Supporting Information

Novel Approach for the Stereocontrolled Construction of Eudesmane Skeleton: A Concise Synthesis of (±)-Balanitol

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Experimental Section

General

For flash column chromatography, silica gel (200~300 mesh) and light petroleum ether (PE, b.p. 60~90 ^{o}C) were used. IR spectra were recorded on a Nicolet FT-170SX spectrometer as liquid films. ^{1}H and ^{13}C NMR spectra were taken on a Bruker AM-400 spectrometer with TMS as an internal standard and $CDCl_3$ as solvent. Mass spectra were determined on a VG ZAB-HS or a Bruker APEXII 47e spectrometer. Melting points were measured on Kofler hot stage and uncorrected.

1-Methyl-3-(4-methyl-3-pentenyl)-7-oxabicyclo[2, 2, 1]heptan-2-one (6). –To a stirred solution of LHMDS(1.0 M, 1.0 mL) in dry THF (5 mL) was added dropwise a solution of 1-methyl-7-oxabicyclo[2, 2, 1]heptan-2-one (**5**) (126 mg, 1.0 mmol) in THF (2 mL) at –78 ^{o}C under Ar atmosphere. The resulting mixture was stirred at that temperature for 2 hr and homoprenyl iodide (210 mg, 1.0 mmol) in 2 mL of THF was added dropwise to the reaction mixture. The reaction mixture was allowed to warm to room temperature overnight. The reaction was quenched with 1 mL of saturated aqueous NH_4Cl, extracted with ether (50 mL × 3). The combined organic layers were washed with 1N HCl, saturated aqueous $NaHCO_3$, water, brine respectively, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography to yield the corresponding *exo*-homoprenylated oxabicyclic ketone (135 mg, 65%) as a colorless oil. ^{1}H NMR (400 MHz): δ 1.45 (3H, s, 1-Me), 1.63, 1.71 (each 3H, br s, 4′-Me×2), 1.91~2.20 (8H, m), 4.49 (1H, d, *J* = 5.1 Hz, 4-H), 5.11 (1H, t, *J* = 7.0 Hz, CH=) *ppm*; FTIR ν_{max} 3020, 2981, 1754, 1215, 757 cm^{-1}; LRMS(EI) *m/z* 208(M^+, 3), 180(3), 122(10), 111(15), 69(51), 43(100); HRMS(EI) *m/z* $[M]^+$ 208.1463 ($C_{13}H_{20}O_2$ requires 208.1463).

3-Dimethyl-3-(4-methyl-3-pentenyl)-7-oxabicyclo[2, 2, 1]heptan-2-one (6). –To a stirred solution of LDA (1.0 M in THF, 0.58 mL, 0.58 mmol) in dry THF (5 mL)

was added dropwise a solution of 1-methyl-3-(4-methyl-3-pentenyl)-7-oxabicyclo[2,2,1]heptan-2-one (120 mg, 0.58 mmol) in THF (2 mL) at –78 ^{o}C under Ar atmosphere. The resulting mixture was stirred at that temperature for 2 hr, to which CH_3I (56 μL, 124 mg, 0.87 mmol, 1.5 equiv.) in 2 mL of THF was added dropwise. The reaction mixture was allowed to warm to room temperature overnight and quenched with 1 mL of saturated aqueous NH_4Cl, extracted with ether (50 mL × 3). The combined organic layers were washed with 1N HCl, saturated aqueous $NaHCO_3$, water, brine respectively, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography to give *exo*-methylated oxabicyclic ketone **6** (97 mg, 75%) as a colorless oil. ^{1}H NMR (400 MHz): δ 1.13 (3H, s, 3-Me), 1.37 (3H, s, 1-Me), 1.54 and 1.61 (each 3H, br s, 4′-Me×2), 1.83~1.89 (6H, m), 2.04~1.10 (2H, m), 4.22 (1H, m, 4-H), 4.99 (1H, t, *J* = 7.4 Hz, CH=) *ppm*; FTIR ν_{max} 3020, 2976, 1753, 1215, 757 cm^{-1}; LRMS(EI) *m/z* 222(M^+, 4), 208(8), 151(34), 69(47), 43(100); HRMS(ESI) *m/z* $[M+H]^+$ 223.1693 ($C_{14}H_{23}O_2$ requires 223.1693).

1, 3-Dimethyl-2-methylenyl-3-(4-methyl-3-pentenyl)-7-oxabicyclo[2, 2, 1]hep-tane (7). –To a stirred suspension of methyltriphenylphosphonium iodide (212 mg, 0.52 mmol) in THF (2 mL) at 0 ^{o}C under Ar was added dropwise *n*-butyllithium (1.6 M in hexane, 0.34 mL, 0.54 mmol). The resulting mixture was stirred at room temperature for 2 hr, to which a solution of oxabicyclic ketone **6** (95 mg, 0.43 mmol) in THF (1 mL) was added dropwise. After the reaction mixture was stirred for 24 hr, the suspension was filtrated and the filtrate was dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography to yield the 1, 4-epoxy diene **7** (80 mg, 84%) as a colorless oil. ^{1}H NMR (400 MHz): δ 1.13 (3H, s, 3-Me), 1.50 (3H, s, 1-Me), 1.62 and 1.69(each 3H, br s, 4′-Me×2), 1.76~1.86 (6H, m), 2.08~2.13 (2H, m), 4.07 (1H, d, *J* = 4.4 Hz, 4-H), 4.58 and 4.69(each 1H, br s, CH_2=); FTIR ν_{max} 3018, 2978, 1215, 757, 669 cm^{-1}; LRMS(EI) *m/z* 220(M^+, 10), 205(7), 177(20), 163(27), 69(42), 43(100); HRMS(EI) *m/z* $[M]^+$ 220.1753 ($C_{15}H_{24}O$ requires 220.1827).

4-Eudesmene-1β, 11-diol (9). –A mixture of 1, 4-epoxy diene **7** (80.0 mg, 0.36 mmol) in 0.5 mL of 88% formic acid was stirred at 20 ^{o}C for 1.5 h under Ar atomsphere. The resulting mixture was poured into 100 mL of ether, the organic layer was washed with saturated aqueous $NaHCO_3$ several times until pH 7-8, and dried ($MgSO_4$). The solvent was evaporated in vacuum and the crude product was purified by silica gel chromatography to yield the corresponding C-1 formate **10** (31 mg, 32%) of 4-eudesmene-1β, 11-diol (**9**) as a colorless oil, along with a mixture of unidentifiable nonpolar materials. ^{1}H NMR (400 MHz): δ 1.03 (3H, s, 10-Me), 1.14 (6H, s, 11-Me×2), 1.08~1.19 (2H, m), 1.59 (3H, br s, 4-Me), 1.60~1.78 (4H, m), 1.95~2.22 (4H, m), 2.58 (1H, dt, *J* = 13.6, 2.6 Hz), 4.76 (1H, m, 1-H), 8.06 (1H, s, CHO *ppm*; ^{13}C NMR (100 MHz): δ 18.5, 22.7, 24.0, 26.3, 26.7, 27.3, 27.3, 31.4, 38.4, 38.6, 49.6, 72.6, 80.5, 124.1, 133.3, 161.1 *ppm*; FTIR ν_{max} 3378, 3020, 2924, 1215, 757 cm^{-1}; LRMS(EI) *m/z* 266(M^+, 7), 248(53), 202(43), 159(88), 131(71), 59(100); HRMS(EI) *m/z* $[M]^+$ 266.1894 ($C_{16}H_{26}O_3$ requires 266.1882).

To a solution of C-1 formate **10** (30 mg, 0.11 mmol) in 0.3 mL of *tert*-BuOH was added a solution of 1N NaOH (0.2 mL) at room temperature. The resulting mixture was stirred for 2 hr, and brine (5 mL) was added. The mixture was extracted with ether (50 mL × 3), washed with 1N HCl (5 mL), saturated aqueous $NaHCO_3$ (5 mL), brine, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography to yield 4-eudesmene-1β, 11-diol (**9**) (25 mg, 95%) as white needles, mp. 152~154 ^{o}C. ^{1}H NMR (400 MHz): δ 1.02 (3H, s, 10-Me), 1.22 (6H, s, 11-Me×2), .1.17~1.27 (2H, m), 1.67~1.73 (4H, m), 1.97~2.17 (4H, m), 2.63 (1H, dt, *J* = 13.9, 2.6 Hz), 1.60 (3H, br s, 4-Me), 3.47 (1H, m, 1-H) *ppm*; ^{13}C NMR (100 MHz): 17.3, 19.0, 22.9, 26.5, 26.7, 27.1, 27.2, 31.9, 38.9, 39.5, 49.8, 72.7, 78.4, 123.9, 133.6 *ppm*; FTIR ν_{max} 3389, 3020, 2928 cm^{-1}; LRMS(EI) *m/z* 238(M^+, 4), 220(27), 187(22), 119(20), 86(69), 84(100), 43(34); HRMS(ESI, Bruker APEXII 47e) *m/z* $[M+Na]^+$ 261.1828 ($C_{15}H_{26}O_2Na$ requires 261.1825).

(±)-Balanitol (2). –To a solution of 4-eudesmene-1β, 11-diol (**9**) (25 mg, 0.1 mmol) in 0.5 mL of acetic acid was added Adams' catalyst (PtO_2, 5 mg, from Aldrich), and the resulting mixture was hydrogenated (1 atm) at room temperature for 24 hr. The reaction mixture was filtrated, the resulting filtrate was concentrated and purified by silica gel chromatography to afford the title compound **2** (25 mg, 100%) as white solids, mp. 133~135 ^{o}C. ^{1}H NMR (400 MHz): δ 0.88 (3H, d, *J* = 8 Hz, 4-Me), 0.90 (3H, s, 10-Me), 1.20(6H, s, 11-Me×2), 1.18~1.27 (1H, m), 1.35~1.39 (4H, m), 1.54~1.70 (7H, m), 1.86 (1H, dt, J = 12.4, 3.2 Hz), 3.22 (1H, br d, *J* = 9.3 Hz, 1-H) *ppm*; ^{13}C NMR (100 MHz): δ 14.0, 14.9, 22.6, 26.4, 27.0, 27.3, 27.3, 31.5, 33.2, 39.3, 40.3, 45.9, 49.8, 72.8, 80.5 *ppm*; FTIR ν_{max} 3389, 3019 cm^{-1}; LRMS(EI) *m/z* 240(M^+, 2), 225(19), 182(52), 164(24), 123(37), 59(100); HRMS(EI) *m/z* $[M]^+$ 240.2027 ($C_{15}H_{28}O_2$ requires 240.2089).