CHAPTER II
CHAPTER II

Stereoselectivity in the Alkylation of C$_7$-Substituted-
trans-Hydrindanone $\beta$-Ketoesters

II.1 Introduction:

Stereoselectivity in the alkylation of $\beta$-ketoesters present in trans-decalones, the 6,6-fused bicyclic ring systems have been described in the previous chapter. In continuation, it is logical to extend this study to trans-hydrindanones, the 5,6-fused bicyclic systems 1, 2, 3. Hydrindanones are ubiquitous in nature. Most importantly they occur as C-D ring portion of steroidal skeleton and vitamin-D.$^{1-4}$ This carbon framework is also found in many bicyclic and polycyclic terpenoids. Thus, it is not surprising that synthesis of trans-hydrindanes had engaged many eminent organic chemists during 1950-70, the golden age for steroid synthesis.$^{1-4}$ Robinson$^5$, Woodward, Ireland$^7$ and Djerassi$^8$ to name a few, were pioneers in this area. Due to its inherent importance, synthesis and chemistry of trans-hydrindanes continue to attract attention of synthetic organic chemists$^9$. Our studies on the synthesis and alkylation of trans-C$_7$-substituted 6-methoxycarbonylhydrindan-5-ones, 1, 2, 3 are described (Scheme II.1) in this chapter. The present studies on hydrindanone systems in comparison with our earlier observations on decalone systems will show light on the role
of annulated 5-membered ring in the stereoselectivity involved in the alkylation reactions.

II.2 Results from alkylation reactions:

The alkylation on 6-methoxycarbonyl-trans-hydrindan-5-ones, 1, 2, 3 were conducted with two alkylation agents viz., methyl iodide and benzyl bromide using potassium carbonate in acetone. Stereoselectivity observed in this reaction is gathered in Table II.1.

II.3. Determination of configuration of the alkylated products and analysis of their $^1$H and $^{13}$C NMR spectral data.

The assignment of configuration to Z and E-alkylated products in the hydrindanone systems is based on the analysis of their proton and carbon-13 NMR spectra. The knowledge gained in analyzing NMR spectra of decalone systems have been extrapolated to the present cases and is described in the following.

1. By analogy with the work of Kuehne and Middleton C$_6$-Me group resonances for E-alkylated products appeared upfield, $S = 1.29$ppm, $13 = 1.27$ppm, compared to Z-alkylated products, $4 = 1.45$ppm, $12 = 1.36$ppm.
Table II.1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate number</th>
<th>Product distribution&lt;sub&gt;a,b&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Z : E</td>
</tr>
<tr>
<td>1</td>
<td>1</td>
<td>71 : 29</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>16 : 84</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>05 : 95</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td>05 : 95</td>
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<td>5</td>
<td>3</td>
<td>60 : 40</td>
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<tr>
<td>6</td>
<td>3</td>
<td>05 : 95</td>
</tr>
</tbody>
</table>

<sup>a</sup>) Ratios were fixed based on the integration of silent signals in <sup>1</sup>H NMR (400 MHz) of the total reaction mixture from at least two runs for each case.

<sup>b</sup>) Alkylation products formed in below 5% could not be isolated.
The angular methyl groups in E-methylated and benzylated products of ketoesters 9 and 11 appeared at 0.83 and 0.80 ppm respectively in $^1$H NMR and 16.48, 17.02 ppm in $^{13}$C NMR spectra (Table II.2).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>$^{1}$H NMR δ ppm</th>
<th>$^{13}$C NMR δ ppm</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>1.45</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>1.27</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9</td>
<td>1.29</td>
<td>0.83</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>--</td>
<td>0.80</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>1.36</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>13</td>
<td>1.27</td>
<td></td>
</tr>
</tbody>
</table>

These values not only confirm trans-ring junction in bicyclic system (in compounds with cis-ring junction, the angular methyl group resonates around 1.1 ppm and 22 ppm in $^1$H NMR and $^{13}$C NMR respectively)\textsuperscript{9e}, but also are indicative of E-alkylation (if Z-alkylated products were formed, the angular Me resonances occur at about 0.95 ppm)\textsuperscript{9e}.

2. Anisochrony\textsuperscript{12,13} of Z-benzylmethylene, which
appeared as double doublet was larger than the one seen for 
$E$-benzylmethylene (Table II.3).

**TABLE II.3**

![Table II.3](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{(A)}$H(B) ($\Delta \delta$ ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>0.44 ---</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>--- 0.27</td>
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<tr>
<td>3</td>
<td>11</td>
<td>--- 0.07a</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>--- 0.11</td>
</tr>
</tbody>
</table>

*a. As the $J/\Delta V$ is about one, the $\Delta \delta$ value given is only an approximate.

3. Anisochrony of methylene protons of $C_{7a}-\text{COOCH}_2\text{CH}_3$ group was larger in the case of $E$-alkylated products 13, 15 compared to $Z$-alkylated products 12, Table II.4. As described earlier in Chapter I, the larger anisochrony is a result of the greater $\text{syn}$-axial interactions between $C_{7a}$-ethyl ester and $C_6$-methylester in $E$-alkylated products 12 13, 15.

4. $C_6$-Me group carbon resonance was found to occur downfield in $E$-methylated products 5, 9, 13 indicating equatorial-like orientation compared to $Z$-methylated products.
4, 12 in $^{13}$C NMR spectra (Table II.5), indicating axial-like orientation$^{14,15}$ and reverse in $^1$H NMR spectra (Table II.2)

**TABLE II.4**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>C$_7$a-COOCH$_2$ (Å)</th>
<th>$^1H$CH$_2$ (Å)</th>
<th>$^1$H ppm</th>
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<tr>
<td>1</td>
<td>12</td>
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<tr>
<td>2</td>
<td>13</td>
<td></td>
<td></td>
<td>0.14</td>
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<tr>
<td>3</td>
<td>15</td>
<td></td>
<td></td>
<td>0.16</td>
</tr>
</tbody>
</table>

**TABLE II.5**

| Entry | Product |  } |
|-------|---------|----------------------|-----------------|------------|
| 4     | R = H, R' = CH$_3$, R'' = COOCH$_3$ |  } |
| 6     | R = H, R' = C$_6$H$_5$CH$_2$, R'' = COOCH$_3$ |  } |
| 9     | R = CH$_3$, R' = COOCH$_3$, R'' = CH$_3$ |  } |
| 12    | R = COOC$_2$H$_5$, R' = CH$_3$, R'' = COOCH$_3$ |  } |
| 15    | R = COOC$_2$H$_5$, R' = COOCH$_3$, R'' = C$_6$H$_5$CH$_2$ |  } |

**Contd.**
<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>$^{13}$C-NMR $\delta$ (ppm) $^Z$</th>
<th>$^{13}$C-NMR $\delta$ (ppm) $^E$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>21.23</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>21.81</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>23.26</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>21.95</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>13</td>
<td>23.22</td>
<td></td>
</tr>
</tbody>
</table>

5. As noted earlier in the case of 6,6-bicyclic systems the C$_4$-H(ax) resonates at downfield in E-alkylated products, 13 = 3.50 ppm, 15 = 3.47 ppm compared to Z-alkylated products, 12 = 3.13 ppm, (possibly due to two hydrogen bonding interaction, Fig II.1A) in $^1$H NMR spectra, in the case where C$_{7a}$-substituent is an ester.

![Fig.II.1](image)

**Fig.II.1**

Several other interesting features could be noted from the $^1$H NMR spectra of hydrindanone alkylated products. Similar to 6,6-bicyclic systems, there lies a substantial
chemical shift difference in geminal hydrogens present on C7 in many of the hydrindanone alkylated products (possibly due to actual stabilized conformations). In cases where C7a-syn-axial group is an ester, 12 13, 15 and methyl 9, 11, C7-Hβ(eq) appeared downfield compared to C7-Hα (ax) (13, 15, 9, Table II.6). This may possibly be due to the C7-Hα (ax) hydrogen coming in the shielding zone of the carbonyl group at C5 (Table II.6, entry 5-9). In contrast, the C7-Hα (eq) in the cases where C7a-substituent is hydrogen, 5, 7 appears upfield compared to C7-Hβ (Table II.6, entry 1 & 2). This may be due to flattened chair conformation in such way that C7-Hα doesn't come in the shielding zone of the C5-carbonyl group. The assignment for C7-Hα(ax), in cases where C7a-substituent is H, stems from larger vicinal H-H coupling with C7a-H (14 Hz) and C7-Hβ (eq) not only showed smaller geminal coupling but also long range coupling with C1-Hβ (eq) due to extended "W" conformation16 (see experimental). This long range coupling was also observable for C7-Hβ(eq) for other systems where C7a-substituent is Me and COOR.

Fig.II.2

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Table II.6

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>$C_7$-Hβ (ppm)</th>
<th>$C_7$-Hα (ppm)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
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<td>2.00</td>
<td>2.14</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>1.8</td>
<td>2.34</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>a</td>
<td>2.25</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>2.29</td>
<td>2.41</td>
</tr>
<tr>
<td>5</td>
<td>9</td>
<td>2.77</td>
<td>1.41</td>
</tr>
<tr>
<td>6</td>
<td>11</td>
<td>2.52</td>
<td>1.50</td>
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<tr>
<td>7</td>
<td>12</td>
<td>2.32</td>
<td>1.46</td>
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<td>8</td>
<td>13</td>
<td>3.12</td>
<td>1.45</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>3.08</td>
<td>1.56</td>
</tr>
</tbody>
</table>

a. appears as multiplet, buried in other ring protons.

The assignment of characteristic resonances to $^1H$ NMR spectra is based on the application of generalized Karplus equation, and modifications worked out by Haasnoot$^{17}$.

Information regarding the conformation of the molecule can be derived from geminal coupling constants where the two hydrogen atoms involved are present on a carbon atom located next to a π-system. Barfield and Grant$^{18}$ have shown through extensive theoretical work that the geminal internuclear axis perpendicular to the nodal plane of the carbonyl group would result in geminal coupling constant of
about 16-20Hz (Fig.II.3, A) whereas if one of the hydrogen is located on the nodal plane it would result in a geminal coupling constant of 13 Hz or less (Fig.II.3, B)

\[ \text{Fig.II.3} \]

Extending this argument to the present systems it can be noticed from the Table II.7 that the alkylated products 7, 11, 12 have reasonably high geminal coupling constants and therefore, stabilized conformation of the molecule would be in such a way that the plane bisecting geminal hydrogens on C₄ would pass through the carbonyl carbon i.e., the cyclohexanone ring would be in a half-chair conformation rather than twisted-chair. which would place C₄-Hα on the plane of the carbonyl group. On the other hand, in rest of the alkylated products 4, 5, 6, 13, 15 (entry 1, 2, 3, 8, 9), the situation would be more like what is shown in Fig.II.3 B, i.e., α hydrogen lies on the plane of carbonyl II-systems as they show smaller geminal coupling constants.

\[ \text{Fig.II.4} \]
Entry & Product & $C_4 - H\alpha$ (400 MHz)\textsuperscript{a}  \\
 & & (J, Hz)  \\
\hline
1 & 4 & 14.5  \\
2 & 5 & 6.15  \\
3 & 6 & 13.18  \\
4 & 7 & 16.6\textsuperscript{a}  \\
5 & 9 & multiplet\textsuperscript{a}  \\
6 & 11 & 17.65  \\
7 & 12 & 17.8  \\
8 & 13 & 14.65  \\
9 & 15 & 10.54  \\

\textsuperscript{a} Spectra have been recorded at 200 MHz.

Long range extended "W" coupling\textsuperscript{16} which can exist between $C_4-H\alpha$ (eq) and $C_3-H\alpha$ (eq) has been taken into account while assigning these resonances. For e.g., $C_4-H\alpha$ (eq) appeared as a triplet, doublet with the coupling constants, $J_1 = 14.5$ Hz, $J_2 = 3.64$ Hz, showing long range coupling with $C_3-H\alpha$ hydrogen present in $Z$-alkylated product 4.

The assignment of $^{13}C$ resonances for various alkylated
products is based on (a). Off-resonance/SEFT and APT spectra. (b). by analogy with many compounds having similar structures particularly those of C/D rings in carbon resonances of steroids and 18-norsteroids. Assignment of carbon resonances to the alkylated products (4, 5, 6, 7, 9, 11, 12, 13 and 15) are given in Table II.8. Highly informative articles by Stothers19, Metzer20, Djerassi8 and standard books21,22 were used for this purpose (c). the assignments made on the C7a-substituted hydrindanones20 were also taken into consideration (d). calculated spectra were obtained by taking substituent-effects into consideration, such as α-methyl effect, r-gauche effect. An exhaustive review article by Duddeck23, was taken into consideration while obtaining the calculated spectra. Table II.8 gives the $^{13}$C NMR spectral assignments for the alkylated products 4, 5, 6, 7, 9, 11, 12, 13, & 15.
<table>
<thead>
<tr>
<th>C-atom No.</th>
<th>Compound number</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-1</td>
<td>31.37 31.54 31.21 32.54 39.34 39.65 37.40 37.06 37.87</td>
</tr>
<tr>
<td>C-3</td>
<td>30.25 29.99 29.87 26.56 27.80 27.83 27.02 27.06 26.83</td>
</tr>
<tr>
<td>C-3a</td>
<td>46.32 46.69 46.90 46.13 49.26 49.01 40.71 42.24 42.45</td>
</tr>
<tr>
<td>C-4</td>
<td>44.23 48.01 47.63 46.13 42.81 42.68 45.22 45.15 41.36</td>
</tr>
<tr>
<td>C-5</td>
<td>210.49 208.10 207.14 209.32 208.57 207.83 208.09 208.29 207.32</td>
</tr>
<tr>
<td>C-6</td>
<td>57.46 56.08 61.14 63.16 54.06 59.80 60.67 60.60 60.53</td>
</tr>
<tr>
<td>C-7</td>
<td>39.49 43.15 42.62 41.27 49.76 46.81 49.27 49.17 48.52</td>
</tr>
<tr>
<td>C-7a</td>
<td>40.41 41.50 40.77 37.54 40.81 40.84 51.72 51.64 51.70</td>
</tr>
<tr>
<td>C₆COOH₃</td>
<td>174.02 174.54 171.74 172.58 175.29 173.75 175.50 174.80 174.91</td>
</tr>
<tr>
<td>C₆COOCH₃</td>
<td>52.33 52.66 52.86 51.77 52.48 52.46 52.88 52.40 52.36</td>
</tr>
<tr>
<td>C₆CH₃</td>
<td>21.23 21.81 23.65 23.16 21.95</td>
</tr>
<tr>
<td>C₆-C₆H₅CH₂</td>
<td>- 38.56 39.17 42.06 42.06</td>
</tr>
<tr>
<td>C₇aCH₃</td>
<td>- 16.48 17.02</td>
</tr>
<tr>
<td>C₇aCOOH₂CH₂³</td>
<td>- 13.97 13.95 13.96</td>
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<tr>
<td>C₇aCOOCH₃CH₂</td>
<td>- 54.92 54.16 59.59</td>
</tr>
<tr>
<td>C₇aCOOCH₂CH₃</td>
<td>- 175.50 173.45 171.08</td>
</tr>
<tr>
<td>C-1'</td>
<td>- 136.67 136.68 137.07 136.29</td>
</tr>
<tr>
<td>C-2'</td>
<td>- 130.30 130.68 131.32 130.94</td>
</tr>
<tr>
<td>C-3'</td>
<td>- 128.05 128.28 128.00 128.00</td>
</tr>
<tr>
<td>C-4'</td>
<td>- 126.68 126.95 126.83 126.71</td>
</tr>
</tbody>
</table>

4. R = H, R' = CH₃, R" = COOCH₃  
5. R = H, R' = COOCH₃, R" = CH₃  
6. R = H, R' = C₆H₅CH₂, R" = COOCH₃  
7. R = H, R' = COOCH₃, R" = C₆H₅CH₂  
9. R = CH₃, R' = COOCH₃, R" = CH₃  
11. R = CH₃, R' = COOCH₃, R" = C₆H₅CH₂  
12. R = COOC₂H₅, R' = CH₃, R" = COOCH₃  
13. R = COOC₂H₅, R' = COOCH₃, R" = CH₃  
15. R = COOC₂H₅, R' = COOCH₃, R" = C₆H₅CH₂
Following points could be noted from the Table II.8. On the introduction of a C7a-methyl and an ester group, in the place of hydrogen r-gauche effect of about 2 ppm was observed for a C2-carbon atom.

This indicates envelop conformation for 5 membered ring of 5,6 bicyclic systems and the preferred conformation is in such a way that C2-carbon atom is present in gauche position with C7a-methyl or ester group. The r-gauche effect was also observed on C6-carbon atom (about 3 ppm, Table II.8).

II.4. Determination of isomeric ratios

Procedures described for the determination of the epimeric ratios of Z and E-alkylated products in the case of 6,6-bicyclic systems have been followed for the determination of alkylation ratios in this case also.

II.5. Substrate molecules synthesis

Synthesis of substrate molecules, β-ketoesters 1, 2, 3 followed the general protocol of Robinson annulation24 with 2-substituted cyclopentanones with MVK and subsequent reduction25 followed by methoxycarbonylation.26 Since the synthesis of trans C7a-methylhydrindanone 2 and trans-C7a-ethoxycarbonyl-hydrindanone 3 needed major synthetic developmental work, these are discussed in a separate section.
II.6. Results and discussion

Experimental conditions employed to carry out the alkylation as essentially same as what have been employed for 6,6-system alkylation (vide Chapter I). As stated earlier in this chapter, the purpose of the present study on the alkylation of β-ketoesters present in trans-hydrindanone systems is to understand the role of five membered annulated ring, and compare its effects with the corresponding six-membered ring present in trans-decalone systems. C7α-substituent in 5,6-bicyclic system can be treated as occupying a pseudoaxial position because it is present on the five membered ring, therefore, could have a slightly different role to play in determining the ratio of the products. Minimum energy conformations derived from MMX calculations, however, did not indicate much change in dihedral angle at the ring junction from those of 6,6 systems. The dihedral angle between C7α-H and C3α-H (Fig.II.6 A, 173.38°) is almost same as that of corresponding 6,6 system i.e., C5-H and C10-H (Fig.II.6 B, 175.09°), indicating similar type of steric interactions in both cases.

![Diagrams](image_url)

1. Enolate H-C-C-H θ = 173.38°

2. Enolate H-C-C-H θ = 175.09°

Fig.II.6
The results of alkylation reactions on 1, 2, 3 are presented in Table II.9. Methylation of trans-hydrindanone 1 having syn-axial hydrogen led to the formation of the Z, 4 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.7) and E, 5 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.8) products in the ratio of 71:29 (entry 1, Table II.9). This result further confirms the formation of Z-major alkylated product in sterically unhindered cases. Benzylation on the other hand, quite as expected led to the formation of minor Z, 6 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.9) and major E, 7 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.10) benzylated products (E/Z = 84:16, entry 2, Table II.9). This result is a consequence of greater steric demand of the benzyl group and lower electrophilicity of the benzyl carbocation\(^{27}\). It is of interest to note that within experimental error the product ratios were similar to the one observed for 6, 6 systems (vide Chapter I).

Methylation and benzylation on compound 2 having syn-axial methyl group, expectedly, led to the formation of major E-methylated, 9 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.11) and benzylated 11 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.12) products (entry 3, 4, Table II.9). Continuing further methylation and benzylation of trans-hydrindanone \(\beta\)-ketoester having C\(_7\alpha\)-COOC\(_2\)H\(_5\), 3 resulted in a Z-methylated 12 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.13) and E-methylated 13 (\(^1H, \(^{13}C\) NMR & MS spectra, Fig.II.14), E-benzylated 15 (\(^1H, \(^{13}C\) NMR &
Fig.II.7. A. $^1$H NMR (400 MHz) B. $^{13}$C NMR (100 MHz) C. EI (70ev) mass spectrum of trans-6β-methyl-6α-methoxycarbonyl-hydrindan-5-one (4).
Fig. II.8. A. $^1$H NMR (400 MHz) B. $^{13}$C NMR (100 MHz) C. EI (70 ev) mass spectrum of trans-6α-methyl-6β-methoxycarbonyl-hydrindan-5-one (5).

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Fig. II. 9. A. $^1$H NMR (400 MHz) B. $^{13}$C NMR (100 MHz) C. EI (70 ev) mass spectrum of trans-6β-benzyl-6α-methoxycarbonyl-hydrindan-5-one (6).
Fig. II.10. A. $^1$H NMR (400 MHz)  B. $^{13}$C NMR (100 MHz) C. EI (70ev) mass spectrum of trans-6α-benzyl-6β-methoxycarbonyl hydrindan-5-one (7).
Fig. II.11. A. $^1$H NMR (200 MHz) B. $^{13}$C NMR (50 MHz) C. EI (70 eV) mass spectrum of trans-6α, 7αβ-dimethyl-6β-methoxycarbonylhydrindan-5-one (9).
Fig. II.12. A. $^1$H NMR (200 MHz) B. $^{13}$C NMR (50 MHz) C. EI (70ev) mass spectrum of trans-6α-benzyl-7αβ-methyl-6β-methoxycarbonylhydrindan-5-one (11).
Fig. II.13. A. $^1$H NMR (400 MHz) B. $^{13}$C NMR (100 MHz) C. EI (70 eV) mass spectrum of trans-7aβ-ethoxycarbonyl-6β-methyl- 6a-methoxycarbonylhydrindan-5-one (12).
MS spectra, Fig.II.15) benzylated products (entry 5, 6, Table II.9). These results, within experimental error, are similar to the ratios obtained in the case of 6,6 system (Chapter I), except in the case of benzylation (entry 6, Table II.9). In this case almost exclusive formation of E-bound benzylolation was noticed, contrary to what was found for the benzylation of 6,6-system having C_{10}-ester group (Z vs E, 

TABLE II.9

<table>
<thead>
<tr>
<th>Entry R</th>
<th>Substrate</th>
<th>Alkylating agent</th>
<th>Product distribution</th>
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<td>1</td>
<td>H</td>
<td>1</td>
<td>CH$_3$I</td>
</tr>
<tr>
<td>2</td>
<td>H</td>
<td>1</td>
<td>C$_6$H$_5$CH$_2$Br</td>
</tr>
<tr>
<td>3</td>
<td>CH$_3$</td>
<td>2</td>
<td>CH$_3$I</td>
</tr>
<tr>
<td>4</td>
<td>CH$_3$</td>
<td>2</td>
<td>C$_6$H$_5$CH$_2$Br</td>
</tr>
<tr>
<td>5</td>
<td>COOC$_2$H$_5$</td>
<td>3</td>
<td>CH$_3$I</td>
</tr>
<tr>
<td>6</td>
<td>COOC$_2$H$_5$</td>
<td>3</td>
<td>C$_6$H$_5$CH$_2$Br</td>
</tr>
</tbody>
</table>

(a). Ratio's were fixed based on the integration of diagnostic peaks in $^1$H NMR (400 MHz) spectra of the total reaction mixtures from at least two reactions for each case.
Fig. II.14. A. $^1$H NMR (400 MHz)  B. $^{13}$C NMR (100 MHz)  C. EI (70 ev) mass spectrum of trans-7α-ethoxycarbonyl-6α-methyl-6β-methoxycarbonylhydrindan-5-one (13).
Fig. II.15. A. $^1$H NMR (400 MHz)  B. $^{13}$C NMR (100 MHz)  C. EI (70 ev) mass spectrum of trans-6α-benzyl-7αβ-ethoxycarbonyl 6β- methoxycarbonylhydrindan-5-one (15).
we are not sure of the reasons of this anomalous result. Further, theoretical work may clarify the observed results.

During our initial studies on the alkylation of \( \beta \)-keto esters generated from trans and cis-isomeric ketones 31, 32, we isolated a methylation product 9c from cis-4 methoxycarbonyl 7a-methyl hydridn-5-one, 32A (Fig.II.16 & 16A). This compound was fully characterized based on \(^1\)H, \(^{13}\)C and analytical data. The \(^{13}\)C NMR spectrum showed angular methyl group signal at 22.6 ppm, indicating the cis ring junction of the bicyclic system. The fact that the alkylated products generated from \( \text{C}_4 \)-methoxycarbonyl (instead of \( \text{C}_6 \)-methoxycarbonyl) products was made secured on the basis of \(^1\)H NMR data; it showed 4 protons present on adjacent \( \text{C}_6 \) and \( \text{C}_7 \) carbons. The stereochemistry of the \( \text{C}_4 \)-methyl group in the product was fixed as \( \text{E} \) (\( \alpha \)) based on the value of the methyl proton resonance at 1.36 ppm (if it were to be \( \text{B} \) (ax) it would occur around 1.48 ppm and on the basis of general understanding that due to severe steric interactions from \( \text{C}_7a \) methyl group, alkylation from the \( \alpha \) side is favourable).

II.7. Synthesis of substrate molecules

II.7.1. Synthesis of trans-6-methoxycarbonylhydridn-5-one (1)

Synthesis of \( \beta \)-ketoester 1 is given in the Scheme II.2.
Fig. II.16. A. $^1$H NMR (400 MHz) B. $^{13}$C NMR (100 MHz) spectrum of cis-4α,7αβ-dimethyl-4β-methoxycarbonylhydrindan-5-one (9C).
Fig. II.16A. C. DEPT (400 MHz) spectrum D. EI (70ev) mass spectrum of trans-4α,7αβ-dimethyl-4β-methoxycarbonyl-hydr- indan-5-one (9C).
Reagents and conditions: (i) pyrrolidine, benzene, reflux; (ii) MVK, benzene, reflux; (iii) AcOH / H₂O / AcONa (2:2:1) buffer, reflux.

Scheme II.2
To the pyrrolidine enamine 17 prepared from cyclopentanone (16) in 1,4-dioxane, methylvinylketone was added and refluxed for 24 h$^{24b}$. Buffer treatment ($pH = 5$) of the reaction and due workup resulted in enone 19. The enone 19 was subjected to lithium/ammonia reduction$^{25}$ to afford trans-hydrindanone 20 predominantly.$^{25b}$ Subsequent methoxycarbonylation$^{27}$ of the purified trans-isomer (column chromatography) with NaH/dimethylcarbonate(DMC)/benzene at room temperature resulted in the title compound 1, which exists as an equilibrium mixture of keto-enol tautomers, and the enol-form predominating.

The expectation that methoxycarbonylation goes at C$_6$-position rather than C$_4$ generates from torsional angle concept$^{28}$. The hydrindanes can be viewed as resulting from the fusion of a cyclopentane ring and cyclohexane ring. Newman projection formula taking C$_{3a}$-C$_{7a}$ into account (Fig.II.17) shows the demands of cyclopentane at the ring

Fig.II.17
junction of a cis and trans-hydrindane systems. From this projection it can be seen that the half-chair form of cyclohexene (Fig.II.18) accommodates the demands of trans-

\[ \begin{array}{c}
\text{Fig.II.18} \\
\end{array} \]

fusion by 61° and cis-fusion by 42°. Therefore, the position of the double bond shown in the Fig.II.7, i.e., with the double bond between 5 and 6 carbons should correspond to a more stable position for a trans-fusion (as it accomodates the requirement of torsional angle better). Confirmation of this concept came from the chlorination of trans-hydrindanone 20 which resulted in 6-chlorocompound 21 (Scheme II.3)

\[ \begin{array}{c}
\text{Scheme II.3} \\
\end{array} \]

corresponding to the enol with double bond as in Fig.II.18. Confirmation of the methoxycarbonylation occurring at 6-position, as is the case in the present study, also came from the analysis of 1H and 13C NMR spectral data of the title compound 1 and the alkylated products 4 and 5.
11.7.2. Synthesis of *trans*-7a-methyl 6-methoxycarbonylhydrindan-5-one (2)

The route taken for making this compound 2 is shown in

\[
\begin{align*}
\text{Reagents and conditions:} & \quad (i) \ NaOH, \ C_5H_5OH, \ \text{reflux} \\
& \quad (ii) \ Na, \ C_2H_5OH \ (\text{few drops}) \\
& \quad (iii) \ CH_3I, \ K_2CO_3, \ \text{DMF}, \ 95\% \\
& \quad (iv) \ CH_3I, \ K_2CO_3, \ \text{Acetone}, \ 80\%
\end{align*}
\]

A

\[
\begin{align*}
\text{Reagents and conditions:} & \quad (i) \ \text{Conc HCl, reflux} \\
& \quad (ii) \ \text{MVK, conc H}_2\text{SO}_4 \ (\text{cat}) \\
& \quad \text{benzene, reflux} \\
& \quad (iii) \ 10\% \ \text{ethanolic KOH, reflux}
\end{align*}
\]

B

\[
\begin{align*}
\text{Reagents and conditions:} & \quad (i) \ \text{NaBH}_4 / \text{NiCl}_2 \cdot 6\text{H}_2\text{O, MeOH, } -5^\circ \text{C} - 0^\circ \text{C} \\
& \quad (ii) \ \text{PCC, } \text{CH}_3\text{Cl}_2 \\
& \quad (iii) \ (\text{H}_2\text{CO})_2\text{CO, NaH, benzene} \\
& \quad (iv) \ \text{Separate} \\
& \quad (v) \ \text{Conc HCl, reflux}
\end{align*}
\]

Scheme II.4

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in scheme II.4. 2-Methylcyclopentanone 28 on which Robinson’s Robinson’s annulation\textsuperscript{24} was planned enroute to the target molecule, is commercially available but quite expensive\textsuperscript{29}. As this compound was required in large quantities, we had planned to prepare this compound from adipic acid (23, Scheme II.4 A). Alkylation of ethyl 2-oxocyclopentane-carboxylate (25) prepared from diethyl adipate (24) with methyl iodide in DMF resulted in ethyl 1-methyl 2-oxocyclopentane-carboxylate (25, Scheme II.4 A) in quantitative yield. We found that the methylation occurs faster in DMF as solvent than in acetone, reported in the literature\textsuperscript{30}. Decarboxylation of β-ketoester 25 was attempted by following the procedure given in a practical organic chemistry book\textsuperscript{31}. The reported procedure involved hydrolysis of the ester present in ethyl 1-methyl-2-oxocyclopentanecarboxylate (25) under basic conditions (aqueous ethanolic KOH) and subsequent decarboxylation. In our hands the reported procedure didn’t work and the ring opened product, dimethyl 2-methyl adipate (27) was the only product isolated, (Scheme II.5), which had possibly formed

![Chemical structure](image)

\[ 26 \quad (i) \text{ KOH, CH}_3\text{OH, H}_2\text{O, reflux, b dill HCl, (ii) K}_2\text{CO}_3, \text{ CH}_3\text{OH, reflux} \]

\[ 27 \]

Scheme II.5

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via retro-Dieckmann reaction. In fact this observation was recorded in the early literature also\(^3\). Hence, we tried hydrolysis with relatively mild base, \(K_2CO_3\), and this also led to the formation of the ring opened product 27. A thorough literature search revealed that Bouveault\(^3\) in 1898 had reported the preparation of 2-methyl cyclopentanone (26) by acid catalyzed hydrolysis and decarboxylation of the \(\beta\)-ketoester 26. This procedure worked quite well, and the yield of 2-methyl cyclopentanone (28) from the \(\beta\)-ketoester 26 was quantitative, when the reaction was conducted at reflux temperature of conc. HCl.

Reported Robinson annulation on 2-methyl cyclopentanone (28) involved Michael addition under basic conditions (ethanolic KOH)\(^3\) or used expensive reagents\(^3\) to the diketone 29 and further base catalyzed cyclization and dehydration reactions to form the enone 30\(^3\) (Scheme II.4 B). However, reported yield was 35.12\%, based on 2-methylcyclopentanone used. We found that Michael addition under acidic conditions (conc. \(H_2SO_4\)) and intramolecular Aldol condensation and subsequent dehydration under basic conditions (ethanolic KOH) resulted in desired enone 30 in over 88\% yield\(^3\). The reduction of the enone 30 to trans-\(C_7a\)-methylhydrindanone 30 using NaBH\(_4\)/NiCl\(_2\)6H\(_2\)O system (Scheme II.4 B) is described at length, in Chapter IV, Part A, of this thesis. Methoxycarbonylation at \(C_6\)-position of trans-
7α-methylhydrindanone 31 with NaH/DMC/benzene (Scheme II.4 B) afforded the title product 2 (Scheme II.4 B, \( ^1H \), \( ^{13}C \) NMR spectra, Fig.II.19). This β-ketoester also exists as an equilibrium mixture of the keto-enol form with enol form predominating.

II.7.3. trans-7α-Ethoxycarbonyl 6-Methoxycarbonylhydrindan-5-one (3).

The synthesis of this β-ketoester, 3, is given in Scheme II.6. Dauben et al.\(^{36}\) reported that the methylvinylketone

\[
\text{A} \overset{\text{I}}{\longrightarrow} \text{B} \overset{\text{II}}{\longrightarrow} \text{C} \overset{\text{III}}{\longrightarrow} \text{D}
\]

Reagents and conditions - (i) NaO\(C_2\)H\(5\), C\(2\)H\(5\)OH, reflux (ii) Na, C\(2\)H\(5\)OH (few drops), benzene, reflux (iii) MVK, 1 mol % Ni(acac)\(_2\), p-dioxan, 80° C (iv) pyrrolidine, benzene, reflux (v) AcOH/H\(2\)O/NaOAc (2:2:1) buffer, reflux.

\[
\text{B} \overset{\text{H}_2/Pd-C(10\%)}{\longrightarrow} \text{D}
\]

\[
\text{C} \overset{(\text{H}_3\text{CO})_2\text{CO, NaH}}{\longrightarrow} \text{E}
\]

Scheme II.6
Fig.17.19. A. $^1$H NMR (270 MHz) B. SEFT (100 MHz) C. EI (70ev) mass spectrum of trans-7a-methyl-6-methoxy-carbonylhydridan-5-one (2).
addition to ethyl 2-oxocyclopentanecarboxylate (25) under triethylamine catalysis resulted in the diketone 33 which on heating with aluminum t-butoxide in benzene resulted in the enone 34 in 34% overall yield (Scheme II.6A). Even though, this procedure works well for the preparation of diketone 33, it is a time consuming process (7 days) and cyclization also resulted in poor yields. In a systematic search for a better reagent than triethylamine, we tried a number of reagents known to work on closely related substrates. The best results of Michael addition were obtained (quantitative yield) on heating the compound 25 with 1.1 equivalent of MVK and 1% molar solution of Ni(acac)$_2$ in 1,4-dioxane for 18 h. Earlier, Ni(acac)$_2$ was employed in the Michael addition reaction on acyclic dicarbonyl compounds$^{37}$. Dauben's cyclization procedure on the diketone 33, unfortunately requires long periods of reflux 42 h and the use of substantial quantities of aluminum t-butoxide (1.5 equivalents). Later this difficulty was overcome by Scanio et al.$^{38}$ by using pyrrolidine enamine procedure. We have followed this latter procedure for cyclization of diketone 33 to the enone 34 and obtained quantitative yields. Dauben et al.$^{36}$ in his pioneering studies on the stereoselectivity of cyclic enone reduction reported, the catalytic hydrogenation (H$_2$/Pd.-C, ethanol) of the ester enone 34 which led to exclusive formation of cis-7a-ethoxycarbonylhydrindanone 36, in 83% yield$^{36}$. This observation also has been recorded in
one of the leading text books.\textsuperscript{39}

As we required \textit{trans}-ring junction ketoester \textit{35} only, we initially tried the catalytic hydrogenation using EtOAc as a solvent (change from ethanol) with 10\% Pd-C and CaCO\textsubscript{3}. Surprisingly, this reaction resulted in 13\% (GLC, \textsuperscript{1}H NMR) of \textit{trans}-hydrindanone \textit{35} (Scheme II.6B). Later we found that the yield of the \textit{trans}-compound, \textit{35} could be increased to a maximum of 33\% by employing NaBH\textsubscript{4}/NiCl\textsubscript{2}.6H\textsubscript{2}O/MeOH system (Chapter IV, Part A). Subsequent methoxycarbonylation on the ketone \textit{35} using NaH/DMC/benzene afforded the title compound \textit{3} in good yields (78\%) (Scheme II.6C). This compound \textit{3} also exists as an equilibrium mixture of keto-enol form, in which enol form predominates.

II.8. 2D NMR analysis of \textit{trans}-6\textalpha-methoxycarbonyl 6\textbeta-methyl-hydrindan-5-one (4)

During the past decade with the remarkable developments in NMR instrumentation and computer software a wealth of information for the structural determination of organic compounds has become available. With the advent of computer controlled pulse sequences, there resulted a number of ingenious procedures for the generation of one and two dimensional NMR spectra\textsuperscript{13,40-44}. The so-called 2D spectrum really represents a 3 dimensional spectrum but may not be quite obvious because the usual presentation of contour
slices through stacked peaks i.e., peaks representing intensities are perpendicular to the plane of the page. Among the 2D NMR experiments heteronuclear correlated spectroscopy (HETCOR, $^1\text{H}-^{13}\text{C}$) and homonuclear correlated spectroscopy (HOMOCOSY, $^1\text{H}-^1\text{H}$) have become very popular for the structural determination of organic compounds. HETCOSY spectrum correlates the peaks of an $^1\text{H}$ spectrum with the peaks of a proton decoupled $^{13}\text{C}$ NMR spectrum. Its utility goes beyond off-resonance decoupled $^{13}\text{C}$ NMR spectra and the other two dimensional techniques such as APT, DEPT etc., because it shows specific protons attached to each $^{13}\text{C}$ nucleus. The $^1\text{H}$ NMR spectrum is given on $F_1$ axis, proton decoupled $^{13}\text{C}$ NMR spectrum is given on the $F_2$ axis. The $\text{H-C}$ connectivity is shown by a contour peak present at intersection of horizontal lines drawn from $^1\text{H}$ and $^{13}\text{C}$ peaks. The pulse sequences used in typical HETCOR spectrum is given in the Fig.II.20. The pulse sequences use the evolution period, $T_1$ for precessional motion $^1\text{H}$ spins and to measure the degree of precession with the $^{13}\text{C}$. After a $90^\circ_x$ $^1\text{H}$-pulse both components of the $^1\text{H}$ doublet rotate in the $X, Y$ - plane according to the difference in their frequency to that of the carrier (a-c). A $180^\circ_x$ $^{13}\text{C}$ pulse (d) allows for refocussing at (e); $\delta(^1\text{H})$ is retained in the form of angle $\theta$. This information is transferred to the $^{13}\text{C}$ nuclei through $^{13}\text{C}, ^1\text{H}$ spin-spin coupling during the mixing time. Polarization of the $^1\text{H}$-magnetization with a $90^\circ_y$ pulse (g) results in a
Fig. II.20. Pulse sequence and vector representation of a heteroscalar 2D-NMR experiment.
corresponding polarization of $^{13}$C-magnetization which is transformed into transverse magnetization by the $90^\circ_{\alpha}$ $^{13}$C pulse (h). In the remaining mixing time the $^{13}$C vectors precess around their corresponding $^1$H vectors. They are refocussed after $\Delta_n$ and can be detected with simultaneous $^1$H decoupling. The phase modulation obtained depends on the angle $\theta$.

The HETCOR spectrum is much simpler than $^1$H-$^1$H COSY spectrum due to the absence of diagonal peaks, also CH spin coupling is not observed along the F2 axis because the broad band decoupling of protons has been applied during $T_2$. However, due to the $^{13}$C-$^1$H correlation, slight broadening of the peaks in $^1$H NMR spectrum along the F1 axis is seen.

To gain experience with the emerging techniques of two dimensional spectroscopy, and to further confirm the assignments already made, HETCOR spectrum of $Z$-methylated product 4 from trans-6-methoxycarbonylhydrindan-5-one 1 was recorded. The HETCOR spectrum of "$^{13}$C-aliphatic region" is given in Fig.II.21. Correlation of the carbon resonances with that of proton resonances are given in Fig.II.21. These correlations confirm the assignments made on the basis of 1-D $^1$H and $^{13}$C NMR spectral data (experimental). This spectrum clearly indicates that multiplet at 1.1 ppm is due to two protons which can be assigned to $C_1$-$H_B$ and $C_3$-$H_B$.

Electron impact mass spectra (MS) were recorded for the alkylated products (4, 5, 6, 7, 9, 11, 12, 13 & 15) to see whether the epimers differ in their fragmentation pattern or not. It is worthy to note that the epimeric pairs of
1. 6a-Methoxydecaproxyfurylpyrrolodin-5-one (4)

1H NMR Spectrum (CDCl3, 100 MHz)

(\$-isomer)

2C NMR Spectrum (\$-isomer)

(400 MHz, CDCl3)

PG. III. 21. HC COSY (HETCOR) Spectrum of 6a-Methoxydecaproxyfurylpyrrolodin-5-one (4)
alkylated products do not show much difference in their fragmentation pattern excepting minor difference in the intensities of certain peaks. Almost all the products give rise to stable molecular ions (M⁺). The probable paths of fragmentation which are common to all trans-7a-substituted hydrindanone-methylated products (4, 5, 9, 12 12 & 13) and trans-7a-substituted hydrindanone benzylated products (6, 7, 10 & 15) are shown in Chart II.1 and II.2 respectively. The prominent fragment for all the alkylated products is the loss of substituted (methyl, benzyl) acrylate. In the benzylated cases the peak due to tropelium cation is a prominent one. The spectra of the products described here are presented along with their ¹H & ¹³C NMR spectra in appropriate places in the section.

II.9. Minimum energy conformation of the alkylated products

Finally global minimal energy (MMX) calculations were done for alkylated products with PCMODEL programme and the output was given in Figs.II.22 & 23. Minimum energy conformation show envelop conformation for the cyclopentane ring. The substituted cyclohexanone ring seems to stabilize in mere chair conformation, even in cases where angular substituent is methyl or an ester. This observation is in contrast to what was found in 6,6-bicyclic systems (see chapter I) where substituted cyclohexanone ring was in flattened chair/puckered chair conformation.
Chart 1  General mass spectral fragmentation pattern of C7a-substituted 6-methoxycarbony 6-methylated trans-hydrindan-5-one.
Chart 2  General mass spectral fragmentation pattern of C\textsubscript{7}a-substituted 6-methoxycarbony 6-benzylated trans-hydrindan-5-ones.
trans-6α-Methyl-6α-methoxy-carbonylhydridan-5-one (4).

trans-6α-Methyl-6α-methoxy carbonylhydridan-5-one (5).

trans-6α-Benzyl-6α-methoxy-carbonylhydridan-5-one (6).

trans-6α-Benzyl-6α-methoxy carbonylhydridan-5-one (7).

trans-6α, 7αβ-Dimethyl-6α-methoxycarbonylhydridan-5-one (9).

**Fig. II.22.** Global minimal energy conformations of 4, 5, 6, 7 & 9 as determined by molecular mechanics calculations (PCMODEL output)
trans-6α-Benzyl-7αβ-methyl-6β-methoxycarbonylhydridan-5-one (11).

trans-7αβ-Ethoxycarbonyl-6β-methyl-6α-methoxycarbonylhydrindan-5-one (12).

trans-7αβ-Ethoxycarbonyl-6α-methyl-6β-methoxycarbonylhydrindan-5-one (13).

trans-6α-Benzyl-7αβ-ethoxycarbonyl 6β- methoxycarbonylhydrindan-5-one (15).

Fig.II.23. Global minimal energy conformations of 11, 12, 13, & 15 as determined by molecular mechanics calculations (PCMODEL output).
11.10. Experimental

For general experimental conditions see chapter I. experimental section.

11.10.1. Synthesis of substrate molecules

Hydrind-3a(4)-ene-5-one (19)
(5,6,7,8-Tetrahydrindene-5-one)

This compound was prepared following the procedure described by Stork et al.\textsuperscript{22b}. To the pyrrolidine enamine of cyclopentanone (17, 13.7 g, 0.1 mol, prepared from cyclopentanone 16 and pyrrolidine, under PTC conditions (see Chapter I experimental) in 1, 4-dioxan (65 ml) was added methylvinylketone (7 g, 0.1 mol) and the mixture was refluxed was for 24 h. The reaction mixture was diluted with benzene after removing dioxane and was treated with buffer (AcOH/H\textsubscript{2}O/AcONa 2:2:1 pH = 5) at reflux temperature for 3 h. The Usual workup and further purification by column chromatography (SiO\textsubscript{2}, hexane : ethyl acetate 9:1) afforded hydrindeneone 19 (5.7 g, 42\%).

b.p : 110-111/12 mm Hg.
UV \( \lambda \) max : 238 NM.
IR (Neat) \( \nu_{\text{max}} : 1668, 1590 \text{ cm}^{-1} \).

\(^1\)H NMR (90 MHz) : \( \delta \) 1.2-2.9 (11H, m), 5.95 (1H, s, H)

\(^1^3\)C NMR (22.5 MHz) : \( \delta \) 23.03 (t, C-2), 28.44 (t, C-7), 30.94 (t, C-1), 31.91 (t, C-3), 36.57 (t, C-6), 42.10 (d, C-7a), 121.19 (d, C-4), 174.28 (s, C-3a), 198.01 (s, C-5).

**trans-Hydrindan-5-one (20)**

(trans-Tetrahydrindan-5(6H)-one/Bicyclo (4.3.0)monan-3-one)

Procedure of House et al. \(^{16}\) was followed for preparing this compound. A solution of lithium (1g, mol) in 150 ml of liquid ammonia \(^{28b}\) was treated with tetrahydrindanone 18 (3g, 0.022 mol) and t-butanol (2 ml) in ether (50 ml). Following the procedure described earlier in chapter I, for the preparation of trans-decal-3-one, on usual workup and purification by column chromatography (SiO\(_2\), hexane:EtOAc 95:5) resulted in trans-hydrindan-5-one (20) as major product (faster moving compound in TLC, 85% of the mixture) in good yield (2.0g, 70%).

IR (Neat) \( \nu_{\text{max}} : 1716 \text{ cm}^{-1} \).

\(^1\)H NMR(90 MHz) : \( \delta \) 1.2-2.6 (14H, m).

\(^1^3\)C NMR (22.5 MHz) : \( \delta \) 25.79 (t, C-2), 31.96 (t, C-3) 32.29 (t, C-1) 31.96 (t, C-3), 33.91 (t, C-7), 40.85 (d, C-7a), 43.12 (t, C-6), 47.35 (d, C-3a), 49.62 (d, C-4), 212.92 (s, C-5).
trans-6-Methoxycarbonylhydrindan-5(6H)-one (1)

(---)

To sodium hydride (0.5079 g, 0.011 mol, 50 % mineral oil suspension) in dry benzene (12 ml) under a blanket of nitrogen atmosphere, dimethyl carbonate (0.5 g, 0.07 mol) was added at 0°C with vigorous stirring. Subsequently hydrindanone 20 (1.0 g, 0.0072 mol) in benzene (10 ml) was added dropwise. Contents of the flask were stirred for 1/2 h. at 0°C and at room temperature for 12 h. After completion of the reaction (TLC, SiO₂, hexane-ethyl acetate 90:2) excess of NaH was destroyed with cold acetic acid. The precipitate was dissolved in cold water and extracted with diethyl ether (25 ml X 4). After usual workup and further purification of the crude product by column chromatography (SiO₂, hexane : ethylacetate 90:2) resulted in β-ketoester 1 (0.609 g, 42.3%).

IR (Neat) v max : 3200, 1746, 1659, 1611, cm⁻¹

¹H NMR (90 MHz) : δ 1.24-2.65 (2H, m), 3.85 (3H, s, -COOCH₃), 12.25 (1H, s, enolic H).

¹³C NMR (22.5 MHz) : δ 22.71 (t, C-2), 28.17 (t, C-3), 30.64 (t, C-1), 31.16 (t, C-7), 35.58 (t, C-4), 41.43 (d, C-7α), 42.09 (d, C-3α), 50.93 (q, C₆-COOCH₃), 97.36 (s, C-6),
172.92 (s, C₆–COOCH₃), 172.94 (s, C₅), 206.89 (s, C-5).

MS (EI) m/e (relative intensity): 196 (M⁺, 2.5), 196 (100), 164 (68), 136 (37), 108 (20), 80 (20), 67 (15), 55 (21).

HRMS calculated m/e 196.1099 for C₁₁H₁₆O₃
found m/e 196.1104.

Ethyl 1-methyl-2-oxocyclopentanecarboxylate (26)

Ethyl 2-oxo-cyclopentanone (31.2 g, 0.2 mol) prepared from diethyl adipate 23 according to the procedure described in Vogel's book in DMF (150 ml) was added dropwise to anhydrous potassium carbonate (155.29, 0.4 mol) dispersed in DMF. Methyl iodine (42.6 g, 0.3 mol) in DMF was added dropwise under magnetic stirring to the reaction mixture during 30 min. and stirred for another 2 h at room temperature. After the reaction was complete (TLC, SiO₂, hexane : ethylacetate 90:1, no coloration with neutral FeCl₃ test), the reaction mixture was filtered, concentrated under reduced pressure and the residue was taken in water (200 ml) and extracted with diethyl ether (50 ml X 6). The usual workup and purification by distillation (short path) alkylated product 26 (32.3 g, 95%) resulted. This reaction could also be conducted in acetone, but took more time (12h) for completion and the yields are however comparable with DMF
Hydrolysis of the ester in 8-ketoester 26 and further decarboxylation was carried out following the procedure of Bouveault. Ethyl 1-methyl-2-oxo-cyclopentanancarboxylate (26, 15.8 g, 0.1 mol) taken with conc. HCl (30 ml) was refluxed for 2 h. Reaction mixture was poured into 150 ml ice-cold water and extracted with diethyl ether (50 ml X 6) and on usual workup, removal of the solvent and distillation, resulted 2-methyl cyclopentanone 28 (9.0 g, 92%) which could be identified by its characteristic mint smell and other spectral data.

**IR (Neat)** $\nu_{max}$: 3330, 1742, 1738 cm$^{-1}$

$^{1}$H NMR (90 MHz): $\delta$ 1.1 (3H, d, J = 10.2 Hz, -CH$_3$), 1.2-2.86 (7H, m).

**7a-Methylhydrind-3a (4)-ene-5-one (30)**

(7, 7a-Dihydro-7a-methyl 8 (6H)-indenone)
The mixture of 2-methylcyclopentanone (28.8 g, 0.1 mol) and methyl vinyl ketone (7.0 g, 0.1 mol) was refluxed for 12 h in dry benzene (50 ml) with a drop of conc. H2SO4. Reaction mixture was poured in 100 ml ice cold water and layers were separated. Aqueous layer was extracted with benzene (50 ml x 2). After usual workup and removal of solvent resulted in diketone 29 (14.95 g, 89%)\(^3\). The crude product was further purified by column chromatography (SiO\(_2\), hexane : EtOAc 9 : 1) before cyclization was carried out.

IR (Neat) \(\nu_{\text{max}}\) : 2980, 1732, 1716, 1472 cm\(^{-1}\)

The procedure of Caine et al.\(^3\) diketone 29 (14.95 g, mol) taken in 200 ml 10% ethanolic KOH, was refluxed for 30 min. The cooled reaction mixture was neutralized with acetic acid and ethyl alcohol was removed under reduced pressure. The residue of the reaction mixture was taken in water (100 ml) and extracted with diethyl ether (50 ml x 5). After usual workup obtained crude product obtained was submitted for column chromatography (SiO\(_2\), hexane : ethylacetate 9 : 1) to furnish pure enone 30 (11.75 g, 88%).

UV \(\lambda_{\text{max}}\) : 238 nm

IR (Neat) \(\nu_{\text{max}}\) : 2976, 1662, 1458 cm\(^{-1}\)

\(^1\)H NMR (270 MHz) : \(\delta\) 1.15 (3H, s, C\(_7\)-CH\(_3\)), 1.29 - 1.56 (2H, m) 2.07-2.08 (6H, m), 2.31-2.8 (4H, m), 5.76 (1H, s, olefinic H).
\( ^{13}C \) NMR (100 MHz) : 6 21.12 (\( \delta \), C-2), 22.36 (\( \delta \), C7a-CH\(_3\)) 30.74 (\( \delta \), C-3), 33.76 (\( \delta \), C-6), 36.05 (\( \delta \), C-7), 40.80 (\( \delta \), C-1), 42.68 (\( \delta \), C-7a), 121.22 (\( \delta \), C-4), 178.84 (\( \delta \), C-3a), 199.74 (\( \delta \), C-5).

trans-7a-Methylhydrindan-5(6H)-one (31) and cis-7a-methylhydrindan-5(6H)-one (32)

To the enone 30 (3.0g, 0.02 mol) taken in methanol (100 ml) nickel chloride hexahydrate (14.26g, 0.06 mol) was added in three portions (0.02 mol), each time followed by an molar equivalent of sodium borohydride (2.28g, 0.06 mol) at -5°C to -0°C and further stirred for 1/2 h by which time starting enone 30 was absent in the reaction mixture. The reaction mixture was filtered through filter aid Celite and methanol was removed to result in a residue which was subjected to due workup (dichloromethane). This operation resulted in a mixture of isomeric ketones trans, 31, cis, 33 and further reduced products, alcohols in about 4:1 ratio (\(^1\)H NMR). Crude reaction mixture was subjected to oxidation with PCC.\(^{40}\) PCC (5.42g, 0.025 mol) was suspended in dry dichloromethane (100 ml). The mixture of saturated ketones 31, 32 and corresponding alcohols (0.02 mol) in dichloromethane (25 ml) was then added in one portion to the magnetically stirred suspension. After 1 h dry diethyl ether (100 ml) was added and the supernatant solution was decanted from the black gummy material, which was washed with diethyl
ether (50 ml X 4). The combined organic solution was passed through a short pad of Florosil and the solvent was removed by distillation. Reaction mixture was subjected to column chromatography (SiO₂, hexane : ethyl acetate 95 : 5) to result in the mixture of trans and cis ketones 31, 32 (0.039g, 85%) formed in 59 : 41 (¹H NMR) ratio. Since the mixture of 31, 32 were not separated under variety of solvent systems and with different adsorbents (SiO₂, Al₂O₃, neutral, basic ) cis 32 and trans 31 hydrindanones could be separated via methoxycarbonylation, separation and demethoxycarbonylations which was described earlier.¹² (see under preparation of 28). An authentic cis compound was prepared by hydrogenation of enone 10 under catalytic hydrogenation conditions known to afford cis compound 32

cis 7a-methylhydrindan 5(6H)-one (32)

IR (Neat) νmax : 1726, 1468 cm⁻¹
¹H NMR (90 MHz) : δ 1.12 (3H, s, C₇a-CH₃), 1.2-1.21 (9H, m), 2.2 - 2.55 (4H, m).
¹³C NMR (22.5 MHz) : δ 22.20 (t, C-2), 26.79 (q, C₇a-CH₃), 32.54 (t, C-3), 33.82 (t, C-7), 36.87 (t, C-6), 39.81 (s, C-7a), 39.81 (t, C-1), 42.49 (t, C-4), 46.41 (d, C-3a), 213.64 (s, C-5).

180
trans 7a-methylhydridan 5(6H)-one (31).

IR (Neat)  $\nu_{\text{max}}$: 1716, 1470 cm$^{-1}$

$^1$H NMR (270 MHz): $\delta$ 0.96 (3H, s, C7a -CH$_3$), 2.00 - 2.5 (13H, m).

$^{13}$C NMR (100 MHz): $\delta$ 16.30 (q, C$_7$-CH$_3$), 22.04 (t, C-2), 28.18 (t, C-3), 37.03 (t, C-7), 38.05 (t, C-6), 39.16 (t, C-1), 40.40 (s, C-7a), 43.18 (t, C-4), 48.33 (d, C-3a), 212.79 (s, C-5).

trans-6-Methoxycarbonyl 7a-methylhydridan-5-one (2) and cis 6-methoxycarbonyl 7a-methylhydridan-5-one (2C)

The mixture of saturated ketones (32, cis and trans, 31 mixture) was methoxycarbonylated with dimethyl carbonate and sodium hydride in benzene at reflux temperature following the procedure described for the preparation of trans-2-methoxycarbonyl 10-methyl-trans-decal-3-one (chapter I). Thus the mixture of cis, 32 and trans, 31 ketones (0.70g, 0.004 mol) were treated with sodium hydride (0.53g, 0.023 mol, 50% oil suspension) and dimethyl carbonate (2.06g, 0.023 mol) in dry benzene (30 ml) at refluxing temperature which resulted in a mixture of methoxycarbonylated products 2, 2C (0.728g, 75%). The compound which moves faster on TLC ($SiO_2$, hexane
ethyl acetate 98:2) was identified as **trans** compound 2
(\(^1\)H and \(^{13}\)C NMR) constituting 44\% (0.330 g) of the total
reaction mixture and major product slower moving compound on
TLC was identified as **cis** B-ketoester 2C (\(^1\)H and \(^{13}\)H NMR)
and formed in 56\% (0.408 g) ratio of the total mixture.
Both the components were separated and characterized fully.

**trans-6-Methoxycarbonyl 7a-methylhydridan-9-one** (2)

IR (Neat) \(\nu_{\text{max}}\) : 3200, 1716, 1660, cm\(^{-1}\)

\(^1\)H NMR (270 MHz) : \(\delta\) 0.71 (3H, s, \(\text{C}_7\text{a}-\text{CH}_3\)), 1.25-1.34
(3H, m), 1.37-1.81 (4H, m), 1.833 - 2.11 (2H, m), 2.34-2.41
(2H, m), 3.75 (3H, s, -COOC\(_3\)), 12.29 (1H, s, enolic H).

\(^{13}\)C NMR (100 MHz) : \(\delta\) 16.86 (\(+\), \(\text{C}_7\text{a}-\text{CH}_3\)), 21.28 (\(+\), \(\text{C}-2\)),
27.61 (\(+\), \(\text{C}-3\)), 31.80 (\(+\), \(\text{C}-7\)), 36.60 (\(+\), \(\text{C}-1\)), 39.31 (\(+\),
\(\text{C}-4\)), 39.58 (\(+\), \(\text{C}-7\)), 43.18 (\(+\), \(\text{C}-3\)), 51.26 (\(+\), \(\text{C}_6-\text{COOCH}_3\)),
96.95 (\(+\), \(\text{C}-6\)), 173.53 (\(+\), \(\text{C}-5\)), 173.56 (\(+\), \(\text{C}_6-\text{COOCH}_3\)).

MS (EI) (relative intensity) : 210 (\(M^+\), 65), 178 (57), 168
(17), 150 (67), 135 (23), 128 (19), 109 (29), 95 (100), 81
(36), 67 (42), 55 (27), 41 (25).

HRMS calculated for \(\text{C}_{12}\text{H}_{16}\text{O}_3\) \(m/e\) 210.126
found \(m/e\) 210.124.
cis-4-Methoxycarbonyl 7a-methylhydrindan-5-one (2C)

\[
\begin{align*}
\text{IR (Neat)} & \quad \text{\nu}_{\text{max}}: \, 3250, \, 17120, \, 1658, \, \text{cm}^{-1} \\
{^1}H \text{ NMR (270 MHz)} & \quad \delta 1.00 (3H, s, C_7\text{-CH}_3), \, 1.10-2.30 (11H, m), \, 3.75 (3H, s, -COOCH_3), \, 12.11 (1H, s, enolic H), \\
{^{13}}C \text{ NMR (100 MHz)} & \quad \delta 20.71 (\, 4, \, C-3), \, 25.83 (\, 4, \, C_7\text{-CH}_3), \, 30.07, \, 30.85, \, 31.30, \, 36.94, \, 39.47, \, 40.31, \, 43.17 (\, 4, \, C-3a), \, 51.37, \, (C_4\text{-COOCH}_3), \, 95.35, \, 173.06, \, (C_4\text{-COOCH}_3), \, 206.91, \, (C-5).
\end{align*}
\]

Complete assignment of the resonances in spectrum, as the compound was found to be a fast equilibrium mixture of keto-enol tautomers. \textit{trans}, 2 and \textit{cis}, 2C hydrindanones-ketoesters were decarboxymethoxylated separately under acidic conditions (conc. HCl) via hydrolysis and decarboxylation procedure following the experimental details discussed for the preparation of 2-methylcyclopentanone (2B). Thus pure \textit{cis} 32 and \textit{trans} 31 hydrindanones could be obtained whose spectral details were given earlier.

Ethyl 1-(3-oxobutyl)-2-oxo-cyclopentanecarboxylate (33)
This compound is a diketone ester was prepared by following the procedure described by Nelson et al.29 The procedure which was followed is essentially the same to the one described for the preparation of ethyl 1 (1-oxobutyl)-2-oxocyclohexanecarboxylate (Chapter I, experimental section). Thus ethyl-2-oxocyclopentane carboxylate 25 (15.6g, 0.10 mol), methyl vinyl ketone (7.7g, 0.11 mol), nickel (II) acetyl acetonate (0.25g, 1.0 mol.%) and 1, 4-dioxan (15 ml) were heated in a bath maintained at 85°C for 18 h. to afford an oily product 23 (21g, 93%) which gave no violet coloration with neutral FeCl₃ solution indicating the absence of an enol. No further purification was done since it was sufficiently pure enough to carry out cyclization reaction.

IR (Neat) \( \nu_{\text{max}} \): 2962, 1749, 1722, 1452 cm\(^{-1}\)

\( ^{1}H \) NMR (90 MHz) : \( \delta \) 1.21 (3H, t, \( J = 9.1 \) Hz, -\( \text{COOCH}_2\text{CH}_3 \)), 1.75-2.04 (4H, m), 2.28 - 2.72 (6H, m), 2.18 (3H, s, -\( \text{COOCH}_3 \)), 4.18 (2H, q, \( J = 9.1 \) Hz, -\( \text{COOCN}_2\text{CH}_3 \)).

7a-\( \text{Ethoxycarbonyl} \)hydrind-3a(4)-ene-5-one (34)

(Ethyl, 5, 6, 7, 7a,-\( \text{tetrhydrindan-5-one-7a-carboxylate} \))

The procedure described for the preparation of enone,
10-ethoxycarbonyldecal-4-ene-3-one (Chapter I experimental section) was followed for the preparation of this enone 34. Thus the diketone 33 (15g, 0.066 mol) and pyrrolidine (5.7g, 0.1mol) was refluxed for 4 h. in dry hexane and on buffer (pH = 5) treatment and the usual workup gave the crude title compound 34 (12g). Purification was carried out by distillation (bulb to bulb) and column chromatography (SiO₂, hexane : ethylacetate 9:1) to afford pure enone 34 (10g, 73%).

UV λmax : 238 NM

IR (Neat) νmax : 1728, 1677, 1185, cm⁻¹

¹H NMR (90 MHz) : δ 1.12 (3H, t, J = 9.3 Hz, -COOCH₂CH₃), 1.29- 2.00 (4H, m), 2.12-2.44 (6H, m), 4.06 (2H, q, J = 9.4 Hz, -COOCH₂CH₃), 5.76 (1H, s, olefinic H).

¹³C NMR (22.5 MHz) : δ 13.30 (q, C₇a-COOCH₂CH₃), 21.37 (t, C-2), 31.10 (t, C-3), 32.54 (t, C-6), 37.51 (t, C-7), 37.91 (t, C-1), 53.65 (s, C-7a), 60.51 (t, C₇a-COOCH₂CH₃), 122.53 (d, C-4), 169.41 (s, C-3a), 172.39 (s, C₇a-COOCH₂CH₃), 197.27 (s, C-5).

trans-7a-Ethoxycarbonylhydrindan-5-one (35) and cis-7a-Ethoxycarbonylhydrindan-5-one (36)

The procedure of Ideson and Becker followed for the
hydrogenation of decaleneone, described earlier in Chapter I, the unsaturated ketoester 34 (10g, 0.048 mol) in ethyl acetate (100 ml) having 10% Pd-C (0.600 g) and calcium carbonate (0.600g) was hydrogenated (H₂ /40 psi, 4h) to a mixture of two hydrindanones 35, 36 (9.9g, 98%). The faster moving component on TLC which is major isomer (83% of the total mixture) identified as cis, 36 isomer and slower moving component on TLC as minor (13% of the total mixture) is trans, 36 (¹H NMR GLC) after separation by chromatron (SiO₂, hexane : ethyl acetate 95 : 5).

trans-7a-Ethoxycarbonylhydrindan-9-one (35)

IR (Neat) νmax : 1720 cm⁻¹
¹H NMR (90 MHz) : δ 1.12 (3H, t, J = 9.37 Hz, -COOCH₂CH₃), 1.6-2.08 (9H, m), 2.23-2.76 (4H, m), 4.19 (2H, q, J = 9.35Hz, -COOCH₂CH₃).
¹³C NMR (22.5 MHz) : δ 14.29 (q, C₇₋₆-COOCH₂CH₃) 22.58 (t, C-2), 29.55 (t, C-3), 31.87 (t, C-1), 36.96 (t, C-7), 36.96 (t, C-6), 42.15 (t, C-4), 42.52 (d, C-3a), 50.67 (d, C-7a), 60.51 (t, C₇₋₆-COOCH₂CH₃), 176.37 (s, C₇₋₆-COOCH₂CH₃), 211 (s, C-5)

MS calculated for C₁₂H₁₈O₃ m/z 210.1450
found m/z 210.1245
cis-7a-Ethoxycarbonylhydrindan-5-one (36)

IR (Neat) v max : 1725, cm⁻¹

^1H NMR (90 MHz) : δ 1.28 (3H, t, J = 9.4 Hz, -COOCH₂CH₃), 1.48-1.92 (9H, m), 2.28-2.68 (4H, m), 4.21 (2H, q, J = 9.4 Hz, -COOCH₂CH₃).

^13C NMR (22.5 MHz) : δ 14.24 (q, C₇a-COOCH₂CH₃), 22.36 (t, C-2), 27.56 (t, C-3), 32.84 (t, C-1), 35.74 (t, C-7), 38.17 (t, C-6), 42.26 (t, C-4), 48.76 (d, C-3a), 52.21 (s, C-7a), 59.95 (t, C₇a-COOCH₂CH₃), 174.50 (s, C₇a-COOCH₂CH₃), 210.20 (s, C-5).

Note: It has been reported, Dauben et al.⁶ that only cis isomer 36 formed from hydrogenation reaction in 83% yield.

HRMS calculated for C₁₂H₁₈O₃ m/e 210.1460
found m/e 210.1606

trans-7a- Ethoxycarbonyl-6-methoxycarbonylhydrindan-5-one (3)

The procedure described by Chakravarthi et al. was
followed for the preparation of the 6-ketoester 3 which is 
esential same to the one described for 8-ketoester, a 6,6-
bicyclic ketoester (vide Chapter 1, experimental).

Hydrindanone 35 (2.10g, 0.1 mol) in dry benzene (15 ml) was 
added to a mixture of sodium hydride (2.3 g, 0.5 mol, 50% 
mineral oil suspension) and dimethyl carbonate (4.5g, 0.5 
mol) taken in dry benzene (25 ml) at 0°C and under magnetic 
stirring. The reaction was monitored (TLC). After the due 
work-up, and removal of solvent resulted crude product, which 
was subjected to column chromatography (SiO2, hexane : ethyl 
acetate 98:2). The 6-keto-ester 36 obtained as a white low 
melting solid (2.23: 90%).

m. p : 35°C

IR (Neat)  νmax : 3200, 1653, 1611 cm⁻¹

1H NMR (90 MHz) : δ 1.2 (3H, t, J = 8.2 Hz, -COOCH2CH3), 
1.6-2.54 (10H, m), 3.1 (1H, d, J = 15.2 Hz), 3.65 (1H, bs), 
3.75 (3H, s, -COOCH3), 4.08 (2H, q, J = 8.2 Hz, -COOCH2CH3), 
12.23 (1H, s, enolic H).

13C NMR (22.5 MHz) : δ 11.95 (q, C7a-COOCH2CH3), 22.25 
(t, C-2), 22.78 (t, C-3), 31.87 (t, C-1), 32.76 (t, C-7), 
36.52 (t, C-4), 44.14 (d, C-3a), 51.22 (q, C7a-COOCH2CH3), 
51.88 (s, C-7a), 59.95 (t, ), 96.77 (s, C-6), 172.17 (s, 
non-enolic, C-5), 173.17 (s, enolic C-5), 174.82 (s, C7a-

13C NMR indicates that the 6-ketoester is present as a fast 
equilibrium mixture of keto-enol tautomers.
MS (EI) m/e (relative intensity) : 268 (M⁺, 46), 236 (100), 208 (57), 194 (63), 162 (98), 135 (68), 107 (15), 94 (20), 79 (20), 67 (12), 55 (13), 41 (10)

HRMS calculated for C₁₄H₂₀O₅ m/e 268.1311
found m/e 268.1317

II.11. General Representative Procedure for Alkylation Reaction:

The 3-ketoester (0.1 mmol) in acetone (3 ml) was added to the potassium carbonate (0.5 mmol) which was dispersed in dry acetone (5 ml) under magnetic stirring and nitrogen atmosphere. The alkylating agent (methyl iodide/benzyl bromide, 0.5 mmol) in acetone (5 ml) was added over a period of 10 minutes. After 12 h by which time reaction completes (TLC), solid particles (potassium carbonate, potassium iodide, potassium bromide etc.) were filtered and concentrated under reduced pressure. The residue was taken in water and extracted throughly with diethyl ether (20 ml X 5). The crude alkylated products were isolated after due workup as light oil, found negative to the ferric chloride color test. The ¹H NMR spectrum of this crude material was recorded and relative ratios of peaks characteristic to each epimer were calculated. The individual isomers were separated by chromatography (TLC), column chromatography and chromatron) and were characterised.
Analytical samples were obtained by repeated column chromatography by using different solvent system as eluants. The alkyalted products obtained were colorless solids or light yellow oils.

II.11.1. Spectral data for alkyalted products

trans-6β-Methyl-6a-methoxycarbonylyhydrindan-8-one (4, X-isomer, slower moving component in TLC)

\[
\text{IR (Neat) } \nu_{\text{max}} : 1741, 1711 \text{ cm}^{-1}
\]

\[\text{\textsuperscript{1}H NMR (400 MHz)} : \delta 1.33-1.19 (2H, m, C_1-\text{H} & C_3-\text{H}), 1.45 (3H, s, C_6-\text{CH}_3), 1.59-1.63 (1H, m, C_3a-\text{H}), 1.64-1.79 (1H, m, C_7a-\text{H}), 1.80-1.83 (2H, m, C_1-\text{H} & C_3-\text{H}), 1.82-1.92 (2H, m, C_2-\text{H} & \text{H}), 2.00 (1H, dt, J_1 = 11.06 Hz, J_2 = 1.08 Hz, C_7-\text{H}), 2.14 (1H, t, J = 13.06 Hz, C_7-\text{H}), 2.22 (1H, dt, J_1 = 14.50 Hz, J_2 = 3.64 Hz, C_4-\text{H}), 3.71 (\text{t}, \text{C} - \text{COOC}_3\text{H}_3).
\]

\[\text{\textsuperscript{13}C NMR (100 MHz)} : \delta 21.23 (\text{C}_6-\text{CH}_3), 23.05 (\text{C} - 2), 30.25 (\text{C} - 3), 31.37 (\text{C} - 1), 39.49 (\text{C} - 7), 40.41 (\text{C} - 7a), 44.23 (\text{C} - 4), 46.32 (\text{C} - 3a), 52.33 (\text{C} - \text{C}_6-\text{COOC}_3\text{H}_3), 57.46 (\text{C} - 6), 174.02 (\text{C} - \text{C}_6-\text{COOC}_3\text{H}_3), 210.49 (\text{C} - 5).
\]

\[\text{MS (EI, 70eV) } m/e \text{ (relative intensity)} : 210 (M^+, 40), 178
\]
(37), 182 (35), 178 (48), 166 (18), 150 (59), 137 (27), 22 (83), 108 (54), 95 (81), 88 (34), 81 (69), 67 (100), 59 (18), 51 (32), 41 (91).

ERMS calculated for C_{12}H_{18}O_{3} m/e 210.1268,
found m/e 210.1256.

**trans-6α-Methyl-68-methoxycarbonylhydrindan-5-one (S, E-somer, faster moving component in TLC)**

![Chemical Structure](image)

**IR (Neat) v_{max}: 1716, cm^{-1} (S-somer)**

**$^1$H NMR (400 MHz):** δ 1.06 - 1.25 (2H, m), 1.29 (3H, m, C_{6}-CH_{3}), 1.39 - 1.40 (1H, m), 1.42 - 1.53 (2H, m, J_{1} = 6.15 Hz, C_{7}-Ha), 1.60 - 1.87 (4H, m, J_{1} = 6.15 Hz, J_{2} = 4.5 Hz, C_{4}-Ha), 2.04 (1H, dd, J_{1} = 6.15 Hz, J_{2} = 4.5 Hz, C_{4}-HB), 3.71 (3H, s, -COOCH_{3}).

**$^{13}$C NMR (100 MHz):** δ 21.81 (C, C_{6}-CH_{3}), 21.16 (C, C_{2}), 29.99 (C, C-3), 31.54 (C, C-1), 41.50 (C, C-7a), 42.69 (C, C-3a), 43.15 (C, C-7), 48.01 (C, C-4), 52.66 (C, C_{6}-COOCH_{3}), 56.08 (C, C-6), 174.54 (C, C_{6}-COOCH_{3}), 208.10 (C, C-5).

**MS (EI, 70ev) m/e (relative intensity):** 210 (M^+, 59), 182 (43), 178 (48), 166 (18), 150 (59), 137 (27), 122 (83), 108 (54), 95 (81), 88 (33), 81 (70), 67 (100), 59 (18), 53 (11), 41 (96).

ERMS calculated for C_{12}H_{18}O_{3} m/e 210.1256,
found m/e 210.1260.
5-fluoro-68-Dansyl-6a-methoxycarbonylhydrindan-3-one (6, 6-isomer, faster moving component in TLC).

IR (Neat) \( \nu_{\text{max}} \) : 1730, 1715, 1600 cm\(^{-1}\) (6-isomer)

\(^1\)H-NMR (400 MHz) : \( \delta \) 1.07-1.13 (2H, m), 1.19-1.27 (2H, m), 1.38-1.38 (5H, m), 2.25 (1H, t, \( J = 13.18 \) Hz, \( C_7-H_\alpha \)), 2.53 (1H, dd, \( J_1 = 13.18 \) Hz, \( J_2 = 3.42 \) Hz, \( C_4-H_\alpha \)), 2.68 (1H, dd, \( J_1 = 13.18 \) Hz, \( J_2 = 3.42 \) Hz, \( C_4-H_\alpha \)), 2.89 (1H, d, \( J = 13.67 \) Hz, A of AB of -CH\(_2\)C\(_6\)H\(_5\)), 3.23 (1H, d, \( J = 13.67 \) Hz, B of AB of -CH\(_2\)C\(_6\)H\(_5\)), \( \Delta \delta = 0.34 \) ppm, 3.61 (3H, s, -COOCH\(_3\)), 7.07-7.12 and 7.18 (5H, m, aromatic H's).

\(^13\)C-NMR (100 MHz) : \( \delta \) 23.61 (t, C-2), 29.87 (t, C-3), 31.21 (t, C-1), 38.56 (t, C\(_6\)-CH\(_2\)C\(_6\)H\(_5\)10), 40.77 (d, C-7a), 42.62 (t, C-7), 46.90 (d, C-3a), 47.63 (t, C-4), 52.86 (q, C-COOCH\(_3\)), 61.14 (s, C-6), 171.74 (s, C\(_6\)-COOCH\(_3\)), 207.14 (s, C-5), 136.67 (s, C-1'), 130.30 (d, C-2'), 128.05 (d, C-3'), 126.68 (d, C-4').

MS (EI, 70 ev) m/e (relative intensity) : 286 (M\(^+\), 25), 267 (50), 257 (20), 225 (50), 209 (14), 145 (21), 131 (19), 117 (45), 104 (14), 91 (100), 81 (17), 67 (21), 41 (18).

HRMS calculated for C\(_{18}\)H\(_{22}\)O\(_3\) m/e 286.1569,

dead m/e 286.1586.
**trans-6α-Benzyl-6β-methoxycarbonylhydrindan-5-one** (7, E-isomer, slower moving component in TLC).

**IR** (Neat) $\nu_{\text{max}}$: 1736, 1715, 1600 cm$^{-1}$.

$^1$H NMR (400 MHz): $\delta$ 1.30 - 1.40 (1H, m), 1.45-1.55 (1H, m), 1.62-1.89 (4H, m), 2.41 (1H, dd, $J_1 = 13$ Hz, $J_2 = 6$ Hz, C$_7$-H$_{\alpha}$), 2.29 (1H, dd, $J_1 = 12$ Hz, $J_2 = 6$ Hz, C$_7$-H$_{\beta}$), 2.36 (1H, dd, $J_1 = 16$ Hz, $J_2 = 8$ Hz, C$_4$-H$_{\beta}$), 2.45 (1H, ddd, $J_1 = 16$ Hz, $J_2 = 4$ Hz, $J_3 = 3$ Hz, C$_4$-H$_{\alpha}$), 3.18 (1H, d, $J = 13.68$ Hz, A of AB of -CH$_2$C$_6$H$_5$), 3.45 (1H, d, $J = 13.68$ Hz, B of AB of -CH$_2$C$_6$H$_5$, $\Delta\delta = 0.27$ppm), 3.62 (3H, s, -COOCH$_3$), 7.14-7.26 (5H, m, aromatic H's).

$^{13}$C NMR (100 MHz): $\delta$ 24.02 (t, C-2), 26.56 (t, C-3), 32.54 (t, C-1), 37.54 (d, C-7a), 39.17 (t, C-10), 41.27 (t, C-7), 43.13 (t, C-4), 46.13 (d, C-3a), 51.77 (q, C-9), 63.16 (s, C-6), 172.58 (s, C-8), 209.32 (s, C-5), 136.68 (s, C-1'), 130.68 (d, C-2'), 128.28 (d, C-3'), 126.95 (d, C-4').

**MS** (EI, 70ev) m/e (relative intensity): 286 (M$^+$, 100), 267 (41), 254 (45), 225 (92), 208 (23), 181 (38), 172 (22), 141 (13), 128 (13), 115 (10), 91 (30), 41 (10).

**HRMS** calculated for C$_{18}$H$_{22}$O$_3$ m/e 286.1569, found m/e 286.1587.
trans-6a,7α-Dimethyl-6β-methoxycarbonylhydrindan-5-one (9, E-isomer, faster moving component in TLC).

IR (Neat) v max : 1716, cm⁻¹.

1H NMR (200 MHz) :  δ 0.83 (3H, s, C₇α-CH₃), 1.29 (3H, s, C₆-CH₃), 1.12-1.40 (2H, m), 1.41 (1H, d, J = 16.13 Hz, C₇-Hα), 1.52-1.89 (6H, m), 2.52-2.65 (2H, m, C₄-Hα and Hβ), 2.77 (1H, d, J = 13.16 Hz, C₇-Hβ), 3.71 (3H, s, -COOCH₃).

13C NMR (50 MHz) :  δ 16.48 (q, C₇α-CH₃), 21.42 (t, C-2), 23.65 (q, -CH₃ 27.80 (t, C-3), 39.34 (t, C-1), 40.81 (s, C-7α), 42.81 (t, C-4), 49.26 (d, C-3a), 49.76 (t, C-7), 52.48 (q, C₆-COOCH₃), 54.04 (s, C-6), 175.29 (s, C₆-COOCH₃), 208.57 (s, C-5).

MS (EI, 70eV) m/z (relative intensity) : 224 (M⁺, 9), 192 (29), 182 (20), 155 (34), 149 (12), 123 (40), 101 (42), 95 (100), 81 (86), 67 (84), 55 (38), 41 (90).

HRMS calculated for C₁₃H₂₀O₃ m/z 210.1412, found m/z 210.1387.

trans-6a-Benzyl-7α-methyl-6β-Methoxycarbonylhydrindan-5-one

(11, E-isomer)
IR (Neat) \( \nu_{\text{max}} \): 1716, 1725, cm\(^{-1}\).

\(^1H\) NMR (200 MHz): 6 0.80 (3H, s, C\(_7\)\(\beta\)-CH\(_3\)), 1.05-1.86 (8H, m), 1.50 (1H, d, \(J = 17.60\) Hz, C\(_7\)-H\(_{\alpha}\)). 2.52 (3H, unresolved dd, \(J_1 = 17.65\) Hz, \(J_2 = 17.60\) Hz, C\(_4\)-H\(_{\alpha}\), H\(_B\) and C\(_7\)-H\(_{\beta}\)). 3.08 (2H, dd, \(J_1 = 16.15\) Hz, \(J_2 = 112.31\) Hz, \(\Delta\delta = 0.077\) ppm, A and B of AB of -CH\(_2\)C\(_6\)H\(_5\)), 3.60 (3H, s, -COOC\(_3\)) 7.19 - 7.20 (5H, s, aromatic H's).

\(^{13}C\) NMR (50 MHz) = 6 17.02 (q, C\(_7\)\(\alpha\)-CH\(_3\)), 21.58 (t, C-2), 27.83 (t, C-3), 39.65 (t, s, C-1), 40.84 (d, C-7\(\alpha\)), 42.06 (t, C\(_6\)-CH\(_2\)C\(_6\)H\(_5\)), 42.68 (t, C-4), 46.80 (t, C-7), 49.01 (d, C-7\(\alpha\)), 52.46 (q, C\(_6\)-COOCH\(_3\)), 59.80 (s, C-6), 66.80 (t, C-7), 49.01 (d, C-3\(\alpha\)), 52.46 (q, C\(_6\)-COOCH\(_3\)), 59.80 (s, C-6), 173.75 (s, C\(_6\)-COOCH\(_3\)), 207.83 (s, C-5), 137.07 (s, C-1\(\beta\)), 131.32 (d, C-2\(\beta\)), 128.08 (d, C-3\(\beta\)), 126.83 (d, C-4\(\beta\)).

MS (EI, 70eV) m/e (relative intensity): 300 (M\(^{+}\), 17), 282 (13), 268 (10), 240 (28), 209 (12), 155 (14), 145 (28), 117 (29), 95 (41), 91 (100), 81 (33), 67 (30), 55 (13), 41 (18).

IRMS calculated for C\(_{19}\)H\(_{24}\)O\(_3\) m/e 300.1725, found m/e 300.1701.

trans-7\(\alpha\)β-Ethoxycarbonyl-6\(\beta\)-methyl-6\(\alpha\)-methoxycarbonylhydrindan-5-one (12, Z-isomer, slower moving component in TLC)

IR (Neat) \( \nu_{\text{max}} \): 1744, 1717, cm\(^{-1}\).
$^1$H NMR (400 MHz): 6 1.27 (3H, t, J = 8.88 Hz, -COOCH$_2$CH$_3$), 1.36 (3H, s, C$_6$-CH$_3$), 1.46 (1H, d, J = 17.18 Hz, C$_7$-Ha), 1.58 -1.89 (2H, m, ) 2.2 -3.5 ( 2H, m ), 2.32 ( 1H, bd, J1 = 17.8 Hz, J2 = 6 Hz, C$_4$-H8), 2.68 (1H, dd, J1 = 17.18 Hz, J2 = 6.0 Hz, C$_4$-H8), 3.13 (1H, d, J = 17.18 Hz, C$_7$-H8), 3.65 ( 3H, s, -COOCH$_3$), 4.04 ( 1H dq J1 = 10.65 Hz, J2 = 7.3 Hz A of AB of -COOCH$_2$CH$_3$), 4.12 (1H, dq, J1 = 10.65 Hz, J2 = 7.3 Hz B of AB of -COOCH$_2$CH$_3$). $\Delta \delta = 0.08$ppm).

$^{13}$C NMR (100 MHz): 6 13.98 (q, C$_7$a-COOCH$_2$CH$_3$), 21.95 (t, C-2), 23.16 (q, C$_6$-CH$_3$), 27.02 (t, C-3), 37.40 (t, C-1), 40.71 (d, C-3a), 45.22 (t, C-4), 49.27 (t, C-7), 51.72 (s, C-7a), 52.88 (q, C$_6$-COOCH$_3$), 54.92 (t, C$_7$a-COOCH$_2$CH$_3$), 60.67 (s, C-6), 174.82 (s, C$_7$a-COOC$_2$H$_3$) 175.50 (s, C$_6$-COOCH$_3$), 208.09 (s, C-5).

MS (EI,70ev) m/e (relative intensity): 282 ( M', 14), 237 (10), 209 (13), 282 (100), 154 (96), 14 (22), 125 (39), 108 (20), 95 (15), 67 (19), 41 (2).

HRMS calculated for C$_{15}$H$_{22}$O$_{5}$ m/e 282.1467, found m/e 282.1564.

trans-7aR-Ethoxycarbonyl-6a-methyl-6b-methoxycarbonyl - hydr indan-5-one (13, $E$-isomer).

IR (Neat) $\nu_{\max}$: 1742, 1738, cm$^{-1}$
$^1$H NMR (400 MHz): $\delta$ 1.29 (3H, t, $J = 8.89$ Hz, -COOCH$_2$CH$_3$), 1.29 (3H, s, C$_{6}$-CH$_3$), 1.45 (1H, d, $J = 14.16$ Hz, C$_7$-Ha), 1.71-1.79 (5H, m, ) 2.25 -2.29 (2H, m, C$_{3a}$-Ha), 2.52 (1H, bd, J = 14.06 Hz, J2 = 1.95 Hz, C$_4$-Ha), 3.12 (1H, d, $J = 14.16$ Hz, C$_7$-Hb), 3.50 (1H, t, $J = 14.65$ Hz, C$_4$-Hb), 3.64 (1H, s, -COOC$_3$), 4.03 (1H dq J1 = 10.67 Hz, J2 = 7.2 Hz A of AB of -COOCH$_2$CH$_3$), 4.17 (1H, dq, J1 = 10.67 Hz, J2 = 7.2 Hz B of AB of -COOCH$_2$CH$_3$), $\Delta \delta = 0.14$ppm).

$^{13}$C NMR (100 MHz): $\delta$ 13.96 (q, C$_7$-COOCH$_2$CH$_3$), 21.90 (t, C-2), 21.95 (t, C$_6$-CH$_3$), 27.06 (t, C-3), 37.07 (t, C-1), 42.24 (t, C-4), (d, C-3a), 45.15 (t, C-4), 49.27 (t, C-7), 51.64 (s, C-7a), 52.40 (q, C$_6$-COOCH$_3$), 54.16 (t, C$_7$-COOCH$_2$CH$_3$), 60.60 (s, C-6), 173.45 (s, C$_7$-COOCH$_2$CH$_3$), 174.80 (s, C$_6$-COOCH$_3$), 208.29 (s, C-5).

MS (EI,70ev) m/e (relative intensity): 282 (M$^+$, 2), 237 (7), 223(6), 209 (15), 182 (86), 168 (17), 154 (100), 149 (26), 140 (42), 125 (53), 108 (30), 95 (22), 81 (20), 67 (11), 57 (14), 41 (16).

MS calculated for C$_{15}$H$_{22}$O$_5$ m/e 282.1467, found m/e 282.1481.

**Trans-6o-Benzyl-7aβ-ethoxycarbonyl-6β-methoxycarbonylhydrindan-5-ona (15, E-isomer).**

IR (Neat) $\nu_{max}$: 1711, 1738, cm$^{-1}$
$^{1}H$ NMR (400 MHz) : δ 1.26 (3H, t, J = 6.83 Hz, COOCH$_2$CH$_3$), 1.55 - 1.70 (6H, m), 1.56 (1H, d, J = 11.95 Hz, C$_7$-Ha), 2.27 (1H, m, C$_3$-H), 2.50 (1H, dt, J1 = 10.74 Hz, J2 = 3.42 Hz, C$_4$-Ha), 3.06 (1H, d, J = 13.67 Hz A of AB of -CH$_2$C$_6$H$_5$), 3.08 (1H, d, J = 11.95 Hz, C$_7$-H8), 3.17 (1H, d, J = 11.67 Hz, B of AB of -CH$_2$C$_6$H$_5$), 3.47 (1H, t, J = 10.36 Hz, C$_4$-H8), 3.65 (1H, s, -COOCH$_3$), 3.98 (1H dq J1 = 10.35 Hz, J2 = 6.37 Hz A of AB of -COOCH$_2$CH$_3$), 4.14 (1H, dq, J1 = 10.35 Hz, J2 = 6.37 Hz B of AB of -COOCH$_2$CH$_3$) $\Delta$δ = 0.16 ppm.

$^{13}$C NMR (100 MHz) : δ 13.96 (q, C$_{7a}$-COOCH$_2$CH$_3$), 21.82 (t, C-5), 26.83 (t, C-3), 37.87 (t, C-1), 42.06 (t, C$_6$-CH$_2$C$_6$H$_5$), 41.36 (, C-4), 42.06 (t, C$_6$-CH$_2$C$_6$H$_5$), 42.45 (d, C-3a), 48.52 (t, C-7), 51.72 (s, C-7a), 52.36 (q, C$_6$-COOCH$_3$), 59.59 (t, C$_{7a}$-COOCH$_2$CH$_3$), 60.53 (s, C-6), 171.88 (s, C$_{7a}$-COOC$_2$H$_3$), 174.90 (s, C$_6$-COOCH$_3$), 207.32 (s, C-5), 116.29 (s, C-1'), 110.94 (d, C-2'), 128.00 (d, C-3'), 126.71 (d, C-4').

MS (EI, 70eV) m/e (relative intensity) : 158 (M$^+$, 3), 126 (14), 312(12), 253 (12), 168 (44), 182 (90), 154 (97), 140 (69), 125 (42), 117 (29), 81 (16), 67 (24), 41 (14).

HRMS calculated for C$_{21}$H$_{26}$O$_5$ m/e 358.1780,
found m/e 358.1740.

**trans-4a,7aβ-Dimethyl-4β-methoxycarbonylhydridan-5-one (9C)**

![Structural diagram](image)

IR (neat) : 1717, 1472 cm$^{-1}$
$^1$H NMR (400 MHz) : δ 1.08 (3H, s, C$_{7a}$-CH$_3$), 1.39 (3H, s, C$_4$-CH$_3$), 1.55-1.90 (8H, m, ring methylenes), 2.05 (1H, m, C$_{3a}$-H$_A$), 2.42 (1H, ddq, J1 = 16 Hz, J2 = 12.8 Hz, J3 = 9.6 Hz, C$_6$-H$_A$), 2.52 (1H, dd, J1 = 12.8 Hz, J2 = 9.6 Hz, C$_6$-H$_A$), 3.69 (1H, m, C$_4$-COOC$_2$H$_3$)

$^{13}$C NMR (400 MHz) : δ 22.25 (q, C$_7$-CH$_3$), 24.06 (t, C-2), 29.84 (q, C$_4$-CH$_3$), 30.16 (t, C-3), 33.21 (t, C-7), 35.52 (t, C-1), 41.92 (t, C-6), 42.07 (s, C-7a), 51.94 (q, C$_4$-COOC$_2$H$_3$), 54.73 (d, C-3a), 57.07 (s, C-4), 173.31 (s, COOC$_2$H$_3$), 210.48 (s, C-5).

MS (EI, 70ev) m/e (relative intensity) : 224 (M$^+$, 12), 192 (35), 182 (18), 155 (40), 149 (15), 123 (45), 101 (51), 95 (100), 81 (86), 67 (84), 55 (40), 41 (85)
II.12. References


e. *idem. Synth. Commun. 1988, 18, 115. For synthesis of trans-fused CD ring system in optically pure form, see*


c. ref.8d.


    c. See also, Miller, R.B.; Nash, R.D. Tetrahedron 1974, 30, 2961.


29. For example Aldrich quoted 5 gms $11.10


