Addition and correction

A Versatile Enantioselective Synthesis of Barrenazines

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Supporting Information

The stereochemistry of epoxide **10** was assigned through chemical derivatization and X-ray analysis of compound **19**, prepared following the synthetic sequence shown in the scheme.

Experimental

(2*R*,4*S*,5*S*)-Benzyl 4-amino-2-(3-((*tert*-butyldimethylsilyl)oxy)propyl)-5-hydroxypiperidine-1-carboxylate (17**).** To a mixture of azido alcohol **11** (303.5 mg, 0.676 mmol) in THF:H₂O (8 mL, 3:1) at rt, Ph₃P (372.5 mg, 1.42 mmol) was added and the reaction mixture stirred overnight. The solvent was evaporated at reduced pressure and the residue purified by column chromatography (20% MeOH/CH₂Cl₂) to give amino alcohol **17** (254 mg, 0.601 mmol, 89%) as a yellow oil. ¹H NMR (300 MHz, CDCl₃, 25 °C): δ 0.01 (s, 6H), 0.87 (s, 9H), 1.19-1.31 (m, 2H), 1.43-1.57 (m, 2H), 1.76-1.86 (m, 1H), 1.95-2.04 (m, 1H), 2.65 (br s,

3H), 2.84-2.90 (m, 1H), 3.41 (dd, $J = 3.8, 14.4$ Hz, 1H), 3.50-3.61 (m, 3H), 3.82 (d, $J = 14.4$ Hz, 1H), 4.01 (q, $J = 6.9$ Hz, 1H), 5.06-5.17 (m, 2H), 7.28-7.36 (m, 5H) ppm; ^{13}C NMR (75 MHz, CDCl_3 , 25 °C): δ -5.3 (2 $\times$ CH_3), 18.3 (C), 25.9 (3 $\times$ CH_3), 29.6 (CH_2), 29.7 (CH_2), 33.3 (CH_2), 44.4 (CH_2), 52.4 (2 $\times$ CH), 62.8 (CH_2), 67.1 (CH_2), 72.9 (CH), 127.8 (2 $\times$ CH), 127.9 (CH), 128.5 (2 $\times$ CH), 136.7 (C), 156.5 (C) ppm; IR (ATR): 3033, 2951, 2927, 2855, 2359, 2341, 1691, 1498 cm^{-1} ; MS (ESITOF) m/z (%): 423 ($M^+ + \text{H}$, 51), 379 (2); HRMS (ESITOF) m/z calcd for $\text{C}_{22}\text{H}_{39}\text{O}_4\text{N}_2\text{Si}$ ($M^+ + \text{H}$), 423.2673; found, 423.2679.

(2*R*,4*S*,5*S*)-Benzyl 2-(3-((*tert*-butyldimethylsilyl)oxy)propyl)-5-hydroxy-4-(4-methylphenylsulfonamido)piperidine-1-carboxylate (18). To a solution of amino alcohol **17** (44 mg, 0.104 mmol) and Et_3N (73 μL , 0.520 mmol) in CH_2Cl_2 (5 mL) at 0 °C, a solution of tosyl chloride (60.0 mg, 0.312 mmol) in CH_2Cl_2 (3 mL) was added via cannula, and the mixture was warmed at rt overnight. The reaction was quenched by addition of water (5 mL) and extracted with EtOAc (3 $\times$ 10 mL), washed with brine (20 mL), dried with MgSO_4 , filtered and the solvent removed under reduced pressure. Purification by column chromatography (20% MeOH/ CH_2Cl_2) afforded **18** (48 mg, 0.083 mmol, 83%) as a heavy oil. ^1H NMR (300 MHz, CDCl_3 , 25 °C): δ 0.02 (s, 6H), 0.88 (s, 9H), 1.22-1.34 (m, 2H), 1.38-1.54 (m, 2H), 1.65-1.76 (m, 1H), 1.93-2.05 (m, 1H), 2.44 (s, 3H), 2.71 (d, $J = 3.6$ Hz, 1H), 3.07-3.15 (m, 1H), 3.29 (dd, $J = 3.4, 14.8$ Hz, 1H), 3.49-3.60 (m, 2H), 3.76 (br s, 1H), 3.92 (d, $J = 14.8$ Hz, 1H), 3.85-4.04 (m, 1H), 4.97 (d, $J = 6.1$ Hz, 1H), 5.06-5.16 (m, 2H), 7.28-7.39 (m, 7H), 7.76 (d, $J = 8.3$ Hz, 2H) ppm; ^{13}C NMR (75 MHz, CDCl_3 , 25 °C): δ -5.3 (2 $\times$ CH_3), 18.3 (C), 21.5 (CH_3), 25.9 (3 $\times$ CH_3), 29.3 (CH_2), 29.7 (CH_2), 30.9 (CH_2), 43.4 (CH_2), 51.6 (CH), 54.6 (CH), 62.6 (CH_2), 67.3 (CH_2), 70.9 (CH), 127.1 (2 $\times$ CH), 127.8 (2 $\times$ CH), 128.0 (CH), 128.5 (2 $\times$ CH), 129.9 (2 $\times$ CH), 136.5 (C), 136.6 (C), 143.9 (C), 156.3 (C) ppm; IR (ATR): 3466, 3261, 2952, 2927, 2856, 1671 cm^{-1} ; MS (ESITOF) m/z (%): 577 ($M^+ + \text{H}$, 78), 533 (8); HRMS (ESITOF) m/z calcd for $\text{C}_{29}\text{H}_{45}\text{O}_6\text{N}_2\text{SSi}$ ($M^+ + \text{H}$), 577.2762; found, 577.2753.

(2*R*,4*S*,5*S*)-Benzyl 5-hydroxy-2-(3-hydroxypropyl)-4-(4-methylphenylsulfonamido)piperidine-1-carboxylate (19). To a cold solution of **18** (48 mg, 0.083 mmol) in THF (3 mL) at 0 °C, a solution of TBAF (420 μL , 0.416 mmol, 1 M in THF) was added and the resulting mixture stirred overnight. The solvent was evaporated at reduced pressure and the residue purified by column chromatography (20% MeOH/ CH_2Cl_2) to give **19** (34 mg, 0.073 mmol, 88%) as a white solid (mp 137-139 °C, CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3 , 25 °C): δ 1.36-1.85 (m, 5H), 1.96-2.05 (m, 1H), 2.43 (s, 3H), 3.11 (q, $J = 5.5$ Hz, 1H), 3.36 (dd, $J = 2.9, 14.7$ Hz, 1H), 3.53-3.69 (m, 2H), 3.80-3.84 (m, 1H), 3.92 (d, $J = 14.7$ Hz, 1H), 4.05 (q, $J = 6.5$ Hz, 1H), 5.07-5.17 (m, 2H), 5.65 (d, $J = 5.5$ Hz, 1H), 7.30-7.37 (m, 7H), 7.76 (d, $J = 8.3$ Hz, 2H) ppm; ^{13}C NMR (75 MHz, CDCl_3 , 25 °C): δ 21.5 (CH_3), 28.6 (CH_2), 29.2 (CH_2), 29.3 (CH_2), 42.6 (CH_2), 51.0 (CH), 53.6 (CH), 62.3 (CH_2), 67.3 (CH_2), 69.8 (CH), 127.2 (2 $\times$ CH), 127.8 (2 $\times$ CH), 128.2 (CH), 128.5 (2 $\times$ CH), 129.9 (2 $\times$ CH), 136.4 (C),

136.5 (C), 143.9 (C), 156.3 (C) ppm; IR (ATR): 3424, 2936, 2921, 2358, 2325, 1670 cm^{-1} ; MS (ESITOF) m/z (%): 463 ($M^+ + \text{H}$, 31), 419 (100); HRMS (ESITOF) m/z calcd for $\text{C}_{23}\text{H}_{31}\text{O}_6\text{N}_2\text{S}$ ($M^+ + \text{H}$), 463.1897; found, 463.1890.