

Experimental Section

General. Unless otherwise noted, all reactions were performed in oven-dried glassware, sealed with a rubber septum under an atmosphere of argon. Anhydrous tetrahydrofuran (THF), diethyl ether (Et_2O), and dichloromethane (CH_2Cl_2) were purchased from Kanto Chemical Co., Inc. Toluene, pyridine, and diisopropylamine ($i\text{-Pr}_2\text{NH}$) were distilled from CaH_2 . Hexamethylphosphoramide (HMPA) and dimethyl sulfoxide (DMSO) were distilled from CaH_2 under reduced pressure. Benzene (C_6H_6) and methanol (MeOH) were distilled under argon immediately prior to use. Unless otherwise mentioned, materials were obtained from commercial suppliers and used without further purification. Organic extracts were dried over anhydrous MgSO_4 with stirring, filtered through Celite, and concentrated under reduced pressure with the aid of a rotary evaporator. Flash chromatography was carried out using Merck 60 (230–400 mesh) or Cica 60 (spherical/40–100 μm) silica gel. Reaction mixture and chromatography fractions were analyzed by TLC using precoated silica gel 60 F_{254} plates (Merck). Compounds were visualized under a ultraviolet lamp (254 nm) and/or by staining with *p*-anisaldehyde (in EtOH), phosphomolybdic acid (in EtOH), or ammonium molybdate (in 10% H_2SO_4). IR spectra were recorded as liquid films on NaCl plates unless otherwise noted. ^1H NMR spectra were obtained in CDCl_3 at 300 or 400 MHz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane or relative internal CHCl_3 (δ 7.26). *J* values are given in Hertz.

(3aR*,7aS*)-3,3-Dimethyl-3a,4,7,7a-tetrahydroisobenzofuranone (22). A stirred solution of 1,2,3,6-tetrahydrophthalic anhydride (**21**) (12.0 g, 79.0 mmol) in MeOH (120 mL) was refluxed for 3 h, and then the solvent was removed under reduced pressure to give the corresponding half ester (14.6 g, 100%), which was used to the next step without purification.

To a stirred solution of MeMgI , prepared from Mg (26.2 g, 1.08 mol) and MeI (62 mL, 1.00 mol), in Et_2O (300 mL) was added dropwise a Et_2O solution (400 mL) of the above half ester (36.0 g, 0.2 mol) under reflux. After 0.5 h of stirring, 10% H_2SO_4 solution was added until

the starting material disappeared. The mixture was extracted with Et₂O, and the ethereal layer was washed with saturated NaHCO₃, saturated Na₂S₂O₃, and brine. After removal of the solvent, the residue was recrystallized from Et₂O to afford the lactone **22** (24.8 g, 76%) as colorless prisms, mp 68–69 °C. IR (CHCl₃) cm⁻¹: 1755. ¹H NMR (300 MHz): δ 5.73–5.84 (2H, m), 3.09 (1H, tdd, *J*=8.0, 4.5, 1.0), 2.36–2.55 (2H, m), 2.08–2.30 (2H, m), 1.82–1.94 (1H, m), 1.44 (3H, s), 1.39 (3H, s). ¹³C NMR (75 MHz): δ 178.85, 125.61, 125.20, 85.24, 40.94, 37.82, 27.12, 23.21, 22.41, 21.94. MS (*m/z*): 166 (*M*⁺). *Anal.* Calcd for C₁₀H₁₄O₂: C, 72.25; H, 8.48. Found: C, 72.12; H, 8.49.

(3a*R,7a*R**)-7a-(2-Bromo-2-propenyl)-3,3-dimethyl-3,4,7,7a-tetrahydroisobenzofuranone**

(23). To a stirred solution of LDA, prepared from BuLi (19.7 mL, 1.6 M in hexane, 30.9 mmol) and *i*-Pr₂NH (4.76 mL, 33.9 mmol) at –78 °C, in THF (25 mL) was added a THF solution (21 mL) of **22** (3.41 g, 20.6 mmol) at –78 °C. The mixture was allowed to warm to rt. After 1 h of stirring, HMPA (4.3 mL, 24.7 mmol) was added at the same temperature, and then the mixture was recooled to –78 °C. 2,3-Dibromopropene (4.3 mL, 41.1 mmol) was added at –78 °C, and the mixture was stirred at –30 °C for 5 h. After addition of saturated NaHCO₃ at –78 °C, and the resulting mixture was allowed to warm to rt. The mixture was extracted with Et₂O, and the ethereal layer was washed with brine, dried and evaporated to yield an oil, which was chromatographed. Elution with a 6:1 mixture of hexane–EtOAc furnished **23** (5.37 g, 92%) as prisms, mp 56–59 °C. IR (neat) cm⁻¹: 1765. ¹H NMR (300 MHz): δ 5.79–5.86 (1H, m), 5.65–5.73 (2H, m), 5.56–5.58 (1H, m), 3.20 (1H, dd, *J*=14.0, 0.5), 2.56–2.61 (1H, m), 2.55 (1H, d, *J*=14.0), 2.19–2.42 (2H, m), 1.98–2.12 (2H, m), 1.46 (3H, s), 1.29 (3H, s). ¹³C NMR (75 MHz): δ 179.85, 128.80, 125.77, 122.62, 121.83, 85.22, 46.63, 44.06, 41.64, 31.28, 29.73, 23.04, 20.55. MS (*m/z*): 269 (*M*⁺–CH₃), 205 (*M*⁺–Br). *Anal.* Calcd for C₁₃H₁₇BrO₂: C, 54.75; H, 6.00; Br, 28.02. Found: C, 54.82; H, 6.09; Br, 28.10.

(3a*R,7a*R**)-3,3-Dimethyl-7a-(2-propynyl)-3a,4,7,7a-tetrahydroisobenzofuranone (16).** The desired alkyne **16** (25.8 g, 85%), a colorless oil, was obtained from **22** (24.9 g, 150 mmol) and propargyl bromide (20 mL, 225 mmol) in the presence of LDA, prepared from BuLi (125 mL, 1.6 M in hexane, 195 mmol) and diisopropylamine (30 mL, 214 mmol), and HMPA (29 mL, 165 mmol) in a manner similar to that described above. An analytical sample was recrystallized from Et₂O to give **16**, prisms, mp 110–112 °C. IR (neat) cm⁻¹: 3220, 2100 and 1750. ¹H NMR (300 MHz): δ 5.67–5.85 (2H, m), 2.75 (1H, d, *J*=8.0), 2.66 (1H, dd, *J*=16.0, 2.5), 2.43 (1H, dd, *J*=16.0, 2.5), 2.26–2.38 (2H, m), 2.02–2.17 (2H, m), 2.04 (1H, t, *J*=2.5), 1.46 (3H, s), 1.30 (3H, s). ¹³C NMR (75 MHz): δ 179.22, 125.52, 122.97, 85.18, 79.92, 71.47, 43.81, 43.38, 30.39, 29.50, 26.91, 23.01, 20.59. MS (*m/z*): 204 (*M*⁺). *Anal.* Calcd for C₁₃H₁₆O₂: C, 76.44; H, 7.89. Found: C, 76.45; H, 7.84.

(4*R,5*R**)-4-Acetoxymethyl-4-(2-bromo-2-propenyl)-5-(1-hydroxy-1-methylethyl)cyclohexene (24).** To a stirred suspension of LAH (122 mg, 3.20 mmol) in Et₂O (10 mL) was added dropwise a solution of **23** (456 mg, 1.60 mmol) in Et₂O (5 mL). After 15 h of stirring, the solution was cooled to 0 °C, and H₂O (0.12 mL), 10% NaOH (0.12 mL) and H₂O (0.36 mL) were added successively in this order. After 0.5 h of stirring, MgSO₄ was added, and then the resulting suspension was filtered through Celite. The residue was washed several times with Et₂O, and then the combined filtrates were concentrated to provide the product, which was chromatographed. Elution with a 1:1 mixture of hexane–EtOAc gave rise to the corresponding diol (379 mg, 82%) as a yellowish powder. An analytical sample was recrystallized from Et₂O to give the diol, prisms, mp 84–87 °C. IR (neat) cm⁻¹: 3300 (br). ¹H NMR (300 MHz): δ 5.62–5.66 (4H, m), 3.85 (1H, d, *J*=12.0), 3.70 (1H, d, *J*=12.0), 3.50–3.80 (1H, br s), 2.93 (1H, d, *J*=12.0), 2.56 (1H, d, *J*=12.0), 2.28–2.42 (1H, m), 2.20–2.65 (1H, br s), 2.08–2.14 (1H, m), 2.02–2.08 (2H,

m), 1.77 (1H, dd, $J=8.0, 3.0$), 1.38 (3H, s), 1.33 (3H, s). ^{13}C NMR (75 MHz): δ 129.24, 125.35, 124.70, 122.10, 75.48, 65.43, 47.40, 47.13, 42.11, 34.58, 30.13, 26.36, 25.45. MS (m/z): 270 ($\text{M}^+ - \text{H}_2\text{O}$). *Anal.* Calcd for $\text{C}_{13}\text{H}_{21}\text{BrO}_2$: C, 53.99; H, 7.31; Br, 27.63. Found: C, 54.20; H, 7.44; Br, 27.56.

To a stirred solution of the above diol (112 mg, 0.389 mmol) in pyridine (0.32 mL) was added Ac_2O (0.11 mL, 1.17 mmol), and stirring was continued for 16 h at rt. The resulting solution was diluted with H_2O , and the resulting mixture was extracted several times with Et_2O . The combined extracts were washed with 10% HCl, saturated NaHCO_3 , and brine, dried and evaporated to leave an oil, which was chromatographed. Elution with a 2:1 mixture of hexane– EtOAc produced the acetate **24** (119 mg, 93%) as a colorless oil. IR (neat) cm^{-1} : 3479 (br) and 1716. ^1H NMR (300 MHz): δ 5.58–5.71 (4H, m), 4.43 (1H, d, $J=11.0$), 4.32 (1H, d, $J=11.0$), 2.82 (2H, s), 2.03–2.43 (5H, m), 2.08 (3H, s), 1.94 (1H, dd, $J=7.0, 3.0$), 1.32 (3H, s), 1.29 (3H, s). ^{13}C NMR (75 MHz): δ 170.99, 129.34, 125.73, 124.38, 121.80, 75.04, 68.16, 46.90, 46.49, 40.30, 33.83, 32.10, 26.39, 25.62, 21.05. MS (m/z): 312 ($\text{M}^+ - \text{H}_2\text{O}$). HRMS (M/Z) calcd for $\text{C}_{15}\text{H}_{21}\text{BrO}_2$: 312.0725. found: 312.0722.

(4*R,5*R**)-4-Acetoxymethyl-5-(1-hydroxymethylethyl)-4-(2-propynyl)cyclohexene (25).** The desired diol (11.2 g, 99%), a white powder, was produced from **16** (11.0 g, 54.1 mmol) with LAH (4.1 g, 108 mmol) in a manner similar to that described above. An analytical sample was recrystallized from Et_2O to give the diol, prisms, mp 102–103 °C. IR (neat) cm^{-1} : 3400 (br), 3305, and 2105. ^1H NMR (300 MHz): δ 5.60–5.64 (2H, m), 3.84 (1H, d, $J=10.0$), 3.60–3.75 (1H, br s), 3.62 (1H, d, $J=10.0$), 2.50–2.60 (1H, br s), 2.51 (1H, dd, $J=16.0, 2.5$), 2.43 (1H, dd, $J=16.0, 2.5$), 2.24–2.37 (1H, m), 2.11–2.15 (1H, m), 2.05–2.09 (2H, m), 2.05 (1H, t, $J=2.5$), 1.95 (1H, dd, $J=7.0, 5.0$), 1.43 (3H, s), 1.32 (3H, s). ^{13}C NMR (75 MHz): δ 125.46, 124.57, 82.29, 74.99, 71.33,

66.84, 46.34, 41.01, 33.51, 32.28, 28.29, 27.09, 25.53. MS (m/z): 208 (M^+). *Anal.* Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.67. Found: C, 74.88; H, 9.67.

Following the above procedure, **25** (14.2 g, 100%), a white powder, was obtained from the diol (11.1 g, 53.1 mmol), Ac_2O (15 mL, 160 mmol) and pyridine (50 mL). IR (neat) cm^{-1} : 3500 (br), 3310, 2120 and 1740. 1H NMR (300 MHz): δ 5.56–5.70 (2H, m), 4.32 (1H, d, $J=10.0$), 4.29 (1H, d, $J=10.0$), 2.75 (1H, dd, $J=16.0, 2.5$), 2.42 (1H, dd, $J=16.0, 2.5$), 1.94–2.29 (7H, m), 2.06 (3H, s), 1.33 (3H, s), 1.28 (3H, s). ^{13}C NMR (75 MHz): δ 171.08, 125.90, 124.65, 82.70, 74.73, 71.53, 66.40, 47.66, 39.43, 33.56, 33.50, 27.50, 26.30, 26.27, 20.88. MS (m/z): 250 (M^+). HRMS (M/Z) calcd for $C_{15}H_{22}O_3$: 250.1568. found: 250.1549.

(1*R,2*R**,4*S**)-1-Acetoxymethyl-2-(1-hydroxy-1-methylethyl)-5-**

methylenebicyclo[2.2.2]octane (26) and (1*S,5*R**,8*R**)-5-Acetoxymethyl-8-(1-hydroxy-1-methylethyl)-7-tributylstannylmethylbicyclo[3.2.1]oct-2-ene (27).** To a stirred solution of **25** (14.9 g, 61.3 mmol) in a degassed C_6H_6 (1 L) was added slowly a degassed C_6H_6 solution (30 mL) of Bu_3SnH (18.2 mL, 67.7 mmol) and AIBN (250 mg, 1.5 mmol) over a period of 2 h under reflux. After 2 h of refluxing, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (1 L), and then silica gel (1 kg) was added. After being stirred vigorously for 2 days, the mixture was filtered through Celite. The filtrate was concentrated to give an oil, which was chromatographed. Elution with a 3:1 mixture of hexane–EtOAc afforded **27** (16.6 g, 50%) followed by **26**, containing a small amount of tin species. Washing of the crude **26** with hexane provided the bicyclo[2.2.2]octane compound **26** (6.38 g, 32%) as a white powder. **Compound 26**, mp 67–69 °C. IR (neat) cm^{-1} : 3470 (br), 1735, and 1720. 1H NMR (300 MHz): δ 4.77 (1H, q, $J=2.0$), 4.63 (1H, q, $J=2.0$), 4.21 (1H, d, $J=11.0$), 4.12 (1H, d, $J=11.0$), 2.27–2.32 (1H, m), 2.10–2.26 (2H, m), 2.07 (3H, s), 1.73–1.94 (3H, m), 1.58–1.72 (3H, m), 1.33–1.43 (1H, m), 1.32 (3H, s), 1.26 (1H, ddd, $J=11.0, 9.0, 2.0$), 1.18 (3H, s). ^{13}C NMR (75 MHz): δ 171.03,

150.63, 105.66, 74.78, 70.50, 49.24, 41.73, 37.73, 36.29, 32.59, 31.57, 26.09, 24.24, 23.87, 20.94. MS (m/z): 234 ($M^+ - H_2O$). *Anal.* Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.58. Found: C, 71.22; H, 9.39. **Compound 27**; 1H NMR (300 MHz, C_6D_6): δ 5.82-5.92 (1H, m), 5.38 (1H, dt, $J=9.0$, 3.0), 4.32 (2H, s), 2.51 (1H, dq, $J=17.0$, 2.0), 2.18 (1H, qd, $J=8.0$, 4.0), 2.04 (1H, dd, $J=6.0$, 3.0), 1.98 (1H, d, $J=3.0$), 1.83-1.92 (2H, m), 1.75 (3H, s), 1.74 (1H, ddd, $J=17.0$, 4.0, 2.0), 1.51-1.63 (6H, m), 1.30-1.45 (7H, m), 1.28 (3H, s), 1.27 (3H, s), 0.80-1.00 (16H, m), 0.44-0.56 (1H, br s). MS (m/z): 542 (M^+). HRMS (M/Z) calcd for $C_{27}H_{50}O_3^{120}Sn$: 542.2782. found: 542.2799.

4,5-Dihydroisobenzofuranone (33). A stirred solution of phthalide **31** (9.5 g, 70 mmol) in MeOH (70 mL) was added 2N NaOH (70 mL), and the resulting mixture was refluxed for 1 h. After having been cooled to rt, the mixture was well dried by vacuum pump. The dried white powder was used in the next step without purification.

To a stirred solution of the above product in MeOH (40 mL) was added liquid NH_3 (ca. 250 mL), followed by sodium (4.8 g) at $-78^\circ C$. After being refluxed for 1 h, to the mixture was carefully added MeOH (20 mL) followed by H_2O (150 mL). The resulting mixture was stirred at rt for 9 h, and then the solution was acidified with 10% HCl. The resulting mixture was extracted with EtOAc, and the organic layer was washed with brine, dried with Na_2SO_4 , and evaporated to leave an oil, which was used in the next reaction without purification.

To a stirred solution of the above acid in CH_2Cl_2 (100 mL) were added DCC (13.7 mL, 82 mmol) followed by DMAP (460 mg, 3.7 mmol), and then the resulting mixture was allowed to stand at rt for 1 h. After the reaction was completed, the mixture was filtered through Celite, and the residue was washed several times with $CHCl_3$. The combined filtrates were concentrated to afford the residue, which was chromatographed. Elution with a 1:1 mixture of hexane-EtOAc afforded **33** (7.9 g, 77% for 3 steps) as a white powder. An analytical sample was recrystallized from acetone to give **33**, needles, mp $54-57^\circ C$. IR (neat) cm^{-1} : 1732. 1H NMR (300 MHz): δ 6.20 (1H, dt, $J=9.0$, 1.5), 5.94 (1H, dt, $J=9.0$, 4.0), 4.81 (2H, s), 2.54-2.64 (2H, m), 2.42-2.52

(2H, m). ^{13}C NMR (75 MHz): δ 171.93, 158.87, 128.66, 124.44, 116.63, 71.36, 22.00, 20.96. MS (m/z): 136 (M^+). HRMS (M/Z) calcd for $\text{C}_8\text{H}_8\text{O}_2$: 136.0524. found: 136.0520.

(3a*R,7a*S**)-3,3-Dimethyl-3a,6,7,7a-tetrahydroisobenzofuranone (35).** To a stirred solution of **33** (7.43 g, 54.6 mmol) in MeOH (300 mL) was added NaBH_4 (2.07 g, 54.6 mmol) at 0 °C. After 12 h of stirring, the solvent was removed in vacuo. The residue was diluted with Et_2O , and the resulting solution was acidified with 10% HCl. After separation, the organic layer was washed with saturated NaHCO_3 , brine, dried, and evaporated to yield an oil, which was chromatographed. Elution with a 2:1 mixture of hexane–acetone furnished the lactones **34**, a yellow oil, as a 2:1 mixture of *cis* and *trans* isomer, which was used in the next step without separation.

To a stirred solution of MeMgI , prepared from Mg (3.7 g, 151 mmol) and MeI (9.5 mL, 151 mmol), in Et_2O (60 mL) was added dropwise a Et_2O solution (40 mL) of the above product **34** (6.96 g, 50.5 mmol) under gentle refluxing. After 0.5 h of stirring, the reaction mixture was quenched with saturated NH_4Cl , and then the solution was acidified with 10% HCl. The resulting mixture was extracted with EtOAc, and the organic layer was washed with saturated NaHCO_3 , dried, and evaporated to leave the corresponding diol, which was used in the next reaction without purification: ^1H NMR (300 MHz): δ 5.71–5.82 (2H, m), 3.91 (1H, dd, $J=11.0, 9.0$), 3.57 (1H, dd, $J=11.0, 3.5$), 2.76–3.10 (2H, m), 2.28–2.41 (2H, m), 1.95–2.04 (2H, m), 1.58–1.84 (2H, m), 1.38 (3H, s), 1.33 (3H, s).

To a stirred suspension of PDC (30 g, 78.9 mmol) and Florisil (60 g) in CH_2Cl_2 (300 mL) was added a CH_2Cl_2 (50 mL) solution of the above diol, and then the resulting mixture was stirred for 48 h. The mixture was filtered through Celite, and the residue was rinsed with EtOAc. After removal of the solvent, the product was chromatographed. Elution with a 3:1 mixture of hexane–EtOAc provided **35** (3.22 g, 38% for 3 steps from **33**) as a white powder. An analytical sample was recrystallized from Et_2O to furnish **35**, prisms, mp 76–77 °C. IR (neat) cm^{-1} : 1732.

^1H NMR (300 MHz): δ 5.93-6.02 (1H, m), 5.58-5.65 (1H, m), 3.08 (1H, dt, $J=7.5$, 4.0), 2.76 (1H, ddd, $J=7.5$, 2.5, 2.0), 1.91-2.12 (3H, m), 1.69-1.81 (1H, m), 1.46 (3H, s), 1.38 (3H, s). ^{13}C NMR (75 MHz): δ 178.03, 130.60, 123.62, 85.39, 43.44, 39.04, 27.97, 24.51, 20.93, 20.43. MS (m/z): 166 (M^+). Anal. Calcd for $\text{C}_{10}\text{H}_{14}\text{O}_2$: C, 72.26; H, 8.49. Found: C, 72.13; H, 8.50.

(3a*R,7a*R**)-3,3-Dimethyl-7a-(2-propynyl)-3a,6,7,7a-tetrahydroisobenzofuranone (36).** To a stirred solution of *i*-Pr₂NH (3.7 mL, 26.7 mmol) in THF (150 mL) was added BuLi (15.5 mL, 1.6 M in hexane, 24.3 mmol) at -78°C , and the mixture was stirred at 0°C for 15 min, and at -78°C for 15 min. After addition of a THF solution (10 mL) of **35** (2.68 g, 16.2 mmol) at -78°C , the mixture was allowed to warm to rt. After being stirred for 1 h, HMPA (3.4 mL, 19.4 mmol) was added at rt, and then propargyl bromide (2.2 mL, 24.3 mmol) was added at -78°C . The reaction mixture was quenched with saturated NaHCO_3 , and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to provide an oil, which was chromatographed. Elution with a 3:1 mixture of hexane-EtOAc gave the desired product **36**, which was recrystallized from Et_2O to give **36** (2.20 g, 67 %) as yellow prisms, mp $95-97^\circ\text{C}$. IR (neat) cm^{-1} : 3243, 2115 and 1749. ^1H NMR (300 MHz): δ 5.92-6.00 (1H, m), 5.60-5.68 (1H, m), 2.97-3.02 (1H, m), 2.55 (1H, dd, $J=16.0$, 2.5), 2.40 (1H, dd, $J=16.0$, 2.5), 1.97-2.21 (2H, m), 2.08 (1H, t, $J=2.5$), 1.68-1.85 (2H, m), 1.55 (3H, s), 1.30 (3H, s). ^{13}C NMR (75 MHz): δ 178.81, 127.90, 122.05, 83.83, 79.88, 71.44, 46.68, 45.70, 29.38, 27.06, 25.82, 24.92, 20.32. MS (m/z): 205 ($\text{M}^+\text{+H}$). Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$: C, 76.44; H, 7.90. Found: C, 76.39, H, 8.03.

(3*R,4*R**)-4-Acetoxymethyl-3-(1-hydroxy-1-methylethyl)-4-(2-propyl)cyclohexene (37).** To a stirred suspension of LAH (710 mg, 18.7 mmol) in Et_2O (80 mL) was added a Et_2O solution (10 mL) of **36** (1.90 g, 934 μmol) at rt, and the resulting mixture was stirred at rt for 4 h. The reaction was quenched by successive addition of H_2O (0.7 mL), 15% NaOH, (0.7 mL) and H_2O

(2.1 mL). The mixture was dried with MgSO_4 , filtered through Celite. The filtrate was concentrated to leave an oil (1.64 g, 84%), which was used in the next reaction without purification. An analytical sample was recrystallized from Et_2O to give the corresponding diol, as prisms, mp 191–121 °C. IR (neat) cm^{-1} : 3305, 3300 (br) and 2114. ^1H NMR (300 MHz): δ 5.74–5.82 (1H, m), 5.53–5.61 (1H, m), 4.71 (1H, br s), 3.92 (1H, br s), 3.78 (1H, dd, $J=11.0, 1.0$), 3.59 (1H, d, $J=11.0$), 2.50 (1H, dd, $J=15.5, 2.5$), 2.27 (1H, ddd, $J=15.5, 2.5, 1.0$), 2.03–2.19 (2H, m), 1.98 (1H, t, $J=2.5$), 1.93–1.99 (1H, m), 1.48–1.65 (2H, m), 1.34 (3H, s), 1.29 (3H, s). ^{13}C NMR (75 MHz): δ 128.84, 125.69, 82.02, 75.22, 70.24, 65.85, 50.73, 40.79, 33.38, 25.98, 25.10, 23.83, 21.52. MS (m/z): 191 ($\text{M}^+ - \text{OH}$). Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_2$: C, 74.96; H, 9.68. Found: C, 74.61; H, 9.55.

A solution of the above diol (1.03 g, 4.97 mmol) and Ac_2O (1.4 mL, 14.9 mmol) in pyridine (4 mL) was stirred at rt for 4 days. The reaction mixture was diluted with Et_2O , and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with 10 % HCl, brine, dried, and evaporated to leave an oil, which was chromatographed. Elution with a 2:1 mixture of hexane– EtOAc afforded **37** (1.28 g, 100%) as colorless oil. IR (neat) cm^{-1} : 3478 (br), 3295, 2114 and 1716. ^1H NMR (300 MHz): δ 5.75–5.83 (1H, m), 5.55–5.63 (1H, m), 4.38 (1H, d, $J=10.0$), 4.28 (1H, d, $J=10.0$), 2.62 (1H, dd, $J=15.5, 2.5$), 2.43–2.47 (1H, m), 2.38 (1H, dd, $J=15.5, 2.5$), 2.08 (3H, s), 2.00–2.08 (4H, m), 1.65–1.81 (2H, m), 1.35 (3H, s), 1.25 (3H, s). ^{13}C NMR (75 MHz): δ 171.12, 127.93, 127.17, 81.78, 74.75, 71.26, 67.52, 50.68, 39.19, 32.77, 27.12, 26.95, 26.91, 21.75, 20.96. MS (m/z): 250 (M^+). Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_3$: C, 71.97; H, 8.86. Found C, 72.14; H, 8.80.

Radical Cyclization of 37. To a solution of **37** (333 mg, 1.33 mmol) in degassed C_6H_6 (100 mL) was added slowly a degassed C_6H_6 solution (0.4 mL) of Bu_3SnH (0.4 mL, 1.46 mmol) and AIBN (20 mg, 0.133 mmol) over a period of 1 h under reflux, and the mixture was refluxed for 2 h. After removal of the solvent in vacuo, the residue was dissolved in CH_2Cl_2 (30 mL), and then

silica gel (40 g) was added. After stirred vigorously for 2 days, the mixture was filtered through Celite. The filtrate was concentrated to furnish an oil, which was chromatographed. Elution with a 5:1 followed by 3:1 mixture of hexane–EtOAc gave rise to the tricyclo[3.2.1.0^{2,7}]octane product **38** (186 mg, 26%) followed by the bicyclo[3.2.1]octane product **39** (42 mg, 17%) and the desired bicyclo[2.2.2]octane product **26** (156 mg, 47%). **Compound 39**: IR (neat) cm⁻¹: 3502(br) and 1717. ¹H NMR (300 MHz): δ 4.83–4.87 (1H, m), 4.76–4.80 (1H, m), 4.14 (1H, d, *J*=10.0), 4.08 (1H, d, *J*=10.0), 2.74–2.80 (1H, m), 2.32 (1H, dq, *J*=16.0, 2.0), 2.14–2.27 (2H, m), 2.07 (3H, s), 2.04 (1H, tdd, *J*=12.0, 6.0, 2.0), 1.48–1.74 (4H, m), 1.41 (3H, s), 1.31 (3H, s), 1.20–1.42 (2H, m). ¹³C NMR (75 MHz): δ 171.20, 152.83, 104.09, 72.93, 70.98, 54.57, 45.90, 44.28, 42.62, 32.91, 31.45, 28.46, 26.88, 20.90, 17.77. MS (*m/z*): 234 (*M*⁺–H₂O). HRMS (*M/Z*) calcd for C₁₅H₂₂O₂: 234.1619. found: 234.1614. **Compound 38**: IR (neat) cm⁻¹: 3479 (br) and 1717. ¹H NMR (400 MHz): δ 4.03 (1H, d, *J*=11.0), 3.87 (1H, d, *J*=11.0), 2.07 (3H, s), 1.95–2.03 (3H, m), 1.61–1.73 (2H, m), 1.39–1.53 (8H, m), 1.34 (3H, s), 1.29 (3H, s), 1.26–1.37 (6H, m), 1.08–1.19 (1H, m), 1.05 (1H, d, *J*=13.0), 1.02 (1H, d, *J*=13.0), 0.76–0.93 (16H, m), 0.62 (1H, dt, *J*=7.0, 2.5). ¹³C NMR (75 MHz): δ 171.43, 72.35, 70.24, 51.76, 44.05, 42.01, 30.42, 30.25, 29.26, 28.18, 27.44, 24.07, 22.70, 21.61, 20.88, 17.42, 16.72, 13.65, 9.56. MS (*m/z*): 525 (*M*⁺–OH). HRMS (*M/Z*) calcd for C₂₇H₄₉O₂¹²⁰Sn: 525.2755. found: 525.2726.

(1*R,2*S**,4*S**)-1-Acetoxymethyl-2-isopropenyl-5-methylenebicyclo[2.2.2]octane (40)**. To a stirred solution of **26** (2.85 g, 11.3 mmol) in pyridine (50 mL) was added POCl₃ (1.6 mL, 17.0 mmol), and stirring was continued for 20 h at rt. The mixture was diluted with H₂O, and the resulting solution was extracted several times with Et₂O. The combined extracts were washed with 10% HCl, saturated NaHCO₃, and brine, dried, and evaporated to afford an oil, which was chromatographed. Elution with a 20:1 mixture of hexane–EtOAc gave rise to the olefin **40** (2.63 g, 99%) as a colorless oil. IR (neat) cm⁻¹: 1740. ¹H NMR (300 MHz): δ 4.78–4.86 (3H, m), 4.66 (1H, q, *J*=2.0), 3.78 (1H, d, *J*=10.0), 3.73 (1H, d, *J*=10.0), 2.36 (1H, ddd, *J*=10.0, 7.5, 2.0), 2.27–

2.32 (1H, m), 2.21-2.25 (2H, m), 2.04 (3H, s), 1.55-1.90 (8H, m), 1.25-1.37 (1H, m). ^{13}C NMR (75 MHz): δ 171.31, 150.95, 146.85, 113.78, 105.86, 69.80, 45.84, 40.24, 36.75, 36.15, 33.35, 26.01, 23.43, 21.91, 20.81. MS (m/z): 234 (M^+). *Anal.* Calcd for $\text{C}_{15}\text{H}_{22}\text{O}_2$: C, 76.88; H, 9.46. Found: C, 76.83; H, 9.32.

(1*R,2*S**,4*S**)-2-Isopropenyl-5-methylenebicyclo[2.2.2]octane-1-carbaldehyde (41).** To a stirred solution of **40** (2.63 g, 11.2 mmol) in MeOH (120 mL) was added K_2CO_3 (7.8 g, 56.2 mmol), and stirring was continued at rt for 18 h. The solvent was removed under reduced pressure. The reaction mixture was extracted with Et_2O , and the ethereal layer was washed with 10% HCl, saturated NaHCO_3 , and brine, dried and evaporated to furnish an oil, which was chromatographed. Elution with a 5:1 mixture of hexane–EtOAc gave the product (2.18 g, 100%) as a colorless oil. An analytical sample was recrystallized from Et_2O to give the alcohol, needles, mp 45–47 °C. IR (neat) cm^{-1} : 3280 (br). ^1H NMR (300 MHz): δ 4.84-4.90 (2H, m), 4.80 (1H, q, $J=2.0$), 4.67 (1H, q, $J=2.0$), 3.39 (1H, dd, $J=11.0, 5.5$), 3.27 (1H, dd, $J=11.0, 5.5$), 2.26-2.41 (3H, m), 2.11 (1H, dt, $J=15.5, 2.5$), 1.87 (3H, s), 1.53-1.88 (5H, m), 1.46 (1H, t, $J=6.0$), 1.17-1.29 (1H, m). ^{13}C NMR (75 MHz): δ 151.33, 148.71, 113.57, 105.87, 69.16, 46.25, 40.18, 38.81, 36.32, 33.19, 26.16, 23.46, 21.43. MS (m/z): 192 (M^+). *Anal.* Calcd for $\text{C}_{13}\text{H}_{20}\text{O}$: C, 81.19; H, 10.48. Found: C, 81.13; H, 10.53.

To a stirred solution of the above alcohol (314 mg, 1.64 mmol) in Et_3N (6 mL), DMSO (6 mL) and CH_2Cl_2 (6 mL) was added $\text{SO}_3\cdot\text{Py}$ (4.0 g), and stirring was continued for 24 h at rt. The resulting solution was diluted with water, and the resulting mixture was extracted several times with Et_2O . The combined extracts were washed with 10% HCl, saturated NaHCO_3 , and brine, dried, and evaporated to give as oil, which was chromatographed. Elution with a 5:1 mixture of hexane–EtOAc furnished **41** (301 mg, 97%) as a colorless oil. IR (neat) cm^{-1} : 1720. ^1H NMR (300 MHz): δ 9.48 (1H, s), 4.88 (1H, q, $J=2.0$), 4.83-4.85 (1H, m), 4.77-4.80 (1H, m), 4.75 (1H,

q, $J=2.0$), 2.57 (1H, t, $J=9.0$), 2.49 (1H, ddt, $J=15.0, 3.0, 1.5$), 2.33-2.39 (1H, m), 2.16 (1H, dt, $J=15.0, 2.0$), 2.03-2.14 (1H, m), 1.95 (1H, dddd, $J=12.0, 10.0, 4.0, 2.0$), 1.75 (3H, s), 1.52-1.80 (4H, m). ^{13}C NMR (75 MHz): δ 205.56, 148.49, 145.94, 112.85, 107.31, 48.74, 45.08, 37.64, 36.17, 33.39, 25.44, 22.45, 20.44. MS (m/z): 190 (M^+). HRMS (M/Z) calcd for $\text{C}_{13}\text{H}_{18}\text{O}$: 190.1357. found: 190.1364.

(1*R,2*S**,4*S**)-1-[(1*S**,3*Z*)-1-Hydroxy-4-triethylsilyloxy-3,5-hexadienyl]-2-isopropenyl-5-methylenebicyclo[2.2.2]octane (42a)** and **(1*R**,2*S**,4*S**)-1-[(1*R**,3*Z*)-1-Hydroxy-4-triethylsilyloxy-3,5-hexadienyl]-2-isopropenyl-5-methylenebicyclo[2.2.2]octane (42b)**. To a stirred solution of 3-triethylsilyloxy-1,4-pentadiene (2.2 mL, 8.09 mmol) in THF (60 mL) was added *s*-BuLi (8.05 mL, 1.0 M in hexane, 8.05 mmol) at $-78\text{ }^{\circ}\text{C}$. After 0.5 h of stirring, a solution of **41** (1.10 g, 5.78 mmol) in THF (10 mL) was added at the same temperature. The reaction mixture was quenched with saturated NH_4Cl , and the mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to leave an oil, which was chromatographed. Elution with a 15:1 mixture of hexane– Et_2O afforded **42b** (0.575 g, 25%), an colorless oil, followed by **42a** (1.63 g, 73%) as a colorless oil. **Compound 42a**; IR (neat) cm^{-1} : 3425 (br). ^1H NMR (300 MHz): δ 6.19 (1H, dd, $J=16.0, 10.0$), 5.30 (1H, dd, $J=16.0, 1.0$), 4.98 (1H, dd, $J=10.0, 1.0$), 4.78-4.90 (4H, m), 4.67 (1H, q, $J=2.0$), 3.41 (1H, dd, $J=10.0, 2.0$), 2.14-2.38 (5H, m), 2.08 (1H, dq, $J=16.0, 2.0$), 1.87 (3H, s), 1.60-1.88 (5H, m), 1.57 (1H, ddd, $J=12.0, 7.5, 2.0$), 1.30-1.44 (1H, m), 1.00 (9H, t, $J=7.5$), 0.73 (6H, q, $J=7.5$). ^{13}C NMR (75 MHz): δ 151.69, 151.05, 148.74, 135.66, 114.24, 112.63, 112.31, 105.69, 75.72, 47.77, 41.32, 37.48, 36.05, 33.91, 28.26, 26.38, 22.43, 21.09, 6.76, 5.47. MS (m/z): 388 (M^+). *Anal.* Calcd for $\text{C}_{24}\text{H}_{40}\text{O}_2\text{Si}$: C, 74.16; H, 10.37. Found: C, 74.26; H, 10.22. **Compound 42b**; IR(neat) cm^{-1} : 3430 (br). ^1H NMR (300 MHz): δ 6.20 (1H, dd, $J=16.0, 10.0$), 5.30 (1H, dd, $J=16.0, 1.0$), 4.83-5.00 (4H, m), 4.81 (1H, q, $J=2.0$), 4.69 (1H, q, $J=2.0$), 3.39 (1H, dd, $J=10.0, 2.0$), 2.61 (1H, ddd, $J=10.0, 9.0, 1.0$), 2.38-2.47 (1H, m), 2.26-2.36 (2H, m), 2.05-2.17 (2H, m), 1.88 (3H, s), 1.49-

1.91 (6H, m), 1.30-1.42 (1H, m), 1.00 (9H, t, $J=7.5$), 0.73 (6H, q, $J=7.5$). ^{13}C NMR (75 MHz): δ 151.67, 150.49, 149.26, 135.82, 114.28, 112.85, 112.14, 106.01, 74.78, 46.10, 41.39, 36.06, 35.82, 33.54, 27.74, 26.39, 24.10, 20.87, 6.79, 5.47. MS (m/z): 388 (M^+). *Anal.* Calcd for $\text{C}_{24}\text{H}_{40}\text{O}_2\text{Si}$: C, 74.16; H, 10.37. Found: C, 74.34; H, 10.17.

(1*R,2*S**,4*S**)-1-[(1*S**,3*Z*)-1-Acetoxy-4-triethylsilyloxy-3,5-hexadienyl]-2-isopropenyl-5-methylenebicyclo[2.2.2]octane (43).** To a stirred solution of **42a** (2.40 g, 6.17 mmol) and DMAP (1.5 g, 12.4 mmol) in CH_2Cl_2 (40 mL) was added Ac_2O (0.87 mL, 9.26 mmol), and stirring was continued for 24 h at rt. The reaction was quenched with saturated NH_4Cl , and the resulting mixture was extracted with Et_2O , dried, and evaporated to provide an oil, which was chromatographed. Elution with a 10:1 mixture of hexane- Et_2O yielded the acetate **43** (2.62 g, 99%) as a colorless oil. IR (neat) cm^{-1} : 1740 and 1240. ^1H NMR (300 MHz): δ 6.12 (1H, dd, $J=16.0, 10.0$), 5.27 (1H, dd, $J=16.0, 1.0$), 4.94 (1H, dd, $J=10.0, 1.0$), 4.92 (1H, dd, $J=10.0, 2.5$), 4.77-4.83 (3H, m), 4.68 (1H, q, $J=2.0$), 4.65 (1H, dd, $J=8.0, 5.0$), 2.21-2.51 (6H, m), 1.99 (3H, s), 1.88 (3H, s), 1.50-1.90 (5H, m), 1.30-1.44 (1H, m), 1.01 (9H, t, $J=7.5$), 0.72 (6H, q, $J=7.5$). ^{13}C NMR (75 MHz): δ 171.05, 151.10, 150.54, 146.85, 135.75, 114.55, 111.96, 111.70, 106.07, 76.58, 46.93, 40.19, 37.10, 35.91, 33.71, 26.56, 26.47, 23.71, 20.90, 20.64, 6.78, 5.46. MS (m/z): 430 (M^+). HRMS (M/Z) Calcd for $\text{C}_{26}\text{H}_{42}\text{O}_3\text{Si}$: 430.2901. Found: 430.2917.

(\pm)-18,19-Dinor-7 β -acetoxyatis-16-en-4-one (45). A solution of **43** (1.66 g, 3.87 mmol) in toluene (20 mL) was heated at 200 °C in a sealed tube for 2 days. After removal of the solvent, the residue was used in the next reaction without further purification.

To a stirred solution of the above product (209 mg, 0.486 mmol) in THF (5 mL) was added TBAF (1.5 mL, 1.0 M in THF, 1.46 mmol) at rt, and then stirring was continued for 10 min at rt. The resulting solution was diluted with water, and the resulting mixture was extracted with Et_2O . The organic layer was washed with brine, dried, and evaporated to leave an oil, which

was chromatographed. Elution with a 3:1 mixture of hexane–EtOAc gave the ketone **45** (143 mg, 92% for 2 steps) as a white powder. An analytical sample was recrystallized from Et₂O–pentane to give **45**, needles, mp 120–123 °C. IR (CHCl₃) cm⁻¹: 1720 and 1710. ¹H NMR (300 MHz): δ 4.77–4.81 (2H, m), 4.63 (1H, q, *J*=2.0), 2.56 (1H, t, *J*=7.5), 2.18–2.38 (4H, m), 2.07 (3H, s), 1.39–2.02 (13H, m), 1.16–1.30 (1H, m), 0.88 (3H, s). ¹³C NMR (75 MHz): δ 212.69, 170.23, 150.73, 106.07, 74.47, 52.73, 45.17, 42.80, 41.76, 40.97, 37.96, 36.58, 35.96, 28.31, 28.03, 26.76, 22.79, 21.91, 21.14, 12.76. MS (*m/z*): 316(M⁺). *Anal.* Calcd for C₂₀H₂₈O₃: C, 75.91; H, 8.91. Found: C, 75.68; H, 8.78.

(±)-**19-Nor-7β-acetoxy-4,18-epoxyatis-16-ene (46)**. To a stirred suspension of Me₃SO⁺I⁻ (2.2 g, 9.86 mmol) and NaH (315 mg, 50% oil suspension, 6.58 mmol) in DMSO (25 mL) was added a solution of **45** (416 mg, 1.32 mmol) in DMSO (10 mL) at 50 °C. After 3 h of stirring, the reaction was quenched with H₂O, and the resulting mixture was extracted with Et₂O. The ethereal layer was washed with brine, dried, and evaporated to furnish an oil, which was chromatographed. Elution with a 2:1 mixture of hexane–Et₂O gave the epoxide **46** (315 mg, 73%), a white powder, together with the starting material **45** (13.9 mg, 3%). An analytical sample was recrystallized from pentane to give **46**, needles, mp 132–134 °C. IR (CHCl₃) cm⁻¹: 1710. ¹H NMR (300 MHz): δ 4.77 (1H, q, *J*=2.0), 4.71 (1H, t, *J*=2.5), 4.61 (1H, q, *J*=2.0), 2.72 (1H, d, *J*=4.0), 2.18–2.29 (3H, m), 2.09 (3H, s), 1.77–2.04 (5H, m), 1.41–1.74 (8H, m), 1.00–1.36 (4H, m), 1.09 (3H, s). ¹³C NMR (75 MHz): δ 170.61, 151.42, 105.66, 75.48, 59.29, 47.97, 45.69, 41.92, 40.41, 38.74, 38.61, 36.61, 36.18, 34.70, 28.18, 27.67, 26.83, 23.23, 21.29, 18.70, 12.44. MS (*m/z*): 270 (M⁺–CH₃CO₂H). *Anal.* Calcd for C₂₁H₃₀O₃: C, 76.32; H, 9.14. Found: C, 76.32; H, 9.16.

(±)-**Methyl 18-Nor-7β-hydroxyatis-16-en-19-oate (48a)** and (±)-**Methyl 19-Nor-7β-hydroxyatis-16-en-18-oate (48b)**. To a stirred solution of **46** (102.9 mg, 0.312 mmol) in toluene (30 mL)

was added $\text{BF}_3 \cdot \text{OEt}_2$ (0.2 mL, 1.56 mmol) at -20°C , and then stirring was continued for 1 min at the same temperature. The resulting solution was quickly quenched with saturated NaHCO_3 , and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to leave an oil, which was used in the next step without further purification.

To a stirred solution of the above aldehyde, KH_2PO_4 (27 mg, 0.374 mmol) and 2-methyl-2-butene (0.25 mL, 2.34 mmol) in a 5:2 mixture of *t*-BuOH- H_2O (7 mL) was added NaClO_2 (34 mg, 0.468 mmol) at rt. After 2 h of stirring, the resulting mixture was quenched with 10% HCl, and the resulting solution was extracted with Et_2O . The extract was dried over anhydrous Na_2SO_4 , and evaporated under reduced pressure. The residue was used in the next step without further purification.

To a stirred solution of the above carboxylic acid in acetonitrile (5 mL) were added DBU (0.1 mL, 0.95 mmol) followed by MeI (0.1 mL, 1.62 mmol), and then stirring was continued for 2 h at rt. The resulting solution was diluted with H_2O and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to produce an oil, which was chromatographed. Elution with a 10:1 mixture of hexane- Et_2O gave rise to the products (91.5 mg, 81%) as a colorless oil; A small amount of the mixture was separated by silica gel column chromatography. **α -Ester**; An analytical sample was recrystallized from pentane to give the ester, needles, mp $80\text{--}82^\circ\text{C}$. IR (neat) cm^{-1} : 1735 and 1730. ^1H NMR (300 MHz): δ 4.75 (1H, q, $J=2.0$), 4.73 (1H, t, $J=3.0$), 4.59 (1H, q, $J=2.0$), 3.66 (3H, s), 2.38 (1H, t, $J=4.0$), 2.07-2.29 (4H, m), 2.10 (3H, s), 1.76-1.94 (4H, m), 1.68 (1H, t, $J=2.5$), 1.32-1.66 (8H, m), 1.17 (1H, td, $J=12.0, 7.0$), 0.92 (1H, td, $J=12.0, 3.0$), 0.84 (3H, s). ^{13}C NMR (75 MHz): δ 175.95, 170.68, 151.58, 105.35, 75.96, 51.11, 46.71, 42.26, 41.86, 41.51, 39.10, 37.63, 36.94, 36.11, 30.17, 28.38, 27.90, 27.35, 26.74, 21.34, 18.01, 11.32. MS (m/z): 300 ($\text{M}^+ - \text{CH}_3\text{CO}_2\text{H}$). HRMS (M/Z) calcd for $\text{C}_{20}\text{H}_{28}\text{O}_2$: 300.2090. found: 300.2095. **β -Ester**; IR (neat) cm^{-1} : 1725 and 1730. ^1H NMR (300 MHz): δ 4.77 (1H, q, $J=2.0$), 4.62 (1H, q, $J=2.0$), 4.60 (1H, t, $J=2.5$), 3.62 (3H, s), 2.22-2.41 (3H, m), 2.10 (3H, s), 1.11-1.93 (15H, m), 0.93 (3H, s), 0.80-1.05 (2H, m). ^{13}C

NMR (75 MHz): δ 176.57, 170.74, 151.39, 105.67, 75.40, 51.35, 45.80, 44.19, 41.76, 41.48, 38.11, 36.84, 36.78, 36.17, 30.16, 28.23, 27.82, 27.33, 26.88, 21.20, 19.86, 11.74. MS (m/z): 360 (M^+). HRMS (M/Z) calcd for $C_{22}H_{32}O_4$: 360.2299. found: 360.2305.

To a stirred solution of the above mixture (91.5 mg, 0.254 mmol) in MeOH (15 mL) was added K_2CO_3 (240 mg, 1.74 mmol), and stirring was continued at 50 °C. After 20 h of stirring, the solvent was removed under reduced pressure. The residue was extracted with Et_2O , and the ethereal layer was washed with 10% HCl, saturated $NaHCO_3$, brine, dried, and evaporated to afford an oil, which was chromatographed. Elution with a 1:1 mixture of hexane- Et_2O yielded the products **48** (64 mg, 80%) as a white powder. A small amount of the mixture **48** was separated by silica gel column chromatography. **α -Ester 48a**; An analytical sample was recrystallized from MeOH to give **48a**, needles, mp 176–180 °C. IR ($CHCl_3$) cm^{-1} : 3600 (br) and 1710. 1H NMR (300 MHz): δ 4.76 (1H, q, $J=2.0$), 4.63 (1H, q, $J=2.0$), 3.67 (3H, s), 3.50 (1H, t, $J=2.5$), 2.37–2.48 (2H, m), 2.11–2.31 (3H, m), 2.04 (1H, ddd, $J=12.5, 5.0, 2.0$), 1.93 (1H, dt, $J=16.0, 2.0$), 1.50–1.92 (9H, m), 1.32–1.49 (3H, m), 1.07 (1H, td, $J=12.0, 7.0$), 0.92 (1H, td, $J=12.0, 3.0$), 0.83 (3H, s). ^{13}C NMR (75 MHz): δ 176.21, 152.05, 105.26, 73.76, 51.11, 45.83, 42.56, 41.86, 40.92, 39.18, 37.84, 37.73, 36.26, 32.91, 28.38, 28.15, 27.29, 26.97, 18.10, 11.35. MS (m/z): 318 (M^+). Anal. Calcd for $C_{20}H_{30}O_3$: C, 75.43; H, 9.50. Found: C, 75.15; H, 9.86. **β -Ester 48b**; IR ($CHCl_3$) cm^{-1} : 3500 (br) and 1725. 1H NMR (300 MHz): δ 4.77 (1H, q, $J=2.0$), 4.64 (1H, q, $J=2.0$), 3.67 (3H, s), 3.41 (1H, t, $J=2.5$), 2.47 (1H, dq, $J=16.0, 2.5$), 2.22–2.43 (2H, m), 1.37–2.00 (15H, m), 1.29 (1H, dt, $J=13.0, 2.5$), 0.90–1.16 (2H, m), 0.92 (3H, s). ^{13}C NMR (75 MHz): δ 177.00, 152.07, 105.43, 73.05, 51.44, 44.87, 44.28, 42.14, 40.66, 38.11, 37.70, 36.94, 36.32, 30.52, 30.32, 28.55, 27.79, 27.14, 19.94, 11.70. MS (m/z): 318 (M^+). HRMS (M/Z) calcd for $C_{20}H_{30}O_3$: 318.2193. found: 318.2193.

(\pm)-Methyl 7 β -Trimethylsilyloxyatis-16-en-19-oate (49). To a stirred solution of **48** (8.3 mg, 26.1 μ mol) and 2,6-lutidine (0.03 mL, 0.131 mmol) in CH_2Cl_2 (3 mL) was added TMSOTf (0.03

mL, 0.131 mmol), and stirring was continued for 0.5 h at rt. The reaction was quenched with saturated NH_4Cl , and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to give an oil, which was chromatographed. Elution with a 15:1 mixture of hexane– EtOAc provided the silyl ether (9.8 mg, 96%) as a colorless oil. A small amount of the mixture was separated by silica gel column chromatography. **α -Methyl ester**; An analytical sample was recrystallized from MeOH to give the α -ester, prisms, mp 178–181 °C. IR (CHCl_3) cm^{-1} : 1725. ^1H NMR (300 MHz): δ 4.72 (1H, q, $J=2.0$), 4.58 (1H, q, $J=2.0$), 3.65 (3H, s), 3.41 (1H, dd, $J=3.0, 1.5$), 2.40 (1H, dq, $J=16.0, 2.5$), 2.28–2.34 (1H, m), 2.03–2.22 (4H, m), 1.68–1.95 (3H, m), 1.30–1.65 (8H, m), 0.81–1.09 (3H, m), 0.79 (3H, s), 0.10 (9H, s). ^{13}C NMR (75 MHz): δ 176.44, 153.33, 104.61, 74.35, 51.05, 45.51, 42.76, 42.55, 40.62, 39.13, 38.23, 37.72, 36.55, 33.50, 28.50, 28.15, 27.42, 27.06, 18.18, 11.53, 0.32. MS (m/z): 390 (M^+). HRMS (M/Z) calcd for $\text{C}_{23}\text{H}_{38}\text{O}_3\text{Si}$: 390.2588. found: 390,2602. **β -Methyl ester**; ^1H NMR (300 MHz): δ 3.63 (3H, s, CO_2Me), 3.32 (1H, dd $J=3.0, 2.0$, H-7), 0.89 (3H, s, 3H-20).

To a stirred solution of $i\text{-Pr}_2\text{NH}$ (0.3 mL, 2.00 mmol) in THF (5 mL) was added BuLi (1.0 mL, 1.6 M in hexane, 1.60 mmol) at -78 °C, and the mixture was stirred at 0 °C for 15 min, and -78 °C for 15 min. After addition of a solution of the above mixture (77.5 mg, 0.200 mmol) in THF (0.5 mL) at -78 °C, and the mixture was warmed to rt. After being stirred for 1 h, HMPA (0.3 mL, 1.60 mmol) was added at the same temperature. MeI (0.15 mL, 2.00 mmol) was added at -78 °C. The reaction was quenched with saturated NaHCO_3 , and the resulting solution was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to furnish an oil, which was chromatographed. Elution with a 10:1 mixture of hexane– Et_2O gave **49** (75.2 mg, 94%) as a white powder. An analytical sample was recrystallized from acetone to give **49**, needles, mp 146–149 °C. IR (neat) cm^{-1} : 1705. ^1H NMR (300 MHz) δ : 4.72 (1H, q, $J=2.0$), 4.58 (1H, q, $J=2.0$), 3.64 (3H, s), 3.42 (1H, dd, $J=3.0, 2.0$), 2.38 (1H, dq, $J=16.0, 3.0$), 2.12–2.22 (2H, m), 1.97 (1H, ddd, $J=14.0, 12.0, 2.0$), 1.78–1.84 (5H, m), 1.46–1.60 (5H, m), 1.30–1.46 (2H, m), 1.12 (3H, s), 1.06 (1H, td, $J=12.5, 4.0$), 0.96–1.10 (1H, m), 0.91 (1H, td, $J=12.5, 4.0$), 0.76 (3H,

s), 0.10 (9H, s). ^{13}C NMR (75 MHz) δ : 178.59, 153.33, 104.64, 74.28, 51.17, 47.68, 45.92, 43.40, 42.55, 39.39, 38.01, 37.90, 36.66, 28.62, 28.55, 28.20, 27.68, 27.11, 18.79, 11.61, 0.34. MS (m/z): 404 (M^+). *Anal.* Calcd for $\text{C}_{24}\text{H}_{40}\text{O}_3\text{Si}$: C, 71.23; H, 9.96. Found: C, 71.09; H, 9.97.

(\pm)-Methyl Gummiferolate (13b). To a stirred solution of **49** (49.9 mg, 0.124 mmol) in THF (2 mL) was added TBAF (0.4 mL, 1.0 M in THF, 0.371 mmol), and stirring was continued for 4 h at rt. The resulting solution was diluted with H_2O , and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to give rise to an oil, which was chromatographed. Elution with a 1:1 mixture of hexane– Et_2O produced the alcohol (38.4 mg, 94%) as a colorless oil. An analytical sample was recrystallized from acetone to give the alcohol, prisms, mp 175–185 °C. IR (CHCl_3) cm^{-1} : 3600 (br) and 1710. ^1H NMR (300 MHz): δ 4.76 (1H, q, $J=2.0$), 4.63 (1H, q, $J=2.0$), 3.66 (3H, s), 3.51 (1H, t, $J=2.5$), 2.41 (1H, dq, $J=16.0$, 3.0), 2.05–2.28 (3H, m), 1.94 (1H, dt, $J=16.0$, 2.0), 1.92 (1H, dt, $J=14.0$, 3.0), 1.72–1.86 (2H, m), 1.50–1.68 (6H, m), 1.37–1.48 (3H, m), 1.18 (3H, s), 1.04–1.14 (1H, m), 1.07 (1H, td, $J=13.0$, 4.0), 0.92 (1H, td, $J=13.0$, 4.0), 0.79 (3H, s). ^{13}C NMR (75 MHz): δ 178.35, 152.16, 105.25, 73.73, 51.26, 48.10, 46.24, 43.40, 41.89, 39.45, 38.04, 37.54, 36.40, 28.53, 28.20, 27.58, 27.05, 18.74, 11.44. MS (m/z): 332 (M^+). *Anal.* Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_3$: C, 75.86; H, 9.70. Found: C, 75.92; H, 9.69. Spectral data (^1H NMR, IR and MS) of the alcohol were consistent with those reported.⁶

To a stirred solution of angelic acid (40 mg, 0.40 mmol) in toluene (0.3 mL) were added trichlorobenzoyl chloride (0.062 mL, 0.40 mmol) followed by Et_3N (0.055 mL, 0.40 mmol) at rt. After 2 h of stirring, to the mixture was added the above alcohol (2.5 mg, 7.53 μmol), and the resulting mixture was allowed to warm to 80 °C. After 2 days of stirring at the same temperature, the resulting mixture was diluted with Et_2O , and the resulting suspension was filtered through Celite. The residue was washed several times with Et_2O , and then the combined filtrates were concentrated to leave an oil, which was chromatographed. Elution with a 2:3 mixture of hexane– CHCl_3 provided methyl gummiferolate **13b** (1.7 mg, 55%) as a colorless oil; IR (CHCl_3)

cm⁻¹: 1715 and 1705. ¹H NMR (300 MHz) δ : 6.06 (1H, qq, $J=7.0, 1.5$), 4.85 (1H, t, $J=3.0$), 4.75 (1H, q, $J=2.0$), 4.59 (1H, q, $J=2.0$), 3.65 (3H, s), 2.05-2.28 (4H, m), 2.02 (3H, dq, $J=7.0, 1.0$), 1.92-1.95 (3H, m), 1.72-1.92 (3H, m), 1.13-1.67 (8H, m), 1.09 (3H, s), 0.82-1.09 (4H, m), 0.82 (3H, s). MS (m/z): 414 (M^+). HRMS (M/Z) Calcd for C₂₆H₃₈O₄: 414.2768. Found: 414.2758. Spectral data (¹H NMR, IR and MS) of methyl gummiferolate (**13b**) were identical with those reported.⁶

(1*R**,5*R**,8*R**)-4,4-Dimethyl-9-methylene-2-oxo-3-oxatricyclo[6.2.1.0^{1,5}]undecane (**19**), (1*R**,5*R**,7*S**)-4,4-Dimethyl-8-methylene-2-oxo-3-oxatricyclo[5.2.2.0^{1,5}]undecane (**50**) and (1*R**,5*R**,6*S**)-4,4-Dimethyl-2-oxo-11-tributylstannylmethyl-3-oxatricyclo[4.3.2.0^{1,5}]undec-7-ene (**51**). To a stirred solution of **16** (5.47 g, 26.8 mmol) in a degassed C₆H₆ (400 mL) was added slowly a degassed C₆H₆ solution (10 mL) of Bu₃SnH (7.6 mL, 28.1 mmol) and AIBN (44 mg, 0.268 mmol) over a period of 2 h under reflux. After 2 h of refluxing, the solvent was removed under reduced pressure. The residue was dissolved in CH₂Cl₂ (400 mL), and then silica gel (400 g) was added. After being stirred vigorously for 2 days, the mixture was filtered through Celite. The filtrate was concentrated to give an oil, which was chromatographed. Elution with a 5:1 mixture of hexane–EtOAc afforded **51** (660 mg, 5%), followed by a mixture of **19** and **50** (5.15 g, **19** : **50** = 18 : 1, 93%), containing a small amount of tin species.

After recrystallization of the mixture from Et₂O, **19** (4.55 g, 82%), colorless prisms, mp 57–59 °C, was obtained. IR (neat) cm⁻¹: 1740. ¹H NMR (300 MHz) δ : 4.99-5.02 (1H, m), 4.84-4.88 (1H, m), 2.82 (1H, dt, $J=15.0, 2.5$), 2.75-2.79 (1H, m), 2.23-2.32 (1H, m), 2.02-2.15 (2H, m), 1.83 (1H, dd, $J=11.0, 2.5$), 1.72 (1H, dd, $J=11.0, 4.5$), 1.39-1.61 (3H, m), 1.44 (3H, s), 1.37 (3H, s). ¹³C NMR (75 MHz) δ : 179.78, 154.71, 106.45, 85.16, 51.67, 49.77, 45.35, 39.66, 34.26, 30.63, 30.51, 24.59, 16.87. MS (m/z): 206 (M^+). Anal. Calcd for C₁₃H₁₈O₂: C, 75.69; H, 8.80. Found: C, 75.51; H, 8.94.

(1R*,2R*,5R*)-1-Acetoxymethyl-2-(1-hydroxy-1-methylethyl)-6-

methylenebicyclo[3.2.1]octane (52). To a stirred suspension of LAH (290 mg, 7.75 mmol) in Et₂O (20 mL) was added dropwise a solution of **19** (399 mg, 1.94 mmol) in Et₂O (15 mL). After 15 h of stirring, the solution was cooled to 0 °C, and H₂O (0.3 mL), 10% NaOH (0.3 mL) and H₂O (0.9 mL) were successively added in this order. After 0.5 h of stirring, MgSO₄ was added, and then the resulting suspension was filtered through Celite. The residue was washed several times with Et₂O, and then the combined filtrates were concentrated to leave an oil, which was chromatographed. Elution with a 2:1 mixture of hexane–EtOAc gave the diol (392 mg, 97%) as a white powder, mp 124–126 °C. IR (neat) cm⁻¹: 3400 (br). ¹H NMR (300 MHz): δ 4.82–4.86 (1H, m), 4.76–4.80 (1H, m), 3.91 (1H, d, *J*=10.5), 3.41 (1H, d, *J*=10.5), 2.64–2.70 (1H, m), 2.36–2.45 (1H, m), 2.16 (1H, dt, *J*=16.5, 2.5), 1.44–1.89 (8H, m), 1.43 (3H, s), 1.33 (3H, s), 1.20–1.30 (1H, m). ¹³C NMR (75 MHz): δ 155.41, 103.62, 76.10, 72.23, 50.50, 49.44, 47.53, 43.09, 36.76, 34.41, 32.07, 28.27, 21.46. MS (*m/z*): 192 (*M*⁺–H₂O). *Anal.* Calcd for C₁₃H₂₂O₂: C, 74.24; H, 10.54. Found: C, 74.04; H, 10.64.

To a stirred solution of the diol (354 mg, 1.69 mmol) in pyridine (2 mL) was added Ac₂O (0.5 mL, 5.05 mmol), and stirring was continued for 16 h at rt. The resulting solution was diluted with H₂O and the resulting mixture was extracted with Et₂O. The combined extracts were washed with 10% HCl, saturated NaHCO₃, and brine, dried, and evaporated to furnish the product, which was chromatographed. Elution with a 2:1 mixture of hexane–EtOAc gave the acetate **52** (423 mg, 100%) as a white powder, mp 45–47 °C. IR (neat) cm⁻¹: 3430 (br), 1735. ¹H NMR (300 MHz): δ 4.82–4.86 (1H, m), 4.76–4.80 (1H, m), 4.50 (1H, d, *J*=10.0), 4.14 (1H, d, *J*=10.0), 2.65–2.71 (1H, m), 2.35–2.65 (1H, br s), 2.28–2.32 (2H, m), 2.06 (3H, s), 1.33–1.92 (7H, m), 1.37 (3H, s), 1.30 (3H, s). ¹³C NMR (75 MHz): δ 171.15, 154.79, 103.58, 75.13, 71.74, 50.68, 46.99, 45.57, 43.14, 35.67, 33.83, 31.72, 28.53, 21.18, 20.85. MS (*m/z*): 235 (*M*⁺–OH). *Anal.* Calcd for C₁₅H₂₄O₃: C, 71.39; H, 9.59. Found: C, 71.35; H, 9.61.

(1*R,2*S**,5*R**)-2-Isopropenyl-6-methylenebicyclo[3.2.1]octane-1-methanol (53).** To a stirred solution of **52** (358 mg, 1.43 mmol) in pyridine (15 mL) was added POCl₃ (0.4 mL, 4.30 mmol), and stirring was continued for 20 h at rt. The resulting solution was diluted with water, and the mixture was extracted several times with Et₂O. The combined extracts were washed with 10% HCl, saturated NaHCO₃, brine, dried, and evaporated to produce an oil, which was chromatographed. Elution with a 10:1 mixture of hexane–EtOAc gave the olefin (320 mg, 96%) as a colorless oil. IR (neat) cm⁻¹: 1740. ¹H NMR (300 MHz): δ 4.85–4.89 (1H, m), 4.79–4.84 (3H, m), 4.00 (1H, d, *J*=10.0), 3.87 (1H, d, *J*=10.0), 2.69–2.75 (1H, m), 2.22–2.42 (3H, m), 2.04 (3H, s), 1.73–2.00 (6H, m), 1.52–1.62 (1H, m), 1.48 (1H, dd, *J*=14.0, 5.0), 1.35 (1H, ddt, *J*=11.0, 5.0, 1.0). ¹³C NMR (75 MHz): δ 171.17, 154.60, 148.50, 113.52, 104.26, 70.21, 47.53, 45.76, 42.96, 42.91, 35.06, 32.07, 24.40, 23.96, 20.71. MS (*m/z*): 234 (*M*⁺). *Anal.* Calcd for C₁₅H₂₂O₂: C, 76.88; H, 9.46. Found: C, 76.64; H, 9.57.

To a stirred solution of the above olefin (3.97 g, 16.9 mmol) in MeOH (150 mL) was added K₂CO₃ (3.5 g, 25.4 mmol), and stirring was continued at rt. After 18 h of stirring, the solvent was removed under reduced pressure. The reaction mixture was extracted with Et₂O, and the ethereal layer was washed sequentially with 10% HCl, NaHCO₃, brine, dried, and evaporated to provide an oil, which was chromatographed. Elution with a 5:1 mixture of hexane–EtOAc furnished the alcohol **53** (3.12 g, 96%) as a white powder, mp 54–56 °C. IR (neat) cm⁻¹: 3350 (br). ¹H NMR (300 MHz): δ 4.85–4.90 (2H, m), 4.80–4.84 (2H, m), 3.59 (1H, d, *J*=10.5), 3.44 (1H, d, *J*=10.5), 2.69–2.76 (1H, m), 2.41 (1H, d, *J*=7.0), 2.32 (1H, dt, *J*=15.0, 2.5), 2.24 (1H, dq, *J*=15.0, 2.0), 1.72–2.00 (4H, m), 1.89 (3H, s), 1.52–1.61 (1H, m), 1.43 (1H, dd, *J*=13.0, 4.0), 1.32 (1H, ddt, *J*=11.0, 5.0, 1.5). ¹³C NMR (75 MHz): δ 155.08, 150.46, 113.13, 104.15, 69.84, 48.35, 48.10, 43.11, 43.08, 35.24, 32.34, 24.30, 24.25. MS (*m/z*): 192 (*M*⁺). *Anal.* Calcd for C₁₃H₂₀O: C, 81.19; H, 10.48. Found: C, 80.84; H, 10.66.

(1R*,2S*,5R*)-1-[(1R*,3Z)-1-Hydroxy-4-triethylsilyloxy-3,5-hexadienyl]-2-isopropenyl-6-methylenebicyclo[3.2.1]octane (54a) and **(1R*,2S*,5R*)-1-[(1S*,3Z)-1-Hydroxy-4-triethylsilyloxy-3,5-hexadienyl]-2-isopropenyl-6-methylenebicyclo[3.2.1]octane (54b)**. To a stirred solution of **53** (1.77 g, 9.20 mmol) in a mixture of Et₃N (25 mL), DMSO (25 mL) and CH₂Cl₂ (25 mL) was added SO₃·Py (6.0 g, 37.7 mmol), and stirring was continued for 24 h at rt. The mixture was diluted with water, and the resulting mixture was extracted several times with Et₂O. The combined extracts were washed with 10% HCl, saturated NaHCO₃, brine, dried, and evaporated to yield an oil, which was chromatographed. Elution with a 15:1 mixture of hexane-Et₂O gave the aldehyde (1.73 g, 99%) as a colorless oil. IR (neat) cm⁻¹: 1715. ¹H NMR (300 MHz): δ 9.68 (1H, s), 4.91-4.94 (2H, m), 4.85-4.88 (1H, m), 4.77-4.79 (1H, m), 2.75-2.81 (1H, m), 2.65 (1H, d, *J*=7.0), 2.39 (2H, t, *J*=2.0), 1.64-2.00 (5H, m), 1.76 (3H, s), 1.48-1.57 (1H, m). ¹³C NMR (75 MHz): δ 205.48, 152.05, 145.97, 113.95, 105.32, 57.50, 46.51, 43.05, 40.80, 33.21, 31.22, 24.43, 22.64. MS (*m/z*): 190 (*M*⁺). HRMS (*M/Z*) calcd for C₁₃H₁₈O: 190.1357. found: 190.1362.

To a stirred solution of 3-triethylsilyloxy-1,4-pentadiene (3.2 mL, 11.9 mmol) in THF (80 mL) was added *n*-BuLi (11.5 mL, 1.0 M in hexane, 11.9 mmol) at -78 °C. After 0.5 h of stirring, a solution of the aldehyde (1.73 g, 9.12 mmol) in THF (10 mL) was added at the same temperature. The reaction was quenched with saturated NH₄Cl, and the resulting solution was extracted with Et₂O. The ethereal layer was extracted with Et₂O. The organic layer was washed with brine, dried, and evaporated to afford an oil, which was chromatographed. Elution with a 15:1 mixture of hexane-Et₂O led to a mixture of α-OH and β-OH **54** (1.63 g, α : β = 1 : 3, 96%) as a colorless oil. A small amount of the mixture was separated by HPLC. **Mixture of α-OH and β-OH**; IR (neat) cm⁻¹: 3425 (br). *Anal.* Calcd for C₂₄H₄₀O₂Si: C, 74.16; H, 10.37. Found: C, 73.79; H, 10.69. α-OH; IR (neat) cm⁻¹: 3500 (br). ¹H NMR (300 MHz): δ 6.20 (1H, dd, *J*=16.0, 10.0), 5.31 (1H, dd, *J*=16.0, 1.0), 4.81-4.502 (6H, m), 3.45-3.55 (1H, m), 2.70-2.76 (1H, m), 2.60 (1H, dd, *J*=7.0, 1.0), 2.12-2.42 (4H, m), 1.75-2.04 (2H, m), 1.94 (3H, s), 1.20-1.62 (4H, m),

1.00 (9H, t, $J=7.5$), 0.82-0.93 (1H, m), 0.72 (6H, q, $J=7.5$). ^{13}C NMR (75 MHz): δ 154.98, 151.49, 150.58, 135.81, 113.98, 112.47, 112.23, 104.25, 47.57, 43.38, 41.47, 36.78, 31.93, 30.33, 29.70, 29.00, 24.98, 24.40, 6.79, 5.52. MS (m/z): 388 (M^+). HRMS (M/Z) calcd for $\text{C}_{24}\text{H}_{40}\text{O}_2\text{Si}$: 388.2795. found: 388.2832. **β -OH**; IR (neat) cm^{-1} : 3410 (br). ^1H NMR (300 MHz): δ 6.19 (1H, dd, $J=16.0, 10.0$), 5.32 (1H, dd, $J=16.0, 1.0$), 5.00 (1H, dd, $J=10.0, 1.0$), 4.78-4.89 (5H, m), 3.61 (1H, dt, $J=10.0, 1.5$), 2.67-2.74 (1H, m), 2.58 (1H, dt, $J=16.0, 2.5$), 2.40 (1H, ddd, $J=14.0, 5.0, 1.5$), 2.33 (1H, d, $J=7.5$), 2.16 (1H, ddd, $J=14.0, 10.0, 8.0$), 1.40-2.04 (8H, m), 1.86 (3H, s), 1.02 (9H, t, $J=7.5$), 0.72 (6H, q, $J=7.5$). ^{13}C NMR (75 MHz): δ 155.39, 151.54, 149.35, 135.58, 113.70, 112.58, 112.17, 104.15, 73.47, 50.56, 48.41, 42.76, 38.58, 33.85, 32.02, 29.38, 25.12, 24.65, 6.78, 5.49. MS (m/z): 388(M^+). HRMS (M/Z) calcd for $\text{C}_{24}\text{H}_{40}\text{O}_2\text{Si}$: 388.2795. found: 388.2762.

(\pm)-18,19-Dinor-7 β -acetoxykaur-16-en-4-one (56) and (\pm)-18,19-Dinor-7 α -acetoxykaur-16-en-4-one (57). To a stirred solution of **54** (2.17 g, 5.58 mmol) and DMAP (1.36 g, 11.2 mmol) in CH_2Cl_2 (50 mL) was added Ac_2O (0.80 mL, 8.37 mmol) at rt, and stirring was continued for 24 h at rt. The reaction was quenched with saturated NH_4Cl , and the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to give an oil, which was chromatographed. Elution with a 10:1 mixture of hexane- Et_2O afforded the acetates (2.62 g, 98%) as a colorless oil; An analytical samples of both acetates obtained by further purification. **α -Acetate**; IR (neat) cm^{-1} : 1735. ^1H NMR (300 MHz): δ 6.13 (1H, dd, $J=16.0, 10.0$), 5.26 (1H, dd, $J=16.0, 1.0$), 4.90-4.97 (2H, m), 4.84-4.87 (1H, m), 4.80-4.83 (1H, m), 4.71-4.78 (3H, m), 2.66-2.72 (1H, m), 2.36-2.50 (4H, m), 2.14-2.23 (1H, m), 2.00 (3H, s), 1.85 (3H, s), 1.36-2.00 (6H, m), 0.98 (9H, t, $J=7.5$), 0.69 (6H, q, $J=7.5$). MS (m/z): 430 (M^+). HRMS (M/Z) calcd for $\text{C}_{26}\text{H}_{42}\text{O}_3\text{Si}$: 430.2901. found: 430.2883. **β -Acetate**; IR (neat) cm^{-1} : 1740. ^1H NMR (300 MHz): δ 6.13 (1H, dd, $J=16.0, 10.0$), 5.27 (1H, dd, $J=16.0, 1.0$), 5.13 (1H, dd, $J=10.0, 3.0$), 4.95 (1H, dd, $J=10.0, 1.0$), 4.83-4.90 (4H, m), 4.66 (1H, dd, $J=8.0, 5.0$), 2.64-2.71 (1H, m), 2.55 (1H, dt,

$J=16.0, 2.5$), 2.26-2.48 (3H, m), 1.90-2.13 (2H, m), 2.01 (3H, s), 1.89 (3H, s), 1.65-1.82 (2H, m), 1.20-1.62 (3H, m), 1.01 (9H, t, $J=7.5$), 0.72 (6H, q, $J=7.5$). ^{13}C NMR (75 MHz): δ 171.20, 154.62, 150.55, 148.15, 135.76, 114.28, 112.05, 111.64, 104.50, 75.22, 49.51, 48.57, 42.49, 39.33, 34.56, 31.87, 27.29, 24.69, 24.33, 20.96, 6.79, 5.50. MS (m/z): 430 (M^+). HRMS (M/Z) calcd for $\text{C}_{26}\text{H}_{42}\text{O}_3\text{Si}$: 430.2901. found: 430.2904.

A solution of the above acetates (2.29 g, 5.33 mmol) in toluene (36 mL) was heated at 200 °C in a sealed tube for 2 days. After removal of the solvent, the residue was used without further purification.

To a stirred solution of the above tetracyclic silyl enol ethers **55** in THF (50 mL) was added TBAF (7.5 mL, 1.0 M in THF, 7.47 mmol) at rt, and stirring was continued for 10 min at rt. The resulting solution was diluted with water and the resulting mixture was extracted with Et_2O . The organic layer was washed with brine, dried, and evaporated to furnish the ketone, which was recrystallized from Et_2O to give **56** (843 mg, 50% for 2 steps). The resulting residue was chromatographed on silica gel with toluene– EtOAc (10:1 v/v) to give **57** (319 mg, 19% for 2 steps) followed by **56** (116 mg, 7% for 2 steps) as a white powder. **Compound 56**; An analytical sample was recrystallized from Et_2O to give **56**, prisms, mp 164–167 °C. IR (neat) cm^{-1} : 1735 and 1715. ^1H NMR (300 MHz) δ : 4.87 (1H, t, $J=2.5$), 4.82-4.85 (1H, m), 4.77-4.81 (1H, m), 2.68-2.74 (1H, m), 2.62 (1H, dd, $J=11.0, 2.5$), 2.28-2.37 (2H, m), 2.17-2.25 (1H, m), 2.14 (1H, dt, $J=16.0, 2.5$), 2.05 (3H, s), 1.50-2.05 (11H, m), 1.42 (1H, td, $J=12.0, 5.0$), 1.30 (1H, dd, $J=12.0, 5.0$), 0.93 (3H, s). ^{13}C NMR (75 MHz) δ : 212.86, 170.36, 153.88, 104.26, 77.95, 52.49, 47.94, 46.63, 45.20, 43.88, 43.17, 40.56, 38.42, 38.31, 32.69, 23.74, 21.85, 21.22, 18.38, 15.54. MS (m/z): 256 ($\text{M}^+ - \text{CH}_3\text{CO}_2\text{H}$). Anal. Calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$: C, 75.91; H, 8.91. Found: C, 75.93; H, 8.86. **Compound 57**; An analytical sample was recrystallized from pentane to give **57**, needles, mp 114–117 °C. IR (neat) cm^{-1} : 1725 and 1705. ^1H NMR (300 MHz) δ : 4.85-4.89 (1H, m), 4.78-4.82 (1H, m), 4.68 (1H, dd, $J=11.0, 4.0$), 2.67-2.73 (1H, m), 2.26-2.39 (4H, m), 2.05 (3H, s), 1.50-2.04 (12H, m), 1.44 (1H, d, $J=7.5$), 1.31 (1H, td, $J=12.0, 5.0$), 0.95 (3H, s). ^{13}C

NMR (75 MHz): δ 211.28, 171.08, 154.12, 104.32, 75.20, 56.76, 52.67, 47.77, 44.00, 42.85, 42.46, 40.36, 38.37, 32.68, 32.25, 24.36, 21.76, 21.14, 18.77, 15.63. MS (m/z): 256(M^+ -CH₃CO₂H). *Anal.* Calcd for C₂₀H₂₈O₃: C, 75.91; H, 8.91. Found: C, 75.81; H, 8.85.

(±)-19-Nor-7β-acetyloxy-4,18-epoxykaur-16-ene (58). To a stirred suspension of Me₃SO⁺I⁻ (2.86 g, 13.0 mmol) and NaH (374 mg, 50% oil dispersion, 7.80 mmol) in DMSO (30 mL) was added **56** (411 mg, 1.30 mmol) at 50 °C. After 5 h of stirring, the reaction was quenched with water, and the resulting mixture was extracted with Et₂O. The ethereal layer was washed with brine, dried, and evaporated to leave an oil, which was chromatographed. Elution with a 1:1 mixture of hexane–Et₂O gave the epoxide **58** (310 mg, 72%) as a white powder. An analytical sample was recrystallized from pentane to give **58**, needles, mp 126–128 °C. IR (neat) cm⁻¹: 1740 and 1240. ¹H NMR (300 MHz) δ : 4.75–4.84 (3H, m), 2.72 (1H, d, *J*=4.0), 2.69 (1H, t, *J*=4.0), 2.24 (1H, d, *J*=4.0), 2.20 (1H, dq, *J*=16.0, 2.0), 2.08 (1H, dt, *J*=16.0, 2.5), 2.07 (3H, s), 1.85–2.02 (5H, m), 1.39–1.72 (8H, m), 1.20–1.28 (2H, m), 1.13 (3H, s), 0.96–1.08 (1H, m). ¹³C NMR (75 MHz) δ : 170.76, 154.39, 103.91, 79.04, 59.57, 48.51, 47.91, 46.66, 45.37, 43.40, 40.00, 39.87, 39.18, 38.34, 34.50, 32.97, 24.24, 21.34, 19.04, 17.72, 15.99. MS (m/z): 270(M^+ -CH₃CO₂H). *Anal.* Calcd for C₂₁H₃₀O₃: C, 76.32; H, 9.14. Found: C, 76.34; H, 9.16.

(±)-Methyl 18-Nor-7β-acetoxykaur-16-en-19-oate (59a) and (±)-Methyl 19-Nor-7β-acetoxykaur-16-en-18-oate (59b). To a stirred solution of **58** (149 mg, 0.452 mmol) in toluene (45 mL) was added BF₃·OEt₂ (0.3 mL, 2.26 mmol) at –20 °C, and then stirring was continued for 1 min at the same temperature. The reaction was quickly quenched with saturated NaHCO₃, and the resulting mixture was extracted with Et₂O. The ethereal layer was washed with brine, dried, and evaporated to provide an oil, which was used in the next step without further purification.

To a stirred solution of the above aldehyde, KH₂PO₄ (100 mg, 0.543 mmol) and 2-methyl-2-butene (0.2 mL, 1.81 mmol) in a 5:2 mixture of *t*-BuOH–H₂O (7 mL) was added

NaClO₂ (153 mg, 1.36 mmol) at rt. After 2 h of stirring, the reaction was quenched with 10% HCl, and the resulting solution was extracted with Et₂O. The organic layer was dried over anhydrous Na₂SO₄, and the solvent was evaporated under reduced pressure. The residue was used in the next step without further purification.

To a stirred solution of the above carboxylic acid in acetonitrile (5 mL) were added DBU (0.14 mL, 0.904 mmol) followed by MeI (0.12 mL, 1.81 mmol), and stirring was continued for 2 h at rt. The mixture was diluted with water, and the resulting solution was extracted with Et₂O. The ethereal layer was washed with brine, dried, and evaporated to furnish an oil, which was chromatographed. Elution with a 5:1 mixture of hexane–EtOAc gave the methyl esters **59** (128 mg, 78%) as a colorless oil. A small amount of the mixture was separated by silica gel column chromatography. **α -Ester 59a**; An analytical sample was recrystallized from Et₂O to give the α -ester **59a**, plates, mp 127–130 °C. IR (neat) cm⁻¹: 1738 and 1732. ¹H NMR (300 MHz): δ 4.79–4.83 (2H, m), 4.74–4.78 (1H, m), 3.65 (3H, s), 2.65–2.71 (1H, m), 2.34 (1H, t, *J*=4.0), 2.04–2.27 (4H, m), 2.07 (3H, s), 1.81–1.99 (4H, m), 1.75 (1H, dt, *J*=14.0, 2.5), 1.22–1.68 (8H, m), 0.77–1.00 (1H, m), 0.89 (3H, s). ¹³C NMR (75 MHz): δ 175.92, 170.76, 154.48, 103.79, 79.53, 51.06, 49.56, 47.06, 45.08, 43.49, 42.46, 41.30, 40.07, 38.64, 38.30, 33.09, 31.43, 28.26, 21.35, 18.48, 17.48, 14.90. MS (*m/z*): 360 (*M*⁺). *Anal.* Calcd for C₂₂H₃₂O₄: C, 73.30; H, 8.95. Found: C, 73.21; H, 8.87. **β -Ester 59b**; An analytical sample was recrystallized from Et₂O to give β -ester **59b**, plates, mp 123–128 °C. IR (neat) cm⁻¹: 1738 and 1732. ¹H NMR (300 MHz): δ 4.80–4.84 (1H, m), 4.75–4.80 (1H, m), 4.68 (1H, t, *J*=2.5), 3.62 (3H, s), 2.67–2.73 (1H, m), 2.05–2.38 (4H, m), 2.08 (3H, s), 1.41–1.98 (11H, m), 1.20–1.30 (2H, m), 0.98 (3H, s), 0.86–0.98 (2H, m). ¹³C NMR (75 MHz): δ 176.60, 170.82, 154.44, 103.96, 78.92, 51.34, 48.77, 46.90, 45.31, 43.88, 43.38, 41.13, 38.64, 38.49, 37.79, 33.12, 30.11, 28.20, 21.23, 20.18, 17.56, 14.72. MS (*m/z*): 360 (*M*⁺). HRMS (*M/Z*) calcd for C₂₂H₃₂O₄: 360.2301. found: 360.2270.

(±)-Methyl 18-Nor-7β-trimethylsilyloxykaur-16-en-19-oate (**60a**) and (±)-Methyl 19-Nor-7β-trimethylsilyloxykaur-16-en-18-oate (**60b**). To a stirred solution of **59** (124 mg, 0.343 mmol) in MeOH (10 mL) was added K₂CO₃ (142 mg, 1.03 mmol), and stirring was continued at 50 °C for 24 h. After removal of the solvent under reduced pressure, the residue was extracted with Et₂O, and the ethereal layer was washed with 10% HCl, saturated NaHCO₃, brine, dried, and evaporated to leave an oil, which was chromatographed. Elution with a 1:1 mixture of hexane–Et₂O afforded the alcohols (95.4 mg, 87%) as a white powder. A small amount of the mixture was separated by silica gel column chromatography. **α-Ester**; An analytical sample was recrystallized from Et₂O to give the α-ester, prisms, mp 169–173 °C. IR (CHCl₃) cm⁻¹: 3496 (br) and 1732. ¹H NMR (300 MHz): δ 4.78–4.86 (2H, m), 3.66 (3H, s), 3.61 (1H, t, *J*=2.5), 2.65–2.72 (1H, m), 2.38 (1H, t, *J*=4.0), 2.08–2.34 (5H, m), 1.79–1.98 (3H, m), 1.32–1.74 (9H, m), 1.19 (1H, dd, *J*=11.0, 5.0), 0.82–0.96 (1H, m), 0.87 (3H, s). ¹³C NMR (75 MHz): δ 176.24, 154.98, 103.78, 77.24, 51.08, 48.62, 48.45, 45.26, 43.68, 42.79, 40.25, 40.13, 38.75, 38.54, 34.07, 33.38, 28.26, 18.59, 17.59, 14.99. MS (*m/z*): 318 (M⁺). *Anal.* Calcd for C₂₀H₃₀O₃: C, 75.43; H, 9.50. Found: C, 75.48; H, 9.43. **β-Ester**; IR (CHCl₃) cm⁻¹: 3496 (br) and 1720. ¹H NMR (300 MHz): δ 4.79–4.86 (2H, m), 3.67 (3H, s), 3.53 (1H, t, *J*=2.5), 2.66–2.72 (1H, m), 2.25–2.40 (3H, m), 1.76–1.98 (4H, m), 1.43–1.74 (10H, m), 1.33 (1H, dt, *J*=13.0, 2.5), 1.18 (1H, dd, *J*=11.0, 5.0), 0.85–1.01 (1H, m), 0.98 (3H, s). ¹³C NMR (75 MHz): δ 177.01, 155.09, 103.78, 76.49, 51.40, 48.22, 47.74, 45.48, 43.94, 43.58, 40.28, 38.67, 37.93, 33.39, 31.37, 30.26, 20.27, 17.66, 14.81. MS (*m/z*): 318 (M⁺). HRMS (*M/Z*) calcd for C₂₀H₃₀O₃: 318.2195. found: 318.2190.

To a stirred solution of the above alcohols (88.8 mg, 0.279 mmol) and 2,6-lutidine (0.15 mL, 0.838 mmol) in CH₂Cl₂ (10 mL) was added TMSOTf (0.2 mL, 0.838 mmol) at rt, and stirring was continued for 0.5 h at rt. The resulting solution was treated with saturated NH₄Cl, and the resulting mixture was extracted with Et₂O. The ethereal layer was washed with brine, dried, and evaporated to yield an oil, which was chromatographed. Elution with a 15:1 mixture of hexane–EtOAc gave the silyl ethers **60** (106 mg, 98%) as a colorless oil. A small amount of

the mixture was separated by silicagel column chromatography. **α -Ester 60a**; An analytical sample was recrystallized from acetone to give the α -ester **60a**, colorless prisms, mp 121–123 °C. IR (CHCl₃) cm⁻¹: 1731. ¹H NMR (300 MHz): δ 4.74–4.80 (2H, m), 3.65 (3H, s), 3.50–3.55 (1H, m), 2.61–2.68 (1H, m), 2.25–2.31 (1H, m), 2.00–2.23 (5H, m), 1.75–1.97 (3H, m), 1.31–1.70 (8H, m), 1.14 (1H, dd, J =10.5, 4.5), 0.85–0.95 (1H, m), 0.84 (3H, s), 0.09 (9H, s). ¹³C (75 MHz): δ 176.47, 156.09, 103.12, 77.91, 51.03, 48.89, 48.51, 46.16, 44.00, 43.00, 40.10, 40.06, 38.74, 38.43, 34.92, 33.36, 28.46, 18.70, 17.68, 15.13, 0.40. MS(m/z): 390 (M^+). *Anal.* Calcd. for C₂₃H₃₈O₃Si: C, 70.72; H, 9.81. Found: C, 70.50; H, 9.94. **β -Ester 60b**; An analytical sample was recrystallized from acetone to give the β -ester **60b**, prisms, mp 112–115 °C. IR (CHCl₃) cm⁻¹: 1733. ¹H NMR (300 MHz): δ 4.74–4.81 (2H, m), 3.63 (3H, s), 3.44 (1H, dd, J =3.0, 1.5), 2.63–2.69 (1H, m), 2.29 (1H, dd, J =11.0, 3.0), 2.20 (1H, dd, J =15.0, 2.0), 2.04 (1H, dt, J =16.0, 2.5), 1.99 (1H, td, J =11.0, 2.0), 1.73–1.85 (3H, m), 1.42–1.70 (8H, m), 1.09–1.19 (2H, m), 0.81–0.97 (2H, m), 0.95 (3H, s), 0.07 (9H, s). ¹³C NMR (75 MHz): δ 176.89, 155.91, 103.23, 77.04, 51.26, 48.77, 47.48, 46.36, 44.22, 43.94, 40.16, 38.61, 38.48, 37.96, 33.54, 31.86, 29.98, 20.26, 17.74, 14.91, 0.28. MS (m/z): 390 (M^+). HRMS (M/Z) calcd for C₂₃H₃₈O₃Si: 390.2590. found: 390.2607.

(\pm)-Methyl 7 β -Hydroxykaur-16-en-19-oate (14b). To a stirred solution of *i*-Pr₂NH (0.4 mL, 2.73 mmol) in THF (5 mL) was added BuLi (1.4 mL, 1.6 M in hexane, 2.18 mmol) at –78 °C, and the mixture was stirred at 0 °C for 15 min, and at –78 °C for 15 min. After addition of a solution of **60** (106 mg, 0.273 mmol) in THF (1 mL), the mixture was warmed to rt. After 1 h of stirring, HMPA (0.4 mL, 2.18 mmol) was added at rt, and then MeI (0.2 mL, 2.73 mmol) was added at –78 °C. The reaction was quenched with saturated NaHCO₃, and the resulting mixture was extracted with Et₂O. The ethereal layer was washed with brine, dried, and evaporated to afford an oil, which was chromatographed. Elution with a 10:1 mixture of hexane–Et₂O gave rise to the ester (89.6 mg, 81%) as a colorless oil. IR (neat) cm⁻¹: 1720. ¹H NMR (300 MHz): δ 4.73–

4.80 (2H, m), 3.62 (3H, s), 3.53 (1H, dd, $J=3.5, 1.5$), 2.60-2.67 (1H, m), 2.11-2.21 (2H, m), 2.03 (1H, dt, $J=16.0, 2.5$), 1.92 (1H, ddd, $J=14.0, 12.0, 2.0$), 1.73-1.86 (4H, m), 1.36-1.65 (7H, m), 0.98-1.23 (2H, m), 1.11 (3H, s), 0.88 (1H, td, $J=12.5, 4.0$), 0.80 (3H, s), 0.09 (9H, s). ^{13}C NMR (75 MHz): δ 178.64, 156.05, 103.15, 77.75, 51.12, 48.89, 48.60, 46.92, 46.16, 43.99, 43.35, 40.36, 39.01, 38.58, 37.98, 33.65, 29.76, 28.62, 19.15, 17.89, 15.37, 0.46. MS (m/z): 404 (M^+). HRMS (M/Z) calcd for $\text{C}_{24}\text{H}_{40}\text{O}_3\text{Si}$: 404.2745. found: 404.2756.

To a stirred solution of the above ester (82.1 mg, 0.203 mmol) in THF (3 mL) was added TBAF (0.6 mL, 1.0 M in THF, 0.610 mmol), and stirring was continued for 4 h at rt. The mixture was diluted with H_2O , and then the resulting mixture was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to provide as oil, which was chromatographed. Elution with a 1:1 mixture of hexane- Et_2O yielded the alcohol **14b** (70.0 mg, 100%) as a white powder. An analytical sample was recrystallized from acetone to give **14b**, prisms, mp 163–165 °C. IR (neat) cm^{-1} : 3500 (br), 1720 and 1700. ^1H NMR (300 MHz): δ 4.76-4.82 (2H, m), 3.63 (3H, s), 3.60 (1H, t, $J=2.5$), 2.62-2.69 (1H, m), 2.13-2.24 (3H, m), 2.04 (1H, ddd, $J=14.0, 12.0, 2.0$), 1.95 (1H, dt, $J=14.0, 3.0$), 1.76-1.86 (2H, m), 1.71 (1H, dd, $J=12.0, 3.0$), 1.38-1.66 (8H, m), 1.15-1.27 (1H, m), 1.15 (3H, s), 1.05 (1H, td, $J=12.0, 5.0$), 0.83-0.94 (1H, m), 0.82 (3H, s). ^{13}C NMR (75 MHz): δ 178.46, 155.12, 103.73, 77.13, 51.20, 49.04, 48.15, 47.21, 45.29, 43.68, 43.32, 40.42, 39.07, 38.66, 37.92, 33.50, 29.03, 28.53, 19.09, 17.84, 15.26. MS (m/z): 332 (M^+). *Anal.* Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_3$: C, 75.86; H, 9.70. Found: C, 75.92; H, 9.65. Spectral data (^1H NMR and MS) of **14b** were identical with those reported.²⁰

(±)-Methyl 7-Oxokaur-16-en-19-oate (14d). To a stirred suspension of Florisil (90 mg), PCC (30 mg, 137 μmol) and NaOAc (3.0 mg, 34.3 μmol) in CH_2Cl_2 (1 mL) was added a solution of **14b** (22.8mg, 68.7 μmol) in CH_2Cl_2 (2 mL) at rt. After 1.5 h of stirring, the resulting suspension was filtered through Celite. The residue was washed several times with Et_2O , and then the combined filtrates were concentrated to leave an oil, which was chromatographed. Elution with a

5:1 mixture of hexane–EtOAc provided **14d** (22.8 mg, 100%) as a white powder. An analytical sample was recrystallized from pentane to yield **14d**, plates, mp 75–78 °C. IR (neat) cm^{-1} : 1720 and 1700. ^1H NMR (300 MHz): δ 4.83–4.89 (2H, m), 3.68 (3H, s), 3.21 (1H, dt, $J=16.0, 2.5$), 3.03 (1H, t, $J=14.0$), 2.70–2.77 (1H, m), 2.66 (1H, dd, $J=14.0, 2.5$), 2.19–2.29 (1H, m), 2.06 (1H, dd, $J=10.0, 2.5$), 1.34–2.02 (11H, m), 1.18 (3H, s), 1.04 (3H, s), 0.97–1.10 (1H, m), 0.86 (1H, td, $J=12.0, 3.5$). ^{13}C NMR (75 MHz): δ 213.37, 177.41, 153.68, 104.55, 57.85, 54.89, 54.42, 51.49, 43.96, 42.82, 40.56, 40.44, 39.45, 38.95, 37.81, 32.60, 28.21, 18.91, 17.88, 14, 82. MS (m/z): 330 (M^+). HRMS (M/Z) calcd for $\text{C}_{21}\text{H}_{30}\text{O}_3$: 330.2193. found: 330.2202. Spectral data (^1H NMR, IR and MS) of **14d** were identical with those reported.²¹

(\pm)-**7-Oxokaurenolide (20)**. A stirred solution of **14d** (10.4 mg, 32 μmol), CuBr_2 (22 mg, 95 μmol) and LiCl (13.0 mg, 320 μmol) in DMF (3 mL) was refluxed for 8 h in a sealed tube. The mixture was poured into water, and the resulting solution was extracted with Et_2O . The ethereal layer was washed with brine, dried, and evaporated to yield the product, which was chromatographed. Elution with a 3:1 mixture of hexane–EtOAc gave rise to **20** (5.0 mg, 51%) as a white powder. An analytical sample was recrystallized from acetone–petroleum ether provided **20**, needles, mp 217–218 °C. IR (neat): cm^{-1} : 1771, 1715. ^1H NMR (300 MHz): δ 5.05–5.08 (1H, m), 4.89–4.93 (1H, m), 4.86 (1H, d, $J=6.0$), 2.67–2.75 (1H, m), 2.04–2.40 (5H, m), 1.98 (1H, dd, $J=11.5, 5.0$), 1.15–1.75 (9H, m), 1.32 (3H, s), 0.97–1.12 (1H, m), 0.71 (3H, s). MS (m/z): 314 (M^+). HRMS (M/Z) calcd for $\text{C}_{20}\text{H}_{26}\text{O}_3$: 314.1881. found: 314.1884. Spectral data (^1H NMR, IR and MS) of **20** were identical with those reported.¹²