Accessing inherently chiral multifunctional structures by desymmetrization of wide-rim calix[4]arene triamine

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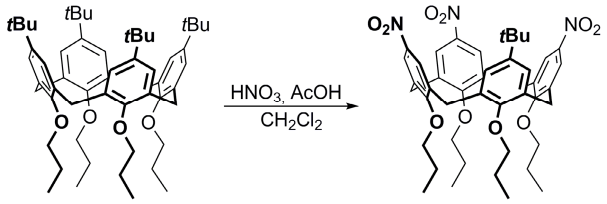
Supplementary Information

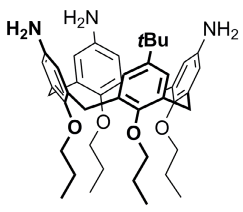
Contents

Synthesis and characterization of novel compounds

General experimental methods: ^{1}H and ^{13}C NMR spectra were acquired on Bruker Avance 400 and Avance 600 instruments at 20 ºC and chemical shifts are reported as ppm referenced to solvent signals. ESI mass spectra were obtained from Sciex TripleTOF 5600+. ECD spectra were obtained from JASCO J-815 ECD spectrometer, path length 1 mm. Optical rotations were measured on a Krüss P8000 polarimeter. Chemicals received from commercial sources were used without further purification.

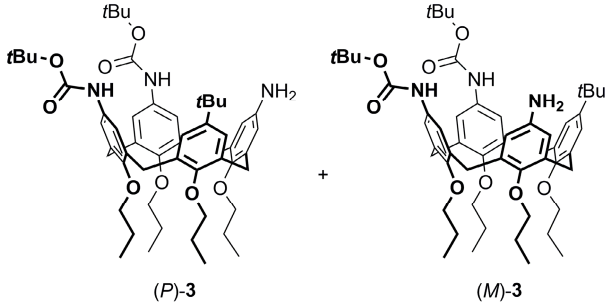


*Calixarene **1*** was prepared by selective nitration of *p-tert*-butylcalix[4]arene tetrakis-*n*-propyl ether[S1] according to the published procedure[S2] with slight modifications: To a stirred solution of *p-tert*-butylcalix[4]arene tetrakis-*n*-propyl ether (4.00 g, 4.9 mmol) in dichloromethane (200 ml) glacial acetic acid (10.0 ml) was added. To the resultant solution, aqueous nitric acid (65%, 50.8 ml, 0.731 mol) was slowly added, and the mixture was stirred at room temperature for 3–4 h, and conversion of the starting material into a single nitration product was monitored by TLC. Nitration can also be initiated by adding a small amount of sodium nitrite, which allows the process to be completed in 10–40 min. The reaction was quenched upon addition of water, and the reaction products were exctracted with dichloromethane. The organic phase was washed with water, brine, filtered through a paper filter and the filtrate was evaporated to dryness under reduced pressure. The residue was purified by column chromatography (silica, gradient from *n*-hexane/dichloromethane 2:1 to dichloromethane) followed by re-crystallization from a dichloromethane/methanol solvent mixture. Yield 2.34 g (61%). The analytical data of the obtained sample were the same as described in the original paper.



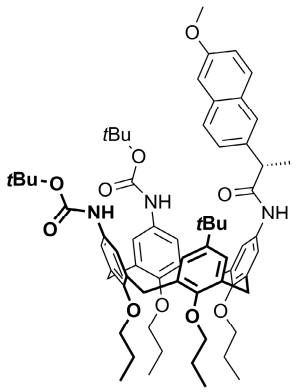
*Triamine **2***. To a solution of calixarene **1** (1.92 g, 2.45 mmol) in toluene (150 ml) a catalytic amount of the ethanol-washed Raney nickel was added. The mixture was vigorously stirred under hydrogen atmosphere (~1 bar) at room temperature for 24 h. The mixture was filtered through a paper filter and the filtrate was evaporated to dryness under reduced pressure. Yield 1.56 g (91%), white solid. M.p. 135–137 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (s, 2H, ArH), 6.30 (s, 2H, ArH), 5.79 (d, 2H, ^{4}J = 2.8 Hz, ArH), 5.70 (s, 2H, ^{4}J = 2.8 Hz, ArH), 4.37 (d, 2H, ^{2}J = 13.2 Hz, $ArCH_2Ar$), 4.31 (d, 2H, ^{2}J = 13.2 Hz, $ArCH_2Ar$), 3.90–3.84 (m, 2H, OCH_2), 3.82–3.77 (m, 2H,

OCH_2), 3.68–3.62 (m, 4H, OCH_2), 3.00 (d, 2H, ^2J = 13.2 Hz, $ArCH_2Ar$), 2.90 (d, 2H, ^2J = 13.2 Hz, $ArCH_2Ar$), 1.95–1.79 (m, 8H, $OCH_2C\underline{H}_2$), 1.25 (s, 9H, $C(CH_3)_3$), 1.05 (t, 6H, ^3J = 7.5 Hz, $CH_2C\underline{H}_3$), 0.88 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.87 (t, 3H, ^3J = 7.5 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.14, 150.59, 149.34, 143.95, 140.32, 139.94, 136.71, 135.13, 134.70, 134.30 (C_{Ar}), 125.28, 115.69, 115.67, 115.49 (CH_{Ar}), 76.77, 76.57, 76.35 (OCH_2), 33.92 ($\underline{C}(CH_3)_3$), 31.61 ($C(\underline{C}H_3)_3$), 31.30, 31.07 ($ArCH_2Ar$), 23.28, 23.01, 22.84 ($OCH_2\underline{C}H_2$), 10.63, 9.98, 9.93 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 732.4143 $[M+K]^+$ for $C_{44}H_{59}KN_3O_4$ (732.4137).

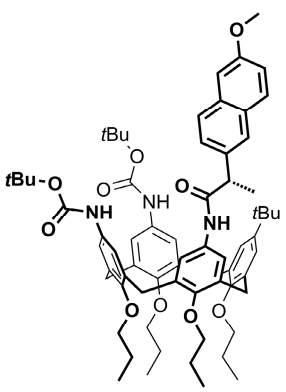


(*P*)-**3** (*M*)-**3**

Bis-Boc-protected calixarene ***3***. To a vigorously stirred solution of triamine **2** (1.24 g, 1.79 mmol) in dry dichloromethane (25 ml) a solution of Boc_2O (0.779 g, 3.57 mmol) in dry dichloromethane (25 ml) was added dropwise and the mixture was stirred at room temperature for 24 h. The solvent was removed under reduced pressure and the residue was purified by column chromatography (silica, gradient from *n*-hexane/ethyl acetate 6:1 to *n*-hexane/ethyl acetate 3:1). Yield 0.475 g (30%), white solid. M.p. 157–159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41 (bs, 1H, NH_{Boc}), 7.16 (bs, 1H, NH_{Boc}), 7.00 (d, 1H, ^4J = 2.3 Hz, ArH), 6.96 (d, 1H, ^4J = 2.3 Hz, ArH), 6.86 (bs, 1H, ArH), 6.33 (bs, 1H, ArH), 6.02 (bs, 1H, ArH), 5.92 (bs, 1H, ArH), 5.63 (d, 1H, ^4J = 2.5 Hz, ArH), 5.53 (d, 1H, ^4J = 2.5 Hz, ArH), 4.38 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 4.36 (d, 1H, ^2J = 13.7 Hz, $ArCH_2Ar$), 4.35 (d, 1H, ^2J = 12.9 Hz, $ArCH_2Ar$), 4.32 (d, 1H, ^2J = 13.1 Hz, $ArCH_2Ar$), 3.95–3.79 (m, 4H, OCH_2), 3.67–3.56 (m, 4H, OCH_2), 3.11 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 3.05 (d, 1H, ^2J = 13.7 Hz, $ArCH_2Ar$), 3.00 (d, 1H, ^2J = 12.9 Hz, $ArCH_2Ar$), 2.99 (d, 1H, ^2J = 13.1 Hz, $ArCH_2Ar$), 1.93–1.76 (m, 8H, $OCH_2C\underline{H}_2$), 1.53 (s, 9H, $OC(CH_3)_3$), 1.39 (s, 9H, $OC(CH_3)_3$), 1.31 (s, 9H, $ArC(CH_3)_3$), 1.05 (t, 3H, ^3J = 7.4 Hz, CH_3), 1.04 (t, 3H, ^3J = 7.4 Hz, CH_3), 0.85 (t. 3H, ^3J = 7.4 Hz, CH_3), 0.83 (t, 3H, ^3J = 7.4 Hz, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.48 (C_{Ar}), 154.82 (C=O), 153.73, 153.28 (C_{Ar}), 152.94 (C=O), 149.30, 144.22, 139.47, 137.06, 137.04, 135.77, 135.44, 134.63, 134.61, 134.09, 133.80, 131.84, 131.66 (C_{Ar}), 125.81, 125.43, 124.41, 123.67, 118.96, 118.84, 115.13, 115.04 (CH_{Ar}), 80.06, 78.93 ($O\underline{C}(CH_3)_3$), 76.79, 76.49, 76.44, 76.32 (OCH_2), 34.00 ($Ar\underline{C}(CH_3)_3$), 31.63 ($ArC(\underline{C}H_3)_3$), 31.31, 31.26, 31.09, 31.02 ($ArCH_2Ar$), 28.42, 28.36 ($OC(\underline{C}H_3)_3$), 23.37, 23.35, 22.98, 22.81 ($OCH_2\underline{C}H_2$), 10.77, 10.75, 9.85, 9.82 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 894.5631 $[M+H]^+$ for $C_{54}H_{76}N_3O_8$ (894.5627).



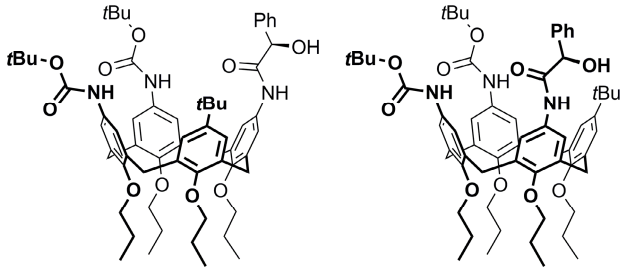
(*P*,*S*)-**4a**



(*M*,*S*)-**4b**

*Bis-Boc-protected diastereomers (P,S)-**4a** and (M,S)-**4b***. To a cooled (0–5 °C) solution of calixarene **3** (0.484 g, 0.54 mmol) and (*S*)-naproxen (0.15 g, 0.65 mmol) in dry dichloromethane (15 ml) DIC (0.253 ml, 1.62 mmol) and DMAP (0.032 g, 0.27 mmol) were added at stirring. The mixture was stirred at room temperature for 24 h and then washed with aqueous HCl (2 M), water, brine, dried and the solvent was evaporated under reduced pressure. The residue was subjected to column chromatography (silica, gradient from *n*-hexane/ethyl acetate 9:1 to *n*-hexane/ethyl acetate 7:1) and calixarenes (*M*,*S*)-**4a** and (*P*,*S*)-**4b** were eluted successively. Compound (*P*,*S*)-**4a**: Yield 0.143 g (24%), white solid. M.p. 157–159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75–7.67 (m, 3H, ArH_{Nap}), 7.43–7.37 (m, 1H, ArH_{Nap}), 7.17–7.11 (m, 2H, ArH_{Nap}), 6.81 (bs, 2H, NH), 6.77–6.60 (m, 3H, ArH), 6.50 (bs, 1H, ArH), 6.43 (bs, 1H, ArH), 6.30 (bs, 1H, ArH), 6.16 (bs, 1H, NH), 6.11 (bs, 1H, ArH), 4.38 (d, 1H, ^{2}J = 12.8 Hz, $ArCH_2Ar$), 4.36 (d, 1H, ^{2}J = 12.8 Hz, $ArCH_2Ar$), 4.34 (1H, ^{2}J = 13.3 Hz, $ArCH_2Ar$), 4.31 (d, 1H, ^{2}J = 13.3 Hz, $ArCH_2Ar$), 3.92 (s, 3H, OCH_3), 3.83–3.69 (m, 9H, OCH_2+C(O)CH), 3.09 (d, 1H, ^{2}J = 12.8 Hz, $ArCH_2Ar$), 3.06 (d, 1H, ^{2}J = 12.8 Hz, $ArCH_2Ar$), 3.05 (d, 1H, ^{2}J = 13.3 Hz, $ArCH_2Ar$), 2.96 (d, 1H, ^{2}J = 13.3 Hz, $ArCH_2Ar$), 1.94–1.78 (m, 8H, $OCH_2C\underline{H}_2$), 1.59 (d, 3H, ^{3}J = 7.0 Hz, $CHC\underline{H}_3$), 1.48 (s, 9H, $C(CH_3)_3$), 1.45 (s, 9H, $C(CH_3)_3$), 1.09 (s, 9H, $C(CH_3)_3$), 1.00–0.87 (m, 12H, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ =171.95 (C=O), 157.63 (C_{Ar}), 154.26 (C=O), 153.54 (C_{Ar}), 153.16 (C=O), 152.87, 152.60, 144.44, 136.67, 135.53, 135.40, 135.29, 134.62, 134.57, 133.89, 133.84, 133.66, 131.81, 131.71, 131.45 (C_{Ar}), 129.20 (CH_{Ar}), 128.92 (C_{Ar}), 127.54, 126.25, 126.17, 125.28, 125.18, 121.09, 120.33, 119.86, 119.82, 119.07, 118.89, 118.68, 105.58 (CH_{Ar}), 79.98 ($O\underline{C}(CH_3)_3$), 76.67 (OCH_2), 55.27 (OCH_3), 47.41 (C(O)$\underline{C}$H), 33.79 ($\underline{C}(CH_3)_3$), 31.37 ($C(\underline{C}H_3)_3$), 31.15, 31.08, 31.05, 30.96 ($ArCH_2Ar$), 28.40, 28.34 ($C(\underline{C}H_3)_{3\ Boc}$), 23.20, 23.11, 23.06, 22.92 ($OCH_2\underline{C}H_2$), 19.00 ($CH\underline{C}H_3$), 10.36, 10.31, 10.20, 10.11 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 1123.6737 $[M+NH_4]^+$ for $C_{68}H_{91}N_4O_{10}$ (1123.6730). Compound (*M*,*S*)-**4b**: Yield 0.125 g (21%), white solid. M.p. 177–179 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.66 (m, 3H, ArH_{Nap}), 7.41–7.35 (m, 1H, ArH_{Nap}), 7.19–7.10 (m, 2H, ArH_{Nap}), 6.86 (bs, 1H, ArH), 6.79 (bs, 1H, ArH), 6.76–6.62 (m, 3H, ArH, NH), 6.57 (bs, 1H, ArH), 6.53 (bs, 1H, ArH), 6.34 (bs, 1H, ArH), 6.23–6.04 (m, 3H, ArH+NH), 4.40–4.28 (m, 4H, $ArCH_2Ar$), 3.93 (s, 3H, OCH_3), 3.85–3.66 (m, 9H, OCH_2+C(O)CH), 3.13–2.92 (m, 4H, $ArCH_2Ar$), 1.94–1.77 (m, 8H, $OCH_2C\underline{H}_2$), 1.62 (d, 3H,

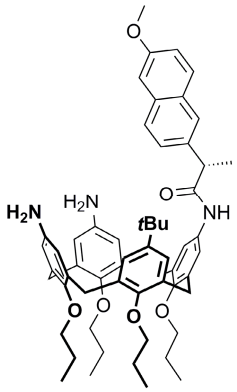
^3J = 7.0 Hz, CHC<u>H</u>$_3$), 1.48 (s, 9H, C(CH$_3$)$_3$), 1.46 (s, 9H, C(CH$_3$)$_3$), 1.02 (s, 9H, C(CH$_3$)$_3$), 1.00–0.81 (m, 12H, CH$_2$C<u>H</u>$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 172.17 (C=O), 157.72 (C_{Ar}), 154.31 (C=O), 153.53 (C_{Ar}), 153.22 (C=O), 152.81, 152.62, 144.30, 136.37, 135.43, 135.31, 135.26, 134.74, 134.65, 134.13, 133.79, 133.71, 131.97, 131.66, 131.33 (C_{Ar}), 129.24 (CH_{Ar}), 128.97 (C_{Ar}), 127.60, 126.30, 126.05, 125.26, 125.03, 120.53, 120.29, 120.20, 119.78, 119.15, 118.80, 118.71, 105.60 (CH_{Ar}), 80.00 (O<u>C</u>(CH$_3$)$_3$), 76.68 (OCH$_2$), 55.30 (OCH$_3$), 47.29 (C(O)<u>C</u>H), 33.73 (Ar<u>C</u>(CH$_3$)$_3$), 31.33 (ArC(<u>C</u>H$_3$)$_3$), 31.16, 31.10, 31.01, 30.99 (ArCH$_2$Ar), 28.39, 28.37 (OC(<u>C</u>H$_3$)$_3$), 23.16, 23.12, 23.07, 22.93 (OCH$_2$<u>C</u>H$_2$), 18.33 (CH<u>C</u>H$_3$), 10.38, 10.33, 10.17, 10.12 (CH$_2$<u>C</u>H$_3$) ppm. ESI-MS *m*/*z*: 1123.6738 [M+NH$_4$]$^+$ for $C_{68}H_{91}N_4O_{10}$ (1123.6730).



(*P*,*R*)-**5a** (*M*,*R*)-**5b**

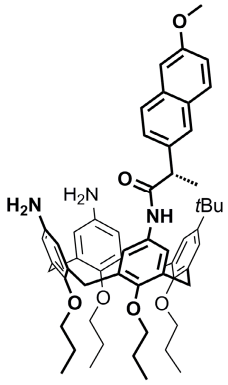
*Bis-Boc-protected diastereomers (P,R)-**5a** and (M,R)-**5b***. To a cooled (0–5 °C) solution of (*R*)-mandelic acid (0.454 g, 2.99 mmol) and N-hydroxysuccinimide (0.344 g, 2.99 mmol) in dry acetone (10 ml), a solution of DCC (0.615 g, 2.99 mmol) in dry acetone (10 ml) was added dropwise at strirring. The mixture was stirred at cooling for 2 h and then a solution of calixarene **3** (0.89 g, 0.996 mmol) in dry acetone (10 ml) was added. The mixture was stirred at room temperature for 24 h. The precipitate formed was separated by filtration, washed with acetone and discarded. The combined filtrates were evaporated under reduced pressure, and the residue was dissolved in dichloromethane. The solution was washed with water and brine, dried and the solven was evaporated. The residue was subjected to column chromatography (silica, gradient from *n*-hexane/ethyl acetate 7:1 to *n*-hexane/ethyl acetate 4:1) and fractions containing calixarenes (*P*,*R*)-**5a** and (*M*,*R*)-**5b** were eluted successively, from which pure compounds were obtained upon recrystallization from *n*-hexane. Compound (*P*,*R*)-**5a**: Yield 0.417 g (41%), white solid. M.p. 160–162 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.94 (bs, 1H, NH), 7.45–7.40 (m, 2H, ArH$_{Ph}$), 7.31–7.19 (m, 3H, ArH$_{Ph}$), 7.17 (bs, 1H, ArH), 7.09 (bs, 1H, ArH), 7.02 (bs, 1H, ArH), 6.97 (bs, 1H, ArH), 6.92 (bs, 1H, ArH), 6.40 (bs, 1H, ArH), 6.00–5.80 (m, 4H, ArH+NH), 5.09 (d, 1H, ^3J = 4.3 Hz, C<u>H</u>(OH)Ph), 4.45–4.32 (m, 4H, ArCH$_2$Ar), 3.97–3.85 (m, 4H, OCH$_2$), 3.69–3.62 (m, 2H, OCH$_2$), 3.62–3.54 (m, 2H, OCH$_2$), 3.13–2.99 (m, 4H, ArCH$_2$Ar), 1.95–1.75 (m, 8H, OCH$_2$C<u>H</u>$_2$), 1.54 (s, 9H, C(CH$_3$)$_3$), 1.43 (s, 9H, C(CH$_3$)$_3$), 1.35 (s, 9H, C(CH$_3$)$_3$), 1.07 (t, 3H, ^3J = 7.4 Hz, CH$_2$C<u>H</u>$_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, CH$_2$C<u>H</u>$_3$), 0.88–0.81 (m, 6H, CH$_2$C<u>H</u>$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 170.23 (C=O), 155.24 (C_{Ar}), 154.31 (C=O), 153.75 (C_{Ar}), 153.17 (C=O), 152.27, 152.07, 144.68, 138.83, 137.11, 136.75, 135.54, 135.22, 134.65, 134.59,

133.73, 133.44, 131.93, 131.59, 131.35 (C_{Ar}), 128.31, 127.84, 126.19, 125.47, 119.89, 119.88, 119.72, 119.55, 119.47, 119.46, 119.28 (CH_{Ar}), 81.39, 80.18 (O<u>C</u>$(CH_3)_3$), 76.87, 76.75, 76.56, 76.30 (OCH_2), 74.46 (CH(OH)), 34.06 (Ar<u>C</u>$(CH_3)_3$), 31.71 (ArC(<u>C</u>$H_3)_3$), 31.46, 31.14, 30.87 ($ArCH_2Ar$), 28.43, 28.30 (OC(<u>C</u>$H_3)_3$), 23.40, 23.34, 22.91, 22.84 ($OCH_2\underline{C}H_2$), 10.75, 10.71, 9.83, 9.77 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 1050.5811 $[M+Na]^+$ for $C_{62}H_{81}NaN_3O_{10}$ (1050.5814). Compound (*M*,*R*)-**5b**: Yield 0.299 g (29%), white solid. M.p. 152–154 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (bs, 1H, NH), 7.44–7.38 (m, 2H, ArH_{Ph}), 7.31–7.20 (m, 4H, ArH+ArH_{Ph}), 7.04 (bs, 2H, ArH), 6.92 (bs, 1H, ArH), 6.88 (d, 1H, ^4J = 2.3 Hz, ArH), 6.43 (bs, 1H, ArH), 6.00–5.70 (m, 4H, ArH+NH), 5.12 (d, 1H, ^3J = 4.6 Hz, C<u>H</u>(OH)Ph), 4.44–4.32 (m, 4H, $ArCH_2Ar$), 3.96–3.84 (m, 4H, OCH_2), 3.70–3.62 (m, 2H, OCH_2), 3.62–3.55 (m, 2H, OCH_2), 3.12–3.02 (m, 4H, $ArCH_2Ar$), 1.95–1.75 (m, 8H, $OCH_2C\underline{H}_2$), 1.52 (s, 9H, $C(CH_3)_3$), 1.42 (s, 9H, $C(CH_3)_3$), 1.36 (s, 9H, $C(CH_3)_3$), 1.07 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.87–0.80 (m, 6H, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.53 (C=O), 155.32 (C_{Ar}), 154.23, 154.21 (C=O), 153.57 153.10, 152.55, 152.14, 144.51, 138.77, 136.81, 136.77, 136.54, 135.67, 135.39, 134.50, 134.43, 133.97, 132.08, 131.32 (C_{Ar}), 128.42, 128.04, 126.47, 125.68, 125.64, 120.14, 119.67, 119.57, 119.38, 118.84, 118.65 (CH_{Ar}), 81.32, 79.94 (O<u>C</u>$(CH_3)_3$), 76.93, 76.76, 76.56, 76.28 (OCH_2), 74.37 (CH(OH)), 34.07 (Ar<u>C</u>$(CH_3)_3$), 31.70 (ArC(<u>C</u>$H_3)_3$), 31.49, 31.48, 31.27, 31.12 ($ArCH_2Ar$), 28.41, 28.27 (OC(<u>C</u>$H_3)_3$), 23.39, 23.33, 22.89, 22.81 ($OCH_2\underline{C}H_2$), 10.74, 10.70, 9.83, 9.76 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 1050.5812 $[M+Na]^+$ for $C_{62}H_{81}NaN_3O_{10}$ (1050.5814).



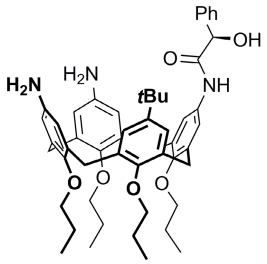
*Diamine (M,S)-**6a***. To a stirred solution of calixarene (*P*,*S*)-**4a** (0.128 g, 0.12 mmol) in dry dichloromethane (10 ml) trifluoroacetic acid (0.41 ml, 5.51 mmol) was added and the mixture was stirred for 2 h at room temperature. Saturated aqueous $NaHCO_3$ was added, the organic phase was separated, washed with water and brine, dried and the solvent was evaporated under reduced pressure. Yield 0.103 g (98%), white solid. M.p. 148–150 °C. ^{1}H NMR (400 MHz, $CDCl_3$, major conformer): δ = 8.38 (s, 1H, NHCO), 7.76–7.66 (m, 2H, ArH_{Nap}), 7.65–7.61 (m, 1H, ArH_{Nap}), 7.37–7.31 (m, 1H, ArH_{Nap}), 7.17–7.07 (m, 2H, ArH_{Nap}), 7.06 (d, 1H, ^4J = 2.2 Hz, ArH), 6.99 (d, 1H, ^4J = 2.2 Hz, ArH), 6.43 (d, 1H, ^4J = 2.6 Hz, ArH), 6.37 (d, 1H, ^4J = 2.6 Hz, ArH), 5.92 (d, 1H, ^4J = 2.2 Hz, ArH), 5.83 (d, 1H, ^4J = 2.2 Hz, ArH), 5.21 (d, 1H, ^4J = 2.6 Hz, ArH), 5.18 (d, 1H, ^4J = 2.6 Hz, ArH), 4.38 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.31 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 4.30 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 4.22 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 3.90 (s, 3H, OCH_3), 3.90–3.85 (m, 2H, OCH_2),

3.83–3.77 (m, 2H, OCH_2), 3.70–3.59 (m, 3H, OCH_2+C<u>H</u>CH_3), 3.54–3.48 (m, 2H, OCH_2), 3.11 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.97 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 2.93 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 2.79 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 1.93–1.71 (m, 8H, $OCH_2C\underline{H}_2$), 1.54 (d, 3H, ^3J = 7.2 Hz, $CHC\underline{H}_3$), 1.38 (s, 9H, $C(CH_3)_3$), 1.07 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.03 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.83 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.80 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major conformer): δ = 174.06 (C=O), 157.58, 155.69, 153.84, 150.93, 149.19, 144.12, 140.00, 138.86, 137.53, 137.23, 137.08, 136.07, 135.75, 134.26, 134.19, 134.10, 134.00, 133.28, 131.35 (C_{Ar}), 129.23, (CH_{Ar}) 128.74 (C_{Ar}), 127.17, 126.81, 125.85, 125.58, 125.48, 124.98, 118.99, 116.07, 115.88, 114.86, 114.68, 105.45 (CH_{Ar}), 76.66, 76.43, 76.30, 76.26 (OCH_2), 55.23 (OCH_3), 46.64 (C(O)<u>C</u>H), 34.03 (<u>C</u>$(CH_3)_3$), 31.70 (C(<u>C</u>$H_3)_3$), 31.17, 31.15, 31.01, 30.96 ($ArCH_2Ar$), 23.39, 23.35, 22.94, 22.66 ($OCH_2\underline{C}H_2$), 18.94 ($CH\underline{C}H_3$), 10.79, 9.73 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 906.5416 $[M+H]^+$ for $C_{58}H_{72}N_3O_6$ (906.5416).

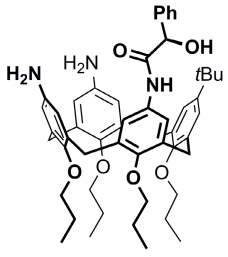


*Diamine (P,S)-**6b*** was prepared as described for compound (*M*,*S*)-**6a** from calixarene (*M*,*S*)-**4b** (0.081 g, 0.073 mmol) and trifluoroacetic acid (0.260 ml, 3.5 mmol) in dry dichloromethane (6.5 ml). Yield 0.065 g (98%), white solid. M.p. 156–158 °C ^{1}H NMR (400 MHz, $CDCl_3$, major conformer): δ = 8.39 (s, 1H, N<u>H</u>CO), 7.66–7.61 (m, 2H, ArH_{Nap}), 7.59–7.56 (m, 1H, ArH_{Nap}), 7.30–7.27 (m, 1H, ArH_{Nap}), 7.13–7.06 (m, 2H, ArH_{Nap}), 7.00 (d, 1H, ^4J = 2.4 Hz, ArH), 6.92 (d, 1H, ^4J = 2.4 Hz, ArH), 6.46 (d, 1H, ^4J = 2.7 Hz, ArH), 6.41 (d, 1H, ^4J = 2.7 Hz, ArH), 5.91 (d, 1H, ^4J = 2.4 Hz, ArH), 5.70 (d, 1H, ^4J = 2.4 Hz, ArH), 5.36 (d, 1H, ^4J = 2.7 Hz, ArH), 4.98 (d, 1H, ^4J = 2.7 Hz, ArH), 4.34 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.30 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.27 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.22 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 3.91 (s, 3H, OCH_3), 3.89–3.76 (m, 5H, OCH_2+C<u>H</u>CH_3), 3.64–3.56 (m, 2H, OCH_2), 3.52–3.46 (m, 2H, OCH_2), 3.08 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.81 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.87 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.58 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 1.90–1.70 (m, 8H, $OCH_2C\underline{H}_2$), 1.49 (d, 3H, ^3J = 7.1 Hz, $CHC\underline{H}_3$), 1.27 (s, 9H, $C(CH_3)_3$), 1.06 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.02 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.80 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.80 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major conformer): δ = 173.65 (C=O), 157.58, 155.69, 153.91, 151.10, 149.14, 144.10, 139.97, 138.86, 137.72, 137.65, 137.46, 136.15, 135.67, 134.21, 134.16, 134.06, 133.85, 133.29, 131.33 (C_{Ar}), 128.96, (CH_{Ar}) 128.76 (C_{Ar}), 127.00, 126.45, 126.42, 125.97, 125.83, 125.47, 125.25, 119.08, 116.18, 115.96, 114.79, 114.68, 105.57 (CH_{Ar}), 76.68, 76.43, 76.32, 76.25 (OCH_2), 55.26 (OCH_3), 46.72 (C(O)<u>C</u>H), 33.94 (<u>C</u>$(CH_3)_3$), 31.62 (C(<u>C</u>$H_3)_3$), 31.15, 31.09, 31.01

(ArCH$_2$Ar), 23.41, 23.37, 22.95, 22.70 (OCH$_2$CH$_2$), 19.18 (CHCH$_3$), 10.81, 9.75, 9.73 (CH$_2$CH$_3$) ppm. ESI-MS *m*/*z*: 906.5416 $[M+H]^+$ for $C_{58}H_{72}N_3O_6$ (906.5416).

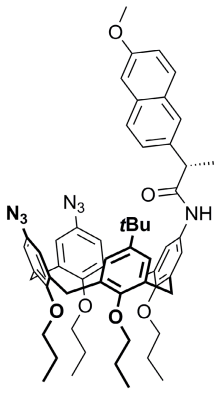


*Diamine (M,R)-**7a*** was prepared as described for compound (*M*,*S*)-**6a** from calixarene (*P*,*R*)-**5a** (0.417 g, 0.406 mmol) and trifluoroacetic acid (1.0 ml, 13.4 mmol) in dry dichloromethane (25 ml). Yield 0.337 g (99%), white solid. M.p. 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$, major conformer): δ = 8.88 (s, 1H, NH), 7.32–7.25 (m, 5H, ArH$_{Ph}$), 7.07 (d, 1H, ^4J = 2.4 Hz, ArH), 6.99 (d, 1H, ^4J = 2.4 Hz, ArH), 6.47 (d, 1H, ^4J = 2.7 Hz, ArH), 6.45 (d, 1H, ^4J = 2.7 Hz, ArH), 5.84 (d, 1H, ^4J = 2.5 Hz, ArH), 5.72 (d, 1H, ^4J = 2.5 Hz, ArH), 5.44 (d, 1H, ^4J = 2.8 Hz, ArH), 5.02 (d, 1H, ^4J = 2.8 Hz, ArH), 4.86 (s, 1H, CH(OH)Ph), 4.38 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 4.32 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 4.30 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 4.25 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 3.95–3.76 (m, 4H, OCH$_2$), 3.76 (s, 1H, CH(OH)), 3.65–3.60 (m, 2H, OCH$_2$), 3.54–3.48 (m, 2H, OCH$_2$), 3.12 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 2.98 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 2.91 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 2.85 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 1.91–1.71 (m, 8H, OCH$_2$CH$_2$), 1.38 (s, 9H, C(CH$_3$)$_3$), 1.08 (t, 3H, ^3J = 7.4 Hz, CH$_2$CH$_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, CH$_2$CH$_3$), 0.81 (t, 3H, ^3J = 7.4 Hz, CH$_2$CH$_3$), 0.80 (t, 3H, ^3J = 7.4 Hz, CH$_2$CH$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major conformer): δ = 172.06 (C=O), 155.73, 154.19, 151.07, 149.43, 144.30, 140.14, 140.10, 138.42, 137.58, 137.56, 136.21, 135.75, 134.68, 134.23, 134.20, 134.11, 130.33 (C$_{Ar}$), 128.55, 128.37, 128.03, 125.93, 125.52, 125.48, 124.46, 116.16, 116.02, 115.05, 114.84 (CH$_{Ar}$), 76.72, 76.48, 76.33, 76.23 (OCH$_2$), 73.29 (CH(OH)), 34.04 (ArC(CH$_3$)$_3$), 31.74 (ArC(CH$_3$)$_3$), 31.24, 31.15, 31.02, 31.00 (ArCH$_2$Ar), 23.42, 23.39, 22.93, 22.70 (OCH$_2$CH$_2$), 10.81, 9.73, 9.69 (CH$_2$CH$_3$) ppm. ESI-MS *m*/*z*: 828.4943 $[M+H]^+$ for. $C_{52}H_{66}N_3O_6$ (828.4946).



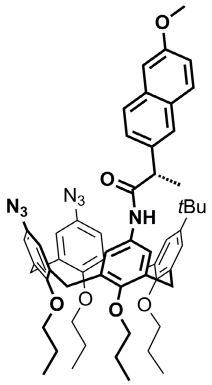
*Diamine (P,R)-**7b*** was prepared as described for compound (*M*,*S*)-**6a** from calixarene (*M*,*R*)-**5b** (0.31 g, 0.302 mmol) and trifluoroacetic acid (1.0 ml, 13.4 mmol) in dry dichloromethane (25 ml). Yield 0.337 g (99%), white solid. M.p. 146–148 °C. ^{1}H NMR (400 MHz, $CDCl_3$, major conformer): δ = 8.73 (s, 1H, NH), 7.42–7.28 (m, 5H, ArH$_{Ph}$), 7.05 (d, 1H, ^4J = 2.3 Hz, ArH), 7.02 (d, 1H, ^4J = 2.3 Hz, ArH), 6.49 (d, 1H, ^4J = 2.7 Hz, ArH), 6.43 (d, 1H, ^4J = 2.7 Hz, ArH), 6.02 (d, 1H, ^4J = 2.4 Hz, ArH), 5.78 (d, 1H, ^4J = 2.4 Hz, ArH), 5.37 (d, 1H, ^4J = 2.8 Hz, ArH), 5.30 (d, 1H, ^4J = 2.8 Hz, ArH), 4.91 (s, 1H, CH(OH)Ph), 4.40 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 4.33 (d, 1H, ^2J = 13.4 Hz, ArCH$_2$Ar), 4.32 (d, 1H, ^2J = 13.5 Hz, ArCH$_2$Ar), 4.26 (d, 1H,

^2J = 13.5 Hz, $ArCH_2Ar$), 3.97–3.75 (m, 4H, OCH_2), 3.76 (s, 1H, CH(O<u>H</u>)), 3.67–3.60 (m, 2H, OCH_2), 3.57–3.49 (m, 2H, OCH_2), 3.09 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 3.01 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.97 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 2.84 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 1.91–1.73 (m, 8H, $OCH_2C\underline{H}_2$), 1.36 (s, 9H, $C(CH_3)_3$), 1.08 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.82 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.81 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major conformer): δ = 171.54 (C=O), 155.64, 153.74, 150.92, 149.50, 144.31, 140.18, 139.99, 138.64, 137.58, 137.18, 135.91, 135.83, 134.52, 134.40, 134.39, 134.00, 130.69 (C_{Ar}), 128.64, 128.25, 127.36, 125.88, 125.53, 123.63, 123.31, 116.08, 115.90, 115.29, 114.97 (CH_{Ar}), 76.81, 76.54, 76.40, 76.21 (OCH_2), 73.59 (CH(OH)), 34.05 ($Ar\underline{C}(CH_3)_3$), 31.71 ($ArC(\underline{C}H_3)_3$), 31.31, 31.28, 31.08, 30.98 ($ArCH_2Ar$), 23.41, 23.40, 22.89, 22.71 ($OCH_2\underline{C}H_2$), 10.80, 9.78, 9.72 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 828.4941 $[M+H]^+$ for. $C_{52}H_{66}N_3O_6$ (828.4946).

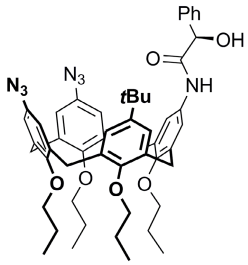


*Bis(azide) (P,S)-**8a***. An aqueous solution of HNO_2 freshly prepared from $NaNO_2$ (0.037 g, 0.53 mmol), water (0.25 ml) and H_2SO_4 (96%, 0.021 ml, 0.379 mmol) at 0–5 °C was added to a stirred solution of calixarene (*M*,*S*)-**6a** (0.048 g, 0.053 mmol) in a mixture of CH_3CN (0.5 ml) and THF (0.5 ml) at 0–5 °C. The mixture was stirred for 15 min at 0–5 °C and a solution of NaN_3 (0.017 g, 0.256 mmol) in water (0.1 ml) was added. The stirring was continued for 1 h at 0–5 °C and then for 1 h at room temperature. The mixture was diluted with H_2O and the products were extracted with dichloromethane. The organic fraction was washed with water and brine, dried and the solvent was evaporated. The residue was purified by column chromatography (silica, gradient from *n*-hexane/ethyl acetate 6:1 to *n*-hexane/ethyl acetate 3:1). Yield 0.026 g (51%), white solid. M.p. 128–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73–7.66 (m, 3H, ArH_{Nap}), 7.41–7.37 (m, 1H, ArH_{Nap}), 7.17–7.09 (m, 2H, ArH_{Nap}), 6.85 (d, 1H, ^4J = 2.2 Hz, ArH), 6.79 (d, 1H, ^4J = 2.2 Hz, ArH), 6.76 (d, 1H, ^4J = 2.7 Hz, ArH), 6.74 (s, 1H, NHCO), 6.46 (d, 1H, ^4J = 2.7 Hz, ArH), 6.45 (d, 1H, ^4J = 2.7 Hz, ArH), 6.13 (d, 1H, ^4J = 2.2 Hz, ArH), 6.06 (d, 1H, ^4J = 2.7 Hz, ArH), 5.92 (d, 1H, ^4J = 2.7 Hz, ArH), 4.40 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 4.36 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 4.35 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 4.32 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 3.91 (s, 3H, OCH_3), 3.89–3.61 (m, 9H, OCH_2+$C\underline{H}CH_3$), 3.11 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 3.08 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 3.03 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 2.98 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 1.93–1.77 (m, 8H, $OCH_2C\underline{H}_2$), 1.57 (d, 3H, ^3J = 7.0 Hz, $CHC\underline{H}_3$), 1.18 (s, 9H, $C(CH_3)_3$), 1.01 (t, 3H,

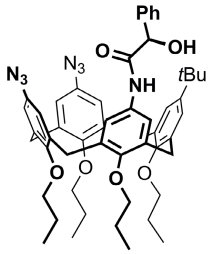
^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.98 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.92 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.89 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.88 (C=O), 157.63, 154.52, 154.31, 153.56, 152.93, 144.99, 137.08, 136.72, 136.66, 136.48, 135.49, 135.10, 134.49, 133.88, 133.80, 133.69, 132.93, 132.77, 131.65 (C_{Ar}), 129.24, (CH_{Ar}) 128.97 (C_{Ar}), 127.52, 126.16, 126.00, 125.84, 125.32, 121.31, 119.63, 119.04, 118.92, 118.54, 118.04, 117.99, 105.57 (CH_{Ar}), 76.84, 76.77, 76.75 (OCH_2), 55.28 (OCH_3), 47.75 (C(O)$\underline{C}$H), 33.86 ($\underline{C}(CH_3)_3$), 31.41 (C($\underline{C}H_3)_3$), 31.16, 31.12, 31.06, 30.89 ($ArCH_2Ar$), 23.19, 23.18, 23.17, 22.90 ($OCH_2\underline{C}H_2$), 19.08 (CH$\underline{C}H_3$), 10.44, 10.11, 9.99 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 975.5496 $[M+NH_4]^+$ for $C_{58}H_{71}N_8O_6$ (975.5491).



*Bis(azide) (M,S)-**8b*** was prepared as described for compound (*P*,*S*)-**8a** from amine (*P*,*S*)-**6b** (0.045 g, 0.0497 mmol), $NaNO_2$ (0.034 g, 0.497 mmol), water (0.33 ml), H_2SO_4 (96%, 0.020 ml, 0.360 mmol), NaN_3 (0.016 g, 0.249 mmol), CH_3CN (0.5 ml) and THF (0.5 ml). Yield 0.032 g (66%), white solid. M.p. 128–130 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74–7.67 (m, 3H, ArH_{Nap}), 7.40–7.35 (m, 1H, ArH_{Nap}), 7.18–7.09 (m, 2H, ArH_{Nap}), 6.76 (s, 1H, NHCO), 6.74 (d, 1H, ^4J = 2.2 Hz, ArH), 6.72 (d, 1H, ^4J = 2.2 Hz, ArH), 6.66 (d, 1H, ^4J = 2.5 Hz, ArH), 6.53 (d, 1H, ^4J = 2.7 Hz, ArH), 6.47 (d, 1H, ^4J = 2.7 Hz, ArH), 6.21 (d, 1H, ^4J = 2.5 Hz, ArH), 6.00 (bs, 2H, ArH), 4.38 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 4.38 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 4.35 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 4.33 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 3.92 (s, 3H, OCH_3), 3.87–3.64 (m, 9H, OCH_2+C$\underline{H}CH_3$), 3.08 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 3.06 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 3.04 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 3.03 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 1.93–1.79 (m, 8H, $OCH_2C\underline{H}_2$), 1.59 (d, 3H, ^3J = 7.1 Hz, $CHC\underline{H}_3$), 1.09 (s, 9H, $C(CH_3)_3$), 1.01 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.98 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.92 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.91 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.10 (C=O), 157.63, 154.48, 154.25, 153.58, 153.08, 144.79, 137.09, 136.57, 136.55, 136.41, 135.58, 134.94, 134.29, 134.07, 133.90, 133.71, 133.02, 132.82, 131.56 (C_{Ar}), 129.24, (CH_{Ar}) 129.00 (C_{Ar}), 127.59, 126.09, 126.05, 125.56, 125.25, 120.75, 120.56, 119.03, 119.02, 118.56, 118.17, 117.95, 105.57 (CH_{Ar}), 76.82, 76.76, 76.68 (OCH_2), 55.28 (OCH_3), 47.64 (C(O)$\underline{C}$H), 33.76 ($\underline{C}(CH_3)_3$), 31.32 (C($\underline{C}H_3)_3$), 31.13, 31.07, 30.92 ($ArCH_2Ar$), 23.17, 23.16, 23.15, 22.89 ($OCH_2\underline{C}H_2$), 18.74 (CH$\underline{C}H_3$), 10.42, 10.09, 10.00 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 975.5503 $[M+NH_4]^+$ for $C_{58}H_{71}N_8O_6$ (975.5491).

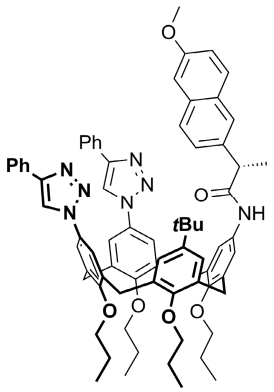


*Bis(azide) (P,R)-**9a*** was prepared as described for compound (*P*,*S*)-**8a** from amine (*M*,*R*)-**7a** (0.337 g, 0.407 mmol), $NaNO_2$ (0.449 g, 6.51 mmol), water (4 ml), H_2SO_4 (96%, 0.262 ml, 4.72 mmol), NaN_3 (0.317 g, 4.89 mmol), CH_3CN (15 ml) and THF (15 ml). Yield 0.24 g (68%), white solid. M.p. 143–145 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (s, 1H, NH), 7.42–7.38 (m, 2H, ArH_{Ph}), 7.37–7.28 (m, 3H, ArH_{Ph}), 6.91 (d, 1H, ^4J = 2.4 Hz, ArH), 6.88 (d, 1H, ^4J = 2.4 Hz, ArH), 6.60 (d, 1H, ^4J = 2.7 Hz, ArH), 6.58 (d, 1H, ^4J = 2.7 Hz, ArH), 6.48 (d, 1H, ^4J = 2.5 Hz, ArH), 6.34 (d, 1H, ^4J = 2.5 Hz, ArH), 5.95 (d, 1H, ^4J = 2.7 Hz, ArH), 5.89 (d, 1H, ^4J = 2.7 Hz, ArH), 5.07 (d, 1H, ^3J = 3.4 Hz, C<u>H</u>(OH)Ph), 4.41 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.39 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.38 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.37 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 3.93–3.79 (m, 4H, OCH_2), 3.78–3.62 (m, 4H, OCH_2), 3.33 (d, 1H, ^3J = 3.4 Hz, CH(O<u>H</u>)), 3.14–3.03 (m, 4H, $ArCH_2Ar$), 1.94–1.79 (m, 8H, $OCH_2C\underline{H}_2$), 1.23 (s, 9H, $C(CH_3)_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.01 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.91 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.89 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.60 (C=O), 154.72, 154.50, 153.43, 153.22, 145.03, 139.26, 137.34, 137.04, 136.39, 135.31, 135.03, 134.70, 134.29, 133.96, 133.11, 132.85, 130.78 (C_{Ar}), 128.78, 128.60, 126.80, 125.85, 125.49, 121.08, 120.24, 119.07, 118.76, 118.04, 117.89 (CH_{Ar}), 76.89, 76.84, 76.71 (OCH_2), 74.43 (CH(OH)), 33.92 ($ArC(CH_3)_3$), 31.49 ($ArC(\underline{C}H_3)_3$), 31.19, 31.09, 30.99 ($ArCH_2Ar$), 23.23, 23.14, 22.88 ($OCH_2\underline{C}H_2$), 10.52, 10.02, 9.93 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 902.4574 $[M+Na]^+$ for $C_{52}H_{61}NaN_7O_6$ (902.4576).

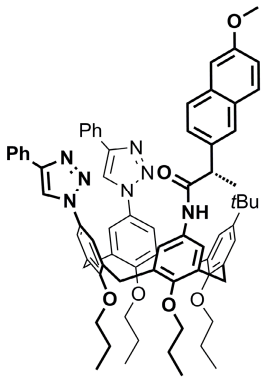


*Bis(azide) (M,R)-**9b*** was prepared as described for compound (*P*,*S*)-**8a** from amine (*P*,*R*)-**7b** (0.25 g, 0.302 mmol), $NaNO_2$ (0.334 g, 4.84 mmol), water (3.9 ml), H_2SO_4 (96%, 0.194 ml, 3.50 mmol), NaN_3 (0.236 g, 3.63 mmol), CH_3CN (14 ml) and THF (14 ml). Yield 0.165 g (62%), white solid. M.p. 157–159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (s, 1H, NH), 7.43–7.38 (m, 2H, ArH_{Ph}), 7.38–7.28 (m, 3H, ArH_{Ph}), 6.92 (d, 1H, ^4J = 2.4 Hz, ArH), 6.88 (d, 1H, ^4J = 2.4 Hz, ArH), 6.60–6.54 (m, 3H, ArH), 6.32 (d, 1H, ^4J = 2.4 Hz, ArH), 6.00 (d, 1H, ^4J = 2.7 Hz, ArH), 5.90 (d, 1H, ^4J = 2.7 Hz, ArH), 5.06 (d, 1H, ^3J = 3.6 Hz, C<u>H</u>(OH)Ph), 4.45–4.33 (m, 4H, $ArCH_2Ar$), 3.92–3.79 (m, 4H, OCH_2), 3.78–3.62 (m, 4H, OCH_2), 3.37 (d, 1H, ^3J = 3.6 Hz, CH(O<u>H</u>)), 3.15–3.02 (m, 4H, $ArCH_2Ar$), 1.95–1.79 (m, 8H, $OCH_2C\underline{H}_2$), 1.24 (s, 9H, $C(CH_3)_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.01 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.92 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.89 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.67 (C=O), 154.70, 154.47, 153.43, 153.22, 145.04, 139.26, 137.29, 136.96, 136.40, 135.29, 135.12, 134.64, 134.26, 133.97, 133.07, 132.91, 130.89 (C_{Ar}), 128.79, 128.60, 126.89, 125.84, 125.50,

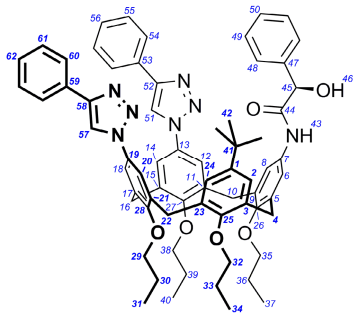
121.11, 120.05, 119.02, 118.74, 118.05, 117.93 (CH_{Ar}), 76.90, 76.86, 76.72 (OCH_2), 74.36 (CH(OH)), 33.93 (Ar<u>C</u>$(CH_3)_3$), 31.47 (ArC(<u>C</u>$H_3)_3$), 31.20, 31.10, 31.08, 30.99 ($ArCH_2Ar$), 23.23, 23.15, 22.87 (OCH_2<u>C</u>H_2), 10.51, 10.03, 9.94 (CH_2<u>C</u>H_3) ppm. ESI-MS *m*/*z*: 902.4569 $[M+Na]^+$ for $C_{52}H_{61}NaN_7O_6$ (902.4576).



*Bis(triazole) (P,S)-**10a***. To a solution of calixarene (*P*,*S*)-**8a** (0.217 g, 0.23 mmol) in dry toluene (9 ml) CuCl (0.0068 g, 0.068 mmol), phenylacetylene (0.10 ml, 0.91 mmol) and triethylamine (2.25 ml) were added and the mixture was stirred at 60 °C under inert atmosphere for 30 h. The solvents were removed under reduced pressure, the residue was dissolved in dichloromethane and washed continuously (for 2 h) with aqueous HCl (2 M) at vigorous stirring. The organic phase was separated, washed with water, dried, and the solvent was evaporated. The product was purified by column chromatography (silica, gradient from dichloromethane to dichloromethane/ethanol 100:1) followed by crystallization from *n*-hexane. Yield 0.19 g (72%), white solid. M.p. 175–177 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1H, ArH_{Trz}), 7.91–7.82 (m, 4H, ArH_{Ph}), 7.79 (s, 1H, ArH_{Trz}), 7.52–7.48 (m, 3H, ArH_{Nap}), 7.45–7.38 (m, 5H, $ArH_{Ph,}$, ArH), 7.36–7.27 (m, 4H, ArH_{Ph}+$ArH_{Nap,}$), 7.04–6.95 (m, 3H, ArH+ArH_{Nap}), 6.92 (d, 1H, ^4J = 2.3 Hz, ArH), 6.89 (s, 1H, NHCO), 6.81 (d, 1H, ^4J = 2.5 Hz, ArH), 6.74 (d, 1H, ^4J = 2.5 Hz, ArH), 6.57 (d, 1H, ^4J = 2.4 Hz, ArH), 6.08 (d, 1H, ^4J = 2.2 Hz, ArH), 4.58 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.54 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 4.45 (d, 1H, ^2J = 13.8 Hz, $ArCH_2Ar$), 4.41 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 4.08–3.60 (m, 11H, OCH_2+OCH_3), 3.51 (q, 1H, ^3J = 7.0 Hz, C(O)CH), 3.33 (d, 1H, ^2J = 13.8 Hz, $ArCH_2Ar$), 3.22 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 3.16 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 3.15 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.02–1.80 (m, 8H, OCH_2C<u>H</u>$_2$), 1.25 (d, 3H, ^3J = 7.0 Hz, CHC<u>H</u>$_3$), 1.16 (s, 9H, C$(CH_3)_3$), 1.09 (t, 3H, ^3J = 7.4 Hz, CH_2C<u>H</u>$_3$), 1.04 (t, 3H, ^3J = 7.4 Hz, CH_2C<u>H</u>$_3$), 0.96 (t, 3H, ^3J = 7.4 Hz, CH_2C<u>H</u>$_3$), 0.94 (t, 3H, ^3J = 7.4 Hz, CH_2C<u>H</u>$_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.89 (C=O), 157.37, 157.29, 156.49, 154.66, 153.17, 148.01, 147.98, 145.29, 137.41, 136.82, 136.73, 136.48, 135.23, 134.94, 134.71, 133.87, 133.42, 133.09, 131.38, 131.33, 131.32, 130.44, 130.16 (C_{Ar}), 129.13, 128.98, 128.79 (CH_{Ar}), 128.77 (C_{Ar}), 128.40, 128.14, 127.01, 126.22, 126.18, 125.83, 125.81, 125.63, 125.33, 123.13, 121.80, 121.09, 120.30, 120.22, 120.09, 118.70, 118.41, 117.67, 105.44 (CH_{Ar}), 77.19, 77.03, 76.91, 76.88 (OCH_2), 55.22 (OCH_3), 46.43 (C(O)<u>C</u>H), 33.96 (<u>C</u>$(CH_3)_3$), 31.41 (C(<u>C</u>$H_3)_3$), 31.30, 31.25, 31.05, 30.97 ($ArCH_2Ar$), 23.34, 23.28, 23.20, 22.90 (OCH_2<u>C</u>H_2), 19.38 (CH<u>C</u>H_3), 10.59, 10.52, 10.07, 9.93 (CH_2<u>C</u>H_3) ppm. ESI-MS *m*/*z*: 1162.6173 $[M+H]^+$ for $C_{74}H_{80}N_7O_6$ (1162.6165).

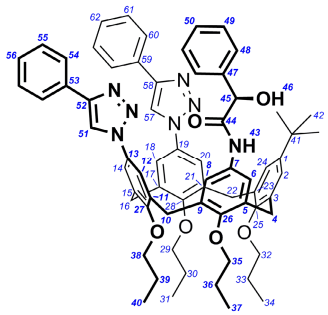


*Bis(triazole) (M,S)-**10b*** was prepared as described for compound (*P*,*S*)-**10a** from bis(azide) (*M*,*S*)-**8b** (0.20 g, 0.21 mmol), phenylacetylene (0.092 ml, 0.84 mmol), CuCl (0.0062 g, 0.063 mmol) and triethylamine (2.25 ml) in toluene (9 ml). Yield 0.154 g (63%), white solid. M.p. 179–181 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (s, 1H, ArH_{Trz}), 7.97–7.86 (m, 4H, ArH_{Ph}), 7.84 (s, 1H, ArH_{Trz}), 7.69–7.66 (m, 1H, ArH_{Nap}), 7.63–7.58 (m, 2H, ArH_{Nap}), 7.52–7.27 (m, 9H, $ArH_{Ph,}$+ArH_{Nap}+ArH), 7.11–7.06 (m, 2H, ArH_{Nap}), 6.93 (d, 1H, ^{4}J = 2.3 Hz, ArH), 6.87 (s, 1H, NHCO), 6.84–6.79 (m, 2H, ArH), 6.62 (d, 1H, ^{4}J = 2.5 Hz, ArH), 6.53 (d, 1H, ^{4}J = 2.3 Hz, ArH), 5.82 (d, 1H, ^{4}J = 2.2 Hz, ArH), 4.60 (d, 1H, ^{2}J = 13.6 Hz, $ArCH_2Ar$), 4.51 (d, 1H, ^{2}J = 13.8 Hz, $ArCH_2Ar$), 4.47 (d, 1H, ^{2}J = 13.8 Hz, $ArCH_2Ar$), 4.35 (d, 1H, ^{2}J = 13.3 Hz, $ArCH_2Ar$), 4.10–3.78 (m, 9H, OCH_2+OCH_3), 3.70–3.63 (m, 2H, OCH_2), 3.56 (q, 1H, ^{3}J = 7.0 Hz, C(O)CH), 3.33 (d, 1H, ^{2}J = 13.8 Hz, $ArCH_2Ar$), 3.24 (d, 1H, ^{2}J = 13.8 Hz, $ArCH_2Ar$), 3.21 (d, 1H, ^{2}J = 13.6 Hz, $ArCH_2Ar$), 3.01 (d, 1H, ^{2}J = 13.3 Hz, $ArCH_2Ar$), 2.02–1.78 (m, 8H, $OCH_2C\underline{H}_2$), 1.22 (d, 3H, ^{3}J = 7.0 Hz, $CHC\underline{H}_3$), 1.10 (t, 3H, ^{3}J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.08 (s, 9H, $C(CH_3)_3$), 1.04 (t, 3H, ^{3}J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.93 (t, 3H, ^{3}J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.92 (t, 3H, ^{3}J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.82 (C=O), 157.54, 157.40, 156.35, 154.73, 153.07, 148.16, 147.88, 145.24, 137.80, 137.14, 136.85, 136.41, 134.88, 134.87, 134.39, 134.16, 133.49, 132.99, 131.46, 131.33, 131.29, 130.44, 130.14 (C_{Ar}), 129.96, 129.72, 129.34 (CH_{Ar}), 128.97 (C_{Ar}), 128.93, 128.85, 128.36, 128.22, 127.10, 126.19, 126.06, 125.86, 125.82, 125.57, 125.46, 122.54, 122.08, 121.57, 120.50, 119.76, 118.67, 117.97, 105.48 (CH_{Ar}), 77.24, 76.86, 76.81 (OCH_2), 55.28 ($O\underline{C}H_3$), 46.16 (C(O)$\underline{C}$H), 33.87 ($\underline{C}(CH_3)_3$), 31.35 ($C(\underline{C}H_3)_3$), 31.26, 31.21, 30.86 ($ArCH_2Ar$), 23.33, 23.32, 23.13, 22.89 ($OCH_2\underline{C}H_2$), 18.40 ($CH\underline{C}H_3$), 10.63, 10.58, 9.99, 9.90 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 1162.6171 $[M+H]^+$ for $C_{74}H_{80}N_7O_6$ (1162.6165).



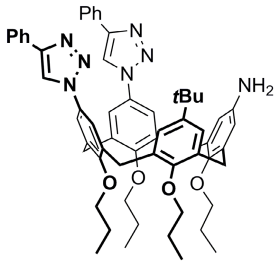
*Bis(triazole) (P,R)-**11a***. To a solution of calixarene (*P*,*R*)-**9a** (0.240 g, 0.27 mmol) in THF (12 ml) a freshly prepared solution of $CuSO_4 \cdot 5H_2O$ (0.067 g, 0.27 mmol) and sodium ascorbate (0.107 g, 0.54 mmol) in water (2 ml) was added followed by phenylacetylene (0.12 ml, 1.09 mmol) and the mixture was stirred at 60 °C under inert atmosphere for 30 h. The solvents were removed under reduced pressure, the residue was dissolved in dichloromethane and washed continuously (for 2 h) with aqueous HCl (2 M) at vigorous stirring. The organic phase was separated, washed with water, dried, and the solvent was evaporated. The product was purified

by column chromatography (silica, gradient from dichloromethane to dichloromethane/ethanol 100:1). Yield 0.251 g (85%), white solid. M.p. 173–175 °C. ^{1}H NMR (600 MHz, $CDCl_3$): 8.29 (s, 1H, ArH_{Trz}[51]), 8.04 (s, 1H, NH[43]), 7.95–7.92 (m, 2H, ArH_{Ph}[54]), 7.69 (d, 1H, ^4J = 2.6 Hz, ArH[14]), 7.68–7.67 (m, 2H, ArH_{Ph}[60]), 7.66 (s, 1H, ArH_{Trz}[57]), 7.53 (d, 1H, ^4J = 2.6 Hz, ArH[12]), 7.46–7.42 (m, 2H, ArH_{Ph}[55]), 7.39–7.30 (m, 4H, ArH_{Ph}[56,61,62]), 7.25–7.22 (m, 2H, ArH_{Ph}[48]), 7.14 (d, 1H, ^4J = 2.4 Hz, ArH[2]), 7.13–7.06 (m, 4H, ArH[24,49,50]), 6.80 (d, 1H, ^4J = 2.5 Hz, ArH[6]), 6.62 (d, 1H, ^4J = 2.6 Hz, ArH[18]), 6.35 (d, 1H, ^4J = 2.6 Hz, ArH[20]), 6.06 (d, 1H, ^4J = 2.5 Hz, ArH[8]), 5.58 (d, 1H, ^3J = 5.2 Hz, CH(O<u>H</u>)[46]), 4.64 (d, 1H, ^3J = 5.2 Hz, C<u>H</u>(OH)[45]), 4.63 (d, 1H, ^2J = 13.8 Hz, $ArCH_2Ar$[16ax]), 4.58 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$[22ax]), 4.51 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$[10ax]), 4.41 (d, 1H, ^2J = 13.0 Hz, $ArCH_2Ar$[4ax]), 4.20–3.93 (m, 4H, OCH_2[38,32]), 3.84–3.75 (m, 2H, OCH_2[29]), 3.67–3.59 (m, 2H, OCH_2[35]), 3.35 (d, 1H, ^2J = 13.8 Hz, $ArCH_2Ar$[16eq]), 3.25 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$[10eq]), 3.22 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$[22eq]), 3.14 (d, 1H, ^2J = 13.0 Hz, $ArCH_2Ar$[4eq]), 2.05–1.91 (m, 6H, $C\underline{H}_2CH_3$[39,33,30]), 1.90–1.83 (m, 2H, $C\underline{H}_2CH_3$[36]), 1.35 (s, 9H, $C(CH_3)_3$[42]), 1.16 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$[31]), 1.09 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$[37]), 0.94 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$[40]), 0.93 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$[34]) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.04 (*44*), 157.88 (*27*), 156.27 (*28*), 155.09 (*25*), 152.17 (*26*), 148.24 (*52*), 147.62 (*58*), 145.48 (*1*), 139.28 (*47*), 138.21 (*11*), 137.49 (*15*), 135.86 (*21*), 135.81 (*3*), 134.65 (*23*), 134.63 (*17*), 133.99 (*5*), 132.34 (*9*), 131.71 (*7*), 131.46 (*13*), 131.33 (*19*), 130.48 (*53*), 129.53 (*59*), 129.01 (*61*), 128.80 (*55*), 128.57 (*62*), 128.20 (*56*), 128.11 (*50*), 127.66 (*49*), 126.64 (*2*), 126.47 (*48*), 125.92 (*54*), 125.66 (*24*), 125.50 (*60*), 121.39 (*20*), 120.82 (*12*), 120.67 (*14*), 120.48 (*18*), 120.00 (*6*), 119.54 (*8*), 118.52 (*57*), 117.89 (*51*), 77.38 (*29*), 77.21 (*35*), 76.73 (*32*), 76.71 (*38*), 73.87 (*45*), 34.16 (*41*), 31.63 (*42*), 31.32 (*22*), 31.29 (*16*), 31.23 (*4*), 31.10 (*10*), 23.44 (*30*), 23.42 (*36*), 23.06 (*33*), 22.83 (*39*), 10.75 (*37*), 10.73 (*31*), 9.86 (*40*), 9.75 (*34*) ppm. ESI-MS *m*/*z*: 1106.5513 $[M+Na]^+$ for $C_{68}H_{73}NaN_7O_6$ (1106.5515).



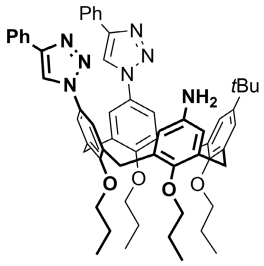
*Bis(triazole) (M,R)-**11b*** was prepared as described for compound (*P,R*)-**11a** from calixarene (*M,R*)-**9b** (0.164 g, 0.187 mmol), phenylacetylene (0.082 ml, 0.75 mmol), $CuSO_4 \cdot 5H_2O$ (0.047 g, 0.187 mmol), sodium ascorbate (0.074 g, 0.374 mmol) in CuCl (0.0056 g, 0.056 mmol), in a mixture of THF (9 ml) and water (1.5 ml). Yield 0.179 g (89%), white solid. M.p. 172–174 °C. ^{1}H NMR (600 MHz, $CDCl_3$): 8.31 (s, 1H, ArH_{Trz}[51]), 8.24 (s, 1H, NH[43]), 7.93–7.90 (m, 2H, ArH_{Ph}[54]), 7.73 (d, 1H, ^4J = 2.6 Hz, ArH[14]), 7.71 (s, 1H, ArH_{Trz}[57]), 7.68–7.65 (m, 2H, ArH_{Ph}[60]), 7.45–7.41 (m, 2H, ArH_{Ph}[55]), 7.39 (d, 1H, ^4J = 2.6 Hz, ArH[12]), 7.36–7.24 (m, 6H, ArH_{Ph}[48,56,61,62]),

7.19–7.11 (m, 5H, ArH[2,24,49,50]), 6.94 (d, 1H, ^4J = 2.5 Hz, ArH[8]), 6.58 (d, 1H, ^4J = 2.6 Hz, ArH[20]), 6.37 (bs, 1H, CH(OH)[46]), 6.32 (d, 1H, ^4J = 2.6 Hz, ArH[18]), 6.05 (d, 1H, ^4J = 2.5 Hz, ArH[6]), 4.66 (bs, 1H, CH(OH)[45]), 4.63 (d, 1H, ^2J = 13.9 Hz, $ArCH_2Ar^{16ax}$), 4.58 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar^{22ax}$), 4.49 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar^{10ax}$), 4.46 (d, 1H, ^2J = 13.0 Hz, $ArCH_2Ar^{4ax}$), 4.20–3.98 (m, 4H, OCH_2[38,32]), 3.82–3.76 (m, 2H, OCH_2[29]), 3.68–3.60 (m, 2H, OCH_2[35]), 3.34 (d, 1H, ^2J = 13.9 Hz, $ArCH_2Ar^{16eq}$), 3.23 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar^{22eq}$), 3.22 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar^{10eq}$), 3.17 (d, 1H, ^2J = 13.0 Hz, $ArCH_2Ar^{4eq}$), 2.04–1.91 (m, 6H, CH_2CH_3[39,33,30]), 1.91–1.83 (m, 2H, CH_2CH_3[36]), 1.39 (s, 9H, $C(CH_3)_3$[42]), 1.16 (t, 3H, ^3J = 7.4 Hz, CH_2CH_3[31]), 1.10 (t, 3H, ^3J = 7.4 Hz, CH_2CH_3[37]), 0.94 (t, 3H, ^3J = 7.4 Hz, CH_2CH_3[34]), 0.93 (t, 3H, ^3J = 7.4 Hz, CH_2CH_3[40]) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.08 (*44*), 157.89 (*27*), 156.34 (*28*), 155.13 (*25*), 152.06 (*26*), 148.17 (*52*), 147.50 (*58*), 145.50 (*1*), 139.26 (*47*), 138.16 (*11*), 137.39 (*15*), 135.92 (*21*), 135.67 (*3*), 134.82 (*23*), 134.40 (*17*), 133.78 (*5*), 132.40 (*9*), 131.86 (*7*), 131.51 (*19*), 131.46 (*13*), 130.51 (*53*), 129.39 (*59*), 128.96 (*61*), 128.79 (*55*), 128.52 (*62*), 128.15 (*56*), 128.12 (*50*), 127.64 (*49*), 126.62 (*48*), 126.33 (*2*), 125.88 (*54*), 125.84 (*24*), 125.40 (*60*), 122.37 (*20*), 121.13 (*14*), 120.98 (*12*), 120.86 (*18*), 119.68 (*6*), 119.19 (*57*), 118.85 (*8*), 118.40 (*51*), 77.44 (*29*), 77.23 (*35*), 76.75 (*38*), 76.68 (*32*), 73.92 (*45*), 34.18 (*41*), 31.66 (*42*), 31.35 (*22*), 31.30 (*10*), 31.23 (*16*), 31.11 (*4*), 23.45 (*30*), 23.44 (*36*), 23.03 (*33*), 22.81 (*39*), 10.78 (*37*), 10.74 (*31*), 9.82 (*34*), 9.77 (*40*) ppm. ESI-MS *m*/*z*: 1106.5508 $[M+Na]^+$ for $C_{68}H_{73}NaN_7O_6$ (1106.5515).

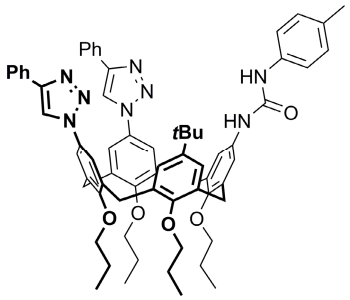


*Amine (P)-**12a***. A mixture of calixarene (*P*,*S*)-**10a** (0.128 g, 0.11 mmol), *t*BuOK (0.493 g, 4.40 mmol) *n*-butanol (6 ml) and DMSO (0.35 ml) was stirred at 120 °C for 24 h. After cooling to room temperature, the mixture was concentrated under reduced pressure, diluted with diethyl ether, and the solution was washed with water and brine, dried and the solvent was evaporated. The residue was purified by column chromatography (silica, gradient from dichloromethane to dichloromethane/ethanol 100:1). Yield 0.081 g (77%). This compound was also prepared by the same method from calixarene (*P*,*R*)-**11a** (0.165 g, 0.152 mmol) and *t*BuOK (0.681 g, 6.08 mmol) in a mixture of *n*-butanol (8.25 ml) and DMSO (0.50 ml). Yield 0.129 g (89%), white solid. M.p. 150–152 °C. $[\alpha]_D^{23}$ –35.0 (*c* 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (s, 1H, ArH_{Trz}), 7.93–7.89 (m, 2H, ArH_{Ph}), 7.77–7.73 (m, 2H, ArH_{Ph}), 7.71 (s, 1H, ArH_{Trz}), 7.50–7.26 (m, 8H, ArH_{Ph}+ArH), 7.01 (d, 1H, ^4J = 2.3 Hz, ArH), 6.99 (d, 1H, ^4J = 2.3 Hz, ArH), 6.78 (d, 1H, ^4J = 2.5 Hz, ArH), 6.71 (d, 1H, ^4J = 2.5 Hz, ArH), 5.64 (d, 1H, ^4J = 2.6 Hz, ArH), 5.59 (d, 1H, ^4J = 2.6 Hz, ArH), 4.61 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 4.55 (d,

1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 4.44 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 4.38 (d, 1H, ^2J = 13.1 Hz, $ArCH_2Ar$), 4.14–3.77 (m, 6H, OCH_2), 3.71–3.60 (m, 2H, OCH_2), 3.33 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 3.23 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 3.14 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 3.05 (d, 1H, ^2J = 13.1 Hz, $ArCH_2Ar$), 2.03–1.82 (m, 8H, $OCH_2C\underline{H}_2$), 1.25 (s, 9H, $C(CH_3)_3$), 1.11 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.05 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.94 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.93 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.80, 156.20, 155.00, 148.71, 148.09, 147.67, 145.03, 140.73, 138.21, 136.98, 136.19, 135.55, 134.90, 134.57, 134.44, 133.06, 131.42, 131.23, 130.42, 130.27 (C_{Ar}), 129.72, 128.85, 128.23, 128.18, 126.05, 125.83, 125.52, 125.35, 120.78, 120.46, 120.08, 119.60, 117.77, 117.68, 114.86, 114.27 (CH_{Ar}), 77.26, 77.10, 76.85, 76.76 (OCH_2), 34.03 ($\underline{C}(CH_3)_3$), 31.58 ($C(\underline{C}H_3)_3$), 31.37, 31.30, 31.22 ($ArCH_2Ar$), 23.37, 23.36, 23.13, 22.93 ($OCH_2\underline{C}H_2$), 10.70, 10.63, 9.98, 9.90 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 950.5329 $[M+H]^+$ for $C_{60}H_{68}N_7O_4$ (950.5327).

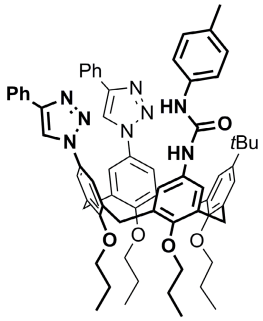


*Amine (M)-**12b*** was prepared as described for compound (*P*)-**12a** from calixarene (*M*,*S*)-**10b** (0.148 g, 0.127 mmol) and *t*BuOK (0.569 g, 5.08 mmol) in a mixture of *n*-butanol (6 ml) and DMSO (0.35 ml). Yield 0.097 g (80%). This compound was also prepared by the same method from calixarene (*M*,*R*)-**11b** (0.150 g, 0.139 mmol) and *t*BuOK (0.623 g, 5.56 mmol) in a mixture of *n*-butanol (8 ml) and DMSO (0.5 ml). Yield 0.112 g (85%). $[\alpha]_D^{23}$ +38.0 (*c* 0.55, $CHCl_3$). The NMR data were identical to those of compound (*P*)-**12a**.

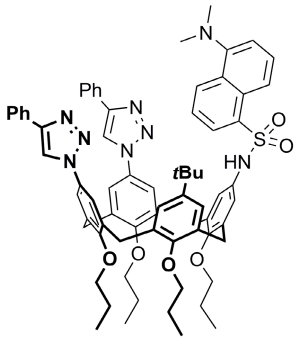


*Urea (P)-**13a***. To a solution of calixarene (*P*)-**12a** (0.021 g, 0.0221 mmol) in dry toluene (2 ml) triethylamine (0.0092 ml, 0.0661 mmol) was added followed by *p*-tolyl isocyanate (0.0042 ml, 0.0333 mmol). The mixture was stirred at 60 °C for 4 h and left and then allowed to stay overnight at room temperature. The solvent was evaporated and the residue was purified by column chromatography (silica, gradient from dichloromethane to dichloromethane/ethanol 200:1). Yield 0.020 g (84%), white solid. M.p. 178–180 °C. $[\alpha]_D^{23}$ +38.4 (*c* 0.3, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (s, 1H, ArH_{Trz}), 7.91–7.86 (m, 2H, ArH_{Ph}), 7.82–7.78 (m, 2H, ArH_{Ph}), 7.77 (s, 1H, ArH_{Trz}), 7.73 (d, 1H, ^4J = 2.6 Hz, ArH), 7.44–7.29 (m, 7H, ArH_{Ph}+ArH), 7.14 (d, 1H, ^4J = 2.3 Hz, ArH), 7.10 (d, 1H, ^4J = 2.3 Hz, ArH), 7.08–7.03 (m, 2H, ArH_{Tol}), 6.88 (s, 1H, NH), 6.85–6.80 (m, 2H, ArH_{Tol}), 6.75 (s, 1H, NH), 6.57 (d, 1H, ^4J = 2.5 Hz, ArH), 6.43 (d, 1H, ^4J = 2.5 Hz, ArH), 6.01 (d, 1H, ^4J = 2.3 Hz, ArH), 5.93 (d, 1H, ^4J = 2.3 Hz, ArH), 4.61

(d, 1H, ^2J = 13.7 Hz, $ArCH_2Ar$), 4.55 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.48 (d, 1H, ^2J = 13.7 Hz, $ArCH_2Ar$), 4.44 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.20–3.95 (m, 4H, OCH_2), 3.80–3.72 (m, 2H, OCH_2), 3.70–3.63 (m, 2H, OCH_2), 3.33 (d, 1H, ^2J = 13.7 Hz, $ArCH_2Ar$), 3.25 (d, 1H, ^2J = 13.7 Hz, $ArCH_2Ar$), 3.20 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 3.15 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.16 (s, 3H, $ArCH_3$), 2.04–1.80 (m, 8H, CH_2CH_3), 1.35 (s, 9H, $C(CH_3)_3$), 1.11 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 1.14 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.91 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.90 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.99, 156.65, 155.25, 153.77, 152.92, 148.47, 148.18, 145.34, 138.65, 137.20, 136.82, 136.08, 136.01, 134.54, 133.93, 132.54, 131.39, 131.35, 131.27, 131.11, 130.38, 129.61 (C=O, C_{Ar}), 128.93, 128.92, 128.81, 128.67, 128.19, 126.66, 125.89, 125.85, 125.52, 124.53, 124.35, 122.65, 121.29, 120.71, 120.63, 120.36, 118.71, 117.81 (CH_{Ar}), 77.51, 76.95, 76.72, 76.65 (OCH_2), 34.15 ($\underline{C}(CH_3)_3$), 31.67 ($C(\underline{C}H_3)_3$), 31.37, 31.26, 31.20 ($ArCH_2Ar$), 23.47, 23.44, 23.03, 22.85 ($OCH_2\underline{C}H_2$), 20.59 ($ArCH_3$), 10.87, 10.73, 9.81, 9.74 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 1083.5855 $[M+H]^+$ for $C_{68}H_{75}N_8O_5$ (1083.5855).

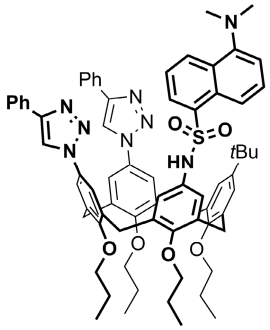


*Urea (M)-**13b*** was prepared as described for compound (*P*)-**13a** from calixarene (*M*)-**12b** (0.021 g, 0.0221 mmol), *p*-tolyl isocyanate (0.0042 ml, 0.0333 mmol) and triethylamine (0.0092 ml, 0.0661 mmol) in toluene (2 ml). Yield 0.021 g (88%). $[\alpha]_D^{23}$ –40.9 (*c* 0.3, $CHCl_3$). The NMR data were identical to those of compound (*P*)-**13a**.



*Sulfonamide (M)-**14a***. To a solution of calixarene (*P*)-**12a** (0.021 g, 0.0221 mmol) in dry dichloromethane (1 ml) a solution of dansyl chloride (0.0089 g, 0.033 mmol) in dry dichloromethane (1 ml) was added dropwise. The solution was stirred at room temperature for 24 h, the solvent was evaporated, and the residue was purified by column chromatography (silica, gradient from dichloromethane to dichloromethane/ethanol 100:1). Yield 0.024 g (92%), off-white solid. M.p. 189–191 °C. $[\alpha]_D^{23}$ –8.0 (*c* 0.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.40–8.35 (m, 1H, ArH_{Naph}), 8.32–8.27 (m, 1H, ArH_{Naph}), 8.18 (s, 1H, ArH_{Trz}), 7.96–7.91 (m, 2H, ArH_{Ph}), 7.86–7.82 (m, 2H, ArH_{Ph}), 7.81 (s, 1H, ArH_{Trz}), 7.80–7.76 (m, 1H, ArH_{Naph}), 7.51 (d, 1H, ^4J = 2.6 Hz, ArH), 7.47–7.41 (m, 3H, ArH_{Ph}), 7.39–7.31 (m, 3H, ArH_{Ph}), 7.30–7.25 (m, 2H, ArH_{Naph}), 7.15 (d, 1H, ^4J = 2.6 Hz, ArH), 7.09–7.04 (m, 1H, ArH_{Naph}), 6.90 (d, 1H, ^4J = 2.3 Hz, ArH), 6.70 (d, 1H, ^4J = 2.3 Hz, ArH), 6.67

(d, 1H, ^4J = 2.3 Hz, ArH), 6.64 (d, 1H, ^4J = 2.3 Hz, ArH), 6.42 (s, 1H, NH), 5.95 (d, 1H, ^4J = 2.3 Hz, ArH), 5.76 (d, 1H, ^4J = 2.3 Hz, ArH), 4.56 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 4.48 (d, 1H, ^2J = 13.3 Hz, $ArCH_2Ar$), 4.37 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 4.27 (d, 1H, ^2J = 13.2 Hz, $ArCH_2Ar$), 4.03–3.76 (m, 6H, OCH_2), 3.69–3.60 (m, 2H, OCH_2), 3.31 (d, 1H, ^2J = 13.6 Hz, $ArCH_2Ar$), 3.18 (d, 1H, ^2J = 13.4 Hz, $ArCH_2Ar$), 3.04 (d, 1H, ^2J = 13.5 Hz, $ArCH_2Ar$), 2.88–2.79 (m, 7H, $ArCH_2Ar$+$N(CH_3)_2$), 1.98–1.78 (m, 8H, $OCH_2C\underline{H}_2$), 1.11–1.06 (m, 12H, $CH_2C\underline{H}_3$+$C(CH_3)_3$), 1.03 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.91 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$), 0.90 (t, 3H, ^3J = 7.4 Hz, $CH_2C\underline{H}_3$) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.45, 156.28, 154.61, 154.40, 151.49, 148.47, 148.10, 145.26, 137.49, 136.87, 136.32, 135.15, 134.79, 134.78, 134.61, 134.14, 133.42, 131.58, 131.42, 130.44, 130.36 (C_{Ar}), 129.89 (CH_{Ar}), 129.83, 129.73, 129.45 (C_{Ar}), 129.19, 128.84, 128.68, 128.20, 128.18, 128.13, 126.03, 125.86, 125.73, 125.64, 125.23, 125.07, 122.78, 121.44, 120.56, 120.14, 119.40, 118.79, 117.92, 115.00 (CH_{Ar}), 77.25, 77.00, 76.90, 76.74 (OCH_2), 45.37 ($N(CH_3)_2$), 33.85 ($\underline{C}(CH_3)_3$), 31.44 ($C(\underline{C}H_3)_3$), 31.28, 31.21, 30.96, 30.93 ($ArCH_2Ar$), 23.31, 23.30, 23.09, 22.92 ($OCH_2\underline{C}H_2$), 10.59, 10.56, 9.96, 9.89 ($CH_2\underline{C}H_3$) ppm. ESI-MS *m*/*z*: 1183.5833 $[M+H]^+$ for $C_{72}H_{79}N_8O_6S$ (1183.5838).



*Sulfonamide (P)-**14b*** was prepared as described for compound (*M*)-**14a** from calixarene (*M*)-**12b** (0.021 g, 0.0221 mmol) and dansyl chloride (0.0089 g, 0.033 mmol) in dichloromethane (2 ml). Yield 0.024 g (92%). $[\alpha]_D^{23}$ +8.6 (*c* 0.2, $CHCl_3$). The NMR data were identical to those of compound (*M*)-**14a**.

NMR spectra of novel compounds

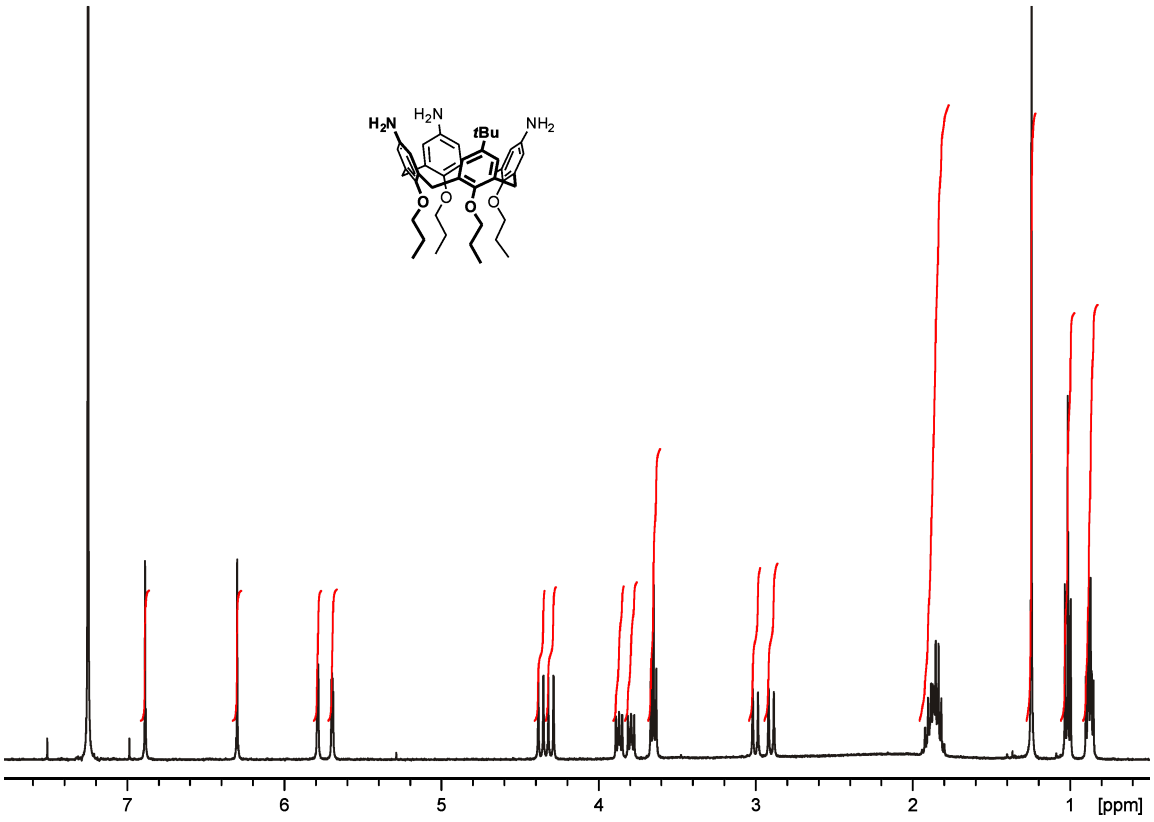


Figure S1. ^{1}H NMR spectrum of calixarene **2** (400 MHz, $CDCl_3$).

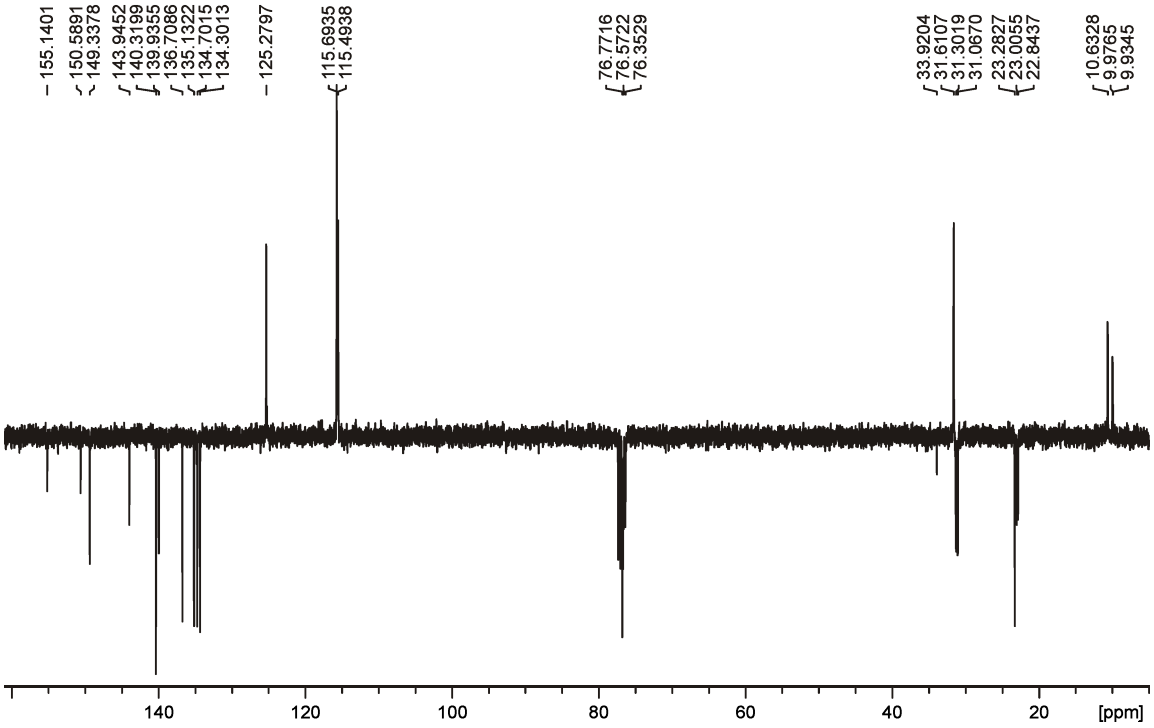


Figure S2. ^{13}C NMR spectrum (APT) of calixarene **2** (100 MHz, $CDCl_3$).

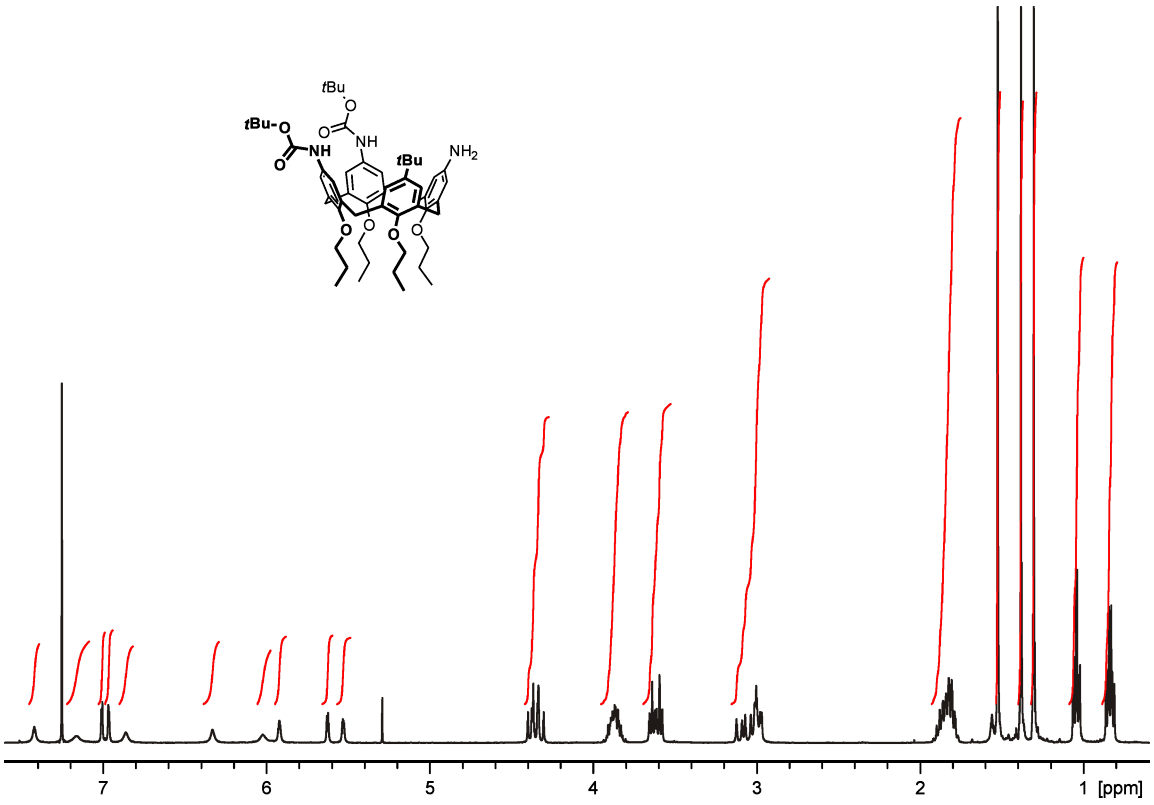


Figure S3. ^{1}H NMR spectrum of calixarene **3** (400 MHz, $CDCl_3$).

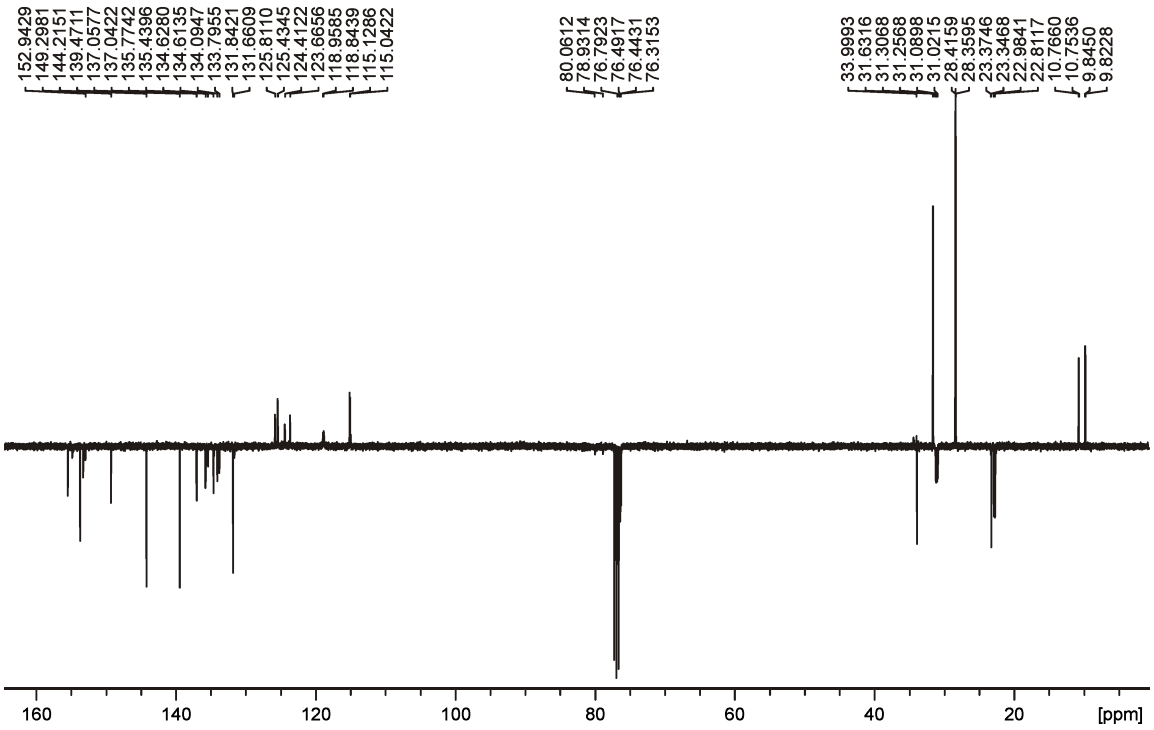


Figure S4. ^{13}C NMR spectrum (APT) of calixarene **3** (100 MHz, $CDCl_3$).

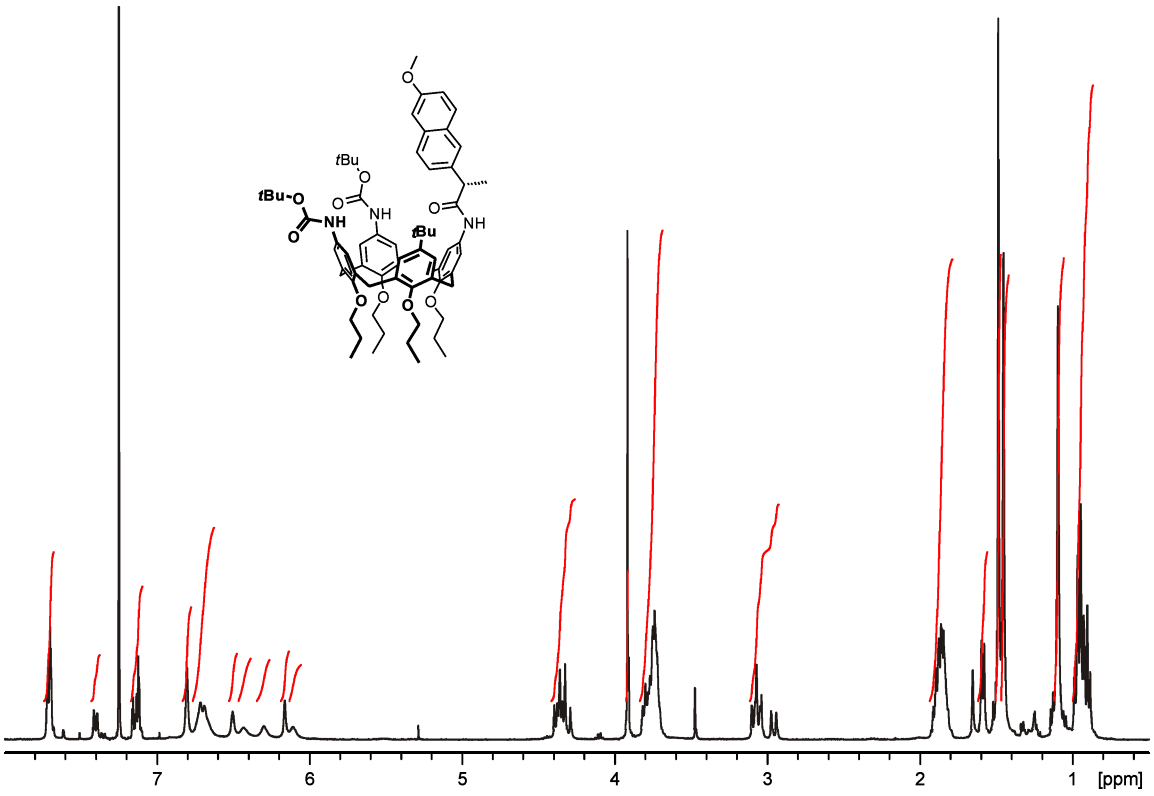


Figure S5. ^{1}H NMR spectrum of calixarene (*P*,*S*)-**4a** (400 MHz, $CDCl_3$).

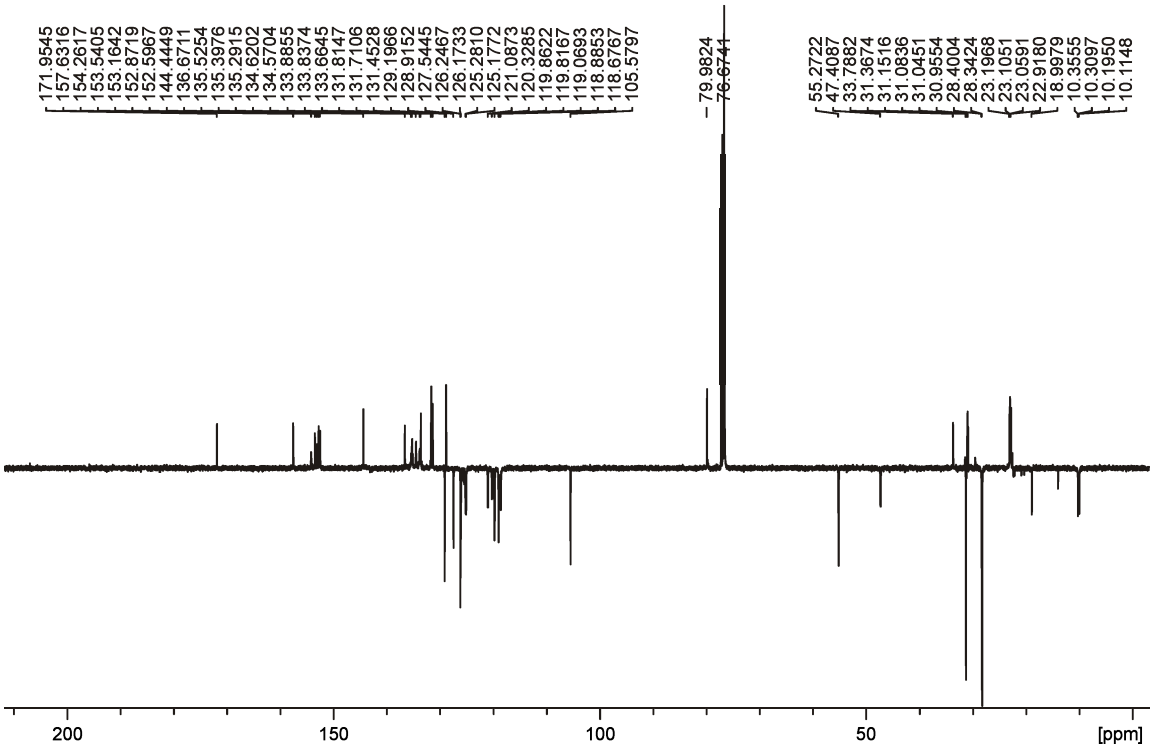


Figure S6. ^{13}C NMR spectrum (APT) of calixarene (*P*,*S*)-**4a** (100 MHz, $CDCl_3$).

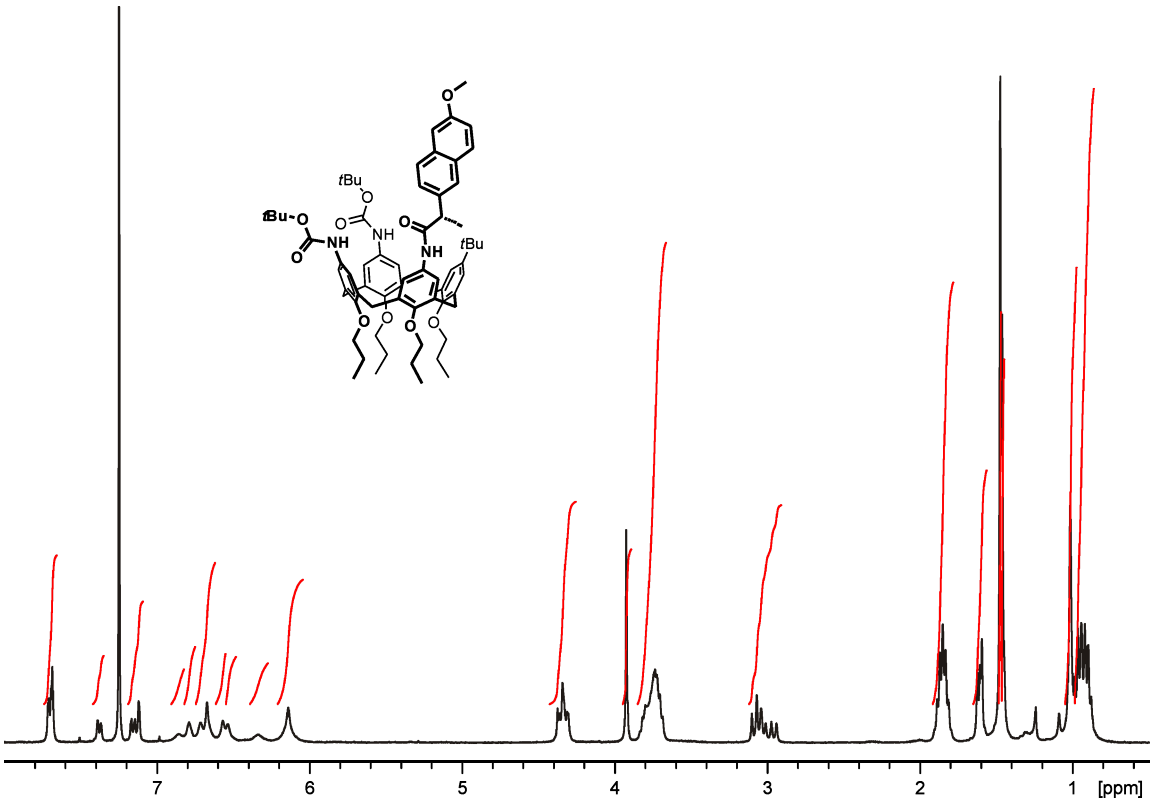


Figure S7. ^{1}H NMR spectrum of calixarene (*M*,*S*)-**4b** (400 MHz, $CDCl_3$).

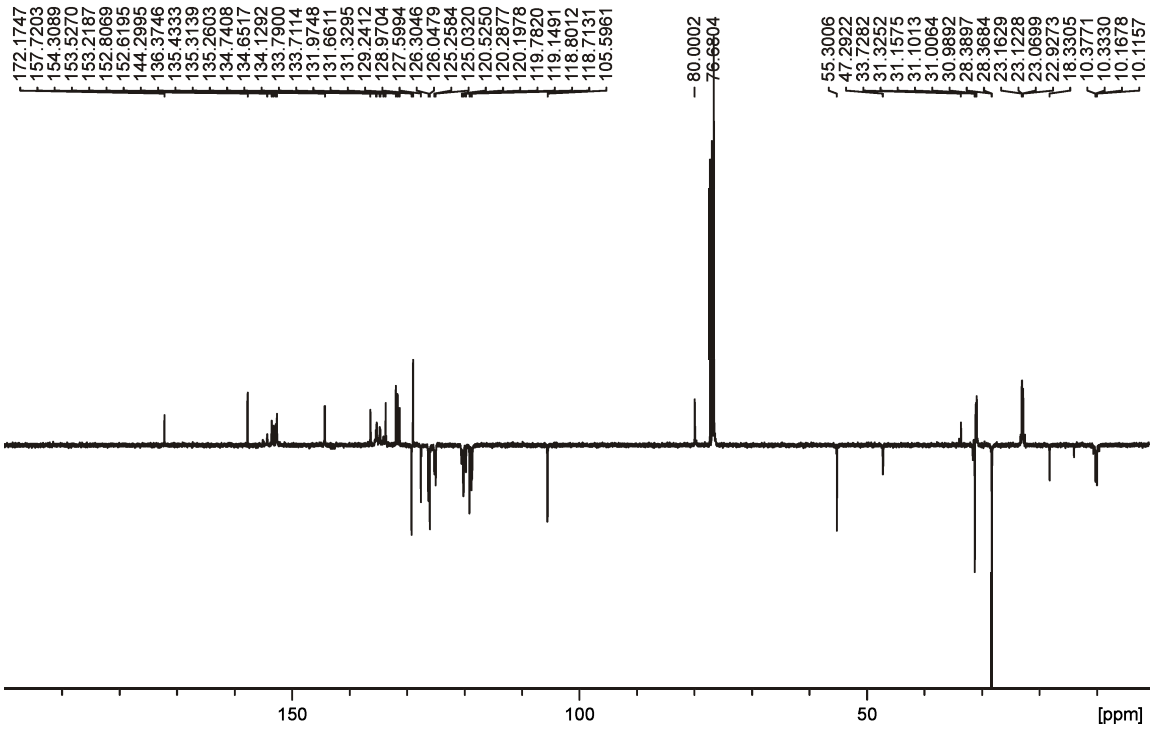


Figure S8. ^{13}C NMR spectrum (APT) of calixarene (*M*,*S*)-**4b** (100 MHz, $CDCl_3$).

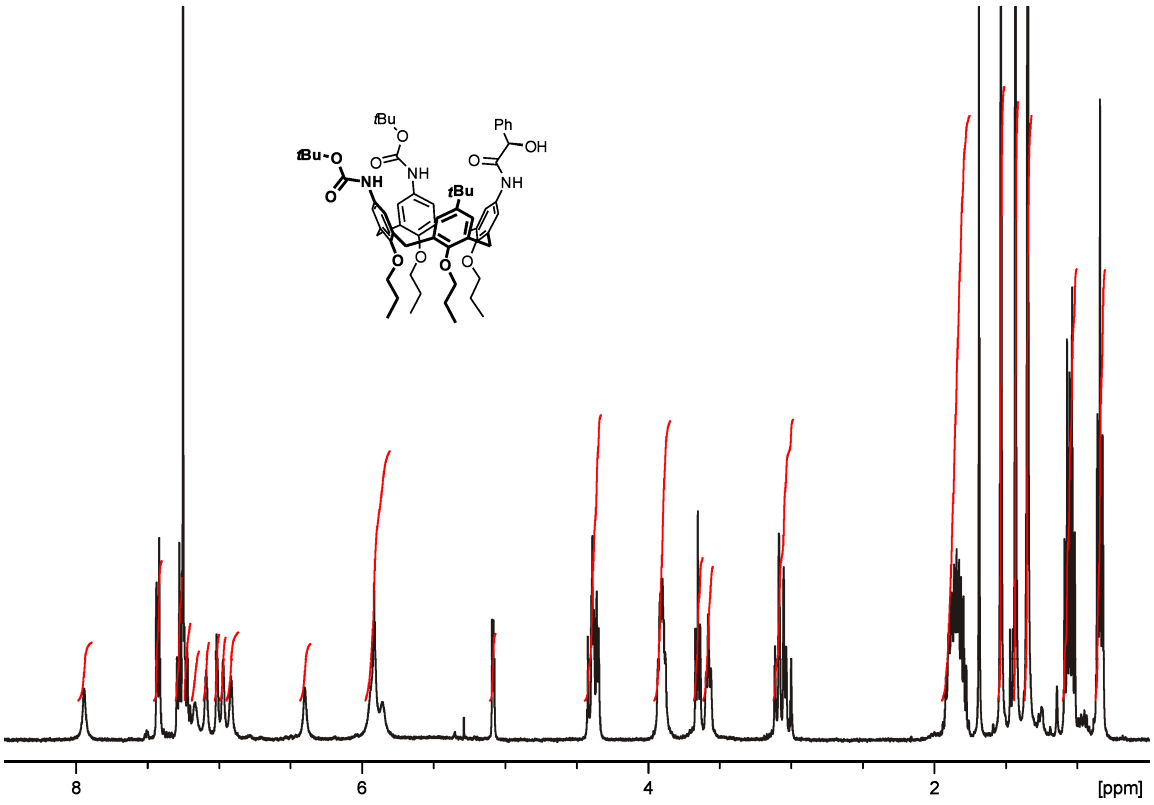


Figure S9. ^{1}H NMR spectrum of calixarene (*P*,*R*)-**5a** (400 MHz, $CDCl_3$).

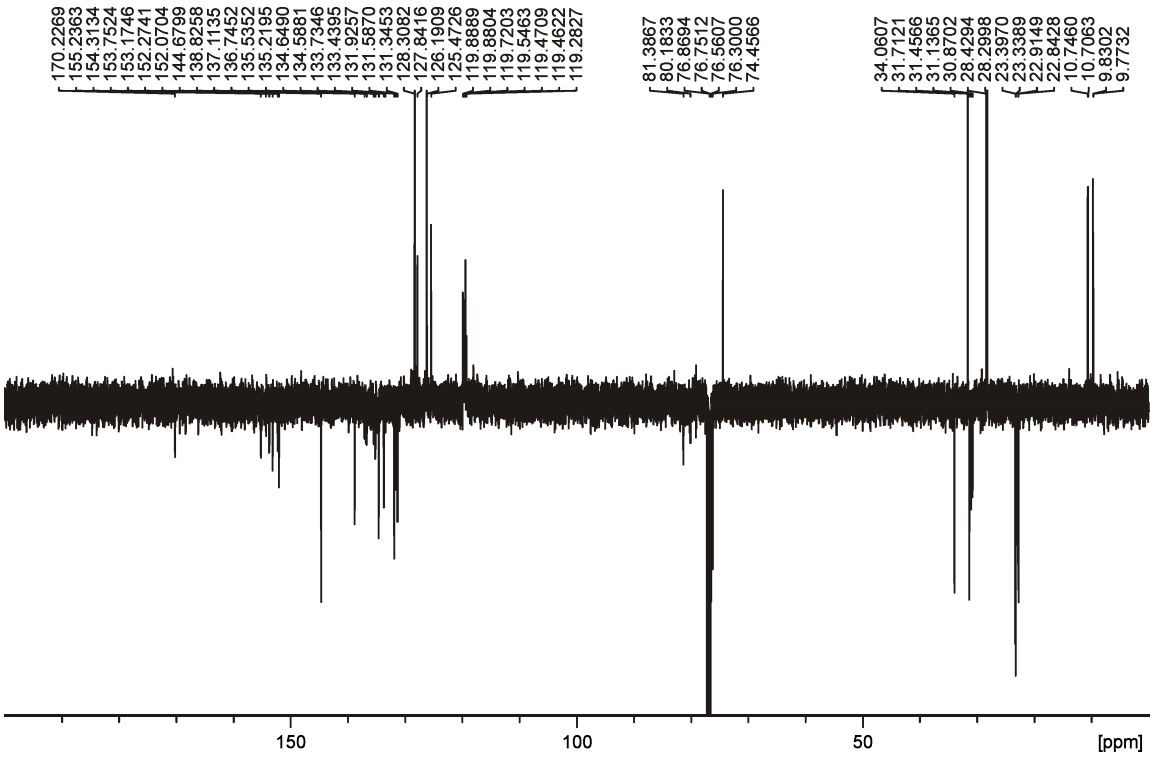


Figure S10. ^{13}C NMR spectrum (APT) of calixarene (*P*,*R*)-**5a** (100 MHz, $CDCl_3$).

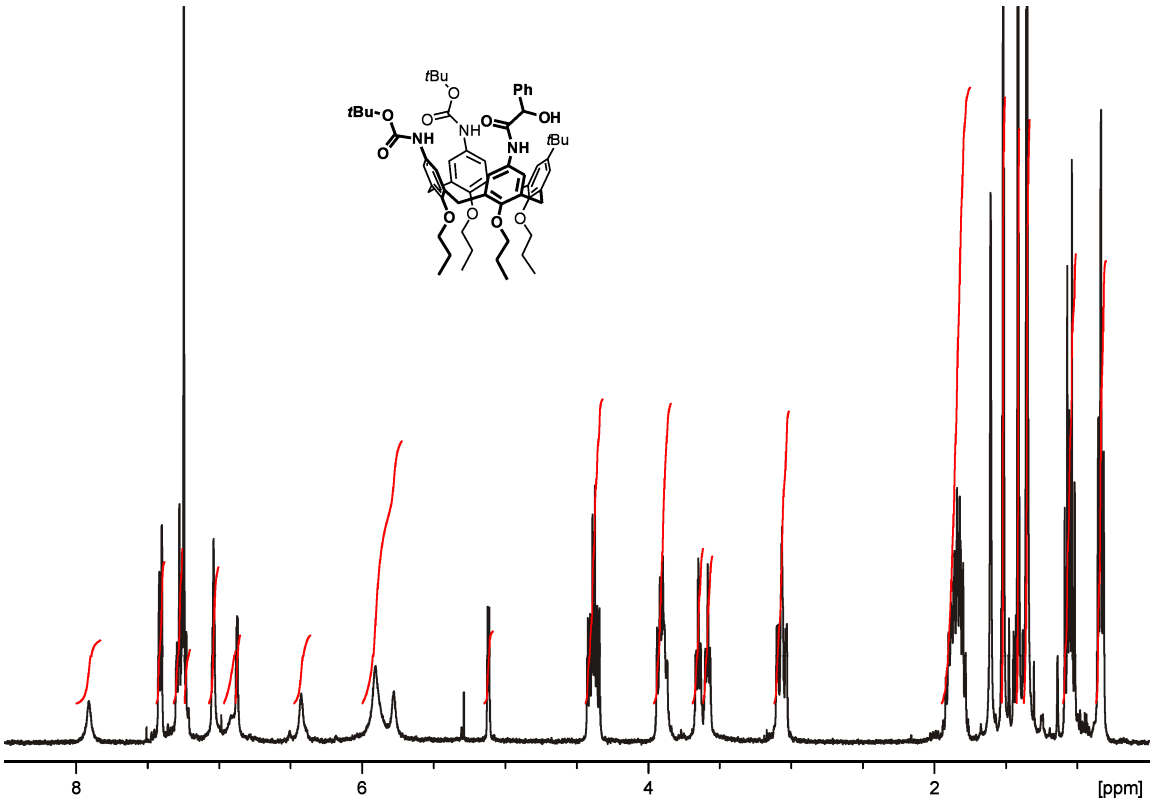


Figure S11. ^{1}H NMR spectrum of calixarene (*M*,*R*)-**5b** (400 MHz, $CDCl_3$).

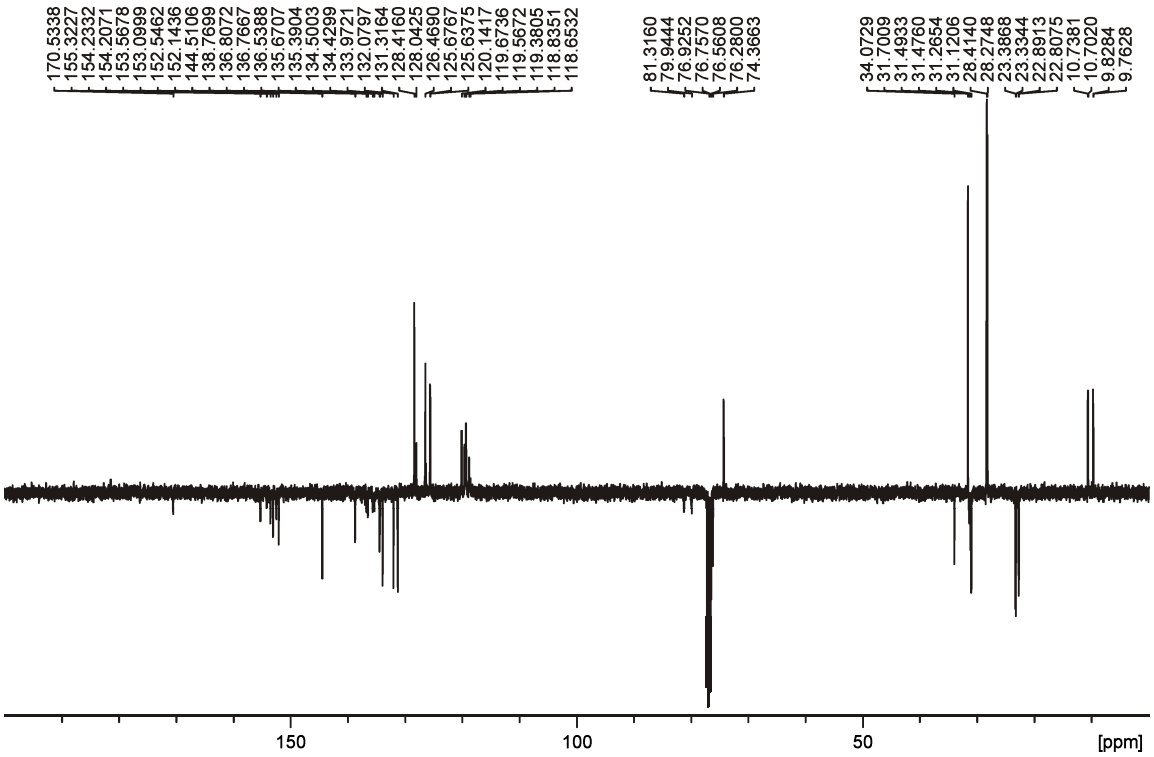


Figure S12. ^{13}C NMR spectrum (APT) of calixarene (*M*,*R*)-**5b** (100 MHz, $CDCl_3$).

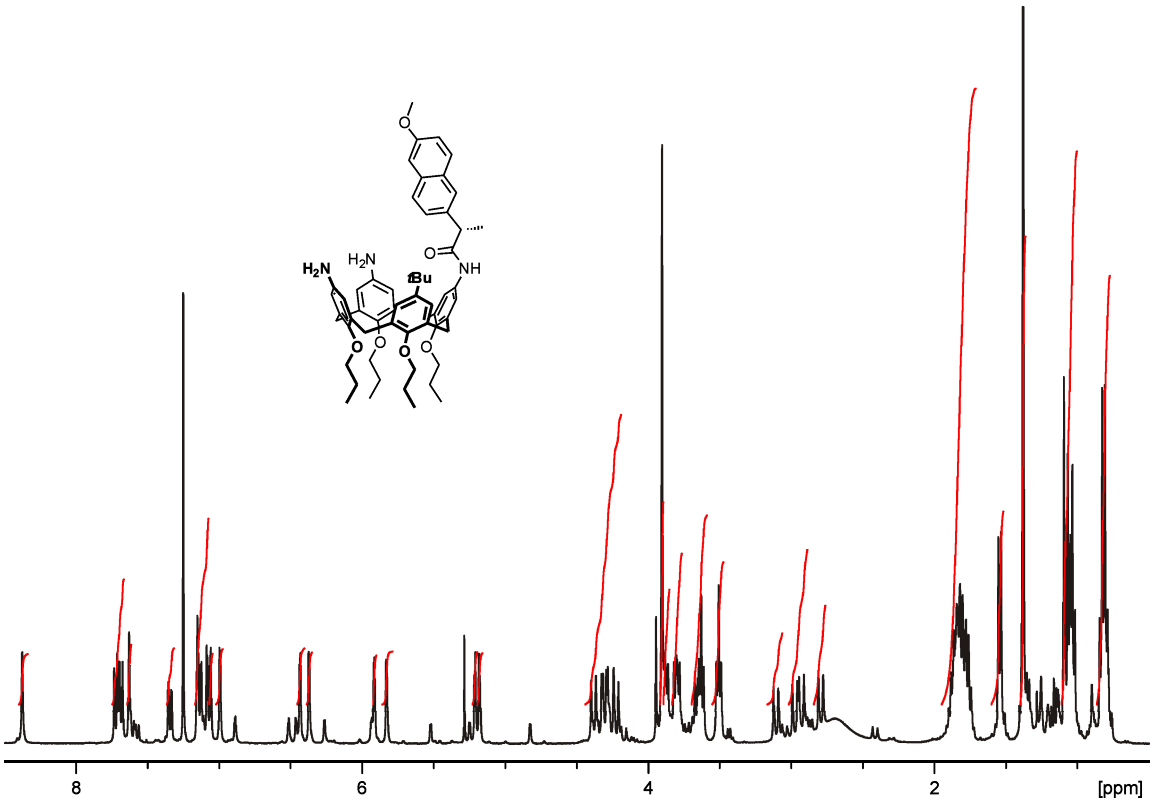


Figure S13. ^{1}H NMR spectrum of calixarene (*M*,*S*)-**6a** (400 MHz, $CDCl_3$).

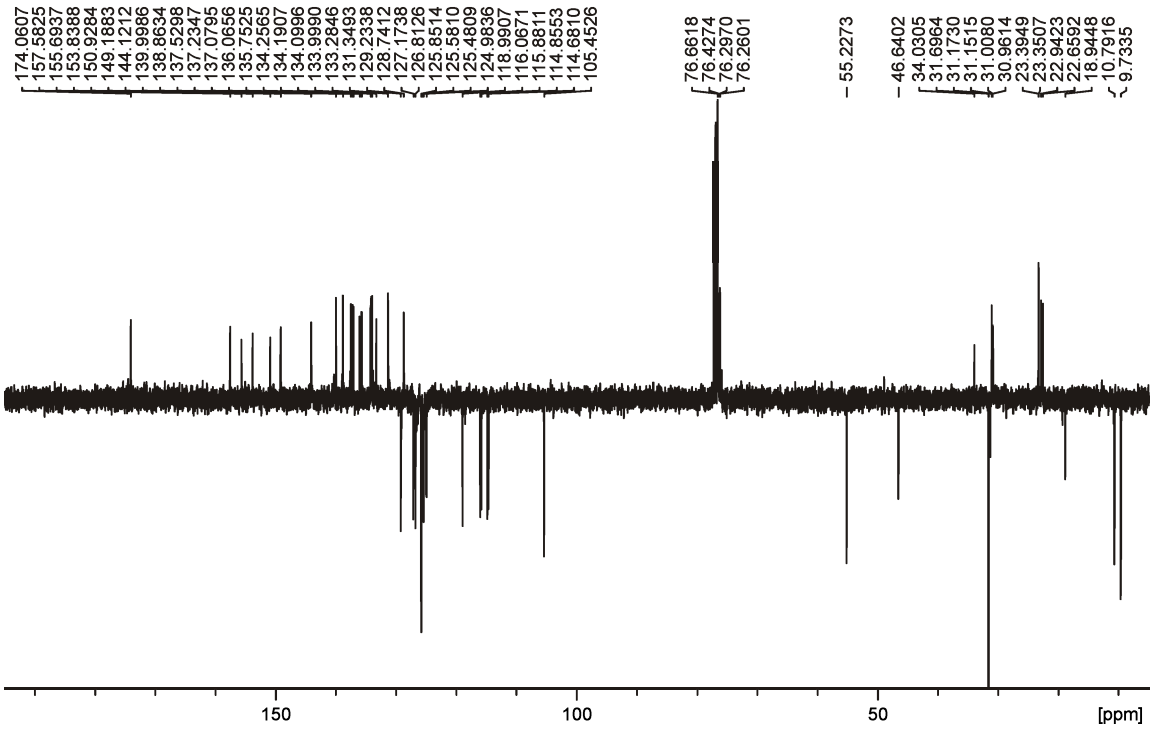


Figure S14. ^{13}C NMR spectrum (APT) of calixarene (*M*,*S*)-**6a** (100 MHz, $CDCl_3$).

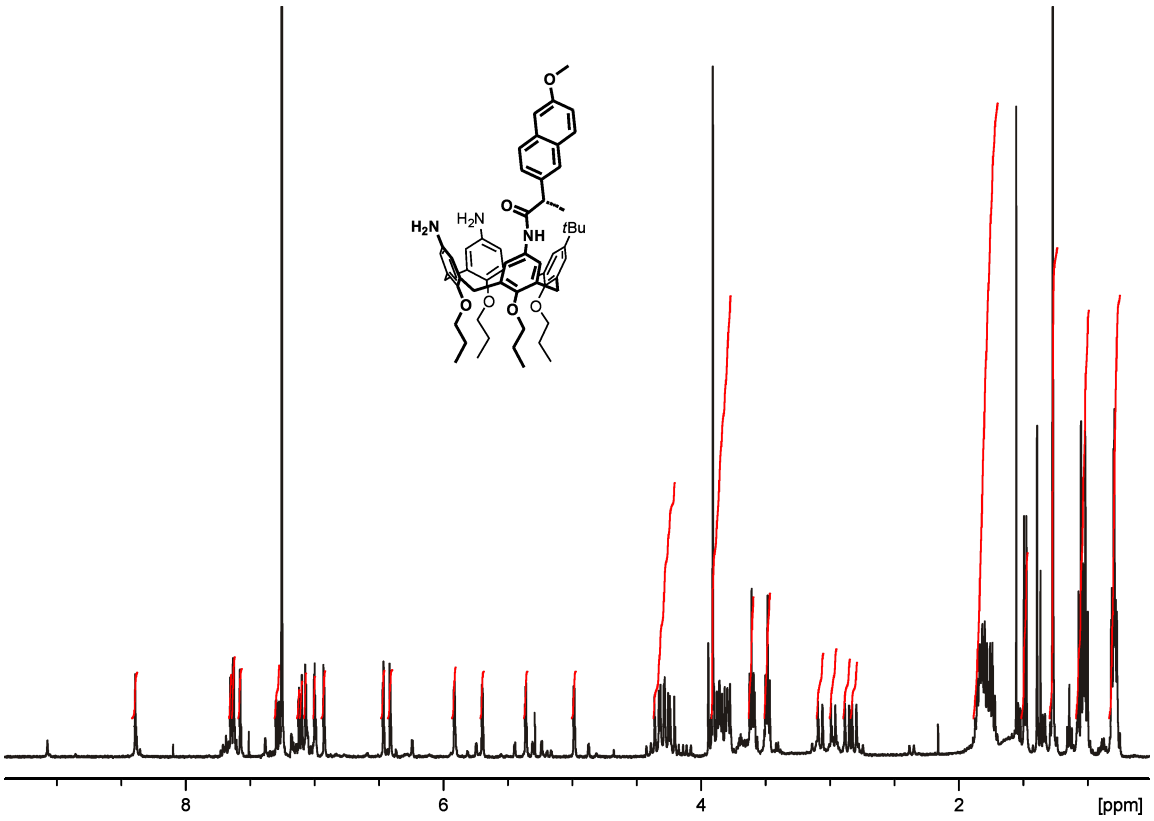


Figure S15. ^{1}H NMR spectrum of calixarene (*P*,*S*)-**6b** (400 MHz, $CDCl_3$).

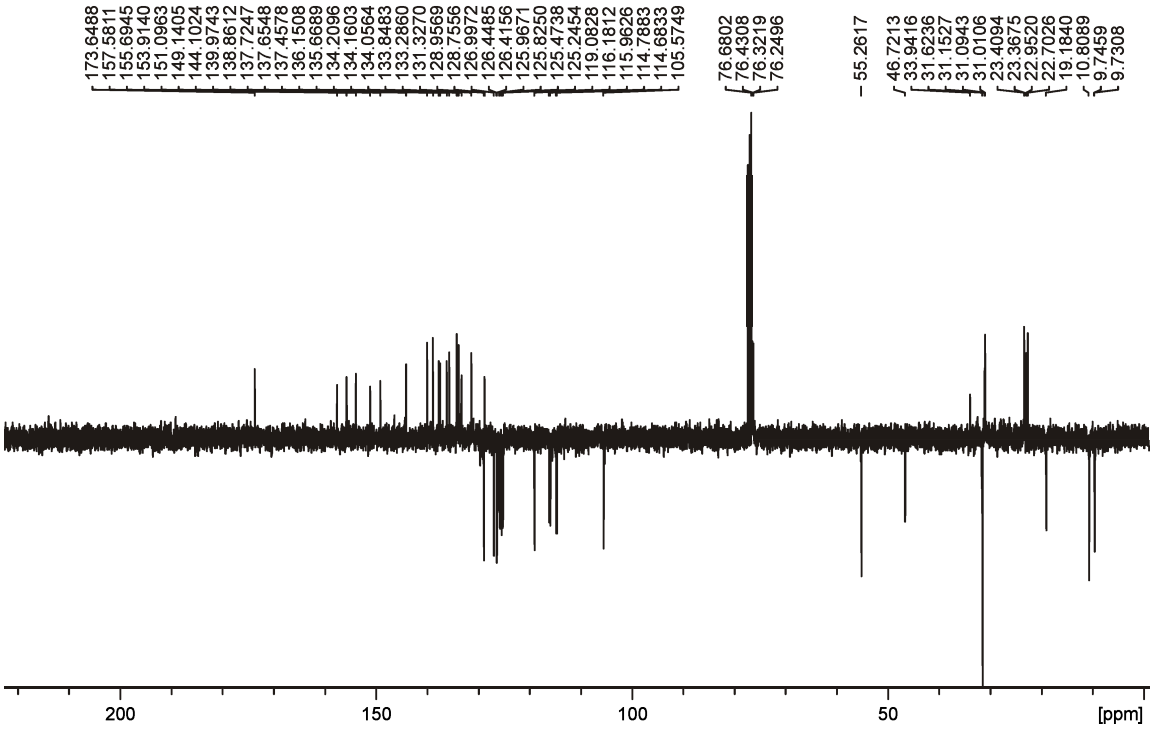


Figure S16. ^{13}C NMR spectrum (APT) of calixarene (*P*,*S*)-**6b** (100 MHz, $CDCl_3$).

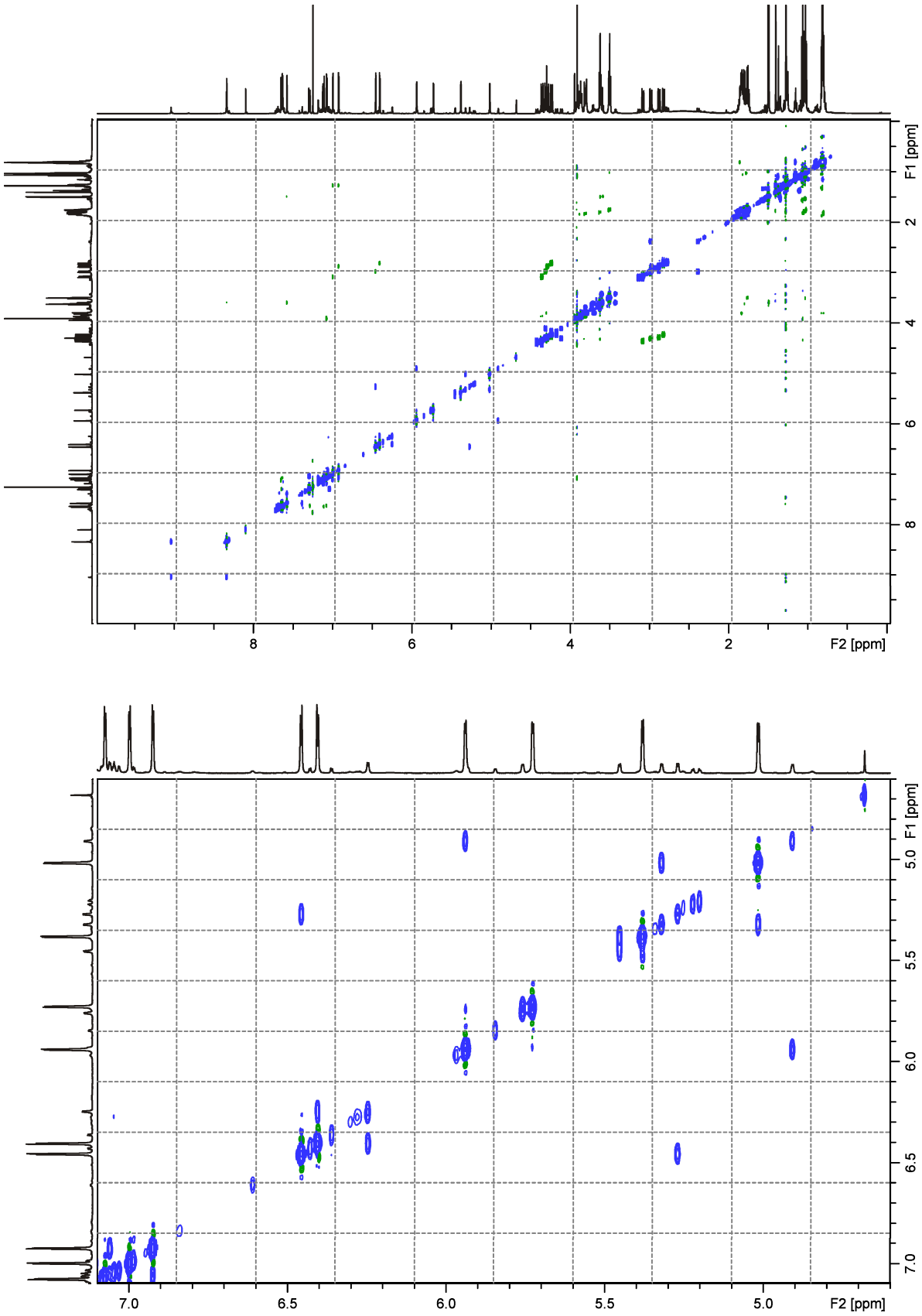


Figure S17. Full (top) and a part of (bottom) 2D EXSY spectrum of calixarene (*P*,*S*)-**6b** (600 MHz, $CDCl_3$, phase-sensitive NOESY sequence, t_m 0.4 s); positive NOE cross-peaks are colored green, negative exchange cross-peaks correlating signals from the major and minor conformers are colored blue.

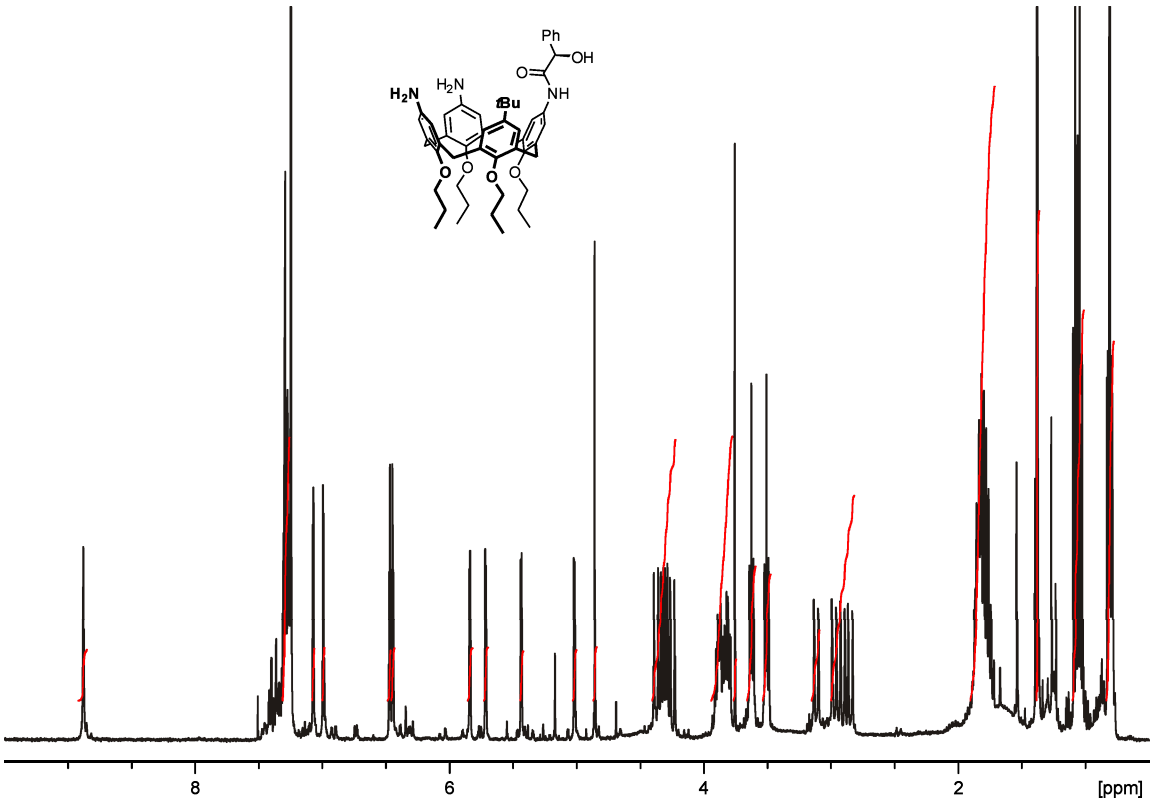


Figure S18. ^{1}H NMR spectrum of calixarene (*M*,*R*)-**7a** (400 MHz, $CDCl_3$).

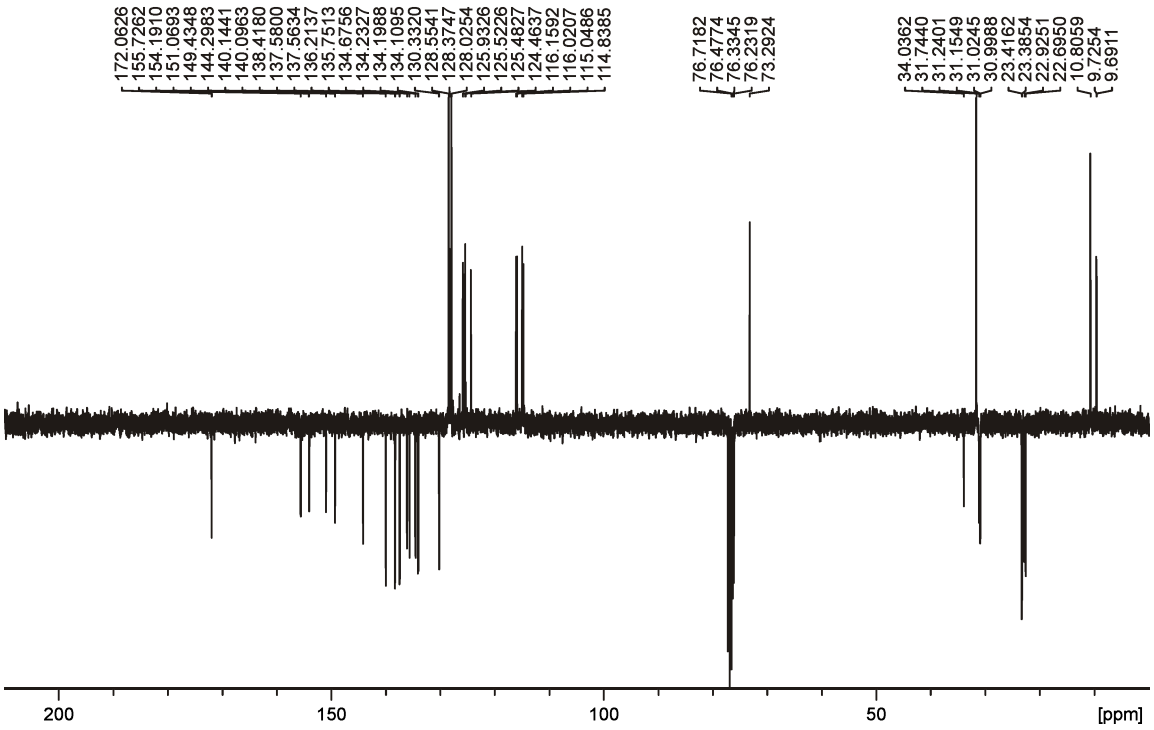


Figure S19. ^{13}C NMR spectrum (APT) of calixarene (*M*,*R*)-**7a** (100 MHz, $CDCl_3$).

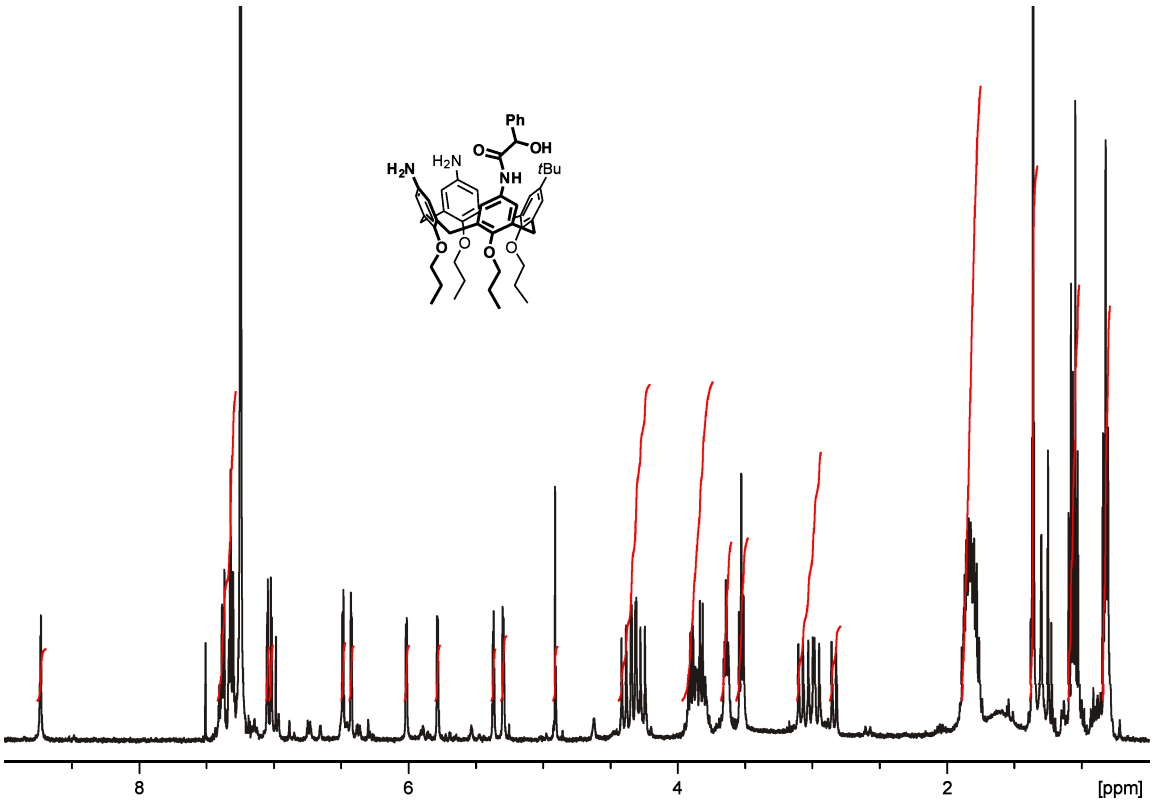


Figure S20. ^{1}H NMR spectrum of calixarene (*P*,*R*)-**7b** (400 MHz, $CDCl_3$).

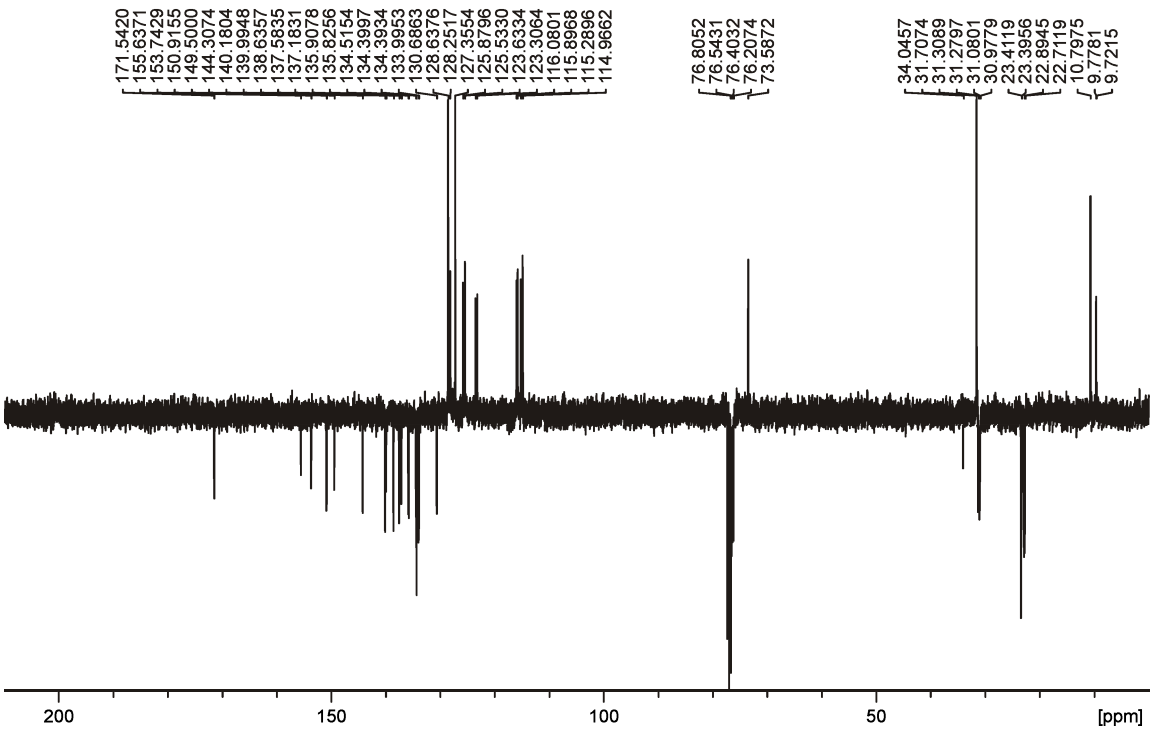


Figure S21. ^{13}C NMR spectrum (APT) of calixarene (*P*,*R*)-**7b** (100 MHz, $CDCl_3$).

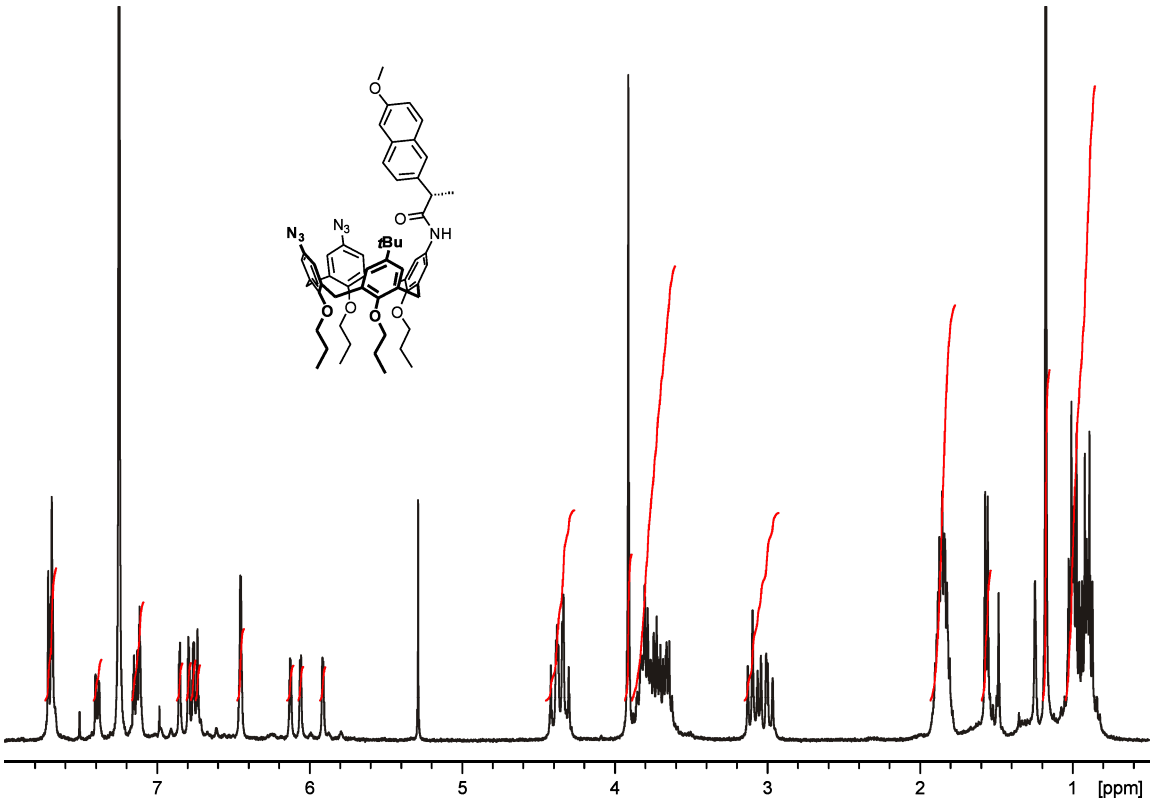


Figure S22. ^{1}H NMR spectrum of calixarene (*P*,*S*)-**8a** (400 MHz, $CDCl_3$).

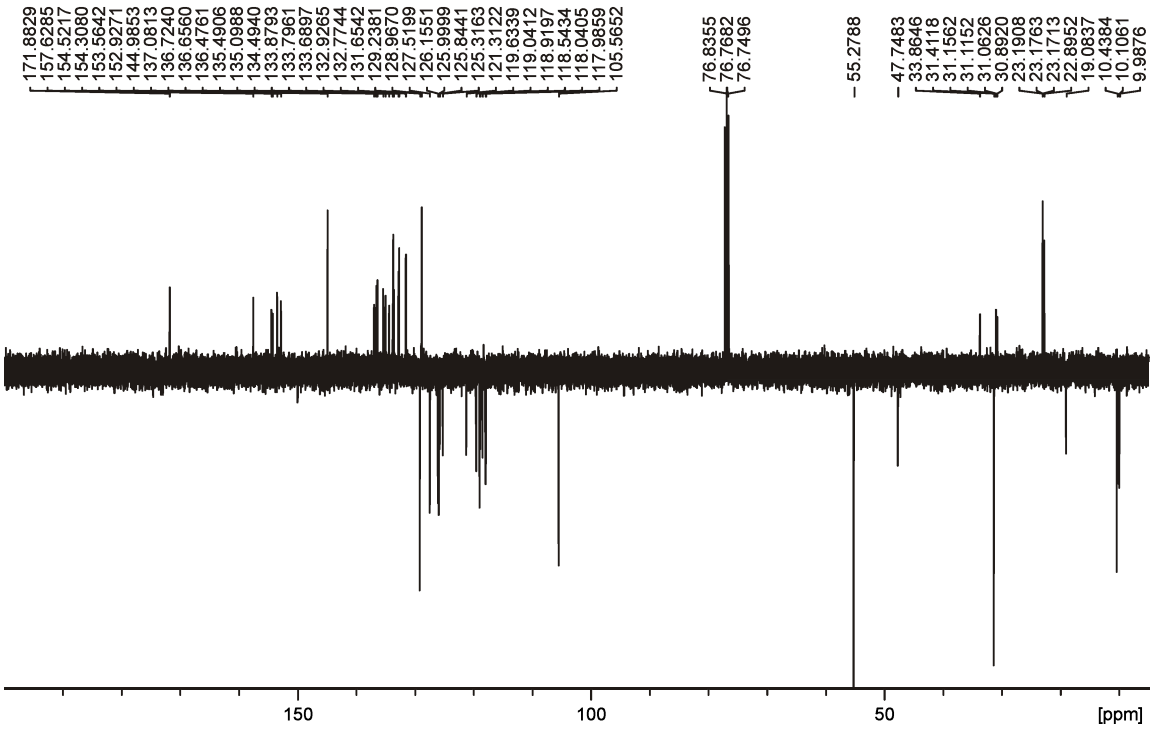


Figure S23. ^{13}C NMR spectrum (APT) of calixarene (*P*,*S*)-**8a** (100 MHz, $CDCl_3$).

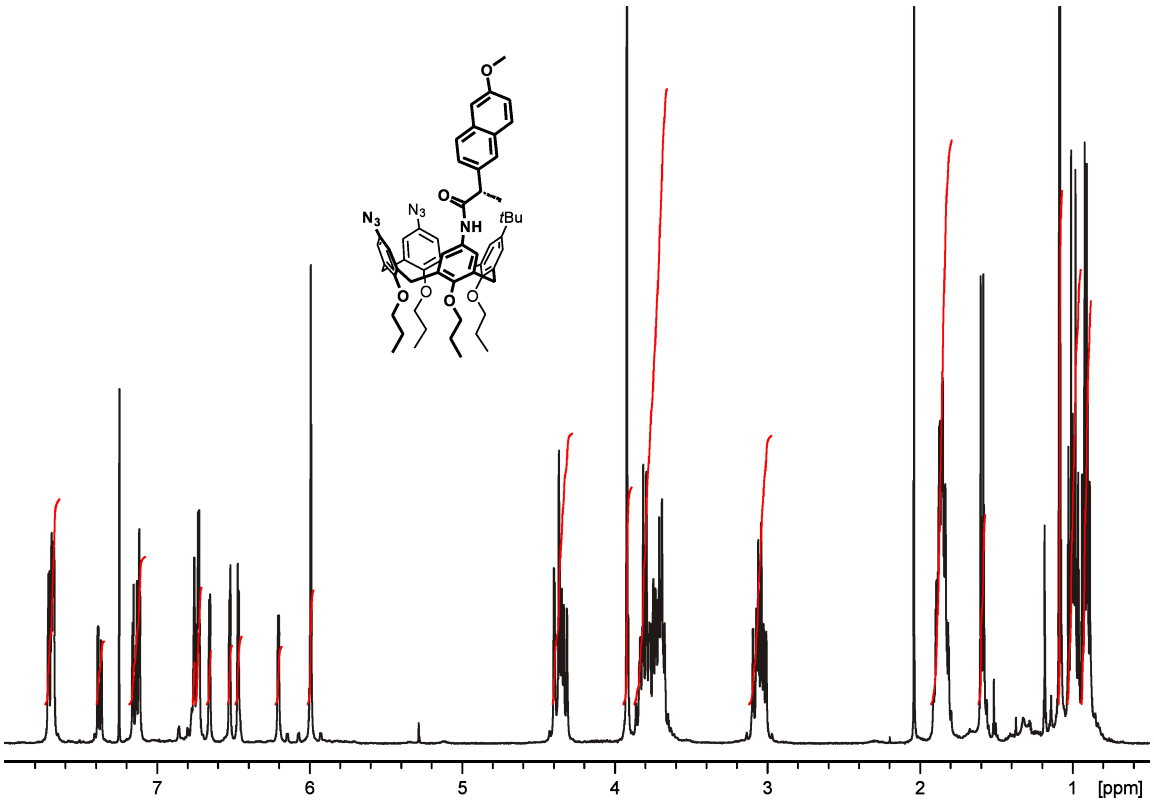


Figure S24. ^{1}H NMR spectrum of calixarene (*M*,*S*)-**8b** (400 MHz, $CDCl_3$).

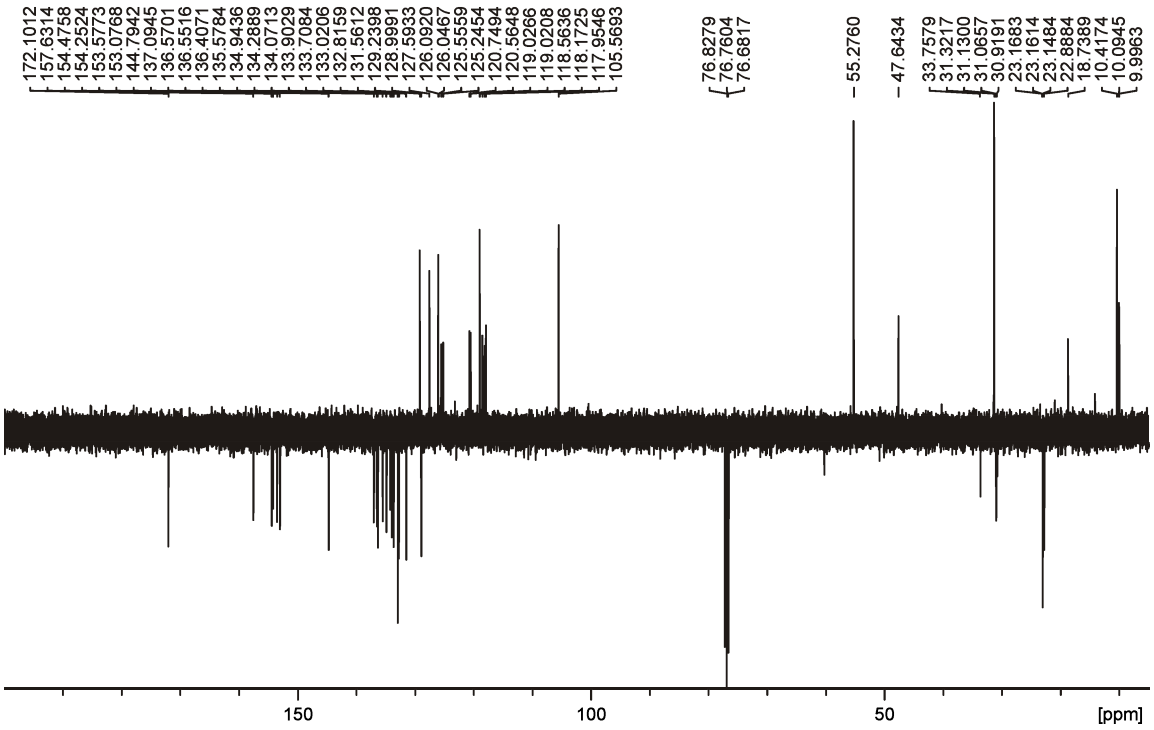


Figure S25. ^{13}C NMR spectrum (APT) of calixarene (*M*,*S*)-**8b** (100 MHz, $CDCl_3$).

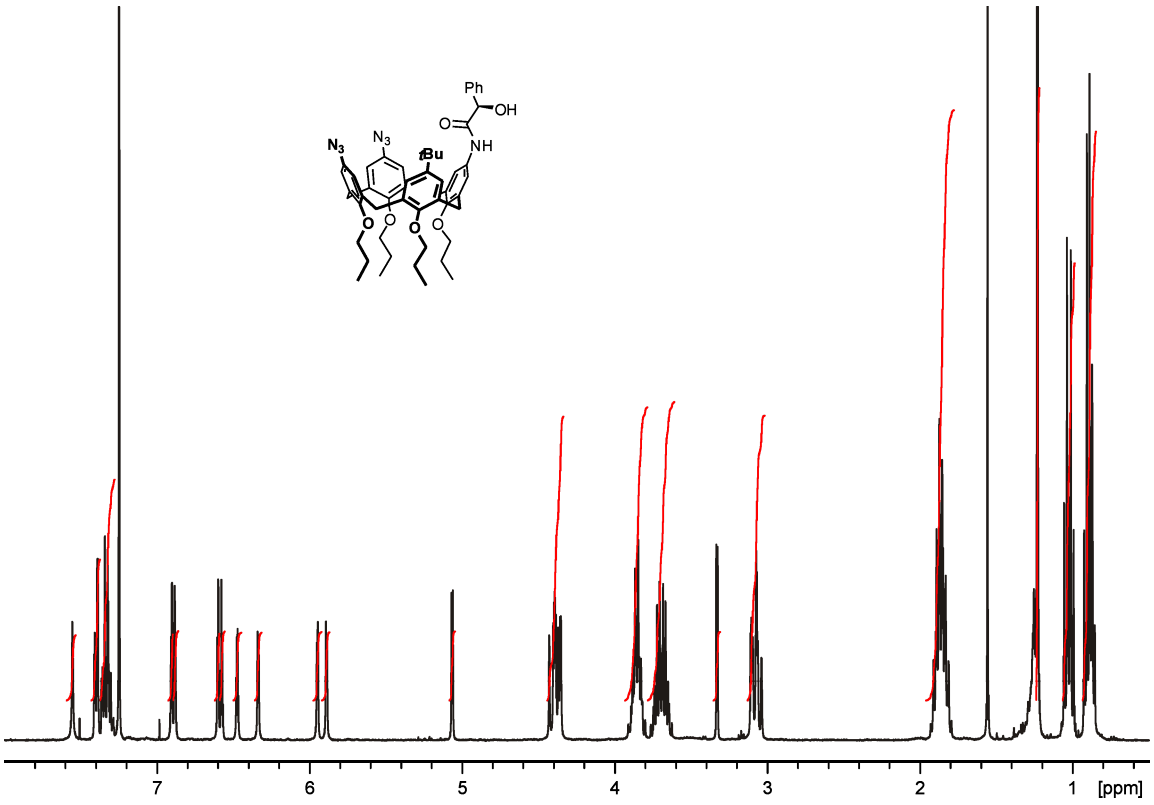


Figure S26. ^{1}H NMR spectrum of calixarene (*P*,*R*)-**9a** (400 MHz, $CDCl_3$).

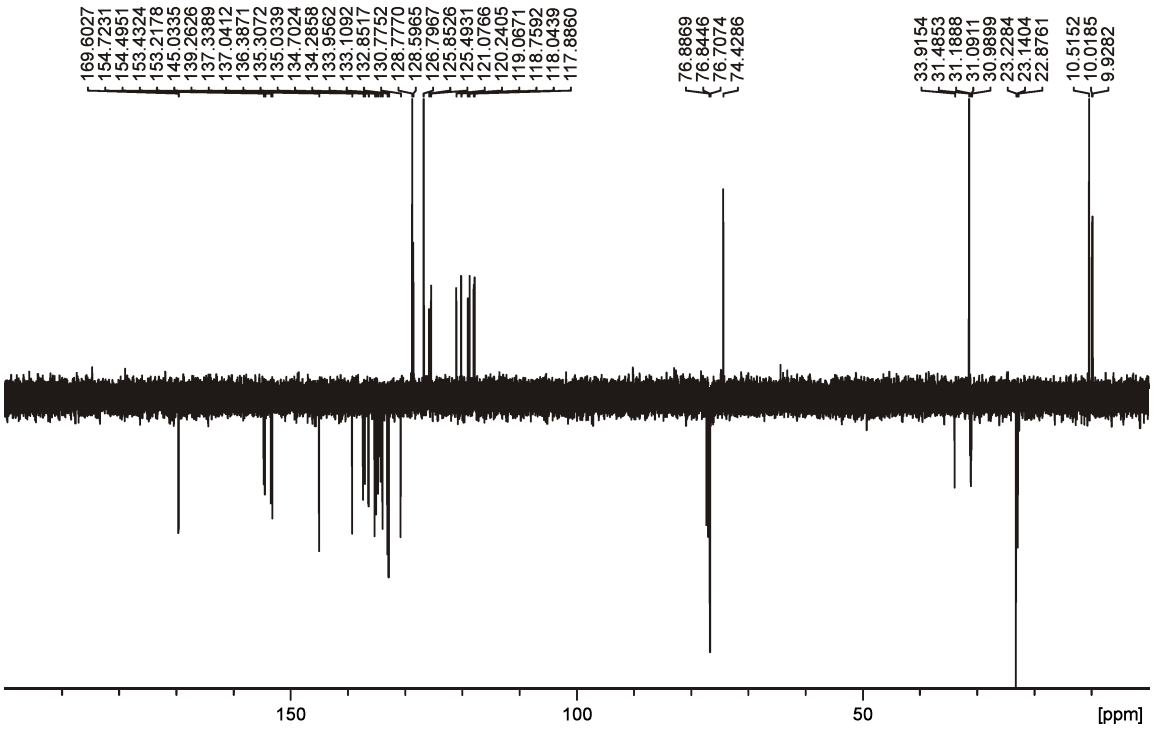


Figure S27. ^{13}C NMR spectrum (APT) of calixarene (*P*,*R*)-**9a** (100 MHz, $CDCl_3$).

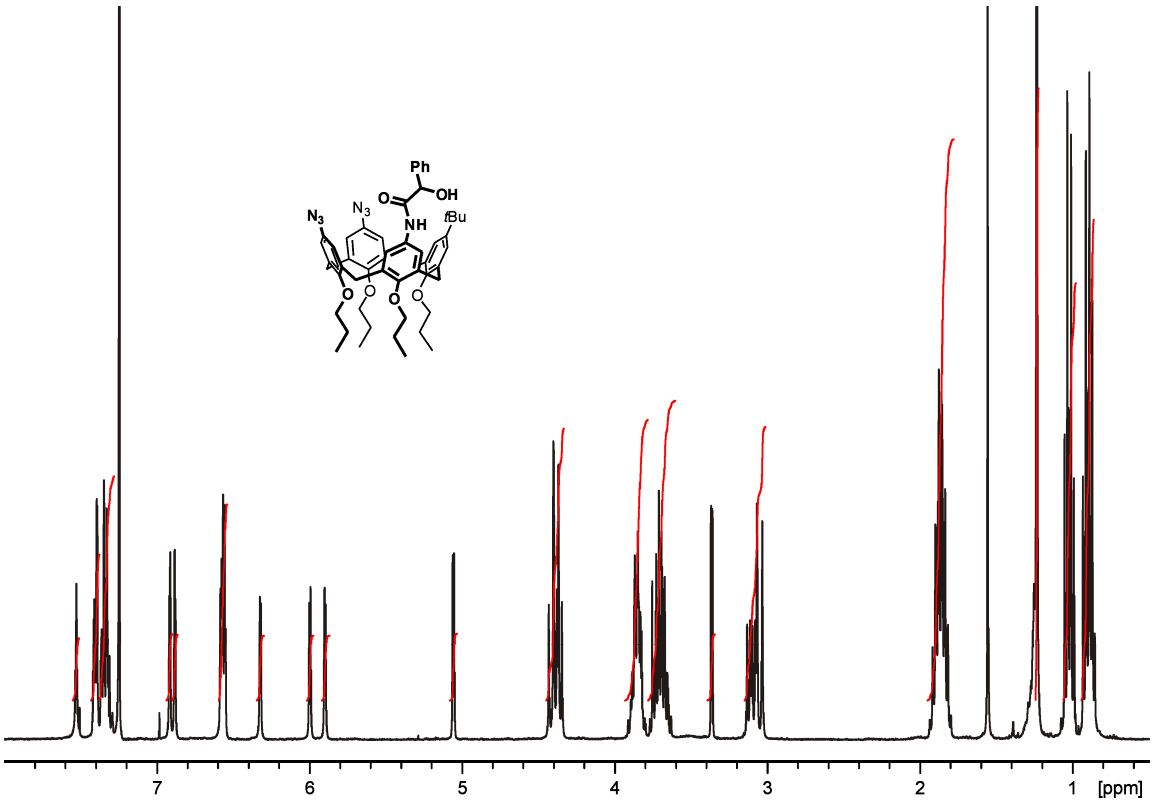


Figure S28. ^{1}H NMR spectrum of calixarene (*M*,*R*)-**9b** (400 MHz, $CDCl_3$).

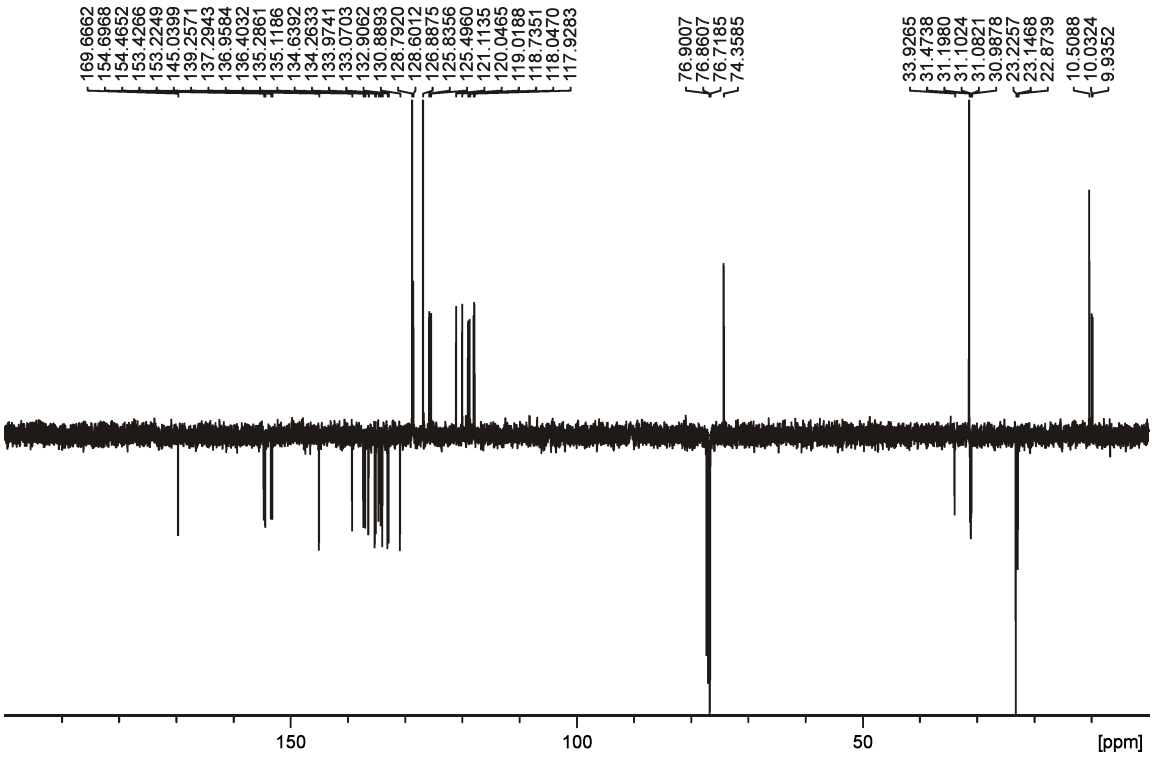


Figure S29. ^{13}C NMR spectrum (APT) of calixarene (*M*,*R*)-**9b** (100 MHz, $CDCl_3$).

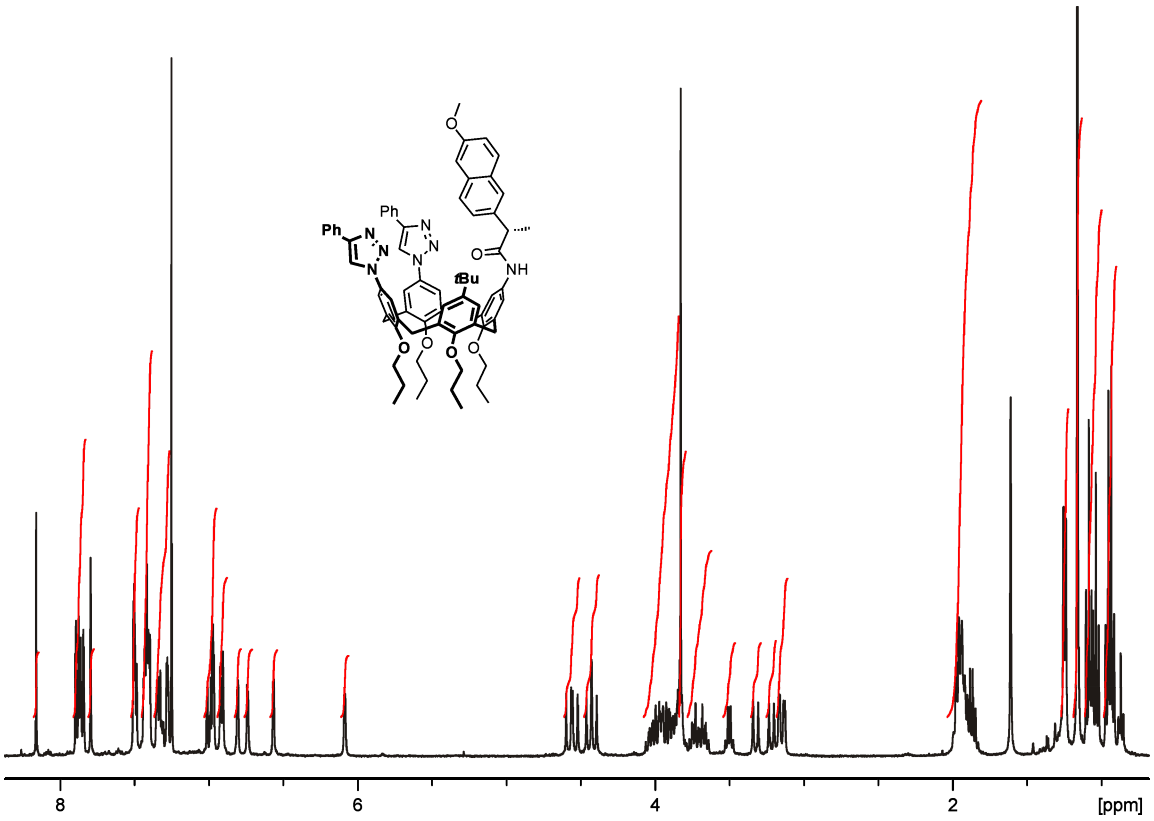


Figure S30. ^{1}H NMR spectrum of calixarene (*P*,*S*)-**10a** (400 MHz, $CDCl_3$).

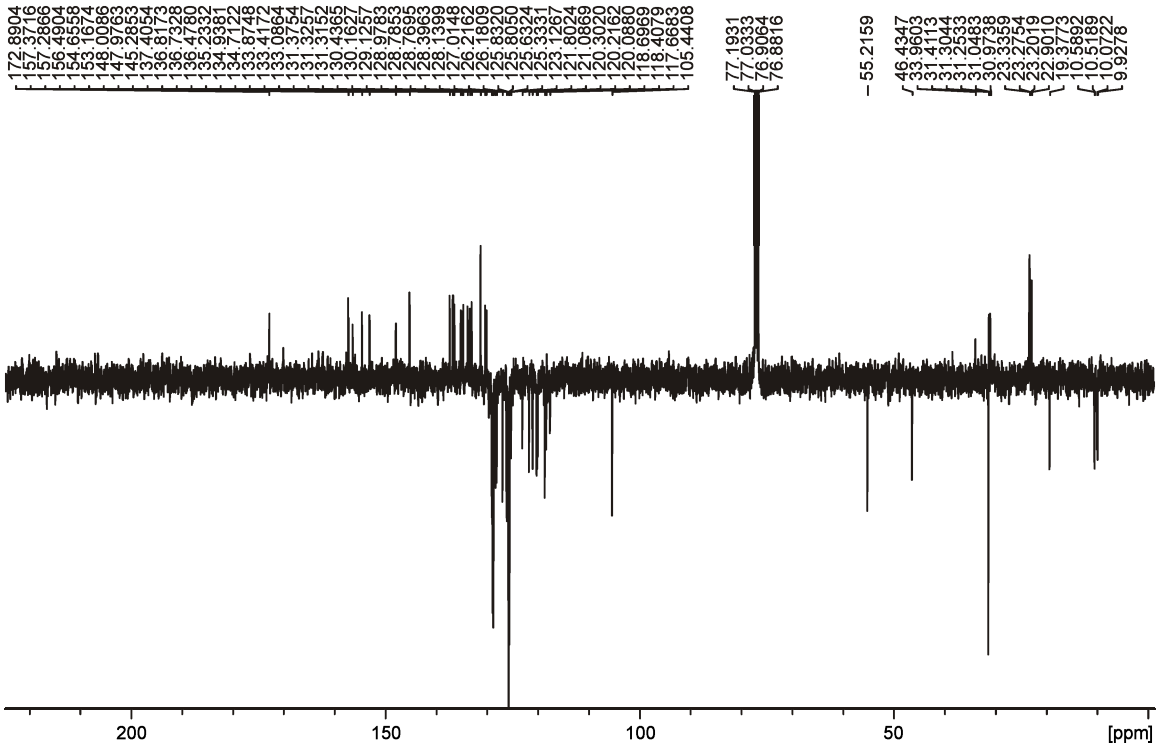


Figure S31. ^{13}C NMR spectrum (APT) of calixarene (*P*,*S*)-**10a** (100 MHz, $CDCl_3$).

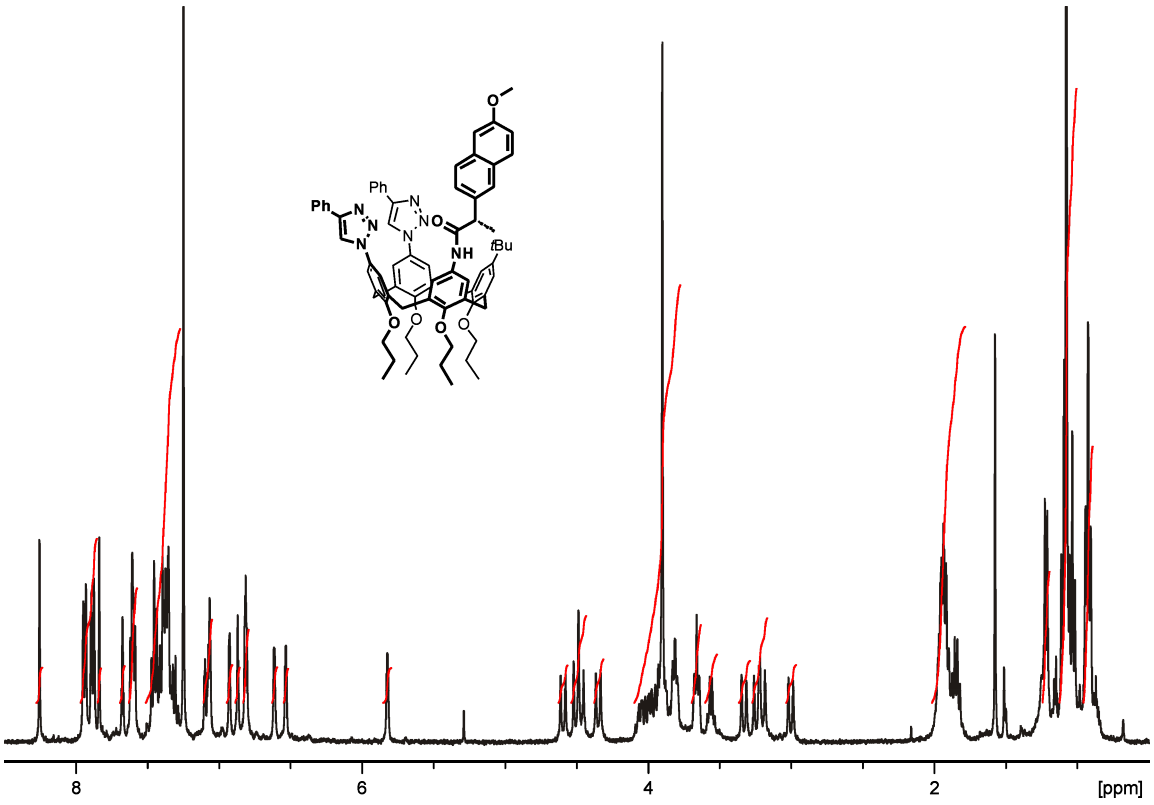


Figure S32. ^{1}H NMR spectrum of calixarene (*M*,*S*)-**10b** (400 MHz, $CDCl_3$).

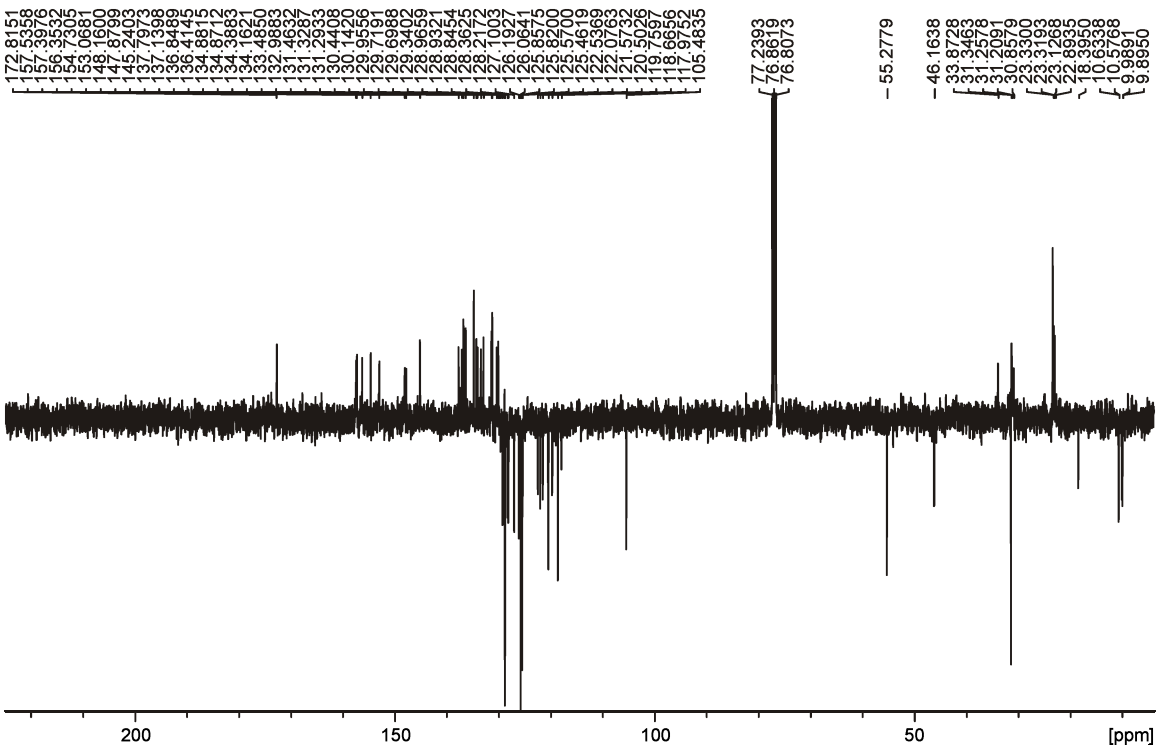


Figure S33. ^{13}C NMR spectrum (APT) of calixarene (*M*,*S*)-**10b** (100 MHz, $CDCl_3$).

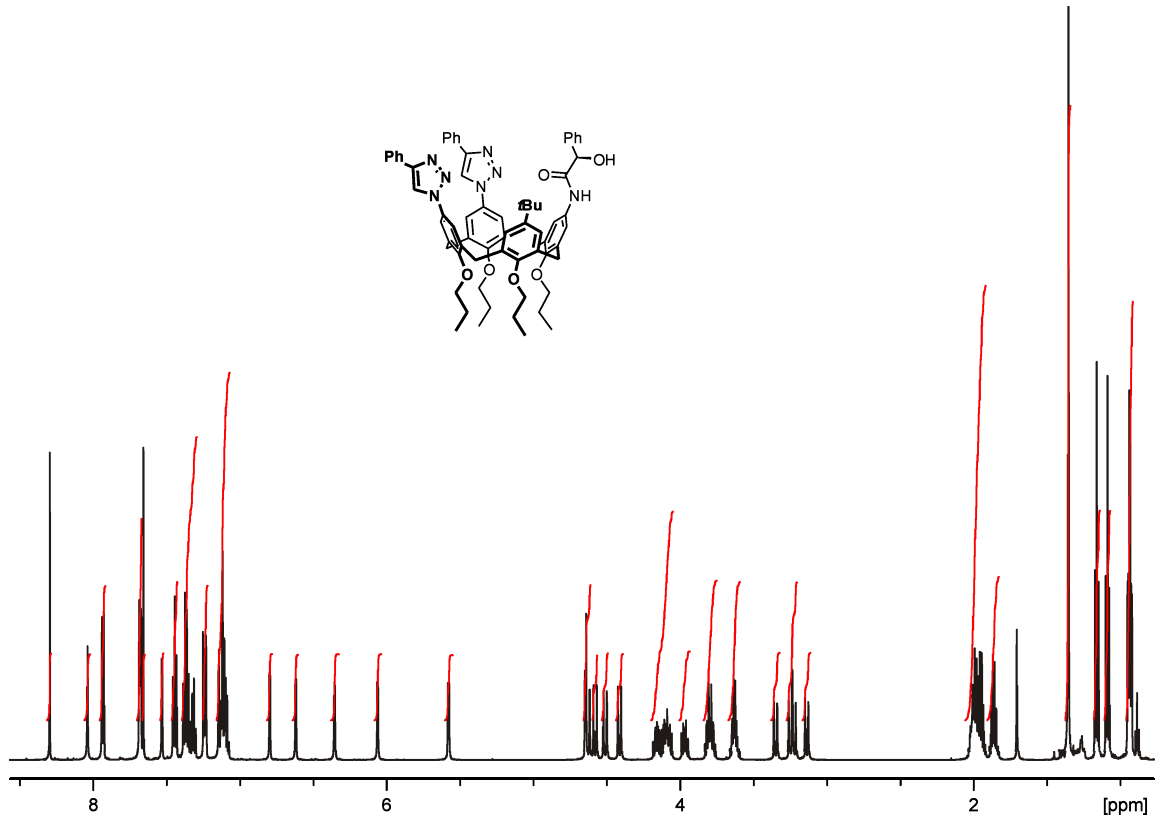


Figure S34. ^{1}H NMR spectrum of calixarene (*P*,*R*)-**11a** (600 MHz, $CDCl_3$).

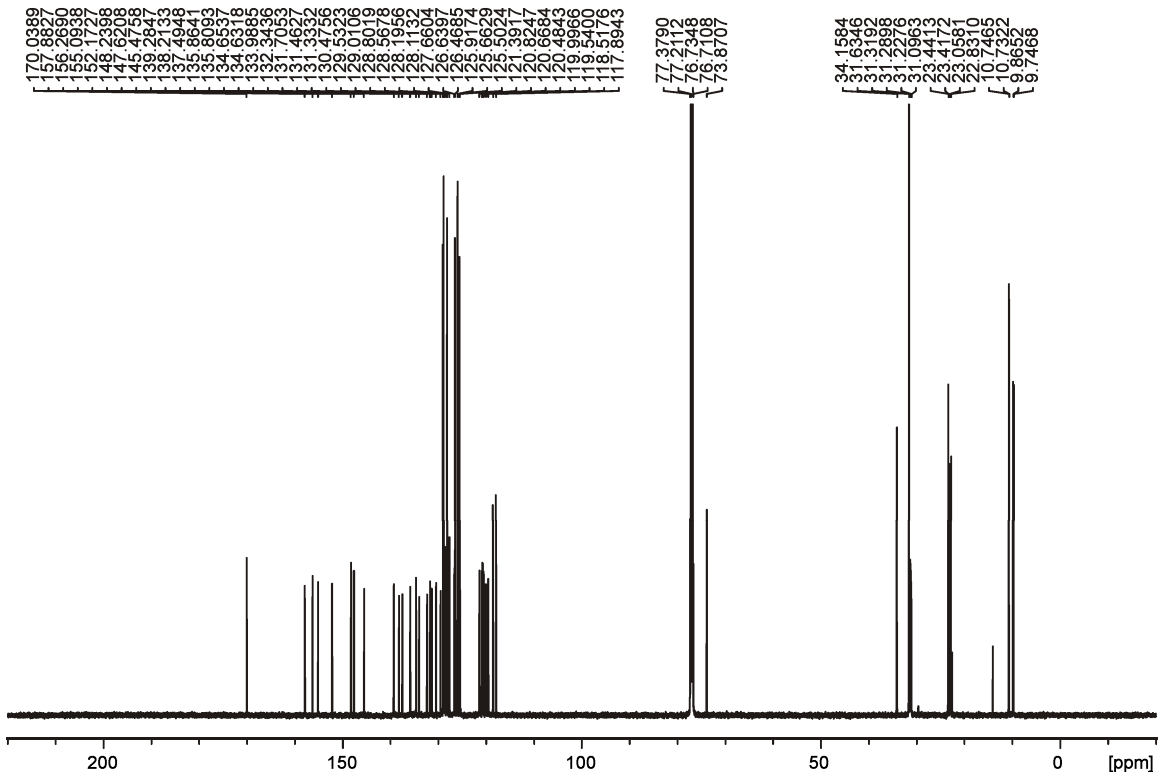


Figure S35. ^{13}C NMR spectrum of calixarene (*P*,*R*)-**11a** (150 MHz, $CDCl_3$).

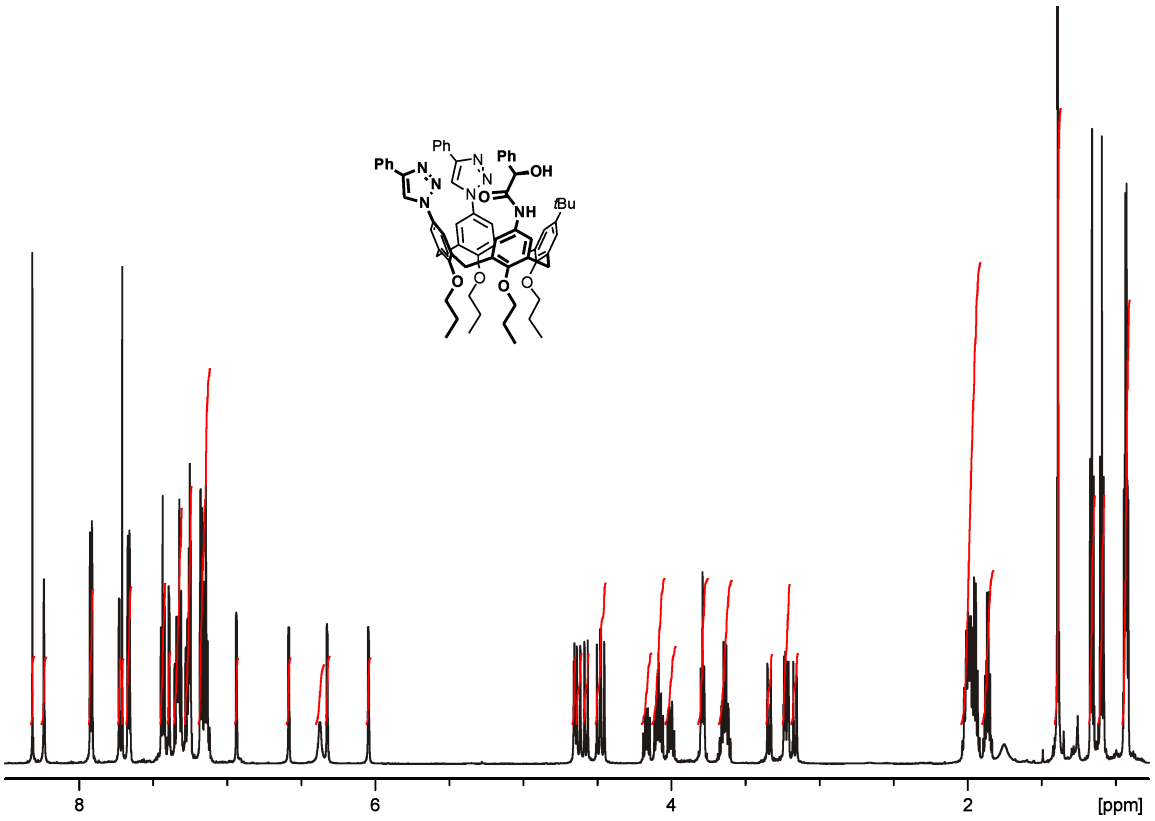


Figure S36. ^{1}H NMR spectrum of calixarene (*M*,*R*)-**11b** (600 MHz, $CDCl_3$).

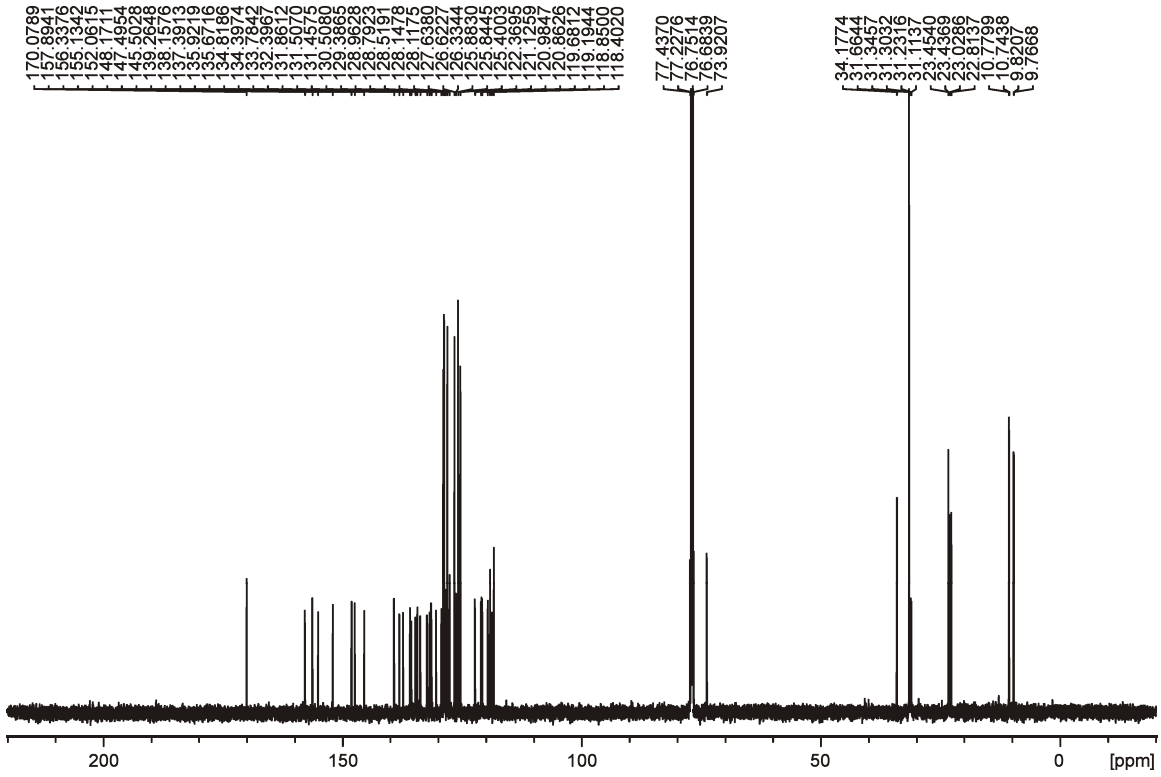


Figure S37. ^{13}C NMR spectrum of calixarene (*M*,*R*)-**11b** (150 MHz, $CDCl_3$).

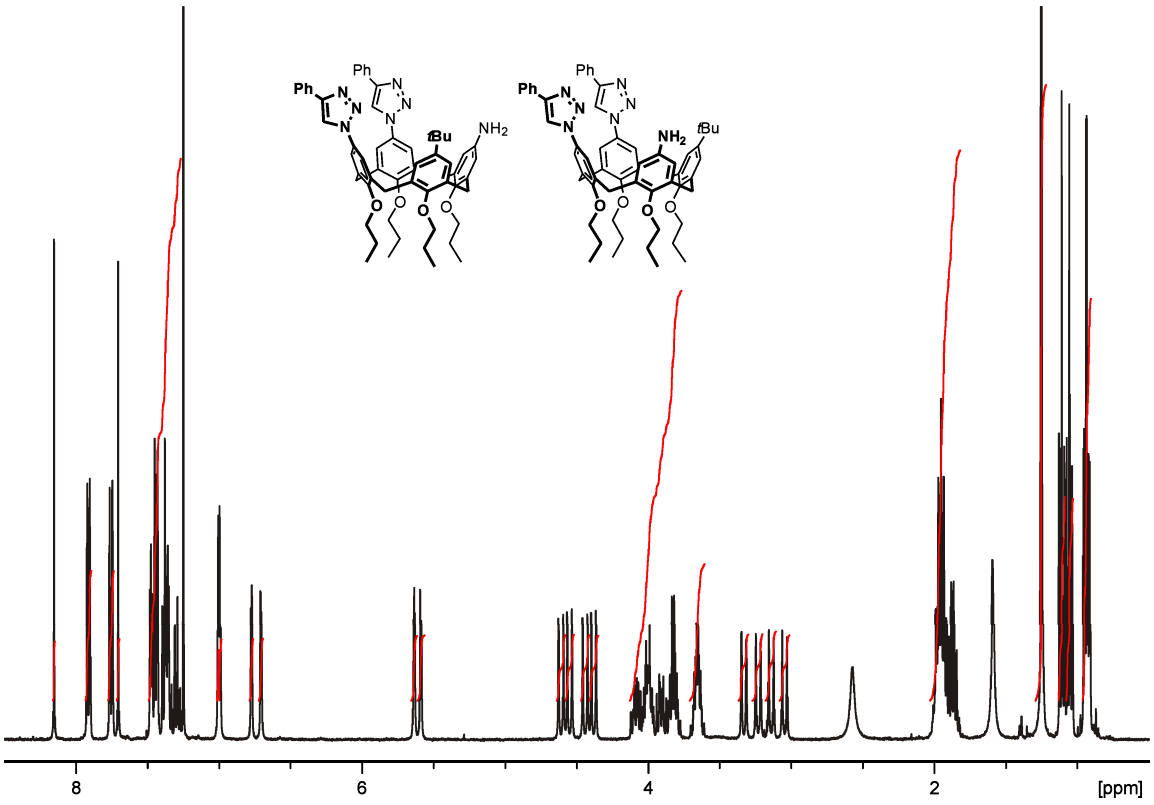


Figure S38. ^{1}H NMR spectrum of calixarene (*P*)-**12a**/(*M*)-**12b** (400 MHz, $CDCl_3$).

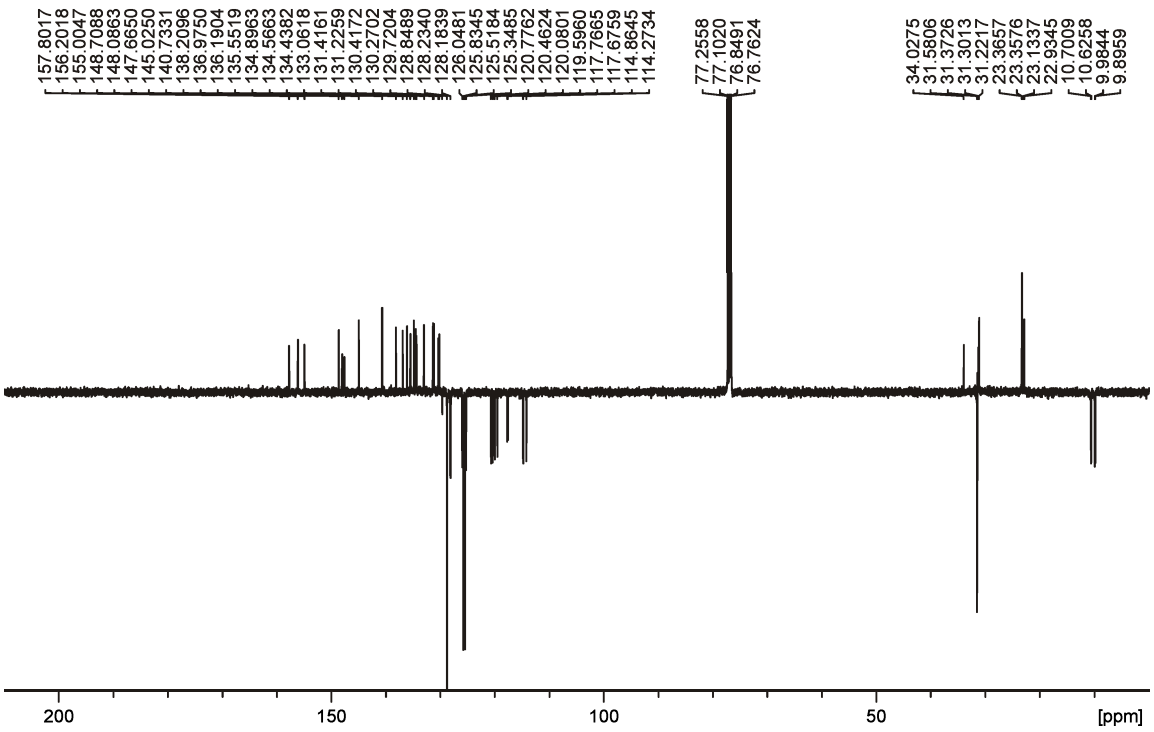


Figure S39. ^{13}C NMR spectrum (APT) of calixarene (*P*)-**12a**/(*M*)-**12b** (100 MHz, $CDCl_3$).

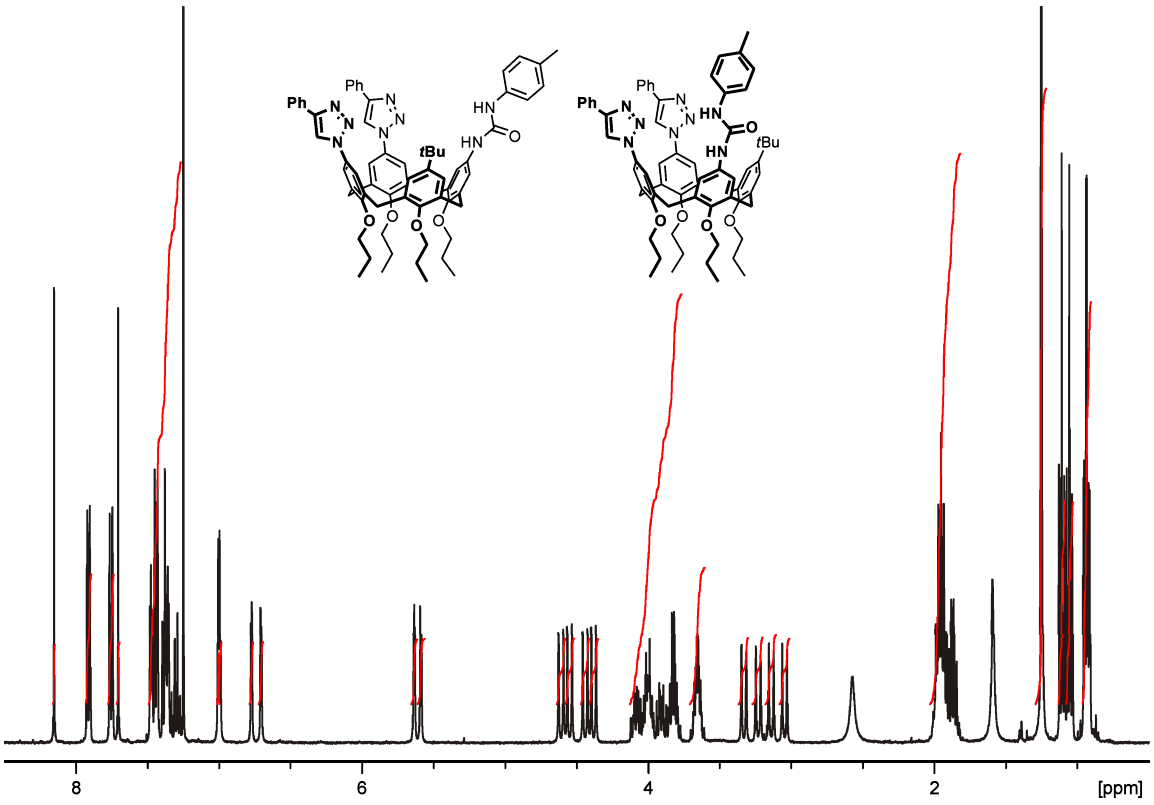


Figure S40. ^{1}H NMR spectrum of calixarene (*P*)-**13a**/(*M*)-**13b** (400 MHz, $CDCl_3$).

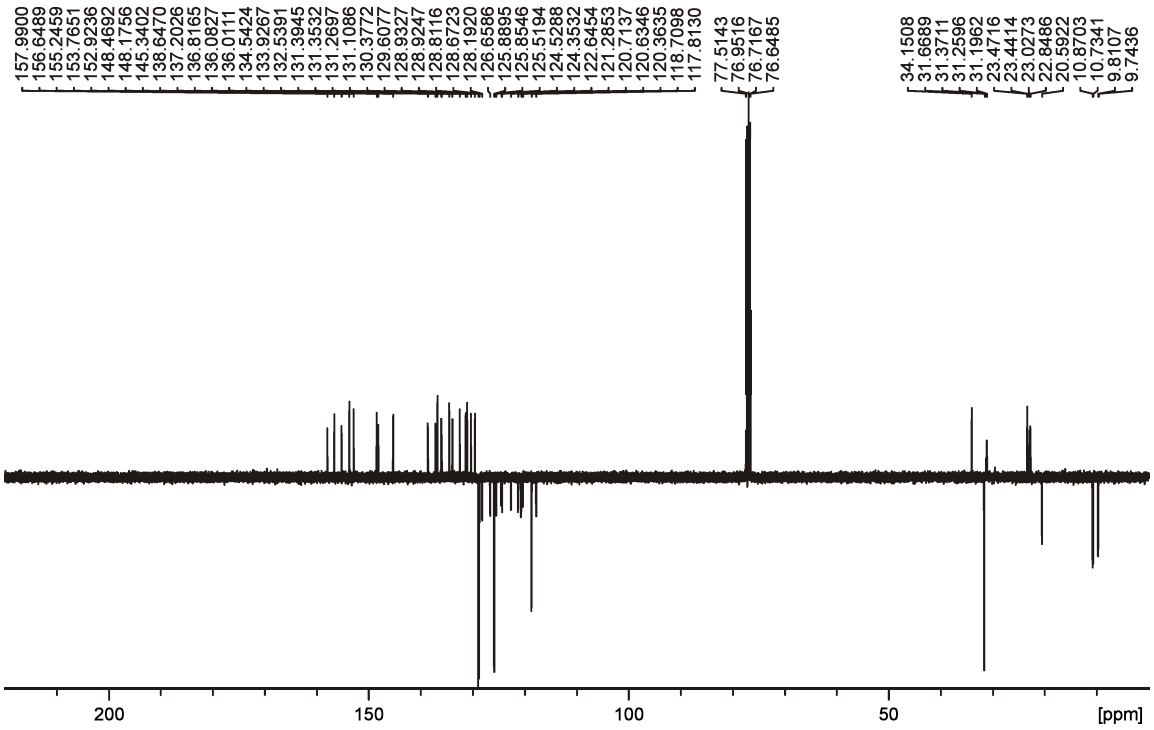


Figure S41. ^{13}C NMR spectrum (APT) of calixarene (*P*)-**13a**/(*M*)-**13b** (100 MHz, $CDCl_3$).

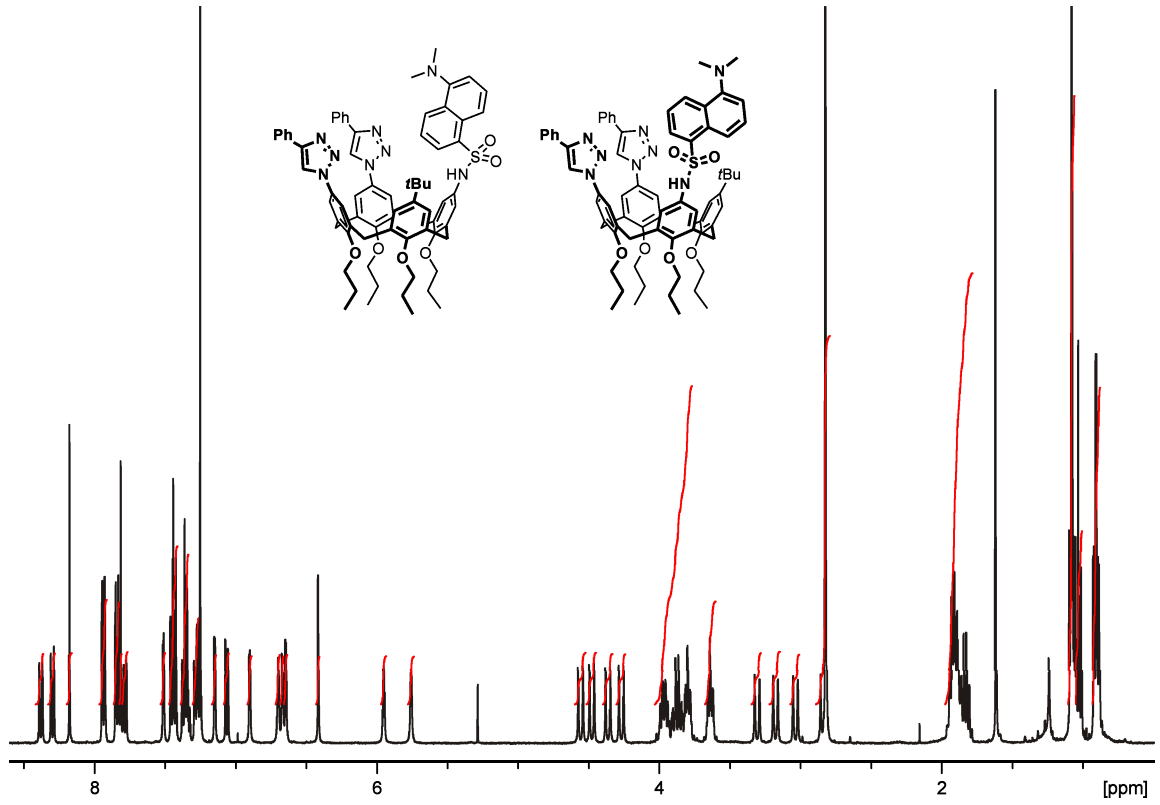


Figure S42. ^{1}H NMR spectrum of calixarene (*M*)-**14a**/(*P*)-**14b** (400 MHz, $CDCl_3$).

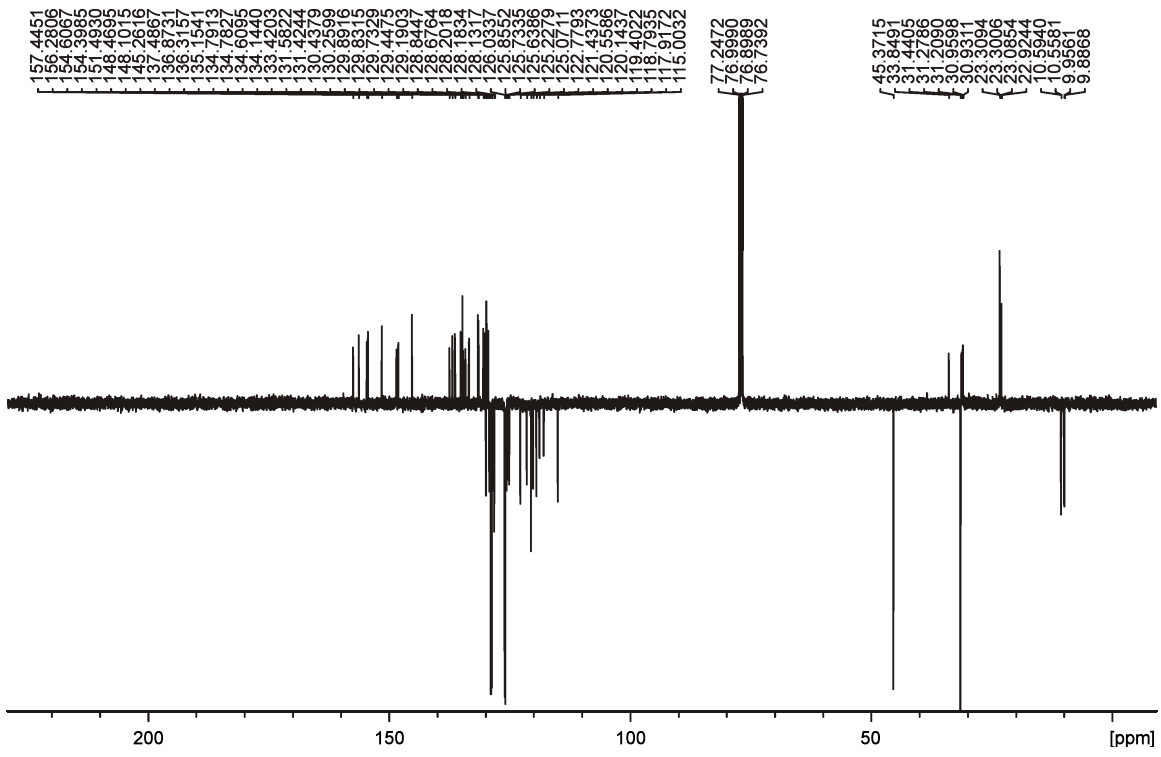


Figure S43. ^{13}C NMR spectrum (APT) of calixarene (*M*)-**14a**/(*P*)-**14b** (100 MHz, $CDCl_3$).

Details of chiral HPLC experiments

Enantiomeric purity of the optically active compounds was determined by chiral HPLC with a Hitachi LaChrome Elite-2000 chromatograph with a UV detector using Daicel columns (0.46 × 25 cm) at room temperature. The chromatograms were processed with the MultiKhrom program. The chiral HPLC data are summarized in Table S1.

The optical purity of the used (*S*)-naproxen (99.6% ee) and (*R*)-mandelic acid (>99.9% ee) was determined after their conversion to methyl esters using a Chiralcel OD-H column. Conditions for the separation of naproxen methyl esters: *n*-hexane/*i*-PrOH 95/5, 1.0 mL/min, 254 nm; the racemic sample was prepared by the base-catalyzed racemization of (*S*)-naproxen followed by estericifation. Conditions for the separation of mandelic acid methyl esters: *n*-hexane/*i*-PrOH 80/20, 1.0 mL/min, 220 nm; the racemic sample was prepared by mixing the methyl esters of the commercially available (*R*)-mandelic acid and (*S*)-mandelic acid.

Enantiomeric purity of the chiral calixarene ureas (*P*)-**13a** and (*M*)-**13b** was determined using a Chiralcel OJ-H column, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, 254 nm. The measurements were carried out in two time-separated series for ureas (*P*)-**13a**$_{\mathbf{SNap}}$/(*M*)-**13b**$_{\mathbf{SNap}}$ and (*P*)-**13a**$_{\mathbf{RMA}}$/(*M*)-**13b**$_{\mathbf{RMA}}$, respectively, which results in slightly different retention times of the enantiomers due to different ambient temperatures.

Table S1. Chiral HPLC data for (*S*)-naproxen methyl ester, (*R*)-mandelic acid methyl ester and calixarenes (*P*)-**13a**, (*M*)-**13b**.

Sample	Retention time1, min	Area1, mV s (%)	Retention time2, min	Area2, mV s (%)
rac-naproxen methyl ester	7.01	1723.484 (50.00)	8.13	1723.252 (50.00)
(*S*)-naproxen methyl ester	7.06	2.153 (0.18)	8.18	1223.409 (**99.82**)
(*R*)-mandelic acid methyl ester + (*S*)-mandelic methyl ester	5.98	1850.390 (52.87)	9.03	1649.685 (47.13)
(*R*)-mandelic methyl ester	5.98	0.487 (0.02)	8.98	2928.013 (**99.98**)
(*P*)-**13a**$_{\mathbf{SNap}}$ + (*M*)-**13b**$_{\mathbf{SNap}}$	6.53	796.153 (51.43)	12.32	751.835 (48.57)
(*P*)-**13a**$_{\mathbf{SNap}}$	6.52	220.426 (7.27)	12.15	2812.954 (**92.73**)
(*M*)-**13b**$_{\mathbf{SNap}}$	6.52	1289.834 (**94.51**)	12.32	74.964 (5.49)
(*P*)-**13a**$_{\mathbf{RMA}}$ + (*M*)-**13b**$_{\mathbf{RMA}}$	6.85	1502.683 (50.43)	15.11	1476.952 (49.57)
(*P*)-**13a**$_{\mathbf{RMA}}$	6.85	7.980 (0.29)	14.95	2786.333 (**99.71**)
(*M*)-**13b**$_{\mathbf{RMA}}$	6.79	4421.831 (**99.62**)	15.06	16.776 (0.38)

Details of X-ray diffraction measurements

The X-ray study was performed for a single suitable needle-like crystal (0.04×0.04×0.32 mm). The diffraction data were collected on a Bruker D8 Venture diffractometer using graphite monochromatized MoKα radiation (INCOATEC IμS 3.0) in ω-scan mode with 120 s per frame (step 0.5°); detector PHOTON III in sensitive mode. Longer time resulted in a significant number of topped low-angle reflections without any increase in intensity of reflections at $2\theta > 42°$, while the use of CuKα radiation (INCOATEC IμS 3.0) with various collection time in three different areas (d > 2.5 Å; 1.0 Å < d < 3 Å; 0.8 Å < d < 1.1 Å) did not result in better diffraction data because at d < 1.1 Å there were no reflections measured even when 120 s per frame was used. Absorption correction based on measurements of equivalent reflections was applied (SADABS-2016/2, Bruker 2016/2). The structure was solved by direct methods (SHELXT 2018/2)[S3] and refined by full matrix least-squares on F^2 with anisotropic thermal parameters for all non-hydrogen atoms (SHELXL 2018/3)[S4] as implemented in the Olex2 package.[S5] The hydrogen atoms were placed in calculated positions and refined using a riding model. Crystallographic details are presented in Table S2.

Table S2. Details of the X-ray crystal data collection and structure refinement for compound (*M*)-**14a**.

Empirical formula	$C_{72}H_{78}N_8O_6S$
M_w	1183.48
Temperature (K)	100(2)
Size (mm)	0.32 x 0.04 x 0.04
Cryst. system	orthorhombic
Space group	$P2_12_12_1$
a (Å)	17.721(6)
b (Å)	26.054(8)
c (Å)	28.742(9)
V (Å^3)	13271(7)
Z	8
θ range (deg)	$1.56 < \theta < 25.12$
collected/unique reflections	293482 / 23537
Completeness to θ (%)	99.7
data/restraints/params	23537 / 34 / 1627
Goodness of fit on F^2	1.012
Final *R* indices ($I > 2\sigma(I)$)	R1 = 0.0751 wR2 = 0.1480
Largest diff peak/hole (e/Å^3)	0.41 / −0.28
Flack parameter	0.03(8)

Energy-minimized structures of complexes

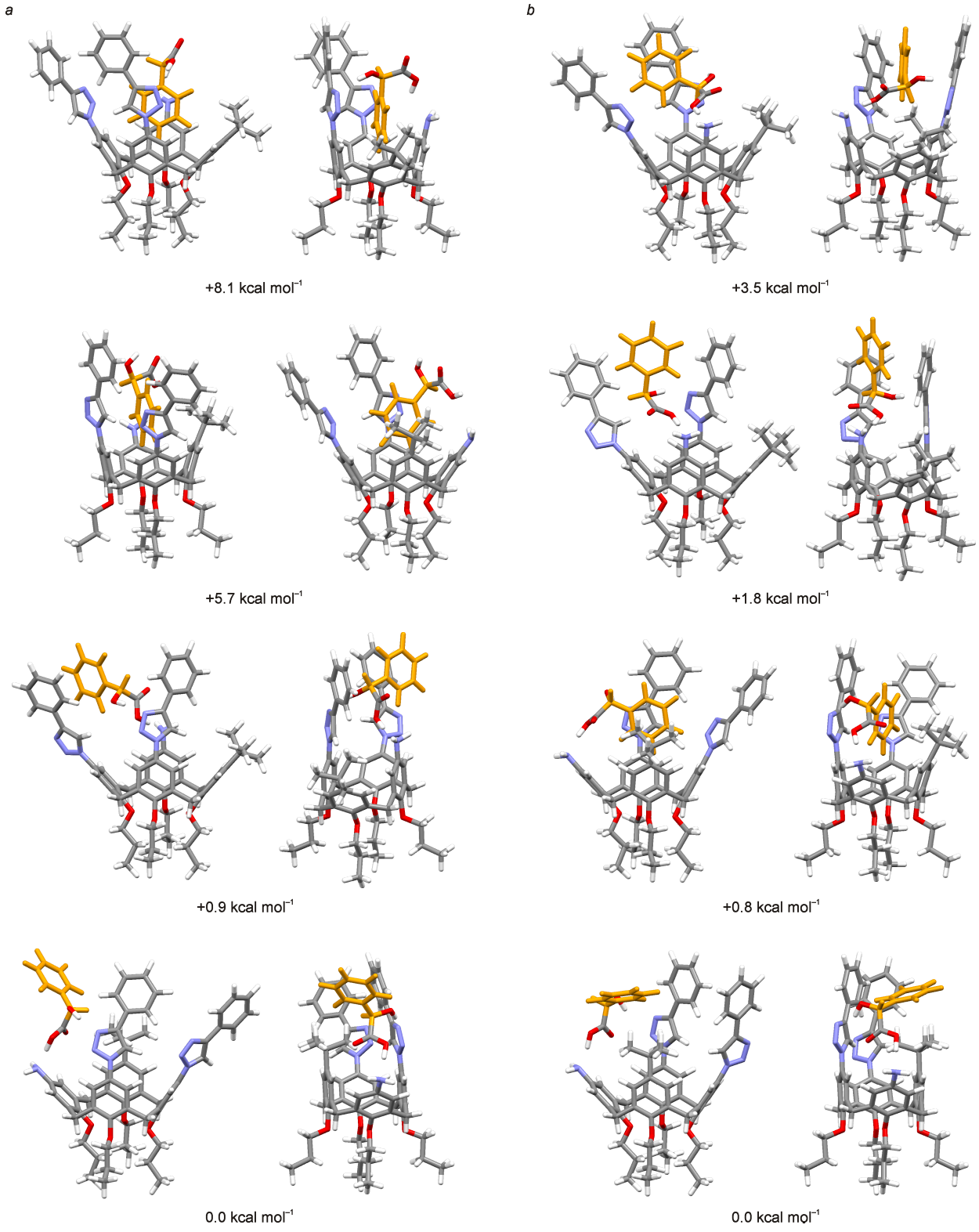


Figure S44. Energy-minimized structures (each in two projections) and relative full-electron energies of the (*R*)-mandelic acid complexes of amines (*P*)-**12a** (*a*) and (*M*)-**12b** (*b*); energy values are given relative to the most stable complex in both series; here and below: PBE0/def2-SVP, gCP, D4, CPCM (chloroform), ORCA 6.0.1 package.

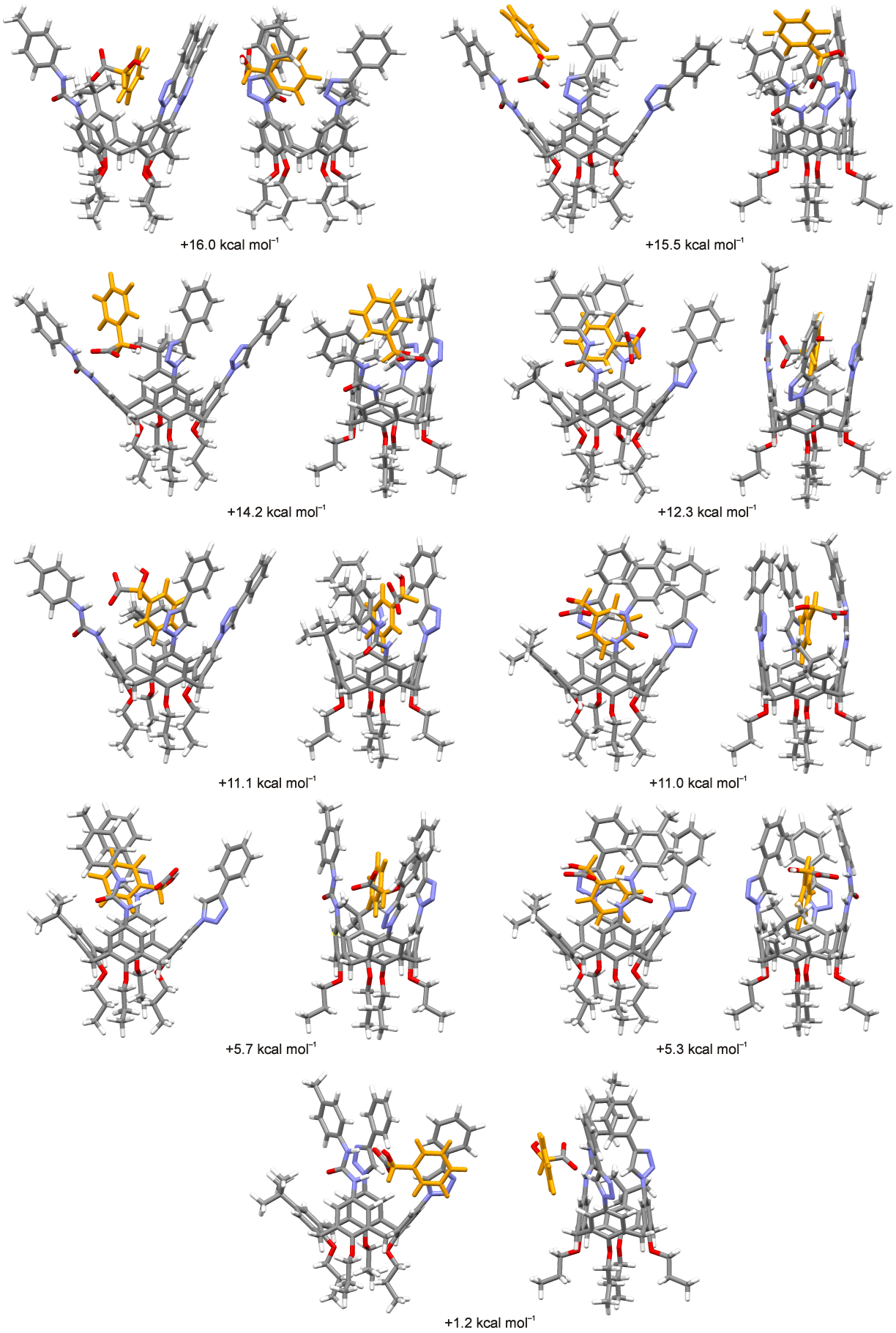


Figure S45. Energy-minimized structures (each in two projections) and relative full-electron energies of the (*R*)-mandelate-anion complexes of urea (*P*)-**13a**; energy values are given relative to the most stable complex among those presented in Figs. S45 and S46.

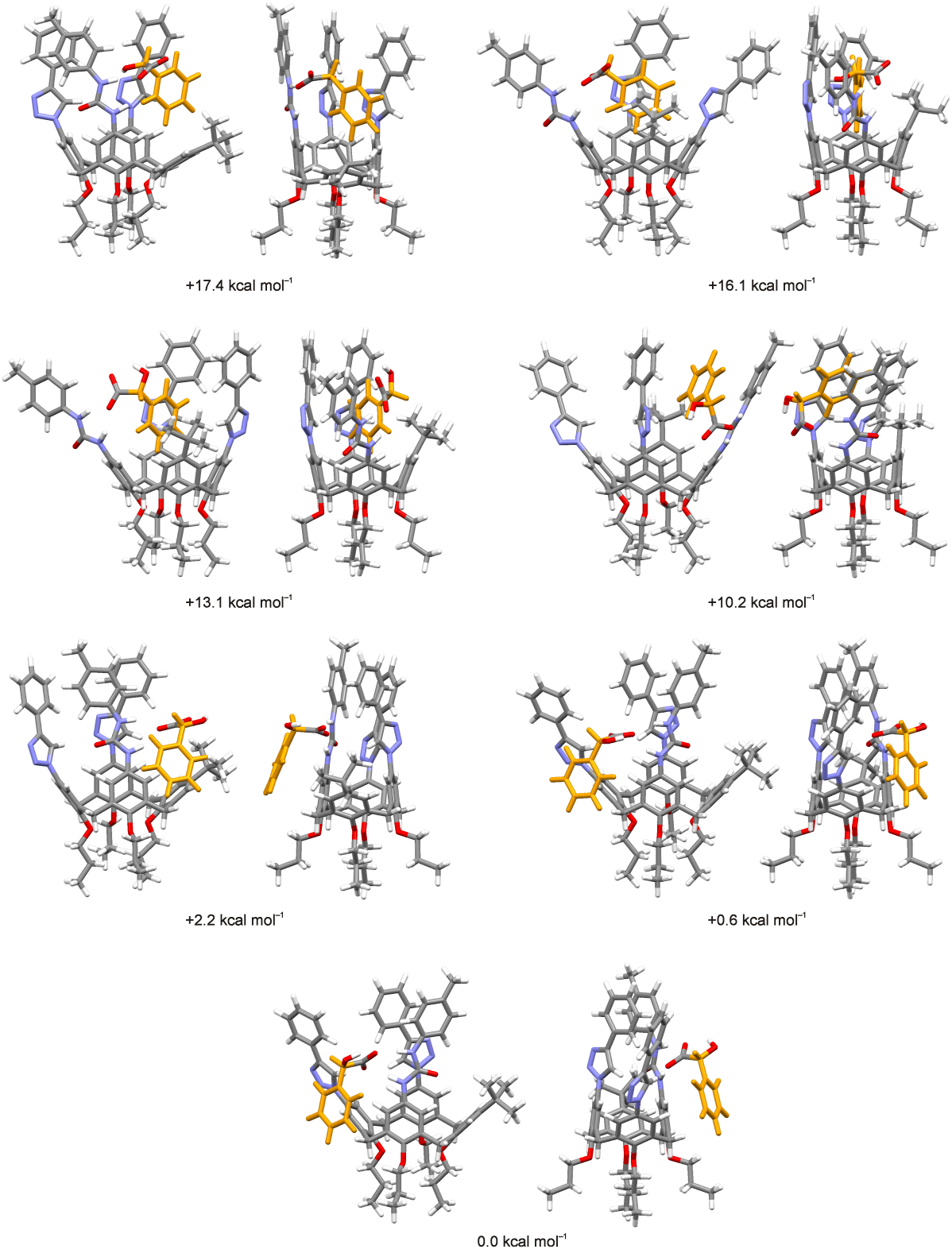


Figure S46. Energy-minimized structures (each in two projections) and relative full-electron energies of the (*R*)-mandelate-anion complexes of urea (*M*)-**13b**; energy values are given relative to the most stable complex among those presented in Figs. S45 and S46.

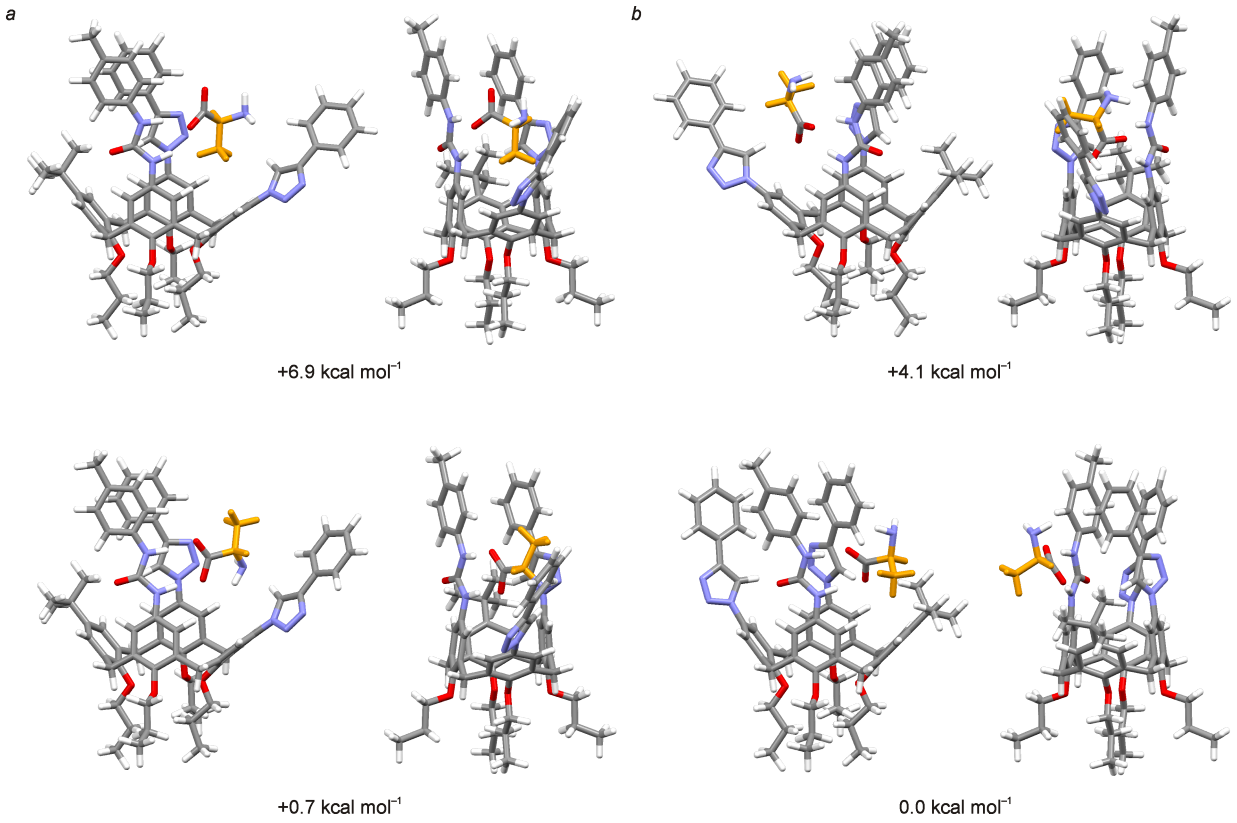


Figure S47. Energy-minimized structures (each in two projections) and relative full-electron energies of the (*L*)-alaninate-anion complexes of ureas (*P*)-**13a** (*a*) and (*M*)-**13b** (*b*); energy values are given relative to the most stable complex in both series.

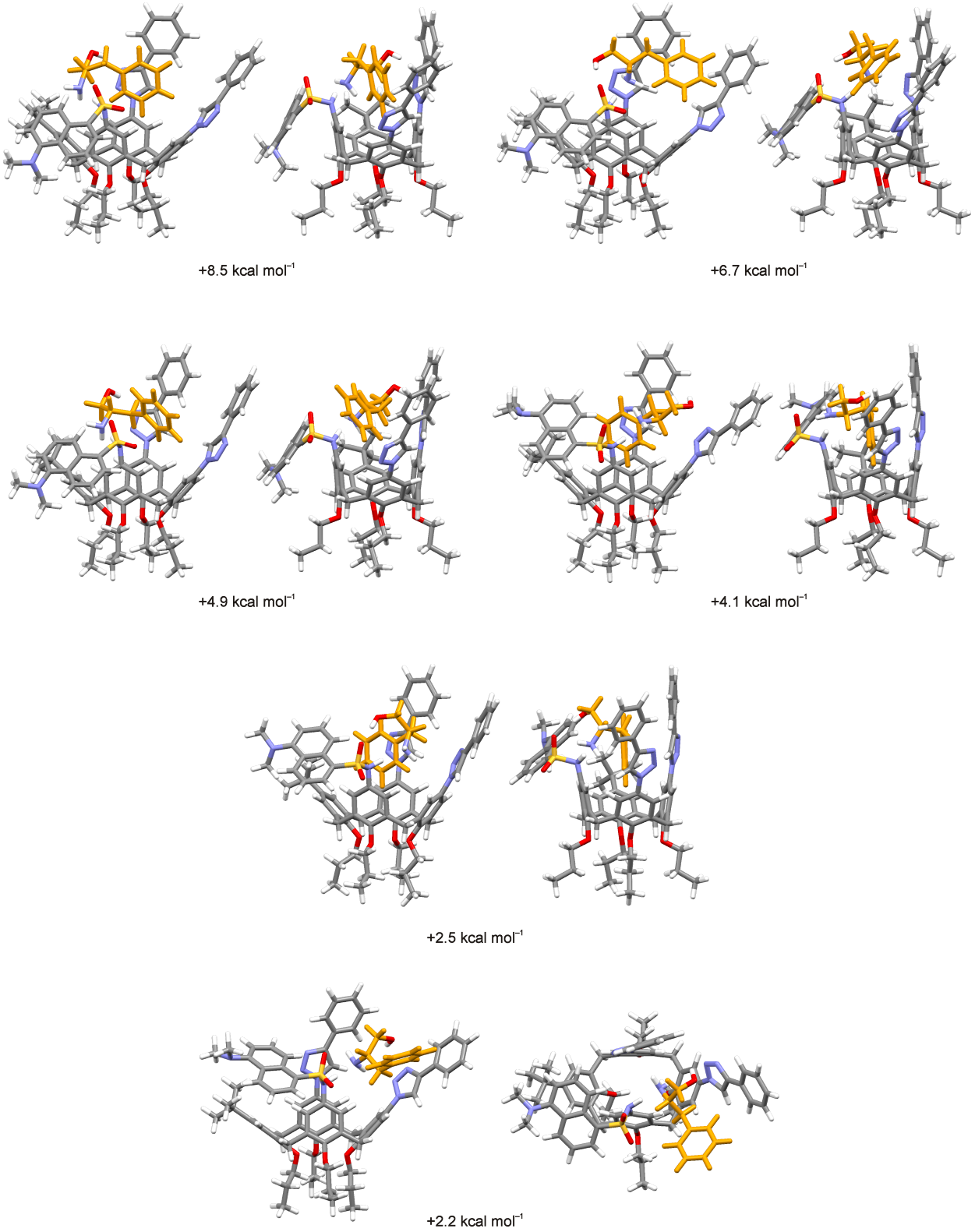


Figure S48. Energy-minimized structures (each in two projections) and relative full-electron energies of the (*L*)-phenylalaninol complexes of sulfonamide (*M*)-**14a**; energy values are given relative to the most stable complex among those presented in Figs. S48 and S49.

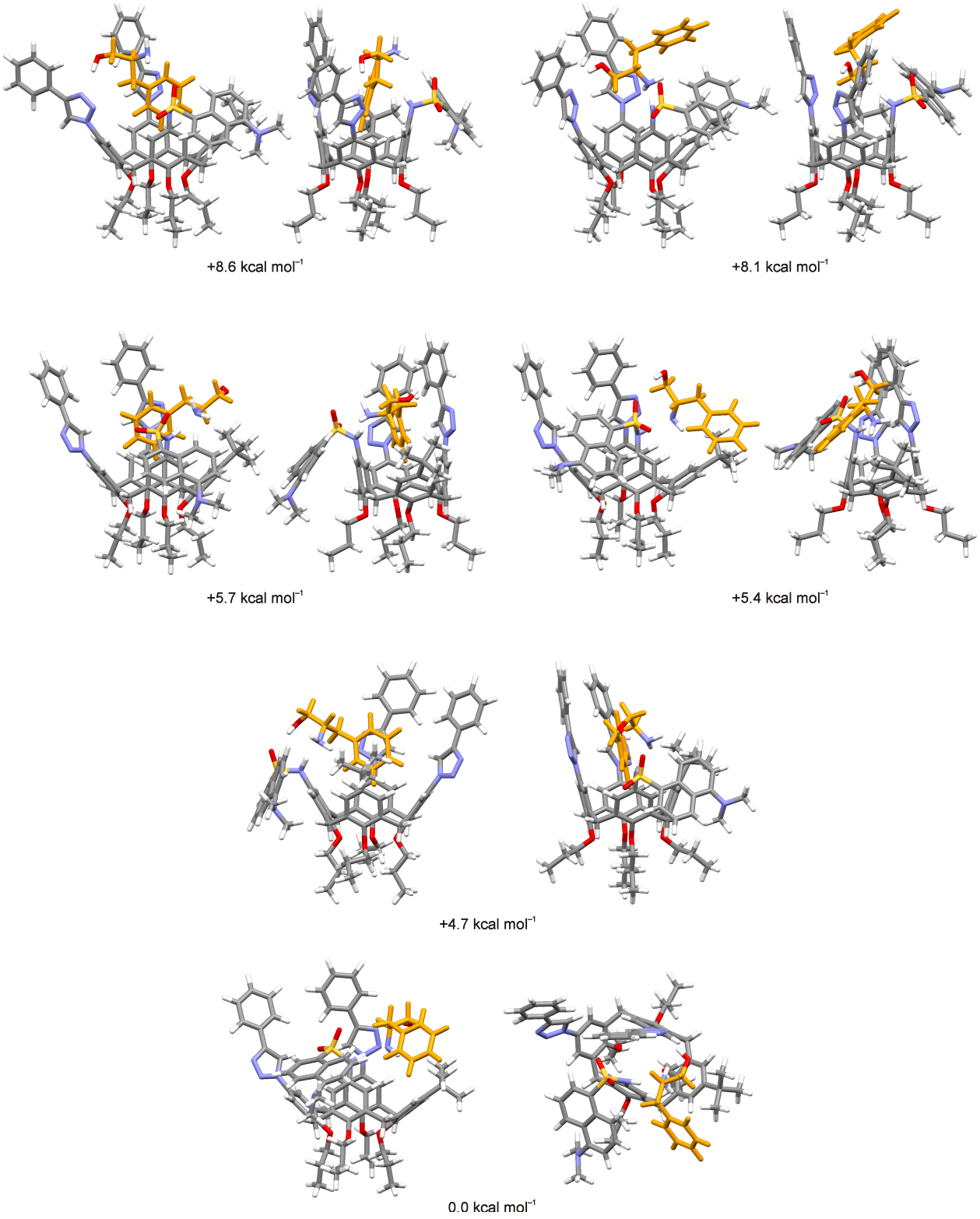


Figure S49. Energy-minimized structures (each in two projections) and relative full-electron energies of the (*L*)-phenylalaninol complexes of sulfonamide (*P*)-**14b**; energy values are given relative to the most stable complex among those presented in Figs. S48 and S49.

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S5. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J Appl Crystallogr*, 2009, **42**, 339–341.