Development of the Interrupted Nazarov Cyclization of Allenyl Vinyl Ketones, with Application to the Total Synthesis of the Cyclooctane Natural Product Roseadione

by

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Submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy at

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Halifax, Nova Scotia
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There is no such thing as failure - only success and learning experiences.
LIST OF FIGURES

Figure 1 Nazarov reactivity increases with α-substitution ........................................... 8
Figure 2 Steric rationale behind increased reactivity of allenyl vinyl ketones ............ 12
Figure 3 Type 1, Type 2, and Type 3 AVKs ................................................................. 26
Figure 4 X-ray crystal structure (ORTEP) of compound 38 ................................. 46
Figure 5 X-ray crystal structure (ORTEP) of compound 50 ................................. 49
Figure 6 Conformations of AVKs calculated as calculated by QTAIM methods (RI-MP2/cc-pvdz) ......................................................................................... 52
Figure 7 X-ray crystal structure (ORTEP) of compound 67 ................................. 56
Figure 8 X-ray structure (ORTEP) of compound 85 ............................................. 62
Figure 9 X-ray crystal structure of compound 90 .................................................... 99
Figure 10 a) Selected atomic charges and b) delocalization indices for the oxyallyl cations 153 - 155, in their lowest-energy conformations, as calculated using RI-MP2/cc-pvdz ................................................................. 118
Figure 11 Reactions of AVKs 26 and 35 with trans-piperylene occur with the same regioselectivity ............................................................. 119
Figure 12 Magnitude of KIEs of atoms at position(s) a and/or b of 185 – 187 could discriminate between concerted and stepwise mechanisms in reactions with AVKs ........................................................................ 206
LIST OF SCHEMES

Scheme 1  Pericyclic reactions are concerted, involve $\pi$–electrons, and proceed through a cyclic transition state .....................................................2

Scheme 2  The five sub-divisions of pericyclic reactions ........................................3

Scheme 3  Mechanism of the Nazarov reaction ......................................................4

Scheme 4  Diastereospecificity in the Nazarov cyclization for both a) thermal and b) photochemical processes .........................................................5

Scheme 5  Enantioselective Nazarov cyclization promoted by a chiral Lewis acid ......5

Scheme 6  Nazarov reactions often give non-regioselective elimination .................6

Scheme 7  Silicon-directed Nazarov reactions give regioselective elimination ........7

Scheme 8  Fluorine-directed Nazarov reactions give regioselective elimination ........7

Scheme 9  Rationale behind the design of the polarized Nazarov reaction ................9

Scheme 10 The polarized Nazarov reaction with only one “polar” $\alpha$-subsituent ....9

Scheme 11 The interrupted Nazarov reaction ..........................................................10

Scheme 12 An intramolecular Nazarov reaction .....................................................11

Scheme 13 Hashmi’s approach to the Nazarov cyclization of allenyl vinyl ketones ....11

Scheme 14 Tius’ approach to the Nazarov cyclization of allenyl vinyl ketones .......13

Scheme 15 Allenyl ethers undergo amine-intercepted interrupted Nazarov reactions ..14

Scheme 16 Total synthesis of racemic trichodiene ....................................................15

Scheme 17 Total synthesis of racemic siliphinene ...................................................15

Scheme 18 Total synthesis of racemic roseophilin ..................................................16

Scheme 19 Total synthesis of racemic terpestacin ..................................................17

Scheme 20 Hypothetical interrupted Nazarov reaction of allenyl vinyl ketones .......18

Scheme 21 Synthetic route to access allenyl ketones 20 .....................................20

Scheme 22 Alternative synthetic route to access allenyl ketones 20 .................20
Scheme 23 General synthetic route to access AVKs 23 ........................................ 21
Scheme 24 Regioselective synthesis of alcohol 25b ............................................... 23
Scheme 25 Synthesis of AVKs 26 – 32 ................................................................. 23
Scheme 26 Attempted oxidation of alcohols 25b and 25d was unsuccessful .......... 24
Scheme 27 Synthesis of AVKs 35 – 37 ................................................................. 25
Scheme 28 Origin of alcohol oxygen is from TFA-trapped intermediate 39 ........... 46
Scheme 29 Reactions of AVKs 35 – 37 in the presence of trifluoroacetic acid ........ 48
Scheme 30 Reactions of AVKs 35 – 37 in the presence of BF₃·Et₂O and SiO₂ .......... 50
Scheme 31 Proposed mechanism for formation of 67 from 30 in presence of InCl₃ .... 56
Scheme 32 Comparison of sublimed and residual TiBr₄ ..................................... 58
Scheme 33 Proposed mechanism for the synthesis of multifunctionalized cyclopent-2-enones from AVKs ................................................................. 59
Scheme 34 Scope of Br₂/TiBr₄-mediated Nazarov reaction of AVKs .................... 60
Scheme 35 Reaction of AVK 26 with Br₂/TFA ....................................................... 62
Scheme 36 Tandem Nazarov/[4 + 3] reaction ....................................................... 95
Scheme 37 Tandem Nazarov/[3 + 2] reaction ....................................................... 96
Scheme 38 Nazarov reaction followed by single carbon-carbon bond formation .... 96
Scheme 39 Proposed equilibration of bicyclic ketones to a single ring system via ring-opening to a zwitterionic intermediate ............................................. 100
Scheme 40 Reaction of AVK 36 with 2,3-dimethylbutadiene ............................. 102
Scheme 41 Ring-opening of silyl-substituted [3 + 2] products at room temperature ... 104
Scheme 42 Attempted interrupted Nazarov reaction of AVK 26 with 113 .......... 106
Scheme 43 Reactions of AVKs 27 and 29 with 3,4-dimethoxystyrene ................... 108
Scheme 44 Michael reactions of AVK 26 with pyrrole .................................... 112
Scheme 45 Michael reactions of AVK 26 with indole ..................................... 114
Scheme 46 Reactions of AVKs 27 and 29 with N-methylindole and 2,3-dimethylindole ................................................................. 114

Scheme 47 Bulkier reagents favour products trapped at position c ..................... 116

Scheme 48 Proposed transition state model leading to 138 ............................. 117

Scheme 49 a) Geometry of cycloaddition that would lead to [4 + 3] product 86a. b) Alternative stepwise pathway that would lead to the undetected epimer 86b ............................................................................. 120

Scheme 50 Geometry of cycloaddition that would lead to [4 + 3] product 91a ........ 121

Scheme 51 Formation of compound 128 via a dipolar [3 + 2]/ring opening process... 122

Scheme 52 Retrosynthetic disconnection of (+)-roseadione (162) leading to AVK 164 ............................................................................. 181

Scheme 53 Intramolecular [4 + 3] cyclizations in which the tether was a) unsubstituted, or b) substituted, at the dienylic position .................... 182

Scheme 54 Intramolecular [4 + 3] cyclization in which substitution at the dienylic position of the tether and on the five-membered ring results was “matched” ........................................................................ 183

Scheme 55 Intramolecular [4 + 3] cyclization in which substitution at the dienylic position of the tether and on the five-membered ring results was “mismatched” .................................................................. 184

Scheme 56 Some alternative methods for the construction of eight-membered ring systems ...................................................................... 185

Scheme 57 Retrosynthetic disassembly of AVK 164 ........................................ 187

Scheme 58 Synthesis of ketone 176a ................................................................. 188

Scheme 59 Proposed Petersen olefination strategy for the synthesis of thioacetal 175a ............................................................................. 189

Scheme 60 Synthesis of dithiane 177a, with failed elaboration into thioacetal 175a... 190

Scheme 61 Second-generation proposal for the synthesis of acetal 175 ............... 190

Scheme 62 Failed attempts at the synthesis of vinyl halides 182a-d .................... 191

Scheme 63 Synthesis of alkenes 182e and 182f ..................................................... 192

Scheme 64 Synthesis of ketal 177b, with failed elaboration into acetals 175b-c ...... 192
Scheme 65  Unsuccessful synthesis of dienones 183a-b ................................. 193

Scheme 66  Retrosynthetic disconnection of (+)-roseadione (162) leading to ketone 163a .............................................................. 205
LIST OF TABLES

Table 1  Synthesis of homopropargyl and allenyl vinyl alcohols ..................... 22
Table 2  Screening for suitable promoters for the Nazarov reaction of AVK 26 ........ 45
Table 3  Scope of the TFA-initiated Nazarov reaction of AVKs ....................... 47
Table 4  Screening of other halogen-bearing Lewis acids for the interrupted
Nazarov cyclization of AVK 26 ................................................. 53
Table 5  Scope of indium-mediated Nazarov reaction of AVKs ....................... 55
Table 6  Scope of TiBr\textsubscript{4}-mediated Nazarov reaction of AVKs ............... 57
Table 7  Scope of I\textsubscript{2}/TFA-mediated Nazarov reaction of AVKs ............... 61
Table 8  Reactions of AVK 26 with butadiene derivatives ............................ 98
Table 9  Reactions of AVKs 27, 29, 35, and 37 with butadiene derivatives ...... 101
Table 10 Reactions of AVK 26 with allylsilanes ........................................ 103
Table 11 Reactions of AVK 26 with electron-rich alkenes ............................ 105
Table 12 Reactions of AVK 26 with styrenes ............................................. 107
Table 13 Reactions of AVK 26 with cyclic dienes ....................................... 109
Table 14 Reactions of AVK 26 with N-substituted pyrroles ........................... 111
Table 15 Reactions of AVK 26 with substituted indoles ............................... 113
ABSTRACT

The development of the interrupted Nazarov cyclization of allenyl vinyl ketones is presented. The intermediate oxyallyl cation, derived from an allenyl vinyl ketone, may be trapped efficiently by a divergent array of nucleophilic species generating functionalized cyclopent-2-enone products. Allenyl vinyl ketones are also a versatile source of cyclic molecules via a tandem reaction sequence terminated via reaction with acyclic dienes, cyclic dienes, aza-heterocycles, electron-rich alkenes, or styrenes by the formation of an additional ring by a [4 + 3] and/or [3 + 2] cyclization or by the formation of one additional carbon-carbon bond. The bicyclic compounds generated by these processes are densely substituted, and would be difficult to access as succinctly in other ways. The products of these interrupted Nazarov reactions generally reflect excellent regio- and stereoselectivity in the trapping reaction. In some instances, equilibrating conditions were shown to enhance the proportion of one product at the expense of another or to provide a different carbon skeleton. This process appears fairly general, and can be conducted with unsubstituted or alkyl, aromatic, or heteroaromatic allenyl vinyl ketones. The exceptional affinity of allenyl vinyl ketones to undergo interrupted Nazarov reactions is likely a result of the increased longevity of the intermediate oxyallyl cation, due in part to the increased resonance stabilization provided by the allene unit. The high regioselectivity noted in the trapping process was computationally and experimentally confirmed to be a result of a localization of the positive charge in the intermediate oxyallyl cation.

The application of this recently developed methodology towards the synthesis of the natural product (+)-roseadione is also described. The tandem Nazarov/[4 + 3] cascade of allenyl vinyl ketones provides a unique manner in which to access the tricyclic core of this cyclooctanoid natural product, a molecule which, to date, has never been synthesized.
LIST OF ABBREVIATIONS AND SYMBOLS USED

α          alpha
Å           angstrom
β           beta
δ           chemical shift or partial charge
Δ           heat
Ac          acetate
aq          aqueous
AVK         allenyl vinyl ketone
Bn          benzyl
br          broad
BOC         tert-butoxycarbonyl
n-Bu        normal-butyl
t-Bu        tertiary-butyl
cod         1,5-cyclooctadiene
COSY        correlation spectroscopy
Cp          cyclopentadiene
Cy          cyclohexyl
d           doublet
DABCO       1,4-diazabicyclo[2.2.2]octane
dba         dibenzylidene acetone
DCE         1,2-dichloroethane
dd          doublet of doublets
ddd         doublet of doublet of doublets
DEPT        distortionless enhancement by polarization transfer
DMAP        dimethylaminopyridine
DMF         dimethylformamide
DMP         Dess-Martin periodinane
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
</tr>
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<tr>
<td>DMS</td>
<td>dimethylsulfide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethylsulfoxide</td>
</tr>
<tr>
<td>dpff</td>
<td>1,1’-bis(diphenylphosphino)ferrocene</td>
</tr>
<tr>
<td>dq</td>
<td>doublet of quartets</td>
</tr>
<tr>
<td>dr</td>
<td>diastereomeric ratio</td>
</tr>
<tr>
<td>dt</td>
<td>doublet of triplets</td>
</tr>
<tr>
<td>E</td>
<td>trans</td>
</tr>
<tr>
<td>EDG</td>
<td>electron donating group</td>
</tr>
<tr>
<td>equiv</td>
<td>equivalent(s)</td>
</tr>
<tr>
<td>ESI</td>
<td>electrospray ionization</td>
</tr>
<tr>
<td>Et</td>
<td>ethyl</td>
</tr>
<tr>
<td>EWG</td>
<td>electron withdrawing group</td>
</tr>
<tr>
<td>FT</td>
<td>Fourier transform</td>
</tr>
<tr>
<td>h</td>
<td>hour(s)</td>
</tr>
<tr>
<td>HMBC</td>
<td>heteronuclear multiple bond coherence</td>
</tr>
<tr>
<td>HMDS</td>
<td>hexamethyldisilazide</td>
</tr>
<tr>
<td>HOMO</td>
<td>highest occupied molecular orbital</td>
</tr>
<tr>
<td>HRMS</td>
<td>high resolution mass spectrometry</td>
</tr>
<tr>
<td>HSQC</td>
<td>heteronuclear single quantum coherence</td>
</tr>
<tr>
<td>Hz</td>
<td>hertz</td>
</tr>
<tr>
<td>IR</td>
<td>infrared</td>
</tr>
<tr>
<td>$^{n}J_{XX}$</td>
<td>$n$ bond coupling constant between atom X and atom X’</td>
</tr>
<tr>
<td>KIE</td>
<td>kinetic isotope effect</td>
</tr>
<tr>
<td>LA</td>
<td>Lewis acid</td>
</tr>
<tr>
<td>LDA</td>
<td>lithium diisopropyl amide</td>
</tr>
<tr>
<td>LUMO</td>
<td>lowest unoccupied molecular orbital</td>
</tr>
<tr>
<td>m</td>
<td>multiplet</td>
</tr>
<tr>
<td>Me</td>
<td>methyl</td>
</tr>
<tr>
<td>Symbol</td>
<td>Definition</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>min</td>
<td>minute(s)</td>
</tr>
<tr>
<td>MHz</td>
<td>megahertz</td>
</tr>
<tr>
<td>MOC</td>
<td>methyloxy carbonyl</td>
</tr>
<tr>
<td>mol</td>
<td>mole(s)</td>
</tr>
<tr>
<td>mp</td>
<td>melting point</td>
</tr>
<tr>
<td>Ms</td>
<td>methanesulfonyl</td>
</tr>
<tr>
<td>NOE</td>
<td>nuclear Overhauser effect</td>
</tr>
<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>ORTEP</td>
<td>Oak Ridge thermal ellipsoid plot</td>
</tr>
<tr>
<td>PG</td>
<td>protecting group</td>
</tr>
<tr>
<td>Ph</td>
<td>phenyl</td>
</tr>
<tr>
<td>PMP</td>
<td>para-methoxyphenyl</td>
</tr>
<tr>
<td>ppm</td>
<td>parts per million</td>
</tr>
<tr>
<td>i-Pr</td>
<td>iso-propyl</td>
</tr>
<tr>
<td>n-Pr</td>
<td>normal-propyl</td>
</tr>
<tr>
<td>PTP</td>
<td>para-(trifluoromethyl)phenyl</td>
</tr>
<tr>
<td>q</td>
<td>quartet</td>
</tr>
<tr>
<td>QTAIM</td>
<td>quantum theory of atoms in molecules</td>
</tr>
<tr>
<td>rt</td>
<td>room temperature</td>
</tr>
<tr>
<td>s</td>
<td>singlet</td>
</tr>
<tr>
<td>SOMO</td>
<td>singly occupied molecular orbital</td>
</tr>
<tr>
<td>TBS</td>
<td>tert-butyldimethylsilyl</td>
</tr>
<tr>
<td>t</td>
<td>triplet</td>
</tr>
<tr>
<td>td</td>
<td>triplet of doublets</td>
</tr>
<tr>
<td>TEA</td>
<td>triethylamine</td>
</tr>
<tr>
<td>Tf</td>
<td>trifluoromethanesulfonyl</td>
</tr>
<tr>
<td>TFA</td>
<td>trifluoroacetic acid</td>
</tr>
<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
</tr>
<tr>
<td>--------------</td>
<td>-----------</td>
</tr>
<tr>
<td>TIPS</td>
<td>triisopropylsilyl</td>
</tr>
<tr>
<td>TLC</td>
<td>thin layer chromatography</td>
</tr>
<tr>
<td>TMEDA</td>
<td>tetramethylethylenediamine</td>
</tr>
<tr>
<td>TMP</td>
<td>2,4,6-trimethoxyphenyl</td>
</tr>
<tr>
<td>TMS</td>
<td>trimethylsilyl</td>
</tr>
<tr>
<td>TOF</td>
<td>time-of-flight</td>
</tr>
<tr>
<td>tq</td>
<td>triplet of quartets</td>
</tr>
<tr>
<td>Ts</td>
<td>toluenesulfonyl</td>
</tr>
<tr>
<td>p-TSA</td>
<td>para-toluenesulfonic acid</td>
</tr>
<tr>
<td>UV</td>
<td>ultraviolet</td>
</tr>
<tr>
<td>Z</td>
<td>cis</td>
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CHAPTER 1. INTRODUCTION

1.1 New Reaction Discovery

Organic synthesis has come a long way in the past century. With the advent of increasingly sophisticated instruments as tools for both synthesis and characterization, chemists are now able to conduct and analyze a plethora of chemical transformations in rapid succession. This has facilitated the discovery of new reagents and catalysts that can now essentially conduct any imagined transformation. As a result, our understanding of chemical reactivity and reaction mechanism has increased drastically, culminating in the invention of a multitude of new reactions and allowing for the synthesis of the most complex of molecular targets.\(^1\)

Though the wide range of synthetic transformations available today is impressive, many reaction processes are far from perfect. Ideally, the synthesis of a single complex target would be accomplished in high yield and a minimal number of steps through the selection of a series of chemo-, regio-, and stereoselective transformations, with readily available starting materials using inexpensive and non-toxic reagents. However, several important transformations continue to rely on expensive and/or toxic reagents for optimal results. Furthermore chemo-, regio-, and stereoselectivity issues often necessitate the use of a lengthy sequence in order obtain a specific molecular target. Finally, in many instances a particular transformation will consistently result in low yield, or fail entirely, for a particular substrate class. Thus, much research in organic chemistry is still devoted to new reaction discovery, which can then be applied to the synthesis of complex molecular targets in a more rapid and efficient manner.\(^1\)
1.2 Pericyclic Reactions

Pericyclic reactions are among the most powerful and best understood chemical transformations available to the synthetic chemist, mainly as a result that many reactions will predictably lead to products in high levels of regio-, chemo-, and diastereoselectivity. Hence, pericyclic reactions have long been exploited in the construction of complex ring systems.

The defining feature of pericyclic reactions is that the reorganization of chemical bonds that occurs as a result of a starting material being converted into a product occurs in a concerted manner through a cyclic transition state, and thus unlike most chemical transformations, pericyclic reactions do not involve any intermediates (Scheme 1).

```
\[ \begin{array}{c}
  \text{||} \\
  \text{\rightarrow} \\
  \text{[\text{\textcircled{\+}}]} \\
  \text{\rightarrow} \\
  \text{\textcircled{}} \\
\end{array} \]
```

Scheme 1 Pericyclic reactions are concerted, involve π-electrons, and proceed through a cyclic transition state.

Pericyclic reactions may be categorized according to five sub-divisions: cycloadditions, electrocyclizations, sigmatropic rearrangements, group-transfer reactions, and cheletropic reactions (Scheme 2). Cycloadditions result in the formation of two or more σ-bonds between the termini of two or more conjugated systems, electrocyclizations result in the formation of one σ-bond between the termini of a conjugated system, sigmatropic rearrangements result in the conversion of one σ-bond into another σ-bond as a substituent migrates across a π-system, group-transfer reactions result in the conversion of one π-bond into one σ-bond as a substituent migrates, and
cheletropic reactions result in the conversion of a lone pair and a $\pi$-bond into two $\sigma$-bonds. An example of each is given in Scheme 2.

a) **Cycloaddition** (e.g. Diels-Alder reaction)

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{Me}
\end{array}
+ \begin{array}{c}
\text{OTMS}
\end{array} \xrightarrow{\Delta \text{ or } BF_3 \cdot OEt_2} \begin{array}{c}
\text{H} \\
\text{Ome}
\end{array}
\]

b) **Electrocyclization**
(e.g. 6$\pi$ electrocyclization)

\[
\begin{array}{c}
\text{H}
\end{array} \xrightarrow{\Delta} \begin{array}{c}
\text{H}
\end{array}
\]

c) **Sigmatropic Rearrangement**
(e.g. Cope rearrangement)

\[
\begin{array}{c}
\text{H}
\end{array} \xrightarrow{\Delta} \begin{array}{c}
\text{H}
\end{array}
\]

d) **Group Transfer Reaction**
(e.g. ene reaction)

\[
\begin{array}{c}
\text{H}
\end{array} \xrightarrow{\Delta} \begin{array}{c}
\text{H}
\end{array}
\]

e) **Cheletropic Reaction**
(e.g. Simmons-Smith reaction)

\[
\begin{array}{c}
\text{H}
\end{array} + \begin{array}{c}
\text{CH}_2\text{I}_2 \xrightarrow{\text{Zn-Cu}} \begin{array}{c}
\text{H}
\end{array}
\]

Scheme 2 The five sub-divisions of pericyclic reactions.

With the advent of chiral catalysts, many pericyclic reactions have been developed to favour a high degree of enantioselectivity. Thus, pericyclic reactions continue to have an important role in the synthesis of complex natural products.

### 1.3 The Nazarov Reaction

A pericyclic reaction that is rapidly gaining popularity for the formation of five-membered rings is the Nazarov reaction, a 4$\pi$ electrocyclization that traditionally yields cyclopent-2-enones from divinyl ketones (Scheme 3).\(^2\)\(^3\) This reaction is usually initiated
by a Brønsted or Lewis acid, generating a pentadienyl cation (1) that undergoes ring closure to generate a cyclic oxyallyl carbocation (2), which undergoes deprotonation to yield a cyclopent-2-enone (3).

Scheme 3 Mechanism of the Nazarov reaction.

1.3.1 Stereoselectivity in the Nazarov Reaction

Ring closure of the Nazarov reaction is diastereospecific, and is governed by the Woodward-Hoffman rules. When the reaction is initiated by an acid catalyst, the HOMO is involved, and thus the substituents at both termini rotate in the same direction (conrotation) (Scheme 4a). The reaction can also be photochemically initiated, in which case the SOMO (generated by the promotion of a HOMO electron to the LUMO) is involved, and thus the substituents at both termini rotate in opposite directions (disrotation) (Scheme 4b).
Scheme 4 Diastereospecificity in the Nazarov cyclization for both a) thermal and b) photochemical processes.

Furthermore, the electrocyclization step may proceed in either a clockwise or counterclockwise manner (termed torquoselectivity), generating a mixture of enantiomers. Many recent efforts have been directed towards the achievement of an enantioselective Nazarov reaction using chiral Lewis acids that promote torquoselectivity and generate a single enantiomer (Scheme 5).\(^4\)

Scheme 5 Enantioselective Nazarov cyclization promoted by a chiral Lewis acid.
1.3.2 Regioselectivity in the Nazarov Reaction

One drawback of the Nazarov reaction, however, is that the regioselectivity of the proton elimination step is often poor, which can generate a mixture of products in some cases (Scheme 6).

Scheme 6 Nazarov reactions often give non-regioselective elimination.

A general solution to this problem was introduced by Denmark and co-workers with the introduction of a trialkylsilyl group,\(^5\) which ensures controlled collapse of the cyclopentadienyl cation due to the stabilization associated with the positive charge \(\beta\) to the silicon atom (Scheme 7).\(^6\)
Scheme 7 Silicon-directed Nazarov reactions give regioselective elimination.

Following the success of the silicon-directed Nazarov cyclizations, Ichikawa and co-workers have recently pioneered fluorine-directed Nazarov cyclizations, which take advantage of the $\beta$-destabilization of a positive charge by fluorine atoms to ensure regioselective elimination (Scheme 8).

Scheme 8 Fluorine-directed Nazarov reactions give regioselective elimination.

### 1.3.3 Steric Influence of $\alpha$-Substituents in the Nazarov Reaction

Another drawback of the Nazarov reaction is that often very strong acids are required to promote cyclization. However, cyclization efficiency can be greatly increased with the introduction of one or more alkyl substituents $\alpha$ to the carbonyl group (Figure...
This is largely attributed to an increase in the population of \textit{s-trans} enone conformers, which are predominantly in the orientation required for cyclization.

\[ \begin{array}{ccc}
\text{\textit{s-trans}/\textit{s-trans}} & \text{\textit{s-trans}/\textit{s-cis}} & \text{\textit{s-cis}/\textit{s-cis}} \\
\includegraphics[width=0.3\textwidth]{diagram.png} & & \\
R^1, R^2 = \text{alkyl} & R^1 = \text{alkyl}, R^2 = H & R^1, R^2 = H \\
\end{array} \]

\textit{decreasing Nazarov reactivity}

Figure 1 Nazarov reactivity increases with \(\alpha\)-substitution.

When there are no \(\alpha\)-substituents, the divinyl ketone will prefer to adopt an \textit{s-cis/s-cis} conformation to minimize steric interactions between the two sets of methylene protons. However, when \(\alpha\)-substituents are introduced, the unfavourable steric interactions experienced in the \textit{s-cis} conformation are much greater than those experienced by the methylene protons, and thus the \textit{s-trans} conformation is favoured.

\subsection*{1.4 The Polarized Nazarov Reaction}

The rate of the Nazarov reaction is also sensitive to electronic factors. This was first investigated systematically by Frontier and co-workers, who designed divinyl ketones containing one electron-rich double bond (\textit{vinyl nucleophile}) and one electron-poor double bond (\textit{vinyl electrophile}), which allowed for a “push/pull” mechanism (Scheme 9).
Scheme 9 Rationale behind the design of the polarized Nazarov reaction.

Frontier and co-workers noted a tremendous acceleration in the reaction rate with such polarized substrates – reaction times of only two hours were required to effect quantitative conversion of substrates such as 4 using a mild Lewis acid such as Cu(OTf)$_2$. As an additional advantage, the elimination step was regioselective, regenerating the “nucleophilic” double bond due to stabilization of the α-positive charge by the electron donating group (or similarly destabilization of the positive charge by the electron withdrawing group). Furthermore, Frontier and co-workers noted that the addition of only one electron-donating or electron-withdrawing group at either α-position was necessary for good reactivity, although the addition of the electron-rich 2,4,6-trimethoxyphenyl at one β-position was needed to achieve higher yields (Scheme 10).

Scheme 10 The polarized Nazarov reaction with only one “polar” α-subsituent.
1.5 The Interrupted Nazarov Reaction

West and co-workers have shown that the oxyallyl cationic intermediate of the Nazarov reaction can undergo trapping by a suitable nucleophile in lieu of the elimination step (Scheme 11), and this group has since coined reactions of this type as “interrupted” Nazarov reactions.¹⁰

The source of the nucleophile can be from the acid itself, as shown in Scheme 11, or can be present in the reaction mixture. West has shown this reaction to be highly successful with many nucleophilic species such as alkenes,¹¹ arenes,¹² halides,¹³ and hydride.¹⁴ The West group has even demonstrated that an intramolecular cascade process involving internal alkenes can be initiated, forming a complex ring system (Scheme 12).¹⁵ In the case of 5, six new stereocenters have been formed diastereoselectively in one step!
1.6 The Nazarov Reaction of Allenyl Vinyl Ketones

The Hashmi group was the first to report that when one of the alkenes of a divinyl ketone is replaced by an allene, a significant rate enhancement is observed, and that allenyl vinyl ketones undergo Nazarov cyclization spontaneously during silica gel chromatography to generate their corresponding cyclopent-2-enones (Scheme 13).16
It has been postulated that the increase in reactivity seen with allenyl vinyl ketones with respect to their divinyl ketone analogues is twofold. The first is a result of the alleviation of the steric strain of the sp-hybridized central carbon upon cyclization. The second is conformational in nature. A higher number of molecules might prefer to adopt the reactive s-trans conformation required for Nazarov cyclization, as steric interactions would be at a minimum (Figure 2).²ᵃ

![Figure 2 Steric rationale behind increased reactivity of allenyl vinyl ketones.](image)

However, the results of Hashmi and co-workers did not seem general (3 examples, 24%, 54%, and 59% yield),¹⁶ and it was not until extensive work by the Tius group with allenyl ethers that allenyl vinyl ketones were popularized as substrates.¹⁷ Allenyl ethers (6) have been shown by Tius and co-workers to be extremely reactive – these molecules are not usually isolable, as following their formation they cyclize spontaneously on work-up to generate the corresponding Nazarov-cyclized products (Scheme 14).¹⁸
Scheme 14 Tius’ approach to the Nazarov cyclization of allenyl vinyl ketones.

It is noteworthy that the elimination product is not observed in this case – the major product is usually a 5-alkylidene-2-hydroxycyclopent-2-enone (7) (Scheme 14), though the Tius group has also shown that if an amine is present in the reaction mixture, 4-amino-2-methoxycyclopent-2-ones (8) can be generated as well (Scheme 15). The Tius group has recently shown that similar products can also be generated via trapping with indoles.
Scheme 15 Allenyl ethers undergo amine-intercepted interrupted Nazarov reactions.

1.7 Synthetic Applications of the Nazarov Reaction

The power of any synthetic methodology is demonstrated in its successful application to the synthesis of a complex natural product. Hence, selected total syntheses utilizing variants of the Nazarov reaction that have been previously discussed are listed below.

1.7.1 Use of the “Normal” Nazarov Reaction in Synthesis

Harding and co-workers synthesized racemic trichodiene (9) in 1990, using the Nazarov reaction as a key step. The Nazarov reaction was chosen as the natural product contains two adjacent quaternary stereocenters, and the diastereospecific nature of the Nazarov reaction would ensure total \( \text{trans} \) selectivity (Scheme 16).
Scheme 16 Total synthesis of racemic trichodiene.

Miesch and co-workers utilized the silicon-directed Nazarov cyclization to synthesize the core of racemic silphinene (12) in 1997.\textsuperscript{22} The benzyl group of 10 ensured counterclockwise conrotation generating the desired diastereomer (11), and the TMS group of 10 directed regioselective elimination (Scheme 17).

Scheme 17 Total synthesis of racemic siliphinene.

1.7.2 Use of the Polarized Nazarov Reaction in Synthesis

Frontier and co-workers recently utilized the polarized Nazarov cyclization to assemble the substituted pyrrole core (13) of racemic roseophilin (14) diastereoselectively (Scheme 18).\textsuperscript{3b}
1.7.3 Use of the Nazarov Cyclization of Allenyl Ethers in Synthesis

Tius and co-workers have used the Nazarov cyclization of allenyl ethers to assemble the core 2-hydroxycyclopent-2-enone unit (15) in their total synthesis of racemic terpestacin (16) (Scheme 19).\(^\text{23}\)
1.8 Proposed Exploitation of Allenyl Vinyl Ketones in Interrupted Nazarov Reactions

We hypothesized that allenyl vinyl ketones (AVKs) of the general type 17 might be particularly well suited to undergo interrupted Nazarov reactions, due to the proposed longevity of oxyallyl cation 18, as a result of the increased resonance stabilization provided by the allene unit. In addition, the alternative elimination pathway generating a cyclopent-2-enone necessitates the intermediacy of fulvene 19, and is thus likely disfavoured. Furthermore, the oxyallyl cation 18 generated from AVKs has, theoretically, three positions to which a nucleophile might add, and thus such a process has the potential to rapidly generate a diverse set of cyclopent-2-enone containing compounds in one step, depending on reaction conditions, from a single, simple, starting material (Scheme 20).
Scheme 20 Hypothetical interrupted Nazarov reaction of allenyl vinyl ketones.
CHAPTER 2. SYNTHESIS OF ALLENYL VINYL KETONES

2.1 Introduction

The synthesis of the starting AVKs (17) will be discussed initially. They are interesting compounds in themselves, as at the initiation of this project there had been no general route reported for their preparation, isolation, and characterization. Based on the studies conducted by the Hashmi group (Section 1.4), it was anticipated that a route could indeed be developed to obtain isolable compounds, but reaction conditions would likely need to be chosen carefully to avoid silica gel chromatography of the final products, as the Hashmi group has shown that they do not survive this purification step (Scheme 13).

The allenyl ketone functionality itself is relatively stable, and there exist numerous traditional methods for its preparation. For allenyl ketones bearing a hydrogen atom on the allene unit adjacent to the carbonyl (20), the most commonly utilized method employs oxidation of a homopropargyl alcohol to the corresponding homopropargyl ketone (Scheme 21). These homopropargyl alcohols are easily synthesized via a Barbier coupling of a terminal propargyl-metal species with an aldehyde (metal = tin, mercury, zinc, or indium), and oxidized using the Dess-Martin periodinane (DMP). Base-induced isomerization yields the allenyl ketone. This isomerization happens in an extremely facile manner with weak bases, generally carbonate or tertiary amine bases, or aluminum oxide. Indeed, terminal homopropargyl ketones are often difficult to isolate as isomerization takes place very readily, even in the presence of silica gel, and thus the allenyl ketone is often obtained quantitatively following chromatography.
Scheme 21. Synthetic route to access allenyl ketones 20.

An alternative, well-used method for the synthesis of AVKs 20, is through the $S_N2'$ displacement of an alkoxide from propargyl alcohols 22 by hydride (Scheme 22)\(^2\). Propargyl alcohols 22 are easily accessed through the addition of the alkynyl lithium derived from 21 to an aldehyde.

Scheme 22 Alternative synthetic route to access allenyl ketones 20.

Allenyl ketones bearing an alkyl group on the allene unit adjacent to the carbonyl (23), on the other hand, are often generated via oxidation of the corresponding allenyl alcohols (Scheme 23); the Swern protocol (DMSO/oxallyl chloride)\(^2\) or Dess-Martin periodinane (DMP) have been shown to be equally effective in this instance. The allenyl alcohols are readily available via a Barbier coupling of an alkyl-substituted propargyl-metal species with an aldehyde (metal = tin, mercury, zinc, or indium).
2.2 Allenyl Vinyl Ketone Synthesis

A series of homopropargyl and allenyl alcohols were synthesized through a Barbier-type coupling procedure (as described in 2.1), using indium\(^{28}\) or zinc\(^{29}\) metal (Table 1). In general, indium metal provided higher overall yields of product. In the case of terminal propargyl-metal species however (entries 3, 5, 15), it is noteworthy that the reaction proceeds with low regioselectivity using indium metal, generating both homopropargyl and allenyl alcohols in a 1.5:1 ratio, respectively. Zinc metal, on the other hand provides homopropargyl alcohols exclusively, albeit in low yield (entries 4, 6, 16). Choice of solvent in both cases also proved important. For reactions mediated by indium, the addition of less methanol, switching from methanol to THF, or switching from saturated aqueous NH\(_4\)Cl to water, results in unconsumed starting material. For reactions mediated by zinc, the MeOH/NH\(_4\)Cl ratio proved important – the addition of less saturated aqueous NH\(_4\)Cl results in unconsumed starting material.

Scheme 23 General synthetic route to access AVKs 23.
Table 1 Synthesis of homopropargyl and allenyl vinyl alcohols.

![Chemical structure](image)

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<sup>a</sup>Conditions: A = indium powder (1.1 equiv), aldehyde (1 equiv), propargyl bromide (1.1 equiv), NH<sub>4</sub>Cl/MeOH (1:3). B = zinc dust (3.3 equiv), aldehyde (1 equiv), propargyl bromide (1.3 equiv), NH<sub>4</sub>Cl/MeOH (5:1),<sup>b</sup> isolated yields.

In order to obtain the allenyl alcohol exclusively as well, the propargyl alcohol derived from α-methylcinnamylaldehyde and propargyl ether 21 was subjected to LiAlH<sub>4</sub> (as described in 2.1), resulting in compound 25b in high yield (Scheme 24).
Oxidation of the allenyl alcohols proved more challenging. “Standard” protocols utilized for similar substrates such as the Swern oxidation or DMP (see Section 2.1) failed, as did other mild reagents such as tetrapropylammonium perruthenate/N-morpholine-N-oxide,\(^3\) \(o\)-iodoxybenzoic acid,\(^3\) and DMP buffered with NaHCO\(_3\) or pyridine. In all cases the starting material was decomposed. However, success was obtained utilizing MnO\(_2\). For allenyl alcohols bearing an alkyl substituent on the allene unit adjacent to the carbonyl and a hydrogen atom on the alkene unit (25a, 25e – 25f), oxidation to the corresponding allenyl ketones proceeded smoothly in 37 – 79% yield (Scheme 25). It is noteworthy that these yields are isolated yields following chromatography on silica gel. This is in contrast to the compounds synthesized by the Hashmi group, which bear a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit. Hashmi’s compounds do not survive chromatography on silica gel (section 1.4).\(^1\)
Unfortunately, this protocol was not amenable to allenyl alcohols bearing an alkyl substituent on the alkene unit adjacent to the carbonyl (Scheme 26), as these derivatives were resistant to oxidation under these conditions resulting in the near quantitative recovery of starting material, even when the more aggressive BaMnO₄ was used as the oxidant.

Scheme 26 Attempted oxidation of alcohols 25b and 25d was unsuccessful.

However, allenyl vinyl ketones bearing a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit (35 and 37), were able to be synthesized from their corresponding homopropargyl alcohols in a two-step oxidation/isomerization sequence (Scheme 27), in 36 – 56% yield. Use of DMP, buffered with NaHCO₃, as oxidant in the first step proved essential. Use of DMP alone failed, as did the Swern protocol, o-iodoxybenzoic acid, and Jones reagent (CrO₃/H₂SO₄), all of which resulted in decomposition of the starting material. Although oxidations with MnO₂ and BaMnO₄ were also attempted, as seen with the allenyl alcohols 25b and 25d, starting material was recovered. For the second, base-mediated isomerization step, triethylamine and K₂CO₃ powder were equally effective, but NaHCO₃, Na₂CO₃, or basic Al₂O₃ all resulted in the decomposition of 33. The yields of this two-step process were determined by ¹H NMR spectroscopy (using 1,3,5-trimethoxybenzene as an internal standard), as attempted purification by silica gel chromatography results only in the
isolation of products of Nazarov cyclization, as observed by the Hashmi group for similar derivatives (Section 1.4). Finally, this method is also amenable to the synthesis of the unsubstituted derivative 36, which bears a hydrogen atom at both positions α to the carbonyl, although in this case the second base-mediated isomerization step is unnecessary; oxidation of the homopropargyl alcohol 24c provides AVK 36 directly. Furthermore, this is an isolated yield following purification by column chromatography, which parallels the reactivity of allenyl vinyl ketones bearing a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit (Scheme 25).

![Scheme 27 Synthesis of AVKs 35 – 37.](image)

For simplicity, AVKs bearing an alkyl substituent on the allene unit adjacent to the carbonyl and a hydrogen atom on the alkene unit will henceforth be categorized as Type 1 AVKs, AVKs bearing a hydrogen atom on the allene unit adjacent to the carbonyl and an alkyl substituent on the alkene unit will be henceforth categorized as Type 2
AVKs, and AVKs bearing a hydrogen atom at both positions α to the carbonyl will be referred to as Type 3 AVKs (Figure 3).

![Chemical Structures]

**Figure 3.** Type 1, Type 2, and Type 3 AVKs.

### 2.3 Summary

Two general methods have been developed for the synthesis and isolation of a variety of allenyl vinyl ketones. Type 1 AVKs were prepared in two steps from commercially available materials, through oxidation of their corresponding allenyl alcohol, in overall yields ranging from 21 – 70%. Type 1 AVKs were found to be fairly stable, as they could be subjected to purification by silica gel chromatography and subsequently stored for prolonged periods. Type 2 AVKs were prepared in three steps from commercially available materials, through oxidation of their corresponding propargyl ketones, in overall yields of 13 - 23%. Type 2 AVKs were found to be much less stable than Type 1 AVKs, and could not be chromatographed or stored for prolonged periods. Type 3 AVKs were prepared in a similar manner as Type 2 AVKs. In contrast to Type 2 AVKs, but similar to Type 1 AVKs, these were amenable to chromatographic purification and could be stored for prolonged periods.
2.4 Experimental Section

2.4.1 General Considerations

All non-aqueous reactions were conducted using oven-dried glassware under an N₂ atmosphere. Reagents were used as received from a commercial supplier without further purification. *p*-Trifluoromethyl-trans-cinnamylaldehyde\(^3\text{5}\) and 1-bromo-2-butyne\(^3\text{6}\) were prepared according to literature procedures. Ms. Rhonda Stoddard is thanked for assistance with the preparation of compounds 24b, 24c, 33, 35, and 36.

Dichloromethane was used freshly distilled from calcium hydride. Tetrahydrofuran and diethyl ether were used freshly distilled from sodium/benzophenone. Ethyl acetate and hexanes were distilled prior to use for column chromatography. All other solvents were used as received.

Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F\(_{254}\)), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or *o*-vanillin in ethanol/H₂SO₄ and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. \(^1\)H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with CDCl₃ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). \(^1\)\(^3\)C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with CDCl₃ as solvent. \(^1\)\(^9\)F NMR spectra were recorded at 225 MHz on a Bruker Avance spectrometer. Infrared spectra were recorded from thin films on a Bruker VECTOR 22 FT-IR instrument using
CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (¹H, ¹³C, and DEPT-135) and two dimensional (COSY, HSQC, and HMBC) NMR spectral data. The ¹H and ¹³C NMR spectra of all compounds may be found in Appendix A.

2.4.2 Preparation and Characterization Data

(E)-4-Methyl-1-phenylhexa-1,4,5-trien-3-ol (25a)

Procedure 1: A saturated aqueous solution of ammonium chloride (30 mL) was added to a methanolic (10 mL) solution of 1-bromo-2-butyne (1.35 mL, 13 mmol) and trans-cinnamylaldehyde (1.7 mL, 13 mmol), and the mixture was cooled to 0°C. Indium powder (100 mesh) (1.7 g, 15 mmol) was then added in four portions (over twenty minutes), and the solution was stirred vigourously for 1 h. The solution was then diluted with diethyl ether, filtered through a pad of Celite, added to a separatory funnel containing a saturated aqueous solution of NaCl, and extracted with diethyl ether (×2). The combined extracts were dried with anhydrous MgSO₄, concentrated, and the product was purified by column chromatography (10% diethyl ether in pentanes) to provide 25a (2.2 g, 88%) as a colourless oil: IR (film) 3356, 1959, 1600 (w) cm⁻¹; ¹H NMR δ: 7.38
(2H, m, H3’), 7.30 (2H, m, H2’), 7.23 (1H, m, H4’), 6.62 (1H, d, J = 16.0 Hz, H1), 6.21 (1H, dd, J = 16.0, 6.8 Hz, H2), 4.86 (2H, dq, J = 3.1, 3.1 Hz, H6), 4.67 (1H, m, H3), 2.11 (1H, br s, OH), 1.74 (3H, t, J = 3.1 Hz, H7); ¹³C NMR δ: 204.7 (C5), 136.5 (C1’), 131.4 (C1), 129.7 (C2), 128.5 (2C, C2’), 127.7 (C4’), 126.5 (2C, C3’), 101.6 (C4), 77.7 (C6), 73.2 (C3), 14.7 (C7); HRMS (ESI): 209.0937, [C₁₃H₁₄ONa]⁺ requires 209.0937. NMR data matches lit.37, 38

Procedure 2: A saturated aqueous solution of ammonium chloride (130 mL) was added to a methanol (25 mL) solution of trans-cinnamylaldehyde (7.5 mL, 60 mmol) and 1-bromobut-2-yne (6.8 mL, 78 mmol). The mixture was cooled in an ice bath and vigourously stirred as zinc dust (15 g, 0.22 mol) was added in 4 portions over 30 min at 0 °C. Stirring was continued for 1 h at rt. The solution was filtered through a pad of Celite, and extracted with diethyl ether (×2). The combined ether extracts were washed with brine, dried over MgSO₄, and concentrated. The residue was subjected to flash chromatography (10% diethyl ether in pentanes) to provide 25a (2.8 g, 25%) as a pale yellow oil.

(E)-2-Methyl-1-phenylhex-1-en-5-yn-3-ol (24b) and (E)-2-methyl-1-phenylhexa-1,4,5-trien-3-ol (25b)

According to Procedure 1 for 25a: indium powder (2.0 g, 17 mmol), propargyl bromide (2.0 g, 17 mmol) and α-methyl-trans-cinnamaldehyde (2.2 mL, 16 mmol)
yielded 24b (1.5 g, 51%) and 25b (0.82 g, 28%) as colourless oils; for 24b: IR (film) 3380, 3297, 2128, 1605 cm\(^{-1}\); \(^1\)H NMR δ: 7.34 (2H, m, H3’), 7.23 (2H, m, H2’), 7.11 (1H, m, H4’), 6.60 (1H, m, H1), 4.37 (1H, m, H3), 2.58 (2H, m, H4), 2.19 (1H, d, J = 3.7 Hz, OH), 2.09 (1H, t, J = 2.7 Hz, H6), 1.89 (3H, d, J = 1.4 Hz, H7); \(^{13}\)C NMR δ: 138.4 (C2), 137.2 (C1’), 129.0 (2C, C2’), 128.1 (2C, C3’), 126.6 (C4’), 126.5 (C2), 80.6 (C5), 75.5 (C6), 70.9 (C3), 26.1 (C4), 13.5 (C7); HRMS (ESI) 209.0941, \([C_{13}H_{14}ONa]^+\) requires 209.0937. NMR data matches lit.\(^39,40\) For 25b: IR 3370, 1958, 1605 (w) cm\(^{-1}\); \(^1\)H NMR δ: 7.33 (2H, m), 7.29 (2H, m), 7.22 (1H, m), 6.59 (1H, m), 5.34 (1H, q, J = 6.5 Hz), 4.96 (2H, d, J = 6.6, 2.7 Hz), 4.74 (1H, m), 2.01 (1H, br s), 1.89 (3H, d, J = 1.4 Hz); \(^{13}\)C NMR δ: 207.4, 139.0, 137.6, 129.2 (2C), 128.3 (2C), 126.8, 126.1, 93.8, 78.5, 75.3, 13.9; HRMS (ESI) 209.0929, \([C_{13}H_{14}ONa]^+\) requires 209.0937. \(^1\)H NMR data matches lit.\(^41\)

According to Procedure 2 for 25a: zinc dust (17 g, 0.26 mol), propargyl bromide (12 g, 0.10 mol) and \(\alpha\)-methyl-\(\alpha\)-trans-cinnamaldehyde (10 mL, 0.08 mol) yielded 24b (5.5 g, 37%) as a colourless oil.

Procedure 3: A 2.5 M solution of \(n\)-butyllithium in hexanes (34 mL, 0.086 mol) was added to a -78 \(^\circ\) C solution of tetrahydro-2-(2-propynyloxy)-2\(H\)-pyran (10 mL, 0.071 mol) in THF (100 mL), stirred for 1 h, and then \(\alpha\)-methyl-\(\alpha\)-trans-cinnamaldehyde (10 mL, 0.071 mol) was added. The reaction was stirred at rt overnight, and then diluted with ether. The organic layer was washed with water, brine, dried with MgSO\(_4\), then concentrated. The crude residue was dissolved in Et\(_2\)O (50 mL), added dropwise to a slurry of LiAlH\(_4\) (5.0 g, 0.13 mol) in Et\(_2\)O (125 mL) at 0 \(^\circ\) C, and stirred for 1 h. Water (15 mL), 10% NaOH (aq) (15 mL), and additional water (15 mL) were then added
successively, and the mixture was stirred at rt for 1 h until a white precipitate formed. Anhydrous MgSO₄ was then added, and the mixture was filtered, then concentrated. The residue was subjected to flash chromatography (25% diethyl ether in pentanes) to provide **25b** (10.4 g, 79%) as a colourless oil.

(\(E\))-1-Phenylhex-1-en-5-yn-3-ol (24c) and (\(E\))-1-phenylhexa-1,4,5-trien-3-ol (25c)

According to Procedure 1 for **25a**: indium powder (2.0 g, 17 mmol), propargyl bromide (2.0 g, 17 mmol) and trans-cinnamaldehyde (2.0 mL, 16 mmol) yielded **24c** (1.3 g, 48%) and **25c** (0.81 g, 30%) as colourless oils; for **24c**: IR (film) 3391, 3296, 2128, 1605 cm\(^{-1}\); \(^1\)H NMR δ: 7.39 (2H, m), 7.32 (2H, m), 7.28 (1H, m), 6.66 (1H, d, \(J = 16\) Hz), 6.28 (1H, dd, \(J = 16, 6.3\) Hz), 4.48 (1H, m), 2.58 (1H, ddd, \(J = 17, 5.9, 2.7\) Hz), 2.52 (1H, ddd, \(J = 17, 6.0, 2.7\) Hz), 2.16 (1H, br s), 2.09 (1H, t, \(J = 2.7\) Hz); \(^{13}\)C NMR δ: 136.3, 131.3, 129.9, 128.6, 127.9, 126.6, 80.2, 71.1, 70.7, 27.7; HRMS (ESI) 195.0788, \([C_{12}H_{12}ONa]^+\) requires 195.0780. NMR data matches lit.\(^{37, 40, 42}\) For **25c**: IR 3406, 1605 (w) cm\(^{-1}\); \(^1\)H NMR δ: 7.39 (2H, m), 7.32 (2H, m), 7.25 (1H, m), 6.64 (1H, d, \(J = 16\) Hz), 6.27 (1H, d, \(J = 16\) Hz), 5.37 (1H, q, \(J = 6.5\) Hz), 4.93 (2H, d, \(J = 6.6, 2.4\) Hz), 4.87 (1H, m), 1.13 (1H, d, \(J = 6.3\) Hz); \(^{13}\)C NMR δ: 207.3, 136.5, 130.7, 130.4, 128.6 (2C), 127.9, 126.6 (2C), 93.9, 78.3, 70.5; HRMS (ESI) 195.0772, \([C_{12}H_{12}ONa]^+\) requires 195.0780. NMR data matches lit.\(^{42}\)
According to Procedure 2 for 25a: zinc dust (35 g, 0.53 mol), propargyl bromide (25 g, 0.21 mol) and trans-cinnaldehyde (20 mL, 0.16 mmol) yielded 24c (21 g, 76%) as a yellow oil.

\[(E)-2,4\text{-Dimethyl-1-phenylhexa-1,4,5-trien-3-ol (25d)}\]

\[
\begin{align*}
\text{Ph} & \\
\text{OH} & \\
\end{align*}
\]

According to Procedure 1 for 25a: indium powder (2.0 g, 17 mol), 1-bromo-2-butyne (1.5 ml, 17 mmol) and \(\alpha\)-methyl-trans-cinnaldehyde (2.2 mL, 16 mmol) yielded 31 (2.7 g, 84%) as a colourless oil; IR 3406, 1963, 1605 (w) cm\(^{-1}\); \(^1\)H NMR \(\delta: 7.34 (2H, m), 7.30 (2H, m), 7.23 (1H, m), 6.56 (1H, m), 4.95 (2H, m), 4.54 (1H, m), 2.07 (1H, d, \(J = 2.2\) Hz), 1.82 (3H, d, \(J = 1.3\) Hz), 1.67 (3H, t, \(J = 3.2\) Hz); \(^13\)C NMR \(\delta: 204.6, 137.8, 137.6, 129.2 (2C), 128.3 (2C), 127.7, 126.8, 101.4, 78.7, 78.1, 15.1, 13.1\); HRMS (ESI) 223.1083, [C\(_{14}\)H\(_{16}\)ONa]\(^+\) requires 223.1093.

According to Procedure 2 for 25a: zinc dust (1.4 g, 22 mmol), 1-bromo-2-butyne (0.85 ml, 8.9 mmol) and \(\alpha\)-methyl-trans-cinnaldehyde (0.95 mL, 6.8 mmol) yielded 25d (0.41 g, 30%) as a colourless oil.
4-Methylhexa-1,4,5-trien-3-ol (25e)

According to Procedure 1 for 25a: acrolein (1.8 mL, 27 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded 25e (0.95 g, 58%) as a colourless oil: IR (film) 3444, 1960 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 5.86 (1H, ddd, \(J = 17.1, 10.4, 6.3\) Hz), 5.31 (1H, dd, \(J = 17.1, 1.3\) Hz), 5.19 (1H, dd, \(J = 10.4, 1.3\) Hz), 4.84 (2H, dq, \(J = 3.2, 3.2\) Hz), 4.50 (1H, m), 1.93 (1H, br s), 1.70 (3H, t, \(J = 3.2\) Hz); \(^13\)C NMR \(\delta\): 204.6, 138.4, 115.8, 101.3, 77.5, 73.5, 14.5; HRMS (ESI): 133.0632, [C\(_7\)H\(_8\)ONa]+ requires 133.0624.

\((E)\)-3-Methylhepta-1,2,5-trien-4-ol (25f)

According to Procedure 1 for 25a: trans-crotonaldehyde (1.1 mL, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded 25f (1.5 g, 90%) as a colourless oil: IR (film) 3357, 1959 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 5.73 (1H, dq, \(J = 15.3, 6.7\) Hz), 5.50 (1H, dd, \(J = 15.3, 7.4\) Hz), 4.83 (2H, m), 4.42 (1H, m), 2.09 (1H, br s), 1.72 (3H, d, \(J = 6.7\) Hz), 1.68 (3H, t, \(J = 3.1\) Hz); \(^13\)C NMR \(\delta\): 204.3, 131.4, 128.0, 101.9, 77.5, 73.2, 17.6, 14.7; HRMS (ESI): 147.0789, [C\(_8\)H\(_{12}\)ONa]+ requires 147.0780.
(E)-3,7-Dimethylocta-1,2,5-trien-4-ol (25g)

According to Procedure 1 for 25a: trans-4-methyl-2-pentenal (1.55 mL, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded 25g (1.7 g, 85%) as a colourless oil: IR (film) 3375, 1960 cm⁻¹; ¹H NMR δ: 5.67 (1H, dd, J = 15.6, 6.6 Hz), 5.41 (1H, dd, J = 15.6, 6.9 Hz), 4.78 (2H, dq, J = 3.1, 3.1 Hz), 4.43 (1H, m), 2.46 (1H, br s), 2.31 (1H, m), 1.67 (3H, t, J = 3.1 Hz), 1.00 (6H, d, J = 6.8 Hz); ¹³C NMR δ: 204.5, 139.5, 127.2, 101.7, 77.3, 73.0, 30.5, 22.0 (2C), 14.4; HRMS (ESI): 175.1087, [C₁₀H₁₆ONa]⁺ requires 175.1093.

(E)-1-(4-Methoxyphenyl)-4-methylhexa-1,4,5-trien-3-ol (25h)

According to Procedure 1 for 25a: p-methoxy-trans-cinnamylaldehyde (2.2 g, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded 25h (2.1 g, 74%) as a colourless oil: IR (film) 3386, 1958, 1607 cm⁻¹; ¹H NMR δ: 7.32 (2H, d, J = 8.8 Hz), 6.85 (2H, d, J = 8.8 Hz), 6.58 (1H, d, J = 15.8 Hz), 6.07 (1H, dd, J = 15.8, 6.9 Hz), 4.86 (2H, dq, J = 3.1, 3.1 Hz), 4.64 (1H, m), 3.82 (3H, s), 1.97 (1H, br s), 1.74 (3H, t, J = 3.1 Hz); ¹³C NMR δ: 204.6, 159.3, 130.9, 129.3, 127.8 (2C), 127.5,
(E)-4-Methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-ol (25i)

According to Procedure 1 for 25a: \( p \)-trifluoromethyl-trans-cinnamylaldehyde (1.9 g, 9.7 mmol), indium powder (1.2 g, 11 mmol), and 1-bromo-2-butyne (1.0 mL, 11 mmol) yielded 25i (2.2 g, 91%) as a colourless oil: IR (film) 3384, 1960, 1616, 1327 cm\(^{-1} \); \(^1\)H NMR \( \delta \): 7.57 (2H, d, \( J = 8.3 \) Hz), 7.48 (2H, d, \( J = 8.3 \) Hz), 6.68 (1H, d, \( J = 15.9 \) Hz), 6.32 (1H, dd, \( J = 15.9, 6.4 \) Hz), 4.89 (2H, dq, \( J = 3.1, 3.1 \) Hz), 4.71 (1H, m), 2.22 (1H, br s), 1.75 (3H, t, \( J = 3.1 \) Hz); \(^{13}\)C NMR \( \delta \): 204.8, 140.1, 132.4, 129.6, 129.5 (q, \( J = 33 \) Hz), 126.7 (2C), 125.5 (2C, q, \( J = 3.6 \) Hz), 124.1 (q, \( J = 270 \) Hz), 101.3, 77.8, 73.0, 14.6; \(^{19}\)F NMR \( \delta \): −63.8 (s); HRMS (ESI): 277.0799, [C\(_{14}\)H\(_{13}\)F\(_3\)ONa]\(^{+}\) requires 277.0811.

(E)-1-(Furan-2-yl)-4-methylhexa-1,4,5-trien-3-ol (25j)

According to Procedure 1 for 25a: trans-3-(2-furyl)acrolein (1.6 g, 13 mmol), indium powder (1.7 g, 15 mmol), and 1-bromo-2-butyne (1.4 mL, 15 mmol) yielded 25j
(1.5 g, 65%) as a yellow oil: IR (film) 3383, 1959 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.34 (1H, d, \(J = 1.6\) Hz), 6.46 (1H, d, \(J = 15.8\) Hz), 6.36 (1H, dd, \(J = 3.3, 1.8\) Hz), 6.25 (1H, d, \(J = 3.3\) Hz), 6.17 (1H, dd, \(J = 15.8, 6.5\) Hz), 4.85 (2H, dq, \(J = 3.1, 3.1\) Hz), 4.65 (1H, m), 2.06 (1H, br s), 1.73 (3H, t, \(J = 3.1\) Hz); \(^1\)C NMR \(\delta\): 204.7, 152.3, 142.0, 128.2, 119.3, 111.3, 108.2, 101.4, 77.6, 72.9, 14.5; HRMS (ESI): 199.0739, [C\(_{11}\)H\(_{12}\)O\(_2\)Na]\(^+\) requires 199.0730.

\((E)\)-1-Cyclohexenylbut-3-yn-1-ol (24k) and \((E)\)-1-cyclohexenylbuta-2,3-dien-1-ol (25k)

\[
\begin{array}{c}
\text{OH} \\
\text{24k} \\
\text{25k}
\end{array}
\]

According to Procedure 1 for 25a: indium powder (2.0 g, 17 mmol), propargyl bromide (2.0 g, 17 mmol) and 1-cyclohexene-1-carboxaldehyde (1.8 mL, 16 mmol) yielded 24k (0.93 g, 39%) and 25k (0.60 g, 25%) as colourless oils; for 24k: IR 3308, 2124 (w) cm\(^{-1}\); \(^1\)H NMR \(\delta\): 5.75 (1H, m), 4.15 (1H, m), 2.46 (2H, m), 2.04 (4H, m), 1.99 (1H, m), 1.94 (1H, m), 1.61 (4H, m); \(^1\)C NMR \(\delta\): 138.3, 124.1, 81.4, 74.3, 70.7, 25.1, 24.0, 22.7, 22.6; HRMS (ESI) 173.0948, [C\(_{10}\)H\(_{14}\)ONa]\(^+\) requires 173.0937. NMR data matches lit.\(^{43}\) For 25k: IR 3366, 1958 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 5.76 (1H, m), 5.26 (1H, q, \(J = 6.4\) Hz), 4.90 (2H, dd, \(J = 6.7, 2.7\) Hz), 4.54 (1H, m), 2.02 (4H, m), 1.81 (1H, br s), 1.61 (4H, m); \(^1\)C NMR \(\delta\): 207.2, 139.0, 123.6, 93.9, 78.1, 73.9, 25.2, 24.1, 22.7 (2C); HRMS (ESI) 173.0941, [C\(_{10}\)H\(_{14}\)ONa]\(^+\) requires 173.0937.
According to Procedure 2 for 25a: zinc dust (23 g, 0.35 mol), propargyl bromide (18 g, 0.15 mol) and 1-cyclohexene-1-carboxaldehyde (13 mL, 0.11 mol) yielded 24k (2.1 g, 13%) as a colourless oil.

**(E)-4-Methyl-1-phenylhexa-1,4,5-trien-3-one (26)**

![Chemical Structure](image)

Activated MnO₂ (19 g, 0.21 mol) was added in four portions (over one hour) to a vigourously stirring solution of allenyl vinyl alcohol 25a (2.0 g, 11 mmol) in dichloromethane (110 mL) at room temperature. The solution was stirred for 3 h, filtered through a pad of Celite, concentrated, and the product was purified via column chromatography to provide 26 (1.55 g, 79%) as an off-white solid: mp 64–67 °C; IR (film) 1958, 1929, 1660, 1607 cm⁻¹; ¹H NMR δ: 7.63 (1H, d, J = 15.8 Hz, H1), 7.54 (2H, m, H3’), 7.40 (1H, d, J = 15.8 Hz, H2), 7.36 (3H, m, H2’, H4’), 5.24 (2H, q, J = 3.0 Hz, H6), 1.91 (3H, t, J = 3.0 Hz, H7); ¹³C NMR δ: 216.2 (C5), 189.2 (C3), 141.6 (C1), 134.9 (C1’), 130.0 (C4’), 128.7 (2C, C2’), 128.2 (2C, C3’), 121.7 (C2), 105.0 (C4), 78.9 (C6), 13.4 (C7); HRMS (ESI): 207.0784, [C₁₃H₁₂ONa]⁺ requires 207.0780.
4-Methylhexa-1,4,5-trien-3-one (27)

\[
\begin{align*}
\text{O} & \quad \text{H} \\
\end{align*}
\]

According to the procedure for 26: allenyl vinyl alcohol 4a (0.50 g, 4.5 mmol) and MnO₂ (7.9 g, 0.090 mol) yielded 27 (0.18 g, 37%) as a colourless oil: IR (film) 1959, 1934, 1685, 1651 cm⁻¹; \(^1\)H NMR δ: 7.05 (1H, dd, \(J = 17, 11\) Hz), 6.29 (1H, d, \(J = 17\) Hz), 5.61 (1H, d, \(J = 11\) Hz), 5.21 (2H, q, \(J = 3.0\) Hz), 1.86 (3H, t, \(J = 3.0\) Hz); \(^{13}\)C NMR δ: 216.5, 189.5, 131.3, 126.9, 104.2, 78.8, 13.0; HRMS (ESI): 131.0473, [C\(_7\)H\(_8\)ONa]⁺ requires 131.0467.

(E)-3-Methylhepta-1,2,5-trien-4-one (28)

\[
\begin{align*}
\text{O} & \quad \text{H} \\
\end{align*}
\]

According to the procedure for 26: allenyl vinyl alcohol 4b (1.3 g, 10 mmol) and MnO₂ (18 g, 0.20 mol) yielded 28 (0.55 g, 43%) as a colourless oil: IR (film) 1954, 1935, 1673, 1628 cm⁻¹; \(^1\)H NMR δ: 6.89 (1H, dq, \(J = 15.4, 6.8\) Hz), 6.78 (1H, d, \(J = 15.4\) Hz), 5.17 (2H, q, \(J = 3.0\) Hz), 1.88 (3H, d, \(J = 6.8\) Hz), 1.84 (3H, t, \(J = 3.0\) Hz); \(^{13}\)C NMR δ: 214.8, 188.0, 140.1, 125.3, 102.8, 75.5, 16.5, 11.9; HRMS (ESI): 145.0626, [C\(_8\)H\(_{10}\)ONa]⁺ requires 145.0624. NMR data matches lit.\(^{44}\)
(E)-3,7-Dimethylocta-1,2,5-trien-4-one (29)

\[
\begin{align*}
(\text{E})-3,7-\text{Dimethylocta-1,2,5-trien-4-one (29)}
\end{align*}
\]

According to the procedure for 26: allenyl vinyl alcohol 4c (1.3 g, 8.7 mmol) and \(\text{MnO}_2\) (15 g, 0.17 mol) yielded 29 (1.0 g, 77%) as a colourless oil: IR (film) 1959, 1935, 1671, 1625 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 6.86 (1H, dd, \(J = 15.5, 6.8\) Hz), 6.71 (1H, d, \(J = 15.5\) Hz), 5.17 (2H, q, \(J = 3.0\) Hz), 2.46 (1H, m), 1.85 (3H, t, \(J = 3.0\) Hz), 1.06 (6H, d, \(J = 6.8\) Hz); \(^{13}\)C NMR \(\delta\): 216.2, 190.0, 152.7, 122.3, 104.5, 78.6, 31.1, 21.4 (2C), 13.4; HRMS (ESI): 173.0935, \([\text{C}_{10}\text{H}_{14}\text{ONa}]^+\) requires 173.0937.

(E)-1-(4-Methoxyphenyl)-4-methylhexa-1,4,5-trien-3-one (30)

\[
\begin{align*}
(\text{E})-1-(4-\text{Methoxyphenyl})-4-\text{methylhexa-1,4,5-trien-3-one (30)}
\end{align*}
\]

According to the procedure for 26: allenyl vinyl alcohol 4e (1.9 g, 9.0 mmol) and \(\text{MnO}_2\) (16 g, 0.18 mol) yielded 30 (1.3 g, 68%) as a yellow solid: mp 56–58 °C; IR (film) 1961, 1933, 1653, 1594 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.60 (1H, d, \(J = 16\) Hz), 7.51 (2H, d, \(J = 8.8\) Hz), 7.29 (1H, d, \(J = 16\) Hz), 6.89 (2H, d, \(J = 8.8\) Hz), 5.23 (2H, q, \(J = 3.0\) Hz), 3.83 (3H, s), 1.91 (3H, t, \(J = 3.0\) Hz); \(^{13}\)C NMR \(\delta\): 216.0, 189.3, 161.3, 141.5, 129.9 (2C), 127.7, 119.6, 114.2 (2C), 105.0, 78.8, 55.3, 13.5; HRMS (ESI): 237.0886, \([\text{C}_{14}\text{H}_{14}\text{O}_{2}\text{Na}]^+\) requires 237.0891.
(E)-4-Methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-one (31)

According to the procedure for 26: allenyl vinyl alcohol 4f (2.2 g, 8.6 mmol) and MnO₂ (15 g, 0.17 mol) yielded 31 (1.5 g, 69%) as an off-white solid: mp 57–59 °C; IR (film) 1963, 1930, 1663, 1610, 1325 cm⁻¹; ¹H NMR δ: 7.62 (5H, m), 7.46 (1H, d, J = 16 Hz), 5.29 (2H, q, J = 3.0 Hz), 1.92 (3H, t, J = 3.0 Hz); ¹³C NMR δ: 216.4, 188.8, 139.6, 138.4, 131.4 (q, J = 33 Hz), 128.2 (2C), 125.6 (2C, q, J = 3.6 Hz), 123.8 (q, J = 270 Hz), 123.8, 105.1, 79.2, 13.3; ¹⁹F NMR δ: -63.8 (s); HRMS (ESI): 275.0646, [C₁₄H₁₁F₃ONa]⁺ requires 275.0654.

(E)-1-(Furan-2-yl)-4-methylhexa-1,4,5-trien-3-one (32)

According to the procedure for 26: allenyl vinyl alcohol 4e (1.5 g, 8.7 mmol) and MnO₂ (15 g, 0.17 mmol) yielded 32 (1.1 g, 73%) as a yellow solid: mp 67–68 °C; IR (film) 1972, 1938, 1655, 1599 cm⁻¹; ¹H NMR δ: 7.47 (1H, d, J = 1.8 Hz), 7.38 (1H, d, J = 16 Hz), 7.27 (1H, d, J = 16 Hz), 6.64 (1H, d, J = 3.4 Hz), 6.47 (1H, dd, J = 3.4, 1.8 Hz), 5.25 (2H, q, J = 3.0 Hz), 1.90 (3H, t, J = 3.0 Hz); ¹³C NMR δ: 216.1, 189.2, 151.6, 144.4,
128.0, 119.5, 115.4, 112.4, 105.0, 79.0, 13.4; HRMS (ESI): 197.0565, \([\text{C}_{11}\text{H}_{10}\text{O}_{2}\text{Na}]^+\) requires 197.0573.

\((E)-2\text{-Methyl-1-phenylhex-1-en-5-yn-3-one} \ (33) \text{ and (E)-2-methyl-1-phenylhexa-1,4,5-trien-3-one} \ (35)\)

\[
\begin{align*}
\text{33} & \quad \text{35}
\end{align*}
\]

Dess-Martin periodinane (1.5 g, 3.5 mmol) was added to a vigorously stirring solution of propargyl alcohol \(24b\) (0.5 g, 2.7 mmol) and sodium bicarbonate (2.3 g, 27 mmol) in CH\(_2\)Cl\(_2\) (25 mL) at rt. After 45 min saturated aqueous solutions of sodium bicarbonate and sodium thiosulfate were added (25 mL each), as well as a small amount of diethyl ether, and the mixture was stirred until both layers went clear. The mixture was extracted thoroughly with CH\(_2\)Cl\(_2\), and the organic layer was washed with brine, dried over MgSO\(_4\), and concentrated under vacuum, yielding \(33\) as a pale yellow oil: IR (film) 1641 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.58 (1H, q, \(J = 1.4\) Hz, H1), 7.43 (4H, m, H2', H3'), 7.37 (1H, m, H4'), 3.74 (2H, d, \(J = 2.8\) Hz, H4), 2.29 (1H, t, \(J = 2.8\) Hz, H6), 2.10 (3H, d, \(J = 1.4\) Hz, H7); \(^1\)C NMR \(\delta\): 194.8 (C3), 140.5 (C1), 135.8 (C2), 135.4 (C1'), 129.8 (2C, C2'), 128.8 (C4'), 128.5 (2C, C3'), 77.3 (C5), 72.9 (C6), 29.7 (C4), 13.3 (C7); HRMS (ESI) 207.0781, \([\text{C}_{13}\text{H}_{12}\text{ONa}]^+\) requires 207.0780. Without further purification, propargyl ketone \(33\) was dissolved in CH\(_2\)Cl\(_2\) (25 mL), and potassium carbonate (0.41 g, 3.0 mmol) was added. After stirring at rt for 20 min, the solution was filtered and concentrated under vacuum, yielding \(35\) as a red oil (0.18 g, 36%): IR (film) 1967, 1943, 1650, 1601 cm\(^{-1}\);
\(^1\)H NMR \(\delta\) 7.50 (1H, m), 7.41 (5H, m), 6.34 (1H, \(t, J = 6.6\) Hz), 5.21 (2H, d, \(J = 6.6\) Hz), 2.12 (3H, d, \(J = 1.9\) Hz); \(^{13}\)C NMR \(\delta\) 215.8, 193.0, 139.3, 137.2, 135.7, 133.2, 129.7, 128.4, 92.5, 78.5, 13.9; HRMS (ESI) 185.0968, \([\text{C}_{13}\text{H}_{13}\text{ONa}]^+\) requires 185.0961. Note: the yield of AVK 35 in the crude reaction mixture was determined by \(^1\)H NMR, using 1,3,5-trimethoxybenzene as an internal standard, and was used without further purification.

\((E)-1\)-Phenylhexa-1,4,5-trien-3-one (36)

\[
\text{O} \\
\text{Ph} \\
\text{36}
\]

Dess-Martin periodinane (3.2 g, 7.5 mmol) was added to a vigorously stirring, room temperature solution of propargyl alcohol 24c (1.0 g, 5.8 mmol) and sodium bicarbonate (4.9 g, 58 mmol) in CH\(_2\)Cl\(_2\) (60 mL). After 45 min, saturated aqueous solutions of sodium bicarbonate (60 mL) and sodium thiosulfate (60 mL) were added, as well as diethyl ether (ca. 30 mL), and the mixture was stirred until both layers were clear. The mixture was extracted thoroughly with CH\(_2\)Cl\(_2\), and the combined organic layers were washed with brine, dried over MgSO\(_4\), and concentrated under vacuum. Flash chromatography of the residue (10% diethyl ether in pentane) provided 36 (0.27 g, 27%) as a yellow oil: IR (film) 1958, 1931, 1664, 1606 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.57 (1H, d, \(J = 16\) Hz), 7.39 (2H, m), 7.26 (3H, m), 7.21 (1H, d, \(J = 16\) Hz), 6.03 (1H, t, \(J = 6.5\) Hz), 5.34 (2H, d, \(J = 6.5\) Hz); \(^{13}\)C NMR \(\delta\): 216.5, 188.5, 142.7, 134.6, 130.4, 128.9, 128.4, 121.8,
97.5, 79.8; HRMS (ESI) 193.0632, $[\text{C}_{12}\text{H}_{10}\text{ONa}]^{+}$ requires 193.0624. NMR data matches lit.$^{45}$

$(E)$-1-Cyclohexenylbut-3-yn-1-one (34) and $(E)$-1-cyclohexenylbuta-2,3-dien-1-one (37)

According to the procedure for 33: Dess-Martin periodinane (2.4 g, 5.6 mmol), propargyl alcohol 24k (0.65 g, 4.3 mmol) and sodium bicarbonate (3.6 g, 43 mmol) yielded 34 as a pale yellow oil; IR 1677, 1641 cm$^{-1}$; $^1$H NMR $\delta$: 6.97 (1H, m), 3.56 (2H, d, $J = 2.8$ Hz), 2.27 (4H, m), 2.23 (1H, t, $J = 2.8$ Hz), 1.64 (4H, m); $^{13}$C NMR $\delta$: 293.6, 142.0, 138.0, 72.6, 29.0, 26.2, 23.2, 21.8, 21.4; HRMS (ESI) 171.0786, $[\text{C}_{10}\text{H}_{12}\text{ONa}]^{+}$ requires 171.0780. According to the procedure for 35: crude 34 and potassium carbonate (0.65 g, 4.7 mmol) yielded 37 as a red oil (0.36 g, 56%); IR 1963, 1936, 1641 cm$^{-1}$; $^1$H NMR $\delta$: 6.91 (1H, m), 6.25 (1H, t, $J = 6.5$ Hz), 5.16 (2H, d, $J = 6.5$ Hz), 2.27 (4H, m), 1.64 (4H, m); $^{13}$C NMR $\delta$: 215.5, 191.2, 140.8, 139.4, 91.7, 78.6, 26.1, 23.6, 21.9, 21.6; HRMS (ESI) 171.0782, $[\text{C}_{10}\text{H}_{12}\text{ONa}]^{+}$ requires 171.0780. Note: the yield of allenyl vinyl ketone 37 in the crude reaction mixture was determined by $^1$H NMR, using 1,3,5-trimethoxybenzene as an internal standard, and was used without further purification.
CHAPTER 3. THE INTERRUPTED NAZAROV CYCLIZATION OF ALLENYL VINYL KETONES WITH HETEROATOM NUCLEOPHILES

3.1 Introduction

Although it had been documented that AVKs could undergo Nazarov cyclization in the presence of silica gel (Section 1.6), the reactivity of AVKs in the presence of protic or Lewis acids had remained unexplored. Hence, the behavior of AVKs in the presence of Lewis and protic acids well known to promote Nazarov cyclizations will be discussed initially. We chose AVK 26 as a test substrate, as it was hypothesized that the phenyl ring would decrease its susceptibility to side reactions, such as Michael additions or polymerization products. Furthermore, 26 should also yield simpler NMR spectra, resulting in more facile interpretation of NMR spectra of crude reaction products.

3.2 Initial Screening Conditions for Interrupted Nazarov Cyclizations

AVK 26 was exposed to a variety of Lewis and protic acids, as outlined in Table 2. The only cyclized product isolated in each case was interrupted Nazarov product 38, as a single regioisomer in which interception of the intermediate oxyallyl cation solely occurred at position $a$. In all cases, the double bond from the end of the allene unit had migrated into the ring. No product with an exocyclic double bond was isolated. Furthermore, no cyclopent-2-enone product resulting from the elimination of a proton was detected. Trifluoroacetic acid was clearly the best acid for the formation of 38 (entry 1). It is interesting to note that when the Lewis acids BF$_3$-Et$_2$O, Cu(OTf)$_2$, and TiCl$_4$ were utilized, only intractable material resulted. This may have been the result of a strong associative interaction between the counterion and the metal center, resulting in a lack of
suitable nucleophilic species present to trap the intermediate oxyallyl cation, leading to alternative pathways resulting in the decomposition of 26.

Table 2 Screening for suitable promoters for the Nazarov reaction of AVK 26.

![Chemical structure](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>acid(^a)</th>
<th>yield of 38 (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>TFA(^c)</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>Amberlyst-15</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>(p)-TSA</td>
<td>71</td>
</tr>
<tr>
<td>4</td>
<td>HCl</td>
<td>0(^d)</td>
</tr>
<tr>
<td>5</td>
<td>BF(_3)(\cdot)Et(_2)O</td>
<td>0(^e)</td>
</tr>
<tr>
<td>6</td>
<td>Cu(OTf)(_2)</td>
<td>0(^e)</td>
</tr>
<tr>
<td>7</td>
<td>Sc(OTf)(_3)</td>
<td>54</td>
</tr>
<tr>
<td>8</td>
<td>Yb(OTf)(_3)</td>
<td>70(^f)</td>
</tr>
<tr>
<td>9</td>
<td>TiCl(_4)</td>
<td>0(^e)</td>
</tr>
</tbody>
</table>

\(^a\)All reactions were slowly warmed from -78 °C until completion by TLC, \(^b\)isolated yields, \(^c\)initial product was the TFA adduct, \(^d\)isolated Michael addition products, \(^e\)resulted in intractable material, \(^f\)resulted in a 1:1 mixture of cis and trans isomers.

The origin of the alcohol oxygen was from the initially formed trifluoroacetyl or sulfonyl esters. This was obvious from the NMR spectra of the crude cyclization product from the reaction of AVK 26 with TFA. The major signals were attributable to the ester 39, and its solvolysis must have occurred readily during chromatography on basic alumina (Scheme 28).
Scheme 28 Origin of alcohol oxygen is from TFA-trapped intermediate 39.

With the exception of Yb(OTf)$_3$ (entry 8), which produced 38 along with its cis diastereomer as a 1:1 mixture, all other acids produced compound 38 as a single trans diastereomer. The trans stereochemistry of 38 was confirmed by X-ray crystallography (Figure 4). The relative stereochemistry was established prior to hydrolysis of the TFA-ester 39, because the relative stereochemistry of 39 was also trans, as was confirmed by comparison of its $^1$H NMR coupling constants with those of compound 38. This was likely a result of steric interactions of the incoming nucleophile with the substituent at C4.

Figure 4 X-ray crystal structure (ORTEP) of compound 38.
3.3 Scope of Trifluoroacetic Acid-Mediated Interrupted Nazarov Cyclizations

The substrate scope of the TFA-mediated Nazarov reaction was initially evaluated with the remainder of the Type 1 AVKs 27 – 32, as shown below in Table 3.

Table 3 Scope of the TFA-initiated Nazarov reaction of AVKs.

<table>
<thead>
<tr>
<th>R</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>27 - 32</td>
<td>40</td>
<td>89</td>
</tr>
<tr>
<td>27 - 32</td>
<td>41a = trans, 41b = cis (88, dr 3:1)</td>
<td></td>
</tr>
<tr>
<td>27 - 32</td>
<td>42</td>
<td>90</td>
</tr>
<tr>
<td>27 - 32</td>
<td>43, MeO</td>
<td>&gt;99</td>
</tr>
<tr>
<td>27 - 32</td>
<td>44, F3C</td>
<td>64</td>
</tr>
<tr>
<td>27 - 32</td>
<td>45</td>
<td>58</td>
</tr>
</tbody>
</table>

\(a0.01 \text{ M, } b\text{isolated yields.}\)

The reaction appeared to be general when the enone moiety of the starting ketone was substituted at the β-position by hydrogen, alkyl, aromatic, or activated aromatic groups. It was unclear why yields were lower when deactivated aromatic and
heteroaromatic derivatives were utilized. It is probable that this was due to the increased likelihood of oligomerization through decomposition pathways, such as those initiated by Michael addition reactions for example, as a result of the increased reaction times. All cyclized products (except 41) showed complete trans selectivity. This relative stereochemistry was confirmed by the magnitude of the $^1$H NMR coupling constants with those of compound 38. The ratio of the diastereomers of 41 was determined by integration of the corresponding signals in the $^1$H NMR spectrum. That only 28 gave a significant amount of cis alcohol 41b further implies that the stereochemistry of the trapping reaction is a sole result of steric interactions of the incoming nucleophile with the substituent at C4.

The reaction was then evaluated with the Type 2 AVKs 35 and 37, and the Type 3 AVK 36 (Scheme 29). Type 2 and Type 3 AVKs clearly exhibited divergent reactivity
from Type 1 AVKs. For example, although Type 3 AVK 36 reacted cleanly in the presence of TFA, the product 46 was the result of conjugate addition to the allene. Type 2 AVK 35 also reacted readily in the presence of TFA; however the Nazarov elimination product 47 was the sole product isolated, in 48% yield. Type 2 AVK 37 gave mainly 48, which represented an intercepted Nazarov product where the oxygen nucleophile had attacked position $a$, with parallel regio- and stereoselectivity to AVKs of Type 1. The relative stereochemistry of 48 was confirmed by X-ray crystallographic analysis of its 3,5-dinitrobenzoate 50 (Figure 5).

![Figure 5 X-ray crystal structure (ORTEP) of compound 50.](image)

### 3.4 Reactivity of AVKs of Type 2 and Type 3 in the Absence of Nucleophilic Species

The susceptibility of Type 2 AVKs 35 and 37, and Type 3 AVK 36, to undergo a traditional Nazarov cyclization, resulting in elimination of a proton from the oxyallyl cationic intermediate, was briefly probed. It was necessary to choose acid
promoters that do not generate nucleophilic species, which might compete with proton elimination to trap the oxyallyl cation or pre-emptively add to the allene’s central carbon prior to Nazarov cyclization. Thus, silica gel and BF$_3$·Et$_2$O were chosen for the task (Scheme 30).

Scheme 30 Reactions of AVKs 35 – 37 in the presence of BF$_3$·Et$_2$O and SiO$_2$.

In the presence of silica gel, AVKs 35 and 37 produced some of the corresponding Nazarov elimination products 47 (41%) and 49 (14%). This observation paralleled the reactivity observed by Hashmi for AVKs with this substitution pattern.$^{16}$ Conversely, AVK 36 remained unreacted in the presence of silica gel. This result paralleled the reactivity observed with AVK 26, which also does not bear an alkyl substituent on the alkene unit. Treatment of 35 and 37 with BF$_3$·Et$_2$O at -78 °C for 10 minutes led to complex mixtures, although 23% of the Nazarov product 49 was isolated following the reaction of the latter. On the other hand, 36 was much more tolerant of the acid, and after one hour the Nazarov product...
was obtained in 64% yield. There had been no evidence of a cyclized product following reaction of AVK 26 with BF$_3$·Et$_2$O; only intractable material resulted (cf. Table 2).

### 3.5 Mechanistic Rationale for the Reactivity Differences of AVKs of Type 1, Type 2, and Type 3

The differences in reactivity of AVKs of Type 1, Type 2, and Type 3 can be rationalized as a subtle interplay between steric and electronic factors. An alkyl substituent on the allene, such as in AVKs of Type 1, is clearly beneficial by inhibiting alternative allene reactions. It is proposed that an alkyl group on the allene attenuates the reactivity at the central carbon of the allene, by electron donation and/or by steric hindrance, allowing the Nazarov pathway to dominate. Furthermore, it is hypothesized that an alkyl group on the alkene or the allene accelerates the Nazarov reaction. In addition, calculations$^{\dagger}$ revealed that the alkyl group on the alkene exerts a significant influence on the conformation, and thus the reactivity, of the AVK (Figure 6). An $s$-$trans$-$s$-$trans arrangement must resemble the transition state geometry for the Nazarov cyclization. The $s$-$trans$-$s$-$trans conformation is more than 12 kJ·mol$^{-1}$ higher in energy than an $s$-$cis$-$s$-$trans conformation for AVK’s 26 and 36. In contrast, the $s$-$trans$-$s$-$trans conformation is the lowest-energy conformation for AVK 35.

$^{\dagger}$Calculations were performed by Gavin Heverly-Coulson, using the Q-Chem 3.1$^{46}$ and AIMAll (Version 10.03.25)$^{47}$ software packages.
Thus, the role of the alkyl group in AVKs of Type 1 (26) appears to be to allow Nazarov reactions to predominate through the inhibition of alternative allene reactions, likely through both steric and electronic means. The role of the alkyl group in AVKs of Type 3 (35) appears to be to allow Nazarov reactions to predominate not by the inhibition of alternative allene reactions, but through conformational acceleration of the Nazarov reaction. Although AVKs of Type 2, which bear no α-alkyl substituents, are clearly capable of cyclization as evidenced by the formation of 51, attempts to elicit an interrupted Nazarov process would be likely to be pre-empted by a more rapid acid-mediated reaction of the allene. The production of cyclopent-2-enone products resulting from elimination of a proton, as sole or major by-products in addition to interrupted Nazarov products, from Type 3 AVKs 35 and 37 is likely a result of the retarded rate of the interrupted Nazarov process due to the steric hindrance imparted by the alkyl group at position α of the intermediate oxyallyl cation.
3.6 Screening of Other Lewis Acids for the Interrupted Nazarov Cyclization

Treatment of AVK 26 with TiCl₄ had led to the rapid destruction of the substrate (Table 2). However, White and West have observed the trapping of a Nazarov intermediate by chloride when a cyclization had been promoted by TiCl₄ (Scheme 11). In the same study, the West group had also observed trapping by fluoride, bromide, and iodide ion when TiF₄, TiBr₄, or TiI₄ had been used, respectively. Thus, we decided to evaluate the Nazarov reactions of an AVK with other titanium-based Lewis acids as well as with other Lewis acids bearing halogen counterions. The hope was that interrupted Nazarov reactions of the AVK might produce halogenated cyclopent-2-enones (Table 4).

Table 4 Screening of other halogen-bearing Lewis acids for the interrupted Nazarov cyclization of AVK 26.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Acid</th>
<th>Compound</th>
<th>X¹</th>
<th>X²</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>InCl₃</td>
<td>52</td>
<td>H</td>
<td>Cl</td>
<td>35</td>
</tr>
<tr>
<td>2</td>
<td>InBr₃</td>
<td>53</td>
<td>H</td>
<td>Br</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>InI₃</td>
<td>54</td>
<td>H</td>
<td>I</td>
<td>32</td>
</tr>
<tr>
<td>4</td>
<td>AlCl₃</td>
<td>--</td>
<td>---</td>
<td>---</td>
<td>0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>FeCl₃</td>
<td>--</td>
<td>---</td>
<td>---</td>
<td>0&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>AuCl₃</td>
<td>55</td>
<td>Cl</td>
<td>H</td>
<td>32</td>
</tr>
<tr>
<td>7</td>
<td>TiBr₄</td>
<td>56</td>
<td>Br</td>
<td>H</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td>TiI₄</td>
<td>57</td>
<td>H</td>
<td>H</td>
<td>90</td>
</tr>
<tr>
<td>9</td>
<td>TiCl₃</td>
<td>--</td>
<td>---</td>
<td>---</td>
<td>0&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Isolated yields, <sup>b</sup>intractable material, <sup>c</sup>isolated Michael addition products.
In the presence of TiI₄, AVK 26 provided cyclopent-2-enone 57 as the sole product (entry 9). This represented not only a Nazarov cyclization but also a reduction. It seemed likely that 57 was derived from an iodinated cyclopentenone by de-iodination, a process for which there is precedence in work by West.¹³ Halogenated cyclopent-2-enones in which the oxyallyl cation had been intercepted at position a exclusively were produced in 80% yield using TiBr₄ (entry 7) and 32% using AuCl₃ (entry 6). The trans stereochemistry of 56 and 57 was confirmed by the magnitude of the ¹H NMR coupling constants to those of compound 38. Conversely, indium-based Lewis acids (entries 1 - 3) yielded products trapped at position c, only. This could be a consequence of the large effective size of indium, in addition to the long In-O bond, which might block attack of the nucleophile at position a of the oxyallyl cation intermediate.

3.7 Scope of Indium-Mediated Interrupted Nazarov Cyclizations

The substrate scope of the indium-initiated interrupted Nazarov reaction was evaluated with AVKs 27 - 32 as shown below in Table 5. In all cases, products trapped at position c were obtained exclusively. No products of trapping at position a were ever detected, although yields of the interrupted Nazarov products were consistently low. It is interesting to note that AVK 30 (R = p-OMePh) gave none of the anticipated interrupted Nazarov product when InCl₃ was used as a promoter. The dimer 67 was isolated instead. This must have been due to one molecule of 30 undergoing a Nazarov cyclization, followed by trapping of the oxyallyl cation by another molecule of 30 in a [3+2] fashion (Scheme 31). What is curious about this result is that the cycloaddition involved position a of the oxyallyl cation, whereas all other indium-mediated reactions involved position c.
Table 5 Scope of indium-mediated Nazarov reaction of AVKs.

\[
\begin{align*}
\text{27 - 31} & \xrightarrow{\text{InX}_3 (5 \text{ equiv), CH}_2\text{Cl}_2^a} \text{58 - 66} \\
\text{58; } X = \text{Cl (31)} & \quad \text{59; } X = \text{I (34)} \\
\text{60; } X = \text{Cl (20)} & \quad \text{61; } X = \text{I (9)} \\
\text{62; } X = \text{Cl (21)} & \quad \text{63; } X = \text{I (9)} \\
\text{64; } X = \text{I (26)} & \quad \text{65; } X = \text{Cl (23)} \\
\text{66; } X = \text{I (13)} & \\
\end{align*}
\]

\(^a0.01 \text{ M, } ^b\text{isolated yields.}\)

Although interception of an oxyallyl cation by electron-rich alkenes had been reported by West,\(^{11}\) this type of dimerization had not been reported before. It is particularly interesting to note the high yield of this reaction (83\% at 0.01 M). The structure of 67 was confirmed by X-ray crystallography (Figure 7). The complete retention of stereochemistry of the alkene double bond suggested that the mechanism of the \([3 + 2]\) reaction might be a concerted process. This result offered significant promise.
for the use of AVKs in tandem reactions involving first a Nazarov cyclization followed
by a [4+3] or [3+2] cycloaddition, with dienes and/or activated alkene derivatives.

Scheme 31 Proposed mechanism for formation of 67 from 30 in presence of InCl₃.

Figure 7 X-ray crystal structure (ORTEP) of compound 67.
3.8 Scope of Titanium-Mediated Interrupted Nazarov Cyclizations

The substrate scope of the TiBr₄-mediated interrupted Nazarov reaction was evaluated with AVKs 26 – 32, as shown below in Table 6.

Table 6 Scope of TiBr₄-mediated Nazarov reaction of AVKs.

Unfortunately, the excellent yields and regioselectivity noted in Table 4 for AVK 26 proved irreproducible, on average producing a 1:1 ratio of products trapped at position a and position c of the oxyallyl cationic intermediate (the trans stereochemistry of
compounds substituted at C4 was determined through analysis of $^1$H NMR coupling constants). Reactions with TiI$_4$ yielded similar results, in addition to a number of products resulting from the abstraction of iodide, amounts of which also proved irreproducible. These discrepancies showed a high dependence on the exact batch of the commercially acquired reagent. In an attempt to rectify this issue, five grams of newly acquired TiBr$_4$ was carefully sublimed. Upon re-subjection of AVK 26 to both the newly sublimed TiBr$_4$, as well as the impure residue, we were surprised to find that while the purified TiBr$_4$ reproduced the poor regioselectivity noted in Table 6, the residual TiBr$_4$ resulted in the sole formation of the trapped product 56 (Scheme 32). The reason for this disturbing result is unknown at this time.

Scheme 32 Comparison of sublimed and residual TiBr$_4$.

3.9 Synthesis of Doubly Functionalized Cyclopent-2-enones via the Initial Addition of Bromine or Iodine

We were inspired to attempt the synthesis of doubly functionalized cyclopent-2-enones, in which a nucleophile had formally added to both positions $a$ and $c$ of the intermediate oxyallyl cation. Theoretically, this could be achieved by initial halogenation of the conjugated end of the allene unit of the AVK with bromine or iodine. Then, protic or Lewis acid-induced isomerization should provide a halogenated divinyl ketone, which
could then undergo a Nazarov cyclization. Interception of the intermediate oxyallyl cation with a suitable nucleophile followed by elimination of HBr (or HI) would then provide a cyclopent-2-enone functionalized at positions \( a \) and \( c \) (Scheme 33).

Scheme 33 Proposed mechanism for the synthesis of multifunctionalized cyclopent-2-enones from AVKs.

AVK 26 (\( R = \text{Ph} \)) was first treated with \( \text{Br}_2 \) and then \( \text{TiBr}_4 \) at -78 ℃, which led to the doubly brominated cyclopentenone 76 in good overall yield (Scheme 34). This reaction was normally conducted in one-pot, although the intermediate dibromide 74 could be isolated, in quantitative yield, if necessary. The reaction was equally effective for AVKs 30 and 31 (\( R = \text{p-PhOMe} \) and \( \text{p-PhCF}_3 \)), less effective for AVK 28 (\( R = \text{Me} \)), and did not result in any cyclized product for AVKs 27 and 29 (\( R = \text{H} \) and \( \text{i-Pr} \)). This was mainly a result of competing bromination of the alkene double-bond for AVKs 27 - 39, as careful inspection of the \(^1\text{H} \) and \(^{13}\text{C} \) NMR spectra of the crude products revealed.
Scheme 34 Scope of Br₂/TiBr₄-mediated Nazarov reaction of AVKs.

TiCl₄ and TiBr₄ were less effective at producing doubly functionalized cyclopent-2-enones. TiCl₄ produced mixtures of diastereomers, whereas TiI₄ resulted in a significant amount of dehalogenated byproduct as a result of iodide abstraction. Finally, products substituted at position c by iodine as a result of prior addition of I₂ also failed to be produced in reasonable yield when titanium-based Lewis acids were used. In this case, complex mixtures of cyclopent-2-enone species were produced as a result of significant amounts of iodide abstraction.

Trifluoroacetic acid, however, proved to be a more effective promoter when iodine was added initially (Table 7), with the remainder of the material largely being the intermediate iodinated divinyl ketone, as determined by careful inspection of the ¹H NMR spectra of the crude reaction product. In this case, silica gel chromatography was utilized to hydrolyze the intermediate TFA-ester instead of basic alumina, in order to preserve the sensitive allyl-iodide functionality.
Table 7 Scope of I$_2$/TFA-mediated Nazarov reaction of AVKs.

\[
\text{26 - 30} \xrightarrow{1) \text{I}_2 \text{ (1 equiv), 1 h}} \text{79 - 83} \\
\text{79} (18) \quad \text{80a = trans} \quad \text{80b = cis} \quad \text{81} (45) \quad \text{79 (18)} \\
\text{82} (61) \quad \text{83} (32)
\]

\[\text{a} 0.01 \text{ M, } \text{b} \text{isolated yields.}\]

Unfortunately, this reaction failed to produce brominated cyclopent-2-enone species when bromine was added prior to TFA. Only the halogenated divinyl ketone $84$ was recovered after 24 hours (Scheme 35), even with stirring for prolonged reaction times. The (E)-stereochemistry of the brominated double bond was confirmed via the X-ray crystal structure of the tetrabrominated derivative $85$ (Figure 8).
3.10 Summary

A variant of the Nazarov cyclization has been presented in which the intermediate oxyallyl cation derived from an allenyl vinyl ketone has been trapped by trifluoroacetate. Al₂O₃-promoted solvolysis then provided a 5-hydroxycyclopent-2-enone. When there was a substituent at C4 in the product, then the predominant or exclusive stereochemistry of the product was trans. This intermolecular trapping of a Nazarov cyclization by an oxygen nucleophile offers an opportunity for the production of a variety of cyclopent-2-enones bearing oxygen functionality at the 5-position in good to excellent yield.
We have also ascertained that AVKs can undergo Nazarov cyclizations in which the intermediate carbocation can be trapped by a halogen at either position \( a \) or position \( c \) of the oxyallyl cationic intermediate. However, the efficiency of this process is highly dependent on the Lewis acid and the substituent on the alkene, with yields ranging from very good to essentially zero. The AVK bearing a simple phenyl substituent (26) was generally the best substrate. We observed the first instance of a formal [3+2] cycloaddition involving a carbocation intermediate being captured by unreacted substrate to generate the dimeric product. This offers significant promise for AVKs as future candidates for tandem Nazarov/[3+2] (or [4+3]) reactions with other alkene or diene partners.

Finally, the presence of an alkyl group \( \alpha \) to the ketone on either the alkene or the allene of an AVK has a very significant impact on the efficacy of Nazarov reactions and interrupted Nazarov reactions. An alkyl substituent on the allene is beneficial by inhibiting alternative allene reactions and likely by accelerating the Nazarov reaction. An alkyl substituent on the alkene accelerates the Nazarov reaction, but interception of the intermediate oxyallyl cation by a nucleophile is retarded by steric hindrance.

**3.11 Experimental Section**

**3.11.1 General Considerations**

All reactions were conducted using oven-dried glassware under an \( \text{N}_2 \) atmosphere. Reagents were used as received from a commercial supplier without further purification. Titanium bromide (ca. 1 M in dichloromethane) and titanium iodide (ca. 0.5 M in dichloromethane) solutions were prepared within an mBraun glovebox apparatus.
Dichloromethane was used freshly distilled from calcium hydride. Ethyl acetate and hexanes were distilled prior to use for column chromatography.

Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F$_{254}$), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or o-vanillin in ethanol/H$_2$SO$_4$ and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 µm particle size, 230 – 240 mesh).

Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. $^1$H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with CDCl$_3$ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). $^{13}$C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with CDCl$_3$ as solvent. $^{19}$F NMR spectra were recorded at 235 MHz on a Bruker Avance spectrometer. Infrared spectra were recorded from thin films on a Bruker VECCTOR 22 FT-IR instrument using CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional ($^1$H, $^{13}$C, and DEPT-135) and two dimensional (COSY, HSQC, and HMBC) NMR spectral data. The $^1$H and $^{13}$C NMR spectra of all compounds may be found in Appendix A, the Cartesian coordinates (including additional computed data) for compounds 26, 35, and 36 may be found in Appendix B, and the X-ray crystallographic data for compounds 38, 50, 67, and 85 may be found in Appendix C.
3.11.2 Preparation and Characterization Data

*(trans)-3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl trifluoroacetate (39) and *(trans)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)*

Trifluoroacetic acid (0.20 mL, 2.8 mmol) was added dropwise to a solution of AVK 26 (0.10 g, 0.56 mmol) in CH₂Cl₂ (50 mL) at -78 °C, and the solution was stirred for 2 h. The solution was washed with saturated aqueous NaHCO₃, the aqueous layer was re-extracted with CH₂Cl₂ (×2), and the combined CH₂Cl₂ layers were dried with Na₂SO₄ and concentrated to provide crude 39 as a yellow oil: IR (film) 1793, 1719, 1603 (w), 1151 cm⁻¹; ¹H NMR δ: 7.35 (3H, m), 7.13 (2H, m), 5.31 (1H, d, J = 3.2 Hz), 3.89 (1H, br d, J = 3.2 Hz), 1.86 (6H, s); ¹³C NMR δ: 199.1, 169.0, 156.8 (q, J = 43 Hz), 138.0, 136.1, 129.1 (2C), 127.9, 127.7 (2C), 114.4 (q, J = 285 Hz), 81.9, 54.5, 15.5, 8.4; ¹⁹F NMR δ: -75.5 (s); HRMS (ESI): 321.0685, [C₁₅H₁₃F₃O₃Na]⁺ requires 321.0709. The ester 39 was loaded onto a column of Al₂O₃ (activated, basic) with 20% ethyl acetate in hexanes, and the column was flushed with this solvent. Then, elution of the column with MeOH provided 38 (0.11 g, 96%) as colourless needles: mp 78–79 °C; IR (film) 3406, 1702, 1638, 1602 (w) cm⁻¹; ¹H NMR δ: 7.33 (2H, m, H3’), 7.27 (1H, m, H4’), 7.13 (2H, m, H2’), 4.11 (1H, br t, J ≈ 3 Hz, H5), 3.78 (1H, br s, OH), 3.67 (1H, br d, J ≈ 3 Hz, H4), 1.81 (3H, s, H7), 1.79 (3H, s, H6); ¹³C NMR δ: 207.9 (C1), 169.4 (C3), 139.8 (C1’),
134.9 (C2), 128.8 (2C, C3’), 127.9 (2C, C2’), 127.2 (C4’), 80.2 (C5), 57.7 (C4), 15.4 (C7), 8.2 (C6); HRMS (ESI): 225.0873, \([C_{13}H_{14}O_2Na]^+\) requires 225.0886.

5-Hydroxy-2,3-dimethylcyclopent-2-enone (40)

![Structure of 5-Hydroxy-2,3-dimethylcyclopent-2-enone (40)](image)

According to the procedure for 38: AVK 27 (0.060 g, 0.56 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 3 h to yield 40 (0.062 g, 89%) as a colourless solid: mp 48–49 °C (lit.\(^{50}\) rac-40 <30 °C; lit.\(^{51}\) (-)-40 40–45 °C); IR (film) 3397, 1701, 1638 cm\(^{-1}\); \(^1\)H NMR δ: 4.22 (1H, dd, \(J = 6.7, 3.0\) Hz), 3.15 (1H, br s), 2.88 (1H, dd, \(J = 18.0, 6.7\) Hz), 2.45 (1H, br dd, \(J = 18.0, 3.0\) Hz), 2.06 (3H, s), 1.72 (3H, s); \(^{13}\)C NMR δ: 209.2, 168.1, 133.7, 71.3, 40.3, 17.2, 7.8; HRMS (ESI): 149.0585, \([C_7H_{10}O_2Na]^+\) requires 149.0573.

(trans)-5-Hydroxy-2,3,4-trimethylcyclopent-2-enone (41a) and (cis)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)

![Structures of (trans)-5-Hydroxy-2,3,4-trimethylcyclopent-2-enone (41a) and (cis)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)](image)

According to the procedure for 38: AVK 28 (0.070 g, 0.57 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 2 h to yield 0.070 g (88%) of a 3:1 mixture of 41a/41b (as determined by integration of the \(^1\)H NMR spectrum), colourless
oil: IR (film) 3398, 1700, 1638 cm⁻¹; HRMS (ESI): 163.0726, [C₈H₁₂O₂Na]⁺ requires 163.0730; the following NMR data were taken from the spectra of the mixture: for 41a: 
¹H NMR δ: 3.76 (1H, d, J = 3.1 Hz), 2.91 (1H, m), 2.60 (1H, br s), 2.00 (s, 3H), 1.72 (s, 3H), 1.31 (d, 3H, J = 7.2 Hz); ¹³C NMR δ: 207.6, 170.8, 133.3, 79.3, 45.4, 16.1, 14.5, 8.1; for 41b: ¹H NMR δ: 4.21 (1H, d, J = 6.5 Hz), 2.90 (2H, m), 2.04 (3H, s), 1.72 (3H, s), 1.08 (3H, d, J = 7.2 Hz); ¹³C NMR δ: 208.8, 173.0, 132.3, 74.0, 42.8, 15.5, 14.4, 7.8.

(trans)-5-Hydroxy-4-isopropyl-2,3-dimethylcyclopent-2-enone (42)

![Chemical structure of 42](image)

According to the procedure for 38: AVK 29 (0.090 g, 0.60 mmol) was reacted with trifluoroacetic acid (0.22 mL, 3.0 mmol) for 2 h to yield 42 (0.091 g, 90%) as a colourless solid: mp 73–74 °C; IR (film) 3396, 1691, 1638 cm⁻¹; ¹H NMR δ: 3.91 (1H, d, J = 2.8 Hz), 3.68 (1H, br s), 2.59 (1H, br d, J = 2.8 Hz), 2.56 (1H, m), 2.00 (3H, s), 1.72 (3H, s), 1.16 (3H, d, J = 6.9 Hz), 0.72 (3H, d, J = 6.9 Hz); ¹³C NMR δ: 208.6, 170.8, 134.6, 71.1, 56.1, 26.6, 21.1, 16.2, 14.9, 7.9; HRMS (ESI): 191.1033, [C₁₀H₁₆O₂Na]⁺ requires 191.1043.
(trans)-5-Hydroxy-4-(4-methoxyphenyl)-2,3-dimethylcyclopent-2-enone (43)

According to the procedure for 38: AVK 30 (0.12 g, 0.56 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 1.5 h to yield 43 (0.13 g, 99%) as a colourless solid: mp 101–102 °C; IR (film) 3406, 1701, 1638, 1612 cm⁻¹; ¹H NMR δ: 7.05 (2H, d, J = 8.8 Hz), 6.88 (2H, d, J = 8.8 Hz), 4.07 (1H, d, J = 3.0 Hz), 3.81 (3H, s), 3.62 (1H, br d, J = 3.0 Hz), 3.27 (1H, br s), 1.81 (3H, s), 1.80 (3H, s); ¹³C NMR δ: 207.9, 169.6, 158.8, 134.7, 131.8, 128.9 (2C), 114.3 (2C), 80.4, 56.8, 55.2, 15.3, 8.2; HRMS (ESI): 255.0989, [C₁₄H₁₆O₃Na]⁺ requires 255.0992.

(trans)-5-Hydroxy-2,3-dimethyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (44)

According to the procedure for 38: AVK 31 (0.14 g, 0.56 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 4 h to yield 44 (0.096 g, 64%) as a colourless solid: mp 146–147 °C; IR (film) 3242, 1699, 1642, 1617, 1421 cm⁻¹; ¹H NMR δ: 7.63 (2H, d, J = 8.2 Hz), 7.28 (2H, d, J = 8.2 Hz), 4.09 (1H, br t, J = 2.7 Hz), 3.75 (1H, br s), 3.36 (1H, d, J = 2.7 Hz), 1.84 (3H, s), 1.83 (3H, s); ¹³C NMR δ: 207.1, 168.0, 144.0, 135.6, 129.8 (q, J = 33 Hz), 128.4 (2C), 126.0 (2C, q, J = 3.5 Hz), 124.0 (q, J = 273 Hz),
According to the procedure for 38: AVK 32 (0.10 g, 0.57 mmol) was reacted with trifluoroacetic acid (0.20 mL, 2.8 mmol) for 3 h to yield 45 (0.061 g, 56%) as an off-white solid: mp 52–53 °C; IR (film) 3406, 1704, 1642 cm⁻¹; ¹H NMR δ: 7.37 (1H, d, \(J = 1.9\) Hz), 6.36 (1H, dd, \(J = 3.2, 1.9\) Hz), 6.29 (1H, d, \(J = 3.2\) Hz), 4.35 (1H, t, \(J = 2.9\) Hz), 3.81 (1H, br d, \(J = 2.9\) Hz), 3.23 (1H, br s), 1.87 (3H, s), 1.79 (3H, s); ¹³C NMR δ: 206.8, 166.6, 152.0, 142.4, 134.4, 110.4, 108.2, 76.7, 50.7, 15.2, 8.2; HRMS (ESI): 215.0677, \([\text{C}_{11}\text{H}_{12}\text{O}_3\text{Na}]^+\) requires 215.0679.

\[(\text{trans})-4-(\text{Furan}-2-\text{yl})-5\text{-hydroxy}-2,3\text{-dimethylcyclopent-2-enone}\ (45)\]

\[(E)-4\text{-Oxo-6-phenylhexa-1,5-dien-2-yl} \ 2,2,2\text{-trifluoroacetate}\ (46)\ \text{and}\ (3Z,5E)-4\text{-hydroxy-6-phenylhexa-3,5-dien-2-one}\ (46a)\]

Trifluoroacetic acid (0.16 mL, 2.1 mmol) was added to a solution of AVK 36 (0.070 g, 0.41 mmol) in CH₂Cl₂ (40 mL) at -78 °C, and stirred for 2 h. The mixture was poured into a separatory funnel containing a saturated solution of sodium bicarbonate, the
organic layer was removed, and additional CH₂Cl₂ (×2) was used to extract the aqueous layer. The organic layers were combined and concentrated under vacuum to yield 46 (0.11 g, 92%) as a yellow oil which was not subjected to further purification: ¹H NMR δ: 7.62 (1H, d, J = 16 Hz), 7.55 (2H, m), 7.41 (3H, m), 6.79 (1H, d, J = 16 Hz), 5.28 (1H, d, J = 2.9 Hz), 5.14 (1H, d, J = 2.9 Hz), 3.67 (2H, s); ¹³C NMR δ: 193.4, 155.2 (q, J = 43 Hz), 148.6, 144.7, 134.0, 131.1, 129.1 (2C), 128.6 (2C), 124.6, 114.4 (q, J = 290 Hz), 107.2, 44.7; ¹⁹F NMR δ: -75.9 (s). Within 24 h 46 hydrolyzed to 46a: ¹H NMR δ: 7.62 (1H, d, J = 16 Hz), 7.52 (2H, m), 7.38 (3H, m), 6.48 (1H, d, J = 16 Hz), 5.69 (1H, s), 2.21 (3H, s); ¹³C NMR δ: 199.4, 177.4, 141.0, 135.0, 130.4, 129.1 (2C), 128.2 (2C), 122.4, 101.5, 27.3. NMR data of 46a matches lit.⁵²

4-Methylene-3-phenylcyclopent-2-enone (51)

BF₃·OEt₂ (0.070 mL, 0.60 mmol) was added to a -78 °C solution of AVK 36 (0.070 g, 0.41 mmol) in CH₂Cl₂ (40 mL). The solution was stirred for 1 h, and then poured into a separatory funnel containing a saturated solution of sodium bicarbonate. The organic layer was removed, and additional CH₂Cl₂ (×2) was used to extract the aqueous layer. The combined organic layers were concentrated under vacuum. Flash chromatography of the residue (10 to 20% EtOAc in hexanes) provided 51 (0.045 g, 64%) as a yellow oil: IR (film) 1721, 1695, 1610 (w) cm⁻¹; ¹H NMR δ: 7.47 (5H, m, H2', 70
H3', H4'), 6.37 (1H, m, H2), 5.51 (1H, m, H6a), 5.43 (1H, m, H6b), 3.22 (2H, m, H5);

\[^{13}\text{C} \text{ NMR} \delta: 204.5 (\text{C}1), 170.6 (\text{C}3), 143.6 (\text{C}1'), 133.4 (\text{C}4), 133.3 (\text{C}2), 130.1 (\text{C}4'), 128.9 (2\text{C}, \text{C}3'), 128.4 (2\text{C}, \text{C}2'), 113.8 (\text{C}6), 41.5 (\text{C}5); \ \text{HRMS (ESI) 193.0628, } [\text{C}_{12}\text{H}_{10}\text{ONa}]^+ \text{ requires 193.0624.} \ ^{1}\text{H} \ \text{NMR data matches lit.}^{53}

2-Methyl-4-methylene-3-phenylcyclopent-2-enone (47)

![2-Methyl-4-methylene-3-phenylcyclopent-2-enone (47)](image)

**Procedure 1:** trifluoroacetic acid (0.20 mL, 2.6 mmol) was added to a solution of AVK 35 (0.010 g, 0.54 mmol) in CH\(_2\)Cl\(_2\) (55 mL) at -78 °C, and stirred for 30 min. The mixture was poured into a separatory funnel containing a saturated solution of sodium bicarbonate, the organic layer was removed, and additional CH\(_2\)Cl\(_2\) (∗2) was used to extract the aqueous layer. The organic layers were combined and concentrated under vacuum to yield 47 (0.048 g, 48%) as a yellow oil following flash chromatography (20% EtOAc in hexanes): IR (film) 1703, 1612 cm\(^{-1}\); \(^{1}\text{H} \ \text{NMR} \delta: 7.47 (3\text{H}, \text{m}), 7.34 (2\text{H}, \text{m}), 5.29 (1\text{H}, \text{s}), 5.22 (1\text{H}, \text{s}), 3.19 (2\text{H}, \text{s}), 1.88 (3\text{H}, \text{s}); \ ^{13}\text{C} \ \text{NMR} \delta: 205.2, 164.5, 143.7, 141.1, 133.2, 128.8, 128.5 (4\text{C}), 110.9, 39.7, 9.4; \ \text{HRMS (ESI) 185.0962, } [\text{C}_{13}\text{H}_{13}\text{O}]^+ \text{ requires 185.0961.}

**Procedure 2:** SiO\(_2\) (0.12 g, 2.7 mmol) was added to a solution of AVK 35 (0.10 g, 0.54 mmol) in CH\(_2\)Cl\(_2\) (5 mL) at rt, and this was stirred overnight. The mixture was filtered and concentrated under vacuum, and flash chromatography (10 to 20% EtOAc in
hexanes) of the residue yielded 47 (0.041 g, 41%) as a yellow oil.

\((3aR^*, 7aS^*)-7a\text{-Hydroxy-3-methyl-3a,4,5,6,7,7a-hexahydro-1H-inden-1-one (48)} \) and 3-methylene-2,3,4,5,6,7-hexahydro-1H-inden-1-one (49)

![Chemical structures of 48 and 49](image)

Trifluoroacetic acid (0.20 mL, 2.6 mmol) was added to a solution of AVK 35 (0.080 g, 0.54 mmol) in CH\(_2\)Cl\(_2\) (55 mL) at -78 °C, and this was stirred for 30 min. The mixture was poured into a separatory funnel containing a saturated solution of sodium bicarbonate, the organic layer was removed, and additional CH\(_2\)Cl\(_2\) (×2) was used to extract the aqueous layer. The organic layers were combined and concentrated under vacuum. The crude product was then subjected to column chromatography (Al\(_2\)O\(_3\), basic, activated, using 20% EtOAc in hexanes then MeOH), which provided 48 (0.052 g, 58%) and 49 (0.009 g, 10%) as yellow oils. For 48: IR (film) 3437, 1695, 1610 cm\(^{-1}\); \(^1\)H NMR δ: 5.94 (1H, m), 2.76 (1H, m), 2.64 (1H, br s), 2.10 (3H, t, \(J = 1.3\) Hz), 1.89 (1H, m), 1.72 (1H, m), 1.61 (4H, m), 1.46 (1H, m), 1.27 (1H, m); \(^13\)C NMR δ: 210.9, 179.1, 126.9, 78.1, 50.3, 32.3, 22.9, 20.7, 18.8, 17.7; HRMS (ESI) 189.0884, [C\(_{10}\)H\(_{14}\)O\(_2\)Na\(^+\)] requires 189.0886. For 49: IR 1704, 1641 cm\(^{-1}\); \(^1\)H NMR δ: 5.24 (1H, s), 5.11 (1H, s), 2.98 (2H, s), 2.45 (2H, m), 2.26 (2H, m), 1.76 (2H, m), 1.70 (2H, m); \(^13\)C NMR δ: 204.9, 165.7, 43.9, 143.1, 107.1, 40.1, 23.1, 22.0, 21.8, 20.6; HRMS (ESI) 171.0785, [C\(_{10}\)H\(_{12}\)ONa\(^+\)] requires 171.0780.
(3aR*,7aS*)-3-Methyl-1-oxo-3a,4,5,6,7,7a-hexahydro-1H-inden-7a-yl-3,5-dinitrobenzoate (50)

Triethylamine (1 mL, 7.2 mmol) and then 3,5-dinitrobenzoyl chloride (0.48, 2.1 mmol) were added to solution of 48 (0.17 g, 1.0 mmol) and DMAP (0.13 g, 1.1 mmol) in CH$_2$Cl$_2$ (25 mL) at rt. The solution was stirred for 18 h, diluted with ethyl acetate, and washed successively with aqueous solutions of 1 M HCl, 10% NaOH, saturated NaHCO$_3$, and brine. The solution was dried over Na$_2$SO$_4$ and concentrated under vacuum. Flash chromatography of the residue (10 to 25% EtOAc in hexanes) provided 50 (0.24 g, 67%), as a peach-coloured solid: mp 176–179 °C; IR (film) 1720, 1619 cm$^{-1}$; $^1$H NMR δ: 9.24 (1H, m), 9.12 (2H, m), 6.14 (1H, s), 3.39 (1H, m), 2.18 (3H, s), 2.14 (1H, m), 1.87 (2H, m), 1.70 (4H, m), 1.42 (1H, m); $^{13}$C NMR δ: 203.3, 176.1, 161.4, 148.8, 133.8, 129.8 (2C), 128.3, 122.8, 85.6, 47.0, 30.0, 22.4, 20.5, 18.8, 17.7; HRMS (ESI) 383.0847, [C$_{17}$H$_{16}$N$_2$O$_7$Na]$^+$ requires 383.0850.
3-Methylene-2,3,4,5,6,7-hexahydro-1H-inden-1-one (49)

![Structure](image)

According to the procedure for 51: BF₃·OEt₂ (0.070 mL, 0.60 mmol) was reacted with AVK 37 (0.080 g, 0.54 mmol) to yield 49 (0.018 g, 23%) as a yellow oil.

According to Procedure 2 for 47: SiO₂ (0.12 g, 2.7 mmol) was reacted with AVK 37 (0.080 g, 0.54 mmol) to yield 49 (0.011 g, 14%) as a yellow oil.

(trans)-5-Chloro-2,3-dimethyl-4-phenylcyclopent-2-enone (55)

![Structure](image)

Gold trichloride (0.27 g, 0.70 mmol) was added at once to a solution of AVK 26 (0.025 g, 0.14 mmol) in CH₂Cl₂ (15 mL) at -78 °C, and the mixture was stirred for 15 min. The black mixture was washed with saturated aqueous NaHCO₃, the aqueous layer was extracted with CH₂Cl₂ (×2), and the combined CH₂Cl₂ layers were dried with Na₂SO₄ and concentrated under vacuum. The residue was purified by column chromatography on silica gel (10% EtOAc in hexanes) to provide 55 as a colourless oil (0.010 g, 32%): IR (film) 1717, 1645, 1603 (w) cm⁻¹; ′H NMR δ: 7.35 (3H, m), 7.13 (2H, m), 4.10 (1H, d, J = 2.8 Hz), 3.91 (1H, br d, J = 2.8 Hz), 1.87 (6H, s); ′C NMR δ: 201.1,
169.0, 138.8, 135.9, 129.2 (2C), 127.9, 127.6 (2C), 61.8, 60.1, 15.6, 8.6; HRMS (ESI): 243.0529, \([\text{C}_{13}\text{H}_{13}\text{ClONa}]^+\) requires 243.0547.

3-(Chloromethyl)-2-methyl-4-phenylocyclopent-2-enone (52)

A solution of AVK 26 (0.10 g, 0.56 mmol) in \(\text{CH}_2\text{Cl}_2\) (50 mL) was cooled to \(-78^\circ\text{C}\), and indium trichloride (0.60 g, 2.8 mmol) was added. The mixture was allowed to warm slowly until completion of the reaction, as evidenced by TLC (3.5 h). The reaction mixture was then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigorously. Additional dichloromethane was added, the aqueous layer was extracted (\(\times 2\)), and the combined organic layers were dried with \(\text{Na}_2\text{SO}_4\), concentrated, and the product was purified by column chromatography (10% \(\text{EtOAc}\) in hexanes) to provide 52 (0.040 g, 35%) as a colourless oil: IR (film) 1711, 1652, 1602 (w) cm\(^{-1}\); \(^1\text{H NMR}^\delta: 7.33 (2\text{H}, \text{m, H3'}), 7.28 (1\text{H}, \text{m, H4'}), 7.14 (2\text{H}, \text{m, H2'}), 4.34 (1\text{H}, \text{d, } J = 12 \text{ Hz, H7a}), 4.24 (1\text{H}, \text{m, H4}), 3.81 (1\text{H}, \text{d, } J = 12 \text{ Hz, H7b}), 2.98 (1\text{H}, \text{dd, } J = 19, 2.3 \text{ Hz, H5a}), 2.47 (1\text{H}, \text{dd, } J = 19, 2.3 \text{ Hz, H5b}), 1.88 (3\text{H, s, H6}); \(^{13}\text{C NMR}^\delta: 208.7 (\text{C1}), 166.2 (\text{C3}), 140.7 (\text{C1'}), 139.2 (\text{C2}), 129.1 (2\text{C, C3'}), 127.5 (3\text{C, C2', C4'}), 44.9 (\text{C4}), 44.2 (\text{C5}), 38.0 (\text{C7}), 8.3 (\text{C6}); \text{HRMS (ESI)}: 243.0547, [\text{C}_{13}\text{H}_{13}\text{ClONa}]^+\) requires 243.0533.
3-(Bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)

According to the procedure for 52: AVK 26 (0.10 g, 0.56 mmol) was reacted with indium tribromide (1.0 g, 2.8 mmol) for 2 h to yield 53 (0.040 g, 29%) as a colourless oil: IR (film) 1710, 1647, 1602 \text{(w)} \text{ cm}^{-1}; \text{^1H NMR } \delta: 7.34 \text{ (2H, m)}, 7.28 \text{ (1H, m)}, 7.14 \text{ (2H, m)}, 4.28 \text{ (1H, m)}, 4.20 \text{ (1H, d, } J = 10 \text{ Hz)}, 3.69 \text{ (1H, d, } J = 10 \text{ Hz)}, 3.01 \text{ (1H, dd, } J = 19, 7.3 \text{ Hz)}, 2.51 \text{ (1H, dd, } J = 19, 2.4 \text{ Hz)}, 1.85 \text{ (3H, s)}; \text{^{13}C NMR } \delta: 208.7, 166.6, 140.7, 139.0, 129.1 \text{ (2C)}, 127.5 \text{ (3C)}, 45.1, 44.2, 24.7, 8.4; \text{ HRMS (ESI): 287.0034, } [\text{C}_{13}\text{H}_{13}\text{BrONa}]^{+} \text{ requires 287.0042.}

3-(Iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (54)

According to the procedure for 52: AVK 26 (0.10 g, 0.56 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 1.5 h to yield 54 (0.055 g, 32%) as a colourless oil: IR (film) 1707, 1641, 1602 \text{(w)} \text{ cm}^{-1}; \text{^1H NMR } \delta: 7.38 \text{ (2H, m)}, 7.31 \text{ (1H, m)}, 7.14 \text{ (2H, m)}, 4.36 \text{ (1H, m)}, 4.13 \text{ (1H, d, } J = 9.3 \text{ Hz)}, 3.66 \text{ (1H, d, } J = 9.3 \text{ Hz)}, 3.03 \text{ (1H, dd, } J = 19, 7.4 \text{ Hz)}, 2.56 \text{ (1H, dd, } J = 19, 2.4 \text{ Hz)}, 1.74 \text{ (3H, s)}; \text{^{13}C NMR } \delta: 208.7, 168.5, 140.9,
137.5, 129.2 (2C), 127.5, 127.4 (2C), 45.4, 44.2, 8.5, -2.8; HRMS (ESI): 334.9881, [C\textsubscript{13}H\textsubscript{13}IONa]\textsuperscript{+} requires 334.9903.

3-(Chloromethyl)-2-methylcyclopent-2-enone (58)

\[
\text{\includegraphics[width=0.1\textwidth]{58.png}}
\]

According to the procedure for 52: AVK 27 (0.060 g, 0.56 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 5 h to yield 58 (0.025 g, 31%) as a colourless oil: IR (film) 1704, 1654 cm\textsuperscript{-1}; \textsuperscript{1}H NMR δ: 4.36 (2H, s), 2.69 (2H, m), 2.46 (2H, m), 1.77 (3H, s); \textsuperscript{13}C NMR δ: 209.4, 164.3, 138.7, 40.2, 34.0, 27.6, 8.0; HRMS (ESI): 167.0231, [C\textsubscript{7}H\textsubscript{9}ClONa]\textsuperscript{+} requires 167.0234.

3-(Iodomethyl)-2-methylcyclopent-2-enone (59)

\[
\text{\includegraphics[width=0.1\textwidth]{59.png}}
\]

According to the procedure for 52: AVK 27 (0.060 g, 0.56 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 2 h to yield 59 (0.045 g, 34%) as a colourless oil: IR (film) 1694, 1639 cm\textsuperscript{-1}; \textsuperscript{1}H NMR δ: 4.16 (2H, s), 2.76 (2H, m), 2.52 (2H, m), 1.66 (3H, s); \textsuperscript{13}C NMR δ: 209.5, 166.5, 137.4, 34.1, 28.2, 8.1, -1.2; HRMS (ESI): 258.9570, [C\textsubscript{7}H\textsubscript{9}IONa]\textsuperscript{+} requires 258.9590.
3-(Chloromethyl)-2,4-dimethylcyclopent-2-enone (60)

![60]

According to the procedure for 52: AVK 28 (0.070 g, 0.57 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 4 h to yield 60 (0.018 g, 20%) as a colourless oil: IR (film) 1708, 1650 cm\(^{-1}\); \(^1\)H NMR δ: 4.42 (1H, d, \(J = 12\) Hz), 4.33 (1H, d, \(J = 12\) Hz), 3.10 (1H, m), 2.71 (1H, dd, \(J = 19, 6.5\) Hz), 2.05 (1H, dd, \(J = 19, 2.2\) Hz), 1.77 (3H, s), 1.23 (1H, d, \(J = 7.2\) Hz); \(^{13}\)C NMR δ: 208.4, 168.1, 138.6, 42.8, 37.8, 33.8, 18.7, 8.2; HRMS (ESI): 181.0385, [C\(_8\)H\(_{11}\)ClNa]\(^+\) requires 181.0391.

3-(Iodomethyl)-2,4-dimethylcyclopent-2-enone (61)

![61]

According to the procedure for 52: AVK 28 (0.060 g, 0.57 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 2 h to yield 61 (0.012 g, 8%) as a colourless oil: IR (film) 1703, 1638 cm\(^{-1}\); \(^1\)H NMR δ: 4.18 (1H, d, \(J = 9.4\) Hz), 4.14 (1H, d, \(J = 9.4\) Hz), 3.18 (1H, m), 2.73 (1H, dd, \(J = 19, 6.8\) Hz), 2.11 (1H, dd, \(J = 19, 2.4\) Hz), 1.65 (3H, s), 1.21 (3H, d, \(J = 7.2\) Hz); \(^{13}\)C NMR δ: 208.4, 170.2, 137.3, 42.9, 34.3, 19.0, 8.3, -3.8; HRMS (ESI): 272.9723, [C\(_{8}\)H\(_{11}\)Iona]\(^+\) requires 272.9747.
3-(Chloromethyl)-4-isopropyl-2-methylcyclopent-2-enone (62)

![Chemical structure of 62](image)

According to the procedure for 52: AVK 29 (0.090 g, 0.6 mmol) was reacted with indium trichloride (0.66 g, 3.0 mmol) for 4.5 h to yield 62 (0.023 g, 21%) as a colourless oil: IR (film) 1707, 1650 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 4.43 (1H, d, \(J = 12\) Hz), 4.22 (1H, d, \(J = 12\) Hz), 3.11 (1H, m), 2.35 (1H, dd, \(J = 19, 6.8\) Hz), 2.23 (2H, m), 1.79 (3H, s), 1.33 (3H, d, \(J = 6.9\) Hz), 0.62 (3H, d, \(J = 6.9\) Hz); \(^13\)C NMR \(\delta\): 208.8, 166.4, 139.9, 44.7, 38.1, 34.8, 27.3, 21.7, 14.9, 8.1; HRMS (ESI): 209.0693, [C\(_{10}\)H\(_{15}\)ClONa]\(^+\) requires 209.0704.

3-(Iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (63)

![Chemical structure of 63](image)

According to the procedure for 52: AVK 29 (0.090 g, 0.60 mmol) was reacted with indium triiodide (1.5 g, 3.0 mmol) for 2.5 h to yield 63 (0.015 g, 9%) as a colourless oil: IR (film) 1702, 1638 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 4.21 (1H, d, \(J = 9.5\) Hz), 4.08 (1H, d, \(J = 9.5\) Hz), 3.23 (1H, m), 2.38 (1H, dd, \(J = 19, 6.8\) Hz), 2.26 (1H, dd, \(J = 19, 2.4\) Hz), 2.16 (1H, m), 1.65 (3H, s), 1.03 (3H, d, \(J = 6.8\) Hz), 0.62 (3H, d, \(J = 6.8\) Hz); \(^13\)C NMR \(\delta\): 208.8, 168.5, 138.6, 45.1, 34.8, 27.5, 21.6, 14.7, 8.2, -3.3; HRMS (ESI): 301.0044, [C\(_{10}\)H\(_{15}\)IONa]\(^+\) requires 301.0060.
3-(Iodomethyl)-4-(4-methoxyphenyl)-2-methylcyclopent-2-enone (64)

According to the procedure for 52: AVK 30 (0.12 g, 0.56 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 1 h to yield 64 (0.049 g, 26%) as a colourless oil: IR (film) 1702, 1639, 1610 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.05 (2H, d, \(J = 8.7\) Hz), 6.86 (2H, d, \(J = 8.7\) Hz), 4.31 (1H, m), 4.12 (1H, d, \(J = 9.3\) Hz), 3.80 (3H, s), 3.67 (1H, d, \(J = 9.3\) Hz), 3.01 (1H, dd, \(J = 19, 7.2\) Hz), 2.52 (1H, dd, \(J = 19, 2.5\) Hz), 1.73 (3H, s); \(^{13}\)C NMR \(\delta\): 208.9, 168.7, 158.9, 137.2, 132.8, 128.4 (2C), 114.5 (2C), 55.3, 44.6, 44.3, 8.5, - 2.7; HRMS (ESI): 365.0009, [C\(_{14}\)H\(_{15}\)IO\(_2\)Na\(^{+}\)] requires 365.0014.

3-(Chloromethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (65)

According to the procedure for 52: AVK 31 (0.14 g, 0.56 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 5 h to yield 65 (0.037 g, 23%) as a colourless oil: IR (film) 1712, 1654, 1620, 1327 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.60 (2H, d, \(J = 8.2\) Hz), 7.28 (2H, d, \(J = 8.2\) Hz), 4.37 (1H, d, \(J = 12\) Hz), 4.33 (1H, m), 3.79 (1H, d, \(J = 12\) Hz), 3.01 (1H, dd, \(J = 19, 7.3\) Hz), 2.44 (1H, dd, \(J = 19, 2.4\) Hz), 1.89 (3H, s); \(^{13}\)C NMR \(\delta\): 207.8, 165.2, 144.9, 139.9, 129.9 (q, \(J = 33\) Hz), 128.0 (2C), 126.1 (2C, q, \(J = 3.5\) Hz), 124.0 (q,
$J = 270 \text{ Hz}, 44.7, 43.9, 37.9, 8.4$; $^{19}$F NMR $\delta$: -63.5 (s); HRMS (ESI): 289.0603, $[\text{C}_{14}\text{H}_{12}\text{F}_{3}\text{ClOH}]^+$ requires 289.0602.

3-(Iodomethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (66)

![Chemical Structure of 66](image)

According to the procedure for 52: AVK 31 (0.14 g, 0.56 mmol) was reacted with indium triiodide (1.4 g, 2.8 mmol) for 3 h to yield 66 (0.028 g, 13%) as a colourless oil: IR (film) 1705, 1642, 1619, 1326 cm$^{-1}$; $^1$H NMR $\delta$: 7.61 (2H, d, $J = 8.2$ Hz), 7.28 (2H, d, $J = 8.2$ Hz), 4.45 (1H, m), 4.44 (1H, d, $J = 9.5$ Hz), 3.61 (1H, d, $J = 9.5$ Hz), 3.06 (1H, dd, $J = 19, 7.4$ Hz), 2.53 (1H, dd, $J = 19, 2.5$ Hz), 1.76 (3H, s); $^{13}$C NMR $\delta$: 207.8, 167.4, 145.1, 138.2, 130.0 (q, $J = 33$ Hz), 127.9 (2C), 126.2 (2C, q, $J = 3.5$ Hz), 126.1 (q, $J = 270$ Hz), 45.2, 43.9, 8.6, -3.3; $^{19}$F NMR $\delta$: -63.5 (s); HRMS (ESI): 402.9754, $[\text{C}_{14}\text{H}_{12}\text{F}_{3}\text{IONa}]^+$ requires 402.9777.
According to the procedure for 52: AVK 30 (0.12 g, 0.56 mmol) was reacted with indium trichloride (0.60 g, 2.8 mmol) for 3 h to yield 67 (0.049 g, 82%) as a white solid: mp 115 – 117 °C; IR (film) 1958, 1932, 1769, 1673, 1610 cm⁻¹; ¹H NMR δ: 6.99 (2H, d, \(J = 8.8\) Hz, H2’’’), 6.98 (2H, d, \(J = 8.8\) Hz, H2’’), 6.82 (2H, d, \(J = 8.8\) Hz, H3’’’), 6.81 (2H, d, \(J = 8.8\) Hz, H3’’), 5.16 (1H, dq, \(J = 15, 3.0\) Hz, H4’a), 5.13 (1H, d, \(J = 2.3\) Hz, H8a), 5.10 (1H, dq, \(J = 15, 3.0\) Hz, H4’’b), 4.81 (1H, d, \(J = 2.3\) Hz, H8b), 3.84 (1H, dd, \(J = 6.7, 4.4\) Hz, H3), 3.78 (6H, s, H11, H12), 3.72 (1H, t, \(J = 2.3\) Hz, H5), 3.70 (1H, d, \(J = 6.7\) Hz, H2), 2.72 (1H, d, \(J = 4.4\) Hz, H4), 1.83 (3H, t, \(J = 3.0\) Hz, H10), 0.83 (3H, s, H9); ¹³C NMR δ: 216.2 (C3’’’), 213.3 (C7), 198.1 (C1’’’), 158.7 (C4’’’), 158.4 (C4’’), 152.1 (C6), 134.8 (C1’’’), 133.6 (C1’’), 129.3 (2C, C2’’’), 128.5 (2C, C2’’), 114.1 (2C, C3’’’), 114.0 (2C, C3’’’), 107.9 (C8), 103.8 (C2’), 79.8 (C4’’), 55.2 (2C, C11, C12), 54.4 (C1), 53.6 (C4), 51.1 (C3), 47.0 (C2), 45.0 (C5), 13.5 (C10), 9.9 (C9); HRMS (ESI): 451.1854, [C₂₈H₂₅O₄Na]⁺ requires 451.1880.
Procedure 1: A solution of AVK 26 (0.10 g, 0.56 mmol) in CH$_2$Cl$_2$ (50 mL) was cooled to –78 °C, and a solution of titanium bromide (1.0 M in CH$_2$Cl$_2$) (2.8 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm to warm slowly for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigorously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers dried with Na$_2$SO$_4$. The product was purified by column chromatography (10% EtOAc in hexanes) to yield 56 (0.12 g, 80%) as a colourless oil: IR (film) 1714, 1644, 1602 (w) cm$^{-1}$; $^1$H NMR δ: 7.38 (3H, m), 7.12 (2H, m), 4.19 (1H, d, $J = 2.5$ Hz), 4.03 (1H, br d, $J = 2.5$ Hz), 1.88 (3H, s), 1.87 (3H, s); $^{13}$C NMR δ: 201.5, 169.1, 138.9, 135.8, 129.2 (2C), 128.0, 127.4 (2C), 60.7, 50.4, 15.7, 8.7; HRMS (ESI): 287.0042, [C$_{13}$H$_{13}$BrONa]$^+$ requires 287.0047.

Procedure 2: A solution of AVK 26 (0.10 g, 0.56 mmol) in CH$_2$Cl$_2$ (50 mL) was cooled to –78 °C, and a solution of freshly sublimed titanium bromide (1.0 M in CH$_2$Cl$_2$) (2.8 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm to warm slowly for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigorously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers dried with Na$_2$SO$_4$. 

(trans)-5-Bromo-2,3-dimethyl-4-phenylcyclopent-2-enone (56) and 3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)
The product was purified by column chromatography (10% EtOAc in hexanes) to yield 56 (0.030 g, 23%) and 53 (0.030 g, 23%) as colourless oils.

5-Bromo-2,3-dimethylcyclopent-2-enone (68) and 3-(bromomethyl)-2-methylcyclopent-2-enone (69)

According to Procedure 2 for 56 and 53: AVK 27 (0.045 g, 0.42 mmol) was reacted with titanium tetrabromide (2.1 mL, 2.1 mmol) to yield 68 (0.013 g, 16%) and 69 (0.013 g, 16%) as colourless oils. For 68: IR (film) 1711, 1648 cm⁻¹; ¹H NMR δ: 4.35 (1H, dd, J = 2.2, 6.8 Hz), 3.19 (1H, dd, J = 6.8, 19 Hz), 2.82 (1H, br dd, J = 2.2, 19 Hz), 1.77 (3H, s), 1.56 (3H, s); ¹³C NMR δ: 202.3, 167.3, 134.5, 43.1, 41.4, 17.2, 8.3; HRMS (ESI): 188.9907, [C₇H₁₀BrO]⁺ requires 188.9910. For 69: IR (film) 1698, 1640 cm⁻¹; ¹H NMR δ: 4.22 (2H, s), 2.70 (2H, m), 2.49 (2H, m), 1.76 (3H, s); ¹³C NMR δ: 209.5, 164.5, 138.8, 34.1, 28.0, 26.7, 8.1; HRMS (ESI): 210.9734, [C₇H₉BrO₂Na]⁺ requires 210.9729.

(trans)-5-Bromo-2,3,4-trimethylcyclopent-2-enone (70) and 3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (71)

According to Procedure 2 for 56 and 53: AVK 28 (0.060 g, 0.56 mmol) was
reacted with titanium tetrabromide (2.8 mL, 2.8 mmol) to yield 70 (0.022 g, 19%) and 71 (0.022 g, 19%) as colourless oils. For 70: IR (film) 1711, 1645 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 3.92 (1H, d, \(J = 2.5\) Hz), 2.97 (1H, m), 1.76 (3H, s), 2.02 (3H, s), 1.28 (3H, d, \(J = 7.3\) Hz); \(^{13}\)C NMR \(\delta\): 201.0, 171.2, 134.2, 50.0, 49.1, 16.9, 14.9, 8.5; HRMS (ESI): 224.9873, \([C_8H_{11}BrONa]^+\) requires 224.9885. For 71: IR (film) 1702, 1641 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 4.26 (1H, d, \(J = 11\) Hz), 4.18 (1H, d, \(J = 11\) Hz), 3.13 (1H, m), 2.72 (1H, dd, \(J = 6.7, 19\) Hz), 2.07 (1H, dd, \(J = 2.2, 19\) Hz), 1.65 (3H, s), 1.22 (3H, d, \(J = 7.2\) Hz); \(^{13}\)C NMR \(\delta\): 208.4, 168.3, 138.7, 42.9, 34.1, 24.2, 18.7, 18.0, 8.2; HRMS (ESI): 224.9870, \([C_8H_{11}BrONa]^+\) requires 224.9885.

\[(trans)-5\text{-Bromo-4-isopropyl-2,3-dimethylcyclopent-2-enone (72)}\text{ and 3-}(\text{bromomethyl)-4-isopropyl-2-methylcyclopent-2-enone (73)}\]

\[\text{According to Procedure 2 for 56 and 53: AVK 29 (0.090 g, 0.60 mmol) was reacted with titanium tetrabromide (3.0 mL, 3.0 mmol) to yield 72 (0.025, 18%) and 73 (0.025 g, 18%) as colourless oils. For 72: IR (film) 1711, 1645 cm}^{-1}; \(^1\)H NMR \(\delta\): 4.10 (1H, d, \(J = 1.9\) Hz), 3.01 (1H, m), 2.25 (1H, m), 2.00 (3H, s), 1.77 (3H, s), 1.17 (3H, d, \(J = 6.9\) Hz), 0.64 (3H, d, \(J = 6.9\) Hz); \(^{13}\)C NMR \(\delta\): 201.9, 170.2, 135.4, 59.9, 42.5, 27.9, 21.2, 15.4 (2C), 8.4; HRMS (ESI): 253.0183, \([C_{10}H_{15}BrONa]^+\) requires 253.0198. For 73: IR (film) 1702, 1638 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 4.28 (1H, d, \(J = 10\) Hz), 4.11 (1H, d, \(J = 10\) Hz), 3.15 (1H, m), 2.37 (1H, dd, \(J = 6.7, 19\) Hz), 2.23 (1H, dd, \(J = 2.3, 19\) Hz), 2.21 (1H, m), \]
1.77 (3H, s), 1.03 (3H, d, $J = 6.9$ Hz), 0.62 (3H, d, $J = 6.9$ Hz); $^{13}$C NMR $\delta$: 208.8, 166.7, 139.9, 44.9, 34.8, 27.3, 24.5, 21.7, 14.9, 8.1; HRMS (ESI): 253.0202, $[C_{10}H_{15}BrONa]^+$ requires 253.0198.

2,3-Dimethyl-4-phenylcyclopent-2-enone (57)

![Diagram of compound 57]

According to Procedure 1 for 56: AVK 26 (0.10 g, 0.56 mmol) was reacted with titanium tetraiodide (0.5 M in CH$_2$Cl$_2$) (5.6 mL, 2.8 mmol) for 48 h to yield 57 (0.090 g, 90%) as a colourless oil: IR (film) 1702, 1649, 1602 (w) cm$^{-1}$; $^1$H NMR $\delta$: 7.35 (2H, m), 7.28 (1H, m), 7.12 (2H, m), 3.81 (1H, m), 2.89 (1H, dd, $J = 19, 7.1$ Hz), 2.36 (1H, dd, $J = 19, 2.3$ Hz), 1.82 (3H, s), 1.79 (3H, s); $^{13}$C NMR $\delta$ (ppm): 208.9, 171.4, 142.1, 137.1, 128.9, 127.3, 127.0, 49.1, 44.5, 15.5, 8.2; HRMS (ESI): 209.0937, $[C_{13}H_{14}ONa]^+$ requires 209.0942.

(trans)-5-Bromo-3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (75)

![Diagram of compound 75]

A solution of AVK 28 (0.070 g, 0.56 mmol) in CH$_2$Cl$_2$ (50 mL) was cooled to $-78$ °C, and a solution of bromine (1M in CH$_2$Cl$_2$) (0.56 mL, 0.56 mmol) was added
dropwise. After stirring for 15 min, a solution of titanium bromide (1M in dichloromethane) (2.8 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm slowly and stirred at room temperature for 10 h. The reaction mixture was then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, the aqueous layer was extracted (×2), and the combined organic layers were dried with Na$_2$SO$_4$, concentrated, and the product purified by column chromatography (10% EtOAc in hexanes) to yield 75 (0.034 g, 22%) as a colourless oil: IR (film) 1712, 1633 cm$^{-1}$; $^1$H NMR δ: 4.24 (1H, d, $J$ = 11 Hz), 4.13 (1H, d, $J$ = 11 Hz), 4.03 (1H, d, $J$ = 2.9 Hz), 3.28 (1H, m), 1.83 (3H, s), 1.35 (3H, d, $J$ = 7.3 Hz); $^{13}$C NMR δ: 200.8, 165.7, 136.9, 49.8, 46.3, 23.3, 16.6, 8.7; HRMS (ESI): 302.8965, [C$_8$H$_{10}$Br$_2$ONa]$^+$ requires 302.8991.

(\textit{trans})-5-Bromo-3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (76)

![Chemical structure of 76](image)

According to the procedure for 75: AVK 26 (0.10 g, 0.56 mmol) was reacted with bromine (0.56 mL, 0.56 mmol) and titanium tetrabromide (2.8 mL, 2.8 mmol) to yield 76 (0.15 g, 79%) as a white solid: mp 84–86 °C; IR (film) 1717, 1642, 1601 (w) cm$^{-1}$; $^1$H NMR δ: 7.37 (3H, m), 7.15 (2H, m), 4.42 (1H, br d, $J$ = 2.7 Hz), 4.33 (1H, d, $J$ = 2.5 Hz), 4.21 (1H, d, $J$ = 11 Hz), 3.69 (1H, d, $J$ = 11 Hz), 1.94 (3H, s); $^{13}$C NMR δ: 201.5, 164.2,
According to the procedure for 75: AVK 30 (0.12 g, 0.56 mmol) was reacted with bromine (0.56 mL, 0.56 mmol) and titanium tetrabromide (2.8 mL, 2.8 mmol) to yield 77 (0.15 g, 70%) as a colourless oil: IR (film) 1717, 1642, 1601 (w) cm$^{-1}$; $^1$H NMR δ: 7.07 (2H, d, $J = 9.0$ Hz), 6.90 (2H, d, $J = 9.0$ Hz), 4.36 (1H, br d, $J = 2.6$ Hz), 4.29 (1H, d, $J = 2.6$ Hz), 4.19 (1H, d, $J = 11$ Hz), 3.81 (3H s), 3.70 (1H, d, $J = 11$ Hz), 1.92 (3H, s); $^{13}$C NMR δ: 201.5, 164.3, 159.6, 137.4, 129.5 (2C), 128.7 (2C), 114.8, 56.4, 55.3, 50.3, 23.9, 8.9; HRMS (ESI): 394.9251, [C$_{14}$H$_{14}$Br$_2$O$_2$Na]$^+$ requires 394.9253.

(\textit{trans})-5-Bromo-3-(bromomethyl)-2-methyl-4-(4-(trifluoromethyl)phenyl)cyclopent-2-enone (78)

According to the procedure for 75: AVK 31 (0.10 g, 0.56 mmol) was reacted with bromine (0.56 mL, 0.56 mmol) and titanium tetrabromide (2.8 mL, 2.8 mmol) to yield 78
(0.15 g, 65%) as a colourless oil: IR (film) 1705, 1642, 1619, 1326 cm⁻¹; ¹H NMR δ: 7.67 (2H, d, J = 8.2 Hz), 7.32 (2H, d, J = 8.2 Hz), 4.49 (1H, br d, J = 2.8 Hz), 4.31 (1H, d, J = 2.8 Hz), 4.24 (1H, d, J = 11 Hz), 3.67 (1H, d, J = 11 Hz), 1.96 (3H, s); ¹³C NMR δ: 200.6, 163.1, 141.8, 138.4, 130.8 (q, J = 33 Hz), 128.2 (2C), 126.5 (2C, q, J = 3.8 Hz), 123.7 (q, J = 270 Hz), 56.9, 49.7, 23.7, 9.0; ¹⁹F NMR δ: -63.8 (s); HRMS (ESI): 432.8989, [C₁₄H₁₁Br₂F₃ONa]^+ requires 432.9021.

5-Hydroxy-3-(iodomethyl)-2-methylcyclopent-2-enone (79)

![Structure](image)

A solution of AVK 27 (0.060 g, 0.56 mmol) in CH₂Cl₂ (50 mL) was cooled to –78 °C, and iodine (0.14 g, 0.56 mmol) was added. After stirring for 1 h, the solution was re-cooled to –78 °C, and trifluoroacetic acid (0.20 mL, 2.8 mmol) was added dropwise. The mixture was allowed to warm to room temperature and stirred for 48 h. The reaction mixture was then poured into a separatory funnel containing saturated aqueous sodium bicarbonate, and shaken vigourously. Additional dichloromethane was added, and the aqueous layer was extracted (×2). The combined organic layers were washed with a 10% aqueous solution of sodium thiosulfate, then dried with Na₂SO₄ and concentrated. The intermediate trifluoroacetate ester was hydrolyzed via SiO₂ chromatography by loading the product with 10% EtOAc in hexanes, and after one hour commencing elution (10%, then 20%, EtOAc in hexanes) to yield 79 (0.025 g, 18%) as an orange wax: IR (film) 3385,
1702, 1632 cm$^{-1}$; $^1$H NMR $\delta$: 4.34 (1H, dd, $J = 6.9, 3.0$ Hz), 4.17 (1H, d, $J = 9.3$ Hz), 4.11 (1H, d, $J = 9.3$ Hz), 3.11 (1H, dd, $J = 17, 6.9$ Hz), 2.80 (1H, br s), 2.68 (1H, br dd, $J = 17, 3.0$ Hz), 1.69 (3H, s); $^{13}$C NMR $\delta$: 208.9, 164.5, 134.6, 71.6, 37.1, 8.1, -2.0; HRMS (ESI): 274.9536, [C$_7$H$_9$IO$_2$Na]$^+$ requires 274.9539.

$^{(trans)}$-5-Hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80a) and $^{(cis)}$-5-hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80b)

According to the procedure for 79: AVK 28 (0.070 g, 0.56 mmol) was reacted with iodine (0.14 g, 0.56 mmol) and trifluoroacetic acid (0.20 mL, 2.8 mmol) to yield 0.062 g (40%) of a 2.5:1 mixture of 80a/80b (as determined by integration of the $^1$H NMR spectrum), yellow oil: IR (film) 3397, 1704, 1627 cm$^{-1}$; HRMS (ESI): 288.9684, [C$_8$H$_{11}$IO$_2$Na]$^+$ requires 288.9696; the following NMR data were taken from the spectra of the mixture: for 80a: $^1$H NMR $\delta$: 4.16 (1H, d, $J = 9.5$ Hz), 4.12 (1H, d, $J = 9.5$ Hz), 3.96 (1H, d, $J = 3.1$ Hz), 3.06 (1H, br s), 3.01 (1H, m), 1.68 (3H, s), 1.37 (3H, d, $J = 7.2$ Hz); $^{13}$C NMR $\delta$: 207.2, 167.0, 134.7, 79.5, 42.8, 15.6, 8.3, -4.9; for 80b: $^1$H NMR $\delta$: 4.26 (1H, d, $J = 7.2$ Hz), 4.23 (1H, d, $J = 9.5$ Hz), 4.08 (1H, d, $J = 9.5$ Hz), 2.95 (1H, br s), 3.31 (1H, s), 1.70 (3H, s), 1.13 (3H, d, $J = 7.2$ Hz); $^{13}$C NMR $\delta$: 209.0, 169.3, 133.4, 74.4, 40.0, 14.7, 8.1, -3.6.
(trans)-5-Hydroxy-3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (81)

According to the procedure for 79: AVK 29 (0.090 g, 0.60 mmol) was reacted with iodine (0.15 g, 0.60 mmol) and trifluoroacetic acid (0.22 mL, 3.0 mmol) to yield 81 (0.080 g, 45%) as a yellow oil: IR (film) 3424, 1706, 1628 cm\(^{-1}\); \(^1\)H NMR: 4.24 (1H, d, \(J = 9.5 \text{ Hz}\)), 4.14 (1H, d, \(J = 2.9 \text{ Hz}\)), 4.04 (1H, d, \(J = 9.5 \text{ Hz}\)), 3.07 (1H, m), 2.77 (1H, br s), 2.48 (1H, m), 1.68 (3H, s), 1.19 (3H, d, \(J = 6.9 \text{ Hz}\)), 0.77 (3H, d, \(J = 6.9 \text{ Hz}\)); \(^{13}\)C NMR: 208.1, 167.2, 136.1, 71.8, 53.0, 26.5, 21.4, 16.5, 8.6, -4.0; HRMS (ESI): 316.9992, [C\(_{10}\)H\(_{15}\)I\(_2\)O\(_2\)Na\(^+\)] requires 317.0009.

(trans)-5-Hydroxy-3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (82)

According to the procedure for 79: AVK 26 (0.10 g, 0.56 mmol) was reacted with iodine (0.14 g, 0.56 mmol) and trifluoroacetic acid (0.20 mL, 2.8 mmol) to yield 82 (0.11 g, 61%) as an orange wax: IR (film) 3418, 1698, 1635, 1602 cm\(^{-1}\); \(^1\)H NMR: 7.38 (2H, m), 7.33 (1H, m), 7.21 (2H, m), 4.36 (1H, d, \(J = 3.0 \text{ Hz}\)), 4.18 (1H, br d, \(J = 3.0 \text{ Hz}\)), 4.14 (1H, d, \(J = 9.5 \text{ Hz}\)), 3.65 (1H, d, \(J = 9.5 \text{ Hz}\)), 2.81 (1H, br s), 1.77 (3H, s); \(^{13}\)C NMR:
According to the procedure for 79: AVK 30 (0.12 g, 0.56 mmol) was reacted with iodine (0.14 g, 0.56 mmol) and trifluoroacetic acid (0.20 mL, 2.8 mmol) to yield 83 (0.065 g, 32%) as an orange wax: IR (film) 3422, 1704, 1630, 1611 cm⁻¹; ¹H NMR δ: 7.13 (2H, d, J = 8.7 Hz), 6.91 (2H, d, J = 8.7 Hz), 4.33 (1H, br t, J = 2.5 Hz), 4.12 (1H, d, J = 9.2 Hz), 3.82 (3H, s), 3.66 (1H, d, J = 9.2 Hz), 2.82 (1H, d, J = 2.5 Hz), 1.76 (3H, s); ¹³C NMR δ: 207.0, 166.2, 159.2, 135.3, 130.4, 129.1 (2C), 114.6 (2C), 80.6, 55.3, 53.4, 8.7, -3.7; HRMS (ESI): 380.9929, [C₁₄H₁₃IO₃Na]⁺ requires 380.9958.

(1E)-4,5-Dibromo-4-methyl-1-phenylhexa-1,5-dien-3-one (74)

A -78 °C CH₂Cl₂ (14 mL) solution of AVK 26 (0.025 g, 0.14 mmol) was reacted with bromine (0.14 mL, 1 M solution in CH₂Cl₂), and was stirred for 15 min. The reaction mixture was then concentrated, and the product purified by column
chromatography (10% EtOAc in hexanes) to yield 74 (0.040, 99%) as a colourless oil: IR (film) 1694, 1611 cm\(^{-1}\); \(^1\)H NMR δ: 7.82 (1H, d, \(J = 16\) Hz, H1), 7.58 (2H, m, H3’), 7.40 (3H, m, H2’, H4’), 7.11 (1H, d, \(J = 16\) Hz, H2), 6.59 (1H, d, \(J = 3.0\) Hz, H6a), 5.98 (1H, d, \(J = 3.0\) Hz, H6b), 2.12 (3H, s, H7); \(^{13}\)C NMR δ: 189.4 (C3), 145.2 (C1), 134.4 (C1’), 130.8 (C4’), 130.5 (C5), 128.9 (2C, C2’), 128.7 (2C, C3’), 123.0 (C6), 120.1 (C2), 68.4 (C4), 27.4 (C7); HRMS (ESI): 364.9113, [C\(_{13}\)H\(_{12}\)Br\(_2\)ONa]\(^+\) requires 364.9147.

\((1\text{E,4E})\)-5,6-Dibromo-4-methyl-1-phenylhexa-1,4-dien-3-one (84)

\[\begin{align*}
\text{(84)} & \\
\text{(84)}
\end{align*}\]

A -78 °C CH\(_2\)Cl\(_2\) (14 mL) solution of AVK 26 (0.025 g, 0.14 mmol) was reacted with bromine (0.14 mL, 1 M solution in CH\(_2\)Cl\(_2\)), and after 15 minutes trifluoroacetic acid (0.70 mmol, 0.10 mL) was added, and the mixture was let to warm to room temperature overnight. The mixture was then washed with saturated aqueous sodium bicarbonate, and the aqueous layer back-extracted with dichloromethane. The combined organic layers were dried with Na\(_2\)SO\(_4\), concentrated, and the product purified by column chromatography (10% EtOAc in hexanes) to yield 84 (0.038, 99%) as a colourless oil: IR (film) 1650, 1617, 1605 cm\(^{-1}\); \(^1\)H NMR δ: 7.62 (1H, d, \(J = 16\) Hz, H1), 7.61 (2H, m, H3’), 7.44 (3H, m, H2’, H4’), 6.83 (1H, d, \(J = 16\) Hz, H2), 4.34 (2H, s, H6), 2.12 (3H, s, H7); \(^{13}\)C NMR δ: 194.8 (C3), 148.1 (C1), 141.3 (C4), 133.8 (C1’), 131.4 (C4’), 129.1 (2C,
C2’), 128.8 (2C, C3’), 125.1 (C5), 124.3 (C2), 36.0 (C6), 21.7 (C7); HRMS (ESI): 364.9129, [C_{13}H_{12}Br_{2}ONa]^+ requires 364.9147.

(1S^*,2R^*,4E)-1,2,5,6-Tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)

A -78 °C CH₂Cl₂ (14 mL) solution of AVK 26 (0.025 g, 0.14 mmol) was reacted with bromine (0.28 mL, 1 M solution in CH₂Cl₂), and after 15 minutes trifluoroacetic acid (0.70 mmol, 0.10 mL) was added, and the mixture was warmed to room temperature and stirred for 18 h. The mixture was then washed with saturated aqueous sodium bicarbonate, and the aqueous layer back-extracted with dichloromethane. The combined organic layers were dried with Na₂SO₄, concentrated, and the product purified by column chromatography (10% EtOAc in hexanes) to yield 85 (0.070, 99%) as a colourless solid: mp 85–87 °C; IR (film) 1702, 1603 cm⁻¹; ¹H NMR δ: 7.41 (5H, m), 5.47 (1H, d, J = 12 Hz), 5.31 (1H, d, J = 12 Hz), 4.60 (1H, d, J = 11 Hz), 4.55 (1H, d, J = 11 Hz), 2.30 (3H, s); ¹³C NMR δ: 192.3, 137.8, 137.5, 134.1, 129.5, 128.9 (2C), 128.2 (2C), 49.5, 49.4, 35.1, 21.3; HRMS (ESI): 522.7469, [C_{13}H_{12}Br_{4}ONa]^+ requires 522.7514.
CHAPTER 4. THE INTERRUPTED NAZAROV CYCLIZATION OF ALLENYL VINYL KETONES WITH CARBON-CARBON BOND FORMATION

4.1 Introduction

Oxyallyl cations are intermediates in the Nazarov cyclization, but they are also integral in the synthesis of seven-membered carbocycles via [4 + 3] cyclizations with 1,3-dienes.\(^{54}\) The intermolecular reaction has been shown to proceed efficiently with furan and cyclopentadiene, but the analogous reaction with acyclic dienes has remained underexplored likely because this process can be complicated by alternative [4 + 2] and [3 + 2] cyclizations and by competing decomposition pathways.\(^{55}\) Recently, the cyclic oxyallyl cations generated by Nazarov cyclization have been shown to be effective partners in intermolecular [4 + 3] cyclizations with furan, cyclopentadiene, and a few acyclic dienes (Scheme 36).\(^{11d}\) The reaction is highly facially selective, as evidenced by the orientation of the phenyl substituent, which is in an \textit{exo} position. Furthermore, the reaction also takes place with high diastereoselectivity via a compact transition state, as evidenced by the reaction with furan and cyclopentadiene, in which \textit{“endo”}-products are formed exclusively.

![Scheme 36 Tandem Nazarov/[4 + 3] reaction.](image)

Furthermore, there are two reports of Nazarov cyclizations being followed by intramolecular [3 + 2] cyclizations (Scheme 37).\(^{11a,b,56}\) This reaction is highly
diastereoselective for products in which the substituents are oriented in an \textit{exo} position.

![Scheme 37 Tandem Nazarov/[3 + 2] reaction.](image)

There are also some examples in which, instead of the expected [4 + 3] or [3 + 2] reactions, compounds in which only a single carbon-carbon bond had been formed were produced as the sole or major product (Scheme 38).\textsuperscript{11a,12}

![Scheme 38 Nazarov reaction followed by single carbon-carbon bond formation.](image)

Based on our studies with trapping the oxyallyl cationic intermediate derived from the Nazarov cyclization of an AVK with heteroatom nucleophiles, there are at least four reasons why an AVK presents an especially well suited coupling partner for subsequent cyclization reactions: 1. An AVK is a particularly reactive substrate for the Nazarov reaction, cyclizing rapidly under acidic conditions to generate the oxyallyl cation. 2. The oxyallyl cation is stabilized by extra conjugation, and simple loss of a proton to generate a double bond might be unfavourable as the product would be a fulvene. Thus, the oxyallyl cation would be more likely to be trapped. 3. The products resulting from either [4 + 3] or [3 + 2] cyclizations would contain an exocyclic methylene
unit, providing a good synthetic handle for further transformations. 4. The oxyallyl cation has two unencumbered positions to which a nucleophile might add readily, which would allow for the production of diverse cyclopentenone-containing ring systems.

4.2 Synthesis of Bicyclic Ketones by Reaction with Substituted Butadiene Derivatives

AVK 26 was treated with BF₃·Et₂O in the presence of various methyl-substituted butadienes (Table 8). Reactions were rapid (5 min at –78 °C) and yielded products of [4 + 3] and [3 + 2] cyclizations onto positions a and b of the oxyallyl cationic intermediate. BF₃·Et₂O was chosen as the acid for most reactions because no nucleophilic species, which might compete with a carbon-nucleophile to trap the oxyallyl cation derived from 26, had been seen to be generated from this Lewis acid (Table 2). Furthermore, whereas BF₃·Et₂O elicited the quantitative formation of 90 (entry 4) in 5 min, InCl₃ and Cu(OTf)₂ gave 90 more slowly (2 h) and in yields of only 59% and 68%, respectively. Although InCl₃ is known to give the product of trapping with chloride at position c, the reaction with the diene must be much faster because chlorinated products were not observed when the diene was added. This was true of other experiments involving alkenes with InCl₃ (vide infra). It is interesting to note that the much more electron-rich trans-1-methoxy-3-trimethylsilyloxy-1,3-butadiene did not yield any Nazarov product with 26 (entry 5).
Table 8 Reactions of AVK 26 with butadiene derivatives.

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>[4 + 3]</th>
<th>[3 + 2]</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>product ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = Me, R&lt;sup&gt;2&lt;/sup&gt; = H, R&lt;sup&gt;3&lt;/sup&gt; = H, R&lt;sup&gt;4&lt;/sup&gt; = H</td>
<td>86a</td>
<td>87</td>
<td>51</td>
<td>86a/87 1:2.7</td>
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<td>2</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = Me, R&lt;sup&gt;3&lt;/sup&gt; = H, R&lt;sup&gt;4&lt;/sup&gt; = H</td>
<td>–</td>
<td>88</td>
<td>54</td>
<td></td>
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<tr>
<td>3</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = H, R&lt;sup&gt;3&lt;/sup&gt; = Me, R&lt;sup&gt;4&lt;/sup&gt; = H</td>
<td>89a,b&lt;sup&gt;b&lt;/sup&gt;</td>
<td>–</td>
<td>56</td>
<td>89a/89b 1:2.8</td>
</tr>
<tr>
<td>4</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = H, R&lt;sup&gt;3&lt;/sup&gt; = Me, R&lt;sup&gt;4&lt;/sup&gt; = Me</td>
<td>90</td>
<td>–</td>
<td>99</td>
<td></td>
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<tr>
<td>5</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = OMe, R&lt;sup&gt;2&lt;/sup&gt; = H, R&lt;sup&gt;3&lt;/sup&gt; = H, R&lt;sup&gt;4&lt;/sup&gt; = OTMS</td>
<td>–</td>
<td>–</td>
<td>–</td>
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</table>

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>[4 + 3]</th>
<th>[3 + 2]</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>product ratio</th>
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</thead>
<tbody>
<tr>
<td>6</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = H</td>
<td>–</td>
<td>91a</td>
<td>85</td>
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<tr>
<td>7</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = Me, R&lt;sup&gt;2&lt;/sup&gt; = H</td>
<td>92</td>
<td>93a,b&lt;sup&gt;d&lt;/sup&gt;</td>
<td>71</td>
<td>92/93a,b 1:2</td>
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<tr>
<td>8</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = Me</td>
<td>–</td>
<td>94a,b&lt;sup&gt;e&lt;/sup&gt;</td>
<td>49</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields, <sup>b</sup> 89a R<sup>3</sup> = Me, R<sup>4</sup> = H; 89b R<sup>3</sup> = H, R<sup>4</sup> = Me, <sup>c</sup> intractable material, <sup>d</sup> 93a R<sup>1</sup> endo, 93b R<sup>1</sup> exo, ratio 1:1, <sup>e</sup> 94a R<sup>1</sup> endo, 94b R<sup>1</sup> exo, ratio 5:1.
The regioselectivity of all cyclizations (with the exception of entry 3), as determined by detailed analysis of the 2D NMR data of the products, was high. The X-ray crystal structure of 90 showed that the phenyl group was in an exo position (Figure 9), and NOE measurements showed that every product had the phenyl group in an exo position, indicating a high degree of facial selectivity. As the only [4 + 3] product using trans-piperylene was 86a (entry 1), this reaction also exhibits a high degree of “exo”-diastereoselectivity, suggesting that the reaction proceeds through an extended transition state. This is in contrast to similar experiments by the West group with oxyallyl cations derived from divinyl ketones, in which “endo”-products had been obtained exclusively (cf. Scheme 36).11d

Figure 9 X-ray crystal structure of compound 90.

All products were stable with BF₃·Et₂O at −78 °C, but with BF₃·Et₂O at room temperature over a period of hours some compounds equilibrated. One may presume that this much slower process involved ring cleavage to give the enolate and the delocalized cation, which then re-cyclized. The [3 + 2] product 87 equilibrated to a 2.2:1 mixture of the [4 + 3] compound 86a and the epimer 86b. On the other hand, compound 88
remained unchanged in the presence of BF$_3$-Et$_2$O. Re-subjecting the mixture of 92 and 93a,b to BF$_3$-Et$_2$O provided 95 in 75% yield. This remarkable outcome indicated that each compound underwent ring-opening, and then reclosure of the enolate onto position $c$ (Scheme 39). Compound 95 represented the product of a formal [5 + 4] cyclization of the oxyallyl cation with the diene. Hence, in every instance in Table 8 where the reaction products were mixtures of different sized ring-systems, addition of more BF$_3$-Et$_2$O to the mixture resulted in confluence to a single ring-system.

![Scheme 39 Proposed equilibration of bicyclic ketones to a single ring system via ring opening to a zwitterionic intermediate.](image)

The reaction was also evaluated with other Type 1 AVKs, 27 and 29, as well as Type 2 AVKs 35 and 37 (Table 9). NOE measurements showed that every product had the phenyl group in an $exo$ position, indicating a high degree of facial selectivity. All reactions proceeded with high regio- and stereoselectivity, producing products with similar connectivity to that of AVK 26. As the only [4 + 3] products using trans-piperylene were 98 (entry 3) and 101 (entry 6) for AVKs 35 and 37 respectively, this reaction also exhibits a high degree of “$exo$”-diastereoselectivity. The stereo- and regiochemistry of the reactions was determined by NOE measurements and analysis of the 2D NMR spectra (COSY, HSQC, and HMBC) of the products.
Table 9 Reactions of AVKs 27, 29, 35, and 37 with butadiene derivatives.

<table>
<thead>
<tr>
<th>entry</th>
<th>AVK</th>
<th>diene</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>product ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = H, R&lt;sup&gt;3&lt;/sup&gt; = Me</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = H, R&lt;sup&gt;5&lt;/sup&gt; = Me, R&lt;sup&gt;6&lt;/sup&gt; = Me</td>
<td>71</td>
<td>96</td>
</tr>
<tr>
<td>2</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = H, R&lt;sup&gt;2&lt;/sup&gt; = i-Pr, R&lt;sup&gt;3&lt;/sup&gt; = Me</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = H, R&lt;sup&gt;5&lt;/sup&gt; = Me, R&lt;sup&gt;6&lt;/sup&gt; = Me</td>
<td>64</td>
<td>97</td>
</tr>
<tr>
<td>3</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = Me, R&lt;sup&gt;2&lt;/sup&gt; = Ph, R&lt;sup&gt;3&lt;/sup&gt; = H</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = Me, R&lt;sup&gt;5&lt;/sup&gt; = H, R&lt;sup&gt;6&lt;/sup&gt; = H</td>
<td>50</td>
<td>98</td>
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<td>4</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = Me, R&lt;sup&gt;2&lt;/sup&gt; = Ph, R&lt;sup&gt;3&lt;/sup&gt; = H</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = H, R&lt;sup&gt;5&lt;/sup&gt; = Me, R&lt;sup&gt;6&lt;/sup&gt; = Me</td>
<td>79</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>R&lt;sup&gt;1&lt;/sup&gt; = Me, R&lt;sup&gt;2&lt;/sup&gt; = Ph, R&lt;sup&gt;3&lt;/sup&gt; = H</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = H, R&lt;sup&gt;5&lt;/sup&gt; = H, R&lt;sup&gt;6&lt;/sup&gt; = Me</td>
<td>73</td>
<td>100a/100b 1:4&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>6</td>
<td>R&lt;sup&gt;1&lt;/sup&gt;, R&lt;sup&gt;2&lt;/sup&gt; = -(CH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;4&lt;/sub&gt;-, R&lt;sup&gt;3&lt;/sup&gt; = H</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = Me, R&lt;sup&gt;5&lt;/sup&gt; = H, R&lt;sup&gt;6&lt;/sup&gt; = H</td>
<td>48</td>
<td>101</td>
</tr>
<tr>
<td>7</td>
<td>R&lt;sup&gt;1&lt;/sup&gt;, R&lt;sup&gt;2&lt;/sup&gt; = -(CH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;4&lt;/sub&gt;-, R&lt;sup&gt;3&lt;/sup&gt; = H</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = H, R&lt;sup&gt;5&lt;/sup&gt; = Me, R&lt;sup&gt;6&lt;/sup&gt; = Me</td>
<td>74</td>
<td>102</td>
</tr>
<tr>
<td>8</td>
<td>R&lt;sup&gt;1&lt;/sup&gt;, R&lt;sup&gt;2&lt;/sup&gt; = -(CH&lt;sub&gt;2&lt;/sub&gt;)&lt;sub&gt;4&lt;/sub&gt;-, R&lt;sup&gt;3&lt;/sup&gt; = H</td>
<td>R&lt;sup&gt;4&lt;/sup&gt; = H, R&lt;sup&gt;5&lt;/sup&gt; = H, R&lt;sup&gt;6&lt;/sup&gt; = Me</td>
<td>65</td>
<td>103a/103b 1:1.3&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields, <sup>b</sup> 100a R<sup>5</sup> = Me, R<sup>6</sup> = H; 100b R<sup>5</sup> = H, R<sup>6</sup> = Me, <sup>c</sup> 103a R<sup>5</sup> = Me, R<sup>6</sup> = H; 103b R<sup>5</sup> = H, R<sup>6</sup> = Me.

The only product of Type 3 AVK 36 and 2,3-dimethylbutadiene in the presence of BF<sub>3</sub>·Et<sub>2</sub>O was the Diels-Alder adduct 104, the result of a [4 + 2] reaction across the allene unit (Scheme 40). This result again highlighted the key role of an alkyl group at either α-position of the carbonyl group of the AVK, in order to facilitate Nazarov reactions at the expense of side reactions initiated via additions to the allenyl central carbon, as discussed in Section 3.3.
Scheme 40 Reaction of AVK 36 with 2,3-dimethylbutadiene.

4.3 Synthesis of Bicyclic Ketones and/or Cyclopent-2-enones by Reaction with Activated Alkenes

AVK 26 was also treated with either BF₃·Et₂O, Cu(OTf)₂, or InCl₃ in the presence of various allylsilanes (Table 10). When BF₃·Et₂O was added to 26 and allyltrimethylsilane, two Nazarov products formed very rapidly. One (105) was the product of addition to position α of the oxyallyl cation, but the major product was the [3 + 2] product 106a. The relative stereochemistry was determined by measurement of NOEs and the magnitude of the ¹H NMR coupling constants, and the regiochemistry was determined by analysis of the 2D NMR spectra (COSY, HSQC, and HMBC) of the products. When Cu(OTf)₂ was employed as the Lewis acid, the reaction was slower and three products were obtained: 105, 106a, and 107, of which 107 was the result of capture at position β. With InCl₃ the reaction had approximately the same rate as with Cu(OTf)₂, 107 was the major product, and there was none of the [3 + 2] product. Utilization of a more robust silane, allyltriisopropylsilane, resulted in an increased proportion of the [3 + 2] product 106b in the presence of either BF₃·Et₂O or InCl₃. Allyltriethoxysilane with BF₃·Et₂O gave a poor yield of the [3 + 2] product 106c, but no other Nazarov product was detected.
Table 10 Reactions of AVK 26 with allylsilanes.

\[
\text{26} + \text{SiX}_3 \xrightarrow{\text{Lewis acid}} \begin{array}{c}
\text{105} \\
\text{106a-c} \\
\text{107}
\end{array}
\]

\[
\begin{array}{cccc|ccc}
\text{entry} & \text{X} & \text{Lewis acid} & \text{time} & \text{yields (\%)}^a \\
1 & \text{Me} & \text{BF}_3\text{Et}_2\text{O}^b & 5 \text{ min} & 27 & 54 (106a) & – \\
2 & \text{Me} & \text{Cu(OTf)}_2^c & 1.5 \text{ h} & 20 & 10 (106a) & 42 \\
3 & \text{Me} & \text{InCl}_3^c & 2 \text{ h} & 22 & – & 56 \\
4 & \text{i-Pr} & \text{BF}_3\text{Et}_2\text{O}^b & 5 \text{ min} & 19 & 57 (106b) & – \\
5 & \text{i-Pr} & \text{InCl}_3^c & 2 \text{ h} & 27 & 28 (106b) & 13 \\
6 & \text{OEt} & \text{BF}_3\text{Et}_2\text{O}^b & 5 \text{ min} & – & 15 (106c) & – \\
\end{array}
\]

\(^a\) Isolated yields, \(^b\) 2 equiv of allylsilane, 1.1 equiv of BF\(_3\)Et\(_2\)O, 
\(^c\) 5 equiv of allylsilane, 5 equiv of Lewis acid.

The trimethylsilyl [2.2.1]-compound 106a could be converted in 5 h to 105 in moderate yield in the presence of BF\(_3\)Et\(_2\)O at room temperature, but a minor product was the trimethylsilyl [3.2.1]-compound 109a (Scheme 41). This minor compound would have been the result of cyclization of intermediate 108a in concert with a shift of the silyl group. This sort of process had been anticipated, but not observed, by West in their study of interception of Nazarov reactions with allylsilanes\(^{11a}\). When the more robust triisopropylsilyl [2.2.1]-compound 106b was stirred with BF\(_3\)Et\(_2\)O at room temperature,
not only was the analogous recyclization of 108b evident, it led to the triisopropylsilyl [3.2.1]-compound 109b in very good yield.

Scheme 41 Ring-opening of silyl-substituted [3 + 2] products at room temperature.

Alternatively, exposure of the crude mixture of 105 and 106a, obtained following work-up of the reaction of AVK 26 with allyltrimehtysilane and BF$_3$·Et$_2$O, gave similar results as in Scheme 41. However, the addition of excess BF$_3$·Et$_2$O to the initial mixture of AVK 26 and allyltrimehtysilane, prior to work-up, led to poorer results: whilst 106a was completely consumed upon warming to room temperature, 105 was obtained in only 33% overall yield following chromatography.

Oxygen-substituted alkenes intercepted the oxyallyl cation with high facial selectivity by nucleophilic attack at position a or by the formation of [3 + 2] products (Table 11). The relative stereochemistry was determined by measurement of NOEs and the magnitude of the $^1$H NMR coupling constants, and the regiochemistry was determined by analysis of the 2D NMR spectra (COSY, HSQC, and HMBC) of the
products. A silyl enol ether and an enol acetate (entries 1 and 2) trapped the oxyallyl cation inefficiently to give low yields of 110 and 111, respectively. The enol ether, n-propoxyethene, gave two types of products, 110 and 112, in high overall yield (entry 3). However, the [3 + 2] product 112, in contrast with 106a,b, simply decomposed when treated with BF3·Et2O at room temperature. Further substitution of the double bond, as in entries 4 and 5, led to products of trapping at position a, and 113 and 114 were not accompanied by [3 + 2] products. The [3 + 2] product 112 was obtained as an epimeric mixture, but it is important to note that the formation of 113 was stereoselective. The relative stereochemistry of compound 113 was established by a J-correlated NMR method.57,58

Table 11 Reactions of AVK 26 with electron-rich alkenes.a

<table>
<thead>
<tr>
<th>entry</th>
<th>alkene</th>
<th>products and yieldsb</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R¹ = H, R² = H, R³ = TMS</td>
<td>110 (35%) -</td>
</tr>
<tr>
<td>2</td>
<td>R¹ = H, R² = H, R³ = Ac</td>
<td>- 111 (18%)</td>
</tr>
<tr>
<td>3</td>
<td>R¹ = H, R² = H, R³ = nPr</td>
<td>110 (59%) 112 (41%)c</td>
</tr>
<tr>
<td>4</td>
<td>R¹ = Me, R² = H, R³ = Et</td>
<td>113 (86%)d -</td>
</tr>
<tr>
<td>5</td>
<td>R¹ = H, R² = Me, R³ = Me</td>
<td>114 (60%)e -</td>
</tr>
</tbody>
</table>

a 2 equiv alkene, 1.1 equiv BF3·Et2O, b isolated yields, c ether group exo/endo 5:1, d ca. 90% the isomer shown, e included an inseparable by-product from subsequent reaction of 114.
In the light of the entries 1 and 4 in Table 11, it was somewhat surprising that introduction of neither the tert-butyldimethylsilyl enol ether derived from cyclopentanone nor a cyclic enol ether, dihydropyran, gave any trapped Nazarov product. Also, \(N\)-vinylpyrrolidinone, as well as the enamine derived from cyclopentanone and pyrrolidine, failed to produce any isolable interrupted Nazarov product – only intractable material was obtained. It is probable that if the alkene or diene is too electron-rich, it will add via a Michael reaction to the central allenic carbon of the AVK before the AVK has undergone the Nazarov reaction. Evidence for this comes from an attempted reaction with an excess of the electron-rich cyclobutene derivative 115 (Scheme 42). The \(^1\)H NMR spectrum of the initial product mixture showed signals mainly for the Michael product 116 and residual 115. The stereochemistry of the C3-C4 double bond was determined by observation of NOEs. Although the isolated yield of 116 following flash chromatography was low, it was subsequently established that 116 decomposed rapidly on silica gel.

![Scheme 42 Attempted interrupted Nazarova reaction of AVK 26 with 113.](image)

Styrenes afforded only [3 + 2] products as single diastereomers (Table 12). The relative stereochemistry was confirmed by NOE measurements, and the regiochemical outcome was determined by analysis of the 2D NMR spectra of the products. Styrene itself (entry 1) gave a poor yield of 117, and an electron-poor derivative (entry 2) did not trap the oxyallyl cation at all. On the other hand, electron-donation was clearly
advantageous (entries 3-5). Reaction of 26 with the trans-isomer provided 120 in a yield that was slightly higher (entry 5) than the yield from the less substituted styrene (entry 3), but the corresponding cis-isomer failed to trap the oxyallyl cation (entry 6). This curious result may reflect reduced electron-donation by the methoxyphenyl group into the alkene moiety in the cis isomer, and it is consistent with a hypothesis that the kinetic route to the [3 + 2] products might be concerted, or at least very rapid, at –78 °C because bond rotation in an intermediate carbocation could have given 120 from the cis isomer.

Table 12 Reactions of AVK 26 with styrenes.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>styrene</th>
<th>product and yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(R^1, R^2, R^3, R^4 = H)</td>
<td>117 (15%)</td>
</tr>
<tr>
<td>2</td>
<td>(R^1, R^2, R^3 = H; R^4 = \text{CF}_3)</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>(R^1, R^2, R^3 = H; R^4 = \text{OMe})</td>
<td>118 (52%)</td>
</tr>
<tr>
<td>4</td>
<td>(R^1, R^2 = H; R^3, R^4 = \text{OMe})</td>
<td>119 (76%)</td>
</tr>
<tr>
<td>5</td>
<td>(R^1 = \text{Me}; R^2, R^3 = H; R^4 = \text{OMe})</td>
<td>120 (59%)</td>
</tr>
<tr>
<td>6</td>
<td>(R^1, R^3 = H; R^2 = \text{Me}; R^4 = \text{OMe})</td>
<td>–</td>
</tr>
</tbody>
</table>

\(\text{a}\) 2 equiv styrene, 1.1 equiv BF\(_3\)-\(\text{Et}_2\)O, \(\text{b}\) isolated yields.

The reaction was also briefly evaluated with AVKs 27 and 29 (Scheme 43). In the presence of 3,4-dimethoxystyrene, AVKs 27 and 29 rapidly formed the [3 + 2] products 121 and 122. In both cases, only the exo-diastereomer was produced, as confirmed by NOE measurements.
The reactions of allyltrimethylsilane and \( p \)-methoxystyrene were also evaluated with Type 2 and Type 3 AVKs \( 35 \text{–} 37 \), however complex mixtures were obtained. NMR analysis of the product mixtures suggested that the bulk of the material had reacted directly with the allene moiety of the AVK.

### 4.4 Synthesis of Functionalized Cyclopent-2-enones by Reaction With Cyclic Diienes

When some cyclic dienes were mixed with AVK \( 26 \) and \( \text{BF}_3 \cdot \text{Et}_2\text{O} \), the Nazarov reactions were interrupted readily by the cyclic dienes, but it was surprising that no products of \([4 + 3]\) cyclization were detected. Only one carbon-carbon bond formed (Table 13), and the relative stereochemistry of the products was determined by comparison of \(^1\text{H} \) NMR coupling constants.

Furan, which has been used in a number of \([4 + 3]\) cyclizations with oxyallyl cations,\(^{54}\) trapped only at position \( \text{a} \) to provide \( 123 \) when the reaction was mediated by \( \text{BF}_3 \cdot \text{Et}_2\text{O} \) (entry 1). Whilst the use of \( \text{Cu(OTf)}_2 \) elicited similar results to \( \text{BF}_3 \cdot \text{Et}_2\text{O} \), \( \text{InCl}_3 \) promoted the formation of a minor amount of \( 124 \) via capture at position \( \text{c} \) (entry 2). Reaction with thiophene led to intractable material, however pyrrole provided \( 125 \) as a single compound, trapped at position \( \text{a} \), in 54\% yield (entry 3). Intractable material was
Table 13 Reactions of AVK 26 with cyclic dienes.

<table>
<thead>
<tr>
<th>entry</th>
<th>diene</th>
<th>Lewis acid</th>
<th>products</th>
<th>yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>product ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>BF₃Et₂O&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="image" alt="Product 123" /></td>
<td>-</td>
<td>64&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>InCl₃&lt;sup&gt;d&lt;/sup&gt;</td>
<td><img src="image" alt="Product 123" /></td>
<td><img src="image" alt="Product 124" /></td>
<td>123/124 3.5:1</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>BF₃Et₂O&lt;sup&gt;e&lt;/sup&gt;</td>
<td><img src="image" alt="Product 125" /></td>
<td>-</td>
<td>54</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>BF₃Et₂O&lt;sup&gt;e&lt;/sup&gt;</td>
<td><img src="image" alt="Product 126" /></td>
<td><img src="image" alt="Product 127" /></td>
<td>126/127 1:5.5</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>BF₃Et₂O&lt;sup&gt;e&lt;/sup&gt;</td>
<td><img src="image" alt="Product 128" /></td>
<td>-</td>
<td>70</td>
</tr>
</tbody>
</table>

<sup>a</sup> Isolated yields, <sup>b</sup> 10 equiv furan, 1.1 equiv BF₃·Et₂O, 5 min, <sup>c</sup> in addition, there was 10% of a product where one furan added to two of 123 at position α, <sup>d</sup> 5 equiv furan, 5 equiv InCl₃, 2 h, <sup>e</sup> 2 equiv diene, 1.1 equiv BF₃·Et₂O, 5 min, <sup>f</sup> in addition, there was 8% of the product of the Diels–Alder reaction of the diene with the allene of 26.

obtained when cyclopentadiene or 6,6-dimethylfulvene were added, but addition of 1,2,3,4,5-pentamethylcyopentadiene led to the formation of a minor product 126, by
interception at position \( a \) of the oxyallyl cation intermediate, and a major product 127, by capture at the less sterically hindered position \( c \) (entry 4). Using 1,3-cyclohexadiene to trap the oxyallyl cation provided only 128, as a single diastereomer (entry 5). The relative stereochemistry of 128 was established by a \( J \)-correlated NMR method.\(^{57,58}\)

A series of \( N \)-substituted pyrroles was then evaluated under the reaction conditions (Table 14). The relative stereochemistry of the products substituted at C4 was determined by the magnitude of their \(^1H\) NMR coupling constants. As with pyrrole itself, the predominant Nazarov product with \( N \)-alkyl-, \( N \)-aryl-, and \( N \)-silyl-pyrroles involved carbon-carbon bond formation at position \( a \) of the oxyallyl cation (entries 1–5). The modest yields of Nazarov products in these cases were mostly a result of a competing Michael addition pathway, generating products such as 140 (Scheme 44). The ratio of Nazarov product 125 to Michael adduct 140, for example, was 3:1 by integration of the \(^1H\) NMR spectrum of the crude reaction mixture. Interception of the Nazarov reaction was also attempted with 2-ethyl-, 3,4-diethyl-, and 3-ethyl-2,4-dimethylpyrrole, but these compounds failed to be incorporated into any cyclopent-2-enone product. It appeared by \(^1H\) NMR spectroscopy of the crude product mixtures that 26 was reacting mainly by Michael reactions with the pyrroles. Utilization of different Lewis acids, such as \( \text{Sc(OTf)}_3 \) or \( \text{InCl}_3 \), led to no Nazarov product. Only the Michael adduct 140 was isolated (Scheme 43); observation of NOEs established the (\( Z \))-geometry. No Michael product was detected for pyrroles with electron-withdrawing groups on the nitrogen atom however (entries 6–9), and much, or all, of the Nazarov product arose by interception at position \( c \). With \( N \)-mesyl and \( N \)-tosyl pyrrole, the low yields obtained with \( \text{BF}_3 \cdot \text{OEt}_2 \)
Table 14 Reactions of AVK 26 with N-substituted pyrroles.$^a$

![Reaction scheme](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>pyrrole R</th>
<th>product(s)</th>
<th>yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Me</td>
<td>129</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>Bn</td>
<td>130</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>Ph</td>
<td>131</td>
<td>67</td>
</tr>
<tr>
<td>4</td>
<td>PMP</td>
<td>132</td>
<td>41</td>
</tr>
<tr>
<td>5</td>
<td>TIPS</td>
<td>133</td>
<td>31</td>
</tr>
<tr>
<td>6</td>
<td>MOC</td>
<td>134/136 (1:1)$^c$</td>
<td>23</td>
</tr>
<tr>
<td>7</td>
<td>BOC</td>
<td>135/137 (1.4:1)$^c$</td>
<td>33</td>
</tr>
<tr>
<td>8</td>
<td>Ms</td>
<td>138</td>
<td>11 (41)$^d$</td>
</tr>
<tr>
<td>9</td>
<td>Ts</td>
<td>139</td>
<td>10 (44)$^d$</td>
</tr>
</tbody>
</table>

$^a$ 2 equiv pyrrole, 1.1 equiv BF$_3$·Et$_2$O, $^b$isolated yields, $^c$ determined by integration of the $^1$H NMR spectra of the crude reaction products, $^d$yields in parentheses were obtained when InCl$_3$ (2 equiv) was used as the Lewis acid.

were improved fourfold by using InCl$_3$ as the Lewis acid (entries 8-9), and Michael-addition products were not detected with these pyrroles. The reason for this increase in yield using InCl$_3$ is as yet unclear.
Scheme 44 Michael reactions of AVK 26 with pyrrole.

A series of substituted indoles was then evaluated under the reaction conditions (Table 15). The relative stereochemistry of the products substituted at C4 was determined by comparison of their $^1$H NMR coupling constants. Interrupted Nazarov reactions mediated by BF$_3$·OEt$_2$ took place in higher yield with indoles than with pyrroles. Michael products made up less than 10% of the product mixtures, and cyclopent-2-enones could be produced in good to excellent yield. The regioselectivity for the trapping, i.e., positions $a$ versus $c$ of the oxyallyl cation, was modest. Notably, methyl substitution at C2 of the indole (entries 4 and 5) led to a greater proportion of the Nazarov product that had been trapped at position $c$. Although trapping with a more electron-rich derivative, 5-methoxyindole (entry 2), did not affect the yield or selectivity of the reaction, N-tosylindole (entry 6), a more electron-poor analogue, failed to generate any trapped product under the same reaction conditions. However, when InCl$_3$ was employed, Nazarov products 146a and 146b were obtained (1:1 ratio).
Table 15 Reactions of AVK 26 with substituted indoles.\textsuperscript{a}

\[ BF_3 \cdot Et_2O \rightarrow \text{26} \]

\[ R^1 = H, \text{Me, Ts} \]
\[ R^2 = H, \text{Me} \]
\[ R^3 = H, \text{OMe} \]

<table>
<thead>
<tr>
<th>entry</th>
<th>products</th>
<th>ratio of product(s)\textsuperscript{b}</th>
<th>combined yield (%)\textsuperscript{c}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>141a,b</td>
<td>2.3-3.7:1</td>
<td>88-93</td>
</tr>
<tr>
<td></td>
<td>(R\textsuperscript{1}, R\textsuperscript{2}, R\textsuperscript{3} = H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>142a,b</td>
<td>2.5-3.9:1</td>
<td>71-92</td>
</tr>
<tr>
<td></td>
<td>(R\textsuperscript{1}, R\textsuperscript{2} = H, R\textsuperscript{3} = OMe)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>143a,b</td>
<td>3.2-3.6:1</td>
<td>88-90</td>
</tr>
<tr>
<td></td>
<td>(R\textsuperscript{1} = Me, R\textsuperscript{2}, R\textsuperscript{3} = H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>144a,b</td>
<td>1.1-1.6:1</td>
<td>58-60</td>
</tr>
<tr>
<td></td>
<td>(R\textsuperscript{1}, R\textsuperscript{3} = H, R\textsuperscript{2} = Me)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>145a,b</td>
<td>1.2-1.4:1</td>
<td>87-90</td>
</tr>
<tr>
<td></td>
<td>(R\textsuperscript{1}, R\textsuperscript{2} = Me, R\textsuperscript{3} = H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>146a,b</td>
<td>1:1</td>
<td>0(49)\textsuperscript{d}</td>
</tr>
<tr>
<td></td>
<td>(R\textsuperscript{1} = Ts, R\textsuperscript{2}, R\textsuperscript{3} = H)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a} 2 equiv indole, 1.1 equiv BF\textsubscript{3} \cdot Et\textsubscript{2}O, \textsuperscript{b} range from three trials, determined by integration of the \textsuperscript{1}H NMR spectra of the crude reaction products, \textsuperscript{c} isolated yields, range from two trials, \textsuperscript{d} yields in parentheses were obtained when InCl\textsubscript{3} (2 equiv) was used as the Lewis acid.

As with pyrrole, when the reaction was assessed with Sc(OTf)\textsubscript{3} the Michael adduct 147 was obtained in 38% yield and no Nazarov product was observed, whereas use of InCl\textsubscript{3} led to Michael adduct 147 in only 19% yield (Scheme 45). Observation of NOEs established the (Z)-geometry of 147.
Replacement of the phenyl group of AVK 26 with a hydrogen, as in AVK 27, or an isopropyl group, as in AVK 29, might be expected to be significant in terms of the reactivity of the AVKs and the regioselectivity of the Nazarov reactions with substituted indoles (Scheme 46). Similarly to AVK 26, the less substituted AVK 27 reacted rapidly with 1-N-methyl- and 1,2-dimethylindole, but the regioselectivity was much improved. Only the products of trapping at the position corresponding to a (148 and 149) were obtained. The reactions of AVK 29 were also rapid and much more regioselective than those of AVK 26, with 150 being the only significant Nazarov product with
N-methylindole, and 151a and 151b being produced in a ratio of 4.3:1 with 1,2-dimethylindole.

The interrupted Nazarov reaction with cyclic dienes does not appear to be amenable to AVKs of Type 2 or Type 3, however. When AVKs 35 – 37 were reacted with a variety of cyclic dienes (furan, 1,3-cyclohexadiene, N-phenylpyrrole, 5-methoxyindole) in the presence of BF$_3$·OEt$_2$, complex mixtures were obtained. NMR analysis of the product mixtures suggested that the bulk of the material had reacted directly with the allene moiety of the AVK.

### 4.5 Mechanistic Rationale for the Observed Regio- and Stereoselectivity in Interrupted Nazarov Reactions of Allenyl Vinyl Ketones

In general, most interrupted Nazarov reactions of AVKs proceeded with high or exclusive regio- and stereoselectivity. For single bond formation, position $a$ of the oxyallyl cation intermediate appeared to be the preferred site of bond formation, although in certain cases products at trapped position $c$ predominated. When three new stereocenters were formed, the reaction also appeared to be highly stereoselective. In the cases where two bonds are formed simultaneously, as with butadiene derivatives, the less hindered end of the diene also reacted regioselectively at position $a$. Furthermore, the reaction was also highly stereoselective for the formation of products in which the substituents are oriented in an exo position. We wished to develop a mechanistic rationale for the observed regio- and stereoselectivity in the Nazarov reaction of AVKs, in order to allow further generalizations to be made in terms of reactivity and selectivity.
4.5.1 Implications of Regioselectivity of Interrupted Nazarov Reactions of AVKs with Cyclic Dienes

Sterically unhindered substrates such as furan, $N$-substituted pyrroles, indole, $N$-methylindole, and 1,3-cyclohexadiene trapped predominantly at position $a$, whereas dienes with increasing substitution near the reacting carbons, such as indoles substituted at the 2-position and 1,2,3,4,5-pentamethylcyclopentadiene, provided competitive or selective amounts of product trapped at position $c$ (Scheme 47). A substituent at the $\beta$-alkenyl position of the AVK also showed a strong influence on the regioselectivity of the trapping process, with unsubstituted AVK 27 and isopropyl-substituted AVK 29 yielding increased or exclusive formation of products trapped at position $a$ relative to the phenyl-substituted AVK 26 (Scheme 47). Hence, the regioselectivity of the trapping process showed a strong dependence upon the substitution pattern present in both reacting partners, and regioselectivity became worse with increasing substitution near the reacting

![Scheme 47 Bulkier reagents favour products trapped at position c.](image-url)
carbons. These results suggested that position $a$ is the electronically preferred trapping site, whereas position $c$ becomes favoured for sterically encumbered substrates.

The observed tendency of $N$-substituted pyrroles bearing MOC, BOC, mesyl, or tosyl groups to produce increasing or exclusive amounts of products trapped at position $c$ in the presence of BF$_3$·OEt$_2$ might be explained by invoking a transition state similar to 152, which might direct attack of the pyrrole to position $c$ in these cases (Scheme 48).

![Scheme 48 Proposed transition state model leading to 138.](image)

### 4.5.2 Computational Investigation of the Oxyallyl Cationic Intermediate

The atomic charge on each atom of the oxyallyl cations 153 – 155, derived from AVKs 26, 35, and 36 respectively, was determined computationally$^\dagger$ using QTAIM$^{48}$ (Figure 10a). There were no significant differences in the lengths of the bonds between adjacent sp$^2$ carbons for 153 – 155 (Figure 10b). The lengths of the bonds between adjacent sp$^2$ carbons were all approximately 1.43 Å, except the exocyclic bond was always shorter ($ca.$ 1.37 Å). However, important differences were revealed in the delocalization indices (Figure 10c),$^{60}$ which are estimates of bond population by pairs of

$^\dagger$Calculations were performed by Gavin Heverly-Coulson, using the Q-Chem 3.1$^{46}$ and AIMAll (Version 10.03.25)$^{47}$ software packages.
Figure 10 a) Selected atomic charges, b) bond lengths, and c) delocalization indices for the oxyallyl cations 153-155, in their lowest-energy conformations, as calculated using RI-MP2/cc-pvdz.49

electrons. Regardless of the presence or the position of the methyl group, the bond from the oxygen-bearing carbon to $b$ and the carbon-carbon bond to $c$ had larger indices than the bond from the oxygen-bearing carbon to $a$, which pointed to position $a$ as the most electrophilic carbon in all three oxyallyl cations. Hence, the computational results suggest that position $a$ of the oxyallyl cation derived from AVKs is indeed the electronically preferred site of trapping in interrupted Nazarov cyclizations.
4.5.3 Implications of Regioselectivity of Interrupted Nazarov Reactions of AVKs with Butadiene Derivatives

The regioselectivity of all cyclizations of AVK 26 with butadienes (Table 8), with the exception of entry 3, was high, and this could be rationalized as arising from the most reactive cationic site in the oxyallyl cation 153 being a and significant amounts of charge in the diene moieties at the transition states. More importantly, Nazarov reactions of both AVKs 26 and 35 in the presence of trans-piperylene gave 86a and 97 as the only [4 + 3] products. The regioselectivity of these cyclizations was the same. In both cases, the unsubstituted end of the diene reacted at position a of the oxyallyl cation (Figure 11). This is further experimental corroboration of the computational result that the electronic bias in the oxyallyl cations derived from AVK’s 26 and 35, i.e., 153 and 154, is position a, regardless of the position of the alkyl substituent.

![Figure 11 Reactions of AVKs 26 and 35 with trans-piperylene occur with the same regioselectivity.](image)

4.5.4 Implications of Stereoselectivity of Interrupted Nazarov Reactions of AVKs with Butadiene Derivatives

Nazarov reactions of AVKs 26 and 35 in the presence of trans-piperylene also gave the [4 + 3] products 86a and 97, as single stereoisomers.
Calculations\(^8\) showed that the epimer of 86\(a\), 86\(b\), is 3.0 kJ-mol\(^{-1}\) lower in energy. These findings would be consistent with a concerted, but asynchronous, cycloaddition mechanism via an extended geometry similar to 156 for the formation of the [4 + 3] products (Scheme 49a), in lieu of a stepwise one which might be expected to generate 86\(b\) preferentially (Scheme 49b).

Scheme 49. a) Geometry of cycloaddition that would lead to [4 + 3] product 86\(a\), and b) Alternative stepwise pathway that would lead to the undetected epimer 86\(b\).

This was consistent with a computational study involving the reaction of butadiene with a metal-bound acyclic oxyallyl species, which had suggested a concerted pathway to be lower in energy than a stepwise one for adducts resulting from extended transition states.\(^{62}\) Although cyclic oxyallyl cations generally proceed through a compact

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\(^8\)Calculations were performed by Gavin Heverly-Coulson, HF/6-31G//HF/6-311G(d,p) using Gaussian 03, Revision C.02.\(^{61}\)
geometry in intermolecular [4 + 3] reactions with dienes, extended transition states might be more energetically accessible for oxyallyl cations derived from AVKs as the methylene unit would relieve some of the steric crowding that would be present otherwise.

A concerted reaction would require the diene to assume an s-cis conformation. s-Cis conformations would be disfavoured for the dienes in entries 2, 6, and 8 (Table 8), and these dienes gave no [4 + 3] products, but provided [3 + 2] products, only, in moderate to good yield. In contrast, the dienes in entries 1, 3, 4, and 7 (Table 8) have more accessible s-cis conformers, and these dienes did afford [4 + 3] products. It was significant that 87, 88, and 91a were the only [3 + 2] products in entries 1, 2, and 6, indicating a high degree of stereoselectivity in this cyclization, also. This might be expected for a cycloaddition via a geometry similar to 157 (Scheme 50) or a very rapid stepwise reaction, although the stepwise formation of [3 + 2] products might be considered a 5-(enolendo)-exo-trig closure, a disfavoured process. The product 91a in entry 6 was compared with its (undetected) epimer 91b computationally, and it was 91b that was lower in energy by 2.2 kJ mol\(^{-1}\), suggesting that 91a formed as the result of a concerted reaction.

Scheme 50 Geometry of cycloaddition that would lead to [4 + 3] product 91a.
4.5.5 Implications of Stereoselectivity of Interrupted Nazarov Reactions of AVK 26 with 1,3-Cyclohexadiene and (Z)-Ethylpropenylether

The interrupted Nazarov reaction of AVK 26 with (Z)-ethylpropenylether and 1,3-cyclohexadiene led to the stereoselective production of compounds 113 and 128, respectively (cf. Tables 11 and 13). The position of the diene moiety in 128 is intriguing because loss of a proton from a putative intermediate 158 should be expected to lead to a more substituted diene. However, a dipolar [3 + 2] cyclization involving the enol oxygen would give 159 as an intermediate,\textsuperscript{15} and conjugate elimination/ring opening during work-up would result in the preferential formation of 128 (Scheme 51). The formation of 113 from 26 might also take place in a similar manner, through the formation of a transient intermediate analogous to 159, produced by a [3 + 2] process involving the enol oxygen. It has been suggested by the calculations of Cramer and Barrows\textsuperscript{62} that a dipolar [3 + 2] cycloaddition can be comparable, or even lower, in energy to all-carbon [3 + 2] and [4 + 3] cycloadditions, depending on the nature of the oxyallyl cation and the diene involved. In the case of the reactions of AVK 26 with (Z)-ethylpropenylether and 1,3-cyclohexadiene, it is plausible that the direct formation of [4 + 3] or all-carbon [3 + 2] products would suffer from considerable steric hindrance in transition state geometries.

Scheme 51 Formation of compound 128 via a dipolar [3 + 2]/ring opening process.
similar to 156 and 157 (cf. Schemes 49a and 50), which might disfavour these pathways relative to a dipolar [3 + 2] cycloaddition pathway.

4.6 Summary

In summary, it has been shown that an AVK is a versatile source of cyclic molecules via a cascade reaction sequence beginning with a Lewis acid-mediated Narazov cyclization and then interception of the intermediate oxyallyl cation by various acyclic dienes, cyclic dienes, electron-rich alkenes, and styrenes by the formation of an additional ring by a [4 + 3] and/or [3 + 2] cyclization or by the formation of one additional carbon-carbon bond. The bicyclic compounds generated in this way are densely substituted, and would be difficult to access as succinctly in other ways. The products of these interrupted Nazarov reactions generally reflect excellent regio- and stereoselectivity in the trapping reaction. In some instances, equilibrating conditions were shown to enhance the proportion of one product at the expense of another or to provide a different carbon skeleton. This process is amenable to unsubstituted, alkyl-substituted, or aromatic-substituted allenyl vinyl ketones.

In general, the trapping process was regioselective for interception of the oxyallyl cation at position $a$, regardless of the placement of the $\alpha$-substituent of the AVK. Computational data showed that this is likely a result of position $a$ being the electronically preferred site for trapping. In the formation of single carbon-carbon bonds, the regioselectivity of the trapping process showed a strong dependence upon the substitution pattern present in both reacting partners, and the regioselectivity became worse with increasing substitution near the reacting carbons. This suggested that,
although position $a$ is the electronically preferred trapping site, position $c$ is the sterically preferred trapping site.

The process was also determined to be highly stereoselective, especially with respect to the formation of the bicyclic ketones. Preliminary data suggest that this result might be the outcome of a concerted, but highly asynchronous, reaction. The high stereoselectivity noted in the formation of the cyclopent-2-enone containing products was proposed to arise as a result of a dipolar $[3 + 2]$ cyclization, or a very rapid stepwise reaction involving the enol oxygen, followed by conjugate ring opening of the resultant cyclic enol ether.

The results of this study contribute to a more complete understanding of the interrupted Nazarov cyclization of allenyl vinyl ketones, and should allow for further generalizations to be made in terms of reactivity and regioselectivity, with respect to related substrate classes. These findings will be invaluable in the design of feasible synthetic approaches involving Nazarov cyclizations of allenyl vinyl ketones, particularly in the stereocontrolled generation of bicyclo[4.2.1]nones.

4.7 Experimental Section

4.7.1 General Considerations

All reactions were conducted using oven-dried glassware under an N$_2$ atmosphere. Reagents were used as received from a commercial supplier without further purification. 1-(Methanesulfonyl)pyrrole$^{64,65}$ and 1-(toluenesulfonyl)pyrrole$^{64-66}$ were prepared according to the literature procedures. Mr. François LeFort is thanked for assistance with the preparation of compounds 125, 129 – 133, 135, 137, and 139. Ms.
Rhonda Stoddard is thanked for assistance with the preparation of compounds 98 - 100.

Dichloromethane was used freshly distilled from calcium hydride. Ethyl acetate and hexanes were distilled prior to use for column chromatography.

Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F_{254}), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or o-vanillin in ethanol/H_2SO_4 and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. \(^1\)H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with CDCl\(_3\) as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). \(^13\)C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with CDCl\(_3\) as solvent. Infrared spectra were recorded from thin films on a Bruker VECTOR 22 FT-IR instrument using CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (\(^1\)H, \(^13\)C, and DEPT-135) and two dimensional (COSY, HSQC, and HMBC) NMR spectral data. The \(^1\)H and \(^13\)C NMR spectra of all compounds, and the DEPT-135, COSY, HSQC, HMBC, and J-HMBC spectra (including detailed analysis of the J-HMBC spectra) for compounds 113 and 128, may be found in Appendix A. The Cartesian coordinates (including additional computed data) for compounds 86a, 86b, 91a, 91b, and 153 - 155, may be found in Appendix B, and the X-ray crystallographic data for compound 90 can be found in Appendix C.
4.7.2 Preparation and Characterization Data

\((1R^*, 6S^*, 7R^*)-1,3,4\text{-}\text{Trimethyl-8-methylene-7-phenylbicyclo[4.2.1]}\text{-}\text{non-3-en-9-one}(90)\)

\[\text{Procedure 1:}\] A solution of AVK 26 (0.050 g, 0.28 mmol) and 2,3-dimethyl-1,3-butadiene (0.060 mL, 0.56 mmol) in CH\(_2\)Cl\(_2\) (25 mL) was cooled to –78 °C, and BF\(_3\)·OEt\(_2\) (0.01 mL, 0.08 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH\(_2\)Cl\(_2\) layer was removed, and additional CH\(_2\)Cl\(_2\) (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na\(_2\)SO\(_4\) and then concentrated under reduced pressure. Flash chromatography of the residue (SiO\(_2\) using 2.5% EtOAc in hexanes) provided 90 (0.075 g, 99%) as a colourless solid: mp 101–103 °C; IR (film) 1738, 1601 (w) cm\(^{-1}\); \(^1\)H NMR δ: 7.26 (2H, m, H3’), 7.17 (1H, m, H4’), 7.00 (2H, m, H2’), 5.05 (1H, d, \(J = 2.1\) Hz, H10a), 4.83 (1H, d, \(J = 2.3\) Hz, H10b), 3.61 (1H, br s, H7), 2.66 (1H, m, H6), 2.48 (1H, br d, \(J = 16\) Hz, H5a), 2.42 (1H, dd, \(J = 16, 6.3\) Hz, H5b), 2.31 (1H, d, \(J = 16\) Hz, H2a), 2.04 (1H, d, \(J = 16\) Hz, H2b), 1.80 (3H, s, H13), 1.78 (3H, s, H12), 1.27 (3H, s, H11); \(^1\)C NMR δ: 222.7 (C9), 157.4 (C8), 146.4 (C1’), 128.7 (2C, C3’), 127.7 (C4), 127.2 (2C, C2’), 126.2 (C4’), 125.6 (C3), 109.2 (C10), 55.3 (C6), 53.9 (C1), 51.0 (C7), 50.8 (C2), 39.9 (C5), 23.8 (2C, C12, C13), 20.8 (C11); HRMS (ESI) 289.1557, [C\(_{19}\)H\(_{22}\)ONa]\(^+\) requires 289.1563.
Procedure 2: A solution of AVK 26 (0.025 g, 0.14 mmol) and 2,3-dimethyl-1,3-butadiene (0.080 mL, 0.70 mmol) in CH₂Cl₂ (15 mL) was cooled to −78 °C, and Cu(OTf)₂ (0.25 g, 0.70 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography of the residue (SiO₂ using 2.5% EtOAc in hexanes) provided 90 (0.025 g, 68%) as a colourless solid.

Procedure 3: A solution of AVK 26 (0.025 g, 0.14 mmol) and 2,3-dimethyl-1,3-butadiene (0.16 mL, 1.4 mmol) in CH₂Cl₂ (15 mL) was cooled to −78 °C, and InCl₃ (0.31 g, 1.4 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography of the residue (SiO₂ using 2.5% EtOAc in hexanes) provided 90 (0.045 g, 59%) as a colourless solid.
Following Procedure 1 for 90: AVK 26 (0.050 g, 0.28 mmol) and trans-piperylene (0.060 mL, 0.60 mmol) were reacted with BF$_3$OEt$_2$ (0.01 mL, 0.08 mmol) to yield 86a (0.012 g, 17%) and 87 (0.024 g, 34%) as colourless oils. For 86a: IR (film) 1742, 1604 (w) cm$^{-1}$; $^1$H NMR $\delta$: 7.27 (2H, m), 7.21 (1H, m), 7.07 (2H, m), 5.53 (1H, m), 5.47 (1H, m), 5.00 (1H, d, $J = 2.4$ Hz), 4.79 (1H, d, $J = 2.4$ Hz), 3.62 (1H, br s), 2.75 (1H, m), 2.43 (2H, m), 2.13 (1H, m), 1.26 (3H, s), 1.06 (3H, dd, $J = 6.7, 1.5$ Hz); $^{13}$C NMR $\delta$: 222.0, 154.5, 145.7, 135.0, 128.6 (2C), 128.1 (2C), 126.4, 124.0, 112.2, 57.5, 55.2, 51.9, 40.0, 33.1, 19.7, 16.7; HRMS (ESI) 275.1405, [C$_{18}$H$_{20}$ONa]$^+$ requires 275.1406. For 87: IR (film) 1771, 1604 (w) cm$^{-1}$; $^1$H NMR $\delta$: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.44 (1H, dq, $J = 15, 6.6$ Hz), 5.10 (1H, m), 5.08 (1H, d, $J = 2.1$ Hz), 4.82 (1H, d, $J = 2.1$ Hz), 3.78 (1H, br s), 2.44 (1H, td, $J = 10, 4.6$ Hz), 2.25 (1H, d, $J = 4.6$ Hz), 2.19 (1H, dd, $J = 13, 10$ Hz), 1.74 (1H, dt, $J = 13, 4.6$ Hz), 1.67 (3H, d, $J = 6.5$ Hz), 1.03 (3H, s); $^{13}$C NMR $\delta$: 215.5, 153.5, 143.3, 131.9, 128.6 (2C), 127.3 (2C), 126.8, 126.6, 107.9, 52.7, 52.3, 47.9, 44.8, 32.5, 17.8, 9.7; HRMS (ESI) 275.1400, [C$_{18}$H$_{20}$ONa]$^+$ requires 275.1406.
Compound 87 (0.009 g, 0.04 mmol) was dissolved in CH$_2$Cl$_2$ (4 mL) at rt, and BF$_3$·OEt$_2$ (0.2 mmol, 0.03 mL) was added. The mixture was stirred for 8 h, diluted with CH$_2$Cl$_2$, and washed with saturated NaHCO$_3$. After re-extraction with CH$_2$Cl$_2$, the combined organic layers were dried over Na$_2$SO$_4$, and concentrated. Purification by flash chromatography (2.5% EtOAc in hexanes) yielded 0.005 g (56%) of a 2.2:1 mixture of 86a and 86b (as determined by integration of the $^1$H NMR spectrum). The following NMR data for 86b were taken from the spectra of the mixture: $^1$H NMR δ: 7.27 (2H, m), 7.18 (1H, m), 7.04 (2H, m), 5.72 (1H, m), 5.56 (1H, m), 5.05 (1H, d, $J = 2.3$ Hz), 4.89 (1H, d, $J = 2.3$ Hz), 3.67 (1H, br s), 2.72 (1H, m), 2.40 (1H, overlapped), 2.34 (1H, m), 2.23 (1H, m) 1.31 (3H, s), 0.95 (3H, d, $J = 7.0$ Hz); $^{13}$C NMR δ: 220.1, 160.1, 146.7, 135.0, 128.7 (2C), 127.0 (2C), 126.3, 122.9, 109.6, 55.8, 55.2, 51.9, 45.6, 31.1, 20.3, 15.3.

(1$R^*$,3$R^*$,4$S^*$,6$S^*$)-1-Methyl-2-methylene-3-phenyl-6-((Z)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (88)

According to Procedure 1 for 90: AVK 26 (0.050 g, 0.28 mmol) and cis-piperylene (0.060 mL, 0.60 mmol) were reacted with BF$_3$·OEt$_2$ (0.01 mL, 0.08 mmol) to yield 88 (0.038 g, 54%) as a colourless solid: mp 72–75 °C; IR (film) 1773, 1602 (w) cm$^{-1}$; $^1$H NMR δ: 7.26 (2H, m, H3’’), 7.19 (1H, m, H4’’), 7.09 (2H, m, H2’’), 5.54 (1H,
dq, $J = 11, 6.8 \text{ Hz, H2}'$), 5.12 (1H, d, $J = 1.9 \text{ Hz, H8a}$), 5.07 (1H, tq, $J = 11, 1.9 \text{ Hz, H1'}$), 4.85 (1H, d, $J = 1.9 \text{ Hz, H8b}$), 3.82 (1H, br s, H3), 2.87 (1H, td, $J = 11, 4.7 \text{ Hz, H6}$), 2.27 (1H, d, $J = 4.7 \text{ Hz, H4}$), 2.22 (1H, dd, $J = 13, 11 \text{ Hz, H5a}$), 1.69 (1H, dt, $J = 13, 4.7 \text{ Hz, H5b}$), 1.63 (3H, dd, $J = 6.8, 1.9 \text{ Hz, H3}'$), 1.06 (3H, s, H9); $^{13}$C NMR δ: 215.1 (C7), 153.5 (C2), 143.3 (C1'''), 131.4 (C1''), 128.6 (2C, C3'''), 127.3 (2C, C2'''), 126.7 (C4'''), 125.2 (C1'), 108.0 (C8), 52.8 (C3), 52.1 (C1), 47.9 (C4), 38.5 (C6), 32.8 (C5), 13.0 (C3'), 9.1 (C9); HRMS (ESI) 275.1398, [C$_{18}$H$_{20}$ONa]$^+$ requires 275.1406.

(1$R^*$,6$S^*$,7$R^*$)-1,4-Dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89a) and (1$R^*$,6$S^*$,7$R^*$)-1,3-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89b)

According to Procedure 1 for 90: AVK 26 (0.050 g, 0.28 mmol) and isoprene (0.060 mL, 0.60 mmol) reacted in the presence of BF$_3$OEt$_2$ (0.01 mL, 0.08 mmol) to yield 0.040 g (56%) of a 1:2.8 mixture of 89a and 89b (as determined by integration of the $^1$H NMR spectrum); IR (film) 1745, 1602 (w) cm$^{-1}$; HRMS (ESI) 275.1403, [C$_{18}$H$_{20}$ONa]$^+$ requires 275.1406. The following NMR data were taken from the spectra of the mixture: for 89a: $^1$H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.03 (2H, m), 5.43 (1H, m), 5.07 (1H, d, $J = 2.2 \text{ Hz}$), 4.83 (1H, d, $J = 2.2 \text{ Hz}$), 3.65 (1H, br s), 2.76 (1H, m), 2.39 (1H, br d, $J = 17 \text{ Hz}$), 2.30 (1H, dd, $J = 17, 4.9 \text{ Hz}$), 2.20 (1H, br d, $J = 16 \text{ Hz}$), 2.15 (1H, dd, $J = 16, 6.0 \text{ Hz}$), 1.81 (3H, s), 1.30 (3H, s); $^{13}$C NMR δ: 221.8, 158.2, 146.3, 132.6,
128.7 (2C), 127.3 (2C), 126.3, 121.8, 109.6, 55.0, 54.6, 51.8, 43.7, 36.7, 28.2, 21.0; for

89b: $^1$H NMR $\delta$: 7.26 (2H, m), 7.19 (1H, m), 7.03 (2H, m), 5.47 (1H, m), 5.07 (1H, d, $J = 2.1$ Hz), 4.87 (1H, d, $J = 2.2$ Hz), 3.70 (1H, m), 2.76 (1H, m), 2.47 (1H, m), 2.41 (1H, m), 2.18 (1H, overlapped), 1.98 (1H, d, $J = 16$ Hz), 1.72 (3H, s), 1.31 (3H, s); $^{13}$C NMR $\delta$: 222.3, 157.8, 146.4, 134.5, 128.7 (2C), 121.2 (2C), 126.3, 120.3, 109.4, 55.9, 53.2, 51.7, 47.4, 33.1, 28.4, 21.6.

$(1R^*,3R^*,4S^*,6S^*)$-1-Methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)

According to Procedure 1 for 90: AVK 26 (0.050 g, 0.28 mmol) and 4-methyl-1,3-pentadiene (0.065 mL, 0.56 mmol) reacted in the presence of BF$_3$OEt$_2$ (0.01 mL, 0.08 mmol) to yield 91a (0.064 g, 85%) as a colourless solid: mp 68–70 °C; IR (film) 1771, 1604 (w) cm$^{-1}$; $^1$H NMR $\delta$: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.10 (1H, d, $J = 2.4$ Hz), 4.83 (1H, d, $J = 2.4$ Hz), 4.81 (1H, d, $J = 10$ Hz), 3.80 (1H, br s), 2.74 (1H, td, $J = 10, 4.5$ Hz), 2.23 (1H, d, $J = 4.5$ Hz), 2.21 (1H, dd, $J = 10, 13$ Hz), 1.71 (3H, br d, $J = 0.9$ Hz), 1.67 (1H, dt, $J = 13, 4.5$ Hz), 1.62 (3H, br d, $J = 1.2$ Hz), 1.03 (3H, s); $^{13}$C NMR $\delta$: 215.5, 153.7, 143.3, 133.4, 128.5 (2C), 127.3 (2C), 126.6, 126.0, 107.8, 52.7, 52.4, 47.9, 39.9, 33.2, 25.7, 18.1, 9.1; HRMS (ESI) 289.1557, [C$_{19}$H$_{22}$ONa]$^+$ requires 289.1563.
(1R*,6S*,7R*)-1,2,2,4-Tetramethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (92), (1R*,2R*,4R*,5S*)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93a), and (1R*,2S*,4R*,5S*)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93b)

According to Procedure 1 for 90: AVK 26 (0.050 g, 0.28 mmol) and 2,4-dimethyl-1,3-pentadiene (0.070 mL, 0.56 mmol) reacted in the presence of BF₃·OEt₂ (0.01 mL, 0.08 mmol) to provide 0.055 g (71%) of a 1.2:1.1:1.0 mixture of 10, 11a, and 11b respectively (as determined by integration of the ¹H NMR spectrum), as an inseparable mixture; IR (film) 1773, 1739, 1602 (w) cm⁻¹; HRMS (ESI) 303.1724, [C₂₀H₂₄ONa]⁺ requires 303.1719. The following NMR data were taken from the spectra of the mixture: for 92: ¹H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.03 (2H, m), 5.27 (1H, br s), 5.02 (1H, d, J = 2.4 Hz), 4.81 (1H, d, J = 2.4 Hz), 3.56 (1H, m), 2.64 (1H, m), 2.43 (1H, br d, J = 17 Hz), 2.25 (1H, overlapped), 1.79 (3H, s), 1.21 (3H, s), 1.12 (3H, s), 0.94 (3H, s); ¹³C NMR δ: 221.1, 157.1, 146.6, 136.5, 128.9, 128.6 (2C), 127.8 (2C), 126.3, 112.9, 59.7, 55.1, 51.4, 40.3, 36.6, 28.8, 25.8, 24.6, 17.0; for 93a: ¹H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.09 (2H, m), 5.29 (1H, br s), 5.13 (1H, d, J = 2.1 Hz), 5.01 (1H, d, J = 2.1 Hz), 3.61 (1H, br s), 2.64 (1H, m), 2.35 (1H, dd, J = 12, 5.4 Hz), 2.13 (1H, m), 1.79 (1H, d, J = 12 Hz), 1.71 (3H, s), 1.67 (3H, s), 1.28 (3H, s), 1.14 (3H, s); ¹³C NMR δ: 221.1, 157.1, 146.6, 136.5, 128.9, 128.6 (2C), 127.8 (2C), 126.3, 112.9, 59.7, 55.1, 51.4, 40.3, 36.6, 28.8, 25.8, 24.6, 17.0; for 93b: ¹H NMR δ: 7.26 (2H, m), 7.18 (1H, m),
According to Procedure 1 for 90: AVK 26 (0.050 g, 0.28 mmol) and 2,5-dimethyl-2,4-hexadiene (0.080 mL, 0.56 mmol) reacted in the presence of BF$_3$OEt$_2$ (0.01 mL, 0.08 mmol) to yield 0.040 g (49%) of a 5:1 mixture of 94a and 94b (as determined by integration of the $^1$H NMR spectrum); IR (film) 1771, 1603 (w) cm$^{-1}$; HRMS (ESI) 317.1876, [C$_{21}$H$_{26}$ONa]$^+$ requires 317.1876. The following NMR data were taken from the spectra of the mixture: for 94a: $^1$H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.10 (2H, m), 5.07 (1H, d, $J = 2.3$ Hz), 4.83 (1H, d, $J = 11$ Hz), 4.82 (1H, d, $J = 2.3$ Hz), 4.15 (1H, br s), 2.45 (1H, d, $J = 11$ Hz), 1.89 (1H, m), 1.75 (3H, br d, $J = 1.0$ Hz), 1.62 (3H, br d, $J = 1.2$ Hz), 1.28 (3H, s), 0.97 (3H, s), 0.87 (3H, s); $^{13}$C NMR δ: 215.0, 154.1, 143.4, 134.4, 128.6 (2C), 127.5 (2C), 126.5, 121.4, 107.0, 60.3, 55.1, 52.7, 46.2, 36.4, 26.9, 26.0, 25.2, 17.9, 9.6; for 94b: $^1$H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.10 (2H, m), 5.13 (1H, m), 5.02 (2H, m), 4.01 (1H, br s), 2.29 (1H, d, $J = 10$ Hz), 1.89 (1H, m), 1.79 (3H, br d, $J = 113$
0.9 Hz), 1.63 (3H, br d, \( J = 1.2 \) Hz), 1.09 (3H, s), 1.05 (3H, s), 1.00 (3H, s); \(^{13}\)C NMR δ: 215.0, 147.8, 143.4, 136.3, 128.6 (2C), 127.5 (2C), 126.5, 120.0, 111.3, 60.4, 56.9, 49.5, 46.5, 36.6, 31.7, 26.3, 21.1, 18.5, 11.2.

(\(7R^*,10S^*,4Z\))-3,3,5,9-Tetramethyl-10-phenylbicyclo[5.2.1]deca-1(9),4-dien-8-one (95)

A mixture of 92, 93a, and 93b (1.2:1.1:1.0, respectively) (0.008 g, 0.03 mmol) was dissolved in CH\(_2\)Cl\(_2\) (3 mL) at rt, and BF\(_3\)-OEt\(_2\) (0.2 mmol, 0.03 mL) was added. The mixture was stirred for 3 h, diluted with CH\(_2\)Cl\(_2\), and washed with saturated NaHCO\(_3\). After re-extraction with CH\(_2\)Cl\(_2\), the combined organic layers were dried over Na\(_2\)SO\(_4\), and concentrated. Purification by flash chromatography (10% EtOAc in hexanes) yielded 95 (0.006 g, 75%) as a colourless oil; IR (film) 1705, 1637, 1601 (w) cm\(^{-1}\); \(^1\)H NMR δ: 7.26 (2H, m, H3’), 7.21 (1H, m, H4’), 7.14 (2H, m, H2’), 5.49 (1H, br q, \( J = 1.4 \) Hz, H4), 4.12 (1H, s, H10), 2.78 (1H, t, \( J = 6.0 \) Hz, H7), 2.56 (1H, d, \( J = 12 \) Hz, H2a), 2.52 (1H, d, \( J = 12 \) Hz, H2b), 2.46 (1H, dd, \( J = 13, 6.0 \) Hz, H6a), 2.42 (1H, dd, \( J = 13, 6.0 \) Hz, H6b), 1.74 (3H, s, H11), 1.73 (3H, d, \( J = 1.4 \) Hz, H14), 1.35 (3H, s, H13), 1.13 (3H, s, H12); \(^{13}\)C NMR δ: 211.4 (C8), 176.1 (C1), 142.5 (C1’), 135.5 (C4), 135.3 (C5), 132.3 (C9), 128.7 (2C, C3’), 127.3 (2C, C2’), 126.8 (C4’), 56.7 (C10), 54.4 (C7), 45.3 (C2), 41.4
(1R*,6S*)-1,3,4-Trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (96)

According to Procedure 1 for 90: AVK 27 (0.025 g, 0.23 mmol) and 2,3-dimethyl-1,3-butadiene (0.050 mL, 0.44 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.01 mL, 0.08 mmol) to yield 96 (0.031 g, 71%) as a colourless oil; IR (film) 1747 cm$^{-1}$; $^1$H NMR $\delta$: 4.92 (1H, t, $J = 2.1$ Hz), 4.90 (1H, t, $J = 2.1$ Hz), 2.63 (2H, m), 2.40 (1H, br d, $J = 16$ Hz), 2.32 (1H, m), 2.23 (2H, m), 1.94 (1H, d, $J = 16$ Hz), 1.73 (3H, s), 1.65 (3H, s), 1.16 (3H, s); $^{13}$C NMR $\delta$: 222.9, 152.4, 127.5, 125.4, 106.1, 53.0, 50.7, 45.4, 39.8, 32.5, 23.8 (2C), 20.0; HRMS (ESI) 213.1254, [C$_{13}$H$_{18}$ONa]$^+$ requires 213.1250.

(1R*,6S*,7R*)-7-Isopropyl-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (97)

According to Procedure 1 for 90: AVK 29 (0.040 g, 0.27 mmol) and 2,3-dimethyl-1,3-butadiene (0.060 mL, 0.56 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.01
mL, 0.08 mmol) to yield 97 (0.040 g, 64%) as a colourless oil; IR 1747; \(^1\)H NMR δ: 4.98 (2H, m), 2.43 (2H, m), 2.36 (1H, m), 2.19 (2H, m), 1.95 (1H, d, \(J = 16\) Hz), 1.86 (1H, m), 1.72 (3H, s), 1.63 (3H, s), 1.16 (3H, s), 0.89 (3H, d, \(J = 6.9\) Hz), 0.65 (3H, d, \(J = 6.9\) Hz); \(^1^3\)C NMR δ: 224.0, 157.0, 127.3, 125.8, 106.2, 53.8, 51.1, 50.9, 48.3, 40.4, 33.6, 23.8 (2C), 20.4, 20.1, 17.2; HRMS (ESI) 255.1710, \([C_{16}H_{24}ONa]^+\) requires 255.1719.

\((1R^*,5R^*,6S^*,8S^*)-1,5\text{-}\text{Dimethyl}-7\text{-}\text{methylene}-8\text{-}\text{phenylbicyclo}\[4.2.1\]\text{non}\text{-}3\text{-}\text{en}\text{-}9\text{-}\text{one}\) (98)

![Chemical structure](image)

According to the procedure for 99: AVK 35 (0.10 g, 0.54 mmol) and \textit{trans}-piperylene (0.30 mL, 3.0 mmol) were reacted with BF\(^3\)OEt\(_2\) (0.070 mL, 0.60 mmol) to yield 98 (0.068 g, 50%) as a colourless oil: IR (film) 1741, 1601 cm\(^{-1}\); \(^1\)H NMR δ: 7.25 (3H, m), 7.00 (2H, m), 5.65 (1H, m), 5.47 (1H, m), 5.15 (1H, t, \(J = 2.0\) Hz), 4.92 (1H, t, \(J = 2.0\) Hz), 3.76 (1H, m), 3.10 (1H, m), 2.59 (1H, m), 2.34 (1H, dd, \(J = 17, 7.5\) Hz), 2.11 (1H, m), 1.30 (3H, d, \(J = 7.5\) Hz), 0.68 (3H, s); \(^1^3\)C NMR δ: 222.5, 149.4, 144.0, 135.1, 129.5, 128.1, 126.4, 125.3, 113.6, 60.0, 58.2, 53.8, 43.2, 36.1, 20.7, 20.4; HRMS (ESI) 275.1400, \([C_{18}H_{20}ONa]^+\) requires 275.1406.
BF₃·OEt₂ (1.1 equiv) was added to a solution of AVK 35 (0.10 g, 0.54 mmol) and 2,3-dimethylbutadiene (0.30 mL, 2.7 mol) in CH₂Cl₂ (55 mL) at -78 °C. The solution was stirred for 10 min, and it was poured into a separatory funnel containing a saturated solution of sodium bicarbonate. The aqueous layer was extracted thoroughly with CH₂Cl₂. The combined organic solutions were dried over MgSO₄ and concentrated under vacuum. Flash chromatography of the residue (2.5% EtOAc in hexanes) yielded 99 (0.11 g, 79%) as a colourless oil: IR (film) 1743, 1597 cm⁻¹; ¹H NMR δ: 7.22 (2H, m), 7.17 (1H, m), 6.92 (2H, m), 5.11 (1H, t, J = 1.9 Hz), 4.87 (1H, t, J = 1.9 Hz), 3.63 (1H, m), 3.24 (1H, m), 2.54 (1H, br d, J = 16 Hz), 2.42 (1H dd, J = 16, 7.7 Hz), 2.25 (1H, d, J = 16 Hz), 2.18 (1H, d, J = 16 Hz), 1.81 (3H, s), 1.72 (3H, s), 0.68 (3H, s); ¹³C NMR δ: 222.9, 152.1, 144.5, 129.1, 128.6, 128.1, 126.7, 126.5, 111.1, 57.9, 54.9, 53.4, 50.6, 41.7, 24.6, 23.9, 20.3; HRMS (ESI) 289.1556, [C₁₉H₂₂ONa]+ requires 289.1563.
(1R*,6S*,8S*)-1,3-Dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100a) and (1R*,6S*,8S*)-1,4-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100b)

According to the procedure for 99: AVK 35 (0.10 g, 0.54 mmol) and isoprene (0.30 mL, 3.0 mmol) were reacted with BF₃·OEt₂ (0.070 mL, 0.60 mmol) to yield 0.098 g (73%) of a 4:1 mixture of 100a and 100b (as determined by integration of the ¹H NMR spectrum); IR (film) 1748, 1605 (w) cm⁻¹; HRMS (ESI) 275.1398, [C₁₈H₂₀O₃Na]⁺ requires 275.1406. The following NMR data were taken from the spectra of the mixture: for 100a: ¹H NMR δ: 7.24 (2H, m), 7.18 (1H, m), 6.94 (2H, m), 5.47 (1H, m), 5.13 (1H, m), 4.93 (1H, m), 3.73 (1H, m), 3.32 (1H, m), 2.48 (1H, overlapped), 2.29 (2H, m), 2.10 (1H, overlapped), 1.74 (3H, s), 0.72 (3H, s); ¹³C NMR δ: 222.3, 152.2, 144.5, 134.5, 128.8 (2C), 128.5 (2C), 126.6, 121.1, 110.9, 58.8, 55.4, 52.5, 43.5, 38.3, 28.2, 20.7; for 100b: ¹H NMR δ: 7.24 (1H, m), 7.18 (2H, m), 6.94 (2H, m), 5.47 (1H, m), 5.15 (1H, m), 4.92 (1H, m), 3.73 (1H, m), 3.32 (1H, m), 2.48 (2H, m), 2.10 (1H, overlapped), 1.98 (1H, m), 1.81 (3H, s), 0.71 (3H, s); ¹³C NMR δ: 222.1, 152.5, 144.2, 133.3, 128.8 (2C), 128.5 (2C), 126.6, 121.5, 111.3, 58.7, 54.1, 53.7, 47.6, 35.1, 29.0, 20.2.
(1R*,3R*,8S*,12S*)-12-Methyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (101)

According to the procedure for 99: AVK 37 (0.080 g, 0.54 mmol) and trans-piperylene (0.30 mL, 3.0 mmol) were reacted with BF$_3$OEt$_2$ (0.070 mL, 0.60 mmol) to yield 101 (0.053 g, 48%) as a colourless oil: IR (film) 1748 cm$^{-1}$; $^1$H NMR $\delta$: 5.46 (1H, m), 5.24 (1H, m), 5.02 (1H, m), 4.97 (1H, m), 2.93 (1H, m), 2.58 (1H, m), 2.40 (1H, m), 2.13 (2H, m), 1.94 (1H, m), 1.82 (1H, m), 1.59 (2H, m), 1.29 (3H, d, $J = 7.5$ Hz), 1.14 (3H, m), 0.94 (1H, m); $^{13}$C NMR $\delta$: 221.4, 151.4, 132.6, 125.2, 108.2, 56.0, 53.0, 49.4, 42.2, 36.6, 34.4, 30.5, 23.6, 22.6, 20.7; HRMS (ESI) 239.1397, [C$_{15}$H$_{20}$ONa]$^+$ requires 239.1406.

(1R*,3R*,8S*)-10,11-Dimethyl-2-methylenetricyclo[6.4.1.0^{3,8}]triscadec-10-en-13-one (102)

According to the procedure for 99: AVK 37 (0.080 g, 0.54 mmol) and 2,3-dimethyl-1,3-butadiene (0.30 mL, 2.7 mmol) were reacted with BF$_3$OEt$_2$ (0.070 mL, 0.60 mmol) to yield 102 (0.089 g, 74%) as a colourless oil: IR (film) 1746 cm$^{-1}$; $^1$H NMR $\delta$:...
4.94 (1H, m), 4.86 (1H, m), 2.99 (1H, m), 2.55 (1H, br d, $J = 17$ Hz), 2.40 (1H, dd, $J = 13$, 6.3 Hz), 2.33 (1H, dd, $J = 17$, 6.3 Hz), 2.17 (1H, m), 2.03 (1H, m), 1.89 (1H, m), 1.63 (3H, s), 1.60 (3H, s), 1.58 (2H, m), 1.13 (3H, m), 0.86 (1H, m); $^{13}$C NMR δ: 220.9, 152.7, 125.5, 124.8, 105.3, 54.0, 49.8 (2C), 49.4, 40.8, 33.9, 30.9, 24.3, 23.7, 23.2, 22.7; HRMS (ESI) 253.1553, [C$_{16}$H$_{22}$ONa]$^+$ requires 253.1563.

(1$R^*$,3$R^*$,8$S^*$)-10-Methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]triscadec-10-en-13-one (103a) and (1$R^*$,3$R^*$,8$S^*$)-11-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]triscadec-10-en-13-one (103b)

According to the procedure for 99: AVK 37 (0.080 g, 0.54 mmol) and isoprene (0.30 mL, 3.0 mmol) were reacted with BF$_3$OEt$_2$ (0.070 mL, 0.60 mmol) to yield 0.072 g (65%) of a 1.3:1 mixture of 103a and 103b (as determined by integration of the $^1$H NMR spectrum); IR (film) 1748 cm$^{-1}$; HRMS (ESI) 239.1393, [C$_{15}$H$_{20}$ONa]$^+$ requires 239.1406. The following NMR data were taken from the spectra of the mixture: for 103a: $^1$H NMR δ: 5.24 (1H, m), 4.99 (1H, m), 4.88 (1H, m), 3.07 (1H, m), 2.41 (2H, m), 2.21 (1H, dd, $J = 18$, 5.4 Hz), 2.17 (1H, m), 2.09 (1H, dd, $J = 17$, 5.7 Hz), 1.95 (1H, m), 1.81 (1H, m), 1.64 (3H, s), 1.59 (3H, m), 1.14 (3H, m), 0.89 (1H, m); $^{13}$C NMR δ: 220.3, 152.9, 131.4, 121.3, 105.3, 54.7, 50.5, 48.6, 42.4, 36.8, 34.0, 30.6, 27.3, 24.3, 23.2; for 103b: $^1$H NMR δ: 5.19 (1H, m), 4.99 (1H, m), 4.89 (1H, m), 3.07 (1H, m), 2.50 (1H, br d, $J = 17$ Hz), 2.41 (2H, overlapped), 2.17 (1H, m), 1.95 (1H, m), 1.86 (1H, br d, $J = 17$ Hz), 2.41 (2H, overlapped)
141 Hz), 1.81 (1H, m), 1.66 (3H, s), 1.59 (3H, m), 1.14 (3H, m), 0.89 (1H, m); $^{13}$C NMR δ: 220.2, 152.8, 132.7, 119.7, 105.9, 53.5, 50.5, 49.4, 46.4, 33.9, 33.8, 30.9, 28.5, 24.2, 23.1.

(E)-1-(3,4-Dimethyl-6-methylene cyclohex-3-enyl)-3-phenylprop-2-en-1-one (104)

BF$_3$OEt$_2$ (1.1 equiv) was added to a solution of AVK 36 (0.070 g, 0.41 mmol) and 2,3-dimethylbutadiene (0.25 mL, 2.2 mol) in CH$_2$Cl$_2$ (40 mL) at -78 °C. The solution was stirred for 1 h, and it was poured into a separatory funnel containing a saturated solution of sodium bicarbonate. The aqueous layer was extracted thoroughly with CH$_2$Cl$_2$. The combined organic solutions were dried over MgSO$_4$ and concentrated under vacuum. Flash chromatography of the residue (2.5% EtOAc in hexanes) yielded 104 (0.051 g, 51%) as an off-white solid: mp 71–74 °C; IR (film) 1695, 1614 cm$^{-1}$; $^1$H NMR δ: 7.63 (1H, d, $J = 16$ Hz), 7.55 (2H, m), 7.38 (3H, m), 6.97 (1H, d, $J = 16$ Hz), 4.98 (1H, m), 4.86 (1H, m), 3.57 (1H, t, $J = 5.7$ Hz), 2.74 (1H, d, $J = 19$ Hz), 2.69 (1H, d, $J = 19$ Hz), 2.63 (1H, br d, $J = 19$ Hz), 1.65 (1H, br d, $J = 19$ Hz), 1.68 (3H, s), 1.62 (3H, s); $^{13}$C NMR δ: 199.4, 144.8, 142.6, 134.9, 130.6, 129.1 (2C), 128.6 (2C), 124.8, 124.3, 124.1, 110.9, 54.2, 39.6, 34.4, 19.0, 18.9; HRMS (ESI) 275.1403, [C$_{18}$H$_{20}$ONa]$^+$ requires 275.1406.
(trans)-5- Allyl-2,3-dimethyl-4-phenylcyclopent-2- enone (105), (1R*,3R*,4S*,6R*)-1-methyl-2-methylene-3-phenyl-6-((trimethylsilyl)methyl)bicyclo[2.2.1]heptan-7-one (106a), and 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2- enone (107)

Procedure 1: A solution of AVK 26 (0.050 g, 0.28 mmol) and allyltrimethylsilane (0.090 mL, 0.56 mmol) in CH₂Cl₂ (25 mL) was cooled to –78 °C, and BF₃·OEt₂ (0.040 mL, 0.31 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography of the residue (2.5%, then 10%, EtOAc in hexanes) provided 105 (0.020 g, 27%) and 106a (0.045 g, 54%). For 105: colourless oil; IR (film) 1702, 1650, 1604 (w) cm⁻¹; ¹H NMR δ: 7.31 (2H, m), 7.24 (1H, m), 7.07 (2H, m), 5.70 (1H, m), 5.10 (1H, d of narrow m, J = 17 Hz), 5.02 (1H, d of narrow m, J = 10 Hz), 3.50 (1H, br d, J ≈ 3 Hz), 2.58 (1H, m), 2.40 (1H, m), 2.28 (1H, ddd, J = 8.9, 4.3, 2.5 Hz), 1.80 (6H, s); ¹³C NMR δ: 210.1, 170.3, 141.8, 136.3, 135.6, 128.8 (2C), 127.9 (2C), 126.9, 117.0, 55.3, 54.7, 35.6, 15.5, 8.3; HRMS (ESI) 249.1242, [C₁₆H₁₈ONa]⁺ requires 249.1250. For 106a: colourless solid; mp 78–79 °C; IR (film) 1763, 1603 (w) cm⁻¹; ¹H NMR δ: 7.27 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.05 (1H, d, J = 2.2 Hz), 4.79 (1H, d, J = 2.2 Hz), 3.76 (1H, br s), 2.22 (1H, d, J = 4.7 Hz), 2.15 (1H, dd, J = 13, 10 Hz), 1.95 (1H, m), 1.53 (1H, dd, J = 13, 4.9 Hz), 1.10 (3H, s), 0.76 (1H, dd, J = 14, 2.5 Hz), 0.27
(1H, t, J = 14 Hz), 0.03 (9H, s); \(^{13}\)C NMR δ: 215.5, 154.4, 143.4, 128.6 (2C), 127.3 (2C), 126.6, 107.4, 53.1, 52.5, 48.2, 37.9, 34.4, 20.8, 9.3, -0.6 (3C); HRMS (ESI) 321.1644, [C\(_{19}\)H\(_{26}\)OSiNa]\(^{+}\) requires 321.1645.

**Procedure 2:** A solution of AVK 26 (0.025 g, 0.14 mmol) and allyltrimethylsilane (0.11 mL, 0.070 mmol) in CH\(_2\)Cl\(_2\) (15 mL) was cooled to –78 °C, and Cu(OTf)\(_2\) (0.25 g, 0.070 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH\(_2\)Cl\(_2\) layer was removed, and additional CH\(_2\)Cl\(_2\) (\(\times 2\)) was used to re-extract the aqueous layer. The combined organic layers were dried over Na\(_2\)SO\(_4\) and then concentrated under reduced pressure. Flash chromatography of the residue (2.5%, then 10%, EtOAc in hexanes) provided 105 (0.008 g, 20%), 106a (0.003 g, 10%), and 105 (0.013 g, 42%). For 107: colourless oil; IR (film) 1702, 1643, 1602 (w) cm\(^{-1}\); \(^{1}\)H NMR δ: 7.32 (2H, m), 7.25 (1H, m), 7.09 (2H, m), 5.70 (1H, m), 4.98 (1H, d of narrow m, J = 15 Hz), 4.95 (1H, d of narrow m, J = 7.4 Hz), 3.94 (1H, m), 2.90 (1H, dd, J = 19, 7.0 Hz), 2.51 (1H, m), 2.36 (1H, dd, J = 19, 2.2 Hz), 2.18 (1H, m), 2.09 (2H, m), 1.80 (3H, s); \(^{13}\)C NMR δ: 209.3, 174.1, 142.0, 137.5, 137.1, 129.0 (2C), 127.4 (2C), 127.1, 115.6, 47.0, 44.7, 31.2, 28.5, 8.4; HRMS (ESI) 249.1244, [C\(_{16}\)H\(_{18}\)ONa]\(^{+}\) requires 249.1250.

**Procedure 3:** A solution of AVK 26 (0.025 g, 0.14 mmol) and allyltrimethylsilane (0.23 mL, 1.4 mmol) in CH\(_2\)Cl\(_2\) (15 mL) was cooled to –78 °C, and InCl\(_3\) (0.31 g, 1.4 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH\(_2\)Cl\(_2\) layer was removed, and additional CH\(_2\)Cl\(_2\) (\(\times 2\)) was used to re-extract the aqueous layer. The combined organic
layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography of the residue (10% EtOAc in hexanes) provided 105 (0.014 g, 22%) and 107 (0.036 g, 56%).

(trans)-5- Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105), (1R*,3R*,4S*,6R*)-1-methyl-2-methylene-3-phenyl-6-((triisopropylsilyl)methyl)bicyclo[2.2.1]heptan-7-one (106b), and 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)

According to Procedure 1 for 105 and 106a: AVK 26 (0.050 g, 0.28 mmol) and allyltriisopropylsilane (0.13 mL, 0.56 mmol) were reacted in the presence of BF₃·OEt₂ (0.040 mL, 0.31 mmol) to yield 105 (0.012 g, 19%) and 106b (0.061 g, 57%). For 106b: colourless oil; IR (film) 1771, 1603 (w) cm⁻¹; ¹H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.09 (2H, m), 5.07 (1H, d, J = 2.2 Hz), 4.80 (1H, d, J = 2.2 Hz), 3.76 (1H, br s), 2.24 (1H, d, J = 4.8 Hz), 2.19 (1H, dd, J = 12, 10 Hz), 2.06 (1H, m), 1.59 (1H, dt, J = 12, 4.6 Hz), 1.16 (3H, s), 1.05 (21H, m), 0.89 (1H, dd, J = 14, 1.9 Hz), 0.30 (1H, t, J = 14 Hz); ¹³C NMR δ: 215.3, 154.5, 143.3, 128.6 (2C), 127.3 (2C), 126.6, 107.5, 53.4, 52.6, 48.2, 37.8, 34.6, 18.8 (6C), 13.1, 11.4 (3C), 9.4; HRMS (ESI) 405.2587, [C₂₅H₃₈OSiNa]⁺ requires 405.2584.

According to Procedure 3 for 105 and 107: AVK 26 (0.050 g, 0.28 mmol) and allyltriisopropylsilane (0.34 mL, 1.4 mmol) were reacted with InCl₃ (0.31 g, 1.4 mmol) to yield 105 (0.018 g, 27%), 106b (0.030 g, 28%), and 107 (0.008 g, 13%).
(1R*,3R*,4S*,6R*)-1-Methyl-2-methylene-3-phenyl-6-((triethoxysilyl)methyl)bicyclo[2.2.1]heptan-7-one (106c)

According to Procedure 1 for 105 and 106a: AVK 26 (0.050 g, 0.28 mmol) and allyltriethoxysilane (0.13 mL, 0.56 mmol) were reacted in the presence of BF₃·OEt₂ (0.040 mL, 0.31 mmol) to yield 106c (0.016 g, 15%) as a colourless oil; IR (film) 1770, 1604 (w) cm⁻¹; ¹H NMR δ: 7.26 (2H, m), 7.18 (1H, m), 7.08 (2H, m), 5.06 (1H, d, J = 2.2 Hz), 4.80 (1H, d, J = 2.2 Hz), 3.82 (6H, q, J = 7.0 Hz), 3.77 (1H, br s), 2.20 (2H, m), 2.07 (1H, m), 1.73 (1H, dt, J = 13, 4.7 Hz), 1.23 (9H, t, J = 7.0 Hz), 0.84 (1H, dd, J = 15, 2.7 Hz), 0.32 (1H, dd, J = 15, 13 Hz); ¹³C NMR δ: 215.6, 154.2, 143.4, 128.5 (2C), 127.3 (2C), 126.6, 107.7, 58.5 (3C), 52.9, 52.5, 48.2, 36.3, 33.6, 18.3 (3C), 14.7, 9.2; HRMS (ESI) 411.1955, [C₂₂H₃₂O₄SiNa]⁺ requires 411.1962.

(trans)-5-Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105) and (1R*,3R*,5S*,6R*)-1-methyl-7-methylene-6-phenyl-3-(trimethylsilyl)bicyclo[3.2.1]octan-8-one (108a)

Compound 106a (0.025 g, 0.083 mmol) was dissolved in CH₂Cl₂ (8 mL) at rt, and BF₃·OEt₂ (0.4 mmol, 0.05 mL) was added. The mixture was stirred for 5 h, diluted with
CH₂Cl₂, and washed with saturated NaHCO₃. After re-extraction with CH₂Cl₂, the combined organic layers were dried over Na₂SO₄, and concentrated. Purification by flash chromatography (2.5%, then 10% EtOAc in hexanes) yielded 105 (0.013 g, 69%) and 108a (0.005 g, 20%). For 108a: colourless solid, mp 141–143 °C; IR (film) 1738, 1603 (w) cm⁻¹; ¹H NMR δ: 7.24 (2H, m), 7.17 (1H, m), 7.01 (2H, m), 5.08 (1H, d, J = 2.1 Hz), 4.97 (1H, d, J = 2.1 Hz), 3.80 (1H, br s), 2.56 (1H, m), 2.18 (1H, m), 1.96 (1H, td, J = 14, 2.5 Hz), 1.79 (2H, m), 1.41 (1H, m), 1.19 (3H, s), -0.02 (9H, s); ¹³C NMR δ: 222.3, 155.4, 145.7, 128.7 (2C), 127.2 (2C), 126.3, 109.3, 55.3 (2C), 50.5, 50.4, 39.5, 18.3, 16.6, 3.3 (3C); HRMS (ESI) 321.1646, [C₁₉H₂₆OSiNa]⁺ requires 321.1645.

(trans)-5- Allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105) and (1R*,3R*,5S*,6R*)-1-methyl-7-methylene-6-phenyl-3-(triisopropylsilyl)bicyclo[3.2.1]octan-8-one (108b)

Compound 106b (0.020 g, 0.052 mmol) was dissolved in CH₂Cl₂ (5 mL) at rt, and BF₃·OEt₂ (0.2 mmol, 0.03 mL) was added. The mixture was stirred for 3 h, diluted with CH₂Cl₂, and washed with saturated NaHCO₃. After re-extraction with CH₂Cl₂, the combined organic layers were dried over Na₂SO₄, and concentrated. Purification by flash chromatography (2.5%, then 10% EtOAc in hexanes) yielded 105 (0.001 g, 8%) and 108b (0.018 g, 85%). For 108b: colourless solid: mp 79–81 °C; IR (film) 1742, 1603 (w) cm⁻¹; ¹H NMR δ: 7.24 (2H, m), 7.17 (1H, m), 7.01 (2H, m), 5.08 (1H, d, J = 2.1 Hz),
5.00 (1H, d, J = 2.1 Hz), 3.74 (1H, br s), 2.58 (1H, m), 2.23 (2H, m), 2.05 (1H, dd, J = 14, 13 Hz), 1.83 (2H, m), 1.19 (3H, s), 1.09 (21H, m); 13C NMR δ: 221.8, 155.3, 145.5, 128.7 (2C), 127.1 (2C), 126.3, 109.1, 55.8, 55.7, 51.2, 50.5, 40.2, 19.1 (6C), 16.7, 15.4, 11.2 (3C); HRMS (ESI) 405.2575, [C25H38OSiNa]+ requires 405.2584.

(1'R*,2R*,5'R*)-2-(3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)

A solution of AVK 26 (0.050 g, 0.28 mmol) and 1-ethoxypropene (3:1 cis/trans mixture) (0.060 mL, 0.54 mmol) in CH2Cl2 (25 mL) was cooled to –78 °C, and BF3·OEt2 (0.040 mL, 0.31 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH2Cl2 layer was removed, and additional CH2Cl2 (∗2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na2SO4 and then concentrated under reduced pressure. Flash chromatography of the residue (10% EtOAc in hexanes) provided 113 (0.057 g, 76%) as a colourless oil: IR (film) 1724, 1701, 1602 (w) cm –1; 1H NMR δ: 9.57 (1H, br d, J = 0.6 Hz, H1), 7.32 (2H, m, H3’’), 7.26 (1H, m, H4’’), 7.02 (2H, m, H2’’), 3.45 (1H, br d, J≈ 3 Hz, H5’’), 3.04 (1H, m, H2), 2.83 (1H, dd, J = 4.2, 3.2 Hz, H1’), 1.82 (3H, s, H5), 1.81 (3H, s, H4), 1.01 (3H, d, J = 7.0 Hz, H3); 13C NMR δ: 208.1 (C2’), 202.9 (C1), 171.1 (C4’), 140.9 (C1’’), 137.2 (C3’), 129.1 (2C, C3’’), 127.7 (2C, C2’’),
127.3 (C4’’), 55.0 (C1’), 51.9 (C5’), 47.4 (C2), 15.5 (C5), 8.9 (C3), 8.3 (C4); HRMS (ESI) 265.1202, [C16H18O2Na]+ requires 265.1199.

2-((trans)-3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and (trimethylsilyl)oxyethene (0.16 g, 0.56 mmol) were reacted with BF₃·OEt₂ (0.040 mL, 0.32 mmol) to yield 110 (0.022 g, 35%) as a colourless oil; IR (film) 1724, 1701, 1602 (w) cm⁻¹; ¹H NMR δ: 9.72 (1H, br t, J = 1.3 Hz), 7.34 (2H, m), 7.28 (1H, m), 7.08 (2H, m), 3.48 (1H, br d, J = 2.5 Hz), 2.94 (1H, m), 2.73 (1H, m), 2.71 (1H, m), 1.83 (3H, s), 1.82 (3H, s); ¹³C NMR δ: 208.3, 200.4, 169.9, 140.8, 136.3, 129.0 (2C), 127.6 (2C), 127.3, 55.9, 50.4, 44.1, 15.4, 8.4; HRMS (ESI) 251.1046, [C₁₅H₁₆O₂Na]⁺ requires 251.1043.

1-Methyl-6-methylene-7-oxo-5-phenylbicyclo[2.2.1]heptan-2-yl acetate (111)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and vinyl
acetate (0.050 mL, 0.54 mmol) were reacted with BF₃·OEt₂ (0.040 mL, 0.32 mmol) to yield 111 (0.014 g, 18%) as a colourless oil; IR (film) 1779, 1743, 1603 (w) cm⁻¹; ¹H NMR δ: 7.26 (2H, m), 7.21 (1H, m), 7.09 (2H, m), 5.32 (1H, d, J = 2.4 Hz), 5.08 (1H, d, J = 2.4 Hz), 4.94 (1H, dd, J = 8.4, 2.4 Hz), 3.75 (1H, br s), 2.46 (1H, dd, J = 15, 8.4 Hz), 2.38 (1H, d, J = 5.1 Hz), 2.06 (3H, s), 1.96 (1H, m), 1.19 (3H, s); ¹³C NMR δ: 213.1, 170.3, 147.4, 142.2, 128.7 (2C), 127.2 (2C), 127.0, 112.9, 72.4, 53.1, 52.4, 47.4, 35.4, 21.0, 7.7; HRMS (ESI) 293.1143, [C₁₇H₁₈O₃Na]⁺ requires 293.1148.

2-((trans)-3,4-Dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110) and (1R*,3S*,4R*,6S*)- and (1R*,3S*,4R*,6R*)-1-methyl-2-methylene-3-phenyl-6-propoxybicyclo[2.2.1]heptan-7-one (112)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and n-propoxypentene (0.060 mL, 0.54 mmol) were reacted in the presence of BF₃·OEt₂ (0.040 mL, 0.32 mmol) to give 110 (0.037 g, 58%) as a colourless oil and 0.031 g (41%) of 112 as a 5:1 mixture of inseparable epimers (as determined by integration of the ¹H NMR spectrum). For 112: IR (film) 1779, 1603 (w) cm⁻¹; HRMS (ESI) 293.1511, [C₁₈H₂₂O₂Na]⁺ requires 293.1512; the following NMR data are taken from the spectra of the mixture: major isomer: ¹H NMR δ: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.22 (1H, d, J = 2.5 Hz), 4.97 (1H, d, J = 2.5 Hz), 3.69 (1H, br s), 3.49 (1H, m), 3.45 (1H, m), 3.30 (1H, m), 2.32 (1H, d, J = 5.0 Hz), 2.24 (1H, dd, J = 13, 7.7 Hz), 1.98 (1H, ddd, J = 149
13, 5.0, 2.2 Hz), 1.55 (2H, m), 1.23 (3H, s), 0.90 (3H, t, $J = 7.5 \text{ Hz}$); $^{13}\text{C NMR } \delta$: 214.4, 149.3, 142.8, 128.5 (2C), 127.3 (2C), 126.7, 111.0, 78.2, 70.8, 54.8, 52.6, 47.5, 35.6, 23.0, 10.7, 7.8; minor isomer: $^1\text{H NMR } \delta$: 7.26 (2H, m), 7.19 (1H, m), 7.09 (2H, m), 5.12 (1H, d, $J = 2.5 \text{ Hz}$), 4.96 (1H, d, $J = 2.5 \text{ Hz}$), 3.80 (1H, m), 3.70 (1H, overlapped), 3.49 (1H, overlapped), 3.45 (1H, overlapped), 2.43 (1H, m), 2.35 (1H, d, $J = 4.8 \text{ Hz}$), 1.76 (1H, d, $J = 14, 3.2 \text{ Hz}$), 1.55 (2H, m), 1.29 (3H, s), 0.93 (3H, t, $J = 7.5 \text{ Hz}$); $^{13}\text{C NMR } \delta$: 212.7, 146.4, 143.4, 128.5 (2C), 127.4 (2C), 126.6, 111.2, 76.9, 71.7, 56.6, 52.5, 49.0, 35.5, 23.1, 10.9, 10.6.

$(\text{trans})$-2,3-Dimethyl-5-(2-oxopropyl)-4-phenylcyclopent-2-enone (114) and by-product

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and 2-methoxypropene (0.050 mL, 0.52 mmol) were reacted with BF$_3$·OEt$_2$ (0.040 mL, 0.32 mmol) to yield 114 and a by-product (tentative structure above) with the mass of 114 plus 2-methoxypropene (0.031 g, 60%) as an inseparable mixture (3.3:1, respectively, as determined by integration of the $^1\text{H NMR}$ spectrum); the following NMR data were taken from the spectra of the mixture: for 114: $^1\text{H NMR } \delta$: 7.35 (2H, m), 7.28 (1H, m), 7.10 (2H, m), 3.52 (1H, narrow m), 2.92 (1H, dd, $J = 17, 4.4 \text{ Hz}$), 2.73 (1H, dd, $J = 17, 7.7 \text{ Hz}$), 2.60 (1H, m), 2.10 (3H, s), 1.81 (3H, s), 1.80 (3H, s); $^{13}\text{C NMR } \delta$: 208.9, 206.9, 169.8, 141.2, 136.2, 128.9 (2C), 127.7 (2C), 127.1, 55.7, 51.6, 43.5, 29.8, 15.4, 8.4; for
the by-product: $^1$H NMR (diagnostic signals only) $\delta$: 3.20 (3H, s), 1.23 (3H, s), 1.22 (3H, s); $^{13}$C NMR $\delta$: 209.2, 207.7, 169.4, 141.4, 136.2, 128.8 (2C), 127.7 (2C), 127.0, 74.4, 52.5, 51.7, 49.3, 44.4, 24.9, 24.8, 15.4, 8.4; HRMS (ESI) for 114: 265.1202, [C$_{16}$H$_{18}$O$_2$Na]$^+$ requires 265.1199; for the by-product: 337.1774, [C$_{20}$H$_{26}$O$_3$Na]$^+$ requires 337.1774.

**Trimethyl((1E,3Z)-4-methyl-1-phenyl-5-(1-(trimethylsilyloxy)cyclobutyl)hexa-1,3,5-trien-3-yloxy)silane (116)**

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and 1,2-bis(trimethylsilyloxy)cyclobutene (0.36 mL, 1.4 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.040 mL, 0.31 mmol) to yield 34 (0.014 g, 12%) as a yellow oil after silica gel chromatography (10% EtOAc in hexanes); IR (film) 1787, 1601 (w) cm$^{-1}$; $^1$H NMR $\delta$: 7.32 (4H, m), 7.21 (1H, m), 6.97 (1H, d, $J = 16$ Hz), 6.68 (1H, d, $J = 16$ Hz), 2.85 (1H, dd, $J = 16$, 11 Hz), 2.77 (1H, dd, $J = 16$, 11, 5.3), 2.37 (1H, td, $J = 11$, 5.3), 2.08 (1H, t, $J = 5.3$ Hz), 1.91 (3H, s), 0.29 (9H, s), 0.18 (9H, s); $^{13}$C NMR $\delta$: 207.7, 147.6, 147.0, 137.2, 128.6 (2C), 128.1, 128.0, 127.4, 126.5 (2C), 123.9, 122.1, 118.1, 94.8, 40.2, 27.6, 18.1, 1.6, 0.8; HRMS (ESI): 437.1932, [C$_{23}$H$_{34}$Si$_2$O$_3$Na]$^+$ requires 437.1939.
(1R*,3R*,4S*,6S*)-1-Methyl-2-methylene-3,6-diphenylbicyclo[2.2.1]heptan-7-one (35)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and styrene (0.065 mL, 0.56 mmol) reacted in the presence of BF₃·OEt₂ (0.01 mL, 0.08 mmol) to yield 117 (0.012 g, 15%) as a colourless oil; IR (film) 1764, 1601 (w) cm⁻¹; ¹H NMR δ: 7.29 (4H, m), 7.23 (2H, m), 7.14 (2H, m), 7.06 (2H, m), 5.15 (1H, d, J = 2.5 Hz), 4.86 (1H, d, J = 2.5 Hz), 3.91 (1H, br s), 3.12 (1H, dd, J = 11, 5.8 Hz), 2.46 (2H, m), 2.25 (1H, dt, J = 13, 5.2 Hz), 0.79 (3H, s); ¹³C NMR δ: 215.7, 153.3, 143.2, 143.0, 128.6 (4C), 128.0 (2C), 127.4 (2C), 127.0, 126.7, 108.1, 53.2, 52.6, 48.6, 47.4, 34.1, 9.8; HRMS (ESI) 311.1400, [C₂₁H₂₀ONa]+ requires 311.1406.

(1R*,3R*,4S*,6S*)-6-(4-Methoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]heptan-7-one (118)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and p-vinylanisole (0.060 mL, 0.56 mmol) were reacted in the presence of BF₃·OEt₂ (0.01 mL, 0.08 mmol) to yield 118 (0.047 g, 52%) as a colourless solid: mp 131–133 °C; IR (film)
1772, 1611 cm⁻¹; ¹H NMR δ: 7.28 (2H, m, H3''), 7.21 (1H, m, H4''), 7.13 (2H, m, H2''), 6.97 (2H, br d, J = 8.7 Hz, H2'), 6.84 (2H, br d, J = 8.7 Hz, H3''), 5.13 (1H, d, J = 2.2 Hz, H8a), 4.85 (1H, d, J = 2.2 Hz, H8b), 3.89 (1H, br s, H3), 3.80 (3H, s, H10), 3.08 (1H, dd, J = 11, 5.8 Hz, H6), 2.45 (2H, m, H3a, H4), 2.20 (1H, dt, J = 13, 5.1 Hz, H3b), 0.78 (3H, s, H9); ¹³C NMR δ: 215.9 (C7), 158.5 (C4'), 153.4 (C2), 143.2 (C1''), 135.0 (C1'), 128.9 (2C, C2''), 127.4 (2C, C2''), 126.7 (C4''), 113.9 (2C, C3'), 107.8 (C8), 55.2 (C10), 53.3 (C1), 52.5 (C3), 48.6 (C4), 46.7 (C6), 34.3 (C3), 9.8 (C9); HRMS 341.1507, [C₂₂H₂₂O₂Na]⁺ requires 341.1512.

(1R*,3R*,4S*,6S*)-6-(3,4-Dimethoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]heptan-7-one (119)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and 3,4-dimethoxystyrene (0.080 mL, 0.54 mmol) reacted in the presence of BF₃·OEt₂ (0.01 mL, 0.08 mmol) to yield 119 (0.074 g, 76%) as a colourless solid: mp 113–116 °C; IR (film) 1771, 1611 (w) cm⁻¹; ¹H NMR δ: 7.29 (2H, m), 7.21 (1H, m), 7.13 (2H, m), 6.80 (1H, d, J = 8.3 Hz), 6.61 (1H, dd, J = 8.3, 2.1 Hz), 6.56 (1H, d, J = 2.1 Hz), 5.14 (1H, d, J = 2.2 Hz), 4.86 (1H, d, J = 2.2 Hz), 3.89 (1H, br s), 3.87 (6H, s), 3.06 (1H, dd, J = 11, 5.5 Hz), 2.46 (2H, m), 2.22 (1H, dt, J = 13, 5.1 Hz), 0.81 (3H, s); ¹³C NMR δ: 216.0, 153.3, 148.8, 147.9, 143.2, 135.6, 128.6 (2C), 127.3 (2C), 126.7, 120.0, 111.0, 110.8, 108.0, 55.8, 53.3, 52.5, 48.6, 47.1, 34.3, 9.7; HRMS 371.1617, [C₂₃H₂₄O₃Na]⁺ requires 371.1618.
(1R*,2S*,3R*,4S*,5S*)-2-(4-Methoxyphenyl)-1,3-dimethyl-6-methylene-5-phenyl bicyclo[2.2.1]-heptan-7-one (120)

According to the procedure for 113: AVK 26 (0.050 g, 0.28 mmol) and trans-anethole (0.080 mL, 0.53 mmol) were reacted with BF₃·OEt₂ (0.01 mL, 0.08 mmol) to yield 120 (0.055 g, 59%) as a colourless solid: mp 129–131 °C; IR (film) 1768, 1611 cm⁻¹; ¹H NMR δ: 7.29 (2H, m), 7.21 (1H, m), 7.16 (2H, m), 6.98 (2H, d, J = 8.7 Hz), 6.83 (2H, d, J = 8.7 Hz), 5.08 (1H, d, J = 2.1 Hz), 4.81 (1H, d, J = 2.1 Hz), 4.15 (1H, br s), 3.79 (3H, s), 2.49 (1H, d, J = 7.1 Hz), 2.41 (1H, m), 2.36 (1H, d, J = 4.0 Hz), 1.27 (3H, d, J = 6.8 Hz), 0.78 (3H, s); ¹³C NMR δ: 215.5, 158.6, 154.0, 143.3, 134.0, 129.3 (2C), 128.6 (2C), 127.6 (2C), 126.6, 113.9 (2C), 107.0, 56.8, 55.3, 55.2, 54.1, 44.0, 38.6, 16.0, 9.9; HRMS (ESI) 355.1659, [C₂₃H₂₄O₂Na]⁺ requires 355.1669.

(1R*,2S*,4S*)-2-(3,4-Dimethoxyphenyl)-1-methyl-6-methylenebicyclo[2.2.1]heptan-7-one (121)

According to the procedure for 113: AVK 27 (0.025 g, 0.23 mmol) and 3,4-dimethoxystyrene (0.070 mL, 0.47 mmol) were reacted in the presence of BF₃·OEt₂ (0.01
mL, 0.08 mmol) to yield 121 (0.049 g, 79%) as a colourless oil; IR (film) 1772, 1611 (w) cm⁻¹; ¹H NMR δ: 6.77 (1H, d, J = 8.3 Hz), 6.57 (1H, dd, J = 8.3, 2.1 Hz), 6.51 (1H, d, J = 2.1 Hz), 4.97 (1H, t, J = 2.3 Hz), 4.90 (1H, d, J = 2.3 Hz), 3.86 (3H, s), 3.85 (3H, s), 2.93 (1H, dd, J = 11, 5.3 Hz), 2.74 (1H, m), 2.54 (1H, dt, J = 16, 2.2 Hz), 2.42 (1H, t, J = 4.5 Hz), 2.25 (1H, dd, J = 13, 11 Hz), 2.14 (1H, m), 0.73 (3H, s); ¹³C NMR δ: 216.2, 148.8, 148.7, 147.8, 135.8, 119.9, 110.9, 110.6, 105.4, 55.8 (2C), 52.8, 47.6, 40.8, 35.0, 34.2, 9.5; HRMS 295.1305, [C₁₇H₂₀O₃Na]⁺ requires 295.1305.

(1R⁺,3R⁺,4S⁺,6S⁺)-6-(3,4-Dimethoxyphenyl)-3-isopropyl-1-methyl-2-methylene bicyclo[2.2.1]heptan-7-one (122)

According to the procedure for 113: AVK 29 (0.040 g, 0.27 mmol) and 3,4-dimethoxystyrene (0.080 mL, 0.54 mmol) reacted in the presence of BF₃·OEt₂ (0.01 mL, 0.08 mmol) to yield 122 (0.068 g, 81%) as a colourless oil; IR (film) 1773, 1610 cm⁻¹; ¹H NMR δ: 6.77 (1H, d, J = 8.3 Hz), 6.57 (1H, dd, J = 8.2, 2.1 Hz), 6.52 (1H, d, J = 2.1 Hz), 5.05 (1H, d, J = 2.2 Hz), 4.96 (1H, d, J = 2.2 Hz), 3.85 (6H, s), 2.91 (1H, dd, J = 11, 5.3 Hz), 2.57 (1H, m), 2.34 (1H, d, J = 4.6 Hz), 2.20 (1H, dd, J = 13, 11 Hz), 2.13 (1H, dt, J = 13, 5.3 Hz), 1.88 (1H, m), 1.02 (3H, d, J = 6.9 Hz), 0.77 (3H, d, J = 6.9 Hz), 0.72 (3H, s); ¹³C NMR δ: 217.4, 153.8, 148.7, 147.8, 135.7, 120.1, 110.9, 110.7, 104.7, 55.8 (2C), 53.6, 53.4, 47.7, 42.3, 34.0, 31.9, 21.4, 17.8, 9.5; HRMS 371.1768, [C₂₀H₂₆O₃Na]⁺ requires 337.1774.
(1''R*,4S*,5R*)-5-(Cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

A solution of AVK 26 (0.050 g, 0.28 mmol) and 1,3-cyclohexadiene (0.055 mL, 0.56 mmol) in CH₂Cl₂ (25 mL) was cooled to −78 °C, and BF₃·OEt₂ (0.01 mL, 0.08 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography of the residue (2.5%, then 10%, EtOAc in hexanes) provided 128 (0.043 g, 58%) as a colourless oil; IR (film) 1697, 1645, 1601 (w) cm⁻¹; ¹H NMR δ: 7.30 (2H, m, C3’), 7.24 (1H, m, C4’), 7.08 (2H, m, C2’), 5.88 (2H, m, H3’’, H4’’), 5.71 (1H, m, H5’’), 5.53 (1H, dd, $J = 9.2, 3.2$ Hz, H2’’), 3.84 (1H, br d, $J = 2.5$ Hz, C4), 3.07 (1H, m, C1’’), 2.51 (1H, dd, $J = 4.9, 2.5$ Hz, C5), 2.11 (1H, m, H6’’a), 1.98 (1H, m, H6’’b), 1.81 (6H, s, H6, H7); ¹³C NMR δ: 209.8 (C1), 171.2 (C3), 142.1 (C1’), 137.6 (C2), 128.9 (C2’’), 128.8 (2C, C3’’), 127.8 (2C, C2’’), 126.8 (C4’), 125.7 (C5’’), 124.7 (C3’’), 123.7 (C4’’), 58.7 (C5), 53.1 (C4), 34.5 (C1’’), 24.3 (C6’’), 15.5 (C7), 8.2 (C6); HRMS (ESI) 287.1396, [C₁₀H₂₀ONa]⁺ requires 287.1406.
(trans)-5-(Furan-2-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (123), 3-(furan-2-ylmethyl)-2-methyl-4-phenylcyclopent-2-enone (124), and (trans,trans)-5,5'-(furan-2,5-diyl)bis(2,3-dimethyl-4-phenyl-cyclopent-2-enone) (160)

**Procedure 1:** A solution of AVK 26 (0.050 g, 0.28 mmol) and furan (0.20 mL, 2.8 mmol) in CH₂Cl₂ (25 mL) was cooled to −78 °C, and BF₃·OEt₂ (0.040 mL, 0.31 mmol) was added. The mixture was stirred for 5 min, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography of the residue (10%, then 25%, EtOAc in hexanes) provided 123 (0.038 g, 54%) and 160 (0.013 g, 22%). For 123: colourless oil; IR (film) 1708, 1649, 1601 (w) cm⁻¹; ¹H NMR δ: 7.38 (3H, m), 7.31 (1H, m), 7.12 (2H, m), 6.31 (1H, dd, J = 3.2, 2.0 Hz), 6.16 (1H, d, J = 3.2 Hz), 4.01 (1H, br d, J = 3.2 Hz), 3.58 (1H, d, J = 3.2 Hz), 1.89 (3H, s), 1.86 (3H, s); ¹³C NMR δ: 205.0, 170.3, 151.1, 142.0, 140.9, 136.2, 129.0 (2C), 127.5 (2C), 127.3, 110.3, 107.3, 55.8, 55.2, 15.6, 8.5; HRMS (ESI) 253.1224, [C₁₇H₁₇O₂]⁺ requires 253.1223. For 160 (1.8:1 inseparable mixture of diastereomers): IR (film) 1708, 1648, 1602 (w) cm⁻¹; HRMS (ESI) 459.1931, [C₃₉H₂₈O₃Na]⁺ requires 459.1931; the following NMR data are taken from spectra of the mixture: **major isomer:** ¹H NMR δ: 7.32 (4H, m), 7.27 (2H, m), 7.08 (4H, m), 6.07 (2H, s), 3.94 (2H, br d, J ≈ 2.5 Hz), 3.53 (2H, overlapped), 1.87 (6H, s), 1.86 (6H, s); ¹³C NMR δ: 204.9, 170.0,
150.6, 140.9, 136.3, 129.0 (4C), 127.6 (4C), 127.2, 107.8, 55.9, 55.3, 15.6, 8.5; minor isomer: $^1$H NMR $\delta$: 7.32 (4H, m), 7.27 (2H, m), 7.08 (4H, m), 6.07 (2H, s), 3.94 (2H, br d, $J \approx 2.5$ Hz), 3.53 (2H, overlapped), 1.87 (6H, s), 1.86 (6H, s); $^{13}$C NMR $\delta$: 205.0, 170.2, 150.8, 140.9, 136.3, 128.9 (4C), 127.7 (4C), 127.2, 107.4, 56.1, 55.2, 15.6, 8.5.

Procedure 2: A solution of AVK 26 (0.025 g, 0.14 mmol) and furan (0.10 mL, 1.4 mmol) in CH$_2$Cl$_2$ (15 mL) was cooled to $-78 \, ^\circ$C, and InCl$_3$ (0.31 g, 1.4 mmol) was added. The mixture was stirred for 2 h, then poured into a separatory funnel containing saturated aqueous sodium bicarbonate. The CH$_2$Cl$_2$ layer was removed, and additional CH$_2$Cl$_2$ ($\times$2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na$_2$SO$_4$ and then concentrated under reduced pressure. Flash chromatography of the residue (10% EtOAc in hexanes) provided 123 (0.039 g, 54%) and 124 (0.011 g, 15%). For 124: colourless oil; IR (film) 1707, 1651, 1601 (w) cm$^{-1}$; $^1$H NMR $\delta$: 7.31 (3H, m), 7.25 (1H, m), 7.07 (2H, m), 6.27 (1H, dd, $J = 3.1, 1.9$ Hz), 5.90 (1H, d, $J = 3.1$ Hz), 3.89 (1H, m), 3.72 (1H, d, $J = 16$ Hz), 3.27 (1H, d, $J = 16$ Hz), 2.89 (1H, dd, $J = 19, 7.1$ Hz), 2.39 (1H, dd, $J = 19, 2.2$ Hz), 1.85 (3H, s); $^{13}$C NMR $\delta$: 209.1, 169.5, 150.4, 141.8, 141.7, 138.2, 128.9 (2C), 127.5 (2C), 127.1, 110.4, 107.1, 46.9, 44.5, 28.0, 8.2; HRMS (ESI) 275.1050, [C$_{17}$H$_{16}$O$_2$Na]$^+$ requires 275.1043.
(trans)-2,3-Dimethyl-4-phenyl-5-(1H-pyrrol-2-yl)cyclopent-2-enone (125)

A solution of AVK 26 (0.10 g, 0.56 mmol) and pyrrole (0.080 mL, 1.1 mmol) in CH$_2$Cl$_2$ (25 mL) was cooled to –78 °C, and BF$_3$·OEt$_2$ (0.080 mL, 0.62 mmol) was added. The mixture was stirred for 5 min at –78 °C before it was poured into a separatory funnel containing saturated aqueous NaHCO$_3$. The CH$_2$Cl$_2$ layer was removed, and additional CH$_2$Cl$_2$ ($\times$2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na$_2$SO$_4$ and then concentrated under reduced pressure. Flash chromatography (10% EtOAc in hexanes with 2.5% triethylamine, and then 25% EtOAc in hexanes with 2.5% triethylamine) of the residue provided 125 (0.093 g, 66%) as a yellow oil: IR (film) 3374, 1697, 1645, 1601 cm$^{-1}$; $^1$H NMR $\delta$: 9.18 (1H, br s, $\text{NH}$), 7.39 (2H, m, H3’’), 7.32 (1H, m, H4’’), 7.25 (1H, m, H2’’), 6.74 (1H, m, H4’), 6.13 (1H, dd, $J = 6.0$, 2.8 Hz, H3’), 6.08 (1H, m, H2’), 4.08 (1H, br d, $J \approx 3$ Hz, H5), 3.57 (1H, d, $J = 2.8$ Hz, H4’), 1.86 (3H, s, H7), 1.81 (3H, br s, H6); $^{13}$C NMR $\delta$: 208.2 (C1), 171.6 (C3), 141.3 (C1’’), 136.0 (C2), 129.3 (2C, C3’’), 128.1 (C1’), 128.0 (2C, C2’’), 127.7 (C4’’), 117.8 (C4’), 108.2 (C3’), 105.0 (C2’), 56.3 (C5), 53.8 (C4), 15.9 (C7), 8.7 (C6); HRMS (ESI) 274.1190, [C$_{17}$H$_{17}$NONa]$^+$ requires 274.1202.
(trans)-4-Methyl-5-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-1-phenylhexa-1,5-dien-3-one (126), 2-methyl-3-((1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)methyl)-4-phenylcyclopent-2-enone (127), and (1'R*,2'R*,4'S*,6'R*,7'S*)-1-(1,2,4,5,6,7-hexamethyl-3-methylenebicyclo[2.2.1]hept-5-en-2-yl)-3-phenylprop-2-en-1-one (161)

According to the procedure for 128: AVK 26 (0.050 g, 0.28 mmol) and 1,2,3,4,5-pentamethylcyclopentadiene (0.090 mL, 0.56 mmol) were reacted in the presence of BF₃·OEt₂ (0.040 mL, 0.31 mmol) to provide 126 (0.018 g, 11%), 127 (0.11 g, 61%), and the Diels–Alder adduct 161 (0.011 g, 8%). For 126: colourless solid, mp 91–93 °C; IR (film) 1698, 1655, 1604 (w) cm⁻¹; ¹H NMR δ: 7.22 (2H, m), 7.19 (1H, m), 6.84 (2H, m), 2.47 (1H, br d, J = 2.3 Hz), 2.30 (1H, d, J = 2.3 Hz), 1.82 (3H, s), 1.80 (3H, s), 1.75 (3H, s), 1.63 (3H, s), 1.52 (3H, s), 1.22 (3H, s), 1.15 (3H, s); ¹³C NMR δ: 211.3, 169.5, 142.4, 142.1, 138.5, 136.4, 136.0, 133.7, 128.3 (2C), 127.8 (2C), 126.5, 58.6, 57.3, 52.4, 18.3, 15.3, 11.3, 11.0, 10.9, 9.9, 8.1; HRMS (ESI) 343.2032, [C₂₃H₂₈ONa]⁺ requires 343.2032.

For 127: colourless solid, mp 105–107 °C; IR (film) 1701, 1633, 1601 (w) cm⁻¹; ¹H NMR δ: 7.26 (2H, m), 7.20 (1H, m), 6.85 (2H, m), 3.41 (1H, m), 2.71 (1H, d, J = 14 Hz), 2.63 (1H, dd, J = 19, 7.0 Hz), 2.31 (1H, d, J = 14 Hz), 1.97 (1H, dd, J = 19, 2.0 Hz), 1.85 (3H, s), 1.83 (3H, s), 1.75 (3H, s), 1.65 (3H, s), 1.15 (3H, s), 0.90 (3H, s); ¹³C NMR δ: 209.7, 173.1, 143.1, 141.1, 140.1, 137.7, 134.5, 134.1, 128.6 (2C), 127.2 (2C), 126.4, 56.1, 45.7, 45.3, 33.5, 23.5, 11.3, 11.0, 10.2, 9.7, 9.1; HRMS (ESI) 343.2041, [C₂₃H₂₈ONa]⁺ requires 343.2032. For 161: colourless solid, mp 68–70 °C; IR (film) 1964,
1936, 1671, 1602 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.41 (3H, m), 7.33 (3H, m), 6.68 (1H, d, \(J = 16\) Hz), 5.00 (1H, s), 4.80 (1H, s), 1.82 (1H, q, \(J = 6.4\) Hz), 1.56 (3H, s), 1.32 (3H, s), 1.28 (3H, s), 1.17 (3H, s), 1.03 (3H, s), 0.68 (3H, d, \(J = 6.4\) Hz); \(^{13}\)C NMR \(\delta\): 202.9, 160.4, 140.5, 136.0, 135.5, 132.5, 129.7, 128.8 (2C), 128.1 (2C), 123.9, 103.4, 62.5, 60.2, 58.8, 58.4, 21.9, 12.1, 11.9, 10.2, 9.9, 7.1; HRMS (ESI) 321.2221, \([\text{C}_{23}\text{H}_{29}\text{O}]^+\) requires 321.2213.

\textit{(trans)-2,3-Dimethyl-5-(1-methyl-1H-pyrrol-2-yl)-4-phenylcyclopent-2-enone (129)}

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\text{129}
\end{align*}
\]

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and 1-methylpyrrole (0.10 mL, 1.1 mmol) reacted in the presence of BF\(_3\)-OEt\(_2\) (0.080 mL, 0.62 mmol) to yield 129 (0.048 g, 32%) as a pale yellow solid: mp 170–173 \(^\circ\)C; IR (film) 1698, 1650, 1605 cm\(^{-1}\); \(^1\)H NMR \(\delta\): 7.33 (2H, m), 7.27 (1H, m), 7.13 (2H, m), 6.55 (1H, m), 6.06 (1H, t, \(J = 3.3\) Hz), 5.88 (1H, dd, \(J = 3.3, 1.8\) Hz), 3.89 (1H, br d, \(J \approx 3\) Hz), 3.57 (1H, d, \(J = 2.5\) Hz), 3.46 (3H, s), 1.87 (3H, s), 1.84 (3H, br s); \(^{13}\)C NMR \(\delta\): 206.8, 169.9, 141.3, 135.6, 129.8, 129.0 (2C), 127.6 (2C), 127.3, 122.7, 106.9, 105.4, 57.7, 53.9, 34.4, 15.6, 8.6; HRMS (ESI) 288.1354, \([\text{C}_{18}\text{H}_{19}\text{NONa}]^+\) requires 288.1359.
(trans)-2,3-Dimethyl-5-(1-benzyl-1H-pyrrol-2-yl)-4-phenylcyclopent-2-enone (130)

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and 1-benzylpyrrole (0.18 g, 1.1 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.080 mL, 0.62 mmol) to give 7 (0.095 g, 50%) as a colourless solid: mp 137–139 °C; IR (film) 1702, 1648, 1602 cm$^{-1}$; $^1$H NMR $\delta$: 7.22 (3H, m), 7.13 (3H, m), 6.95 (2H, m), 6.76 (2H, m), 6.60 (1H, dd, $J = 2.7$, 1.8 Hz), 6.14 (1H, dd, $J = 3.5$, 2.7 Hz), 5.96 (1H, dd, $J = 3.5$, 1.8 Hz), 5.07 (1H, d, $J = 16$ Hz), 4.87 (1H, d, $J = 16$ Hz), 3.82 (1H, br d, $J \approx 3$ Hz), 3.46 (1H, d, $J = 3.1$ Hz), 1.81 (6H, br s); $^{13}$C NMR $\delta$: 206.8, 170.0, 141.1, 138.2, 135.7, 130.0, 129.1 (2C), 128.7 (2C), 127.6 (2C), 127.4, 127.3, 126.5 (2C), 122.6, 107.6, 106.4, 57.9, 54.0, 51.0, 15.7, 8.7; HRMS (ESI) 364.1671, [C$_{24}$H$_{23}$NONa]$^+$ requires 364.1672.

(trans)-2,3-Dimethyl-4-phenyl-5-(1-phenyl-1H-pyrrol-2-yl)cyclopent-2-enone (131)

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and 1-phenylpyrrole (0.16 g, 1.1 mmol) were reacted in the presence of BF$_3$·OEt$_2$ (0.080 mL, 0.62 mmol) to yield 131 (0.13 g, 67%) as a pale yellow solid: mp 132–133 °C; IR (film) 1705, 1650, 1599 cm$^{-1}$; $^1$H NMR $\delta$: 7.18 (6H, m), 7.12 (2H, m), 6.88 (2H, m), 6.74 (1H,
dd, $J = 3.2, 1.7$ Hz), 6.24 (1H, t, $J = 3.2$ Hz), 6.00 (1H, dd, $J = 3.2, 1.7$ Hz), 3.77 (1H, br d, $J \approx 3$ Hz), 3.55 (1H, d, $J = 2.9$ Hz), 1.78 (3H, br s), 1.77 (3H, s); $^{13}$C NMR $\delta$: 207.4, 170.1, 141.1, 139.9, 135.9, 131.4, 129.1 (2C), 129.0 (2C), 127.6 (4C), 127.3, 127.1, 123.0, 108.7, 107.1, 59.7, 53.9, 15.7, 8.8; HRMS (ESI) 350.1513, $[C_{23}H_{21}NONa]^+$ requires 350.1515.

(trans)-5-(1-(4-Methoxyphenyl)-1H-pyrrol-2-yl)-2,3-dimethyl-4-phenyl-cyclopent-2-enone (132)

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and 1-(4-methoxyphenyl)pyrrole (0.19 g, 1.1 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.080 mL, 0.62 mmol) to yield 132 (0.082 g, 41%) as an off-white solid: mp 115–117 °C; IR (film) 1705, 1649, 1605 cm$^{-1}$; $^1$H NMR $\delta$: 7.20 (3H, m), 7.03 (2H, d, $J = 8.9$ Hz), 6.89 (2H, m), 6.69 (3H, m), 6.21 (1H, t, $J = 3.2$ Hz), 5.98 (1H, dd, $J = 3.5, 1.7$ Hz), 3.75 (3H, s), 3.75 (1H, overlapped), 3.51 (1H, d, $J = 2.8$ Hz), 1.78 (3H, br s), 1.77 (3H, s); $^{13}$C NMR $\delta$: 207.5, 170.1, 159.0, 141.2, 135.9, 132.9, 131.6, 129.0 (2C), 128.4 (2C), 127.7 (2), 127.2, 123.2, 114.1 (2C), 108.3, 106.7, 59.6, 55.7, 53.9, 15.7, 8.8; HRMS (ESI) 380.1623, $[C_{24}H_{23}NO_2Na]^+$ requires 380.1621.
*(trans)-2,3-Dimethyl-4-phenyl-5-(1-(triisopropylsilyl)-1H-pyrrol-2-yl)cyclopent-2-enone (133)*

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and 1-(triisopropylsilyl)pyrrole (0.25 mL, 1.1 mmol) reacted in the presence of BF₃·OEt₂ (0.080 mL, 0.62 mmol) to yield 133 (0.070 g, 31%) as a pale yellow oil: IR (film) 1706, 1652, 1609 cm⁻¹; ¹H NMR δ: 7.31 (2H, m), 7.26 (1H, m), 7.12 (2H, m), 6.70 (1H, t, J = 2.4 Hz), 6.63 (1H, m), 6.13 (1H, m), 3.80 (1H, br d, J ≈ 3 Hz), 3.46 (1H, d, J = 2.8 Hz), 1.84 (6H, m), 1.40 (3H, m), 1.07 (18H, m); ¹³C NMR δ: 209.1, 169.6, 142.3, 136.5, 129.2 (2C), 128.0 (2C), 127.2, 124.7, 122.8, 122.1, 109.4, 59.5, 55.0, 18.2, 15.8, 12.0, 8.9; HRMS (ESI) 430.2535, [C₂₆H₃₇NOSiNa]⁺ requires 430.2537.

*Methyl-2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1H-pyrrole-1-carboxylate (134) and methyl-2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1H-pyrrole-1-carboxylate (136)*

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and methyl pyrrole-1-carboxylate (0.13 mL, 1.1 mmol) reacted in the presence of BF₃·OEt₂ (0.080 mL, 0.62 mmol) to yield 0.038 g (23%) of an inseparable 1:1 mixture of 134 and 136 (as
determined by integration of the $^1$H NMR spectrum); IR (film) 1748, 1704, 1656, 1602 cm$^{-1}$; HRMS (ESI) 332.1249, [C$_{19}$H$_{19}$NO$_3$Na]$^+$ requires 332.1257. The following NMR data were taken from the spectra of the mixture: for 134: $^1$H NMR $\delta$: 7.32 (1H, m), 7.26 (2H, m), 7.18 (1H, dd, $J = 3.3, 1.6$ Hz), 7.08 (2H, m), 6.10 (1H, t, $J = 3.3$ Hz), 5.90 (1H, m), 3.95 (2H, overlapped), 3.70 (3H, br s), 1.87 (3H, s), 1.85 (3H, br s); for 136: $^1$H NMR $\delta$: 7.32 (1H, m), 7.26 (3H, m), 7.08 (2H, m), 6.08 (1H, t, $J = 3.3$ Hz), 5.75 (1H, s), 3.98 (1H, d, $J = 17$ Hz), 3.95 (4H, overlapped), 3.64 (1H, d, $J = 17$ Hz), 2.89 (1H, dd, $J = 19, 7.2$ Hz), 2.33 (1H, dd, $J = 19, 2.2$ Hz), 1.77 (3H, s); $^{13}$C NMR $\delta$: 209.7, 206.0, 171.7, 168.1, 151.3, 151.2, 142.2, 141.3, 138.3, 136.3, 130.3 (2C), 129.0 (4C), 128.1 (2C), 127.6 (2C), 127.3, 127.1, 122.4, 121.5, 114.1, 111.1, 111.0, 57.3, 54.0 (2C), 53.9, 47.4, 45.1, 29.3, 15.6, 8.8, 8.4.

**tert-Butyl-2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1H-pyrrole-1-carboxylate (135) and tert-butyl-2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1H-pyrrole-1-carboxylate (137)**

According to the procedure for 125: AVK 26 (0.10 g, 0.56 mmol) and tert-butyl pyrrole-1-carboxylate (0.19 mL, 1.1 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.080 mL, 0.62 mmol) to yield 0.064 g (33%) of an inseparable 1.4:1 mixture of 135 and 137 (as determined by integration of the $^1$H NMR spectrum); IR (film) 1744, 1707, 1651, 1601 cm$^{-1}$; HRMS (ESI) 374.1722, [C$_{22}$H$_{25}$NO$_3$Na]$^+$ requires 374.1727; the following
NMR data were taken from the spectra of the mixture: for 135: $^1$H NMR δ: 7.29 (2H, m), 7.24 (1H, m), 7.15 (1H, dd, $J = 3.3, 1.7$ Hz), 7.01 (2H, m), 6.04 (1H, t, $J = 3.3$ Hz), 5.73 (1H, m), 3.94 (1H, d, $J = 17$ Hz), 3.92 (1H, overlapped), 3.62 (1H, d, $J = 17$ Hz), 2.90 (1H, dd, $J = 19, 7.1$ Hz), 2.36 (1H, dd, $J = 19, 2.0$ Hz), 1.76 (3H, s), 1.46 (9H, s); for 137: $^1$H NMR δ: 7.29 (2H, m), 7.24 (1H, m), 7.20 (1H, dd, $J = 3.3, 1.8$ Hz), 7.09 (2H, m), 6.06 (1H, t, $J = 3.3$ Hz), 5.91 (1H, s), 3.91 (1H, overlapped), 3.86 (1H, m), 1.84 (6H, s), 1.50 (9H, s); $^{13}$C NMR δ: 209.8, 206.1, 172.2, 167.8, 149.6, 149.4, 142.4, 141.5, 138.5, 136.2, 130.2 (2C), 129.1 (4C), 128.2 (2C), 127.7 (2C), 127.3, 127.2, 122.6, 121.6, 113.3, 110.3, 110.2, 84.0, 83.8, 57.4 (2C), 47.6, 45.1, 29.3, 28.2, 28.1, 15.7, 8.9, 8.5.

2-Methyl-3-((1-(methylsulfonyl)-1H-pyrrol-2-yl)methyl)-4-phenylcyclopent-2-enone (138)

**Procedure 1:** A solution of AVK 26 (0.10 g, 0.56 mmol) and 1-(methanesulfonyl)pyrrole (0.16 g, 1.1 mmol) in CH$_2$Cl$_2$ (25 mL) was cooled to $-78$ °C, and BF$_3$-OEt$_2$ (0.080 mL, 0.62 mmol) was added. The mixture was stirred for 5 min at $-78$ °C before it was poured into a separatory funnel containing saturated aqueous NaHCO$_3$. The CH$_2$Cl$_2$ layer was removed, and additional CH$_2$Cl$_2$ (∗2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na$_2$SO$_4$ and then concentrated under reduced pressure. Flash chromatography (25% EtOAc in hexanes with 2.5% triethylamine, then 50% EtOAc in hexanes with 2.5% triethylamine) of the
residue provided 138 (0.021 g, 11%) as a pale yellow oil: IR (film) 1700, 1645, 1602 cm⁻¹; ¹H NMR δ: 7.26 (4H, m), 7.09 (1H, dd, J = 3.3, 1.7 Hz), 7.02 (2H, m), 6.21 (1H, t, J = 3.3 Hz), 5.86 (1H, m), 3.99 (1H, m), 3.92 (1H, d, J = 17 Hz), 3.50 (1H, d, J = 17 Hz), 2.94 (1H, dd, J = 19, 7.1 Hz), 2.78 (3H, s), 2.39 (1H, dd, J = 19, 2.3 Hz), 1.83 (3H, s); ¹³C NMR δ: 209.0, 169.8, 141.8, 139.5, 129.2 (6C), 127.4 (4C), 127.5 (2C), 122.5, 114.5, 111.9, 47.0, 44.9, 42.5, 27.7, 8.7; HRMS (ESI) 352.0992, [C₁₈H₁₉NO₃SNa]⁺ requires 352.0978.

Procedure 2: A solution of AVK 26 (0.10 g, 0.56 mmol) and 1-(methanesulfonyl)pyrrole (0.16 g, 1.1 mmol) in CH₂Cl₂ (25 mL) was cooled to −78 °C, and InCl₃ (0.24 g, 1.1 mmol) was added. The mixture was stirred for 2 h before it was poured into a separatory funnel containing saturated aqueous NaHCO₃. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography (25% EtOAc in hexanes with 2.5% triethylamine, then 50% EtOAc in hexanes with 2.5% triethylamine) of the residue provided 138 (0.075 g, 41%) as a pale yellow oil.

2-Methyl-4-phenyl-3-((1-(para-toluenesulfonyl)-1H-pyrrol-2-yl)methyl)cyclopent-2-enone (139)

According to Procedure 1 for 138: AVK 26 (0.10 g, 0.56 mmol) and 1-(p-
toluenesulfonyl)pyrrole (0.25 g, 1.1 mmol) were reacted in the presence of BF$_3$OEt$_2$
(0.080 mL, 0.62 mmol) to yield 139 (0.022 g, 10%) as a pale yellow oil: IR (film) 1703,
1648, 1597 cm$^{-1}$; $^1$H NMR $\delta$: 7.50 (2H, m), 7.35 (1H, m), 7.26 (5H, m), 6.94 (2H, m),
6.21 (1H, $t$, $J = 3.3$ Hz), 5.72 (1H, m), 3.88 (1H, d, $J = 17$ Hz), 3.66 (1H, m), 3.40 (1H, d,
$J = 17$ Hz), 2.70 (1H, dd, $J = 19$, 7.1 Hz), 2.44 (3H, s), 2.29 (1H, dd, $J = 19$, 2.1 Hz), 1.75
(3H, s); $^{13}$C NMR $\delta$: 209.0, 169.8, 145.0, 141.6, 139.0, 136.1, 130.0 (2C), 129.2, 128.9
(2C), 127.4 (2C), 127.1, 126.5 (2C), 123.3, 114.6, 111.3, 47.0, 44.6, 27.6, 21.7, 8.4;
HRMS (ESI) 428.1279, [C$_{24}$H$_{23}$NO$_3$SNa]$^+$ requires 428.1291.

According to Procedure 2 for 138: AVK 26 (0.10 g, 0.56 mmol) and 1-(p-
toluenesulfonyl)pyrrole (0.25 g, 1.1 mmol) were reacted in the presence of InCl$_3$ (0.24 g,
1.1 mmol) to yield 139 (0.099 g, 44%) as a pale yellow oil.

(1$E$,4$Z$)-4-Methyl-1-phenyl-5-(1$H$-pyrrol-2-yl)hexa-1,4-dien-3-one (140)

Procedure 1: A solution of AVK 26 (0.025 g, 0.14 mmol) and pyrrole (0.020 mL,
0.28 mmol) in CH$_2$Cl$_2$ (7 mL) was cooled to −78 °C, and Sc(OTf)$_3$ (0.14 g, 0.28 mmol)
was added at once. The mixture was stirred for 45 min, then poured into a separatory
funnel containing a saturated aqueous solution of NaHCO$_3$. Following addition of
CH$_2$Cl$_2$, the aqueous layer was re-extracted with additional CH$_2$Cl$_2$ ($\times$2). The combined
organic extracts were dried over Na$_2$SO$_4$ and concentrated under reduced pressure, and
the product was purified by flash chromatography (10% ethyl acetate in hexanes, and then 25% ethyl acetate in hexanes) to yield \( \text{140} \) (0.015 g, 42%) as an orange oil: IR (film) 3334, 1650, 1591, 1578 cm\(^{-1}\); \(^1\)H NMR \( \delta \): 9.20 (1H, br s), 7.49 (1H, d, \( J = 16 \) Hz), 7.39 (2H, m), 7.32 (3H, m), 6.73 (1H, m), 6.57 (1H, d, \( J = 16 \) Hz), 6.36 (1H, m), 6.20 (1H, m), 2.21 (3H, s), 2.07 (3H, s); \(^{13}\)C NMR \( \delta \): 198.6, 142.4, 135.0, 133.2, 132.3, 130.8, 130.2, 128.8 (2C), 128.2 (2C), 126.0, 119.4, 110.4, 109.7, 20.1, 17.6; HRMS (ESI) 274.1203, [C\(_{17}\)H\(_{17}\)NONa]\(^+\) requires 274.1202.

Procedure 2: A solution of AVK \( \text{26} \) (0.025 g, 0.14 mmol) and pyrrole (0.020 mL, 0.28 mmol) in CH\(_2\)Cl\(_2\) (7 mL) was cooled to –78 °C, and InCl\(_3\) (0.060 g, 0.28 mmol) was added at once. The mixture was stirred for 2 h, then poured into a separatory funnel containing a saturated aqueous solution of NaHCO\(_3\). Following addition of CH\(_2\)Cl\(_2\), the aqueous layer was re-extracted with additional CH\(_2\)Cl\(_2\) (×2). The combined organic extracts were dried over Na\(_2\)SO\(_4\) and concentrated under reduced pressure, and the product was purified by flash chromatography (10% ethyl acetate in hexanes, and then 25% ethyl acetate in hexanes) to yield \( \text{140} \) (0.009 g, 26%) as an orange oil.

\((\text{trans})\)-5-(1H-Indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a) and 3-((1H-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (141b)

![141a](image1)

A solution of AVK \( \text{26} \) (0.10 g, 0.56 mmol) and indole (0.13 g, 1.1 mmol) in CH\(_2\)Cl\(_2\) (25 mL) was cooled to –78 °C, and BF\(_3\)-OEt\(_2\) (0.080 mL, 0.62 mmol) was added.
The mixture was stirred for 5 min at –78 °C before it was poured into a separatory funnel containing saturated aqueous NaHCO₃. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure provided a mixture of 141a and 141b (3.7:1, respectively, (as determined by integration of the crude ¹H NMR spectrum). Flash chromatography (10%, then 35%, EtOAc in hexanes) of the residue yielded 141a (0.11 g, 68%), still contaminated with < 10% 141b, as a pale orange solid, and 0.030 g (20%) of a sample containing a mixture of 141a and 141b. For 141a: IR (film) 3302, 1692, 1648, 1598 cm⁻¹; ¹H NMR δ: 8.09 (1H, br s), 7.31 (4H, m), 7.13 (4H, m), 7.00 (1H, m), 6.91 (1H, s), 3.93 (1H, br d, J ≈ 3 Hz), 3.74 (1H, d, J = 2.8 Hz), 1.94 (3H, br s), 1.90 (3H, s); ¹³C NMR δ: 209.1, 170.4, 142.0, 136.8, 129.1 (2C), 127.9 (2C), 127.3, 126.6, 122.6, 122.4, 119.7, 119.4, 113.8, 111.5, 58.9, 54.5, 15.8, 8.8; HRMS (ESI) 324.1361, [C₂₁H₁₉NONa]⁺ requires 324.1359. The following data for 141b were taken from spectra of a mixture of 141a and 141b: ¹H NMR δ: 8.11 (1H, overlapped), 7.31 (4H, overlapped), 7.13 (4H, overlapped), 7.01 (2H, overlapped), 3.93 (1H, overlapped), 3.80 (1H, m), 3.35 (1H, d, J = 16 Hz), 2.80 (1H, dd, J = 19, 7.1 Hz), 2.33 (1H, dd, J = 19, 2.3 Hz), 2.04 (3H, s); ¹³C NMR δ: 209.9, 173.9, 142.4, 137.1, 136.4, 129.0 (2C), 127.8 (2C), 127.2, 124.9, 122.9, 122.5, 119.8, 118.7, 111.5, 111.3, 46.5, 44.9, 25.3, 8.9.
(trans)-5-(5-Methoxy-1H-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a) and 3-((5-methoxy-1H-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (142b)

Following the procedure for 141a and 141b: AVK 26 (0.10 g, 0.56 mmol) and 5-methoxyindole (0.16 g, 1.1 mmol) were reacted in the presence of BF$_3$OEt$_2$ (0.080 mL, 0.62 mmol) to yield a 3.8:1 mixture of 142a and 142b (ratios determined by integration of crude $^1$H NMR spectrum). Flash chromatography gave a sample of 142a (0.095 g, 53%), contaminated with < 10% 19b, as a yellow solid, and 0.022 g (39%) of a sample containing a mixture of 142a and 142b. For 142a: IR (film) 3347, 1694, 1644, 1602 cm$^{-1}$; $^1$H NMR $\delta$: 8.08 (1H, br s), 7.30 (3H, m), 7.16 (3H, m), 6.86 (1H, m), 6.79 (1H, m), 6.52 (1H, s), 3.87 (1H, br d, $J \approx 3$ Hz), 3.76 (1H, d, $J = 2.9$ Hz), 3.63 (3H, s), 1.93 (3H, br s), 1.88 (3H, s); $^{13}$C NMR $\delta$: 209.1, 170.4, 154.0, 142.1, 136.8, 131.9, 129.1 (2C), 129.0, 128.0 (2C), 127.8, 127.4, 123.0, 112.4, 112.2, 101.3, 59.1, 55.8, 54.3, 15.7, 8.8; HRMS (ESI) 354.1463, [C$_{22}$H$_{21}$NO$_2$Na]$^+$ requires 354.1465. The following data for 142b were taken from spectra of a mixture of 142a and 142b: $^1$H NMR $\delta$: 8.01 (1H, overlapped), 7.31 (3H, overlapped), 7.25 (1H, m), 7.03 (2H, m), 6.86 (1H, s), 6.75 (1H, m), 6.74 (1H, m), 3.89 (1H, overlapped), 3.87 (1H, overlapped), 3.83 (3H, s), 3.31 (1H, d, $J = 16$ Hz), 2.81 (1H, dd, $J = 19$, 7.2 Hz), 2.33 (1H, dd, $J = 19$, 2.3 Hz), 2.04 (3H, s); $^{13}$C NMR $\delta$: 209.9, 173.8, 154.3, 142.5, 137.0, 131.5, 129.0 (2C), 127.8 (2C), 127.2,
123.6, 112.7, 112.2, 111.0, 100.4, 56.0, 46.5, 44.9, 25.2, 8.9.

(trans)-2,3-Dimethyl-5-(1-methyl-1H-indol-3-yl)-4-phenylcyclopent-2-enone (143a) and 2-methyl-3-((1-methyl-1H-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (143b)

Following the procedure for 141a and 141b: AVK 26 (0.10 g, 0.56 mmol) and 1-methylindole (0.14 mL, 1.1 mmol) were reacted in the presence of BF₃·OEt₂ (0.080 mL, 0.62 mmol) to yield a 3.2:1 mixture of 143a and 143b (ratios determined by integration of crude ¹H NMR spectrum). Flash chromatography gave a sample of 143a (0.10 g, 56%), contaminated with < 10% 143b, as a yellow oil, and 0.060 g (33%) of a sample containing a mixture of 143a and 143b. For 143a: IR (film) 1703, 1648, 1602 cm⁻¹; ¹H NMR δ: 7.33 (2H, m), 7.27 (2H, m), 7.19 (1H, m), 7.12 (3H, m), 6.99 (1H, m), 6.83 (1H, s), 3.92 (1H, br d, J ≈ 3 Hz), 3.73 (1H, d, J = 2.5 Hz), 3.71 (3H, s), 1.93 (3H, br s), 1.89 (3H, s); ¹³C NMR δ: 209.2, 170.3, 142.0, 137.6, 136.8, 129.1 (2C), 127.9 (2C), 127.3, 127.2, 127.0, 121.9, 119.5, 119.2, 112.2, 109.6, 59.2, 54.4, 32.9, 15.8, 8.8; HRMS (ESI) 338.1505, [C₂₂H₂₁ONa]⁺ requires 338.1515. The following data for 143b were taken from spectra of a mixture of 143a and 143b: ¹H NMR δ: 7.31 (4H, overlapped), 7.20 (1H, m), 7.09 (1H, m), 7.01 (3H, m), 6.61 (1H, s), 3.92 (1H, overlapped), 3.83 (1H, m), 3.74 (3H, s), 3.34 (1H, d, J = 15 Hz), 2.81 (1H, dd, J = 19, 7.1 Hz), 2.34 (1H, dd, J = 19, 2.1 Hz), 2.04 (3H, s); ¹³C NMR δ: 209.9, 174.0, 142.5, 137.2, 137.0, 129.0 (2C), 127.8 (2C), 127.5, 127.2, 122.0, 119.3, 118.9, 109.7, 109.5, 46.5, 44.9, 25.1, 8.9.
(trans)-2,3-Dimethyl-5-(2-methyl-1H-indol-3-yl)-4-phenylcyclopent-2-enone (144a) and 2-methyl-3-((2-methyl-1H-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (144b)

According to the procedure for 141a and 141b: AVK 26 (0.10 g, 0.56 mmol) and 2-methylindole (0.14 g, 1.1 mmol) were reacted in the presence of BF₃·OEt₂ (0.080 mL, 0.62 mmol) to yield 144a (0.059 g, 37%) and 144b (0.037 g, 23%). For 144a: pale yellow solid, mp 175–178 °C; IR (film) 3336, 1695, 1644, 1602 cm⁻¹; ¹H NMR δ: 7.94 (1H, br s), 7.30 (2H, m), 7.25 (1H, m), 7.21 (1H, m), 7.05 (3H, m), 6.96 (2H, m), 3.90 (1H, br d, J ≈ 3 Hz), 3.60 (1H, d, J = 3.1 Hz), 1.97 (3H, br s), 1.94 (3H, s), 1.91 (3H, s); ¹³C NMR δ: 209.3, 170.2, 142.0, 137.5, 135.8, 133.4, 129.1 (2C), 127.7 (2C), 127.2, 127.1, 121.2, 119.5, 118.2, 110.7, 108.8, 58.4, 54.5, 15.7, 11.8, 8.9; HRMS (ESI) 338.1507, [C₂₂H₂₁NONa]⁺ requires 338.1515. For 144b: pale yellow solid, mp 190–193 °C; IR (film) 3343, 1690, 1638, 1602 cm⁻¹; ¹H NMR δ: 7.79 (1H, br s), 7.31 (3H, m), 7.26 (1H, m), 7.16 (2H, m), 7.05 (1H, m), 6.92 (2H, m), 3.94 (1H, d, J = 16 Hz), 3.68 (1H, m), 3.37 (1H, d, J = 16 Hz), 2.81 (1H, dd, J = 19, 7.2 Hz), 2.28 (1H, dd, J = 19, 2.2 Hz), 2.08 (3H, s), 1.89 (3H, s); ¹³C NMR δ: 209.9, 174.5, 142.6, 137.3, 135.4, 132.6, 128.9 (2C), 128.7, 127.7 (2C), 127.0, 121.5, 119.7, 118.0, 110.5, 106.8, 46.3, 45.1, 24.7, 11.4, 8.9; HRMS (ESI) 338.1515, [C₂₂H₂₁NONa]⁺ requires 338.1515.
(trans)-5-(1,2-Dimethyl-1H-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (145a) and 3-((1,2-dimethyl-1H-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (145b)

According to the procedure for 141a and 141b: AVK 26 (0.10 g, 0.56 mmol) and 1,2-dimethylindole (0.16 g, 1.1 mmol) were reacted in the presence of BF$_3$·OEt$_2$ (0.080 mL, 0.62 mmol) to yield 145a (0.11 g, 62%) and 145b (0.052 g, 28%). For 145a: pale yellow solid, mp 164–166 °C; IR (film) 1702, 1648, 1602 cm$^{-1}$; $^1$H NMR δ: 7.31 (2H, m), 7.25 (2H, m), 7.12 (1H, m), 7.06 (2H, m), 6.97 (2H, m), 3.90 (1H, br d, $J \approx 3$ Hz), 3.65 (1H, d, $J = 3.2$ Hz), 3.61 (3H, s), 2.03 (3H, s), 1.97 (3H, br s), 1.94 (3H, s); $^{13}$C NMR δ: 209.3, 169.9, 142.1, 137.4, 137.2, 135.0, 129.1 (2C), 127.7 (2C), 127.1, 126.1, 120.9, 119.1, 118.2, 109.0, 108.0, 58.6, 54.9, 29.8, 15.7, 10.5, 8.9; HRMS (ESI) 352.1667, [C$_{23}$H$_{23}$NOna]$^+$ requires 352.1672. For 145b: pale yellow solid, mp 199–201 °C; IR (film) 1698, 1641, 1602 cm$^{-1}$; $^1$H NMR δ: 7.25 (4H, m), 7.16 (1H, m), 7.12 (1H, m), 7.01 (1H, m), 6.86 (2H, m), 3.92 (1H, d, $J = 16$ Hz), 3.62 (1H, m), 3.61 (3H, s), 3.37 (1H, d, $J = 16$ Hz), 2.74 (1H, dd, $J = 19, 7.4$ Hz), 2.24 (1H, dd, $J = 19, 2.2$ Hz), 2.04 (3H, s), 1.85 (3H, s); $^{13}$C NMR δ: 209.9, 174.5, 142.7, 137.1, 136.8, 134.4, 128.9 (2C), 127.8, 127.6 (2C), 127.0, 121.0, 119.2, 118.0, 108.8, 105.9, 46.2, E45.1, 29.8, 25.0, 10.0, 8.9; HRMS (ESI) 352.1676, [C$_{23}$H$_{23}$NOna]$^+$ requires 352.1672.
(trans)-2,3-Dimethyl-4-phenyl-5-(1-tosyl-1H-indol-3-yl)cyclopent-2-enone (146a) and 2-methyl-4-phenyl-3-((1-tosyl-1H-indol-3-yl)methyl)cyclopent-2-enone (146b).

A solution of AVK 26 (0.10 g, 0.56 mmol) and 1-(toluenesulfonyl)indole (0.30 g, 1.1 mmol) in CH₂Cl₂ (25 mL) was cooled to –78 °C, and InCl₃ (0.24 g, 1.1 mmol) was added. The mixture was stirred for 2 h before it was poured into a separatory funnel containing saturated aqueous NaHCO₃. The CH₂Cl₂ layer was removed, and additional CH₂Cl₂ (×2) was used to re-extract the aqueous layer. The combined organic layers were dried over Na₂SO₄ and then concentrated under reduced pressure. Flash chromatography (20%, then 33%, EtOAc in hexanes) of the residue provided 146a (0.064 g, 25%) and 146b (0.061 g, 24%). For 146a: colourless solid, mp 76–78 °C; IR (film) 1708, 1650, 1605 cm⁻¹; ¹H NMR δ: 7.94 (1H, m), 7.74 (2H, d, J = 8.5 Hz), 7.33 (4H, m), 7.27 (1H, m), 7.22 (2H, d, J = 8.5 Hz), 7.08 (3H, m), 7.03 (1H, m), 3.80 (1H, br d, J ≈ 3 Hz), 3.67 (1H, d, J = 3.0 Hz), 2.34 (3H, s), 1.92 (3H, br s), 1.89 (3H, s); ¹³C NMR δ: 207.1, 170.4, 145.1, 141.2, 136.9, 135.6, 135.3, 130.1 (3C), 129.3 (2C), 127.8 (2C), 127.6, 127.1 (2C), 125.0, 123.8, 120.2, 120.1, 113.9, 58.1, 53.7, 21.8, 15.8, 8.8; HRMS (ESI) 478.1424, [C₂₈H₂₅NO₃SNa]⁺ requires 478.1447. For 146b: colourless solid, mp 61–63 °C; IR (film) 1704, 1650, 1601 cm⁻¹; ¹H NMR δ: 8.01 (1H, m), 7.75 (2H, d, J = 8.4 Hz), 7.31 (4H, m), 7.25 (2H, d, J = 8.4 Hz), 7.19 (2H, m), 7.08 (1H, s), 6.93 (2H, m), 3.79 (1H, d, J = 16 Hz), 3.67 (1H, m), 3.28 (1H, d, J = 16 Hz), 2.82 (1H, dd, J = 19, 7.2 Hz), 2.36 (s, 3H), 2.34 (1H, dd, J = 19, 2.1 Hz), 1.92 (3H, s); ¹³C NMR δ: 209.3, 171.1, 145.3, 141.8, 138.1, 175
135.5, 135.4, 130.5, 130.1 (2C), 129.2 (2C), 127.7 (2C), 127.5, 127.0 (2C), 125.2, 124.4, 123.5, 119.3, 117.9, 114.1, 46.7, 44.8, 25.2, 21.8, 8.9; HRMS (ESI) 478.1431, [C$_{28}$H$_{25}$NO$_3$SNa]$^+$ requires 478.1447.

(1E,4Z)-5-((1H-Indol-3-yl)-4-methyl-1-phenylhexa-1,4-dien-3-one (147)

According to Procedure 1 for 140: AVK 26 (0.025 g, 0.14 mmol) and indole (0.032 g, 0.28 mmol) were reacted with Sc(OTf)$_3$ (0.14 g, 0.28 mmol) to yield 147 (0.016 g, 38%) as a yellow oil: IR (film) 3325, 1646, 1596, 1578 cm$^{-1}$; $^1$H NMR δ: 8.21 (1H, br s), 7.73 (1H, m), 7.29 (1H, m), 7.23 (4H, m), 7.13 (2H, m), 6.89 (1H, d, $J = 2.5$ Hz), 6.75 (2H, m), 6.14 (1H, d, $J = 16$ Hz), 2.35 (3H, s), 2.08 (3H, s); $^{13}$C NMR δ: 198.0, 138.5, 137.0, 136.8, 136.6, 135.4, 129.2, 127.7 (2C), 127.2 (2C), 126.1, 122.8, 120.6, 120.1, 119.3, 111.6 (2C), 20.7, 16.3; HRMS (ESI) 324.1358, [C$_{21}$H$_{19}$NONa]$^+$ requires 324.1359.

According to Procedure 2 for 140: AVK 26 (0.025 g, 0.14 mmol) and indole (0.032 g, 0.28 mmol) were reacted with InCl$_3$ (0.060 g, 0.28 mmol) to yield 147 (0.008 g, 19%) as a yellow oil.
2,3-Dimethyl-5-(1-methyl-1H-indol-3-yl)cyclopent-2-enone (148)

According to the procedure for 141a and 141b: AVK 27 (0.075 g, 0.69 mmol) and 1-methylindole (0.17 mL, 1.4 mmol) were reacted in the presence of BF₃·OEt₂ (0.090 mL, 0.76 mmol) to yield 148 (0.084 g, 51%), as a colourless oil: IR (film) 1697, 1654 cm⁻¹; ¹H NMR δ: 7.37 (1H, m, H₄''), 7.28 (1H, m, H₇''), 7.20 (1H, m, H₆''), 7.05 (1H, m, H₅''), 6.95 (1H, s, H₂''), 3.84 (1H, dd, J = 7.3, 2.7 Hz, H₅), 3.72 (3H, s, H₈), 3.12 (1H, dd, J = 18, 7.3 Hz, H₄a), 3.12 (1H, br dd, J = 18, ~3 Hz, H₄b), 2.11 (3H, s, H₇), 1.81 (3H, s, H₆); ¹³C NMR δ: 209.8 (C₁), 168.6 (C₃), 137.5 (C₈''), 135.7 (C₂), 127.2 (C₉''), 126.8 (C₂''), 121.9 (C₆''), 119.2 (C₄''), 119.1 (C₅''), 112.9 (C₃''), 109.6 (C₇''), 43.1 (C₅), 41.2 (C₄), 32.8 (C₈), 17.3 (C₇), 8.4 (C₆); HRMS (ESI) 262.1190, [C₁₆H₁₇NONa]⁺ requires 262.1202.

5-(1,2-Dimethyl-1H-indol-3-yl)-2,3-dimethylcyclopent-2-enone (149)

According to the procedure for 141a and 141b: AVK 27 (0.075 g, 0.69 mmol) and 1,2-dimethylindole (0.20 g, 1.4 mmol) were reacted in the presence of BF₃·OEt₂ (0.12 mL, 0.84 mmol) to yield 149 (0.091 g, 52%), as a yellow oil (contained <10% of an
inseparable product that likely arose by trapping at position c): IR (film) 1704, 1650 cm$^{-1}$; $^1$H NMR $\delta$: 7.22 (1H, m), 7.10 (1H, m), 7.02 (1H, m), 6.95 (1H, m), 3.76 (1H, dd, $J = 7.3$, 3.0 Hz), 3.65 (3H, s), 3.01 (1H, dd, $J = 18$, 7.3 Hz), 2.71 (1H, br dd, $J = 18$, 3 Hz), 2.36 (3H, s), 2.15 (3H, s), 1.84 (3H, s); $^{13}$C NMR $\delta$: 210.4, 168.6, 137.0, 136.2, 134.3, 126.2, 120.9, 119.1, 118.0, 109.2, 109.0 43.2, 40.8, 29.8, 17.4, 10.8, 8.6; HRMS (ESI) 276.1362, [C$_{17}$H$_{19}$NONa]$^+$ requires 276.1359.

**{(trans)-4-Isopropyl-2,3-dimethyl-5-(1-methyl-1H-indol-3-yl)cyclopent-2-enone (150)}**

![Diagram of the molecule 150](image)

According to the procedure for 141a and 141b: AVK 29 (0.10 g, 0.67 mmol) and 1-methylindole (0.17 mL, 1.4 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.090 mL, 0.76 mmol) to yield 150 (0.15 g, 81%), as a white solid (contained <10% of an inseparable product that likely arose by trapping at position c): IR (film) 1704, 1654 cm$^{-1}$; $^1$H NMR $\delta$: 7.26 (2H, m), 7.18 (1H, m), 7.01 (1H, m), 6.89 (1H, s), 3.72 (3H, s), 3.51 (1H, d, $J = 2.6$ Hz), 3.01 (1H, m), 2.28 (1H, m), 2.09 (3H, s), 1.82 (3H, s), 1.01 (3H, d, $J = 6.9$ Hz), 0.77 (3H, d, $J = 6.9$ Hz); $^{13}$C NMR $\delta$: 209.3, 171.4, 137.6, 136.5, 127.4, 126.7, 121.8, 119.4, 119.1, 113.8, 109.6, 57.1, 44.6, 32.8, 28.7, 21.6, 16.1, 15.6, 8.5; HRMS (ESI) 304.1661, [C$_{19}$H$_{23}$NONa]$^+$ requires 304.1672.
(trans)-5-(1,2-Dimethyl-1H-indol-3-yl)-4-isopropyl-2,3-dimethylcyclopent-2-enone (151a) and 3-((1,2-dimethyl-1H-indol-3-yl)methyl)-4-isopropyl-2-methylcyclopent-2-enone (151b)

According to the procedure for 141a and 141b: AVK 29 (0.10 g, 0.67 mmol) and 1,2-dimethylindole (0.19 g, 1.3 mmol) reacted in the presence of BF$_3$·OEt$_2$ (0.090 mL, 0.76 mmol) to yield a 3.9:1 mixture of 151a and 151b (ratios determined by integration of crude $^1$H NMR spectrum). Flash chromatography afforded a sample of 151a (0.095 g, 53%), still contaminated with < 10% of 151b, as a yellow solid, and 0.060 g (26%) of a sample containing a mixture of 151a and 151b. For 151a: IR (film) 1700, 1654 cm$^{-1}$; $^1$H NMR $\delta$: 7.21 (1H, m), 7.09 (1H, m), 7.02 (1H, m), 6.93 (1H, m), 3.63 (3H, s), 3.44 (1H, d, $J = 2.8$ Hz), 3.04 (1H, m), 2.38 (3H, s), 2.26 (1H, m), 2.11 (3H, s), 1.83 (3H, s), 0.92 (3H, d, $J = 6.9$ Hz), 0.81 (3H, d, $J = 6.9$ Hz); $^{13}$C NMR $\delta$: 209.9, 171.3, 137.1, 137.0, 134.0, 126.5, 120.7, 118.9, 118.1, 109.9, 109.0, 56.8, 44.0, 29.8, 28.3, 21.4, 16.2, 15.5, 11.0, 8.6; HRMS (ESI) 318.1835, [C$_{20}$H$_{25}$NONa]$^+$ requires 318.1828. The following data for 151b were taken from spectra of a mixture of 151a and 151b: $^1$H NMR $\delta$: 7.31 (1H, m), 7.26 (1H, m), 7.16 (1H, m), 7.04 (1H, m), 3.98 (1H, d, $J = 16$ Hz), 3.68 (3H, s), 3.59 (1H, d, $J = 16$ Hz), 2.62 (1H, m), 2.36 (3H, s), 2.11 (2H, overlapped), 2.00 (3H, s), 0.85 (3H, d, $J = 7.0$ Hz), 0.64 (3H, d, $J = 7.0$ Hz); $^{13}$C NMR $\delta$: 210.4, 175.0, 136.8, 136.7, 133.8, 127.8, 121.1, 119.4, 117.9, 108.9, 106.5, 45.4, 34.9, 29.9, 27.8, 24.8, 22.0, 14.8, 10.7, 8.6.
CHAPTER 5. PROGRESS TOWARDS THE TOTAL SYNTHESIS OF (+)-ROSEADIONE

5.1 Introduction

(+)-Roseadione (162), a tricyclic diterpene with a dicyclopenta[a,d]cyclooctanoid skeleton, was isolated from the leaves and stems of the tropical shrub Hypoestes rosea, collected near Akure, Nigeria.67 Besides the interest inspired by its molecular complexity, roseadione and molecules of its structural family also have significance in terms of their broad-ranging biological activity.68 Although there have been studies directed towards the total synthesis of other natural products containing the dicyclopenta[a,d]cyclooctanoid framework, to date (+)-roseadione has yet to succumb to total synthesis. The tandem Nazarov/[4 + 3] cascade of allenyl vinyl ketones provides a unique manner in which to access the tricyclic core of this cyclooctanoid natural product. With this in mind, we postulated that the [5,8,5]-tricylic core could be accessed via compound 163, which could be constructed via a regio- and doubly diastereoselective tandem Nazarov cyclization/[4 + 3] cycloaddition strategy from AVK 164 (Scheme 52). The requisite facial and endo selectivity for the [4 + 3] cyclization of the oxyallyl cation derived from AVK 164 has moderate precedent, based on work by Harmata and co-workers (Section 5.1.1).
5.1.1 Intramolecular [4 + 3] Cyclization of Cyclic Oxyallyl Cations for the Synthesis of Eight-Membered Ring Systems

Although the [4 + 3] cyclization of an oxyallyl cation and a diene is a common strategy for the synthesis of seven-membered ring systems, when a five-membered ring oxyallyl cation is utilized the cyclization can be a powerful means in which to generate an eight-membered carbocycle via a formal [4 + 4] process. As previously mentioned (Section 4.1), intermolecular reactions are generally limited to the utilization of furan and cyclopentadiene as diene partners. However, the intramolecular variant appears to be more general, and cyclized products can be produced in high yields for a variety of diene partners under a number of different reaction conditions. Unfortunately, despite the high overall yields commonly reported, the diastereoselectivity of the reaction is often quite poor. However, in an elegant study *en route* to their total synthesis of dactylool, and inspired by the work of Giguere on the diastereoselectivity of [4 + 3] cyclizations of allylic cations derived from allylsilanes, Harmata and co-workers noted that careful placement of stereocenters in the system can result in high levels of stereoselectivity. For example, reaction of substrate 165 proceeded with modest selectivity for the *endo* product 166a over the *exo* product 166b (Scheme 53a), but with substitution adjacent to...
the diene unit as in 167, the reaction resulted in a significant increase in selectivity for the 

*endo* product 168a (Scheme 53b).69

![Scheme 53 Intramolecular [4 + 3] cyclizations in which the tether was a) unsubstituted, or b) substituted, at the dienyl position.](image)

In the reaction of compound 167, the formation of the *exo* product 168b was the result of addition to the opposite face of the oxyallyl cation, with respect to the formation of *endo* product 168a. An appropriately placed substituent on the five-membered ring should effectively block that face of the oxyallyl cation, resulting in an increase in *endo* selectivity. Such was indeed the case with compound 169, which provided the *endo* product 170 almost exclusively (Scheme 54).69
Scheme 54 Intramolecular [4 + 3] cyclization in which substitution at the dienylic position of the tether and on the five-membered ring results was “matched”.

The high facial and endo/exo selectivity in the reaction of compound 169 was postulated to be a result of a conformational preference, due to a minimization of steric interactions, for the transition state 171 involving the oxyallyl cation derived from 169, which led to compound 170. It is important to recognize, however, that this example is representative of a “matched” case. In an alternative scenario where the stereocenter adjacent to the diene and the stereocenter on the five-membered ring are mismatched, multiple products are formed. Such was the case with the epimer of 169, compound 172, which produced roughly equal amounts of all four possible [4 + 3] products 173a-d (Scheme 55).69
5.1.2 Alternative Methods for the Synthesis of Eight-Membered Ring Systems

The synthesis of eight-membered ring systems is not only valuable from the context of the synthesis of cyclooctanoid natural products, but also as a result of their ability to be subsequently transformed into other useful products through various ring expansion, contraction, or cleavage reactions. Thus, in addition to the [4 + 3] cyclization of cyclopentenyl cations, there exist a number of strategies for the synthesis of cyclooctanoid ring systems, with the consequence that there are several reviews devoted to the subject.\textsuperscript{68, 71} Some of these strategies are depicted below in Scheme 56. More traditional approaches invoke a 3,3-sigmatropic rearrangement and/or ring expansion of smaller ring systems, through reactions such as the anionic oxy-Cope process (Scheme 56a)\textsuperscript{72} or the Grob fragmentation (Scheme 56b),\textsuperscript{73} and have been well-studied. Metal-mediated cyclizations, such as a palladium-catalyzed allylic substitution (Scheme 56c),\textsuperscript{74}
Scheme 56 Some alternative methods for the construction of eight-membered ring systems.
a nickel-catalyzed [4 + 4] cyclization (Scheme 56d), a rhodium-catalyzed [5 + 2 + 1] cyclization (Scheme 56e), and a ruthenium-catalyzed ring-closing metathesis strategy (Scheme 56f), are more recent developments and continue to garner increasing attention both in the context of methodology development and their use in synthesis. It is worth mentioning that each of the examples highlighted in Scheme 56 was utilized as the key step in the synthesis of a cyclooctanoid natural product.

5.2 Retrosynthetic Disassembly of AVK 164

The retrosynthetic strategy devised for AVK 164 is outlined below in Scheme 57. Briefly, AVK 164 could be accessed from Barbier coupling of propargyl bromide with aldehyde 174, followed by oxidation with the use of DMP, through the method discussed previously in Section 2.2. Aldehyde 174 would be accessed via deprotection of acetal 175, followed by aldolization with formaldehyde. Acetal 175 could theoretically be derived by the union of ketone 176 and an organometallic species derived from protected cyclopentenone 177. Ketone 176 should be attainable in enantiopure form from (-)-carvone (178).
Scheme 57 Retrosynthetic disassembly of AVK 164.

5.3 Progress Towards the Synthesis of the First Key Intermediate, Acetal 175

The synthesis of ketone 176a was accomplished as depicted in Scheme 58 below. (-)-Carvone (178) was transformed into its acetate 179 in 47% overall yield via a three-step procedure proceeding through a chemoselective hydrogenation of the exocyclic double bond using Adam’s catalyst,78 a stereo- and regioselective LiAlH₄-mediated reduction of the enone carbonyl,79 and protection of the resultant alcohol with acetyl chloride. cis-Carvotanacetol acetate (179) was then transformed into ketone 176a via ozonolysis in 56% yield, which proceeded with simultaneous chemoselective protection
of the aldehyde functionality in one-pot as its dimethyl acetal. It was necessary to use acetate-protected *cis*-carvotanacetol 179 for the ozonolysis step – when benzyl and *tert*-butyldimethylsilyl derivatives were utilized, only decomposition of the starting material resulted.

Scheme 58. Synthesis of ketone 176a.

Initially, we envisioned coupling fragments 176a and 177a through a Petersen olefination strategy (Scheme 59). This procedure was chosen as it is notable for its overall high \((E)/(Z)\) selectivity, and conditions can be carefully chosen in which to yield either the \((E)\)- or the \((Z)\)-isomer. This method offers considerable advantages over more traditional carbonyl olefination methods, such as Wittig\(^8\) or Julia\(^9\) reactions, which typically give poor \((E)/(Z)\)-selectivity with ketones.
Compound 177a was readily available from iodinated cyclopent-2-enone 180, which was transformed into its TMS-derivative 181 through a Negishi cross-coupling with methyltrimethylsilylmagnesium chloride, which was subsequently converted into its dithiolane derivative 177a with ethanedithiol in 12% overall yield (Scheme 60). Although transformation into its dioxolane derivative was also attempted, compound 184 decomposed in the presence of ethylene glycol, or its trimethylsilyl protected derivative. Unfortunately, in subsequent reactions, compound 177a did not react with ketone 176a, returning both starting materials intact under most circumstances. This was later determined to be a result of our failure to deprotonate 177a, under all conditions attempted (LDA, nBuLi, nBuLi/TMEDA, nBuLi/HMPA, tBuLi, nBuLi/tBuOK).
Scheme 60 Synthesis of dithiane 177a, with failed elaboration into thioacetal 175a.

A strategy involving the union of alkene 182 and compound 177b was then envisioned, which could theoretically be stereoselectivity joined through a variety of palladium-mediated cross-coupling reactions, to generate acetal 175 (Scheme 61).

Scheme 61 Second-generation proposal for the synthesis of acetal 175.

It was initially proposed to employ compound 177 in a Negishi cross-coupling reaction\textsuperscript{85} with vinyl iodide 182a or vinyl bromide 182c (Scheme 62). However, attempts to prepare either substrate by a Takai olefination procedure\textsuperscript{86} (182a), or a Corey-Fuchs reaction\textsuperscript{87} followed by a stereoselective dehalogenation\textsuperscript{88} (182c), failed. In the former case, multiple alkene-containing products were produced, as determined by careful analysis of the crude \textsuperscript{1}H NMR spectrum, whereas in the latter case only decomposition of
the starting material resulted upon treatment with either CBr₄/PPh₃ or CBr₄/Zn. Similarly, exposure of the tert-butyl dimethylsilyl protected derivative 176b, which was obtained from acetate 176a in 36% yield, to the reaction conditions mentioned above also failed to produce 182b or 182d. Marginal success did result upon exposure of 176b to chromium(II)chloride and iodoform in the presence of 2,6-(di-t-butyl)pyridine for three hours, however the yield was unacceptably low (ratio of 182d to 176b was only 1:7 as determined by integration of crude ¹H NMR spectrum), and prolonged reaction times only led to degradation of the product.

It was next decided to join compound 177 to compound 182 via a Heck cross-coupling protocol. Fortunately, the requisite alkenes 182e and 182f were able to be produced in good yields via a Wittig reaction with methyltriphenylphosphonium bromide (Scheme 63).
Compound 177b, which was readily available via bromination of cyclopent-2-enone followed by protection with ethyleneglycol, was then exposed to Pd$_2$(dba)$_3$/PtBu$_3$ and N-methyldicyclohexylamine in the presence of alkenes 182e and 182f (Scheme 64). This particular catalyst system and base were chosen as it has been reported that this particular combination has exceptional activity with regards to both sterically hindered and electronically deactivated substrates. Unfortunately, no reaction resulted and only starting material was recovered following several days of stirring at room temperature.

Reasoning that the failed production of compounds 175b and 175c was a result of the failure of the palladium catalyst to undergo oxidative addition with ketal 177b as a
result of steric hindrance about the bromine atom, alkenes 182e and 182f were then exposed to Pd(tBu)₄ and N-methyldicyclohexylamine in the presence of iodo cyclopent-2-enone (180) (Scheme 65). Unfortunately, once again no reaction resulted and starting material was recovered, along with some dimerized 180, following several days of stirring at room temperature.

Scheme 65 Unsuccessful synthesis of dienones 183a-b.

5.4 Summary

A strategy for the total synthesis of the cyclooctane natural product (+)-roseadione (162), utilizing the tandem Nazarov/[4 + 3] cyclization of allenyl vinyl ketones, has been presented. Unfortunately, although a number of direct precursors to the first key intermediate 175 have been synthesized, a successful route has yet to be developed for the preparation of acetal 175.
5.5 Experimental Section

5.5.1 General Considerations

All reactions were conducted using oven-dried glassware under an N₂ atmosphere. Reagents were used as received from a commercial supplier without further purification.

Dichloromethane and benzene were used freshly distilled from calcium hydride. Tetrahydrofuran and diethyl ether were used freshly distilled from sodium/benzophenone. Anhydrous methanol was purchased from Sigma-Aldrich and used as received. Ethyl acetate and hexanes were distilled prior to use for column chromatography.

Thin layer chromatography was conducted using pre-coated silica plates with plastic backing (EMD chemicals, silica gel 60 F₂₅₄), using UV light (254 nm) as a visualizing agent and potassium permanganate in aqueous KOH and heat, or o-vanillin in ethanol/H₂SO₄ and heat, as developing agents. Column chromatography was carried out on silica gel purchased from Silicycle (40 – 63 μm particle size, 230 – 240 mesh).

Melting points are uncorrected, and were acquired using a Fisher-Johns apparatus. ¹H NMR spectra were recorded at 500 MHz on a Bruker Avance spectrometer with CDCl₃ as solvent (7.24 ppm) and TMS as internal reference (0.00 ppm). ¹³C NMR spectra were recorded at 125 MHz on a Bruker Avance spectrometer with CDCl₃ as solvent. Infrared spectra were recorded from thin films on a Bruker VECtor 22 FT-IR instrument using CsI plates. High resolution mass spectra were acquired by Mr. Xiao Feng, on a Bruker microTOF Focus orthogonal ESI-TOF mass spectrometer.

The carbon and hydrogen atoms of select compounds were assigned following detailed analysis of their one dimensional (¹H, ¹³C, and DEPT-135) and two dimensional
(COSY, HSQC, and HMBC) NMR spectral data. The $^1$H and $^{13}$C NMR spectra of all compounds may be found in Appendix A.

5.5.2 Preparation and Characterization Data

2-Iodocyclopent-2-enone (180)

![Iodocyclopent-2-enone (180)]

Iodine (54 g, 0.20 mol) was added to a 1:1 solution of pyridine and Et$_2$O (160 mL), and stirred for 20 min. Cyclopent-2-enone (2 mL, 0.025 mol) was added dropwise, the solution was cooled to 0 °C, and additional cyclopent-2-enone (6.2 mL, 0.075 mmol) was then added dropwise. The solution was brought to rt, stirred for 2 h, then washed successively with 1 M HCl (aq) ($\times 2$), 10% Na$_2$S$_2$O$_3$ (aq) ($\times 3$), and brine. The Et$_2$O layer was then dried with MgSO$_4$, filtered, and concentrated to provide 180 (10 g, 65%) as a yellow solid: mp 69–71 °C (lit. $^{93}$ 70–71 °C); $^1$H NMR δ: 8.06 (1H, t, $J = 2.8$ Hz), 2.82 (2H, m), 2.51 (2H, m); $^{13}$C NMR δ: 203.8, 169.7, 102.4, 31.0, 30.7.

2-((Trimethylsilyl)methyl)cyclopent-2-enone (181)

![2-((Trimethylsilyl)methyl)cyclopent-2-enone (181)]

A 1 M solution of (trimethylsilyl)methylmagnesium chloride in THF (34 mL, 0.034 mol) was added dropwise to a –78 °C solution of flame-dried ZnBr$_2$ (7.6 g, 0.034
mol) in THF (300 mL), and warmed to rt over 1 h. A solution of 180 (3.5 g, 0.017 mol) and Pd(PPh3)4 (0.60 g, 0.51 mmol) in DMF/THF (80 mL, 1:1) was then added rapidly by cannula, and stirred 1 h. The mixture was then diluted with ether/hexanes (1:1), washed with saturated NH4Cl (aq) (∗3), water (∗2), brine, dried with MgSO4, and concentrated. Flash chromatography of the residue (SiO2 using 10% EtOAc in hexanes) provided 181 (1.8 g, 64%) as a yellow oil; IR (film) 1711, 1649 cm−1; 1H NMR δ: 7.12 (1H, m), 2.55 (2H, m), 2.38 (2H, m), 1.66 (2H, d, J = 1.2 Hz), -0.01 (9H, s); 13C NMR δ: 210.0, 154.5, 144.1, 34.2, 26.4, 14.6, -1.5 (3C). HRMS (ESI) 191.0863 [C9H16OSiNa]+ requires 191.0863.

(1,4-Dithiaspiro[4.4]non-6-en-6-ylmethyl)trimethylsilane (177a)

A solution of 181 (1.6 g, 9.1 mmol) and 1,2-ethanethiol (1.0 mL, 12 mmol) in MeOH (35 mL) was cooled to 0 °C, and BF3·OEt2 (1.5 mL, 12 mmol) was added. The mixture was stirred for 2 h, then warmed to rt, and stirred for an additional 18 h. The solution was diluted with EtOAc, washed with saturated NaHCO3 (aq), then brine, dried with MgSO4, and concentrated. Flash chromatography of the residue (SiO2 using hexanes) provided 177a (0.65 g, 30%) as a yellow oil; 1H NMR δ: 5.42 (1H, br s), 3.29 (4H, m), 2.48 (2H, t, J = 6.3 Hz), 2.30 (2H, m), 1.63 (2H, d, J = 2.8 Hz), 0.07 (9H, s); 13C NMR δ: 143.1,
6-Bromo-1,4-dioxaspiro[4.4]non-6-ene (177b)

A solution of Br₂ (1.6 mL, 0.13 mol) in CH₂Cl₂ (20 mL) was added dropwise, over 1 h, to a 0 °C solution of cyclopent-2-enone (2.5 mL, 0.030 mol) in CH₂Cl₂ (20 mL). Then a solution of Et₃N (6 mL, 0.045 mol) in CH₂Cl₂ (20 mL) was added dropwise over 1 h, while the solution was maintained at a 0 °C. The solution was then stirred for 2 h at rt, filtered, and washed successively with 1 M HCl (aq) (×2), saturated NaHCO₃ (aq), water, and brine. The CH₂Cl₂ layer was dried over MgSO₄, and concentrated. The crude residue was then dissolved in benzene (350 mL). Ethylene glycol (5 mL, 0.090 mol) and p-TSA (0.050 g, 0.26 mmol) were added, and the solution was heated at reflux for 24 h, with azeotropic removal of water. The solution was cooled to room temperature, dried with K₂CO₃, and filtered over a pad of SiO₂ to provide 177b (12 g, 99%) as a yellow oil; ¹H NMR δ: 6.18 (1H, t, J = 2.8 Hz), 4.19 (2H, m), 3.99 (2H, m), 2.37 (2H, m), 2.17 (2H, t, J = 6.2 Hz); ¹³C NMR δ: 36.8, 123.9, 117.7, 65.9, 34.4, 28.7; NMR data matches lit.⁹¹
(1R,5R)-5-Isopropyl-2-methylcyclohex-2-enyl acetate (179)

PtO₂ (0.15 g, 0.67 mmol), then (-)-carvone (10 mL, 0.066 mol), were added to a dry 100 mL flask. The flask was then evacuated and backfilled with hydrogen gas (∗3), and stirred for 48 h under a balloon filled with H₂ (until ¹H NMR of a small aliquot showed complete reduction of the exocyclic double bond). The mixture was then diluted with Et₂O, filtered through a short pad of SiO₂, and concentrated. The crude residue was then dissolved in Et₂O (50 mL), added dropwise to a −78 °C solution of LiAlH₄ (1.3 g, 0.034 mol) in Et₂O (50 mL), and stirred for 30 min. Water (3 mL), 10% NaOH (3 mL), and additional water (3 mL) were then added successively, and the mixture was then stirred at rt for 1 h until a white precipitate formed. Anhydrous MgSO₄ was then added, and the mixture was filtered, then concentrated. The crude residue was then dissolved in CH₂Cl₂ (600 mL), and cooled to 0 °C. DMAP (8.1 g, 0.066 mol), Et₃N (70 mL, 0.5 mol), and acetyl chloride (0.92 mL, 0.013 mol) were then added successively. The mixture was stirred for 1 h, diluted with CH₂Cl₂, and then washed successively with 1 M HCl (aq) (∗3), 10% NaOH (aq), saturated NaHCO₃ (aq), and brine. The CH₂Cl₂ layer was then dried with Na₂SO₄, concentrated, and purification by column chromatography (SiO₂ with 5% EtOAc in hexanes) provided 179 (6.1 g, 47%) as a colourless oil; IR (film) 1736 cm⁻¹; ¹H NMR δ: 5.59 (1H, m, H3), 5.41 (1H, m, H1), 2.12 (1H, m, H6a), 2.08 (3H, s,
H1’), 1.99 (1H, m, H4a), 1.78 (1H, m, H4b), 1.62 (3H, q, J = 1.3 Hz, H7), 1.49 (2H, m, H5, H2’’), 1.25 (1H, m, H6b), 0.88 (1H, d, J = 6.6 Hz, H1’’a), 0.87 (1H, d, J = 6.6 Hz, H1’’b); 13C NMR δ: 171.3 (C2’), 133.1 (C2), 126.6 (C3), 73.8 (C1), 39.4 (C5’’), 33.0 (C6), 32.3 (C2’’), 29.0 (C4), 21.5 (C1’), 19.9 (C1’’a), 19.6 (C1’’b), 19.0 (C7); HRMS (ESI) 219.1352 [C12H20O2Na]+ requires 219.1356.

(3R,5S)-5-Isopropyl-7,7-dimethoxy-2-oxoheptan-3-yl acetate (176a)

A solution of 179 (5.7 g, 0.029 mol) in CH2Cl2/MeOH (600 mL, 1:1) was cooled to −70 °C. Ozone was bubbled through the solution for 1 h, and then excess ozone was removed by bubbling N2 through the solution for 30 min. DMS (40 mL) was then added, the solution was allowed to slowly warm to rt, and was stirred for 18 h. The mixture was concentrated, and the crude residue was dissolved in EtOAc, washed with water (×3), then brine. The EtOAc layer was then dried with Na2SO4, concentrated, and purified by column chromatography (SiO2 with 10%, then 20%, EtOAc in hexanes) to provide 176a (4.5 g, 56%) as a colourless oil; IR (film) 1745, 1731 cm−1; 1H NMR δ: 5.03 (1H, dd, J = 10, 2.8 Hz, H3), 4.41 (1H, t, J = 5.4 Hz, H7), 3.31 (3H, s, H8a), 3.30 (3H, s, H8b), 2.17 (3H, s, C1), 2.14 (3H, s, C1’), 1.78 (1H, m, C2’’), 1.60 (5H, m, H4, H5, H6), 0.88 (3H, d, J = 6.8 Hz, H1’’a), 0.85 (3H, d, J = 6.8 Hz, H1’’b); 13C NMR δ: 205.9 (C2), 170.8 (C2’), 103.7 (C7), 77.7 (C3), 53.0 (2C, C8), 36.3 (C5), 33.9 (C6), 31.5 (C4), 30.4 (C2’’), 26.2
(C1), 20.9 (C1’), 19.5 (C1’’a), 18.4 (C1’’b); HRMS (ESI) 297.1662 [C14H26O5Na]+ requires 297.1672.

(3R,5S)-3-(tert-Butyldimethylsilyloxy)-5-isopropyl-7,7-dimethoxyheptan-2-one (176b)

A solution of saturated aqueous potassium carbonate (2.5 mL) was added to a solution of 176a (1.5 g, 6.0 mmol) in methanol (50 mL). After stirring for 30 min at rt, the reaction mixture was diluted with diethyl ether, and the organic layer was washed with saturated NH4Cl (aq) (x2), then brine, dried with MgSO4, and concentrated. The crude residue was then dissolved in CH2Cl2 (50 mL), cooled to 0 °C, and DMAP (0.045 g, 0.37 mmol), imidazole (0.54 g, 7.9 mmol), and tert-butyldimethylsilyl chloride (0.95 g, 6.3 mmol) were added successively. The reaction mixture was stirred at rt for 18 h, then washed with water, brine, dried with Na2SO4, and concentrated. Purification by column chromatography (SiO2 with 10% EtOAc in hexanes) provided 176b (0.75 g, 36%) as a colourless oil; IR (film) 1715 cm⁻¹; ¹H NMR δ: 4.42 (1H, t, J = 5.8 Hz, H7), 4.0 (1H, dd, J = 7.9, 5.0 Hz, H3), 3.32 (3H, s, H8a), 3.28 (3H, s, H8b), 2.15 (3H, s, C1), 1.81 (1H, m, C2’’), 1.61 (1H, m, H6a), 1.57 (1H, m, H4a), 1.51 (1H, m, H6b), 1.46 (1H, m, H4b), 1.39 (1H, m, H5), 0.92 (9H, s, H3’’), 0.84 (3H, d, J = 6.9 Hz, H1’’a), 0.82 (3H, d, J = 6.9 Hz, H1’’b), 0.08 (3H, s, H1’a), 0.04 (3H, s, H1’b); ¹³C NMR δ: 212.3 (C2), 103.7 (C7), 73.0
(C3), 53.6 (C8a), 52.0 (C8b), 36.1 (C5), 35.8 (C4), 33.8 (C6), 29.5 (C2’’), 26.0 (3C, C3’), 24.7 (C1), 18.8 (C1’’a), 18.6 (C1’’b), 18.2 (C2’’), -4.7 (C1’a), -4.8 (C1’b); HRMS (ESI) 369.2432 [C_{18}H_{38}O_{4}SiNa]^{+} requires 369.2432.

(3R,5S)-5-Isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yl acetate (182e)

A solution of methyltriphenylphosphonium bromide (0.25 g, 0.66 mmol) in THF (1 mL) was cooled to 0 °C, and a 1 M solution of NaHMDS in THF (0.70 mL, 0.70 mmol) was added dropwise. The resultant bright yellow solution was stirred at rt for 30 min, and then a solution of 176a (0.12 g, 0.44 mmol) in THF (1 mL) was added. The mixture was stirred for 1 h, diluted with diethyl ether, and the organic layer was washed with saturated NH₄Cl (aq) (×2), then brine (×2). The organic layer was then dried with MgSO₄ and concentrated, and purification of the residue by column chromatography (SiO₂ with 10% EtOAc in hexanes) provided 182e (0.085 g, 71%) as a colourless oil; IR (film) 1741 cm⁻¹; ¹H NMR δ: 5.22 (1H, dd, J = 8.0, 6.2 Hz, H3), 4.96 (1H, m, H9a), 4.89 (1H, m, H9b), 4.42 (1H, t, J = 5.6 Hz, H7), 3.30 (6H, s, H8), 2.05 (3H, s, H1’), 1.80 (1H, m, H2’’), 1.73 (3H, s, H1), 1.63 (2H, m, H4a, H6a), 1.44 (3H, m, H4b, H5, H6b), 0.86 (3H, d, J = 6.8 Hz, H1’’a), 0.84 (3H, d, J = 6.8 Hz, H1’’b); ¹³C NMR δ: 170.6 (C2’’), 143.7 (C2), 113.1 (C9), 103.7 (C7), 76.3 (C3), 52.7 (2C, C8), 36.1 (C5), 34.1 (C6), 33.3
According to the procedure for 182e: methyltriphenylphosphonium bromide (0.39 g, 1.1 mmol), NaHMDS (1.2 mL, 1.2 mmol), and 176b (0.25 g, 0.72 mmol) were reacted to yield 182f (0.19 g, 76%) as a colourless oil; IR (film) cm⁻¹; ¹H NMR δ: 4.83 (1H, m, H9a), 4.75 (1H, m, H9b), 4.42 (1H, dd, J = 6.2, 5.3 Hz, H7), 4.07 (1H, dd, J = 7.1, 5.7 Hz, H3), 3.32 (3H, s, H8a), 3.30 (3H, s, H8b), 1.79 (1H, m, H2”), 1.68 (3H, s, H1), 1.58 (1H, m, H6a), 1.51 (1H, m, H4a), 1.42 (2H, m, H5, H6b), 1.24 (1H, m, H4b), 0.88 (9H, s, H3”), 0.84 (3H, d, J = 6.8 Hz, H1”a), 0.82 (3H, d, J = 6.8 Hz, H1”b), 0.05 (3H, s, H1’a), 0.00 (3H, s, H1’b); ¹³C NMR δ: 148.4 (C2), 111.0 (C9), 104.0 (C7), 75.8 (C3), 53.3 (C8a), 52.4 (C8b), 37.8 (C4), 36.0 (C5), 33.8 (C6), 29.3 (C2”), 26.1 (3C, C3”), 18.9 (C1”a), 18.6 (C1”b), 18.4 (C2”), 16.8 (C1), -4.4 (C1’a), -4.8 (C1’b); HRMS (ESI) 367.2645 [C₁₉H₄₀O₃SiNa]⁺ requires 367.2639.
6.1 Summary of the Thesis

The results detailed in Chapter 2 of this thesis described general synthetic pathways for the synthesis of a variety of \( \alpha \)-functionalized allenyl vinyl ketones. Chapter 3 of this thesis divulged initial studies for the use of these compounds as substrates for the interrupted Nazarov cyclization. Considerable success in the trapping of heteroatom nucleophiles was noted, with the best results obtained with AVKs bearing an alkyl group on the allene unit, and it was determined that \( \alpha \)-substitution plays a significant role in the reactivity patterns of AVKs. It is likely that an alkyl group on the allene attenuates the reactivity at the central carbon of the allene, by electron donation and/or by steric hindrance, allowing the intramolecular Nazarov pathway to dominate. For AVKs not bearing an alkyl group on the allene unit, it was discovered that an alkyl group on the alkene unit was necessary to achieve an interrupted Nazarov cyclization, which was rationalized, and confirmed computationally, to be a result of conformational acceleration of the Nazarov reaction. AVKs bearing no \( \alpha \)-substituents did not cyclize under interrupted Nazarov conditions, and only participated in alternative allene reactions.

The results detailed in Chapter 4 of this thesis expanded this methodology to carbon-carbon formation. A variety of cyclopent-2-enones or bicyclic ketones were produced from a range of reaction partners, including acyclic dienes, cyclic dienes, aza-heterocycles, electron-rich alkenes, or styrenes, with the type of product formed dependent on the nucleophilic species employed. In most cases, the products were formed in very high regio- and stereoselectivity. A combined computational and experimental
investigation implied that the regiochemical outcome of the reaction was predominantly a result of an electronic bias in the intermediate oxyallyl cation, which resulted in the preferential formation of cyclopent-2-enones substituted at the 5-position, or bicyclic ketones in which initial bond formation had occurred at the same position. The high stereoselectivity in the formation of the bicyclic ketones from acyclic dienes was investigated through a comparison of the relative energies of the products formed, and it was determined that this was likely a result of a highly organized transition state derived from a concerted reaction, which would take place through an extended (or “exo”) geometry.

The results of this thesis should allow for further generalizations to be made, in terms of reactivity and regioselectivity with respect to related substrate classes, for the interrupted Nazarov reaction of allenyl vinyl ketones. As a result, the interrupted Nazarov cyclization of allenyl vinyl ketones has potential as a useful alternative to other synthetic approaches utilized for the stereocontrolled synthesis of cyclooctanoid natural products. The results described in Chapter 5 of this thesis are the beginning of the realization of this aim.

6.2 Future Work

The results detailed in Chapter 5 of this thesis summarize the current progress towards the total synthesis of (+)-roseadione, which would showcase the interrupted Nazarov cyclization of allenyl vinyl ketones for the construction of the cyclooctanoid ring system. As described in Chapter 5, progress towards the successful implementation of the key Nazarov step is ongoing. However, following its successful application for the
production of compound 163a, the synthesis of (+)-roseadione is proposed to be completed in a manner in agreement with the retrosynthetic analysis devised in Scheme 66 below. Briefly, lactonization then reductive ring opening of the tricyclic ketone 163a, followed by a deketalization, then 1,4-reduction of the revealed enone with \textit{in situ} triflation of the resultant enolate, and finally a Negishi cross-coupling with methylmagnesium bromide would yield advanced intermediate 184. It is envisioned that compound 184 could then be transformed into (+)-roseadione through a chemoselective oxidative cleavage of the exocyclic alkene, followed by deprotection and oxidation of the secondary alcohol unit.

Scheme 66 Retrosynthetic disconnection of (+)-roseadione (162) leading to ketone 163a.
Finally, it is also worth developing a firmer mechanistic rationale for the [4 + 3] and [3 + 2] cyclizations discussed in Chapter 4. Of particular interest is elucidation of whether the reactions are concerted or stepwise, for both the acyclic dienes, and activated alkene derivatives. This can in principle be accomplished through determination of the magnitude of the $^{13}\text{C}$ and $^2\text{H}$ KIEs of the reacting atoms, for instance positions $a$ and $b$ in compounds \textbf{185} - \textbf{187} (Figure 12). The measured KIEs can then be compared to theoretical KIEs, calculated for both a concerted and stepwise process, to determine which is the better fit with the experimental data. The $^{13}\text{C}$ and $^2\text{H}$ KIE data of compounds \textbf{185} – \textbf{187} would be obtained by NMR methods, at natural abundance.

Figure 12 Magnitude of KIEs of atoms at position(s) $a$ and/or $b$ of \textbf{185} – \textbf{187} could discriminate between concerted and stepwise mechanisms in reactions with AVKs.
REFERENCES


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211


APPENDIX A. NMR Spectral Data

$^1$H NMR (500 MHz, CDCl$_3$) of (E)-2-methyl-1-phenylhex-1-en-5-yn-3-ol (24b)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-2-methyl-1-phenylhex-1-en-5-yn-3-ol (24b)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-1-phenylhex-1-en-5-yn-3-ol (24c)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-1-phenylhex-1-en-5-yn-3-ol (24c)
$^{1}H$ NMR (500 MHz, CDCl$_3$) of (E)-1-cyclohexenylbut-3-yn-1-ol (24k)

$^{13}C$ NMR (125 MHz, CDCl$_3$) of (E)-1-cyclohexenylbut-3-yn-1-ol (24k)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-4-methyl-1-phenylhexa-1,4,5-trien-3-ol (25a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-4-methyl-1-phenylhexa-1,4,5-trien-3-ol (25a)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-2-methyl-1-phenylhexa-1,4,5-trien-3-ol (25b)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-2-methyl-1-phenylhexa-1,4,5-trien-3-ol (25b)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-1-phenylhexa-1,4,5-trien-3-ol (25c)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-1-phenylhexa-1,4,5-trien-3-ol (25c)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-2,4-dimethyl-1-phenylhexa-1,4,5-trien-3-ol (25d)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-2,4-dimethyl-1-phenylhexa-1,4,5-trien-3-ol (25d)
$^1$H NMR ($\text{CDCl}_3$, 500 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-ol (25e)

$^{13}$C NMR ($\text{CDCl}_3$, 125 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-ol (25e)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-3-methylhepta-1,2,5-trien-4-ol (25f)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-3-methylhepta-1,2,5-trien-4-ol (25f)
$^1\text{H NMR (CDCl}_3, 500 \text{ MHz) spectrum of (E)-3,7-dimethylocta-1,2,5-trien-4-ol (25g)}$

$^{13}\text{C NMR (CDCl}_3, 125 \text{ MHz) spectrum of (E)-3,7-dimethylocta-1,2,5-trien-4-ol (25g)}$
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-ol (25h)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-ol (25h)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-ol (25i)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-ol (25i)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-ol (25j)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-ol (25j)
$^1$H NMR (500 MHz, CDCl₃) of (E)-1-cyclohexenylbuta-2,3-dien-1-ol (25k)

$^{13}$C NMR (125 MHz, CDCl₃) of (E)-1-cyclohexenylbuta-2,3-dien-1-ol (25k)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-4-methyl-1-phenylhexa-1,4,5-trien-3-one (26)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-4-methyl-1-phenylhexa-1,4,5-trien-3-one (26)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-one (27)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 4-methylhexa-1,4,5-trien-3-one (27)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-3-methylhepta-1,2,5-trien-4-one (28)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-3-methylhepta-1,2,5-trien-4-one (28)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-3,7-dimethylocta-1,2,5-trien-4-one (29)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-3,7-dimethylocta-1,2,5-trien-4-one (29)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-one (30)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-1-(4-methoxyphenyl)-4-methylhexa-1,4,5-trien-3-one (30)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-one (31)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-4-methyl-1-(4-(trifluoromethyl)phenyl)hexa-1,4,5-trien-3-one (31)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-one (32)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-1-(furan-2-yl)-4-methylhexa-1,4,5-trien-3-one (32)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-2-methyl-1-phenylhex-1-en-5-yn-3-one (33)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-2-methyl-1-phenylhex-1-en-5-yn-3-one (33)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-1-cyclohexenylbut-3-yn-1-one (34)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-1-cyclohexenylbut-3-yn-1-one (34)
\[ {^1}\text{H NMR (500 MHz, CDCl}_3\text{)} \text{ of (E)-2-methyl-1-phenylhexa-1,4,5-trien-3-one (35)} \]

\[ {^{13}}\text{C NMR (125 MHz, CDCl}_3\text{)} \text{ of (E)-2-methyl-1-phenylhexa-1,4,5-trien-3-one (35)} \]
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-1-phenylhexa-1,4,5-trien-3-one (36)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-1-phenylhexa-1,4,5-trien-3-one (36)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-1-cyclohexenylbuta-2,3-dien-1-one (37)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-1-cyclohexenylbuta-2,3-dien-1-one (37)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl trifluoroacetate (39)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl trifluoroacetate (39)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 5-hydroxy-2,3-dimethylcyclopent-2-enone (40)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 5-hydroxy-2,3-dimethylcyclopent-2-enone (40)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)- (41a) and (cis)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)- (41a) and (cis)-5-hydroxy-2,3,4-trimethylcyclopent-2-enone (41b)
\(^1\)H NMR (CDCl\(_3\), 500 MHz) spectrum of \((\text{trans})\)-5-hydroxy-4-isopropyl-2,3-dimethylcyclopent-2-enone (42)

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz) spectrum of \((\text{trans})\)-5-hydroxy-4-isopropyl-2,3-dimethylcyclopent-2-enone (42)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylcyclopent-2-enone (43)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-hydroxy-4-(4-methoxyphenyl)-2,3-dimethylcyclopent-2-enone (43)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-hydroxy-2,3-dimethyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (44)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-hydroxy-2,3-dimethyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (44)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-4-(furan-2-yl)-5-hydroxy-2,3-dimethylcyclopent-2-enone (45)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-4-(furan-2-yl)-5-hydroxy-2,3-dimethylcyclopent-2-enone (45)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-4-oxo-6-phenylhexa-1,5-dien-2-yl 2,2,2-trifluoroacetate (46)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-4-oxo-6-phenylhexa-1,5-dien-2-yl 2,2,2-trifluoroacetate (46)
$^1$H NMR (500 MHz, CDCl$_3$) of (3$^Z$, 5$^E$)-4-hydroxy-6-phenylhexa-3,5-dien-2-one (46a)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (3$^Z$, 5$^E$)-4-hydroxy-6-phenylhexa-3,5-dien-2-one (46a)
$^1$H NMR (500 MHz, CDCl$_3$) of 2-methyl-4-methylene-3-phenylcyclopent-2-enone (47)

$^{13}$C NMR (125 MHz, CDCl$_3$) of 2-methyl-4-methylene-3-phenylcyclopent-2-enone (47)
$^1$H NMR (500 MHz, CDCl$_3$) of (3a$R^*$,7a$S^*$)-7a-hydroxy-3-methyleneoctahydro-1$H$-inden-1-one (48)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (3a$R^*$,7a$S^*$)-7a-hydroxy-3-methyleneoctahydro-1$H$-inden-1-one (48)
$^1$H NMR (500 MHz, CDCl$_3$) of 3-methylene-2,3,4,5,6,7-hexahydro-1$H$-inden-1-one (49)

$^{13}$C NMR (125 MHz, CDCl$_3$) of 3-methylene-2,3,4,5,6,7-hexahydro-1$H$-inden-1-one (49)
\(^1\)H NMR (500 MHz, CDCl\(_3\)) of (3a\(R^*, 7a^S^*\))-1-methylene-3-oxooctahydro-1\(H\)-inden-3a-yl 3,5-dinitrobenzoate (50)

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)) of (3a\(R^*, 7a^S^*\))-1-methylene-3-oxooctahydro-1\(H\)-inden-3a-yl 3,5-dinitrobenzoate (50)
$^1$H NMR (500 MHz, CDCl$_3$) of 4-methylene-3-phenylcyclopent-2-enone (51)

$^{13}$C NMR (125 MHz, CDCl$_3$) of 4-methylene-3-phenylcyclopent-2-enone (51)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-phenylcyclopent-2-enone (52)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-phenylcyclopent-2-enone (52)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (53)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (54)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (54)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-chloro-2,3-dimethyl-4-phenylcyclopent-2-enone (55)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-chloro-2,3-dimethyl-4-phenylcyclopent-2-enone (55)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-bromo-2,3-dimethyl-4-phenylcyclopent-2-enone (56)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-bromo-2,3-dimethyl-4-phenylcyclopent-2-enone (56)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2,3-dimethyl-4-phenylcyclopent-2-enone (57)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2,3-dimethyl-4-phenylcyclopent-2-enone (57)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(chloromethyl)-2-methylcyclopent-2-enone (58)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(chloromethyl)-2-methylcyclopent-2-enone (58)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (59)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (59)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(chloromethyl)-2,4-dimethylcyclopent-2-enone (60)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(chloromethyl)-2,4-dimethylcyclopent-2-enone (60)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (61)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (61)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(chloromethyl)-4-isopropyl-2-methylcyclopent-2-enone (62)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(chloromethyl)-4-isopropyl-2-methylcyclopent-2-enone (62)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (63)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (63)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(iodomethyl)-4-(4-methoxyphenyl)-2-methyl-cyclopent-2-enone (64)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(iodomethyl)-4-(4-methoxyphenyl)-2-methyl-cyclopent-2-enone (64)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (65)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(chloromethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (65)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (66)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(iodomethyl)-2-methyl-4-(4-(trifluoromethyl)-phenyl)cyclopent-2-enone (66)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*, 2S^*, 3R^*, 4R^*, 5R^*$)-2,5-bis(4-
methoxyphenyl)-1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylenebicyclo[2.2.1] 
heptan-7-one (67)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*, 2S^*, 3R^*, 4R^*, 5R^*$)-2,5-bis(4-
methoxyphenyl)-1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylenebicyclo[2.2.1] 
heptan-7-one (67)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 5-bromo-2,3-dimethylcyclopent-2-enone (68)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 5-bromo-2,3-dimethylcyclopent-2-enone (68)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(bromomethyl)-2-methylcyclopent-2-enone (69)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(bromomethyl)-2-methylcyclopent-2-enone (69)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-bromo-4-methyl-2,3-dimethylcyclopent-2-enone (70)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-bromo-4-methyl-2,3-dimethylcyclopent-2-enone (70)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (71)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (71)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-bromo-4-isopropyl-2,3-dimethylcyclopent-2-enone (72)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-bromo-4-isopropyl-2,3-dimethylcyclopent-2-enone (72)
\(^1\)H NMR (CDCl\(_3\), 500 MHz) spectrum of 3-(bromomethyl)-4-isopropyl-2-methylcyclopent-2-enone (73)

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz) spectrum of 3-(bromomethyl)-4-isopropyl-2-methylcyclopent-2-enone (73)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (E)-4,5-dibromo-4-methyl-1-phenylhexa-
1,5-dien-3-one (74)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (E)-4,5-dibromo-4-methyl-1-phenylhexa-
1,5-dien-3-one (74)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-bromo-3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (75)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-bromo-3-(bromomethyl)-2,4-dimethylcyclopent-2-enone (75)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-bromo-3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (76)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-bromo-3-(bromomethyl)-2-methyl-4-phenylcyclopent-2-enone (76)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (77)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of *trans*-5-bromo-3-(bromomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (77)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-bromo-3-(bromomethyl)-2-methyl-4-(4- (trifluoromethyl)phenyl)cyclopent-2-enone (78)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-bromo-3-(bromomethyl)-2-methyl-4-(4- (trifluoromethyl)phenyl)cyclopent-2-enone (78)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 5-hydroxy-3-(iodomethyl)-2-methylcyclopent-2-enone (79)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 5-hydroxy-3-(iodomethyl)-2-methylcyclopent-2-enone (79)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-(80a) and cis-5-hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-(80a) and cis-5-hydroxy-3-(iodomethyl)-2,4-dimethylcyclopent-2-enone (80b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-hydroxy-3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (81)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-hydroxy-3-(iodomethyl)-4-isopropyl-2-methylcyclopent-2-enone (81)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (82)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of *trans*-5-hydroxy-3-(iodomethyl)-2-methyl-4-phenylcyclopent-2-enone (82)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of trans-5-hydroxy-3-(iodomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (83)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of trans-5-hydroxy-3-(iodomethyl)-4-(4-methoxy-phenyl)-2-methylcyclopent-2-enone (83)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$E$,4$E$)-5,6-dibromo-4-methyl-1-phenylhexa-1,4-dien-3-one (84)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$E$,4$E$)-5,6-dibromo-4-methyl-1-phenylhexa-1,4-dien-3-one (84)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (erythro,4E)-1,2,5,6-tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)

$^{13}$C NMR (CDCl$_3$, 120 MHz) spectrum of (erythro,4E)-1,2,5,6-tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*$,2$S^*$,6$S^*$,7$R^*$)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*$,2$S^*$,6$S^*$,7$R^*$)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*$,2$S^*$,6$S^*$,7$R^*$)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a), and (1$R^*$,2$R^*$,6$S^*$,7$R^*$)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*$,2$S^*$,6$S^*$,7$R^*$)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a), and (1$R^*$,2$R^*$,6$S^*$,7$R^*$)-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)
\(^1\)H NMR (CDCl\(_3\), 500 MHz) spectrum of \((1R*,3R*,4S*,6S*)-1\)-methyl-2-methylene-3-phenyl-6-\(((E)\)-prop-1-enyl\)bicyclo[2.2.1]heptan-7-one (87)

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz) spectrum of \((1R*,3R*,4S*,6S*)-1\)-methyl-2-methylene-3-phenyl-6-\(((E)\)-prop-1-enyl\)bicyclo[2.2.1]heptan-7-one (87)
\(^1\)H NMR (CDCl\textsubscript{3}, 500 MHz) spectrum of (1\textsuperscript{R},3\textsuperscript{R},4\textsuperscript{S},6\textsuperscript{S})-1-methyl-2-methylene-3-phenyl-6-((Z)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (88)

\(^{13}\)C NMR (CDCl\textsubscript{3}, 125 MHz) spectrum of (1\textsuperscript{R},3\textsuperscript{R},4\textsuperscript{S},6\textsuperscript{S})-1-methyl-2-methylene-3-phenyl-6-((Z)-prop-1-enyl)bicyclo[2.2.1]heptan-7-one (88)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of $(1R^*,6S^*,7R^*)$-1,4-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89a) and $(1R^*,6S^*,7R^*)$-1,3-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of $(1R^*,6S^*,7R^*)$-1,4-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89a) and $(1R^*,6S^*,7R^*)$-1,3-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (89b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*,6S^*,7R^*$)-1,3,4-trimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (90)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$^R$,3$^R$,4$^S$,6$^S$)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$^R$,3$^R$,4$^S$,6$^S$)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*$,6$S^*$,7$R^*$)-1,2,2,4-tetramethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (92), (1$R^*$, 2$R^*$,4$R^*$,5$S^*$)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93a), and (1$R^*$,2$S^*$,4$R^*$,5$S^*$)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenyl-bicyclo[2.2.1]heptan-7-one (93b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*$,6$S^*$,7$R^*$)-1,2,2,4-tetramethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (92), (1$R^*$, 2$R^*$,4$R^*$,5$S^*$)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]heptan-7-one (93a), and (1$R^*$,2$S^*$,4$R^*$,5$S^*$)-1,2-dimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenyl-bicyclo[2.2.1]heptan-7-one (93b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^\ast$,2$R^\ast$,4$R^\ast$,5$R^\ast$)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]-heptan-7-one (94a) and (1$R^\ast$,2$S^\ast$,4$R^\ast$,5$R^\ast$)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]-heptan-7-one (94b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^\ast$,2$R^\ast$,4$R^\ast$,5$R^\ast$)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]-heptan-7-one (94a) and (1$R^\ast$,2$S^\ast$,4$R^\ast$,5$R^\ast$)-1,3,3-trimethyl-6-methylene-2-(2-methylprop-1-enyl)-5-phenylbicyclo[2.2.1]-heptan-7-one (94b)
\(^1\)H NMR (CDCl\(_3\), 500 MHz) spectrum of \((7R^*,10S^*)\)-3,3,5,9-tetramethyl-10-phenylbicyclo[5.2.1]deca-1(9),4-dien-8-one (95)

\(^{13}\)C NMR (CDCl\(_3\), 125 MHz) spectrum of \((7R^*,10S^*)\)-3,3,5,9-tetramethyl-10-phenylbicyclo[5.2.1]deca-1(9),4-dien-8-one (95)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of $(1R^*,6S^*)$-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (96)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of $(1R^*,6S^*)$-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (96)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*$,6$S^*$,7$R^*$)-7-isopropyl-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (97)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*$,6$S^*$,7$R^*$)-7-isopropyl-1,3,4-trimethyl-8-methylenebicyclo[4.2.1]non-3-en-9-one (42)
$^1$H NMR (500 MHz, CDCl$_3$) of (1$R^*$,5$R^*$,6$S^*$,8$S^*$)-1,5-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (98)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (1$R^*$,5$R^*$,6$S^*$,8$S^*$)-1,5-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (98)
$^1$H NMR (500 MHz, CDCl$_3$) of (1$R^*$,6$S^*$,8$S^*$)-1,3,4-trimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (99)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (1$R^*$,6$S^*$,8$S^*$)-1,3,4-trimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (99)
$^1$H NMR (500 MHz, CDCl$_3$) of (1$R^*$,6$S^*$,8$S^*$)-1,3-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100a) and (1$R^*$,6$S^*$,8$S^*$)-1,4-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100b)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (1$R^*$,6$S^*$,8$S^*$)-1,3-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100a) and (1$R^*$,6$S^*$,8$S^*$)-1,4-dimethyl-7-methylene-8-phenylbicyclo[4.2.1]non-3-en-9-one (100b)
$^1$H NMR (500 MHz, CDCl$_3$) of $(1R^*,3R^*,8S^*,12S^*)$-12-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]triscadec-10-en-13-one (101)

$^{13}$C NMR (125 MHz, CDCl$_3$) of $(1R^*,3R^*,8S^*,12S^*)$-12-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]triscadec-10-en-13-one (101)
$^1$H NMR (500 MHz, CDCl$_3$) of (1$R^*,3R^*,8S^*$)-10,11-dimethyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]triscadec-10-en-13-one (102)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (1$R^*,3R^*,8S^*$)-10,11-dimethyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]triscadec-10-en-13-one (102)
$^{1}$H NMR (500 MHz, CDCl$_3$) of (1$R^*$,3$R^*$,8$S^*$)-10-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]trisdec-10-en-13-one (103a) and (1$R^*$,3$R^*$,8$S^*$)-11-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]trisdec-10-en-13-one (103b)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (1$R^*$,3$R^*$,8$S^*$)-10-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]trisdec-10-en-13-one (103a) and (1$R^*$,3$R^*$,8$S^*$)-11-methyl-2-methylenetricyclo[6.4.1.0$^{3,8}$]trisdec-10-en-13-one (103b)
$^1$H NMR (500 MHz, CDCl$_3$) of (E)-1-(3,4-dimethyl-6-methylene cyclohex-3-enyl)-3-phenylprop-2-en-1-one (104)

$^{13}$C NMR (125 MHz, CDCl$_3$) of (E)-1-(3,4-dimethyl-6-methylene cyclohex-3-enyl)-3-phenylprop-2-en-1-one (104)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-allyl-2,3-dimethyl-4-phenylcyclopent-2-enone (105)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of $(1R^*,3R^*,4S^*,6R^*)$-1-methyl-2-methylene-3-phenyl-6-((trimethylsilyl)methyl)bicyclo[2.2.1]-heptan-7-one (106a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of $(1R^*,3R^*,4S^*,6R^*)$-1-methyl-2-methylene-3-phenyl-6-((trimethylsilyl)methyl)bicyclo[2.2.1]-heptan-7-one (106a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of ($1^R$*,$3^R$*,$4^S$*,$6^R$*)-1-methyl-2-methylene-3-phenyl-6-((triisopropylsilyl)methyl) bicyclo[2.2.1]heptan-7-one (106b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of ($1^R$*,$3^R$*,$4^S$*,$6^R$*)-1-methyl-2-methylene-3-phenyl-6-((triisopropylsilyl)methyl) bicyclo[2.2.1]heptan-7-one (106b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$^R^*,3R^*,4S^*,6R^*$)-1-methyl-2-methylene-3-phenyl-6-((triethoxysilyl)methyl)bicyclo[2.2.1] heptan-7-one (106c)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$^R^*,3R^*,4S^*,6R^*$)-1-methyl-2-methylene-3-phenyl-6-((triethoxysilyl)methyl)bicyclo[2.2.1]heptan-7-one (106c)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(but-3-enyl)-2-methyl-4-phenylcyclopent-2-enone (107)
$^{1}H$ NMR (CDCl$_3$, 500 MHz) spectrum of ($1R^*,3R^*,5S^*,6R^*$)-1-methyl-7-methylene-6-phenyl-3-(trimethylsilyl)bicyclo[3.2.1]octan-8-one (109a)

$^{13}C$ NMR (CDCl$_3$, 125 MHz) spectrum of ($1R^*,3R^*,5S^*,6R^*$)-1-methyl-7-methylene-6-phenyl-3-(trimethylsilyl)bicyclo[3.2.1]octan-8-one (109a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*$,3$R^*$,5$S^*$,6$R^*$)-1-methyl-7-methylene-6-phenyl-3-(triisopropylsilyl)bicyclo[3.2.1]octan-8-one (109b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*$,3$R^*$,5$S^*$,6$R^*$)-1-methyl-7-methylene-6-phenyl-3-(triisopropylsilyl)bicyclo[3.2.1]octan-8-one (109b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)acetaldehyde (110)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 1-methyl-6-methylene-7-oxo-5-phenylbicyclo[2.2.1]heptan-2-yl acetate (111)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 1-methyl-6-methylene-7-oxo-5-phenylbicyclo[2.2.1]heptan-2-yl acetate (111)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of ($1R^*,3S^*,4R^*,6S^*$)- and ($1R^*,3S^*,4R^*,6R^*$)-1-methyl-2-methylene-3-phenyl-6-propoxybicyclo-[2.2.1]heptan-7-one (112)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of ($1R^*,3S^*,4R^*,6S^*$)- and ($1R^*,3S^*,4R^*,6R^*$)-1-methyl-2-methylene-3-phenyl-6-propoxybicyclo-[2.2.1]heptan-7-one (112)
$^1$H NMR (CDCl₃, 500 MHz) spectrum of (1'R*,2S*,5'R*)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)

$^{13}$C NMR (CDCl₃, 125 MHz) spectrum of (1'R*,2S*,5'R*)-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)
DEPT-135 spectrum of \((1'R^*,2S^*,5'R^*)-2-(3,4\text{-dimethyl-2-oxo-5-phenylcyclopent-3-enyl})\)propanal (113)

COSY spectrum of \((1'R^*,2S^*,5'R^*)-2-(3,4\text{-dimethyl-2-oxo-5-phenylcyclopent-3-enyl})\)propanal (113)
HSQC spectrum of \((1'R^*,2S^*,5'R^*)-2-(3,4\text{-}dimethyl\text{-}2\text{-}oxo\text{-}5\text{-}phenyleclopent-3\text{-}enyl)propanal\) (113)

HMBC spectrum of \((1'R^*,2S^*,5'R^*)-2-(3,4\text{-}dimethyl\text{-}2\text{-}oxo\text{-}5\text{-}phenyleclopent-3\text{-}enyl)propanal\) (113)
$J$-HMBC spectrum of $(1'R^*,2S^*,5'R^*)$-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)

Details of $J$-HMBC spectrum of $(1'R^*,2S^*,5'R^*)$-2-(3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)propanal (113)

$^2J_{H2-C5'}$
\( {^2J_{H2-C1'}} \)

\( {^3J_{H1'-C3}} \)
$^{2}J_{H1'-C2}$

$^{3}J_{H1'-C1''}$
Critical data from \( J \)-HMBC spectrum of \((1'R^*,2S^*,5'R^*)-2-(3,4\text{-dimethyl-2-oxo-5-phenylcyclopent-3-enyl})propanal \) (113)

![Diagram of molecular structure](image)

Measured \( J_{HH} \) and \( J_{CH} \) with respect to the C2-C1' segment in compound 113

<table>
<thead>
<tr>
<th>( J_{HH} )</th>
<th>nuclei</th>
<th>measured value (Hz)</th>
<th>magnitude estimation</th>
<th>stereorelation</th>
</tr>
</thead>
<tbody>
<tr>
<td>( J_{H2-H1'} )</td>
<td>H2-H1'</td>
<td>4.2</td>
<td>small</td>
<td>gauche</td>
</tr>
<tr>
<td>( J_{H2-C5'} )</td>
<td>H2-C5'</td>
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<tr>
<td>( J_{H1'-C3} )</td>
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<td>anti</td>
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<tr>
<td>( J_{C1'-C5'} )</td>
<td>H1'-C5'</td>
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<td>large</td>
<td>gauche to C2'</td>
</tr>
<tr>
<td>( J_{H1'-C2} )</td>
<td>H1'-C2</td>
<td>7.1</td>
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<td>gauche to C1</td>
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Measured \( J_{HH} \) and \( J_{CH} \) with respect to the C1'-C5' segment in compound 113

<table>
<thead>
<tr>
<th>( J_{HH} )</th>
<th>nuclei</th>
<th>measured value (Hz)</th>
<th>magnitude estimation</th>
<th>stereorelation</th>
</tr>
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<td>H1'-H5'</td>
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<td>anticlinal</td>
</tr>
<tr>
<td>( J_{H1'-C1''} )</td>
<td>H1'-C1''</td>
<td>7.0</td>
<td>large</td>
<td>synclinal</td>
</tr>
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$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-5-(2-oxopropyl)-4-phenylcyclopent-2-enone (114) and by-product

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-5-(2-oxopropyl)-4-phenylcyclopent-2-enone (114) and by-product
$^{1}H$ NMR (CDCl$_{3}$, 500 MHz) spectrum of trimethyl((1E,3Z)-4-methyl-1-phenyl-5-(1-(trimethylsilyloxy)cyclobutyl)hexa-1,3,5-trien-3-yloxy)silane (116)

$^{13}C$ NMR (CDCl$_{3}$, 125 MHz) spectrum of trimethyl((1E,3Z)-4-methyl-1-phenyl-5-(1-(trimethylsilyloxy)cyclobutyl)hexa-1,3,5-trien-3-yloxy)silane (116)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$^R$*,3$^R$*,4$^S$*,6$^S$*)-1-methyl-2-methylene-3,6-diphenylbicyclo[2.2.1]heptan-7-one (117)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$^R$*,3$^R$*,4$^S$*,6$^S$*)-1-methyl-2-methylene-3,6-diphenylbicyclo[2.2.1]heptan-7-one (117)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$^R$*,3$R$*,4$S$*,6$S$*)-6-(4-methoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]heptan-7-one (118)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$^R$*,3$R$*,4$S$*,6$S$*)-6-(4-methoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]heptan-7-one (118)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$^R$*,3$^R$*,4$^S$*,6$^S$*)- 6-(3,4-dimethoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]-heptan-7-one (119)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$^R$*,3$^R$*,4$^S$*,6$^S$*)- 6-(3,4-dimethoxyphenyl)-1-methyl-2-methylene-3-phenylbicyclo[2.2.1]-heptan-7-one (119)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R^*$,2$S^*$,3$R^*$,4$S^*$,5$S^*$)-2-(4-methoxyphenyl)-1,3-dimethyl-6-methylene-5-phenylbicyclo[2.2.1]-heptan-7-one (120)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R^*$,2$S^*$,3$R^*$,4$S^*$,5$S^*$)-2-(4-methoxyphenyl)-1,3-dimethyl-6-methylene-5-phenylbicyclo[2.2.1]-heptan-7-one (120)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$^R$,2$^5$,4$^5$*)-2-(3,4-dimethoxyphenyl)-1-methyl-6-methylenebicyclo[2.2.1]heptan-7-one (121)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$^R$,2$^5$,4$^5$*)-2-(3,4-dimethoxyphenyl)-1-methyl-6-methylenebicycle[2.2.1]heptan-7-one (121)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of \((1R^*,3R^*,4S^*,6S^*)\)-6-(3,4-dimethoxyphenyl)-3-isopropyl-1-methyl-2-methylenebicyclo[2.2.1]-heptan-7-one (122)

\[ \text{Spectrum Image} \]

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of \((1R^*,3R^*,4S^*,6S^*)\)-6-(3,4-dimethoxyphenyl)-3-isopropyl-1-methyl-2-methylenebicyclo[2.2.1]-heptan-7-one (122)

\[ \text{Spectrum Image} \]
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-(furan-2-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (123)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-(furan-2-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (123)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-(furan-2-ylmethyl)-2-methyl-4-phenylcyclopent-2-enone (124)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-(furan-2-ylmethyl)-2-methyl-4-phenylcyclopent-2-enone (124)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1H-pyrrol-2-yl)cyclopent-2-enone (125)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1H-pyrrol-2-yl)cyclopent-2-enone (125)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-4-methyl-5-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-1-phenylhexa-1,5-dien-3-one (126)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-4-methyl-5-(1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)-1-phenylhexa-1,5-dien-3-one (126)
$^1\text{H}$ NMR (CDCl$_3$, 500 MHz) spectrum of 2-methyl-3-((1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)methyl)-4-phenylcyclopent-2-enone (127)

$^{13}\text{C}$ NMR (CDCl$_3$, 125 MHz) spectrum of 2-methyl-3-((1,2,3,4,5-pentamethylcyclopenta-2,4-dienyl)methyl)-4-phenylcyclopent-2-enone (127)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (I''R*,4S*,5R*)-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (I''R*,4S*,5R*)-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)
DEPT-135 spectrum of \((1''R^*,4S^*,5R^*)\)-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

COSY spectrum of \((1''R^*,4S^*,5R^*)\)-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)
HSQC spectrum of \((1''R^*,4S^*,5R^*)-5\text{-}(\text{cyclohexa-2,4-dienyl})\text{-}2,3\text{-}\text{dimethyl-4-phenylcyclopent-2-enone (128)}\)

HMBC spectrum of \((1''R^*,4S^*,5R^*)-5\text{-}(\text{cyclohexa-2,4-dienyl})\text{-}2,3\text{-}\text{dimethyl-4-phenylcyclopent-2-enone (128)}\)
J-HMBC spectrum of \((1''R^*,4S^*,5R^*)\)-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

Details of J-HMBC spectrum of \((1''R^*,4S^*,5R^*)\)-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

\(^3\)J H5-C6''
$^{2}J_{H5-C1''}$

$^{3}J_{H5-C1'}$
Critical data from $J$-HMBC spectrum of $\left(1''R^*,4S^*,5R^*\right)$-5-(cyclohexa-2,4-dienyl)-2,3-dimethyl-4-phenylcyclopent-2-enone (128)

Measured $^3J_{H,H}$ and $^2,^3J_{C,H}$ with respect to the C5-C1" segment in compound 128

<table>
<thead>
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<th>$^2,^3J_{H,X}$</th>
<th>nuclei</th>
<th>measured value (Hz)</th>
<th>magnitude estimation</th>
<th>stereorelation to H5</th>
</tr>
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<tr>
<td>$^3J_{H,H}$</td>
<td>H5–H1&quot;</td>
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<td>gauche</td>
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<tr>
<td>$^3J_{C,H}$</td>
<td>H5–C6&quot;</td>
<td>7.4</td>
<td>large</td>
<td>anti</td>
</tr>
<tr>
<td>$^2J_{C,H}$</td>
<td>H5–C1&quot;</td>
<td>7.2</td>
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<td>gauche to C2&quot;</td>
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</table>

Measured $^3J_{H,H}$ and $^2,^3J_{C,H}$ with respect to the C5-C4 segment in compound 128

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<th>$^2,^3J_{H,X}$</th>
<th>nuclei</th>
<th>measured value (Hz)</th>
<th>magnitude estimation</th>
<th>stereorelation to H5</th>
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</thead>
<tbody>
<tr>
<td>$^3J_{H,H}$</td>
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<tr>
<td>$^2J_{C,H}$</td>
<td>H5–C1'</td>
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<td>large</td>
<td>synclinal</td>
</tr>
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</table>
$^1$H NMR (CDCl₃, 500 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-methyl-1H-pyrrol-2-yl)-4-phenylcyclopent-2-enone (129)

$^{13}$C NMR (CDCl₃, 125 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-methyl-1H-pyrrol-2-yl)-4-phenylcyclopent-2-enone (129)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-benzyl-1H-pyrrol-2-yl)-4-phenylcyclopent-2-enone (130)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-benzyl-1H-pyrrol-2-yl)-4-phenylcyclopent-2-enone (130)
$^1\text{H NMR (CDCl}_3, \text{ 500 MHz)}$ spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1-phenyl-1H-pyrrol-2-yl)cyclopent-2-enone (131)

$^{13}\text{C NMR (CDCl}_3, \text{ 125 MHz)}$ spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1-phenyl-1H-pyrrol-2-yl)cyclopent-2-enone (131)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of \((\text{trans})-5-(1-(4\text{-methoxyphenyl}-1\text{H}-\text{pyrrol-2-yl})-2,3\text{-dimethyl-4-phenyl-cyclopent-2-enone (132)}\)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1-(triisopropylsilyl)-1H-pyrrol-2-yl)cyclopent-2-enone (133)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1-(triisopropylsilyl)-1H-pyrrol-2-yl)cyclopent-2-enone (133)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of methyl 2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1H-pyrrole-1-carboxylate (134) and methyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1H-pyrrole-1-carboxylate (136)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of methyl 2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1H-pyrrole-1-carboxylate (134) and methyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1H-pyrrole-1-carboxylate (136)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of tert-butyl 2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1H-pyrrole-1-carboxylate (135) and tert-butyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1H-pyrrole-1-carboxylate (137)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of tert-butyl 2-((trans)-3,4-dimethyl-2-oxo-5-phenylcyclopent-3-enyl)-1H-pyrrole-1-carboxylate (135) and tert-butyl 2-((2-methyl-3-oxo-5-phenylcyclopent-1-enyl)methyl)-1H-pyrrole-1-carboxylate (137)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-methyl-3-((1-(methylsulfonyl)-1H-pyrrol-2-yl)methyl)-4-phenylcyclopent-2-enone (138)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-methyl-3-((1-(methylsulfonyl)-1H-pyrrol-2-yl)methyl)-4-phenylcyclopent-2-enone (138)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-methyl-4-phenyl-3-((1-(para-toluenesulfonyl)-1H-pyrrol-2-yl)methyl)cyclopent-2-enone (139)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-methyl-4-phenyl-3-((1-(para-toluenesulfonyl)-1H-pyrrol-2-yl)methyl)cyclopent-2-enone (139)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$E,4Z$)-4-methyl-1-phenyl-5-(1$H$-pyrrol-2-yl)hexa-1,4-dien-3-one (140)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$E,4Z$)-4-methyl-1-phenyl-5-(1$H$-pyrrol-2-yl)hexa-1,4-dien-3-one (140)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-(1H-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-(1H-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-($1H$-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a) and 3-((1$H$-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (141b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-($1H$-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (141a) and 3-((1$H$-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (141b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-(5-methoxy-1$H$-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-(5-methoxy-1$H$-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-(5-methoxy-$1H$-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a) and 3-((5-methoxy-$1H$-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (142b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-(5-methoxy-$1H$-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (142a) and 3-((5-methoxy-$1H$-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (142b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-methyl-1$H$-indol-3-yl)-4-phenylcyclopent-2-enone (143a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-methyl-1$H$-indol-3-yl)-4-phenylcyclopent-2-enone (143a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-methyl-1H-indol-3-yl)-4-phenylcyclopent-2-enone (143a) and 2-methyl-3-((1-methyl-1H-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (143b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-5-(1-methyl-1H-indol-3-yl)-4-phenylcyclopent-2-enone (143a) and 2-methyl-3-((1-methyl-1H-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (143b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-5-(2-methyl-1H-indol-3-yl)-4-phenylcyclopent-2-enone (144a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-5-(2-methyl-1H-indol-3-yl)-4-phenylcyclopent-2-enone (144a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-methyl-3-((2-methyl-1H-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (144b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-methyl-3-((2-methyl-1H-indol-3-yl)methyl)-4-phenylcyclopent-2-enone (144b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-(1,2-dimethyl-1H-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (145a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-(1,2-dimethyl-1H-indol-3-yl)-2,3-dimethyl-4-phenylcyclopent-2-enone (145a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-((1,2-dimethyl-1H-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (145b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-((1,2-dimethyl-1H-indol-3-yl)methyl)-2-methyl-4-phenylcyclopent-2-enone (145b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1-tosyl-1H-indol-3-yl)cyclopent-2-enone (146a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-2,3-dimethyl-4-phenyl-5-(1-tosyl-1H-indol-3-yl)cyclopent-2-enone (146a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-methyl-4-phenyl-3-((1-tosyl-1H-indol-3-yl)methyl)cyclopent-2-enone (146b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-methyl-4-phenyl-3-((1-tosyl-1H-indol-3-yl)methyl)cyclopent-2-enone (146b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1E,4Z)-5-(1H-indol-3-yl)-4-methyl-1-phenylhexa-1,4-dien-3-one (147)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1E,4Z)-5-(1H-indol-3-yl)-4-methyl-1-phenylhexa-1,4-dien-3-one (147)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2,3-dimethyl-5-(1-methyl-1$H$-indol-3-yl)cyclopent-2-enone (148)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2,3-dimethyl-5-(1-methyl-1$H$-indol-3-yl)cyclopent-2-enone (148)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 5-(1,2-dimethyl-1H-indol-3-yl)-2,3-dimethylcyclopent-2-enone (149)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 5-(1,2-dimethyl-1H-indol-3-yl)-2,3-dimethylcyclopent-2-enone (149)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-4-isopropyl-2,3-dimethyl-5-(1-methyl-1H-indol-3-yl)cyclopent-2-enone (150)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-4-isopropyl-2,3-dimethyl-5-(1-methyl-1H-indol-3-yl)cyclopent-2-enone (150)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans)-5-(1,2-dimethyl-1$H$-indol-3-yl)-4-isopropyl-2,3-dimethylcyclopent-2-enone (151a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans)-5-(1,2-dimethyl-1$H$-indol-3-yl)-4-isopropyl-2,3-dimethylcyclopent-2-enone (151a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3-((1,2-dimethyl-1$H$-indol-3-yl)methyl)-4-isopropyl-2-methylcyclopent-2-enone (151b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 3-((1,2-dimethyl-1$H$-indol-3-yl)methyl)-4-isopropyl-2-methylcyclopent-2-enone (151b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (trans,trans)-5,5$'$(furan-2,5-diyl)bis(2,3-dimethyl-4-phenyl-cyclopent-2-enone (160)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (trans,trans)-5,5$'$(furan-2,5-diyl)bis(2,3-dimethyl-4-phenyl-cyclopent-2-enone (161)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1'R*,2'R*,4'S*,6'R*,7'S*)-1-(1,2,4,5,6,7-hexamethyl-3-methylenebicyclo[2.2.1]hept-5-en-2-yl)-3-phenylprop-2-en-1-one (162)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1'R*,2'R*,4'S*,6'R*,7'S*)-1-(1,2,4,5,6,7-hexamethyl-3-methylenebicyclo[2.2.1]hept-5-en-2-yl)-3-phenylprop-2-en-1-one (162)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (3$R$,5$S$)-5-isopropyl-7,7-dimethoxy-2-oxoheptan-3-yl acetate (176a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (3$R$,5$S$)-5-isopropyl-7,7-dimethoxy-2-oxoheptan-3-yl acetate (176a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (3R,5S)-3-(tert-butyldimethylsilyloxy)-5-isopropyl-7,7-dimethoxyheptan-2-one (176b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (3R,5S)-3-(tert-butyldimethylsilyloxy)-5-isopropyl-7,7-dimethoxyheptan-2-one (176b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1,4-dithiaspiro[4.4]non-6-en-6-ylmethyl)trimethylsilane (177a)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1,4-dithiaspiro[4.4]non-6-en-6-ylmethyl)trimethylsilane (177a)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 6-bromo-1,4-dioxaspiro[4.4]non-6-ene (177b)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 6-bromo-1,4-dioxaspiro[4.4]non-6-ene (177b)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of (1$R$,5$R$)-5-isopropyl-2-methylcyclohex-2-enyl acetate (179)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (1$R$,5$R$)-5-isopropyl-2-methylcyclohex-2-enyl acetate (179)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-iodocyclopent-2-enone (180)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-iodocyclopent-2-enone (180)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 2-((trimethylsilyl)methyl)cyclopent-2-enone (181)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of 2-((trimethylsilyl)methyl)cyclopent-2-enone (181)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of 3$R$,5$S$)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yl acetate (182e)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of (3$R$,5$S$)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yl acetate (182e)
$^1$H NMR (CDCl$_3$, 500 MHz) spectrum of ((3$R,5S$)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yloxy)tert-butyl dimethylsilane (182f)

$^{13}$C NMR (CDCl$_3$, 125 MHz) spectrum of ((3$R,5S$)-5-isopropyl-7,7-dimethoxy-2-methylhept-1-en-3-yloxy)tert-butyl dimethylsilane (182f)
APPENDIX B. Additional Computational Data and Cartesian Coordinates

Summary of relative energies of the conformations of 26, 36, and 37

For 26:

\[
\begin{align*}
\text{Ph} &= \text{C} \quad 21.5 \text{ KJ mol}^{-1} \\
\text{O} &= \text{C} \quad 0 \text{ KJ mol}^{-1} \\
\text{Ph} &= \text{no local minimum} \\
\text{C} &= 12.7 \text{ KJ mol}^{-1}
\end{align*}
\]

For 35:

\[
\begin{align*}
\text{Ph} &= \text{C} \quad 9.0 \text{ KJ mol}^{-1} \\
\text{O} &= \text{C} \quad 6.9 \text{ KJ mol}^{-1} \\
\text{Ph} &= \text{C} \quad 5.5 \text{ KJ mol}^{-1} \\
\text{Ph} &= \text{no local minimum}
\end{align*}
\]

For 36:

\[
\begin{align*}
\text{Ph} &= \text{C} \quad 10.5 \text{ KJ mol}^{-1} \\
\text{O} &= \text{C} \quad 0 \text{ KJ mol}^{-1} \\
\text{Ph} &= \text{C} \quad 15.9 \text{ KJ mol}^{-1} \\
\text{Ph} &= \text{C} \quad 12.3 \text{ KJ mol}^{-1}
\end{align*}
\]

Cartesian coordinates for 26, s-cis-s-cis conformation

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C  -2.418903  1.095233 -0.037941
C  -2.997358 -1.261008  0.074497
C  -3.779561  1.424313 -0.040685
H  -1.673081  1.894103 -0.0832
C  -4.359958 -0.931233  0.071883
H  -2.686719 -2.310077  0.119206
C  -4.756785  0.414082  0.014421
H  -4.082115  2.474765 -0.086773
H  -5.11222 -1.724424  0.114451
H  -5.818898  0.676005  0.011796
O   2.026245 -1.674996  0.058406
C   3.030274  0.49808  -0.018995
C  -4.252008 -0.029855  0.018948
C  -4.623544 -0.554137  0.058704
H   5.964873 -0.735334  1.014117
H   5.984394 -0.832299 -0.862311
C  -2.828453  1.998074 -0.096034
H  -2.263082  2.276313 -1.00044
H   2.27132  2.369416  0.779684
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Energy = -576.019759448 au

384
Cartesian coordinates for 26, s-cis-s-trans conformation

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H & \quad -5.374353 \quad 0.050858 \quad 0.061889 \\
\text{Energy} & = -576.027957914 \text{ au}
\end{align*}

\textbf{Cartesian coordinates for 26, \textit{s-trans-s-trans} conformation\textsuperscript{46-49}}

\begin{tabular}{cccc}
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Atom & x & y & z \\
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C & 2.14042 & 1.07286 & 0.02447 \\
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C & -2.34326 & 0.98813 & -0.61821 \\
C & -2.33412 & -0.97248 & 0.81522 \\
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H & -1.78095 & -1.71901 & 1.39527 \\
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H & -4.27135 & -1.80918 & 1.30225 \\
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\end{tabular}
36, the $s\text{-}\text{trans}-s\text{-}\text{cis}$ conformation converged to the $s\text{-}\text{trans}-s\text{-}\text{trans}$ conformation.

**Cartesian coordinates for 36, $s\text{-}\text{cis}-s\text{-}\text{cis}$ conformation**

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Cartesian coordinates for 36, s-cis-s-trans conformation

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Energy = -536.833441146 au
Energy = -536.837427503 au
**Cartesian coordinates for 36, *s*-trans-*s*-cis conformation**

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### Cartesian coordinates for 36, *s-trans-s-trans* conformation\(^{46,49}\)

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**Cartesian coordinates for 37, s-cis-s-cis conformation**^46-49^

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Energy = -576.017821916 au

**Cartesian coordinates for 37, s-cis-s-trans conformation**

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Energy = -576.018650048 au
Cartesian coordinates for 37, *s-trans-s-cis* conformation\textsuperscript{46,49}

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**Cartesian coordinates for 37, s-trans-s-trans conformation**

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Energy = -576.021265102 au

Cartesian coordinates for oxyallyl cation 153$^{46-49}$

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### Cartesian coordinates for $(1R^*,2S^*,6S^*,7R^*)$-1,2-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86a)$^{61}$

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**Basis set for geometry optimization:** RH/6-31G; **Number of imaginary frequencies:** 0

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401
Energy HF/6-31G//HF/6-311G(d,p): \(-768.2692219\) Hartrees

Cartesian coordinates for \((1R^*,2R^*,6S^*,7R^*)-1,2\text{-dimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (86b)}\)

Basis set for geometry optimization: RH/6-31G; Number of imaginary frequencies: 0

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Energy HF/6-31G//HF/6-311G(d,p): $-768.270356$ Hartrees

Cartesian coordinates for $(1R^*,3R^*,4S^*,6S^*)$-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91a)$^6$
Energy HF/6-31G//HF/6-311G(d,p): -807.3094439 Hartrees

Cartesian coordinates for (1R*,3R*,4S*,6R*)-1-methyl-2-methylene-6-(2-methylprop-1-enyl)-3-phenylbicyclo[2.2.1]heptan-7-one (91b)

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Energy HF/6-31G//HF/6-311G(d,p): \(-807.3102898\) Hartrees
APPENDIX C. X-ray Crystallographic Data

*(trans)*-5-hydroxy-2,3-dimethyl-4-phenylcyclopent-2-enone (38)

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<tr>
<td>Crystal Colour, Habit</td>
<td>colourless, needle</td>
</tr>
<tr>
<td>Crystal Dimensions</td>
<td>0.38 X 0.23 X 0.12 mm</td>
</tr>
<tr>
<td>Crystal System</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Lattice Type</td>
<td>C-centered</td>
</tr>
<tr>
<td>Indexing Images</td>
<td>4 oscillations @ 300.0 seconds</td>
</tr>
<tr>
<td>Detector Position</td>
<td>127.40 mm</td>
</tr>
<tr>
<td>Pixel Size</td>
<td>0.100 mm</td>
</tr>
<tr>
<td>Lattice Parameters</td>
<td>[a = 18.7028(14) , \text{Å}, \quad b = 5.9021(2) , \text{Å}, \quad c = 20.8680(12) , \text{Å}, \quad \beta = 106.022(3) , ^{\circ}, \quad V = 2214.0(2) , \text{Å}^3 ]</td>
</tr>
<tr>
<td>Space Group</td>
<td>( \text{C2/c} ) (#15)</td>
</tr>
<tr>
<td>Z value</td>
<td>8</td>
</tr>
<tr>
<td>( D_{\text{calc}} )</td>
<td>1.213 g/cm(^3)</td>
</tr>
<tr>
<td>( F_{\text{000}} )</td>
<td>864.00</td>
</tr>
</tbody>
</table>
\( \mu(\text{MoK}\alpha) \)  \hspace{2cm} 0.805 cm\(^{-1}\)

**Intensity Measurements**

**Diffractometer**  
Rigaku RAXIS-UNKNOWN

**Radiation**  
\( \text{MoK}\alpha(\lambda = 0.71070 \text{ Å}) \)  
graphite monochromated

**Data Images**  
60 exposures

\( \omega \) oscillation Range  
20.0 - 140.0\(^{\circ}\)

**Exposure Rate**  
456.0 sec./\(^{\circ}\)

\( \omega \) oscillation Range  
20.0 - 200.0\(^{\circ}\)

**Exposure Rate**  
456.0 sec./\(^{\circ}\)

**Detector Position**  
127.40 mm

**Pixel Size**  
0.100 mm

\( 2\theta_{\text{max}} \)  
144.7\(^{\circ}\)

**No. of Reflections Measured**  
Total: 41835  
Unique: 18822 (R\(_{\text{int}} \) = 0.035)

** Corrections**  
Lorentz-polarization

Absorption  
(trans. factors: 0.819 - 0.990)

Secondary Extinction  
(coefficient: 1.47210e+001)

**Structure Solution and Refinement**

**Structure Solution**  
Direct Methods (SHELX97)
Refinement

Full-matrix least-squares on F

Function Minimized

$\sum w (|F_o| - |F_c|)^2$

Least Squares Weights

Chebychev polynomial with 3 parameters: 9.8132, 5.0194, 6.4664,

2$\theta_{\text{max}}$ cutoff

52.0°

Anomalous Dispersion

All non-hydrogen atoms

No. Observations ($I > 3.00\sigma(I)$)

1841

No. Variables

178

Reflection/Parameter Ratio

10.34

Residuals: $R (I > 3.00\sigma(I))$

0.0634

Residuals: $R_w (I > 3.00\sigma(I))$

0.0795

Goodness of Fit Indicator

1.076

Max Shift/Error in Final Cycle

0.004

Maximum peak in Final Diff. Map

0.51 e-/Å³

Minimum peak in Final Diff. Map

-0.25 e-/Å³

(3a$R^*$,7a$S^*$)-3-Methyl-1-oxo-3a,4,5,6,7,7a-hexahydro-1H-inden-7a-yl-3,5-dinitrobenzoate (50)

Crystal Data

Empirical Formula

C$_{17}$H$_{16}$O$_7$N$_2$

Formula Weight

360.32
<table>
<thead>
<tr>
<th><strong>Crystal Colour, Habit</strong></th>
<th>colourless, plate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Crystal Dimensions</strong></td>
<td>0.27 X 0.13 X 0.09 mm</td>
</tr>
<tr>
<td><strong>Crystal System</strong></td>
<td>triclinic</td>
</tr>
<tr>
<td><strong>Lattice Type</strong></td>
<td>Primitive</td>
</tr>
<tr>
<td><strong>Indexing Images</strong></td>
<td>4 oscillations @ 300.0 seconds</td>
</tr>
<tr>
<td><strong>Detector Position</strong></td>
<td>127.40 mm</td>
</tr>
<tr>
<td><strong>Pixel Size</strong></td>
<td>0.100 mm</td>
</tr>
<tr>
<td><strong>Lattice Parameters</strong></td>
<td></td>
</tr>
<tr>
<td>a</td>
<td>10.9142(12) Å</td>
</tr>
<tr>
<td>b</td>
<td>11.9957(12) Å</td>
</tr>
<tr>
<td>c</td>
<td>13.3277(7) Å</td>
</tr>
<tr>
<td>α</td>
<td>87.550(11) °</td>
</tr>
<tr>
<td>β</td>
<td>76.214(11) °</td>
</tr>
<tr>
<td>γ</td>
<td>89.882(15) °</td>
</tr>
<tr>
<td>V</td>
<td>1693.0(3) Å³</td>
</tr>
<tr>
<td><strong>Space Group</strong></td>
<td>P-1 (#2)</td>
</tr>
<tr>
<td><strong>Z value</strong></td>
<td>4</td>
</tr>
<tr>
<td><strong>Dcalc</strong></td>
<td>1.414 g/cm³</td>
</tr>
<tr>
<td><strong>F000</strong></td>
<td>752.00</td>
</tr>
<tr>
<td><strong>μ(MoKα)</strong></td>
<td>1.114 cm⁻¹</td>
</tr>
</tbody>
</table>

**Intensity Measurements**

<table>
<thead>
<tr>
<th><strong>Diffractometer</strong></th>
<th>Rigaku RAXIS-UNKNOWN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Radiation</strong></td>
<td>MoKα(λ = 0.71070 Å)</td>
</tr>
<tr>
<td></td>
<td>graphite monochromated</td>
</tr>
<tr>
<td>Parameter</td>
<td>Value</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Detector Aperture</td>
<td>0 mm x 0 mm</td>
</tr>
<tr>
<td>Data Images</td>
<td>45 exposures</td>
</tr>
<tr>
<td>ω oscillation Range</td>
<td>160.0 - 190.0°</td>
</tr>
<tr>
<td>Exposure Rate</td>
<td>300.0 sec./°</td>
</tr>
<tr>
<td>ω oscillation Range</td>
<td>113.8 - 188.8°</td>
</tr>
<tr>
<td>Exposure Rate</td>
<td>300.0 sec./°</td>
</tr>
<tr>
<td>ω oscillation Range</td>
<td>51.0 - 175.0°</td>
</tr>
<tr>
<td>Exposure Rate</td>
<td>300.0 sec./°</td>
</tr>
<tr>
<td>Detector Position</td>
<td>127.40 mm</td>
</tr>
<tr>
<td>Pixel Size</td>
<td>0.100 mm</td>
</tr>
<tr>
<td>2θmax</td>
<td>71.2°</td>
</tr>
<tr>
<td>No. of Reflections Measured</td>
<td>Total: 23233</td>
</tr>
<tr>
<td></td>
<td>Unique: 12273 (R_{int} = 0.042)</td>
</tr>
<tr>
<td>Corrections</td>
<td>Lorentz-polarization</td>
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<tr>
<td></td>
<td>Absorption</td>
</tr>
<tr>
<td></td>
<td>(trans. factors: 0.809 - 0.990)</td>
</tr>
<tr>
<td>Structure Solution and Refinement</td>
<td></td>
</tr>
<tr>
<td>Structure Solution</td>
<td>Direct Methods (SHELX97)</td>
</tr>
<tr>
<td>Refinement</td>
<td>Full-matrix least-squares on F</td>
</tr>
<tr>
<td>Function Minimized</td>
<td>$\Sigma \ w \ (</td>
</tr>
</tbody>
</table>
Least Squares Weights
Chebychev polynomial with 3 parameters
8.7104,-1.0291,6.8722,

$2\theta_{\text{max}}$ cutoff
60.0°

Anomalous Dispersion
All non-hydrogen atoms

No. Observations (I>3.00σ (I))
4429

No. Variables
470

Reflection/Parameter Ratio
9.42

Residuals: R (I>3.00σ (I))
0.0496

Residuals: Rw (I>3.00σ (I))
0.0529

Goodness of Fit Indicator
1.161

Max Shift/Error in Final Cycle
0.000

Maximum peak in Final Diff. Map
0.31 e⁻/Å³

Minimum peak in Final Diff. Map
-0.20 e⁻/Å³

2,5-Bis(4-methoxyphenyl)-1-methyl-3-(2-methylbuta-2,3-dienoyl)-6-methylene bicyclo[2.2.1]heptan-7-one (67)

Crystal Data

Empirical Formula
C$_{28}$H$_{28}$O$_{4}$

Formula Weight
428.53

Crystal Colour, Habit
colourless, needle-plate

Crystal Dimensions
0.34 X 0.13 X 0.04 mm
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal System</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Lattice Type</td>
<td>Primitive</td>
</tr>
<tr>
<td>Indexing Images</td>
<td>4 oscillations @ 300.0 seconds</td>
</tr>
<tr>
<td>Detector Position</td>
<td>127.40 mm</td>
</tr>
<tr>
<td>Pixel Size</td>
<td>0.100 mm</td>
</tr>
<tr>
<td>Lattice Parameters</td>
<td>a = 13.1142(11) Å</td>
</tr>
<tr>
<td></td>
<td>b = 11.7261(11) Å</td>
</tr>
<tr>
<td></td>
<td>c = 14.7870(13) Å</td>
</tr>
<tr>
<td></td>
<td>β = 90.486(6) °</td>
</tr>
<tr>
<td></td>
<td>V = 2273.8(3) Å</td>
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<tr>
<td>Space Group</td>
<td>P2₁/a (#14)</td>
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<tr>
<td>Z value</td>
<td>4</td>
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<tr>
<td>Dcalc</td>
<td>1.252 g/cm³</td>
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<tr>
<td>F000</td>
<td>912.00</td>
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<tr>
<td>μ(MoKα)</td>
<td>0.825 cm⁻¹</td>
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<tr>
<td>Intensity Measurements</td>
<td></td>
</tr>
<tr>
<td>Diffractometer</td>
<td>Rigaku RAXIS-UNKNOWN</td>
</tr>
<tr>
<td>Radiation</td>
<td>MoKα(λ = 0.71070 Å)</td>
</tr>
<tr>
<td></td>
<td>graphite monochromated</td>
</tr>
<tr>
<td>Detector Aperture</td>
<td>0 mm x 0 mm</td>
</tr>
<tr>
<td>Data Images</td>
<td>24 exposures</td>
</tr>
<tr>
<td>ω Oscillation Range</td>
<td>40.0 - 164.0°</td>
</tr>
<tr>
<td>Description</td>
<td>Value</td>
</tr>
<tr>
<td>-------------------------------------------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Exposure Rate</td>
<td>600.0 sec./°</td>
</tr>
<tr>
<td>Detector Position</td>
<td>127.40 mm</td>
</tr>
<tr>
<td>Pixel Size</td>
<td>0.100 mm</td>
</tr>
<tr>
<td>2θ_{\text{max}}</td>
<td>72.8°</td>
</tr>
<tr>
<td>No. of Reflections Measured</td>
<td>Total: 17805</td>
</tr>
<tr>
<td></td>
<td>Unique: 9087 (R_{int} = 0.059)</td>
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<tr>
<td>Corrections</td>
<td>Lorentz-polarization</td>
</tr>
<tr>
<td>Structure Solution and Refinement</td>
<td></td>
</tr>
<tr>
<td>Structure Solution</td>
<td>Direct Methods (SHELX97)</td>
</tr>
<tr>
<td>Refinement</td>
<td>Full-matrix least-squares on F</td>
</tr>
<tr>
<td>Function Minimized</td>
<td>$\Sigma w \left(</td>
</tr>
<tr>
<td>Least Squares Weights</td>
<td>Chebychev polynomial with 3 parameters</td>
</tr>
<tr>
<td></td>
<td>14.0989,-6.7772,10.5568,</td>
</tr>
<tr>
<td>2θ_{\text{max}} cutoff</td>
<td>54.0°</td>
</tr>
<tr>
<td>Anomalous Dispersion</td>
<td>All non-hydrogen atoms</td>
</tr>
<tr>
<td>No. Observations (I&gt;3.00σ (I))</td>
<td>2883</td>
</tr>
<tr>
<td>No. Variables</td>
<td>317</td>
</tr>
<tr>
<td>Reflection/Parameter Ratio</td>
<td>9.09</td>
</tr>
<tr>
<td>Residuals: R (I&gt;3.00σ (I))</td>
<td>0.0552</td>
</tr>
<tr>
<td>Residuals: Rw (I&gt;3.00σ (I))</td>
<td>0.0612</td>
</tr>
<tr>
<td>Goodness of Fit Indicator</td>
<td>1.143</td>
</tr>
</tbody>
</table>
Max Shift/Error in Final Cycle

0.000

Maximum peak in Final Diff. Map

0.28 e\(^{-}/Å^3\)

Minimum peak in Final Diff. Map

-0.23 e\(^{-}/Å^3\)

(1S\(^*\),2R\(^*\),4E)-1,2,5,6-Tetrabromo-4-methyl-1-phenylhex-4-en-3-one (85)

Crystal Data

Empirical Formula

C\(_{13}\)H\(_{12}\)Br\(_4\)O

Formula Weight

503.85

Crystal Colour, Habit

colourless, plate

Crystal Dimensions

0.25 X 0.17 X 0.03 mm

Crystal System

monoclinic

Lattice Type

Primitive

Indexing Images

4 oscillations @ 1500.0 seconds

Detector Position

127.40 mm

Pixel Size

0.100 mm

Lattice Parameters

a = 11.619(3) Å
b = 5.6336(14) Å
c = 13.014(4) Å
β = 115.711(11) °
V = 767.5(4) Å\(^3\)

Space Group

P2\(_1\) (#4)

Z value

2
| **Dcalc** | 2.180 g/cm$^3$ |
| **F000** | 476.00 |
| **μ(MoKα)** | 105.037 cm$^{-1}$ |

**Intensity Measurements**

| **Diffractometer** | Rigaku RAXIS-UNKNOWN |
| **Radiation** | MoKα ($λ = 0.71070$ Å) graphite monochromated |
| **Data Images** | 33 exposures |
| **ω oscillation Range** | 30.0 - 60.0° |
| **Exposure Rate** | 480.0 sec./° |
| **ω oscillation Range** | 53.8 - 188.8° |
| **Exposure Rate** | 480.0 sec./° |
| **Detector Position** | 127.40 mm |
| **Pixel Size** | 0.100 mm |
| **2θmax** | 145.9° |
| **No. of Reflections Measured** | Total: 15882  
Unique: 13242 ($R_{\text{int}} = 0.086$)  
Friedel pairs: 3455 |
| **Corrections** | Lorentz-polarization Absorption  
(trans. factors: 0.185 - 0.730)  
Secondary Extinction  
(coefficient: 3.93220e+001) |
<table>
<thead>
<tr>
<th><strong>Structure Solution and Refinement</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Structure Solution</strong></td>
<td>Direct Methods (SHELX97)</td>
</tr>
<tr>
<td><strong>Refinement</strong></td>
<td>Full-matrix least-squares on $F^2$</td>
</tr>
<tr>
<td><strong>Function Minimized</strong></td>
<td>$\sum w (Fo^2 - Fc^2)^2$</td>
</tr>
<tr>
<td><strong>Least Squares Weights</strong></td>
<td>Chebychev polynomial with 3 parameters: 14515.5000, 19188.5000, 0.0000,</td>
</tr>
<tr>
<td><strong>$2\theta_{\text{max}}$ cutoff</strong></td>
<td>60.0°</td>
</tr>
<tr>
<td><strong>Anomalous Dispersion</strong></td>
<td>All non-hydrogen atoms</td>
</tr>
<tr>
<td><strong>No. Observations ($I&gt;3.60\sigma(I)$)</strong></td>
<td>1905</td>
</tr>
<tr>
<td><strong>No. Variables</strong></td>
<td>175</td>
</tr>
<tr>
<td><strong>Reflection/Parameter Ratio</strong></td>
<td>10.89</td>
</tr>
<tr>
<td><strong>Residuals: R1 ($I&gt;3.60\sigma(I)$)</strong></td>
<td>0.0892</td>
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<tr>
<td><strong>Residuals: wR2 ($I&gt;3.60\sigma(I)$)</strong></td>
<td>0.0844</td>
</tr>
<tr>
<td><strong>Goodness of Fit Indicator</strong></td>
<td>1.275</td>
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<tr>
<td><strong>Flack Parameter (Friedel pairs = 3455)</strong></td>
<td>0.22(4)</td>
</tr>
<tr>
<td><strong>Max Shift/Error in Final Cycle</strong></td>
<td>0.015</td>
</tr>
<tr>
<td><strong>Maximum peak in Final Diff. Map</strong></td>
<td>$1.91 \text{ e}^-/\text{Å}^3$</td>
</tr>
<tr>
<td><strong>Minimum peak in Final Diff. Map</strong></td>
<td>$-1.82 \text{ e}^-/\text{Å}^3$</td>
</tr>
</tbody>
</table>
(1R*,6S*,7R*)-1,3,4-Trimethyl-8-methylene-7-phenylbicyclo[4.2.1]non-3-en-9-one (90)

**Crystal Data**

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
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</thead>
<tbody>
<tr>
<td>Empirical Formula</td>
<td>C\textsubscript{19}H\textsubscript{22}O</td>
</tr>
<tr>
<td>Formula Weight</td>
<td>266.38</td>
</tr>
<tr>
<td>Crystal Colour, Habit</td>
<td>colourless, plate</td>
</tr>
<tr>
<td>Crystal Dimensions</td>
<td>0.36 X 0.24 X 0.13 mm</td>
</tr>
<tr>
<td>Crystal System</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Lattice Type</td>
<td>Primitive</td>
</tr>
<tr>
<td>Indexing Images</td>
<td>4 oscillations @ 300.0 seconds</td>
</tr>
<tr>
<td>Detector Position</td>
<td>127.40 mm</td>
</tr>
<tr>
<td>Pixel Size</td>
<td>0.100 mm</td>
</tr>
<tr>
<td>Lattice Parameters</td>
<td>a = 12.3808(5) Å</td>
</tr>
<tr>
<td></td>
<td>b = 7.1865(2) Å</td>
</tr>
<tr>
<td></td>
<td>c = 17.5078(8) Å</td>
</tr>
<tr>
<td></td>
<td>β = 98.452(2)°</td>
</tr>
<tr>
<td></td>
<td>V = 1540.83(10) Å\textsuperscript{3}</td>
</tr>
<tr>
<td>Space Group</td>
<td>P2\textsubscript{1}/a (#14)</td>
</tr>
<tr>
<td>Z value</td>
<td>4</td>
</tr>
<tr>
<td>D\textsubscript{calc}</td>
<td>1.148 g/cm\textsuperscript{3}</td>
</tr>
<tr>
<td>F000</td>
<td>576.00</td>
</tr>
<tr>
<td>μ(MoKα)</td>
<td>0.686 cm\textsuperscript{-1}</td>
</tr>
</tbody>
</table>

**Intensity Measurements**

<p>| Diffractometer                    | Rigaku RAXIS-RAPID          |</p>
<table>
<thead>
<tr>
<th><strong>Radiation</strong></th>
<th>MoKα(λ = 0.71070 Å) graphite monochromated</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Data Images</strong></td>
<td>51 exposures</td>
</tr>
<tr>
<td><strong>ω oscillation Range</strong></td>
<td>70.0 - 198.0°</td>
</tr>
<tr>
<td><strong>Exposure Rate</strong></td>
<td>360.0 sec./°</td>
</tr>
<tr>
<td><strong>ω oscillation Range</strong></td>
<td>72.5 - 202.5°</td>
</tr>
<tr>
<td><strong>Exposure Rate</strong></td>
<td>360.0 sec./°</td>
</tr>
<tr>
<td><strong>Detector Position</strong></td>
<td>127.40 mm</td>
</tr>
<tr>
<td><strong>Pixel Size</strong></td>
<td>0.100 mm</td>
</tr>
<tr>
<td><strong>2θmax</strong></td>
<td>71.5°</td>
</tr>
<tr>
<td><strong>No. of Reflections Measured</strong></td>
<td>Total: 23169, Unique: 5766 (Rint = 0.019)</td>
</tr>
<tr>
<td><strong>Corrections</strong></td>
<td>Lorentz-polarization</td>
</tr>
</tbody>
</table>

**Structure Solution and Refinement**

- **Structure Solution**: Direct Methods (SHELX97)
- **Refinement**: Full-matrix least-squares on F
- **Function Minimized**: \( \sum w (|F_o| - |F_c|)^2 \)
- **Least Squares Weights**: Chebychev polynomial with parameters 7.9587, 5.3376, 5.8881
- **2θmax cutoff**: 60.0°
- **Anomalous Dispersion**: All non-hydrogen atoms
- **No. Observations (I>3.00σ(I))**: 3007
- **No. Variables**: 203
- **Reflection/Parameter Ratio**: 14.81
<table>
<thead>
<tr>
<th>Description</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residuals: R (I&gt;3.00σ(I))</td>
<td>0.0526</td>
</tr>
<tr>
<td>Residuals: Rw (I&gt;3.00σ(I))</td>
<td>0.0693</td>
</tr>
<tr>
<td>Goodness of Fit Indicator</td>
<td>1.078</td>
</tr>
<tr>
<td>Max Shift/Error in Final Cycle</td>
<td>0.000</td>
</tr>
<tr>
<td>Maximum peak in Final Diff. Map</td>
<td>0.23 e⁻/Å³</td>
</tr>
<tr>
<td>Minimum peak in Final Diff. Map</td>
<td>-0.22 e⁻/Å³</td>
</tr>
</tbody>
</table>