Synthesis of (+)-Casuarine

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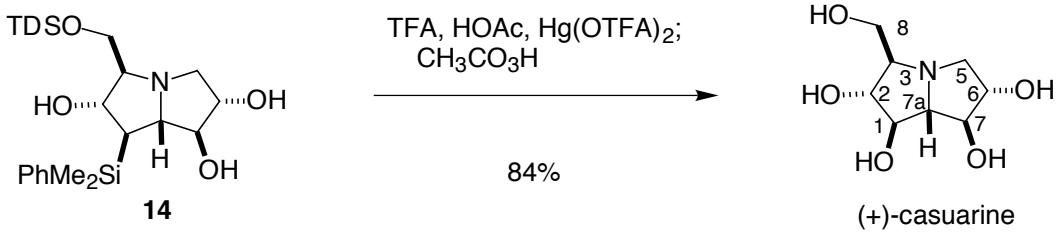
SUPPORTING INFORMATION

(1*R*,2*R*,3*R*,6S,7*R*,7a*R*)-Hexahydro-3-(hydroxymethyl)-1*H*-pyrrolizine-1,2,6,7-tetraol [Casuarine] ((+)-1).



Mercuric trifluoroacetate (462.7 mg, 1.08 mmol, 1.5 equiv.) was added to a solution of (-)-**14** (337 mg, 0.723 mmol, 1 equiv) in CF_3CO_2H (4 mL), $CHCl_3$ (4 mL), and HOAc (2 mL) and was stirred at rt for 60 min. The reaction mixture was then cooled to 0 ˚C and peroxyacetic acid (37% in HOAc, 12 mL)was added dropwise, after which the cooling bath was removed and the solution was stirred at rt for 18 h. The reaction mixture was cooled to 0 ºC and slowly quenched with Me_2S, maintaining the internal temperature ≤ 15 °C, until a negative starch/I_2 test was achieved. The contents of the flask were transferred to a column of BioRad AG 50W-X8 resin (10 g), which was then washed with H_2O (40 mL) to remove non-amine containing products, and then with 2 M NH_4OH (80 mL) to elute casuarine. Evaporation of the NH_4OH eluate afforded a pale-yellow powder which was recrystallized from EtOH to provide 84.4 mg of casuarine (57%). The mother liquor was concentrated and redissolved in MeOH (5 mL). 10% Palladium on carbon and 10 drops of HOAc were added and the mixture was stirred under 1 atm of H_2 for 16 h. The catalyst was removed by filtration through Celite, then was rinsed with MeOH (100 mL) and concentrated. The resulting, pale-yellow oil was transferred to a column of BioRad

AG 50W-X8 resin (10 g), then was washed with H_2O (40 mL) to remove acetic acid, and then with 2 M NH_4OH (80 mL) to elute casuarine. Evaporation of the NH_4OH eluate afforded a pale-yellow powder which was recrystallized (2 crops) from EtOH to provide 40.3 mg of casuarine (27%). The combined crops were treated with pentane and concentrated to azeotropically remove the remaining EtOH for a combined yield of 124.7 mg (84%) of casuarine as a white powder.

Analytical data for (+)-**1**

M.P. 180-181°C (EtOH)

Rotation $[\alpha]_D^{27} = +10.8°$ (H_2O), c = 1.020)

^{1}H NMR: (500 MHz, D_2O)
4.21-4.24 (m, 2H, H(C6), H(C7)), 4.19 (t, *J* = 8.1, 1H, H(C1)), 3.81 (t, *J* = 8.8, 1H, H(C2)), 3.78 (dd, *J* = 11.7, 3.7, 1H, H(C8)), 3.63 (dd, *J* = 11.7, 6.6, 1H, H(C8)), 3.29 (dd, *J* = 12.1, 4.3, 1H, H(C5)), 3.10 (dd, *J* = 8.3, 2.9, 1H, H(C7a)), 3.07 (ddd, *J* = 8.8, 6.6, 3.7, 1H, H(C3)), 2.94 (dd, *J* = 12.1, 3.6, 1H, H(C5))

^{13}C NMR: (125 MHz, D_2O))
79.15 (C7), 78.14 (C1), 77.77 (C6), 77.03 (C2), 72.03 (C7a), 70.26 (C3), 62.74 (C8), 58.31 (C5)

IR: (KBr)
3362 (br, s), 2970 (m), 2922 (m), 2890 (m), 2859 (m), 1444 (m), 1369 (w), 1322 (m), 1274 (m), 1225 (w), 1193 (w), 1167 (s), 1167 (s), 1114 (m), 1088 (m), 1047 (s), 1037 (s), 999 (s), 974 (m), 954 (w), 871 (w)

MS (FAB)
279 (100), 206 (M^++1, 80), 149 (60), 135 (22), 119 (49)

Analysis $C_8H_{15}NO_5$ (205.21)
Calc. C, 46.82; H, 7.37; N, 6.83
Found C, 46.59; H, 7.28; N, 6.49

TLC: R_f = 0.35 (CH_2Cl_2/ MeOH/NH_4OH; 5/5/1)