.), or Reagent Grade benzene was stored over sodium and used without further purification.

Boron trifluoride etherate was distilled under aspirator pressure from calcium hydride and stored in the refrigerator in sealed glass vials until needed.

Tert-butyl alcohol was refluxed over and then distilled from sodium. However, Mallinkrodt Analytical
Reagent Grade tert-butyl alcohol was used successfully without further purification.

*Diglyme* (bis-(2-methoxyethyl)ether) was distilled from NaAlH₄(OCH₂CH₂OCH₃)₂.

Diethyl succinate was distilled under reduced pressure and stored over Linde 4A molecular sieves.

Ethyl ether of anhydrous grade was stored over sodium.

Pyridine was distilled from either barium oxide or calcium hydride and stored over Linde 4A molecular sieves.

Tetrahydrofuran was distilled from lithium aluminum hydride after stirring over magnesium sulfate overnight.

Thionyl chloride was distilled from phosphorus pentoxide and stored in the refrigerator in a desiccator over calcium sulfate.

Toluene was azeotropically distilled and then distilled from NaAlH₄(OCH₂CH₂OCH₃)₂.

p-Toluenesulfonyl chloride was purified according to Pelletier's method.¹⁸

Triethylamine was distilled from phenylisocyanate, then distilled from calcium hydride, and stored over potassium hydroxide.

b. Miscellaneous Materials, Reagents, Procedures

*Column chromatography* was performed on Sephadex LH-20 (Pharmacia Fine Chemicals, Piscataway, N.J.), or
on alumina (M. Woelm, Germany), or on silica gel (Bio Sil A, Bio-Rad Laboratories, Richmond, California). Mesh size, elution solvents, and column dimensions are specified for each particular separation or purification process described.

Analytical thin layer chromatography was performed on 5 x 20 cm glass plates poured with a 250μ-thick coating of silica gel (HF 254 + 366 for tlc acc. to Stahl, distributed by Brinkmann Instruments Co.). The plates were prepared from a w/w 1:3 slurry of silica gel in water, air dried overnight, and then activated overnight in a 110° oven. The plates were allowed to equilibrate with atmospheric moisture before use.

Preparative thin layer chromatography utilized 750μ-thick 20 x 20 cm silica gel plates. Preparation and activation was as described above for the analytical tlc plates.

Diazomethane was generated from Diazald (N-methyl-N-nitroso-p-toluenesulfonamide) (Aldrich Chemical Co.) in 0.01 mole amounts according to the directions on the label.

Methyllithium was either obtained commercially (Alfa Chemical Company, San Leandro, California) or was prepared according to Schöllkopf et al. and standardized by titrating the charge-transfer complex formed between
methyllithium and 2,2'-bipyridine with sec-butyl alcohol.\textsuperscript{20} Diisobutylaluminum hydride was obtained as a neat liquid (Texas Alkyls, Houston, Texas). Solutions were prepared in hexane in a dry box and stored in the refrigerator under nitrogen until needed.

Corning Filters for Photosensitized Isomerization had the transmission characteristics described in Figure 3.\textsuperscript{21} Nuclear Overhauser Effect Experiments were performed on samples in CDCl\textsubscript{3} solution. The sample was degassed with a very fine argon stream for at least 30 min before the nmr tube was sealed. Enhancements were determined by averaging at least five integrations (except for the case of compound 58, where the peaks were cut out and weighed). The nuclear Overhauser enhancement is reported as the percentage increase over the integrated intensity obtained with irradiation of a "control" area (an area where there are no peaks).

Potassium tert-Butoxide was freshly prepared (unless otherwise noted) in a dry apparatus, under nitrogen, using dry tert-butyl alcohol. Equivalent results were obtained when the potassium tert-butoxide was prepared under a slight positive pressure of nitrogen using a mercury column (according to Johnson and Schneider\textsuperscript{22}) or when an atmospheric pressure of nitrogen was attained by the use of an oil
bubbler. In either case, strict adherence to the precautions involving the handling of potassium is strongly recommended.

Metallic potassium was cut into small chunks in a mortar under sodium-dried xylene and quickly transferred to a tared beaker which also contained dry xylene. The potassium was weighed, rapidly blotted, and transferred to the tert-butyl alcohol which was contained in a round-bottomed flask equipped with a condenser, addition funnel, magnetic stirring bar, and a nitrogen inlet. After the requisite amount of potassium had been added, the solution was refluxed, with stirring, until all of the potassium had dissolved. When all of the reagents and equipment were properly dried, dissolution of the potassium generally required approximately 3 hr.
Figure 3. Percent transmission curves for Corning filters.
B. Syntheses and Properties of Compounds

1. Acyclic Diisopropyldiene Compounds

a. Ethyl Hydrogen Isopropyldienesuccinate, 25

Compound 25 was prepared in a flame-dried apparatus, under nitrogen, according to the literature by the dropwise addition of a mixture of acetone (14.7 ml, 0.2 mol) and diethyl succinate (50.5 ml, 0.3 mol) to a solution of freshly prepared potassium tert-butoxide (9.25 g K, 0.237 mol) in 250 ml of refluxing tert-butyl alcohol. The reaction mixture was allowed to reflux an additional 45 min after addition was complete.

After most of the solvent was removed under aspirator pressure, the mixture was made acidic with 3 N HCl, and the remainder of the tert-butyl alcohol was removed. The aqueous layer was extracted with ether, the combined organic layers were washed with water, and then extracted with 10% aqueous Na₂CO₃. The combined Na₂CO₃ layers were acidified with 6 N HCl (with chilling in an ice/water bath), extracted with ether, and dried. Evaporation of the solvent yielded 36.84 g (98%) of the half-acid ester, 25.

Nmr (neat) δ 1.28 (t, 3H), 1.91 (s, 3H), 2.15 (s, 3H), 3.41 (broad s, 2H), 4.17 (q, 2H), 11.0 (broad s, 1H, D₂O exchangeable).
b. **Diethyl Isopropylidenesuccinate, 26**

The half-acid ester 25 (36.85 g, 0.197 mol) was mixed with 100 ml of absolute ethanol, 300 ml of benzene, and a few drops of concd H₂SO₄ and refluxed overnight using a Dean-Stark apparatus for azeotropic water removal. The Dean-Stark apparatus was drained periodically and the reaction mixture was replenished with ethanol and benzene as necessary. The reaction mixture was cooled to room temperature and ether was added. This mixture was washed repeatedly with ~3% aqueous K₂CO₃ until a basic wash was obtained. The organic layer was dried (MgSO₄) before solvent was removed under aspirator pressure. The remaining oil was distilled through a short fractionating column under reduced pressure to obtain the diester 26 in ca. 75% yield.

Bp 79 - 81°/0.1 mmHg, (lit. 76°/0.6 mmHg and 100 - 102°/2 mmHg); nmr (CDCl₃) δ 1.21 (t, 3H, J = 7 Hz), 1.24 (t, 3H, J = 7 Hz), 1.84 (s, 3H), 2.11 (s, 3H), 3.34 (s, 2H), 4.08 (2H, q, J = 7 Hz), 4.13 (q, 2H, J = 7Hz).

See Figure A-1 (Appendix) for the nmr spectrum of compound 26.

c. **Ethyl Hydrogen Diisopropylidenesuccinate, 27**

Condensation of acetone with compound 26 was performed in a dry apparatus, under nitrogen, according to
Thus, acetone (14.7 ml, 0.20 mol) plus diethyl isopropylidene succinate, 26 (36.4 g, 0.17 mol) were added dropwise to a refluxing solution of potassium tert-butoxide (10.92 g K, 0.28 mol) in 250 ml of tert-butanol. Reflux was ceased 45 min after addition of the above solution was complete. Work-up as described for compound 25, above, yielded 28.5 g (90%) of the half-acid ester, 27.

\[ \text{Nmr (CDCl}_3 \text{) } \delta 1.18 \text{ (t, 3H, } J = 7 \text{ Hz), 1.21 (t, 3H, } J = 7 \text{ Hz), 1.82 (s, 3H), 2.08 (s, 3H), 3.29 (s, 2H), 4.04 (q, 2H, } J = 7 \text{ Hz), 4.09 (q, 2H, } J = 7 \text{ Hz).} \]

See Figure A-2 (Appendix) for the nmr spectrum of compound 27.

d. 2,3-Diisopropylidene-1,4-butanediol, 28

Because attempted Fischer esterification of the half-acid ester 27 resulted in extensive isomerization, compound 27 was reduced as the acid-ester to the diol 28. Compound 27 (17.6 g, 0.078 mol) in 50 ml of benzene was added dropwise, under nitrogen, at room temperature, to a stirred solution of 75 ml (~10% excess) of 60% Red-al (NaAlH\(_2\)(OCH\(_2\)CH\(_2\)OCH\(_3\))\(_2\), Aldrich Chemical Co.) in 200 ml of benzene. Addition was at such a rate as to maintain gentle reflux of the solvent.

The reaction mixture was refluxed for ~2 hr, cooled, and hydrolyzed carefully with water and then with suf-
ficient 1 N KOH to obtain two clear layers. The benzene layer was separated and the aqueous layer was extracted repeatedly with benzene or chloroform (the low yield of diol 28 is attributed partly to its water solubility). The organic extracts were combined, washed with water, dried (MgSO₄), and concentrated. A yield of 5.3 g (40%) was realized after distillation.

Bp 95 - 100°/0.15 mmHg; later solidified; mp 46 - 47°; nmr (CDCl₃) δ 1.57 (s, 6H), 1.78 (s, 6H), 3.69, 4.29 (AB quartet, 4H, J_AB = 11.5 Hz), 4.51 (s, 2H, D₂O exchangeable); ¹³C nmr (CDCl₃) δ 19.29, 21.40, 61.56, 131.31, 133.07; uv (cyclohexane) λ_max 238 nm (ε 1,100); density (flotation) 1.05 g/cm³; ir (neat) 3280 cm⁻¹ (s), 2910 (s), 1640 (w), 1435 (m), 985 (s); exact mass for compound 28 - H₂O 152.1201 (calcd for C₁₀H₁₆O 152.1201).

See Figures A-3, A-4, A-5, and A-6 (Appendix) for the proton nmr, ¹³C nmr, ir, and mass spectra, respectively, for compound 28.

e. 2,3-Diisopropylidene-1,4-dibromobutane, 29

Triphenylphosphine dibromide was prepared in a flame-dried system, under nitrogen, by the dropwise addition of bromine (5.8 ml, 0.106 mol) to a suspension of triphenylphosphine (27.9 g, 0.106 mol) in 250 ml of dry acetonitrile at 0°.
To this cream-colored suspension was added 2,3-di-isopropylidene-1,4-butanediol \( \text{28} \) (9.04 g, 0.0531 mol) in 100 ml of dry acetonitrile over a period of 20 min. (Two equivalents of triethylamine were added for some runs; this seemed to improve the yield slightly.)

After 45 min at ice/water temperature, the suspension of white solid in an orange solution was filtered and evaporated down to a residue at or below room temperature. The residue was washed repeatedly with 30/60 pet ether and these washes were evaporated down at or below room temperature. Off-white crystals formed immediately. Recrystallization from pentane was done rapidly by solvent evaporation in a nitrogen stream. The yield was 4.62 g (29.4%) of clear, colorless plates.

Mp 62 - 63°; nmr (CDCl\(_3\)) \( \delta \) 1.70 (s, 6H), 1.88 (s, 6H), 4.10, 4.25 (AB quartet, 4H, \( J_{AB} = 20 \) Hz); ir (KBr) 1634 cm\(^{-1} \) (w), 1429 (m), 1368 (w), 1191 (s); mass spectrum m/e (rel intensity) 296 (0.05), 215 - 217 (0.2), 115 (0.85).

See Figures A-7, A-8, and A-9 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 29.

f. 2,3-Diisopropylidene-1,4-diazidobutane, \( \text{30} \)

Dibromide \( \text{29} \) (150 mg, 0.507 mmol) in 25 ml of 95% ethanol was added dropwise to NaN\(_3\) (0.3 g, 4.6 mmol) in
40 ml of 95% ethanol. The flask was flushed with nitrogen, capped, and stirred overnight at room temperature.

The reaction mixture was evaporated down to a residue under reduced pressure at room temperature. The residue was taken up in ether and water, the water layer was extracted with two portions of ether, and the combined ether layers were dried (MgSO₄). Evaporation of the solvent at or below room temperature yielded 102 mg (91.5%) of the yellow oil 30.

Nmr (CDCl₃) δ 1.70 (s, 6H), 1.83 (s, 6H), 3.70, 4.08 (AB quartet, 4H, Jₐₜₜ = 13 Hz); ir (neat) 2080 cm⁻¹ (s), 1645 (w), 1440 (m), 1260 (m); no molecular ion, exact mass for compound 30 - N₅ 150.1281 (calcd for C₁₀H₁₆N₁ 150.1283).

See Figures A-10, A-11, and A-12 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 30.

g. 2,3-Diisopropylidene-1,4-diethoxybutane, 31

Sodium (42 mg, 1.82 mmol) was dissolved carefully in 20 ml of absolute ethanol and the dibromide 29 (160 mg, 0.54 mmol) was added as a solid. The reaction mixture was flushed with nitrogen, capped, and stirred overnight at room temperature.

The reaction mixture was evaporated to a residue, taken up in ether and water, and extracted with a total
of three portions of ether. The ether layer was dried
(MgSO₄) and concentrated using a rotary evaporator to
yield ca. 76% of the crude diethoxy compound 31.

Purification of compound 31 was difficult; neither
molecular distillation (bp 64 - 65°/ 0.25 - 0.1 mmHg)
nor preparative tlc (silica gel, benzene:CHCl₃ 4:1)
produced a clean product.

Nmr (CDCl₃) δ 1.21 (t, 6H, J = 7 Hz), 1.65 (s, 6H),
1.83 (s, 6H), 3.46 (q, 4H, J = 7 Hz), 4.02 (s, 4H).

See Figure A-13 (Appendix) for the nmr spectrum of
compound 31.

h. 2,3-Diisopropylidene-1,4-dicyanobutane, 32

The dibromide 29 (0.516 g, 1.74 mmol), dissolved in
15 ml of dimethyl sulfoxide was added dropwise to KCN
(1.0 g, 15.4 mmol) suspended in 50 ml of dimethyl sulfox-
ide. The flask was flushed with nitrogen, capped, and
stirred overnight at room temperature.

The reaction mixture was taken up in water and pen-
tane and extracted a total of 3 times with pentane. The
pentane layer was washed with 4 small portions of water
and dried (MgSO₄). Evaporation of solvent yielded 123 mg
(37.6%) of a clear oil. (Yield was generally variable
and purification by preparative tlc on silica gel (CHCl₃:
benzene 1:1) was sometimes necessary.)
Nmr (CDCl₃) δ 1.69 (s, 6H), 1.83 (s, 6H), 3.70, 4.07 (AB quartet, 4H, Jₐₜ = 14 Hz); ir (neat) 2240 cm⁻¹ (m); exact mass 188.1299 (calcd for C₁₂H₁₆N₂ 188.1314).

See Figures A-14, A-15, and A-16 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 32.

i. 2,3-Diisopropylidene-1,4-butanedithiolacetate, 33

Dibromide 29 (57 mg, 0.19 mmol) was added to thiolacetic acid (0.25 ml, 3.52 mmol) plus 3.50 ml of 1.0 N NaOH in 10 ml of acetone. The reaction mixture was stirred overnight at room temperature.

The reaction mixture was taken up in ether and water and extracted with 3 portions of ether. After drying (MgSO₄), solvent was removed and purification was effected by preparative tlc on silica gel (benzene:CHCl₃ 4:1).

Nmr (CDCl₃) δ 1.47 (s, 6H), 1.68 (s, 6H), 2.18 (s, 6H), 3.52, 3.69 (AB quartet, 4H, Jₐₜ = 13 Hz); ir (neat) 1675 cm⁻¹ (s).

See Figures A-17 and A-18 (Appendix) for the nmr and ir spectra for compound 33.

j. 2,3-Diisopropylidene-1,4-butanediacetate, 34

Compound 34 was prepared by two routes; either by direct acetylation of the diol 28 or by reaction of the dibromide 29 with sodium acetate.
In the first method, diol 28 (0.25 g, 1.47 mmol) was refluxed for 3.75 hr in a solution of 25 ml of pyridine and 5 ml of acetic anhydride. When cool, the reaction mixture was diluted with ether and extracted with 4 portions of 5% HCl, two portions of 10% Na₂CO₃, followed by two portions of water. Solvent was removed under aspirator pressure, yielding the diacetate, 34.

The alternate method of preparation involved the addition of the dibromide 29 (150 mg, 0.507 mmol) to a suspension of NaOAc·3H₂O (187 mg, 1.37 mmol) in 35 ml of acetonitrile. The reaction mixture was stirred overnight at room temperature and then evaporated down to a residue under aspirator pressure. The residue was taken up in water and the water layer was extracted twice with ether. Drying (MgSO₄) and solvent removal yielded the crude diacetate, 34.

\[ \text{Nmr (CS}_2\text{)} \delta 1.56 (s, 6H), 1.80 (s, 6H), 1.89 (s, 6H) 4.62 (s, 4H). \]

See Figure A-19 (Appendix) for the nmr spectrum of compound 34.

\[ \text{Diisopropylidenedesuccinic acid, 35} \]

Half-acid ester 27, when refluxed for 1 hr in 10% aqueous KOH yielded, after acidification, diacid 35, which could be recrystallized from hot ethanol.
Nmr (DMSO-d$_6$) $\delta$ 1.67 (s, 6H), 2.10 (s, 6H); mp 208 - 209° (dec), (lit. $^{24}$ 230° (dec)).

See Figures A-20 and A-21 (Appendix) for the nmr and ir spectra for compound 35.

1. Dimethyl Diisopropylidenediisocinate, 36

Treatment of diacid 35, suspended in ethanol, with ethereal diazomethane, yielded the diester 36. (Attempted Fischer esterification of the diacid 35 resulted in extensive isomerization.)

Nmr (CDCl$_3$) $\delta$ 1.63 (s, 6H), 2.22 (s, 6H), 3.63 (s, 6H); mp 69 - 71°.

See Figure A-22 (Appendix) for the nmr spectrum of compound 36.

m. 3,4-Diisopropylidene-2,5-dimethyl-2,5-hexanediol, 37

Dimethyl ester 36 (0.82 g, 3.63 mmol) in 30 ml of absolute ether was added dropwise to a mixture of methyllithium (20 ml, 1.7 M in hexane) and 100 ml of ether at room temperature. The reaction mixture was stirred overnight at room temperature under nitrogen.

Still under a nitrogen atmosphere, the reaction mixture was cooled in an ice bath and water was added cautiously until all active methyllithium was destroyed and two clear layers were obtained. The aqueous and ether layers
were separated and the aqueous layer extracted again with ether. The combined ether layers were dried (MgSO₄) and concentrated under reduced pressure, without applying heat.

Purification was effected by column chromatography on silica gel (Bio Sil A, 200-375 mesh) using as the eluent 5% MeOH in CHCl₃.

Mp 56 - 58°; nmr (CDCl₃) δ 1.45 (s, 6H), 1.58 (s, 6H), 1.65 (s, 6H), 1.89 (s, 6H), 2.42 (broad s, 2H, D₂O exchangeable); ir (nujol) 3230 cm⁻¹ (s, br), 1360 (doublet); mass spectrum m/e (rel intensity) 226 (M⁺ not observable), 208 (0.48), 193 (1.0), 150 (0.81), 135 (0.89), 95 (0.11).

See Figures A-23, A-24, and A-25 (Appendix) for nmr, ir, and mass spectra, respectively, for compound 37.

2. Cyclic 5-Membered Ring Diisopropylidene Compounds

a. 3,4-Diisopropylidenediarylorganothiophene, 38

A solution of dibromide 29 (0.150 g, 0.507 mmol) in 15 ml of 95% ethanol was added dropwise to Na₂S·9H₂O (0.159 g, 0.66 mmol) dissolved in a mixture of 5 ml of water and 50 ml of 95% ethanol. After addition was complete (~ 5 min), the flask was flushed with nitrogen, sealed, and allowed to stir overnight at room temperature.

The reaction mixture was evaporated to dryness, taken up in ether and water, extracted twice with ether, and dried (MgSO₄). Evaporation of solvent yielded 52 mg (61%)
of a white solid.

Mp 48 - 49°; nmr (CDCl₃) δ 1.63 (s, 6H), 1.77 (s, 6H), ~3.36 (broad, 4H); ir (neat) 2910 cm⁻¹ (m), 2945 (m), 1640 (w), 1435 (m), 1257 (m), 1130 - 1100 (m, broad), 780 (m); exact mass 168.0966 (calcd for C₁₀H₁₆S 168.0972).

See Figures A-26, A-27, and A-28 (Appendix) for nmr, ir, and mass spectra, respectively, for compound 38.

b. 3,4-Diisopropylidenedtetrahydrothiophene-1-oxide, 39

Compound 38 (52 mg, 0.31 mmol) was taken up in 3 ml of dry dichloromethane and was chilled in an ice/water bath. A solution of 85% m-chloroperbenzoic acid (62 mg, 0.31 mmol "pure" mCPBA) in 3 ml of dry dichloromethane was added dropwise. A drying tube was attached and the reaction was allowed to warm up to room temperature overnight.

The reaction mixture was washed with a weak solution of Na₂S₀₃ and then with 3% Na₂CO₃. These aqueous washes were combined and back-extracted with dichloromethane. The dichloromethane layers were combined and dried (MgSO₄). Upon evaporation of solvent, 50 mg (87.5%) of the oil, 39, was obtained.

Nmtr (CDCl₃) δ 1.70 (s, 6H), 1.79 (s, 6H), ~3.54 (broad, 4H); ir (neat) 1654 cm⁻¹ (w), 1035 (s); exact mass 184.0921 (calcd for C₁₀H₁₆SO 184.0921).
See Figures A-29, A-30, and A-31 (Appendix) for nmr, ir, and mass spectra, respectively, for compound 39.

c. 3,4-Diisopropylidenetetrahydrothiophene-1,1-dioxide, 40

Compound 38 (36.9 mg, 0.22 mmol) was dissolved in 2 ml of dry dichloromethane and cooled in an ice/water bath. A solution of 85% m-chloroperbenzoic acid (93.2 mg, 0.46 mmol "pure" mCPBA) in 3 ml of dry dichloromethane was added dropwise. A drying tube was attached and the reaction mixture was allowed to warm to room temperature overnight.

The reaction mixture was washed in succession with dilute Na₂SO₃ and Na₂CO₃, and dried (MgSO₄). Evaporation of solvent yielded a solid residue, shown to be impure by nmr and tlc. After 3 recrystallizations from pentane/ether an impurity still remained. Preparative tlc on silica gel (benzene:CHCl₃ 1:1) afforded pure compound 40. Yield was not determined.

Mp 133-135°; nmr (CDCl₃) δ 1.68 (s, 6H), 1.79 (s, 6H), 3.78 (broad d, 4H); ir (neat) 1645 cm⁻¹ (w), 1294 (s), 1085 (s); exact mass 200.0866 (calcd for C₁₀H₁₆O₂S 200.0870).

See Figures A-32, A-33, and A-34 (Appendix) for nmr, ir, and mass spectra, respectively, for compound 40.
d. 3,4-Diisopropylidene-N-methylpyrrolidine, 41

2,3-Diisopropylidene-1,4-dibromobutane 29, (181.8 mg, 0.40 mmol) in 10 ml of acetonitrile was added dropwise to methylamine (2 ml, 25% in water) in 50 ml of acetonitrile. The reaction flask was flushed with nitrogen, capped, and stirred overnight at room temperature.

The reaction mixture was evaporated to a residue under aspirator pressure and taken up in chloroform and 3% HCl. The acidic extract was made basic with 7.5% Na₂CO₃ and extracted with three portions of chloroform. The organic layer was dried briefly (K₂CO₃). Evaporation of the solvent yielded 59.1 mg (89.5%) of compound 41.

Nmr (CDCl₃) δ 1.65 (s, 6H), 1.72 (s, 6H), 2.41 (s, 3H), 3.12 (s, 4H); ir (neat) 2760 cm⁻¹ (m), 1640 (broad, m), 1445 (m); mass spectrum m/e (rel intensity) 165 (0.11), 150 (0.29).

See Figures A-35, A-36, and A-37 (Appendix) for nmr, ir, and mass spectra, respectively, for compound 41.

e. 3,4-Diisopropylidene-N-benzylpyrrolidine, 42

A solution of dibromide 29 (150 mg, 0.507 mmol) in 15 ml of acetonitrile was added dropwise to a solution of benzylamine (55 µl, 0.507 mmol) in 40 ml of acetonitrile. The reaction vessel was flushed with nitrogen, capped, and allowed to stir overnight at room temperature.
The reaction mixture was evaporated down to a residue, taken up in 3% HCl and washed with two portions of ether. The acidic aqueous layer was made basic with 7.5% Na₂CO₃ and extracted with two portions of ether, which were combined and dried (MgSO₄). Evaporation of solvent yielded 66 mg (54%) of compound 42.

Nmr (CDCl₃) δ 1.61 (s, 6H), 1.69 (s, 6H), 3.30 (s, 4H), 3.73 (s, 2H), 7.25 - 7.43 (m, 5H); ir (neat) 2698 cm⁻¹ (m), 1673 (m), 1450 (m), 1372 (m); exact mass 241.1818 (calcd for C₁₇H₂₃N). See Figures A-38, A-39, and A-40 for the nmr, ir, and mass spectra, respectively, for compound 42.

f. 3,4-Diisopropylidenetetrahydrofuran, 43

Compound 43 was prepared by two independent methods. The diol 28 (5.48 g, 0.0322 mol) in 30 ml of anhydrous ether was added very slowly, under nitrogen, to a suspension of NaH (99%, 2.4 g, 0.1 mol) in 100 ml of absolute ether. The solution was refluxed overnight under nitrogen and then cooled in a dry ice/CCl₄ slush (-23°) before dropwise addition of recrystallized para-toluenesulfonyl chloride (12.4 g, 0.065 mol) in 100 ml of absolute ether. After 2 hr at -23°, an ice/water bath was applied. After 2 hr at 0°, the reaction mixture was allowed to warm to room temperature for 1 hr.
The reaction mixture was filtered, the liquid was concentrated, and the reaction mixture was filtered again. The oil remaining could be purified by distillation or by column chromatography on silica gel (Bio Sil A, 200 - 325 mesh, benzene:CHCl$_3$ 4:1).

Compound 43 could be alternatively synthesized by the addition of the dibromide 29 (20 mg, 0.068 mmol) to a solution of 3 ml of 1.0 N NaOH in 2 ml of ethanol. After stirring overnight at room temperature, the reaction mixture was diluted with water and extracted with two portions of ether. Evaporation of solvent after a brief drying period (MgSO$_4$) yielded the tetrahydrofuran 43, which could be purified by preparative tlc on silica gel (benzene: CHCl$_3$ 4:1).

Bp 32°/0.05 mmHg; nmr (CDCl$_3$) δ 1.71 (s, 12H), 4.32 (s, 4H); ir (neat) 1185 cm$^{-1}$.

See Figures A-41, A-42, and A-43 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 43.

g. 3,4-Diisopropylidene-N,N-dimethylpyrrolidinium bromide, 44

Dibromide 29 (100 mg, 0.34 mmol) dissolved in 15 ml of acetonitrile, was added to a solution of dimethylamine hydrochloride (0.857 g, 10.4 mmol) plus 1.0 N NaOH (10.4 ml, 10.4 mmol) in 50 ml of acetonitrile and stirred overnight at room temperature.
The reaction mixture was concentrated to a volume of 20 ml, taken up in 1 N KOH, and extracted with three portions of ether. The combined ether extracts were dried (MgSO₄) and evaporated down to yield 4 mg of a yellow oil which was shown by nmr to be a complex mixture.

The aqueous layer was concentrated to a residue and stirred overnight with chloroform. The chloroform solution was filtered, dried (MgSO₄), and evaporated down to yield a mixture whose major component was the salt, 44.

Nmr (acetone-d₆) δ 1.78 (s, 6H), 1.85 (s, 6H), 3.59 (s, 3H), 4.58 (s, 2H).

h. 3,4-Diisopropylidene-1,1-dicarbethoxycyclopentane, 45

Diethyl malonate (96 mg, 0.6 mmol) was added to commercially available potassium tert-butoxide (146 mg, 1.3 mmol) dissolved in 50 ml of anhydrous ether under a dry nitrogen atmosphere. A solution of 2,3-diisopropylidene-1,4-dibromobutane 29 (150 mg, 0.507 mmol) in 50 ml of anhydrous ether was added dropwise. The reaction mixture was stirred overnight at room temperature under a dry nitrogen atmosphere.

The yellow reaction mixture was chilled in an ice/water bath and water was added until two clear layers were obtained. The aqueous layer was extracted with two portions of ether, which were combined and dried (MgSO₄). Evaporation of solvent yielded an oily residue which
was composed of the starting dibromide, diethyl malonate, and the desired product, 45. Purification was effected by preparative tlc on silica gel using double elution with benzene as the solvent. The yield was not determined.

\[
\text{Nmr (CDCl}_3) \delta 1.24 (t, 6H, J = 7 \text{ Hz}), 1.60 (s, 6H), 1.73 (s, 6H), 2.88 (s, 4H), 4.16 (q, 4H, J = 7 \text{ Hz}); \text{ ir (neat) 1728 cm}^{-1} (s), 1235 (m), 1165 (m); \text{ exact mass 294.1828 (calcd for C}_{12}\text{H}_{26}O_4 294.1831)}.
\]

See Figures A-44, A-45, and A-46 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 45.

\(i. 3,4\)-Diisopropylidene-2,2,5,5-tetramethyltetrahydrofuran, 46

Compound 37 cyclodehydrated upon standing in solution for several days, or upon heating to 80°, to the tetrahydrofuran, 46.

\[
\text{Nmr (CDCl}_3) \delta 1.22 (\text{broad s, 6H}), 1.51 (\text{broad s, 6H}), 1.59 (s, 6H), 1.77 (s, 6H).
\]

See Figure A-47 (Appendix) for the nmr spectrum of compound 46.
3. Cyclic 6-Membered Ring Diisopropylidene Compounds

a. 3,4-Diisopropylidene-1,2-dimethylhexahydropyridazine, 47

The dibromide $29$ (2.22 g, 7.50 mmol) was added as a solid to a solution of sym-dimethylhydrazine hydrochloride (1.54 g, 8.50 mmol, Aldrich Chemical Co.) in a mixture of 34 ml of 1.0 N NaOH (34 mmol) and 200 ml of acetonitrile. The reaction vessel was flushed with nitrogen, capped, and stirred at room temperature overnight.

The reaction mixture was evaporated down to a residue under aspirator pressure and then taken up in 3% HCl and chloroform. The chloroform layer was separated, dried (MgSO$_4$), and concentrated to yield 1.04 g (ca. 60%) of the hydrochloride salt of compound 47. Recrystallization from benzene (rapidly, in a nitrogen stream) yielded fine white needles.

For the hydrochloride salt of compound 47: Mp 130 - 132° (dec); nmr (CDCl$_3$) $\delta$ 1.68 (s, 6H), 1.81 (s, 6H), 2.90 (s, 6H), 3.74, 3.77 (AB quartet, 4H, J = 13 Hz).

See Figures A-48, A-49, and A-50 (Appendix) for the nmr, ir, and mass spectra, respectively, for the hydrochloride salt of compound 47.

The free hydrazine $47$ was obtained by treatment of the above hydrochloride salt with 1 N KOH, and then extraction into chloroform. The chloroform extract was dried (MgSO$_4$) and concentrated to yield the free base $47$. 
For the free base 47: Nmr (CDCl₃) δ 1.56 (s, 6H), 1.69 (s, 6H), 2.49 (s, 6H), 3.42 (s, 4H); ir (neat) 2755 cm⁻¹ (m), 1652 (w), 1445 (m); exact mass 194.1780 (calcd for C₁₂H₂₂N₂ 194.1783).

See Figures A-51, A-52 (Appendix) for the proton nmr and the ¹³C nmr spectra for compound 47.

b. 3,4-Diisopropylidene-1,2-dibenzylhexahydropyridazine, 48

Benzaldehyde azine was prepared according to the literature by the dropwise addition of hydrazine hydrate (99-100%, 0.5 ml, 0.01 mol "pure" H₂NNH₂) to a stirred solution of benzaldehyde (2.0 g, 0.019 mol) in 50 ml of ether which was immersed in an ice/water bath. After 15 min at ice/water temperature, several spatula-fulls of anhyd K₂CO₃ were added and the stirring and cooling were continued for an additional 15 min. The ether solution was decanted off, dried again (MgSO₄), filtered, and evaporated down at or below room temperature to yield 1.72 g (87%) of a crude yellow solid. Recrystallization from pentane/ether afforded 0.90 g (46%) of benzaldehyde azine as yellow needles.

Mp 90 - 91° (lit. 92 - 93°); nmr (CDCl₃) δ 7.4 - 7.6 (m, 6H), 7.8 - 8.0 (m, 4H), 8.66 (s, 2H); ir (nujol) 1460 cm⁻¹ (s).

Because the reduction of benzaldehyde azine with Red-al (NaAlH₂(OC₂H₅)₂), lithium aluminum hydride,
and sodium borohydride proved unsatisfactory, it was necessary to use the procedure of Blair and Gardner\textsuperscript{27} to effect the reduction of the azine with diborane to sym-dibenzylhydrazine. Diborane was generated in an apparatus constructed according to Zweifel and Brown\textsuperscript{28} by the addition of freshly distilled boron trifluoride etherate (14.2 ml, 0.115 mol) in 50 ml of dry diglyme to sodium borohydride (2.3 g, 0.605 mol) in 80 ml of dry diglyme. The diborane so generated was bubbled into a solution of benzaldehyde azine (3.0 g, 0.0144 mol) in 160 ml of dry diglyme maintained at 15 - 20° by slight cooling. When the reduction was complete, the originally yellow solution became colorless.

Anhyd HCl was bubbled into the reaction vessel. The white precipitate which formed was collected by suction filtration and dried in vacuo to yield 1.85 g (ca. 48%) of sym-dibenzylhydrazine hydrochloride.

Nmr for sym-dibenzylhydrazine hydrochloride (CF$_3$CO$_2$H) $\delta$ 4.42 (s, 4H), 7.37 (s, 10H); ir (KBr) 3200 cm$^{-1}$ (s), 3000 - 2400 (broad, s), 1450 (s); mass spectrum m/e (rel intensity) 212 (0.27), 121 (0.37), 91 (1.0).

To sym-dibenzylhydrazine hydrochloride (0.145 g, 0.507 mmol) was added 3 ml of 1.0 N NaOH and 40 ml of acetonitrile. A solution of the dibromide\textsuperscript{29} (150 mg, 0.507 mmol) in a total of 15 ml of acetonitrile was added
dropwise, the flask was flushed with nitrogen, capped, and stirred overnight.

Solvent was removed and the residue was taken up in ether and 3% HCl. The ether layer was extracted with two more portions of 3% HCl, which were combined and made basic with 7.5% Na$_2$CO$_3$. Extraction of the basic solution with three portions of ether, drying (MgSO$_4$), and evaporation of the solvent yielded 44 mg (25%) of a yellow oil which could be crystallized from ether to yield white needles.

Mp 69 - 73°; nmr (CDCl$_3$) $\delta$ 1.64 (s, 12H), 3.31, 3.61 (ring AB quartet, 4H, $J_{AB} = 15.5$ Hz), 3.77, 4.09 (benzyl AB quartet, 4H, $J_{AB} = 13.5$ Hz), 7.21 (s, 10H); ir (nujol) 2825 cm$^{-1}$ (s), 1445 (m); exact mass 346.2404 (calcd for C$_{24}$H$_{30}$N$_2$ 346.2409).

See Figures A-53, A-54, and A-55 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 48.

c. 3,4-Diisopropylidene-8-phenyl-1,6,8-triazobicyclo[4.3.0]nonane-7,9-dione, 49

4-Phenylurazole (120 mg, 0.68 mmol, Aldrich Chemical Co.) was mixed with 1.36 ml of 1.0 N NaOH (1.36 mmol) and was then taken up in 15 ml of hexamethylphosphoramide (HMPA). The dibromide 29 (200 mg, 0.675 mmol) was added, the reaction vessel was flushed with nitrogen, capped, and stirred overnight at room temperature.
The reaction mixture was taken up in pentane, water, and a few ml of 1 N KOH, and was extracted with three portions of pentane. The combined pentane extract was washed four times with water, dried (MgSO₄), and evaporated down to yield 94 mg (45%) of solid compound 49. Recrystallization was performed from hexane.

Mp 131 - 132° (lit. 8b 131.5 - 133°); nmr (CDCl₃) δ 1.71 (coupled s, 6H), 1.87 (s, 6H), 3.92, 4.75 (AB quartet, 4H, J = 13 Hz), 7.3 - 7.5 (m, 5H), (cf. lit. 8 nmr measured in CCl₄); ir (KBr) 1760 cm⁻¹ (m), 1690 (s), 1400 (s), 1240 (m).

See Figures A-56 and A-57 (Appendix) for the nmr and ir spectra for compound 49.

4. Dineopentylidene Compounds

a. Trans-2,5-di-tert-butyl-3,4-dicarbomethoxy-2,5-dihydrothiophene-1,1-dioxide, 51

m-Chloroperbenzoic acid (85%, 149 mg, 0.664 mmol "pure" MCPBA) dissolved in 8 ml of dry dichloromethane was added to trans-2,5-di-tert-butyl-3,4-dihydrothiophene 50 (104 mg, 0.331 mmol) dissolved in 10 ml of dry dichloromethane which was cooled to ice/water temperature. The flask was capped with a drying tube and allowed to warm to room temperature overnight.

The reaction mixture was washed once with dilute Na₂SO₃ and once with dilute Na₂CO₃. These washes were
combined and back-extracted with dichloromethane. The 
organic layers were combined and dried (MgSO₄). Evapor­
ation of solvent yielded 115 mg (99+%) of a white powder. 

Mp 187.0 - 187.5°; nmr (CDCl₃) $\delta$ 1.24 (s, 18H), 3.82 
(s, 6H), 3.88 (s, 2H).

See Figures A-58 and A-59 (Appendix) for the nmr 
and ir spectra for compound 51.

b. **Dimethyl (E,Z)-Dineopentyldienesuccinate, 52** 

Pyrolysis of sulfone 51 on a hundred mg scale was 
performed in a test tube over an open flame, taking care 
to avoid undue sublimation of the sulfone before pyro-
lysis. Molecular distillation (60 - 90°/0.1 - 0.15 
mmHg) afforded ca. 90% of a clear, colorless oil.

Nmr (CDCl₃) $\delta$ 1.16 (s, 9H), 1.25 (s, 9H), 3.70 (s, 
6H), 5.82 (s, 1H), 6.83 (s, 1H).

See Figures A-60 and A-61 (Appendix) for the nmr 
and mass spectra for compound 52.

c. **Dimethyl (E,E)-Dineopentyldienesuccinate, 53**

Photosensitized isomerization³¹ of compound 52 was 
performed in dilute CDCl₃ solution with benzophenone as the 
sensitizer. The solution was degassed for ~15 min in 
an argon stream, sealed, and subjected to irradiation
with a 550-Watt Hanovia mercury lamp using a Corning 0-52 filter (cutoff 360 nm). After 24 hr, a photostationary state consisting of 24.5% of the \((E,E)\)-isomer 53, 6% of the \((Z,Z)\)-isomer 54, and 69.5% of the \((E,E)\)-isomer 52 (determined by nmr integration) was obtained. Separation of these compounds could be effected by preparative tlc on silica gel (double elution with benzene:CHCl₃ 4:1).

Approximate \(r_f\)'s were: benzophenone, 0.75; the \((Z,Z)\)-isomer 54, 0.55; the \((E,Z)\)-isomer 52, 0.5; and the \((E,E)\)-isomer 53, 0.4.

These stereoisomers were distinguished by their nmr spectra. The structural assignments were based on the large down-field nmr chemical shift expected for the vinyl proton when it is cis to the carbomethoxy group (and is therefore influenced by the carbonyl deshielding cone).

Nmr for the \((E,E)\)-isomer (CDCl₃) \(\delta\) 1.11 (s, 18H), 3.71 (s, 6H), 6.86 (s, 1H).

See Figure A-62 (Appendix) for the nmr spectrum of compound 53.

d. Dimethyl \((Z,Z)\)-Dineopentylidenesuccinate, 54

Compound 54 could be produced as a byproduct in the synthesis of compound 53, or obtained in slightly higher yield (ca. 15%) by the photosensitized isomerization of a degassed solution of compound 52 using acetophenone as
the sensitizer. Irradiation was performed with a 550-Watt Hanovia mercury lamp using a Corning 0-54 filter (cutoff 310 nm).

\[ \text{Nmr (CDCl}_3\text{)} \delta 1.09 (s, 18H), 3.76 (s, 6H), 5.43 (s, 2H). \]

See Figure A-63 (Appendix) for the nmr spectrum for compound 54.

e. (E,Z)-2,3-Dineopentylidene-1,4-butanediol, 55

Reduction of the (E,Z)- and (E,E)-diesters 52 and 53 with Red-al (NaAlH\textsubscript{2}(OCH\textsubscript{2}CH\textsubscript{2}OCH\textsubscript{3})\textsubscript{2}), LiAlH\textsubscript{4}, AlH\textsubscript{3},\textsuperscript{33} and LiAlH\textsubscript{3}(OCH\textsubscript{2}CH\textsubscript{3})\textsuperscript{34} under a variety of conditions proved unsatisfactory and it was therefore necessary to employ diisobutylaluminum hydride for these reductions.

The (E,Z)-diester 52 (6.5 mg) was dissolved in 5 ml of sodium-dried ether and cooled in an ice/water bath. Diisobutylaluminum hydride (1.5 ml, ~0.7 M in hexane) was added through a septum via a hypodermic syringe.

After 50 min, water was added cautiously, plus enough 5% NaOH to obtain two clear layers. The aqueous layer was extracted with three portions of ether, which were combined and dried (MgSO\textsubscript{4}). Evaporation of solvent at or below room temperature under aspirator pressure yielded compound 55.

\[ \text{Nmr (CDCl}_3\text{)} \delta 1.08 (s, 9H), 1.19 (s, 9H), 4.03 (s, 2H), 4.36 (s, 2H), 5.33 (s, 1H), 5.43 (s, 1H). \]
See Figure A-64 (Appendix) for the nmr spectrum of compound 55.

f. \((E,E)-3,4\text{-Dineopentylidene}-2,5\text{-dimethyl}-2,5\text{-hexanediol}, \, 56\)

An excess of methyllithium in ether was added at 0\(^\circ\) to compound 53 (ca. 15 mg) in 10 ml of ether. The reaction mixture was stirred overnight under nitrogen at room temperature.

Water and a small amount of KOH were added to the reaction mixture. The aqueous layer was extracted with three portions of ether, which were combined and dried (MgSO\(_4\)). Solvent was removed at or below room temperature under aspirator pressure. Preparative tlc on silica gel (benzene:CHCl\(_3\) 4:1) afforded compound 56.

Nmr (CDCl\(_3\)) \(\delta\) 1.09 (s, 18H), 1.51 (s, 12H), 5.54 (s, 2H); ir (neat) 3330 cm\(^{-1}\) (m).

See Figure A-65 (Appendix) for the nmr spectrum of compound 56.

g. \((E,E)-2,3\text{-Dineopentylidene}-1,4\text{-butanediol}, \, 57\)

To 37 mg of the \((E,E)\)-diester 53 in 10 ml of sodium-dried ether was added via a septum 2 ml of \(~0.7\, \text{M~diisobutylaluminum hydride in hexane.}\)

After 1 hr at 0\(^\circ\), water was added, followed by 5% NaOH until two clear layers were obtained. The basic
aqueous layer was extracted with four portions of ether, which were combined and dried over MgSO₄.

Preparative tlc on silica gel using 5% MeOH in CHCl₃ two times was necessary to obtain pure compound 57.

That the geometry about the double bonds of diol 57 was (E,E), as assigned, was established by the observation of a 20% nuclear Overhauser enhancement of the vinyl proton resonance upon irradiation at the methylene frequency. The isomeric (Z,Z)-diol 58 exhibited no nuclear Overhauser enhancement of the vinyl proton resonance upon irradiation at the methylene frequency.

Nmr (CDCl₃) δ 1.11 (s, 18H), 4.07 (s, 4H), 5.42 (s, 2H); exact mass 226.1933 (calcd for C₁₄H₂₆O₂ 226.1933).

See Figures A-66, A-67, and A-68 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 57.

h. (Z,Z)-2,3-Dineopentylidene-1,4-butanediol, 58

Compound 54 (4.1 mg) was dissolved in 10 ml of sodium-dried ether and cooled in an ice/water bath. Diisobutylaluminum hydride in hexane (1.5 ml, ~ 0.7 M) was added via a septum. After 1 hr at 0°, work-up was performed as described for compound 55, above.

Assignment of the stereochemistry about the double bonds in compound 58 was based on the absence of an observable nuclear Overhauser effect upon irradiation at the methylene frequency, whereas a nuclear Overhauser
enhancement of 20% was observed for the isomeric diol 57.

Nmr (CDCl$_3$) $\delta$ 1.20 (s, 18H), 4.26 (s, 4H), 5.42 (s, 2H); exact mass 226.1931 (calcd for C$_{14}$H$_{26}$O$_2$ 226.1933).

See Figures A-69 and A-70 (Appendix) for the nmr and mass spectra for compound 58.

i. (E,Z)-3,4-Dineopentyldiene-2,2,5,5-tetramethyltetrahydrofuran, 59

Diol 59 cyclodehydrated, with concomitant double-bond isomerization, overnight in CDCl$_3$ solution in the refrigerator to the tetrahydrofuran 59. This reaction was accompanied by apparent polymerization. Tetrahydrofuran 59 was purified by preparative tlc on silica gel (benzene:CHCl$_3$ 4:1), although some polymeric material was still present at this point.

Nmr (CDCl$_3$) $\delta$ 0.92 (s, 9H), 1.07 (s, 3H), 1.11 (s, 9H), 1.29 (impurity), 1.37 (s, 3H), 1.79 (s, 3H), 1.86 (s, 3H); mass spectrum (gcms) m/e (rel intensity) 264 (0.015), 249 (0.06), 207 (0.52), 137 (1.0).

See Figures A-71 and A-72 (Appendix) for the nmr and mass spectra for compound 59.
5. Miscellaneous 1,3-Dienes

a. 1,2-Diisopropylidene-3,3,4,4-tetramethylcyclobutane, 60

Compound 60 was synthesized according to the literature in 75 - 78% analytical yield by heating neat tetramethyl allene in a sealed tube for 9 days at 142 - 143°. Cyclobutane 60 was collected as the third peak (peak 1: tetramethyl allene; peak 2: unidentified) by preparative vpc using a Carbowax (15% on Chromosorb W) 10' x 3/8" column operating at 130°.

Nmr (CCl₄) δ 1.05 (s, 12H), 1.61 (s at 60 mHz, 12H).

b. Ethyl Hydrogen (E)-Benzyldienesuccinate, 61

Preparation of compound 61 was performed under nitrogen using a flame-dried apparatus. A mixture of benzaldehyde (26 ml, 0.25 mol) and diethyl succinate (42 ml, 0.25 mol) in 100 ml of tert-butyl alcohol was added dropwise to a refluxing solution of potassium tert-butoxide (11.83 g K, 0.304 mol) in 500 ml of tert-butyl alcohol. After addition was complete (~45 min), the orange solution was refluxed for an additional hr.

The cooled reaction mixture was hydrolyzed with water, most of the tert-butyl alcohol was removed under aspirator pressure, and the oil was taken up in ether and 7.5% Na₂CO₃. The organic layer was extracted twice with 7.5% Na₂CO₃. These extracts were combined, cooled in an ice/water bath, and made acidic with 4 N HCl. The acidic
aqueous layer was extracted twice with ether, the ether extracts were combined, dried (MgSO₄), and the solvent was removed. The reaction product was subjected to esterification without further characterization.

c. Diethyl (E)-Benzyldienesuccinate, 62

Compound 61 was refluxed with excess absolute ethanol, benzene, and a few drops concd H₂SO₄ overnight using a Dean-Stark apparatus to azeotropically remove the water. Ethanol and benzene were added to the reaction mixture as necessary.

The cooled reaction mixture was washed with water and then repeatedly with ~3% Na₂CO₃ until a basic wash was obtained. The organic layer was dried and solvent was removed to yield the diester 62 (27.5% overall yield for these first two steps).

Nmr (CDCl₃) δ 1.2. (t, 3H, J = 4 Hz), 1.28 (t, 3H, J = 4 Hz), 3.48 (s, 2H), 4.12 (q, 2H, J = 4 Hz), 4.14 (q, 2H, J = 4 Hz), 7.27 - 7.34 (m, 5H), 7.86 (s, 1H).

See Figure A-73 (Appendix) for the nmr spectrum of compound 62.

d. Ethyl Hydrogen (E,E)-Dibenzylidienesuccinate, 63

Compound 62 (5.59 g, 0.0213 mol) plus benzaldehyde (3 ml, 0.0298 mol) were mixed and added dropwise, under nitrogen, to a refluxing solution of potassium tert-
butoxide (1.16 g K, 0.0298 mol) in 200 ml of \textit{tert}-butyl alcohol.\textsuperscript{11b} The reaction mixture was refluxed for 1 hr after addition was complete.

Work-up was performed as described for compound 61. Yield was not determined.

e. \textbf{Diethyl (E,E)-Dibenzylidenesuccinate, 64}

The half-acid ester 63 was esterified with excess absolute ethanol, benzene, and a few drops of concd $\text{H}_2\text{SO}_4$, using a Dean-Stark apparatus for azeotropic water removal. The Dean-Stark apparatus was drained periodically and more ethanol and benzene were added to the reaction mixture, as necessary. Work-up was performed as described for the diester 62.

Nmr (CDCl$_3$) $\delta$ 1.08 (t, 6H, $J = 4$ Hz), 4.12 (q, 4H, $J = 4$ Hz), 7.18 - 7.48 (m, 10H), 7.88 (s, 2H).

See Figure A-74 (Appendix) for the nmr spectrum of compound 64.

f. \textbf{(E,E)-3,4-Dibenzylidene-2,5-dimethyl-2,5-hexanediol, 65}

Compound 64 (0.79 g, 2.26 mmol) was dissolved in 80 ml of anhydrous ether and added dropwise, under nitrogen, to 30 ml of $\sim$0.5 M methyl lithium in ether.\textsuperscript{11c} The reaction mixture was refluxed for 1 hr, then cooled in an ice/water bath, and carefully hydrolyzed with water. The ether layer was separated and the aqueous layer was
extracted with two more portions of ether. The combined ether layers were dried (MgSO₄) and concentrated at or below room temperature to yield 0.7 g of a crude yellow oil.

Purification was accomplished by preparative tlc on silica gel (5% MeOH in CHCl₃).

Nmr (CDCl₃) δ 1.16 (s, 6H), 1.61 (s, 6H), 6.85 (s, 2H), 7.2 - 7.7 (m, 10H); ir (neat) 3310 cm⁻¹ (s, broad), 1150 (s).

See Figures A-75 and A-76 (Appendix) for the nmr and ir spectra for compound 65.

g. (E,E)-3,4-Dibenzylidene-2,2,5,5-tetramethyltetrahydrofuran, 66

A sealed tube of diol 65 in CDCl₃ was held overnight at 80°. The tetrahydrofuran 66 thus obtained was purified by preparative tlc on silica gel (benzene:CHCl₃ 4:1).

Nmr (CDCl₃) δ 1.53 (s, 12H), 6.28 (s, 2H), 6.8 - 7.5 (m, 10H); ir (nujol) 1370 cm⁻¹ (doublet).

See Figures A-77 and A-78 (Appendix) for the nmr and ir spectra for compound 66.

h. Ethyl Hydrogen (E)-α-Benzylidene-α'-isopropylidene-succinate, 67a

A solution of diethyl isopropylidenesuccinate 26 (22.32 g, 0.104 mol) and benzaldehyde (11.68 g, 0.11
mol, from a freshly-opened bottle) in 50 ml of tert-butyl alcohol was added dropwise, under nitrogen, to a refluxing solution of potassium tert-butoxide (4.67 g K, 0.119 mol) in 150 ml of tert-butyl alcohol. Addition was completed in 25 min, and the reaction mixture was then refluxed for 1 hr.

The reaction mixture was hydrolyzed with 3 N HCl and extracted several times with ether. The combined ether layer was extracted repeatedly with 7.5% Na₂CO₃ until a strongly basic extract was obtained. This basic aqueous extract was cooled in an ice/water bath, made acidic with 6 N HCl, and extracted with three portions of ether. Evaporation of solvent after a brief drying period (MgSO₄) yielded 16.8 g (59%) of a viscous yellow oil.

i. Dimethyl (E)-α-Benzylidene-α'-isopropylidene-succinate, 68

Compound 67a was purified by hydrolysis to the diacid in refluxing 1 N KOH. After a 2 hr reaction time, the reaction mixture was acidified with 3% HCl. The pale yellow crystals that separated were dried in vacuo.

For the diacid: Mp 214.5 - 215°; nmr (acetone-d₆)
δ 1.61 (s, 3H), 2.21 (s, 3H), 7.32 - 7.52 (m, 5H), 7.78 (s, 1H); ir (KBr) ~3000 cm⁻¹ (broad, s), 1675 (s).
See Figures A-79 and A-80 (Appendix) for the nmr and ir spectra for the hydrolysis product of compound 67a.

The above diacid was suspended in ethanol and esterified with excess ethereal diazomethane to yield the dimethyl ester 68.

Nmr (CDCl₃) δ 1.57 (s, 3H), 2.21 (s, 3H), 3.65 (s, 3H), 3.77 (s, 3H), 7.24 - 7.45 (m, 5H), 7.74 (s, 1H); ir (neat) 1730 cm⁻¹ (s), 1220 (s).

See Figure A-81 (Appendix) for the nmr spectrum of compound 68.

j. Dimethyl (Z)-α-Benzylidene-α′-isopropylidene-
succinate, 69

A few milligrams of benzophenone was added to diester 68 in CDCl₃ solution contained in a thin-walled nmr tube. The sample was degassed in a nitrogen stream and irradiated for 17 hr using a 550-Watt Hanovia mercury lamp and a Corning 0-52 filter. The stereoisomer 69 was formed in 50% analytical yield (determined by nmr integration).

Nmr (as a mixture with compound 68, in CDCl₃) 1.99 (s, 3H), 2.21 (s, 3H), 3.63 (s, 3H), 3.68 (s, 3H), 6.73 (s, 1H), 7.2 - 7.5 (m, 5H).

See Figure A-82 (Appendix) for the nmr spectrum of compound 69.
k. (E)-3-Benzylidene-4-isopropylidene-2,5-dimethyl-2,5-hexanediol, 70

Compound 68 (0.40 g, 1.46 mmol) in 50 ml of anhydrous ether was added dropwise to 35 ml of 0.52 M methyl lithium in ether under a dry nitrogen atmosphere. After addition was complete the bright orange solution was refluxed for 1 hr and allowed to cool to room temperature overnight.

The reaction mixture was chilled in an ice/water bath before careful hydrolysis with water. The organic and aqueous layers were separated and the aqueous layer was extracted with two more portions of ether. The combined ether layer was washed once with water and dried briefly (MgSO₄). Solvent was removed at or below room temperature to yield 0.39 g (97%) of a crude yellow oil.

Nmr (CDCl₃) δ 1.27 (s, 3H), 1.42 (s, 3H), 1.56 (s, 3H), 1.62 (s, 3H), 1.75 (s, 3H), 1.90 (s, 3H), 6.67 (s, 1H), 7.2 - 7.5 (m, 5H).

See Figures A-83 and A-84 (Appendix) for the nmr and ir spectra for compound 70.

(In a subsequent preparation attempt, compound 70 spontaneously cyclodehydrated to the tetrahydrofuran, 71, and it was therefore not possible to isolate the diol 70.)

1. (E)-3-Benzylidene-4-isopropylidene-2,2,5,5-tetramethyl-tetrahydrofuran, 71

Compound 70 was heated to 75° in CDCl₃ solution in an nmr tube. After 30 min, an nmr spectrum indicated
that almost complete conversion to the tetrahydrofuran 71 had occurred. Purification was effected by preparative tlc on silica gel (benzene:CHCl₃ 4:1).

The stereochemistry about the double bond in the tetrahydrofuran 71 was established on the basis of the large upfield nmr chemical shift for the "inside" isopropylidene methyl group caused by the shielding of the phenyl ring. This assignment was further corroborated by the observation of a 20% nuclear Overhauser enhancement of the vinyl proton intensity upon irradiation at the neighboring geminal methyl frequency (see Results and Discussion).

Nmr (CDCl₃) δ 1.22 (s, 3H), 1.34 (s, 6H), 1.51 (s, 6H), 1.72 (s, 3H), 6.21 (s, 1H), 7.22 (m, 5H); 13C nmr (CDCl₃) δ 146.72, 139.05, 136.76, 127.78, 126.81, 126.11, 120.11, 120.83, 79.02, 78.91, 29.41, 28.62, 25.27, 21.14.

See Figures A-85, A-86, A-87, and A-88 (Appendix) for the proton nmr, 13C nmr, ir, and mass spectra, respectively, for compound 71.

m. (Z)-3-Benzylidene-4-isopropylidene-2,5-dimethyl-2,5-hexanediol, 72

The photolysis sample containing a 1:1 mixture of geometric isomers 68 and 69, plus a small amount of benzophenone, was refluxed with excess methyllithium in ether for 1 hr under nitrogen and allowed to stir overnight at room temperature.
Hydrolysis with water, extraction twice with ether, and drying (MgSO₄) yielded a 1:1 mixture of diols 70 and 72 plus 1,1-diphenylethanol.

n. (Z)-3-Benzylidene-4-isopropylidene-2,2,5,5-tetramethyl-tetrahydrofuran, 73

The crude reaction mixture containing a 1:1 mixture of diols 70 and 72 plus 1,1-diphenylethanol was taken up in CC₁₄ and refluxed over Linde 4A molecular sieves for 2 hr. Evaporation of solvent yielded a 1:1 mixture of tetrahydrofurans 71 and 73 plus some 1,1-diphenylethylene. Separation of these products was achieved by preparative tlc on silica gel (benzene:CHCl₃ 4:1). Approximate r_f's were: 1,1-diphenylethylene, 0.9; compound 73, 0.5; and compound 71, 0.4.

Nmr (CDCl₃) δ 1.21 (s, 6H), 1.44 (s, 6H), 1.86 (s, 3H), 2.04 (s, 3H), 6.56 (s, 1H), ~7.2 (m, 5H).

See Figure A-89 (Appendix) for the nmr spectrum of compound 73.

o. 3-Benzyl-4-isopropenyl-2,2,5,5-tetramethyl-2,5-dihydrofuran, 74

Attempts to isomerize compound 71 directly to compound 73 under the following conditions resulted in formation of the 1,5-hydrogen shift product, 74, in high yield: (1) compound 71 plus iodine, direct irradiation in CDCl₃; (2) compound 71 plus iodine, heated to 130 -
135° for 17 hr; (3) compound 71 plus benzophenone sensitizer, irradiation using a Corning 0-52 filter for 17 hr; (4) compound 71 plus iodine in benzene, heated to 75 - 80° for 4 days.

Nmr (CDCl₃) δ 1.19 (s, 6H), 1.39 (s, 6H), 1.74 (d, 3H, J = 1.5 Hz), 3.31 (s, 2H), 4.93 (dq, 2H, J = 1.5 Hz, J = 16 Hz), 7.06 - 7.21 (m, 5H).

See Figure A-90 (Appendix) for the nmr spectrum of compound 74.

p. Diisopropylidenesuccinic anhydride, 75

The diacid 35 (4.45 g, 0.0225 mol) was suspended in 30 ml of acetic anhydride. When a few drops of concd H₂SO₄ were added, the solution became homogeneous and took on a yellow color. The reaction mixture was warmed for 45 min on a water bath maintained at 70° and then cooled to room temperature.

The reaction mixture was poured onto ice and ether was added. The aqueous layer was separated and extracted again with ether. The combined ether layer was washed with four portions of 3% Na₂O₃, at which time a basic wash was obtained. The ether layer was dried (MgSO₄), filtered, and evaporated down to yield a solid. Recrystallization of the product from pentane/ether afforded 2.48 g (61.5%) of white needles.
Mp 53 - 53.5° (lit. 36 56 - 58°); nmr (CDCl₃) δ 1.96 (s, 6H), 2.38 (s, 6H); ir (nujol) 1795 cm⁻¹ (m), 1740 (s).

See Figures A-91 and A-92 (Appendix) for the nmr and ir spectra for compound 75.

q. 2,5-Dimethyl-4-(hydrazinocarbonylhydrochloride)-2,4-hexadiene-3-carboxylic acid, 76

To the anhydride 75 (1.62 g, 9.0 mmol) in 50 ml of ether was added hydrazine hydrate (99-100%, 0.65 ml, 13 mmol "pure" H₂NNH₂). A gummy solid immediately settled out. The reaction mixture was allowed to stand overnight.

The gummy white solid was dissolved in a small amount of 7.5% Na₂CO₃ and then 6 N HCl was added carefully until the solution was just acidic toward blue litmus. The fine white powder that formed was collected by suction filtration and was dried in vacuo to yield 0.83 g (37%) of compound 76.

Nmr (DMSO-d₆) δ 1.62 (s, 3H), 1.76 (s, 3H), 2.04 (s, 6H); ir (KBr) 3200 cm⁻¹ (broad, s), 1720 (s), 1600 (s).

See Figures A-93, A-94, and A-95 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 76.

r. 2,5-Dimethyl-4-(aminocarbonyl)-2,4-hexadiene-3-carboxylic acid, 77

Ten ml of concd NH₄OH (58%) was added to the anhydride 75 (0.267 g, 1.48 mmol). After stirring for 30 min at room temperature, a clear solution was obtained.
After 1 hr at room temperature, the reaction mixture was chilled in an ice/water bath and was carefully acidified with 6 N HCl. The white precipitate which formed immediately was collected by suction filtration and dried in vacuo to yield 0.215 g (74%) of compound 77.

\[ \text{Ir (KBr) } 3305 \text{ cm}^{-1} \text{ (s), } 3160 \text{ (s), } 1700 \text{ (m), } 1650 \text{ (s).} \]

See Figures A-96 and A-97 (Appendix) for the IR and mass spectra for compound 77.

s. 2,5-Dimethyl-4-(N-methylaminocarbonyl)-2,4-hexadiene-3-carboxylic acid, 78

Compound 78 was prepared by two methods. In a procedure similar to that of Brundrett and White,\textsuperscript{37} the diacid 35 (1.0 g, 5.05 mmol) was pulverized with 1,3-dimethyl urea (0.5 g, 5.68 mmol) and heated, under nitrogen, for 1 hr at 160°.

The yellow melt was cooled under nitrogen and then dissolved in a mixture of chloroform and water. The chloroform layer was separated, dried (MgSO\textsubscript{4}), and the solvent was removed. An NMR of the yellow oil indicated that it was a complex mixture. Crystallization of compound 78 occurred when the neat oil was stored overnight in the refrigerator.

In an alternate method of preparation, 0.5 ml of methylamine in water (25%) was added to the anhydride 75.
(0.5 g, 2.78 mmol) dissolved in 20 ml of ether. The reaction mixture was refluxed for 25 min and then cooled to room temperature.

The reaction mixture was acidified with 3% HCl. The ether and water layers were separated and the aqueous layer was extracted with two more portions of ether. The combined ether layer was dried (MgSO₄), and the solvent was removed to yield a crystalline 1:1 mixture (determined by nmr) of the starting anhydride 75 and the product 78. This crude mixture was dissolved in 2% Na₂CO₃ and ether. The basic layer was removed, acidified with 6 N HCl, and extracted with ether to yield the pure amide-acid 78.

Mp 157 - 158.5°; nmr (acetone-d₆) δ 1.68 (s, 3H), 1.75 (s, 3H), 1.95 (s, 3H), 2.00 (s, 3H), 2.84 and 2.89 (singlets, 3H); ir (KBr) 3305 cm⁻¹ (s), 1730 (s), 1665 (m), 1600 (s).

See Figures A-98, A-99, and A-100 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 78.

t. 2,5-Dimethyl-4-(N,N-dimethylaminocarbonyl)-2,4-hexadiene-3-carboxylic acid, 79

The anhydride 75 (0.762 g, 4.23 mmol) and dimethylamine hydrochloride (0.839 g, 10 mmol) were added to 30 ml of 1 N NaOH. The reaction mixture was capped and stirred at room temperature. The progress of the reaction was
monitored by tlc in the following manner: an aliquot was removed from the reaction mixture, acidified with 3 N HCl, and extracted with ether. The ether was dried (MgSO₄), filtered, and treated with ethereal diazomethane. Analytical tlc (benzene:CHCl₃ 4:1) showed the presence of the anhydride 75, the dimethyl ester 36, and the methyl ester of the product 79 at approximate r_f's of 0.5, 0.3, and 0.0, respectively.

After two days at room temperature, the entire reaction mixture was washed with ether and acidified with 3 N HCl. The oil which formed was extracted into ether and dried (MgSO₄). Evaporation of the solvent afforded an off-white solid which was recrystallized from pentane/acetone to yield clear, colorless rods. The yield was not determined.

Mp 105 - 106°; nmr (acetone-d₆) δ 1.70 (s, 3H), 1.77 (s, 6H), 1.97 (s, 3H), 3.03 (s, 3H), 3.23 (s, 3H).

See Figures A-101, A-102, and A-103 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 79.

u. 2,3,7,8-Tetraisopropylidene-perhydro-1,4,6,9-tetraketo-pyridazine[1,2-a]pyridazine, 80

To the hydrazide-acid 76 (0.584 g, 2.35 mmol) suspended in 50 ml of chloroform was added 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide HCl (0.480 g, 2.50
mmol, 98\%, Aldrich Chemical Co.). The reaction flask was stoppered and allowed to remain at room temperature. After 1 hr, the solution became homogeneous.

After a reaction period of two days, the chloroform layer was washed with two portions of water. The aqueous wash was back-extracted with one portion of chloroform and the combined chloroform layers were dried (K$_2$CO$_3$), filtered, and evaporated down at or below room temperature to yield compound 80. (Yields were variable and often compound 80 was obtained as a mixture with the isomeric 81.)

The structure of compound 80 was distinguishable from that of 81 on the basis of its mass spectrum (molecular ion at m/e 356, but no peak at 178) and its ir spectrum (1730 cm$^{-1}$; 6-membered ring).

Mp 164 - 165°; nmr (CDCl$_3$) $\delta$ 1.92 (s, 12H), 2.37 (s, 12H); ir (KBr) 1730 cm$^{-1}$ (s); mass spectrum exact mass 356.1730 (calcd for C$_{20}$H$_{24}$N$_2$O$_4$ 356.1736).

See Figures A-104, A-105, and A-106 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 80.

v. N,N-Bis(3,4-diisopropylidenedesuccinimide), 81

The following reaction was performed under nitrogen in dry apparatus using dry reagents. Compound 76 (0.149 g,
0.602 mmol) was dissolved in triethylamine (0.12 ml, 0.86 mmol) and 50 ml of sodium-dried benzene and added dropwise over a period of 20 min to a mixture of thionyl chloride (0.17 ml, 2.38 mmol) and triethylamine (0.25 ml, 1.79 mmol) in 100 ml of sodium-dried benzene. During this addition period, the reaction mixture was maintained just above the freezing point of benzene with an ice/water bath.

The reaction mixture was warmed to room temperature, and then washed in succession with water, 3% HCl (producing an acidic wash), and then 3% Na₂CO₃ (producing a basic wash). The benzene layer was dried (K₂CO₃), filtered, and evaporated down at or below room temperature to yield 50 mg (23%) of compound 81. (Yields were variable and often compound 81 was obtained in conjunction with isomeric compound 80 and a third, unidentified compound.)

The structure of compound 81 was established on the basis of its mass spectrum (m/e 178, corresponding to half of the dimer) and its ir spectrum (1790 cm⁻¹, corresponding to the 5-membered imide ring).

Mp 178 - 179°C; nmr (acetone-d₆) δ 1.82 (s, 12H), 2.15 (s, 12H); ir (KBr) 1790 cm⁻¹ (s), 1650 (s); mass spectrum exact mass for (molecular ion)/2 178.0863 (calcd for C₁₀H₁₂NO₂ 176.0868).
See Figures A-107, A-108, and A-109 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 81.

w. 2,5-Dimethyl-4-carbethoxy-2,4-hexadiene-3-carbonyl chloride, 82

Dry apparatus and dry reagents were employed throughout this synthesis. Thionyl chloride (3 ml, 0.03 mol) was added to an ice-cooled solution of the half-acid ester 27 (4.94 g, 0.028 mol) in 35 ml of benzene plus triethylamine (4.2 ml, 0.03 mol).

After 30 min at ice temperature, the reaction mixture was filtered and most of the benzene was removed under aspirator pressure (exposure to air was minimized). The reaction mixture was transferred to a small round-bottomed flask for distillation, the last traces of benzene and thionyl chloride were removed in a nitrogen stream, and the product was vacuum-distilled to yield 2.07 g (30%) of a viscous yellow oil.

Bp 74 - 79°/0.15 mmHg; nmr (CDCl₃) δ 1.25 (t, 3H, J = 7 Hz), 1.84 (s, 6H), 2.17 (s, 3H), 2.29 (s, 3H), 4.17 (q, 2H, J = 7 Hz); ir (neat) 1765 -1 (s), 1595 (s), 1195 (m); mass spectrum m/e (rel intensity) no molecular ion; loss of Cl 209 (0.125), 112 (0.22).

See Figures A-110, A-111, and A-112 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 82.
x. 2,5-Dimethyl-3-carbethoxy-4-(1-menthyl oxy carbonyl)-2,4-
bisadiene, \(83\)

Dry reagents and a dry apparatus were used throughout this synthesis, and the reaction was performed under nitrogen. \(\text{-Menthol (1.25 g, 8.0 mmol)}\) was added as a solid to a solution of the acid chloride 82 (2.07 g, 8.45 mmol) and triethylamine (1.25 ml, 9.0 mmol) in 100 ml of benzene. The reaction mixture was stirred at room temperature for 1 hr.

Water and ether were added and the reaction mixture was washed with 3% HCl (an acidic wash was produced) and then 3.5% \(\text{K}_2\text{CO}_3\) (a basic wash was produced). The organic layer was dried (\(\text{MgSO}_4\)), filtered, and evaporated down under aspirator pressure to yield a yellow oil. Analytical tlc (benzene:CHCl\(_3\) 4:1) indicated the presence of at least five components; the major one was \(\text{-menthol}\).

Compound 83 could be purified by column chromatography (200 - 325 mesh Bio Sil A, benzene:CHCl\(_3\) 4:1) or by preparative tlc on silica gel (benzene:CHCl\(_3\) 4:1).

Partial nmr (CDCl\(_3\)) \(\delta\) 1.76 (s, 6H), 2.09 (s, 3H), 2.10 (s, 3H); ir (neat) 1710 cm\(^{-1}\) (s), 1205 (s); mass spectrum m/e (rel intensity) no molecular ion, loss of menthol 226 (0.04), 180 (0.13), 117 (1.00).

See Figures A-113, A-114, and A-115 (Appendix) for the nmr, ir, and mass spectra, respectively, for compound 83.
A mixture of acetophenone (2.8 ml, 0.0233 mol) and diethyl isopropylidenesuccinate 26 (5.0 g, 0.0233 mol) in 30 ml of tert-butyl alcohol were added dropwise, under nitrogen, to a refluxing solution of freshly prepared potassium tert-butoxide (1.0 g K, 0.0256 mol) in 100 ml of tert-butyl alcohol. The cloudy orange reaction mixture was refluxed for 2.5 hr after addition was complete.

Water was added to the cooled reaction mixture and most of the tert-butyl alcohol was removed under aspirator pressure. Ether was added to the reaction product and the organic layer was extracted with two portions of 7.5% Na₂CO₃. These basic aqueous extracts were combined, cooled in an ice/water bath, and acidified with 6 N HCL. The acidic solution was extracted with three portions of ether. The ether extracts were combined, dried (MgSO₄), filtered, and concentrated under reduced pressure to yield 3.65 g (55%) of a bright yellow oil. Nmr showed the oil to be a 2:1 mixture of the half-acid esters 84 and 85. Structural assignments were based on the upfield nmr chemical shift observed for the "inside" methyl group in compound 85.³⁵

Compound 84: Mp 113 - 114°; nmr (CDCl₃) δ 0.89 (t, 3H, J = 7 Hz), 2.00 (s, 3H), 2.08 (s, 3H), 2.31 (s, 3H), 3.88 (q, 2H, J = 7 Hz), 7.1 - 7.3 (m, 5H).
See Figure A-116 (Appendix) for the nmr spectrum of compound 84.

Compound 85: (as a mixture with compound 84) nmr (CDCl₃) δ 1.30 (t, 3H, J = 7 Hz), 1.60 (s, 3H), 1.94 (s, 3H), 2.51 (s, 3H), 4.21 (q, 2H, J = 7 Hz), 7.1 - 7.3 (m, 5H).

z. (Z)- and (E)-2-Methyl-5-phenyl-2,4-hexadiene-3,4-dicarboxylic acid, 86 and 87

Hydrolysis of the crude reaction mixture from the Stobbe condensation of acetophenone with diethyl isopropylidenesuccinate 26 proved to be an efficient method for impurity removal but did not readily allow separation of the isomeric diacids 86 and 87.

The crude mixture of half-acid esters 84 and 85 (4.18 g, 0.0145 mol) was refluxed for 1 hr in 150 ml of 12.5% aqueous KOH.

The cooled hydrolysis mixture was acidified with 6 N HCl. The gummy solid which separated was recrystallized from ethanol/water to yield a mixture of the diacids 86 and 87. Structural assignments were again based on the upfield nmr chemical shift of the "inside" methyl group for compound 87.35

Mp of the mixture of compound 86 and 87: 219 - 225°; nmr of compound 86 (acetone-d₆) δ 1.93 (s, 3H), 1.99 (s, 3H), 2.22 (s, 3H), 7.25 (s, 5H); nmr of compound 87
(acetone-d$_6$) $\delta$ 1.57 (s, 3H), 1.86 (s, 3H), 2.45 (s, 3H), 7.25 (s, 5H); ir of the mixture of compounds 86 and 87 (KBr) $\sim$ 3000 cm$^{-1}$ (broad, s), $\sim$ 1700 (broad).

See Figures A-117 and A-118 (Appendix) for the nmr and ir spectra, respectively, for the mixture of compounds 86 and 87.

aa. (Z)- and (E)-2-Methyl-5-phenyl-2,4-hexadiene-3,4-dicarboxylic acid, dimethyl ester, 88 and 89

The mixture of diacids 86 and 87 was suspended in ethanol and treated with ethereal diazomethane (freshly generated from Diazald, Aldrich Chemical Co.) until the solids were dissolved and the yellow color of excess diazomethane persisted.

The solvent was removed to yield a yellow oil which was shown by nmr to consist of a mixture of diesters 88 and 89. Structural assignments were based on the upfield nmr chemical shift for the "inside" methyl group in compound 89. 35

Nmr of compound 88 (CDCl$_3$) $\delta$ 1.91 (s, 3H), 1.99 (s, 3H), 2.24 (s, 3H), 3.37 (s, 3H), 3.69 (s, 3H), 7.1 - 7.3 (m, 5H); nmr of compound 89 (CDCl$_3$) $\delta$ 1.54 (s, 3H), 1.87 (s, 3H), 2.45 (s, 3H), 3.63 (s, 3H), 3.71 (s, 3H), 7.1 - 7.3 (m, 5H); ir of a mixture of compounds 88 and 89 (neat) 1720 cm$^{-1}$ (s).
See Figures A-119 and A-120 (Appendix) for the nmr and ir spectra for the mixture of compounds 88 and 89.

bb. (Z)- and (E)-Diols 90 and 91

A mixture of diesters 88 and 89 (ca. 100 mg) in 10 ml of absolute ether was added dropwise, under nitrogen, to a large excess of methyllithium (15 ml of 1.7 M in ether, Alfa Chemical Co.) in 50 ml of absolute ether. The bright yellow reaction mixture was refluxed for 30 min after addition was complete and was then stirred overnight under nitrogen.

The reaction mixture was cooled in an ice/water bath and water was cautiously added just until two clear layers were obtained. The aqueous and ether layers were separated and the aqueous layer was extracted with two more portions of ether. The ether layers were combined, dried (MgSO₄), filtered, and concentrated under aspirator pressure at or below room temperature to yield an oil. The nmr spectrum consisted of a very complex methyl region, although there were no resonances in the olefinic region.

Cyclodehydration was attempted two times: (1) by refluxing the above oil, in chloroform, over Linde 4A molecular sieves for 2 hr, and (2) by refluxing the oil in carbon tetrachloride (without molecular sieves) for
2 hr. In both cases, complex mixtures were obtained (tlc analysis, benzene:CHCl₃ 4:1) which may have included elimination products. The reaction products were not investigated further.

cc. Ethyl Hydrogen (E)-Neopentylidenesuccinate, 92

Trimethylacetaldehyde, sodium bisulfite addition compound (technical grade, Aldrich Chemical Co., 3.0 g, 15.7 mmol) was hydrolyzed with 40 ml of 3 N HCl and extracted with four portions of ether (total volume of 50 ml). The ether extracts were combined, dried (MgSO₄), and filtered. Diethyl succinate (2.60 ml, 15.5 mmol) was added to the solution of trimethylacetaldehyde in ether, and this mixture was then added, dropwise, to a solution of potassium tert-butoxide (0.64 g K, 16.4 mmol) in 75 ml of tert-butyl alcohol at room temperature. After addition was complete, the reaction mixture was refluxed for 1 hr.

The cooled reaction mixture was acidified with 3 N HCl and most of the tert-butyl alcohol was removed. Water was added and the mixture was extracted with three portions of ether. The ether extracts were combined, dried (MgSO₄), filtered, and evaporated down to yield a light yellow oil which was shown by nmr to consist of a mixture of
the product 92 and ethyl hydrogen succinate. The half-acid ester 92 was esterified without further characterization.

dd. Diethyl (E)-Neopentylidene succinate, 93

The oil 92 was mixed with 30 ml of absolute ethanol, 50 ml of benzene, and four drops of concd H₂SO₄ and refluxed overnight using a Dean-Stark apparatus for azeotropic water removal.

The cooled reaction mixture was diluted with ether and washed with several portions of 5% Na₂CO₃ (until a basic wash was obtained). The organic layer was dried (MgSO₄), filtered, and evaporated down. The clear yellow oil was transferred to a smaller vessel and vacuum distilled to yield 0.76 g (20.2% yield for these two steps) of a clear, colorless, viscous oil.

Bp 89 - 90°/0.5 mmHg; nmr (CDCl₃) δ 1.20 (s, 9H), 1.25 (t, 3H, J = 7 Hz), 1.28 (t, 3H, J = 7 Hz), 6.99 (s, 1H).

See Figure A-121 (Appendix) for the nmr spectrum of compound 93.
C. Dynamic Nmr Measurements and Computer Programs

The dynamic nmr data were obtained on either the Varian HA-100 or Varian XL-100 spectrometers. The digital temperature read-out attached directly to the probe of the HA-100 spectrometer was calibrated against the chemical shifts of ethylene glycol and methanol and found to be accurate to ±1°.38,39 The oil-filled nmr tube containing a thermocouple which was used to determine the probe temperature on the XL-100 was similarly calibrated.39 All measurements were made after sufficient time was allowed for thermal equilibration of the sample. All dynamic behavior was found to be fully reversible (after completion of a series of high- or low-temperature experiments, the ambient temperature spectrum was recorded again.)

Complete line-shape analysis was performed using the in-house programs ABEX (adapted to the Digital Equipment Corporation PDP-11 computer by T. T. Bopp and G. Gulden, treatment according to Lynden-Bell40) and DNMR3 (adapted to the PDP-11 by T. T. Bopp, treatment according to Kleier and Binsch41). Data analysis was performed using NMREA (written for the PDP-11 by T. T. Bopp and N. Liu). NMREA performs unweighted linear least squares on the \( \tau \) vs. temperature data, and calculates the activation parameters from the slope and intercepts of \( \ln \tau \) vs. \( 1/T \).
III. RESULTS AND DISCUSSION

A. Syntheses

This section presents the synthetic schemes for the various new compounds which were prepared, and is followed by a summary of general trends and observations concerning the syntheses.

1. Acyclic Diisopropylidene Compounds

The acyclic compounds 25 - 37 were synthesized according to Scheme 1.

2. Cyclic Five-membered Ring Diisopropylidene Compounds

The five-membered cyclic diisopropylidene compounds 38 - 46 were obtained according to Scheme 2.

3. Cyclic Six-membered Ring Diisopropylidene Compounds

The hexahydropyridazines 47 and 48 and the urazole 49 were synthesized according to Scheme 3.

4. Dineopentylidene Compounds

The dineopentylidene compounds, inaccessible via the double Stobbe condensation, were synthesized according to Scheme 4.
5. Miscellaneous 1,3-Dienes

Schemes 5, 6, 7, 8, 9, and 10 outline the syntheses of additional 1,3-dienes.

6. Unsuccessful Synthetic Attempts

Scheme 11 details the attempts made to obtain seven-membered cyclic carbonates, sulfinates, and boronates. Miscellaneous unsuccessful synthetic attempts are shown in Scheme 12.
Scheme 1

Acyclic Diisopropylidene Compounds
Scheme 2

Cyclic Five-membered Ring Diisopropylidene Compounds
R⁻ - K⁺ = potassium phthalimide

29

CH₃NHCH₂CH₂NHCH₃

sodium napthalene

\( \text{dimethyl acetylene dicarboxylate} \) CH₃CN

\( \text{H₂NNH₂} \)

\( \text{NCH₃} \)

\( \text{NHCH₃} \)

\( \text{N(CH₃)₂} \)

\( \text{N-NH₂} \)

\( \text{CO₂Me} \)

\( \text{CO₂Me} \)
Scheme 3
Cyclic Six-membered Ring Diisopropylidene Compounds

\[
\begin{align*}
\text{CH}_3\text{NNNCH}_3 & \quad 47 \\
\text{Br} & \quad 29 \\
\text{PhCH}_2\text{NNNCH}_2\text{Ph} & \quad 48 \\
\text{HN} & \quad 49 \\
\text{HN} & \quad \text{NPh} \\
2 \text{ equ NaOH} & 
\end{align*}
\]
Scheme 4
Dineopentyldene Compounds

Scheme diagram with chemical structures and reactions.
Scheme 5
Miscellaneous 1,3-Dienes

\[ \text{cycloaddition} \rightarrow \text{product} \]

Scheme 6
Miscellaneous 1,3-Dienes

\[ \text{reactions} \rightarrow \text{products} \]
Scheme 7

Miscellaneous 1,3-Dienes

\[ \text{26} \xrightarrow{\text{PhCHO}} \text{67a} \quad \text{67b} \]

\[ \text{67a} \quad R=H, R'=\text{Et} \quad \text{67b} \quad R=\text{Et}, R'=\text{H} \]

\[ \text{1) KOH/}H^+ \]
\[ \text{2) CH}_2\text{N}_2 \]

\[ \text{69} \xrightarrow{\text{hν/ sens}} \text{68} \]

\[ \text{1) CH}_3\text{Li} \]
\[ \text{2) H}_2\text{O} \]

\[ \Delta \]

\[ \text{71} \]

\[ \text{72} \xrightarrow{\Delta} \text{73} \]
Scheme 8

Miscellaneous 1,3-Dienes

```
\[ \text{CO}_2\text{H} \quad \text{CO}_2\text{H} \]
\[ \text{CONNH}_2\cdot\text{HCl} \]
\[ \text{H}_2\text{NNHz} \quad \text{NH}_4\text{OH} \quad \text{CH}_3\text{NH}_2 \]
\[ \text{CO}_2\text{H} \quad \text{CONH}_2 \quad \text{(CH}_3\text{)}_2\text{NH} \]
\[ \text{SOCl}_2 \quad \text{Et}_3\text{N} \]
\[ \text{CON(CH}_3\text{)}_2 \]
```

80

81
Scheme 9

Miscellaneous 1,3-Dienes

\[
\text{Scheme 9}
\]

\[
\begin{align*}
\text{I-menthol} & \quad \xrightarrow{\text{SOCl}_2} \quad \text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{I-menthol} & \quad \xrightarrow{\text{1-menthol}} \quad \text{CO}_2\text{Et} & \quad \text{CO}_2\text{Et} \\
\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2 & \quad \xrightarrow{\text{28}} \quad \text{OH} & \quad \text{OH}
\end{align*}
\]
Scheme 10

Miscellaneous 1,3-Dienes

\[
\begin{align*}
\text{26} & \xrightarrow{\text{acetophenone, } tBuOK} \text{84, 85} \\
\text{1) KOH} & \xrightarrow{2) H^+} \text{86, 87} \\
\left[\begin{array}{c}
\text{88, 89} \\
\text{90, 91}
\end{array}\right] & \xrightarrow{\Delta} \text{elimination}
\end{align*}
\]
Scheme 11
Unsuccessful Attempts to Obtain Cyclic Seven-membered Ring Compounds

N,N'-carbonyl diimidazole $\xrightarrow{\Delta}$

[Chemical Structures]

N$_2$N'-carbonyl diimide addition

[Chemical Reactions]

$Na_2CO_3$/$EtOH$

$Ag_2CO_3$/$abs$EtOH$
Scheme 12

Miscellaneous Unsuccessful Synthetic Attempts
Scheme 12, continued

Miscellaneous Unsuccessful Synthetic Attempts

\[ \text{EtOH} \xrightarrow{H^+} \text{CO}_2\text{Et} \xrightarrow{\text{CHO}} \text{CO}_2\text{Et} \xrightarrow{\text{tBuOK}} \text{CO}_2\text{H} \]

\[ \text{EtOH} \xrightarrow{\text{CHO}} \text{CO}_2\text{Et} \xrightarrow{\text{tBuOK}} \text{CO}_2\text{Et} \xrightarrow{\text{CHO}} \text{CO}_2\text{H} \]
Scheme 12, continued

Miscellaneous Unsuccessful Synthetic Attempts

\[
\text{NaAlH}_2(OCH_2CH_2OCH_3)_2 \quad \text{or LiAlH}_4 \text{ under various conditions}
\]

\[
\begin{array}{c}
\text{CO}_2\text{Et} \\
\text{CO}_2\text{Et}
\end{array}
\xrightarrow{\text{diisopropyl ketone}}
\begin{array}{c}
\text{CO}_2\text{Et} \\
\text{CO}_2\text{H}
\end{array}
\]

\[
\begin{array}{c}
\text{CO}_2\text{Et} \\
\text{CO}_2\text{Et}
\end{array}
\xrightarrow{\text{p-NO}_2\text{-acetophenone}}
\begin{array}{c}
\text{CO}_2\text{H}
\end{array}
\]
7. Summary of Syntheses

a. Generality of the Stobbe Condensation

Scheme 13 below, details the generally accepted mechanism for the Stobbe condensation. Because a cyclic intermediate is involved which must be in the proper (trans) orientation for elimination to occur in the irreversible step, the (E) isomer, with the bulkier group "inside" is usually obtained.

Scheme 13
Mechanism of the Stobbe Condensation
Table 1 lists the \((E)/(Z)\) ratios obtained during this work from the Stobbe condensation with various aldehydes and ketones.
Table 1

(E)/(Z) Product Ratios from the Stobbe Condensation

<table>
<thead>
<tr>
<th>Reactants</th>
<th>Product*</th>
<th>(E)/(Z) Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Reactant" /></td>
<td><img src="image2" alt="Product" /></td>
<td>100% (E)</td>
</tr>
<tr>
<td><img src="image3" alt="Reactant" /></td>
<td><img src="image4" alt="Product" /></td>
<td>100% (E)</td>
</tr>
<tr>
<td><img src="image5" alt="Reactant" /></td>
<td><img src="image6" alt="Product" /></td>
<td>100% (E)</td>
</tr>
</tbody>
</table>
Table 1, continued

(E)/(Z) Product Ratios from the Stobbe Condensation

<table>
<thead>
<tr>
<th>Reactants</th>
<th>Product*</th>
<th>(E)/(Z) Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO₂Et HO CH₃CPh</td>
<td><img src="image1" alt="Product 1" /></td>
<td>~1:2</td>
</tr>
<tr>
<td>CO₂Et CO₂Et</td>
<td><img src="image2" alt="Product 2" /></td>
<td>100% (E)</td>
</tr>
</tbody>
</table>

*only the (E) isomer is shown
Although the double Stobbe condensation proved to be an efficient reaction for construction of the vicinal diisopropylidene skeleton, it was shown to be of limited value for the introduction of bulkier vicinal dialkylidene/diarylidene groups. Whereas high yields were realized (>90%) for the condensation of diethyl succinate with acetone, the yields with benzaldehyde were lower, and with pivalaldehyde, lower still (ca. 18%). Diisopropyl ketone would not condense with diethyl succinate. The influence of steric hindrance upon the yield of the Stobbe condensation has been previously documented by Newman and Linsk, who reported that compound 94 would not condense with diethyl succinate when either \( R'' = \text{CH}_3 \) or both \( R \) and \( R' = \text{CH}_3 \).
This work employed potassium tert-butoxide exclusively as the condensing base. It was found by Gordon\textsuperscript{44} that when sodium hydride was used as the base for the second condensation (that of a diethyl alkylidene or arylidene-succinate with another mole of ketone) that tri-condensation products such as compounds $\sim 95$ and $\sim 96$ could be isolated.

\begin{center}
\includegraphics[width=0.5\textwidth]{structures.png}
\end{center}

\subsubsection*{b. Tendency for Five-membered Ring Formation}

The favorable nature of five-membered ring formation in compounds containing the vic-dialkylidene moiety was evidenced by the essentially spontaneous cyclodehydration of tertiary diols $37$, $56$, $65$, $70$, and $72$ to their respective tetrahydrofurans, and was supported by the relatively high yields obtained in reactions of the dibromide $\sim 29$ according to Scheme 2. The tendency for five-membered ring formation was so great that even under reaction conditions involving
very large excesses of dimethylamine, reaction of the dibromide 29 afforded only the quaternary salt, 44.

Formation of the six-membered ring compounds 47, 48, and 49 was less favorable than for the five-membered series in terms of yield, as was the synthesis of the acyclic compounds 30 - 34 according to Scheme 1.

Attempts to prepare seven- and eight-membered vic-dialkyldiene compounds were unsuccessful.

c. The Dineopentylidene Series of Compounds

Because the double Stobbe condensation proved to be ineffectual for construction of the dineopentylidene skeleton, the reaction pathway outlined in Scheme 4 was utilized for the preparation of these compounds. These studies were greatly facilitated by the generous donation of one gram of the dihydrothiophene diester 50 by Professor R. M. Kellogg of the University of Groningen, The Netherlands.

Although reduction of the (E,Z) diester 52 and the (Z,Z) diester 54 with diisobutylaluminum hydride to the corresponding diols 55 and 58 proceeded cleanly, reduction of the (E,E) isomer 53 was accompanied by extensive rearrangement. The (E,E) diol 57 could be separated from the complex reaction mixture by preparative thin layer chromatography on silica gel.
The diastereotopic methylene protons of the diol 57 should be anisochronous; however, compound 57 exhibited only three nmr peaks in the solvents deuteriochloroform, carbon tetrachloride, carbon disulfide, benzene-d$_6$, and pyridine-d$_5$. Splitting of the tert-butyl singlet was observed in the presence of the chiral shift reagent Eu(tfc)$_3$, indicating that 57 is chiral at room temperature, as expected.
B. Dynamic Nmr Results

Table 2 summarizes the dynamic nmr (dnmr) results, and is followed by detailed descriptions of the individual experiments (in the order that they are listed in the table), and then by a section discussing the possible sources and magnitudes of error in these measurements. The last section summarizes these results and points out trends that were observed.

1. Table of Dnmr Results

Table 2 lists the dynamic nmr results that were obtained for the dissymmetric 1,3-dienes studied.
Table 2

Dynamic NMR Data

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cmpd #</th>
<th>R</th>
<th>Coalescence Temp °C</th>
<th>Solvent</th>
<th>$\Delta G^\ddagger_c$ kcal/mol</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Diagram]</td>
<td>46</td>
<td>$R_1 = R_2 = R_4 = \text{CH}_3$</td>
<td>48</td>
<td>CDCl₃</td>
<td>16.19&lt;sup&gt;a&lt;/sup&gt;, 16.1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>[Diagram]</td>
<td>71</td>
<td>$R_1 = R_2 = \text{CH}_3$, $R_3 = \text{Ph}$, $R_4 = \text{H}$</td>
<td>-78</td>
<td>HCCl₂F</td>
<td>10.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>[Diagram]</td>
<td>28</td>
<td>$R = \text{OH}$</td>
<td>138</td>
<td>nitrobenzene-d₅</td>
<td>20.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>[Diagram]</td>
<td>29</td>
<td>$R = \text{Br}$</td>
<td>109</td>
<td>diphenyl ether</td>
<td>20.57&lt;sup&gt;a&lt;/sup&gt;, 19.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>[Diagram]</td>
<td>32</td>
<td>$R = \text{CN}$</td>
<td>109</td>
<td>diphenyl ether</td>
<td>19.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>[Diagram]</td>
<td>33</td>
<td>$R = \text{SCOCH}_3$</td>
<td>~140</td>
<td>nitrobenzene-d₅</td>
<td>~20.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
### Table 2, continued

**Dynamic Nmr Data**

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cmpd #</th>
<th>R</th>
<th>Coalescence Temp °C</th>
<th>Solvent</th>
<th>$\Delta G_c^\ddagger$ kcal/mol</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>60</td>
<td></td>
<td>&lt;127</td>
<td>HCCl₂F</td>
<td>&lt;8</td>
</tr>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>47</td>
<td>R=CH₃</td>
<td>~ -112</td>
<td>CS₂</td>
<td>~8 &lt;sup&gt;b&lt;/sup&gt;,&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>~ -30</td>
<td>CDCl₃</td>
<td>11.9&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+109</td>
<td>diphenyl ether</td>
<td>19.1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>48</td>
<td>R=CH₂Ph</td>
<td>~ -46</td>
<td>CDCl₃</td>
<td>10.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>+131</td>
<td>nitrobenzene-d₅</td>
<td>20.4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>38</td>
<td>R=S</td>
<td>30</td>
<td>CDCl₃</td>
<td>15.16&lt;sup&gt;a&lt;/sup&gt;, 15.0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>39</td>
<td>R=SO</td>
<td>30</td>
<td>CDCl₃</td>
<td>15.1&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>40</td>
<td>R=SO₂</td>
<td>36</td>
<td>CDCl₃</td>
<td>15.45&lt;sup&gt;a&lt;/sup&gt;, 15.3&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
Table 2, continued

Dynamic Nmr Data

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cmpd #</th>
<th>R</th>
<th>Coalescence Temp °C</th>
<th>Solvent</th>
<th>$\Delta G^\ddagger$ kcal/mol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41</td>
<td>R=NCH$_3$</td>
<td>&lt;-100</td>
<td>acetone-d$_6$</td>
<td></td>
<td>$&lt; 8.4^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>42</td>
<td>R=NCH$_2$Ph</td>
<td>-95</td>
<td>CCl$_2$F$_2$:CS$_2$ 1:1</td>
<td></td>
<td>$8.7^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>43</td>
<td>R=O</td>
<td>-109</td>
<td>CCl$_2$F$_2$</td>
<td></td>
<td>$8.16^a, 8.0^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>R=C(CO$_2$Et)$_2$</td>
<td>-46</td>
<td>CCl$_2$F$_2$</td>
<td></td>
<td>$11.3^a, 11.1^b$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>53</td>
<td></td>
<td></td>
<td></td>
<td>bromo-benzene-d$_5$</td>
<td>$&gt; 24^d$</td>
</tr>
</tbody>
</table>
Table 2, continued

Dynamic Nmr Data

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cmpd #</th>
<th>R</th>
<th>Coalescence Temp °C</th>
<th>Solvent</th>
<th>ΔG° kcal/mol</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Chemical Structure" /></td>
<td>52</td>
<td></td>
<td>&lt; 25</td>
<td>CDCl₃</td>
<td>&lt;15³³</td>
</tr>
</tbody>
</table>

³³From complete line-shape analysis; treatment according to Lynden-Bell, adapted to the PDP-ll computer by T.T. Bopp.

³³Calculated from the Eyring rate equation:

\[ \Delta G_c = 4.57T_c \left[ 9.97 + \log_{10} \left( \frac{T_c}{(\Delta \gamma_{AB}^2 + 6J_{AB}^2)^{1/2}} \right) \right] \]

³³Determined by ¹³C nmr.

³³Determined in the presence of the chiral shift reagent Eu(tfc)₃.
2. Dynamic Nmr Results for Individual Compounds

a. 3,4-Diisopropylidene-2,2,5,5-tetramethyltetrahydrofuran, \( \text{46} \)

The ambient temperature nmr spectrum of compound \( \text{46} \) consisted of two sharp singlets for the gem-dimethyl protons (see Figure A-47, Appendix). Variable temperature nmr yielded two sharp singlets for the high field resonances at low temperatures. Upon warming, the usual coalescence phenomenon was observed at 48°, and at high temperatures, the spectra exhibited one sharp singlet for the four saturated methyl groups. Complete line-shape analysis (assuming the parameters \( J = 0, \Delta v = 30.5 \text{ Hz}, \) and \( T_2 = 0.21 \text{ sec} \), \(^{49}\) using deuteriochloroform as the solvent) produced the calculated spectra, samples of which are shown in Figure 4. An Arrhenius plot of eighteen points over the temperature range surrounding coalescence is shown in Figure 5. Arrhenius parameters \( E_a = 16.22 \text{ kcal/mol} \) with \( \log A = 12.85 \) were obtained from these data. A similar transition theory analysis yielded \( \Delta H^\ddagger = 15.58 \text{ kcal/mol}, \Delta S^\ddagger = -1.89 \text{ cal/mol-deg}, \) and \( \Delta G^\ddagger_{48} = 16.19 \text{ kcal/mol}. \) Table 3 lists the line-shape analysis data obtained for compound \( \text{46} \).
Figure 4. Experimental (left) and calculated dnmr spectra for compound 46.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 16.22 KCAL
LOG A = 12.8458

TRANSITION STATE ACTIVATION PARAMETER
DELTA H = 15.58 KCAL
DELTA S = -1.896 CAL/DEG.
AT A COALESCENCE TEMPERATURE OF 48.0 C
DELTA G = 16.19 KCAL

Figure 5. Arrhenius plot for compound 46.
Table 3
Dynamic NMR Data for Compound 46

3, 4- DIISOPROPYLIDENE-2, 2, 5, 5- TETRAMETHYLTETRAHYDROFURAN

<table>
<thead>
<tr>
<th>TEMP C</th>
<th>TAU</th>
<th>1000/T</th>
<th>LN(1/TAU)</th>
<th>CALC.</th>
<th>DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>17.9</td>
<td>2.0000E-01</td>
<td>3.4358</td>
<td>1.6094</td>
<td>1.5386</td>
<td>0.0708</td>
</tr>
<tr>
<td>20.7</td>
<td>1.8000E-01</td>
<td>3.4031</td>
<td>1.7148</td>
<td>1.8058</td>
<td>-0.0910</td>
</tr>
<tr>
<td>24.7</td>
<td>1.0000E-01</td>
<td>3.3574</td>
<td>2.3026</td>
<td>2.1788</td>
<td>0.1238</td>
</tr>
<tr>
<td>27.8</td>
<td>8.0000E-02</td>
<td>3.3228</td>
<td>2.5257</td>
<td>2.4610</td>
<td>0.0647</td>
</tr>
<tr>
<td>31.0</td>
<td>7.0000E-02</td>
<td>3.2879</td>
<td>2.6593</td>
<td>2.7463</td>
<td>-0.0871</td>
</tr>
<tr>
<td>35.1</td>
<td>4.7000E-02</td>
<td>3.2441</td>
<td>3.0576</td>
<td>3.1032</td>
<td>-0.0456</td>
</tr>
<tr>
<td>39.4</td>
<td>3.5000E-02</td>
<td>3.1995</td>
<td>3.3524</td>
<td>3.4675</td>
<td>-0.1151</td>
</tr>
<tr>
<td>42.6</td>
<td>2.7000E-02</td>
<td>3.1671</td>
<td>3.6119</td>
<td>3.7321</td>
<td>-0.1202</td>
</tr>
<tr>
<td>43.9</td>
<td>2.2000E-02</td>
<td>3.1541</td>
<td>3.8167</td>
<td>3.8381</td>
<td>-0.0214</td>
</tr>
<tr>
<td>46.0</td>
<td>1.8000E-02</td>
<td>3.1333</td>
<td>4.0174</td>
<td>4.0074</td>
<td>0.0099</td>
</tr>
<tr>
<td>46.7</td>
<td>1.7000E-02</td>
<td>3.1265</td>
<td>4.0745</td>
<td>4.0634</td>
<td>0.0111</td>
</tr>
<tr>
<td>47.8</td>
<td>1.4500E-02</td>
<td>3.1158</td>
<td>4.2336</td>
<td>4.1509</td>
<td>0.0828</td>
</tr>
<tr>
<td>48.8</td>
<td>1.3000E-02</td>
<td>3.1061</td>
<td>4.3428</td>
<td>4.2298</td>
<td>0.1130</td>
</tr>
<tr>
<td>51.7</td>
<td>1.1000E-02</td>
<td>3.0783</td>
<td>4.5099</td>
<td>4.4561</td>
<td>0.0537</td>
</tr>
<tr>
<td>54.2</td>
<td>9.5000E-03</td>
<td>3.0548</td>
<td>4.6565</td>
<td>4.6480</td>
<td>0.0085</td>
</tr>
<tr>
<td>57.5</td>
<td>8.0000E-03</td>
<td>3.0243</td>
<td>4.8283</td>
<td>4.8768</td>
<td>-0.0485</td>
</tr>
<tr>
<td>61.1</td>
<td>6.2000E-03</td>
<td>2.9918</td>
<td>5.0832</td>
<td>5.1626</td>
<td>-0.0704</td>
</tr>
<tr>
<td>66.7</td>
<td>3.5000E-03</td>
<td>2.9425</td>
<td>5.6550</td>
<td>5.5650</td>
<td>0.0900</td>
</tr>
</tbody>
</table>

ARRHENIUS PARAMETERS:
ACTIVATION ENERGY = 16.22 KCal.
LOG A = 12.8458

TRANSITION STATE ACTIVATION PARAMETERS:
DELTA H = 15.58 KCal.
DELTA S = -1.893 CAL./DEG.

AT A COALESCENCE TEMPERATURE OF 47.5 DEGREES C
DELTA G = 16.19 KCal.
b. (E)-Benzylidene-4-isopropylidene-2,2,5,5-tetramethyl-tetrahydrofuran, 71

Compound 71 was prepared for comparison to the similarly constituted diene, 15b, which Pasto et al. synthesized in optically active form.\textsuperscript{10}

\begin{center}
\begin{tikzpicture}
\node at (0,0) {\includegraphics[width=0.4\textwidth]{71.png}};
\node at (0,-1) {15b};
\end{tikzpicture}
\end{center}

In order to establish that the stereochemistry about the double bond in 71 was correct, a nuclear Overhauser experiment was performed. Irradiation at one of the saturated gem-dimethyl lines resulted in a 20\% enhancement of the vinyl proton resonance, whereas irradiation at the isopropylidene resonances (and at the other saturated gem-dimethyl line) had no effect upon the intensity of the olefinic proton signal.

This stereochemical assignment was further corroborated by the high field absorption (δ 1.22) of the "inside" isopropylidene methyl group which resides in the shielding area above the phenyl ring,\textsuperscript{35} and ultimately by synthesis of the geometric isomer, 73 (see Scheme 7).

Because the ambient temperature nmr spectrum of compound 71 exhibited only two sharp singlets for the 2- and 5-
gem-dimethyl groups (in addition to low field aromatic and vinyl absorptions, and two singlets for the isopropylidene methyl groups) (see Figure A-85, Appendix), a $^{13}$C nmr was obtained to determine whether the pairs of saturated methyl resonances were truly equivalent or whether these groups were accidentally isochronous. There was but one $^{13}$C nmr resonance observed for the methyl groups on C2 and one for the methyls on C5, as shown in Figure A-86 (Appendix).

The chemical shift equivalence of these saturated gem-dimethyl groups was further established by the behavior of compound 71 in the presence of the shift reagent Eu(fod)$_3$-d$_{27}$. A large contact shift was observed for the gem-dimethyl groups, although the chemical shifts of the diastereotopic groups remained isochronous. (Compound 71 did not complex with the chiral shift reagent, Eu(tfc)$_3$, presumably for steric reasons.)

The nmr spectrum of compound 71, when measured below -78° in dichlorodifluoromethane, consisted of four separate saturated methyl resonances. A $\Delta G_{-78}^+$ of 10.0 kcal/mol was estimated from the coalescence temperature. The data presented above require that racemization of the diene system be rapid at ambient temperature. Therefore, the dynamic process with a $\Delta G_C^+$ of 10.0 kcal/mol is assigned to racemization of the diene system, rather than to restricted
phenyl rotation or to slowed methyl rotation, both of which should have much lower free energy barriers.
The high temperature dynamic nmr behavior of diol 28 was observed in several solvents: quinoline, α-chloronapthalene, and nitrobenzene-d$_5$. The fact that the coalescence temperature was virtually identical in these three solvents (T$_c$ ranged from 138 to 142 degrees) seemed to indicate that hydrogen bonding is unimportant in the transition state for racemization, suggesting an s-trans geometry for the latter.

It was not possible to obtain a good computer fit for the nmr lineshapes of compound 28 unless it was assumed that the chemical shift difference, $\delta \nu_{AB}$, was temperature-dependent. The chemical shift difference decreased with temperature and was extrapolated to a constant value of 40.0 Hz for temperatures in excess of 145°. Complete line-shape analysis of thirteen points surrounding coalescence for compound 28 (constant parameters $J_{AB} = 11.5$ Hz, $T_2 = 0.200$ sec, using α-chloronaphthalene as the solvent) yielded an activation energy of 16.52 kcal/mol, $\Delta H^\ddagger = 15.71$ kcal/mol, $\Delta S^\ddagger = -11.97$ cal/mol-deg, and $\Delta G^\ddagger_{138} = 20.63$ kcal/mol. Calculated and experimental spectra for compound 28 are shown in Figure 6, and Table 4 lists the dnmr data. Figure 7 is the Arrhenius plot for compound 28.

In order to further illustrate that diol 28 is chiral at room temperature, its nmr spectrum was recorded in the
presence of the chiral shift reagent, Eu(tfc)$_3$. The splitting of the methylene AB quartet into two separate quartets showed that diastereomeric association complexes were present and indicated that compound 28 is chiral on the nmr time scale at room temperature. The results of the interaction of compound 28 with the chiral shift reagent are shown in Figure 8.
Figure 6. Experimental (left) and calculated dnmr spectra for compound 28.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 16.52 KCAL
LOG A = 10.7519

TRANSITION STATE ACTIVATION PARAMETER
DELTA H = 15.71 KCAL
DELTA S = -11.967 CAL/DEG.
AT A COALESCENCE TEMPERATURE OF 138.0° C
DELTA G = 20.63 KCAL

Figure 7. Arrhenius plot for compound 28.
Table 4

Dynamic NMR Data for Compound 23

2,3-DIISOPROPYLIDENE-1,4-BUTANEDIOL

<table>
<thead>
<tr>
<th>TEMP C</th>
<th>TAU</th>
<th>1000/T</th>
<th>LN(1/TAU)</th>
<th>CALC.</th>
<th>DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>90.0</td>
<td>1.500E-01</td>
<td>2.7537</td>
<td>1.8971</td>
<td>1.8667</td>
<td>0.0304</td>
</tr>
<tr>
<td>110.0</td>
<td>4.600E-02</td>
<td>2.6099</td>
<td>3.0791</td>
<td>3.6155</td>
<td>0.0176</td>
</tr>
<tr>
<td>120.0</td>
<td>2.600E-02</td>
<td>2.5436</td>
<td>3.6497</td>
<td>3.6134</td>
<td>0.0363</td>
</tr>
<tr>
<td>130.0</td>
<td>1.900E-02</td>
<td>2.4805</td>
<td>3.9633</td>
<td>4.1378</td>
<td>-0.1745</td>
</tr>
<tr>
<td>140.0</td>
<td>9.300E-03</td>
<td>2.4204</td>
<td>4.6777</td>
<td>4.6369</td>
<td>0.0408</td>
</tr>
<tr>
<td>145.0</td>
<td>7.600E-03</td>
<td>2.3915</td>
<td>4.8796</td>
<td>4.8775</td>
<td>0.0021</td>
</tr>
<tr>
<td>150.0</td>
<td>6.000E-03</td>
<td>2.3632</td>
<td>5.1160</td>
<td>5.1124</td>
<td>0.0036</td>
</tr>
<tr>
<td>155.0</td>
<td>4.600E-03</td>
<td>2.3356</td>
<td>5.3815</td>
<td>5.3418</td>
<td>0.0399</td>
</tr>
<tr>
<td>160.0</td>
<td>4.000E-03</td>
<td>2.3087</td>
<td>5.5215</td>
<td>5.5659</td>
<td>-0.0445</td>
</tr>
<tr>
<td>165.0</td>
<td>3.000E-03</td>
<td>2.2823</td>
<td>5.8091</td>
<td>5.7349</td>
<td>0.0242</td>
</tr>
<tr>
<td>170.0</td>
<td>2.500E-03</td>
<td>2.2566</td>
<td>5.9915</td>
<td>5.9990</td>
<td>-0.0075</td>
</tr>
<tr>
<td>175.0</td>
<td>2.000E-03</td>
<td>2.2314</td>
<td>6.2146</td>
<td>6.2083</td>
<td>0.0063</td>
</tr>
<tr>
<td>180.0</td>
<td>1.600E-03</td>
<td>2.2068</td>
<td>6.4378</td>
<td>6.4129</td>
<td>0.0248</td>
</tr>
</tbody>
</table>

ARRHENIUS PARAMETERS:
ACTIVATION ENERGY = 16.52 KCAL.
LOG A = 10.7519

TRANSITION STATE ACTIVATION PARAMETERS:
DELTA H = 15.71 KCAL.
DELTA S = -11.967 CAL./DEG.

AT A COALESCEENCE TEMPERATURE OF 138.0 DEGREES C
DELTA G = 20.63 KCAL.
ALL PAU
Figure 8. Nmr spectra of compound 28 in the presence of the chiral shift reagent Eu(tfc)$_3$. 

- a) 500 Hz sweep width. No shift reagent.
- b) 500 Hz sweep width. 14.5 mol% Eu(tfc)$_3$.
- c) 1000 Hz sweep width. 19.6 mol% Eu(tfc)$_3$.
- d) 1000 Hz sweep width. 44.3 mol% Eu(tfc)$_3$. 
d. 2,3-Diisopropylidene-1,4-dibromobutane, \( \text{29} \)

The chemical shifts for compound \( \text{29} \) were dependent upon temperature, and it was not possible to achieve a good computer fit of the experimental data assuming a constant chemical shift difference. Consequently, the chemical shift difference was decreased as the temperature was increased. An activation energy of 19.49 kcal/mol was calculated, assuming constant parameters of \( J_{\text{AB}} = 10 \) Hz and \( T_2 = 0.212 \) sec, using diphenyl ether as the solvent. The transition state parameters were calculated as \( \Delta H^\ddagger = 18.73 \) kcal/mol, \( \Delta S^\ddagger = -4.82 \) cal/mol-deg, and \( \Delta G_{109}^\ddagger = 20.57 \) kcal/mol. Log A was 12.28.

The results of the line-shape analysis for compound \( \text{29} \) are shown in Figures 9 and 10. Table 5 lists the dnmr data.

The nmr sample of the dibromide \( \text{29} \) became progressively more purple in color as the high temperature nmr spectra were recorded. However, no new peaks were observed in the nmr spectrum, and upon cooling the sample and re-recording the spectrum, the original spectrum was again observed.
Figure 9. Experimental (left) and calculated dnmr spectra for compound 29.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 19.49 KCAL
LOG A = 12.2826

TRANSITION STATE ACTIVATION PARAMETER
DELTA H = 18.73 KCA
DELTA S = -4.919 CAL./DEG.
AT A COALESCENCE TEMPERATURE OF 109.0°C
DELTA G = 20.57 KCAL

Figure 10. Arrhenius plot for compound 29.
Table 5
Dynamic Nmr Data for Compound 29

2,3-DIISOPROPYLIDENE-1,4-DIBROMOBUTANE

DATA

<table>
<thead>
<tr>
<th>TEMP C</th>
<th>TAU</th>
<th>1000/T</th>
<th>LN(1/TAU)</th>
<th>CALC.</th>
<th>DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>92.5</td>
<td>2.5000E-01</td>
<td>2.7349</td>
<td>1.3863</td>
<td>1.4641</td>
<td>-0.0778</td>
</tr>
<tr>
<td>94.9</td>
<td>1.8000E-01</td>
<td>2.7170</td>
<td>1.7148</td>
<td>1.6390</td>
<td>0.0758</td>
</tr>
<tr>
<td>97.9</td>
<td>1.6000E-01</td>
<td>2.6951</td>
<td>1.8326</td>
<td>1.8544</td>
<td>-0.0218</td>
</tr>
<tr>
<td>100.5</td>
<td>1.3000E-01</td>
<td>2.6763</td>
<td>2.0402</td>
<td>2.0382</td>
<td>0.0020</td>
</tr>
<tr>
<td>103.2</td>
<td>1.0000E-01</td>
<td>2.6571</td>
<td>2.3026</td>
<td>2.2265</td>
<td>0.0761</td>
</tr>
<tr>
<td>106.6</td>
<td>8.5000E-02</td>
<td>2.6333</td>
<td>2.4651</td>
<td>2.4598</td>
<td>0.0053</td>
</tr>
<tr>
<td>109.4</td>
<td>7.5000E-02</td>
<td>2.6140</td>
<td>2.5903</td>
<td>2.6480</td>
<td>-0.0585</td>
</tr>
</tbody>
</table>

ARRHENIUS PARAMETERS:
ACTIVATION ENERGY = 19.49 KCAL.
\[ \log A = 12.2826 \]

TRANSITION STATE ACTIVATION PARAMETERS:
DELTA H = 18.73 KCAL.
DELTA S = -4.819 CAL./DEG.

AT A COALESCENCE TEMPERATURE OF 109.0 DEGREES C
DELTA G = 20.57 KCAL.
e. 2,3-Diisopropylidene-1,4-dicyanobutane, 32

A free energy of activation of 19.0 kcal/mol was estimated for compound 32 from its coalescence temperature of 109°, measured in diphenyl ether. It was not possible to obtain good computer matches for the experimental nmr spectra for compound 32, although the chemical shift difference and T₂ were both varied in attempts to match the spectra.
f. 2,3-Diisopropylidene-1,4-butanedithiolacetate, 33

It was not possible to obtain a good computer fit for the experimental dnmr spectra for compound 33, although the chemical shift difference, $\Delta \nu_{AB}$, was varied in attempts to match the spectra.

A free energy of activation of $\Delta G^{+} = 20.9$ kcal/mol was estimated from the coalescence temperature in nitrobenzene-<sub>d</sub><sub>5</sub>. 16
g. 1,2-Diisopropylidene-3,3,4,4-tetramethylcyclobutane, \( \sim \)

Low temperature \( \text{ddnmr} \) was attempted for compound \( \sim \) in both carbon disulfide and in dichlorodifluoromethane. Although line-broadening was observed at \(-127^\circ\), splitting of the gem-dimethyl groups was not observed. An upper limit of \( \Delta G^\neq = 8 \text{ kcal/mol} \) can be estimated from these data.\(^{16}\)
h. 4,5-Diisopropylidene-1,2-dimethylhexahydropyridazine, 47

The ambient temperature nmr spectrum of compound 47 in deuteriochloroform consisted of isopropylidene resonances, a singlet for the N-methyl groups, and a singlet for the ring methylene protons (see Figure A-51, Appendix). The accidental equivalence of the ring methylene protons was removed in all other solvents employed (diphenyl ether, α-chloronapthalene, benzene-d₆, and dichlorodifluoromethane: carbon disulfide 1:1), where they appeared as an AB quartet at ambient temperature. Upon cooling in dichlorodifluoromethane:carbon disulfide 1:1 solution, the AB quartet seemed to undergo coalescence phenomena at ~-45°, and reappeared as a different AB quartet (J_AB unchanged, Δν_AB larger). When measured in deuteriochloroform (in which the ring methylene protons appeared as a singlet at room temperature), the low temperature dnmr spectra showed a clean broadening of the methylene protons at -30° and the appearance of an AB quartet below this temperature. These data allow estimation of ΔG° = 11.9 kcal/mol for the -30° process in compound 47. Figure 11 shows representative dnmr spectra for compound 47.

An attempt to fit the low temperature proton nmr spectra for compound 47 using complete line-shape analysis proved futile. It was assumed that this complication arose because the relative populations of the N-methyl groups
in the axial-axial (aa), the equatorial-axial (ea), and
the equatorial-equatorial (ee) conformations were functions
of temperature. As the temperature was lowered and the
nitrogen inversion was slowed, the relative conformer
populations were also changing.

This behavior was corroborated by $^{13}$C low temperature
nmr experiments on compound 47. (spectral assignments were
based on the off-resonance $^{13}$C nmr spectrum of compound
47.) At $\sim$-41°, the ring methylene resonance broadened
and at still lower temperatures it became sharp again.
This rate process was attributed to a slowing of the N-
methyl aa $\leftrightarrow$ ee interconversion with a concomitant and
significant increase in the population of ee over aa.
At very low temperatures ($\sim$-112°) a similar process occurred;
this time however, both the N-methyl resonance and the ring
methylene carbon underwent spectral broadening. At -135°,
the N-methyl carbons and the ring methylene carbons were
again sharp singlets. This final process was attributed
to a slowing of the "easy" and only remaining inversion,
that of ee $\leftrightarrow$ ea, with the ee conformer again remaining
predominant over the ea conformer.

The dynamical behavior of similar cyclic hydrazines
27, 28, and 29 has been extensively studied in other
laboratories.
Anderson investigated a varied series of hydrazines, including 97 - 99, by proton nmr and established barriers of ~10 - 12 kcal/mol for "nitrogen inversion." Subsequent $^{13}$C investigations of similar hydrazines showed this "nitrogen inversion" process to be far more complex than set forth by Anderson. Katritzky, using dipole moment measurements, established that there were more conformers present in compound 97 than solely the ee conformation assumed by Anderson's proton nmr work.

In a later paper, Katritzky summarized the three types of energy barriers available to cyclic hydrazines: 1) a barrier of ~12 kcal/mol, attributable to ring inversions which require a crossing of the substituents on the nitrogen in the transition state; 2) an intermediate process of ~10 - 11 kcal/mol which involves nitrogen inversion but not concomitant ring inversion, and 3) a low-energy barrier of ~8 kcal/mol which involves nitrogen inversions where no substituent crossing occurs.
In further $^{13}$C nmr experiments, Nelsen established the presence of ea and ee conformers in compound $\tilde{\jmath}$.

For the similarly constituted hydrazines $\tilde{\jmath}$8 and $\tilde{\jmath}$9, Takeuchi et al. found that only the ea conformation was present at low temperatures.

The data obtained in this work indicate that compound $\tilde{\jmath}$ is similar to Takeuchi's case, in that only one conformer is predominant at low temperatures.

A higher-energy dynamic process was also observed for hydrazine $\tilde{\jmath}$. The ring methylene protons, which appeared as an AB quartet in the ambient temperature nmr spectrum recorded in diphenyl ether, coalesced at +109° to a singlet. A value of $\Delta G^\neq = 19.1$ kcal/mol was calculated for this process. Figure 12 shows representative high temperature dnmr spectra for compound $\tilde{\jmath}$.

These data indicate that compound $\tilde{\jmath}$ demonstrates the three barriers for cyclic hydrazines predicted by Katritzky. The free energy barrier of 19.1 kcal/mol is assigned to the ring inversion process which involves racemization of the diisopropylidene system. The middle free energy barrier of 11.9 kcal/mol is assigned to nitrogen-nitrogen inversions which require a passing of the nitrogen substituents in the transition state, and the low energy barrier of $\sim$8 kcal/mol is assigned to nitrogen inversions where no substituent crossing is involved.
Addition of the chiral shift reagent $\text{Eu(tfc)}_3^{46}$ to the hydrazine $47$ was unsuccessful due to the extremely strong paramagnetic complexes formed which resulted (even in very low concentrations) in extensive broadening of the nmr lines.
Figure 11. Experimental dnmr spectra for compound 47. (The diastereotopic methylene protons were accidentally equivalent at ambient temperature in CDCl₃.)
Figure 12. Experimental high temperature dnmr spectra for compound 47.
As in the case of hydrazine 47, compound 48 also displayed low temperature and high temperature coalescence phenomena. The low temperature nmr spectra, measured in deuteriochloroform, involved the appearance of new AB quartets for both the benzyl protons and for the ring methylene protons, although it is uncertain whether actual coalescence or merely chemical shift changes occurred. A value of \( \Delta G_c^\ddagger = 10.0 \text{ kcal/mol} \) can be extracted from these data for the low temperature process, which is attributed to slowed nitrogen inversion. Figure 13 shows representative low temperature dnmr spectra for compound 48.

In the high temperature nmr spectra, recorded in nitrobenzene-d_5, the ring methylene protons went through what appeared to be a cross-over in chemical shifts before coalescence was observed. The benzyl protons seemed better behaved and the coalescence temperature for the molecule was taken as that of the benzyl protons (131°). This higher-energy process, attributed to ring inversion, was calculated to have \( \Delta G_c^\ddagger = 20.4 \text{ kcal/mol} \). Experimental high temperature dnmr spectra are shown in Figure 14.

Addition of the chiral shift reagent Eu(tfc)_3 to compound 48 gave results similar to those for compound 47.
Figure 13. Experimental low temperature dnmr spectra for compound 48.
Figure 14. Experimental high temperature dnmr spectra for compound 48.
j. 3,4-Diisopropylidnetetrahydrothiophene, 38

The room temperature nmr spectrum of sulfide 38 was that of a molecule undergoing a conformational change at an intermediate rate: the high-field region consisted of the two singlets expected for the isopropylidene groups, and the methylene ring protons appeared as a very broad peak (see Figure A-26, Appendix). A singlet was observed for the methylene protons above the coalescence temperature of 30°, and upon cooling the nmr sample, an AB quartet appeared for these diastereotopic protons. Complete line-shape analysis (assuming the constant parameters $J_{\text{AB}} = 12$ Hz, $\Delta\nu_{\text{AB}} = 29.66$, and $T_2 = 0.212$ sec, using deuteriochloroform as the solvent) produced the calculated spectra shown in Figure 15. An Arrhenius plot of ten points in the region surrounding coalescence (see Figure 16) yielded an activation energy of 11.86 kcal/mol, and transition state parameters were calculated as $\Delta H^\ddagger = 11.26$ kcal/mol, $\Delta S^\ddagger = -12.86$ cal/mol-deg, with a $\Delta G_{30^\ddagger} = 15.16$ kcal/mol. The dnmr data for compound 38 are listed in Table 6.
Figure 15. Experimental (left) and calculated dnmr spectra for compound 38.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 11.86 KCAL
LOG $\Lambda = 10.4248$

TRANSITION STATE ACTIVATION PARAMETER
$\Delta H = 11.26$ KCAL
$\Delta S = -12.858$ CAL/DEG.
AT A COALESCEENCE TEMPERATURE OF 30.0 C
$\Delta G = 15.16$ KCAL

Figure 16. Arrhenius plot for compound 38.
### Table 6
Dynamic Nmr Data for Compound 38

<table>
<thead>
<tr>
<th>TEMP C</th>
<th>TAU</th>
<th>1000/T</th>
<th>LN(1/TAU)</th>
<th>CALC.</th>
<th>DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>20.6</td>
<td>2.5000E-02</td>
<td>3.4043</td>
<td>3.6807</td>
<td>3.6053</td>
<td>0.0035</td>
</tr>
<tr>
<td>23.8</td>
<td>2.0000E-02</td>
<td>3.3676</td>
<td>3.9120</td>
<td>3.7043</td>
<td>0.0077</td>
</tr>
<tr>
<td>25.3</td>
<td>1.8000E-02</td>
<td>3.3504</td>
<td>4.0174</td>
<td>4.0053</td>
<td>0.0121</td>
</tr>
<tr>
<td>27.7</td>
<td>1.7000E-02</td>
<td>3.3237</td>
<td>4.0745</td>
<td>4.1649</td>
<td>-0.0903</td>
</tr>
<tr>
<td>28.5</td>
<td>1.5000E-02</td>
<td>3.3151</td>
<td>4.1997</td>
<td>4.2175</td>
<td>-0.0178</td>
</tr>
<tr>
<td>29.6</td>
<td>1.3000E-02</td>
<td>3.3031</td>
<td>4.3428</td>
<td>4.2894</td>
<td>0.0534</td>
</tr>
<tr>
<td>31.1</td>
<td>1.2000E-02</td>
<td>3.2868</td>
<td>4.4223</td>
<td>4.3866</td>
<td>0.0363</td>
</tr>
<tr>
<td>32.6</td>
<td>1.1000E-02</td>
<td>3.2706</td>
<td>4.5099</td>
<td>4.4020</td>
<td>0.0271</td>
</tr>
<tr>
<td>36.5</td>
<td>9.0000E-03</td>
<td>3.2295</td>
<td>4.7105</td>
<td>4.7287</td>
<td>-0.0181</td>
</tr>
<tr>
<td>40.4</td>
<td>7.0000E-03</td>
<td>3.1893</td>
<td>4.9618</td>
<td>4.9634</td>
<td>-0.0066</td>
</tr>
</tbody>
</table>

**Arrhenius Parameters:**
- Activation Energy = 11.86 KCAL.
- \( \log A = 10.4248 \)

**Transition State Activation Parameters:**
- \( \Delta H = 11.26 \) KCAL.
- \( \Delta S = -12.858 \) CAL./DEG.

At a coalescence temperature of \( 30.0 \) DEGREES C
- \( \Delta G = 15.16 \) KCAL.
k. 3,4-Diisopropylidene-tetrahydrothiophene-1-oxide, 39

Oxidation of the sulfide 38 with one equivalent of 
\textit{m}-chloroperbenzoic acid added an additional and config-
urationally stable element of dissymmetry. Consequently, 
diastereomers were observed at low temperatures.

The ambient temperature nmr spectrum consisted of 
the two isopropylidene singlets and a broad region assigned 
to the ring methylene protons (see Figure A-29, Appendix).
At high temperatures, an AB quartet was observed for these 
protons; at temperatures below the coalescence point (30°), 
two AB quartets were observed. (See Figure 17 for represent-
ative experimental dnmr spectra for compound 39.) A value 
of $\Delta G^\ddagger = 15.1$ kcal/mol was calculated for the ring inversion 
process in this compound.
Figure 17. Experimental dnmr spectra for compound 39.
1. 3,4-Diisopropylidenetetrahydrothiophene-1,1-dioxide, \( \text{40} \)

Further oxidation of the sulfide \( \text{38} \) to the sulfone \( \text{40} \) again restored symmetry to the molecule, and the temperature dependent nmr spectra were again those of a simple AB exchange process. Complete line-shape analysis was performed assuming constant parameters of \( J_{AB} = 14 \) Hz, \( \Delta v_{AB} = 29.88 \) Hz, and \( T_2 = 0.212 \) sec, using deuterio-chloroform as the solvent. Figure 18 shows calculated and experimental dnmr spectra for compound \( \text{40} \), and the Arrhenius plot from these data is shown in Figure 19. An activation energy of 12.09 kcal/mol was calculated, and the transition state parameters were \( \Delta H^\ddagger = 11.48 \) kcal/mol and \( \Delta S^\ddagger = -12.86 \) cal/mol-deg. At a coalescence temperature of 36°, \( \Delta G^\ddagger_c \) was calculated as 15.45 kcal/mol. The dnmr data for compound \( \text{40} \) are listed in Table 7.
Figure 18. Experimental (left) and calculated dnmr spectra for compound 40.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 12.09 KCAL
LOG A = 10.4319

TRANSITION STATE ACTIVATION PARAMETER
DELTA H = 11.48 KCAL
DELTA S = -12.664 CAL/DEG.
AT A COALESCENCE TEMPERATURE OF 36.0 C
DELTA G = 15.45 KCAL

Figure 19. Arrhenius plot for compound 40.
Table 7
Dynamic Nmr Data for Compound 40

3,4-DIISOPROPYLIDENETETRAHYDROTHIOPHENE-1,1-DIOXIDE

<table>
<thead>
<tr>
<th>TEMP C</th>
<th>TAU</th>
<th>1000/T</th>
<th>LN(1/TAU)</th>
<th>CALC.</th>
<th>DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.0</td>
<td>3.0000E-02</td>
<td>3.3767</td>
<td>3.5066</td>
<td>3.4003</td>
<td>0.0253</td>
</tr>
<tr>
<td>29.0</td>
<td>2.0000E-02</td>
<td>3.3096</td>
<td>3.7120</td>
<td>3.5006</td>
<td>0.0234</td>
</tr>
<tr>
<td>31.0</td>
<td>1.9000E-02</td>
<td>3.2879</td>
<td>3.7633</td>
<td>4.0210</td>
<td>-0.0577</td>
</tr>
<tr>
<td>32.0</td>
<td>1.7000E-02</td>
<td>3.2771</td>
<td>4.0745</td>
<td>4.0006</td>
<td>-0.0120</td>
</tr>
<tr>
<td>34.0</td>
<td>1.5000E-02</td>
<td>3.2557</td>
<td>4.1797</td>
<td>4.2164</td>
<td>-0.0166</td>
</tr>
<tr>
<td>35.0</td>
<td>1.4000E-02</td>
<td>3.2452</td>
<td>4.2607</td>
<td>4.2006</td>
<td>-0.0119</td>
</tr>
<tr>
<td>36.0</td>
<td>1.3000E-02</td>
<td>3.2347</td>
<td>4.3428</td>
<td>4.3445</td>
<td>-0.0017</td>
</tr>
<tr>
<td>37.0</td>
<td>1.2000E-02</td>
<td>3.2242</td>
<td>4.4228</td>
<td>4.4079</td>
<td>0.0149</td>
</tr>
<tr>
<td>40.0</td>
<td>1.0000E-02</td>
<td>3.1934</td>
<td>4.6052</td>
<td>4.5250</td>
<td>0.0094</td>
</tr>
<tr>
<td>42.0</td>
<td>9.0000E-03</td>
<td>3.1731</td>
<td>4.7105</td>
<td>4.7191</td>
<td>-0.0085</td>
</tr>
<tr>
<td>43.0</td>
<td>8.0000E-03</td>
<td>3.1631</td>
<td>4.8203</td>
<td>4.7801</td>
<td>0.0482</td>
</tr>
<tr>
<td>46.0</td>
<td>7.0000E-03</td>
<td>3.1533</td>
<td>4.9618</td>
<td>4.9610</td>
<td>0.0009</td>
</tr>
<tr>
<td>52.0</td>
<td>5.0000E-03</td>
<td>3.0755</td>
<td>5.2933</td>
<td>5.3127</td>
<td>-0.0144</td>
</tr>
</tbody>
</table>

Arrhenius Parameters:
Activation Energy = 12.09 KCAL.
Log A = 10.4319

Transition State Activation Parameters:
Delta H = 11.48 KCAL.
Delta S = -12.864 CAL./DEG.
At a Coalescence Temperature of 36.0 Degrees C
Delta G = 15.45 KCAL.
m. 3,4-Diisopropylidene-N-methylpyrrolidine, 41

Solubility problems were encountered with compound 41 at low temperatures. In both dichlorodifluoromethane and in dichlorodifluoromethane:carbon disulfide:acetone-d$_6$ 2:2:1, line-broadening due to freezing of the sample was observed. No evidence of coalescence was observed in acetone-d$_6$ at -100°, which sets an upper limit of ~8.4 kcal/mol on $\Delta G^\ddagger$ for compound 41.$^{16}$
n. 3,4-Diisopropylidene-N-benzylpyrrolidine, 42

The ambient temperature nmr spectrum for compound 42 consisted of two singlets for the isopropylidene groups, a singlet for the ring methylene protons, a singlet for the benzyl protons, and an aromatic multiplet (see Figure A-38, Appendix).

The diastereotropic benzyl protons became non-equivalent in the nmr spectrum at -95°, whereas the ring methylene protons remained a singlet at temperatures as low as -120°. It was not possible to obtain a good computer fit of the experimental nmr spectra, although the chemical shift difference was varied in attempts to fit the spectra. \( \Delta G^\ddagger \) was calculated as 8.7 kcal/mol from the coalescence temperature of -95°. 16

Although two processes, ring flipping and nitrogen inversion, are available to compound 42, the distinction between these processes cannot be made based upon the dnmr behavior of this compound.
o. 3,4-Diisopropylidenetetrahydrofuran, \( \text{43} \)

Although the isopropylidene groups in compound 43 appeared as a singlet at 100 mHz in both deuteriochloroform and in dichlorodifluoromethane, this accidental equivalence was removed when the spectrum was measured in benzene-\( d_6 \).

Complete line-shape analysis yielded the calculated dnmr spectra shown in Figure 20. Constant parameters were: \( J = 10.5 \text{ Hz}, \Delta \nu_{\text{AB}} = 22.7 \), and \( T_2 = 0.25 \text{ sec} \). The solvent was dichlorodifluoromethane. An activation energy of 6.58 kcal/mol was calculated, with \( \Delta H^\ddagger = 6.26 \text{ kcal/mol} \) and \( \Delta S^\ddagger = -11.52 \text{ cal/mol-deg} \). The free energy of activation was calculated as 8.16 kcal/mol at a coalescence temperature of -109°. (See Figure 21 for the Arrhenius plot of twenty points surrounding the region of coalescence.) The dnmr data for compound 43 are listed in Table 8.
Figure 20. Experimental (left) and calculated dnmr spectra for compound 43.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 6.58 KCAL
LOG A = 10.4537

TRANSITION STATE ACTIVATION PARAMETER
DELTA H = 6.26 KCAL
DELTA S = -11.507 CAL./DEG.
AT A COALESCENCE TEMPERATURE OF -109.0 C
DELTA G = 8.15 KCAL

Figure 21. Arrhenius plot for compound 43.
Table 8
Dynamic Nmr Data for Compound 43

3,4 DIISOPROPYLDIENETETRAHYDROFURAN

DATA

<table>
<thead>
<tr>
<th>TEMP C</th>
<th>TAU</th>
<th>1000/T</th>
<th>LN(1/TAU)</th>
<th>CALC.</th>
<th>DIFF</th>
</tr>
</thead>
<tbody>
<tr>
<td>-94.4</td>
<td>5.0000E-03</td>
<td>5.5944</td>
<td>5.2983</td>
<td>5.5446</td>
<td>-0.2463</td>
</tr>
<tr>
<td>-99.7</td>
<td>7.0000E-03</td>
<td>5.7654</td>
<td>4.9618</td>
<td>4.7735</td>
<td>-0.166</td>
</tr>
<tr>
<td>-102.0</td>
<td>8.5000E-03</td>
<td>5.8428</td>
<td>4.7677</td>
<td>4.7217</td>
<td>0.0458</td>
</tr>
<tr>
<td>-103.8</td>
<td>1.0000E-02</td>
<td>5.9047</td>
<td>4.6052</td>
<td>4.5163</td>
<td>0.0889</td>
</tr>
<tr>
<td>-105.6</td>
<td>1.3000E-02</td>
<td>5.9644</td>
<td>4.5220</td>
<td>4.3062</td>
<td>0.0366</td>
</tr>
<tr>
<td>-106.7</td>
<td>1.4000E-02</td>
<td>6.0700</td>
<td>4.2677</td>
<td>4.1756</td>
<td>0.0931</td>
</tr>
<tr>
<td>-107.7</td>
<td>1.5000E-02</td>
<td>6.0441</td>
<td>4.1997</td>
<td>4.0553</td>
<td>0.1444</td>
</tr>
<tr>
<td>-109.5</td>
<td>2.0000E-02</td>
<td>6.1106</td>
<td>3.7120</td>
<td>3.5352</td>
<td>0.0766</td>
</tr>
<tr>
<td>-110.4</td>
<td>2.4000E-02</td>
<td>6.1444</td>
<td>3.7227</td>
<td>3.7233</td>
<td>0.0064</td>
</tr>
<tr>
<td>-111.7</td>
<td>2.7000E-02</td>
<td>6.1939</td>
<td>3.6119</td>
<td>3.5595</td>
<td>0.0525</td>
</tr>
<tr>
<td>-112.3</td>
<td>2.8000E-02</td>
<td>6.2170</td>
<td>3.5755</td>
<td>3.4630</td>
<td>0.0926</td>
</tr>
<tr>
<td>-112.7</td>
<td>3.0000E-02</td>
<td>6.2325</td>
<td>3.5064</td>
<td>3.4316</td>
<td>0.0749</td>
</tr>
<tr>
<td>-113.9</td>
<td>3.5000E-02</td>
<td>6.2794</td>
<td>3.3524</td>
<td>3.2761</td>
<td>0.0763</td>
</tr>
<tr>
<td>-115.7</td>
<td>4.5000E-02</td>
<td>6.3512</td>
<td>3.1011</td>
<td>3.0384</td>
<td>0.0627</td>
</tr>
<tr>
<td>-116.1</td>
<td>5.0000E-02</td>
<td>6.3674</td>
<td>2.9757</td>
<td>2.9043</td>
<td>0.0109</td>
</tr>
<tr>
<td>-116.9</td>
<td>7.5000E-02</td>
<td>6.4000</td>
<td>2.5903</td>
<td>2.0769</td>
<td>-0.2064</td>
</tr>
<tr>
<td>-118.3</td>
<td>9.0000E-02</td>
<td>6.4662</td>
<td>2.4079</td>
<td>2.6576</td>
<td>-0.2496</td>
</tr>
<tr>
<td>-119.6</td>
<td>1.0000E-01</td>
<td>6.5125</td>
<td>2.3026</td>
<td>2.5042</td>
<td>-0.2016</td>
</tr>
<tr>
<td>-123.7</td>
<td>1.5000E-01</td>
<td>6.6712</td>
<td>1.9771</td>
<td>1.9126</td>
<td>-0.0154</td>
</tr>
<tr>
<td>-129.3</td>
<td>3.0000E-01</td>
<td>6.9517</td>
<td>1.2040</td>
<td>1.0500</td>
<td>0.1540</td>
</tr>
</tbody>
</table>

ARRHENIUS PARAMETERS:
ACTIVATION ENERGY = 6.58 Kcal.
LOG A = 10.4537

TRANSITION STATE ACTIVATION PARAMETERS:
DELTA H = 6.26 Kcal.
DELTA S = -11.523 Cal./deg.

AT A COALESCENCE TEMPERATURE OF -107.7 DEGREES C
DELTA G = 8.16 Kcal.
The ambient temperature nmr spectrum of compound 45 consisted of the expected isopropylidene resonances, the ethyl triplet and quartet, and a singlet for the ring methylene protons (see Figure A-44, Appendix). At temperatures below -45°, the ring methylene protons split into an AB quartet. This phenomenon should have been accompanied by a similar change in the diastereotopic methylene protons of the ethyl group. Failure to observe this splitting may have been due to a near-zero value for the chemical shift differences for these methylene protons.

Complete line-shape analysis was performed for compound 45, assuming constant parameters $J_{AB} = 15 \text{ Hz}$, $\Delta^\nu_{AB} = 21.2$, and $T_2 = 0.106$. The solvent was dichlorodifluoromethane. The calculated dnmr spectra are shown in Figure 22. An activation energy of 10.57 kcal/mol was calculated, and $\Delta H = 10.12 \text{ kcal/mol}$, $\Delta S = -5.36 \text{ cal/mol-deg}$, and $\Delta G_{45} = 11.34 \text{ kcal/mol}$. (See Figure 23 for the Arrhenius plot of the dnmr data for compound 45.) The dnmr data are listed in Table 9.
Figure 22. Experimental (left) and calculated dnmr spectra for compound 45.
ARRHENIUS PARAMETERS
ACTIVATION ENERGY = 10.57 KCAL
LOG A = 11.9398

TRANSITION STATE ACTIVATION PARAMETER
DELTA H = 10.12 KCAL
DELTA S = -5.353 CAL/DEG.
AT A COALESCENCE TEMPERATURE OF -46.0 C
DELTA G = 11.34 KCAL

Figure 23. Arrhenius plot for compound 45.
Table 9
Dynamic Nmr Data for Compound 45

3,4-DIISOPROPYLDENE-1,1-DICARBOXYCYCLOPENTANE

<table>
<thead>
<tr>
<th>DATA</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TEMP C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-34.7</td>
<td>6.0000E-03</td>
<td>4.1938</td>
<td>5.1160</td>
<td>5.1268</td>
<td>-0.0748</td>
</tr>
<tr>
<td>-39.9</td>
<td>7.0000E-03</td>
<td>4.2872</td>
<td>4.6095</td>
<td>4.6095</td>
<td>0.0169</td>
</tr>
<tr>
<td>-43.5</td>
<td>1.1000E-02</td>
<td>4.3545</td>
<td>4.5092</td>
<td>4.5092</td>
<td>0.1736</td>
</tr>
<tr>
<td>-46.7</td>
<td>1.7000E-02</td>
<td>4.4160</td>
<td>4.0745</td>
<td>4.0745</td>
<td>0.0655</td>
</tr>
<tr>
<td>-48.8</td>
<td>2.5000E-02</td>
<td>4.4573</td>
<td>3.6809</td>
<td>3.6809</td>
<td>-0.1003</td>
</tr>
<tr>
<td>-51.6</td>
<td>3.0000E-02</td>
<td>4.5137</td>
<td>3.5044</td>
<td>3.5044</td>
<td>0.0169</td>
</tr>
<tr>
<td>-53.5</td>
<td>4.0000E-02</td>
<td>4.5527</td>
<td>3.2189</td>
<td>3.2189</td>
<td>-0.0632</td>
</tr>
<tr>
<td>-54.6</td>
<td>4.5000E-02</td>
<td>4.5756</td>
<td>3.1011</td>
<td>3.1011</td>
<td>-0.0591</td>
</tr>
<tr>
<td>-55.5</td>
<td>5.0000E-02</td>
<td>4.5945</td>
<td>2.9957</td>
<td>2.9957</td>
<td>-0.0638</td>
</tr>
<tr>
<td>-61.9</td>
<td>9.0000E-02</td>
<td>4.7337</td>
<td>2.4079</td>
<td>2.4079</td>
<td>0.0886</td>
</tr>
</tbody>
</table>

ARRHENIUS PARAMETERS:
ACTIVATION ENERGY = 10.57 KCAL.
LOG A = 11.9398

TRANSITION STATE ACTIVATION PARAMETERS:
DELTA H = 10.12 KCAL.
DELTA S = -5.362 CAL./DEG.

AT A COALESCENCE TEMPERATURE OF -45.0 DEGREES C
DELTA G = 11.34 KCAL.
q. Dimethyl (E,E)-Dineopentylidenesuccinate, 53

Because the diastereotopic methylene protons of the diol 57 were accidentally equivalent in the nmr in all solvents tested (deuteriochloroform, carbon tetrachloride, carbon disulfide, benzene-d₆, and pyridine-d₅; see Figure A-66, Appendix, and Results and Discussion, part A, section 7c), an estimate for the energy barrier to racemization for the vicinal (E,E) dineopentylidene system was made based on the diester, 53. The dynamic nmr behavior of the (E,E) diester 53 was observed in the presence of the chiral shift reagent, Eu(tfc)₃.11c,46,48

At 150°C (the highest temperature accessible using bromobenzene-d₅ as the solvent) the signals corresponding to the diastereomeric association complexes showed incipient coalescence, placing a lower limit of 24 kcal/mol on the free energy of activation for compound 53.16
r. Dimethyl (E,Z)-Dineopentylidenesuccinate, $\text{52}$

In contrast to the (E,E)-dineopentylidene compound $\text{53}$, the isomeric compound $\text{52}$ did not show diastereomeric association complexes in the presence of Eu(tfc)$_3$ at room temperature. Low temperature dnnmr on compound $\text{52}$ was complicated by early and extreme line-broadening, presumably due to an increase in the paramagnetism of the shift reagent as the temperature was lowered. The very low shift reagent:substrate ratio employed in a second attempt to determine the dnnmr barrier in diene $\text{52}$ did not improve the results, and the same line-broadening effect was observed. An upper limit of 15 kcal/mol for the free energy barrier for compound $\text{52}$ can be inferred from these data. $^{16}$
3. Error Involved in the Dnmr Results

Determination of thermodynamic parameters by the use of dynamic nmr and complete line-shape analysis involves recording nmr spectra at a series of temperatures and then visually matching the nmr spectra with computer-generated lineshapes. Generally, the coupling constant $J_{AB}$, the chemical shift difference $\Delta \nu_{AB}$, and the lifetime in the absence of exchange $T_2$, are read from the slow exchange nmr spectrum and are kept constant during line-shape analysis. The correlation time $\tau$ is then varied until a theoretical spectrum is generated which matches an experimental spectrum that was recorded at a known temperature. (See Introduction, section C, for a further discussion of the use of dynamic nmr for the determination of free energies of activation.)

This section discusses the various errors which could be introduced in the course of spectra acquisition or during complete line-shape analysis. The source of errors can be divided into several areas.

The accuracy of temperature measurement is of prime concern. The digital temperature read-out attached directly to the probe of the Varian HA-100 spectrometer was calibrated against the chemical shifts of the methanol and ethylene glycol protons and was found to be accurate to $\pm 1^\circ$. An oil-filled nmr tube with a thermocouple attached to the digital temperature read-out for the Varian XL-100 spectrometer
was similarly calibrated and found to be accurate to \( \pm 1.38,39 \).

Determination of the temperature of coalescence from the spectra in hand probably introduces the largest error as far as temperature measurements are concerned. A coalescence temperature uncertainty to \( \pm 5^\circ \) would imply that the free energy of activation is known to within \( \sim \pm 0.3 \) kcal/mol, whereas \( \Delta S \) is somewhat more sensitive and varies by \( \sim 3\% \).

The judgment factor inherent in the complete line-shape analysis method is difficult to quantify. The values determined in the temperature region immediately surrounding coalescence are undoubtedly the most accurate, since it is here that the line shape is changing most dramatically. Generally, a change in \( \tau \) of \( \sim 4\% \) in this region would give a noticeable change in the calculated spectrum. The \( \tau \) values at temperatures far from the coalescence point (\( \pm 15 - 20^\circ \)) are much less sensitive to a variation in \( \tau \), and it is here that the uncertainty involved becomes large.

In several of the compounds studied in this work (notably compounds 32, 33, and 42) the chemical shift difference appeared to be variable with temperature. It is particularly difficult to measure \( \Delta \nu_{AB} \) accurately in the critical temperature region just below coalescence, due to the line shape changes which are occurring here. Furthermore, virtually indistinguishable calculated spectra can be obtained by
varying two of more parameters at the same time (e.g., $T_2$ and $\Delta \nu_{AB}$). For these reasons, accurate line-shape analysis was impossible with several of these 1,3-dienes.

It should be noted, however, that although the coalescence temperature for the diene-diol 28 was measured using both the HA-100 and the XL-100 spectrometers, in three different solvents, the results yielded coalescence temperatures with a range from 138 - 142°.
4. Discussion of Dynamic Nmr Results\textsuperscript{57}

a. Cyclic 1,3-Dienes

The "buttressing" effect, or the steric repulsion of the "outside" diene substituents with the groups in the 1,4-positions of the diene backbone, has been studied extensively by Mannschreck \textit{et al.}\textsuperscript{11} The large difference in the free energies of activation for enantiomerization of tetrahydrofurans 43 and 46 (8.16 kcal/mol and 16.2 kcal/mol, respectively) is attributed to this effect.

The large increase in the free energy of activation in going down the periodic table in heteroatom substitution (\(R = 0\) to \(R = S\)) is illustrated by comparing the free energy of activation of 8.16 kcal/mol for the tetrahydrofuran 43 with the value of 15.16 kcal/mol for the tetrahydrothiophene 38. This increase is attributed to increases in the C-R bond lengths, leading to more crowding elsewhere in the molecule.

An eclipsing effect\textsuperscript{58} has been suggested as the cause for the slight increase in the free energy of activation observed upon increased sulfur oxidation state in the series: sulfide 38, sulfoxide 39, and sulfone 40. The differences in the free energies of activation for these compounds are small and this effect is probably negligible.

The predicted nitrogen and ring inversion barriers\textsuperscript{52-56} that were observed for the cyclic hydrazines 47 and 48
are described in detail in the Results and Discussion, section B, parts 2h and 2i.

b. Acyclic 1,3-Dienes

Whereas the cyclic 1,3-dienes are constrained to enantiomerize via a cis-coplanar transition state, a transoid transition state for enantiomerization is probably involved for the acyclic 1,3-dienes. [See the dnmr results for compound 28 in a hydrogen-bonding and non-hydrogen-bonding solvent (Results and Discussion, section B, part 2c) and the CNDO/2 results for a model 1,3-diene (Results and Discussion, section D).]

The values for the free energies of activation for the acyclic diisopropylidene 1,3-dienes 28, 29, 32, and 33 are very similar (19.0 to 20.9 kcal/mol), which seems to indicate that the nature of the 1,4-substituents has little effect upon the energy barrier to racemization.

The importance of the "buttressing" effect is again illustrated by a comparison of dimethyl diisopropylidene-succinate 36 and the reduced diene-diol 28 in the presence of the chiral shift reagent Eu(tfc)$_3$. The diene-diol 28 exhibits diastereomeric association complexes at room temperature when complexed with a chiral shift reagent (see Results and Discussion, section B, part 2c), whereas dimethyl diisopropylidene-succinate 36 does not. The
20.6 kcal/mol free energy of activation for the diene-diol 29 can thus be compared to a maximum value of ~15 kcal/mol for the dimethyl ester 36.
C. Resolution Attempts

Several attempts were made to resolve the dissymmetric 1,3-diene-diol 28 and the urazole 49. None of these attempts was successful. The rationale for the methods employed and the reasons to which their lack of success may be attributed are described below.

1. Metal Complexes

a. Nickel (II) Complexes

Nickel (II) is known to form complexes whose structures are interconvertible and thus fluxional. It was hypothesized that the diene-diol 28 would complex with a nickel (II) compound which contained a chiral ligand, and that upon complexing, the interaction would be strong enough to force the fluxional diene-diol 28 into either a predominantly d or l conformation.

Bis(l-leucinato)nickel (II) dihydrate was prepared according to the literature. It was highly insoluble in ordinary solvents and did not appear to complex with the diene-diol 28.

The ligand (+)-2,3-α-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphino)butane [(+)-DIOF] was synthesized according to the literature. Although the nickel complex was prepared according to the literature, it was not stable to the atmosphere and much difficulty was encountered in its characterization.
Similar difficulty was encountered in the synthesis of a nickel complex with 1-sparteine 101 as a ligand. The preparation of a sparteine-nickel complex was subsequently reported in the literature. 63

b. Platinum (II) Complex

The compound Pt(α-d-(1-naphthyl)ethylamine)Cl₂(C₂H₄) was prepared according to the literature, starting from a platinum crucible. 64 Resolution of both the diene-diol 28 and the phenyl urazole 49 was attempted according to the method described by Cope. 65 Both compounds failed
to coordinate with the platinum complex, presumably for steric reasons.

2. Chiral Reducing Agent

A new chiral reducing agent was prepared by the addition of an equal molar amount of 2,3-O-isopropylidene-1-threitol 102 to lithium aluminum hydride. When applied to the reduction of acetophenone, this reagent produced (+)-1-phenylethanol in 28% optical purity (enantiomeric excess determined both by the use of the chiral shift reagent Eu(tfc)$_3$ and by polarimetric measurement after chromatographic purification).

Unfortunately, this chiral reducing agent did not effect the reduction of the diester 36; the ester was recovered unreacted from the reaction mixture.
3. Reduction of the Chiral Ester $83$

The chiral ester $83$ was prepared according to Scheme 9 (Results and Discussion, section A). Reduction for one hour at $0^\circ$ with Red-al $[\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2]$ afforded the diene-diol $28$. (Work-up was performed at $0^\circ$.) No optical induction was observed, within experimental error, either by polarimetry of the $0^\circ$ solution or by the rapid nmr measurement of the cold sample in the presence of the optically active shift reagent, $\text{Eu(tfc)}_3$.46

![Chemical structure](image)

$83$ $\rightarrow$ $28$

(no optical induction)

4. Column Chromatography on (−)-TAPA-impregnated Silica Gel

The Newman reagent, (−)-α-(2,4,5,7-tetranitro-9-fluorenlylideneminoxy)propionic acid [(−)-TAPA 103] has been used to resolve optical isomers via the diastereomeric charge-transfer complexes it forms with aromatic compounds.68
A sample of (-)-TAPA was prepared according to the literature, and in a procedure similar to that of Mikes et al., silica gel was impregnated with (-)-TAPA (3.4 per cent, by weight). A chromatography column (1" x 39") was packed with the (-)-TAPA-impregnated silica gel as a slurry in 1:1 dichloromethane:cyclohexane and allowed to equilibrate in the cold room at 5°. The column was charged with a 0.45 gram sample of the urazole. Excessive bleeding of (-)-TAPA from the column occurred in solvents polar enough to elute the urazole (e.g., pure dichloromethane) and it was therefore not possible to obtain a stable column.
5. Classical Resolution Attempts

Several attempts were made to functionalize both the diene-diol 28 and the urazole 49 for resolution by classical means (salt formation).

a. Reaction of the Diene-diol 28 with Phthalic Anhydride

In a method similar to that reported by Mannschreck et al.,11e the diene-diol 28 was refluxed with excess phthalic anhydride in pyridine. An nmr and a tlc of the reaction products indicated that a very complex mixture had been obtained. This approach was not pursued further.
b. Attempts to Functionalize Compound 49

Numerous attempts were made to prepare an analog of compound 49 with an acid or amino group on the phenyl ring. The strategy was to prepare a substituted 4-phenylurazole 104.

Unsubstituted 4-phenylurazole was not susceptible to transamination with either para-aminobenzoic acid, para-aminoacetophenone hydrochloride, or \( \text{d-}(1\text{-naphthyl})\text{-ethylamine} \). Attempted pyrolysis of compound 105 with \( \text{d-}(1\text{-naphthyl})\text{-ethylamine} \), para-aminoacetophenone hydrochloride, or para-aminobenzoic acid did not yield the desired 4-phenylurazoles. Likewise unsuccessful was the Friedel-Crafts acylation of 4-phenylurazole in nitrobenzene using either zinc chloride or aluminum chloride as the catalyst. Attempted Friedel-Crafts acylation of compound 49 in benzene yielded an anomalous product 106. (Spectral data for compound 106 are shown in Figures A-123, A-124, and A-125 in the Appendix.) The carbethoxy-substituted 4-phenylurazole was not obtained by attempted ring closure of either the ortho- or para-substituted compound 107, using either aqueous potassium hydroxide or anhydrous potassium \( \text{tert} \)-butoxide as the base.
D. CNDO/2 Calculation for a Model 1,3-Diene System

CNDO/2 calculations \(^{73}\) were performed on the model diene system \(^{108}\) using "normal" bond lengths and bond angles, \(^{74}\) and assuming that no deformational freedom other than rotation about the central sp\(^2\) - sp\(^2\) single bond exists. The minimum-energy conformation of the methyl hydrogen atoms was determined using the program MESUBS. \(^{75}\) Functions were written in APL using the rotational matrices described by Cotton, \(^{76}\) in order to determine the atomic coordinates of the model system after a rotation of \(\Theta^\circ\) about the central sp\(^2\) - sp\(^2\) single bond. A similar APL function was written to determine the methyl-methyl internuclear distances.

As expected for systems of this type, \(^{77}\) the total energies calculated seemed unreasonable, although it was possible to compare the relative energies. Figure 24 shows a plot of relative energy vs. dihedral angle. It can be seen that the minimum energy conformation calculated is one in which there is an \(\sim 100^\circ\) dihedral angle (from s-cis-coplanar) between the planes described by the pi bonds. This angle, which requires that the methyl groups be twice their van der Waals radius apart, agrees well with the skew angle of 104.8\(^\circ\) obtained from an x-ray crystallographic study of the diene-diol \(^{28}\). \(^{78}\)
CH₃
CH₃

108
The low energy conformation (dihedral angle of 100° from s-cis) was taken as zero energy. The other data points were shifted on this scale.

Data points for dihedral angles 0° (s-cis), 30°, and 40° had energy values greater than 100 kcal/mol relative to the low energy conformation of 100°.

Figure 24. Results of CNDO/2 calculations for the model diene system 108.
E. $^{13}$C $T_1$ Measurement for the Diene-diol 28

Carbon 13 spin-lattice relaxation times ($T_1$'s) have been shown to correlate with molecular geometry, non-bonded interactions, and molecular motion. It was hypothesized that the differences in the steric interactions felt by the "inside" and "outside" methyl groups in the diene-diol 28 would be reflected in slowed methyl rotation, or a "cog-wheeling" effect.

A $T_1$ experiment was performed on compound 28 using the inversion-recovery pulse sequence $^{79}$ (180° - $\tau$ - 90° - $T$)$_n$ with a delay time of 20 seconds. The results, plotted in Figure 25, show that there is no difference, within experimental error, in the spin-lattice relaxation times for the "inside" and "outside" methyl groups in compound 28.

The overall spin-lattice relaxation time is composed of contributions from four major relaxation mechanisms: dipole-dipole relaxation, spin-rotation relaxation, chemical shift anisotropy, and scalar relaxation. $^{79}$ A more complete experiment would include determination of the magnitude of these individual contributions to the overall relaxation rate. Although the overall relaxation times are similar for the "inside" and "outside" isopropylidene methyl groups, the differences in steric interactions may be reflected in the individual contributions to the overall relaxation rates.
Figure 25. Spin-lattice relaxation time results for compound 28.
IV. APPENDIX

Spectral Data for Synthetic Products
Figure A-2. Hmr spectrum (CDCl₃) of compound 27.
Figure A-4. $^{13}$C Nmr spectrum (CDCl$_3$) of compound 28.
Figure A-5. Ir spectrum (neat) of compound 28.
Figure A-6. Mass spectrum (70 eV) of compound 28.
Figure A-7. Nmr spectrum (CDCl$_3$) of compound 29.
Figure A-8. Ir spectrum (KBr) of compound 29.
Figure A-9. Mass spectrum (70 eV) of compound 29.
Figure A-10. Nmr spectrum (CDCl₃) of compound 30.
Figure A-11. IR spectrum (neat) of compound 30.
Peak mass = 150.128121 ± 0.00600

<table>
<thead>
<tr>
<th>C</th>
<th>H</th>
<th>N</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Max</td>
<td>12</td>
<td>6</td>
<td>8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula Wt</th>
<th>Mmu</th>
<th>R+DB</th>
<th>C</th>
<th>H</th>
<th>N</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>149.107876</td>
<td>-0.2</td>
<td>4.5</td>
<td>9</td>
<td>13</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>149.103854</td>
<td>3.8</td>
<td>0.5</td>
<td>4</td>
<td>13</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>149.105197</td>
<td>2.5</td>
<td>0.0</td>
<td>6</td>
<td>15</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Formula Wt</th>
<th>Mmu</th>
<th>R+DB</th>
<th>C</th>
<th>H</th>
<th>N</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>150.128277</td>
<td>-0.2</td>
<td>3.5</td>
<td>10</td>
<td>16</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>150.122912</td>
<td>6.8</td>
<td>0.0</td>
<td>3</td>
<td>14</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>150.124255</td>
<td>3.9</td>
<td>-0.5</td>
<td>5</td>
<td>16</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Figure A-12. Mass spectrum (70 eV) of compound 30.
Figure A-13. Nmr spectrum (CDCl$_3$) of compound 31.
Figure A-15. IR spectrum (neat) of compound 32.
Peak Mass = 188.129910 ± 0.006000

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Max</td>
<td>15</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Formula wt 188.131351, Mnu -1.4, R+DB 6.0

C     H     N
112    16     2

Figure A-16. Mass spectrum (70 eV) of compound 32.
Figure A-18. IR spectrum (neat) of compound 33.
Figure A-21. IR spectrum (nujol) of compound 35.
Figure A-24. IR spectrum (nujol) of compound 37.
Figure A-25. Mass spectrum (20 eV) of compound 37.
Figure A-27. IR spectrum (neat) of compound 38.
Figure A-29. Nmr spectrum (CDCl$_3$) of compound 39.
Figure A-30. Ir spectrum (neat) of compound 39.
Figure A-31. Mass spectrum (70 eV) of compound 39.
Figure A-33. IR spectrum (neat) of compound 40.
Figure A-34. Mass spectrum (70 eV) of compound 40.
Figure A-36. Ir spectrum (neat) of compound 41.
Figure A-38. Nmr spectrum (CDCl₃) of compound 42.
Figure A-39. IR spectrum (neat) of compound 42.
Figure A-40. Mass spectrum (70 eV) of compound 42.
Figure A-41. Nmr spectrum (CDCl$_3$) of compound 43.
Figure A-42. IR spectrum (neat) of compound 43.
Figure A-43. Mass spectrum (70 eV) of compound 43.
Figure A-44. Nmr spectrum (CDCl₃) of compound `45`. 
Figure A-45. IR spectrum (neat) of compound 45.
Figure A-46. Mass spectrum (70 eV) of compound 45.
Figure A-48. Nmr spectrum (CDCl₃) of the hydrochloride salt of compound 47.
Figure A-49. IR spectrum (nujol) of the hydrochloride salt of compound 47.
Figure A-50. Mass spectrum (70 eV) of the hydrochloride salt of compound 47.
Figure A-51. Nmr spectrum (CDCl₃) of compound 47.
Figure A-52. $^{13}$C Nmr spectrum (CS$_2$) of compound 47.
Figure A-53. Nmr spectrum (CDCl₃) of compound 48.
Figure A-54. Ir spectrum (nujol) of compound 48.
**Figure A-55.** Mass spectrum (70 eV) of compound 48.
Figure A-56. Nmr spectrum (CDCl₃) of compound 49.
Figure A-57. Ir spectrum (KBr) of compound 49.
Figure A-59. Nmr spectrum (CDCl₃) of compound 5l.
Figure A-59. IR spectrum (KBr) of compound 51.
Figure A-60. Nmr spectrum (CDCl$_3$) of compound 52.
Figure A-61. Mass spectrum (70 eV) of compound 52.
Figure A-62. Nmr spectrum (CDCl₃) of compound 53.
Figure A-63. Nmr spectrum (CDCl3) of compound 54.
Figure A-64. Nmr spectrum (CDCl₃) of compound 55.
Figure A-67. IR spectrum (neat) of compound 57.
Figure A-68. Mass spectrum (70 ev) of compound 57.
Figure A-69. Nmr spectrum (CDCl₃) of compound S8.
Figure A-70. Mass spectrum (70 eV) of compound 58.
Figure A-71. Nmr spectrum (CDCl₃) of compound 59.
Figure A-72. Mass spectrum (70 eV) of compound 59.
Figure A-73. Nmr spectrum (CDCl₃) of compound 62.

diethyl succinate
Figure A-74. Nmr spectrum (CDCl₃) of compound 62.
Figure A-75. Nmr spectrum (CDCl₃) of compound 65.
Figure A-76. IR spectrum (neat) of compound 65.
Figure A-78. IR spectrum (nujol) of compound 66.
Figure A-79. Nmr spectrum (acetone-$d_6$) of the hydrolysis product of compound 67a.
Figure A-80. Ir spectrum (KBr) of the hydrolysis product of compound 67a.
Figure A-81. Nmr spectrum (CDCl₃) of compound 68.
Figure A-82. Nmr spectrum (CDCl$_3$) of a mixture of compounds 68 and 69.
Figure A-84. IR spectrum (neat) of compound 70.
Figure 4-85. Nmr spectrum (CDCl₃) of compound 71.
Figure A-86. $^{13}$C Nmr spectrum (CDCl$_3$) of compound 71.
Figure A-90. Nmr spectrum (CDCl₃) of compound 74.
Figure A-92. IR spectrum (nujol) of compound 75.
Figure A-93. Nmr spectrum (DMSO-d$_6$) of compound 76.
Figure A-94. IR spectrum (KBr) of compound 76.
Figure A-96. IR spectrum (KBr) of compound 77.
Figure A-99. IR spectrum (KBr) of compound 78.
Figure A-100. Mass spectrum (70 eV) of compound 78.
Figure A-101. Near spectrum (acetone-d$_6$) of compound 79.
Figure A-102. IR spectrum (KBr) of compound 79.
Figure A-103. Mass spectrum (70 eV) of compound 79.
Figure A-105. IR spectrum (KBr) of compound 80.
Figure A-106. Mass spectrum (70 eV) of compound 80.
Figure A-108. IR spectrum (KBr) of compound 81.
Peak mass = 178.086321 ± 0.006

<table>
<thead>
<tr>
<th>C</th>
<th>H</th>
<th>N</th>
<th>O</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>0</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

Formula wt. 178.086806
Mmu -0.5
R+DB 5.5

C 10 H 12 N 1 O 2

Figure A-109. Mass spectrum (70 eV) of compound 81.
Figure A-111. IR spectrum (neat) of compound 82.
Figure A-113. Nmr spectrum (CDCl₃) of compound 83.
Figure A-114. Ir spectrum (neat) of compound 83.
Figure A.115. Mass spectrum (70 eV) of compound 81.
Figure A-116. Nmr spectrum (CDCl₃) of compound 84.
Figure A-117. Nmr spectrum (acetone-$d_6$) of a mixture of compounds 86 and 87.
Figure A-118. IR spectrum (KBr) of a mixture of compounds 86 and 87.
Figure A-119. Nmr spectrum (CDCl₃) of a mixture of compounds 88 and 89.
Figure A-120. IR spectrum (neat) of a mixture of compounds 88 and 89.
Figure A-121. Nmr spectrum (CDCl₃) of compound 93.
Figure A-122. Ir spectrum (neat) for compound 93.
Figure 124. IR spectrum (KBr) of compound 106.
Figure A-125. Mass spectrum (70 eV) of compound 106.


14. For general reviews dealing with the use of dnmr to detect hindered rotation and inversion, see:
a) G. Binsch, *Top. Stereochem.*, 3, 97 - 192 (1968);

15. For reviews dealing with the theoretical and mathematical aspects of chemical exchange and nmr line-shape analysis, see:
   a) C. S. Johnson, Jr., *Adv. Magn. Reson.*, 1, 33 - 102 (1965);


21. This figure was taken from the Corning Laboratory Glass Color Filter Catalog CF-3, Corning Glass Works, Corning, New York, 1965, p. 8.


29. We are grateful to Professor R. M. Kellogg, The University of Groningen, The Netherlands, for a generous gift of compound 50.


33. a) M. J. Jorgenson, Tetrahedron *Lett.*, 559 - 562 (1962);

   b) L. F. Fieser and M. Fieser, *op. cit.*, p. 34.


35. Shielding in this type of system is well known. See, for example: D. J. Pasto, *J. Org. Chem.*, 41, 1061 - 1063 (1976), and references cited.


39. These calibrations were performed by Phil Dahlstrom and Jim Hunecke.


44. Work performed in the Chemistry Department, University of Hawaii, by Berner J. Gordon, on leave from Saginaw Valley College, Spring 1974.


46. Eu(tfc)₃ is Aldrich Chemical Company's tris-(3-trifluoromethyl-hydroxymethylene)-d-camphorate), europium (III) derivative.

47. Some of these dnmr results have been published: L. W. Jelinski and E. F. Kiefer, J. Am. Chem. Soc., 98, 281 - 282 (1976).

48. Determination of internal rotational rates in the presence of optically active reagents has been reported:
a) A. Mannschreck, V. Jonas, and B. Kolb, Angew. Chem., Int. Ed. Engl., 12, 909 - 910 (1973);

49. $T_2$ was taken as $(1/\pi)(1/\Delta \nu_1/2)$ where $\Delta \nu_1/2$ is the width of a peak at half-height in the absence of exchange.

50. Eu(fod)$_3$-d$_{27}$ is Merck, Sharp, and Dohme's tris-(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-d$_6$-4,6-octanedione-d$_3$) europium (III).

51. For a review on hindered rotation involving the tetrahedral carbon atom, see: M. Oki, Angew. Chem., Int. Ed., Engl., 15, 87 - 93 (1976), and in particular, reference 31 cited therein.


57. Some of this material has been published. See references 45 and 47.


   
b) P. W. Feit, *J. Med. Chem.*, 7, 14 - 17 (1964);
   
   


   
b) R. N. Keller, *Inorg. Synth.*, 2, 247 - 250 (1946);
   
   

66. M. A. Bennett, Australian National University, personal communication.


   b) A. Krebs, J. Odenthal, and H. Kimling, *Tetrahedron Lett.*, 4663 - 4666 (1975);


70. This compound was prepared by the stannous chloride reduction of commercially available para-nitroacetophenone.


72. This compound was prepared by the addition of ethyl cyanato- benzoate to ethoxycarbonylhydrazine [O. Diels, *Chem. Ber.*, 47, 2183 - 2195 (1914)] in a method similar to that of G. Zinner and W. Deucker, *Arch. Pharm.*, 294, 370 - 372 (1961);
The para-isocyanato-benzoate was commercially available (Aldrich Chemical Co.); synthesis of the ortho-isomer has not been previously reported. It was synthesized in good yield from phthalic anhydride by the treatment of the following reagents: Fischer esterification with ethanol; thionyl chloride; sodium azide; heat (80°).

73. CNDO/2 Program, Quantum Chemistry Program Exchange Library, Indiana University.


75. MESUBS Program, Quantum Chemistry Program Exchange Library, Indiana University.


