

# **Stereoselective synthesis of 1,6-dioxaspirolactones from spiro-cyclopropanecarboxylated sugars: Total synthesis of dihydro-pyrenolide D**

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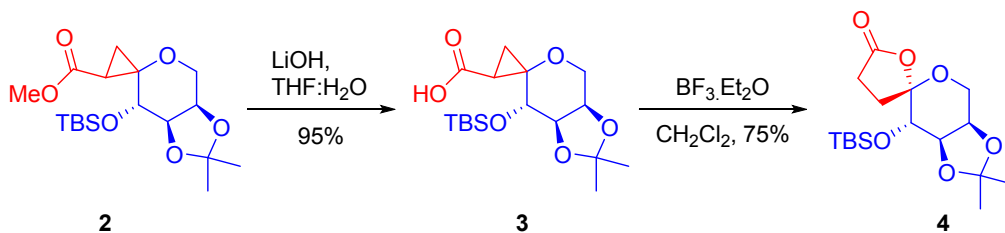
## **Supporting Information**

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## 1. General:

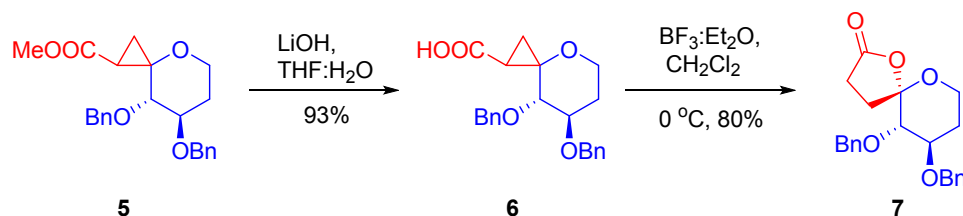
All the reactions were carried out under nitrogen or argon atmosphere and monitored by thin layer chromatography (TLC) using silica gel GF<sub>254</sub> plates with detection by charring with 5% (v/v) H<sub>2</sub>SO<sub>4</sub> in methanol or by phosphomolybdic acid (PMA) stain or by ultra violet (UV) detection. All the chemicals were purchased from local suppliers and Sigma-Aldrich Chemicals Company. Solvents used in the reactions were distilled over dehydrating agents. Dry toluene was prepared by using sodium and benzophenone. Silica-gel (100-200 mesh) was used for column chromatography. <sup>1</sup>H, <sup>13</sup>C, DEPT, COSY, NOESY spectra were recorded on Bruker 400 MHz and 500 MHz spectrometer in CDCl<sub>3</sub>. <sup>1</sup>H NMR chemical shifts were reported in ppm ( $\delta$ ) with TMS as internal standard ( $\delta$  0.00) and <sup>13</sup>C NMR were reported in chemical shifts with solvent reference (CDCl<sub>3</sub>,  $\delta$  77.00). Infrared (IR) spectra were recorded with a JASCO FT/IR-5300 pulse Fourier transform infrared spectrometer. High resolution mass spectra (HRMS) were recorded with a Bruker maXis ESI-TOF spectrometer.



**Compound 3:** To a stirred solution of spiro-cyclopropanecarboxylated sugar **2** (400 mg, 1.07 mmol) in THF (10 mL), aqueous 0.2N LiOH (5.3 mL) was added. The reaction mixture was stirred for 3 h at room temperature, then poured into water, neutralized with 1N HCl, (2 mL) and extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with water (100 mL), brine (100 mL), and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, filtered and concentrated in *vacuo*. The obtained crude product was further purified by the silica-gel column chromatography provided carboxylic acid **3** (365 mg) in 95% yield as a mixture of diastereomers (please see the supporting

spectra). **IR (neat)**:  $\nu_{\max}$  2980, 2964, 2925, 2865, 1703, 1451, 1380, 1248, 1122, 1002, 832, 782  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{17}\text{H}_{30}\text{O}_6\text{Si}+\text{Na}$  381.1709, found 381.1710.

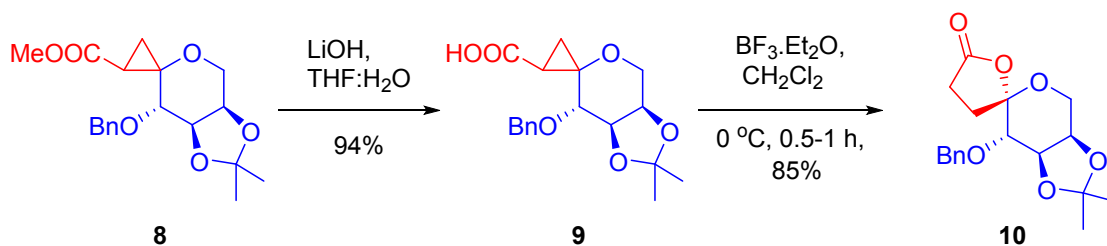
**Compound 4**: To a cooled (0 °C) solution of spiro-cyclopropanecarboxylic acid **3** (80 mg, 0.22 mmol) in dry dichloromethane (4 mL), was added borontrifluoride-diethyletherate ( $\text{BF}_3\cdot\text{Et}_2\text{O}$ ) (5.4  $\mu\text{L}$ , 0.04 mmol). The reaction mixture was stirred for 1 h while allowing the temperature to come to 25 °C. During the reaction, the colour was changed to pale red colour. After completion of the reaction (monitored by TLC), it was quenched with triethylamine. Removal of solvent under reduced pressure followed by silica-gel column chromatography afforded compound **4** (60 mg, 75%) as a colourless solid. **IR (neat)**:  $\nu_{\max}$  2975, 2942, 2931, 2881, 2848, 1774, 1385, 1243, 1210, 1122, 1078, 1056, 914, 848, 788  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**:  $\delta$  4.24-4.26 (m, 1H), 4.18 (t, 1H,  $J = 2.8$  Hz), 4.15 (t, 1H,  $J = 3.2$  Hz), 4.08 (d, 1H,  $J = 13.6$  Hz), 3.68 (d, 1H,  $J = 6.8$  Hz), 2.65-2.74 (m, 1H), 2.43-2.59 (m, 2H), 2.10 (ddd, 1H,  $J = 3.2$  Hz,  $J = 9.2$  Hz,  $J = 14.0$  Hz), 1.55 (s, 3H), 1.37 (s, 3H), 0.88 (s, 9H), 0.19 (s, 3H), 0.12 (s, 3H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  175.7, 109.1, 108.3, 77.1, 74.2, 73.2, 61.9, 29.8, 28.2, 27.8, 26.2, 25.7, 18.0, -3.8, -5.2. **HRMS (ESI)** calcd for  $\text{C}_{17}\text{H}_{30}\text{O}_6\text{Si}+\text{Na}$  381.1709, found 381.1712.  $[\alpha]_D^{25} = -90.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



**Compound 6**: Compound **6** was synthesized from **5** following the procedure described for compound **3**, yield 93%. **IR (neat)**:  $\nu_{\max}$  3029, 2925, 2870, 1725, 1692, 1456, 1210, 1100, 1067, 744, 700  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_5+\text{Na}$  391.1521, found 391.1521.

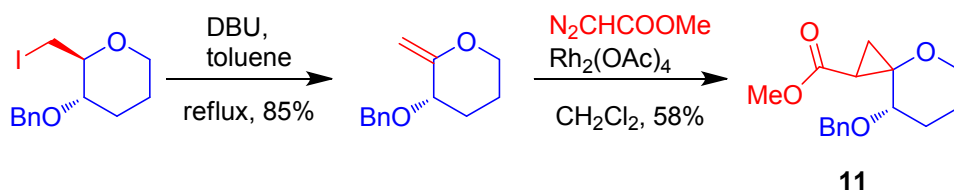
**Compound 7**: Compound **7** was synthesized from **6** following the procedure described for compound **4**, yield 80%. **IR (neat)**:  $\nu_{\max}$  3024, 2920, 1780, 1456, 1363, 1215, 1095, 908, 733, 700  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )**:  $\delta$  7.28-7.36 (m, 10H), 5.06 (d, 1H,  $J = 11.5$  Hz), 4.71 (d, 1H,  $J = 6.0$  Hz), 4.69 (d, 1H,  $J = 3.0$  Hz), 4.62 (d, 1H,  $J = 11.5$  Hz), 3.99 (ddd, 1H,  $J = 5.0$  Hz,  $J = 9.5$

Hz,  $J = 14.0$  Hz), 3.82-3.89 (m, 1H), 3.76 (ddd, 1H,  $J = 1.5$  Hz,  $J = 5.5$  Hz,  $J = 12.0$  Hz), 3.42 (d, 1H,  $J = 9.5$  Hz), 2.54-2.61 (m, 1H), 2.48 (ddd, 1H,  $J = 6.0$  Hz,  $J = 10.5$  Hz,  $J = 18.0$  Hz), 2.21 (ddd, 1H,  $J = 7.0$  Hz,  $J = 10.0$  Hz,  $J = 17.0$  Hz), 2.11-2.15 (m, 1H), 1.95 (ddd, 1H,  $J = 5.5$  Hz,  $J = 10.0$  Hz,  $J = 15.5$  Hz), 1.71-1.79 (m, 1H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  175.8, 138.2, 137.9, 128.4, 127.8, 127.7, 109.1, 81.7, 77.5, 75.2, 71.8, 61.4, 31.1, 30.8, 28.4. HRMS (ESI) calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_5 + \text{Na}$  391.1521, found 391.1522.  $[\alpha]_D^{25} = -71.7$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



**Compound 9:** Compound 9 was synthesized from 8 by following the procedure described for compound 3, yield 94%. IR (neat):  $\nu_{\text{max}}$  2985, 2925, 1703, 1456, 1385, 1221, 1111, 1084, 848, 744, 706  $\text{cm}^{-1}$ . HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{22}\text{O}_6 + \text{Na}$  357.1314, found 357.1312.

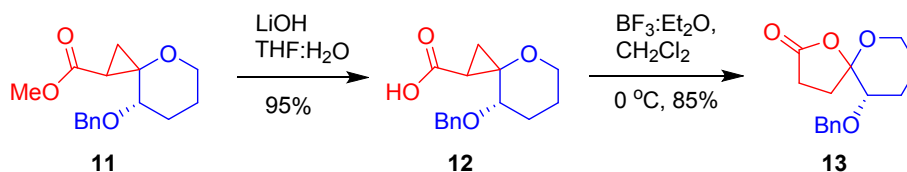
**Compound 10:** Compound 10 was synthesized from 9 by following the procedure described for compound 4, yield 85%. IR (neat):  $\nu_{\text{max}}$  3030, 2986, 2931, 2871, 2849, 1780, 1457, 1375, 1205, 1117, 1084, 909, 745  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.29-7.34 (m, 5H), 4.96 (d, 1H,  $J = 12.0$  Hz), 4.66 (d, 1H,  $J = 12.0$  Hz), 4.43 (dd, 1H,  $J = 5.5$  Hz,  $J = 7.0$  Hz), 4.27 (ddd, 1H,  $J = 1.0$  Hz,  $J = 3.0$  Hz,  $J = 5.5$  Hz), 4.16 (dd, 1H,  $J = 3.0$  Hz,  $J = 13.5$  Hz), 4.08 (d, 1H,  $J = 13.5$  Hz), 3.51 (d, 1H,  $J = 7.5$  Hz), 2.51-2.65 (m, 2H), 2.36 (ddd, 1H,  $J = 7.5$  Hz,  $J = 10.0$  Hz,  $J = 17.5$  Hz), 2.01 (ddd, 1H,  $J = 5.0$  Hz,  $J = 10.0$  Hz,  $J = 15.5$  Hz), 1.54 (s, 3H), 1.39 (s, 3H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  175.6, 137.6, 128.4, 128.0, 127.9, 109.3, 107.4, 78.1, 77.1, 73.2, 72.7, 61.9, 30.3, 28.2, 28.1, 26.2. HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{22}\text{O}_6 + \text{Na}$  357.1314, found 357.1315.  $[\alpha]_D^{25} = -71.5$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



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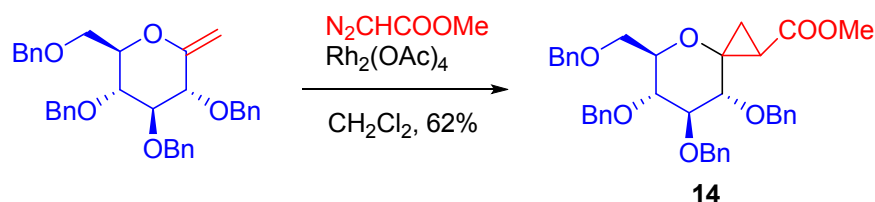
**Compound 11:** To a solution of (3*S*)-3-(benzyloxy)-2-(iodomethyl)tetrahydro-2*H*-pyran ( 8.0 g, 24 mmol) in toluene (100 mL) at 0 °C was added DBU (9 mL, 60.24 mmol), drop wise over a period of 10 min. The reaction mixture was brought to 25 °C and heated at reflux for 1.5 h. After completion of the reaction, the mixture was diluted with ethyl acetate. The solution was taken into a separating funnel and washed with water, brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated and the obtained residue was purified by column chromatography to give the *exo*-cyclic olefin (4.2 g) as a colourless liquid in 85% yield. **IR (neat):**  $\nu_{\max}$  2958, 2920, 2849, 1720, 1452, 1364, 1271, 1172, 1117, 1035, 723 cm<sup>-1</sup>. **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  7.29-7.39 (m, 5H), 4.70 (dd, 1H, *J* = 2.8 Hz, *J* = 12.0 Hz), 4.65 (d, 1H, *J* = 3.2 Hz), 4.46 (dd, 1H, *J* = 2.8 Hz, *J* = 12.0 Hz), 4.40 (d, 1H, *J* = 2.8 Hz), 4.00-4.06 (m, 1H), 3.81-3.87 (m, 2H), 2.06-2.14 (m, 1H), 1.93-1.98 (m, 2H), 1.58-1.66 (m, 1H). **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):**  $\delta$  158.4, 138.6, 128.3, 127.9, 127.6, 127.5, 94.6, 73.4, 70.0, 69.2, 29.5, 21.7. **HRMS (ESI)** calcd for C<sub>13</sub>H<sub>16</sub>O<sub>2</sub>+H 205.1229, found 205.1227.

To a stirred suspension of *exo*-cyclic glycol (1.0 g, 4.9 mmol) and Rh<sub>2</sub>(OAc)<sub>4</sub> (43.0 mg, 0.098 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (20 mL), a solution of methyl diazoacetate (1.36 mL, 14.70 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (40 mL) was added drop wise, over a period of 1 h, After completion of the reaction, the reaction mixture was concentrated in *vacuo* and the obtained crude product was purified by silica-gel column chromatography (eluent: 10-20% EtOAc in Hexane) to give desired spiro-cyclopropanecarboxylate **11** (0.78 g) in 58% yield as a mixture of diastereomers. **IR (neat):**  $\nu_{\max}$  3057, 3019, 2958, 2838, 1726, 1490, 1430, 1358, 1265, 1254, 1194, 1156, 1073, 882, 739, 706 cm<sup>-1</sup>. **HRMS (ESI)** calcd for C<sub>16</sub>H<sub>20</sub>O<sub>4</sub>+H 277.1440, found 277.1443.

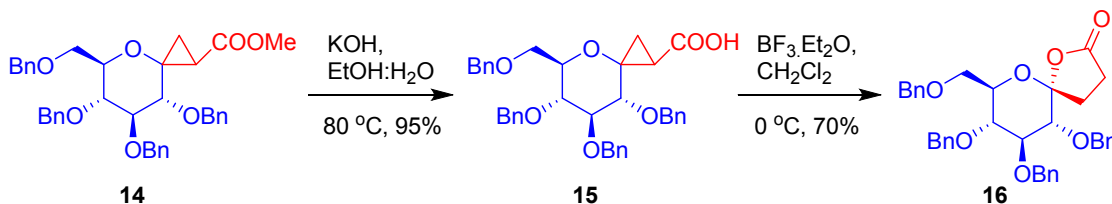


**Compound 12:** Compound **12** was synthesized from **11** by following the procedure described for compound **3**, yield 95%. **IR (neat):**  $\nu_{\max}$  3063, 3030, 2926, 1742, 1506, 1452, 1358, 1227, 1079, 1024, 745, 690 cm<sup>-1</sup>. **HRMS (ESI)** calcd for C<sub>15</sub>H<sub>18</sub>O<sub>4</sub>+H 263.1283, found 263.1280.

**Compound 13:** Compound **13** was synthesized from **12** by following the procedure described for compound **4**, yield 85%. Compound **13** was obtained as an inseparable mixture of *S,S* and *R,S* diastereomers in 55:45 ratio respectively (please see the supporting spectra). **IR (neat):**  $\nu_{\max}$  3063, 3024, 2942, 2887, 1786, 1501, 1457, 1358, 1271, 1221, 1194, 1095, 1063, 909, 734, 701  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{15}\text{H}_{18}\text{O}_4+\text{H}$  263.1283, found 263.1282.



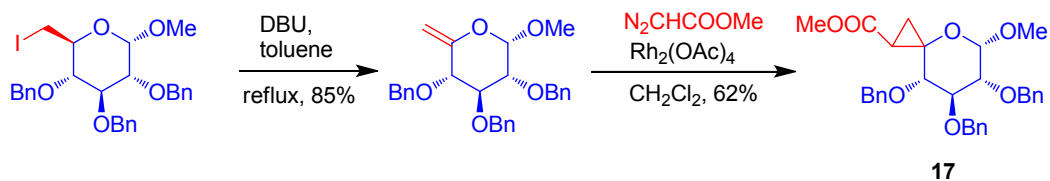
**Compound 14:** Compound **14** was synthesized from 2,6-Anhydro-3,4,5,7-tetra-*O*-benzyl-1-deoxy-D-glucohept-1-enitol<sup>1</sup> by following the procedure described for compound **11**, yield 62%. **IR (neat):**  $\nu_{\max}$  3091, 3056, 3029, 2942, 2869, 1736, 1627, 1496, 1453, 1343, 1249, 1210, 1164, 1094, 1066, 1025, 913, 844, 822  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{38}\text{H}_{40}\text{O}_7+\text{Na}$  631.2672, found 631.2672.



**Compound 15:** To a solution of spiro-cyclopropanecarboxylated sugar **14** (350 mg, 0.574 mmol) in EtOH/ $\text{H}_2\text{O}$  (15 mL, 2:1) was added KOH (226 mg, 4.04 mmol) and the mixture was stirred at 80 °C for 2 h, after completion of the reaction (by TLC), 1/3 of the solvent was removed in *vacuo* at 50 °C. The obtained suspension was diluted with  $\text{H}_2\text{O}$  (60 mL), and extracted with ethyl acetate (100 mL). The aqueous phase was acidified with 1N HCl, and the solution was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with brine solution (50 mL), dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Evaporation of the solvent under reduced pressure provided the crude product which was purified by the silica-gel column chromatography to obtain the spiro-cyclopropanecarboxylic acid **15** (324 mg, 95%) as a colourless thick oil. **IR (neat):**  $\nu_{\max}$  3085,

3056, 3029, 2920, 2863, 1696, 1496, 1453, 1360, 1205, 1094, 1026, 911  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{37}\text{H}_{38}\text{O}_7+\text{Na}$  617.2515, found 617.2517.

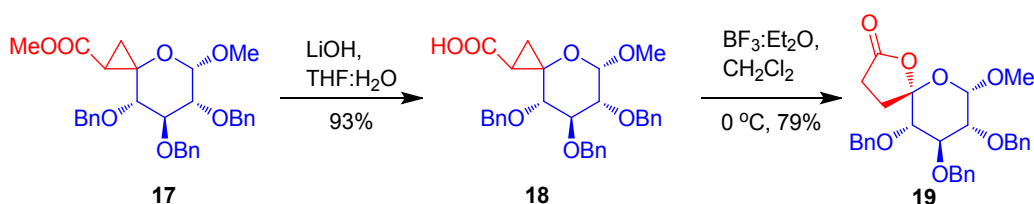
**Compound 16:** To a cooled (0 °C) solution of spiro-cyclopropanecarboxylic acid **15** (100 mg, 0.16 mmol) in dry dichloromethane (5 mL) was added  $\text{BF}_3\cdot\text{Et}_2\text{O}$  (20.5  $\mu\text{L}$ , 0.16 mmol) and the mixture was stirred for 5 h at the room temperature. After completion of the reaction (by checking TLC), the reaction was quenched by the addition of triethylamine. The reaction mixture was concentrated under reduced pressure, followed by silica-gel column chromatography afforded the compound **16** (70 mg, 70%) as colourless solid. **IR (neat):**  $\nu_{\text{max}}$  3090, 3063, 3030, 2926, 2865, 1780, 1501, 1452, 1364, 1265, 1210, 1106, 909, 734, 701  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.28-7.39 (m, 20H), 5.05 (d, 1H,  $J = 11.6$  Hz), 4.96 (d, 1H,  $J = 4.8$  Hz), 4.77 (d, 1H,  $J = 11.6$  Hz), 4.74 (s, 1H), 4.73 (d, 1H,  $J = 12.0$  Hz), 4.64 (d, 1H,  $J = 11.2$  Hz), 4.50 (d, 1H,  $J = 12.0$  Hz), 4.46 (d, 1H,  $J = 12.0$  Hz), 4.14 (t, 1H,  $J = 6.8$  Hz), 3.97-4.09 (m, 3H), 3.51-3.60 (m, 2H), 2.45-2.63 (m, 2H), 2.19 (ddd, 1H,  $J = 7.2$  Hz,  $J = 11.6$  Hz,  $J = 16.8$  Hz), 2.05 (ddd, 1H,  $J = 6.4$  Hz,  $J = 10.4$  Hz,  $J = 16.4$  Hz).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):** 175.7, 138.4, 138.0, 137.8, 137.8, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 127.6, 108.9, 80.9, 77.5, 75.3, 74.8, 74.2, 73.4, 72.9, 72.6, 68.2, 30.7, 28.5. **HRMS (ESI)** calcd for  $\text{C}_{37}\text{H}_{38}\text{O}_7+\text{Na}$  617.2515, found 617.2518.  $[\alpha]_D^{25} = +28.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



**Compound 17:** To a solution of methyl 6-deoxy-6-iodo-2,3,4-tri-*O*-benzyl- $\alpha$ -D-glucopyranoside<sup>2</sup> (4.0 g, 6.96 mmol) in toluene (60 mL) at 0 °C was added DBU (3.12 mL, 20.90 mmol), drop wise over a period of 10 min. The reaction mixture was brought to 25 °C and heated at reflux for 1.5 h. After completion of the reaction, the mixture was diluted with ethyl acetate. The solution was taken into a separating funnel and washed with water, brine, dried over anhydrous  $\text{Na}_2\text{SO}_4$ , concentrated and the obtained residue was purified by silica-gel column chromatography to give methyl 2,3,4-tri-*O*-benzyl- $\alpha$ -D-xylo-hex-5-enopyranoside<sup>2</sup> (2.65 g, 85%) as a colourless semisolid. **IR (neat):**  $\nu_{\text{max}}$  3068, 3035, 2920, 1731, 1501, 1452, 1353, 1090, 1024, 734, 701  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR**

(400 MHz, CDCl<sub>3</sub>): δ 7.27-7.39 (m, 15H), 4.92 (d, 1H, *J* = 10.4 Hz), 4.89 (s, 1H), 4.88 (d, 1H, *J* = 10.8 Hz), 4.84 (d, 1H, *J* = 12.0 Hz), 4.79 (d, 2H, *J* = 2.4 Hz), 4.72 (d, 1H, *J* = 0.8 Hz), 4.69 (d, 1H, *J* = 12.0 Hz), 4.64 (d, 1H, *J* = 3.2 Hz), 3.99 (t, 1H, *J* = 9.2 Hz), 3.91 (dt, 1H, *J* = 0.8 Hz, *J* = 8.8 Hz), 3.62 (dd, 1H, *J* = 3.2 Hz, *J* = 9.2 Hz), 3.44 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 153.6, 138.6, 138.0, 137.9, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 99.0, 96.9, 81.2, 79.5, 79.2, 75.8, 74.5, 73.6, 55.4. HRMS (ESI) calcd for C<sub>28</sub>H<sub>30</sub>O<sub>5</sub>+H 447.2171, found 447.2173.

To a stirred suspension of methyl 2,3,4-tri-*O*-benzyl- $\alpha$ -D-xylo-hex-5-enopyranoside (1.1 g, 2.46 mmol) and Rh<sub>2</sub>(OAc)<sub>4</sub> (10.8 mg, 0.02 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added drop wise, over a period of 1 h, a solution of methyl diazoacetate (0.68 mL, 7.39 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (40 mL). After completion of the reaction, the reaction mixture was concentrated in *vacuo* and the obtained crude product was purified by silica gel column chromatography (eluent: 10-20% EtOAc in Hexane) to give desired spiro-cyclopropanecarboxylate **17** (0.80 g, 62%) as a mixture of diastereomers. IR (neat):  $\nu_{\max}$  3084, 3057, 3029, 2920, 2854, 1719, 1500, 1451, 1358, 1199, 1166, 1051, 914, 739, 695 cm<sup>-1</sup>. HRMS (ESI) calcd for C<sub>31</sub>H<sub>34</sub>O<sub>7</sub>+Na 541.2202, found 541.2204.

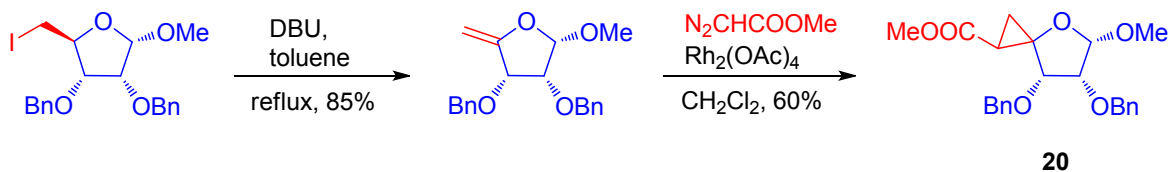


**Compound 18:** Compound **18** was synthesized from **17** following the procedure described for compound **3**, yield 93%. IR (neat):  $\nu_{\max}$  3062, 3024, 2920, 2859, 1698, 1495, 1451, 1358, 1166, 1100, 1056, 733, 695 cm<sup>-1</sup>. HRMS (ESI) calcd for C<sub>30</sub>H<sub>32</sub>O<sub>7</sub>+Na 527.2046, found 527.2045.

**Compound 19:** Compound **19** was synthesized from **18** following the procedure described for compound **4**, yield 79%. IR (neat):  $\nu_{\max}$  3057, 3024, 2926, 2849, 1786, 1495, 1457, 1358, 1221, 1073, 915, 739, 701 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.27-7.36 (m, 15H), 5.00 (d, 1H, *J* = 11.6 Hz), 4.94 (d, 1H, *J* = 10.8 Hz), 4.93 (d, 1H, *J* = 11.2 Hz), 4.78-4.80 (m, 2H), (4.74 (d, 1H, *J* = 11.6 Hz), 4.68 (d, 1H, *J* = 11.6 Hz), 4.01 (t, 1H, *J* = 9.6 Hz), 3.54 (s, 3H), 3.47-3.52 (m, 2H), 2.46-2.66 (m, 2H), 2.04-2.16 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 175.2, 138.4, 138.2, 137.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.6, 106.5, 102.1, 82.0, 80.9, 80.2, 76.0, 75.3, 74.6,

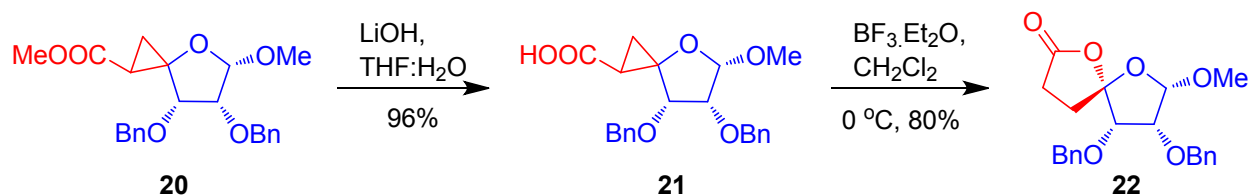


57.6, 30.6, 28.1. **HRMS (ESI)** calcd for  $C_{30}H_{32}O_7+Na$  527.2046, found 527.2048.  $[\alpha]_D^{25} = -15.9$  (C = 1.0,  $CHCl_3$ ).



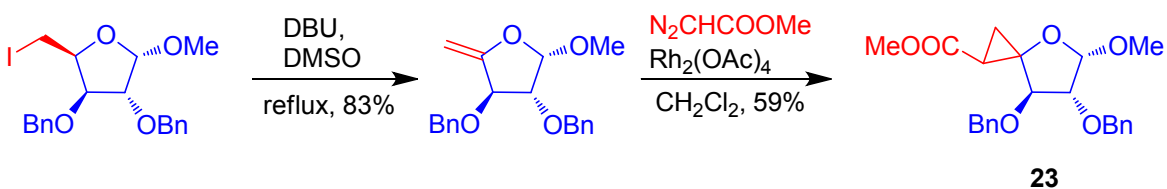
**Compound 20:** To a solution of methyl 5-deoxy-5-iodo-2,3-di-*O*-benzyl- $\alpha$ -D-ribofuranoside<sup>3</sup> (1.3 g, 2.38 mmol) in toluene (15 mL) at 0 °C was added DBU (0.89 mL, 5.97 mmol), drop wise over a period of 10 min. The reaction mixture was brought to 25 °C and heated at reflux for 1.5 h. After completion of the reaction (by monitoring TLC), the mixture was diluted with ethyl acetate (50 mL). The solution was taken into a separating funnel and washed with water, brine, dried over anhydrous  $Na_2SO_4$ , concentrated and the obtained residue was purified by column chromatography to give methyl 5-deoxy-2,3-di-*O*-benzyl- $\alpha$ -D-*erythro*-pent-4-eno-furanoside<sup>4</sup> (0.66 g, 85%) as a colourless liquid. **IR (neat):**  $\nu_{max}$  3090, 3068, 3035, 2926, 2865, 1720, 1501, 1457, 1353, 1112, 1024, 745, 695  $cm^{-1}$ . **<sup>1</sup>H NMR (400 MHz,  $CDCl_3$ ):**  $\delta$  7.32-7.40 (m, 10H), 5.16 (d, 1H,  $J = 2.0$  Hz), 4.66 (d, 2H,  $J = 2.8$  Hz), 4.63 (d, 2H,  $J = 3.6$  Hz), 4.55 (s, 1H), 4.39 (d, 1H,  $J = 4.8$  Hz), 4.28 (s, 1H), 3.84 (dd, 1H,  $J = 2.4$  Hz,  $J = 4.8$ ), 3.45 (s, 3H). **<sup>13</sup>C NMR (100 MHz,  $CDCl_3$ ):**  $\delta$  158.5, 137.6, 137.4, 128.5, 128.1, 128.0, 127.9, 106.8, 85.0, 78.7, 75.9, 72.2, 71.5, 56.5. **HRMS (ESI)** calcd for  $C_{20}H_{22}O_4+H$  327.1596, found 327.1593.

The above methylenated product (0.326 g, 1 mmol) was cyclopropanated following the procedure described for compound **17** to obtain the spiro-cyclopropanecarboxylate **20** (0.24 g, 60%) as a mixture of diastereomers (please see the supporting spectra). **IR (neat):**  $\nu_{max}$  3095, 3068, 3035, 2953, 2925, 1725, 1495, 1456, 1374, 1325, 1215, 1155, 739, 706  $cm^{-1}$ . **HRMS (ESI)** calcd for  $C_{23}H_{26}O_6+H$  399.1808, found 399.1809.



**Compound 21:** Compound **21** was synthesized from **20** by following the procedure described for compound **3**, yield 96%. **IR (neat):**  $\nu_{\text{max}}$  3035, 2920, 2859, 1703, 1451, 1407, 1265, 1210, 1150, 1111, 1040, 739, 695  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_6+\text{Na}$  407.1471, found 407.1473.

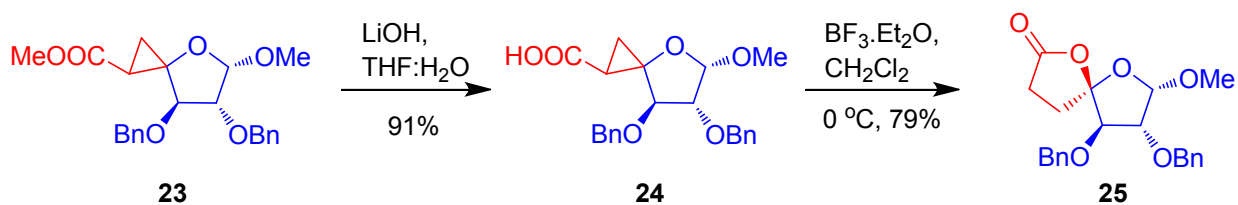
**Compound 22:** Compound **22** was synthesized from **21** by following the procedure described for compound **4**, yield 80%. **IR (neat):**  $\nu_{\text{max}}$  3068, 3035, 2920, 2860, 1786, 1731, 1501, 1452, 1265, 1030, 882, 739, 695  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.31-7.39 (m, 10H), 5.00 (d, 1H,  $J = 1.5$  Hz), 4.71 (d, 1H,  $J = 12.5$  Hz), 4.67 (s, 1H), 4.63 (d, 1H,  $J = 12.0$  Hz), 4.57 (d, 1H,  $J = 12.0$  Hz), 4.32 (d, 1H,  $J = 4.5$  Hz), 4.00 (dd, 1H,  $J = 1.5$  Hz,  $J = 4.5$  Hz), 3.39 (s, 3H), 2.67-2.76 (m, 2H), 2.49 (ddd, 1H,  $J = 8.5$  Hz,  $J = 13.0$  Hz,  $J = 17.5$  Hz), 2.18-2.24 (m, 1H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta$  175.6, 137.5, 137.2, 128.5, 128.5, 127.9, 127.8, 127.7, 115.4, 106.3, 81.3, 80.3, 73.3, 72.6, 55.6, 29.6, 28.1. **HRMS (ESI)** calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_6+\text{Na}$  407.1471, found 407.1474.  $[\alpha]_D^{25} = +21.6$  ( $c = 0.78$ ,  $\text{CHCl}_3$ ).



**Compound 23:** To a solution of methyl 5-deoxy-5-iodo-2,3-di-O-benzyl- $\alpha$ -D-xylofuranoside (0.80 g, 1.47 mmol) in dimethyl sulfoxide (DMSO) (12 mL) at 0 °C was added DBU (0.54 mL, 3.67 mmol), drop wise over a period of 5 min. The reaction mixture was brought to 25 °C and heated at reflux for 3 h in presence of 3 Å molecular sieves. After completion of the reaction, water (20 mL) was added and the reaction mixture was extracted with diethyl ether. The solution

was taken into a separating funnel and washed with water, brine and dried over anhydrous  $\text{Na}_2\text{SO}_4$ , concentrated and the obtained residue was purified by column chromatography to give methyl 5-deoxy-2,3-di-*O*-benzyl- $\alpha$ -D-*threo*-pent-4-eno-furanoside (0.40 g, 83%) as a colourless liquid. **IR (neat)**:  $\nu_{\text{max}}$  3057, 3024, 2926, 2871, 1731, 1704, 1660, 1501, 1452, 1205, 1090, 734, 706  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**:  $\delta$  7.31-7.41 (m, 10H), 5.13 (d, 1H,  $J = 2.0$  Hz), 4.70 (s, 2H), 4.62 (d, 1H,  $J = 11.6$  Hz), 4.61 (t, 1H,  $J = 2.0$  Hz), 4.57 (d, 1H,  $J = 11.6$  Hz), 4.39 (m, 1H), 4.29 (t, 1H,  $J = 1.6$  Hz), 4.03 (dd, 1H,  $J = 2.0$  Hz,  $J = 3.2$  Hz), 3.24 (s, 3H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  159.6, 137.6, 137.2, 128.5, 128.5, 128.0, 128.0, 127.9, 108.3, 86.4, 85.0, 79.7, 72.0, 71.2, 56.3. **HRMS (ESI)** calcd for  $\text{C}_{20}\text{H}_{22}\text{O}_4 + \text{H}$  327.1596, found 327.1592.

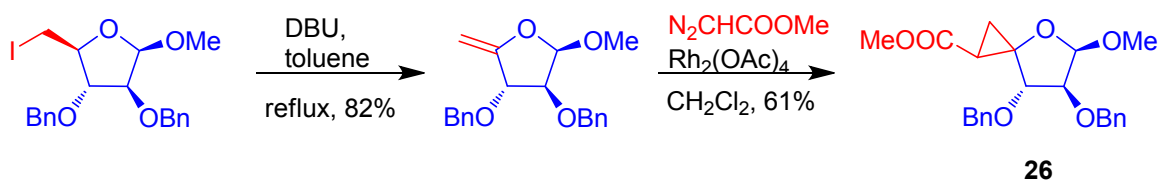
The above methylenated product (270 mg, 0.82 mmol) was cyclopropanated following the procedure described for compound **17** to obtain spiro-cyclopropanecarboxylate **23** (195 mg, 59%) as a mixture of diastereomers (please see the supporting spectra). **IR (neat)**:  $\nu_{\text{max}}$  3062, 3029, 2920, 2854, 1741, 1500, 1451, 1369, 1265, 1100, 1018, 739, 700  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{23}\text{H}_{26}\text{O}_6 + \text{Na}$  421.1627, found 421.1626.



**Compound 24**: Compound **24** was synthesized from **23** by following the procedure described for compound **3**, yield 91%. **IR (neat)**:  $\nu_{\text{max}}$  3029, 2920, 2848, 1698, 1500, 1451, 1407, 1308, 1210, 1095, 1023, 952, 739, 695  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_6 + \text{Na}$  407.1471, found 407.1472.

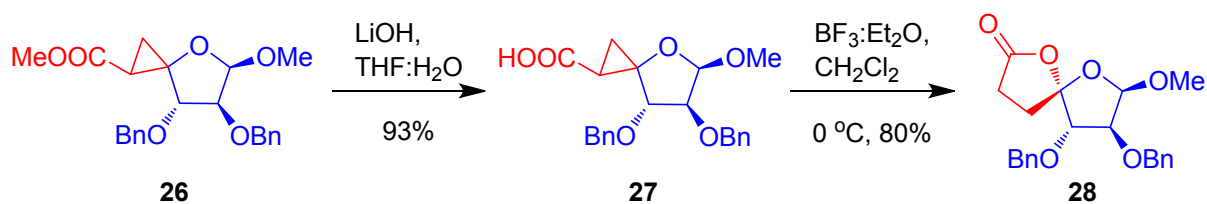
**Compound 25**: Compound **25** was synthesized from **24** by following the procedure described for compound **4**, yield 79%. **IR (neat)**:  $\nu_{\text{max}}$  3029, 2920, 2848, 1785, 1730, 1643, 1451, 1402, 1248, 1084, 908, 739, 695  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )**:  $\delta$  7.29-7.41 (m, 10H), 4.94 (d, 1H,  $J = 3.6$  Hz), 4.82 (d, 1H,  $J = 12.0$  Hz), 4.66 (d, 1H,  $J = 6.0$  Hz), 4.63 (d, 1H,  $J = 7.2$  Hz), 4.57 (d, 1H,  $J = 11.6$  Hz), 4.26 (dd, 1H,  $J = 3.6$  Hz,  $J = 7.6$  Hz), 3.96 (d, 1H,  $J = 7.2$  Hz), 3.41 (s, 3H), 2.60-2.68 (m, 1H), 2.44-2.55 (m, 1H), 2.16-2.22 (m, 2H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  174.7, 137.4,

137.3, 128.4, 128.1, 127.9, 111.4, 108.1, 85.7, 83.8, 72.7, 72.4, 55.9, 29.9, 28.2. **HRMS (ESI)** calcd for C<sub>22</sub>H<sub>24</sub>O<sub>6</sub>+Na 407.1471, found 407.1471.  $[\alpha]_D^{25} = -10.3$  ( $c = 0.73$ , CHCl<sub>3</sub>).



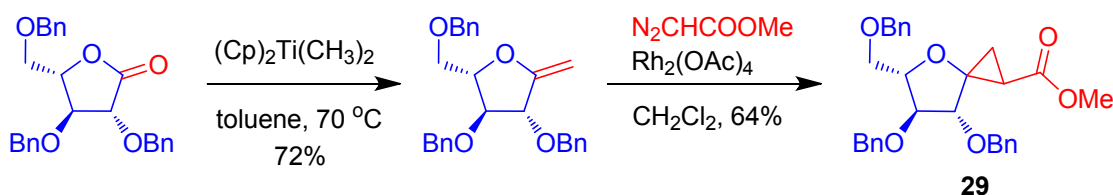
**Compound 26:** To a solution of methyl 5-deoxy-5-iodo-2,3-di-*O*-benzyl- $\beta$ -D-arabinofuranoside (1.8 g, 3.47 mmol) in toluene (20 mL) at 0 °C was added DBU (1.46 mL, 10.42 mmol), drop wise over a period of 10 min. The reaction mixture was brought to 25 °C and heated at reflux for 1.5 h. After completion of the reaction, the mixture was diluted with ethyl acetate, taken into a separating funnel and washed with water, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, concentrated and the obtained residue was purified by silica gel column chromatography to give the *exo*-cyclic-olefin (0.93 g, 82%) as colourless liquid. **IR (neat):**  $\nu_{\max}$  3084, 3068, 3030, 2931, 2876, 1715, 1501, 1457, 1358, 1210, 1112, 1024, 739, 706 cm<sup>-1</sup>. **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):**  $\delta$  7.32-7.39 (m, 10H), 5.11 (d, 1H,  $J = 1.6$  Hz), 4.70 (s, 2H), 4.62 (d, 1H,  $J = 11.6$  Hz), 4.61 (t, 1H,  $J = 2.0$  Hz), 4.57 (d, 1H,  $J = 11.6$  Hz), 4.39 (m, 1H), 4.29 (t, 1H,  $J = 1.6$  Hz), 4.03 (dd, 1H,  $J = 2.0$  Hz,  $J = 3.2$  Hz), 3.24 (s, 3H). **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):**  $\delta$  159.6, 137.6, 137.2, 128.5, 128.5, 128.0, 127.9, 127.8, 108.3, 86.4, 84.9, 79.7, 72.0, 71.2, 56.2. **HRMS (ESI)** calcd for C<sub>20</sub>H<sub>22</sub>O<sub>4</sub>+H 327.1596, found 327.1596.

The above obtained methylenated product (600 mg 1.84 mmol) was cyclopropanated by following the procedure described for compound **17** to obtain the spiro-cyclopropanecarboxylate **26** (450 mg, 61%) as a mixture of diastereomers (please see the supporting spectra). **IR (neat):**  $\nu_{\max}$  3057, 3035, 2953, 2920, 2848, 1719, 1500, 1456, 1440, 1380, 1265, 1199, 1155, 1100, 739, 700 cm<sup>-1</sup>. **HRMS (ESI)** calcd for C<sub>23</sub>H<sub>26</sub>O<sub>6</sub>+H 399.1808, found 399.1808.



**Compound 27:** Compound **27** was synthesized from **26** following the procedure described for compound **3**, yield 93%. **IR (neat):**  $\nu_{\text{max}}$  3068, 3029, 2920, 2859, 1703, 1500, 1456, 1270, 1210, 1100, 1029, 952, 733, 700  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_6+\text{H}$  385.1651, found 385.1654.

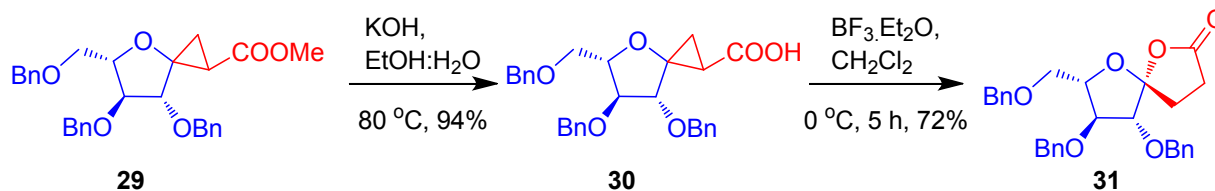
**Compound 28:** Compound **28** was synthesized from **27** following the procedure described for compound **4**, yield 80%. **IR (neat):**  $\nu_{\text{max}}$  3084, 3057, 3030, 2920, 2854, 1780, 1501, 1452, 1369, 1210, 904, 739, 701  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.28-7.37 (m, 10H), 4.92 (d, 1H,  $J = 3.6$  Hz), 4.79 (d, 1H,  $J = 12.0$  Hz), 4.64 (d, 1H,  $J = 6.0$  Hz), 4.61 (d, 1H,  $J = 6.8$  Hz), 4.55 (d, 1H,  $J = 12.0$  Hz), 4.24 (dd, 1H,  $J = 3.6$  Hz,  $J = 7.6$  Hz), 3.94 (d, 1H,  $J = 7.6$  Hz), 3.39 (s, 3H), 2.44-2.66 (m, 2H), 2.15-2.20 (m, 2H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta$  174.8, 137.4, 137.3, 128.5, 128.1, 127.9, 127.8, 111.4, 108.1, 85.7, 83.8, 72.7, 72.4, 55.9, 29.9, 28.2. **HRMS (ESI)** calcd for  $\text{C}_{22}\text{H}_{24}\text{O}_6+\text{Na}$  407.1471, found 407.1472.  $[\alpha]_D^{25} = +14.9$  ( $c = 0.76$ ,  $\text{CHCl}_3$ ).



**Compound 29:** 2,3,5-tri-*O*-benzyl-L-arabinoic acid  $\gamma$ -lactone<sup>5</sup> (1.0 g, 2.39 mmol) was dissolved in dry toluene (20 mL) and cyclopentadienyldimethyl titanocene (4.0 mL of a 20% w/w solution in toluene) was added slowly at room temperature, then the reaction mixture was stirred in the dark

at 70 °C under argon for 24 h or until TLC showed disappearance of the starting material. The brown reaction mixture was concentrated, and subjected to silica-gel column chromatography, using hexane/ethyl acetate (containing 1% triethylamine) to give the corresponding *exo*-cyclic enol ether product (0.72 g, 72%) as a colourless liquid. **IR (neat):**  $\nu_{\max}$  3066, 3028, 2936, 2875, 2249, 1723, 1496, 1453, 1350, 1271, 1205, 1089, 1026, 906, 726  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.29-7.33 (m, 15 H), 4.64-4.76 (m, 4H), 4.58-4.61 (m, 2H), 4.46-4.50 (m, 2H), 4.09-4.10 (m, 1H), 4.01-4.05 (m, 2H), 3.81-3.83 (m, 1H), 3.75-3.77 (m, 1H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta$  155.9, 138.5, 138.2, 138.1, 128.4, 128.4, 127.7, 127.7, 97.9, 76.9, 76.2, 72.6, 72.5, 71.6, 71.4, 66.9. **HRMS (ESI)** calcd for  $\text{C}_{27}\text{H}_{28}\text{O}_4+\text{H}$  417.2066, found 417.2062.

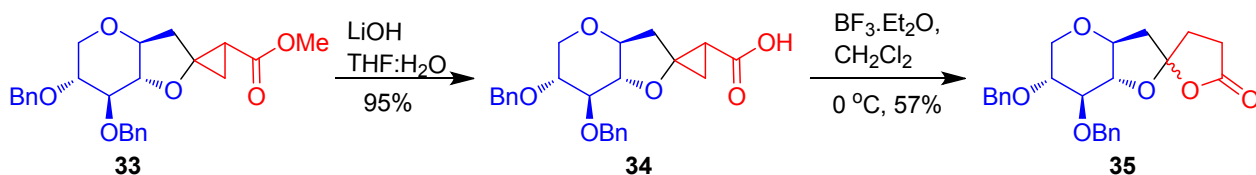
The obtained methylenated product (830 mg 1.98 mmol) was cyclopropanated by following the procedure described for compound **17** to provide spiro-cyclopropanecarboxylate **29** (620 mg, 64%) as a mixture of diastereomers (please see the supporting spectra). **IR (neat):**  $\nu_{\max}$  2923, 2852, 1722, 1496, 1453, 1364, 1264, 1209, 1164, 1071, 1027, 888, 843, 804, 733  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{30}\text{H}_{32}\text{O}_6+\text{Na}$  511.2097, found 511.2100.



**Compound 30:** To a solution of spiro-cyclopropanecarboxylated sugar **29** (200 mg, 0.41 mmol) in EtOH/ $\text{H}_2\text{O}$  (10 mL, 2:1) was added KOH (161 mg, 2.88 mmol) at room temperature, and the reaction mixture was stirred at 80 °C for 2 h. After completion of the reaction (by TLC) 1/3 of the solvent was removed in *vacuo*. The obtained residue was diluted with water (40 mL), and once extracted with ethyl acetate (50 mL). The aqueous phase was acidified with 1N HCl and extracted with ethyl acetate (3  $\times$  50 mL). The combined organic layers were washed with brine solution (100 mL), dried over  $\text{Na}_2\text{SO}_4$ , and evaporated. The obtained crude product was purified by the silica-gel column chromatography to furnish the spiro-cyclopropanecarboxylic acid **30** (183 mg, 94%).

**IR (neat):**  $\nu_{\max}$  3059, 3018, 2926, 2853, 1693, 1496, 1453, 1317, 1264, 1186, 1069, 1026, 882  $\text{cm}^{-1}$ . **<sup>1</sup>H NMR (ESI)** calcd for  $\text{C}_{29}\text{H}_{30}\text{O}_6+\text{Na}$  497.1940, found 497.1945.

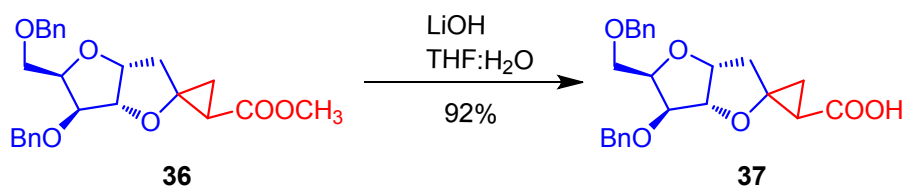
**Compound 31:** To a cooled (0 °C) solution of spiro-cyclopropanecarboxylic acid **30** (30 mg, 0.06 mmol) in dry dichloromethane (3 mL) was added  $\text{BF}_3\cdot\text{Et}_2\text{O}$  (7.76  $\mu\text{L}$ , 0.06 mmol) and stirred the reaction mixture for 5 h at the room temperature. After completion of the reaction by checking TLC, the reaction mixture was quenched by addition of triethylamine, then concentrated by using rotary evaporator. Purification of the obtained residue over silica-gel column chromatography gave the spiro lactone **31** (22 mg, 72%) as a single diastereomer. **IR (neat):**  $\nu_{\max}$  2922, 2853, 1781, 1741, 1602, 1496, 1453, 1365, 1263, 1208, 1124, 1095, 1051, 1027, 910, 858, 801, 737  $\text{cm}^{-1}$ . **<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.28-7.43 (m, 15H), 5.09 (d, 1H,  $J = 11.6$  Hz), 4.79 (d, 1H,  $J = 12.4$  Hz), 4.74 (d, 1H,  $J = 12.4$  Hz), 4.73 (d, 1H,  $J = 11.6$  Hz), 4.66 (d, 1H,  $J = 12$  Hz), 4.63 (d, 1H,  $J = 12$  Hz), 4.04 (d, 1H,  $J = 9.6$  Hz), 4.00 (dd, 1H,  $J = 2.8$  Hz,  $J = 10.0$  Hz), 3.89 (dd, 1H,  $J = 1.6$  Hz,  $J = 12.4$  Hz), 3.84 (d, 1H,  $J = 1.6$  Hz), 3.81 (d, 1H,  $J = 12.8$  Hz), 2.57-2.66 (m, 2H), 2.26 (ddd, 1H,  $J = 7.2$  Hz,  $J = 10.0$  Hz,  $J = 17.2$  Hz), 2.09 (ddd, 1H,  $J = 5.6$  Hz,  $J = 10.4$  Hz,  $J = 16.0$  Hz). **<sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta$  175.7, 138.0, 128.4, 127.9, 127.8, 109.2, 79.4, 77.6, 75.5, 73.2, 72.2, 71.8, 63.7, 30.7, 28.4. **HRMS (ESI)** calcd for  $\text{C}_{29}\text{H}_{30}\text{O}_6+\text{Na}$  497.1940, found 497.1942.  $[\alpha]_D^{25} = +57.5$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



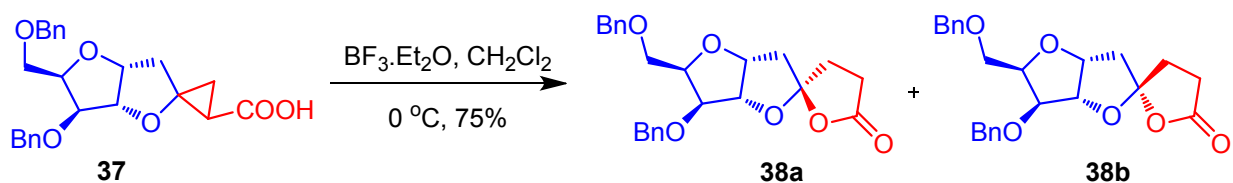
**Compound 34:** Compound **34** was synthesized from **33**<sup>6</sup> by following the procedure described for compound **3**, yield 95%. **IR (neat):**  $\nu_{\max}$  3063, 3024, 2926, 2854, 1726, 1682, 1501, 1452, 1413, 1128, 1101, 1056, 914, 843, 728, 701  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{24}\text{H}_{26}\text{O}_6+\text{Na}$  433.1627, found 433.1626.

**Compound 35:** Compound **35** was synthesized from **34** by following the procedure described for compound **4**, as mixture of inseparable diastereomers in 1:1 ratio. Yield 57%. **IR (neat):**  $\nu_{\max}$  3084,

3062, 3029, 2920, 2854, 1780, 1500, 1456, 1281, 1144, 1095, 1045, 903, 744, 695  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{24}\text{H}_{26}\text{O}_6+\text{Na}$  433.1627, found 433.1629.



**Compound 37:** Compound **37** was synthesized from **36**<sup>6</sup> following the procedure described for compound **3**, yield 92%. **IR (neat):**  $\nu_{\text{max}}$  3068, 3035, 2931, 2865, 1786, 1682, 1490, 1452, 1216, 1073, 1030, 909, 838, 739  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{24}\text{H}_{26}\text{O}_6+\text{Na}$  433.1627, found 433.1628.

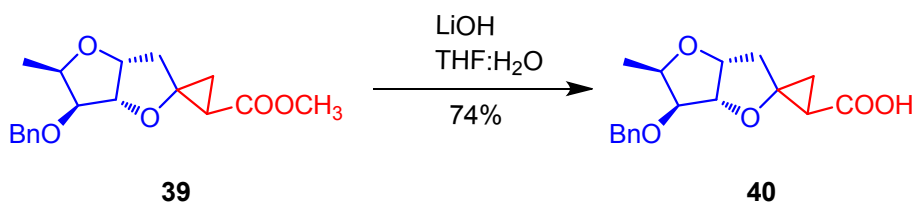


**Compound 38a, 38b:** Compounds **38a** and **38b** were synthesized from **37** by following the procedure described for compound **4**, yield 75%. Obtained as a mixture of diastereomers in 8:7 ratio, respectively.

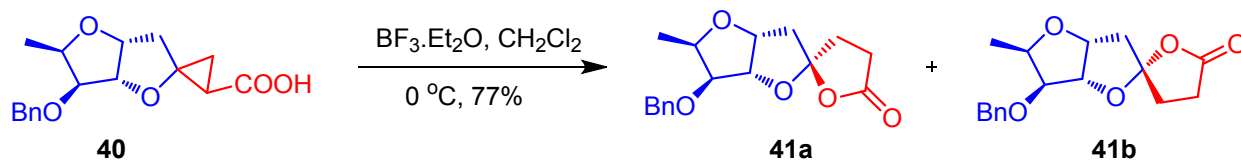
**Compound 38a:** **IR (neat):**  $\nu_{\text{max}}$  3062, 3024, 2953, 2914, 2859, 1785, 1725, 1456, 1270, 1078, 897, 744, 689  $\text{cm}^{-1}$ . **<sup>1</sup>H NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.28-7.36 (m, 10H), 5.06-5.09 (m, 1H), 4.76 (d, 1H,  $J = 4.8$  Hz), 4.66 (dd, 2H,  $J = 12.0$  Hz,  $J = 20.4$  Hz), 4.53 (d, 1H,  $J = 12$  Hz), 4.49 (d, 1H,  $J = 12.0$  Hz), 4.20-4.22 (m, 1H), 4.00 (d, 1H,  $J = 3.2$  Hz), 3.74 (d, 1H,  $J = 2.8$  Hz), 3.73 (d, 1H,  $J = 4.0$  Hz), 2.67-2.82 (m, 2H), 2.54 (ddd, 1H,  $J = 4.4$  Hz,  $J = 7.6$  Hz,  $J = 18.0$  Hz), 2.34-2.38 (m, 2H), 2.17-2.21 (m, 1H). **<sup>13</sup>C NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta$  175.6, 137.9, 137.4, 128.5, 128.4, 127.9, 127.8, 127.7, 116.7, 86.2, 81.6, 81.0, 79.4, 73.6, 71.9, 68.1, 43.5, 31.4, 28.7. **HRMS (ESI)** calcd for  $\text{C}_{24}\text{H}_{26}\text{O}_6+\text{Na}$  433.1627, found 433.1627.  $[\alpha]_D^{25} = -11.2$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



**Compound 38b: IR (neat):**  $\nu_{\max}$  3068, 3029, 2920, 2865, 1774, 1725, 1500, 1451, 1352, 1265, 1193, 1078, 908, 733, 706  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.28-7.35 (m, 10H), 4.98 (t, 1H,  $J = 5.6$  Hz), 4.78 (d, 1H,  $J = 4.8$  Hz), 4.68 (q, 1H,  $J = 5.2$  Hz), 4.66 (d, 1H,  $J = 12.0$  Hz), 4.62 (d, 1H,  $J = 12.0$  Hz), 4.54 (d, 2H,  $J = 12.0$  Hz), 4.14 (d, 1H,  $J = 5.2$  Hz), 3.69 (d, 2H,  $J = 5.6$  Hz), 2.71-2.80 (m, 1H), 2.62 (d, 1H,  $J = 15.2$  Hz), 2.52 (ddd, 1H,  $J = 4.4$  Hz,  $J = 8.0$  Hz,  $J = 18.0$  Hz), 2.27-2.37 (m, 2H), 2.15-2.20 (m, 1H).  **$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):**  $\delta$  175.6, 137.9, 137.4, 128.5, 128.4, 127.9, 127.8, 127.7, 116.7, 86.2, 81.6, 81.0, 79.4, 73.6, 71.9, 68.1, 43.5, 31.4, 28.7. **HRMS (ESI)** calcd for  $\text{C}_{24}\text{H}_{26}\text{O}_6 + \text{Na}$  433.1627, found 433.1628.  $[\alpha]_D^{25} = -5.7$  ( $c = 0.85$ ,  $\text{CHCl}_3$ ).



**Compound 40:** Compound **40** was synthesized from **39**<sup>6</sup> by following the procedure described for compound **3**, yield 74%. **IR (neat):**  $\nu_{\max}$  3030, 2926, 2854, 1780, 1720, 1682, 1446, 1347, 1271, 1178, 1084, 1079, 909, 739, 701  $\text{cm}^{-1}$ . **HRMS (ESI)** calcd for  $\text{C}_{17}\text{H}_{20}\text{O}_5 + \text{H}$  305.1389, found 305.1388.

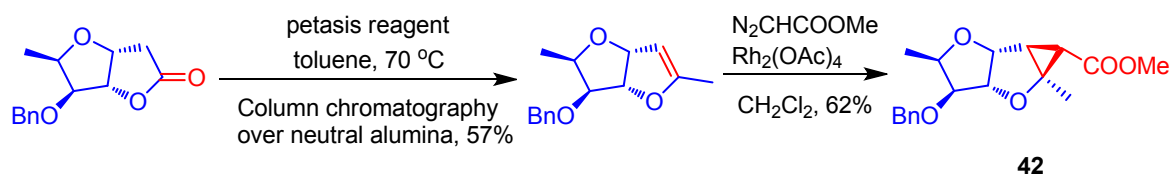


**Compound 41a and 41b:** Compounds **41a** and **41b** were synthesized from **40** by following the procedure described for compound **4**, 77% yield. **41a** and **41b** were obtained as a mixture of diastereomers in 3:2 ratio, respectively.

**Compound 41a: IR (neat):**  $\nu_{\max}$  3057, 3030, 2926, 2871, 1780, 1452, 1347, 1090, 1057, 898, 739, 701  $\text{cm}^{-1}$ .  **$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):**  $\delta$  7.29-7.35 (m, 5H), 5.01-5.04 (m, 1H), 4.75 (d, 1H,  $J = 5.2$  Hz), 4.71 (d, 1H,  $J = 12.0$  Hz), 4.50 (d, 1H,  $J = 12.0$  Hz), 4.07-4.09 (m, 1H), 3.75 (d, 1H,  $J =$

3.6 Hz), 2.65-2.80 (m, 2H), 2.53 (ddd, 1H,  $J = 4.4$  Hz,  $J = 7.6$  Hz,  $J = 17.6$  Hz), 2.32-2.37 (m, 2H), 2.08 (dd, 1H,  $J = 4.0$  Hz,  $J = 14.8$  Hz), 1.30 (d, 3H,  $J = 6.4$  Hz).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  175.6, 137.6, 128.4, 127.8, 127.6, 116.6, 86.7, 82.4, 80.3, 75.8, 71.7, 43.5, 31.2, 28.7, 13.4. **HRMS (ESI)** calcd for  $\text{C}_{17}\text{H}_{20}\text{O}_5 + \text{Na}$  327.1208, found 327.1208.  $[\alpha]_D^{25} = -9.6$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

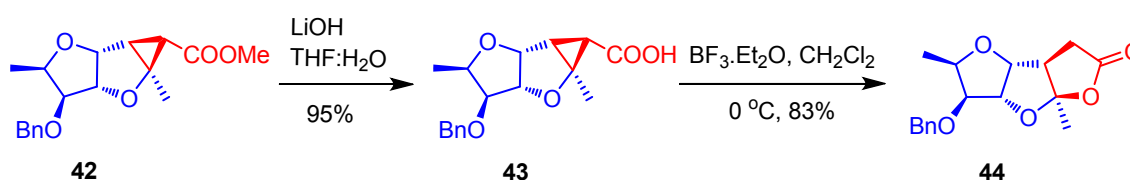
**Compound 41b: IR (neat):**  $\nu_{\text{max}}$  3068, 3030, 2931, 1780, 1495, 1457, 1347, 1189, 1073, 904, 838, 745, 706  $\text{cm}^{-1}$ .  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.29-7.35 (m, 5H), 5.02-5.29 (m, 1H), 4.75 (d, 1H,  $J = 5.2$  Hz), 4.71 (d, 1H,  $J = 12.4$  Hz), 4.49 (d, 1H,  $J = 12.4$  Hz), 4.03-4.14 (m, 1H), 3.74 (d, 1H,  $J = 3.2$  Hz), 2.65-2.80 (m, 2H), 2.53 (ddd, 1H,  $J = 4.8$  Hz,  $J = 7.6$  Hz,  $J = 18.0$  Hz), 2.32-2.37 (m, 2H), 2.08 (dd, 1H,  $J = 4.0$  Hz,  $J = 14.8$  Hz), 1.30 (d, 3H,  $J = 6.0$  Hz).  $^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  175.7, 137.8, 128.4, 127.8, 127.5, 116.4, 89.8, 84.0, 80.2, 76.5, 72.1, 44.3, 33.1, 28.6, 14.0. **HRMS (ESI)** calcd for  $\text{C}_{17}\text{H}_{20}\text{O}_5 + \text{Na}$  327.1208, found 327.1211.  $[\alpha]_D^{25} = -8.3$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).



**Compound 42:** 3,6-anhydro-5-*O*-benzyl-2,7-di-deoxy-D-ido-heptono-2,4-lactone (3.5 g, 14.11 mmol) was dissolved in dry toluene (70 mL) and cyclopentadienyldimethyl titanocene (23.48 mL of a 20% w/w solution in toluene) was added slowly at room temperature, then the reaction mixture was stirred in the dark at 70 °C under argon for a period of 24 h or until TLC showed disappearance of the starting material. The brown reaction mixture was concentrated, and subjected to column chromatography using neutral alumina in hexane/ethyl acetate without adding triethylamine to give the unsaturated methyl product (2.0 g, 57%). (If the column has done in presence of triethylamine, methylenated product was obtained). **IR (neat):**  $\nu_{\text{max}}$  2958, 2926, 2849, 1736, 1671, 1463, 1391, 1205, 1079, 1024, 734  $\text{cm}^{-1}$ .  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.27-7.37 (m, 5H), 5.39 (d, 1H,  $J = 6.0$  Hz), 4.88 (d, 1H,  $J = 6.8$  Hz), 4.72-4.77 (m, 2H), 4.57 (dd, 1H,  $J = 2.0$  Hz,  $J = 12.4$

Hz), 3.78-3.81 (m, 2H), 1.82 (s, 3H), 1.33 (d, 3H,  $J = 2.4$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  159.7, 137.9, 128.4, 127.8, 127.7, 96.4, 86.8, 84.4, 83.4, 73.3, 71.7, 13.4, 13.0. HRMS (ESI) calcd for  $\text{C}_{15}\text{H}_{18}\text{O}_3 + \text{Na}$  269.1154, found 269.1155.

The obtained *endo*-cyclic olefin (1.0 g, 4.06 mmol) was cyclopropanated, by following the procedure described for compound **17**, to obtain the corresponding cyclopropane carboxylate **42** (0.8 g, 62%). IR (neat):  $\nu_{\text{max}}$  3057, 2926, 2860, 1731, 1446, 1331, 1216, 1156, 1079, 854, 734  $\text{cm}^{-1}$ . HRMS (ESI) calcd for  $\text{C}_{18}\text{H}_{22}\text{O}_5 + \text{Na}$  341.1365, found 341.1364.

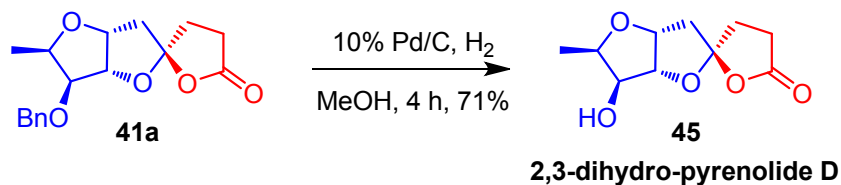


**Compound 43:** Compound **43** was synthesized from **42** by following the procedure described for compound **3**, yield 95%. IR (neat):  $\nu_{\text{max}}$  3063, 3030, 2926, 2865, 1720, 1687, 1463, 1331, 1227, 1084, 860, 734  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.28-7.35 (m, 5H), 5.82 (d, 1H,  $J = 6.0$  Hz), 4.94 (d, 1H,  $J = 4.8$  Hz), 4.65 (d, 1H,  $J = 12.0$  Hz), 4.49 (d, 1H,  $J = 12.4$  Hz), 4.29 (d, 1H,  $J = 4.4$  Hz), 4.09 (d, 1H,  $J = 4.0$  Hz), 3.68 (s, 1H), 2.26 (d, 1H,  $J = 4.0$  Hz), 1.64 (s, 3H), 1.31 (d, 3H,  $J = 6.0$  Hz), 0.88 (t, 1H,  $J = 5.2$  Hz).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  175.6, 137.7, 128.4, 127.9, 127.6, 85.7, 84.3, 83.5, 76.4, 74.1, 71.9, 34.2, 27.9, 13.5, 13.3. HRMS (ESI) calcd for  $\text{C}_{17}\text{H}_{20}\text{O}_5 + \text{Na}$  327.1208, found 327.1206.

**Compound 44:** Compound **44** was synthesized from **43** following the procedure described for compound **4**, in 83% yield. IR (neat):  $\nu_{\text{max}}$  3068, 3024, 2931, 2849, 1775, 1501, 1446, 1386, 1243, 1090, 1030, 909, 843, 728  $\text{cm}^{-1}$ .  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta$  7.29-7.36 (m, 5H), 4.76 (d, 1H,  $J = 4.0$  Hz), 4.69 (d, 1H,  $J = 12.0$  Hz), 4.55 (d, 1H,  $J = 4.0$  Hz), 4.53 (d, 1H,  $J = 12.0$  Hz), 4.23-4.27 (m, 1H), 3.91 (d, 1H,  $J = 3.5$  Hz), 2.96 (dd, 1H,  $J = 11.0$  Hz,  $J = 18.5$  Hz), 2.88 (dd, 1H,  $J = 2.5$  Hz,  $J = 11.0$  Hz), 2.60 (dd, 1H,  $J = 3.0$  Hz,  $J = 18.5$  Hz), 1.68 (s, 3H), 1.29 (d, 3H,  $J = 6.5$  Hz).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.5, 137.4, 128.5, 127.9, 127.6, 118.2, 88.1, 86.1, 82.1, 72.2,

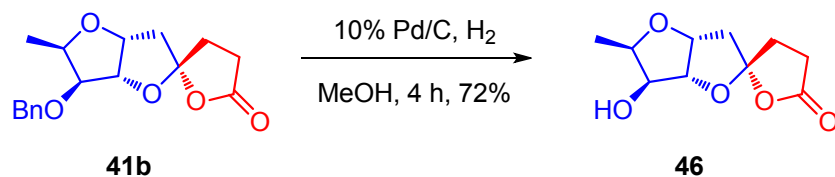
51.1, 33.8, 24.0, 13.8. **HRMS (ESI)** calcd for C<sub>17</sub>H<sub>20</sub>O<sub>5</sub>+Na 327.1208, found 327.1210.  $[\alpha]_D^{25} = -44.1$  ( $c = 1.0$ , CHCl<sub>3</sub>).

#### Synthesis of 2,3-dihydro-pyrenolide D (Compound 45):



To a stirred solution of compound **41a** (40 mg, 0.13 mmol), in MeOH (5 mL) was hydrogenated over 10% Pd/C (5 mg), under hydrogen atmosphere for 4 h at 25 °C. The catalyst was filtered off and the filtrate was concentrated. The crude product was purified by silica-gel column chromatography using hexane/ethyl acetate (containing 1% triethylamine) to give 2,3-dihydro-pyrenolide D **45** (20 mg, 71%) as colourless solid. **IR (neat)**:  $\nu_{\text{max}}$  3424, 2942, 2871, 1780, 1649, 1446, 1194, 1052, 898, 816 cm<sup>-1</sup>. **<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)**:  $\delta$  5.01-5.05 (m, 1H), 4.63 (d, 1H,  $J = 5.2$  Hz), 4.02-4.08 (m, 2H), 2.68-2.83 (m, 2H), 2.55 (ddd, 1H,  $J = 3.2$  Hz,  $J = 8.8$  Hz,  $J = 17.6$  Hz), 2.34-2.43 (m, 2H), 2.10 (dd, 1H,  $J = 4.0$  Hz,  $J = 14.8$  Hz), 1.30 (d, 3H,  $J = 6.0$  Hz). **<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)**:  $\delta$  175.7, 116.6, 89.4, 79.9, 76.0, 75.4, 43.4, 31.1, 28.7, 12.8. **HRMS (ESI)** calcd for C<sub>10</sub>H<sub>14</sub>O<sub>5</sub>+Na 237.0739, found 237.0741.  $[\alpha]_D^{25} = +10.1$  ( $c = 1.0$ , CHCl<sub>3</sub>).

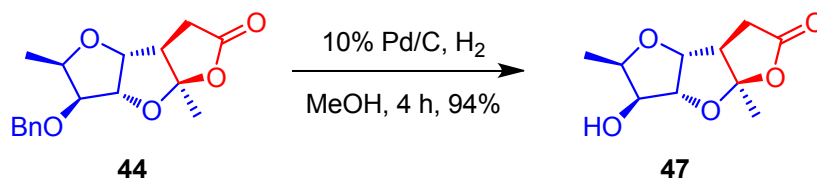
#### 4-*epi*-2,3-dihydro-pyrenolide D (Compound 46):



To a stirred solution of compound **41b** (20 mg, 0.06 mmol), in MeOH (3 ml) was hydrogenated over 10% Pd/C (4 mg) under hydrogen atmosphere for 4 h at 25 °C. The catalyst was filtered off

and the filtrate was concentrated. The crude product was purified by silica-gel column chromatography using hexane/ethyl acetate (containing 1% triethylamine) to give the 4-*epi*-2,3-dihydro-pyrenolide **46** (10 mg, 72%) as colourless solid. **IR (neat)**:  $\nu_{\max}$  3419, 2936, 2871, 1764, 1736, 1643, 1441, 1276, 1194, 1057, 893, 816  $\text{cm}^{-1}$ .  **$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**:  $\delta$  4.93 (t, 1H,  $J = 5.6$  Hz), 4.68 (d, 1H,  $J = 4.8$  Hz), 4.59-4.66 (m, 1H), 4.11 (d, 1H,  $J = 2.8$  Hz), 2.77 (dt, 1H,  $J = 10.0$  Hz,  $J = 17.6$  Hz), 2.60 (d, 1H,  $J = 15.2$  Hz), 2.53 (ddd, 1H,  $J = 4.4$  Hz,  $J = 6.8$  Hz,  $J = 17.6$  Hz), 2.34 (dd, 1H,  $J = 3.2$  Hz,  $J = 10.0$  Hz), 2.32 (d, 1H,  $J = 10.0$  Hz), 2.18-2.25 (m, 1H), 1.27 (d, 3H,  $J = 6.4$  Hz).  **$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  175.8, 116.5, 92.2, 80.2, 77.1, 76.4, 44.3, 33.2, 28.6, 13.4. **HRMS (ESI)** calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_5 + \text{Na}$  237.0739, found 237.0739.  $[\alpha]_D^{25} = +6.1$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

#### Compound 47:



To a stirred solution of compound **44** (30 mg, 0.09 mmol), in MeOH (4 mL) was hydrogenated over 10% Pd/C (5 mg) under hydrogen atmosphere for 4 h at 25°C. The catalyst was filtered off and the filtrate was concentrated. The crude product was purified by silica-gel column chromatography using hexane/ethyl acetate (containing 1% triethylamine) to give the product **47** (20 mg, 94%) as colourless solid. **IR (neat)**:  $\nu_{\max}$  3424, 2926, 2865, 2854, 1775, 1501, 1452, 1386, 1249, 1084, 1035, 920, 838, 734, 701  $\text{cm}^{-1}$ .  **$^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ )**:  $\delta$  4.63 (d, 1H,  $J = 4.60$  Hz), 4.56 (d, 1H,  $J = 3.6$  Hz), 4.17-4.23 (m, 2H), 2.97 (dd, 1H,  $J = 10.8$  Hz,  $J = 18.4$  Hz), 2.87 (dd, 1H,  $J = 2.4$  Hz,  $J = 10.8$  Hz), 2.61 (dd, 1H,  $J = 2.8$  Hz,  $J = 18.4$  Hz), 2.23 (d, 1H,  $J = 4.8$  Hz), 1.68 (s, 3H), 1.28 (d, 3H,  $J = 6.0$  Hz).  **$^{13}\text{C NMR}$  (100 MHz,  $\text{CDCl}_3$ )**:  $\delta$  173.7, 118.4, 88.7, 87.9, 77.4, 75.6, 51.2, 33.9, 24.0, 13.2. **HRMS (ESI)** calcd for  $\text{C}_{10}\text{H}_{14}\text{O}_5 + \text{Na}$  237.0739, found 237.0735.  $[\alpha]_D^{25} = -11.9$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ).

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