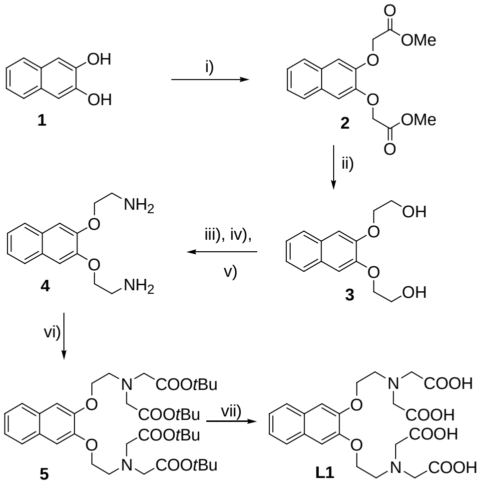
Supporting Information for b804195d

Experimental procedures related to the synthetic protocol reported in Scheme 2.



Compound 2

To a stirred suspension of 2,3-naphthalenediol (0.500 g, 3.1 mmol) and powdered potassium carbonate (1.725 g, 12.5 mmol) in acetone (40 mL), methyl bromoacetate (1.15 mL, 12.5 mmol) was added dropwise. The mixture was refluxed for 2 h and then filtered and the filtrate evaporated *in vacuo*. The residue is redissolved in dichloromethane (20 mL) and the organic solution washed with aq. 0.1N NaOH (3x25mL), dried over Na$_2$SO$_4$, filtered and evaporated, obtaining diester **2**. Yield 0.890 g (94%). M.p. 111-113°C. Mass spectrum (ESI) 305.0 (MH$^+$). Calc. for C$_{16}$H$_{16}$O$_6$: 304.1 u.m.a.. ^{1}H-NMR (CDCl$_3$): 7.62 (m, 2H), 7.30 (m, 2H), 7.06 (s, 2H), 4.79 (s, 4H), 3.77 (s, 6H). ^{13}C-NMR (CDCl$_3$): 169.2 [C], 147.7 [C], 129.5 [C], 126.6 [CH], 124.9 [CH], 109.4 [CH], 66.1 [CH$_2$], 52.4 [CH$_3$].

Compound 3

To a stirred suspension of compound **2** (2.00 g, 6.6 mmol) in ethanol (50 mL) at 0°C, sodium borohydride (2.50 g, 66 mmol) was added portionwise. The reaction mixture was brought to room temperature, then refluxed for 3 h. After cooling to r.t., conc. aq. 37% HCl (5 mL) was slowly added to destroy residual hydrides. The suspension was filtered and the solid residue washed thoroughly with water and dried under vacuum, obtaining compound **3**. Yield 1.18 g (72%). M.p. 146-147°C. Mass spectrum (ESI) 249.2 (MH$^+$). Calc. for C$_{14}$H$_{16}$O$_4$: 248.1 u.m.a.. ^{1}H-NMR (CD$_3$OD): 7.62 (m, 2H), 7.26 (m, 2H), 7.19 (s, 2H), 4.14 (t, 4H, J = 4.7 Hz), 3.92 (t, 4H, J = 4.6 Hz). ^{13}C-NMR (CD$_3$OD): 150.3 [C], 130.0 [C], 127.4 [CH], 125.2 [CH], 109.8 [CH], 71.8 [CH$_2$], 61.6 [CH$_2$].

Compound 4

Compound **3** (750.0 mg, 3.0 mmol) and ethyldiisopropylamine (3.60 mL, 21 mmol) were dissolved in dry ethyl acetate (20 mL). The solution was stirred and cooled at -10°C and methanesulfonyl chloride (1.25 mL, 18 mmol) was added dropwise, maintaining the reaction temperature below 0°C. After the addition the reaction mixture was stirred for 3 h, then transferred in a separatory funnel where it was washed respectively with 0.1 N aq. HCl (3x20 mL) and saturated aq. NaHCO$_3$ (3x20 mL). The organic solution was finally dried over anhydrous Na$_2$SO$_4$, filtered and evaporated *in vacuo*, obtaining crude bis(methanesulfonyloxy) derivative as an amorphous off-white solid. Mass spectrum (ESI) 405.6 (MH$^+$). Calc. for C$_{16}$H$_{20}$O$_8$S: 404.5 u.m.a.. ^{1}H-NMR (CDCl$_3$): 7.68 (m, 2H), 7.37 (m, 2H), 7.16 (s, 2H), 4.65 (t, 4H, J = 4.2 Hz), 4.38 (t, 4H, J = 4.2 Hz), 3.18 (s, 6H). ^{13}C-NMR (CDCl$_3$): 147.9 [C], 129.4 [C], 126.4 [CH], 124.9 [CH], 109.0 [CH], 67.9 [CH$_2$], 66.7 [CH$_2$], 37.8 [CH$_3$].

The crude dimesyloxy derivative (0.525 g, 1.3 mmol), potassium phthalimidate (0.48 g, 2.6 mmol) and potassium carbonate (0.715 g, 5.2 mmol) were suspended in anhydrous DMF (3.5 mL) and stirred under nitrogen atmosphere at 100°C for 6 h. Insolubles and inorganic salts were filtered away and the filtrate evaporated *in vacuo*. The semisolid residue was taken up in dichloromethane (25 mL), washed with aq. 0.1N NaOH (3x25mL), dried over anhydrous Na$_2$SO$_4$, filtered and evaporated. The solid product was recrystallized from ethanol/water, giving 405 mg of pure bis(phthalimido) derivative.

M.p. 175-180°C. Mass spectrum (ESI) 507.1 (MH$^+$). Calc. for C$_{30}$H$_{22}$N$_2$O$_6$: 506.2 u.m.a.. ^{1}H-NMR (CDCl$_3$): 7.87 (m, 4H), 7.71 (m, 4H), 7.61 (m, 2H), 7.29 (m, 2H), 7.14 (s, 2H), 4.30 (t, 4H, J = 6.0 Hz), 4.17 (t, 4H, J = 6.0 Hz). ^{13}C-NMR (CDCl$_3$): 168.5 [C], 148.9 [C], 134.4 [CH], 132.5 [C], 129.8 [CH], 126.8 [CH], 125.8 [CH], 124.8 [CH], 109.7 [CH], 65.9 [CH$_2$], 37.4 [CH$_2$].

To a stirred suspension of the bis(phthalimido) derivative (400 mg, 0.79 mmol) in ethanol (5 mL), hydrazine hydrate (395 mg, 7.9 mmol) was added and the whole mixture was heated to reflux for 2h. The white precipitate was filtered and washed with cold ethanol (2 mL); filtrate and washings were pooled and evaporated *in vacuo*. The residue was dissolved in dichloromethane (25 mL) and extracted with 0.1N aq. HCl. The joint aqueous extracts were basified with NaOH and extracted with dichloromethane (3x10 mL). The organic extracts were dried over anhydrous Na$_2$SO$_4$, filtered and evaporated, obtaining compound **4** (301 mg).

M.p. 106-107°C. Mass spectrum (ESI) 247.2 (MH$^+$). Calc. for C$_{14}$H$_{18}$N$_2$O$_2$: 246.1 u.m.a.. ^{1}H-NMR (CDCl$_3$): 7.66 (m, 2H), 7.33 (m, 2H), 7.15 (s, 2H), 4.14 (t, 4H, J = 5.1 Hz), 3.18 (t, 4H, J = 5.2 Hz), 1.83 (bs, 4H). ^{13}C-NMR (CDCl$_3$): 149.2 [C], 129.4 [C], 126.4 [CH], 124.4 [CH], 108.5 [CH], 71.2 [CH$_2$], 41.6 [CH$_2$].

Compound 5

Compound **4** (300.0 mg, 1.22 mmol) and potassium carbonate (1.35 g, 9.76 mmol) are suspended in acetonitrile (15 mL). *t*-Butyl bromoacetate (1.43 g, 7.31 mmol) is slowly added dropwise at room temperature and then the reaction mixture is stirred for 48 h. Inorganic salts are filtered and the filtrate evaporated *in vacuo*; the waxy residue is charged on a silica gel chromatographic column, from which tetraester 5 was eluted (eluant petroleum ether/ethyl acetate 7/3), obtaining the pure product as a light yellow oil.

Yield 530 mg (62%).