Traceless Stereoinduction for the Enantiopure Synthesis of substituted cyclopent-2-enones: Total Synthesis of (-)-Teuclatriol and (+)-Orientalol-F

Dissertation
Zur Erlangung des Doktorgrades

Dr. rer. nat.

Der Fakultät für Chemie und Pharmazie

Der Universität Regensburg

Vorgelegt von
Nanaji Arisetti

aus Palakonda (Indien)

Regensburg 2105
Die Arbeit wurde angeleitet von: Prof. Dr. Oliver Reiser

Promotionsgesuch eingereicht am: 05. May 2015


Prüfungsausschuss:  Vorsitz: Prof. Dr. Axel Jacobi von Wangelin

1. Gutachter: Prof. Dr. Oliver Reiser

2. Gutachter: Prof. Dr. Sabine Amslinger

3. Gutachter: Prof. Dr. Robert Wolf
For All Chemistry Nobel Laureates

“A Man has always to be busy with his thoughts if anything is to be accomplished”

-Antonie van Leeuwenhoek
Der experimentelle Teil der vorliegenden Arbeit wurde unter der Leitung von Herrn Prof. Dr. Oliver Reiser in der Zeit von Oktober 2011 bis März 2015 am Institute für Organische Chemie der Universität Regensburg angefertigt.

Herrn Prof. Dr. Oliver Reiser möchte ich herzlich für die Überlassung des äußerst interessanten Themas, die anregenden Diskussionen und seine stete Unterstützung während der Durchführung Arbeit danken.
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<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ar</td>
<td>Aryl</td>
</tr>
<tr>
<td>atm.</td>
<td>atmosphere</td>
</tr>
<tr>
<td>Bn</td>
<td>Benzyl</td>
</tr>
<tr>
<td>Boc</td>
<td>tert-butylxycarbonyl</td>
</tr>
<tr>
<td>c</td>
<td>concentration</td>
</tr>
<tr>
<td>d</td>
<td>days</td>
</tr>
<tr>
<td>dba</td>
<td>dibenzylideneacetone</td>
</tr>
<tr>
<td>DCC</td>
<td>N,N'-dicyclohexylcarbodimide</td>
</tr>
<tr>
<td>DCM</td>
<td>dichloromethane</td>
</tr>
<tr>
<td>DIPEA</td>
<td>N,N-diisopropylethylamine</td>
</tr>
<tr>
<td>DMAP</td>
<td>dimethyl aminopyridine</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>EA</td>
<td>ethyl acetate</td>
</tr>
<tr>
<td>ee</td>
<td>enantiomeric excess</td>
</tr>
<tr>
<td>ent</td>
<td>enantiomer</td>
</tr>
<tr>
<td>eq.</td>
<td>Equation</td>
</tr>
<tr>
<td>equiv.</td>
<td>Equivalents</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
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<td>EtOH</td>
<td>Ethanol</td>
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<tr>
<td>g</td>
<td>gram</td>
</tr>
<tr>
<td>H</td>
<td>hours</td>
</tr>
<tr>
<td>HPLC</td>
<td>high pressure liquid Chromatography</td>
</tr>
<tr>
<td>HRMS</td>
<td>high resolution mass spectrometry</td>
</tr>
<tr>
<td>'Pr</td>
<td>iso-propyl</td>
</tr>
<tr>
<td>'PrOH</td>
<td>iso-propanol</td>
</tr>
<tr>
<td>IR</td>
<td>infrared spectroscopy</td>
</tr>
<tr>
<td>L</td>
<td>liter</td>
</tr>
<tr>
<td>LiHMDS</td>
<td>lithium bis(trimethylsilyl)amide</td>
</tr>
<tr>
<td>Me</td>
<td>Methyl</td>
</tr>
<tr>
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<td>acetonitrile</td>
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<td>millimoles</td>
</tr>
<tr>
<td>mL</td>
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</tr>
<tr>
<td>m.p.</td>
<td>melting point</td>
</tr>
<tr>
<td>MS</td>
<td>mass spectroscopy</td>
</tr>
<tr>
<td>n-Bu</td>
<td>n-butyl</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>Nu</td>
<td>nucleophile</td>
</tr>
<tr>
<td>PE</td>
<td>petrol ether</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>quant.</td>
<td>Quantitative</td>
</tr>
<tr>
<td>rt</td>
<td>room temperature</td>
</tr>
<tr>
<td>rac</td>
<td>racemic</td>
</tr>
<tr>
<td>p</td>
<td>pressure</td>
</tr>
<tr>
<td>t</td>
<td>time</td>
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**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>T</td>
<td>temperature</td>
</tr>
<tr>
<td>TBAF</td>
<td>tetrabutyl ammoniumfluoride</td>
</tr>
<tr>
<td>TBDMS</td>
<td>tert-butyldimethyl silyl</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>V</td>
<td>volume</td>
</tr>
<tr>
<td>W</td>
<td>watt</td>
</tr>
</tbody>
</table>
A. INTRODUCTION

1. Bioactive substituted cyclopent-2-enone compounds and its derivatives

Cyclopent-2-enone is one of the most important core structure in many bioactive prostaglandin derivatives and sesquiterpenes. Prostaglandins are a group of physiologically active compounds having hormone like effects.\(^1\) Every prostaglandin contains 20 carbon atoms. Prostaglandins show wide range of activities. They regulates cell growth, calcium ion levels, hormones, inflammation, and act on parietal cells in the stomach wall to inhibit acid secretion.\(^2\) The biological activity of cyclopent-2-enone containing compounds is manifested in their ability to undergo conjugate addition with various biological nucleophiles such as L-cysteine or thiol containing enzymes (E-SH). Based on the SAR studies it was concluded that the cyclopent-2-enone moiety enhances the cytotoxic activity.\(^3\) 5-(1'-hydroxy)-4-disubstituted cyclopent-2-enones 1 (Fig 1) act against malignant tumors.\(^4\) Cyclopent-2-enone prostaglandin derivatives show anti-inflammatory and antiviral activity and inhibit NF-κB activation in human cell stimulated with tumor necrosis factor-α. The prostaglandin analog 2 acts against L1210 murine leukemia cells with IC\(_{50}\)= 4.0 (µg/mL).\(^5\) TEI-9826 3 was shown to retain \textit{in vivo} activity against cis-platin-resistant tumors.\(^6\) The IC\(_{50}\) value of TEI-9826 for the inhibition of human ovarian cancer is 7.5 µM. 15-deoxy -12-iso-Δ\(^7\)-PGA\(_1\) 4 shows promising anti-proliferative activity with IC\(_{50}\)= 0.23 (µg/mL) on colon 26 cancer cells.\(^3\) Prostaglandin-A\(_1\) (PGA\(_1\))\(^2\) 5 causes renal vasodilatation, increase urine sodium excretion and lower the arterial pressure in hypertensive patients (Fig 1).

![Chemical structures](image.png)

\(\text{Figure 1: Bioactive cyclopent-2-enone prostaglandin derivatives.}\)
2. Literature precedents for the synthesis of substituted cyclopent-2-enones and prostaglandin derivatives

The consecutive addition of two side chains to the cyclopent-2-enone core (three-component coupling in one pot) is a well known procedure in prostaglandin synthesis. A one pot, high yield construction of the whole prostaglandin skeleton is accomplishable by combination of the copper-mediated conjugate addition of alkyl or alkenyl nucleophiles to 4-siloxy cyclopent-2-enones followed by trapping the intermediate enolate with aldehydes. Deprotection of 4-siloxy followed by dehydration gives prostaglandin derivatives. Since organo cuprates have been widely used for the addition of organic groups to the β-position of the α,β-unsaturated carbonyls, it is known that the cuprate mediated conjugate addition of nucleophiles, followed by trapping intermediate enolate with strong electrophiles useful for synthesis of substituted cyclopent-2-enones or prostaglandin derivatives.

In 1975, Gilbert Stork et al. reported the synthesis of PGF$_{2\alpha}$ 9 (Scheme 1) from 6 by using E-vinyl iodide 7 as nucleophile and HCHO$^7$ as electrophile. The resulting 8 was converted in 5 further steps to the prostaglandin 9.$^8$

\[
\begin{align*}
\text{Scheme 1: Stork approach to the PGF$_{2\alpha}$.}
\end{align*}
\]

Ryoji Noyori et al. developed new routes for the prostaglandin derivatives 12, 15, and 17 from cyclopent-2-enone 10 (Scheme 2).$^9$ They synthesized various prostaglandin derivatives by trapping an intermediate enolate with different types of aldehydes followed by deprotection and dehydration of –OTBS group. The 1-octenyl substituent of 17, was derived from 1-octyne through the 1-octenyl zirconocene, which has been formed in situ from 1-octyne and Schwartzs reagent,$^{10}$ followed by treatment with t-BuLi.
Scheme 2: Noyori approach towards the prostaglandin derivatives.

Smitrovich et al. developed a Cu(I) catalyzed addition of alkylzirconocenes to the $\alpha,\beta$-unsaturated carbonyl compounds (Scheme 3).\(^{11}\) This method allows the synthesis of substituted cyclopentanones from cyclopent-2-enoens. In the presence of 3-10 mol% of Cu(I) salts, alkylzirconocenes react readily with $\alpha,\beta$-unsaturated carbonyl compounds. The reaction yields are sensitive to the presence of Lewis acids and bases. Steric hindrances as well as a broad range of functional groups are tolerated. Cyclopent-2-ene 19 readily underwent tandem conjugate addition with hexyl zirconocene 18 (which has been formed \textit{in situ} from 1-hexene and Schwartz reagent) followed by aldol reaction with benzaldehyde in the presence of 10 mol% of CuBrMe$_2$S gave 20 in 58% yield with 2:1 mixture of epimers.
A. INTRODUCTION

Scheme 3: Synthesis of substituted cyclopentanone by Smitrovich et al.

In the year, 1994 Lipshutz B. H. et al. reported enantiopure synthesis of substituted cyclopentanones and non-prostaglandin skeletal from cyclopent-2-enone 25. In this case, alkenyl zirconocene acts as nucleophiles, which has been derived from the corresponding terminal alkyne by using Schwartz reagent. This was a one pot 6 steps sequence could be developed for the synthesis of prostaglandin and non-prostaglandin skeletons of type 24. This method involves the trans metalation between a organozirconium to a cuprate species (Scheme 4). Alkenyl zirconocenes 22, which upon exposure to Me3ZnLi (which has been derived from Me2Zn and MeLi) in THF at -78 °C effects the transmetalation. After conjugate addition, the trapping of the resulting enolate 23 with aldehydes is rapid at -78 °C and affords aldol adduct 24 as mixture of diastereomers with respect to the newly formed stereo center (Table 1).

Scheme 4: Catalytic Cuprate-induced vinyl ligand 1,4-addition to 25 by Lipshutz et al.
**Table 1**: Synthesis of 4-alkenyl substituted cyclopentane derivatives by Lipshutz *et al*.

![Chemical reaction](image.png)

<table>
<thead>
<tr>
<th>Entry</th>
<th>1-alkyne</th>
<th>enone</th>
<th>aldehyde</th>
<th>product</th>
<th>yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>OTIPS</td>
<td></td>
<td></td>
<td></td>
<td>80(^a)</td>
</tr>
<tr>
<td>2</td>
<td>OTIPS</td>
<td></td>
<td>COMe</td>
<td></td>
<td>74(^b)</td>
</tr>
<tr>
<td>3</td>
<td>BnO</td>
<td></td>
<td></td>
<td></td>
<td>75(^c)</td>
</tr>
<tr>
<td>4</td>
<td>BnO</td>
<td></td>
<td>TMS</td>
<td></td>
<td>74(^b)</td>
</tr>
<tr>
<td>5</td>
<td>OTMS</td>
<td></td>
<td></td>
<td></td>
<td>79(^d)</td>
</tr>
<tr>
<td>6</td>
<td>MEMO</td>
<td></td>
<td></td>
<td></td>
<td>83(^b)</td>
</tr>
</tbody>
</table>

\(^a\) One isomer by \(^1\)H-NMR. \(^b\) Two isomers by \(^1\)H-NMR. \(^c\) Five isomers by \(^1\)H-NMR. \(^d\) Four isomers by \(^1\)H-NMR.

With cyclopent-2-enone as starting material, various successful examples were developed by combination of different alkynes and aldehydes providing yields between 70-80%. The number of
epimers was based on substituents on alkyne as well as aldehyde. Alkyne with no substituents gave only one isomer (entry 1, Table 1) and alkyne with substituent’s furnished epimers more than two (entry 2-6, Table 1).

In the year 2002, Kobayashi et al. reported the application of Ni-catalysis for the synthesis of enantiopure cyclopentanoid molecules 30. They have developed the installation of aryl and alkenyl groups on to the readily available monoacetate 26 using lithium borate 27 and nickel catalyst in the presence of additive gave 4-substituted hydroxy cyclopentenes 28.

**Scheme 5**: a) General route for synthesis of aldol adducts 30. b) Synthetic route to Δ7-PGA methyl ester by Kobayashi et al.

Among several additives t-BuCN and NaI in ratio of 13:1 was found to be the best additive. The oxidation of 28 furnished 29, followed by trapping of the resulting enolate of 29 with aldehydes gave
A. INTRODUCTION

4-substituted cyclopent-2-enone 30 (Table 2). After treatment with a base such as LDA at -78 °C followed by trapping of resulting enolate with aldehydes afforded an aldol adduct 30 (Table 2). They reported synthesis of Δ7-PGA methyl ester 35 from 31 and 32 by using this methodology as key step (Scheme 5).

The yield of aldol adducts 30 depend on time and temperature, it was shown that the intermediate enolate is unstable. The authors found that 60 min and >-50 °C were suitable reaction parameters for aldol adduct formation. The assignment of the anti and syn aldols 30 was made by using coupling constants between H^a and H^b. The anti-aldols show $J_{a,b} = 7-9$ Hz and syn-aldols shows $J_{a,b} = 3$ Hz. In all cases, aromatic aldehydes gave nearly the same ratio of epimers (entry 1-3, 5, 7 and 8, Table 2), whereas aliphatic aldehyde provided anti-aldol as the major diastereomer (entry 4, 6 and 9, Table 2).
### A. INTRODUCTION

**Table 2: Synthesis of 4,5-disubstituted cyclopent-2-enone derivatives 29 by Kobayashi et al.**

![Chemical Reaction](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>enone&lt;sup&gt;a&lt;/sup&gt;</th>
<th>base</th>
<th>aldehyde</th>
<th>yield[%]&lt;sup&gt;b&lt;/sup&gt;</th>
<th>anti: syn&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Enone 1" /></td>
<td>LDA</td>
<td>OHC=C=Ph</td>
<td>85</td>
<td>2:1</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Enone 2" /></td>
<td>LiCA</td>
<td>OHC=C=Ph</td>
<td>88</td>
<td>4.8:1</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Enone 3" /></td>
<td>LHMDS</td>
<td>OHC=C=Ph</td>
<td>86</td>
<td>3.5:1</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Enone 4" /></td>
<td>LDA</td>
<td>iPrCHO</td>
<td>66</td>
<td>&gt;20:1&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="Enone 5" /></td>
<td>LDA</td>
<td>OHC=C=Ph</td>
<td>83</td>
<td>4.2:1</td>
</tr>
<tr>
<td>6</td>
<td><img src="image" alt="Enone 6" /></td>
<td>LDA</td>
<td>iPrCHO</td>
<td>72</td>
<td>&gt;20:1&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>7</td>
<td><img src="image" alt="Enone 7" /></td>
<td>LDA</td>
<td>PhCHO</td>
<td>74</td>
<td>2.5:1</td>
</tr>
<tr>
<td>8</td>
<td><img src="image" alt="Enone 8" /></td>
<td>LDA</td>
<td>OHC=C=Ph</td>
<td>72</td>
<td>2.4:1</td>
</tr>
<tr>
<td>9</td>
<td><img src="image" alt="Enone 9" /></td>
<td>LDA</td>
<td>iPrCHO</td>
<td>75</td>
<td>13:1</td>
</tr>
</tbody>
</table>

a) Synthesized from 29 by using oxidation. b) Calculated from the isolated yields. c) *Anti:* *syn* aldols determined by coupling constants. d) Determined by $^1$H NMR.
A. INTRODUCTION

Approximately at the same time, Feringa et al. published their results of the synthesis of enantiopure substituted cyclopentanones 37 by using catalytic tandem 1,4-addition and aldol reaction in the presence of a catalyst generated in situ from Cu(OTf)$_2$ and phosphoramidate 38.$^{18}$ They used alkyl zinc compounds$^{19}$ as nucleophiles in the presence of aromatic aldehydes. Enantioselectivities were obtained up to 94% and de up to 97:3. Alternatively, PGE$_1$ methyl ester 43 could be synthesized from the compound 39 and zinc compound 41 applying the conditions developed for the synthesis of 37. The key compound 42 was obtained in 60% yield and a 87:13 ratio of epimers, which was further converted to PGE$_1$-methyl ester 43 in five steps (Scheme 6b).

Scheme 6: a) General method for synthesis of enantiopure substituted cyclopentanones by Feringa et al. b) Synthetic route to PGE$_1$-methyl ester.

In the year 2006, Helmchen et al. reported synthesis of enantiopure 2,4-disubstituted cyclopent-2-enones 50 by iridium catalyzed allylic alkylations.$^{20}$ The key steps involved in their synthesis are iridium catalyzed allyl alkylation, acylation and ring closing metathesis. In this case, sodium enolates
A. INTRODUCTION

of Weinreb amides\textsuperscript{21} \textbf{44}, allylic carbonates \textbf{45} and Grignard reagents are the starting materials. Enolate \textbf{44} and carbonate \textbf{45} are reacted with each other in the presence of iridium catalyst and ligand \textbf{46}\textsuperscript{22-24} gave amide \textbf{47} with high stereoinduction through the catalyst. Saponification with NaOH and decarboxylation at 180 °C gave amide \textbf{48}. After Grignard reaction at -78 °C followed by ring closing metathesis\textsuperscript{25} on \textbf{49} the 2,4-disubstituted cyclopent-2-enones \textbf{50} were obtained as products with high enantiomeric excess (Scheme 7).

\begin{center}
\includegraphics[width=\textwidth]{scheme7.png}
\end{center}

\textbf{Scheme 7}: Iridium catalyzed synthesis of substituted cyclopent-2-enones by Helmchen \textit{et al}.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|}
\hline
\textbf{Entry} & \textbf{Substr.} & \textbf{R}\textsuperscript{1} & \textbf{R}\textsuperscript{2} & \textbf{yield [%]}\textsuperscript{a} & \textbf{ee [%]}\textsuperscript{b} \\
\hline
1 & (R)-\textbf{47} & Ph & H & 66 & 97 \\
2 & (R)-\textbf{47} & Ph & Ph & 55 & 96 \\
3 & (R)-\textbf{47} & Me & Me & 44 & 95 \\
4 & (R)-\textbf{47} & n-octyl & H & 56 & 96 \\
5 & (R)-\textbf{47} & n-octyl & Me & 56 & n.d. \\
\hline
\end{tabular}
\caption{Examples of 4-substituted cyclopent-2-enone derivatives by Helmchen \textit{et al}.}
\end{table}

\textsuperscript{a) Yields based on 44+45. b) Determined by HPLC on chiral column.}

On the other hand, in 2014 Hartwig \textit{et al}. published enantioselective allylic substitution of unstabilized enolates \textbf{52} (derived from \textbf{51}) by using iridium catalysis.\textsuperscript{26} In this case, unstabilized
enolates 52 and allylic carbonates 53 are starting materials. These two starting materials react with each other in the presence of [Ir(COD)Cl]₂ and ligand (ent)-46 to afford allylated products 54 having new stereo center at the β-position to the keto group. The additives played a key role for the reaction of allylic carbonate with enolate. Among the several additives tested, it was found that KF with 18-crown-6 is key to the success of the reaction. The β-allylated unsaturated ketone 54 should be useful intermediates for synthesis of enantiopure 4-substituted cyclopent-2-enones 55 by using ring-closing metathesis (Scheme 8).

Scheme 8: Iridium catalyzed synthesis of β-substituted unsaturated ketones by Hartwig et al.

Moreover, recently Nakajima group published synthesis of enantiopure 4-substituted cyclopent-2-enones 59 from dienones 56 (Table 4). The key steps involved O-monoacyltartaric acid catalyzed enantioselective conjugate addition of boronic acids to dienones followed by Ru-catalyzed RCM. With styryl boronic acid as starting material various successful examples are presented by changing the substituents on dienone providing mono styrylated products in 42-81% and ee with 86-94% along with bis styrylated product 60 (Table 4).
Table 4: Synthesis of mono-styryl enones by Nakajima et al.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>58[equiv]</th>
<th>MeOH[equiv]</th>
<th>59[%]</th>
<th>ee[%]</th>
<th>60[%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph</td>
<td>1.2</td>
<td>2.4</td>
<td>79</td>
<td>86</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>Ph</td>
<td>1.0</td>
<td>2.0</td>
<td>78</td>
<td>86</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
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<tr>
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<td>2.0</td>
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<td>88</td>
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<td>2.0</td>
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<td>94</td>
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<tr>
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<td>2.0</td>
<td>56</td>
<td>89</td>
<td>15</td>
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</table>

The actual reaction time was 24 h. To suppress the amount of 60, the reaction time was reduced to 14 h. On the other hand, using exactly 1 equivalent of boronic acid 58 significantly suppressed the yield of 60 (entry 3 and 7, Table 4). The higher amount of boronic acid favors the formation 60 in equal yield with respect to the 59 (entry 4, Table 4). With compound 59a in their hand, they concentrated on the construction of cyclopent-2-enone by using RCM reaction. Various Ru-catalysts were tested for ring closing metathesis. The Schrodi-Grubbs catalyst in the presence of 1, 6-heptadiene (additive) gave desired product in moderate yield (entry 1, Table 5). The Grubbs-II also showed similar activity in the presence of additive (entry 2, Table 5). The Grubbs-I catalyst failed completely in this RCM (entry 3, Table 5). When switched to Hoveyda-Grubbs II catalyst gave better
A. INTRODUCTION

results. 15 mol% of Hoveyda-Grubbs II furnished desired compound 61 in 84% yield after 48 h (entry 4, Table 5). Whereas lowers the amount to 10 mol% provides desired compound 61 in very good yield 98% after 24 h (entry 7, Table 5). The additive diene generates active Ru- species from the catalyst, which would promote less reactive enones into the RCM reaction.

Table 5: Synthesis of 4-substituted cyclopent-2-enones using RCM by Nakajima et al.
A. INTRODUCTION

- The catalyst (5 mol %) was added every 24 h (15 mol %).
- The catalyst was added in one portion.
- In toluene at 80 °C.
- With 1, 6-heptadine (0.4 equiv).
- Without 1,6-heptadiene.
- With diallyl ether (0.2 equiv).

Entry 9 provides a derivative 62 with n-octyl group. After successive RCM with Hoveyda-Grubbs II in the presence of 1,6-heptadiene at 80 °C for 24 h furnished 4-octyl cyclopent-2-enone 63 in 76% yield, which is know intermediate for TEI-9826 (Scheme 9).

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\[ \text{Scheme 9: Synthesis of enantiopure 4-octyl cyclopent-2-enone by Nakajima et al.} \]

TEI-9826 3 is one of the most prominent anti-cancer drugs. Many groups reported the synthesis of this anti-tumor agent. In 2003, Monneret et al. reported the synthesis of TEI-9826 from commercially available propargyl alcohol 64 in 11 steps.\textsuperscript{33c} Key steps involved in their synthesis are a Claisen rearrangement\textsuperscript{34} and a RCM. However, no experimental details have been published. In 2006, Helmchen et al. synthesized this molecule from (E)-methyl undec-2-enyl carbonate 65, Weinreb amide 66 and vinyl magnesium bromide by using iridium catalyzed allylic substitution followed by Ru-catalyzed ring closing metathesis.\textsuperscript{20}
A. INTRODUCTION

Scheme 10: Various synthetic approaches towards the TEI-9826.

Iqbal and co-workers reported the synthesis of TEI-9826 by using Pauson-Khand reaction between TMS-acetylene 67 and norbornadiene 68, which gave rise to cyclopent-2-enone core.\textsuperscript{33b} Zurawinski et al. described the synthesis of TEI-9826 from cyclopent-2-enone derivative 69 in 7 steps.\textsuperscript{33a} The key steps were involved here, Horner-Wadsworth-Emmons-olefination\textsuperscript{35} followed by aldol reaction. Recently Hartwig et al. accomplished from silylenol ether 70 and compound 71 in 6 steps by using iridium catalyzed enantioselective allylic substitution of unstabilized silyl enol ethers and subsequent RCM with Grubbs-II catalyst (Scheme 10).\textsuperscript{26} Moreover, all the above methods need more than two pots, harsh conditions and longer reaction time for the synthesis of prostaglandin derivatives.

3. **Bio-active guananes and guianolides**

Guaianes and guianolides,\textsuperscript{36} represent one of the largest subgroup of naturally occurring sesquiterpenes and lactones exhibiting strong biological activity.\textsuperscript{37,38} Plants containing different guananes and guianolides as the active principles have been used in traditionally medicine for treating cancer, inflammatory etc. Guaianes consisting of 5,7-bicyclic hydroazulene system and guianolides consisting 5,7,5-tricyclic system.
A. INTRODUCTION

**Figure 2**: Bioactive guaiane sesquiterpenes.

Guaianes are 5,7-bicyclic sesquiterpenes, widely obtained from many plants. These molecules exhibit strong anti-tumor, anti-inflammatory and anti-diabetic activities. The functionalities on guaiane core structure affect the nature of activity in biological systems. The representative members shown below exemplify the structural diversity found within this class of compounds. Teuclatriol 72 isolated from *teucrium leucocladum*,\(^\text{40}\) shows a significant anti-proliferative activity against human activated peripheral blood lymphocytes with IC\(_{50}\) = 72.5 µg/mL.\(^\text{41}\) Another guaiane molecule with exo-methylene group teucladiol 73 also isolated from *teucrium leucocladum*,\(^\text{40}\) exhibit moderate anti-cancer activity on human breast cancer cell lines. Molecule 74 from acorus calamus, shows promising anti-diabetic activity on a insulin mediated glucose consumption model of HepG2 cells.\(^\text{42}\) Kadsuguain-A 75 isolated from *piper kadsura*, shows moderate anti-neuroinflammatory activity.\(^\text{43}\) Guaiiane core structure with Oxygen bridge also exhibits strong bioactivity. Chrysothol 76 isolated from *chrysothamnus viscidiflorus*, shows anti-cancer activity on human breast cancer cells.\(^\text{44,45}\) Buchariol 77 which was isolated from *salvia bucharica*, shows cytotoxic activity against a panel of human cancer lines.\(^\text{46,47}\) Orientalol-F 78 isolated from *Alisma orientalis* acts anti-diabetic.\(^\text{48}\) Another similar molecule englerin-A 79 was isolated from *phyllanthus engleri*, and shows anti cancer activity on human renal cancer cell lines\(^\text{49}\) (Fig 2).
A. INTRODUCTION

The pseudo-guaianolide skeleton along with the 5,7-bicyclic hydroazulene ring system often contains a third ring, an unsaturated \( \alpha \)-methylene-\( \gamma \)-butyro lactone fused to the 7 membered ring. Along with structural diversity guaianolides exhibit strong biological activity. Here we showed some bio-active molecules with guaian 8,12-olide core structure. Helenalin 81 is a sesquiterpene lactone found in *Arnica Montana* has a variety of observed anti-inflammatory and antitumor activities. Helenalin\(^{50}\) has been shown to selectively inhibit the NF-\( \kappa B \), which plays a key role in the regulating immune response. The sesquiterpen lactone carpesiolin\(^{51}\) 82 shows significant inhibitory activity against *Cochliobolus miyabeanus*. On the other hand, sesquiterpenoid lactone 80\(^{52}\) was found to be submicromolar inhibitors against LPS-induced nitric oxide production in RAW264.7 macrophages (Fig 3).

![Chemical structures](image)

**Figure 3**: Bioactive pseudoguaianolide sesquiterpenes

4. **Pot economy in natural product synthesis by using cascade sequence**

The total synthesis of natural products and biologically active compounds, such as pharmaceuticals and agrochemicals, has reached an extraordinary level of sophistication. The efficient total synthesis of natural products has always been a critical issue for organic chemists. A lot of effort has been devoted to the development of an ideal synthesis. When synthesizing molecules, one not only has to consider efficiency but also sustainability, such as atom economy, step economy, redox economy, protecting-group-free\(^{53}\) and toxic metal free synthesis also contribute to sustainability. Only a single reaction solvent, workup procedure, and purification step may be required to provide a product that would otherwise have to be made over the course of several individual steps.

![Chemical reaction](image)

**Scheme 11**: Robinson approach to the tropinone.
As such, cascade reaction/ domino reaction/ tandem reaction can be considered as one pot economy reaction. A cascade reaction is an efficient method to achieve several transformations and by forming several bonds, while at the same time save purifications steps, and thus minimize chemical waste and time. Indeed, cascade reactions have attracted the attention of organic chemists, since Robinson’s one pot synthesis of tropinone (Scheme 11). Subsequent classic examples include the endiandric acid-C 87 cascade by Black and co-workers through the electrocyclic reactions (Scheme 12a). Radical based synthesis of hirsutene 89 and other triquinane natural products by Curran and co-workers are the other prominent examples. They used tandem radical approach starting from intermediate 88, which leads to tricyclic core of hirsutene 89 in a one pot operation (Scheme 12b).

**Scheme 12**: a) Black electrocyclic cascade for endiandric acid-C. b) Radical cyclization cascade for hirsutene by Curran et al.

Hayashi and co-workers reported one-pot synthesis of (-)-oseltamivir 94 by using an asymmetric Michael reaction of aldehyde 90 with (Z) - N-2-nitroethynylacetamide 92 catalyzed by diphenyl prolinol silyl ether. They used two one-pot sequences for the target. In the first one pot operation, they achieved core structure of (-)-oseltimivir 93 by using an asymmetric enantioselective Michael addition, Horner-Wadsworth-Emmons reaction followed by cyclization. In the next one pot operation, they achieved six further transformations, which led to the target 94 with good yield (Scheme 13).
A. INTRODUCTION

Scheme 13: Pot economy cascade for (-)-Oseltamivir by Hayashi et al.

On the other hand, the same group reported synthesis of PGE$_1$-methyl ester 43 by using a three-pot cascade. In the first pot they achieved the synthesis of cyclopentane core 98 with two stereogenic centers by using an enantio selective Michael addition, Horner-Wadsworth-Emmons followed by cyclization, which was reduced selectively to 99 by using (-)-diisopinocamphenyl chloroborane. A further one pot protocol combining 4 transformations was then demonstrated, which led to PGE$_1$-methyl ester with 14% overall yield (Scheme 14).$^{63}$

Scheme 14: Three pot economy for PGE$_1$-metghyl ester by Hayashi et al.
A. INTRODUCTION

5. Protecting group free access to the natural product synthesis

Total synthesis is a big tool for synthesis of derivatives of naturally occurring bioactive molecules with different functionalization. When we start synthesis of some complex molecules, selectivity plays a crucial role. One strategy that allows the differentiation of similar functional groups is the use of protecting groups. Nevertheless, adding protecting group and removal of protecting group needs 2 steps, thus reducing yield and requiring more reagents. It is therefore desirable to develop reaction sequences that avoid the use of protecting groups. Some prominent examples are shown in the following: In 1917 Robinson reported the synthesis of tropinone from the simple starting materials succinaldehyde, methylamine and acetone di-carboxylic acid. This one may be considered first protecting group free synthesis as well as one pot synthesis. In 1968, Danieshfsky et al. reported the total synthesis of racemic patchouli alcohol 102 from 100 and 101 without using any protecting groups.64 In his synthesis, each intermediate has limited reactive sites and diminishing chemo selective transformations (Scheme 15a). Phil. S. Baran et al. reported the first synthesis of ambiguine-H 104 by using a protecting group free strategy.65 They used commercially available material 103 as starting material by using direct indole coupling in the presence of copper salts as key step66 (Scheme 15b).

Scheme 15: Protecting group free strategy for Patchouli alcohol by Danishefsky et al (a), (+)-ambiguine-H by Baran et al (b).

Moreover, in 2008 B. M. Stoltz group reported first synthesis of cyantwigin-F 106 from di-allyl succinate 105 without using any protecting groups.67 The key steps involved double enantioselective alkylation68 in the presence of Pd2(dba)3 and PHOX ligand followed by RCM (Scheme 16a). Alois Fürstner et al. reported the total synthesis of ecklonialactone 108 without using any protecting groups and alkyne metathesis as key step (Scheme 16b).69 In 2010, D. Ma et al. reported the total synthesis of englerin-A 79 from 109 by using gold-catalyzed cyclization of keto enynes and without using any protecting groups (Scheme 16c).70 The protecting group free synthesis needs intermediates with active sites, which are diminishing chemoselective transformations.
A. INTRODUCTION

Scheme 1: Protecting group free approach to the various natural products.

Recently J. K. Taylor et al. reported first total synthesis of Dievidiamine 112 from commercially available materials 110 and 111. The key steps include the first example of an organometallic addition into a DHED adduct and Stille coupling between two sterically hindered alkenes. Moreover, they completed the synthesis without using any protecting groups; this could be an example of protecting group free synthesis (Scheme 17).

Scheme 16: Protecting group free approach to the various natural products.

Scheme 17: Protecting group free approach to the Dievodiamine by Taylor et al.
6. Kinetic resolution

Many of the building blocks in biological systems and bioactive natural products are mostly available in pure enantiomeric forms. Their synthesis as well as that of analogues needs an asymmetric synthetic strategy. The enantioselective synthesis can be achieved by using chiral catalysts or achiral catalysts with chiral ligands. Separation of enantiomers from racemic mixture by using kinetic resolution is a well known strategy in asymmetric synthesis. Two enantiomers in racemic mixture react with different rates with a chiral reagent, resulting in an enantiomeric excess of an unreacted enantiomer in a racemic mixture. The first kinetic resolution reported by Louis Pasteur. However, Marckwald and McKenze reported the first synthetic kinetic resolution in 1899. They separated enantiopure (+)-113 from (±)-113 by using enantioselective esterification with 114. In which (+)-113 reacts faster than (-)-113, gave ester 115, saponification on 115 furnished (+)-113 in pure enantiomeric form (Scheme 18).

Scheme 18: Kinetic resolution of racemic mandelic acid by Marckwald and McKenze.

B. M. Trost et al. published asymmetric synthesis of butenolides 118. In this case, palladium catalyst forms a chiral complex with ligand 127. The two enantiomers of butenolide generated π-allylpalladium complex 117a and 117b with Pd-catalyst. These 2 complexes undergo interconversion with each other. If interconversion is fast relative to nucleophilic addition one of the complexes reacts with nucleophile faster than the other, then effective dynamic kinetic resolution would be result (Scheme 19).
A. INTRODUCTION

Scheme 19: Kinetic resolution of butenolides by using Pd-\((R,R)\)-Trost complex by Trost et al.

G. Fu et al. reported kinetic resolution of secondary alcohols 120 as enantipure acetates 122 by using a planar-chiral DMAP analogue 121 in the presence of 119 (as acetylation agent) and triethyl amine gave selectivities ranging from 12-52. In these cases, enantioselectivity observed are better than previously reported non-enzymatic asymmetric acylation catalyst (Scheme 20).75

Scheme 20: Kinetic resolution of racemic secondary alcohols by G. Fu et al.

Recently O.Reiser et al. published enantioselective synthesis of 4-hetero substituted cyclopent-2-enones 126 from (t)-125. In this case, they used Pd-catalyzed kinetic resolution of (t)-125 with various nucleophiles in the presence of ligand 127. Excellent enantioselectivities of both substitution products 126 and recovered starting material (+)-125 were obtained even at low catalyst loading (Scheme 21). This method could be useful for synthesis of various starting materials for cyclopentanoid bioactive molecules and prostaglandin derivatives.76
7. Conclusion

Since last 40 years, the synthesis of substituted cyclopent-2-enones was expanded significantly. Prostaglandins exhibit a broad range of biological activity and stimulate the development of research in their synthesis. As there are more and more number of prostaglandins discovered, the full evaluation of their bioactivity is still of current interest. Besides this, methods were developed to synthesize substituted cyclopent-2-enones from various starting materials, which were highly valuable in view of growing interest in their synthesis. On the other hand, cyclopentanoid sesquiterpenes are also exhibit a broad range of bioactivity. Therefore, the total synthesis of sesquiterpenes plays an important role in inventing new methods in organic synthesis.
B. Main Part

1. One pot synthesis of substituted cyclopent-2-enones by using a traceless stereoinducing directing group

1.1 Introduction
Substituted cyclopent-2-enones represent one of the most important core structures in many bioactive prostaglandin derivatives and sesquiterpenes. Prostaglandins\textsuperscript{1} are a group of physiologically active compounds having hormone like effects. They show wide range of activities, such as regulating cell growth, calcium ion levels, hormones, inflammation, and they act on parietal cells in the stomach wall to inhibit acid secretion.\textsuperscript{2} Cyclopent-2-enone compounds have been shown, to react by conjugate addition with various biological nucleophiles such as L-cysteine or thiol containing enzymes (E-SH). Based on the SAR studies it was concluded that cyclopent-2-enone moiety enhances the cytotoxic activity. 5-(1-hydroxy)-4-substituted cyclopent-2-enones \textbf{1} (Fig 1, Introduction part) act against malignant tumors. Cyclopent-2-enone prostaglandin derivatives showed anti-inflammatory and antiviral activity, and inhibit NF-κB activation in human cells stimulated with tumor necrosis factor-α.\textsuperscript{77} Based on the biological activity of such substituted cyclopent-2-enones many groups have reported the synthesis this moiety by using chiral pool, chiral reagents and various catalytically strategies.\textsuperscript{78} Addition of organo lithium or Grignard reagents to cyclopent-2-enones in the presence of copper (I) salts followed by trapping of the resultion enolate intermediate with an aldehyde is a well known process for synthesis of prostaglandin derivatives. However, extensive studies along this line have revealed that such direct vicinal functionalization is not easy to achieve. The difficulty is presumably attributable to the complex nature of the reaction system, which causes a facile double bond migration of the initial formed enolate \textbf{129}, causing concomitant dehydration to give undesired products \textbf{132}. By using highly reactive electrophiles, such side reactions are avoided.\textsuperscript{79}
As I showed in introduction, with the pioneering work of Noyori et al. utilizing 4-siloxy-2-cyclopentenone 10 as a key building block for the synthesis of prostaglandins, a reliable strategy towards enantioselective cyclopentenones was established, being broadly applied by many. Conjugate anti-addition of nucleophiles to 10 in the 3-position controlled by the adjacent siloxy group followed by an aldol reaction in the 2-position anti to the nucleophile just introduced was developed. Subsequently, the siloxy group can be eliminated to generate the substituted 2-cyclopentenone. With the advent of asymmetric conjugate additions, it was demonstrated that 2-cyclopentenone could be used directly as a starting material for the synthesis of enantioselective cyclopentanones (Scheme 2, Introduction part). Other strategies towards the target structure have been reported as well, however, mixtures of epimers at C-1', often in ratios close to 1:1, are generally obtained with only few exceptions that require sterically demanding aldehydes. In my thesis, I have found that the pseudoequatorially oriented 4-siloxy-2-cyclopentenone 128 and 131 act as traceless stereodirecting elements that not only relay 1,2- but also remote 1,4-stereocontrol in a cascade of nucleophile addition/aldol reaction/elimination sequence (Scheme 23).
3.5 Scheme 23: Stereoselective synthesis of 5-(1-hydroxy)-4-substituted cyclopent-2-enones.

1.2 Synthesis of (R)-125 and (S)-134:
(R)-125 and (S)-134 are readily available in enantiopure form from the bulk chemical furfurylalcohol 135 in a two-step sequence. In the first step, (±)-136 was synthesized on kilogram scale from 135 by an acid catalyzed Piancatelli rearrangement\(^8\) carried out in a micro reactor setup afforded (±)-136 in 87% yield, which was converted to (±)-125 with (Boc)\(_2\)O and Et\(_3\)N gave (±)-125 in 85% yield (Scheme 24).\(^8\)

With the compound (±)-125 in our hand we decided to synthesize (R)-125 and (S)-134 via a Trost-Tsuji asymmetric allylation technology.\(^8\) Reacting 4-methoxy phenol 137 as nucleophile with (±)-125 in the presence of Pd\(_2\)(dba)\(_3\)CHCl\(_3\) and 127 gave corresponding 4-methoxy phenol substituted compound (S)-134 along with unreacted (R)-125. The yield and ee of the (R)-125 and (S)-134 depend on the equivalents of the 137 (Table 6).
Table 6: Optimization studies for (R)-125 and (S)-129.

<table>
<thead>
<tr>
<th>Entry</th>
<th>(±)-125 (mmol)</th>
<th>137 (mmol)</th>
<th>Pd2(dba)3.CHCl (mol%)</th>
<th>127 (mol%)</th>
<th>Cs2CO3 (equiv)</th>
<th>Yield (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(R)-125</td>
<td>(S)-134</td>
<td>(R)-125</td>
<td>(S)-134</td>
<td></td>
<td></td>
<td></td>
</tr>
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</tr>
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<td>55</td>
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<td>1.25</td>
<td>4.62</td>
<td>0.37</td>
<td>48</td>
<td>40</td>
</tr>
<tr>
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<td>1.00</td>
<td>3.70</td>
<td>0.30</td>
<td>41</td>
<td>44</td>
</tr>
<tr>
<td>6</td>
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<td>0.25</td>
<td>0.20</td>
<td>3.70</td>
<td>0.30</td>
<td>45</td>
<td>44</td>
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<tr>
<td>7</td>
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<td>0.25</td>
<td>0.40</td>
<td>3.70</td>
<td>0.30</td>
<td>41</td>
<td>48</td>
</tr>
</tbody>
</table>

[a] General procedure: (±)-125 (0.5 mmol), 137, Pd2(dba)3.CHCl, 127, Cs2CO3, DCM (6 mL), 0 °C, 2.5 h. [b] Pd2(dba)3.CHCl, 127, Cs2CO3, based on 137. [c] Isolated yields after column chromatography.

When we used 137 in lower amounts, the formation (S)-134 with good enantiomeric excess but low yield is achieved (entry 1, Table 6). However, the higher amount of 137 favors the (R)-125 with good yield and enantiomeric excess (entry 5, Table 6). Decreasing the amount of the Pd-catalyst from 1 mol% to 0.4 mol% was tolerated well, while a decrease to 0.2 mol% gave some better results for both (R)-125 and (S)-134 (entries 5, 6 and 7). We have resolved (±)-125 on 50 g scale with 137 (0.5 equiv) under the conditions shown in entry 5, giving rise to (R)-125 (42%, >99% ee) and (S)-134 (48%, >92% ee).

1.3 Synthesis of (+)-133 and (-)-133
Copper (I)-catalyzed Grignard additions to (R)-125 followed by trapping of the resulting enolate with aldehydes were investigated next. First it was set out to identify best copper (I) source for the envisioned one pot operation. Test reactions were performed with (R)-125, isopropenyl magnesiumbromide and trans-2-methyl-2-butenal (Table 7): Using copper (I) iodide in THF, the desired adduct (+)-133g was obtained with 48% yield (entry 1, Table 7). Switching to diethyl ether, the yield decreased to 38% (entry 2, Table 7). Variation of the copper(I)-species by adding PBu3, which has been shown to be stabilize the intermediate oregano copper reagent, also gave
disappointing yields (entries 4-6, Table 7). Higher order cyanocuprates \(^{88}\) were examined next: Applying CuCN\(\cdot\)2LiCl in combination with Grignard reagents in THF—afforded (+)-133g with an improved yield of 66% (entry 7, Table 7). Further variation of solvent demonstrated that the mixture of THF and diethyl ether led to lower yields than THF alone (entries 3, 6 and 9, Table 7). These results suggest that the CuCN\(\cdot\)2LiCl mixture \(^{89,90}\) in THF proved to be the best condition for the one-pot strategy, offering good yields in short reaction times.

**Table 7: Optimization studies for one pot strategy.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Copper source</th>
<th>Solvent</th>
<th>Temperature (°C)</th>
<th>Time (min)</th>
<th>Yield[^d]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1[a]</td>
<td>Cul</td>
<td>THF</td>
<td>−78 °C, 30 min, then −45 °C to −78 °C</td>
<td>80 min</td>
<td>48%</td>
</tr>
<tr>
<td>2[a]</td>
<td>Cul</td>
<td>Et(_2)O</td>
<td>−78 °C, 30 min, then −45 °C to −78 °C</td>
<td>80 min</td>
<td>38%</td>
</tr>
<tr>
<td>3[a]</td>
<td>Cul</td>
<td>THF:Et(_2)O[^a]</td>
<td>−78 °C</td>
<td>80 min</td>
<td>44%</td>
</tr>
<tr>
<td>4[b]</td>
<td>Cul+PBu(_3)</td>
<td>THF</td>
<td>rt to −78 °C</td>
<td>45 min</td>
<td>38%</td>
</tr>
<tr>
<td>5[b]</td>
<td>Cul+PBu(_3)</td>
<td>Et(_2)O</td>
<td>rt to −78 °C</td>
<td>45 min</td>
<td>32%</td>
</tr>
<tr>
<td>6[b]</td>
<td>Cul+PBu(_3)</td>
<td>THF:Et(_2)O[^a]</td>
<td>rt to −78 °C</td>
<td>45 min</td>
<td>38%</td>
</tr>
<tr>
<td>7[c]</td>
<td>CuCN+LiCl</td>
<td>THF</td>
<td>−40 °C to −78 °C</td>
<td>10 min</td>
<td>66%</td>
</tr>
<tr>
<td>8[d]</td>
<td>CuCN+LiCl</td>
<td>Et(_2)O</td>
<td>−40 °C to −78 °C</td>
<td>15 min</td>
<td>45%</td>
</tr>
<tr>
<td>9[d]</td>
<td>CuCN+LiCl</td>
<td>THF:Et(_2)O[^a]</td>
<td>−40 °C to −78 °C</td>
<td>15 min</td>
<td>51%</td>
</tr>
</tbody>
</table>

[^a]: (R)-125 (0.38 mmol, 1 equiv), Cul (1.62 equiv), iso-propenylmagnesium bromide (1.62 equiv), aldehyde (1.68 equiv), solvent (8 mL). [b]: (R)-125 (0.38 mmol, 1 equiv), Cul (1 equiv), PBu\(_3\) (2 equiv), iso-propenylmagnesium bromide (1 equiv), aldehyde (1.68 equiv), solvent (8 mL). [c]: (R)-125 (0.38 mmol, 1 equiv), CuCN (3 equiv), LiCl (6 equiv), iso-propenylmagnesium bromide (3 equiv), aldehyde (1.68 equiv), solvent (10 mL). [d]: Yields obtained after column chromatography. [a]: THF:Et\(_2\)O (3:1, 10 mL).

Under the optimized conditions, the addition of organometal compounds to (R)-125 followed by trapping of the resulting intermediate enolates was investigated: Irrespective of the Grignard reagent
employed (aryl-, vinyl- and alkyl) or the aldehydes (aromatic, $\alpha,\beta$-unsaturated or aliphatic) the adducts (-)-133 were obtained with high stereoselectivity. The level of enantioselectivity is determined by the anti-selectivity of the Grignard reagent in the initial conjugate addition to (R)-125, and small differences in selectivity are observed correlating with its steric bulk (Table 8). Introducing a vinyl group as the smallest nucleophile investigated, the enantioselectivity was ≥95% ee, while octyl, isopropenyl, cyclohexyl and phenyl generally gave ≥99% ee with the exception of (+)-133i (98% ee). Good yields (59-77%) were obtained in all cases with the exception of octyl magnesiumbromide, which gave rise to (+)-133-x (30-38%). It was subsequently found (vide infra) that this Grignard reagent gave considerable higher yields when (S)-134, being pseudo enantiomeric to (R)-125, was used.

**Table 8:** One pot strategy of (R)-125 with different Grignard reagents and aldehydes.
All products were obtained with ≥ 99\% de as determined by $^1$HNMR of the crude products. Enantioselectivities (133a-d, 133f-h, 133n, o, p and r, 133s, 133t: ≥ 99\% ee, 133i: 98\% ee; 133k: 96\% ee, 133m: ≥95\% ee,) of (+)-133 for each Grignard reagent were determined by chiral HPLC of the pure against a racemic reference samples of 133a-d, f-h, n-p and r, s, t and from these data extrapolated to 133e, j, l, q and u-x.

Employing the 4-OPMP derivative (S)-134 as starting material gave access to the enantiomeric cycopentenones (-)-133 with equally good selectivity. Gratifyingly, good yields were obtained in all cases, even for octyl magnesium bromide (Table 9).
Table 9: One pot strategy of (S)-134 with different Grignard reagents and aldehydes.

![Chemical structure](image)

\[ \text{CuCN:LiCl} \quad R^2\text{MgX} \quad R^1\text{CHO} \]

\[ -78 \, ^\circ C \]

\[ 10 \text{ min (one pot)} \]

\[ >95\% \text{ ee, (S)-134} \]

Single stereo isomer

17 entries

Yields=59-80%

<table>
<thead>
<tr>
<th>R^2\text{MgBr}</th>
<th>(-)-133</th>
<th>R^1</th>
</tr>
</thead>
<tbody>
<tr>
<td>\text{MgBr}</td>
<td><img src="image" alt="Chemical structure" /></td>
<td><img src="image" alt="Chemical structure" /> a (72%)</td>
</tr>
<tr>
<td>\text{MgBr}</td>
<td><img src="image" alt="Chemical structure" /> d (66%)</td>
<td><img src="image" alt="Chemical structure" /> e (68%)</td>
</tr>
<tr>
<td>\text{MgBr}</td>
<td><img src="image" alt="Chemical structure" /> h (72%)</td>
<td><img src="image" alt="Chemical structure" /> i (66%)</td>
</tr>
<tr>
<td><img src="image" alt="Chemical structure" /></td>
<td><img src="image" alt="Chemical structure" /> k (75%)</td>
<td><img src="image" alt="Chemical structure" /> l (68%)</td>
</tr>
</tbody>
</table>
All products were obtained with ≥95% d.r. as determined by $^1$HNMR of the crude products. (-)-133a, c, d, g, h, j, k, l, n and r: 94% ee (Chiral HPLC against reference samples reference).

As depicted in Scheme 25, upon addition of a nucleophile to (R)-125, the enantiopure enolate 138 is formed, which is then converted to the aldol adduct (+)-133 by reacting with an aldehyde. The excellent stereocontrol achieved for (+)-133 at the C-1′-position can be understood by the terminating anti-elimination of ROH (R=–OBoc) from intermediate 139, which we reckon is initially formed along with (epi)-139 (Scheme 25).

**Scheme 25:** Stereochemical model for the remote 1,4-stereoccontrol of the −OBoc group.

139 can adopt a favorable conformation that triggers elimination to (+)-133, while in (epi)-139, the conformation that is required to invoke R-OH elimination suffers from steric repulsion caused by the axial position of R$_1$.

1.4 Applications of the methodology towards biologically relevant cyclopent-2-enones

Prostaglandins are lipid compounds having hormone type activities that are found in many tissues and organs. They are produced following the sequential oxidation of arachidonic acid by
cyclooxygenase and have a wide variety of effects in bio-systems. Prostaglandins are responsible for constriction and dilation of vascular smooth muscle, regulate calcium movement, regulate hormones, and control cell growth.\(^{94,95}\) Owing to the bioactivity of these compounds, many groups reported syntheses of these molecules by consecutive addition of two side chains to the enantiopure 4-oxo cyclopent-2-enones 10 in the presence of Cu (I)-salts (Scheme 2, Introduction part). All these methods need separate reaction steps, quite drastic reaction conditions and longer reaction times. To overcome these problems, we decided to use the strategy developed above for the synthesis of some prostaglandins and derivatives thereof.

![Scheme 26: One-pot synthesis of anti tumor agents 2 and 3.](image)

Compound 2, acts against L1210 murine leukemia cells with IC\(_{50}\) = 4.0 (µg/mL),\(^5\) could be obtained from (R)-125 by using n-butyl magnesium bromide as Grignard reagent and heptanal as trapping reagent for the intermediate enolate in 38% yield. The anti-tumor agent 3 (TEI-9826) was synthesized from (S)-134 by using n-octyl magnesiumbromide as Grignard reagent and trapping the resulting
enolate by methyl-6-formylhexanoate afforded 140, which was used for the next dehydration with MsCl\(^{6}\) in the same flask without further separation gave 3 in 48% yield (Scheme 26).

Scheme 27: Synthesis of 141 and 143.

Two more prostaglandin derivatives 141 (butyl derivative of 3) and 143 (methyl ester of 4) could be obtained starting from (S)-134. To synthesize 141 we used n-butyl magnesiumbromide as nucleophile and methyl-6-formylhexanoate. The resulting aldol adduct was then dehydrated by using MsCl and DMAP to give rise 141 in 42% yield. Using vinyl zirconium instead of Grignard reagents was also possible. We were able to synthesize 143 in 45 % yield starting from (S)-134, 1-octyne, Schwartz’s reagent (Cp₂ZrHCl) and methyl-6-formylhexanoate giving rise to 142, followed by dehydration to 143. The later strategy could be in general useful for the synthesis of prostaglandin derivatives with alkenyl groups at C4, without the need to transmetallate another organometal precursor (Scheme 27).\(^{97}\)
2. Studies towards the synthesis of teuclatriol and iso-teucladiol

2.1 Isolation and bioactivity

The second aim of this work is synthesis of some bioactive guaiane natural products by using the previously described one-pot strategy as key step. Here we successfully achieved the total synthesis of teuclatriol 72, iso-teucladiol 144 (Fig 4).

![Structures of teuclatriol 72 and teucladiol 144](image)

Figure 4: Structure of teuclatriol 72 and teucladiol 144.

Teuclatriol (72) is another guaiane sesquiterpene was isolated from *teucrium leucocladum*. This compound showed a significant anti-proliferative activity on human activated peripheral blood lymphocytes with IC$_{50}$ = 72.5 µg/ml. A number of sesquiterpene lactones have shown anti-inflammatory and anti-cancer activity. Various studies revealed that these lactones most likely induce their immunoinhibitory activity through apoptosis. Teuclatriol does not have a lactone ring, its anti-proliferative activity probably follows a different mode of action. Using bioassay-guided fractionation, it appears that teuclatriol is one of the responsible compounds for the immunoinhibitory activity of *Salvia mirzayanni*.

2.2 Retrosynthetic analysis

In our retro synthesis, the main goal was to achieve an adduct 146 with 4 contiguous stereo centers in a single step by using our one-pot strategy. We envisioned that the target molecule 72 can be obtained from compound 144 by hydration of the double bond. 144 might be obtained from 145 via stereo selective methylation. Compound 145 was expected to arise from aldol adduct 146 through ring closing metathesis followed by selective reduction of $\alpha,\beta$-unsaturated double bond. Aldol adduct 146 could be accomplished by kinetic resolution of racemic achiral aldehyde (±)-148 with enantiopure enolate 147 (Scheme 28).
2.3 Kinetic resolution of racemic enolates

Kinetic resolution is a well known process for the separation of enantiomers from a racemic mixture. In this process, one of the enantiomer reacts faster than the other enantiomer with a chiral reagent. In 2010 Vanderwal and co-workers reported the kinetic resolution of racemic enolates 151 by using enantiopure achiral aldehyde (-)-148. Using aldehyde (-)-148 (95% ee) in the reaction of the racemic enolate 151 afforded aldol adduct 152 in 38% yield with 83% ee. Apparently, (-)-148 underwent epimerization under the reaction conditions. The authors therefore noted that an ideal enantioselective synthesis would incorporate enantioenriched enolate, but the asymmetric conjugate addition of sp2-hybridized organometallics to the cyclopentenone is not a well-developed process. From adduct 152 five steps were needed to complete the synthesis of teucldiol 73 (Scheme 29).

Scheme 28: Retrosynthetic analysis of teuclatriol 72.
2.4 Kinetic resolution of racemic aldehyde \((\pm)-149\) and synthesis of teuclatriol

Using our one-pot strategy demonstrated that racemic \(\alpha\)-chiral aldehydes \((\pm)-154\) are resolved allowing the one-step construction of cyclopent-2-enones 156 with 4-contiguous stereocenters. Extending the stereochemical model to \(\alpha\)-chiral aldehydes \((\pm)-154\) suggests that 155 is favored over \((\text{epi})-155\): By placing the smallest substituent (hydrogen) on the \(\alpha\)-center axial to minimize 1,3-interactions with the cyclopentanone moiety allows \(R^1\) in 156 to orient away from the chair conformation, being most favorable to trigger the elimination of Boc-OH (Scheme 30).
Scheme 30: Stereochemical model for the remote 1,4-stereocontrol of the –OBoc group with achiral aldehydes.

As depicted in the retrosynthetic analysis of 72 (Scheme 28), the guaiane core 145 could be obtained from aldol adduct 146. Reacting (R)-125, isopropenyl magnesiumbromide and aldehyde (±)-148 gave aldol adduct 146 in 68% yield and with >99% ee and. With this compound 146 in our hand, we further proceeded towards the teuclatriol 72 (Scheme 31).

Scheme 31: Kinetic resolution of aldehyde (±)-148 by using enantiopure (R)-125.

With this compound 146 in our hand, we further proceeded towards the teuclatriol 72. Ring closing metathesis (92% yield) gave rise to 157 followed by selective reduction of its α,β-unsaturated double bond using Ph₂SiH₂ in the presence of Pd(TPP)₄ afforded 145 in 80% yield. The alcohol function in the resulting 145 was protected by reaction with TESCl to yield 158 in 88%. Regio and stereoselective methylation of 158 by MeLi, CeCl₃ in THF at -78 °C followed by deprotection with
TBAF\textsuperscript{107, 108} afforded diol 144 in 76% yield. The final step in our synthesis was hydration of the alkene double bond to a tertiary alcohol at C-10. Initially, oxymercuration-deoxymercuration\textsuperscript{109} on 144 was applied, however compound 72 was obtained low yield and accompanied with undesired side products. Gratifyingly, cobalt-catalyzed hydration in the presence of PhSiH\textsubscript{3} and oxygen\textsuperscript{110, 111} afforded teuclatriol 72 in 52% yield along with 10-\textit{epi} teuclatriol 159 in 20% yield (Scheme 32).

Scheme 32: End game for teuclatriol.

The spectroscopic data (\textsuperscript{1}H NMR, \textsuperscript{13}C NMR, UV and HRMS) and optical rotation were in accordance with literature.\textsuperscript{46}
### Table 10. $^1$H and $^{13}$C NMR chemical shift comparison of synthetic and natural (-)-teuclatriol.

<table>
<thead>
<tr>
<th></th>
<th>$^1$H NMR chemical shift comparison</th>
<th>$^{13}$C NMR chemical shift comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$^1$H NMR synthetic (CDCl$_3$-600 MHz)</td>
<td>$^1$H NMR natural (CDCl$_3$-500 MHz)</td>
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<tr>
<td>4.13 (dt)</td>
<td>4.13 (dd)</td>
<td>81.11</td>
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<tr>
<td>1.98-1.93 (m)</td>
<td>1.94 (dd)</td>
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<tr>
<td>1.86 (td)</td>
<td>1.85 (m)</td>
<td>71.40</td>
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<tr>
<td>1.81-1.76 (m)</td>
<td>1.77 (m)</td>
<td>55.25</td>
</tr>
<tr>
<td>1.74 (d)</td>
<td>1.73 (m)</td>
<td>52.03</td>
</tr>
<tr>
<td>1.69 (dd)</td>
<td>1.68 (m)</td>
<td>47.99</td>
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<tr>
<td>1.59-1.56 (m)</td>
<td>1.56 (m)</td>
<td>45.48</td>
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<tr>
<td>1.39 (dd)</td>
<td>1.38 (m)</td>
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<td>1.36 (dd)</td>
<td>1.36 (m)</td>
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<td>1.26 (s)</td>
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<td>1.25 (s)</td>
<td>1.23 (s)</td>
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<td>1.08 (m)</td>
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<td>1.02 (d)</td>
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<td>0.97 (d)</td>
<td>0.97 (d)</td>
<td>21.14</td>
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</table>
Table 11. $^1$H and $^{13}$C NMR chemical shift comparison of synthetic and natural (−)-10 epi-teuclatriol.

<table>
<thead>
<tr>
<th>$^1$H NMR synthetic (CDCl$_3$-300 MHz)</th>
<th>$^1$H NMR natural (CDCl$_3$-300 MHz)</th>
<th>$^{13}$C NMR synthetic (CDCl$_3$-75 MHz)</th>
<th>$^{13}$C NMR natural (CDCl$_3$-50.3 MHz)</th>
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</tr>
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<td>2.22 (dd)</td>
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<td>1.29 (s)</td>
<td>1.29 (s)</td>
<td>71.3</td>
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<td>1.17 (s)</td>
<td>1.20 (s)</td>
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<td></td>
<td>19.9</td>
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</table>

2.5 Studies towards Kadsuguain-A

Kadsuguain-A 75 is a guaianesquiterpene, which was isolated from *piper kadsura*. Based on our previous synthesis of 78, we assume that an intermediate 145 could be useful starting material for the synthesis of C-7 epimer of (ent)-75. Reaction of 145 with Co (acac)$_2$ and PhSiH$_3$ in the presence of oxygen gave 160 in 72% yield. We expected that the newly formed C10-OH would be in anti position to the C1-H. Unfortunately, we have observed the newly formed C10-OH group was in syn to the C1-H. Based on the proposed mechanism (scheme 33b), we thought that the intermediate peroxocobalt complex reacts with alkene from the less hindered side and form 145a, which provides us 160 as a major compound. The next step of our synthesis was the introduction of an exomethylene group in 160. Wittig methylenation, gave the expected product 161 only in low yield. Selective methylenation in the presence of TiCl$_4$ and magnesium in DCM/THF mixture afforded the desired target 161 in 62% yield (Scheme 33a). However, the newly synthesized molecule 161 showed a different configuration at C7 and C10 positions with respect to (ent)-75.
3. Studies towards the orientalol-F 78 and englerin-A 79

3.1 Isolation and bioactivity

Guaianes are representatives of the largest group among naturally occurring sesquiterpenes.  
Orientalol-F 78 is an oxo-bridged guaianesesquiterpene isolated from *Alismaorientalis* JUZEP and has been widely cultivated in China and Japan; its dried rhizomes have been used as folk medicines to treat diabetes. Another oxo-bridged guaianesesquiterpene is englerin-A 79, which was isolated from
**B. Main Part**

*Phyllanthus engleri* in Zimbabwe and Tanzania region. It showed a 1000-fold selectivity against six of eight renal cancer cell lines with IC₅₀ values 1-87 nM. The C-9 glycolate ester moiety is important for the anti-cancer activity for the engelrin-A, because the glycolic acid is well known metabolite of ethylene glycol that causes acute renal toxicity in mammals (Fig 5).

![Orientalol-F 78 and Englerin-A 79](image)

**Figure 5**: Structure of orientalol-F 78 and englerin-A 79.

### 3.2 Retro synthetic analysis

As depicted in scheme 34, we envisioned that the mercuric salt 162 could be the common intermediate for the targets 78 and 79. 78 could be obtained from 162 through reductive demercuration, followed by inversion of C9-OH.

![Scheme 34](image)

**Scheme 34**: Retrosynthetic analysis of orientalol-F 78 and englerin-A 79.
B. Main Part

162 was expected to arise from 163 by allylation, RCM\textsuperscript{117} and subsequent oxymercuration. Ketone 163 might be accessed from an unsaturated aldehyde 164 by umpolung method. Aldehyde 164 could be assembled from enone 165 through the selective reduction of \( \alpha,\beta \)-unsaturated double bond, methylation and subsequent oxidation.

3.3 Previous reports for orientalol-F and englerin-A

Up to date only two groups have reported the synthesis of the orientalol-F. In 2009, Echavarren \textit{et al.} reported the first synthesis of oriental-F 78 from 166 by gold-catalyzed cycloaddition of functionalized ketoenynes.\textsuperscript{118} In 2012, Wang \textit{et al.} achieved the synthesis of 78 from 167 and 168 by 4+3 cycloaddition\textsuperscript{119} catalyzed by a proline derivative in the key step (Scheme 35).

![Scheme 35: Previous reports for Orientalol-F.](image)

Based on its strong bioactivity against renal cancer cell lines many groups focused on the synthesis of 79. In 2009 M. Christmann \textit{et al.} reported the first synthesis of 79 from commercially available nepatalactone 169 in 15 steps and found that the assignment of the absolute stereochemistry in naturally occurring 79 has been wrong.\textsuperscript{120} In 2010, D. Ma \textit{et al.} and Echavarren \textit{et al.} achieved the synthesis of 79 by gold catalyzed cyclization of enynes as key step from 109 and 170.\textsuperscript{70,121} Notably the synthesis developed by D. Ma is protecting group free. In the same year, Nicolaou \textit{et al.} reported the synthesis of 79 in 25 steps from 171.\textsuperscript{122}
Scheme 36: Previous reports for Englerin-A.

The synthesis of W. J. Chain et al. (2012)\textsuperscript{123} feuters SmI\(_2\) mediated reductive cyclization between 172 and 173 as key step and K. Takahashi et al. (2012)\textsuperscript{124} showcase CrCl\(_2\) catalyzed enantio selective Barbier allylation\textsuperscript{125} as key step for 79. Moreover, P. Metz et al. (2013),\textsuperscript{126} and J. Zhang et al. (2014)\textsuperscript{127} also synthesized 79 starting from 176 and 177 (Scheme 36).
3.4 Towards the construction of guaiane core structure of 78 and 79

3.4.1 Synthesis of aldehyde 164

The total synthesis of 78 and 79, began by subjecting (S)-134, isopropenyl magnesiumbromide and formaldehyde to the conditions developed for our one-pot operation to cyclopentenones, giving rise 165 in 66% yield as a single stereoisomer (Scheme 37).

\[
\text{(S)-134} \xrightarrow{\text{CuCN, LiCl, BrMg, HCHO, -78 °C}} 165 \quad 66\%
\]

Scheme 37: Synthesis of enone 165 by using one pot strategy on (S)-134.

The next step of our synthesis consisted of the selective reduction of the \(\alpha,\beta\)--unsaturated double bond in 165. The combination of catalytic amounts of ZnCl\(_2\) and to the Pd(TPP)\(_4\) in the presence of stoichiometric amounts of a hydride source has proved to be efficient in conjugate reductions of \(\alpha,\beta\)-unsaturated double bonds.\(^{105,151,152}\) First Bu\(_3\)SnH was tried as hydride source, however no reduction was observed at room temperature after 24 h.\(^{128}\) In contrast, Ph\(_2\)SiH\(_2\) as hydride source furnished 178 in 75% yield after 30 minutes at room temperature (Scheme 38).\(^{105}\)

\[
\text{165} \xrightarrow{\text{Ph}_2\text{SiH}_2, \text{ZnCl}_2, \text{Pd(TPP)}_4, \text{CHCl}_3, \text{rt, 30 min}} 178 \quad 75\%
\]

Scheme 38: Selective reduction of \(\alpha,\beta\)--unsaturated double bond in 165.

As the next step, the chemo selective methylation of 178 by MeLi, CeCl\(_3\) in THF at -78 °C was carried out to afford syn-diol 179\(_a\) in 70% and anti-diol 179\(_b\) in 15% (Scheme 39).
Scheme 39: Synthesis of diol 179a by using MeCeCl₂.

Next, we planned to do an oxidation of the primary alcohol on syn-179a followed by dehydration to arrive at aldehyde 164. When compound 179a was subjected to the conditions of the Dess-Martin oxidation¹²⁹ aldehyde 180 was obtained in 90% yield, which could be dehydrated to 164 in 55% yield in the presence of MsCl, Et₃N and DMAP. Alternatively, oxidation of 179a under the conditions of a Swern oxidation¹³¹ directly furnished 164¹³⁰ in 54% yield. On the other hand, 179b under the Swern conditions furnished epi-180 in low yield (Scheme 40).

Scheme 40: Synthesis of aldehyde 164.

3.4.2 Umpolung strategy

Umpolung is known as a chemical modification of a functional group with reversal of polarity, a concept that was developed D. Seebach and E. J. Corey.¹³² It is a very important tool for the generation of carbanion synthons. A well-known Umpolung reagent in organic synthesis is the cyanide ion. For example, cyanide is a key catalyst in the benzoin condensation.¹³³ The net result in a benzoin condensation is that a bond is formed between two carbons that are normally electrophiles.
Moreover, dithiane chemistry is a classic example for Umpolung reaction. In aldehyde compounds, the carbonyl carbon behaves as an electrophile and oxygen behave like nucleophile, but if the aldehyde is converted to a 1,3-dithiane the polarity can be reversed by deprotonation, thus a carbanion synthon can be generated (Scheme 41).

Scheme 41: General Umpolung strategy in organic synthesis for the generation of carbanion synthons.

The next steps in our synthesis are concerned with the construction of the guaiane core structure being present in 78 and 79. The reaction of aldehyde 164 with isopropyl dithiane (Umpolung synthon) in the presence of n-BuLi at -78 °C furnished 187 in 95% yield with 9:1 ratio. Exposure of allylalcohol 187 to the conditions of deprotection (NCS, AgNO₃ in 9:1 (MeCN:H₂O)) gave hydroxyl ketone 163 in 75% yield (Scheme 42).

Scheme 42: Synthesis of 163 by Umpolung.

The next aim was to achieve the stereoselective allylation of 163 followed by RCM. Barbier-type allylation of 163 with allyl bromide in the presence of zinc in DMF did not give the desired product after 24 h. However, when allyl magnesiumbromide as an allylating agent at 0 °C was employed, diol 188 was obtained in 78% yield as a single diastereomeric.
\(\alpha\)-hydroxy group in 163 favors the addition of Grignard reagent through the 163a, which provides us 188 as a major diastereomer. With 188 hand, the cyclization to obtain 189 was investigated. During the past decade, ring-closing metathesis developed as a powerful tool for the formation of carbon-carbon bonds with concurrent cyclization. Which has been utilized for the synthesis of complex natural products. Reaction of diol 188 with Grubbs-II catalyst in DCM, after 3 h at refluxed temperature gave guaiane core 189 in 92% yield (Scheme 43).

\[
\text{Scheme 43: Synthesis of guaiane core compound 189.}
\]

3.4.3 Construction of oxo-bridge ring

Having the guaiane core compound 189 in hand, the next aim was the construction of the oxo-bridge ring to complete the synthesis of 78 and 79. Phenyl selenium chloride was investigated to initiate the desired intramolecular cyclization. Subjecting 189 to the PhSeCl and \(\text{K}_2\text{CO}_3\) in DCM afforded the corresponding cyclized selenide compound 190 in 65% yield, which was used directly for the next elimination step. \(\text{NaIO}_4\) in MeOH-H\(_2\)O and \(\text{H}_2\text{O}_2\) in THF were tested for the elimination of the PhSe-group in 190. However, both of these procedures failed to produce compound 191 (Scheme 44).

\[
\text{Scheme 44: Formation oxo-bridge core in 189 by using selenide chemistry.}
\]
As an alternative, we turned our focus to an oxymercuration-deoxymercuration sequence. Reaction of compound 189 with Hg(OAc)$_2$ in DCM followed by treatment with aq. NaCl solution gave organomercuric compound 162 which was not further purified but directly subjected to the reduction with NaBH$_4$ at -78 °C in methanol to give rise to epi-orientalol-F 192 in 62% yield (over 2 steps). Alternatively, 162 could be converted to 193 by oxidation with NaBH$_4$, O$_2$ (bubbling) in DMF in 58% yield over two steps (Scheme 45).

Scheme 45: Formation oxo-bridge core in 189 by oxymercuration method.

### 3.5 The end game for orientalol-F 78 and englerin-A 79

192 was oxidized with Dess-Martin reagent to give enone 194 in quantitative yield after 1 h at room temperature. Luche reduction$^{146,147}$ (NaBH$_4$, CeCl$_3$·7H$_2$O) reduction of 194 the afforded final molecule orientalol-F 78 in 94% yield as a single stereoisomer (Scheme 46a). Alternatively, 193 was oxidized with Dess-Martin reagent followed by reduction with NaBH$_4$ in MeOH (72% over 2 steps) to give rise to 196 as a single stereoisomer. We thought that the oxo-bridge ring might form complex with intermediate borane (BH$_4$), which favors the attack of hydride nucleophile from the same side and leads to 78 and 196 as a majors. The diol-196 is known intermediate for englerin-A 79$^{70}$ (Scheme 46b).
The spectroscopic data (\(^1\)H NMR, \(^{13}\)C NMR, UV and HRMS) and optical rotation were in accordance with literature.\(^{48}\) In order to unambiguously prove the correct relative and absolute stereochemistry of (+)-orientalol-F 78 according to our synthetic route, a X-ray crystal structure was desired. Since orientalol-F 78 was obtained only as pale yellow oil, we synthesized a derivative, i.e. epoxy-orientalol-F 197 by treatment of 78 with m-CPBA in dry DCM at 0 °C in 88% yield,\(^{148}\) which upon recrystallization from heptane afforded crystals suitable for X-ray analysis (Scheme 47).

**Scheme 46**: End game for orientalol-F and englerin-A.
B. Main Part

Scheme 47: Synthesis of epoxy-orientalol-F 197 for X-ray analysis.

One-pot reactions are especially efficient method to rapidly achieve several transformations with the necessity for work-up and purification, which minimizes the generation of chemical waste and safes time. Our previous described individual steps showed only the desired transformations as clean spot-to-spot reactions on TLC. We therefore investigated if the guaiane core 192 or 193 can be constructed enroute to 78 and 79 from 163 without isolation of any intermediates. We started our one pot operation with allylation of 163 by using allylmagnesium bromide (1.5 equiv.) at 0 °C (the excess Grignard reagent was quenched by stirring the reaction in the open air).

Scheme 48: Pot economy for 192 and 193.
After 1.5 h the solvent was removed under reduced pressure, the crude was directly used for ring closing metathesis reaction with Grubbs-II catalyst in DCM in the same flask. After 3 h of reflux, Hg(OAc)$_2$ was added at room temperature to the same flask without evaporation of solvent. After 15 h at room temperature the reaction was quenched with aq. NaCl, yield in 162 (cf. Scheme 45) as crude product. In different reaction pots, 162 was done converted to 192 and 193 as described above. Overall 192 was obtained in 45% yield (over 4 steps starting from 163) and 193 was obtained in 40% yield (over 4 steps starting from 162) (Scheme 48).

3.6 Other efforts for 78 and 79

With the successful synthesis of orientaol-F 78 (total synthesis) and englerin-A 79 (formal synthesis), we next turned our focus to different aldehydes for trapping the intermediate enolate that is generated after nucleophile addition to (R)-125, which would provide alternative intermediates that might be useful towards the target molecules 78 and 79.

Scheme 49: Synthesis of 199.

We began this study with the synthesis of 199. We subjected compound (R)-125, isopropenyl magnesium bromide and 198 to our one pot conditions, giving rise to aldol adduct 199 in 80% yield (Scheme 49). The next step of our synthesis was the selective reduction of the $\alpha,\beta$-unsaturated double bond in 199. However, 199 possessing an allylic alcohol functionality gave 200 only in low yield under various reduction conditions with Pd (TPP). It was thought that the presence of the allylic –OH system, which is very reactive towards the Pd (0) catalysts and forms Pd-allyl type complex 201, interferes with the desired double bond reduction. Raney-Ni exhibits a good selectivity towards conjugate reduction of $\alpha,\beta$–unsaturated double bonds in THF. However, with 199 as substrate we observed no conversion after 24h at room temperature. Another alternative is the, Lewis acid catalyzed selective reduction of $\alpha,\beta$–unsaturated double bonds. Attempts to convert 199 to 200 by an InCl$_3$ catalyzed process with NaBH$_4$ as stoichiometric reductant was also met with no success (Scheme 50).
Scheme 50: Selective reduction of \(\alpha,\beta\)-unsaturated double bond in 199.

We therefore planned to protect the allylic alcohol double bond in 199 to prevent a reaction with Pd(0). We synthesized compound 202 from 199 using m-CPBA in DCM at 0 °C. Subsequent reaction with Pd(TPP)_4, Ph_2SiH_2 in the presence of ZnCl_2 gave 203 in only 26% yield (Scheme 51a). Then we switched to protect free hydroxyl group in 199. We treated compound 199 with TESCl giving rise to 204. Subsequent treatment with Pd(TPP)_4, Ph_2SiH_2 and ZnCl_2 resulted on in decomposition of 204 after 30 min at room temperature (Scheme 51b).
B. Main Part

Scheme 51: Selective reduction of $\alpha,\beta$-unsaturated bond in derivatives of 199.

Addition of nucleophile to the $\alpha,\beta$-unsaturated system in the presence of Cu (I) salts affords 1,4-addition products. Copper hydrides however are not readily accessible. Cul catalyzed selective 1, 4- addition of hydride to the $\alpha,\beta$-unsaturated system in the presence of LiAlH$_4$ is known. We subjected therefore, compound 199 to the combination of Cul and LiAlH$_4$ in a mixture of DMPU:THF at $-78^\circ$C, yielding the desired 200 in 82 % yield after 3 h (Scheme 52).

Scheme 52: Selective reduction of $\alpha,\beta$-unsaturated double bond in 199 with copper hydride.

We next converted 200 to the methylated compound 205 with MeLi in the presence of CeCl$_3$ at $-78^\circ$C, which was obtained as a syn/anti mixture (2:3). The epoxide 206 was obtained from syn-205 by epoxidation with m-CPBA in 80% yield. For the final rearrangement of epoxide to the ketone 207, we planned to use an acid catalyzed rearrangement. We treated epoxide 206 with BF$_3$·Et$_2$O in DCM, which resulted in decomposition after 30 min at 0 $^\circ$C and also applying TfOH in DCM gave no better results. Keto group formation could not be observed even after longer reaction time in both cases (Scheme 53).
Scheme 53: Towards 78 and 79.

Having been unsuccessful to convert of 206 into 207, we turned our focus to use aldehyde 210, which is similar to the aldehyde 148 (with \( \alpha \)-hydroxy group). As we have shown in our retrosynthetic analysis (Scheme 54a), compound 208 could be a useful intermediate for the construction oxo-bridged guaiane core of 78 by using ring-closing metathesis, which can then be used for the synthesis of 78 and 79. 208 was expected to arise from (\( R \))-125, isopropenyl magnesium bromide and aldehyde 210. Aldehyde 210 synthesized from commercially available methyl isopropyl ketone 211. Silyl enol ether 212 was obtained from 211 by treatment with LDA followed by trapping the intermediate enolate with TMSCl in 70% yield. This was used directly for the Rubottom oxidation with m-CPBA affording 213 in 80% yield. 213 was converted to 210 by allylation with allyl magnesium bromide (75% yield) followed by Swern oxidation (70% yield). 210 was found to be very stable at room temperature (Scheme 54b). The reaction of (\( R \))-125, isopropenyl magnesium bromide and aldehyde 210 according to our one-pot protocol gave the desired compound 215, albeit in very low yield (10%). We thought that the protonation of the intermediate enolate might retard the formation of desired product in reasonable yield. Using the TES protected aldehyde 216 however gave also no conversion after 2 h at \(-78^\circ C\) (Scheme 54b).
4. Studies towards the synthesis of pseudoguaianolide core structure

Based on SAR studies it has been shown that almost all known bioactive pseudoguaianolides possess an $\alpha,\beta$-unsaturated lactone ring with an exomethylene group. This unsaturated lactone moiety enhances the cytotoxicity. The high toxicity can be attributed to the inhibition of DNA synthesis. Based on this bioactivity we tried to construct pseudoguaianolide core structure for our building block by using our one pot strategy.
Scheme 55: Retrosynthetic analysis for pseudoguaianolide core.

As outlined in scheme 55, aldehyde 220 was required for the construction of pseudoguaianolide core structure 217. Before that, we first used known literature aldehyde 221\textsuperscript{163} for the trapping of the intermediate enolate that is formed after Grignard addition to (R)-125. We subjected compound (R)-125, isopropenyl magnesiumbromide and aldehyde 221 to the one-pot protocol to produce aldol adduct 222 in 62\% yield. In the next step, we used Grubbs-II catalyzed ring closing metathesis to produce the unnatural pseudoguaianolide core structure 223, having a 8-membered ring, in 45\% yield (Scheme 56). However, the newly formed 223 was showed cytotoxicity against RAW264 cell lines with 240 \( \mu \text{M} \).

Scheme 56: Synthesis of unnatural pseudoguaianolide core structure 222.
Table 12: Anti-inflammatory activity of 223.

<table>
<thead>
<tr>
<th>compound</th>
<th>MTT IC&lt;sub&gt;50&lt;/sub&gt; [µM]</th>
<th>inhibition of NO production [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>minimum (conc [µM])</td>
</tr>
<tr>
<td></td>
<td>208.6 ± 11.7</td>
<td>44.8 ± 2.9 (25)</td>
</tr>
</tbody>
</table>

We next focused on the construction of 217 with aldehyde 220. As outlined in Scheme 55, the core structure 217 could be obtained from an aldol adduct 218, which we can easily achieved from compound (R)-125, aldehyde 220 and isopropenyl magnesiumbromide. Aldehyde 220 can be easily accessed from aldehyde 221 by treatment with Grubbs-II catalyst and MeOH as solvent. We used (R)-125, isopropenyl magnesiumbromide and aldehyde 220 to our one-pot protocol gave aldol adduct 218 in 64% yield. After successive ring closing metathesis with Grubbs-II catalyst afforded the natural pseudoguaianolide core structure 217 in 84% yield (Scheme 57).
With compound 218 in hand, we planned to synthesize anti-inflammatory drug 80. We began our studies with selective reduction of $\alpha,\beta$-unsaturated double bond in 218. We first focused on Pd (TPP)$_4$ catalyzed selective reduction of $\alpha,\beta$-unsaturated double bond in 218 in the presence of Ph$_2$SiH$_2$ as hydride source and obtained desired product 224 in very low yield. When we switched to Bu$_3$SnH under the above conditions, it gave decomposition after 1 h at room temperature. It was thought that the presence of allylic lactone system, which is very reactive towards the Pd (0) catalysts and forms Pd-allyl type complex 225. This may retard the attack of Pd (0) to the $\alpha,\beta$-unsaturated system (Scheme 58).
B. Main Part

Scheme 58: Selective reduction of \( \alpha,\beta \)-unsaturated double bond in 217.

Raney-Ni catalyzed selective conjugate reduction of \( \alpha,\beta \)-unsaturated double bond in THF was met with no success. We next focused on copper hydride for selective reduction of \( \alpha,\beta \)-unsaturated double bond in 218. When we subjected, compound 218 to the Cul and LiAlH4 in the mixture of DMPU:THF at -78 °C, the 1,4-adduct 224 was obtained in 80% yield after 3 h (Scheme 58). After successful reduction of the unsaturated double bond in 218, we directly applied Grubbs-II catalyzed ring closing metathesis to 224 in toluene at refluxed temperature to give rise to the pseudoguaianolide core structure 226 in 85% yield. 226 furnished 227 with TESCl and imidazole in
94% yield, and was then envisioned to be used for a stereoselective methylation to produce 228. Unfortunately, all attempts of this methylation failed. When we applied methylation conditions (MeLi, THF, -78 °C, 4 h and MeLi, CeCl₃, -78 °C, 8 h), it gave many undesired spots on TLC (Scheme 59).

Scheme 59: Synthetic route to the 80.

5. Conclusion

In conclusion, the readily available (R)-125 and (S)-134 allow the stereoselective synthesis of (+)-133 and (-)-133 with excellent selectivity and operational simplicity without using any harsh conditions, allowing the rapid assembly of natural scaffolds with complex architecture. The methodology described here offers a versatile approach for asymmetric synthesis of simple to complex various cyclopentanoid bioactive molecules. The first synthesis of (-)-teuclatriol 72 was achieved with 20% overall yield. This method allows the facile access to get guaiane and pseudoguaianolide core structures without using any protecting groups. On the other hand, with this method we have successfully finished total synthesis of (+)-orientalol-F 78 and formal synthesis of englerin-A 79 from our building block (R)-125.
C. Summary

In the first chapter, an application for (R)-125 and (S)-134 on the basis of copper(I)-catalyzed Grignard additions followed by trapping of the resulting intermediate enolate with aldehydes were investigated. Adducts (+)-133 and (-)-133 could be synthesized from (R)-125 and (S)-134 in a facile procedure with a decent yields (Scheme 60).

Scheme 60: Overview of (+)-133, (-)-133 and prostaglandin derivatives.
Excellent diastereo and enantioselectivities were obtained for adducts \((+)-133a-x\) and \((-)-133 a-r\). The scope of participating Grignard reagents and aldehydes is very broad: aliphatic, aromatic and alkenyl organomagnesium compounds could be applied. This method provides a potentially useful access to a variety of bioactive cyclopentanoid prostaglandin derivatives such as TEI-9826 3, compound 2, 141 and 143 (Scheme 60).

In the second chapter, a successful synthesis of teuclatriol 72 from \((R)-125\) has been demonstrated. The key steps involved were a one-pot construction of cyclopent-2-enone 146 with 4 contiguous stereo centers, ring-closing metathesis, selective reduction of a \(\alpha,\beta\)-unsaturated bond and subsequent chemoselective methylation. The first synthesis of \((-)\)-teuclatriol 72 was achieved with 26% overall yield in six steps (Scheme 61).

![Scheme 61: Synthesis of 72.](image)

In the third chapter, a successful total synthesis of orientalol-F 78 from \((S)-134\) has been demonstrated. The key steps involved were a, one-pot construction of 165, an Umpolung, ring-closing metathesis and subsequent formation of an oxo-bridge ring by oxymercuration. Compound 162 furnished diol 196, which is a known intermediate for englerin-A 79 (Scheme 62).
C. Summary

Scheme 62: Synthesis of 78 and 79.

Moreover, different aldehydes have been used for trapping the intermediate enolate that is generated after nucleophile addition to (R)-125, which would provide alternative intermediates that might be useful towards the target molecules 78 and 79. A study of a one-pot economy was carried out on 163 to get directly the desired 192 and 193 without isolation and purification of intermediates (Scheme 63).

Scheme 63: Overview of one pot operation on 163.
In the fourth chapter, a successful construction of a pseudoguaianolide core structure 217 has been demonstrated.

**Scheme 64**: Synthesis of 217 and 223.

In this synthesis, the new aldehyde 220 was synthesized from known aldehyde 221 via Grubbs-II catalyst. Later, selective reduction of the α,β-unsaturated bond was carried out on compound 218, which could be a useful intermediate for compound 80. Moreover, the synthesis of unnatural pseudoguaianolide core structure 223 and its bioactivity has been demonstrated (Scheme 64).
D. Experimental Part

1. General

\textbf{\textsuperscript{1}H-NMR-Spectra} were recorded on Bruker Avance 300, Bruker Avance 400, Bruker Avance 600, Varian Inova 600, Bruker DRX-400 with a H/C/P/F QNP gradient probe and Bruker Avance 500 with a dual carbon/proton CPDUL cryoprobe. The chemical shift is given in [ppm], calibration is set on chloroform-d1 (7.26 ppm). The spectra were evaluated in 1st order and the coupling constants are given in Herth [Hz]. The following abbreviations for the spin multiplicity were used: \textbf{s} = singlet, \textbf{d} = doublet, \textbf{t} = triplet, \textbf{q} = quartet, \textbf{qt} = quintet, \textbf{m} = multiplet, \textbf{dd} = doublet of doublet, \textbf{dt} = doublet of triplet, \textbf{ddd} = doublet of double doublet, \textbf{sept} = septet. The used deuterated solvents are given separately.

\textbf{\textsuperscript{13}C-NMR-Spectra} were recorded on Bruker Avance 300, Bruker Avance 400, Bruker Avance 600, Varian Inova 600, Bruker DRX-400 with a H/C/P/F QNP gradient probe and Bruker Avance 500 with a dual carbon/proton CPDUL cryoprobe. The chemical shift is given in [ppm], calibration is set on chloroform-d1 (77.16 ppm). The multiplicity of signals were detected by DEPT 135 and 90 (DEPT-Distortionless Enhancement by Polarization Transfer) and are given as: + = primary and tertiary C-atom (positive DEPT 135 signal; tertiary C-atom: DEPT 90 signal), - = secondary C-atom (negative DEPT 135 signal), Cq = quaternary C-atom (DEPT-signal intensity zero).

\textbf{Melting points} were measured on a Büchi SMP-20 in a silicon oil bath. The melting points are uncorrected.

\textbf{Infrared-Spectra} were recorded on a Bio-Rad Excalibur Series or Mattson Genesis Series FT-IR. Solid compounds were measured in KBr film, liquid compounds as a neat film between NaCl-plates. The wave numbers are given in [cm\textsuperscript{-1}].

\textbf{Masspectrometry} was performed on a Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000, Nermag quadrupoles, VG-ZAB high resolution double focusing and VG Autospec-Q tandem hybrid with EBEqQ configuration. The percentage set in brackets gives the peak intensity related to the basic peak (I=100%). High Resolution Mass Spectrometry HRMS: The molecular formula was proven by the calculated precise mass.

\textbf{Elemental Analysis} was prepared by the micro analytic section University of Regensburg using a Vario EL III or Mikro-Rapid CHN (Heraeus).
**Optical rotation** was measured at room temperature on a 241 MC Perkin-Elmer polarimeter at a wavelength of 589 nm (Na-D) in a 1 dm or 0.1 dm cell. The concentration is given in (g/100 mL).

**X-ray analysis** was performed by the crystallography laboratory of the University of Regensburg (STOE-IPDS, Stoe & Cie GmbH).

**Chiral High Performance Liquid Chromatography** was carried out using. Column: LabID 80/ Daicel Chemical Industries LTD./ CHIRALCEL (OD-H) (Lot No. ODH0CE-GB060)/ Cellulose tris (3,5-dimethylphenyl carbamate) / coated on 5 μm silica gel/ 250 mm x 4.6 mm ID/ part DAIC 14325 and CHIRALCEL OJ-H, 4.6 x 250 mm, 10 μm. LC system: Agilent 1100/3: DAD G1315B [DE03010828]/COLCOM G1316A [DE14925491] / ALS G1313A [DE23922434] / BIN pump GG1312A [DE43618259]/ HP 1050 DEGASSER.

**Thin Layer Chromatography (TLC)** was prepared on TLC- aluminium sheets (Merck, silica gel 60 F254, 0.2 mm). Detection in UV-light λ = 254 nm, staining with Iodine, Mostain, molybdatophosphoric acid (5% in ethanol), KMnO4 solution and vanillin-sulfuric acid.

**Ozone-Generator** For ozone generation a Fischer process technology ozone generator OZ 500 MM was used, supplied by an oxygen tank.

**Solvents** Absolute solvents were prepared according to usual lab procedures or taken from MB-SPS solvent purification system. EtOAc, Hexanes and DCM were purified ny distillation before used. Further solvents and reagents were p.a. quality. Reaction with oxygen- and moisture sensitive reactants was performed in oven dried and in vacuo heated reaction flasks under pre-dried inert gas (nitrogen or argon) atmosphere. For cooling temperatures <-78 oC dry ice/acetone mixture was used.
2. Procedure for the synthesis of (R)-125 and (S)-134 in 50 gram scale:

To a solution of 4-hydroxy-2-cyclopentenone (±)-136 (36.76 g, 375 mmol) and Boc₂O (98.21 g, 450 mmol) in THF (375 mL) were added triethylamine (63 mL, 450 mmol) and DMAP (0.75 g). After the reaction mixture was stirred at room temperature for 30 min, the solvent was removed under reduced pressure. After purification on silica (hexanes/ EtOAc 5:1) obtained (±)-125 (64.87 g, 87%).

Physical state: White solid;
TLC: R_f = 0.33 (hexanes/ EtOAc 9:1, UV-active, stains dark brown with vanillin);
M.P = 39 °C;
^1H NMR (300 MHz, CDCl₃): δ 7.60 (dd, J = 5.7, 2.4 Hz, 1H), 6.33 (dd, J = 5.7, 1.3 Hz, 1H), 5.71 (ddt, J = 3.6, 2.3, 1.8 Hz, 1H), 2.84 (dd, J = 18.7, 6.4 Hz, 1H), 2.40 (dd, J = 18.7, 2.2 Hz, 1H), 1.51 (s, 9H);
^13C NMR (75 MHz, CDCl₃): δ = 204.6, 158.6, 152.7, 137.2, 83.3, 74.2, 41.0, 27.8, 27.8, 27.8;
IR (neat) (cm⁻¹) ν_max : 1730, 1716;
HRMS (m/z): calcd for C₁₀H₁₄O₄ (M⁺) 198.0892, found 198.0896.

Under nitrogen atmosphere to a solution of (±)-125 (50.00 g, 252.52 mmol, 2.0 equiv) 137 (15.67 g, 126.26 mmol, 1.0 equiv) and Cs₂CO₃ (12.17 g, 37.37 mmol, 0.296 equiv) in DCM (1000 mL) at 0 °C was added the catalyst solution, being separately prepared by stirring Pd₂(dba)₃CHCl₃ (1.31 g, 1.262 mmol, 1 mol% Pd based on 137) and ligand (R,R)-127 (3.07 g, 4.44 mmol, 0.035 equiv) in DCM (500 mL) until the initially purple solution turned yellow-brown (4-5 min). After 2.5 h of stirring at 0 °C,
D. Experimental Part

solvent was removed under reduced pressure. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) (R)-125 (21.00 g, 42%, >99% ee) and (S)-134 (24.75g, 48%, > 92% ee) were obtained.

**Compound (R)-125:**

**Physical state:** brown oil;

**TLC:** R_\text{f} = 0.33 (hexanes/ EtOAc 9:1, UV-active, stains dark brown with vanillin);

[\alpha]_D^25 = 94 (c 1.1, CHCl_3);

^1H NMR (300 MHz, CDCl_3): δ 7.60 (dd, J = 5.7, 2.4 Hz, 1H), 6.33 (dd, J = 5.7, 1.3 Hz, 1H), 5.71 (ddt, J = 3.6, 2.3, 1.8 Hz, 1H), 2.84 (dd, J = 18.7, 6.4 Hz, 1H), 2.40 (dd, J = 18.7, 2.2 Hz, 1H), 1.51 (s, 9H);

^13C NMR (75 MHz, CDCl_3): δ = 204.6, 158.6, 152.7, 137.2, 83.3, 74.2, 41.0, 27.8, 27.8, 27.8;

**IR (neat) (cm^{-1})** ν_{\text{max}}: 1730, 1716;

**HRMS (m/z):** calcd for C_{10}H_{14}O_4 (M^+)^+ 198.0892, found 198.0896.

**Compound (S)-134:**

**Physical state:** pale brown color solid;

**TLC:** R_\text{f} = 0.43 (hexanes/ EtOAc 3:1, UV-active, stains dark green with vanillin);

M.P. = 64 °C;

[\alpha]_D^25 = 8.62 (c 1.00, CHCl_3);

^1H NMR (300 MHz, CDCl_3): δ = 7.70 (dd, J=5.7, 2.4 Hz, 1H), 6.98 – 6.71 (m, 4H), 6.35 (dd, J=5.7, 1.3 Hz, 1H), 5.37 (ddd, J=5.8, 3.4, 2.2 Hz, 1H), 3.78 (s, 3H), 2.85 (dd, J=18.4, 6.0 Hz 1H), 2.45 (dd, J=18.4, 2.2 Hz, 1H);

^13C NMR (75 MHz, CDCl_3): δ = 205.28, 159.90, 154.62, 151.31, 136.40, 116.71, 116.71, 114.89, 114.89, 76.07, 55.72, 41.90;

**IR (neat) (cm^{-1})** ν_{\text{max}}: 1706, 1506, 1353, 1107, 1027, 821;

**HRMS (m/z):** calcd for C_{12}H_{13}O_3 (M+H)^+ 205.0859, found 205.0863.
3. Synthesis and characterization of (+)-133.

**General Procedure A:** To a stirred solution of CuCN (0.102 g, 1.14 mmol, 3.0 equiv) and anhydrous LiCl (0.096 g, 2.28 mmol, 6.0 equiv) in THF (4 mL) was added the Grignard reagent (1.14 mmol, 3.0 equiv) dropwise at –40 °C. The reaction mixture was cooled to –78 °C upon which a solution of (R)-125 (0.075 g, 0.38 mmol, 1.0 equiv) in THF (1 mL) was added. After 4 min of stirring, aldehyde (0.63 mmol, 1.68 equiv) was added. After the starting material had disappeared (ca. 5 min, monitored by TLC), NH₄Claq (5 mL) was added and the reaction mixture was extracted with Et₂O (2x 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude was purified by flash chromatography on silica.

**Compound (+)-133a:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) phenylmagnesium bromide (0.94 M solution in THF, 1.2 mL, 1.14 mmol) and hexanal (0.063 g, 0.078 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 5:1 to 3:1) title compound was obtained in 72% yield (0.071 g).

**Physical state:** pale yellow oil;

**TLC:** Rₐ = 0.31 (hexanes/ EtOAc 5:1, UV-active, stains orange with vanillin);

[^25]D: 215.3 (c 0.32, CHCl₃);

**1H NMR (300 MHz, CDCl₃)** δ 7.62 (dd, J = 5.6, 2.4 Hz, 1H), 7.38 – 7.26 (m, 3H), 7.19 – 7.14 (m, 2H), 6.29 (dd, J = 5.6, 2.1 Hz, 1H), 3.87 (ddd, J = 7.4, 6.2, 2.4 Hz, 2H), 3.76 (s, 1H), 2.44 (dd, J = 8.2, 2.9 Hz, 1H), 1.66 – 1.47 (m, 2H), 1.33 – 1.12 (m, 6H), 0.82 (t, J = 6.8 Hz, 3H);

**13C NMR (75 MHz, CDCl₃)** δ 212.96, 167.19, 140.52, 132.95, 129.11, 129.11, 127.51, 127.51, 127.51, 72.24, 59.01, 50.91, 35.26, 31.71, 24.55, 22.58, 14.02;

**IR (neat) (cm⁻¹)** νmax: 3425, 2953, 2931, 2858, 1689, 1590, 1454, 1278, 1179, 1076, 1048, 1030, 757, 700, 616, 494;

**HRMS (m/z):** calcd for C₁₇H₂₂NaO₂(M+Na)⁺ 281.1512, found 281.1510.
Compound (+)-133b: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) phenylmagnesium bromide (0.94 M solution in THF, 1.2 mL, 1.14 mmol) and trans-2-pentenal (0.053 g, 0.062 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) title compound was obtained in 68% yield (0.063 g).

Physical state: brown color oil;
TLC: R_f = 0.28 (hexanes/ EtOAc 5:1, UV-active, stains brown with vanillin);
[^a]D^25 313.28 (c 0.28, CHCl_3);

^1^H NMR (300 MHz, CDCl_3) δ 7.64 (dd, J = 5.6, 2.5 Hz, 1H), 7.37 – 7.24 (m, 3H), 7.15 – 7.05 (m, 2H), 6.30 (dd, J = 5.6, 2.1 Hz, 1H), 5.85 (dt, J = 15.2, 6.1 Hz, 1H), 5.41 – 5.29 (m, 1H), 4.29 (t, J = 8.3 Hz, 1H), 3.91 – 3.81 (m, 2H), 2.48 (dd, J = 8.6, 2.7 Hz, 1H), 2.13 – 2.00 (m, 2H), 0.97 (t, J = 7.4 Hz, 3H);

^13^C NMR (75 MHz, CDCl_3) δ 121.57, 167.37, 140.47, 136.20, 132.89, 128.91, 128.91, 128.80, 127.78, 127.78, 127.36, 74.29, 59.30, 50.51, 25.06, 12.98;
IR (neat) (cm\(^{-1}\)) \(\nu_{\text{max}}\): 3415, 2962, 1689, 1589, 1493, 1454, 1335, 1179, 1030, 969, 897, 758, 699, 533, 505;
HRMS (m/z): calcd for C_{16}H_{18}NaO_2 (M+Na)^+ 265.1199, found 265.1200.

Compound (+)-133c: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) phenylmagnesium bromide (0.94 M solution in THF, 1.2 mL, 1.14 mmol) and trans-2-decenal (0.098 g, 0.11 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) title compound was obtained in 70% yield (0.083 g).

Physical state: yellow oil;
TLC: R_f = 0.31 (hexanes/ EtOAc 5:1, UV-active, stains dark red with vanillin);
[^a]D^25 219.5 (c 0.56, CHCl_3);

^1^H NMR (600 MHz, CDCl_3) δ 7.64 (dd, J = 5.6, 2.5 Hz, 1H), 7.34 – 7.30 (m, 2H), 7.28 – 7.26 (m, 1H), 7.11 (dd, J = 5.2, 3.3 Hz, 2H), 6.29 (dd, J = 5.6, 2.1 Hz, 1H), 5.83 – 5.77 (m, 1H), 5.38 (ddt, J = 15.3, 7.8, 1.4 Hz, 1H), 4.30 (t, J = 8.1 Hz, 1H), 3.86 (dd, J = 4.8, 2.4 Hz, 1H), 2.50 (dd, J = 8.4, 2.7 Hz, 1H), 2.02 (qt, J = 10.8, 4.1 Hz, 2H), 1.34 (ddd, J = 12.0, 4.8, 2.3 Hz, 2H), 1.32 – 1.23 (m, 9H), 0.88 (t, J = 7.1 Hz, 3H);

^13^C NMR (151 MHz, CDCl_3) δ 212.32, 167.25, 140.48, 134.83, 132.86, 129.56, 128.89, 128.89, 127.72, 127.72, 127.32, 74.18, 59.28, 50.43, 32.06, 31.77, 29.22, 29.14, 28.85, 22.65, 14.08;
D. Experimental Part

IR (neat) (cm⁻¹) ν_max: 3361, 2926, 2855, 1690, 1511, 1454, 1234, 1036, 827, 700, 637, 537, 497;

HRMS (m/z): calcd for C_{21}H_{28}NaO_2 (M+Na)^+ 335.1982, found 335.1983.

**Compound (+)-133d:** The title compound was prepared (R)-125 (0.075 g, 0.38 mmol) phenylmagnesium bromide (0.94 M solution in THF, 1.2 mL, 1.14 mmol) and 4-methoxy benzaldehyde (0.086 g, 0.076 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 5:1 to 3:1) title compound was obtained in 78% yield (0.087 g).

**Physical state:** green color oil;

**TLC:** R_f = 0.2 (hexanes/ EtOAc 5:1, UV-active, stains dark brown with vanillin);

[α]_D^{25} 242.0 (c 0.53, CHCl_3);

^1H NMR (300 MHz, CDCl_3) δ 7.60 (dd, J = 5.6, 2.5 Hz, 1H), 7.23 – 7.16 (m, 2H), 7.17 – 7.06 (m, 3H), 6.84 – 6.77 (m, 2H), 6.56 – 6.48 (m, 2H), 6.34 (dd, J = 5.6, 2.1 Hz, 1H), 4.74 (d, J = 9.5 Hz, 1H), 4.45 (s, 1H), 3.80 (s, 3H), 3.67 – 3.59 (m, 1H), 2.66 (dd, J = 9.5, 2.6 Hz, 1H);

^13C NMR (75 MHz, CDCl_3) δ 213.0, 167.5, 159.7, 140.1, 133.1, 132.9, 128.6, 128.6, 128.6, 127.1, 127.1, 127.0, 113.8, 113.8, 75.0, 60.9, 55.4, 50.2;

IR (neat) (cm⁻¹) ν_max: 3445, 2836, 1689, 1612, 1587, 1513, 1454, 1247, 1174, 1031, 833, 701, 635, 538, 496;

HRMS (m/z): calcd for C_{19}H_{18}NaO_2 (M+Na)^+ 317.1148, found 317.1150.

**Compound (-)-133e:** The title compound was prepared (R)-125 (0.075 g, 0.38 mmol) phenylmagnesium bromide (0.94 M solution in THF, 1.2 mL, 1.14 mmol) and benzaldehyde (0.067 g, 0.064 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 5:1 to 3:1) title compound was obtained in 72% yield (0.072 g).

**Physical state:** white powder;

**TLC:** R_f = 0.35 (hexanes/ EtOAc 5:1, UV-active, stains pale brown with vanillin);

[α]_D^{25} 235.0 (c 0.16, CHCl_3);

^1H NMR (300 MHz, CDCl_3) δ 7.62 (dd, J = 5.6, 2.5 Hz, 1H), 7.30 (d, J = 7.3 Hz, 5H), 7.15 – 7.04 (m, 3H), 6.49 – 6.41 (m, 2H), 6.36 (dd, J = 5.6, 2.0 Hz, 1H), 4.78 (d, J = 9.5 Hz, 1H), 4.69 – 4.35 (m, 1H), 3.66 (dd, J = 4.7, 2.4 Hz, 1H), 2.66 (dd, J = 9.5, 2.6 Hz, 1H);

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**D. Experimental Part**

**13C NMR (75 MHz, CDCl₃) δ 213.05, 167.61, 140.71, 139.92, 132.90, 128.56, 128.49, 128.46, 127.41, 127.06, 127.06, 127.06, 75.55, 60.76, 50.10;**

**IR (neat)** (cm⁻¹) νₘₐₓ: 3392, 1677, 1590, 1492, 1437, 1340, 1266, 1196, 1034, 902, 853, 796, 752, 695, 638, 555, 484;

**HRMS (m/z):** calcd for C₁₈H₁₆NaO₂ (M+Na)⁺ 287.1150, found 287.1149.

**Compound (+)-133f**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) isopropenylmagnesium bromide (1.0 M solution in THF, 1.14 mL, 1.14 mmol) and acrolein (0.036 g, 0.042 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 7:1 to 5:1) title compound was obtained in 64% yield (0.043 g).

**Physical state:** yellow oil;

**TLC:** Rₚ = 0.57 (hexanes/EtOAc 3:1, UV-active, stains brown with vanillin);

**[α]D²⁵:** 235.2 (c 0.14, CHCl₃);

**1H NMR (300 MHz, d₆-Acetone) δ 7.67 (dd, J = 5.7, 2.6 Hz, 1H), 6.14 (dd, J = 5.7, 2.0 Hz, 1H), 5.86 (ddd, J = 5.6 Hz, 1H), 5.35 – 5.24 (m, 1H), 5.12 – 5.05 (m, 1H), 4.84 – 4.80 (m, 1H), 4.76 (dd, J = 5.7, 0.8 Hz, 1H), 4.52 – 4.41 (m, 1H), 4.32 (d, J = 3.6 Hz, 1H), 3.50 (dd, J = 5.3, 2.4 Hz, 1H), 1.79 – 1.75 (m, 3H);

**13C NMR (75 MHz, d₆-Acetone) δ 209.55, 167.52, 146.75, 138.73, 134.21, 115.84, 112.45, 73.32, 57.55, 51.24, 21.30;

**IR (neat)** (cm⁻¹) νₘₐₓ: 3468, 3390, 2973, 1689, 1645, 1587, 1438, 1378, 1273, 1184, 1052, 992, 897, 785, 667, 535, 495;

**HRMS (m/z):** calcd for C₁₁H₁₄NaO₂ (M+Na)⁺ 201.099, found 201.098.

**Compound (+)-133g**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) isopropenylmagnesium bromide (1.0 M solution in THF, 1.14 mL, 1.14 mmol) and trans-2-methyl-2-butenal (0.053 g, 0.06 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 7:1 to 5:1) title compound was obtained in 66% yield (0.052 g).

**Physical state:** yellow oil;

**TLC:** Rₚ = 0.62 (hexanes/EtOAc 3:1, UV-active, stains brown with vanillin);

**[α]D²⁵:** 250.2 (c 0.37, CHCl₃);
Compound (+)-133h: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) isopropenylmagnesium bromide (1.0 M solution in THF, 1.14 mL, 1.14 mmol) and trans-2-decenal (0.098 g, 0.11 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 10:1) title compound was obtained in 70% yield (0.073 g).

Physical state: pale yellow oil;

TLC: R<sub>f</sub> = 0.7 (hexanes/EtOAc 5:1, UV-active, stains brown with vanillin);

[α]<sub>D</sub><sup>25</sup> = 121.8 (c 0.71, CHCl<sub>3</sub>);

<sup>1</sup>H NMR (300 MHz, d<sub>6</sub>-Acetone) δ 7.32 (dd, J = 5.6, 2.5 Hz, 1H), 6.19 – 6.07 (m, 1H), 5.46 (qt, J = 19.5, 9.7 Hz, 1H), 4.86 – 4.47 (m, 1H), 4.67 (d, J = 0.7 Hz, 1H), 4.38 (s, 1H), 3.94 (d, J = 10.1 Hz, 1H), 3.13 (q, J = 2.3 Hz, 1H), 2.38 – 2.24 (m, 1H), 1.58 – 1.54 (m, 6H), 1.53 – 1.49 (m, 3H);

<sup>13</sup>C NMR (75 MHz, d<sub>6</sub>-Acetone): δ 212.89, 167.14, 141.82, 134.62, 131.78, 122.90, 113.03, 78.41, 51.61, 50.96, 18.16, 11.99, 9.68;

IR (neat) (cm<sup>-1</sup>) v<sub>max</sub>: 3489, 3462, 2916, 1682, 1647, 1586, 1504, 1440, 1410, 1378, 1343, 1261, 1187, 1026, 943, 898, 831, 793, 640, 624, 538, 464;

HRMS (m/z): calcd for C<sub>13</sub>H<sub>18</sub>NaO<sub>2</sub>(M+Na)<sup>+</sup> 229.1199, found 229.1196.

Compound (+)-133i: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) isopropenylmagnesium bromide (1.0 M solution in THF, 1.14 mL, 1.14 mmol) and 4-dimethylamino benzaldehyde (0.098 g, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 10:1) title compound was obtained in 62% yield (0.064 g).
Physical state: yellow colored oil;

TLC: $R_f = 0.13$ (hexanes/ EtOAc 5:1, UV-active, stains dark green with vanillin);

$[\alpha]_D^{25} = 170.1$ ($c$ 0.6, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.51 (dd, $J = 5.6$, 2.6 Hz, 1H), 7.23 – 7.16 (m, 2H), 6.73 – 6.64 (m, 2H), 6.20 (dd, $J = 5.6$, 2.0 Hz, 1H), 4.59 (dd, $J = 5.3$, 3.8 Hz, 2H), 4.29 (d, $J = 4.1$ Hz, 2H), 3.13 (dd, $J = 4.4$, 2.2 Hz, 1H), 2.92 (s, 6H), 2.53 (dd, $J = 9.2$, 2.3 Hz, 1H), 1.34 (s, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 212.90, 168.07, 150.72, 143.64, 132.72, 129.19, 128.02, 128.02, 113.07, 112.41, 112.41, 75.26, 57.28, 51.57, 40.72, 40.72, 20.17;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3445, 2968, 2855, 2798, 1685, 1614, 1522, 1444, 1346, 1219, 1185, 1163, 1055, 944, 899, 814, 739, 538;

HRMS (m/z): calcd for C$_{17}$H$_{21}$NaNO$_2$ (M+Na)$^+$ 294.1572, found 294.1572.

**Compound (+)-133j**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) isopropenylmagnesium bromide (1.0 M solution in THF, 1.14 mL, 1.14 mmol) and pyridine 4-carbaldehyde (0.068 g, 0.06 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 3:1 to 1:1) title compound was obtained in 59% yield (0.052 g).

Physical state: pale brown colored oil;

TLC: $R_f = 0.25$ (hexanes/ EtOAc 6:1, UV-active, stains green with vanillin);

$[\alpha]_D^{25} = 198.6$ ($c$ 0.18, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.53 (d, $J = 4.5$ Hz, 2H), 7.50 (dd, $J = 5.7$, 2.6 Hz, 1H), 7.28 (t, $J = 5.5$ Hz, 2H), 6.22 (dd, $J = 5.7$, 2.0 Hz, 1H), 4.79 (d, $J = 8.5$ Hz, 2H), 4.63 – 4.59 (m, 1H), 4.35 (s, 1H), 3.17 (dd, $J = 4.7$, 2.2 Hz, 1H), 2.52 (dd, $J = 8.5$, 2.7 Hz, 1H), 1.41 (s, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 211.41, 167.92, 149.97, 149.97, 149.52, 142.40, 132.89, 122.08, 122.08, 113.84, 74.14, 55.63, 51.29, 19.56;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3424, 3174, 2358, 2326, 1699, 1603, 1559, 1416, 1271, 1186, 1067, 1003, 906, 815, 652, 574, 468;

HRMS (m/z): calcd for C$_{14}$H$_{15}$NaNO$_2$ (M+Na)$^+$ 252.1101, found 252.110.

**Compound (+)-133k**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) vinylmagnesium bromide (0.80 M solution in THF, 1.4 mL, 1.14 mmol) and 3, 5-di methoxy benzaldehyde (0.105 g, 0.63 mmol) according to
the general procedure A. After purification on silica (hexanes/ EtOAc 5:1 to 2:1) title compound was obtained in 72% yield (0.075 g).

**Physical state:** yellow oil;

**TLC:** \( R_f \) = 0.15 (hexanes/ EtOAc 5:1, UV-active, stains dark brown with vanillin);

\([\alpha]^D_{25}\) = 143.9 (c 0.14, CHCl₃);

**\(^1\)H NMR (300 MHz, CDCl₃)** \( \delta \) 7.59 (td, \( J = 5.5, 2.5 \) Hz, 1H), 6.53 (d, \( J = 2.3 \) Hz, 2H), 6.39 (t, \( J = 2.3 \) Hz, 1H), 6.23 (dd, \( J = 5.7, 2.0 \) Hz, 1H), 5.30 (ddd, \( J = 13.5, 10.2, 7.3 \) Hz, 1H), 4.85 (d, \( J = 10.2 \) Hz, 1H), 4.74 – 4.63 (m, 2H), 4.59 (s, 1H), 3.77 (d, \( J = 7.1 \) Hz, 6H), 3.22 – 3.14 (m, 1H), 2.42 (dd, \( J = 9.5, 3.0 \) Hz, 1H);

**\(^{13}\)C NMR (75 MHz, CDCl₃)** \( \delta \) 212.11, 166.98, 160.84, 143.21, 136.41, 132.99, 116.17, 116.17, 104.99, 104.99, 100.25, 75.22, 57.79, 55.42, 47.78;

**IR (neat) (cm\(^{-1}\)) V\(_{\text{max}}\):** 3465, 2939, 1686, 1596, 1507, 1463, 1346, 1295, 1204, 1153, 1058, 920, 837, 633, 538, 500;

**HRMS (m/z):** calcd for C₁₆H₁₈NaO₄ (M+Na)\(^+\) 297.1099, found 297.1099.

**Compound (+)-133l:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) vinylmagnesium bromide (0.80 M solution in THF, 1.4 mL, 1.14 mmol) and trans-2-methyl-2-butenal (0.053 g, 0.06 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) title compound was obtained in 68% yield (0.050 g).

**Physical state:** pale red colored oil;

**TLC:** \( R_f \) = 0.35 (hexanes/ EtOAc 5:1, UV-active, stains dark brown with vanillin);

\([\alpha]^D_{25}\) = 136.3 (c 0.45, CHCl₃);

**\(^1\)H NMR (300 MHz, CDCl₃)** \( \delta \) 7.52 (dt, \( J = 5.6, 3.0 \) Hz, 1H), 6.16 (dd, \( J = 5.6, 2.1 \) Hz, 1H), 5.65 – 5.47 (m, 2H), 5.08 – 4.94 (m, 2H), 4.00 (d, \( J = 10.2 \) Hz, 1H), 3.13 – 3.03 (m, 1H), 2.25 (dd, \( J = 10.2, 2.7 \) Hz, 1H), 1.74 – 1.62 (m, 1H), 1.62 – 1.55 (m, 6H);

**\(^{13}\)C NMR (75 MHz, CDCl₃)** \( \delta \) 213.67, 167.15, 136.70, 135.24, 132.86, 124.00, 117.03, 79.14, 53.61, 49.03, 13.04, 10.71;

**IR (neat) (cm\(^{-1}\)) V\(_{\text{max}}\):** 3418, 2920, 1682, 1585, 1510, 1440, 1345, 1233, 1100, 1036, 912, 828, 734, 632, 536, 498;

**HRMS (m/z):** calcd for C₁₂H₁₆NaO₂ (M+Na)\(^+\) 215.1150, found 215.1150.
**Compound (+)-133m:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) vinylmagnesium bromide (0.80 M solution in THF, 1.4 mL, 1.14 mmol) and trans-4-methyl-2-pentenal (0.062 g, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 7:1 to 3:1) title compound was obtained in 64% yield (0.050 g).

**Physical state:** yellow oil;

**TLC:** \( R_f = 0.31 \) (hexanes/EtOAc 5:1, UV-active, stains dark brown with vanillin);

\[ [\alpha]_{D}^{25} = 147.4 \text{ (c 0.11, CHCl}_3) \];

\[^1^H\text{NMR (300 MHz, } d_6\text{-Acetone)} \delta 7.70 (dd, J = 5.7, 2.6 \text{ Hz, 1H}), 6.12 (dd, J = 5.7, 2.1 \text{ Hz, 1H}), 5.95 – 5.82 (m, 1H), 5.73 – 5.63 (m, 1H), 5.42 (ddd, J = 15.5, 6.5, 1.2 \text{ Hz, 1H}), 5.11 (ddt, J = 12.9, 10.2, 1.3 \text{ Hz, 2H}), 4.39 (dt, J = 9.3, 4.7 \text{ Hz, 1H}), 3.55 – 3.46 (m, 1H), 2.32 (dd, J = 6.1, 2.6 \text{ Hz, 1H}), 2.22 (dd, J = 13.5, 6.7 \text{ Hz, 1H}), 2.08 – 2.03 (m, 1H), 0.94 (dd, J = 6.8, 0.9 \text{ Hz, 6H});

\[^{13}C\text{NMR (75 MHz, } d_6\text{-Acetone)} \delta 210.03, 167.04, 139.83, 139.59, 134.07, 127.70, 115.95, 73.09, 58.21, 48.22, 31.50, 22.69, 22.64;

**IR (neat) (cm\(^{-1}\))** \( \nu_{\text{max}}:3474, 2959, 2872, 1694, 1637, 1587, 1467, 1346, 1182, 974, 917, 790, 631, 539, 498; \)

**HRMS \((m/z)\):** calcd for \( C_{13}H_{18}NaO_2(\text{M+Na})^+ \) 229.1199, found 229.1194.

**Compound (+)-133n:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) cyclohexylmagnesium bromide (0.80 M solution in THF, 1.4 mL, 1.14 mmol) and octanal (0.081 g, 0.098 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 10:1 to 5:1) title compound was obtained in 77% yield (0.085 g).

**Physical state:** pale green oil;

**TLC:** \( R_f = 0.52 \) (hexanes/EtOAc 5:1, UV-active, stains brown with vanillin);

\[ [\alpha]_{D}^{25} = 136.75 \text{ (c 0.25, CHCl}_3) \];

\[^1^H\text{NMR (600 MHz, } CDCl_3) \delta 7.70 (dd, J = 5.8, 2.6 \text{ Hz, 1H}), 6.14 (dd, J = 5.8, 1.9 \text{ Hz, 1H}), 3.63 (dd, J = 12.3, 6.4 \text{ Hz, 1H}), 2.59 (td, J = 4.4, 2.1 \text{ Hz, 1H}), 2.17 (dd, J = 7.7, 2.1 Hz, 1H), 1.81 – 1.74 (m, 2H), 1.72 – 1.65 (m, 3H), 1.55 (t, J = 5.5 Hz, 3H), 1.51 (s, 2H), 1.35 – 1.24 (m, 11H), 1.22 – 1.17 (m, 2H), 1.16 – 1.11 (m, 1H), 0.87 (d, J = 7.1 Hz, 3H);
D. Experimental Part

$^{13}$C NMR (151 MHz, CDCl$_3$) δ 212.69, 167.57, 133.33, 72.70, 53.51, 40.94, 35.58, 31.80, 31.55, 29.59, 29.53, 29.28, 26.50, 26.32, 26.30, 25.66, 22.63, 14.07;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3440, 2922, 2852, 1687, 1449, 1183, 1052, 891, 631, 534, 496;

HRMS ($m/z$): calcd for C$_{19}$H$_{32}$ NaO$_2$ (M+Na)$^+$ 315.2295, found 315.2286.

Compound (+)-133o: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) cyclohexylmagnesium bromide (0.8 M solution in THF, 1.4 mL, 1.14 mmol) and 4-methoxy benzaldehyde (0.086 g, 0.076 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 5:1 to 3:1) title compound was obtained in 72% yield (0.082 g).

Physical state: brown colored oil;

TLC: $R_f = 0.22$ (hexanes/ EtOAc 5:1, UV-active, stains dark brown with vanillin);

$[\alpha]_{D}^{25}$: 196.2 (c 0.48, CHCl$_3$);

$^1$H NMR (600 MHz, CDCl$_3$) δ 7.65 (dd, $J = 5.8$, 2.6 Hz, 1H), 7.30 – 7.27 (m, 2H), 6.89 – 6.85 (m, 2H), 6.15 (dd, $J = 5.8$, 1.9 Hz, 1H), 4.57 (d, $J = 9.3$ Hz, 1H), 4.46 (s, 1H), 3.81 (s, 3H), 2.43 (d, $J = 1.5$ Hz, 1H), 2.39 (dd, $J = 9.3$, 2.2 Hz, 1H), 1.56 (dd, $J = 14.0$, 11.2 Hz, 3H), 1.35 – 1.29 (m, 2H), 1.02 – 0.94 (m, 3H), 0.88 – 0.82 (m, 2H), 0.63 (td, $J = 11.9$, 3.2 Hz, 1H);

$^{13}$C NMR (151 MHz, CDCl$_3$) δ 212.95, 168.22, 159.45, 133.71, 132.68, 128.06, 128.06, 113, 68, 113.68, 75.23, 55.33, 55.03, 50.45, 39.92, 31.09, 28.95, 26.34, 26.21, 26.17;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3422, 2923, 2851, 1686, 1613, 1513, 1448, 1247, 1174, 1035, 632, 536, 495;

HRMS ($m/z$): calcd for C$_{19}$H$_{24}$ NaO$_3$ (M+Na)$^+$ 323.1618, found 323.1620.

Compound (+)-133p: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) cyclohexylmagnesium bromide (0.8 M solution in THF, 1.4 mL, 1.14 mmol) and trans-2-decenal (0.098 g, 0.11 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 5:1) title compound was obtained in 75% yield (0.090 g).

Physical state: yellow oil;

TLC: $R_f = 0.48$ (hexanes/ EtOAc 5:1, UV-active, stains dark brown with vanillin);

$[\alpha]_{D}^{25}$: 140.71 (c 0.73, CHCl$_3$);
D. Experimental Part

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.69 (dd, $J = 5.8$, 2.6 Hz, 1H), 6.13 (dd, $J = 5.8$, 1.9 Hz, 1H), 5.70 (dt, $J = 15.0$, 6.7 Hz, 1H), 5.52 – 5.39 (m, 1H), 4.05 (t, $J = 8.2$ Hz, 1H), 3.77 (d, $J = 9.8$ Hz, 1H), 2.54 (td, $J = 4.4$, 2.1 Hz, 1H), 2.23 (dd, $J = 8.6$, 2.0 Hz, 1H), 2.09 – 1.99 (m, 2H), 1.72 (dd, $J = 21.3$, 8.2 Hz, 3H), 1.63 (d, $J = 11.7$ Hz, 3H), 1.48 (dd, $J = 11.5$, 8.0, 3.5 Hz, 1H), 1.35 (dd, $J = 13.2$, 5.7 Hz, 2H), 1.24 (d, $J = 12.7$ Hz, 9H), 1.12 (ddd, $J = 12.6$, 9.6, 5.9 Hz, 3H), 0.87 (t, $J = 6.6$ Hz, 3H);

$^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 212.70, 168.98, 134.40, 132.49, 129.73, 74.21, 55.94, 44.80, 33.73, 32.14, 31.83, 31.80, 29.69, 29.45, 29.23, 29.21, 29.17, 29.05, 27.14, 22.63, 14.07;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3418, 2920, 2852, 1690, 1586, 1449, 970, 536;

HRMS ($m/z$): calcd for C$_{21}$H$_{34}$NaO$_2$ (M+Na)$^+$ 341.2451, found 341.2451.

**Compound (+)-133q**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) cyclohexylmagnesium bromide (0.8 M solution in THF, 1.4 mL, 1.14 mmol) and cyclohexanal (0.071 g, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 5:1) title compound was obtained in 70% yield (0.073 g).

**Physical state**: yellow oil;

TLC: $R_f = 0.42$ (hexanes/ EtOAc 5:1, UV-active, stains orange with vanillin);

$[\alpha]_{D}^{25}$: 186.2 (c 0.75, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.70 (dd, $J = 5.8$, 2.5 Hz, 1H), 6.13 (dd, $J = 5.8$, 2.0 Hz, 1H), 3.44 – 3.37 (m, 1H), 3.16 (s, 1H), 2.63 (td, $J = 4.6$, 2.2 Hz, 1H), 2.36 (dd, $J = 7.0$, 2.4 Hz, 1H), 1.81 – 1.65 (m, 10H), 1.30 (t, $J = 7.2$ Hz, 2H), 1.21 (dd, $J = 7.9$, 4.2 Hz, 5H), 1.02 (d, $J = 22.4$ Hz, 3H), 0.91 – 0.84 (m, 2H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 213.13, 167.39, 133.58, 77.37, 51.63, 50.04, 41.31, 40.73, 31.56, 30.53, 29.42, 27.17, 26.60, 26.47, 26.37, 26.37, 26.03;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3444, 2928, 2850, 1686, 1588, 1511, 1449, 1183, 1059, 576, 420;

HRMS ($m/z$): calcd for C$_{18}$H$_{28}$NaO$_2$ (M+Na)$^+$ 299.1982, found 299.1985.

**Compound (+)-133r**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) cyclohexylmagnesium bromide (0.8 M solution in THF, 1.4 mL, 1.14 mmol) and benzaldehyde (0.067 g, 0.064 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 5:1) title compound was obtained in 74% yield (0.076 g).

**Physical state**: yellow oil;
D. Experimental Part

**TLC:** $R_f = 0.45$ (hexanes/ EtOAc 5:1, UV-active, stains brown with vanillin);

$\left[\alpha\right]_D^{25} = 220.3$ (c 0.39, CHCl$_3$);

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.65 (dd, $J = 5.8$, 2.6 Hz, 1H), 7.38 – 7.36 (m, 2H), 7.36 – 7.32 (m, 2H), 7.31 – 7.28 (m, 1H), 6.16 (dd, $J = 5.8$, 2.0 Hz, 1H), 4.62 (d, $J = 9.3$ Hz, 1H), 4.55 (s, 1H), 2.46 (td, $J = 4.4$, 2.2 Hz, 1H), 2.40 (dd, $J = 9.3$, 2.3 Hz, 1H), 1.61 – 1.52 (m, 3H), 1.28 (dd, $J = 10.7$, 8.9 Hz, 2H), 1.02 – 0.91 (m, 3H), 0.86 – 0.80 (m, 1H), 0.79 – 0.73 (m, 1H), 0.60 (qd, $J = 12.2$, 3.6 Hz, 1H);

$^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 212.88, 168.23, 141.40, 132.67, 128.32, 128.32, 128.18, 126.88, 126.88, 75.67, 54.91, 50.34, 39.81, 31.02, 28.86, 26.31, 26.18, 26.15;

IR (neat) (cm$^{-1}$) $\nu_{max}$: 3451, 2922, 2850, 1683, 1585, 1449, 1192, 1045, 903, 803, 760, 703, 550;

HRMS (m/z): calcd for C$_{18}$H$_{22}$NaO$_2$ (M+Na)$^+$ 293.1512, found 293.1504.

**Compound (+)-133s:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) octylmagnesium bromide (1.0 M solution in Et$_2$O, 1.14 mL, 1.14 mmol) and benzaldehyde (0.067 g, 0.064 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 10:1 to 5:1) title compound was obtained in 30% yield (0.035 g).

**Physical state:** pale yellow oil;

**TLC:** $R_f = 0.44$ (hexanes/ EtOAc 5:1, UV-active, stains pink with vanillin);

$\left[\alpha\right]_D^{25} = 111.0$ (c 0.15, CHCl$_3$);

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.65 (dd, $J = 5.7$, 2.5 Hz, 1H), 7.38 (dd, $J = 8.2$, 1.3 Hz, 2H), 7.36 – 7.33 (m, 2H), 7.32 – 7.28 (m, 1H), 6.17 (dd, $J = 5.7$, 1.9 Hz, 1H), 4.74 (s, 1H), 4.64 (d, $J = 9.7$ Hz, 1H), 2.50 (ddd, $J = 7.4$, 5.0, 2.4 Hz, 1H), 2.27 (dd, $J = 9.7$, 2.4 Hz, 1H), 1.26 (dd, $J = 14.1$, 6.7 Hz, 2H), 1.22 – 1.12 (m, 4H), 1.07 – 0.92 (m, 8H), 0.87 (t, $J = 7.3$ Hz, 3H);

$^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 213.03, 169.22, 141.38, 132.27, 128.43, 128.43, 128.24, 126.88, 126.88, 75.43, 57.33, 44.53, 32.69, 31.76, 29.22, 29.10, 29.06, 26.19, 22.60, 14.07;

IR (neat) (cm$^{-1}$) $\nu_{max}$: 3441, 2923, 2853, 1686, 1585, 1511, 1455, 1200, 1044, 702, 632, 544, 494;

HRMS (m/z): calcd for C$_{20}$H$_{28}$NaO$_2$ (M+Na)$^+$ 323.1982, found 323.1980.

**Compound (+)-133t:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) octylmagnesium bromide (1.0 M solution in Et$_2$O, 1.14 mL, 1.14 mmol) and trans-2-decenal (0.098 g, 0.11 mL, 0.63 mmol)
D. Experimental Part

according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 5:1) title compound was obtained in 31% yield (0.041 g).

**Physical state:** yellow oil;

**TLC:** $R_f = 0.52$ (hexanes/ EtOAc 5:1, UV-active, stains brown with vanillin);

$[\alpha]_D^{25} 48.5 \text{ (c 0.18, CHCl}_3\text{)}$;

$^1\text{H NMR (600 MHz, CDCl}_3\text{)} \delta 7.69 (dd, J = 5.8, 2.6 \text{ Hz, 1H}), 6.13 (dd, J = 5.8, 1.9 \text{ Hz, 1H}), 5.72 – 5.67 (m, 1H), 5.48 – 5.43 (m, 1H), 4.05 (t, J = 8.2 \text{ Hz, 1H}), 2.54 (dt, J = 4.3, 2.1 \text{ Hz, 1H}), 2.23 (dd, J = 8.5, 2.0 \text{ Hz, 1H}), 2.06 – 2.02 (m, 2H), 1.78 – 1.73 (m, 2H), 1.69 – 1.62 (m, 4H), 1.47 (ddd, J = 15.4, 7.8, 3.8 \text{ Hz, 1H}), 1.40 – 1.31 (m, 3H), 1.28 (ddd, J = 14.7, 10.2, 5.6 \text{ Hz, 10H}), 1.22 – 1.18 (m, 2H), 1.18 – 1.09 (m, 3H), 0.88 (t, J = 7.0 \text{ Hz, 6H});

$^{13}\text{C NMR (151 MHz, CDCl}_3\text{)} \delta 212.54, 168.02, 134.39, 132.93, 129.87, 74.55, 53.39, 50.59, 40.69, 32.13, 31.77, 31.45, 29.75, 29.17, 29.15, 29.09, 26.48, 26.30, 26.29, 22.65, 22.65, 14.07, 14.07;

**IR (neat) (cm$^{-1}$)** $\nu_{\text{max}}$: 3430, 2922, 2852, 1692, 1464, 970, 909, 733, 631, 542, 498;

**HRMS (m/z):** calcld for C$^{23}$H$^{40}$ NaO$^2_2$ (M+Na)$^+$ 371.2921, found 371.2922.

**Compound (+)-133u:** The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) octylmagnesium bromide (1.0 M solution in Et$_2$O, 1.14 mL, 1.14 mmol) and octanal (0.081 g, 0.098 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 5:1) title compound was obtained in 34% yield (0.042 g).

**Physical state:** pale yellow oil;

**TLC:** $R_f = 0.58$ (hexanes/ EtOAc 5:1, UV-active, stains pale brown with vanillin);

$[\alpha]_D^{25} 52.6 \text{ (c 0.85, CHCl}_3\text{)}$;

$^1\text{H NMR (600 MHz, CDCl}_3\text{)} \delta 7.69 (dd, J = 5.7, 2.5 \text{ Hz, 1H}), 6.13 (dd, J = 5.7, 1.9 \text{ Hz, 1H}), 3.79 (s, 1H), 3.67 (t, J = 8.1 \text{ Hz, 1H}), 2.67 – 2.63 (m, 1H), 2.02 (dd, J = 8.4, 2.3 \text{ Hz, 1H}), 1.64 (ddd, J = 10.7, 9.3, 5.3 Hz, 1H), 1.59 – 1.52 (m, 3H), 1.51 – 1.46 (m, 1H), 1.43 – 1.37 (m, 2H), 1.34 – 1.25 (m, 19H), 0.88 (td, J = 7.0, 3.6 Hz, 6H);

$^{13}\text{C NMR (151 MHz, CDCl}_3\text{)} \delta 213.03, 168.58, 132.84, 129.87, 74.55, 53.39, 50.59, 40.69, 32.66, 29.56, 29.41, 29.28, 26.91, 25.39, 22.63, 22.65, 14.07, 14.07;

**IR (neat) (cm$^{-1}$)** $\nu_{\text{max}}$: 3438, 2924, 2854, 1690, 1465, 1314, 1262, 1186, 634, 537, 497;

**HRMS (m/z):** calcld for C$^{21}$H$^{38}$ NaO$^2_2$ (M+Na)$^+$ 345.2764, found 345.2764.
**Compound (+)-133v:** The title compound was prepared from (**R**)-125 (0.075 g, 0.38 mmol) octylmagnesium bromide (1.0 M solution in Et₂O, 1.14 mL, 1.14 mmol) and 4-nitro benzaldehyde (0.096 g, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) title compound was obtained in 38% yield (0.050 g).

**Physical state:** pale yellow oil;

**TLC:** $R_f = 0.23$ (hexanes/ EtOAc 5:1, UV-active, stains pale brown with vanillin);

$[\alpha]_{D}^{25} = 126.6$ (c 0.85, CHCl₃);

$^1$H NMR (600 MHz, CDCl₃) δ 8.25 – 8.23 (m, 2H), 7.68 (dd, $J = 5.7$, 2.5 Hz, 1H), 7.60 – 7.58 (m, 2H), 6.20 (dd, $J = 5.7$, 1.9 Hz, 1H), 4.84 (s, 1H), 4.81 (d, $J = 9.5$ Hz, 1H), 2.52 (ddd, $J = 7.4$, 5.0, 2.4 Hz, 1H), 2.26 (dd, $J = 9.5$, 2.5 Hz, 1H), 1.27 – 1.23 (m, 2H), 1.20 – 1.12 (m, 4H), 1.03 (dd, $J = 13.4$, 7.7 Hz, 5H), 0.99 – 0.92 (m, 3H), 0.86 (t, $J = 7.3$ Hz, 3H);

$^{13}$C NMR (151 MHz, CDCl₃) δ 211.95, 169.06, 148.56, 147.77, 132.44, 127.79, 127.79, 123.71, 123.71, 74.47, 56.87, 44.17, 32.90, 31.71, 29.26, 29.16, 29.05, 26.31, 22.58, 14.03;

IR (neat) (cm⁻¹) $\nu_{max}$: 3398, 2926, 2854, 1689, 1524, 1347, 1191, 856, 756, 536, 494;

HRMS (m/z): calcd for C$_{21}$H$_{28}$NO$_6$ (M+HCOO) -, 390.1922, found 390.1922.

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**Compound (+)-133w:** The title compound was prepared from (**R**)-125 (0.075 g, 0.38 mmol) octylmagnesium bromide (1.0 M solution in Et₂O, 1.14 mL, 1.14 mmol) and isobutanal (0.046 g, 0.058 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) title compound was obtained in 32% yield (0.033 g).

**Physical state:** pale brown oil;

**TLC:** $R_f = 0.54$ (hexanes/ EtOAc 5:1, UV-active, stains pale brown with vanillin);

$[\alpha]_{D}^{25} = 103.2$ (c 0.65, CHCl₃);

$^1$H NMR (300 MHz, CDCl₃) δ 7.70 (dd, $J = 5.7$, 2.4 Hz, 1H), 6.14 (dd, $J = 5.7$, 1.9 Hz, 1H), 3.80 (s, 1H), 3.47 (ddd, $J = 8.6$, 3.2, 2.4 Hz, 1H), 2.70 – 2.61 (m, 1H), 2.13 (dd, $J = 8.6$, 2.4 Hz, 1H), 1.86 (dt, $J = 9.4$, 6.4, 2.9 Hz, 1H), 1.67 (s, 1H), 1.27 (s, 13H), 1.05 (d, $J = 6.8$ Hz, 3H), 0.96 (d, $J = 6.7$ Hz, 3H), 0.91 – 0.86 (m, 3H);

$^{13}$C NMR (75 MHz, CDCl₃) δ 213.72, 168.67, 132.95, 76.86, 53.21, 45.32, 33.37, 31.83, 31.44, 29.71, 29.43, 29.20, 26.70, 22.64, 20.33, 15.58, 14.09;
D. Experimental Part

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3486, 2925, 2856, 1686, 1512, 1465, 1236, 1042, 792, 632, 536, 501;

HRMS ($m/z$): calcd for $\text{C}_{17}\text{H}_{30}\text{NaO}_2\{(\text{M+Na})^+\}$, 289.2138, found 289.2136.

**Compound (+)-133x**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) octylmagnesium bromide (1.0 M solution in Et$_2$O, 1.14 mL, 1.14 mmol) and 4-methoxy benzaldehyde (0.086 g, 0.076 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/ EtOAc 7:1 to 3:1) title compound was obtained in 36% yield (0.045 g).

**Physical state**: pale brown oil;

**TLC**: $R_f = 0.25$ (hexanes/ EtOAc 5:1, UV-active, stains deep brown with vanillin);

[α]$_D^{25}$: 114.2 (c 0.65, CHCl$_3$);

$^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 7.65 (dd, $J = 5.7, 2.5$ Hz, 1H), 7.31 – 7.28 (m, 2H), 6.89 – 6.86 (m, 2H), 6.15 (dd, $J = 5.7, 1.9$ Hz, 1H), 4.69 (s, 1H), 4.58 (d, $J = 9.7$ Hz, 1H), 3.80 (s, 3H), 2.90 – 2.25 (m, 1H), 2.26 (dd, $J = 9.7, 2.4$ Hz, 1H), 1.26 (dd, $J = 14.5, 7.2$ Hz, 2H), 1.21 – 1.14 (m, 4H), 1.09 – 0.95 (m, 8H), 0.87 (t, $J = 7.3$ Hz, 3H);

$^{13}$C NMR (151 MHz, CDCl$_3$) $\delta$ 213.12, 169.24, 159.48, 133.69, 132.26, 128.04, 128.04, 113.75, 113.75, 113.75, 74.96, 57.43, 55.24, 44.59, 32.74, 31.77, 29.25, 29.17, 29.10, 26.23, 22.60, 14.06;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3463, 2926, 2854, 1686, 1613, 1513, 1464, 1303, 1246, 1173, 1036, 834, 632, 539, 497;

HRMS ($m/z$): calcd for $\text{C}_{21}\text{H}_{30}\text{NaO}_3\{(\text{M+Na})^+\}$, 353.2087, found 353.209.
D. Experimental Part

Table 11. Coupling constants $^{3}J_{Ha-Hb}$ of (+)-133.

![Diagram of compound (+)-133]

<table>
<thead>
<tr>
<th>Compound</th>
<th>$^{3}J_{Ha-Hb}$</th>
<th>$\delta_{ppm}^{a}$</th>
<th>Compound</th>
<th>$^{3}J_{Ha-Hb}$</th>
<th>$\delta_{ppm}^{a}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)-133a</td>
<td>8.21</td>
<td>2.44</td>
<td>(+)-133m</td>
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<td>2.26</td>
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<td>(+)-133b</td>
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<td>(+)-133n</td>
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<td>2.17</td>
</tr>
<tr>
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<td>2.5</td>
<td>(+)-133o</td>
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</tr>
<tr>
<td>(+)-133d</td>
<td>9.46</td>
<td>2.66</td>
<td>(+)-133p</td>
<td>8.6</td>
<td>2.23</td>
</tr>
<tr>
<td>(+)-133e</td>
<td>9.5</td>
<td>2.66</td>
<td>(+)-133q</td>
<td>7.0</td>
<td>2.36</td>
</tr>
<tr>
<td>(+)-133f</td>
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<td>2.36</td>
<td>(+)-133r</td>
<td>9.3</td>
<td>2.40</td>
</tr>
<tr>
<td>(+)-133g</td>
<td>10.1</td>
<td>2.31</td>
<td>(+)-133s</td>
<td>9.7</td>
<td>2.27</td>
</tr>
<tr>
<td>(+)-133h</td>
<td>8.4</td>
<td>2.33</td>
<td>(+)-133t</td>
<td>8.5</td>
<td>2.23</td>
</tr>
<tr>
<td>(+)-133i</td>
<td>9.2</td>
<td>2.53</td>
<td>(+)-133u</td>
<td>8.4</td>
<td>2.02</td>
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<td>(+)-133j</td>
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<td>(+)-133v</td>
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<td>2.26</td>
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<td>(+)-133w</td>
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<tr>
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<td>10.2</td>
<td>2.25</td>
<td>(+)-133x</td>
<td>9.7</td>
<td>2.26</td>
</tr>
</tbody>
</table>

Kobayashi et al.\textsuperscript{15} had established that for compound (+)-133 (anti-diols) $^{3}J_{Ha-Hb}$ is in the range of 8.4 to 9.7 Hz, while for the corresponding syn-diols $^{3}J_{Ha-Hb}$ is around 3 Hz.

All (-)-133 derivatives were synthesized from (S)-134 by using previous one pot conditions according to general procedure A.
D. Experimental Part

**Note**: Characterization: Spectral data of (-)-133 a, b and c were matched with (+)-133 d, e and c.

$[\alpha]_D^{25}$: (-)-133a = -232.0 (c 0.53, CHCl$_3$), (-)-133b = -228.0 (c 0.15, CHCl$_3$), (-)-133c = -202.0 (c 0.56, CHCl$_3$).

**Note**: Characterization: Spectral data of (-)-133 d, e, f and g were matched with (+)-133 f, g, h and i.

$[\alpha]_D^{25}$: (-)-133d = -230.0 (c 0.14, CHCl$_3$), (-)-133b = -222.0 (c 0.37, CHCl$_3$), (-)-133c = -110.0 (c 0.71, CHCl$_3$), (-)-133g = n.d.

**Note**: Characterization: Spectral data of (-)-133 h, i and j were matched with (+)-133 k, l and m.

$[\alpha]_D^{25}$: (-)-133h = -130.0 (c 0.14, CHCl$_3$), (-)-133i = n.d, (-)-133j = -141.0 (c 0.14, CHCl$_3$).

**Note**: Characterization: Spectral data of (-)-133 k, l and m were matched with (+)-133 n, o and p.

$[\alpha]_D^{25}$: (-)-133k = -127.0 (c 0.39, CHCl$_3$), (-)-133l = -188.0 (c 0.48, CHCl$_3$), (-)-133m = -129.0 (c 0.73, CHCl$_3$).
D. Experimental Part

Note

Characterization: Spectral data of of (-)-133n, o, p, q and r were matched with (+)-133 t, u, v, x and s.

\[ [\alpha]_D^{25} \] (-)-133n = -39.0 (c 0.19, CHCl₃), (-)-133o, p, q and r = n.d.

4. Synthesis and characterization of natural products

**Compound 2**: The title compound was prepared from (R)-125 (0.075 g, 0.38 mmol) n-butyl magnesiumbromide (0.90 M solution in THF, 1.24 mL, 1.14 mmol) and heptanal (0.068 g, 0.084 mL, 0.63 mmol) according to the general procedure A. After purification on silica (hexanes/EtOAc 10:1 to 5:1) 2 was obtained in 38% yield (0.037 g).

**Physical state**: pale yellow oil;

**TLC**: Rf = 0.4 (hexanes/EtOAc 5:1, UV-active, stains pale brown with vanillin);

\[ [\alpha]_D^{25} \] = 48.6 (c 0.18, CHCl₃);

**1H NMR (300 MHz, CDCl₃)** δ 7.70 (dd, J = 5.7, 2.5 Hz, 1H), 6.14 (dd, J = 5.7, 1.9 Hz, 1H), 3.87 (s, 1H), 3.68 (dd, J = 9.3, 4.8 Hz, 1H), 2.65 (ddd, J = 7.9, 5.6, 2.3 Hz, 1H), 2.04 – 2.00 (m, 1H), 1.67 – 1.62 (m, 1H), 1.58 – 1.47 (m, 4H), 1.38 – 1.24 (m, 11H), 0.93 – 0.85 (m, 6H).

**13C NMR (75 MHz, CDCl₃)** δ 213.20, 168.76, 132.86, 72.32, 55.94, 44.98, 35.59, 33.55, 31.85, 29.29, 29.09, 25.37, 24.79, 22.64, 14.11, 13.96;

**IR (neat) (cm⁻¹)**: 3373, 2954, 2925, 2857, 1686, 1511, 1466, 1357, 1234, 1100, 1038, 827, 733, 529, 489;

**HRMS (m/z)**: calcd for C₁₆H₂₈NO₂ (M+Na)⁺ 275.1982, found 275.1982.

**Compound 3** [(-)-TEI-9826]: To a stirred solution of CuCN (0.202 g, 2.25 mmol, 3.0 equiv) and anhydrous LiCl (0.190 g, 4.5 mmol, 6.0 equiv) in anhydrous THF (10 mL) was added octyl magnesiumbromide (0.9 M in Et₂O, 2.5 mL, 2.25 mmol, 3.0 equiv) dropwise at −40 °C under stirring. After the addition was completed, the reaction mixture was cooled to −78 °C. To this mixture was added a solution of (S)-134 (0.153 g, 0.75 mmol, 1.0 equiv) in
anhydrous THF (6 mL) at −78 °C. After 4 min of stirring at −78 °C, methyl-6-formylhexanoate (0.199 g, 1.26 mmol, 1.68 equiv) was added. After the reaction was completed (ca. 5 min, monitored by TLC) the mixture was quenched by adding NH₄Claq (5 mL) and allowed to warm to room temperature. The aqueous layer was removed with a pipette and the crude was dried under high vacuum. To a solution of the residue in DCM (10 mL) were added 4-(dimethylamino)-pyridine (0.486 g, 3.98 mmol) and methane sulfonyl chloride (0.16 mL, 1.98 mmol) at ambient temperature. After stirring for 15 h, aqueous HCl solution was added. The layers were separated and the aqueous layer was extracted with EtOAc (3x 15 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc 5:1)) to give (−)-TEI-9826 3 was obtained in 48% yield (0.12 g, 4 steps in one pot).

**Physical state:** yellow oil;

**TLC:** Rᵢ = 0.36 (hexanes/EtOAc 5:1, UV-active, stains brown with vanillin);

[α]D²⁵ᵣ = −129.4 (c 0.43, CHCl₃); lit.¹ [α]D²⁵ᵣ = −121 (c=0.58, CHCl₃), lit.³ [α]D²⁵ᵣ = 119 (c=1.10, CHCl₃, ent-3);

**¹H NMR (400 MHz, CDCl₃)** δ 7.55 – 7.49 (m, 1H), 6.51 (t, J = 7.7 Hz, 1H), 6.31 (dd, J = 6.0, 1.8 Hz, 1H), 3.66 (s, 3H), 3.49 – 3.42 (m, 1H), 2.30 (t, J = 7.5 Hz, 2H), 2.28 – 2.15 (m, 2H), 1.81 (dd, J = 9.7, 4.0 Hz, 1H), 1.65 (dd, J = 15.5, 7.6 Hz, 2H), 1.55 – 1.47 (m, 3H), 1.41 – 1.34 (m, 2H), 1.30 – 1.21 (m, 12H), 0.87 (t, J = 6.9 Hz, 3H).

**¹³C NMR (100 MHz, CDCl₃)** δ 197.2, 174.2, 162.2, 138.3, 135.4, 135.0, 51.7, 43.5, 34.1, 32.7, 32.0, 30.0, 29.6, 29.4, 29.1, 28.5, 26.1, 25.0, 22.8, 14.3;

**IR (neat) (cm⁻¹)** ν̃max: 3373, 2954, 2925, 2857, 1686, 1511, 1466, 1357, 1234, 1100, 1038, 827, 733, 529, 489;

**HRMS (m/z):** calcd for C₂₁H₃₄O₃ (M⁺) 334.2508, found 334.2504.

**Compound 141:** To a stirred solution of CuCN (0.33 g, 3.67 mmol, 3.0 equiv) and anhydrous LiCl (0.310 g, 7.35 mmol, 6.0 equiv) in anhydrous THF (13 mL) was added n-butyl magnesiumbromide (0.91 M in Et₂O, 4.0 mL, 3.67 mmol, 3.0 equiv) dropwise at −40 °C under stirring. After the addition was completed, the reaction mixture was cooled to −78 °C. To this mixture was added a solution of (S)-134 (0.25 g, 1.225 mmol, 1.0 equiv) in anhydrous THF (2.5 mL) at −78 °C. After 4 min of stirring at −78 °C, methyl-6-formylhexanoate (0.32 g, 2.06 mmol, 1.68 equiv) was added. After the reaction was completed (ca. 5 min, monitored by TLC) the mixture was quenched by adding NH₄Claq (10 mL) and allowed to warm to room temperature. The aqueous layer was removed with a pipette and the crude was dried under high vacuum. To a solution of the residue in DCM (18 mL)
D. Experimental Part

were added 4-(dimethylamino)-pyridine (0.79 g, 6.90 mmol) and methane sulfonylchloride (0.25 mL, 3.45 mmol) at ambient temperature. After stirring for 15 h, aqueous HCl solution was added. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic extracts were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc 5:1) to give 141 in 42% yield (0.145 g, 4 steps in one pot).

**Physical state:** yellow oil;

**TLC:** Rₜ = 0.36 (hexanes/EtOAc 5:1, UV-active, stains brown with vanillin);

[α]₂⁵° = −121.0 (c 0.5, CHCl₃);

**¹H NMR (300 MHz, CDCl₃)** δ 7.48 (ddd, J = 6.0, 2.6, 0.9 Hz, 1H), 6.46 (t, J = 7.7 Hz, 1H), 6.26 (dd, J = 6.0, 1.9 Hz, 1H), 3.60 (s, 3H), 3.44–3.37 (m, 1H), 2.28–2.16 (m, 4H), 1.77 (ddd, J = 12.9, 5.8, 3.3 Hz, 1H), 1.64–1.54 (m, 2H), 1.51–1.41 (m, 3H), 1.36–1.17 (m, 6H), 0.84–0.79 (m, 3H);

**¹³C NMR (75 MHz, CDCl₃)** δ 197.1, 174.1, 162.1, 138.1, 138.4, 134.5, 134.8, 134.9, 134.1, 32.1, 28.9, 28.9, 28.3, 28.0, 24.7, 22.8, 13.95;

**IR (neat)** (cm⁻¹) νmax: 3373, 2954, 2925, 2857, 1686, 1511, 1466, 1357, 1234, 1100, 1038, 827, 733, 529, 489;

**HRMS (m/z):** calcd for C₁₇H₂₆O₃ (M)⁺ 278.1882, found 278.1880.

**Compound 143:** To a 25 mL 3-neck round bottom flask equipped with a stir bar and septum was added Cp₂Zr(H)Cl (0.39 g, 1.5 mmol) followed by 4 mL of THF and 1-octyne (0.225 mL, 1.5 mmol). Thw two-phase mixture shielded from light and allowed to stir for 30 min at room temperature. This mixture was the cooled to -78 °C, and at this temperature was added MeLi (1.6 M in Et₂O, 0.94 mL, 1.5 mmol), dropwise over 1 min. At the same time, to another round bottom flask was added CuCN (0.0068g, 0.075 mmol), followed by 1 mL of THF. The mixture was cooled to -78 °C, and Me₂Zn (2.0 M in heptanes, 0.39 mL, 0.75 mmol) was added dropwise, followed quickly by dropwise addition of MeLi (0.58 mL, 1.1 mmol). After 5 min this three phase slurry was placed in an ice-bath for 10 min. This solution was then cooled back to -78 °C and the solution containing methyl vinyl zirconocene, still at -78 °C was transferred to the flask, containing the zincate/catalytic cuprate mixture. After 5 min of stirring (S)-134 (0.153 g, 0.75 mmol, 1.0 equiv) in 1.0 mL THF was added during 5 min. After 5 min of additional stirring methyl-6-formylhexanoate (0.2 g, 1.26 mmol) was added. After 5 min stirring the mixture was quenched with aq. NH₄Cl (5 mL). The layers were
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separated and the aqueous layer was extracted with EtOAc (2x10 mL). The combined extracts were washed with brine (10 mL), dried, filtered and concentrated to give crude oil, which was directly subjected to the next step.

To a solution of the residue in DCM (12 mL) were added 4-(dimethylamino)-pyridine (0.52 g, 4.29 mmol) and methane sulfonylchloride (0.16 mL, 2.15 mmol) at ambient temperature. After stirring for 15 h, aqueous HCl solution was added. The layers were separated and the aqueous layer was extracted with EtOAc (3x 20 mL). The combined organic extracts were dried over Na$_2$SO$_4$, filtered and concentrated under reduced pressure. The residue was purified by column chromatography (hexanes/EtOAc 5:1) to give 143 in 45% yield (0.113 g).

Physical state: yellow oil;
TLC: $R_f = 0.63$ (hexanes/EtOAc 3:1, UV-active, stains pale brown with vanillin);
$[\alpha]_D^{25} = -110.0$ (c 0.5, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.34 (ddd, $J = 5.8, 2.6, 0.7$ Hz, 1H), 6.58 (t, $J = 7.7$ Hz, 1H), 6.30 (dd, $J = 5.9, 1.9$ Hz, 1H), 5.63 (dd, $J = 14.7, 7.3$ Hz, 1H), 5.15 (ddt, $J = 15.3, 8.5, 1.3$ Hz, 1H), 3.96 (d, $J = 8.5$ Hz, 1H), 3.65 (s, 3H), 2.24 (ddd, $J = 14.8, 13.8, 7.4$ Hz, 4H), 2.01 (dd, $J = 12.2, 5.7$ Hz, 2H), 1.60 (dd, $J = 15.1, 7.5$ Hz, 2H), 1.49 – 1.40 (m, 2H), 1.36 – 1.23 (m, 10H), 0.87 (dd, $J = 7.8, 4.7$ Hz, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 196.8, 174.1, 161.1, 137.2, 136.9, 134.4, 133.8, 127.4, 51.6, 47.3, 33.9, 32.4, 31.7, 29.3, 28.9, 28.8, 28.6, 28.2, 24.7, 22.6, 14.1;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3373, 2954, 2925, 2857, 1686, 1511, 1357, 1110, 1038, 827, 733, 529;

HRMS (m/z): calcd for C$_{21}$H$_{32}$O$_3$ (M)$^+$ 332.2351, found 332.2350.

**Compound 146:** To a stirred solution of CuCN (0.503 g, 5.61 mmol, 3.0 equiv) and anhydrous LiCl (0.472 g, 11.2 mmol, 6.0 equiv) in anhydrous THF (20 mL) was added iso propenyl magnesium bromide (0.83 M solution in THF, 5.61 mmol, 6.85 mL, 3.0 equiv) dropwise at $-40^\circ$C under stirring. After the addition was completed, the reaction mixture was cooled to $-78^\circ$C. To this mixture was added a solution of (R)-125 (0.37 g, 1.87 mmol, 1.0 equiv) in anhydrous THF (5 mL) at $-78^\circ$C. After 4 min of stirring at $-78^\circ$C, 1-148 (0.471 g, 0.374 mmol, 2.0 equiv) was added. After the reaction was completed (ca. 5 min) the mixture was quenched by adding NH$_4$Cl$_{aq}$ (30 mL). Then the mixture was allowed to warm to room temperature. The layers were separated, and the aqueous layer was extracted with Et$_2$O (2x15 mL). The combined organic extracts were dried over Na$_2$SO$_4$, filtered and
D. Experimental Part

the solvent was removed under reduced pressure. After purification on silica (hexanes/EtOAc 7:1) 146 was obtained in 68% yield (0.316 g).

**Physical state:** brown color oil;

**TLC:** $R_f = 0.62$ (hexanes/EtOAc 5:1, UV-active, stains dark brown with vanillin);

$\left[\alpha\right]_{D}^{25} = 100.7$ (c 0.42, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.60 – 7.49 (dd, $J = 5.6$, 2.6 Hz, 1H), 6.21 (dd, $J = 5.6$, 2.1 Hz, 1H), 5.81 (ddt, $J = 17.1$, 10.0, 7.1 Hz, 1H), 5.04 (ddd, $J = 17.1$, 3.5, 1.6 Hz, 1H), 4.99 – 4.90 (m, 3H), 4.00 (t, $J = 1.4$ Hz, 1H), 3.93 – 3.83 (m, 1H), 3.24 (dd, $J = 4.8$, 2.4 Hz, 1H), 2.44 (dd, $J = 9.2$, 2.7 Hz, 1H), 2.25 – 2.14 (m, 2H), 1.88 (ddt, $J = 13.8$, 6.9, 4.8 Hz, 1H), 1.66 (d, $J = 0.8$ Hz, 3H), 1.51 (t, $J = 5.5$ Hz, 1H), 0.93 (dt, $J = 13.2$, 6.6 Hz, 6H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 213.58, 167.62, 142.98, 139.01, 133.37, 115.46, 114.51, 72.76, 53.58, 51.39, 46.46, 30.96, 29.02, 20.87, 19.38, 18.97;

IR (neat) (cm$^{-1}$) $v$ max: 3473, 2957, 2928, 1743, 1686, 1589, 1414, 1369, 1279, 1177, 1056, 901, 795, 658, 624, 531, 496;

HRMS (m/z): calcd for C$_{16}$H$_{24}$NaO$_2$ (M+Na)$^+$ 271.1669, found 271.1669.

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**Compound 157:** A flask containing 146 (0.39 g, 1.57 mmol) was outfitted with a reflux condenser and evacuated and backfilled with dry nitrogen. Deoxygenated DCM (85 mL) was added, and the solution was heated to reflux (44 °C). A solution of Grubbs-II catalyst (0.09 g, 0.11 mmol) in deoxygenated DCM (5 mL) was added to the reaction mixture. The light brown reaction mixture was refluxed (44 °C) for 1.5 h and was then cooled to room temperature. The solvent was removed under reduced pressure. After purification on silica (hexanes/EtOAc 5:1 to 3:1) 157 was obtained in 94% yield (0.325 g).

**Physical state:** pale brown color oil;

**TLC:** $R_f = 0.53$ (hexanes/EtOAc 5:1, UV-active, stains dark brown with vanillin);

$\left[\alpha\right]_{D}^{25} = -25.6$ (c 0.25, CHCl$_3$);

$^1$H NMR (300 MHz, Acetone-$d_6$) $\delta$ 8.03 – 7.90 (dd, $J = 5.7$, 2.6 Hz, 1H), 6.12 (dd, $J = 5.9$, 2.8 Hz, 1H), 5.57 – 5.49 (m, 1H), 4.23 – 4.15 (m, 1H), 3.60 (dd, $J = 10.1$, 8.8 Hz, 1H), 2.54 (dd, $J = 9.7$, 5.3 Hz, 1H), 2.04 (dt, $J = 8.7$, 4.3 Hz, 1H), 1.96 (t, $J = 4.1$ Hz, 1H), 1.87 (dd, $J = 2.3$, 0.9 Hz, 3H), 1.81 – 1.62 (m, 2H), 1.57 – 1.48 (m, 1H), 1.02 (d, $J = 6.6$ Hz, 3H), 0.93 (d, $J = 5.8$ Hz, 3H).
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13C NMR (75 MHz, Acetone-d6) δ 212.17, 164.59, 136.88, 132.72, 127.66, 49.59, 49.54, 47.10, 29.56, 27.87, 26.58, 22.16, 21.68, 21.42;
IR (neat) (cm⁻¹) ν max: 3429, 2957, 2873, 1682, 1539, 1446, 1368, 1271, 1068, 976, 737, 632, 540, 497;
HRMS (m/z): calcd for C14H20NaO2 (M+Na)⁺ 243.1463, found 243.1463

Compound 145: The 157 (0.21 g, 0.95 mmol, 1.0 equiv) was dissolved in CHCl₃ (7.5 mL, filtered through basic alumina) along with diphenylsilane (0.29 ml, 1.62 mmol, 1.7 equiv) and zinc chloride (0.067 g, 0.49 mmol, 0.52 equiv). Pd (PPh₃)₄ (0.015 g, 0.012 mmol, 0.013 equiv) was added and the mixture was stirred (inert atmosphere was not required) at room temperature for 20 min. The solvent was removed under reduced pressure and the crude was purified by column chromatography (hexanes/EtOAc 5:1) 145 was obtained in 80% yield (0.170 g).
Physical state: white color solid;
TLC: Rf = 0.56 (hexanes/EtOAc 5:1, stains brown with vanillin);
[α]D²⁵ = –63.5 (c 0.1, CHCl₃);
M.P.: 74 °C;
¹H NMR (300 MHz, CDCl₃): δ 5.58 (dd, J = 8.8, 1.3 Hz, 1H), 4.13 – 4.01 (m, 1H), 3.33 (t, J = 1.4 Hz, 1H), 2.57 (d, J = 11.6 Hz, 1H), 2.46 – 2.26 (m, 4H), 2.25 – 2.11 (m, 1H), 1.89 (dd, J = 17.4, 8.8 Hz, 1H), 1.71 (d, J = 7.0 Hz, 3H), 1.66 (ddd, J = 11.3, 7.7, 2.4 Hz, 1H), 1.61 – 1.49 (m, 1H), 1.29 (td, J = 10.1, 4.3 Hz, 1H), 1.00 (d, J = 6.6 Hz, 3H);
¹³C NMR (75 MHz, CDCl₃): δ 223.93, 137.29, 127.81, 71.21, 59.00, 49.21, 42.26, 37.85, 28.58, 26.93, 24.92, 21.98, 21.47, 20.99;
IR (neat) (cm⁻¹) ν max: 3525, 2964, 2870, 1721, 1443, 1408, 1284, 1241, 1159, 1064, 1033, 975, 864, 796, 636, 522;
HRMS (m/z): calcd for C₁₄H₂₂NaO₂ (M+Na)⁺ 245.1512, found 245.1513.

Compound 158: To a solution of 145 (0.044 g, 0.2 mmol) in anhydrous DMF (0.3 mL) was added imidazole (0.078 g, 1.15 mmol), DMAP (0.008 g, 0.06 mmol) and triethyl chlorosilane (1.46 mL, 0.83 mmol). The clear reaction mixture was stirred at room temperature for 1 h, then directly subjected to column chromatography (hexanes/EtOAc 10:1) without further work-up to afford 158 in 88% yield (0.059 g).
D. Experimental Part

**Physical state:** yellow color oil;

**TLC:** $R_f = 0.79$ (hexanes/EtOAc 7:1, stains brown with vanillin staining);

$[\alpha]^{25}_D = -48.7$ (c 0.14, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.54 (dd, $J = 8.1$, 1.3 Hz, 1H), 4.20 (dt, $J = 6.6$, 2.0 Hz, 1H), 2.62 (d, $J = 12.7$ Hz, 1H), 2.51 – 2.39 (m, 1H), 2.37 – 2.16 (m, 3H), 2.13 – 1.97 (m, 1H), 1.86 (dd, $J = 17.8$, 8.1 Hz, 1H), 1.73 (d, $J = 1.2$ Hz, 3H), 1.61 – 1.50 (m, 2H), 1.25 (t, $J = 7.4$ Hz, 1H), 0.97 – 0.94 (m, 6H), 0.92 – 0.86 (m, 9H), 0.74 – 0.59 (m, 6H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 219.56, 136.09, 127.75, 70.98, 62.55, 49.66, 43.01, 37.03, 28.71, 26.19, 25.35, 22.21, 21.38, 21.25, 7.31, 5.66;

**IR (neat) (cm$^{-1}$) $\nu_{max}$:** 2954, 2874, 1743, 1457, 1243, 1075, 999, 830, 738, 632, 534, 501;

**HRMS (m/z):** calcd for C$_{20}$H$_{37}$O$_2$Si (M+H)$^+$ 337.2485, found 337.2488.

**Compound 144 [(−)-4β,6β-dihydroxy-1α,5β(H)-guai-9-ene]:** CeCl$_3$ 7H$_2$O (0.146 g, 0.39 mmol) was placed in 25 mL schlenck flask and, heated at 140 oC in vacuo (0.01 mmHg) for 3.5 h, and then cooled. Dry THF (1.7 mL) was added while stirring under N$_2$, and the solution was stirred for 2 h at room temperature under N$_2$ atmosphere. The resulting suspension was cooled to −78 oC, and MeLi (1.6 M solution in Et$_2$O, 0.24 mL, 0.17 mmol) was added. The resulting pale brown color mixture was stirred for 30 min, and then 158 (0.06 g, 0.18 mmol) in THF (1 mL) was added dropwise, and the mixture was stirred for a further 4 h at −78 oC. The reaction mixture was treated with a NH$_4$Cl aq (15 mL), filtered through Celite and extracted with EtOAc (2x25 mL). The combined organic extracts were dried over Na$_2$SO$_4$ and evaporated under reduced pressure to give the crude product. Which was used for the next step without further purification.

Ta a solution of above crude in dry THF (2 mL) was added TABF (1 M solution in THF, 0.17 mL) at 0 oC during 5 min. The reaction mixture was stirred at room temperature until the starting material disappeared (ca. 30 min). The solvent was removed under reduced pressure and the residue was purified on silica (hexanes/EtOAc 10:1 to 3:1) to give rise to 144 in 76% yield (0.032 g, over 2 steps).

**Physical state:** pale yellow oil;

**TLC:** $R_f = 0.13$ (hexanes/EtOAc 2:1, stains deep blue with vanillin);

$[\alpha]^{25}_D = -9.5$ (c 0.44, CHCl$_3$); lit.$^7$ $[\alpha]^{25}_D = 10.5$ (c 0.60, CHCl$_3$) for natural (−)-4β,6β-dihydroxy-1α,5β(H)-guai-9-ene;
D. Experimental Part

\(^1\)H NMR (600 MHz, CDCl\(_3\)) \(\delta\) 5.57 – 5.43 (m, 1H), 4.21 – 4.06 (m, 1H), 2.36 (d, \(J = 16.7\) Hz, 2H), 2.34 – 2.19 (m, 2H), 2.08 (dd, \(J = 12.0, 9.5\) Hz, 1H), 1.89 – 1.68 (m, 5H), 1.66 (s, 3H), 1.64 – 1.54 (m, 1H), 1.31 (s, 3H), 1.29 – 1.20 (m, 1H), 1.02 (d, \(J = 6.6\) Hz, 3H), 0.98 – 0.93 (m, 3H);

\(^{13}\)C NMR (151 MHz, CDCl\(_3\)) \(\delta\) 139.22, 126.18, 81.12, 72.42, 57.46, 50.49, 42.32, 39.90, 28.45, 26.59, 24.33, 24.17, 23.11, 21.41, 21.36;

IR (neat) (cm\(^{-1}\)) \(\tilde{v}_{\text{max}}\): 3420, 3310, 2957, 2936, 2868, 1475, 1447, 1387, 1367, 1340, 1150, 1126, 1025, 963, 940, 573, 543;

HRMS (m/z): calcd for C\(_{15}\)H\(_{26}\)NaO\(_2\) (M+Na)\(^+\) 261.1825, found 261.1825.

\((-\text{-Teuclatriol 72 and \((-\text{-10-epi teuclatriol 159: 144}}\)

(0.056 g, 0.24 mmol) and cobalt acetylacetonate (0.012 g, 0.047 mmol) were dissolved in THF (2 mL). Oxygen was bubbled through the solution for 1 h at room temperature, upon which PhSiH\(_3\) (0.15 mL, 0.94 mmol)\(^8\) was added. The resulting reaction mixture was stirred at room temperature for 14 h in the presence of oxygen. The mixture was diluted with EtOAc, the solvent was evaporated and the crude was purified by column chromatography (hexanes/EtOAc 3:1 to 1:1) to give rise to \textbf{72} in 52% yield (0.032 g) and \textbf{159} in 20% yield (0.012 g).

\((-\text{-Teuclatriol:}}\)

\textbf{Physical state:} yellow color oil;

\textbf{TLC:} \(R_f = 0.23\) (hexanes/EtOAc 2:1, stains blue with vanillin);

\([\alpha]_{D}^{35}\) \(-16.8\) (c 0.59, CHCl\(_3\)), lit.\(^9\) \([\alpha]_{D}^{24}\): 16.9 (c 0.43, CHCl\(_3\)) for natural (+)teuclatriol;

\(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta\) 4.13 (dt, \(J = 13.4, 4.6\) Hz, 1H), 1.98 – 1.93 (m, 1H), 1.86 (td, \(J = 10.5, 3.1\) Hz, 1H), 1.81 – 1.76 (m, 1H), 1.74 (d, \(J = 10.4\) Hz, 1H), 1.69 (dd, \(J = 8.1, 6.0\) Hz, 2H), 1.67 – 1.64 (m, 1H), 1.59 – 1.56 (m, 1H), 1.55 – 1.51 (m, 1H), 1.39 (dd, \(J = 6.2, 3.4\) Hz, 2H), 1.36 (dd, \(J = 6.5, 3.3\) Hz, 1H), 1.34 – 1.29 (m, 1H), 1.27 (d, \(J = 3.5\) Hz, 3H), 1.25 (d, \(J = 4.2\) Hz, 3H), 1.17 – 1.13 (m, 1H), 1.08 (dd, \(J = 8.3, 4.4\) Hz, 1H), 1.02 (d, \(J = 6.6\) Hz, 3H), 0.97 (d, \(J = 6.6\) Hz, 3H);

\(^{13}\)C NMR (151 MHz, CDCl\(_3\)): \(\delta\) 81.11, 75.47, 71.40, 55.25, 52.03, 47.99, 45.48, 41.10, 29.56, 23.16, 23.07, 22.14, 21.50, 21.14, 20.50;

IR (neat) (cm\(^{-1}\)) \(\tilde{v}_{\text{max}}\): 3420, 2960, 2934, 2872, 1508, 1463, 1376, 1218, 1145, 1106, 1036, 902, 852, 789, 675, 635, 564, 471;
HRMS (m/z): calcd for C_{15}H_{28}NaO_{3} (M+Na)^+ 279.193, found 279.1931.

(−)-10-epi teuclatriol:

Physical state: pale yellow color oil;

TLC: R_f = 0.15 (hexanes/EtOAc 2:1, stains deep blue with vanillin);

[α]_D^{25} = −17.2 (c 0.39, CHCl₃), lit.⁹ [α]_D^{24} = +17.8 (c 0.29, CHCl₃) for natural (+)-10-epi teuclatriol;

¹H NMR (300 MHz, CDCl₃): δ 4.10 (dt, J = 8.5, 4.4 Hz, 1H), 2.26 – 2.18 (m, 1H), 1.92 – 1.84 (m, 1H), 1.80 – 1.72 (m, 2H), 1.72 – 1.67 (m, 2H), 1.67 – 1.60 (m, 2H), 1.58 (dd, J = 5.4, 2.5 Hz, 1H), 1.54 (dd, J = 7.1, 2.0 Hz, 1H), 1.39 (ddd, J = 17.1, 10.4, 3.2 Hz, 2H), 1.29 (s, 3H), 1.25 (s, 1H), 1.21 (s, 1H), 1.17 (d, J = 6.7 Hz, 3H), 1.14 (dd, J = 6.8, 2.6 Hz, 1H), 1.00 (t, J = 5.5 Hz, 3H), 0.96 (d, J = 6.6 Hz, 3H);

¹³C NMR (75 MHz, CDCl₃): δ 81.28, 73.19, 71.37, 54.02, 51.63, 46.87, 45.90, 40.93, 29.93, 29.81, 23.67, 23.30, 21.37, 21.25, 19.97;

IR (neat) (cm⁻¹) ν_max: 3420, 2960, 2934, 2872, 1508, 1463, 1376, 1218, 1145, 1036, 902, 852, 789, 675, 635, 564, 471;

HRMS (m/z): calcd for C_{15}H_{28}NaO_{3} (M+Na)^+ 279.193, found 279.1931.

Compound 160: Compound 145 (0.025 g, 0.112 mmol) and Co(acac)$_2$ (0.006 g, 0.022 mmol) were dissolved in THF (1.2 mL), and the solution was cooled to 0 °C. Oxygen was bubbled through the solution for 2 h, and PhSiH₃ (0.055 mL, 0.448 mmol) was added afterwards. The reaction was stirred 18 h at room temperature in the presence of Oxygen balloon. Then the reaction was diluted with EtOAc and filtered through the silica gel. The solvent was removed and the crude was purified by column chromatography gave 160 in 62% yield (0.0165 g).

Physical state: white solid;

TLC: R_f = 0.21 (hexanes/EtOAc 1:1, stains deep brown with vanillin);

M.P.: 96 °C;

[α]_D: n.d.;

¹H NMR (300 MHz, CDCl₃): δ 3.99 (d, J = 3.4 Hz, 1H), 2.59 (t, J = 9.1 Hz, 1H), 2.52 – 2.22 (m, 2H), 2.19 – 2.08 (m, 1H), 2.05 – 1.94 (m, 2H), 1.90 – 1.81 (m, 2H), 1.68 (dd, J = 15.7, 6.6 Hz, 2H), 1.53 – 1.28 (m, 3H), 1.25 (s, 3H), 1.16 (dd, J = 14.8, 8.2 Hz, 1H), 0.96 (dd, J = 9.9, 6.6 Hz, 6H);

¹³C NMR (75 MHz, CDCl₃): δ 225.01, 71.6, 54.95, 51.07, 47.11, 46.63, 37.58, 29.66, 28.90, 23.84, 21.82, 21.41, 21.11, 20.26;
D. Experimental Part

IR (neat) (cm⁻¹) \( \tilde{\nu}_{\text{max}} \): n.d.

HRMS (m/z): calcd for C₁₅H₂₂O₃ (M+H)⁺ 241.173, found 241.1731

Compound 161: To a suspension of Mg (0.0192 g, 0.8 mmol), TiCl₄ (0.022 mL, 0.2 mmol) in DCM (0.4 mL) at 0 °C was added over a 2 min of 160 (0.024 g, 0.1 mmol) in mixture of DCM: THF (0.3 mL: 0.2 mL). After being stirred for 1.5 h at the same temperature, quenched with aq. K₂CO₃ (1 mL). The resulting mixture was extracted with EtOAc (5 mL) followed by washed with brine. The solution was dried, filtered and concentrated under reduced pressure. The crude was purified by column chromatography (hexanes: EtOAc- 5:1) gave 161 in 48% yield (0.012 g).

Physical state: colorless oil;

TLC: \( R_f = 0.39 \) (hexanes/EtOAc 7:1, stains deep blue with vanillin);

\([\alpha]^{25}_D\): n.d.;

\(^1\)H NMR (300 MHz, CDCl₃): \( \delta \) 5.10 (s, 1H), 4.91 – 4.86 (m, 1H), 3.82 (dd, \( J = 7.8, 3.6 \) Hz, 1H), 2.67 (ddd, \( J = 10.1, 7.9, 2.2 \) Hz, 1H), 2.34 (dd, \( J = 15.3, 7.4 \) Hz, 1H), 2.28 – 2.16 (m, 1H), 1.89 – 1.82 (m, 2H), 1.78 – 1.69 (m, 2H), 1.69 – 1.59 (m, 3H), 1.50 – 1.43 (m, 2H), 1.42 – 1.30 (m, 3H), 1.20 (s, 3H), 0.97 (dd, \( J = 6.6, 3.0 \) Hz, 6H);

\(^13\)C NMR (75 MHz, CDCl₃): \( \delta \) 156.81, 105.39, 75.60, 72.19, 51.07, 50.4, 48.59, 46.58, 33.45, 29.99, 29.91, 26.82, 21.39, 21.22, 20.4;

IR (neat) (cm⁻¹) \( \tilde{\nu}_{\text{max}} \): n.d.;

HRMS (m/z): calcd for C₁₅H₂₂O₃ (M+H)⁺ 239.193, found 239.1931.

Compound 165: To a suspension of Cul (4.53 g, 23.87 mmol, 1.623 equiv) in THF (140 mL) was added isopropenyl magnesiumbromide (0.6 M in THF, 39.8 ml, 23.87 mmol, 1.623 equiv) dropwise at -78 °C. The solution was allowed to warm up to -45 °C upon which a solution of (S)-134 (3 g, 14.7 mmol, 1 equiv) in THF (36 mL) was added. After 10 min of stirring, the resulting solution was again cooled to -78 °C and HCHO (generated from 13.674 g, 441 mmol, 30 eq. of paraformaldehyde at 150°C) was passed through the above reaction mixture until disappearance of the starting material. Upon which the reaction was quenched with sat.NH₄Cl solution. Aqueous layer was extracted with ether (4×150 mL). The combined organic phases were washed with brine (200 mL), dried (Na₂SO₄) and the solvent was
removed under reduced pressure. The crude was purified by flash chromatography on silica (hexanes/EtOAc 5:1 to 2:1) to give compound 165 in 66% yield (1.48 g).

**Physical state:** deep yellow oil;

**TLC:** Rf = 0.23 (hexanes/EtOAc 3:1, UV-active, stains dark green with vanillin);

\[ \alpha_D^{25} = 144.46 \text{ (c 1.00, CHCl}_3) \];

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 7.64 (dd, \( J = 5.7, 2.4 \) Hz, 1H), 6.23 (dd, \( J = 5.7, 2.1 \) Hz, 1H), 4.93 – 4.83 (m, 1H), 4.81 (d, \( J = 0.5 \) Hz, 1H), 3.99 (dd, \( J = 10.7, 5.2 \) Hz, 1H), 3.83 – 3.65 (m, 1H), 3.38 (dd, \( J = 4.6, 2.3 \) Hz, 1H), 2.48 (s, 1H), 2.34 (dddd, \( J = 6.4, 4.7, 3.0 \) Hz, 1H), 1.73 (dt, \( J = 20.4, 10.2 \) Hz, 3H);

\(^13\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 211.27, 166.90, 144.04, 133.60, 112.84, 61.78, 52.82, 51.25, 20.46;

IR (neat) (cm\(^{-1}\)) \( \nu_{\text{max}} \): 3418, 1691, 1511, 1057, 895;

HRMS (m/z): calcd for C\(_9\)H\(_{13}\)O\(_2\)(M+H)\(^+\) 153.0910, found 153.0908.

**Compound 178:** To a solution of 165 (2.28 g, 15.0 mmol) in CHCl\(_3\) (120 ml) was added Ph\(_2\)SiH\(_2\) (4.8 ml, 25.5 mmol, 1.7 equiv), ZnCl\(_2\) (1.06 g, 7.8 mmol, 0.52 equiv) followed by Pd(PPh\(_3\))\(_4\) (225 mg, 0.2 mmol, 0.015 equiv). The resulting dark green colored mixture was stirred at room temperature for 30 min. The solvent was removed under reduced pressure and the crude was purified by flash column chromatography (hexanes/EtOAc 5:1), 178 was obtained in 75% yield (1.74 g).

**Physical state:** deep brown oil;

\[ \alpha_D^{23} = 72.72 \text{ (c 1.00, CHCl}_3) \];

\(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) 4.88 – 4.86 (m, 1H), 4.84 (d, \( J = 0.6 \) Hz, 1H), 3.84 (dd, \( J = 11.3, 4.2 \) Hz, 1H), 3.65 (dd, \( J = 11.3, 6.2 \) Hz, 1H), 2.66 (td, \( J = 11.9, 5.8 \) Hz, 1H), 2.50 – 2.40 (m, 1H), 2.31 (dddd, \( J = 11.9, 5.8, 3.9, 1.3 \) Hz, 2H), 2.23 – 2.08 (m, 2H), 1.77 (s, 3H), 1.74 – 1.64 (m, 1H);

\(^13\)C NMR (75 MHz, CDCl\(_3\)): \( \delta \) 221.01, 144.63, 111.83, 60.51, 54.07, 46.37, 38.04, 26.63, 19.37.

**Compound 179:** CeCl\(_3\).7H\(_2\)O (18.5 g, 49.8 mmol, 4.058 equiv) was placed in 500 mL three-necked flask and heated at 140° in vacuo (0.1 mmHg) for 3 h, and then cooled to room temperature. THF (75 mL) was added, and the suspension was stirred at room temperature for 2.5 h under N\(_2\) atmosphere. The resulting suspension was cooled to -78°C, and methyl lithium (1.6 M in Et\(_2\)O, 30 ml, 49.2 mmol, 4.06 equiv) was added. The resulting pale brown colored mixture was stirred for 30 min, ketone 178 (1.88 g, 12.27 mmol, 1 equiv) in THF (45 mL) was
added dropwise, and the mixture stirred for a further 4 h at -78 °C. The reaction mixture was treated with a saturated solution of NH₄Cl, filtered through Celite and extracted with EtOAc (4×150 mL). The combined organic layers were dried (Na₂SO₄) and concentrated under reduced pressure. The crude was purified by flash column chromatography (hexanes/ EtOAc 7:1 to 3:1) to give 179a-syn diol (1.48 g, 70%) 179b-anti diol (330 mg, 15%) as white solids.

Syn diol: 179a

1H NMR (300 MHz, CDCl₃) δ = 4.76 (s, 1H), 4.74 – 4.71 (m, 1H), 3.88 (dd, J=11.3, 3.1 Hz, 1H), 3.73 – 3.65 (m, 1H), 2.89 – 2.81 (m, 1H), 2.78 (d, J=4.8 Hz, 2H), 1.92 (dt, J=12.6, 8.1, 6.1 Hz, 1H), 1.77 – 1.69 (m, 2H), 1.68 (s, 3H), 1.56 (ddd, J=10.9, 4.8, 3.3 Hz, 1H), 1.52 – 1.43 (m, 1H), 1.38 (s, 3H);

13C NMR (75 MHz, CDCl₃) δ = 146.93, 110.67, 81.58, 60.75, 52.44, 46.86, 41.52, 28.34, 27.94, 19.28.

Data was in accordance with literature.

Anti diol: 179b

1H NMR (300 MHz, CDCl₃) δ = 4.71 (s, 1H), 4.69 (dd, J=3.0, 1.6 Hz, 1H), 3.71 (dd, J=10.7, 4.7 Hz, 1H), 3.67 – 3.57 (m, 1H), 2.40 (s, 2H), 2.24 – 2.06 (m, 2H), 1.87 – 1.73 (m, 2H), 1.72 (s, 3H), 1.70 – 1.55 (m, 2H), 1.29 (s, 3H);

13C NMR (75 MHz, CDCl₃) δ = 146.84, 110.74, 80.62, 63.13, 53.04, 47.50, 40.27, 26.94, 23.05, 18.75.

Data was in accordance with literature.

Compound 164: To a solution of DMSO (3.06 g, 2.78 ml, 39 mmol, 5.27 equiv) in CH₂Cl₂ (16 mL) was added oxalyl chloride (1.66 ml, 20 mmol, 2.702 equiv) at -78° C. The resulting mixture was stirred at this temperature for 30 min and solution of 179a-syn diol (1.258 g, 7.4 mmol, 1 equiv) in CH₂Cl₂ (10 mL) was added over 30 min. The resulting mixture was stirred for 3 h, Et₃N (11.8 mL, 84.32 mmol, 11.395 equiv) was added and the mixture was warmed to room temperature. The resulting mixture was diluted with cold water followed by extraction with DCM (4×50 mL). The combined organic layers were washed with brine (100mL) and dried. The solvent was removed under reduced pressure to give crude, which was purified by flash column chromatography (hexanes/ EtOAc 5:1) to give 164 in 52% yield (0.58 g).

Physical state: deep pink color oil;

R⁰ = 0.75 (hexanes/ EtOAc 3:1, stains deep blue with vanilin);

[α]D²³ = 58.7 (c 1, CHCl₃). (lit [α]D²³ = 56.1 c 1, CHCl₃);

1H NMR (300 MHz, CDCl₃) δ = 9.97 (s, 1H), 4.71 – 4.68 (m, 1H), 4.63 – 4.59 (m, 1H), 3.61 (d, J=9.3 Hz, 1H), 2.62 (dt, J=17.9, 8.2 Hz, 1H), 2.52 – 2.38 (m, 1H), 2.18 (d, J=1.2 Hz, 3H), 2.14 – 2.02 (m, 2H), 1.68 (s, 3H).
D. Experimental Part

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta = 188.00, 163.74, 146.8, 139.13, 109.73, 50.74, 39.43, 28.55, 20.48, 14.56\).

Data was in accordance with literature.

**Compound 187:** Under nitrogen atmosphere to a solution of 2-Isopropyl-1,3-dithiniae (0.5 g, 2.975 mmol, 0.649 equiv) in THF (8.5 mL) was added dropwise n-BuLi (1.44 M, 3.15 mL, 4.533 mmol, 0.990 equiv) at -25 °C. The resultant clear solution was stirred at the same temperature for 2 h. After cooling down to -78 °C, aldehyde 164 (0.687 g, 4.58 mmol, 1 equiv) in THF (3 mL) was added dropwise. The reaction mixture was stirred for 1 h, then quenched with saturated solution of NH\(_4\)Cl and warmed to ambient temperature. The layers were separated and aqueous layer was extracted with ether (3×50 mL). The combined organic layers were washed with brine (50 mL), dried (Na\(_2\)SO\(_4\)), filtered and concentrated under vacuo. The crude was purified by flash column chromatography (hexanes/ EtOAc 99.5:0.5 to 98:2) to give 187 in 70% yield (1.0 g).

**Physical state:** colorless syrup; 

\(R_f = 0.64\) (hexanes/ EtOAc 10:1, stains deep blue with vanilin);

\([\alpha]_D^{29} = 62.5\) (c 0.85, CHCl\(_3\));

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta = 4.92\) (d, \(J=7.4\) Hz, 2H), 4.78 – 4.71 (m, 1H), 4.00 (d, \(J=8.7\) Hz, 1H), 2.97 (ddd, \(J=14.1, 9.0, 4.0\) Hz, 1H), 2.89 – 2.81 (m, 2H), 2.79 – 2.71 (m, 2H), 2.50 – 2.30 (m, 2H), 2.20 (dd, \(J=16.3, 9.9\) Hz, 1H), 2.12 – 2.02 (m, 1H), 1.93 (dd, \(J=12.0, 6.0\) Hz, 2H), 1.80 – 1.74 (m, 6H), 1.63 – 1.57 (m, 1H), 1.24 (d, \(J=6.9\) Hz, 3H), 1.14 (d, \(J=6.8\) Hz, 3H);

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta = 152.42, 141.08, 134.28, 110.13, 74.66, 64.67, 53.74, 37.36, 35.16, 29.41, 26.43, 24.41, 20.16, 19.11, 18.51, 15.17;

**IR (neat) (cm\(^{-1}\))** \(\nu_{max}: 3539, 2922, 1637, 1436, 1380, 1017, 894, 803;

**HRMS (ESI):** calcd for C\(_{17}\)H\(_{29}\)OS\(_2\) (M+H\(^+\)) 313.1654, found 313.1653.

**Compound 163:** The \(\alpha\)-hydroxydithiane 187 (1.079 g, 3.46 mmol) was dissolved in acetonitrile (5 mL) and was added at once to a well stirred solution of NCS (1.40 g, 10.4 mmol, 3 equiv) and AgNO\(_3\) (2.05 g, 12.1 mmol, 3.497 equiv) in 50 mL of 90% aq.MeCN at 0 °C, stirring was continued for 30 min at the same temperature and then treated with sat.Na\(_2\)S\(_2\)O\(_3\) solution (25 mL). The reaction mixture was extracted with ether (2×100 mL), then combined organic layers were washed with aq.Na\(_2\)CO\(_3\) (50 mL), water (50 mL) and brine (50 mL), dried, filtered and concentrated under vacuo.
The crude was purified by flash column chromatography on silica (hexanes/ EtOAc 98:2) to give 163 in 75% yield (0.58 g).

**Physical state:** pale red color oil;

$R_f = 0.36$ (hexanes/ EtOAc 10:1, stains blue with vanilin);

$[\alpha]_{D}^{23} = 405.1$ (c 0.52, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta = 5.06$ (s, 1H), 4.67 (d, $J=1.5$ Hz, 1H), 4.61 (dd, $J=2.1$, 1.4 Hz, 1H), 3.46 (s, 1H), 3.08 (d, $J=9.2$ Hz, 1H), 2.74 – 2.62 (m, 1H), 2.48 (dt, $J=10.0$, 7.6, 1.1 Hz, 1H), 2.33 – 2.21 (m, 1H), 2.05 – 1.93 (m, 1H), 1.85 (d, $J=1.2$ Hz, 3H), 1.70 (ddd, $J=8.8$, 4.4, 2.1 Hz, 1H), 1.65 (s, 3H), 1.11 – 1.05 (m, 6H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta = 214.24$, 149.62, 142.41, 132.19, 110.52, 72.94, 54.79, 37.90, 35.99, 28.33, 19.59, 18.21, 17.80, 14.42;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3540, 2970, 2936, 1712, 1382, 1005, 884;

HRMS (EI-MS): calcd for C$_{14}$H$_{23}$O$_2$ (M+H)$^+$ 223.1693, found 223.1693.

**Compound 188:** Under nitrogen atmosphere to a solution of $\alpha$–hydroxyketone 163 (475 mg, 2.14 mmol, 1 equiv) in THF (38 mL) was added a solution of allyl magnesiumbromide (0.55 M in Et$_2$O, 15.56 mL, 3.21 mmol, 1.5 equiv) at 0 $^\circ$C, and was stirred at the same temperature for 1.5 h. The reaction mixture was quenched with saturated solution of NH$_4$Cl. The layers were separated and the aqueous layer was extracted with ether (2×50 mL). The combined organic extracts were washed with brine (50 mL) and dried. The solvent was removed under reduce pressure. The crude was purified by flash column chromatography (hexanes/ EtOAc 10:1) to give 188 in 72% yield (0.41 g).

**Physical state:** light red color oil;

$R_f = 0.41$ (hexanes/ EtOAc 7:1, stains blue with vanilin);

$[\alpha]_{D}^{23} = 72.9$ (c 0.48, CHCl$_3$);

$^1$H NMR (300 MHz, CDCl$_3$) $\delta = 6.03$ (ddq, $J=20.7$, 10.4, 7.6 Hz, 1H), 5.17 – 5.00 (m, 2H), 4.83 (d, $J=2.3$ Hz, 1H), 4.69 (dd, $J=2.4$, 1.3 Hz, 1H), 4.54 (d, $J=5.8$ Hz, 1H), 3.68 (d, $J=9.0$ Hz, 1H), 2.44 – 2.34 (m, 3H), 2.26 – 2.11 (m, 2H), 2.06 – 1.94 (m, 1H), 1.80 – 1.72 (m, 6H), 1.62 – 1.53 (m, 1H), 1.29 – 1.24 (m, 1H), 0.99 (d, $J=6.9$ Hz, 3H), 0.90 – 0.85 (m, 1H), 0.83 (dd, $J=6.7$, 3.4 Hz, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta = 152.70$, 140.10, 135.77, 134.55, 117.5, 109.62, 77.99, 73.55, 53.66, 39.31, 37.31, 33.75, 29.19, 20.22, 17.48, 14.85;

IR (neat) (cm$^{-1}$) $\nu_{\text{max}}$: 3547, 2979, 1638, 1439, 1371, 1059, 1371, 998, 893;

HRMS (EI-MS): calcd for C$_{17}$H$_{29}$O$_2$ (M+H)$^+$ 265.2162, found 265.2164.
D. Experimental Part

**Compound 189**: A flask containing diol 188 (400 mg, 1.515 mmol, 1 equiv) was outfitted with a reflux condenser and evacuated and backfilled with dry N₂. DCM (100 mL) was added, and the solution was heated to reflux. A solution of Grubbs-II catalyst (66 mg, 0.0778 mmol, 0.117 equiv) in DCM (6.6 mL) was added to the reaction mixture, and the light brown color mixture was refluxed further for 3 h. The solvent was removed under reduced pressure and crude was purified by flash chromatography (hexanes/ EtOAc 5:1) to give **189** in 95% yield (0.34 g).

**Physical state**: Pale brown color oil; Rf = 0.25 (hexanes/ EtOAc 5:1, stains deep blue with vanilin);

\[ [\alpha]_{D}^{23} = 90.0 \text{ (c 1.07, CHCl₃)}; \]

**¹H NMR (300 MHz, Acetone) \(\delta\)** = 5.37 – 5.29 (m, 1H), 4.43 (s, 1H), 3.72 (d, \(J = 4.2\) Hz, 1H), 3.24 (t, \(J = 9.1\) Hz, 1H), 2.33 (dd, \(J = 5.1, 1.9\) Hz, 1H), 2.28 (dt, \(J = 3.7, 2.6\) Hz, 1H), 2.18 – 2.09 (m, 1H), 2.06 (dd, \(J = 4.5, 2.3\) Hz, 1H), 2.03 – 1.96 (m, 3H), 1.89 (dd, \(J = 1.9, 1.0\) Hz, 3H), 1.79 – 1.74 (m, 1H), 1.72 (d, \(J = 1.0\) Hz, 3H), 1.06 (d, \(J = 6.8\) Hz, 3H), 0.91 – 0.86 (m, 3H);

**¹³C NMR (75 MHz, Acetone) \(\delta\)** = 141, 137.53, 134.16, 121, 81.75, 78.29, 53.40, 38.93, 35.98, 32.98, 29.75, 23.81, 18.72, 18.64, 15.81;

**IR (neat) \(\text{cm}^{-1}\) \(\text{vmax}\)**: 3472, 2961, 2914, 1741, 1445, 1373, 1072, 1013;

**HRMS (EI-MS)**: calcd for C₁₅H₂₅O₂ (M+H)⁺ 237.1849, found 237.1843.

**Compound 192**: Under nitrogen atmosphere to a solution of diol 189 (182 mg, 0.771 mmol, 1 equiv) in DCM (38 mL) was added Hg (OAc)₂ (302.5 mg, 0.951 mmol, 1.233 equiv) at room temperature. The reaction mixture was stirred for 15 h. To this resultant mixture was added water and extracted with ether (4×50 mL). The combined organic layers were washed with water (100 mL), brine (100 mL), dried (Na₂SO₄) and filtered. The solvent was removed under reduced pressure to give crude 162. This was used for the next step without further purification.

To the above crude 162 in dry MeOH (23 mL), was added NaBH₄ (500 mg, 5.11 mmol) at -78 °C. The resulting mixture was warmed to room temperature and stirred for 3 h. The reaction mixture was treated with water, extracted with EtOAc (2×100 mL). The combined organic layers were washed with brine (50 mL), water (50 mL), dried and filtered. The crude was concentrated under reduced pressure and purified by flash chromatography (hexanes/ EtOAc 3:1) to give **192** in 62% yield (0.11 g).

**Physical state**: colorless oil;

\(R_f = 0.6 \text{ (hexanes/ EtOAc 5:1, stains blue with vanilin);}\n
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[α]_D^23 = 38.2 (c 0.25, CHCl₃);

**1H NMR (300 MHz, CDCl₃)** δ = 4.44 (s, 1H), 2.68 (t, J=7.5 Hz, 1H), 2.26 (dt, J=24.9, 11.3 Hz, 2H), 1.94 (dd, J=13.1, 6.2 Hz, 1H), 1.89 (s, 3H), 1.85 – 1.74 (m, 2H), 1.73 – 1.59 (m, 2H), 1.51 (d, J=4.3 Hz, 1H), 1.36 – 1.23 (m, 2H), 1.19 (d, J=6.9 Hz, 6H);

**13C NMR (75 MHz, CDCl₃)** δ = 133.49, 133.01, 86.66, 84.41, 73.89, 57.59, 39.05, 31.74, 31.68, 28.61, 24.00, 23.97, 18.12, 17.26, 14.64;

**IR (neat) (cm⁻¹) v_max =** 3490, 2965, 2932, 2878, 1470, 1375, 1176, 1072, 1013, 901;

**HRMS (EI-MS):** calcd for C₁₅H₂₃O₂ (M+H)^+ = 237.1849, found 237.1852.

**Compound 194:** Under nitrogen atmosphere to a solution of alcohol 192 (185 mg, 0.783 mmol, 1 equiv) in DCM (38 mL) was added Dess-Martin periodinane (370 mg, 0.870 mmol, 1.12 equiv) at 0°C. The resulting mixture was warmed to ambient temperature and stirred for 1 h, then treated with saturated Na₂S₂O₃ solution (20 mL), followed by addition of sat. NaHCO₃ solution (20 mL) after 15 min. The resultant mixture was stirred for additional 15 min. The organic layer was separated and the aqueous layer was extracted with DCM (3×100 mL). The combined organic layers were washed with water (100 mL), brine (100 mL), dried over Na₂SO₄. The solvent was removed under reduced pressure, to give enone 194, which was used for the next step without further purification (0.36 g, 98%).

R_f = 0.87 (hexanes/ EtOAc 5:1, stains brown with vanilin);
[α]_D^23 = -1.4 (c 0.47, CHCl₃);

**1H NMR (300 MHz, CDCl₃)** δ = 3.22 (s, 1H), 2.59 – 2.42 (m, 1H), 2.35 – 2.23 (m, 1H), 2.16 (dt, J=13.7, 6.9 Hz, 1H), 2.08 (dd, J=3.3, 2.3 Hz, 3H), 2.05 – 1.85 (m, 3H), 1.68 – 1.61 (m, 1H), 1.54 – 1.35 (m, 2H), 1.33 (s, 3H), 1.03 (dd, J=6.9, 2.0 Hz, 6H);

**13C NMR (75 MHz, CDCl₃)** δ = 199.88, 154.45, 131.90, 91.07, 84.39, 57.90, 38.86, 33.27, 30.57, 30.04, 25.98, 24.61, 18.41, 17.30, 15.96;

**IR (neat) (cm⁻¹) v_max =** 2965, 2877, 1689, 1625, 1375, 1268, 1077, 1004, 883;

**HRMS (EI-MS):** calcd for C₁₅H₂₃O₂ (M+H)^+ 235.1693, found 235.1696.

**Orientalol-F 78:** Under nitrogen atmosphere to a stirred solution of crude 194 (81 mg, 0.346 mmol, 1 equiv) and CeCl₃·7H₂O (260 mg, 0.696 mmol, 2.011 equiv) in MeOH (10 mL) was added NaBH₄ (26.2 mg, 0.696 mmol, 2.011 equiv) at 0 °C. The mixture was stirred at room temperature for 20 h, then quenched by addition of water and extracted with EtOAc (2×50 mL). The combined organic layers were washed
with water (25 mL), brine (25 mL), dried, filtered and concentrated under reduce pressure. The crude was purified by flash chromatography (hexanes/ EtOAc 5:1) gave 78 (Orientalol-F) in 94% yield (0.076 g).

**Physical state:** pale yellow oil;

Rf= 0.6 (hexanes/ EtOAc 5:1, stains blue with vanilin);

[α]D23 = 12.4 (c 0.67, DCM). (lit-[α]D23 = 12.2 (c 0.5, DCM);

1H NMR (300 MHz, CDCl3) δ = 4.47 – 4.39 (m, 1H), 2.73 – 2.63 (m, 1H), 2.39 – 2.15 (m, 2H), 1.96 (dd, J=13.8, 6.9 Hz, 1H), 1.89 (dd, J=3.2, 2.3 Hz, 3H), 1.85 – 1.75 (m, 2H), 1.73 – 1.60 (m, 2H), 1.58 – 1.46 (m, 1H), 1.28 (dddd, J=10.8, 9.7, 6.5, 2.5 Hz, 2H), 1.21 – 1.18 (m, 3H), 1.03 (t, J=6.9 Hz, 6H);

13C NMR (75 MHz, CDCl3) δ = 133.49, 133.0, 86.65, 84.41, 73.89, 57.59, 39.05, 31.73, 31.68, 28.60, 24.03, 23.97, 18.11, 17.26, 14.64;

IR (neat) (cm⁻¹) νmax= 3490, 2965, 2931, 2878, 1469, 1375, 1177, 1072, 901;

HRMS (EI-MS): calcd for C15H25O2 (M+H)+ 237.1849, found 237.1852. Data was in accordance with literature.

**Compound 197:** Under nitrogen atmosphere m-CPBA (70%, 252 mg, 1.02 mmol, 1.2 equiv) was added to a stirred solution of 78 (200 mg, 0.85 mmol, 1 equiv) in DCM (4 mL) at 0°C. The resultant mixture was stirred for 2 h at the same temperature, then quenched with saturated Na2CO3 solution (3 mL), and diluted with water (10 mL). The aqueous layer was extracted twice with DCM (2×15 mL). The combined organic extracts were washed with water (10 mL), brine (10 mL) dried and filtered. The solvent was removed under reduced pressure to give 197 as a white crystalline compound. This was used for the recrystallization from n-heptane without further purification.

Rf= 0.50 (hexanes/ EtOAc 3:1, stains deep blue with vanilin).

[α]D23 = 0.64 (c 0.36, CHCl3);

M.P = 68 °C;

1H NMR (300 MHz, CDCl3) δ = 4.34 (s, 1H), 2.16 (d, J=9.4 Hz, 1H), 2.04 – 1.75 (m, 6H), 1.75 – 1.68 (m, 1H), 1.67 (s, 3H), 1.65 – 1.40 (m, 3H), 1.26 (s, 3H), 1.03 (dd, J=8.9, 6.9 Hz, 6H);

13C NMR (75 MHz, CDCl3) δ = 86.67, 83.97, 73.55, 72.11, 71.76, 52.07, 34.58, 33.22, 31.99, 28.85, 24.54, 21.5, 17.81, 17.53, 16.72;

IR (neat) (cm⁻¹) νmax= 3406, 2970, 2895, 1474, 1375, 1085, 1005, 888, 722;

HRMS (EI-MS): calcd for C15H23O3 (M+H)+ 253.1798, found 253.1797.
Under N\textsubscript{2} atmosphere allyl magnesiumbromide (0.55 M in Et\textsubscript{2}O, 15.56 mL, 3.21 mmol, 1.5 equiv) was added to a solution of 163 (475 mg, 2.14 mmol, 1 equiv) in THF (38 mL) at 0 °C and stirring was continued for 1.5 h at the same temperature. The solvent was removed under reduced pressure, then dry DCM (100 mL) was added to this residue followed by addition Grubbs-II catalyst (66 mg, 0.0778 mmol, 0.117 equiv) in CH\textsubscript{2}Cl\textsubscript{2} (6.6 mL) at room temperature. The resultant brown colored solution was refluxed for 3 h, to this solution was added Hg(OAc)\textsubscript{2} (520 mg, 1.622 mmol, 2.1 equiv) at ambient temperature. The resultant mixture was stirred for 15 h at the same temperature, and then quenched by addition of brine (75 mL). The aqueous layer was removed with pipette, and the resultant organic phase was concentrated in vacuo. To this residue in dry MeOH (50 mL) was added NaBH\textsubscript{4} (1 g, 10.2 mmol) at -78 °C. The reaction mixture was stirred at room temperature for 3 h, then the reaction was quenched with water, and extracted with EtOAc (4 X 50 mL). The combined organic layers were washed with brine (50 mL), water (50 mL) dried, filtered and concentrated in vacuo. The crude was purified by flash chromatography on silica (hexanes/ EtOAc 3:1) to give 192 (0.23 g, 45%) as colorless oil.

Oxygen was bubbled through the solution of NaBH\textsubscript{4} (210 mg, 5.55 mmol) in dry DMF (20 mL) for 45 min at room temperature, at which point suspension of residue (the crude obtained after
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Oxymercuration step from the above procedure) in dry DMF (20 mL) was introduced dropwise with syringe pump with continuous oxygen bubbling during 1 h. Upon, completion of the addition the resulting mixture was stirred with continuous oxygen bubbling at the same temperature for 30 min, and the reaction mixture was filtered through Celite pad, and washed celite pad with EtOAc, combined organic phases were washed with water, dried, filtered and concentrated in vacuo. The crude was purified by flash chromatography (hexanes/ EtOAc 3:1 to 1:1) to give 193 (0.22 g, 40%) as white color powder.

Rf = 0.25 (hexanes/ EtOAc 5:1, stains deep blue with vanilin).

[α]D23 = 11.8 (c .49, CH2Cl2);

1H NMR (300 MHz, CDCl3) δ 4.39 (s, 1H), 3.93 (t, J = 6.7 Hz, 1H), 2.78 – 2.64 (m, 1H), 2.43 – 2.19 (m, 3H), 2.01 – 1.93 (m, 1H), 1.85 (d, J = 6.6 Hz, 3H), 1.64 – 1.49 (m, 3H), 1.37 (d, J = 8.7 Hz, 1H), 1.33 – 1.25 (m, 1H), 1.19 (s, 3H), 1.06 (dd, J = 6.9, 3.4 Hz, 6H).

13C NMR (75 MHz, CDCl3) δ 133.7, 132.2, 86.8, 85.6, 73.5, 73.4, 56.1, 40.5, 38.9, 30.9, 23.6, 18.8, 17.8, 17.2, 14.6;

IR (neat) (cm⁻¹) v_max = 3490, 3398, 2965, 2931, 2878, 1469, 1375, 1181, 1031, 901;

HRMS (EI-MS): calcd for C15H24O3 (M+H)+ 252.1726, found 253.173.

Under nitrogen atmosphere to a solution of diol 193 (252 mg, 1 mmol, 1 equiv) in DCM (20 mL) was added Dess-Martin periodinane (1.272 g, 3 mmol, 3 equiv) at 0°C. The resulting mixture was stirred for 4 h at the room temperature, then quenched with saturated Na2S2O3 solution (40 mL) followed by addition of sat.NaHCO3 solution (40 mL) after 15 min. The resulting mixture was stirred for additional 15 min. The organic layer was separated and the aqueous layer was extracted with DCM (3×100 mL). The combined organic layers were washed with water (100 mL), brine (100 mL), and dried over Na2SO4. Solvent was removed in vacuo, to give di ketone 195, which was unstable at room temperature.
To a solution of the above crude di ketone 195 in dry MeOH (15 mL) was added NaBH$_4$ (38 mg, 1 mmol, 1 equiv) at 0 °C. After 30 min of stirring at the same temperature, the reaction mixture was quenched with saturated aq. NH$_4$Cl and extracted twice with EtOAc (20 mL). The combined organic phases were washed with brine and dried over Na$_2$SO$_4$. The residue was concentrated in vacuo and the crude was purified by flash chromatography (hexanes/ EtOAc 3:1 to 1:1) to give 196 as a white color powder in 72% yield (0.18 g).

R$_f$= 0.25 (hexanes/ EtOAc 5:1, stains deep blue with vanilin).

[α]$_D$$^2$3 = 2.8 (c 0.49, CH$_2$Cl$_2$);

$^1$H NMR (300 MHz, CDCl$_3$) δ 4.55 (s, 1H), 3.95 (dd, J = 10.7, 6.2 Hz, 1H), 2.83 (s, 1H), 2.39 (dd, J = 10.3, 6.7 Hz, 2H), 2.29 – 2.21 (m, 1H), 2.16 – 2.08 (m, 1H), 2.07 – 1.99 (m, 1H), 1.91 (d, J = 5.1 Hz, 3H), 1.89 – 1.76 (m, 2H), 1.66 (dd, J = 13.5, 6.2 Hz, 2H), 1.26 (s, 3H), 1.00 (dd, J = 7.7, 7.1 Hz, 6H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 133.5, 133.4, 84.8, 81.9, 81.3, 74.1, 57.5, 39.3, 39.0, 31.1, 22.8, 21.6, 17.2, 16.8, 14.6;

IR (neat) (cm$^{-1}$) $\nu_{max}$ = 3490, 3398, 2965, 2931, 2878, 1469, 1375, 1181, 1031, 901;

HRMS (EI-MS): calcd for C$_{15}$H$_{24}$O$_3$ (M+H)$^+$ 252.1726, found 253.173.

Compound 199: According to general procedure A: To a stirred solution of CuCN (3.12 g, 34.85 mmol, 3.0 equiv) and anhydrous LiCl (2.97 g, 69.69 mmol, 6.0 equiv) in THF (120 mL) was added iso propenylmagnesium bromide (1.18 M solution in THF, 34.85 mmol, 30 mL, 3.0 equiv) dropwise at –40 °C. The reaction mixture was cooled to –78 °C upon which a solution of (R)-125 (2.3 g, 11.61 mmol, 1.0 equiv) in THF (15 mL) was added. After 4 min of stirring, 198 (1.96 g, 19.52 mmol, 1.68 equiv) was added. After the starting material had disappeared, aq. NH$_4$Cl (100 mL) was added and the reaction mixture was extracted with Et$_2$O (2x150 mL). The combined organic extracts were dried over Na$_2$SO$_4$, filtered and the solvent was removed under reduced pressure. After purification on silica (hexanes/EtOAc 5:1) 199 was obtained in 81% yield (1.95 g).

R$_f$= 0.33 (hexanes/ EtOAc 5:1, UV-active, stains bluish-green with vanilin).

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.51 (dd, J = 5.7, 2.5 Hz, 1H), 6.16 (dd, J = 5.7, 2.0 Hz, 1H), 5.21 – 5.15 (m, 1H), 4.82 – 4.80 (m, 1H), 4.68 (s, 1H), 4.42 (t, J = 8.9 Hz, 1H), 3.69 (s, 1H), 3.14 (dd, J = 4.5, 2.2 Hz, 1H), 2.26 (dd, J = 8.6, 2.5 Hz, 1H), 1.67 (dd, J = 6.4, 1.3 Hz, 6H), 1.62 (s, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 212.4, 167.6, 143.8, 136.7, 133.2, 125.1, 113.4, 69.2, 55.4, 52.0, 25.7, 20.2, 18.5;
HRMS (EI-MS): calcd for C_{13}H_{18}O_2Na (M+Na)^+ 229.1307, found 229.1310.

**Compound 200:** To a solution of α,β-unsaturated compound 199 (0.15 g, 0.728 mmol) in CHCl_3 (6 mL) was added Ph_3SiH_2 (0.23 ml, 1.24 mmol, 1.7 equiv), ZnCl_2 (0.051 g, 0.38 mmol, 0.52 equiv) and Pd (PPh_3)_4 (0.011 g, 0.011 mmol, 0.015 equiv). The mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure, the crude was purified by flash column chromatography (hexanes/ EtOAc 5:1) to give 200 as pale brown oil in 28% yield (0.043 g).

To a solution of α,β-unsaturated compound 199 (0.029 g, 0.14 mmol) in THF (0.5 mL) was added Bu_3SnH (0.08 ml, 0.28 mmol, 2.0 equiv), ZnCl_2 (0.042 g, 0.308 mmol, 2.2 equiv) and Pd (PPh_3)_4 (0.005 g, 0.0042 mmol, 0.03 equiv). The mixture was stirred at room temperature for 3 h. The solvent was removed under reduced pressure, the crude was purified by flash column chromatography on silica (hexanes/ EtOAc 5:1) to give 200 as pale brown oil in 30% yield (0.045 g).

To a suspension of LiAlH_4 (0.332 g, 8.73 mmol) in THF (38 mL) at -78 °C was added CuI (1.66 g, 8.73 mmol) dissolved in THF: DMPU (4:1, 38 mL). The resulting mixture was stirred for 1 h at the same temperature, and then added 199 (1.8 g, 8.73 mmol) in THF (4 mL). After stirring 2 h at -78 °C, the mixture was quenched with aq. NH_4Cl (50 mL) followed by ether (100 mL). The aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure gave crude. The crude was purified by flash chromatography (hexanes/ EtOAc 3:1) gave 200 in 82% yield (1.5 g).

R_f = 0.25 (hexanes/ EtOAc 5:1, stains brown with vanillin).

^1H NMR (300 MHz, CDCl_3) δ 5.36 – 5.28 (m, 1H), 4.82 – 4.77 (m, 2H), 4.47 (ddd, J = 9.0, 6.0, 2.8 Hz, 1H), 3.12 (d, J = 3.3 Hz, 1H), 2.69 (td, J = 11.1, 6.6 Hz, 1H), 2.46 – 2.36 (m, 1H), 2.33 – 2.18 (m, 2H), 2.10 – 2.03 (m, 1H), 1.73 (s, 3H), 1.72 – 1.70 (m, 1H), 1.66 (dd, J = 9.7, 1.3 Hz, 6H);

^13C NMR (75 MHz, CDCl_3) δ 221.2, 145.5, 135.9, 124.9, 111.6, 68.4, 57.2, 47.3, 38.4, 26.9, 25.7, 19.1, 18.2;

HRMS (EI-MS): calcd for C_{13}H_{30}O_2Na (M+Na)^+ 231.1466, found 231.1467.
Compound 202: Under the nitrogen atmosphere to a solution of 199 (0.064 g, 0.31 mmol) in DCM (3 mL) at 0 °C was added m-CPBA (0.152 g, 2.0 equiv) at once. The reaction mixture was allowed to stir for 20 min at the same temperature. The solvent was removed under reduced pressure and the crude was purified by flash column chromatography (hexanes/ EtOAc 2:1) gave 202 in 88% yield (0.061 g).

Rf= 0.28 (hexanes/ EtOAc 3:1, UV-active, stains deep pink with vanilin).

\(^1\text{H NMR (300 MHz, CDCl}_3\) \(\delta\) 7.61 (dd, \(J = 5.7, 2.5\) Hz, 1H), 6.24 (dd, \(J = 5.7, 2.1\) Hz, 1H), 4.90 (p, \(J = 1.4\) Hz, 1H), 4.83 (d, \(J = 0.6\) Hz, 1H), 3.78 (dd, \(J = 7.7, 4.9\) Hz, 1H), 3.56 (dd, \(J = 4.7, 2.2\) Hz, 1H), 3.16 (d, \(J = 7.7\) Hz, 1H), 2.43 (dd, \(J = 4.9, 2.9\) Hz, 1H), 1.75 – 1.72 (m, 3H), 1.33 (d, \(J = 3.3\) Hz, 6H);

\(^{13}\text{C NMR (75 MHz, CDCl}_3\) \(\delta\) 209.2, 166.7, 143.9, 134.0, 113.3, 70.1, 64.8, 60.5, 53.8, 51.7, 24.8, 20.2, 19.3;

HRMS (El-MS): calcd for C\(_{13}\)H\(_{20}\)O\(_3\) (M+H)\(^+\) 223.126, found 223.1261.

Compound 203: To a solution of \(\alpha,\beta\)–unsaturated compound 202 (0.07 g, 0.315 mmol) in CHCl\(_3\) (3 mL) was added Ph\(_2\)SiH\(_2\) (0.099 ml, 0.535 mmol, 1.7 equiv), ZnCl\(_2\) (0.022 g, 0.388 mmol, 0.16 equiv) and Pd (PPh\(_3\))\(_4\) (0.005 g, 0.004 mmol, 0.015 equiv), and the mixture was stirred at the room temperature for 30 min. The solvent was removed under reduced pressure, the crude was purified by flash column chromatography (hexanes/ EtOAc 5:1) to give 203 as pale brown oil in 28% yield (0.02 g).

Rf= 0.31 (hexanes/ EtOAc 7:1, stains blue with vanilin).

\(^1\text{H NMR (300 MHz, CDCl}_3\) \(\delta\) 4.96 – 4.88 (m, 2H), 4.26 – 4.16 (m, 2H), 3.74 (d, \(J = 4.6\) Hz, 1H), 3.53 (d, \(J = 3.7\) Hz, 1H), 3.02 – 2.87 (m, 1H), 2.52 – 2.42 (m, 1H), 2.33 – 2.28 (m, 1H), 2.28 – 2.16 (m, 2H), 1.79 (s, 3H), 1.64 (s, 3H), 1.54 (s, 3H);

\(^{13}\text{C NMR (75 MHz, CDCl}_3\) \(\delta\) 223.4, 144.5, 112.6, 78.1, 72.3, 66.9, 57.4, 47.4, 39.0, 30.5, 27.0, 26.5, 19.2;

HRMS (El-MS): calcd for C\(_{13}\)H\(_{21}\)O\(_3\) (M+H)\(^+\) 225.141, found 225.140.

Compound 205: CeCl\(_3\).7H\(_2\)O (1.63 g, 4.36 mmol, 4.05 equiv) was placed in a 25 mL three-necked flask and heated at 140° in vacuo (0.1 mmHg) for 3 h, and then cooled to room temperature. THF (10 mL)
was added and stirring was continued for 2.5 h at room temperature. The resulting suspension was cooled to -78°C, and methyl lithium (1.49 M in Et₂O, 3.0 ml, 4.315 mmol, 4.01 equiv) was added. The resulting pale brown colored mixture was stirred for 1 h, ketone 200 (0.224 g, 1.07 mmol, 1.0 equiv) in THF (5 ml) was added, and the reaction mixture was stirred for further 4 h at the same temperature. The reaction mixture was quenched with aq.NH₄Cl solution, filtered through Celite and extracted with EtOAc (4×15 ml). The combined organic layers were dried (Na₂SO₄). The solvent was removed under reduced pressure, the products were separated by flash column chromatography (hexanes/ EtOAc 7:1 to 3:1) to give 205-syn diol (0.074 g, 30%) 205-anti diol (0.11 g, 46%) as colorless oils.

**205-syn diol:**
- Rₚ = 0.72 for syn and 0.6 for anti (hexanes/ EtOAc 5:1, stains pale blue with vanillin);
- ¹H NMR (300 MHz, CDCl₃) δ 5.36 – 5.26 (m, 1H), 4.68 (s, 2H), 4.52 (dd, J = 9.2, 6.6 Hz, 1H), 2.58 (dd, J = 17.1, 8.9 Hz, 1H), 1.90 – 1.81 (m, 1H), 1.78 – 1.72 (m, 2H), 1.68 (s, 3H), 1.66 (s, 6H), 1.57 – 1.44 (m, 2H), 1.42 (s, 3H), 1.39 – 1.24 (m, 2H);
- ¹³C NMR (75 MHz, CDCl₃) δ 147.4, 134.3, 127.2, 110.4, 81.3, 70.3, 56.0, 49.7, 42.3, 31.0, 29.4, 25.7, 19.5, 18.2;
- HRMS (EI-MS): calcd for C₁₄H₂₅O₂ (M+H)+ 225.1776, found 225.177.

**205-anti diol:**
- Rₚ = (hexanes: ethyl acetate=5:1);
- ¹H NMR (300 MHz, CDCl₃) δ 5.11 – 5.00 (m, 1H), 4.58 – 4.49 (m, 2H), 4.40 (t, J = 9.6 Hz, 1H), 3.36 (s, 1H), 2.26 – 2.14 (m, 1H), 1.96 (dd, J = 28.5, 18.0 Hz, 2H), 1.86 – 1.76 (m, 2H), 1.75 – 1.70 (m, 1H), 1.67 – 1.64 (m, 6H), 1.61 (d, J = 1.2 Hz, 3H), 1.51 – 1.43 (m, 1H), 1.36 (s, 3H);
- ¹³C NMR (75 MHz, CDCl₃) δ 147.8, 135.1, 126.9, 109.9, 80.8, 71.1, 55.9, 47.1, 40.0, 27.9, 55.6, 23.0, 18.6, 18.4;
- HRMS (EI-MS): calcd for C₁₄H₂₅O₂ (M+H)+ 225.1776, found 225.177.

**Compound 206:** Under nitrogen to a solution of 205 syn-diol (0.052 g, 0.233 mmol) in DCM (3 ml) was added m-CPBA (0.084 g, 1.1 equiv) at once at 0 °C. The reaction mixture was allowed to stir for 20 min at the same temperature. The solvent was removed under reduced pressure and the crude was purified by flash column chromatography (hexanes/ EtOAc 2:1) gave 206 in 85% yield (0.046 g).

Rₚ = 0.35 (hexanes/ EtOAc 2:1, stains deep blue with vanillin);
**D. Experimental Part**

\[ ^1H \text{ NMR (300 MHz, CDCl}_3\] \( \delta \) 4.74 – 4.65 (m, 2H), 3.56 – 3.46 (m, 1H), 2.70 (d, \( J = 8.7 \text{ Hz} \), 1H), 2.32 – 2.23 (m, 1H), 2.22 – 2.15 (m, 1H), 1.91 – 1.79 (m, 2H), 1.75 (s, 3H), 1.73 – 1.65 (m, 1H), 1.61 – 1.38 (m, 2H), 1.31 (d, \( J = 6.5 \text{ Hz} \), 6H), 1.26 (d, \( J = 7.2 \text{ Hz} \), 1H), 1.22 (s, 3H);

\[ ^13C \text{ NMR (75 MHz, CDCl}_3\] \( \delta \) 146.8, 110.7, 80.8, 72.5, 67.4, 62.2, 52.7, 46.3, 39.4, 28.5, 24.5, 23.0, 19.7, 19.3;

**HRMS (EI-MS):** calcd for \( C_{14}H_{25}O_3 \) (M+H)\(^+\) 241.1725, found 241.1728.

To a solution of i-Pr\(_2\)NH (2.8 mL, 20 mmol) in THF (30 mL) was added n-BuLi (1.45 M in hexanes, 13.8 mL, 20 mmol) at 0 °C and the resulting solution was stirred for 30 min at the same temperature, then cooled to -78 °C. Ketone 211 (2.14 mL, 20 mmol) was added dropwise and the resulting mixture was stirred for 45 min at -78 °C, and was then added TMSCl (3.0 mL, 24 mmol) followed by quenched with aq. NH\(_4\)Cl. The reaction was warmed to room temperature. The aqueous layer was extracted with Et\(_2\)O. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure gave crude 212 which we can use directly for the next step.

To the above crude 212 solution in DCM (125 mL) was added m-CPBA (5.94 g) at 0 °C. The reaction mixture was allowed to warm room temperature during 30 min, and was quenched with water. The aqueous layer was extracted with DCM. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure gave crude 213.

To the above crude 213 (0.83 g, 4.74 mmol) in Et\(_2\)O(30 mL) was added allyl magnesium bromide (0.74 M in Et\(_2\)O, 19 mL, 14.22 mmol) at 0 °C. The reaction was stirred at the same temperature for 30 min and was allowed to warm to room temperature for 30 min. The reaction was quenched with aq. NH\(_4\)Cl and extracted twice with Et\(_2\)O. The combined organics were washed with brine; dried, filtered
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and removed solvent under reduced pressure gave crude. This crude was purified by flash column (hexanes/ EtOAc 7:1) gave diol 214 in 70% yield (0.72 g).

Rf = 0.64 (hexanes/ EtOAc 10:1, stains blue with vanilin).

$^1$H NMR (300 MHz, CDCl$_3$) δ 5.92 – 5.70 (m, 1H), 5.07 – 5.03 (m, 1H), 5.00 (ddd, $J = 5.3, 2.3, 1.3$ Hz, 1H), 3.48 – 3.35 (m, 2H), 2.18 (dddd, $J = 13.4, 9.0, 7.0, 3.7$ Hz, 3H), 1.80 (dq, $J = 13.5, 6.8$ Hz, 1H), 0.87 (d, $J = 7.0$ Hz, 6H), 0.11 – 0.04 (m, 9H);

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 145.8, 118.0, 75.6, 65.9, 39.2, 33.5, 17.7, 17.4, 3X0.00(TMS);

HRMS (EI-MS): calcd for C$_{11}$H$_{25}$O$_2$Si (M+H)$^+$ 217.155, found 217.157.

To the above diol 214 (0.084 g, 0.392 mmol) in DCM (1.2 mL) was added DMSO (0.29 mL, 4.11 mmol) followed by the addition of iPr$_2$NEt (0.35 mL, 2.03 mmol) after 15 min at 0°C. To this solution was added Py.SO$_3$ complex (0.193 g, 1.21 mmol). The reaction mixture was stirred at the same temperature for an hour, and was quenched with aq. NaHCO$_3$ followed by extraction with DCM. The combined organics were washed with brine, dried, filtered and concentrated under reduced pressure. The resulting crude was purified by flash column (hexanes/ EtOAc 7:1) gave aldehyde 210 in 80% yield (0.045g).

Rf = 0.65 (hexanes/ EtOAc 5:1, stains pale brown with vanilin).

$^1$H NMR (300 MHz, CDCl$_3$) δ 9.53 (s, 1H), 5.78 – 5.57 (m, 1H), 5.16 – 5.12 (m, 1H), 5.09 (d, $J = 1.1$ Hz, 1H), 3.15 (s, 1H), 2.51 (dt, $J = 1.9, 1.1$ Hz, 1H), 2.49 (dd, $J = 2.6, 1.2$ Hz, 1H), 2.01 (dd, $J = 13.7, 6.8$ Hz, 1H), 1.01 (d, $J = 6.8$ Hz, 3H), 0.89 – 0.86 (m, 3H);

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 205.2, 131.8, 119.4, 81.8, 38.8, 32.7, 17.0, 16.0;

HRMS (EI-MS): calcd for C$_{15}$H$_{24}$O$_3$ (M+H)$^+$, found.

Compound 215: According to general procedure A: To a stirred solution of CuCN (0.051mmol, 0.561 mmol, 3.0 equiv) and anhydrous LiCl (0.048 g, 1.122 mmol, 6.0 equiv) in THF (2 mL) was added isopropenylmagnesium bromide (0.92 M solution in THF, 0.561 mmol, 0.61 mL, 3.0 equiv) dropwise at −40°C. The reaction mixture was cooled to −78°C upon which a solution of (R)-125 (0.038 g, 0.187 mmol, 1.0 equiv) in THF (0.5 mL) was added. After 4 min of stirring at −78°C, 210 (0.053 g, 0.37 mmol, 2.0 equiv) was added. After the reaction was completed (ca. 5 min), the mixture was quenched with NH$_4$Cl$_{aq}$ (100 mL) and the aqueous layer was extracted with Et$_2$O (2x5 mL). The combined organic extracts were washed with brine, dried, filtered and the solvent was removed under reduced pressure. After purification on silica (hexanes/EtOAc 7:1-5:1) 215 was obtained in 12% yield (0.006 g).

Rf= 0.25 (hexanes/ EtOAc 5:1, UV-active, stains blue with vanilin);
**Experimental Part**

**1H NMR (300 MHz, CDCl₃)** δ 7.68 (dd, J = 5.7, 2.2 Hz, 1H), 6.21 (dd, J = 5.7, 2.1 Hz, 1H), 6.09 – 5.94 (m, 1H), 5.15 – 5.01 (m, 2H), 4.95 (dd, J = 3.8, 2.3 Hz, 2H), 4.51 (s, 1H), 3.89 (d, J = 7.6 Hz, 1H), 3.81 (q, J = 2.5 Hz, 1H), 2.84 (d, J = 8.7 Hz, 1H), 2.63 (dd, J = 3.1, 1.7 Hz, 1H), 2.38 (dd, J = 14.5, 7.0 Hz, 2H), 1.95 (dd, J = 13.7, 6.9 Hz, 1H), 1.71 (s, 3H), 1.13 (d, J = 6.8 Hz, 3H), 0.83 (d, J = 7.0 Hz, 3H);

**13C NMR (75 MHz, CDCl₃)** δ 212.1, 169.0, 142.9, 135.6, 134.0, 116.7, 114.8, 72.9, 54.1, 53.1, 37.6, 36.1, 23.9, 19.5, 17.5, 14.6;

**HRMS (EI-MS):** calcd for C₁₈H₂₄O₃ (M+H)⁺ 264.1726, found 265.1732.

**Compound 222:** According to general procedure A: To a stirred solution of CuCN (0.215 g, 2.4 mmol, 3.0 equiv) and dried LiCl (0.202 g, 4.8 mmol, 6.0 equiv) in THF (8 mL) was added isopropenylmagnesium bromide (0.92 M solution in THF, 2.4 mmol, 2.6 mL, 3.0 equiv) dropwise at –40 °C. The reaction mixture was cooled to –78 °C upon which a solution of (R)-125 (0.16 g, 0.8 mmol, 1.0 equiv) in THF (2 mL) was added. After 4 min successive stirring at –78 °C, aldehyde 221 (0.21 g, 1.34 mmol, 1.68 equiv) was added. After the reaction was completed (ca. 10 min), the mixture was quenched with aq. NH₄Cl (10 mL), and the reaction mixture was extracted with Et₂O (2x25 mL). The combined organic extracts were washed with brine (25 mL), dried over Na₂SO₄, filtered and concentrated under vacuo. The crude was purified by flash chromatography on silica (hexanes/EtOAc 5:1 to 2:1) obtained enone 222 in 66 % yield (0.145 g).

**Physical state:** deep yellow oil;

**TLC:** Rₜ = 0.3 (hexanes/EtOAc 2:1, UV-active, stains pale green with vanillin);

**[α]D²⁵:** n.d.

**1H NMR (300 MHz, CDCl₃)** δ 7.49 (dd, J = 5.7, 2.4 Hz, 1H), 6.22 (dd, J = 5.6, 2.2 Hz, 1H), 5.85 – 5.69 (m, 1H), 5.15 (s, 1H), 5.12 – 5.08 (m, 1H), 4.96 – 4.92 (m, 1H), 4.90 (s, 1H), 4.68 – 4.58 (m, 2H), 3.77 – 3.72 (m, 1H), 3.16 (dd, J = 5.3, 2.6 Hz, 1H), 2.81 (dd, J = 16.9, 9.2 Hz, 1H), 2.49 – 2.33 (m, 3H), 2.19 (dd, J = 16.9, 9.1 Hz, 1H), 2.10 – 2.05 (m, 1H), 1.59 (s, 3H);

**13C NMR (75 MHz, CDCl₃)** δ 212.31, 176.04, 167.66, 142.14, 133.32, 132.41, 119.15, 115.30, 79.76, 69.52, 52.65, 51.35, 43.95, 38.32, 28.29, 18.47;

**IR (neat) (cm⁻¹) νmax:** 3485, 2919, 1773, 1686, 1440, 1229, 967, 905, 535, 494;

**HRMS (m/z):** calcd for C₁₆H₂₄O₃ (M+H)⁺ 277.1361, found 277.1362.
D. Experimental Part

**Compound 223**: A flask containing enone 222 (0.146 g, 0.53 mmol) was outfitted with reflux condenser and evacuated and backfilled with N₂ 3 times. Deoxygenated DCM (25 mL) was added, and the solution was heated to reflux (40 °C). A solution of Grubbs-II catalyst (0.045 g) in deoxygenated DCM (2.5 mL) was added to the reaction mixture. The light brown reaction mixture was refluxed for 48 h and was then cooled to room temperature. The solvent was removed under reduced pressure. After purification on silica (hexanes/ EtOAc 5:1 to 2:1) 223 was obtained in 45 % yield (0.059 g).

**Physical state**: pale yellow oil;

**TLC**: R_f = 0.5 (hexanes/ EtOAc 1:1, UV-active, stains deep brown with vanillin);

[α]_D^25°: n.d.;

^1^H NMR (300 MHz, CDCl₃) δ 7.66 (dd, J = 5.7, 2.2 Hz, 1H), 6.27 (dd, J = 5.7, 2.3 Hz, 1H), 5.33 (d, J = 6.6 Hz, 1H), 4.86 – 4.76 (m, 2H), 3.73 (t, J = 9.9 Hz, 1H), 3.46 (d, J = 1.6 Hz, 1H), 2.97 (ddt, J = 18.0, 5.4, 2.6 Hz, 1H), 2.85 – 2.67 (m, 2H), 2.60 – 2.49 (m, 1H), 2.37 – 2.24 (m, 1H), 2.11 (dd, J = 10.2, 4.3 Hz, 1H), 1.64 – 1.60 (m, 3H);

^13^C NMR (75 MHz, CDCl₃) δ 211.16, 175.54, 165.95, 134.44, 133.88, 121.54, 80.22, 74.27, 56.26, 46.24, 44.75, 35.81, 33.77, 20.79;

IR (neat) (cm⁻¹) ν_max: 2923, 1780, 1690, 1578, 1414, 1261, 1045, 985, 898, 539, 497;

HRMS (m/z): calcd for C₁₄H₁₇O₄ (M+H)^+ 249.105, found 249.1044.

**Compound 220**: To a solution of the aldehyde 221 (0.057 g, 0.37 mmol, 1 equiv) in dry MeOH (0.075 M) was added Grubbs-II catalyst (10 mol %) at room temperature. The suspension was then heated at 60° C. After 10 minutes, the catalyst completely dissolved and the resulting deep brown color solution was stirred at same temperature for further 15 h. After reaction was completed the solvent was removed under vacuo. The residue was purified by flash chromatography (hexanes/ EtOAc 5:1 to 2:1) the isomerized aldehyde 220 was obtained in 85 % yield (E/Z- 5:1, 0.049 g).

**Physical state**: deep brown oil;

**TLC**: R_f = 0.13 (hexanes/ EtOAc 2:1, stains deep green with vanillin);

[α]_D^25°: 147.36 (c 0.11, CHCl₃);

^1^H NMR (300 MHz, CDCl₃) δ; ^1^H NMR (300 MHz, CDCl₃) δ 9.75 – 9.71 (m, 1H), 5.96 – 5.78 (m, 1H), 5.63 – 5.45 (m, 1H), 3.30 – 3.14 (m, 1H), 2.93 – 2.83 (m, 1H), 2.79 – 2.70 (m, 1H), 2.53 (dt, J = 14.4, 6.6 Hz, 1H), 1.79 – 1.72 (m, 3H);

^13^C NMR (75 MHz, CDCl₃) δ 197.15, 173.99, 132.27, 127.11, 79.32, 53.13, 28.84, 17.72;
D. Experimental Part

IR (neat) (cm⁻¹) $v_{\text{max}}$: 3080, 2980, 2841, 1774, 1727, 1419, 1359, 1193, 921;

HRMS ($m/z$): calcd for $C_{8}H_{11}O_{3}$ (M+H)⁺ 155.0703, found 155.0702.

**Compound 218:** According to general procedure A: To a stirred solution of CuCN (0.215 g, 2.4 mmol, 3.0 equiv) and dried LiCl (0.202 g, 4.8 mmol, 6.0 equiv) in THF (8 mL) was added isopropenylmagnesium bromide (0.92 M solution in THF, 2.4 mmol, 2.6 mL, 3.0 equiv) dropwise at −40 °C. The reaction mixture was cooled to −78 °C upon which a solution of ($R$)-125 (0.16 g, 0.8 mmol, 1.0 equiv) in THF (2 mL) was added. After 4 min successive stirring at −78 °C, aldehyde 220 (0.21 g, 1.34 mmol, 1.68 equiv) was added. After the reaction was completed (ca. 10 min), the mixture was quenched by adding aq. $\text{NH}_4 \text{Cl}$ (10 mL), and the reaction mixture was extracted with $\text{Et}_2\text{O}$ (2x25 mL). The combined organic extracts were washed with brine (25 mL), dried over $\text{Na}_2\text{SO}_4$, filtered and concentrated under vacuo. The crude was purified by flash chromatography on silica (hexanes/ $\text{EtOAc}$ 5:1 to 2:1) obtained enone 218 in 66 % yield (0.145 g).

**Physical state:** deep yellow oil;

TLC: $R_f$ = 0.3 (hexanes/ $\text{EtOAc}$ 2:1, UV-active, stains pale green with vanillin);

$[\alpha]_D^{25}$: 11.1 (c 0.11, CHCl₃);

$^1\text{H NMR}$ (300 MHz, $\text{CDCl}_3$) $\delta$: $^1\text{H NMR}$ (300 MHz, $\text{CDCl}_3$) $\delta$ 7.54 (dd, $J = 5.6$, 2.4 Hz, 1H), 6.28 – 6.23 (m, 1H), 5.95 – 5.77 (m, 1H), 5.49 – 5.37 (m, 1H), 5.00 – 4.96 (m, 2H), 4.91 (dd, $J = 15.8$, 7.4 Hz, 1H), 4.70 (d, $J = 6.2$ Hz, 1H), 3.75 (d, $J = 5.4$ Hz, 1H), 3.29 – 3.20 (m, 1H), 2.90 – 2.80 (m, 1H), 2.37 – 2.22 (m, 2H), 2.13 (dt, $J = 10.2$, 3.4 Hz, 1H), 1.75 – 1.71 (m, 3H), 1.64 (s, 3H);

$^{13}$C NMR (75 MHz, $\text{CDCl}_3$) $\delta$: 212.44, 175.95, 167.79, 142.16, 133.23, 132.92, 127.72, 115.32, 81.86, 68.21, 52.48, 51.51, 46.56, 28.42, 18.45, 17.86;

IR (neat) (cm⁻¹) $v_{\text{max}}$: 3485, 2919, 1773, 1686, 1440, 1229, 1188, 967, 905, 728, 535, 494;

HRMS ($m/z$): calcd for $C_{16}H_{21}O_{4}$ (M+H)⁺ 277.1361, found 277.1362.

**Compound 217:** A flask containing enone 218 (0.145 g, 0.53 mmol) was outfitted with reflux condenser and evacuated and backfilled with $\text{N}_2$ 3 times. Deoxygenated DCM (25 mL) was added, and the solution was heated to reflux (40 °C). A solution of Grubbs-II catalyst (0.045 g) in deoxygenated DCM (2.5 mL) was added to the reaction mixture. The light brown reaction mixture was refluxed for 15 h and was then cooled to room temperature. The solvent was removed under reduced pressure. After purification on silica (hexanes/ $\text{EtOAc}$ 5:1 to 2:1) 217 was obtained in 84 % yield (0.104 g).
Physical state: deep brown oil;

TLC: R_f = 0.5 (hexanes/ EtOAc 1:1, UV-active, stains deep brown with vanillin);

[α]_D^25: 17.4 (c 0.18, CHCl_3);

^1^H NMR (300 MHz, CDCl_3) δ 7.80 (dd, J = 5.9, 2.0 Hz, 1H), 6.30 (dd, J = 5.9, 2.6 Hz, 1H), 5.86 – 5.82 (m, 1H), 4.91 – 4.83 (m, 2H), 3.50 (d, J = 2.6 Hz, 1H), 2.95 – 2.87 (m, 1H), 2.49 – 2.44 (m, 1H), 2.24 (ddd, J = 10.1, 6.1, 2.5 Hz, 1H), 2.13 – 2.08 (m, 1H), 1.99 (td, J = 4.1, 2.2 Hz, 1H), 1.87 (s, 3H);

^13^C NMR (75 MHz, CDCl_3) δ 209.77, 175.32, 162.15, 136.67, 134.12, 126.58, 78.63, 74.63, 55.04, 48.87, 45.41, 34.24, 19.97;

IR (neat) (cm⁻¹) ν max: 2923, 1780, 1690, 1578, 1414, 1261, 1227, 1045, 985, 898, 734, 631, 539, 497;

HRMS (m/z): calcd for C_{13}H_{15}O_4 (M+H)^+ 235.0969, found 235.0965.

Compound 226: To a suspension of LiAlH_4 (0.0038 g, 0.1 mmol) in THF (0.45 mL) at -78 °C was added CuI (0.019 g, 0.1 mmol) dissolved in THF: DMPU (4:1, 0.45 mL). The resulting mixture was stirred for 1 h at the same temperature, and then was added 217 (0.024 g, 0.1 mmol) in THF (0.1 mL). After stirring 2 h at -78 °C, the mixture was quenched with aq. NH_4Cl (5 mL) followed by ether (10 mL). The aqueous layer was extracted twice with Et_2O. The combined organic extracts were washed with brine, dried, filtered and concentrated under reduced pressure gave crude. The crude was purified by flash chromatography (hexanes/ EtOAc 3:1) gave 226 in 76% yield (0.018 g).

Physical state: pale yellow oil;

TLC: R_f = 0.48 (hexanes/ EtOAc 1:1, stains deep brown with vanillin);

[α]_D^25: n.d.;

^1^H NMR (300 MHz, CDCl_3) δ 5.77 (s, 1H), 5.14 (d, J = 10.4 Hz, 1H), 4.03 (dd, J = 9.1, 5.0 Hz, 1H), 3.54 (s, 1H), 3.11 – 2.99 (m, 1H), 2.67 – 2.56 (m, 2H), 2.43 (ddd, J = 22.7, 12.0, 5.8 Hz, 3H), 2.26 – 2.16 (m, 2H), 1.83 (d, J = 1.4 Hz, 3H);

^13^C NMR (75 MHz, CDCl_3) δ 221.0, 175.8, 139.1, 126.6, 76.0, 65.7, 59.1, 46.6, 42.2, 37.2, 29.6, 26.8, 22.0;

IR (neat) (cm⁻¹) ν max: 2923, 1780, 1690, 1578, 1414, 1261, 1227, 1045, 985;

HRMS (m/z): calcd for C_{13}H_{17}O_4 (M+H)^+ 237.105, found 237.1049.
1. NMR Spectra:

(R)-125, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

(5)-134, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

(+)-133a, CDCl₃, 300 MHz

CDCl₃, 75 MHz
(+)-133a, HSQC, CDCl₃, 600 MHz
E. Appendix

(+)-133b, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

(+)-133c, CDCl$_3$, 600 MHz

CDCl$_3$, 151 MHz
(+)-133c, HSQC, CDCl₃, 600 MHz
E. Appendix

(+)-133e, CDCl₃, 300 MHz

[Chemical structure diagram]

CDCl₃, 75 MHz

[Chemical spectrum diagram]
E. Appendix

(+)-133f, d₆-Acetone, 300 MHz

D₆-Acetone, 75 MHz
(±)-133g, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

(+)-133h, d$_6$-Acetone, 300 MHz

D$_6$-Acetone, 75 MHz
E. Appendix

(+)-133i, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

\[ \text{(+)-133j, CDCl}_3, 300 \text{ MHz} \]

\[ \text{CDCl}_3, 75 \text{ MHz} \]
E. Appendix

(+)-133k, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

(+)-133m, d$_6$-Acetone, 300 MHz

D$_6$-Acetone, 75 MHz
E. Appendix

(+)-133n, CDCl₃, 600 MHz

CDCl₃, 151 MHz
E. Appendix

(+)-133o, CDCl₃, 600 MHz

CDCl₃, 151 MHz
(+)-133o, HSQC, CDCl$_3$, 600 MHz
E. Appendix

(+)-133p, HSQC, CDCl₃, 600 MHz
E. Appendix

(+)-133q, CDCl₃, 300 MHz

CDCl₃, 75 MHz
(+)-133r, CDCl₃, 600 MHz

CDCl₃, 151 MHz
(+)-133r, HSQC, CDCl₃, 600 MHz
E. Appendix

(+)-133s, CDCl₃, 600 MHz

CDCl₃, 151 MHz
(+)-133s, HSQC, CDCl₃, 600 MHz
E. Appendix

\( \text{CDCl}_3, \text{600 MHz} \)

\( \text{CDCl}_3, \text{151 MHz} \)
E. Appendix

(+)-133t, HSQC, CDCl$_3$, 600 MHz
E. Appendix

(+)-133u, CDCl₃, 600 MHz

CDCl₃, 151 MHz
(+)-133u, HSQC, CDCl₃, 600 MHz
E. Appendix

(+)-133v, CDCl$_3$, 600 MHz

CDCl$_3$, 151 MHz
E. Appendix

(+)-133v, HSQC, CDCl₃, 600 MHz
E. Appendix

(+)-133w, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

(+)-133x, CDCl₃, 600 MHz

CDCl₃, 151 MHz
(+)-133x, HSQC, CDCl₃, 600 MHz
E. Appendix

2, CDCl₃, 300 MHz
E. Appendix

3, CDCl₃, 400 MHz

CDCl₃, 100 MHz
E. Appendix

141, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

143, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

146, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

145, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
COSY, CDCl$_3$, 600 MHz

Noesy, CDCl$_3$, 600 MHz
E. Appendix

158, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

![NMR spectrum, CDCl₃, 600 MHz]

**144, CDCl₃, 600 MHz**

![NMR spectrum, CDCl₃, 151 MHz]

**CDCl₃, 151 MHz**
E. Appendix

HSQC, CDCl₃, 600 MHz

HMBC, CDCl₃, 600 MHz
E. Appendix

COSY, CDCl$_3$, 600 MHz

Noesy, CDCl$_3$, 600 MHz
E. Appendix

72, CDCl$_3$, 600 MHz

CDCl$_3$, 151 MHz
10 *epi*-leucatriol

159, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

160, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

161, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

165, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

178, CDCl$_3$, 300 MHz

CDCI3, 75 MHz
E. Appendix

179a-syn, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

179b-anti, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

164, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

163, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

188, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

189, $d_6$-Acetone, 300 MHz

$d_6$-Acetone, 75 MHz
E. Appendix

\[ \text{192, CDCl}_3, 300 \text{ MHz} \]

\[ \text{CDCl}_3, 75 \text{ MHz} \]
E. Appendix

194, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

78 (+)-Orientalol-F, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

197, CDCl₃, 300 MHz

CDCl₃, 75 MHz
196, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

\[ \text{199, CDCl}_3, 300 \text{ MHz} \]

\[ \text{CDCl}_3, 75 \text{ MHz} \]
202, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

203, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

206, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

214a, CDCl$_3$, 300 MHz

CDCl$_3$, 75 MHz
E. Appendix

\[ \text{HO} \]
\[ \text{HO} \]

214b, CDCl\textsubscript{3}, 300 MHz

CDCl\textsubscript{3}, 75 MHz
E. Appendix

210, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

215, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

222, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

223, CDCl₃, 300 MHz

CDC13, 75 MHz
E. Appendix

220, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

218, CDCl₃, 300 MHz

CDCl₃, 75 MHz
217, CDCl₃, 300 MHz

CDCl₃, 75 MHz
E. Appendix

226, CDCl₃, 300 MHz

CDCl₃, 75 MHz
2. HPLC data:

HPLC condition: (CHIRALCEL OJ-H, Hept: iPrOH-99:1, 1.0 mL/min, 215 nm)

Table 6, entry-1
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HPLC condition: (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

**Table 6, entry-1**

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Totals: 3.67788e4 866.52394
E. Appendix

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Totals : 3.44234e4 792.16082

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Totals : 1.46111e4 342.18576
### 50 g scale

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Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals : 2.33833e4 966.77435

Pure

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Totals : 2.43745e4 954.45892
E. Appendix

Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals: 2.07622e4 698.08887

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Totals: 2.32976e4 624.16785

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**E. Appendix**

![Chemical Structure](image1)

**Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)**

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**Totals:**

1.97707e4  802.82189

**Pure**

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**Totals:**

2.15171e4  744.00293
E. Appendix

\[+\text{-133d} \text{ Racemic} \] (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals : 3.81344e4 490.66869

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Totals : 1.93902e4 216.71927

223
E. Appendix

(+)-133f Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals : 2.10265e4 1340.97461

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Totals : 2.09386e4 1406.85852
E. Appendix

Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals : 1.87879e4 1034.39142

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Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals: 1.48036e4 1181.84427

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Totals: 1.61348e4 1460.01709
E. Appendix

Racemic (Phenomenex Lux Cellulose-2, n-Hep: iPrOH-1:1, 0.5 mL/min, 254 nm)

Peak Results:

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Peak Results:

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</table>
E. Appendix

Racemic (Chiralpak AS-H, n-Hep: iPrOH-7:3, 0.5 mL/min, 215 nm)

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E. Appendix

(+)-133m Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals: 1.81927e4 1257.35022

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Totals: 1.78757e4 1349.30622
Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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<tbody>
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<td>BB</td>
<td>0.1746</td>
<td>6796.20410</td>
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<td>BV</td>
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<td>6852.02930</td>
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Total: 136482e4 1077.36514

Pure

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Total: 1.45538e4 1261.4923
### E. Appendix

**Racemic** (Phenomenex Lux Cellulose-2, n-Hep: iPrOH-7:3, 0.5 mL/min, 215 nm)

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Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals : 1.42511e4 1089.72354

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Totals : 1.28671e4 1104.21106
Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals: 2.43129e4 933.62619

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<td>1.94189e4</td>
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Totals: 1.94189e4 821.36072
## Appendix

![Racemic](image)

**Racemic** (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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<th>Height</th>
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<td>[min]</td>
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Totals: 2.30124e4 1035.13162

**Pure**

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<td>[mAU]</td>
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Totals: 1.09369e4 539.99188
E. Appendix

Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

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Totals : 9254.29541 822.41055

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Totals : 8418.02637 815.6677
Racemic (Daicel CHIRALCEL OD-H, Hex: iPrOH-9:1, 0.5 mL/min, 220 nm)

Peak RetTime    Type    Width  Area     Height     Area     %
#   [min]         [min]   [mAU*s]     [mAU]        %
----|--------|-----|---------|-----------|---------|-----|
1  13.188   BV   0.261   8066.14697  476.19882  49.8447
2  14.235   VB   0.2916  8116.41406  431.12695  50.1553

Totals :                  1.61826e4   907.32578

Pure

Peak RetTime    Type    Width  Area     Height     Area     %
#   [min]         [min]   [mAU*s]     [mAU]        %
----|--------|-----|---------|-----------|---------|-----|
1  13.014   BB   0.2496  1.18239e4  727.64905 100.0000

Totals :                  1.18239e4   727.64905
### E. Appendix

![Chemical Structure](image)

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<th>Height</th>
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<td>[min]</td>
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<td>[mAU]</td>
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Totals: 3.81344e4 490.66869

![Graph 1](image)

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Totals: 3.91793e4 565.11511
### Peak RetTime Type Width Area Height Area

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### Peak RetTime Type Width Area Height Area

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E. Appendix

\[ \text{(-)-133g} \]

**Peak Results:**

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<th>Quantity [% Area]</th>
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**Peak Results:**

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E. Appendix

\[
\text{(-)-133h}
\]

\[
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\text{Index} & \text{Name} & \text{Time (Min)} & \text{Quantity (mAU)} & \text{Height (mAU)} & \text{Area (mAU Min)} & \text{Area %} \\
\hline
1 & \text{UNKNOWN} & 37.65 & 49.81 & 554.4 & 706.0 & 49.812 \\
2 & \text{UNKNOWN} & 53.44 & 50.19 & 443.5 & 711.3 & 50.188 \\
\hline
\text{Total} & & & 100.00 & 967.8 & 1417.3 & 100.000 \\
\hline
\end{array}
\]
E. Appendix

\[
\text{(-)-133j}
\]
E. Appendix

(-)-133k

<table>
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<th>Area [mAU Min]</th>
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E. Appendix

![Chemical Structure](image1)

(-)-133r

![Graph](image2)

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<th>Name</th>
<th>Time [Min]</th>
<th>Quantity [% Area]</th>
<th>Height [mAU]</th>
<th>Area [mAU Min]</th>
<th>Area % [%]</th>
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![Graph](image3)

<table>
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<th>Quantity [% Area]</th>
<th>Height [mAU]</th>
<th>Area [mAU Min]</th>
<th>Area % [%]</th>
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3. X-Ray structure of *epoxy*-Orientalol-F 197:

![Image of molecular structure]

Table 1. Crystal data and structure refinement for 197.

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<td>Empirical formula</td>
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</tr>
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<td>Temperature/K</td>
<td>123.01(10)</td>
</tr>
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</tr>
<tr>
<td>Space group</td>
<td>P2_{1}2_{1}2_{1}</td>
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<tr>
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<td>6.08287(12)</td>
</tr>
<tr>
<td>b/Å</td>
<td>9.5429(2)</td>
</tr>
<tr>
<td>c/Å</td>
<td>24.1276(6)</td>
</tr>
<tr>
<td>α/°</td>
<td>90</td>
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<td>β/°</td>
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<td>γ/°</td>
<td>90</td>
</tr>
<tr>
<td>Volume/Å³</td>
<td>1400.56(5)</td>
</tr>
</tbody>
</table>
Z  
\( \rho_{\text{calc}} / \text{cm}^3 \)  1.197  
\( \mu / \text{mm}^{-1} \)  0.650  
F(000)  552.0  
Crystal size/\( \text{mm}^3 \)  0.1731 \times 0.1344 \times 0.1244  
Radiation  CuK\( \alpha \) (\( \lambda = 1.54184 \))  
2\( \theta \) range for data collection/\(^\circ \)  7.32 to 147.52  
Index ranges  -7 \( \leq h \leq 6, -11 \leq k \leq 7, -29 \leq l \leq 26 \)  
Reflections collected  6079  
Independent reflections  2648 [\( R_{\text{int}} = 0.0205, R_{\text{sigma}} = 0.0214 \)]  
Data/restraints/parameters  2648/0/166  
Goodness-of-fit on \( F^2 \)  1.079  
Final R indexes [\( I > 2\sigma (I) \)]  \( R_1 = 0.0374, wR_2 = 0.1038 \)  
Final R indexes [all data]  \( R_1 = 0.0399, wR_2 = 0.1061 \)  
Largest diff. peak/hole / e \( \text{Å}^{-3} \)  0.39/-0.23  
Flack parameter  0.0(2)  

Table 2. Fractional Atomic Coordinates (\( \times 10^4 \)) and Equivalent Isotropic Displacement Parameters (\( \text{Å}^2 \times 10^3 \)) for l274. \( U_{eq} \) is defined as 1/3 of of the trace of the orthogonalised \( U_{ij} \) tensor.

<table>
<thead>
<tr>
<th>Atom</th>
<th>( x )</th>
<th>( y )</th>
<th>( z )</th>
<th>( U(\text{eq}) )</th>
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<td>2393.8(5)</td>
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<td>4114.7(19)</td>
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Table 3. Anisotropic Displacement Parameters (Å²×10³) for l274. The Anisotropic displacement factor exponent takes the form: \(-2\pi^2[h^2a^*2U_{11}+2hka*b*U_{12}+...].\)

<table>
<thead>
<tr>
<th>Atom</th>
<th>U₁₁</th>
<th>U₂₂</th>
<th>U₃₃</th>
<th>U₁₂</th>
<th>U₁₃</th>
<th>U₂₃</th>
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<td>25.6(5)</td>
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<td>4.2(6)</td>
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<td>4.3(6)</td>
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<td>1.3(6)</td>
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<td>Length/Å</td>
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<td>------</td>
<td>------</td>
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<td>-------</td>
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Table 4. Bond Lengths for l274.

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Table 5 Bond Angles for l274.
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<th>A</th>
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<th>d(D-A)/Å</th>
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\(^1\text{X},-1/2+Y,1/2-Z; ^2\text{1-X},1/2+Y,1/2-Z\)

Table 6. Hydrogen Bonds for I274.
Table 7. Torsion Angles for l274.

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<th>B</th>
<th>C</th>
<th>D</th>
<th>Angle/°</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>Angle/°</th>
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<td>C2</td>
<td>C3</td>
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<td>C6</td>
<td>C7</td>
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<td>C1</td>
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<td>C14</td>
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<td>C10</td>
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<td>C14</td>
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<td>C5</td>
<td>C12</td>
<td>C13</td>
<td>C14</td>
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<td>C12</td>
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<td>C6</td>
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<td>C14</td>
<td>C13</td>
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</tr>
<tr>
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<td>C7</td>
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Table 8. Hydrogen Atom Coordinates (Å×10\(^4\)) and Isotropic Displacement Parameters (Å\(^2\)×10\(^3\)) for 1274.

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<td>1176</td>
<td>47</td>
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Experimental

Single crystals of C_{15}H_{24}O_{3} [l274] were []. A suitable crystal was selected and [] on a SuperNova, Single source at offset), Atlas diffractometer. The crystal was kept at 123.01(10) K during data collection.
Using Olex2 [1], the structure was solved with the [2] structure solution program using and refined with the [3] refinement package using minimisation.

2. 
3. 

Crystal structure determination of [l274]

**Crystal Data** for C_{15}H_{24}O_{3} (M =252.34 g/mol): orthorhombic, space group P2_12_12_1 (no. 19), a = 6.08287(12) Å, b = 9.5429(2) Å, c = 24.1276(6) Å, V = 1400.56(5) Å³, Z = 4, T = 123.01(10) K, μ(CuKα) = 0.650 mm^{-1}, Dcalc = 1.197 g/cm³, 6079 reflections measured (7.32° ≤ θ ≤ 147.52°), 2648 unique (R_{int} = 0.0205, R_{sigma} = 0.0214) which were used in all calculations. The final R₁ was 0.0374 (I>2σ(I)) and wR₂ was 0.1061 (all data).

Refinement model description

Number of restraints - 0, number of constraints - ?.

Details:

1. Others

Fixed Uiso: H2A(0.04) H2B(0.04) H2O(0.037) H3A(0.04) H3B(0.04) H5(0.034)
H7(0.029) H8(0.044) H9A(0.052) H9B(0.052) H9C(0.052) H10A(0.072) H10B(0.072) H10C(0.072) H11A(0.049) H11B(0.049) H11C(0.049) H12A(0.047) H12B(0.047) H13A(0.047) H13B(0.047) H15A(0.045) H15B(0.045) H15C(0.045) Fixed X: H2A(0.4387) H2B(0.4323) H3A(0.3413) H3B(0.3764) H5(-0.1851) H7(-0.0917) H8(0.1843) H9A(-0.2403) H9B(-0.1913) H9C(-0.1574) H10A(0.3245) H10B(0.0818) H10C(0.1499) H11A(-0.0342) H11B(-0.0004) H11C(-0.2202) H12A(0.0991) H12B(-0.0622) H13A(0.3942) H13B(0.2484) H15A(0.5329) H15B(0.3836) H15C(0.5172) Fixed Y: H2A(0.4232) H2B(0.3506) H3A(0.5557) H3B(0.6311) H5(0.6268) H7(0.3537) H8(0.1392) H9A(0.1976) H9B(0.1638) H9C(0.0449) H10A(0.1754) H10B(0.2014) H10C(0.0499) H11A(0.5953) H11B(0.7411) H11C(0.6521) H12A(0.8307) H12B(0.8345) H13A(0.781) H13B(0.8395) H15A(0.5151) H15B(0.5084) H15C(0.6482) Fixed Z: H2A(0.1365) H2B(0.0762) H3A(0.0361) H3B(0.0952) H5(0.1415) H7(0.1834) H8(0.1303) H9A(0.0853) H9B(0.149) H9C(0.103) H10A(0.0415) H10B(0.018) H10C(0.0408) H11A(-0.0003) H11B(0.0314) H11C(0.0409) H12A(0.1176) H12B(0.1703) H13A(0.1699) H13B(0.2205) H15A(0.2229) H15B(0.2775) H15C(0.263) This report has been created with Olex2, compiled on 2014.06.27 svn.r2953 for OlexSys. Please let us know if there are any errors or if you would like to have additional features.
4. Curriculum Vitae

Personal data:

Name: Nanaji Arisetti

Date of birth: 01.07.1987 in Andhra Pradesh, India

Marital status: Unmarried

Nationality: Indian

Education:

2011-2015 PhD thesis at the University of Regensburg under supervision of Prof. Dr. Oliver Reiser, as a fellow of DAAD

2009-2011 Junior Research Fellow (JRF) at the Indian Institute of Chemical Technology (IICT), Hyderabad:

Organic transformations by using nano-sized Metal oxides (Baeyer-Villiger oxidation Reactions)

2007-2009 Master of Science at the Andhra University, Visakhapatnam, India

Bioinorganic Chemistry

2004-2007 Bachelor of Science at the Andhra University, Visakhapatnam, India

Chemistry, Botany, Zoology (CBZ)

Languages:

Telugu (Native)

English
Professional references:

Prof. Dr. Oliver Reiser
University of Regensburg
Institute of Organic Chemistry
Universitätsstr 31
D-93053 Regensburg
Germany
Phone: +49-941-9434631
E-mail: oliver.reiser@chemie.uni-regensburg.de

5. List of Publications:


6. Poster Presentation and Scientific Meetings:

1. Participated in “Indian Science Congress (ISCA)” held at, Andhra University, India on 1st to 7th January 2008.

2. National Symposium on “Current Development in Organic Chemistry” held at Department of Chemistry (Organic Division) Andhra University, India on 12th & 14th Dec- 2008.

3. Participated in “International Symposium on Analytical Chemistry” at Andhra University, India during November 2-7, 2008.
Participated in “INDO-NIMS Workshop on Advanced Materials” held at Indian Institute of Chemical Technology (IICT, India) Dec-22-23rd, 2009.

Participated in 12th CRSI National symposium held at IICT organized by Chemical Research Society of India (CRSI) during February 2-5, 2010.

Participated in Heidelberg Forum of Molecular Catalysis (HFMC), held at Heidelberg University, Germany 2013 (Poster presentation).

Participated in GDCh-Wissenschaftsforum Chemie, held at Darmstadt University, Germany, Oct-01-04, 2013 (Poster presentation).

Participated in 4th INDIGO PhD research conference, held at University of Regensburg, Germany Oct 6-10, 2013.
F. References:


F. References:


47. Tundis, R.; Loizzo, M. R.; Menichini, F.; Bonesi, M.; Colica, C.; Menichini, F. *Chemistry and Biodiversity* 2011, 8, 1152-1162.


F. References:


F. References:


F. References:


F. References:


F. References:


F. References:


G. Acknowledgement

I wish to express my sincere gratitude towards my research supervisor Prof. Dr. Oliver Reiser, whose knowledge and vast experience has inspired me at every stage of my tenure and helped me achieve these targets. His suggestions, constructive criticisms and constant encouragement made me to grow as chemist, as well as a good researcher.

I thank Prof. Oliver Reiser Secretary Mrs. Antje Weigert for her help and support regarding all the academic office work at the university and matters related to VISA throughout my stay in Regensburg.

I am grateful to DAAD (German Academic Exchange Service) for the financial support throughout my PhD study. Besides the financial support for my PhD study, the DAAD gave me an opportunity to know about Germany, its people and its culture. I am very much thankful to DAAD in that regard. I am thankful to all my teachers who taught the wonderful language Deutsch, at Goethe-Institute, Mannheim during my DAAD six month language course.

I am very grateful for the technical support provided by Dr. Peter Kreitmeier, Klaus Döring, Helena Konkel, Roxane Harteis and Brigitte Eichenseher. They did all kinds of jobs that made everyday life much easier.

I am thankful to Dr. Sabine Amslinger for her discussions and suggestions on bioactive molecules, which I worked in early part of my PhD work.

I thank all my lab colleagues for keeping friendly atmosphere in the lab and cooperation throughout my research. My special thanks to: Francesca Besostri, Soraia Fernandes, Saerom Park, Viktor Kais, Daniel Dobler, Corina Eichenseer, Thomas Ertl, Sabine Kerres, Martin Hofmann, Verena Lehner, Matthias Gnhan, Benjamin Kastl, Christian Faderal, Thomas Rawner, Daniel Rackl, Santosh Pagire, Andreas Okun, Christian Lankes, Dr. Andreas Kreuzer, Matthias Knorn, Sabine Fürst, Dr. Lee, Dr. Jian Zhi, Dr. Adela Carillo, Dr. Paul Kohls, Dr. Quirin Kainz, Dr. Andreas Bergmann, Dr. Datta Bagal, Dr. Ludwig Pilsl, Dr. Roland Linhardt, Dr. Kathrin Ulbrich, Dr. Michael Pirtsch, Dr. Sudipta Roy, Dr. Michael Schwarz, Dr. Pietro Di Stefano, Dr. Julian Bodensteiner, Dr. Suja Paria, Dr. Sebastian Wittmann, Dr. Klaus Harrar.
Declaration

Herewith I declare that I have made this existing work single-handedly. I have only used the stated utilities.

Regensburg, 04.05.2015

Nanaji Arisetti