Bridged to Fused Ring Interchange. Methodology for the Construction of Fused Cycloheptanes and Cyclooctanes. Total Syntheses of Ledol, Ledene, and Compressanolide

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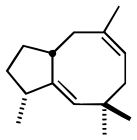
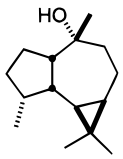
The type two intramolecular Diels−Alder reaction (T2IMDA) is an efficient method for the formation of medium rings. The methodology is particularly effective for the construction of seven- and eight-membered rings. A strategy for the synthesis of functionalized cycloheptanes and cyclooctanes has been developed that involves a bridged to fused ring interchange. The T2IMDA provides a synthesis for rigid bridged bicyclic molecules that can be stereoselectively elaborated before ozonolysis of the bridgehead double bond. Following oxidative cleavage, aldol condensation provides fused bicyclic ring systems that otherwise are difficult to synthesize. This methodology is amenable to the synthesis of terpene natural products. This is demonstrated here through total syntheses of (±)-ledol and (±)-ledene and a formal synthesis of (±)-compressanolide.

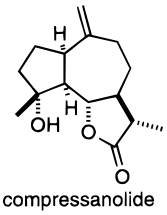
Many terpene natural products are characterized by five−eight or five−seven fused ring systems.[1] Examples include precapnelladiene,[2] ledol,[3] and compressanolide.[4] These molecules represent a significant challenge to synthetic chemists due to their stereochemical complexity and the presence of a medium-sized ring.



precapnelladiene



ledol

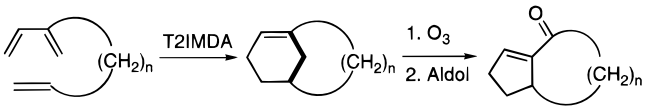


compressanolide

Due to the high entropic and enthalpic barrier to formation, seven- and eight-membered rings are often the most difficult to form.[5] As a result, many synthetic approaches for their formation involve a rearrangement or fragmentation of a more easily accessed ring system. Direct cyclizations of acyclic precursors to form seven- and eight-membered rings are less common. Two recent reviews illustrate these points.[6]

The type two intramolecular Diels−Alder reaction (T2IMDA) is an efficient method for the formation of medium rings.[7] The carbocycle is imbedded within a bicyclo [*n*.3.1] framework (Scheme 1). The methodology is particularly effective for the construction of seven- and eight-membered rings and has been used for a direct entry into the taxane[8] and esperamicin ring systems.[9]

Scheme 1



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The T2IMDA differs from the type one intramolecular Diels−Alder reaction in that the dienophile is tethered to the diene at the 2-position of the diene rather than at the 1-position.

Herein, we describe a method for converting the bicyclo [*n*.3.1] ring system (**1**) into a fused five−seven or five−eight construction (Scheme 1). Oxidative cleavage of the bridgehead double bond liberates a dicarbonyl compound which is condensed in an aldol cyclization. We refer to this strategy as *bridged to fused ring interchange.*[10]

[⊗] Abstract published in *Advance ACS Abstracts,* September 15, 1996.

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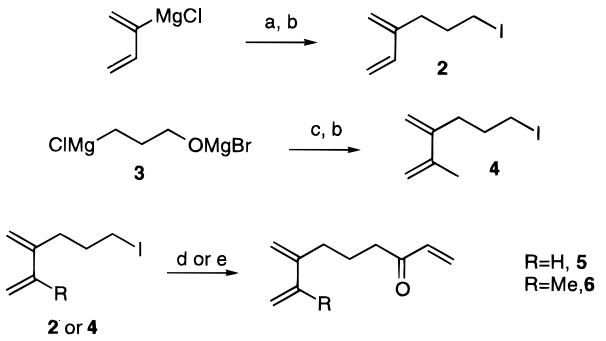
Scheme 2[a]



[a] Reagents: (a) 3-(*tert*-butyldimethylsiloxy)-1-iodopropane, Li_2CuCl_4 and then HF, 73%; (b) Ph_3P, I_2, pyridine, 70−80%; (c) CuBr and then 2-methyl-1-buten-3-yne, 46%; (d) Zn and then acryloyl chloride, $Pd(PPh_3)_4$, 70−80%; (e) lithiomethoxyallene and then HCl, 77%.

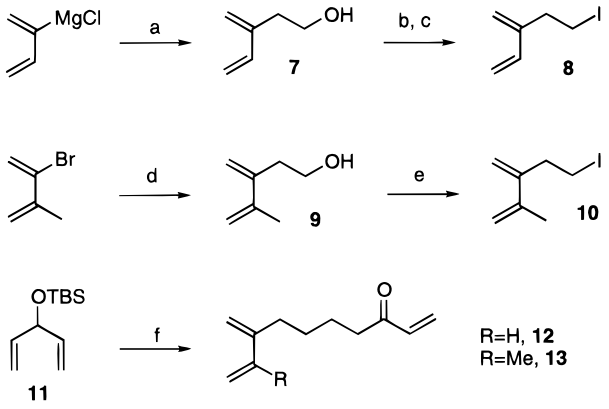
Setting stereochemistry in medium rings can be difficult due to their conformational flexibility.[11] An attractive feature of the above methodology is that it provides an opportunity to take advantage of the conformational rigidity of the bridged bicyclic intermediate **1** to set stereochemistry in the medium-sized ring *prior* to oxidative cleavage.

Bridged to fused ring interchange is useful for the synthesis of terpene natural products. Its use in the syntheses of compressanolide, ledol, and ledene is described below.

Results and Discussion

Synthesis of Diels−Alder Precursors. Our overall strategy for assembly of the Diels−Alder precursors involved attachment of a four or five atom tether to the 2-position of a diene, followed by installation of the dienophile. Trienes **5** and **6** were synthesized as outlined in Scheme 2. Chloroprene Grignard was coupled[12] with protected 3-iodopropanol to give 2-(3-hydroxypropyl)-1,3 butadiene in 46% yield. Conversion of this alcohol to the iodide **3** was accomplished using triphenylphosphine and molecular iodine. The synthesis of diene **4** begins with the Normant Grignard **3**,[13] which is converted to its cuprate and then added to 2-methyl-but-1-en-3-yne.[14] Although this reaction proceeds in moderate yield, it represents a convenient entry to this 2-substituted diene. The resulting alcohol is transformed to the iodide **4** as before. The iodopropyl dienes thus formed are converted to organozincs and coupled with acryloyl chloride under palladium catalysis to yield **5** and **6**.[15] Alternatively, alkylation of lithio methoxyallene[16] with **4** followed by hydrolysis gives triene **6** in 77% yield.

Scheme 3[a]



[a] Reagents: (a) ethylene oxide, 48%; (b) MsCl, Et_3N; (c) NaI, acetone, 56% for two steps; (d) t-BuLi and then ethylene oxide, 62%; (e) Ph_3P, I_2, pyridine, 72%; (f) s-BuLi, **8** or **10**, and then HF, 50−55%.

The Diels−Alder precursors **12** and **13** were synthesized by the coupling[17] of 3-(*tert*-butyldimethylsiloxy)-1,4-pentadiene[18] with alkyl iodides **8** and **10** (Scheme 3). The needed diene fragment **8** was synthesized from chloroprene Grignard by first quenching with ethylene oxide to generate 3-methylene-4-pentenol **7**.[19] Subsequent transformation of the alcohol to the iodide via the mesylate gave 3-methylene-5-iodopentene (**8**).

In a similar fashion, diene fragment **10** was synthesized from 2-bromo-3-methyl-1,3-butadiene (Scheme 3).[20] Following lithium halogen exchange to form 2-lithio-3-methyl-1,3-butadiene, ethylene oxide was added to give alcohol **9**. Formation of the tosylate in pyridine followed by displacement with iodide produced 5-iodo-2-methyl-3-methylene-1-pentene (**10**).

Metalation of (*tert*-butyldimethylsilyloxy)-1,4-pentadiene with *sec*-butyllithium followed by treatment with alkyl iodide **8** or **10** resulted in the formation of silyl enol ethers.[17] Alkylation occurred with high selectively at the γ position. The enol ether was not purified but immediately subjected to HF in acetonitrile to produce trienes **12** and **13** in 50−55% yield.[21]

The Diels−Alder precursor **16** was assembled from THP protected 6-iodo-hexanol. Copper(II) catalyzed coupling of chloroprene Grignard with this iodide incorporated the diene portion of the molecule furnishing **14**.[12] Subsequent deprotection of the alcohol and oxidation to the aldehyde produced 7-methylene-8-nonenal **15**. Finally, the aldehyde **15** was condensed with triethyl phosphonoacetate to produce ester triene **16**.

Type Two Intramolecular Diels−Alder Reactions. Trienes **5**, **6**, **12**, **13**, and **16** underwent cycloaddition to give the corresponding bicyclo ring systems (Scheme 5).

Several features of the T2IMDA reactions shown in Scheme 5 deserve comment. In contrast to the lengthy reaction times necessary for the thermal cycloadditions of **5**, **12**, and **16**, the Lewis acid-catalyzed T2IMDA of **6**

(11) (a) Anet, F. A. L. *Conformational Analysis*; Chiurdoglu, G., Ed.; Academic: New York, 1971. (b) Anet, F. A. L.; Anet, R. *Top. Curr. Chem.* **1974**, *45*, 169. (c) Dale, J. *Stereochemistry and Conformational Analysis*; Verlag Chemie: New York, 1978. (d) Petasis, N. A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757 and references cited therein. (e) However, numerous examples can be found of stereoselective transformations involving medium-sized rings. See for example, Still, W. C.; Galynker, I. *Tetrahedron* **1981**, *37*, 3981.

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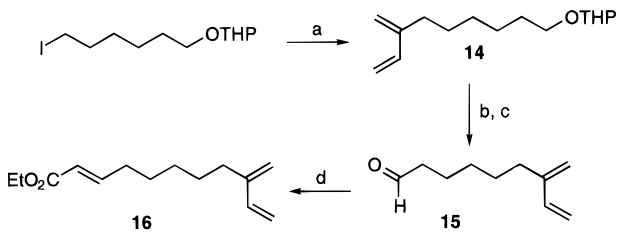
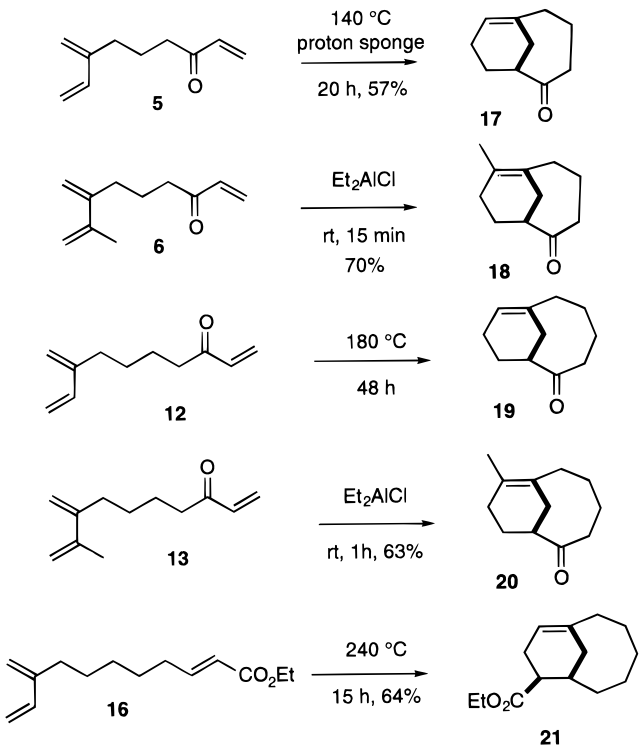
Scheme 4[a]



[a] Reagents: (a) chloroprene Grignard, Li_2CuCl_4, 73%; (b) PPTS, EtOH; (c) Swern oxidation, 80% for two steps; (d) triethyl phosphonoacetate, NaH, 85%.

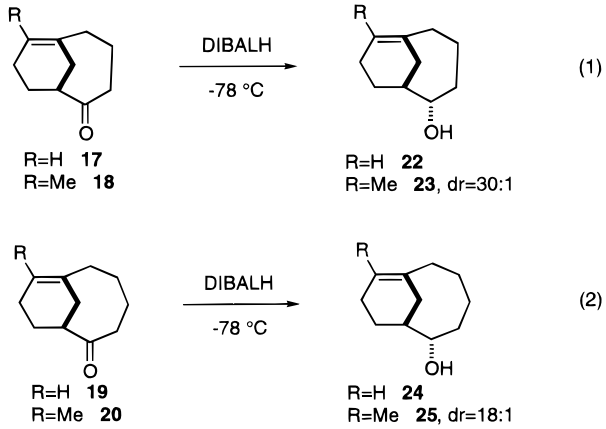
Scheme 5



and **13** proceeded within 1 h. The use of a Lewis acid to catalyze the T2IMDA shortens reaction times and lowers the temperature required for cyclization.[8b] However, trienes **5** and **12** proved to be quite sensitive under these conditions. When the cyclization of **5** was carried out thermally with added proton sponge (30 mol %), a significant improvement in yield was observed. Cycloadduct **19** was not purified, instead the methyl ether of the alcohol resulting from the reduction of **19** was isolated in 58% yield from the triene **12**.

Stereoselective Functionalization. The problems inherent in the stereospecific elaboration of medium rings may be ameliorated by carrying out chemical transformations on related bridged bicyclic systems. The conformationally restricted bridged bicyclic ring system offers the potential for stereochemical control of functional group manipulation. Following these transformations, liberation of the medium ring would permit delivery of a stereoselectively functionalized molecule. The examples cited below illustrate this strategy.

The reduction of ketone **18** (eq 1) by DIBALH at −78 °C resulted in a 30:1 preference for formation of the α-alcohol **23**. In a similar fashion, ketone **20** (eq 2) was reduced to alcohol **25** with 18:1 diastereoselectivity. Ketones **17** and **19** were also reduced with high selectivity (>95:5).



The stereoselectivity observed for these transformations can be understood by examining the conformational biases of ketones **18** and **20** (Figure 1). In their lowest energy conformations (as determined by Monte Carlo conformational search), the *β*-face of each of these molecules is exposed, while the α-face is effectively shielded by the cup shape of the molecule.

Regioselective and Stereoselective Methylation of Ketone 20. Studies performed on the methylation of ketone **20** produced surprising results.[22] When ketone **20** was subjected to conditions of kinetic enolate formation (−78 to −30 °C, 1.2 equiv of LDA, addition of the ketone to LDA), subsequent alkylation with methyl iodide occurred *mainly at the C-1 carbon* (**26**) corresponding to methylation of the bridgehead enolate (Scheme 6). The ratio of C_1 to C_3 methylation (**26**:**27**), as determined by GC of the crude reaction mixture, was 37:1.

The regioisomers could be unambiguously distinguished by DEPT NMR experiments on the isolated isomers (see Experimental Section). A DEPT experiment conducted on ketone **26** showed a quaternary bridgehead carbon and no tertiary carbons. Ketone **27**, however, displayed no quaternary carbons but instead possessed two tertiary carbons corresponding to the bridgehead carbon and the C-3 carbon.

In contrast, enolate formation under thermodynamic conditions (0 °C, 0.98 equiv of KHMDS, addition of KHMDS to the ketone over 0.5 h) followed by treatment with methyl iodide resulted in mainly the C-3 alkylation product **27**. The ratio of C-3 methylation to C-1 methylation (**27**:**26**) was 40:1 as determined by GC of the crude reaction mixture. The C-3 methylated product consisted of an 8:1 mixture of diastereomers.

The origin of this unusual selectivity can be explained by a combination of conformational and thermodynamic factors peculiar to the bridged structure of bicyclo[5.3.1]-

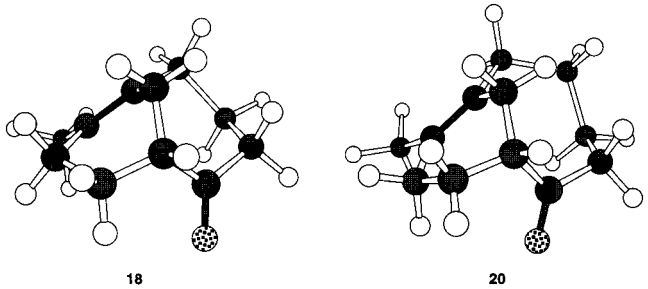
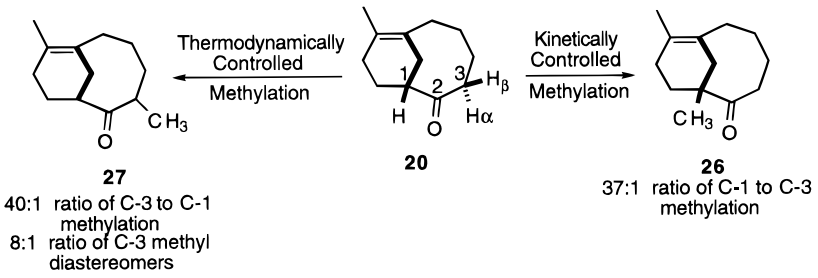


Figure 1. MM2 lowest energy conformers for ketones **18** and **20**.

Scheme 6



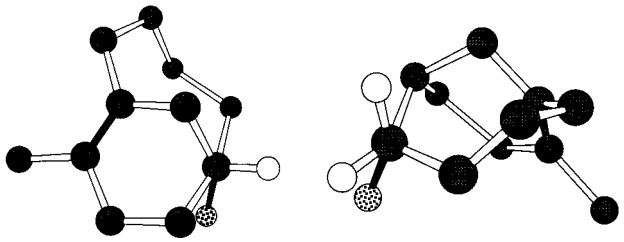


Figure 2. M2-calculated lowest energy conformer of bicyclo-[5.3.1]undecenone **20**.

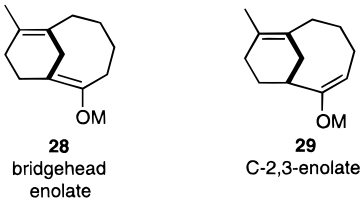


Figure 3. Bridgehead enolate **28** and C-2,3-enolate **29** of bicyclo[5.3.1]undecene **20**.

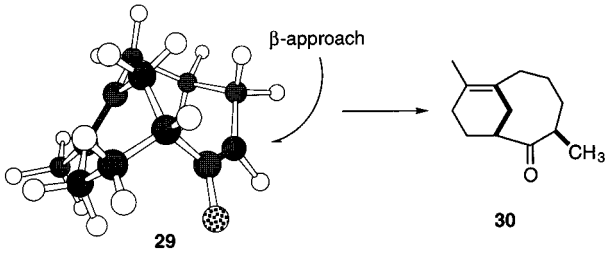


Figure 4. The calculated lowest energy conformer by MM2 of the 2,3-enolate **29** showing attack of the methyl electrophile on the β-face resulting in **30**.

undecenone ring system **20**.[23] Stereoelectronics mandate that kinetic deprotonation is optimal with a 90° C−H dihedral angle to the carbonyl σ plane.[24] Inspection of the lowest energy conformation of **20** (MM2) reveals H_{c1} has a dihedral angle of 100° (Figure 2). In contrast, $H_{c-3\beta}$ has an angle of 145°. Deprotonation of $H_{c-3\alpha}$, which would result in a high energy trans cyclooctene enolate, also has an unfavorable dihedral angle of 32°. The observed 37:1 ratio of the C-1 to C-3 methylated products indicates a strong preference for the *kinetic deprotonation* of H_{c1} resulting in formation of the *most highly substituted enolate*.[25]

The stereoelectronic bias favoring deprotonation of H_{c1} results in formation of a *bridgehead enolate* **28** (Figure 3). This enolate is expected to be thermodynamically disfavored due to the strain involved in formation of an additional bridgehead double bond.[26] Molecular mechanics (MM2) calculations reveal a 3 kcal/mol difference in energy favoring the 2,3-enolate **29** over the bridgehead enolate **28**. Not surprisingly, under equilibrating conditions, the thermodynamically more stable 2,3-enolate **29** is favored. Additional evidence that the C-2,3 enolate **29** is thermodynamically more stable comes from the observation that if KHMDS is added rapidly to ketone **20**, subsequent alkylation with CH_3I results in a C-3 to C-1 methylation (**27**:**26**) ratio of only 3:1.

Alkylation at C-3 of the 2,3-enolate of **20** proceeds with a 8:1 selectivity. We expect that the conformation of the bicyclo[5.3.1]undecenone 2,3-enolate biases formation of the β C-3 methyl diastereomer **30**. In the calculated (MM2) lowest energy conformer of this enolate, the β face is most accessible to electrophilic attack suggesting the β-methyl is the major diastereomer formed in this reaction (Figure 4).[27] The results of the two alkylation experiments constitutes a complete reversal of the usual regioselectivity observed in enolate alkylations.[28]

The preceding results have been utilized in a strategy for the direct functionalization of the bridgehead position. Under conditions of *kinetic control*, enolization of the bicyclo[5.3.1]undecenone **20** followed by treatment with Davis's 2-sulfonyl oxaziridine afforded a 77% yield of alcohol **31** (eq 3).[29] NMR analysis (500 MHz) of the crude reaction mixture indicates a 30:1 ratio in favor of the bridgehead hydroxyl **31**.

The bicyclo[5.3.1]undecene ring system is a key substructural feature of the taxane natural products. Bridgehead enolization/hydroxylation of these systems has been used in both model studies[22,30] and in the total synthesis of taxol.[31]

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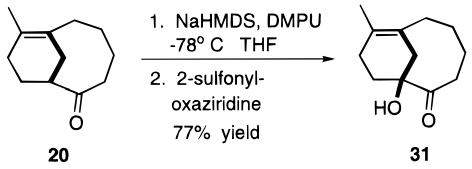


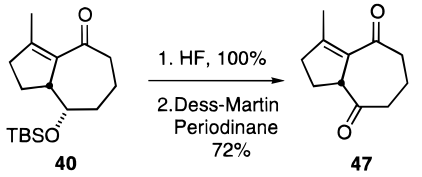
20 **31** (3)

Bridged to Fused Ring Interchange. Prior to oxidative cleavage, the bicyclic alcohols **22**, **23**, and **25** were protected as TBS ethers, and alcohol **24** was protected as its methyl ether **34** (Scheme 7). Similarly, the carbethoxy cycloadduct **21** was reduced with DIBALH and the alcohol protected as its methyl ether **36**.

The ozonolysis of these bridgehead alkenes proceeds with facility (Scheme 8). Introduction of ozone into a solution of the bicyclic intermediates **32**−**36** in methanol followed by triphenylphosphine reductive workup, gave dicarbonyl species in high yields.

To determine the most efficient method for aldol cyclization, a variety of conditions were surveyed. As can be seen in Scheme 8, aldol condensation of dicarbonyl compounds **38**, **41**, and **42** proceeded best under basic conditions to generate fused ring systems **40**, **43**, and **44** in 95%, 64%, and 75% yields, respectively. In contrast, **37** and **45** were subjected to buffered acid (PPTS) conditions to afford **39** and **46** in 94% and 62% yields, respectively (Scheme 8). Under the thermodynamic conditions employed, the more stable fused ring system is obtained rather than the more strained bridged ring system. These overall transformations achieve the first examples of bridged to fused ring interchange to generate fused ring systems.

The expediency of the overall transformation is illustrated with the following example. With intermediate **40** in hand, a formal synthesis of compressanolide is readily achieved (eq 4). Deprotection of the TBS ether followed by oxidation led to **47**, which has been converted to compressanolide by Vandewalle.[4b]

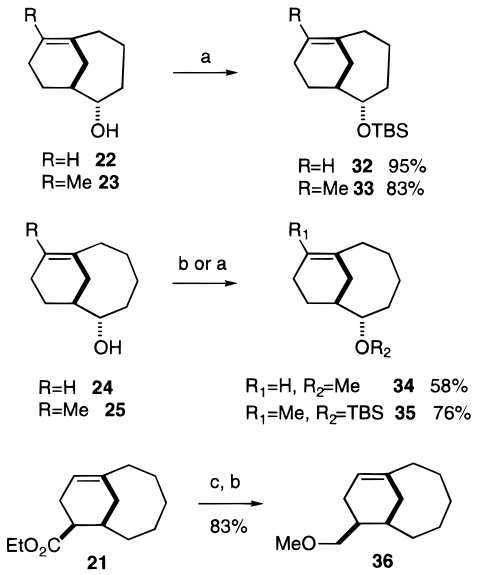


40 **47** (4)

Total Synthesis of Aromadendrane Sesquiterpenes. The aromadendranes are a class of sesquiterpene natural products found in a number of plant species.[32] Structurally, they are characterized by a dimethyl cyclopropane unit fused to a hydroazulene core. The aromadendranes have been found to possess a variety of biological activities.[32,33] Ledol is representative of this class and shows antifungal activity against *Coriolus renatus*.[34]

Although much work has been done on the synthesis of hydroazulenes, there have been few synthetic studies of the aromadendranes. Buchi and co-workers synthesized (−)-aromadendrene using a ring expansion of a decalin system as the key step and, in doing so, unambiguously established the stereochemistry of this natural product and its relatives.[35] Marshall and Ruth carried out the cyclization of a cyclodecadienol derivative to gain access to the hydroazulene ring system. Installation of a *gem*-dimethyl cyclopropane afforded these workers globulol, which is epimeric to ledol.[36] Iwata and co-workers have studied the preparation of aromadendranes starting from carene. Their strategy uses two aldol reactions to sequentially append the seven- and the five-membered rings to the existing cyclopropane.[33]

Scheme 7[a]



[a] Reagents: (a) TBSCl, imidazole; (b) MeI, NaH; (c) DIBALH.

Wijnberg, de Groot, Gijsen, and their co-workers have studied the aromadendranes extensively. They have developed syntheses of alloaromadendranediols using a decalin ring expansion[37] and have demonstrated the value of the aromadendranes as chiral starting materials for natural products synthesis.[38] In addition, these workers have carried out partial syntheses of (−)-globulol, (−)-epiglobulol, (−)-ledol, and (+)-viridiflorol starting from (+)-aromadendrene.[3]

The bridged to fused ring interchange methodology described above provides an efficient method for the total synthesis of (±)-ledol from triene **6** (Scheme 9).[39] This approach exploits the concave nature of cycloadduct **18** and hydroazulenes **48** and **49** to direct the delivery of reagents in a stereocontrolled manner.

The synthesis begins with cycloadduct **18** (prepared above). When this bicyclic ketone is treated with MeLi at −78 °C, **50** is formed exclusively in 91% yield. The origin of this stereoselection can be understood by examining the conformational bias of the ketone (eq 5).[40] The lowest energy conformation[41] presents the exo face of the carbonyl to reagents. This results in high levels

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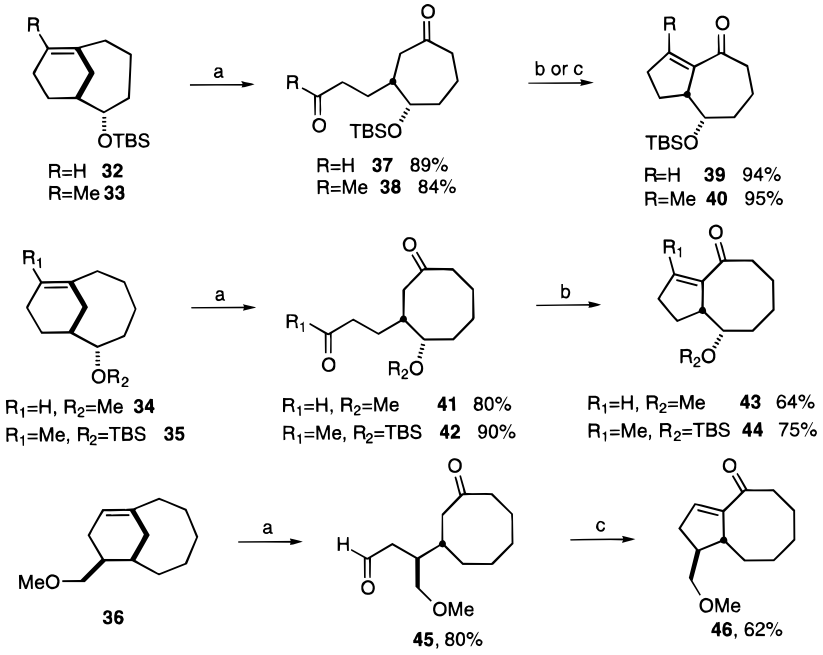
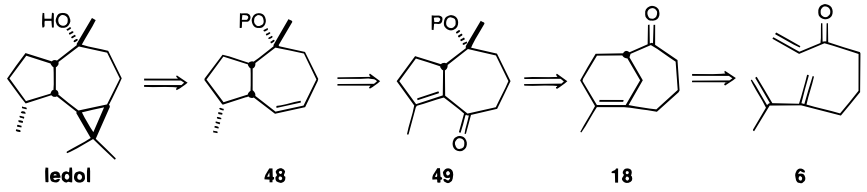
(41) As obtained using Monte Carlo conformational searching in Macromodel V4.5 available from the Department of Chemistry, Columbia University, New York, NY 10027.

Scheme 8[a]

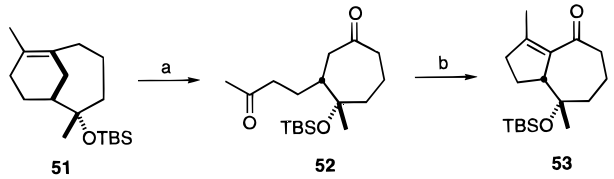


[a] Reagents: (a) O_3, MeOH; (b) KOH, MeOH; (c) PPTS, PhH, reflux.

Scheme 9

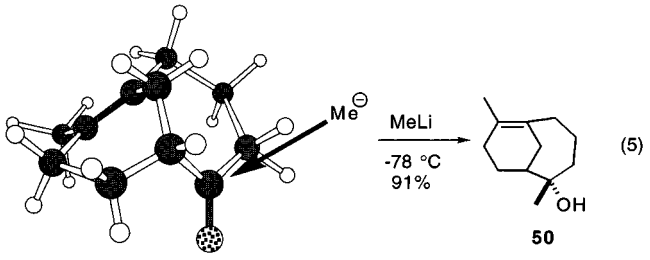


Scheme 10[a]



[a] Reagents: (a) O_3, MeOH, 67%; (b) KOH, MeOH, 97%.

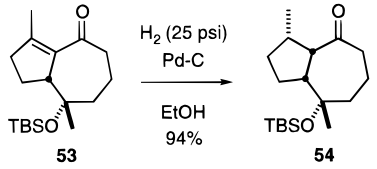
of stereocontrol. The tertiary alcohol thus formed can be efficiently protected (92% yield) using TBSOTf in pyridine/CH_2Cl_2.



(5)

The bridged to fused ring interchange is initiated by treating the protected alcohol with ozone at −78 °C (Scheme 10). After a reductive workup with trimethyl phosphite, the diketone **52** is obtained. Cyclization is accomplished with KOH in MeOH to give enone **53**.

The ring fusion stereochemistry of ledol requires a cis addition of hydrogen to **53**. An example from the literature suggested that this ring system would be amenable to medium pressure catalytic hydrogenation.[42] In the event, treatment of **53** with 25 psi of hydrogen in EtOH over Pd−C afforded 94% of a single diastereomer which was assigned as structure **54** based on ^{1}H NMR coupling constants and NOESY spectra.



(6)

Installation of the dimethylcyclopropane moiety was accomplished as follows. Conversion of **54** to the enol phosphate, followed by reduction with lithium in ammonia,[43] gave alkene **55** (Scheme 11). Dibromocyclopropanation employed Seyferth's reagent.[44] Gem-dimethylation was best performed with the mixed cuprate derived from MeLi and CuCN.[45] Removal of the TBS protecting group with TBAF in refluxing THF gave (±)-ledol which had spectroscopic properties consistent with the assigned structure and was found to be identical to an authentic sample.[46]

(42) Mehta, G.; Krishnamurthy, N.; Karra, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 5765.
(43) Ireland, R. E.; Pfister, G. *Tetrahedron Lett.* **1969**, 2145.
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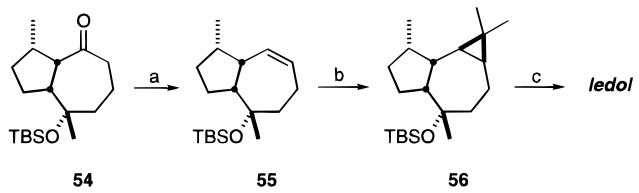
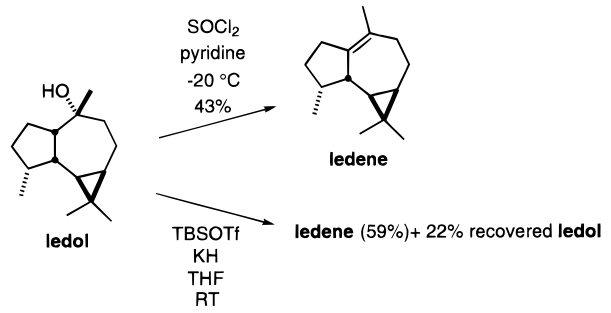
Scheme 11[a]



[a] Reagents: (a) (i) LDA, and then $(EtO)_2POCl$, (ii) Li, NH_3, 45%; (b) (i) $PhHgCBr_3$, PhH, reflux, (ii) MeLi, CuCN, 69%; (c) TBAF, THF, reflux, 59%.

Scheme 12



With ledol in hand, we hoped to prepare other aromadendrane natural products by manipulating the alcohol functionality. Quantities of ledol sufficient for experimentation were obtained by following the work cited above,[3] which showed that ledol can be prepared in two steps from alloaromadendrene.

Treatment of ledol with thionyl chloride in pyridine led to the exclusive formation of ledene in 43% yield. The use of other dehydrating agents (Burgess,[47] Martin sulfurane[48]) led to mixtures of olefins. An intriguing result was obtained when we attempted to silylate ledol with *tert*-butyldimethylsilyl triflate using potassium hydride as the base. Elimination occurred to give ledene in 59% yield along with 22% recovered ledol.

This work represents the first syntheses of ledol and ledene from compounds other than aromadendrane starting materials.

In summary, the type two intramolecular Diels−Alder, when coupled with bridged to fused ring interchange, provides an efficient method for the synthesis of fused 5,7 and 5,8 ring systems. The intermediate bicyclic species can be stereoselectively elaborated prior to ozonolysis of the bridgehead double bond, thus providing a stereoselective synthesis of functionalized cycloheptanes and cyclooctanes that are otherwise difficult to synthesize. Following cleavage, aldol condensations provide fused bicyclic structures. This methodology is amenable to the synthesis of terpene natural products as evidenced by the total syntheses of compressanolide, ledol, and ledene described above. Development of this methodology for the synthesis of other fused polycyclic natural products continues in our lab.

Experimental Section

General. Most of the solvents used were distilled from drying agents (CaH_2 or Na/benzophenone) just before use. Reactions were run in oven-dried or flame-dried glassware under a positive nitrogen atmosphere unless otherwise stated. Drying of organic solutions was accomplished using $MgSO_4$. *In vacuo* as used in the Experimental Section refers to rotary evaporation using a rotavapor.

Thin layer chromatography (TLC) analyses were run on plates precoated with 0.25 mm of silica gel containing 60F-254 indicator. Flash chromatography was run using 230−400 mesh silica gel.

Proton nuclear magnetic resonance spectra (^1H NMR) were recorded on 250, 300, and 500 MHz spectrometers. High resolution mass spectra were obtained by EI (22 or 70 eV) or CI (isobutane or ammonia).

Alloaromadendrene was obtained from Fluka Chemie AG.

4-Methylenehex-5-en-1-ol. To a stirred solution of 1-iodo 3-(*tert*-butyldimethylsiloxy)propane (5 g, 16.66 mmol) and Li_2CuCl_4[12] (1.7 mL of a 1 M solution, 1.7 mmol) in THF (50 mL) at 0 °C was added chloroprene Grignard (31 mL of a 0.7 M solution, 21.7 mmol). This was stirred overnight as the cooling bath warmed slowly to rt. The mixture was then poured into saturated NH_4Cl solution and extracted with ether. The combined organics were dried, concentrated *in vacuo*, and then treated with HF (10 mL) in acetonitrile (190 mL). After approximately 30 min, the reaction was quenched with aqueous Na_2CO_3 and extracted with ether. The combined organics were washed with saturated $NaHCO_3$ solution and brine. The organic phase was dried and concentrated *in vacuo*, and the resulting residue was flushed through a plug of silica and concentrated again to give the alcohol (1.37 g, 73%). FTIR (NaCl, cm^{-1}) 3344, 3089, 2943, 1597, 1061; ^1H NMR (500 MHz, $CDCl_3$) δ 6.33 (dd, J = 11.0, 17.6 Hz, 1H), 5.20 (d, J = 17.6 Hz, 1H), 5.02 (d, J = 10.6 Hz, 1H), 4.98 (s, 1H), 4.97 (s, 1H), 3.60 (t, J = 6.6 Hz, 2H), 3.07 (br s, 1H), 2.24 (t, J = 7.7 Hz, 2H), 1.71 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 145.8, 138.7, 115.8, 113.3, 62.2, 30.9, 27.5; HRMS (EI) calcd for $C_7H_{12}O$ (M^+) 112.08875, observed (M^+) 112.0884.

2-(3-Hydroxypropyl)-3-methyl-1,3-butadiene. To a stirred solution of 3-chloro-1-propanol (16.7 mL, 200 mmol) in THF (500 mL) at 0 °C was added MeMgBr (73 mL of a 2.8 M solution, 205 mmol). After stirring for 30 min, the reaction was warmed and Mg (5 g, 205 mmol) was added. The reaction was heated at reflux for 2.5 h and was then cannula transferred to a solution of CuBr (14.3g, 100 mmol) in THF (100 mL) at −50° C. After 1.5 h, 2-methylbut-1-en-3-yne[14] (9.5 mL, 100 mmol) was added. This mixture was stirred for 2.5 h as the bath slowly warms to rt. The mixture was treated with 6 N HCl and was extracted with ether. The combined organics were extracted with brine and saturated $NaHCO_3$ and were then dried and concentrated. Chromatography (15% ethyl acetate:hexanes; SiO_2) gave the alcohol (5.85g, 46%). FTIR (NaCl, cm^{-1}) 3332, 3093, 2947, 1597, 1442, 1057, 891; ^1H NMR (300 MHz, $CDCl_3$) δ 5.07 (s, 2H), 4.95 (s, 2H), 3.60 (m, 2H), 2.6−2.9 (br s, 1H), 2.32 (dd, J = 7.4, 7.9 Hz, 2H), 1.87 (s, 3H), 1.70 (m, 3H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 147.2, 142.3, 112.6, 112.1, 62.2, 31.5, 29.7, 21.0; HRMS (EI) calcd for $C_8H_{15}O$ (MH^+) 127.1122, observed (MH^+) 127.1124.

1-Iodo-4-methylenehex-5-ene (2). To a stirred solution of the alcohol (9.4 g, 83.9 mmol) in CH_2Cl_2 (300 mL) and pyridine (13.5 mL) at 0 °C were added triphenylphosphine (30.7 g, 117 mmol) and iodine (32 g, 126 mmol). When TLC analysis showed the reaction to be complete, the mixture was filtered into a separatory funnel. The organics were washed with 1 N HCl, saturated $NaHSO_3$, H_2O, and saturated $NaHCO_3$. After drying and concentration in vacuo, the residue was flushed through a plug of silica (petroleum ether). The filtrate was concentrated *in vacuo* to give the iodopropyl diene (12.96 g, 70%). FTIR (NaCl, cm^{-1}) 3085, 2935, 1593, 1427, 1214, 1168, 899; ^1H NMR (500 MHz, $CDCl_3$) δ 6.35 (t, J = 11.0, 17.6 Hz, 1H), 5.24 (d, J = 17.6 Hz, 1H), 5.07 (d, J = 11.0 Hz, 1H), 5.05 (s, 1H),5.04 (s, 1H), 3.20 (m, 2H), 2.33 (m, 2H), 2.0 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 144.3, 138.3, 116.6, 113.6, 31.9, 31.6, 6.7; HRMS (EI) calcd for $C_7H_{11}I$ (M^+) 221.9905, observed (M^+) 221.9905.

A similar procedure gave **1-iodo-4-methylene-5-methylhex-5-ene (4)** in 78% yield. FTIR (NaCl, cm^{-1}) 2946, 1597, 1222, 895; ^1H NMR (500 MHz, $CDCl_3$) δ 5.13 (s, 1H), 5.08 (s, 1H), 5.01 (s, 1H), 5.00 (s, 1H), 3.19 (t, J = 6.8 Hz, 2H), 2.40 (t,

(46) Sample obtained from Prof. Joannes B. P. A. Wijnberg. See reference 3 for spectral data and leading references on ledol.

(47) Burgess, E. M.; Penton, Jr., H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.

(48) Paul, I. C.; Martin, J. C.; Perozzi, E. F. *J. Am. Chem. Soc.* **1972**, *94*, 5010.

J = 6.8 Hz, 2H), 2.0 (m, 2H), 1.90 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 145.9, 142.1, 113.2, 113.0, 34.3, 32.4, 21.1, 7.0; HRMS (CI) calcd for $C_8H_{13}I$ (M^+) 236.0061, observed (M^+) 236.0070.

7-Methylene-8-methyl-1,8-nonadien-3-one (6). Method A (after Tamaru et al.[15]). 2-(3-Iodopropyl)-3-methyl-1,3-butadiene (320 mg, 1.36 mmol) and zinc−copper couple (136 mg, 2.08 mmol) were stirred in benzene (3 mL) and DMF (0.2 mL) at rt for 1 h. The reaction was heated at 60 °C for 3.5 h. Acryloyl chloride (75mL, 0.9 mmol) and $Pd(PPh_3)_4$ (46 mg, 0.04 mmol) were added as a suspension in benzene (3 mL). When the exothermic reaction subsided, the mixture was poured into saturated NH_4Cl solution, and this was extracted with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. Radial chromatography (2.5% to 5% ethyl acetate:hexanes; SiO_2) gave the triene (103 mg, 70%).

Method B. To a solution of methoxyallene[16] (2.65 g, 37.9 mmol) in THF (40 mL) at −35 °C was added n-BuLi (12.6 mL of a 2.0 M solution, 25.25 mmol). The reaction was stirred for 1.25 h while maintaining the temperature below −25 °C. 2-(3-Iodopropyl)-3-methyl-1,3-butadiene (2.98 g, 12.6 mmol) was added as a solution in THF (10 mL). After 1 h, excess 1 N HCl was added and the mixture was stirred for 45 min. The mixture was then diluted with ether, and the organics were further washed once with brine and once with saturated $NaHCO_3$. The organics were dried and concentrated *in vacuo*. Chromatography of the residue (5% ether:petroleum ether; SiO_2) gave the triene (1.6 g, 9.76 mmol, 77%) and cycloadduct **18** (50 mg, 0.3 mmol, 2%). FTIR (NaCl) 2951, 1701, 1682, 1616, 1597, 1403, 895 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.30 (dd, J = 1.46, 10.6 Hz, 1H), 6.20 (m, 1H), 5.78 (dd, J = 1.1, 10.6 Hz, 1H), 5.07 (overlapping singlets, 2H), 4.95 (s, 1H), 4.93 (s, 1H), 2.57 (m, 2H), 2.28 (t, J = 7.5 Hz, 2H), 1.87 (s, 3H), 1.80 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.4, 147.1, 142.2, 136.4, 127.5, 112.5, 112.3, 38.9, 32.8, 22.7, 20.8; HRMS (EI) calcd for $C_{11}H_{16}O$ (M^+) 164.1200, observed 164.1201.

A procedure similar to method A using 2-(3-iodopropyl)-1,3-butadiene gave **7-methylene-1,8-nonadien-3-one (5)** in 80% yield. FTIR (NaCl) 3089, 2939, 1701, 1682, 1616, 1597, 1404, 991, 899 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.30 (m, 3H), 5.80 (dd, J = 1.24, 10.4 Hz, 1H), 5.24 (d, J = 17.6 Hz, 1H), 5.28 (m, 3H), 2.61 (t, J = 7.3 Hz, 2H), 2.24 (t, J = 7.6 Hz, 2H), 1.83 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 200.6, 145.5, 138.5, 136.6, 128.0, 116.2, 113.5, 39.0, 30.7, 22.2; HRMS (EI) calcd for $C_{10}H_{14}O$ (M^+) 150.1044, observed 150.1046.

1-Iodo-3-methylene-4-pentene (8). To a solution of 3-methylenepent-4-en-1-ol[19] (13.55 g, 0.138 mol), triethylamine (23 mL, 0.166 mol), and CH_2Cl_2 (500 mL) at 0 °C was added methanesulfonyl chloride (12.8 mL, 0.166 mol) dropwise. After 1 h, the reaction mixture was extracted sequentially with water, saturated $NaHCO_3$, and brine. The organic layer was then dried, concentrated *in vacuo*, and taken up in acetone (300 mL) to which NaI (62 g, 0.414 mol) was added. The solution was stirred at rt for 12 h and then refluxed for 4 h at which time it was added to a 5% aqueous $NaHSO_3$ solution and extracted with petroleum ether. The combined organic layers were extracted with saturated $NaHSO_3$, dried, and concentrated *in vacuo*. The oil was passed through silica gel, eluted with petroleum ether, and distilled (36 °C at 1.9 mmHg) to yield the iodopentene (16.06 g, 0.077 mol, 56%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.35 (dd, J =17.7, 10.6 Hz, 1H), 5.26−5.07 (m, 4H), 3.30 (dd, J = 8.2, 7.5 Hz, 2H), 2.81 (dd, J = 8.1, 7.5 Hz, 2H). ^{13}C (75.4 MHz, $CDCl_3$) δ 145.1, 137.8, 117.7, 114.0, 36.5, 3.6. IR (neat) 3090, 2960, 1590, 1420, 1230 cm^{-1}. HRMS (EI) calcd for C_6H_9I (M^+) 207.9749, observed 207.9743.

3-Methylene-4-methyl-4-penten-1-ol (9). To a solution of freshly distilled 2-bromo-3-methyl-1,3 butadiene[20] (4.035 g, 27.4 mmol) in THF (40 mL) at −78 °C was added *tert*-butyllithium (39 mL of a 1.4 M solution in pentane, 54.9 mmol). The solution was stirred for 5 h when ethylene oxide (2.0 mL, 41.1 mmol) was added and the cold bath removed. After 2 h, the solution was added to half saturated NaH_2PO_4 and extracted with ether. The combined organic layers were dried and concentrated *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 3:7 ether to petroleum ether to recover the alcohol (1.91 g, 16.9 mmol, 62% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.25−5.0 (m, 4H), 3.74 (t, J = 6.4 Hz, 2H), 2.58 (t, J = 6.4 Hz, 2H), 1.90 (s, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.2, 142.4, 114.7, 113.5, 61.7, 37.2, 21.3. IR (FTIR, neat) 3330, 2950, 1600 cm^{-1}. HRMS (CI) calcd for $C_7H_{13}O$ (MH^+) 113.0963, observed 113.0961.

1-Iodo-4-methyl-3-methylene-4-pentene (10). A solution of the alcohol **9** (3.56 g, 31.8 mmol) in pyridine (9 mL) was cooled to 0 °C and then charged with tosyl chloride (6.36 g, 33.4 mmol). The solution was stirred at 0 °C for 10 min and then 4 h at rt when it was added to water and extracted with ether. The combined ether layers were extracted with 5% HCl, saturated $NaHCO_3$, and brine and then dried and reduced to an oil *in vacuo*. The oil was taken up in acetone (150 mL), and NaI (49.5 g, 330 mmol) was added. The solution was stirred at rt for 16.5 h when it was added to water and extracted with petroleum ether. The combined organic layers were dried, reduced to an oil *in vacuo*, and chromatographed on silica gel eluted with petroleum ether to recover the iodo diene (4.317 g, 19.4 mmol, 65% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.2−5.0 (m, 4H), 3.28 (t, J = 7.8 Hz, 2H), 2.86 (t, J = 7.8 Hz, 2H), 1.91 (s, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 146.7, 141.7, 114.5, 113.2, 38.8, 21.3, 4.7. HRMS (CI) calcd for $C_7H_{12}I$ (MH^+) 222.9981, observed 222.9995.

8-Methylene-1,9-decadien-3-one (12). To a solution of 3-(*tert*-butyldimethylsiloxy)-1,4-pentadiene (460.7 mg, 2.33 mmol) in THF (2.5 mL) at −78 °C was added *sec*-butyllithium (1.7 mL of a 1.35 M solution in cyclohexane, 2.33 mmol) dropwise over 10 min. After 35 min, 5-iodo-3-methylenepentene (**6**) (485 mg, 2.33 mmol) was added. The solution was stirred for 30 min at −78 °C when it was added to saturated NH_4Cl and extracted with petroleum ether. The combined organic layers were extracted with brine, dried, and reduced to an oil *in vacuo*. The pale yellow oil was taken up in 5% HF (37% aqueous) in CH_3CN (25 mL) and stirred at rt for 30 min at which time it was added to saturated $NaHCO_3$ and extracted with ether. The combined ether layers were extracted with saturated $NaHCO_3$ and brine and then dried and reduced to an oil *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 7% ether in petroleum ether to recover the triene (209.4 mg, 1.28 mmol, 55%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.41−6.32 (m, 2H), 6.21 (dd, J = 17.6, 1.3 Hz, 1H), 5.81 (dd, J = 10.2, 1.3 Hz, 1H), 5.21 (d, J = 17.6 Hz, 1H), 5.07−4.99 (m, 3H), 2.62 (t, J = 7.2 Hz, 2H), 2.24 (t, J = 7.4 Hz, 2H), 1.70−1.63 (m,2H), 1.57−1.50 (m,2H). ^{13}C NMR (75.4 MHz, CDCl) δ 201.1, 146.2, 139.1, 136.8, 128.2, 116.1, 113.4, 39.7, 31.4, 27.9, 24.1. IR (neat) 3090, 1700, 1680 cm^{-1}. HRMS calcd for $C_{11}H_{16}O$ (M^+) 164.1200, observed 164.1198.

8-Methylene-9-methyl-1,9-decadien-3-one (13). To a solution of 3-(*tert*-butyldimethylsilyloxy)-1,4-pentadiene (1.59 g, 8.03 mmol) in THF (8.5 mL) at −78 °C was added *sec*-butyllithium (5.95 mL of a 1.35 M solution in cyclohexane, 8.03 mmol) dropwise over 15 min. The solution was then stirred for 30 min when the alkyl iodide **10** (1.67 g, 8.03 mmol) was added. THF (2 mL) was used to rinse the syringe which contained the alkyl iodide, and this was added to the reaction solution. After 30 min, the mixture was added to an aqueous solution of half saturated NH_4Cl and extracted with petroleum ether. The combined organic layers were dried, concentrated to an oil *in vacuo*, and taken up with 5% HF (37% aqueous) in acetonitrile (80 mL). The resulting solution was stirred at rt for 30 min when it was added to aqueous saturated $NaHCO_3$ and extracted with ether. The combined ether layers were extracted with saturated $NaHCO_3$, dried, and concentrated *in vacuo*. The resulting oil was chromatographed with silica gel eluted with 3% ether in petroleum ether to recover the triene (729 mg, 4.07 mmol, 51% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37−6.3 (m, 1H), 6.21 (d, J = 17.5 Hz, 1H), 5.81 (d, J = 10.0 Hz, 1H), 5.06 (d, J = 11.3, 2H), 4.95 (d, J = 8.1Hz, 2H), 2.60 (t, J = 7.3 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 1.84 (s, 3H), 1.6 (m, 2H), 1.5 (m, 2H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 201.2, 147.7, 142.8, 136.8, 126.2, 112.8, 112.4, 33.7, 33.6, 28.6, 24.1, 21.4. IR (FTIR, neat) 2940, 1700, 1680, 1600 cm^{-1}. HRMS (CI) calcd for $C_{12}H_{19}O$ (MH^+) 179.1431, observed 179.1427.

6-Iodohexanol, Tetrahydropyranyl Ether. A solution of the mono-THP protected 1,6 hexanediol (16.71 g, 82.7 mmol), triethylamine (13.8 mL, 99.3 mmol), and CH_2Cl_2 (200 mL) was

cooled to 0 °C. The solution was charged with methanesulfonyl chloride (7.7 mL, 99.3 mmol) and stirred for 45 min at 0** °C when it was extracted with water and saturated $NaHCO_3$. The organic layer was dried and the solvent removed *in vacuo*. The residue was taken up in acetone (25 mL) and NaI (74.5 mg, 496 mmol) added. The solution was stirred at rt for 20 h when it was added to water and extracted with ether. The combined organic layers were dried, and the solvent was removed *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 5% ether in petroleum ether to recover the THP protected iodohexanol (16.40 g, 52.4 mmol, 64%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.51 (t, J = 3.5 Hz, 1H), 3.8 (m, 1H), 3.66 (dt, J = 9.6, 6.7 Hz, 1H), 3.4 (m, 1H), 3.31 (dt, J = 9.6, 6.4 Hz, 1H), 3.13 (t, J = 7.0 Hz, 2H), 1.80−1.29 (m, 14H). ^{13}C NMR (75.4 MHz), $CDCl_3$ δ 98.8, 67.3, 62.3, 33.4, 30.7, 30.3, 29.5, 28, 25.2, 19.6, 7.0. IR (FTIR, neat) 2940, 1435 cm^{-1}. HRMS (CI) calcd for $C_{11}H_{22}IO_2$ (MH^+) 313.0662, observed 313.0670.

7-Methylene-8-nonen-1-ol, Tetrahydropyranyl Ether (14). The THP protected 6-iodohexanol (3.0725 g, 9.85 mmol) was taken up with THF (18 mL) and Li_2CuCl_4 (9.85 mL of a 0.10 molar solution in THF, 0.985 mmol) added. A stock solution of chloroprene Grignard (11.4 mL of a 1.3 M solution in THF, 14.8 mmol) was added dropwise over 10 min. The solution was allowed to stir for 16 h when it was poured into an aqueous solution (20 mL of saturated NH_4Cl and 80 mL of water) and extracted with ether. The organic layers were combined, dried, and concentrated *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 3% ether in petroleum ether to yield the THP-diene compound (1.71 g, 7.15 mmol, 73% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.37 (dd, J = 17.6, 10.7 Hz, 1H), 5.22 (d, J = 17.6 Hz, 1H), 5.0 (m, 3H), 4.58 (t, J = 3.5 Hz, 1H), 3.87−3.70 (m, 2H), 3.52−3.35 (m, 2H), 2.20 (t, J = 7.3 Hz, 2H), 1.36−1.82 (m, 14H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 146.7, 139.2, 115.7, 113.3, 99.1, 67.9, 62.6, 31.5, 31.0, 29.9, 29.7, 28.3, 26.4, 25.7, 19.9. IR (FTIR, neat) 1594, 1033 cm^{-1}. HRMS (CI) calcd for $C_{15}H_{27}O_2$ (MH^+) 239.2003, observed 239.2004.

7-Methylene-8-nonen-1-ol. A solution of the THP protected alcohol **14** (1.71 g, 7.18 mmol) in ethanol (55 mL) was charged with pyridinium *p*-toluenesulfonate (0.18 g, 0.718 mmol) and stirred at 55 °C for 5 h. The ethanol was then removed *in vacuo* and the resulting oil chromatographed on silica gel eluted with 1:4 ether:petroleum ether to yield the alcohol (0.995 g, 6.42 mmol, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.35 (dd, J = 10.8, 17.6 Hz, 1H), 5.21 (d, J = 17.6 Hz, 1H), 5.05−4.97 (m, 3H), 3.61 (t, J = 6.2 Hz, 2H), 2.20 (t, J = 7.5 Hz, 2H), 2.05 (br s, 1H), 1.58−1.33 (m, 8H). ^{13}C (75.4 MHz, $CDCl_3$) δ 146.6, 139.1, 115.7, 113.2, 63.0, 32.9, 31.4, 29.5, 28.3, 25.8. IR (FT, neat) 3334, 1594 cm^{-1}. HRMS (CI) calcd for $C_{10}H_{19}O$ (MH^+) 155.1435, observed 155.1428.

7-Methylene-8-nonen-1-al (15). To a three-neck round bottom flask equipped with two addition funnels were added oxalyl chloride (3.58 mL, 41.0 mmol) and CH_2Cl_2 (85 mL). The solution was cooled to −78 °C when DMSO (6.3 mL, 89.5 mmol) was added as a solution in CH_2Cl_2 (17 mL) over 15 min. After stirring for 10 min, 7-methylene-8-nonen-1-ol **14** (5.74 g, 37.3 mmol) was added as a solution in CH_2Cl_2 (35 mL). The reaction mixture was allowed to stir for 15 min when Et_3N (26 mL, 186.5 mmol) was added over 20 min. The cold bath was removed and the solution warmed to rt. Water was then added and the solution stirred for 10 min. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The organic layers were combined, dried, and concentrated to an oil *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 3% ether in petroleum ether to recover the aldehyde (4.75 g, 31.0 mmol, 84%). ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.75 (t, J = 1.8 Hz, 1H), 6.35 (dd, J = 10.8, 17.6 Hz, 1H), 5.20 (d, J = 17.6 Hz, 1H), 5.06−4.96 (m, 3H), 2.42 (dt, J = 1.7, 7.3 Hz, 2H), 2.20 (t, J = 7.4 Hz, 2H), 1.71−1.31 (m, 6H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 202.9, 146.4, 139.1, 115.9, 113.3, 44.0, 31.3, 29.2, 28.0, 22.1. IR (FT, neat) 1726, 1595 cm^{-1}. HRMS (CI) calcd for $C_{10}H_{17}O$ (MH^+) 153.1278, observed 153.1283.

Ethyl 9-Methylene-2,10-undecadienoate (16). Sodium hydride (52 mg of a 50% dispersion in mineral oil, 1.09 mmol) was taken up in THF (1 mL) and cooled to 0 °C. Triethyl phosphonoacetate (210 μL, 1.07 mmol) was added dropwise. The solution was stirred for 1 h at 0 °C when the aldehyde **15** (162.1 mg, 1.07 mmol) was added as a solution in THF (1 mL). The flask previously containing the aldehyde was rinsed with THF (0.5 mL) and added to the reaction flask. The reaction mixture was stirred for 2 h when it was added to water (40 mL) and brine (5 mL). The aqueous layer was extracted with ether, and the ether layers were combined, dried, and concentrated *in vacuo*. The resulting oil was radially chromatographed on silica gel eluted with 2% ether in petroleum ether to yield the triene (192.5 mg, 0.863 mmol, 81% yield trans product, also 8.0 mg, 3% cis triene). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97 (dt, J = 15.4, 7.1 Hz, 1H), 6.37 (dd, J = 10.8, 17.6 Hz, 1H), 5.82 (dt, J = 15.6, 1.5 Hz, 1H), 5.22 (d, J = 17.6 Hz, 1H), 5.07−4.98 (m, 3H), 4.19 (q, J = 7.2 Hz, 2H), 2.23−2.18 (m, 4H), 1.56−1.32 (m, 6H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 166.9, 149.5, 146.5, 139.1, 121.5, 115.8, 113.3, 60.3, 32.3, 31.4, 29.2, 28.1, 28.0, 14.4. IR (FT, neat) 1722, 1655 cm^{-1}. HRMS (CI) calcd for $C_{14}H_{23}O_2$ (MH^+) 223.1697, observed 223.1689.

2-Oxobicyclo[4.3.1]dec-6-ene (17). The trienone **5** (162 mg, 1.08 mmol) and proton sponge (69 mg, 0.32 mmol) were stirred in xylenes (50 mL) at reflux for 20 h. After cooling, the solvent was removed *in vacuo*. Radial chromatography (5% ether:petroleum ether, SiO_2) gave the bridgehead alkene (93 mg, 57%). FTIR (NaCl) 2935, 1701, 1442, 899 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.47 (d, J = 6.2 Hz, 1H) 2.83 (ddd, J = 3.3, 11.7, 14.7 Hz, 1H), 2.55 (m, 1H), 2.49 (m, 1H), 2.30 (m, 1H), 2.22 (ddd, J = 2.6, 5.9, 11.4 Hz, 1H), 2.15 (dt, J = 5.9, 11.4 Hz, 1H), 2.00 (m, 4H), 1.76 (m, 2H), 1.42 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 216.4, 144.8, 123.4, 46.9, 41.6, 35.6, 32.3, 31.6, 24.0, 21.0; HRMS (EI) calcd for $C_{10}H_{14}O$ (M^+) 150.1044, observed 150.1046.

2-Oxo-7-methylbicyclo[4.3.1]dec-6-ene (18). To a stirred solution of triene **6** (138 mg, 0.84 mmol) in CH_2Cl_2 (20 mL) at rt was added Et_2AlCl (0.23 mL of a 1.8 M solution, 0.42 mmol). TLC analysis showed the reaction to be complete in less than 15 min. The residue was poured into a solution of sodium bicarbonate and Rochelle's salt. This was extracted twice with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. Radial chromatography (5% diethyl ether:petroleum ether; SiO_2) gave the bridgehead alkene (96 mg, 70%). FTIR (NaCl) 2938, 1697, 1442 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.85 (m, 1H), 2.62 (m, 1H), 2.50 (m, 1H), 2.42 (m, 1H), 2.22 (m, 1H), 2.06−1.68 (m, 8H), 1.58 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 216.5, 135.7, 130.5, 47.1, 42.0, 32.8, 32.6, 30.0, 27.4, 24.0, 17.8; HRMS (EI) calcd for $C_{11}H_{16}O$ (M^+) 164.1200, observed 164.1200.

2-Oxobicyclo[5.3.1]undec-7-ene (19). A solution of the triene **12** (746 mg, 4.55 mmol) in toluene (100 mL) was added to a resealable Carius tube and freeze-thaw degassed for four cycles. The solution was heated in an oil bath at 180 °C for 48 h when the toluene was evaporated *in vacuo* to recover the crude cycloadduct (725.7 mg, 97%) which was carried on to the next step without purification. UV (6.4×10^{-4} M in hexanes) λ_{max}= 196 nm, ϵ = 2900.

2-Oxo-8-methylbicyclo[5.3.1]undec-7-ene (20). A solution of the triene **13** (579.0 mg, 3.25 mmol) in CH_2Cl_2 (90 mL) at rt was charged with Et_2AlCl (108 mL of a 1.5 M solution in hexane, 0.16 mmol, 0.05 equiv). The resulting solution was stirred for 1 h when it was added to an aqueous solution of saturated $NaHCO_3$ (150 mL) and saturated Na,K-tartrate (20 mL) and then extracted with CH_2Cl_2. The organic layers were combined, dried, and reduced to an oil *in vacuo*. The product was isolated from the crude mixture with silica gel eluted with 5% ether in petroleum ether to recover the ketone (364.2 mg, 2.05 mmol, 63% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.5 (m, 2H), 2.41 (dt, J = 11.3, 1.3 Hz, 1H), 2.3 (m, 1H), 2.05−1.75 (m, 7H), 1.51 (m, 1H), 1.53 (s, 3H), 1.1 (m, 1H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 214.5, 131.5, 129.0, 47.8, 42.4, 29.6, 28.4, 27.4, 27.3, 25.4, 23.0, 18.7. IR (FTIR, neat) 2929, 1699 cm^{-1}. HRMS (EI) calcd for $C_{12}H_{18}O$ (M^+) 178.1353, observed 178.1364. UV (5.3×10^{-4} M in hexanes) λ_{max} = 208 nm, ϵ = 5200.

1β-H-10β-Carbethoxybicyclo[5.3.1]undec-7-ene (21). A solution of the triene **16** (334.5 mg, 1.51 mmol) in xylenes (30 mL) was degassed for four freeze-pump-thaw cycles in a

resealable Carius tube. The tube was then placed into an oil bath at 240 °C for 15 h. The resulting solution was chromatographed on silica gel eluted initially with petroleum ether and then 2% ether in petroleum ether to yield the cycloadduct (214.3 mg, 0.965 mmol, 64% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.55 (br s, 1H), 4.14 (q, J = 7.1 Hz, 2H), 2.35−1.29 (m, 16H), 1.26 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 177.0, 140.7, 120.7, 60.5, 44.2, 36.0, 35.9, 35.6, 30.0, 29.1, 28.8, 25.8, 25.3,14.5. IR (FT, neat) 1731 cm^{-1}. HRMS (EI) calcd for $C_{14}H_{22}O_2$ (M^+) 222.1619, observed 222.1602.

1β-H-10β-(Hydroxymethyl)bicyclo[5.3.1]undec-7-ene. To a solution of the ester **21** (361.8 mg, 1.63 mmol) and toluene (10 mL) at −78 °C was added DIBALH (2.4 mL of a 1.5 molar solution in toluene, 3.59 mmol). The solution was stirred for 15 min when water (30 mL), saturated K,Na-tartrate (20 mL), and ether (20 mL) were added. The resulting solution was stirred for 1 h at rt when the layers were separated. The aqueous layer was extracted with ether. The combined ether layers were dried, concentrated *in vacuo*, and chromatographed on silica gel eluted with 3:7 ether:petroleum ether to yield the alcohol (286.1 mg, 1.59 mmol, 98% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.58 (m, 1H), 3.54 (m, 2H), 2.27 (dt, J = 6.5, 15.0 Hz, 1H), 2.15−2.11 (m, 3H), 1.86−1.61 (m, 3H), 1.58−1.48 (m, 6H), 1.41−1.29 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 141.1, 121.5, 67.3, 41.5, 36.1, 36.0, 35.1, 30.1, 29.2, 28.9, 26.5, 25.4. IR (FT, neat) 3327, 1467 cm^{-1}. HRMS calcd for $C_{12}H_{20}O$ (M^+) 180.1513, observed 180.1524.

1β-H-2α-Hydroxy-8-methylbicyclo[5.3.1]undec-7-ene (25). To a solution of the ketone **20** (276 mg, 1.55 mmol) in toluene (20 mL) at −78 °C was added DIBALH (1.1 mL of a 1.5 M solution in toluene, 1.63 mmol, 1.05 equiv) dropwise. The solution was stirred for 45 min when it was added to water (50 mL), saturated Na,K-tartrate (50 mL), and ether (50 mL). The resulting emulsion was stirred for 2 h when two layers separated. The aqueous layer was extracted with ether, and the ether layers were combined, dried, and reduced to an oil *in vacuo*. The oil was chromatographed on silica gel eluted with 7:13 ether:petroleum ether to recover the α-alcohol (248.9 mg, 1.38 mmol, 89% yield) and the β-alcohol (10 mg, 0.06 mmol, 3.5% yield). Characterization of the α-alcohol: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.7 (m, 1H), 2.6 (m, 1H), 2.4 (m, 1H), 2.1 (m, 1H), 1.85−2.0 (m, 4H), 1.72 (s, 3H), 1.7 (m, 3H), 1.5 (m, 3H), 1.35 (m, 2H), 1.2 (m, 1H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 131.2, 129.8, 79.1, 38.6, 33.4, 33.0, 32.8, 30.1, 30.0, 25.7, 20.8, 18.0. HRMS (EI) calcd for $C_{12}H_{20}O$ (M^+) 180.1509, observed 180.1505. Anal. Calcd for $C_{12}H_{20}O$: C, 79.92; H, 11.20. Observed: C, 80.22; H, 11.53.

1,8-Dimethyl-2-oxobicyclo[5.3.1]undec-7-ene (26). To a solution of LDA (477 μL of a 0.48 M solution in THF/hexanes, 0.23 mmol) and DMPU (400 μL) at −78 °C was added the ketone **20** (34.0 mg, 0.19 mmol) in THF (200 μL) dropwise. The flask previously containing the ketone was washed with THF (200 μL) and added to the reaction mixture. The reaction was stirred for 20 min when it was warmed to −30 °C, and methyl iodide (35.5 μL, 0.56 mmol) was added in 1 portion. After 1 h at −30 °C, the solution was quenched with saturated NH_4Cl and extracted with petroleum ether. The combined organic layers were dried, concentrated *in vacuo*, and radially chromatographed on silica gel eluted with 3% ether:petroleum ether to recover methylated product (23.4 mg of an inseparable mixture consisting mainly of bridgehead methyl regioisomer and a minor amount of the methylene methyl regioisomer, 0.12 mmol, 64% yield) and starting material (0.5 mg, 1%). By gas/liquid chromatography of the crude reaction mixture it was determined that the mixture of the methylated products was approximately a 37:1 mixture favoring the bridgehead methyl product **26**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.53 (dt, J = 11.3, 1.0 Hz, 1H), 2.40 (ddd, J = 13.9, 11.5, 7.1 Hz, 1H), 2.31 (dd, J = 14.9, 3.4 Hz, 1H), 2.23 (m, 1H), 2.17 (t, J = 10.6 Hz, 1H), 2.07 (m, 2H, 1.85 (m, 6H), 1.52 (s, 3H), 1.34 (m, 1H), 1.06 (s, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 216.4, 131.6, 128.4, 49.8, 40.5, 35.2, 31.9, 30.0, 29.5, 27.3, 24.8, 23.9, 18.7. IR (FTIR, neat) 1697, 1454 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{20}O$ (M^+) 192.1509, observed 192.1516.

3,8-Dimethyl-2-oxobicyclo[5.3.1]undec-7-ene (27). A solution of the ketone **20** (88.0 mg, 0.494 mmol) in THF (1.2 mL) was cooled to 0 °C when a solution of potassium bis(trimethylsilyl)amide (970 μL of a 0.5 M solution in toluene, 0.484 mmol) was added dropwise over 30 min. The solution was stirred for 15 min at 0 °C when methyl iodide (92 μL, 1.48 mmol) was added in one portion. After 1.5 h at 0 °C and 15 min at rt, saturated NH_4Cl was added. The resulting solution was added to water and extracted with ether. The combined organic layers were dried, concentrated *in vacuo*, and radially chromatographed on silica gel eluted with 3% ether in petroleum ether to recover methylated product (69.0 mg of the major methylene methyl diastereomer, 0.359 mmol, 73%; 8.0 mg of the minor diastereomer, 0.042 mmol, 8%) and starting material (7.1 mg, 0.039, 8%). By gas/liquid chromatography of the crude reaction mixture it was determined that the ratio of the regioisomers was 40:1 in favor of the methylene methyl over the bridgehead methyl. Further analysis provided a 8:1 ratio of diastereomers of the methylene methyl products. Characterization of the main diastereomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.87 (m, 2H), 2.54 (ddd, J = 7.9, 7.4, 4.2 Hz, 1H), 2.35 (dd, J = 13.5, 2.0 Hz, 1H), 2.06 (app dd, J = 7.8, 4.7 Hz, 2H), 1.95 (m, 1H), 1.83 (m, 1H), 1.76 (s, 3H), 1.7−1.5 (m, 6H), 0.99 (d, J = 7.1 Hz, 3H). ^{13}C NMR (125.8 Hz) δ 219.5, 131.4, 130.3, 48.0, 41.8, 35.8, 31.2, 30.4, 29.3, 24.9, 22.5, 18.6, 18.5. HRMS (EI) calcd for $C_{13}H_{20}O$ (M^+) 192.1509, observed 192.1517. Characterization of the minor diastereomer. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.67 (m, 2H), 2.58 (m, 1H), 2.33 (m, 2H), 2.03 (m, 3H), 1.90 (m, 3H), 1.55 (m, 2H), 1.53 (s, 3H), 1.05 (m, 1H), 0.99 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 216.5, 131.6, 128.7, 47.9, 44.6, 35.3, 29.8, 28.4, 26.8, 26.7, 22.8, 20.4, 18.7. IR (FTIR, neat) 2929, 1702 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{20}O$ (M^+) 192.1509, observed 192.1506.

1-Hydroxy-8-methyl-2-oxobicyclo[5.3.1]undec-7-ene (31). To a solution of NaHMDS (290 μL of a 1.0 M solution in THF, 0.29 mmol), DMPU (400 μL), and THF at −78 °C was added the ketone **20** (43.4 mg, 0.243 mmol) in THF (200 μL) at −78 °C dropwise. THF (200 μL) was used to rinse the flask previously containing the ketone and was added to the reaction. The reaction was stirred for 30 min when the 2-sulfonyl oxiziridine[29] (95.4 mg, 0.37 mmol) was added as a solution in THF (200 μL). The reaction was stirred at −78 °C for 12 h, −60 °C for 5 h, and then slowly warmed to −25 °C at which time it was quenched with saturated NH_4Cl and extracted with ether. The combined ether layers were dried, concentrated *in vacuo*, and chromatographed on silica gel eluted with 3:7 ether:petroleum ether to recover alcohol (30.1 mg of a mixture of regioisomers, 65% yield) and starting material (5.0 mg, 12% yield). Proton NMR of the product mixture shows approximately a 30:1 ratio of regioisomeric alcohols favoring the bridgehead alcohol. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.8 (br s, 1H), 2.57 (m, 2H), 2.45 (m, 1H), 2.40 (m, 2H), 2.23 (d, J = 13.5 Hz, 1H), 1.98 (ddd, J = 15.6, 7.0, 3.0 Hz, 1H), 1.95 (m, 2H), 1.77 (m, 2H), 1.73 (s, 3H), 1.67 (m, 3H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 214.9, 131.3, 129.3, 80.0, 39.6, 37.5, 32.2, 31.2, 30.3, 27.3, 25.8, 18.5. IR (FTIR, neat) 3408 (br), 2925, 1693 cm^{-1}. HRMS (EI) calcd for $C_{12}H_{18}O_2$ (M^+) 194.1302, observed 194.1301.

2-Hydroxy-7-methylbicyclo[4.3.1]dec-6-ene (23). To a stirred solution of ketone **18** (544 mg, 3.32 mmol) in toluene (50 mL) at −78 °C was added DIBALH (2.4 mL of a 1.5 M solution, 3.65 mmol) dropwise. TLC analysis showed the reaction to be complete in 20 min at which time the reaction mixture was poured into 50 mL of a half-saturated solution of Rochelle's salt and 50 mL of ether. This was stirred for 30 min when two layers form. The organics were separated, and the aqueous layer was extracted with ether. The combined organics were dried and concentrated *in vacuo*. Radial chromatography (20% ethyl acetate:hexanes; SiO_2) gave the alcohol (510 mg, 93%). FTIR (NaCl) 3351, 2939, 1454, 1034 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.60 (ddd, J = 3.0, 5.3, 11.0 Hz, 1H), 2.44 (m, 1H), 2.38 (dt, J = 4.1, 12.8 Hz, 1H), 2.03 (m, 2H), 1.93 (m, 1H), 1.84 (d, J = 2.6 Hz, 2H), 1.76 (m, 1H), 1.72 (s, 3H), 1.65 (m, 1H), 1.51 (m, 1H), 1.36 (m, 2H), 1.17 (m, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 132.8, 130.5, 78.5, 36.7, 30.8, 30.2, 28.8, 28.7, 22.0, 21.6, 18.1; HRMS (CI) calcd for $C_{11}H_{19}O$ (MH^+) 167.1435, observed 167.1429. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Observed: C, 79.08; H, 11.12.

A similar procedure starting with ketone **17** gave **2-hydroxybicyclo[4.3.1]dec-6-ene (22)** in 98% yield. FTIR (NaCl) 3359, 2935, 1454, 1038 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.69 (m, 1H), 3.55 (m, 1H), 2.44 (m, 1H), 2.36 (m, 1H), 2.10 (m, 1H), 2.02 (ddd, J = 8.1, 10.3, 18.7 Hz, 1H), 1.84 (m, 3H), 1.68 (m, 2H), 1.50 (m, 2H), 1.36 (m, 2H), 1.16 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.7, 126.9, 78.5, 36.1, 34.5, 30.6, 27.6, 23.5, 22.0, 21.8; HRMS (CI) calcd for $C_{10}H_{17}O$ (MH^+) 153.1279, observed 153.1281.

2-(*tert*-Butyldimethylsiloxy)bicyclo[4.3.1]dec-6-ene (32). To a stirred solution of alcohol **22** (123 mg, 0.809 mmol) and imidazole (165 mg, 2.43 mmol) in DMF (2 mL) was added TBSCl (241 mg, 1.6 mmol). The reaction was heated to 40 °C for 20 h and was then poured into water and extracted with petroleum ether. The combined organics were dried and concentrated *in vacuo*. Radial chromatography (petroleum ether; SiO_2) gave the protected alcohol (204 mg, 95%). FTIR (NaCl) 2931, 1469, 1080 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.68 (m, 1H), 3.50 (ddd, J = 3.7, 5.9, 14.3 Hz, 1H), 2.34 (m, 2H), 2.07 (m, 1H), 2.00 (m, 1H), 1.81 (m, 3H), 1.69 (m, 1H), 1.58 (m, 1H), 1.48 (m, 1H), 1.34 (m, 3H), 0.85 (s, 9H), 0.01 (two s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 139.9, 127.0, 78.8, 36.9, 34.7, 31.3, 27.6, 25.8, 23.5, 22.4, 22.0, 18.1, −4.7, −4.8; HRMS (CI) calcd for $C_{16}H_{31}OSi$ (MH^+) 267.2143, observed 267.2134.

A similar procedure starting with alcohol **23** gave **2-(*tert*-butyldimethylsiloxy)-7-methylbicyclo[4.3.1]dec-6-ene (33)** in 83% yield. FTIR (NaCl) 2931, 1083, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.55 (m, 1H), 2.34 (m, 2H), 2.0 (m, 2H), 1.90 (m, 1H), 1.8 (d, J = 3.7 Hz, 2H), 1.72 (m overlapping with s, 4H), 1.6−1.45 (m, 2H), 1.4 (m, 2H), 1.2 (m, 1H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 132.7, 130.6, 78.8, 37.4, 31.5, 30.3, 28.9, 28.7, 25.8, 22.2, 22.1, 18.2, 18.1, −4.7, −4.8; HRMS (EI) calcd for $C_{17}H_{32}OSi$ (M^+) 280.2221, observed 280.2211.

1*β*-H-2α-Methoxybicyclo[5.3.1]undec-7-ene (34). DIBALH (430 μL of a 1.5 M solution in toluene, 416 μmol) was added dropwise to a solution of cycloadduct **24** (88.2 mg, 0.538 mmol) and toluene (5 mL) at −78 °C. After 1 h, the cold bath was removed and the reaction mixture allowed to warm to rt. Water (4 mL), ether (6 mL), and a saturated Na,K-tartrate solution (6 mL) were then added. The solution was stirred vigorously for 30 min when the layers were separated and the aqueous layer extracted with ether. The organic layers were combined, dried, and concentrated *in vacuo*. The resulting oil was taken up in THF (3 mL) and NaH (39 mg, 1.61 mmol) was added. The solution was heated to reflux for 1 h and then cooled to rt after which time MeI (170 μL, 2.69 mmol) was added. The solution was stirred for 12 h when it was added to water and extracted with petroleum ether. The petroleum ether layers were combined, dried, and concentrated *in vacuo*. The crude oil was chromatographed on silica gel eluted with 3% ether in petroleum ether to yield the methyl ether (55.8 mg, 0.31 mmol, 58% yield from the triene). ^1H NMR (300 MHz, $CDCl_3$) δ 5.70 (t, J = 3.6 Hz, 1H), 3.29 (s, 3H), 3.15−3.19 (m, 1H), 2.64 (m, 1H), 2.27−2.31 (m, 1H), 1.18−2.16 (m, 13H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 141.2, 123.8, 88.0, 55.9, 36.3, 34.3, 31.9, 30.8, 29.9, 25.6, 23.5, 20.9. IR (neat) 2930, 2810, 1460 cm^{-1}. HRMS (EI) calcd for $C_{12}H_{20}O$ (M^+) 180.1513, observed 180.1501.

1*β*-H-8-Methyl-2α-(*tert*-butyldimethylsiloxy)bicyclo-[5.3.1]undec-7-ene (35). To a solution of the alcohol **25** (63.3 mg, 0.35 mmol), imidazole (60 mg, 0.88 mmol, 2.5 equiv), and DMF (200 μL) at 0 °C was added TBDMSCl (116.6 mg, 0.77 mmol, 2.2 equiv). The solution was stirred at 0 °C for 5 min then for 2 days at 35−40 °C when it was added to water and extracted with petroleum ether. The combined organic layers were dried, reduced to an oil *in vacuo*, and chromatographed on silica gel eluted with petroleum ether to recover the protected alcohol (87.6 mg, 0.30 mmol, 85% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 3.6 (m, 1H), 2.6 (m, 1H), 2.3 (m, 1H), 2.1 (m, 1H), 1.9 (m, 3H), 1.8 (m, 1H), 1.72 (s, 3H), 1.62 (m, 2H), 1.5 (m, 2H), 1.3 (m, 4H), 0.859 (s, 9H), 0.023 (s, 6H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 131.2, 129.8, 79.4, 39.4, 34.3, 33.2, 33.0, 30.3, 30.2, 26.1, 25.6, 21.4, 18.4, 18.1, −4.5. HRMS (EI) calcd for $C_{18}H_{34}OSi$ (M^+) 294.2370, observed 294.2368.

1*β*-H-10*β*-(Methoxymethyl)bicyclo[5.3.1]undec-7-ene (36). A suspension of 1*β*-H-10*β*-(hydroxymethyl)bicyclo[5.3.1]-undec-7-ene (266.9 mg, 1.48 mmol) and NaH (85.4 mg, 1.78 mmol) in THF (10 mL) was heated to reflux for 1 h when it was cooled to rt. Methyl iodide (138 mL, 2.22 mmol) was added and the solution stirred at rt for 20 h at which time it was added to water (25 mL), brine (5 mL), and ether (10 mL). The layers were shaken and separated, and the aqueous layer was further extracted with ether. The combined ether layers were dried, concentrated, and chromatographed on silica gel eluted with 2% ether in petroleum ether to yield the methyl ether (244.3 mg, 1.26 mmol, 85%). ^1H NMR (300 MHz, $CDCl_3$) δ 5.56 (m, 1H), 3.34 (s, 3H), 3.31 (dd, J = 6.9, 9.0 Hz, 1H), 3.23 (dd, J = 6.8, 9.1 Hz, 1H), 2.27−2.20 (m, 1H), 2.13−2.08 (m, 3H), 1.85−1.78 (m, 3H), 1.64−1.52 (m, 6H), 1.39−1.27 (m, 3H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 140.9, 121.7, 77.6, 59.0, 38.7, 36.1, 35.9, 35.4, 30.1, 29.3, 28.7, 26.9, 25.5. IR (neat) 1446 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{22}O$ (M^+) 194.1669, observed 194.1679.

***cis*-3-(2-Formylethyl)-4-(*tert*-butyldimethylsiloxy)-cycloheptan-1-one (37).** Ozone was bubbled through a solution of the TBS ether **32** (258 mg, 0.97 mmol) in CH_2Cl_2 (30 mL) and MeOH (10 mL) at −78 °C until the characteristic blue color appears. The reaction was then purged of ozone with oxygen, and triphenylphosphine (382 mg, 1.5 mmol) was added. The reaction was allowed to warm to rt and was stirred for 1.5 h. The solvent was then removed *in vacuo*, and the residue was radially chromatographed (40% ether:petroleum ether; SiO_2) to give the keto aldehyde (258 mg, 89%). FTIR (NaCl) 2931, 1724, 1700, 1057, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.76 (s, 1H), 3.98 (d, J = 5.5 Hz, 1H), 2.87 (dd, J = 10.6, 14.7 Hz, 1H), 2.45 (m, 4H), 2.10 (dd, J = 2.2, 15.0 Hz, 1H), 1.97 (m, 2H), 1.75 (m, 2H), 1.52 (m, 3H), 0.89 (s, 9H), 0.05 (two s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 213.6, 201.7, 72.2, 43.6, 42.7, 41.6, 40.6, 36.8, 26.0, 25.8, 18.1, 17.3, −4.2, −5.0; HRMS (CI) calcd for $C_{16}H_{31}O_3Si$ (MH^+) 299.2041, observed 299.2039.

A similar procedure starting with silyl ether **33** gave ***cis*-3-(3-oxobutyl)-4-(*tert*-butyldimethylsiloxy)cycloheptan-1-one (38)** in 84% yield. FTIR (NaCl) 2931, 1705, 1053, 837 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.93 (d, J = 5.3 Hz, 1H), 2.39 (m, 1H), 2.8 (m, 4H), 2.09 (s, 3H), 2.06 (m, 1H), 2.01 (m, 2H), 1.66 (m, 2H), 1.47 (m, 3H), 0.85 (s, 9H), 0.01 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 219.2, 213.3, 72.1, 42.2, 41.2, 39.6, 39.0, 35.2, 28.0, 25.8, 23.6, 15.6, 14.8, −7.5, −8.3; HRMS (EI) calcd for $C_{17}H_{32}O_3Si$ (M^+) 312.2119, observed 312.2104.

7*β*-H-6α-(*tert*-Butyldimethylsiloxy)bicyclo[5.3.0]dec-1(10)-en-2-one (39). The keto aldehyde **37** (117 mg, 0.39 mmol) and PPTS (20 mg, 0.08 mmol) were stirred in benzene (20 mL) at reflux in a Dean−Stark apparatus. After 9 h, TLC analysis showed the reaction to be complete. The mixture was added to water and was extracted with ether. The combined organics were dried and concentrated *in vacuo* to give the fused enone (103 mg, 94%). FTIR (NaCl) 2931, 1681, 1612, 1254, 1099, 837 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 6.79 (m, 1H), 3.97 (m, 1H), 3.04 (m, 1H), 2.53 (m, 1H), 2.44 (m, 2H), 2.33 (m, 1H), 2.17 (m, 1H), 1.98 (m, 1H), 1.82 (m, 2H), 1.64 (m, 2H), 0.81 (s, 9H), 0.01 (two s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 200.4, 143.6, 143.3, 73.0, 50.4, 44.9, 37.9, 31.8, 29.5, 25.7, 18.2, 18.0, −4.2, −5.3; HRMS (CI) calcd for $C_{16}H_{29}O_2Si$ (MH^+) 281.1935, observed 281.1927.

7*β*-H-6α-(*tert*-Butyldimethylsiloxy)-10-methylbicyclo-[5.3.0]dec-1(10)-en-2-one (40). To a stirred solution of the diketone **38** (191 mg, 0.61 mmol) in MeOH (30 mL) was added KOH (840 mg, 15 mmol). The reaction was heated to 60 °C for 20 h when TLC analysis showed the reaction was complete. The mixture was cooled and poured into saturated NH_4Cl. This was extracted with ether. The combined organics were dried and concentrated *in vacuo* to give the fused enone (170 mg, 95%). FTIR (NaCl) 2931, 1670, 1612, 1254, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.94 (m, 1H), 3.1 (m, 1H), 2.45 (m, 3H), 2.3 (m, 1H), 2.06 (d, J = 1.1 Hz, 3H), 2.05−1.8 (m, 3H), 1.64 (m, 3H), 0.81 (s, 9H), 0.01 (two s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 202.2, 157.2, 134.2, 73.6, 52.3, 45.8, 39.4, 38.0, 28.1, 25.6, 18.4, 17.9, 16.8, −4.1, −5.3; HRMS (EI) calcd for

$C_{17}H_{30}O_2Si$ (M^+) 294.2014, observed 294.2016. Anal. Calcd for $C_{17}H_{30}O_2Si$: C, 69.33; H, 10.27. Observed: C, 69.31; H, 10.26.

4α-Methoxy-3α-(2-formylethyl)cyclooctan-1-one (41). A solution of the methyl ether **34** (22.4 mg, 0.124 mmol) in methanol (2.5 mL) was cooled to −78 °C with a dry ice−acetone bath. A stream of ozone gas in oxygen was bubbled through the solution until it turned a light blue color. Nitrogen gas was then bubbled through the solution for 5 min after which time triphenylphosphine (65 mg, 0.248 mmol) was added. The cold bath was removed and the solution allowed to warm to rt. The solution was concentrated *in vacuo*, and the resulting oil was chromatographed on silica gel eluted with 3:1 ether: petroleum ether to yield the keto-aldehyde (19.2 mg, 0.0992 mmol, 80% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.79 (t, J = 1.5 Hz, 1H), 3.27 (s, 3H), 3.22−3.25 (m, 1H), 2.51−2.63 (m, 4H), 2.26−2.32 (m, 2H), 2.12 (dd, J = 14.3, 3.0 Hz, 1H), 1.71−1.91 (m, 6H), 1.29−1.32 (m, 2H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 216.3, 202.5, 81.6, 57.2, 42.9, 42.1, 41.9, 39.1, 28.3, 28.0, 24.2, 23.3. IR (neat) 2940, 1720, 1700, 1470 cm^{-1}. HRMS (EI) calcd for $C_{12}H_{20}O_3$ (M^+) 212.1411, observed 212.1434.

4α-(*tert*-Butyldimethylsiloxy)-3α-(3-oxobutyl)cyclooctan-1-one (42). A solution of the alkene **35** (98 mg, 0.33 mmol) in methanol (10 mL) and CH_2Cl_2 (5 mL) was cooled to −78 °C when ozone was bubbled through the solution until the characteristic blue color appeared. Triphenylphosphine (130 mg, 0.50 mmol, 1.5 equiv) was then added and the cold bath removed. After 2 h at rt, the solvent was removed *in vacuo* and petroleum ether (20 mL) added. The suspension was filtered and the petroleum ether removed *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 2:3 ether:petroleum ether to recover the diketone (96.7 mg, 0.296 mmol, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.77 (m, 1H), 2.65 (dd, J = 15.1, 11.4 Hz, 1H), 2.5 (m, 1H), 2.50 (dt, J = 2.5, 7.3 Hz, 2H), 2.25 (m, 2H), 2.17 (s, 3H), 2.00 (dd, J = 15.1, 2.5 Hz, 1H), 1.9−1.5 (m, 6H), 1.25 (m, 2H), 0.88 (s, 9H), 0.030 (s, 6H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 216.9, 208.6, 73.6, 42.9, 41.5, 41.4, 39.4, 33.7, 30.1, 28.7, 27.1, 26.0, 22.8, 18.2, −3.8, −4.7. IR (FTIR, neat) 2930, 1700 cm^{-1}. HRMS (CI) calcd for $C_{18}H_{35}O_3Si$ (MH^+) 327.2346, observed 327.2365.

8β-H-7α-Methoxybicyclo[6.3.0]undec-1(11)-en-2-one (43). The keto aldehyde **41** (47.3 mg, 0.223 mmol) was taken up in 0.4 M KOH in methanol (5 mL) and the solution heated to 40 °C. After 7 h the solution was added to water and extracted with ether. The organic layers were combined, dried, and concentrated *in vacuo*. The resulting oil was chromatographed on silica gel eluted with 1:3 ether:petroleum ether to yield the bicyclic enone (27.7 mg, 0.143 mmol, 64% yield). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (t, J = 2.6 Hz, 1H), 3.45 (dt, J = 2.5, 7.6 Hz, 1H), 3.29 (s, 3H), 3.17−3.28 (m, 1H), 2.81 (dt, J = 5.3, 11.9 Hz, 1H), 2.54−2.56 (m, 1H), 2.20−2.37 (m, 3H), 1.60−2.05 (m, 6H), 1.42−1.42 (m, 1H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 202.6, 145.6, 143.7, 83.8, 57.2, 49.4, 39.3, 32.8, 31.5, 28.6, 28.3, 18.6. IR (FTIR, neat) 2930, 1670, 1600 cm^{-1}. HRMS calcd for $C_{12}H_{18}O_2$ (M^+) 194.1306, observed 194.1302.

8β-H-7α-(*tert*-Butyldimethylsiloxy)-11-methylbicyclo-[6.3.0]undec-1(11)-en-2-one (44). A solution of the diketone **42** (38.9 mg, 0.13 mmol) in 0.49 M KOH in methanol (11 mL) was warmed to 60 °C for 28 h when it was added to saturated NH_4Cl and extracted with ether. The combined ether layers were dried, reduced to an oil *in vacuo*, and chromatographed on silica gel eluted with 1:9 ether:petroleum ether to recover the cyclized five−eight fused ring system (27.6 mg, 0.090 mmol, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (dt, J = 3.0, 8.8 Hz, 1H), 3.30 (d, J = 9.8 Hz, 1H), 2.75 (dt, J = 5.41, 11.5 Hz, 1H), 2.68 (p, J = 8.8 Hz, 1H), 2.3−2.2 (m, 2H), 2.09 (s, 3H), 1.8−1.65 (m, 6H), 1.45 (m, 1H), 1.3 (m, 1H), 0.83 (s, 9H), 0.43 (s, 3H), 0.12 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 204.7, 158.2, 134.2, 76.3, 51.0, 41.3, 40.5, 34.8, 29.5, 28.5, 26.0, 20.5, 18.1, 17.1, −3.96, −4.68. IR (FTIR, neat) 2933, 1672 cm^{-1}. HRMS (EI) calcd for $C_{18}H_{32}O_2Si$ (M^+) 308.2163, observed 308.2162.

3α-[1β-(Methoxymethyl)-2-formylethyl]cyclooctan-1-one (45). A solution of the bridgehead alkene **36** (185.4 mg, 0.955 mmol) in methanol (10 mL) at −78 °C was treated with a stream of ozone in oxygen until the characteristic blue color appeared. The cold bath was then removed and triphenylphosphine (376 mg, 1.43 mmol) added. The suspension was stirred for 2 h when the methanol was removed *in vacuo* and the resulting oil chromatographed on silica gel eluted with 3:2 ether:petroleum ether to yield the keto-aldehyde (173.1 mg, 0.763 mmol, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.72 (t, J = 1.9 Hz, 1H), 3.41 (dd, J = 5.3, 9.4 Hz, 1H), 3.28 (s, 3H), 3.25 (dd, J = 7.0, 9.4 Hz, 1H), 2.50−2.15 (m, 8H), 1.88−1.82 (m, 2H), 1.65−1.60 (m, 2H), 1.47−1.28 (m, 4H). ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 216.7, 201.9, 74.2, 59.0, 44.5, 44.2, 42.9, 39.4, 39.1, 30.9, 27.5, 24.9, 24.1. IR (FTIR, neat) 1722, 1699 cm^{-1}. HRMS (CI) calcd for $C_{13}H_{23}O_3$ (MH^+) 227.1645, observed 227.1649.

8β-H-9β-(Methoxymethyl)bicyclo[6.3.0]undec-1(11)-en-2-one (46). A solution of the keto aldehyde **45** (104.5 mg, 0.462 mmol) in benzene (15 mL) was charged with PPTS (23.2 mg, 0.0925 mmol, 0.2 equiv). The solution was heated to reflux and a Dean−Stark trap used to remove the water. After two days, the solution was added to water and extracted with ether. The combined organic layers were dried and reduced to an oil *in vacuo*. The resulting oil was radially chromatographed on silica gel eluted with 1:3 ether:petroleum ether to recover the cyclic enone (59.8 mg, 0.288 mmol, 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.62 (t, J = 2.4 Hz, 1H), 3.34 (s, 3H), 3.28 (dd, J = 7.8, 9.1 Hz, 1H), 3.23 (dd, J = 7.2, 9.1 Hz, 1H), 2.90 (br d, J = 2 Hz, 1H), 2.82 (m, 1H), 2.63 (ddt, J = 19.3, 8.0, 2.4 Hz, 1H), 2.24−2.31 (m, 2H), 2.14 (dt, J = 19.2, 2.8 Hz, 1H), 1.88−1.80 (m, 1H), 1.79−1.75 (m, 2H), 1.68−1.63 (m, 1H), 1.58−1.50 (m, 2H), 1.47−1.37 (m, 2H). ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 203.4, 147.2, 139.8, 75.7, 58.7, 47.2, 46.5, 39.4, 37.1, 34.1, 28.5, 25.7, 25.7. IR (FT, neat) 1675, 1602 cm^{-1}. HRMS (EI) calcd for $C_{13}H_{20}O_2$ (M^+) 208.1462, observed 208.1475.

7β-H-6α-Hydroxy-10-methylbicyclo[5.3.0]dec-1(10)-en-2-one. To a stirred solution of the TBS ether **40** (54 mg, 0.18 mmol) in acetonitrile (25 mL) was added HF (49%, 0.5 mL). After 2 h, the reaction was quenched with saturated $NaHCO_3$. This mixture was extracted with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. Radial chromatography (20% to 50% ethyl acetate:hexanes; SiO_2) gave the alcohol (33 mg, 100%). FTIR (NaCl) 3371, 2924, 1658, 1597 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.96 (m, 1H), 3.21 (m, 1H), 2.54 (m, 1H), 2.47 (m, 2H), 2.37 (m, 1H), 2.12 (s, 3H), 2.08 (m, 2H), 1.79 (m, 1H), 1.70 (m, 4H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 202.0, 160.6, 132.5, 72.8, 51.5, 45.6, 39.5, 37.3, 27.7, 18.1, 17.1; HRMS (EI) calcd for $C_{11}H_{16}O_2$ (M^+) 180.1149, observed 180.1146. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.947. Observed: C, 72.90; H, 9.00.

7β-H-10-Methylbicyclo[5.3.0]dec-1(10)-ene-2,6-dione (47). To a solution of the alcohol (33 mg, 0.18 mmol) in CH_2Cl_2 (10 mL) was added Dess−Martin periodinane (109 mg, 0.26 mmol). When TLC showed the reaction to be complete, the mixture was diluted with ether and was poured into 1 N NaOH. The organics were further washed with water and brine and were then dried and concentrated *in vacuo* to give the fused diketone (23 mg, 72%). FTIR (NaCl) 2924, 1709, 1674, 1608 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.98 (m, 1H), 2.82 (ddd, J = 3.7, 11.8, 17.7 Hz, 1H), 2.59 (m, 1H), 2.34 (ddd, J = 4.4, 8.8, 17.7 Hz, 2H), 2.10 (d, J = 1.5 Hz, 1H), 2.09 (m, 3H), 1.89 (m, 2H), 1.79 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 209.8, 199.3, 160.5, 130.8, 58.0, 43.7, 43.6, 39.4, 23.6, 20.8, 17.0; HRMS (CI) calcd for $C_{11}H_{15}O_2$ (MH^+) 179.1071, observed 179.1065.

1β-H-2α-Hydroxy-2, 7-dimethylbicyclo[4.3.1]dec-6-ene (50). To a stirred solution of the ketone (461 mg, 2.81 mmol) in THF (20 mL) at −78 °C was added MeLi (4 mL of a 1.4 M solution in ether, 5.62 mmol). After 30 min, the reaction was warmed to rt and was quenched with saturated NH_4Cl. The mixture was extracted twice with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. GC analysis of the crude reaction mixture showed only one diastereomer. Radial chromatography (10% ethyl acetate:hexanes; SiO_2) gave the tertiary alcohol (460 mg, 2.56 mmol, 91%). FTIR (NaCl) 3390, 2927, 1454, 1373, 1107 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) 2.38 (m, 1H), 2.04 (m, 3H), 1.87 (m, 3H), 1.71 (s, 3H), 1.68 (m, 2H), 1.54 (m, 1H), 1.33 (m, 1H), 1.27 (s, 3H), 1.23 (m, 1H), 1.12 (m, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 132.6, 130.9,

76.4, 42.3, 36.1, 30.3, 29.3, 28.7, 28.5, 23.6, 20.9, 18.0; HRMS (CI) calcd for $C_{12}H_{20}O$ (M^+) 180.1513, observed 180.1516.

1β-H-2α-(*tert*-Butyldimethylsiloxy)-2,7-dimethylbicyclo-[4.3.1]dec-6-ene (51). To a stirred solution of the alcohol (520 mg, 2.88 mmol) in CH_2Cl_2 (20 mL) and pyridine (0.7 mL, 8.7 mmol) at 0 °C was added *tert*-butyldimethylsilyl triflate (1 mL, 4.33 mmol). The reaction was allowed to warm to rt. When the reaction was complete by TLC, the mixture was diluted with hexanes and was poured into saturated $NaHCO_3$. Following trituration, the organics were separated and were further washed once with brine. The organics were dried and concentrated *in vacuo*. Radial chromatography (hexanes; SiO_2) gave the silyl ether (780 mg, 2.65 mmol, 92%). FTIR (NaCl) 2931, 1122, 833 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.36 (m, 1H), 2.06−1.92 (m, 3H), 1.87 (m, 1H), 1.78 (m, 2H), 1.72 (s, 3H), 1.7−1.5 (m, 3H), 1.35 (m, 1H), 1.30 (s, 3H), 1.26 (m, 1H), 1.15 (m, 1H), 0.83 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 132.7, 131.0, 79.5, 43.7, 36.7, 30.6, 29.1, 28.7, 28.3, 25.9, 24.6, 21.1, 18.3, 18.0, −1.7, −2.0; HRMS (CI) calcd for $C_{18}H_{34}OSi$ (M^+) 294.2337, observed 294.2377.

***cis*-3-(3-Oxobutyl)-4-(*tert*-Butyldimethylsiloxy)-4-methylcycloheptan-1-one (52).** Ozone was bubbled through a solution of the TBS ether **51** (400 mg, 1.37 mmol) in MeOH (25 mL) at −78 °C until the characteristic blue color appeared. The reaction was then purged of ozone with oxygen and trimethyl phosphite (0.3 mL, 2.5 mmol) was added. The reaction was allowed to warm to rt and was stirred for 1.5 h. The mixture was poured into saturated ammonium chloride and was extracted thrice with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. The residue was radially chromatographed (10 to 20% ethyl acetate:hexanes; SiO_2) to give the diketone (300 mg, 0.92 mmol, 67%). FTIR (NaCl) 2935, 1705, 1254 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.97 (dd, J = 10.3, 13.6 Hz, 1H), 2.56 (ddd, J = 5.1, 8.8, 17.6 Hz, 1H), 2.46−2.28 (m, 3H), 2.11 (s, 3H), 2.09−1.90 (m, 4H), 1.55 (m, 1H), 1.45 (m, 1H), 1.33 (s, 3H), 1.3 (m, 2H), 0.89 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 215.1, 209.1, 76.9, 47.0, 44.3, 43.9, 43.3, 42.0, 30.8, 29.9, 26.7, 25.1, 19.2, 18.5, −1.1, −1.5; HRMS (CI) calcd for $C_{18}H_{35}O_3Si$ (MH^+) 327.2355, observed 327.2360.

7β-H-6α-(*tert*-Butyldimethylsiloxy)-6,10-dimethylbicyclo[5.3.0]dec-1(10)-en-2-one (53). To a stirred solution of the diketone **52** (48 mg, 0.147 mmol) in MeOH (15 mL) was added KOH (390 mg, 7 mmol). The reaction was heated to 60 °C for 3 h when TLC analysis showed the reaction was complete. The mixture was cooled and poured into saturated NH_4Cl. This was extracted with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo* to give the fused enone (45 mg, 0.146 mmol, 99%). FTIR (NaCl) 2931, 1678, 1616 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.91 (m, 1H), 2.42 (m, 2H), 2.35 (m, 1H), 2.27 (m, 1H), 2.01 (s, 3H), 1.88 (m, 2H), 1.77 (m, 2H), 1.60 (m, 2H), 1.23 (s, 3H), 0.76 (s, 9H), 0.02 (two s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 202.1, 155.5, 136.8, 75.9, 56.7, 45.3, 45.1, 38.3, 29.4, 25.7, 24.9, 19.8, 18.4, 17.0, −1.95, −2.35; HRMS (CI) calcd for $C_{18}H_{32}O_2Si$ (M^+) 308.2170, observed 308.2165.

1β-H-7β-H-6α-(*tert*-Butyldimethylsiloxy)-6β,10α-dimethyl bicyclo[5.3.0]decan-2-one (54). The enone **53** (74 mg, 0.227 mmol) and Pd−C (10%, 40 mg) in EtOH (10 mL) were treated with hydrogen (25 psi) and shaken in a Parr apparatus. After 4.5 h, the reaction mixture was filtered through Celite and concentrated *in vacuo* to give one diastereomer of saturated ketone (65.8 mg, 0.212 mmol, 94%). FTIR (NaCl) 2927, 1693, 1461, 1254, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.65 (dd, J = 7.7, 8.1 Hz, 1H), 2.37 (m, 2H), 2.26 (m, 2H), 2.0 (m, 4H), 1.82 (m, 1H), 1.64 (dt, J = 4.0, 18.0 Hz, 1H), 1.45 (m, 2H), 1.18 (s, 3H), 0.91 (d, J = 7.0 Hz, 3H), 0.83 (s, 9H), 0.05 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 214.8, 77.7, 58.9, 53.5, 45.1, 39.5, 38.6, 32.5, 27.9, 25.8, 25.5, 22.4, 18.1, 16.5, −1.89, −1.98; HRMS (CI) calcd for $C_{18}H_{34}O_2Si$ (M^+) 310.2326, observed 310.2327.

1β-H-7β-H-6α-(*tert*-Butyldimethylsiloxy)-6β,10α-dimethylbicyclo[5.3.0]dec-2-ene (55). To a stirred solution of diisopropylamine (0.16 mL, 1.18 mmol) in THF (1.5 mL) at −30 °C was added n-BuLi (0.36 mL of a 2.0 M solution, 0.71 mmol). To this was added the ketone **54** (73.4 mg, 0.237 mmol) as a solution in tetramethylethylenediamine (0.4 mL). After 10 min, the cold bath was removed and diethyl chlorophosphonate (0.17 mL, 1.18 mmol) was added. After 1 h, the reaction mixture was poured into ice-water and was extracted with CH_2Cl_2. The combined organics were washed with brine and then were dried and concentrated *in vacuo*. The oil obtained was dissolved in t-BuOH (0.07 mL) and THF (5 mL) and was added to a solution of lithium (excess) in liquid ammonia. After 1 h, the reaction was carefully quenched with NH_4Cl. This was extracted thrice with CH_2Cl_2. The combined organics were dried and concentrated *in vacuo*. Radial chromatography (hex; SiO_2) gave the alkene (31.3 mg, 0.106 mmol, 45%). FTIR (NaCl) 2954, 1466, 1254, 1115 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.65 (m, 1H), 5.40 (d, J = 12.1 Hz, 1H), 2.32 (m, 1H), 2.2−1.95 (m, 4H), 1.68 (m, 3H), 1.54 (m, 1H), 1.36 (s, 3H), 1.25 (m, 1H), 1.13 (m, 1H), 1.01 (d, J = 7.0 hz, 3H), 0.84 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 130.0, 128.0, 77.3, 56.5, 49.3, 44.0, 39.8, 36.3, 30.3, 28.5, 25.9, 24.9, 23.8, 18.2, 16.2, −1.81, −1.92; HRMS (CI) calcd for $C_{18}H_{35}OSi$ (MH^+) 295.2457, observed 295.2449.

***O*-(*tert*-Butyldimethylsilyl)ledol (56)**. To a solution of the alkene (34.7 mg, 0.118 mmol) in benzene (3 mL) was added $PhHgCBr_3$ (187 mg, 0.354 mmol). The reaction was heated to reflux. After 2 h, TLC showed the reaction to be incomplete, and more $PhHgCBr_3$ (62 mg, 0.117 mmol) was added. Thirty minutes later, the reaction was complete and was cooled to rt. The mixture was filtered through Celite and the filter pad was rinsed with hexanes. The filtrate was concentrated *in vacuo*, and the residue was added as a solution in THF (2 mL) to a mixture of CuCN (211 mg, 2.36 mmol) and MeLi (3.94 mL of a 1.2 M solution, 4.73 mmol) in THF (1 mL) at −78 °C. After 18 h, MeI (0.3 mL) was added, and the mixture was poured into saturated $NaHCO_3$. This was extracted thrice with CH_2Cl_2. The combined organics were dried and concentrated. Radial chromatography (hexanes; SiO_2) gave the dimethylcyclopropane compound (27.5 mg, 0.82 mmol, 69%). FTIR (NaCl) 2927, 1466, 1373, 1254, 1122, 1076, 1038, 1007 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.99 (m, 1H), 1.91 (m, 1H), 1.84 (m, 1H), 1.8−1.7 (m, 4H), 1.55 (m, 1H), 1.48 (m, 1H), 1.26 (m, 1H), 1.23 (s, 3H), 1.02 (s, 3H), 0.916 (d, J = 6.8 Hz, 3H), 0.914 (s, 3H), 0.85 (s overlapping a d, J = 6.8 Hz, 10H), 0.62 (m, 1H), 0.18 (appwerent t, J = 9.5 Hz, 1H), 0.06 (s, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 77.8, 58.0, 40.2, 38.95, 38.85, 31.1, 29.4, 28.6, 27.3, 26.0, 24.9, 22.8, 20.3, 18.4, 17.6, 16.4, 16.1, −1.65, −1.7; HRMS (EI) calcd for $C_{21}H_{40}OSi$ (M^+) 336.2846, observed 336.2857.

Ledol. The silyl ether **56** (4.5 mg, 0.013 mmol) was treated with tetrabutylammonium fluoride (0.5 mL of a 1 M solution in THF). The reaction was heated to reflux. Eight hours later, the mixture was added to water and this was extracted thrice with ether. The combined organics were dried and concentrated. Radial chromatography (15% ethyl acetate:hexanes; SiO_2) gave ledol (1.7 mg, 0.0077 mmol, 59%). FTIR (NaCl) 3336, 2935, 1462, 1377, 1111 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.25 (br s, 1H), 2.08 (m, 1H), 1.98 (m, 1H), 1.9−1.75 (m, 4H), 1.72−1.67 (m, 3H), 1.32−1.19 (m, 2H), 1.14 (s, 3H), 1.04 (s, 3H), 0.98 (s, 3H), 0.93 (d, J = 7.2 Hz, 3H), 0.72 (ddd, J = 6.0, 9.2, 11.5 Hz, 1H), 0.33 (dd, J = 9.5, 9.9 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 74.6, 53.7, 40.8, 39.2, 38.4, 30.8, 30.5, 28.6, 25.0, 24.6, 23.4, 20.3, 19.2, 16.0, 15.4; HRMS (CI) calcd for $C_{15}H_{26}O$ (M^+) 222.1982, observed 222.1978.

Ledene. Method A. To a stirred solution of ledol (7.6 mg, 0.034 mmol) in pyridine (1 mL) at −20 °C was added thionyl chloride (0.05 mL, 0.68 mmol). After 5 min, the reaction was quenched with saturated $NaHCO_3$ and this was extracted thrice with CH_2Cl_2. The combined organics were dried and concentrated. Radial chromatography (hexanes; SiO_2) gave ledene (3 mg, 0.0147 mmol, 43%).

Method B. To a stirred solution of ledol (23 mg, 0.014 mmol) in THF (2 mL) at 0 °C was added KH (5 mg, 0.15 mmol). The reaction was warmed to rt briefly, and was then recooled to 0 °C, and was treated with *tert*-butyldimethylsilyl triflate (24 μL, 0.104 mmol). When the reaction did not proceed, excess KH was added. The reaction was allowed to stir overnight, and the mixture was then added to saturated

$NaHCO_3$ and was extracted thrice with CH_2Cl_2. The combined organics were dried and concentrated. Radial chromatography (gradient elution: hexanes to 10% ethyl acetate:hexanes; SiO_2) gave ledene (12.6 mg, 0.062 mmol, 59%) and recovered ledol (5.1 mg, 0.023 mmol, 22%).

Characterization for Ledene. FTIR (NaCl) 2924, 1458, 1373 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 2.57 (dd, J = 9.2, 9.5 Hz, 1H), 2.4 (m, 1H), 2.21 (m, 2H), 2.05 (m, 2H), 1.71 (m, 1H), 1.65 (m, 1H), 1.57 (s, 3H), 1.26 (m, 2H), 1.06 (s, 3H), 0.99 (s, 3H), 0.95 (d, J = 7.2 Hz, 3H), 0.67 (dd, J = 9.5, 11.1 Hz, 1H), 0.55 (ddd, J = 5.2, 9.5, 11.1 Hz, 1H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 140.0, 124.7, 40.0, 37.3, 36.6, 32.6, 31.7, 30.4, 28.4, 25.4, 22.2, 21.8, 18.6, 15.69, 15.65; HRMS (EI) calcd for $C_{15}H_{24}$ (M^+) 204.1878, observed 204.1875.

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Supporting Information Available: ^1H and ^{13}C NMR spectra for all compounds reported (108 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of this journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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