Supporting Information: A New Family of Macrocycles Produced by Sequential Claisen-Schmidt Condensations

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(1a) 3,4:15,16-Dibenzo-5,14-dioxa-bicyclo[16.3.1]docosa-1,3,15,17-tetraen-22-one

To an ethanolic solution (95%, 3 L) of 1,8-bis(2-formylphenoxy)octane¹ (6.00 g, 17.0 mmol) and cyclohexanone (1.66 g, 17.0 mmol) was added aqueous NaOH (30 g/ 72 ml, 750 mmol) in one portion. After stirring for 7 days at rt, the ethanol was removed in vacuo to give a brown oil. The oil was acidified with 1.0 M HCl and extracted with dichloromethane (3 x 150 mL). The combined organic extracts were dried over anhydrous MgSO₄ and the solvent removed in vacuo to give a crude orange-yellow solid (5.736 g). Recrystallisation of a portion of the crude product (730 mg) from dichloromethane/hexane yielded fine, yellow crystals (196 mg, 22%).

Mp: 126-127°C;

¹H NMR (300 MHz, CDCl₃): δ 7.77 (s, 2H, CH), 7.28 (ddd, *J* = 7.8, 1.7 Hz, 2H, arom.CH), 7.22 (dd, *J* = 7.6, 1.4 Hz, 2H, arom.CH), 6.97 (ddd, *J* = 7.5, 0.6 Hz, 2H, arom.CH), 6.92 (dd, *J* = 6.9 Hz, 2H, arom.CH), 3.96 (m (AA'BB'), *J* = 5.3 Hz, 4H, OCH₂), 2.77 (td, *J* = 6.2, 1.7 Hz, 4H, CCH₂), 1.76-1.64 (m, 6H, CH₂), 1.47-1.37 (m, 8H, CH₂);

¹³C NMR (75 MHz, CDCl₃): δ 193.1, 157.9, 138.3, 132.1, 130.1, 129.6, 126.6, 120.4, 113.3, 70.1, 30.2, 30.0, 28.6, 27.1, 24.7;

IR (cm⁻¹): 2935, 2917, 2853, 1670, 1616, 1595, 1484, 1448, 1287, 1277, 1242, 1165, 1137, 1107, 1045, 1033, 976, 965, 940, 750;

MS (ES⁺, 35 mV): 417.4 (M+H⁺, 100%), 833.5 (2M+H⁺ or [2+2]+H⁺, 10%);

Microanalysis found (calc.): C 80.8% (80.73%), O 11.6% (11.52%), H 7.6% (7.74%).

¹ Brody, M. S.; Williams, R. M.; Finn, M. G. *J. Am. Chem. Soc.* **1997**, *119*, 3429.

(1b) 3,4:15,16-Dibenzo-5,8,11,14-tetraoxa-bicyclo[16.3.1]docosa-1,3,15,17-tetraen-22-one

To an ethanolic solution (95%, 3 L) of 1,8-bis(2-formylphenoxy)3,6-dioxaoctane¹ (6.28 g, 17.5 mmol) and cyclohexanone (1.72 g, 17.5 mmol) was added aqueous KOH (12 g/ 30ml, 214 mmol) in one portion. After stirring at rt for 7 days, the yellow solution was neutralised with 1.0 M HCl and the solvent removed in vacuo. Water (200 mL) was added to the residue and the organic material was extracted with dichloromethane (3 x 150 mL). The organic extract was dried over anhydrous MgSO₄ and the solvent was removed in vacuo to give an orange-yellow crude solid (7.11 g). Recrystallisation of the crude product from dichloromethane/heptane yielded yellow crystals (3.95 g, 55%).

Mp: 144-145°C;

¹H NMR (400 MHz, CDCl₃): δ 7.64 (s, 2H, CH), 7.28 (ddd, *J* = 8.2, 7.4, 1.7 Hz, 2H, arom.CH), 7.20 (dd, *J* = 7.5, 1.7 Hz, 2H, arom.CH), 6.98 (ddd, *J* = 7.5, 7.4, 0.9 Hz, 2H, arom.CH), 6.87 (dd, *J* = 8.2, 0.9 Hz, 2H, arom.CH), 4.10 (m (AA'BB'), *J* = 4.2 Hz, 4H, ArOCH₂), 3.86 (m (AA'BB'), *J* = 4.2 Hz, 4H, OCH₂), 3.77 (sh s, 4H, OCH₂), 2.72 (td, *J* = 4.2 Hz, 4H, CCH₂), 1.66 (p, *J* = 4.2 Hz, 2H, CH₂);

¹³C NMR (100 MHz, CDCl₃): δ 194.1, 157.3, 139.4, 132.2, 130.4, 129.8, 126.3, 120.8, 112.4, 71.9, 70.4, 69.5, 28.6, 24.7;

IR (cm⁻¹): 2920, 2862, 1670, 1616, 1594, 1493, 1445, 1276, 1247, 1225, 1171, 1136, 1103, 1050, 973, 929, 914, 903, 755, 743;

MS (ES⁺, 35 mV): 443.2 (M+Na⁺, 100%), 421.3 (M+H⁺, 20%), 863.5 (2M+Na⁺ or [2+2]+Na⁺, 11%);

Microanalysis found (calc.): C 74.19% (74.26%), H 6.60% (6.71%).

(2c) 3,4:9,10:18,19:24,25-Tetrabenzo-5,8,20,23-tetraoxa-tricyclo[25.3.1.1^{12,16}]-dotriaconta-1,3,9,11,16,18,24,26-octaene-31,32-dione

To an ethanolic solution (95%, 1.83 L) of 1,2-bis(2-formylphenoxy)ethane² (10.1 g, 37.4 mmol) and cyclohexanone (5.53 g, 56.3 mmol) was added aqueous NaOH (22.5 g/ 45 mL, 563 mmol) in one portion. After stirring at rt for 6 d, a bright yellow precipitate was filtered from the reaction. The precipitate was washed thoroughly with 1.0 M HCl and water, and dried in an oven (90°C) to constant weight (10.3 g). A portion of the precipitate (920 mg) was washed with hot chloroform to afford the macrocycle as a bright yellow powder (380 mg, 34 %).

Mp: solid turns brown at 292-293°C and melts sharply at 297-298°C;

¹H NMR (400 MHz, CDCl₃): δ 7.97 (s, 4H, CH), 7.30 (dd, *J* = 7.6, 1.2 Hz, 8H, arom.CH), 7.25 (ddd, *J* = 7.8, 1.7 Hz, 4H, arom.CH), 6.95 (ddd, *J* = 7.5 Hz, 4H, arom.CH), 6.86 (dd, *J* = 8.3, 0.8 Hz, 4H, arom.CH), 4.44 (s, 8H, OCH₂), 2.80 (td, *J* = 5.7, 1.7 Hz, 8H, CCH₂), 1.74 (p, *J* = 5.7 Hz, 4H, CH₂);

¹³C NMR (75 MHz, CDCl₃): δ 190.1, 157.1, 137.3, 132.3, 131.1, 129.6, 126.6, 120.5, 111.9, 66.6, 29.4, 23.8;

IR (cm⁻¹): 2953, 1661, 1596, 1483, 1446, 1296, 1280, 1238, 1223, 1158, 1130, 1108, 1040, 966, 949, 925, 902, 865, 815, 757;

MS (ES⁺, 35 mV): 687.4 (M+Na⁺, 100%), 665.3 (M+H⁺, 28%);

Microanalysis found (calc.): C 79.40% (79.50%), O 14.43% (14.44%), H 5.98% (6.06%).

² Simion, C.; Simion, A.; Mitoma, Y.; Nagashima, S.; Kawaji, T.; Hashimoto, I.; Tashiro, M. *Heterocycles* **2000**, 53, 2459.

(2d) 3,4:12,13:21,22:30,31-Tetrabenzo-5,8,11,23,26,29-hexaoxa-tricyclo-[31.3.1.1^{15,19}]octatriaconta-,3,12,14,19,21,30,32-octaene-37,38-dione

To an ethanolic solution (95%, 1.0 L) of 1,5-bis(2-formylphenoxy)3-oxapentane² (4.98 g, 15.8 mmol) and cyclohexanone (1.701 g, 17.3 mmol) was added aqueous NaOH (14.1 g/ 15 mL, 351 mmol) in one portion. After stirring at rt for 6 d, a yellow precipitate was filtered from the reaction. The precipitate was washed thoroughly with 1.0 M HCl and water, and dried in an oven (90°C) to constant weight (4.61 g). Recrystallisation of a portion of the precipitate (1.00 g) from chloroform yielded the macrocycle as yellow crystals (0.33 g, 25%).

Mp: 227-229°C;

¹H NMR (400MHz, CDCl₃): δ 7.98 (s, 4H, CH), 7.31-7.26 (m, 8H, arom.CH), 6.98-6.93 (m, 8H, arom.CH), 4.20 (t, *J* = 5.5 Hz, 8H, OCH₂), 4.02 (t, *J* = 5.5 Hz, 8H, OCH₂), 2.84 (m, *J* = 6.1, 1.7 Hz, 8H, CCH₂), 1.74 (p, *J* = 6.1 Hz, 4H, CH₂);

¹³C NMR (100MHz, CDCl₃): δ 190.6, 158.0, 136.8, 132.5, 130.7, 130.1, 125.9, 120.5, 112.4, 70.3, 68.2, 29.2, 24.0;

IR (cm⁻¹): 2919, 2861, 1669, 1615, 1594, 1493, 1445, 1276, 1247, 1171, 1136, 1108, 1050, 973, 929, 903, 859, 817, 755;

MS (ES+, 35mV): 775.3 (M+Na⁺, 100%);

Microanalysis found (calc.): C 76.62% (76.57%), H 6.31% (6.43%).