Supplementary Material (ESI) for Chemical Communications

Calix-Tris-Tröger's Bases – A New Cavitand Family

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S2 … Preparation of aminoamide **3c**

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S3 … Preparation of *throne*-**1c**

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EXPERIMENTAL PART

All ^{1}H and ^{13}C NMR experiments were recorded at 300.08 and 75.46 MHz, respectively. Chemical shifts δ (ppm) are referenced to the internal standard Me_4Si for both ^{1}H and ^{13}C NMR spectra; the coupling constants *J* are given in Hertz (Hz). The correlation techniques g-HSQC, g-COSY, 1D NOESY (mixing time 600 ms) were recorded under common conditions. The g-HMBC spectra were recorded with parameters of $^{1}J_{CH}$ coupling 180 Hz (parameter j1hx at Varian Mercury NMR machine) and $^{n}J_{CH}$ coupling 8 Hz (parameter jnhx at Varian Mercury NMR machine). The chemical shifts and coupling constants for H^{7a}, H^{7b}, H^{8a}, H^{8b}, H^{9a} and H^{9b} in *calix*-**1b** and *calix*-**1c** were determined by simulation as six-spins system by MestRe-C 4.4.6 (Mestrelab Research, Spain). Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-640697 (*calix*-**1c**) and CCDC-640698 (*throne*-**1c**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk). The preparations of compounds **2b**, **3b**, **4b**, *throne*-**1b**, **2a**, **3a** and **4a**, and unsuccessful attempt of *throne*-**1a** preparation were described previously.[6a]

Preparation of nitroamide **2c**

5-methoxy-2-nitrobenzoic acid (12.9 g, 65.5 mmol) was refluxed with $SOCl_2$ (40 mL) in toluene (50 mL) for 5 h. The volatile part of reaction mixture was evaporated and residue codestilated with toluene (2×20 mL). Residual brown oil was added to solution of 1,3,5-triaminobenzene (2.02 g, 16.4 mmol) in pyridine (20 mL) and DMF (40 mL). Reaction mixture was stirred 12 h at room temperature and 1 h at 50 °C. After cooling, 1 L of water was added. The formed precipitate of **2c** (6.10 g, 63% yield) was filtered off, washed with methanol (100 mL) and dichlormethane (150 mL). Additional part of **2c** (0.75 g, 8% yield) was obtained from the organic part of the filtrate. ^{1}H NMR (DMSO-d_6): 3.92 (9H, s, OCH_3), 7.20 (6H, m), 7.87 (3H, s), 8.15 (3H, d, 8.5), 10.69 (3H, s, NH). ^{13}C APT NMR (DMSO-d_6): 56.57 (OCH_3), 106.69 (CH), 114.22 (CH), 115.33 (CH), 126.92 (CH), 135.67, 138.68, 139.41, 163.51, 164.16. Elemental analysis for $C_{30}H_{24}N_6O_{12}$ calcd: 54.55 %C, 3.66 %H, 12.72 %N; found: 54.22 %C, 3.93 %H, 12.82 %N.

Preparation of aminoamide **3c**

A flask was charged with 1.00 g (1.5 mmol) of **2c**, 100 mg of Pd/C (10%), 50 mL of methanol, and 10 mL of DMF. The mixture was stirred over night under H_2 atmosphere. The catalyst was filtrated off through cellite and the filtrate was concentrated *in vacuo* to obtained 0.86 g of **3c** (100% yield). ^{1}H NMR (DMSO-d_6): 3.72 (9H, s), 5.80-6.20 (6H, br s), 6.72 (3H, d, 8.8), 6.89 (3H, dd, 8.8, 2.8), 7.20 (3H, d, 2.8), 7.81 (3H, s), 10.08 (3H, br s). ^{13}C APT NMR (DMSO-d_6): 55.61

(OCH_3), 109.70 (CH), 112.67 (CH), 115.83, 117.96 (CH), 119.92 (CH), 139.03, 143.58, 149.52, 167.50. HRMS (FAB^+) for $C_{30}H_{31}N_6O_6$ (MH^+) calcd: 571.2305; found: 571.2298, and for $C_{30}H_{30}N_6O_6$ (M^+) calcd: 570.2227; found: 570.2214.

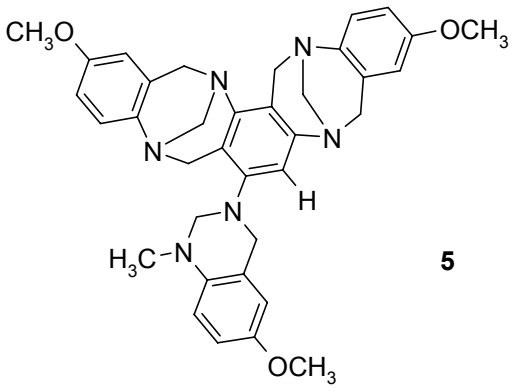
Preparation of hexaamine **4c**

3.5 M toluene solution of LAH (18 mL, 63 mmol) was slowly added to **3c** (1.30 g, 2.3 mmol) in dioxane (40 mL). Then the reaction mixture was refluxed for 14 h. The flask was placed into ice bath and 6 mL of water, followed by 7 mL of aqueous solution of NaOH (15%) and 10 mL of water were cautiously added. The mixture was filtered and the filtrate was evaporated *in vacuo* to obtain 1.12 g of **4c** (93% yield). ^{1}H NMR (DMSO-d_6): 3.57 (9H, s), 3.91 (6H, d, 5.5), 4.45 (6H, br s), 5.30 (6H, m), 6.54 (6H, m), 6.69 (3H, t, 1.6). ^{13}C APT NMR (DMSO-d_6): 44.12 (CH_2), 55.23 (OCH_3), 87.64 (CH), 112.22 (CH), 114.38 (CH), 115.51 (CH), 125.32, 139.80, 150.20, 150.89. LRMS (FAB^+): for $C_{30}H_{37}N_6O_3$ (MH^+) calcd: 529.29; found: 529.29.

Preparation of *throne*-**1c**

Hexaamine **4c** (1.21 g, 2.3 mmol) and 1.00 g of paraformaldehyde were added to trifluoroacetic acid (145 mL). The reaction mixture was stirred 1 h at 50 °C, then diluted with ice water (1 L), and conc. aq. ammonia was added to pH 14. The mixture was extracted with CH_2Cl_2 (3×150 mL). The organic parts were combined, washed with brine, dried over Na_2SO_4, and evaporated *in vacuo* to dryness. By repeating column chromatography on silica (CH_2Cl_2/EtOAc/ethanol 250:250:12) 80 mg of by-product **5** (6% yield) 320 mg of crude Tris-TB *throne*-**1c** were obtained. The crystallization of crude *throne*-**1c** from CH_2Cl_2/acetone gave 240 mg (18% yield) of pure *throne*-**1c**.

By-product ***5***: ^{1}H NMR ($CDCl_3$): 2.80 (3H, s, NCH_3), 3.71 (3H, s, OCH_3), 3.73 (3H, s, OCH_3), 3.75 (3H, s, OCH_3), 3.91 (1H, d, 16.7), 3.95 (1H, d, 10.8), 4.01 (1H, d, 15.8), 4.02 (1H, d, 13.3), 4.04 (1H, d, 10.6), 4.13 (1H, d, 12.7), 4.18 (1H, d, 15.6), 4.19 (1H, d, 12.2), 4.28 (3H, m), 4.46 (1H, d, 16.9), 4.47 (1H, d, 17.1), 4.52 (1H, d, 17.9), 4.56 (1H, d, 17.2), 4.59 (1H, d, 16.6), 6.41 (1H, d, 2.9), 6.46 (1H, d, 2.8), 6.50 (1H, t, 1.7), 6.67 (1H, s), 6.78 (4H, m), 7.07 (1H, d, 8.8), 7.11 (1H, d, 8.8). ^{13}C APT NMR ($CDCl_3$): 38.93 (NCH_3), 53.60 (CH_2), 55.25 (CH_2), 55.29 (OCH_3), 55.35 (OCH_3), 55.55 (CH_2), 55.64 (OCH_3), 55.84 (CH_2), 59.08 (CH_2), 66.76 (CH_2), 67.00 (CH_2), 71.05 (CH_2), 110.54 (CH), 110.68 (CH), 111.73 (CH), 113.17 (CH), 113.20 (CH), 113.82 (CH), 113.97 (CH), 115.76 (CH), 117.98, 118.77, 123.75, 126.20 (CH), 126.27 (CH), 128.60, 128.75, 140.33, 140.77, 140.92, 145.82, 147.53, 148.00, 152.54, 155.86, 155.96. HRMS (FAB^+): for $C_{36}H_{39}N_6O_3$ (MH^+) calcd: 603.3084; found: 603.3056. Based on these characteristics and 2D NMR spectra (g-COSY, g-HSQC, g-HMBC) the following structure was deduced.



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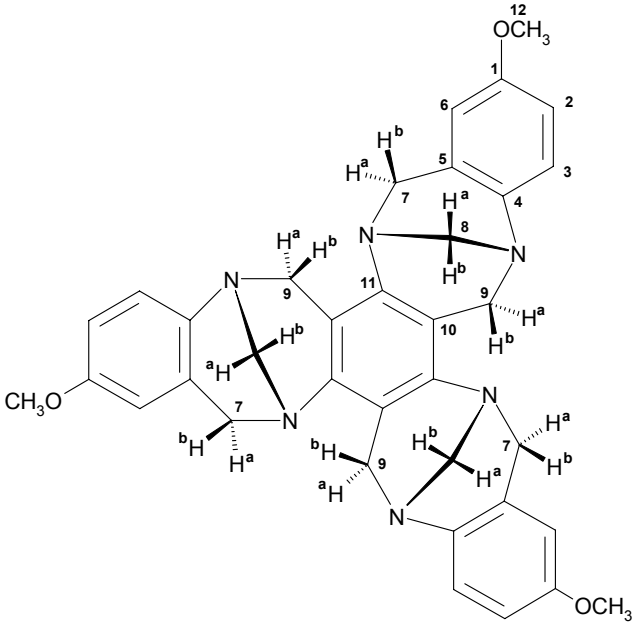
Throne-**1c**: ^{1}H NMR ($CDCl_3$): 3.60 (1H, d, 16.8), 3.65 (3H, s), 3.72 (3H, s), 3.73 (3H, s), 3.82 (1H, d, 16.5), 3.88 (1H, d, 16.7), 4.08 (1H, d, 12.8), 4.10 (1H, d, 12.2), 4.16 (1H, d, ~13), 4.18 (1H, d, ~13), 4.19 (2H, s), 4.29 (1H, d, 17.4), 4.36 (1H, d, 17.0), 4.41-4.52 (5H, m), 4.53 (1H, d, 17.4), 4.56 (1H, d, 17.0), 6.25 (1H, d, 2.9), 6.41 (1H, d, 2.9), 6.45 (1H, d, 2.9), 6.69 (1H, dd, 8.8, 2.9), 6.76 (1H, dd, 8.8, 2.9), 6.78 (3H, dd, 8.8, 2.9), 7.08 (1H, d, 8.8), 7.12 (1H, d, 8.8), 7.15 (3H, d, 8.8). ^{13}C APT NMR ($CDCl_3$): 54.67 (2×CH_2), 55.08 (2×CH_2), 55.31 (OCH_3), 55.36 (OCH_3), 55.38 (OCH_3), 55.57 (CH_2), 56.19 (CH_2), 66.69 (CH_2), 66.74 (CH_2), 66.97 (CH_2), 110.53 (CH), 110.66 (2×CH), 113.80 (CH), 114.08 (CH), 114.46 (CH), 117.94, 118.25, 119.02, 125.84 (CH), 126.28 (CH), 126.38 (CH), 128.38, 128.50, 128.54, 140.82, 140.94, 141.17, 143.94, 144.26 (2×C), 155.92, 155.99, 156.09. HRMS (FAB$^+$): for $C_{36}H_{37}N_6O_3$ (MH^+) calcd: 601.2927; found: 601.2939.

Preparation of *calix*-**1c** by diastereiosomeration

Throne-**1c** (54 mg) was dissolved in 5 mL of TFA and warmed at 110 °C for 15 h. The obtained mixture of *throne*-**1c** and *calix*-**1c** in ratio 97:3 was separated by preparative TLC (Uniplate Silica Gel GF, 20 cm × 20 cm × 0.1 cm, with PA zone, CH_2Cl_2/CH_3OH 97:3). The diastereoisomer *throne*-**1c** was subject of next diastereoisomerization. The collected portions of *calix*-**1c** from five isomerizations gave 6 mg (11% yield). The single crystal for X-ray analysis was obtained by crystalization from mixture CH_2Cl_2/CH_3OH. The ^{1}H and ^{13}C chemical shifts in NMR spectra were assigned based on g-COSY, g-HSQC, g-HMBC and 1D NOEDIF spectra analogously to assignment on bisTB derivatives.[6c]



Calix-**1c**: ^{1}H NMR ($CDCl_3$): 3.64 (9H, s, H12), 3.65 (3H, d, 16.8, H7^a), 4.18 (3H, d, 17.7, H9^a) , 4.18 (3H, d, 12.3, H8^a or H8^b), 4.20 (3H, d, 12.3, H8^a or H8^b), 4.48 (3H, d, 16.8, H7^b), 4.66 (3H, d, 17.7, H9^b), 6.28 (3H, d, 2.9, H6), 6.71 (3H, dd, 8.8, 2.9, H2), 7.11 (3H, d, 8.8, H3). ^{13}C NMR ($CDCl_3$): 54.91 C7, 55.35 C12, 56.09 C9, 66.39 C8, 110.67 C6, 114.49 C2, 120.40 C10, 125.98 C3, 128.23 C5, 141.26 C4, 144.31 C11, 156.16 C1. HRMS (FAB$^+$): for $C_{36}H_{37}N_6O_3$ (MH^+) calcd: 601.2927; found: 601.2908.

One-pot preparation of *throne*-**1b**

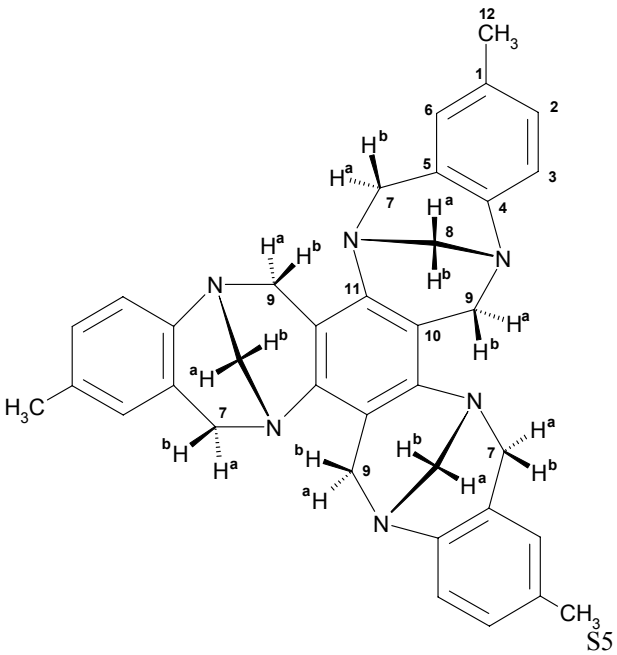
A vial was charged with 86 mg (0.70 mmol) of 1,3,5-triaminobenzene, 249 mg (2.32 mmol) of *p*-toluidine and 199 mg (equiv. of 6.63 mmol of CH_2O) of paraformaldehyde, and 4 mL of TFA was added. The vial was closed with a cup, and the mixture was vigorously stirred for 24 h in 60 °C oil bath. The mixture was cool down and diluted with 200 mL of water, and alkalized by adding of 5 mL of conc. aqueous ammonium. The mixture was extracted with CH_2Cl_2 (2 x 20 mL). The organic parts were dried over $MgSO_4$ and evaporated *in vacuo* to dryness. Repeating separation on preparative TLC (CH_2Cl_2/CH_3OH 100:3) gave 8 mg (2% yield) of *throne*-**1b**. The NMR characteristics confirm the identity with the compound isolated previously.[6c]

Throne-**1b**: ^{1}H NMR ($CDCl_3$): 2.18 (3H, s, CH_3), 2.24 (6H, m, $2CH_3$), 3.60 (1H, d, 16.5), 3.73 (1H, d, 16.8), 3.86 (1H, d, 16.5), 4.00-4.65 (15H, m), 6.54 (1H, s), 6.70 (1H, s), 6.74 (1H, s), 6.86-7.14 (6H, m). ^{13}C APT NMR ($CDCl_3$): 20.88 (CH_3), 21.90 (CH_3), 20.96 (CH_3), 54.39 (CH_2), 54.42 (CH_2), 55.11 (CH_2), 55.17 (CH_2), 55.24 (CH_2), 56.25 (CH_2), 66.59 ($2CH_2$), 66.85 (CH_2), 117.70 (C), 118.13 (C), 118.82 (C), 124.42 (CH), 124.99 (CH), 125.07 (CH), 126.87 (CH), 126.92 (CH), 127.19 (C), 127.35 (2C), 127.38 (CH), 127.90 (CH), 127.98 (CH), 128.04 (CH), 133.36 (C), 133.38 (C), 133.48 (C), 143.74 (C), 144.03 (C), 144.07 (C), 144.99 (C), 145.09 (C), 145.34 (C). HRMS (FAB^+): for $C_{36}H_{37}N_6$ (MH^+) calcd: 553.3080; found: 553.3056.

Preparation of *calix*-**1b** by diastereiosomeration

Throne-**1b** (17 mg) was dissolved in 2 mL of TFA and warmed at 110 °C for 17 h. The obtained mixture of *throne*-**1b** and *calix*-**1b** in ratio 97:3 was separated by preparative TLC (Uniplate Silica Gel GF, 20 cm × 20 cm × 0.1 cm, with PA zone, CH_2Cl_2/CH_3OH 92:2) to give about 1 mg of *calix*-**1b**. The ^{1}H and ^{13}C chemical shifts in NMR spectra were assigned based on gCOSY, gHSQC, gHMBC and 1D NOEDIF spectra analogously to assignment on bisTB derivatives.[6c]

Calix-**1b**: ^{1}H NMR ($CDCl_3$): 2.16 (9H, s, H12), 3.59 (3H, d, 16.8, H7^a), 4.16 (3H, d, 12.4, H8^a or H8^b), 4.20 (3H, d, 12.4, H8^a or H8^b), 4.21 (3H, d, 16.6, H9^a), 4.45 (3H, d, 16.7, H7^b), 4.65 (3H, d, 17.6, H9^b), 6.56 (3H, d, 1.4, H6), 6.94 (3H, dd, 8.1, 1.9, H2), 7.06 (3H, d, 8.1, H3). ^{13}C NMR ($CDCl_3$): 20.76 C12, 54.63 C7, 56.12 C9, 66.29 C8, 120.32 C10, 124.71 C3, 127.20 C5, 127.42 C6, 128.06 C2, 133.55 C1, 144.25 C11, 145.77 C4.



Approximation of cavity volume calculation

The volume of the *calix*-**1c** was calculated from X-ray data as the volume of truncated cone with following definition. The nitrogen atoms of central benzene define almost equilateral triangle with side 0.49 nm and the circumscribed circle d_1 = 0.65 nm. The oxygen atoms define almost equilateral triangle with side 0.85 nm and the circumscribed circle d_2 = 0.98 nm. The distance of the triangle centroids is h = 0.55 nm. The dimensions must be decreased by van der Waals diameter; let's use a correction by 0.16 nm. The volume of the free space for guest is 0.078 nm^3.