

# Control of the Stereochemistry of C14 Hydroxyl During the Total Synthesis of Withanolide E and Physachenolide C

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## Experimental Techniques, materials and Instrumentation

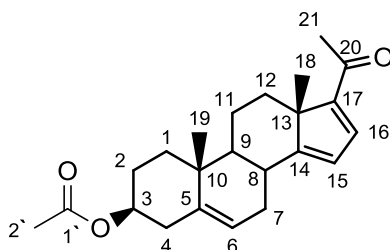
**General:** Commercially available chemical reagents and starting materials were purchased from Sigma-Aldrich, Alfa Aesar and Carbosynth and used without any additional purification. All solvents were of reagent grade. Petroleum ether (PE) refers to the fraction of petroleum spirit boiling in the range of 60 to 80 °C. Where stated, mixtures of solvents are referred to as volume-to-volume (v/v) ratios. Synthesised compounds were purified by flash chromatography using high-purity silica gel (Fluorochem: LC4025), pore size 40-63 µm (CAS Number: 7631-86-9). The analytical thin layer chromatography was conducted on Merck silica gel 60 F254 aluminium backed plates (catalogue number 1.05554.0001, VWR). TLC plates were visualised under ultraviolet light lamp (254 nm), or by dipping in basic potassium permanganate (KMnO<sub>4</sub>) solution.

Proton and carbon nuclear magnetic resonance (<sup>1</sup>H and <sup>13</sup>C NMR) spectra were recorded using Bruker AMX400 spectrometer operating at 400 MHz and 101 MHz respectively. Deuterated chloroform (CDCl<sub>3</sub>) was used as the NMR solvent unless otherwise stated. Chemical shifts are reported in parts per million (δ, ppm). <sup>1</sup>H NMR chemical shifts are reported relative to an internal reference (tetramethylsilane) or residual proton signals of the solvent. Coupling constants (J) are expressed in Hertz (Hz). The splitting patterns in NMR spectra are reported with the following abbreviations; singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint.), multiplet (m), double doublet (dd), double triplet (dt), double double doublet (ddd), triple double doublet (tdd) and broad (br). <sup>13</sup>C NMR chemical shifts are reported relative to the signal of the solvent. Where necessary, correlation spectroscopy (COSY), nuclear overhauser enhanced spectroscopy (NOESY), heteronuclear multiple quantum correlation spectroscopy (HMQC) for <sup>13</sup>C/<sup>1</sup>H nuclei, and distortionless enhancement by polarization transfer (DEPT) technique were employed to confirm the assignment of NMR spectra.

Routine infrared (IR) spectra were recorded on a Perkin-Elmer Spectrum 100 FT-IR spectrometer. Spectra are reported in wavenumbers (cm<sup>-1</sup>).

Routine LC-MS was used to monitor the reaction on Waters, Micromass Quattro Ultima in the electrospray (ES), positive (+ve) electrospray. High resolution accurate mass determination was performed using a Thermo Orbitrap LTQ XL spectrometer.

## Compound 7



To a stirred solution of 16-dehydropregnenolone acetate (**3**) (10.0 g, 28.05 mmol) in dry ether (300 ml) was slowly added anhydrous potassium acetate (15.0 g) in glacial acetic acid (130 ml). The mixture was cooled to 0° C in an ice bath and bromine (4.49 g, 28.05 mmol) in acetic acid (100 ml) was added dropwise over a period of 4 hours. The reaction mixture was stirred at 0° C for further 2 hours and then at room temperature overnight. The reaction mixture was partitioned between diethyl ether (400 ml) and water (500 ml). Organic extract was then washed with aqueous potassium carbonate (500 ml × 2), dried over MgSO<sub>4</sub> and stripped of solvent under reduced pressure to afford 5,6 dibromo as white foam. This was used for the next step without further purification.

NBS (9.99 g, 56.10 mmol) & AIBN (40.0 mg) were added to a solution of this white foam in EtOAc (150 ml) and the resulting mixture was heated to reflux under nitrogen atmosphere for 1 hour. The reaction mixture was cooled to room temperature and stripped of solvent under reduced pressure. The resulting residue was suspended in diethyl ether (500 ml), and the solid succinimide was filtered. The filtrate was stripped of solvent under reduced pressure to afford **6** as white foam which was dissolved in acetone (120 ml). Sodium iodide (20.0 g) was added and the mixture was heated to reflux for 3.5 hours under a nitrogen atmosphere. The acetone was removed under reduced pressure and the residue was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (400 ml) and washed aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution to remove iodine by-product. Organic extract was dried over MgSO<sub>4</sub> and solvent was removed under reduced pressure to afford brown solid. Silica gel column chromatography (5-10% EtOAc in PE) afforded compound **7** (3.92 g, 39%) as a pale yellow solid.

<sup>1</sup>H NMR δ 0.81 (1H, td, *J* = 12.9, 5.1 Hz, CH<sub>2</sub> - 12), 1.04 (1H, td, *J* = 11.4, 5.3 Hz, CH - 9), 1.09 – 1.20 (1H, m, CH<sub>2</sub> - 1), 1.14 (3H, s, CCH<sub>3</sub> - 19), 1.19 (3H, s, CCH<sub>3</sub> - 18), 1.56 - 1.70 (3H, m, CH<sub>2</sub> - 11, CH<sub>2</sub> - 2), 1.83 - 1.93 (2H, m, CH<sub>2</sub> - 2, CH<sub>2</sub> - 1), 2.03 (3H, s, CCH<sub>3</sub> - 2'), 2.18 – 2.27 (2H, m,

$\text{CH}_2$  - 7), 2.32 (3H, m,  $\text{CCH}_3$  - 21), 2.35 (2H, dd,  $J = 12.1, 3.4$  Hz,  $\text{CH}_2$  - 4), 2.43 – 2.53 (2H, m,  $\text{CH}$  - 8,  $\text{CH}_2$  - 12), 4.60 (1H, ddd,  $J = 10.8, 8.4, 4.7$  Hz,  $\text{CH}$  - 3), 5.45 – 5.49 (1H, m,  $\text{CH}$  - 6), 6.02 (1H, t,  $J = 2.1$  Hz,  $\text{CH}$  - 15), 7.22 (1H, d,  $J = 2.3$  Hz,  $\text{CH}$  - 16).

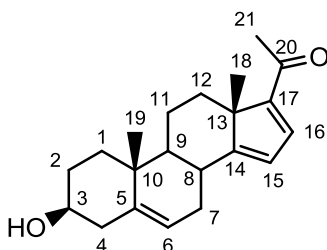
$^{13}\text{C}$  NMR  $\delta$  18.7 ( $\text{CCH}_3$ , 18), 19.8 ( $\text{CCH}_3$ , 19), 21.0 ( $\text{CH}_2$ , 11), 21.7 ( $\text{CCH}_3$  - 2'), 27.0 ( $\text{CCH}_3$  - 21), 28.0 ( $\text{CH}_2$ , 2), 29.2 ( $\text{CH}_2$ , 7), 32.6 ( $\text{CH}$ , 8), 35.9 ( $\text{CH}_2$ , 12), 37.6 ( $\text{CH}_2$ , 1), 37.8 ( $\text{CH}$ , 10), 38.3 ( $\text{CH}_2$ , 4), 53.8 ( $\text{C}$ , 13), 54.3 ( $\text{CH}$ , 9), 74.0 ( $\text{CH}$ , 3), 119.5 ( $\text{CH}$ , 15), 122.0 ( $\text{CH}$ , 6), 139.7 ( $\text{C}$ , 5), 142.1 ( $\text{CH}$ , 16), 155.1 ( $\text{C}$ , 17), 170.8 ( $\text{C}$  - 1'), 173.3 ( $\text{C}$  - 14), 192.9 ( $\text{C}$  - 20).

**Mass Spectrum** (ESI+),  $m/z$ , 355.34 [ $\text{M} + \text{H}$ ] $^+$ , 377.34 [ $\text{M} + \text{Na}$ ] $^+$ , 295.35 [ $\text{C}_{21}\text{H}_{27}\text{O}$ ] $^+$ , 731.37 [ $\text{M} \times 2 + \text{Na}$ ] $^+$ .

**IR:** 1727  $\text{cm}^{-1}$  (C=O stretch), 1032  $\text{cm}^{-1}$  (C-O stretch).

**HRMS:** (ESI+),  $m/z$ , found = 355.2292, calculated for  $\text{C}_{23}\text{H}_{31}\text{O}_3$  [ $\text{M} + \text{H}$ ] $^+$  = 355.2273.

### Compound 8



To a stirred solution of **7** (3.92 g, 11.06 mmol) in t-butanol (50 ml) was added KOH (3.10 g, 5eq.) in  $\text{H}_2\text{O}$  (5 ml). The resulting mixture was stirred at 30 °C overnight. Solvent was removed under reduced pressure and water (300 ml) was added. The resulting suspension was filtered and washed with water. The solid was dried under high vacuum overnight to afford compound **8** (3.45 g, 100%) as an off-white solid.

$^1\text{H}$  NMR  $\delta$  0.81 (1H, td,  $J = 12.8, 5.0$  Hz,  $\text{CH}_2$  - 12), 1.04 (2H, ddd,  $J = 22.9, 12.5, 4.6$  Hz,  $\text{CH}$  - 9,  $\text{CH}_2$  - 1), 1.13 (3H, s,  $\text{CCH}_3$  - 19), 1.19 (3H, s,  $\text{CCH}_3$  - 18), 1.47 - 1.72 (3H, m,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 11), 1.80 - 1.94 (2H, m,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 1), 2.14 – 2.38 (4H, m,  $\text{CH}_2$  - 4,  $\text{CH}_2$  - 7), 2.32 (3H, m,  $\text{CCH}_3$  - 21), 2.48 (2H, ddd,  $J = 9.9, 6.5, 3.2$  Hz,  $\text{CH}$  - 8,  $\text{CH}_2$  - 12), 3.53 (1H, ddd,  $J = 16.0, 11.1, 4.9$  Hz,  $\text{CH}$  - 3), 5.45 (1H, d,  $J = 2.4$  Hz,  $\text{CH}$  - 6), 6.01 (1H, d,  $J = 1.8$  Hz,  $\text{CH}$  - 15), 7.22 (1H, d,  $J = 2.2$  Hz,  $\text{CH}$  - 16).

$^{13}\text{C}$  NMR  $\delta$  18.7 ( $\text{CCH}_3$ , 18), 19.8 ( $\text{CCH}_3$ , 19), 21.0 ( $\text{CH}_2$ , 11), 27.0 ( $\text{CCH}_3$  - 21), 29.2 ( $\text{CH}_2$ , 7), 31.9 ( $\text{CH}_2$ , 2), 32.7 ( $\text{CH}$ , 8), 36.0 ( $\text{CH}_2$ , 12), 37.7 ( $\text{C}$ , 10), 37.8 ( $\text{CH}_2$ , 1), 42.5 ( $\text{CH}_2$ , 4), 53.8 ( $\text{C}$ ,

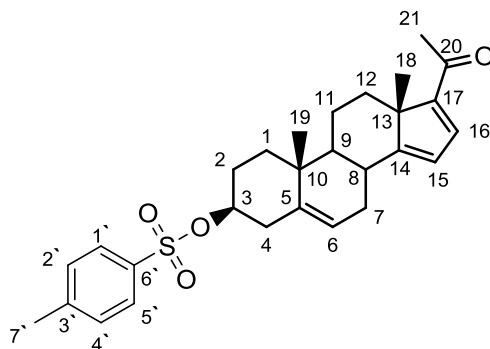
13), 54.4 (CH, 9), 72.0 (CH, 3), 119.4 (CH, 15), 121.1 (CH, 6), 140.8 (C, 5), 142.2 (CH, 16), 155.1 (C, 17), 173.6 (C - 14), 193.0 (C - 20).

**Mass Spectrum** (ESI+),  $m/z$ , 313.34 [M + H]<sup>+</sup>, 335.34 [M + Na]<sup>+</sup>, 295.35 [C<sub>21</sub>H<sub>27</sub>O]<sup>+</sup>.

**IR:** 3425 cm<sup>-1</sup> (OH stretch), 1631 cm<sup>-1</sup> (C=O stretch), 1027 cm<sup>-1</sup> (C-O stretch).

**HRMS:** (ESI+),  $m/z$ , found = 313.2184, calculated for C<sub>21</sub>H<sub>29</sub>O<sub>2</sub> [M + H]<sup>+</sup> = 313.2168.

### Compound 9



Tosyl chloride (2.39 g, 12.55 mmol) was added to a stirred solution of **8** (1.31 g, 4.18 mmol) in pyridine (10 ml) at room temperature. After 28 hours, water (300 ml) was added. The organic mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (50 ml × 3). The organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure to afford compound **9** (1.62 g, 83%) as an off-white solid.

**<sup>1</sup>H NMR** δ 0.78 (1H, td,  $J$  = 13.1, 4.3 Hz, CH<sub>2</sub> - 12), 0.93 – 1.08 (1H, m, CH - 9, CH<sub>2</sub> - 1), 1.09 (3H, s, CCH<sub>3</sub> - 19), 1.18 (3H, s, CCH<sub>3</sub> - 18), 1.49 - 1.65 (2H, m, CH<sub>2</sub> - 11), 1.70 - 1.89 (3H, m, CH<sub>2</sub> - 1, CH<sub>2</sub> - 7), 2.11 – 2.39 (3H, m, CH<sub>2</sub> - 2, CH<sub>2</sub> - 4), 2.32 (3H, m, CCH<sub>3</sub> - 21), 2.39 – 2.53 (3H, m, CH<sub>2</sub> - 4, CH - 8, CH<sub>2</sub> - 12), 4.39 – 4.28 (1H, m, CH - 3), 5.38 – 5.48 (1H, m, CH - 6), 6.00 (1H, app. t,  $J$  = 2.1 Hz, CH - 15), 7.21 (1H, d,  $J$  = 2.4 Hz, CH - 16), 7.33 (2H, d,  $J$  = 8.2 Hz, 2' & 4'), 7.86 (2H, d,  $J$  = 8.5 Hz, 1' & 5').

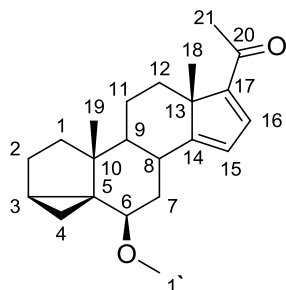
**<sup>13</sup>C NMR** δ 18.7 (CCH<sub>3</sub>, 18), 19.6 (CCH<sub>3</sub>, 19), 21.0 (CH<sub>2</sub>, 11), 22.0 (CCH<sub>3</sub> - 7'), 27.0 (CH<sub>3</sub>, 21), 28.8 (CH<sub>2</sub>, 7), 29.2 (CH<sub>2</sub>, 2), 32.5 (CH, 8), 35.9 (CH<sub>2</sub>, 12), 37.5 (CH<sub>2</sub>, 1), 37.6 (C, 10), 39.2 (CH<sub>2</sub>, 4), 53.8 (C - 13), 54.2 (CH, 9), 82.3 (CH, 3), 119.6 (CH, 15), 123.0 (CH, 6), 128.0 (CH, 1' & 5'), 130.1 (CH - 2' & 4'), 135.0 (C - 3'), 139.0 (C - 5), 142.0 (CH, 16), 144.8 (C - 6'), 155.2 (C, 17), 173.0 (C - 14), 193.0 (C - 20).

**Mass Spectrum** (ESI+),  $m/z$ , 467.43 [M + H]<sup>+</sup>, 295.45 [C<sub>21</sub>H<sub>27</sub>O]<sup>+</sup>.

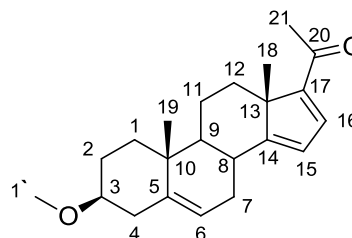
IR: 1640  $\text{cm}^{-1}$  (C=O stretch), 1342 & 1166  $\text{cm}^{-1}$  (S=O stretch), 932-810  $\text{cm}^{-1}$  (S-O stretch).

HRMS: (ESI+),  $m/z$ , found = 467.2283, calculated for  $\text{C}_{28}\text{H}_{35}\text{O}_4\text{S}$   $[\text{M} + \text{H}]^+ = 467.2256$ .

### Compound 5 & 10



**5**



**10**

Pyridine (0.82 ml, 10.17 mmol) was added to a stirred solution of compound **9** (1.58 g, 3.39 mmol) in anhydrous methanol (10 ml) at room temperature and the mixture was heated to reflux for 4 hours. The reaction mixture was cooled to room temperature and extracted with saturated  $\text{NaHCO}_3$  solution (300 ml) and  $\text{CH}_2\text{Cl}_2$  (200 ml  $\times$  3). The organic extracts were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel column chromatography (3-5% EtOAc in PE) afforded compound **5** (928 mg, 84%) as an off-white solid and compound **10** (127 mg, 12%) as a pale yellow solid.

### Compound 5

$^1\text{H NMR}$   $\delta$  0.50 (1H, dd,  $J = 8.0$  &  $5.2$  Hz,  $\text{CH}_2$  - 4), 0.68 (1H, app. t, 4.4 Hz  $\text{CH}_2$  - 4), 0.74 – 1.01 (4H, m,  $\text{CH}_2$  - 12,  $\text{CH}$  - 9,  $\text{CH}$  - 3,  $\text{CH}_2$  - 1), 1.14 (3H, s,  $\text{CCH}_3$  - 19), 1.22 (3H, s,  $\text{CCH}_3$  - 18), 1.40 – 1.78 (6H, m,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 11,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 2), 2.21 (4H, dt,  $J = 13.3$ , 2.9 Hz,  $\text{CH}_2$  - 7), 2.31 (3H, s,  $\text{CCH}_3$  - 21), 2.47 (1H, dt,  $J = 3.1$ , 3.1  $\text{CH}_2$  - 12), 2.75 (1H, app. t,  $J = 11.63$  Hz,  $\text{CH}$  - 8), 2.91 (1H, t,  $J = 2.8$  Hz,  $\text{CH}$  - 6), 3.37 (3H, s,  $\text{OCH}_3$  - 1'), 5.98 (1H, app. t,  $J = 2.02$  Hz,  $\text{CH}$  - 15), 7.22 (1H, d,  $J = 2.3$  Hz,  $\text{CH}$  - 16).

$^{13}\text{C NMR}$   $\delta$  13.6 ( $\text{CH}_2$ , 4), 19.2 ( $\text{CH}_3$ , 18), 19.7 ( $\text{CH}_3$ , 19), 21.8 ( $\text{CH}$ , 3), 23.0 ( $\text{CH}_2$ , 11), 25.2 ( $\text{CH}_2$ , 2), 27.0 ( $\text{CH}_3$ , 21), 31.9 ( $\text{CH}$ , 8), 33.4 ( $\text{CH}_2$ , 7), 34.2 ( $\text{CH}_2$ , 1), 35.2 ( $\text{C}$ , 10), 36.8 ( $\text{CH}_2$ , 12), 44.4 ( $\text{C}$ , 5), 52.6 ( $\text{CH}$ , 9), 54.1 ( $\text{C}$ , 13), 57.1 ( $\text{CH}_3$ , 1'), 82.3 ( $\text{CH}$ , 6), 118.4 ( $\text{CH}$ , 15), 142.2 ( $\text{CH}$ , 16), 155.1 ( $\text{C}$ , 17), 174.9 (C-14) 192.9 ( $\text{C}$ , 20).

**Mass Spectrum** (ESI+),  $m/z$ , 327.35  $[\text{M} + \text{H}]^+$ , 349.34  $[\text{M} + \text{Na}]^+$ , 295.34  $[\text{M} - \text{OMe}]^+$ , 675.49  $[\text{M}\times 2 + \text{Na}]^+$ .

IR: 1084 cm<sup>-1</sup> (C-O stretch), 1637 cm<sup>-1</sup> (C=O stretch).

HRMS: (ESI+), *m/z*, found = 327.2339, calculated for C<sub>22</sub>H<sub>31</sub>O<sub>2</sub> [M + H]<sup>+</sup> = 327.2324.

### Compound 10

<sup>1</sup>H NMR δ 0.81 (1H, td, *J* = 12.8, 5.1 Hz, CH<sub>2</sub> - 12), 0.97 – 1.10 (2H, m, CH - 9, CH<sub>2</sub> - 1), 1.12 (3H, s, CCH<sub>3</sub> - 19), 1.20 (3H, s, CCH<sub>3</sub> - 18), 1.38 - 1.52 (1H, m, CH<sub>2</sub> - 2), 1.56 - 1.71 (2H, m, CH<sub>2</sub> - 11), 1.88 (1H, t, *J* = 3.4 Hz, CH<sub>2</sub> - 1), 1.94 (1H, dd, *J* = 9.8, 7.0 Hz, CH<sub>2</sub> - 1), 2.14 – 2.24 (3H, m, CH<sub>2</sub> - 4, CH<sub>2</sub> - 7), 2.32 (3H, s, CH<sub>3</sub> - 21), 2.37 – 2.53 (3H, m, CH<sub>2</sub> - 4, CH - 8, CH<sub>2</sub> - 12), 3.00 - 3.11 (1H, m, CH - 3), 3.35 (3H, s, OCH<sub>3</sub> - 1'), 5.45 (1H, app. d, *J* = 4.9 Hz, CH - 6), 6.01 (1H, app. t, *J* = 2.0 Hz, CH - 15), 7.22 (1H, d, *J* = 2.3 Hz, CH - 16).

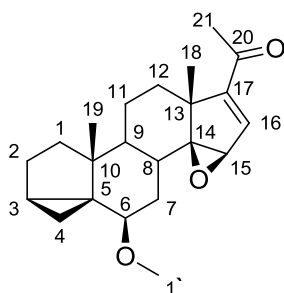
<sup>13</sup>C NMR δ 18.7 (CCH<sub>3</sub>, 18), 19.8 (CCH<sub>3</sub>, 19), 21.0 (CH<sub>2</sub>, 11), 27.0 (CCH<sub>3</sub> - 21), 28.2 (CH<sub>2</sub>, 2), 29.3 (CH<sub>2</sub>, 7), 32.7 (CH-8), 36.1 (CH<sub>2</sub>, 12), 37.8 (CH<sub>2</sub>, 1), 38.2 (C, 10), 39.0 (CH<sub>2</sub>, 4), 53.9 (C, 13), 54.6 (CH, 9), 56.0 (CH<sub>3</sub> - 1'), 80.5 (CH, 3), 119.4 (CH, 15), 121.0 (CH, 6), 141.0 (C, 5), 142.1 (CH, 16), 155.1 (C, 17), 173.6 (C - 14), 193.0 (C - 20).

Mass Spectrum (ESI+), *m/z*, 327.44 [M + H]<sup>+</sup>, 349.34 [M + Na]<sup>+</sup>, 295.35 [M - OMe]<sup>+</sup>.

IR: 1637 cm<sup>-1</sup> (C=O stretch), 1057 cm<sup>-1</sup> (C-O stretch).

HRMS: (ESI+), *m/z*, found = 327.2341, calculated for C<sub>22</sub>H<sub>31</sub>O<sub>2</sub> [M + H]<sup>+</sup> = 327.2324.

### Compound 11



mCPBA (75%, 520 mg, 3.01 mmol) was added to a stirred solution of compound **5** (740 mg, 2.27 mmol) in CHCl<sub>3</sub> (25 ml) at room temperature. After 2.5 hours, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> aqueous solution (0.5 M, 50 ml) was added. The reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 ml × 3) and the combined organic extracts were washed with saturated NaHCO<sub>3</sub> aqueous solution (100 ml). The organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel column chromatography (5 – 10 % EtOAc in PE) afforded epoxide **11** (632 mg, 81%) as a white solid as well as unreacted compound **5** (73.0 mg, 10%).

**<sup>1</sup>H NMR**  $\delta$  0.41 (1H, dd,  $J = 8.0$  &  $5.2$  Hz,  $\text{CH}_2$  - 4), 0.59 (1H, app. t,  $4.4$  Hz  $\text{CH}_2$  - 4), 0.75 – 1.06 (6H, m,  $\text{CH}_2$  - 1,  $\text{CH}$  - 3,  $\text{CH}_2$  - 11,  $\text{CH}_2$  - 7,  $\text{CH}$  - 8,  $\text{CH}_2$  - 12), 0.99 (3H, s,  $\text{CCH}_3$  - 19), 1.28 (3H, s,  $\text{CCH}_3$  - 18), 1.29 - 1.53 (3H, m,  $\text{CH}_2$  - 11,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 2), 1.67 (1H, tdd,  $J = 12.1, 7.9, 4.2$ ,  $\text{CH}_2$  - 2), 1.93 (1H, dt,  $J = 13.2, 2.9$  Hz,  $\text{CH}_2$  - 7), 2.18 (3H, s,  $\text{CH}_3$  - 21), 2.34 (1H, dt,  $J = 3.3, 3.3$  Hz,  $\text{CH}_2$  - 12), 2.40 (1H, td,  $J = 12.1, 2.7$  Hz,  $\text{CH}$  - 9), 2.73 (1H, t,  $J = 2.8$  Hz,  $\text{CH}$  - 6), 3.24 (3H, s,  $\text{OCH}_3$  - 1'), 3.69 (1H, d,  $J = 0.7$  Hz,  $\text{CH}$  - 15), 6.82 (1H, s,  $\text{CH}$  - 16).

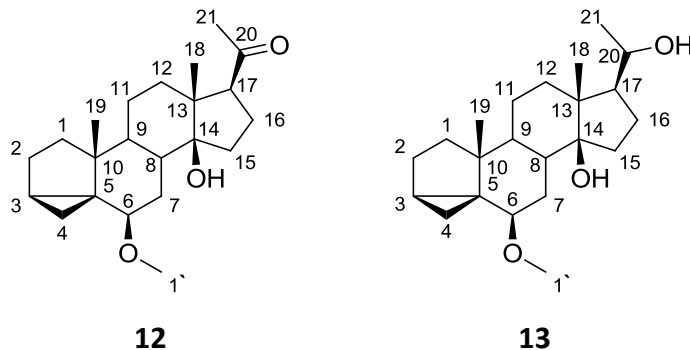
**<sup>13</sup>C NMR**  $\delta$  13.1 ( $\text{CH}_2$ , 4), 16.9 ( $\text{CH}_3$ , 18), 19.2 ( $\text{CH}_3$ , 19), 21.6 ( $\text{CH}_2$ , 11), 21.8 ( $\text{CH}$ , 3), 24.9 ( $\text{CH}_2$ , 2), 27.4 ( $\text{CH}_3$ , 21), 28.5 ( $\text{CH}$ , 9), 29.9 ( $\text{CH}_2$ , 7), 33.4 ( $\text{CH}_2$ , 1), 35.2 ( $\text{C}$ , 10), 36.7 ( $\text{CH}_2$ , 12), 43.8 ( $\text{C}$ , 5), 46.7 ( $\text{CH}$ , 8), 48.1 ( $\text{C}$ , 13), 56.6 ( $\text{CH}_3$ , 1'), 59.2 ( $\text{CH}$ , 15), 74.7 ( $\text{C}$ , 14), 81.6 ( $\text{CH}$ , 6), 140.5 ( $\text{CH}$ , 16), 158.4 ( $\text{C}$ -17) 196.1 ( $\text{C}$ , 20).

**Mass Spectrum** (ESI+),  $m/z$ , 343.34 [ $\text{M} + \text{H}$ ]<sup>+</sup>, 365.34 [ $\text{M} + \text{Na}$ ]<sup>+</sup>, 311.34 [ $\text{M} - \text{OMe}$ ]<sup>+</sup>, 707.38 [ $\text{M} \times 2 + \text{Na}$ ]<sup>+</sup>.

**IR:** 1665  $\text{cm}^{-1}$  (C=O stretch), 1089  $\text{cm}^{-1}$  (C-O stretch).

**HRMS:** (ESI+),  $m/z$ , found = 343.2286, calculated for  $\text{C}_{22}\text{H}_{31}\text{O}_3$  [ $\text{M} + \text{H}$ ]<sup>+</sup> = 343.2273.

### Compounds 12 and 13



The epoxide **11** (200.0 mg, 0.58 mmol) was added to dry THF (15 ml) containing  $\text{LiAlH}_4$  (200.0 mg) and the mixture was refluxed under  $\text{N}_2$  for 1 hour. The reaction mixture was cooled to room temperature and filtered. Solvent was removed under reduced pressure and residue extracted with diethyl ether (30 ml  $\times$  3) and water (100 ml). The residue was purified by column chromatography (5-40% EtOAc in PE) to afford compound **12** (84.0 mg, 42%) as white solid and compound **13** (47.0 mg, 23%) as white solid.

### Compound 12



**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 0.41 (1H, dd, *J* = 8.0 & 5.2 Hz, CH<sub>2</sub> - 4), 0.59 (1H, app. t, 4.4 Hz, CH<sub>2</sub> - 4), 0.82 (4H, tdd, *J* = 11.8, 7.8, 3.6 Hz, CH<sub>2</sub> - 1, CH - 3), 0.94 (3H, s, CCH<sub>3</sub> - 19), 0.97 (2H, dd, *J* = 12.6, 3.9 Hz, CH - 8), 1.10 – 1.22 (3H, m, CH<sub>2</sub> - 7, CH<sub>2</sub> - 12), 1.18 (3H, s, CCH<sub>3</sub> - 18), 1.29 – 1.53 (6H, m, CH<sub>2</sub> - 1, CH<sub>2</sub> - 11, CH<sub>2</sub> - 16, CH<sub>2</sub> - 15, CH<sub>2</sub> - 2), 1.62 – 1.97 (3H, m, CH<sub>2</sub> - 2, CH - 9, CH<sub>2</sub> - 15), 2.04 (1H, dd, *J* = 9.0, 3.7 Hz, CH<sub>2</sub> - 16), 2.08 (3H, s, CH<sub>3</sub> - 21), 2.14 (1H, dt, *J* = 13.6, 2.9 Hz, CH<sub>2</sub> - 7), 2.79 (1H, t, *J* = 2.8 Hz, CH - 6), 3.20 (1H, t, *J* = 9.3 Hz, CH - 17) 3.27 (3H, s, OCH<sub>3</sub> - 1').

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 13.3 (CH<sub>2</sub>, 4), 19.2 (CH<sub>3</sub>, 19), 19.2 (CH<sub>3</sub>, 18), 21.4 (CH, 3), 21.6 (CH<sub>2</sub>, 11), 24.8 (CH<sub>2</sub>, 16), 24.9 (CH<sub>2</sub>, 2), 30.6 (CH<sub>2</sub>, 7), 30.7 (CH<sub>2</sub>, 15), 31.1 (CH<sub>2</sub>, 12), 32.0 (CH<sub>3</sub>, 21), 33.6 (CH<sub>2</sub>, 1), 34.8 (C, 10), 36.5 (CH, 9), 43.6 (C, 5), 43.7 (CH, 8), 48.4 (C, 13), 56.6 (CH<sub>3</sub>, 1'), 61.4 (CH, 17), 82.2 (CH, 6), 86.4 (C-14) 210.6 (C, 20).

**Mass Spectrum** (ESI+), *m/z*, 369.34 [M + Na]<sup>+</sup>, 315.34 [C<sub>21</sub>H<sub>31</sub>O<sub>2</sub>]<sup>+</sup>, 297.35 [C<sub>21</sub>H<sub>30</sub>O]<sup>+</sup>, 715.48 [MX<sub>2</sub> + Na]<sup>+</sup>.

**IR:** 3449 cm<sup>-1</sup> (OH stretch), 1703 cm<sup>-1</sup> (C=O stretch), 1075 cm<sup>-1</sup> (C-O stretch).

**HRMS:** (ESI+), *m/z*, found = 315.2339, calculated for C<sub>21</sub>H<sub>31</sub>O<sub>2</sub> [M - OMe]<sup>+</sup> = 315.2324.

### Compound 13

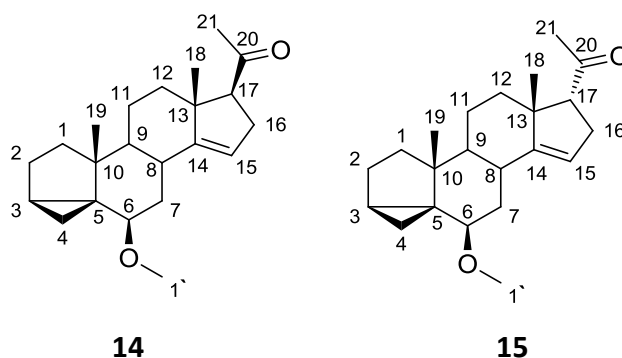
**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 0.46 (1H, dd, *J* = 8.0 & 5.2 Hz, CH<sub>2</sub> - 4), 0.64 (1H, app. t, 4.4 Hz, CH<sub>2</sub> - 4), 0.84 – 1.05 (5H, m, CH<sub>2</sub> - 1, CH - 3, CH - 8, CH<sub>2</sub> - 12, CH<sub>2</sub> - 7), 1.01 (3H, s, CCH<sub>3</sub> - 19), 1.16 (3H, s, CCH<sub>3</sub> - 21 R/S), 1.18 (3H, s, CCH<sub>3</sub> - 21 R/S), 1.19 (3H, s, CCH<sub>3</sub> - 18), 1.20 – 1.36 (1H, m, CH<sub>2</sub> - 2), 1.39 – 1.57 (2H, m, CH<sub>2</sub> - 1, CH<sub>2</sub> - 2), 1.65 (1H, dt, *J* = 13.0, 3.2 Hz, CH<sub>2</sub> - 12), 1.70 – 1.93 (4H, m, CH<sub>2</sub> - 15, CH<sub>2</sub> - 16), 2.07 (1H, q, *J* = 9.5 Hz, CH - 17), 2.23 (1H, dt, *J* = 13.5, 2.9 Hz, CH<sub>2</sub> - 7), 2.84 (1H, t, *J* = 2.7 Hz, CH - 6), 3.33 (3H, s, OCH<sub>3</sub> - 1'), 3.73 (1H, dq, *J* = 10.3, 6.1 Hz, CH - 20 R/S), 3.87 (1H, p, *J* = 6.2 Hz, CH - 20 R/S), 5.29 (1H, s, OH).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 13.6 (CH<sub>2</sub>, 4), 19.6 (CH<sub>3</sub>, 19), 20.6 (CH<sub>3</sub>, 18), 21.9 (CH, 3), 22.0 (CH<sub>2</sub>, 11), 24.4 (CH<sub>2</sub>, 16), 24.5 (CH<sub>3</sub>, 21), 25.3 (CH<sub>2</sub>, 2), 30.5 (CH<sub>2</sub>, 12), 30.6 (CH<sub>2</sub>, 7 & 15), 33.9 (CH<sub>2</sub>, 1), 35.4 (C, 10), 36.6 (CH, 9), 44.0 (C, 5), 44.3 (CH, 8), 47.1 (C, 13), 56.2 (CH, 17), 56.9 (CH<sub>3</sub>, 1'), 68.4 (CH, 20 R/S), 70.1 (CH, 20 R/S), 82.7 (CH - 6) 86.8 (C, 14).

**Mass Spectrum** (ESI+), *m/z*, 371.44 [M + Na]<sup>+</sup>

**IR:** 1705 cm<sup>-1</sup> (C=O stretch), 1076 cm<sup>-1</sup> (C-O stretch).

## Compound 14 & 15



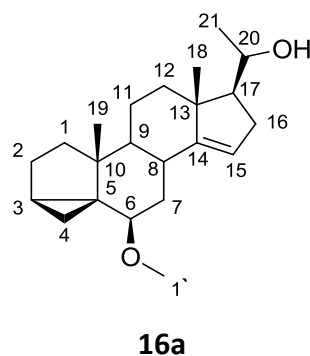
To a stirred solution of **5** (5.0 g, 15.31 mmol) in anhydrous toluene (80 ml) was added triphenyltin hydride (10.77 g, 30.63 mmol) & AIBN (30 mg) and the reaction mixture was refluxed under nitrogen for 10 hours with addition of AIBN (15 mg) every hour. Solvent was removed under reduced pressure and methanol was added to the resulting solid. Silica gel column chromatography (3 % EtOAc in PE) afforded mixture of **14** & **15** (1.94 g, 39%) as a white solid as well as mixture of **14** & **15** and unreacted compound **5** (2.1 g, 42%).

**Mass Spectrum** (ESI+),  $m/z$ , 329.45  $[M + H]^+$ , 351.45  $[M + Na]^+$ , 679.49  $[M \times 2 + Na]^+$ , 297.45  $[M - OMe]^+$ .

**IR:** 1090  $\text{cm}^{-1}$  (C-O stretch), 1707  $\text{cm}^{-1}$  (C=O stretch).

**HRMS:** (ESI+),  $m/z$ , found = 329.2471, calculated for  $\text{C}_{22}\text{H}_{33}\text{O}_2$   $[M + H]^+ = 329.2480$ .

## Compound 16a-d



To a stirred solution of **14** & **15** (1.04 g, 3.15 mmol) in methanol (30 ml) &  $\text{CH}_2\text{Cl}_2$  (10 ml) was added  $\text{NaBH}_4$  (238 mg 6.29 mmol) at room temperature. After 40 minutes, dilute HCl (200 ml) was added. The reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (100 ml  $\times$  3) and the combined organic extracts were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel column chromatography (5 % EtOAc in PE) afforded **16a** (602 mg, 58%) as a white solid and an inseparable mixture of **16a-d** (330 mg, 32%) as a white solid.

$^1\text{H NMR}$   $\delta$  0.45 (1H, dd,  $J = 5.2$  &  $5.1$  Hz,  $\text{CH}_2$  - 4), 0.65 (1H, app. t, 4.2 Hz, 4.5 Hz  $\text{CH}_2$  - 4), 0.80 – 0.93 (3H, m,  $\text{CH}_2$  - 9,  $\text{CH}$  - 1, CH - 3), 1.04 (3H, s,  $\text{CCH}_3$  - 19), 1.06 (3H, s,  $\text{CCH}_3$  - 18), 1.17 & 1.18 (3H, s,  $\text{CCH}_3$  - 21), 1.24 - 1.34 (1H, m,  $\text{CH}_2$  - 12), 1.36 - 1.55 (6H, m,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 11), 1.70 - 1.80 (2H, m,  $\text{CH}$  - 17,  $\text{CH}_2$  - 2), 1.83 - 1.92 (1H, m,  $\text{CH}_2$  - 16), 2.05 – 2.20 (2H, m,  $\text{CH}_2$  - 12,  $\text{CH}_2$  - 16), 2.41 (1H, app. t,  $J = 11.9, 11.8$  Hz,  $\text{CH}$  - 8), 2.84 (1H, t,  $J = 3.0$  Hz,  $\text{CH}$  - 6), 3.34 (3H, s,  $\text{OCH}_3$  - 1'), 3.89 – 3.97 (1H, m,  $\text{CH}$  - 20), 5.14 (1H, app. q,  $J = 2.2$  Hz,  $\text{CH}$  - 15).

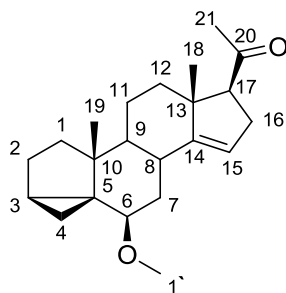
$^{13}\text{C NMR}$   $\delta$  13.5 ( $\text{CH}_2$ , 4), 18.9 ( $\text{CH}_3$ , 18), 19.3 ( $\text{CH}_3$ , 19), 21.8 ( $\text{CH}$ , 3), 23.9 ( $\text{CH}_2$ , 11), 24.0 ( $\text{CH}_3$ , 21), 25.3 ( $\text{CH}_2$ , 2), 30.5 ( $\text{CH}$ , 8), 33.6 ( $\text{CH}_2$ , 7), 34.0 ( $\text{CH}_2$ , 1), 34.0 ( $\text{CH}_2$ , 16), 35.2 ( $\text{C}$ , 10), 43.2 ( $\text{CH}_2$ , 12), 43.9 ( $\text{C}$ , 5), 47.7 ( $\text{C}$ , 13), 47.9 ( $\text{CH}$ , 9), 57.0 ( $\text{CH}_3$ , 1'), 61.1 ( $\text{CH}_2$ , 17), 69.8 ( $\text{C}$ , 20), 82.6 ( $\text{CH}$ , 6), 116.8 ( $\text{CH}$ , 15), 155.7 ( $\text{C}$ , 14).

**Mass Spectrum** (ESI+),  $m/z$ , 353.45 [ $\text{M} + \text{Na}$ ] $^+$ , 299.35 [ $\text{M} - \text{OMe}$ ] $^+$ , 281.35 [ $\text{C}_{21}\text{H}_{29}$ ] $^+$ .

**IR:** 1084  $\text{cm}^{-1}$  (C-O stretch), 3425  $\text{cm}^{-1}$  (OH stretch).

**HRMS:** (ESI+),  $m/z$ , found = 299.2388, calculated for  $\text{C}_{22}\text{H}_{33}\text{O}_2$  [ $\text{M} - \text{OMe}$ ] = 299.2375.

### Compound 14 from 16a



To a stirred solution of **16a** (100 mg, 0.30 mmol) in  $\text{CH}_2\text{Cl}_2$  (5 ml) was added PDC (228 mg, 0.60 mmol) at room temperature and stirred for 2 days. Saturated  $\text{Na}_2\text{S}_2\text{O}_3$  aqueous solution (200 ml) was added. The reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (50 ml  $\times$  3) and the combined organic extracts were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel column chromatography (3 % EtOAc in PE) afforded **14** (78 mg, 78%) as a white solid.

$^1\text{H NMR}$   $\delta$  0.47 (1H, dd,  $J = 5.1$  &  $5.2$  Hz,  $\text{CH}_2$  - 4), 0.66 (1H, app. t, 4.4 Hz,  $\text{CH}_2$  - 4), 0.84 – 0.95 (3H, m,  $\text{CH}_2$  - 1,  $\text{CH}$  - 9, CH - 3), 0.89 (3H, s,  $\text{CCH}_3$  - 18), 1.04 (3H, s,  $\text{CCH}_3$  - 19), 1.37 -

1.60 (6H, m,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 12,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 11), 1.69 – 1.80 (1H, m,  $\text{CH}_2$  - 2), 2.10 – 2.24 (3H, m,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 12,  $\text{CH}_2$  - 16), 2.39 (1H, app. t,  $J$  = 11.5, 11.5 Hz,  $\text{CH}$  - 8), 2.15 (3H, s,  $\text{CCH}_3$  - 21), 2.73 – 2.82 (1H, m,  $\text{CH}_2$  - 16), 2.85 (1H, t,  $J$  = 2.9 Hz,  $\text{CH}$  - 6), 2.93 (1H, dd,  $J$  = 8.1, 8.2 Hz,  $\text{CH}$  - 17), 3.34 (3H, s,  $\text{OCH}_3$  - 1'), 5.16 (1H, app. q,  $J$  = 2.2 Hz,  $\text{CH}$  - 15).

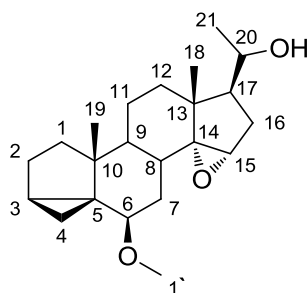
$^{13}\text{C}$  NMR  $\delta$  13.5 ( $\text{CH}_2$ , 4), 19.0 ( $\text{CH}_3$ , 18), 19.3 ( $\text{CH}_3$ , 19), 21.8 ( $\text{CH}$ , 3), 24.0 ( $\text{CH}_2$ , 11), 25.2 ( $\text{CH}_2$ , 2), 30.5 ( $\text{CH}$ , 8), 31.6 ( $\text{CH}_2$ , 16), 31.7 ( $\text{CH}_3$ , 21), 33.6 ( $\text{CH}_2$ , 7), 34.0 ( $\text{CH}_2$ , 1), 35.0 ( $\text{C}$ , 10), 42.6 ( $\text{CH}_2$ , 12), 43.9 ( $\text{C}$ , 5), 48.1 ( $\text{CH}$ , 9), 48.8 ( $\text{C}$ , 13), 56.0 ( $\text{CH}_3$ , 1'), 65.9 ( $\text{CH}_2$ , 17), 82.5 ( $\text{CH}$ , 6), 117.2 ( $\text{CH}$ , 15), 152.3 ( $\text{C}$ , 14), 209.8 ( $\text{C}$ , 20).

**Mass Spectrum** (ESI+),  $m/z$ , 351.35 [ $\text{M} + \text{Na}$ ] $^+$ , 297.35 [ $\text{M} - \text{OMe}$ ] $^+$ .

**IR**: 1090  $\text{cm}^{-1}$  (C-O stretch), 1707  $\text{cm}^{-1}$  (C=O stretch).

**HRMS**: (ESI+),  $m/z$ , found = 329.2471, calculated for  $\text{C}_{22}\text{H}_{33}\text{O}_2$  [ $\text{M} + \text{H}$ ] $^+$  = 329.2480.

## Compound 19



mCPBA (75%, 70 mg, 0.41 mmol) was added to a stirred solution of compound **16a** (41 mg, 0.12 mmol) in  $\text{CHCl}_3$  (3 ml) at room temperature. After 3 hours,  $\text{Na}_2\text{S}_2\text{O}_3$  aqueous solution (0.5 M, 50 ml) was added. The reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (100 ml  $\times$  3) and the combined organic extracts were washed with saturated  $\text{NaHCO}_3$  aqueous solution (100 ml). The organic extracts were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel column chromatography (10 % EtOAc in PE) afforded epoxide **19** (36 mg, 84%) as a white solid.

$^1\text{H}$  NMR  $\delta$  0.44 (1H, dd,  $J$  = 5.2 & 5.2 Hz,  $\text{CH}_2$  - 4), 0.65 (1H, app. t, 4.5 Hz,  $\text{CH}_2$  - 4), 0.85 – 0.95 (2H, m,  $\text{CH}_2$  - 1,  $\text{CH}$  - 3), 1.01 (3H, s,  $\text{CCH}_3$  - 18), 1.06 (3H, s,  $\text{CCH}_3$  - 19), 1.14 & 1.15 (3H,

s, CCH<sub>3</sub> - 21), 1.17 – 1.26 (2H, m, CH - 9, CH<sub>2</sub> - 16), 1.38 - 1.59 (8H, m, CH<sub>2</sub> - 7, CH - 17, CH<sub>2</sub> - 1, CH<sub>2</sub> - 2, CH<sub>2</sub> - 11, CH<sub>2</sub> - 12), 1.78 – 1.86 (1H, m, CH<sub>2</sub> - 2), 1.87 – 1.96 (2H, m, CH<sub>2</sub> - 12, CH<sub>2</sub> - 16), 2.54 (1H, dt, *J* = 11.0 Hz, CH - 8), 2.79 (1H, t, *J* = 2.9 Hz, CH - 6), 3.34 (3H, s, OCH<sub>3</sub> - 1'), 3.38 (1H, app. s, CH - 15), 3.66 – 3.74 (1H, m, CH - 20).

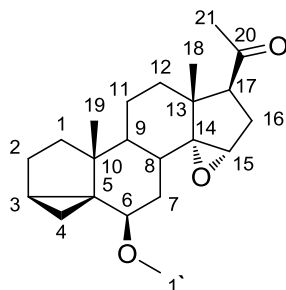
<sup>13</sup>C NMR δ 13.5 (CH<sub>2</sub>, 4), 15.5 (CH<sub>3</sub>, 18), 19.4 (CH<sub>3</sub>, 19), 21.4 (CH, 3), 22.7 (CH<sub>2</sub>, 11), 24.0 (CH<sub>3</sub>, 21), 25.1 (CH<sub>2</sub>, 2), 27.8 (CH, 8), 30.3 (CH<sub>2</sub>, 7), 30.7 (CH<sub>2</sub>, 16), 33.7 (CH<sub>2</sub>, 1), 34.7 (C, 10), 36.2 (CH<sub>2</sub>, 12), 41.6 (C, 13), 43.8 (C, 5), 44.4 (CH, 9), 51.3 (CH, 17), 56.9 (CH<sub>3</sub>, 1'), 58.3 (CH, 15), 69.3 (CH, 20), 74.3 (C, 14), 82.4 (CH, 6).

**Mass Spectrum** (ESI+), *m/z*, 347.44 [M + H]<sup>+</sup>, 315.45 [M - OMe]<sup>+</sup>, 297.35 [M - OMe, - H<sub>2</sub>O]<sup>+</sup>, 279.35 [M - OMe, - 2H<sub>2</sub>O]<sup>+</sup>.

**IR:** 3488 cm<sup>-1</sup> (OH stretch), 1073 cm<sup>-1</sup> (C-O stretch).

**HRMS:** (ESI+), *m/z*, found = 347.2597, calculated for C<sub>22</sub>H<sub>35</sub>O<sub>3</sub> [M + H]<sup>+</sup> = 347.2586.

## Compound 17



From **14**: mCPBA (75%, 100 mg, 0.58 mmol) was added to a stirred solution of compound **14** (78 mg, 0.24 mmol) in CHCl<sub>3</sub> (5 ml) at room temperature. After 3 hours, Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> aqueous solution (0.5 M, 50 ml) was added. The reaction mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 ml × 3) and the combined organic extracts were washed with saturated NaHCO<sub>3</sub> aqueous solution (100 ml). The organic extracts were dried over MgSO<sub>4</sub> and concentrated under reduced pressure. Silica gel column chromatography (10 % EtOAc in PE) afforded epoxide **17** (76 mg, 93%) as a white solid.

From **19**: To a stirred solution of **19** (23 mg, 0.07 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3 ml) was added PDC (160 mg, 0.42 mmol) at room temperature and stirred for 2 days. Saturated Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> aqueous

solution (50 ml) was added. The reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (30 ml  $\times$  3) and the combined organic extracts were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel column chromatography (10 % EtOAc in PE) afforded **17** (18 mg, 78%) as a white solid.

$^1\text{H NMR}$   $\delta$  0.44 (1H, dd,  $J = 5.2$  &  $5.2$  Hz,  $\text{CH}_2$  - 4), 0.65 (1H, app. t, 4.5 Hz,  $\text{CH}_2$  - 4), 0.81 (3H, s,  $\text{CCH}_3$  - 18), 0.85 – 0.95 (2H, m,  $\text{CH}_2$  - 1, CH - 3), 1.05 (3H, s,  $\text{CCH}_3$  - 19), 1.27 (1H, app. dt, 11.9, 11.9 Hz, CH - 9), 1.37 - 1.64 (6H, m,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 11), 1.69 – 1.87 (2H, m,  $\text{CH}_2$  - 12,  $\text{CH}_2$  - 2), 1.89 – 1.96 (1H, m,  $\text{CH}_2$  - 16), 1.98 (1H, t,  $J = 3.4$  Hz,  $\text{CH}_2$  - 12), 2.00 – 2.07 (1H, m,  $\text{CH}_2$  - 16), 2.08 (3H, s,  $\text{CCH}_3$  - 21), 2.47 – 2.56 (2H, m, CH - 8, CH - 17), 2.79 (1H, t,  $J = 2.9$  Hz, CH - 6), 3.32 (3H, s,  $\text{OCH}_3$  - 1'), 3.44 (1H, app. s, CH - 15).

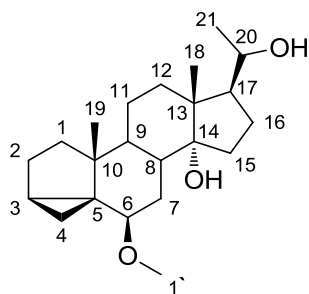
$^{13}\text{C NMR}$   $\delta$  13.6 ( $\text{CH}_2$ , 4), 16.4 ( $\text{CH}_3$ , 18), 19.4 ( $\text{CH}_3$ , 19), 21.5 (CH, 3), 23.0 ( $\text{CH}_2$ , 11), 25.2 ( $\text{CH}_2$ , 2), 27.8 (CH, 8), 28.1 ( $\text{CH}_2$ , 16), 30.4 ( $\text{CH}_2$ , 7), 31.6 ( $\text{CH}_3$ , 21), 33.8 ( $\text{CH}_2$ , 1), 34.8 (C, 10), 35.4 ( $\text{CH}_2$ , 12), 42.7 (C, 13), 43.8 (C, 5), 44.4 (CH, 9), 57.0 ( $\text{CH}_3$ , 1'), 57.3 (CH, 17), 58.2 (CH, 15), 73.4 (C, 14), 82.3 (CH, 6), 209.2 (C, 20).

**Mass Spectrum** (ESI+),  $m/z$ , 313.35 [M - OMe] $^+$ , 295.35 [M - OMe, -  $\text{H}_2\text{O}$ ] $^+$ , 277.25 [M - OMe, -  $2\text{H}_2\text{O}$ ] $^+$ .

**IR:** 1098  $\text{cm}^{-1}$  (C-O stretch), 1704  $\text{cm}^{-1}$  (C=O stretch).

**HRMS:** (ESI+),  $m/z$ , found = 345.2442, calculated for  $\text{C}_{22}\text{H}_{33}\text{O}_3$  [M + H] $^+$  = 345.2430.

## Compound 23



The epoxide **19** (300 mg, 0.87 mmol) was added to dry THF (5 ml) containing  $\text{LiAlH}_4$  (33 mg, 0.87 mmol) and the mixture was refluxed under  $\text{N}_2$  for overnight. The reaction mixture was cooled to room temperature and filtered. Solvent was removed under reduced pressure and residue extracted with diethyl ether (30 ml  $\times$  3) and water (50 ml). The residue was purified

by column chromatography (30% EtOAc in PE) to afford compound **23** (185 mg, 61%) as white solid and 55 mg of **19** was also recovered.

$^1\text{H NMR}$   $\delta$  0.44 (1H, dd,  $J = 5.2$  &  $5.2$  Hz,  $\text{CH}_2$  - 4), 0.65 (1H, app. t, 4.5 Hz,  $\text{CH}_2$  - 4), 0.84 – 0.95 (2H, m,  $\text{CH}_2$  - 1, CH - 3), 0.96 (3H, s,  $\text{CCH}_3$  - 18), 1.06 (3H, s,  $\text{CCH}_3$  - 19), 1.17 & 1.19 (3H, s,  $\text{CCH}_3$  - 21), 1.20 – 1.89 (14H, m,  $\text{CH}_2$  - 16, CH - 9,  $\text{CH}_2$  - 11,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 15,  $\text{CH}_2$  - 12), 2.00 (1H, q,  $J = 9.4$  Hz, CH - 17), 2.14 (1H, dt,  $J = 12.0$  Hz, CH - 8), 2.84 (1H, t,  $J = 2.9$  Hz, CH - 6), 3.33 (3H, s,  $\text{OCH}_3$  - 1'), 3.74 – 3.81 (1H, m, CH - 20).

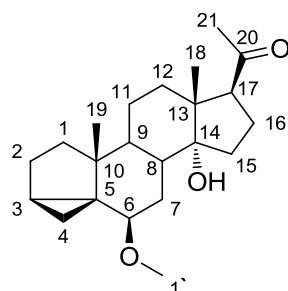
$^{13}\text{C NMR}$   $\delta$  13.6 ( $\text{CH}_2$ , 4), 16.9 ( $\text{CH}_3$ , 18), 19.6 ( $\text{CH}_3$ , 19), 21.7 ( $\text{CH}_2$ , 11), 21.8 (CH, 3), 24.3 ( $\text{CH}_3$ , 21), 25.0 ( $\text{CH}_2$ , 16), 25.3 ( $\text{CH}_2$ , 2), 31.0 ( $\text{CH}_2$ , 7), 32.8 ( $\text{CH}_2$ , 12), 33.4 ( $\text{CH}_2$ , 15), 33.5 (CH, 8), 33.8 ( $\text{CH}_2$ , 1), 35.6 (C, 10), 41.0 (CH, 9), 44.0 (C, 5), 47.1 (C, 13), 53.8 (CH, 17), 57.0 ( $\text{CH}_3$ , 1'), 70.7 (CH, 20), 82.9 (CH, 6), 86.0 (C, 14).

**Mass Spectrum** (ESI+),  $m/z$ , 371.44 [ $\text{M} + \text{Na}$ ] $^+$ , 299.45 [ $\text{M} - \text{OMe}, - \text{H}_2\text{O}$ ] $^+$ , 281.45 [ $\text{M} - \text{OMe}, - 2\text{H}_2\text{O}$ ] $^+$ .

**IR:** 1075  $\text{cm}^{-1}$  (C-O stretch), 3403  $\text{cm}^{-1}$  (OH stretch).

**HRMS:** (ESI+),  $m/z$ , found = 371.2549, calculated for  $\text{C}_{22}\text{H}_{36}\text{O}_3\text{Na}$  [ $\text{M} + \text{Na}$ ] $^+$  = 371.2562.

## Compound 24



To a stirred solution of **23** (73 mg, 0.21 mmol) in  $\text{CH}_2\text{Cl}_2$  (3 ml) was added PDC (394 mg, 1.01 mmol) at room temperature and stirred overnight. Saturated  $\text{Na}_2\text{S}_2\text{O}_3$  aqueous solution (50 ml) was added. The reaction mixture was extracted with  $\text{CH}_2\text{Cl}_2$  (30 ml  $\times$  3) and the combined organic extracts were dried over  $\text{MgSO}_4$  and concentrated under reduced pressure. Silica gel column chromatography (20 % EtOAc in PE) afforded **23** (56 mg, 77%) as a white solid.

$^1\text{H NMR}$   $\delta$  0.44 (1H, dd,  $J = 5.2$  &  $5.2$  Hz,  $\text{CH}_2$  - 4), 0.64 (1H, app. t, 4.5 Hz,  $\text{CH}_2$  - 4), 0.77 (3H, s,  $\text{CCH}_3$  - 18), 0.81 – 0.93 (2H, m,  $\text{CH}_2$  - 1, CH - 3), 1.03 (3H, s,  $\text{CCH}_3$  - 19), 1.33 – 1.57 (7H, m,  $\text{CH}$  - 9,  $\text{CH}_2$  - 1,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 15,  $\text{CH}_2$  - 16), 1.61 - 1.85 (5H, m,  $\text{CH}_2$  - 11,  $\text{CH}_2$  - 2,  $\text{CH}_2$  - 7,  $\text{CH}_2$  - 12), 1.90 – 1.98 (1H, m,  $\text{CH}_2$  - 12), 2.09 (3H, s,  $\text{CCH}_3$  - 21), 2.10 – 2.17 (1H, m,  $\text{CH}$  - 8), 2.22 – 2.31 (1H, m,  $\text{CH}_2$  - 16), 2.83 (1H, t,  $J = 2.9$  Hz,  $\text{CH}$  - 6), 3.19 (1H, t,  $J = 8.75$  Hz,  $\text{CH}$  - 17), 3.31 (3H, s,  $\text{OCH}_3$  - 1').

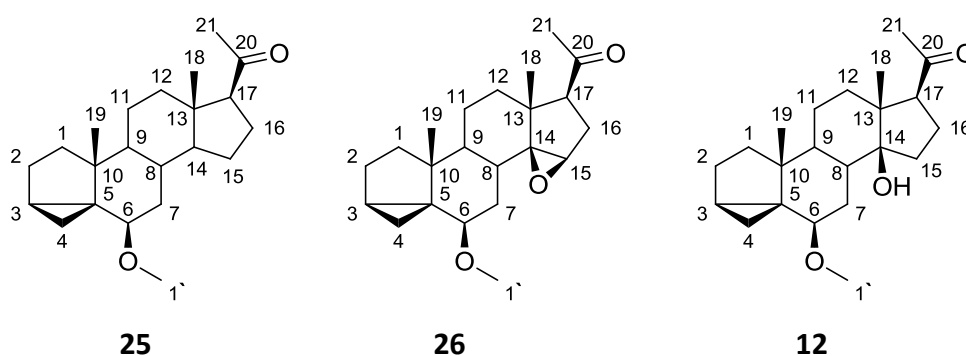
$^{13}\text{C NMR}$   $\delta$  13.5 ( $\text{CH}_2$ , 4), 17.8 ( $\text{CH}_3$ , 18), 19.5 ( $\text{CH}_3$ , 19), 21.8 ( $\text{CH}$ , 3), 21.8 ( $\text{CH}_2$ , 11), 21.9 ( $\text{CH}_2$ , 16), 25.3 ( $\text{CH}_2$ , 2), 31.1 ( $\text{CH}_2$ , 7), 31.7 ( $\text{CH}_3$ , 21), 31.9 ( $\text{CH}_2$ , 12), 33.4 ( $\text{CH}_2$ , 15), 33.5 ( $\text{CH}$ , 8), 33.8 ( $\text{CH}_2$ , 1), 35.4 ( $\text{C}$ , 10), 40.8 ( $\text{CH}$ , 9), 43.9 ( $\text{C}$ , 5), 48.6 ( $\text{C}$ , 13), 56.9 ( $\text{CH}_3$ , 1'), 60.0 ( $\text{CH}$ , 17), 82.6 ( $\text{CH}$ , 6), 86.2 ( $\text{C}$ , 14), 210.9 ( $\text{CH}$ , 20).

**Mass Spectrum** (ESI+),  $m/z$ , 369.44 [ $\text{M} + \text{Na}$ ] $^+$ , 297.35 [ $\text{M} - \text{OMe}, - \text{H}_2\text{O}$ ] $^+$ , 279.35 [ $\text{M} - \text{OMe}, - 2\text{H}_2\text{O}$ ] $^+$ .

**IR:** 1096  $\text{cm}^{-1}$  (C-O stretch), 1691  $\text{cm}^{-1}$  (C=O stretch), 3547  $\text{cm}^{-1}$  (OH stretch).

**HRMS:** (ESI+),  $m/z$ , found = 369.2397, calculated for  $\text{C}_{22}\text{H}_{34}\text{O}_3\text{Na}$  [ $\text{M} + \text{Na}$ ] $^+$  = 369.2406.

### Compound **25** from hydrogenation of **11**



To a solution of epoxide **11** (200.0 mg, 0.58 mmol) in methanol (7 ml) was added Pd/C (30.0 mg) and stirred under  $\text{H}_2$  (g) overnight. The reaction mixture was filtered and concentrated. The residue was subjected to column chromatography (3-40% EtOAc in PE) to afford compound **25** as a pale yellow oil (33.0 mg, 17%), compound **26** as a clear oil (68.0 mg, 34%) and compound **12** as a white solid (75.0 mg, 37%).



### Compound 25

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 0.44 (1H, dd, *J* = 8.0 & 5.1 Hz, CH<sub>2</sub> - 4), 0.64 (1H, *J* = 9.7, 5.1 Hz, CH<sub>2</sub> - 4), 0.77 – 0.93 (2H, m, CH - 3, CH<sub>2</sub> - 1), 0.99 (3H, s, CCH<sub>3</sub> - 19), 0.99 – 1.82 (13H, m, CH - 9, CH<sub>2</sub> - 12, CH - 8, CH<sub>2</sub> - 11, CH<sub>2</sub> - 1, CH<sub>2</sub> - 2, CH - 14, CH<sub>2</sub> - 7, CH<sub>2</sub> - 15), 1.27 (3H, s, CCH<sub>3</sub> - 18), 2.02 - 2.18 (3H, m, CH<sub>2</sub> - 12, CH<sub>2</sub> - 16), 2.13 (3H, s, CCH<sub>3</sub> - 21), 2.75 (2H, t, *J* = 9.2 Hz, CH - 17), 2.79 (1H, t, *J* = 2.8 Hz, CH - 6), 3.33 (3H, s, OCH<sub>3</sub> - 1').

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 13.6 (CH<sub>2</sub>, 4), 19.4 (CH<sub>3</sub>, 19), 21.7 (CH, 3), 23.1 (CH<sub>2</sub>, 11), 23.3 (CH<sub>2</sub>, 16), 23.6 (CH<sub>2</sub>, 15), 24.9 (CH<sub>3</sub>, 18), 25.3 (CH<sub>2</sub>, 2), 28.7 (CH, 8), 29.0 (CH<sub>2</sub>, 12), 32.2 (CH<sub>3</sub>, 21), 33.9 (CH<sub>2</sub>, 1), 35.3 (C, 5), 36.0 (CH<sub>2</sub>, 7), 40.0 (CH, 9), 43.6 (C, 10), 44.6 (C, 13), 52.7 (CH, 14), 57.0 (CH<sub>3</sub>, 1'), 64.9 (CH, 17), 82.9 (CH, 6), 210.6 (C, 20).

**Mass Spectrum** (ESI+), *m/z*, 331.44 [M + H]<sup>+</sup>, 353.34 [M + Na]<sup>+</sup>, 299.34 [C<sub>21</sub>H<sub>31</sub>O]<sup>+</sup>, 683.59 [MX<sub>2</sub> + Na]<sup>+</sup>.

**IR:** 1705 cm<sup>-1</sup> (C=O stretch), 1100 cm<sup>-1</sup> (C-O stretch).

**HRMS:** (ESI+), *m/z*, found = 331.2651, calculated for C<sub>22</sub>H<sub>35</sub>O<sub>2</sub> [M + H]<sup>+</sup> = 331.2637.

### Compound 26

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>) δ 0.43 (1H, dd, *J* = 8.0 & 5.2 Hz, CH<sub>2</sub> - 4), 0.61 (1H, app. t, 4.4 Hz, CH<sub>2</sub> - 4), 0.77 – 1.05 (4H, m, CH<sub>2</sub> - 1, CH - 3, CH<sub>2</sub> - 7, CH - 8), 1.02 (3H, s, CCH<sub>3</sub> - 19), 1.09 – 1.26 (2H, m, CH<sub>2</sub> - 12), 1.36 (3H, s, CCH<sub>3</sub> - 18), 1.28 – 1.56 (4H, m, CH<sub>2</sub> - 1, CH<sub>2</sub> - 11, CH<sub>2</sub> - 2), 1.71 (1H, tdd, *J* = 12.1, 7.9, 4.3 Hz, CH<sub>2</sub> - 2), 1.88 – 1.98 (2H, m, CH<sub>2</sub> - 7, CH<sub>2</sub> - 16), 2.11 (3H, s, CH<sub>3</sub> - 21), 2.06 – 2.18 (1H, m, CH<sub>2</sub> - 16), 2.38 (1H, td, *J* = 12.0, 2.7 Hz, CH - 9), 2.64 (1H, dd, *J* = 10.2, 7.5 Hz, CH - 17), 2.75 (1H, t, *J* = 2.9 Hz, CH - 6), 3.28 (3H, s, OCH<sub>3</sub> - 1'), 3.35 (1H, s, CH - 15).

**<sup>13</sup>C NMR** (101 MHz, CDCl<sub>3</sub>) δ 13.4 (CH<sub>2</sub>, 4), 19.5 (CH<sub>3</sub>, 19), 20.0 (CH<sub>3</sub>, 18), 22.1 (CH, 3), 22.2 (CH<sub>2</sub>, 11), 25.2 (CH<sub>2</sub>, 2), 27.8 (CH<sub>2</sub>, 16), 28.5 (CH, 9), 29.9 (CH<sub>2</sub>, 7), 31.5 (CH<sub>2</sub>, 12), 32.1 (CH<sub>3</sub>, 21), 33.7 (CH<sub>2</sub>, 1), 35.5 (C, 10), 43.3 (C, 13), 43.9 (C, 5), 47.2 (CH, 8), 56.9 (CH<sub>3</sub>, 1'), 57.7 (CH, 17), 58.4 (CH, 15), 73.1 (C, 14), 81.9 (CH-6) 208.8 (C, 20).

**Mass Spectrum** (ESI+), *m/z*, 367.34 [M + Na]<sup>+</sup>, 313.34 [C<sub>21</sub>H<sub>29</sub>O<sub>2</sub>]<sup>+</sup>, 711.48 [MX<sub>2</sub> + Na]<sup>+</sup>.

**IR:** 1704 cm<sup>-1</sup> (C=O stretch), 1091 cm<sup>-1</sup> (C-O stretch).

**HRMS:** (ESI+), *m/z*, found = 345.2450, calculated for C<sub>22</sub>H<sub>33</sub>O<sub>3</sub> [M + H]<sup>+</sup> = 345.2430.

