Chemical Communications

Electronic Supplementary Information

Induction of chirality in porphyrin/(bis)calixarene assemblies: a mixed covalent/non-covalent *vs* a fully non-covalent approach

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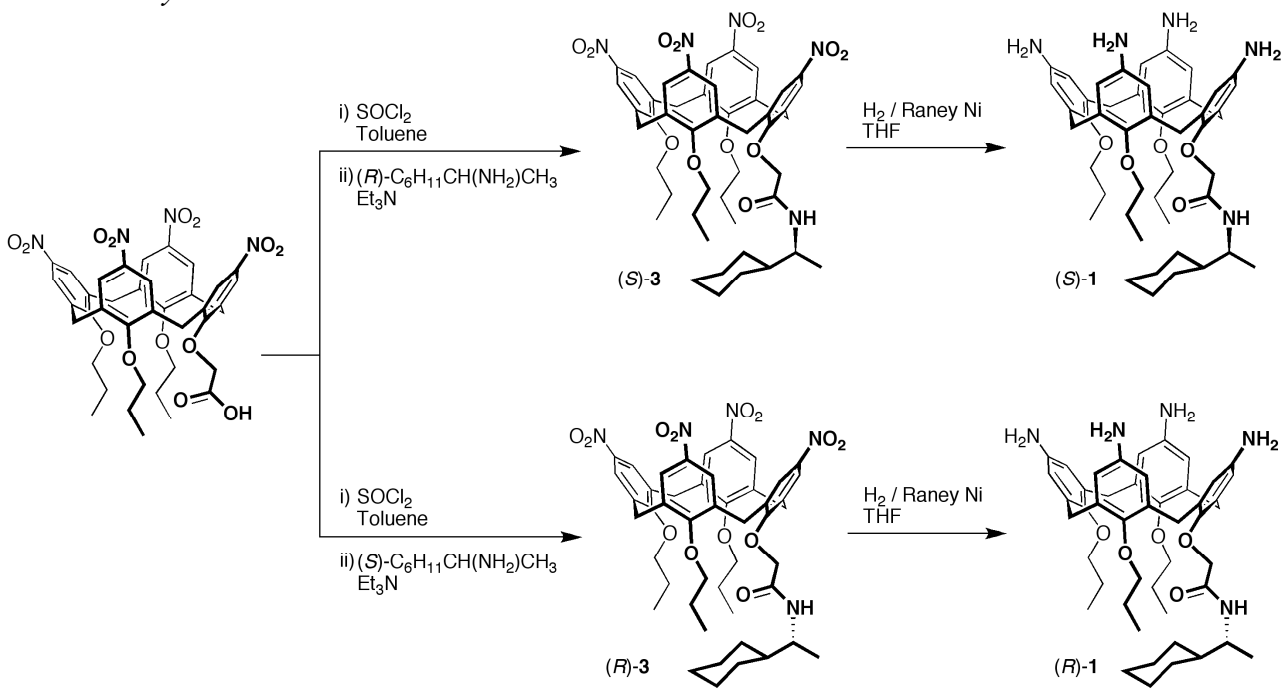
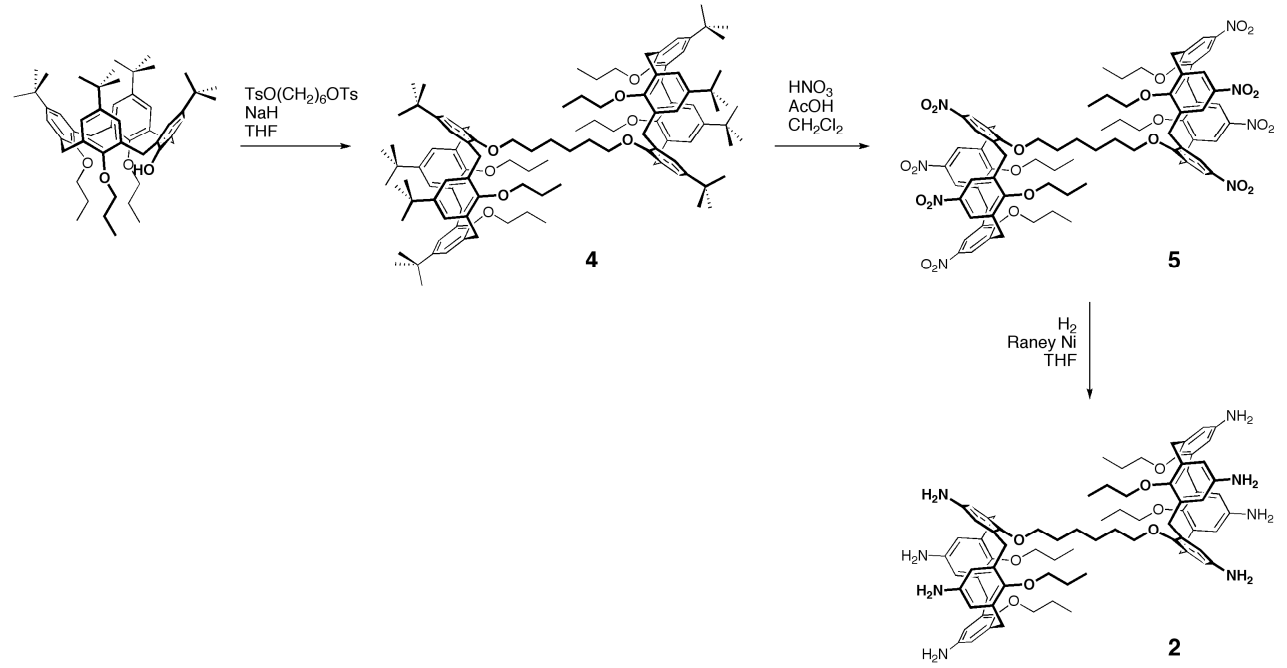
Experimental

General. Unless otherwise stated, ^{1}H (300 or 500 MHz) and ^{13}C (75 or 125 MHz) NMR spectra were obtained at 25 °C in $CDCl_3$ (using TMS as an internal standard). Solvents were dried by standard methods prior to use; other chemicals were reagent grade and were used without further purification. Column chromatography was performed on silica gel (Merck, 230–400 mesh). All reactions were carried out under a nitrogen atmosphere.

Calixarene synthesis overviews



Scheme S1. The syntheses of calix[4]arenes (*S*)-**1** and (*R*)-**1**.



Scheme S2. The synthesis of bis-calix[4]arene **2**.

Synthetic procedures

5,11,17,23-Tetranitro-25,26,27-tripropoxy-28-[(*R*)-1-cyclohexylethylaminocarbonylmethoxy] calix[4]arene (*R*)-3.
A stirred mixture of *p*-nitro-25,26,27-tripropoxy-28-carboxymethoxycalix[4]arene[1] (350 mg, 0.44 mmol) and $SOCl_2$ (3.5 mL) in dry toluene (5 mL) was heated at reflux for 3 h. Upon cooling, the mixture was concentrated to dryness under vacuum, and taken up in dry toluene (5 mL). Evaporation of the solvent afforded the $SOCl_2$-free acid chloride, which was dissolved in dry CH_2Cl_2 (5 mL) and cooled to –10 °C. To this solution a mixture of (*R*)-(–)-1-cyclohexylethylamine (70 mg, 0.55 mmol) and triethylamine (55 mg, 0.55 mmol) in CH_2Cl_2 (2 mL) was added via cannula. The reaction mixture was stirred for an additional 5 h, and stopped by addition of 0.1 N HCl (5 mL). The organic layer was washed with water, then with brine and dried over Na_2SO_4. The solid residue was purified by column chromatography (SiO_2, cyclohexane–ethyl acetate 2:1, v/v) to afford the pure amide (*R*)-**3** as a pale yellow solid (0.348 g, 88% yield). ^{1}H NMR (500 MHz) δ 7.86 (bs, 4 H), 7.32 (s, 2 H), 7.25 (s, 2 H), 6.07 (d, J = 8.5 Hz, 1 H), 4.55 (d, J = 13.5 Hz, 2 H), 4.52 (d, J = 14.0 Hz, 2 H), 4.42 (s, 2 H), 4.12–3.97 (m, 6 H), 3.87 (t, J = 7.5 Hz, 2 H), 3.48, 3.47, 3.44 (3×d, J = 14.0 Hz, ratio 1:1:2, 4 H), 1.95–1.84 (m, 6 H), 1.78–1.64 (m, 6 H), 1.44–0.95 (m, 18 H) ppm; ^{13}C NMR (125 MHz) δ 166.2, 161.94, 161.90, 160.9, 159.6, 143.4, 143.0, 136.1, 135.7, 134.7, 134.6, 134.3, 134.2, 124.8, 124.6, 123.9, 123.7, 123.6, 77.9, 77.63, 77.60, 74.0, 49.5, 43.1, 31.3, 31.2, 29.4, 29.0, 26.9, 26.2, 26.1, 26.0, 23.31, 23.28, 23.26, 18.0, 10.4, 9.97, 9.95 ppm.

5,11,17,23-Tetraamino-25,26,27-tripropoxy-28-[(*R*)-1-cyclohexylethylaminocarbonylmethoxy] calix[4]arene (*R*)-1. A mixture of nitrocalix[4]arene (*R*)-**3** (49 mg, 0. 054 mmol) and Raney/Ni in THF (10 mL) was stirred under H_2 (1 atm) at room temperature for 18 h, and then filtered on celite. The solvent was evaporated under reduced pressure, and the residual solid was triturated with cyclohexane and collected by suction filtration to afford the tetra-amine (*R*)-**1** (39 mg, 93%). ^{1}H NMR (500 MHz) δ 6.90 (d, J = 9.2 Hz, 1 H), 6.33, 5.90, 5.76 (bs×3, ratio 2:1:1, 8 H), 4.31–4. 18 (m, 6 H), 4.04–3.96 (m, 1 H), 3.88–3.74 (m, 4 H), 3.62 (t, J = 6.9 Hz, 2 H), 3.00–2.88 (m, 4 H), 2.80 (bs, 8 H), 1.89–1.74 (m, 9 H), 1.70–1.65 (m, 1 H), 1.45–1.38 m, 1 H), 1.28–1.11 (m, 7 H), 1.07–0.99 (m, 5 H), 0.88 (t, J = 7.5 Hz, 6 H) ppm; ^{13}C NMR (125 MHz) δ 168.9, 150.3, 150.1, 149.4, 148.4, 141.0, 140.4, 136.9, 136.3, 136.2, 134.5, 133.4, 116.3, 116.1, 115.9, 76.5, 76.4, 74.0, 49.0, 43.2, 31.3, 31.24, 31.16, 31.0, 29.7, 29.2, 26.3, 26.1, 23.3, 23.0, 22.9, 18.1, 10.7, 10.1 ppm.

The relevant calix[4]arene enantiomers (*S*)-**3** and (*S*)-**1** were obtained in a similar way by using (*S*)-(+)-1-cyclohexylethylamine in place of its (*R*)-(–) enantiomer. The NMR spectra of the two enantiomers were superimposable.

1,6-Bis{5,11,17,23-tetra-*p*-*tert*-butyl-25,26,27-tripropoxy-28-[oxy]calix[4]arene}hexane (4).
To a stirred mixture of 25,26,27-tripropoxy-*p*-*tert*-butilcalix[4]arene[2] (387 mg, 0.5 mmol) and NaH (24 mg, 1.0 mmol) in anhydrous THF (10 mL), 1,6-bis[(*p*-tolylsulfonyl)oxy]hexane[3] (0.25 mmole) was added as a solid. The mixture was refluxed for 18–24 h. Progress of the reaction was monitored by following the disappearance of the reagents by TLC (cyclohexane/CH_2Cl_2 7:3, v/v). The cooled mixture was treated with a few drops of methanol, to destroy any NaH excess, and the solvent was evaporated. The residue was partitioned between 1N HCl and dichloromethane. The organic layer was washed with $NaHCO_3$, then with water, dried over Na_2SO_4 and concentrated to dryness. The solid obtained after trituration with MeOH was further purified by recrystallization from

1 M. Regayeg, F. Vocanson, A. Duport, B. Blondeau, M. Perrin, A. Fort and R. Lamartine, *Material Sciences and Engineering C*, 2002, **21**, 131.
2 K. Iwamoto, K. Araki and S. Shinkai, *J. Org. Chem*., 1991, **56**, 4955.
3 V. Pejanović, V. Piperski, D. Uglješić-Kilibarda, J. Tasić, M. Dačević, L. Medić-Mijačević. E. Gunić, M. Popsavin and V. Popsavin, *Eur. J. Medicinal Chem*., 2006, **41**, 503.

CH_3CN/CH_2Cl_2 (70% yield). ^{1}H NMR (300 MHz) δ 6.81, 6.77 (s, 8 H each), 4.44, 4.43 (2×d, J = 12.5 Hz, 4 H each), 3.91 (t, J = 7.5 Hz, 4 H), 3.86–3.81 (overlapped t, 12 H), 3.13, 3.12 (2×d, J = 12.5 Hz, 4 H each), 2.12–2.01 (m, 16 H), 1.51 (bs, 4 H), 1.11, 1.08 (2×s, 36 H each), 1.02, 1.00 (2×t, ratio 2:1, J = 7.5 Hz, 18 H) ppm; ^{13}C NMR (75 MHz) δ 153.8, 153.7, 153.6, 144.18, 144.16, 144.09, 134.0, 133.7, 124.9, 124.8, 76.9, 75.3, 33.81, 33.77, 31.48, 31.43, 31.1, 30.6, 26.5, 23.3, 23.2, 10.4, 10.3 ppm.

1,6-Bis{5,11,17,23-tetra-nitro-25,26,27-tripropoxy-28-[oxy]calix[4]arene}hexane (5).
To a chilled solution of *p-tert*-butylcalix[4]arene dimer **4** (163 mg, 0.1 mmol) in a mixture of CH_2Cl_2 (3 mL) and glacial acetic acid (3 mL) was added 100% HNO_3 (1.0 mL, ~ 24 mmol). The reaction mixture was stirred at room temperature until the initial black purple color had turned orange (ca 4 h). The mixture was poured into water (20 mL), and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with water (2 × 20 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was triturated with MeOH to give a product (88% yield) which was pure enough for subsequent manipulations. ^{1}H NMR (300 MHz) δ 7.70, 7.68, 7.44, 7.41 (4×s, 2 H each), 4.51, 4.49 (2×d, J = 14.0 Hz, 4 H each), 4.02–3.89 (m, 16 H),), 3.41, 3.39 (2×d, J = 14.0 Hz, 4 H each),1.97–1.84 (m, 12 H), 1.53–1.42 (m, 4 H), 1.04, 0.98 (2×t, J = 7.5 Hz, ratio 1:2, 18 H) ppm; ^{13}C NMR (75 MHz) δ 161.9, 161.4, 161.3, 142.8, 135.7, 135.6, 135.2, 135.1, 124.3, 124.1, 123.74, 123.66, 77.7, 77.6, 75.9, 31.1, 30.2, 25.9, 23.25, 23.21, 10.2, 10.1 ppm.

1,6-Bis{5,11,17,23-tetra-amino-25,26,27-tripropoxy-28-[oxy]calix[4]arene}hexane (2).
A mixture of octa-nitro derivative **5** (0.1 mmol) and Raney-Ni in freshly distilled THF (15 mL) was stirred at room temperature under H_2 (atm) till decoloration of the initially yellow solution (1–1.5 h, monitoring by ^{1}H NMR). The reaction mixture was then subjected to filtration through a celite pad, which was thoroughly washed with AcOEt. Concentration of the filtrate to dryness yielded the octa-amino derivative **2** in almost quantitative yield as an off-white solid, which was used without further purification. ^{1}H NMR δ 6.07, 6.05 (2×s, 16 H), 4.30 (d, J = 13.2 Hz, 8 H), 3.77–3.69 (overlapping t, 16 H), 2.91 (d, J = 13.2 Hz, 8 H), 2.41 (bs, 16 H), 1.90–1.82 (16 H), 1,33, 1.29 (2×s, 16 H), 0.94 (t, J = 7.5 Hz, 18 H) ppm; ^{13}C NMR (75 MHz) δ 150.1, 150.02, 149.96, 140.1, 135.7, 135.5, 115.8, 76.6, 74.9, 40.9, 31.1, 30.2, 26.3, 23.1, 10.37, 10.33 ppm.

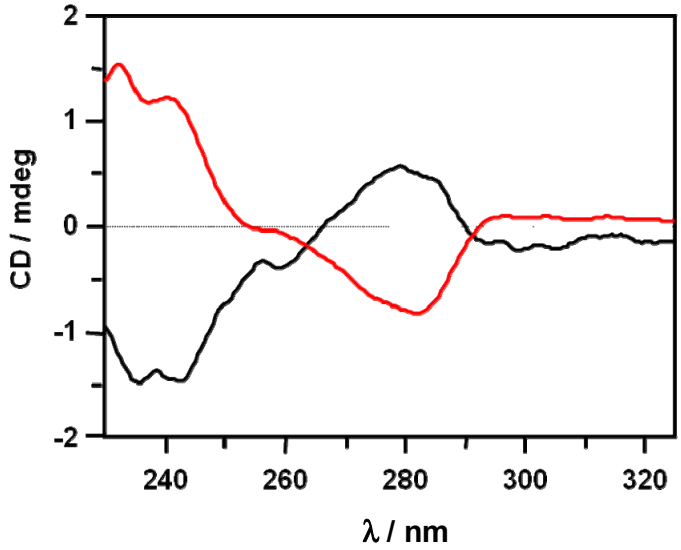


Figure S1: CD spectra of 50 µM aqueous solutions (pH 2.5) of calix[4]arenes (*R*)-**1** (black trace) and (*S*)-**1** (red trace).

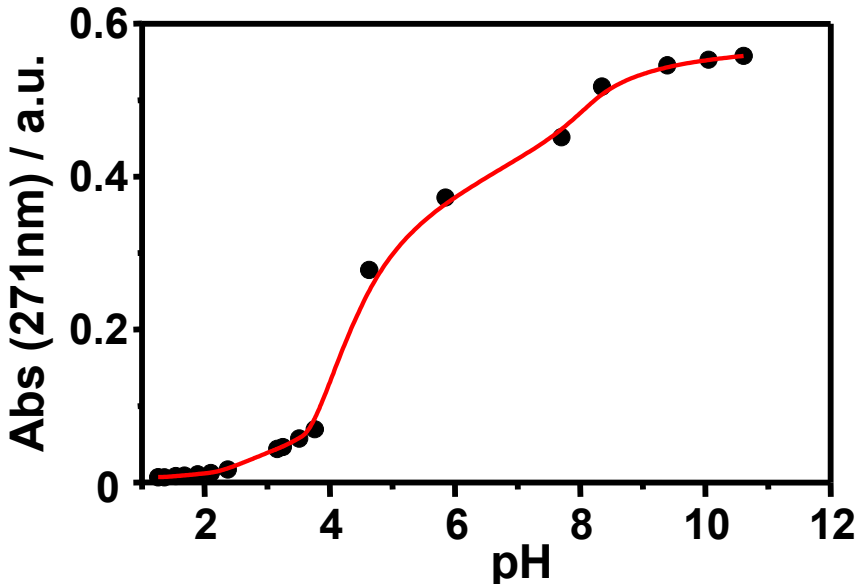


Figure S2: Spectrophotometric pH titration of a 4 µM aqueous solution of calix[4]arene (*R*)-**1** with aqueous HCl.

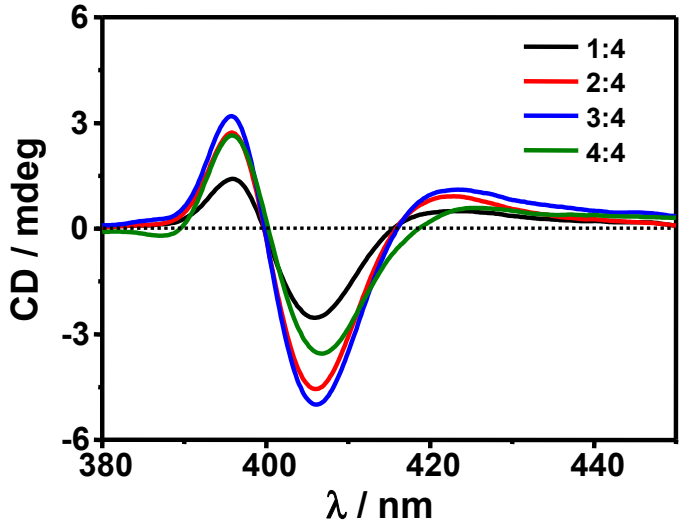


Figure S3: CD spectra of aqueous solutions (pH 2.5) of the 1:4 (black trace) 2:4 (red trace), 3:4 (blue trace) and 4:4 (green trace) binary **CuTPPS**/(*S*)-**1** assemblies ([(*S*)-**1**] = 4 μM).

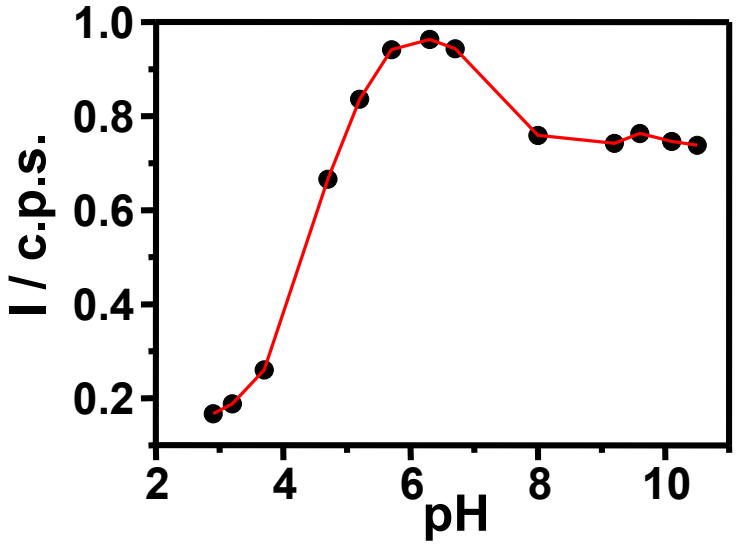


Figure S4: Spectrophotometric pH titration of a 4 mM aqueous solution of bis-calix[4]arene **2** with aqueous HCl. I and c.p.s. stand for intensity and counts per second, respectively.

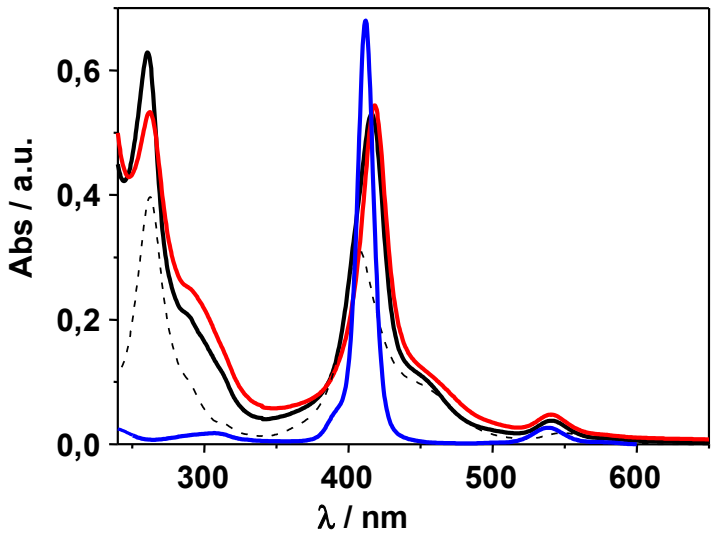


Figure S5: Absorption spectra of aqueous solutions of the ternary 1:4:4 assembly ([**CuTPPS**] = 1.5 μM: [**2**] = 6 μM: [Δ-$[Ru(phen)_3]^{2+}$] = 6 μM) at pH 5.5 (black trace) and pH 9.0 (red trace). The dashed trace refers to an aqueous solution of the binary 1:4 complex **CuTPPS**/Δ-$[Ru(phen)_3]^{2+}$ (1.5 and 6 μM, respectively) at pH 9.0, while the blue one pertains to **CuTPPS** (1.5 μM) at pH 9.0.