Supplementary Information

Novel pH responsive calix[8]arene hydrogelators: self-organization processes at nanometric scale

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Synthesis of polyelectrolyte calix[8]arene derivatives

Calix[8]arene derivatives **1** (yield = 52%) and **3** (yield = 78%) were synthesized following the procedure described in ref. 20

Synthesis of Calix[8]arene derivatives **6**

Succinic anhydride (86.4 mg, 0.863 mmol) was added to a solution of octa-*p*-amino-octa-*O*-propoxycalix[8]arene (45.0 mg, 0.0345 mmol) in dry pyridine (4.0 mL). The solution was stirred for 24 hours, then the solvent was evaporated and the residue was washed 4 times by sonication in CH_2Cl_2/Et_2O 1/1 (6 mL) and centrifugated. The white powdery compound was then dried under vacuum giving 68 mg of pure compound **6** as free acid (yield = 94%). The corresponding sodium salt utilized for gelations and NMR experiments was obtained adding 8 molar equivalents of NaOH to a water suspension of compound **6** free acid.

Synthesis of Calix[8]arene derivatives **7**

Adipic acid monomethylester (61.3 μL, 0.414 mmol), HOBT (65.3 mg, 0.483 mmol) and DCC (92.6 mg, 0.449 mmol) were dissolved in 2.5 mL of 1/1 solution of dry DMF/CH_2Cl_2 and stirred in a round flask at room temperature for 15 min, then octa-*p*-amino-octa-*O*-propoxycalix[8]arene (45.0 mg, 0.0345 mmol), previously dissolved in 2 mL of 1/1 solution of dry DMF/CH_2Cl_2, was added. The reaction was stirred overnight. The mixture was filtered and the organic solvent was

removed under vacuum. The residue was purified by flash chromatography on silica gel using a gradient of CH_2Cl_2/EtOH, from 98:2 to 94:6 giving 47 mg of pure octa-(adipic-acid monomethylester)-octa-*O*-propoxycalix[8]arene (yield = 56%). Pure compound was dissolved in MeOH (1 mL) and 2 mL of NaOH 1M were added, the mixture was stirred for 3 hours at 50 C° then cooled and slowly added in HCl 1M (5 ml) under vigorously stirring. The precipitate was centrifuged, then washed 3 times with HCl 0.5M and water. Product was dried under vacuum yielding pure compound **7** as free acid in quantitative yield. The corresponding sodium salt utilized for gelations and NMR experiments was obtained adding 8 molar equivalents of NaOH to a water suspension of compound **7** free acid.

Spectral data of compounds **1**, **3**, **6** and **7**

Octa-glycine-octa-*O*-propoxycalix[8]arene trifluoroacetate (**1**). ^{1}H NMR (400 MHz, CD_3OD, 297 K) δ=0.80 (t, *J* = 7.2 Hz, 24 H, $OCH_2CH_2CH_3$), 1.56 (m, 16 H, $OCH_2CH_2CH_3$), 3.49 (bt, 16 H, $OCH_2CH_2CH_3$), 3.73 (bs, 16 H, CH_2NH_2), 3.95 (bs, 16 H, $ArCH_2Ar$), 7.25 (s, 16 H, ArH). ^{13}C NMR (100.62 MHz, CD_3OD, 297 K) δ = 11.1 ($OCH_2CH_2\mathbf{C}H_3$), 24.5 ($OCH_2\mathbf{C}H_2CH_3$), 31.6 ($Ar\mathbf{C}H_2Ar$), 42.0 ($CO\mathbf{C}H_2NH_2$), 76.1 ($O\mathbf{C}H_2CH_2CH_3$), [113.8, 116.8, 119.7, 122.6 ($\mathbf{C}F_3COO^-$)], 121.9 (2 x aromatic >CH), 134.6 (aromatic >***C***-O), 135.8 (2 x aromatic >***C***-CH_2), 153.7 (aromatic >***C***-NH), [162.5, 162.9, 163.3, 163.6 ($CF_3\mathbf{C}OO^-$)], 165.0 (***C***ONH).ES-MS calcd for $C_{96}H_{128}N_{16}O_{16}$ 1763.1856 ($M+H^+$), found 1762.2.

Octa-gaba-octa-*O*-propoxycalix[8]arene trifluoroacetate (**3**). ^{1}H NMR (400 MHz, CD_3OD, 297 K) δ=0.81 (t, *J* = 7.2 Hz, 24 H, $OCH_2CH_2CH_3$), 1.57 (m, 16 H, $OCH_2CH_2CH_3$), 1.97 (m, 16 H, $COCH_2CH_2CH_2NH_2$), 2.45 (t, *J* = 6.8 Hz, 16 H, $COCH_2CH_2CH_2NH_2$) 2.99 (t, 16 H, *J* = 7.2 Hz, $COCH_2CH_2CH_2NH_2$), 3.51 (t, *J* = 6.4 Hz 16 H, $OCH_2CH_2CH_3$), 3.96 (bs, 16 H, $ArCH_2Ar$), 7.24 (s, 16 H, ArH). ^{13}C NMR (100.62 MHz, CD_3OD, 297 K) δ = 11.2 ($OCH_2CH_2\mathbf{C}H_3$), 24.3

($OCH_2\boldsymbol{C}H_2CH_3$), 24.5 ($COCH_2\boldsymbol{C}H_2CH_2NH_2$), 31.4 (Ar$\boldsymbol{C}H_2$Ar), 34.4 (CO$\boldsymbol{C}H_2CH_2CH_2NH_2$), 40.4 ($COCH_2CH_2\boldsymbol{C}H_2NH_2$), 76.0 (O$\boldsymbol{C}H_2CH_2CH_3$), [113.8, 116.8, 119.7, 122.6 ($\boldsymbol{C}F_3COO^-$)], 122.2 (2 x aromatic >CH), 135.1 (aromatic >$\boldsymbol{C}$-O), 135.7 (2 x aromatic >$\boldsymbol{C}$-CH_2), 153.4 (aromatic >$\boldsymbol{C}$-NH), [162.5, 162.9, 163.3, 163.6 ($CF_3\boldsymbol{C}OO^-$)], 172.4 ($\boldsymbol{C}$ONH). ES-MS calcd for $C_{112}H_{160}N_{16}O_{16}$ 1987.6176 ($M+H^+$), found 1986.5.

Octa-succinic-acid-octa-*O*-propoxycalix[8]arene sodium salt (**6**). ^{1}H NMR (400 MHz, CD_3OD/D_2O 1:1, 297 K) δ = 0.75 (t, *J* = 7.2 Hz, 24 H, $OCH_2CH_2\boldsymbol{CH_3}$), 1.52 (m, 16 H, $OCH_2\boldsymbol{CH_2}CH_3$), 2.47 (t, *J* = 6.0 Hz, 16 H, $COCH_2\boldsymbol{CH_2}COOH$), 2.56 (t, *J* = 6.0 Hz, 16 H, $CO\boldsymbol{CH_2}CH_2COOH$), 3.46 (bt, 16 H, $O\boldsymbol{CH_2}CH_2CH_3$), 3.96 (bs, 16 H, $ArCH_2Ar$), 7.19 (s, 16 H, ArH). ^{13}C NMR (100.62 MHz, CD_3OD/D_2O 1:1, 297 K) δ = 10.9 ($OCH_2CH_2\boldsymbol{C}H_3$), 24.0 ($OCH_2\boldsymbol{C}H_2CH_3$), 31.0 (Ar$\boldsymbol{C}H_2$Ar), 34.1 ($COCH_2\boldsymbol{C}H_2COOH$), 34.3 (CO$\boldsymbol{C}H_2CH_2COOH$), 75.8 (O$\boldsymbol{C}H_2CH_2CH_3$), 122.3 (2 x aromatic >CH), 134.5 (aromatic >$\boldsymbol{C}$-O), 135.4 (2 x aromatic >$\boldsymbol{C}$-CH_2), 153.0 (aromatic >$\boldsymbol{C}$-NH) 174.4 ($\boldsymbol{C}$ONH) 181.5 ($\boldsymbol{C}OO^-$). ES-MS calcd for $C_{112}H_{136}N_8O_{32}$ 2107.3544 ($M + H^+$), found 2106.4.

Octa-adipic-acid-octa-*O*-propoxycalix[8]arene sodium salt (**7**). ^{1}H NMR (400 MHz, D_2O, 297 K) δ=0.56 (t, *J* = 7.2 Hz, 24 H, $OCH_2CH_2\boldsymbol{CH_3}$), 1.38 (m, 16 H, $OCH_2\boldsymbol{CH_2}CH_3$), 1.51 (m, 32 H, $COCH_2\boldsymbol{CH_2}\boldsymbol{CH_2}CH_2CO$), 2.09 (t, *J* = 7.2 Hz, 16 H, $COCH_2CH_2CH_2\boldsymbol{CH_2}COOH$), 2.25 (t, *J* = 6.8 Hz, 16 H, $CO\boldsymbol{CH_2}CH_2CH_2CH_2COOH$), 3.30 (bt, 16 H, $O\boldsymbol{CH_2}CH_2CH_3$), 3.88 (bs, 16 H, $ArCH_2Ar$), 7.08 (s, 16 H, ArH). ^{13}C NMR (100.62 MHz, CD_3OD/D_2O 3:1, 297 K) δ = 11.1 ($OCH_2CH_2\boldsymbol{C}H_3$), 24.3 ($OCH_2\boldsymbol{C}H_2CH_3$), 26.8 and 27.0 ($COCH_2\boldsymbol{C}H_2\boldsymbol{C}H_2CH_2COOH$), 31.3 (Ar$\boldsymbol{C}H_2$Ar), 37.7 [$COCH_2(CH_2)_2\boldsymbol{C}H_2COOH$], 38.6 [$CO\boldsymbol{C}H_2(CH_2)_2CH_2COOH$], 75.9 (O$\boldsymbol{C}H_2CH_2CH_3$), 122.4 (2 x aromatic >CH), 134.9 (aromatic >$\boldsymbol{C}$-O), 135.4 (2 x aromatic >$\boldsymbol{C}$-CH_2), 153.1 (aromatic >$\boldsymbol{C}$-NH) 174.9 ($\boldsymbol{C}$ONH) 183.2 ($\boldsymbol{C}OO^-$). ES-MS calcd for $C_{128}H_{168}N_8O_{32}$ 2331.7864 ($M+H^+$), found 2330.3.

Atomic Force Microscopy (AFM) instrument and conditions

The gels were characterized at the nanometer scale by means of Atomic Force Microscopy (AFM) with a Multimode Nanoscope IIIa (Digital Instruments, Santa Barbara, USA) with both 10 and 125 μm scanners. Images were acquired in tapping mode. Sharpened silicon nitride probes with a radius of 30 nm and a nominal spring constant, k=0.06 Nm-1 were employed (Veeco probes). To estimate roughness scan areas of 10×10 μm^2 were imaged and analysed by using Nanoscope RIII software, providing the standard deviation of measured heights (Rq).