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Calixarene alpha-ketoacetylenes: versatile platforms for reaction with hydrazine nucleophile

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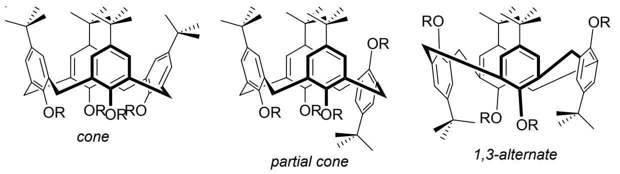
Experimental



Scheme S1. Three main conformations of calix[4]arenes: *cone, partial cone, and 1,3-alternate.*

Materials and methods

Solvents and reagents were purified according to known procedures before use.[1] All commercial reagents (Acros, Alfa Aesar, Lancaster) were used without further purification. The (thia)calixarenes **1** have been prepared using previously reported procedures.[2,3]

Purity of substances was controlled by TLC method on Silufol UV 254 and Fluka 0.060-0.2 mm plates using a VL-6.LC (6W–254 nm tube) ultraviolet lamp. Column chromatography was performed by using silica as a stationary phase (particle diameter is 0.035-0.070 mm and pore size is 60 Å). Melting points of substances were determined on a BOETIUS compact heating table equipped with an RNMK 05 visual inspection unit. IR spectra were recorded on a Bruker Vector 22 FT-IR spectrometer in KBr pellets in the wavenumber range of 400–4000 cm^{-1}.

High-resolution MALDI mass spectra were recorded on a Ultraflex III TOF/TOF mass spectrometer (Bruker Daltonik GmbH, Germany) in reflectron mode (resolution is 10000) using Nd:YAG laser, $\lambda = 266$ nm. The composition provided the relative error of mass measurement of less than 3.9 ppm. A total of 0.5 μL of the *para*-nitroaniline (*p*-NA) matrix solution (10 mg/mL, CH_3CN) and 0.5 μL of the mixture, which consists of specimen (1 mg/mL $CHCl_3$) and reference substance (PEG-1000, PEG-1500 with the concentration of 1 mg/mL in CH_3CN) with the addition of CsCl (1 mg/mL, H_2O), were sequentially deposited onto the metallic MTP AnchorChip^{TM} target using the dried-droplet method and evaporated. The data were obtained using the Flex Control program (Bruker Daltonik GmbH, Germany) and processed using the FlexAnalysis 3.0 program (Bruker Daltonik GmbH, Germany).

1D and 2D NMR experiments (^{13}C DEPT, $^{13}C/^{1}H$ HMBC, $^{13}C/^{1}H$ HSQC) were carried out on a Bruker Avance 400 NMR spectrometer in $CDCl_3$. As an internal standard, the residual signal of $CHCl_3$ (δ_H 7.26 ppm and δ_C 77.16 ppm) was used. Residual solvent peaks were found in some cases at δ_H 1.55 (H_2O), 1.09 and 3.49 (MeOH), and 3.39 and 0.92 ppm (*i*-BuOH). The signal assignment was done on the basis of 2D HSQC and HMBC experiments. The protons have the same numbers as the carbons to which they are attached.

Synthetic procedures

General procedure for synthesis of alkynones 2,3. The mixture of 157 μmol (0.125 equiv.) copper(I) iodide and 71 μmol (0.057 equiv.) $PdCl_2(PPh_3)_2$ were stirred in 60 mL of THF for 30 min in argon atmosphere. Then, 1.25 mmol (1 equiv.) of (thia)calix[4]arene **1**, 20 mL triethylamine, and 6 mmol (4 equiv.) of benzoyl chloride were added. The mixture was maintained upon stirring for 5 h in argon atmosphere at room temperature. After 5 h, the precipitate was filtered, the filtrate was evaporated, and the residue was dissolved in 20 mL of diethyl ether, 50 mL of hexane was added, the precipitate was filtered and purified using column chromatography (eluent – hexane/ethylacetate = 4:1).

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((4-oxo-4-phenylbut-2-yn-1-yl)oxy)calix[4]arene (**2a** *cone*) (1.20 g, 79%). mp 120 °C. R_f (hexane : ethylacetate = 4 : 1) 0.36. ν_{max}/cm^{-1} (Fig. S1) 2229 (C≡C) and 1648 (C=O). δ_H(400 MHz; $CDCl_3$) (Fig. S2) 7.98 (8 H, d, $J_{1,3}$ 8.0 Hz, H_{13}), 7.52 (4 H, t, $J_{1,3}$ 7.4 Hz, H_{15}), 7.38 (8 H, t, $J_{1,3}$ 8.0 Hz, H_{14}), 6.86 (8 H, s, H_3), 5.18 (8 H, s, H_8), 4.66 (4 H, AB-d, $J_{1,2}$ –12.8 Hz, $H_{5(ax)}$), 3.32 (4 H, AB-d, $J_{1,2}$ –12.8 Hz, $H_{5(eq)}$), 1.10 (36 H, s, H_7). δ_C(100 MHz; $CDCl_3$) (Fig. S3) 177.6 (C_{11i}), 152.3 (C_{1i}), 146.5 (C_{4i}), 136.4 (C_{12i}), 134.4 (C_{15}), 134.4 (C_{2i}), 129.7 (C_{13}), 128.7 (C_{14}), 125.4 (C_3), 91.5 (C_{10i}), 84.9 (C_{9i}), 61.5 (C_8), 34.2 (C_{6i}), 32.6 (C_5), 31.4 (C_7). HRMS-MALDI (Fig. S4): ($C_{84}H_{80}O_8$) *m/z* calcd: 1349.4902 $[M+Cs]^+$. found: 1349.4862 $[M+Cs]^+$.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((4-oxo-4-phenylbut-2-yn-1-yl)oxy)calix[4]arene (**2b** *partial cone*) (1.34 g, 88%). mp 104 °C. R_f (hexane : ethylacetate = 4 : 1) 0.36. ν_{max}/cm^{-1} (Fig. S5) 2229 (C≡C), 1638 (C=O). δ_H(400 MHz; $CDCl_3$) (Fig. S6) 8.04 (2 H, d, $J_{1,3}$ 8.0 Hz, H_{13}), 8.01 (4 H, d, $J_{1,3}$ 8.0 Hz, H_{13+}), 7.79 (2 H, d, $J_{1,3}$ 8.0 Hz, $H_{13'}$), 7.59 (4 H, m, H_{15}), 7.5–7.4 (8 H, m, $H_{3'}+H_{14}$), 7.32 (2 H, t, $J_{1,3}$ 8.0 Hz, $H_{14'}$), 7.15 (2 H, s, H_3), 7.05 (2 H, AB-d, $J_{1,4}$ –2.2 Hz, H_{3+}), 6.64 (2 H, AB-d, $J_{1,4}$ –2.2 Hz, $H_{3+'}$), 4.84 (2 H, AB-d, $J_{1,2}$ –16.8 Hz, H_{8+}), 4.78 (2 H, AB-d, $J_{1,2}$ –16.8 Hz, H_{8+}), 4.63 (2 H, s, H_8), 4.62 (2 H, s, $H_{8'}$), 4.39 (2 H, AB-d, $J_{1,2}$ –13.4 Hz, $H_{5(ax)}$), 3.96 (2 H, AB-d, $J_{1,2}$ –14.4 Hz, $H_{5'}$), 3.90 (2 H, AB-d, $J_{1,2}$ –14.4 Hz, $H_{5'}$), 3.26 (2 H, AB-d, $J_{1,2}$ –13.4 Hz, $H_{5(eq)}$), 1.38 (9 H, s, H_7), 1.36 (9 H, s, $H_{7'}$), 1.07 (18 H, s, H_{7+}). δ_C(100 MHz; $CDCl_3$) (Fig. S7) 177.5 (C_{11i}), 177.4 (2 signals, C_{11i}), 153.8 ($C_{1i'}$), 152.7 (C_{1i+}), 151.5 (C_{1i}), 147.1 (C_{4i}), 146.1 (C_{4i+}), 145.1 ($C_{4i'}$), 136.6 ($C_{12i/12i'/12i+}$), 136.5 ($C_{12i/12i'/12i+}$), 136.4 ($C_{12i/12i'/12i+}$), 136.1 (C_{2i}), 134.4 (2 signals, C_{15}), 134.0 ($C_{15'}$), 133.2 ($C_{2i'}$), 132.7 (C$_{2i+}$), 132.0 (C$_{2i+'}$), 129.7 (3 signals, C$_{13/13'/13+}$), 128.8 (C$_{14/14+}$), 128.7 (C$_{14/14+}$), 128.5 (C$_{14'}$), 128.5 (C$_{3'}$), 126.3 (C$_{3+}$), 126.1 (C$_3$), 125.9 (C$_{3+'}$), 92.7 (C$_{10i}$), 90.5 (C$_{10i'}$), 90.0 (C$_{10i+}$), 84.9 (C$_{9i+}$), 84.8 (C$_{9i}$), 84.4 (C$_{9i'}$), 60.9 (C$_{8+}$), 58.9 (C$_8$), 58.8 (C$_{8'}$), 38.2 (C$_{5'}$), 34.4 (C$_{6i}$), 34.2 (C$_{6i'}$), 34.0 (C$_{6i+}$), 32.8 (C$_5$), 31.8 (C$_{7'}$), 31.8 (C$_7$), 31.5 (C$_{7+}$). HRMS-MALDI (Fig. S8): ($C_{84}H_{80}O_8$) *m*/*z* calcd: 1349.4902 [M+Cs]$^+$. found: 1349.4858 [M+Cs$^+$].

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((4-oxo-4-phenylbut-2-yn-1-yl)oxy)calix[4]arene (**2c** *1,3-alternate*) (1.38 g, 91%). mp 222 °C. R_f (hexane : ethylacetate = 4 : 1) 0.34. v_{max}/cm^{-1} (Fig. S9) 2229 (C≡C) and 1638 (C=O). δ_H(400 MHz; CDCl$_3$) (Fig. S10) 7.98 (8 H, d, $J_{1,3}$ 7.6 Hz, H$_{13}$), 7.59 (4 H, t, $J_{1,3}$ 6.9 Hz, H$_{15}$), 7.44 (8 H, t, $J_{1,3}$ 7.4 Hz H$_{14}$), 7.22 (8 H, s, H$_3$), 4.08 (8 H, s, H$_8$), 4.01 (8 H, s, H$_5$), 1.24 (36 H, s, H$_7$). δ_C(100 MHz; CDCl$_3$) (Fig. S11) 177.3 (C$_{11i}$), 152.7 (C$_{1i}$), 146.5 (C$_{4i}$), 136.5 (C$_{12i}$), 134.3 (C$_{15}$), 129.7 (C$_{13}$), 128.7 (C$_{14}$), 127.4 (C$_{2i}$), 127.4 (C$_3$), 91.4 (C$_{10i}$), 84.8 (C$_{9i}$), 58.3 (C$_8$), 39.1 (C$_5$), 34.2 (C$_{6i}$), 31.5 (C$_7$). HRMS-MALDI (Fig. S12): ($C_{84}H_{80}O_8$) *m*/*z* calcd: 1349.4902 [M+Cs]$^+$. found: 1349.4850 [M+Cs]$^+$.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((4-oxo-4-phenylbut-2-yn-1-yl)oxy)thiacalix[4]arene (**3a**) (1.35 g, 84%). mp 102 °C. R_f (hexane : ethylacetate = 4 : 1) 0.36. v_{max}/cm^{-1} (Fig. S13) 2233 (C≡C) and 1648 (C=O). δ_H(400 MHz; CDCl$_3$) (Fig. S14) 8.06 (8 H, d, $J_{1,3}$ 7.2 Hz, H$_{12}$), 7.60 (8 H, s, H$_3$), 7.58 (4 H, br m, H$_{14}$), 7.45 (8 H, t, $J_{1,3}$ 8.0 Hz, H$_{13}$), 5.05 (8 H, s, H$_7$), 1.20 (36 H, s, H$_6$). δ_C(100 MHz; CDCl$_3$) (Fig. S15) 177.4 (C$_{10i}$), 156.5 (C$_{1i}$), 147.6 (C$_{4i}$), 136.6 (C$_{11i}$), 134.3 (C$_{14}$), 132.3 (C$_3$), 129.8 (C$_{12}$), 128.8 (C$_{2i}$), 128.7 (C$_{13}$), 90.1 (C$_{9i}$), 84.7 (C$_{8i}$), 58.0 (C$_7$), 34.4 (C$_{5i}$), 31.3 (C$_6$). HRMS-MALDI (Fig. S16): ($C_{80}H_{72}O_8S_4$) *m*/*z* calcd: 1421.3159 [M+Cs]$^+$. found: 1421.3100 [M+Cs]$^+$.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((5-oxo-5-phenylpent-3-yn-1-yl)oxy)thiacalix[4]arene **3b**) (1.40 g, 83%). mp 171 °C. R_f (hexane : ethylacetate = 4 : 1) 0.43. v_{max}/cm^{-1} (Fig. S17) 2237 (C≡C) and 1648 (C=O). δ_H(400 MHz; CDCl$_3$) (Fig. S18) 8.09 (8 H, d, $J_{1,3}$ 7.2 Hz, H$_{13}$), 7.61 (4 H, t, $J_{1,3}$ 7.2 Hz, H$_{15}$), 7.48 (8 H, t, $J_{1,3}$ 7.6 Hz, H$_{14}$), 7.43 (8 H, s, H$_3$), 4.20 (8 H, t, $J_{1,3}$ 8.8 Hz, H$_7$), 1.97 (8 H, t, $J_{1,3}$ 8.8 Hz, H$_8$), 1.34 (36 H, s, H$_6$). δ_C(100 MHz; CDCl$_3$) (Fig. S19) 177.8 (C$_{11i}$), 155.5 (C$_{1i}$), 147.7 (C$_{4i}$), 136.7 (C$_{12i}$), 134.3 (C$_{15}$), 129.7 (C$_{13}$), 128.7 (C$_{14}$), 128.2 (C$_{2i}$), 127.3 (C$_3$), 90.7 (C$_{10i}$), 81.0 (C$_{9i}$), 64.3 (C$_7$), 34.7 (C$_{5i}$), 31.5 (C$_6$), 19.4 (C$_8$). HRMS-MALDI (Fig. S20): ($C_{84}H_{80}O_8S_4$) *m*/*z* calcd: 1477.3785 [M+Cs]$^+$. found: 1477.3798 [M+Cs]$^+$.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((6-oxo-6-phenylhex-4-yn-1-yl)oxy)thiacalix[4]arene (**3c**) (1.61 g, 92%). mp 124 °C (decomp.). R_f (hexane : ethylacetate = 4 : 1) 0.52. v_{max}/cm^{-1} (Fig. S21) 2229 (C≡C) and 1638 (C=O). δ_H(400 MHz; CDCl$_3$) (Fig. S22) 8.14 (8 H, d, $J_{1,3}$ 9.2 Hz, H$_{14}$), 7.60 (4 H, t, $J_{1,3}$ 6.4 Hz, H$_{16}$), 7.49 (8 H, t, $J_{1,3}$ 7.6 Hz, H$_{15}$), 7.41 (8 H, s, H$_3$), 4.07 (8 H, t, $J_{1,3}$ 7.2 Hz, H$_7$), 2.22 (8 H, t, $J_{1,3}$ 7.2 Hz, H$_9$), 1.42 (8 H, t, $J_{1,3}$ 7.2 Hz, H$_8$), 1.27 (36 H, s, H$_6$). δ_C(100 MHz; CDCl$_3$) (Fig. S23) 177.9 (C$_{12i}$), 156.6 (C$_{1i}$), 146.5 (C$_{4i}$), 137.0 (C$_{13i}$), 134.1 (C$_{16}$), 129.7 (C$_{14}$), 128.7 (C$_{15}$), 128.4 (C$_3$), 127.6 (C$_{2i}$), 95.7 (C$_{11i}$), 80.4 (C$_{10i}$), 67.3 (C$_7$), 34.5 (C$_{5i}$), 31.5 (C$_6$), 27.2 (C$_8$), 16.2 (C$_9$). HRMS-MALDI (Fig. S24): ($C_{88}H_{88}O_8S_4$) *m*/*z* calcd: 1533.4411 [M+Cs]$^+$. found: 1533.4351 [M+Cs]$^+$.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis((7-oxo-7-phenylhept-5-yn-1-yl)oxy)thiacalix[4]arene (**3d**) (1.66 g, 91%). mp 136 °C (decomp.). R_f (hexane : ethylacetate = 4 : 1) 0.38. v_{max}/cm^{-1} (Fig. S25) 2229 (C≡C), 1638 (C=O). δ_H(400 MHz; CDCl$_3$) (Fig. S26) 8.13 (8 H, d, $J_{1,3}$ 7.2 Hz, H$_{15}$), 7.59 (4 H, t, $J_{1,3}$ 7.2 Hz, H$_{17}$), 7.47 (8 H, t, $J_{1,3}$ 7.6 Hz, H$_{16}$), 7.35 (8 H, s, H$_3$), 3.93 (8 H, t, $J_{1,3}$ 7.6 Hz, H$_7$), 2.39 (8 H, t, $^3J_{HH}$ 7.6 Hz, H$_{10}$), 1.57 (8 H, t, $J_{1,3}$ 7.2 Hz, H$_9$), 1.33 (8 H, t, $J_{1,3}$ 6.0 Hz, H$_8$), 1.26 (36 H, s, H$_6$). δ_C(100 MHz; CDCl$_3$) (Fig. S27) 178.2 (C$_{13i}$), 157.4 (C$_{1i}$), 145.8 (C$_{4i}$), 137.0 (C$_{14i}$), 134.1 (C$_{17}$), 129.7 (C$_{15}$), 128.7 (C$_{16}$), 128.5 (C$_3$), 128.5 (C$_{2i}$), 95.8 (C$_{12i}$), 80.0 (C$_{11i}$), 68.7 (C$_7$), 34.4 (C$_{5i}$), 31.5 (C$_6$), 28.7 (C$_8$), 24.7 (C$_9$), 19.2 (C$_{10}$). HRMS-MALDI (Fig. S28): ($C_{92}H_{96}O_8S_4$) *m*/*z* calcd: 1589.5037 [M+Cs]$^+$. found: 1589.5008 [M+Cs]$^+$.

General procedure for synthesis of pyrazoles 4. The mixture of 2 g (1.64 mmol) of compound **2** and 0.4 mL (80 mmol) hydrazine hydrate was refluxed in 120 mL of *i*-BuOH for 4 h under inert atmosphere. The reaction mixture was evaporated, the residue was washed with 100 mL of hexane and the precipitate was filtered.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis-O-[(1-*benzylpyrazolyl*)-4-*methoxy]calix[4]arene* (**4a** *cone*) (1.44 g, 69%). mp 176 °C. v_{max}/cm^{-1} (Fig. S29) 3356 (NH) and 1480 (C=N). δ_H(400 MHz; CDCl$_3$) (Fig. S30) 7.73 (8 H, d, $J_{1,3}$ 8.0 Hz, H$_{13}$), 7.33 (8 H, t, $J_{1,3}$ 8.0 Hz, H$_{14}$), 7.27 (4 H, t, $J_{1,3}$ 8.0 Hz, H$_{15}$), 6.86 (8 H, s, H$_3$), 6.33 (4 H, s, H$_{10}$), 4.95 (8 H, s, H$_8$), 4.17 (4 H, AB-d, H$_{5(ax)}$, $J_{1,2}$ –12.8 Hz), 3.12 (4 H, AB-d, H$_{5(eq)}$, $J_{1,2}$ –12.8 Hz), 1.09 (36 H, s, H$_7$). δ_C(100 MHz; CDCl$_3$) (Figs. S31,S32) 152.7 (C$_{1i}$), 151.3 (C$_{11i}$), 146.2 (C$_{4i}$), 141.8 (C$_{9i}$), 133.9 (C$_{2i}$), 133.2 (C$_{12i}$), 128.7 (C$_{14}$), 127.7 (C$_{15}$), 125.9 (C$_{13}$), 125.7 (C$_3$), 101.8 (C$_{10}$), 68.5 (C$_8$), 34.0 (C$_{6i}$), 31.5 (C$_7$), 31.2 (C$_5$). HRMS-MALDI (Fig. S33): ($C_{84}H_{88}N_8O_4$) *m*/*z* calcd: 1405.5978 [M+Cs]$^+$. found: 1405.5927 [M+Cs]$^+$.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis-O-[(1-*benzylpyrazolyl*)-4-*methoxy]calix[4]arene* (**4b** *partial cone*) (1.65 g, 79%). mp 169 °C. v_{max}/cm^{-1} (Fig. S34) 3355 (NH) and 1479 (C=N). δ_H(400 MHz; CDCl$_3$) (Fig. S35) 7.88 (4 H, d, $J_{1,3}$ 8.0 Hz, H$_{13+}$), 7.57 (2 H, d, $J_{1,3}$ 8.0 Hz, H$_{13'}$), 7.50 (2 H, d, $J_{1,3}$ 8.0 Hz, H$_{13}$), 7.44 (4 H, t, H$_{14+}$), 7.36 (4 H, m, H$_{15+,14/14'}$), 7.31 (2 H, t, $J_{1,3}$ 8.0 Hz, H$_{14'/14}$), 7.23 (2 H, s, H$_{15,15'}$), 7.22 (2 H, AB-d, $J_{1,4}$ –2.0 Hz, H$_{3+}$), 7.08 (2 H, s, H$_{3'}$), 7.01 (2 H, AB-d, $J_{1,4}$ –2.0 Hz, H$_{3+'}$), 6.93 (2 H, s, H$_3$), 6.34 (2 H, s, H$_{10+}$), 5.98 (1 H, s, H$_{10}$), 5.75 (1 H, s, H$_{10'}$), 5.06 (2 H, AB-d, $J_{1,2}$ –16.8 Hz, H$_{8+}$), 4.78 (2 H, AB-d, $J_{1,2}$ –16.8 Hz, H$_{8+}$), 4.49 (2 H, s, H$_8$), 4.02 (2 H, AB-d, $J_{1,2}$ –13.4 Hz, H$_{5'}$), 3.91 (2 H, AB-d, $J_{1,2}$ –14.4 Hz, H$_{5'}$), 3.90 (2 H, AB-d, $J_{1,2}$ –14.4 Hz, H$_{5(ax)}$), 3.09 (2 H, s, H$_{8'}$), 3.03 (2 H, AB-d, $J_{1,2}$ –13.4 Hz, H$_{5(eq)}$), 1.20 (18 H, s, H$_{7+}$), 1.02 (9 H, s, H$_7$), 0.97 (9 H, s, $H_{7'}$). δ_C(100 MHz; $CDCl_3$) (Figs. S36–S38) 153.2 ($C_{1i'}$), 152.8 (C_{1i+}), 151.5 (C_{11i+}), 150.8 ($C_{11i'}$), 150.0 (C_{1i}), 149.1 (C_{11i}), 147.8 (C_{4i+}), 147.2 ($C_{4i'}$), 146.3 (C_{4i}), 142.1 (C_{9i}), 141.7 (C_{9i+}), 140.5 ($C_{9i'}$), 136.5 (C_{2i}), 133.8 ($C_{12i/12i'}$), 133.7 (C_{2i+}), 133.5 ($C_{2i+'}$), 133.3 ($C_{2i'}$), 132.6 (C_{12i+}), 131.9 ($C_{12i'/12i}$), 129.0 (C_{14+}), 128.6 ($C_{14/14'}$), 128.4 ($C_{14'/14}$), 128.3 (C_{15+}), 127.9 (C_{15}), 127.3 ($C_{15'}$), 126.6 ($C_{3'}$), 126.2 (C_{13+}), 126.1 (C_{3+}), 126.0 ($C_{3+'}$), 125.8 ($C_{13'}$), 125.6 (C_{13}), 125.3 (C_3), 103.5 (C_{10}), 100.8 (C_{10+}), 99.8 ($C_{10'}$), 68.0 (C_8), 66.7 (C_{8+}), 62.7 ($C_{8'}$), 38.8 ($C_{5'}$), 34.3 (C_{6i+}), 34.2 (C_{6i}), 33.9 ($C_{6i'}$), 31.4 (C_{7+}), 31.2 (C_7), 31.1 ($C_{7'}$), 30.6 (C_5). HRMS-MALDI (Fig. S39): ($C_{84}H_{88}N_8O_4$) *m/z* calcd: 1405.5978 $[M+Cs]^+$. found: 1405.5915 $[M+Cs]^+$.

Details of assignment of ^1H and ^{13}C nuclei in pyrazole **4b**.

In ^1H NMR spectrum of pyrazole **4b** (Fig. S35), a set of signals at a 1:1:2 ratio was observed for the protons of phenyl ring of substituent (13, doublets at 7.8–7.3 ppm), pyrazole (10, singlets from 6.34 to 5.75 ppm), methylene units at ether oxygen atom (8, AB quadruplet at 5.07–4.76 ppm and two singlets at 4.49 and 3.09 ppm), benzene rings of calixarene platform (3, AB quadruplet at 7.23–7.03 ppm and two singlets at 7.07 and 6.92 ppm), and *tert*-butyl fragments (7, singlets from 1.20 to 0.97 ppm). Bridging methylene units appear as two AB-quadruplets, the one at ~4.00 ppm corresponding to 5' and another one at 3.89–3.07 ppm corresponding to 5. The only unresolved part of the spectrum is in the range of 7.45–7.23 ppm, where protons 14 and 15 give resonance signals.

A double integral intensity of the peaks of protons indicated as "+" allowed us to distinguish them from other protons. In order to correlate other signals of protons and carbon atoms in compound **4b** and assign hydrogen and carbon atoms 14 and 15 in phenyl ring of substituent, 2D NMR experiments were carried out (Figs. S37,S38). Analysis of $^{13}C/^1H$ HMBC experiment is given in Fig. S38. At the first stage, the signals of C atoms indicated as + (except for 14 and 15) were assigned from HSQC cross peaks (Fig. S37), in addition to bridging units 5 and 5'. Then, the signals of aromatic protons 3 were determined from $C_5/H_{3,3+}$ and $C_{5'}/H_{3',3+'}$ correlations. Cross peaks of $C_{6i}/H_{3,7}$ and $C_{6i'}/H_{3',7'}$ indicated *tert*-butyl groups 7 and 7'. To correlate the signals of protons and carbon atoms at the lower rim of macrocycle 4b, cross peaks $C_{1i'}/H_5$ and $C_{1i'}/H_{5'}$ were informative, because carbon atoms 1i and 1i' gave cross peaks with 8 and 8', respectively. Further analysis was performed in the following order of HMBC correlations: $C_{8,8'}$–$H_{10,10'}$–$C_{11i,11i'}$–$H_{13,13'}$–$C_{15,15'}$. The latter unit of this chain has indicated the location of the protons 15 of phenyl group at 7.23 ppm. Finally, we derived the location of the protons 14 at 7.44, 7.36, and 7.31 ppm by a process of elimination, which was supported by the cross peaks C_{12i+}/H_{14+} and $C_{12i,12i'}/H_{14,14'}$, though we were not able to distinguish 14 from 14', because atoms 12 and 14 do not display other correlations in HMBC spectra.

5,11,17,23-tetra-tert-butyl-25,26,27,28-tetrakis-O-[(1-*benzylpyrazolyl*)-4-*methoxy]calix[4]arene* (**4c** *1,3-alternate*) (1.82 g, 87%). mp 182 °C. ν_{max}/cm^{-1} (Fig. S40) 3351 (NH) and 1479 (C=N). δ_H(400 MHz; $CDCl_3$) (Fig. S41) 7.78 (8 H, d, $J_{1,3}$ 8.0 Hz, H_{13}), 7.39 (8 H, t, $J_{1,3}$ 8.0 Hz, H_{14}), 7.29 (4 H, t, $J_{1,3}$ 8.0 Hz, H_{15}), 6.79 (8 H, s, H_3), 6.26 (4 H, s, H_{10}), 4.75 (8 H, s, H_8), 3.66 (8 H, s, H_5), 0.98 (36 H, s, H_7). δ_C(100 MHz; $CDCl_3$) (Fig. S42) 153.1 (C_{1i}), 151.8 (C_{11i}), 147.0 (C_{4i}), 140.8 (C_{9i}), 134.1 (C_{12i}), 132.5 (C_{2i}), 128.8 (C_{14}), 127.6 (C_{15}), 126.0 (C_{13}), 125.9 (C_3), 99.9 (C_{10}), 64.0 (C_8), 39.2 (C_5), 34.0 (C_{6i}), 31.2 (C_7). HRMS-MALDI (Fig. S43): ($C_{84}H_{88}N_8O_4$) *m/z* calcd: 1405.5978 $[M+Cs]^+$. found: 1405.6020 $[M+Cs]^+$.

Crystallography

Data set for single crystal of compound **2c** was collected on a Bruker AXS Kappa APEX Duo diffractometer with graphite-monochromated Cu Kα radiation (λ = 1.54178 Å) at T = 198(2) K. Programs used: data collection APEX2[4], data reduction SAINT[5], multi-scan absorption correction SADABS[6] structure solution SHELXS[7], structure refinement by full-matrix least-squares against F^2 using SHELXL[7]. Hydrogen atoms were placed into calculated positions and refined as riding atoms.

Crystal data for $C_{84}H_{80}O_8$, M = 1217.48 g/mol, tetragonal, space group $I4_1/a$ (No. 88), Z = 4, a = 13.0450(4), c = 40.2669(12) Å, V = 6852.3(5) Å^3, ρ_{calc} = 1.180 g·cm^{-3}, μ=0.586 mm^{-1}, 17469 reflections collected ($-14 \le h \le 15$, $-15 \le k \le 15$, $-47 \le l \le 47$), θ range = 3.56^0 to 68.26^0, 3122 independent (R_{int} = 0.0225) and 2917 observed reflections [$I \geq 2\sigma(I)$], 211 refined parameters, R_1 = 0.0462, wR^2 = 0.1272, max. residual electron density 0.222 (-0.285) e Å^{-3}.

CCDC 1579205 contains the supplementary crystallographic data for this paper.

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Compound 2a

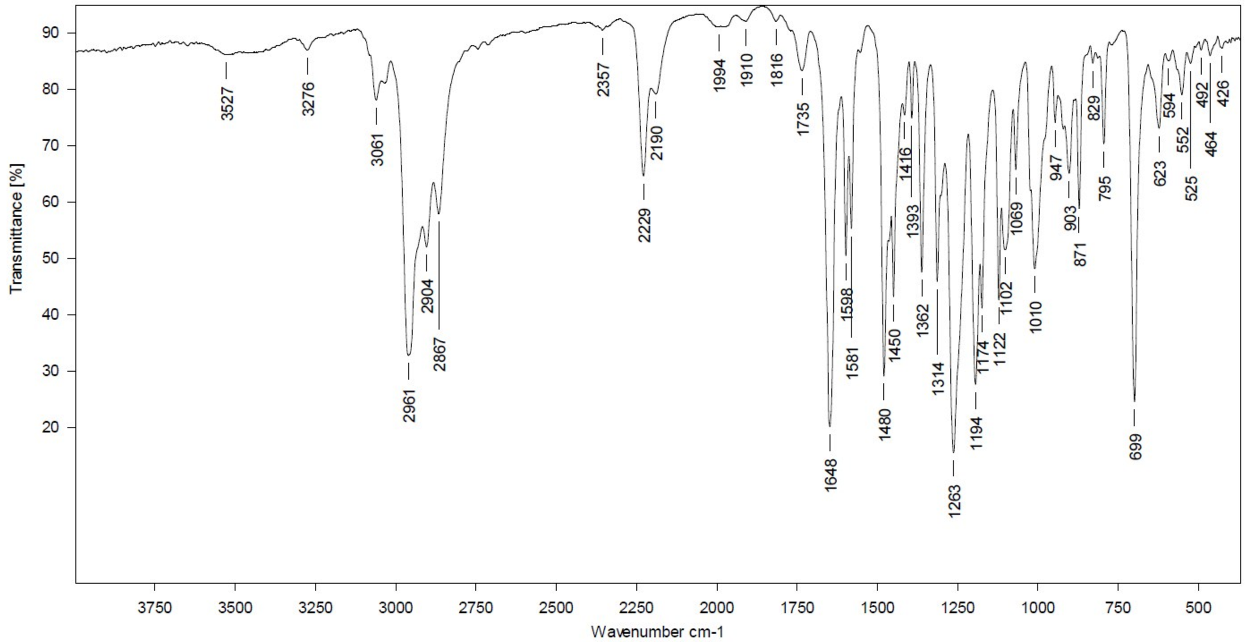


Fig. S1. FT IR spectrum of compound **2a** (KBr, 293K).

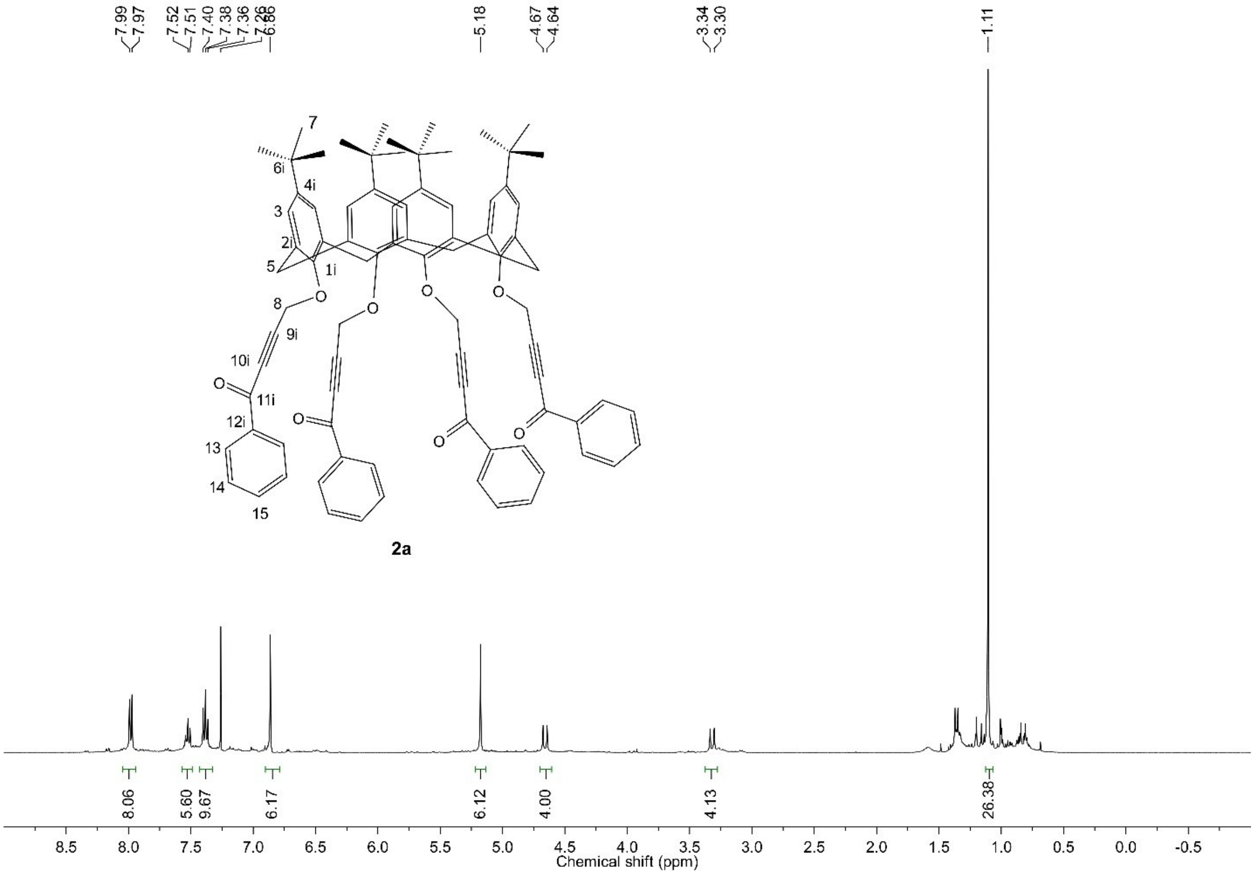


Fig. S2. ^{1}H NMR spectrum of compound **2a** (CDCl$_3$, 400 MHz, 298 K).

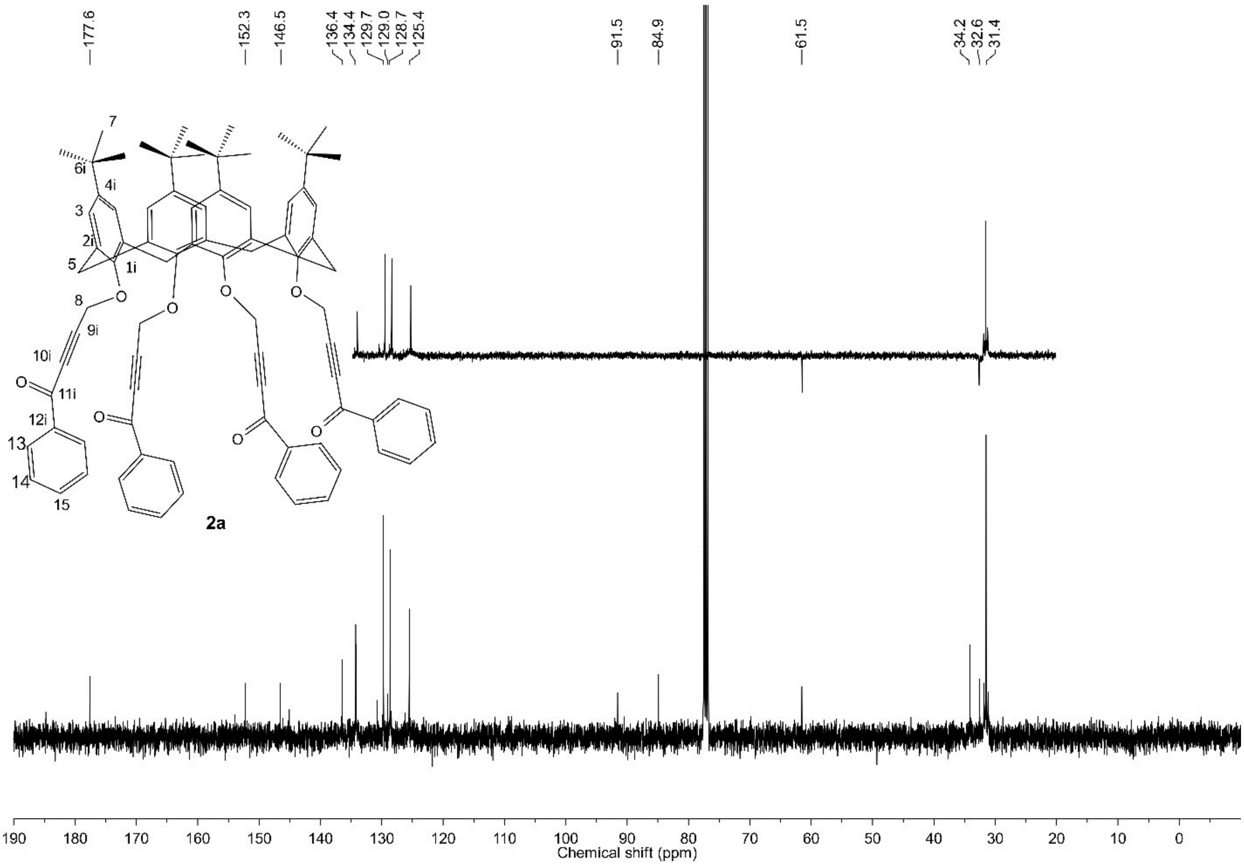


Fig. S3. ^{13}C NMR spectrum of compound **2a** ($CDCl_3$, 100 MHz, 298 K).

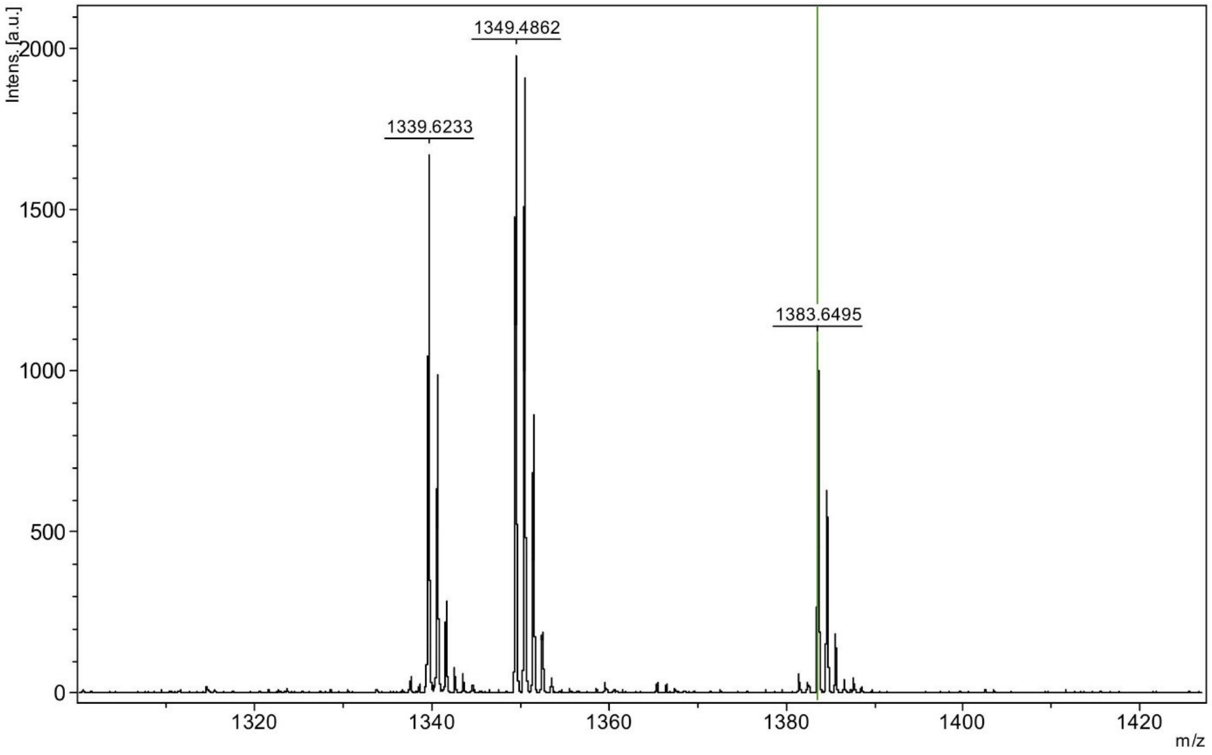


Fig. S4. HRMS spectrum of compound **2a**+CsCl (*p*-nitroaniline, PEG-1000 standard).

Compound 2b

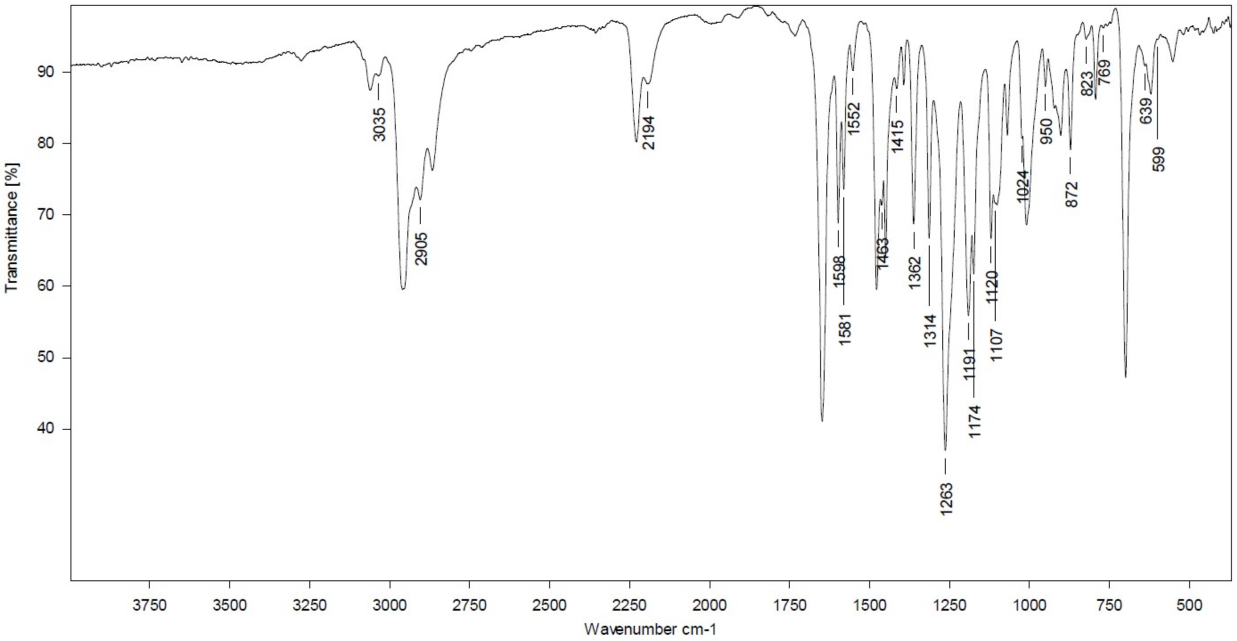


Fig. S5. FT IR spectrum of compound **2b** (KBr, 293K).

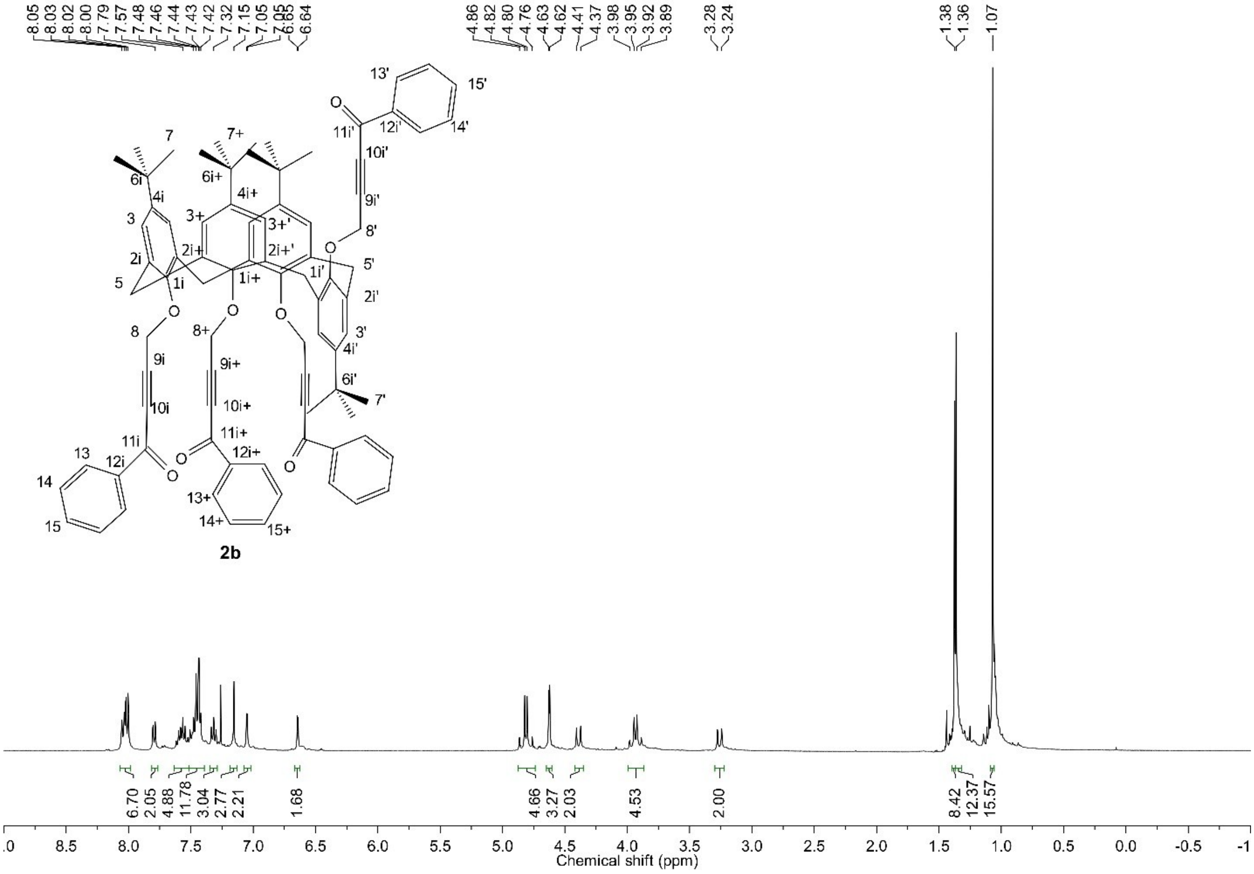


Fig. S6. ^{1}H NMR spectrum of compound **2b** (CDCl$_3$, 400 MHz, 298 K).

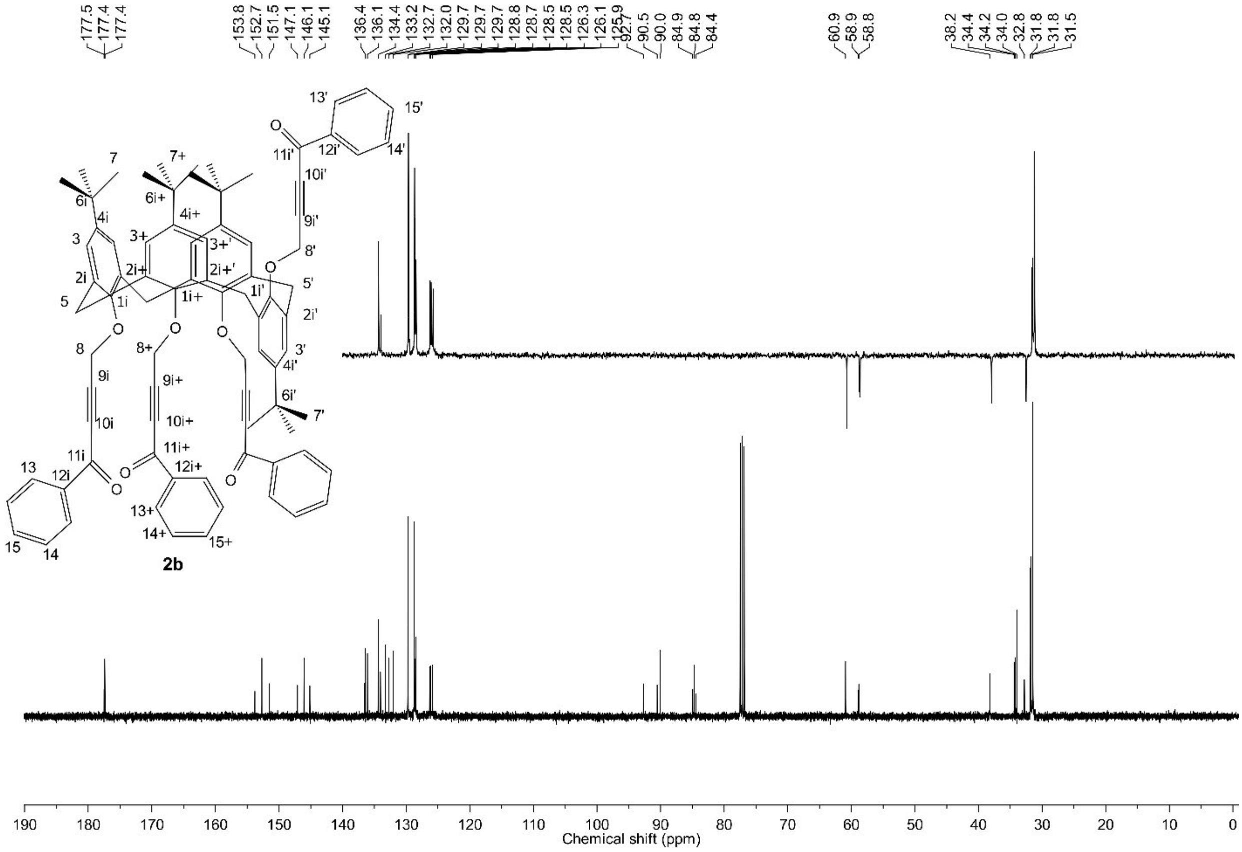


Fig. S7. ^{13}C NMR spectrum of compound **2b** (CDCl$_3$, 100 MHz, 298 K).

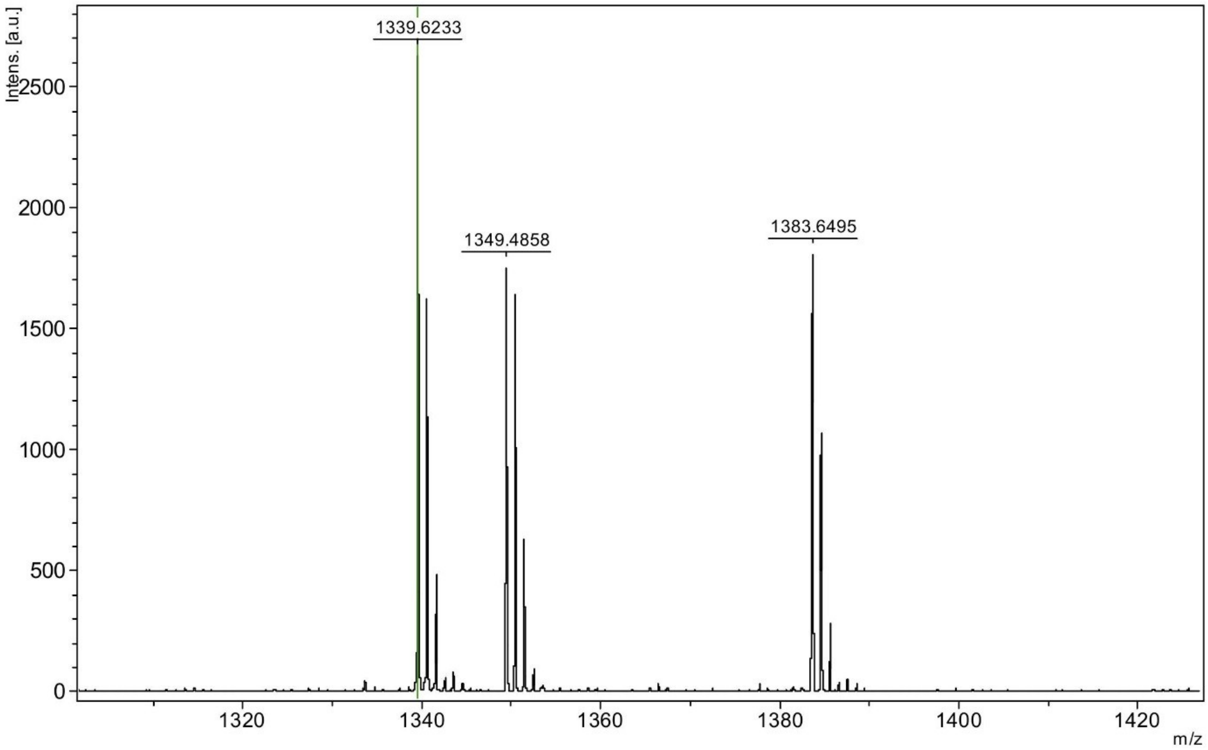


Fig. S8. HRMS spectrum of compound **2b**+CsCl (*p*-nitroaniline, PEG-1000 standard).

Compound 2c

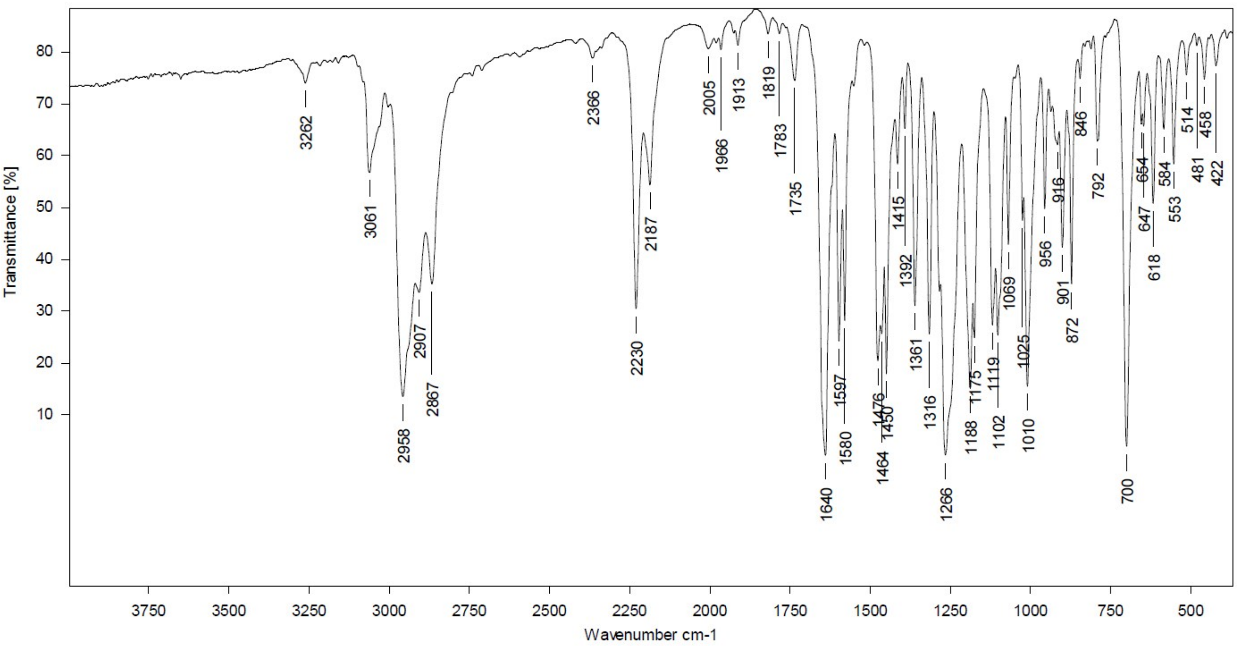


Fig. S9. FT IR spectrum of compound **2c** (KBr, 293K).

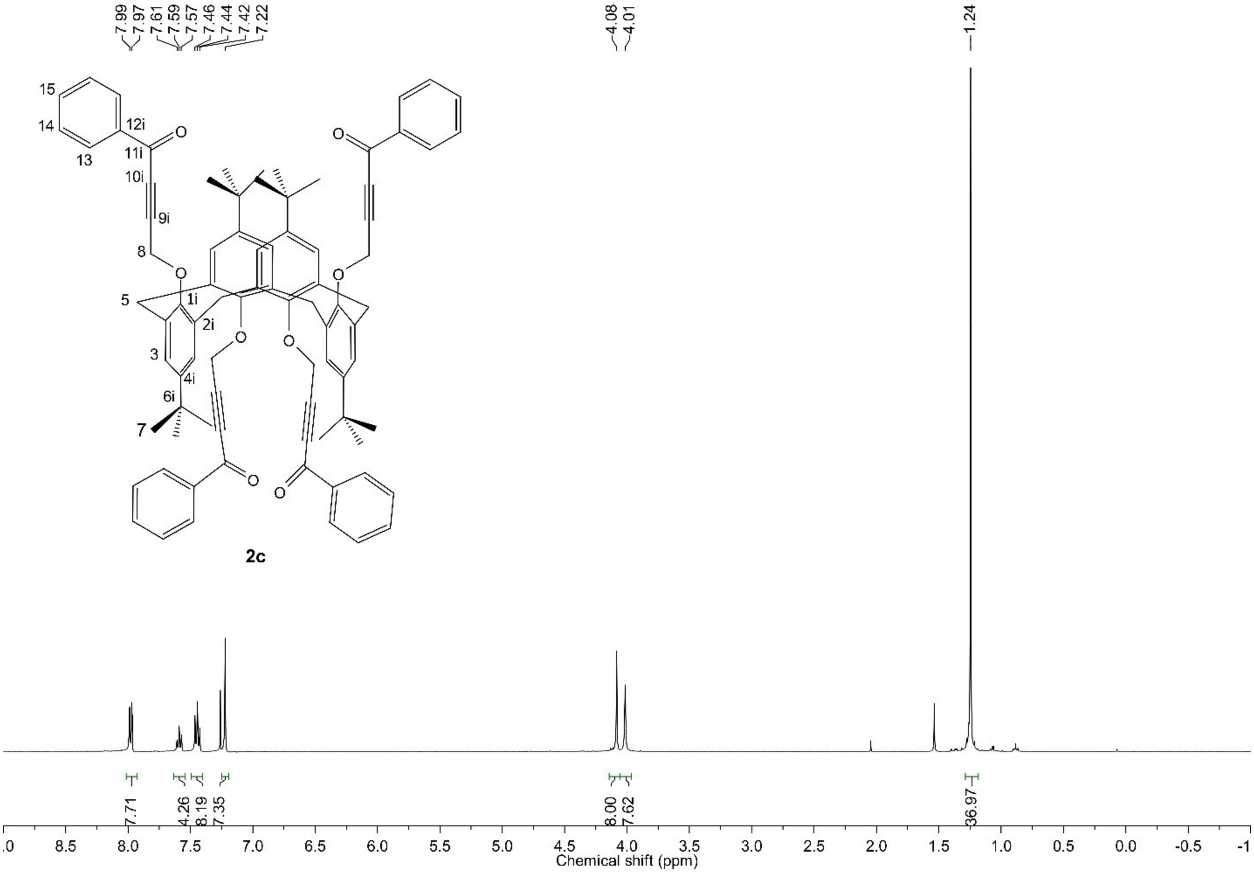


Fig. S10. ^{1}H NMR spectrum of compound **2c** (CDCl$_3$, 400 MHz, 298 K).

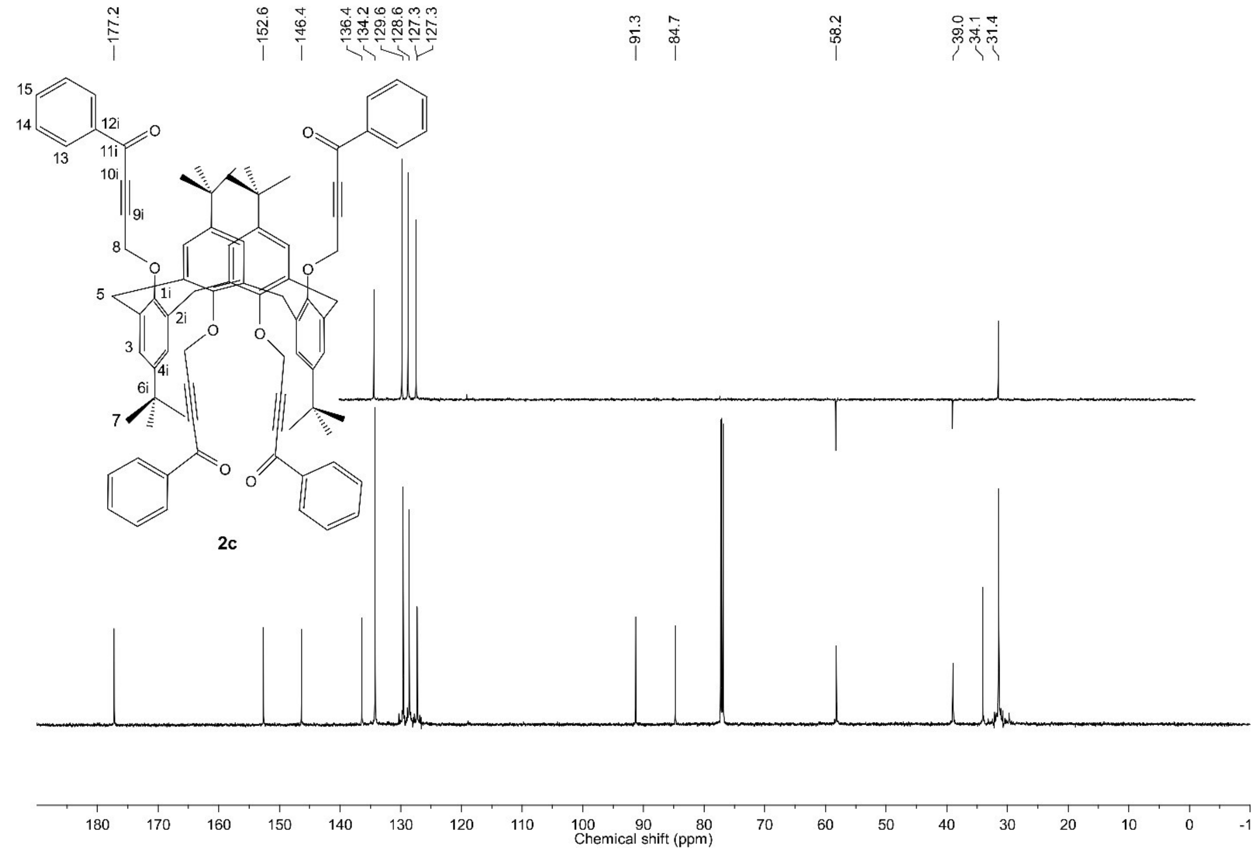


Fig. S11. ^{13}C NMR spectrum of compound **2c** ($CDCl_3$, 100 MHz, 298 K).

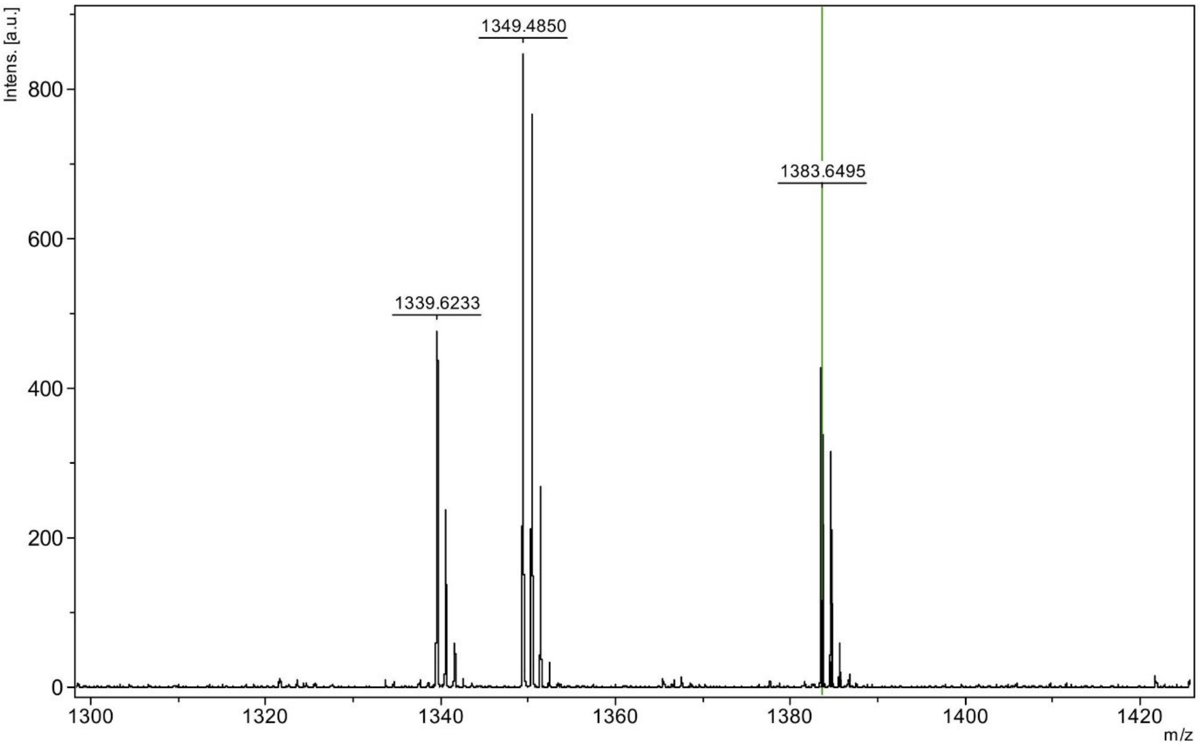


Fig. S12. HRMS spectrum of compound **2c**+CsCl (*p*-nitroaniline, PEG-1000 standard).

Compound 3a

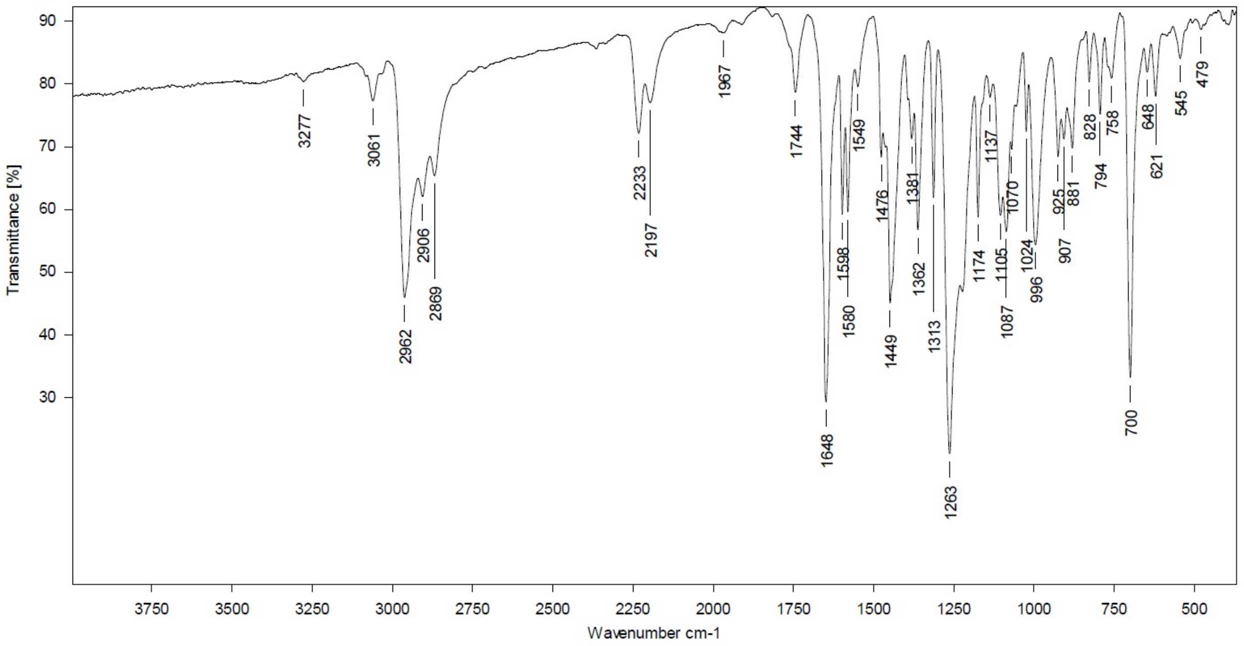


Fig. S13. FT IR spectrum of compound **3a** (KBr, 293K).

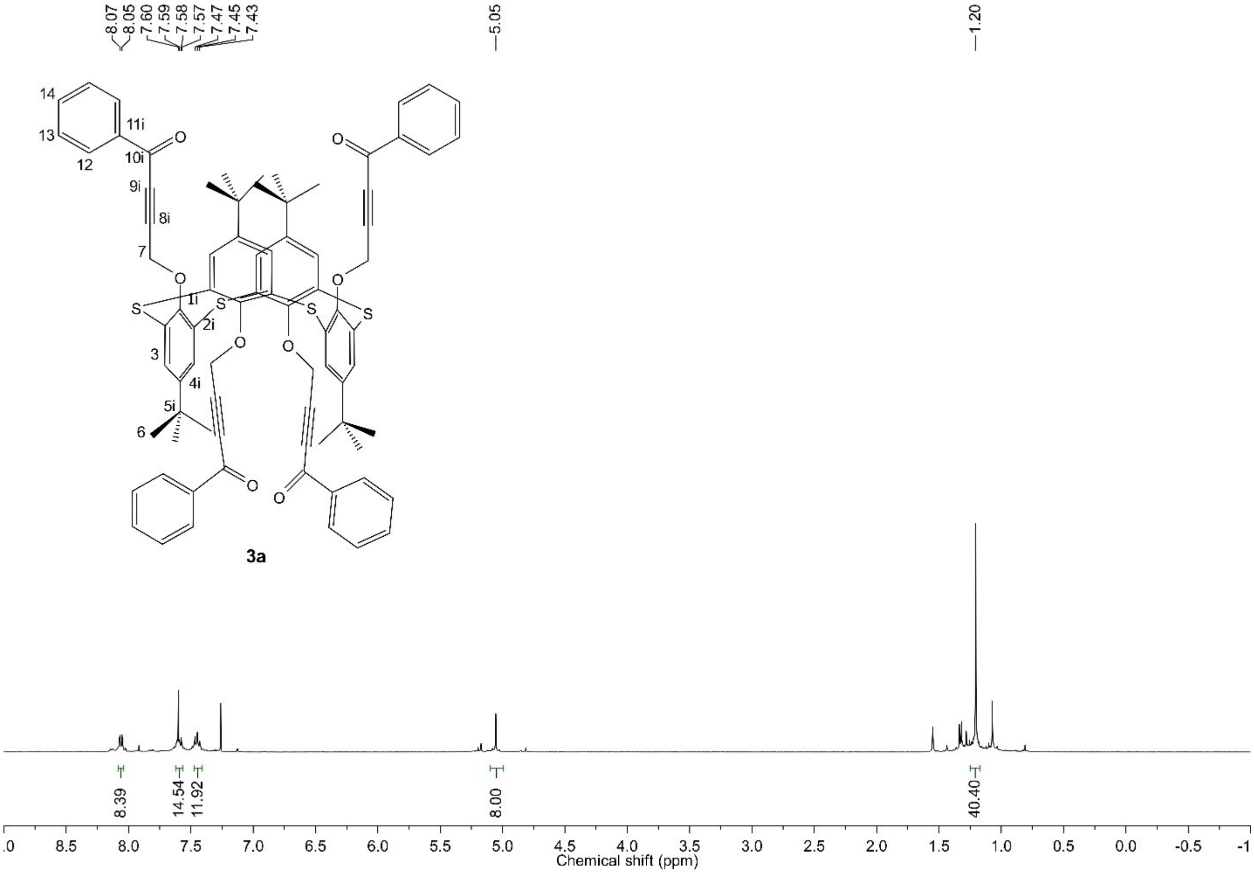


Fig. S14. ^{1}H NMR spectrum of compound **3a** ($CDCl_3$, 400 MHz, 298 K).

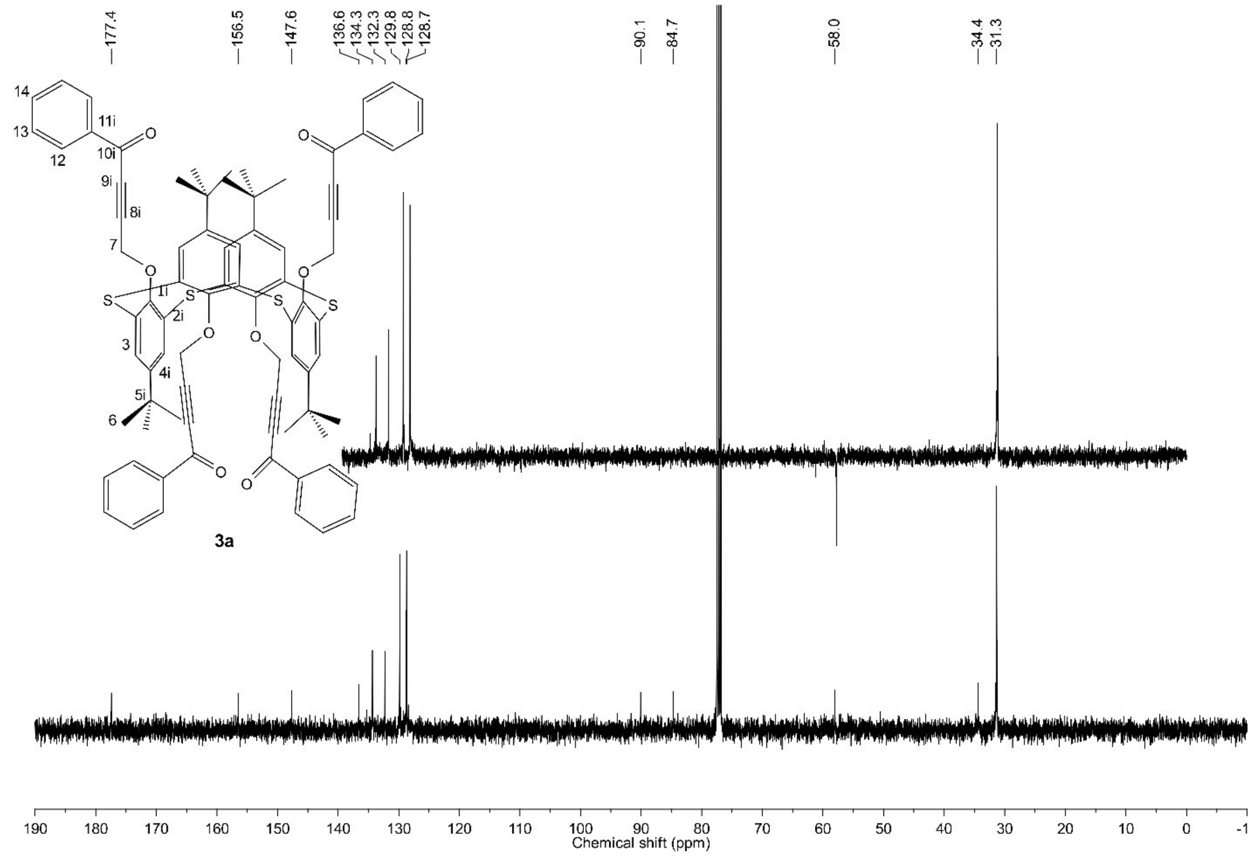


Fig. S15. ^{13}C NMR spectrum of compound **3a** ($CDCl_3$, 100 MHz, 298 K).

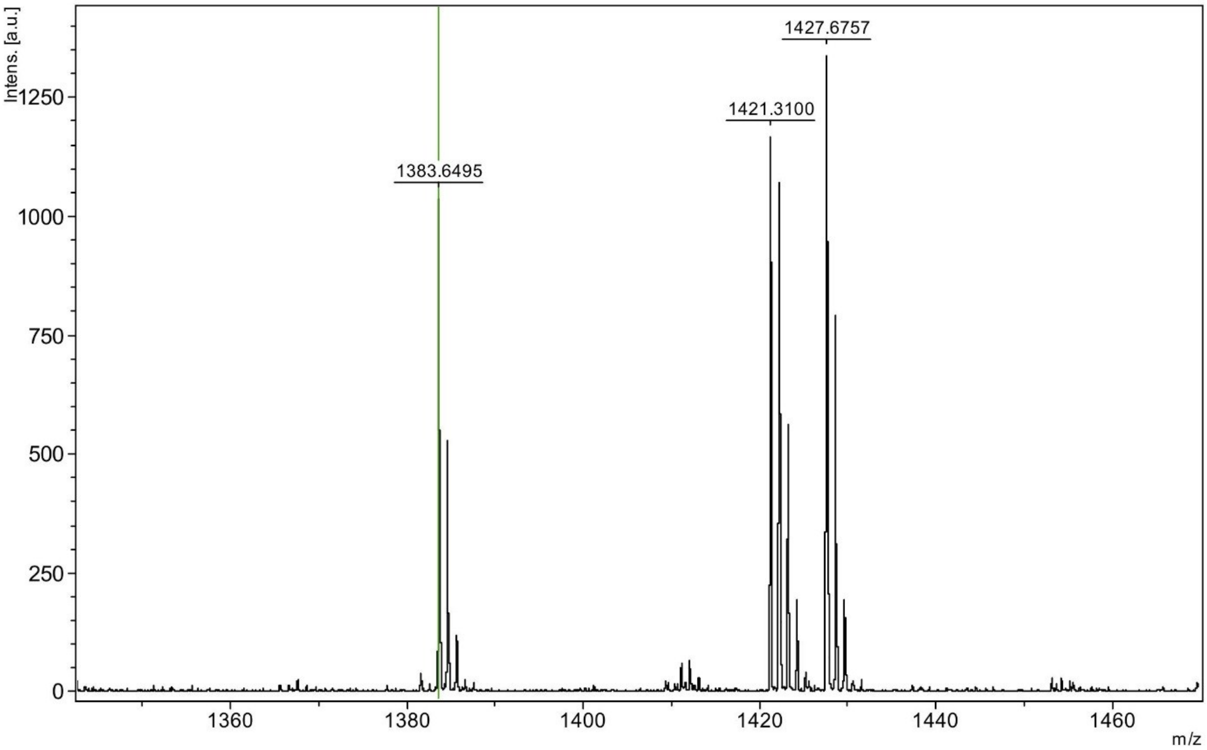


Fig. S16. HRMS spectrum of compound **3a**+CsCl (*p*-nitroaniline, PEG-1500 standard).

Compound 3b

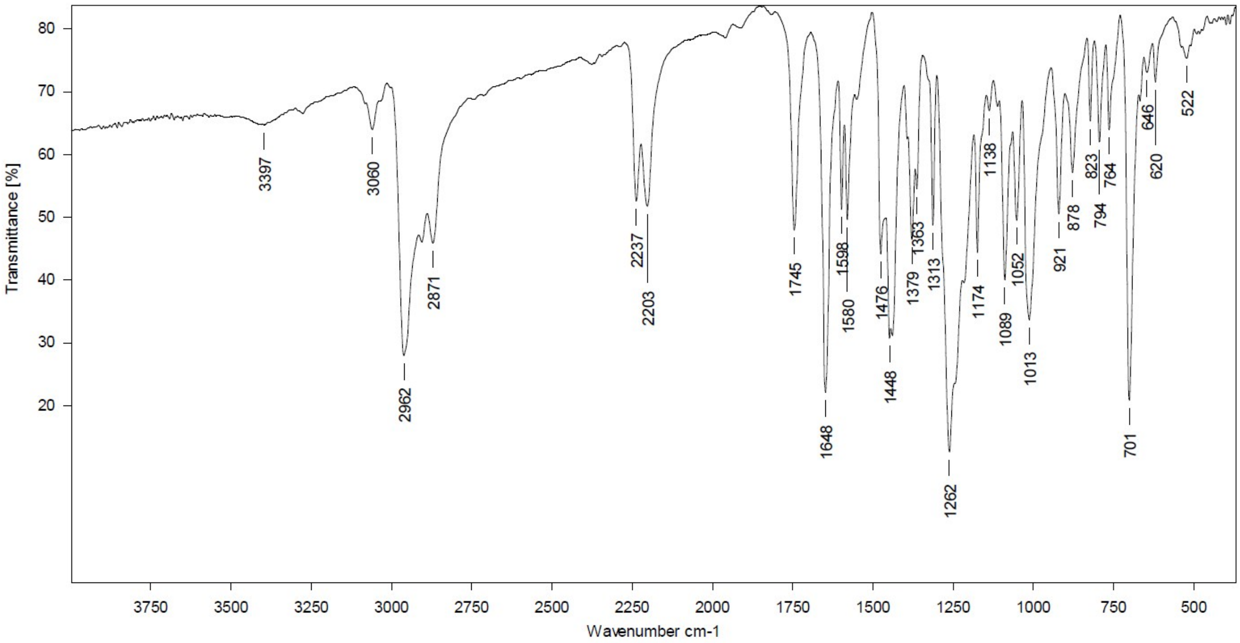


Fig. S17. FT IR spectrum of compound **3b** (KBr, 293K).

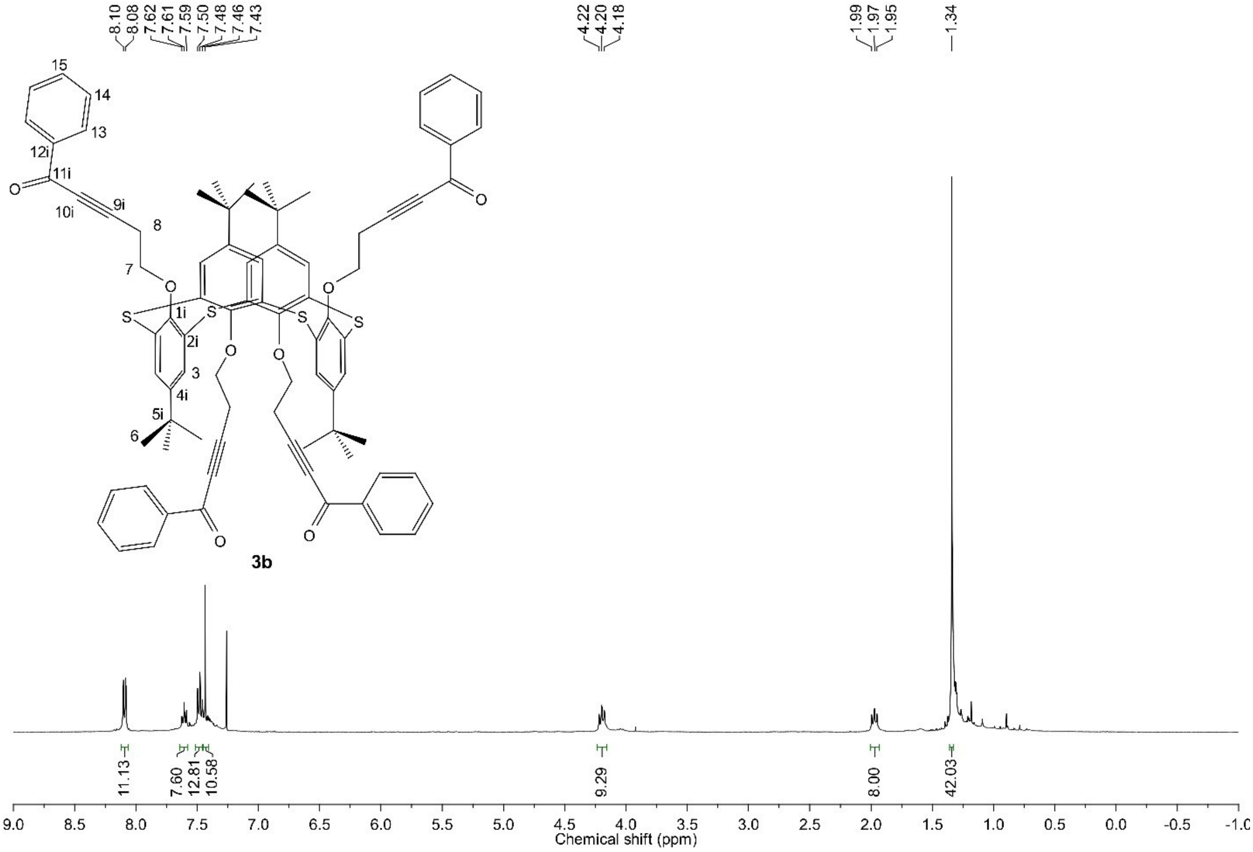


Fig. S18. ^{1}H NMR spectrum of compound **3b** ($CDCl_3$, 400 MHz, 298 K).

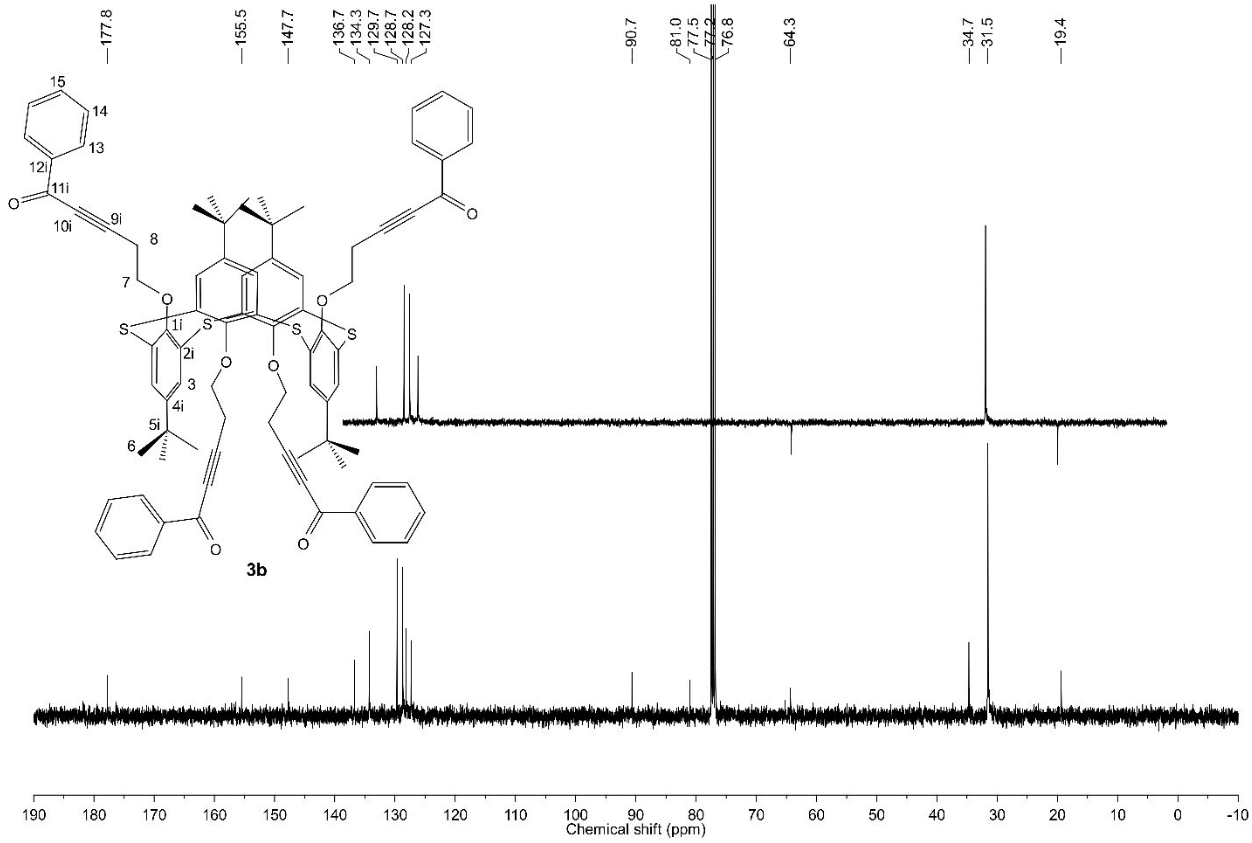


Fig. S19. ^{13}C NMR spectrum of compound **3b** ($CDCl_3$, 100 MHz, 298 K).

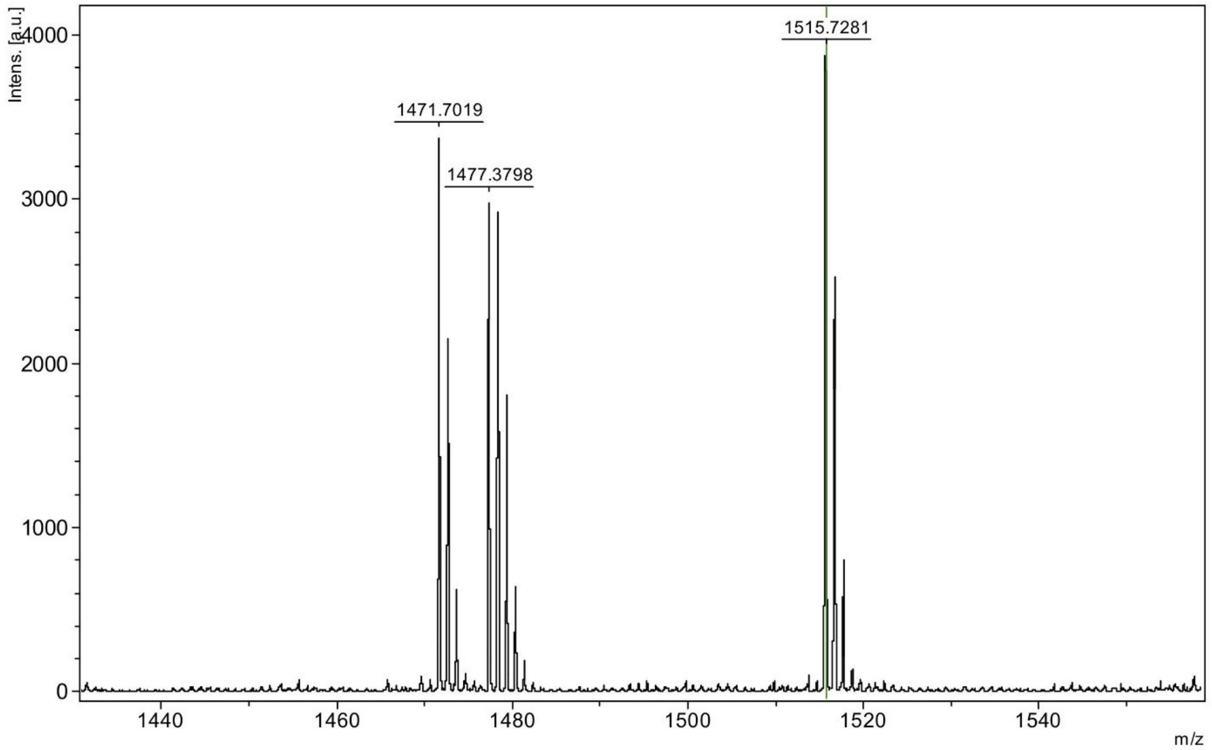


Fig. S20. HRMS spectrum of compound **3b**+CsCl (*p*-nitroaniline, PEG-1500 standard).

Compound 3c

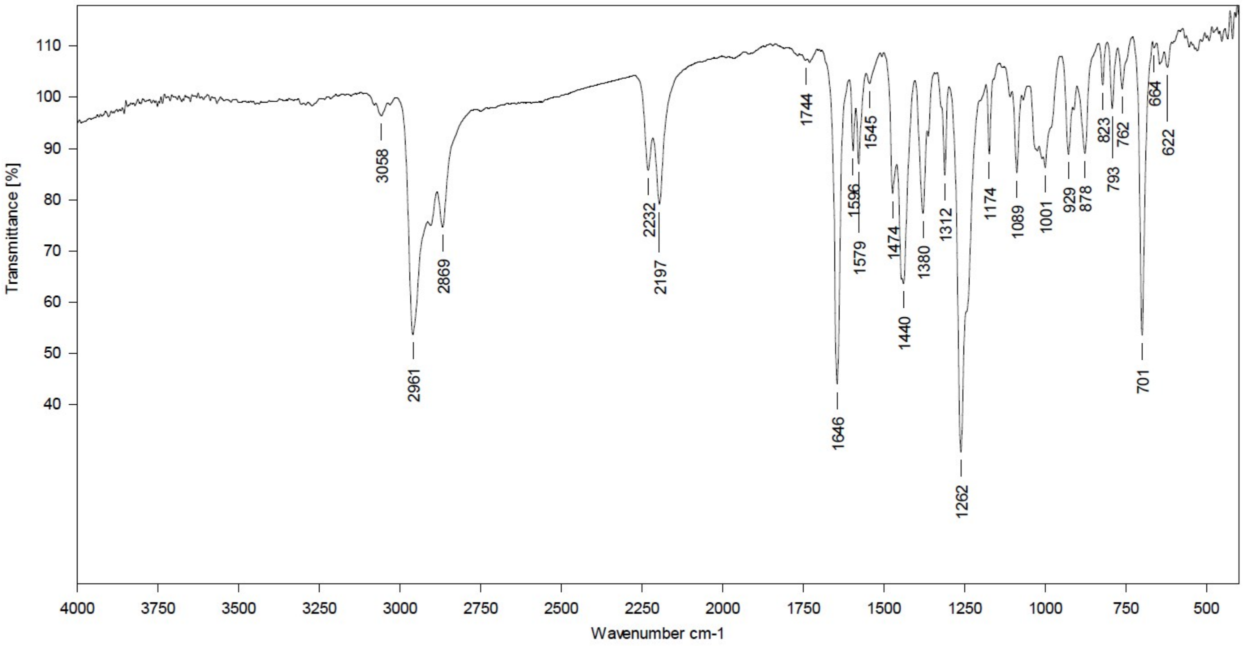


Fig. S21. FT IR spectrum of compound **3c** (KBr, 293K).

Fig. S22. ^{1}H NMR spectrum of compound **3c** ($CDCl_3$, 400 MHz, 298 K).

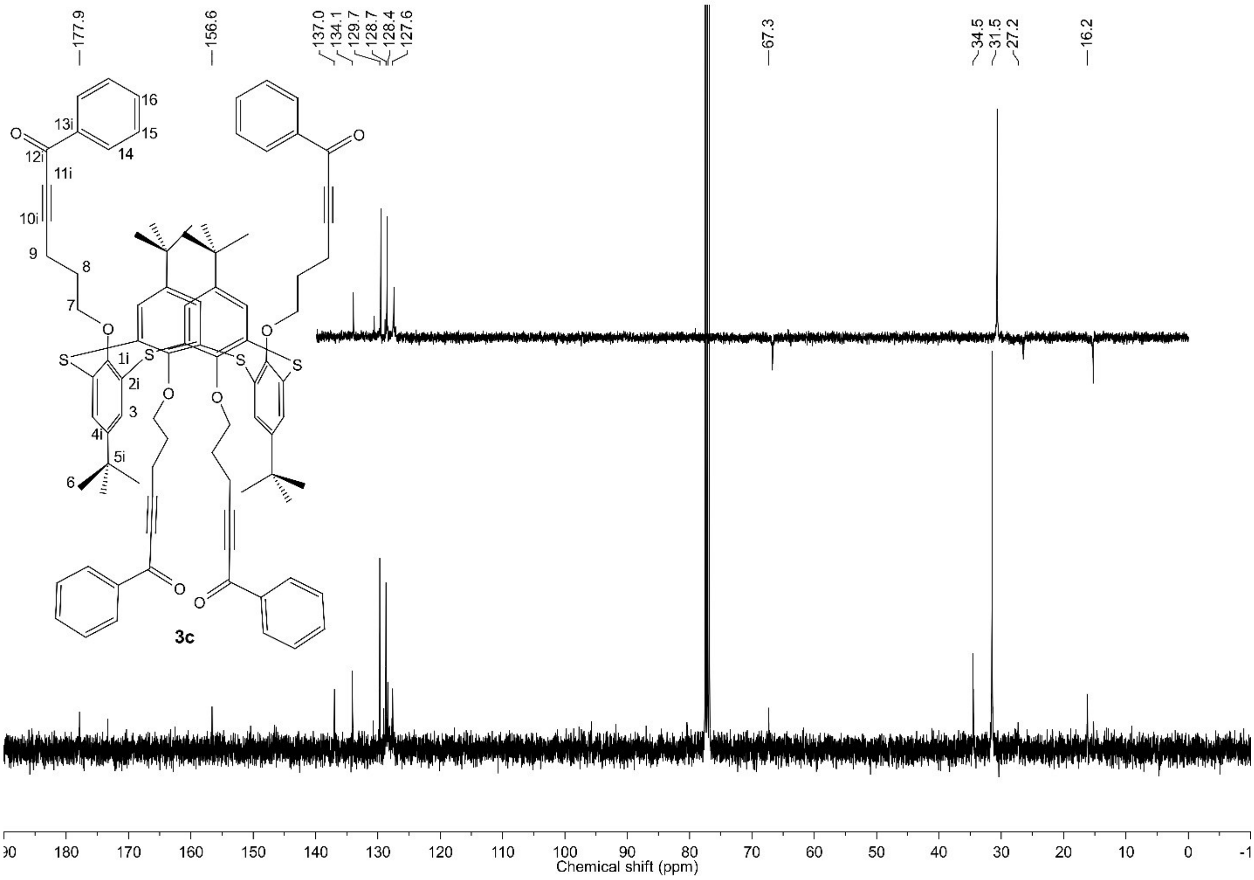


Fig. S23. ^{13}C NMR spectrum of compound **3c** ($CDCl_3$, 100 MHz, 298 K).

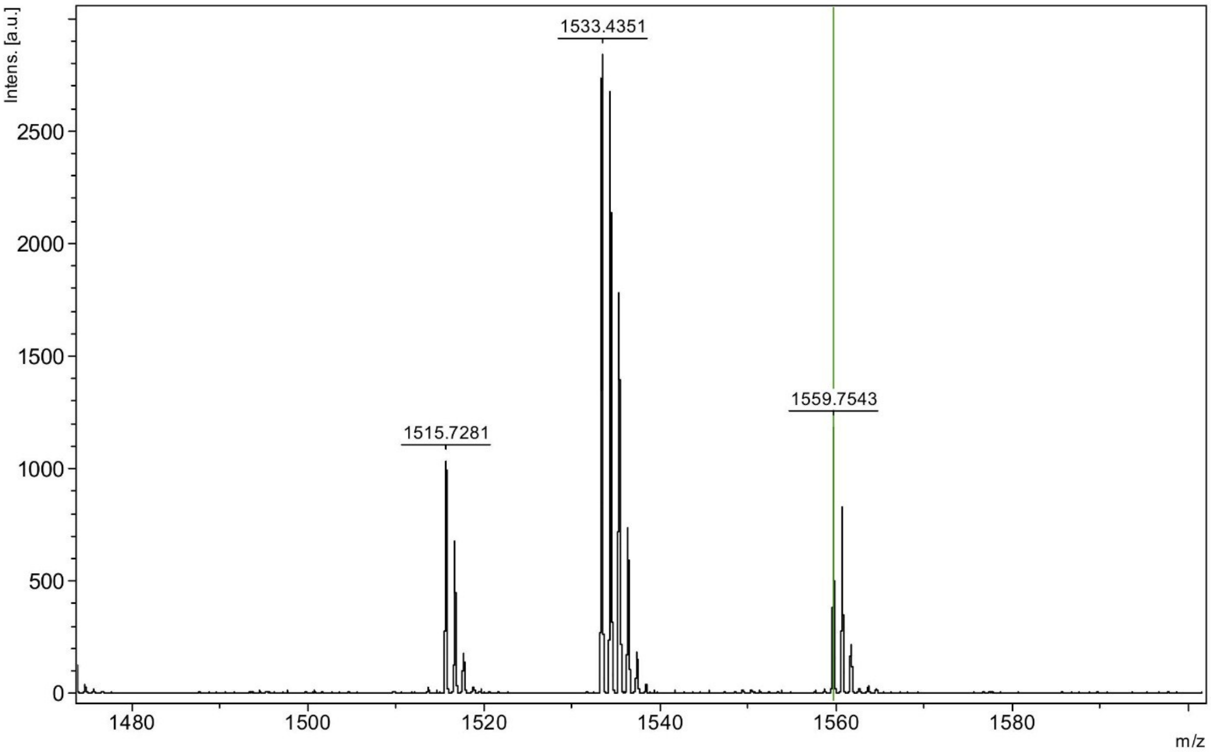


Fig. S24. HRMS spectrum of compound **3c**+CsCl (*p*-nitroaniline, PEG-1500 standard).

Compound 3d

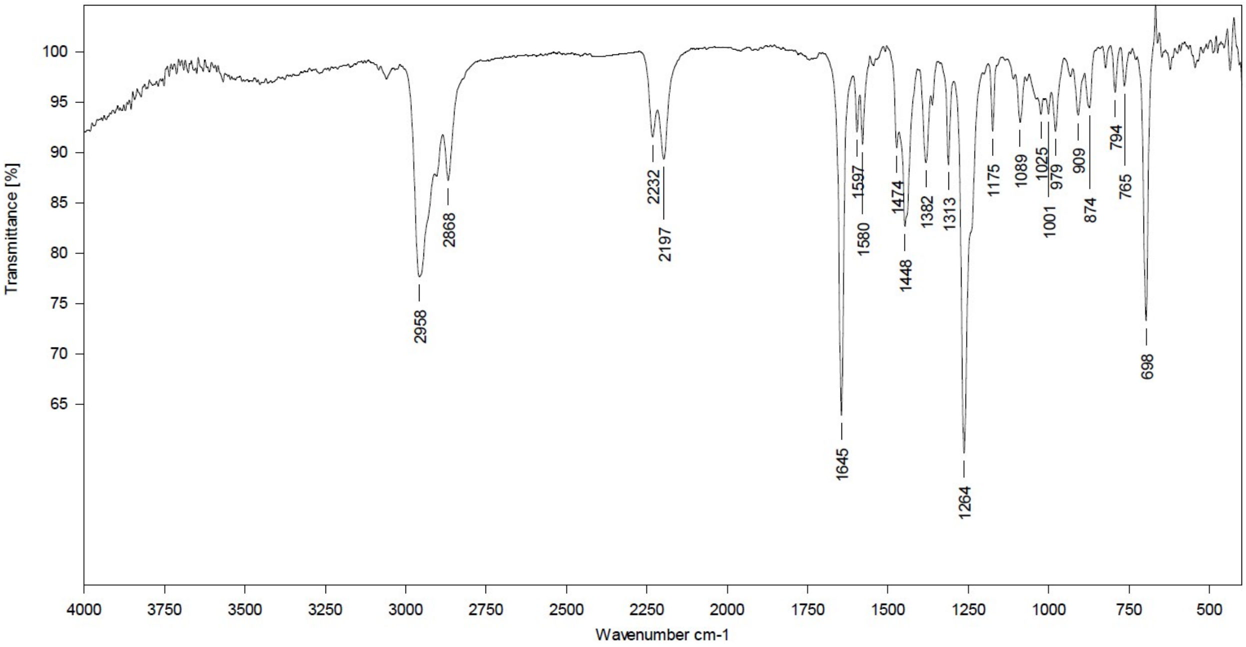


Fig. S25. FT IR spectrum of compound **3d** (KBr, 293K).

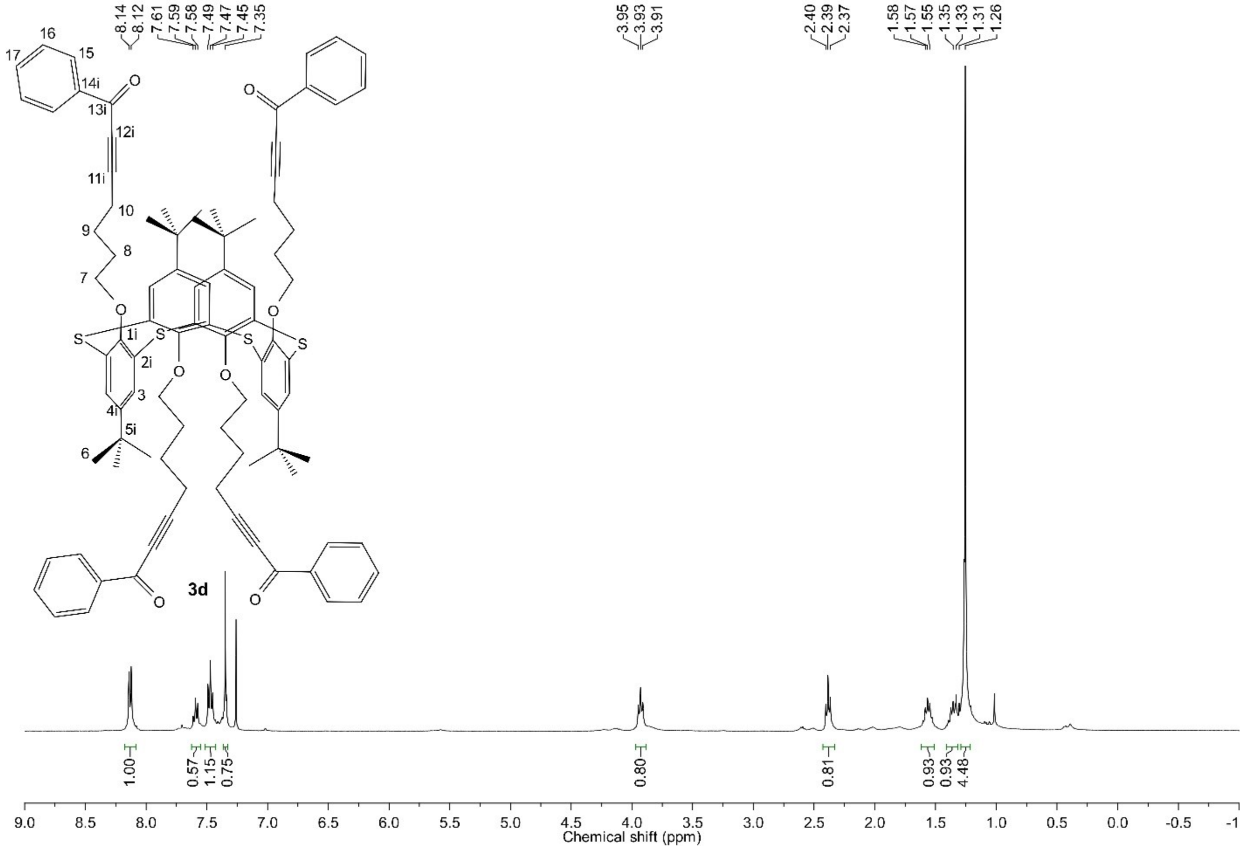


Fig. S26. ^{1}H NMR spectrum of compound **3d** ($CDCl_3$, 400 MHz, 298 K).

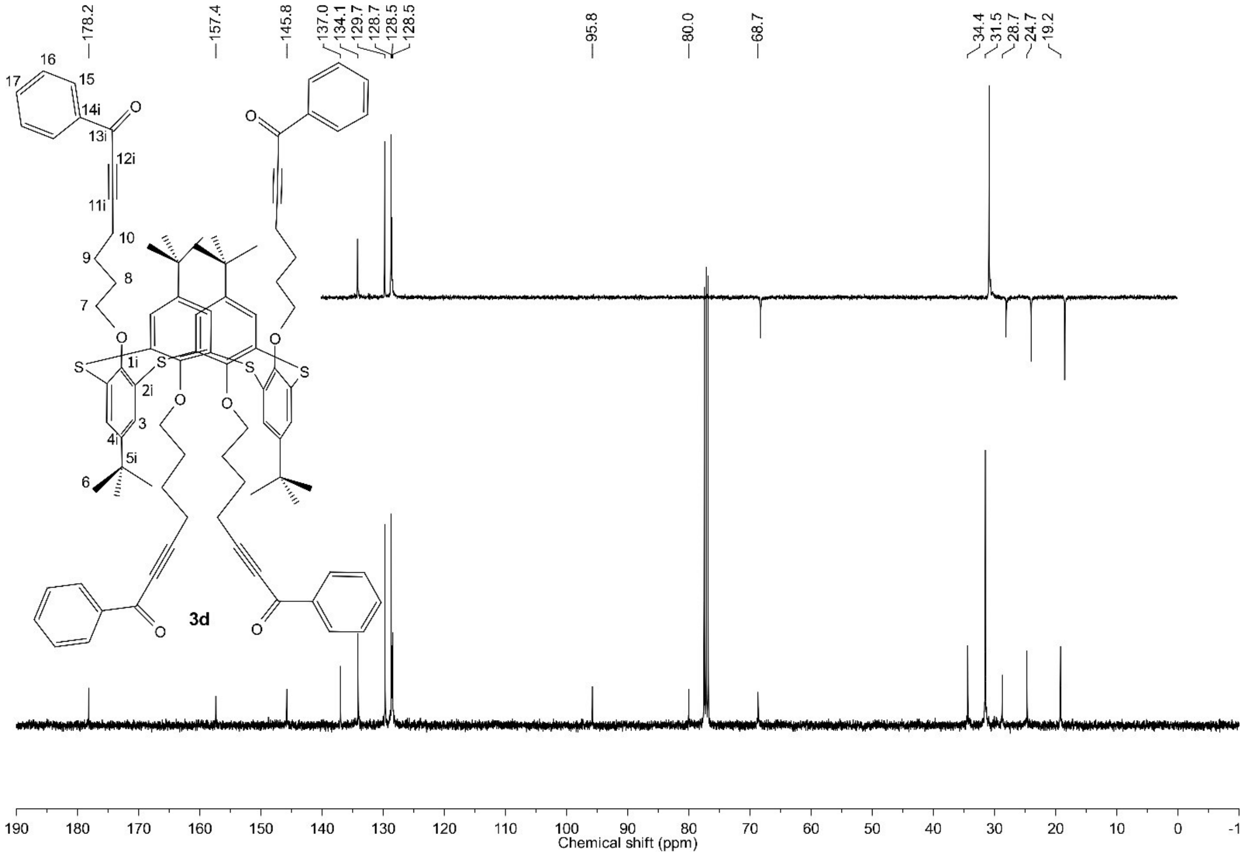


Fig. S27. ^{13}C NMR spectrum of compound **3d** ($CDCl_3$, 100 MHz, 298 K).

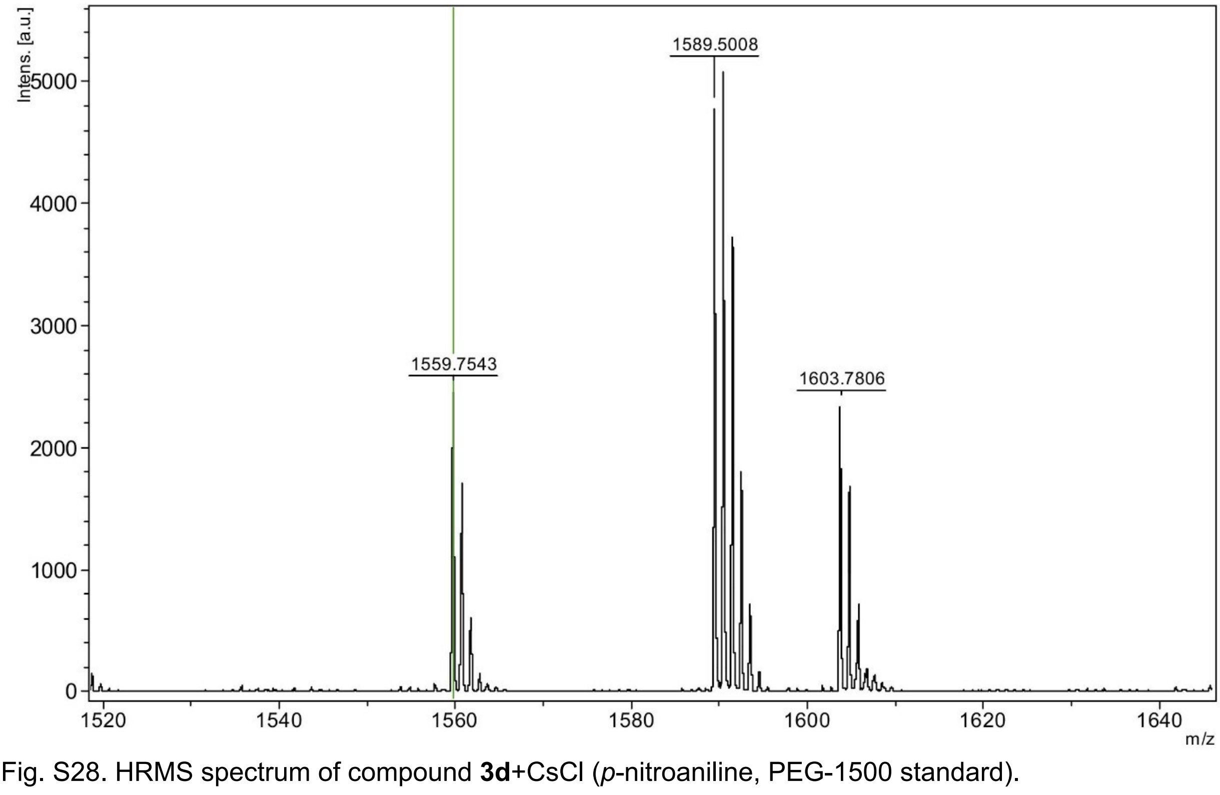


Fig. S28. HRMS spectrum of compound **3d**+CsCl (*p*-nitroaniline, PEG-1500 standard).

Compound 4a

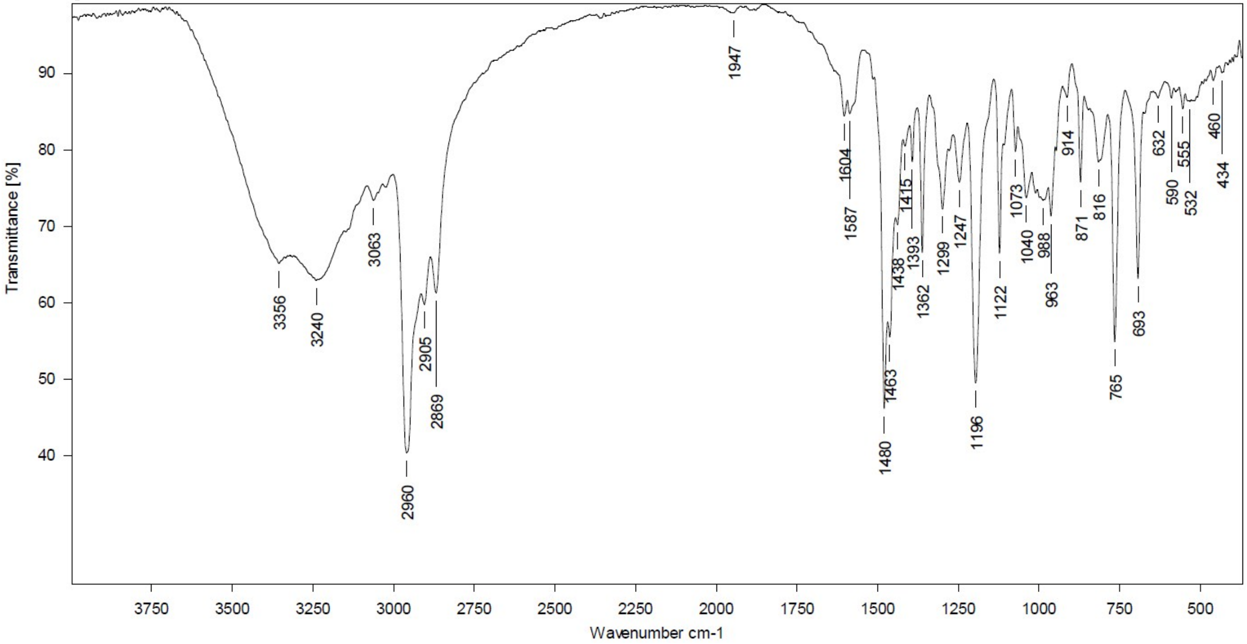


Fig. S29. FT IR spectrum of compound **4a** (KBr, 293K).

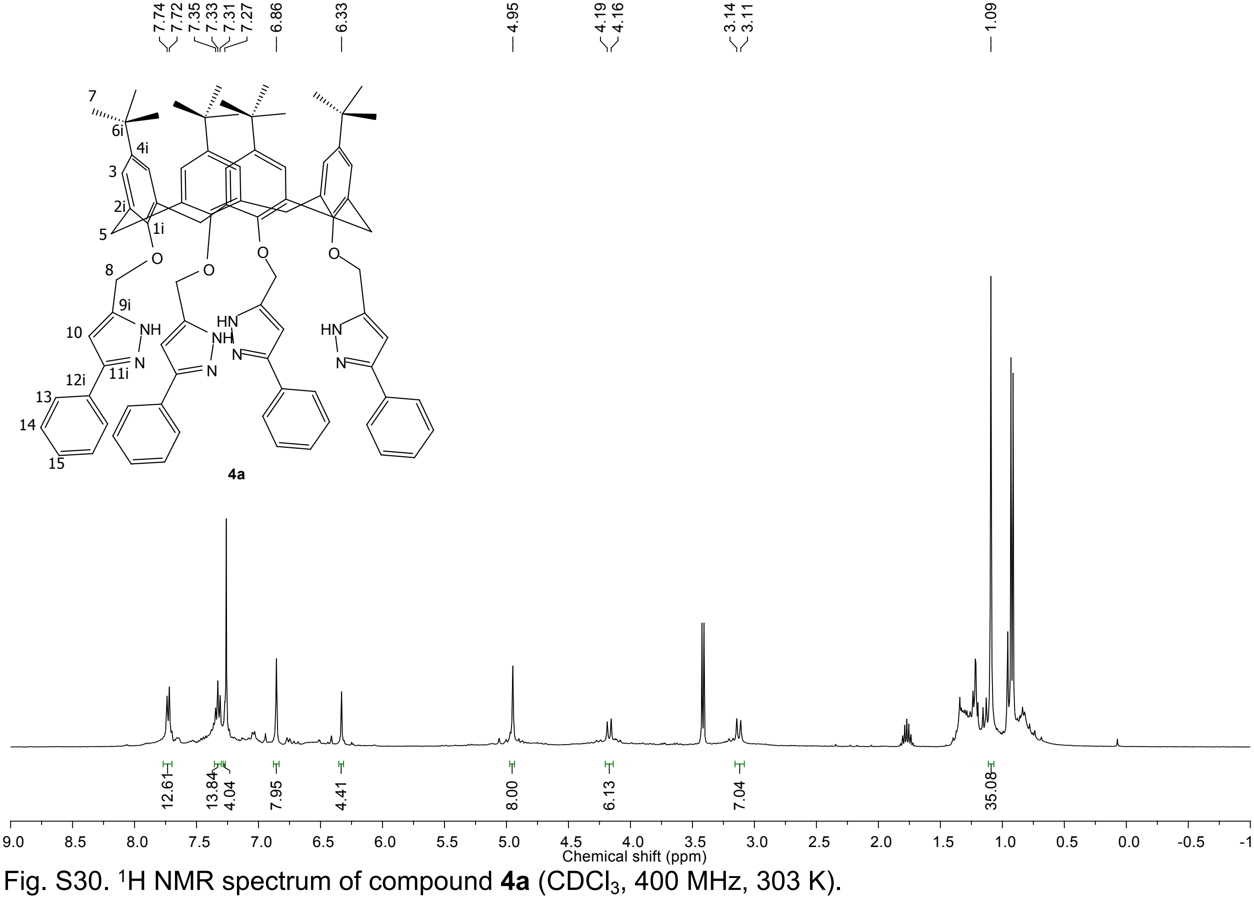


Fig. S30. ^{1}H NMR spectrum of compound **4a** ($CDCl_3$, 400 MHz, 303 K).

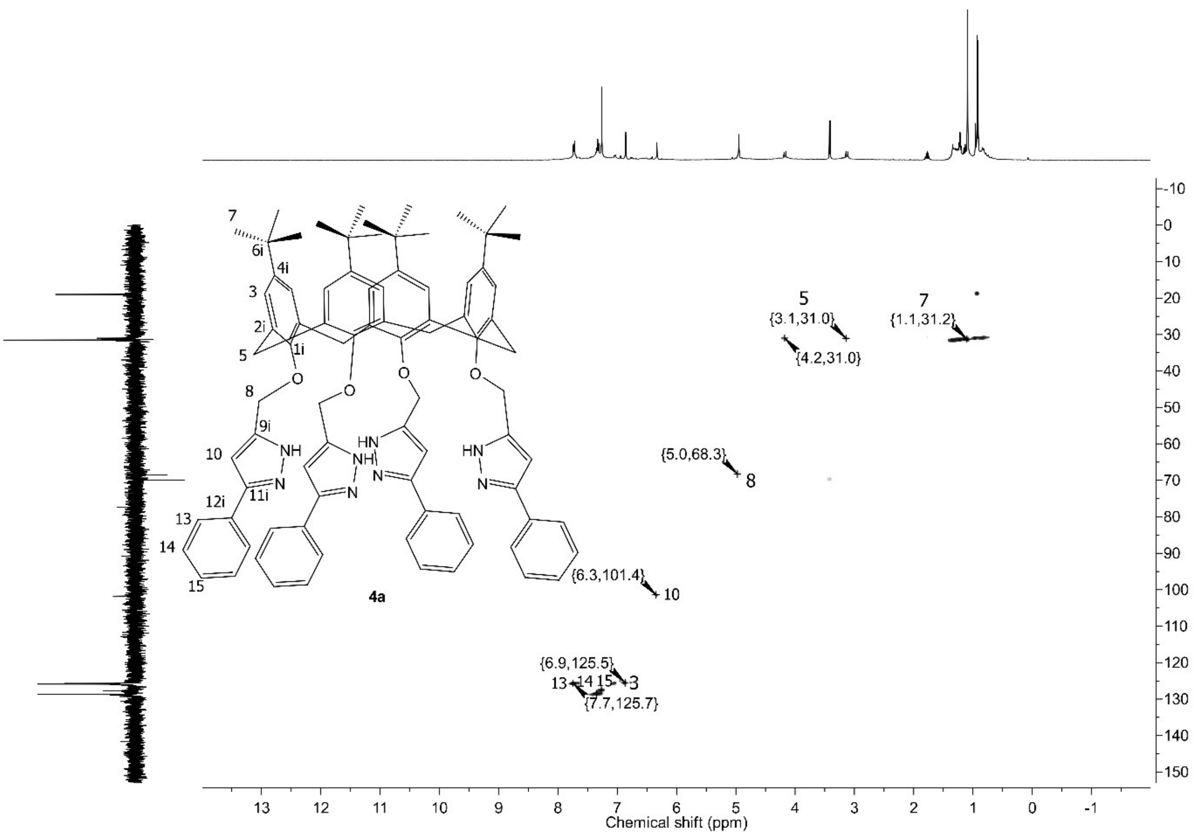
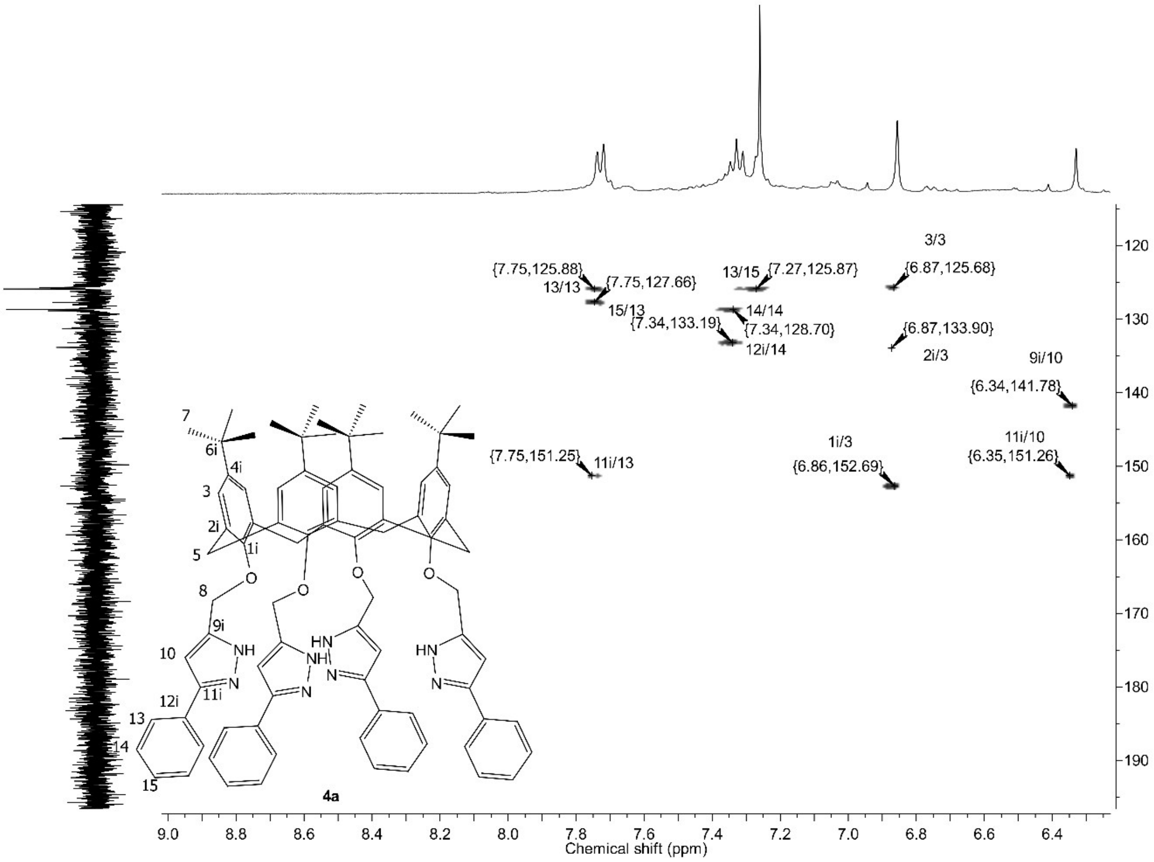


Fig. S31. $^{13}C/^{1}H$ HSQC NMR spectrum of compound **4a** ($CDCl_3$, 100 MHz, 298 K).



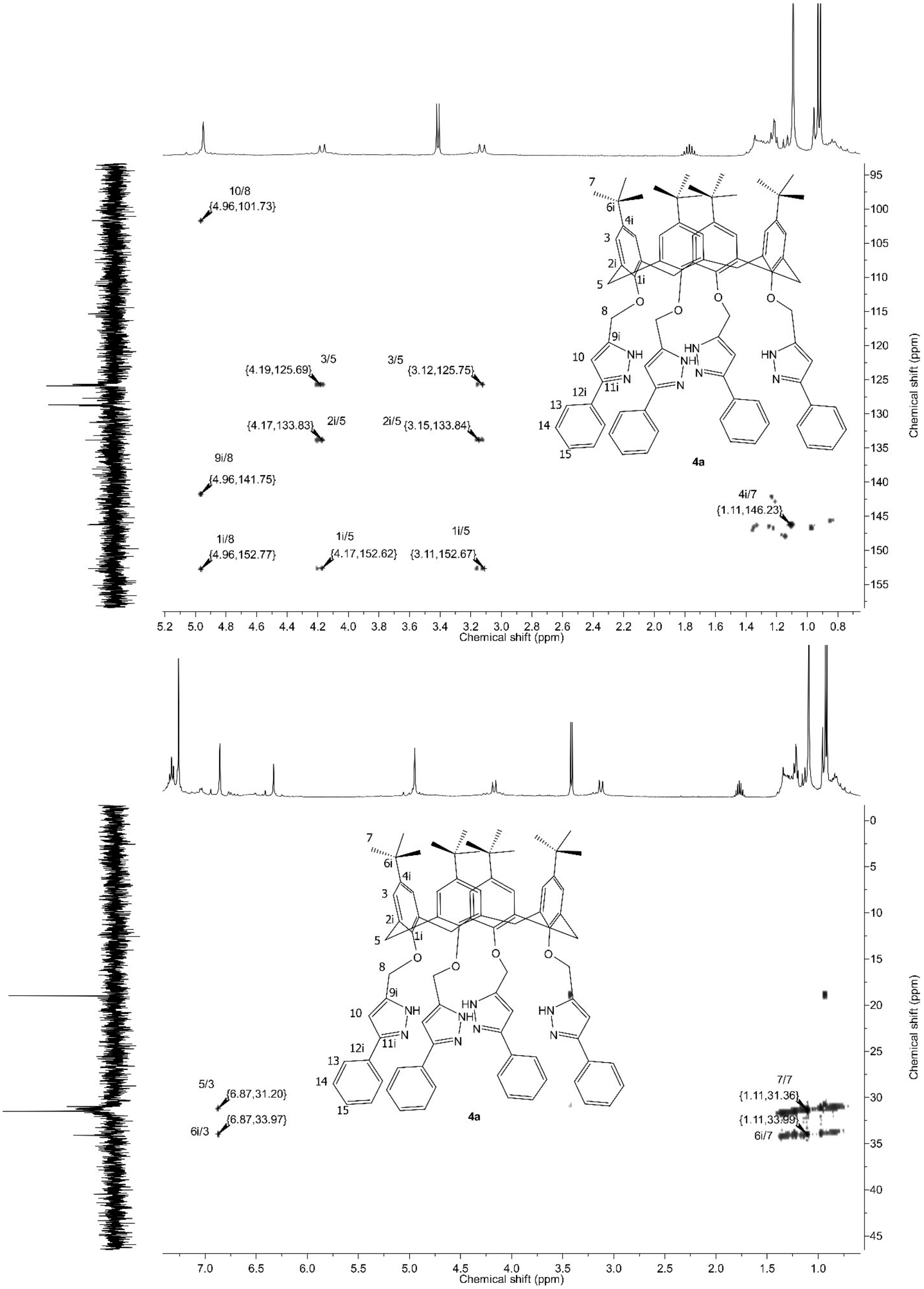


Fig. S32. ^{13}C/^{1}H HMBC NMR spectrum of compound **4a** (CDCl$_3$, 100 MHz, 298 K).

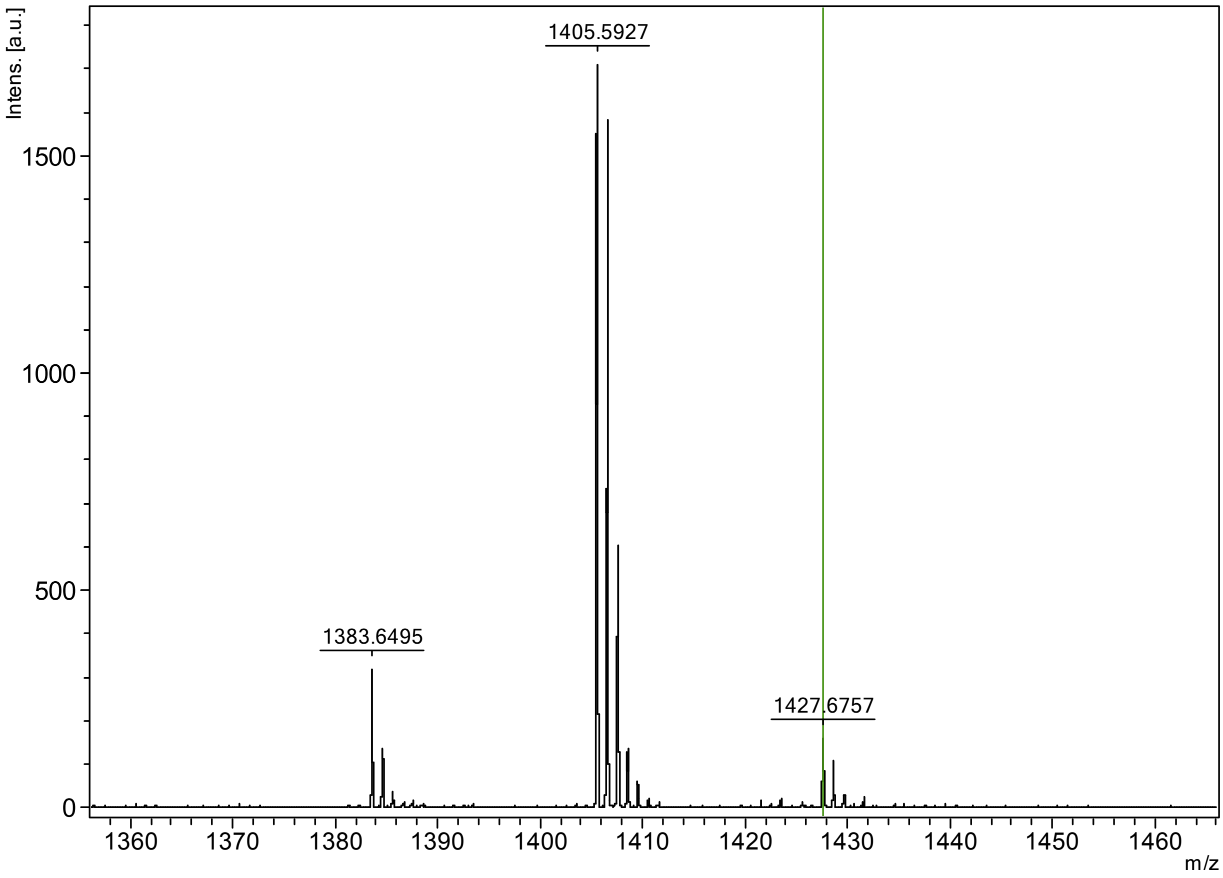


Fig. S33. HRMS spectrum of compound **4a**+CsCl (*p*-nitroaniline, PEG-1000 standard).

Compound 4b

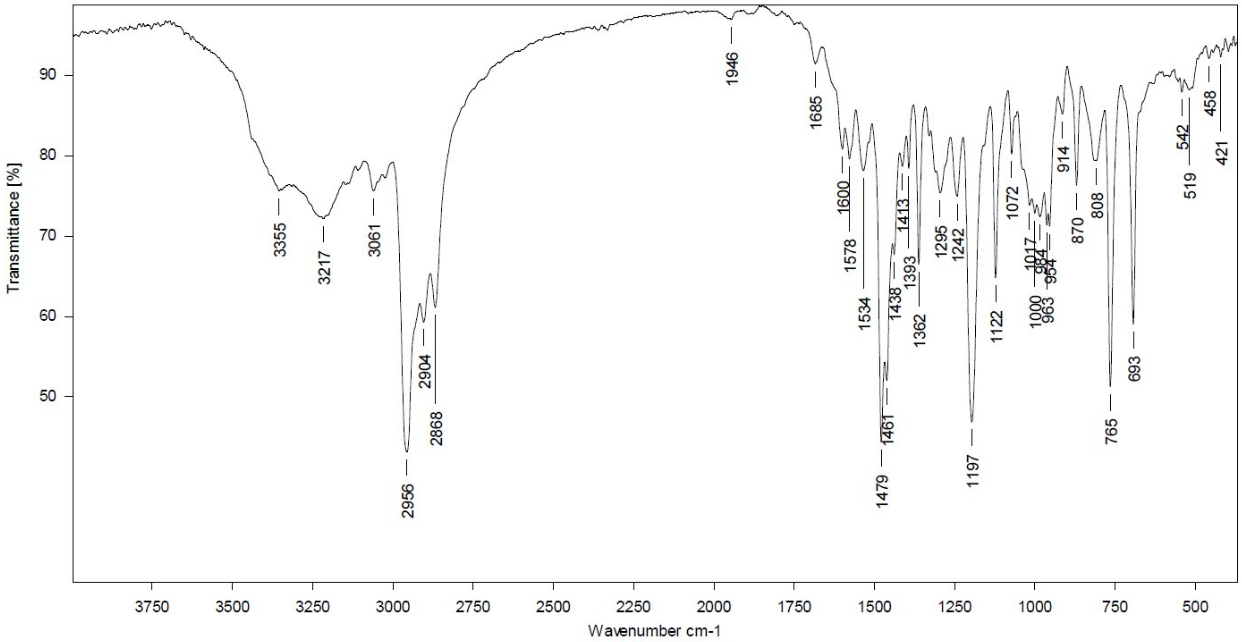


Fig. S34. FT IR spectrum of compound **4b** (KBr, 293K).

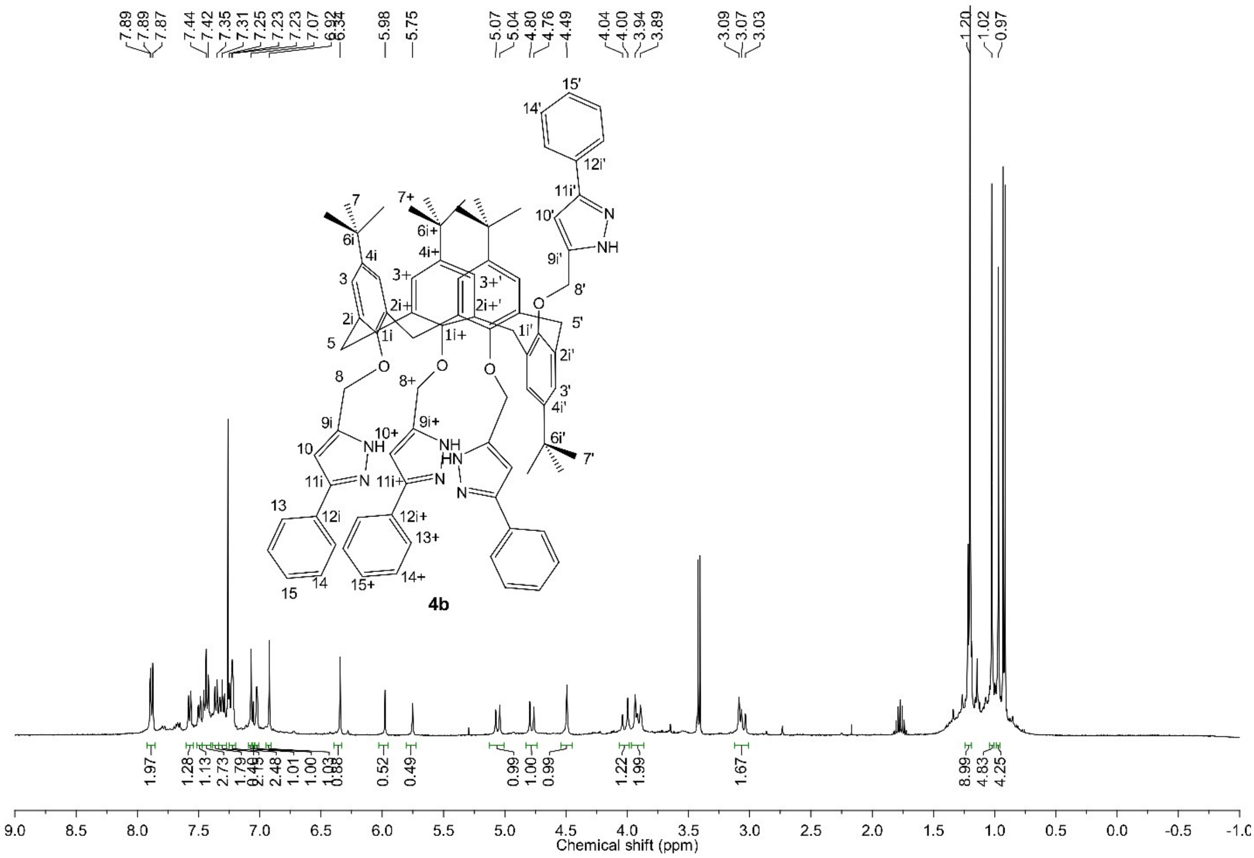


Fig. S35. ^{1}H NMR spectrum of compound **4b** ($CDCl_3$, 400 MHz, 303 K).

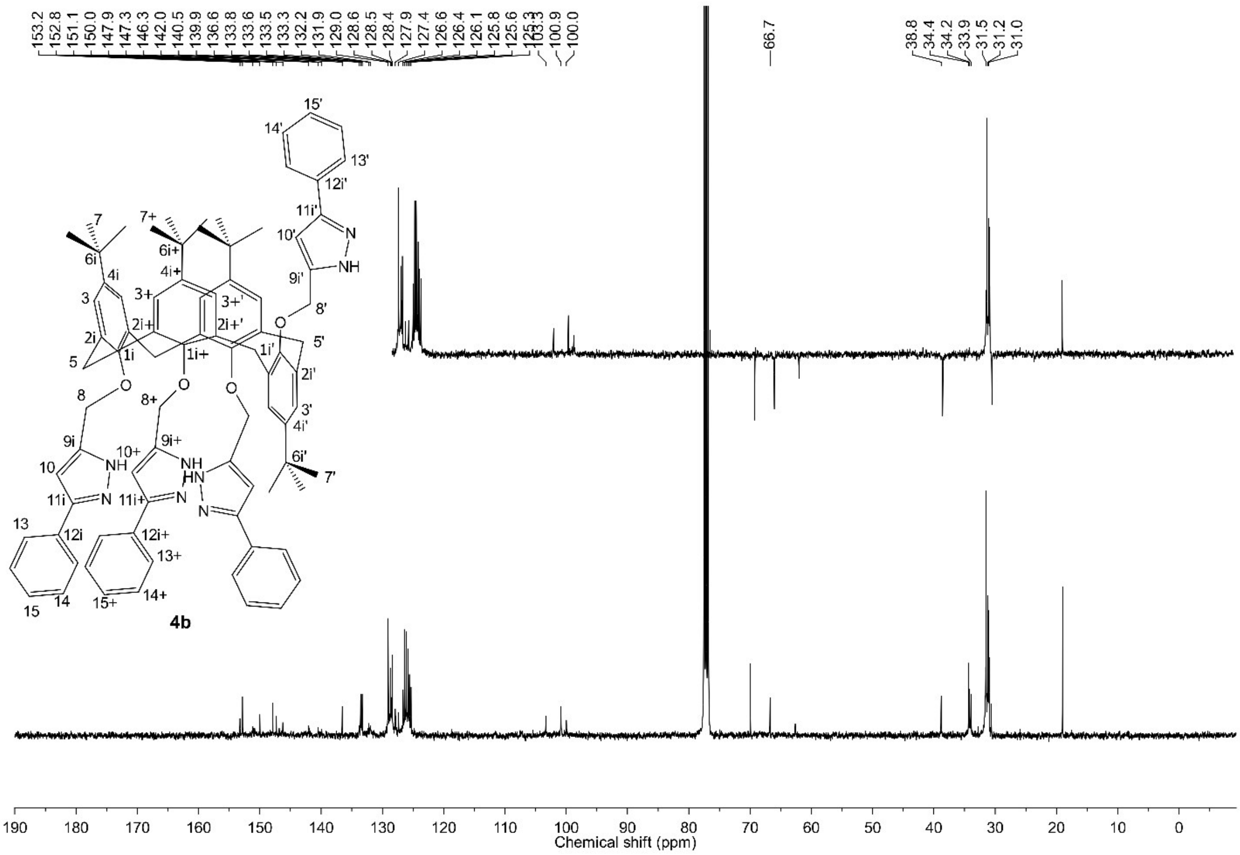


Fig. S36. ^{13}C NMR spectrum of compound **4b** ($CDCl_3$, 100 MHz, 298 K).

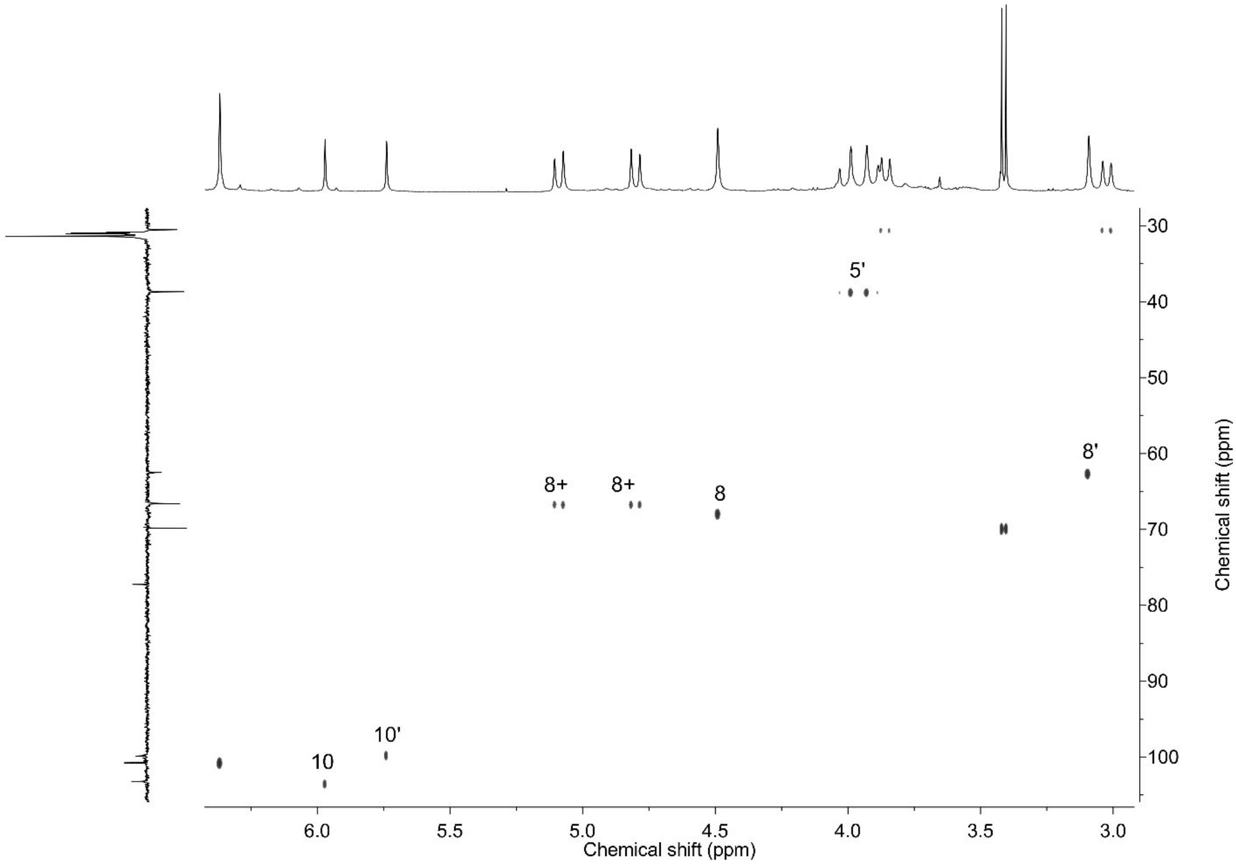
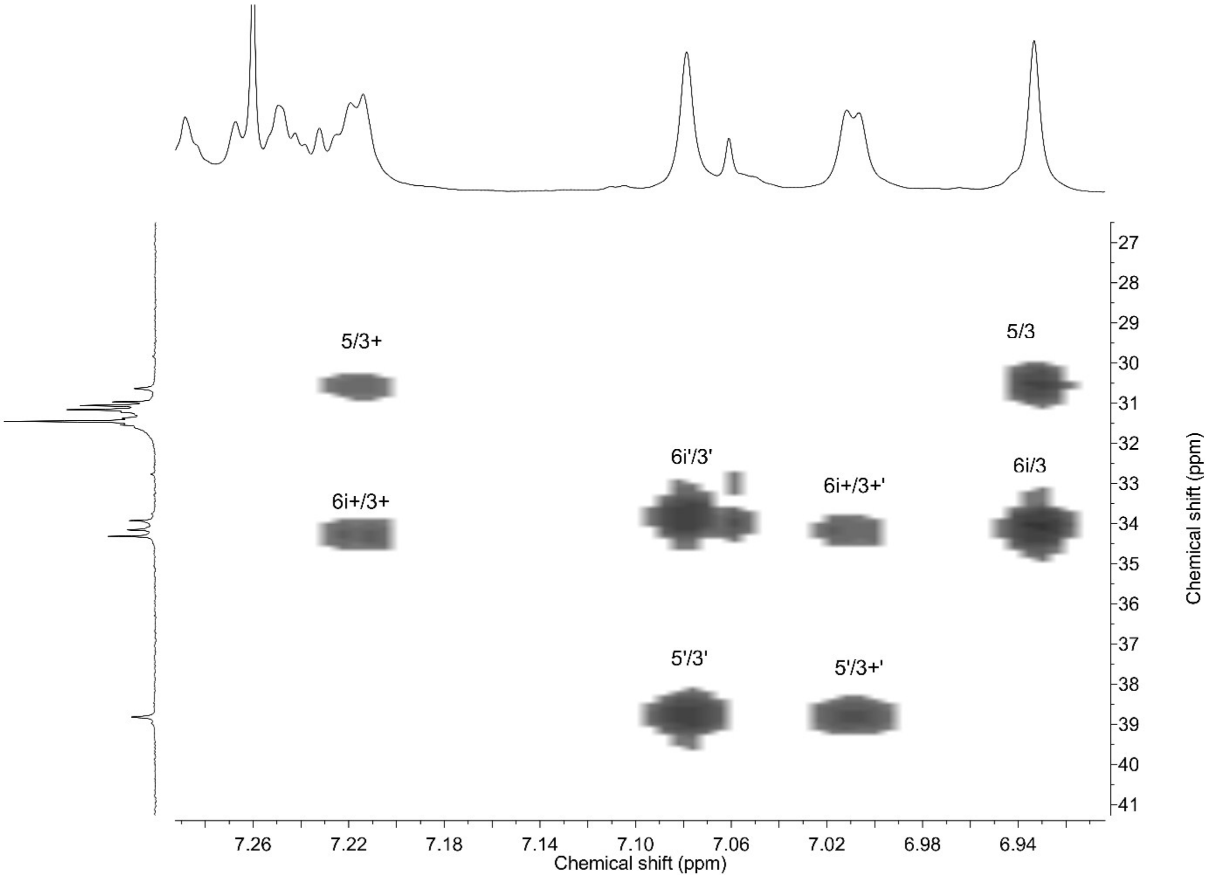


Fig. S37. ^{13}C/^{1}H HSQC NMR spectrum of compound **4b** ($CDCl_3$, 100 MHz, 298 K).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5/3
6i'/3'
6i+/3+'
6i/3
6i+/3+
5'/3'
5'/3+'
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-28
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-30
-31
-32
-33
-34
-35
-36
-37
-38
-39
-40
-41
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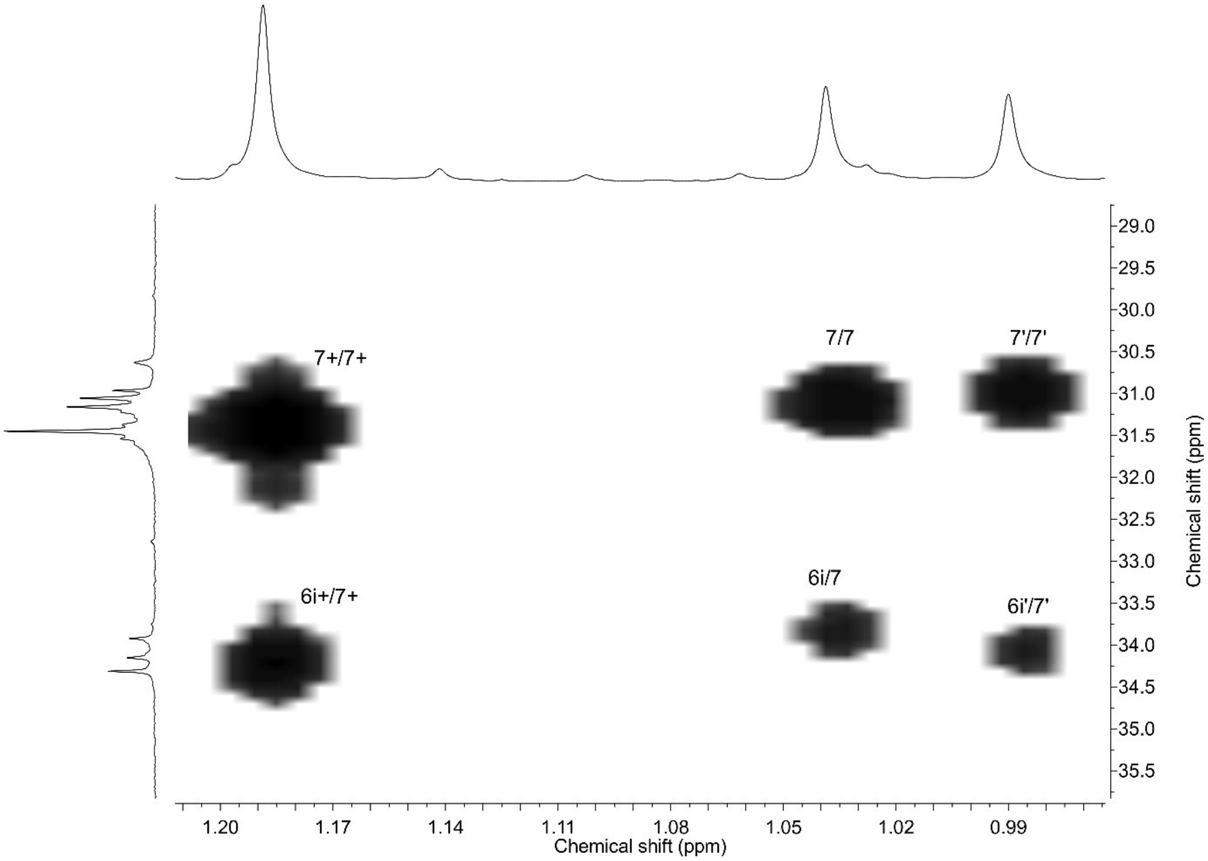
7.22
7.18
7.14
7.10
7.06
7.02
6.98
6.94
Chemical shift (ppm)


7+/7+
7/7
7'/7'
6i+/7+
6i/7
6i'/7'
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-29.5
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-31.0
-31.5
-32.0
-32.5
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-34.5
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Chemical shift (ppm)
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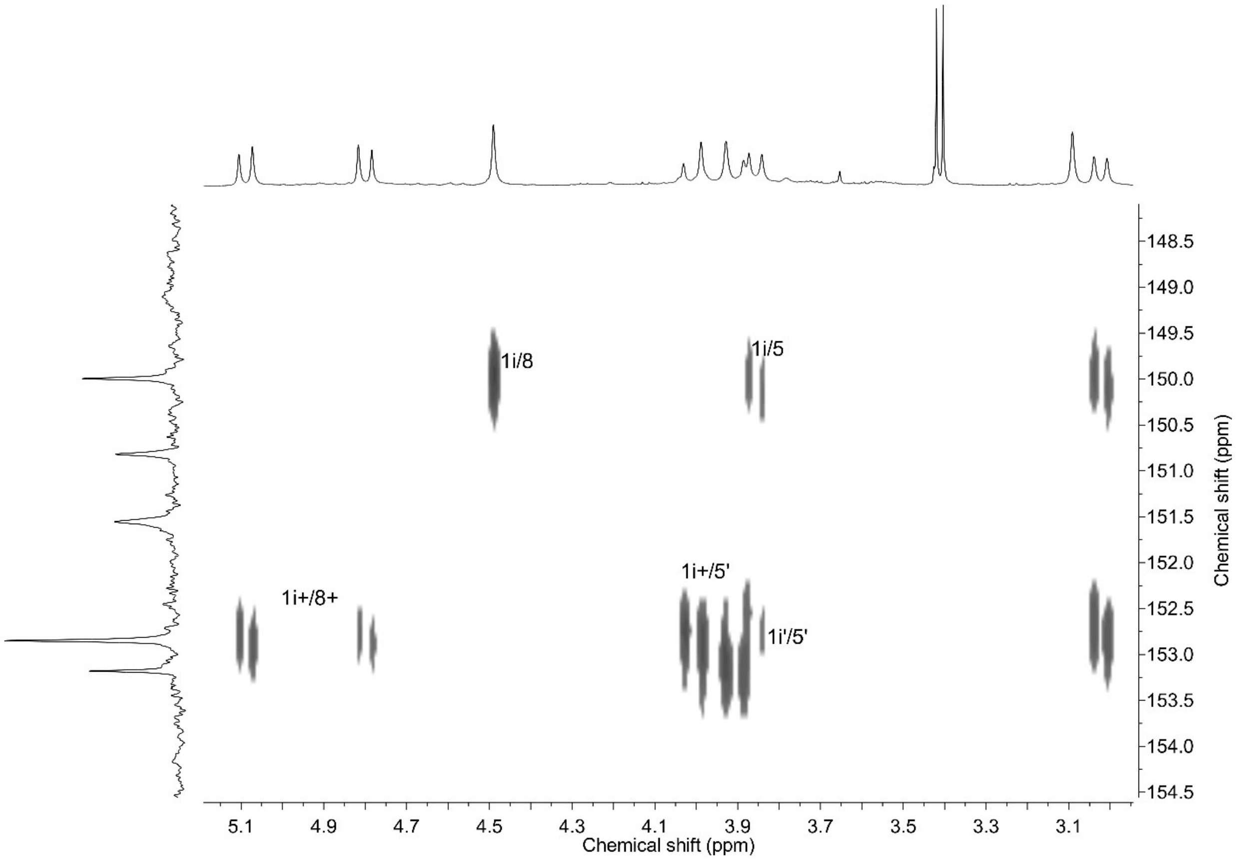
1.05
1.02
0.99
Chemical shift (ppm)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1i+/5'
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151.5
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153.0
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154.5
Chemical shift (ppm)
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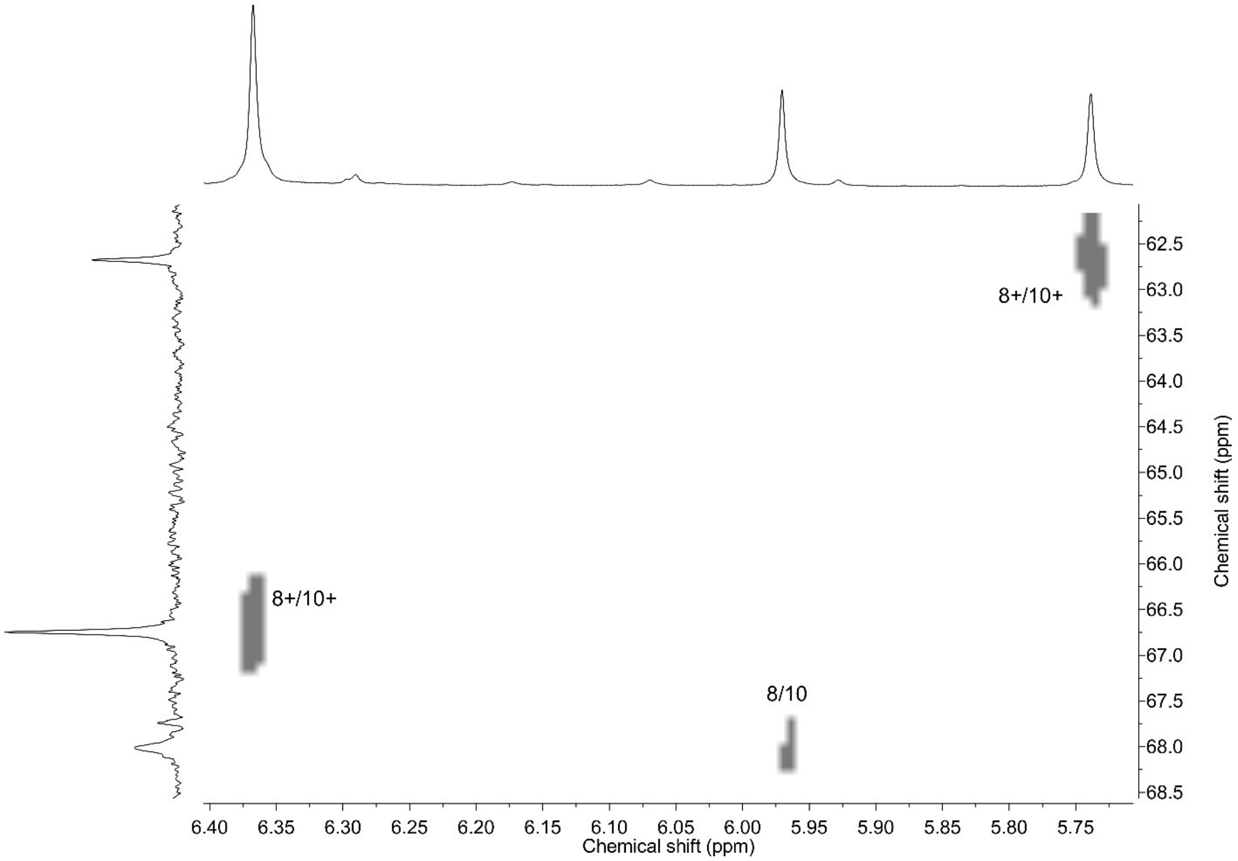
3.5
3.3
3.1
Chemical shift (ppm)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66.5
67.0
67.5
68.0
68.5
Chemical shift (ppm)
6.40
6.35
6.30
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6.05
6.00
5.95
5.90
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5.80
5.75
Chemical shift (ppm)

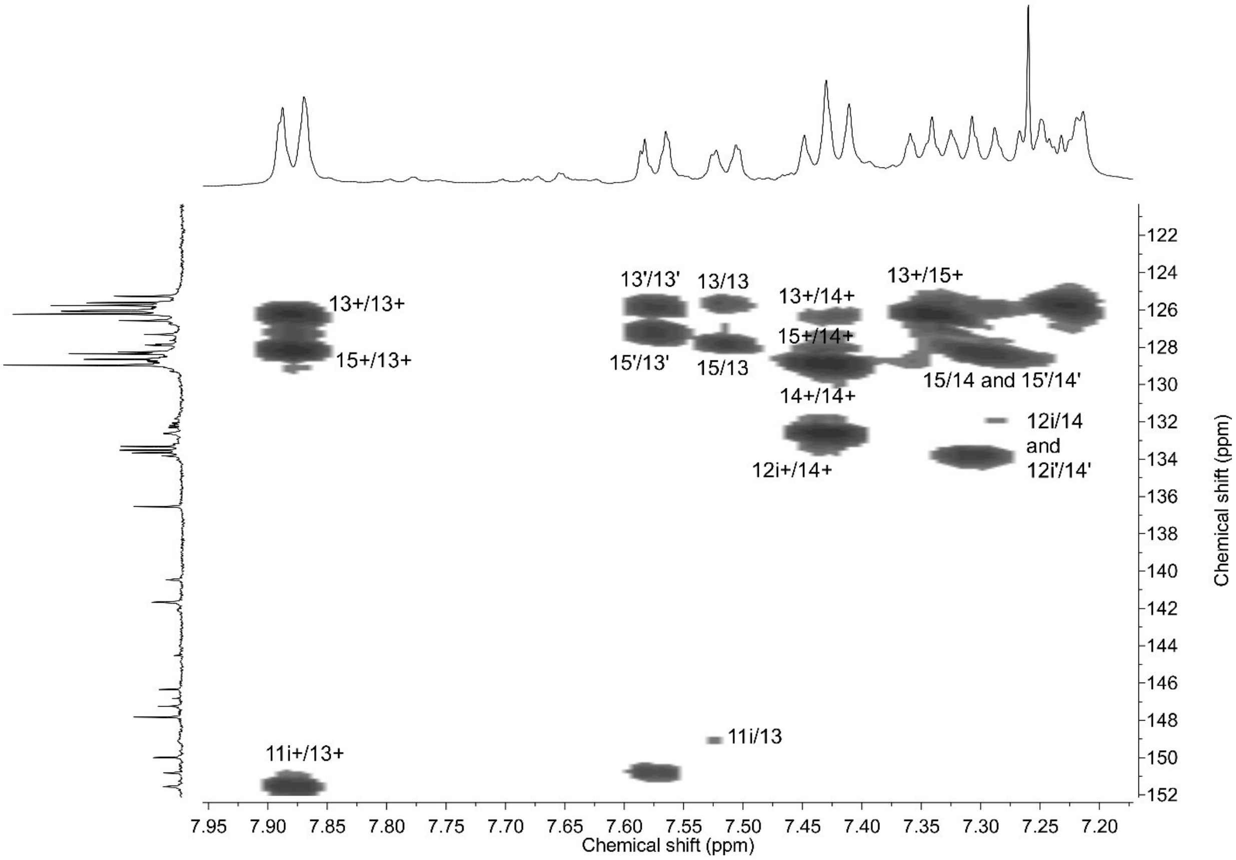

Fig. S38. Partial $^{13}C/^{1}H$ HMBC NMR spectra of compound **4b** ($CDCl_3$, 100 MHz, 298 K).

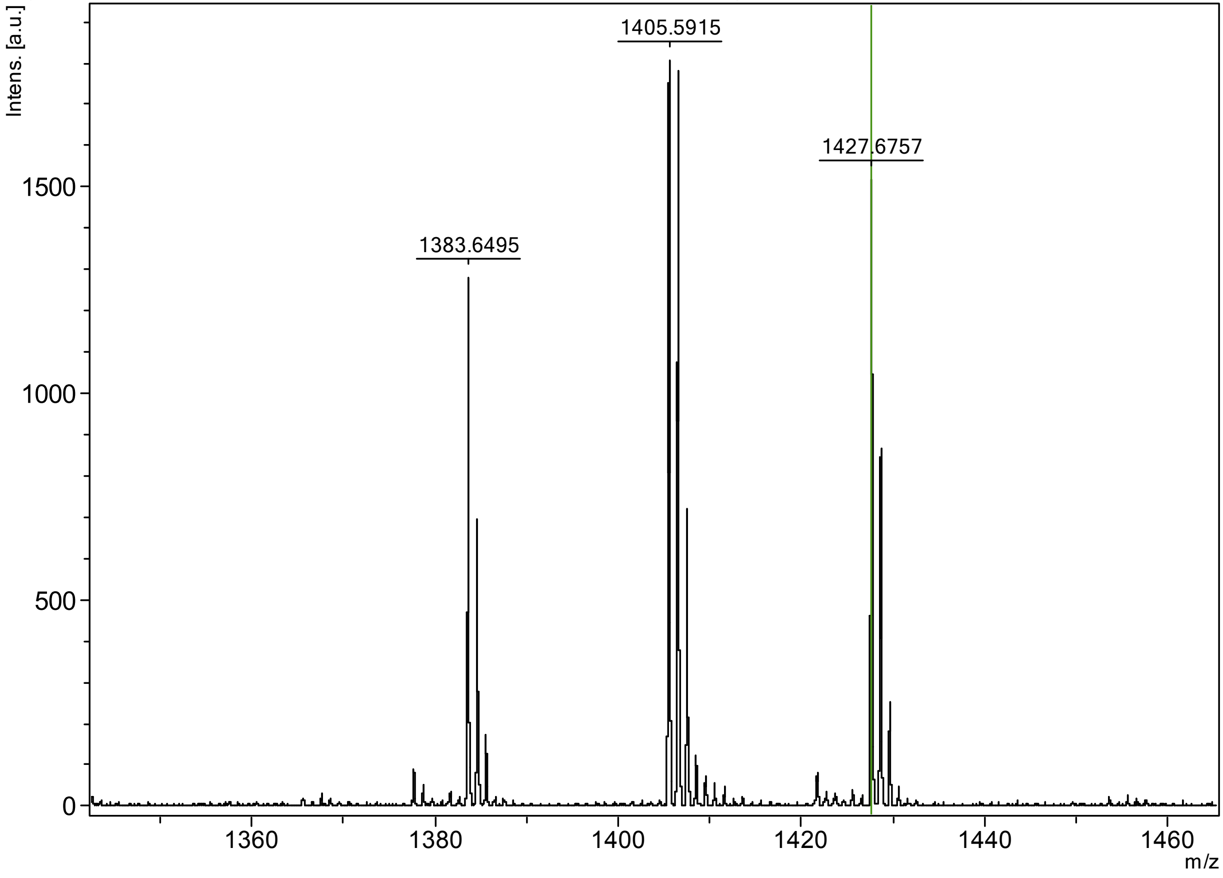

Fig. S39. HRMS spectrum of compound **4b**+CsCl (*p*-nitroaniline, PEG-1000 standard).

Compound 4c

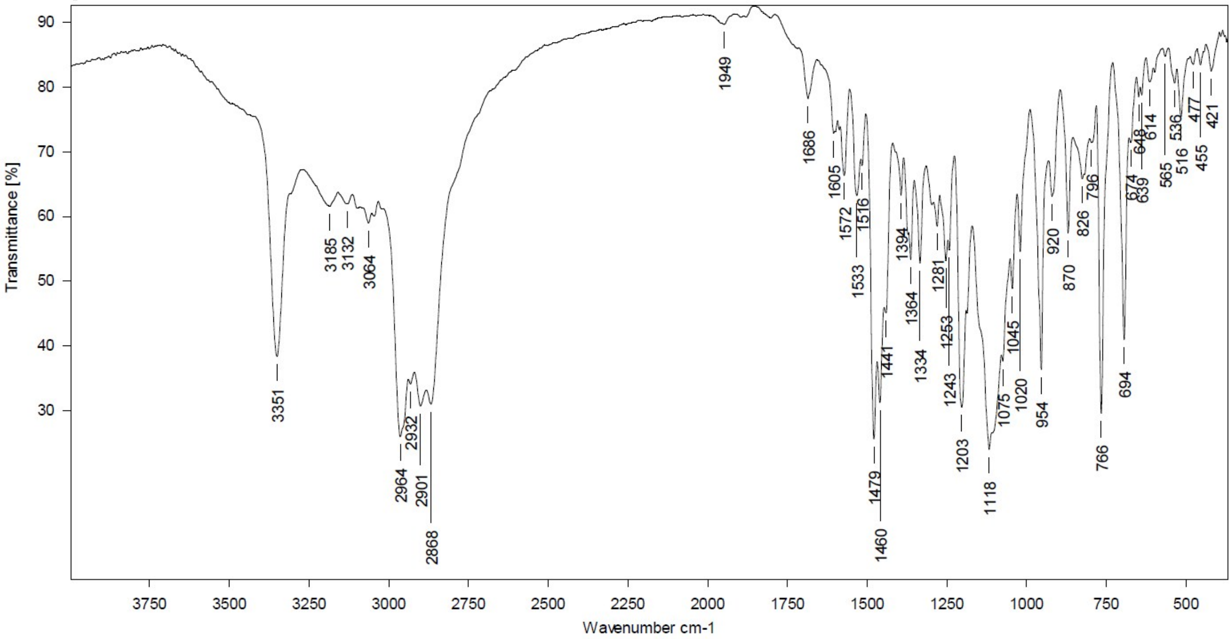

Fig. S40. FT IR spectrum of compound **4c** (KBr, 293K).

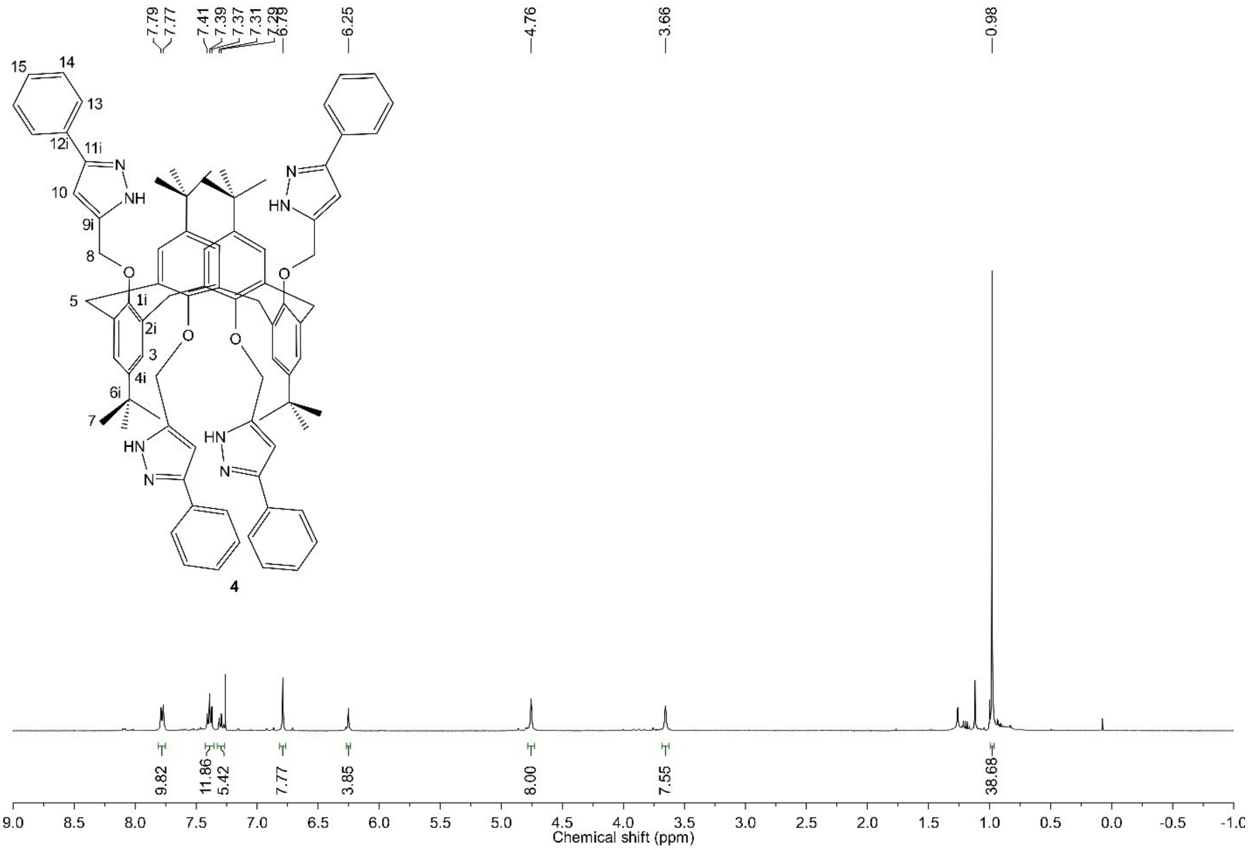

Fig. S41. ^{1}H NMR spectrum of compound **4c** ($CDCl_3$, 400 MHz, 298 K).

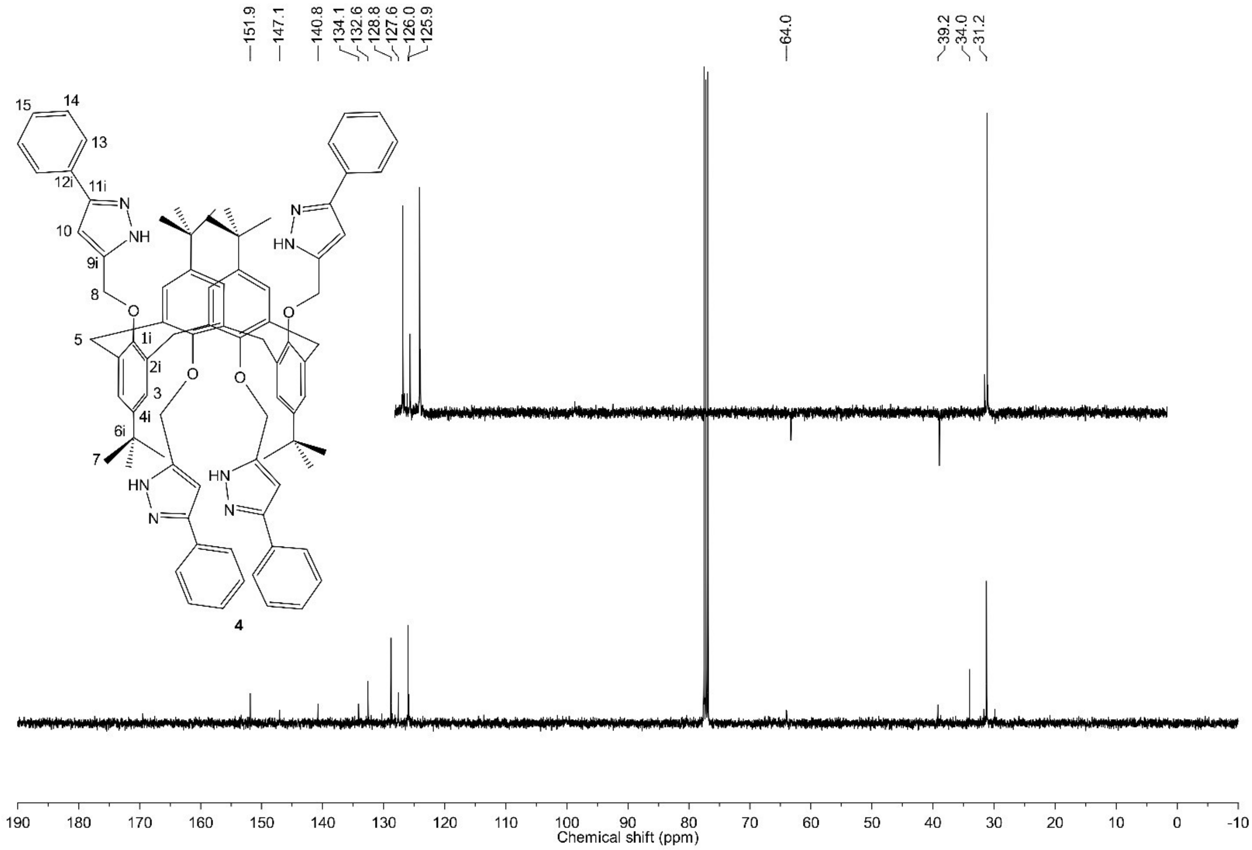

Fig. S42. ^{13}C NMR spectrum of compound **4c** ($CDCl_3$, 100 MHz, 298 K).

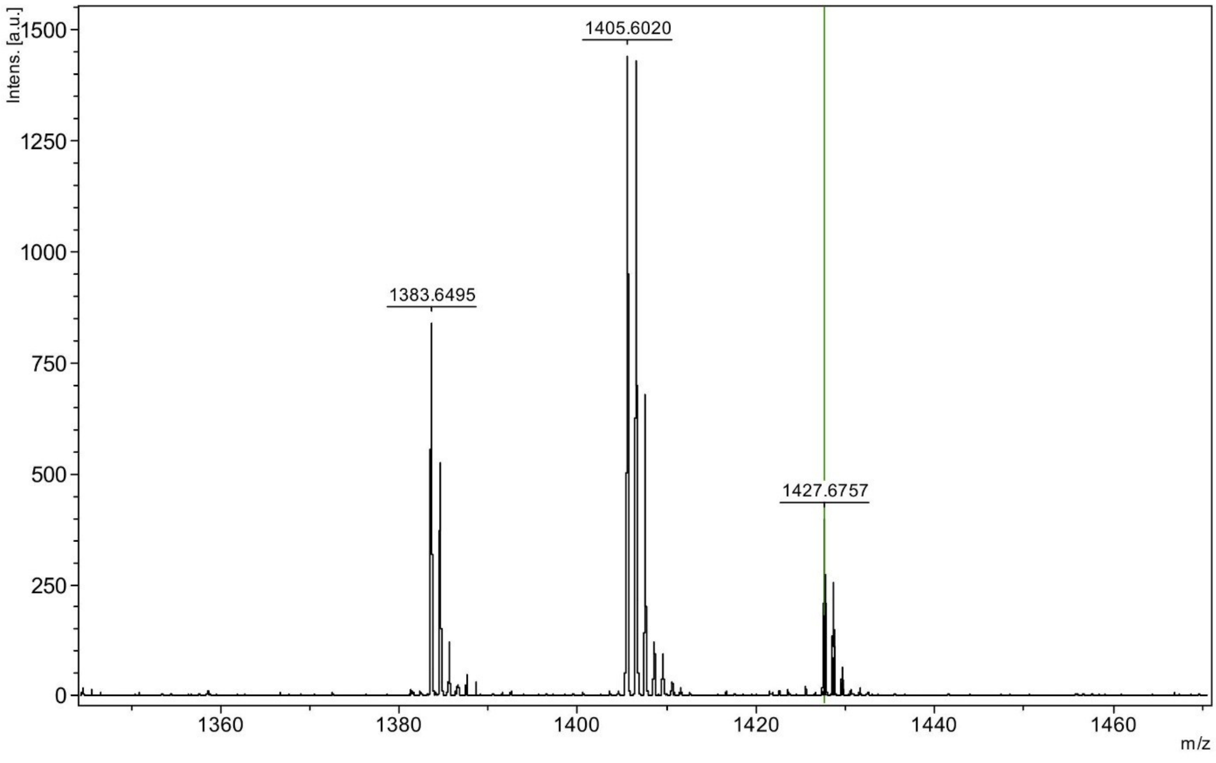

Fig. S43. HRMS spectrum of compound **4c**+CsCl (*p*-nitroaniline, PEG-1000 standard).