Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Novel Octacationic-Resorcin[4]arenes Featuring Quaternary Ammonium Groups as Multivalent Biocides

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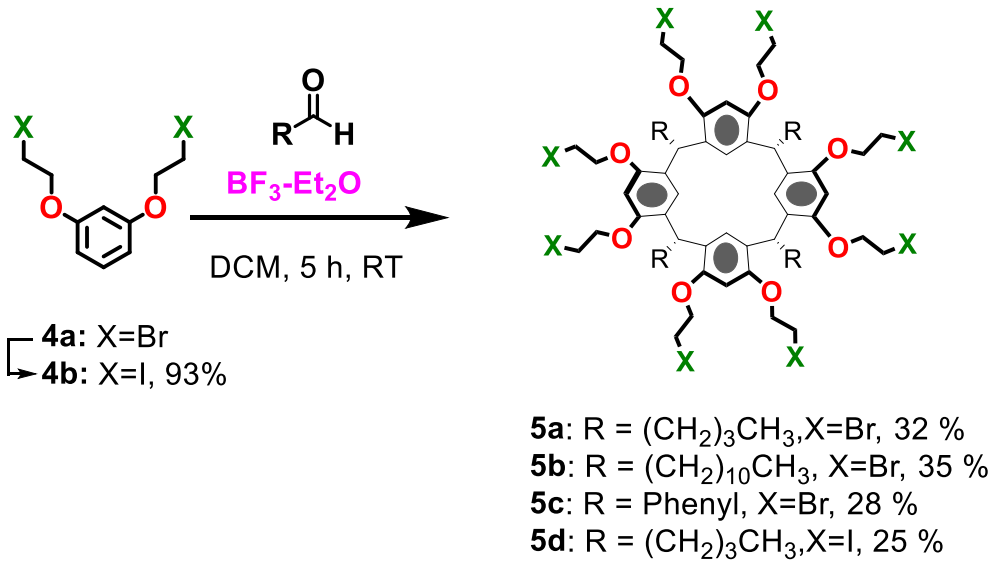
General Comments

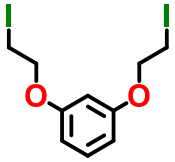
All chemical reagents grade was used without further purification and were used as purchased from Sigma Aldrich, TCI or Fluorochem. Reaction temperatures were measured externally. Reactions were monitored by TLC, using Macherey-Nagel silica gel plates (0.20 mm) and visualized by UV light 254 nm, or by spraying with H_2SO_4−$Ce(SO_4)_2$. The reactions requiring anhydrous conditions were carried out in an inert atmosphere (nitrogen), using anhydrified solvents and treating, before use, the glassware with vacuum/N_2 cycles. The yields shown below refer to chromatographically and spectroscopically pure products (^{1}H NMR). NMR spectra were recorded on a Bruker Avance-600 [600 (1H) and 150 MHz (13C)], Avance-400 [400 (1H) and 100 MHz (13C)], Avance-300 MHz [300 (1H) and 75 MHz (13C)] or Avance-250 MHz [250 (1H) and 62.5 MHz (13C)] spectrometers. The chemical shifts are given in ppm (*δ*); multiplicities in *s* singlet, *d* doublet, *t* triplet, *dd* double doublet, *m* multiplet and the coupling constants *J* in Hertz; for the spectra recorded in $CDCl_3$ the $CHCl_3$ signal was used as an internal standard (*δ* 7.26 ^{1}H, 77.16 ^{13}C), in CD_3OD the CH_3OH signal was used (*δ* 3.31 ^{1}H), in D_2O the H_2O signal was used (*δ* 4.79 ^{1}H), in CD_3CN the CD_3CN signal was used (*δ* 1.94 ^{1}H, 1.36 e 118.26 ^{13}C); for the spectra recorded in TCDE the tetrachloroethane signal was used as an internal standard (δ 5.98 ^{1}H, 73.78 ^{13}C). Standard pulse programs, provided by the manufacturer, were used for 2D COSY-45 and 2D HSQC, experiments. HR MALDI/ESI mass spectra were recorded on a Bruker Solarix FT-ICR mass spectrometer equipped with a 7T magnet. The samples recorded in MALDI were prepared by mixing 10 µL of analyte in dichloromethane (1 mg/mL) with 10 µL of solution of 2,5-dihydroxybenzoic acid (10 mg/mL in Methanol). The mass spectra were calibrated externally, and a linear calibration was applied.

Synthesis of derivatives 4b and 5a-d



Scheme S1. Synthesis of derivatives **5a-d**.

Derivative 4b:



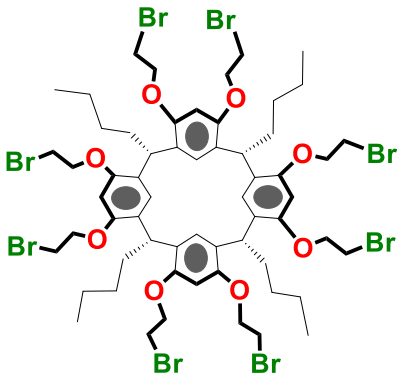
4b

Derivative **4a** (0.20 g) was dissolved in acetone (0.15 M); then NaI (4 equiv) was added. The resulting mixture was heated to 60 °C for 24 hours. The solvent was evaporated under reduced pressure. The product was dissolved in $CHCl_3$ and washed with H_2O. The organic phase was dried over sodium sulfate and concentrated to give a white solid with a yield of 93% (0.24 g, 0.57 mmol), mp 117-119 °C. **^{1}H NMR** (300 MHz, $CDCl_3$, 298 K): δ 7.19 (t, *J*=8.3, Ar*H*, 1H), 6.53 (dd, J_1=8.3, J_2=2.3, Ar*H*, 2H), 6.47 (t, *J*=2.3, Ar*H*, 1H), 4.23 (t, *J*=6.8, OCH_2, 4H), 3.41 (t, *J*=6.8, CH_2I, 4H); **^{13}C NMR** (62.5 MHz, $CDCl_3$, 298 K): 159.4, 130.3, 107.8, 102.5, 68.8, 1.1; **HRMS (ESI)** m/z $[M+H]^+$ calcd for $C_{10}H_{13}I_2O_2^+$: 418.8999. found. 418.8997.

General Procedure for synthesis of derivative 5a-d.

A solution of derivative **4a-b** (500 mg, 1.0 equiv), appropriate aldehyde (1.0 equiv) and boron trifluoride etherate (2 equiv) in dry CH_2Cl_2(0.15 M) was stirred at room temperature for 24 h. Subsequently the solvent was evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 (30 mL) and the mixture was washed with an aqueous saturated solution of $NaHCO_3$ (30 mL). Finally, the organic layer was washed with brine (2x20 mL), and the organic phases were dried over sodium sulfate and concentrated to give a solid light brown. The crude product was purified by chromatographic column on silica gel.

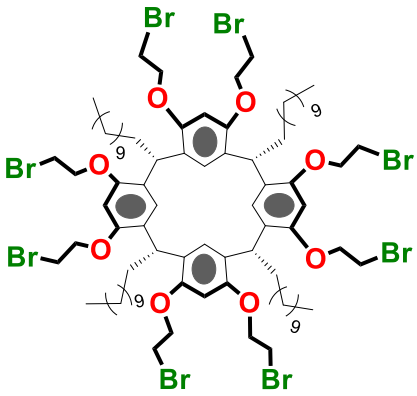
Derivative 5a:



5a

General procedure applied to derivative **4a** and pentanal gave derivative **5a.** The product was isolated by flash chromatography on silica gel using a gradient of *n*-hexane/CH_2Cl_2 (60/40→50/50) as a white powder with a yield of 32 % (193 mg, 0.12 mmol); mp 127-130 °C: **^{1}H NMR** (600 MHz, TCDE, 353 K): *δ* 6.52 (broad, Ar*H,* meta to OCH_2, 4H), 6.14 (s, Ar*H*, ortho to OCH_2, 4H), 4.41 (t, *J* =7.0 Hz, ArC*H*Ar, 4H), 4.00 and 3.90 (broad, OCH_2, 16H), 3.33 (broad, CH_2Br, 16H), 1.71 (broad, -CHCH_2CH_2, 8H), 1.20 (m, CH_2CH_2CH_3, 16H), 0.74 (br t, CH_2CH_3, 12H); **^{13}C NMR** (150 MHz, TCDE, 353 K): *δ* 154.2, 126.6, 99.6, 69.1, 35.6, 34.3, 30.2, 29.7, 22.8, 14.0; **HRMS (MALDI)** m/z $[M+Na]^+$ calcd for $C_{60}H_{80}Br_8O_8Na^+$: 1590.9145. found. 1590.9194.

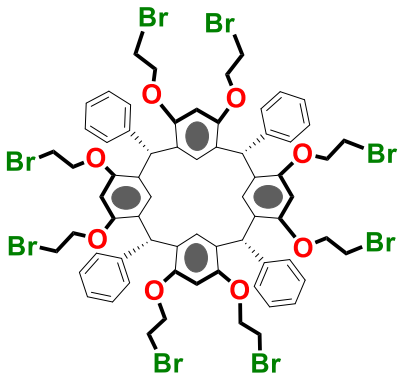
Derivative 5b:



5b

General procedure applied to derivative **4a** and dodecanal gave derivative **5b.** The product was isolated by flash chromatography on silica gel using a gradient of n-hexane/CH_2Cl_2 (60/40→50/50) as a white powder with a yield of 35 % (265 mg, 0.14 mmol); mp 84-87 °C: **^{1}H NMR** (600 MHz, TCDE, 353 K): δ 6.51 (broad, Ar*H*, meta to OCH_2, 4H), 6.15 (s, Ar*H*, ortho to OCH_2, 4H), 4.42 (t, *J*=7.11 Hz, ArC*H*Ar, 4H), 4.02 and 3.91 (broad, OC*H*$_2$, 16H), 3.35 (broad, C*H*$_2$Br, 16H), 1.71 (broad, CHC*H*$_2$$(CH_2)_9CH_3$, 8H), 1.13 (overlapped, $CH_2(CH_2)_9CH_3$, 72H), 0.76 (broad t, $CH_2(CH_2)_9CH_3$, 12H); **^{13}C NMR** (150 MHz, TCDE, 353 K): δ 154.2, 127.6, 126.6, 99.6, 69.1, 35.6, 34.7, 31.8, 29.9, 29.7, 29.6, 29.6, 29.5, 29.5, 29.2, 28.0; **HRMS (MALDI)** m/z $[M+K]^+$ calcd for $C_{88}H_{136}Br_8O_8K^+$: 1999.3278. found. 1999.3225.

Derivative 5c:

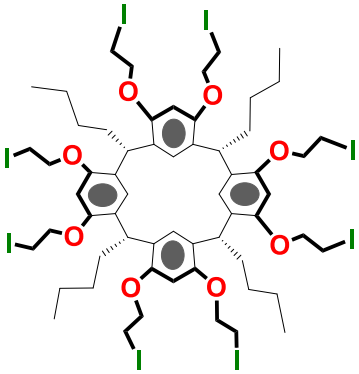


5c

General procedure applied to derivative **4a** and benzaldehyde gave derivative **5c.** The product was isolated by flash chromatography on silica gel using a gradient of n-hexane/CH_2Cl_2 (60/40→50/50) as a white powder with a yield of 28 % (178 mg, 0.11 mmol); mp 234-236 °C: **^{1}H NMR** (300 MHz, $CDCl_3$, 298K) (boat conformation): δ 6.96 (overlapped,

Ar*H*, 12H), 6.67 (overlapped, Ar*H*, 8H), 6.38 (overlapped, Ar*H*, 4H), 6.23 (s, Ar*H*, 2H), 5.85 (s, ArC*H*Ar, 4H), 5.70 (s, Ar*H*, 2H), 4.13 (broad, OCH_2, 16H), 3.35 (broad, CH_2Br, 16H); **^{13}C NMR** (75 MHz, $CDCl_3$, 298K): δ 154.2, 154.0, 141.7, 131.6, 128.6, 128.1, 127.3, 126.4, 125.3, 125.0, 98.8, 96.7, 68.6, 68.2, 42.6, 29.0, 28.6; **HRMS (MALDI)** m/z $[M+Na]^+$ calcd for $C_{68}H_{64}Br_8O_8Na^+$:1670.7919 found. 1670.7983.

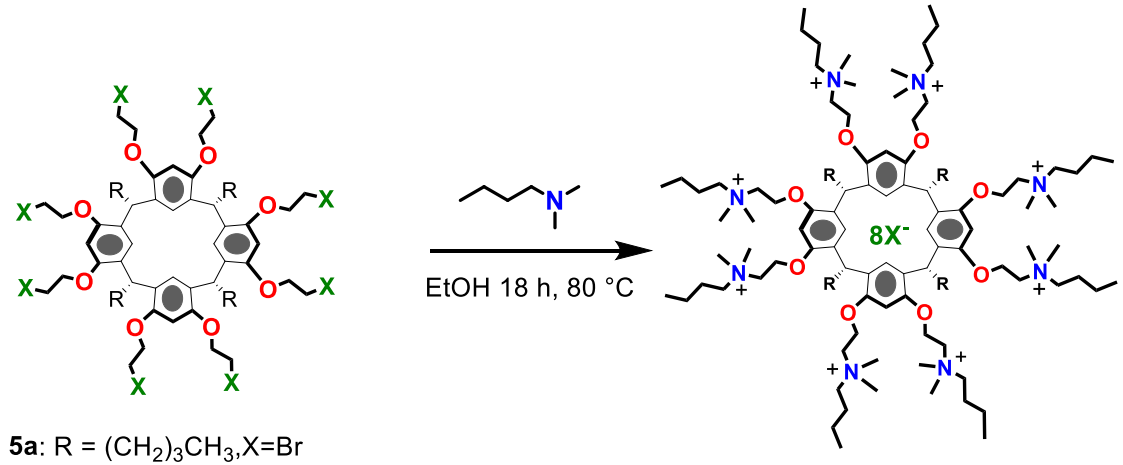
Derivative 5d:



5d

General procedure applied to derivative **4b** and pentanal gave derivative **5d.** The product was isolated by flash chromatography on silica gel using a gradient of n-hexane/CH_2Cl_2 (60/40→50/50) as a white powder with a yield of 25 % (145 mg, 74.8 µmol): **^{1}H NMR** (600 MHz, TCDE, 353 K): δ 6.53 (broad, Ar*H*, meta to OCH_2, 4H), 6.14 (s, Ar*H*, ortho to OCH_2, 4H), 4.44 (broad, ArC*H*Ar, 4H), 3.96 (broad, OCH_2, 16H), 3.16 (broad, CH_2Br, 16H), 1.72 (broad, CHC$H_2$$(CH_2)_2CH_3$, 8H), 1.20 (overlapped with H_2O, $CH_2(CH_2)_2CH_3$, 16H), 0.77 (broad t, $CH_2(CH_2)_2CH_3$, 12H); **^{13}C NMR** (150 MHz, TCDE, 353 K): δ 157.5, 131.0, 130.0, 103.2, 73.4, 39.0, 37.8, 33.6, 26.2, 17.2, 5.1; **HRMS (MALDI)** m/z $[M+Na]^+$ calcd for $C_{60}H_{80}I_8O_8Na^+$: 1966.8103. found. 1966.8351.

Synthesis of derivatives ResQAC^{R}(X^{-})$_8$



5a: R = $(CH_2)_3CH_3$,X=Br
5b: R = $(CH_2)_{10}CH_3$, X=Br
5c: R = Phenyl, X=Br
5d: R = $(CH_2)_3CH_3$,X=I

ResQAC^{R}(X^{-})$_8$

R = $(CH_2)_3CH_3$, X=Br, 85 %
R = $(CH_2)_{10}CH_3$, X=Br, 76 %
R = Phenyl, X=Br, 77 %
R = $(CH_2)_3CH_3$, X=I, 87 %

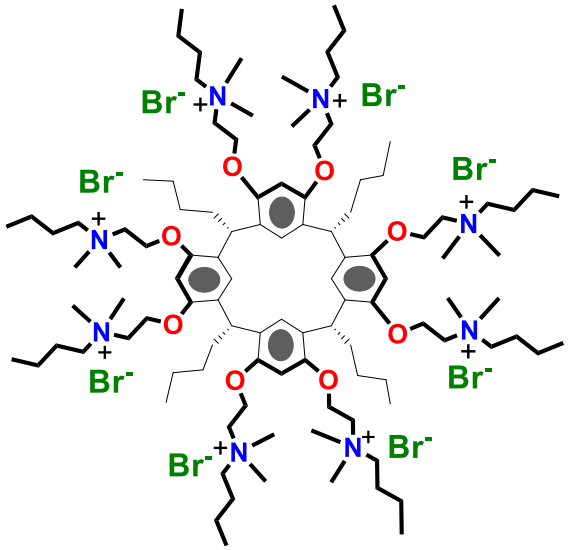
ResQAC^{R}(NO_3^-)$_8$ ← $AgNO_3$, CH_3CN, 30 min, 25°C

R = $(CH_2)_3CH_3$, 92 %
R = $(CH_2)_{10}CH_3$, 95 %
R = Phenyl, 90 %

Scheme S2. Synthesis of derivatives **ResQAC^{R}(X^{-})$_8$**

General procedure. Derivative **5a-d** (30 mg, 1 equiv) was dissolved in EtOH (20.0 mM); then N,N-dimethylbutylamine (300 equiv) was added. The resulting mixture was heated to 80 °C in a pressure tube for 18 hours. The solvent was evaporated under pressure and the product was washed with diethyl ether. The solid obtained was dried *in vacuo*.

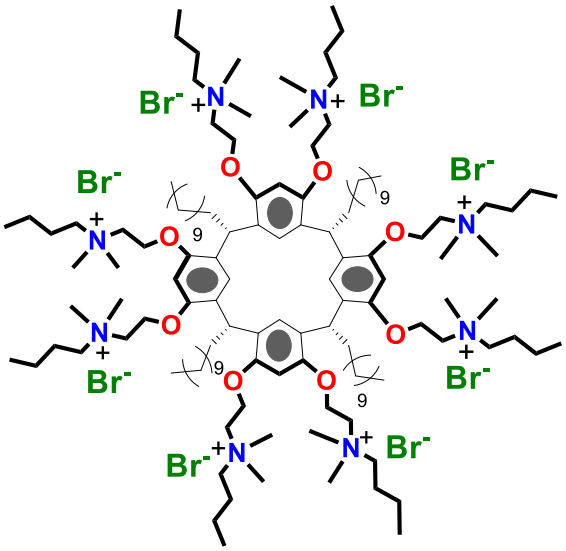
ResQAC^{butyl}(Br$^-$)$_8$:



ResQAC^{butyl} (Br$^-$)$_8$

The product **ResQAC^{butyl}(Br$^-$)$_8$** was obtained in 85 % of yield (39 mg, 16 µmol); mp 206-208 °C: **^{1}H NMR** (400 MHz, CD_3OD, 298 K): δ 7.26 (s, Ar*H*, 2H), 7.08 (s, Ar*H*, 2H), 6.72 (s, Ar*H*, 2H), 6.11 (s, Ar*H*, 2H), 4.91 (overlapped, OC*H*$_2$, 8H), 4.47 (overlapped, ArC*H*Ar and OC*H*$_2$, 8H), 4.26 (overlapped, OC*H*$_2$, 4H), 4.03 (overlapped, C*H*$_2$N, 8H), 3.75 (overlapped, C*H*$_2$N, 4H), 3.64 (overlapped, C*H*$_2$N and NC*H*$_2$(CH$_2$)$_2$CH$_3$, 20H), 3.39 (overlapped, N(C*H*$_3$)$_2$ 24H), 3.15 (overlapped, -N(C*H*$_3$)$_2$, 24H), 1.84 (overlapped, CHC*H*$_2$(CH$_2$)$_2$CH$_3$ and NCH$_2$C*H*$_2$CH$_2$CH$_3$, 24H), 1.48 (overlapped, NCH$_2$CH$_2$C*H*$_2$CH$_3$, 16H), 1.33 (overlapped, CHCH$_2$(C*H*$_2$)$_2$CH$_3$, 16H), 1.07 (overlapped, NCH$_2$(CH$_2$)$_2$C*H*$_3$, 24H), 0.87 (t, *J*=6.74 Hz, -CHCH$_2$(CH$_2$)$_2$C*H*$_3$, 12H); **^{13}C NMR** (125 MHz, CD_3OD, 298 K): δ 155.9, 154.7, 129.6, 128.5, 127.3, 124.5, 102.0, 99.8, 66.8, 66.7, 64.7, 64.0, 63.9, 52.4, 52.1, 52.0, 37.4, 35.8, 32.0, 25.8, 24.2, 20.8, 14.6, 14.2, 14.1; **HRMS (ESI)** m/z [M+5Br]$^{3+}$ calcd for $C_{108}H_{200}Br_5N_8O_8^{3+}$: 712.3795. found. 712.3797.

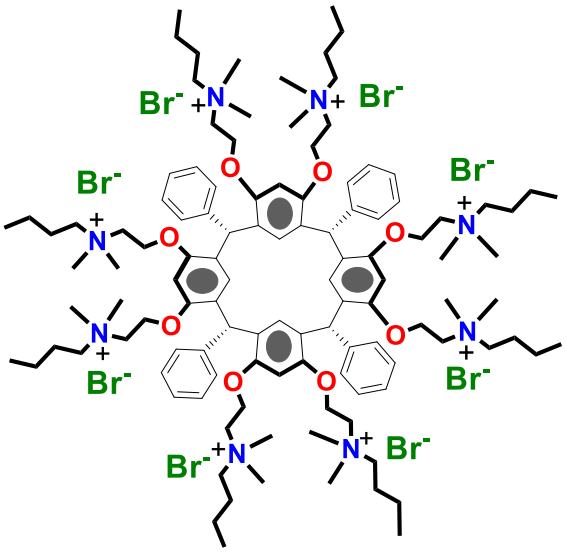
ResQAC^{undecyl} (Br$^-$)$_8$:



ResQAC^{undecyl} (Br$^-$)$_8$

The product **ResQAC^{undecyl} (Br$^-$)$_8$** was obtained in 76 % of yield (32 mg, 12 µmol); mp 127-131 °C: **^{1}H NMR** (600 MHz, CD_3OD, 298 K): *δ* 7.25 (s, Ar*H*, 2H), 7.08 (s, Ar*H*, 2H), 6.71 (s, Ar*H*, 2H), 6.11 (s, Ar*H*, 2H), 4.90 (overlapped, OC*H*$_2$, 8H), 4.47 (overlapped, ArC*H*Ar and OC*H*$_2$, 8H), 4.26 (overlapped, OC*H*$_2$, 4H), 4.04 (overlapped, C*H*$_2$N, 8H), 3.78 (overlapped, C*H*$_2$N, 4H), 3.59 (overlapped, C*H*$_2$N and NC*H*$_2$(CH$_2$)$_2$CH$_3$, 20H), 3.39 (overlapped, N(C*H*$_3$)$_2$ 24H), 3.14 (overlapped, N(C*H*$_3$)$_2$, 24H), 1.84 (overlapped, CHC*H*$_2$(CH$_2$)$_9$CH$_3$ and -NCH$_2$C*H*$_2$CH$_2$CH$_3$, 24H), 1.47 (overlapped, -NCH$_2$CH$_2$C*H*$_2$CH$_3$, 16H), 1.26 (overlapped, -CHCH$_2$(C*H*$_2$)$_9$CH$_3$, 72H), 1.05 (overlapped, -NCH$_2$(CH$_2$)$_2$C*H*$_3$, 24H), 0.88 (t, *J*=7.14 Hz, -CHCH$_2$(CH$_2$)$_9$C*H*$_3$, 12H); **^{13}C NMR** (150 MHz, CD_3OD, 298 K): *δ* 155.9, 154.7, 129.4, 128.4, 128.4, 127.4, 124.6, 102.0, 99.9, 66.8, 66.7, 64.8, 64.1, 63.9, 52.4, 52.2, 52.0, 37.3, 36.2, 33.1, 31.6, 31.2, 31.0, 30.9, 30.6, 29.8, 25.8, 25.8, 23.8, 20.8, 14.5, 14.2, 14.1; **HRMS (ESI)** m/z [M+5Br]$^{3+}$ calcd for $C_{136}H_{256}Br_5N_8O_8^{3+}$: 843.5266 found. 843.5234.

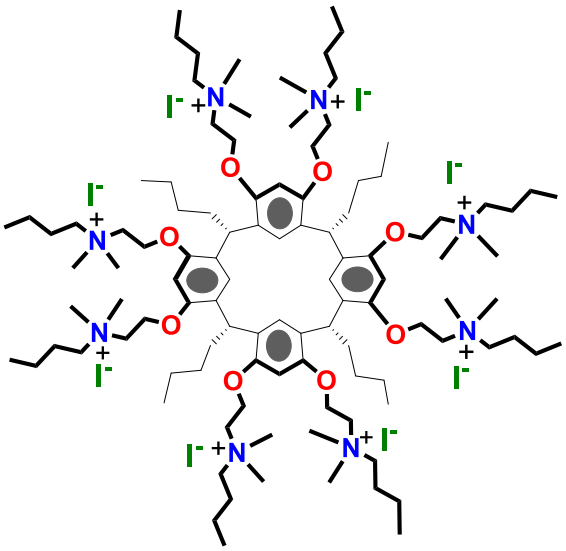
ResQAC^{phenyl} (Br$^-$)$_8$:



ResQAC^{phenyl} (Br$^-$)$_8$

Derivative **5c** (30 mg, 1 equiv) was dissolved in a mixture EtOH/DMF:1/1 (20.0 mM). The product **ResQAC^{phenyl} (Br$^-$)$_8$** was obtained in 77 % of yield (34 mg, 14 µmol); mp > 300°C dec.: **^{1}H NMR** (600 MHz, CD_3OD, 298 K): δ 7.12 (t, J=7.70 Hz, Ar*H*, 8H), 6.99 (overlapped, Ar*H*, 8H), 6.66 (broad, Ar*H*, 8H), 6.36 (s, Ar*H*, 2H), 5.79 (s, ArC*H*Ar, 4H), 5.66 (s, Ar*H*, 2H), 4.59 (overlapped, OCH_2, 16H), 3.75 (overlapped, CH_2N, 16H), 3.42 (overlapped, NCH_2CH$_2$CH$_2$CH$_3$, 16H), 3.11 (s, N(CH_3)$_2$, 12H), 2.97 (s, N(CH_3)$_2$, 12H), 2.91 (overlapped, -N(CH_3)$_2$, 24H), 1.75 (overlapped, NCH$_2$CH_2CH$_2$CH$_3$, 16H), 1.38 (overlapped, NCH$_2$CH$_2$CH_2CH$_3$, 16H), 0.99 (overlapped, NCH$_2$(CH$_2$)$_2$CH_3, 24H); **^{13}C NMR** (150 MHz, CD_3OD, 298 K): δ 154.4, 153.9, 141.8, 132.2, 129.3, 128.6, 128.2, 126.2, 125.4, 124.8, 99.1, 98.4, 65.4, 63.3, 63.2, 62.9, 51.5, 50.9, 50.6, 50.4, 43.1, 24.3, 24.2, 19.3, 12.7, 12.6; **HRMS (ESI)** m/z [M+4Br]$^{4+}$ calcd for $C_{116}H_{184}N_8O_8Br_4^{4+}$: 534.5235. found. 534.5271.

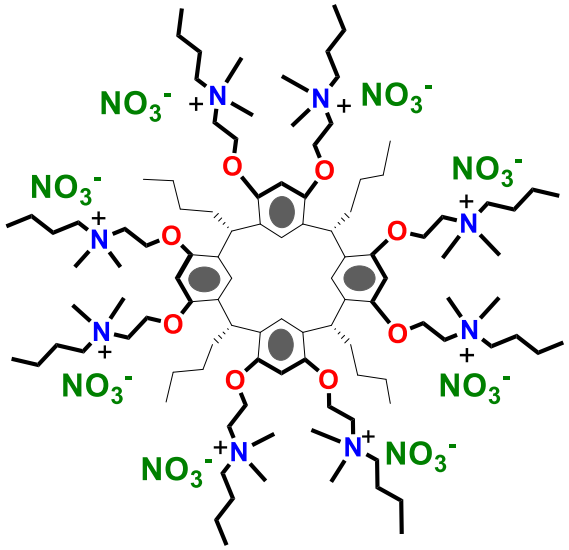
ResQAC^{butyl}(I^-)$_8$:



ResQAC^{butyl} (I^-)$_8$

The product **ResQAC^{butyl} (I^-)$_8$** was obtained in 87 % of yield (37 mg, 13.4 µmol); mp 209-211: **^{1}H-NMR** (400 MHz, CD_3OD, 298 K): δ 7.26 (s, -Ar*H*, 2H), 7.05 (s, -Ar*H*, 2H), 6.75 (s, -Ar*H*, 2H), 6.09 (s, -Ar*H*, 2H), 4.49 and 3.96 (overlapped, -C*H*$(CH_2)_3CH_3$ and -NC*H*$_2(CH_2)_2CH_3$ 20H), 3.96 and 3.13 (overlapped, -N(C*H*$_3)_2$ 48H), 3.60 (overlapped, -OC*H*$_2$, 32H), 1.85 and 1.73 (overlapped, -CHC*H*$_2(CH_2)_2CH_3$ and -$CHCH_2$(C*H*$_2)_2CH_3$ 24H), 1.46 and 1.32 (overlapped, -NCH_2(C*H*$_2)_2CH_3$ 32H), 1.04 and 0.88 (overlapped, -$NCH_2(CH_2)_2$C*H*$_3$ and -$CHCH_2(CH_2)_2$C*H*$_3$, 36H). **^{13}C NMR** (150 MHz, TCDE, 353 K): δ 152.8, 151.5, 126.5, 125.4, 124.3, 121.2, 99.7, 97.4, 63.7, 63.3, 61.9, 61.5, 61.2, 60.9, 50.1, 50.0, 49.8, 49.5, 34.3, 32.7, 29.0, 22.7, 21.2, 17.7, 11.9, 11.5, 11.4. **HRMS (ESI)** m/z $[M+6I]^{2+}$ calcd for $C_{108}H_{200}N_8O_8I_6^{2+}$: 1249.4873. found. 1249.4893.

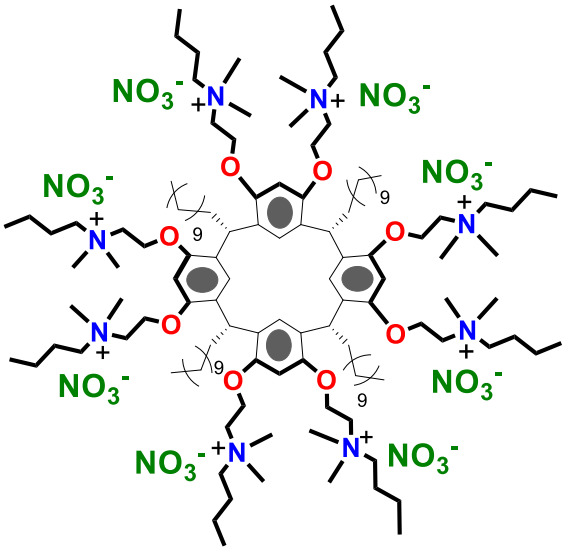
ResQAC^{butyl}(NO_3^-)$_8$:



ResQAC^{butyl} (NO_3^-)$_8$

Macrocycle **ResQAC^{butyl}(Br^-)$_8$** (10 mg, 1 equiv) was dissolved in CH_3CN (4.0 mM) and $AgNO_3$ (8 equiv) was added. The solution was stirred for 30 minutes at room temperature, and a white precipitate was obtained. The mixture was filtered, and the solvent was evaporated *in vacuo*. **ResQAC^{butyl}(NO_3^-)$_8$** was obtained with a yield of 92 % (8.6 mg, 3.87 µmol); mp 220-225 °C: **^{1}H NMR** (600 MHz, CD_3CN, 298 K): *δ* 7.25 (s, Ar*H*, 2H), 7.09 (s, Ar*H*, 2H), 6.74 (s, Ar*H*, 2H), 6.10 (s, Ar*H*, 2H), 4.47 and 4.05 (overlapped, -C*H*$(CH_2)_3CH_3$ and NC*H*$_2(CH_2)_2CH_3$, 20H), 3.67 (overlapped OC*H*$_2$, 32H), 3.41 and 3.16 (overlapped, N(C*H*$_3)_2$, 48H), 1.90 (overlapped, CHC*H*$_2$C*H*$_2$C*H*$_2CH_3$, 24H), 1.50 (overlapped, NCH$_2$(C*H*$_2)_2CH_3$, 32H), 1.07 (t, NCH$_2(CH_2)_2$C*H*$_3$, 24H), 0.90 (overlapped, -CHCH$_2(CH_2)_2$C*H*$_3$, 12H). **^{13}C NMR** (150 MHz, CD_3CN, 298 K): *δ* 154.8, 153.3, 128.1, 127.1, 125.9, 122.9, 100.5, 97.7, 65.4, 65.1, 63.5, 62.7, 62.2, 62.1, 51.3, 51.0, 50.7, 36.1, 34.2, 30.7, 24.3, 22.8, 19.3, 13.5, 13.0. **HRMS (ESI)** m/z $[M+5NO_3]^{3+}$ calcd for $C_{108}H_{200}N_{13}O_{23}^{3+}$: 682.8299. found. 682.8320.

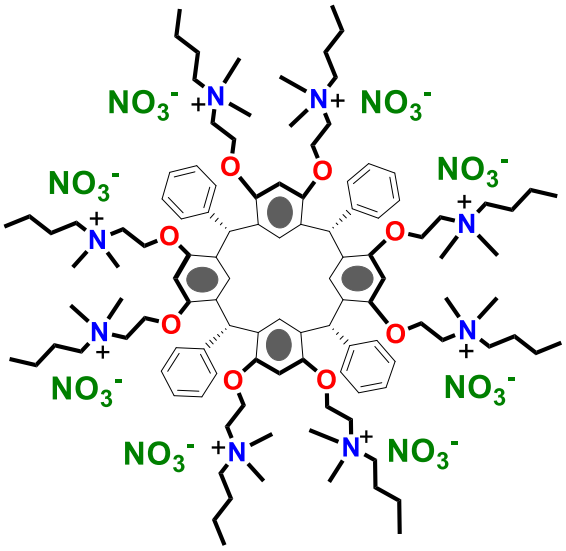
ResQAC^{undecyl}(NO_3^-)$_8$:



ResQAC^{undecyl} (NO_3^-)$_8$

Macrocycle **ResQAC^{undecyl} (Br^-)$_8$** (10 mg, 1 equiv) was dissolved in CH_3CN (4.0 mM) and $AgNO_3$ (8 equiv) was added. The solution was stirred for 30 minutes at room temperature, and a white precipitate was obtained. The mixture was filtered and the solvent was evaporated *in vacuo*. **ResQAC^{undecyl} (NO_3^-)$_8$** was obtained in 95 % of yield (9 mg, 3.4 µmol); mp 132-135 °C: **^{1}H NMR** (600 MHz, CD_3CN, 298 K): δ 7.24 (s, Ar*H*, 2H), 7.09 (s, Ar*H*, 2H), 6.75 (s, Ar*H*, 2H), 6.08 (s, Ar*H*, 2H), 4.91 (overlapped, OC*H*$_2$, 8H), 4.44 (overlapped, -C*H*$(CH_2)_3CH_3$ and OC*H*$_2$, 12H), 4.00 (overlapped, C*H*$_2$N, 8H), 3.69 (overlapped, C*H*$_2$N and NC*H*$_2(CH_2)_2CH_3$, 24H), 3.35 (overlapped, N(C*H*$_3)_2$, 24H), 3.16 (overlapped, N(C*H*$_3)_2$, 24H), 1.77 (overlapped, -CHC*H*$_2(CH_2)_9CH_3$ and $NCH_2CH_2CH_2CH_3$, 24H), 1.45 (overlapped, $NCH_2CH_2CH_2CH_3$, 16H), 1.27 (overlapped, $CHCH_2(CH_2)_9CH_3$, 72H), 1.02 (overlapped, -$NCH_2(CH_2)_2CH_3$, 24H), 0.89 (t, *J*=6.95 Hz, -$CHCH_2(CH_2)_9CH_3$, 12H); **^{13}C NMR** (150 MHz, CD_3CN, 298 K): δ 154.5, 153.2, 128.1, 127.0, 126.0, 123.0, 101.4, 99.1, 65.4, 65.1, 63.6, 63.3, 62.9, 62.6, 51.7, 51.7, 51.5, 51.2, 36.0, 34.7, 31.7, 30.1, 29.8, 29.7, 29.6, 29.5, 29.2, 28.6, 24.4, 22.4, 19.4, 13.4, 13.2, 13.0; **HRMS (ESI)** m/z $[M+5NO_3]^{3+}$ calcd for $C_{136}H_{256}N_{13}O_{23}^{3+}$: 813.6426. found. 813.6460.

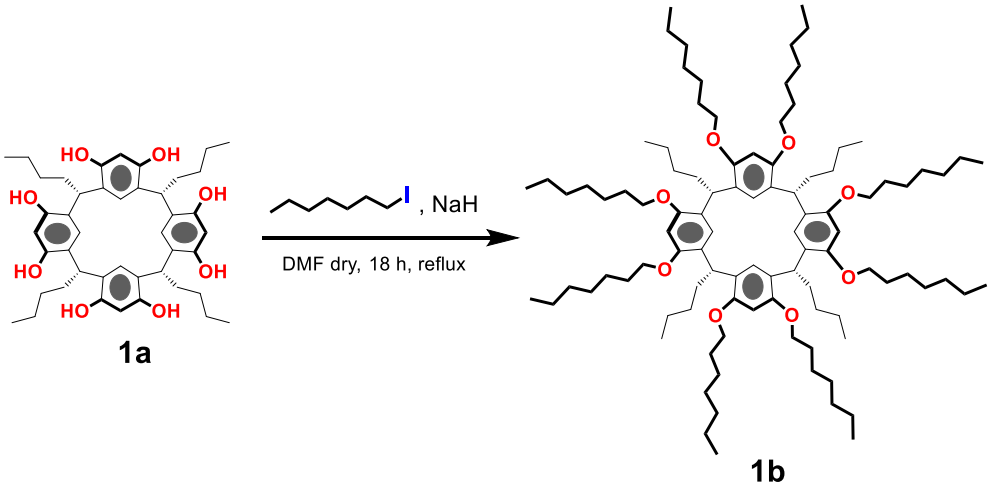
ResQAC^{phenyl} (NO_3^-)$_8$:



ResQAC^{phenyl} (NO_3^-)$_8$

Macrocycle **ResQAC^{phenyl} (Br^-)$_8$** (10 mg, 1 equiv) was dissolved in CH_3CN (4.0 mM) and $AgNO_3$ (8 equiv) was added. The solution was stirred for 30 minutes at room temperature, and a white precipitate was obtained. The mixture was filtered and the solvent was evaporated *in vacuo*. **ResQAC^{phenyl} (NO_3^-)$_8$** was obtained in 90 % of yield (8 mg, 3.7 µmol); mp > 300°C dec.: **^{1}H NMR** (400 MHz, CD_3OD, 298 K): δ 7.03 (overlapped, Ar*H*, 14H), 6.82 (s, - Ar*H*, 2H), 6.65 (overlapped, Ar*H*, 8H), 6.36 (s, Ar*H*, 2H), 5.78 (s, ArC*H*Ar, 4H), 5.66 (s, Ar*H*, 2H), 4.57 (overlapped, OCH_2, 16H), 3.74 (overlapped, CH_2N, 16H), 3.04 (s, N(CH_3)$_2$, 12H), 2.93 (s, N(CH_3)$_2$, 12H), 2.87 (overlapped, N(CH_3)$_2$, 24H), 1.69 (overlapped, -$NCH_2CH_2CH_2CH_3$, 16H), 1.35 (overlapped, -$NCH_2CH_2CH_2CH_3$, 16H), 1.00 (overlapped, -$NCH_2(CH_2)_2CH_3$, 24H); **^{13}C NMR** (125 MHz, CD_3OD, 298 K): δ 154.4, 154.1, 141.9, 132.3, 129.4, 128.6, 128.1, 126.3, 125.3, 124.8, 98.0, 97.5, 65.4, 65.3, 63.1, 62.9, 62.4, 62.2, 51.1, 50.4, 50.4, 50.0, 43.1, 24.2, 19.3, 12.6, 12.5; **HRMS (ESI)** m/z $[M+5NO_3]^{3+}$ calcd for $C_{116}H_{184}N_{13}O_{23}^{3+}$: 709.1204. found. 709.1219.

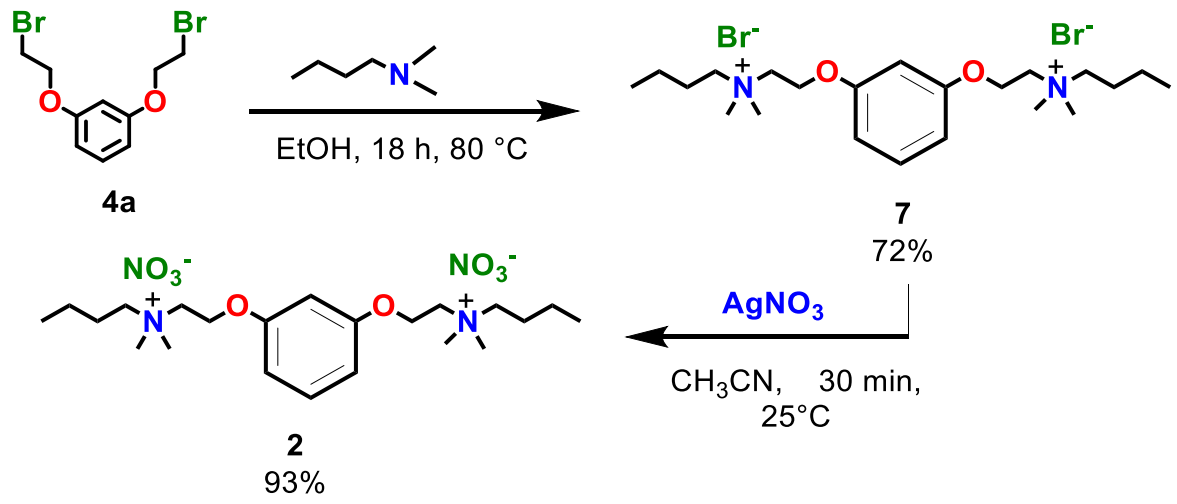
Synthesis of derivative 1b



Scheme S3. Synthesis of derivative **1b.**

Procedure. A mixture of derivative **1a**, synthesized and characterized according to the reported procedure[S1], (500 mg, 0.70 mmol) and 22 mL of DMF dry was heated to 60°C with stirring under a nitrogen atmosphere. After, NaH 60% (1.16 g, 29 mmol) were added and the system is left for 30 minutes. After the necessary time, 3.45 mL (21 mmol) of 1-iodoheptane were added and the mixture was stirrer for 18 h at reflux temperature. After this time, if the reaction has gone to completion, the work-up was carried out by eliminating the solvent in vacuo. Subsequently, 100 mL of 1N HCl were added. The product was extracted with ethyl acetate (3x100 mL). The combined organic phases were washed with 100 mL of H_2O. Once the organic phase has been recovered, it was dried by adding Na_2SO_4 and subsequently filtered and the solvent removed under vacuum. The crude product was purified by flash chromatography on silica gel using Petroleum ether/chloroform = 85/15 as eluent. Macrocycle **1b** was obtained in 31 % of yield (326 mg, 0.22 mmol); mp 46-48 °C: **^{1}H NMR** (600 MHz, TCDE, 353 K): *δ* 6.58 (s, Ar*H*, 4H), 6.23 (s, Ar*H*, 4H), 4.50 (t, *J*=6.82 Hz C*H*$(CH_2)_3CH_3$, 4H), 3.79 (broad, OC*H*$_2$, 8H), 3.58 (broad, OC*H*$_2$, 8H), 1.81 (broad, CHC*H*$_2(CH_2)_2CH_3$, 8H), 1.61 (broad, OCH_2CH_2, 16H), 1.32 (overlapped, $OCH_2CH_2(CH_2)_4CH_3$ and $CHCH_2(CH_2)_2CH_3$, 80H), 0.88 (overlapped, $OCH_2CH_2(CH_2)_4CH_3$ and $CHCH_2(CH_2)_2CH_3$, 36H); **^{13}C NMR** (150 MHz, TCDE, 353 K): *δ* 155.1, 126.1, 98.5, 68.6, 35.6, 34.3, 31.6, 30.4, 29.7, 29.4, 29.0, 25.9, 22.8, 22.4, 13.8. **HRMS (MALDI)** m/z $[M]^+$ calcd for $C_{100}H_{168}O_8Na^+$: 1521.2665. found. 1521.2657.

Synthesis of derivative 2



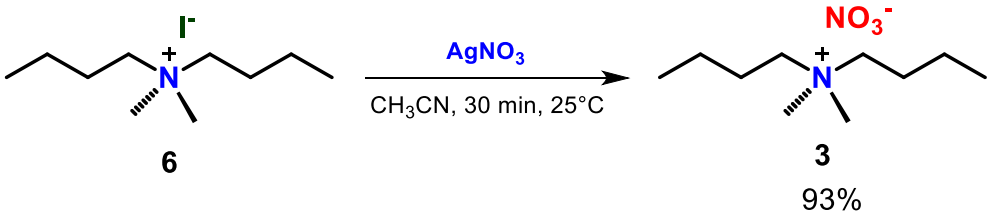
Scheme S4. Synthetic scheme for the synthesis of derivative **2**

Derivative 7. Derivative **4a** (200 mg, 1 equiv) was dissolved in EtOH (20.0 mM); then N,N-dimethylbutylamine (100 equiv) was added. The resulting mixture was heated to 80 °C in a pressure tube for 18 hours. The solvent was evaporated under pressure and the product was washed with diethyl ether. The solid obtained was dried *in vacuo*. The product **7** was obtained as white powder in 72 % of yield (234 mg, 0.44 mmol); **^{1}H NMR** (300 MHz, CD_3OD, 298 K): *δ* 7.25 (t, *J*=8.19 Hz, Ar*H*, 1H), 6.79 (t, *J*=2.14 Hz, Ar*H*, 1H), 6.68 (dd, J_1=8.19 Hz, J_2=2.14 Hz, Ar*H*, 2H), 4.55 (broad, -OC$H_2$$CH_2$N-, 4H), 3.90 (broad, -$OCH_2C$$H_2$N-, 4H), 3.53 (m, -NC$H_2$$CH_2CH_2CH_3$, 4H), 3.28 (s, -N(C$H_3$)$_2$, 12H), 1.83 (m, -$NCH_2C$$H_2$$CH_2CH_3$, 4H), 1.43 (m, -$NCH_2CH_2C$$H_2$$CH_3$, 4H), 1.04 (t, *J*=6.95, -$NCH_2CH_2CH_2C$$H_3$, 6H). **^{13}C NMR** (75 MHz, CD_3OD, 298 K): *δ* 159.0, 130.3, 117.1, 108.3, 101.7, 65.5, 62.9, 62.3, 51.5, 24.5, 19.5, 12.9. **HRMS (ESI)**: m/z $[M+Br]^+$ calcd for $C_{22}H_{42}N_2O_2Br^+$: 445.2424 found. 445.2416.

Derivative 2. Derivative **7** (10 mg, 1 equiv) was dissolved in CH_3CN (4.0 mM) and $AgNO_3$ (2 equiv) was added. The solution was stirred for 30 minutes at room temperature, and a white precipitate was obtained. The mixture was filtered and the solvent was evaporated *in vacuo*. The product **2** was obtained as white powder in 93 % of yield (8.7 mg, 17.7 µmol). **^{1}H NMR** (600 MHz, CD_3OD, 298 K): *δ* 7.26 (t, *J*=8.54 Hz, Ar*H*, 1H), 6.67 (overlapped, Ar*H*, 3H), 4.48 (broad, OC$H_2$$CH_2$N, 4H), 3.81 (broad, $OCH_2C$$H_2$N, 4H), 3.44 (m, NC$H_2$$CH_2CH_2CH_3$, 4H), 3.20 (s, N(C$H_3$)$_2$, 12H), 1.82 (m, $NCH_2C$$H_2$$CH_2CH_3$, 4H), 1.43 (m, -$NCH_2CH_2C$$H_2$$CH_3$, 4H), 1.02 (t, *J*=7.43, -$NCH_2CH_2CH_2C$$H_3$, 6H). **^{13}C NMR** (150 MHz,

CD_3OD, 298 K): δ 158.8, 130.2, 107.8, 101.4, 65.4, 62.7, 61.6, 50.8, 24.2, 19.3, 12.5. **HRMS (ESI)**: m/z $[M]^{2+}$ calcd for $C_{22}H_{42}N_2O_2^{2+}$: 183.1618 found. 183.1616.

Synthesis of derivative 3



6 **3** 93%

Scheme S5. Synthesis of derivative **3**.

Derivative **6** (200 mg, 0.701 mmol), synthesized and characterized according to the reported procedure[S2], was dissolved in CH_3CN (0.1 M), and $AgNO_3$ (2 equiv) was added. The solution was stirred for 30 minutes at room temperature, and a white precipitate was obtained. The mixture was filtered, and the solvent was evaporated *in vacuo* to afford **3** as white powder in 93 % of yield (143 mg, 0.652 mmol). **^{1}H NMR** (600 MHz, CD_3CN, 298 K): δ 3.24 (t, J = 8.50 Hz, $NCH_2CH_2CH_2CH_3$, 4H), 3.00 (s, $N(CH_3)_2$, 6H), 1.67 (m, $NCH_2CH_2CH_2CH_3$, 4H), 1.33 (m, $NCH_2CH_2CH_2CH_3$, 4H), 0.94 (t, J = 0.94, $NCH_2CH_2CH_2CH_3$, 6H). **^{13}C NMR** (75 MHz, CD_3CN, 298 K): δ 65.0, 51.5, 25.3, 20.6, 14.1; **HRMS (ESI)** m/z $[M]^+$ calcd for $C_{10}H_{24}N^+$: 158.1903. found. 158.1907.

Microbiological assays and bacterial strains

The minimum inhibitory concentration (MIC) and the minimum lethal dose (MLD) of each compound were estimated using protocols recommended by the National Committee for Clinical Laboratory Standards (NCCLS) and the cellular density of 5 x 10^5 colony forming units (CFU)/mL. Gram-positive and Gram-negative bacteria, *Stapylococcus aureus* and *Escherichia coli*, respectively, were inoculated into Luria Bertani medium (10 g/L Tryptone, 5g/L yeast extract, 5g/L NaCl), in the presence of increasing concentrations of each compound (0, 1, 2, 5, 10, 15, 30, 70, 140, 280 □g/mL), incubated 14-16 hours at 37 °C, with constant shaking (220 rpm), and the effects on their growth evaluated by turbidity, measuring the optical density at 600nm (OD600), and count plate agar method and colony forming units (CFU) determination. The MIC was defined as the minimum compound concentration that does not change the turbidity compared to time 0 (that is the MIC100). The MLD was estimated by plate count method and was defined as the minimum compound

concentration at which the number of CFU/mL resulted equal to 0. Briefly, after the MIC measuring, inoculants with concentration of each compound ≥ MIC were opportunely diluted and spread on LB agar(15g/L) medium, incubated 24 h a 37 °C and CFU counted. MIC and MLD values were obtained from at least three independent experiments each in triplicate and reported as mean ± standard deviation. *E. coli* (strain JM109) was purchased from Promega (http://www.promega.com, accessed 2024). *S. aureus* was derived from the collection deposited in the microbiology laboratory directed by prof. G. Vigliotta at the University of Salerno.

Cell viability assay

To evaluate cell viability, a MTT assay on a human keratinocyte cell line (HaCat) was performed. HaCat cells were obtained from Interlab Cell Line Collection, National Institute for Cancer Research (Genoa, Italy). Cells were cultured in Dulbecco's Modified Eagle medium (Life Technologies, Milan, Italy) supplemented with 10% (v/v) fetal bovine serum, 0.2 mM L-glutamine, 50 units/mL penicillin and 50 µg/mL streptomycin. Cells were maintained at 37 °C in a 5% CO_2 atmosphere and passaged twice a week. To perform the viability assay, cells were seeded in 96-well plates and treated, after 24 h, with different concentrations of each compound for 24 h. Then, MTT was added to the medium (0.25 mg/ml) and incubated at 37 °C for 1 h to allow the formation of formazan crystals. Finally, crystals were solubilized in DMSO and absorbances were registered at 595 nm and 655 nm in a microplate spectrophotometer (SpectraMax Mini, Molecular Devices). The background signals at 655 nm were subtracted from 595 nm signals and cell viability was expressed as per cent of viability with the respect to vehicle (DMSO)-treated cells.

NMR spectra of derivative 4b

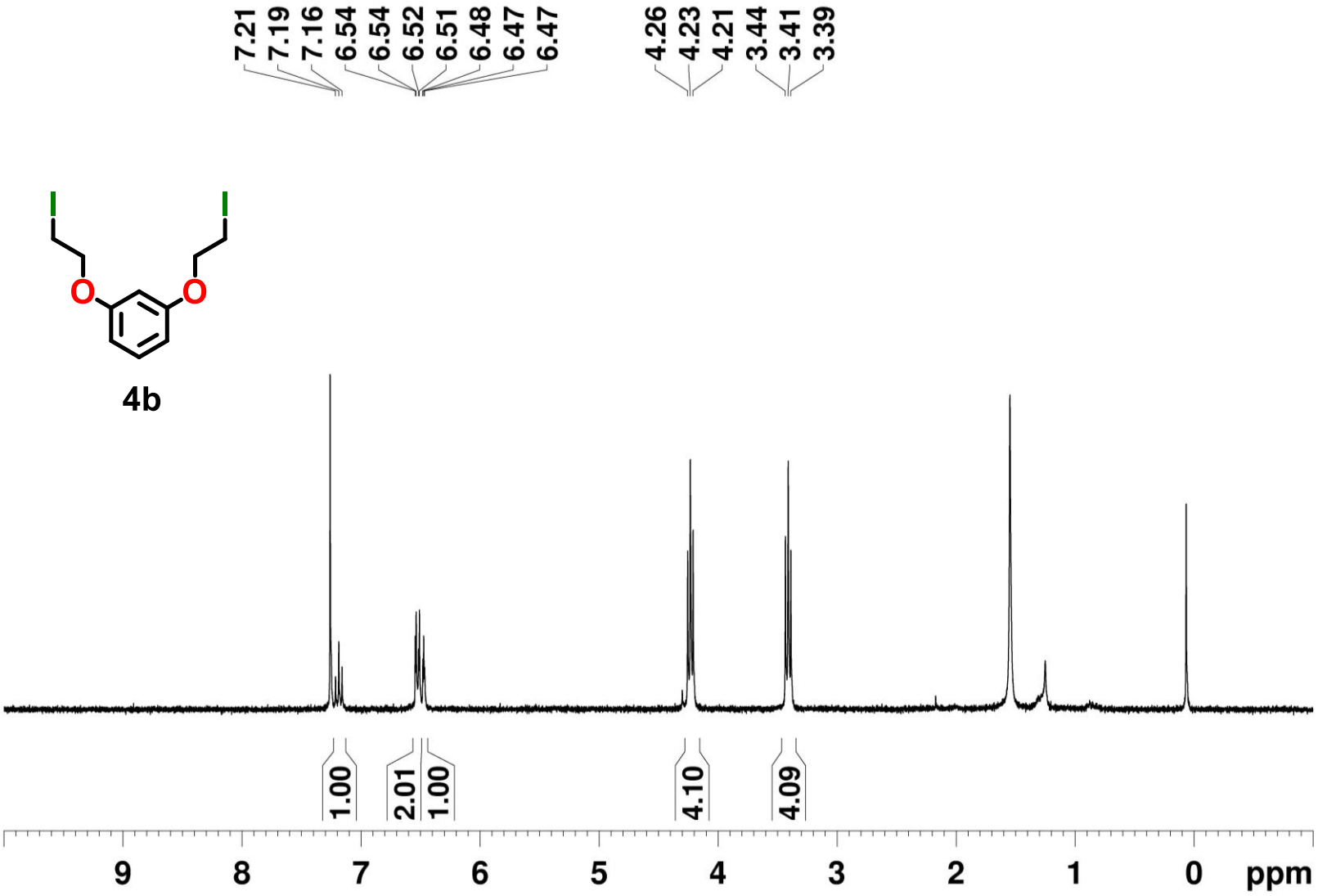


Figure S1. ^{1}H NMR spectrum (300 MHz, $CDCl_3$, 298 K) of derivative **4b**.

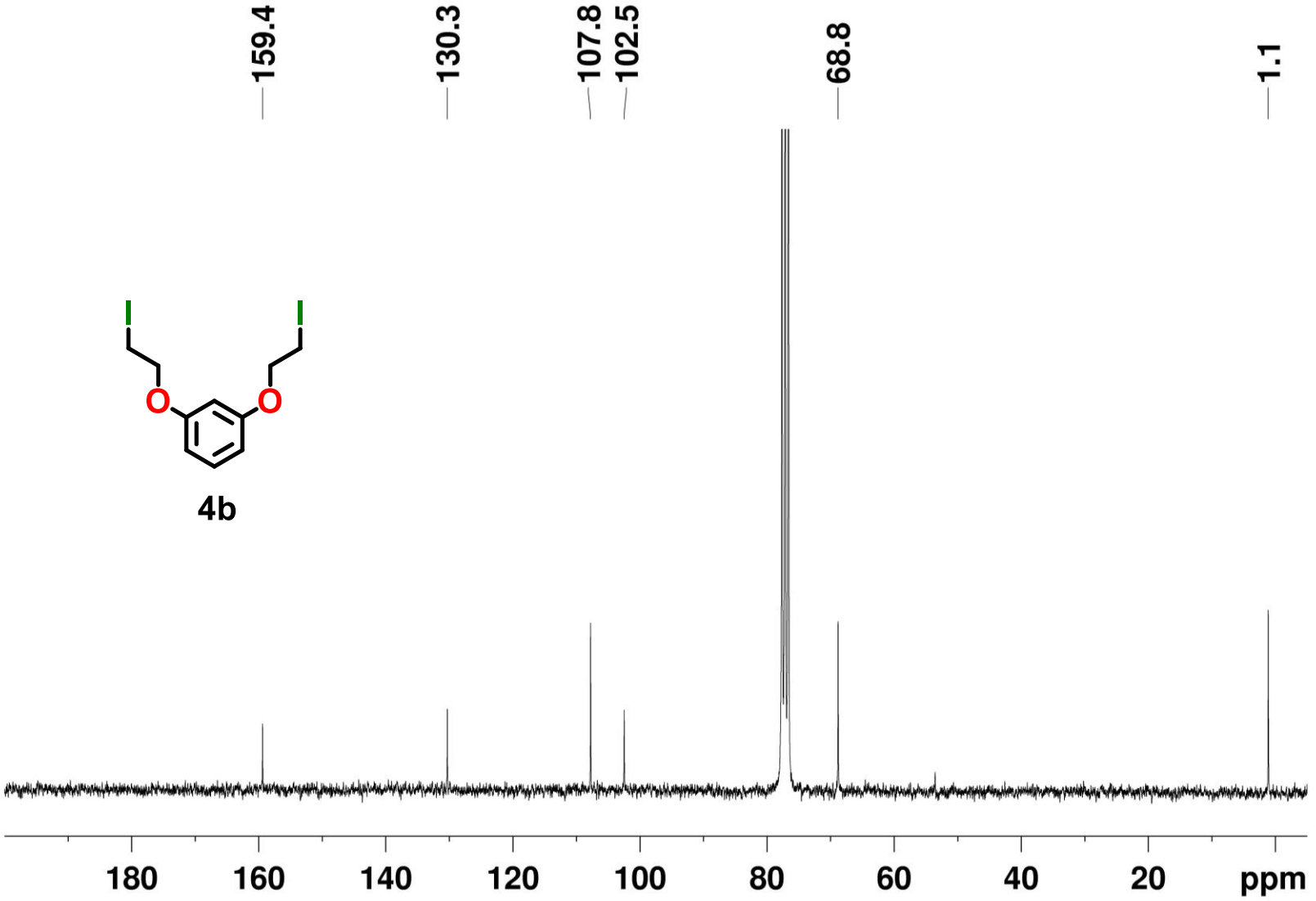


Figure S2. ^{13}C NMR spectrum (62.5 MHz, $CDCl_3$, 298 K) of derivative **4b**.

HRMS MALDI spectrum of derivative 4b

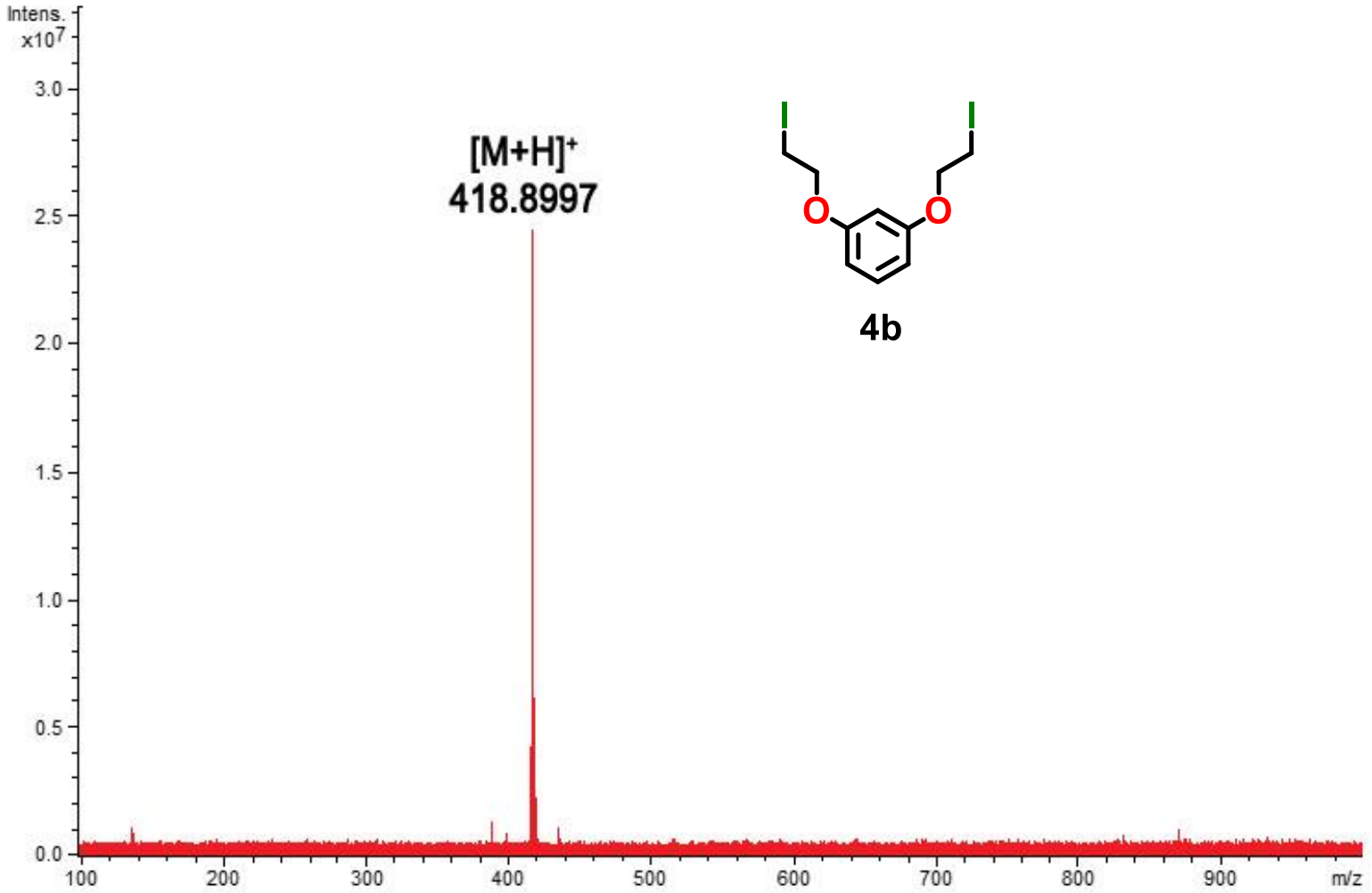


Figure S3. HRMS MALDI of derivative **4b**.

NMR spectra of derivative 5a

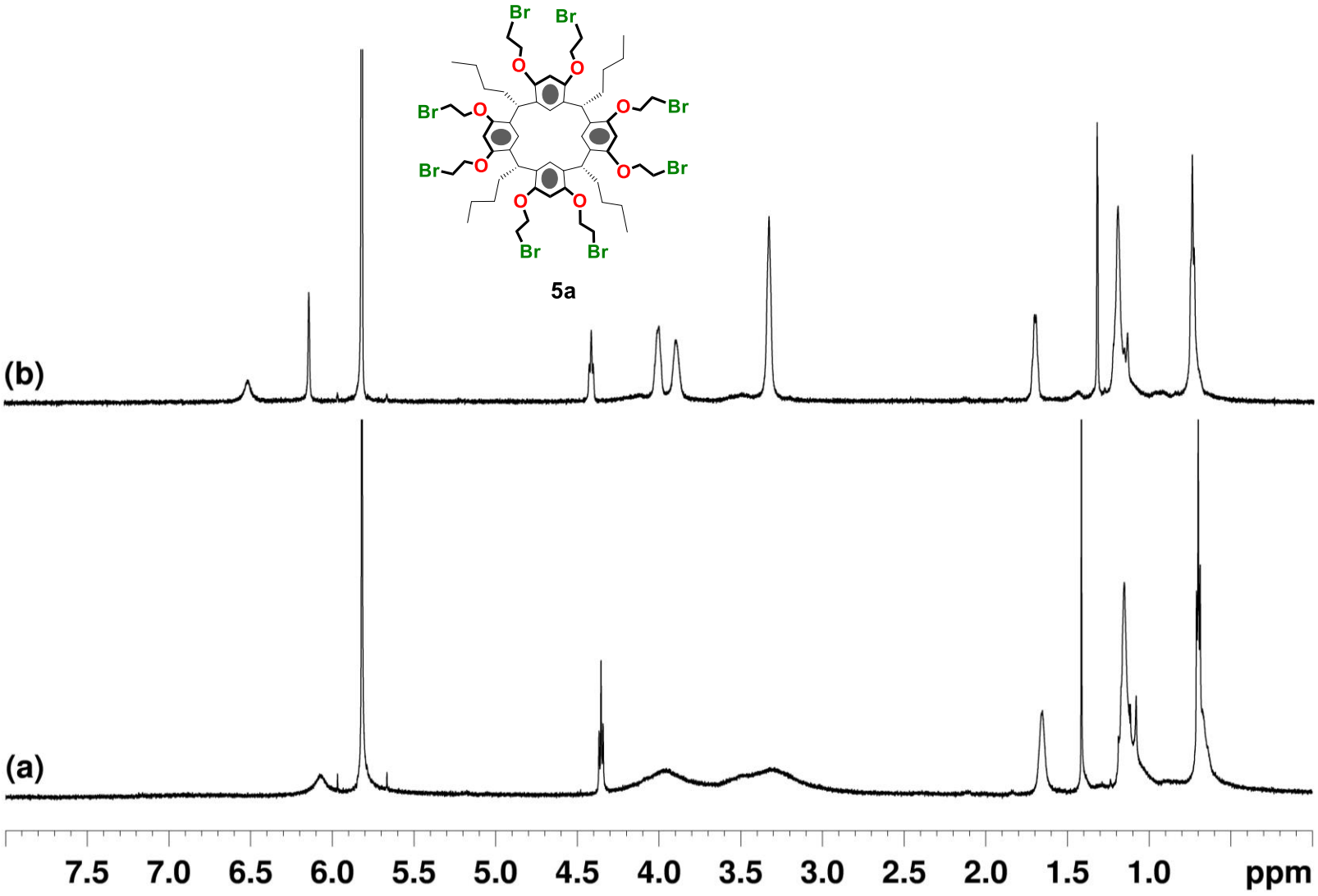


Figure S4. ^{1}H NMR spectra (600 MHz, TCDE) of derivative **5a** (a) at 298 K (b) at 353 K.

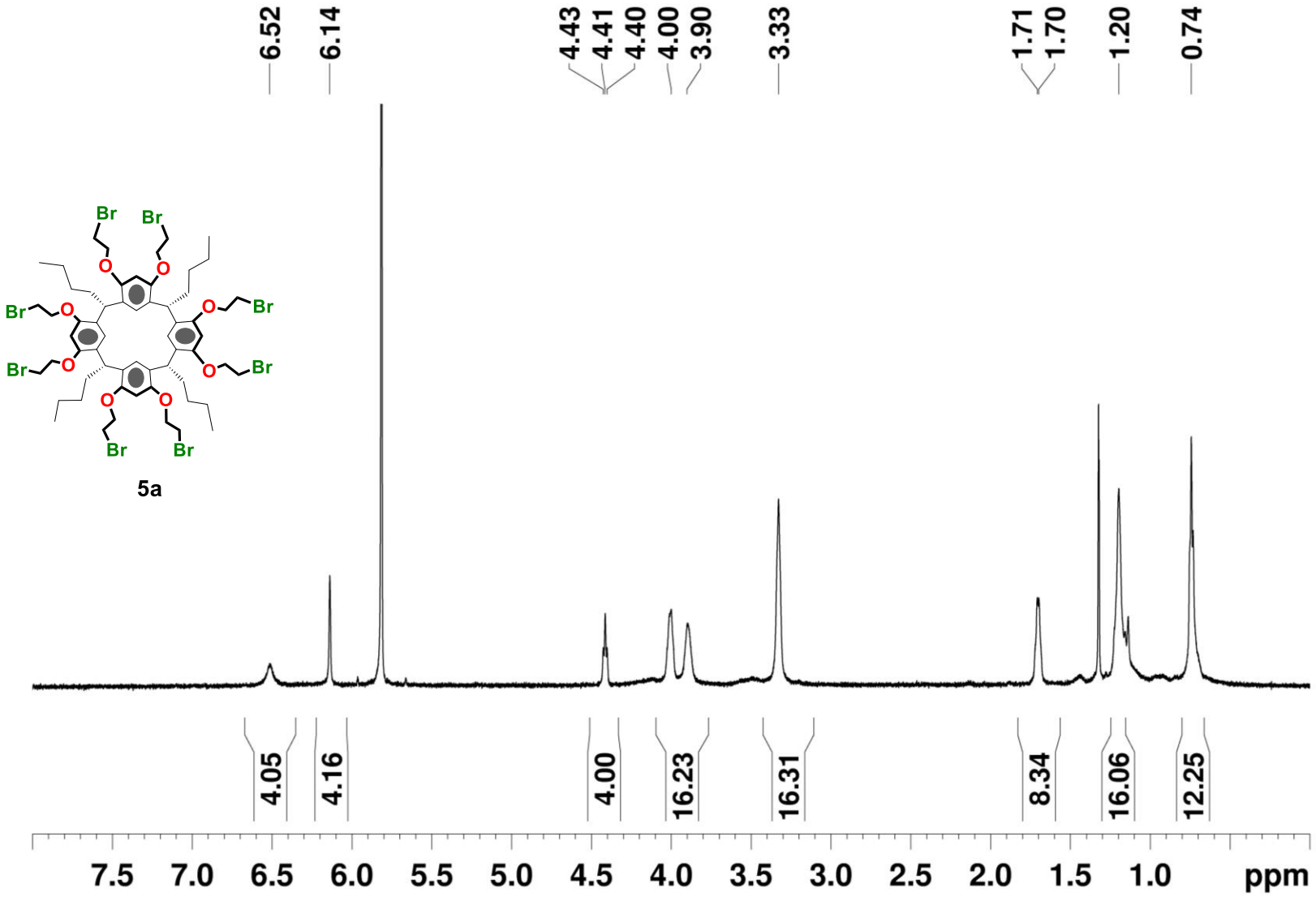


Figure S5. ^{1}H NMR spectrum (600 MHz, TCDE, 353 K) of derivative **5a**.

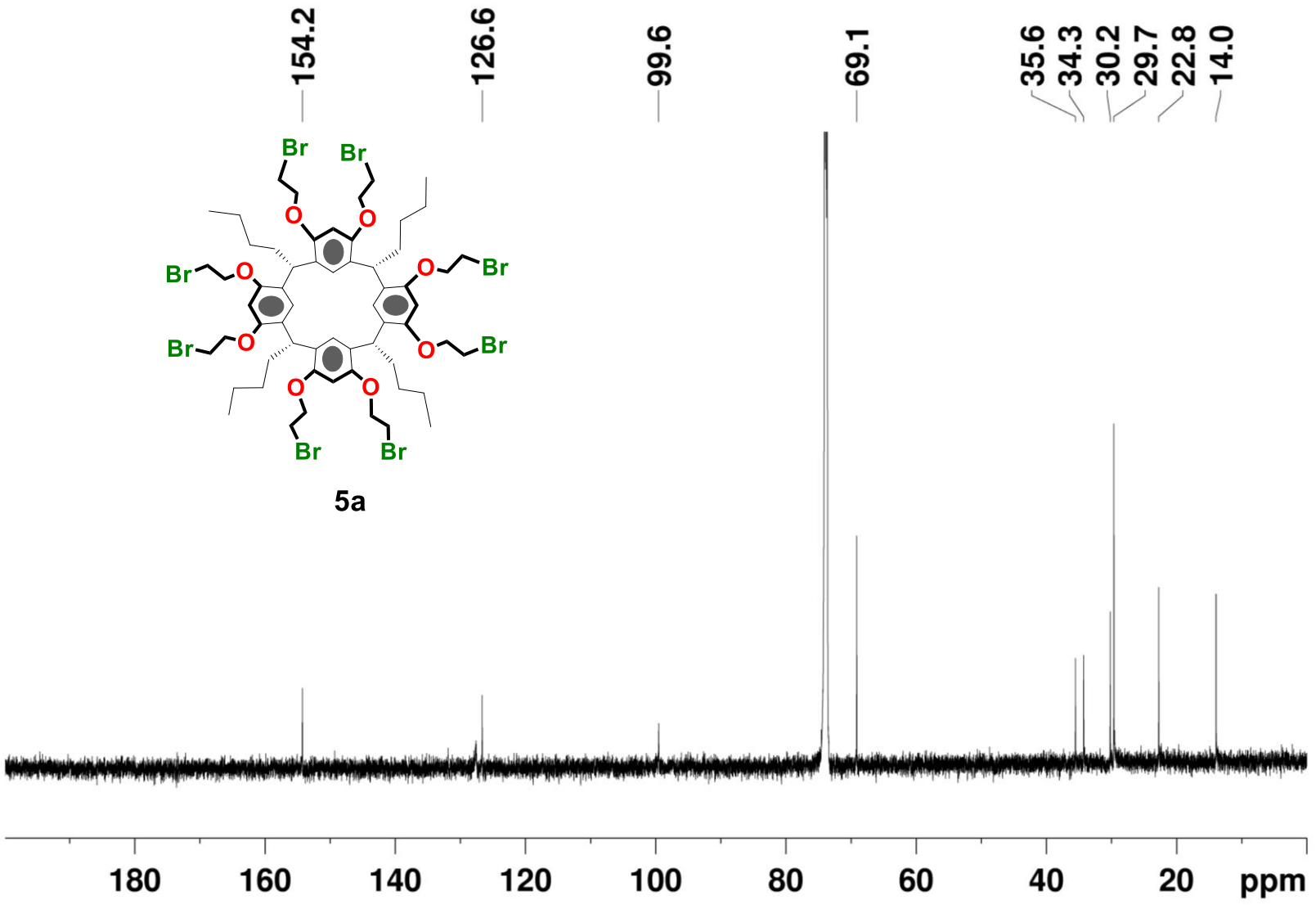
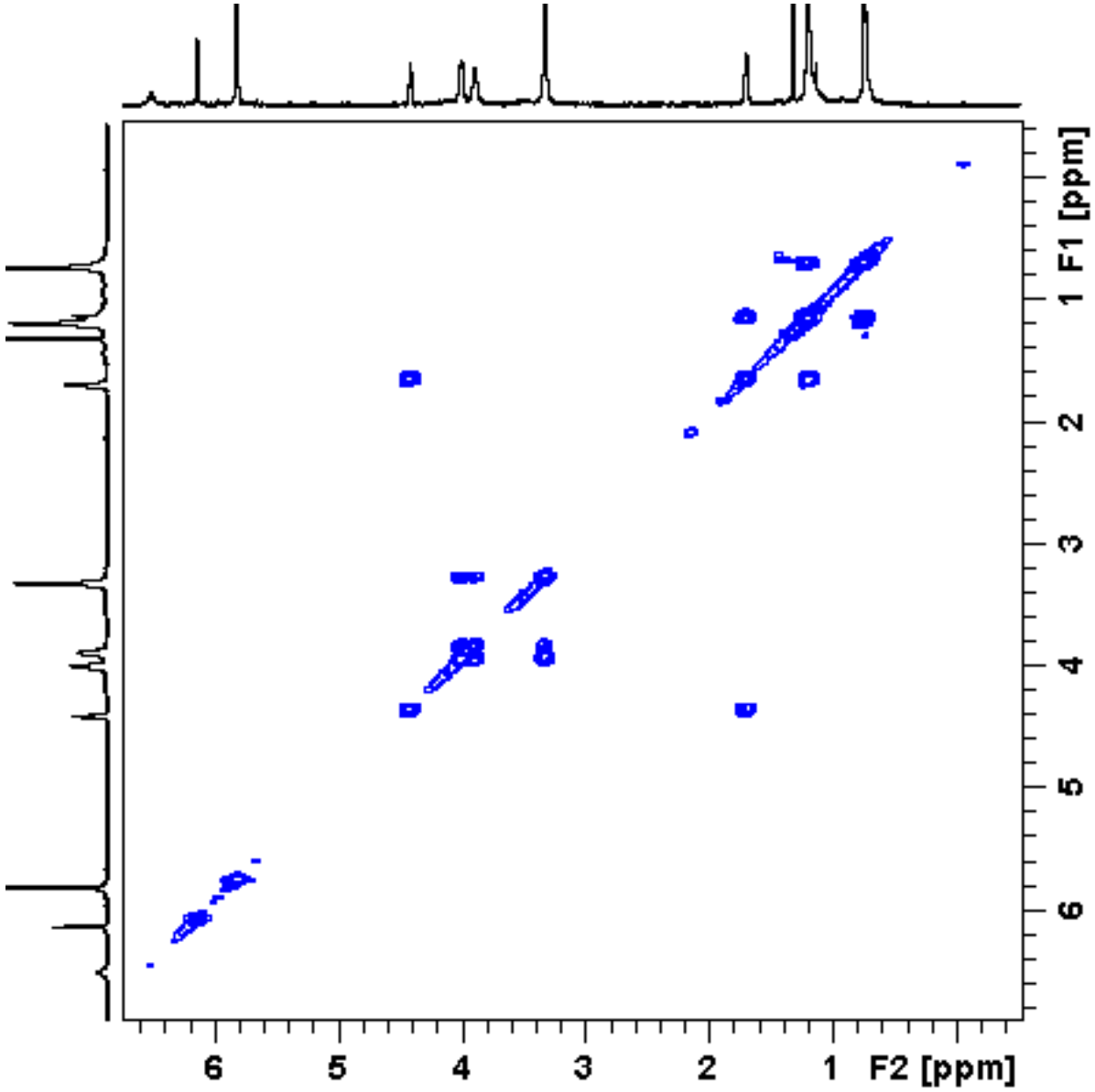
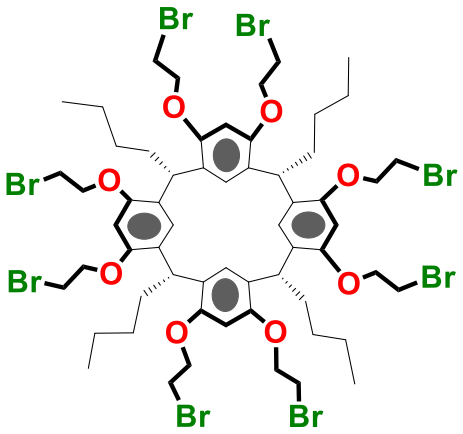


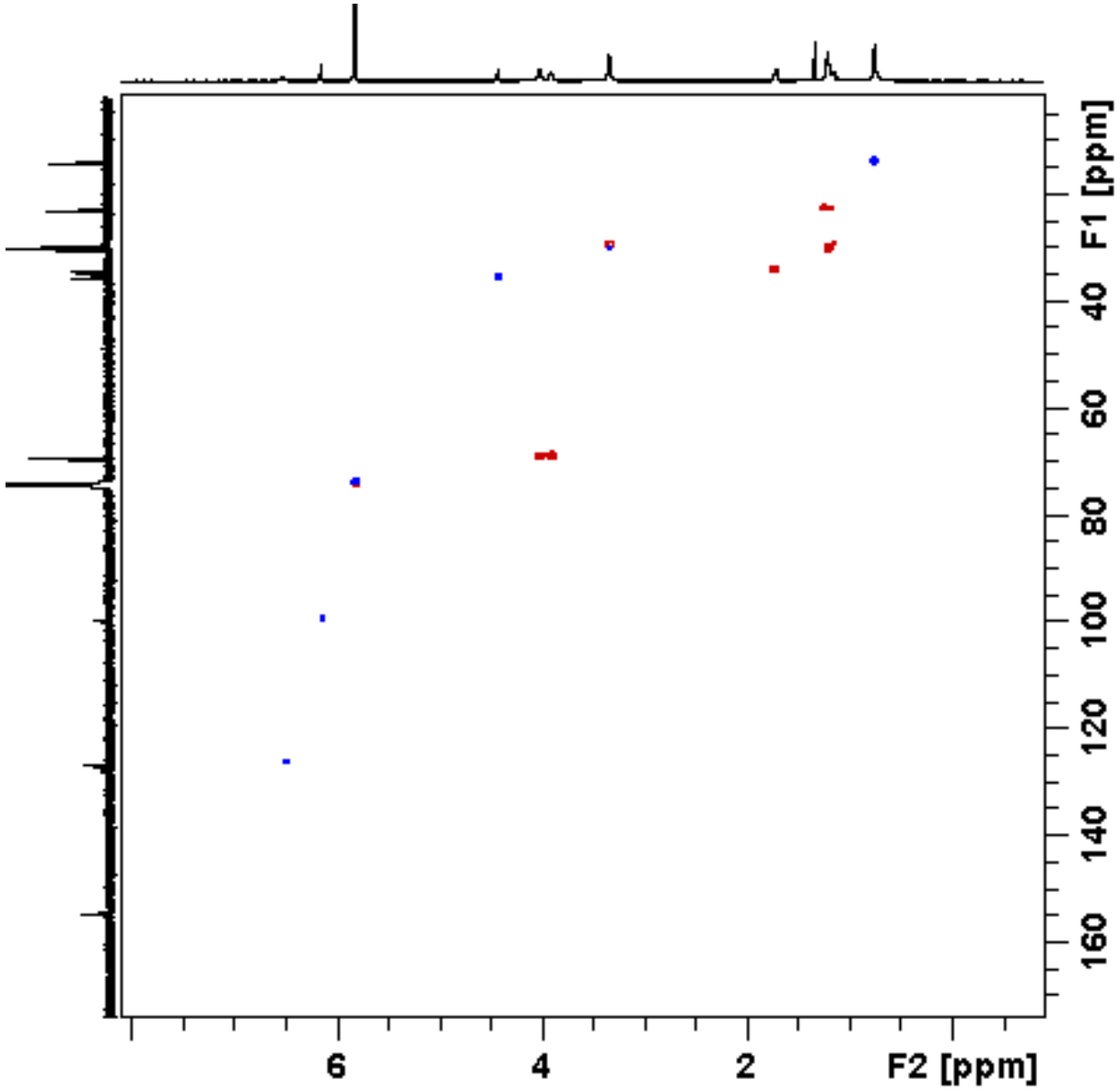
Figure S6. ^{13}C NMR spectrum (150 MHz, TCDE, 353 K) of derivative **5a**.

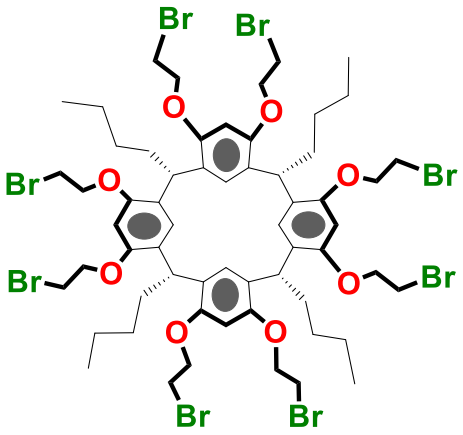




5a

Figure S7. 2D COSY spectrum (600 MHz, TCDE, 353 K) of derivative **5a**.





5a

Figure S8. 2D HSQC spectrum (600 MHz, TCDE, 353 K) of derivative **5a**.

HRMS MALDI spectrum of derivative 5a

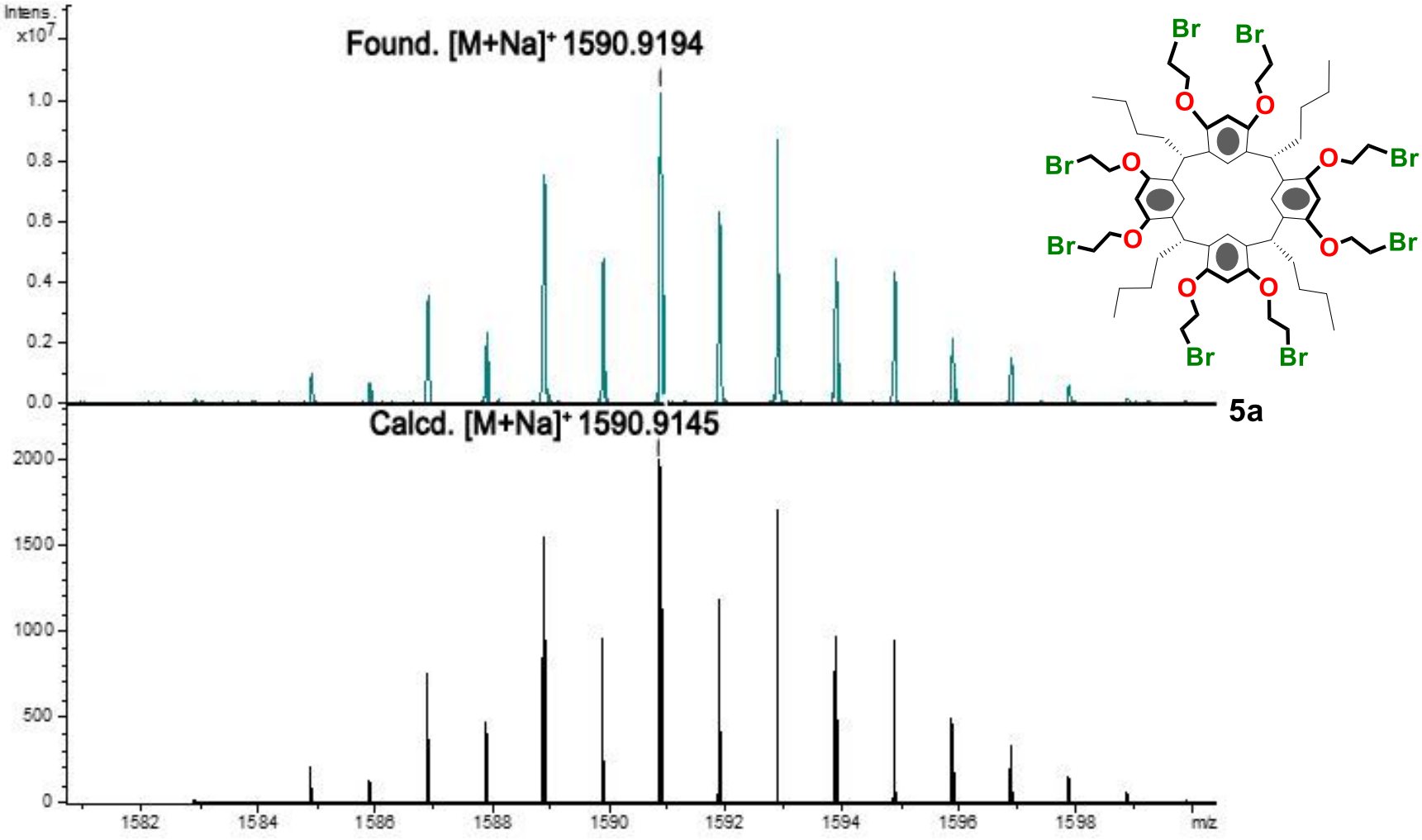


Figure S9. HRMS MALDI spectrum of derivative **5a**

NMR spectra of derivative 5b

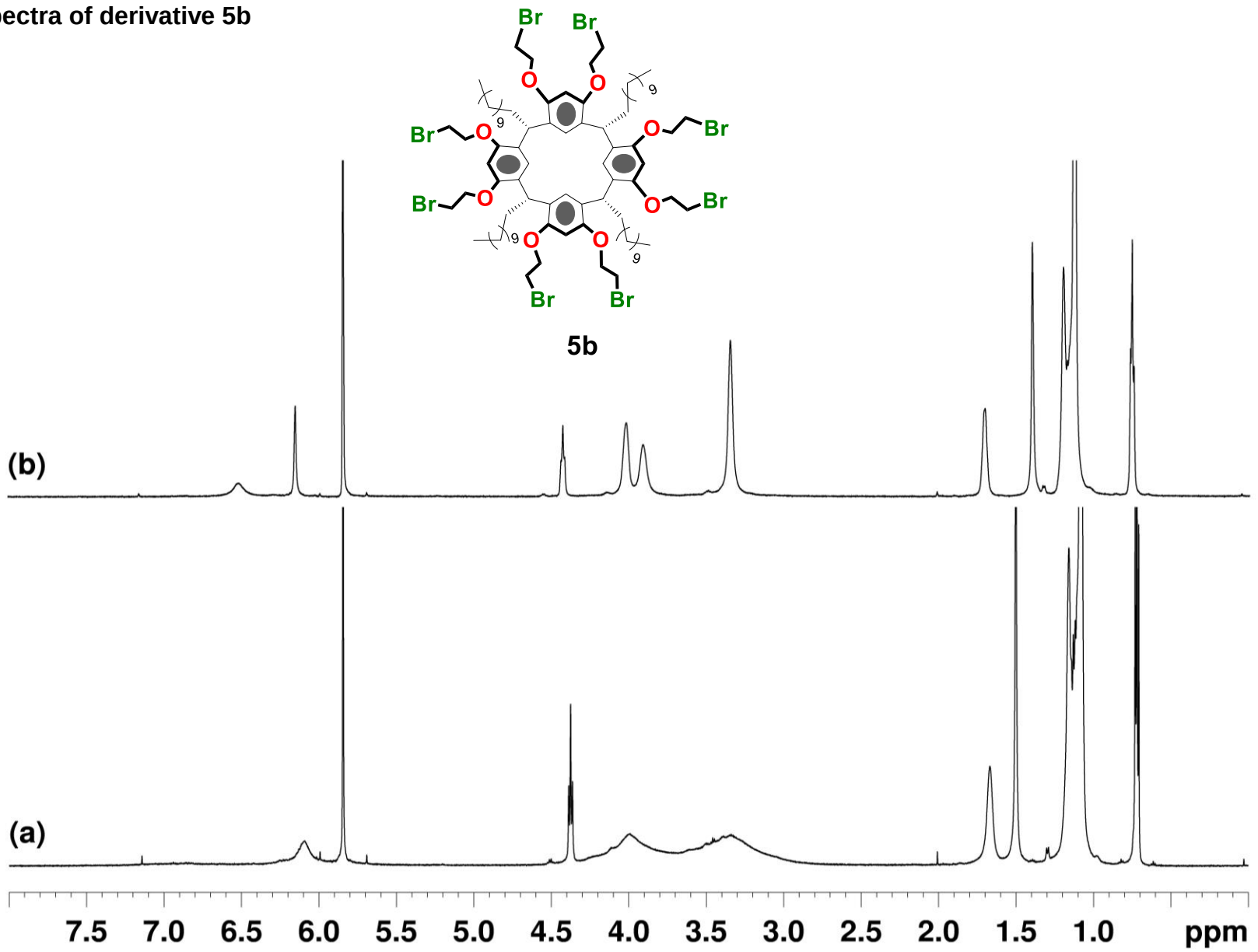


Figure S10. ^{1}H NMR spectra (600 MHz, TCDE) of derivative **5b** (a) at 298 K (b) at 353 K.

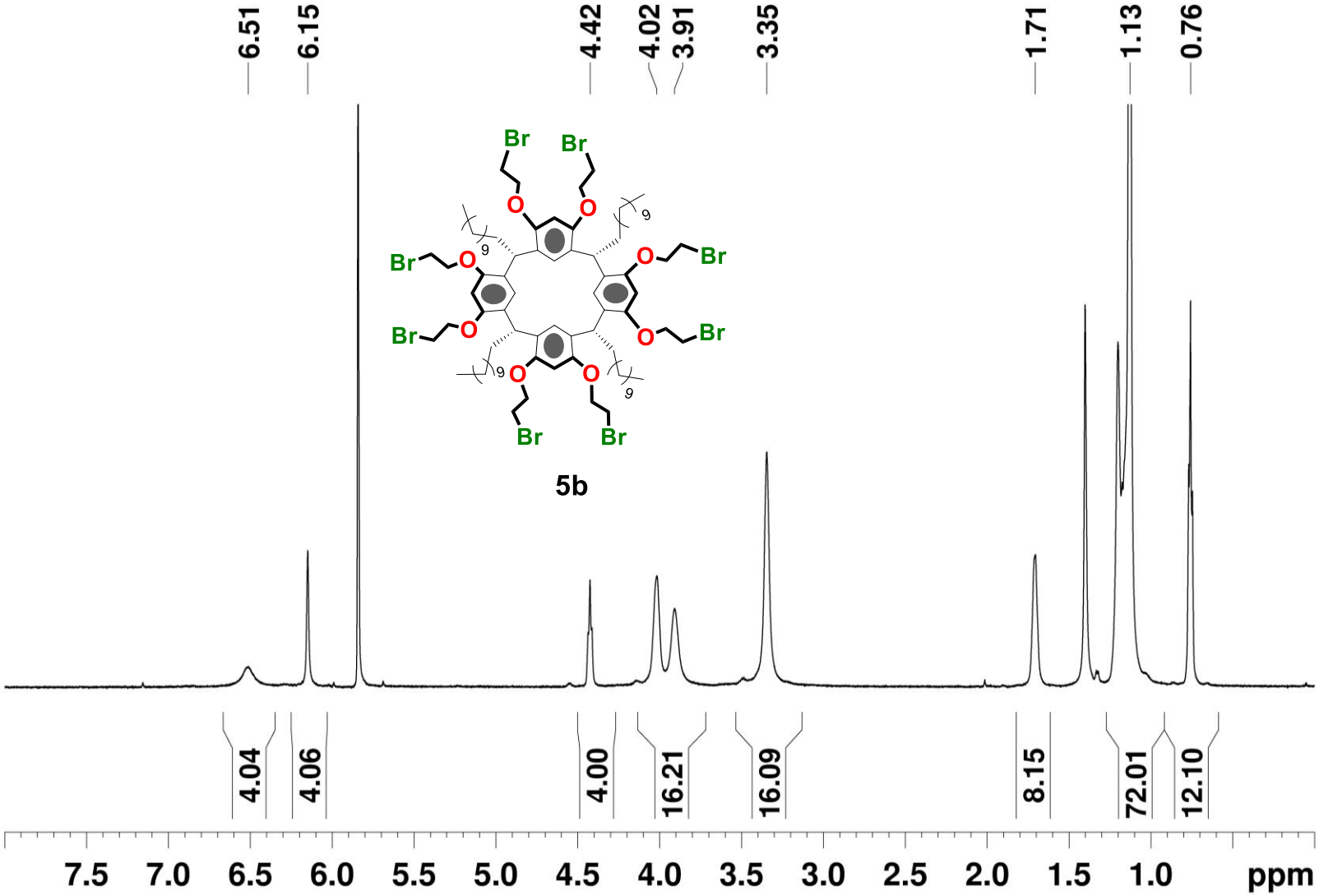


Figure S11. ^{1}H NMR spectrum (600 MHz, TCDE, 353 K) of derivative **5b**.

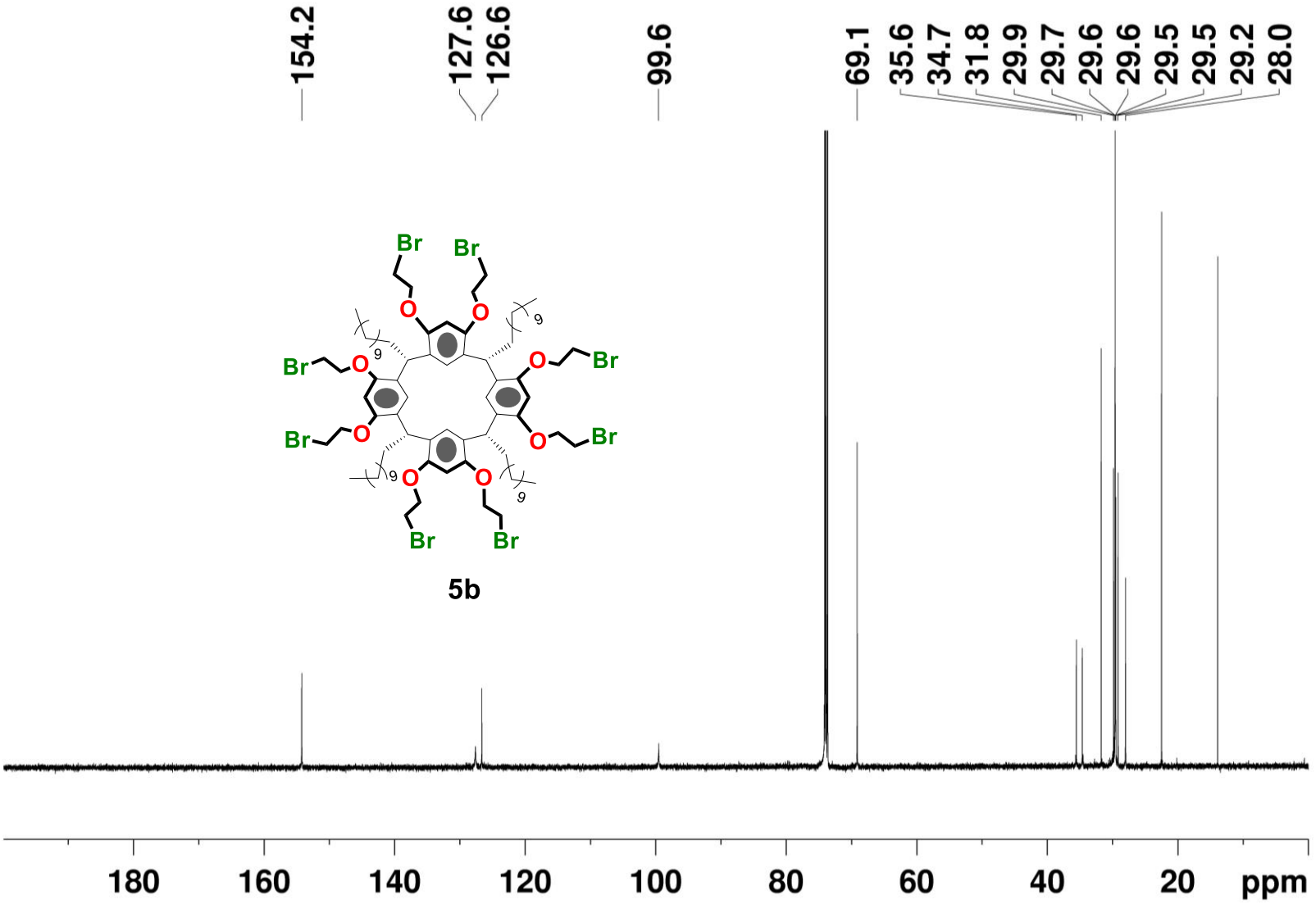


Figure S12. ^{13}C NMR spectrum (150 MHz, TCDE, 353 K) of derivative **5b**.

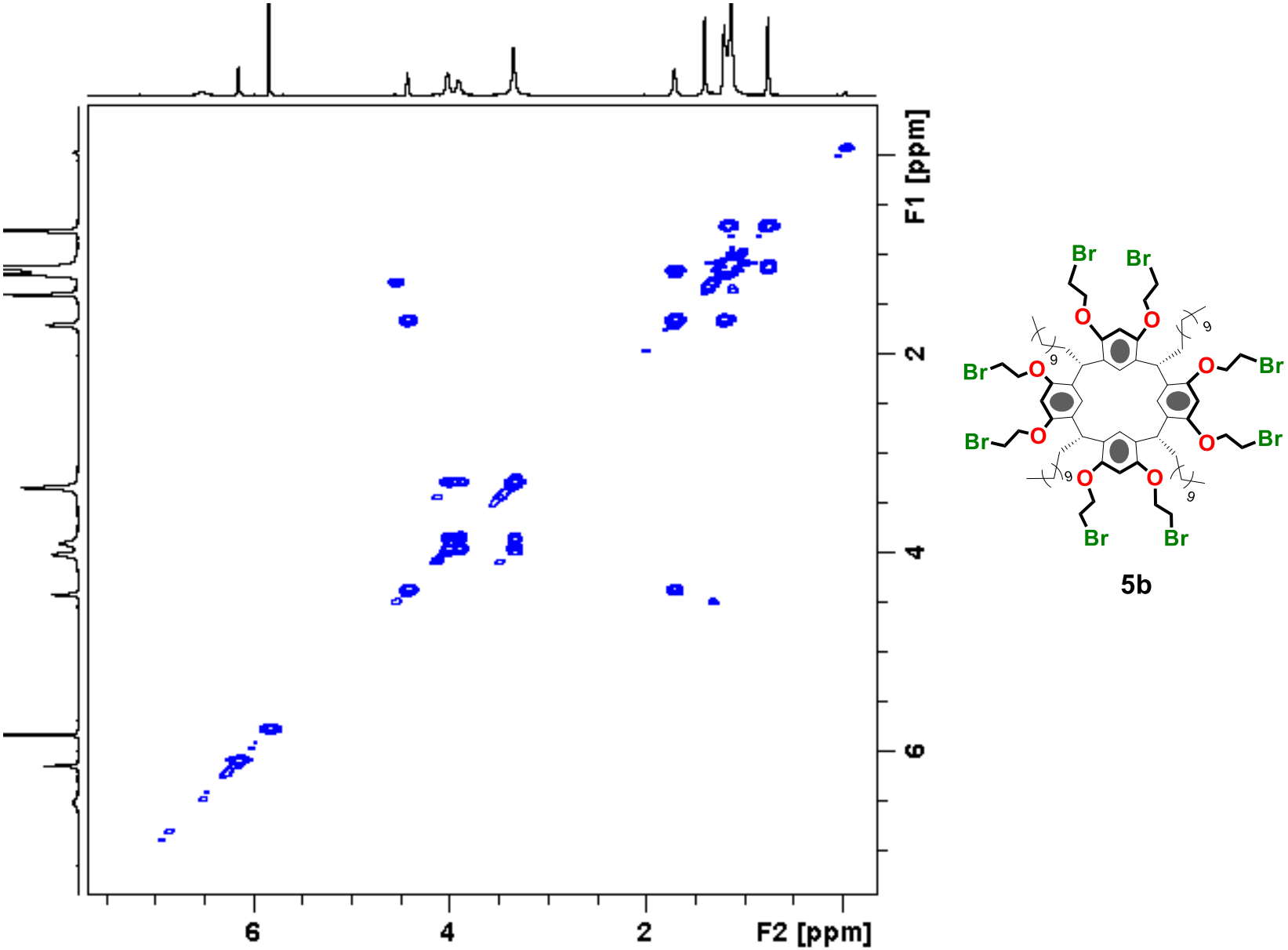
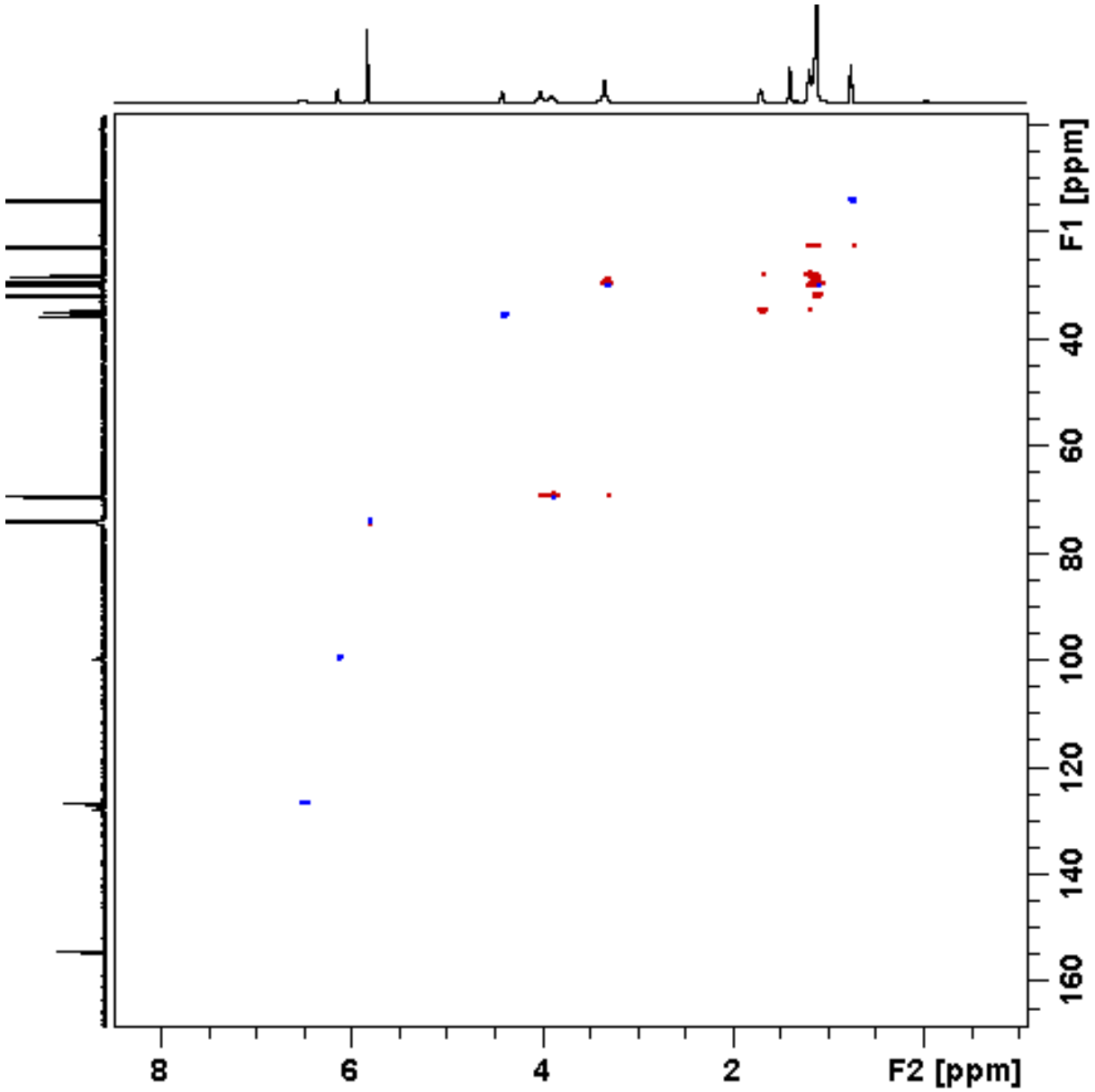
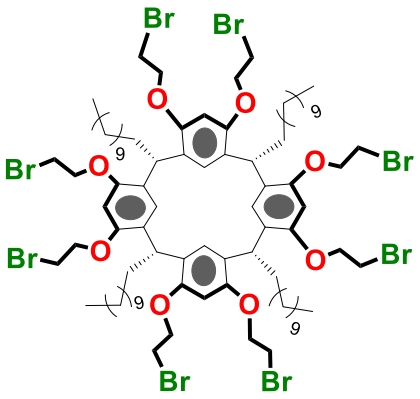


Figure S13. 2D COSY spectrum (600 MHz, TCDE, 353 K) of derivative **5b**.





5b

Figure S14. 2D HSQC spectrum (600 MHz, TCDE, 353 K) of derivative **5b**.

HRMS MALDI spectrum of derivative 5b

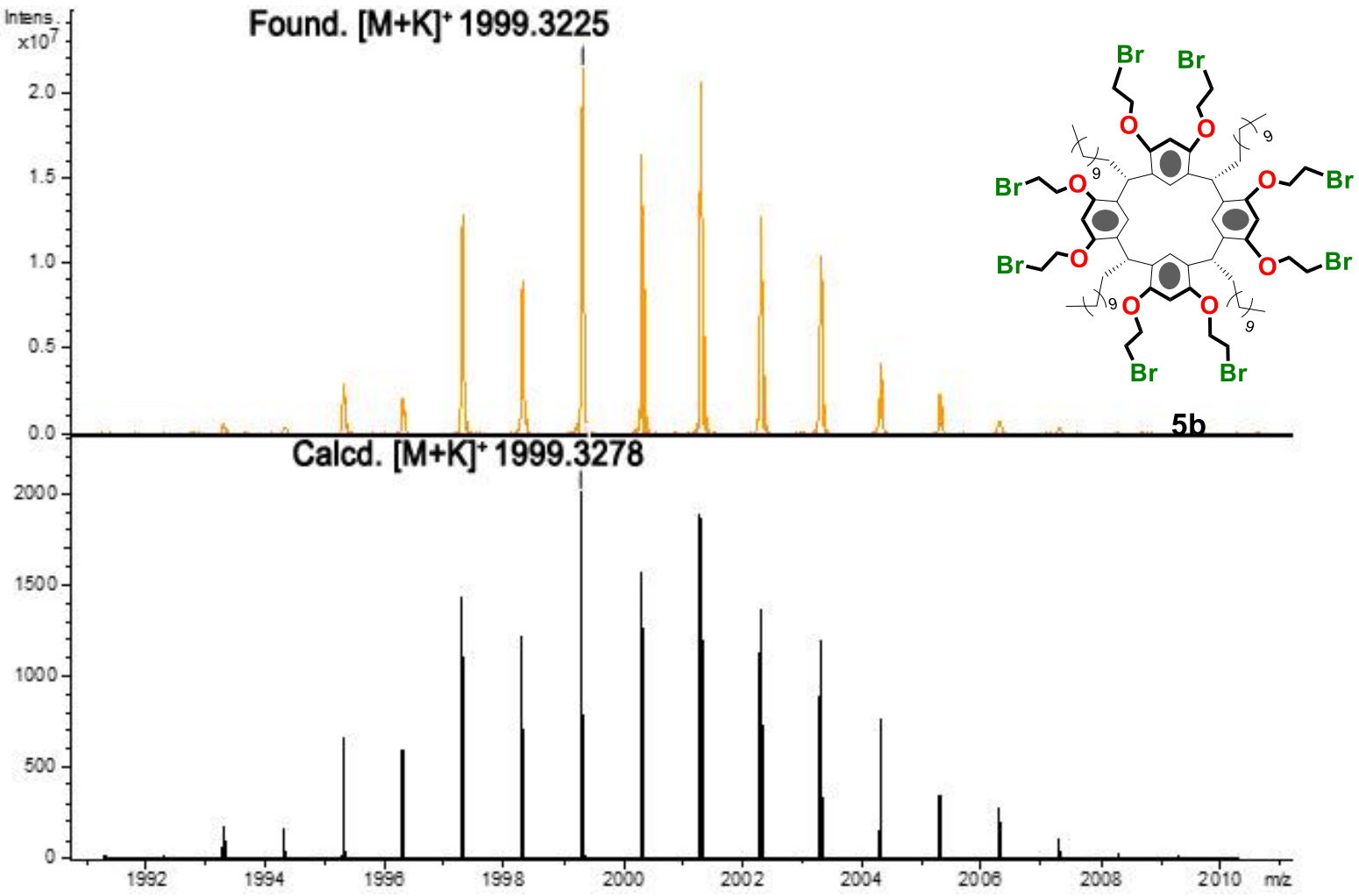


Figure S15. HRMS MALDI spectrum of derivative **5b**

NMR spectra of derivative 5c

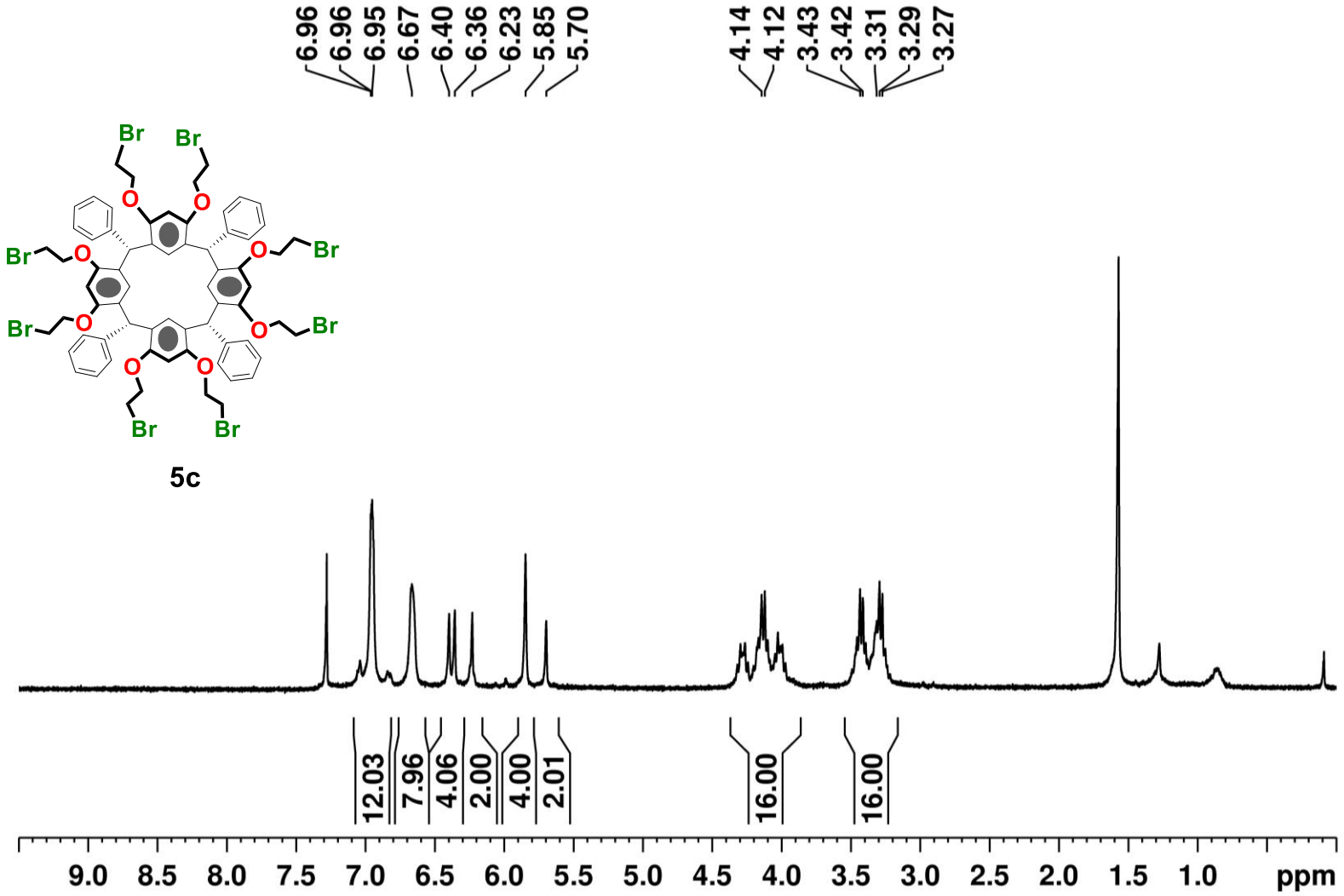


Figure S16. ^{1}H NMR spectrum (300 MHz, $CDCl_3$, 298K) of derivative **5c**.

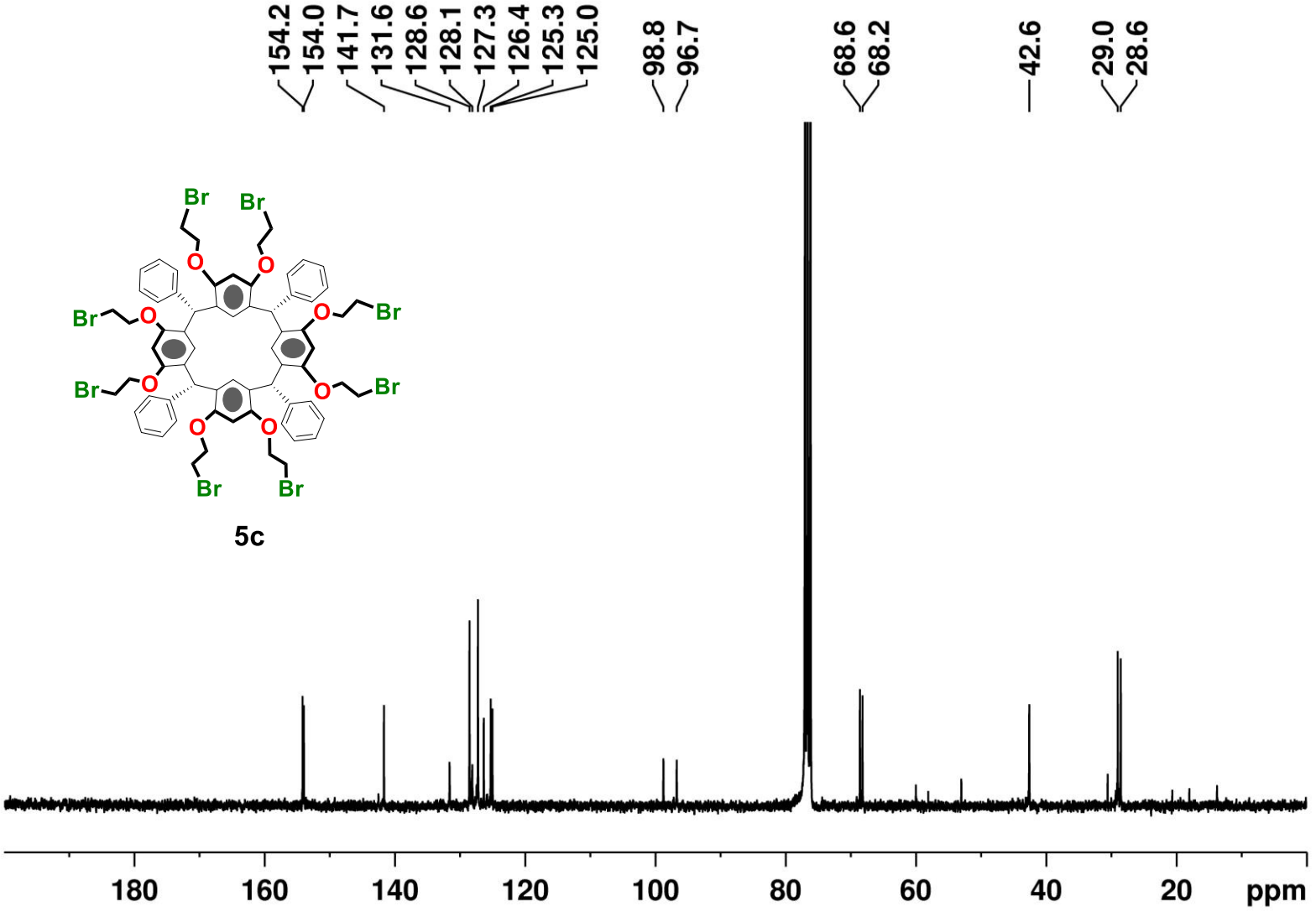
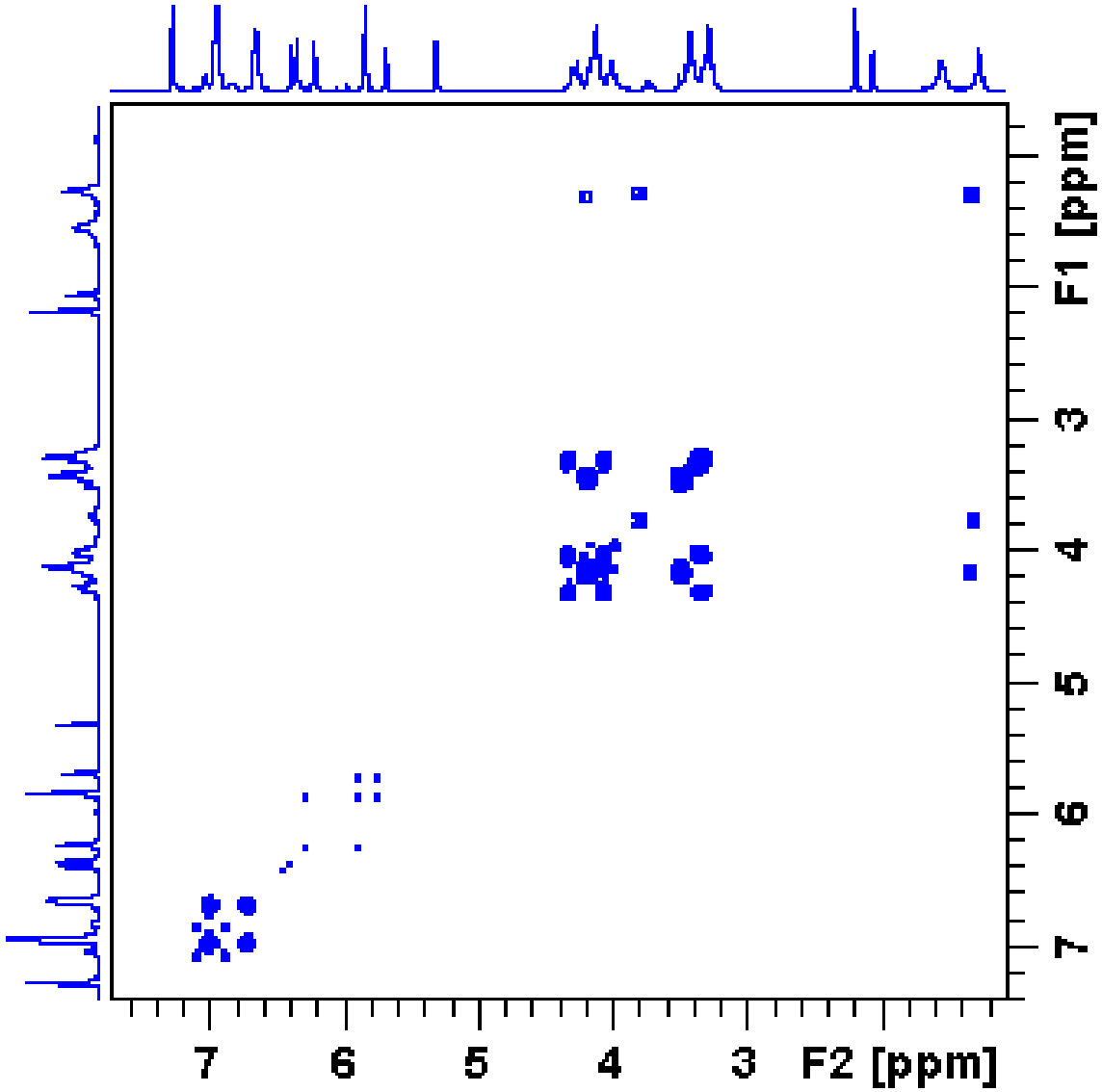
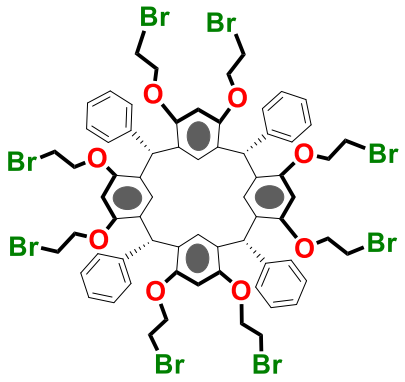


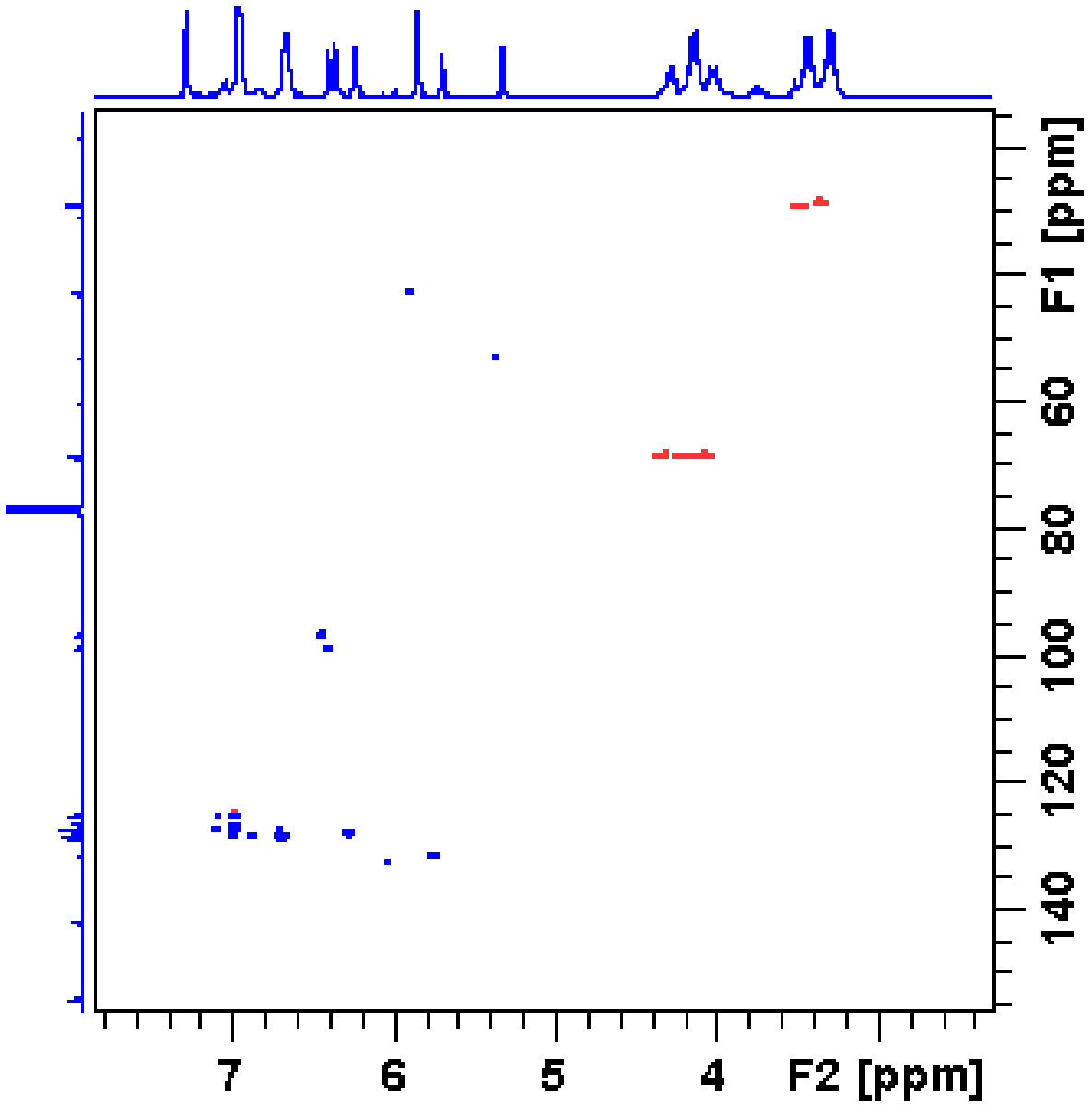
Figure S17. ^{13}C NMR spectrum (75 MHz, $CDCl_3$, 298K) of derivative **5c**.

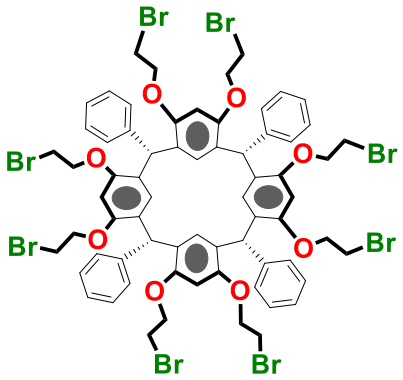




5c

Figure S18. 2D COSY spectrum (400 MHz, $CDCl_3$, 298 K) of derivative **5c**.





5c

Figure S19. 2D HSQC spectrum (400 MHz, $CDCl_3$, 298 K) of derivative **5c**.

HRMS MALDI spectrum of derivative 5c

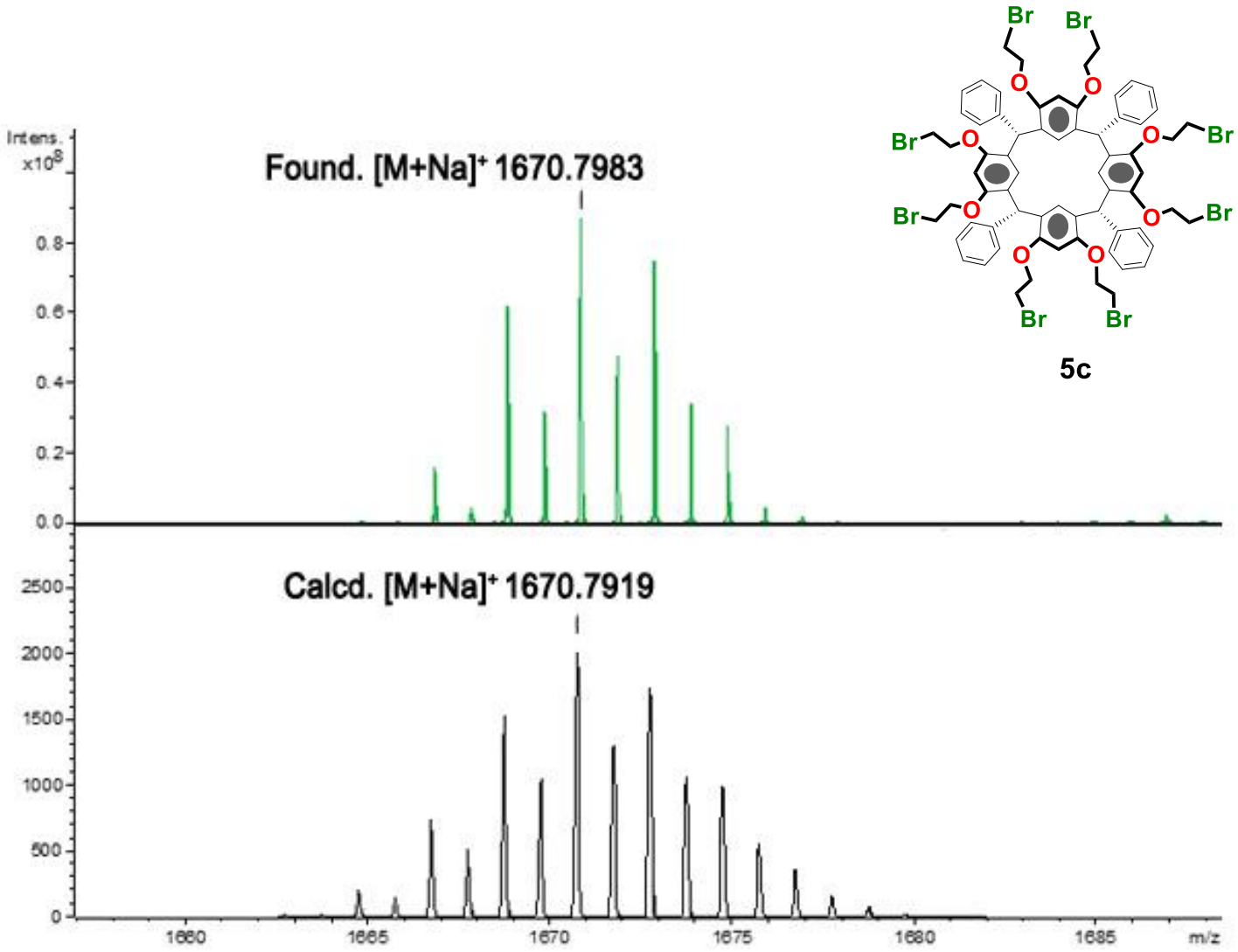


Figure S20. HRMS MALDI spectrum of derivative **5c.**

NMR spectra of derivative 5b

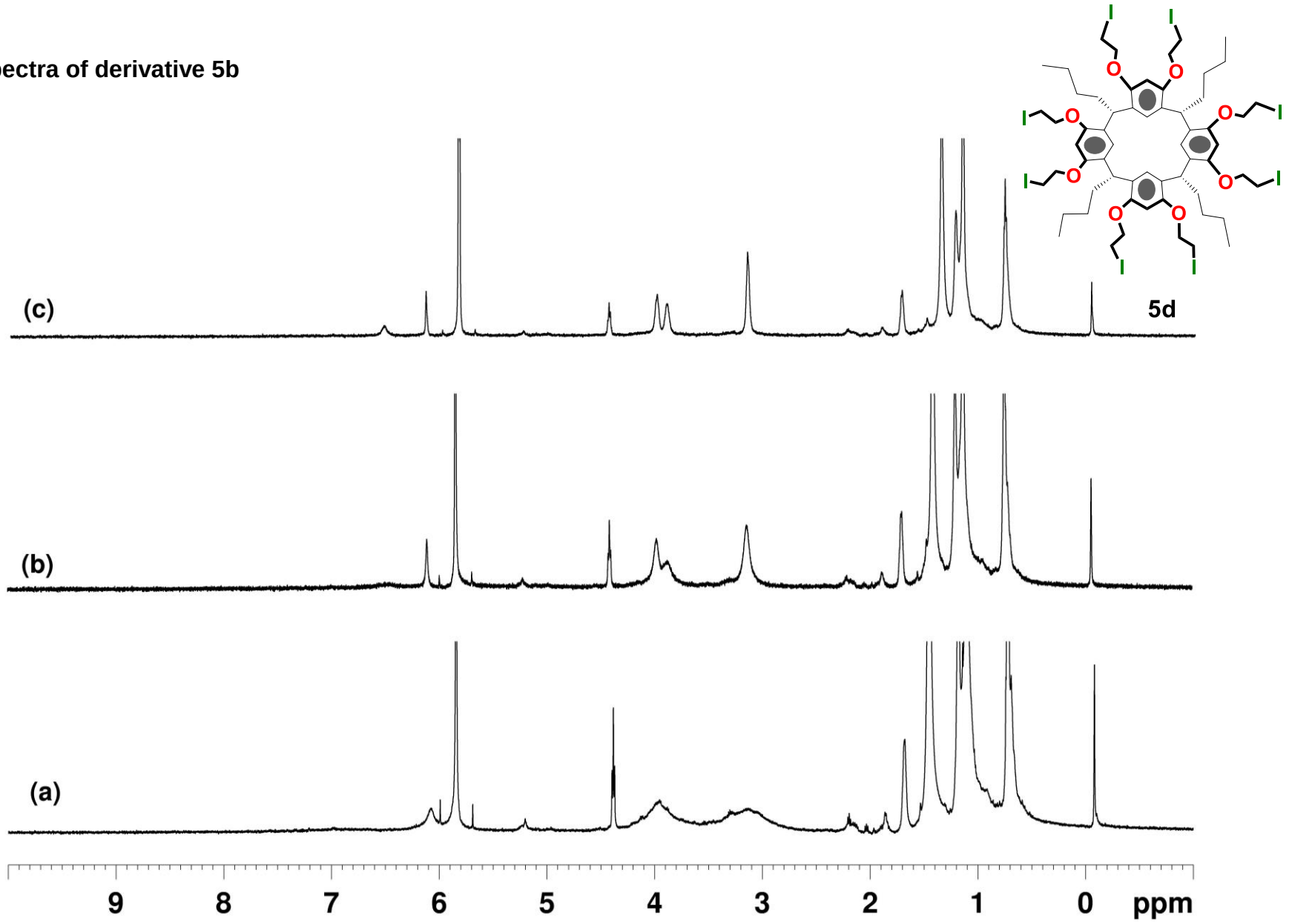


Figure S21. ^{1}H NMR spectra (600 MHz, TCDE) of derivative **5d** (a) at 298 K (b) at 323 K. (c) at 353 K.

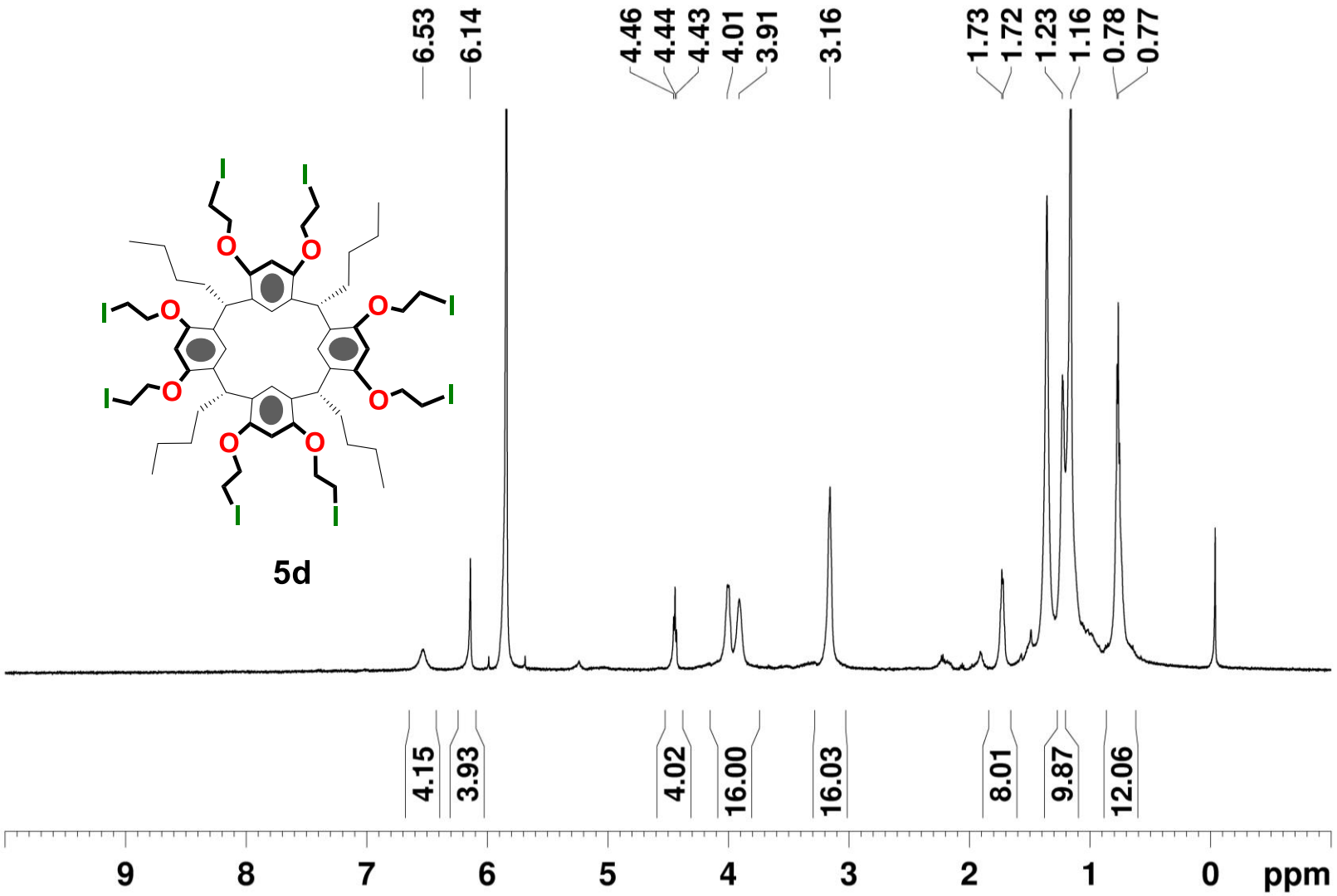


Figure S22. ^{1}H NMR spectrum (600 MHz, TCDE, 353 K) of derivative **5d**.

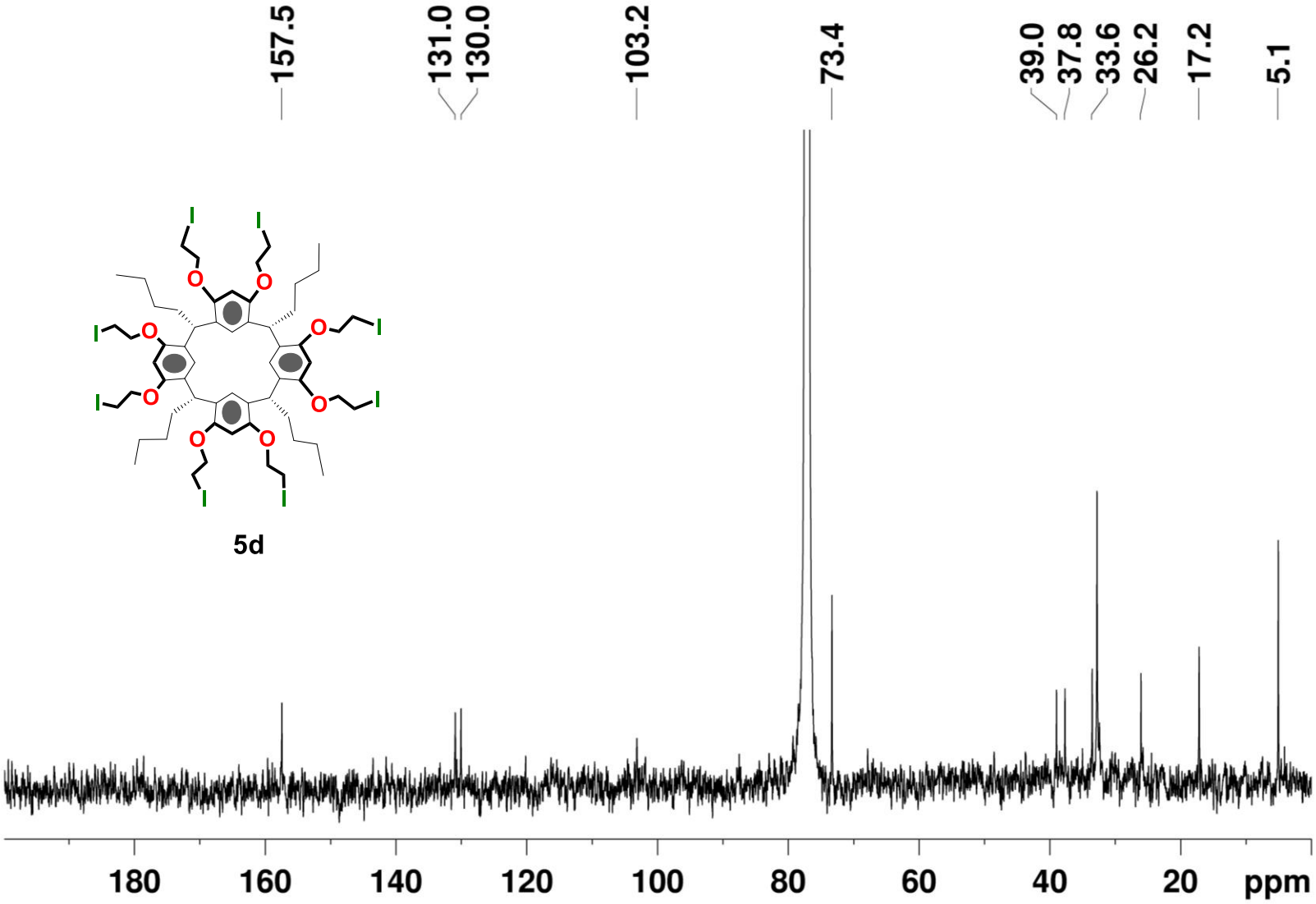
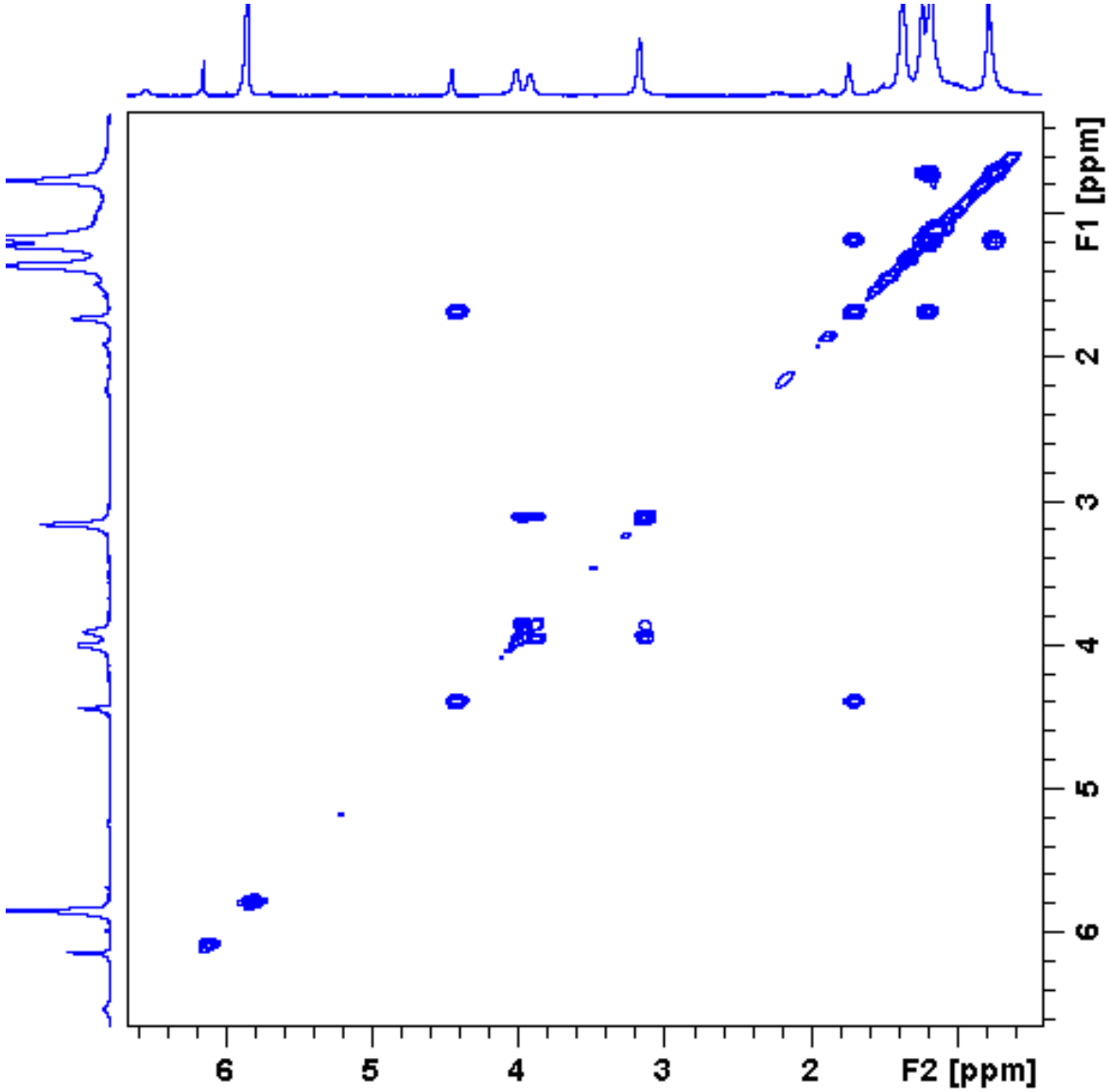
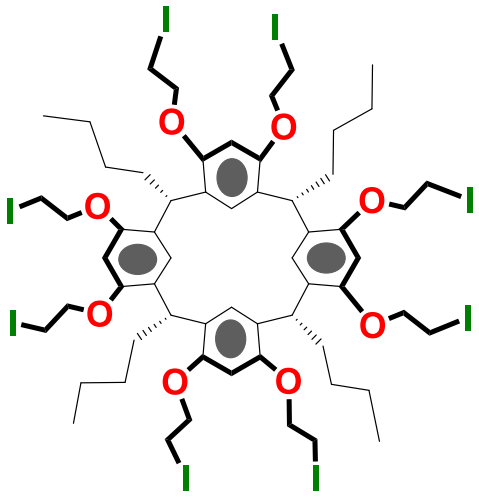


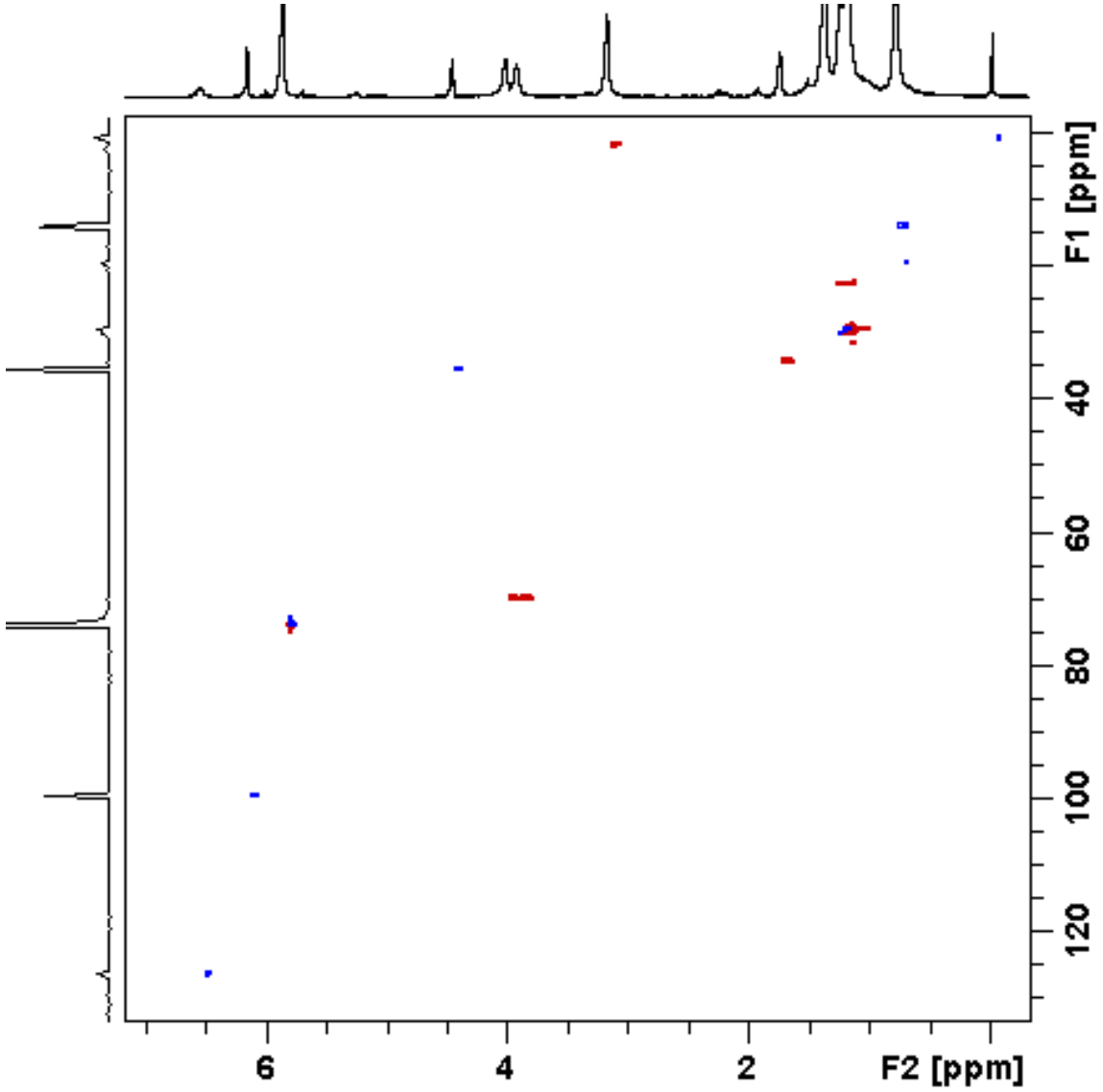
Figure S23. ^{13}C NMR spectrum (150 MHz, TCDE, 353 K) of derivative **5d**.

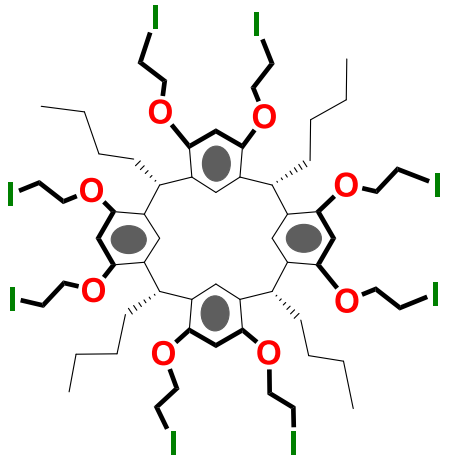




5d

Figure S24. 2D COSY spectrum (600 MHz, TCDE, 353 K) of derivative **5d**.





5d

Figure S25. 2D HSQC spectrum (600 MHz, TCDE, 353 K) of derivative **5d**.

HRMS MALDI spectrum of derivative 5d

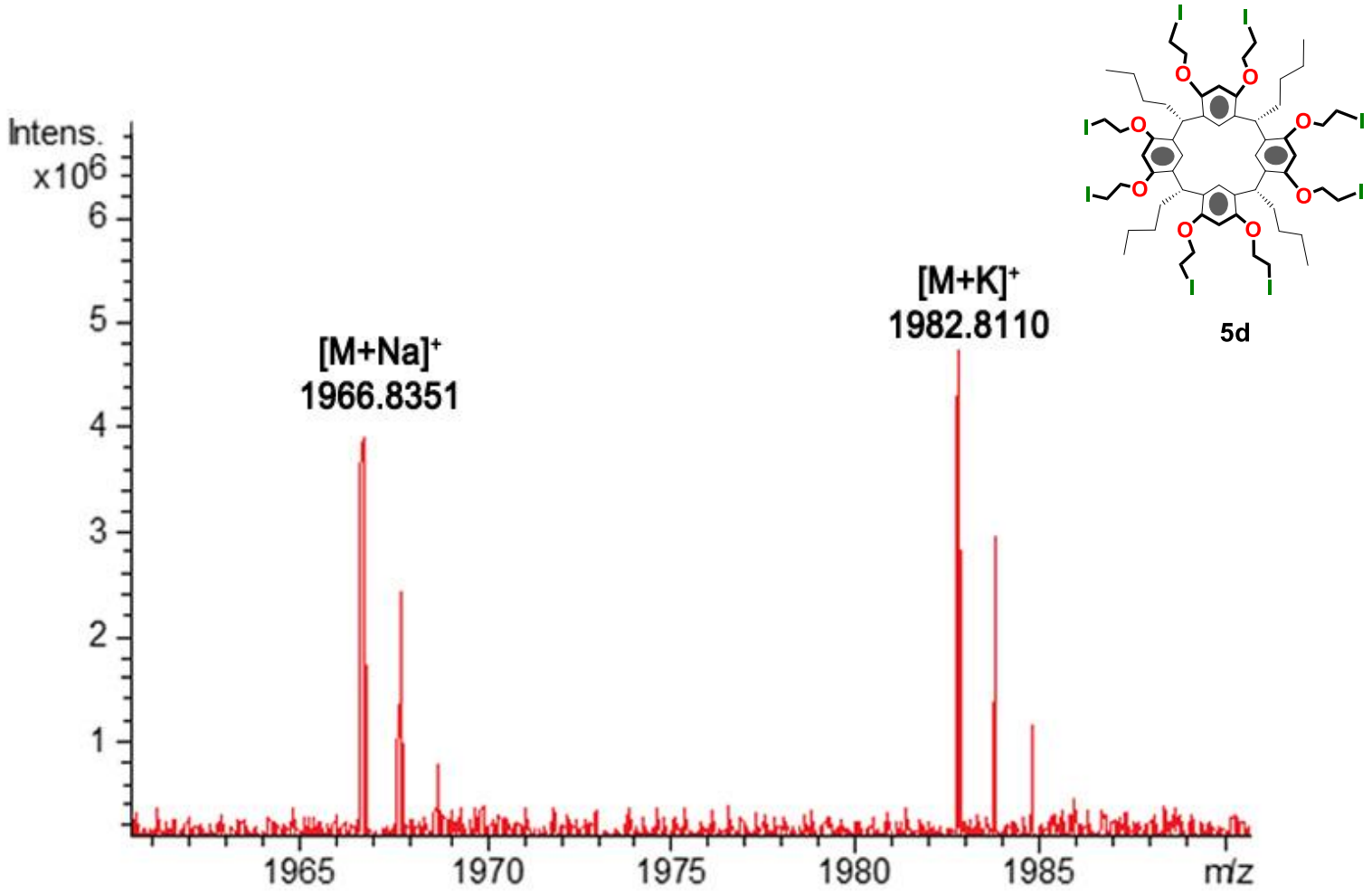


Figure S26. HRMS MALDI spectrum of derivative **5d**

NMR spectra of ResQAC^{butyl}(Br$^-$)$_8$

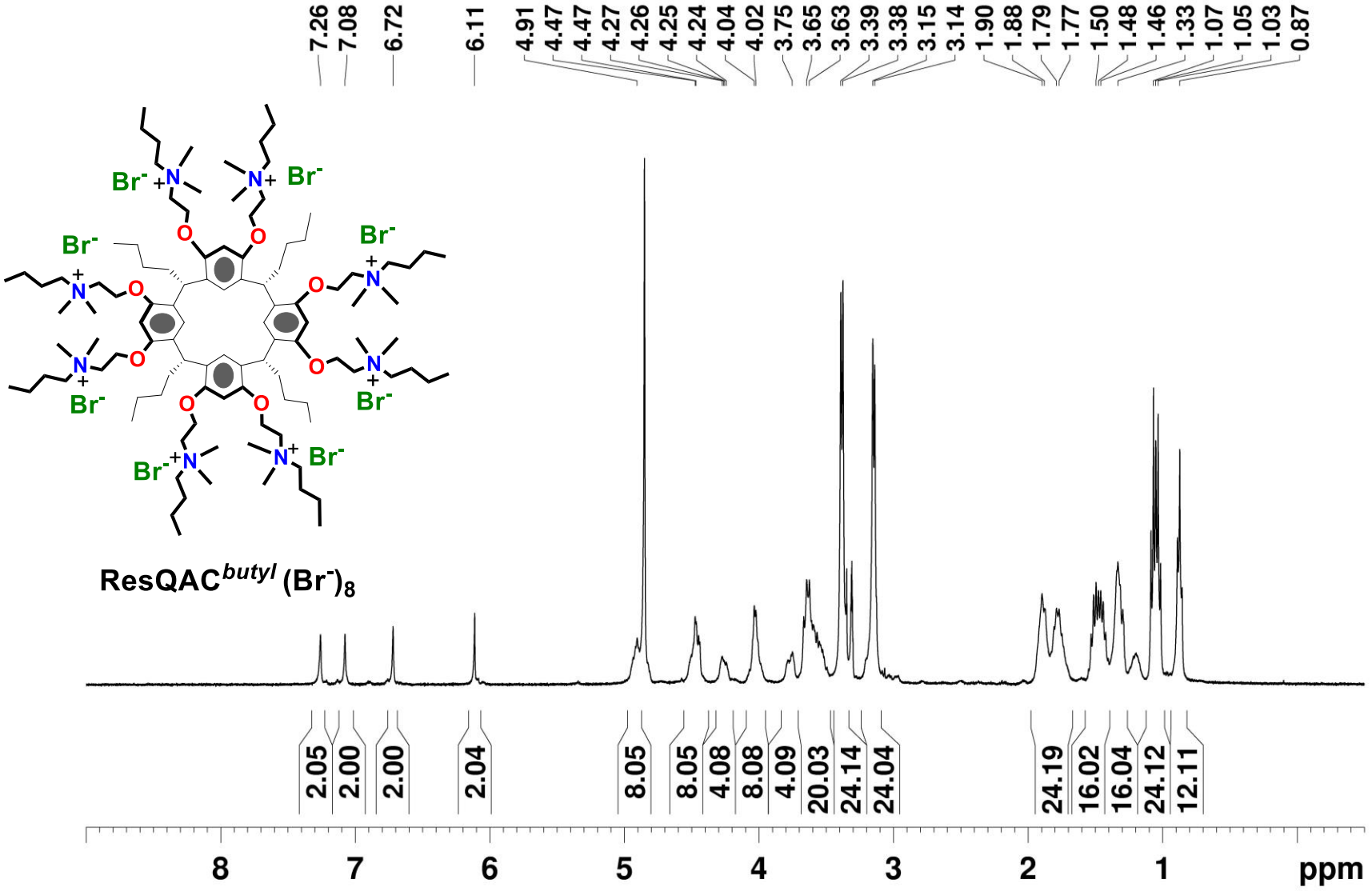


Figure S27. ^{1}H NMR spectrum (400 MHz, CD_3OD, 298 K) of **ResQAC^{butyl}(Br$^-$)$_8$**.

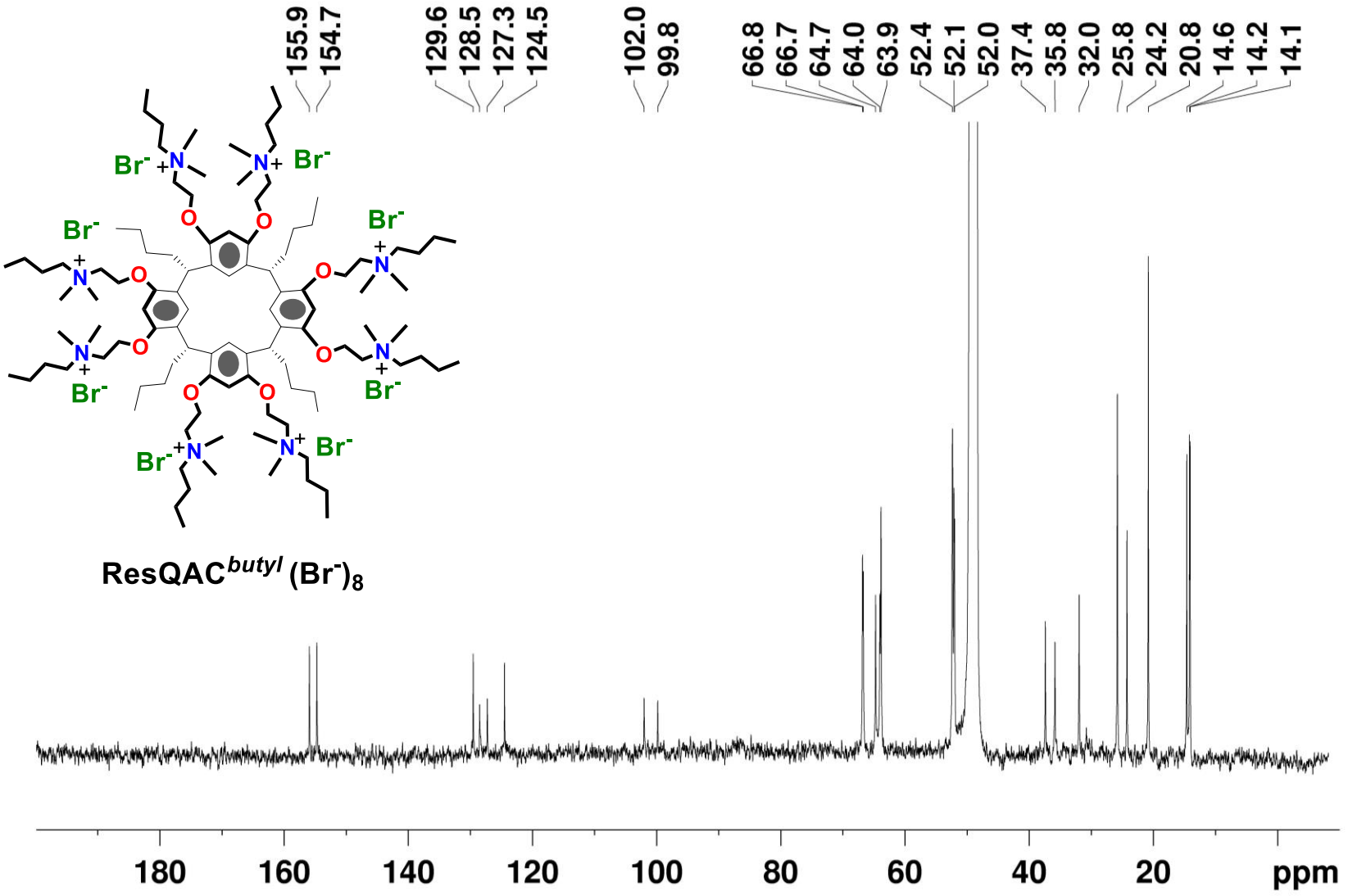
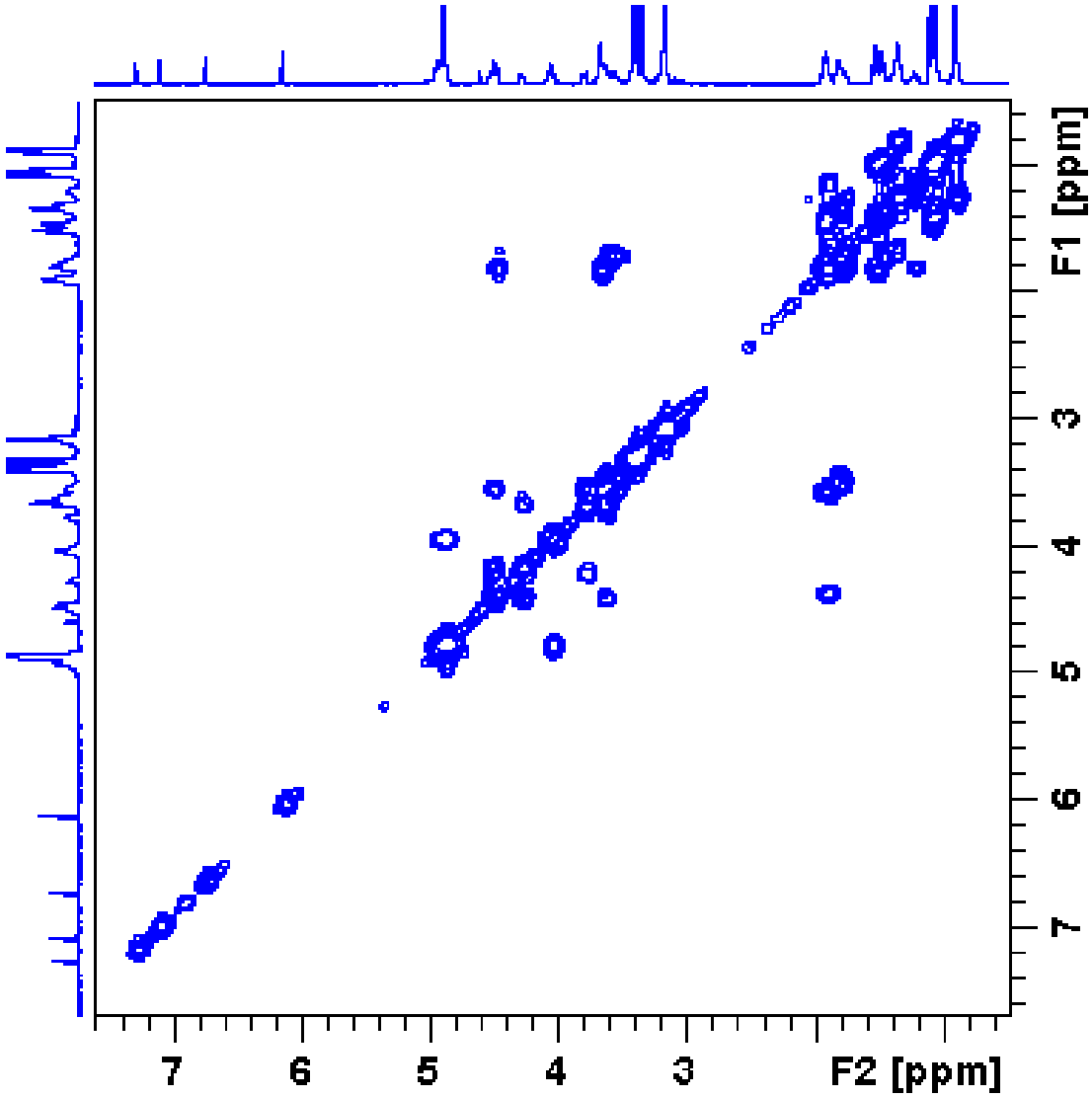


Figure S28. ^{13}C NMR spectrum (125 MHz, CD_3OD, 298 K) of **ResQAC^{butyl}(Br$^-$)$_8$**.



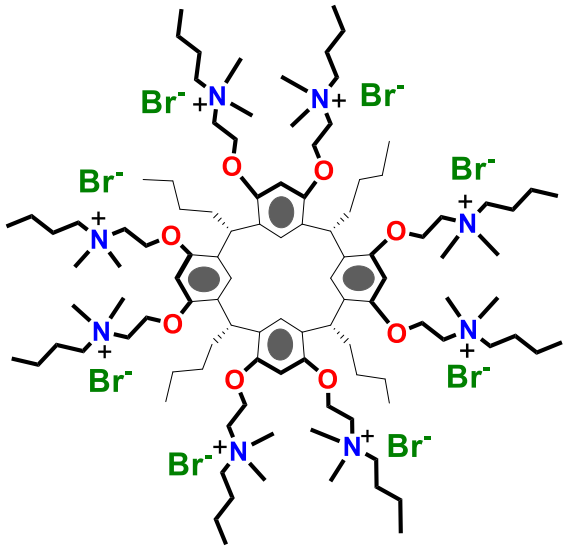
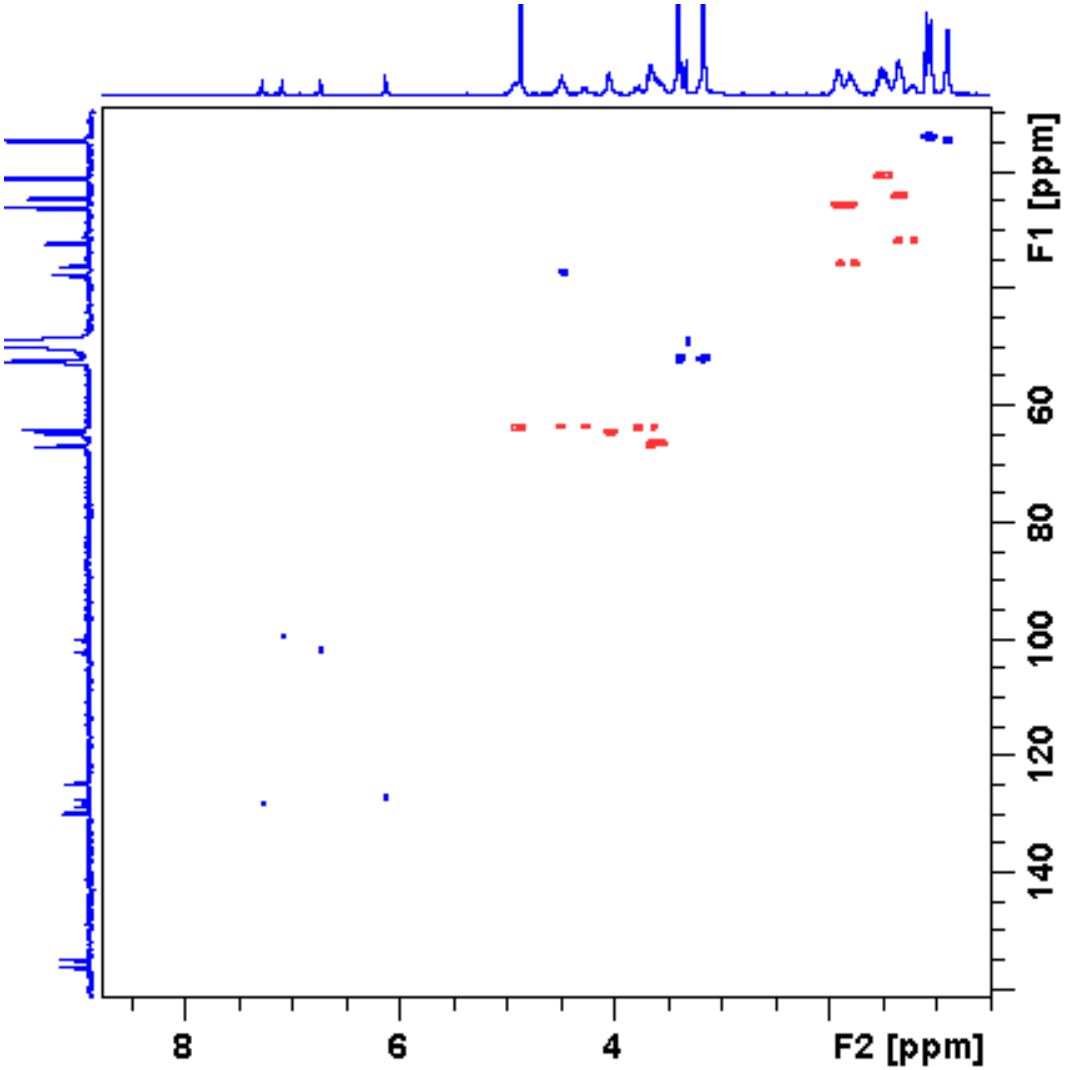
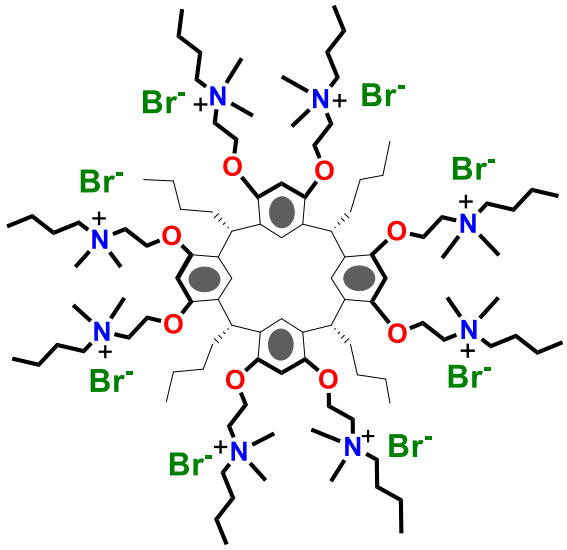


Figure S29. 2D COSY spectrum (400 MHz, CD_3OD, 298 K) of **ResQAC^{butyl}(Br$^-$)$_8$**.





ResQAC^{butyl} (Br$^-$)$_8$

Figure S30. 2D COSY spectrum (400 MHz, CD_3OD, 298 K) of **ResQAC^{butyl}(Br$^-$)$_{8.8}$**

HT NMR spectra of ResQAC^{butyl}(Br$^-$)$_8$

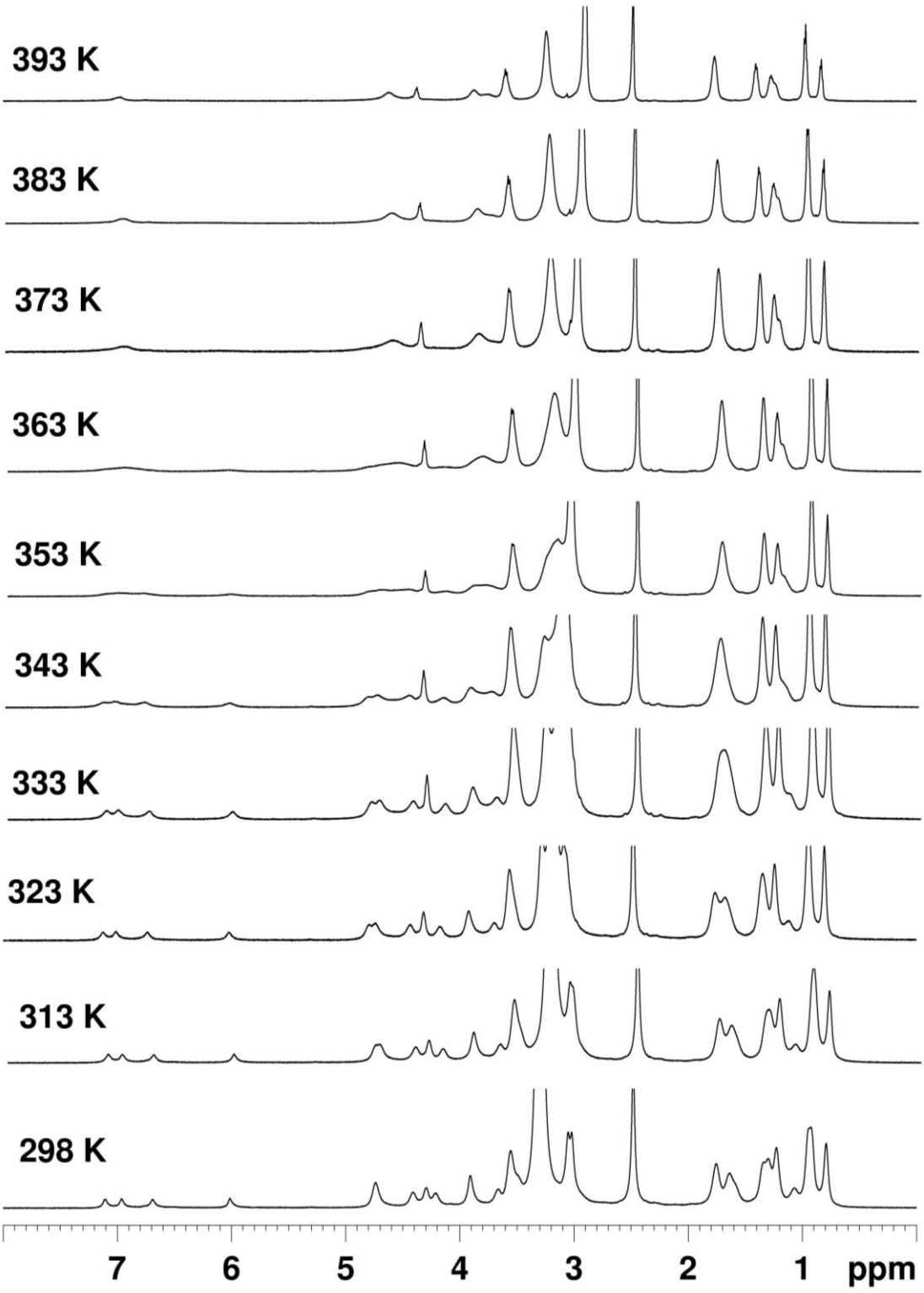


Figure S31. ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{butyl}(Br$^-$)$_8$**.

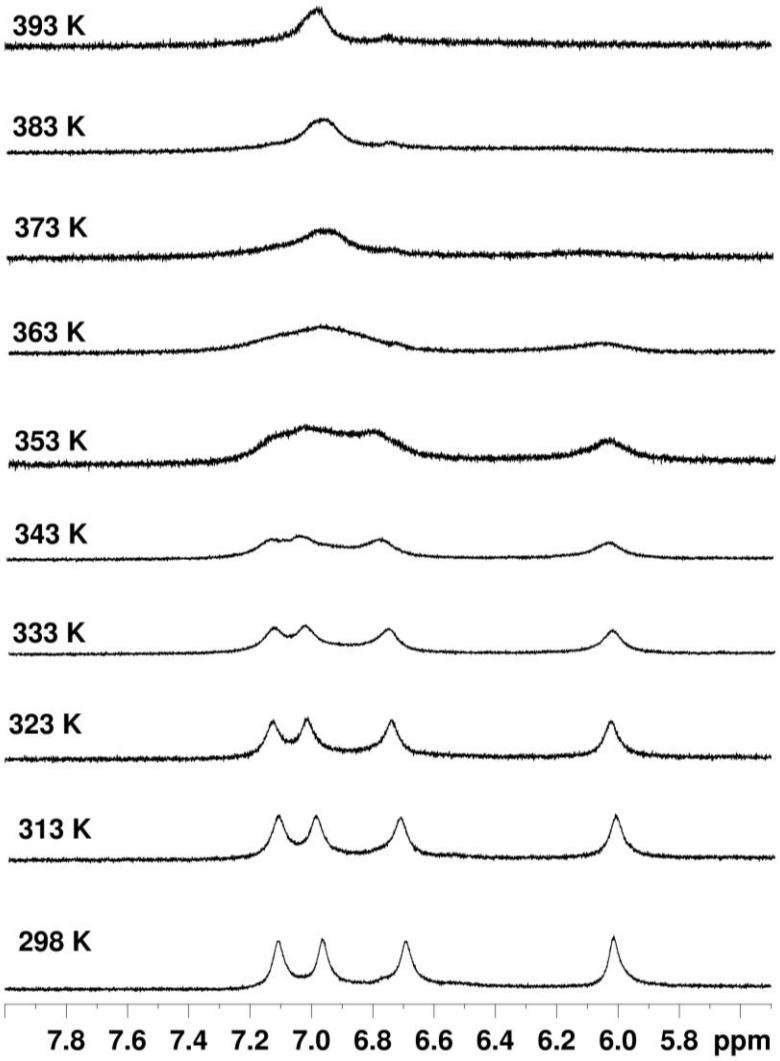


Figure S32. Aromatic portion of ^{1}H NMR spectra (600 MHz, DMSO-d_6) of **ResQAC^{butyl}(Br^{-})$_8$**.

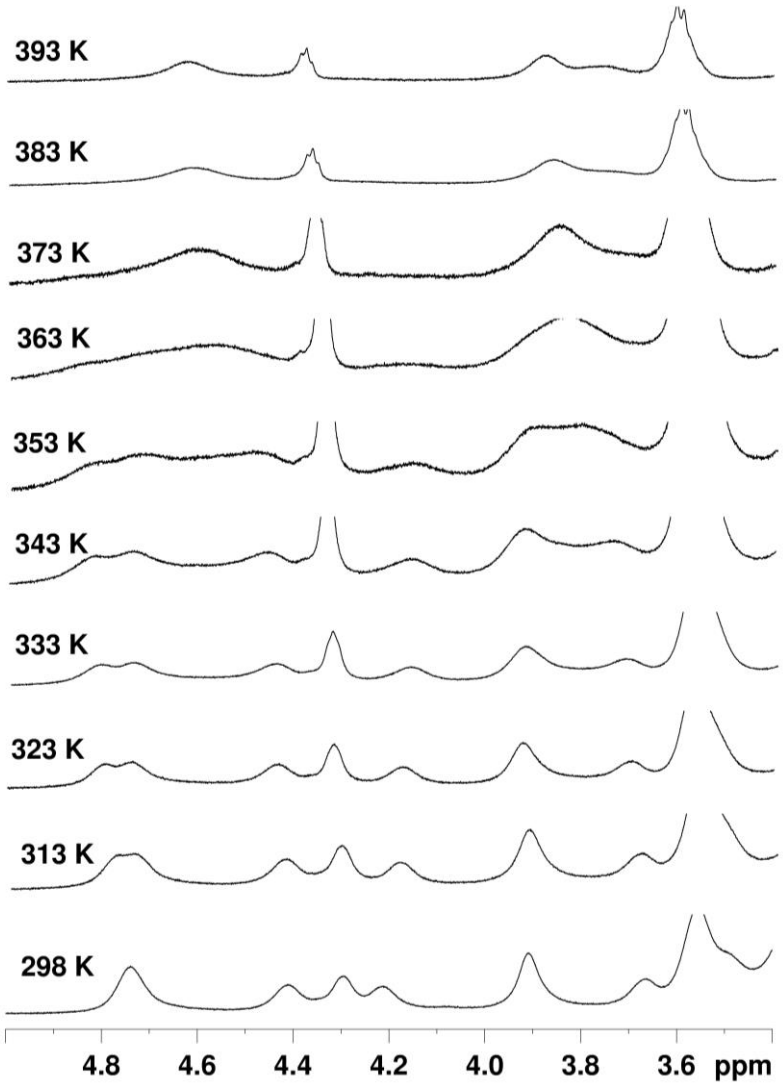


Figure S33. portion of ^{1}H NMR spectra (600 MHz, DMSO-d_6) of **ResQAC^{butyl}(Br^{-})$_8$**.

HRMS ESI spectrum of ResQAC^{butyl}(Br$^-$)$_8$

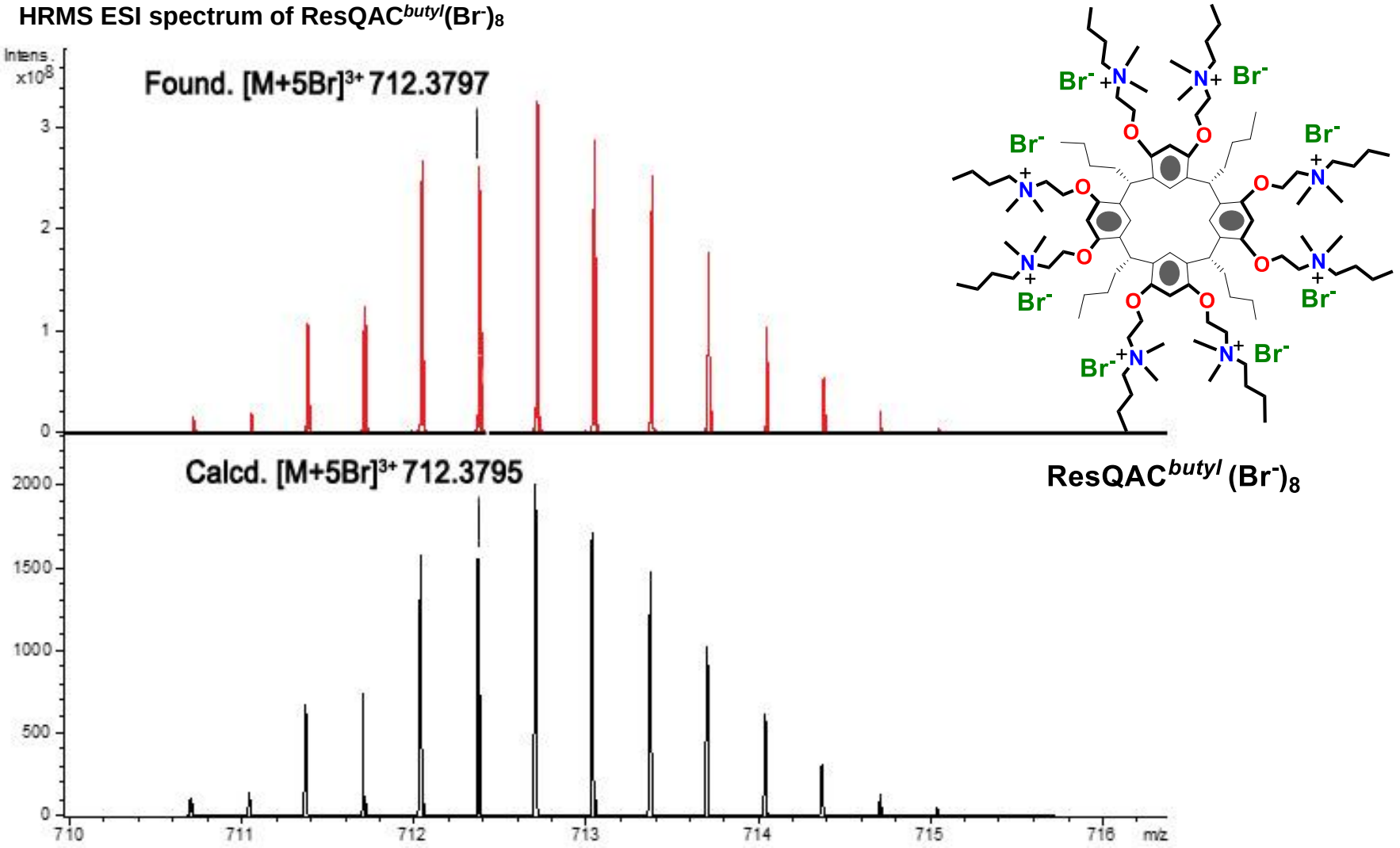


Figure S34. HRMS ESI spectrum of **ResQAC^{butyl}(Br$^-$)$_8$.**

NMR spectra of ResQAC^{undecyl}(Br$^-$)$_8$

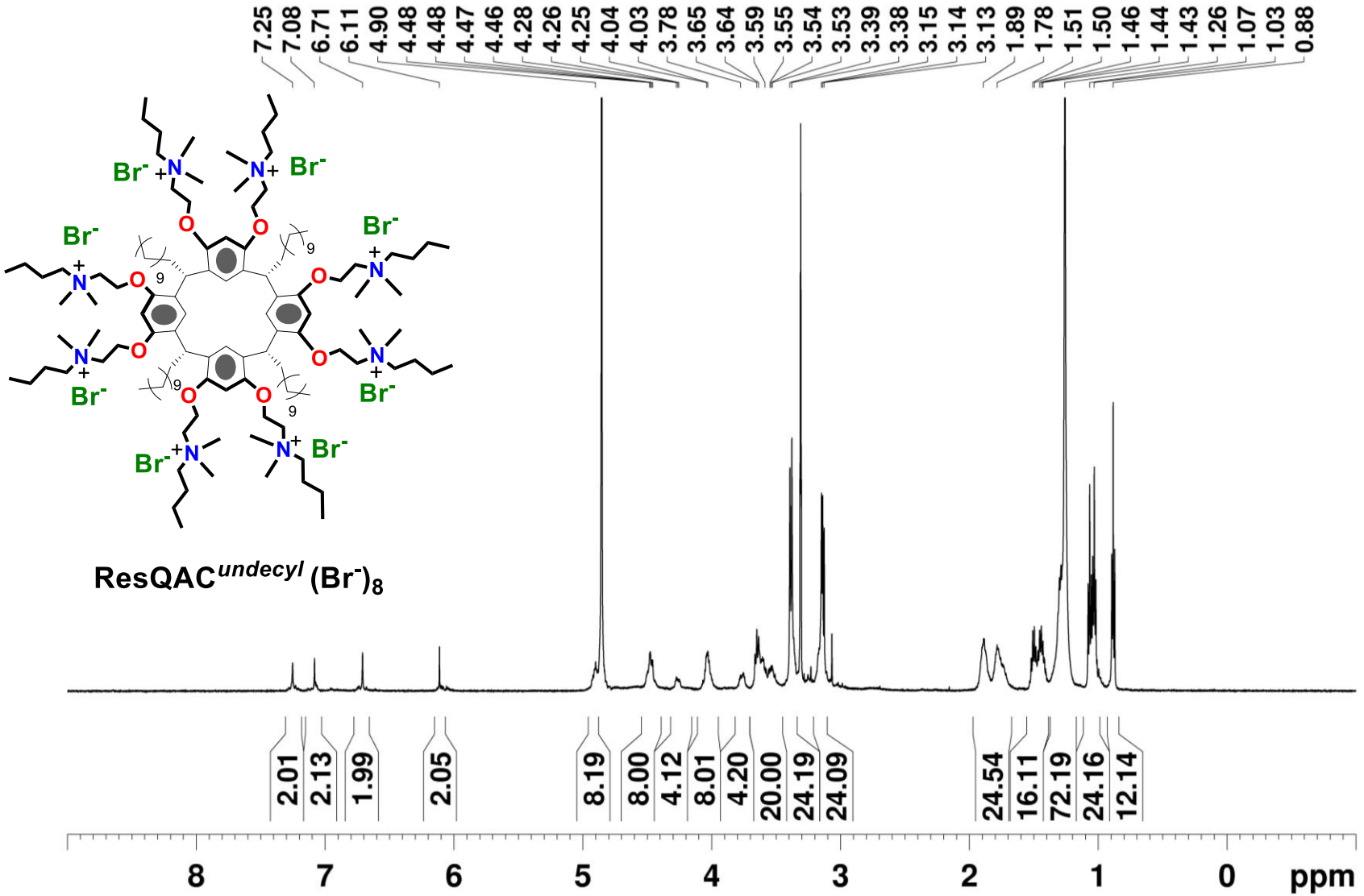


Figure S35. ^{1}H NMR spectrum (600 MHz, CD_3OD, 298 K) of **ResQAC^{undecyl}(Br$^-$)$_8$**.

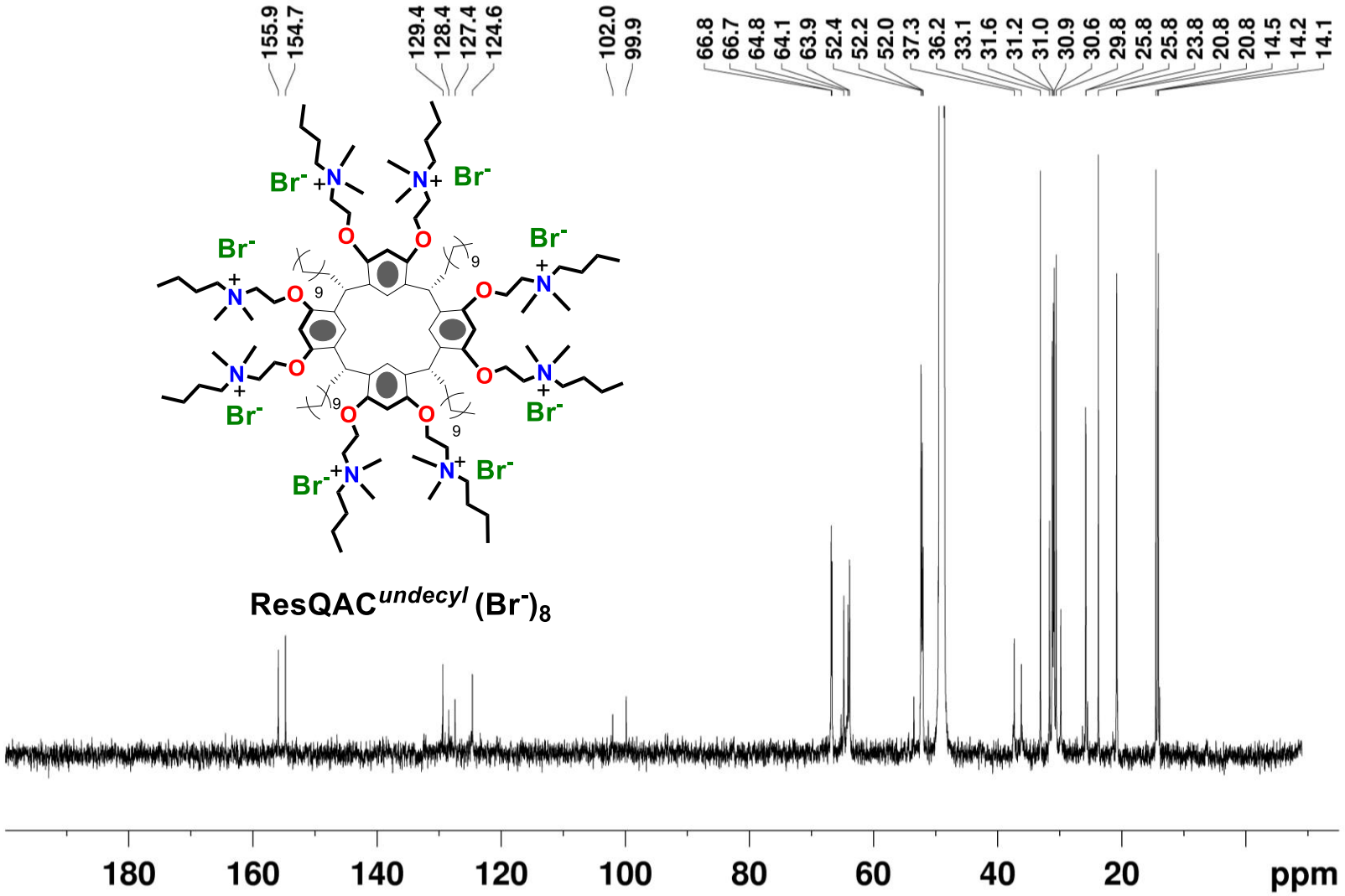
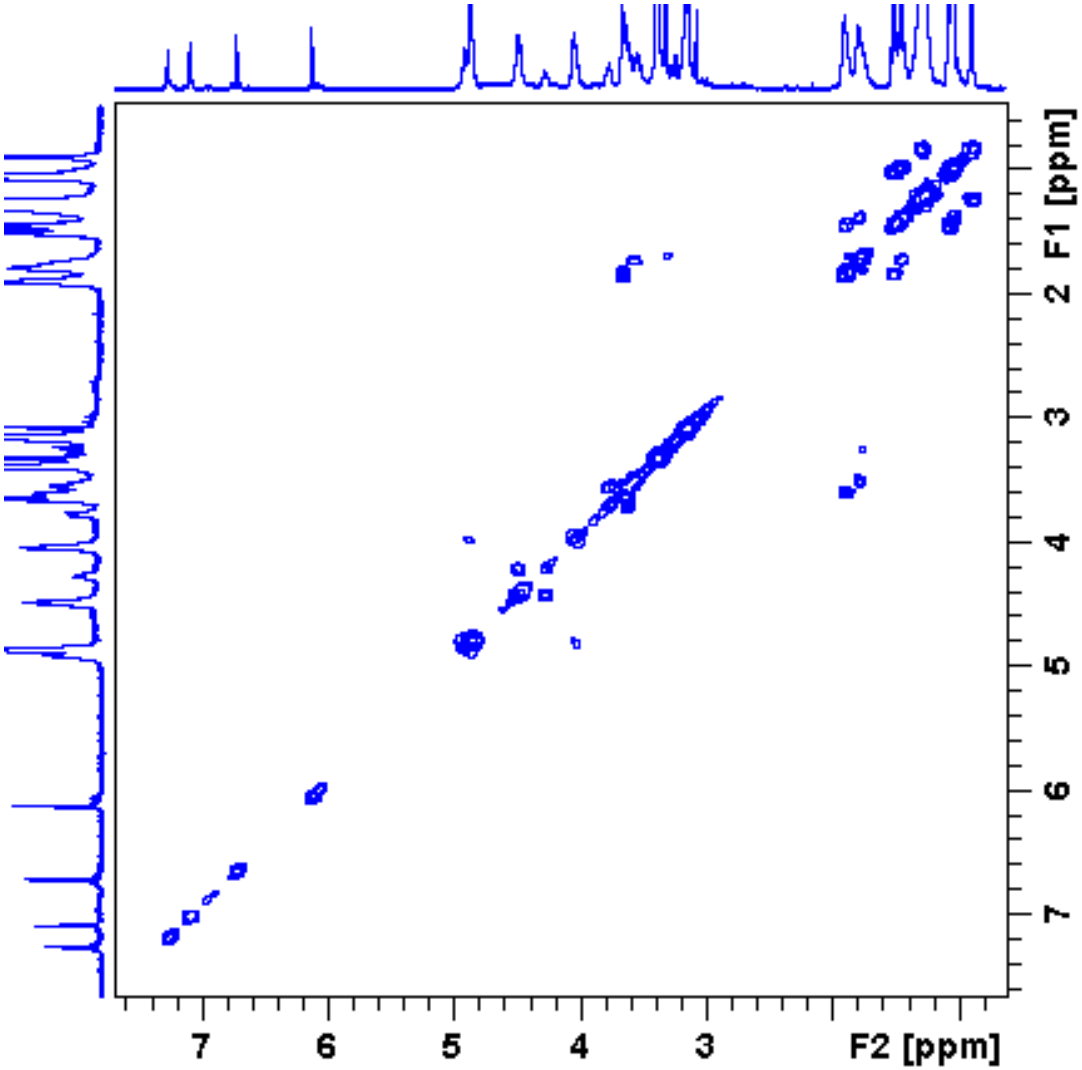
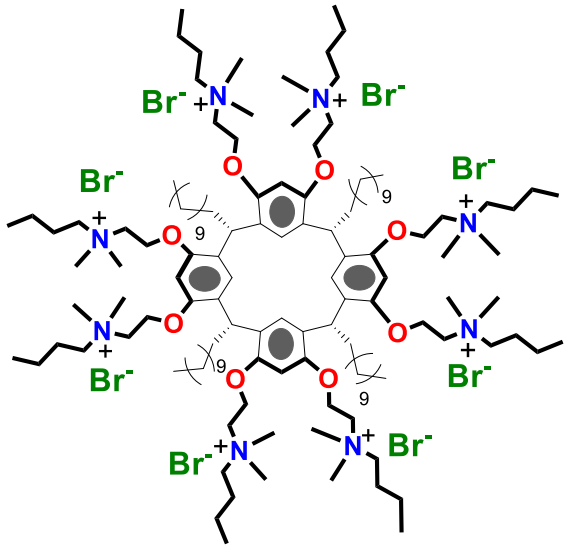


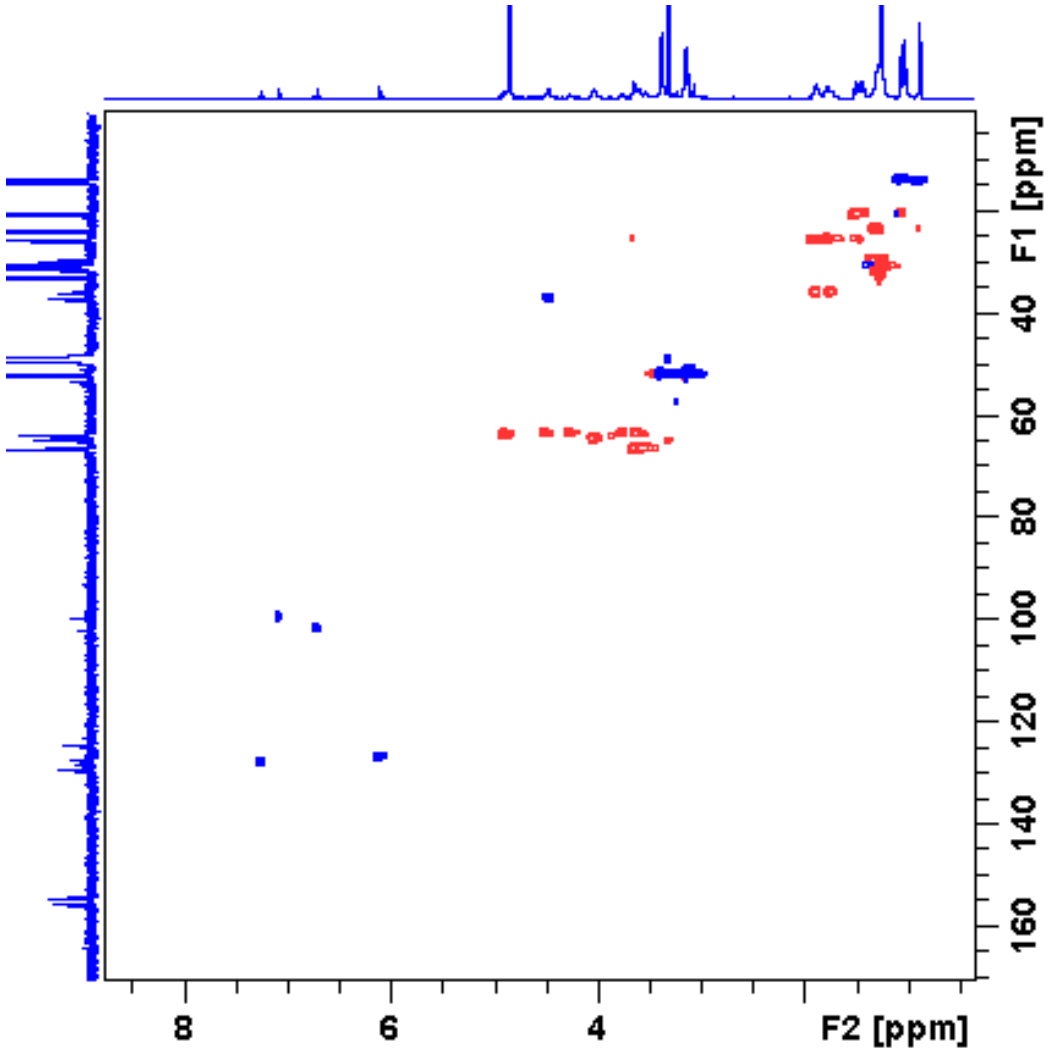
Figure S36. ^{13}C NMR spectrum (150 MHz, CD_3OD, 298 K) of **ResQAC^{undecyl}(Br$^-$)$_8$**.

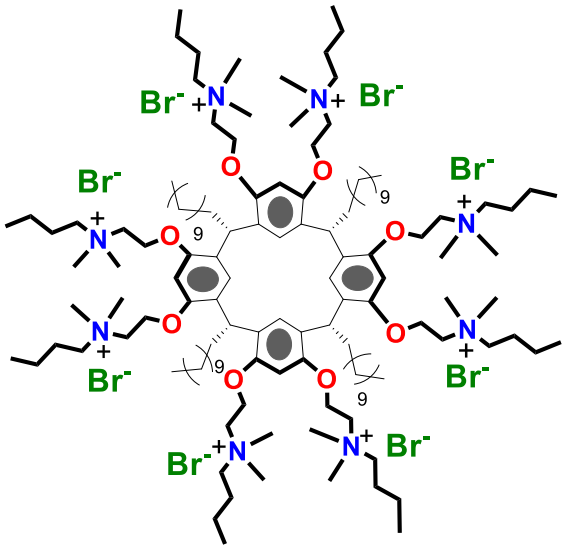




ResQAC^{undecyl} (Br$^-$)$_8$

Figure S37. 2D COSY spectrum (600 MHz, CD_3OD, 298 K) of **ResQAC^{undecyl}(Br$^-$)$_8$**.





ResQAC^{undecyl} (Br$^-$)$_8$

Figure S38. 2D HSQC spectrum (600 MHz, CD_3OD, 298 K) of **ResQAC^{undecyl}(Br$^-$)$_8$**.

HT NMR spectra of ResQAC^{undecyl}(Br$^-$)$_8$

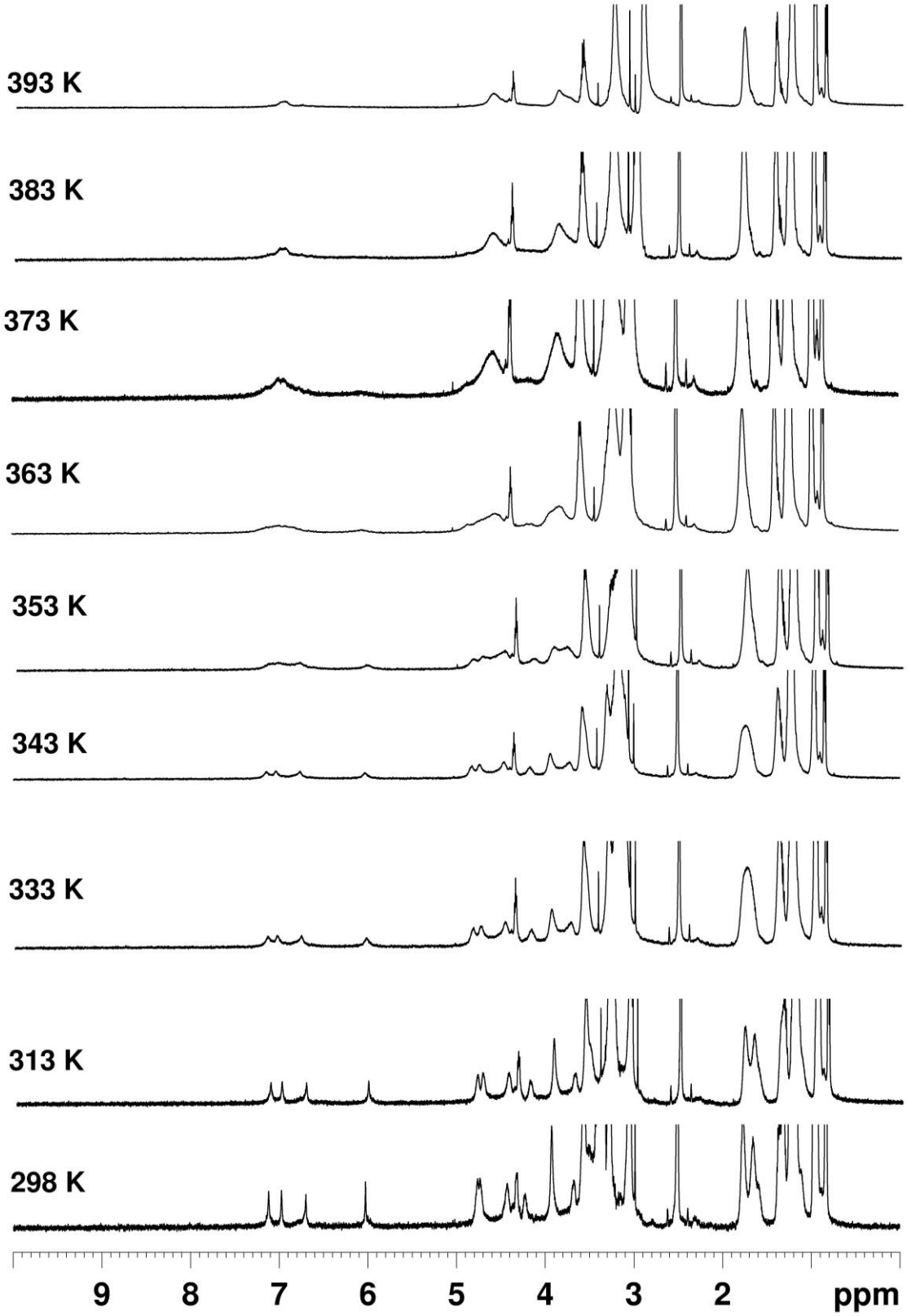


Figure S39. ^{1}H NMR Spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{undecyl}(Br$^-$)$_8$**.

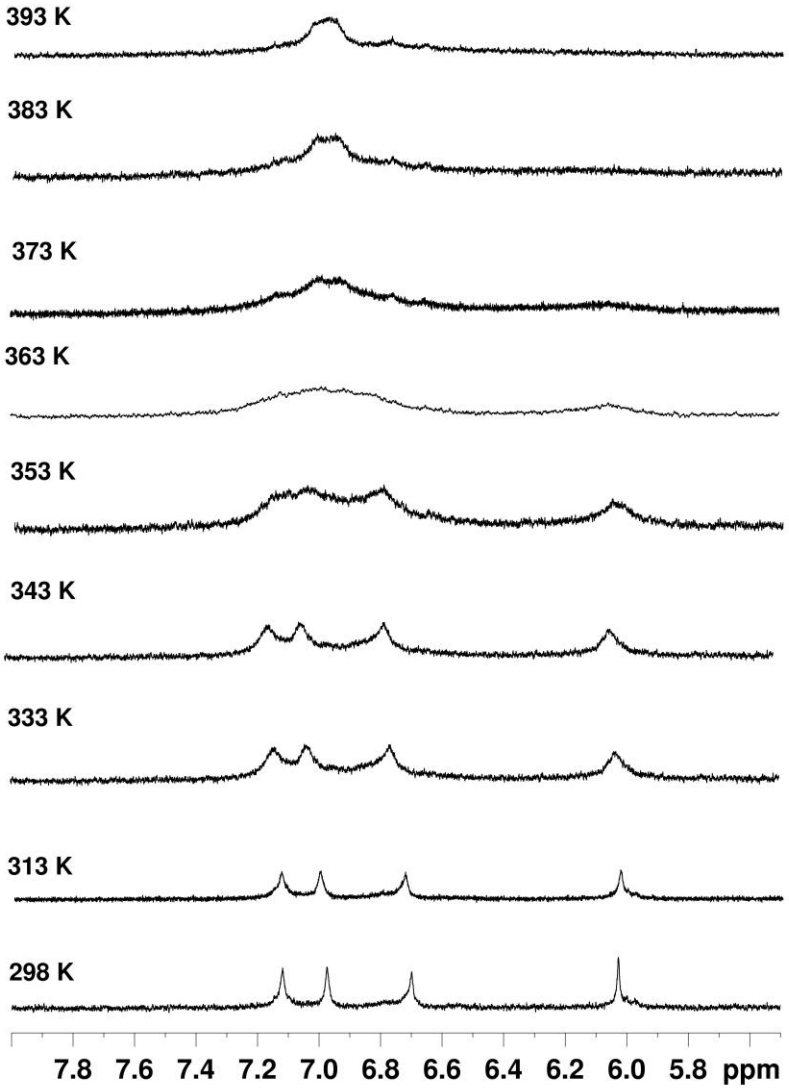


Figure S40. Aromatic portion of ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{undecyl}(Br$^-$)$_8$**

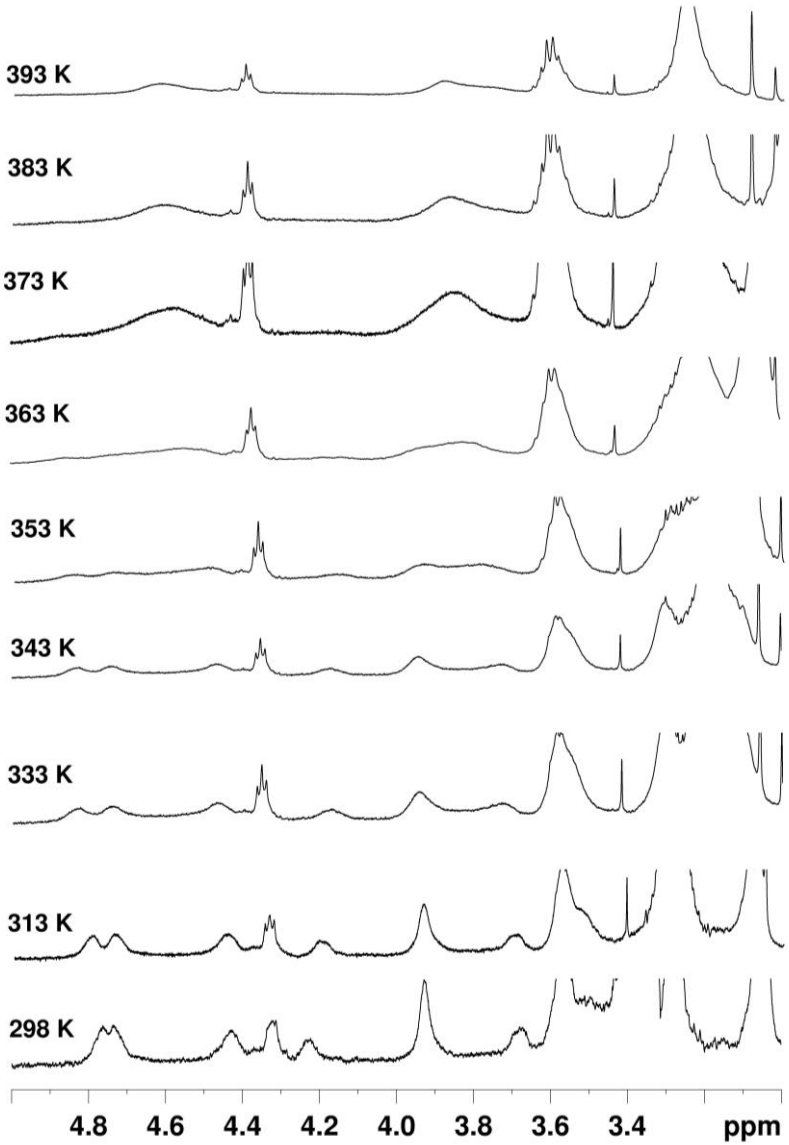


Figure S41. portion of ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{undecyl}(Br$^-$)$_8$**

HRMS ESI spectrum of ResQAC^{undecyl}(Br$^-$)$_8$

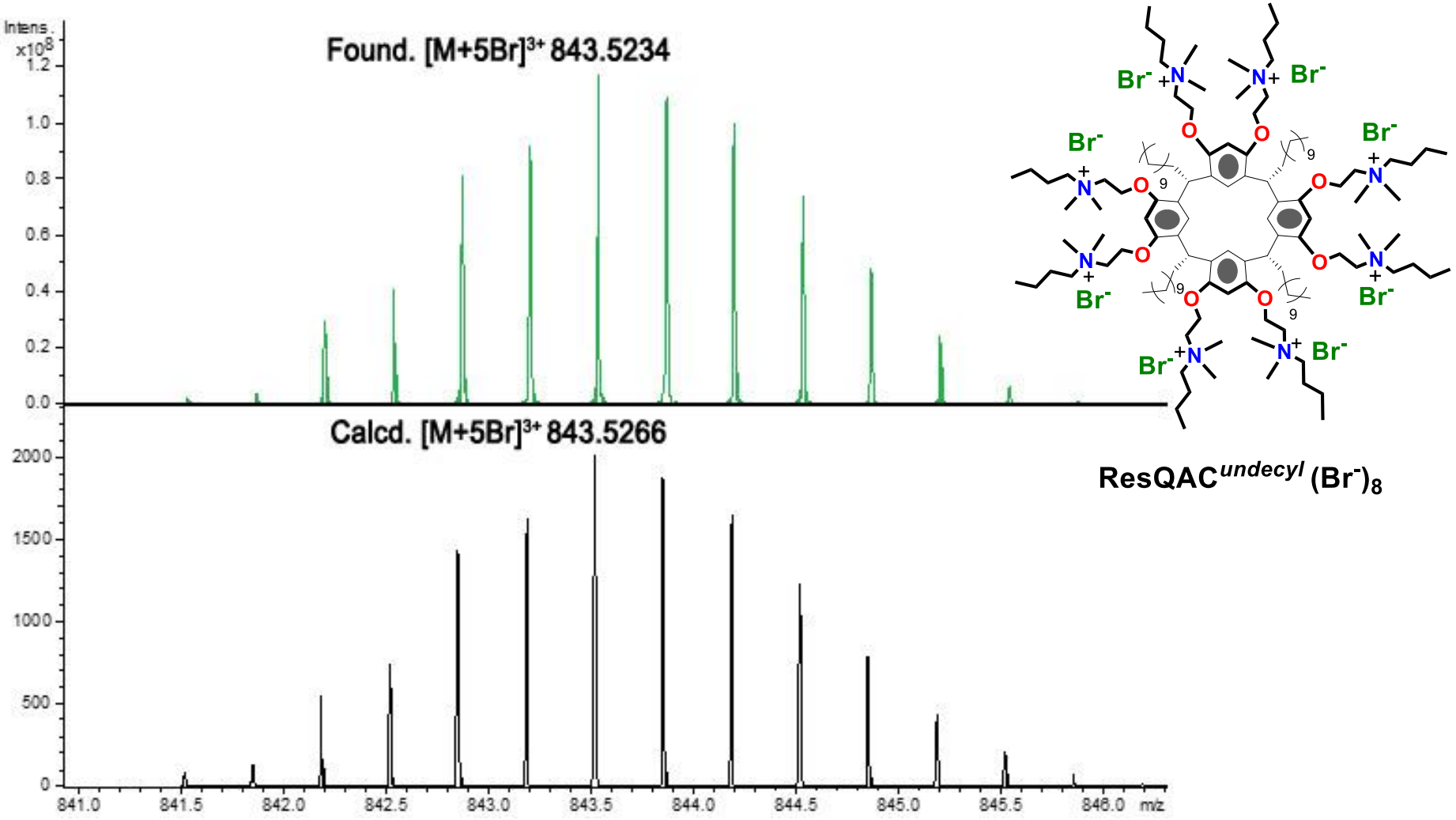


Figure S42. HRMS ESI spectrum of **ResQAC^{undecyl}(Br$^-$)$_8$**

NMR spectra of ResQAC^{phenyl}(Br$^-$)$_8$

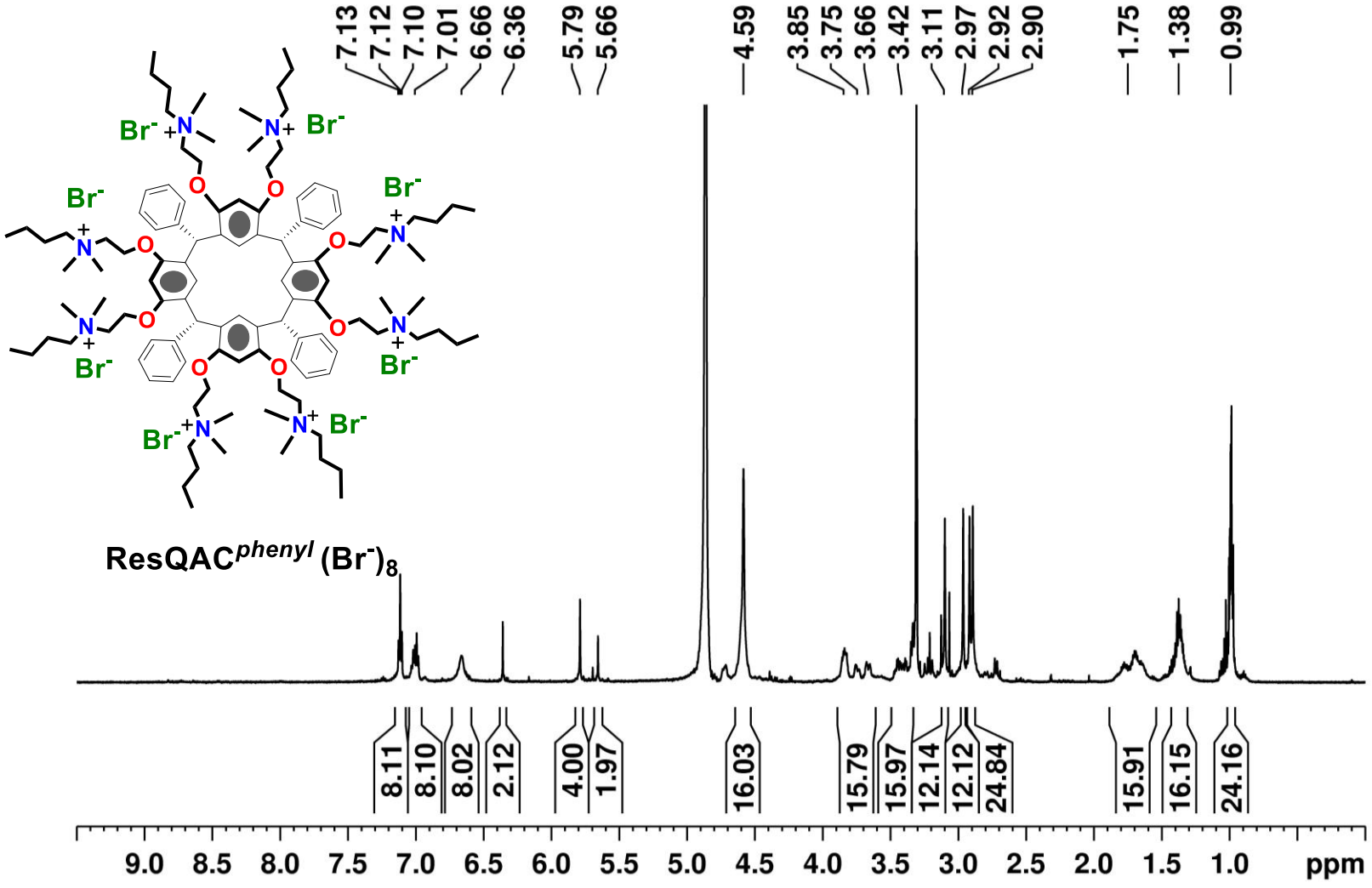


Figure S43. ^{1}H NMR spectrum (600 MHz, CD_3OD, 298 K) of **ResQAC^{phenyl}(Br$^-$)$_8$**.

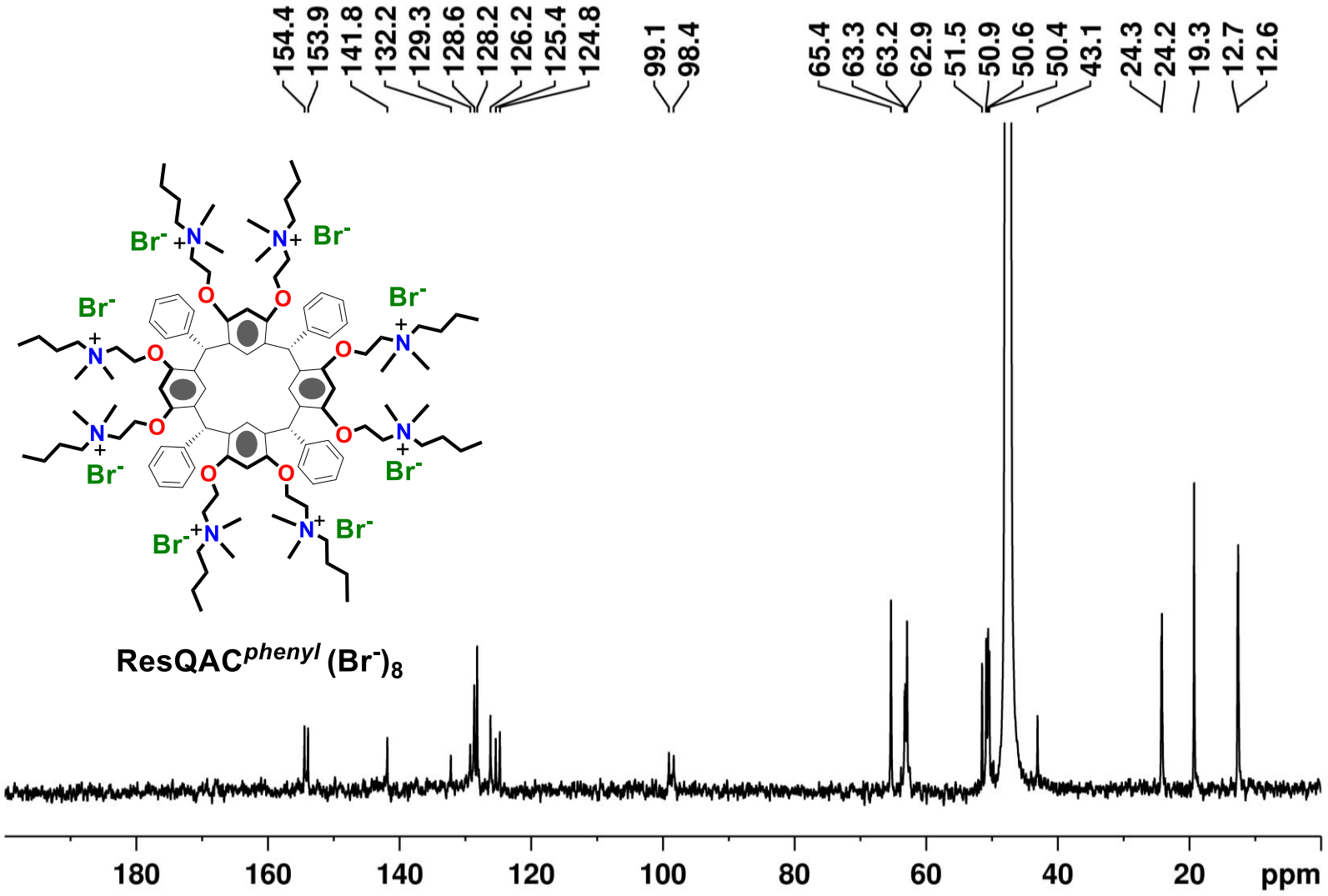


Figure S44. ^{13}C NMR spectrum (150 MHz, CD_3OD, 298 K) of **ResQAC^{phenyl}(Br$^-$)$_8$**.

HT NMR spectra of ResQAC^{phenyl}(Br$^-$)$_8$

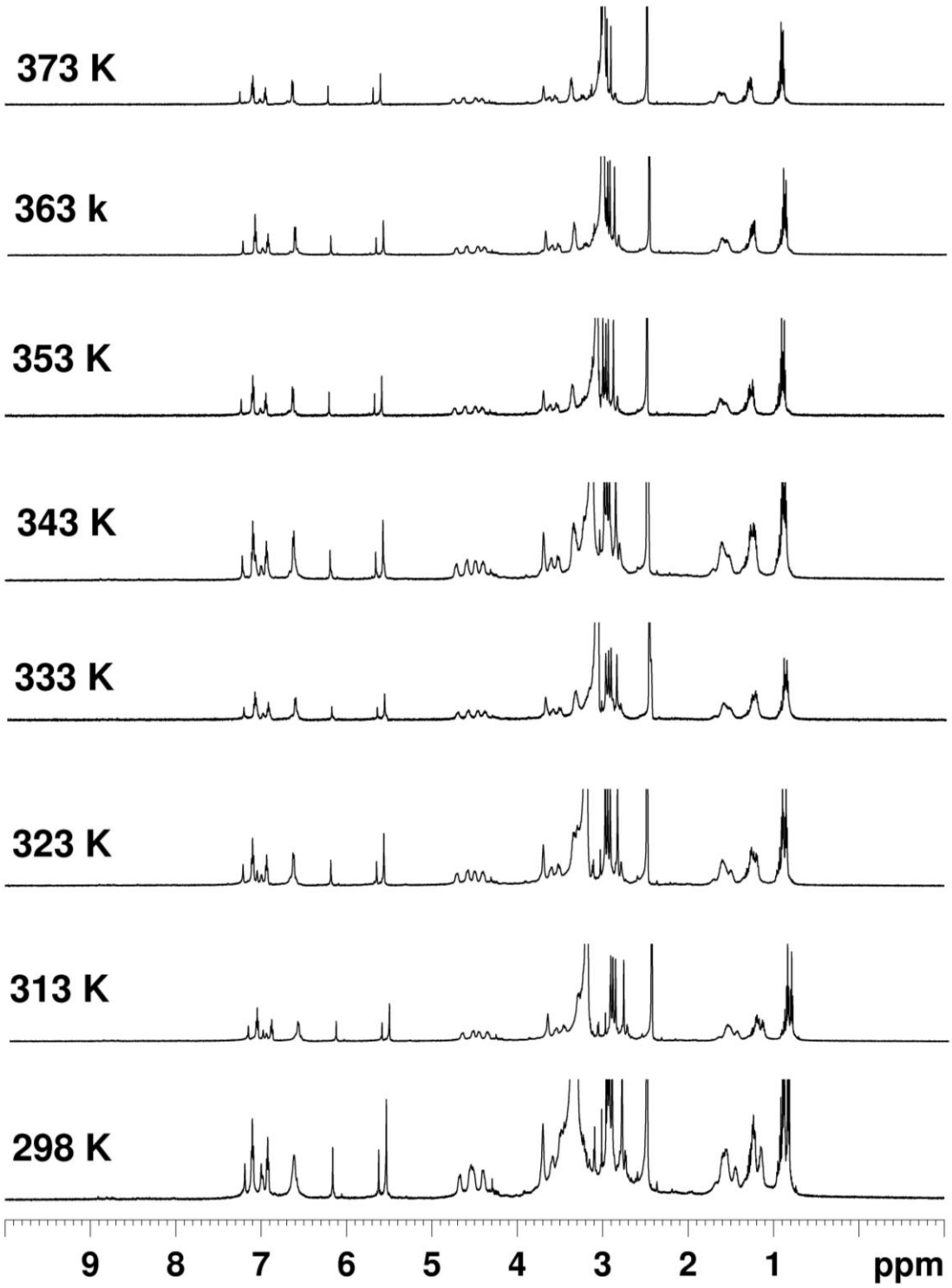


Figure S45. ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{phenyl}(Br$^-$)$_8$**

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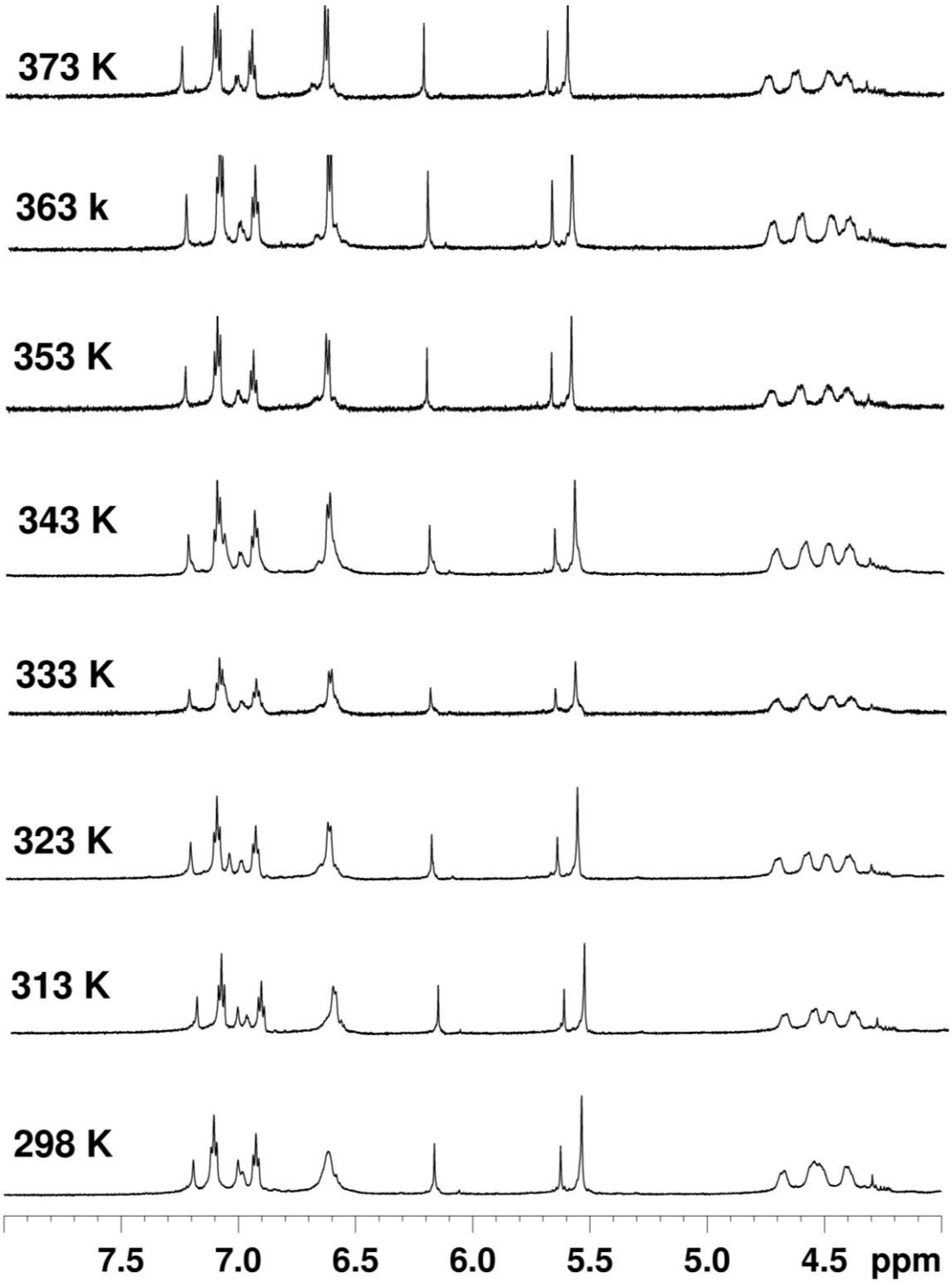


Figure S46. Portion of ^{1}H NMR spectra (600 MHz, DMSO-d_6) of **ResQAC^{phenyl}(Br^{-})$_8$**.

HRMS ESI spectrum of ResQAC^{phenyl}(Br$^-$)$_8$

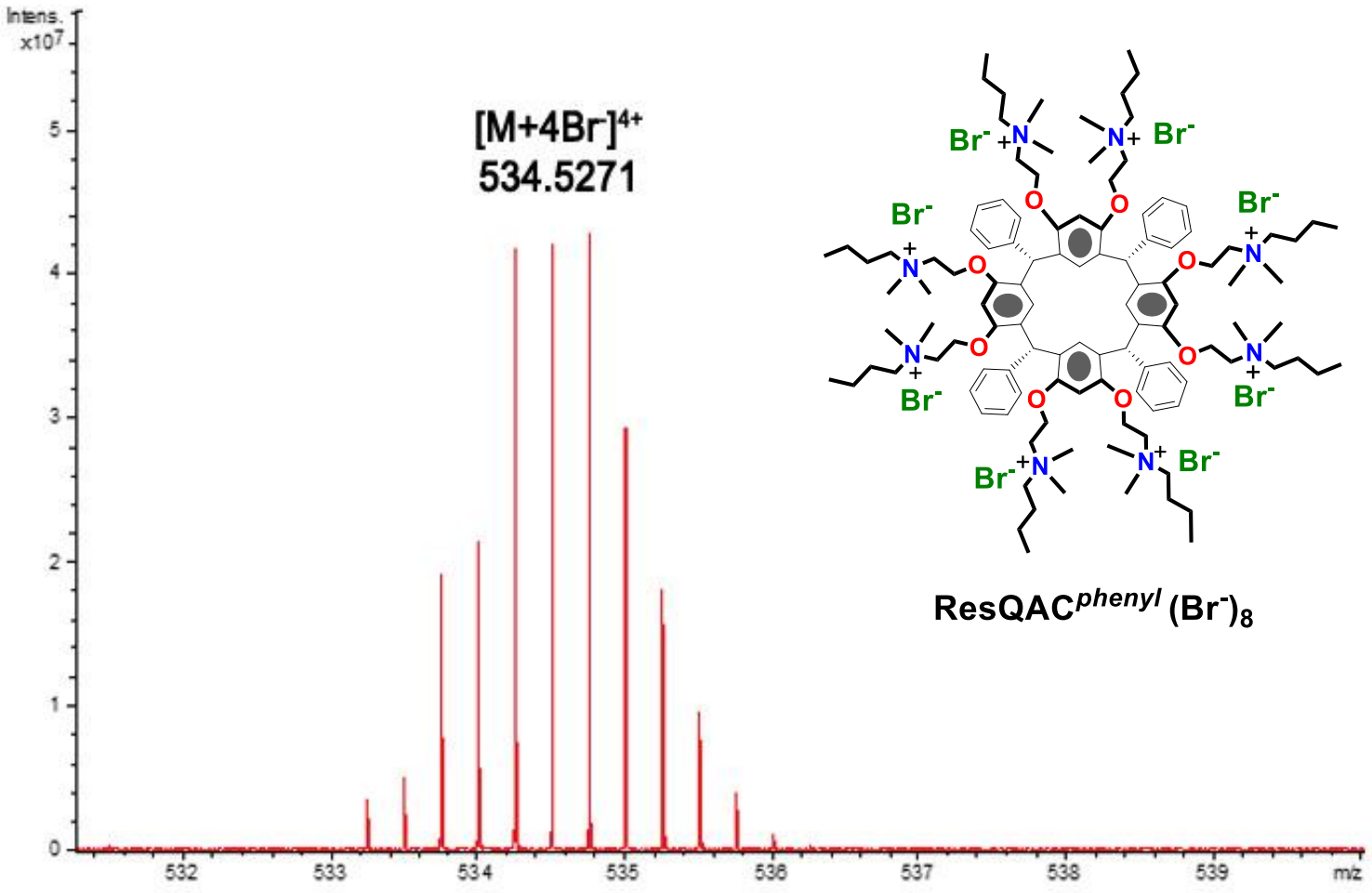


Figure S47. HRMS ESI spectrum of **ResQAC^{phenyl}(Br$^-$)$_8$**

NMR spectra of ResQAC^{butyl}(I$^-$)$_8$

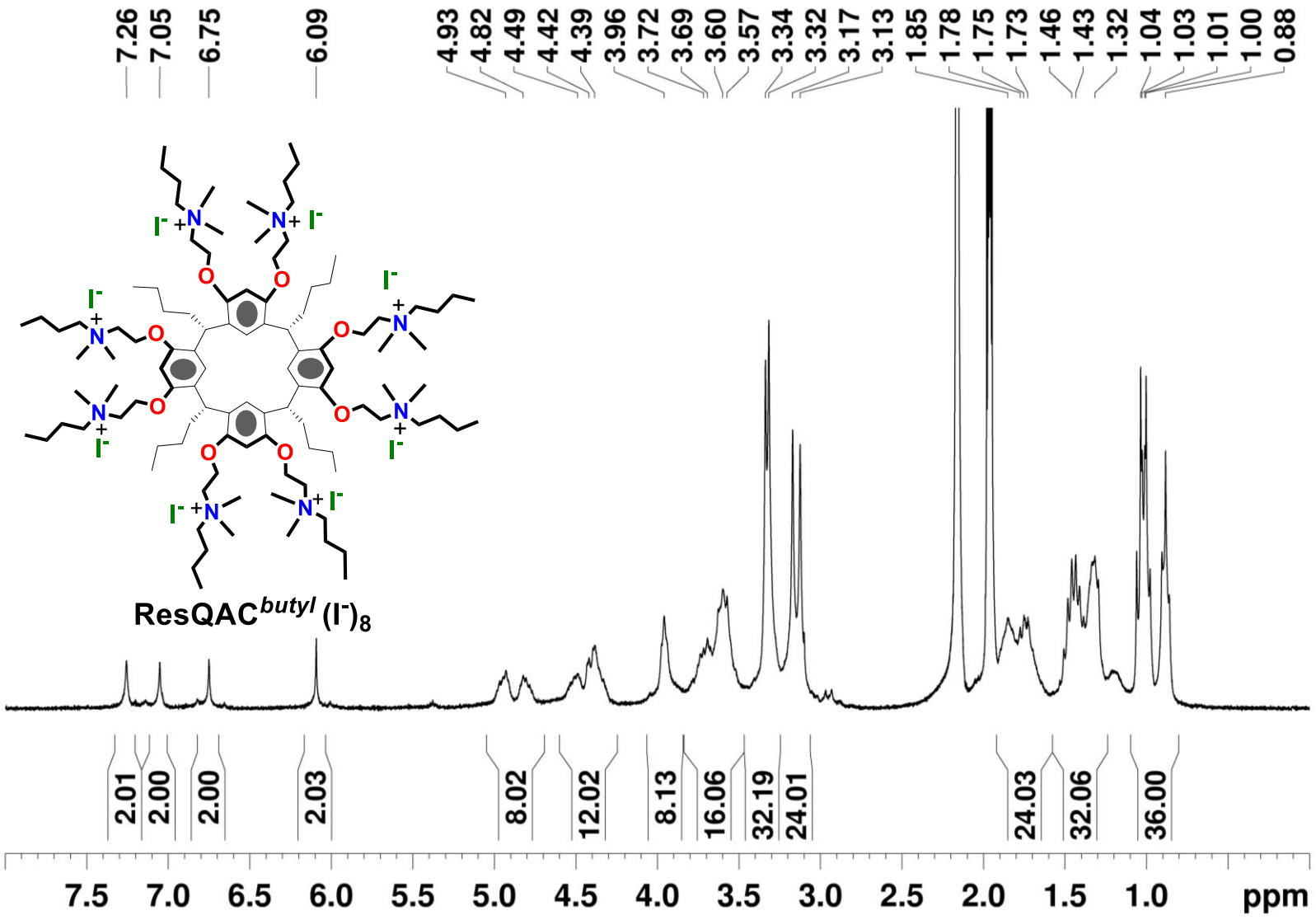


Figure S48. ^{1}H NMR spectrum (400 MHz, CD_3CN, 298 K) of **ResQAC^{butyl}(I$^-$)$_8$**.

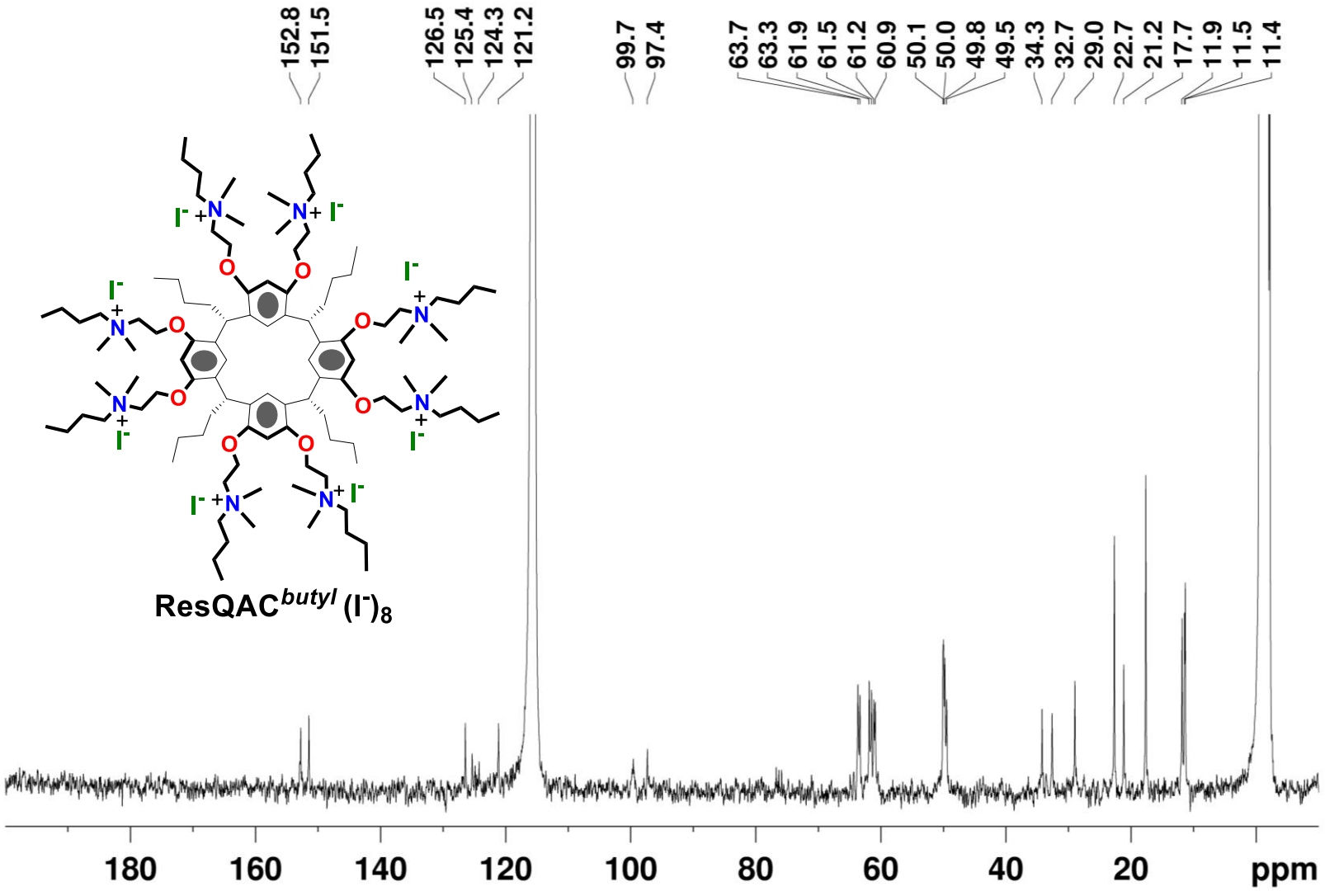


Figure S49. ^{13}C NMR spectrum (75 MHz, CD_3CN, 298 K) of **ResQAC^{butyl}(I$^-$)$_8$**

HRMS ESI spectrum of ResQAC^{butyl}(I^-)$_8$

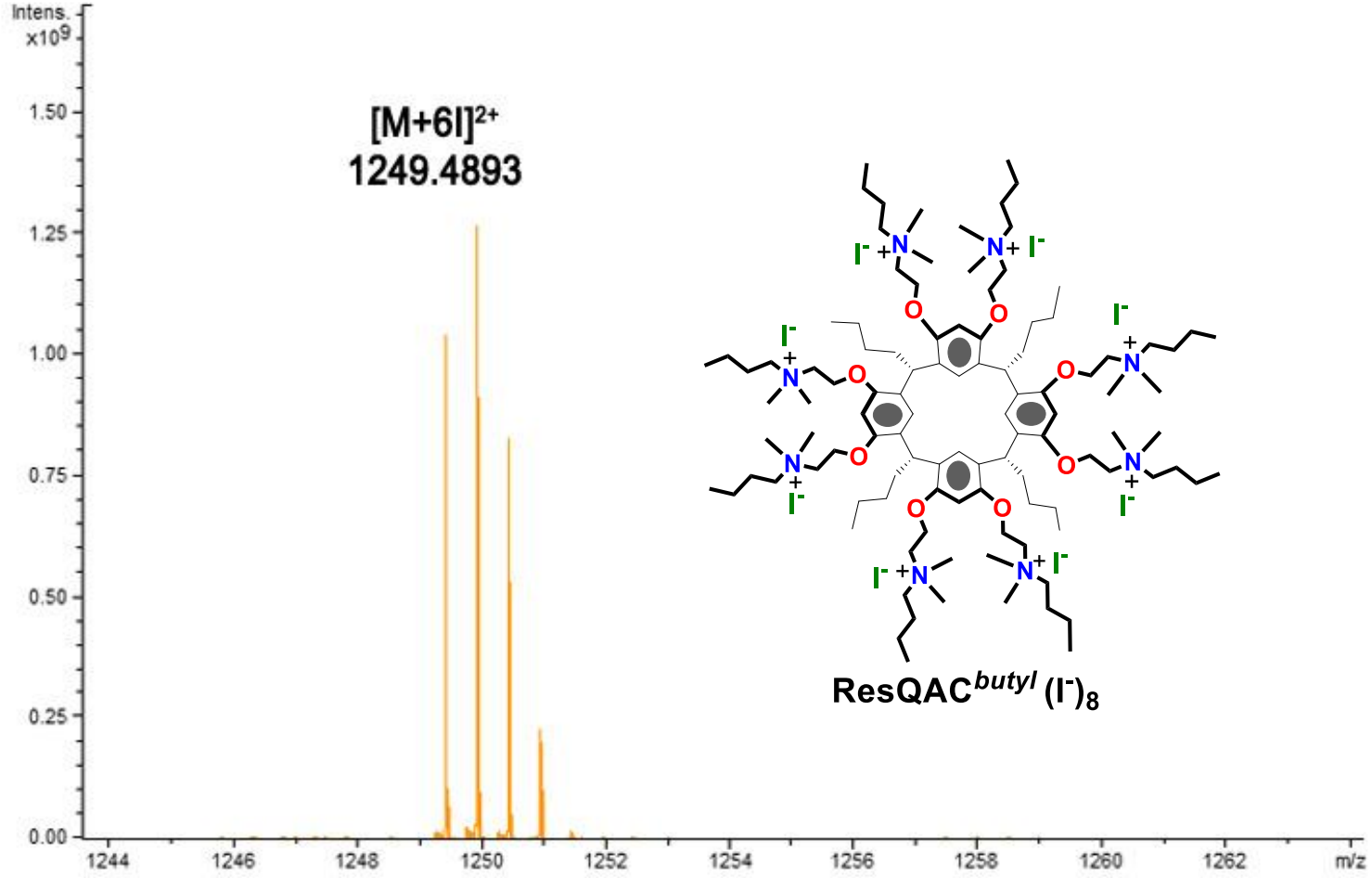


Figure S50. HRMS ESI spectrum of **ResQAC^{butyl}(I^-)$_8$**

NMR spectra of ResQAC^{butyl}(NO_3^-)$_8$

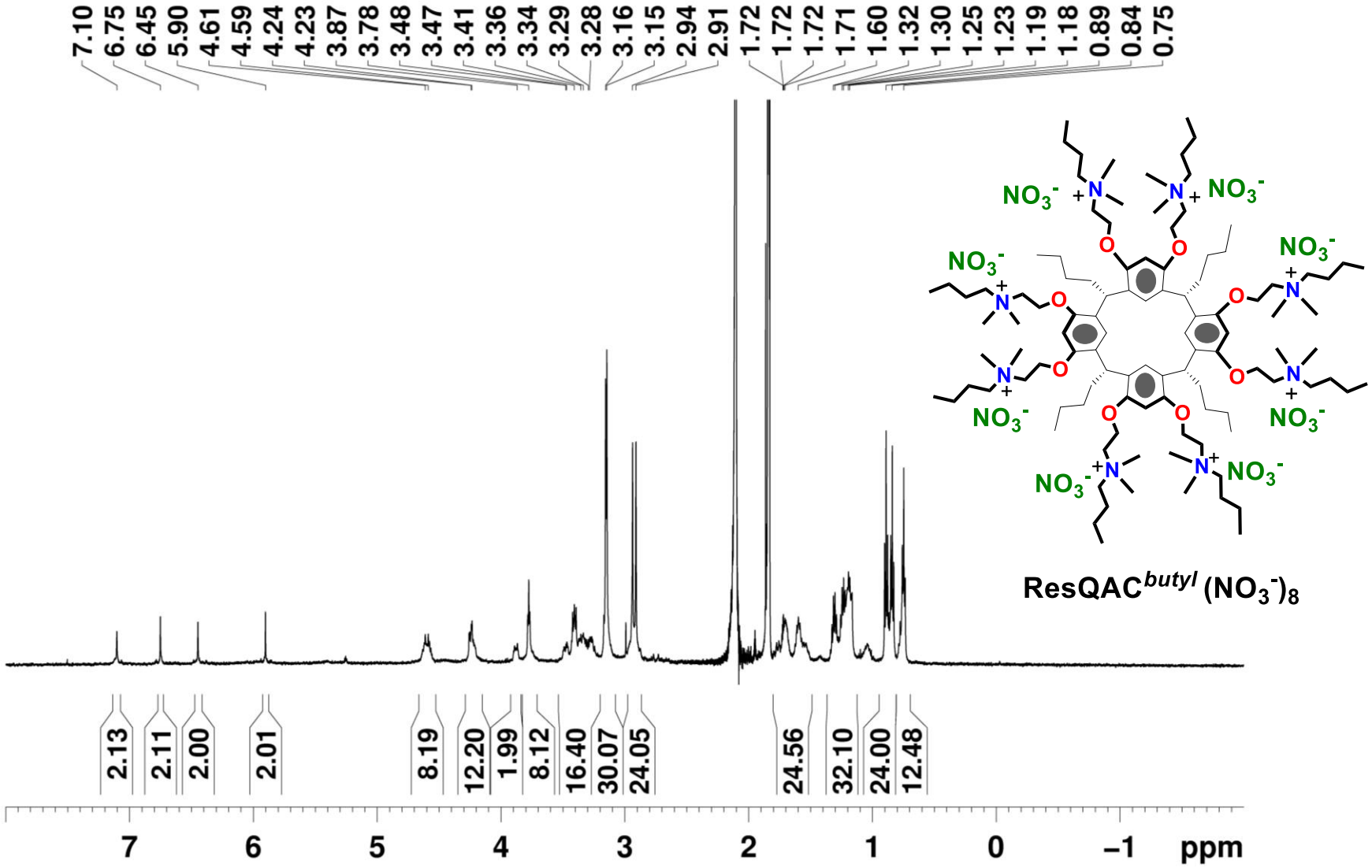


Figure S51. ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of **ResQAC^{butyl}(NO_3^-)$_8$**.

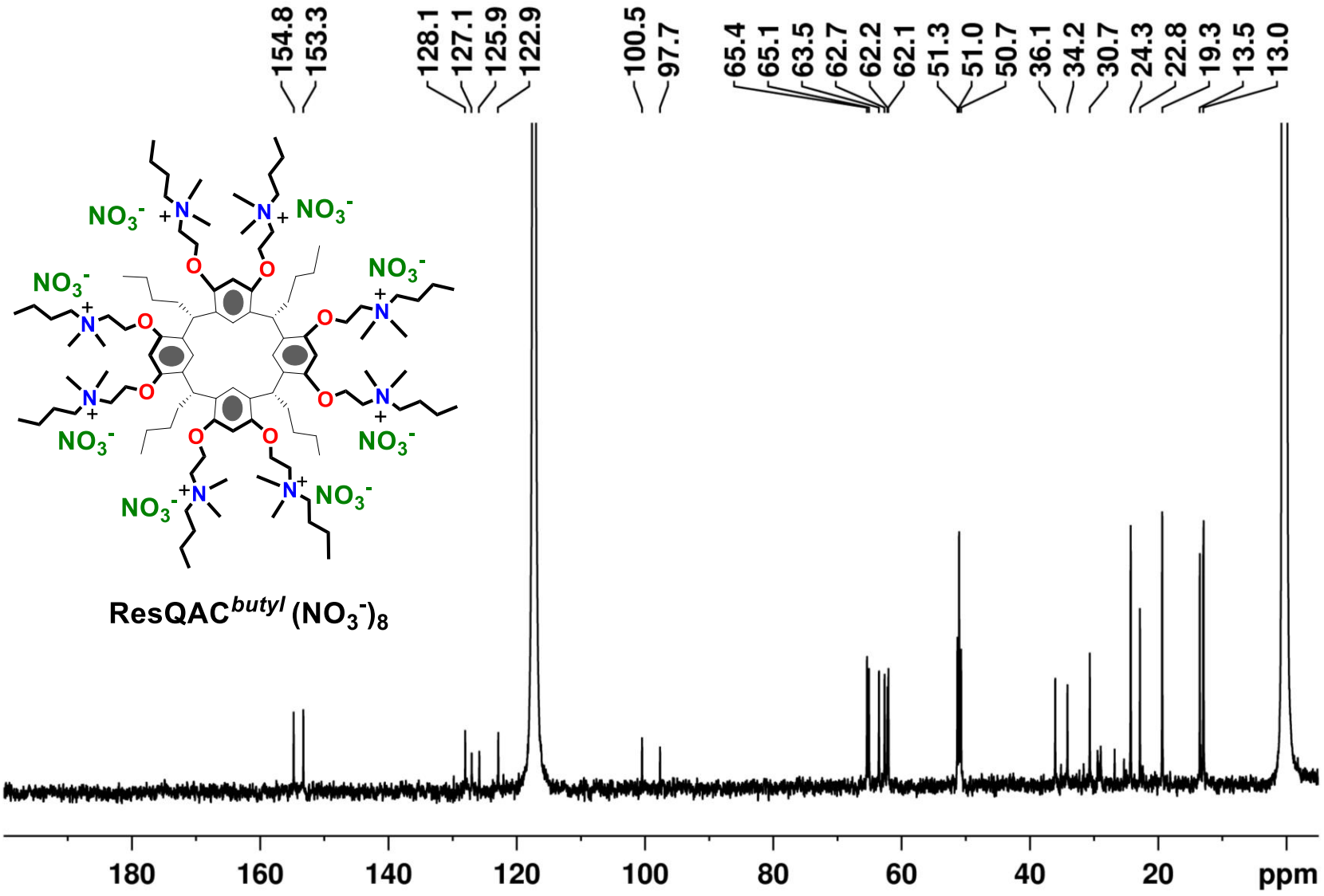


Figure S52. ^{13}C NMR spectrum (150 MHz, CD_3CN, 298 K) of **ResQAC^{butyl}(NO_3^-)$_8$**.

HT NMR spectra of ResQAC^{butyl}(NO_3^-)$_8$

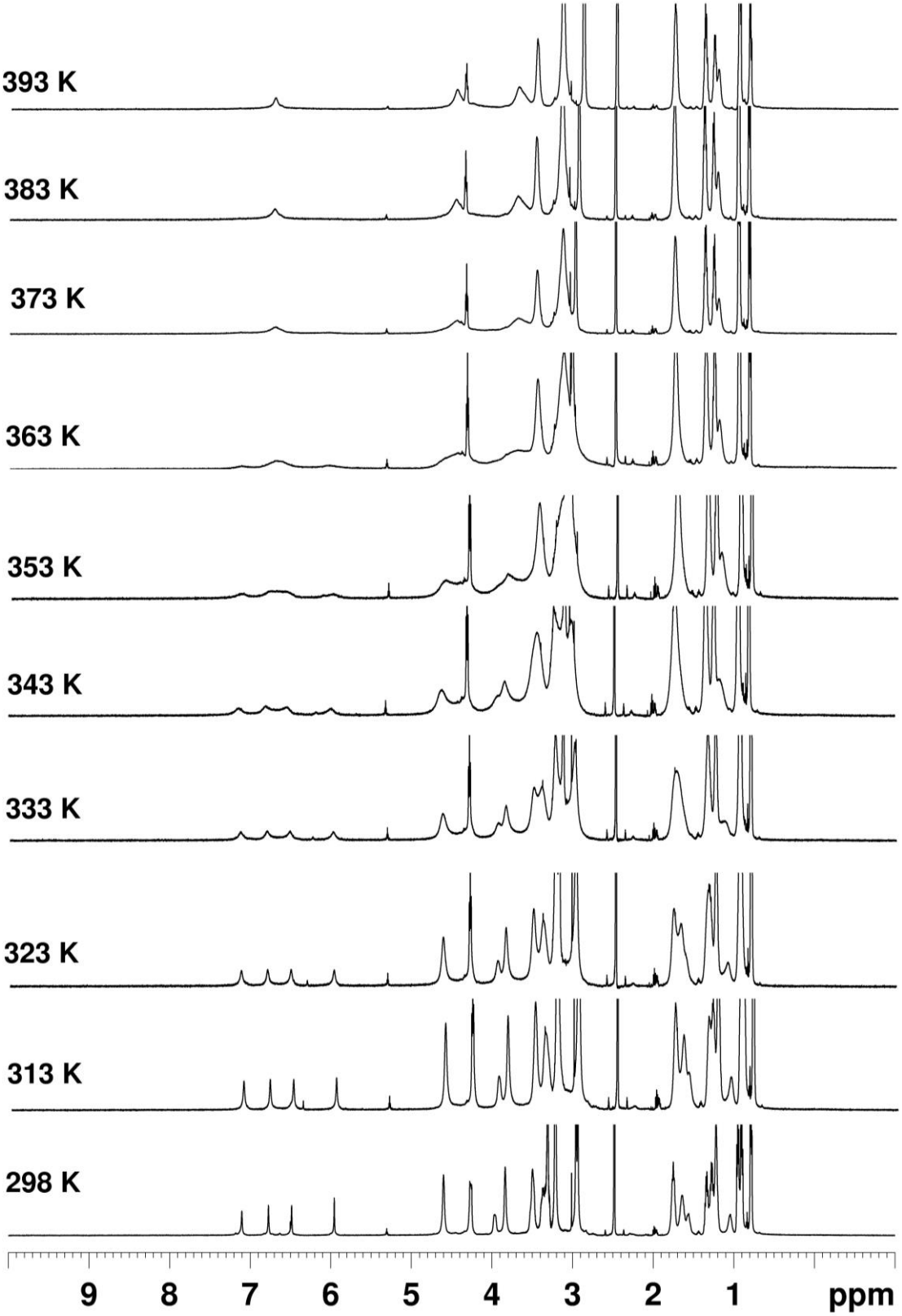


Figure S53. ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{butyl}(NO_3^-)$_8$**.

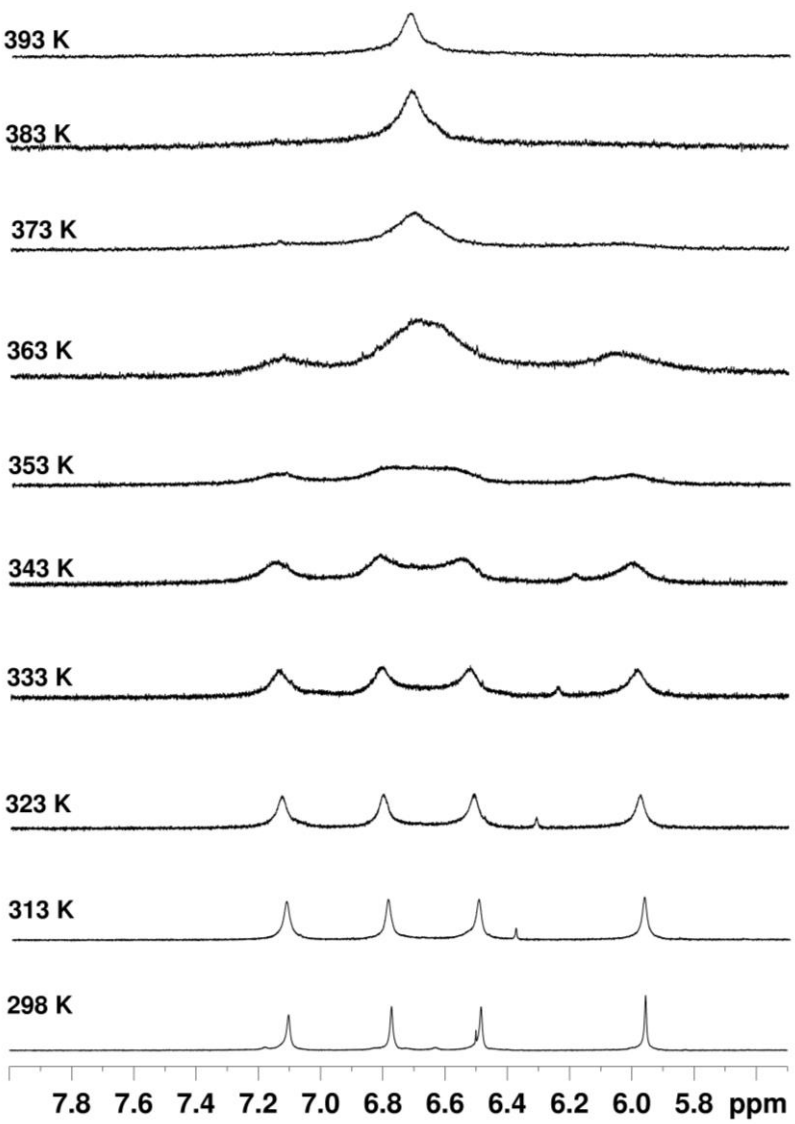


Figure S54. Aromatic portion of ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{butyl}(NO$_3^-$)$_8$**

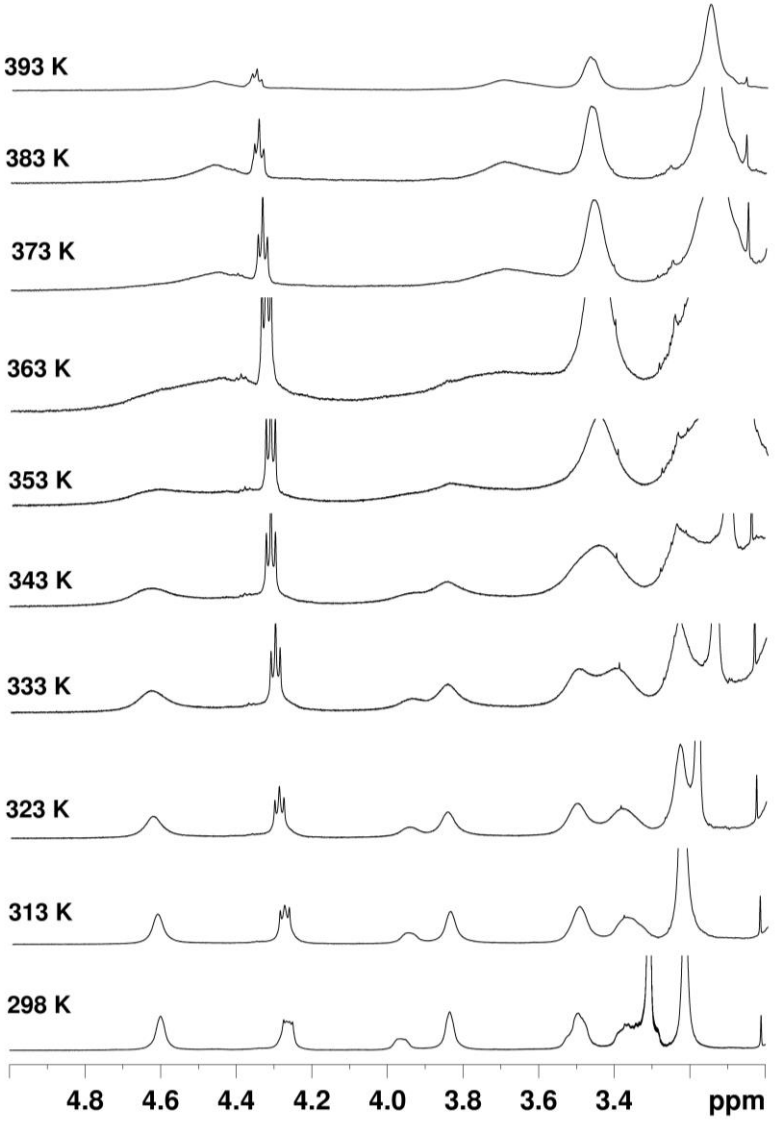


Figure S55. portion of ^{1}H NMR spectra (600 MHz, DMSO-d$_6$) of **ResQAC^{butyl}(NO$_3^-$)$_8$**

HRMS ESI spectrum of ResQAC^{butyl}(NO_3^-)$_8$

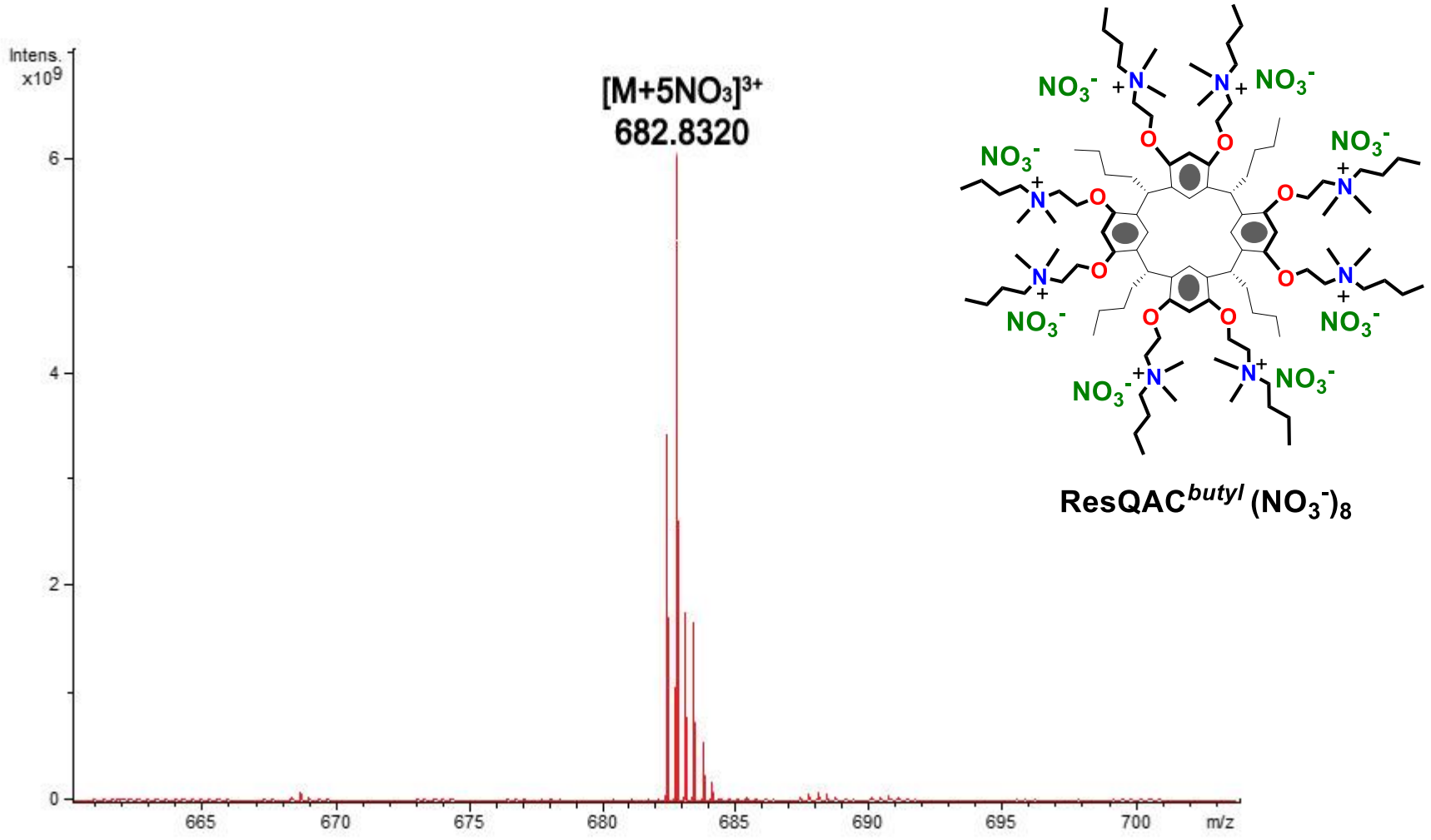


Figure S56. HRMS ESI spectrum of **ResQAC^{butyl}(NO_3^-)$_8$**

NMR spectra of ResQAC^{undecyl}(NO_3^-)$_8$

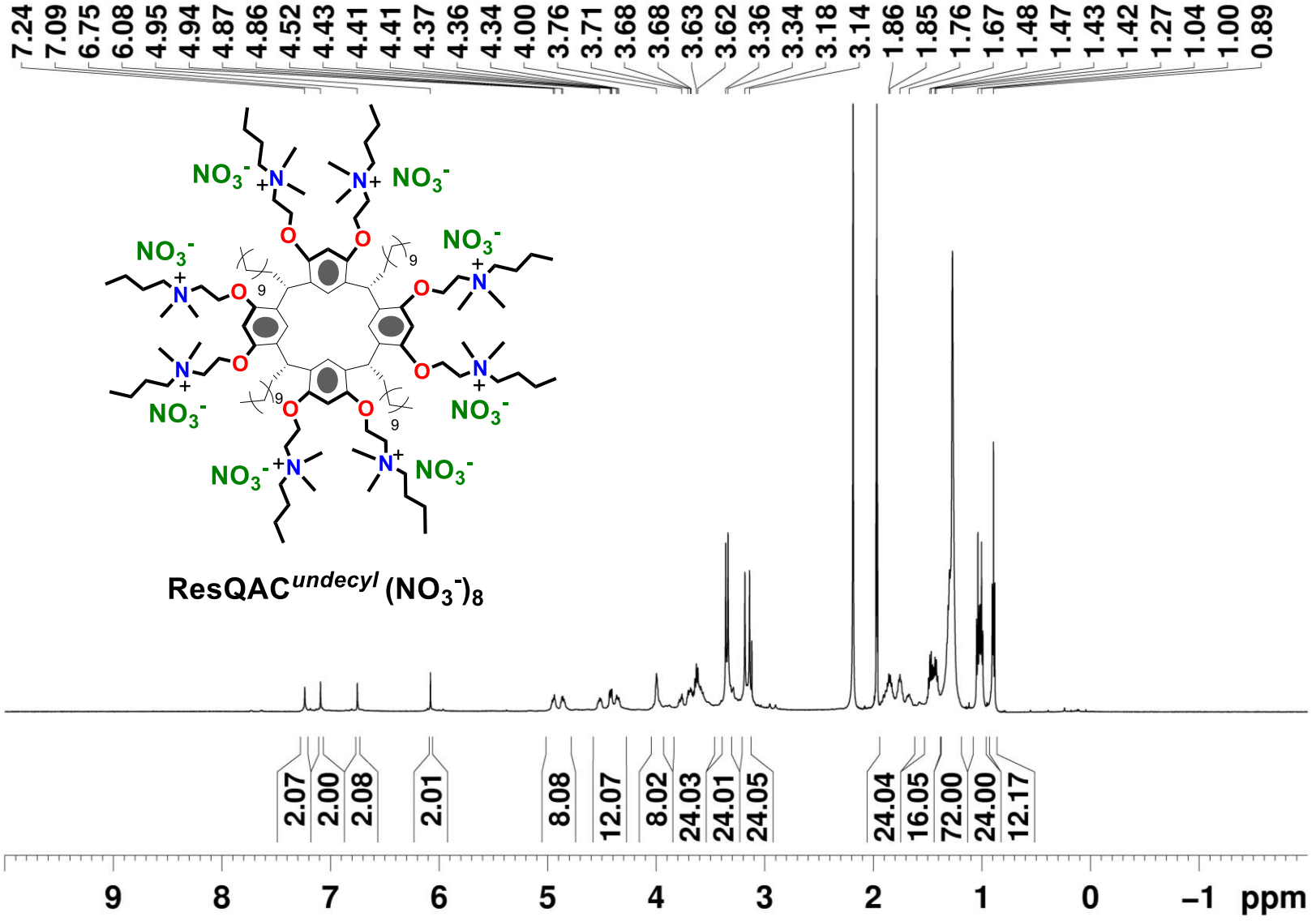


Figure S57. ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of **ResQAC^{undecyl}(NO_3^-)$_8$**.

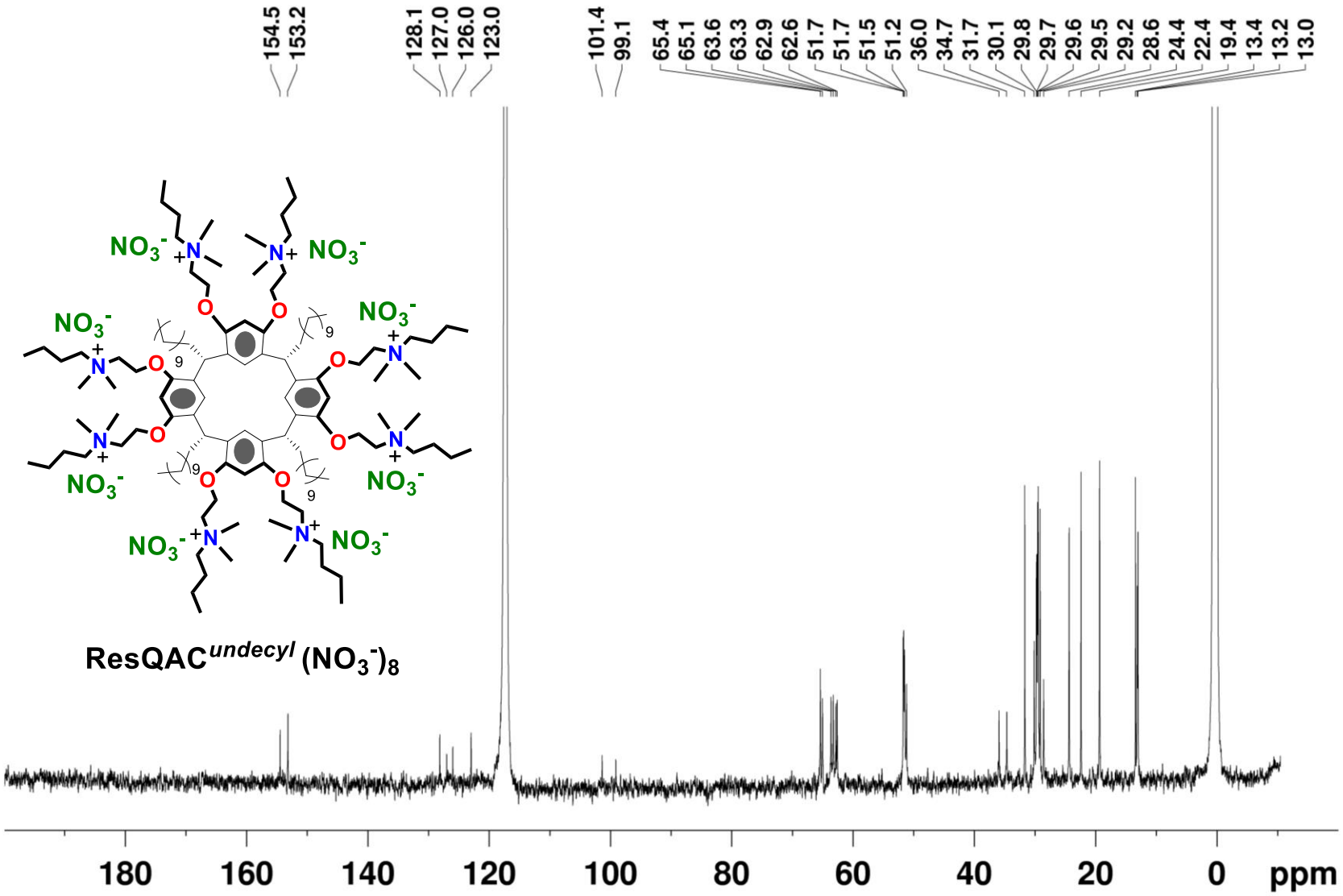
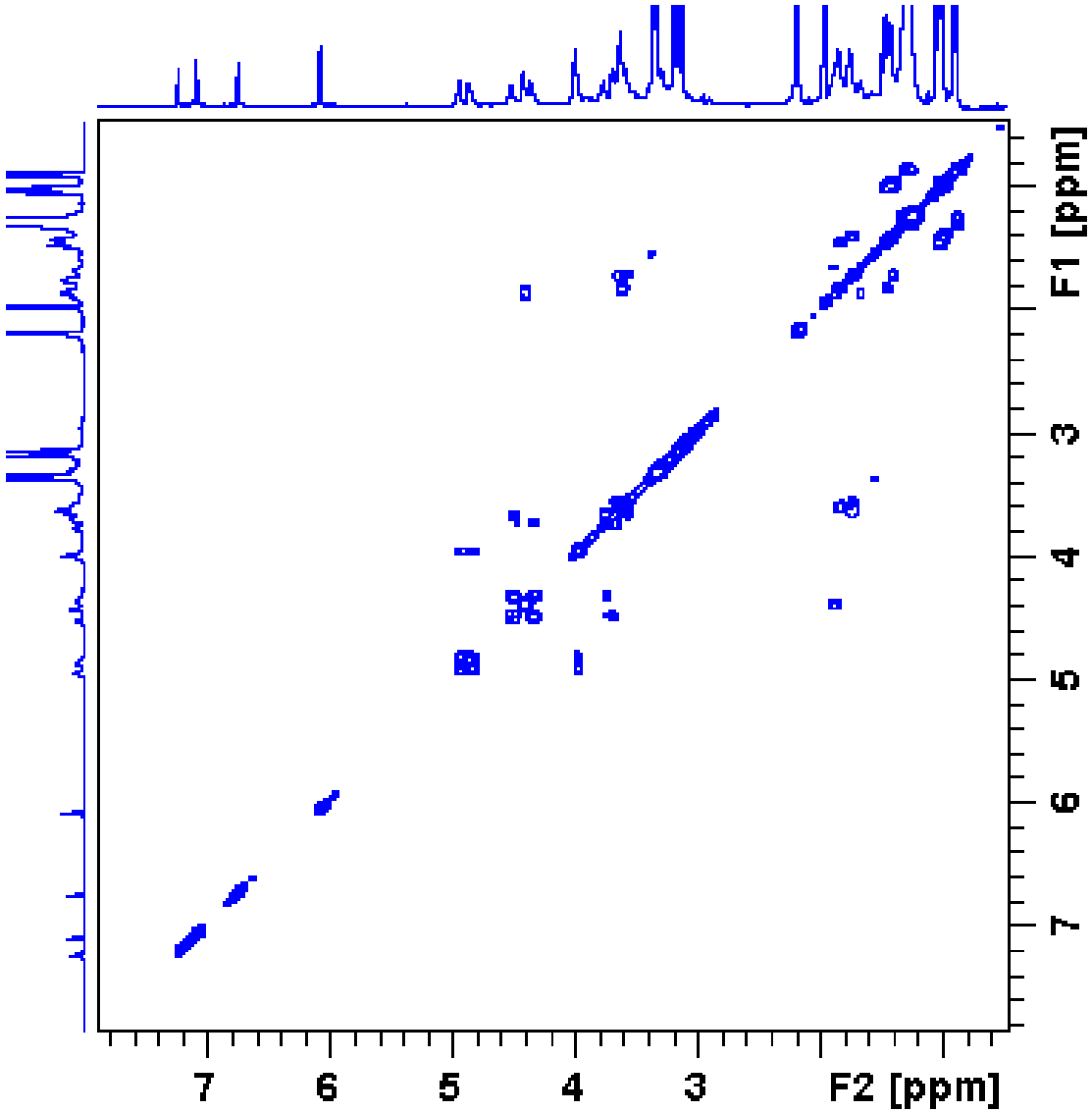
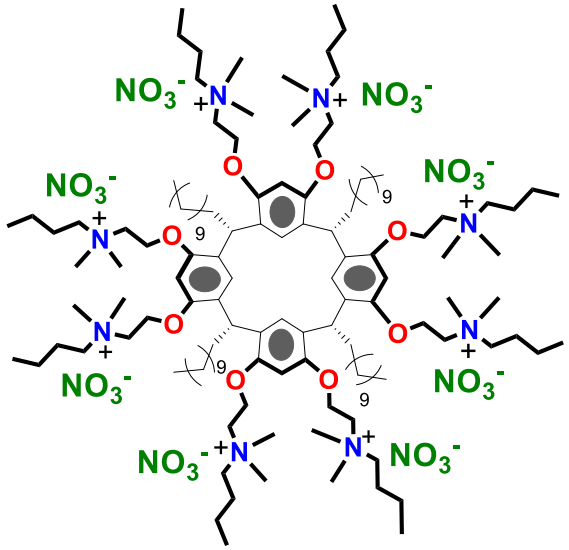


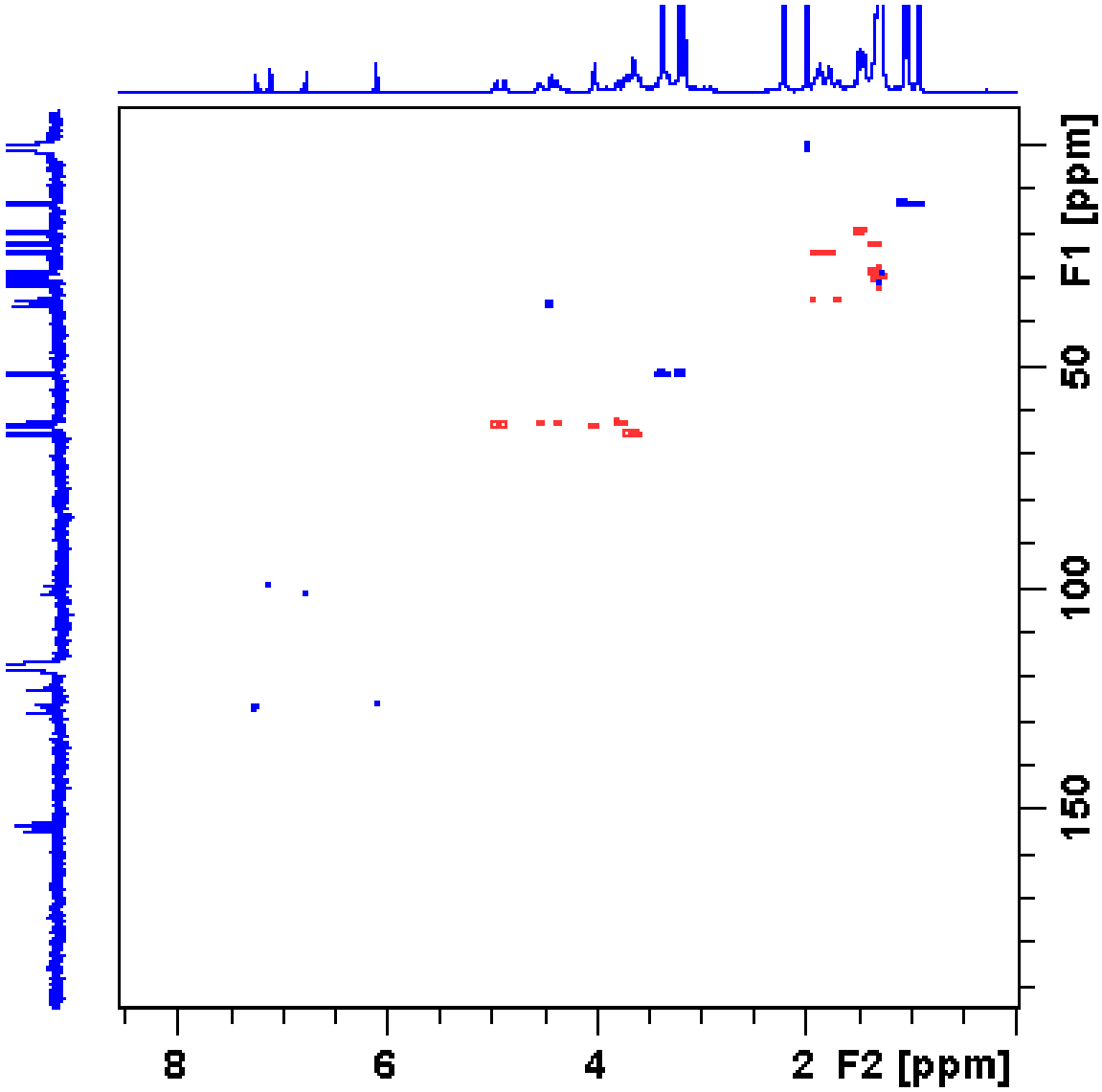
Figure S58. ^{13}C NMR spectrum (150 MHz, CD_3CN, 298 K) of **ResQAC^{undecyl}(NO_3^-)$_8$**.

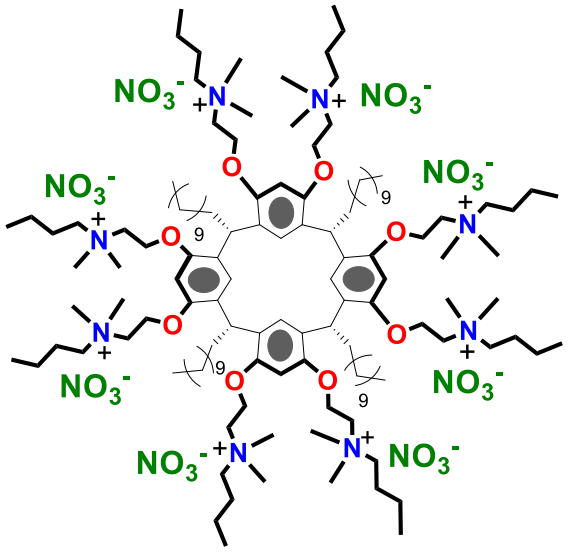




ResQAC^{undecyl} (NO_3^-)$_8$

Figure S59. 2D COSY spectrum (600 MHz, CD_3CN, 298 K) of **ResQAC^{undecyl}(NO_3^-)$_8$.**





ResQAC^{undecyl} (NO_3^-)$_8$

Figure S60. 2D HSQC spectrum (600 MHz, CD_3CN, 298 K) of **ResQAC^{undecyl}(NO_3^-)$_8$.**

HRMS ESI spectrum of ResQAC^{undecyl}(NO_3^-)$_8$

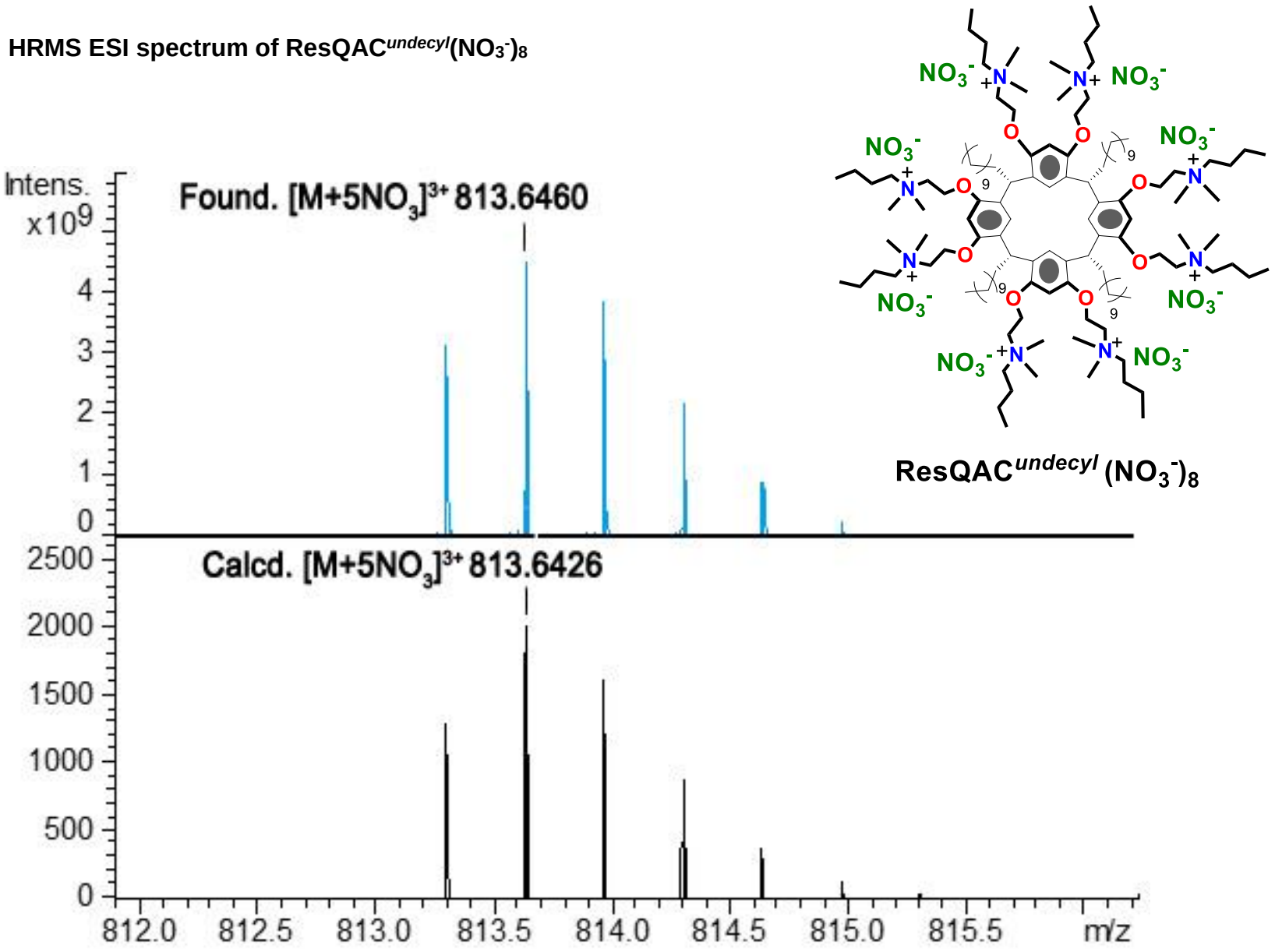


Figure S61. HRMS ESI spectrum of **ResQAC^{undecyl}(NO_3^-)$_8$**

NMR spectra of ResQAC^{phenyl}(NO_3^-)$_8$

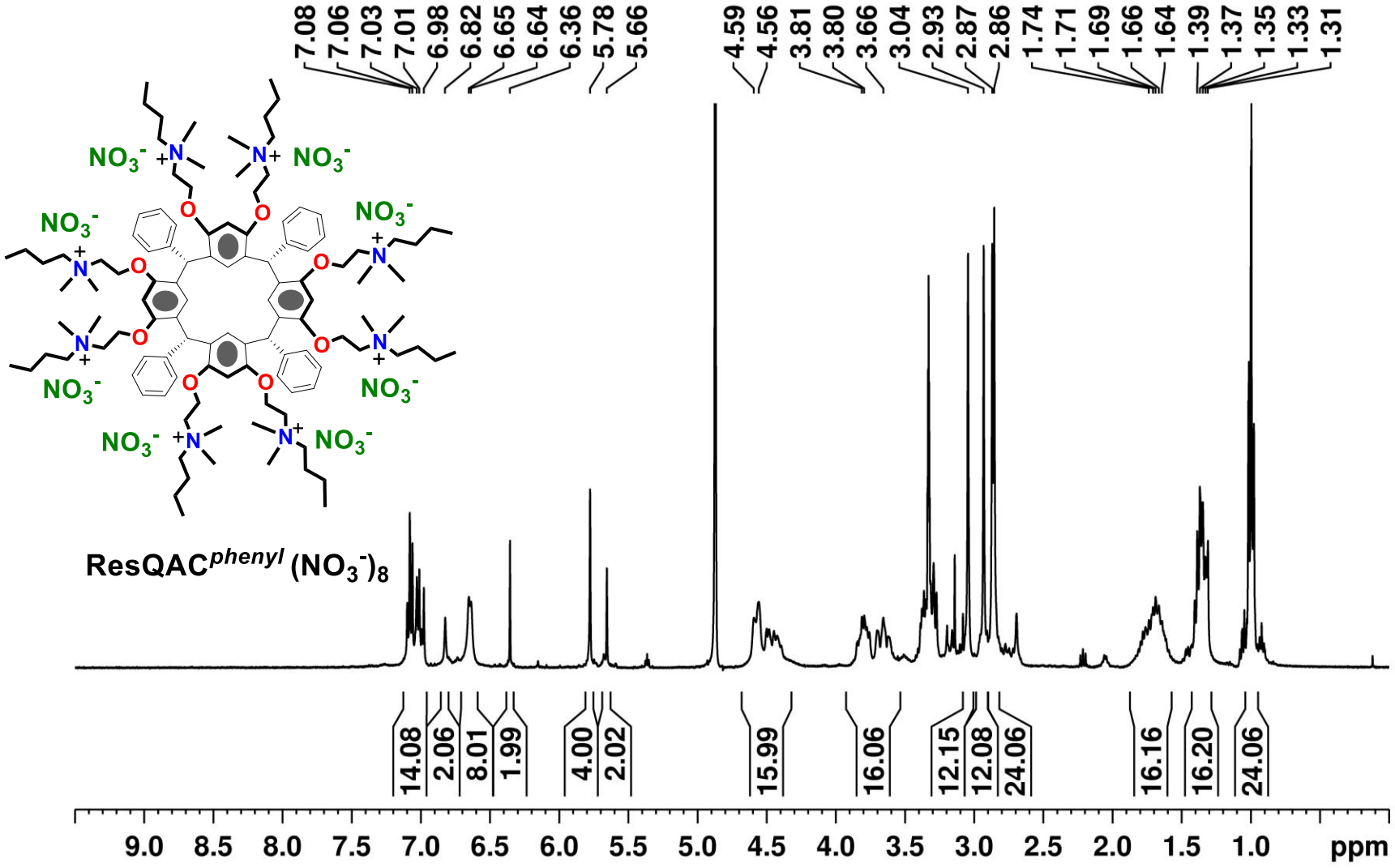


Figure S62. ^{1}H NMR spectrum (400 MHz, CD_3OD, 298K) of **ResQAC^{phenyl}(NO_3^-)$_8$**.

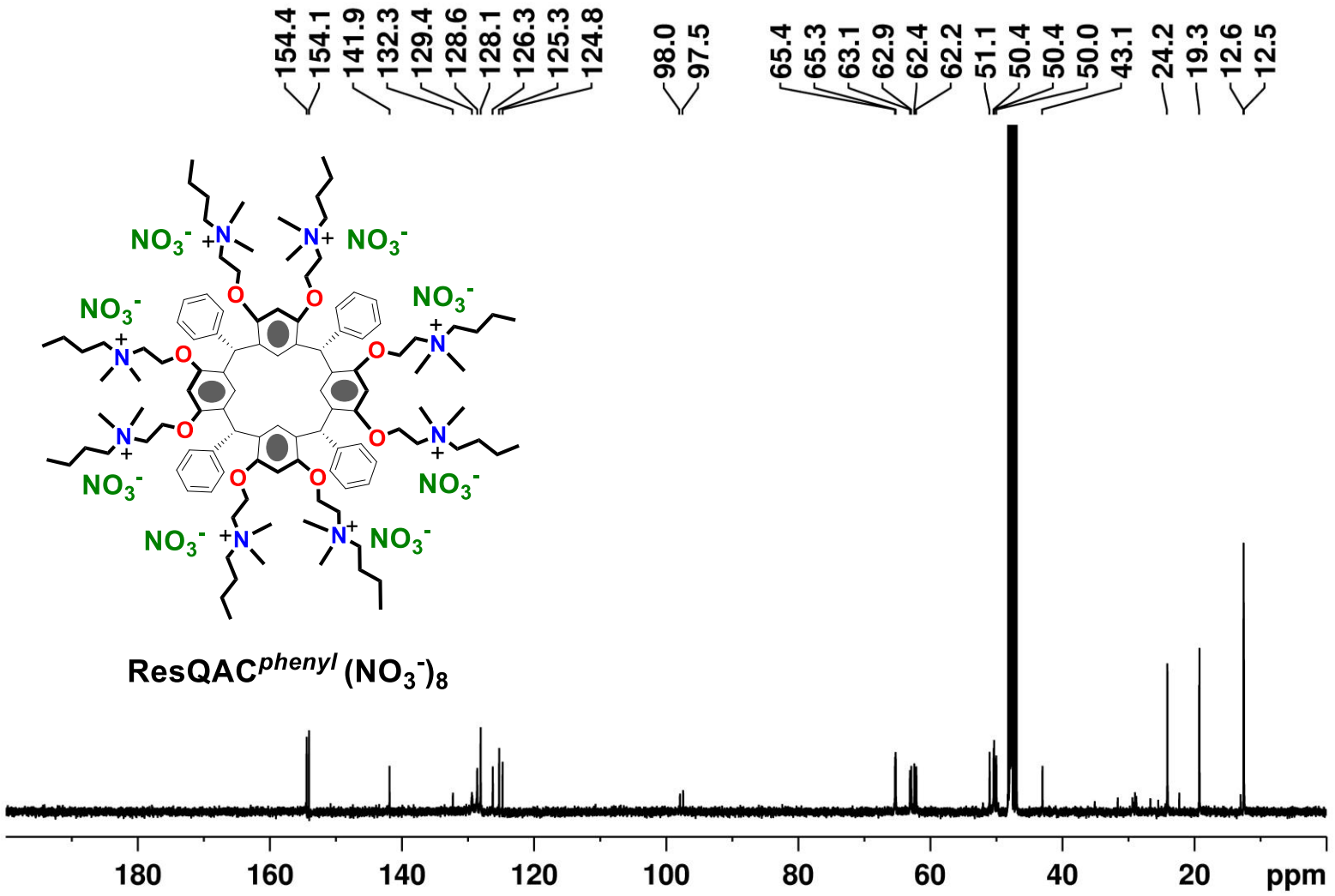


Figure S63. ^{13}C NMR spectrum (125 MHz, CD_3OD, 298K) of **ResQAC^{phenyl}(NO_3^-)$_8$**.

HRMS ESI spectrum of ResQAC^{phenyl}(NO_3^-)$_8$

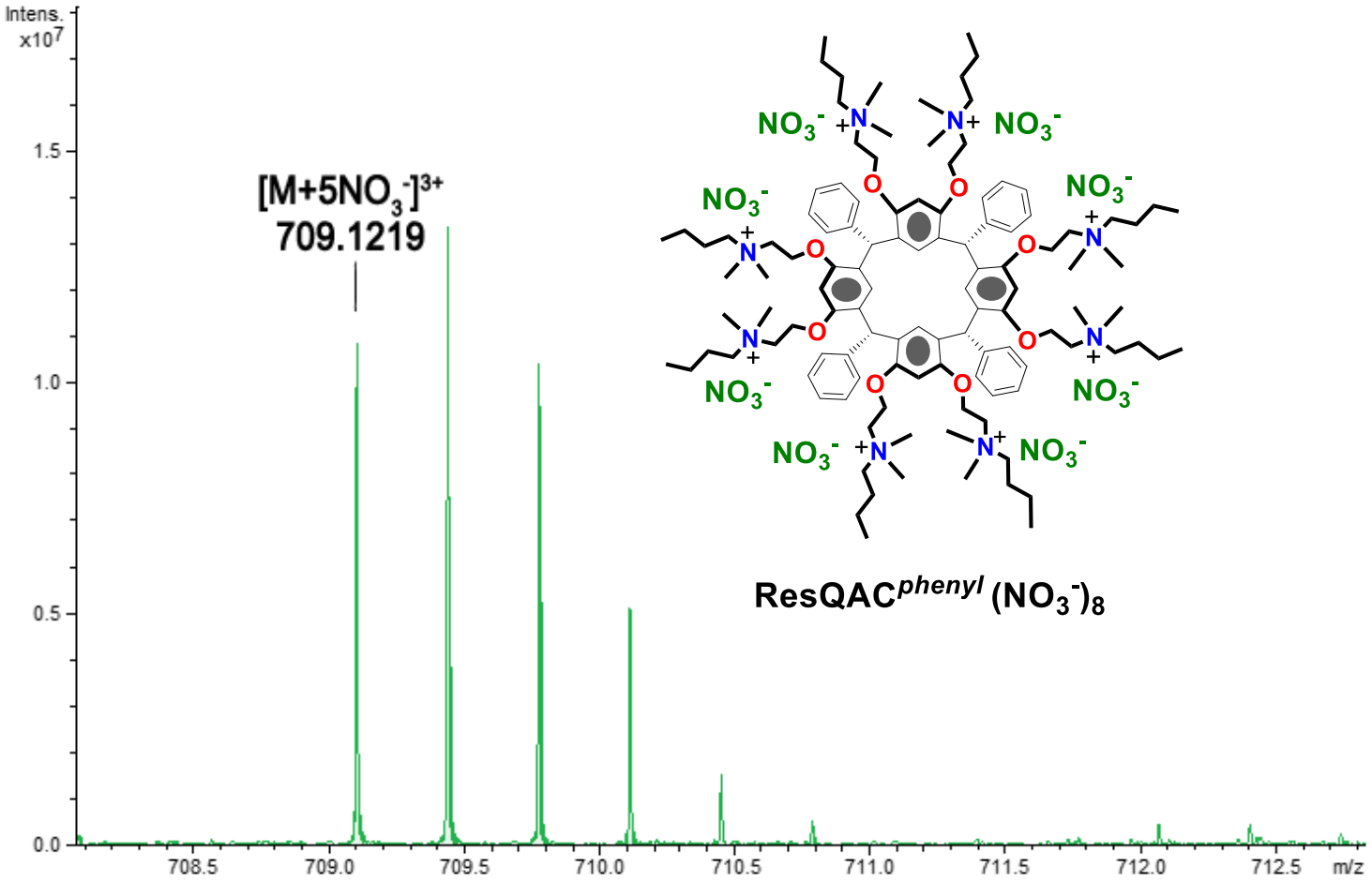


Figure S64. HRMS ESI spectrum of **ResQAC^{phenyl}(NO_3^-)$_8$.**

NMR spectra of derivative 1b

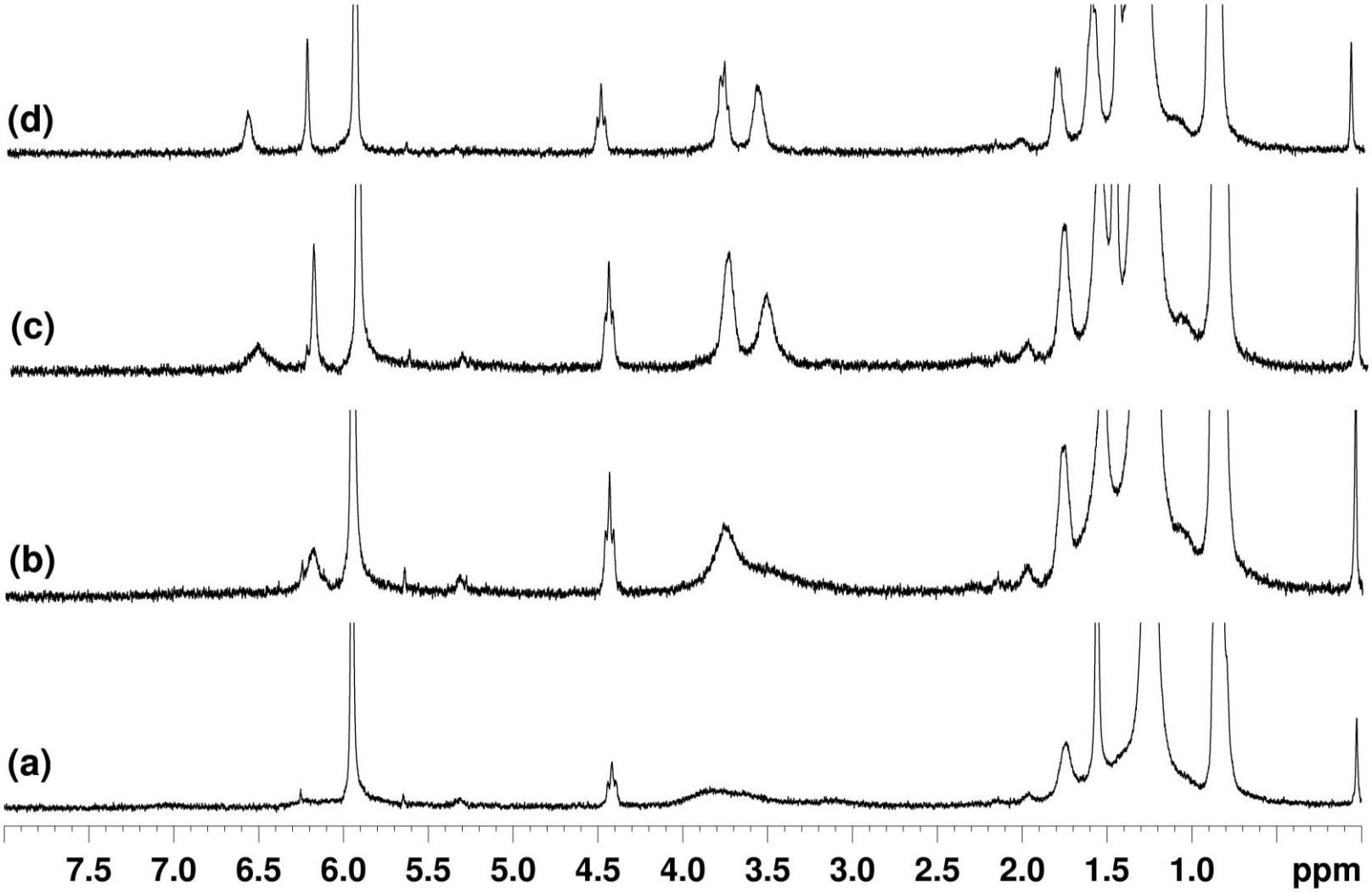


Figure S65. ^{1}H NMR spectra (600 MHz, TCDE) of derivative **1b** at (a) 298 k; (b) 313 k; (c) 333 k; (d) 353 k.

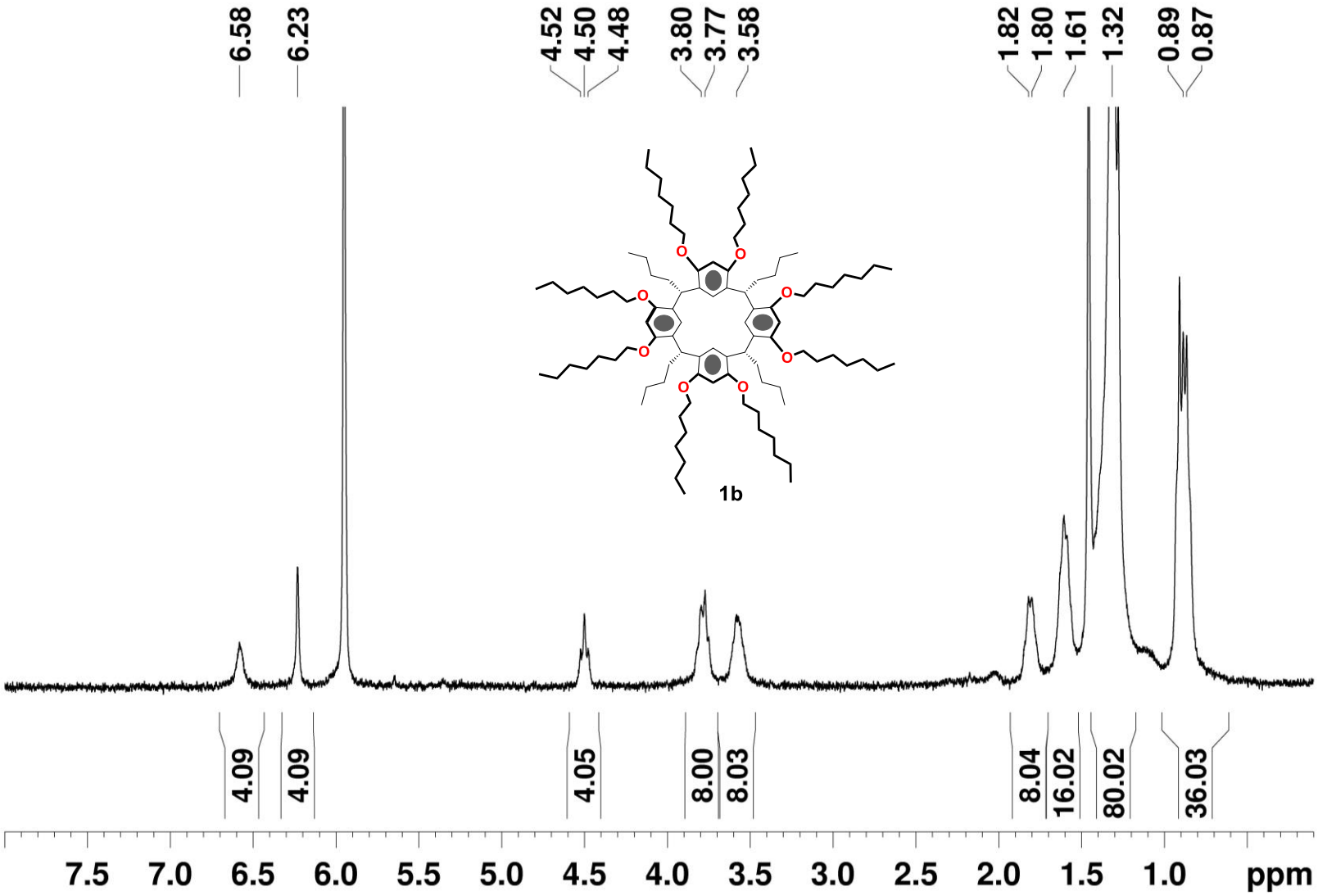


Figure S66. ^{1}H NMR spectrum (600 MHz, TCDE, 353K) of derivative **1b**.

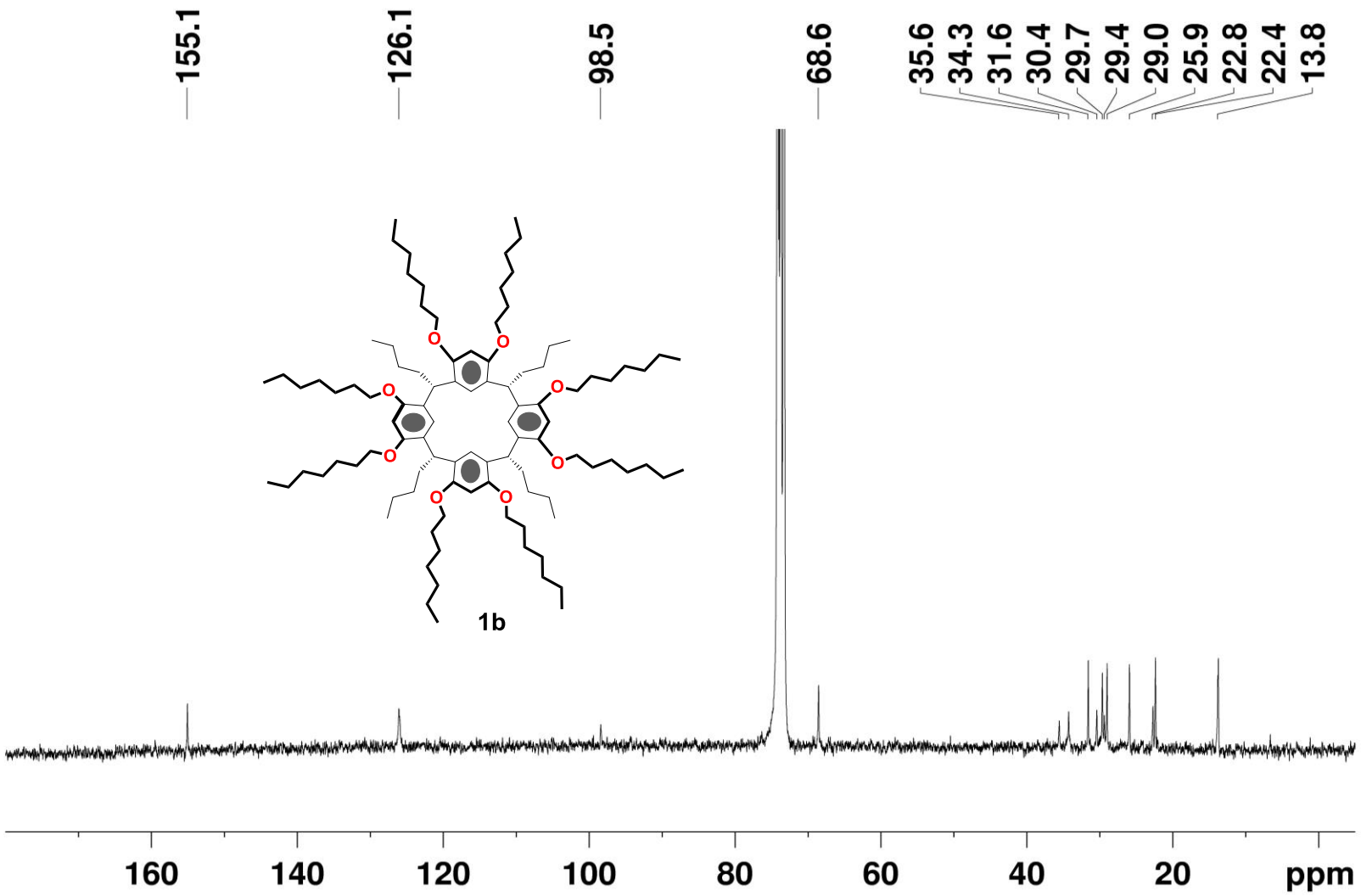


Figure S67. ^{13}C NMR spectrum (150 MHz, TCDE, 353K) of derivative **1b**.

HRMS ESI spectrum of derivative 1b

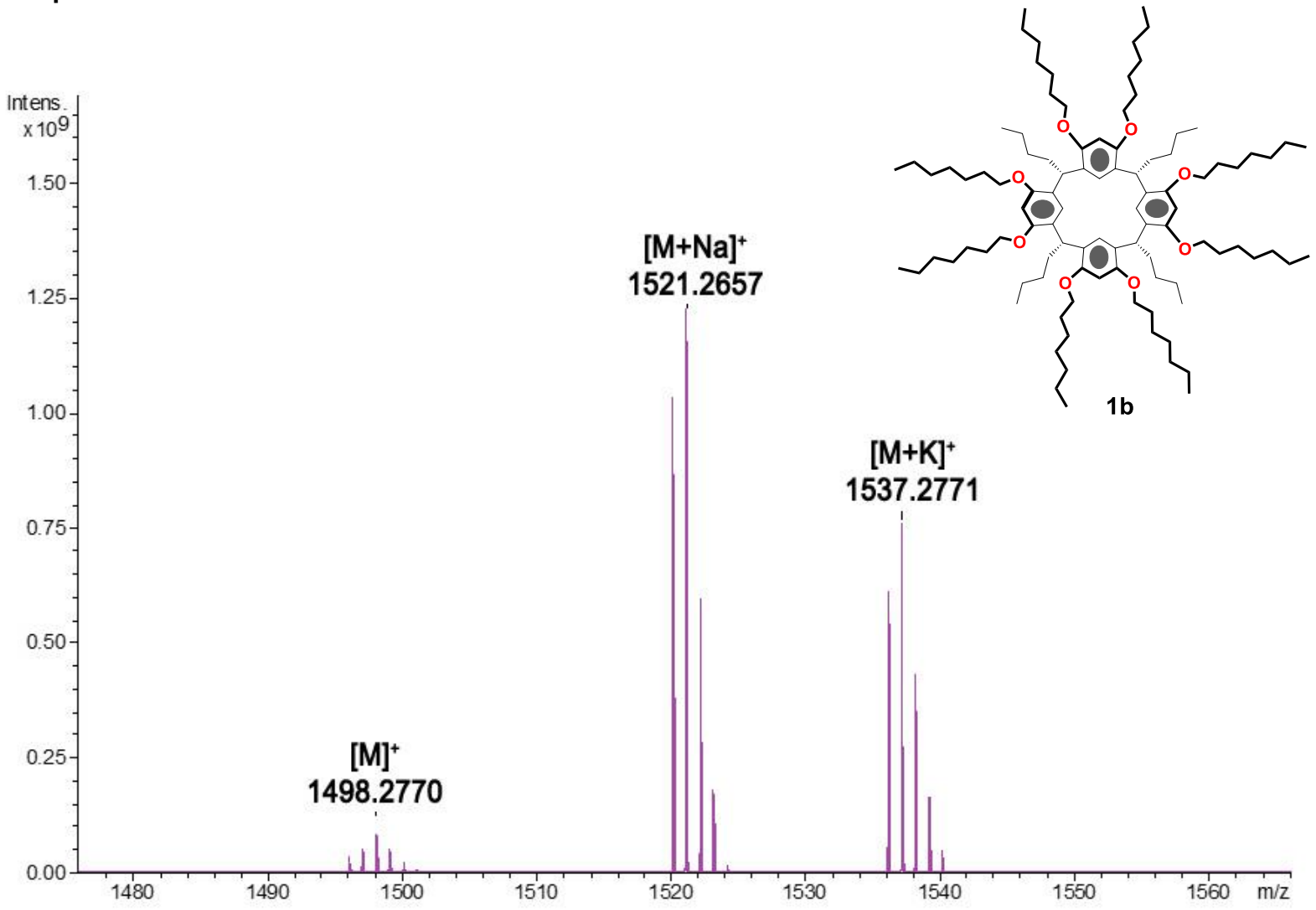


Figure S68. HRMS ESI spectrum of derivative **1b**

NMR spectra of derivative 3

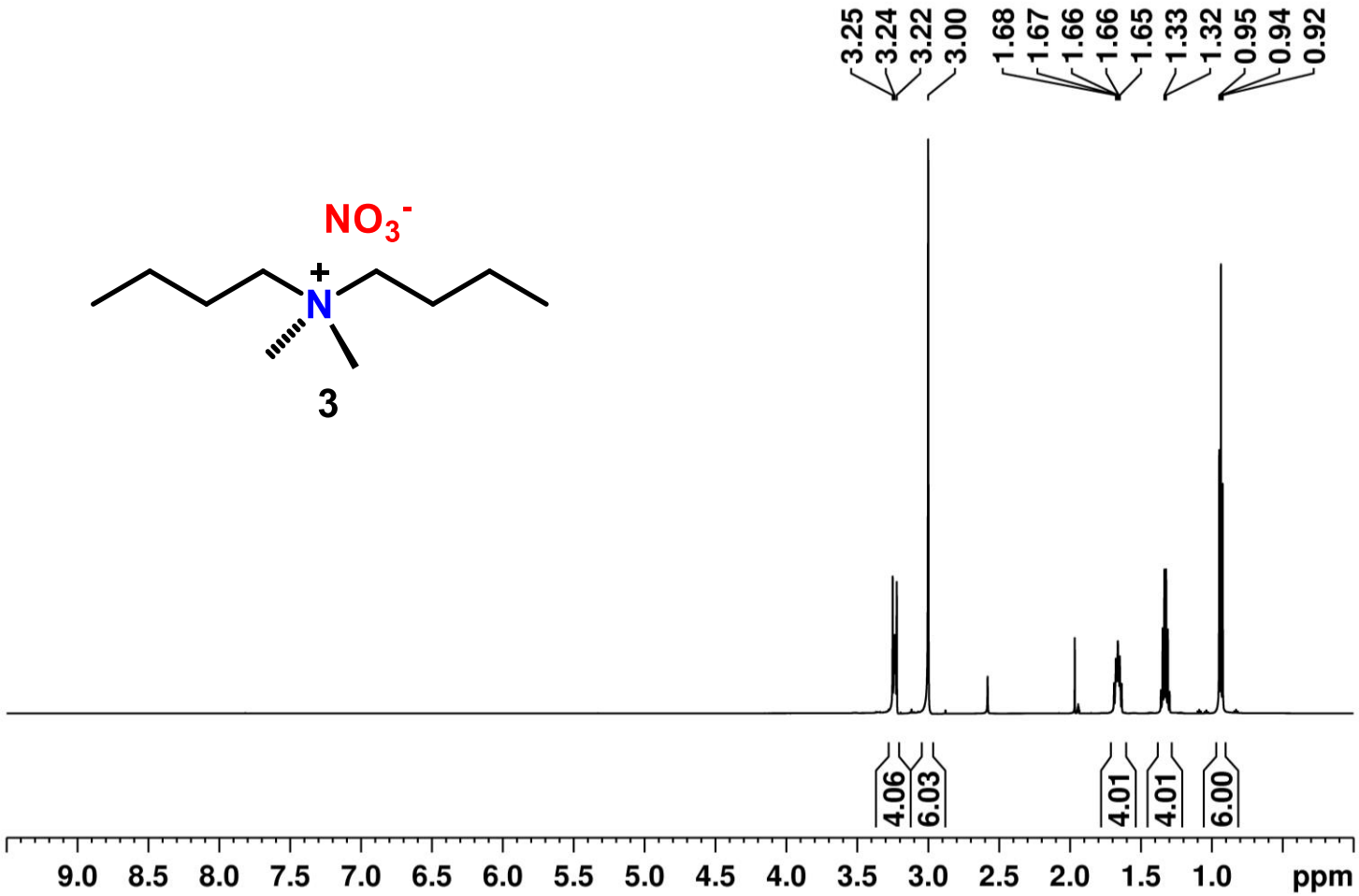


Figure S69. ^{1}H NMR spectrum (600 MHz, CD_3CN, 298 K) of derivative **3**.

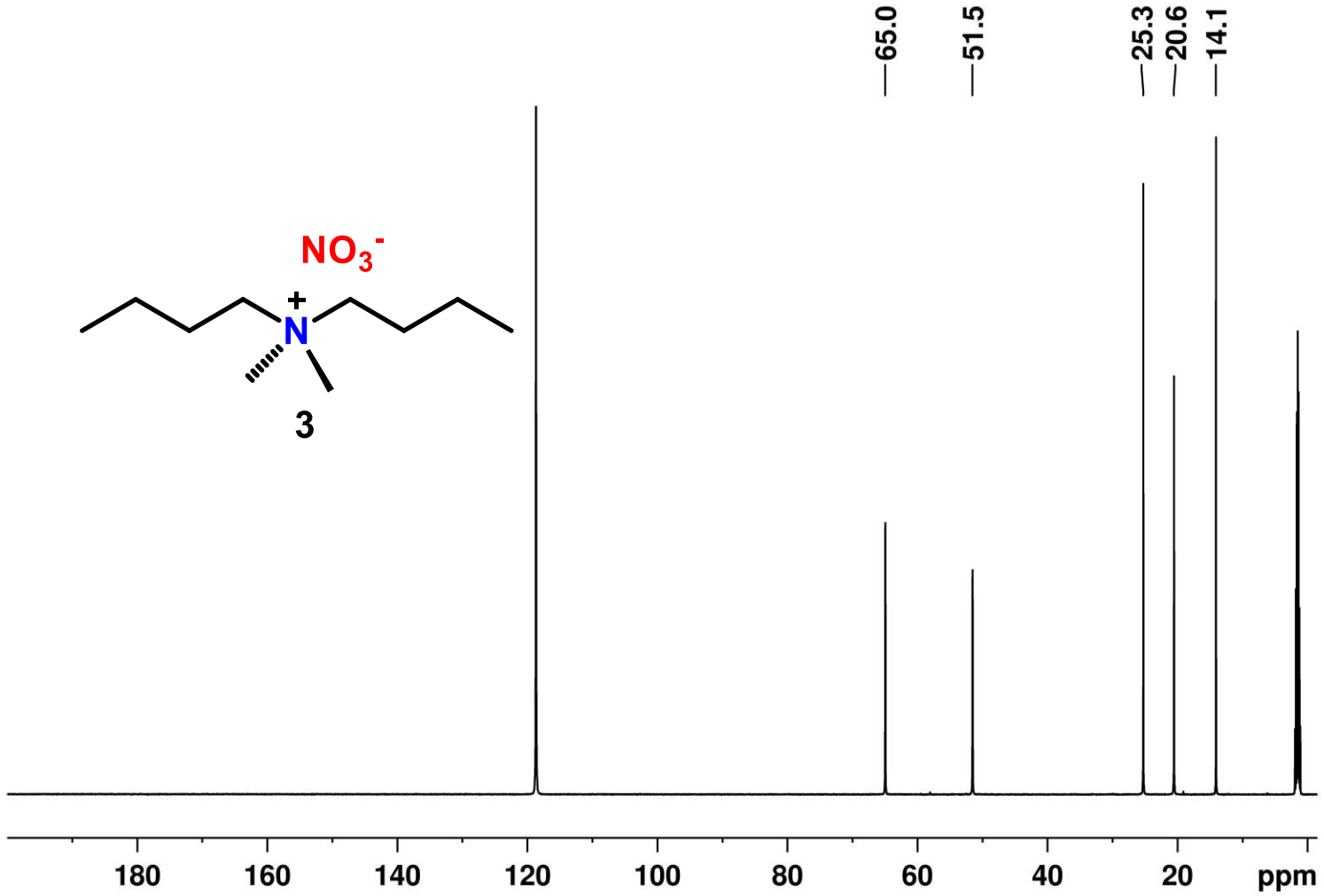


Figure S70. ^{13}C NMR spectrum (75 MHz, CD_3CN, 298 K) of derivative **3**.

HRMS ESI spectrum of derivative 3

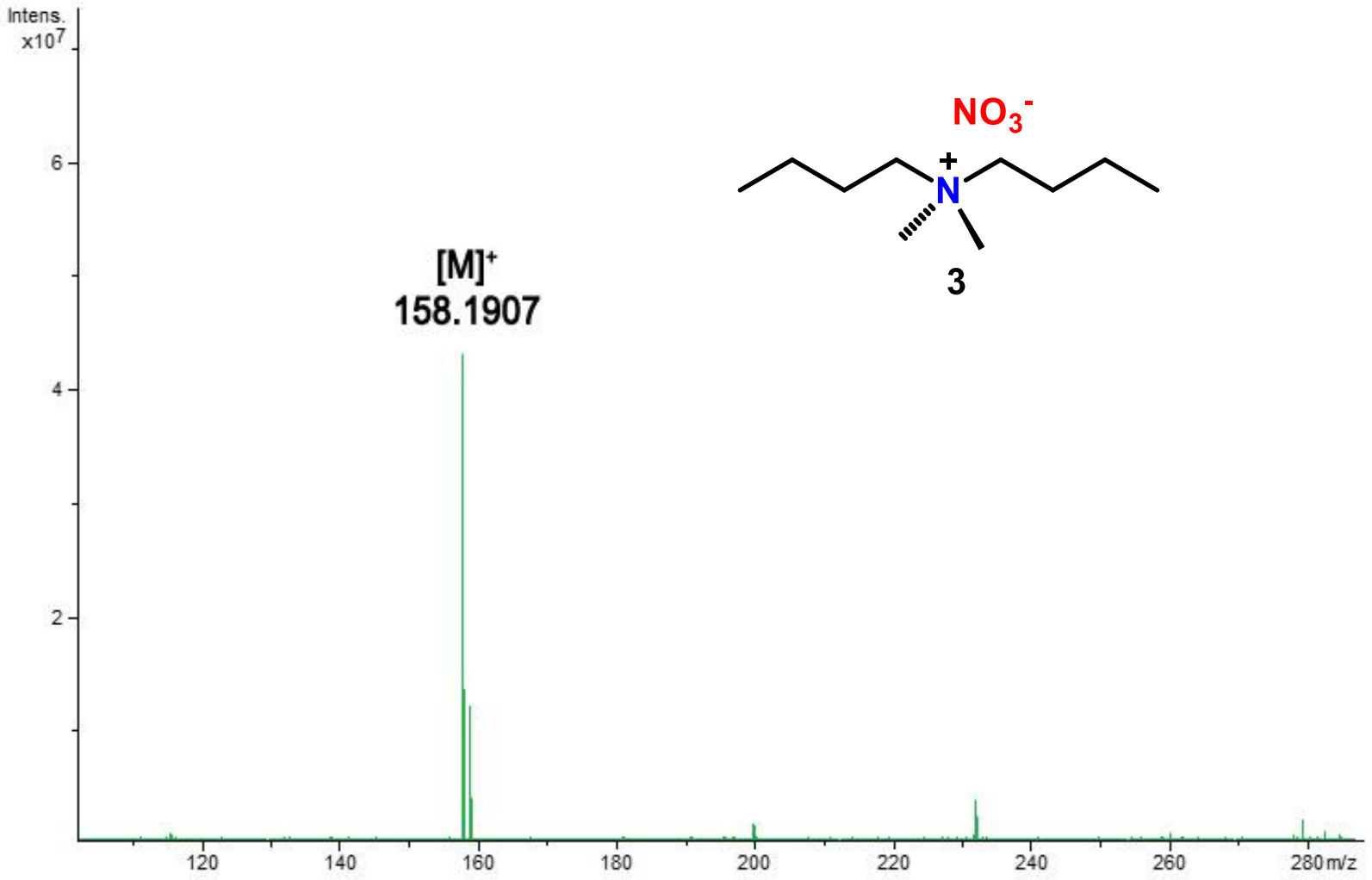


Figure S71. HRMS ESI spectrum of derivative **3**

NMR spectra of derivative 7

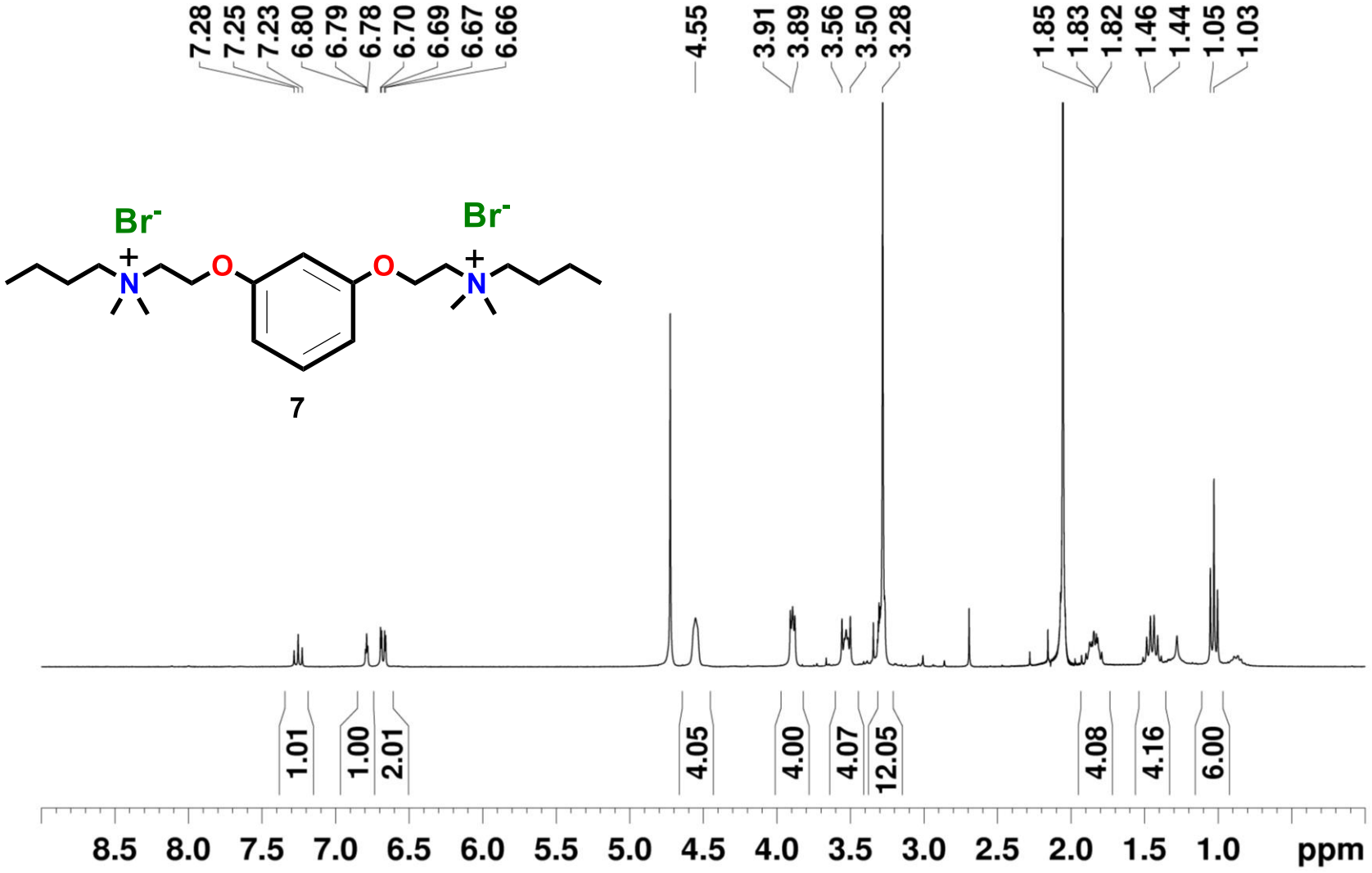


Figure S72. ^{1}H NMR Spectrum (300 MHz, CD_3OD, 298 K) of derivative **7**.

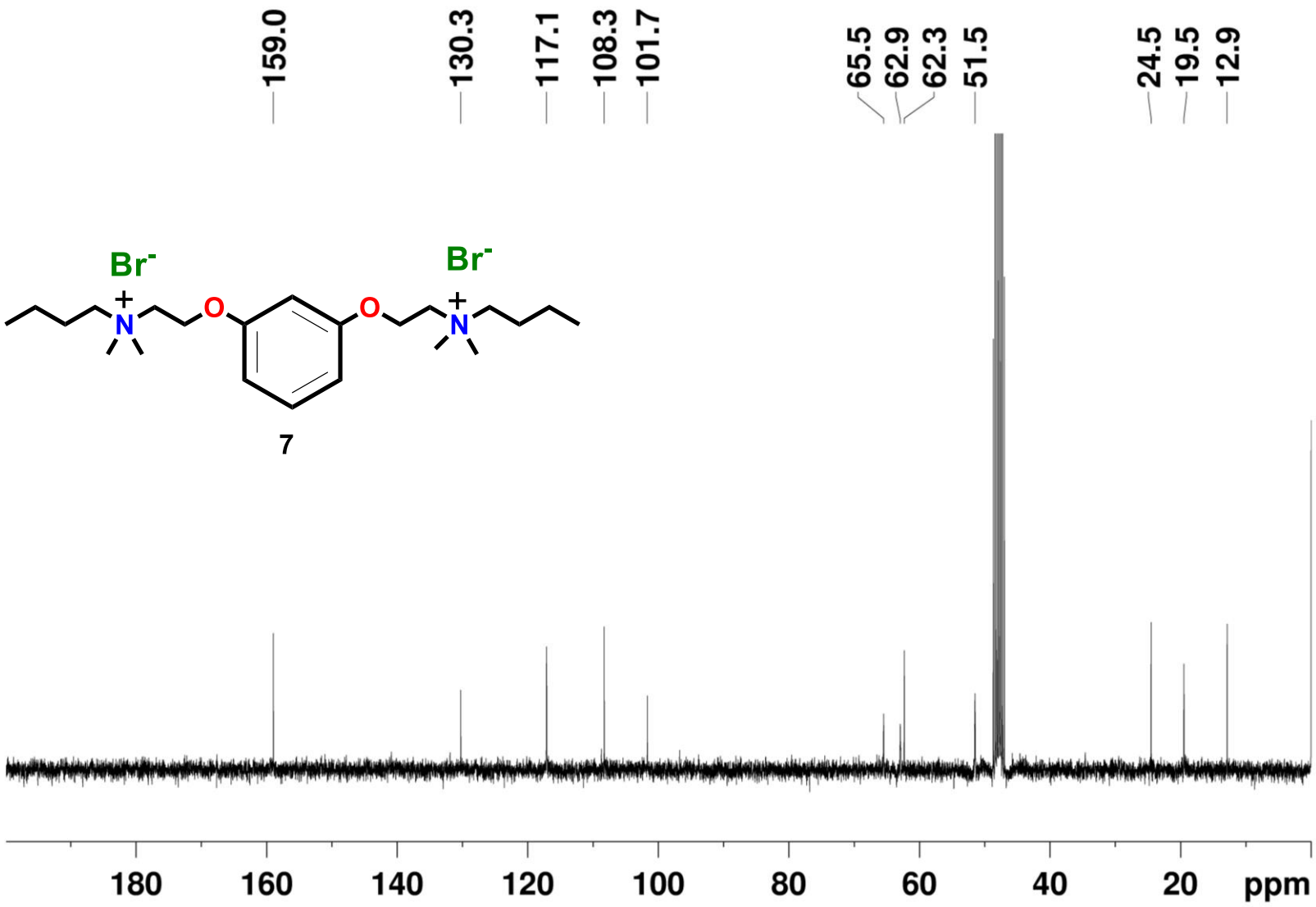


Figure S73. ^{13}C NMR spectrum (300 MHz, CD_3OD, 298 K) of derivative **7**.

HRMS ESI spectrum of derivative 7

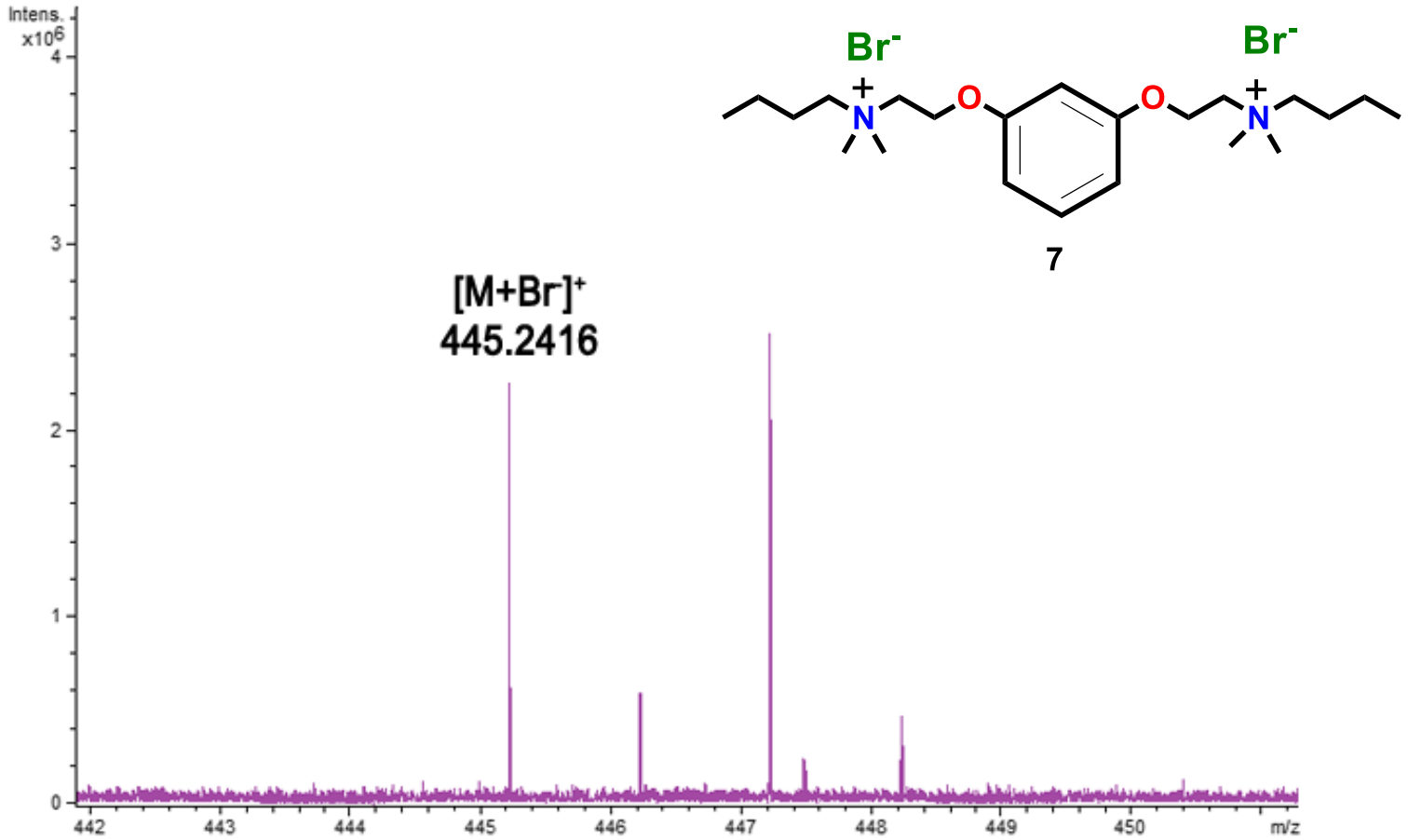


Figure S74. HRMS ESI spectrum of derivative **7**.

NMR spectra of derivative 2

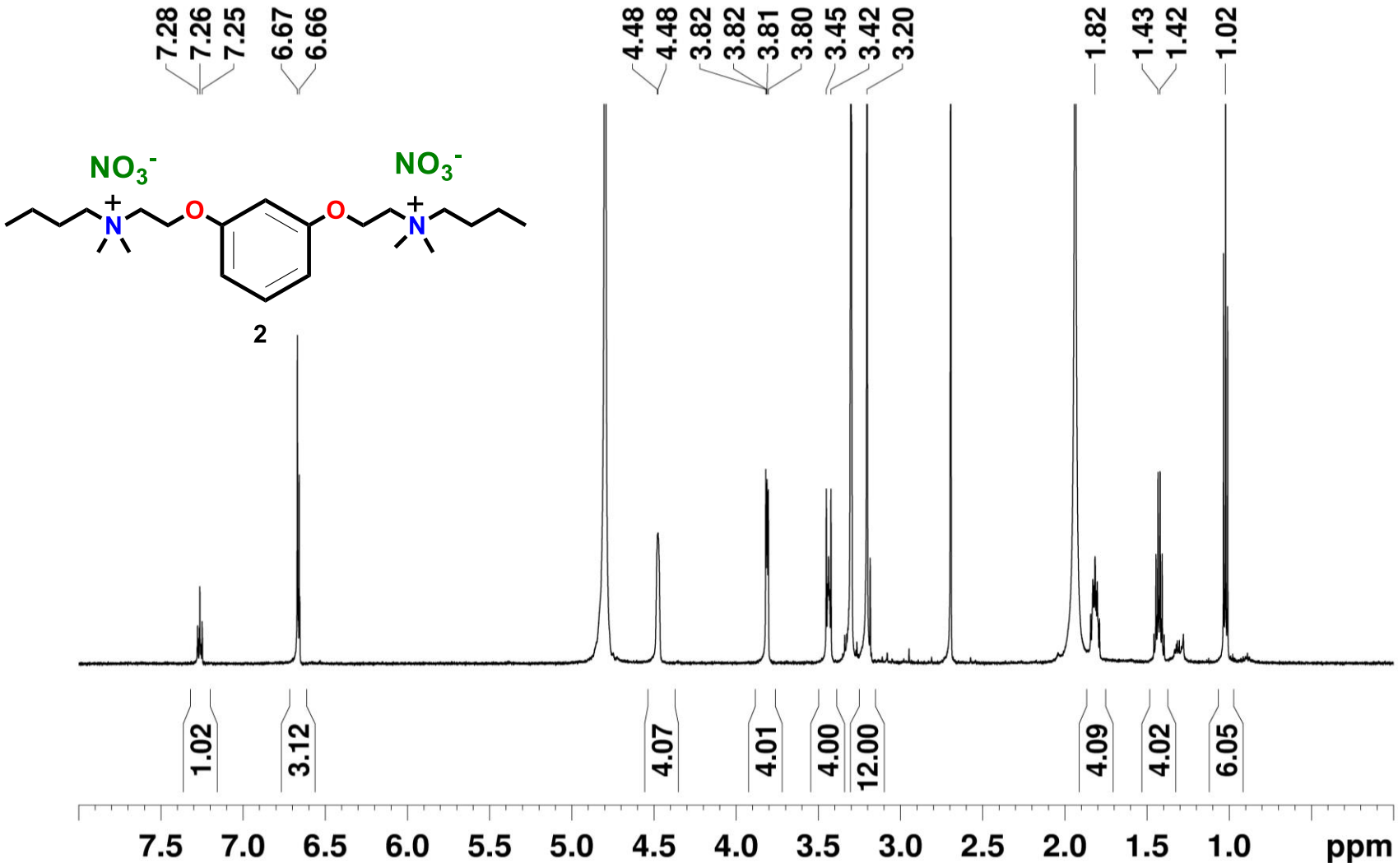


Figure S75. ^{1}H NMR spectrum (600 MHz, CD_3OD, 298 K) of derivative **2**.

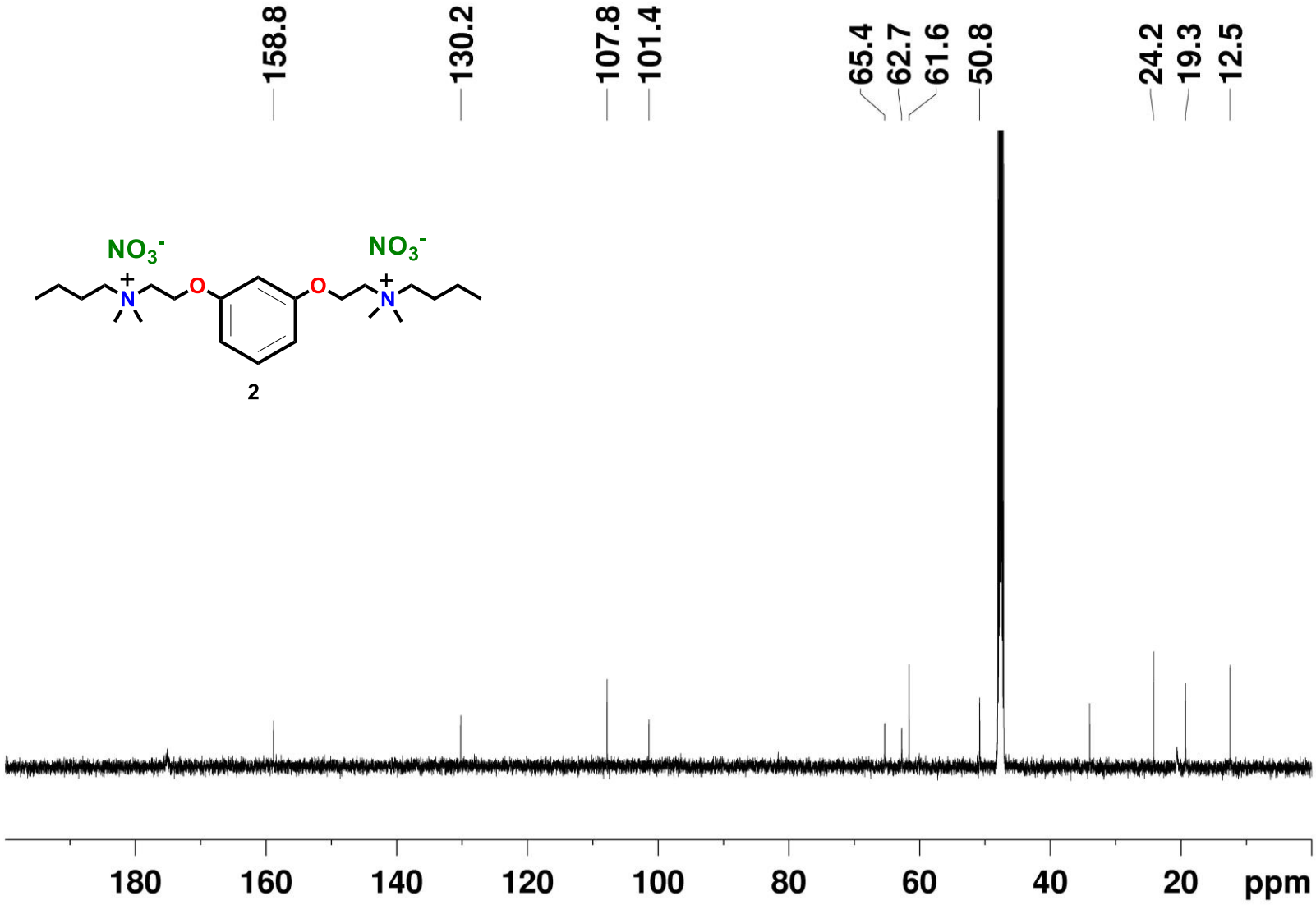
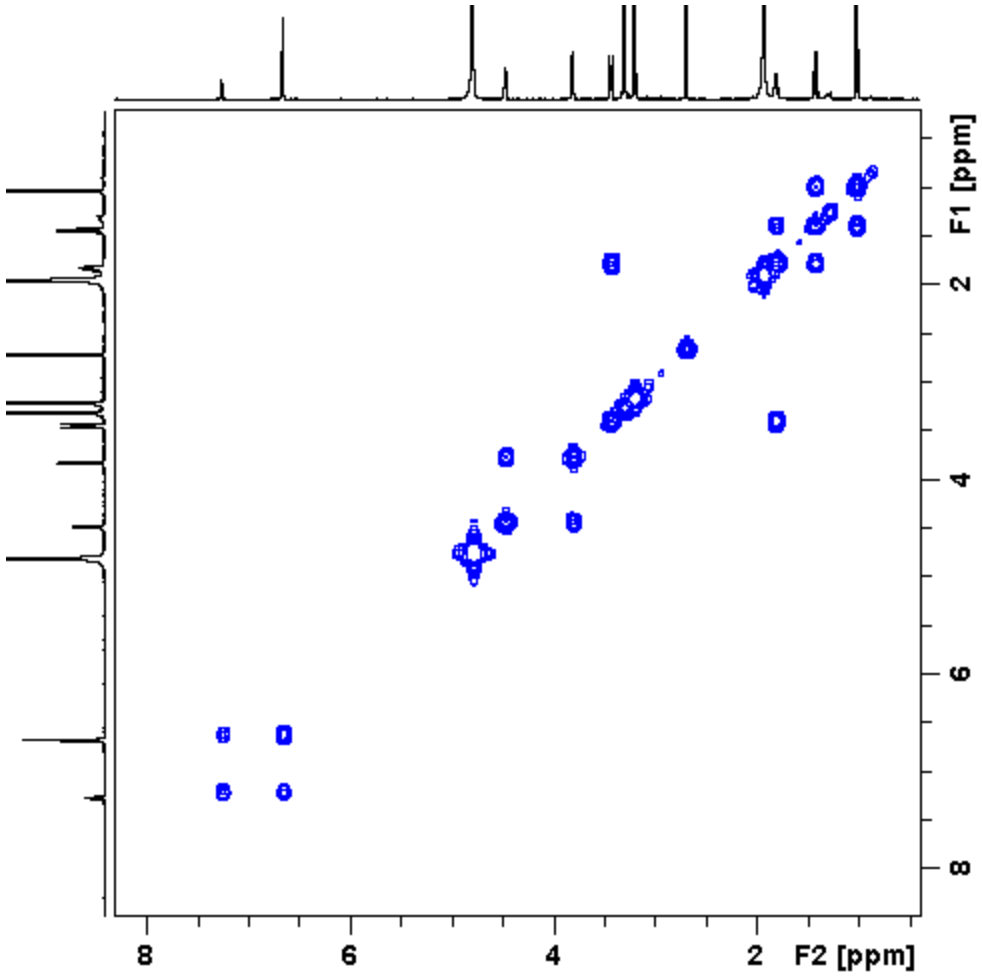
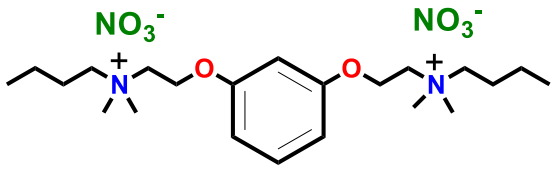


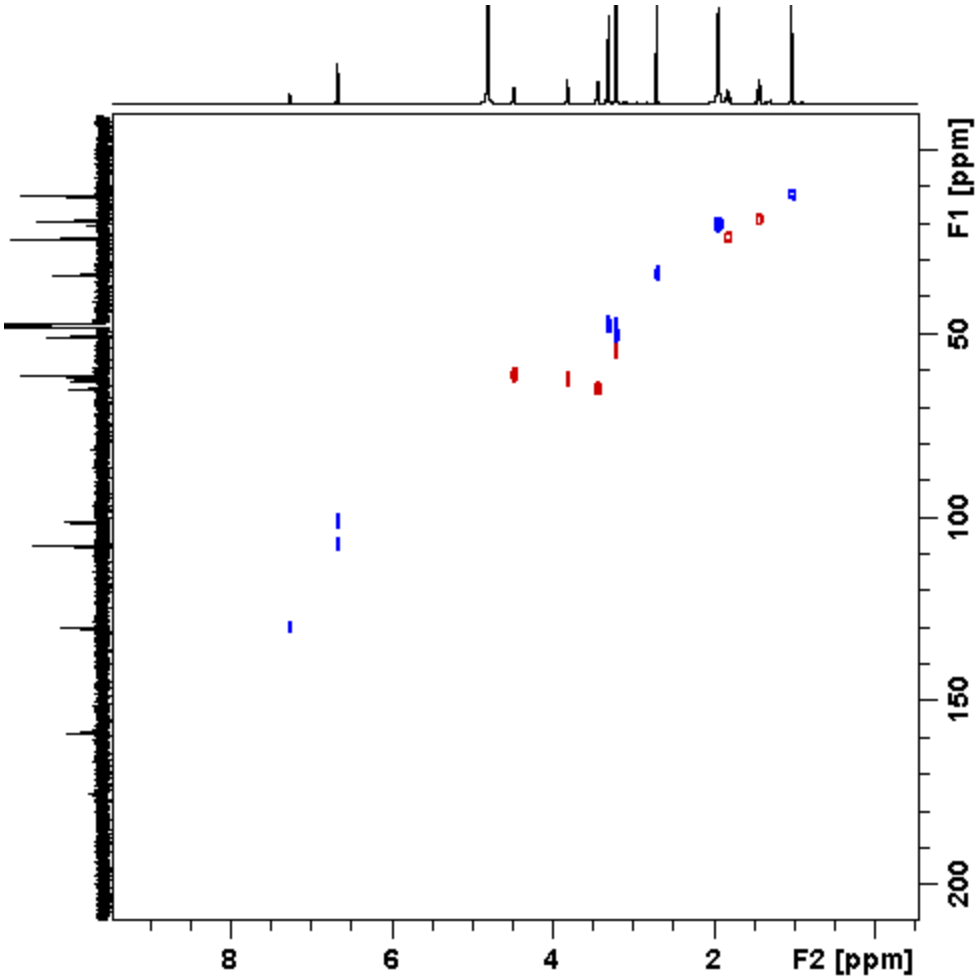
Figure S76. ^{13}C NMR spectrum (150 MHz, CD_3OD, 298 K) of derivative **2**

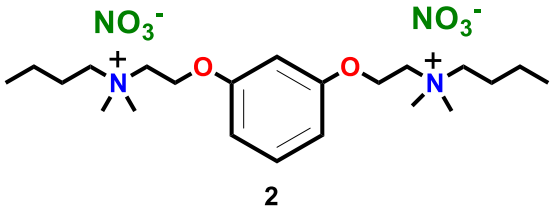




2

Figure S77. 2D COSY spectrum (600 MHz, CD_3OD, 298 K) of derivative **2**.





2

Figure S78. 2D HSQC spectrum (600 MHz, CD_3OD, 298 K) of derivative **2**.

HRMS ESI spectrum of derivative 2

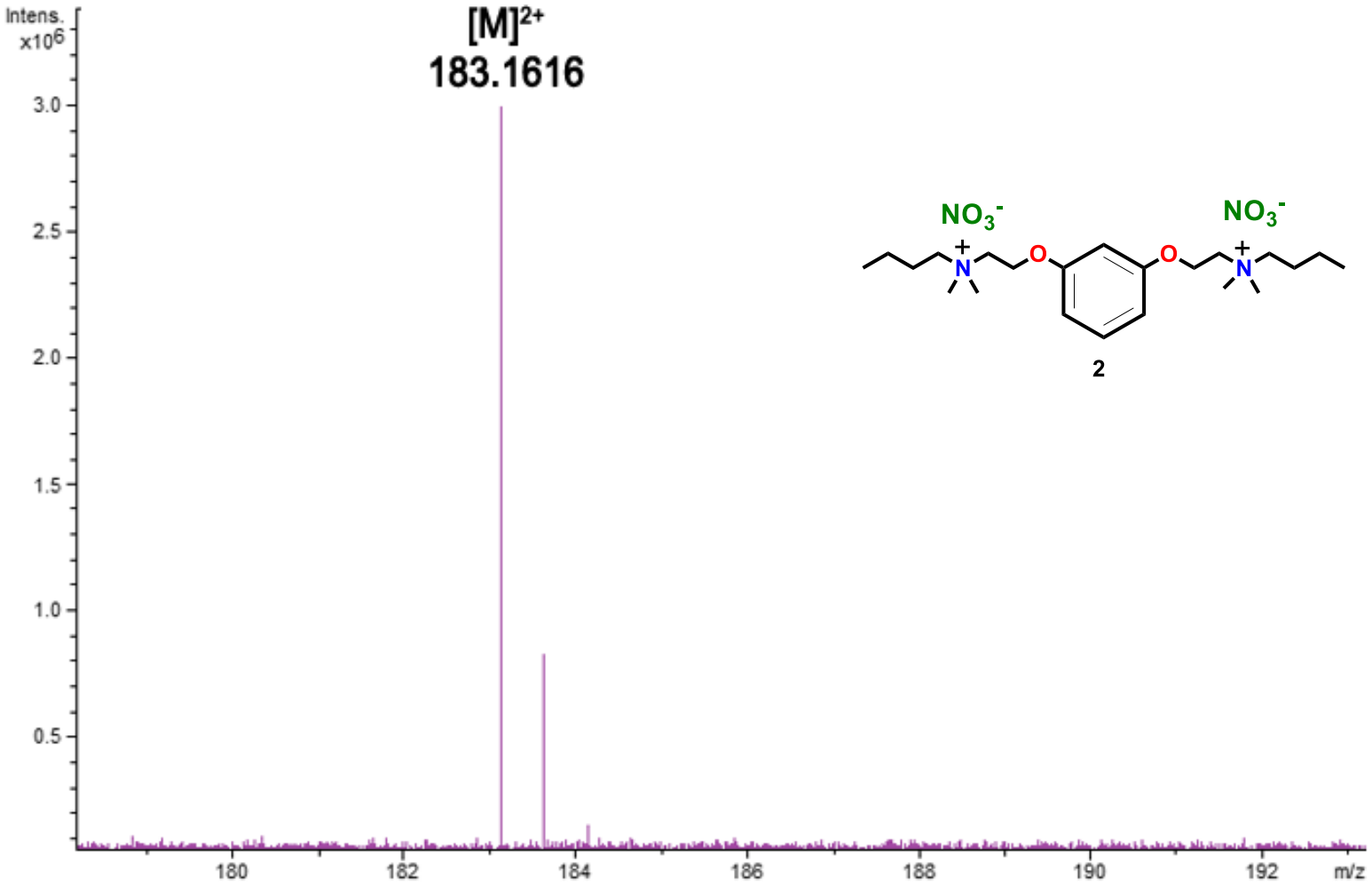


Figure S79. HRMS ESI spectrum of derivative **2**

X-ray structure refinement details of ResQAC^{butyl}(I$^-$)$_8$

Single crystals suitable for X-Ray diffraction were obtained by slow evaporation of solution containing **ResQAC^{butyl}(I$^-$)$_8$** in CH_3OH/H_2O. Data collection was carried out at the XRD1 beamline of the Elettra synchrotron (Trieste, Italy) using the rotating-crystal method, with a monochromatic wavelength of 0.7000 Å and a Dectris Pilatus 2 M area detector. Single crystals were dipped in paratone cryoprotectant, mounted on a nylon loop and flash-frozen under a nitrogen stream at 100 K. Diffraction data were indexed and integrated using the XDS package,[s3] while scaling was carried out with XSCALE.[s4] The structure was solved using the SHELXT program and structure refinement was performed with SHELXL-18[s5,s6] by full-matrix least-squares (FMLS) methods on F^2, operating through the WinGX GUI.[s7]

All three structures crystallised in the P-1 space group. Non-hydrogen atoms were refined anisotropically, except for carbon and oxygen atoms with occupancy factor less than 0.5 (see below). Hydrogen atoms were included in idealised positions and refined using the riding model. Crystallographic data and refinement details are reported in Table S1.

ResQAC^{butyl}(I$^-$)$_8$ contains one **ResQAC^{butyl}(I$^-$)$_8$** formula unit in the asymmetric unit. The iodide anions showed severe disorder and were modelled in 9 different sites, some with 2- or 3-position disorder. Thus, 3 iodide ions were refined at full occupancy, 2 at full occupancy with 2-position disorder (0.5/0.5 occupancy factors for each), 1 at full occupancy with 3 position disorder (0.40/0.40/0.2 occupancy factors), 1 at partial occupancy with 2 position disorder (0.45/0.45 occupancy factors) and 2 at partial occupancy (0.60 and 0.50 occupancy factors). Disorder was also present in various chains containing the quaternary ammonium cations. This disorder was not modelled at the electron density in these regions was too poor to allow reliable identification of all possible positions. In each of these cases the model includes only the most prominent chain positions, refined at full occupancy and with DFIX, DANG and SIMU restraints applied during refinement to selected bond lengths, bond angles and anisotropic thermal factors. The cell also contained residual electron density attributed to water solvent molecules. This was not modelled but was accounted for using the Platon squeeze tool.[S8] The residual electron density of 224 electrons/cell in a total potential solvent area volume of 803 Å^3 (11.5% of the cell volume) can be attributed to circa 22 water molecules per cell.

Table #1 Crystal data and structure refinements for **ResQAC^{butyl}(I^-)$_8$**

	ResQAC^{butyl}(I^-)$_8$
Empirical formula	$(C_{108}H_{200}N_8\ O_8)^{8+}$ $8I^-$ $11H_2O$
Formula weight	2801.95
Temperature (K)	100(2)
Wavelength (Å)	0.7
Crystal system	Triclinic
Space group	P -1
Unit cell Dimensions (Å. °)	a = 13.730(1) b = 21.819(2) c = 24.380(3) α = 106.798(5) β = 93.307(6) γ = 93.547(6)
Volume (Å^3)	6957(1)
Z	2
ρ_{calcd} (g/cm^3)	1.338
μ (mm^{-1})	1.736
F(000)	2832
θ (°)	0.862 – 27.818
Limiting indices	-18≤ h ≤18 -29≤ k ≤29 -32≤ l ≤32
Reflections collected	208758
Independent Reflections	34130
R_{int}	0.0299
Independent reflections [I>2σ(I)]	21140
Parameters / Restraints	1222 / 207
GooF	1.631
Final *R* indices [I>2σ(I)]	
R_1[a]	0.1247
wR2[b]	0.3851
R indices (all data)	
R_1[a]	0.1472
wR2[b]	0.4161
Largest differences in peak/ hole (e Å^{-3})	2.457/-2.116
CCDC code	

[a] $R^1 = \Sigma(|Fo| - |Fc|)/\Sigma|Fo|$. [b] $wR2 = \{\Sigma[w(|Fo|^2 - |Fc|^2)^2]/\Sigma[w(|Fo|^2)^2]\}^{1/2}$

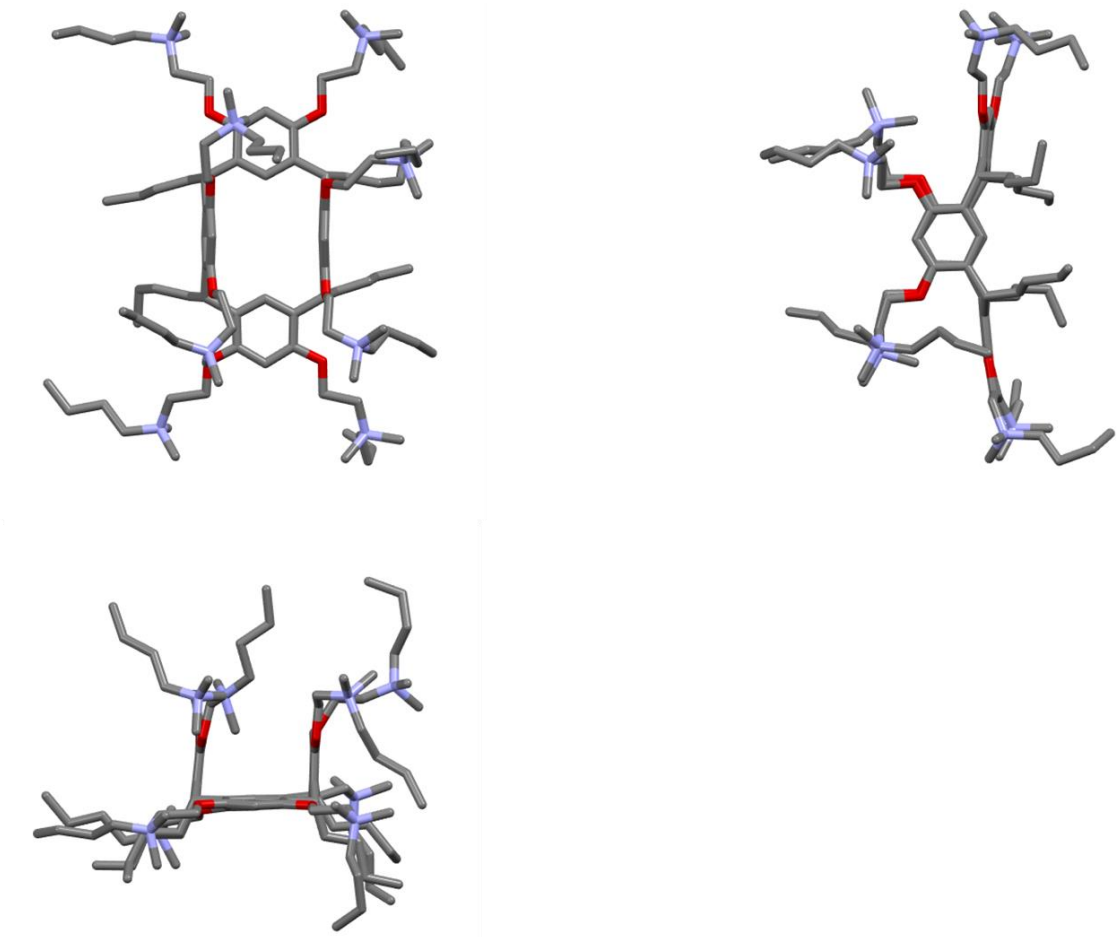


Figure S80. Orthogonal views of the crystallographically independent molecule of **ResQAC^{butyl}(I$^-$)$_8$**

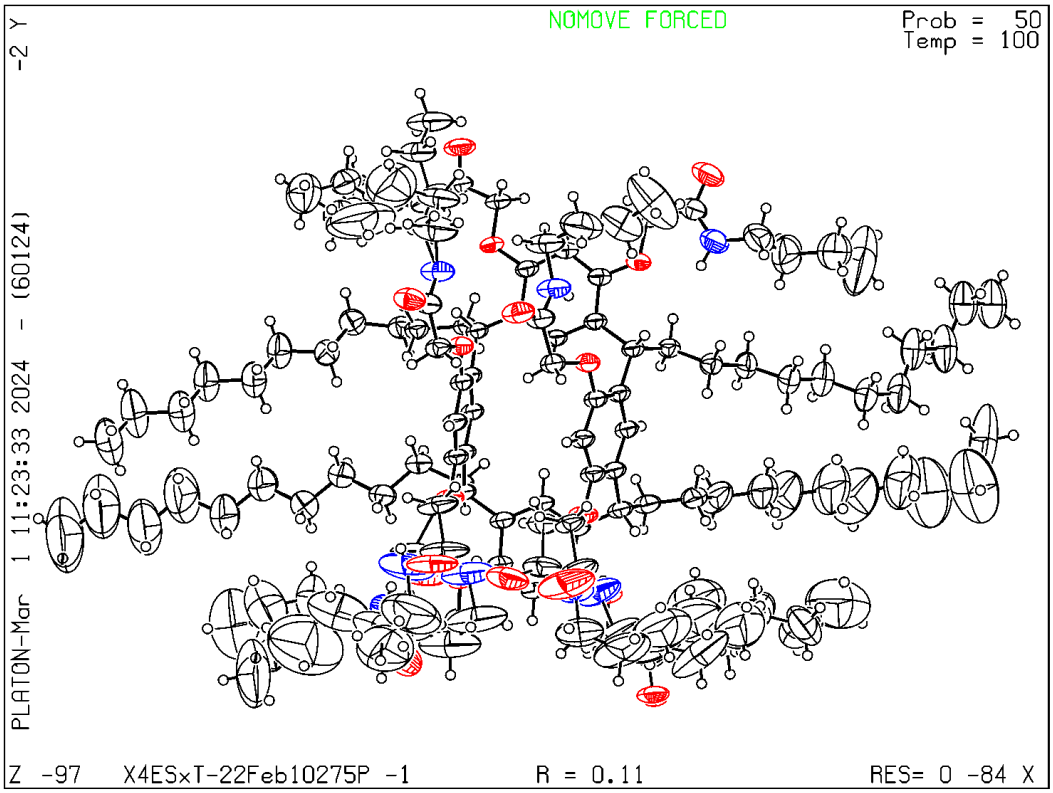


Figure S81. ORTEP drawing of the asymmetric unit of **ResQAC^{butyl}(I$^-$)$_8$**

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S4. Kabsch, W., *Acta Crystallogr. Sect. D Biol. Crystallogr.* **2010**, *66*, 133–144.

S5. Sheldrick, G.M., *Acta Crystallogr. Sect. A Found. Crystallogr.* **2015**, *71*, 3–8.

S6. Sheldrick, G.M., *Acta Crystallogr. Sect. C* **2015**, *71*, 3–8.

S7. Farrugia, L. J. *J. Appl. Crystallogr*. **2012**, *45*, 849–85.

S8. Spek, A. L., *Acta Cryst.* **2015**, *71*, 9-18.