Electronic Supplementary Material (ESI) for Chemical Communications.

Electronic Supplementary Information for

Intermolecular hydrogen bonding in calix[5]arene derived cavitands regulates the molecular recognition of fullerenes.

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1 Materials and methods

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification, and synthesis grade solvents were used. Reaction progress was monitored using thin layer chromatography (TLC) on Macherey-Nagel Xtra SIL G/UV254 silica gel plates. Flash column chromatography was performed on silica gel 60 (40-60 μm SiO_2). ^1H and ^{13}C NMR spectra were acquired at 298 K unless otherwise stated, at 400 MHz and 101 MHz respectively. A Bruker Ultrashield AVANCE III 400 spectrometer equipped with a 5 mm BBI probe and a Bruker ASCEND 400 spectrometer equipped with a 5 mm BBFO probe were used. NMR spectra were internally referenced to tetramethylsilane (TMS) for ^1H, and to the solvent signal for ^{13}C. The NMR data are reported as follows: chemical shift (δ) in ppm from TMS, multiplicity (bs = broad singlet, s = singlet, d= doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration (^1H) and assignment. IR spectra were recorded on an Agilent Cary 630 FT-IR spectrometer equipped with an ATR sampling accessory. High resolution mass spectra (HRMS) were acquired on a Bruker micrOTOF-QII instrument with an ESI source. Samples were introduced into the mass spectrometer ion source by direct infusion through a syringe pump and were externally calibrated using sodium formate. UV-Vis spectra were recorded on an Agilent 8452 UV-vis spectrophotometer equipped with a cryostat from Unisoku Co., using a 1 cm quartz cell.

2 Open data access

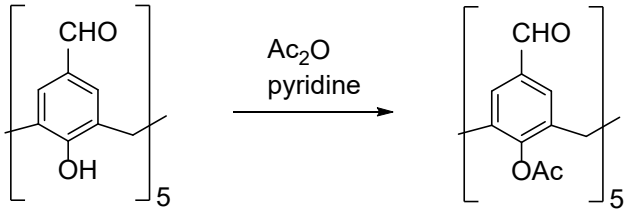
Links to available raw data

Spectroscopic data: https://doi.org/10.34810/data780

Computational data: https://doi.org/10.19061/iochem-bd-4-63

3 Synthetic procedures

5,11,17,23,29-Pentaformyl-31,32,33,34,35-pentaacetylcalix[5]arene (3).



2 **3**

In a round-bottom flask was placed pentaformyl calixarene **2**[1] (1.16 g, 1.73 mmol) and pyridine (3.6 ml, 37.59 mmol). Acetic anhydride (3.6 ml, 44.7 mmol) was added dropwise and the solution was stirred overnight. After this time, TLC (DCM/MeOH 95:5) showed that the reaction was not finished, so the mixture was heated to 40 °C and further stirred for 1 h. The reaction was then quenched by addition of HCl 1M (10 ml) and the mixture was extracted with DCM and washed with HCl 1M. The organic phase was dried (anh. Na_2SO_4), filtered, and concentrated in vacuo yielding a dark oil, which was purified by flash column chromatography (SiO_2, DCM/MeOH 100:0 to 95:5) to obtain **3** as white solid (800 mg, 53% yield).

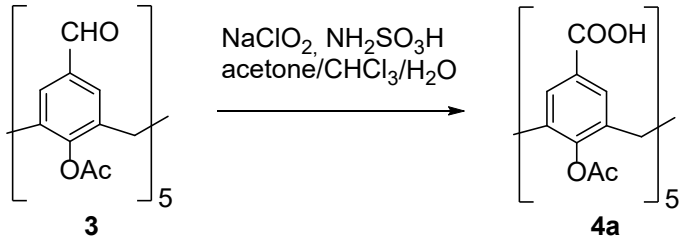
^1H NMR (400 MHz, DMSO-*d6*, 340 K) δ 9.93 (s, 5H, CHO), 7.77 (s, 10H, CH), 3.75 (s, 10H, CH_2), 1.79 (s, 15H, CH_3) ppm.

^{13}C NMR (101 MHz, DMSO-*d6*, 340 K) δ 191.4 (CO), 167.3 (CO), 151.4 (Cq), 133.6 (Cq), 133.0 (Cq), 130.4 (CH), 31.1 (CH_2), 19.2 (CH_3) ppm.

HRMS (ESI+) m/z calc. for: $C_{50}H_{40}O_{15}Na^+$ ([M+Na]$^+$): 903.2259; found 903.2314. m/z calc. for: $(C_{50}H_{40}O_{15})_2Na^+$ ([2M+Na]$^+$): 1784.4661; found 1784.4746.

IR ν 3620, 3505, 3371, 3020, 2937, 2839, 2734, 2398, 2319, 2215, 2102, 1756, 1691, 1595, 1433, 1370, 1283, 1176, 1121, 1006, 895, 818, 735, 694, cm^{-1}.

5,11,17,23,29-Pentacarboxy-31,32,33,34,35-pentaacetylcalix[5]arene (4a)



In a round bottom flask, calix[5]arene pentaaldehyde **3** (751 mg, 0.852 mmol) was dissolved in 200 mL of an acetone/$CHCl_3$ mixture (3:1). A solution of sulfamic acid (1.210 g, 12.463 mmol) in 7 mL of deionized H_2O is added at once. Then, a solution of sodium chlorite (80% w/w, 981 mg, 9.045 mmol) in 7 mL of deionized H_2O is added dropwise during a 5-minute period. The resulting pale yellow solution is stirred for 24 h at room temperature. After this time, the reaction mixture is quenched by addition of 1M HCl (30 mL). The volatiles are removed under reduced pressure, and white solids precipitate from the aqueous mixture. The resulting suspension is triturated in an ultrasonic bath and the solids are filtered and washed with deionized water. The resulting solid is dried under high vacuum in a desiccator with P_2O_5, and 854 mg of the title product are obtained as a white powder (98% yield).

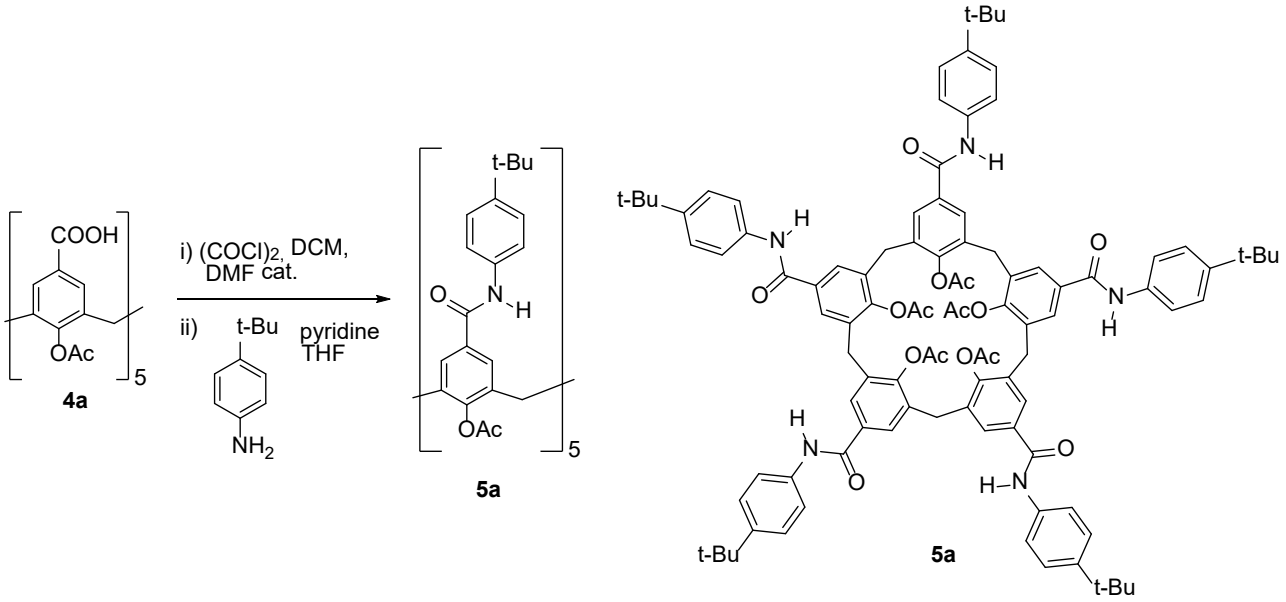
^{1}H NMR (400 MHz, DMSO, 340 K) δ 7.79 (bs, 10H, CH), 3.68 (bs, 10H, CH_2), 1.75 (bs, 15H, CH_3) ppm.

^{13}C NMR (101 MHz, DMSO, 340 K) δ 167.4 (CO), 166.1 (CO), 150.2 (Cq), 132.2 (Cq), 130.3 (CH), 128.2 (Cq), 31.3 (CH_2), 19.0 (CH_3) ppm.

HRMS (ESI−) m/z calc. for $C_{50}H_{39}O_{20}^-$ ([M−H]$^-$): 959.2040; found 959.2025. m/z calc. for $C_{100}H_{79}O_{40}^-$ ([2M−H]$^-$): 1920.4187; found 1920.4111. m/z calc. for $(C_{50}H_{39}O_{20})_2Na^-$ ([2M−2H+Na]$^-$): 1942.4006; found 1942.3912.

IR ν 3469, 3144, 2939, 2629, 2542, 2318, 2113, 1693, 1598, 1424, 1368, 1283, 1209, 1158, 1006, 905, 775, 678 cm^{-1}.

Cavitand 5a



In a round bottom flask, calix[5]arene pentaacid **4a** (110 mg, 0.114 mmol) was suspended in anh. DCM (11 mL) under a nitrogen atmosphere. Two drops of anh. DMF were then added followed by oxalyl chloride (1.8 mL of 2.0 M solution in DCM, 3.6 mmol). The mixture gradually became homogeneous, and after stirring for 18 h at room temperature the solvent was removed under reduced pressure. The residue was redissolved in anh. THF (5.5 mL) and then added dropwise to a solution of 4-*tert*-butylaniline (192 μL, 1.20 mmol) and anh. pyridine (92 μL, 1.14 mmol) in anh. THF (5.5 mL). The mixture was stirred for 20 h at room temperature under a nitrogen atmosphere. The reaction was quenched by addition of HCl 1M and extracted with DCM. The

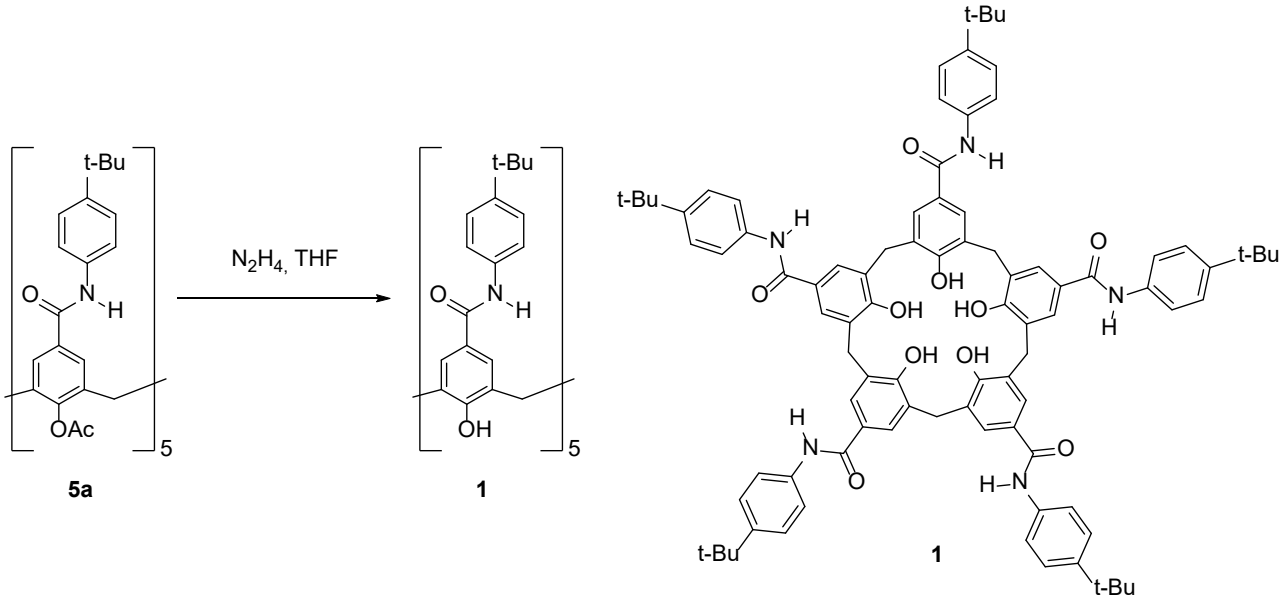
organic layer was washed with water, dried (anh. Na_2SO_4) and concentrated in vacuo. The crude product was subjected to flash chromatography (SiO_2, DCM/EtOAc from 100:0 to 70:30). The resulting solid was dissolved in the minimal amount of $CHCl_3$, precipitated by addition of *n*-pentane, and triturated in an ultrasonic bath. After drying under high vacuum, 122 mg (63%) of the title product were obtained as a light brown powder.

^{1}H NMR (400 MHz, DMSO-d_6, 340 K) δ 9.95 (s, 5H, NH), 7.84 (s, 10H, CH_{Ar}), 7.63 (d, J = 8.2 Hz, 10H, CH_{Ar}), 7.36 (d, J = 8.7 Hz, 10H, CH_{Ar}), 3.73 (s, 10H, CH_2), 1.87 (s, 15H, CH_3), 1.31 (s, 45H, CH_3).

^{13}C NMR (101 MHz, DMSO-d_6, 340 K) δ 167.8 (CO), 164.1 (CO), 149.2 (Cq), 145.9 (Cq), 136.1 (Cq), 132.4 (Cq), 131.8 (Cq), 128.9 (CH), 124.8 (CH), 120.0 (CH), 33.7 (Cq), 30.9 (CH_3), 19.3 (CH_3) ppm.

HRMS (ESI+) m/z calc. for $C_{100}H_{105}N_5O_{15}Na^+$ ([M+Na]$^+$): 1639.7532; found 1639.7530. m/z calc. for $C_{100}H_{105}N_5O_{15}Na^{+2}$ ([M+2Na]$^{+2}$): 831.3712; found 831.3701.

Cavitand 1



In a round bottom flask, peracetylated cavitand **5a** (100 mg, 0.062 mmol) was dissolved in 2 mL of THF and then N_2H_4 (0.6 mL of a 1.0 M solution in THF, 0.62 mmol) was added. After stirring overnight, the reaction was quenched by addition of HCl 0.1 M. The mixture was then extracted with DCM, and the organic layers were dried over anh. Na_2SO_4 and concentrated in vacuo. The resulting solids were triturated in Et_2O by sonication, filtered, rinsed with fresh Et_2O and dried under high vacuum. The product was further purified by trituration in the minimal amount of refluxing MeOH, yielding 63 mg (72%) of an off-white powder.

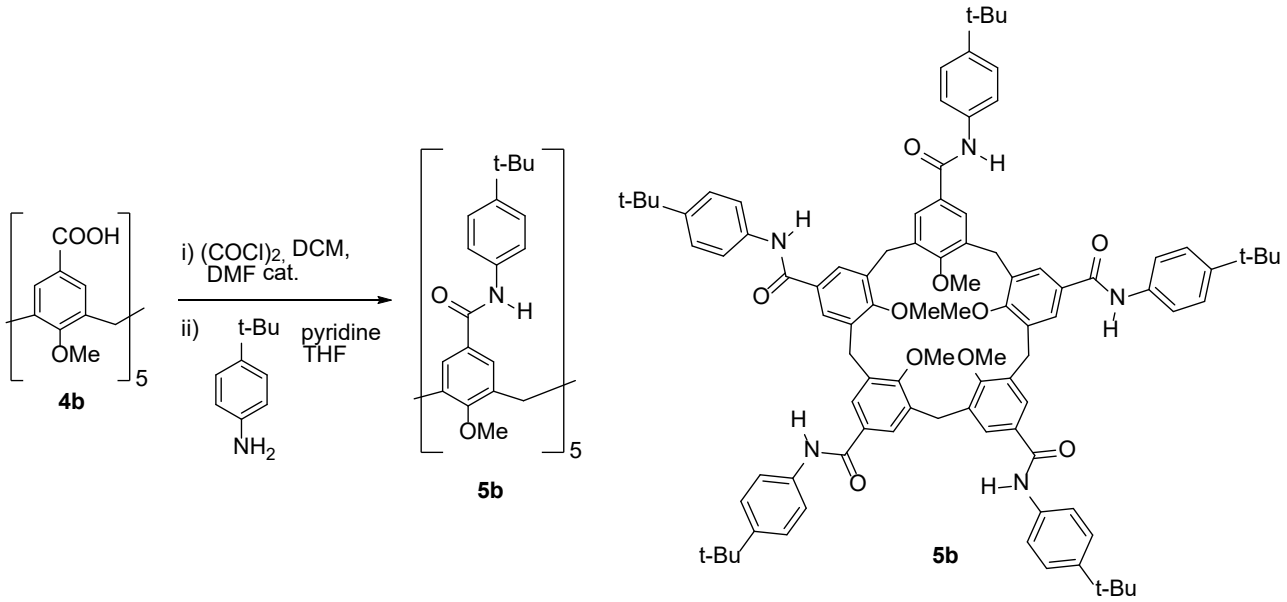
^{1}H-RMN (400 MHz, DMSO-d_6, 298 K) δ 9.89 (s, 5H), 7.82 (s, 10H), 7.60 (d, J = 8.6 Hz, 10H), 7.30 (d, J = 8.8 Hz, 10H), 3.98 (s, 10H), 1.25 (s, 45H) ppm.

^{13}C-RMN (101 MHz, DMSO-d_6, 298 K) δ 165.2 (CO), 154.7 (Cq), 145.6 (Cq), 136.7 (Cq), 129.0 (CH), 127.5 (Cq), 126.6 (Cq), 125.1 (CH), 120.1 (CH), 34.0 (Cq), 31.2 (CH_3), 30.9 (CH_2) ppm.

HRMS (ESI+) m/z calc. for $C_{90}H_{94}N_5O_{10}Na_3^+$ ([M-H+3Na]$^{+2}$): 737.3358; found: 737.3346. m/z calc. for $C_{90}H_{94}N_5O_{10}Na_2^+$ ([M-H+2Na]$^+$) 1451.6824; found: 1451.6822

IR ν 3611, 3244, 2955, 2315, 2079, 1646, 1597,1517, 1475, 1399, 1322, 1194, 1117, 829, 752 cm^{-1}.

Cavitand 5b



In a round bottom flask, **4b**[1, 2] (102 mg, 0.122 mmol) was suspended in anh. DCM (12 mL) under a nitrogen atmosphere. Two drops of anh. DMF were then added followed by oxalyl chloride (2.0 mL of 2.0 M solution in DCM, 4.0 mmol). The mixture gradually became homogeneous, and after stirring for 18 h at room temperature the solvent was removed under reduced pressure. The residue was redissolved in anh. THF (6 mL) and then added dropwise to a solution of 4-*tert*-butylaniline (290 µL, 1.82 mmol) and anh. pyridine (97 µL, 1.21 mmol) in anh. THF (6 mL). The mixture was stirred for 20 h at room temperature under a nitrogen atmosphere. The reaction was quenched by addition of HCl 1M and extracted with DCM. The organic layer was washed with water, dried (anh. Na_2SO_4) and concentrated in vacuo. The crude product was subjected to flash chromatography (SiO_2, DCM/EtOAc from 100:0 to 70:30). The resulting solid was dissolved in the minimal amount of $CHCl_3$, precipitated by addition of *n*-pentane, and triturated in an ultrasonic bath. After drying under high vacuum, 137 mg (74%) of the title product were obtained as a light brown powder.

^{1}H-RMN (400 MHz, DMSO-d_6) δ 9.99 (s, 5H), 7.72 (s, 10H), 7.60 (d, J = 8.8 Hz, 10H), 7.28 (d, J = 8.9 Hz, 10H), 4.00 (s, 10H), 3.40 (s, 15H), 1.26 (s, 45H).

^{13}C NMR (101 MHz, DMSO-d_6) δ 165.5 (CO), 159.3 (Cq), 146.2 (Cq), 137.1 (Cq), 134.3 (Cq), 130.7 (Cq), 129.2 (CH), 125.5 (CH), 120.6 (CH), 61.1 (CH_3), 34.5 (Cq), 31.7 (CH_3), 30.4 (CH_2)* ppm.

* The methylene resonance is not observed in the 1D ^{13}C spectrum, probably due to bad relaxation. It appears however as a well-defined cross peak in the corresponding ^{1}H – ^{13}C HSQC spectrum.

HRMS (ESI+) m/z calc. for $C_{95}H_{105}N_5O_{10}Na^+$ ($[M+Na]^+$): 1499.7786; found: 1499.7773.

4 Additional NMR and HRMS data.

^{1}H NMR spectra of 5b in different conditions

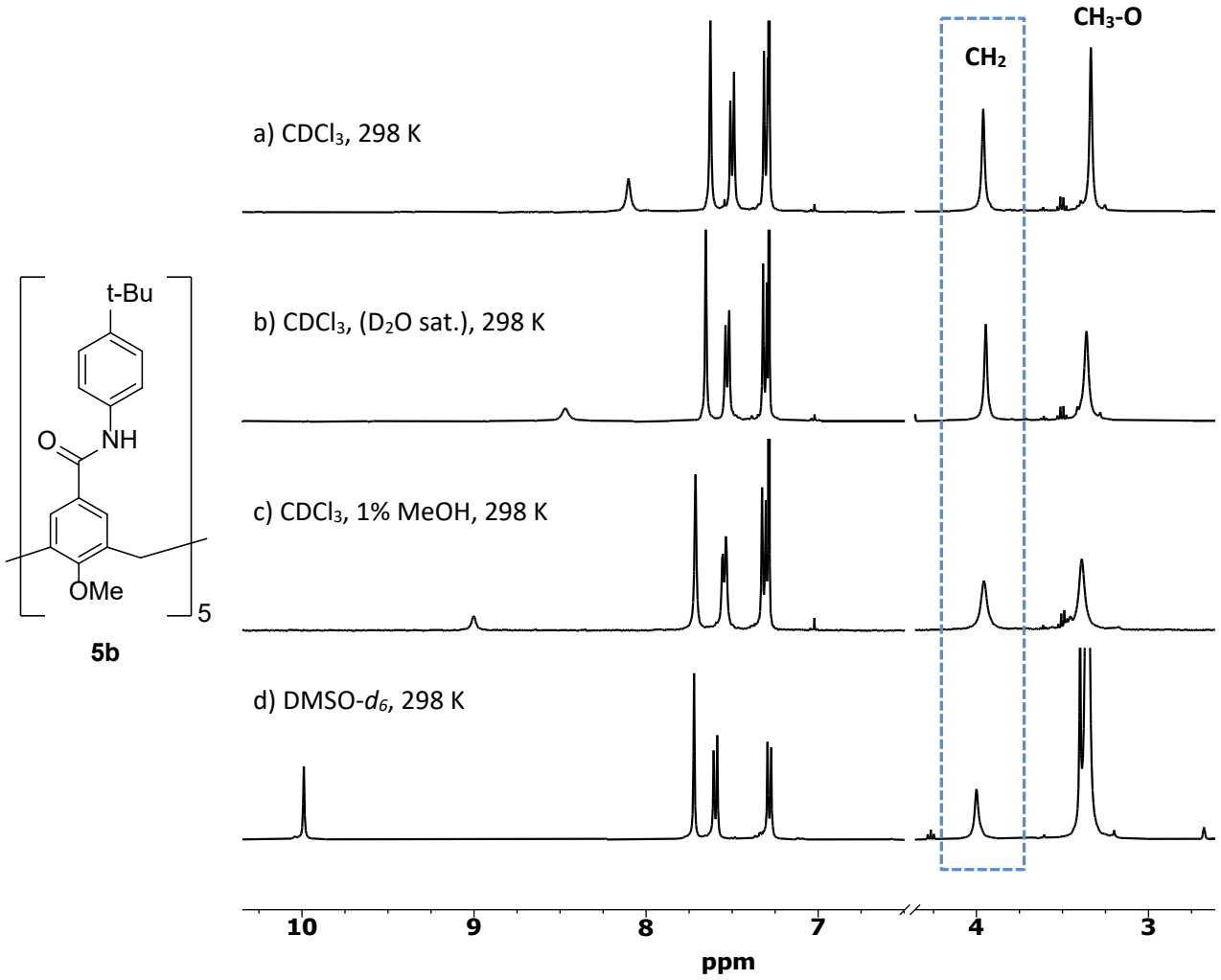


Figure S1. ^{1}H NMR analysis of **5b** in solution: a) $CDCl_3$, 298 K; b) D_2O saturated $CDCl_3$, 298 K; c) $CDCl_3$ with 1% MeOH, 273 K; d) DMSO-d_6, 298 K.

^{1}H NMR spectra: binding of C_{60} in 1.

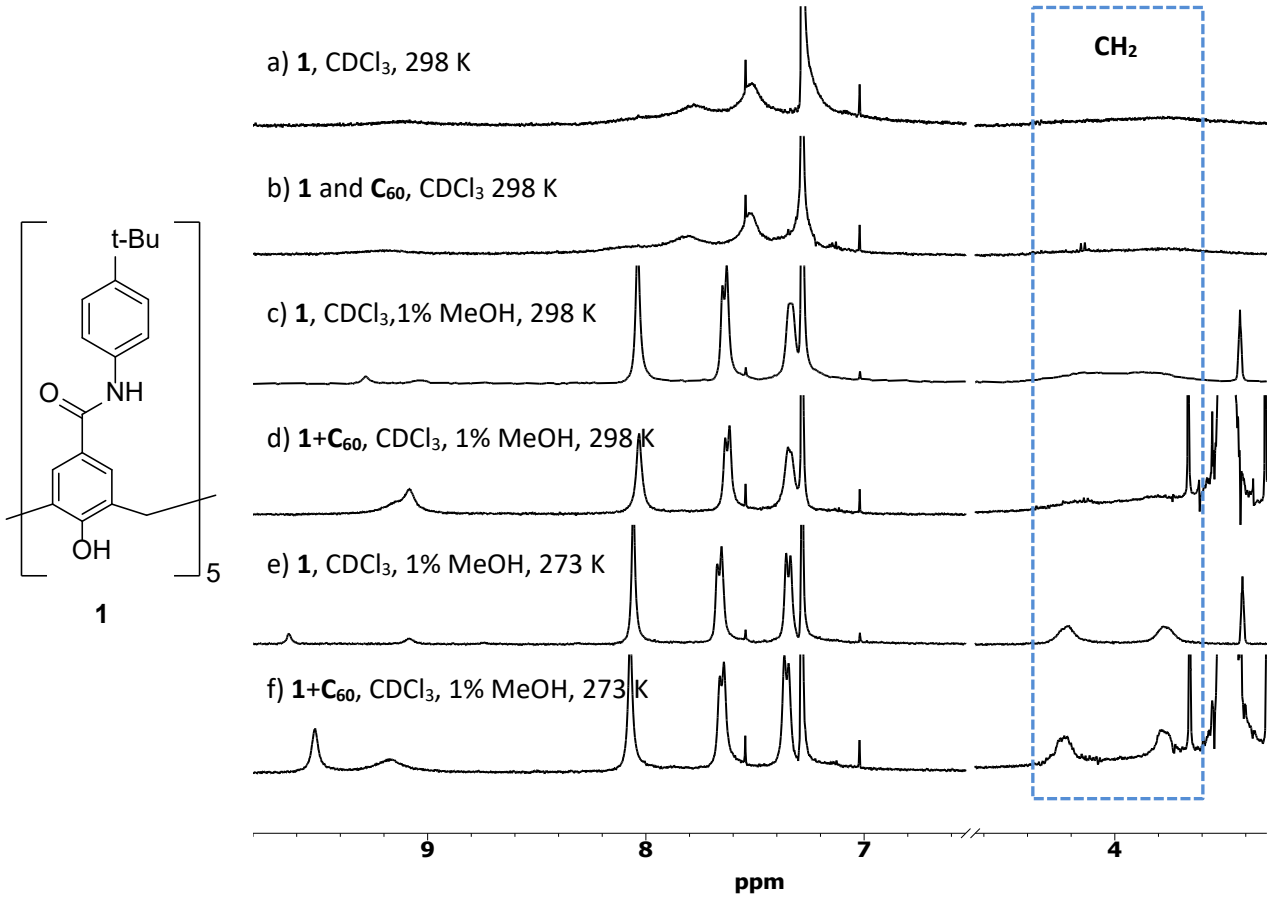


Figure S2. ^{1}H NMR binding test of $\mathbf{C_{60}}$ with **1**. a) **1**, $CDCl_3$, 298 K; b) **1** and $\mathbf{C_{60}}$, $CDCl_3$ 298 K; c) **1**, $CDCl_3$,1% MeOH, 298 K; d) **1**+$\mathbf{C_{60}}$, $CDCl_3$, 1% MeOH, 298 K; e) **1**, $CDCl_3$, 1% MeOH, 273 K; f) **1**+$\mathbf{C_{60}}$, $CDCl_3$, 1% MeOH, 273 K.

HRMS spectra: binding of C_{60} in 1.

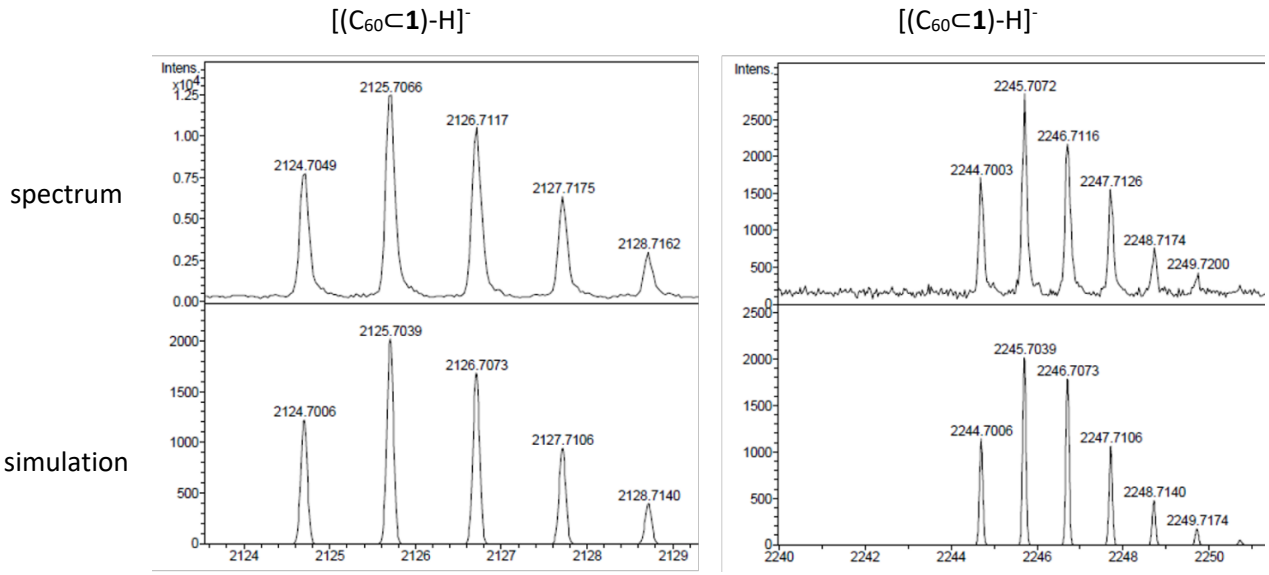
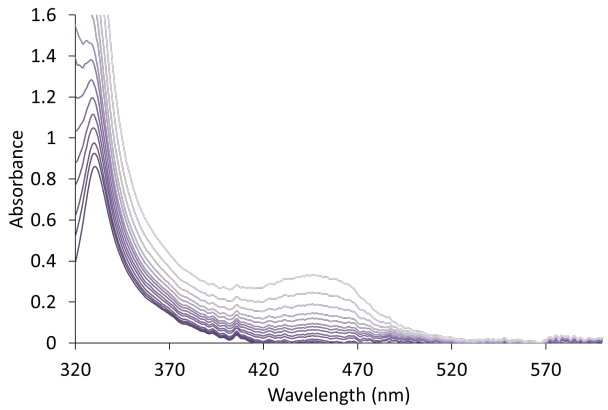
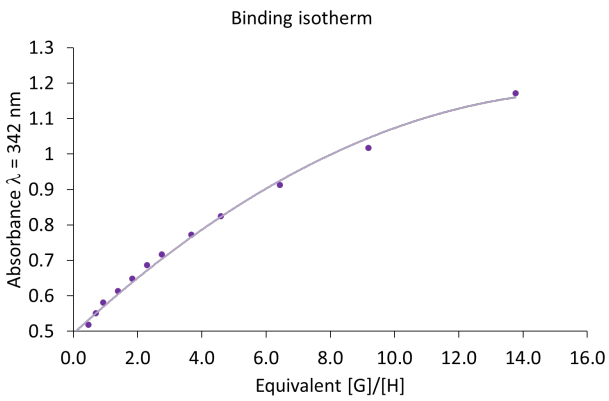


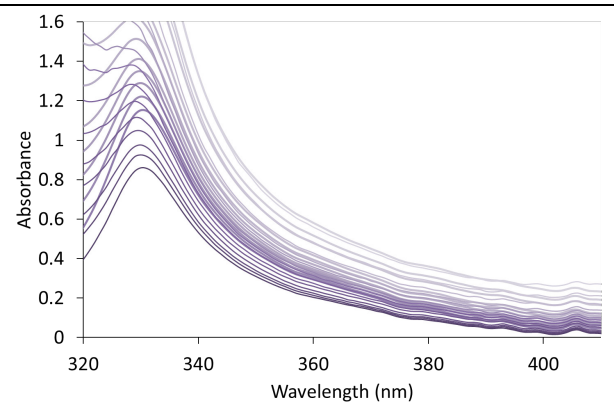
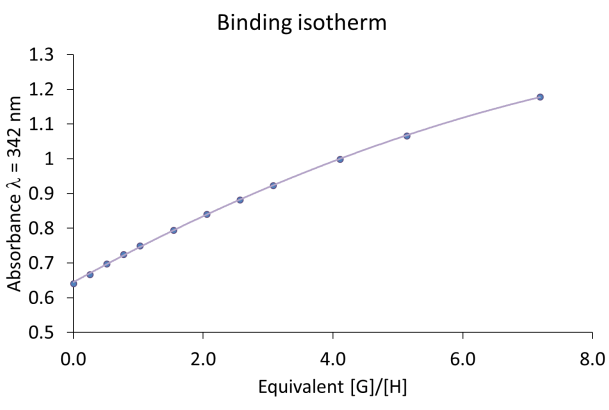
Figure S3. ESI(-) HRMS of complexes C_{60}⊂**1** and C_{70}⊂**1**.

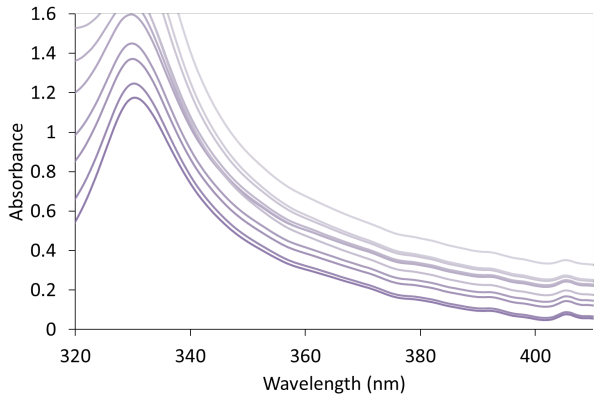
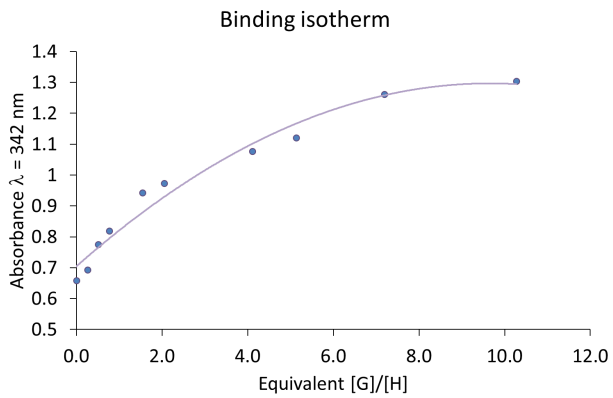
5 UV-Vis titration experiments.

All titrations were performed in a mixture of $CHCl_3$/*o*-DCB (90:10, v/v) on an Agilent 8452 UV-vis spectrophotometer using a 1 cm quartz cell. The temperature was controlled with a cryostat from Unisoku Co. Stock solutions of fullerene (C_{60} or C_{70}) in the mixture of solvents were prepared with a concentration of *ca.* $2 \cdot 10^{-5}$ M (solution **A**). Solutions of the host (**1**) in the mixture of solvents at a concentration of *ca.* $6.6 \cdot 10^{-4}$ M were prepared either in the aforementioned mixture of solvents (solution **B**) or in the same mixture containing methanol (0.3% v/v, [MeOH]/[**1**] = 10^2) (solution **C**). Titrations were carried out at the indicated temperature by adding increasing amounts of solution **B** or **C** to an initial 2 mL volume of solution **A**, recording the UV-Vis spectrum after each addition. Absorbance values were extracted and fitted to a binding isotherm using Bindfit.[3-4] The titrations were repeated three times. The K_a values are reported as the mean value of the replicates, and the error is expressed as the confidence interval at 95% confidence, based on the standard deviation of the three experiments.

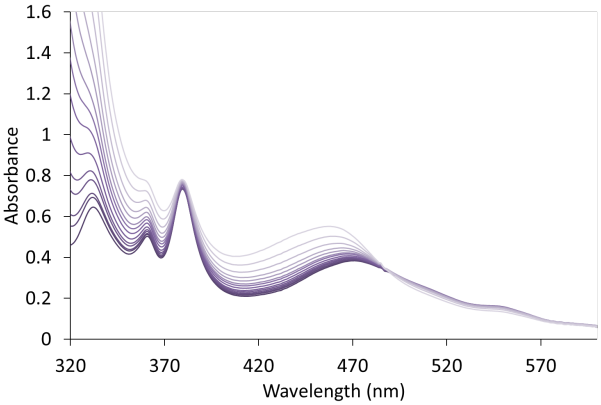
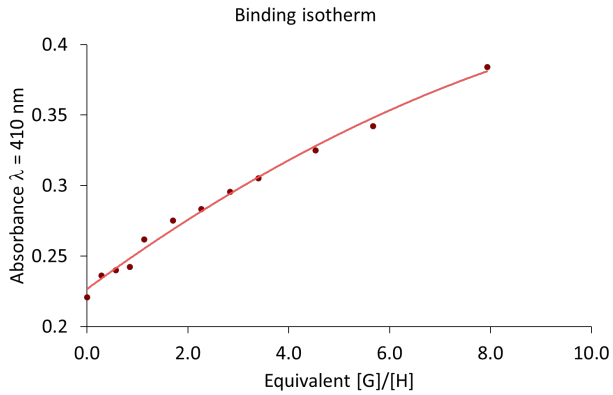
Binding of C_{60}

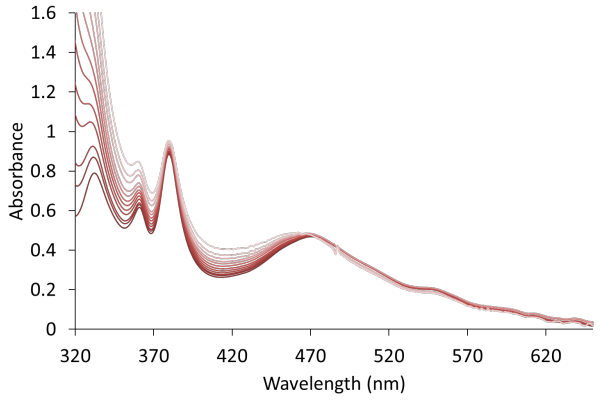
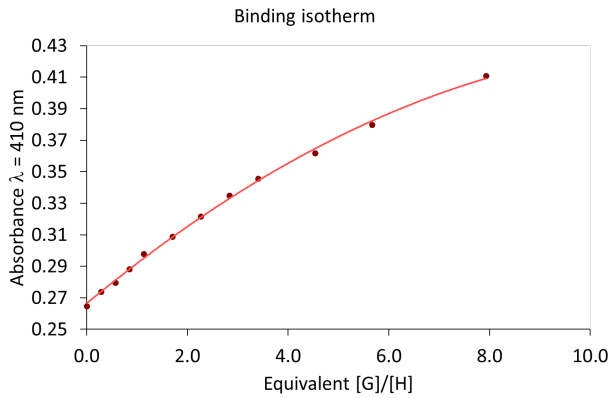
1 + C_{60}, T = 298 K	$K_a = 6500 \pm 20$ M^{-1}
	

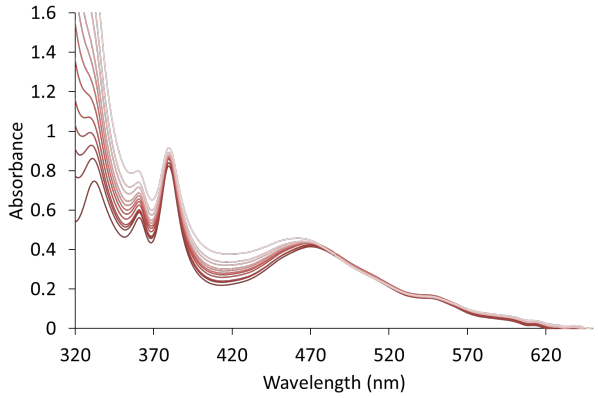
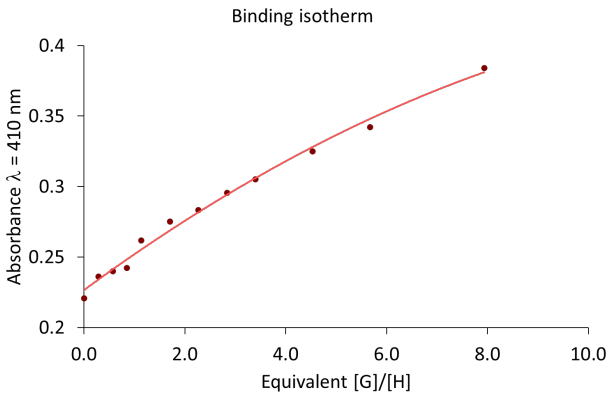
1 + C_{60}, T = 283 K	$K_a = 3061 \pm 3$ M^{-1}
	

1 + C_{60} + MeOH, T = 283 K	K_a = 33000 ± 7000 M^{-1}
	

Binding of C_{70}

1 + C_{70}, T = 298 K	K_a = 4020 ± 20 M^{-1}
	

1 + C_{70}, T = 283 K	K_a = 7010 ± 20 M^{-1}
	

1 + C_{70} + MeOH, T = 283 K	K_a = 6020 ± 50 M^{-1}
	

6 Molecular modelling studies

Geometries of all stationary points were optimized without symmetry constraints with the Gaussian 16 program,[5] including solvent effects corrections of a chloroform solution computed with the polarizable continuum model (PCM). For the complex **1**·5(MeOH) the optimization was carried out using the DFT B3LYP hybrid exchange-correlation functional with a DG-DZVP basis set and GD3BJ energy corrections for dispersion. For the fullerene complexes C_{60}⊂**1**·5(MeOH) and C_{70}⊂**1**·5(MeOH) the optimization was carried out at the PM7 semiempirical level.

The buried volume for **1**·5(MeOH) was computed with the channel finder tool available in the 3V website,[6-7] using a 1.4 Å and 30 Å inner and outer probe radii respectively. Molecular models were generated with Chimera 1.10.2.

7 References

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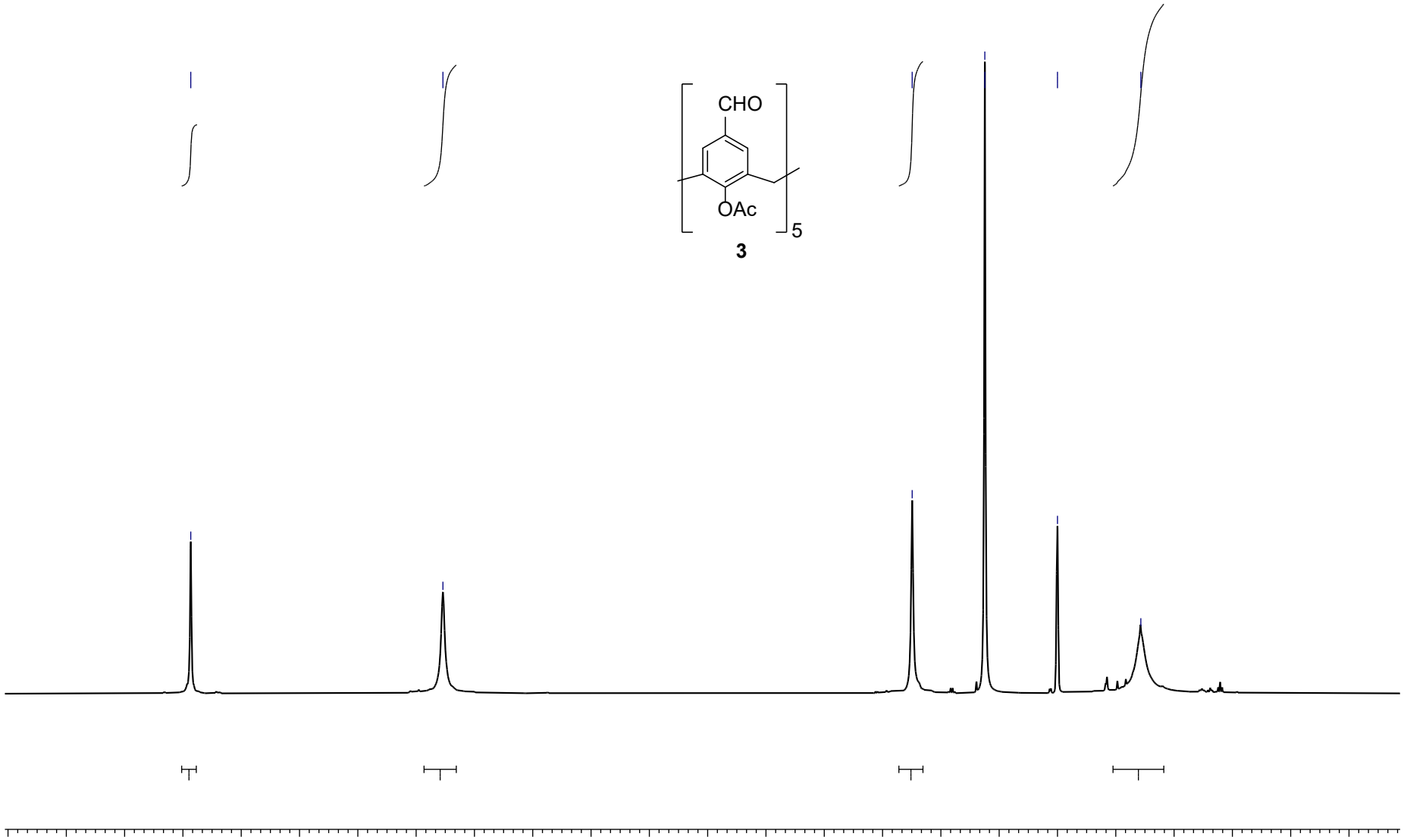
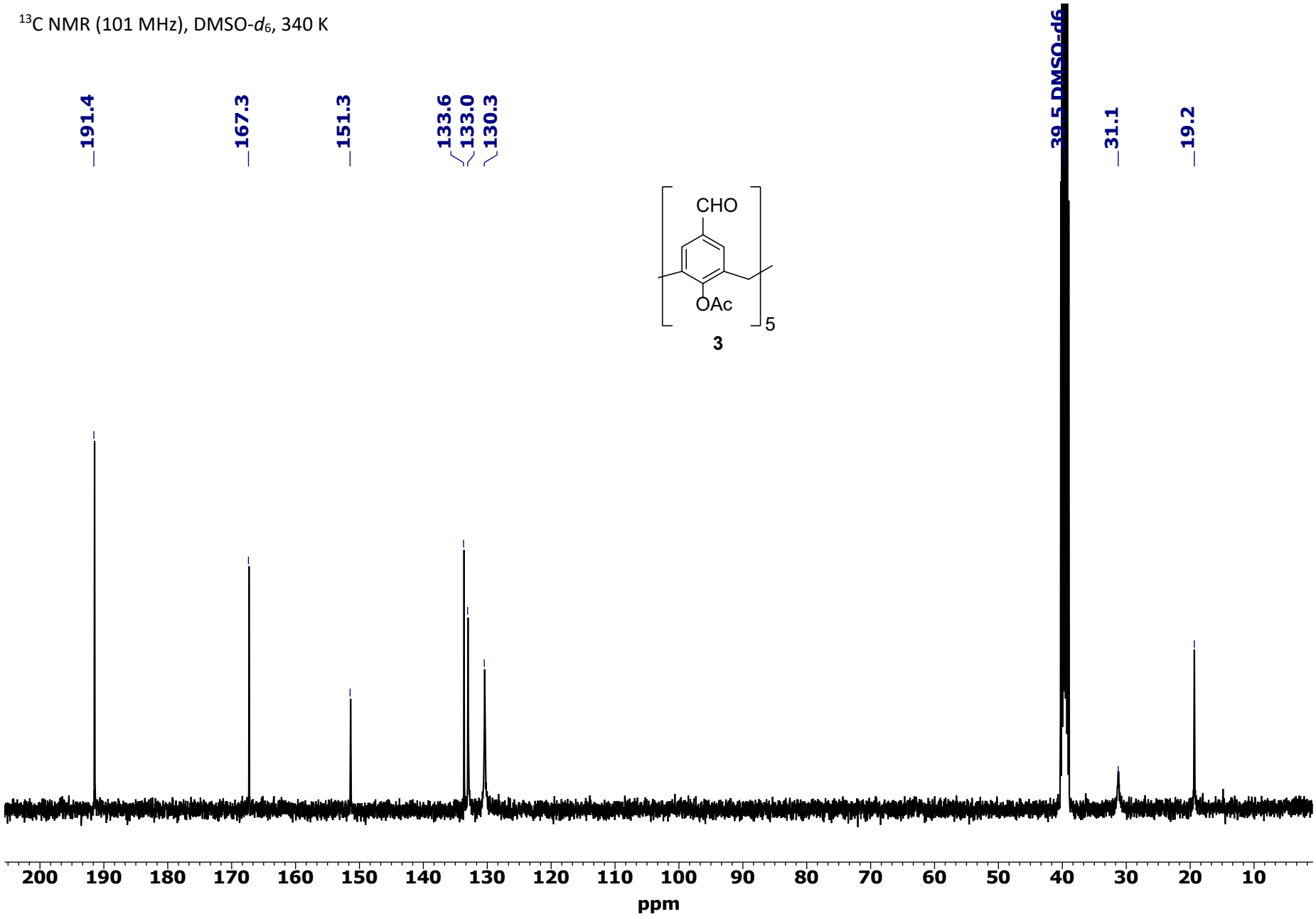
8 NMR Spectra of new compounds.

^{1}H NMR (400 MHz), DMSO-d_6, 340 K

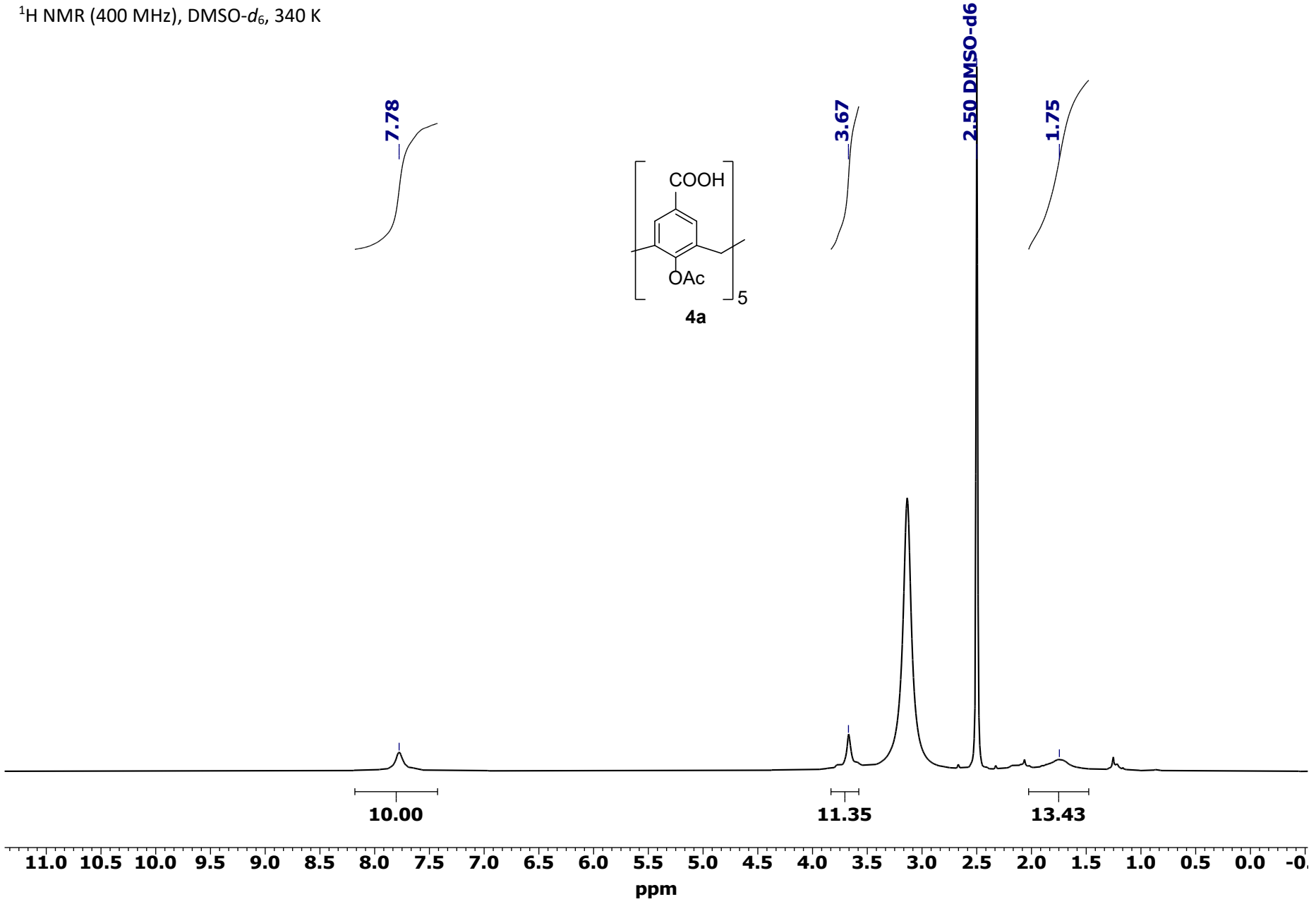


3

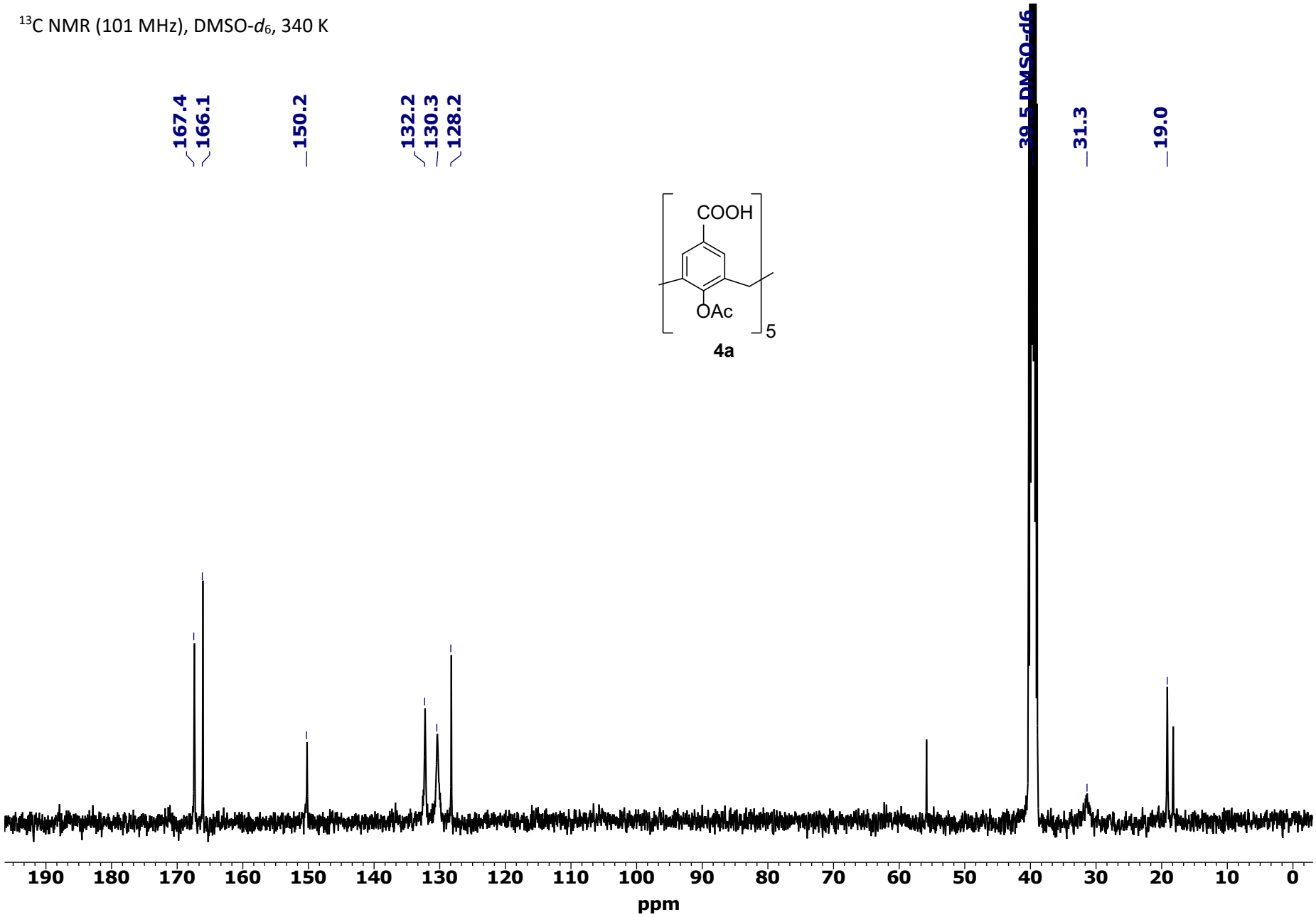
^{13}C NMR (101 MHz), DMSO-d_6, 340 K



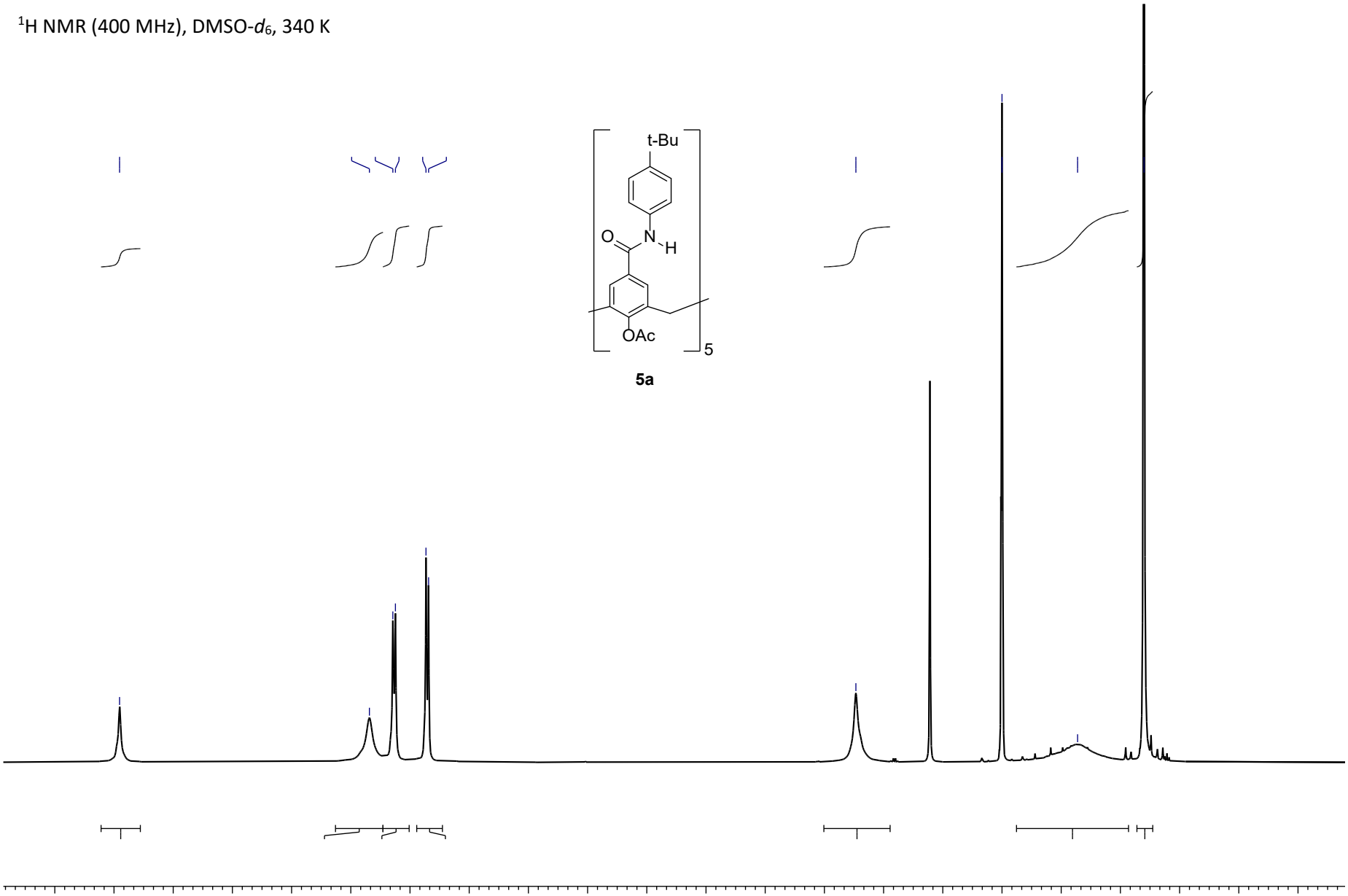
^{1}H NMR (400 MHz), DMSO-d_6, 340 K



^{13}C NMR (101 MHz), DMSO-d_6, 340 K

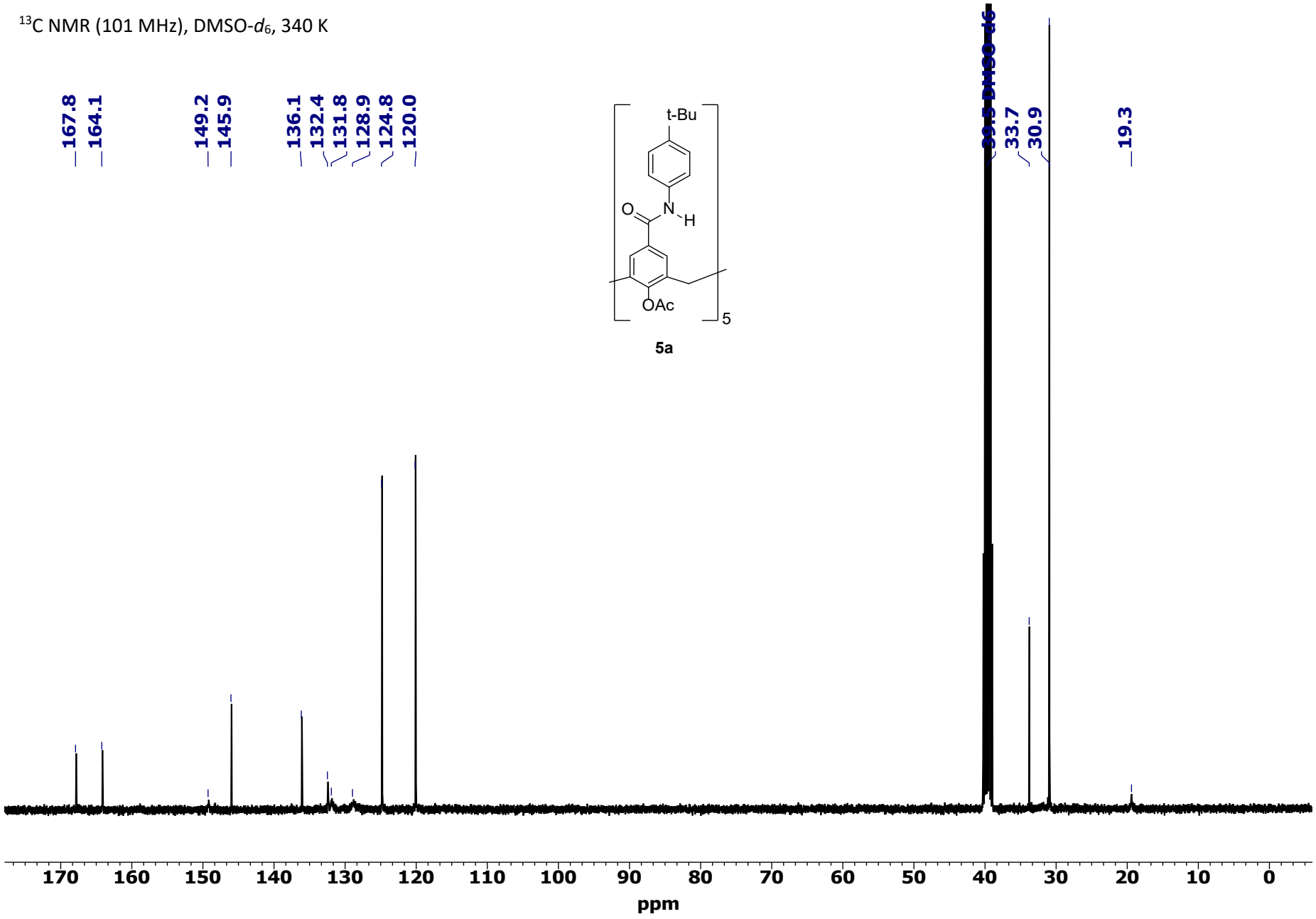


^{1}H NMR (400 MHz), DMSO-d_6, 340 K



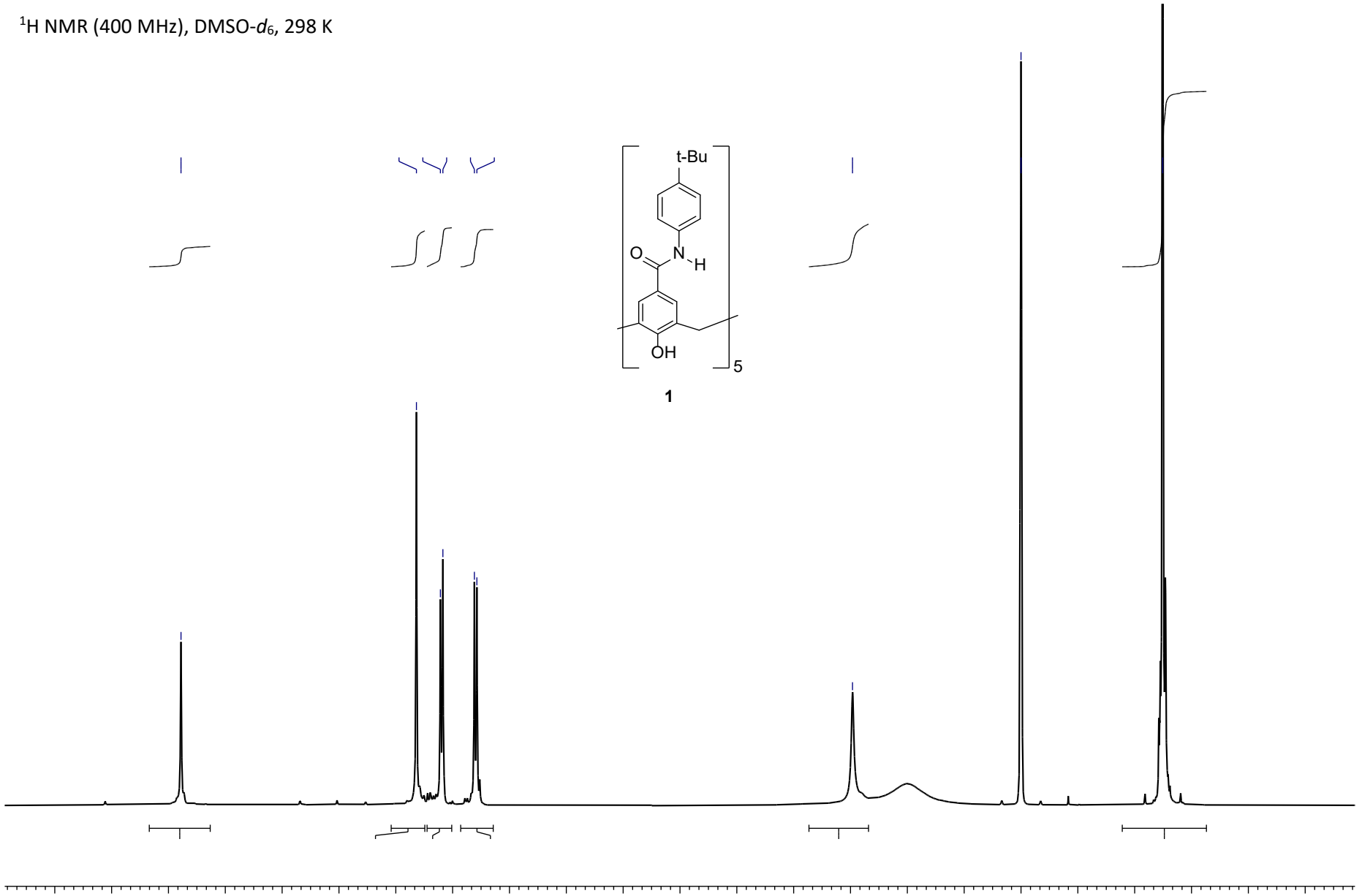
5a

^{13}C NMR (101 MHz), DMSO-d_6, 340 K



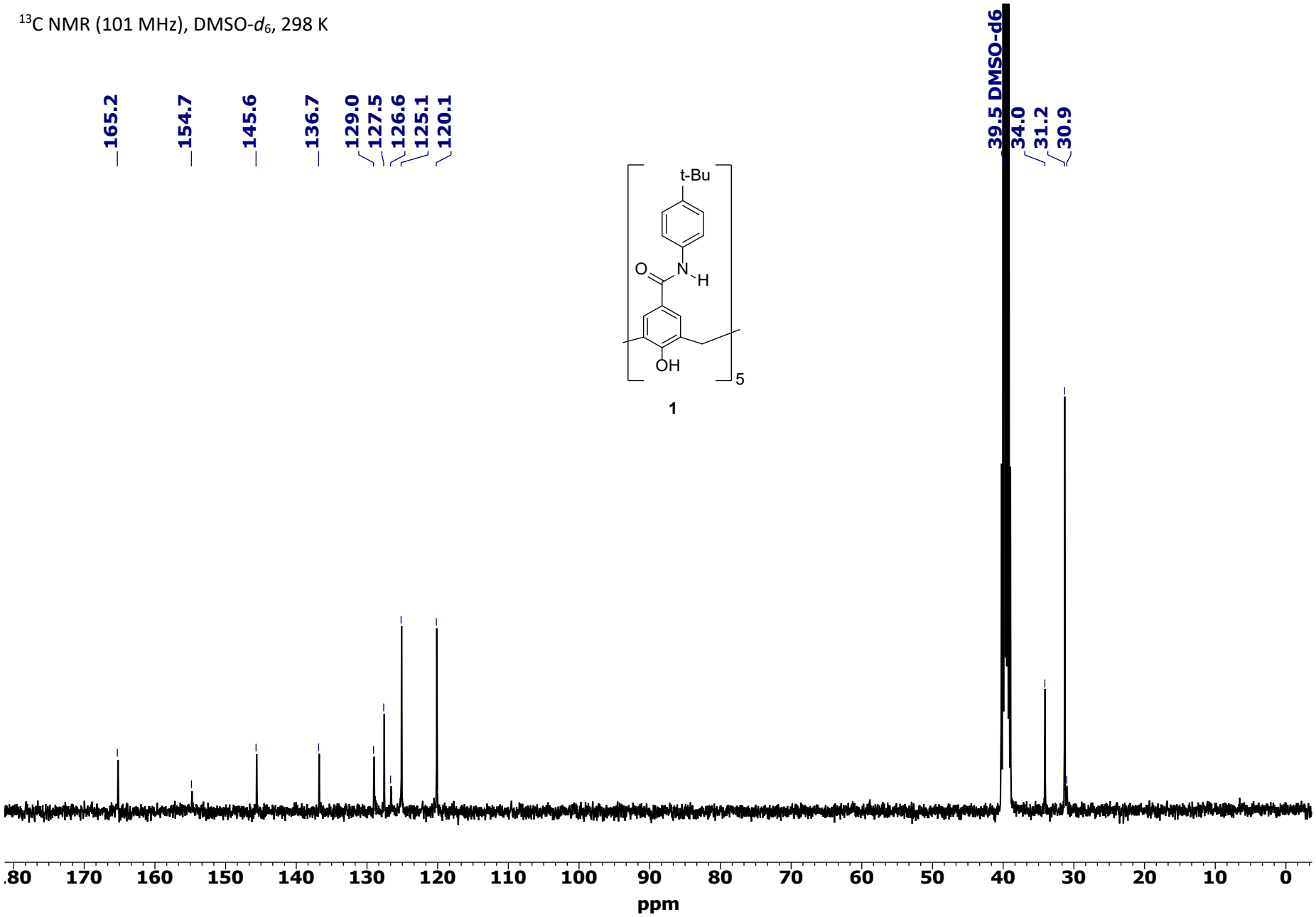
5a

^{1}H NMR (400 MHz), DMSO-d_6, 298 K

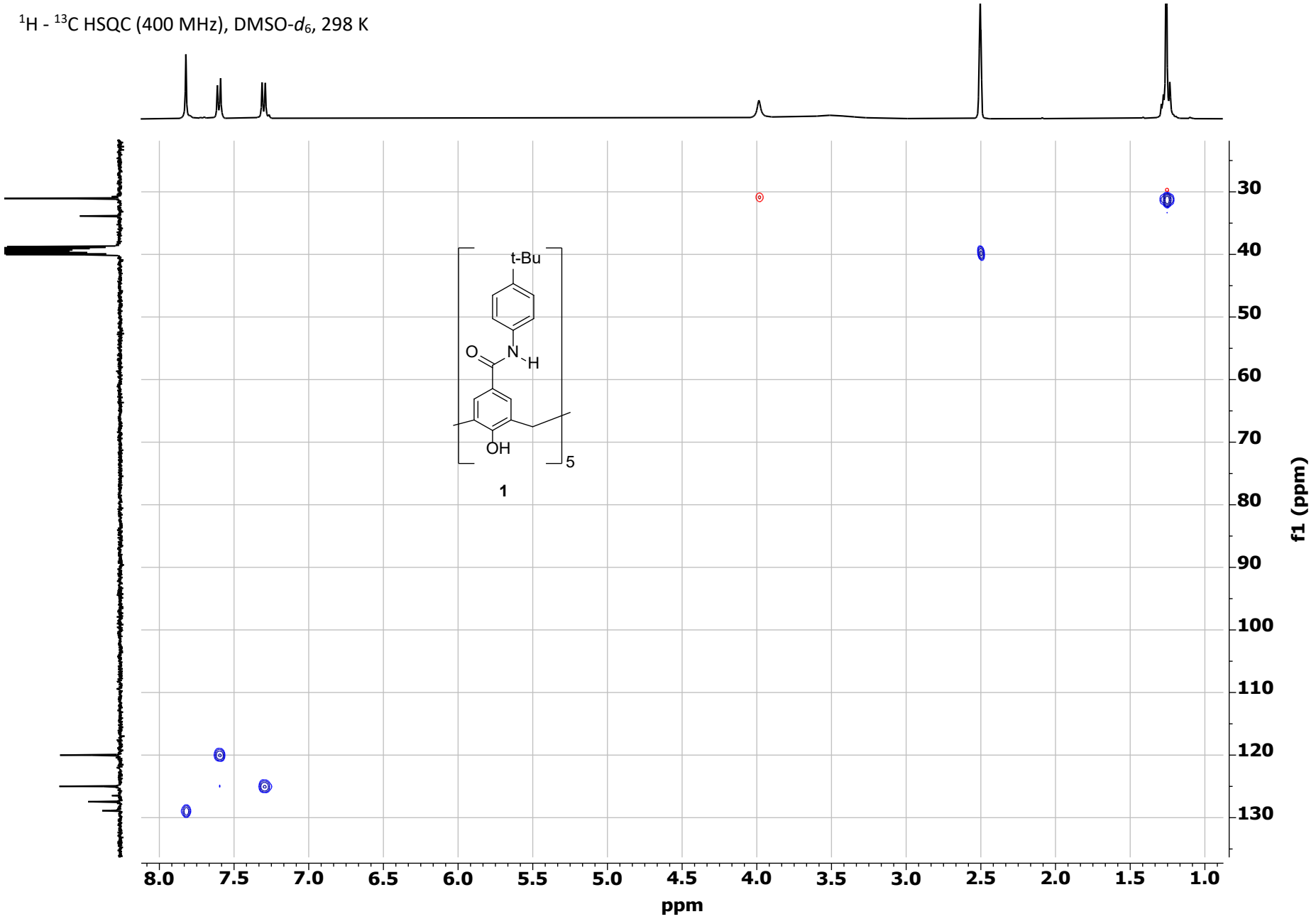


1

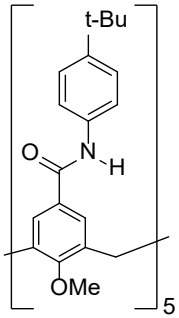
^{13}C NMR (101 MHz), DMSO-d_6, 298 K



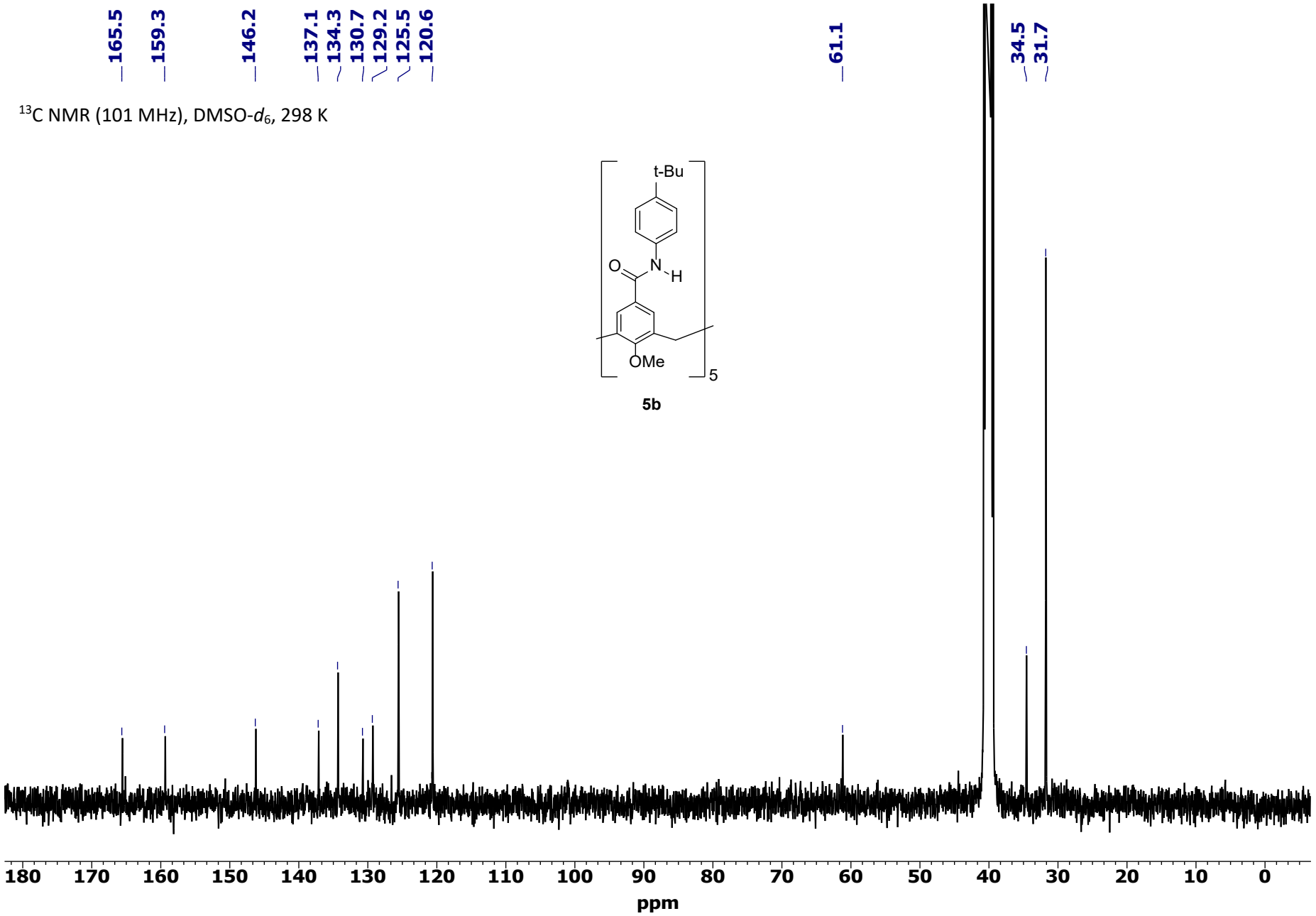
^{1}H - ^{13}C HSQC (400 MHz), DMSO-d_6, 298 K



^{1}H NMR (400 MHz), DMSO-d_6, 298 K

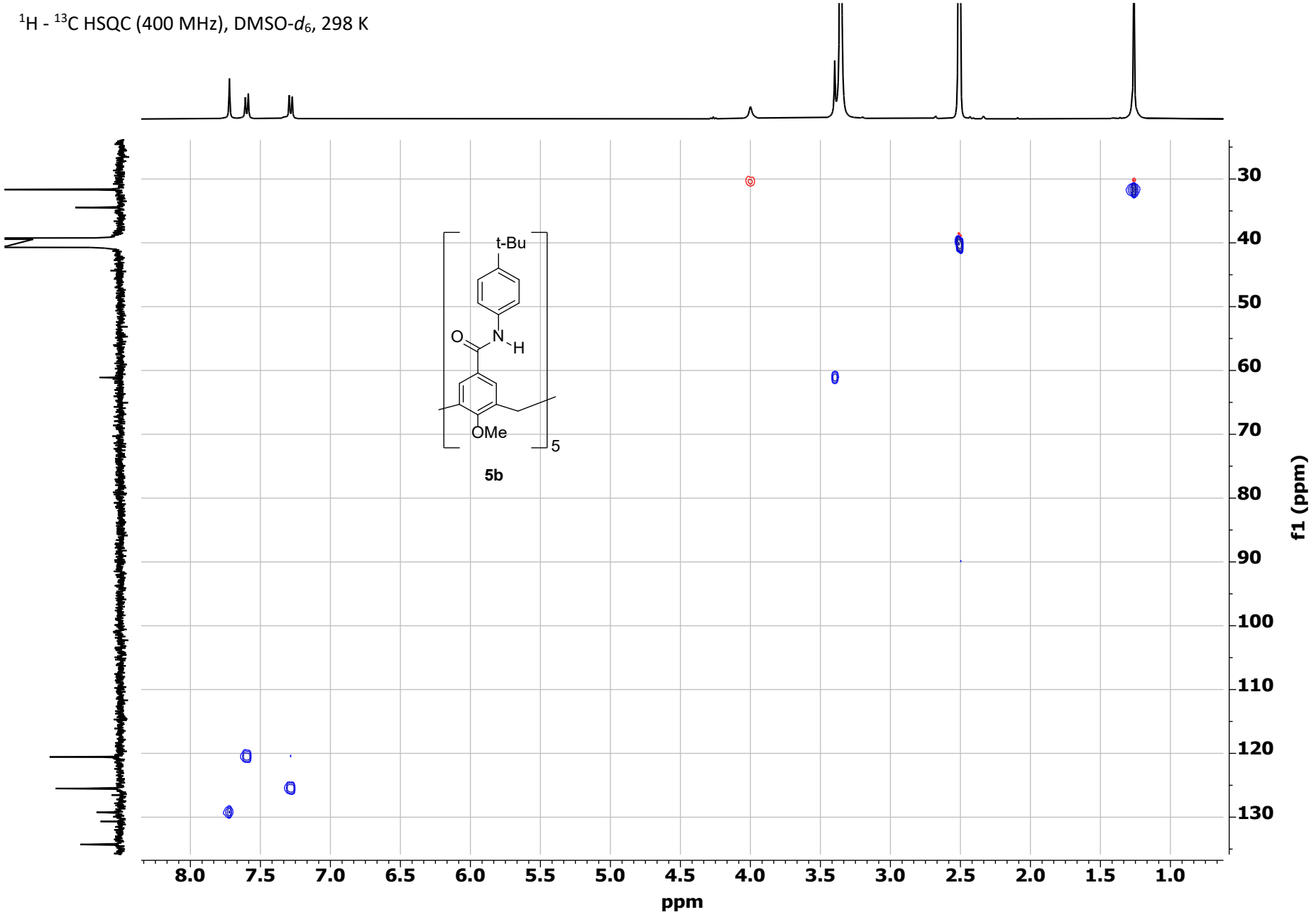


5b


165.5
159.3
146.2
137.1
134.3
130.7
129.2
125.5
120.6
61.1
34.5
31.7
^{13}C NMR (101 MHz), DMSO-d_6, 298 K
t-Bu
O
N
H
OMe
5
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

5b

^{1}H - ^{13}C HSQC (400 MHz), DMSO-d_6, 298 K

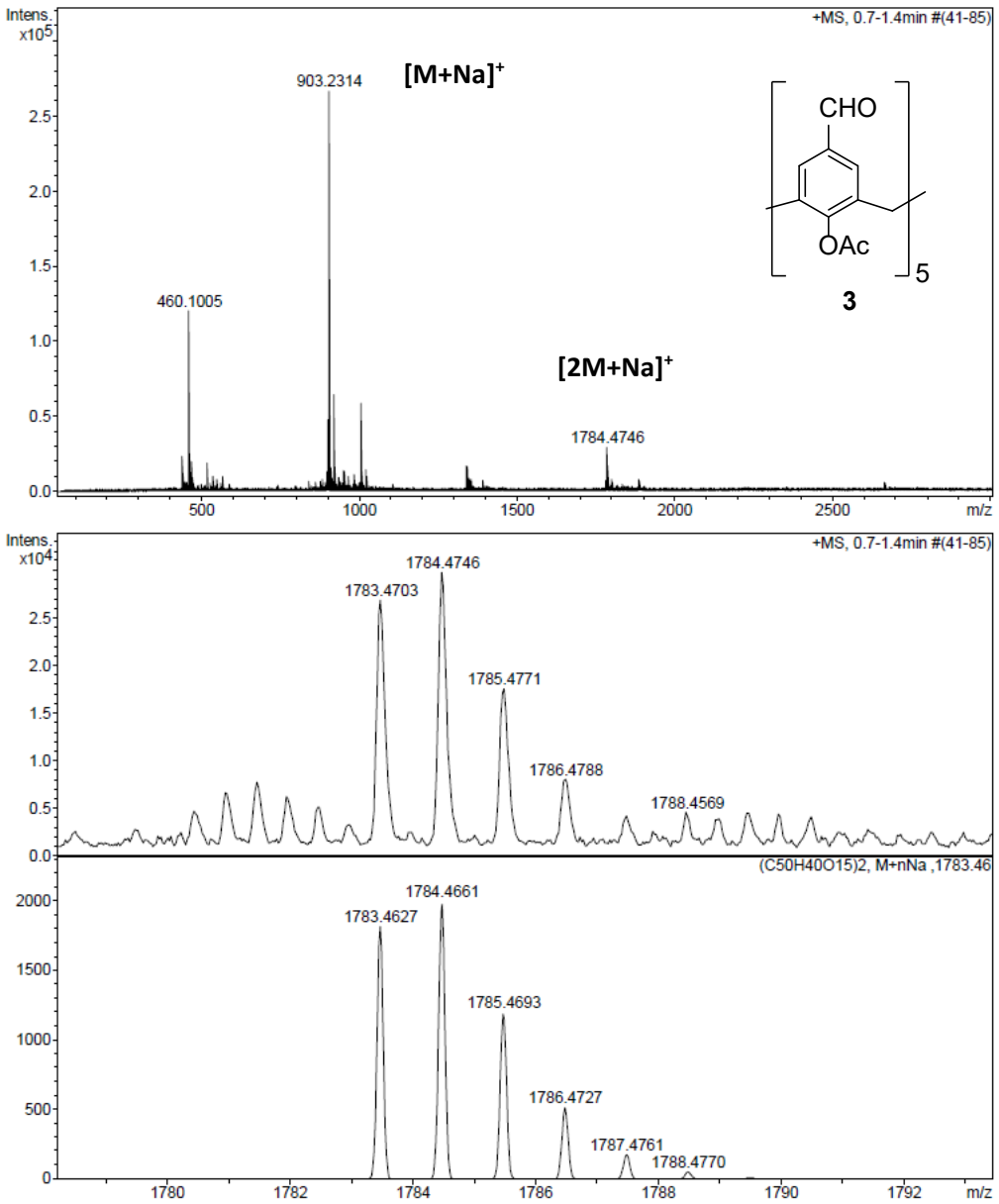


9 HRMS spectra of new compounds

Generic Display Report

Analysis Info

Acquisition Date	28/2/2022 9:24:54		
Analysis Name	X:\QTOF files\Àngel Oliveras\Ruben Alvarez\20220228\20220228000004.d		
Method	tune_wide.m	Operator	Univ. Girona
Sample Name	RAY CHO[C5]OAc	Instrument	micrOTOF-Q II
Comment			



Generic Display Report

Analysis Info

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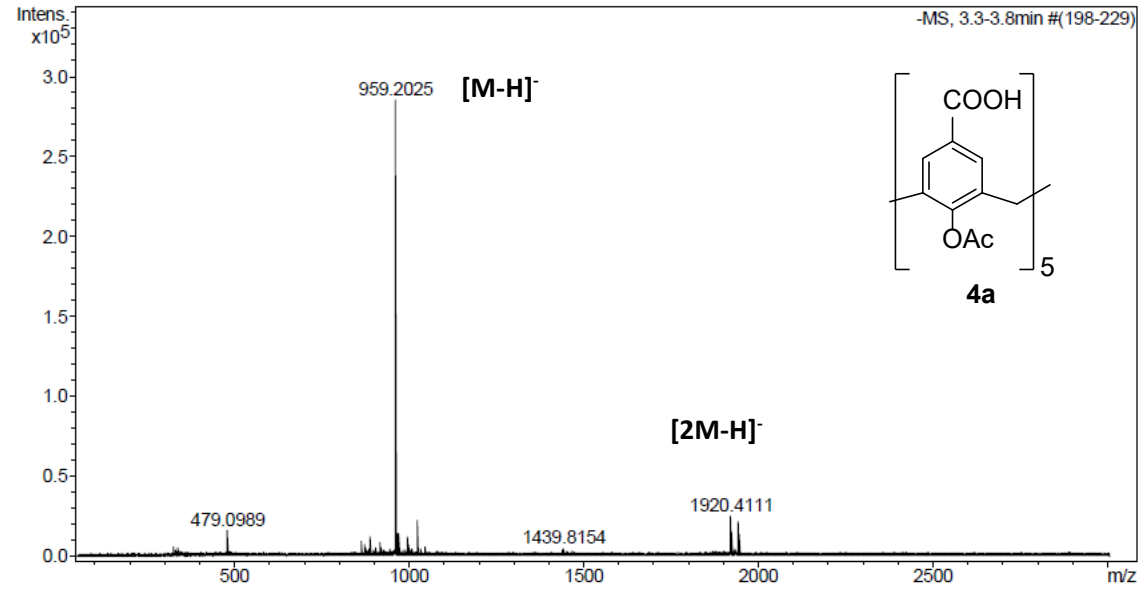
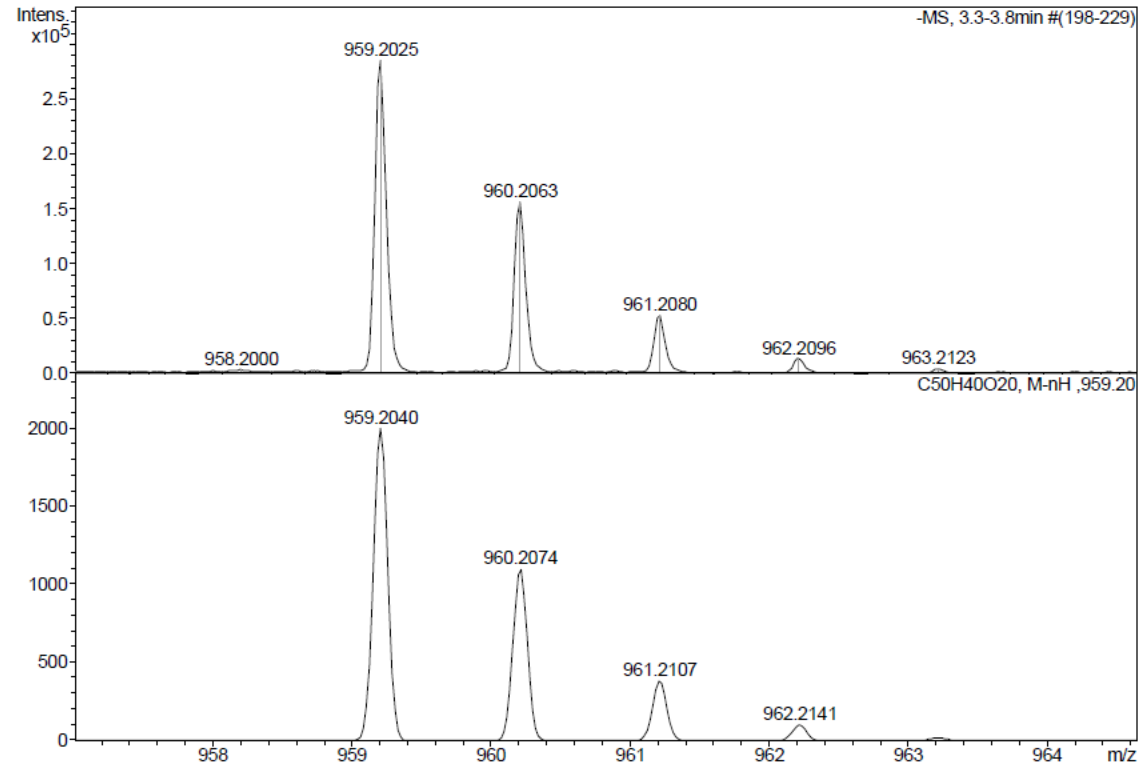
Sample Name	RAY COOH[C5]OAc	Instrument	micrOTOF-Q II
Comment			





Generic Display Report

Analysis Info

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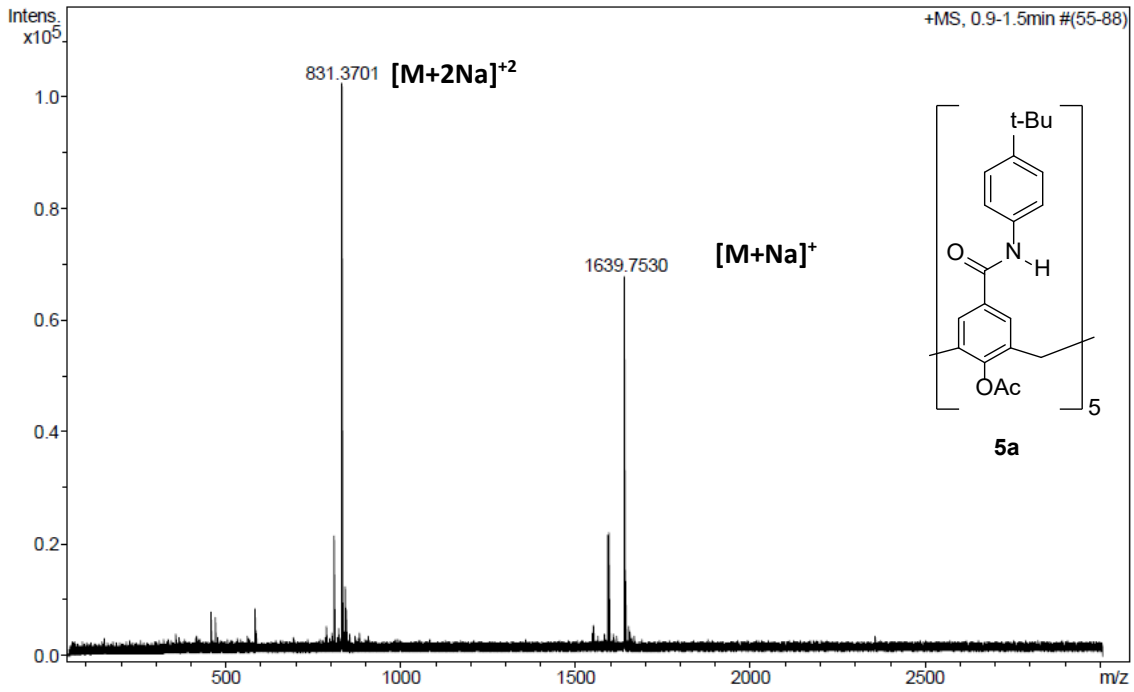
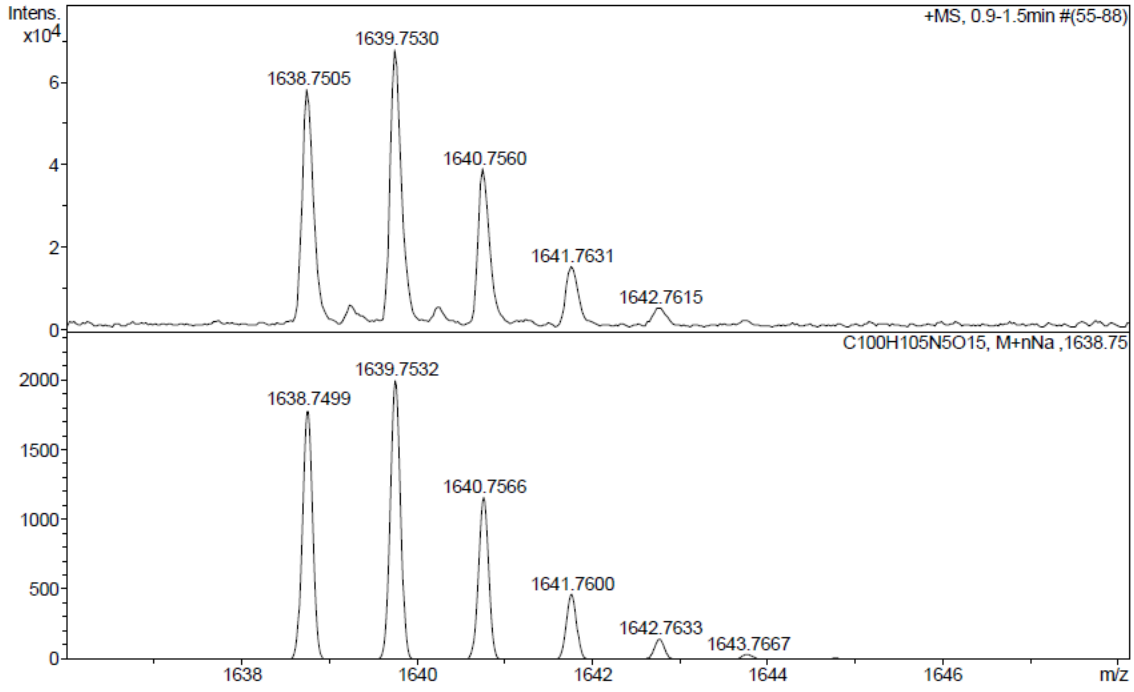
Sample Name	ASV017	Instrument	micrOTOF-Q II
Comment			





Generic Display Report

Analysis Info

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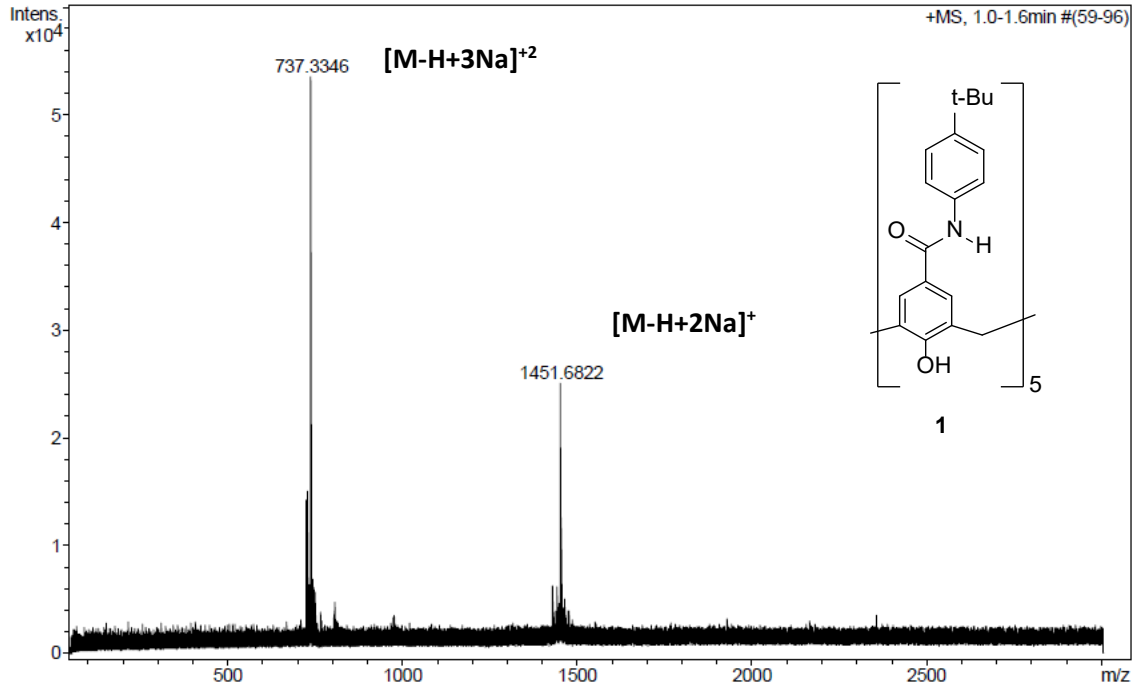
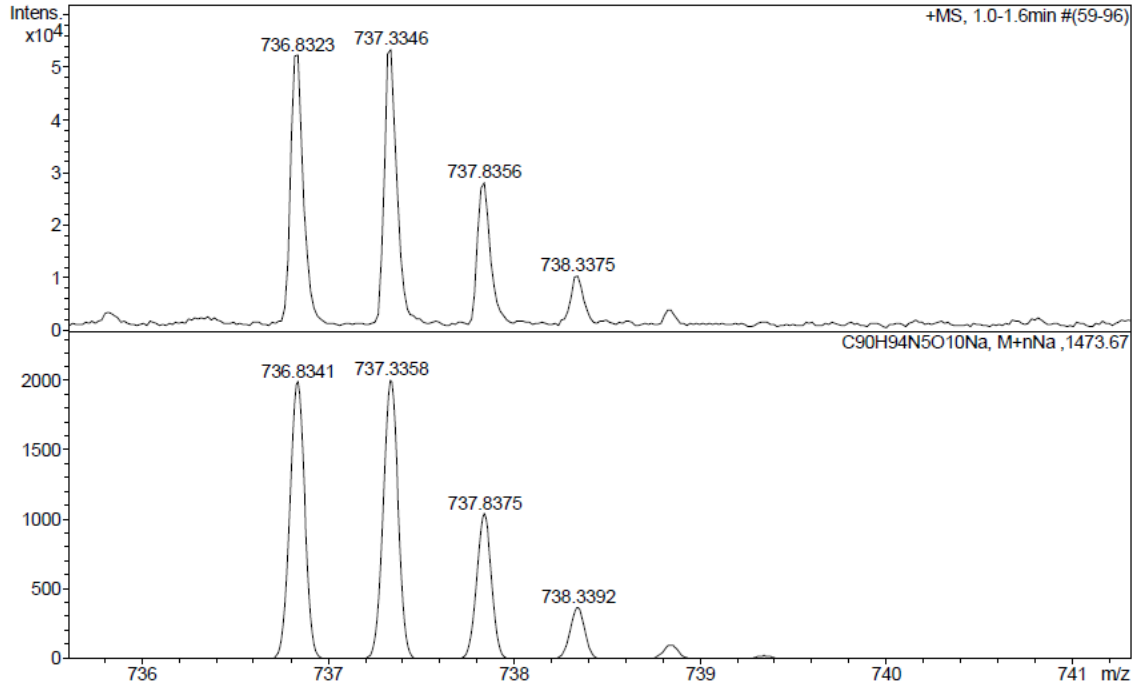
Comment			





Generic Display Report

Analysis Info

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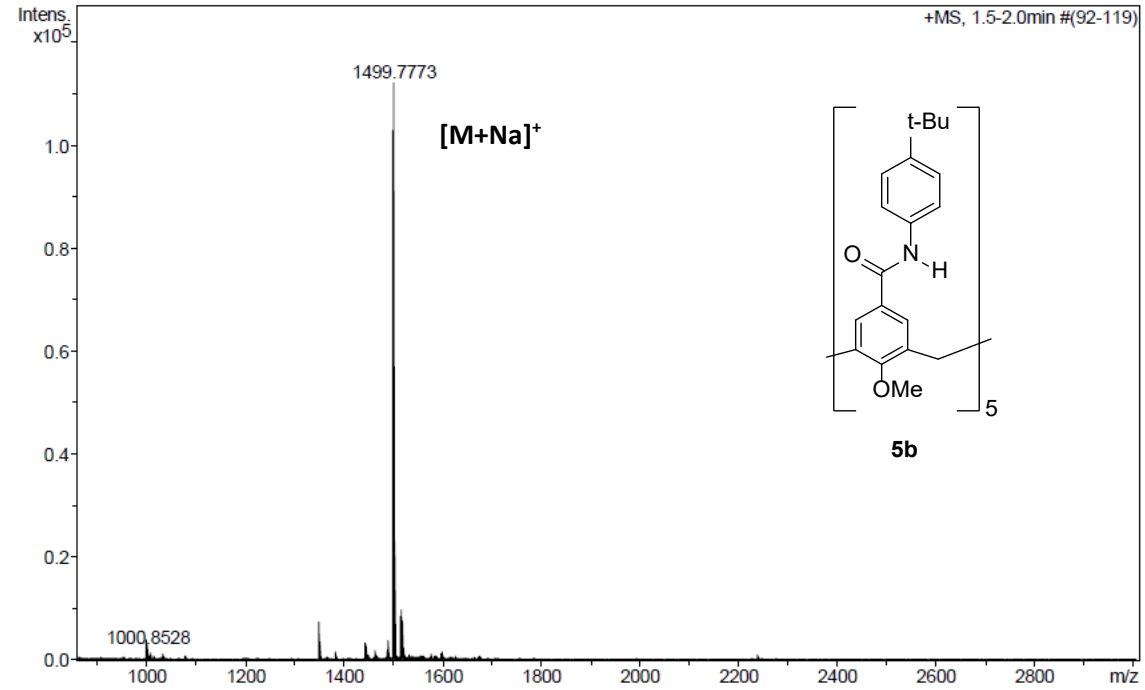
Comment			



5b