

Guest Exchange of Dimeric Capsules Formed by Tetra-urea Calix[4]arenes

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Synthesis

***p*-tert-Butylcalix[4]arene monopentyl ether.** A mixture of *p*-tert-butylcalix[4]arene (2.92 g, 4.5 mmol), K₂CO₃ (0.373 g, 2.7 mmol) and *n*-pentylbromide (1.69 ml, 2.04 g, 13.5 mmol) in dry acetonitrile (25 ml) was refluxed for 19 h. After cooling the reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The product was re-crystallized from chloroform/methanol and then purified by the column chromatography (chloroform/hexane, 1:1). Yield 49% (1.6 g), mp 215-216 °C. δ_{H} (400 MHz; CDCl₃) 10.18 (s, 1H, OH), 9.59 (s, 2H, OH), 7.08 (s, 2H, ArH), 7.05 (br d, 2H, ArH), 7.03 (s, 2H, ArH), 6.96 (br d, 2H, ArH), 4.35 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 4.27 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 4.12 (m, 2H, OCH₂), 3.43 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 3.40 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 2.15 (m, 2H, CH₂), 1.62 (m, 2H, CH₂), 1.51 (m, 2H, CH₂) and 1.01 (t, *J* 7.2 Hz, 3H, CH₃). FD-MS *m/z* 719.7 (100%), 720.7 (48), 721.6 (25) [M+H]⁺ for C₄₉H₆₆O₄·H (720.07).

***p*-tert-Butylcalix[4]arene 1,2-dipentyl ether.** To a stirred suspension of *p*-tert-butylcalix[4]arene (5.84 g, 9.0 mmol) in DMSO (39 ml) the aqueous solution of NaOH (40%, 5.4 ml, 77 mmol) was added. The mixture was stirred at 50 °C for 20 min and then *n*-pentylbromide (4.5 ml, 36 mmol) was added. The reaction mixture was stirred at 60 °C for 2 days. After cooling, water (200 ml) was added and the solid formed was separated, washed with water and dried. The product was crystallized from acetonitrile to give 3.37 g of the product. The filtrate was concentrated and the rest was separated by column chromatography (chloroform/hexane, 2:1) to give additionally 1.40 g of the product. Yield 67% (4.77 g), mp 130-132 °C. δ_{H} (400 MHz; CDCl₃) 8.88 (s, 2H, OH), 6.99 (d, *J* 1.4 Hz, 2H, ArH), 6.97 (d, *J* 2.0 Hz, 2H, ArH), 6.96 (d, *J* 1.7 Hz, 2H, ArH), 6.90 (d, *J* 1.4 Hz, 2H, ArH), 4.48 (d, *J* 12.3 Hz, 1H, ArCH₂Ar), 4.31 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 4.30 (d, *J* 13.3 Hz, 1H, ArCH₂Ar), 4.06 (m, 2H, OCH₂), 3.89 (m, 2H, OCH₂), 3.32 (m, 4H, ArCH₂Ar), 2.08 (m, 4H, CH₂), 1.47 (m, 8H, CH₂), 1.20 (s, 18H, C(CH₃)₃), 1.10 (s, 18H, C(CH₃)₃) and 0.97 (t, *J* = 6.8 Hz, 6H, CH₃). FD-MS *m/z* 788.9 (100%), 789.8 (63), 790.9 (17) [M]⁺ for C₅₄H₇₆O₄ (788.57).

***p*-tert-Butylcalix[4]arene tripentyl ether.** A suspension of *p*-tert-butylcalix[4]arene (2.92 g, 4.5 mmol) in dry DMF (56 ml) was heated to 70 °C for 2 h. After cooling, Ba(OH)₂·8H₂O (4.96 g, 15.7 mmol) and BaO (4.46 g, 30.3 mmol) followed by *n*-pentylbromide (5.6 ml, 44.9 mmol) were added and the stirring was continued for 4 days at room temperature. Water (280 ml) was added and the solid formed was separated, washed with water, dissolved in chloroform (150 ml) and washed with 1N HCl (15 ml) and then with water. The organic phase was dried and the solvent evaporated. The product was re-precipitated from chloroform/methanol. Yield 84% (3.25 g), mp 158-159 °C. δ_{H} (400 MHz; CDCl₃) 7.11 (s, 2H, ArH), 7.03 (s, 2H, ArH), 6.50 (s, 2H, ArH), 6.49 (s, 2H, ArH), 5.69 (s, 1H, OH), 4.36 (d, *J* 12.6 Hz, 2H, ArCH₂Ar), 4.32 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 3.89 (br t, *J* 8.2 Hz, 2H, OCH₂), 3.77 (t, *J* 7.0 Hz, 4H, OCH₂), 3.21 (d, *J* 12.9 Hz, 2H, ArCH₂Ar), 3.15 (d, *J* 12.6 Hz, 2H, ArCH₂Ar), 2.29 (m, 2H, CH₂), 1.90 (m, 4H, CH₂), 1.41 (m, 12H, CH₂), 1.32 (s, 9H, C(CH₃)₃), 1.31 (s, 9H, C(CH₃)₃), 0.95 (m, 9H, CH₃) and 0.81 (s, 18H, C(CH₃)₃). FD-MS *m/z* 858.9 (100%), 859.7 (60), 860.7 (23) [M]⁺ for C₅₉H₈₆O₄ (858.65).

General procedure for the synthesis of mixed p-tert-butylcalix[4]arene pentyl-methyl ethers 2. The appropriate partially pentylated *p*-tert-butylcalix[4]arene (2 mmol) was dissolved in THF (30 ml). NaH (1.2 mol per mol of OH) was added followed, after 30 min, by (CH₃O)₂SO₂ (1.2 mol per mol of OH). The suspension was stirred under reflux for 5 h, cooled, quenched with water (1 ml) and the solvent evaporated. The residue was dissolved in dichloromethane, washed with 1N HCl, water and brine, dried and, after the solvent evaporation, re-precipitated from chloroform/methanol. Due to a high conformational flexibility, no clear NMR data can be presented for **2-4_{MMMP}**, **2-4_{MMPP}** and **2-4_{MPPP}**.

***p*-tert-Butylcalix[4]arene trimethyl-monopentyl ether 2_{MMMP}.** Yield 95%, mp 197-200 °C. FD-MS *m/z* 761.7 (100%), 762.7 (52), 763.6 (12) [M+H]⁺ for C₅₂H₇₂O₄·H (761.55).

***p*-tert-Butylcalix[4]arene 1,2-dimethyl-3,4-dipentyl ether 2_{MMPP}**. Yield 77%, mp 82-83 °C. FD-MS *m/z* 817.1 (100%), 818.1 (59), 819.1 (17) [M+H]⁺ for C₅₆H₈₀O₄·H (817.61).

***p*-tert-Butylcalix[4]arene monomethyl-tripentyl ether 2_{MPPP}**. Yield 74%, mp 149-150 °C. FD-MS *m/z* 873.9 (100%), 874.8 (86), 875.8 (24) [M+H]⁺ for C₆₀H₈₈O₄·H (873.68).

General procedure for the preparation of tetranitrocalixarenes 3. To a stirred solution of the tetraether **2** (1.5 mmol) in dichloromethane (50 ml) glacial acetic acid (3.4 ml, 60 mmol) and fuming HNO₃ (2.5 ml, 60 mmol) were added. The mixture was stirred at room temperature for 2 h and then quenched with water (50 ml). The organic phase was separated, washed repeatedly with water and dried. The solvent was evaporated and the product was precipitated from chloroform/methanol.

***p*-Nitro-calix[4]arene trimethyl-monopentyl ether 3_{MMMP}**. Yield 60%, mp 286-288 °C (decomp). FD-MS *m/z* 715.7 (100%), 716.7 (41), 717.7 (11) [M]⁺ for C₃₆H₃₆N₄O₁₂ (716.23).

***p*-Nitro-calix[4]arene 1,2-dimethyl-3,4-dipentyl ether 3_{MMPP}**. Yield 74%, mp 252-254 °C. FD-MS *m/z* 772.5 (100%), 773.5 (54), 774.5 (10) [M]⁺ for C₄₀H₄₄N₄O₁₂ (772.30).

***p*-Nitro-calix[4]arene monomethyl-tripentyl ether 3_{MPPP}**. Yield 77%, mp 222-224 °C. FD-MS *m/z* 829.5 (100%), 830.5 (46), 831.5 (11) [M+H]⁺ for C₄₄H₅₂N₄O₁₂·H (829.37).

General procedure for the preparation of tetraaminocalixarenes 4. A catalytic amount of Raney nickel (washed with ethanol) was added to a solution of tetranitrocalixarene **3** (1 mmol) in toluene (50 ml) and the mixture was stirred at room temperature under H₂ for 10 h. The suspension was filtered and the filtrate evaporated to give the corresponding tetraamine.

***p*-Amino-calix[4]arene trimethyl-monopentyl ether 4_{MMMP}**. Yield 80%, mp 190-192 °C (decomp). FD-MS *m/z* 595.9 (100%), 596.9 (45), 597.9 (10) [M]⁺ for C₃₆H₄₄N₄O₄ (596.34).

***p*-Amino-calix[4]arene 1,2-dimethyl-3,4-dipentyl ether 4_{MMPP}**. Yield 85%, mp 145-147 °C (decomp). FD-MS *m/z* 652.0 (100%), 652.9 (50), 654.0 (13) [M]⁺ for C₄₀H₅₂N₄O₄ (652.40).

***p*-Amino-calix[4]arene monomethyl-tripentyl ether 4_{MPPP}**. Yield 90%, mp 210-212 °C. FD-MS *m/z* 709.8 (100%), 710.8 (54), 711.8 (10) [M+H]⁺ for C₄₄H₆₀N₄O₄·H (709.47).

Calix[4]arene 1,3-dipentyl-2,4-dibenzyl ether SI1. To a stirred solution of calix[4]arene 1,3-dibenzyl ether (0.725 g, 1.2 mmol) in THF (27 ml) and DMF (3 ml) NaH (0.23 g, 9.6 mmol) was added followed, after 15 min, by 1-bromopentane (1.19 ml, 9.6 mmol). The mixture was stirred for 48 h under nitrogen and then quenched with methanol. The solvent was evaporated and the resultant oil was treated with water. The solid formed was washed with methanol and re-crystallized from dichloromethane/methanol. Yield 58% (0.52 g), mp 207-209 °C. δ_H(400 MHz; CDCl₃) 7.47 (m, 4H, ArH_{Bz}), 7.33 (m, 6H, ArH_{Bz}), 6.89 (d, *J* 7.3 Hz, 4H, ArH), 6.77 (t, *J* 7.5 Hz, 2H, ArH), 6.44-6.28 (m, 6H, ArH), 4.83 (s, 4H, OCH₂Ph), 4.43 (d, *J* 13.4 Hz, 4H, ArCH₂Ar), 3.85 (m, 4H, OCH₂), 3.12 (d, *J* 13.4 Hz, 4H, ArCH₂Ar), 1.70 (m, 4H, CH₂), 1.13 (m, 4H, CH₂), 1.03 (m, 4H, CH₂) and 0.84 (t, *J* 7.3 Hz, 6H, CH₃). δ_C(100 MHz; CDCl₃) 157.32, 154.93, 137.99, 136.22, 134.16 (C_{Ar}), 129.02, 128.55, 128.14, 127.80, 127.46, 122.29, 121.81 (CH_{Ar}), 76.95, 74.97 (OCH₂), 31.11 (ArCH₂Ar), 29.42, 27.95, 22.58 (CH₂), and 14.31 (CH₃). FD-MS *m/z* 743.9 (100%), 744.9 (53), 746.0 (14) [M]⁺ for C₅₂H₅₆O₄ (744.42).

***p*-Iodo-calix[4]arene 1,3-dipentyl-2,4-dibenzyl ether SI2**. A suspension of AgCF₃CO₂ (0.63 g, 2.86 mmol) in chloroform (60 ml) was refluxed for 15 min under nitrogen. A solution of calixarene **SI1** (0.41 g, 0.55 mmol) in chloroform (15 ml) was added and the solution was refluxed for additional 15 min. Iodine (0.73 g, 2.86 mmol) was placed in the elbow of a Y-tube, and the vapor of chloroform was passed over it, slowly delivering I₂ into the reaction mixture. After the addition was completed, the mixture was refluxed for 30 min, cooled and quenched with NaHSO₃ (1.5 g) in water (5 ml). The reaction mixture was filtered and the filtrate washed with 10% NaHSO₃, water and dried. The solvent was removed and the product re-precipitated from chloroform/methanol. Yield 79% (0.54 g), mp 225-227 °C. δ_H(400 MHz; CDCl₃) 7.40-7.29 (m, 10H, ArH_{Bz}), 7.22 (s, 4H, ArH), 6.75 (s, 4H, ArH), 4.76 (s, 4H, OCH₂Ph), 4.21 (d,

J 13.4 Hz, 4H, ArCH₂Ar), 3.77 (m, 4H, OCH₂), 2.97 (d, J 13.4 Hz, 4H, ArCH₂Ar), 1.60 (m, 4H, CH₂), 1.10 (m, 4H, CH₂), 0.96 (m, 4H, CH₂) and 0.82 (t, J 7.3 Hz, 6H, CH₃). δ_{C} (100 MHz; CDCl₃) 156.95, 154.81, 137.79 (C_{Ar}), 137.32, 136.88 (CH_{Ar}), 136.82, 136.03 (C_{Ar}), 129.34, 128.32, 128.29 (CH_{Ar}), 86.67, 85.93 (C_{Ar}), 77.46, 75.20 (OCH₂), 30.49 (ArCH₂Ar), 29.11, 27.77, 22.48 (CH₂) and 14.25 (CH₃). FD-MS m/z 1247.5 (100%), 1248.5 (60), 1249.5 (13) [M]⁺ for C₅₂H₅₂I₄O₄ (1248.00).

***p*-Phthalimido-calix[4]arene 1,3-dipentyl-2,4-dibenzyl ether SI3.** A mixture of calixarene SI2 (0.50 g, 0.4 mmol), phthalimide (0.71 g, 4.8 mmol), Cu₂O (0.69 g, 4.8 mmol) and 2,4,6-collidine (20 ml) was stirred at 170 °C under nitrogen for 48 h. The reaction mixture was filtered and filtrate concentrated *in vacuo* to give a black oil. Washing with ethanol gave the solid from which the product was separated by the column chromatography (gradient from dichloromethane to dichloromethane/ethanol, 20:1). Yield 25% (0.13 g), mp 322-324 °C (decomp). δ_{H} (400 MHz; CDCl₃) 7.76 (m, 4H, ArH_{PhI}), 7.66 (m, 4H, ArH_{PhI}), 7.52 (m, 4H, ArH_{PhI}), 7.43-7.28 (m, 10H, ArH_{Bz}), 7.22 (m, 8H, ArH + ArH_{PhI}), 6.65 (s, 4H, ArH), 4.83 (s, 4H, OCH₂Ph), 4.56 (d, J 13.0 Hz, 4H, ArCH₂Ar), 3.94 (m, 4H, OCH₂), 3.28 (d, J 13.0 Hz, 4H, ArCH₂Ar), 1.74 (m, 4H, CH₂), 1.12 (m, 4H, CH₂), 0.98 (m, 4H, CH₂) and 0.85 (t, J 7.2 Hz, 6H, CH₃). δ_{C} (100 MHz; CDCl₃) 167.13, 166.32 (C=O), 156.57, 153.94, 150.10, 137.48, 136.11 (C_{Ar}), 133.84 (CH_{Ar}), 133.42 (C_{Ar}), 133.05 (CH_{Ar}), 131.95, 131.72 (C_{Ar}), 129.24, 128.32, 128.05, 126.36, 126.19 (CH_{Ar}), 125.63 (C_{Ar}), 123.25, 122.66 (CH_{Ar}), 77.56, 75.27 (OCH₂), 31.26 (ArCH₂Ar), 29.33, 27.85, 22.55 (CH₂) and 14.37 (CH₃). FD-MS m/z 1324.6 (100%), 1325.5 (65), 1326.5 (40) [M]⁺ for C₈₄H₆₈N₄O₁₂ (1324.48).

***p*-Amino-calix[4]arene 1,3-dipentyl-2,4-dibenzyl ether 4_{PPPB}.** A mixture of calixarene SI3 (0.13 g, 0.095 mmol), hydrazine hydrate solution (80%, 2.3 ml, 38 mmol) and ethanol (10 ml) was refluxed overnight, cooled and ethanol evaporated. The rest was diluted with water and the solid formed was filtered, washed with water and dried. Yield 93% (0.071 g), mp 214-216 °C (decomp). δ_{H} (400 MHz; CDCl₃) 7.44 (m, 4H, ArH_{Bz}), 7.30 (m, 6H, ArH_{Bz}), 6.27 (s, 4H, ArH), 5.85 (s, 4H, ArH), 4.75 (s, 4H, OCH₂Ph), 4.27 (d, J 13.4 Hz, 4H, ArCH₂Ar), 3.73 (m, 4H, OCH₂), 3.06 (br s, 8H, NH₂), 2.87 (d, J 13.4 Hz, 4H, ArCH₂Ar), 1.67 (m, 4H, CH₂), 1.12 (m, 4H, CH₂), 1.02 (m, 4H, CH₂) and 0.82 (t, J 7.2 Hz, 6H, CH₃). δ_{C} (100 MHz; CDCl₃) 150.49, 148.52, 140.68, 140.11, 138.23, 136.61, 134.71 (C_{Ar}), 128.94, 127.96, 127.52, 115.87, 115.53 (CH_{Ar}), 76.82, 74.91 (OCH₂), 31.23 (ArCH₂Ar), 29.25, 27.99, 22.56 (CH₂) and 14.28 (CH₃). FD-MS m/z 804.6 (100%), 805.6 (65), 806.6 (22) [M]⁺ for C₅₂H₆₀N₄O₄ (804.46).

4-[(2-hexyloctyl)oxy]acetanilide 6. A mixture of 4-acetamidophenol **5** (4.62 g, 30.6 mmol) and K₂CO₃ (4.22 g, 30.6 mmol) was stirred in acetone (80 ml) for 30 min. 1-Bromo-2-hexyloctane (7.37 g, 26.6 mmol) was added, and the reaction mixture was stirred at reflux for 6 days, cooled and filtered. The filtrate was concentrated and separated by the column chromatography (dichloromethane) to give the product as an oil. Yield 69% (6.32 g). δ_{H} (400 MHz; CDCl₃) 7.35 (d, J 8.9 Hz, 2H, ArH), 7.09 (s, 1H, NH), 6.83 (d, J 8.9 Hz, 2H, ArH), 3.78 (d, J 5.7 Hz, 2H, OCH₂), 2.14 (s, 3H, C(O)CH₃), 1.74 (m, 1H, CH), 1.50-1.20 (m, 20H, OCH₂) and 0.87 (t, J 6.8 Hz, 6H, CH₃). FD-MS m/z 347.8 (100%), 348.8 (26), 349.8 (3) [M]⁺ for C₂₂H₃₇NO₂ (347.28).

4-[(2-hexyloctyl)oxy]aniline 7. A mixture **6** (3.47 g, 10 mmol), NaOH (8 g, 200 mmol) dissolved in water (20 ml) and ethanol (100 ml) was refluxed for 6 h under nitrogen. The mixture was concentrated, and products were extracted with diethyl ether. The organic layer was washed with water and dried over NaOH. Evaporation of the solvent gave the product as an oil. Yield 96% (2.93 g). δ_{H} (400 MHz; CDCl₃) 6.73 (m, 2H, ArH), 6.63 (m, 2H, ArH), 3.74 (d, J 6.0 Hz, 2H, OCH₂), 3.39 (br s, 2H, NH₂), 1.72 (m, 1H, CH), 1.49-1.20 (m, 20H, OCH₂) and 0.87 (t, J 6.8 Hz, 6H, CH₃). FD-MS m/z 305.7 (100%), 306.8 (22), 307.8 (2) [M]⁺ for C₂₀H₃₅NO (305.27).

Kinetic studies

Fig. S1-S10 contain the informative regions of ¹H NMR spectra of all the tetraurea dimers in the beginning of the kinetic measurements (*a*) and after a deep conversion (*b*). The signals from which the conversion was monitored are marked with arrows. The first order rate constants for separate kinetic runs are collected in Table S1.

Table S1 Pseudo-first order rate constants obtained from the slopes of $\ln(C_0/C)$ vs. t plots

Tetra-urea	run	k, h^{-1}	averaged k, h^{-1}
δ_{MMMM}	1	0.45	0.47 ± 0.03 (6.4%)
	2	0.46	
	3	0.50	
δ_{MMMP}	1	0.36	0.37 ± 0.02 (5.4%)
	2	0.37	
	3	0.39	
δ_{MPMP}	1	0.35	0.35 ± 0.02 (5.7%)
	2	0.36	
	3	0.33	
δ_{MMPP}	1	0.082	0.090 ± 0.008 (8.9%)
	2	0.091	
	3	0.097	
δ_{MPPP}	1	0.053	0.052 ± 0.003 (5.8%)
	2	0.055	
	3	0.049	
δ_{PPPP}	1	0.025	0.027 ± 0.003 (11.1%)
	2	0.030	
	3	0.026	
δ_{PBPB}	1	0.0082	0.0082 ± 0.0001 (1.2%)
	2	0.0081	
	3	0.0082	
δ_{BBBB}	1	0.00033	0.00026 ± 0.00007 (26.9%)
	2	0.00023	
	3	0.00022	
δ_{PHPH}	1	0.030	0.031 ± 0.002 (6.5%)
	2	0.031	
	3	0.033	
δ_{HHHH}	1	0.0037	0.0039 ± 0.0003 (7.7%)
	2	0.0039	
	3	0.0042	

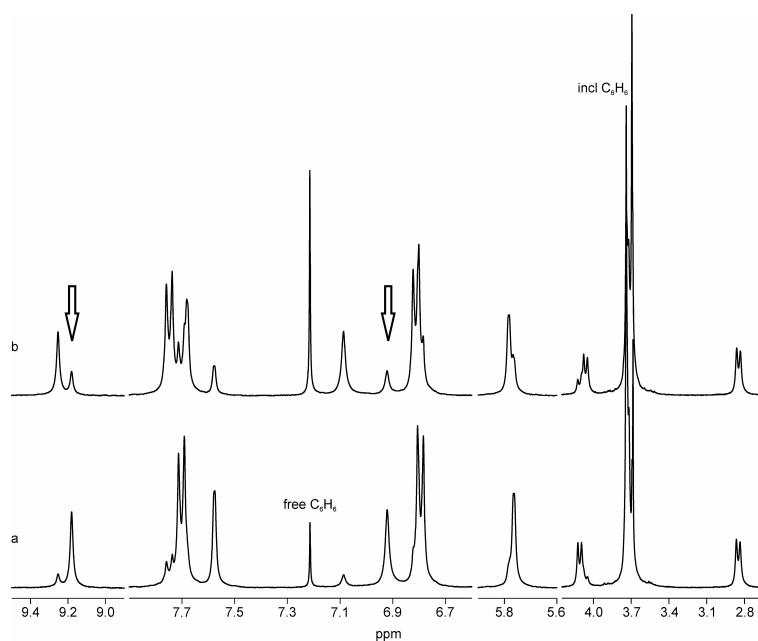


Fig. S1 $\delta_{MMMM}\text{-C}_6\text{H}_6\text{-}\delta_{MMMM}$ in cyclohexane- d_{12} .

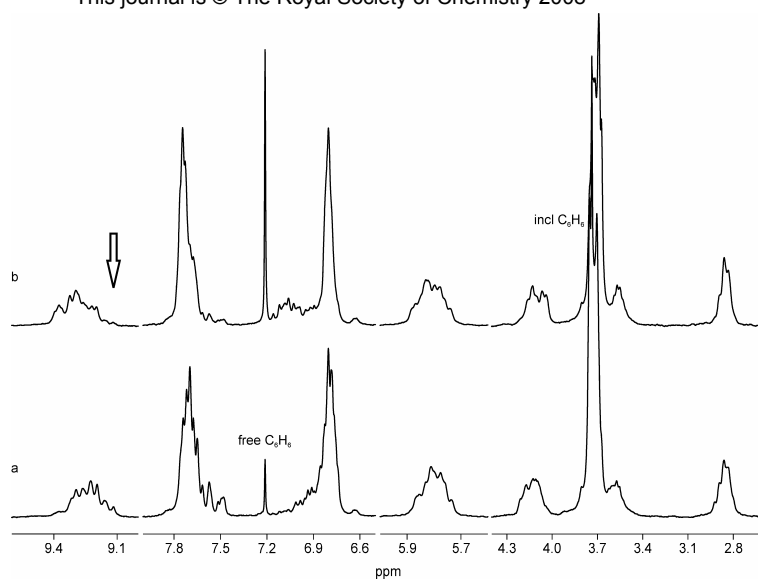


Fig. S2 $8_{\text{MMMP}} \cdot \text{C}_6\text{H}_6 \cdot 8_{\text{MMMP}}$ in cyclohexane- d_{12} .

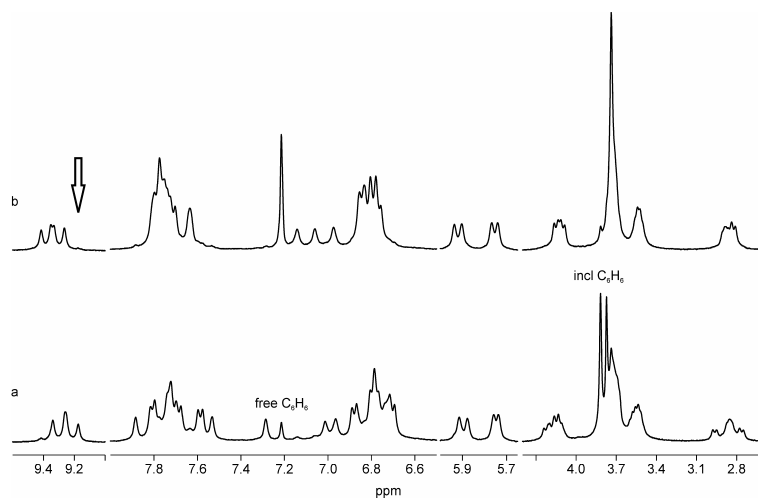


Fig. S3 $8_{\text{MPMP}} \cdot \text{C}_6\text{H}_6 \cdot 8_{\text{MPMP}}$ in cyclohexane- d_{12} .

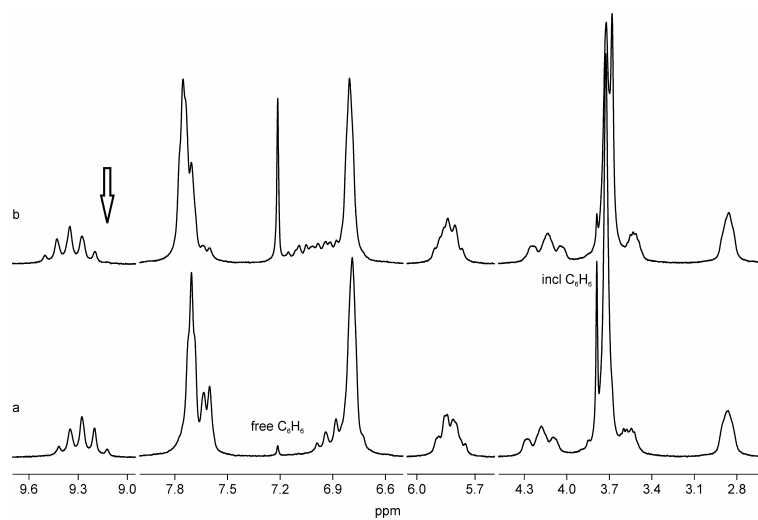


Fig. S4 $8_{\text{MMPP}} \cdot \text{C}_6\text{H}_6 \cdot 8_{\text{MMPP}}$ in cyclohexane- d_{12} .

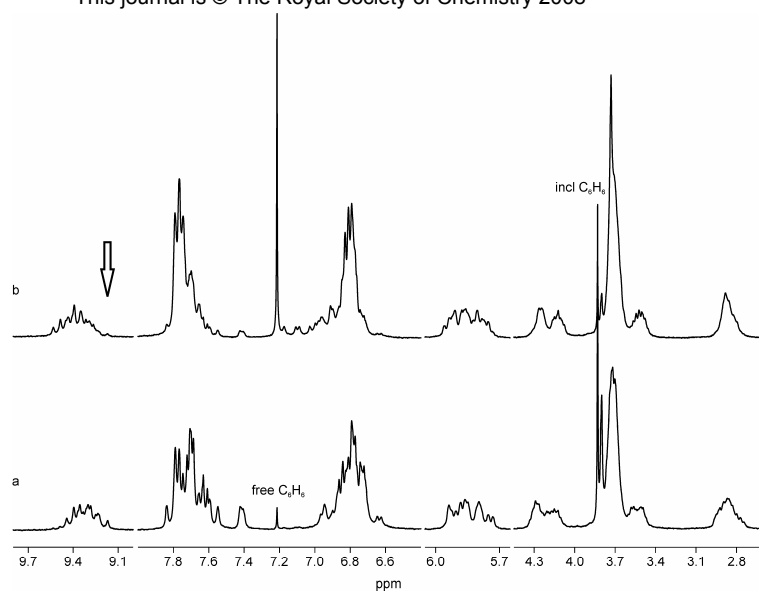


Fig. S5 8MPPP·C₆H₆·8MPPP in cyclohexane-*d*₁₂.

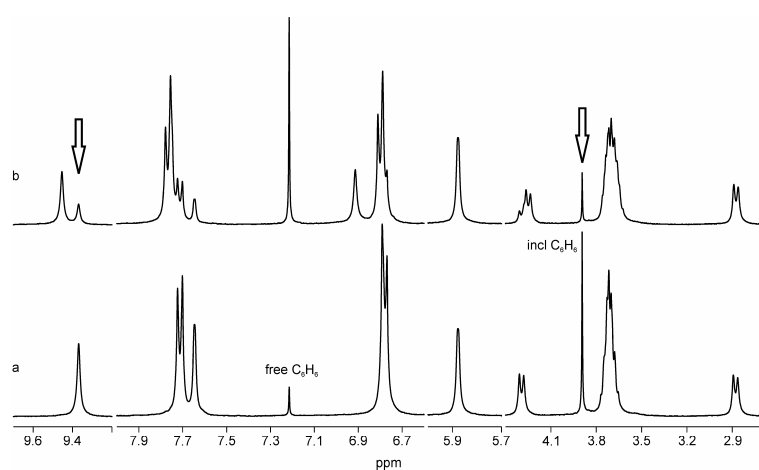


Fig. S6 8PPPP·C₆H₆·8PPPP in cyclohexane-*d*₁₂.

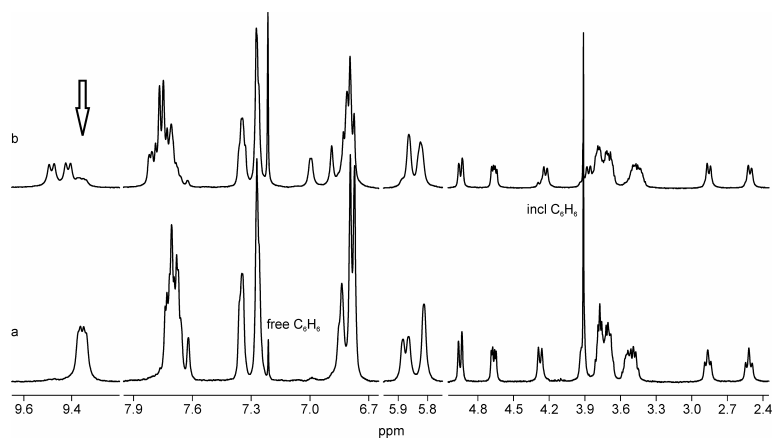


Fig. S7 8PBPB·C₆H₆·8PBPB in cyclohexane-*d*₁₂.

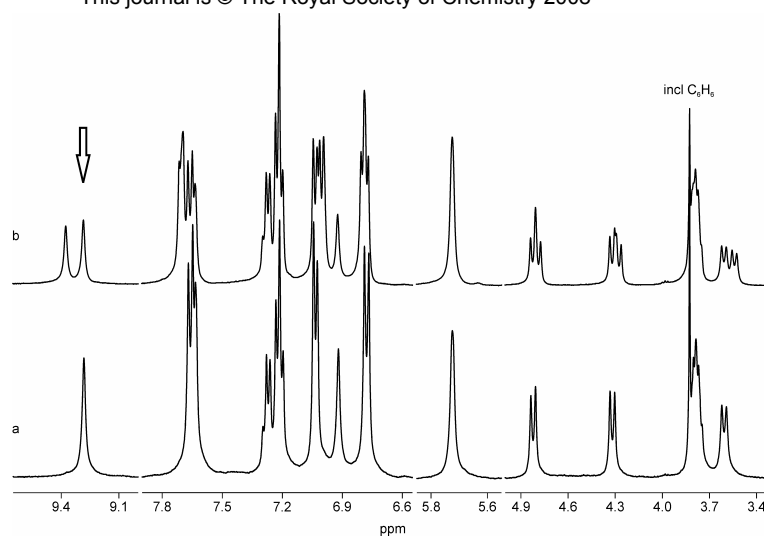


Fig. S8 8_{BBBB}·C₆H₆·8_{BBBB} in cyclohexane-*d*₁₂.

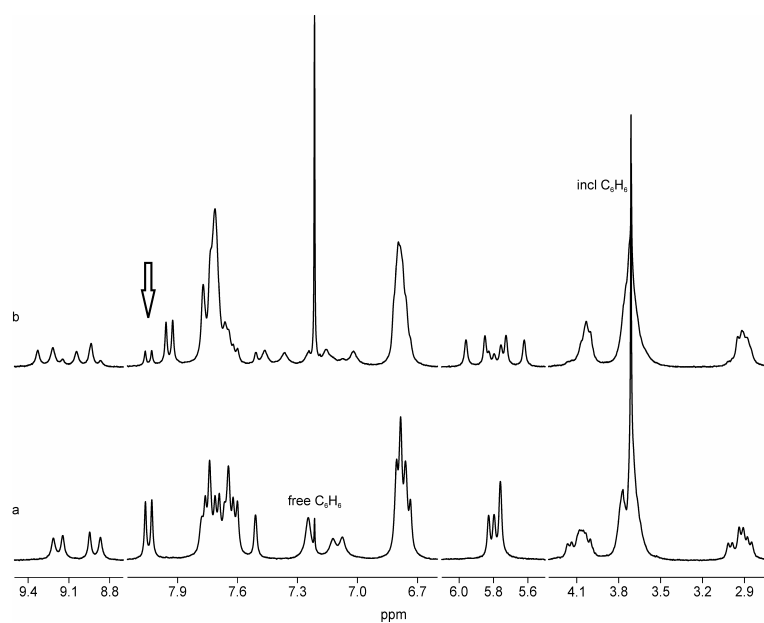


Fig. S9 8_{PHPH}·C₆H₆·8_{PHPH} in cyclohexane-*d*₁₂.

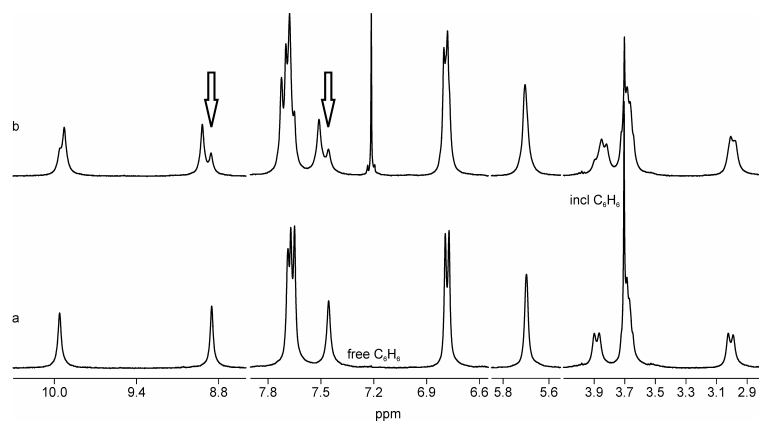


Fig. S10 8_{HHHH}·C₆H₆·8_{HHHH} in cyclohexane-*d*₁₂.