

# Supplementary Material (ESI) for Chemical Communications  
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## CHEMICAL COMMUNICATIONS

# Conformational diastereoisomerism in a chiral pretzelane

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# Supporting Information

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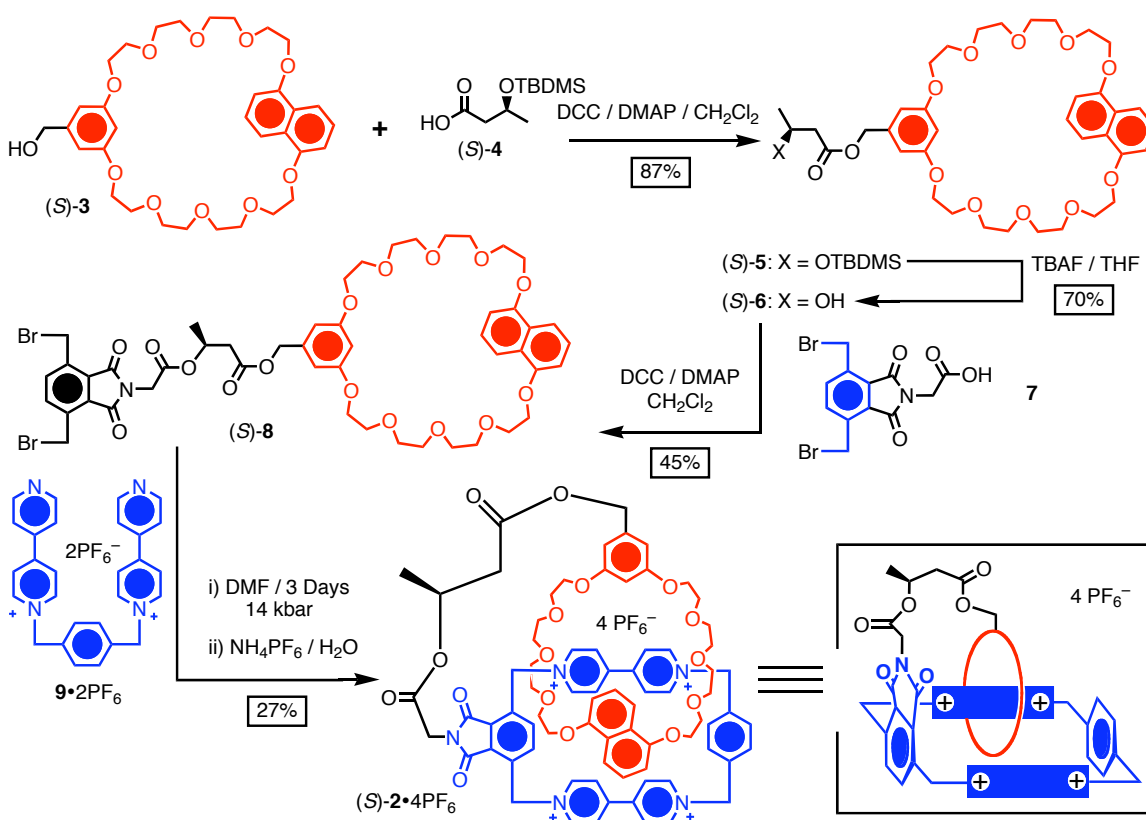
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## Experimental Section

### Preparation of the Chiral Pretzelane (*S*)-(PM)-2•4PF<sub>6</sub> and Its Precursors

The synthesis of the crown ether-containing dibromide precursor **8** and the following clipping reaction to prepare the chiral pretzelane (*S*)-(PM)-2•4PF<sub>6</sub> are described in Scheme S1. Reaction of **3**<sup>1</sup> carrying a symmetrically positioned hydroxyl group with the carboxylic acid (*S*)-**4**<sup>2</sup> gave the compound (*S*)-**5**. Removal of the TBDMS protecting group generated the alcohol (*S*)-**6**, which underwent esterification with the carboxylic acid derivative **7**<sup>3</sup> to afford the key intermediate, the dibromide (*S*)-**8**. Formation of (*S*)-(PM)-2•4PF<sub>6</sub> was achieved in 27% yield by allowing (*S*)-**8** and the **9**•2PF<sub>6</sub><sup>4</sup> to stir in DMF for 3 days at 14 kbar and then exchanging the counterions.



**Scheme S1.** Synthesis of the chiral pretzelane (*S*)-(P)-2•4PF<sub>6</sub>, which is the minor diastereoisomer

**General Methods:** Reagents were purchased from Aldrich or synthesized as described. The compounds **3**,<sup>1</sup> (*S*)-**4**,<sup>2</sup> **7**,<sup>3</sup> and **9**•2PF<sub>6</sub><sup>4</sup> were prepared according to literature procedures. Solvents were purified according to literature procedures.<sup>5</sup> Thin-layer chromatography (TLC) was carried out using aluminum sheets, precoated with silica gel 60F (Merck 5554). The plates were inspected by UV-light, prior to development with iodine vapor. Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. Proton and carbon nuclear magnetic resonance spectra (<sup>1</sup>H-NMR and <sup>13</sup>C-NMR) were recorded on a Bruker Avance500 or ARX500, using the deuterated solvent as lock and the residual protiated solvent as internal standard. All chemical shifts are quoted using the  $\delta$  scale, and all coupling constants (*J*) are expressed in Hertz (Hz). Electrospray mass spectra (ESI-MS) were measured on a VG ProSpec triple focusing mass spectrometer. Matrix-Assisted Laser Desorption Ionization (MALDI) mass spectra were obtained using dihydroxybenzoic acid as the supporting matrix.

**(S)-5:** A mixture of the crown ether **3**<sup>1</sup> (0.35g, 0.56 mmol), the carboxylic acid (*S*)-**4** (0.12 g, 0.56 mmol), 1,3-dicyclohexylcarbodiimide (DCC) (0.17 g, 0.84 mmol) and 4-dimethylaminopyridine (DMAP) (cat. amount) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) was stirred for 1 h at room temperature. The resulting suspension was filtered, the filtrate was evaporated and the residue was subjected to column chromatography (SiO<sub>2</sub>:hexanes/EtOAc 1:3) to give (*S*)-**5** (0.40 g, 87%).  $[\alpha]_D^{22} = +5.6$  (*c* = 0.85, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 298 K):  $\delta$  = 7.85 (d, *J* = 8.5 Hz, 2 H), 7.30 (t, *J* = 8.1 Hz, 2 H), 6.76 (d, *J* = 7.6 Hz, 2 H), 6.43 (d, *J* = 2.2 Hz, 2 H), 6.20 (t, *J* = 2.2 Hz, 1 H), 4.97 (s, 2 H), 4.28 (m, 1 H), 4.25 (t, *J* = 4.5 Hz, 4 H), 4.12 (t, *J* = 4.5 Hz, 4 H), 3.98 (t, *J* = 4.5 Hz, 4 H), 3.85–3.78 (m, 4 H), 3.71–3.66 (m, 12 H), 3.64–3.63 (m, 4 H), 2.52 (dd, *J* = 7.6, 14.6 Hz, 1 H), 2.40 (dd, *J* = 5.4, 14.6 Hz, 1 H), 1.18 (d, *J* = 6.1 Hz, 3 H), 0.85 (s, 9 H), 0.049 (s, 3 H), 0.025 (s, 3 H); <sup>13</sup>C

NMR (CDCl<sub>3</sub>, 125 MHz, 298 K):  $\delta$  = 171.3, 159.9, 154.2, 137.7, 126.7, 125.0, 114.5, 106.7, 105.6, 100.6, 71.0, 70.8, 70.7, 70.6, 69.6, 69.5, 68.0, 67.2, 65.9, 65.7, 44.7, 25.6, 23.8, 17.8, -4.6, -5.1; HRMS (MALDI) C<sub>43</sub>H<sub>64</sub>O<sub>13</sub>Si: [M + Na]<sup>+</sup>, calcd 839.4008, found 839.4014.

**(S)-6:** (*S*)-**5** (0.32 g, 0.39 mmol) was dissolved in THF (5ml) and a THF solution of tetrabutylammonium fluoride (TBAF) (0.5 mL, 1 M) was added at 0 °C. The mixture was stirred overnight at room temperature, followed by the addition of saturated NH<sub>4</sub>Cl solution (10 mL). The product was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 10 mL). The combined organic layer was evaporated, and the residue was subjected to column chromatography (SiO<sub>2</sub>: EtOAc) to give (*S*)-**6** as a colorless oil (0.19 g, 70%). [ $\alpha$ ]<sub>D</sub><sup>22</sup> = +6.9 (*c* 2.45, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 298 K):  $\delta$  = 7.84 (d, *J* = 8.4 Hz, 2 H), 7.29 (t, *J* = 8.0 Hz, 2 H), 6.76 (d, *J* = 7.6 Hz, 2 H), 6.42 (d, *J* = 2.2 Hz, 2 H), 6.20 (t, *J* = 2.2 Hz, 1 H), 5.01 (d, *J* = 3.9 Hz, 2 H), 4.24 (t, *J* = 4.5 Hz, 4 H), 4.19 (m, 1 H), 3.97 (t, *J* = 4.5 Hz, 4 H), 3.83 (t, *J* = 4.5 Hz, 4 H), 3.79–3.77 (m, 4 H), 3.71–3.66 (m, 12 H), 3.64–3.62 (m, 4 H), 2.97 (br s, 1 H), 2.53–2.42 (m, 2 H), 1.20 (d, *J* = 6.3 Hz, 3 H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz, 298 K):  $\delta$  = 172.5, 159.9, 154.2, 137.4, 126.7, 125.0, 114.5, 106.6, 105.6, 100.7, 70.9, 70.8, 70.7, 70.6, 69.6, 69.4, 68.0, 67.3, 66.1, 64.1, 42.7, 22.4; HRMS (MALDI) C<sub>37</sub>H<sub>50</sub>O<sub>13</sub>: [M + Na]<sup>+</sup>, calcd 725.3144, found 725.3113.

**(S)-8:** A mixture of the alcohol (*S*)-**6** (0.15 g, 0.21 mmol), the carboxylic acid derivative **7**<sup>3</sup> (89 mg, 0.23 mmol), DCC (64 mg, 0.31 mmol) and DMAP (cat. amount) in CH<sub>2</sub>Cl<sub>2</sub> (5 mL) was stirred for 1 h at room temperature. The resulting suspension was filtered, the filtrate was evaporated, and the residue was subjected to column chromatography (SiO<sub>2</sub>:EtOAc) to give the dibomide (*S*)-**8** as a sticky solid (0.10 g, 45%). [ $\alpha$ ]<sub>D</sub><sup>22</sup> = -6.5 (*c* 1.20, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz, 298 K):  $\delta$  = 7.83 (d, *J* = 8.5 Hz, 2 H), 7.67 (s,

2 H), 7.27 (t,  $J = 8.1$  Hz, 2 H), 6.74 (d,  $J = 7.6$  Hz, 2 H), 6.43 (d,  $J = 2.2$  Hz, 2 H), 6.20 (t,  $J = 2.2$  Hz, 1 H), 5.36 (m, 1 H), 5.01 (s, 2 H), 4.92 (s, 4 H), 4.34 (d,  $J = 2.4$  Hz, 2 H), 4.23 (t,  $J = 4.5$  Hz, 4 H), 3.97 (t,  $J = 4.5$  Hz, 4 H), 3.84 (t,  $J = 4.5$  Hz, 4 H), 3.78–3.76 (m, 4 H), 3.70–3.65 (m, 12 H), 3.63–3.62 (m, 4 H), 2.68 (dd,  $J = 7.5, 15.7$  Hz, 1 H), 2.55 (dd,  $J = 5.7, 15.7$  Hz, 1 H), 1.33 (d,  $J = 6.7$  Hz, 3 H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz, 298 K):  $\delta = 169.4, 166.3, 166.2, 159.9, 154.2, 137.5, 137.0, 136.4, 128.3, 126.6, 125.0, 114.5, 106.7, 105.7, 100.7, 70.9, 70.8, 70.7, 70.6, 69.6, 69.4, 69.2, 68.0, 67.3, 66.3, 40.5, 38.8, 25.7, 19.7$ ; HRMS (MALDI)  $\text{C}_{49}\text{H}_{57}\text{Br}_2\text{NO}_{16}$ :  $[M + \text{Na}]^+$ , calcd 1096.1936, found 1096.1984.

**(*S*)-(PM)-2•4PF<sub>6</sub>**: A solution of (*S*)-**8** (78 mg, 72  $\mu\text{mol}$ ) and the dicationic salt **9•2PF<sub>6</sub><sup>4</sup>** (51 mg, 72  $\mu\text{mol}$ ) in DMF (4 mL) was stirred at room temperature under 14 kbar for 3 days. The solvent was removed under reduced pressure and the residue was subjected to column chromatography ( $\text{SiO}_2$ : MeOH/aqueous  $\text{NH}_4\text{Cl}$  (2M)/ $\text{MeNO}_2$  7:2:1). The purple fractions containing the product were combined and concentrated. Solid  $\text{NH}_4\text{PF}_6$  was added to the residue to precipitate (*S*)-(PM)-**2•4PF<sub>6</sub>** as a purple solid (38 mg, 27%). M.p. 228°C (dec.);  $^1\text{H}$  NMR of the major diastereoisomer (*S*)-(M)-**2•4PF<sub>6</sub>** ( $\text{CD}_3\text{COCD}_3$ , 500 MHz, 298 K):  $\delta = 9.27$  (d,  $J = 6.6$  Hz, 1 H), 9.19 (d,  $J = 6.6$  Hz, 1 H), 8.88 (d,  $J = 6.6$  Hz, 1 H), 8.73 (d,  $J = 6.6$  Hz, 1 H), 8.65–8.59 (m, 3 H), 8.54 (d,  $J = 8.3$  Hz, 1 H), 8.43 (d,  $J = 8.3$  Hz, 1 H), 8.05 (d,  $J = 8.1$  Hz, 1 H), 8.00–7.92 (m, 3 H), 7.43 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 7.41 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 7.38 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 7.36 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 7.28 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 7.27 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 7.00 (dd,  $J = 8.1, 2.4$  Hz, 1 H), 6.95 (t,  $J = 1.5$  Hz, 1 H), 6.81 (t,  $J = 1.5$  Hz, 1 H), 6.67 (d,  $J = 13.7$  Hz, 1 H), 6.62–6.60 (m, 3 H), 6.29 (d,  $J = 7.9$  Hz, 1 H), 6.24 (d,  $J = 7.9$  Hz, 1 H), 6.02 (t,  $J = 7.9$  Hz, 1 H), 5.91–5.85 (m, 3 H), 5.78–5.73 (m, 3 H), 5.71 (t,  $J = 1.5$  Hz, 1 H), 5.61 (d,  $J = 1.5$  Hz, 1 H), 5.51 (t,  $J = 1.5$  Hz, 1 H), 5.41 (t,  $J = 1.5$  Hz, 1 H), 5.31 (t,  $J = 1.5$  Hz, 1 H), 5.21 (t,  $J = 1.5$  Hz, 1 H), 5.11 (t,  $J = 1.5$  Hz, 1 H), 5.01 (t,  $J = 1.5$  Hz, 1 H), 4.91 (t,  $J = 1.5$  Hz, 1 H), 4.81 (t,  $J = 1.5$  Hz, 1 H), 4.71 (t,  $J = 1.5$  Hz, 1 H), 4.61 (t,  $J = 1.5$  Hz, 1 H), 4.51 (t,  $J = 1.5$  Hz, 1 H), 4.41 (t,  $J = 1.5$  Hz, 1 H), 4.31 (t,  $J = 1.5$  Hz, 1 H), 4.21 (t,  $J = 1.5$  Hz, 1 H), 4.11 (t,  $J = 1.5$  Hz, 1 H), 4.01 (t,  $J = 1.5$  Hz, 1 H), 3.91 (t,  $J = 1.5$  Hz, 1 H), 3.81 (t,  $J = 1.5$  Hz, 1 H), 3.71 (t,  $J = 1.5$  Hz, 1 H), 3.61 (t,  $J = 1.5$  Hz, 1 H), 3.51 (t,  $J = 1.5$  Hz, 1 H), 3.41 (t,  $J = 1.5$  Hz, 1 H), 3.31 (t,  $J = 1.5$  Hz, 1 H), 3.21 (t,  $J = 1.5$  Hz, 1 H), 3.11 (t,  $J = 1.5$  Hz, 1 H), 3.01 (t,  $J = 1.5$  Hz, 1 H), 2.91 (t,  $J = 1.5$  Hz, 1 H), 2.81 (t,  $J = 1.5$  Hz, 1 H), 2.71 (t,  $J = 1.5$  Hz, 1 H), 2.61 (t,  $J = 1.5$  Hz, 1 H), 2.51 (t,  $J = 1.5$  Hz, 1 H), 2.41 (t,  $J = 1.5$  Hz, 1 H), 2.31 (t,  $J = 1.5$  Hz, 1 H), 2.21 (t,  $J = 1.5$  Hz, 1 H), 2.11 (t,  $J = 1.5$  Hz, 1 H), 2.01 (t,  $J = 1.5$  Hz, 1 H), 1.91 (t,  $J = 1.5$  Hz, 1 H), 1.81 (t,  $J = 1.5$  Hz, 1 H), 1.71 (t,  $J = 1.5$  Hz, 1 H), 1.61 (t,  $J = 1.5$  Hz, 1 H), 1.51 (t,  $J = 1.5$  Hz, 1 H), 1.41 (t,  $J = 1.5$  Hz, 1 H), 1.31 (t,  $J = 1.5$  Hz, 1 H), 1.21 (t,  $J = 1.5$  Hz, 1 H), 1.11 (t,  $J = 1.5$  Hz, 1 H), 1.01 (t,  $J = 1.5$  Hz, 1 H), 0.91 (t,  $J = 1.5$  Hz, 1 H), 0.81 (t,  $J = 1.5$  Hz, 1 H), 0.71 (t,  $J = 1.5$  Hz, 1 H), 0.61 (t,  $J = 1.5$  Hz, 1 H), 0.51 (t,  $J = 1.5$  Hz, 1 H), 0.41 (t,  $J = 1.5$  Hz, 1 H), 0.31 (t,  $J = 1.5$  Hz, 1 H), 0.21 (t,  $J = 1.5$  Hz, 1 H), 0.11 (t,  $J = 1.5$  Hz, 1 H).

= 7.9 Hz, 1 H), 4.86 (d,  $J = 17.1$  Hz, 1 H), 4.83 (dd,  $J = 12.5, 2.5$  Hz, 1 H), 4.62 (dd,  $J = 12.5, 2.5$  Hz, 1 H), 4.54 (d,  $J = 17.1$  Hz, 1 H), 4.52–3.45 (m, 32 H), 3.29 (dd,  $J = 11.4, 2.5$  Hz, 1 H), 3.07 (dd,  $J = 11.4, 2.5$  Hz, 1 H), 2.50 (d,  $J = 8.1$  Hz, 1 H), 2.44 (d,  $J = 8.1$  Hz, 1 H); MS (ESI): 1783.4 [ $M - PF_6$ ]<sup>+</sup>, 818.9 [ $M - 2PF_6$ ]<sup>2+</sup>, 497.6 [ $M - 3PF_6$ ]<sup>3+</sup>; HRMS (ESI) C<sub>77</sub>H<sub>81</sub>F<sub>24</sub>N<sub>5</sub>O<sub>17</sub>P<sub>4</sub>: [ $M - PF_6$ ]<sup>+</sup>, calcd 1554.1606, found 1554.1638.

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