Total Synthesis of (−)-α-Acoradiene and (−)-α-Cedrene

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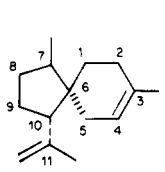
An efficient nine-step stereospecific synthesis of (−)-α-acoradiene (**1**) using *cis,trans*-puleganolide (**4**), derived from (+)-pulegone, as starting material is described. Alkylation of lactone **4** with 1-iodo-3,3-ethylenedioxybutane (**6**) is followed by a *tert*-butoxide in DMF induced elimination to introduce an isopropenyl group. Esterification, removal of the protecting ketal group, and Claisen cyclization with *tert*-butoxide in DMF gives the desired spiro[4.5]decanedione **13**. Dione **13** is converted to an enol ether with diazopropane, which is reduced with $LiAlH_4$ to afford dienone **20**. Reaction of **20** with methylenetriphenylphosphorane and reduction of the resulting triene with sodium in ammonia affords diene **1**. The synthesis of (−)-α-acoradiene (**1**) constitutes a formal total synthesis of (−)-α-cedrene (**2**).

The sesquiterpene α-acoradiene (**1**)[1-3] is known to occur



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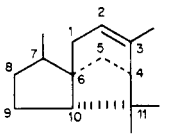

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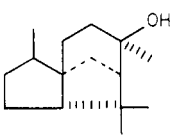

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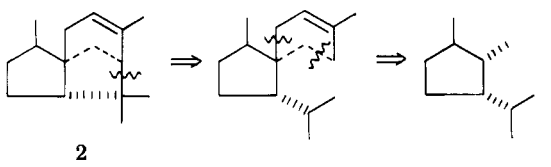
along with α-cedrene (**2**)[4] and cedrol (**3**) in the wood of *Juniperus rigida*. Our interest in the previously unsynthesized α-acoradiene (**1**) came from a retrosynthetic analysis of α-cedrene (**2**, Scheme I) which suggested the obvious connection between the acorane, cedrane, and iridoid (methylcyclopentane)[5] ring systems. *cis,trans*-Puleganolide (**4**),[6] derived from (+)-pulegone (**5**), appeared to be an appropriate choice as a starting material since it has the same relative and absolute configuration found in **1**. Our plan was to specifically alkylate **4**, construct the spiro[4.5]decane ring system, and then manipulate the functional groups in order to arrive at α-acoradiene (**1**). Herein we describe the successful completion of this stragedy.

Early attempts to alkylate **4** employing potassium *tert*-butoxide failed to afford even a trace of desired product. However, alkylation of **4** by generation of the enolate anion using 1 equiv of LDA at −78 °C followed by addition of 1-iodo-3,3-ethylenedioxybutane (**6**) in HMPA afforded **7** in 51% yield (Scheme II).[8] Although the yield

Scheme I



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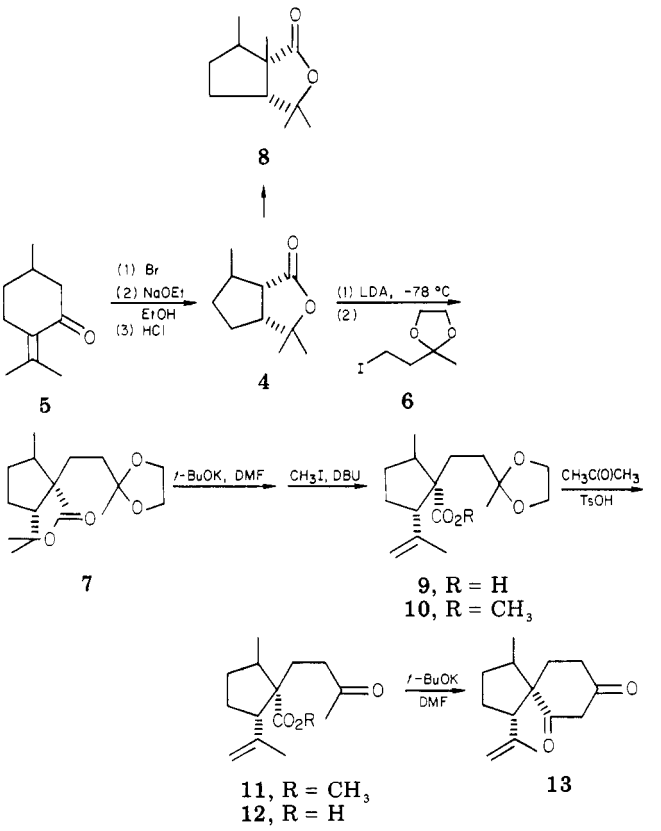
Scheme II



8

5 **4** **6**

7

9, R = H
10, R = CH_3

11, R = CH_3
12, R = H

13

is not extremely high, the only other compounds found in the product mixture were starting materials. All three compounds are easily separated by distillation or chro-

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(6) (a) Wolinsky, J.; Wolf, H.; Gibson, T. *J. Org. Chem.* **1963**, *28*, 274. (b) Eustace, E.; Wolinsky, J. *J. Org. Chem.* **1972**, *37*, 3376.

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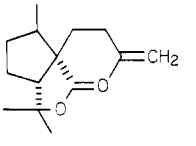
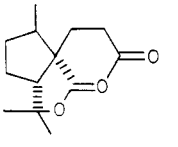
(8) Alternatively, lactone **4** was alkylated with 4-iodo-2-methyl-1-butene, the resulting terminal olefin **7a** was ozonized, and the ketone **7b** was ketalized to yield lactone **7**. Attempts to cyclize keto lactone **7b** using LDA gave unidentified products.



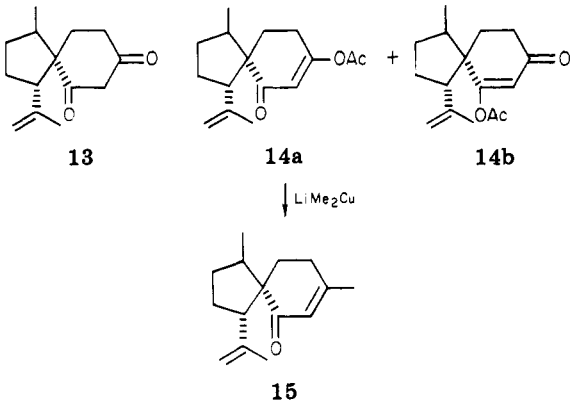
7a



7b

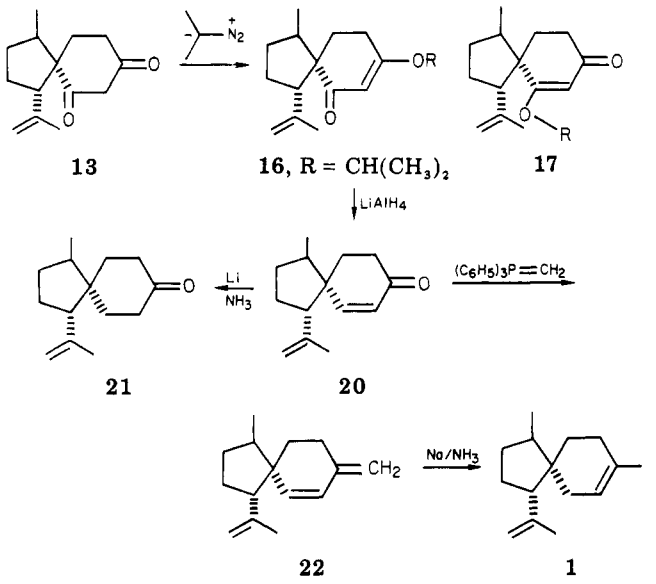
0022-3263/83/1948-0670$01.50/0

Scheme III



13 14a 14b 15

Scheme IV



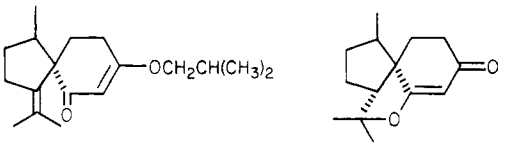
13 16, R = $CH(CH_3)_2$ 17 21 20 22 1

matography, and since the starting materials can be recycled, the alkylation is in essence quantitative. Note also that the alkylation appears to occur exclusively from the top face of the molecule, avoiding the formation of a highly strained trans-fused ring juncture.[9] To confirm the configuration of the ring juncture, lactone **4** was alkylated with methyl iodide to yield the methyl lactone **8**. Saponification of **8** followed by acidification gave back lactone **8**, with no sign of the formation of a hydroxycarboxylic acid, which would have been the case if a trans ring juncture had been present.[10]

Lactone **7** cleanly underwent a base-induced elimination in high yield by using slightly less than 1 equiv of potassium *tert*-butoxide in hot dimethylformamide[6b,11] to yield unsaturated acid **9**, where the desired isopropenyl group has been introduced at C-10. Acid **9** was esterified by using 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and methyl iodide,[12] the ketal **10** was hydrolyzed,[13] and the keto ester **11** was then cyclized with potassium *tert*-butoxide in DMF to give spirodione **13** in 69% overall isolated yield from lactone **7**. Use of potassium *tert*-butoxide in *tert*-butyl alcohol[4a] in the cyclization of keto ester **11** also gave spirodione **13** but in much reduced yield and invariably produced keto acid **12** as a byproduct.[14]

To complete the acorane skeleton, a methyl group at C-3 and a double bond between C-3 and C-4 must be introduced. The first approach attempted involved a cuprate addition[15] to the appropriate keto enol acetate **14a** (Scheme III) obtained by treatment of **13** with acetic anhydride in pyridine at room temperature.[16] Exposure of **14a** to 1 equiv of lithium dimethylcuprate at −78 °C gave the dienone **15** in 80% yield. Unfortunately, attempts to remove the carbonyl group in **15** by thioketalization–desulfurization failed.[2d,17]

To surmount this problem, a second approach was pursued wherein the carbonyl group at C-5 in spirodione **13** was removed by the classic procedure of enol ether formation followed by lithium aluminum hydride reduction and acid workup.[18] Attempts to prepare the required enol ether **16** using diazomethane,[19b] diethyl sulfate, and potassium carbonate in acetone or Me_2SO,[19a] or isobutyl tosylate and potassium carbonate in Me_2SO gave nearly equal amounts[21] of enol ethers **16** and **17** (R = CH_3, C_2H_5, or i-C_4H_9). Isobutyl alcohol and *p*-toluenesulfonic acid in benzene[20] produced a mixture where undesirable byproducts **18** and **19** predominated. The use of the more bulky



18 19

diazopropane[22] proved to be reasonably successful and afforded a mixture of **16** and **17** (R = isopropyl) in a 2:1 ratio (Scheme IV). After isolation of the desired enol ether **16** (R = isopropyl) by chromatography, it was reduced with $LiAlH_4$ and worked up with dilute sulfuric acid to afford dienone **20** in 56% yield.

Reduction of the conjugated double bond in **20** with lithium in liquid ammonia in the presence of *tert*-butyl alcohol[23] gave enone **21** that was identical with an intermediate Corey[4c] has used in a total synthesis of cedrol (**3**). The preparation of **21** constitutes a formal synthesis of cedrol (**3**).

To complete the synthesis of α-acoradiene (**1**), the reaction of methylenetriphenylphosphorane[24] with dienone **20** was used to introduce the missing carbon atom at C-3, and a 1,4-reduction[25,2b] of the resulting triene **22** employing

(9) Hudlicky, T.; Short, R. P. *J. Org. Chem.* **1982**, *47*, 1525 report that the alkylation of the flexible methyl pulegenate occurs from the least hindered side of the molecule with the alkyl group entering from the side opposite the methyl group. With the rigid lactone **4** the avoidance of a highly strained trans lactone ring juncture forces the alkylation to occur from the same side as the methyl group.

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(16) Enol acetate formation is reversible under these conditions, and the product distribution is thermodynamically controlled. The formation of enol acetate **14a** is favored since steric crowding is less severe when enolization occurs at a site furthest removed from substituents.

(17) Sondheimer, F.; Rosenthal, D. *J. Am. Chem. Soc.* **1958**, *80*, 3995.

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(24) Greenwald, R.; Chaykovsky, M.; Corey, E. J. *J. Org. Chem.* **1963**, *28*, 1128.

sodium in liquid ammonia selectively placed a double bond in the required C-3 position. (−)-α-Acoradiene (1) was obtained in a 70% overall yield from **20**. The NMR and IR spectra of the synthetic diene, purified by GLPC, agree well with the spectra reported in the literature for the natural product.[1] Synthetic α-acoradiene (1) shows an optical rotation of −39.6°, which is somewhat higher than the rotation of −36.7° reported in the literature.[1]

Tomita and Hirose[1] found that exposure of 1 to ethanolic hydrogen chloride afforded (−)-α-cedrene (**2**) in greater than 80% yield. The successful synthesis of 1 therefore constitutes a formal total synthesis of (−)-α-cedrene.

Experimental Section

All melting points were obtained with a Thomas Hoover capillary melting point apparatus and are uncorrected. NMR spectra were recorded on a Varian Associates A-60 spectrometer at 60 MHz or on a Perkin-Elmer Model R-32 spectrometer at 90 MHz. Infrared spectra were obtained with a Perkin-Elmer Infracord Model 137-B. Ultraviolet spectra were recorded on a Cary 15 spectrophotometer. Mass spectra were provided by the Purdue University Mass Spectral Service. Optical rotation measurements were taken on a Rudolph Research Autopol III polarimeter. Microanalyses were performed by Dr. C. S. Yeh and associates.

1-(3,3-Ethylenedioxybutyl)-*cis*,*trans*-puleganolide (7). A solution of 20 g (0.119 mol) of *cis*,*trans*-puleganolide (**4**) in 125 mL of THF was slowly added through an addition funnel to a stirred solution of 0.119 mol of LDA in 125 mL of THF at −78 °C under argon. After this stirred for 20 min, 47.535 g (0.196 mol) of 1-iodo-3,3-ethylenedioxybutane[26] (**6**) dissolved in 25.2 mL (0.143 mol) of HMPA was added, and the temperature was allowed to rise to −40 °C. The temperature was maintained at −40 °C for 72 h, and the reaction was quenched at −40 °C with saturated NH_4Cl solution. The mixture was extracted with ether, and the ether extract was washed with 10% HCl solution. The ether was dried ($MgSO_4$), and the solvents were removed to give 50 g of crude **7**. Flash chromatography[27] (silica gel, 30% ethyl acetate/pentane) afforded 17.042 g (51% yield) of **7**: IR (neat) 1754 cm^{-1} (C=O); NMR ($CDCl_3$) 1.05 (d, 3, J = 7 Hz, CH_3), 1.30 (s, 3, CH_3), 1.35 and 1.42 (s's, 6, $(CH_3)_2C$), 3.95 ppm (s, 4, OCH_2CH_2O); mass spectrum, m/e (relative intensity) 282 (1), 267 (9), 238 (3), 223 (2), 205 (75), 177 (2), 168 (9), 151 (4), 99 (3), 87 (100).

Anal. Calcd for $C_{14}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 67.93; H, 9.40.

1-(3-Methyl-3-butenyl)-*cis*,*trans*-puleganolide (7a). Alkylation of **4** with 4-iodo-2-methyl-1-butene as described above gave a 49% yield of lactone **7a**; bp 98–99 °C (0.05 mmHg); IR (neat) 1754 (C=O), 889 cm^{-1} (=CH_2); NMR ($CDCl_3$) 1.04 (d, 3, J = 7 Hz, CH_3), 1.35 and 1.42 (s's, 6, $(CH_3)_2C$), 1.71 (s, 3, CH_3), 4.7 ppm (br s, 2, C=CH_2); mass spectrum, m/e (relative intensity) 236 (16), 221 (8), 213 (8), 188 (94), 143 (69), 81 (48), 59 (50), 43 (98), 41 (100).

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.23; H, 10.24. Found: C, 76.46; H, 10.43.

Ozonolysis of Lactone 7a. Ozone was passed through a solution of 4.062 g (17.210 mmol) of lactone **7a** in 13 mL of methanol cooled to −60 °C until a light blue color persisted. The system was flushed with nitrogen, and 1.74 mL (23.660 mmol) of dimethyl sulfide was added. The solution was stirred at −10 °C for 1 h, at 0 °C for 1 h, and then at room temperature for 1 h. The solvent was removed and the residue taken up in ether. The ether solution was washed with water, dried ($MgSO_4$), and evaporated to yield 4.012 g of crude **7b**. Flash chromatography (silica gel, 30% ethyl acetate/pentane) afforded 2.908 g (71% yield) of **7b**: IR (neat) 1754 (C(O)O), 1718 cm^{-1} (C=O); NMR ($CDCl_3$) 0.9 (d, 3, J = 7 Hz, CH_3), 1.35 and 1.46 (s's, 6, $(CH_3)_2C$), 2.15 ppm (s, 3, CH_3); mass spectrum, m/e (relative intensity) 238 (15), 223 (16), 196 (13), 195 (8), 168 (97), 123 (23), 121 (35), 94 (98), 55 (22), 43 (100).

Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.54; H, 9.31. Found: C, 70.44; H, 9.19.

Ketalization of **7b** using ethylene glycol and *p*-toluenesulfonic acid gave ketal **7** in 98% yield.

1-Methyl-*cis*,*trans*-puleganolide (8). Alkylation of 0.5 g of lactone **4** with 0.47 g of methyl iodide as described above gave 0.460 g of crude 1-methyl-*cis*,*trans*-puleganolide (**8**, 80% by NMR):IR (neat) 1751 cm^{-1} (C=O); NMR ($CDCl_3$) 0.9 (d, 3, J = 7 Hz, CH_3) 1.21 (s, 3, CH_3CCO), 1.31 and 1.4 ppm (s's, 6, $(CH_3)_2C$).

A solution of 0.40 g (2.198 mmol) of 1-methyl-*cis*,*trans*-puleganolide (**8**) in 20% ethanolic KOH was refluxed for 12 h. The crude reaction mixture was added to water and extracted with ether. The aqueous layer was then acidified to pH <1 with 5 N H_2SO_4 and extracted with ether. The ether extract was dried ($MgSO_4$) and the ether removed to afford 0.36 g of crude lactone **8**.

Based-Induced Elimination of Lactone 7. To a stirred slurry of 1.361 g (12.131 mmol) of potassium *tert*-butoxide in 10 mL of dry DMF at 120 °C was added 3.527 g (12.510 mmol) of lactone **7** in 15 mL of dry DMF. The solution was heated to 140–144 °C for 4 h, cooled to room temperature, and poured over ice. The mixture was extracted with ether to remove polymeric and starting materials. The remaining aqueous layer was then acidified with 5% HCl and extracted with ether, and the ether was washed with water. Drying ($MgSO_4$) and removal of ether gave 3.157 g of crude acid **9**: IR (neat) 3333–2500 (CO_2H), 1695 (C=O), 892 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.98 (d, 3, J = 7 Hz, CH_3), 1.31 (s, 3, CH_3), 1.7 (br s, 3, CH_3), 3.9 (s, 4, OCH_2CH_2O), 4.75 and 4.8 (s's, 2, C=CH_2), 9.7 ppm (vbr s, 1, CO_2H).

Esterification of Acid 9. To a stirred mixture of 1.589 g (11.196 mmol) of methyl iodide and 1.704 g (11.196 mmol) of DBU in 15 mL of benzene was added 3.157 g (11.196 mmol) of the above crude acid **9**. The mixture was stirred for 3 h at room temperature and refluxed for 1 h. After this cooled to room temperature, water was added, and the reaction mixture was extracted with ether. Drying ($MgSO_4$) and removal of solvents afforded 3.009 g of crude ester **10**. Flash chromatography (silica gel 50% ether/pentane) gave 2.871 g (80% overall yield from lactone **7**) of ester **10**: IR (neat) 1724 (C=O), 889 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.96 (d, 3, J = 7 Hz, CH_3), 1.3 (s, 3, CH_3), 1.62 (br s, 3, CH_3), 3.6 (s, 3, CO_2CH_3), 3.92 (s, 4, OCH_2CH_2O), and 4.71 and 4.8 ppm (s's, 2, C=CH_2); mass spectrum, m/e (relative intensity) 296 (3), 221 (2), 182 (8), 175 (6), 149 (2), 135 (6), 121 (6), 107 (7), 87 (100).

Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 69.06; H, 9.66.

Deketalization of Ester 10. A mixture of 2.758 g (9.317 mmol) of ester **10**, 155 mg (0.816 mmol) of *p*-TsOH, and 155 mL of acetone was refluxed for 14 h. After this cooled to room temperature 20 mL of saturated $NaHCO_3$ solution was added and the acetone removed by rotary evaporation. The residue was extracted with ether and the ether washed with water. Drying ($MgSO_4$) and removal of solvents gave 2.302 g of crude keto ester **11**. Flash chromatography (silica gel, 50% ether/pentane) afforded 1.996 g (85% yield) of keto ester **11**: IR (neat) 1724 (C=O), 889 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.95 (d, 3, J = 7 Hz, CH_3), 1.68 (br s, 3, CH_3), 2.15 (s, 3, CH_3C=O), 3.62 ppm (s, 3, CO_2CH_3); mass spectrum, m/e (relative intensity) 252 (4), 234 (6), 221 (11), 182 (69), 139 (33), 135 (47), 133 (9), 121 (25), 91 (21), 43 (100).

Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59. Found: C, 71.19; H, 9.84.

Cyclization of Keto Ester 11 with Potassium *tert*-Butoxide–DMF. To a stirred of 5.739 g (51.151 mmol) of potassium *tert*-butoxide in 205 mL of DMF was slowly added, by addition funnel, 6.7843 g (26.922 mmol) of keto ester **11** in 68 mL of DMF. After stirring for 3 h at room temperature, the reaction mixture was poured onto ice. The aqueous mixture was extracted with ether, acidified with 20% HCl with cooling, and extracted with methylene chloride. The methylene chloride extract was washed with water and dried ($MgSO_4$), and the solvent was removed to give 5.8533 g (98% yield) of ene dione **13**: mp 100–101 °C (recrystallized from hexane); IR (Nujol) 3333–2778 (=COH), 1587 (C=O), 881 cm^{-1} (=CH_2); NMR ($CDCl_3$; a mixture of dione and keto enol) 0.85 and 0.88 (d's, 6, J = 7 Hz, CH_3), 1.6 (br s, 3, CH_3), 4.65 and 4.7 (s's, 2, C=CH_2), 4.8 (s, 2, C=CH_2), 5.45 (br s, 1, HC=C—O), 8.59 ppm (br s, 1, C=COH); mass spectrum, m/e (relative intensity) 220 (0.4), 205 (0.4), 177 (0.7), 165 (3), 162 (6),

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139 (7), 107 (4), 93 (10), 82 (6), 67 (10), 44 (20), 43 (9), 42 (14), 41 (100).

Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.46; H, 9.22.

Preparation of Enol Acetates 14a and 14b. A mixture of 1.229 g (5.586 mmol) of crude dione **13**, 2 mL of pyridine, and 1.4 mL of acetic anhydride was stirred at room temperature for 17 h. Pyridine and acetic anhydride were removed via vacuum distillation and the residue was dissolved in ether. The ether solution was washed with saturated $NaHCO_3$ solution and dried ($MgSO_4$), and the ether was removed to give 1.081 g of crude enol acetates **14a** and **14b**. Flash chromatography (silica gel, 20% ethyl acetate/pentane) afforded 0.746 g (50% overall yield from **11**) of enol acetate **14a**: IR (neat) 1770 ($OC(O)CH_3$), 1667 (C=C—C=O), 893 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.84 (d, 3, J = 7 Hz, CH_3), 1.6 (s, 3, CH_3), 2.15 (s, 3, O_2CCH_3), 4.7 (br s, 2, C=CH_2), 5.8 ppm (d, 1, J = 2 Hz, C=CH); mass spectrum, m/e (relative intensity) 262 (4), 220 (12), 202 (6), 164 (16), 163 (4), 162 (4), 139 (13), 121 (3), 91 (6), 69 (12), 67 (8), 55 (11), 53 (8), 43 (100).

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.37; H, 8.63.

Later fractions contained 0.075 g (~5% overall yield from **11**) of enol acetate **14b**: IR (neat) 1783 ($OC(O)CH_3$), 1681 (C=C—C=O), 885 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.95 (d, 3, J = 7 Hz, CH_3), 1.73 (s, 3, CH_3), 2.14 (s, 3, O_2CCH_3), 4.75 and 4.85 (s's, C=CH_2), 6.11 ppm (s, 1, C=CH).

Preparation of Dienone 15. To a solution of 0.722 g (2.757 mmol) of enol acetate **14a** in 10 mL of ether at −78 °C under argon was added, by double-headed needle, 1 equiv of lithium dimethylcuprate [0.525 g (2.757 mmol) of CuI, 3.7 mL of 1.5 M CH_3Li, and 10 mL ether]. After 1 h the reaction was quenched at 20 °C with 3 N HCl in ether followed by addition of water. The ether layer was separated, filtered through Celite, and dried ($MgSO_4$), and the ether was removed to give 0.5814 g of crude dienone **15**. Flash chromatography (silica gel, 20% ethyl acetate/pentane) afforded 0.4761 g (80% yield) of dienone **15**: IR (neat) 1653 (C=O), 885 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.84 (d, 3, J = 7 Hz, CH_3), 1.6 (s, 3, CH_3), 1.9 (br s, 3, CH_3), 4.65 and 4.71 (s's, 2, C=CH_2), 5.84 ppm (m, 1, C=CH); mass spectrum, m/e (relative intensity) 219 (100), 218 (37), 175 (13), 163 (17), 162 (22), 161 (10), 160 (18), 150 (15), 147 (10), 137 (23), 135 (14), 121 (13), 82 (32), 43 (7), 41 (44).

Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.36; H, 10.37.

Reaction of Dione 13 with Diazopropane. A mixture of 0.2 g (0.909 mmol) of dione **13**, 50 mL of ether, and excess diazopropane was allowed to stand at 0 °C for 10 min and at room temperature for 2 h. The excess diazopropane and ether were removed to yield 0.258 g of crude enols **16** and **17**. Flash chromatography (silica gel, 40% ethyl acetate/pentane) afforded 0.134 g (60% yield) of enol ether **16**: IR (neat) 1653 (C=O), 1613 (C=C), 885 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.84 (d, 3, J = 7 Hz, CH_3), 1.2 (d, 3, J = 7 Hz, CH_3), 1.25 (d, 2, J = 7 Hz, CH_3), 4.4 (heptet, 1, J = 7 Hz, CH), 4.7 (m, 2, C=CH_2), 5.33 ppm (br s, 1, HC=C); mass spectrum, m/e (relative intensity) 262 (37), 220 (12), 207 (57), 205 (13), 181 (18), 177 (17), 165 (100), 163 (23), 162 (19), 152 (46), 139 (95), 137 (26), 121 (24), 85 (44), 84 (96). Later fractions yielded 0.078 g (30% yield) of enol ether **17**: IR (neat) 1653 (C=O), 1592 (C=C), 885 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.86 (d, 3, J = 7 Hz, CH_3), 1.24 (d, 6, J = 7 Hz, $(CH_3)_2C$), 1.69 (s, 3, CH_3), 4.35 (h, 1, J = 7 Hz, CH), 4.65 and 4.71 (s's, 2, C=CH_2), 5.32 ppm (s, 1, HC=C); mass spectrum, m/e (relative intensity) 262 (6), 202 (16), 165 (36), 163 (33), 155 (24), 149 (28), 139 (33), 137 (26), 135 (16), 121 (58), 112 (46), 108 (47), 107 (45), 84 (56), 69 (100).

Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found for enol ether **16**: C, 77.63; H, 10.08. Found for enol ether **17**: C, 77.57; H, 9.97.

Preparation of Dienone 20. A solution of 0.274 g (0.939 mmol) of enol ether **16** in 1 mL of ether was added dropwise with stirring to a mixture of 0.018 g (0.491 mmol) of $LiAlH_4$ and 2 mL of ether. After refluxing for 0.5 h, the reaction mixture was allowed to cool to room temperature, and water was slowly added to quench the reaction. The mixture was poured into 1.5 mL of 10% H_2SO_4 (ice cold) and extracted with ether, and the ether extract was washed with saturated $NaHCO_3$ solution and dried ($MgSO_4$). The ether was removed, affording 0.240 g of crude dienone **20**. Flash chromatography (silica gel, 20% ethyl acetate/pentane) yielded 0.107 g (56%) of dienone **20**: UV λ_{max}^{MeOH} 230 nm (log ϵ 3.78); $[\alpha]^{25}_D$ −135.3° (c 0.5, methanol); IR (neat) 1695 (C=O), 889 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.95 (d, 3, J = 7 Hz, CH_3), 1.68 (s, 3, CH_3), 4.75 and 4.82 (s's, 2, C=CH_2), 5.93 (d, 1, J = 10 Hz, HC=C), 6.68 ppm (d, 1, J = 10 Hz, HC=C); mass spectrum, m/e (relative intensity) 204 (32), 189 (37), 162 (38), 148 (20), 147 (48), 133 (29), 121 (37), 119 (21), 106 (44), 105 (55), 94 (44), 91 (83), 79 (100), 77 (63), 67 (91).

Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.34; H, 9.92.

Preparation of Enone 21. A solution of 0.1 g (0.490 mmol) of dienone **20** and 0.05 mL (0.490 mmol) of *tert*-butyl alcohol in 0.5 mL of ether was added dropwise to a mixture of 7.5 mg (1.078 g/atom) of lithium in 10 mL of ammonia at −40 °C. After stirring for 30 min, the reaction was quenched with excess NH_4Cl and the NH_3 allowed to evaporate. The ether solution was washed with water and dried ($MgSO_4$), and the solvent was removed to yield 0.107 g of crude enone **21**. Flash chromatography (silica gel, methylene chloride) afforded 0.072 g (72% yield) of enone **21**: $[\alpha]^{25}_D$ −20.7° (c 0.5, methanol); IR (neat) 1727 (C=O), 890 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.95 (d, 3, J = 7 Hz, CH_3), 1.78 (s, 3, CH_3), 4.73 and 4.89 ppm (s's, 2, C=CH_2); mass spectrum, m/e (relative intensity) 206 (2), 163 (3), 149 (2), 138 (3), 136 (6), 123 (6), 109 (10), 107 (9), 95 (13), 93 (16), 83 (14), 82 (100), 68 (79), 55 (39), 43 (8).

Preparation of Triene 22. To 0.62 mL of a 1.04 M solution of methylsulfinyl carbanion in Me_2SO was added a solution of 0.263 g (0.735 mmol) of methyltriphenylphosphonium bromide in 1 mL of Me_2SO under argon. After 5 min 0.1 g (0.490 mmol) of dienone **20** in 1 mL of Me_2SO was added, and the solution was stirred at room temperature for 35 min.[28] The mixture was then poured into an equal volume of water and extracted with pentane. The pentane extract was washed with 50% Me_2SO/H_2O, water, dried ($MgSO_4$), and plug filtered through silica gel, and the pentane was removed affording 87 mg (88% yield) of **22**: UV λ_{max}^{MeOH} 237 nm (log ϵ 4.33); IR (neat) 1647 (C=C), 881 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.85 (d, 3, J = 7 Hz, CH_3), 1.65 (s, 3, CH_3), 4.73 (m, 4, C=CH_2), 5.46 (d, 1, J = 10 Hz, HC=C), 6.1 ppm (d, 1, J = 10 Hz, HC=C); mass spectrum, m/e (relative intensity) 202 (15), 187 (10), 159 (13), 146 (16), 131 (33), 120 (33), 118 (36), 105 (49), 93 (19), 92 (25), 91 (100), 79 (33), 77 (36), 69 (51), 55 (48).

Anal. Calcd for $C_{15}H_{22}$: C, 89.04; H, 10.96. Found: C, 88.87; H, 11.09.

(−)-α-Acoradiene (1). A solution of triene **22** in 1 mL of ether was added dropwise to a solution of 38.3 mg (1.665 g/atom) of sodium in 20 mL of liquid ammonia under argon. After stirring 30 min, the reaction was quenched with NH_4Cl and the NH_3 allowed to evaporate. The ether solution was washed with water and dried ($MgSO_4$), and the ether was removed to afford 40.4 mg (100% yield, 80% pure by glpc) of α-acoradiene (**1**). An analytical sample was prepared by preparative GLPC (10% OV-101): $[\alpha]^{25}_D$ −39.6° (c 0.3 hexane); IR (neat) 1642 (C=C), 885 cm^{-1} (=CH_2); NMR ($CDCl_3$) 0.85 (d, 3, J = 7 Hz, CH_3), 1.68 (br s, 3, CH_3), 4.61 and 4.8 (s's, 2, C=CH_2), 5.21 ppm (m, 1, HC=C); mass spectrum, m/e (relative intensity) 204 (9), 189 (6), 161 (11), 147 (38), 121 (66), 119 (100), 107 (27), 105 (67), 93 (77), 91 (55), 77 (38), 67 (43), 55 (45), 43 (22).

Anal. Calcd for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.40; H, 11.89.

Registry No. **1**, 24048-44-0; **4**, 78247-16-2; **5**, 89-82-7; **6**, 53750-51-9; **7**, 84370-33-2; **7a**, 84370-45-6; **7b**, 84370-46-7; **9**, 84370-34-3; **10**, 84370-35-4; **11**, 84370-36-5; **13**, 84370-37-6; **14a**, 84370-38-7; **14b**, 84370-39-8; **15**, 84370-40-1; **17**, 84370-42-3; **20**, 84415-14-5; **21**, 84370-43-4; **22**, 84370-44-5; **16**, 84370-41-2; 2-diazopropane, 2684-60-8; 4-iodo-2-methyl-1-butene, 53750-52-0.

(28) If the reaction mixture was allowed to stir for a longer time, the yield decreased drastically.