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PART I
A VINYL SULFONE-MEDIATED DIELS-ALDER APPROACH TO THE
REGIOCONTROLLED ELABORATION OF 2-CYCLOHEXENONES

PART II
CONSTRUCTION OF FUSED 4-CYCLOOCTENONES BY CLAISEN
REARRANGEMENT AND APPROACHES TO THE
SYNTHESIS OF PRECAPNELLADIENE

Presented in Partial Fulfillment of the Requirements
for the Degree
DOCTOR OF PHILOSOPHY

By
WILLIAM ALVIN KINNEY, B.S.

* * * * * *

The Ohio State University
1984

Reading Committee:  Approved By
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Dr. Harold Shechter  Advised
Dr. Matthew S. Platz  Department of Chemistry
To Donald and Joan Kinney
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Special thanks go to Marlene Pease for her expertise in typing this manuscript.

Finally, I want to thank Professor Leo A. Paquette for an efficient environment in which to work and the freedom to pursue my research problem as I chose, although those choices were not always productive.
VITA

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PUBLICATIONS


FIELD OF STUDY

Major Field: Organic Chemistry
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PART I

A VINYL SULFONE-MEDIATED DIELS-ALDER APPROACH TO THE
REGIOCONTROLLED ELABORATION OF 2-CYCLOHEXENONES
CHAPTER 1

A NEW SYNTHON FOR THE REGIOSPECIFIC $\gamma$-ALKYLATION OF 2-CYCLOHEXENONES

Introduction

The acquisition of specifically substituted 2-cyclohexenones has occupied synthetic chemists for many years due to the wide utility of such intermediates in organic synthesis.\(^1\) Particular emphasis has been directed toward incorporation of groups at the $\gamma$-position, because of the value of 4-substituted 2-cyclohexenones in strategies directed toward natural products, e.g. as precursors to zingiberene (1)\(^2\) and anticapsin (2).\(^3\) However, functionalization at this position directly from 2-cyclohexenones is notoriously difficult for reasons outlined below.
Methods for generation of specific dienolates from α,β-unsaturated carbonyls have evolved over several decades leading to relatively routine substitution at the α'- and α-positions through alkylation chemistry. For example, kinetic deprotonation of 3 at the α'-carbon (Scheme I, A) with strong base yields dienolate 4 which when treated with methyl iodide affords exclusively 5. However, under equilibrating conditions (Scheme I, B) the thermodynamic dienolate 6 is formed; subsequent electrophile capture occurs exclusively at the α-position. Even when the γ-carbon is activated as in Hagemann's ester (7), the thermodynamic dienolate undergoes predominant α-alkylation (Scheme I, C).
SCHEME I

A. \[ \text{compound 3} \xrightarrow{\text{NCH(CH}_3)_2\text{Li, THF, 0°C}} \text{compound 4} \]
   \[ \xrightarrow{\text{CH}_3\text{I}} \text{compound 5} \]
   \[ \text{85%} \quad \text{(Ref. 4)} \]

B. \[ \text{compound} \xrightarrow{\text{KOT-Bu, t-BuOH, reflux}} \text{compound} \xrightarrow{\text{CH}_3\text{I}} \]
   \[ \text{(Ref. 5)} \]
   \[ \text{compound} \]
   \[ \text{44%} \quad \text{+} \quad \text{compound} \]
   \[ \text{9%} \]
   \[ \text{(Ref. 6)} \]

C. \[ \text{compound 7} \xrightarrow{1.) \text{NaOEt, EtOH, 65°C}} \text{compound} \]
   \[ \xrightarrow{2.) \text{CH}_3\text{I}} \text{compound} \]
   \[ \text{83%} \quad \text{+} \quad \text{compound} \]
   \[ \text{(4 : 1)} \]

D. \[ \text{compound} \xrightarrow{1.) >1 \text{equiv \ LDA, -78°C}} \text{compound} \]
   \[ \xrightarrow{2.) \text{CH}_3\text{I}} \text{compound} \]
   \[ \text{(70%)} \quad \text{(Ref. 7)} \]

D. \[ \text{compound} \xrightarrow{1.) <1 \text{equiv \ LDA, rt}} \text{compound} \]
   \[ \xrightarrow{2.) \text{CH}_3\text{I}} \text{compound} \]
   \[ \text{(73%)} \]
β-Enamino ketones (Scheme I, D) represent the only examples where substitution at the Y-position predominates.

As a direct consequence of the above, this important class of intermediates has necessarily been generated indirectly by a variety of means (Scheme II). The oldest and most straightforward method involves Birch reduction of p-substituted anisoles and acid hydrolysis of the resulting diene (Scheme II, A). Depending on the availability of the appropriate aromatic compound, this route is quite efficient. Stork developed the other most commonly used synthesis of these materials (Scheme II, B): alkylation of 1,3-cyclohexanedione enol ethers, reduction with lithium aluminum hydride, and acid hydrolysis. Though very convenient, this route does not permit the attachment of unprotected oxidized functionality on the side chain. Two more exotic methods have been introduced recently (Scheme II, C, D) by Wenkert and Birch. The former, involving copper bronze-catalyzed addition of ethyl diazoacetate, is limited by poor regiocontrol and low yields. Addition of nucleophiles to tricarbonylmethoxycyclohexadienyliiron cations followed by
SCHEME II

A. \[
\text{C}_{6}\text{H}_{4}OMe} \xrightarrow{1.) \text{Na, NH}_3, \text{EtOH}} \text{C}_2\text{H}_2 \xrightarrow{2.) \text{H}^+, \text{EtOH reflux}} \text{C}_2\text{H}_2 \xrightarrow{\text{H}_2\text{SO}_4} \text{C}_2\text{H}_2 (\text{Ref. 8})
\]

B. \[
\text{C}_{6}\text{H}_4\text{OMe} \xrightarrow{1.) \text{LDA}} \text{C}_{6}\text{H}_4\text{O}C\text{C} = \text{CH}_2 \xrightarrow{1.) \text{LAH}} \text{C}_2\text{H}_2 (\text{80%})
\]

C. \[
\text{C}_{6}\text{H}_4\text{OMe} \xrightarrow{\text{EtOCCCHN}_2, \text{Cu}} \text{C}_{6}\text{H}_4\text{O}C\text{CCH}_2\text{CH}_3 + \text{C}_{6}\text{H}_4\text{OMe} \xrightarrow{\text{HCl, EtOH}} \text{C}_2\text{H}_2 (\text{Ref. 10})
\]

D. \[
\text{C}_{6}\text{H}_4\text{OMe} \xrightarrow{1.) \text{SiMe}_3} \text{C}_{6}\text{H}_4\text{Fe(CO)}_3 \xrightarrow{2.) \text{Ce(IV), AcOH}} \text{C}_2\text{H}_2 (63\%)
\]
SCHEME II (Cont'd.)

E. $\text{CHO} \xrightarrow{\text{K}_2\text{CO}_3} \text{1.} \xrightarrow{\text{2.}} \text{H}^+$

F. $\text{1.} \xrightarrow{\text{LDA}} \text{2.} \xrightarrow{\text{TMSCl}} (77\%)$

G. $\text{Me}_3\text{N}^+\text{OH}^- \xrightarrow{\text{MeOH}} \text{HCl} \xrightarrow{\text{DMSO}} (95\%)$

H. $\text{1.} \xrightarrow{\text{MeCO}_2\text{H}} \text{2.} \xrightarrow{\text{H}^+} \xrightarrow{\text{Me}_2\text{SO}_4} \text{NaOH} (85\%)$

I. $\text{MeO}_2\text{C} \xrightarrow{\text{1.}} \xrightarrow{\text{2.}} \text{H}^+$

(Ref. 12)

(24%)

(Ref. 13)

(57%)

(Ref. 3)

(Ref. 14)

(Ref. 15)

(1 : 8)

(79%)
oxidation cleanly affords 4-substituted 2-cyclohexenones. However, the generality of this process is yet to be demonstrated. Another procedure (Scheme II, E), involving enamine-methyl vinyl ketone condensations, is fairly efficient if the appropriately substituted acetaldehyde moiety is readily available, as in this case in which (+)-citronellal is involved. Recent work by Fleming (Scheme II, F) has shown that zinc bromide-catalyzed alkylation of O-silylated dienolates leads to 4-substituted cyclohexenones in a few isolated examples. Finally, 1,6-addition of methyl nitroacetate to 4-methylene-cyclohex-2-enone (Scheme II, G), Baeyer-Villiger fragmentation of 1-methoxy-bicyclo[2.2.2]oct-5-enones (Scheme II, H), and cycloaddition of methyl acrylate with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Scheme II, I) afford a series of homologous 4-substituted esters expediently. Although these procedures are highly imaginative, all are in some way restricted in substrate structure.

In considering a general strategy to achieve net substitution at the \( \gamma \)-position, we were attracted to a solution which involved the Diels-Alder reaction of a terminal olefin with Danishefsky's diene\(^{15} \) (Figure 1). Unactivated olefins, however, lack both regiocontrol
Figure 1. Diels-Alder Strategy to 4-Substituted 2-Cyclohexenones

and the π-acceptor ability for addition to even such reactive dienes. An activating group was, therefore, required; further, its ultimate replacement by an R group had to be readily effected. Earlier experimentation in this laboratory (Scheme III) demonstrated the use of phenyl vinyl sulfone as a suitable terminal olefin equivalent in cycloadditions.
Regiospecificity was observed in the Diels-Alder reaction and the sulfone group was converted to a desired side chain via alkylation and desulfonylation chemistry in excellent yields. It was also known\textsuperscript{17,18} that unsaturated sulfonyl anions generally react in a regiocontrolled manner at the position $\alpha$ to the sulfonyl substituent (Scheme IV).
Thus, the combination of this cumulative experience led to the choice of 9 as a possible synthon for the 4-(2-cyclohexenyl) anion 10.
Results and Discussion

It was our initial hope that 9, efficiently prepared from phenyl vinyl sulfone and Danishefsky's diene (Scheme V), would be the solution to the longstanding problem of achieving γ-alkylation of 2-cyclohexenones. When 9 was alkylated with excess electrophile a mixture of products 11 and 12 was observed. Because of this weak regiocontrol, ketal 13 was prepared (Scheme VI) by direct ketalization of the Diels-Alder adduct in a one pot synthesis in 85% yield.
It was our expectation that anion 14 derivable from 13 would exhibit heightened nucleophilicity at the carbon atom directly bonded to the phenylsulfonyl substituent because the ketal group would eliminate carbonyl activation and provide steric congestion at the other position. Indeed, when 13 was deprotonated with sodium hydride in dimethylformamide and treated with the desired alkylating agent, the conversion proceeded efficiently and with regiospecificity affording 15 (Table I).
SCHEME VI

\[
\begin{align*}
\text{Me} & \quad \text{PPTS} \\
\text{wet acetone} & \\
CC & DMF \\
(TsOH) & \\
\text{16% NaPO}_4 & \\
\text{MeOH} & \\
\text{SO}_2\text{Ph} & \\
\text{I} & \\
\text{0} & \\
\text{U} & \\
\text{PPTS} & \\
wet acetone & \\
\text{R-SO}_2\text{Ph} & \\
\text{I} & \\
\text{15} & \\
\text{R-X} & \\
\text{6% Na(Hg)} & \\
\text{Na}_2\text{HPO}_4 & \\
\text{MeOH} & \\
\text{95% EtOH} & \\
\text{17 (major)} & \\
\text{I} & \\
\text{R} & \\
\text{18} & \\
\text{19} & \\
\text{R} & \\
\text{16} & \\
\end{align*}
\]
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*Values derived from product quantities isolated because accurate ¹H NMR integration was not possible.

*Longer heating gave rise to an equilibrium ratio of 69:31.
In general, the alkylation products were characterized via their enones 16 after deketalization with pyridinium p-toluenesulfonate (PPTS)\textsuperscript{19} in wet acetone. When preliminary examination of the direct desulfonylation of 16 with various reagents did not proceed as well as desired, we turned to the reduction of 15 with 6% sodium amalgam in Na\textsubscript{2}HPO\textsubscript{4}-buffered methanol.\textsuperscript{20} These reactions were usually complete within 30 min at room temperature, the pendant functional groups were not chemically altered, and yields of pure products generally bordered on quantitative. A preponderance of the more thermodynamically favored $\beta,\gamma$-unsaturated ketal 17 was routinely observed (\textsuperscript{1}H NMR analysis, Table I). In fact, treatment of the mixture with tlc grade silica gel afforded exclusively 17. Acid hydrolysis of these mixtures delivered the target cyclohexenones 18 $\rightarrow$ 19. In most instances, \textsuperscript{1}H NMR spectroscopy and/or chromatographic separation indicated the predominance of the $\alpha,\beta$ isomer 18, as expected. Little effort was made to determine the precise positions of equilibrium for these product pairs since this issue has been previously examined by others\textsuperscript{21} and is reasonably well understood.
The \( \beta,\gamma \) isomer 19 can be prepared exclusively by treatment of the ketal isomers with PPTS in wet acetone.\(^{22}\) These conditions are apparently sufficient to isomerize the unusually labile ketal olefins but not the product cyclohexenones.

It should be recognized that no difficulties were encountered in separating 18 from 19 by standard chromatography on silica gel. Accordingly, either double bond isomer is available in a pure state for further synthetic manipulation. Since the overall yields from 13 to the individual cyclohexenones are very good, this sulfonyl ketal is viewed as a useful, readily accessible, stable synthon for 10.

When 13 was condensed with 4-bromo-2-butanone ethylene ketal\(^{23}\) as before (Scheme VII), 20 resulted (85\%). Following independent conversion to 21 and 22, these diketones were exposed to alcoholic potassium hydroxide. In the first instance, the pair of highly crystalline bicyclic keto alcohols 23a and 24a was formed and isolated in yields of 72\% and 11\%, respectively. Preliminary structural assignment to these obviously epimeric (\(^1\)H NMR comparison) products was based on the premise that intramolecular aldol
SCHEME VII

1.) Na(Hg)$_2$, Na$_2$HPO$_4$, CH$_3$OH

Ph$_3$CH$_2$OH, KOH, CH$_3$OH

2.) CH$_3$Li

18
cyclization might well occur more rapidly from that conformation in which the carbonyl dipoles are opposed (see A). Some support for this conclusion was provided by the more highly shielded nature of the methyl singlet in 23a (δ 1.20) relative to 24a (δ 1.39), but these data are hardly conclusive. Consequently, 22 was comparably cyclized and the exclusive aldol product (23b) having a methyl singlet at δ 1.21 was sequentially hydrogenated and exposed to methyllithium. The diol so produced (25) was seen by 1H and 13C NMR analysis to be devoid of a plane of symmetry. Since the second methyl group in 25 is certain to have entered from the exo direction, the original alkyl substituent is required to be endo, in confirmation of the original structural hypothesis.

Synthesis of Zingiberenol

In an effort to delineate more fully the scope and limitations of the present methodology, application to the synthesis of a monocyclic natural product was viewed as desirable. Zingiberenol (26), a sesquiterpene alcohol recently isolated from the essential oil of Zingiber officinale Rosc,24 was of particular
SCHEME VIII

13

NaH, DMF

1. Na(Hg)
2. PPTS
3. NaOCH₃

CH₃OH

26

29

27

28

O

O

O

O

O

20
interest because of the need to effect the alkylation of 13 with a secondary tosylate \(28\)\(^{25}\) in its synthesis (Scheme VIII). By utilization of those conditions previously outlined, 29 was obtained as a mixture of diastereomers (47%) whose separation into two pure components could be accomplished readily by MPLC. Accompanying 29 was the aromatic sulfone 30 (15%), evidently the oxidized end product of a sequence initiated by 0-alkylation of 27. Following desulfonylation of 29 and hydrolysis to the conjugated enone, reaction with methyllithium furnished both 26 and 31. The desired trans isomer predominated (2.4:1) and was easily isolated in a pure state following chromatography. Although the sample of 26 prepared in this manner consisted of a mixture of two diastereomers, its infrared spectrum was superimposable upon that published for the naturally occurring substance.

**Conclusion**

The methodology described in this chapter has been demonstrated to be capable of introducing a wide variety of substituents and therefore provides a valuable addition to the repertoire of the synthetic
organic chemist. Obviously, the assets of this and other schemes must necessarily be weighed against other strategy considerations in the choice of an appropriate method for a given synthetic challenge. Extension of this approach to the \( \text{C}_5 \)-substitution of 2-cyclohexenones will be described in the following chapter. A particular advantage of this scheme is thereby illustrated.
CHAPTER 2

EXTENSION OF METHODOLOGY TO THE REGIOCONTROLLED ELABORATION OF 5-SUBSTITUTED AND 4,5-DISUBSTITUTED 2-CYCLOHEXENONES

Introduction

As mentioned in the previous chapter, kinetic and thermodynamic dienolates afford \( C_6^- \) and \( C_2^- \)-alkylated 2-cyclohexenones, respectively. The methodology developed in our laboratory, as well as others, facilitates introduction of groups at \( C_4^- \). Nucleophiles can be selectively added to enones in a 1,2 or 1,4 manner to deliver \( C_1^- \) and \( C_3^- \)-substituted materials. This leaves only the \( C_5^- \)-position, which has not received significant attention. This is due mostly to its inaccessibility via electrophilic or nucleophilic means, because of the lack of endogenous activation (Figure 2).
There has certainly been a necessity for strategies incorporating C₅-substitution both for the synthesis of monocyclic natural products, e.g. bilobanone (32) and cryptomerion (33), and for the synthesis of more complex structures not obviously related to 2-cyclohexenones, e.g. 34 as a precursor to coriolin (35). As the latter example suggests, an approach which affords C₄,C₅-disubstituted materials is highly desirable. Such methodology would also facilitate application to such natural products as curvularin (36).

The available methods for incorporation of appendages at the elusive C₅-position can be divided into
three categories (Scheme IX). Danishefsky (Scheme IX, A) has exploited the Diels-Alder reaction in the synthesis of cycloalkenones. The groups attached to the dienophile are transferred to the C\textsubscript{4}– and C\textsubscript{5}– positions of the product cyclohexenones. Birch and Semmelhack have independently developed schemes involving specific addition of nucleophiles to anisole-metalcarbonyl complexes (Scheme IX, B). Finally, classical annulation approaches have been utilized, for instance in the synthesis of bilobanone (32) (Scheme IX, C).
SCHEME IX

A.

\[ \text{MeO}_2\text{C} \quad + \quad \text{Me}^\text{OTMS} \quad \xrightarrow{1. \Delta} \quad \text{Me}^\text{OTMS} \quad \xrightarrow{2. \text{H}^+} \]

\[ \begin{align*} 
\text{CO}_2\text{Me} & \quad (20\%) \\
\text{CO}_2\text{Me} & \quad (5\%) \\
\text{CO}_2\text{Me} & \quad (5\%)
\end{align*} \]

B.

\[ \text{Fe(CO)}_3 \quad \xrightarrow{1. \Delta} \quad \text{PCC} \quad \xrightarrow{2. \text{H}^+} \]

\[ \text{( Ref. 15c) } \]

\[ \text{( Ref. 31) } \]
SCHEME IX (Cont'd.)

1. CF₃CO₂H
2. NH₄OH

(Ref. 32)

Ref. 27c
The Diels-Alder approach, inspired by Danishefsky and outlined in Chapter 1 (Figure 3, A), can be applied expediently to this challenge. The reactivity of the dienophile must be reversed (Figure 3, B) to afford net incorporation of appendages at C$_5$. The monosubstituted vinyl sulfone 39 would be expected to deliver the requisite regiocontrol. The phenylsulfonyl substituent could then be removed reductively to deliver 38 or could be converted to another group (Figure 3, C) by alkylation prior to removal, yielding 41. Therefore, 39 should behave as a useful olefin equivalent for both 37 and 40 in reaction with Danishefsky's diene.

**Results and Discussion**

In order to arrive rapidly at 39, recourse was made to the selenosulfonation of terminal alkenes. The thermal$^{33}$ and photochemical versions$^{34}$ of Se-phenyl benzeneselenolsulfonate addition to olefins were initially examined. Although both procedures provided the desired regioselectivity, the photochemical conditions proved substantially cleaner, more efficient, and easier to execute. It should be noted that because the selenolsulfonate reagent is both
Figure 3. Diels-Alder Strategy to 4- or 5-Monosubstituted and 4,5-Disubstituted 2-Cyclohexenones
thermally and photochemically labile, it should be wrapped in aluminum foil and kept cold for extended storage. Vinyl sulfones 43, 45, and 47 proved to be readily accessible by appropriate selenosulfonation of 42, 44, and 46 respectively and subsequent oxidative elimination (Scheme X).

**SCHEME X**

\[
\begin{align*}
\text{SiMe}_3 \quad & \text{PhSeSO}_2\text{Ph, hv} \quad \text{PhS}_2 \quad \text{SiMe}_3 \\
42 & \quad 43 \\
\text{PhS}_2 & \quad 44 \\
45 & \quad \text{OSi} \\
46 & \quad \text{OSi} \\
47 & \quad \text{OSi}
\end{align*}
\]

Also in this laboratory,\textsuperscript{35a} the tolerance of this procedure to a wide range of functional groups was seen, as evidenced by the suitability of such terminal
alkenes as phenyl allyl ether, trimethylvinylsilane, and acrolein dimethyl acetal.

Synthesis of 5-Substituted 2-Cyclohexenones

Crouse\textsuperscript{35a} demonstrated the utility of this procedure in generating a single substituent at C\textsubscript{5} in 2-cyclohexenones. Thus, reaction of 48 with the diene 49 afforded 50 after thermolysis and hydrolysis (Scheme XI). Reduction with zinc in acetic acid delivered 5-n-butyl-2-methyl-2-cyclohexenone (51). Those cycloadditions involving monosubstituted vinyl sulfones proved to be more sluggish than the phenyl vinyl sulfone examples, requiring refluxing xylenes in contrast to refluxing benzene, probably because of steric influences. At these temperatures, substantial decomposition of the diene occurred occasionally if the vinyl sulfone was not carefully purified.

Synthesis of 4,5-Disubstituted 2-Cyclohexenones

Vinyl sulfones 43, 45, and 47 were heated with 1-methoxy-3-(trimethylsilyl)oxybutadiene and ketalized
directly (Table II). Due to the acid lability of the tert-butyldimethylsilyloxy substituent in two of these substrates, the use of p-toluenesulfonic acid as ketalization catalyst necessitated resilylation prior to product isolation. Under these conditions, the \( \beta,\gamma \)-unsaturated ketals were formed as the predominant products. Since the subsequent step involves deprotonation, which provides the same allylic anion from either olefin, the isomeric ketals are directly usable without purification.
<table>
<thead>
<tr>
<th>Vinyl Sulfone</th>
<th>Ketal</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>![Structure 52]</td>
<td>88%</td>
</tr>
<tr>
<td>45</td>
<td>![Structure 53]</td>
<td>35%</td>
</tr>
<tr>
<td>47</td>
<td>![Structure 54]</td>
<td>74%</td>
</tr>
</tbody>
</table>
That the generation and trapping of these unsymmetrical anions is reasonably regioselective can be clearly seen in the conversion of 52 to 55 (Scheme XII). Notwithstanding the rather sterically congested environment about the \( \alpha \) sulfonyle carbon in this allylic intermediate, the charge affinity of the sulfonyle group dominates to deliver 55 rather cleanly (62% yield). Deketalization proceeded smoothly to give 56 (97%), the reductive desulfoniylation of which with zinc in acetic acid efficiently (80%) delivered \( \beta,\gamma \)-enone 57. Independent equilibration with sodium carbonate in methanol was required to arrive at 58.

For the remaining syntheses summarized in Table III, the phenylsulfonyle group was cleaved with sodium amalgam prior to ketal hydrolysis. This particular sequence was followed to avoid complications which had been encountered earlier during zinc reductions on substrates containing allylic substituents at C\(_4\).

It should be mentioned that somewhat reduced alkylation yields were realized when more bulky electrophiles such as 3-(trimethylsilyl)-2-butenyl iodide and geranyl bromide were utilized (Table III). These observations are attributed to reasonably competitive
SCHEME XII

1. NaOH, DMF (62%)

2. Br

(97%)

55

Py • HOTs

aq acetone

56

Me₃Si

PhSO₂

Zn, HOAc

(80%)

58

Na₂CO₃

CH₃OH (65%)

57
TABLE III. SEQUENTIAL ALKYLATION, REDUCTION, HYDROLYSIS, AND EQUILIBRATION OF 52, 53, and 54

<table>
<thead>
<tr>
<th>Ketal Electrophile</th>
<th>Yield</th>
<th></th>
<th>Yield</th>
<th></th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td></td>
<td>71</td>
<td></td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>53</td>
<td></td>
<td>35</td>
<td></td>
<td>69</td>
<td></td>
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<tr>
<td>54</td>
<td></td>
<td>41</td>
<td></td>
<td>71</td>
<td></td>
</tr>
<tr>
<td>54</td>
<td></td>
<td>29</td>
<td></td>
<td>75</td>
<td></td>
</tr>
</tbody>
</table>

- **52**: Br, \( R^1 = \text{CH}_2\text{CH}_2\text{SiMe}_3 \), \( R^2 = \text{CH}_2\text{CH} = \text{CH}_2 \)
- **53**: I, SiMe₃, \( R^1 = (\text{CH}_2)_4\text{OSi}^+ \), \( R^2 = \text{CH}_2\text{CH} = \text{C(\text{CH})}_3\text{SiMe}_3 \)
- **54**: Br, CH₃, CH₃, \( R^1 = \text{CH}_2\text{OSi}^+ \), \( R^2 = \text{geranyl} \)
- **54**: Br, O,C₆H₅, \( R^1 = \text{CH}_2\text{OSi}^+ \), \( R^2 = (\text{CH}_2)_2\text{OCH}_2\text{C}_6\text{H}_5 \)
α-alkylation arising because of steric interaction with R'. Small quantities of dialkylated product were therefore formed. The yield data which are cited refer to the amounts of pure γ-alkylated product obtained subsequent to MPLC purification.

In those equilibration studies involving 3-cyclohexenones 62a and 62b which carry a methylol side chain at C5, intramolecular cyclization to the oxabicyclo[3.2.1]octanones 64 occurs partially during base treatment. This phenomenon is understandably not observed when the hydroxy group is held more remotely as in 61b. As a direct consequence of their large polarity differences, the chromatographic separation of 63 from 64 can be readily accomplished.

\[ \text{62} \xrightarrow{\text{No}_2\text{CO}_3} \xrightarrow{\text{CH}_3\text{OH}} \text{63} \xrightarrow{} \text{64} \]

\( a, R = \text{geranyl} \); \( b, R = (\text{CH}_2)_2\text{OCH}_2\text{C}_6\text{H}_5 \)
Conclusion

The versatility of vinyl sulfones as terminal olefin and disubstituted olefin equivalents has been documented (Figure 3). When coupled with Danishefsky's diene, full regiocontrol was achieved and a convenient elaboration of 2-cyclohexenones was realized. Substitution at C$_4$ and C$_5$ was easily accomplished by proper choice of terminal olefins and electrophiles, providing usefully functionalized appendages. Undoubtedly, this scheme can be profitably applied to the synthesis of natural products, such as those mentioned earlier: bilobanone (32), cryptomerion (33) and curvularin (36). The utility of vinyl sulfones as alkene equivalents, providing $\pi$-acceptor ability and regiocontrol, however, is not limited to this particular problem and should be applied to other challenges in which a Diels-Alder strategy would be expedient.
EXPERIMENTAL

Melting points were determined in open capillaries with a Thomas-Hoover apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 467 instrument. Proton magnetic resonance spectra were obtained with Varian EM-360, EM-390, Bruker WP-200, and WM-300 spectrometers. Carbon spectra were recorded with Bruker WP-80, WP-200, and WM-300 instruments. Mass spectra were determined on AEI-MS9 and Kratos MS-30 spectrometers at an ionization potential of 70 eV. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.
A solution of phenyl vinyl sulfone\textsuperscript{[16]} (5.86g, 35 mmol) and 1-methoxy-3-(trimethylsilyl)-oxybutadiene\textsuperscript{[15]} (6.62g, 85% purity, 38.4 mmol) in 7 mL of benzene was refluxed under argon for 28h. The cooled reaction mixture was poured into 0.1 N hydrochloric acid (35 mL) and tetrahydrofuran (70 mL). Stirring was continued vigorously for 40 min, after which benzene (70 mL) was added and the aqueous layer was removed. The organic layer was washed with water (3x70 mL) and brine (70 mL), dried, and evaporated to yield a red-brown oil. The residue was purified on silica gel (150g, elution with 40% ethyl acetate in hexanes) to afford 7.1g (87%) of 9 as a marginally crystalline material; IR (CHCl\textsubscript{3}, cm\textsuperscript{-1}) 3010, 1690, 1448, 1316, 1205, 1150, 1085; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textsuperscript{\delta} 8.0-7.3 (m, 5H), 6.9 (dd, \textit{J} = 10 and 4 Hz, 1H), 6.1 (dd, \textit{J} = 10 and 2 Hz, 1H), 4.2-3.8 (m, 1H), 2.9-2.0 (series of m, 4H); m/e (M\textsuperscript{+}) calcd 236.0507, obs 236.0514.
4-Methyl-4-(benzenesulfonyl)-2-cyclohexenone (11)

To a cold (0°C) suspension of sodium hydride (54 mg of 50%, 1.1 mmol) in dimethylformamide \(^{18}\) (15 mL) under argon was injected a solution of 9 (195 mg, 0.82 mmol) in dimethylformamide (10 mL). Immediately thereafter methyl iodide (0.20 mL, 3.2 mmol) was added and the solution was stirred at rt overnight. The reaction mixture was poured into water (150 mL) and extracted with ether (4x75 mL). The combined organic extracts were washed with water (75 mL) and brine (75 mL), dried, and concentrated in vacuo yielding 196 mg (93%) of a crude mixture of 11 and 12 (56:44 ratio—\(^1\)H NMR analysis). The two isomers were readily separated by preparative tlc purification on silica gel (elution with 45% ethyl acetate in hexanes) affording 104 mg (51%) of 11, mp 91.5-93.0°C, and 70 mg (32%) of 12, mp 96.5-97.5°C.

For 11: IR (CHCl\(_3\), cm\(^{-1}\)) 3020, 1688, 1445, 1308, 1205, 1148, 1072; \(^1\)H NMR (CDCl\(_3\)) \(\delta 8.0-7.4\) (m, 5H), 6.73 (d, \(J = 11\) Hz, 1H), 6.07 (d, \(J = 11\) Hz, 1H),
2.8-1.9 (series of m, 4H), 1.53 (s, 3H); m/e (M⁺) calcd 250.0663, obs 250.0671.

Anal. Calcd for C₁₃H₁₄O₃S: C, 62.38; H, 5.64.
Found: C, 62.36; H, 5.65.

For 12: IR (CHCl₃, cm⁻¹) 3020, 2930, 1685, 1450, 1310, 1210, 1150, 1073; ¹H NMR (CDCl₃) δ 8.0-7.4 (m, 5H), 6.46 (br s, 1H), 2.8-1.8 (series of m, 4H), 1.76 (s, 3H), 1.45 (s, 3H); m/e (M⁺) calcd 264.0820, obs 264.0826.

Anal. Calcd for C₁₄H₁₆O₃S: C, 63.61; H, 6.10.
Found: C, 63.26; H, 6.00.

4,4-Ethylenedioxy-1-(benzenesulfonyl)cyclohexene (13)

![Structure of 4,4-Ethylenedioxy-1-(benzenesulfonyl)cyclohexene (13)]

A solution of phenyl vinyl sulfone (3.91 g, 23.2 mmol) and 1-methoxy-3-(trimethylsilyl)-oxybutadiene (4.98 g, 85% purity, 24.5 mmol) in benzene (10 mL) was heated at reflux for 28 hr. After cooling, ethylene glycol (3.5 g), p-toluenesulfonic acid (300 mg), and benzene (15 mL) were added, and the reaction mixture was heated with removal of water for an additional 23 h, cooled, diluted with
more solvent (40 mL), and extracted successively with saturated sodium bicarbonate solution (20 mL), water (20 mL), and brine (20 mL). The organic phase was dried and concentrated and the residue was chromatographed on silica gel (40 g, elution with 30% ethyl acetate in hexane). Crystallization of the product from ether afforded 5.53 g (85%) of pure 13 as colorless crystals, mp 77-78°C; IR (CHCl₃, cm⁻¹) 3010, 2880, 1647, 1444, 1368, 1300, 1200, 1150, 1118, 1088; ¹H NMR (CDCl₃) δ 7.9-7.3 (m, 5 H), 6.92-6.72 (m, 1 H), 3.86 (s, 4 H), 2.5-2.2 (m, 4 H), 1.68 (t, J = 6 Hz, 2 H); m/z (M⁺) calcd 280.0769, obs 280.0776.

6,6'-Ethylendioxy-3-methyl-3-(benzenesulfonyl)cyclohexene (15a)

A cold (0°C), magnetically stirred suspension of sodium hydride (101 mg of 50%, 2.1 mmol) in dry dimethylformamide (25 mL) was treated under argon with a solution of 13 (400 mg, 1.43 mmol) in 25 mL of the same
solvent. Immediately thereafter, methyl iodide (0.28 mL, 4.50 mmol) was added and the reaction mixture was stirred at room temperature for 5.5 h, poured into water (150 mL) and extracted with ether (4x75 mL). The combined organic layers were washed with water (75 mL) and brine (75 mL) prior to drying and solvent evaporation. Crystallization of the residue from ether furnished 350 mg (83%) of 15a as colorless crystals, mp 94-96°C; IR (CHCl₃, cm⁻¹) 3010, 2880, 1445, 1302, 1205, 1145, 1073; ¹H NMR (CDCl₃) δ 7.8-7.3 (m, 5 H), 5.88 (d, J = 10 Hz, 1 H), 5.78 (d, J = 10 Hz, 1 H), 3.77 (m, 4 H), 2.4-2.0 (m, 1 H), 1.9-1.5 (m, 3 H), 1.35 (s, 3 H).

Found: C, 61.09; H, 6.13.

The ketal group in 15a (317 mg, 1.08 mmol) was cleanly removed by heating at reflux with PPTS (73 mg) in wet acetone (11 mL) for 3 h. Following solvent evaporation, the residue was dissolved in ether (150 mL) and this solution was shaken in turn with 5% sodium bicarbonate solution (50 mL), 1 M hydrochloric acid (30 mL), and brine (30 mL) prior to drying. Concentration in vacuo and crystallization from ether gave 11 as colorless crystals, 255 mg (94%).
4-Methyl-2-cyclohexenone (18a) and 4-Methyl-3-cyclohexenone (19a)

Dry methanol (18 mL, distilled from magnesium methoxide) was introduced via syringe into a nitrogen-blanketed solution of 15a (530 mg, 1.80 mmol). Following the addition of disodium hydrogen phosphate (1.0 g) and pulverized 6% sodium amalgam\(^{20}\) (3.2 g), the reaction mixture was stirred until tlc analysis indicated the disappearance of starting material (2.5 h). Insoluble material was separated by filtration and the product was partitioned between ether (150 mL) and water (25 mL). The organic phase was washed with brine (25 mL), dried, and evaporated to give 248 mg (89%) of a liquid consisting predominantly of 17a (41:59 ratio-NMR analysis); IR (neat, cm\(^{-1}\)) 3010-2800, 1515, 1440, 1250, 1170, 1120, 1060, 850; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.54 (br d, 0.4 H), 5.29 (m, 0.6 H), 4.86 (d, \(J = 5\) Hz, 0.4 H), 3.98 (s, 2.4 H), 3.80 (br s, 1.6 H), 2.4-1.6 (m, 8.6 H).
The mixture of isomeric ketals (94 mg, 0.61 mmol) dissolved in 95% ethanol (15 mL) containing p-toluene-sulfonic acid (300 mg) was heated at reflux for 20.5 h. The majority of the solvent was removed on a rotary evaporator and the product was partitioned between ether (25 mL) and 5% sodium bicarbonate solution (15 mL). The organic phase was washed with brine, dried, and evaporated. $^1$H NMR analysis indicated the ratio of 18a to 19a to be 80:20. Chromatography on silica gel (5 g, dichloromethane elution) gave 19a (15 mg, 22%) and 18a (35 mg, 52%) in pure form.

For 18a: IR (neat, cm$^{-1}$) 3000-2800, 1690, 1460, 1395, 1380, 1255, 830, 750; $^1$H NMR (CDCl$_3$) $\delta$ 6.77 (br d, $\mathcal{J} = 11$ Hz, 1 H), 5.92 (dd, $\mathcal{J} = 11$ and 3 Hz, 1 H), 2.7-1.6 (series of m, 5 H), 1.17 (d, $\mathcal{J} = 7$ Hz, 3 H); m/e (M$^+$) calcd 110.0732, obs 110.0735.

For 19a: $^1$H NMR (CDCl$_3$) $\delta$ 5.40 (br s, 1 H), 2.82 (br s, 2 H), 2.46 (m, 4 H), 1.79 (br s, 3 H).
6,6-Ethlenedioxy-3-allyl-3-(benzenesulfonyl)cyclohexene (15b)

Alkylation of 13 (1.00 g, 3.57 mmol) with 50% sodium hydride (258 mg, 5.38 mmol) and allyl bromide (0.62 mL, 7.16 mmol) in 50 mL of dimethylformamide was accomplished with 3.5 h of stirring. Workup as before and chromatography of the resulting oil on silica gel (60 g, elution with 25% ethyl acetate in hexane) afforded a colorless oil which crystallized from ether to give 877 mg (77%) of 15b as a white powder, mp 81-83°C; IR (CHCl₃, cm⁻¹) 3090-2840, 1448, 1305, 1210, 1144, 1083, 930; H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.88 (d, J = 10 Hz, 1 H), 5.75 (d, J = 10 Hz, 1 H), 5.7-5.4 (m, 1 H), 5.2-4.9 (m, 2 H), 3.84 (s, 4 H), 2.7-1.5 (series of m, 6 H).

Hydrolysis of 15b (800 mg, 2.50 mmol) was carried out in wet acetone (20 mL) containing PPTS (150 mg) at the reflux temperature for 3 h. Subsequent workup and concentration in vacuo afforded 656 mg (95%) of 3-allyl-3-(benzenesulfonyl)-2-cyclohexenone as a colorless oil; IR (CHCl₃, cm⁻¹) 3100-2850, 1690, 1448,
1307, 1225, 1143, 1082, 924; $^1$H NMR (CDCl$_3$) $\delta$ 7.9-7.4 (m, 5 H), 6.64 (d, $\beta J = 11$ Hz, 1 H), 6.18 (d, $\beta J = 11$ Hz, 1 H), 5.8-5.4 (m, 1 H), 5.2-5.0 (m, 2 H), 2.8-2.2 (m, 6 H); m/z (M$^+$) calcd 276.0820, obs 276.0827.

4- Allyl-2-cyclohexenone (18b) and 4-allyl-3- cyclohexenone (19b)

Rapid (30 min), clean reduction of 15b (557 mg, 1.74 mmol) with 1.10 g of Na$_2$HPO$_4$ and 5.5 g of 6% Na(Hg) was seen. Workup and solvent removal yielded 307 mg (98%) of a 31:69 mixture of $\alpha$, $\beta/\beta$, $\gamma$ isomers; IR (neat, cm$^{-1}$) 3070, 3000-2800, 1655, 1635, 1605, 1430, 1240, 1205, 1150, 1110, 1050, 905, 850; $^1$H NMR (CDCl$_3$) $\delta$ 6.0-4.8 (m, 4.3 H), 3.99 (s, 2.8 H), 3.83 (br s, 1.2 H), 2.9-1.6 (series of m, 7.7 H).

Deketalization and equilibration was achieved by heating this mixture (275 mg, 1.52 mmol) with 59 mg of $p$-toluenesulfonic acid in 15 mL of 95% ethanol for 11 h. Subsequent workup and silica gel chromatography (20 g, elution with 10% ether in pentane) afforded 59 mg
(28%) of 19b followed by 93 mg (45%) of 18b (73% combined yield).

For 18b: IR (neat, cm⁻¹) 3100-2800, 1680, 1385, 1280, 1200, 985, 910; ¹H NMR (CDCl₃) δ 6.85 (br d, J = 11 Hz, 1 H), 5.96 (dd, J = 11 and 3 Hz, 1 H), 6.0-5.5 (m, 1 H), 5.3-4.9 (m, 2 H), 2.6-1.5 (series of m, 7 H); m/e (M⁺) calcd 136.0888, obs 136.0884.

For 19b: IR (neat, cm⁻¹) 3100-2800, 1720, 1640, 1510, 1430, 1340, 1180, 910; ¹H NMR (CDCl₃) δ 6.0-5.5 (m, 1 H), 5.47 (br s, 1 H), 5.2-4.9 (m, 2 H), 2.9-2.7 (m, 4 H), 2.45 (br s, 4 H); m/e (M⁺) calcd 136.0888, obs 136.0884.

6,6-Ethylendioxy-3-prenyl-3-
(benzenesulfonyl)cyclohexene (15c)

Comparable alkylation of 13 (1.00 g, 3.57 mmol) with 50% sodium hydride (258 mg, 5.38 mmol) and prenyl bromide (898 mg, 6.02 mmol) in dimethylformamide (50 mL) afforded 1.13 g (91%) of 15c as a white
powder, mp 91-92.5°C, after silica gel chromatography (70 g, elution with 15% ethyl acetate in hexane); IR (CHCl₃, cm⁻¹) 3080-2820, 1445, 1300, 1200, 1140, 1070; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.86 (d, J = 10 Hz, 1 H), 5.72 (d, J = 10 Hz, 1 H), 5.07 (m, 1 H), 3.83 (br s, 4 H), 2.7-1.8 (series of m, 6 H), 1.69 (s, 3 H), 1.62 (s, 3 H).

When 15c (343 mg, 0.98 mmol) was heated with pyridinium tosylate (77 mg) in wet acetone (20 mL) under reflux for 4 h, conversion to ketone 16c occurred: 260 mg (87%), colorless needles, mp 90-91°C (from ether); IR (CHCl₃, cm⁻¹) 3080-2840, 1690, 1450, 1310, 1230, 1148, 1088; ¹H NMR (CDCl₃) δ 8.0-7.3 (m, 5 H), 6.60 (d, J = 10 Hz, 1 H), 6.19 (d, J = 10 Hz, 1 H), 4.96 (m, 1 H), 2.7-1.8 (series of m, 6 H), 1.64 (2s, 6 H).

Desulfonylation of 15c (458 mg, 1.32 mmol) was performed as before with 830 mg of Na$_2$HPO$_4$ and 4.1 g of 6% Na(Hg) in 20 mL of dry methanol over a period of 40 min. Workup and concentration afforded 275 mg (100%) of ketal consisting of $\beta,\gamma$-(66%) and $\alpha,\beta$-unsaturated isomers (34%); IR (neat, cm$^{-1}$) 3000-2800, 1660, 1610, 1440, 1370, 1240, 1210, 1110, 1050, 850; $^1$H NMR (CDCl$_3$) $\delta$ 5.55 (br d, $\mathcal{J} = 5$ Hz, 0.3 H), 5.30 (br s, 0.7 H), 5.14 (br t, $\mathcal{J} = 7$ Hz, 1 H), 4.88 (d, $\mathcal{J} = 5$ Hz, 0.3 H), 3.98 (s, 2.8 H), 3.83 (s, 1.2 H), 2.8-2.5 (m, 2 H), 2.3-2.0 (m, 5.7 H), 1.74 (s, 3 H), 1.64 (s, 3 H).

Hydrolysis of this material (234 mg, 1.12 mmol) with p-toluenesulfonic acid (50 g) in 95% ethanol (reflux, 11 h) afforded a 62:38 mixture of $\alpha,\beta$- and $\beta,\gamma$-unsaturated ketones. Chromatography on silica gel (20 g, elution with 5% ether in pentane) gave 58 mg of crude 19c and 112 mg (61%) of pure 18c. Preparative
tli chromatography of 19c (silica gel, elution with 30% ether in pentane) afforded 48 mg of pure enone (87% combined yield).

For 18c: IR (neat, cm\(^{-1}\)) 3050-2800, 1680, 1450, 1380, 1240, 1200; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.83 (br d, \(J = 11\) Hz, 1 H), 5.95 (dd, \(J = 11\) and 2Hz, 1 H), 5.15 (br t, \(J = 7\) Hz, 1 H), 2.6-2.0 (m, 7 H), 1.77 (s, 3 H), 1.67 (s, 3 H); m/e (M\(^+\)) calcd 164.1201, obs 164.1199.

For 19c: IR (neat, cm\(^{-1}\)) 3050-2800, 1725, 1445, 1375, 1335, 1190, 840, 790; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.43 (br s, 1 H), 5.13 (br t, \(J = 7\) Hz, 1 H), 2.9-2.6 (m, 4 H), 2.5-2.3 (m, 4 H), 1.76 (s, 3 H), 1.66 (s, 3 H); m/e (M\(^+\)) calcd 164.1201, obs 164.1198.

6,6-Ethylenedioxy-3-benzyl-3-(benzenesulfonyl)cyclohexene (15d)

From 1.00 g (3.57 mmol) of 13, 258 mg (5.38 mmol) of 50% sodium hydride, and 1.02 g (6.0 mmol) of benzyl bromide in dimethylformamide (50 mL) (rt, 4 h), there was obtained
1.07 g (81%) of 15d as a colorless solid, mp 106-107°C (from ether); IR (CHCl₃, cm⁻¹) 3100-2860, 1450, 1310, 1230, 1150, 1125, 1090; ¹H NMR (CDCl₃) δ 8.1-7.4 (m, 5 H), 7.16 (br s, 5 H), 5.94 (d, J = 10 Hz, 1 H), 5.80 (d, J = 10 Hz, 1 H), 3.63 (br s, 4 H), 3.22 (br s, 2 H), 2.3-1.1 (series of m, 4 H).

Hydrolysis of this material (704 mg, 1.90 mmol) in wet acetone (20 mL) containing pyridinium tosylate (153 mg) (reflux, 4 h) yielded 486 mg (78%) of ketone 16d as colorless needles, mp 108-110°C, after recrystallization from ether; IR (CHCl₃, cm⁻¹) 3100-2840, 1685, 1450, 1310, 1250, 1148, 1090; ¹H NMR (CDCl₃) δ 8.0-7.4 (m, 5 H), 7.3-7.0 (m, 5 H), 6.83 (d, J = 11 Hz, 1 H), 6.13 (d, J = 11 Hz, 1 H), 3.37 (d, J = 15 Hz, 1 H), 3.16 (d, J = 15 Hz, 1 H), 2.6-1.6 (series of m, 4 H); m/z (M⁺) calcd 326.0977, obs 326.0982.

4-Benzyl-2-cyclohexenone (18d) and 4-Benzyl-3-cyclohexenone (19d)

Application of the general desulfonylation procedure to 15d (404 mg, 1.09 mmol) through the agency of Na$_2$HPO$_4$ (700 mg) and 6% Na(Hg) (3.5 g) in dry methanol (18 mL) for 1.5 h afforded 250 mg (100%) of a mixture of $\beta,\gamma$- (68%) and $\alpha,\beta$-unsaturated ketals (32%); IR (neat, cm$^{-1}$) 3100-2800, 1660, 1605, 1490, 1450, 1240, 1210, 1105, 1050, 690; $^1$H NMR (CDCl$_3$) $\delta$ 7.23 (br s, 5 H), 5.62 (br d, 0.3 H), 5.34 (br m, 0.7 H), 4.90 (d, $\mathcal{J}$ = 6 Hz, 0.3 H), 3.97 (s, 2.8 H), 3.83 (s, 1.2 H), 3.4-3.2 (m, 2 H), 2.4-1.6 (series of m, 5.7 H).

Deketalization and equilibration was achieved by refluxing 217 mg (0.94 mmol) of this mixture in 95% ethanol (12 mL) containing p-toluenesulfonic acid (50 mg) for 24 h. $^1$H NMR analysis of the crude product indicated 18d and 19d to be present in a 68:32 ratio. Silica gel chromatography (20 g, elution with 5% ether in pentane) yielded 56 mg of impure 19d followed by 114 mg (65%) of pure 18d. Preparative tlc of 19d (silica
gel, 30% ether in pentane) afforded 31 mg of pure enone (83% combined yield).

For 18d: IR (neat, cm⁻¹) 3100-2800, 1685, 1500, 1460, 1390, 1255, 1210, 835; ¹H NMR (CDCl₃) δ 7.4-7.0 (m, 5 H), 6.81 (br d, J = 11 Hz, 1 H), 5.96 (d, J = 11 Hz, 1 H), 2.78 (d, J = 2 Hz, 2 H), 2.9-1.5 (series of m, 5 H); m/z (M⁺) calcd 186.1044, obs 186.1050.

For 19d: IR (neat, cm⁻¹) 3100-2800, 1715, 1490, 1450, 1335, 1190, 1070, 690; ¹H NMR (CDCl₃) δ 7.5-7.1 (m, 5 H), 5.50 (br m, 1 H), 3.38 (br s, 2 H), 3.0-2.7 (m, 2 H), 2.5-2.2 (m, 4 H); m/z (M⁺) calcd 186.1044, obs 186.1048.

6,6-Ethylenedioxy-3-(4'-p-tolylpentyl)-3-(benzenesulfonyl) cyclohexene (15e)

Alkylation of 13 (803 mg, 2.86 mmol) with 1.17 g (4.85 mmol) of (4-p-tolyl)-pentyl bromide (DMF, rt, 6 h) afforded a dark yellow oil which was purified by silica gel chromatography (60 g, elution with 10% ethyl acetate in hexane). There was isolated 1.13 g (89%) of 15e as a
colorless oil; IR (CHCl$_3$, cm$^{-1}$) 3080-2840, 1514, 1450, 1303, 1220, 1145, 1087; $^1$H NMR (CDCl$_3$) $\delta$ 7.9-7.3 (m, 5 H), 7.03 (s, 4 H), 5.9-5.6 (m, 2 H), 3.81 (br s, 4 H), 2.29 (s, 3 H), 2.8-1.1 (series of m, 11 H), 1.18 (d, J = 7 Hz, 3 H).

Hydrolysis of this product (1.01 g, 2.29 mmol) in the predescribed manner (PPTS, wet acetone) afforded 844 mg (93%) of ketone 16e as a colorless immobile oil; IR (CHCl$_3$, cm$^{-1}$) 3080-2840, 1687, 1450, 1310, 1240, 1143, 1080; $^1$H NMR (CDCl$_3$) $\delta$ 7.9-7.4 (m, 5 H), 7.01 (br s, 4 H), 6.51 (dd, J = 11 and 3 Hz, 1 H), 6.12 (d, J = 11 Hz, 1 H), 2.29 (s, 3 H), 2.7-1.1 (m, 11 H), 1.17 (d, J = 7 Hz, 3 H); m/z (M$^+$) calcd 396.1759, obs 396.1770.
4-(4'-p-tolylpentyl)-2-cyclohexenone (18e) and 4-(4'-p-tolylpentyl)-3-cyclohexenone (19e)

Reductive desulfonylation of 15e (470 mg) with 700 mg of Na$_2$HPO$_4$ and 3.5 g of 6% Na(Hg) cleanly afforded 288 mg (90%) of ketal isomers (63% of $\beta$, $\gamma$ and 37% $\alpha$, $\beta$); IR (neat, cm$^{-1}$) 3000-2800, 1655, 1610, 1510, 1240, 1210, 1110, 1050, 810; $^1$H NMR (CDCl$_3$) $\delta$ 7.07 (s, 4 H), 5.51 (br d, $\beta$ = 5 Hz, 0.4 H), 5.24 (br m, 0.6 H), 4.85 (br d, $\beta$ = 5 Hz, 0.4 H), 3.96 (s, 2.4 H), 3.81 (br s, 1.6 H), 2.65 (q, $\beta$ = 7 Hz, 1 H), 2.33 (s, 3 H), 2.4-1.2 (series of m, 11.6 H), 1.22 (d, $\beta$ = 7 Hz, 3 H).

Heating of this mixture (254 mg, 0.84 mmol) for 16 h in 95% ethanol (12 mL) containing 60 mg of p-toluene-sulfonic acid gave a 70:30 mixture of 18e and 19e ($^1$H NMR analysis). Chromatography on silica gel (20 g, elution with 5% ether in pentane) gave 64 mg of impure 19e and 124 mg (57%) of pure 18e. Preparative tlc chromatography (silica gel, elution with 30% ether in pentane) of the crude 19e afforded 54 mg (25%) of pure enone.
For 18e: IR (neat, cm⁻¹) 3050-2800, 1680, 1510, 1450, 1390, 1250, 810; ¹H NMR (CDCl₃) δ 7.06 (s, 4 H), 6.74 (br d, J = 10 Hz, 1 H), 5.90 (dd, J = 10 and 3 Hz, 1 H), 2.67 (q, J = 7 Hz, 1 H), 2.32 (s, 3 H), 2.5-1.1 (series of m, 11 H), 1.23 (d, J = 7 Hz, 3 H); m/£ (M⁺) calcd 256.1827, obs 256.1821.

For 19e: IR (neat, cm⁻¹) 3060-2800, 1720, 1510, 1450, 1185, 810; ¹H NMR (CDCl₃) δ 7.06 (s, 4 H), 5.37 (br m, 1 H), 2.32 (s, 3 H), 2.9-1.1 (series of m, 13 H), 1.24 (d, J = 6 Hz, 3 H); m/£ (M⁺) calcd 256.1827, obs 256.1821.

6,6-Ethlenedioxy-3-(3'-phenylthiopropyl)-3-(benzenesulfonyl)cyclohexene (15f)

Alkylation of 13 (446 mg, 1.59 mmol) with 50% sodium hydride (115 mg, 2.40 mmol) and 3-phenylthio-1-bromopropane (637 mg, 2.75 mmol) in dimethylformamide (30 mL) followed by silica gel chromatography (30 g, elution with 20% ethyl acetate in hexane) afforded 15f (627 mg, 92%) as a clear immobile oil; IR (CHCl₃, cm⁻¹) 3100-2840, 1590,
1485, 1450, 1443, 1305, 1230, 1143, 1083, 1025; $^1$H NMR (CDCl$_3$) $\delta$ 7.9-7.4 (m, 5 H), 7.24 (m, 5 H), 5.88 (d, $J_1 = 10$ Hz, 1 H), 5.72 (d, $J_1 = 10$ Hz, 1 H), 3.82 (br s, 4 H), 2.88 (t, $J_2 = 6$ Hz, 2 H), 2.4-1.0 (series of m, 8 H).

Hydrolysis of this product (573 mg, 1.33 mmol) as previously described (PPTS, wet acetone) furnished 471 mg (92%) of ketone 16f as colorless crystals, mp 61-62.5°C (from ether); IR (CHC{l}_3, cm$^{-1}$) 3090-2840, 1690, 1587, 1480, 1450, 1440, 1308, 1225, 1142, 1082; $^1$H NMR (CDCl$_3$) $\delta$ 7.9-7.4 (m, 5 H), 7.23 (s, 5 H), 6.54 (d, $J_2 = 11$ Hz, 1 H), 6.11 (d, $J_2 = 11$ Hz, 1 H), 2.87 (t, $J_2 = 6$ Hz, 2 H), 2.7-1.5 (series of m, 8 H).

4-(3'-Phenyliothiopropy1)-2-cyclohexenone (18f) and 4-(3'-Phenyliothiopropy1)-3-cyclohexenone (19f)

Reductive desulfonylation of 15f (475 mg, 1.10 mmol) with 708 mg of \( \text{Na}_2\text{HPO}_4 \) and 3.5 g of 6% \( \text{Na(Hg)} \) during 1.5 h led to the isolation of 295 mg (92%) of ketal isomers (67% \( \beta,\gamma \) and 33% \( \alpha,\beta \)); IR (neat, cm\(^{-1}\)) 3100-2800, 1655, 1605, 1580, 1480, 1435, 1240, 1210, 1100, 1050, 730, 680; \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 7.5-7.0 (m, 5 H), 5.58 (br d, 0.3 H), 5.32 (br m, 0.7 H), 4.88 (br d, \( \mathcal{J} = 6 \) Hz, 0.3 H), 3.98 (s, 2.8 H), 3.82 (br s, 1.2 H), 2.92 (t, \( \mathcal{J} = 6 \) Hz, 2 H), 2.3-1.6 (series of m, 9.7 H).

The isomeric ketals (269 mg, 0.93 mmol) were stirred under reflux in 95% ethanol with p-toluenesulfonic acid for 19 h to give a 47:53 mixture of 18f and 19f (\(^1\)H NMR analysis). Chromatography on silica gel (15 g, 10% ether in pentane) afforded 101 mg (44%) of 19f and 99 mg (43%) of 18f (combined yield of 87%) as colorless oils.
For 18f: IR (neat, cm$^{-1}$) 3000-2800, 1680, 1585, 1480, 1440, 1385, 1245, 730, 680; $^1$H NMR (CDCl$_3$) $\delta$ 7.4-7.0 (m, 5 H), 6.76 (br d, $\mathcal{J} = 11$ Hz, 1 H), 5.94 (dd, $\mathcal{J} = 10$ and 2 Hz, 1 H), 3.1-1.4 (series of m, 11 H); m/e (M$^+$) calcd 246.1078, obs 246.1070.

For 19f: IR (neat, cm$^{-1}$) 3000-2800, 1720, 1585, 1480, 1440, 1190, 1020, 730, 680; $^1$H NMR (CDCl$_3$) $\delta$ 7.4-7.0 (m, 5 H), 5.44 (br m, 1 H), 3.0-2.7 (m, 4 H), 2.5-1.6 (series of m, 8 H); m/e (M$^+$) calcd 246.1078, obs 246.1085.

6,6-Ethyleneedioxy-3-(2'-tetrahydrofuranomethyl)-3-(benzenesulfonyl)cyclohexene (15g)

![Diagram of 6,6-Ethyleneedioxy-3-(2'-tetrahydrofuranomethyl)-3-(benzenesulfonyl)cyclohexene (15g)]

Reaction of 13 (1.00 g, 3.57 mmol) with 50% sodium hydride in oil (269 mg, 5.60 mmol) and 2-(iodomethyl)tetrahydrofuran (1.37 g, 6.46 mmol) in dimethylformamide (50 mL) as previously described (9 h) and silica gel chromatography of the product (elution with 20% ethyl acetate in hexane) gave 103 mg of unreacted 13 and 888 mg (76%, corrected for recovery) of 15g as a white crystalline...
powder, mp 94-100°C (from ether); IR (CHCl₃, cm⁻¹)
3100-2800, 1450, 1305, 1145, 1085; ¹H NMR (CDCl₃) δ
7.9-7.3 (m, 5 H), 6.0-5.7 (m, 2 H), 3.81 (s, 4 H), 4.1-
3.5 (m, 3 H), 2.4-1.4 (series of m, 10 H).

Hydrolysis of this product (831 mg, 2.28 mmol) in
wet acetone (24 mL) containing pyridinium tosylate (300
mg) in the predescribed manner gave enone 16g as a
thick colorless oil (730 mg, 100%); IR (CHCl₃, cm⁻¹)
3080-2840, 1690, 1450, 1310, 1230, 1150, 1085; ¹H NMR
(CDCl₃) δ 7.9-7.4 (m, 5 H), 6.73 (d, J = 11 Hz, 1 H),
6.21 (d, J = 11 Hz, 0.5 H), 6.09 (d, J = 11 Hz, 0.5 H),
4.2-3.6 (m, 3 H), 2.8-1.3 (series of m, 10 H).

Preparative tlc on silica gel (elution with 50% ethyl acetate in hexane) served to separate the two
diastereomers, the first being a crystalline solid, mp
87.5-89.5°C, and the second a colorless oil.

Anal. Calcd for C₁₇H₂₀O₄S:  C, 63.73; H, 6.29.
Found:  C, 63.54; H, 6.33.
Reductive desulfonylation of 15g (322 mg, 0.88 mmol) with 550 mg of Na$_2$HPO$_4$ and 2.8 g of 6% Na(Hg) was complete in 1 h and afforded 187 mg (95%) of ketal isomers (64% $\beta,\gamma$ and 36% $\alpha,\beta$); IR (neat, cm$^{-1}$) 3000-2800, 1655, 1605, 1430, 1360, 1240, 1210, 1110, 1055; $^1$H NMR (CDCl$_3$) $\delta$ 5.64 (br d, $J = 6$ Hz, 0.4 H), 5.38 (br s, 0.6 H), 4.90 (d, $J = 6$ Hz, 0.4 H), 3.96 (s, 2.4 H), 3.83 (s, 1.6 H), 4.1-3.6 (m, 3 H), 2.4-1.3 (series of m, 11.6 H).

Acid hydrolysis of this product (157 mg, 0.70 mmol) in the manner described above furnished 18g and 19g in a 69:31 ratio ($^1$H NMR analysis). Preparative tlc chromatography on silica gel (elution with 40% ether in pentane) gave 91 mg (72%) of the same mixture. No success was realized in attempts to separate the isomers; IR (neat, cm$^{-1}$) 3000-2800, 1720, 1680, 1445, 1385, 1245, 1210, 1060; $^1$H NMR (CDCl$_3$) $\delta$ 6.96 (br d, $J = 10$ Hz, 0.7 H), 5.97 (dd, $J = 10$ and 3 Hz, 0.7 H),
5.55 (br s, 0.3 H), 4.1-3.6 (m, 3 H), 2.9-1.4 (series of m, 11.3 H); m/e (M+) calcd 180.1150, obs 180.1142.

6,6-Ethylenedioxy-3-geranyl-3-(benzenesulfonyl)cyclohexene (15h)

Reaction of 13 (400 mg, 1.43 mmol) with 110 mg (2.29 mmol) of 50% sodium hydride and 0.54 mL (2.72 mmol) of geranyl bromide in 30 mL of dimethylformamide followed by silica gel chromatography (gradient elution with 10-20% ethyl acetate in hexane) afforded 564 mg (94%) of an oil which later crystallized from ether-hexane, mp 77.5-79°C; IR (CHCl₃, cm⁻¹) 3080-2810, 1450, 1305, 1145, 1075; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.84 (d, J = 11 Hz, 1 H), 5.73 (d, J = 11 Hz, 1 H), 5.04 (br t, 2 H), 3.82 (s, 4 H), 2.59 (d, J = 7 Hz, 2 H), 2.3-1.5 (series of m, 17 H).

Hydrolysis of this product (493 mg, 1.18 mmol) in wet acetone (25 mL) containing PPTS (150 mg) as before, followed by filtration through silica gel (20 g, elution with 20% ethyl acetate in hexane), yielded 420
mg (96%) of enone 16h as a colorless oil; IR (CHCl₃, cm⁻¹) 3080-2840, 1690, 1450, 1390, 1310, 1145, 1085; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 6.58 (d, J = 11 Hz, 1 H), 6.17 (d, J = 11 Hz, 1 H), 4.86 (br t, 2 H), 2.62 (d, J = 7 Hz, 2 H), 2.8-1.4 (series of m, 17 H); m/e (M⁺) calcd 372.1759, obs 372.1751.


4-Geranyl-2-cyclohexenone (18h) and 4-Geranyl-3-cyclohexenone (19h)

Reductive desulfonylation of 15h (432 mg, 1.04 mmol) was achieved during 17 h with 700 mg of Na₂HPO₄ and 3.6 g of 6% Na(Hg). Workup and solvent removal furnished 288 mg (100%) of ketal isomers (62% βγ and 38% αβ) as a colorless oil; IR (neat, cm⁻¹) 3000-2800, 1650, 1600, 1435, 1370, 1235, 1200, 1105, 1045; ¹H NMR (CDCl₃) δ 5.6-4.8 (m, 3.4 H), 3.99 (s, 2.4 H), 3.83 (br s, 1.6 H), 2.8-1.5 (series of m, 20.6 H).
Acid hydrolysis of this product (257 mg, 0.93 mmol) in 95% ethanol (12 mL) containing p-toluene-sulfonic acid (50 mg) for 4 h delivered a 64:36 mixture of 19h and 18h. Silica gel chromatography (elution with 10% ether in pentane) afforded 124 mg (57%) of 19h and 79 mg (36%) of 18h (93% combined yield).

Heating for 24 h gave a 69:31 distribution of the same enones.

For 18h: IR (neat, cm⁻¹) 3000-2800, 1680, 1440, 1380, 1245, 1205; $^1$H NMR (CDCl₃) δ 6.82 (br d, J = 11 Hz, 1 H), 5.96 (br d, J = 11 Hz, 1 H), 5.3-4.9 (m, 2 H), 2.6-1.5 (series of m, 20 H); m/e (M⁺) calcd 232.1827, obs 232.1834.

For 19h: IR (neat, cm⁻¹) 3000-2800, 1720, 1440, 1375, 1190; $^1$H NMR (CDCl₃) δ 5.44 (br m, 1 H), 5.3-5.0 (m, 2 H), 3.0-1.5 (series of m, 21 H); m/e (M⁺) calcd 232.1827, obs 232.1834.
**6,6-Ethylendioxy-3-(4'-carboethoxybutyl)-3-(benzenesulfonyl)cyclohexene (15i)**

The anion of 13 (1.00 g, 3.58 mmol) was prepared with 50% sodium hydride (274 mg, 5.71 mmol) in dimethylformamide (25 mL) and added to a solution of ethyl 6-iodovalerate (1.83 g) in 25 mL of the same solvent. Chromatography of the product on silica gel (elution with 20% ethyl acetate in hexane) afforded 15i as a colorless, mobile oil (1.34 g, 92%); IR (CHCl₃, cm⁻¹) 3080-2875, 1735, 1450, 1305, 1240, 1145, 1075; ¹H NMR (CDCl₃) δ 7.9-7.3 (m, 5 H), 5.90 (d, J = 11 Hz, 1 H), 5.81 (d, J = 11 Hz, 1 H), 4.08 (q, J = 7 Hz, 2 H), 3.83 (s, 4 H), 2.4-1.2 (series of m, 12 H), 1.24 (t, J = 7 Hz, 3 H).

Hydrolysis of this product (1.27 g, 3.11 mmol) in wet acetone (25 mL) containing PPTS (300 mg) (reflux, 2 h), filtration through silica gel (20 g, elution with 20% ethyl acetate in hexane), and crystallization from ether gave 910 mg (80%) of enone 16i as colorless needles, mp 56-59°C; IR (CHCl₃, cm⁻¹) 3080-2860, 1735, 1695, 1450, 1380, 1310, 1190, 1145, 1085; ¹H NMR
(CDCl$_3$) $\delta$ 7.9-7.4 (m, 5 H), 6.60 (d, $J = 11$ Hz, 1 H), 6.15 (d, $J = 11$ Hz, 1 H), 4.07 (q, $J = 7$ Hz, 2 H), 2.6-1.2 (series of m, 12 H), 1.22 (t, $J = 7$ Hz, 3 H).

Anal. Calcd for C$_{19}$H$_{24}$O$_5$S: C, 62.62; H, 6.64.

Found: C, 62.78; H, 6.71.

4-(4'-Carboethoxybutyl)-2-cyclohexenone (18i) and 4-(4'-Carboethoxybutyl)-3-cyclohexenone (19i)

Reductive desulfonylation of 15i (342 mg, 0.84 mmol) with Na$_2$HPO$_4$ (550 mg) and 6% Na(Hg) (2.8 g) in the usual manner (20 mL of dry ethanol) for 1.5 h gave a mixture of ketals (159 mg, 71%) in a ratio of 56% $\beta$, $\gamma$ and 44% $\alpha$, $\beta$; IR (neat, cm$^{-1}$) 3000-2800, 1735, 1655, 1610, 1370, 1240, 1210, 1110, 1040, 850; $^1$H NMR (CDCl$_3$) $\delta$ 5.56 (br d, $J = 5$ Hz, 0.4 H), 5.30 (br s, 0.6 H), 4.89 (d, $J = 5$ Hz, 0.4 H), 4.13 (q, $J = 7$ Hz, 2 H), 3.99 (s, 2.4 H), 3.84 (s, 1.6 H), 2.4-1.4 (series of m, 13.6 H), 1.28 (t, $J = 7$ Hz, 3 H).

Deketalization was achieved without affecting the ester functionality by refluxing the above material
(127 mg, 0.47 mmol) for 19 h in 95% ethanol (15 mL) containing p-toluenesulfonic acid (100 mg). The 69:31 mixture of 18i and 19i was separated into its components by preparative tlc on silica gel (elution with 40% ether in pentane). There was obtained 21 mg (20%) of 19i and 59 mg (56%) of 18i.

For 18i: IR (neat, cm⁻¹) 3000-2800, 1735, 1680, 1450, 1410, 1370, 1240, 1180, 1090, 1025; ¹H NMR (CDCl₃) δ 6.85 (br d, J = 10 Hz, 1 H), 5.96 (dd, J = 10 and 3 Hz, 1 H), 4.15 (q, J = 7 Hz, 2 H), 2.6-1.3 (series of m, 13 H), 1.29 (t, J = 7 Hz, 3 H); m/e (M⁺) calcd 224.1412, obs 224.1405.

For 19i: IR (neat, cm⁻¹) 3000-2800, 1730, 1440, 1370, 1185, 1020; ¹H NMR (CDCl₃) δ 5.46 (br s, 1 H), 4.15 (q, J = 7 Hz, 2 H), 2.9-2.7 (br s, 2 H), 2.5-1.9 (series of m, 8 H), 1.8-1.3 (m, 4 H), 1.29 (t, J = 7 Hz, 3 H); m/e (M⁺) calcd 224.1412, obs 224.1405.
The anion of 13 (1.80 g, 6.42 mmol) was generated at 0°C with 50% sodium hydride (503 mg, 10.5 mmol). 1-Bromo-3,3-
edtylenedioxybutane (1.20 g, 6.15 mmol) was introduced and the reaction mixture was stirred at room temperature for 1.5 h when an equivalent amount of electrophile was added. A third 1.20 g sample of bromide was added 18 h later. After a total reaction of 42 h, the slurry was poured into water (50 mL) and chloroform (100 mL) was added. The aqueous phase was extracted with chloroform (2 × 100 mL) and the combined organic layers were washed with water (6 × 50 mL) and brine (100 mL) before drying. Chloroform was removed on a rotary evaporator and residual dimethylformamide was removed under high vacuum overnight. MPLC on silica gel (elution with 70% ethyl acetate in petroleum ether) afforded 990 mg of unreacted 13 and 946 mg (83%) of 20, mp 114-116°C (from ethyl acetate); IR (CHCl₃, cm⁻¹) 3040-2830, 1445, 1295,
1H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.88 (d, J = 11 Hz, 1 H), 5.72 (d, J = 11 Hz, 1 H), 3.86 (s, 4 H), 3.82 (s, 4 H), 2.3-1.5 (series of m, 8 H), 1.28 (s, 3 H).

Hydrolysis of 20 (113 mg, 0.29 mmol) in wet acetone (15 mL) containing 100 mg of PPTS was complete after 23 h at the reflux temperature. The usual workup afforded 80 mg (90%) of 21 as a colorless oil which later crystallized, mp 110-112°C (from dichloromethane-ether); IR (CHCl₃, cm⁻¹) 3100-2840, 1720, 1690, 1445, 1300, 1140, 1080; 1H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 6.64 (d, J = 11 Hz, 1 H), 6.12 (d, J = 11 Hz, 1 H), 2.8-2.1 (series of m, 8 H), 2.17 (s, 3 H). This material was used without further purification.

Cyclization of 21

A solution of 21 (342 mg, 1.12 mmol) in 2% methanolic potassium hydroxide solution (20 mL) was stirred at room temperature for 4 h and poured into 50
72 mL of water previously saturated with ether. The product was extracted into ether (150 mL) and the resulting organic phase was washed with brine (50 mL) prior to drying and evaporation. MPLC on silica gel (elution with 70% ethyl acetate in petroleum ether) gave 246 mg (72%) of 23a and 36 mg (11%) of 24a as colorless crystalline solids.

For 23a: mp 166-168°C (from ether-pentane); IR (CHCl₃, cm⁻¹) 3600-3300, 3100-2840, 1680, 1445, 1375, 1305, 1145, 1080, 1010, 990, 900; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 7.03 (dd, J = 11 and 3 Hz, 1 H), 6.11 (d, J = 11 Hz, 1 H), 2.8-1.5 (series of m, 8 H), 1.20 (s, 3 H); ¹³C NMR (CDCl₃) ppm 198.32, 143.52, 134.84, 134.41, 132.59, 130.17, 129.26, 129.26, 67.42, 64.50, 54.79, 32.83, 29.97, 28.52, 22.08; m/e (M⁺) calcd 306.0926, obs 306.0933.


For 24a: mp 178-179°C (from ether-pentane); IR (CHCl₃, cm⁻¹) 3600-3300, 3100-2840, 1675, 1445, 1375, 1305, 1145, 1080, 1000, 940, 920; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 7.04 (dd, J = 10 and 2 Hz, 1 H), 6.19 (d, J = 10 Hz, 1 H), 2.5-1.5 (series of m, 8 H), 1.40 (s, 3 H); ¹³C NMR (CDCl₃) ppm 198.58, 143.92, 134.93, 134.57,
Desulfonylation of 20 (596 mg, 1.51 mmol) was conducted during 1 h as before with 952 mg of Na₂HPO₄ and 4.84 g of 6% Na(Hg) in dry methanol (20 mL). Customary workup gave 368 mg (96%) of ketal isomers as a colorless liquid; IR (CHCl₃, cm⁻¹) 3000-2800, 1655, 1610, 1375, 1230, 1110, 1050, 940, 855; H NMR (CDCl₃) δ 5.56 (br d, J = 6 Hz, 0.4 H), 5.29 (br s, 0.6 H), 4.87 (d, J = 6 Hz, 0.4 H), 3.98 (s, 2.4 H), 3.94 (s, 4 H), 3.80 (s, 1.6 H), 2.3-1.6 (series of m, 9.6 H), 1.35 (s, 3 H). Hydrolysis of this product (30 mg, 0.12 mmol) in the usual manner for 18 h furnished 16 mg (82%) of pure 22 as a colorless liquid; IR (neat, cm⁻¹) 3000-2800, 1720, 1420, 1360, 1190, 1160, 965, 785; H NMR (CDCl₃) δ 5.41 (br s, 1 H), 2.9-2.0 (series of m, 10 H), 2.17 (s, 3 H); m/z (M⁺) calcd 166.0994, obs 166.0997.
Cyclization of 22

A solution of 22 (555 mg) in 2% methanolic potassium hydroxide (20 mL) was stirred at room temperature for 5 h, then poured into water (50 mL) and extracted with chloroform (4 x 50 mL). The combined organic phases were washed with brine (50 mL), dried, and evaporated. Silica gel chromatography of the residue (elution with 40% ethyl acetate in petroleum ether) afforded 246 mg (51%) of 23b and 68 mg of recovered 22. Recrystallization of 23b from ether-pentane yielded a fluffy white solid, mp 92-93.5°C; IR (CHCl₃, cm⁻¹) 3600, 3560-3220, 3080-2820, 1670, 1440, 1380, 1300, 1260-1170, 1090, 970, 890, 840; ¹H NMR (CDCl₃) δ 6.86 (m, 1 H), 6.01 (d, J = 9 Hz, 1 H), 2.7-1.3 (series of m, 9H), 1.21 (s, 3 H); ¹³C NMR (CDCl₃) ppm 201.42, 152.56, 130.41, 68.70, 55.47, 31.86, 30.40 (2C), 29.61, 22.09; m/e (M⁺) calcd 166.0994, obs 166.0997.

Anal. Calcd for C₁₀H₁₄O₂: C, 72.26; H, 8.49.
Found: C, 71.89; H, 8.48.
Hydrogenation of 23b

A solution of 23b (164 mg) in ethyl acetate (9 mL) was hydrogenated in a Parr apparatus at 42 psi for 17 h over a 10% palladium on carbon catalyst. Filtration through Celite and evaporation of the filtrate gave 170 mg of dihydro derivative, mp 100-102°C (from ether-pentane); IR (CHCl₃, cm⁻¹) 3600, 3560-3300, 3000-2820, 1695, 1450, 1380, 1295, 1225, 1100, 970, 895; ¹H NMR (CDCl₃) δ 2.6-1.4 (series of m, 13 H), 1.18 (s, 3 H); m/e (M⁺) calcd 168.1150, obs 168.1155.

exo-2,endo-8-Dimethylbicyclo[3.3.1]nonane-endo-2,exo-8-diol (25)

A cold (0°C) solution of dihydro-23b (137 mg, 0.81 mmol) in dry ether (20 mL) and tetrahydrofuran (2 mL) was blanketed with nitrogen and treated with 1.90 mL of 1.3 M
ethereal methyllithium (2.47 mmol). The reaction mixture was allowed to warm to room temperature where it was treated with additional methyllithium (0.70 mL) after 6 h. After a total reaction time of 11 h, saturated ammonium chloride solution (50 mL) was added and the product was extracted into chloroform (2 x 75 mL). The combined organic layers were washed with water (50 mL) and brine (50 mL), dried, and evaporated. MPLC of the residue on silica gel (elution with 45% ethyl acetate in petroleum ether) afforded 45 mg of unreacted dihydro-23b, 19 mg of an unidentified substance, and 47 mg (46%) of 25, a colorless solid, mp 148.5-149.5°C (from dichloromethane-ether); IR (KBr, cm⁻¹) 3500-3200, 3000-2800, 1125, 1105, 920; ¹H NMR (CDCl₃) δ 2.3-1.1 (series of m, 14 H), 1.47 (s, 3 H), 1.42 (s, 3 H); ¹³C NMR (CD₃CN) ppm 73.41 (2C), 52.92, 36.85 (2C), 33.11, 31.85, 30.78, 29.57, 29.37, 28.06; m/z (M⁺-H₂O) calcd 166.1357, obs 166.1361.

Anal. Calcd for C₁₁H₂₀O₂: C, 71.70; H, 10.94. Found: C, 71.45; H, 10.87.
6,6-Ethlenedioxy-3-(2'-(6'-methyl-5'-heptenyl))-3-(benzenesulfonyl)cyclohexene (29)

Inverse addition of the anion of 13 (6.00 g, 21.4 mmol), prepared as above, to 2-toluenesulfonyloxy-6-methyl-5-heptene (10.29 g, 36.4 mmol) in a total volume of 100 mL of dimethylformamide, followed by preparative HPLC on a Waters Prep 500 instrument (silica gel, elution with 25% ethyl acetate in petroleum ether), afforded 857 mg (15%) of 30 and 2.75 g (47%) of 29 in addition to 1.87 g of unreacted 13. The two diastereomers of 29 could be separated by careful MPLC purification (silica gel, elution with 30% ethyl acetate in petroleum ether).

For 30: IR (CHCl₃, cm⁻¹) 3040-2820, 1595, 1445, 1310, 1260, 1150, 1100; ¹H NMR (CDCl₃) δ 8.0-7.8 (m, 2 H), 7.85 (d, J = 9 Hz, 2 H), 7.6-7.4 (m, 3 H), 6.95 (d, J = 9 Hz, 2 H), 5.09 (br t, J = 6 Hz, 1 H), 4.2-3.3 (m, 5 H), 2.3-1.1 (series of m, 4 H), 1.68 (s, 3 H), 1.60 (s, 3 H), 1.15 (d, J = 7 Hz, 3 H); m/z (M⁺) calcd 388.1708, obs 388.1716.
For 29a: IR (CHCl₃, cm⁻¹) 3040-2800, 1440, 1385, 1290, 1215, 1135, 1115, 920; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.80, 5.72 (ABq, J = 11 Hz, 2 H), 4.98 (br t, J = 6 Hz, 1 H), 3.80 (br s, 4 H), 2.4-1.0 (series of m, 9 H), 1.66 (s, 3 H), 1.59 (s, 3 H), 1.25 (d, J = 7 Hz, 3 H).

For 29b: IR (CHCl₃, cm⁻¹) 3040-2800, 1445, 1385, 1290, 1135, 1115, 920; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.82, 5.65 (ABq, J = 11 Hz, 2 H), 5.10 (br m, 1 H), 3.81 (br s, 4 H), 2.3-1.0 (series of m, 9 H), 1.70 (s, 3 H), 1.63 (s, 3 H), 0.96 (d, J = 7 Hz, 3 H).

4-(2'-(6'Methyl-5'-hepteny1))-3-cyclohexenone

Desulfonylation of 29 (2.39 g, 6.13 mmol) was achieved in 1 h upon reaction with Na₂HPO₄ (3.0 g) and 6% Na(Hg) (12.5 g) in dry methanol (20 mL). Workup yielded 1.44 g (94%) of the isomeric ketals (54% β,γ; 46% α,β); IR (neat, cm⁻¹) 3000-2800, 1650, 1605, 1450, 1370, 1240, 1210, 1110, 1055, 860; ¹H NMR (CDCl₃) δ 5.52 (d, J = 6 Hz, 0.5 H), 5.24 (br s, 0.5 H), 5.05 (br t, J = 7 Hz, 1 H), 4.86
(d, J = 6 Hz, 0.5 H), 3.95 (s, 2 H), 3.79 (s, 2 H),
2.3-1.0 (series of m, 10.5 H), 1.69 (s, 3 H), 1.60 (s, 3 H), 0.99 (d, J = 7 Hz, 3 H).

Exclusive formation of the β,γ-enone was realized upon refluxing this mixture (1.41 g, 5.63 mmol) in wet acetone (25 mL) containing 300 mg of PPTS for 5 h. Pure product was obtained following MPLC purification (silica gel, elution with 5% ethyl acetate in petroleum ether): 875 mg (75%); IR (neat, cm⁻¹) 3000-2820, 1725, 1450, 1370, 1185, 1110; ¹H NMR (CDCl₃) δ 5.42 (br s, 1 H), 5.05 (br t, J = 6 Hz, 1 H), 2.9-1.1 (series of m, 11 H), 1.69 (s, 3 H), 1.60 (s, 3 H), 1.02 (d, J = 6 Hz, 3 H); m/£ (M⁺) calcd 206.1670, obs 206.1665.

4-(2'-(6'-Methyl-5'-heptenyl))-2-cyclohexenone

The desired α,β-enone was obtained by treating the β,γ-unsaturated isomer (361 mg) with a methanolic sodium methoxide solution (from 43 mg of sodium and 7 mL of dry methanol) at 60°C for 5 min. The reaction mixture was poured
onto ice (30 g) and acetic acid (1 mL). The product was extracted into ether (3 x 50 mL) and the combined organic layers were washed with 5% sodium bicarbonate solution (2 x 30 mL) and brine (50 mL) prior to drying and solvent evaporation. MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether) led to the recovery of the β,γ isomer (105 mg) and the isolation of the conjugated enone (148 mg, 58%); IR (neat, cm⁻¹) 3000-2800, 1685, 1610, 1510, 1445, 1375, 825; ¹H NMR (CDCl₃) δ 6.80 (br d, J = 10 Hz, 1 H), 5.96 (dd, J = 10 Hz, 1 H), 5.06 (br t, J = 6 Hz, 1 H), 2.6-1.0 (series of m, 10 H), 1.70 (s, 3 H), 1.62 (s, 3 H), 0.92 (d, J = 7 Hz, 1.5 H), 0.88 (d, J = 7 Hz, 1.5 H); m/z (M⁺) calcd 206.1670, obs 206.1664.

Zingiberenol (26)

A cold (0°C) solution of the conjugated enone from above (75 mg, 0.36 mmol) in dry ether (7 mL) was blanketed with nitrogen and treated with ethereal methyllithium (0.35 mL of 1.3 M, 0.45 mmol). The reaction
mixture was stirred at room temperature for 11 h prior to the addition of saturated ammonium chloride solution. Ether (150 mL) was introduced and the organic layer was washed with water (50 mL) and brine (50 mL) before drying. Silica gel chromatography of the residue obtained upon solvent evaporation (elution with 10% ethyl acetate in petroleum ether) afforded 49 mg (61%) of zingiberenol (26) and 21 mg (26%) of its isomer 31.

For 26: IR (neat, cm\(^{-1}\)) 3350, 3000-2800, 1450, 1375, 1115, 1040, 970, 910, 735, 710; \(^1^H\) NMR (CDCl\(_3\)) \(\delta\) 5.6-5.3 (m, 2 H), 5.05 (br t, \(J = 6\) Hz, 1 H), 2.2-1.0 (series of m, 11 H), 1.72 (s, 3 H), 1.64 (s, 3 H), 1.31 (s, 3 H), 0.84 (d, \(J = 6\) Hz, 1.5 H), 0.80 (d, \(J = 6\) Hz, 1.5 H); m/\(\alpha\) (M\(^+\)) calcd 222.1983, obs 222.1990.

For 31: IR (neat, cm\(^{-1}\)) 3350, 3000-2800, 1445, 1370, 1110, 900, 730; \(^1^H\) NMR (CDCl\(_3\)) \(\delta\) 5.7-5.4 (m, 2 H), 5.06 (br t, \(J = 6\) Hz, 1 H), 2.2-1.0 (series of m, 11 H), 1.69 (s, 3 H), 1.62 (s, 3 H), 1.28 (s, 3 H), 0.86 (d, \(J = 6\) Hz, 1.5 H), 0.82 (d, \(J = 6\) Hz, 1.5 H); m/\(\alpha\) (M\(^+\)) calcd 222.1983, obs 222.1990.
trans-1-(Benzenesulfonyl)-4-(trimethylsilyl)-1-butene

(43)

\[ \text{PhSO}_2\equiv\text{SiMe}_3 \]

A solution of 4-(trimethylsilyl)-1-butene\textsuperscript{36} (1.41 g, 11.0 mmol) and Se-phenyl benzeneselenol-sulfonate\textsuperscript{34} (1.70 g, 5.7 mmol) in carbon tetrachloride (15 mL) was placed in two small pyrex tubes and irradiated with a bank of 2537 Å lamps in a Rayonet reactor for 1.5 h. The solvent was evaporated, the residue was taken up in dichloromethane (50 mL), and 15\% hydrogen peroxide (5 mL) was added with vigorous stirring at 0°C. After 30 min, the reaction mixture was warmed to room temperature. Following an identical time interval, the solution was poured into 5\% sodium bicarbonate solution (30 mL) and dichloromethane (20 mL). The organic phase was washed once more with bicarbonate solution (30 mL) and brine (50 mL) before drying and evaporation. The resulting oil was chromatographed on silica gel (MPLC, elution with 10\%
ethyl acetate in petroleum ether) to give 1.43 g (93%)
of 43 after removal of solvent under high vacuum
overnight; IR (neat, cm\(^{-1}\)) 2960-2860, 1625, 1445, 1320,
1250, 1145, 1080, 855, 830, 750, 680; \(^1\)H NMR (CDCl\(_3\)) \(\delta\)
7.9-7.4 (m, 5 H), 7.08 (dt, \(J = 15\) and 6 Hz, 1 H), 6.32
(d, \(J = 15\) Hz, 1 H), 2.4-2.1 (m, 2 H), 0.8-0.6 (m, 2
H), 0.06 (s, 9 H); \(m/e\) (M\(^+\)) calcd 268.0953, obs
268.0971.

Found:  C, 57.76; H, 7.45.

**trans-1-(Benzenesulfonyl)-6-(**tert-**butyldimethylsilyloxy)-1-hexene (45)**

![Chemical Structure](image)

The silyl ether was prepared by reacting 5-hexen-1-ol (1.18 mL, 9.97 mmol) with imidazole (0.80 g) and **tert**-butyldimethylsilyl chloride (2.60 g) in dimethylformamide (50 mL) under nitrogen at room temperature for 20 h. The reaction mixture was poured into ether
(200 mL) and extracted with water (100 mL, 2 x 50 mL) and brine (100 mL). After drying and solvent evaporation, distillation gave 1.39 g (65%) of product, bp 98°C (20 torr).

Photolysis of this substance (1.34 g, 6.25 mmol) with Se-phenyl benzeneselenolsulfonate (1.20 g, 4.04 mmol) in carbon tetrachloride (15 mL) as before furnished 1.27 g (89%) of 45 after MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether); IR (neat, cm⁻¹) 2980-2810, 1620, 1440, 1320, 1245, 1140, 1080, 825, 770, 680; ¹H NMR (CDCl₃) δ 8.0-7.5 (m, 5 H), 7.02 (dt, J = 15 and 6 Hz, 1 H), 6.34 (d, J = 15 Hz, 1 H), 3.63 (m, 2 H), 2.5-2.2 (m, 2 H), 1.7-1.5 (m, 4 H), 0.93 (s, 9 H), 0.09 (s, 6 H); m/z (M⁺) calcd 339.1450, obs 339.1458.

Anal. Calcd for C₁₆H₂₇O₃SSi: C, 60.97; H, 8.53. Found: C, 60.94; H, 8.53.
trans-1-(Benzenesulfonyl)-3-(tert-butyldimethylsilyloxy)-1-propene (47)

The tert-butyldimethylsilyl ether of allyl alcohol (bp 49-50°C at 20 torr) (1.14 g, 6.61 mmol) was similarly converted to 47 upon irradiation with the selenolsulfonate (1.02 g, 3.43 mmol) in carbon tetrachloride solution (15 mL). MPLC purification on silica gel (elution with 10% ethyl acetate in petroleum ether) gave 909 mg (85%) of 47 as a colorless solid which melted upon warming to room temperature; IR (neat, cm⁻¹) 2980-2820, 1630, 1440, 1310, 1250, 1140, 1080, 860, 830, 770, 680; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 7.05 (dt, J = 14 and 3 Hz, 1 H), 6.60 (dt, J = 14 and 2 Hz, 1 H), 4.4-4.3 (m, 2 H), 0.92 (s, 9 H), 0.09 (s, 6 H); m/e (M⁺) calcd 297.0981, obs 297.0987.

Anal. Calcd for C₁₅H₂₄O₃SSi: C, 57.64; H, 7.74. Found: C, 57.57; H, 7.72.
Cycloaddition-Ketalization of 43

A solution containing 43 (3.98 g, 14.8 mmol) and Danishefsky's diene (3.30 g of 85% purity, 16.3 mmol) in xylene (16 mL) was refluxed under nitrogen for 55 h. The cooled reaction mixture was transferred to a larger round-bottomed flask and benzene (20 mL), ethylene glycol (2 g), and a catalytic quantity of p-toluenesulfonic acid were added. Azeotropic removal of water was carried out over 24 h, followed by the customary workup. HPLC (silica gel, elution with 15% ethyl acetate in petroleum ether) afforded 1.07 g of unreacted 43 and 3.62 g (88%) of 52 as a mixture of the two isomers. Recrystallization of the mixture gave 1.92 g of \( \Delta^3 \)-52. The mother liquor was rechromatographed and re-crystallized to provide an additional 0.50 g of \( \Delta^3 \)-52 as a colorless crystalline solid, mp 76-78.5°C (from ether-pentane). Careful MPLC of the residue (silica gel, elution with 16% ethyl acetate in petroleum ether) yielded pure \( \Delta^2 \)-52 as a colorless oil.
For $\Delta^3$-52: IR (CHCl$_3$, cm$^{-1}$) 3060-2820, 1630, 1440, 1300, 1140, 1080, 850, 830; $^1$H NMR (CDCl$_3$) δ 8.0-7.4 (m, 5 H), 7.00 (t, $\Delta = 4$ Hz, 1 H), 3.98 (s, 4 H), 2.8-2.5 (m, 2 H), 2.0-1.2 (series of m, 5 H), 0.6-0.2 (m, 2 H), -0.03 (s, 9 H).

For $\Delta^2$-52: IR (neat, cm$^{-1}$) 3000-2800, 1440, 1300, 1240, 1150-1100, 1075, 1050, 1015, 940, 770, 720, 680; $^1$H NMR (CDCl$_3$) δ 8.0-7.5 (m, 5 H), 5.89 (s, 2 H), 4.0-3.6 (m, 5 H), 2.4-1.5 (m, 5 H), 0.7-0.3 (m, 2 H), 0.01 (s, 9 H).

Cycloaddition-Ketalization of 45

A solution of 45 (1.21 g, 3.41 mmol) and Danishefsky's diene (760 mg of 85% purity, 3.75 mmol) in xylene (6 mL) was refluxed for 48 h under nitrogen. Ethylene glycol (650 mg), benzene (20 mL), and p-toluenesulfonic acid (25 mg) were added and azeotropic removal of water was continued for 20 h. Workup as before but with ethyl acetate as solvent gave 53 and some desilylated product. Reprotection of the hydroxyl group with
imidazole (255 mg, 3.74 mmol) and tert-butyldimethyl-silyl chloride (515 mg, 3.42 mmol) in dimethylformamide (18 mL) was therefore effected (22 h) prior to MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether). There was obtained 542 mg of unreacted 45 and 311 mg (35%) of $\Delta^3$-53; IR (neat, cm$^{-1}$) 3000-2800, 1675, 1600, 1450, 1300, 1250, 1150-1000, 830, 770, 680; $^1$H NMR (CDCl$_3$) δ 8.0-7.4 (m, 5 H), 7.0-6.8 (br t, 1 H), 4.0-3.8 (m, 4 H), 3.7-3.5 (m, 2 H), 2.7-2.5 (m, 2 H), 2.0-1.1 (series of m, 9 H), 0.95 (s, 9 H), 0.08 (s, 6 H).

Cycloaddition-Ketalization of 47

A solution of 47 (1.00 g, 3.2 mmol) and Danishefsky's diene (720 mg of 85% purity, 3.5 mmol) in xylene (5 mL) was refluxed until black in color (23 h) under nitrogen in base-washed glassware. The solution was transferred to a flask having twice the volume and benzene (20 mL), ethylene glycol (600 mg), and p-toluenesulfonic acid (25 mg) were added. Removal of
water azeotropically during 17 h followed by the predescribed workup but with ethyl acetate as solvent afforded a ketal mixture. This oil was dissolved in dry dimethylformamide (18 mL) and resilylated with imidazole (240 mg, 3.5 mmol) and tert-butylidimethylsilyl chloride (480 mg, 3.2 mmol) at room temperature under nitrogen for 18 h. MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether) yielded 139 mg of unreacted 47 and 863 mg (74%) of 54 as a mixture of β,γ- and α,β-isomers (77:23); IR (neat, cm⁻¹) 3000-2800, 1465, 1440, 1390, 1355, 1300, 1250, 1150-1050, 1020, 940, 830, 770, 720, 680; ¹H NMR (CDCl₃) δ 8.0-7.5 (m, 5 H), 7.07 (t, J = 4 Hz, 0.8 H), 5.89 (s, 0.4 H), 4.0-3.6 (m, 6.2 H), 2.7-1.3 (series of m, 4.6 H), 0.90 (m, 9 H), 0.03 (m, 6 H).

Alkylation of 52 A. l-Bromo-4-p-tolylpentane

Alkylation of 52 (506 mg, 1.33 mmol) with sodium hydride (134 mg of 50% in oil, 2.79 mmol) and l-bromo-4-p-tolylpentane (646 mg, 2.68 mmol) in dry dimethylformamide (25 mL)
during 20 h, followed by the customary workup and MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether) gave 183 mg (20%) of dialkylated product and 444 mg (62%) of 55; IR (CHCl₃, cm⁻¹) 3040-2800, 1510, 1440, 1290, 1240, 1130, 1075, 935, 850, 830, 680, 590; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 7.06 (br s, 4 H), 6.0-5.1 (m, 2 H), 4.1-3.5 (m, 4 H), 2.31 (s, 3 H), 2.8-0.5 (series of m, 14 H), 1.22 (d, J = 8 Hz, 1.5 H), 1.20 (d, J = 8 Hz, 1.5 H), 0.02 (s, 9 H).

5-(2'-(Trimethylsilyl)ethyl)-4-(4'-p-tolylpentyl)-3-cyclohexenone (57)

Deketalization was effected by refluxing a solution of 55 (385 mg, 0.71 mmol) and PPTS (90 mg) in wet acetone (12 mL) for 16 h. The usual workup and concentration under high vacuum afforded 56 (342 mg, 97%) as a colorless oil; IR (neat, cm⁻¹) 3100-2800, 1680, 1580, 1510, 1450, 1380, 1300, 1250, 1130, 1070, 880-800; ¹H NMR (CDCl₃) δ 8.0-7.5 (m, 5 H), 7.3-7.0 (m, 5 H), 6.3-
6.0 (m, 1 H), 2.30 (s, 3 H), 2.9-0.5 (series of m, 14 H), 1.23 (d, \( J = 7 \) Hz, 1.5 H), 1.19 (d, \( J = 7 \) Hz, 1.5 H), 0.04 (s, 9 H).

A solution of 56 (257 mg, 0.52 mmol) in glacial acetic acid (10 mL) was stirred with zinc dust (340 mg, 5.2 mg-at) at room temperature under nitrogen for 24 h. The solution was filtered into 5% sodium bicarbonate solution (100 mL) and ether (150 mL) was added. Solid sodium bicarbonate was slowly added until neutralization was complete. The ethereal layer was washed again with the bicarbonate solution (50 mL) and brine (50 mL) prior to drying and solvent evaporation. MPLC of the residue on silica gel (elution with 5% ethyl acetate in petroleum ether) afforded 148 mg (80%) of 57 as a colorless liquid; IR (neat, cm\(^{-1}\)) 3000-2800, 1720, 1510, 1240, 1145, 870-800; \(^1\)H NMR (CDCl\(_3\)) \( \delta \) 7.11 (s, 4 H), 5.37 (m, 1 H), 2.34 (s, 3 H), 2.9-1.1 (series of m, 14 H), 1.24 (d, \( J = 8 \) Hz, 3 H), 0.7-0.3 (m, 2 H), 0.00 (s, 9 H); m/e (M\(^+\)) calcd 356.2535, obs 356.2543.
5-(2'-((Trimethylsilyl)ethyl))-4-(4'-p-tolylpentyl)-2-cyclohexenone (58)

Equilibration to the 2-isomer was cleanly achieved by refluxing a mixture of 57 (21 mg) and sodium carbonate (2 mg) in methanol (6 mL) for 9 h. The reaction mixture was cooled, poured into saturated brine, and extracted with ether. The combined organic layers were washed with water (25 mL) and brine (25 mL) before drying and solvent evaporation. MPLC on silica gel (elution as above) afforded recovered 57 (4 mg) and 58 (11 mg, 65%); IR (neat, cm⁻¹) 3040-2800, 1680, 1510, 1450, 1410, 1385, 1245, 870-800; ¹H NMR (CDCl₃) δ 7.13 (s, 4 H), 6.79 (dd, J = 10 and 3 Hz, 1 H), 5.93 (br d, J = 10 Hz, 1 H), 1.36 (s, 3 H), 2.8-1.0 (series of m, 13 H), 1.24 (d, J = 7 Hz, 3 H), 0.7-0.3 (m, 2 H), 0.00 (s, 9 H); m/z (M⁺) calcd 356.2535, obs 356.2545.

Alkylation of 52. B. Allyl Bromide

From 503 mg (1.32 mmol) of 52, 144 mg (3.0 mmol) of 50% sodium hydride, and 0.23 mL (2.66 mmol) of allyl bromide (25 mL of dry DMF, room temperature, 22 h), there was isolated by MPLC on silica gel (elution with 17% ethyl acetate in petroleum ether) 65 mg (11%) of dialkylation products and 395 mg (71%) of 59a; IR (neat, cm⁻¹) 3100-2800, 1440, 1390, 1300, 1240, 1130, 1075, 1020, 925, 830, 765, 720, 680; ¹H NMR (CDCl₃) δ 8.0-7.4 (m, 5 H), 6.2-5.1 (m, 5 H), 4.3-3.7 (m, 4 H), 3.2-1.2 (series of m, 7 H), 0.9-0.2 (m, 2 H), 0.13 (s, 9 H).
5-(2'-{(Trimethylsilyl)ethyl})-4-allyl-2-cyclohexenone (61a)

The ketal sulfone 59a (236 mg, 0.56 mmol) was reduced with 2.0 g of 6% Na(Hg) and 357 mg of Na$_2$HPO$_4$ in dry methanol (12 mL) during 3.5 h as before. The resulting double bond isomer mixture was directly taken up in wet acetone (12 mL) to which 40 mg of PPTS was added. This reaction mixture was heated at reflux for 17 h and worked up in the usual manner to furnish pure $\beta,\gamma$-unsaturated ketone (96 mg, 72%) after MPLC on silica gel (elution with 5% ethyl acetate in petroleum ether); IR (neat, cm$^{-1}$) 3100-2800, 1720, 1630, 1410, 1240, 1160, 980, 900, 830; $^1$H NMR (CDCl$_3$) $\delta$ 6.0-5.6 (m, 1 H), 5.44 (br t, 1 H), 5.2-4.9 (m, 2 H), 2.9-2.7 (m, 4 H), 2.6-2.3 (m, 3 H), 1.7-1.2 (m, 2 H), 0.8-0.2 (m, 2 H), -0.03 (s, 9 H); m/e (M$^+$) calcd 236.1596, obs 236.1602.

Heating this substance (92 mg) with sodium carbonate (3 mg) in absolute methanol (20 mL) for 10 h, followed by the standard isolation procedure and MPLC
(elution as before) furnished 12 mg of recovered $\Delta^3$-isomer and 41 mg (51%) of 61a; IR (neat, cm$^{-1}$) 3100-2800, 1680, 1390, 1245, 910, 855, 830, 750; $^1$H NMR (CDCl$_3$) $\delta$ 6.80 (dd, $J = 10$ and 2 Hz, 1 H), 5.92 (br d, $J = 10$ Hz, 1 H), 6.0-5.5 (m, 1 H), 5.3-5.0 (m, 2 H), 2.7-1.7 (m, 5 H), 1.7-1.2 (m, 3 H), 0.7-0.3 (m, 2 H), -0.05 (s, 9 H); $^{13}$C NMR (CDCl$_3$) ppm 199.84, 153.37, 135.27, 129.04, 117.61, 41.40, 41.02, 40.03, 36.48, 26.97, 12.75, -1.84; m/e (M$^+$) calcd 236.1596, obs 236.1602.


Alkylation of 53. (E)-2-(Trimethylsilyl)-3-iodopropene

A 630 mg (1.35 mmol) sample of 53 was treated with 196 mg (4.08 mmol) of 50% sodium hydride and 1.03 g (4.05 mmol) of (E)-2-(trimethylsilyl)-3-iodopropene$^{37}$ in dimethylformamide (25 mL) for 17.5 h. Workup and
solvent evaporation under high vacuum gave an oil which was chromatographed (MPLC) on silica gel (elution with 15% ethyl acetate in petroleum ether). There was obtained 171 mg (35%) of 59b and 226 mg of unreacted 53; IR (neat, cm⁻¹) 3000-2800, 1460, 1440, 1385, 1300, 1245, 1150-1050, 830; ¹H NMR (CDCl₃) δ 8.0-7.4 (m, 5 H), 6.1-5.8 (m, 2 H), 4.0-3.4 (m, 6 H), 1.73 (br s, 3 H), 2.4-1.1 (series of m, 11 H), 0.96 (s, 9 H), 0.10 (m, 15 H).

5-(4'-Hydroxybutyl)-4-(3-(trimethylsilyl)-2'-butenyl)-2'-cyclohexenone (61b)

Sulfone ketal 59b (288 mg, 0.52 mmol) was reduced with 365 mg of Na₂HPO₄ and 3.2 g of 6% Na(Hg) in dry methanol (13 mL) for 1.5 h. The residue remaining after workup was heated at reflux in a solution of PPTS (30 mg) in wet acetone (13 mL) for 22 h. MPLC on silica gel (elution with 44% ethyl acetate in petroleum...
ether) afforded 105 mg (69%) of isomerically pure β,γ-
unsaturated enone; IR (neat, cm⁻¹) 3600-3200, 3000-
2800, 1710, 1415, 1245, 830; ¹H NMR (CDCl₃) δ 5.69 (m,
1 H), 5.36 (m, 1 H), 3.55 (t, J = 5 Hz, 2 H), 2.9-2.0
(series of m, 8 H), 1.66 (br s, 3 H), 1.6-1.1 (m, 6 H),
0.06 (s, 9 H); m/£ (M⁺) calcd 294.2015, obs 294.2023.

Equilibration of this substance (98 mg) was
achieved by heating with sodium carbonate (2 mg) in
absolute methanol under nitrogen for 6 h. MPLC on
silica gel (elution with 44% ethyl acetate in petroleum
ether) furnished 7 mg of recovered Δ³-isomer and 61 mg
(67%) of 6lb; IR (neat, cm⁻¹) 3600-3200, 3000-2800,
1680, 1245, 1055, 830; ¹H NMR (CDCl₃) δ 6.76 (dd, J =
11 and 2 Hz, 1 H), 5.93 (d, J = 11 Hz, 1 H), 5.7-5.5
(m, 1 H), 3.58 (t, J = 5 Hz, 2 H), 2.6-1.8 (m, 6 H),
1.67 (br s, 3 H), 1.6-1.1 (m, 9 H), 0.06 (s, 9 H); ¹³C
NMR (CDCl₃) ppm 199.81, 153.75, 135.18, 129.05, 128.87,
62.78, 41.84, 41.24, 38.75, 33.11, 32.80, 30.92, 22.73,
14.72, -2.08; m/£ (M⁺) calcd 294.2015, obs 294.2023.
Alkylation of 54. A. Geranyl Bromide

A 282 mg (0.66 mmol) sample of 54 was treated with 80 mg (1.67 mmol) of 50% NaH and 0.26 mL (1.31 mmol) of geranyl bromide in dry dimethylformamide (15 mL) for 19 h. Workup as before and MPLC on silica gel (elution with 17% ethyl acetate in petroleum ether) afforded 153 mg (41%) of 59c; IR (neat, cm⁻¹) 3000-2800, 1450, 1390, 1300, 1250, 1135, 1080, 1030, 940, 830, 770, 720, 680; ¹H NMR (CDCl₃) δ 7.9-7.4 (m, 5 H), 5.84 (s, 2 H), 5.3-4.9 (m, 2 H), 4.3-3.5 (m, 6 H), 2.2-1.8 (m, 6 H), 1.8-1.6 (m, 9 H), 1.6-1.1 (m, 3 H), 0.96 (s, 9 H), 0.13 (s, 6 H).
5-Hydroxymethyl-4-geranyl-3-cyclohexenone (62a)

Reductive desulfonation of 59c (209 mg, 0.37 mmol) was accomplished with 260 mg of Na$_2$HPO$_4$ and 2.27 g of 6% Na(Hg) in dry methanol (12 mL) during 3.5 h. The residue after workup was refluxed with 30 mg of PPTS in wet acetone (12 mL). MPLC on silica gel (elution with 44% ethyl acetate in petroleum ether) furnished 69 mg (71%) of 62a; IR (neat, cm$^{-1}$) 3600-3100, 3000-2800, 1715; $^1$H NMR (CDCl$_3$) $\delta$ 5.60 (m, 1 H), 5.3-5.0 (m, 2 H), 3.64 (d, $J = 4$ Hz, 2 H), 3.0-2.8 (m, 4 H), 2.7-2.5 (m, 3 H), 2.2-2.0 (m, 4 H), 1.8-1.6 (m, 9 H); m/e (M$^+$) calcd 262.1933, obs 262.1939.
Base-Promoted Equilibration of 62a

A solution of 62a (60 mg) in absolute methanol (12 mL) containing sodium carbonate (1.5 mg) was heated at reflux for 6.5 h. Workup in the pre-described manner (dichloromethane extraction) and silica gel chromatography (MPLC, elution with 45% ethyl acetate in petroleum ether) gave the cyclized product 64a (7 mg, 13%), unchanged 62a (6 mg), and the conjugated enone 63a (27 mg, 50%).

For 63a: IR (neat, cm⁻¹) 3600-3100, 3100-2800, 1675, 1440, 1380, 1080; ¹H NMR (CDCl₃) δ 6.86 (dd, J = 10 and 3 Hz, 1 H), 5.98 (dd, J = 10 and 2 Hz, 1 H), 5.3-4.9 (m, 2 H), 3.8-3.6 (m, 2 H), 2.6-1.8 (series of m, 10 H), 1.7-1.5 (m, 9 H), 1.5-1.2 (m, 1 H); ¹³C NMR (CDCl₃) ppm 199.39, 153.85, 138.16, 131.65, 128.81, 124.11, 120.82, 64.13, 41.22, 39.80, 29.42, 37.61, 30.67, 26.52, 25.70, 17.71, 16.29; m/e (M⁺) calcd 262.1933, obs 262.1926.

For 64a: IR (neat, cm⁻¹) 3000-2800, 1725, 1445, 1380, 1060; ¹H NMR (CDCl₃) δ 5.3-4.9 (m, 2 H), 4.3-3.7
Alkylation of 54. B. 2-Benzylxoyethyl Bromide

A 640 mg (1.51 mmol) sample of 54 was treated with 126 mg (2.62 mmol) of 50% NaH and 567 mg (2.63 mmol) of 2-benzylxoyethyl bromide in dimethylformamide (25 mL) for 18.5 h. Workup and MPLC on silica gel (elution with 30% ethyl acetate in petroleum ether) led to the isolation of C-2 monoalkylated product (115 mg), dialkylation products (106 mg) and 59d (247 mg, 29%); IR (neat, cm⁻¹) 3100-2800, 1450, 1385, 1360, 1290, 1250, 1200, 1150-1000, 830; $^1$H NMR (CDCl₃) δ 8.0-7.4 (m, 5 H), 7.33 (s, 5 H), 6.1-5.8 (m, 2 H), 4.6-3.6 (series of m, 10 H), 2.6-1.5 (series of m, 5 H), 0.94 (2s, 9 H), 0.09 (m, 6 H).
5-Hydroxymethyl-4-(2'—benzyloxyethyl)-3-cyclohexenone (62b)

Reductive desulfonylation of 59d (229 mg, 0.41 mmol) was accomplished with 260 mg of Na₂HPO₄ and 1.5 g of 6% Na(Hg) in dry methanol during 4 h. The resulting oil was hydrolyzed with 30 mg of PPTS in wet acetone (12 mL) at the reflux temperature (22 h). MPLC on silica gel (elution with 60% ethyl acetate in petroleum ether) afforded 80 mg (75% overall) of 62b as the sole product; IR (neat, cm⁻¹) 3600–3200, 3100–2800, 1710, 1450, 1400, 1355, 1195, 1100–1000, 730, 690; ¹H NMR (CDCl₃) δ 7.36 (s, 5 H), 5.67 (br s, 1 H), 4.51 (br s, 2 H), 3.7–3.5 (m, 4 H), 2.9–2.3 (m, 8 H); m/z (M⁺) calcd 260.1412, obs 260.1420.
Base-Promoted Equilibration of 62b

Treatment of 62b (75 mg) in a totally analogous manner afforded cyclized product 64b (18 mg, 26%), recovered starting material (6 mg), and conjugated enone 63b (26 mg, 38%).

For 63b: IR (neat, cm\(^{-1}\)) 3600-3200, 3000-2800, 1675, 1450, 1120-1050, 740, 640; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.36 (s, 5 H), 6.85 (dd, \(\Delta = 9\) and 3 Hz, 1 H), 5.98 (br d, \(\Delta = 9\) Hz, 1 H), 4.50 (s, 2 H), 3.7-3.4 (m, 4 H), 2.6-1.5 (series of m, 7 H); \(^13\)C NMR (CDCl\(_3\)) ppm 199.22, 153.57, 137.99, 128.64, 128.53, 127.87, 127.76, 73.31, 67.84, 64.23, 41.66, 39.47, 34.82, 32.42; m/e (M\(^+\)) calcd 260.1412, obs 260.1426.

For 64b: IR (neat, cm\(^{-1}\)) 3000-2800, 1720, 1450, 1360, 1200, 1100, 735, 690; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 7.34 (s, 5 H), 4.51 (s, 2 H), 4.1-3.5 (m, 5 H), 2.6-1.5 (series of m, 8 H); m/e (M\(^+\)) calcd 260.1412, obs 260.1400.
REFERENCES


8b Birch, A.J.; Mukherji, S.M. Ibid. 1949, 2531.


10 Wenkert, E.; Goodwin, T.E.; Ranu, B.C. 1977, 42, 2137.


19 Sterzycki, R. *Synthesis* 1979, 724.


Examples of this transformation will appear later in this discussion, e.g. \( 20 \rightarrow 22 \).


PART II

CONSTRUCTION OF FUSED 4–CYCLOOCTENONES BY CLAISEN REARRANGEMENT AND APPROACHES TO THE SYNTHESIS OF PRECAPNELLADIENE
INTRODUCTION

In recent years, there have been several bicyclic marine natural products discovered which contain eight-membered rings (Figure 1). Three of these sesquiterpenes incorporate the identical carbon skeleton composed of the unprecedented bicyclo[6.3.0]undecane ring system. Dactylol (1) was isolated from a Caribbean sea hare, *Aplysia dactylomela*, and its structure and absolute configuration were determined by chemical degradation and NMR studies.\(^1\) The isolation of 1 from red seaweeds of the genus *Laurencia* has also been reported\(^2\) and it was suggested that the sea hare concentrates dactylol while grazing on the latter species. Another metabolite isolated from *Laurencia poitei* is poitediol (2), whose three-dimensional structure was elucidated by x-ray crystallography.\(^2\) The soft coral *Capnella imbricata* contains yet another sesquiterpene of the same carbon skeleton, precapnelladiene (3).\(^3\) Its structure was determined by high field NMR with the assistance of the CONGEN computer program, which
Figure 1. Bicyclic Natural Products Containing Eight-Membered Rings

generates possible structures and isomers. The relative stereochemistry was not established and a total synthesis of epiprecapnelladiene⁴ was therefore required to prove the configuration of the natural material. A unique terpenoid structure is represented by neolemnanyl acetate (4), which was isolated from the Pacific soft coral Lemnalia africana.⁵ X-ray crystallography was utilized to elucidate its structure.
Figure 2. Tricyclic Natural Products Containing Eight-Membered Rings
Much of the work in the synthesis of eight-membered rings has been directed at more elaborate tricyclic natural products (Figure 2), which have been known for over a decade. These diterpenes and sesterterpenes include pleuromutilin (5), the ophiobolins typified by ophiobolin F (6), the fusicoccins of which cotylenol (7) is an example, and the ceroplastols represented by ceroplastol I (8). Although there have been many creative approaches to the molecules described above, and these have been primarily oriented toward suitable elaboration of eight-membered rings, only one total synthesis has appeared in the literature, i.e. of pleuromutilin (5).

The procedures most commonly employed to construct eight-membered rings in natural products synthesis (Scheme I) can be organized into three general categories. Dutta and Boeckman (Scheme I, A, B) demonstrated methods involving the cleavage of bicyclo[3.3.1]nonanes with base to afford cyclooctenecarboxylic acids in studies directed at the ophiobolins. The second reaction type includes a [2+2]
SCHEME I

A.\[
\begin{array}{c}
\text{OTs} \\
\text{NaOEt, EtOH} \\
\text{KOH, MeOH} \\
\end{array}
\]
(Ref. 10)

B.\[
\begin{array}{c}
\text{LiAl(OEt-Bu)₃H} \\
\text{TsCl, py} \\
\text{NaOMe} \\
\end{array}
\]
(33%)
(Ref. 11)

C.\[
\begin{array}{c}
\text{DMAD} \\
\text{H₂O} \\
\end{array}
\]
(40%)
(Ref. 12)

D.\[
\begin{array}{c}
\text{hv} \\
(77\%) \\
\text{NaOH, H₂O} \\
\text{Na₂RuO₄} \\
(58\%) \\
\text{Li, NH₃} \\
\text{H₂CrO₄} \\
\text{CH₃N₂} \\
(44\%) \\
\end{array}
\]
SCHEME I (Cont'd.)

E.

\[
\text{hv} \quad (98\%) \quad \text{KOH} \quad \text{EtOH} \quad (33\%) 
\]

(Ref. 4)

F.

\[
\text{MgBr} \quad \text{KH, THF} \quad 55^\circ \text{C, 30 min} \quad (35\%) 
\]

(Ref. 14)

G.

\[
\text{ether} \quad \text{KH, THF} \quad 25^\circ \text{C, 45 min} \quad \begin{array}{c}
(49\%) \\
(13\%) 
\end{array} 
\]

(Ref. 15)
SCHEME I (Cont'd.)

H.

\[ \text{ester} \xrightarrow{\text{Cp}_2\text{Li}, -78^\circ C, 1 h} \text{intermediate} \]

\[ \text{intermediate} \xrightarrow{\text{CH}_3\text{I}, \text{rt}, 2 h} \text{product} \]

(Ref. 16)

I.

\[ \text{acetyl chloride} + \text{alkene} \xrightarrow{100^\circ C, 41 h} \text{products} \]

\[ \text{product} \]

(Ref. 17)
annulation followed by ring opening (Scheme I, C-E).
Dauben and Hart applied the reaction of enamines with acetylenic esters to achieve expansion of the six-membered ring en route to the ophiobolin nucleus. More commonly, this kind of ring enlargement incorporates a high yielding intramolecular [2+2] photochemical addition and a subsequent Grob fragmentation as accomplished by Coates and Pattenden. Finally, Cope rearrangements of divinylcyclobutanes have been seen in many applications (Scheme I, F-I). Kahn illustrated an example of an oxy-anionic Cope rearrangement, which theoretically could be employed in the synthesis of pleuromutilin (5). Gadwood has demonstrated this scheme as well, and has recently utilized it in a total synthesis of poitediol (2). The most successful exploitation of this method was Paquette's synthesis of the ophiobolin skeleton in 96% yield. Danheiser generated an unactivated divinylcyclobutane system in situ, by the [2+2] cycloaddition of a vinyl ketene with 1-vinylcyclopentene, which required elevated temperatures and produced low yields of a five-eight fused ring system. With the exception of Paquette's example (Scheme I, H) all of these procedures are fairly inefficient (<50% yield) and further investigations are warranted.
A new method for the elaboration of eight-membered rings by Claisen rearrangement will be introduced in the following discussion. It is well known that 2-vinyl-5-methylenetetrahydrofurans (9) undergo [3,3]-sigmatropic rearrangement to afford 4-cycloheptenones (Scheme II). Therefore, it would be expected that
thermolysis of 10 would similarly deliver 4-cyclo-octenones. In fact, one would predict that this process would be more facile in the latter case because less ring strain would be involved when proceeding through the chair transition state. Bicyclic molecules should be accessible from 11. Many creative studies of allyl vinyl ether systems have been reported, some of which resemble 10 (Scheme III). However in 12 and 13, the vinyl portion is not exocyclic and rearrangement affords the six-membered carbocycle. Systems such as these are much more accessible than 10, because the endocyclic double bond is favored thermodynamically in cyclic ether systems. Studies have revealed that 2-methylenetetrahydropyrans are significantly less stable than 2-methylenetetrahydrofurans (K^endo/exo:K^endo/exo = 500:1). This was attributed to the fact that the lone pairs on oxygen are oriented poorly for resonance with the exocyclic double bond in hydropyrans. Therefore, it was a major concern that 10 might behave differently (Scheme IV) than the furan 9 and isomerize to 14 before Claisen rearrangement delivering 15. It was with this understanding that the project was undertaken.
SCHEME III

A.  
\[ \text{12} \xrightarrow{240^\circ C, 25 \text{ min}} \text{13} \]  
(65%)  
(Ref. 23)

B.  
\[ \text{PhSe} \xrightarrow{1. \text{NaIO}_4} \xrightarrow{2. \text{toluene, reflux, 18 h}} \text{14} \]  
(81%)  
(Ref. 24)  
(cis:trans, 7:2)

C.  
\[ \text{13} \xrightarrow{1. 105^\circ C} \xrightarrow{2. \text{HCl}} \text{15} \]  
(63%)  
(Ref. 25)
RESULTS AND DISCUSSION

Model Studies

Before undertaking the total synthesis of precapnelladiene (3), it seemed prudent to examine the feasibility of this Claisen rearrangement on several model systems. Construction of ring systems resembling the precapnelladiene (3) and neolemnanyl acetate (4) skeletons was the goal. Therefore, allyl vinyl ethers 16, 17, and 18 were prepared and their thermal reactions studied (Scheme V).

The [3,3]-sigmatropic rearrangement of 16 was expected to afford 19, which contains the basic 5,8-ring system of precapnelladiene. Treatment of keto
SCHEME V

16 \[\rightarrow \Delta \rightarrow \] 19

17 \[\rightarrow \Delta \rightarrow \] 19

18 \[\rightarrow \Delta \rightarrow \] 20

3

4
ester 21 with vinyl magnesium bromide delivered a single isomer 22 as a consequence of attack from the less hindered side and spontaneous lactonization (Scheme VI). Olefination of 22 was efficiently accomplished with Tebbe reagent (23)\(^{30}\) to yield 16. Transfer of 16 in toluene solution to a potassium hydroxide-coated soft glass tube,\(^{22b}\) in order to minimize isomerization to 24, followed by thermolysis yielded 19 and 25. Major product 19 contained the desired eight-membered ring as evidenced by a characteristically high carbonyl chemical shift in its \(^{13}\)C NMR spectrum (214.39 ppm). Also observed as a minor product was 25, from Claisen rearrangement of 24 after isomerization to the endocyclic olefin.

Model system 17 (Scheme V) ought to deliver a carbon skeleton more closely resembling precanelladiene in that two additional methyl groups have been included. It was anticipated that their incorporation might create a steric problem in the rearrangement. Lactone 26 was prepared by addition of 2-methylpropen-1-yl lithium to 21 (Scheme VII). Treatment of 26 with Tebbe reagent followed by pyrolysis afforded a pair of unexpected isomers 27a and 27b.
The methyl groups in 17 appear to encourage elimination by donating charge density into the developing allylic cation. It seemed possible that the potassium hydroxide, coated on the tubes, was causing cleavage. Therefore, 17 was heated in an uncoated pyrex tube, which again delivered 27b. Although these results were discouraging, 17 differs in one important way from 28,
SCHEME VII

1.) Tebbe (23)
2.) 176°C
18 h
(61%)

17

21

\[ \text{ether (37\%)} \]

26

[Diagram of chemical reactions and structures]

27a + 27b

28
which is required for the synthesis of precapnelladiene. It was possible that only syn-elimination of 17 was occurring and replacement of \( H_d \) with a methyl group as in 28 would preclude operation of this pathway.

It was anticipated that the neolemnanyl acetate skeleton (4), minus one methyl group, would be accessible from 18 (Scheme V). This final model system was prepared as before by olefination of the appropriate lactone (30) (Scheme VIII). Thermolysis of 18 delivered 20 as the major product, which contains the desired 6,8-ring system. Again, a minor product (31) was observed from isomerization of 18 prior to rearrangement. The possibility of eliminating this isomerization by prior introduction of unsaturation as in lactone 32 was next considered. Olefination with Tebbe reagent afforded the fixed exocyclic olefin 33; however, pyrolysis did not afford the desired product.
SCHEME VIII

\[
\text{Scheme VIII}
\]

\[
\text{1.) Tebbe (23)}
\]

\[
\text{2.) } 192 \, ^\circ \text{C}
\]

\[
\text{46 h}
\]

\[
\begin{align*}
\text{29} & \xrightarrow{\text{THF}} \text{30} \\
& \text{(36%)}
\end{align*}
\]

\[
\begin{align*}
\text{18} & \xrightarrow{\text{H}_2\text{O}_2} \text{33}
\end{align*}
\]

\[
\begin{align*}
\text{20} & \text{(37%)} \\
\text{31} & \text{(13%)}
\end{align*}
\]

\[
\begin{align*}
\text{32} & \xrightarrow{\text{1.) Tebbe}} \text{33}
\end{align*}
\]

\[
\begin{align*}
\text{30} & \xrightarrow{\text{LDA}} \text{32} \\
& \text{PhSeCl} \\
& \text{H}_2\text{O}_2
\end{align*}
\]

\[
\text{(72%)}
\]
Approaches to the Synthesis of Precapnelladiene

There are three primary challenges that must be addressed in the synthesis of precapnelladiene (3). The strategy must include efficient construction of the eight-membered ring, regioselective introduction of unsaturation, and stereoselective orientation of the C-1 methyl group (Figure 3). By implementation of the Claisen rearrangement, two of the requirements are satisfied. Thermolysis of 35 should afford the 4-cyclooctenone 34, which incorporates one properly disposed olefin and a suitable handle for selective insertion of the other. The stereochemistry can be defined in cyclopentanone 37, which embodies the proper cis-relationship. In order to simplify the spectral analysis of stereoisomers, 36a was first synthesized which contains only two asymmetric centers.

Preparation of 36a and 37

Initially 36 was prepared as an inseparable mixture of cis-and trans-isomers by alkylation of the pyrrolidine enamine of 2-methylcyclopentanone with
methyl acrylate (Scheme IX).\textsuperscript{31} Only a moderate yield of the desired alkylation product (36) was observed. The two isomeric methyl groups were clearly distinguished in the 300 MHz $^1$H NMR spectrum of 36 as two doublets in a ratio of 2:1. The minor isomer was later determined to be 36a by preparing the cis-compound in a pure state. Equilibration of 36 with acid or base did not alter the proportion. Consequently, it would
appear that the thermodynamic distribution had already been achieved.

**SCHEME IX**

The mixture of isomers was converted to pure 36a by a four step sequence (Scheme X). Reduction of 36
with sodium borohydride proceeded uneventfully. However, the dehydration of 40 was more problematic, affording 42 and 43 as side products. Other dehydration reagents were examined, but reaction with phosphorus oxychloride gave the best results. Hydroboration of 41 with 9-BBN\textsuperscript{32d} cleanly provided a single isomer 40a with the proper \textit{cis}-orientation. Oxidation with pyridinium chlorochromate\textsuperscript{33} afforded 36a in
greater than 95% purity (300 MHz $^1$H NMR integration). Although this scheme was very stereoselective, it was less than efficient and an alternative means to prepare 36a was desired.

Conia reported$^{34}$ that 45 was synthesized by copper-catalyzed conjugate addition of the Grignard reagent of 4-bromo-1-butene to 2-cyclopentenone, followed by ene cyclization (Scheme XI). This sequence was conveniently repeated in 54% and 25% yields and has recently been improved to 76% and 48%. This was achieved by utilizing (n-Bu)$_3$P and CuI as the cuprate catalyst and by scaling up the ene reaction to 10 g runs at 325°C for 6-8 hours in a large Carius tube.$^{35}$

Baeyer-Villiger oxidation of 45 with m-chloroperbenzoic acid expediently provided 43a. This lactone was cleaved to afford the corresponding hydroxy ester with catalytic sodium methoxide in methanol. In order to minimize conversion of the hydroxy ester back to the stable cis-fused lactone (43a), oxidation was performed immediately to give 36a in 63% yield (74% based on recovered 43a) (Figure 4). Additionally, 37 can be prepared as a single isomer by this scheme.
SCHEME XI

Methylation of 43a occurred only from the convex face of the molecule, and subsequent ring opening and oxidation delivered 37 efficiently (Figure 5).
Figure 4. 300 MHz $^1$H NMR Spectrum of 36a as Prepared from 43a
Figure 5. 300 MHz $^1$H NMR Spectrum of 37
Claisen Rearrangements

Because of the lack of success in the Claisen rearrangement of 17 in the model studies, two additional systems 28 and 47 were examined, before attempting to construct the precapnelladiene skeleton directly from 35 (Figure 6). It was feared that 28 and 35 would cleave when heated, as was seen in 17, which would necessitate laborious introduction of the geminal methyl groups after the rearrangement of 47. Even if cleavage of 28 and 35 did not occur, steric interaction between the three methyl groups in 35 might cause the Claisen rearrangement to be unfavorable relative to isomerization of the exocyclic double bond, which would require methylation of the product derived from 28 to afford the precapnelladiene nucleus.

The best scenario began to unfold with the preparation of 28 (Scheme XII). Treatment of 36a with 2-methylpropen-1-yllithium prior to quenching at \(-78^\circ\text{C}\) gave a mixture of 48 and 49 (Figure 7) in 54% yield. Conversion of 48 to 49 was readily accomplished by treatment with sodium hydride at \(-78^\circ\text{C}\) and by warming to room temperature. Lactone 49 was combined with
Tebbe reagent to provide 28, which was then heated at 200°C for about two days. Rearrangement products 50 (Figure 8) and 51 were isolated, which indicated that the C-1 methyl group precluded syn-elimination as had been hoped.
SCHEME XII

\[ \text{36a} \rightarrow \text{ether} \rightarrow -78^\circ C \]

\[ \text{49 (25%)} + \text{48 (29%)} \]

1.) Tebbe (23)
2.) 200°C, 44 h

\[ \text{NaH, THF} \rightarrow -78^\circ C \rightarrow \text{rt} \]

(72%)

\[ \text{28} \]

\[ \text{50 (38%)} + \text{51 (32%)} \]
Figure 7. 200 MHz $^1$H NMR Spectrum of 49
Figure 8. 300 MHz $^1$H NMR Spectrum of 50
Another surprising and satisfying result was seen when the thermal reaction of 47 was investigated (Scheme XIII). Lactone 52 was conveniently synthesized by treating 37 with vinyl lithium at $-78^\circ C$ and briefly warming the reaction mixture to ambient temperature. Olefination of 52 afforded 47, which when thermolyzed provided exclusively 53 in 91% yield as a mixture of isomers (Figures 9 and 10) (2.8:1 ratio of 53b:53a). Epimerization apparently occurred when 53 interacted with the potassium hydroxide in the tube. The stability of the exocyclic double bond in 47 can be attributed to the inaccessibility of the only proton adjacent to the olefin. Without speculating about the mechanism of the 1,3-shift, the specifically oriented $\alpha$-methyl group in the lactone prevented this process from operating.
SCHEME XIII

1. Tebbe (23)
2. 200 °C 48 h (91%)

 Ether

\(-78 °C \rightarrow rt\) (62%)

52

47
Figure 9. 300 MHz $^1$H NMR Spectrum of 53a
Figure 10. 300 MHz $^1$H NMR Spectrum of 53b
The precapnelladiene skeleton was expediently prepared in an analogous manner from 35 (Scheme XIV). Treatment of 37 with 2-methylpropen-1-yllithium provided a single stereoisomer 54 (Figure 11). Allyl
vinyl ether 35, available from 54, incorporates the properly disposed methyl groups to eliminate the undesired cleavage and isomerization products upon heating. Thermolysis of 35 in a base coated tube afforded 34 in 87% yield over two steps (Figures 12 and 13) (3.4:1 ratio of 34b:34a).

CONCLUSION

This novel method for the construction of fused 4-cyclooctenones has been proven to be very efficient in selected examples and was especially well suited for the elaboration of the precapnelladiene nucleus (34). It is expected that the last double bond will be successfully introduced to complete the total synthesis of 3. Initial attempts to implement this by reduction with sodium borohydride and dehydration with phosphorus oxychloride were frustrated by transannular reactions. Currently, other means are being investigated to accomplish this task. Experimentation is also underway to apply this scheme to the synthesis of other bicyclic natural products (Figure 1).
Figure 11. 50 MHz $^{13}$C NMR Spectrum of 54
Figure 12. 200 MHz $^1\text{H}$ NMR Spectrum of 34a
Figure 13. 200 MHz $^1$H NMR Spectrum of 34b
**EXPERIMENTAL**

*cis*-7a-Ethenylhexahydrocyclopenta[b]pyran-2(3H)-one (22)

Vinyl bromide was added via an addition funnel to magnesium turnings (490 mg, 20 mmol) in tetrahydrofuran (5 mL) until all the magnesium was consumed (initiation with 1,2-dibromo-ethane). After dilution with additional solvent (13 mL), the mixture was cooled to $-78^\circ\text{C}$ and 2131 (1.70 g, 10 mmol) in tetrahydrofuran (5 mL) was added dropwise over 10 min and stirred at $-78^\circ\text{C}$ for 3 h. The solution was allowed to warm for 20 min, quenched with saturated ammonium chloride solution, poured into water (50 mL), and acidified with acetic acid. The product was extracted into ether (3x50 mL) and the combined organic layers were washed with saturated sodium bicarbonate solution, dried, and evaporated. The residue was chromatographed on silica gel (MPLC, elution with 10% ethyl acetate in petroleum ether) affording 415 mg
(25%) of 22; IR (neat, cm\(^{-1}\)) 3000-2840, 1740, 1255, 1170, 1100, 1000, 925; \(^1\)H NMR (CDCl\(_3\)) \& 6.0-5.0 (m, 3H), 2.5-1.4 (series of m, 11 H); \(^13\)C NMR (CDCl\(_3\)) ppm 172.29, 140.68, 113.79, 93.07, 40.58, 40.36, 29.59, 26.48, 22.48, 21.50; m/e (M\(^+\)) calcd 166.0994, obs 166.0978.

Anal. Calcd for C\(_{10}\)H\(_{14}\)O\(_2\): C, 72.26; H, 8.49. Found: C, 72.12; H, 8.55.

Preparation of 23

A solution of titanocene dichloride (6.00 g, 24.1 mmol) and 2 M trimethylaluminum (26 mL, 52 mmol) in toluene was prepared under argon.\(^{30}\) After 48 h, all volatiles were removed under high vacuum and the residue was dissolved in dry deoxygenated toluene (30 mL). The molarity of the reagent was determined by combining 1 mL of the stock solution with methyl benzoate (0.10 mL, 0.80 mmol) and pyridine (2 drops) in an NMR tube under argon. After 12 h, the ratio of methyl singlets in the
\[^{1}\text{H NMR} \text{ spectrum of this mixture indicated 74\% conversion to product. Therefore, the concentration of reagent was approximately 0.59 \text{ M}.}\]

cis-7a-Ethenyloctahydro-2-methylenecyclopenta[b]pyran (16)

A solution of 22 (101 mg, 0.61 mmol), pyridine (1 drop), tetrahydrofuran (0.5 mL), and toluene (1.5 mL) was prepared under argon. The mixture was cooled to 0\degree C and 0.55 M Tebbe reagent (23) (1.3 mL, 0.71 mmol) in toluene was added dropwise. After being stirred for 90 min at 25\degree C, the solution was again cooled to 0\degree C and quenched with 15\% sodium hydroxide solution (0.30 mL). After gas evolution had ceased, ether was added and the mixture was dried, filtered, and evaporated. The residue was passed through a short column (6x3 cm) of basic alumina (Act. III, elution with petroleum ether) to provide 92 mg (92\%) of 16; IR (neat, cm\(^{-1}\)) 3000-2820, 1650, 1450, 1270, 1110, 1015, 915; \[^{1}\text{H NMR} (\text{CCl}_4) \delta 6.1-4.9 \text{ (m, 3}\]"
H), 4.13 (br s, 1 H), 3.85 (br s, 1 H), 2.3-1.2 (series of m, 11 H); m/e (M⁺) calcd 164.1201, obs 164.1204.

1,2,3,3a,4,5,7,8-Octahydro-6H-cyclopentacycloocten-6-one (19)

A solution of 16 (57 mg) in toluene (1 mL) was sealed under vacuum in a potassium hydroxide-coated soft glass tube²²b (7 mm O.D.) and heated at 175°C for 23 h. The resulting pale yellow solution was evaporated and the residue was purified on silica gel (MPLC, elution with 10% ethyl acetate in petroleum ether). There was isolated 16 mg (28%) of 25, followed by 24 mg (42%) of 19.

For 19: IR (neat, cm⁻¹) 3000-2800, 1710, 1440, 1335; ¹H NMR (CDCl₃) δ 5.44 (br t, 1 H), 2.8-2.1 (series of m, 9 H), 1.9-1.3 (m, 6 H); ¹³C NMR (CDCl₃) ppm 214.39, 149.74, 119.66, 47.66, 41.21, 40.12, 34.50, 33.48, 32.01, 24.34, 23.83; m/e (M⁺) calcd 164.1202, 164.1192.
Anal. Calcd for C_{11}H_{16}O: C, 80.44; H, 9.82.
Found: C, 80.04; H, 9.82.

For 25: IR (neat, cm^{-1}) 3000-2800, 1710, 1435, 1355, 1160; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \delta 5.35 (m, 1 H), 2.6-2.1 (m, 6 H), 2.14 (s, 3 H), 2.0-1.0 (m, 6 H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}) ppm 211.83, 144.91, 115.26, 48.30, 40.99, 33.07, 31.03, 29.69, 27.91, 27.53, 23.31; m/z (M\textsuperscript{+}) calcd 164.1202, obs 164.1191.

cis-Hexahydro-7a-(2-methyl-1-propenyl)cyclopenta[b]pyran-2(3H)-one (26)

An argon-blanketed, magnetically stirred solution\textsuperscript{15a} of 1-bromo-2-methylpropene (3.0 mL, 29 mmol) in ether (60 mL) was cooled to -78°C, treated with 2.0 M \textit{tert}-butyllithium (15.0 mL, 30 mmol) in pentane, and allowed to warm to 0°C for 30 min. After the temperature was returned to -78°C, 21 (1.70 g, 10 mmol) in cold (-78°C) ether (5 mL) was added rapidly via canula. After 25 min, tetrahydrofuran (25 mL) was added, the reaction mixture was
allowed to warm over 20 min, treated with saturated ammonium chloride solution, poured into brine (50 mL), and extracted with ether (3x50 mL). The combined organic layers were dried and concentrated in vacuo. Chromatography of the residue on silica gel (MPLC, elution with 15% ethyl acetate in petroleum ether) afforded 720 mg (37%, 55% based on recovered 21) of 26 as well as 562 mg of 21.

For 26: IR (neat, cm\(^{-1}\)) 3000-2800, 1740, 1450, 1260, 1185, 1010; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.30 (m, 1 H), 2.38 (t, \(J = 6\) Hz, 2 H), 2.3-1.0 (series of m, 9 H), 1.79 (d, \(J = 2\) Hz, 3 H); \(^13\)C NMR (CDCl\(_3\)) ppm 173.11, 138.12, 127.34, 92.25, 43.26, 40.36, 30.08, 27.08, 26.97, 22.65, 21.88, 19.31; m/z (M\(^+\)) calcd 194.1307, obs 194.1261.

Anal. Calcd for C\(_{12}\)H\(_{18}\)O\(_2\): C, 74.19; H, 9.34. Found: C, 73.91; H, 9.34.
4-[2-(2-Methyl-1-propenyl)-1-(and 2- )cyclopenten-1-yl]-2-butanone (27)

Olefination of 26 (100 mg, 0.51 mmol) was achieved by admixing toluene (1.5 mL), tetrahydrofuran (0.5 mL), pyridine (one drop), and 0.52 M Tebbe reagent (23) (1.1 mL, 0.57 mmol) in toluene (dropwise at 0°C) with stirring for 90 min. After the usual workup, $^1$H NMR spectroscopy indicated formation of the exocyclic olefin. This material was transferred with toluene (1 mL) to a base-coated soft glass tube, sealed under vacuum, and heated at 176°C for 18 h. Chromatography by MPLC (silica gel, elution with 5% ethyl acetate in petroleum ether) yielded 60 mg (61%) of 27; IR (neat, cm$^{-1}$) 3000-2800, 1720, 1440, 1360, 1160; $^1$H NMR (CDCl$_3$) $\delta$ 5.8-5.4 (m, > 1 H), 2.8-1.3 (series of m, < 10 H), 2.12 (s, 3 H), 1.79 (br s, 6 H); m/e (M$^+$) calcd 192.1514, obs 192.1521.
Methyl α,1-Dimethyl-2-oxocyclohexanepropanoate (29)

To a cooled (0°C) solution\(^\text{37}\) of 2-methylcyclohexanone (41.4 g, 0.369 mol) and sodium methoxide (2.0 g, 37 mmol) in tetrahydrofuran (500 mL) was added methyl methacrylate (40 mL, 0.37 mol) in tetrahydrofuran (40 mL) dropwise. The mixture was stirred for 3 h at 0°C and 20 h at rt, poured into 5% hydrochloric acid (1000 mL), and extracted with ether (2x300 mL). The combined organic phases were washed with brine, dried, and evaporated. Distillation of the residual oil afforded 44.0 g (56%) of 29, bp 101-102°C/0.7 mm; IR (neat, cm\(^{-1}\)) 3000-2800, 1740, 1710, 1460, 1380, 1315, 1165, 990; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.61 (s, 1.5 H), 3.57 (s, 1.5 H), 2.48-1.34 (series of m, 11 H), 1.13 (d, \(J = 7\) Hz, 1.5 H), 1.09 (d, \(J = 7\) Hz, 1.5 H), 1.02 (s, 1.5 H), 1.01 (s, 1.5 H); m/e (M\(^+\)) calcd 212.1412, obs 212.1416.
(4aΩ,8aΩ)-8a-Ethenyloctahydro-3,4a-dimethyl-2H-1-
benzopyran-2-one (30)

Vinyl magnesium bromide was prepared in the usual manner (2 h) from magnesium turnings (7.2 g, 0.30 mol), vinyl bromide (18 mL, 0.25 mol), and tetrahydrofuran (100 mL) and stirred for an additional 2.5 h. After the reaction mixture was diluted with tetrahydrofuran (100 mL) and cooled (-78°C), 29 (40 g, 0.19 mol) in the same solvent (30 mL) was added dropwise. The cooling bath was removed and 30 min later saturated ammonium chloride solution was added. The oil obtained after the usual workup was distilled to deliver 26.1 g of crude material, bp 109-120°C/0.7 mm (54% pure by MPLC, 36% yield). This material was chromatographed before use by MPLC or HPLC with one recycle (silica gel, elution with 5% ethyl acetate in petroleum ether) to afford pure 30; IR (neat, cm⁻¹) 3000-2840, 1735, 1465, 1250-1100, 1000, 935; ¹H NMR (CDCl₃) δ 6.54-5.86 (m, 1 H), 5.39-5.11 (m, 2 H), 2.63-2.58 (m, 1 H), 1.90-1.38 (series of m, 10 H), 1.21 (d, J = 7 Hz, 1.5 H), 1.20 (d, J = 7 Hz, 1.5
H), 1.04 (s, 2.4 H), 0.98 (s, 0.6 H); m/e (M+ ) calcd 208.1463, obs 208.1485.

Anal. Calcd for C_{13}H_{20}O_{2}: C, 74.96; H, 9.68.
Found: C, 74.71; H, 9.74.

2,3,4,4a,5,6,8,9-Octahydro-4a,6-dimethyl-7(1H)-benzocyclooctenone (20)

A cold (-40°C) solution of 30 (311 mg, 1.49 mmol), toluene (2 mL), tetrahydrofuran (1 mL), and pyridine (1 drop) was treated with 0.52 M Tebbe reagent (23) (3.2 mL, 1.7 mmol) in toluene. After 90 min at 25°C, the reaction mixture was cooled (-20°C) and quenched with 15% sodium hydroxide solution (0.45 mL). The warmed solution was diluted with petroleum ether, dried, filtered, and concentrated. The residue in toluene was transferred to a base-coated soft glass tube with 0.25 mL of toluene and sealed. Thermolysis at 192°C for 46 h yielded an oil which was chromatographed on silica gel (MPLC, elution with 3% ethyl acetate in petroleum
ether) to afford 40 mg (13%) of 31 and 113 mg (37%) of 20.

For 20: IR (neat, cm\(^{-1}\)) 3000-2820, 1705, 1450, 1375, 1260; \(^1H\) NMR (CDCl\(_3\)) \(\delta\) 5.35-5.27 (m, 1 H), 2.97-1.20 (series of m, 15 H), 1.18-1.07 (m, 6 H); \(^{13}C\) NMR (CDCl\(_3\)) ppm 216.82, 215.41, 147.57, 145.02, 120.36, 119.91, 47.98, 47.53, 44.79, 42.55, 40.89, 40.76, 38.78, 35.91, 27.80, 27.41, 23.71, 22.81, 22.36, 22.11, 20.96, 19.24; m/z (M\(^+\)) calcd 206.1671, obs 206.1697.

Anal. Calcd for C\(_{14}H_{22}O\): C, 81.50; H, 10.75. Found: C, 81.55; H, 10.78.

For 31: IR (neat, cm\(^{-1}\)) 3000-2800, 1710, 1450, 1360, 1135; \(^1H\) NMR (CDCl\(_3\)) \(\delta\) 5.30 (td, \(J = 4\) and 2 Hz, 1 H), 2.35-1.17 (series of m, 12 H), 2.13 (s, 3 H), 1.15 (s, 3 H), 1.11 (s, 3 H); \(^{13}C\) NMR (C\(_6\)D\(_6\)) ppm 210.93, 142.83, 117.28, 47.84, 47.01, 42.41, 35.58, 33.92, 32.58, 28.87, 25.49, 24.85, 24.59, 22.61; m/z (M\(^+\)) calcd 206.1671, obs 206.1706.
cis-8a-Ethenyl-4a,5,6,7,8,8a-hexahydro-3,4a-dimethyl-2H-1-benzopyran-2-one (32)

A lithium diisopropylamide solution was prepared at 0°C from diisopropylamine (2.0 mL, 14 mmol), 1.55 M n-butyllithium (8.4 mL, 13 mmol) in hexane, and tetrahydrofuran (20 mL). To the cooled (-78°C) solution was added 30 (2.41 g, 11.6 mmol) in tetrahydrofuran (5 mL) over 10 min. After an additional 55 min, phenylselenenyl chloride (2.52 g, 13.2 mmol) in the same solvent (5 mL) was added with stirring for 1 h. The reaction mixture was warmed for 10 min, quenched with saturated ammonium chloride solution, and worked up in the usual manner. The α-phenylseleno lactone was dissolved in dichloromethane (200 mL), cooled to 0°C, and oxidized with 15% hydrogen peroxide (40 mL) for 30 min. After returning to rt during 30 min, the dichloromethane layer was extracted with saturated sodium bicarbonate solution (100 mL), and dried. The residue was purified on silica gel (MPLC, elution with 5% ethyl acetate in petroleum ether) to yield 1.73 g (72%) of 32; IR (neat,
cm\(^{-1}\)) 3000–2810, 1720, 1450, 1365, 1210–1080, 1020, 930, 880; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 6.41–5.96 (m, 1 H), 6.25 (br s, 0.2 H), 6.18 (br s, 0.8 H), 5.40–5.15 (m, 2 H), 1.87 (d, \(J = 2\) Hz, 2.4 H), 1.79 (d, \(J = 2\) Hz, 0.6 H), 1.78–1.44 (series of m, 8 H), 1.20 (s, 0.6 H), 1.07 (s, 2.4 H); m/e (M\(^+\)) calcd 206.1307, obs 206.1324.

**Anal.** Calcd for C\(_{13}\)H\(_{18}\)O\(_2\): C, 75.69; H, 8.80. Found: C, 75.65; H, 8.95.

**Methyl 3-Methyl-2-oxocyclopentanepropanoate (36)**

The pyrrolidine enamine\(^{31}\) of 2-methylcyclopentanone\(^{39}\) (1.0 g, 6.6 mmol) was dissolved in 9 mL of dry methanol, treated with 0.60 mL (6.7 mmol) of methyl acrylate, and heated at reflux for 3 h. Following addition of 1 mL of water, reflux was continued for an additional hour. The methanol was removed in vacuo and the residue was taken up into 75 mL of ether. The organic layer was washed with 5% hydrochloric acid (2x25 mL) and brine (25 mL) prior to drying. Concentration in vacuo afforded a mixture of
three products which were purified by MPLC (silica gel, elution with 12% ethyl acetate in petroleum ether) to yield 570 mg (47%) of 36, 180 mg (15%) of 38, and 200 mg (11%) of dialkylation product 39.

For 36: IR (neat, cm\(^{-1}\)) 3000-2800, 1740, 1440, 1370, 1250, and 1170; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.65 (s, 3 H), 2.4-2.3 (m, 2 H), 2.2-2.0 (m, 6 H), 1.7-1.6 (m, 2 H), 1.08 (d, \(J = 7\) Hz, 2 H), 1.04 (d, \(J = 7\) Hz, 1 H).

For 38: IR (neat, cm\(^{-1}\)) 3000-2800, 1740, 1450, 1370, 1200, 1070; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.67 (s, 3 H), 2.5-1.5 (series of m, 10 H), 1.01 (s, 3 H).

For 39: IR (neat, cm\(^{-1}\)) 3000-2800, 1740, 1440, 1370, 1200; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 3.68 (s, 6 H), 2.5-1.5 (series of m, 13 H), 1.01 (s, 1.5 H), 0.94 (s, 1.5 H); m/z (M\(^+\)) calcd 270.1467, obs 270.1453.
Methyl 2-Hydroxy-3-methylcyclopentanepropanoate (40)

Reduction of 36 (27.4 g, 149 mmol) was achieved by treatment with 4.40 g (117 mmol) of sodium borohydride at 0°C in 350 mL of anhydrous methanol. The mixture was stirred for 30 min intervals at 0°C and 25°C, quenched with 5% hydrochloric acid (100 mL), concentrated in vacuo, and diluted with water (100 mL). The aqueous layer was extracted with ether (3x130 mL) and the combined ethereal layers were washed with 75 mL of saturated sodium bicarbonate solution and 75 mL of brine, dried, and evaporated to yield 23.50 g (85%) of pure alcohol 40; IR (neat, cm⁻¹) 3450, 3000-2800, 1740, 1445, 1250, 1170; ¹H NMR (CDCl₃) δ 3.7 (br s, 1 H), 3.66 (s, 3 H), 2.5-1.2 (series of m, 10 H), 1.2-0.9 (m, 3 H); m/e (M⁺) calcd 186.1256, obs 186.1289.
Methyl 3-Methyl-1-(and 2-)cyclopentene-1-propanoate (41)

Dehydration of 364 mg (1.96 mmol) of 40 with 0.35 mL (3.83 mmol) of phosphorus oxychloride in 10 mL of dry pyridine was performed at 60°C over 17 h. The reaction mixture was quenched with 50 mL of water and extracted with ether (2x50 mL). The combined organic layers were washed with 2x25 mL of 10% hydrochloric acid and with 25 mL of saturated sodium bicarbonate solution prior to drying. Chromatography of the residue on silica gel (MPLC, elution with 5% ethyl acetate in petroleum ether) afforded 153 mg (46%) of 41, 78 mg (19%) of 42, and upon increasing the polarity of eluent (27% ethyl acetate in petroleum ether) 66 mg (22%) of 43.

For 41: IR (neat, cm⁻¹) 3000-2800, 1745, 1440, 1250, 1170; ¹H NMR (CDCl₃) δ 5.25 (br s, 1 H), 3.67 (s, 3 H), 2.8-1.2 (series of m, > 9 H), 0.96 (d, J = 7 Hz, < 3 H); m/z (M⁺) calcd 168.1150, obs 168.1188.
For 42: $^1\text{H NMR (CDCl}_3\text{)} \delta$ 4.3-3.9 (m, 1 H), 3.78 (s, 3 H), 2.6-1.3 (series of m, 10 H), 1.2-1.0 (series of d, $J = 7$ Hz, 3 H).

For 43: IR (neat, cm$^{-1}$) 3000-2800, 1745, 1460, 1250, 1180, 1065, 1020; $^1\text{H NMR (CDCl}_3\text{)} \delta$ 4.52-4.27 (m, 1 H), 2.7-1.2 (series of m, 10 H), 1.09 (d, $J = 7$ Hz, 3 H).

**Methyl (1α,2β,3α)-2-hydroxy-3-methylcyclopentane-propanoate (40a)**

Hydroboration$^{32}$ of 41 (1.18 g, 7.03 mmol) was accomplished with 860 mg (7.04 mmol) of 9-BBN in 10 mL of dry tetrahydrofuran for 24 h at reflux under argon. This solution was cooled to 0°C and treated simultaneously with 3 mL of 3 M sodium hydroxide and 3 mL of 30% hydrogen peroxide. Following warming to rt, ether (75 mL) was added and the aqueous layer was removed. The organic phase was washed with 20 mL of 1% sodium carbonate solution, 20 mL of saturated sodium sulfite solution, and 20 mL of
brine prior to drying. MPLC purification of the residue (silica gel, elution with 30% ethyl acetate in petroleum ether) afforded 391 mg of recovered 41 and 609 mg (47%, 70% based on recovered 41) of 40a; IR (neat, cm⁻¹) 3450, 3000-2800, 1750, 1450, 1175, 1060; ¹H NMR (CDCl₃) δ 3.65 (s, 3 H), 3.2-3.0 (m, 1 H), 2.6-2.2 (m, 3 H), 2.0-1.1 (series of m, 8 H), 1.02 (d, J = 6 Hz, 3 H); ¹³C NMR (C₆D₆) ppm 173.89, 85.24, 51.04, 46.61, 42.35, 32.74, 29.67, 29.56, 27.40, 18.07; m/e (M⁺) calcd 186.1256, obs 186.1281.

Anal. Calcd for C₁₀H₁₈O₃: C, 64.49; H, 9.74. Found: C, 64.52; H, 9.78.

*Methyl cis-3-Methyl-2-oxocyclopentane propanoate (36a)*

A suspension of pyridinium chlorochromate (104 mg, 0.48 mmol), sodium acetate (8 mg, 0.10 mmol), and Celite (300 mg) in 3 mL of dry dichloromethane was prepared under nitrogen. Alcohol 40a (79 mg, 0.42 mmol) in 3 mL of dichloromethane was introduced and the reaction mixture was
stirred overnight (18 h). The slurry was filtered through Celite (subsequently rinsed with 50 mL of ether), and the filtrate was washed with 5% hydrochloric acid (20 mL) and 5% sodium bicarbonate solution (20 mL), dried, and evaporated. The residue was purified on silica gel (MPLC, elution with 20% ethyl acetate in petroleum ether) to give 73 mg (94%) of 96% isomerically pure 36a (determined by 300 MHz $^1$H NMR integration); IR (neat, cm$^{-1}$) 3000-2800, 1740, 1440, 1165; $^1$H NMR (CDCl$_3$) $\delta$ 3.65 (s, 3 H), 2.41 (t, $J = 8$ Hz, 2 H), 2.2-1.9 (m, 6 H), 1.6-1.5 (m, 2 H), 1.05 (d, $J = 7$ Hz, 3 H); m/e (M$^+$) calcd 184.1100, obs 184.1110.

$^{(1\alpha,5\alpha,8\beta)}$-8-methyl-2-bicyclo[3.3.0]octanone (45)

The copper catalyzed addition of the Grignard reagent from 4-bromo-1-butene to 2-cyclopentenone afforded 44 in 54% yield, bp 50-90°C/0.6 mm (lit.$^{34}$ bp 67°C/0.2 mm).

Pyrolysis of 44 (7.90 g) in 15 sealed thick walled 8 mm OD pyrex tubes was performed at 325°C over 90 min.
The crude contents were washed out with ether, combined, concentrated by distillation, and distilled to afford 2.0 g (25%) of pure 45, bp 42-52°C/0.7 mm; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textdelta 3.0-2. (series of m, 11 H), 0.93 (d, \textlambda = 6 Hz, 3 H).

(4a\alpha,7\beta,7\alpha\alpha)-Hexahydro-7-methylcyclopenta[b]pyran-2(3\beta)-one (43a)

Baeyer-Villiger oxidation of 45 (1.52 g, 11.0 mmol) in 30 mL of dichloromethane was realized with 80\% m-chloroperbenzoic acid (3.1 g, 14 mmol) during 48 h. The solution was diluted with 30 mL of solvent, washed with 30 mL of saturated sodium bicarbonate solution and brine prior to drying. The residue was chromatographed on silica gel (MPLC, elution with 22\% ethyl acetate in petroleum ether) to provide 1.29 g (76\%) of 43a; IR (neat, cm\textsuperscript{-1}) 3000-2840, 1745, 1465, 1260, 1190, 1150-1000; \textsuperscript{1}H NMR (CDCl\textsubscript{3}) \textdelta 4.45 (t, \textlambda = 5 Hz, 1 H), 2.46-1.41 (series of m, 10 H),
1.09 (d, J = 7 Hz, 3 H); m/e (M+) calcd 154.0994, obs 154.1023.

**Anal.** Calcd for C₉H₁₄O₂: C, 70.10; H, 9.15.
Found: C, 70.01; H, 9.20.

**Preparation of 36a from 43a**

Catalytic sodium methoxide (14 mg) was added to a solution of 43a (115 mg, 0.74 mmol) in dry methanol (11 mL). After overnight stirring, the methanol was removed in vacuo and the residue was dissolved in ether, washed with brine, dried, and concentrated. The resulting hydroxy ester in dichloromethane (5 mL) was combined with a slurry of pyridinium chlorochromate (243 mg, 1.13 mmol), Celite (300 mg), and sodium acetate (18 mg, 0.22 mmol) in dichloromethane (5 mL) under argon. After 5 h, the usual work up and MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether) afforded 86 mg (63%, 74% based on recovered 43a) of 36a and 18 mg of 43a.
The 300 MHz $^1$H NMR spectrum of 36a was identical to that prepared by the previous route.

(3α,4α,7β,7α)-Hexahydro-3,7-

dimethylcyclopenta[b]pyran-2(3H)-one (46)

To a cold (0°C) solution of diisopropylamine (0.87 mL, 6.2 mmol) in tetrahydrofuran (14 mL) under argon was added 3.9 mL (6.0 mmol) of 1.55 M n-butyllithium in hexane. The reagent was cooled to -78°C and lactone 43a (920 mg, 5.96 mmol) in tetrahydrofuran (6 mL) was added dropwise over 10 min. After an additional 20 min, the enolate was quenched with methyl iodide (0.39 mL, 6.3 mmol) and stirring was continued for 30 min. After the cooling bath was removed for 10 min, saturated ammonium chloride solution was added and the reaction mixture was poured into brine and extracted with ether. The organic layer was dried and evaporated. Chromatography of the resulting oil on silica gel (elution with 12% ethyl acetate in petroleum ether) yielded 870 mg (87%)
Methyl [1α(S*),3α1-α,3-Dimethyl-2-oxocyclopentane propanoate (37)

A solution of 487 mg (2.89 mmol) of 46 and 24 mg of sodium methoxide in 15 mL of dry methanol was stirred for 5 h, treated with 0.5 mL of saturated ammonium chloride solution, and freed of methanol in vacuo. The residue was dissolved in ether, dried, concentrated, and added in 5 mL of dry dichloromethane to 950 mg (4.41 mmol) of pyridinium chlorochromate, 1.3 g of Celite, 70 mg (0.85 mmol) of sodium acetate, and 10 mL of dichloromethane. Workup and chromatography on silica gel (MPLC, elution
with 8% ethyl acetate in petroleum ether) after 3 h afforded 406 mg (71%, 89% based on recovered 46) of 37 and 100 mg of 46; IR (neat, cm⁻¹) 3000-2840, 1740, 1460, 1380, 1180; ¹H NMR (CDCl₃) δ 3.34 (s, 3 H), 2.58 (sxt, J = 7 Hz, 1 H), 1.96-1.03 (m, 8 H), 1.00 (d, J = 7 Hz, 3 H), 0.88 (d, J = 7 Hz, 3 H); ¹³C NMR (CDCl₃) ppm 219.73, 176.23, 51.02, 45.98, 42.21, 38.06, 34.74, 28.80, 26.94, 17.30, 15.25; m/z (M⁺) calcd 198.1256, obs 198.1230.

(4α,7β,7αa)-Hexahydro-7-methyl-7a-(2-methyl-1-propenyl)cyclopenta[b]pyran-2(3H)-one (49)

A solution of 2-methylpropyl-l-yllithium in ether (20 mL) was prepared¹⁵ by dissolving 0.84 mL (8.0 mmol) of 1-bromo-2-methylpropene in ether and injecting 4.2 mL (8.0 mmol) of 1.9 M tert-butyllithium in pentane at -78°C under argon. After being stirred at 0°C for 30 min, the reagent was cooled to -78°C and a solution of 36a (509 mg, 2.76 mmol) in 4 mL of cold (-78°C) ether was
introduced via canula. After 20 min, acetic acid (0.48 mL, 8.4 mmol) was added, and the reaction mixture was warmed to 25°C, poured into saturated sodium bicarbonate solution (25 mL), and extracted with ether (3x25 mL) prior to drying. Chromatography of the residue on silica gel (elution with 10% ethyl acetate in petroleum ether) yielded 194 mg (29%) of 48, 143 mg (25%) of 49, and 158 mg (31%) of recovered 36 as a mixture of cis and trans isomers.

Conversion from 48 to 49 was accomplished by adding 48 (190 mg, 0.79 mmol) dropwise in anhydrous tetrahydrofuran (6 mL) to a cold (-78°C) slurry of sodium hydride (60 mg of 50%, 1.25 mmol) in tetrahydrofuran (6 mL). The cooling bath was removed and the reaction mixture allowed to warm to room temperature over 1 h. Saturated ammonium chloride solution was added and the solution was poured into brine (25 mL). Extraction with ether (3x30 mL), drying, and purification of the residue by MPLC (silica gel, elution with 10% ethyl acetate in petroleum ether) afforded 119 mg (72%) of 49.

For 48: IR (neat, cm⁻¹) 3550, 3000-2800, 1740, 1440, 1370, 1270-1150; ¹H NMR (CDCl₃) δ 4.96 (m, 1 H), 3.65 (s, 3 H), 2.4-2.2 (m, 2 H), 1.9-1.3 (series of m,
8 H), 1.86 (d, $J = 1$ Hz, 3 H), 1.71 (d, $J = 1$ Hz, 3 H), 0.91 (d, $J = 6$ Hz, 3 H); $^{13}$C NMR ($C_6D_6$) ppm 174.03, 134.34, 129.31, 83.77, 50.97, 45.77, 32.98, 29.92, 28.17, 27.90, 24.83, 18.98, 12.97; m/e (M⁺) calcd 240.1726, obs 240.1701.

For 49: IR (neat, cm⁻¹) 3000-2820, 1740, 1460, 1260, 1180, 1045, 1000; $^1$H NMR (CDCl₃) δ 5.01 (m, 1 H), 2.39 (t, $J = 7$ Hz, 2 H), 2.2-1.4 (series of m, 8 H), 1.74 (d, $J = 1$ Hz, 3 H), 1.69 (d, $J = 1$ Hz, 3 H), 0.98 (d, $J = 7$ Hz, 3 H); $^{13}$C NMR (CDCl₃) ppm 172.78, 135.98, 125.81, 94.05, 46.27, 42.60, 30.57, 27.79, 26.47, 21.83, 19.04, 12.15; m/e (M⁺) calcd 208.1464, obs 208.1436.

Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.86; H, 9.65.
trans-1,2,3,3a,4,5,7,8-Octahydro-1,8,8-trimethyl-6H-cyclopentacycloocten-6-one (50)

Olefination of 49 (80 mg, 0.38 mmol) was achieved with pyridine (1 drop), tetrahydrofuran (0.5 mL), toluene (1 mL), and 0.56 M Tebbe reagent (23) (0.68 mL, 0.38 mmol) during 20 min at \(-40^\circ C\) and 15 min at \(25^\circ C\). The reaction mixture was quenched at \(-20^\circ C\), diluted with petroleum ether, dried, and evaporated. The residual oil was filtered through basic alumina (Act.III, elution with petroleum ether), concentrated in vacuo, transferred with 0.75 mL of toluene to a potassium hydroxide-coated soft glass tube, sealed, and heated (200°C, 44 h). The resulting pale yellow solution was purified on silica gel (MPLC, elution with 3% ethyl acetate in petroleum ether) affording 25 mg (32%) of 51 and 30 mg (38%) of 50.

For 50: IR (neat, \(cm^{-1}\)) 3000-2800, 1700, 1450, 1365, 1300, 1210; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.28 (br s, 1 H), 3.12 (m, 1 H), 2.90 (d, \(J = 15\) Hz, 1 H), 2.64 (td, \(J = 13\) and \(6\) Hz, 1 H), 2.5-2.2 (m, 2 H), 2.31 (d, \(J = 15\) Hz, 1 H), 1.9-1.1 (series of m, 6 H), 1.09 (d, \(J = 7\) Hz, 1 H), 1.04 (d, \(J = 6\) Hz, 1 H), 0.80 (d, \(J = 6\) Hz, 1 H), 0.31 (s, 3 H).
Hz, 3 H), 1.08 (s, 3 H), 1.06 (s, 3 H); $^{13}$C NMR (CDCl$_3$) ppm 213.82, 145.56, 129.93, 56.02, 41.08, 40.65, 38.63, 35.90, 33.20, 31.71, 31.35, 30.87, 29.85, 20.89; m/e (M$^+$) calcd 206.1657, obs 206.1625.

Anal. Calcd for C$_{14}$H$_{22}$O: C, 81.50; H, 10.75. Found: C, 81.47; H, 10.90.

For 51: IR (neat, cm$^{-1}$) 3000-2800, 1710, 1455, 1360, 1195; $^1$H NMR (CDCl$_3$) $\delta$ 4.94 (m, 1 H), 2.6-2.2 (m, 3 H), 2.18 (s, 3 H), 1.9-1.2 (series of m, 6 H), 1.17 (s, 3 H), 0.99 (d, $J = 7$ Hz, 3 H), 0.88 (s, 3 H); $^{13}$C NMR (C$_6$D$_6$) ppm 209.64, 147.29, 127.30, 58.44, 41.44, 35.76, 35.25, 32.95, 31.03, 30.46, 30.20 (2C), 25.47, 19.15; m/e (M$^+$) calcd 206.1671, obs 206.1625.

(3α,4α,7β,7α)-7a-Ethenylhexahydro-3,7-dimethylcyclopentab[bl]pyran-2(3H)-one (52)

A solution of vinyl lithium in ether was prepared by adding excess vinyl bromide (0.40 mL, 5.7 mmol) via a cold syringe to cold (-78°C) ether (10 mL) under argon and then by adding
2.0 M tert-butyllithium (0.80 mL, 1.6 mmol) in pentane. After 30 min, a cold (−78°C) solution of 37 (141 mg, 0.71 mmol) in ether (5 mL) was injected via canula. The reaction mixture was maintained at −78°C for 20 min and allowed to warm to 25°C over 20 min before being quenched with saturated ammonium chloride solution. The usual workup and purification on silica gel (MPLC, elution with 4% ethyl acetate in petroleum ether) afforded 86 mg (62%) of 52; IR (neat, cm⁻¹) 3000-2840, 1735, 1460, 1385, 1340, 1235, 1195, 1135, 1075, 985, 930; ¹H NMR (CDCl₃) 6 5.71-5.62 (m, 1 H), 5.30-5.22 (m, 2 H), 2.58-2.54 (m, 1 H), 2.26 (br s, 1 H), 1.96-1.43 (series of m, 7 H), 1.24 (d, J = 6 Hz, 3 H), 0.96 (d, J = 6 Hz, 3 H); ¹³C NMR (CDCl₃) ppm 174.75, 139.76, 116.25, 94.60, 45.28, 41.18, 31.34, 30.36, 28.94, 26.20, 17.13, 11.66; m/z (M⁺) calcd 194.1307, obs 194.1294.

Anal. Calcd for C₁₂H₁₈O₂: C, 74.19; H, 9.34.
Found: C, 74.32; H, 9.47.
Tebbe reagent (23) (1.10 mL of 0.56 M, 0.62 mmol) was added dropwise to a cold (-40°C) solution of 52 (112 mg, 0.58 mmol), pyridine (1 drop), toluene (1 mL), and tetrahydrofuran (0.5 mL). After 20 min, the reaction mixture was warmed to rt for 10 min, recooled to -20°C, and quenched. Workup as usual and filtration through basic alumina delivered a colorless oil, which was transferred with 0.55 mL of toluene to a base-coated soft glass tube. The carefully annealed tube was heated in a tube furnace (200°C, 48 h) and the solution concentrated and chromatographed on silica gel (MPLC, 3% ethyl acetate in petroleum ether). There was isolated 27 mg (24%) of 53a and 75 mg (67%) of 53b.

For 53a: IR (neat, cm⁻¹) 3000-2800, 1710, 1450, 1375, 1210, 1155, 1095; ¹H NMR (CDCl₃) δ 5.60 (br t, J = 7 Hz, 1 H), 2.8-2.1 (series of m, 7 H), 1.9-1.1 (series of m, 6 H), 1.10 (d, J = 7 Hz, 3 H), 1.03 (d, J = 7 Hz, 3 H); m/z (M⁺) calcd 192.1514, obs 192.1499.
For 53b: IR (neat, cm$^{-1}$) 3000-2800, 1710, 1455, 1380, 1195, 910, 840; $^1$H NMR (CDCl$_3$) $\delta$ 5.40 (br t, $J = 8$ Hz, 1 H), 3.0-2.1 (series of m, 7 H), 1.8-1.2 (series of m, 6 H), 0.99 (d, $J = 7$ Hz, 3 H), 0.98 (d, $J = 7$ Hz, 3 H); $^{13}$C NMR (C$_6$D$_6$) ppm 213.41, 153.87, 119.89, 46.87, 42.66, 41.95, 41.83, 39.91, 33.59, 33.01, 23.62, 21.06, 19.40; m/z (M$^+$) calcd 192.1514, obs 192.1495.

Anal. Calcd for C$_{13}$H$_{20}$O: C, 81.20; H, 10.48. Found: C, 81.11; H, 10.54.

(3$\alpha$,4$\alpha$,7$\beta$,7$\alpha$)-Hexahydro-3,7-dimethyl-7a-(2-methyl-1-propenyl)cyclopenta[b]pyran-2(3$\alpha$)-one (54)

A solution of 2-methylpropen-1-yllithium (1.85 mmol) in ether (25 mL) was prepared as before and cooled to $-78^\circ$C under argon. The keto ester (37) (336 mg, 1.69 mmol) in cold ($-78^\circ$C) ether (8 mL) was injected via canula and reacted for 30 min before being warmed to 25$^\circ$C over 10 min. The quenched reaction mixture was worked up as usual and purified on silica gel (MPLC, elution with 5%
ethyl acetate in petroleum ether) affording 220 mg (58%) of 54; IR (neat, cm⁻¹) 3000-2800, 1720, 1450, 1375, 1330, 1225, 1180, 1115, 1060, 975; ¹H NMR (CDCl₃) δ 4.99 (br s, 1 H), 2.8-1.4 (series of m, 9 H), 1.80 (d, J = 1 Hz, 3 H), 1.75 (d, J = 1 Hz, 3 H), 1.25 (d, J = 7 Hz, 3 H), 1.01 (d, J = 7 Hz, 3 H); ¹³C NMR (CDCl₃) ppm 174.48, 135.98, 125.50, 94.98, 45.99, 42.64, 30.75, 30.12, 29.20, 27.84, 25.61, 18.78, 17.19, 11.98; m/z (M⁺) calcd 222.1620, obs 222.1580.

Anal. Calcd for C₁₄H₂₂O₂: C, 75.63; H, 9.97. Found: C, 75.84; H, 10.05.

(1α,3αβ)-1,2,3,3a,4,5,7,8-Octahydro-1,5,8,8-tetramethyl-6H-cyclopentacycloocten-6-one (34)

Lactone 54 (112 mg, 0.50 mmol) was reacted with Tebbe reagent (23) (0.98 mL of 0.59 M, 0.58 mmol) in the pre described manner. The colorless oil, isolated upon purification, was transferred with toluene (0.75 mL) to a base-coated soft glass tube. Thermolysis (200°C, 44 h) and
purification on silica gel (MPLC, elution with 1.5% ethyl acetate in petroleum ether) cleanly afforded 22 mg (20%) of 34a and 74 mg (67%) of 34b.

For 34a: IR (neat, cm\(^{-1}\)) 3000-2800, 1710, 1450, 1370, 1320; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.10 (br s, 1 H), 3.09 (d, \(J = 13\) Hz, 1 H), 3.09 (m, 1 H), 2.72 (m, 1 H), 2.34 (m, 1 H), 2.12 (d, \(J = 13\) Hz, 1 H), 1.8-1.1 (series of m, 6 H), 1.24 (s, 3 H), 1.06 (s, 3 H), 1.02 (d, \(J = 7\) Hz, 3 H), 0.92 (d, \(J = 6\) Hz, 3 H); m/e (M\(^+\)) calcd 220.1827, obs 220.1830.

For 34b: IR (neat, cm\(^{-1}\)) 3000-2800, 1700, 1450, 1370; \(^1\)H NMR (CDCl\(_3\)) \(\delta\) 5.26 (br s, 1 H), 3.1-2.3 (series of m, 3 H), 2.75 (d, \(J = 15\) Hz, 1 H), 2.38 (d, \(J = 15\) Hz, 1 H), 1.8-1.1 (series of m, 6 H), 1.08 (d, \(J = 7\) Hz, 3 H), 1.04 (s, 3 H), 1.02 (s, 3 H), 0.97 (d, \(J = 7\) Hz, 3 H); \(^{13}\)C NMR (CDCl\(_3\)) ppm 215.46, 146.38, 129.54, 56.16, 42.54, 40.65, 39.39, 38.44, 35.65, 32.81, 31.70, 31.15, 31.06, 20.91, 15.81; m/e (M\(^+\)) calcd 220.1827; obs 220.1784.
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