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Intramolecular Additions of Allylsilanes in Triquinane Synthesis. Studies Directed Toward the Total Synthesis of (±)-Hirsutene.§

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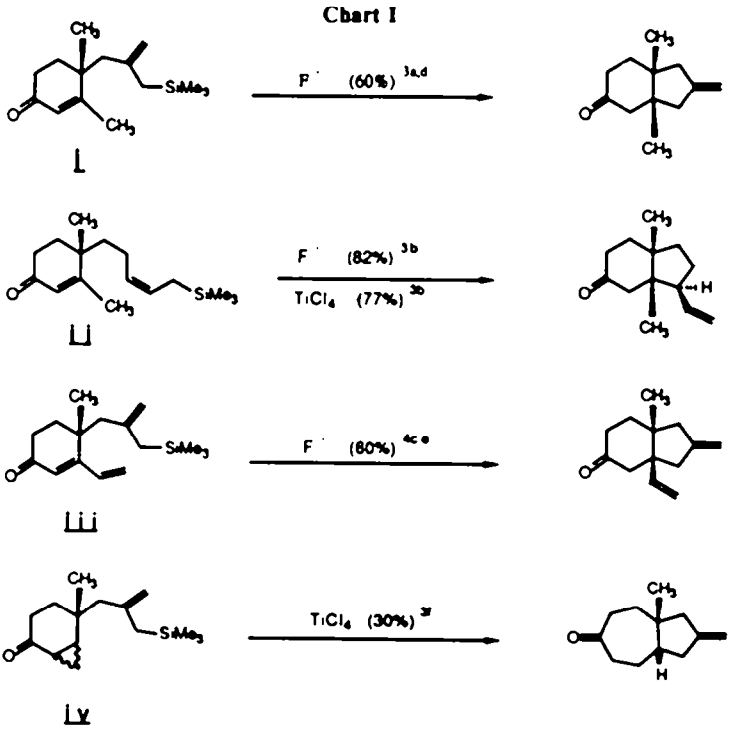
Summary: The straightforward construction of the cis, anti, cis-cyclopenta[a]pentalene skeleton characteristic of (±)-hirsutene was achieved via the intramolecular addition of two functionalized cyclopentane rings linked by a one-carbon tether.

Introduction: In light of the remarkable versatility and broad synthetic utility demonstrated to date, it is not surprising that reactions of allylsilanes are becoming an increasingly popular method for inter- and intramolecular carbon-carbon bond formation.[2] Our contributions in this active field of research have focused on the construction of polycyclic systems via intramolecular addition of allylsilanes to electrophilic olefins. Chart I illustrates four cyclizations, developed in our laboratories, which annulate a cyclopentane ring.[3] Methods for the efficient annulation of six-, seven-, and eight-membered rings have also been developed.[4]

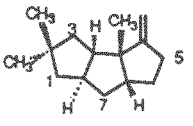
Chart I



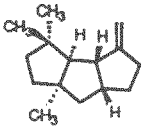
§ Dedicated to Professor R. K. Hill on the occasion of his receipt of *The Josiah Meigs Award for Excellence In Teaching*, the highest award for teaching at **The University of Georgia.**

The linearly fused triquinanes hirsutene[5a] (1) and capnellene[5b] (2) have been a proving ground for the development of new cyclopentane annulation methods.[6,7] Examination of these sesquiterepenes reveals four assymetric centers, three quaternary centers, and the cis, anti, cis-cyclopenta[a]pentalene skeleton (Fig. 1). Note that these sesquiterpenes differ only in the placement of the methyl substitutents. Despite the multitude of reported syntheses, only Mehta,[7h] Little[7b,8a,b] and Curran[8c] have developed general approaches to both these families of triquinanes. We have sought to prepare these isomeric natural products by a general route featuring organosilicon chemistry to construct their basic carbon skeleton. Here we report our studies directed towards a total synthesis of (±)-hirsutene.

Figure 1



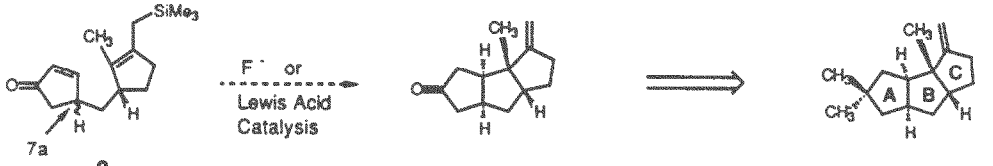
HIRSUTENE (1)



CAPNELLENE (2)

Our approach to the condensed cyclopentane rings features the construction of the central five-membered ring via an allylsilane cyclization of two functionalized cyclopentane rings linked by a one-carbon tether (Eq.1). At first glance, this strategy appears to have a stereochemical problem not found in other routes,[9] since only one of the two diastereomers of 3 can cyclize to yield a tricyclic ketone with the correct stereochemical relationships.[10]

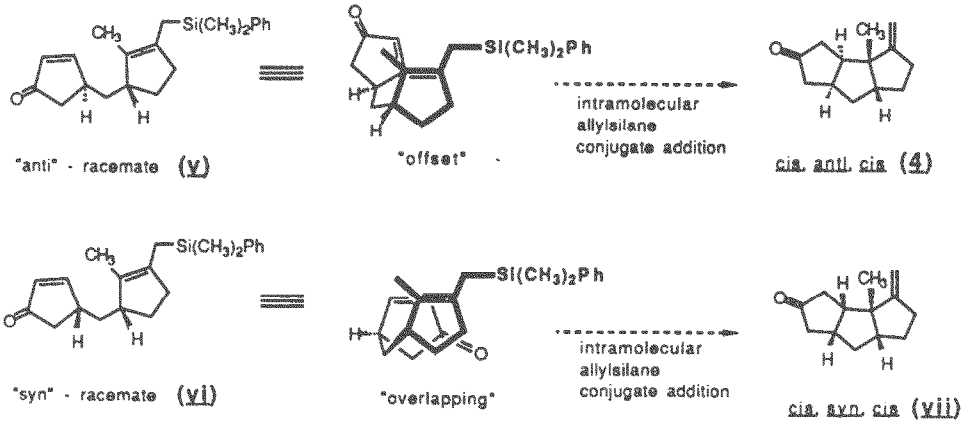
Equation 1



3 4 1

Our stereochemical prediction that only ketone 4 will be produced is based on examination of molecular models of the two racemic diastereomers involved, the "anti"-racemate (v) and the "syn"-racemate (vi) (Eq. 2). Trajectory requirements for successful Michael addition demand that in the transition state the two planar units achieve a par-

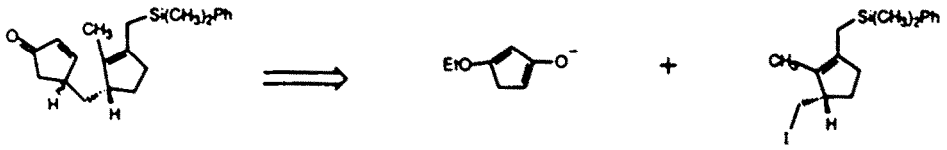
Equation 2



allel orientation.[11] When this relationship is obtained in the "syn"-racemate (vi), the two five-membered rings must eclipse one another, whereas in the "anti"-racemate v, the two rings will be offset. This suggests that the transition state for cyclization of the "anti"-isomer will be far less congested than that of the "syn"-isomer. Thus we expected the "anti"-stereoisomer to cyclize more rapidly than the "syn"-isomer. More importantly, under either fluoride ion or Lewis acid catalysis, the "syn"-racemate should equilibrate into the requisite "anti"-isomer, thus producing only tricycle 4. This possibility was intriquing, and served as the impetus for this study.

Since substrate 3 should be readily prepared using well-established alkylation methodology, our retrosynthetic analysis was simplified to the synthesis of iodide 6 (Eq. 3).

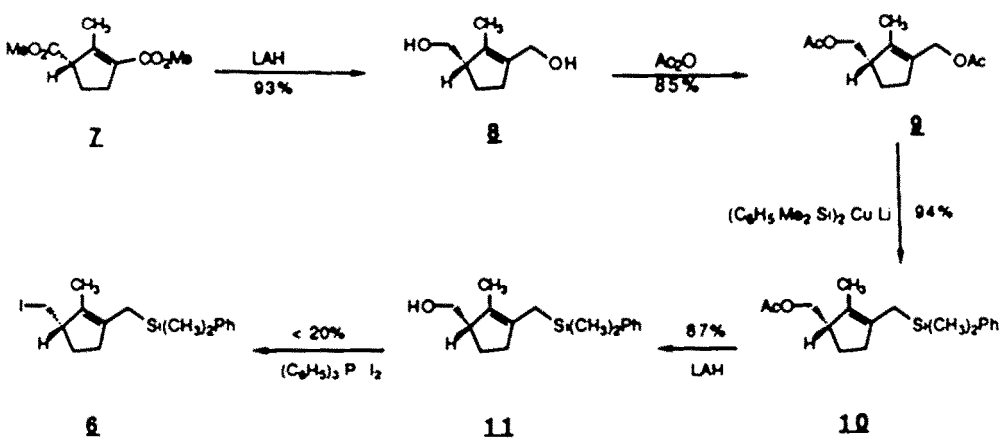
Equation 3



3 5 6

Results and Discussion: Key intermediate 3 was prepared using the route shown in Eq. 4. Our synthesis began with diester 7, prepared from commerically available cyclopropyltriphenylphosphonium bromide via Fuchs' procedure.[12] Reduction of 7, followed by acetylation, afforded diacetate 9 in 64% overall yield. This diacetate permitted us to introduce the allylsilane moiety based on Fleming and Pearce's report that allylic acetates readily undergo displacement by organosilicon cuprates to generate allylsilanes.[13] Indeed, the allylic acetate of 9 was converted into an allylsilane moiety in 94% yield. Reduction of the acetate with LAH unmasked the primary hydroxyl group in 87% yield (cf. 11). We have found that formation of non-allylic alkyl iodides in the presence of allylsilanes using Finkelstein conditions often results in desilylation.[14] The use of diiodotriphenylphosphorane[15] often avoids this problem. Thus alcohol 11 was directly converted into iodide 6 without loss of the allylsilane functionality; however, this iodide proved to be quite unstable.

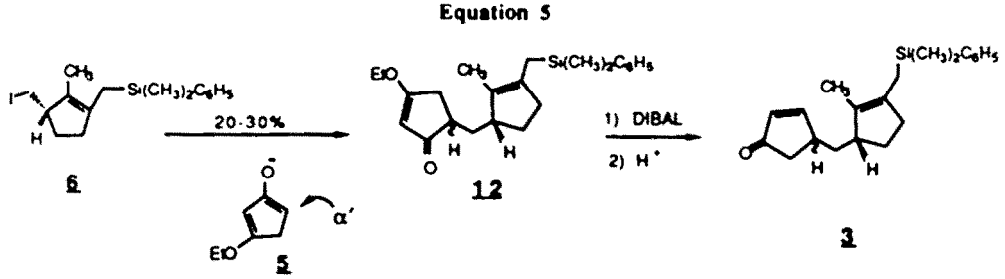
Equation 4



7 8 9 6 11 10

Alkylation of the kinetic enolate of 3-ethoxy-2-cyclopenten-1-one (5)[16] with 6 proceeded in low yield (10→20%), due to the competitive decomposition of 6 during the reaction. Considerable effort was directed toward increasing the nucleophilicity of the enolate by introducing activating groups such as phenyl selenyl, phenyl sulfinyl, or benzyl oxycarbonyl at the α'-position of 5. Nevertheless, these alkylations also occurred in low yield. DIBAL reduction of 12, followed by mild acid hydrolysis, completed a synthesis of enone 3 (Eq. 5), but the overall yield of this three-step sequence was unacceptable [<15%].

Equation 5

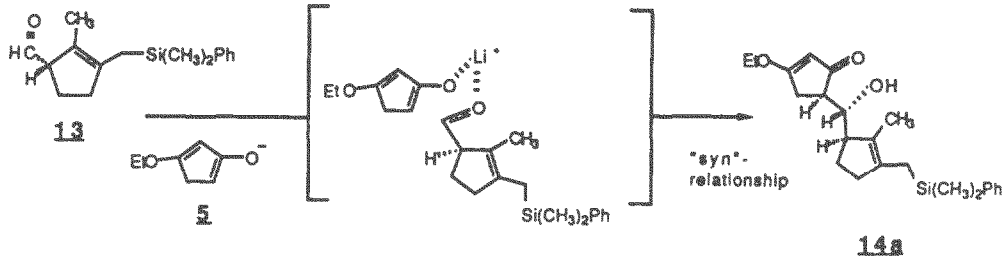


6 5 12 3

The difficulties described above led us to employ a crossed-aldol condensation rather than alkylation to efficiently link the "A" and "C" rings. Oxidation of alcohol **11** using dipyridine chromic anhydride complex[17] provided aldehyde **13** is 50% yield (Eq. 6).[18] The aldol condensation between **5** and **13** coupled the two cyclopentane rings in good yield (75%); isomeric adducts **14a**, **14b**, and **14c** were obtained in roughly 6:1:1 ratio, respectively. Since the stereochemistry of the C(6a) and C(7a) methines ultimately controls the C(3a)-C(3b) geometry, the introduction of a hydroxyl group at C(7) is of little consequence and merely requires its removal at a later stage.

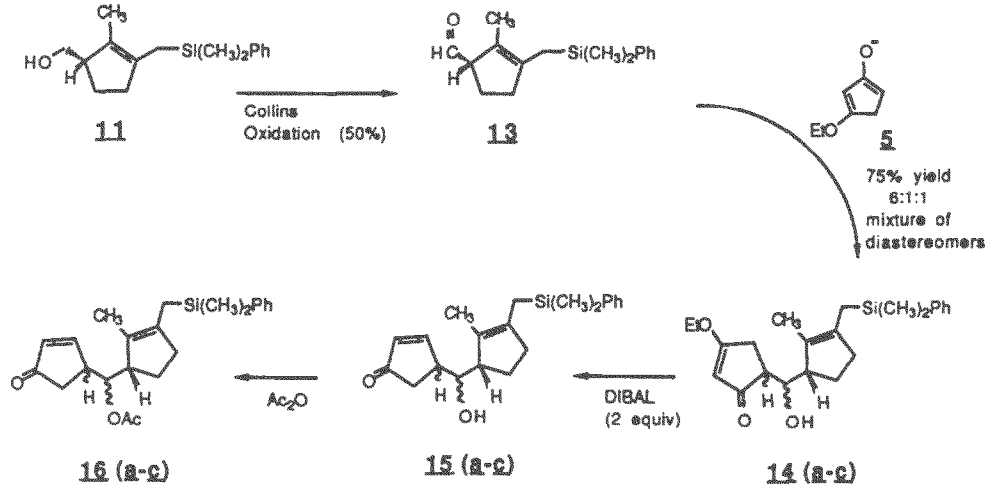
In an important series of papers, J.E. Dubois showed that enolates of cyclic ketones, which must be E for geometric reasons, give rise mainly to threo aldols.[21] Later work by Heathcock[22a] and Noyori[22b] with similar systems supports the conclusion that E-enolates give threo aldols selectively while Z-enolates furnish erythro isomers as the predominant products. Extension of these studies to our aldol coupling dictates that the major isomer (**14a**) has the wrong relationship between C(7a) and C(6a) required for a synthesis of hirsutene. This analysis accentuates the need for an equilibration prior to formation of a tricyclic adduct (Eq. 6).

Equation 6



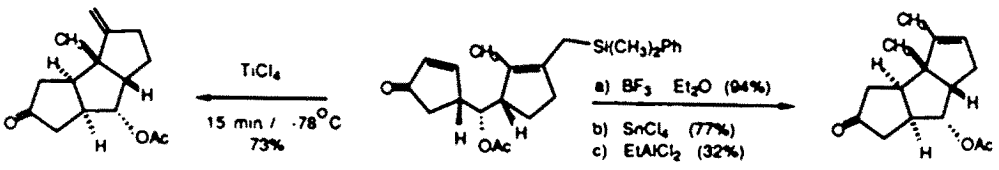
Initially, only the major isomer **14a** was studied.[23] Conversion of **14a** to **15a** was achieved using two equivalents of DIBAL, followed by mild acid hydrolysis (Eq. 7). As anticipated, use of only one equivalent of hydride ion resulted in a retro-aldol reaction. Compound **15a** was acetylated to preclude protodesilylation in the cyclization step.

Equation 7



Cyclization of **16a** using boron trifluoride etherate, tin tetrachloride, or ethylaluminum dichloride resulted in tricyclic ketone **17a** (Eq. 8). It is noteworthy that isomerization of the C(9) olefin also occurred using these catalysts. Further study showed that brief exposure of **16a** to 1.5 equivalents of titanium tetrachloride at low tem-

Equation 8

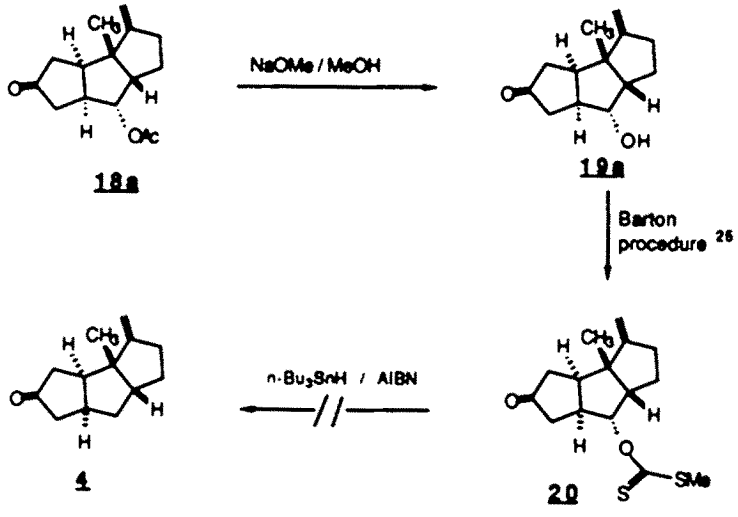


18a 16a 17a

peratures generated tricyclic ketone **18a**, which possesses the required exocyclic double bond, in 73% yield. More importantly, NMR studies suggested that **18a** has the cis, anti, cis-cyclopenta[a]pentalene skeleton as required, thus implying that the desired equilibration of diastereoisomers had indeed occurred. The use of coupling constants to assign the stereochemical relationships of triquinane ring junctions, however, is tenous. Instead, completion of our hirsutene synthesis would confirm our structural assignments.[24]

With ketone **18a** in hand, we expected that the following three transformations would proceed directly to hirsutene: (1) saponification; (2) deoxygenation of the C(7)-hydroxyl group; and (3) conversion of the C(2) carbonyl unit into a gem-dimethyl group. Alcohol **19a** was prepared by transesterification using sodium methoxide in methanol. However, attempts to selectively deoxygenate the "B" ring via tri-n-butyltin hydride reduction of xanthate **20** failed presumably due to competing enolization of the C(2) ketone (Eq. 9).[25]

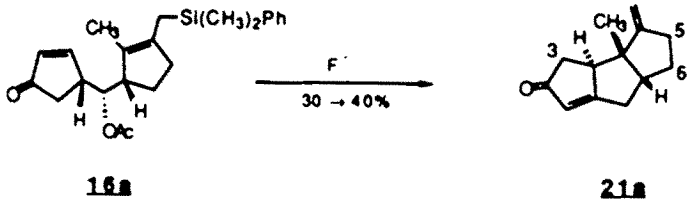
Equation 9



18a 19a 4 20

Deoxygenation of the central cyclopentane ring was fortuitously achieved during the fluoride ion-induced cyclization of **16a** which afforded enone **21a** in 30→40% yield (Eq. 10). Further study with other nonnucleophilic bases has shown that under the basic conditions employed [fluoride ion in DMF/HMPA], loss of

Equation 10

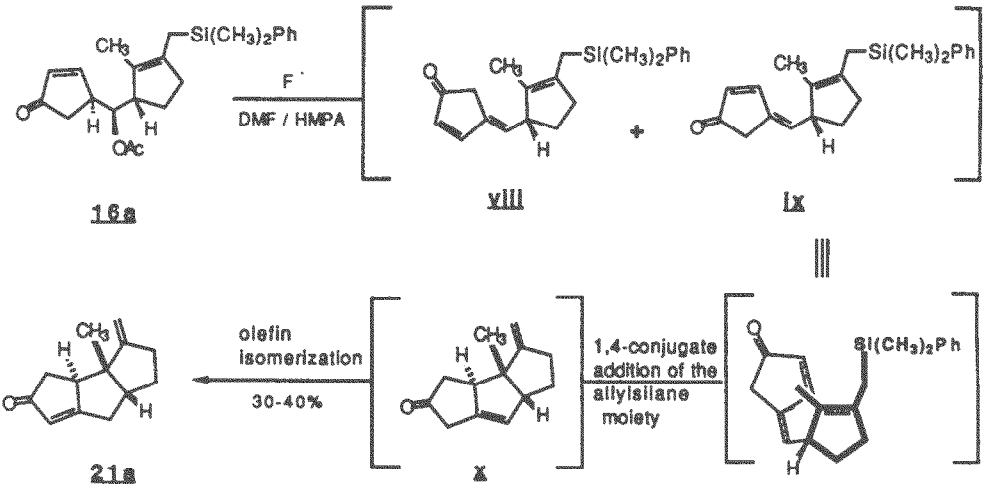


16a 21a

the acetic acid residue generates a mixture of conjugated dienones (viii and ix), only one of which can cyclize in a 1,4-fashion due to geometric constraints; olefin isomerization of x results in the isolation of enone **21a** (Eq. 11). The stereochemistry indicated for C(3a), C(3b), and C(6a) is based upon analysis of the disposition of the two

reactive centers of dienone ix prior to bond formation. Since enone 21a has most of the salient features of hirsutene, it became a key intermediate in our synthesis.

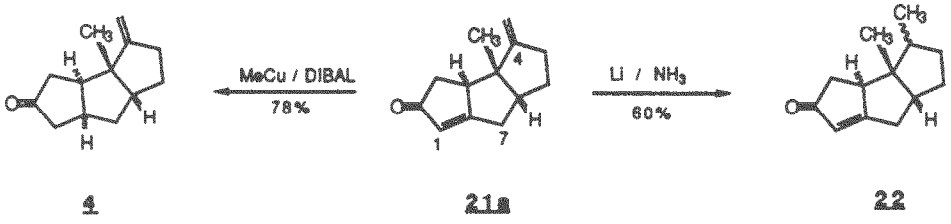
Equation 11



Although dissolving metal reduction of the C(1)-C(7a) double bond of 21a would furnish ketone 4, terminal olefinic bonds can also be reduced by metal-ammonia reagents in the presence of a proton source.[26] We hoped that the enone moiety of 21a would reduce faster than the exocyclic double bond. However, experimentation showed that treatment of 21a with lithium in ammonia and tert-butanol reduced only the exocyclic olefin (cf. 22).

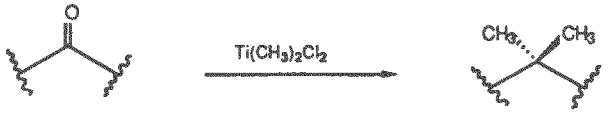
Enone 21a was converted to ketone 4 in 90% yield via the 1,4-addition of hydride ion using Tsuda and Saegusa's procedure.[27] Although this 1,4-reduction was also achieved using hydrosilane-rhodium (I) complex,[28] the isolation of 4 was severely plagued by silicon-containing byproducts.

Equation 12



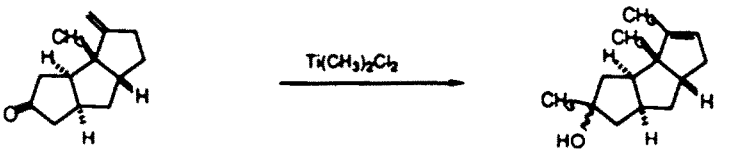
We felt that the conversion of ketone 4 to hirsutene could be achieved in a single step. For example, Reetz and co-workers have reported that simple ketones can be converted into gem-dimethyl groups in high yield using dimethyltitanium dichloride under mild conditions.[29] However, brief treatment of less than one equivalent of this reagent to 4 resulted in alcohol 23 (Eq. 14).[30] Although the formation of a tertiary alcohol is a normal re-

Equation 13



action intermediate, the isomerization of the exocyclic olefin under the reaction conditions mandated that this method be abandoned.[31]

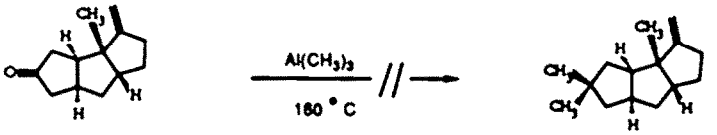
Equation 14



4 23

Alternative one-pot methods were also examined. For example, Meister and Mole have reported that simple tertiary alcohols, ketones, and carboxylic acids are exhaustively methylated by reaction with excess trimethylaluminum at elevated temperatures.[32] However, heating ketone 4 with trimethylaluminum failed to provide hirsutene (Eq. 15).

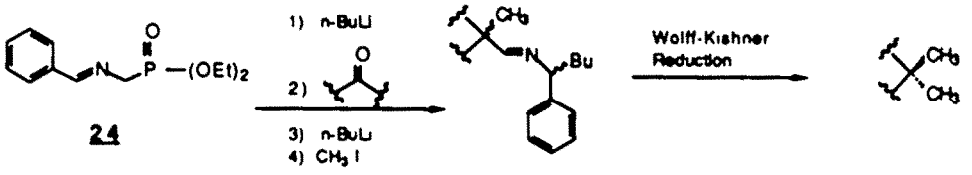
Equation 15



4 1

A three-step procedure introduced by Martin and co-workers to generate quaternary carbon atoms with two substitutents of differing functionalitiy was also investigated.[33] In this method a ketone is homologated to an α-alkylated aldehyde and methylated via the *in situ* generation of a metalloenamine (Eq. 16). Subsequent Wolff-Kishner reduction of the imine intermediate (xi) would complete our hirsutene synthesis.

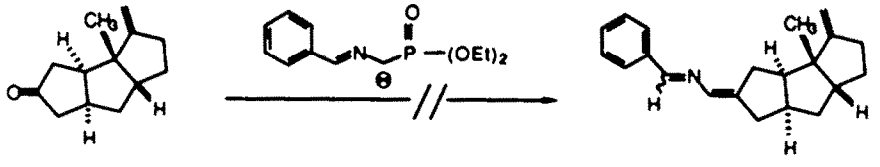
Equation 16



24 xi

Although simple ketones were converted to geminal dimethyl groups in 60% overall yield via the above sequence, the condensation of the ylide of 24[34] with 4 failed (Eq. 17).

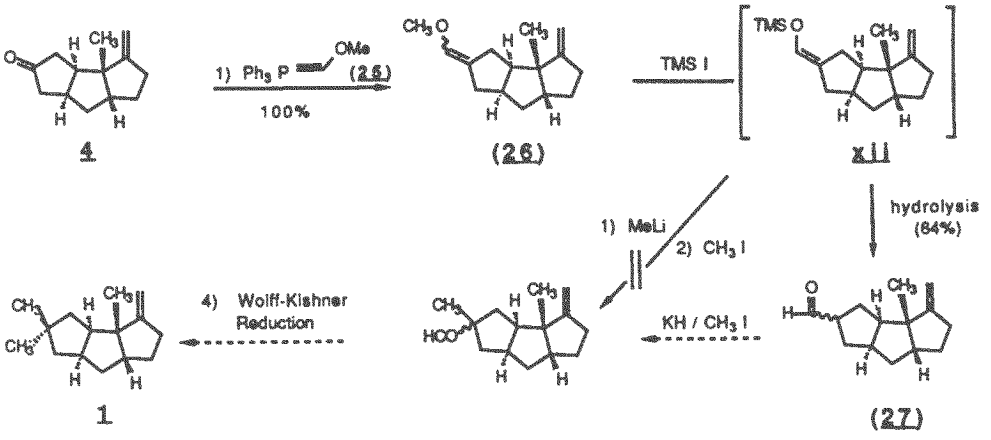
Equation 17



4

We have recently turned to more classical procedures to achieve the transformation of 4 into hirsutene (Eq. 18).

Equation 18



Wittig olefination of 4 using (methoxymethylene)triphenylphosphorane (25) afforded enol ether 26 in nearly quantitative yield. Others have noted that hydrolysis of analogous methyl enol ethers proceed slowly using mild protic acids.[35] The tendency for the exocyclic olefin to isomerize upon exposure to acids prompted us to use iodotrimethylsilane[36] to achieve demethylation. We envisioned a one-pot procedure whereby the silyl enol ether (xii) generated *in situ* could be alkylated directly. Although reaction of 26 with TMSI furnished aldehyde 27 in 64% yield within minutes, the intermediate silyl enol ether could not be isolated or alkylated.

Aldehyde 27 is our most advance intermediate. We are optimistic that the alkylation of the enolate derived from aldehyde 27,[37] followed by Wolff-Kishner reduction, will soon provide (±)-hirustene. Although incomplete, this study demonstrates the usefulness of intramolecular allylsilane additions to assemble polycyclic systems as well as some of the limitations of this methodology. Such knowledge will faciliate the design of synthetic routes to more complex natural products.

Experimental Section:

General: Routine ^1H NMR spectra were recorded at 90 MHz on a Varian EM 390 spectrometer. Chemical shifts are reported in ppm relative to tetramethylsilane as 0.00 ppm. ^1H NMR data are presented as follows: chemical shift (multiplicity, number of protons, coupling constants in Hertz). Fourier transform NMR spectra were determined on a JEOL FX-90Q 90MHz (^1H)/22.5 MHz (^{13}C) instrument , a JEOL FX 270 MHz (^1H) / 67.5 MHz (^{13}C) instrument, or a BRUCKER AM250 250 MHz (^1H) / 62.5 (^{13}C) instrument. Carbon multiplicities were determined by the DEPT {"Distortionless Enhancement by Polarization Transfer"} experiments with ^1H-decoupling and by QUAT experiments which give ^1H-decoupled spectra for ^{13}C-nuclei which are not protonated. Infrared (IR) spectra were recorded as a thin film between polished sodium chloride plates on a Perkin-Elmer 197 Grating Infrared Spectrometer. All adsorption bands are reported in wave numbers (cm^{-1}), which were calibrated against the 1601 cm^{-1} absorption band of polystyrene. Low resolution mass spectra were recorded on a Finnigan 4023 Chromatograph-Mass Spectrometer by a direct probe and are expressed in m/z units. Microanalysis was performed by Atlantic Microlab, Inc., Atlanta, Georgia.

Anhydrous tetrahydrofuran (THF) and diethyl ether were prepared by refluxing with, and distillation from, sodium/benzophenone under a nitrogen atmosphere in a recycling still. Anhydrous dimethylformamide (DMF) and hexamethylphosphoramide (HMPA) were prepared by refluxing over and distillation from calcium hydride under a dry nitrogen atmosphere and stored over 4A molecular sieves. Anhydrous toluene and diisopropyl amine were prepared by refluxing over and distillation from calcium hydride and stored over sodium metal and potassium hydroxide pellets, respectively. Diisobutylaluminum hydride is abbreviated as DIBAL.

All reactions were run under an inert atmosphere of nitrogen, and monitored by TLC analysis until the starting material was completely consumed. Unless otherwise indicated, all ethereal workups consisted of the

following procedure: The reaction mixture was quenched at room temperature with saturated aqueous ammonium chloride. The solvent was removed under reduced pressure on a rotary evaporator and the residue was taken up in ether, washed with brine and dried over anhydrous magnesium sulfate. Filtration, followed by concentration at reduced pressure on a rotary evaporator and at 0.1 torr to constant weight, afforded a crude residue which was purified by flash chromatography with MN silica gel 60 (230-400 mesh ASTM) and distilled reagent grade solvents.

(±)-2-Methyl-1-cyclopentene-1,3-dimethanol (8): To a mechanically stirred suspension of 2.30 g (61.0 mmol) of lithium aluminum hydride in 110 mL of dry ether was added a solution of 6.85 g (30.0 mmol) of diethyl (±)-1-cyclopentene-1-carboxylate (7) dissolved in 20 mL of ether at -78°C for 90 min and allowed to warm to room temperature overnight (13 h). The reaction mixture was added to 500 mL of reagent grade ether and 4 mL of water was added dropwise over a 1-h period. The ethereal phase was dried over anhydrous magnesium sulfate, filtered and concentrated. The resulting crude diol 8 (3.98 g, 93%) was homogeneous by TLC analysis (ether, R_f 7 = 0.96, R_f 8 = 0.10), and was used without further purification or characterization: ^{1}H NMR ($CDCl_3$) δ 1.62 (br s, 3H), 1.75-2.25 (m, 4H), 2.25-2.60 (m, 2H), 2.60-2.90 (m, 1H), 3.56 (d, 2H, J=5Hz), 4.12 (br s, 2H); IR (film) 3650-3050, 2940, 2870, 1440, 1380, 1080, 1040, 1000 cm^{-1}; mass spectrum, m/z 142 (M^+).

(±)-2-methyl-1-cyclopentene-1,3-dimethanol diacetate (9): To a solution of 3.98 g (28.0 mmol) of diol 8 in 60 mL of dry THF at room temperature was added 6.80 mL (84.1 mmol) of pyridine. Acetic anhydride (7.93 mL, 84.1 mmol) was added and the resulting reaction mixture was stirred for 14 h. Evaporation of the solvent afforded a crude residue which was diluted with 500 mL of ether and washed with saturated $CuSO_4$ (2 x 50 mL), water (25 mL), saturated $NaHCO_3$ (2 x 50 mL) and brine (25 mL). The ethereal phase was dried over anhydrous magnesium sulfate, filtered and concentrated. Purification by chromatography on silica gel (elution with hexanes/ether, 5:1 → 1:1) afforded 5.40 g (85%) of diacetate 9 which was homogeneous by TLC analysis (hexanes/ether, 1:2, R_f 8 = 0.05, R_f 9 = 0.86): ^{1}H NMR ($CDCl_3$) δ 1.72 (br s, 3H), 1.85-2.25 (m, 8H), 2.25-2.45 (m, 2H), 2.78-2.92 (m, 1H), 3.95-4.20 (m, 2H), 4.63 (ABq, 2H, Δ_{AB} = 23Hz, J = 7Hz); ^{13}C NMR ($CDCl_3$) 171.0 (s), 170.8 (s), 137.3 (s), 132.5 (s), 66.1 (t), 60.7 (t), 49.1 (d), 32.7 (t), 25.9 (t), 20.6 (q), 20.6 (q), 12.5 (q) ppm; IR (film) 2950, 2850, 1735, 1440, 1380, 1360, 1220, 1025, 960 cm^{-1}; mass spectrum, m/z 166 (M-60; M-HOAc).

(±)-3-[(Dimethylphenylsilyl)methyl]-2-methyl-2-cyclopentene-1-methanol acetate (10): Phenyldimethylchlorosilane (3.87 mL, 23.4 mmol) was added to 818 mg of finely cut lithium metal suspended in 45 mL of dry THF. After being stirred for 90 min the solution turned dark red. Continued vigorous stirring for 3 h produced a brownish solution which was transferred (via canula) to a suspension of 1.47 g (16.4 mmol) of copper (I) cyanide in 20 mL of dry THF at 0°C. After 90 min, the reaction mixture was cooled to -60°C and 2.64 g (11.7 mmol) of diacetate 9 in 20 mL of dry THF was added. The resulting mixture was stirred at -60°C for 12 h. The reaction mixture was quenched by pouring onto 800 mL of a 1:1 mixture of saturated aqueous NH_4Cl / saturated aqueous Na_2CO_3 and extracted with ether (4 x 200 mL portions). The combined organic extracts were dried over anhydrous magnesium sulfate, filtered and concentrated. Purification by chromatography on silica gel (elution with hexanes/ether, 20:1 → 5:1) gave 6.64 g (94%) of 10 which was homogeneous by TLC analysis (hexanes/ether, 2:1, R_f 9 = 0.40, R_f 10 = 0.85): ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 6H), 1.40 (br s, 3H), 1.70 (br s, 2H), 1.80-2.20 (m, 7H), 2.55-2.85 (m, 1H), 3.62-4.15 (m, 2H), 7.10-7.48 (m, 5H); ^{13}C NMR ($CDCl_3$) 171.3 (s), 139.2 (s), 135.1 (s), 133.5 (d), 133.5 (d), 129.0 (d), 127.9 (s), 127.7 (d), 127.7 (d), 67.0 (t), 48.8 (d), 36.8 (t), 26.2 (t), 21.0 (q), 18.8 (t), 12.8 (q), -2.5 (q), -2.5 (q) ppm; IR (film) 3070, 3050, 2960, 1735, 1430, 1380, 1360, 1250, 1120, 1040, 840, 940, 900 cm^{-1}; mass spectrum, m/z 242 (M-60; M-HOAc).

(±)-3-[(Dimethylsilyl)methyl]-2-cyclopentene-1-methanol (11): To a suspension of 335 mg (8.81 mmol) of lithium aluminum hydride in 30 mL of dry ether at -45°C was added dropwise a solution of acetate 10 (2.66 g, 8.81 mmol) in 20 mL of ether over a 20-min period. The reaction mixture was stirred for 1 h at -45°C, warmed to room temperature over a 3-h period and then quenched by pouring onto reagent grade ether. The ethereal phase was dried over anhydrous magnesium sulfate, filtered and concentrated. Purification by chromatography on silica gel (elution with hexanes/ether, 10:1 → 1:2) gave 2.0 g (87%) of alcohol 11 which was

homogeneous by TLC analysis (hexanes/ether, 2:1, R_f **10** in 0.85, R_f **11** = 0.50): ^{1}H NMR ($CDCl_3$) δ 0.28 (s, 6H), 1.40 (br s, 3H), 1.50-1.90 (m, 5H), 1.93-2.25 (m, 2H), 2.45-2.80 (m, 1H), 3.46 (d, 2H, J = 5Hz), 7.13-7.49 (m, 5H); ^{13}C NMR ($CDCl_3$) 139.0 (s), 135.9 (s), 133.4 (d), 133.4 (d), 129.0 (d), 127.7 (d), 127.7 (d), 127.3 (s), 64.6 (t), 52.0 (d), 37.2 (t), 25.5 (t), 18.9 (t), 12.5 (q), -2.5 (q), -2.7 (q) ppm; IR (film) 3650-3100, 3060, 3040, 3000, 2950, 2900, 2860, 1660, 1580, 1420, 1400, 1380, 1320, 1240, 1160, 1110, 1040, 1020, 1000, 830, 790, 730, 710, 695 cm^{-1}; mass spectrum, m/z 260 (M^+).

(±)-3-[(Dimethylphenylsilyl)methyl]-2-methyl-2-cyclopentene-1-carboxaldehyde (13): Chromium trioxide (1.29 g, 13.0 mmol) was added in three equal portions over a 15-min period to 2.10 mL (25.9 mmol) of pyridine in 20 mL of dry methylene chloride. After stirring for 15 min at room temperature 750 mg (2.88 mmol) of alcohol **11** in 5 mL of dry methylene chloride was added. The reaction mixture was stirred for 3 h and then quenched by pouring onto wet reagent grade ether. The ethereal phase was washed with 10% NaOH (2 x 200 mL), saturated $CuSO_4$ (4 x 25 mL), water (20 mL) and brine (2 x 25 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered and concentrated. Purification by chromatography on silica gel (elution with hexanes/ether, 50:1) gave 378 mg (51%) of aldehyde **13** which was homogeneous by TLC analysis (hexanes/ether, 2:1, R_f **11** = 0.50, R_f **13** = 0.88): ^{1}H NMR ($CDCl_3$) δ 0.30 (s, 6H), 1.43 (s, 3H), 1.80 (ABq, 2H, Δ_{AB} = 23.4 Hz, J = 13.5 Hz), 1.84-2.00 (m, 2H), 2.00-2.30 (m, 2H), 3.00-3.20 (m, 1H), 7.28-7.40 (m, 3H), 7.43-7.55 (m, 2H), 9.33 (d, 1H, J = 5Hz); ^{13}C NMR ($CDCl_3$) 202.3 (d), 139.0 (s), 138.6 (s), 133.4 (d), 133.4 (d), 129.1 (d), 127.7 (d), 127.7 (d), 123.9 (s), 62.9 (d), 37.7 (t), 22.8 (t), 19.3 (t), 13.0 (q), -2.5 (q), -2.5 (q) ppm; IR (film) 3100, 3080, 2980, 2940, 2830, 2730, 1725, 1435, 1385, 1255, 1175, 1160, 1120, 840, 720, 700 cm^{-1}; mass spectrum, m/z 258 (M^+).

(±)-5-[[3-[(Dimethylphenylsilyl)methyl]-2-methyl-2-cyclopenten-1-yl]hydroxymethyl]-3-ethoxy-2-cyclopenten-1-one 14 (a-c): Tetrahydrofuran (500 μL) was added to n-butyllithium (1.0 mL, 2.48 mmol, 2.5 M in hexane) from which the hexanes had been removed under vacuum. The resulting solution was cooled to 0°C and 0.36 mL (2.6 mmol) of diisopropylamine was added. After cooling to -78°C, a solution of 286 mg (2.27 mmol) of 3-ethoxy-2-cyclopenten-1-one (**5**) in 1 mL of dry THF containing 0.38 mL (2.2 mmol) of HMPA was added over a 1-h period. After an additional 30 min at -78°C, 556 mg (2.16 mmol) of aldehyde **13** in 1 mL of dry THF was added. The reaction mixture was stirred at -78°C for 4 h and then quenched with solid NH_4Cl. Evaporation of the solvent provided 790 mg of crude residue which TLC analysis indicated consisted of three components. This mixture was added directly onto a silica gel column. Chromatography (elution with hexanes/ether, 4:1) afforded 428 mg (52%) of aldol adduct **14a** which was homogeneous by TLC analysis (ether, R_f **5** = 0.27, R_f **14a** = 0.80): ^{1}H NMR ($CDCl_3$) δ 0.30 (s, 3H), 0.31 (s, 3H), 1.38 (t, 3H, J = 7Hz), 1.49 (s, 3H), 1.76 (ABq, 2H, Δ_{AB} = 34.2 Hz, J = 16Hz), 1.80-1.94 (m, 2H), 1.96-2.20 (m, 2H), 2.28 (dd, 1H, J = 16Hz, 2Hz), 2.41-2.55 (m, 2H), 2.64 (dd, 1H, J = 16Hz, 7Hz), 3.70 (dd, 1H, J = 16 Hz, 2Hz), 3.75 (s, 1H), 4.03 (q, 2H, J = 7Hz), 4.54 (br s, 1H), 7.28-7.38 (m, 3H), 7.43-7.55 (m, 2H); ^{13}C NMR ($CDCl_3$) 210.0 (s), 189.6 (s), 139.5 (s), 134.6 (s), 133.5 (d), 133.5 (d), 128.7 (d), 128.0 (s), 127.6 (d), 127.6 (d), 103.6 (d), 71.7 (d), 67.9 (t), 53.1 (d), 47.2 (d), 37.2 (t), 32.0 (t), 21.1 (t), 19.0 (t), 14.1 (q), 12.2 (q), -2.33 (q), -2.3 (q) ppm; IR (film) 3650-3450, 3080, 3060, 2950, 2850, 1680, 1600, 1480, 1440, 1380, 1350, 1300, 1250, 1200, 1170, 1120, 1030, 920, 830, 720 cm^{-1}; mass spectrum, m/z 249 [M-135, M-$Si(CH_3)_2C_6H_5$].

Continued elution gave 143 mg (17%) of a diastereomeric aldol adduct **14b** which was homogeneous by TLC analysis (ether, R_f **5** = 0.27, R_f **14b** = 0.70): ^{1}H NMR ($CDCl_3$) δ 0.31 (s, 3H), 0.32 (s, 3H), 1.36 (t, 3H, J = 7Hz), 1.52 (s, 3H), 1.65 (ABq, 2H, Δ_{AB} = 31Hz, J = 11Hz), 1.82-1.98 (m, 2H), 1.98-2.22 (m, 2H), 2.30 (dd, 1H, J = 16Hz, 1Hz), 2.51 (d, 1H, J = 8Hz), 2.58-2.68 (m, 1H), 2.76-2.86 (m, 1H), 3.88 (dd, 1H, J = 12Hz, 3Hz), 4.07 (q, 2H, J = 7Hz), 4.82-4.96 (m, 1H), 5.27 (s, 1H), 7.30-7.40 (m, 3H), 7.50-7.60 (m, 2H); ^{13}C NMR ($CDCl_3$) 209.9 (s), 190.1 (s), 139.2 (s), 135.9 (s), 133.4 (d), 133.4 (d), 128.9 (d), 127.8 (s), 127.6 (d), 127.6 (d), 103.5 (d), 74.5 (d), 67.9 (t), 54.5 (d), 46.6 (d), 37.4 (t), 32.4 (t), 24.7 (t), 18.9 (t), 14.0 (q), 14.0 (q), -2.3 (q), -2.3 (q) ppm; IR (film) 3500-3300, 3080, 2950, 2900, 2850, 1680, 1590, 1420, 13380, 1340, 1245, 1190, 1105, 1075, 1020, 975, 865, 835, 800, 705, 695, 660 cm^{-1}; mass spectrum, m/z 249 [M-135; M-$Si(CH_3)_2C_6H_5$].

Further elution afforded 144 mg (17%) of a third diastereomeric aldol adduct **14c** which was homogeneous by TLC analysis (ether, R_f **5** = 0.27, R_f **14c** = 0.40): ^{1}H NMR ($CDCl_3$) δ 0.30 (s, 3H), 0.31 (s,

3H), 1.37 (t, 3H, J = 7Hz), 1.40 (s, 3H), 1.15-1.35 (m, 4H), 1.95-2.20 (m, 2H), 2.42-2.64 (m, 2H), 2.72-2.91 (m, 2H), 3.93-4.18 (m, 3H), 4.16 (s, 1H), 5.26 (s, 1H), 7.26-7.36 (m, 3H), 7.40-7.56 (m, 2H); ^{13}C NMR ($CDCl_3$) 206.5 (s), 190.1 (s), 138.9 (s), 136.7 (s), 133.3 (d), 133.3 (d), 128.9 (d), 127.6 (d), 127.6 (d), 127.6 (s), 104.1 (d), 69.5 (d), 67.5 (t), 54.4 (d), 49.7 (d), 37.2 (t), 30.8 (t), 22.7 (t), 19.1 (t), 14.0 (q), 12.6 (q), -2.4 (q), -2.6 (q) ppm; IR (film) 3600-3200, 2925, 1680, 1590, 1420, 1370, 1340, 1245, 1235, 1190, 1110, 1025, 830, 700 cm^{-1}; mass spectrum, m/z 135 (B).

(±)-4-[[3-[(Dimethylphenylsilyl)methyl]-2-methyl-2-cyclopenten-1-yl]hydroxymethyl]-2-cyclopenten-1-one 15 (a-c): To a solution of 205 mg (0.53 mmol) of **14a** in 2 mL of dry toluene at -20°C was added 0.8 mL of a 1.5 M solution of DIBAL-H in toluene [Aldrich]. After the mixture was stirred for 2 h at -20°C, the reaction mixture was quenched with wet reagent grade ether (125 mL). The ethereal phase was washed with 1% HCl (35 mL) and brine (20 mL). The organic phase was dried over anhydrous magnesium sulfate, filtered and concentrated. The crude residue was chromatographed on silica gel (elution with hexanes/ether, 4:1 → 1:1) to afford 151 mg (84%) of enone **15a** which was homogeneous by TLC analysis (hexanes/ether, 1:4, R_f **14a** = 0.68, R_f **15a** = 0.72): ^1H NMR ($CDCl_3$) δ 0.31 (s, 3H), 0.32 (s, 3H), 1.40 (s, 3H), 1.55-1.80 (m, 4H), 1.90 (d, 1H, J = 16Hz), 2.00 (dd, 1H, J = 22Hz, 2Hz), 2.07-2.26 (m, 2H), 2.44 (dd, 1H, J = 22Hz, 8Hz), 2.51-2.75 (m, 1H), 2.90-3.04 (m, 1H), 3.47 (dd, 1H, J = 8Hz, 2Hz), 6.23 (dd, 1H, J = 6Hz, 2Hz), 7.30-7.43 (m, 3H), 7.45-7.58 (m, 2H), 7.97 (dd, 1H, J = 6Hz, 2Hz); ^{13}C NMR ($CDCl_3$) 209.1 (s), 167.8 (d), 138.6 (s), 138.0 (s), 134.0 (d), 133.3 (d), 133.3 (d), 129.2 (d), 127.8 (d), 127.8 (d), 126.4 (s), 73.7 (d), 53.8 (d), 45.2 (d), 37.4 (t), 37.4 (t), 20.7 (t), 19.3 (t), 12.0 (q), -2.4 (q), -2.5 (q) ppm; IR (film) 3650-3250, 3100, 2950, 1710, 1680, 1600, 1440, 1420, 1360, 1200, 1105, 1040, 840, 825, 800, 720 cm^{-1}; mass spectrum, m/z 322 (M-18).

(**15b**): Addition of 1 mL of DIBAL-H (1.5 M) to 290 mg (0.755 mmol) of **14b**, using the procedure described for the preparation of **15a**, gave 257 mg (100%) of enone **15b** which homogeneous by TLC analysis (hexanes/ether, 1:10, R_f **14b** = 0.63, R_f **15b** = 0.68): ^1H NMR ($CDCl_3$) δ 0.32 (s, 3H), 0.36 (s, 3H), 1.54 (s, 3H), 1.81 (ABq, 2H, Δ_{AB} = 38Hz, J = 16Hz), 1.90-2.34 (m, 6H), 2.40 (dd, 1H, J = 19Hz, 6.6 Hz), 2.64-2.76 (m, 1H), 2.90-3.01 (m, 1H), 3.50 (dd, 1H, J = 7.5Hz, 5Hz), 6.22 (dd, 1H, J = 6Hz, 2Hz), 7.31-7.43 (m, 3H), 7.45-7.58 (m, 2H), 7.79 (dd, 1H, J = 6Hz, 2Hz); ^{13}C NMR ($CDCl_3$) 209.4 (s), 166.4 (d), 138.6 (s), 138.6 (s), 134.7 (d), 133.5 (d), 133.5 (d), 129.1 (d), 127.8 (d), 127.8 (d), 126.8 (s), 77.7 (d), 54.0 (d), 46.1 (d), 38.4 (t), 37.3 (t), 27.5 (t), 19.4 (t), 14.9 (q), -2.2 (q), -2.4 (q) ppm; IR (film) 3600-3200, 3070, 3040, 2930, 1710, 1680, 1590, 1430, 1410, 1340, 1250, 1190, 1110, 950, 830, 710 cm^{-1}; mass spectrum, m/z 322 (M-18).

(**15c**): Addition of 1.7 mL of DIBAL-H (1.5 M) to 437 mg (1.14 mmol) of **14c**, using the procedure described for the preparation of **15a**, gave 129 mg (33%) of enone **15c** which was homogeneous by TLC analysis (ether, R_f **14c** = 0.27, R_f **15c** = 0.55): ^1H NMR ($CDCl_3$) δ 0.31 (s, 3H), 0.33 (s, 3H), 1.38 (s, 3H), 1.58-1.93 (m, 5H), 2.05-2.29 (m, 2H), 2.43 (d, 1H, J = 3Hz), 2.48 (d, 1H, J = 6Hz), 2.69-2.81 (m, 1H), 2.94-3.05 (m, 1H), 3.58 (dd, 1H, J = 8Hz, 2Hz), 6.19 (dd, 1H, J = 6Hz, 2Hz), 7.28-7.42 (m, 3H), 7.49-7.54 (m, 2H), 7.58 (dd, 1H, J = 6Hz, 3Hz); ^{13}C NMR ($CDCl_3$) 210.1 (s), 164.6 (d), 138.5 (s), 137.2 (s), 135.1 (d), 133.2 (d), 133.2 (d), 128.9 (d), 127.6 (d), 127.6 (d), 126.6 (s), 73.4 (d), 53.2 (d), 45.9 (d), 38.6 (t), 37.3 (t), 21.4 (t), 19.1 (t), 12.1 (q), -2.4 (q), -2.6 (q) ppm; IR (film) 3650-3250, 3070, 3040, 2900, 1710, 1690, 1420, 1270, 1250, 1190, 1110, 1040, 840, 820, 795, 735, 725, 715 cm^{-1}; mass spectrum, m/z 322 (M-18).

(±)-4-[[3-[(Dimethylphenylsilyl)methyl]-2-methyl-2-cyclopenten-1-yl]hydroxymethyl]-2-cyclopenten-1-one acetate 16 (a-c): To a solution of 264 mg (0.776 mmol) of alcohol **15a** in 15 mL of dry THF was added 94 μL (1.2 mmol) of pyridine and 142 mg of 4-dimethylaminopyridine [DMAP]. After stirring for 5 min, 110 μL (1.2 mmol) of acetic anhydride was added and the reaction mixture was stirred for 12 h. Evaporation of the solvent afforded a crude residue which was then diluted with 125 mL of ether and washed with saturated $CuSO_4$ (2 x 15mL), water (10 mL), saturated $NaHCO_3$ (2 x 15mL), water (10 mL) and brine (15 mL). The ethereal phase was dried over anhydrous magnesium sulfate, filtered and concentrated. The crude residue was chromatographed on silica gel (elution with hexanes/ether, 10:1 → 2:1) to afford 289 mg (97%) of acetate **16a** which was homogeneous by TLC analysis (hexanes/ether, 1:2, R_f **15a** = 0.42, R_f **16a** = 0.82): ^1H NMR ($CDCl_3$) δ 0.28 (s, 6H), 1.48 (s, 3H), 1.75 (s, 2H), 1.84 (ABq, 2H, Δ_{AB} = 14Hz, J = 8Hz), 2.03 (s, 3H), 2.04-

2.25 (m, 3H), 2.51 (dd, 1H, J = 22Hz, 8Hz), 2.69-2.81 (m, 1H), 3.13-3.25 (m, 1H), 5.50 (dd, 1H, J = 12Hz, 2Hz), 6.25 (dd, 1H, J = 7Hz, 2Hz), 7.31-7.42 (m, 3H), 7.48-7.61 (m, 3H); ^{13}C NMR ($CDCl_3$) 207.9 (s), 170.1 (s), 164.5 (d), 139.0 (s), 135.8 (s), 134.9 (d), 133.3 (d), 133.3 (d), 128.9 (d), 127.6 (d), 127.6 (d), 127.0 (s), 74.9 (d), 52.5 (d), 44.0 (d), 38.0 (t), 37.2 (t), 22.5 (t), 20.8 (q), 18.7 (t), 12.5 (q), -2.5 (q), -2.5 (q) ppm; IR (film) 3070, 3040, 3020, 2975, 2850, 1735, 1680, 1595, 1450, 1435, 1420, 1380, 1250, 1190, 1115, 1020, 1060, 840, 790, 730 cm^{-1}.

(16b): Treatment of 315 mg (0.926 mmol) of alcohol 15b, using the procedure described for the preparation of 16a, afforded 230 mg (65%) of acetate 16b which was homogeneous by TLC analysis (hexanes/ether, 1:2, R_f 15b = 0.30, R_f 16b = 0.70): ^1H NMR ($CDCl_3$) δ 0.29 (s, 3H), 0.30 (s, 3H), 1.49 (s, 3H), 1.55-1.95 (m, 4H), 2.00 (s, 3H), 2.01-2.23 (m, 3H), 2.36 (dd, 1H, J = 20Hz, 7Hz), 2.80-2.93 (m, 1H), 3.08-3.18 (m,1H), 4.98 (t, 1H, J = 6Hz), 6.20 (dd, 1H, J = 5.5Hz, 2Hz), 7.26-7.38 (m, 3H), 7.43-7.52 (m, 2H), 7.55 (dd, 1H, J = 5.5Hz, 2Hz); ^{13}C NMR ($CDCl_3$) 208.2 (s), 170.2 (s), 163.5 (d), 138.6 (s), 136.5 (s), 135.0 (d), 133.2 (d), 133.2 (d), 128.9 (d), 127.5 (d), 127.5 (d), 127.5 (s), 76.8 (d), 51.8 (d), 42.8 (d), 38.3 (t), 36.9 (t), 25.3 (t), 20.8 (q), 18.8 (t), 13.6 (q), -2.6 (q), -2.6 (q) ppm; IR (film) 3070, 3050, 3020, 2940, 2890, 1710, 1650, 1590, 1430, 1370, 1230, 1190, 1110, 1030, 830, 820, 790, 700, 640 cm^{-1}; mass spectrum, m/z 322 (M-60; M-HOAc).

(16c): Treatment of 129 mg (0.380 mmol) of alcohol 15c, using the procedure described for the preparation of 16a, afforded 122 mg (84%) of 16c which was homogeneous by TLC analysis (hexanes/ether, 1:5, R_f 15c = 0.55, R_f 16c = 0.82): ^1H NMR ($CDCl_3$) δ 0.27 (s, 6H), 1.47 (s, 3H), 1.63-1.85 (m, 4H), 1.94 (s, 3H), 1.95-2.28 (m, 3H), 2.32-2.36 (m, 1H), 2.66-2.78 (m, 1H), 3.09-3.18 (m, 1H), 5.17 (dd, 1H, J = 5Hz, 4Hz), 6.18 (dd, 1H, J = 5.5Hz, 2Hz), 7.27-7.37 (m, 3H), 7.43-7.52 (m, 2H), 7.55 (dd, 1H, J = 5.5Hz, 2Hz); ^{13}C NMR ($CDCl_3$) 208.3 (s), 170.0 (s), 164.3 (d), 138.7 (s), 136.1 (s), 134.9 (d), 133.1 (d), 133.1 (d), 128.8 (d), 127.5 (d), 127.5 (d), 126.9 (s), 73.8 (d), 52.1 (d), 45.0 (d), 36.8 (t), 36.8 (t), 23.8 (t), 20.7 (q), 18.7 (t), 12.8 (q), -2.6 (q), -2.6 (q) ppm; IR (film) 3070, 3020, 2940, 1710, 1590, 1420, 1400, 1370, 1230, 1180, 1110, 1020, 950, 820, 780, 710 cm^{-1}; mass spectrum, m/z 322 (M-60; M-HOAc).

(±)-(3aR*, 3bS*, 6aS*, 7S*, 7aS*)-1,3,3a,3b,6,6a,7,7a-Octahydro-7-hydroxy-3b,4-dimethyl-2H-cyclopenta[a]pentalen-2-one acetate (17a): Boron trifluoride etherate (19 μL, 0.16 mmol) was added to 20 mg (0.052 mmol) of 16a in 1.25 mL of dry toluene at 0°C. The reaction mixture was stirred at 0°C for 90 min. Standard ethereal workup afforded an oily residue which was purified on silica gel (elution with hexanes/ether, 5:1) to provide 12 mg (94%) of tricyclic ketone 17a which was homogeneous by TLC analysis (hexanes/ether 2:1, R_f 16a = 0.45, R_f 17a = 0.58): ^1H NMR ($CDCl_3$) δ 1.13 (s, 3H), 1.62 (br s, 3H), 2.01 (s, 3H), 2.08-2.47 (m, 6H), 2.68-2.74 (m, 2H), 2.77-2.90 (m, 1H), 4.95 (dd, 1H, J = 7Hz, 2Hz), 5.14 (br s, 1H); ^{13}C NMR ($CDCl_3$) 218.9 (s), 170.3 (s), 145.3 (s), 122.6 (d), 84.8 (d), 59.5 (s), 57.0 (d), 47.4 (d), 43.6 (d), 40.0 (t), 39.6 (t), 35.8 (t), 21.6 (q), 21.1 (q), 12.6 (q) ppm; IR (film) 3030, 2920, 2850, 1735, 1450, 1400, 1375, 1240, 1160, 1050, 1020, 960, 800 cm^{-1}; mass spectrum, m/z 188 (M-60; M-HOAc).

$EtAlCl_2$-Catalyzed Cyclization of 16a: To a solution of 17 mg (0.0443 mmol) of enone 16a in 1 mL of dry toluene was added 80 μL,(0.12 mmol, 1.5 M in hexanes) of ethylaluminum dichloride at 0°C. After 1 h at 0°C, the reaction mixture was quenched with wet reagent grade ether. Standard ethereal workup provided a crude residue which was purified via chromatography on silica gel (elution with hexanes/ether, 10:1) to afford 3.5 mg (32%) of ketone 17a which was identical to material previously characterized.

$SnCl_4$-Catalyzed Cyclization of 16a: Tin tetrachloride (29 μL, 0.029 mmol, 1.0 M in CH_2Cl_2) was added to 11 mg (0.029 mmol) of acetate 16a in 0.75 mL of dry CH_2Cl_2 at -78°C. After the mixture was stirred for 20 min at -78°C the reaction mixture was quenched with saturated $NaHCO_3$. Standard ethereal workup provided a crude residue which was purified using chromatography on silica gel (elution with hexanes/ether, 10:1) to provide 5.5 mg (77%) of ketone 17a which was identical to material previously characterized.

$TiCl_4$-Catalyzed Cyclization of 16b: Treatment of 20 mg (0.053 mmol) of acetate 16b with titanium tetrachloride (25 μL, 0.228 mmol), using the procedure described for the preparation of 18a except that the

reaction time was increased to 1 h, afforded 3 mg (23%) of tricyclic ketone **17b** which was homogeneous by TLC analysis (hexanes/ether 1:1, R_f **16b** = 0.47, R_f **17b** = 0.41): ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.62 (br s, 3H), 1.96 (s, 3H), 1.96-2.42 (m, 6H), 2.43-2.59 (m, 1H), 2.60-2.72 (m, 1H), 3.00-3.13 (m, 1H), 5.28 (br s, 1H), 5.43 (dd, 1H, J = 7Hz, J = 7Hz); ^{13}C NMR ($CDCl_3$) 219.3 (s), 170.5 (s), 142.9 (s), 125.7 (d), 79.5 (d), 62.1 (s), 55.9 (d), 50.3 (d), 45.9 (d), 40.4 (t), 39.4 (t), 30.2 (t), 27.8 (q), 20.7 (q), 13.6 (q) ppm; mass spectrum, m/z 248 (M^+).

(**17c**): The reaction of 60 mg (0.16 mmol) of acetate **16c** with titanium tetrachloride (19 μL, 0.173 mmol) for 1 h using the procedure described for the preparation of **18a** afforded 12 mg (31%) of tricyclic ketone **17c** which was homogeneous by TLC analysis (hexanes/ether, 1:1, R_f **16c** = 0.40, R_f **17c** = 0.50): ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3H), 1.58 (br s, 3H), 1.90-2.06 (m, 1H), 2.08 (s, 3H), 2.15-2.65 (m, 7H), 2.86-3.04 (m, 1H), 4.72 (dd, 1H, J = 7Hz, 7 Hz), 5.28 (br s, 1H).

(±)-(3a*R, 3b*S**, 6a*S**, 7*S**, 7a*S**)-Decahydro-7-hydroxy-3b-methyl-4-methylene-2*H*-cyclopenta[*a*]-pentalen-2-one acetate (18a)**: Titanium tetrachloride (30 μL, 0.27 mmol) was added to 62 mg (0.16 mmol) of acetate **16a** in 2 mL of dry methylene chloride at -78°C. After being stirred for 15 min at -78°C the reaction mixture was quenched with saturated $NaHCO_3$. [Note that when the reaction was conducted for longer than 15 min, isomerization of exocyclic adduct **18a** to endocyclic adduct **17a** occurred.] The reaction mixture was diluted with ether (85 mL) and washed with saturated $NaHCO_3$ (15 mL) and brine (15 mL). The ethereal phase was dried over anhydrous magnesium sulfate, filtered and concentrated. The crude residue was chromatographed on silica gel (elution with hexanes/ether, 20:1 → 5:1) to yield 29 mg (73%) of tricyclic ketone **18a** which was homogeneous by TLC analysis (hexanes/ether, 2:1, R_f **16a** = 0.45, R_f **18a** = 0.58): ^{1}H NMR ($CDCl_3$) δ 1.17 (s, 3H), 1.57-1.74 (m, 2H), 1.83-1.97 (m, 1H), 1.98 (s, 3H), 2.20-2.50 (m, 6H), 2.55-2.95 (m, 2H), 4.82 (dd, 1H, J = 2Hz, 2Hz), 4.86-4.96 (m, 2H); ^{13}C NMR ($CDCl_3$) 219.2 (s), 170.3 (s), 161.8 (s), 105.9 (t), 82.4 (d), 59.2 (d), 54.6 (s), 52.1 (d), 43.6 (d), 40.3 (t), 39.3 (t), 33.3 (t), 28.0 (t), 25.0 (q), 20.9 (q) ppm; IR (film) 3070, 2925, 2850, 1735, 1650, 1460, 1405, 1375, 1240, 1160, 1020, 960, 890 cm^{-1}; mass spectrum, m/z 248 (M^+).

(**18b**): Treatment of 162 mg (0.42 mmol) of acetate **16b** with titanium tetrachloride (70 μL, 0.64 mmol), using the procedure described for the preparation of **18a**, afforded 57 mg (54%) of ketone **18b** which was homogeneous by TLC analysis (hexanes/ether 1:1, R_f **16b** = 0.47, R_f **18b** = 0.41): ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.45-1.76 (m, 2H), 1.98 (s, 3H), 2.00-2.57 (m, 7H), 2.66 (q, 1H, J = 8Hz), 2.97-3.10 (m, 1H), 4.71 (s, 1H), 5.00 (s, 1H), 5.50 (dd, 1H, J = 5.5 Hz, 5.5Hz); ^{13}C NMR ($CDCl_3$) 219.1 (s), 170.3 (s), 158.6 (s), 106.6 (t), 80.4 (d), 59.1 (d), 56.0 (s), 52.2 (d), 46.0 (d), 41.3 (t), 39.8 (t), 37.3 (t), 31.0 (q), 23.7 (t), 20.8 (q) ppm; IR (film) 2970, 2925, 2870, 1740, 1440, 1405, 1375, 1260, 1240, 1160, 1070, 1020, 975, 900, 800 cm^{-1}; mass spectrum, m/z 248 (M^+).

(**18c**): Treatment of 57mg (0.15 mmol) of acetate **16c** with titanium tetrachloride (25 μL, 0.22 mmol) using the procedure described for the preparation of **18a** afforded 12 mg (32%) of ketone **18c** which was homogeneous by TLC analysis (hexanes/ether, 1:1, R_f **16c** = 0.40, R_f **18c** = 0.50): ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.56-1.86 (m, 2H), 2.08 (s, 3H), 2.10-2.55 (m, 7H), 2.64 (dd, 1H, J = 18Hz, 9Hz), 2.87-3.02 (m, 1H), 4.71 (br s, 1H), 4.79 (dd, 1H, J = 7Hz, 7Hz), 5.11 (br s, 1 H); ^{13} C NMR ($CDCl_3$) 217.5 (s), 171.0 (s), 157.5(s), 107.3 (t), 83.5 (d), 60.5 (d), 53.8(s), 50.0 (d), 47.1 (d), 42.2 (t), 41.8 (t), 35.2 (t), 30.4 (q), 27.1 (t), 21.2 (q) ppm; IR (film) 2970, 1740, 1450, 1370, 1240, 1180-1140, 1070-1000, 890 cm^{-1}; mass spectrum, m/z 248 (M^+).

(±)-(3a*R, 3b*S**, 6a*S**, 7a*S**)-Decahydro-7-hydroxy-3b-methyl-4-methylene-2*H*-cyclopenta[*a*]pentalen-2-one (19a)**: To a solution of 4 mg (0.073 mmol) of sodium methoxide [Fisher] in 0.5 mL of anhydrous methanol was added 18 mg (0.073 mmol) of acetate **18a** in 0.5 mL of anhydrous methanol. After being refluxed for 3 h the reaction mixture was quenched with saturated NH_4Cl (0.5 mL). Standard ethereal workup provided a crude residue which was purified via chromatography on silica gel (elution with hexanes/ether, 15:1 → 3:1) to give 12 mg (77%) of alcohol **19a** which was homogeneous by TLC analysis (hexanes/ether 2:1, R_f **18a** = 0.58, R_f **19a** = 0.38): ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 3H), 1.43-1.59 (m, 1H), 1.62 (q, 1H, J = 2Hz),

1.83-2.83 (m, 10H), 3.96 (dd, 1H, J = 2Hz, 2Hz), 4.80 (t, 1H, J = 2Hz), 4.91 (t, 1H, J = 2Hz); ^{13}C NMR ($CDCl_3$) 221.0 (s), 162.9 (s), 104.5 (t), 80.1 (d), 61.8 (d), 54.3 (s), 52.0 (d), 45.2 (d), 41.0 (t), 39.0 (t), 33.4 (t), 28.1 (t), 25.5 (q) ppm; IR (film) 3550-3300, 2950, 2880, 1730, 1650, 1400, 1170, 1050, 880, 610 cm^{-1}; mass spectrum, m/z 206 (M^+).

(**19b**): Treatment of 57 mg (0.230 mmol) of acetate **18b** with 19 mg (0.345 mmol) of sodium methoxide [Fisher], using the procedure described for the preparation of alcohol **19a**, afforded 34 mg (72%) of alcohol **19b** which was homogeneous by TLC analysis (hexanes/ether 1:1, R_f **18b** = 0.47, R_f **19b** = 0.30): ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.55-1.85 (m, 2H), 1.95-2.64 (m, 9H), 2.78-2.91 (m, 1H), 4.18 (t, 1H, J = 5Hz), 4.66 (s, 1H), 4.95 (s, 1H); ^{13}C NMR ($CDCl_3$) 221.8 (s), 159.9 (s), 105.6 (t), 78.3 (d), 60.7 (d), 55.8 (s), 52.8 (d), 47.2 (d), 42.0 (t), 39.8 (t), 37.8 (t), 31.3 (q), 23.3 (t) ppm; IR (film) 3550-3200, 3070, 2910, 2855, 1715, 1640, 1440, 1420, 1385, 1285, 1220, 1165, 1060, 1000, 965, 865, 610 cm^{-1}.

(±)-(3R*, 3bS*, 6aS*)-3,3a,3b,4,5,6,6a,7-Octahydro-3b-methyl-4-methylene-2H-cyclopenta[a]-pentalen-2-one (21a): To 124 mg (0.39 mmol) of tetra-n-butylammonium fluoride trihydrate which had been placed under vacuum for 30 min was added 1.5 mL of dry DMF and a few activated 4A molecular sieves. After 15 min, the solution was transferred to a reaction vessel containing 100 mg 4A molecular sieves. Hexamethylphosphoramide (115 μL, 0.663 mmol) was added and the reaction mixture was stirred for 15 min. A solution of enone **16a** (85 mg, 0.221 mmol) in 1.5 mL of dry DMF was added dropwise over a 1-h period (via syringe pump). The resulting mixture was stirred at room temperature for 12 h and then quenched with water. Standard ethereal workup provided a crude residue which was purified via chromatography on silica gel (elution with hexanes/ether, 6:1) to afford tricyclic enone **21a** which was homogeneous by TLC analysis (hexanes/ether 1:1, R_f **16a** = 0.65, R_f **21a** = 0.52): ^{1}H NMR ($CDCl_3$) δ 1.22 (s, 3H), 1.75 (d, 1H, J = 4Hz), 1.79-2.40 (m, 5H), 2.42 (t, 2H, J = 4Hz), 2.52-2.75 (m, 2H), 4.86 (s, 1H), 4.91 (s, 1H), 5.75 (s, 1H); ^{13}C NMR ($CDCl_3$) 209.3 (s), 181.0 (s), 155.4 (s), 128.4 (d), 104.4 (t), 39.6 (s), 36.0 (d), 35.3 (t), 33.4 (t), 30.6 (d), 28.8 (t), 25.7 (t), 12.2 (q) ppm; IR (film) 3070, 2930, 2870, 1700, 1605, 1440, 1260, 1240, 1195, 1170, 1080, 1040, 990, 900, 880, 850, 790 cm^{-1}; mass spectrum m/z 188 (M^+).

(±)-(3aR*, 3bS*, 6aS*, 7aS*)-Decahydro-3b,4-dimethyl-2H-cyclopenta[a]pentalen-2-one (22): To 10 mg (0.053 mmol) of enone **21a** and 5 μL of tert-butyl alcohol in 0.5 mL of dry ether was added 5 mL of freshly distilled liquid ammonia. After 2 mg (0.28 mmol) of lithium was added, the reaction mixture was refluxed for 20 min. The reaction mixture was quenched by the addition of solid NH_4Cl and the ammonia was allowed to evaporate. Standard ethereal workup provided a crude residue which was purified by chromatography on silica gel (elution with hexanes/ether, 7:1) to afford 6 mg (60%) of enone **22** which was homogeneous by TLC analysis (hexanes/ether 2:1, R_f **21a** = 0.42, R_f **22** = 0.53): ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.27-1.57 (m, 2H), 1.61 (d, 3H, J = 6.5Hz), 1.88-2.07 (m, 1H), 2.10-2.38 (m, 8H), 5.98 (s, 1H); ^{13}C NMR ($CDCl_3$) 210.3, 182.5, 130.4, 47.8, 38.1, 36.6, 35.4, 31.9, 29.7, 28.3, 14.0, 12.0 ppm.

(±)-(3aR*, 3bS*, 6aS*, 7aS*)-Decahydro-3b-methyl-4-methylene-2H-cyclopenta[a]pentalen-2-one (4): To a solution of 50 μL (0.0702 mmol) of methyl lithium (1.4 M in ether) in 0.20 mL of dry THF at -15°C was added 12 mg (0.064 mmol) of CuI in one portion. After the mixture was stirred for 15 min, 0.20 mL of HMPA followed by 85 μL (0.13 mmol) of DIBAL-H were added to the bright yellow precipitate of methyl copper. After being stirred for 30 min at -15°C, 12 mg (0.064 mmol) of enone **21a** in 0.25 mL of dry THF was added dropwise over a 5-min period. The reaction mixture was stirred for 90 min at -15°C and then quenched with 10% aqueous HCl. Standard ethereal workup provided a crude residue which was purified by chromatography on silica gel (elution with hexanes/ether, 20:1) to afford 9.5 mg (78%) of tricyclic ketone **4** which was homogeneous by TLC analysis (hexanes/ether 1:1, R_f **21a** = 0.52, R_f **4** = 0.75): ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3H), 1.59-2.50 (m, 13H), 4.20 (s, 1H), 4.28 (s, 1H); ^{13}C NMR ($CDCl_3$) 219.7 (s), 157.4 (s), 102.1 (t), 45.0 (t), 38.2 (t), 38.0 (d), 33.5 (d), 32.3 (d), 32.2 (s), 29.9 (t), 29.9 (t), 26.0 (t), 13.5 (q) ppm.

Preparation of enol ether 26: To 123 mg (0.358 mmol) of (methoxymethyl)triphenylphosphonium chloride (**25**) in 0.5 mL of dry THF under argon at 0°C was added 745 μL (0.371 mmol) of potassium

bis(trimethylsilyl)amide [0.5M solution in toluene, Aldrich]. After being stirred for 30 min at 0°C, followed by 30 min at room temperature, 17 mg (0.0895 mmol) of ketone 4 in 800 µL of dry THF was added to the bright red solution. After stirring for 2 h at room temperature, followed by an additional 2 h at 60°C, the reaction mixture was quenched with 0.5 mL of water. The cooled reaction mixture was concentrated, diluted with 5 mL of water and then extracted with hexanes (4 x 20 mL). The combined organic phases were washed with 15 mL of brine, dried over anhydrous magnesium sulfate, filtered and concentrated. The crude residue was chromatographed on silica gel (elution with hexanes/ether, 40:1) to afford 19 mg (100%) of enol ether 26 which was homogeneous by TLC analysis (hexanes/ether, 5:1, R_f 4 = 0.35, R_f 26 = 0.90): ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 1.5H), 1.29 (s, 1.5H), 1.37-2.46 (m, 12H), 2.56 (dd, 1H, J = 18Hz, 8Hz), 3.58 (s, 3H), 4.67 (br s, 1H), 4.74 (br s, 1H), 5.88 (br s, 1H); ^{13}C NMR ($CDCl_3$) 158.5 (s), 158.3 (s), 138.7 (d), 120.3 (s), 101.2 (t), 59.3(q), 41.3 (d), 41.0 (d), 35.4 (t), 33.9 (d), 33.7 (d), 33.4 (t), 33.3 (t), 32.9 (t), 32.6(d), 32.2 (s), 32.0 (d), 30.1 (t), 29.7 (t), 28.2 (t), 26.0 (t), 13.6 (q) ppm; IR (film) 2930, 2870, 2830, 1690, 1650, 1460, 1440, 1230, 1170, 1110, 860 cm^{-1}; mass spectrum, m/z 218 (M^+). These data represent a mixture of E and Z isomers.

Preparation of Aldehyde 27: To 19.5 mg (0.089 mmol) of methyl enol ether 26 in 0.75 mL of acetonitrile under argon at room temperature was added 14 µL (0.0984 mmol) of trimethylsilyl iodide [Aldrich]. After being stirred for 5 min, the reaction mixture was diluted with 60 mL of reagent grade ether and washed with 5 mL of saturated aqueous $Na_2S_2O_3$, 5 mL of saturated sodium bicarbonate and 5 mL of brine. The ethereal phase was dried over anhydrous magnesium sulfate, filtered, concentrated and chromatographed on silica gel (elution with hexanes/ether, 40:1) to afford 11.6 mg (64%) of aldehyde 27 which was homogeneous by TLC analysis (hexanes/ether, 10:1, R_f 26 = 0.50, R_f 27 = 0.30): ^{1}H NMR ($CDCl_3$) δ 1.25-2.41 (m, 16H), 2.88-3.02 (m, 1H), 4.36 (br s, 1H), 4.42 (br s, 1H), 9.62 (br s, 1H).

(±)-(3a*R, 3b*S**, 6a*S**, 7*S**, 7a*S**)-1,3,3a,3b,6,6a,7,7a-Octahydro-7-hydroxy-3b,4-dimethyl-2*H*-cyclopenta[a]pentalen-2-one (29):** To a solution of 21 mg (0.10 mmol) of alcohol 19a in 3 mL of dry ether was added 37 µL (0.30 mmol) of boron trifluoride etherate at 0°C. After being stirred for 3 h at 0°C, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. Standard ethereal workup provided a crude residue which was purified via chromatography on silica gel (elution with hexanes/ether, 6:1 → 2:1) to give 16 mg (77%) of alcohol 29 which was homogeneous by TLC analysis (hexanes/ether 2:1, R_f 19a = 0.38, R_f 29 = 0.38): ^{1}H NMR ($CDCl_3$) δ 1.15 (s, 3H), 1.60 (br s, 3H), 1.95-2.77 (m, 10H), 3.95 (dd, 1H, J = 5Hz, 2Hz), 5.15 (br s, 1H); ^{13}C NMR ($CDCl_3$) 221.4 (s), 146.0 (s), 122.0 (d), 82.4 (d), 59.7 (d), 59.4 (s), 47.2 (d), 45.2 (d), 40.7 (t), 39.3 (t), 35.7 (t), 22.1 (q), 12.7 (q) ppm; mass spectrum, m/z 188 (M^+).

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Footnotes and References:

1. This work was presented in part at the 38th SERM at Louisville, Ky, in November,1986, and at the 194th National Meeting of the ACS in New Orleans, August, 1987. It was taken in part from the Ph.D. dissertation of Jean Defauw, The University of Georgia, 1988.

2. For a comprehensive review of allylsilane chemistry prior to 1981, see: Sakurai, H. Pure and Appl. Chem. **1982**, *54*, 1. For an updated survey of allylsilane chemistry, see: Majetich, G. "Allylsilanes in Organic Synthesis," in *Organic Syntheses, Theory and Applications*; Hudlicky, T. Ed., Jai Press, Inc., Greenwich, CT., **1988**, in press. Two other independent reviews of allylsilane chemistry [by Fleming & Dunogues, and Schinzer] are also in press.

3. **For cyclopentane annulations using allylsilanes, see:** a) Majetich, G.; Desmond, R.; Casares, A. M. Tetrahedron Lett. **1983**, *24*, 1913. b) Majetich, G.; Hull, K.; Defauw, J.; Shawe, T. Ibid. **1985**, *26*, 2755. c) Majetich, G.; Defauw, J.; Hull, K.; Shawe, T. Ibid. **1985**, *26*, 4711. d) Majetich, G.; Desmond, R.; Soria, J. J. Org. Chem. **1986**, *51*, 1753. e) Schinzer, D. Angew. Chem., Int. Ed. **1984**, *23*, 308. f) Unpublished results of Mr. R. Derric Lowery.

4. **For cyclohexane annulations using allylsilanes, see:** a) Majetich, G.; Hull, K.; Desmond, R. Tetrahedron Lett. **1985**, *26*, 2751. b) Majetich, G.; Behnke, M.; Hull, K. J. Org. Chem. **1985**, *50*,

3615. **For cycloheptane annulations using allylsilanes, see:** c) Majetich, G.; Hull, K.; Defauw, J.; Desmond, R. Tetrahedron Lett. **1985**, *26*, 2747. d) Majetich, G.; Ringold, C. Heterocycles **1987**, *25*, 271. e) Majetich, G.; Defauw, J.; Ringold, C. J. Org. Chem. **1988**, *53*, 50. f) Majetich, G.; Hull, K. Tetrahedron **1987**, *43*, 5621. g) Schinzer, D.; Steffen, J.; Solyom, S. J. Chem. Soc., Chem. Commun. **1986**, 829. **For cyclooctane annulations using allylsilanes, see:** reference 4a.

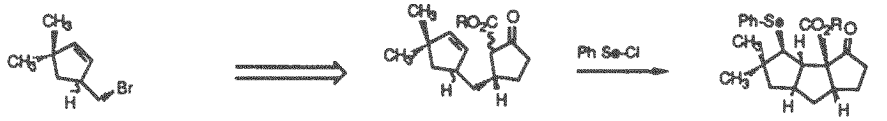
5. **Isolation of hirsutene:** a) Nozoe, S.; Furukawa, J.; Sankawa, U.; Shibata, S. Tetrahedron Lett. **1976**, 195. **Isolation of capnellene:** b) Ayanaglu, E.; Gebreyesus, T.; Beechan, C.M.; Djerassi, C.; Kaisin, M. Tetrahedron Lett. **1978**, 1671.

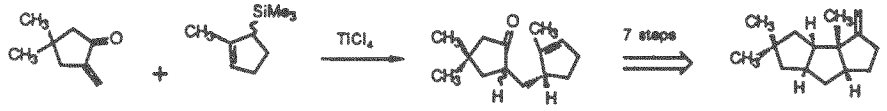
6. For recent reviews on cyclopentane annulations, see: a) Paquette, L.A. Top. Curr. Chem. **1984**, *119*, 1. b) Ramaiah, M. Synthesis **1984**, 529. c) Trost, B.M. Chem. Soc. Rev. **1982**, *11*, 141.

7. For a recent compilation of previous hirsutene total syntheses, see ref. 10 of 7a. See, also: a) Hudlicky, T.; Koszyk, F.J.; Kutchan, T. M.; Sheth, J.P. J. Org. Chem. **1980**, *45*, 5020. b) Little, R.D.; Muller. G.W.; Venegas, M.G.; Carroll, G.L.; Bukhari, A.; Patton, L.; Stone, K. Tetrahedron **1981**, *37*, 4371. c) Magnus, P.; Quagliato, D. A.; Organometallics **1982**, *1*, 1243. d) Dawson, B.A.; Ghosh, A.K.; Jurlina, J.L.; Stothers, J.B. J. Chem. Soc., Chem. Commun. **1983**, 204. e) Little, R. D.; Higby, R.G.; Moeller, K.D. J. Org. Chem. **1983**, *48*, 3139. f) Curran, D. P.; Rakiewicz, D. M. J. Am. Chem. Soc. **1985**, *107*, 1448. g) Disanayaka, B.W.; Weedon, A.C.; J. Chem. Soc.,Chem. Commun. **1985**, 1282. h) Mehta, G.; Murthy, A. N.; Reddy, D.S.; Reddy, A.V. J. Am. Chem. Soc. **1986**, *108*, 3443. i) Funk, R. L.; Bolton, G. L.; Daggett, J. U.; Hansen, M.M.; Horcher, L. H. M. Tetrahedron **1985**, *41*, 3479. j) Curran, D. P.; Rakiewicz, D.M. Tetrahedron **1985**, *41*, 3943. k) Hewson, A.T.; MacPherson, D.T. J. Chem. Soc. Perkin Trans. 1. **1985**, 2625. l) Disanayaka, B.W.; Weedon, A.C. J. Org. Chem. **1987**, *52*, 2905. m) Cossy, J.; Bellotti, D.; Pete, J.P. Tetrahedron Lett. **1987**, *28*, 4547. n) see also ref. 9.

8. a) Little, R. D.; Carroll, G.L. Tetrahedron Lett. **1981**, *22*, 4389. b) Little, R.D.; Carroll, G.L.; Petersen, J. L. J. Am. Chem. Soc. **1983**, *105*, 928. c) Curran, D.P.; Chen, M.-H. Tetrahedron Lett. **1985**, *26*, 4991.

9. Ley and Murray achieved the first hirsutene synthesis featuring an "A + C" approach to directly form the central cyclopentane ring: a) Ley, S. V.; Murray, P.J. J. Chem. Soc., Chem. Commun. **1982**, 1252; b) Ley, S. V.; Murray, P. J.; Palmer, B.D.; Tetrahedron **1985**, *41*, 4765. See, also: c) Funk, R. L.; Bolton, G. L. J. Org. Chem. **1984**, *49*, 5021. d) ref. 7i. Tatsuta and Oda have photochemicallycoupled functionalized A and C rings, followed by skeletal rearrangement, to produce hirsutene. See: e) Tatsuta, K.; Akimoto, K.; Kinoshita, M. J. Am. Chem. Soc. **1979**, *101*, 6116. f) Iyoda, M.; Kushida, T.; Kitami, S.; Oda, M. J. Chem. Soc., Chem. Comm. **1986**, 1049.





10. All structures drawn here represent racemates, only one enantiomer being drawn.

11. a) Baldwin, J. E. J. Chem. Soc., Chem. Commun. **1976**, 734. b) Liotta, C.L.; Burgess, E.M.; Eberhardt, W.H. J. Am. Chem. Soc. **1984**, *106*, 4849.

12. Fuchs, P. L. J. Am. Chem. Soc. **1974**, *96*, 1607.

13. a) Fleming, I.; Pearce, A. J. Chem. Soc. Perkin Trans. **1981**, *1*, 251. b) Fleming, I.; Marchi, D., Jr. Synthesis **1981**, 560.

14. We have observed that when three or more methylene units link the hydroxyl group and the allylsilane unit standard Finkelstein conditions do not result in protodesilylation. Unpublished results of Mr. Jose Soria and Mr. R. D. Lowery.

15. Haynes, R. K.; Holden, M. Aust. J. Chem. **1982**, *35*, 517.

16. Stork, G.; Danheiser, R.L. J. Org. Chem. **1973**, *38*, 1775.

17. Valicenti, A.J.; Holman, R.T. Chemistry and Physics of Lipids **1976**, *17*, 389.

18. Oxidants suchs as PCC, PCC on aluminum oxide,[19] barium manganate,[20] proved inferior to Collins reagent. Other mild oxidative procedures, such as the Swern or Moffat oxidations, proceeded in poor yield.

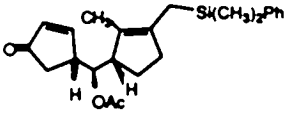
19. Cheng, Y.-S.; Liu, W.-L.; Chen, S.-H. Synthesis **1980**, 223.

20. Firouzabadi, H.; Ghaderi, E. Tetrahedron Lett. **1978**, 839.

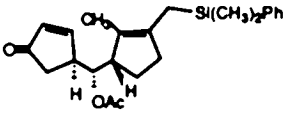
21. a) Dubois, J.E.; Dubois, M. Tetrahedron Lett., **1967**, 4215. b) Dubois, J.E. J. Chem. Soc., Chem. Soc. **1968**, 1567. c) Dubois, J.E.; Dubois, M. Bull. Soc. Chem. Fr. **1969**, 3553. d) Fellmann, P.; Dubois, J. E. Tetrahedron **1978**, *34*, 1349. See, also: e) Leonard, W. R.; Livinghouse, T. Tetrahedron Lett. **1985**, *26*, 6431. f) Gennari, C.; Todeschini, R.; Beretta, M.G.; Favini, G.; Scolastico, C. J. Org. Chem. **1986**, *51*, 612.

22. a) Heathcock, C.H.; Buse, C.T.; Kleschick, W.A.; Pirrung, M.C.; Sohn, J.E.; Lampe, J. J. Org. Chem. **1980**, *45*, 1066. b) Noyori, R.; Nishida, I.; Sakata, J. J. Am. Chem. Soc. **1981**, *103*, 2106.

23 Diastereomers **14b** and **14c** have been converted into enones **16b** and **16c** via the same sequence of reactions as applied to **14a**. Possible structures for **16b** and **16c** are shown below. This work, as well as the cyclizations of these enones, is detailed within the experimental section.



d,l pair



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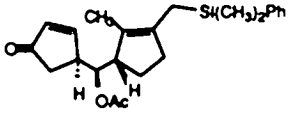

d,l pair

24. The exocyclic olefin of alcohol **19a** was isomerized using boron trifluoride etherate to give alcohol **29**. This crystalline intermediate has been submitted for single-crystal X-ray analysis to verify its structure and via inference those of **16a** through **19a**.

25. For successful deoxygenations of simpler substrates, see: a) Barton, D.H.R.; McCombie, S.W. J. Chem. Soc., Perkin Trans. 1 **1975**, 1574. b) Barton, D.H.R.; Motherwell, W.B.; Stange, A. Synthesis **1981**, 743.

26. For example, hex-1-ene is converted into hexane by sodium and methanol in liquid ammonia, whereas hex-2-ene is not reduced. See: a) Halsall, T.G.; Theobald, D.W.; Walshaw, K.B. J. Chem. Soc. **1964**, 1029. b) Greenffield, H.; Friedel, R.A.; Orchin, M. J. Am Chem. Soc. **1954**, *76*, 1258.

27. a) Tsuda, T.; Hayashi, T.; Satomi, H.; Kawamoto, T.; Saegusa, T. J. Org. Chem. **1986**, *51*, 537. b) Tsuda, T.; Satomi, H.; Hayashi, T.; Saegusa, T. Ibid. **1987**, *52*, 439.

28. Ojima, I.; Kogure, T.; Nagai, Y.; Tetrahedron Lett. **1972**, 5035.

29. a) Reetz, M. T.; Westermann, J.; Kyung, S.-H. Chem. Ber. **1985**, *118*, 1050. b) Reetz, M. T.; Westermann, J.; Steinbach, R.; Wenderoth, B.; Peter, R.; Ostarek, R.; Maus, S. Ibid. **1985**, *118*, 1421.

30. A slight excess of dimethylzinc was used [5%] to insure that unreacted titanium tetrachloride was not present to promote olefin isomerization.

31. Mehta, G.; Rao, K. S. J. Chem. Soc., Chem Commun. **1985**, 1464.

32. Meisters, A.; Mole, T. J. Chem. Soc., Chem. Commun. **1972**, 595.

33. Martin, S. F.; Phillips, G. W.; Puckette, T. A.; Colapret, J.A. J. Am. Chem. Soc. **1980**, *102*, 5866.

34. For the preparation of aminomethyldiethylphosphonate, a precursor for reagent **24**, see : a) Ratcliffe, R.W.; Christensen, B.G. Tetrahedron Lett. **1973**, 4645. For a far superior procedure, see: b) Davidsen, S.K.; Phillips, G. W.; Martin, S. F. Organic Syntheses **1987**, *65*, 119.

35. This Wittig olefination has been utilized by Ikegammi and Mehta in their hirsutetic acid and pentalenene work, respectively. See; a) Shibasaki, M.; Yamazaki, M.; Iseki, K.; Ikegami, S. Tetrahedron Lett. **1982**, *23*, 5311. b) Yamazaki, M.; Shibasaki, M.; Ikegami, S. J. Org. Chem. **1983**, *48*, 4402. c) ref. 31.

36. Jung, M.E.; Lyster, M.A. J. Org. Chem. **1977**, *42*, 3761.

37. For alkylations of similar aldehyde enolates, see: a) ref. 31. b) Ireland, R.E.; Nander, L.N. J. Org. Chem. **1969**, *34*, 142 and references cited therein.