Total Synthesis of (+)-Peloruside A

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Experimental

Compound S1:

1,3-Dithiane (2.8g, 23.3mmol) was dissolved in THF (31ml) and cooled to -10°C . *n*-Butyllithium (1.4M in hexane, 17ml, 23.8mmol) was added and the solution was stirred at -10°C for 2 h and then cooled to -78°C . A solution of (S)-glycidyl tosylate (5g, 22.0mmol) in THF (8ml) was added by cannula, the solution was maintained at -78°C for 4 hours and allowed to warm to room temperature over 2 hours. Saturated aqueous NaHCO_3 was added and the mixture was extracted with ether, dried (Na_2SO_4) and evaporated to give a residue, which was subjected to flash column chromatography to afford the epoxide as a colorless oil (2.6g, 14.9mmol)

To a stirred suspension of CuI (500mg, 2.6mmol) in THF (70 ml) was added vinylmagnesium bromide (1.0M in THF, 22ml, 22mmol) at -50°C and the mixture was stirred for 30 min. Then a solution of the epoxide (2.6g, 14.9mmol) in THF (10 ml) was added by cannula. The resulting mixture was stirred at -40°C for 40 min, allowed to warm to -10°C over 30 min. The reaction mixture was quenched by the addition of saturated aqueous NH_4Cl and the bulk of THF was removed. The residue was extracted with ether, dried (Na_2SO_4) and evaporated to give a residue, which was subjected to flash column chromatography to provide secondary alcohol as a colorless oil (2.8g, 13.7mmol, 63%): NMR data are identical with literature (F. Yokokawa et al. *Tetrahedron* **2001**, 57, 6311).

To a stirred solution of the alcohol prepared above (1.4g, 6.8mmol), imidazole (1.83mg, 27mmol), DMAP (200mg, 1.6mmol) in 5ml DMF was added TESCl (1.6ml, 9.5mmol) at 0°C . The mixture was then stirred at r. t. for 12 h, after TLC show the completion of reaction, 20ml of aq. NaHCO_3 was added and the mixture was extracted with ether, dried (Na_2SO_4) and evaporated to give a residue, which was subjected to flash column chromatography to provide (-)-S1 (2.1g, 98%) as a colorless oil. $[\alpha]_D^{22} = -28.8^{\circ}$ (c 0.13, CHCl_3); IR (thin film, cm^{-1}) 742, 915, 1005, 1088, 1240, 1275, 1373, 1422, 1458, 1640, 2876, 2904, 2953; ^1H NMR (300 MHz, CDCl_3) δ_{H} 0.63 (6H, q, $J = 8.1$ Hz), 0.97 (9H, t, $J = 8.1$ Hz), 1.79-1.94 (3H, m), 2.05-2.15 (1H, m), 2.22-2.27 (2H, m), 2.78-2.93 (4H, m), 3.98-4.06 (1H, m), 4.11 (1H, dd, $J = 6.0$ Hz, 8.4 Hz), 5.03-5.09 (2H, m), 5.71-5.85 (1H, m) ^{13}C NMR (75 MHz, CDCl_3); δ_{C} 5.48, 7.09, 26.35, 30.23, 30.71, 42.57, 42.84, 44.21, 68.64, 117.578, 134.545; HRMS calc. for $\text{C}_{15}\text{H}_{30}\text{OSSi}$ $[\text{M}+\text{H}]$ 319.1586, found 319.1587.

Compound 4:

A stirred mixture of S1 (116mg, 0.36mmol), MeI (0.23ml, 3.7mmol) and CaCO_3 (190mg,

1.9mmol) in 5ml MeCN/H₂O (v:v = 9:1) was heated at 45°C for 2.5 h, cool down to room temperature, the bulk of MeCN was removed. Then the mixture was extracted with ether, dry (Na₂SO₄) and evaporated to give a residue, which was subjected to flash column chromatography to provide aldehyde **2** and was directly used for the next step.

To a solution of oxazolidinone **3** (160 mg, 0.45mmol) in 3 ml of dry toluene was added Et₃N (0.07ml, 0.49mmol) followed by Bu₂BOTf (1 M in CH₂Cl₂, 0.45ml, 0.45mmol) at -50°C. After stirring at -50°C for 1.5 h, aldehyde **2** in 1 ml of toluene was added via cannula. The resulting mixture was warmed to -30°C over 30 min and held at -30°C for 2h. The reaction was quenched by adding 0.8 ml of pH 7 phosphate buffer followed by 0.8 ml of methanol and 0.8 ml of tetrahydrofuran. After 5 min, 0.4 mL of 30% aqueous hydrogen peroxide was added (dropwise). The mixture was then warmed up to 0°C and stirred at 0°C for 1 h, concentrated by rotary evaporation and diluted with aqueous NaHCO₃. This mixture was extracted with ethyl acetate, dried (Na₂SO₄) and evaporated to give a residue, which was subjected to flash column chromatography to provide (+)-**4** (125mg, 61%, 2 steps) as a colorless oil. $[\alpha]_D^{22} = +7.05^\circ$ (c 0.02, CHCl₃); IR (thin film, cm⁻¹) 745, 823, 1108, 1248, 1390, 1456, 1514, 1612, 1708, 1781, 2954, 3502; ¹H NMR (300 MHz, CDCl₃) δ_H 0.64 (6H, q, *J* = 7.8 Hz), 0.97 (9H, t, *J* = 7.8 Hz), 1.71 (1H, ddd, *J* = 2.4, 6.0, 14.4 Hz), 1.87 (1H, ddd, *J* = 6.9, 9.9, 14.4 Hz), 2.22-2.38 (2H, m), 2.71 (1H, dd, *J* = 9.9, 13.5 Hz), 2.96 (1H, d, *J* = 5.7 Hz), 3.27 (1H, dd, *J* = 3.3, 13.5 Hz), 3.81 (3H, s), 3.96-4.12 (2H, m), 4.15-4.27 (2H, m), 4.51 (1H, d, *J* = 11.4 Hz), 4.67-4.74 (2H, m), 5.07-5.15 (2H, m), 5.75-5.89 (1H, m), 6.90 (2H, d, *J* = 8.7 Hz), 7.22-7.40 (7H, m), ¹³C NMR (75 MHz, CDCl₃) δ_C 5.18, 7.04, 37.89, 39.93, 42.01, 55.44, 55.85, 67.00, 71.15, 71.21, 72.99, 79.45, 114.02, 117.69, 127.59, 129.18, 129.42, 129.59, 130.38, 134.52, 135.38, 153.55, 159.79, 170.78; HRMS calc. for C₃₂H₄₅NO₇Si [M+H] 584.3044, found 584.3027.

Compound **5**:

To a stirred solution of **4** (15mg, 0.024mmol) and 2,2-dimethoxypropane (7.4mg, 0.071mmol) in 1.5 ml CH₂Cl₂ was added PPTS (0.6 mg, 0.0024mmol) at 0°C. The stirred mixture was then warm up to r. t. slowly and stirred at r. t. for 2h. The reaction mixture was concentrated by rotary evaporation to give a residue, which was purified by column chromatography to afford (+)-**5** (10mg, 81%) as a colorless oil, $[\alpha]_D^{22} = +39.1^\circ$ (c 0.002, CHCl₃); IR (thin film, cm⁻¹) 701, 1032, 1110, 1248, 1380, 1513, 1612, 1705, 1781, 2928; ¹H NMR (300 MHz, CDCl₃) δ_H 1.28-1.49 (1H, m), 1.34 (3H, s), 1.42 (3H, s), 1.57-1.63 (1H, m), 2.12-2.22 (1H, m), 2.27-2.36 (1H, m), 2.69 (1H, dd, *J* = 13.5, 9.6 Hz), 3.22 (1H, dd, *J* = 13.5, 3.3 Hz), 3.81 (3H, s), 3.82-3.92 (1H, m), 4.14-4.19 (2H, m), 4.30-4.37 (1H, m), 4.56-4.69 (3H, m), 5.06-5.14 (2H, m), 5.48 (1H, d, *J* = 5.4 Hz), 5.73-5.87 (1H, m), 6.89-7.37 (9H, m); ¹³C NMR (75 MHz, CDCl₃) δ_C 19.8, 30.1, 30.9, 38.3, 40.9, 55.5, 56.1, 66.8, 68.8, 69.9, 73.3, 77.0, 98.9, 113.9, 117.4, 127.6, 129.2, 129.6, 130.5, 134.2, 135.5, 153.5, 159.7, 170.6; HRMS calc. for C₂₉H₃₅NO₇ [M-H]⁺ 508.2335, found 508.2338.

Compound 6:

To a stirred solution of **4** (120mg, 0.2mmol) in 5ml CH_2Cl_2 was added proton sponge (642mg, 3.0mmol) followed by trimethyloxonium tetrafluoroborate (444mg, 3.0mmol) at 0°C . After stirring 15 h at room temperature, the reaction was quenched with aq. NaHCO_3 and extracted with CH_2Cl_2 . The extract was washed with sat. aq. NaCl , dried (Na_2SO_4) and evaporated to give a residue, which was filtered through a short column to provide a crude material which was directly used for the next step.

To a stirred solution of crude material prepared above in 2 ml CH_2Cl_2 was added H_2O (0.1ml) followed by DDQ (143mg, 0.63mmol) at 0°C , after stirring at 0°C for 20 min, the ice bath was removed and the mixture was stirred at r. t. for 2h. The mixture was then diluted with 15 ml of saturated aqueous sodium bicarbonate and extracted with CH_2Cl_2 . The organic layers were combined, dried (Na_2SO_4), and evaporated to give a residue which was then dissolved in 1ml CH_2Cl_2 , to this solution was added DIPEA (348mg, 2.7mmol) followed by MOMCl (145mg, 1.8mmol) at 0°C . The resulting mixture was warmed up to r. t. slowly and stirred at r. t. for 15h. Then diluted with 5 ml of saturated aqueous sodium bicarbonate and extracted with ether. The organic layers were combined, dried (Na_2SO_4) and evaporated to give a residue, which was purified by column chromatography afforded (+)-**6** (62mg, 62%, 3 steps) as a colorless oil, $[\alpha]_D^{22}=44.86^\circ$ (c 0.007, CHCl_3); IR (thin film, cm^{-1}) 702, 745, 917, 1007, 1048, 1107, 1153, 1211, 1349, 1387, 1455, 1709, 1783, 2877, 2954; ^1H NMR (300 MHz, CDCl_3) δ_{H} 0.60 (6H, q, $J = 8.1$ Hz), 0.95 (9H, t, $J = 8.1$ Hz), 1.78 (2H, t, $J = 6.3$ Hz), 2.17-2.37 (2H, m), 2.78 (1H, dd, $J = 9.6$, 13.5 Hz), 3.34 (1H, dd, $J = 3.3$, 9.6 Hz), 3.39 (3H, s), 3.40 (3H, s), 3.70-3.76 (1H, m), 3.86-3.94 (1H, m), 4.15-4.22 (2H, m), 4.60-4.67 (1H, m), 4.69 (1H, d, $J = 6.9$ Hz), 4.79 (1H, d, $J = 6.9$ Hz), 5.02-5.11 (2H, m), 5.48 (1H, d, $J = 4.8$ Hz), 5.77-5.92 (1H, m), 7.23-7.37 (5H, m); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} 5.21, 7.19, 37.72, 37.79, 41.65, 55.98, 56.58, 58.78, 66.63, 69.34, 77.20, 78.60, 97.77, 117.44, 127.64, 129.27, 129.74, 135.26, 135.51, 153.43, 171.23; HRMS calc. for $\text{C}_{27}\text{H}_{43}\text{NO}_7\text{Si}$ $[\text{M}+\text{H}]^+$ 522.2887, found 522.2862.

Compound 7:

To a stirred solution of **6** (125mg, 0.24mmol) in 8ml CH_2Cl_2 was added pyridine (50mg, 0.63mmol) at -78°C , ozone was bubbled through the solution until TLC shows the completion of reaction. PPh_3 (125mg, 0.48mmol) was added and the mixture was warmed up to room temperature slowly and stirred at room temperature for 4 hours. Then the reaction mixture was diluted with aq. NaHCO_3 and extracted with CH_2Cl_2 , dried (Na_2SO_4) and evaporated to give a residue, which was subjected to a short column to provide aldehyde **7** as colorless oil and was directly used for the next step. ^1H NMR (300 MHz, CDCl_3) δ_{H} 0.62 (6H, q, $J = 8.1$ Hz), 0.97 (9H, t, $J = 8.1$ Hz), 1.89 (2H, t, $J = 6.6$ Hz), 2.55-2.70 (2H, m), 2.78 (1H, dd, $J = 9.9$, 13.5 Hz), 3.36 (1H, dd, $J = 3.0$, 13.5 Hz), 3.42 (3H, s), 3.43 (3H, s), 3.71-3.79 (1H, m), 4.19-4.24 (2H, m), 4.40-4.48 (1H, m), 4.62-4.69 (1H, m), 4.71 (1H, d, $J = 6.9$ Hz), 4.81 (1H, d, $J = 6.9$ Hz), 5.55 (1H, d, $J = 4.5$ Hz), 7.23-7.40 (5H, m), 9.81 (1H, t, $J = 2.4$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ_{C} 5.08, 7.07, 37.69, 38.55, 50.89, 56.00, 56.58, 58.98, 65.52, 66.68, 76.31, 78.37, 97.73, 127.67, 129.28,

129.73, 135.44, 153.75, 171.14, 202.26.

Compound 9:

To a stirred solution of diisopropylamide (41mg, 0.40mmol) in 5ml THF was added BuLi (1.7M in hexane, 0.23ml, 0.39mmol) at 0°C, the mixture was stirred at 0°C for 30 min. Cooled to -78°C, ketone **S8** (230mg, 0.36mmol) in 2ml THF was added, the reaction was stirred at -78°C for 1 hour and aldehyde **7** in 3ml THF was added. The reaction was stirred at -78°C for 1 min and quenched by 1ml aqueous NH₄Cl. The resulting mixture was warmed up to room temperature in 1 hour and extracted with CH₂Cl₂, dried (Na₂SO₄) and evaporated to give a residue, which was subjected to a short column to provide a mixture of two diastereomers (165mg) as colorless oil. This material was then dissolved in 5ml of CH₂Cl₂ and was cannulated to a stirred mixture of Dess-Martin periodinane (360mg, 0.85mmol) and pyridine (167mg, 2.1mmol) in 10 ml CH₂Cl₂ at 0°C. After stirring at the same temperature for 4 hours, aqueous Na₂S₂O₃ was added followed by aqueous NaHCO₃. Extracted with CH₂Cl₂, the organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue, which was purified by column chromatography to afford (+)-**9** (141mg, 85%) as a colorless oil, $[\alpha]_D^{22} = +25.4^\circ$ (c, 0.01, CHCl₃); IR (thin film, cm⁻¹) 688, 700, 745, 775, 836, 882, 920, 1101, 1153, 1210, 1250, 1387, 1460, 1604, 1708, 1784, 2866, 2954; ¹H NMR (500 MHz, CDCl₃) δ_H 0.01 (3H, s), 0.07 (3H, s), 0.62 (6H, q, *J* = 8.0 Hz), 0.83 (3H, t, *J* = 7.0 Hz), 0.90 (9H, s), 0.94 (9H, t, *J* = 8.0 Hz), 1.05-1.09 (21H, m), 1.10 (3H, s), 1.16-1.23 (5H, m), 1.38-1.45 (1H, m), 1.63-1.77 (5H, m), 1.85 (2H, t, *J* = 6.0 Hz), 2.12-2.19 (1H, m), 2.34-2.41 (1H, m), 2.45 (1H, dd, *J* = 8.0, 14.0 Hz), 2.55 (1H, dd, *J* = 5.0, 14.0 Hz), 2.75-2.83 (1H, m), 3.30 (3H, s), 3.35 (3H, s), 3.34-3.41 (1H, m), 3.42 (3H, s), 3.45 (3H, s), 3.43-3.51 (2H, m), 3.68-3.71 (1H, m), 3.74-3.79 (1H, m), 4.05 (1H, dd, *J* = 1.5, 10.5 Hz), 4.18-4.25 (2H, m), 4.31-4.40 (1H, m), 4.51 (1H, dd, *J* = 2.5, 9.5 Hz), 4.58-4.69 (3H, m), 4.72 (1H, d, *J* = 7.0 Hz), 4.81 (1H, d, *J* = 7.0 Hz), 4.96 (1H, d, *J* = 9.5 Hz), 5.51 (1H, d, *J* = 4.5 Hz), 5.70 (1H, s), 7.26-7.38 (5H, m); ¹³C NMR (125 MHz, CDCl₃) δ_C -4.75, -4.72, 5.02, 7.11, 12.20, 15.53, 18.27, 18.31, 20.98, 22.25, 25.04, 25.11, 29.95, 37.11, 37.71, 38.92, 40.68, 46.69, 54.87, 55.97, 56.33, 56.55, 59.09, 66.12, 66.24, 66.65, 67.21, 67.66, 74.17, 74.40, 76.73, 78.51, 80.43, 97.73, 98.85, 98.97, 127.04, 127.64, 129.26, 129.74, 135.47, 139.19, 153.46, 171.14, 192.52, 199.43.

Compound 10:

To a stirred solution of **9** (152mg, 0.13mmol) in 10ml toluene was added p-toluenesulfonic acid (1.9mg, 0.01mmol) and the mixture was heated at 45°C for 2.5 hours. After TLC shows the completion of reaction, aqueous NaHCO₃ was added. Extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue, which was purified by column chromatography to afford (-)-**10** (81mg, 62%) as a colorless oil, $[\alpha]_D^{22} = -36.69^\circ$ (c, 0.003,

CHCl₃); IR (thin film, cm⁻¹) 688, 701, 775, 836, 882, 920, 1035, 1103, 1196, 1211, 1249, 1349, 1388, 1463, 1596, 1666, 1707, 1782, 2865, 2893, 2944; ¹H NMR (500 MHz, CDCl₃) δ_H 0.01 (3H, s), 0.07 (3H, s), 0.82 (3H, t, *J* = 7.5 Hz), 0.91 (9H, s), 1.05-1.09 (21H, m), 1.10 (3H, s), 1.13-1.23 (5H, m), 1.40-1.45 (1H, m), 1.66-1.80 (5H, m), 2.10-2.25 (3H, m), 2.31-2.39 (1H, m), 2.42 (1H, dd, *J* = 4.0, 16.5 Hz), 2.50 (1H, dd, *J* = 14.0, 16.5 Hz), 2.82 (1H, dd, *J* = 10.0, 13.5 Hz), 3.29 (3H, s), 3.34 (3H, s), 3.38 (1H, dd, *J* = 4.0, 13.5 Hz), 3.43 (3H, s), 3.44 (3H, s), 3.44-3.51 (2H, m), 3.69 (1H, dd, *J* = 4.0, 10.0 Hz), 3.86-3.89 (1H, m), 4.05 (1H, d, *J* = 9.5 Hz), 4.21 (1H, dd, *J* = 2.5, 9.0 Hz), 4.25 (1H, t, *J* = 9.0 Hz), 4.49 (1H, d, *J* = 8.0 Hz), 4.58-4.64 (2H, m), 4.67 (1H, d, *J* = 6.5 Hz), 4.70-4.75 (2H, m), 4.83 (1H, d, *J* = 6.5 Hz), 4.97 (1H, d, *J* = 10.5 Hz), 5.50 (1H, s), 5.65 (1H, d, *J* = 4.5 Hz), 7.26-7.38 (5H, m); ¹³C NMR (125 MHz, CDCl₃) δ_C -4.75, -4.43, 12.19, 12.31, 18.27, 18.28, 18.32, 21.73, 21.87, 25.07, 26.06, 35.27, 37.03, 37.71, 40.73, 41.20, 42.18, 45.03, 55.11, 56.01, 56.42, 56.69, 58.85, 66.32, 66.70, 67.64, 74.39, 75.42, 78.05, 80.58, 97.81, 99.09, 103.34, 127.01, 127.67, 129.28, 129.75, 135.43, 139.25, 153.49, 170.82, 182.90, 193.65; HRMS calc. for C₅₅H₉₅NO₁₃Si₂ [M+Na]⁺ 1056.6240, found 1056.6217.

Compound **S10**:

To a stirred solution of **10** (60mg, 0.058mmol) in 5ml mixture solvent (MeCN/H₂O, v/v = 5:1) was added HF/Pyridine complex (440mg, 4.4mmol) at 0°C and the mixture was stirred at room temperature for 15 hours. After TLC shows the completion of reaction, aqueous NaHCO₃ was added. Extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give the crude diol, which was then dissolved in 1ml CH₂Cl₂. To this solution was added imidazole (30mg, 0.44mmol), DMAP (1.8mg, 0.015mmol) followed by TIPSCl (40mg, 0.20mmol) at 0°C, the resulting mixture was stirred at room temperature for about 10 hours. After TLC shows the completion of reaction, aqueous NaHCO₃ was added. Extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue, which was purified by column chromatography to provide (-)-**S10** (34mg, 65%, 2 steps) as a colorless oil, [α]_D²² = -34.0° (c 0.01, CHCl₃); IR (thin film, cm⁻¹) 882, 919, 1037, 1100, 1211, 1388, 1463, 1594, 1662, 1708, 1781, 2866, 2943, 3468; ¹H NMR (500 MHz, CDCl₃) δ_H 0.85 (3H, t, *J* = 7.5 Hz), 1.04-1.09 (21H, m), 1.10 (3H, s), 1.12-1.18 (4H, m), 1.41-1.51 (2H, m), 1.57-1.61 (2H, m), 1.76 (3H, s), 2.01-2.07 (1H, m), 2.13-2.25 (2H, m), 2.43 (1H, dd, *J* = 4.0, 16.5 Hz), 2.48-2.59 (2H, m), 2.82 (1H, dd, *J* = 9.5, 13.5 Hz), 3.36 (3H, s), 3.37 (3H, s), 3.38-3.42 (2H, m), 3.43 (3H, s), 3.44 (3H, s), 3.56-3.62 (1H, m), 3.64 (1H, dd, *J* = 5.0, 9.0 Hz), 3.85-3.89 (1H, m), 3.95 (1H, dd, *J* = 2.5, 8.5 Hz), 4.21 (1H, dd, *J* = 2.5, 9.0 Hz), 4.26 (1H, t, *J* = 9.0 Hz), 4.54-4.61 (2H, m), 4.64 (1H, d, *J* = 6.5 Hz), 4.67 (1H, d, *J* = 6.5 Hz), 4.70-4.75 (2H, m), 4.83 (1H, d, *J* = 7.0 Hz), 4.97 (1H, d, *J* = 9.5 Hz), 5.50 (1H, s), 5.65 (1H, d, *J* = 4.5 Hz), 7.27-7.39 (5H, m); ¹³C NMR (125 MHz, CDCl₃) δ_C 12.17, 12.21, 18.22, 18.53, 21.38, 22.00, 24.80, 35.36, 37.31, 37.69, 38.12, 41.21, 42.33, 45.36, 55.95, 56.00, 56.26, 56.71, 58.89, 66.46, 66.72, 67.32, 75.44, 75.72, 78.00, 81.52, 97.84, 98.97, 103.57, 127.69, 129.29, 129.74, 131.06, 135.39, 139.61, 153.51, 170.76, 182.62, 193.62;

Compound **11**:

To a stirred solution of **S10** (42mg, 0.045mmol) in 2ml THF was added 0.3ml H₂O and aq. LiOH (1M in H₂O, 0.09ml, 0.09mmol) 0°C, the mixture was stirred at the same temperature for 40 minutes. After TLC shows the completion of reaction, the solution was acidified with acetic acid (adjust to PH = 3) and extracted with ethyl acetate. The organic layers were combined, dried (Na₂SO₄) and evaporated to give the corresponding seco-acid, which was then dissolved in 1ml THF. To this solution was added Et₃N (70mg, 0.69mmol) and trichlorobenzoyl chloride (66mg, 0.27mmol) at 0°C. The reaction mixture was warmed up to room temperature and stirred at the same temperature for 2 hours. Toluene (15ml) was added to the reaction mixture and the resulting diluted solution was added (via syringe pump, 3ml/h) to a solution of DMAP (114mg, 0.93mmol) in toluene (20ml) at room temperature. After continued stirring for 12 hours, the reaction mixture was heated to 90°C and stirred at the same temperature for 6 hour. Aqueous NaHCO₃ was added and extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue, which was subjected to column chromatography to afford (-)-**11** (18mg, 56%, 2 steps) as a colorless oil, [α]_D²² = -81.2° (c 0.005, CHCl₃); IR (thin film, cm⁻¹) 680, 805, 882, 922, 1033, 1096, 1153, 1243, 1332, 1391, 1463, 1595, 1667, 1731, 1759, 2866, 2941; ¹H NMR (500 MHz, CDCl₃) δ _H 0.88 (3H, t, *J* = 7.5 Hz), 1.02-1.11 (21H, m), 1.19 (3H, s), 1.20 (3H, s), 1.23-1.30 (1H, m), 1.45-1.62 (2H, m), 1.71 (3H, s), 1.66-1.82 (2H, m), 1.95-2.05 (2H, m), 2.23 (1H, ddd, *J* = 4.0, 7.0, 15.0 Hz), 2.37 (1H, dd, *J* = 2.5, 16.5 Hz), 2.56 (1H, dd, *J* = 14.0, 16.5 Hz), 2.58-2.64 (1H, m), 3.30 (3H, s), 3.40 (3H, s), 3.40-3.46 (1H, m), 3.41 (3H, s), 3.48 (3H, s), 3.51-3.62 (2H, m), 3.84-3.91 (2H, m), 4.18 (1H, d, *J* = 7.0 Hz), 4.28-4.35 (1H, m), 4.67-4.75 (4H, m), 5.20 (1H, d, *J* = 10.0 Hz), 5.53 (1H, s), 5.80 (1H, dd, *J* = 4.5, 6.5 Hz); ¹³C NMR (75 MHz, CDCl₃) δ _C 12.21, 18.18, 18.29, 20.53, 24.70, 25.15, 29.96, 34.84, 36.34, 38.45, 40.99, 41.97, 45.15, 56.22, 56.71, 58.33, 65.89, 70.63, 74.67, 76.42, 76.75, 77.47, 79.16, 85.01, 96.35, 99.37, 105.17, 131.54, 133.11, 169.39, 180.99, 193.35; HRMS calc. for C₃₉H₇₀NO₁₁Si [M+H]⁺ 743.4766, found 743.4744.

Peloruside A:

To a stirred solution of **11** (15mg, 0.020mmol) and CeCl₃·7H₂O (7.5mg, 0.020mmol) in MeOH (2ml) was added NaBH₄ (0.95mg, 0.025mmol) at -60°C, the reaction mixture was stirred at the same temperature for 40 minutes and quenched with brine. The mixture was warmed up to room temperature, extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give the crude alcohol which was used for the next step immediately without further purification due to instability.

The crude alcohol prepared above was dissolved in 3ml CH₂Cl₂ and treated with solid

NaHCO₃ (9mg, 0.11mmol). To this stirred mixture, purified mCPBA (3.6mg, 0.021mmol) was added at -30°C. The mixture was stirred at the same temperature for 30 minutes and quenched with aqueous NH₄Cl. Extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue which was subjected to a column chromatography to afford alcohol (-)-**12** (7.5mg, 52% for 2 steps) as a colorless oil, $[\alpha]_D^{22} = -66.7^\circ$ (c 0.004, CHCl₃); IR (thin film, cm⁻¹) 680, 805, 882, 920, 1034, 1097, 1152, 1210, 1382, 1463, 1753, 2866, 2942, 3391; ¹H NMR (600 MHz, CD₃OD) δ_H 0.88 (3H, t, $J = 7.8$ Hz), 1.02-1.08 (21H, m), 1.12 (6H, s), 1.18-1.23 (1H, m), 1.25-1.32 (1H, m), 1.40-1.50 (1H, m), 1.53 (1H, ddd, $J = 2.4, 4.2, 12.0$ Hz), 1.67 (3H, s), 1.63-1.73 (1H, m), 1.85 (1H, dd, $J = 12.6, 15.0$ Hz), 1.81-1.92 (1H, m), 1.94-2.08 (1H, m), 2.14 (1H, ddd, $J = 2.4, 6.6, 15.0$ Hz), 2.26-2.36 (1H, m), 2.46-2.54 (1H, m), 3.38 (3H, s), 3.39 (6H, s), 3.34-3.46 (3H, m), 3.57-3.62 (1H, m), 3.73 (1H, d, $J = 3.0$ Hz), 3.84-3.92 (1H, m), 3.94-4.01 (2H, m), 4.08 (1H, ddd, $J = 3.0, 4.8, 11.4$ Hz), 4.26-4.42 (1H, m), 4.51-4.62 (1H, m), 4.63-4.71 (3H, m), 5.01 (1H, d, $J = 10.2$ Hz), 5.47 (1H, br s).

To a stirred solution of **12** (5 mg, 0.0068mmol) in CH₂Cl₂ (2.5ml) was added 2,6-di-tert-butyl pyridine (28mg, 0.15mmol) and Me₃OPBF₄ (15mg, 0.1mmol) at 0°C. The resulting mixture was stirred at 0°C until TLC shows the completion of reaction. Aqueous NaHCO₃ was added, extracted with ethyl acetate. The organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue, which was filtered through a short column (silica gel) to provide a crude material. This material was then dissolved in THF (1.5ml) and treated with 4N HCl (1.5ml) at 0°C, the resulting mixture was warmed up to room temperature and stirred at the same temperature for 3 hours. The reaction was quenched by aqueous NaHCO₃ and extracted with ethyl acetate, the organic layers were combined, dried (Na₂SO₄) and evaporated to give a residue which was subjected to a column chromatography to provide (+)-peloruside A (1.6mg, 43% for 2 steps) as a colorless oil, $[\alpha]_D^{22} = +16.5^\circ$ (c 0.0015, CH₂Cl₂); (lit.:² $[\alpha]_D^{20} = +16^\circ$ (c 0.30, CH₂Cl₂)); IR (thin film, cm⁻¹) 1085, 1155, 1222, 1383, 1456, 1739, 2850, 2929, 3445; ¹H NMR (500 MHz, CDCl₃) δ_H 0.86 (3H, t, $J = 7.5$ Hz), 1.10 (3H, s), 1.12 (3H, s), 1.16-1.21 (1H, m), 1.40-1.46 (2H, m), 1.53 (1H, q, $J = 12.0$ Hz), 1.68 (3H, d, $J = 1.0$ Hz), 1.75-1.82 (1H, m), 1.79 (1H, ddd, $J = 2.5, 5.0, 12.5$ Hz), 2.00-2.18 (4H, m), 2.56-2.66 (1H, m), 2.71 (1H, d, $J = 9.0$ Hz), 3.01 (1H, dd, $J = 3.0, 8.0$ Hz), 3.31 (3H, s), 3.36, (1H, t, $J = 10.5$ Hz), 3.39 (3H, s), 3.48 (3H, s), 3.65 (1H, ddd, $J = 3.0, 7.5, 10.0$ Hz), 3.82 (1H, ddd, $J = 3.0, 5.0, 11.5$ Hz), 3.96-4.02 (1H, m), 4.02 (1H, s), 4.22 (1H, dd, $J = 5.5, 10.5$ Hz), 4.26 (1H, ddd, $J = 2.5, 4.5, 10.5$ Hz), 4.46 (1H, s), 4.53 (1H, d, $J = 9.5$ Hz), 4.91 (1H, m), 5.05 (1H, d, $J = 10.5$ Hz), 5.69 (1H, d, $J = 10.5$ Hz), 6.77 (1H, br. s); ¹³C NMR (125 MHz, CDCl₃) δ_C 12.24, 15.84, 17.45, 20.81, 24.60, 31.67, 32.59, 33.92, 35.70, 43.37, 43.60, 55.70, 56.09, 59.11, 63.49, 66.85, 67.00, 70.30, 70.91, 73.89, 75.90, 77.93, 78.28, 101.91, 131.18, 136.09, 174.01; HRMS calc. for C₂₇H₄₈NO₁₁ [M+Na]⁺ 571.3094, found 571.3079.