PART I: CARBON-13 NUCLEAR MAGNETIC RESONANCE STUDIES OF METAL ENOLATES

- PART II: THE SYNTHESIS AND CYCLIZATION REACTIONS OF  $\omega$ -BROMO KETONES
- PART III: ALKYLATION STUDIES OF THE  $\Delta^{1,9}$ -ENOLATE OF ANTI-6-t-BUTYL-CIS AND TRANS-1-DECALONE

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- PART I: CARBON-13 NUCLEAR MAGNETIC RESONANCE STUDIES OF METAL ENOLATES
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#### SUMMARY

### Part I. The Carbon-13 NMR Spectra of Metal Enolates

The natural abundance  ${}^{13}$ C nmr spectra of several metal enolates were measured in various aprotic solvents including Et,0, THF, and DME. The chemical shifts of the enolate  $\alpha$ -carbon atoms have been compared with the chemical shifts of the same carbon atoms in the corresponding enol acetates and trimethylsilyl enol ethers. The observed chemical shift differences ( $\Delta \delta$ ) between the enolates and the enol acetates appear to be related both to the  $\pi$ -electron density and the reactivity at the enolate a-carbon atom. The following changes increase the magnitude of the chemical shift differences in metal enolates: (1) changing the metal cation from Li<sup>+</sup> to Na<sup>+</sup> to K<sup>+</sup>; (2) changing the solvent from  $Et_2^0$  to THF to DME; (3) addition of 4 mol equiv. of HMP to a Li enolate; and (4) addition of 1 mol equiv. of dicyclohexy1-18-crown-6 polyether to a Na enolate. Those combinations of cation, solvent and added ligands that give the largest value of  $\Delta\delta$  are also the combinations that result in the highest reactivity of the enolate with alkyl halides and in the greatest proportion of 0- to C-acylation in reaction with acetic anhydride. The magnitudes of the chemical shift differences at the enolate  $\alpha$ -carbon atoms are relatively insensitive to the presence or absence of  $\alpha$ -alkyl or  $\alpha$ -phenyl substituents.

Part II. The Synthesis and Cyclization Reactions of w-Bromo Ketones

Various methyl ketones containing terminal vinyl groups have been synthesized by regiospecific alkylations of metal enolates with allyl bromide, by the conjugate addition of  $(CH_2=CH)_2CuLi$  or  $CH_2=CHMgBr$  with a Cu catalyst to enones, and by other procedures. The light-catalyzed radical-chain addition of HBr in pentane solution to these olefins constituted an efficient method for the synthesis of  $\omega$ -bromo ketones.

Utilizing stable solutions of i-Pr2NLi in hexane, a convenient procedure is described for the conversion of methyl  $\omega$ -bromolakyl ketones to mixtures of Li<sup>+</sup> enolates containing predominantly the terminal enolates. Although solutions of these Li<sup>+</sup> enolates in Et<sub>2</sub>O-hexane mixtures are stable at 0°, when activating ligands are added these Li<sup>+</sup> enolates undergo intramolecular cyclization reactions. In the absence of serious geometrical constaints, precursors to cyclohexanone derivatives underwent intramolecular C-alkylation in 60-80% yields. Similar cyclization of precursors to cycloheptanone systems produced mixtures of 5- and 7-membered C-alkylated products, whose proportions varied with the precursor, but the bromo enolate precursor to a cyclopentanone system yielded only 0-alkylated product. A cyclobutanone precursor produced a mixture of O- and C-alkylated four membered ring products in a slow reaction. These results are interpreted in terms of the geometrical requirements and relative rates of intramolecular C- and O-alkylations.

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Part III. Alkylation Studies of the  $\Delta^{1,9}$ -Enolate of

Anti-6-t-Butyl Cis and Trans-1-Decalone

The title enolate, <u>10</u>, was regiospecifically generated from the corresponding 1-decalone via the sequence ketone  $\rightarrow$  enol acetate  $\rightarrow$  silyl enol ether  $\rightarrow$  lithium enolate, and the stereochemistry of its alkylation with CH<sub>3</sub>I was studied. Molecular mechanics calculations were carried out to determine the probable configuration of <u>10</u> in solution. The enolate had abnormal geometry, with its non-oxygenated cyclohexane ring in a twist form. The bridgehead stereochemistry of the methylated product (> 85% <u>cis</u>) was confirmed by a single crystal X-ray diffraction study on its oxime derivative. The stereoselectivity of alkylation is explained in terms of a reactantlike transition state and  $\psi_{e}$  (pseudoequatorial) attack of CH<sub>3</sub>I on the twist form of the non-oxygenated ring.

#### CHAPTER I

#### THE CARBON-13 NMR SPECTRA OF METAL ENOLATES

### Discussion

Enolate anions,  $\underline{1}$ , are members of a group of ambident nucleophiles that react with alkylating or acylating agents to form products with a new bond at carbon or at oxygen.<sup>1</sup> In an earlier study<sup>2</sup> of the



properties and reactions of solutions of metal enolates derived from ketones, comparison of the <sup>1</sup>H nmr spectra for a related set of compounds <u>2a</u>, <u>10</u>, <u>17</u> and <u>23</u>, showed that the vinyl H atom signal moved progressively upfield in the order: enol acetate <u>17</u> (  $\delta$  5.80), trimethylsilyl enol ether <u>23</u> (  $\delta$  5.32), and lithium enolate <u>2a</u> (  $\delta$  5.02 in Et<sub>2</sub>0, 4.93 in THF, and 4.83 in DME). Among the various cations and solvents studied with this enolate system, the cation-solvent combinations that resulted in the greatest upfield shift of the vinyl H atom nmr signal were also the combinations that resulted in the greatest proportion of 0- to C-acylation of the enolate anions and corresponded qualitatively to conditions that favored most rapid reaction of the enolate anion with alkylating agents. Thus, the location of the <sup>1</sup>H nmr signal appeared to offer a useful measure of the reactivity of a metal enolate under various reaction conditions. However, two experimental problems hindered study of the <sup>1</sup>H nmr spectra of metal enolates. First, the total range of <sup>1</sup>H nmr values observed for a particular enolate system was rather small (ca. 0.3 ppm), so that chemical shift differences arising from nearby anisotropic substituents were likely to be as large as those arising from changes in the degree of association and charge distribution of metal enolates. Second, and even more troubling, was the interference from the <sup>1</sup>H nmr signals of the various solvents (Et<sub>2</sub><sup>0</sup>, THF, DME, DMF, etc.) commonly used with metal enolates.

It appeared that both of these problems could be largely alleviated by studying the natural abundance  ${}^{13}$ C nmr spectra of metal enolate solutions. Because of the much larger range of chemical shift values and the relatively narrow linewidths obtainable in  ${}^{13}$ C nmr, the problems arising from interference between solvent peaks and peaks from the metal enolates would be more easily avoided. Of equal importance would be the fact that electron densities at carbon and the atoms bonded to it, but not shielding from neighboring anisotropic substituents, are dominant in determining  ${}^{13}$ C nmr chemical shift values. ${}^{3}$ 

To explore this possibility, a series of metal enolates 2 - 7(Scheme I) of ketones <u>10</u> - <u>15</u> were prepared. Also included in the study<sup>4a</sup> were the corresponding enol acetates <u>17</u> - <u>22</u> as well as selected silyl enol ethers <u>23</u> - <u>26</u>, one enamine <u>9</u>, and the sodium enolate <u>8</u> of diethyl malonate 16.

Although relatively high concentrations (0.5-1.0 M) of metal enolates in solution were required in order to obtain satisfactory natural abundance <sup>13</sup>C nmr spectra in a reasonable period of time (1-3 hr), we found that interference between <sup>13</sup>C nmr signals for the metal









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 $\frac{18}{24}, X = COCH_3$  $\frac{24}{24}, X = Si(CH_3)_3$ 





5, R = H6, R = t-Bu



 $\frac{13}{14}, R = H$   $\frac{14}{14}, R = t-Bu$ 



 $\frac{20}{25}, R = H, X = COCH_3$   $\frac{25}{25}, R = H, X = SiMe_3$   $\frac{21}{26}, R = \underline{t}-Bu, X = COCH_3$   $\frac{26}{26}, R = \underline{t}-Bu, X = SiMe_3$ 





<u>15</u>



<u>22</u>



<u>7</u>





<u>9</u>





<u>27</u>







<u>29</u>

<u> 30</u>

enolates and the solvents was much less of a problem than had been encountered in measurements of <sup>1</sup>H nmr spectra.<sup>2</sup> Consequently, where solubility permitted, satisfactory <sup>13</sup>C nmr spectra of various metal enolates could be obtained in most common solvents used in preparative work including  $\text{Et}_2^0$ , THF, DME, DMF and HMP. The data obtained from the measurements are summarized in Tables 1 and 2. In one case (enolate <u>2a</u> in DME, Table 1), we demonstrated that the chemical shift values were essentially the same for 1.0 <u>M</u> and 0.2 <u>M</u> solutions of the enolate (see Table 1, footnote e).

In order to compare the <sup>13</sup>C nmr data for various metal enolates, we elected to relate the enolate chemical shift data to the analogous data for the corresponding enol acetates. <sup>4b</sup> These serve as neutral model compounds with geometries and substituent patterns similar to the metal enolates. This comparison utilizes the <sup>13</sup>C nmr shift difference  $(\Delta \delta = \delta_{enol acetate} - \delta_{enolate})$  between the  $\alpha$ -carbon atom in a metal enolate and the corresponding carbon atom in the related enol acetate. As can be seen from Tables 1 and 2, the  $\Delta\delta$  values for the  $\alpha$ -carbon atom of monoketone enolates are in the range of +19 to +25 ppm. This upfield shift for the  $\alpha$ -carbon atom is accompanied by a downfield shift of -13 to -23 ppm for the "carbonyl carbon atom" of the enolate. In general, the largest upfield shifts of  $\alpha$ -carbon atoms are accompanied by the largest downfield shifts of the enolate "carbonyl carbon atoms." One factor responsible for the upfield shift of an  $sp^2$  carbon atom signal<sup>2</sup> in the  ${}^{13}$ C nmr (or a hydrogen atom bound to this carbon in the  ${}^{1}$ H nmr<sup>5</sup>) is an increase in the  $\pi$ -electron density at carbon. From studies of various hydrocarbons and the related ions, it has been suggested that an

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Table 1.  $^{13}$ C NMR Data for Phenylacetone Derivatives



| Compound<br>(solvent)                     | Position of <sup>13</sup> C nmr Signals, ppm Relative to TMS |                |       |                             |       |                            |  |  |
|---|--|----------------|-------|-----------------------------|-------|----------------------------|--|--|
|   | р  | o and m        | đ     | α<br>(Δδ) <sup>a</sup>      | C=0   | other<br>C atoms           |  |  |
| <u>10</u> (DME)                           | 127.2  | 129.5<br>129.5 | 135.7 | 50.9                        | 204.3 | 28.8                       |  |  |
| <u>17</u> (DME)                           | 127.5  | 128.9<br>128.9 | 135.4 | 116.6 <sup>b</sup>          | 147.0 | 20.6 <sup>c</sup><br>168.0 |  |  |
| <u>23</u> (DME)                           | 125.1  | 127.7<br>127.7 | 137.1 | 108.7<br>(7.9)              | 148.8 | 23.8<br>0.8                |  |  |
| <u>2a</u> (Et <sub>2</sub> 0)             | 122.3  | 125.8<br>128.4 | 142.1 | 97.8 <sup>d</sup><br>(18.8) | 160.6 | 27.1                       |  |  |
| 2a (Et <sub>2</sub> 0 +<br>5.1 equiv HMP) | 118.5  | 124.6<br>127.0 | 144.3 | 94.1<br>(22.5)              | 166.4 | 28.6                       |  |  |
| <u>2a</u> (THF)                           | 120.9  | 125.5<br>127.5 | 141.8 | 97.1<br>(19.5)              | 162.5 | 28.6                       |  |  |
| <u>2a</u> (THF +<br>3.9 equiv HMP)        | 118.9  | 124.7<br>127.6 | 144.0 | 94.4<br>(22.2)              | 166.0 | 28.7                       |  |  |
| <u>2a</u> (THF +<br>0.9 equiv <u>28</u> ) | 120.5  | 125.1<br>127.5 | 142.5 | 96.4<br>(20.2)              | 163.7 | 28.7                       |  |  |
| <u>2a</u> (THF +<br>1.1 equiv 29)         | 120.5  | 125.1<br>127.6 | 142.5 | 96.5<br>(20.1)              | 163.9 | 28.8                       |  |  |

| Compound<br>(solvent)                                  | Posit | ion of <sup>13</sup> C | nmr Sign | nals, ppm                   | m Relative to TMS |                  |  |  |  |
|--|-------|------------------------|----------|-----------------------------|-------------------|------------------|--|--|--|
|  | р     | o and m                | Ą        | α<br>(Δδ) <sup>a</sup>      | C=0               | other<br>C atoms |  |  |  |
| <u>2a</u> (DME) <sup>e</sup>                           | 120.0 | 125.0<br>127.2         | 143.2    | 95.3<br>(21.3)              | 164.7             | 28.6             |  |  |  |
| $\frac{2a}{4.1}$ (DME + $\frac{1}{4.1}$ equiv HMP)     | 117.7 | 124.1<br>126.6         | 144.8    | 93.1<br>(23.5)              | 167.4             | 28,9             |  |  |  |
| <u>2b</u> (DME)  | 119.2 | 124.1<br>128.2         | 145.1    | 93.4<br>(23.2)              | 169.3             | 29.4             |  |  |  |
| <u>2b</u> (DME +<br>1.0 equiv <u>27</u> ) <sup>f</sup> | 116.4 | 123.1<br>126.7         | 146.0    | 90.7 <sup>g</sup><br>(25.9) | 170.3             | 29.7             |  |  |  |
| <u>2c</u> (DME)  | 118.6 | 123.3<br>128.4         | 145.6    | 91.8<br>(24.8)              | 170.7             | 29.5             |  |  |  |

<sup>a</sup> $\Delta\delta$  is the difference in chemical shift between the  $\alpha$ -carbon of the compound and the  $\alpha$ -carbon of the corresponding enol acetate. <sup>b</sup>The  ${}^{1}J_{CH}$  value was 154 ± 3 Hz. <sup>c</sup>The signals for both CH<sub>3</sub> groups are superimposed. <sup>d</sup>The  ${}^{1}J_{CH}$  value was 146 ± 3 Hz. <sup>e</sup>The values listed are for a 1.0 M solution of the enolate. For a 0.2 M solution, the values were 120.0, 125.0, 127.4, 143.3, 95.3, 164.8 and 28.6 ppm. <sup>f</sup>Within experimental error, the same  ${}^{13}C$  chemical shift values were found with a solution containing 2 mol equiv of the crown ether 27. <sup>g</sup>The  ${}^{1}J_{CH}$  value was 154 ± 3 Hz.

Table 2. <sup>13</sup>C NMR Data for Saturated Carbonyl Derivatives



|                 | Position of <sup>13</sup> C nmr Signals, ppm Relative to TMS |       |   |  |  |  |  |  |
|-----------------|--|-------|---|--|--|--|--|--|
| (solvent)       | α<br>(Δδ) <sup>a</sup>                                       | C=0   | Other C Atoms <sup>b</sup>  |  |  |  |  |  |
| <u>11</u> (DME) | 24.1   | 210.3 | 26.4 (3CH <sub>3</sub> of <u>t</u> -Bu), 44.0 (4°C of <u>t</u> -Bu)   |  |  |  |  |  |
| <u>18</u> (DME) | 98.4   | 162.2 | 20.6 (acetyl CH <sub>3</sub> ), 27.9 (3CH <sub>3</sub> of <u>t</u> -Bu),<br>36.3 (4°C of <u>t</u> -Bu), 167.3 (ester C=O) |  |  |  |  |  |
| 24 (DME)        | 85.5<br>(12.9)   | 166.5 | 0.1 (3CH <sub>3</sub> of Me <sub>3</sub> Si), 28.2 (3CH <sub>3</sub> of <u>t</u> -Bu),<br>36.6 (4°C of <u>t</u> -Bu)      |  |  |  |  |  |
| <u>3</u> (DME)  | 73.5<br>(24.9)   | 176.8 | 29.7 (3CH <sub>3</sub> of <u>t</u> -Bu), 37.5 (4°C of <u>t</u> -Bu)   |  |  |  |  |  |
| <u>12</u> (DME) | 41.7   | 210.0 | 18.3 (2CH <sub>3</sub> ), 27.1 (acetyl CH <sub>3</sub> )  |  |  |  |  |  |

|                       |                             | Position of <sup>13</sup> C nmr Signals, ppm Relative to TMS |  |  |  |  |  |  |  |
|-----------------------|-----------------------------|--|--|--|--|--|--|--|--|
| Compound<br>(solvent) | α<br>(Δδ) <sup>a</sup>      | C=0  | Other C Atoms <sup>b</sup>   |  |  |  |  |  |  |
| <u>19</u> (DME)       | 117.8                       | 139.8  | 16.0 (CH <sub>3</sub> ), 17.3 (CH <sub>3</sub> ), 18.6 (CH <sub>3</sub> ), 20.3<br>(acetyl CH <sub>3</sub> ), 168.4 (ester C=O)                          |  |  |  |  |  |  |
| <u>4</u> (DME)        | 92.3<br>(25.5)              | 150.6  | 18.7 (CH <sub>3</sub> ), 20.4 (CH <sub>3</sub> ), 21.5 (CH <sub>3</sub> )  |  |  |  |  |  |  |
| 20 (DME)              | 113.2 <sup>c</sup>          | 148.5  | 20.5 (acetyl CH <sub>3</sub> ), 22.3 (CH <sub>2</sub> ), 23.2 (CH <sub>2</sub> ),<br>24.0 (CH <sub>2</sub> ), 27.3 (CH <sub>2</sub> ), 167.8 (ester C=O) |  |  |  |  |  |  |
| <u>25</u> (DME)       | 102.8<br>(10.4)             | 149.9  | 0.3 (3CH <sub>3</sub> of Me <sub>3</sub> Si), 22.6 (CH <sub>2</sub> ), 23.3 (CH <sub>2</sub> ),<br>23.8 (CH <sub>2</sub> ), 30.0 (CH <sub>2</sub> )      |  |  |  |  |  |  |
| <u>5</u> (DME)        | 91.7 <sup>d</sup><br>(21.5) | 158.6  | 24.5 (CH <sub>2</sub> ), 25.0 (CH <sub>2</sub> ), 25.5 (CH <sub>2</sub> ), 33.7 (CH <sub>2</sub> )   |  |  |  |  |  |  |
| <u>5</u> (THF)        | 89.6<br>(23.6)              | 159.0  | 25.0 (CH <sub>2</sub> ), 25.6 (CH <sub>2</sub> ), 26.1 (CH <sub>2</sub> ), 33.9 (CH <sub>2</sub> )   |  |  |  |  |  |  |

|                       | Position of <sup>13</sup> C nmr Signals, ppm Relative to TMS |       |  |  |  |  |  |  |
|-----------------------|--|-------|--|--|--|--|--|--|
| Compound<br>(solvent) | $(\Delta\delta)^a$   | C=0   | Other C Atoms <sup>b</sup>   |  |  |  |  |  |
| <u>21</u> (DME)       | 113.0  | 148.4 | 20.5 (acetyl $CH_3$ ), 24.5 $(CH_2)$ , 25.4 $(CH_2)$ ,<br>27.4 (3 $CH_3$ of <u>t</u> -Bu), 28.3 $(CH_2)$ , 32.3 (4°C of <u>t</u> -Bu), 44.0 (CH at C-4), 167.6 (ester C=0)   |  |  |  |  |  |
| <u>26</u> (DME)       | 102.5<br>(10.5)  | 149.7 | 0.0 (3CH <sub>3</sub> of Me <sub>3</sub> Si), 24.4 (CH <sub>2</sub> ), 25.0 (CH <sub>2</sub> ),<br>27.0 (3CH <sub>3</sub> of <u>t</u> -Bu), 30.9 (CH <sub>2</sub> ), 31.9 (4°C<br>of <u>t</u> -Bu), 44.0 (CH at C-4) |  |  |  |  |  |
| <u>6</u> (DME)        | 91.5<br>(21.5)   | 158.4 | 25.9 (CH <sub>2</sub> ), 26.5 (CH <sub>2</sub> ), 27.7 (3CH <sub>3</sub> of<br><u>t</u> -Bu), 32.5 (4°C of <u>t</u> -Bu), 34.5 (CH <sub>2</sub> ),<br>45.7 (CH at C-4)   |  |  |  |  |  |
| <u>22</u> (DME)       | 117.1  | 169.1 | 20.7 (acetyl CH <sub>3</sub> ), 21.7 (CH <sub>2</sub> ), 28.5 (CH <sub>2</sub> ),<br>36.9 (CH <sub>2</sub> ), 166.8 (ester C=O), 197.1<br>(ketone C=O)   |  |  |  |  |  |

|                       | Position of <sup>13</sup> C nmr Signals, ppm Relative to TMS |       |   |  |  |  |  |  |
|-----------------------|--|-------|---|--|--|--|--|--|
| Compound<br>(solvent) | $(\Delta\delta)^{\alpha}$ a                                  | C=0   | Other C Atoms <sup>b</sup>  |  |  |  |  |  |
| 22 (DMF)              | 116.7  | 169.6 | 20.9 (acetyl CH <sub>3</sub> ), 21.5 (CH <sub>2</sub> ), 28.3 (CH <sub>2</sub> ),<br>36.8 (CH <sub>2</sub> ), 167.7 (ester C=O), 197.7<br>(ketone C=O)  |  |  |  |  |  |
| <u>7</u> (DMF)        | 102.3<br>(14.4)  | 193.5 | 22.9 (CH <sub>2</sub> at C-5), 36.6 (2CH <sub>2</sub> at C-4<br>and C-6)  |  |  |  |  |  |
| <u>16</u> (DMF)       | 41.6   | 166.1 | 14.1 (2CH <sub>3</sub> of ethoxyl groups), 61.0 (2CH <sub>2</sub> of<br>ethoxyl groups)   |  |  |  |  |  |
| <u>8</u> (DMF)        | 62.1 <sup>e</sup>  | 171.4 | 15.3 (2CH <sub>3</sub> of ethoxyl groups), 56.1 (2CH <sub>2</sub> of<br>ethoxyl groups)   |  |  |  |  |  |
| <u>9</u> (DME)        | 93.0<br>(20.2) <sup>f</sup>                                  | 142.5 | 23.7 (CH <sub>2</sub> ), 24.0 (CH <sub>2</sub> ), 24.9 (3CH <sub>2</sub> ,<br>cyclohexenyl CH <sub>2</sub> and 2CH <sub>2</sub> at the $\beta$ -positions<br>of pyrrolidine), 47.4 (2CH <sub>2</sub> at $\alpha$ -position of<br>pyrrolidine) |  |  |  |  |  |

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<sup>a</sup> $\Delta\delta$  is the chemical shift difference between the  $\alpha$ -carbon atom of the enol acetate and the  $\alpha$ -carbon atom of the enolate or related derivative. <sup>b</sup>Unless otherwise noted, each <sup>13</sup>C signal corresponds to a single carbon atom. <sup>c</sup>The <sup>1</sup>J<sub>CH</sub> value was 157 ± 3 Hz. <sup>d</sup>The <sup>1</sup>J<sub>CH</sub> value was 145 ± 3 Hz. <sup>e</sup>Since we lacked a suitable model, no measure of  $\Delta\delta$  was made. <sup>f</sup>The  $\Delta\delta$  is relative to 20.

increase by one unit of negative charge in the p orbital of such a carbon atom should result in an upfield shift of 150-160 ppm for the  $^{13}$ C nmr signal<sup>6</sup> and of <u>ca</u>. 10 ppm for the  $^{1}$ H nmr signal of a proton bound to such a carbon atom.<sup>5a, 7</sup>

Studies by Jackman and co-workers 4d on the lithium enolate of isobutyrophenone in various ethereal solvents have shown that changes in the structures of ion-pairs or their aggregates in solution cause a change in the electron distribution of the organic anion which is reflected in the  ${}^{13}$ C nmr chemical shifts, particularly that of the  $\alpha$ carbon atom. In THF-do and dioxolane, for example, lithioisobutyrophenone exists as two rapidly equilibrating tetramers, and the  $^{13}$ C chemical shifts are virtually unaffected upon forming the "ate" complex Li4Cl(enolate)3 with added LiCl. In DME, however, the predominant species in solution has been shown by  ${}^{13}$ C nmr relaxation time studies  ${}^{4d}$ , 22 to be dimeric. Dimer formation evidently effects a substantial increase in charge density at the  $\alpha$ -carbon atom (ca. 4 ppm upfield shift); the addition of LiCl to the DME solution causes apparent reconversion of dimer to tetramer, with a concomitant 4 ppm downfield shift for the  $\alpha$ carbon atom. Since some evidence exists that enolate aggregate structure in solution can influence the course of alkylation, further research in this area is clearly desirable.

The aforementioned upfield shift differences (0.7-1.0 ppm for  $\alpha$ -H atoms and 19-25 ppm for  $\alpha$ -C atoms) observed when metal enolates are compared with the analogous enol acetates suggest that the  $\pi$ -electron density at the  $\alpha$ -carbon atom is greater in the metal enolates than in enol acetates by <u>ca</u>. 12-17% of a unit negative charge. Since there is

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question as to the quantitative relationship between  ${}^{13}$ C nmr chemical shift differences and calculated charge densities, especially in ionic molecules and in molecules containing heteroatoms,  ${}^{3}$ ,  ${}^{8}$  we prefer to discuss the properties of various metal enolates in terms of the measured chemical shift difference parameter  $\Delta\delta$  rather than calculated charge densities. However, it is important to note that  $\Delta\delta$  does appear to be largest in those circumstances where the enolate anions 1 might be expected to have a significant contribution from structure <u>lb</u> with the negative charge concentrated at the  $\alpha$ -carbon atom.

In two cases, enolates 2a and 5, we measured the coupling constants  ${}^{1}J_{CH}$  between the  $\alpha$ -carbon atom and the attached proton. The J values obtained, 145-154 Hz, did not differ appreciably from the J values, 154-157 Hz, for the corresponding enol acetates 17 and 20. These measurements suggest, therefore, that the  $\alpha$ -carbon atom of these enolates is not deformed significantly from a planar sp<sup>2</sup> configuration.

The high order of reactivity observed<sup>9</sup> in reactions of potassium enolates with alkyl halides is compatible with the  $\Delta\delta$  values observed. In DME solution, the  $\Delta\delta$  values decrease regularly in progressing from the K enolate 2c ( $\Delta\delta$  24.8) to the Na enolate 2b ( $\Delta\delta$  23.2) to the Li enolate 2a ( $\Delta\delta$  21.3). The enhanced rate of alkylation of lithium enolates obtained by use of DME rather than  $Et_2^0$  as a reaction solvent<sup>10</sup> is also consistent with the  $\Delta\delta$  values observed. For the lithium enolate 2a, the  $\Delta\delta$  values change with solvent as follows:  $Et_2^0$  ( $\Delta\delta$  18.8), THF ( $\Delta\delta$  19.5), and DME ( $\Delta\delta$  21.3). The addition of 4 equiv. of HMP [sufficient to form the tetracoordinate solvated cation,  $Li(HMP)_4^+$ ], a solvent believed to be one of the most effective for solvation of metal cations,<sup>11</sup> to solutions of the enolate 2a in Et<sub>2</sub>0, THF, or DME increased the values of  $\Delta\delta$  to 22.5, 22.2, and 23.5 ppm, respectively. The largest effect (increasing  $\Delta\delta$  by 3.7 ppm) is consistent with the practice of adding HMP to an Et<sub>2</sub>0 solution of a lithium enolate in order to increase its rate of reaction with an alkyl halide.<sup>12</sup>

Interestingly, the maximum value of  $\Delta\delta$  (25.9) for the  $\alpha$ -carbon atom of enolate <u>2</u> was attained by the addition of 1 mol equiv. of the crown ether <u>27</u> to a solution of the Na enolate <u>2b</u> in DME. Since no further change in the chemical shift values of <u>2b</u> was observed when a second mol equiv. of <u>27</u> was added, the formation of a 1:1 Na<sup>+</sup> cationcrown ether <u>27</u> complex is evidently very favorable. Unfortunately, we were unable to obtain sufficiently concentrated solutions of the K enolate <u>2c</u> in the presence of 1 mol equiv. of either of the crown ethers 27 or 28 to permit nmr measurements.<sup>13</sup>

In contrast to the results obtained with the sodium enolate  $\underline{2b}$ , the addition of 1 mol equiv. of either of the crown ethers  $\underline{28}$  or  $\underline{29}$  to THF solutions of the Li enolate  $\underline{2a}$  had relatively little effect on the chemical shift values. Consequently, it appears that neither of the crown ethers  $\underline{28}$  or  $\underline{29}$  forms a sufficiently stable complex with Li<sup>+</sup> cation to enhance significantly the reactivity of lithium enolates. Since the common synthetically useful methods for the regiospecific generation of metal enolates produce lithium enolates, it is clearly desirable to find a crown ether of proper geometry to form a very stable complex with Li<sup>+</sup> cation. Unfortunately, the low solubility of the crown ether  $\underline{30}$  in ethereal solvents prevented us from obtaining useful  $\underline{13}^{2}$  c nmr

measurements described herein do offer a rather simple experimental method for evaluating the efficacy of various polydentate ligands as additives to enhance the reactivity of metal enolates.

It was also of interest to compare the  $\Delta\delta$  values for the terminal lithium enolate 3 with the corresponding values for enolates 4 - 6 in which alkyl substituents are present at the  $\alpha$ -carbon atom. Earlier work<sup>14</sup> had suggested that metal enolates with no alkyl substituents at the  $\alpha$ -carbon atom are less reactive than analogous metal enolates with  $\alpha$ -alkyl substituents. The  $\Delta\delta$  values for DME solutions of the unsubstituted enolate 3 (AS 24.9) and the enolate 4 (AS 25.5) with two methyl substituents are practically the same and both are greater than the values observed for the cyclohexanone enolates 5 (A $\delta$  21.5) and 6 (A $\delta$  21.5). Even in the case of a DME solution of the Li enolate 2a where some delocalization of negative charge into the p-position of the phenyl ring was evident, the  $\Delta\delta$  value (21.3) was comparable to the values observed with the cyclohexanone enolates 5 and 6. Only in the case of the  $\beta$ diketone enolate 7 where delocalization of the negative charge to two equivalent carbonyl groups was possible did the  $\Delta\delta$  value (14.4) decrease. The decreased value of  $\Delta\delta$  (presumably corresponding to diminished charge density at the enolate  $\alpha$ -carbon atom) is compatible with the general observation that enolates of  $\beta$ -diketones tend to give significant amounts of O-alkyl products upon reaction with alkylating agents.

The several trimethylsilyl enol ethers 23 - 26 examined had observed  $\Delta\delta$  values (7.9-12.9) approximately half as large as the values for the metal enolates, consistent with the fact that these materials are significantly poorer nucleophiles than metal enolates.

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Interestingly, the  $\Delta\delta$  value (20.2) for the one enamine examined was practically the same as the value for the corresponding metal enolate.

In conclusion, the  $\Delta\delta$  values observed with a particular enolate system do appear to vary in a systematic way with changes in the metal cation, the solvent, and added ligands that can coordinate with the metal cation. In general, those combinations of cation, solvent and added ligands that give the largest value of  $\Delta\delta$  are also the combinations that result in the highest reactivity of the enolate with alkyl halides, and in the greatest proportion of O- to C-acylation in reaction with  $Ac_20$ . However, comparison of  $\Delta\delta$  values for structurally different enolates derived from monoketones has not revealed any obvious relationship between the substitution pattern of the enolate anion, its reactivity, and its  $\Delta\delta$  value.

# Experimental Section<sup>15</sup>

#### Reagents and Starting Materials

All ethereal solvents were distilled from  $\text{LiAlH}_4$  immediately before use. Oil dispersions (Alfa Inorganics) of NaH and KH were washed free of oil with purified pentane ( $\text{H}_2\text{SO}_4$  washed, dried, distilled from CaH<sub>2</sub>) immediately before use. Ethereal solutions of halide free CH<sub>3</sub>Li (Foote Mineral Co.) were standardized by previously described methods.<sup>16</sup> Samples of the <u>trans</u>-enol acetate <u>17</u> and the <u>trans</u>-silyl enol ether <u>23</u> were obtained by the previously described<sup>2</sup>, <sup>17</sup> reactions of the <u>trans</u>enolate <u>2b</u> with Ac<sub>2</sub>O or (CH<sub>3</sub>)<sub>3</sub>SiCl. <u>Preparation of the Enol Acetate 19</u><sup>18</sup>

To a solution of 100 ml (108 g, 1.06 mol) of  $Ac_2^{0}$  and 17.2 g

(0.20 mol) of 3-methyl-2-butanone 12 in 240 ml CCl was added 136  $\mu l$ of aqueous 70%  $HC10_4$ . The resulting solution was allowed to stand 4 hr at room temperature, then partitioned between 160 ml of pentane and 160 ml of saturated aqueous NaHCO3. The organic layer was stirred over cold (ca.  $10^{\circ}$ ) saturated aqueous NaHCO<sub>3</sub>, and 160 g of solid NaHCO<sub>3</sub> were added in portions to complete the hydrolysis of acetic anhydride. After extracting the aqueous layer three times with 60 ml portions of pentane, the combined organic phases were dried over anhydrous  $Na_2SO_4$ , filtered and concentrated on a rotary evaporator. Fractional distillation of the residual liquid separated 11.7 g of material, bp 123°-131°,  $\underline{n}^{25}\underline{D}$  1.4201-1.4217. This material was redistilled to afford 10.6 g (41%) of colorless oil, bp  $138^{\circ}-140^{\circ}$ ,  $\underline{n}^{25}\underline{p}$  1.4210 (lit.<sup>19</sup> bp 121° (763 mm),  $\underline{n}^{20}\underline{D}$  1.4222) which gave one peak upon glpc analysis [15% SE-30 on P, ret time 5.6 min  $(\underline{19})$ ] with no ketone  $\underline{12}$  (ret time 2.0 min) or acetic anhydride (ret time 2.9 min) present; nmr (CC1 $_{L}$ ),  $\delta$  2.03 (3H, s, CH\_3CO) with 3 partially resolved multiplets at 1.78, 1.65 and 1.50 (each 3H, allylic  $CH_3$ ); ir  $(CCl_4)$ , cm<sup>-1</sup> 1755 (enol ester C=0) and 1701 (enol C=C).

# Preparation of Solutions for <sup>13</sup>C nmr Study

A. <u>Ketones 11 and 12, Enol Acetates 17 and 19, and Trimethyl-</u> <u>silyl Enol Ether 23</u> - Solutions of these materials were prepared by dissolving 200-400 mg of each purified material in 1.5 ml of 1, 2dimethoxyethane (DME), then adding 0.4 ml of  $C_6D_6$  and 0.2 ml of  $Me_4Si$ .

B. <u>Sodium and Potassium Enolates 2b and 2c</u> - A slurry of one equiv of prewashed KH or NaH (1.5-2.0 mmol per ml of solvent) in DME was treated with ketone <u>10</u> and stirred at 15°-25° until  $H_2$  evolution ceased. Aliquots (1.6 ml) of these solutions were added to 0.4 ml  $C_6D_6$  and 0.2 ml  $Me_4Si$  in <sup>13</sup>C-nmr tubes. The <sup>1</sup>H nmr spectra of these enolates were previously described.<sup>2</sup>

C. Lithium Enolates 2a and 4 ~ A 1.3 <u>M</u> solution of these enolates in DME was obtained by the reaction of the respective enol acetates <u>17</u> and <u>19</u> with a DME solution of MeLi in the usual manner.<sup>16b</sup> Aliquots of these solutions (1.5-2.0 ml) were added to 0.4 ml  $C_6D_6$  and 0.2 ml Me<sub>4</sub>Si for <sup>13</sup>C-nmr measurements.

## Preparation of the Crown Ether 30

The crown ether  $\underline{30}$  was prepared in two steps by a previously described procedure<sup>20</sup> from furan<sup>21</sup> and acetone.

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#### CHAPTER II

PART A. THE SYNTHESIS OF  $\omega$ -BROMO KETONES

Our interest in preparing a group of  $\omega$ -bromo ketones<sup>1a</sup> of the type <u>3</u> as substrates for studying the behavior of the enolate anions <u>2<sup>1b,c,24</sup></u> (Scheme I) led us to the vinyl ketones <u>4</u> as attractive precursors for such bromo ketones. These olefinic intermediates were readily accessible either by regiospecific alkylation of a preformed lithium enolate <u>5</u> with an allyl halide<sup>2</sup> or by the conjugate addition of lithium divinylcuprate (or its equivalent) to an enone <u>6</u>.<sup>3,4</sup>

In this study we prepared the  $\alpha$ -allyl ketones <u>8</u> and <u>10</u> by allylation of the enolates <u>7</u> and <u>9</u> (Scheme II). We also performed a regiospecific alkylation of the enolate <u>9</u> to obtain precursors <u>11-13</u> of the bromo ketone <u>14</u>, a lower homolog of the bromo ketone system <u>3</u>. The  $\alpha$ -allyl ketone <u>16</u> was prepared by an acid catalyzed thermal rearrangement of the diallyl acetal <u>15</u>.<sup>42</sup> The precursor <u>18</u> for another lower homolog of the bromo ketone <u>3</u> was obtained by the previously described<sup>5</sup> reaction of the acid <u>17</u> with MeLi.

To obtain a precursor for a higher homolog of the bromo ketone 3, (Scheme III) the known dienol  $20^6$  was subjected to an oxy-Cope rearrangement<sup>7</sup> to obtain the unsaturated ketone 21, albeit a rather inefficient process. Although this precursor 21 can also be obtained by the reaction of the enone 19 with  $(CH_2=CHCH_2)_2CuLi$ , <sup>18</sup> use of the more readily accessible organometallic reagent,  $CH_2=CHCH_2MgBr$ , with the enone 19 gave primarily the 1,2-addition product even in the presence






















Scheme III (cont.)







added Me,SCuBr catalyst. To explore the possibility that Cu-catalyzed conjugate addition of CH2=CHCH2MgBr would be more efficient with a substrate having a less negative reduction potential than enone 19 ( $E_{red} = -2.08V$  vs SCE), we prepared the enones <u>22</u> [ $E_{red} = -1.80V$  (<u>22a</u>) and -1.79V (22b) vs SCE].<sup>43</sup> The Cu-catalyzed addition of CH<sub>2</sub>=CHCH<sub>2</sub>MgBr to the enones 22 produced cleanly the conjugate adduct 23 that could be cleaved and decarboxylated to form the unsaturated ketone 21. Another higher homolog of 1 was prepared from the acetylenic alcohol  $\underline{24}$  (Scheme III). An acid catalyzed isomerization gave enone  $\underline{25}$ .<sup>38</sup> From consideration of the reduction potential of 25 (-2.11V vs SCE in DME solution), conjugate addition of (ally1) $_2$ CuLi to form <u>26</u> was expected to be only marginally satisfactory.<sup>18</sup> Indeed, the reaction formed almost equal amounts of 26 and 27 (each ca. 30%) with 11-24% recovery of 25. However, the base-catalyzed <sup>7c</sup> rearrangement of 27 in refluxing DME afforded 26 in 78% yield. The 1,4-allyl adduct 26 could also be prepared in higher yield (83-94%) directly from enone 25 by reaction with  $CH_2 = CHCH_2Si(CH_3)_3$  and  $TiCl_4$ .

During our study, the commercially prepared solution of vinyllithium in THF was removed from the market, and we were led to explore the use of vinylmagnesium bromide with a copper(I) catalyst<sup>4</sup> instead of lithium divinylcuprate. We found the use of a THF solution of  $CH_2$ =CHMgBr with the complex  $Me_2S$ -CuBr <sup>3h</sup> as a catalyst to be an effective substitute for  $(CH_2=CH)_2CuLi$  in the preparation of ketones 29, <sup>3a</sup> 31, <sup>14</sup> 34, <sup>3h</sup> and 35<sup>3h</sup> (Scheme IV), provided that the temperature of the reaction solution was maintained at -30 to -40° so that the vinylcopper derivative did not undergo thermal



$$(CH_3)_2 C = CHCCH_3 \qquad \underbrace{(CH_2 = CH)_2 CuLi}_{\text{or } CH_2 = CHMgBr} \qquad CH_2 = CH(CH_3)_2 CH_2 CCH_3 \\ \underbrace{28}_{\text{H}} \qquad + CuBr \cdot S(CH_3)_2 \qquad \underbrace{29}_{\text{H}}$$





Scheme IV (cont.)







+









40, R = H

 $\underline{41}$ , R =  $\underline{t}$ -Bu

I



<u>42a</u>



decomposition  $^{3g,3h,8}$  before reaction with the enone could occur.

The stereochemical preference for axial addition by such Cu(I) reagents<sup>1a,3g,h</sup> was used to advantage in the synthesis of <u>35</u> to introduce an axial vinyl substituent in >90% of the conjugate addition product.

The epimeric ketones <u>35a</u> and <u>35b</u>, as well as <u>36a</u> and <u>36b</u> (Scheme IV) were separable by chromatography. The equilibrium constant for <u>35a</u>  $\longrightarrow$  <u>35b</u> was previously determined <sup>3h</sup> to be 2.3, and was determined for <u>36a</u>  $\longrightarrow$  <u>36b</u> to be <u>ca</u>. 99.

To investigate the conformation in solution of  $\underline{35a}$ , the <sup>1</sup>H nmr spectrum was rerun at 100 MHz to examine the pattern attributable to the -CHCO multiplet at  $\delta 2.4$ -2.6. We obtained partial resolution into three closely spaced lines at 248, 250.5, and 253 Hz; the width at half-height of the envelope containing these peaks was 10 Hz. This observation is compatible with our assigned stereochemistry in which the COCH proton is equatorial and is coupled with two equatorial and one axial adjacent protons (typical J values all 2-3 Hz).

In an earlier study, <sup>3e</sup> the unsaturated ketone <u>38</u> (Scheme IV) had been converted to the bromo ketone <u>39</u> by the reaction sequence: unsaturated ketone <u>38</u>  $\div$  unsaturated ketal  $\div$  alkylborane  $\div$  primary alcohol  $\div$  mesylate  $\div$  primary alkyl bromide <u>39</u>. In exploring an analogous sequence with the ketals <u>40</u> and <u>41</u>, <sup>3h</sup> the tendency of the hydroboration-oxidation product <u>42a</u> to undergo trans-ketalization forming ketal <u>42b</u> and related materials was a troublesome side reaction. We concluded that a more efficient route for the conversion, RCH=CH<sub>2</sub>  $\div$  RCH<sub>2</sub>CH<sub>2</sub>Br, was clearly required. Accordingly, we explored

the addition of anhydrous HBr in a free-radical chain process. Although this reaction has only rarely been applied to molecules containing both a terminal CH=CH, group and a second functional group, 9 it was not apparent that a ketone function would interfere with this reaction if conditions were chosen that would minimize the tendency for the ketone to be present in equilibrium with its enol This expectation proved to be correct. When anhydrous HBr form. gas was passed through pentane solutions<sup>17</sup> of the various unsaturated ketones 8, 10, 16, 18, 21, and 29 (Scheme V), while irradiating with light from a medium pressure Hg lamp, the addition reactions were complete within 5-10 min and practically quantitative yields of the crude bromo ketones 43-48 were obtained. After purification by distillation or column chromatography, the pure bromo ketones 43-48 were obtained. Neither  $^{1}$ H nmr nor  $^{13}$ C nmr measurements gave any indication that these products were contaminated with the isomeric secondary alkyl bromides (the products expected from addition in the Markovnikov sense).

When the reaction conditions used successfully for HBr addition to form bromo ketones 43-48 were applied to the unsaturated ketones 34 and 35 (Scheme VI) we found that the crude products were unstable and rapidly darkened on storage or distillation. The <sup>1</sup>H nmr spectra of each of these crude products contained two sets of extraneous signals, a doublet at  $\delta 1.66-1.68$  (J = 7 Hz, CH<sub>3</sub>) and a multiplet at  $\delta 4.23-4.26$ , an appropriate location for a > CH-Br grouping. A product with the same nmr spectrum as this contaminant was obtained when the unsaturated ketone 34 was allowed to react with











Scheme V (cont.)









Scheme VI (cont.)





aqueous 48% HBr. Thus, we conclude that the contaminants formed along with the bromo ketones <u>49</u> and <u>50</u> are the secondary bromides <u>51</u> (<u>ca</u>. 5% of the product from ketone <u>34</u>) and <u>52</u> (<u>ca</u>. 20-30% of the product from ketone <u>35</u>). These same minor contaminants were also present in bromo ketones <u>49</u> and <u>50</u> formed by the light-catalyzed addition of HBr in pentane to the ketals <u>40</u> and <u>41</u> followed by hydrolysis of the ketals <u>55</u> and <u>56</u>. Consequently, the presence of a ketone function is not responsible for the formation of the secondary bromide by-products. A variety of additional experiments in which special care was taken to insure anhydrous reactants and in which small amounts of H<sub>2</sub>O were deliberately added had little influence on the amount of the by-product that was formed. Therefore, we concluded that the secondary bromides were also being formed by a free radical process.

Since the unsaturated ketones <u>34</u> and <u>35</u> differed from the other ketones studied <u>8</u>, <u>10</u>, <u>16</u>, <u>18</u>, <u>21</u>, and <u>29</u> in containing a tertiary allylic CH grouping, we considered the possibility that reaction of the ketones <u>34</u> and <u>35</u> with a Br atom resulted not only in addition of this radical to form precursors of the primary bromides <u>49</u> and <u>50</u> but also in H atom abstraction to form the allylic radicals <u>53</u>. Further reaction of these allylic radicals <u>53</u> to abstract an H atom from the excess HBr could form the isomeric olefins <u>54</u> that would yield the secondary bromides <u>51</u> and <u>52</u> upon addition of HBr in a radical chain process. There are reported examples<sup>10</sup> of just this type of isomerization in other studies of the free-radical addition of HBr to terminal olefins. To provide additional evidence that the presence of tertiary allylic CH bonds in ketones (which would enhance the stability of allylic radicals such as <u>53</u>) favor this side reaction leading to secondary bromide by-products, we also examined the addition of HBr to the ketone <u>31</u> (Scheme VI), an acyclic system that contains this structural feature. Upon light-catalyzed addition of HBr, the expected bromo ketone product <u>57</u> again contained <u>ca</u>. 5% of a contaminant believed to be the secondary bromide <u>58</u>. In the case of <u>31</u> or <u>34</u>, the small amounts of secondary bromide impurities <u>58</u> or <u>51</u> could be readily separated from the desired primary bromides by chromatography on silica gel.

In the case of ketone 35, however, it was clearly preferable to find reaction conditions which would minimize formation of 52. From previous work,<sup>9,10b</sup> the reaction temperature appeared to be a key factor for selectivity, since the rate of the abstraction process relative to radical addition decreased with decreasing temperatures. Indeed, by conducting the photochemical hydrobromination at 0° in pentane, we obtained 80-85% yields of 50 with only 0-3% yields of 52 after purification by liquid chromatography. When either pure epimer of <u>35</u> was allowed to react with HBr (g) at 0° as described above, a 35:65 ratio of primary bromides <u>50a:50b</u> (Scheme VI) was obtained in overall 80% yield, with comparable amounts (0-3%) of secondary bromide product <u>52</u> being formed in both cases. At 25°, however, the formation of by-products by H atom abstraction was clearly a more serious problem with epimer <u>35b</u> (ca. 32% yield of by-products) than with <u>35a</u> (ca. 5% yield).

# Experimental Section<sup>11</sup>

#### Preparation of the Ketone 29

A solution of 514 mg (2.5 mmol, 10 mol-% based on the enone) of  $Me_2SCuBr$  in 5.2 ml of  $Me_2S$  was diluted with 25 ml of THF and then cooled to  $-55^{\circ}$ . Then a solution of 2.45 g (25 mmol) of the enone 28 in 25 ml of THF was added and the reaction mixture was maintained at -50 to -55° while 37 ml of a THF solution containing 30 mmol of vinyl-MgBr was added, dropwise and with stirring during 30 min. During this process it was important to immerse the entire reaction flask in the cooling bath so that any vinyl-Cu reagent<sup>12</sup> splashed on the walls of the flask did not undergo thermal decomposition. The reaction solution, which successively changed from red to purple to green-black in color, was stirred at -45 to -50° for an additional 30 min and then siphoned into cold, vigorously stirred aqueous 2M In this procedure it was important to keep the reaction HC1. temperature below  $-40^{\circ}$  and to hydrolyze the product by addition of the reaction mixture to aqueous acid. The resulting mixture was extracted with pentane and the organic extract was washed with aqueous NaHCO3, dried, concentrated, and distilled to separate 2.33g (74%) of the ketone 29 as a colorless liquid, bp 59.5°-60.5° (30 mm),  $\underline{n}^{25}\underline{p}$  1.4282 (lit. bp 45-50° (30 mm), <sup>13a</sup> 69-71° (45 mm), <sup>13b</sup>  $\underline{n}^{20}\underline{p}$  1.4375, <sup>13a</sup>  $\underline{n}^{20}\underline{p}$  1.4305<sup>13b</sup>); ir (CCl<sub>4</sub>), 3080, 1720 (C=O), 1640 (C=C), and 925 cm<sup>-1</sup> (RCH=CH<sub>2</sub>); nmr (CCl<sub>4</sub>),  $\delta$ 5.93 (1H, d of d, H<sub>x</sub>, J<sub>trans</sub> = 17.8 Hz,  $J_{cis} = 10.5 \text{ Hz}$ , 4.90 (1H, d of d,  $H_{\dot{a}}$  (trans),  $J_{gem} = 1.3 \text{ Hz}$ ), 4.89 (1H, d of d, H<sub>b</sub> (cis)), 2.35 (2H, s, CH<sub>2</sub>CO), 2.02 (3H, s, CH<sub>3</sub>CO),

and 1.09 (6H, s, gem  $CH_3$ ); uv (95% EtOH), 206 ( $\epsilon$  231) and 235 nm ( $\epsilon$  112); mass spectrum, m/e (rel. intensity), 126 (M<sup>+</sup>, 12), 111 (20), 83 (26), 69 (45), 55 (27), 43 (100), and 41 (42). The natural abundance <sup>13</sup>C-nmr spectrum of <u>29</u> was as follows: <sup>13</sup>C-nmr (CDC1<sub>3</sub>),  $\delta$  (multiplicity in off resonance decoupled spectrum) 206.2 (s), 146.5 (d), 110.3 (t), 54.7 (t), 36.2 (s), 31.9 (q), and 26.9 (q, 2C atoms).

## Preparation of the Ketone 31

A cold (-50 to -55°), red solution was prepared from 205 mg (1.0 mmol) of  $Me_2SCuBr$ , 10 ml of  $Me_2S$ , and 20 mmol of  $CH_2$ =CHMgBr in 65 ml of THF. To this cold mixture was added, dropwise and with stirring during 30 min, a solution of 103 mg (0.50 mmol) of Me<sub>2</sub>SCuBr, 5 ml of  $Me_2S$ , and 840 mg (10 mmol) of the enone <u>30</u> in 10 ml of THF. The resulting solution was stirred at -40 to -50° for 45 min and then siphoned into aqueous  $NH_4C1$ . After the mixture had been treated with aqueous 2 M HCl to dissolve the precipitate that separated, it was made basic with NaHCO3 and extracted with Et20. After the ethereal extract had been washed with aqueous 2  $\underline{M}$  HCl and with aqueous NaHCO<sub>3</sub>, it was dried, concentrated, and distilled to separate 0.70 g (63%) of the ketone <u>31</u> as a colorless liquid, bp 62-63.5° (50 mm),  $\underline{n}^{25}\underline{p}$  1.4213-1.4216 [lit.<sup>14</sup> bp 137-138°,  $\underline{n}^{25}\underline{p}$  1.4193]; ir (CCl<sub>4</sub>), 1720 (C=0), 1640 (C=C), and 925 cm<sup>-1</sup> (CH=CH<sub>2</sub>); nmr (CCl<sub>4</sub>), δ4.7-6.1 (3H, m, vinyl CH), 2.3-3.1 (3H, m, aliphatic CH), 2.03 (3H, s, CH<sub>3</sub>CO), and 1.00 (3H, d, J = 6.5 Hz,  $CH_2$ ); mass spectrum, m/e (rel. intensity), 112 (3), 97 (15), 69 (11), 55 (18), 43 (100), and 41 (20).

#### Preparation of the Vinyl Ketones 35

A 2.05 g (.01 moles, 10 mole % based on enone) portion of  $CuBr(CH_3)_2S$  complex was dissolved in 20 ml  $(CH_3)_2S$ , diluted with 100 ml THF and cooled to  $-60^{\circ}$  under N<sub>2</sub>. The dropwise addition over 15 min of 18.00 g (0.1 moles) enone 33 in 100 ml THF was followed by the addition over 90 min at  $-53^{\circ}$  to  $-55^{\circ}$  of a THF solution containing 0.12 moles vinylmagnesium bromide.<sup>12</sup> The resulting green-black mixture was warmed to -45° and stirred at -43° to -45° for 45 min, then quenched while still cold onto 250 ml 2N HCl. The resulting mixture was filtered through Celite and worked-up as previously described for ketone 29 to yield 16.85 g (81%) of distilled 35 and <u>36</u>, bp 75.5°-78.0° (0.45 mm),  $\underline{n}^{25}\underline{p}$  1.4723 (lit.<sup>3h</sup>  $\underline{n}^{25}\underline{p}$  1.4728). A 3.00 g sample of the crude product from reaction of the enone 33 with CH<sub>2</sub>=CHMgBr and Me<sub>2</sub>SCuBr in THF<sup>1a</sup> [containing (glpc, silicone XE-60 on Chromosorb P) a derivative of the 1,2-adduct (ret. time (190°), 5.2 min, ca. 6%), the ketone 36a (14.0 min, ca. 0.3%), the ketone 35a (18.3 min, ca. 34%), the ketone 36b (20.6 min, ca. 5%), the enone 33 (22.6 min, ca. 3%), and the ketone 35b (26.6 min, ca. 52%)] was chromatographed on a 2.5 x 100 cm column packed with Woelm silica gel (0.032 - 0.064 mm) and eluted with EtOAc-hexane (8:92 v/v). The early fractions contained 188 mg (6%) of liquid,  $\underline{n}^{25}\underline{D}$  1.4865, believed to be p-(sec-buty1)-t-buty1benzene (formed from the 1,2-adduct 37 by dehydration and C=C rearrangement). The spectral properties of the component were: ir (CC1 $_{L}$ ), no OH or C=O absorption; nmr (CCl<sub>4</sub>),  $\delta$ 7.20 (2H, d, J = 8 Hz, aryl CH), 7.00 (2H, d, J = 8 Hz, aryl CH), 2.55 (1H, sextet, J = 7 Hz, benzylic CH),

1.1 - 1.9 (11H, m, aliphatic CH including a t-Bu singlet at 1.28, and 0.6-1.0 (6H, m, two CH<sub>3</sub> groups); mass spectrum, m/e (rel. intensity), 190 (M<sup>+</sup>, 69), 176 (49), 175 (90), 173 (20), 162 (38), 161 (100), 146 (44), 131 (45), 91 (28), 57 (36), and 41 (19). Subsequent chromatographic fractions contained (glpc), in order of elution, 950 mg (32%) of relatively pure ketone 35a, 288 mg (10%) of a mixture of ketones 35a and 35b, and 1.446 g (48%) of relatively pure ketone 35b. Appropriate fractions were combined and rechromatographed to separate 798 mg (27%) of ketone  $\underline{35a}$ ,  $\underline{n}^{25}\underline{D}$  1.4730, that was further purified by short-path distillation to separate a colorless liquid, mp 8.0-8.5°, <u>n</u><sup>25</sup><u>D</u> 1.4731; ir (CC1<sub>4</sub>), 1712 (C=O), 1640 (C=C), and 921 cm<sup>-1</sup> (CH=CH<sub>2</sub>); mass spectrum, m/e (rel. intensity), 208 (M<sup>+</sup>, 0.7), 152 (40), 151 (17), 109 (62), 107 (16), 71 (19), 67 (17), 57 (81), 43 (100), and 41 (30); nmr (CC1<sub>4</sub>),  $\delta$ 4.8-6.3 (3H, m, vinyl CH), 2.7-3.1 (1H, m, allylic CH), 2.4-2.6 (1H, m, COCH), 2.11 (3H, s, COCH3), 0.9-2.1 (7H, m, aliphatic CH), and 0.81 (9H, s, t-Bu).

<u>Anal</u>. Calcd. for C<sub>14</sub>H<sub>24</sub>O: C, 80.71; h, 11.61. Found: C, 80.90; H, 11.74.

Appropriate later fractions that were combined and rechromatographed afforded 1.17 g (39%) of pure (glpc) ketone <u>35b</u>, mp 24-25°,  $\underline{n}^{25}\underline{p}$  1.4728 (lit.  $\underline{n}^{25}\underline{p}$  1.4728, <sup>3h</sup> mp 17.5-18°<sup>1a</sup>) that was identified with a previously described <sup>3h</sup> sample by comparison of ir, nmr, and mass spectra. The natural abundance <sup>13</sup>C nmr spectrum of the ketone <u>35b</u> was as follows: <sup>13</sup>C-nmr (CDCl<sub>3</sub>),  $\delta$ (multiplicity in off resonance decoupled spectrum): 208.8 (s), 136.9 (d), 115.5 (t), 54.2 (d), 41.2 (d), 40.7 (d), 33.7 (t), 32.0 (s), 28.0 (q), 27.2 (q, 3 C atoms), 26,3 (t), and 22.8 (t).

An alternate method for obtaining <u>39b</u> involved low temperature fractional crystallization. Thus, when a solution of 10.4 g of the mixture of ketones <u>35</u> (major) and <u>36</u> (minor) in 15 ml of pentane was slowly cooled to -15 to -20°, the isomer <u>35b</u> separated as white needles that were collected at -25° and washed with cold (-78°) pentane. The crystalline product, mp 17-18°, amounted to 6.75 g (65% recovery) and contained (glpc and nmr analyses) 85-90% of ketone <u>35b</u> and 10-15% of ketone <u>35a</u> with <1% of the stereoisomers <u>36</u>. Recrystallization from pentane separated the pure ketone <u>35b</u>, as shown by comparison of nmr spectra and glpc retention times with an authentic sample.

Ketone <u>35b</u> could also be isolated from the crude mixture of <u>35</u> and <u>36</u> by reaction with 2,4-dinitrophenylhydrazine to form a mixture of 2,4-dinitrophenylhydrazones. Fractional recrystallization from an EtOH-EtOAc mixture separated the 2,4-dinitrophenylhydrazone of ketone <u>35b</u> as orange needles, mp 145.5-147°; nmr (CDCl<sub>3</sub>),  $\delta$ 11.0 (1H, broad, NH), 9.07 (1H, d, J = 2.5 Hz, aryl CH), 8.27 (1H, d of d, J = 2.5 and 9.5 Hz, aryl CH), 7.90 (1H, d, J = 9.5 Hz, aryl CH), 4.8-6.3 (3H, m, vinyl CH), 2.3-3.1 (2H, m, allylic CH and CH-C=N), 2.00 (3H, s, CH<sub>3</sub>C=N), 1.0-2.0 (7H, m, aliphatic CH), and 0.87 (9H, s, <u>t</u>-Bu). Reaction of this solid derivative with a mixture of levulinic acid and aqueous 1 <u>M</u> HCl as previously described<sup>16</sup> afforded a sample of the pure ketone 35b (nmr analysis).

Reaction of the ketone 35b with HOCH<sub>2</sub>CH<sub>2</sub>OH and TsOH in refluxing PhH as previously described<sup>3h</sup> afforded the ketal 41 (a

mixture of epimers), bp 100.5-102° (0.4 mm),  $\underline{n}^{25}\underline{p}$  1.4789 (lit. <sup>3h</sup>  $\underline{n}^{25}\underline{p}$  1.4790), in 85% yield).

Preparation of the Vinyl Ketones 36

Fractions from several reactions containing (glpc, silicone XE-60 on Chromosorb P) primarily the ketones <u>36a</u> (ret. time 10.2 min) and <u>36b</u> (15.4 min) were combined and separated by preparative liquid chromatography on a column packed with silica gel and eluted with EtOAc-hexane (6:94 v/v). The early fractions contained (glpc) the ketone <u>36a</u> separated as a colorless liquid; ir (CCl<sub>4</sub>), 1715 cm<sup>-1</sup> (C=0); nmr (CCl<sub>4</sub>),  $\delta$ 5.6-6.2 (1H, vinyl CH), 4.7-5.2 (2H, m, vinyl CH), 2.77 (1H, m, allylic CH), 1.0-2.3 (11H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.02), and 0.85 (9H, s, <u>t</u>-Bu); mass spectrum, m/e (rel. intensity), 208 (M<sup>+</sup>, 0.5), 152 (13), 109 (26), 71 (23), 58 (100), 57 (50), 43 (69), 42 (18), 41 (24), and 39 (14).

<u>Anal</u>. Calcd for C<sub>14</sub>H<sub>24</sub>O: C, 80.71; H, 11.61. Found: C, 80.81; H, 11.67.

Later chromatographic fractions contained (glpc) the ketone <u>36b</u> separated as a colorless liquid; ir (CC1<sub>4</sub>), 1715 cm<sup>-1</sup> (C=0); nmr (CC1<sub>4</sub>),  $\delta$ 4.8-6.1 (3H, m, vinyl CH), and 0.8-2.6 (21H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 1.99 and a <u>t</u>-Bu singlet at 0.89); mass spectrum, m/e (rel. intensity), 208 (M<sup>+</sup>, 4), 151 (23), 109 (36), 107 (17), 67 (18), 57 (88), 43 (100), and 41 (32).

<u>Anal</u>. Calcd for C<sub>14</sub>H<sub>24</sub>O: C, 80.71; H, 11.61. Found: C, 80.74; H, 11.65.

#### Equilibration of the Ketones 36

The two ketones <u>36</u> were equilibrated to establish which epimer corresponded to the more stable stereoisomer <u>36b</u> with an equatorial acetyl group. A solution of 21 mg of ketone <u>36a</u> and 21 mg of  $\underline{n}-C_{19}H_{40}$  (an internal standard) in 1 ml of MeOH and 1 ml of THF was treated with 5.5 µl (0.2 equiv) of methanolic 3.6 <u>M</u> NaOMe and stirred at 25.0°. Periodically aliquots of the solution were removed, quenched in an aqueous phosphate buffer (pH 7.0), extracted with hexane, dried, and analyzed (glpc, apparatus calibrated with known mixtures). An additional portion (0.3 equiv) of methanolic 3.6 <u>M</u> NaOMe was added after 5 hr. After 140 hr at 25°, the solution contained 1.3% of ketone <u>36a</u> and 98.7% of ketone <u>36b</u> (93% recovery of <u>36</u>). From a comparable experiment starting with the ketone <u>36b</u> after 140 hr at 25° the solution contained >98% of the ketone <u>36b</u> and <2% of the ketone <u>36a</u> (100% recovery of <u>36</u>).

# Preparation of the Alcohol 37

To 10 ml of a cold (0°) THF solution containing the vinyl-MgBr from 20.8 mg-atom of Mg was added, dropwise with stirring over 25 min, a solution of 2.50 g (13.9 mmol) of the enone <u>33</u> in 6 ml of THF. After the resulting solution had been stirred at 25° for 35 min, it was partitioned between aqueous  $NH_4Cl$  and  $Et_20$ . The ethereal solution was dried and concentrated to leave the crude product as a yellow liquid containing (nmr analysis) <u>ca</u>. 73% of the alcohol <u>37</u>, <u>ca</u>. 21% of the ketones <u>35</u> and <u>36</u> and <u>ca</u>. 6% of the enone <u>33</u>. A portion of the crude product was subjected to preparative liquid chromatography on a Merck silica gel column with Et<sub>2</sub>O-PhH (1:49 v/v) as the eluent. After separation of the early fractions containing ketones <u>33</u>, <u>35</u>, and <u>36</u>, the crude alcohol <u>37</u> was collected and further purified by short-path distillation at 0.5 mm. The alcohol <u>37</u> was collected as a colorless liquid that solidified on standing, mp 30.5-32°; ir (CCl<sub>4</sub>), 3590 (OH) and 915 cm<sup>-1</sup> (CH=CH<sub>2</sub>); nmr (CCl<sub>4</sub>),  $\delta$ 4.8-6.3 (4H, m, vinyl CH), 1.5-2.4 (7H, m, aliphatic CH), 1.31 (3H, s, CH<sub>3</sub>-C-O), 1.18 (1H, broad, OH), and 0.87 (9H, s, <u>t</u>-Bu); mass spectrum, m/e (rel. intensity), 208 (M<sup>+</sup>, 7), 190 (39), 133 (100), 106 (60), 105 (53), 91 (94), 57 (80), 55 (38), 43 (37), and 41 (70).

<u>Anal</u>. Calcd for C<sub>14</sub>H<sub>24</sub>O: C, 80.71; H, 11.61. Found: C, 80.62; H, 11.64.

## Preparation of Bromo Ketones - General Procedures

The pentane used as solvent in these reactions was purified by stirring over conc.  $H_2SO_4$  for several days followed by washing with  $H_2O$ , drying over MgSO\_4, and distillation from CaH<sub>2</sub>. In a typical preparation a solution of 10 mmol of the unsaturated ketone in 300 ml of purified pentane was placed in a quartz photochemical reaction vessel and flushed with N<sub>2</sub>. Gaseous HBr was then passed through anhydrous Mg(ClO<sub>4</sub>)<sub>2</sub> drying agent, and into the solution for either 4 min (room temperature reaction) or 8 min (0° reaction) while the solution was irradiated with the light from an Hanovia 450-watt medium pressure Hg lamp. In the low temperature reactions, the photochemical vessel was immersed in an ice bath, and the lamp cooled by circulating cold MeOH from an external, thermostated cooling system. The temperature of the circulating MeOH was monitored amd kept at 0 to  $-1^{\circ}$  at the outlet from the cooling jacket of the photochemical apparatus. The resulting colorless pentane solution was flushed with N<sub>2</sub> to remove most of the HBr and then washed repeatedly with saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>. The resulting organic solution was dried and concentrated under reduced pressure to leave the crude bromo ketone.

## Preparation of Bromo Ketone 45

The light-catalyzed addition of HBr to a solution of 1.90 g (15 mmol) of the ketone <u>29</u> in 300 ml of pentane at room temperature yielded 2.82 g (91%) of the crude bromo ketone <u>45</u> as a pale yellow liquid that darkened on standing. Distillation separated 2.35 g (76%) of the pure bromo ketone <u>45</u> as a colorless liquid, bp 56.5-57.5° (0.45 mm),  $n^{25}$ D 1.4717-1.4720; ir (CCl<sub>4</sub>), 1720 cm<sup>-1</sup> (C=O); nmr (CCl<sub>4</sub>),  $\delta$ 3.1-3.5 (2H, m, CH<sub>2</sub>Br), 2.34 (2H, s, CH<sub>2</sub>CO), 2.08 (3H, s, CH<sub>3</sub>CO), 1.8-2.0 (2H, m, CH<sub>2</sub>), and 1.02 (6H, s, CH<sub>3</sub>); mass spectrum, m/e (rel. intensity), 126 (12), 125 (12), 110 (73), 83 (15), 69 (26), 55 (23), 43 (100), and 41 (26).

<u>Anal</u>. Calcd for C<sub>8</sub>H<sub>15</sub>BrO: C, 46.40; H, 7.25; Br, 38.62. Found: C, 46.44; H, 7.30; Br, 38.45.

The natural abundance  ${}^{13}$ C nmr spectrum of the bromo ketone was as follows:  ${}^{13}$ C-nmr (CDCl<sub>3</sub>),  $\delta$ (multiplicity in off resonance decoupled spectrum) 205.6 (s), 52.5 (t), 44.8 (t), 34.1 (s), 31.9 (q), 28.7 (t), and 26.9 (q, 2 C atoms).

Bromo ketone 45 exhibited a single glpc peak (silicone XE-60 on Chromosorb P); however, a collected sample of the material eluted from this glpc column had ir absorption (3035 and 1670 cm<sup>-1</sup>)

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different from the ketone <u>45</u> suggesting that the bromo ketone may have been converted to an enol ether in the glpc apparatus. Preparation of Bromo Ketones 57 and 58

The photochemical addition of HBr at room temperature to 300 mg (2.68 mmol) of the ketone 31 in pentane gave 530 mg of the crude bromo ketone 57 as a pale yellow oil that rapidly darkened on standing. The nmr spectrum of the crude product exhibited weak absorption not present in the pure bromo ketone 57 in the regions  $\delta 4.0-4.6$  and 1.5-1.7. This absorption may be attributable to the bromo ketone 58 since stirring 137 mg of the unsaturated ketone 31 with 1.5 ml of aqueous 48% HBr for 10 min on a steam bath and then for 90 min at room temperature yielded, after distillation, a crude sample of the bromo ketone 58 as a yellow liquid with distinctive nmr absorption (CC1<sub>4</sub>) at  $\delta$ 3.9-4.4 (m, CHBr); 2.05 (s, COCH<sub>3</sub>), and 1.62 and 1.64 (two overlapping doublets, J = 7 Hz,  $CH_3$ ). Chromatography of the crude bromo ketone 57 on silica gel with an Et<sub>2</sub>O-hexane eluent (1:9 v/v) separated 318 mg (61.5%) of the bromo ketone 57 from a faster and a slower moving component, neither of which contained a C=O function (ir analysis). Distillation afforded the pure bromo ketone 57 as a colorless liquid, bp 60.5-61.5°  $(0.75 \text{ mm}), \underline{n}^{25}\underline{p} 1.4672 - 1.4680; \text{ ir } (CC1_4), 1720 \text{ cm}^{-1} (C=0); \text{ nmr } (CC1_4),$  $\delta$ 3.35 (2H, t, J = 7 Hz, CH<sub>2</sub>Br), 1.5-2.4 (8H, m, aliphatic CH including a  $CH_3$  singlet at 2.05), and 0.9-1.1 (3H, m,  $CH_3$ ); mass spectrum, m/e (rel. intensity), 113 (14), 112 (16), 97 (48), 69 (21), 43 (100), 41 (25), and 39 (11).

<u>Anal</u>. Calcd for C<sub>7</sub>H<sub>13</sub>BrO: C, 43.53; H, 6.80; Br, 41.38. Found: C, 43.72; H, 6.81; Br, 41.18.

# Preparation of the Bromo Ketone 49

A solution of 1.50 g ketone  $\underline{34}^{1a}$  in 300 ml anhydrous pentane was irradiated at room temperature with HBr (g) to yield 2.20 g (96%) of crude bromo ketone as a pale yellow oil. Chromatography on silica gel with an EtOAc-hexane eluent (7:93 v/v) separated 100 mg (4.5%) of secondary bromo ketone <u>51</u>, and 1.80 g (78%) of bromo ketone <u>49</u>. Distillation of fractions containing <u>49</u> at 0.02 mm afforded 1.56 g of material, bp 76.0°-77.0°,  $\underline{n}^{25}\underline{p}$  1.4988-1.4992; ir (CCl<sub>4</sub>), 1705 (C=0); nmr (CCl<sub>4</sub>),  $\delta 3.2$ -3.6 (2H, m, CH<sub>2</sub>Br), and 0.6 to 2.6 (15H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.08); mass spectrum, m/e (rel. intensity), 234 (M<sup>+</sup>, <1), 232 (M<sup>+</sup>, <1), 153 (20), 109 (21), 81 (11), 67 (19), 55 (13), 43 (100), 41 (17), and 39 (8).

<u>Anal</u>. Calcd for  $C_{10}H_{17}BrO$ : C, 51.52; H, 7.36; Br, 34.27. Found: C, 51.59; H, 7.37; Br, 34.30. The bromo ketone <u>51</u> exhibited a quartet (J = 7 Hz with additional partially resolved splitting) at  $\delta 4.23$  (R<sub>2</sub>CH-Br) and a doublet (J = 7 Hz) at  $\delta 1.66$  (CH<sub>3</sub>) in its nmr spectrum. Several experiments performed to learn the origin of impurity <u>51</u> are reported elsewhere.<sup>1a</sup>

#### Preparation of the Bromo Ketones 50

In a typical experiment, a cold (0° or less) solution of 1.90 g (9.13 mmol) of unsaturated ketone 35b in 350 ml of pentane was irradiated with ultraviolet light for 12 min while a stream of anhydrous HBr was passed through the solution. Then the solution

was purged with  $N_2$  (to remove excess HBr), washed with aqueous  $Na_2S_2O_3$ , dried, and concentrated to leave 2.25 g (85%) of crude bromo ketone product as a colorless liquid that contained (nmr analysis ) ca. 35% of 50a and ca. 65% of 50b, but none of the secondary bromide 52 was detected. A 1.00-g aliquot of the product was chromatographed on Woelm silica gel with an EtOAc-hexane eluent (6:94 v/v) to separate 105 mg of earlier fractions containing (nmr analyses) the bromo ketone 50a followed by 453 mg of fractions containing various mixtures of 50a and 50b. Subsequent fractions contained 410 mg of the bromo ketone 50b. The intermediate fractions were rechromatographed on silica gel to separate 228 mg of 50a (total yield 333 mg of 28%) and 208 mg of 50b (total yield 618 mg or 53%). In another comparable hydrobromination of 1.50 g of the vinyl ketone 35b for 10 min at -1 to 0°, chromatography separated 90 mg (ca. 4%) of early fractions containing (nmr) mixtures of dibrominated products and secondary bromide 52 followed by 1.74 g (84%) of fractions containing bromo ketones 50b (ca. 65% of the mixture and 50a (ca. 35% of the mixture).

The ketone <u>50b</u> was obtained as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4969; ir (CCl<sub>4</sub>), 1710 cm<sup>-1</sup> (C=0): <sup>1</sup>H nmr (CCl<sub>4</sub>),  $\delta 3.15-3.5$  (2H, m, CH<sub>2</sub>Br), 2.2-2.5 (1H, m, CHCO), 1.0-2.1 (13H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.08), and 0.87 (9H, s, <u>t</u>-Bu); <sup>13</sup>C nmr (CDCl<sub>3</sub>, multiplicity in off-resonance decoupling), 209.8 (s), 54.3 (d), 40.8 (d), 33.7 (d), 32.1 (s), 31.9 (t), 29.8 (t), 29.3 (t), 28.3 (t), 27.3 (q, 3 C atoms), 26.2 (q), and 22.4 (t) ppm; mass spectrum, m/e (rel. intensity), 290 (M<sup>+</sup>, 0.05), 288 (M<sup>+</sup>, 0.05), 208 (15),

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193 (21), 151 (21), 123 (35), 110 (12), 109 (19), 95 (10), 81 (12), 57 (48), 43 (100), and 41 (27).

The ketone <u>50a</u> was obtained as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4968; ir (CCl<sub>4</sub>), 1710 cm<sup>-1</sup> (C=O); <sup>1</sup>H nmr (CCl<sub>4</sub>);  $\delta 3.37$  (2H, t, J = 7 Hz, CH<sub>2</sub>Br), 1.0-2.6 (14H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.10), and 0.82 (9H, s, <u>t</u>-Bu); mass spectrum, m/e (relative intensity), 290 (M<sup>+</sup>, 0.5), 288 (M<sup>+</sup>, 0.5), 209 (11), 153 (12), 123 (10), 109 (18), 95 (10), 81 (11), 71 (23), 57 (71), 55 (12), 43 (100), and 41 (29).

The most satisfactory analytical method for mixtures of the epimeric bromo ketones 50 utilized the <sup>1</sup>H nmr spectra. The ketone 50b exhibited a <u>t</u>-Bu singlet at  $\delta 0.87$  with a complex multiplet (CH<sub>2</sub>Br) centered at  $\delta 3.33$  while the ketone 50a exhibited a <u>t</u>-Bu singlet at a higher field ( $\delta 0.82$ ) with a triplet (CH<sub>2</sub>Br) at  $\delta 3.37$ . The presence of the secondary bromide 52 in this mixture is readily detected by the presence of a <u>t</u>-Bu singlet at  $\delta 0.89$  and, especially, a CHBr multiplet at  $\delta 4.22$ . When samples of either pure bromo ketone 50a or 50b (from chromatography) were distilled in a short path still (<u>ca. 104° at 0.01 mm</u>), mixtures of the two epimers were obtained. Thus, distillation of pure ketone 50b afforded a colorless liquid,  $n^{25}$  <u>p</u> 1.4970, that contained (nmr analysis) <u>ca</u>. 65% of 50b and ca. 35% of 50a.

<u>Anal</u>. Calcd for C<sub>14</sub>H<sub>25</sub>BrO: C, 58.12; H, 8.73; Br, 27.62. Found: C, 58.20; H, 8.72; Br, 27.49.

When an 835-mg sample of the epimeric vinyl ketone <u>35a</u> in 300 ml of pentane was subjected to the photoinitiated addition of HBr

for 6 min at 25°, the resulting crude bromo ketone product amounted to 1.076 g. Chromatography on silica gel with an EtOAc-hexane eluent (8:92 v/v) separated in earlier fractions 44 mg of an unidentified crude dibrominated product as a colorless solid, mp 104-105.5°, followed by 18 mg (1.5%) of the crude secondary bromide 52 as a colorless liquid; nmr (CC1,),  $\delta 4.22$  (1H, q of d, J = 7 and 2 Hz, CH-Br), and 0.8-2.4 [24H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.15, a CH<sub>3</sub> doublet (J = 7 Hz) at 1.65, and a  $\underline{t}$ -Bu singlet at 0.89]. Later fractions contained 877 mg (76%) of mixtures of bromo ketones 50b (ca. 64%) and 50a (ca. 36%). The similar hydrobromination of 242 mg of vinyl ketone 35b in 300 ml of pentane at 25° for 5 min afforded, after chromatography 114 mg (ca. 32%) of a mixture of dibromo product and secondary bromo ketone 52 and 141 mg (42%) of fractions containing mixtures of bromo ketones 50a and 50b. Thus, it appears that the H atom abstraction leading to by-products 52 is more serious at 25° with the vinyl ketone 35b than with its epimer 35a. The photoinitiated addition of HBr was repeated with a solution of 140.5 mg of the vinyl ketone 35a in 310 ml of pentane at 0° for 6.5 min. After the crude product (183.6 mg) had been chromatographed, the fractions were subjected to the above nmr analysis. From the fraction weights and nmr analysis, the yields were estimated to be 28% of bromo ketone 50a, 52% of bromo ketone 50b, 3% of the secondary bromide 52 and 3% of the dibrominated product.

The addition of HBr at room temperature to a solution of 1.00 g (3.9 mmol) of the unsaturated ketal 41 in 300 ml of

pentane yielded, after distillation, 1.1 g (84%) the crude bromo ketal <u>56</u>, bp 108-109° (0.3 mm),  $\underline{n}^{25}\underline{p}$  1.4972. The spectra of this product indicated the presence of 5-10% of the bromo ketone <u>50</u>; ir (CCl<sub>4</sub>), 1710 cm<sup>-1</sup> (weak, C=0 of ketone <u>50</u>); nmr (CCl<sub>4</sub>), 63.8-4.0 (4H, m, CH<sub>2</sub>-0), 3.1-3.6 (2H, m, CH<sub>2</sub>Br), 1.0-2.4 [14H, m, aliphatic CH including CH<sub>3</sub> singlets at 1.25 (major) and 1.17 (minor)], and two singlets at 0.82 and 0.86 (total 9H, <u>t</u>-Bu groups of two epimers); mass spectrum, m/e (rel. intensity), 319 (2), 317 (2), 109 (7), 87 (100), 57 (13), 43 (28), and 41 (9).

A solution of 300 mg of this crude bromo ketal <u>56</u> and 3 ml of aqueous 1 <u>M</u> HBr in 7 ml of THF was stirred at 25° for 1 hr and then subjected to the previously described<sup>1a</sup> isolation procedure. The crude bromo ketone <u>50</u> (0.25 g or 81%) was distilled to separate the pure bromo ketone <u>50</u> as a colorless liquid, bp 91-93° (0.01 mm),  $n^{25}$ <u>D</u> 1.4960, as a mixture of the two epimers.

PART B. THE CYCLIZATION OF METAL ENOLATES FROM  $\omega\text{-}BROMO$  KETONES

The most common synthetic routes to cyclohexane derivatives involve the reduction of benzene derivatives, use of the Diels-Alder reaction to form intermediate cyclohexenes, or use of the Robinson annelation technique (or related procedures) to form intermediate cyclohexenones. It seemed to us that another rather general synthetic route to cyclohexanone derivatives <u>1</u> (Scheme I) could be based on the cyclization of a regiospecifically generated<sup>20</sup> metal enolate <u>2</u> derived from an  $\omega$ -bromo ketone <u>3</u>. We have noted in Part A of this chapter that the requisite  $\omega$ -bromo ketones <u>3</u> can readily be obtained by

addition of HBr to the vinyl ketones 4 in a free radical chain process.<sup>1a</sup> Superficially the intramolecular C-alkylation reaction (arrows in structure 2) would appear to be straightforward. However, when one imposes the geometrical constraints that the nucleophile (the enolate  $\alpha$ -carbon atom) attack along a path colinear with the C-Br bond<sup>19</sup> and the electron density at the  $\alpha$ -carbon of the enolate is concentrated in orbitals perpendicular to the plane of the enolate anion, then the transition state required for this intramolecular C-alkylation is represented by structure 59 (Scheme VII). In this transition state, three of the carbon atoms lie in a plane perpendicular to the forming C-C bond. A study of molecular models indicates that this transition state 59 can be attained without excessive distortion of normal carbon bond angles when n has values of two or larger to form cyclic ketones 61 with six or more ring members. However, substantial distortion of normal carbon bond angles is required to attain the transition state 59 when n has values one or zero. In such cases an alternative transition state 60 in which the forming C-O bond lies in the plane of the enolate anion with a non-bonded electron pair on the oxygen atom serving as the nucleophile seems much more attractive. In short, these geometrical considerations suggest that these intramolecular alkylation reactions  $59 \rightarrow 61$  should be favorable (or at least feasible) when ketones with six or more ring members (61, n = 2,3,etc.) are being formed but should be unfavorable for the formation of four- and five-membered ketones  $(\underline{61}, n = 0, 1)$ .<sup>21</sup> In these latter cases either intramolecular 0-alkylation  $\underline{60} \rightarrow \underline{62}$ 







<u>61</u>





<u>62</u>

(H<sub>2</sub><sup>l</sup>)<sub>n</sub>

н<sub>2</sub>с

or intermolecular reactions might be expected.

Generation of Enolates and the Formation of 6-Membered Rings

To explore these considerations experimentally, we have examined the behavior of various metal enolates derived from the previously described<sup>1a</sup> bromo ketones. Scheme VIII summarizes our study of bromo ketones 44-46 and 49 that could be converted to 6-membered cyclic ketones. The bromo ketones 3 were converted to the intermediate terminal enolates 2 by the slow addition of the ketones to a slight excess of the strong, sterically hindered base, <u>i</u>-Pr<sub>2</sub>NLi, dissolved in a cold (-60 to 0°) mixture of  $Et_2^0$  and hexane (typically 9:1 v/v). This kinetically controlled deprotonation procedure is known<sup>20</sup> to convert methyl n-alkyl ketones to mixtures of lithium enolates in which the terminal enolate predominates (typically 85% of the enolate mixture) and the proportion of the terminal enolate is even larger (typically 95%) when branching is present at the  $\alpha$ -carbon atom of the alkyl group. The regiospecificity of this enolate generation procedure is illustrated by the conversion of the ketone 46 to its terminal enolate (and subsequently to the ketone 67) in spite of the fact that the internal enolate, stabilized by a phenyl substituent, is substantially more stable at equilibrium. Note that conversion of ketone 46 to its enolates under equilibrating conditions (KOBu-t in t-BuOH) yielded only products 68 and 69 derived from the more stable internal enolate.

Since <u>i</u>-Pr<sub>2</sub>NLi is a sufficiently strong base to deprotonate and cleave solvents such as  $\text{Et}_20$ , THF, and especially DME and HMP [(Me<sub>2</sub>N)<sub>3</sub>PO] at temperatures above 0°, it is not practical to prepare

# Scheme VIII

$$Br(CH_2)_3C(CH_3)_2COCH_3 \xrightarrow[]{1) \underline{i}-Pr_2NLi, Et_20, \\ \underline{hexane, -60^\circ to 0^\circ}}_{2) HMP, 0^\circ to 20^\circ} \xrightarrow[]{63} (55-68\%)$$

$$\xrightarrow[]{44} \\ \underbrace{44} \\ \underbrace{44} \\ \underbrace{63} (55-68\%) \\ \underline{63} (41\%)$$



Scheme VIII (cont.)







stock solutions of <u>i</u>-Pr<sub>2</sub>NLi in these solvents. However, we have found that if commercial solutions of <u>n</u>-BuLi in hexane are diluted with additional hexane or pentane and then treated with 1 mol equiv of <u>i</u>-Pr<sub>2</sub>NH, <u>stable solutions</u> of <u>i</u>-Pr<sub>2</sub>NLi (0.5-0.6 <u>M</u>) in hexane or hexane-pentane mixtures are formed. Provided that these hexane solutions are not cooled or concentrated to induce the irreversible separation of solid <u>i</u>-Pr<sub>2</sub>NLi, they may be standardized<sup>15</sup> (titration with 2,2'-bipyridyl indicator) and stored at 25° without deterioration for weeks. Thus, it is especially convenient to prepare solutions of <u>i</u>-Pr<sub>2</sub>NLi for reactions by adding a known volume of the stable hexane solution to the desired volume of a cold (<0°) ethereal solvent such as Et<sub>2</sub>0 or THF.

Utilizing the above procedures, we were able to generate 0.05 <u>M</u> solutions (dilute solutions were used to disfavor intermolecular reactions) of the lithium bromo enolates  $\underline{2}$  from each of the various bromo ketones studied. At 0° in Et<sub>2</sub>O-hexane solution these lithium bromo enolates (which are presumably aggregated as dimers, trimers, tetramers, <u>etc.</u>)<sup>21</sup> were stable to further change for at least an hour allowing us first to prepare solutions of the lithium bromo enolates  $\underline{2}$  and then to activate these bromo enolates for further reactions by adding ligands (Scheme IX) such as HMP (<u>71</u>, 4 mol equiv per Li<sup>+</sup>), DME (<u>72</u>, excess), triglyme (<u>73</u>, 1 mol equiv per Li<sup>+</sup>), or the 14-crown-4 ether (<u>74</u>, 1 mol equiv per Li<sup>+</sup>).<sup>22</sup> Among these activating ligands, stoichoimetric amounts of HMP appeared to be most effective with stoichiometric amounts of either triglyme <u>73</u> or the crown <u>74</u> affording slightly lower yields in the



$$[(CH_3)_2N]_3P = 0$$
  $H_3CO - CH_2CH_2 - OCH_3$   
 $71 72$ 



<u>73</u>


conversion of bromo ketone  $\underline{45}$  to ketone  $\underline{64}$ . In reactions where the polyethers  $\underline{73}$  or  $\underline{74}$  were used, the LiBr produced as the reaction proceeded formed  $\text{Et}_2^{0-\text{insoluble complexes with these polyethers}}$  facilitating its separation from the remaining reaction products.

Utilizing the above procedures to generate and activate the lithium bromo enolates 2, each of the acyclic bromo ketones 44, 19d45, or 46 could be converted to the corresponding 6-membered cyclic ketone 63, 64, or 67 in 60-70% by reaction at  $0-20^{\circ}$  for 1 hr. Even with bromo ketones 45 and 46 where two structurally isomeric enolates could be formed, by-products derived from the internal enolate (e.g., 68) were minor. In each of these cyclizations (44-46), the main by-product was a complex mixture of higher molecular weight compounds that was apparently derived from intermolecular reaction of the bromo enclate 2 either with itself or with the reaction product. When the bromo ketones 45 and 46 were converted to their enolates with KOBu-t in t-BuOH (conditions that allow enolate equilibration), the major products 65, 66, 68, and 69 were derived from the internal enolates and the typical preference for forming a 6-membered ring by O-alkylation (66 and 68) rather than a 4-membered ring by C-alkylation (65 and 69) was observed. When one considers the relative rates of ring closure of the enolates derived from KOBu-t and the malonates (C1)Br(CH<sub>2</sub>)<sub>n</sub>CH(CO<sub>2</sub>Et)<sub>2</sub>[3-ring > 5-ring > 6-ring > 4-ring]<sup>23</sup> where incorporation of the entire planar enolate system into the cyclic transition state (i.e., structure 59) is not required, the fact that we observe relatively little 6-ring C-alkylation with bromo ketones 45 and 46 under equilibrating conditions suggests that

the transition state 59 (n=2), although attainable, must still possess significant strain. The formation of appreciable quantities of by-product from intermolecular reaction, even at relatively low enolate concentrations, is also in keeping with this idea.

When we turned our attention to the cyclization of the bromo ketone 49, a compound in which the derived terminal enolate and the C-Br bond are held in positions favorable for attaining the transition state 59 (n=2), the yield of intramolecularly cyclized product 70 was significantly improved. We have observed this phenomenon with other cyclizations of bromo ketones to form bicyclic products.<sup>1c,24</sup> For example in the synthesis of 77 (Scheme X),<sup>24</sup> the application of a standard Robinson annulation technique to 4-t-butylcyclohexanone was clearly inappropriate<sup>25</sup> because equilibration during this process ultimately leads to the more stable decalone 79. However, the methodology described in Part A of this chapter converted enone 33 to bromo ketone epimers 50 in good yield, and each epimer was isolable by low pressure liquid chromatography. Kinetic deprotonation of each of the bromo ketones 50b and 50a with i-Pr2NLi (Scheme X) allowed us to obtain each terminal enolate 75 and 76 needed for cyclization to the epimeric decalones 77 and 78. Activation of the enolate 75, either by addition of 4 mol equiv of  $(Me_2N)_3PO$  (HMP) to an Et<sub>2</sub>O solution at 25°<sup>1b,24</sup> or by refluxing a THF solution, <sup>1c,24</sup> resulted in cyclization to form the desired decalone 77 in 76-86% yield. This product was clearly different from the previously described<sup>25</sup>









$$\frac{1) \underline{i} - \Pr_2 \text{NLi, THF}}{2) \text{ reflux}} \xrightarrow{77} (\text{major}) + \frac{78}{78} (\text{minor})$$

diastereoisomer 79. Cyclization of the epimeric enolate 76 in refluxing THF yielded mainly the same decalone 77 indicating that the cyclization was accompanied by epimerization of the starting bromo ketone 50a ( $\rightarrow$ 50b) and/or the initial product 78 ( $\rightarrow$ 77). However, when the cyclization was effected in Et<sub>2</sub>0 with 4 mol equiv. of HMP, the major product was the trans-fused decalone 78 accompanied by lesser amounts of the cis-fused epimer 77. Equilibration of these two decalone epimers with NaOMe in MeOH at 25° produced a mixture containing 6.5% of 78 and 93.5% of 77. Thus, it is clear that the bromo enolate 76 is capable of cyclization, presumably via the twist boat conformer 76b, to form the trans-fused decalone 78. If one considers the  $\Delta G$  values for an axial  $CH_3CO$ -group [1.17 kcal/mol, <sup>26</sup> a crude model for the enolate  $-C(OLi)=CH_2$ ] and an axial  $CH_3CH_2$ -group (1.75 kcal/mol,<sup>26</sup> a model for  $-CH_2CH_2Br$ ), the sum of these  $\Delta G$  values (2.9 kcal/mol) is sufficiently close to the energy difference between chair and twist-boat cyclohexane rings  $(ca. 4 \text{ kcal/mol})^{27}$  that appreciable concentrations of both conformers 76a and 76b would be expected. Thus, the successful cyclization  $50a \rightarrow 78$  is not an unreasonable result.

The foregoing results demonstrate that the projected cyclization  $3 \rightarrow 2 \rightarrow 1$  can be a viable synthetic route to 6-membered cyclic ketones although there is an indication of strain in the 6-membered transition state 59 (n=2) leading to products. One can then anticipate that adding other structural features that would be unfavorable to attaining this transition state 59 (n=2) would prevent formation of a cyclohexanone derivative. This idea is illustrated by the behavior of the bromo ketone <u>48</u> (Scheme XI). In an earlier study, <sup>28</sup> reaction





of this ketone 48 with KOBu-t (equilibrating conditions) in PhH was found to yield the O-alkylated product 83 that would be derived from the more stable enolate 81. We have now treated this bromo ketone 48 with  $\underline{i}$ -Pr<sub>2</sub>NLi under conditions that will clearly favor formation of the less stable, but kinetically favored, enolate 80.<sup>20</sup> After activation with HMP, this mixture of enolates 80 and 81 underwent a relatively slow reaction (accompanied by enolate equilibration) to form the same enol ether 83 observed earlier with only a very minor product corresponding to the cyclohexanone derivative 82. Although we found no indication of the presence of the isomeric enol ether 84, we cannot exclude the possibility that this substance was destroyed or isomerized during our isolation procedure. We attribute the failure of enolate 80 to form the cyclohexanone 82 to the geometrical problem illustrated in structure 85. Since the enolate 80 can at best only adopt a conformation with the bromoalkyl side chain on a pseudoaxial bond (bond a in structure 85) which is not perpendicular to the plane of the enolate, considerable distortion would be required to obtain the colinear arrangement C...C...Br needed in the transition state 59 for C-alkylation. By contrast, reaction of the related keto tosylate 87 with NaH in DME produced the bicyclic ketone 88 in good yield.<sup>28</sup> As indicated in structure 86, the enolate derived from ketone 87 can adopt a conformation with the tosyloxyalkyl side chain on a normal axial bond (bond a in structure 86) allowing the colinear arrangement needed for C-alkylation. Further support for this explanation is found in the successful C-alkylations performed with enolates similar to enolate 80, but possessing 4-carbon  $\omega$ -haloalkyl side chains.<sup>29</sup>

### The Formation of 5- and 4-Membered Rings

Application of the previously discussed procedure to the formation and activation of the enolate from the bromo ketone  $43^{19d}$ (Scheme XII) resulted in the formation of the enol ether 89 and a complex mixture of higher molecular weight products (presumably formed by intermolecular reactions). However, none of the C-alkylated product 90 was detected supporting the earlier hypothesis that it would be very difficult to attain the geometry required for the transition state 59 (n=1). Earlier examples of bromo carbonyl compounds that have reacted with bases to form enol ethers (0-alkylation) rather than 5-membered carbonyl compounds (C-alkylation) include the bromo ester  $91^{30}$  and bromo ketones  $92^{31}$  and  $93.^{32}$  Related phenomena include the reaction of the chloro ketone 94 with base to form only methyl cyclopropyl ketone and no cyclopentanone  $3^{33}$  and the cyclization of the bromo amide 95 to form an O-alkylated imino ether rather than an N-alkylated lactam. <sup>34</sup> All of these examples support the general idea that the synthetic sequence  $59 \rightarrow 61$  is unlikely to be a satisfactory route to cyclopentanone derivatives 61 (n=1). Conversion of the bromo ketone 14 (Scheme XIII) to its Li<sup>+</sup> enolate followed by activation with HMP resulted in a very slow reaction to form a mixture of comparable amounts of the enol ether 96 and the cyclobutanone 97 as well as a mixture of higher molecular weight materials. A similar mixture of O-alkylated and C-alkylated products was reported<sup>35</sup> from the reaction of the tosyloxy ketone 100 with NaH or KH in THF. Although the formation of O-alkylated products such as 96 by way of a transition state of the type  $\underline{60}$  (n=0) is reasonable, the formation of the cyclobutanone products (e.g., 97) by















<u>93</u>



### Scheme XIII













<u>103</u>







<u>105</u>, R = H, or metal cation



<u>97</u> + <u>98</u>

a normal  $S_n^2$  displacement (structure <u>59</u>, n=0) seems most improbable. A further indication that a different pathway may be involved in cyclobutanone formation is provided by earlier studies of the reactions of the related bromo (or tosyloxy) ketones <u>101</u>.<sup>36</sup> The reaction of this ketone with KOH or NaOH in a polar, partially aqueous solvent (H<sub>2</sub>O-dioxan, H<sub>2</sub>O-MeOH) produced a mixture of the "expected" cyclobutanone <u>102</u>, the rearranged cyclobutanone <u>103</u> (frequently the major product), and the acid <u>104</u> resulting from fragmentation. When we subjected the bromo ketone <u>14</u> to similar reaction conditions (KOH in refluxing H<sub>2</sub>O-DME), the major product was NaOAc from fragmentation (see structure <u>99</u>) accompanied by lesser amounts of the "expected" cyclobutanone <u>97</u> and the rearranged cyclobutanone <u>98</u>.

A possible interpretation of these results would involve the initial solvolytic rearrangement of the bromo enol (or enolate) <u>105</u> to the cyclopropanol derivative <u>106</u> (or the related cyclopropylcarbinyl cation, <u>cf.</u> Ref. 36d). This rearrangement <u>105</u>  $\div$  <u>106</u> is, of course, an example of the homoallyl  $\div$  cyclopropylcarbinyl rearrangement. Further base-catalyzed rearrangement of this intermediate (arrows in <u>106</u>) or conversion to the oxaspiropentane <u>107</u> followed by rearrangement would provide pathways to the cyclobutanones <u>97</u> and <u>98</u>. Since the oxaspiropentane <u>107</u> is known<sup>37</sup> to rearrange to a mixture of <u>97</u> (minor) and <u>98</u> (major) when treated with various Lewis acids including Li<sup>+</sup> salts, the fact that the rearranged cyclobutanone <u>98</u> was, at most, the minor product in our reaction indicates that the oxaspiropentane <u>107</u> is not an important intermediate in the reactions we have studied.

### The Formation of 7-Membered Rings

The usual reaction of the bromo ketone 47 (Scheme XIV) with i-Pr<sub>2</sub>NLi followed by activation of the resulting enolate with HMP resulted in a slow reaction (about 2 hr at 0° was required for complete reaction) to form a mixture of comparable amounts of the 7- and 5membered ring products 110 and 111. Authentic samples of these products were obtained by addition of Me<sub>2</sub>CuLi to the enones <u>112</u> and <u>25</u>. Conversion of the bromo ketone 47 to its enolates under equilibrating conditions (KOBu-t in t-BuOH or KH in DME) resulted in the formation of only the 5-membered ring C-alkylated product 111 accompanied by minor amounts of two by-products that may be the enol ethers 113 and 114. This result indicates that cyclization of the enolate 109 to 111 is more rapid than cyclization of enolate 108 to 110. The formation of comparable amounts of 5-membered (111) and 7-membered (110) C-alkylated products from cyclization of the kinetically generated mixture of Li<sup>+</sup> enolates 108 and 109 (mainly 108) is thus attributable to a combination of three factors: (1) kinetically controlled deprotonation of methyl n-alkyl ketones with the hindered base  $\underline{i}$ -Pr<sub>2</sub>NLi typically forms 80-85% of the terminal enolate (e.g., 108) accompanied by 15-20% of the internal enolate (e.g., 109);<sup>20</sup> (2) the reaction of internal enolates with alkyl halides is usually more rapid than the corresponding reaction with terminal enolates that are presumably more highly aggregated;  $^{20,21}$  and (3) intramolecular alkylation to form 5-membered rings is more rapid than the analogous reaction to form 7-membered rings.<sup>23</sup> This latter unfavorable rate factor is further enhanced in the present case because the cyclization  $108 \rightarrow 110$  requires the additional strain of



$$Br(CH_2)_{3}^{CH_3}CHCH_2COCH_3 \xrightarrow{\underline{i}-Pr_2NLi,} Br(CH_2)_{3}^{CH(CH_2)}CH(CH_3)CH_2^{-CH_2}CH_2$$

$$47 \qquad + 108 \qquad 0^{-Li} + 108 \qquad 0^{-Li} + Br(CH_2)_{3}^{-CH(CH_3)}CH - CH_3$$

$$Br(CH_2)_{3}^{-CH(CH_3)}CH - CH_3$$

$$109$$



+ <u>21</u> (-HBr, 3%)



Scheme XIV (cont.)



incorporating a planar enolate system into the cyclic transition state<sup>1b</sup> while the cyclization  $109 \rightarrow 111$  does not have this unfavorable requirement. The relatively slow rate of cyclization  $108 \rightarrow 110$  allowed sufficient time for competing enolate equilibration of 108 and 109 so that a significant amount of the unwanted cyclopentane by-product 111 was produced. By varying the temperature used for this cyclization from the usual range  $0-20^{\circ}$  to  $25^{\circ}$  we were able to shorten the time required for the cyclization from 2 hr to 1 hr and to increase the ratio of 7-membered to 5-membered product from 44:56 to 60:40. However, it appeared that the best way to increase substantially the proportion of 7-member cyclization product was to utilize systems with an alkyl substituent at the  $\alpha$ -carbon of the  $\omega$ -bromoalkyl methyl ketone (to diminish both the equilibrium concentration and the reactivity of the internal enolate)<sup>20</sup> and to use more rigid bromo ketone substrates analogous to 49 or 50 in order to increase the rate of the desired cyclization to a 7-membered ring product.<sup>1c</sup> The attachment of the two reacting functionalities to a preformed ring will favor the proximity of the two reacting centers and can be expected  $^{1b}$  to increase the rate of cyclization.

The desired bromo ketone <u>115</u> was obtained by photochemical hydrobromination of <u>26</u> in 88% yield (a mixture of stereoisomers). Conversion of the bromo ketone <u>115</u> to the enolates <u>116</u> and <u>117</u> under equilibrating conditions (<u>t</u>-BuOK in <u>t</u>-BuOH) resulted in a relatively rapid conversion to the methyl ketone <u>119</u> (86-94%, Scheme XIV) with none of the 7-membered cyclic product <u>118</u> being detected. This result is, of course, compatible with the idea that the intramolecular reaction to form a 5-membered ring is faster than cyclization to form a 7-membered ring.<sup>23</sup> The structure and stereochemistry of methyl ketone <u>119</u> were confirmed by its conversion to the known alcohol <u>120</u>.<sup>40</sup> As we had hoped, kinetic deprotonation of the bromo ketone <u>115</u> with <u>i</u>-Pr<sub>2</sub>NLi exhibited high regiospecificity to form the terminal enolate <u>116</u> and, after cyclization, the ketone <u>118</u>. By carrying out the cyclization in refluxing THF, the yields were 77-84% of the desired ketone <u>118</u> (a mixture of <u>cis</u> and <u>trans</u> isomers), 2% of the isomeric ketone <u>119</u> and 2% of the dehydrobromination product <u>26</u>. When the reaction solvent was either boiling THF or boiling DME, the addition of 4 mol equiv. of HMP to coordinate with the Li<sup>+</sup> cation was unnecessary.

Thus, The cyclization of terminal enolates from bromo ketones such as <u>115</u> constitute an efficient and useful route to perhydroazulene derivatives.<sup>1c,41</sup> Also, with appropriate substitution to disfavor formation of 5-membered ring products, the intramolecular alkylation reaction may be useful in preparing cycloheptanone derivatives 61 (n=3).

# Experimental Section<sup>11</sup>

### Preparation of i-Pr<sub>2</sub>NLi

After 22.8 ml of a hexane solution containing<sup>15b</sup> 34.2 mmol of <u>n</u>-BuLi (Foote Mineral Co.) had been diluted with 30 ml of anhydrous pentane, 4.15 g (41.5 mmol) of <u>i</u>-Pr<sub>2</sub>NH was added dropwise and with stirring during 45 min. Titration<sup>15b</sup> of the resulting colorless solution of <u>i</u>-Pr<sub>2</sub>NLi with a 2,2'-bipyridyl indicator indicated the concentration of the amide to be 0.53 <u>M</u>; at the end point of this titration the color of the solution changed from dark brown to pale yellow green. Such solutions of <u>i</u>-Pr<sub>2</sub>NLi in pentane-hexane mixtures were stable for weeks at 25° provided that they are not cooled or concentrated to induce the irreversible separation of solid <u>i</u>-Pr<sub>2</sub>NLi.

## Cyclization of Bromo Ketone 49 with i-Pr2NLi

To a cold (-60°) solution of 5.94 mmol of  $\underline{i}$ -Pr<sub>2</sub>NLi and several milligrams of 2,2'-bipyridy1 in 11.9 ml of a hexane-pentane mixture and 87.5 ml of Et<sub>2</sub>0 was added, dropwise and with stirring during 10 min, a solution of 1.318 g (5.66 mmol) of the bromo ketone <u>49</u> in 7.5 ml of  $Et_20$ . The resulting yellow-orange solution of the enolate (0.053 M) was warmed to 0°, treated with 4.25 g (23.7 mmol) of HMP, stirred at 0-3° for 20 min, and then allowed to warm to 22° during 20 min. After the resulting mixture had been partitioned between Et<sub>2</sub>O and aqueous NaHCO<sub>3</sub>, the organic layer was dried and concentrated to leave 1.257 g of yellow liquid (containing some HMP). After an aliquot of the crude product had been mixed with a known amount of 2-methylnaphthalene (an internal standard) glpc analysis (silicone XE-60 on Chromosorb P, apparatus calibrated with known mixtures) indicated the presence of 2-methylnaphthalene (retention time 15.0 min), decalone 70 (80% yield, 19.1 min, cis and trans isomers not resolved), and three minor unidentified impurities (5.2, 10.0, and 43.3 min). A 1.018-g aliquot of the crude product was chromatographed on silica gel with an EtOAc-hexane eluent to separate 586 mg (84%) of decalone 70;

distillation of this material gave 550 mg (79%) of decalone  $\underline{70}$ , bp 68-69° (1.0 mm),  $\underline{n}^{25}\underline{p}$  1.4844, that was identified with an authentic sample (an equilibrium mixture of <u>cis</u> and <u>trans</u> isomers) by comparison of glpc retention times and ir, nmr, and mass spectra. The later fractions from the liquid chromatographed contained 62 mg of a crude mixture of higher molecular weight products with ir absorption at 3400 and 1710 cm<sup>-1</sup>.

### Cyclization of Bromo Ketone 50b

In Et<sub>2</sub>O Solution. Following a previously described<sup>1b</sup> Α. procedure, a solution of 386 mg (1.33 mmol) of the bromo ketone 50b in 10 ml of Et<sub>2</sub>0 was added, dropwise and with stirring during 30 min, to a cold (-78°) solution of 1.40 mmol of  $\underline{i}$ -Pr<sub>2</sub>NLi and 2 mg of 2,2'-bipyridyl (an indicator) in 2.7 ml of a pentane-hexane mixture and 20.6 ml of  $Et_20$ . After the resulting soluiton of the enolate  $\underline{75}$  (0.04 M) had been warmed to 0°, 1.00 g (5.58 mmol, 4 mol equiv per Li<sup>+</sup>) of HMP was added and the solution was stirred at 0-2° for 20 min, allowed to warm to 23° during 20 min, and stirred at 23° for 40 min. The reaction mixture was partitioned between  $Et_20$  and aqueous NaHCO<sub>3</sub> and the organic phase was dried and concentrated to leave 317 mg of crude product as a yellow liquid. An aliquot of the crude product was mixed with a known weight of  $\underline{n}-C_{20}H_{42}$  (an internal standard) for glpc analyses (silicone XE-60 on Chromosorb P, apparatus calibrated with known mixtures); the crude product contained several minor unidentified impurities (ret. times 5.2, 6.9, 9.4, and 14.8 min),  $\underline{n}-C_{20}H_{42}$  (28.0 min), the trans-decalone 78 (34.6 min, 2.4% yield), and the cis-decalone 77 (41.5 min, 86% yield). A 275 mg aliquot of the crude product was

chromatographed on Woelm silica gel with an EtOAc-hexane eluent (8:92 v/v) to separate 8.5 mg (3.5%) of an early fraction containing (nmr) the unchanged bromo ketone <u>50b</u> accompanied by small amounts of ketones <u>77</u> and <u>78</u>. Later fractions contained 184 mg (76%) of ketone <u>77</u> that was identified with the subsequently described sample by comparison of ir and nmr spectra and glpc retention times and shown to differ from the previously described<sup>25</sup> decalone diastereoisomer <u>79</u> by comparison of ir spectra.

In THF Solution. To a cold (-70°) solution of 8.11 mmol Β. of  $\underline{i}$ -Pr<sub>2</sub>NLi and 4 mg of 2,2'-bipyridyl (an indicator) in 14.2 ml of a pentane-hexane mixture and 120 ml of THF was added, dropwise and with stirring during 45 min, a solution of 2.233 g (7.73 mmol) of the bromo ketone 50b in 25 ml of THF. The resulting orange solution of the enolate 75 (0.05 M) was warmed to  $-20^{\circ}$  during 10 min and then immersed in a preheated bath and refluxed for 45 min. After the reaction mixture had been subjected to the previously described isolation procedure, the crude product amounted to 1.60 g of red liquid. After an aliquot of the crude product had been mixed with  $\underline{n}-c_{20}H_{42}$ , glpc analysis indicated the presence of ketone 77 (78% yield) and ketone 78 (9% yield). Distillation of the crude product separated 1.29 g (80%) of a mixture of ketones 77 (90% of mixture) and 78 (10% of mixture), bp 115-117° (0.35 mm),  $\underline{n}^{25}\underline{p}$  1.4865-1.4868, and left 0.22 g of a brown higher molecular weight residue. A 1.11-g aliquot of the distillate was chromatographed on Woelm silica gel to separate 83 mg (6%) of the transdecalone 78 and 884 mg (64%) of the cis-decalone 77. These latter fractions were distilled to separate 820 mg of the pure cis-decalone 77

as a colorless liquid, bp  $81-82^{\circ}$  (0.08 mm),  $n^{25} p 1.4859$ ; ir (CCl<sub>4</sub>), 1709 cm<sup>-1</sup> (C=0); uv max (95% EtOH), 299 nm ( $\varepsilon$  18); <sup>1</sup>H nmr (CCl<sub>4</sub>),  $\delta 0.9-2.4$  (15H, m, aliphatic CH) and 0.86 (9H, s, <u>t</u>-Bu); <sup>13</sup>C nmr (CDCl<sub>3</sub>),  $\delta$ , (multiplicity in off-resonance decoupled spectrum), 214.5 (s), 53.1 (d), 41.2 (d), 37.5 (d and t, 2 C atoms), 32.0 (s), 31.4 (t), 27.2 (q, 3 C atoms), 26.8 (t), 25.8 (t), 25.7 (t), and 25.2 (t); mass spectrum, m/e (rel. intensity), 208 (M<sup>+</sup>, 13), 151 (22), 133 (30), 112 (22), 110 (34), 97 (98), 91 (32), 84 (28), 67 (34), 57 (100), 55 (25), and 41 (64).

<u>Anal</u>. Calcd for C<sub>14</sub>H<sub>24</sub>O: C, 80.71; H, 11.61. Found: C, 80.76; H, 11.64.

A collected (glpc) sample of the <u>trans</u>-decalone <u>78</u> was distilled in a short-path still to separate the ketone <u>78</u> as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4853; ir (CCl<sub>4</sub>), 1710 cm<sup>-1</sup> (C=O, spectrum clearly different from the ir spectra of decalones <u>77</u> and <u>79</u>); nmr (CCl<sub>4</sub>),  $\delta$ 1.0-2.4 (15H, m, aliphatic CH) and 0.90 [9H, s, <u>t</u>-Bu (this signal is at 0.04 ppm lower field than the <u>t</u>-Bu signal at 0.86 for the <u>cis</u>-decalone <u>77</u>)]; mass spectrum, m/e (rel. intensity), 208 (M<sup>+</sup>, 12), 152 (24), 123 (20), 110 (35), 97 (21), 67 (22), 57 (100), 55 (24), 44 (24), and 41 (64).

<u>Anal</u>. Calcd for C<sub>14</sub>H<sub>24</sub>O: C, 80.71; H, 11.61. Found: C, 80.89; H, 11.73.

In a larger scale preparation, 6.22 g (29.9 mmol) of a mixture of vinyl ketone epimers 35 (isolated by liquid chromatography) was subjected to light-catalyzed hydrobromination at 0° to yield, after column chromatography, 7.05 g (24.4 mmoles, 82%) of a mixture of epimeric bromo ketones <u>50a</u> and <u>50b</u>. After a solution of this mixture in 30 ml of THF had been added to a cold (-78°) mixture of 400 ml of THF and 52.2 ml of a hexane-pentane solution containing 25.6 mmol of  $(\underline{i}-Pr)_2NLi$ , the resulting solution was refluxed for 75 min and then subjected to the usual isolation procedure. Chromatography of the crude product on silica gel separated 4.13 g (82% based on the bromo ketones <u>50</u> or 66% overall) of a mixture of decalones <u>77</u> and <u>78</u>. Cyclization of the Bromo Ketone 50a

In Et<sub>2</sub>O Solution. A solution of the enolate 76 (0.05 M)Α. was prepared by the slow (40 min) addition of a solution of 475 mg (1.64 mmol) of the bromo ketone 50a in 4 ml of  $Et_20$  to a cold (-70°) solution of 1.73 mmol of i-Pr<sub>2</sub>NLi and 2-3 mg of 2,2'-bipyridyl in 3.2 ml of a pentane-hexane mixture and 25 ml of  $Et_20$ . After the orange enolate solution had been warmed to 0°, 1.24 g (6.92 mmol, 4 mol equiv per Li<sup>+</sup>) of HMP was added and the mixture was stirred at  $0-2^{\circ}$  for 20 min, at 2-22° for 20 min, and at reflux (33°) for 20 min. After the reaction mixture had been partitioned between aqueous  $NaHCO_3$  and  $Et_2O$ , the organic phase was dried, concentrated, taken up in pentane, washed with several portions of aqueous NaCl (to remove residual HMP), and again dried and concentrated. The residual red liquid (328 mg) contained (ir and nmr analysis) a mixture of the starting bromo ketone 50a (no 50b was detected), and the epimeric decalones 77 and 78. Analysis by glpc (silicone XE-60 on Chromosorb P) indicated the presence of several relatively rapidly eluted components (ret. times 6.5, 9.9, and 16.3 min) believed to be various enol ether isomers from decomposition

of the bromo ketone <u>50a</u> in the glpc apparatus, the <u>trans</u>-decalone <u>78</u> (33.4 min, 17% of the decalone product), and <u>cis</u>-decalone <u>77</u> (38.0 min, 83% of the decalone product). From a second comparable reaction (reaction time 20 min at 0-2°, 20 min at 0-25°, and 40 min at 25°) where an aliquot of the crude product was mixed with a weighed amount of  $\underline{n}-\underline{c_{20}H_{42}}$ , the calculated yield (glpc) was 44% of <u>cis</u>-decalone <u>77</u> and 12% of trans-decalone 78.

A 205 mg aliquot of the crude product was chromatographed on Woelm silica gel with an  $Et_2O$ -hexane eluent (1:9 v/v) to separate 92 mg (45%) of early fractions containing (nmr analysis) the bromo ketone 50a (ca. 58% of the mixture) and trans-decalone 78 (ca. 42% of the mixture) and 22 mg (11%) of later fractions containing (nmr analysis) the bromo ketone 50b (ca. 10% of the mixture) and the cis-decalone 77 (ca. 90% of the mixture). In addition 48 mg of fractions containing various minor unidentified components and 33 mg (ca. 16%) of slowly eluted fractions containing higher molecular weight materials (presumably from intermolecular alkylation) were isolated. Based on fraction weights and nmr analysis, the calculated yields were 26% recovery of bromo ketone 50a. 1% of bromo ketone 50b, 19% of transdecalone 78, and 10% of cis-decalone 77. Collected (glpc) samples of the cis-decalone 77 and the trans-decalone 78 were identified with previously described samples by comparison of ir spectra and glpc retention times.

B. In THF solution. A solution of the enolate  $\underline{76}$  (0.05 M) was obtained by the slow (15 min) addition of a solution of 310 mg (1.07 mmol) of the bromo ketone 50a in 2.0 ml of THF to a cold (-60°)

solution of 1.13 mmol of <u>i</u>-Pr<sub>2</sub>NLi and 2 mg of 2,2'-bipyridyl in 2.1 ml of a pentane-hexane mixture and 16.8 ml of THF. The resulting yellow solution was stirred at -60° for 5 min and then immersed in a preheated bath and refluxed for 2 hr. After the reaction mixture had been partitioned between Et<sub>2</sub>O and aqueous NaHCO<sub>3</sub>, the organic layer was dried and concentrated to leave 182 mg of crude red liquid product. A 175 mg aliquot was chromatographed on Woelm silica gel with an Et<sub>2</sub>O-hexane eluent (9:91 v/v) to separate 4 mg of unidentified rapidly eluted material followed by 35 mg (16% yield) of the <u>trans</u>decalone <u>78</u>, 95 mg (44% yield) of the c<u>is</u>-decalone <u>77</u>, and 47 mg (<u>ca</u>. 17% yield) of a mixture of higher molecular materials. Collected (glpc) samples of the decalones <u>77</u> and <u>78</u> were identified with previously described samples by comparison of ir spectra and glpc retention time. Equilibration of Decalones 77 and 78

A solution of 31.2 mg (0.15 mmol) of the <u>trans</u>-decalone <u>78</u>, 15.4 mg of <u>n</u>-C<sub>19</sub>H<sub>40</sub>, and 0.03 mmol of NaOMe in 1.5 ml of MeOH and 1.5 ml of Et<sub>2</sub>O was maintained at 25.0°. Aliquots (0.3 ml) were removed, diluted with 0.3 ml of Et<sub>2</sub>O, and partitioned between hexane and an aqueous buffer (pH 7) at the following time intervals: 0.5, 8, 10, 13, and 31 hr. The hexane phases were concentrated and analyzed by glpc (silicone XE-60 on Chromosorb P, apparatus calibrated with known mixtures); the retention times of the components were: <u>n</u>-C<sub>19</sub>H<sub>40</sub>, 16.0 min; <u>trans</u>-decalone <u>78</u>, 31.1 min; <u>cis</u>-decalone <u>77</u>, 36.3 min. The recovery of ketones <u>77</u> and <u>78</u> in the various aliquots ranged from 96-100% and the composition of the mixture became constant after 10 hr at 6.5% of <u>trans</u>-ketone <u>78</u> and 93.5% of <u>cis</u>-ketone <u>77</u>. Comparable mixtures of  $\underline{77}$  and  $\underline{78}$  were obtained when the <u>cis</u>-ketone  $\underline{77}$  was subjected to the same equilibrating conditions.

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- 11. All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated MgSO4 was employed as a drying agent. The ir spectra were determined with a Perkin Elmer, Model 257, infrared recording spectrophotometer fitted with a grating. The uv spectra were determined with a Cary, Model 14, or a Perkin Elmer, Model 202, recording spectrophotometer. The 60 MHz proton nmr spectra were determined with a Varian, Model A-60 or Model T-60-A, nmr spectrometer and the 100 MHz proton and 13C nmr spectra (25 MHz) were determined with a JEOL Fourier transform spectrometer Model PFT-100. The chemical shift values are expressed in  $\delta$  values (ppm) relative to a Me<sub>4</sub>Si internal standard. The mass spectra were obtained with an Hitachi (Perkin Elmer), Model RMU-7, or a Varian, Model M-66, mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.
- 12. A procedure for the preparation and use of  $(vinyl)_2$ CuLi was described previously in Ref. 3h. The preparation of this same cuprate reagent from (n-Bu<sub>3</sub>P-CuI)<sub>4</sub> and its addition to ketone 28 has been described in Ref. 3a. The vinylmagnesium bromide solution was prepared by adding 72 ml (107 g, 1.0 mole,  $\rho_4^{20}$  = 1.49) twice distilled vinyl bromide in 300 ml THF to 25.5 g Mg turnings (1.05 moles) in 300 ml THF containing 0.1 cc BrCH<sub>2</sub>CH<sub>2</sub>Br as an initiator. The solution was allowed to stand overnight, decanted via cannula, and titrated by the method of Watson and Eastham (ref. 15 below). This preparation gave yields of 80-85% based on the Mg used, and such solutions were stable at room temperature for extended periods of time.
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### CHAPTER III

ALKYLATION STUDIES OF THE  $\Delta^{1,9}$ -ENOLATE OF ANTI-6-t-BUTYL-CIS AND TRANS-1-DECALONE

### Discussion

The alkylation of the 1-decalone enolates  $\underline{2}$  (Scheme I) to form predominately the <u>cis</u>-fused monoalkylated products  $\underline{3}^1$  conformed to the ideas that the alkylation stereochemistry could be explained by invoking transition states  $\underline{5}$  and/or  $\underline{6}$  with reactant-like geometries and that the preferred direction for alkylation normally introduces the alkyl substituent equatorial to the saturated cyclohexane ring (see structure  $\underline{7}$ ). It was of interest to examine the alkylation of a 1-decalone enolate whose geometry was distorted from that normally found (<u>i.e.</u>, <u>5</u> or <u>6</u>) to learn what factor seemed best to account for the alkylation stereochemistry. For that purpose, we have synthesized the 1-decalone derivatives <u>8</u> and  $\underline{9}^2$  and report here the result of reaction of the corresponding lithium enolate 10 with methyl iodide.

A suitable precursor <u>11</u> (Scheme II) for the enolate <u>10</u> could be obtained by enol acetylation of ketone  $\underline{8}^2$  followed by separation of the enol acetates <u>11</u> and <u>12</u> by low-pressure liquid chromatography. However, as found in an earlier study,<sup>1</sup> methylation of the lithium enolate <u>10</u> (accompanied by an equivalent of <u>t</u>-BuOLi) formed from the enol acetate <u>11</u> and MeLi was accompanied by the formation of di- and trimethylated products that complicated the separation and analysis of









Scheme I (cont.)

,R .0 alkylation



\_ \_

95

<u>7</u>













the reaction products. To diminish the amount of polyalkylation we chose to use the enol silyl ether <u>14</u> as a precursor for the enolate <u>10</u> in order to avoid the presence of excess base (<u>t</u>-BuOLi) in the reaction mixture.<sup>3</sup> Although the direct reaction of the ketone <u>8</u> with Me<sub>3</sub>SiCl and Et<sub>3</sub>N<sup>36</sup> formed only the unwanted silyl enol ether <u>13</u>, the indirect method involving generation of the enolate <u>10</u> from the enol acetate <u>11</u> and subsequent quenching of the enolate <u>10</u> with Me<sub>3</sub>SiCl, <sup>3,4</sup> afforded the desired silyl enol ether 14.

Reaction of the enolate 10, generated from the silyl enol ether 14, with MeI for a short period of time (40-60 sec) afforded mixtures containing small amounts of the recovered unalkylated ketones 8 and 9 and two dialkylated products tentatively assigned structures 15 and 16. The major product was the monomethylated ketone 17 isolated as a liquid that appeared to be homogeneous by all the usual criteria. Wolff-Kishner reduction converted this ketone 17 to a hydrocarbon 19 that differed in spectral properties from the previously prepared steroeisomeric hydrocarbons 22 (from ketone 4b),<sup>1</sup> 20 (from ketone 23), 5 and 21 (from ketone 24). However, the <sup>1</sup>H nmr spectrum of our hydrocarbon product indicated the presence of a minor impurity (not separated by glpc) that may be the isomeric hydrocarbon 20 derivable from ketone 18 on Wolff-Kishner reduction. If this is the case then the monomethylated product, cis-ketone 17 obtained from the enolate 10, could contain as much as 13% of the isomeric transketone 18 that we were unable to separate.

To remove any question about the structure and stereochemistry of the major alkylated product, the ketone 17 was converted to its

crystalline oxime derivative  $\underline{25}$  (Scheme III), whose structure was determined by a single crystal x-ray diffraction study<sup>6</sup> to be that shown in Figure 1. The bond lengths and bond angles obtained from the structural determination are listed in Tables 3 and 4. A tabulation of other calculated and observed structure factors may be found in the experimental section.

We have been as yet unable to obtain such structure data on a suitable enol derivative 26, either because the derivatives were oils (26, R = -COPh, -COp-tolyl), or did not yield crystals suitable for x-ray analysis (<u>26</u>, R = -COpBrPh,  $-COp-O_2NPh$ ). Therefore, we have employed the MMI energy minimization scheme developed by Allinger and co-workers<sup>7</sup> to adequately approximate the solution conformation of enolate 10 from molecular model coordinates. A comparison of calculated steric energy differences with experimentally determined AG values from equilibration experiments showed good agreement in the two cases examined. The calculated steric energies for compounds 27 (24.00 kcal/mole) and 28 (25.24 kcal/mole) differed by  $\Delta G = 1.24$  kcal/mole. The experimentally determined<sup>8</sup> Keq (28  $\implies$  27) = 8.01 implied  $\Delta G$  = 1.23 kcal/mole. In the decalone series, compounds 8 and 9 had an experimentally determined Keq = 14.4, implying a  $\Delta G$  = 1.58 kcal/mole. The calculated energy difference between 8 (18.44 kcal/mole) and 9 (20.33 kcal/mole) was 1.89 kcal/mole. Thus, the calculated  $\Delta G$  values compare fairly well with  $\Delta G$  values determined in solution.

As an approximation to the geometry of enolate 10 which was also compatible with the limitations on functional groups involved in
Scheme III







0

H

H

28

<u>t</u>-Bu

Н

















Figure 1. A Perspective View of the Molecular Structure of Oxime 25

| Atoms    | Distance, A<br>(10 <sup>3</sup> · standard<br>deviation) | Atoms     | Distance, Å<br>(10 <sup>3</sup> · standard<br>deviation) |
|----------|--|-----------|--|
| Н – О    | 1.037 (2)  | C7 - C8   | 1.524 (5)  |
| 0 – N    | 1.416 (4)  | C8 - C9   | 1.538 (5)  |
| N - Cl   | 1.277 (4)  | C9 - C1   | 1.523 (5)  |
| C1 - C2  | 1.501 (5)  | C9 - C10  | 1.553 (5)  |
| C2 - C3  | 1.528 (5)  | C9 - C11  | 1.534 (5)  |
| C3 - C4  | 1.512 (5)  | C6 - C12  | 1.555 (5)  |
| C4 - C10 | 1.523 (5)  | C12 - C13 | 1.533 (6)  |
| C10 - C5 | 1.534 (5)  | C12 - C14 | 1.529 (6)  |
| C5 - C6  | 1.531 (5)  | C12 - C15 | 1.530 (6)  |
| C6 - C7  | 1.524 (5)  |           |  |

Table 3. Bond Lengths of the Oxime 25

| Atoms        | Angle,<br>(standard dev | °<br>iation) | Atoms          | Angle,<br>(standard dev | °<br>viation) |
|--------------|-------------------------|--------------|----------------|-------------------------|---------------|
| H - O - N    | 107.9                   | (.2)         | C1 - C9 - C10  | 110.6                   | (.3)          |
| 0 - N - C1   | 113.9                   | (.3)         | C1 - C9 - C11  | 109.4                   | (.3)          |
| N - C1 - C2  | 123.5                   | (.4)         | C8 - C9 - C10  | 109.6                   | (.3)          |
| N - C1 - C9  | 117.0                   | (.3)         | C8 - C9 - C11  | 110.5                   | (.3)          |
| C2 - C1 - C9 | 119.5                   | (.3)         | C10 - C9 - C11 | 109.0                   | (.3)          |
| C1 - C2 - C3 | 110.6                   | (.3)         | C4 - C10 - C5  | 111.6                   | (.3)          |
| C2 - C3 - C4 | 110.8                   | (.3)         | C4 - C10 - C9  | 113.0                   | (.3)          |
| C3 - C4 - C1 | 0 113.1                 | (.3)         | C5 - C10 - C9  | 111.5                   | (.3)          |
| C6 - C5 - C1 | 0 114.4                 | (.3)         | C6 - C12 - C13 | 109.7                   | (.3)          |
| C5 - C6 - C7 | 108.9                   | (.3)         | C6 - C12 - C14 | 1 <b>11.</b> 7          | (.3)          |
| C5 - C6 - C1 | 2 113.8                 | (.3)         | C6 - C12 - C15 | 109.3                   | (.3)          |
| C7 - C6 - C1 | 2 114.5                 | (.3)         | C13 - C12 - C1 | 5 107.4                 | (.4)          |
| C6 - C7 - C8 | 112.2                   | (.3)         | C14 - C12 - C1 | 5 109.4                 | (.4)          |
| C7 - C8 - C9 | 113.2                   | (.3)         | C12 - C13 - C1 | 4 109.3                 | (.4)          |
| C1 ~ C9 ~ C8 | 107.8                   | (.3)         |                |                         |               |

Table 4. Bond Angles of the Oxime 25

the minimization scheme, we utilized the olefin  $\underline{29}$ . This olefin maintained the geometrical constraints present in the ring system of enolate <u>10</u>, and appeared from molecular models to have two favored conformations. The first conformation had the cyclohexane ring bearing the <u>t</u>-butyl group in a twist-boat with the cyclohexene ring in a half-chair; the second had the cyclohexane ring in a halfchair, and the cyclohexene ring in a half-boat. The conformers were minimized by MMI calculations to the geometries shown in Figures 2 and 3, respectively.<sup>9</sup> The final steric energy calculated for the conformation in Figure 2 was 22.07 kcal/mole, and was 30.73 kcal/mole for that in Figure 3. In light of the previously noted agreement of calculated energy differences with relative energies in solution, it appears likely that the conformation in Figure 2 better represents the solution geometry of enolate 10.

It is noteworthy that alkylation of enolate <u>10</u> with  $CH_3I$  led to introduction of the methyl group <u>axial</u> to the saturated cyclohexane ring in <u>17</u>, in contrast to the predominant equatorial alkylation found in enolate geometries such as <u>5</u> and <u>6</u>. The bridgehead olefinic C atom in Figure 2 showed no out-of-plane deformation in its calculated bond angles, thus indicating little, if any, puckering at the enolate  $\alpha$ -C atom. In accordance with the reactant-like transition states previously demonstrated<sup>1,10</sup> in other alkylations, the reaction stereochemistry seems best explained by two factors. First, the steric hindrance to approach by the alkylating agent appears less severe along the reaction coordinate leading to <u>cis</u>-fused product <u>17</u> than that leading to trans-fused ketone <u>18</u>. In addition, the initial



Figure 2. A MMI Energy-Minimized Conformation of Olefin 29 ( $E_{steric} = 22.07 \text{ kcal mole}^{-1}$ )



Figure 3. A MMI Energy-Minimized Conformation of Olefin 29 ( $E_{steric} = 30.73 \text{ kcal mole}^{-1}$ )



Figure 4. A MMI Energy-Minimized Conformation of Ketone 17





deformation of the enolate  $\alpha$ -C atom toward its final sp<sup>3</sup> geometry is less constrained in the direction leading to cis-fused product.

Analysis of the dihedral angles<sup>11b</sup> for the conformer in Figure 2 shows that C-7 and C-10 are essentially isoclinal positions. Thus the <u>t</u>-Bu group at C-6 occupies a  $\psi_e$  position, and by the inherent C<sub>2V</sub> type symmetry in twist forms of cyclohexane,<sup>11</sup> the initial approach of the CH<sub>3</sub>I to C-9 which leads to <u>cis</u>-fused product is a <u>pseudoequatorial</u> attack in a reactant-like transition state. Conformational inversion then leads to the 9-Me axial substituent in the resultant chair form of the final product 17.

# Experimental Section<sup>12</sup>

# Preparation of the Enol Acetates 11 and 12

A solution of 6.54 g (31.4 mmol) of the ketone <u>8</u> and 17.1 g (167 mmol) of  $Ac_2^0$  in 94 ml CCl<sub>4</sub> was treated with 0.5 ml of aqueous 70% HClO<sub>4</sub> and the resulting mixture was allowed to stand at 25° for 20 min. After the reaction mixture had been neutralized with aqueous NaHCO<sub>3</sub>, it was partitioned between aqueous NaHCO<sub>3</sub> and an  $Et_2^0$ -hexane mixture. The organic layer was dried, concentrated, and distilled in a short-path still [bp 97°-115° (0.1 mm)] to separate 6.99 g (89%) of a mixture of enol acetates <u>11</u> and <u>12</u> as a pale yellow liquid. This material contained (glpc, silicone XE-60 on Chromosorb P, apparatus calibrated with known mixtures) 50% of the enol acetate <u>12</u> (ret. time 51.8 min), and 50% of the starting ketone <u>8</u> (44.2 min). This product was subjected to preparative low-pressure liquid

chromatography on silica gel<sup>13</sup> with an EtOAc-hexane eluent (4:96 v/v). Certain of the later chromatographic fractions that were enriched in the unwanted enol acetate isomer 12 were resubjected to the original enol acetylation conditions  $^2$  to reequilibrate the enol acetates <u>11</u> and 12 to a 1:1 mixture. These mixtures were then rechromatographed. In this way the mixture was separated into early fractions containing 2.80 g (36% yield) of the enol acetate 11 (> 98%, glpc analysis) as a colorless liquid,  $\underline{n}^{25}\underline{\underline{D}}$  1.4855; ir (CCl<sub>4</sub>), 1752 (enol ester C=0) and 1704 cm<sup>-1</sup> (weak, C=C); nmr (CC1<sub>Δ</sub>), δ1.0-2.4 (17H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.03) and 0.84 (9H, s, <u>t</u>-Bu); mass spectrum, m/e (rel. intensity), 250 (M<sup>+</sup>, 5), 208 (100), 151 (75), 149 (20), 133 (37), 123 (72), 110(51), 91 (23), 57 (50), 55 (24), 43 (44), and 41 (39);  ${}^{13}$ C-nmr (CDCl<sub>3</sub>, multiplicity on off-resonance decoupling), 167.6 (s), 140.3 (s), 125.0 (s), 42.6 (d), 32.9 (s), 32.0 (d), 30.6 (t), 29.5 (t), 27.0 (q and t, four C atoms), 23.8 (t), 21.7 (t), 21.4 (t), and 20.6 (q) ppm.

<u>Anal</u>. Calcd. for C<sub>16</sub>H<sub>26</sub>O<sub>2</sub>: C, 76.75; H, 10.47; mol wt, 250.1933. Found: C, 77.02; H, 10.72; mol wt, 250.1917.

Later chromatographic fractions contained 2.20 g (28%) of the enol acetate <u>12</u> as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4837; ir (CC1<sub>4</sub>), 1758 (enol ester C=O) and 1690 cm<sup>-1</sup> (C=C); nmr (CC1<sub>4</sub>),  $\delta$ 5.1-5.3 (1H, m, vinyl CH), 1.0-2.5 (16H, m, aliphatic CH including a CH<sub>3</sub>CO singlet at 2.03), and 0.83 (9H, s, <u>t</u>-Bu); mass spectrum, m/e (rel. intensity), 250 (M<sup>+</sup>, 6) 208 (96), 190 (26), 175 (20), 152 (29), 151 (83), 150 (27), 149 (26), 134 (64), 133 (100), 132 (22), 123 (24), 112 (24), 110 (29), 97 (90), 91 (61), 84 (53), 81 (23), 67 (36), 57 (85), 55 (40), 43 (72), and 41 (54); <sup>13</sup>C-nmr (CDCl<sub>3</sub>, multiplicity on off-resonance decoupling), 168.2 (s), 151.6 (s), 112.5 (d), 41.9 (d), 38.4 (d), 34.2 (d), 32.5 (t), 32.0 (s), 27.7 (t), 27.2 (q, 3 C atoms), 26.8 (t), 24.1 (t), 23.1 (t), and 20.8 (q) ppm.

<u>Anal</u>. Calcd for C<sub>16</sub>H<sub>26</sub>O<sub>2</sub>: C, 76.75; H, 10.47; mol wt, 250.1933. Found: C, 77.06; H, 10.70; mol wt, 250.1897.

Subsequent fractions from the chromatography contained 315 mg (4%) of the starting ketone 8. In order to establish the presence of the cis-ring fusion in the enol acetate 12, a solution of 39.6 (0.16 mmol) of the enol acetate 12 and 0.9 ml of aqueous 1 M HCl in 2.4 ml of THF was stirred at 25° for 72 hr. Aliquots of the solution were removed periodically and partitioned between Et<sub>2</sub>0 and aqueous NaHCO3. Each organic layer was mixed with a known weight of  $\underline{n}-C_{19}H_{40}$  (an internal standard) for glpc analysis (silicone XE-60 on Chromosorb P, apparatus calibrated with known mixtures). The retention times for the various components were:  $\underline{n}-C_{19}H_{40}$ , 22.9 min; enol acetate 11 and trans-fused ketone 9, 37.9 min (not resolved); cis-fused ketone 8, 47.8 min; enol acetate 12, 55.2 min. As the hydrolysis proceeded the enol acetate 12 was slowly converted to the cis-ketone 1 accompanied by little if any (4% or less) of the transketone 9 and the enol acetate 11. After 72 hr approximately 60% of the enol acetate 12 had been converted to the cis-ketone 8. Collected (glpc) samples of these two products were identified with authentic samples by comparison of ir spectra and glpc retention times.

# Preparation of the Silyl Enol Ether 13

Following a previously described general procedure, <sup>14</sup> a solution of 500 mg (2.4 mmol) of the ketone  $\underline{8}$ , <sup>2</sup> 485 mg (4.8 mmol) of  $Et_3N$ , and 500 mg (4.6 mmol) of  $Me_3SiCl$  in 1 ml of DMF [distilled, dried over No. 4A Molecular Sieves, and redistilled, bp 43° (6 mm)] was refluxed for 48 hr. The resulting solution was partitioned between a cold (0°) mixture of hexane and aqueous NaHCO3. The organic layer was dried, concentrated, and distilled in a short-path still at 0.55 mm to separate 515 mg (77%) of the crude enol ether 13,  $\underline{n}^{25}\underline{D}$  1.4737, containing (glpc, Carbowax 20M on Chromosorb P) the enol ether 13 (ret. time 21.5 min) and three minor unidentified impurities (11.3, 12.2, and 18.4 min). Under the conditions of this glpc analysis, the retention time of the starting ketone 8 was 56.1 min. The product was chromatographed on silica gel with an EtOAc-hexane eluent (1:39 v/v) to separate the enol ether 13. Distillation in a short-path still at 0.2 mm afforded the pure enol ether 13 as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4738, with ir absorption (CCl<sub>4</sub>) at 1662 cm<sup>-1</sup> (C=C) and lacking ir absorption at 1679  $\rm cm^{-1}$  characteristic of the isomeric enol ether  $\underline{14}$ ; nmr (CC1<sub>4</sub>),  $\delta 4.5-4.8$  (1H, m, vinyl CH), 0.8-2.3 (22H, aliphatic CH including a t-Bu singlet at 0.84), and 0.14 (9H, s,  $Me_3SiO$ ); mass spectrum, m/e (rel. intensity), 280 (M<sup>+</sup>, 23), 223 (21), 175 (30), 169 (40), 156 (81), 134 (20), 133 (78), 129 (20), 91 (38), 75 (54), 73 (100), 57 (49), and 41 (30).

<u>Anal</u>. Calcd for C<sub>17</sub>H<sub>32</sub>OSi: C, 72.77; H, 11.52; mol. wt, 280.222. Found: C, 72.75; H, 11.52; mol. wt., 280.218.

## Preparation of the Silyl Enol Ether 14

A solution of 13.9 mmol of MeLi (halide-free) and 1 mg of 2,2'-bipyridyl (an indicator) in 11.9 ml of  $Et_2^0$  was concentrated to dryness under reduced pressure 15 and then 12 ml of anhydrous DME was added. The resulting solution was cooled to 0° and then a solution of 1.50 g (6.0 mmol) of the enol acetate 11 in 3.0 ml of DME was added, dropwise and with stirring during 10 min. After the resulting red (excess MeLi) solution had been warmed to 25°, it was quenched by the rapid addition of 7.4 ml of a solution prepared by mixing 3.0 ml of Me<sub>3</sub>SiCl (freshly distilled from a mixture with quinoline, bp 57°), 7.5 ml of DME, and 0.75 ml of Et<sub>2</sub>N (freshly distilled from LiAlH,) and then centrifuging the mixture to separate the solid  $Et_3NH^+Cl^-$ . The reaction mixture, from which a white precipitate becan to separate after 20 sec, was stirred at 25° for 30 min and then partitioned between pentane and saturated aqueous NaHCO3 containing excess solid NaHCO3. The organic solution was dried and concentrated, and the residual yellow liquid was chromatographed on silica gel with an EtOAc-hexane eluent (2.5:97.5 v/v) to separate 1.56 g (93%) of the pure silyl ether 14 as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4765; ir (CCl<sub>4</sub>), 1679 cm<sup>-1</sup> (C=C); nmr (CCl<sub>4</sub>), δ0.7-2.4 (23H, m, aliphatic CH including a t-Bu singlet at 0.83) and 0.13 (9H, s, Me<sub>3</sub>SiO); mass spectrum, m/e (rel. intensity), 280 (M<sup>+</sup>, 22), 223 (27), 195 (28), 133 (33), 91 (23), 75 (50), 73 (100), 57 (32), and 41 (25).

<u>Anal</u>. Calcd for C<sub>17</sub>H<sub>32</sub>OSi: C, 72.77; H, 11.52; mol. wt., 280.222. Found: C, 72.81; H, 11.50; mol. wt., 280.220.

## Methylation of the Lithium Enolate 10

A solution of 3.75 mmol of MeLi (halide-free), 875 mg (3.12 mmol) of the silyl ether 14, and 1 mg of 2,2'-bipyridyl (an indicator) in 3 ml of  $\text{Et}_20$  was stirred at 25° for 45 min and then concentrated to dryness under reduced pressure.<sup>15</sup> The residue was treated with 3.2 ml of anhydrous DME and the resulting red (excess MeLi) solution was cooled to 0° and treated with 741 mg (5.21 mmol) of  $CH_3I$ . The resulting mixture was stirred in an ice bath for 40 sec and then quenched by the rapid addition of 5 ml of aqueous 5% HC1. After the reaction mixture had been partitioned between pentane and aqueous NaCl, the organic layer was dried and concentrated. The crude residual yellow liquid (618 mg) contained (glpc, SE-52 on Chromosorb P) two minor components believed to be olefins 30 and 31 (ret. times 12.8 and 14.5 min, both together constituted <u>ca</u>. 2% of the mixture), the previously described  $^2$ trans-ketone 9 (18.3 min, ca. 15%), the cis-ketone 8 (20.0 min, ca. 20%), the monoalkylated ketone 17 (22.0 min, ca. 55%), and an unresolved mixture of two components believed to be dialkylated ketones 15 and 16 (25.1 min, ca. 5%).

A 400-mg aliquot of the crude product was subjected to low-pressure liquid chromatography on silica gel with an EtOAc-hexane eluent (3:97 v/v). The first components eluted amounted to 8.6 mg (2% yield) of colorless liquid with spectral properties corresponding to one or both of the olefins <u>30</u> and <u>31</u>; ir (CCl<sub>4</sub>), no OH or C=O absorption; nmr (CCl<sub>4</sub>), 65.30 (0.5H, broad, vinyl CH), 1.0-2.9 (16H, m, aliphatic CH including a broad singlet at 1.67), and 0.87 (9H, s, <u>t</u>-Bu); mass spectrum, m/e (rel. intensity), 206 (1), 205 (4), 204 (26), 148 (7), 147 (100), 105 (30), 91 (30), 75 (17), 67 (15), and 41 (17).

The next fractions from the chromatograph contained varying mixtures of two components believed to be ketones 15 and 16 (total amount 16.7 mg or 3.4% yield). The more rapidly eluted fractions in this group contained (nmr analysis) mainly the product believed to be ketone <u>15</u> as a colorless liquid,  $\underline{n}^{25}\underline{\underline{p}}$  1.4822; ir (CC1<sub>4</sub>), 1705 cm<sup>-1</sup> (C=O); mass spectrum, m/e (rel. intensity), 236 (M<sup>+</sup>, 32), 161 (24), 138 (64), 125 (100), 119 (23), 109 (43), 95 (49), 81 (53), 79 (20), 69 (21), 68 (20), 67 (41), 57 (85), 55 (45), 43 (25), and 41 (69); nmr (CCl<sub>4</sub>), δ2.0-2.9 (1H, m, CHCO) and 0.8-2.0 [27H, m, aliphatic CH including a CH, singlet at 1.11, a CH<sub>3</sub> doublet (J = 6.6 Hz) at 0.95, and a  $\underline{t}$ -Bu singlet at 0.87]. In  $C_6D_6$  solution, the locations of the CH<sub>3</sub> singlet, the CH<sub>3</sub> doublet, and the t-Bu singlet were 1.25 (A\delta +0.14), 1.07 (A\delta = +0.12), and 0.83 ( $\Delta\delta$  = -0.04), respectively. The downfield shift of both methyl signals in  $C_6 D_6$  solution is consistent with our tentative assignment 15 with both methyl groups equatorial to the cyclohexanone ring. 16

<u>Anal</u>. Calcd for C<sub>16</sub>H<sub>28</sub>O: mol. wt., 236.214. Found: mol. wt., 236.218.

The more slowly eluted fractions in this group of chromatographic fractions contained (nmr analysis) mainly the product believed to be ketone <u>16</u> as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4820; ir (CCl<sub>4</sub>), 1709 cm<sup>-1</sup> (C=0); mass spectrum, m/e (rel. intensity), 236 (M<sup>+</sup>, 10), 179 (24),

161 (32), 138 (64), 125 (100), 109 (45), 95 (54), 84 (25), 81 (56), 69 (20), 67 (40), 57 (85), 55 (40), 43 (28), and 41 (64); nmr (CC1<sub>4</sub>),  $\delta$ 2.0-2.9 (1H, m, CHCO) and 0.8-2.0 [27H, m, aliphatic CH including a CH<sub>3</sub> singlet at 1.07, a CH<sub>3</sub> doublet (J = 6.6 Hz) at 1.00, and a <u>t</u>-Bu singlet at 0.84]. In C<sub>6</sub>D<sub>6</sub> solution, the locations of the CH<sub>3</sub> singlet, the CH<sub>3</sub> doublet, and the <u>t</u>-Bu singlet were 1.04 ( $\Delta\delta$  = -0.03), 1.05 ( $\Delta\delta$  = +0.05), and 0.80 ( $\Delta\delta$  = -0.04), respectively.

The shifts in the methyl signals exhibit no consistent pattern as might be expected for the tentatively assigned structure <u>16</u> since the 1,3-diaxial Me--CH<sub>2</sub> interaction present may force the cyclohexanone ring into a boat conformation. The fact that the amounts of both this isomer and the other dialkylated product <u>15</u> increased at approximately the same rate as the reaction time was lengthened suggests that both products are derived from the further alkylation of the major monoalkylated product 17.

<u>Anal</u>. Calcd for C<sub>16</sub>H<sub>28</sub>O: mol. wt., 236.214. Found: mol. wt., 236.216.

Subsequent fractions from the chromatograph contained 192.3 mg (43% yield) of the monoalkylated ketone <u>17</u> as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4869, that exhibited a single glpc peak (silicone SE-52 on Chromosorb P); ir (CCl<sub>4</sub>), 1709 cm<sup>-1</sup> (C=0); mass spectrum, m/e (rel. intensity), 222 (M<sup>+</sup>, 4.5), 147 (25), 124 (43), 111 (100), 95 (24), 81 (36), 67 (27), 57 (89), 55 (37), 43 (30), and 41 (63); <sup>13</sup>C nmr (CDCl<sub>3</sub>, multiplicity on off-resonance decoupling), 215.7 (s), 48.6 (s), 42.9 (d), 41.1 (d), 37.7 (t), 32.2 (s), 31.2 (t),

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28.0 (t), 27.5 (t), 27.2 (q, three C atoms), 25.4 (t), 22.2 (t), and 19.6 (q) ppm; <sup>1</sup>H nmr (CCl<sub>4</sub>),  $\delta 0.7$ -2.7 (m, aliphatic CH including a CH<sub>3</sub> singlet at 1.10 and a <u>t</u>-Bu singlet at 0.85. In C<sub>6</sub>D<sub>6</sub> solution, the location of the CH<sub>3</sub> and <u>t</u>-Bu singlets were 1.24 ( $\Delta\delta$  = +0.14) and 0.80 ( $\Delta\delta$  = -0.05), respectively. The downfield shift of the methyl signal is consistent with our stereochemical assignment in which the methyl group is equatorial to the cyclohexanone ring.<sup>16</sup>

<u>Anal</u>. Calcd for C<sub>15</sub>H<sub>26</sub>O: C, 81.02; H, 11.79. Found: C, 81.15; H, 11.87.

Subsequent fractions from the chromatograph contained 48.5 mg (11.5% yield) of the <u>trans</u>-ketone <u>9</u> followed by 66.7 mg (16% yield) of the <u>cis</u>-ketone <u>8</u>. Both of these products were identified with previously characterized samples<sup>2</sup> by comparison of ir, nmr, and mass spectra.

A second comparable alkylation experiment was performed with 1.56 g (5.6 mmol) of silyl ether <u>14</u> employing the same temperature and molar concentrations of all reactants used in the previous experiment with a total reaction time of 60 sec rather than 40 sec. The crude liquid product (1.11 g) contained (glpc analysis) a component thought to be one or both of the olefins <u>30</u> or <u>31</u> (ca. 3%), the <u>trans</u>-ketone <u>9</u> (ca. 5%), the <u>cis</u>-ketone <u>8</u> (ca. 6%), the monomethyl ketone <u>17</u> (ca. 74%), and a mixture of dimethyl ketones <u>15</u> and <u>16</u> (ca. 12%). After following the same chromatographic isolation procedure previously described, the isolated yields were: olefins <u>30</u> and/or <u>31</u>, 43.8 mg or 3.8%; ketones <u>15</u> and <u>16</u>, 126.4 mg or 9.6%; ketone <u>17</u>, 709.7 mg or 57.2%; <u>trans</u>-ketone <u>9</u>, 53.7 mg or 4.6%; and and cis-ketone 8, 74.4 mg or 6.4%.

# Preparation of the Hydrocarbon 19

A solution of 190.8 mg (0.86 mmol) of the ketone 17, 215 mg (4.3 mmol) of hydrazine hydrate, and 2.5 ml of diethylene glycol was refluxed for 75 min and then cooled and treated with 103 mg (2.6 mmol) of NaOH. The reaction mixture was again heated to reflux and the two-phase mixture of  $H_2O$ ,  $H_2NNH_2$ , and hydrocarbon <u>19</u> was allowed to distill from the reaction vessel. After the distillate had been partitioned between pentane and aqueous 10% HCl, the organic layer was dried and concentrated to leave 110.7 mg (62%) of the hydrocarbon 19 as a colorless liquid. This material was distilled in a short-path still at 1 mm to separate the hydrocarbon 19 as a colorless liquid,  $\underline{n}^{25}\underline{p}$  1.4770; ir (CCl<sub>4</sub>), no OH or C=O absorption; mass spectrum, m/e (rel. intensity), 208  $(M^+, 7)$ , 152 (38), 151 (37), 150 (30), 137 (57), 109 (33), 96 (31), 95 (100), 83 (24), 81 (47), 69 (22), 67 (28), 57 (52), 55 (32), and 41 (40); <sup>13</sup>C nmr (CDCl<sub>3</sub>, multiplicity in off-resonance decoupling), 41.6 (d), 41.0 (t and d, two C atoms), 32.2 (s), 32.0 (s), 30.4 (t), 28.5 (t), 28.2 (t), 28.0 (q), 27.4 (q, three C atoms), 27.2 (t), 22.8 (t), and 22.1 (t) ppm; <sup>L</sup>H nmr (CC1<sub>4</sub>),  $\delta$ 0.7-2.1 (28H, m, aliphatic CH including a  $CH_3$  singlet at 0.93 and <u>t</u>-Bu singlet at 0.83). The <sup>1</sup>H nmr spectrum also exhibited a small peak at  $\delta$ 0.88 that may be the t-Bu signal for the previously described<sup>17</sup> stereoisomeric hydrocarbon 20 (lit.<sup>17</sup>  $\delta 0.86$  for <u>t</u>-Bu and 0.85 for CH<sub>3</sub>). This extra nmr peak was also present in the spectrum of a sample of the hydrocarbon 19 purified by glpc collection (as noted below hydrocarbons 19 and 20

were not resolved by any glpc column we examined). If this extra peak is attributable to the nmr signal for the <u>t</u>-butyl group of hydrocarbon <u>20</u>, then the relative heights of the two <u>t</u>-butyl nmr signals in our sample would indicate that the <u>cis</u>-hydrocarbon <u>19</u> contains ca. 13% of the isomeric trans-hydrocarbon 20.

However, it was clear from comparison of the ir,  ${}^{1}$ H nmr, and  ${}^{13}$ C nmr spectra for the present sample, hydrocarbon <u>19</u>, and the previously prepared  ${}^{17}$  hydrocarbons <u>20</u> and <u>21</u>, that the three compounds are different. Our hydrocarbon <u>19</u> also differs from the previously described  ${}^{18}$  <u>trans-hydrocarbon 22</u> in its ir and nmr absorption.

<u>Anal</u>. Calcd for C<sub>15</sub>H<sub>28</sub>: C, 86.43; H, 13.54; mol. wt., 208.219. Found: C, 86.29; H, 13.67; mol. wt., 208.223.

Various mixtures of hydrocarbons <u>19</u>, <u>20</u>, and <u>21</u> were examined with a variety of glpc columns. In only two cases, columns were found that would resolve hydrocarbons <u>20</u> and <u>21</u>; Apriezon M on Chromosorb P, <u>21</u>, 39.2 min, and <u>20</u>, 41.2 min; silicone OV-17 on Chromosorb P, <u>21</u>, 35.6 min, and <u>20</u>, 37.1 min. However, with both of these glpc columns and with all others examined, mixtures of the hydrocarbons <u>19</u> and <u>20</u> were not resolved.

# Preparation of the Oxime 25

A solution of 66.6 mg (0.30 mmol) of the ketone <u>17</u>, 25.4 mg (0.37 mmol) of  $\text{HONH}_3^+$ Cl<sup>-</sup>, and 0.1 ml of aqueous 10% NaOH in 0.7 ml of H<sub>2</sub>O and 0.75 ml of EtOH was refluxed for 10 min and then cooled and diluted with 4.5 ml of H<sub>2</sub>O. The crude solid oxime that separated (66.2 mg) was recrystallized from EtOH to separate 54 mg (76%) of

the crude oxime  $\underline{25}$  as colorless needles, mp 152.5-154°. A 16.6-mg portion of this oxime was recrystallized from MeOH to separate 11.7 mg (54% yield) of the pure oxime  $\underline{25}$ , mp 163-164°. The oxime  $\underline{25}$  was allowed to crystallize slowly from a saturated solution in MeOH to separate crystals of the pure oxime, mp 164-165°, that were suitable for x-ray crystallography; ir (CC1<sub>4</sub>), 3610 and 3290 cm<sup>-1</sup> (free and associated OH); nmr (CDC1<sub>3</sub>),  $\delta 3.1$ -3.4 (1H, broad, OH) and 0.8-2.7 (26H, m, aliphatic CH including a CH<sub>3</sub> singlet at 1.25 and a <u>t</u>-Bu singlet at 0.85); mass spectrum, m/e (rel. intensity), 237 (M<sup>+</sup>, 28), 222 (31), 220 (52), 180 (42), 147 (20), 126 (100), 110 (20), 107 (20), 99 (50), 81 (20), 58 (31), 57 (72), 55 (24), 43 (70), and 41 (46).

<u>Anal</u>. Calcd for C<sub>15</sub>H<sub>27</sub>NO: C, 75.89; H, 11.47; N, 5.90. Found: C, 75.68; H, 11.27; N, 5.79.

# X-Ray Crystallographic Data Collection

An oxime derivative crystal with approximate dimensions 0.22 x 0.30 x 0.75 mm was mounted on a glass fiber using epoxy cement such that the longest crystal dimension 0.75 mm was approximately parallel to the fiber axis.

Unit cell parameters and the orientation matrix were determined on a Syntex P2, four circle diffractometer equipped with a graphite monochromator (Bragg 20 angle = 12.2°) using MoK<sub> $\alpha$ </sub> radiation at a takeoff angle of 6.75°. Fifteen reflections whose 20 values ranged from 3.86° to 10.78° were machine-centered and used in least-squares refinement of the lattice parameters and orientation matrix. Unit cell parameters obtained were a = 12.161 (6) Å,<sup>19</sup> b = 12.788 (7) Å, c = 18.69 (1) Å, and V = 2906 (3) Å<sup>3</sup>. The calculated density of 1.08 g cm<sup>-3</sup> for 8 formula units per unit cell agrees with the experimental density of 1.08 g cm<sup>-3</sup> measured by the flotation method using a mixture of  $H_2O$  and CsCl. Omega scans of several low 20 angle reflections gave peak widths at half-height of less than 0.18°, indicating a satisfactory mosaic spread for the crystal.

Axial photographs indicated that the crystal belonged to the orthorhombic system. Intensity data for zero and upper levels were collected at a rapid scan rate and the intensities examined carefully for systematic absences. The absence of  $0K\ell \ \ell = 2n + 1$ , h $0\ell \ \ell = 2n + 1$ , and h $kO \ h + k = 2n + 1$  reflections is consistent with only space group Pccn No. 56.<sup>20</sup>

Intensity data were collected using  $\theta$ -2 $\theta$  scans with x-ray source and monochromator settings identical to those used for determination of the unit cell parameters. A variable scan rate of from 2.93° to 29.3° min was used and a scan width of 2.0° was sufficient to collect all of the peak intensity. Stationary background counts were measured at the beginning (bgd 1) and at the end (bgd 2) of each scan with a total background to scan time ratio, TR, of 1.0. No significant fluctuations were observed in the intensities of three standard reflections (4, 0, 0; 0, 4, 0; 0, 0, 6) monitored every 97 reflections. Intensities were calculated from the total scan count (CT) and background counts by the relationship:

$$I = CT-(TR)(bdg1 + bgd2).$$

The intensities were assigned standard deviations according to the formula

$$\sigma(I) = [CT + (TR)^{2}(bgd1 + bgd2) + (pI)^{2}]^{1/2}$$

from a total of 2583 reflections collected in a complete octant of data out to  $2\theta = 50^{\circ}$ ; 1507 were accepted as statistically above background on the basis that F was greater than  $3\sigma(F)$ . Lorentz and polarization corrections were made in the usual way.

# Solution and Refinement of the Structure for 25

Computations were performed using standard programs;<sup>21</sup> all computations were carried out on the CDC Cyber 74 System. For structure factor calculations the scattering factors were taken from Cromer and Mann's tabulation.<sup>22</sup>

The agreement factors are defined in the usual way as

 $\mathbf{R} = (\Sigma | |\mathbf{F}_{O}| - |\mathbf{F}_{C}| |) / (\Sigma | \mathbf{F}_{O}|)$ 

and

$$R_{w} = \frac{[\Sigma(|F_{o}| - |F_{c}|)(w^{0.5})]}{[\Sigma(|F_{o}|)(w^{0.5})]}$$

In all least squares refinements, the quantity minimized was  $w(|F_o|-|F_c|)^2$ . A weighting scheme based on counting statistics, (w = 2.2/[ $\sigma$  F<sup>2</sup> + 0.002 F<sup>2</sup>]), was employed for calculating R<sub>w</sub> and in least-squares refinement.

The structure was solved using the automatic centrosymmetric direct methods program of SHELX-76. The total number of parameters varied were 180 for 1507 observations. Parameters varied included a scale factor, coordinates of all atoms except hydrogens, anisotropic thermal parameters for all atoms except H atoms, and isotropic thermal parameters for H atoms. Hydrogen atoms were refined in the riding mode. The full-matrix least-squares refinement converged at R = .076 and R<sub>w</sub> = .077. Final positional parameters were listed in Tables 3 and 4.

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- 8. These calculations and experiments were performed in our laboratories by Mr. C. C. Yau.
- 9. The plots in Figures 2 and 3 are modified ORTEP plots performed on a Calcomp plotter and CDC Cyber 74 system, and are based on final atomic coordinates calculated by the MMI program (see ref. 7) after energy minimization.
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- 12. All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated MgSO4 was employed as a drying agent. The ir spectra were determined with a Perkin Elmer, Model 257 or Model 299, infrared recording spectrophotometer fitted with a grating. The uv spectra were determined with a Perkin Elmer, Model 202, recording spectrophotometer. The proton nmr spectra were determined at 60 mHz with a Varian, Model T-60-A, nmr spectrometer and at 100 mHz with a JEOL nmr spectrometer, Model PFT-100. The 13C nmr spectra were determined at 25 mHz with a JEOL Fourier transform spectrometer. Model PFT-100. The chemical shift values are expressed in  $\delta$  values (ppm) relative to a MedSi internal standard. The mass spectra were obtained with an Hitachi (Perkin Elmer), Model RMU-7, mass spectrometer. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere. The anhydrous ethereal solvents were purified by distillation from LiAlH, immediately before use.
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- 21. Programs utilized were Sheldnick's SHELX-76 program, Iber's NUCLS modification of the Busing-Martin-Levy leastsquares program, Doeden's RBANG rigid group orientation program, Stewart's ABSORB absorption correction program from the X-Ray 72 system, and Johnson's ORTEP program.

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## COSERVEC AND CALCULATED STRUCTURE FACTORS FOR OXINE OF METHYLATED DECALONE

| н        | к | Ł      | FQ         | FC   | н  | к  | L   | FC  | FC   | н   | к  | Ļ | FO    | FC   | н  | к   | L   | FĊ       | FC   | н   | к | Ł   | FÛ  | FC    |
|----------|---|--------|------------|------|----|----|-----|-----|------|-----|----|---|-------|------|----|-----|-----|----------|------|-----|---|-----|-----|-------|
| 4        | n | n      | E4         | 65   | 19 | 5  | ٥   |     | 6    | 8   | 12 | ۵ | 19    | -17  | 3  | 3   | 1   | 43       | -42  | 17  | 5 | 1   | 14  | -15   |
| 6        | ñ | a      | 41         | -60  |    | 6  | Ā   | 4.4 | -47  | 10  | 12 | ň | 7     | -6   | Š  | 3   | 1   | 4.8      | -49  | 10  | 5 | -   | 12  | -11   |
| Ă        | ŏ | ň      | 15         | 14   | 2  | ĕ. | ì   | 35  | -33  | 12  | ĩž | ă | 15    | - 15 | 6  | ž   | ĩ   | 24       | 22   | 2   | 6 | - î | 1   | -11   |
| 12       | 5 | ň      | 37         | 36   |    | 6  | ā   | 3.4 | - 37 | 3   | 13 | ñ | 20    | -21  | 7  | š   | - ī | 56       | -55  | 3   | ň | ī   | 11  | 11    |
| 16       | ň | ň      | 15         | 16   | é  | Ă  | 8   | õ   | Ĩ.   | 5   | 13 | ā | 1.6   | -19  | Å  | 3   | ī   | 50       | 47   | L.  | 6 | 1   | 13  | 12    |
| 20       | ñ | ő      | 12         | 12   |    | Å  |     | 11  | 10   | 7   | 13 | ñ | 12    | 11   | à  | 3   | 1   | 20       | -36  | 6   | 6 |     | 29  | -27   |
| 3        | 1 | ō      | 44         | -45  | 10 | 6  | ā   | 47  | 46   | ģ   | 13 | ā | Ĩġ    | ģ    | 10 | 3   | 1   | ģ        |      | 7   | 6 | 1   | 22  | -21   |
| 5        | ī | ā      | 6.1        | 39   | 12 | 6  | å   | 1.0 | -10  | 2   | 16 | Ō | 6     | 7    | 11 | 3   | ĩ   | 13       | -15  | Å   | ň | -   | 1.8 | -19   |
| 7        | ÷ | ō      | 37         | 35   | 14 | 6  | ē   | ç   | -9   | - L | 14 | đ | 11    | 12   | 12 | 3   | ī   |          | 7    | à   | 6 | 1   | ĩ   | 3     |
| ģ        | 1 | Õ      | 6          | 7    | 16 | 6  | ō   | 14  | -14  | 1   | 15 | a | 13    | 13   | 13 | 3   | 1   | 19       | +16  | 10  | 6 | ī   | 12  | 11    |
| 11       | ī | Ğ      | 15         | -1E  | 18 | 6  | ā   | ÷   | -6   | 3   | 15 | õ | 15    | 15   | 14 | 3   | 1   | 18       | 10   | 11  | 6 | ī   | 26  | 27    |
| 13       | 1 | ā      | ġ          | -10  | 1  | 7  | 6   | 2 E | - 24 | 2   | 1  | 1 | 101   | -195 | 15 | 3   | 1   | 18       | -16  | 13  | 6 | 1   | 9   | -10   |
| 17       | 1 | ā      | 5          | 5    | 3  | 7  | ō   | 2 E | -25  | 3   | 1  | ī | 63    | 67   | 16 | 3   | 1   | 11       | -12  | 15  | 6 | 1   | 5   | -2    |
| 0        | 2 | ٥      | 33         | 34   | 5  | 7  | Û   | 12  | · 12 | 4   | 1  | 1 | 101   | 101  | 18 | 3   | 1   | 5        | 5    | 16  | 6 | 1   | 6   | 7     |
| ž        | 2 | Ō      | 169        | -177 | 7  | 7  | 8   | g   | 8    | 5   | 1  | 1 | 33    | 33   | 19 | 3   | 1   | 5        | -4   | 17  | 6 | 1   | 6   | -6    |
| 4        | 2 | a      | 56         | 55   | 9  | 7  | 8   | 27  | -27  | 6   | 1  | 1 | 10    | 12   | 21 | 3   | 1   | 8        | -6   | 19  | E | 1   | 6   | -1    |
| 8        | 2 | Û      | 9          | 8    | 11 | 7  | 8   | ŧ   | -7   | 7   | 1  | 1 | 10    | -11  | 1  | 4   | 1   | 51       | -49  | · 1 | 7 | 1   | 11  | -12   |
| 10       | 2 | 0      | 23         | -29  | 13 | 7  | G   | 8   | - 9  | 8   | 1  | 1 | 8     | -7   | 2  | 4   | 1   | 29       | 27   | 4   | 7 | 1   | 12  | 12    |
| 12       | 2 | Û      | 4          | -3   | 15 | 7  | 0   | 8   | -6   | 9   | 1  | 1 | 3     | -1   | 3  | 4   | 1   | e        | -6   | 5   | 7 | 1   | 7   | -7    |
| 16       | 2 | 0      | 4          | - 3  | 19 | 7  | ĉ   | 6   | -1   | 10  | 1  | 1 | 7     | 6    | 4  | 4   | 1   | 39       | 39   | 6   | 7 | 1   | 27  | -25   |
| 18       | 2 | ۵      | 22         | -21  | 2  | 8  | 4   | 4   | 7    | 11  | 1  | 1 | 3     | -3   | 5  | -4  | 1   | 33       | 30   | 8   | 7 | 1   | 24  | -25   |
| 50       | 2 | 0      | 5          | 1    | E  | 8  | G   | 26  | 26   | 12  | 1  | 1 | 4     | 2    | 6  | -4  | 1   | 19       | 20   | 19  | 7 | 1   | 13  | -12   |
| 1        | 3 | 0      | 32         | 31   | 8  | 8  | G   | 27  | -28  | 13  | 1  | 1 | 16    | 15   | 7  | - 4 | 1   | 16       | 11   | 11  | 7 | 1   | 14  | -15   |
| 3        | 3 | 0      | 40         | 41   | 10 | 8  | ٥   | 18  | 19   | 15  | 1  | 1 | 14    | 14   | 8  | 4   | 1   | e        | 6    | 12  | 7 | 1   | 16  | -16   |
| 5        | 3 | ٥      | ea         | 59   | 12 | 8  | 8   | 15  | 15   | 16  | 1  | 1 | 7     | -7   | 9  | 4   | 1   | 4        | - 3  | 13  | 7 | 1   | 8   | -9    |
| 7        | 3 | Э      | 42         | +2   | 14 | 5  | ٥   | 11  | 11   | 17  | 1  | 1 | 15    | 16   | 10 | 4   | 1   | 31       | - 30 | 15  | 7 | 1   | 5   | 4     |
| 9        | 3 | a      | 50         | 18   | 18 | 8  | Q   | 8   | 7    | 19  | 1  | 1 | 11    | 9    | 11 | 4   | 1   | 12       | 11   | 17  | 7 | 1   | 5   | -1    |
| 13       | 3 | 0      | 7          | -6   | 1  | 9  | G   | 5   | -7   | 1   | 2  | 1 | 96    | - 99 | 12 | - 4 | 1   | 31       | - 31 | 1   |   | 1   | 6   | 6     |
| 15       | 3 | 0      | 16         | -17  |    | 9  | đ   | 13  | -14  | Z   | 2  | 1 | 39    | 39   | 13 | - 4 | 1   | 17       | -18  | 2   | 8 | 1   | 11  | -12   |
| 17       | 3 | 0      | 5          | +4   | 5  | 3  | C   | 31  | -30  | 3   | 2  | 1 | 48    | -47  | 14 | 4   | 1   | 11       | -12  | 3   |   | 1   |     | - 4 7 |
| 19       | 3 | ų      |            | 3    |    | Y  | U A | 44  | -47  | 4   | 2  | 1 | 43    | -40  | 11 |     | 1   | 2        | 4    |     | • | 1   | 12  | -13   |
| 0        | 4 | U<br>A | 113        | -110 |    | 3  | Ľ,  | 32  | - 34 | 2   | 5  | 1 | 4 1 1 | 3    | 13 | -   | 1   | с<br>с п | - 55 | 7   | • | 1   | 11  | - 7 2 |
| <u>د</u> | 4 | u<br>n | 21         | - 20 | 11 | 3  |     | 11  | 17   | 7   | 6  | - | 10    | 15   | -  | -   | 1   | 00       | - 22 | , r | 9 | +   |     | - 32  |
| 2        | 7 |        | 2 -<br>1 1 | _10  | 16 | 2  |     | 10  | å    | é   | 2  | 1 | 10    | 17   | 2  | 6   | 4   | 16       | -16  | 4 0 |   | -   | 11  | 11    |
|          | 7 |        | 10<br>10   | -1-  | 15 | 10 |     | 10  | 2    | 10  | 2  | ÷ | 7     | -5   |    | é   | 4   | 10       | -10  | 11  |   | 1   | 1   | 1 c   |
| 1 ก็     | 7 | 0      | 19         | -21  | 2  | 10 | a   | 1.6 | 15   | 11  | 2  | 1 | Å     | 7    | 5  | 5   | 1   | 24       | 21   | 13  | ă | 1   | ă   | - 7   |
| 12       | L | ā      | 44         | -44  |    | 10 | ċ   |     | 5    | 12  | 2  | 1 | 5     | -6   | 6  | 5   | -   | 1.2      | - 39 | 15  |   | 1   | 7   | 5     |
| 14       | 7 | ň      | 11         | 11   | 6  | 10 | ă   | á   | á    | 16  | 2  | î | 11    | -11  | ž  | 5   | î   | 18       | 17   | 16  | ă | i   | 5   | ĩ     |
| 16       | 4 | G      | 20         | 21   | 10 | 10 | ō   | 17  | 18   | 15  | 2  | ĩ |       | - 9  |    | ŝ   | 1   | 14       | -12  |     | ŝ | 1   | 18  | 17    |
| 20       | 4 | ň      | 11         | 11   | 18 | 10 | ē   | Ē   |      | 16  | 2  | ī | 10    | -10  | ğ  | 5   | ī   | 15       | 15   | 2   | 9 | 1   | 15  | -14   |
| 1        | 5 | 8      | 15         | 14   | 1  | 11 | 0   | ç   | 9    | 17  | 2  | 1 | 9     | 9    | 10 | ŝ   | ī   | 25       | - 25 | 3   | 9 | 1   | 19  | 19    |
| 3        | 5 | Ō      | 13         | 14   | 3  | 11 | 6   | ç   | 10   | 18  | 2  | 1 | 6     | 5    | 11 | 5   | 1   | 16       | 16   | 5   | 9 | 1   | 24  | 25    |
| 5        | 5 | э      | 33         | 30   | 5  | 11 | G   | E   | 7    | 19  | 2  | 1 | 12    | 12   | 12 | 5   | 1   | 5        | -6   | 7   | 9 | 1   | 37  | 38    |
| 7        | 5 | õ      | 2.5        | 56   | 7  | 11 | û   | 1.  | 17   | 20  | ē  | 1 | 10    | 10   | 13 | 5   | 1   | 6        | 6    | 8   | 9 | 1   | 16  | 18    |
| 11       | 5 | Ō      | 21         | 23   | 13 | 11 | ٥   | 5   | -7   | 21  | 2  | 1 | 6     | 1    | 14 | ē.  | 1   | 19       | 19   | 9   | 9 | 1   | 25  | 25    |
| 13       | 5 | 0      | 24         | 23   | 2  | 12 | Q   | 11  | 10   | 1   | 3  | 1 | 33    | 34   | 15 | 5   | 1   | 13       | -13  | 10  | 9 | 1   | 20  | 22    |
| 15       | 5 | 0      | Э          | - 9  | 6  | 12 | 6   | 15  | -19  | 2   | 3  | 1 | 25    | -24  | 16 | 5   | 1   | 7        | -5   | 11  | 9 | 1   | 14  | 14    |

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### DESERVED AND CALCULATED STRUCTURE FACTORS FOR SXIME OF METHYLATED DECALONE

| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | L FO FC  | L | нк    | FC   | FO  | L | ĸ      | н          | FC   | FQ  | L | κ   | н  | FC   | FC   | L      | к | H        | FC  | FO       | L | к   | н   |
|--|----------|---|-------|------|-----|---|--------|------------|------|-----|---|-----|----|------|------|--------|---|----------|-----|----------|---|-----|-----|
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 10 10  | 2 | 11 9  | -29  | 31  | 2 | 6      | 4          | 88   | 91  | z | 3   | 6  | -18  | 19   | 2      | 0 | 11       | 8   | 8        | 1 | 9   | 13  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 7 7    | 2 | 12 9  | -22  | 24  | 2 | 6      | 5          | - 34 | 37  | 2 | 3   | 7  | -19  | 20   | 2      | ٥ | 13       | - 3 | 5        | 1 | ġ   | 14  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 10 11  | ž | 13 9  | -13  | 14  | ž | 6      | 6          | 10   | 9   | 2 | 3   | 8  | 16   | 16   | 2      | Ð | 14       | 6   |          | ī | 10  | 1   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 6 4    | 2 | 16 9  | 12   | 11  | 2 | E      | 7          | 23   | 22  | 2 | 3   | 10 | - 22 | 22   | 2      | ۵ | 15       | -7  | 7        | 1 | 10  | 2   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 21 20  | 2 | 0 10  | 19   | 19  | 2 | E      | 8          | -6   | 7   | 2 | 3   | 11 | 28   | 28   | 2      | 0 | 16       | 8   | 7        | 1 | 10  | 3   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 7 -8   | 2 | 1 10  | 11   | 10  | 2 | 6      | 9          | 4    | 6   | 2 | 3   | 12 | 37   | 38   | 2      | 0 | 18       | +15 | 15       | 1 | 10  | 4   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 18 18  | ž | 2 10  | 29   | 25  | 2 | Ē      | 11         | -7   | â   | 2 | 3   | 13 | 7    | 7    | 2      | 0 | 20       | 21  | 21       | 1 | 10  | 5   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 2 15 15  | 2 | 4 19  | 14   | 14  | 2 | 6      | 12         | 3    | 5   | 2 | 3   | 15 | 7    | 6    | 2      | 0 | 21       | 10  | 11       | 1 | 10  | 7   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 8 7    | ž | 6 10  | 24   | 22  | 2 | Ê      | 13         | - 22 | 22  | Z | 3   | 16 | 192  | 175  | 2      | 1 | Ū        | ģ   | 8        | 1 | 10  | 8   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 17 -18 | 2 | 7 10  | -9   | 8   | 2 | E      | 14         | -10  | 10  | 2 | 3   | 18 | 14   | 13   | 2      | 1 | 1        | - 4 | 5        | 1 | 10  | 11  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 15 14  | 2 | 8 10  | 12   | 12  | 2 | e      | 15         | -5   | 7   | 2 | 3   | 19 | ç 9  | 96   | 2      | 1 | 2        | -7  | 6        | 1 | 10  | 13  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 15 -15 | 2 | 9 10  | - 8  | £   | 2 | £      | 16         | -11  | 10  | 2 | 3   | 20 | 54   | 93   | 2      | 1 | 3        | 5   | 11       | 1 | 10  | 14  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 2 9 -16  | Ż | 10 10 | -4   | 7   | 2 | 6      | 20         | 5    | 5   | 2 | 4   | 0  | -38  | 39   | 2      | 1 | 4        | 11  | 11       | 1 | 11  | 1   |
| 3   11   1   7   -9   €   1   2   40   38   2   4   2   26   25   2   7   2   7   5   9   11   2   7   -4     4   11   1   6   4   7   1   2   12   12   3   4   2   44   43   3   7   2   11   -10   1   11   2   10   -1     5   11   1   15   -16   8   1   2   7   -5   4   4   2   26   -26   -4   7   2   30   -27   2   11   2   12   -12   -12   -12   12   12   12   -12   -12   <  | 2 11 8   | 2 | 16 10 | -11  | 12  | 2 | 7      | 0          | 9    | 8   | 2 | 4   | 1  | 101  | 101  | 2      | 1 | 5        | 8   | 9        | 1 | 11  | 5   |
| 4   11   1   6   4   7   1   2   12   12   3   4   2   44   43   3   7   2   11   -19   1   11   2   10   -1     5   11   1   15   -16   8   1   2   7   -5   4   4   2   26   -26   4   7   2   30   -27   2   11   2   12   -1     7   11   1   18   -20   9   1   2   7   -7   5   4   2   26   -26   4   7   2   30   -27   2   11   2   12   -12   -12   12   12   12   12   -12     | 2 7 -7   | 2 | 9 11  | 5    | 7   | 2 | 7      | 2          | 25   | 26  | 2 | - 4 | 2  | 36   | 40   | 2      | 1 | €        | -9  | 7        | 1 | 11  | 3   |
| 5   11   1   15   -16   8   1   2   7   -5   4   4   2   26   -26   4   7   2   30   -27   2   11   2   12   -1     7   11   1   18   -20   9   1   2   7   -7   5   4   2   26   -26   4   7   2   30   -27   2   11   2   12   -1     7   11   1   18   -20   9   1   7   -7   5   4   2   10   10   5   7   2   12   -12   4   11   2   5     8   11   15   16   10   1   2   22   2   6   4   2   18   -16   6   7   2   6   -11   2   6   -12   12   12   11   7   12   6   -11   7   12   2   11   12   7   11   10   11   2   | 2 10 -10 | 2 | 1 11  | -19  | 11  | 2 | 7      | 3          | 43   | 44  | 2 | 4   | 3  | 12   | 12   | 2      | 1 | 7        | 4   | ó        | 1 | 11  | - 4 |
| 7   11   1   18   -20   9   1   2   7   -7   5   4   2   10   10   5   7   2   12   -12   4   11   2   5     8   11   1   15   16   10   1   2   22   22   6   4   2   18   -16   6   7   2   6   -5   11   2   6     9   11   1   24   -25   11   1   2   16   -11   7   4   2   9   -9   7   7   2   17   18   6   11   2   7     10   11   1   2   11   12   9   4   2   5   -3   8   7   2   11   10   7   11   2   6   -     10   11   1   2   11   12   11   12   6   -   -   11   10   7   11   2   6   -   -   1   | 2 12 -13 | 2 | 2 11  | - 27 | 30  | 2 | 7      | 4          | - 26 | 26  | 2 | 4   | 4  | -5   | 7    | 2      | 1 | 8        | -16 | 15       | 1 | 11  | 5   |
| 8   11   1   5   16   10   1   2   22   6   4   2   18   -16   6   7   2   6   -6   5   11   2   6     9   11   1   24   -25   11   1   2   16   -11   7   4   2   9   -9   7   7   2   17   18   6   11   2   7     10   11   1   8   6   12   11   12   9   4   2   5   -3   8   7   2   11   10   7   11   2   6   -     10   11   1   7   11   12   9   4   2   5   -3   8   7   2   11   10   7   11   2   6   -  | 2 5 3    | 2 | 4 11  | -12  | 12  | 2 | 7      | 5          | 10   | 10  | 2 | 4   | 5  | - 7  | 7    | 2      | 1 | ġ        | -20 | 18       | 1 | 11  | 7   |
| 9 11 1 24 -25 11 1 2 12 -11 7 4 2 9 -9 7 7 2 17 18 6 11 2 7<br>10 11 1 9 6 12 1 2 11 12 9 4 2 5 -3 8 7 2 11 10 7 11 2 6 -  | 266      | 2 | 5 11  | -6   | 6   | 2 | 7      | 6          | -16  | 18  | 2 | 4   | 6  | 22   | 22   | 5      | 1 | 10       | 16  | 15       | 1 | 11  | 8   |
| 10 11 1 9 6 12 1 7 11 12 9 4 7 5 -3 8 7 2 11 10 7 11 2 6 -   | 275      | 2 | 5 11  | 18   | 17  | 2 | 7      | 7          | -9   | 9   | 2 | 4   | 7  | -11  | 12   | 2      | 1 | 11       | -25 | 24       | 1 | 11  | 9   |
|  | 26-6     | 2 | 7 11  | 10   | 11  | 2 | 7      | 8          | -3   | 5   | 2 | - 4 | à  | 12   | 11   | 2      | 1 | 12       | E   | 9        | 1 | 11  | 10  |
| 12 11 1 5 -5 15 1 2 10 11 10 4 2 17 -16 9 7 2 23 23 8 11 2 8   | 6 8 9    | 5 | 8 11  | 23   | 23  | 2 | 7      | 9          | -16  | 17  | 2 | 4   | 10 | 11   | 10   | ē      | 1 | 15       | - 5 | 5        | 1 | 11  | 12  |
| 1 12 1 9 10 16 1 2 7 -6 13 4 2 9 -9 10 7 2 13 12 12 11 2 9   | 2 9 8    | 2 | 12 11 | 12   | 13  | 2 | 7      | 10         | -9   | 9   | 2 | 4   | 13 | -6   | 7    | ĉ      | 1 | 16       | 10  | 9        | 1 | 12  | 1   |
| 3 12 1 7 -7 17 1 2 8 8 14 4 2 7 -8 11 7 2 9 -10 0 12 2 19 -1   | 2 19 -19 | 2 | 0 12  | -10  | 9   | 2 | 7      | 11         | - 8  | 7   | 2 | 4   | 14 | 8    | 8    | 2      | 1 | 17       | -7  | 7        | 1 | 12  | 3   |
| 5 12 1 7 8 18 1 2 6 4 15 4 2 5 4 12 7 2 8 -8 1 12 2 6  | 261      | 2 | 1 12  | -8   | 8   | Z | 7      | 12         | 4    | 5   | z | - 4 | 15 | 4    | E    | 2      | 1 | 18       | 8   | 7        | 1 | 12  | 5   |
| 6 12 1 6 -E 0 2 2 13e -146 16 4 2 11 -11 15 7 2 5 4 2 12 2 19 -2   | 2 19 -20 | 2 | 2 12  | 4    | 5   | 2 | 7      | 15         | -11  | 11  | 2 | - 4 | 16 | -146 | 136  | 2      | 2 | Ū        | -€  | 6        | 1 | 12  | 6   |
| 2 13 1 9 7 1 2 2 12 -11 19 4 2 8 -5 0 6 2 8 8 3 12 2 11 1  | 2 11 12  | Z | 3 12  | 8    | 5   | 2 | 8      | 0          | -5   | 5   | 2 | - 4 | 19 | -11  | 12   | Ż      | 2 | 1        |     | 9        | 1 | 13  | Z   |
| 3 13 1 3 -10 2 2 2 26 25 20 4 2 7 -6 1 8 2 7 -7 4 12 2 14 -1   | 2 14 -14 | 2 | 4 12  | -7   |     | 2 | 8      | 1          | •b   |     | 2 | 4   | 28 | 25   | 26   | ĉ      | 2 | Ž        | -10 |          | 1 | 13  | 3   |
| 5 13 1 7 -8 3 2 2 40 -39 0 5 2 62 -57 2 8 2 9 9 5 12 2 18 1  | 2 18 18  | 2 | 5 12  | 9    | 9   | 2 | e      | 2          | -51  | 62  | 2 | 5   | U  | - 39 | 40   | 2      | 2 | 3        |     | <u> </u> | 1 | 13  | 5   |
| 6 13 1 7 -E 4 2 2 7 -6 1 5 2 15 13 3 8 2 8 -B 6 12 2 7 -   | 2 7 -6   | 2 | 6 12  | - 8  | , a | 2 | 8      | 3          | 13   | 15  | Z | 2   | 1  | ~6   |      | č      | 2 |          |     |          | 1 | 13  | 6   |
|  | 2 0 -4   | ć | / 12  | 10   | 12  | 4 | c      | 4          | 38   | 40  | ~ | 2   | 2  | -42  | 44   | 4      | 2 | 7        | -/  | r        | 1 | 14  | 1   |
| 3141 15-17 622 5 9 5 5 2 4 4 5 8 2 5 7 9 12 2 10 -   | 2 10 -8  | 2 | 9 12  |      | 2   | 2 | 5      | 2          | 4    | 4   | 2 | 2   | 5  | 9    |      | 2      | 4 | <u>د</u> | -1/ | 15       | 1 | 14  |     |
|  |          | 2 | 10 12 | 36   | 26  | 2 | C      |            | -12  | 12  | 2 | 2   |    | +21  | 23   | ~      | 2 | , r      | 4   |          | 1 | 14  | 4   |
|  | 2 6 -4   | 2 | 11 12 | 20   | 22  | 2 | c      | f a        | - 21 | 210 | 2 | 2   | 2  | -10  | 11   | 2      | 2 | 10       | , c | •        | 1 | 14  | 0   |
|  | 2 13 -5  | 5 | 10 12 | 22   |     | 5 | С<br>1 | 4.0        | -6   |     |   | 2   | 7  |      | 2    | с<br>9 | 5 | 11       | - 2 | ź        | + | 1.4 | 4   |
| 1 1 7 1 0 - 2 1 1 2 2 7 - 0 7 7 2 0 - 0 1 0 0 2 9 2 3 1 3 2 0 - 0 1 0 0 2 9 2 3 1 3 2 0 - 0 1 0 0 2 9 2 1 6 1 8 4 1 3 7 6  | 265      | 5 | 6 13  | 1.8  | 16  | 2 | Å      | 12         | -0   | 10  | 5 | 5   | ģ  | -0   |      | ÷      | 2 | 12       | -2  | 7        | 1 | 15  | 2   |
|  | 2 8 -7   | 2 | 5 13  | 7    | 2   | , | A      | 14         | -10  | 11  | 5 | Ē   | 10 | -7   | ,    | -      | 5 | 4 7      | -16 | 1        | ÷ | ÷.  | õ   |
| 1  0  2  10  -10  10  2  1  -1  10  2  1  -10  10  10  10  1  0  10  1   | 2 6 .6   | 5 | 7 13  | 21   | 20  | 2 | ò      | - <b>a</b> | - 21 | 21  | 5 | ŝ.  | 11 | - 6  | é    | -      | 5 | 16       | -10 | 82       | 5 | ň   | 4   |
|  | 2 15 15  | 2 | 0 14  | -я   | ž   | 2 | ó      | 1          | -27  | 27  | 2 | ś   | 12 | -11  | 11   | 2      | 2 | 16       | 183 | 170      | 2 | ñ   | 2   |
|  | 2 6 8    | 2 | 2 14  | 7    | Å   | 2 | é      | 2          | -14  | 13  | 2 | 5   | 13 |      | - î; | 2      | 5 | 17       | 50  | 64       | 2 | 0   | र   |
| $L_{1} = 2$ $L_{2} = 2$ $L_{2} = 2$ $L_{1} = 2$ $L_{2} = 2$ $L_{2} = 2$ $L_{1} = 2$ $L_{2} = 2$ $L_{1} = 2$ $L_{2} = 2$ $L_{2$ | 2 12 -10 | 2 | 3 14  | -8   | ă   | 2 | ċ      | 3          | 18   | 1 A | 2 | 5   | 14 | - 4  | 7    | 2      | 2 | 2.0      | 27  | 26       | 2 | ñ   | ŭ   |
| 5 0 2 18 19 0 3 2 14 14 15 5 2 7 -8 5 9 2 14 -14 5 14 2 5 -  | 2 5 -4   | 2 | 5 14  | -14  | 14  | ž | ġ      | 5          | -8   | Ĩ   | 2 | ś   | 15 | -14  | 14   | ž      | 3 | ā        | 19  | 18       | ž | õ   | 5   |
| 6 0 7 16 16 1 3 7 15 14 16 5 2 · 5 4 6 9 7 17 -17 1 1 3 72 7   | 3 72 72  | J | 1 1   | -12  | 12  | 2 | ģ      | 6          | ŭ    | 5   | 2 | 5   | 16 | 14   | 1 5  | 2      | 3 | 1        | 16  | 16       | 2 | õ   | Ē   |
| 7 0 2 20 22 2 3 2 26 26 17 5 2 5 -4 7 5 2 15 -16 2 1 3 77 8  | 3 77 80  | 3 | 2 1   | -16  | 15  | ž | ç      | ž          | -4   | ś   | 2 | ś   | 17 | 26   | ŽĒ   | 2      | š | 2        | 22  | 20       | ž | ŏ   | 7   |
| 8 9 2 5 5 3 3 2 65 65 0 6 2 41 -38 8 9 2 20 -21 3 1 3 76 7   | 3 76 75  | 3 | J 1   | -21  | 20  | 2 | ġ      | 8          | - 38 | 41  | 2 | 6   | 0  | ē5   | 65   | 2      | 3 | 3        | 5   | 5        | 2 | ā   | 8   |
| 9 0 2 9 14 4 3 2 64 -63 1 6 2 5 3 9 9 2 11 12 4 1 3 52 5   | 3 52 53  | 3 | 4 1   | 12   | 11  | 2 | ç      | ģ          | 3    | 5   | 2 | Ē   | 1  | -E3  | 64   | ē      | 3 | ų,       | 1.  | q        | 2 | ō   | ĝ   |
| 10 0 2 14 15 5 3 2 34 34 2 6 2 33 -32 10 5 2 15 +15 5 1 3 53 5   | 3 53 53  | 3 | 51    | -15  | 15  | 2 | S      | 1 0        | - 32 | 33  | 2 | 6   | 2  | 34   | 34   | 2      | 3 | 5        | 15  | 14       | 2 | 0   | 10  |

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OBSERVED AND CALCULATED STRUCTURE FACTORS FOR CALINE OF HETHYLATED DECALONE

| н   | К   | L | FO  | FC             | H   | ĸ | Ł   | FC     | FC   | н        | ĸ   | L   | FO  | FC   | н   | ĸ   | L    | FĊ    | FC   | н        | ĸ   | L              | FQ         | FG    |
|-----|-----|---|-----|----------------|-----|---|-----|--------|------|----------|-----|-----|-----|------|-----|-----|------|-------|------|----------|-----|----------------|------------|-------|
| 6   | 1   | 3 | 38  | 39             | 16  | 4 | 3   | 5      | - 3  | 2        | 9   | 3   | 4   | 6    | 7   | ۵   | 4    | 30    | 32   | 3        | 3   | 4              | 45         | -47   |
| 7   | ĩ   | 3 | 62  | 50             | 1   | 5 | 3   | 47     | -48  | 3        | 9   | 3   | 18  | 17   | 8   | 0   | 4    | 4     | - 4  | 4        | 3   | 4              | 26         | 25    |
| 8   | - ī | 3 | 13  | -12            | 2   | 5 | 3   | 52     | -50  | 5        | 9   | 3   | 7   | 6    | 10  | 0   | 6    | 41    | 41   | 5        | 3   | 6              | 76         | -75   |
| ā   | 1   | 3 | 5   | -5             | 3   | 5 | 3   | 42     | -43  | 7        | 9   | 3   | 5   | -1   | 11  | ū   | 4    | 20    | +20  | 6        | 3   | 4              | 35         | -35   |
| 10  | 1   | ž | q   | - 8            | 4   | ŝ | 3   | 7 9    | -77  | Å        | ģ   | 3   | 11  | -13  | 12  | ã   | ÷.   | E     | 6    | 8        | 3   | 4              | 20         | 21    |
| 11  | - F | ĩ | é.  |                | e e | 5 | - i | 1.5    | 15   | ă        | á   | 3   | 25  | 26   | 13  | ñ   | Ĺ.   | 10    | -10  | 10       | 3   | À              | 19         | 20    |
| 16  | -   | 1 | 16  | 16             | é   | ŝ |     | 1.0    | 10   | 10       | ć   | 3   | 7   | - 6  | 14  | ň   | ī.   | 22    | 25   | 11       | 3   | 7              | Ťá         | - ă   |
| 46  | -   | 3 |     | 4 3            | ,   | Ē | -   | 16     | 47   | 11       |     | 7   | 4.4 | 1.   | 46  |     | Ĺ    | 20    | - 30 | 12       | 7   | L.             | + 0        | 10    |
| 10  | -   | 3 | 14  | -1             |     | 5 | 1   |        | 13   | 4.3      | 2   | 2   |     | 7    | 1.5 |     |      | 10    | -30  | 11       | 7   | 7              | <b>1</b> 3 | - 5   |
| 10  | *   | 3 |     |                | 4.4 | É | 5   | è      | 5    | 47       | 0   | 7   | á   |      | 47  |     |      | 16    | -16  | 44       | 7   | 7              |            | - 4 4 |
| 24  | -   | 3 | 6.7 | -1.2           | 4.2 |   | -   | с<br>Е | 2    | 1        | 4 0 | 7   | 7   | 2    | 1.1 |     | 1    |       | -10  |          | 7   | 7              | 1          | -11   |
| 1   | 2   | 3 | 42  | -42            | 14  | 2 | 3   | 2      | 5    | -        | 4.0 | 3   | 24  | - 24 | 10  |     | 7    | 4.6   | 16   | 10       |     | 4              | 2          | - 6   |
| Ę   | 2   | 3 | 13  | 40             | 14  | 2 |     | 2      |      | 2        | 10  | 7   | 22  | -21  | 20  | , v | 7    | 12    | 10   | 4        | 7   | 7              |            | -17   |
| 3   | 2   | 3 | 6.3 | 0 7            |     | 2 | -   | 2      | -/   | 3        | 10  | 3   | 47  | ~~   | 24  | U.  |      | 16    | 10   | -        | 7   | 7              | 17         | -17   |
| 4   | 2   | 3 | 60  | 00             | 7.3 | 2 | ÷   | c      | -4   |          | 10  | 3   | 11  | -10  | U I | -   |      | C 4 6 |      | ۲<br>۲   | 1   | 7              | 33         | -31   |
| 2   | 2   | 5 | 16  | 12             | 1   | 0 | 3   |        |      | 5        | 10  | 3   |     | -7   | 1   | 1   |      | 11    |      |          |     | 7              | 20         | 21    |
| 7   | 2   | 3 | 29  | ~ ~ ~          |     |   | 3   | 5      | -4   | <u> </u> | 10  | 3   | 11  |      |     | 1   |      | ~ 4   | -10  | - 1      |     |                |            |       |
| 8   | 2   | 3 | 4.5 | -41            | 3   |   |     |        | -9   |          | 10  | 3   | 10  | 10   | 5   | 1   | 4    | 2     |      | 2        |     |                | 38         | 39    |
| . 9 | 2   | 3 | 43  | 42             |     | 6 | 3   | 17     | -16  | 11       | 10  | - 3 | 5   | -3   | 4   | 1   | - 44 | 15    | 15   | 6        | - 1 | - <del>1</del> | 14         | 14    |
| 10  | 2   | 3 | 9   | 9              | 5   | 6 | 3   | 7      | 8    | 12       | 10  | 3   | 7   | 5    | 5   | 1   | - 4  | 14    | 10   | <u> </u> | -4  | . 4            | 24         | -24   |
| 11  | 5   | 3 | 4   | 5              | 7   | 6 | 3   | - 14   | 13   | 16       | 10  | 3   | 6   | . 4  | 7   | 1   | - 4- | 52    | 50   | 8        | -4  | - 4            | - 14       | -15   |
| 12  | 2   | 3 | 11  | 11             |     | 6 | 3   | 8      | -7   | 1        | 11  | 3   | 10  | - 18 | 8   | 1   | 4    | 38    | 36   | 9        | 4   | - 4            | 7          | -7    |
| 13  | 2   | 3 | 8   | 7              | 9   | 6 | 3   | 19     | -18  | 2        | 11  | 3   | 7   | 6    | 9   | 1   | 4    | 3     | -4   | 10       | 4   | 4              | 6          | 5     |
| 15  | 2   | 3 | 8   | ç              | 10  | 6 | 3   | 4      | 3    | 3        | 11  | 3   | 10  | 12   | 10  | 1   | 4    | 29    | 30   | 11       | 4   | 4              | 9          | 10    |
| 17  | 2   | 3 | - 6 | <del>-</del> € | 12  | 6 | 3   | 19     | 19   | 4        | 11  | 3   | 6   | 5    | 11  | 1   | - 4  | 22    | -21  | 12       | -4  | - 4            | 8          | -8    |
| 1   | 3   | 3 | 23  | 19             | 13  | e | 3   | 13     | 13   | 5        | 11  | 3   | 6   | 4    | 12  | 1   | 4    | 28    | 21   | 13       | 4   |                | 6          | 7     |
| 2   | 3   | 3 | 15  | 20             | 14  | 5 | 3   | 10     | 9    | - 5      | 11  | 3   | 16  | 17   | 13  | 1   | 4    | 18    | -19  | 14       | 4   | - 4-           | 10         | -10   |
| 3   | 3   | 3 | 73  | -70            | 16  | 6 | 3   | 6      | -7   | 7        | 11  | 3   | 15  | -16  | 15  | 1   | 4    | 11    | -12  | 15       | 4   | 4              | 6          | 4     |
| 4   | 3   | 3 | 49  | -58            | 1   | 7 | 3   | 5      | - 9  | 8        | 11  | 3   | 6   | 8    | 16  | 1   | 4    | 13    | 14   | Q        | 5   | - 4            | 8          | 8     |
| 5   | 3   | 3 | 86  | -84            | 2   | 7 | 3   | 8      | 6    | ġ        | 11  | 3   | 6   | -7   | 18  | 1   | 4    | ç     | 10   | 1        | 5   | - 4            | 7          | £     |
| 6   | 3   | 3 | 27  | 26             | 3   | 7 | 3   | 7      | -8   | 16       | 11  | 3   | 6   | -5   | 19  | 1   | 4    | 10    | 9    | 2        | 5   | - 4            | 7          | -9    |
| 7   | 3   | 3 | 29  | -28            | 5   | 7 | 3   | - 4    | 5    | 11       | 11  | 3   | 9   | -9   | 21  | 1   | 4    | 7     | 6    | 3        | 5   | 4              | 36         | 35    |
| 9   | 3   | 3 | 14  | -14            | 1   | 7 | 3   | ε      | - 6  | 2        | 12  | 3   | 11  | 11   | 9   | 2   | 4    | 28    | -29  | 4        | 5   | - 4            | 57         | 57    |
| 11  | 3   | 3 | 9   | - 8            | 8   | 7 | 3   | 19     | -17  | 3        | 12  | 3   | δ   | 4    | 1   | 2   | 4    | 4     | - 3  | 5        | 5   | 4              | 29         | 29    |
| 13  | 3   | 3 | 12  | -11            | 10  | 7 | 3   | E      | 5    | 4        | 12  | 3   | 7   | 7    | 2   | 2   | 4    | 14    | -15  | 6        | 5   | 4              | 12         | -13   |
| 14  | 3   | 3 | 15  | -16            | 12  | 7 | 3   | 7      | 7    | 5        | 12  | 3   | 11  | -12  | 3   | 2   | -4   | 5     | 6    | 8        | 5   | -4             | 11         | 1 Z   |
| 18  | 3   | 3 | 5   | 3              | 17  | 7 | 3   | 6      | 5    | 7        | 12  | 3   | 7   | -8   | - 4 | 2   | 4    | 17    | -16  | 9        | 5   | 4              | 16         | -14   |
| 20  | 3   | 3 | 6   | £              | 2   | 8 | 3   | 5      | 4    | 9        | 12  | 3   | 6   | -4   | 5   | 2   | 4    | 48    | 50   | 12       | 5   | 4              | 7          | 6     |
| 1   | 4   | 3 | 19  | -19            | 3   | 8 | 3   | 8      | 8    | 10       | 12  | 3   | 5   | 4    | 6   | 2   | 4    | 5     | -5   | 13       | 5   | 4              | 20         | -21   |
| 2   | 4   | 3 | 25  | -24            | e   | 8 | 3   | 9      | - 8  | 11       | 12  | 3   | 7   | 4    | 7   | 2   | 4    | 18    | 19   | 14       | 5   | 4              | 11         | -11   |
| 3   | 4   | 3 | 50  | -51            | 8   | 8 | 3   | 21     | - 22 | 1        | 13  | 3   | 10  | 10   | 8   | 2   | 4    | 51    | -49  | 16       | 5   | 4              | 5          | 2     |
| 4   | 4   | 3 | 44  | 41             | ę   | 8 | 3   | 22     | - 22 | 7        | 13  | 3   | 6   | +5   | 10  | 2   | 4    | 8     | 9    | 18       | 5   | 4              | 7          | -3    |
| 5   | 4   | 3 | 63  | -63            | 10  | 8 | 3   | 26     | -21  | 10       | 13  | 3   | 7   | 6    | 11  | S   | 4    | 6     | -6   | 20       | 5   | 4              | 6          | 0     |
| Ē   | 4   | 3 | 94  | 94             | 11  | 0 | 3   | 27     | -28  | 7        | 14  | 3   | 6   | 5    | 12  | 2   | 4    | 8     | -7   | 0        | 6   | 4              | 13         | 12    |
| 7   | 4   | 3 | 7   | -6             | 12  | 8 | 3   | 7      | - 8  | a        | 0   | 4   | 42  | 42   | 13  | 2   | 4    | 11    | 12   | 1        | 6   | 4              | 21         | -20   |
| 8   | 4   | 3 | 24  | 23             | 13  | ā | 3   | 13     | -13  | 1        | ō   | 4   | 30  | 31   | 19  | 2   | 4    | ε     | - 3  | ž        | 6   | 4              | 4          | - 4   |
| 9   | 4   | 3 | 11  | 11             | 14  | ā | 3   | ç      | - 8  | 2        | Û   | 4   | 74  | 74   | 0   | 3   | 4    | 32    | -31  | 3        | 6   | 4              | 41         | +39   |
| 11  | 4   | 3 | 13  | 11             | 16  | ē | 3   | 7      | -7   | 5        | 0   | 4   | 23  | 26   | 1   | 3   | 4    | 14    | -14  | 4        | 6   | 4              | 23         | 22    |
| 13  | 4   | 3 | 6   | 7              | 1   | 9 | 3   | É      | 7    | 6        | 0   | 4   | 15  | 16   | 2   | 3   | 4    | 6£    | -67  | 5        | 6   | 4              | 39         | -37   |

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DESERVED AND CALCULATED STRUCTURE FACTORS FCR. DXIME OF METHYLATED DECALONE

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| н          | ĸ   | ι   | FQ     | FC    | н  | ĸ   | L  | FC  | FĊ   | н   | ĸ | Ĺ  | FQ  | FC    | н        | K        | L | FC  | FÇ   | нк         | L      | FQ | FC          |
|------------|-----|-----|--------|-------|----|-----|----|-----|------|-----|---|----|-----|-------|----------|----------|---|-----|------|------------|--------|----|-------------|
| 6          | 6   | 4   | 6      | 7     | 12 | 10  | 4  | ç   | 8    | 14  | z | 5  | 11  | 11    | 6        | e        | 5 | 22  | -23  | 5 11       | 5      | 5  | -3          |
| 7          | 6   | 4   | 26     | -26   | 15 | 10  | 4  | 6   | 4    | 16  | 2 | 5  | 11  | 11    | 7        | 6        | 5 | 11  | -12  | 7 11       | 5      | 8  | 4           |
| 9          | 6   | 4   | 6      | 7     | 0  | 11  | 4  | 22  | 23   | 1   | 3 | 5  | 24  | -23   | ä        | 6        | 5 | 11  | 10   | 11 11      | 5      | 7  | -7          |
| 10         | 6   | 4   | 14     | -13   | 1  | 11  | 4  | 8   | 6    | 2   | 3 | 5  | 25  | 26    | 10       | 6        | 5 | 5   | 5    | 12 11      | 5      | 10 | -7          |
| 12         | 6   | 4   | 15     | -19   | 2  | 11  | 4  | 21  | 21   | 3   | 3 | 5  | 42  | 38    | 13       | Ē        | 5 | 10  | 12   | 1 12       | 5      | 9  | = 9         |
| 13         | 6   | 4   | 6      | -6    | 3  | 11  | 4  | Ē   | - 9  | 4   | 3 | 5  | 26  | 26    | 1        | 7        | 5 | 12  | 11   | 5 12       | 5      | 6  | ż           |
| 14         | 6   | 4   | ö      | -9    | 4  | 11  | 4  | ō   | 9    | 6   | 3 | 5  | 36  | - 35  | 2        | 7        | 5 | 6   | -7   | 2 13       | 5      | ă  | 6           |
| 0          | 7   | 4   | ġ      | - 6   | £  | 11  | 4  | é   | ġ    | 7   | 3 | 5  | 6   | -7    | 3        | 7        | 5 | 17  | -18  | 5 13       | 5      | 10 | _ <b>o</b>  |
| 2          | 7   | 4   | 22     | - 22  | 7  | 11  | Å. | q   | ģ    | à   | 3 | 5  | 4   | ŝ     | ŭ        | ż        | ŝ | 12  | 12   | 7 13       | ś      | Â  | -6          |
| 3          | 7   | i.  | 4      | - 4   |    | 11  | 4  | 7   | 7    | tõ  | 3 | 5  | 1.6 | 11    | Ś        | 7        | ŝ | 14  | -15  | 8 13       | 5      | š  | - 1         |
| 6          | 7   | 6   | 13     | =13   | ā  | 11  | 6  | 7   | 5    | 11  | 3 | 5  | 24  | -23   | 6        | 7        | 5 | F   | .7   | 2 14       | ś      | 6  | -5          |
| à          | 7   | i.  |        | c     | 10 | 11  | Ĺ. | 1.3 | +2   | 13  | 3 | 5  | 17  | -17   | 9        | ;        | 5 | · 7 | -7   | 1 1 4      | é      | ĕ  | - /         |
| 10         | 7   | 7   | Á      | + A   | ā  | 12  | 4  | 1.5 | -15  | 14  | 3 | ŝ  | 6   |       | 10       | ÷        | ś | 5   | 6    | 0 0        | 6      | 36 | 11          |
| 11         | 7   | 1   | ,<br>A | ,     | 1  | 12  | 4  | Ĩ,  | 1    | 16  | - | 5  | Ă   | -8    | 11       | ,<br>,   | 5 | é   | a    | 2 0        | ě.     | 6  | 2           |
| 14         | 7   | 2   | š      | -10   | ;  | 12  |    | 10  | -1 a | 10  | 4 | 5  | 12  | -12   | 12       | ÷        | 5 | 15  | 16   | 1 1        | 6      |    | 47          |
| 16         | 7   | L.  | , i    | 10    |    | 12  | 1  | 12  | ĥ    | •   | 2 | ŝ. | 21  | - 1 6 | 11       | ÷        | é |     | - a  |            | č      | 77 | 74          |
| 16         | ÷., | 7   | 6      |       | š  | 12  | 2  | 1 6 | -14  | 1   | 1 | 6  | 20  | - 2 4 | 16       | ÷        | 5 | 4.4 | 12   |            | 6      | 21 | 36          |
| 4.0        | 7   | 2   | ä      | 5     |    | 4.2 | 7  | 1,  | -14  |     | 7 | 5  | 23  | -20   | 16       | ÷,       | 2 | 11  | 10   |            | ç      | 23 | 24          |
| 10         | Å   | 2   | 2      | Ā     | ň  | 13  |    |     | -18  | 6   | 2 | 5  |     | -6    | 17       | ÷        | 5 | 6   | 4    | 7 A        | 6      | 14 | 1           |
| -          |     |     | ě      | -10   |    | 4 7 |    |     | - 10 | 7   | 7 | É  | 4.6 | 4.2   |          |          | é |     | å    |            | ć      | 54 |             |
| ۲<br>۲     | 9   |     | 7      | -10   | 2  | 17  | 2  | ć   | -10  |     |   | 2  | 14  | 13    |          |          | 2 | 27  | - 27 | a u<br>a n | 2      | 20 | 53          |
|            |     |     | 21     | 20    |    | 11  | 7  | Ē   | -10  | å   | 7 | Ē  | 26  | 7     |          | 6        | 2 | 21  | -21  | 10 0       | ç      | 0  | _ <b></b> , |
| č          |     | 7   | 4 8    | -17   |    | 13  | 1  | 5   | -7   | 10  | 7 | 5  | 26  | - 14  | 2        |          | 2 | 24  | - 47 | 14 0       | ç      | 20 | - 21        |
| 2          | 0   | 1   | 10     | -11   |    | 1.2 | 7  | 2   |      | 10  | 7 | 2  | 14  | -14   | 2        | Š        | 2 | 14  | -13  | 11 0       | ~      | 30 | 31          |
|            | R R | 4   | 10     |       |    | 13  |    | Ĕ   | -2   | 12  | 4 | 2  | 17  | - 1 # | 9        | C S      | 2 | 2   | - 22 | 13 0       | 6      | 14 | -14         |
| <i>'</i>   | 3   | 7   |        |       |    | 17  | -  |     |      | 4.7 | 7 | -  | ±', | -10   | <u>'</u> | <u> </u> | 2 | 21  | -20  | 15 0       | 6      | 2  | -           |
| 8          | 0   | 4   | 22     | 23    | 1  | 1   | 2  | 20  | 21   | 13  |   | 2  |     | -9    |          | c        | 2 | 12  | -13  | 10 0       | e      | 2  |             |
|            | 0   | 7   |        | 47    | 4  |     | ž  | 15  | 10   | 24  |   | 2  |     | -0    | 7.0      | c        | 2 |     | 2    | 17 0       | 0      |    | u .         |
| 10         |     |     | 12     | 13    | 2  | - 1 | -  | ž   | 11   | 15  | 7 | 2  | 10  | -10   | 11       | 5        | 2 |     | - 4  | 4 1        | 6      | 10 | 1/          |
| 11         |     | 4   | 0      | -0    | c  | . 1 | -  |     |      | 10  | 4 | 2  | 2   | 1     | 1        | ğ        | 2 | 13  | 15   | 1 1        | ç      | 3  |             |
| 12         | 0   | 1   | 2      | -     | C  | -   | 2  | 11  | 10   | 10  | 4 | 2  | C   | -0    | 2        | ž        | 2 | ,   | -9   | 21         | 6      | 14 | 15          |
| 1          | a   |     |        |       | 11 | 1   | ÷  | 20  | - 21 | 19  | - | 2  |     | - 74  | 4        | 2        | 2 |     |      |            | 0      | 11 | 14          |
| 2          | 4   | 4   | 21     | 21    | 12 | 1   | 2  | 36  | - 31 | 1   | 2 | 2  | 34  | - 34  | 5        | 2        | 2 | 15  | 15   | 5 1        | c      |    |             |
| 1          | 4   | 4   | 19     | 19    | 13 | 1   | -  | 11  | 11   | 4   | 2 | 2  | 20  | -20   | •        | 7        | 2 |     |      |            | Ş      | 32 | 31          |
| 2          | 3   | 4   |        | _ 1 0 | 14 | 1   | -  |     | - 2  | 3   | 2 | 2  | 20  |       |          | 3        | 2 | 24  | 27   |            | ç      | 20 | <u> </u>    |
| 5          |     |     | 11     | -10   | 13 | 1   | -  |     |      | 2   | 2 | 2  | 24  | -19   |          |          | 2 | 7   | - 4  |            | ç      | 47 | 40          |
| ſ,         | 3   | 4   | 21     | - 22  | 10 | -   | -  |     | - 0  |     | 2 | 2  | 10  | 10    | 10       | 40       | 2 | 21  | 20   | 10 1       | 2      | 12 | 11          |
| , <u>c</u> |     |     | 21     | - 22  | 11 | 1   | 2  | 11  |      |     | 2 | 2  | 10  | 10    | -        | 10       | 2 | 21  | 20   | 11 1       |        | 14 | -13         |
| 10         | 3   | 4   |        |       | 1  | 2   |    | 12  | -13  |     | 2 | 2  | ž   |       |          | 10       | 2 | ç   | -6   | 12 1       | 6      | 14 | 15          |
| 11         | 3   | 4   |        | 4     |    | 2   | 1  | 15  | 10   | 11  | 2 | 2  | 2   | -0    | 2        | 14       | 2 |     | 2    | 15 1       | , o    | 2  | - {         |
| 14         | 9   | 4   | a      | e     | 3  | 4   | -  | ~   | 20   | 12  | 2 | 2  |     |       | 0        | 10       | 2 | 14  | -13  | 19 1       | 6      |    |             |
| 14         | . 9 | - 4 | 5      | 1     | 4  | Z   | 1  | E   |      | 14  | 5 | 2  | 17  | 17    | ő        | 10       | 5 | 4   | -4   | 2 2        | 6      | 13 | +20         |
| 0          | 10  | 4   | 37     | 57    | 5  | 2   | 2  | 80  | 81   | 15  | 2 | 2  | 07  | 3     |          | 10       | 2 | 5   | 3    | 5 2        | 6      | 5  | 5           |
| 1          | 10  | 4   | 15     | 17    |    | 2   | -  | 22  | 52   | 10  | 2 | 2  |     |       | 11       | 14       | 2 |     | 4    |            | с<br>, |    |             |
| 2          | 10  | 4   | 9      | ç     | 5  | Z   | 5  | 11  | 12   | 17  | 5 | 2  | 6   | -2    | 12       | 10       | 2 | 2   | 1    | 2 Z        | 6      | 10 | 10          |
| 3          | 10  | 4   | 22     | 23    | ç  | 2   | Ĩ  | 16  | 15   | 1   | 6 | 2  | 15  | 15    | 15       | 10       | 2 | 5   | 5    | <u>r</u> 2 | E .    | 33 | 33          |
| 6          | 10  | 4   | 17     | -10   | 10 | 2   | 1  | 22  | 23   | 2   | ÷ | 2  | 10  | - 10  | 14       | 10       | 2 | 8   |      |            | e<br>ć | 51 | 32          |
| 8          | 10  | 4   | 7      | -1    | 11 | 2   | 1  | E   | -6   |     | 6 | 2  |     | - 5   | 2        | 11       | 2 | 14  | -15  | 10 2       | t      | 24 | -24         |
| 9          | 10  | 4   | 7      | 6     | 12 | - 2 | 5  | 11  | 10   | 4   | 6 | 5  | Z7  | - 26  | - 4      | 11       | 5 | 5   | -4   | 1Z Z       | 6      | 8  | 9           |

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### DESERVEC AND CALCULATED STRUCTURE FACTORS FOR DOXINE OF HETHYLATED DECALORE

| н  | ĸ | ι | FO | FC   | н   | к  | L | FC | FC  | н  | к  | Ļ. | FO | FC   | н  | ĸ | r | FC  | FC  | нк     | L | FC | FC  |
|----|---|---|----|------|-----|----|---|----|-----|----|----|----|----|------|----|---|---|-----|-----|--------|---|----|-----|
| 13 | 2 | 6 | 15 | -16  | 8   | 6  | E | 10 | - 9 | 2  | 11 | 6  | 12 | 13   | 17 | 3 | 7 | 6   | 4   | 29     | 7 | 14 | 14  |
| 16 | z | 6 | 6  | 1    | 14  | 6  | 6 | 5  | ۵   | 3  | 11 | 6  | 13 | 14   | 1  | 4 | 7 | 17  | -18 | 89     | 7 | 5  | 2   |
| Ō  | 3 | 6 | 14 | -13  | 16  | 6  | E | 6  | ~ 3 | 6  | 11 | 6  | 8  | 6    | 5  | 4 | 7 | 10  | -9  | ġ ġ    | 7 | 6  | 7   |
| 1  | 3 | E | 4  | - 4  | 0   | 7  | E | 20 | 21  | 11 | 11 | 6  | 6  | 0    | 6  | 4 | 7 | 6   | -6  | 10 9   | 7 | 6  | 5   |
| 2  | 3 | 6 | 17 | -19  | 1   | 7  | € | 28 | -28 | 12 | 11 | 6  | 7  | 5    | 7  | 4 | 7 | 5   | 6   | 13 9   | 7 | 6  | 1   |
| 3  | 3 | 6 | 16 | -16  | 2   | 7  | e | 18 | 20  | 3  | 12 | 6  | 6  | 5    | 8  | 4 | 7 | E   | -2  | 1 10   | 7 | 21 | 21  |
| 4  | 3 | 6 | 10 | -10  | 3   | 7  | £ | 16 | -16 | 4  | 12 | 6  | 6  | -4   | 9  | 4 | 7 | 10  | 9   | 3 10   | 7 | 16 | 16  |
| 5  | 3 | 6 | 11 | -10  | 4   | 7  | E | 11 | -12 | 5  | 12 | 6  | 7  | 7    | 11 | 4 | 7 | 10  | 10  | 4 10   | 7 | 8  | 7   |
| 6  | 3 | 6 | 6  | 8    | 5   | 7  | E | 4  | 2   | 7  | 12 | 6  | 7  | 8    | 13 | 4 | 7 | 11  | -11 | 5 10   | 7 | 6  | 6   |
| 19 | 3 | 6 | 7  | - 8  | £   | 7  | E | 28 | -19 | 8  | 12 | 6  | 7  | 2    | 14 | 4 | 7 | 6   | -7  | 6 10   | 7 | 7  | 8   |
| 11 | 3 | 6 | 6  | E    | 8   | 7  | e | ę  | - 8 | 9  | 12 | 6  | 7  | 4    | 15 | 4 | 7 | 11  | -10 | 7 10   | 7 | 8  | 8   |
| 13 | 3 | 6 | 23 | 25   | 10  | 7  | 6 | ġ  | -10 | 10 | 12 | 6  | 8  | 7    | 2  | 5 | 7 | 16  | -16 | 10 10  | 7 | 8  | 7   |
| 14 | 3 | 6 | 6  | £    | 11  | 7  | E | 7  | ~ 3 | G  | 13 | 6  | 9  | -8   | 3  | 5 | 7 | `_4 | -4  | 12 10  | 7 | e  | 6   |
| 0  | 4 | 6 | 8  | 8    | 12  | 7  | e | 12 | -12 | 2  | 13 | 6  | 8  | -8   | 4  | 5 | 7 | 21  | -22 | 1 11   | 7 | 11 | -11 |
| 1  | 4 | 6 | 11 | 11   | 13  | 7  | 6 | 8  | ~ 8 | 1  | 1  | 7  | 6  | -9   | 5  | 5 | 7 | - 4 | - 4 | 2 11   | 7 | 7  | Ē   |
| 2  | 4 | 6 | 3  | - 9  | 14  | 7  | £ | 6  | -6  | 2  | 1  | 7  | 10 | 9    | 6  | 5 | 7 | 5   | 3   | 3 11   | 7 | 5  | -5  |
| 3  | 4 | 6 | 24 | -24  | 15  | 7  | E | 8  | ~7  | 3  | 1  | 7  | 8  | -8   | 9  | 5 | 7 | 8   | - 4 | - 4 11 | 7 | 5  | 5   |
| 4  | 4 | 6 | 34 | -35  | 0   | 8  | E | 39 | -42 | 4  | 1  | 7  | 9  | 9    | 11 | 5 | 7 | 6   | -7  | 1 12   | 7 | 6  | 0   |
| 5  | 4 | 6 | 44 | -42  | 1   | 8  | ŧ | 17 | -17 | 5  | 1  | 7  | 10 | 11   | 13 | 5 | 7 | 9   | -9  | 7 12   | 7 | 6  | 4   |
| 6  | 4 | 6 | 27 | -28  | 2   | 8  | £ | 13 | 12  | 6  | 1  | 7  | 22 | 21   | 15 | 5 | 7 | 7   | -7  | 2 13   | 7 | 8  | 8   |
| 7  | 4 | Ê | 13 | -10  | 3   | 8  | 6 | 29 | -29 | 8  | 1  | 7  | 15 | -16  | 17 | 5 | 7 | £   | -6  | 4 13   | 7 | 7  | 3   |
| 8  | 4 | 6 | 13 | -14  | 4   | 8  | E | 11 | 11  | 9  | 1  | 7  | 17 | 17   | 1  | 6 | 7 | 15  | -16 | 9 0    | 8 | 12 | -10 |
| 9  | 4 | 6 | 12 | -12  | 6   | 8  | £ | 13 | 15  | 10 | 1  | 7  | 23 | - 25 | 3  | 6 | 7 | 25  | 31  | 1 0    | 8 | 12 | 11  |
| 10 | 4 | 6 | 17 | -1E  | 7   | 8  | E | ç  | -10 | 11 | 1  | 7  | 9  | 9    | 4  | 6 | 7 | 19  | -19 | 30     | â | 21 | 21  |
| 11 | 4 | 6 | 5  | - 3  | e   | 8  | 6 | ġ  | 8   | 13 | 1  | 7  | 4  | 5    | 5  | ε | 7 | 8   | 8   | 4 0    | 6 | 4  | 4   |
| 12 | 4 | 6 | 13 | 13   | 10  | 8  | E | 7  | 8   | 1  | 2  | 7  | 17 | 15   | 8  | ε | 7 | 10  | 10  | 70     | 8 | 34 | -36 |
| 13 | 4 | 6 | 3  | 8    | 12  | 8  | E | 5  | - 3 | 2  | 2  | 7  | 11 | -11  | 13 | £ | 7 | 8   | -5  | 8 Ū    | 8 | 22 | -23 |
| 16 | 4 | 6 | 7  | - £  | 15  |    | E | £  | 3   | 3  | 2  | 7  | 5  | 7    | 15 | € | 7 | 7   | 3   | 90     | 8 | 5  | -5  |
| 0  | 5 | 6 | 37 | - 37 | 16  | 8  | E | 7  | 3   | 4  | 2  | 7  | 3  | -3   | 1  | 7 | 7 | 32  | 33  | 10 0   | 8 | 15 | 14  |
| 1  | 5 | 6 | 4  | - 4  | 0   | 9  | £ | 5  | - 2 | 5  | 2  | 7  | 7  | 7    | 2  | 7 | 7 | 6   | 7   | 11 0   | 8 | 9  | +9  |
| 2  | 5 | 6 | 35 | -35  | 1   | 9  | e | 13 | -13 | 6  | 2  | 7  | 21 | -21  | 3  | 7 | 7 | 21  | 21  | 15 0   | 8 | 7  | ÷5  |
| 3  | 5 | 6 | 30 | 29   | 2   | 9  | E | 14 | 15  | 8  | 2  | 7  | 29 | - 30 | 4  | 7 | 7 | 25  | -27 | 19 Q   | 8 | 7  | 3   |
| 4  | 5 | 6 | 17 | -16  | 3   | 9  | E | 8  | ~8  | 10 | 2  | 7  | 10 | -10  | 5  | 7 | 7 | 9   | 7   | 21     | 8 | 14 | 14  |
| 5  | 5 | ٤ | 31 | 31   | - 4 | 9  | 6 | 11 | 10  | 11 | 2  | 7  | 36 | 37   | 6  | 7 | 7 | 7   | -8  | J 1    | 8 | 3  | ÷ 3 |
| 6  | 5 | 6 | 13 | 12   | 5   | 9  | 6 | 7  | ~5  | 13 | 2  | 7  | 16 | 18   | 7  | 7 | 7 | 4   | -6  | 4 1    | 8 | 7  | e.  |
| 7  | 5 | 6 | 7  | - 8  | Ģ   | 9  | € | 5  | 2   | 14 | 2  | 7  | 5  | 1    | 9  | 7 | 7 | E   | -4  | 51     | 8 | 4  | 2   |
| 8  | 5 | 6 | 13 | 13   | 10  | 9  | E | 8  | - 8 | 15 | 2  | 7  | 7  | 7    | 11 | 7 | 7 | 5   | 2   | 61     | 8 | 14 | 16  |
| 9  | 5 | 6 | 3  | ÷9   | 13  | 9  | £ | 7  | -4  | 1  | 3  | 7  | 6  | -7   | 1  | 8 | 7 | 23  | -24 | 5 1    | 8 | 31 | 31  |
| 10 | 5 | 6 | 8  | 8    | 15  | 9  | E | 7  | - 8 | 3  | 3  | 7  | 13 | -13  | 2  | 8 | 7 | 17  | 16  | 91     | ð | 19 | 18  |
| 12 | 5 | 6 | 7  | 9    | Q   | 10 | E | 10 | -11 | 4  | 3  | 7  | 8  | 7    | 3  | 8 | 7 | 6   | -7  | 10 1   | 8 | 29 | 29  |
| 13 | 5 | 6 | 13 | 12   | 2   | 16 | e | ç  | 9   | 6  | 3  | 7  | 13 | 12   | 4  | 8 | 7 | 9   | 9   | 11 1   | 8 | 12 | 13  |
| 15 | 5 | e | 5  | 2    | 3   | 10 | ŧ | £  | 6   | 7  | 3  | 7  | 12 | -12  | 5  | 8 | 7 | 15  | -16 | 13 1   | 8 | 5  | 3   |
| 18 | 5 | 6 | 6  | 1    | 5   | 19 | € | 10 | 10  | 9  | 3  | 7  | 10 | -8   | 6  | 3 | 7 | 10  | 11  | 16 1   | Ľ | 6  | 4   |
| 1  | 6 | 6 | э  | 10   | 7   | 10 | € | 5  | ~ 2 | 10 | 3  | 7  | 17 | 17   | 7  | 8 | 7 | 11  | -12 | 17 1   | e | 5  | 4   |
| 2  | 6 | 6 | 22 | 22   | 8   | 10 | E | 7  | ~8  | 11 | 3  | 7  | 5  | -5   | 9  | 3 | 7 | s   | -8  | 0 2    | 8 | 10 | -13 |
| 4  | 6 | 6 | 15 | -15  | 13  | 10 | E | 8  | -5  | 12 | 3  | 7  | 17 | 16   | 10 | 8 | 7 | 6   | -5  | 52     | 8 | 8  | 7   |
| 6  | 6 | 6 | 18 | -19  | Q   | 11 | E | 15 | 15  | 14 | 3  | 7  | 8  | -7   | 13 | 8 | 7 | 8   | -6  | 62     | 8 | 11 | 10  |
| 7  | 6 | 6 | 3  | - 8  | 1   | 11 | ε | 5  | 3   | 15 | 3  | 7  | 5  | 5    | 1  | 9 | 7 | 10  | -10 | 72     | 8 | E  | e   |

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### CESERVED AND CALCULATED STRUCTURE FACTORS FOR OXINE CF METHYLATED DECALONE

| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | н      | к   | Ļ        | FC  | FC       | н   | ĸ  | L   | FC       | FC    | н   | к        | Ļ  | FQ | FC   | н   | K | L. | FC  | FC   | нк          | L  | FQ  | ₽C  |
|--|--------|-----|----------|-----|----------|-----|----|-----|----------|-------|-----|----------|----|----|------|-----|---|----|-----|------|-------------|----|-----|-----|
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 8      | 2   | 8        | 9   | Ģ        | 2   | 7  | 8   | 11       | -10   | 8   | 3        | 9  | 16 | -15  | 4   | Q | 10 | £   | -5   | 14 5        | 10 | 7   | - 4 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 9      | 2   | 8        | 10  | 10       | 3   | 7  | . 8 | 21       | 21    | 9   | 3        | 9  | 11 | -10  | 5   | 0 | 10 | 11  | 19   | 06          | 10 | 16  | 16  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 10     | Ż   | 8        | 31  | 33       | 4   | 7  | 8   | 24       | - 25  | 10  | 3        | 9  | 7  | -6   | 6   | 0 | 10 | 11  | 10   | 16          | 10 | 5   | 5   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 11     | 2   | 8        | 14  | -14      | 5   | 7  | 8   | 7        | 8     | 12  | 3        | 9  | 7  | -5   | 7   | 0 | 10 | e   | -6   | 26          | 10 | 17  | 17  |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 14     | 2   | 8        | 7   | - 4      | e   | 7  | 8   | 5        | - 4   | 14  | 3        | 9  | 5  | 3    | 8   | 8 | 10 | 9   | -12  | 46          | 18 | 8   | 9   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 16     | 2   | e        | 6   | -7       |     | 7  | E   | 10       | - 9   | 1   | 4        | 9  | 13 | -14  | 9   | ۵ | 10 | 14  | -15  | 07          | 10 | 12  | -13 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 18     | 2   | 8        | 7   | - 5      | 12  | 7  | - E | 7        | -5    | 2   | 4        | 9  | 11 | -12  | 18  | ۵ | 10 | 1 E | -16  | 1 7         | 10 | 5   | - 4 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 0      | 3   | 8        | 7   | - 7      | 13  | 7  | e   | E        | - 2   | 3   | 4        | 9  | 21 | - 21 | 15  | ß | 10 | 12  | -11  | 27          | 10 | 12  | -11 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 2      | 3   | 8        | 15  | 15       | - 0 | 8  | 8   | 24       | 23    | 5   | 4        | 9  | 9  | -10  | 16  | 0 | 10 | E   | -4   | 67          | 10 | 11  | -10 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 3      | 3   | 8        | 21  | -21      | 1   | 8  | 8   | 12       | -11   | 12  | 4        | 9  | 5  | 3    | ٥   | 1 | 10 | 9   | 9    | 10 7        | 10 | 5   | 1   |
|  | 5      | 3   | 8        | 5   | - 4      | - 4 | 8  | e   | 5        | -1    | 13  | - 4      | 9  | 6  | -1   | 1   | 1 | 10 | 4   | -2   | 11 7        | 10 | 6   | 1   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 6      | 3   | 8        | 7   | Ģ        | 13  | 8  | 8   | 7        | 4     | 15  | 4        | 9  | 6  | 4    | 2   | 1 | 10 | 8   | 7    | 66          | 16 | 14  | 14  |
| 9   3   8   24   23   2   9   8   7   -7   2   5   9   10   10   10   10   7   -7   7   6   1   10   10   7   -7   7   6   1   10   10   7   -7   7   1   13   16   -6   6   9   10   5   -2     11   3   8   6   3   0   10   1   11   11   4   5   9   10   -7   7   1   10   11   -11   9   9   10   -7   7   10   11   11   11   11   11   11   10   6   6   6   10   10   10   7   -6   11   10   9   7   -6   11   10   9   7   -6   11   10   9   7   -6   11   10   7   -7   7   7   7   7   7   7   7   7   11   10   10 <td< td=""><td>7</td><td>3</td><td>8</td><td>5</td><td>3</td><td>0</td><td>9</td><td>. 8</td><td>14</td><td>-14</td><td>1</td><td>5</td><td>9</td><td>7</td><td>~9</td><td>4</td><td>1</td><td>10</td><td>13</td><td>13</td><td>98</td><td>10</td><td>6</td><td>1</td></td<>   | 7      | 3   | 8        | 5   | 3        | 0   | 9  | . 8 | 14       | -14   | 1   | 5        | 9  | 7  | ~9   | 4   | 1 | 10 | 13  | 13   | 98          | 10 | 6   | 1   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 9      | 3   | 8        | 24  | 23       | Ż   | 9  | 8   | 7        | -7    | 2   | 5        | 9  | 10 | -11  | 5   | 1 | 10 | 10  | -9   | 19          | 10 | 7   | +7  |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 10     | 3   | 8        | 5   | 4        | 4   | 9  | 3   | £        | 6     | 3   | 5        | 9  | 7  | -7   | 6   | 1 | 10 | ç   | 7    | 39          | 10 | 5   | • 2 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 11     | 3   | 8        | 6   | 8        | 0   | 10 | 8   | 13       | 11    | - 4 | 5        | 9  | 6  | 7    | 7   | 1 | 1] | 16  | -16  | 49          | 10 | 5   | 3   |
|  | 12     | 3   | 8        | 11  | -11      | 3   | 10 | 8   | 6        | 2     | 5   | 5        | 9  | 10 | -8   | 8   | 1 | 10 | e   | 6    | 69          | 10 | 6   | 1   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 14     | 3   | 8        | 5   | e        | 0   | 11 |     | 13       | 13    | 6   | 5        | 9  | 11 | -10  | 9   | 1 | 10 | 11  | -11  | 99          | 10 | 7   | 4   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | G      | 4   | 8        | 16  | 15       | 2   | 11 | 8   | ė        | 9     | 9   | 5        | 9  | 7  | -6   | 11  | 1 | 10 | £   | a    | <b>ũ</b> 1ũ | 10 | 18  | -19 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 1      | 4   | 8        | 6   | - E      | 4   | 11 | 8   | 18       | 11    | 11  | 5        | 9  | 7  | -6   | 13  | 1 | 10 | 5   | - 3  | 2 10        | 10 | 11  | -11 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 3      | 4   | 8        | 5   | - E      | 7   | 11 | 3   | 7        | 2     | 13  | 5        | 9  | 7  | -5   | 16  | 1 | 10 | 9   | 7    | 5 10        | 10 | 7   | - 8 |
| 6   4   8   9   -7   6   2   2   10   5   -4   1   1   11   9   -9     7   4   8   12   -22   5   1   1   9   7   -6   2   2   10   14   -16   4   1   11   7   -5     9   4   8   12   12   1   9   8   -6   3   2   10   14   -16   4   1   11   7   -5     9   4   8   12   12   7   1   2   2   3   1   7   9   13   12   8   2   10   14   11   11   11   11   11   11   11   11   11   7   9   15   4   11   11   11   7   11   11   11   10   14   11   11   11   11   11   11   11   11   11   11   11   11   11   11   11   | 5      | 4   | 8        | 6   | - 6      | 2   | 12 | 8   | 9        | -5    | 2   | £        | 9  | 18 | -18  | 0   | 2 | 10 | 18  | -16  | 1 11        | 10 | 6   | 5   |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$  | 6      | 4   | 8        | 9   | -7       | e   | 12 | 8   | 7        | 1     | 3   | 6        | 9  | 7  | -6   | 2   | 2 | 10 | 5   | -4   | 1 1         | 11 | 9   | - 9 |
| a   a   a   i   c   a   -a   i   i   c   9   5   -a   4   2   10   c   -a   5   11   c   c   5   5   1   11   | 7      | £., | 8        | 10  | <u> </u> | 1   | 1  | ç   | 7        | - 7   | 8   | 5        | 9  | 8  | -8   | 3   | 2 | 10 | 14  | -16  | 4 1         | 11 | 7   | - 5 |
| 9   4   8   12   12   7   1   9   21   22   14   6   9   7   3   6   2   10   11   11   7   1   11   5   -5     10   4   8   3   -8   8   1   5   25   30   1   7   9   13   12   8   2   10   16   19   5   1   11   | ę      | 4   | 8        | 22  | -22      | Ę   | 1  | ç   | 8        | - 8   | 11  | ε        | 9  | 5  | -6   | 4   | 2 | 10 | £   | -6   | 51          | 11 | E   | e   |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 9      | 4   | 8        | 12  | 12       |     | 1  | ç   | 21       | 22    | 14  | 6        | 9  | .7 | 3    | 6   | 2 | 10 | 11  | - 11 | 7 1         | 11 | 5   | - 5 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 10     | 4   | <u>.</u> |     | - 8      | 8   | 1  | 5   | 29       | 30    | 1   | <u> </u> | 9  | 15 | 12   | 8   | 2 | 10 | 18  | 19   | 5 1         | 11 | 11  | -13 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 12     | 4   | 9        | 12  | -12      | 9   | 1  | 5   | . 7      | 8     | z   | 7        | 9  | 5  | -5   | 9   | ž | 10 |     | -5   | 9 1         | 11 | 8   |     |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 1      | 5   |          | 13  | 13       | 10  | 1  | ŝ   | 12       | 11    | 5   | <u>'</u> | 9  | 18 | 19   | 10  | ž | 10 | ġ   | 8    | 1 2         | 11 | 15  | 11  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | 3      | 5   | 4        | 12  | -1.      | 14  | 1  | 2   | t        | 4     | 2   |          | 9  | 2  |      | 11  | 4 | 10 | 2   | 4    | 3 2         | 11 |     |     |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | -      | 2   | e        | 11  | -1u      | 11  | 1  | 2   | c .      | -0    |     | 4        | 9  | ~  | -7   | 13  | 4 | 10 | ç   | 0    | 4 4         | 11 |     | -11 |
| e   5   e   1   2   2   6   -5   1   | 2      | 5   | 8        | 12  | -14      | 1   | 2  | 2   | e e      |       |     | 4        | 3  | 0  | 4    | 1   | 3 | 10 |     | - 5  | 6 C         | 11 | 14  | 13  |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$   | с<br>7 | 2   | с        | 14  | 24       |     | 2  | ž   |          | -0    | 13  |          | 3  |    | 47   | 4   | 3 | 10 | 17  | 1/   | 11 2        | 11 |     | 1 2 |
| 13   5   6   1   5   12   12   13   14   11   1   15   16   1   15   16   1   16   1   16   1   16   1   16   1   16   1   16   1   16   1   16   1   16   1   17   16   1   19   9   6   -7   9   3   10   10   7   3   3   11   12   14   11   17   16   4   9   9   6   -5   15   3   10   10   7   3   3   11   11   13   11   11   17   14   10   5   5   5   3   11 <td< td=""><td>í<br/>a</td><td>2</td><td>а<br/>а</td><td>7</td><td></td><td>3</td><td>5</td><td>2</td><td>47</td><td>_ + +</td><td>÷.</td><td>-</td><td>0</td><td>14</td><td>1.0</td><td>27</td><td>3</td><td>10</td><td>7</td><td>-0</td><td>1 2</td><td>11</td><td>11</td><td>15</td></td<>                                    | í<br>a | 2   | а<br>а   | 7   |          | 3   | 5  | 2   | 47       | _ + + | ÷.  | -        | 0  | 14 | 1.0  | 27  | 3 | 10 | 7   | -0   | 1 2         | 11 | 11  | 15  |
| 13   5   6   6   1   5   7   7   5   10   12   12   11   14   14   16   5   8   8   7   6   2   9   9   6   -5   15   3   10   10   7   3   3   11   8   7     16   5   8   8   -7   6   2   9   9   6   -5   15   3   10   10   7   3   3   11   8   7     2   6   8   25   -27   9   2   9   6   -6   5   4   10   9   9   7   3   11   8   7     3   6   8   11   11   10   2   9   6   -6   5   4   10   19   9   6   -6   6   4   10   19   -21   3   3   11   6   -4   6   6   4   10   10   -10   1   10   10   | 47     | 2   | 2        | ć   |          | 4   | 2  | ž   | 10       | -13   |     | 0        | 2  | 11 | -7   | , r | 3 | 10 | 12  | -12  | 1 2         | 11 | 12  |     |
| 10   5   6   11   -11   7   2   5   7   16   16   10 </td <td>46</td> <td>5</td> <td>Q<br/></td> <td></td> <td>-7</td> <td>-</td> <td>5</td> <td>è</td> <td>2 U<br/>2</td> <td>20</td> <td>2</td> <td>2</td> <td>ä</td> <td>Å</td> <td>-7</td> <td>16</td> <td>1</td> <td>10</td> <td>10</td> <td>-12</td> <td>23</td> <td>11</td> <td>A A</td> <td>17</td> | 46     | 5   | Q<br>    |     | -7       | -   | 5  | è   | 2 U<br>2 | 20    | 2   | 2        | ä  | Å  | -7   | 16  | 1 | 10 | 10  | -12  | 23          | 11 | A A | 17  |
| 1    | 10     | é   |          | 4.4 |          |     | -  | Ē   |          | 16    |     |          | ő  | 7  | - 7  |     |   | 10 |     | -    | <b>5</b> 3  | ** | • • | • 3 |
| 3   6   8   11   10   2   6   -3   6   9   9   7   -6   5   4   10   9   9   7   3   11   6   -4     6   6   9   11   12   2   5   7   7   10   9   9   7   -6   5   4   10   19   -21   5   3   11   6   -4     7   6   8   6   -6   10   19   -21   5   3   11   5   4     7   6   8   6   -6   -6   6   4   10   10   -10   1   4   11   11   12     8   6   8   5   -2   14   2   6   11   0   8   10   10   -10   1   4   11   11   12   11   11   12   11   11   11   12   11   11   11   12   11   11   11   12   11  | 2      | 2   | a<br>a   | 26  | -27      | 6   | 5  | è   |          | 10    | -   | ā        | ā  | ś  | -2   | 5   | - | 10 | ő   | a a  | 6 3         | 11 | Â   | 7   |
| 6   6   6   9   11   12   2   7   7   10   9   9   6   -6   6   4   10   19   -21   5   3   11   5   4     7   6   8   9   11   12   2   5   7   7   10   9   9   6   -6   6   4   10   19   -21   5   3   11   5   4     7   6   8   6   +6   13   2   5   6   6   10   9   10   10   10   10   -10   1   4   11   11   12   11   12   11   11   12   11   11   12   11   11   12   11   11   12   11   11   11   12   11   11   12   11   11   12   11   11   12   11   12   11   11   12   11   12   11   11   12   11   12   11   11   11  | 7      | 4   |          | 4.1 | - 67     | 10  | 2  | è   | 6        | - 3   | ŝ   | å        | á  | 2  | - 6  | 5   | - | 10 | á   | á    | . 7 3       | 11 | ĥ   |     |
| 7   6   6   -6   1   10   9   16   7   4   10   1   7   6   1   10   9   16   7   4   10   10   7   11   7   6   10   4   10   10   7   6   10   4   10   10   -10   1   4   11   11   12   11   10   6   10   9   16   7   4   10   10   -10   1   4   11   11   12   11   11   12   11   11   11   12   11   11   11   12   11   14   11   11   12   11   11   12   11   11   12   11   15   15   15   15   15   15   16   6   -6   6   4   11   15   15   15   15   16   6   -7   12   11   15   15   15   16   6   -6   6   4   11   6   -7   5 <td< td=""><td>5</td><td>6</td><td></td><td></td><td>11</td><td>12</td><td>2</td><td>č</td><td>7</td><td>7</td><td>10</td><td>ć</td><td>å</td><td>ś</td><td>-6</td><td>ĥ</td><td>2</td><td>10</td><td>19</td><td>-21</td><td>8 3</td><td>11</td><td>š</td><td>Ĩ.</td></td<>  | 5      | 6   |          |     | 11       | 12  | 2  | č   | 7        | 7     | 10  | ć        | å  | ś  | -6   | ĥ   | 2 | 10 | 19  | -21  | 8 3         | 11 | š   | Ĩ.  |
| 8   6   8   5   -2   14   2   1   10   8   10   9   7   6   10   4   10   10   -10   1   4   11   11   12     10   6   8   5   -3   1   3   9   7   7   9   10   9   6   5   4   5   10   12   11   2   4   11   15   15     11   6   8   3   7   2   3   6   9   2   11   9   6   -5   5   5   10   6   -6   6   4   11   6   -7     16   6   4   7   4   3   14   14   3   11   9   6   -5   5   5   10   6   -6   6   4   11   6   -7     16   6   4   7   4   3   11   3   4   11   6   0   11   14   14   11  | ž      | ň   | Ă        | é   | ÷÷       | 13  | 5  | ć   | Ė        |       | 1   | 10       | á  | 19 | 18   | 7   | 4 | 10 |     | 7    | 12 3        | 11 | 7   | 6   |
| 10   6   8   5   -3   1   3   6   7   7   9   10   9   6   5   4   5   10   12   11   2   4   11   15   15     11   6   8   3   7   2   3   9   6   10   12   11   2   4   11   15   15     11   6   8   3   7   2   3   9   6   10   12   11   2   4   11   15   15     16   6   8   7   7   2   3   9   2   11   9   6   3   6   5   10   14   -14   10   10   7   7   3   5   11   14   -14   10   11   7   7   3   5   11   14   -14   11   10   10   7   5   13   5   10   5   4   5   11   14   -11   11   14   -11  | 8      | 6   | ă        | s   | -2       | 14  | 2  | é   | 11       | 10    | ŝ   | ĩŏ       | é  | Ť  | Ĩ    | 10  | 4 | 10 | 10  | -10  | 1 4         | 11 | 11  | 12  |
| 11   6   8   3   7   2   3   9   2   11   9   6   -5   5   5   10   6   -6   6   4   11   6   -7     16   6   8   7   7   3   5   11   9   6   -5   5   5   10   14   -14   13   4   11   6   -7     16   6   8   7   7   3   5   11   10   10   10   14   -14   13   4   11   6   -7   6   -5   5   10   14   -14   13   4   11   6   -7   6   -5   10   14   -14   13   4   11   6   -7   6   -5   5   10   14   -14   13   4   11   6   -7   6   -5   5   10   14   -14   14   14   -14   14   -14   13   4   11   -14   14   -14   10   1  | ٩ñ     | 6   | Ă        | ś   | -3       |     | 7  | ċ   | 7        | -7    | å   | 10       | 9  | 6  | 5    | - 4 | Ę | 10 | 12  | 11   | 2 4         | 11 | 15  | 15  |
| 16 6 8 7 4 3 9 11 9 6 3 6 5 10 14 -14 13 4 11 6 0   0 7 8 8 5 3 5 10 14 -14 13 4 11 6 0   0 7 8 8 5 3 5 10 14 -14 13 4 11 6   1 7 8 8 5 3 5 14 -14 1 0 10 7 5 13 5 10 5 4 4 5 11 14 -14   1 7 8 24 25 6 3 5 14 -14 1 0 10 7 5 13 5 10 5 4 4 5 11 14 -11  | 11     | 6   | ā        | จ้  | 7        | 2   | 3  | c   | é        | ģ     | 2   | 11       | 9  | 6  | -5   | 5   | 5 | 10 | 6   | -6   | 64          | 11 | 6   | -7  |
| 0 7 8 9 8 5 3 5 5 -4 0 0 10 8 -9 7 5 10 7 7 3 5 11 14 -14<br>1 7 8 24 25 6 3 5 14 -14 1 0 10 7 5 13 5 10 5 4 4 5 11 10 -11   | 16     | 6   | a        | Á   | 7        | ŭ   | 3  | ç   | 14       | 14    | 3   | 11       | ģ  | 6  | 3    | 6   | 5 | 10 | 14  | -14  | 13 4        | 11 | 6   | Ċ   |
| 1 7 8 24 25 E 3 5 14 -14 1 0 10 7 5 13 5 10 5 4 4 5 11 14 -11  | õ      | 7   | ě        |     | ė        | Ę   | ž  | ç   | Ē        | -4    | ā   | Ō        | 10 | 8  | -9   | 7   | 5 | 13 | 7   | 7    | 3 5         | 11 | 14  | -14 |
|  | 1      | 7   | Â.       | 24  | 25       | Ē   | 3  | ç   | 14       | -14   | 1   | Ō        | 10 | 7  | 5    | 13  | ş | 10 | 5   | 4    | 4 5         | 11 | 19  | -11 |

133

•

| н  | κ | ι  | FO | FC  | н   | κ | ٤  | FC | FC  | н  | к   | Ľ  | FQ | FC  | н  | ĸ | L  | FC | FC  | н | κ | L  | FO | FC  |
|----|---|----|----|-----|-----|---|----|----|-----|----|-----|----|----|-----|----|---|----|----|-----|---|---|----|----|-----|
| 5  | 5 | 11 | 10 | -11 | 3   | C | 12 | 17 | 16  | 7  | 2   | 12 | 6  | -2  | 11 | 4 | 12 | 8  | -6  | 4 | 2 | 13 | 6  | -6  |
| 7  | 5 | 11 | 3  | - 8 | 4   | 0 | 12 | 9  | - 8 | 8  | 2   | 12 | 7  | 8   | 2  | 5 | 12 | E  | -6  | 3 | 3 | 13 | 5  | 2   |
| 8  | 5 | 11 | 6  | 5   | 6   | ۵ | 12 | 11 | -11 | ٥  | 3   | 12 | 9  | 10  | 3  | 5 | 12 | €  | -6  | 4 | 3 | 13 | 5  | 3   |
| 1  | 6 | 11 | 5  | -7  | 7   | 9 | 12 | 8  | 8   | 1  | 3   | 12 | 9  | -9  | 4  | 5 | 12 | 8  | -7  | 4 | 4 | 13 | 5  | 5   |
| 4  | 6 | 11 | ć  | - E | 8   | 0 | 12 | 7  | - 4 | 3  | 3   | 12 | 14 | -14 | 8  | 5 | 12 | E  | -4  | 5 | 4 | 13 | 5  | 5   |
| 6  | 6 | 11 | 7  | - 4 | 12  | 0 | 12 | 8  | 7   | 6  | 3   | 12 | 6  | 5   | 2  | 6 | 12 | 5  | 3   | Q | a | 14 | 18 | -18 |
| 11 | 6 | 11 | 9  | -7  | ٥   | 1 | 12 | 17 | 17  | 11 | 3   | 12 | 6  | 5   | 4  | Æ | 12 | 5  | 4   | 3 | 0 | 14 | 9  | -9  |
| 1  | 8 | 11 | 15 | -14 | 5   | 1 | 12 | e  | 7   | 1  | 4   | 12 | 6  | -5  | 1  | 7 | 12 | €  | 4   | 1 | 1 | 14 | 8  | 8   |
| 3  | 8 | 11 | 6  | - 4 | - 3 | 1 | 12 | 7  | 5   | S  | 4   | 12 | 5  | -7  | 2  | 1 | 13 | 11 | -12 | 3 | 1 | 14 | 10 | 9   |
| 5  | 8 | 11 | 5  | -5  | 5   | 1 | 12 | £  | 6   | 5  | 4   | 12 | 6  | 2   | 5  | 1 | 13 | 6  | -4  | 5 | 1 | 14 | 7  | 3   |
| 3  | 9 | 11 | 7  | -4  | 12  | 1 | 12 | 7  | 4   | б  | 4   | 12 | 5  | 5   | 7  | 1 | 13 | 6  | 4   | 2 | 2 | 14 | ç  | 7   |
| 5  | 9 | 11 | 5  | Q   | 0   | 2 | 12 | 16 | 15  | 7  | - 4 | 12 | 5  | -2  | 2  | ē | 13 | 12 | -12 | 1 | 3 | 14 | 6  | 5   |
| 1  | 0 | 12 | 6  | 3   | 1   | 2 | 12 | 7  | -6  | 10 | 4   | 12 | 6  | -6  | 3  | 2 | 13 | 14 | 13  | 2 | 3 | 14 | 7  | 7   |
| 2  | 0 | 12 | 15 | -14 | Ę   | 2 | 12 | 10 | -11 |    |     |    |    |     |    |   |    |    |     |   |   |    |    |     |

### DESERVEC AND CALCULATED STRUCTURE FACTORS FOR OXIME OF METHYLATED DECALONE

•

| ATOM         | ×                          | ۲                    | 2                               | U11             | U2 2    | 033      | U23      | U1 3     |
|--------------|----------------------------|----------------------|---------------------------------|-----------------|---------|----------|----------|----------|
| 0            | 0564(1)                    | .4166(2)             | .5507(2)                        | .068(2)         | .048(2) | .074(2)  | 010(1)   | .002(2)  |
| N            | 0017(2)                    | .3823(2)             | .4785(3)                        | .055(2)         | .942(2) | .060(2)  | 008(2)   | 005(2)   |
| C1           | 0029(2)                    | .2842(2)             | .4592(3)                        | .061(2)         | .030(2) | .043(2)  | 005(2)   | 009(2)   |
| CZ           | -,0579(2)                  | .2114(3)             | .5064(3)                        | .078(3)         | .042(2) | .067(3)  | 003(2)   | .011(2)  |
| C 3          | 0371(2)                    | .1385(3)             | .417E(3)                        | .(58(2)         | .042(2) | .074(3)  | ·.000(2) | .001(2)  |
| Č4           | 0263(2)                    | .0832(3)             | 3586(3)                         | .060(2)         | .040(2) | .063(2)  | 006(2)   | 011(2)   |
| C5           | .0863(2)                   | .6994(3)             | .2457(3)                        | . (59(2)        | .049(2) | .045(2)  | 004(2)   | 006 (2)  |
| C6           | .1413(2)                   | .0486(3)             | .3222(3)                        | .053(2)         | .039(2) | .044(2)  | 001(2)   | 005(2)   |
|              | .1703(2)                   | . 1317(3)            | .3996(3)                        | . 055(2)        | .067(3) | .062(3)  | 019(2)   | 011 (2)  |
| Ča           | .1129(2)                   | .1283(3)             | 4625(3)                         | .060(3)         | .059(2) | .055(2)  | 018(2)   | 014(2)   |
| ng           | .05E5(2)                   | .2404(3)             | -386A(3)                        | . 060(2)        | .029(2) | .858(2)  | **001(2) | .002/21  |
| C10          | .0262(2)                   | . 1581 (3)           | .3052(3)                        | . (61(2)        | -142(2) | 642(2)   | .001(2)  | +.012/21 |
| C11          | .0909(3)                   | . 3298(3)            | 3212(4)                         | 101641          | 043121  | .112741  | .003/31  | 162163   |
| C12          | 1964/21                    | 0163(3)              | - 2615(3)                       | . [59(2)        | 059/21  | . (54(2) | - 010/23 | 002/21   |
| 013          | 2521 (3)                   | (626 (4)             | 3645(4)                         | .071(3)         | .093(3) | . 686(3) | +.011(T) | 004(3)   |
| C14          | 2404(3)                    | . 0503(4)            | 177 (4)                         | . 07 8(3)       | .100(4) | . 081(3) | 002(3)   | .027(3)  |
| C15          | - 1676/31                  | - 1078(4)            | 2015/51                         | . 0.8.36 *1     | .075/3) | . 112741 | - 0/9/71 | - 005/43 |
|              | .1030(3)                   |                      |                                 |                 |         | ••••••   |          |          |
| ATCH         | ×                          | ۲                    | Z                               | U               |         |          |          |          |
| нп           | 0670                       | . 49441              | .56941                          | . 05            |         |          |          |          |
| HČ2          | 0336(2)                    | .1652(3)             | .5707(3)                        | . 87 (1)        |         |          |          |          |
| 402          | 1014(2)                    | 25F7(3)              | . 540.2 (3)                     | . (7 (1)        |         |          |          |          |
| HC3          | 1174(2)                    | .1838(3)             | -358 £ (3)                      | . ú9 (1)        |         |          |          |          |
| HC3          | + 1216(2)                  | .0810(3)             | 4553(3)                         | . (7 (1)        |         |          |          |          |
| HCL          | .0.17(2)                   | . (355(3)            | 4176(3)                         | . 06 (1)        |         |          |          |          |
| HC4          | - 0464(2)                  | .0.239(3)            | 2556 (3)                        | . (7 (1)        |         |          |          |          |
| HCS          | .1144(2)                   | . 1541 (3)           | .1931(3)                        | .07(1)          |         |          |          |          |
| NCE          | - 06 76 / 78               |                      | 1061131                         | . 66 (1)        |         |          |          |          |
| H09<br>HC6   | 1167771                    | - 6100733            |                                 | 075/81          |         |          |          |          |
| 400<br>407   | 5167(2)                    |                      | 65714(3)                        | 00/11           |         |          |          |          |
|              | 2006/21                    | 4892/71              | 7520171                         | 007117          |         |          |          |          |
|              | 46399467                   | 4 22/. / 21          | 63526437                        |                 |         |          |          |          |
| HLO<br>UCA   | 1767/21                    | 2690731              | 67142133                        | + LO (1 )       |         |          |          |          |
| 100          | - 0034695                  | 2017/71              |                                 |                 |         |          |          |          |
| HC10         |                            | -2013(3)             | 46442())                        |                 |         |          |          |          |
|              | 4433434                    | 205(3)               | 203-147                         | + 11 (2)        |         |          |          |          |
|              | 0500(7)                    | * 2 6 6 6 7 7 7 1    | 2777761                         | + 17 (67        |         |          |          |          |
| NG11         | • U7 U7 (J)<br>27 46 / 7 1 | • COTIOJ             | 46702147                        | + 7 C (3 )      |         |          |          |          |
| HC13         | +2(0413)                   |                      | + 3 CO C 1 4 J<br>R n 1 C / 6 4 | + 1 6 1 6 7     |         |          |          |          |
| 1013         | 22367531                   | - 444 21.44          | 43015147                        | + 1 1 4 7 7 1   |         |          |          |          |
| HG13<br>HC11 | 007077                     |                      | 4922143                         | 4 1 5 1 2 1     |         |          |          |          |
| HG14         | -2037131                   | + UCJU(4)<br>0050765 | ********                        | • 17 (6)        |         |          |          |          |
| NG 1 4       | *2/91133                   | 4427265              | +1 3D F (4)                     | +11(C)<br>+2/2) |         |          |          |          |
| NG19         | .20/3131                   | +112/147             | 42204143                        | • 12127         |         |          |          |          |
| 4615         | •1269(4)                   | ₹•U/C1(4)            | •1418(5)                        | A12(2)          |         |          |          |          |
| 0045         | 1757/75                    | - 4564765            | 260575                          | 10/71           |         |          |          |          |
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## VITA