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Synthesis of novel highly functionalized triazole-linked calix[4]resorcinols *via* click reaction

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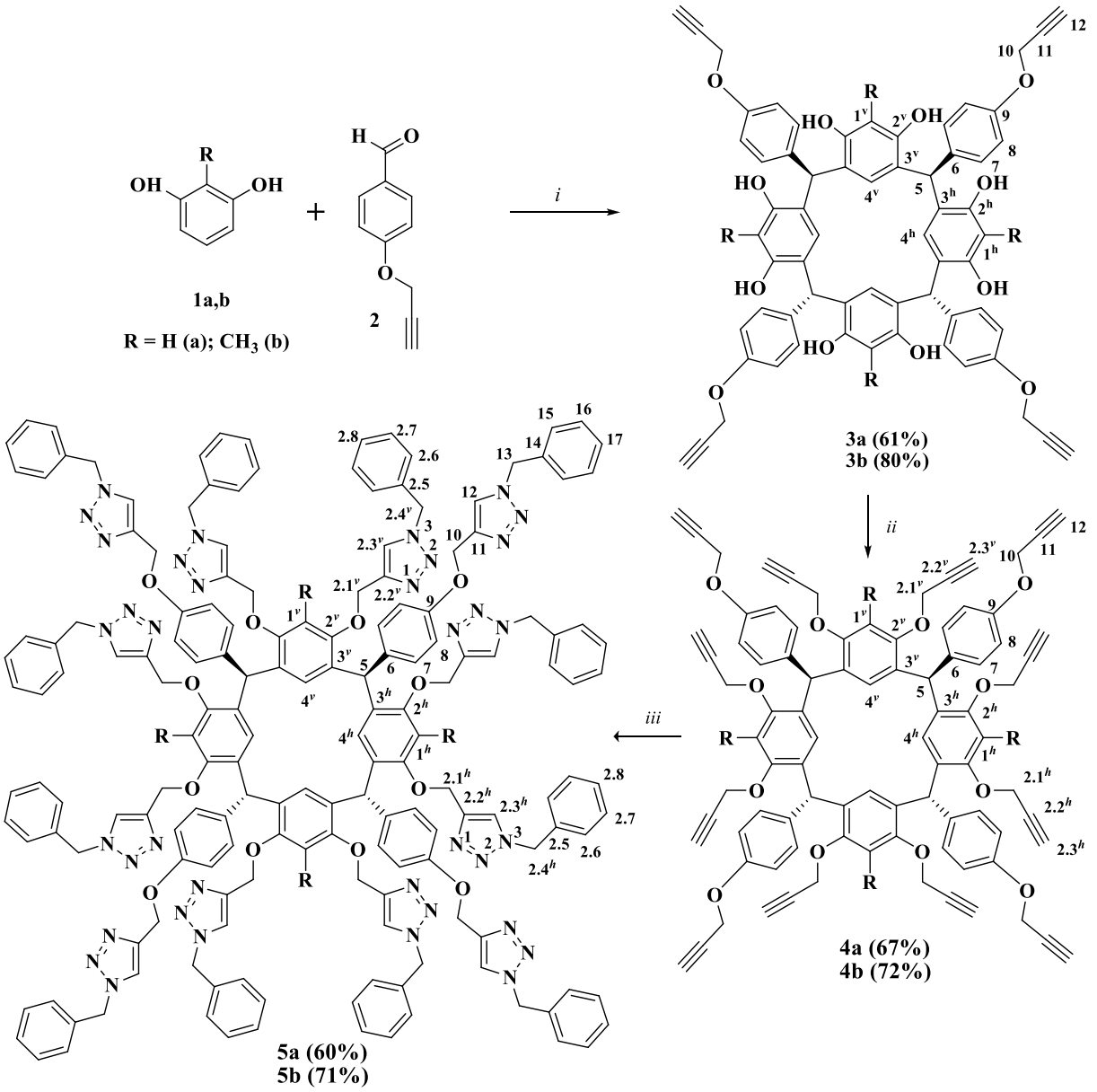
Experimental Section

General

NMR experiments were recorded on a Bruker AVANCE-600 spectrometer at 303 K equipped by 5 mm broadband probehead working at 600.1 MHz in ^{1}H and 150.9 MHz in ^{13}C experiments. Chemical shifts were measured relative to residual protons (^{1}H) or solvent signal (^{13}C). The pulse programs of the COSY, NOESY, HSQC and HMBC experiments were taken from Bruker software library. NMR-experiments were carried out in solutions (30 mmol·l^{-1}) at 303 K. The IR spectra of the compounds as emulsions in Nujol were recorded on a Vector 22 FTIR Spectrometer (Bruker) in the 4000–400 cm^{-1} range at a resolution of 1 cm^{-1}. MALDI mass spectra were run on an Ultra Flex III TOF/TOF mass spectrometer (Bruker Daltonic, Bremen, Germany) operated in the linear mode. Elemental microanalyses data were obtained on a CHN-3 analyzer and they were within ±0.4% of the theoretical values for C and H. The uncorrected melting points were measured on a Boetius hot-stage apparatus. All solvents were dried according to standard protocols.



Scheme S1

Compound 3a: A mixture of resorcinol **1a** (1.03 g, 9.38 mmol) and 4-propargyloxybenzaldehyde **2** (1.50 g, 9.38 mmol) in $CHCl_3$ (25 ml) and TFA (5 ml) was stirred at 60–65 ºC for 32 h under inert atmosphere. The precipitate formed was filtered, and washed sequentially with diethyl ether and acetone. The procedure was repeated until filtrates become coluorless. After drying *in vacuo* (40 ºC, 0.06 Torr), pure **3a** as *rctt*-isomer in the corresponding *chair* conformation was obtained (1.43 g, 61%) as a white powder. Mp > 260 ºC (decomp.). ^{1}H NMR (600.1 MHz, DMSO-d_6, 30 ºC): δ 3.48 (t, $^4J_{HH}$ 2.3 Hz, 4H, H^{12}), 4.62 (d, $^4J_{HH}$ 2.3 Hz, 8H, H^{10}), 5.47 (s, 4H, H5), 5.52 (s, 2H, H4^h), 6.12 (s, 2H, H1^v), 6.27 (s, 2H, H4^v), 6.30 (s, 2H, H1^h), 6.50 (br. m, 16H, H7, H8), 8.41 (s, 4H, OH^h), 8.47 (s, 4H, OH^v). ^{13}C NMR (150.9 MHz, DMSO-d_6, 30 ºC): δ 41.2 (s, C5), 55.3 (s, C10), 77.7 (s, C12), 79.6 (s, C11), 101.5 (s, C1^h), 101.6 (s,

C1^{v}), 116.5 (s, C8), 120.8 (s, C3^{h}), 121.1 (s, C3^{v}), 129.0 (s, C4^{v}), 129.6 (s, C7), 131.6 (s, C4^{h}), 137.1 (s, C6), 152.4 (s, C2^{h}), 152.5 (s, C2^{v}), 154.5 (s, C9). IR ν_{max} (KBr): 2121 (C≡C); 3280 (C≡CH); 3460 (OH) cm^{-1}. Anal. Calcd for $C_{64}H_{48}O_{12}$ (%): C, 76.19; H, 4.76. Found: C, 76.23; H, 4.72. MALDI-MS: *m/z* = 1009.0 $[M+H]^+$, 1031.0 $[M+Na]^+$ (calcd M = 1008.0).

Compound 3b: The *rctt*-isomer **3b** in the *chair* conformation was obtained as a white powder in a yield of 0.53 g (77%) similarly to **3a** from 2-methylresorcinol **1b** (0.47 g, 3.75 mmol) with aldehyde **2** (0.60 g, 3.75 mmol). Mp > 215 ºC (decomp.). ^{1}H NMR (600.1 MHz, DMSO-*d*$_6$, 30 ºC): δ 1.92 (s, 6H, CH$_3^{v}$), 2.09 (s, 6H, CH$_3^{h}$), 3.49 (t, $^4J_{HH}$ 2.3 Hz, 4H, H12), 4.63 (d, $^4J_{HH}$ 2.3 Hz, 8H, H10), 5.32 (s, 2H, H4^{h}), 5.57 (s, 4H, H5), 6.11 (s, 2H, H4^{v}), 6.52 (d, $^3J_{HH}$ 8.4 Hz, 8H, H8), 6.56 (d, $^3J_{HH}$ 8.4 Hz, 8H, H7), 7.16 (s, 4H, OH^{h}), 7.53 (s, 4H, OH^{v}). ^{13}C NMR (150.9 MHz, DMSO-*d*$_6$, 30 ºC): δ 9.5 (s, CH$_3^{v}$), 9.8 (s, CH$_3^{h}$), 42.7 (s, C5), 55.2 (s, C10), 77.7 (s, C12), 79.6 (s, C11), 113.3 (s, C8), 110.4 (s, C1^{h}), 111.0 (s, C1^{v}), 122.1 (s, C3^{h}), 122.8 (s, C3^{v}), 125.6 (s, C4^{v}), 128.9 (s, C4^{h}), 129.9 (s, C7), 136.2 (s, C6), 150.3 (s, C2^{h}), 150.4 (s, C2^{v}), 124.7 (s, C9). IR ν_{max} (KBr): 2120 (C≡C); 3279 (C≡CH); 3492 (OH) cm^{-1}. Anal. Calcd for $C_{68}H_{56}O_{12}$ (%): C, 76.69; H, 5.26. Found: C, 76.65; H, 5.29. MALDI-MS: *m/z* = 1065.0 $[M+H]^+$, 1087.0 $[M+Na]^+$ (calcd M = 1064.0).

Compound 4a: To the suspension of calix[4]resorcinol **3a** (0.5 g, 0.50 mmol) and freshly dried K_2CO_3 (1.1 g, 7.94 mmol) in 45 ml dry acetonitrile propargyl bromide (0.94 g, 7.94 mmol) was added. The mixture was stirred and heated to 90 °C for 24 h under an inert atmosphere. The course of the reaction was controlled by MALDI-MS. The reaction was stopped when only one peak of the fully substituted product was observed. The mixture was then filtered, the solvent was evaporated to dryness. The residue was re-precipitated from chloroform with diethyl ether. After drying *in vacuo* (40 ºC, 0.06 Torr), pure **4a** as *rctt*-isomer in the *chair* conformation was obtained (0.47 g, 72%) as a pale-yellow powder. Mp 204–206 ºC. ^{1}H NMR (600.1 MHz, DMSO-*d*$_6$, 30 ºC): δ 3.43 (s, 4H, H2.3^{h}), 3.46 (s, 4H, H2.3^{v}), 3.50 (s, 4H, H12), 4.46 and 4.64 (dd, $^4J_{HH}$ 2.3 Hz, $^2J_{HH}$ 15.8 Hz, 8H, H2.1^{h}), 4.57 and 4.66 (dd, $^4J_{HH}$ 2.3 Hz, $^2J_{HH}$ 15.8 Hz, 8H, H2.1^{v}), 4.66 (br.m., 8H, H10), 5.56 (s, 4H, H5), 5.64 (s, 2H, H4^{h}), 6.14 (s, 2H, H4^{v}), 6.47 (d, $^3J_{HH}$ 8.6 Hz, 8H, H7), 6.58 (d, $^3J_{HH}$ 8.6 Hz, 8H, H8), 6.73 (s, 2H, H1^{v}), 6.91 (s, 2H, H1^{h}). ^{13}C NMR (150.9 MHz, DMSO-*d*$_6$, 30 ºC): δ 41.6 (s, C5), 55.3 (s, C10), 56.4 (s, C2.1^{h}), 56.7 (s, C2.1^{v}), 77.8 (s, C2.2^{h}), 77.8 (s, C2.2^{v}), 77.9 (s, C11), 79.2 (s, C12), 79.4 (s, C2.3^{h}), 79.5 (s, C2.3^{v}), 99.7 (s, C1^{h}), 100.4 (s, C1^{v}), 113.7 (s, C8), 124.9 (s, C3^{h}), 126.0 (s, C3^{v}), 127.7 (s, C4^{v}), 129.5 (s, C7), 131.1 (s, C4^{h}), 134.5 (s, C6), 153.2 (s, C2^{v}), 153.6 (s, C2^{h}), 155.1 (s, C9). IR ν_{max} (KBr): 2120 (C≡C); 3288 (C≡CH) cm^{-1}. Anal. Calcd for

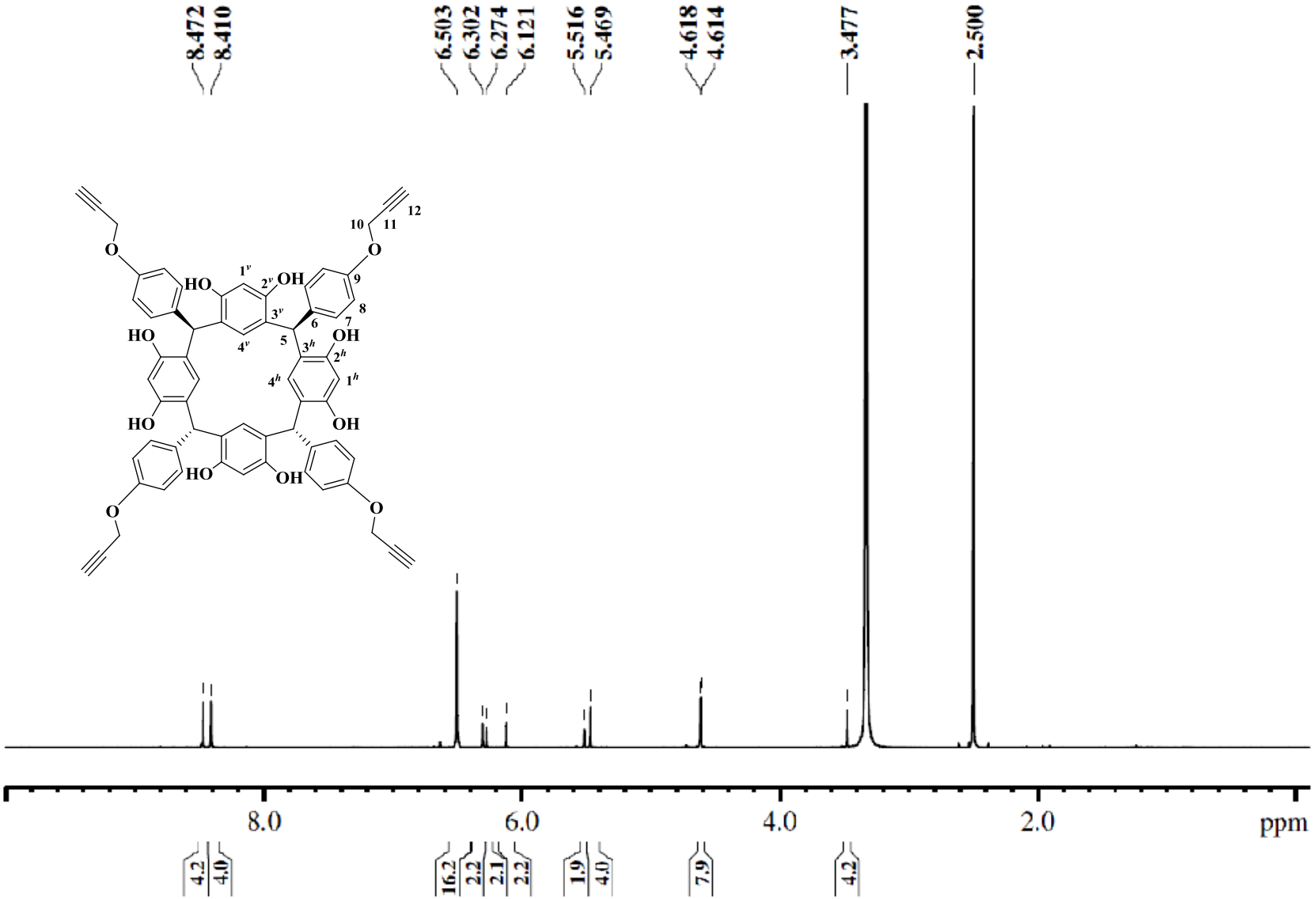
$C_{88}H_{64}O_{12}$ (%): C, 80.49; H, 4.88.Found: C, 80.43; H, 4.84. MALDI-MS: *m/z* = 1313.0 $[M+H]^+$, 1335.0 $[M+Na]^+$, 1351.0 $[M+K]^+$ (calcd M = 1312.0).

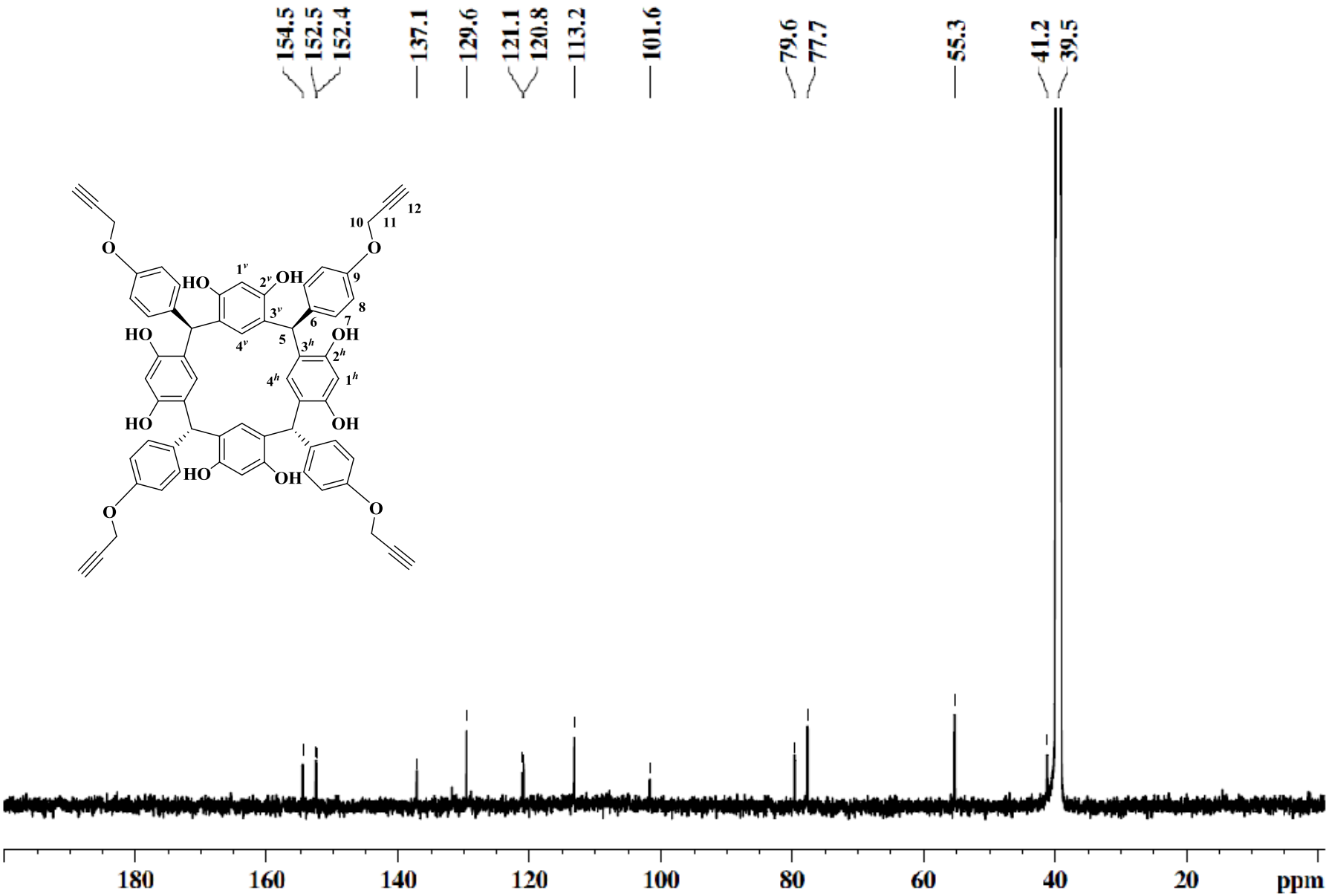
Compound 4b: The *rctt*-isomer **4b** in the *chair* conformation was obtained as a pale-yellow powder in a yield of 0.43 g (67%) similarly to **4a** from calix[4]resorcinol **3b** (0.50 g, 0.50 mmol), K_2CO_3 (1.04 g, 7.94 mmol) and propargyl bromide (0.89 g, 7.52 mmol). Mp 187–188 ºC. ^{1}H NMR (600.1 MHz, DMSO-d_6, 30 ºC): δ 2.17 (s, 6H, $CH_3{}^v$), 2.30 (s, 6H, $CH_3{}^h$), 3.51 (s, 4H, H2.3^h), 3.52 (s, 4H, H2.3^v), 3.55 (s, 4H, H12), 4.12 and 4.40 (dd, $^4J_{HH}$ 1.3 Hz, $^2J_{HH}$ 15.3 Hz, 8H, H2.1^h), 4.19 and 4.52 (dd, $^4J_{HH}$ 1.4 Hz, $^2J_{HH}$ 15.0 Hz, 8H, H2.1^v), 4.67 (br.m., 8H, H10), 5.80 (s, 4H, H5), 5.60 (s, 2H, H4^h), 6.03 (s, 2H, H4^v), 6.52 (d, $^3J_{HH}$ 8.5 Hz, 8H, H7), 6.60 (d, $^3J_{HH}$ 8.5 Hz, 8H, H8). ^{13}C NMR (150.9 MHz, DMSO-d_6, 30 ºC): δ 10.5 (s, $CH_3{}^v$), 10.9 (s, $CH_3{}^h$), 43.3 (s, C5), 55.3 (s, C10), 59.8 (s, C2.1^h), 60.3 (s, C2.1^v), 77.8 (s, C2.3^v), 77.9 (s, C11), 78.2 (s, C2.3^h), 79.3 (s, C12), 79.3 (s, C2.2^h), 79.5 (s, C2.2^v), 113.9 (s, C8), 124.2 (s, C1^h), 124.8 (s, C1^v), 126.2 (s, C4^v), 129.0 (s, C4^h), 129.5 (s, C7), 132.3 (s, C3^h), 133.3 (s, C3^v), 134.2 (s, C6), 153.2 (s, C2^v), 153.4 (s, C2^h), 155.5 (s, C9). IR ν_{max} (KBr): 2126 (C≡C); 3290 (C≡CH) cm^{-1}. Anal. Calcd for $C_{92}H_{72}O_{12}$ (%): C, 80.70; H, 5.26.Found: C, 80.68; H, 5.23. MALDI-MS: *m/z* = 1369.0 $[M+H]^+$, 1407.0 $[M+K]^+$ (calcd M = 1368.0).

Compound 5a: To a suspension of calix[4[resorcinol **4a** (0.20 g, 0.15 mmol), sodium ascorbate (0.07 g, 0.37 mmol) and $CuSO_4{\cdot}5H_2O$ (0.09 g, 0.37 mmol) in 50 ml THF/H_2O (1:1), benzyl azide (0.73 g, 3.66 mmol) was added. The mixture was stirred at 60–65 ºC for 24 h under inert atmosphere. Then the mixture was diluted with $CHCl_3$ (25 ml), washed with H_2O, and concentrated *in vacuo*. The residue was purified by precipitation from chloroform with diethyl ether. After drying *in vacuo* (40 ºC, 0.06 Torr), pure **5a** as *rctt*-isomer in the *chair* conformation was obtained (0.26 g, 60%) as white powder. Mp 105–106 ºC. ^{1}H NMR (600.1 MHz, DMSO-d_6, 30 ºC): δ 4.71 and 4.77 (d, $^2J_{HH}$ 12.2 Hz, 8H, H2.1^h), 4.86 (br.m., 8H, H10), 4.87 and 5.23 (d, $^2J_{HH}$ 12.4 Hz, 8H, H2.1^v), 5.37 (m, 8H, H13), 5.49 (s, 16H, H2.4), 5.51 (s, 4H, H5), 5.81 (s, 2H, H4^h), 6.29 (s, 2H, H4^v), 6.46 (d, ^{3}J 8.8 Hz, 8H, H7), 6.50 (d, ^{3}J 8.8 Hz, 8H, H8), 6.80 (s, 2H, H1^v), 7.07 (s, 2H, H1^h), 7.11 (s, 4H, H2.3^v), 7.28–7.31 (m, 60H, H15–H17, H2.6–H2.8), 7.68 (s, 4H, H2.3^h), 8.00 (s, 4H, H12). ^{13}C NMR (150.9 MHz, DMSO-d_6, 30 ºC): δ 42.1 (s, C5), 52.7 (s, C13), 52.8 (s, C10), 61.1 (s, C10), 62.8 (s, C2.1), 98.6 (s. C1^v), 99.4 (s, C1^h), 113.7 (s, C8), 123.0 (s, C2.3^h), 123. (s, C2.3^v), 123.8 (s, C12), 127.3 (s, C4^v), 127.9 (s, C2.6, C15), 128.1 (s, C2.7, C16), 128.7 (s, C2.8, C17), 128.7 (s, C4^h), 129.7 (s, C7), 133.9 (s, C6), 135.5 (s, C14), 135.8 (s, C2.5), 143.1 (s, C11), 143.7 (s, C2.2^h), 143.9 (s, C2.2^v), 153.8 (s, C2^v), 154.5 (s, C2^h), 155.8 (s, C9). Anal. Calcd for $C_{172}H_{148}O_{12}N_{36}$ (%): C, 70.98; H, 5.09; N, 17.33. Found: C, 70.75; H, 5.16; N, 17.28. MALDI-MS: *m/z* = 1912.0 $[M+H]^+$, 2934.0 $[M+Na]^+$, 2950.0 $[M+K]^+$, 29740 $[M+Cu^+]^+$ (calcd M = 2911.0).

Compound 5b: The *rctt*-isomer **5b** in the *chair* conformation was obtained as a white powder in a yield of 0.46 g (71%) similarly to **5a** from calix[4]resorcinol **4b** (0.20 g, 0.15 mmol), sodium ascorbate (0.07 g, 0.35 mmol), $CuSO_4 \cdot 5H_2O$ (0.9 g, 0.35 mmol) and benzyl azide (0.47 g, 3.51 mmol). Mp 104–106 ºC. ^{1}H NMR (600.1 MHz, DMSO-d_6, 30 ºC): δ 1.97 (s, 6H, CH_3^v), 2.37 (s, 6H, CH_3^h), 4.21 and 4.83 (d, $^2J_{HH}$ 11.1 Hz, 8H, H2.1^v), 4.38 and 4.76 (d, $^2J_{HH}$ 11.0 Hz, 8H, H2.1^h), 4.91 (s, 8H, H10), 5.44 (d, $^2J_{HH}$ 14.9 Hz, 8H, H13), 5.49 (s, 8H, H2.4), 5.59 (s, 8H, H2.4), 5.87 (s, 4H, H5), 5.91 (s, 2H, H4^h), 6.43 (s, 2H, H4^v), 6.52 (s, 16H, H7, H8), 7.11–7.29 (m, 60H, H15–H17, H2.6–H2.8), 7.96 (s, 4H, H2.3), 8.06 (s, 4H, H12), 8.13 (s, 4H, H2.3). ^{13}C NMR (150.9 MHz, DMSO-d_6, 30 ºC): δ 10.1 (s, CH_3^v), 10.8 (s, CH_3^h), 43.3 (s, C5), 52.7 (s, C13), 61.1 (s, C10), 65.2 (s, C2.1^h), 65.4 (C2.1^v), 113.8 (s, C8), 124.2 (s, C1^h, C2.3, C12), 126.5 (s, C4^v), 127.6 (s, C2.6, C15), 127.9 (s, C2.8, C17), 128.6 (s, C2.7, C16), 129.2 (s, C4^h), 129.7 (s, C7), 132.0 (s, C3^h), 133.8 (s, C3^v), 134.1 (s, C6), 135.5 (s, C14), 135.9 (s, C2.5), 143.1 (s, C11), 143.2 (s, C2.2), 153.2 (s, C2^v), 153.8 (s, C2^h), 156.0 (s, C9). ^{15}NMR (61 MHz, DMSO-d_6, 30 ºC): δ 245 (N^3), 348 (N^1), 357 (N^2). Anal. Calcd for $C_{176}H_{156}O_{12}N_{36}$ (%): C, 71.2; H, 5.3; N, 17.0. Found: C, 71.6; H, 5.1; N, 17.4. MALDI-MS: *m/z* = 2968.0 $[M+H]^+$, 2990.0 $[M+Na]^+$, 3006.0 $[M+K]^+$ (calcd M = 2967.0).

Calix[4]resorcinol 3a (*rctt*-isomer in *chair* conformation)

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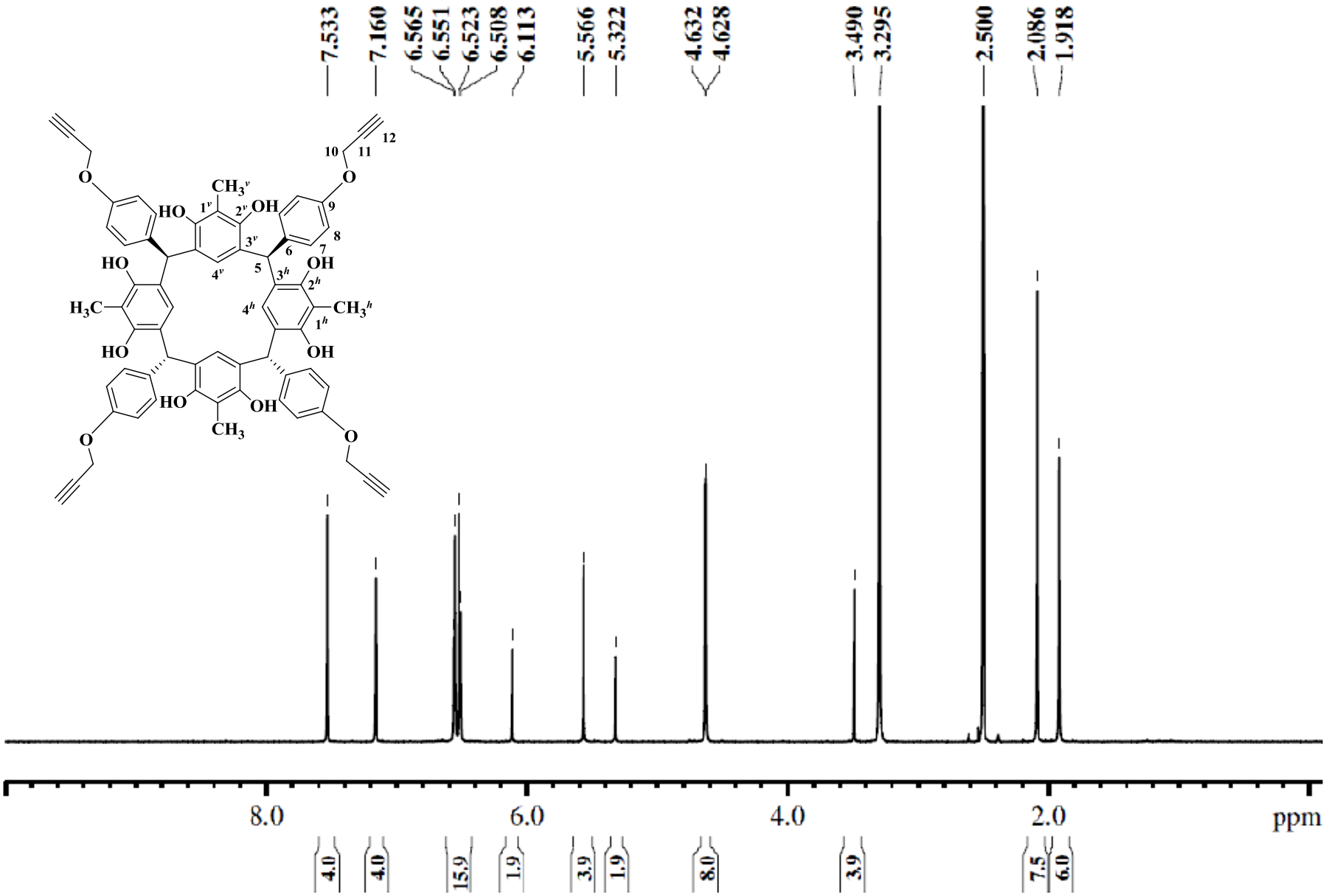

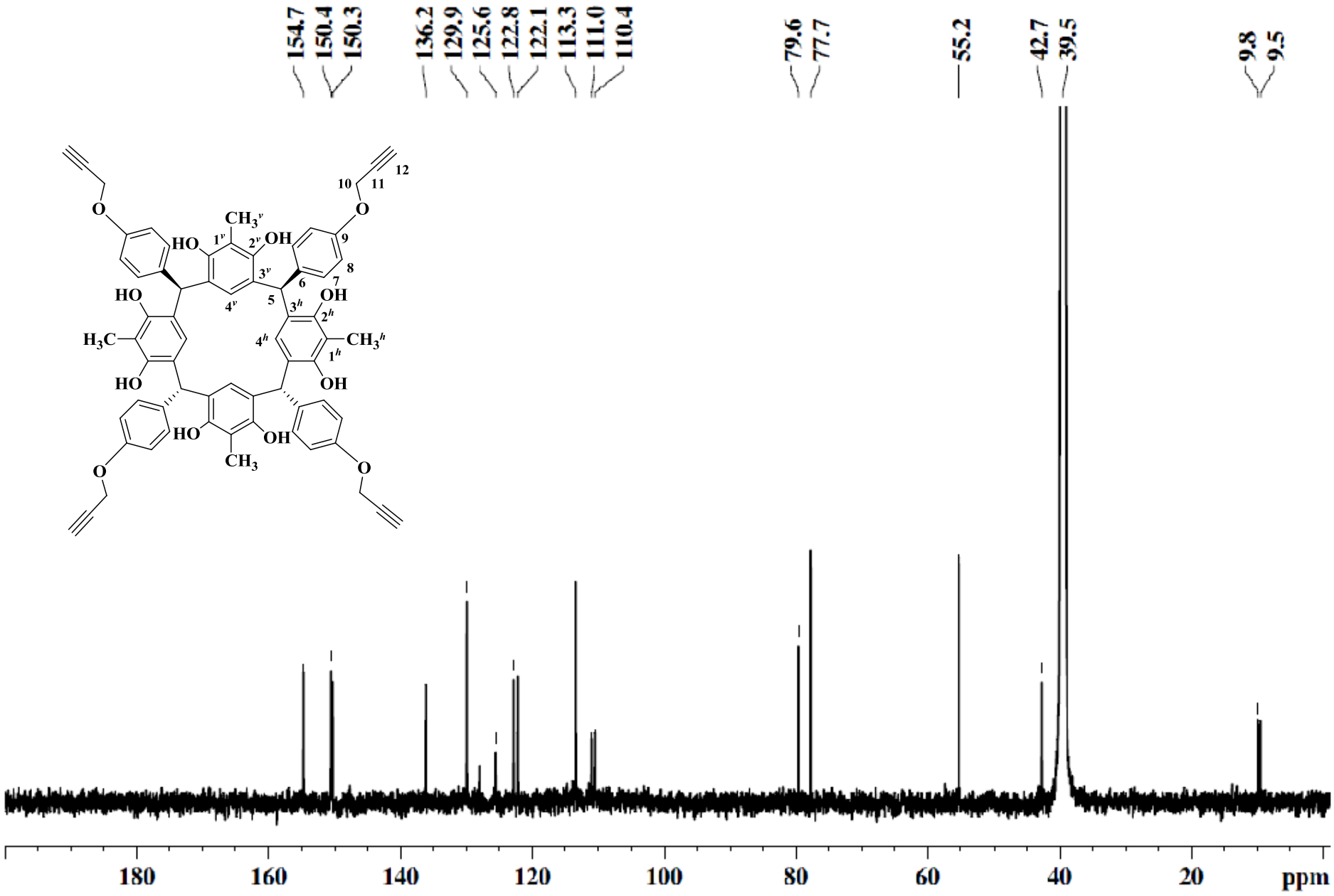
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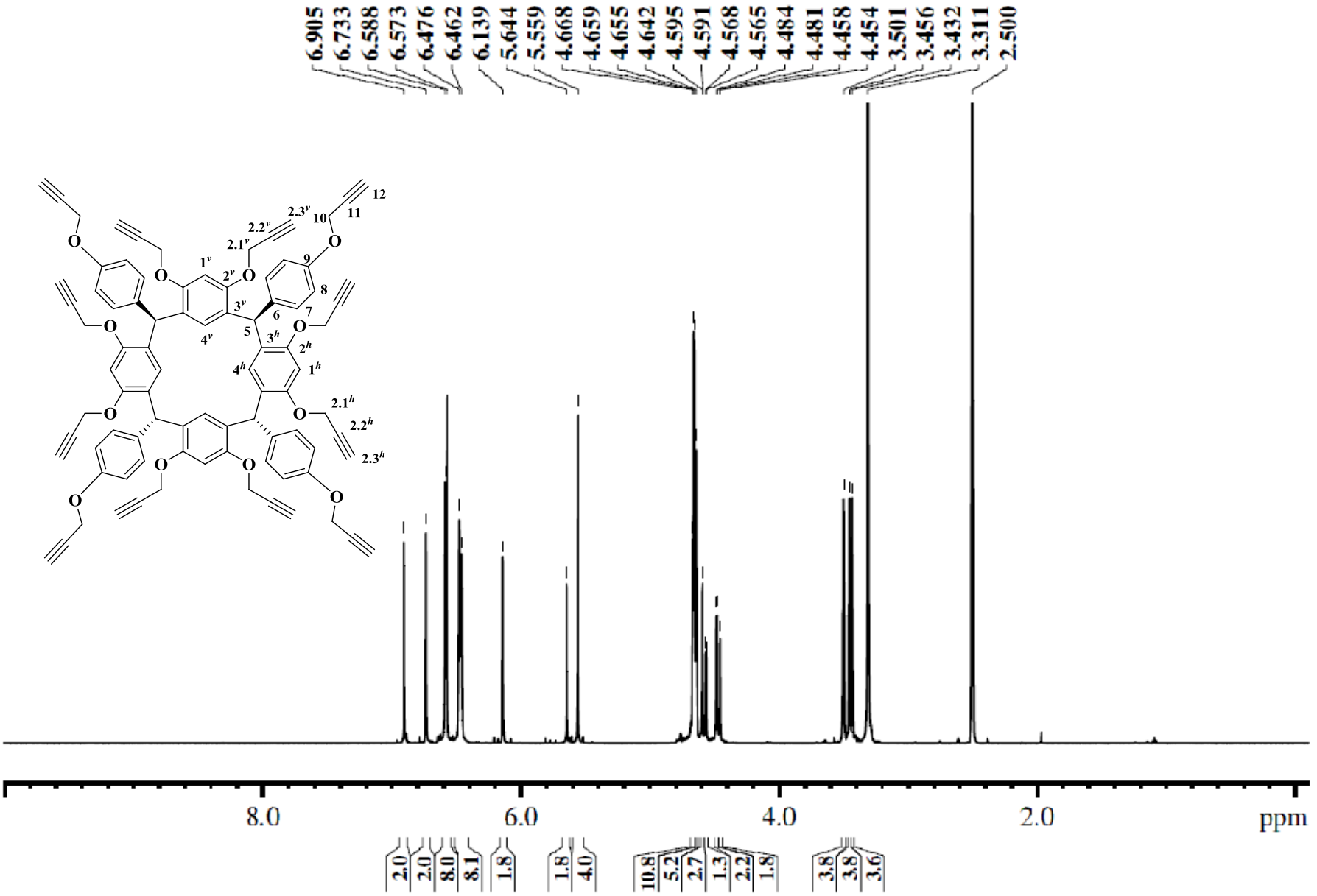

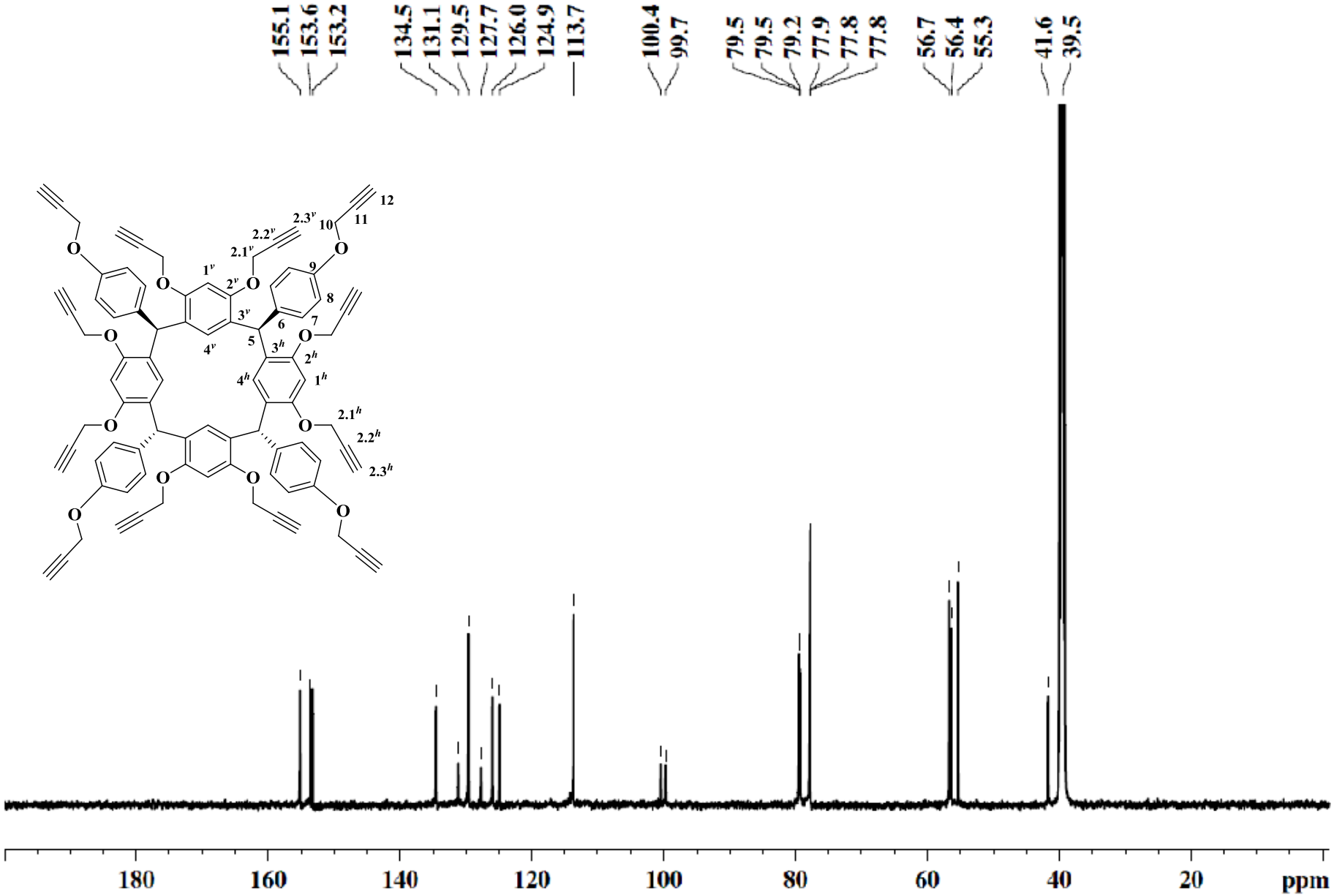
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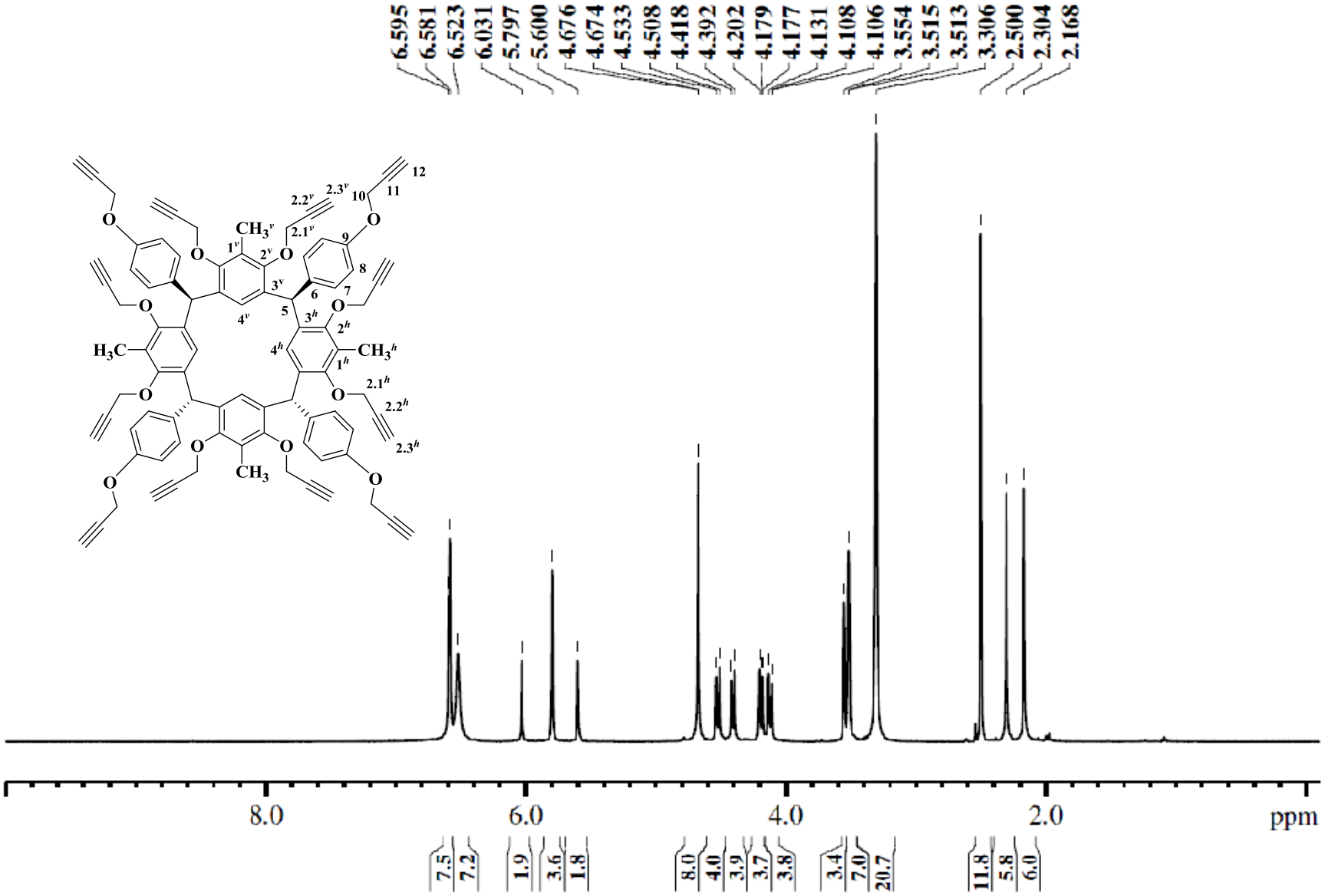
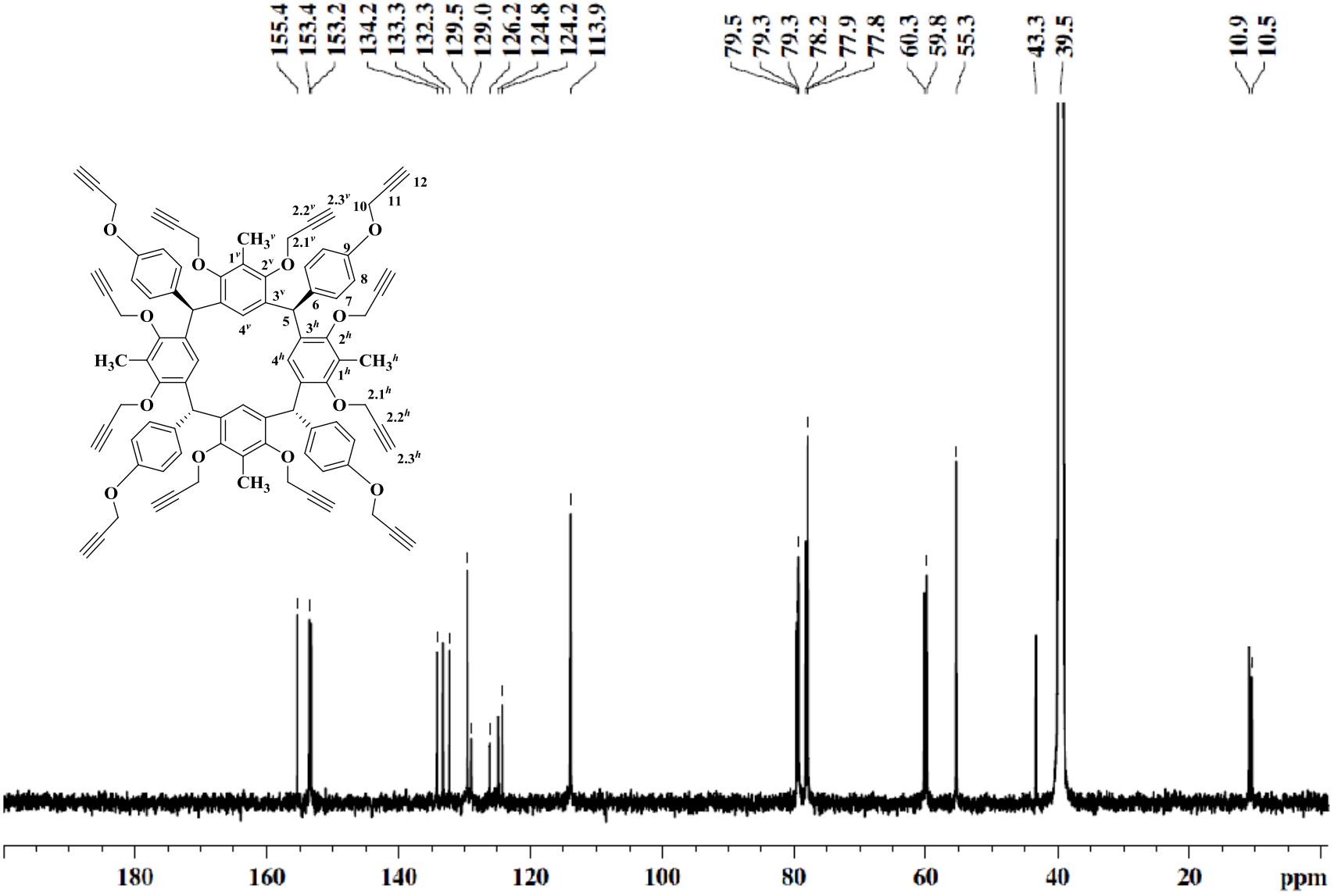
Calix[4]resorcinol 4b (*rctt*-isomer in *chair* conformation)

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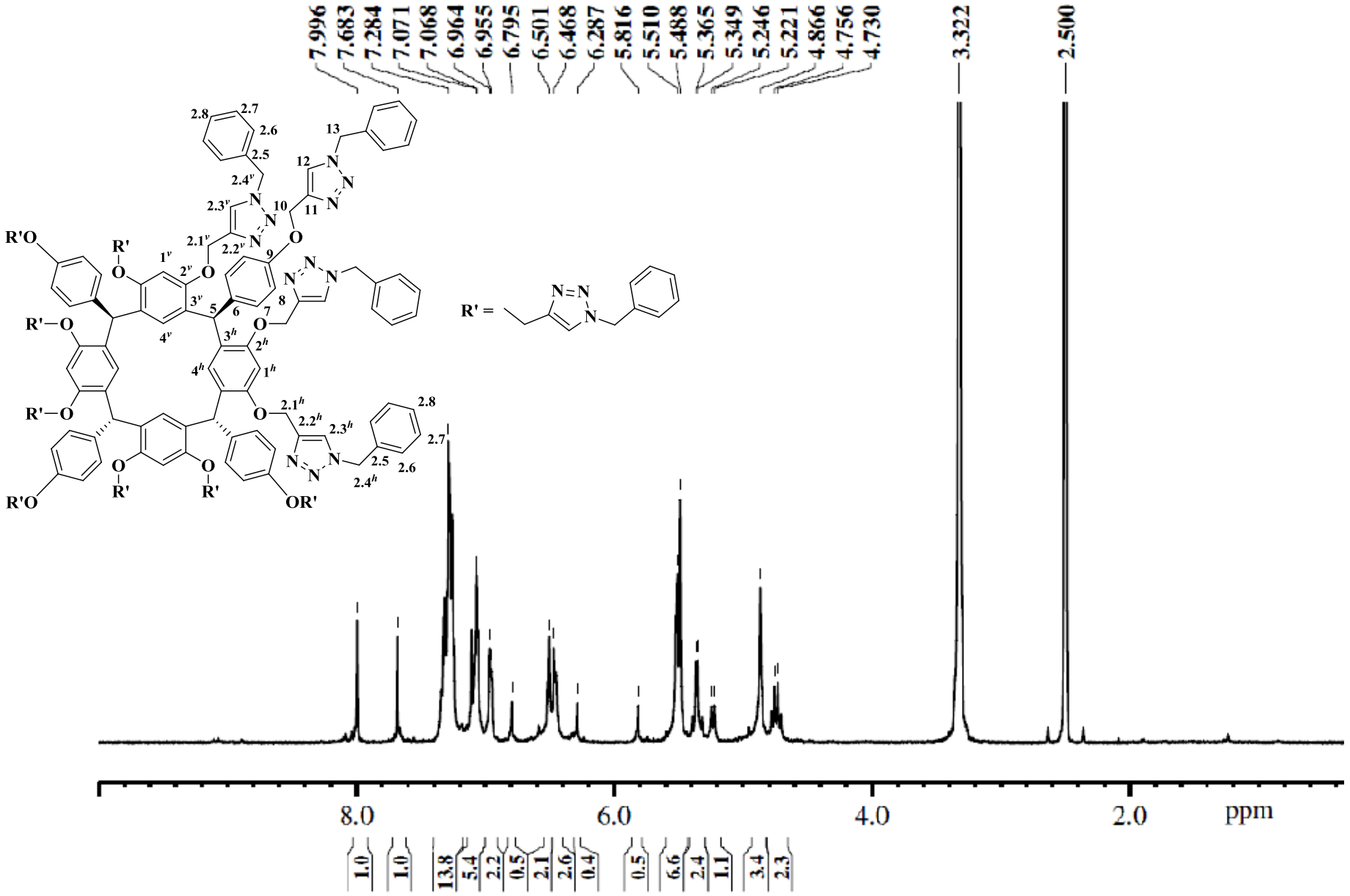
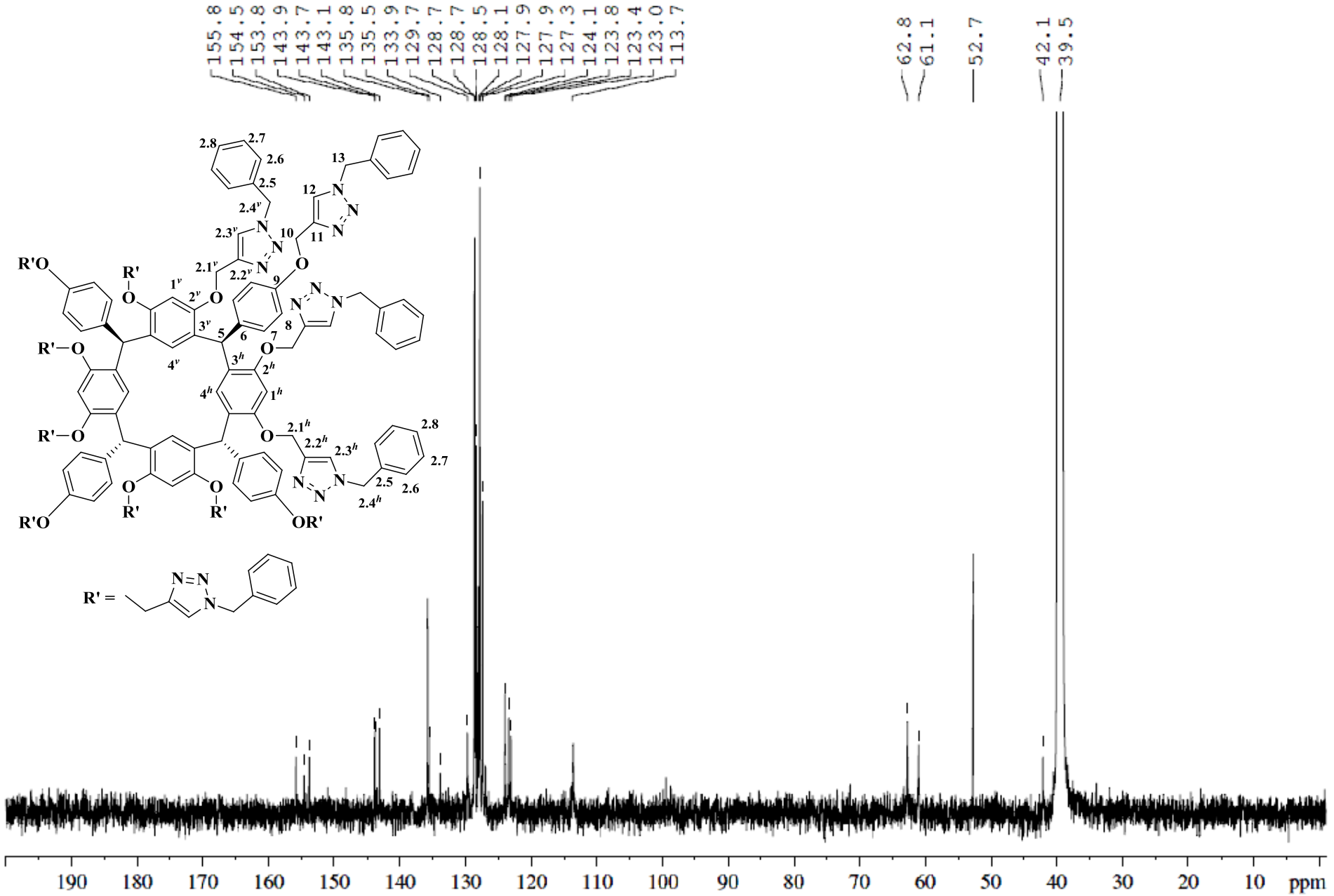
Calix[4]resorcinol 5a (*rctt*-isomer in *chair* conformation)

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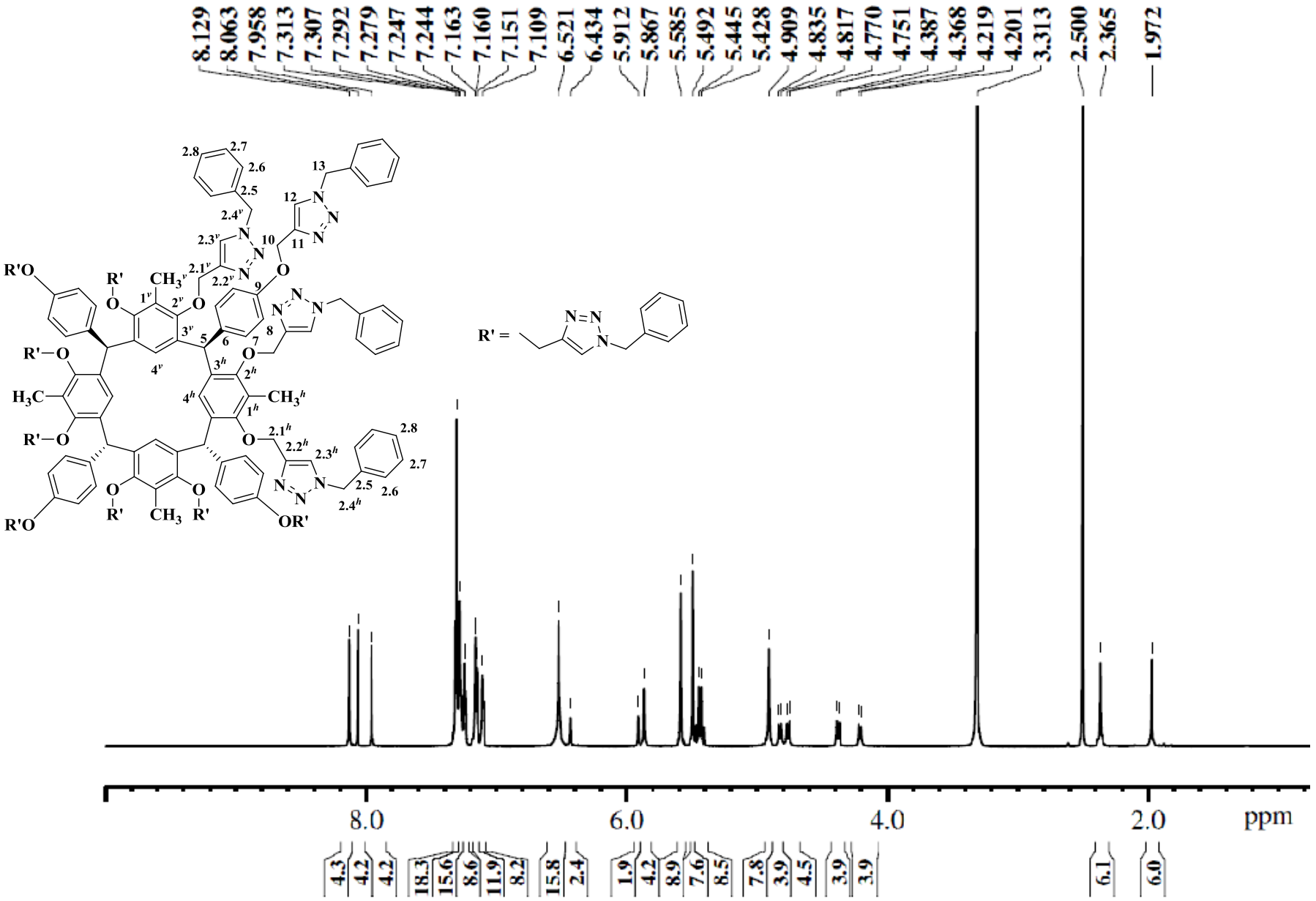
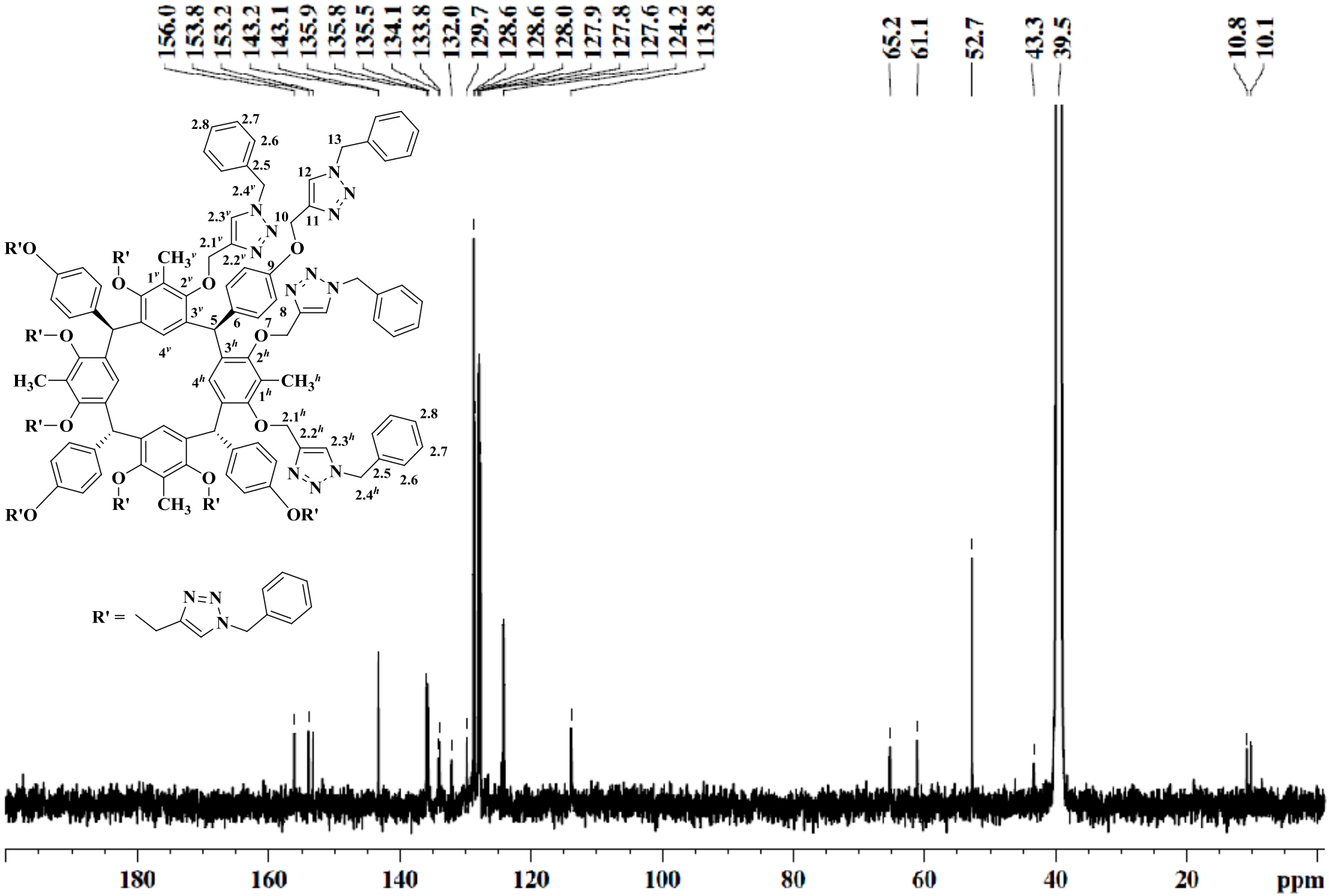
Calix[4]resorcinol 5b (*rctt*-isomer in *chair* conformation)

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