Stereoselective Total Synthesis of Dihydrocorynantheol

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Supporting Information

General Methods. Unless otherwise noted, solvents and reagents were reagent grade and used without purification. CH₂Cl₂, *i*-Pr₂NH and Et₃N were freshly distilled from CaH₂. THF and Et₂O were passed through two columns of neutral alumina. MeOH, CH₃CN and DMF were passed through two columns of molecular sieves. Toluene was passed through a column of neutral alumina and a column of Q5 reactant. Reactions involving air- or moisture-sensitive reagents or intermediates were performed under an inert atmosphere of argon in glassware that had been flame dried. Melting points are uncorrected. Infrared (IR) spectra were recorded either neat on sodium chloride plates or as solutions in CH₂Cl₂ as indicated and are reported in wavenumbers (cm⁻¹). ¹H and ¹³C NMR spectra were obtained as solutions in CDCl₃ or C₆D₆ and chemical shifts are reported in parts per million (ppm) downfield from (CH₃)₄Si (TMS). Coupling constants are reported in hertz (Hz). Spectral splitting patterns are designated as follows: s, singlet; br, broad; d, doublet; t, triplet; q, quartet; m, multiplet and comp, complex multiplet. Signals in the ¹³C NMR that could not be assigned are separated by slashes. Flash column-chromatography was performed using Merck silica gel 60 (230-400 mesh ASTM) according to Still et al.¹

***N*-(2-Ethylbut-3-enyl)-2-(1*H*-indol-3-yl)acetamide (6).** A mixture of **3** (1.29 g, 5.08 mmol) and [(C₆H₁₁)₃P]₂Cl₂RuC₂H₃Ph (42 mg, 0.05 mmol, 1 mol%) in THF (60 mL) was stirred for 29 h at room temperature. A 2 M solution of EtMgCl in Et₂O (10.2 mL, 20.32 mmol) and Cp₂ZrCl₂ (222 mg, 0.76 mmol) were added. The mixture was stirred for 1 h and 2 M aqueous HCl (30 mL) was injected. The layers were separated, and the organic phase was extracted with EtOAc (3 × 30 mL). The combined organic phases were dried (MgSO₄), and the volatiles were removed under reduced pressure. The residue was purified by flash column-chromatography on silica gel, eluting with EtOAc/hexanes (1:1 → 7:3 → EtOAc) to give 926 mg (71%) of **6** as a yellow viscous oil. ¹H NMR (300 MHz) δ 8.79 (brs, 1 H), 7.55-7.09 (comp, 5 H), 5.77 (brs, 1 H), 5.28 (ddd, *J* = 9.0, 9.5, 16.8 Hz, 1 H), 4.76 (dd, *J* = 1.6, 10.2 Hz, 1 H), 4.59 (ddd, *J* = 0.6, 1.6,

16.8 Hz, 1 H), 3.73 (s, 2 H), 3.37 (ddd, $J = 4.9, 8.0, 13.0$, 1 H), 2.86 (ddd, $J = 4.9, 8.0, 13.0$ Hz, 1 H), 1.90-1.80 (m, 1 H), 1.40-1.20 (m, 1 H), 1.20-1.03 (m, 1 H), 0.78 (t, $J = 7.4$ Hz, 3 H); ^{13}C NMR (75 MHz) δ 171.5, 139.6, 136.4, 126.9, 123.8, 122.4, 119.8, 118.7, 116.6, 111.4, 108.7, 45.9, 42.6, 33.3, 24.9, 11.3; IR (neat) 3403, 3277, 2962, 2926, 1650, 1530, 1457, 1340, 918, 741 cm^{-1} ; HRMS (CI) m/z 257.1657 [$\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}$ ($M+1$) requires 257.1653].

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3-Ethyl-2-vinyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-a]quinolizine (11). Freshly distilled POCl_3 (0.23 mL, 2.42 mmol) was added to a suspension of **10** (90 mg, 0.30 mmol) in toluene (4 mL) and the reaction mixture was heated to 100 $^{\circ}\text{C}$ for 1 h. The volatiles were evaporated under reduced pressure and MeOH (6 mL) was added. The solution was cooled to 0 $^{\circ}\text{C}$, and NaBH_4 (92 mg, 2.42 mmol) was added. The reaction mixture was allowed to warm to room temperature over 1 h. A saturated aqueous solution of sat. aq. NaHCO_3 (0.2 mL) was added, and the organic solvent was removed under reduced pressure. The residue was dissolved in EtOAc (6 mL) and the solution was dried (MgSO_4). The solvents were removed under reduced pressure, and the residue was purified by flash column-chromatography on silica gel eluting with EtOAc/hexane (2:1) to furnish 74 mg (87%) of **11** as a yellow solid. Mp = 162-163 $^{\circ}\text{C}$ (EtOAc/hexane); ^1H NMR (300 MHz) δ 7.76 (brs, 1 H), 7.48 (d, $J = 7.2$ Hz, 1 H), 7.28 (d, $J = 7.2$ Hz, 1 H), 7.16-7.06 (comp, 2 H), 5.69-5.62 (m, 1 H), 5.12-5.03 (comp, 2 H), 3.26 (dd, $J = 2.1, 12.0$ Hz, 1 H), 3.19-2.97 (m, 3 H), 2.74 (m, 1 H), 2.62 (dt, $J = 4.2, 10.8$ Hz, 1 H), 2.12-2.01 (comp, 2 H), 1.93 (m, 1 H), 1.70-1.51 (comp, 3 H), 1.11-1.01 (m, 1 H), 0.91 (t, $J = 7.5$ Hz, 3 H); ^{13}C NMR (125 MHz) δ 141.9, 136.0, 134.7, 127.4, 121.3, 119.4, 118.1, 115.0, 110.7, 108.2, 60.1, 59.5, 53.3, 46.6, 41.6, 36.7, 24.3, 21.7, 11.2; IR (CH_2Cl_2) 3189, 2943, 2804, 2750, 1450, 1321, 911, 739 cm^{-1} ; HRMS (CI) m/z 308.1387 [$\text{C}_{18}\text{H}_{18}\text{N}_3\text{O}_2$ ($M+1$) requires 308.1399].

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Dihydrocorynantheol (1). 9-BBN (0.5 M solution in THF, 0.54 mL, 0.27 mmol) was added to a solution of **11** (30 mg, 0.11 mmol) in THF (3 mL) and the reaction mixture was stirred at room temperature for 12 h. The mixture was then cooled to 0 °C, and a 3 M solution of aqueous NaOH (134 µL) and a 30% aqueous solution of H₂O₂ (134 µL) were added. Stirring was continued for 1 h, whereupon EtOAc (3 mL) and sat. aq. NaHCO₃ (3 mL) were added. The layers were separated, and the aqueous phase was extracted with EtOAc (3 × 4 mL). The combined organic layers were dried (MgSO₄), filtered and concentrated under reduced pressure. The residue was purified by flash column-chromatography on silica gel eluting with EtOAc to give 21 mg (66%) of **1** as a pale yellow solid. Mp 175-177 °C (EtOAc), lit.^{2a} 178-180 °C; The ¹H and ¹³C NMR spectra were consistent with those reported in the literature.^{2b,c}

References

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