Competitive hydrogen bonding in supramolecular polymerizations of tribenzylbenzene-1,3,5-tricarboxamides

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Supporting Information

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Molecular Dynamics (MD) simulations

Computational details

All-atom molecular dynamics (MD) simulations, an effective technique to get more insight into molecular order and dynamics of supramolecular systems,[1,2] were performed using AMBER 16 software.[3] We started from prearranged BTA fibers. For this, BTA monomers were built within Discovery Studio 4.0[4] and parametrized with the '*general AMBER force field (GAFF)*'[5]. The partial atomic charges of monomers were calculated using the semiempirical AM1-BCC model[6,7] with the *antechamber* module.[8] Then, these monomers were replicated along the z-axis to build fibers of 12 and 24 BTA units, characterized by a stacking distance (between adjacent BTAs) of 5 *Å*, chosen higher than the characteristic BTA stacking distance of ~3.4 *Å*[9] to avoid biasing the system. Once BTA fibers were built, we performed a 10,000 steps energy minimization consisting in 1,000 steps of steepest descent algorithm, followed by 9,000 cycles of conjugate gradient. After initial energy minimization, BTA fibers underwent 500 ns of MD simulations. Particle velocities in each direction were randomly assigned according to the Maxwell-Boltzmann velocity distribution function at the specified temperature. MD simulations were performed at a temperature of 300 K using a Langevin thermostat with a coupling constant of 1 ps. Non-bonded interactions were calculated with a virtual infinite cutoff. All MD simulations used a time step of 1 fs and were performed in the gas phase (*i.e.* no solvent) to reproduce the low dielectric constant of MCH in which BTAs self-assemble and to reduce the computational cost. The resulting trajectories were visualized using the *VMD* software package[10] and snapshots of the MD trajectories were captured using *PyMOL.*[11]

Position of defects in the fibers. The distance/angle between center-of-mass of BTA cores were calculated using *cpptraj* module[12] of AMBER 16. Each distance/angle was averaged over the entire simulations and plotted for each pair/triad of BTA units sliding in steps of one BTA unit along the fiber (starting from the first BTA unit).

Hydrogen bonds. Intermolecular H-bonds (amide-amide or amide-ether H-bonds) between BTA units were identified using *cpptraj* module of AMBER 16. A donor (D)-acceptor (A) distance cut-off of 3.5 Å and no A-H-D angle cutoff were used to prevent missing any possible hydrogen bonds. Only persistent H-bonds (*i.e.* those present more than 90% of simulation time) were considered.

Helical kink identification. The bending and the kinking of helices were computed using the HELANAL-Plus[13] software which follows the method of Sugeta and Miyazawa.[14] It calculates the local axis of the helix by fitting least square 3D line and sphere to local helix origin points. A local helix axis is defined for a window of four consecutive BTA centers-of-mass. This window then slides along the length of the helix one BTA unit at a time. Local bending angles (one for each window of four consecutive BTA centers-of-mass, except at the ends of the helix) are calculated from the angle between local helix axis and the helix axis (Fig. S4). The region of kink is

characterized by large values of local bending angles at several consecutive window and is identified from 2D-plots of the local bending angle at the position *i* (position of the sliding window of four consecutive BTA units) versus the simulation time. To quantify the number of kinks for each helix, we applied an angle cutoff of 90° above which a kink is considered as an authentic kink, while regions of lower bending angles are considered as straight. This value was chosen for consistency with the fact that BTA cores are not uniaxially stacked on top each other.

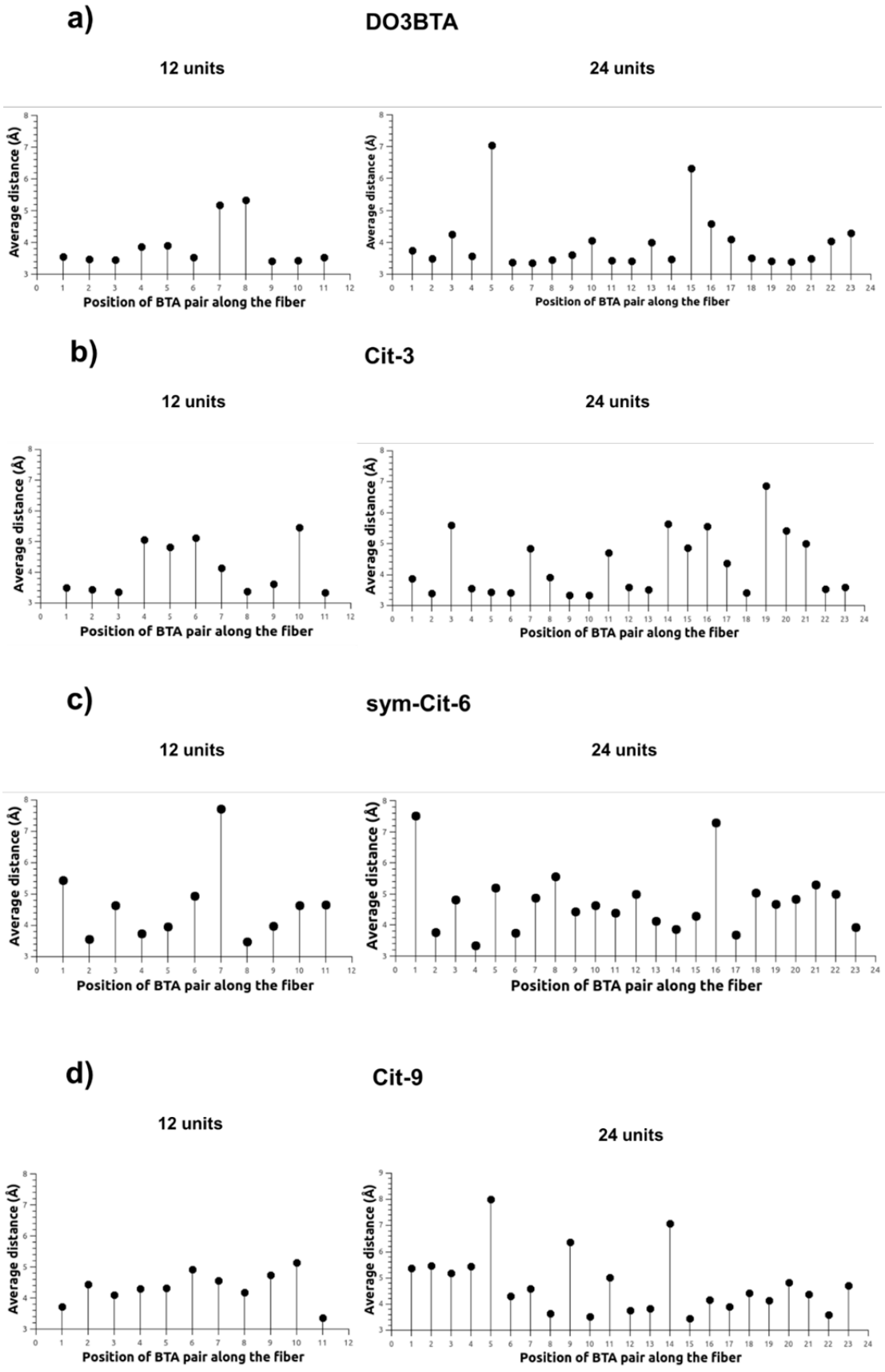


Figure S1. Plots of average distances between pairs of BTA cores for a) **DO3BTA** (reference BTA), b) **Cit-3**, c) **Sym-Cit-6**, d) **Cit-9** fibers of 12 units (left) and 24 units (right).

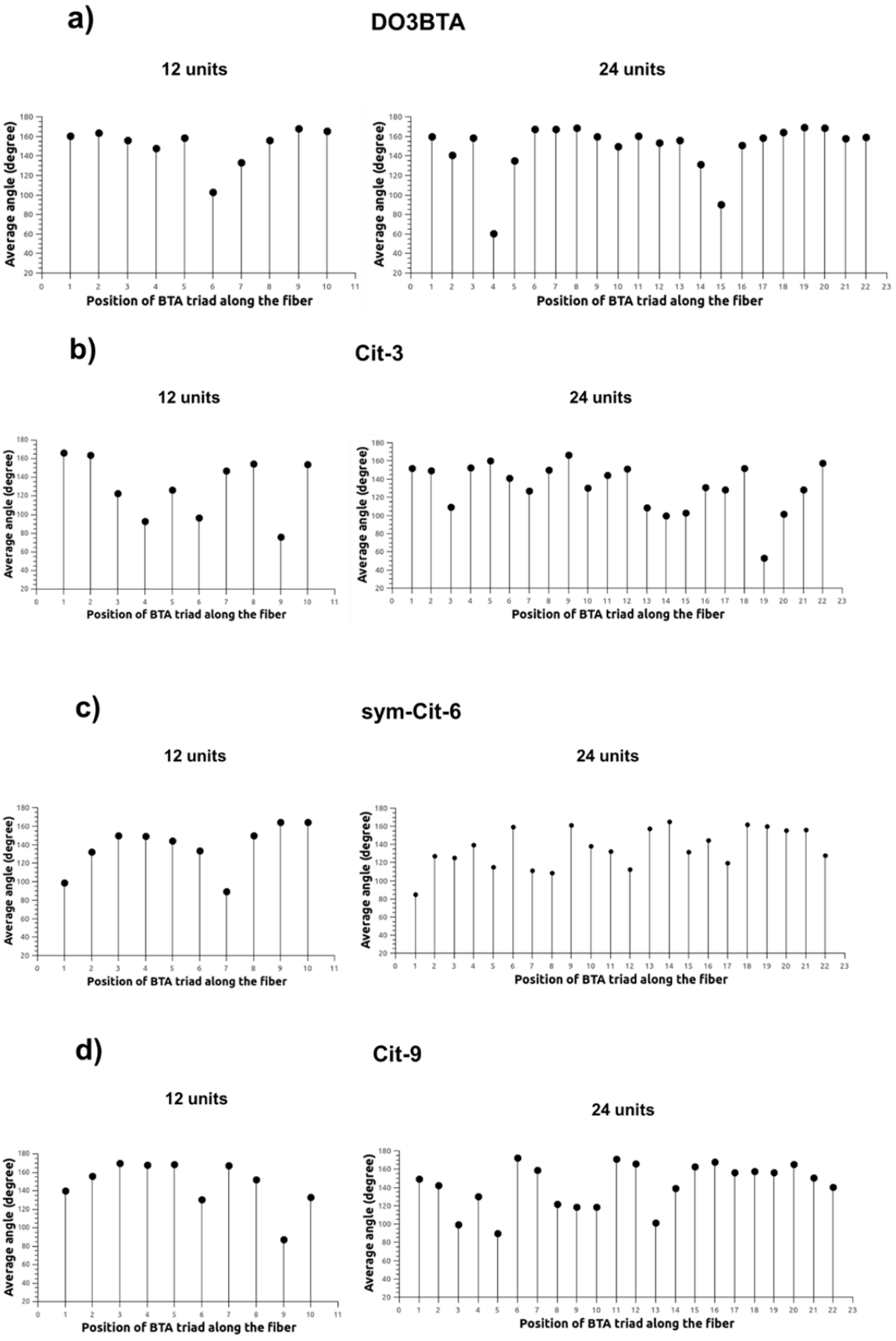


Figure S2. Plots of average angles between triads of BTA cores for a) **DO3BTA** (reference BTA), b) **Cit-3**, c) **Sym-Cit-6**, d) **Cit-9** fibers of 12 units (left) and 24 units (right).

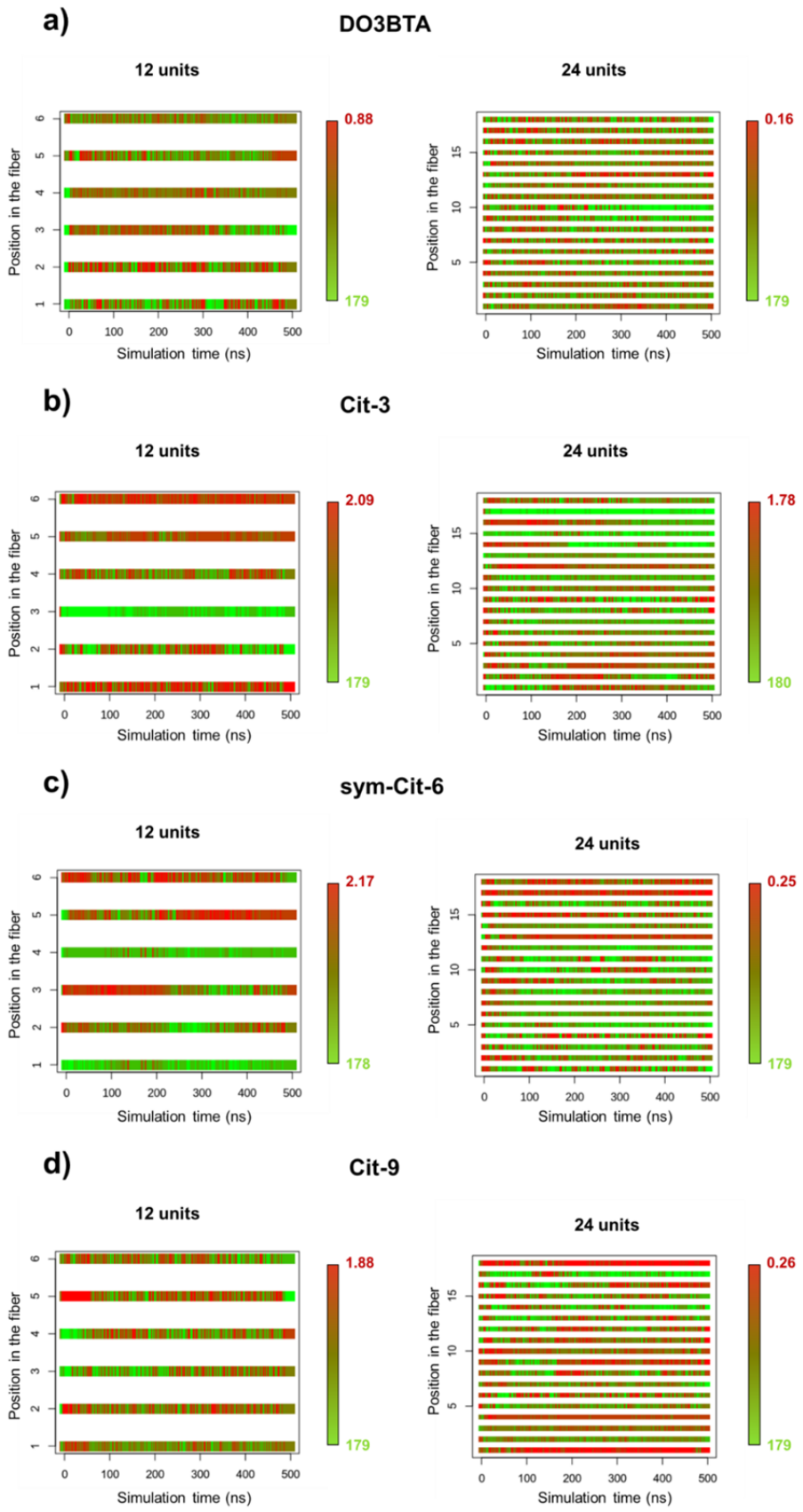


Figure S3. Evolution of the local bending angles at the position *i* (position of the sliding window of four consecutive BTA units) versus the simulation time for a) **DO3BTA** (reference BTA), b) **Cit-3**, c) **Sym-Cit-6**, d) **Cit-9** fibers of 12 units (left) and 24 units (right). Red regions indicate low bending angles values; green regions indicate high bending angles values.

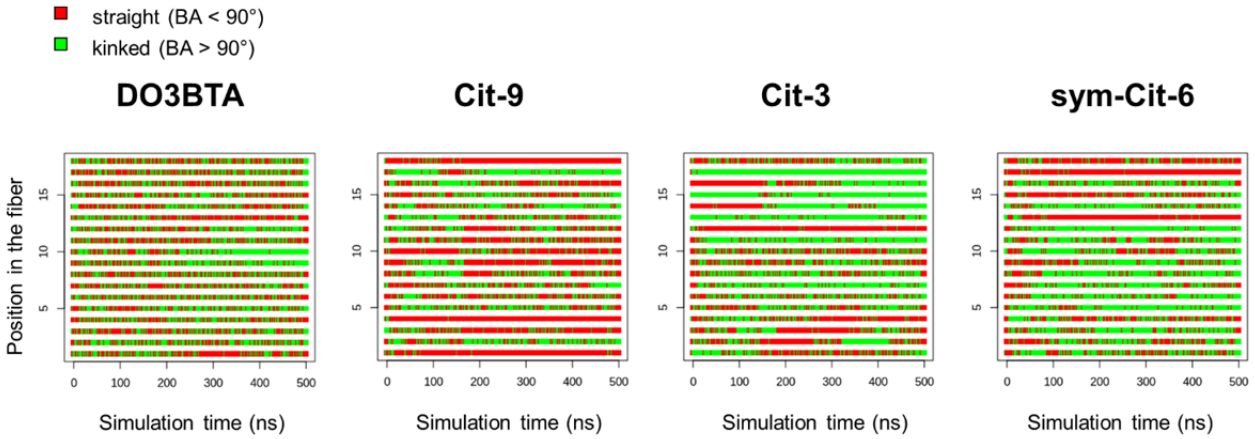


Figure S4. For fibers of 24 BTA units, evolution of the local bending angles at the position along the fiber (position of the sliding window of four consecutive BTA units, see computational details and Fig. S4 for the definition) versus the MD simulation time. Kinked regions appear through a binary color code of bending angles (BA): red regions indicate a straight portion of the fiber (BA < 90°), while green regions indicate kinked portions (BA > 90°). From left to right: **DO3BTA** (reference BTA), **Cit-9**, **Cit-3**, **Sym-Cit-6**.

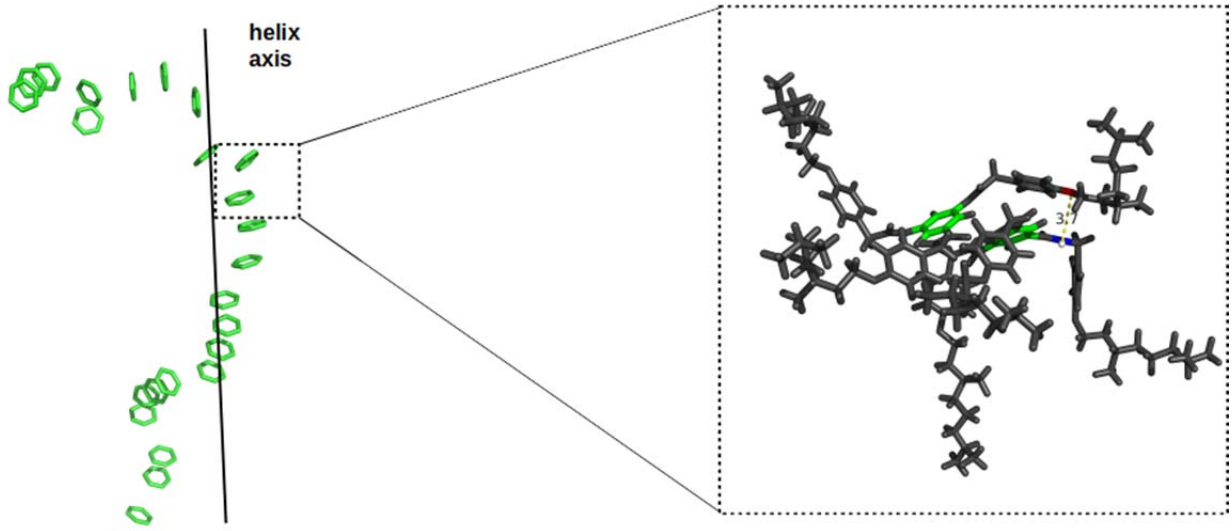


Figure S5. Snapshot of 24 **Cit-3** BTA cores conformation at 40 ns and zoom showing disordering amide-ether hydrogen-bond between the two BTA units where a structural defect is localized.

Full POM and solid state IR results

Table S1. Diffraction spacings in Å for BTA's.

hkl	**DO3BTA**[a]	**C8-3**[b]	**Cit-3**	**Cit-6**	**C8-6**	**C8-9**
T (°C)	140	159	120	124	85	73
1 0 0	17.2	16.0	20.6	24.9	23.0	26.7
1 1 0	9.9	9.1	11.8	–	–	15.5
2 0 0	8.6	8.1	10.3	–	–	13.4
2 1 0	–	–	–	9.4	8.7	–
3 0 0	–	–	–	8.3	7.7	–
3 1 0	–	–	–	6.9	6.5	7.2
halo	5.0	4.8	4.7	4.6	4.6	4.6
interdisc	3.5	3.5	3.5	3.5	3.5	3.5
intercolumn	19.9	18.5	23.8	28.8	26.6	30.8
Density (Z = 1)[c]	0.87	0.89	0.88	0.94	0.97	0.94

[a] P. J. M. Stals, J. F. Haveman, R. Martín-Rapún, C. F. C. Fitié, A. R. A. Palmans, E. W. Meijer, J. Mater. Chem. 2009, 19, 124 – 130.[15] [b] P. J. M. Stals, M. M. J. Smulders, R. Martín-Rapún, A. R. A. Palmans, E.W. Meijer, Chem. Eur. J. 2009, 15, 2071 – 2080.[16] [c] g cm^{-3}

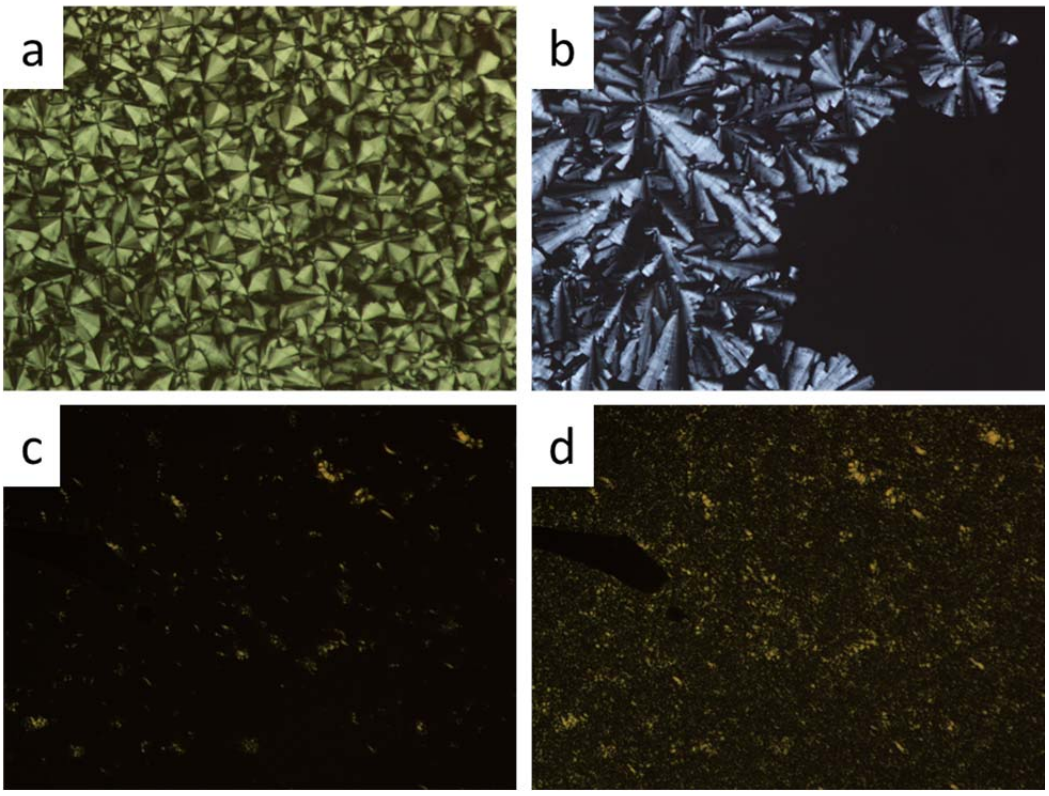


Figure S6. Optical textures (crossed polarizers) obtained after slow cooling from the isotropic state for (a) **C8-3** at 119 °C, (b) **C8-6** at 151 °C, (c) **C8-9** at 66 °C, and (d) **C8-9** at 57 °C.

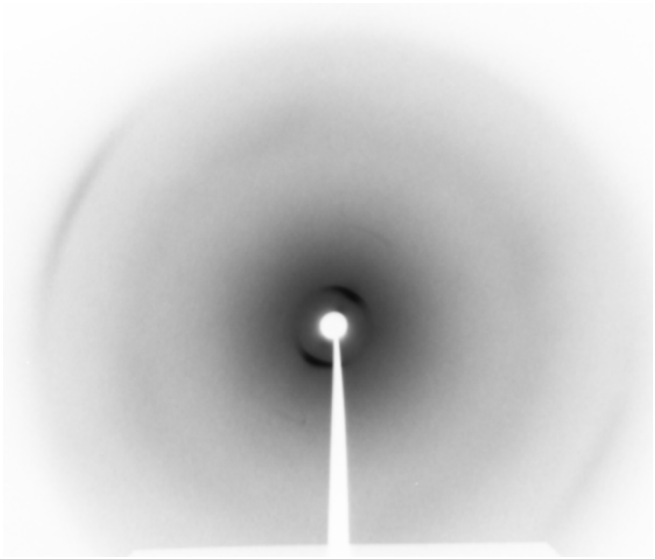


Figure S7. Diffraction pattern observed for aligned **Cit-6** measured at 124 °C./

Instruments and measurements

^{1}H and ^{13}C NMR (400 and 101 MHz respectively) spectra were recorded on a Bruker AV-400 spectrometer and a Bruker Avance 3 HD NanoBay spectrometer. Chemical shifts are given in ppm relative to the solvent residual peak, which was used as internal reference. Coupling constants are given in Hertz. Spectra were processed with *MestReNova 10.0.2* from Mestrelab Research.

MALDI-ToF mass spectrometry was performed on a Bruker Autoflex Speed spectrometer. ESI-MS was performed on a Thermo Finnigan LCQ Fleet ion trap mass spectrometer. FTIR spectroscopy was performed in a *Jasco* FT-IR 4100 instrument with an ATR accessory, in which samples were measured without any preparation, or a PerkinElmer Spectrum Two spectrometer. Solution state IR measurements were performed using NaCl cells. All frequencies of characteristic bands are reported in cm^{-1}.

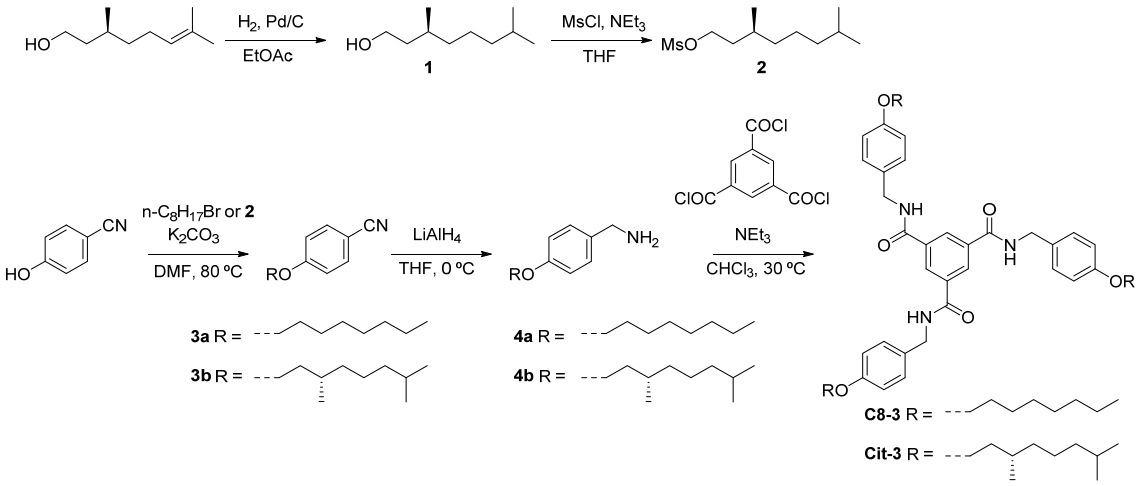
Mesogenic behavior was investigated by polarized light optical microscopy (POM) using an Olympus BS51 Polarizing Optical Microscope fitted with a Linkam THMS600 hot stage.

Differential scanning calorimetry (DSC) experiments were performed on a TA DSC Q-20 and Q-2000 instrument under nitrogen atmosphere in aluminum pans and a scanning rates of 10 °C·min^{-1}. Three consecutive thermal cycles were carried out. The transition temperatures were read at the maximum or the onset of the corresponding peaks in the second or third cycle.

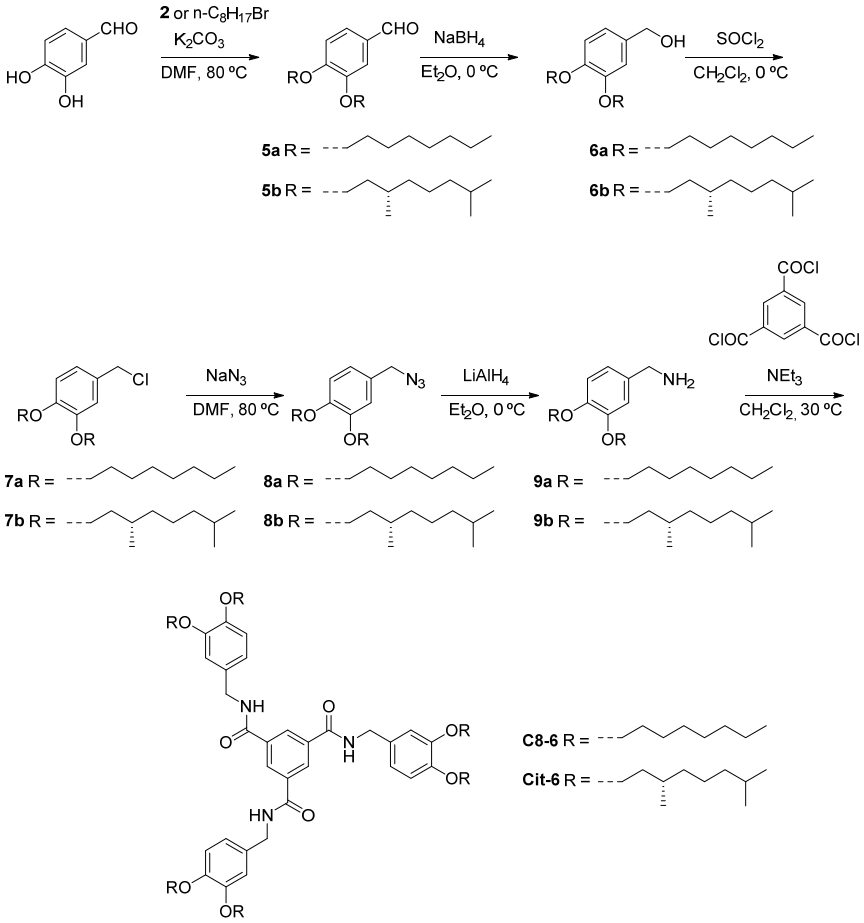
X-Ray diffraction measurements (XRD) were carried out with a Pinhole camera (Anton Paar) operating with a point-focused Ni-filtered Cu-Kα beam. Samples were contained in Lindemann glass capillaries (0.9 or 0.7 mm diameter) and, when necessary, a variable temperature attachment was used to heat the sample. The patterns were collected on flat photographic film perpendicular to the X-ray beam. Bragg's law was used to obtain the spacing ($n \times \lambda = 2 \times d \times \sin\theta$).

CD spectroscopy was measured on a Jasco J-815 spectrometer with a thermostatted PCT-742 or MPTC-490 sample holder. Samples were prepared by dissolving the solid material in MCH in an air-tight vial and heating and sonicating the mixture until no solid material could be observed anymore. Samples were measured in screw-capped cuvettes and cooled at a rate of 1 °C·min^{-1}.

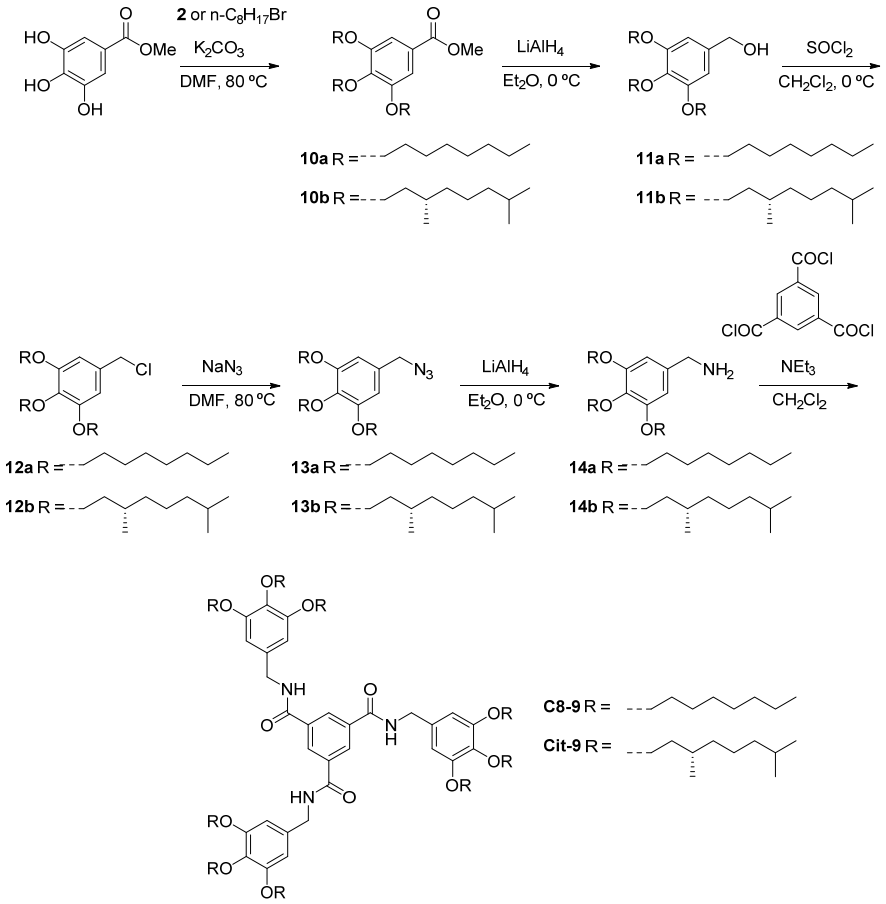
Synthesis details



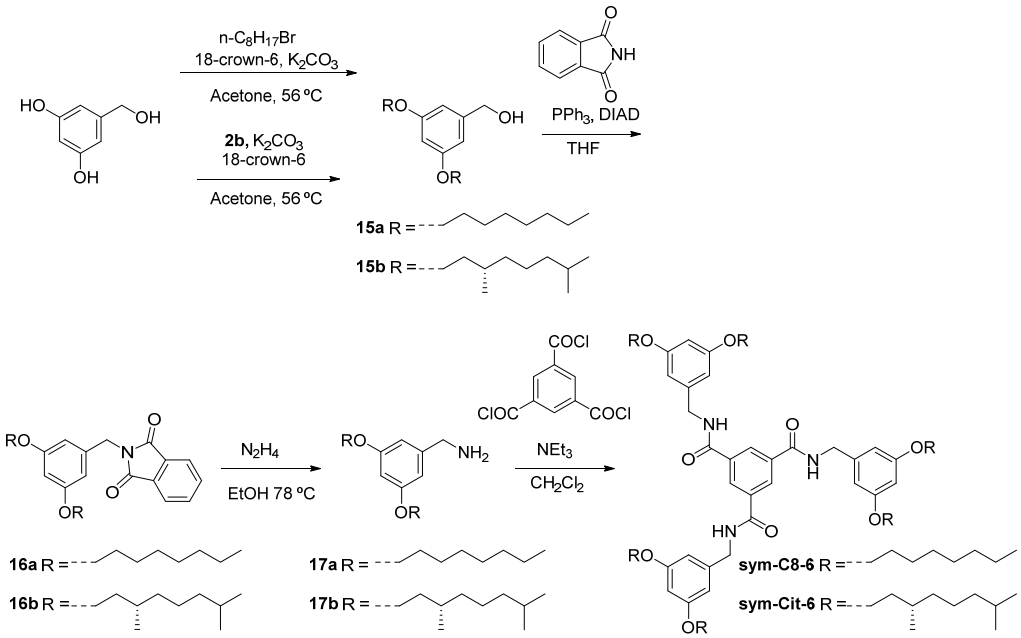
Scheme S1. Synthetic route to **C8-3** and **Cit-3**.



Scheme S2. Synthetic route to **C8-6** and **Cit-6**.



Scheme S3. Synthetic route to **C8-9** and **Cit-9**.

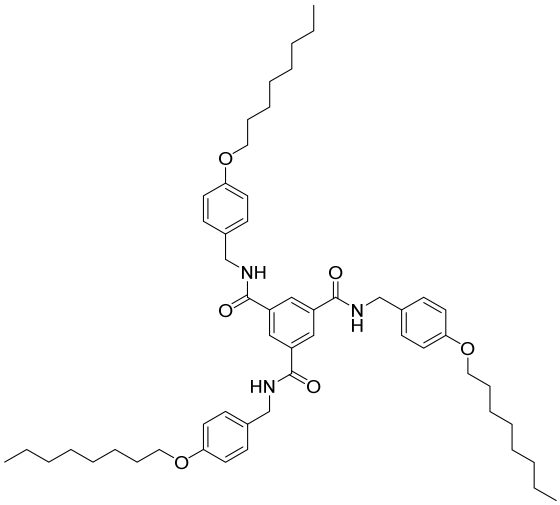


Scheme S4. Synthetic route to **sym-C8-6** and **Sym-Cit-6**.

General procedure for the synthesis of the C3-symmetrical compounds

To a solution of the appropriate benzylamine derivative (0.39 mmol) and trimethylamine (0.42 mmol) in anhydrous dichloromethane or chloroform (10 mL) at 0 °C, 1,3,5-benzenetricarbonyl chloride (0.12 mmol) was added and the reaction mixture was then allowed to reach room temperature (or heated to reflux temperature if the solution was not homogeneous). After 14-18 h the mixture was diluted with dichloromethane (10 mL) and washed with aqueous HCl (1 M, 2 x 10 mL). The organic layer was then dried over anhydrous Na2SO4, filtered and the solvents were removed under reduced pressure. The crude product was purified by column chromatography.

Synthesis of C8-3



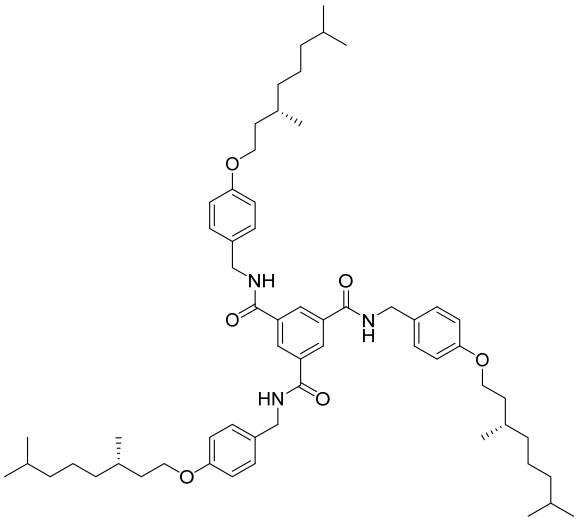
FTIR-ATR (neat): 3244, 3069, 2925, 2854, 1638, 1553, 1511, 1299, 1246, 1232, 1177 cm^{-1}

^{1}H NMR (399 MHz, $CDCl_3$) δ 8.33 (s, 3H), 7.23 (d, *J* = 8.6 Hz, 5H), 6.92 – 6.78 (m, 6H), 6.64 (t, *J* = 5.5 Hz, 3H), 4.54 (d, *J* = 5.5 Hz, 6H), 3.93 (t, *J* = 6.6 Hz, 6H), 1.84 – 1.69 (m, 6H), 1.52 – 1.39 (m, 6H), 1.39 – 1.17 (m, 24H), 1.00 – 0.77 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.34, 158.79, 135.05, 129.34, 129.28, 128.22, 114.80, 77.00, 68.09, 43.91, 31.81, 30.92, 29.35, 29.23, 26.03, 22.65, 14.09.

HRMS (ESI): $C_{54}H_{75}N_3O_6$ $[M+Na]^+$, mass calculated: 884.55, mass found: 884.57; $[M+K]^+$, calculated: 900.53, found: 900.54.

Synthesis of Cit-3



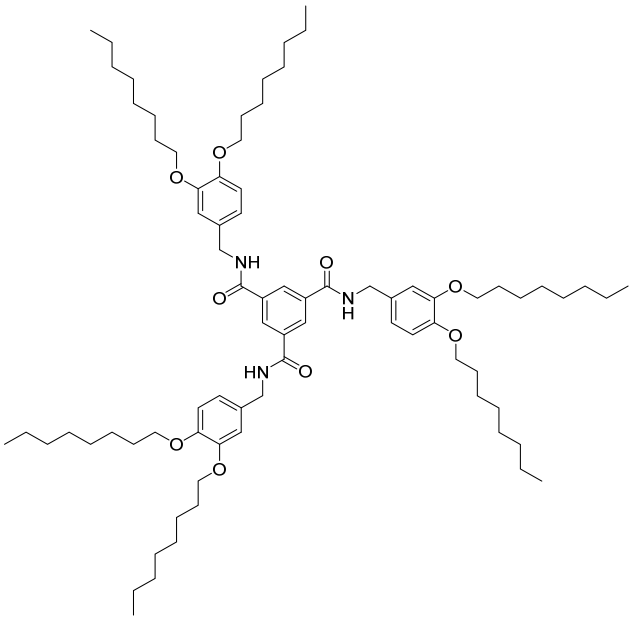
FTIR-ATR (neat): 3231, 3065, 2954, 2925, 2869, 1637, 1556, 1511, 1298, 1246, 1233, 1175 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (s, 3H), 7.26 (s, 6H), 6.87 (d, *J* = 8.6 Hz, 6H), 6.57 (t, *J* = 5.6 Hz, 3H), 4.56 (d, *J* = 5.4 Hz, 6H), 3.99 (d, *J* = 7.0 Hz, 6H), 1.90 – 1.75 (m, 3H), 1.75 – 1.43 (m, 15H), 1.42 – 1.21 (m, 14H), 1.21 – 1.06 (m, 6H), 0.94 (d, *J* = 6.5 Hz, 9H), 0.87 (d, *J* = 6.6 Hz, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.33, 158.79, 135.05, 129.35, 129.28, 128.23, 114.81, 66.41, 43.92, 39.23, 37.29, 36.16, 29.84, 27.96, 24.64, 22.70, 22.60, 19.62.

HRMS (ESI): $C_{60}H_{87}N_3O_6Na$ $[M+Na]^+$, mass calculated: 968.65, mass found: 968.65.

Synthesis of C8-6



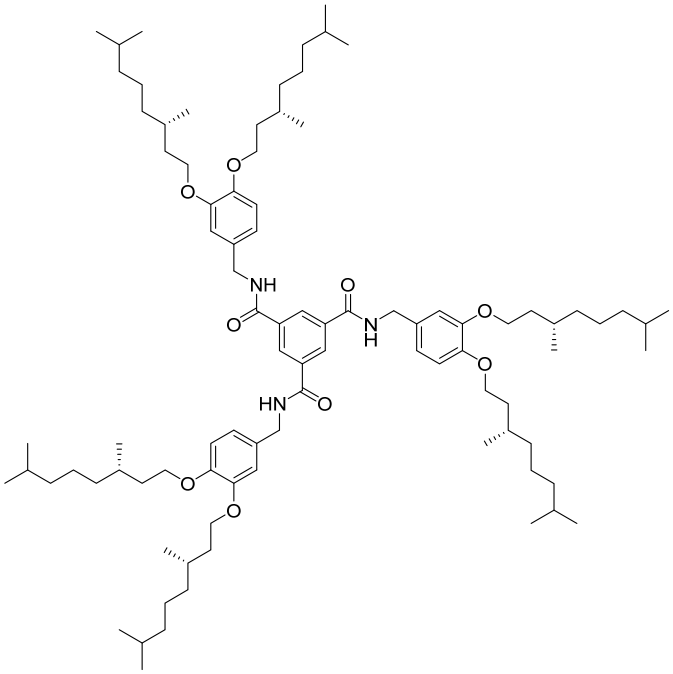
FTIR-ATR (neat): 3237, 3069, 2924, 2855, 1644, 1515, 1264, 1137 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.6 Hz, 3H), 6.87 – 6.64 (m, 11H), 4.50 (d, *J* = 3.2 Hz, 3H), 4.00 – 3.86 (m, 12H), 1.95 – 1.70 (m, 14H), 1.70 – 1.54 (m, 3H), 1.54 – 1.37 (m, 15H), 1.37 – 1.01 (m, 51H), 0.97 – 0.73 (m, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.18, 149.34, 148.74, 134.97, 129.99, 128.34, 120.65, 114.04, 113.98, 69.42, 69.34, 44.36, 31.81, 29.37, 29.37, 29.30, 29.26, 26.02, 26.00, 22.65, 14.08.

HRMS (ESI): $C_{78}H_{123}N_3O_9$ $[M+Na]^+$, mass calculated: 1268.92, mass found: 1268.93. $C_{78}H_{123}N_3O_9K$ $[M+K]^+$, calculated: 1284.89, found: 1284.90.

Synthesis of Cit-6



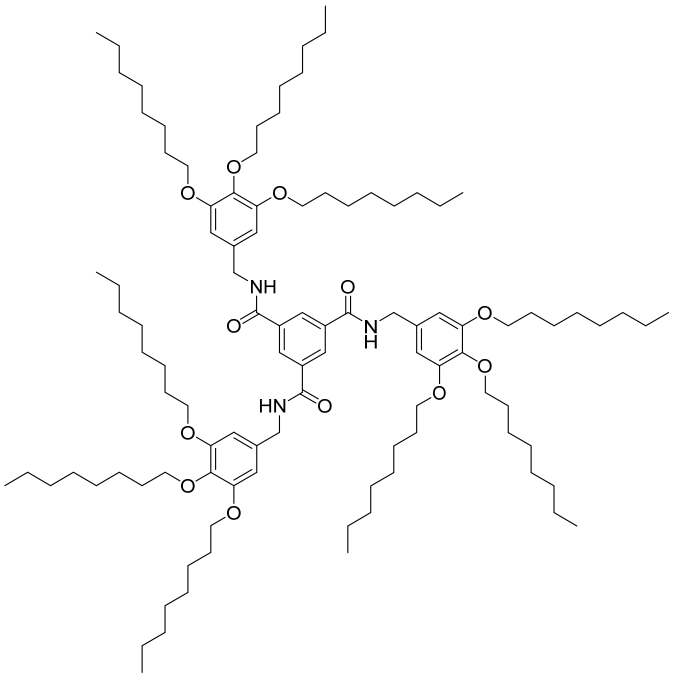
FTIR-ATR (neat): 3237, 3066, 2954, 2926, 2869, 1636, 1514, 1558, 1512, 1468, 1427, 1295, 1263, 1232, 1137 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 3H), 6.83 (s, 9H), 6.65 (t, *J* = 5.4 Hz, 3H), 4.53 (d, *J* = 5.4 Hz, 6H), 4.17 – 3.80 (m, 12H), 1.92 – 1.75 (m, 6H), 1.74 – 1.42 (m, 13H), 1.42 – 1.01 (m, 40H), 0.93 (dd, *J* = 6.5, 2.7 Hz, 18H), 0.86 (dd, *J* = 6.6, 2.4 Hz, 36H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.13, 149.45, 148.88, 135.04, 129.91, 128.24, 120.65, 114.01, 113.95, 67.76, 67.68, 44.40, 39.26, 37.38, 37.35, 36.30, 36.24, 29.91, 27.98, 24.71, 22.70, 22.60, 19.67, 19.66.

HRMS (ESI): $C_{90}H_{147}N_3O_9$ $[M+Na]^+$, mass calculated: 1438.10, mass found: 1437.11.

Synthesis of C8-9



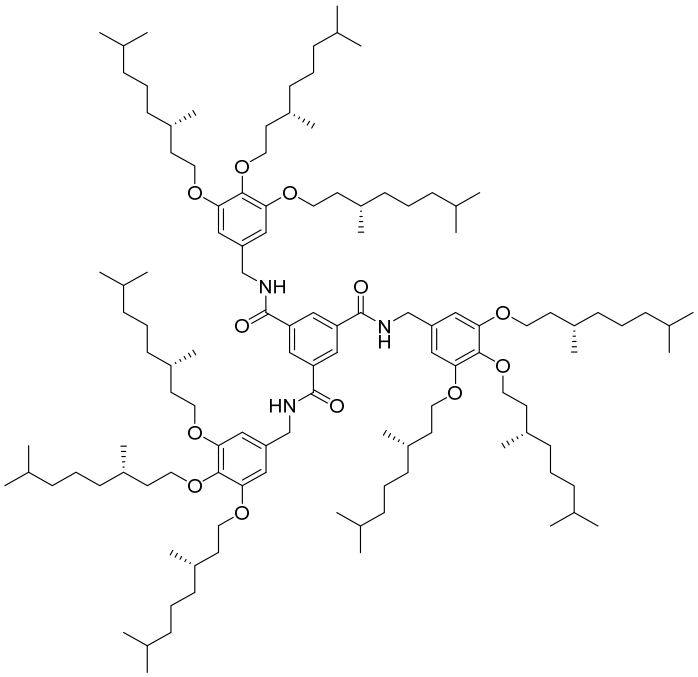
FTIR-ATR (neat): 3230, 3067, 2955, 2922, 2854, 1646, 1628, 1554, 1505, 1440, 1329, 1252, 1231, 1112 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 3H), 6.82 (s, 3H), 6.50 (s, 6H), 4.50 (d, *J* = 4.9 Hz, 6H), 4.13 – 3.79 (m, 19H), 1.87 – 1.63 (m, 19H), 1.55 – 1.39 (m, 19H), 1.39 – 1.12 (m, 78H), 0.99 – 0.70 (m, 29H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.20, 153.42, 137.88, 134.85, 132.23, 128.38, 106.81, 77.00, 73.46, 69.20, 31.90, 31.82, 30.32, 29.55, 29.42, 29.37, 29.28, 26.10, 22.68, 22.66, 14.08.

HRMS (ESI): $C_{102}H_{171}N_3O_{12}Na$ $[M+Na]^+$, mass calculated: 1654.28, mass found: 1654.28. $C_{102}H_{171}N_3O_{12}K$ $[M+K]^+$, calculated: 1670.25, found: 1670.25.

Synthesis of Cit-9



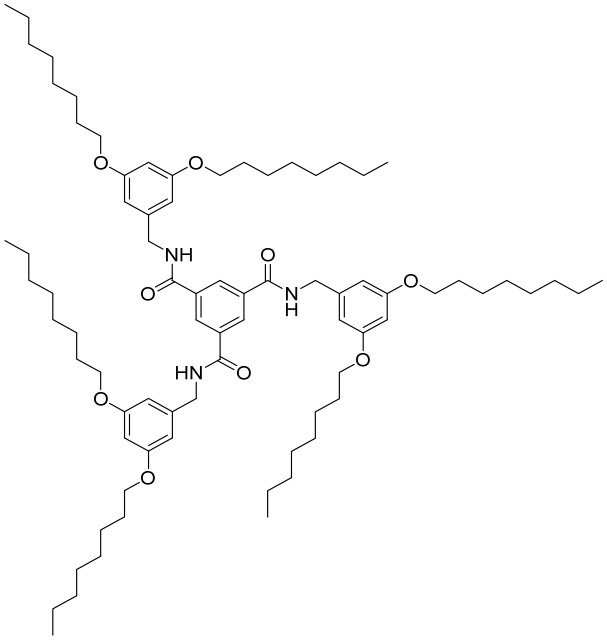
FTIR-ATR (neat): 3317, 2953, 2925, 2869, 1662, 1591, 1535, 1504, 1463, 1438, 1230, 1113 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 3H), 6.57 (t, *J* = 5.5 Hz, 3H), 6.53 (s, 6H), 4.53 (d, *J* = 5.4 Hz, 6H), 4.13 – 3.80 (m, 18H), 1.94 – 1.77 (m, 9H), 1.77 – 1.63 (m, 8H), 1.63 – 1.45 (m, 23H), 1.45 – 1.21 (m, 25H), 1.21 – 1.04 (m, 23H), 0.92 (d, *J* = 6.6 Hz, 18H), 0.92 (d, *J* = 6.6 Hz, 9H), 0.86 (d, *J* = 6.7 Hz, 48H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.00, 153.50, 137.99, 134.97, 132.18, 128.25, 77.00, 71.70, 67.49, 39.37, 39.27, 37.54, 37.40, 37.35, 36.44, 29.80, 29.71, 27.98, 24.73, 24.71, 22.71, 22.62, 22.60, 19.58, 19.55.

HRMS (ESI): $C_{120}H_{207}N_3O_{12}Na$ $[M+Na]^+$, mass calculated: 1906.56, mass found: 1906.57.

Synthesis of Sym-C8-6



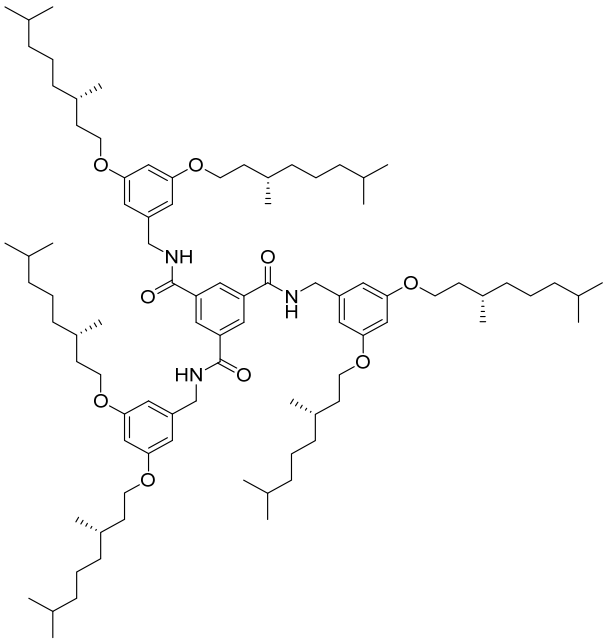
FTIR-ATR (neat): 3330, 2925, 2855, 1664, 1596, 1531, 1460, 1291, 1166, 1060 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 3H), 6.73 (t, J = 5.6 Hz, 3H), 6.44 (d, J = 2.2 Hz, 6H), 6.35 (t, J = 2.2 Hz, 3H), 4.53 (d, J = 5.5 Hz, 6H), 3.90 (t, J = 6.6 Hz, 12H), 1.85 – 1.65 (m, 12H), 1.52 – 1.38 (m, 12H), 1.38 – 1.15 (m, 48H), 0.96 – 0.78 (m, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.31, 160.65, 139.47, 134.99, 128.29, 106.45, 100.46, 68.09, 44.62, 31.81, 29.36, 29.25, 29.23, 26.04, 22.65, 14.09.

HRMS (ESI): $C_{78}H_{123}N_3O_9$ $[M+H]^+$, calculated: 1246.93, found: 1246.95; $[M+Na]^+$, mass calculated: 1268.92, mass found: 1268.92.

Synthesis of Sym-Cit-6



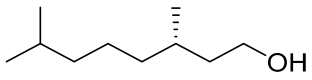
FTIR-ATR (neat): 3332, 3037, 2954, 2927, 2870, 1596, 1532, 1463, 1167 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 3H), 6.65 (t, J = 5.5 Hz, 3H), 6.45 (d, J = 2.2 Hz, 6H), 6.38 (t, J = 2.2 Hz, 3H), 4.54 (d, J = 5.5 Hz, 6H), 4.05 – 3.85 (m, 12H), 1.87 – 1.72 (m, 6H), 1.72 – 1.60 (m, 6H), 1.57 – 1.45 (m, 6H), 1.39 – 1.23 (m, 18H), 1.15 (s, 18H), 0.92 (d, J = 6.5 Hz, 18H), 0.86 (d, J = 6.6 Hz, 36H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.20, 160.69, 139.38, 134.99, 128.27, 106.50, 100.52, 66.40, 44.69, 39.24, 37.31, 36.20, 29.82, 27.97, 24.65, 22.71, 22.60, 19.63.

HRMS (ESI): $C_{90}H_{147}N_3O_9$ $[M+H]^+$, calculated: 1416.12, found: 1415.13; $[M+Na]^+$, mass calculated: 1438.11, mass found: 1438.11.

Synthesis of 1



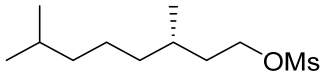
(*S*)-(−)-β-Citronellol (5 g, 31 mmol) was dissolved in ethyl acetate (20 mL) and palladium catalyst (Pd/C 10 % w/w, 250 mg) was added. The suspension and the headspace were deaerated by bubbling nitrogen gas through the suspension. The same operation was then performed with hydrogen. The reaction took place under H2 atmosphere (1 atm) using a balloon which was refilled with hydrogen when needed. When the reaction was complete nitrogen gas was used to replace hydrogen gas in the system. The mixture was subsequently filtered through celite and the solvent was removed under reduced pressure. The product was obtained as colourless liquid (4.14 g, 82 % yield).

FTIR-ATR (neat): 3340, 2954, 2926, 2870, 1457, 1052 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 – 3.60 (m, 2H), 1.67 – 1.44 (m, 3H), 1.43 – 1.18 (m, 5H), 1.18 – 1.01 (m, 3H), 0.89 (d, *J* = 6.6 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 61.23, 39.93, 39.24, 37.35, 29.49, 27.95, 24.66, 22.67, 22.57, 19.61.

Synthesis of 2

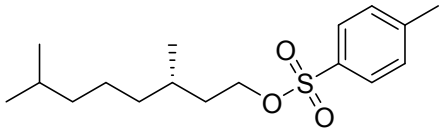


^{1}H NMR (400 MHz, $CDCl_3$) δ 4.32 – 4.20 (m, 2H), 3.00 (s, 3H), 1.85 (bs, 1H), 1.83 – 1.72 (m, 1H), 1.65 – 1.45 (m, 1H), 1.38 – 1.21 (m, 3H), 1.21 – 1.05 (m, 4H), 0.92 (d, J = 6.5 Hz, 4H), 0.86 (d, J = 6.6 Hz, 6H).

FTIR-ATR (neat): 2954, 2928, 2870, 1353, 1173, 940 cm^{-1}.

ESI-MS analysis: $C_{11}H_{24}O_3SNa$ $[M+Na]^+$, mass calculated: 259.13, mass found: 259.13.

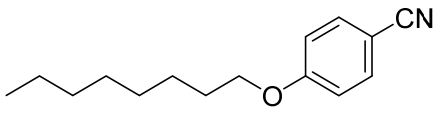
Synthesis of 2b



1 (10.0 g, 63.2 mmol) was dissolved in DCM (50 mL) and Et_3N was added (24.3 mL, 174 mmol). Then, the reaction mixture was cooled to 0 °C under an Ar atmosphere. Subsequently, tosyl chloride (13.5 g, 70.9 mmol) in DCM (40 mL) was slowly added dropwise. The mixture was left to heat up to room temperature and stirred for 23 hours, after which the mixture was evaporated to dryness. The product was obtained as a clear oil after purification through silica gel chromatography using 40% heptane in $CHCl_3$ as eluents with a 87% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.3 Hz, 2H), 4.06 (m, 2H), 2.45 (s, 3H), 1.70-1.63 (m, 1H), 1.52-1.37 (m, 3H), 1.30-1.00 (m, 6H), 0.85 (d, J = 6.7 Hz, 6H, 0.80 (d, J = 6.5 Hz, 3H).

Synthesis of 3a



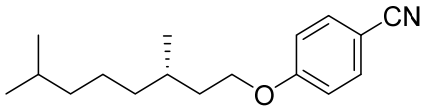
4-cyanophenol (0.63 g, 95 %, 5.00 mmol) and potassium carbonate (1.38 g, 10.00 mmol) were suspended in butanone (15 mL) and heated to reflux temperature under magnetic stirring. After 15 minutes at reflux temperature the 1-bromoctane (0.920 mL, 5.25 mmol) was added dropwise with a syringe. After 16 h a white suspension had been obtained. Water (50 mL) was added and the layers were separated in a separation funnel. The aqueous layer was extracted with ethyl acetate (3x10 mL) and the 4 organic layers were combined and washed with 1 M aqueous NaOH (2x10 mL) and brine (10 mL). After drying over anhydrous sodium sulfate the solvents were removed under reduced pressure. A yellow oil was obtained and used in the next step without further purification.

FTIR-ATR (neat): 2926, 2856, 2224, 1605, 1508, 1257, 1170 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 3.98 (t, *J* = 6.6 Hz, 2H), 1.95 – 1.56 (m, 2H), 1.55 – 1.09 (m, 10H), 0.96 – 0.73 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.41, 133.88, 119.27, 115.12, 103.55, 77.00, 68.37, 31.72, 29.22, 29.13, 28.92, 25.87, 22.58, 14.03.

Synthesis of 3b



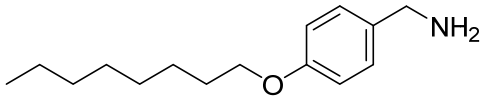
S-(+)-Citronellol (1.00 g, 6.32 mmol), 4-cyanophenol (0.75 g, 6.32 mmol) and diisopropyl azodicarboxylate (1.27 g, 6.32 mmol) were dissolved in dry THF (30 mL) under N_2 atmosphere. Next, the organic solution was cooled in an ice bath and triphenylphosphine (1.66 g, 6.32 mmol) was added. The reaction was allowed to reach room temperature and further stirred 24 hours. Once the reaction was completed, water was added (5 drops) and further stirred 1 hour more. Finally, THF was removed under reduced pressure and the solid obtained was redissolved in an ethyl acetate:hexane (3:7) (60 mL) in an ice bath over 1 hour. The white precipitate obtained was filtered through silica gel and rinsed several times with the same solvent. Finally, the solvent was removed under reduced pressure giving rise to a yellow liquid, which was purified through silica gel column using hexane:ethyl acetate 98:2. **3b** was obtained as a colourless liquid with 61 % yield (1. 06 g, 4.08 mmol).

FTIR-ATR (neat): 2953, 2927, 2870, 2224, 1605, 1508, 1257, 1171 cm^{-1}.

^{1}H NMR (400 MHz, CDCl3) δ 7.73 – 7.42 (m, 2H), 7.07 – 6.75 (m, 2H), 4.26 – 3.82 (m, 2H), 1.90 – 1.77 (m, 1H), 1.73 – 1.44 (m, 3H), 1.41 – 1.05 (m, 5H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.40, 133.91, 119.28, 115.16, 103.61, 66.74, 39.17, 37.18, 35.85, 29.75, 27.93, 24.60, 22.66, 22.56, 19.57.

Synthesis of 4a



A dry round-bottom flask was flushed with dry nitrogen gas for 20 min and $LiAlH_4$ (1 M in THF, 4.33 mL) was added via syringe. The reagent was diluted with dry diethyl ether (10 mL) and the mixture was stirred at 0-4 ºC under nitrogen for 10 min. Then a solution of **3a** (1.00 g, 4.33 mmol) in dry diethyl ether (5 mL) was dropwise added. The mixture turned yellow. After overnight reaction the mixture was diluted with Et_2O (10 mL) and NaOH (3.60 mL) was added in an ice bath to precipitate inorganic salts. After 1 hour stirring the suspension was vacuum filtered and the solid rinsed several times with Et_2O. The solvent was removed under reduced pressure giving rise a yellow oil, which was purified through silica gel column using $CHCl_3$:MeOH:NH_3 90:9:1 as eluent. **4a** was obtained as a white waxy solid with a 64 % yield (653 mg, 2.77 mmol).

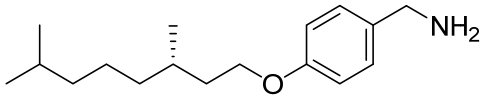
FTIR-ATR (neat): 3271, 2918, 2852, 1511, 1242 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 3.93 (t, *J* = 6.6 Hz, 2H), 3.79 (s, 2H), 2.54 (s, 2H), 1.76 (dq, *J* = 8.1, 6.6 Hz, 2H), 1.50 – 1.39 (m, 2H), 1.39 – 1.12 (m, 13H), 0.95 – 0.78 (m, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.21, 134.06, 128.46, 114.54, 68.03, 45.53, 31.79, 29.34, 29.26, 29.22, 26.03, 22.63, 14.07.

ESI-MS analysis: $C_{15}H_{23}O$ $[M\text{-}NH_2]^+$, mass calculated: 219.17, mass found: 219.17.

Synthesis of 4b



3b (900 mg, 3.46 mmol) was dissolved in dry Et_2O (10 mL) under N_2 and cooled down in an ice bath. Then, $LiAlH_4$ (4.15 mL, 1 M THF) was dropwise added turning the colourless solution to a pale-yellow suspension together with gas release. The reaction was gradually warmed to room temperature and further stirred overnight. The crude was diluted with Et_2O and NaOH (3.60 mL) was added in an ice bath to precipitate inorganic salts. After 1 hour stirring, the suspension was vacuum filtered and the solid rinsed several times with Et_2O. The solvent was removed under reduced pressure giving rise a yellow oil, which was purified through silica gel column using

$CHCl_3$:MeOH:NH_3 90:9:1 as eluent. **4b** was obtained as a yellowish liquid with 86 % yield (770 mg, 2.94 mmol).

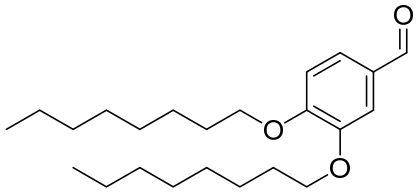
FTIR-ATR (neat): 3277, 2924, 2869, 1513, 1245 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.19 (m, 2H), 6.90 – 6.83 (m, 2H), 4.02 – 3.88 (m, 2H), 3.80 (s, 2H), 3.65 (bs, 2H), 1.87 – 1.74 (m, 1H), 1.74 – 1.43 (m, 3H), 1.39 – 1.21 (m, 3H), 1.21 – 1.06 (m, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.45, 132.46, 128.83, 114.62, 66.34, 45.11, 39.23, 37.29, 36.20, 29.84, 27.95, 24.64, 22.69, 22.59, 19.63.

ESI-MS analysis: $C_{17}H_{27}O$ $[M\text{-}NH_2]^+$, mass calculated: 247.21, mass found: 247.20.

Synthesis of 5a



3,4-dihydroxybenzaldehyde (540 mg, 3.90 mmol) was dissolved in 30 mL of DMF in a Schlenk flask under argon atmosphere. To the solution were added (*S*)-3,7-dimethyloctyl 4-methylbenzenesulfonate (2.05 eq., 2.5 g, 8.0 mmol) and potassium carbonate (3.5 eq., 1.89 g, 13.7 mmol) and the reaction mixture refluxed for 16 hours. The solvent was removed under reduced pressure, the mixture dissolved in chloroform and extracted with water (3 x 20 mL). The organic phase was dried over magnesium sulfate, filtered and the solvent removed. The material was purified by column chromatography with a Biotage Isolera One and a solvent gradient of DCM in Heptane (30 to 50%) to yield **5a** as a yellow oil (3.19 mmol, yield: 82%)

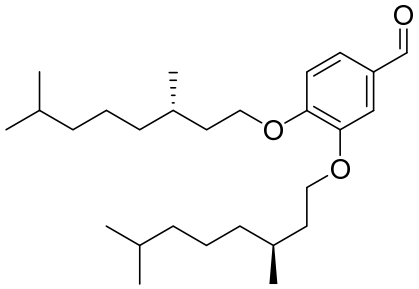
FTIR-ATR (neat): 2921, 2851, 1685, 1589, 1510, 1271, 1236, 1133 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 7.64 – 7.32 (m, 2H), 6.95 (d, *J* = 8.1 Hz, 1H), 4.08 (t, *J* = 6.6 Hz, 2H), 4.04 (t, *J* = 6.6 Hz, 2H), 1.93 – 1.76 (m, 4H), 1.56 – 1.42 (m, 4H), 1.42 – 1.19 (m, 16H), 0.97 – 0.81 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.00, 154.65, 149.40, 129.82, 126.59, 111.70, 110.89, 69.11, 69.09, 31.80, 31.78, 29.32, 29.30, 29.25, 29.23, 29.05, 28.96, 25.97, 25.93, 22.65, 14.09.

ESI-MS analysis: $C_{23}H_{38}O_3Na$ $[M+Na]^+$, mass calculated: 385.27, mass found: 385.27.

Synthesis of 5b



3,4-dihydroxybenzaldehyde (1 g, 7.24 mmol) was dissolved in 40 mL of DMF in a Schlenk flask under argon atmosphere. To the solution 1-bromooctane (2.05 eq., 2.87 g, 14.9 mmol) and potassium carbonate (3.5 eq., 3.5 g, 25.3 mmol) were added and the reaction mixture refluxed for 16 hours. The solvent was removed under reduced pressure, the mixture dissolved in chloroform and extracted with water (3x 20 mL). The organic phase was dried over magnesium sulfate, filtered and the solvent removed. The material was purified by column chromatography with a Biotage Isolera One and a solvent gradient of DCM in Heptane (30 to 50%) to yield 2.45 g of **5b** as a crystalline solid (6.76 mmol, yield: 93%).

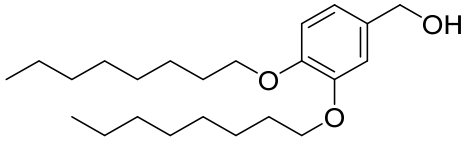
FTIR-ATR (neat): 2926, 2869, 1689, 1595, 1508, 1265, 1132 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.83 (s, 1H), 7.47 – 7.32 (m, 2H), 6.96 (d, *J* = 8.1 Hz, 1H), 4.21 – 3.96 (m, 4H), 1.98 – 1.79 (m, 2H), 1.77 – 1.59 (m, 4H), 1.59 – 1.43 (m, 2H), 1.42 – 1.05 (m, 12H), 0.96 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.4 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.03, 154.62, 149.42, 129.82, 126.64, 111.60, 110.68, 67.50, 67.47, 39.22, 39.20, 37.28, 35.99, 35.86, 29.96, 29.92, 27.97, 24.71, 24.70, 22.69, 22.59, 19.70, 19.68.

ESI-MS analysis: $C_{27}H_{46}O_3Na$ $[M+Na]^+$, mass calculated: 441.33, mass found: 441.33.

Synthesis of 6a



Aldehyde **5a** (1.42 g, 3.91 mmol) was dissolved in dry THF (30 mL), and the mixture was stirred at 0-4 ºC. After 10 min, $NaBH_4$ (0.30 g, 37.83 mmol) was added. After 2 h the reaction was completed by TLC and the mixture was quenched with the addition of aqueous $NaHCO_3$ (5 % w/w, 10 mL). After addition of water (20 mL) the mixture was extracted with CH_2Cl_2 (3 x 10 mL). The organic layers were combined, treated with brine (10 mL) and dried over anhydrous Na_2SO_4. After filtration and removal of the solvents under reduced pressure, the crude was obtained as a thick oil that slowly solidified to yield a waxy solid. The product was purified by flash column chromatography using an eluent gradient from hexanes (100 %) to hexanes/ethyl acetate (5/1). **6a** was obtained as a yellowish liquid with 85 % yield (1.21 g, 3.32 mmol).

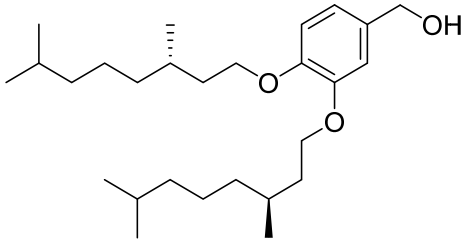
FTIR-ATR (neat): 3282, 2921, 2845, 1593, 1518, 1467, 1429, 1263, 1139 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 – 6.89 (m, 1H), 6.89 – 6.71 (m, 2H), 4.57 (d, *J* = 19.6 Hz, 2H), 3.99 (t, *J* = 6.6 Hz, 2H), 3.98 (t, *J* = 6.7 Hz, 2H), 2.02 – 1.72 (m, 4H), 1.65 (s, 1H), 1.55 – 1.40 (m, 4H), 1.40 – 1.05 (m, 18H), 1.00 – 0.69 (m, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.33, 148.71, 133.69, 119.56, 113.85, 112.97, 69.42, 69.21, 65.36, 31.81, 29.37, 29.29, 29.27, 26.02, 26.01, 22.65, 14.08.

ESI-MS analysis: $C_{23}H_{40}O_3Na$ $[M+Na]^+$, mass calculated: 387.29, mass found: 387.28.

Synthesis of 6b



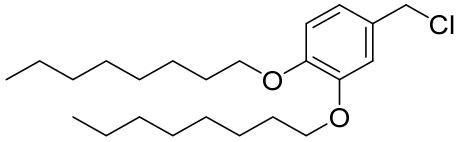
6b was synthesized according to the procedure described for **6a**, using **5b** as starting material (1.15 g, 2.75 mmol), and $NaBH_4$ as reductant (0.21 g, 5.50 mmol). **6b** was obtained as a colourless liquid with 84 % yield (965 mg, 2.31 mmol).

FTIR-ATR (neat): 3372, 2925, 2869, 1512, 1463, 2621, 1135 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 6.96 – 6.79 (m, 6H), 4.61 (s, 2H), 4.16 – 3.80 (m, 8H), 1.96 – 1.77 (m, 3H), 1.76 – 1.42 (m, 13H), 1.42 – 1.21 (m, 12H), 1.21 – 1.03 (m, 11H), 0.98 – 0.90 (m, 8H), 0.90 – 0.82 (m, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.35, 148.72, 133.63, 119.55, 113.70, 112.83, 67.73, 67.53, 65.42, 39.26, 37.35, 36.26, 36.24, 36.20, 36.16, 29.93, 29.91, 27.98, 24.72, 24.71, 22.70, 22.60, 19.69.

Synthesis of 7a



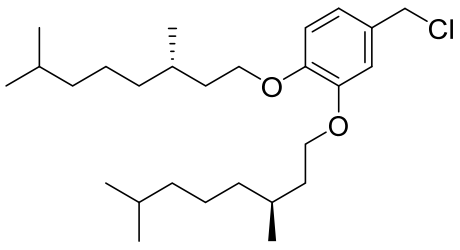
Alcohol **6a** (1.15 g, 3.16 mmol) was dissolved in dry CH_2Cl_2 (10 mL), and the solution was stirred at 0-4 ºC. After 10 min, thionyl chloride (0.32 mL, 4.42 mmol) was added dropwise. After 2 h stirring in a water-ice bath the reaction was still incomplete by TLC and the mixture was allowed to react for 1 h at room temperature before adding another portion of $SOCl_2$ (0.32 mL) at 0-4 ºC. After 2 h the solvents were removed under reduced pressure and the crude was dried under vacuum. The yellow crude finally solidified to a waxy yellowish solid, which was used in the next reaction without any purification.

FTIR-ATR (neat): 2922, 2850, 1603, 1467, 1392, 1270, 1234, 1132 cm^{-1}.

^1H NMR (400 MHz, CDCl3) δ 6.94 – 6.86 (m, 2H), 6.86 – 6.79 (m, 1H), 4.55 (s, 2H), 4.01 (d, *J* = 6.6 Hz, 2H), 3.98 (d, *J* = 6.7 Hz, 2H), 1.90 – 1.74 (m, 5H), 1.53 – 1.41 (m, 4H), 1.41 – 1.13 (m, 19H), 0.99 – 0.79 (m, 7H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.37, 149.23, 129.96, 121.23, 114.20, 113.45, 69.26, 46.75, 31.81, 29.36, 29.26, 29.22, 26.01, 22.66, 14.09.

Synthesis of 7b

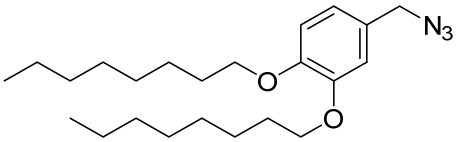


7b was synthesized according to the procedure described for **7a**, using **6b** as starting material (1.00 g, 2.38 mmol), and $SOCl_2$ (0.48 mL, 6.66 mmol) in two portions.

FTIR-ATR (neat): 2952, 2925, 2868, 1511, 1467, 1262 cm^{-1}.

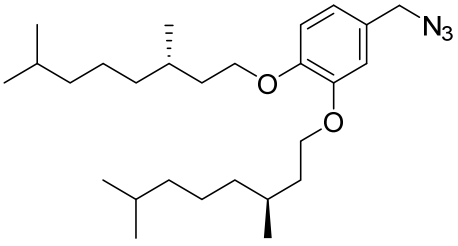
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 – 6.86 (m, 2H), 6.86 – 6.77 (m, 1H), 4.55 (s, 2H), 4.10 – 3.91 (m, 4H), 1.95 – 1.80 (m, 2H), 1.79 – 1.45 (m, 10H), 1.41 – 1.21 (m, 6H), 1.21 – 1.05 (m, 7H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H), 0.87 (d, *J* = 6.6 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.36, 149.22, 129.93, 121.21, 114.06, 113.31, 67.58, 46.78, 39.25, 37.34, 37.33, 36.21, 36.16, 29.92, 29.91, 27.98, 24.73, 24.71, 22.70, 22.60, 19.70, 19.67.
ESI-MS analysis: $C_{27}H_{47}O_2$ $[M\text{-}Cl]^+$, mass calculated: 403.36, mass found: 403.36.

Synthesis of 8a



NaN_3 (0.41 g, 6.32 mmol) was added to a solution of **7a** (theor 3.16 mmol) in dry DMF (9 mL). The mixture was heated to 80 ºC and allowed to react overnight (18 h). The mixture was allowed to reach room temperature, water (30 mL) was added and the product was extracted with a 7/3 mixture of hexanes and ethyl acetate (3 x 20 mL). The organic layers were combined, treated with brine (20 mL), dried over anhydrous Na_2SO_4, filtered and submitted to reduced pressure to remove the solvents.
The product was purified by flash column chromatography using an eluent gradient from hexanes to hexanes/ethyl acetate 98/2.
FTIR-ATR (neat): 2955, 2917, 2849, 2107, 1517, 1467, 1430, 1263, 1238, 1137 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 – 6.68 (m, 3H), 4.25 (s, 2H), 4.00 (t, *J* = 6.7 Hz, 2H), 3.99 (t, *J* = 6.7 Hz, 2H), 1.89 – 1.73 (m, 4H), 1.54 – 1.41 (m, 4H), 1.41 – 1.17 (m, 14H), 0.99 – 0.79 (m, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 149.32, 149.24, 127.79, 120.93, 113.89, 113.64, 69.29, 69.27, 54.78, 31.81, 29.37, 29.26, 26.01, 22.66, 14.08.
ESI-MS analysis: $C_{23}H_{39}N_3O_2Na$ $[M+Na]^+$, mass calculated: 412.29, mass found: 412.29.

Synthesis of 8b



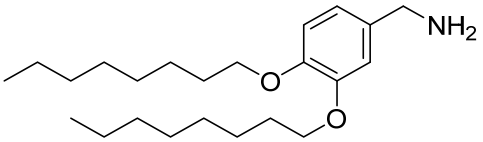
8b was synthesized according to the procedure described for **8a**, using **7b** as starting material (theor 2.38 mmol), and NaN_3 (0.31 g, 4.76 mmol).
FTIR-ATR (neat): 2953, 2925, 2869, 2095, 1512, 1467, 1429, 1262, 1236, 1138 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.93 – 6.72 (m, 3H), 4.25 (s, 2H), 4.14 – 3.75 (m, 3H), 2.01 – 1.76 (m, 2H), 1.75 – 1.44 (m, 5H), 1.39 – 1.05 (m, 11H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.94 (d, *J* = 6.5 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 149.32, 149.23, 127.76, 120.89, 113.75, 113.49, 67.61, 67.58, 54.80, 39.24, 37.34, 36.21, 36.19, 29.91, 27.98, 24.71, 22.69, 22.59, 19.70, 19.69.

ESI-MS analysis: $C_{27}H_{47}N_3O_2Na$ $[M+Na]^+$, mass calculated: 468.36, mass found: 468.35.

Synthesis of 9a

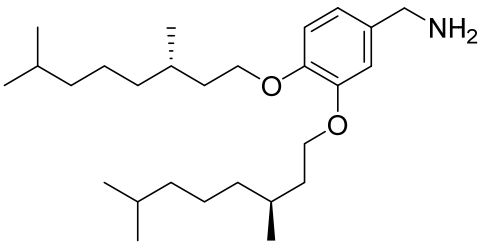


Azide **8a** (0.50 g, 1.29 mmol) was dissolved in dry THF (10 mL) under N_2 atmosphere. After 10 min stirring at 0-4 °C $LiAlH_4$ (1 M in THF, 1.54 mL) was added dropwise via syringe. After 2 h stirring at 0-4 °C no starting material was observed by TLC. The mixture was diluted with diethyl ether (20 mL), and water (0.100 mL) and aqueous 1 M NaOH (0.100 mL) were consecutively added at 0-4 ºC. After 30 min water (0.100 mL) was added and the mixture was stirred at room temperature for 15 min. The mixture was then filtered and the filter cake was washed with diethyl ether (3 x 5 mL). The filtrate was submitted to reduced pressure and the crude was obtained as a waxy yellowish solid after slow solidification. The product was used without further purification.

FTIR-ATR (neat): 3321, 2921, 2850, 1512, 1467, 1268, 1253, 1232, 1135 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 – 6.63 (m, 3H), 4.57 – 4.38 (m, 2H), 4.15 – 3.73 (m, 4H), 2.09 – 1.58 (m, 4H), 1.55 – 1.38 (m, 4H), 1.38 – 1.13 (m, 16H), 0.99 – 0.49 (m, 6H).

Synthesis of 9b



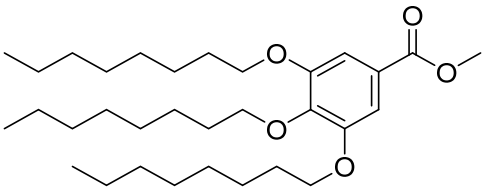
9b was synthesized according to the procedure described for **9a**, using **8b** as starting material (0.50 g, 1.12 mmol), and $LiAlH_4$ as reductant (1 M in THF, 1.35 mL). The product, a yellow oil, was used without further purification.

FTIR-ATR (neat): 2925, 2869, 1510, 1263, 1136 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.88 – 6.63 (m, 3H), 4.57 – 4.38 (m, 1H), 4.15 – 3.73 (m, 4H), 2.09 – 1.58 (m, 4H), 1.55 – 1.38 (m, 4H), 1.38 – 1.13 (m, 16H), 0.99 – 0.49 (m, 6H).

ESI-MS analysis: $C_{27}H_{49}NO_2$ $[M]^+$, mass calculated: 419.38, mass found: 419.37.

Synthesis of 10a



Methyl 3,4,5-trihydroxybenzoate (0.74 g, 4 mmol) and anhydrous potassium carbonate (3.32 g, 24 mmol) were suspended in anhydrous DMF (20 mL). The suspension was heated to 80 °C and after 1 h stirring, 1-bromooctane (2.3 mL 13.2 mmol) was added dropwise via syringe. After 66 h the mixture (dark color) was allowed to reach room temperature and then poured into water (60 mL). The product was extracted with a 70/30 mixture of hexanes and ethyl acetate (3 x 30 mL). The combined organic layers were treated with brine (30 mL), dried over anhydrous Na_2SO_4, filtered and submitted to reduced pressure. The product was then purified by flash column chromatography using an eluent gradient from hexanes (100 %) to a mixture of hexanes and ethyl acetate (95/5). **10a** was obtained as a colourless oil in 71 % yield (1.47 g, 2.82 mmol).

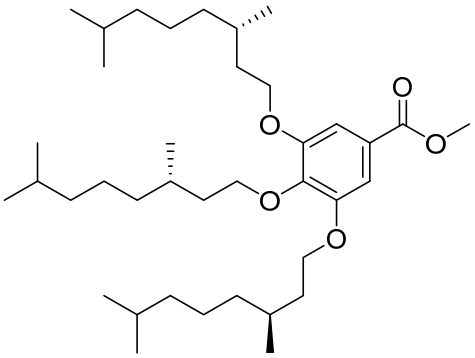
FTIR-ATR (neat): 2924, 2855, 1722, 1587, 1429, 1335, 1217, 1111 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, *J* = 4.6 Hz, 3H), 4.03 (t, *J* = 6.6 Hz, 2H), 4.02 (t, *J* = 6.5 Hz, 4H), 3.90 (s, 3H), 1.90 – 1.69 (m, 6H), 1.55 – 1.42 (m, 6H), 1.42 – 1.16 (m, 24H), 0.99 – 0.78 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.92, 152.79, 142.35, 124.63, 107.96, 73.47, 69.15, 52.08, 31.88, 31.82, 30.31, 29.50, 29.35, 29.33, 29.29, 29.28, 26.06, 26.03, 22.68, 22.66, 14.08.

ESI-MS analysis: $C_{32}H_{57}O_5$ $[M+H]^+$, mass calculated: 521.42, mass found: 521.43

Synthesis of 10b

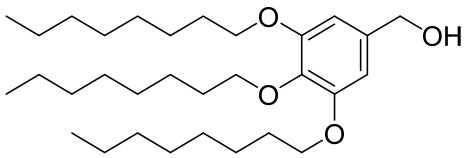


10b was synthesized according to the procedure described for **10a**, using methyl 3,4,5-trihydroxybenzoate (0.74 g, 4 mmol), potassium carbonate (3.32 g, 24 mmol), and (*S*)-3,7-dimethyl-1-octyl methylsulfonate (4.58 g, 19.4 mmol) in dry DMF (20 mL). The product was purified by flash column chromatography using an eluent gradient from hexanes to a 98/2 mixture of hexanes and ethyl acetate, and obtained as a colourless oil (1.24 g, 2.05 mmol, 51 % yield).

FTIR-ATR (neat): 2953, 2869, 1723, 1587, 1435, 1333, 1212, 1112 cm^{-1}.

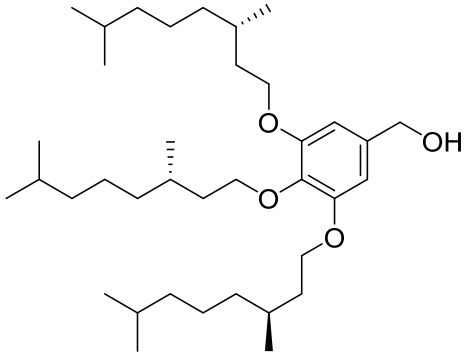
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (s, 2H), 4.24 – 3.95 (m, 6H), 3.89 (s, 3H), 1.93 – 1.76 (m, 3H), 1.76 – 1.66 (m, 3H), 1.66 – 1.44 (m, 4H), 1.42 – 1.22 (m, 6H), 1.22 – 1.05 (m, 9H), 0.94 (d, *J* = 6.6 Hz, 6H), 0.92 (d, *J* = 6.6 Hz, 3H), 0.89 – 0.78 (m, 18H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 166.91, 152.80, 142.31, 124.64, 107.90, 71.66, 67.42, 52.06, 39.33, 39.24, 37.47, 37.31, 36.29, 29.80, 29.61, 27.96, 24.71, 24.69, 22.68, 22.59, 22.57, 19.56, 19.53.
ESI-MS analysis: $C_{38}H_{68}O_5Na[M+Na]^+$, mass calculated: 627.50, mass found: 627.50.

Synthesis of 11a



10a (1.43 g, 2.76 mmol) was dissolved in dry diethyl ether (20 mL), and the colourless solution was stirred at 0-4 °C for 10 min. $LiAlH_4$ (1 M in THF, 2.8 mL) was then added dropwise via syringe (gas evolution). The reaction mixture was allowed to react while the water-ice bath was consumed. After 3 h the mixture was diluted with diethyl ether (40 mL), cooled down to 0-4 °C. Deionized water (0.10 mL) and 1 M NaOH (0.10 mL) were consecutively added. The mixture was stirred for 30 min and other 0.10 mL deionized water were added. The mixture was stirred for 30 min at room temperature and then filtered to remove the formed salts. Evaporation of the solvents under reduced pressure afforded **11a** as a white waxy solid (1.20 g, 2.43 mmol, 88 % yield).
FTIR-ATR (neat): 3289, 2921, 2852, 1590, 1437, 1228, 1113 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (s, 2H), 4.59 (s, 2H), 3.97 (t, *J* = 6.5 Hz, 4H), 3.93 (t, *J* = 6.6 Hz, 2H), 1.92 – 1.65 (m, 6H), 1.52 – 1.39 (m, 6H), 1.39 – 1.09 (m, 24H), 1.00 – 0.78 (m, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.27, 137.62, 135.98, 109.93, 105.36, 73.43, 69.11, 65.68, 31.91, 31.83, 30.32, 29.55, 29.41, 29.37, 29.36, 29.36, 29.29, 26.12, 26.09, 22.69, 22.67, 14.09.
ESI-MS analysis: $C_{31}H_{57}O_4$ $[M+H]^+$, mass calculated: 493.43, mass found: 493.42.

Synthesis of 11b



11b was prepared according the same procedure as **11a** using **10b** (1.15 g, 1.90 mmol) as starting material and $LiAlH_4$ (1 M in THF, 1.90 mL). The product was purified by flash column

chromatography using an eluent gradient from hexanes to hexanes/ethyl acetate (95/5). The product was obtained as a colorless oil (0.93 g, 1.61 mmol, 85 % yield).

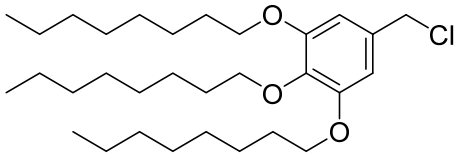
FTIR-ATR (neat): 3357, 2953, 2925, 2869, 1590, 1457, 1437, 1232, 1114 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.59 (s, 2H), 4.15 – 3.86 (m, 6H), 1.93 – 1.76 (m, 3H), 1.76 – 1.64 (m, 3H), 1.64 – 1.43 (m, 6H), 1.43 – 1.21 (m, 9H), 1.21 – 1.04 (m, 9H), 0.93 (d, *J* = 6.6 Hz, 9H), 0.86 (d, *J* = 6.6 Hz, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.27, 137.52, 136.04, 105.24, 71.65, 67.36, 65.65, 39.36, 39.27, 37.52, 37.35, 36.41, 29.82, 29.69, 27.98, 27.96, 24.72, 24.71, 22.70, 22.59, 19.63, 19.57.

ESI-MS analysis: $C37H68O4Na$ $[M+Na]^+$, mass calculated: 599.50, mass found: 599.50.

Synthesis of 12a



11a (1.14 g, 2.32 mmol) was dissolved in dry dichloromethane (10 mL) and stirred for 10 min at 0-4 °C under nitrogen. Thionyl chloride (0.24 mL, 3.25 mmol) was added dropwise followed by DMF (3 drops). The colourless solution turned yellow. After 1 h stirring 0-4 °C the solvents were removed under reduced pressure. Additional dichloromethane was used to favour distillation of the excess of thionyl chloride. **12a** was obtained as a yellow oil and directly used in the next reaction.

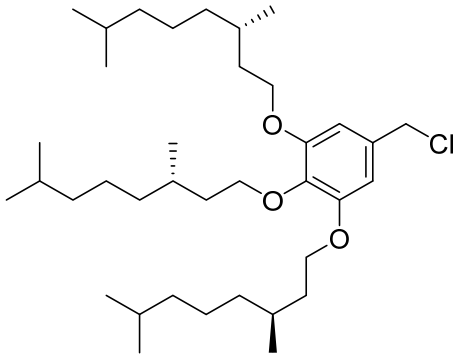
FTIR-ATR (neat): 2924, 2854, 1591, 1506, 1437, 1335, 1235, 1113 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 (s, 2H), 4.51 (s, 2H), 3.97 (t, *J* = 6.5 Hz, 4H), 3.94 (t, *J* = 6.6 Hz, 2H), 1.88 – 1.67 (m, 6H), 1.53 – 1.40 (m, 6H), 1.40 – 1.10 (m, 24H), 0.98 – 0.75 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.19, 138.24, 132.30, 106.98, 71.66, 67.39, 46.99, 39.35, 39.26, 39.17, 37.50, 37.33, 37.31, 37.06, 36.45, 36.36, 29.80, 29.67, 27.98, 24.73, 24.70, 22.70, 22.59, 19.58.

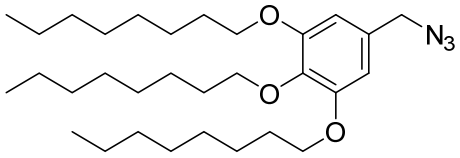
ESI-MS analysis: $C_{31}H_{55}ClO_3Na$ $[M+Na]^+$, mass calculated: 533.37, mass found: 533.37.

Synthesis of 12b



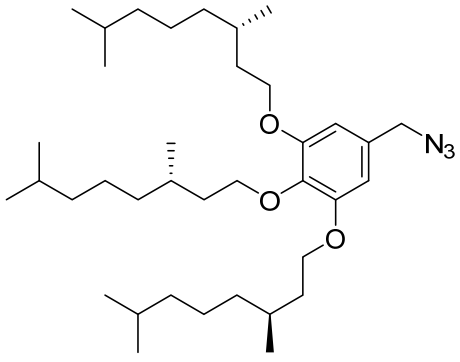
The product was prepared following the same procedure as for **12a** using **11b** (0.88 g, 1.53 mmol), thionyl chloride (0.16 mL, 2.14 mmol), DMF (3 drops) and dry dichloromethane (10 mL).
FTIR-ATR (neat): 2953, 2925, 2869, 1591, 1505, 141464, 1440, 1236, 1114 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (s, 2H), 4.52 (s, 2H), 4.28 – 3.80 (m, 6H), 1.95 – 1.76 (m, 3H), 1.75 – 1.40 (m, 9H), 1.40 – 1.21 (m, 9H), 1.21 – 1.03 (m, 9H), 1.00 – 0.89 (m, 9H), 0.87 (d, *J* = 6.6 Hz, 12H), 0.86 (d, *J* = 6.4 Hz, 6H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.19, 138.24, 132.30, 106.98, 71.66, 67.39, 46.99, 39.35, 39.26, 37.50, 37.34, 37.34, 37.31, 36.36, 29.80, 29.67, 27.98, 24.73, 24.70, 22.70, 22.61, 22.59, 19.58.
ESI-MS analysis: C37H67ClO3 $[M+Na]^+$, mass calculated: 617.47, mass found: 617.46.

Synthesis of 13a



The product was prepared following the same procedure as for **8a** using **12a** (theor 2.32 mmol) and NaN_3 (0.30 g, 4.64 mmol). The product was purified by flash column chromatography using an eluent gradient from hexanes to hexanes/ethyl acetate 99/1. **13a** was obtained as a colourless liquid with 76 % yield (0.93 g, 1.79 mmol).
FTIR-ATR (neat): 2924, 2855, 2097, 1590, 1507, 1436, 1335, 1234, 1113 cm^{-1}.
^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (s, 2H), 4.24 (s, 2H), 3.97 (t, *J* = 6.5 Hz, 4H), 3.94 (t, *J* = 6.6 Hz, 2H), 1.91 – 1.67 (m, 6H), 1.53 – 1.40 (m, 6H), 1.40 – 1.13 (m, 24H), 1.01 – 0.76 (m, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.32, 138.08, 130.32, 106.57, 73.40, 69.13, 55.17, 31.90, 31.82, 30.31, 29.54, 29.37, 29.35, 29.28, 26.09, 26.08, 22.69, 22.67, 14.09.
ESI-MS analysis: $C_{31}H_{55}N_3O_3Na$ $[M+Na]^+$, mass calculated: 540.41, mass found: 540.41.

Synthesis of 13b



The product was prepared following the same procedure as for **8a** using **12b** (theor 1.39 mmol) and NaN_3 (0.18 g, 2.78 mmol). The product was purified by flash column chromatography using an

eluent gradient from hexanes to hexanes/ethyl acetate 98/2. **13b** was obtained as a colourless liquid with 71 % yield (0.60 g, 0.99 mmol).

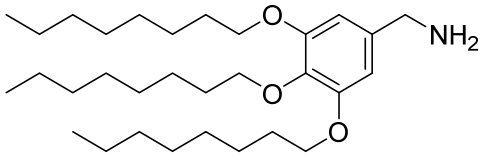
FTIR-ATR (neat): 2953, 2925, 2869, 2097, 1590, 1507, 1437, 1236, 1114 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 6.50 (s, 2H), 4.25 (s, 2H), 4.12 – 3.86 (m, 6H), 1.94 – 1.77 (m, 3H), 1.77 – 1.64 (m, 3H), 1.64 – 1.44 (m, 6H), 1.44 – 1.21 (m, 9H), 1.21 – 1.05 (m, 9H), 0.98 – 0.90 (m, 9H), 0.87 (d, *J* = 6.6 Hz, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.34, 138.10, 130.36, 106.54, 71.64, 67.44, 55.19, 39.36, 39.26, 37.52, 37.34, 37.33, 36.37, 29.81, 29.69, 27.98, 24.73, 24.71, 22.70, 22.61, 22.60, 19.58.

ESI-MS analysis: $C_{37}H_{67}N_3O_3Na$ $[M+Na]^+$, mass calculated: 624.51, mass found: 624.51.

Synthesis of 14a



13a (665 mg, 1.28 mmol) was dissolved in anhydrous diethyl ether (10 mL) under N_2 atmosphere. After 10 min stirring at 0-4 °C, $LiAlH_4$ (1 M in THF, 1.54 mL) was added dropwise via syringe. After 2 h stirring at 0-4 °C no starting material was observed by TLC. The mixture was diluted with diethyl ether (20 mL), and water (0.660 mL) and aqueous 1 M NaOH (0.660 mL) were consecutively added at 0-4 ºC. After 1 h water the mixture was filtered and the filter cake was washed with diethyl ether (3 x 5 mL). The filtrate was submitted to reduced pressure and the crude was obtained as a colorless oil. The product was purified by flash column chromatography using an eluent gradient of ethyl acetate/methanol/NH_4OH (aq) from 10/0/0 to 9/1/0 and finally 9/1/0.1. **14a** was obtained as a waxy white solid with a 48 % yield (0.31 g, 0.61 mmol).

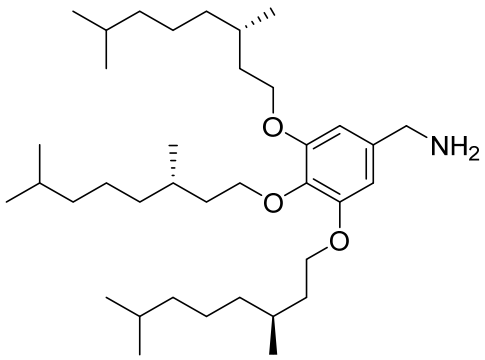
FTIR-ATR (neat): 2920, 2850, 1641, 1591, 1502, 1466, 1435, 1330, 1230, 1115 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 6.54 (s, 2H), 3.96 (t, *J* = 6.5 Hz, 4H), 3.91 (t, *J* = 6.6 Hz, 2H), 3.79 (s, 2H), 3.17 (bs, 2H), 1.85 – 1.65 (m, 6H), 1.54 – 1.39 (m, 6H), 1.39 – 1.13 (m, 24H), 1.04 – 0.53 (m, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.25, 137.31, 135.79, 105.84, 73.39, 69.12, 46.04, 31.89, 31.82, 30.32, 29.55, 29.43, 29.37, 29.29, 26.11, 26.11, 22.67, 22.65, 14.07.

ESI-MS analysis: $C_{31}H_{37}NO_3Na$ $[M+Na]^+$, mass calculated: 514.42, mass found: 514.41.

Synthesis of 14b



14b was prepared following the same procedure as for **14a** using **13b** (396 mg, 0.66 mmol) and $LiAlH_4$ (1 M in THF, 0.79 mL). **14a** was obtained as a yellow oil with a 61 % yield (229 mg, 0.40 mmol).

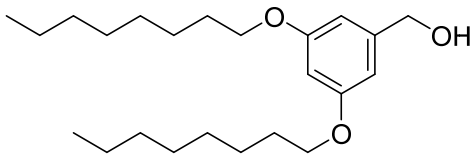
FTIR-ATR (neat): 2953, 2925, 2869, 1589, 1463, 1436, 1232, 1114 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$) δ 6.56 (s, 2H), 4.08 – 3.86 (m, 6H), 3.83 (s, 2H), 3.21 (bs, 3H), 1.94 – 1.76 (m, 3H), 1.76 – 1.62 (m, 3H), 1.62 – 1.43 (m, 6H), 1.43 – 1.20 (m, 10H), 1.20 – 1.03 (m, 8H), 0.93 (d, *J* = 6.4 Hz, 6H), 0.91 (d, *J* = 6.2 Hz, 3H), 0.86 (d, *J* = 6.6 Hz, 18H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.32, 137.42, 135.06, 105.89, 71.64, 67.40, 45.92, 39.36, 39.27, 37.54, 37.39, 37.34, 36.45, 29.81, 29.71, 27.97, 24.73, 24.70, 22.70, 22.61, 22.59, 19.56, 19.55.

ESI-MS analysis: $C_{37}H_{67}O_3$ $[M\text{-}NH_2]^+$, mass calculated: 559.51, mass found: 559.50.

Synthesis of 15a



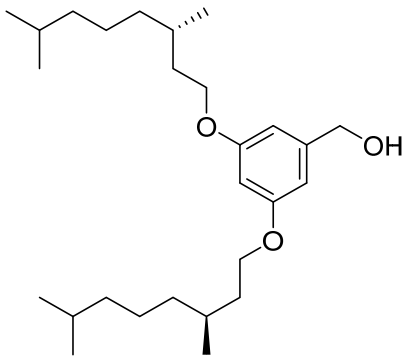
3,5-dihydroxybenzyl alcohol (2.01 g, 14.4 mmol), *n*-octyl bromide (5.33 mL, 30.9 mmol), 18-crown-6 (741 mg, 2.80 mmol) and K_2CO_3 (7.87 g, 56.9 mmol) were suspended in dry acetone (50 mL) under an argon atmosphere. The mixture was refluxed for 16 hours, after which the mixture was cooled to room temperature and subsequently, water (50 mL) was added and the volatile organic solvent was evaporated. Then, DCM (50 mL) was added and the product was extracted into the organic layer. The organic layer was dried over $MgSO_4$, filtered and evaporated. Column chromatography (KP-Sil 100g, heptane to EtOAc) afforded the product (4.65 g, 89%).

^1H NMR (400 MHz, $CDCl_3$) δ 6.50 (d, *J* = 2.2 Hz, 2H), 6.38 (t, *J* = 2.2 Hz, 1H), 4.62 (d, *J* = 5.9 Hz, 2H), 3.93 (t, *J* = 6.6 Hz, 4H), 1.81-1.73 (m, 4H), 1.46-1.40 (m, 4H), 1.37-1.25 (m, 16H), 0.89 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.70, 143.32, 105.21, 100.71, 68.22, 65.65, 31.97, 29.50, 29.41, 29.39, 26.20, 22.81, 14.25.

MALDI-ToF analysis: mass calculated: 364.30, mass found: 365.38 $(M+H^+)$.

Synthesis of 15b



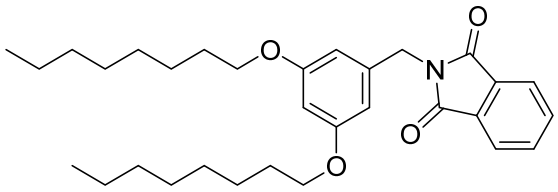
3,5-dihydroxybenzyl alcohol (1.66 g, 11.9 mmol), citronellyl tosylate (7.97 g, 25.5 mmol), 18-crown-6 (632 mg, 2.39 mmol) and K_2CO_3 (6.52 g, 47.2 mmol) were suspended in dry acetone (25 mL) under an argon atmosphere. The mixture was refluxed for 15 hours, after which it was cooled to room temperature and subsequently, the solvent was evaporated. Then, the product was redissolved in DCM (50 mL) and washed with water (50 mL). The aqueous layer was extracted with DCM and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. Column chromatography (KP-Sil 50, 7 vol% EtOAc in heptane) afforded the product (3.43 g, 69%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (d, *J* = 2.2 Hz, 2H), 6.35 (t, *J* = 2.2 Hz, 2H), 4.56 (d, *J* = 5.5 Hz, 2H), 3.93 (m, 4H), 1.84-1.73 (m, 2H), 1.72-1.61 (m, 2H), 1.59-1.47 (m, 4H), 1.37-1.23 (m, 6H), 1.19-1.12 (m, 6H), 0.93 (d, *J* = 6.6 Hz, 6H), 0.87 (d, *J* = 6.7 Hz, 12H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.50, 143.35, 105.08, 100.56, 66.40, 65.24, 39.33, 37.37, 36.29, 29.93, 28.0, 24.74, 22.79, 22.69, 19.71.

MALDI-ToF analysis: mass calculated: 420.36, mass found: 421.37 ($M+H^+$).

Synthesis of 16a



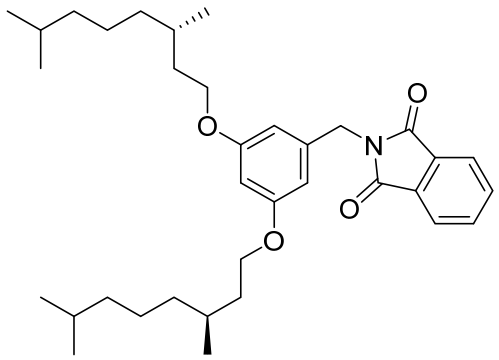
15a (4.44 g, 12.2 mmol), phthalimide (2.24 g, 15.2 mmol) and PPh_3 (2.96 g, 14.6 mmol) were dissolved in dry THF (100 mL) under an argon atmosphere. The solution was cooled to 0 °C using an ice bath and a solution of DIAD (2.87 mL, 14.6 mmol) in dry THF (40 mL) was added using a dropping funnel. Then, the mixture was left to heat up and stir for 3 hours, after which the solvent was evaporated. Pentane (75 mL) was added to the residue to result in the formation of a white precipitate. The supernatant was decanted and evaporated. Column chromatography (KP-Sil 100g, 25% EtOAc in heptane) afforded the product in quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.87 (m, 2H), 7.68-7.73 (m, 2H), 6.55 (d, *J* = 2.2 Hz, 2H), 3.90 (t, *J* = 6.6 Hz, 4H), 1.77-1.68 (m, 4H), 1.45-1.37 (m, 4H), 1.34-1.22 (m, 16H), 0.88 (t, *J* = 7.0 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.14, 160.61, 138.46, 134.09, 132.30, 123.48, 106.98, 100.77, 68.18, 41.83, 31.95, 29.49, 29.38, 29.36, 26.18, 22.83, 22.80, 14.25, 14.24.

MALDI-ToF analysis: mass calculated: 493.32, mass found: 494.45 ($M+H^+$).

Synthesis of 16b



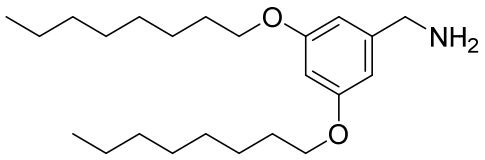
15b (3.43 g, 8.16 mmol) was dissolved in dry THF (100 mL) under an argon atmosphere. Phthalimide (1.51 gram, 10.2 mmol) and PPh_3 (2.78 g, 10.6 mmol) were added and the mixture was cooled to 0 °C using an icebath. Using a dropping funnel, a solution of DIAD (1.93 mL, 9.79 mmol) in dry THF (40 mL) was added, resulting in a yellow solution. The mixture was left to heat up to room temperature and stirred for 4 hours, after which the solvent was evaporated. Then, pentane (100 mL) was added to the yellow oil to precipitate a White solid. The resulting precipitate was filtered off and the filtrate was evaporated. Column chromatography (KP-Sil 100g, 25% $CHCl_3$ in heptane) afforded the product as a viscous oil (3.57 g, 80%).

^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.72 (m, 2H), 6.55 (d, *J* = 2.2 Hz, 2H), 6.34 (t, *J* = 2.2 Hz, 1H), 4.76 (s, 2H), 3.93 (m, 4H), 1.84-1.72 (m, 2H), 1.68-1.58 (m, 2H), 1.54-1.46 (m, 2H), 1.35-1.22 (m, 8H), 1.18-1.10 (m, 6H), 0.91 (d, *J* = 6.6 Hz, 6H), 0.87 (s, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.16, 160.61, 138.47, 134.11, 132.32, 123.50, 106.98, 100.77, 66.48, 41.84, 39.39, 37.44, 36.34, 32.04, 29.94, 28.12, 24.79, 22.86, 22.84, 22.75, 19.78, 14.27.

MALDI-ToF analysis: mass calculated: 549.38, mass found: 550.42 ($M+H^+$).

Synthesis of 17a



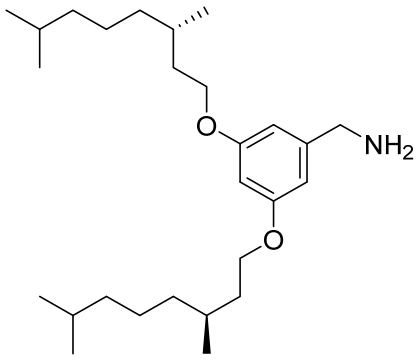
16a (5.61 g, 11.4 mmol) was dissolved in 1:1 EtOH:THF (40 mL). Then, hydrazine monohydrate (5.52 mL, 0.11 mol) was added and the mixture was refluxed overnight. After coooling down to room temperature, DCM (50 mL) was added and the solution was washed with 1M aqueous Na_2CO_3 solution (100 mL). The organic layer was dried over $MgSO_4$, filtered and evaporated to yield the product as a light red oil (3.85 g, 93%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.44 (d, J = 2.2 Hz, 2H), 6.34 (t, J = 2.2 Hz, 1H), 3.93 (t, J = 6.6Hz, 4H), 3.79 (s, 2H), 1.80-1.72 (m, 4H), 1.46-1.38 (m, 4H), 1.37-1.22 (m, 16H), 0.89 (t, J = 7.0 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.67, 145.88, 105.48, 99.76, 68.17, 46.86, 31.96, 29.50, 29.43, 29.39, 26.20, 22.80, 14.24.

ESI-MS analysis: mass calculated: 363.31, mass found: 364.17 ($M+H^+$).

Synthesis of 17b



16b (3.5 g, 6.37 mmol) was dissolved in 1:1 EtOH:THF (20 mL). Then, hydrazine monohydrate (4.83 mL, 63.7 mmol) was added. The mixture was then refluxed overnight and left at room temperature for 1 day, after which a white precipitate was formed. The suspension was dispersed between $CHCl_3$ (50 mL) and 0.5 M aqueous Na_2CO_3 solution (100 mL). The aqueous layer was extracted with $CHCl_3$ (3x25 mL) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated to yield the product as a clear oil in quantitative yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (d, J = 2.2 Hz, 2H), 6.34 (t, J = 2.2 Hz, 2H), 3.96 (m, 4H), 3.79 (s, 2H), 1.86-1.77 (m, 2H), 1.71-1.64 (m, 2H), 1.62-1.53 (m, 4H), 1.37-1.23 (m, 6H), 1.18-1.12 (m, 6H), 0.93 (d, J = 6.6 Hz, 6H), 0.87 (d, J = 6.7 Hz, 12H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 160.67, 145.91, 105.48, 99.79, 66.48, 46.89, 39.41, 37.44, 36.40, 30.01, 28.13, 24.8, 22.86, 22.76, 19.81.

IR spectra of BTA derivatives

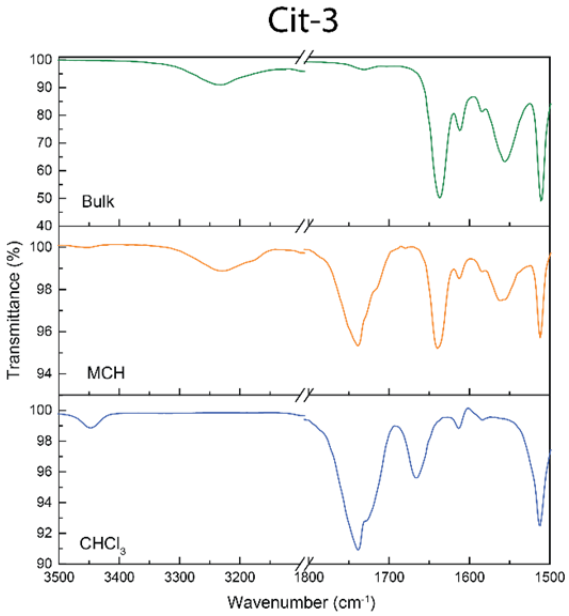


Figure S8. IR spectra of **Cit-3** in the bulk (top panel) and 250 μM solutions in MCH (middle panel) and $CHCl_3$ (bottom panel).

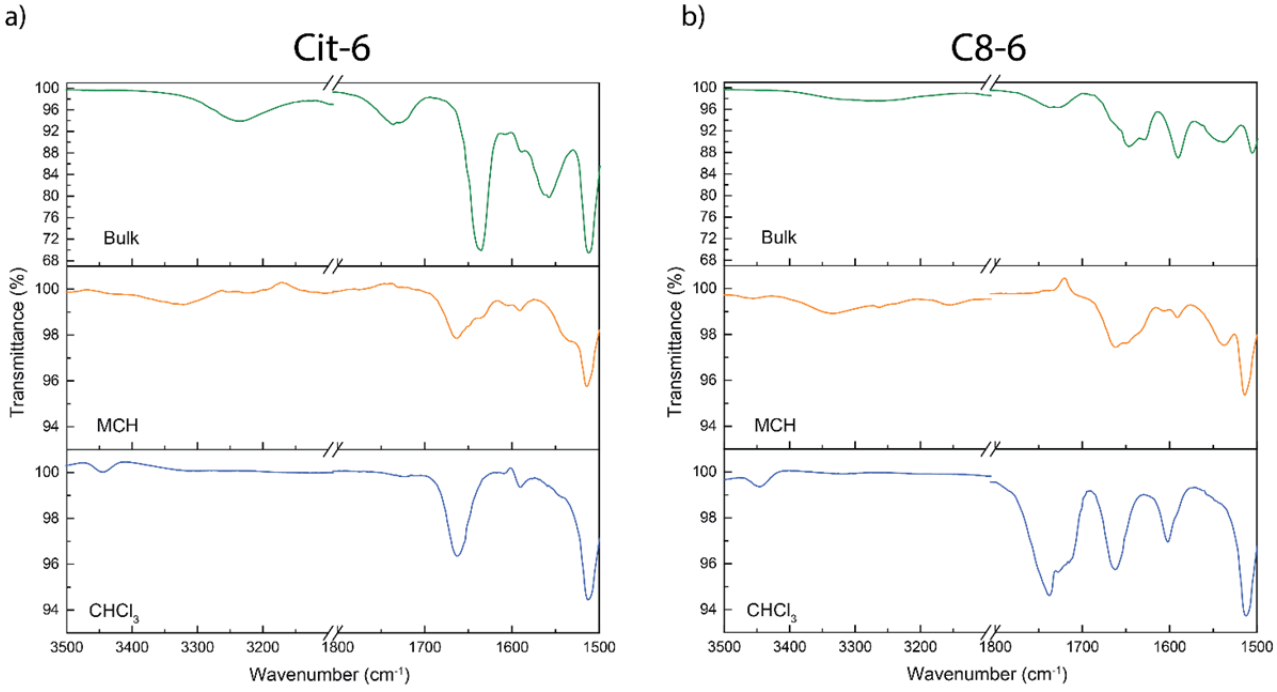


Figure S9. IR spectra of **Cit-6** (a) and **C8-6** (b) in the bulk (top panel) and 250 μM solutions in MCH (middle panel) and $CHCl_3$ (bottom panel).

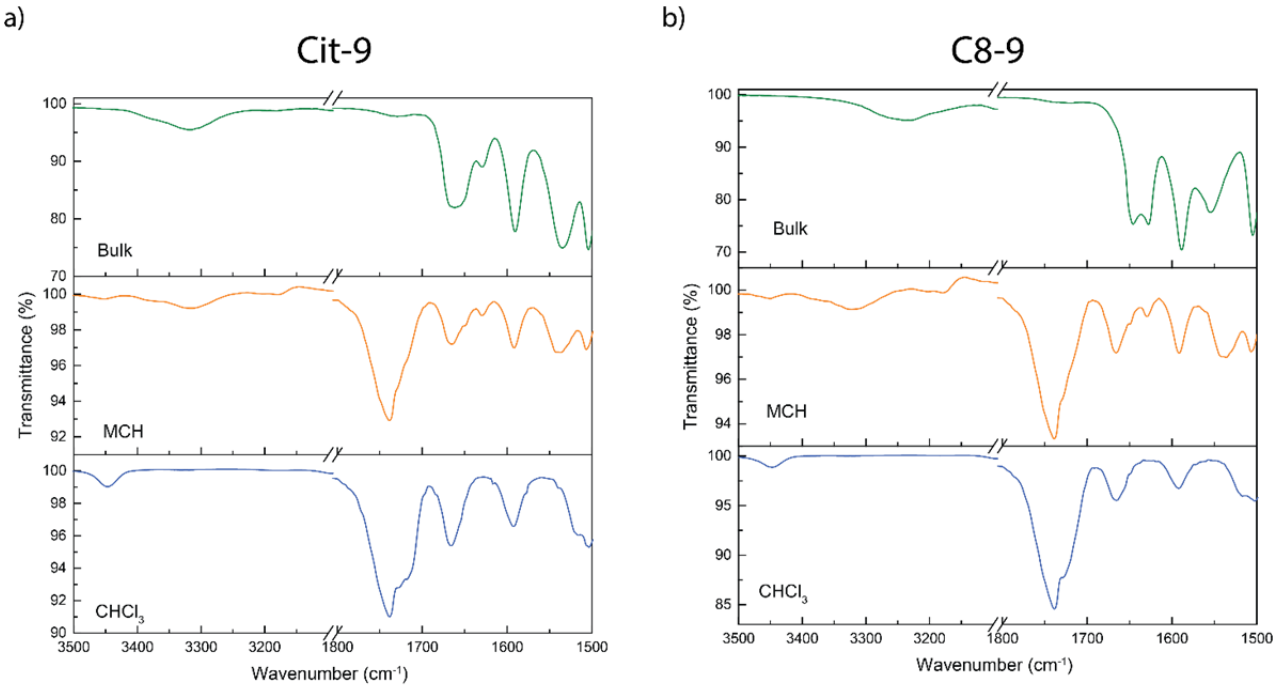


Figure S10. IR spectra of **Cit-9** (a) and **C8-9** (b) in the bulk (top panel) and 250 μM solutions in MCH (middle panel) and $CHCl_3$ (bottom panel).

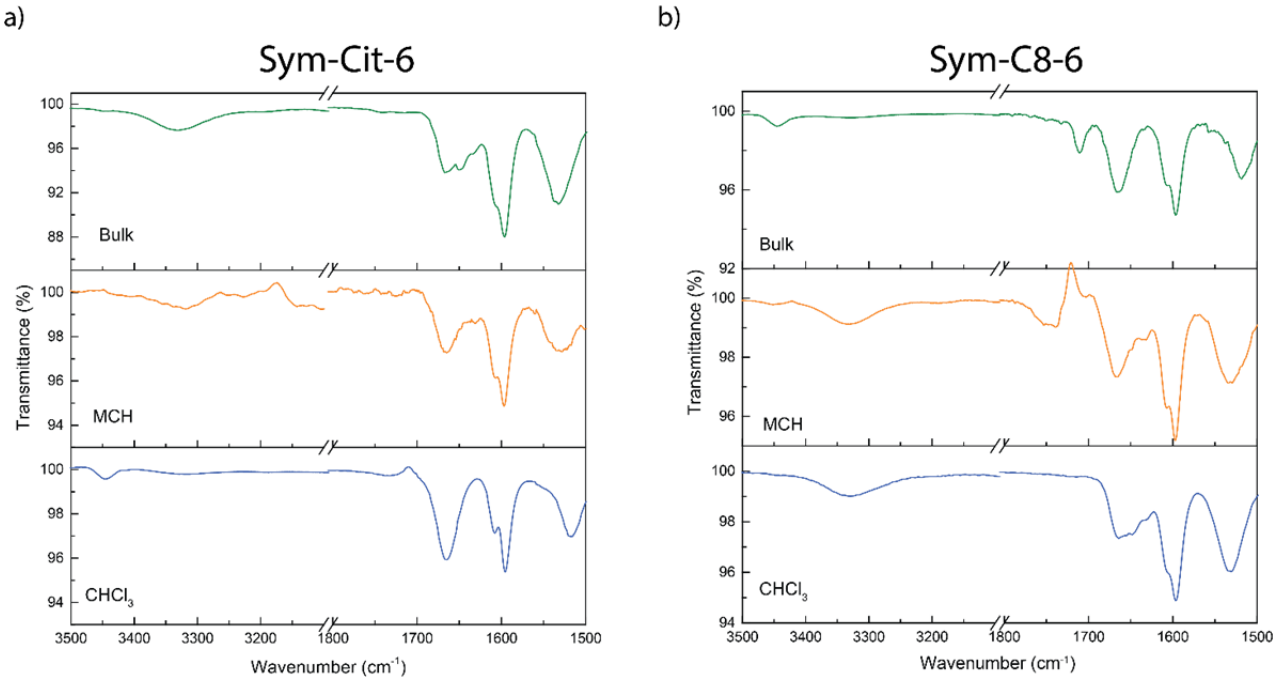


Figure S11. IR spectra of **Sym-Cit-6** (a) and **Sym-C8-6** (b) in the bulk (top panel) and 250 μM solutions in MCH (middle panel) and $CHCl_3$ (bottom panel).

VT-UV and VT-CD spectra of BTA derivatives

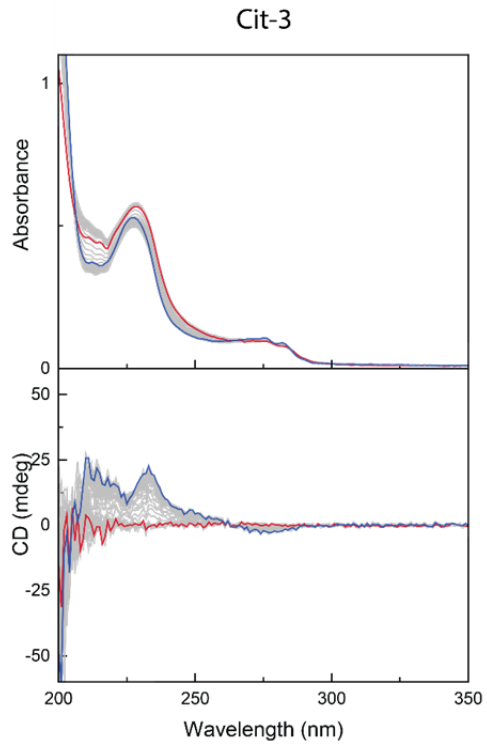


Figure S12. VT-UV (top panel) and VT-CD (bottom panel) spectra of 50 μM solutions of **Cit-3** in MCH. The spectra are measured at regular intervals between 90 °C (red spectrum) and 6 °C (blue spectrum).

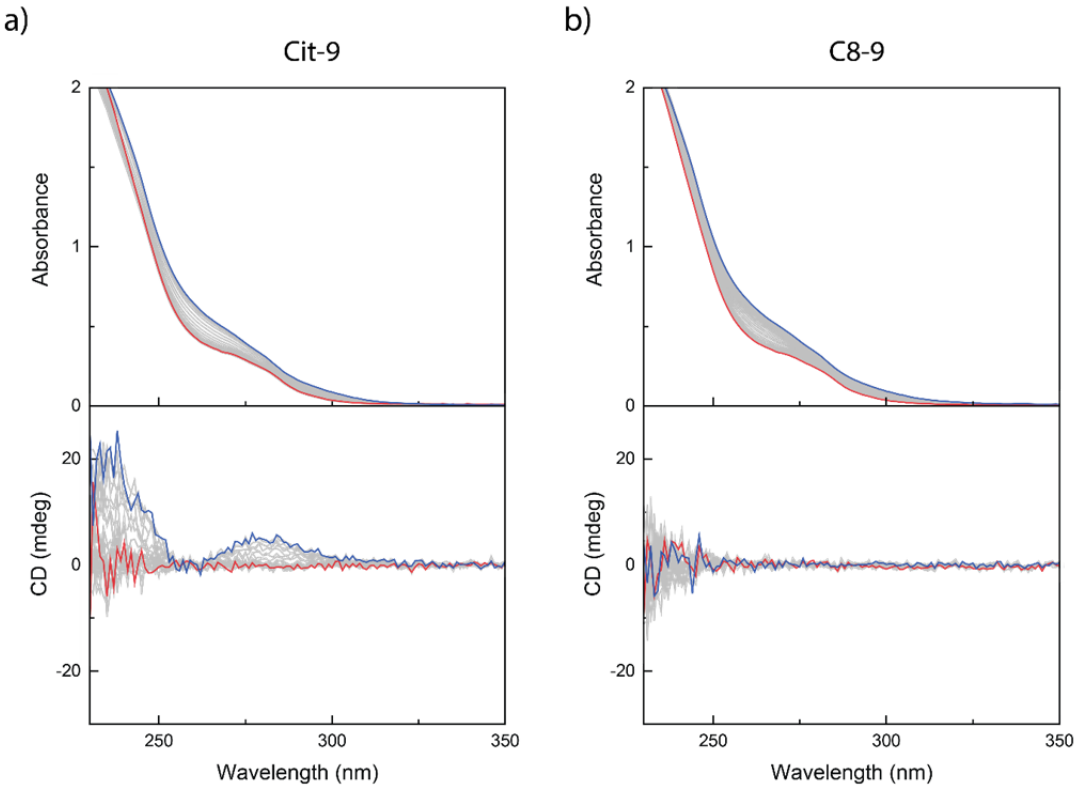


Figure S13. VT-UV (top panel) and VT-CD (bottom panel) spectra of 50 μM solutions of **Cit-9** (a) and **C8-9** (b) in MCH. The spectra are measured at regular intervals between 90 °C (red spectrum) and 6 °C (blue spectrum).

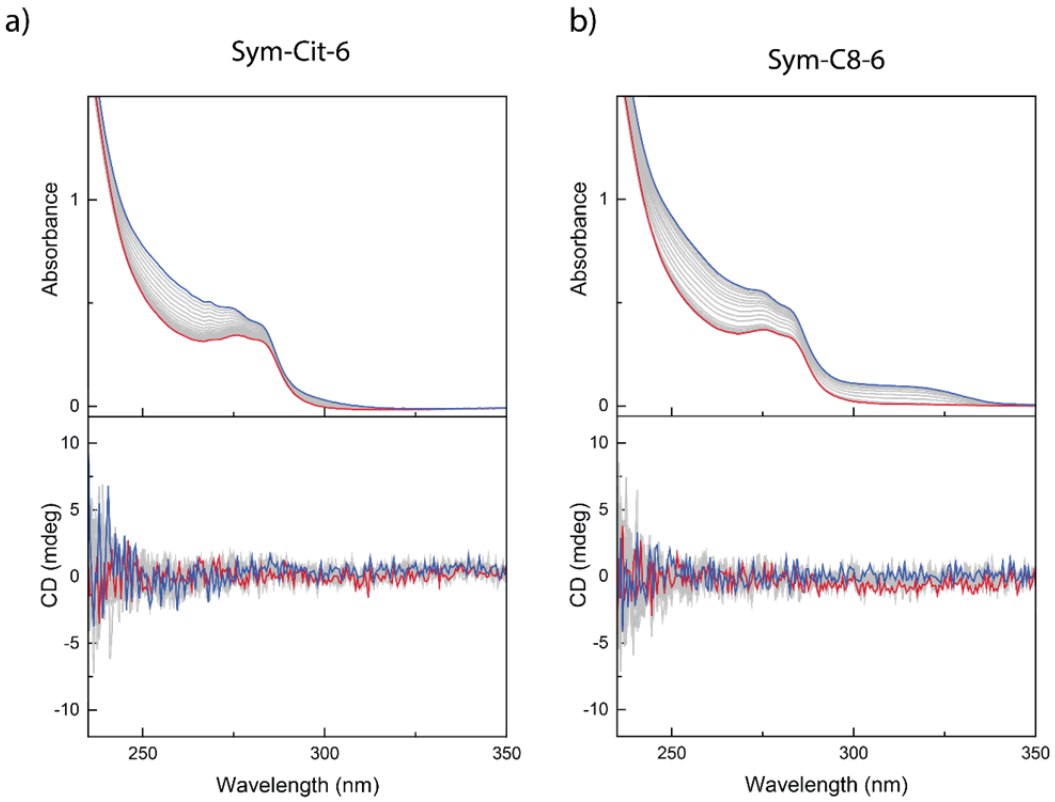


Figure S14. VT-UV (top panel) and VT-CD (bottom panel) spectra of 50 μM solutions of **Sym-Cit-6** (a) and **Sym-C8-6** (b) in MCH. The spectra are measured at regular intervals between 89 °C (red spectrum) and 5 °C (blue spectrum) for **Sym-Cit-6** and 92 °C and 4 °C for **Sym-C8-6** .

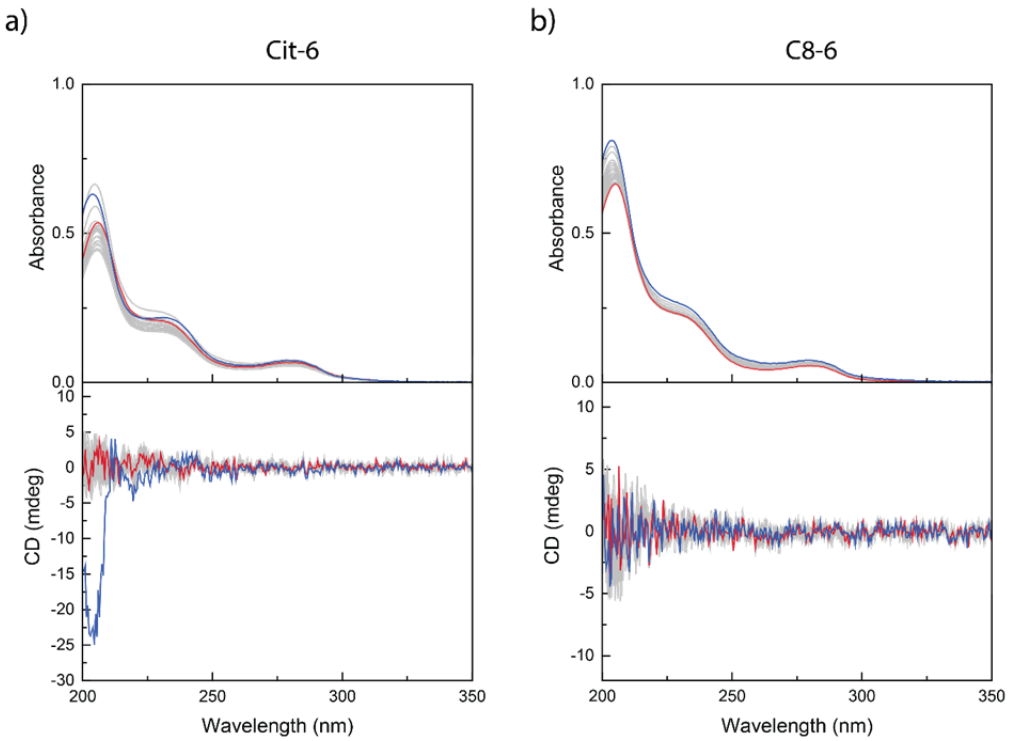


Figure S15. VT-UV (top panel) and VT-CD (bottom panel) spectra of 50 μM solutions of **Cit-6** (a) and **C8-6** (b) in MCH. The spectra are measured at regular intervals between 89 °C (red spectrum) and 5 °C (blue spectrum).

Additional VT-UV and VT-CD cooling curves

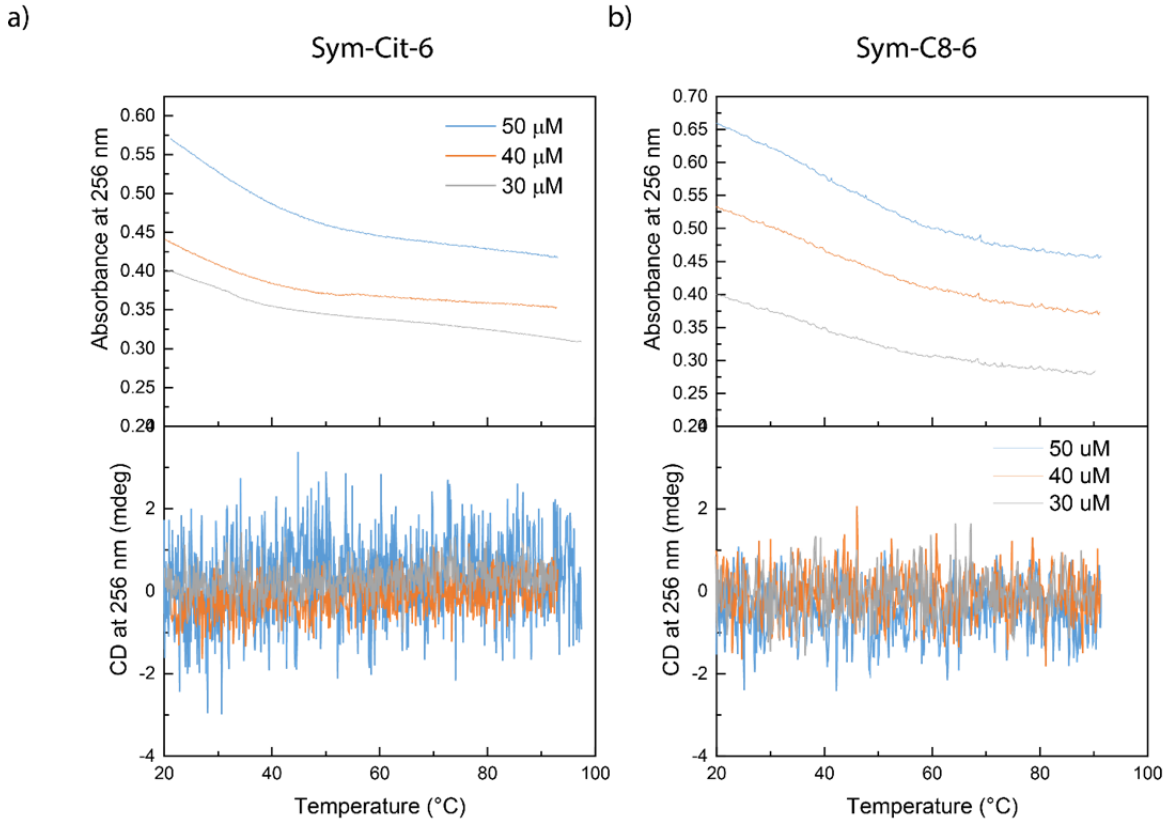


Figure S16. VT-UV (top panels) and VT-CD (bottom panels) cooling curves of **Sym-Cit-6** and **Sym-C8-6** in MCH.

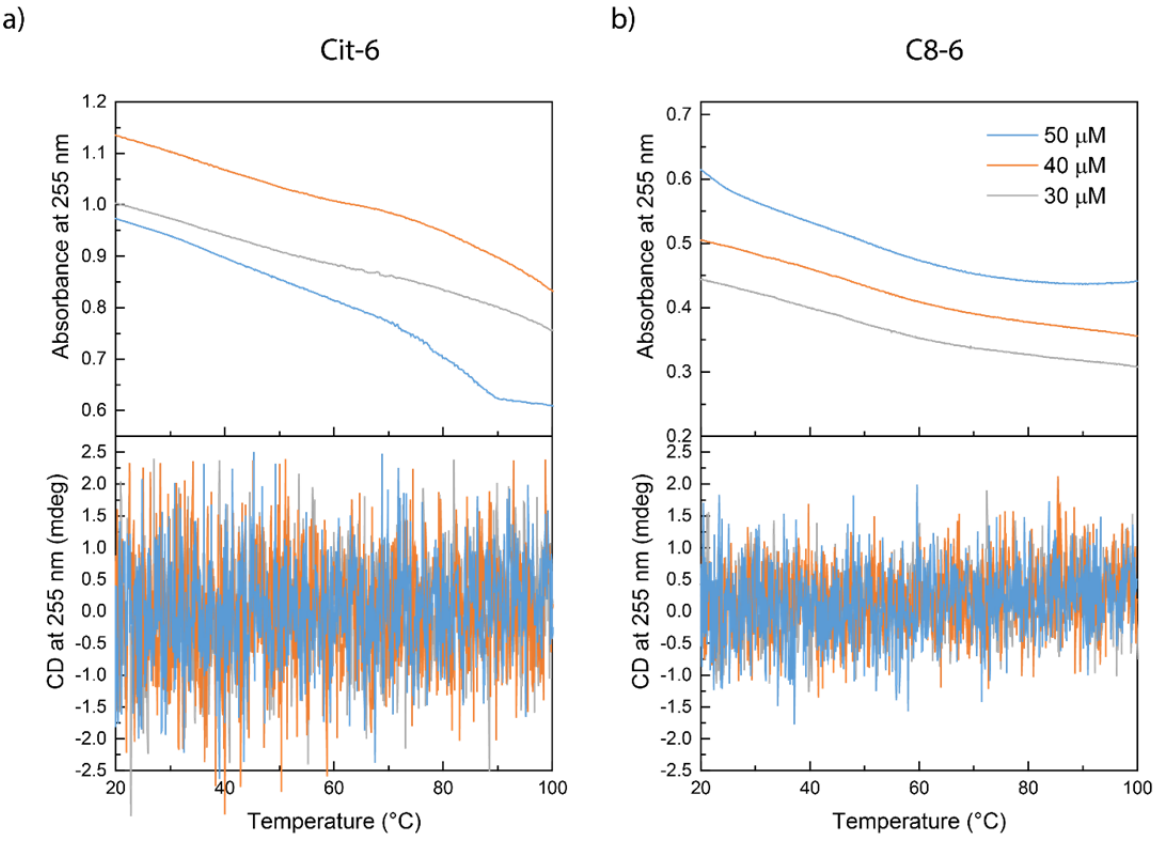


Figure S17. VT-UV (top panels) and VT-CD (bottom panels) cooling curves of **Cit-6** and **C8-6** in MCH.

Fits of cooling curves Cit-3, Cit-9 and C8-9

The fits were obtained by fitting the experimental data with the Matlab software published by ten Eikelder and co-workers.[17]

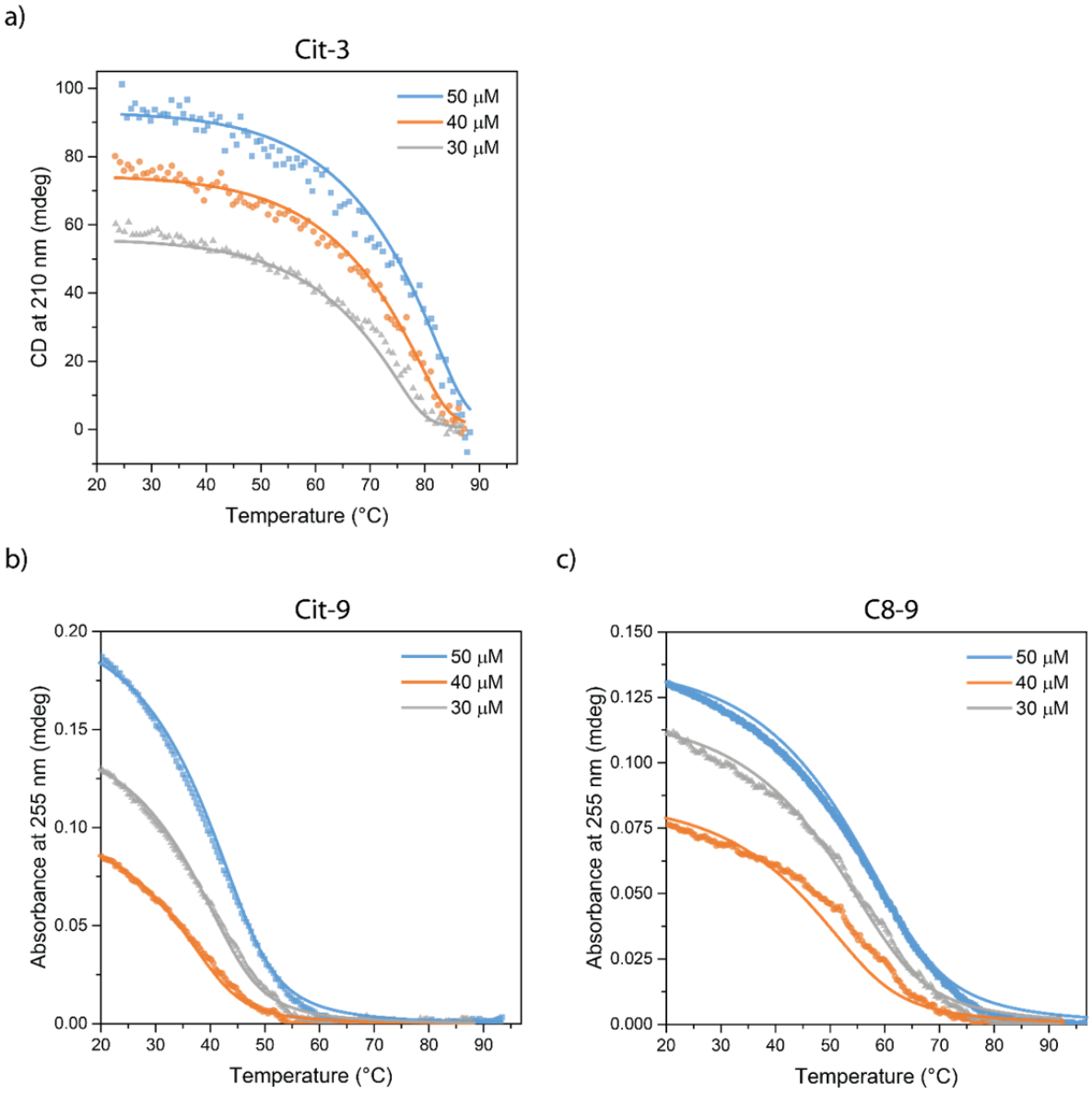
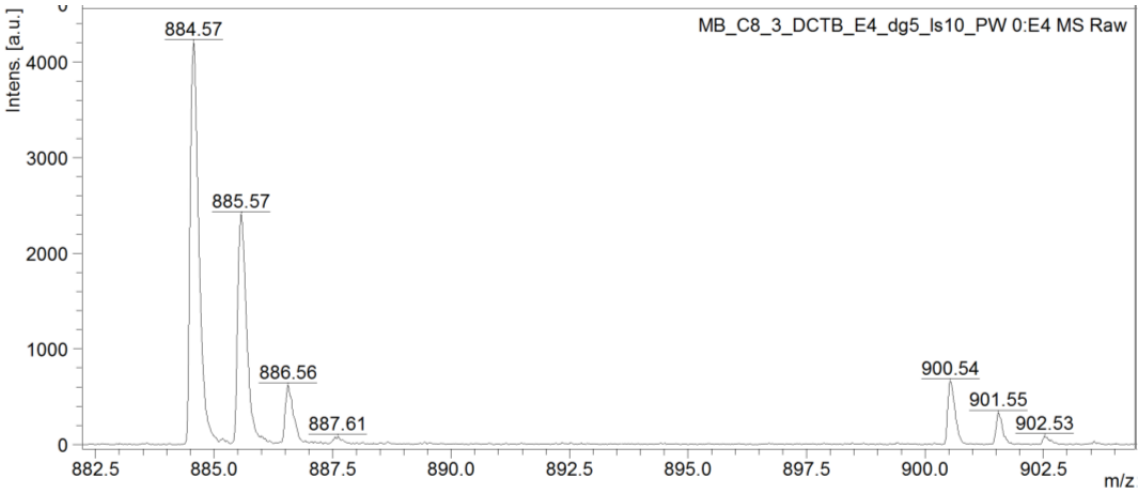


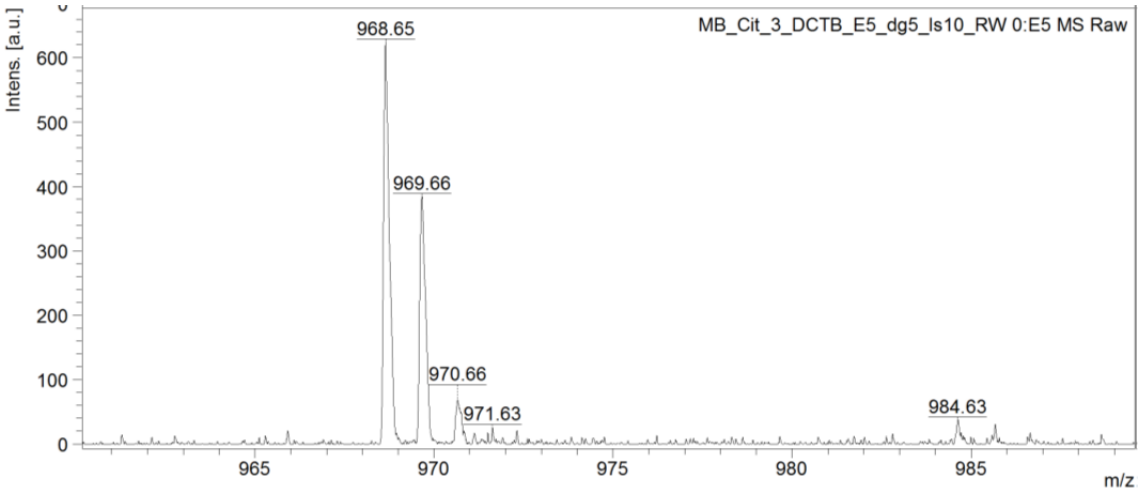
Figure S18. Experimental data (symbols) and fits (solid lines) of the VT-CD experiments of Cit-3 (a), Cit-9 (b) and C8-9 (c). The thermodynamic data obtained is repoted in the main text.

MALDI-TOF mass spectra of the BTA derivatives

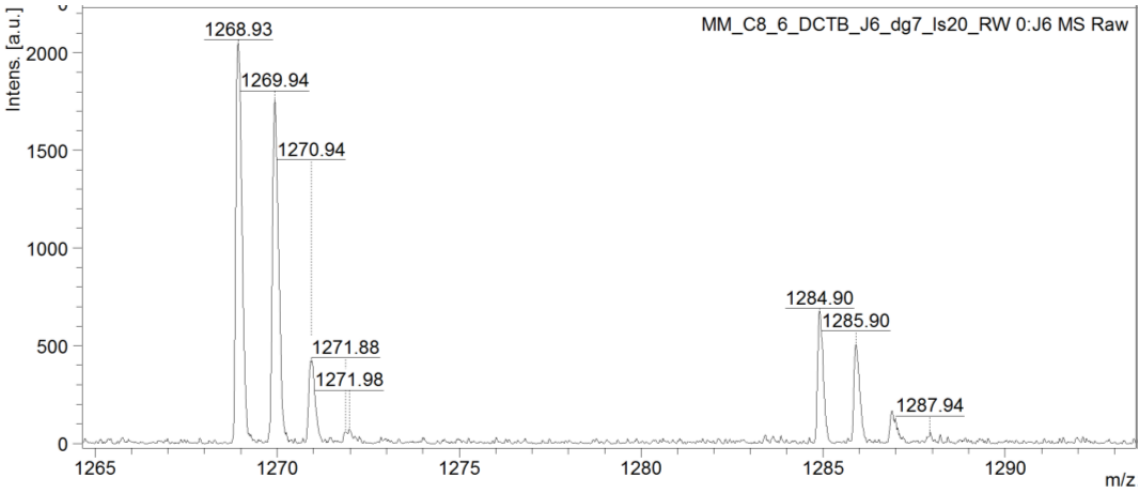
C8-3



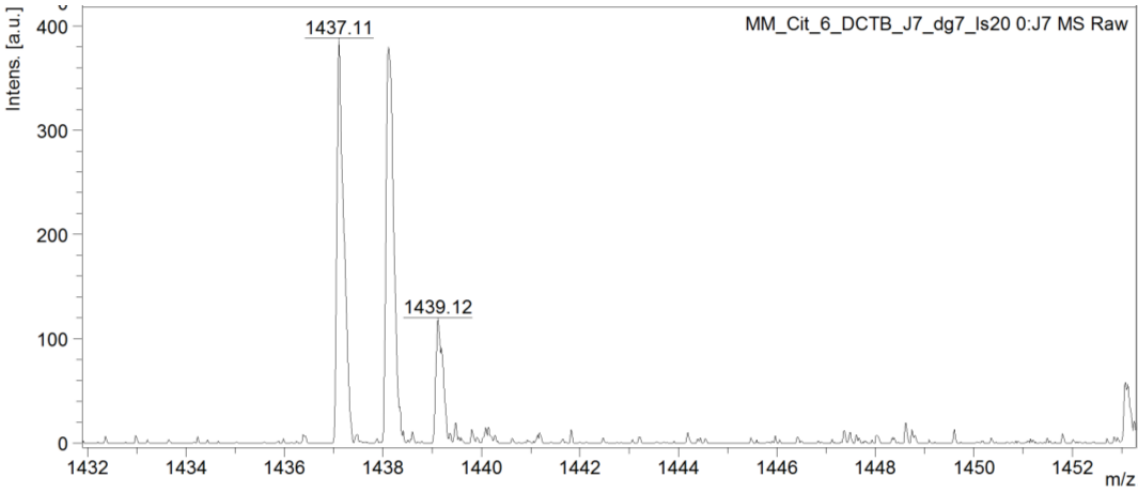
Cit-3



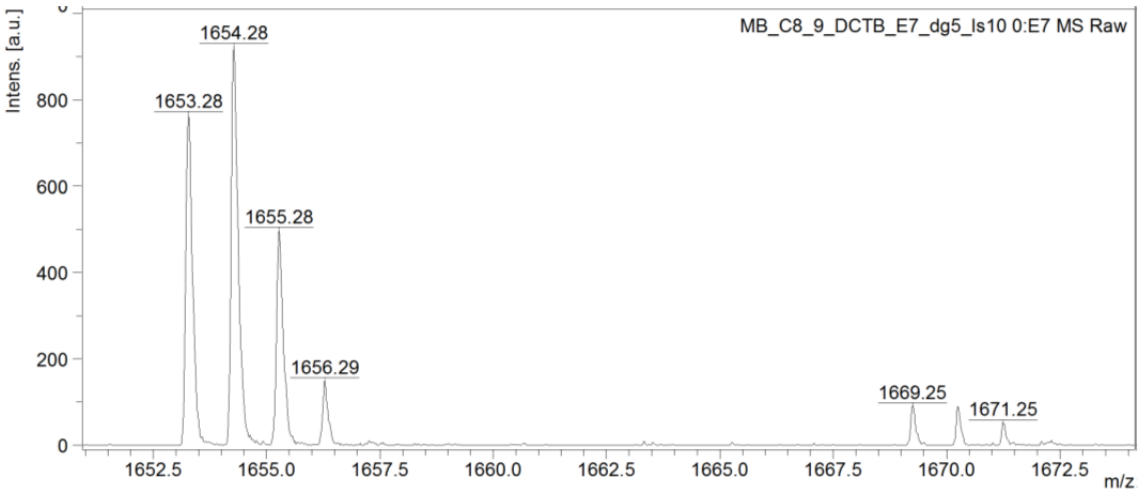
C8-6



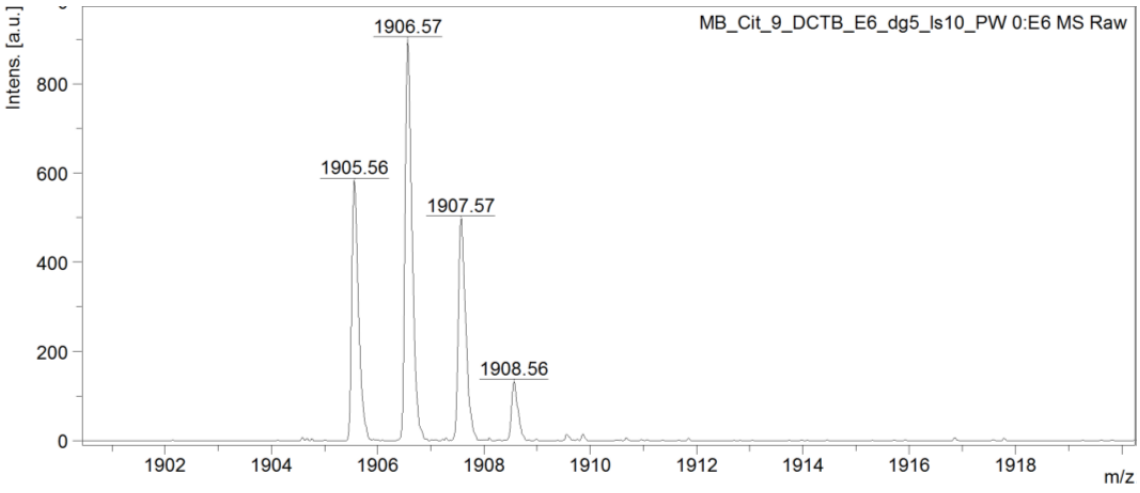
Cit-6



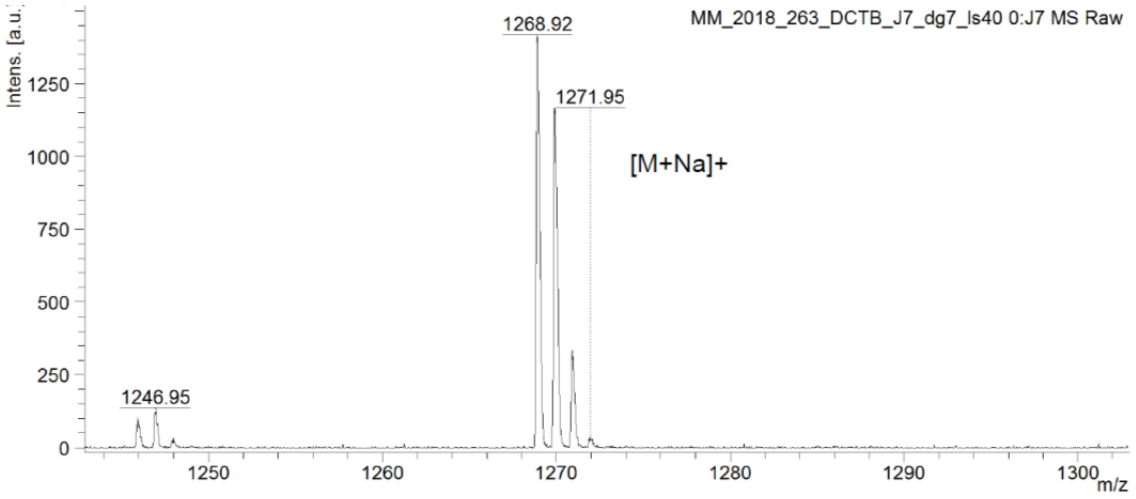
C8-9



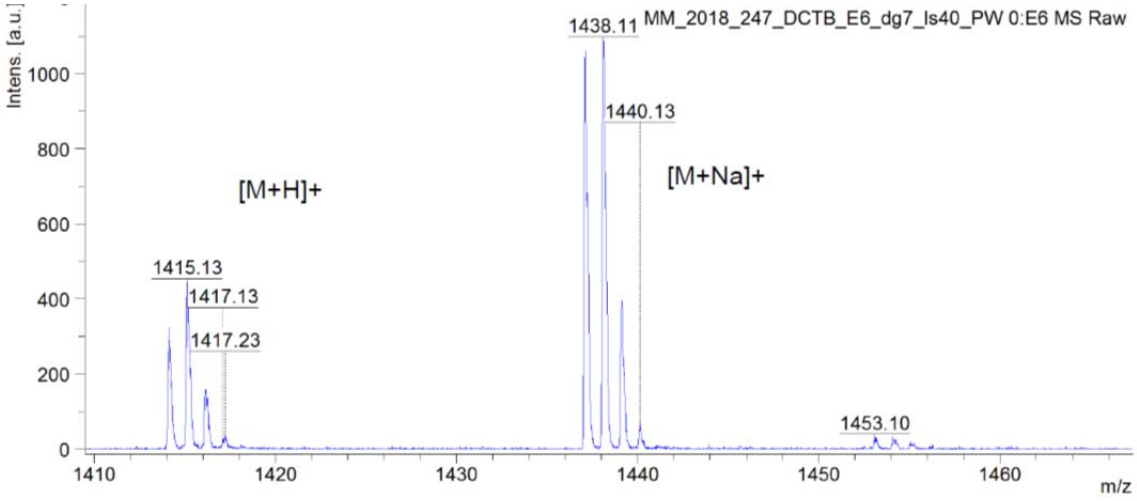
Cit-9



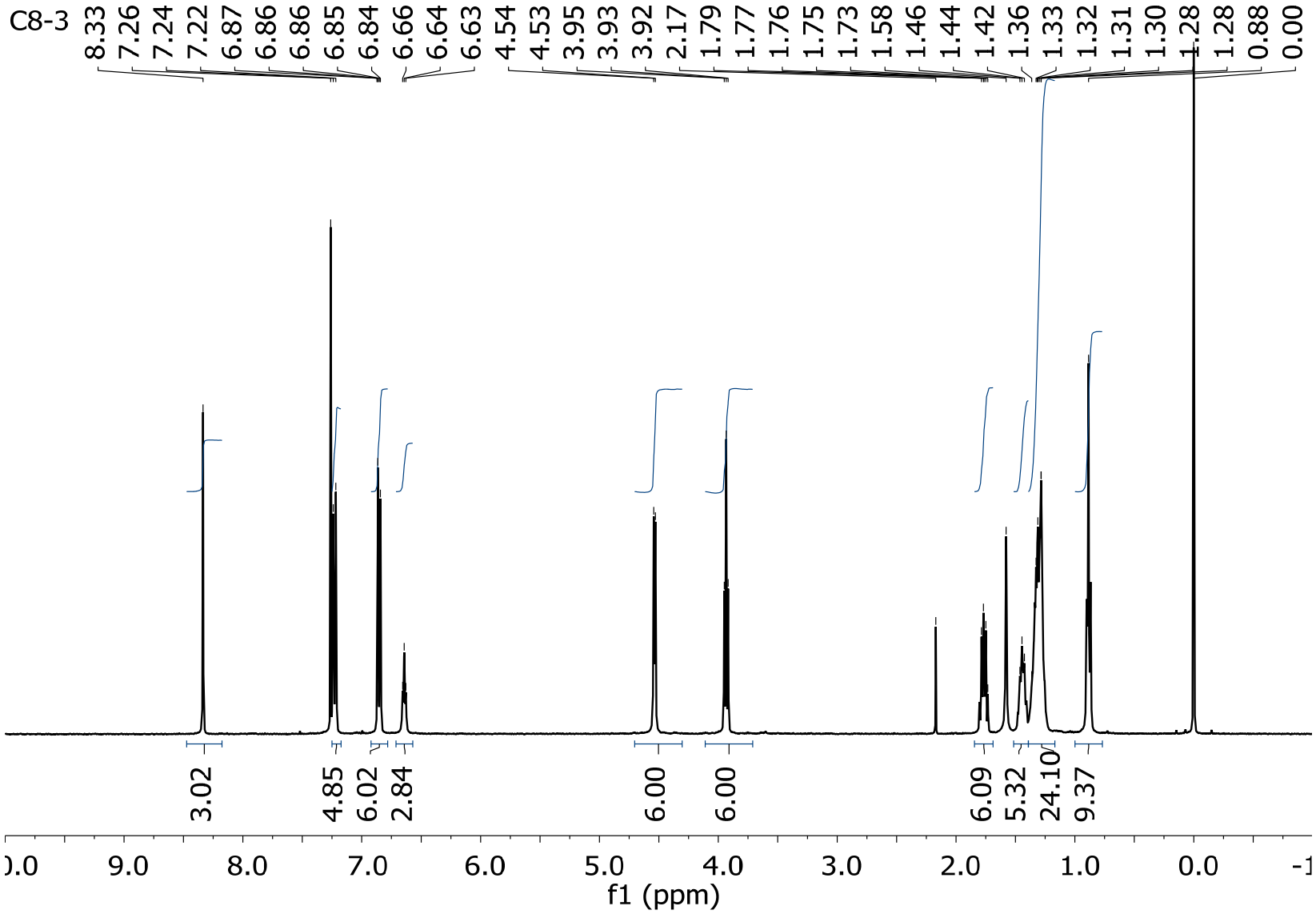
Sym-C8-6

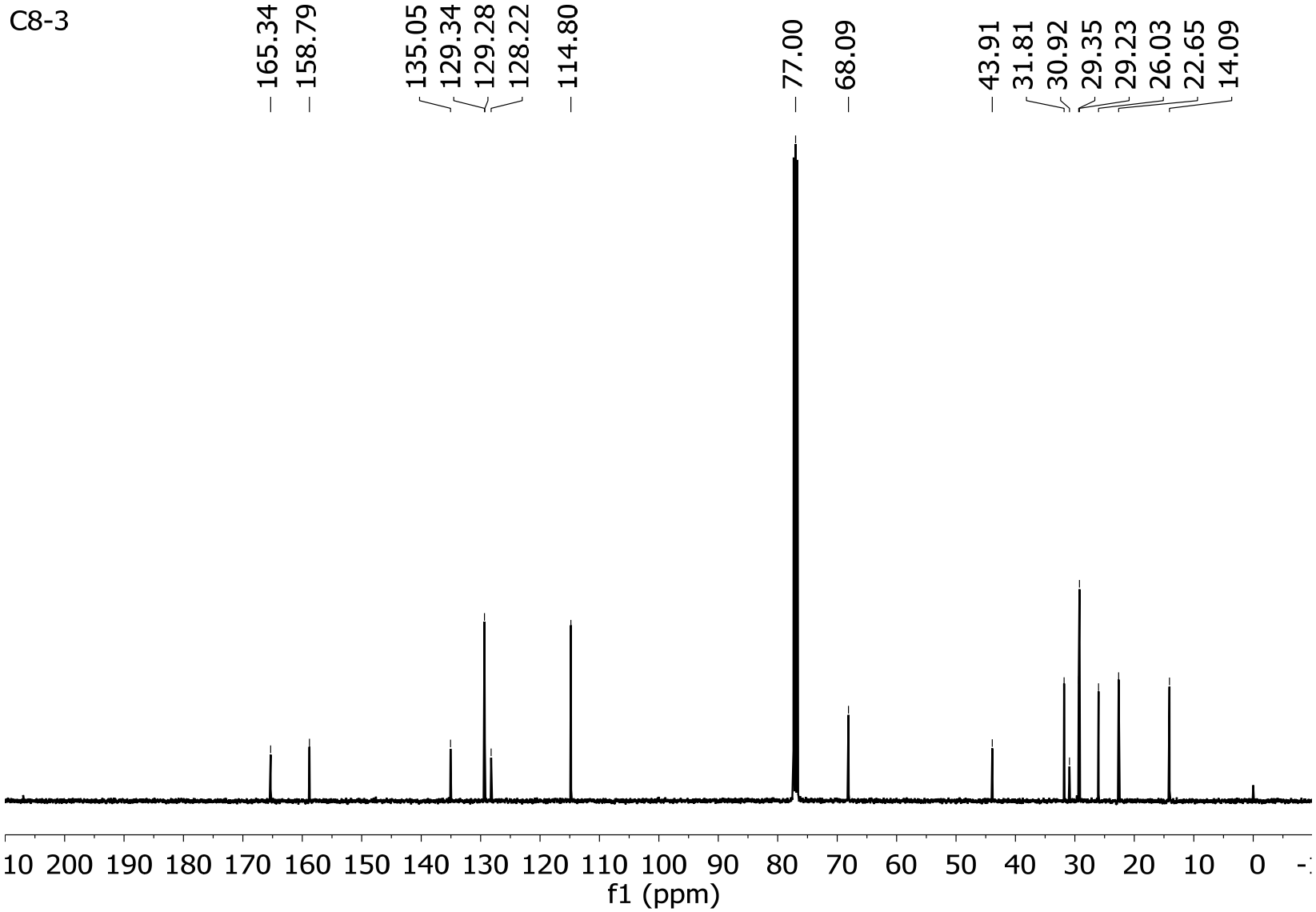


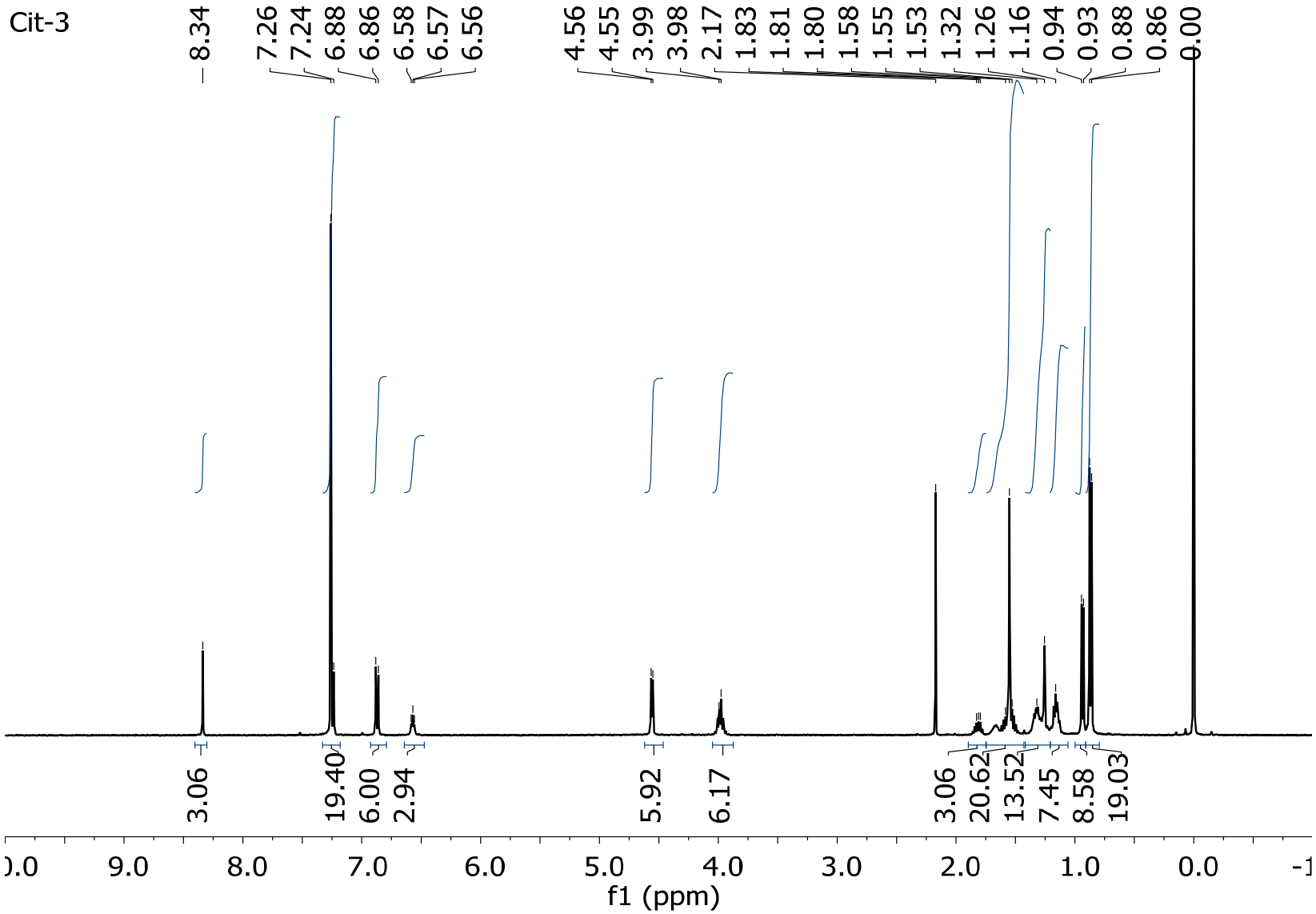
Sym-Cit-6

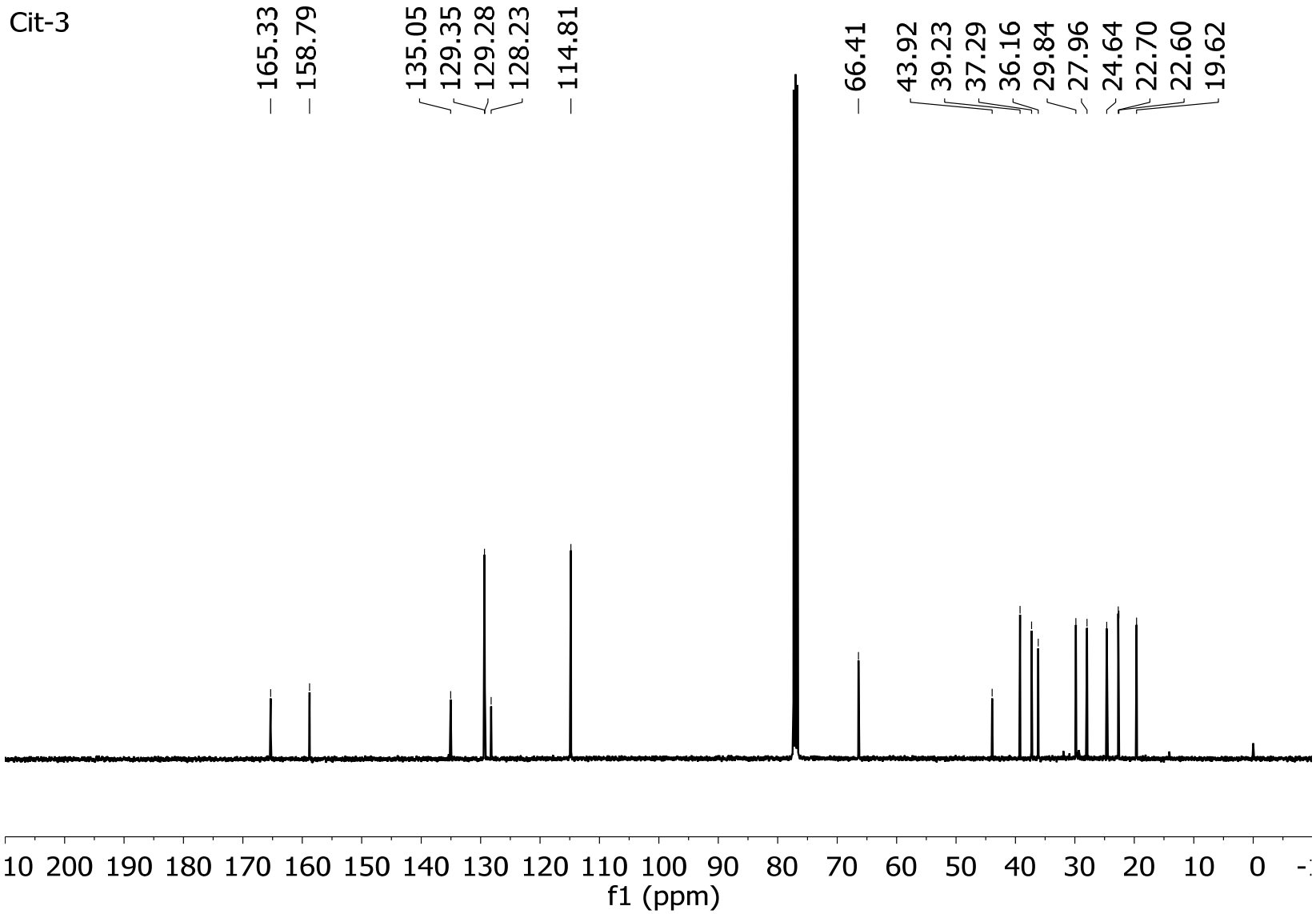


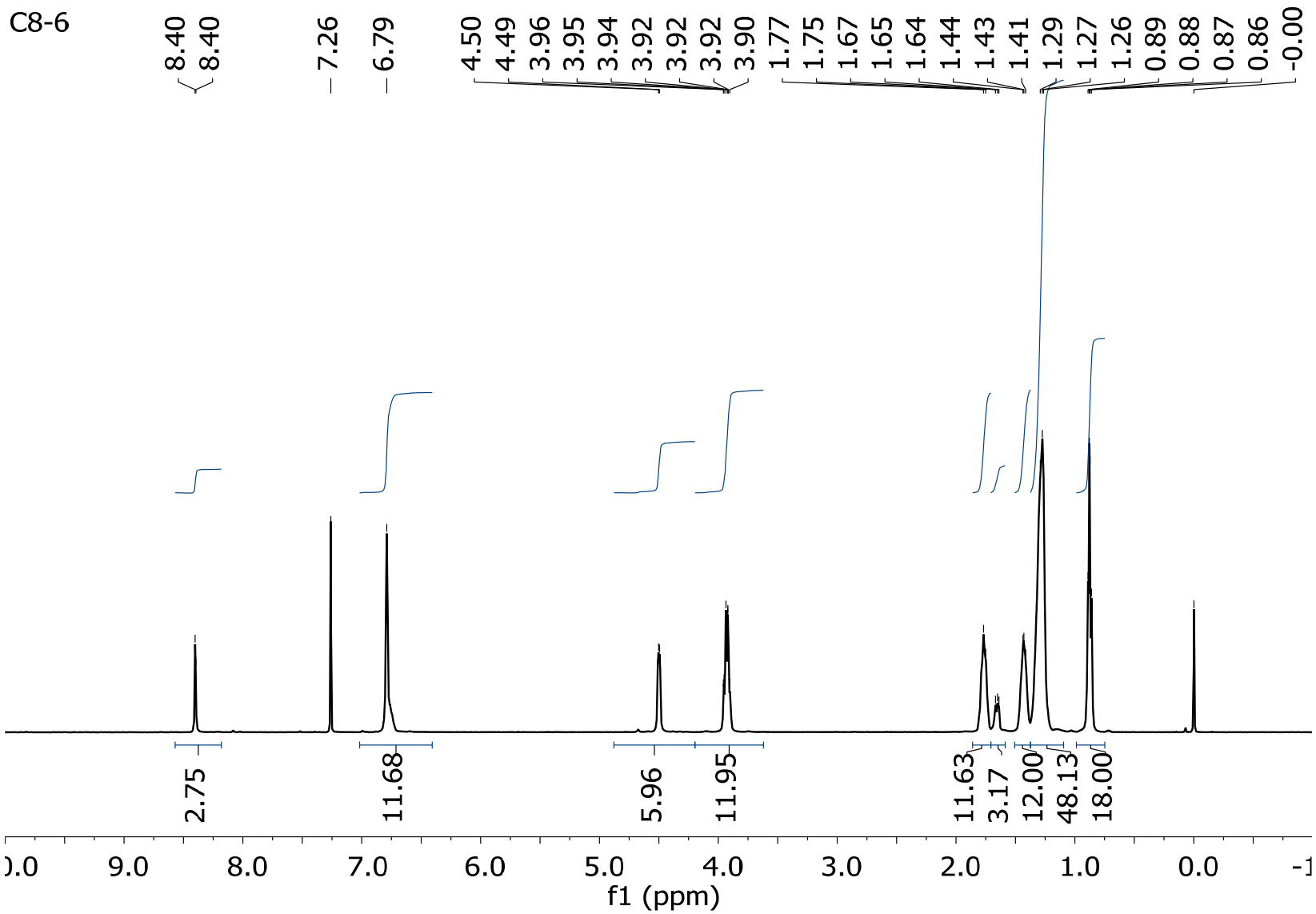
NMR spectra of the BTA derivatives

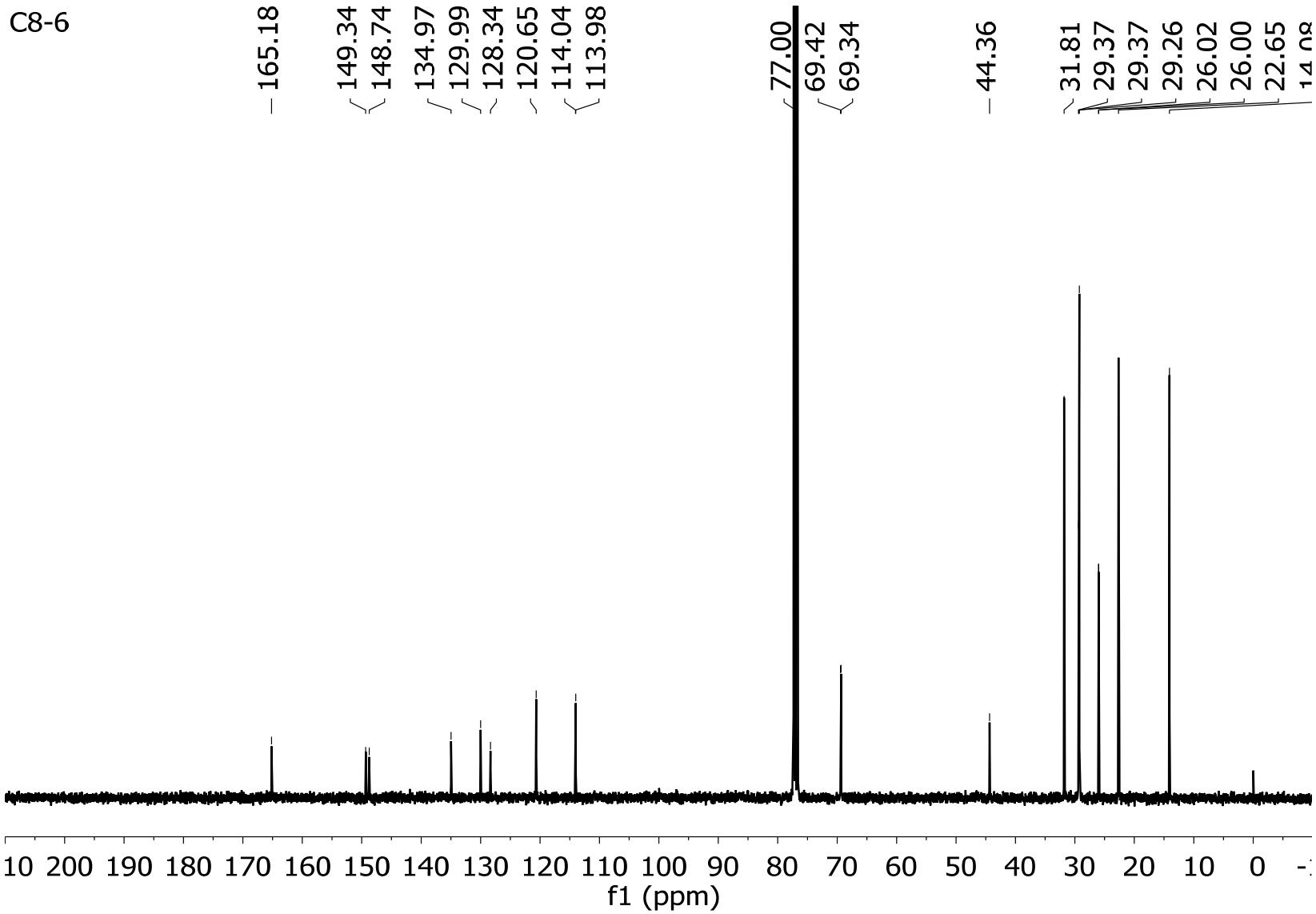


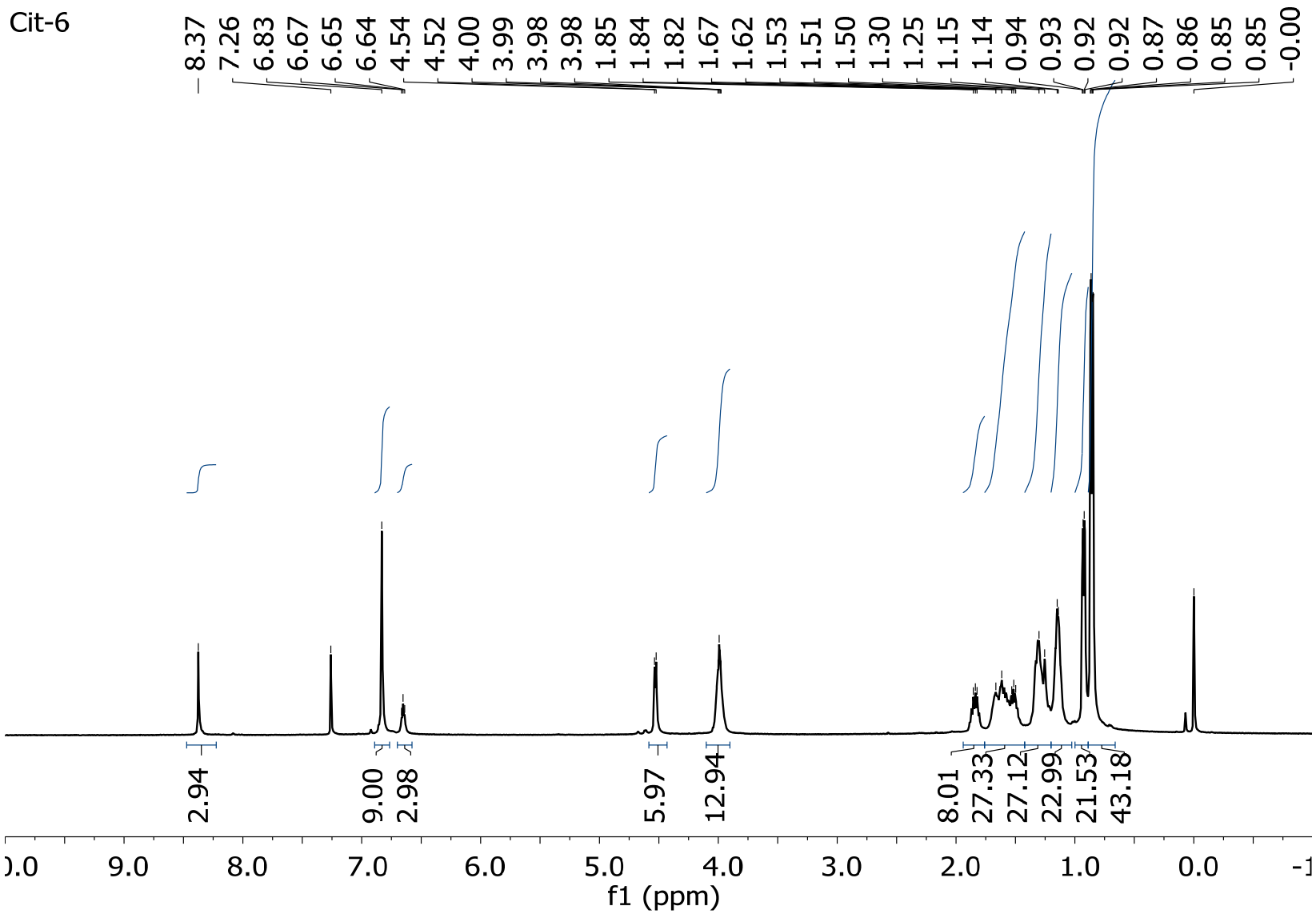

C8-3
165.34
158.79
135.05
129.34
129.28
128.22
114.80
77.00
68.09
43.91
31.81
30.92
29.35
29.23
26.03
22.65
14.09
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Cit-3
8.34
7.26
7.24
6.88
6.86
6.58
6.57
6.56
4.56
4.55
3.99
3.98
2.17
1.83
1.81
1.80
1.58
1.55
1.53
1.32
1.26
1.16
0.94
0.93
0.88
0.86
0.00
3.06
19.40
6.00
2.94
5.92
6.17
3.06
20.62
13.52
7.45
8.58
19.03
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


Cit-3
165.33
158.79
135.05
129.35
129.28
128.23
114.81
66.41
43.92
39.23
37.29
36.16
29.84
27.96
24.64
22.70
22.60
19.62
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


C8-6
8.40
8.40
7.26
6.79
4.50
4.49
3.96
3.95
3.94
3.92
3.92
3.92
3.90
1.77
1.75
1.67
1.65
1.64
1.44
1.43
1.41
1.29
1.27
1.26
0.89
0.88
0.87
0.86
-0.00
2.75
11.68
5.96
11.95
11.63
3.17
12.00
48.13
18.00
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


C8-6
165.18
149.34
148.74
134.97
129.99
128.34
120.65
114.04
113.98
77.00
69.42
69.34
44.36
31.81
29.37
29.37
29.26
26.02
26.00
22.65
f1 (ppm)


Cit-6
8.37
7.26
6.83
6.67
6.65
6.64
4.54
4.52
4.00
3.99
3.98
3.98
1.85
1.84
1.82
1.67
1.62
1.53
1.51
1.50
1.30
1.25
1.15
1.14
0.94
0.93
0.92
0.92
0.87
0.86
0.85
0.85
-0.00
2.94
9.00
2.98
5.97
12.94
8.01
27.33
27.12
22.99
21.53
43.18
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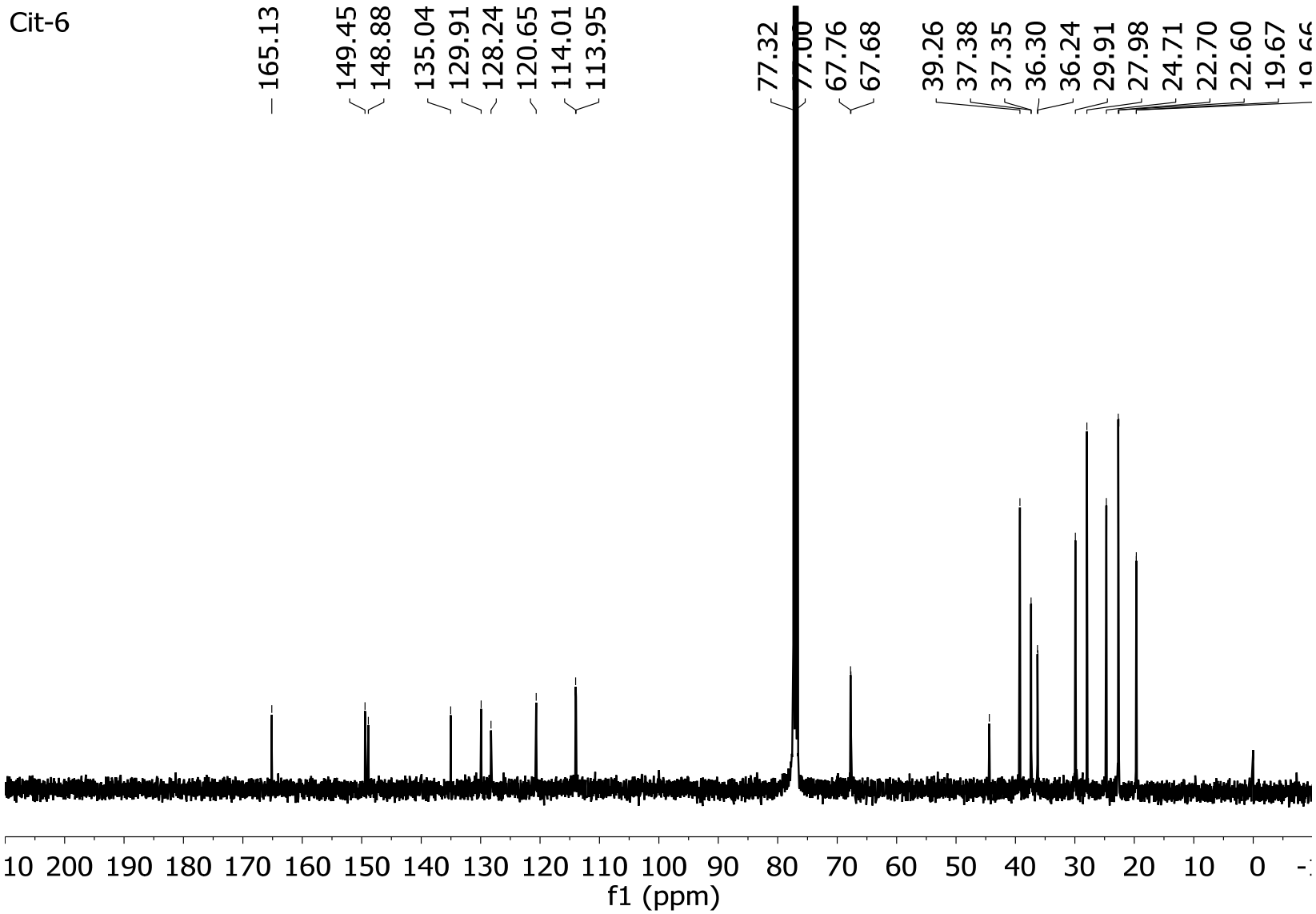
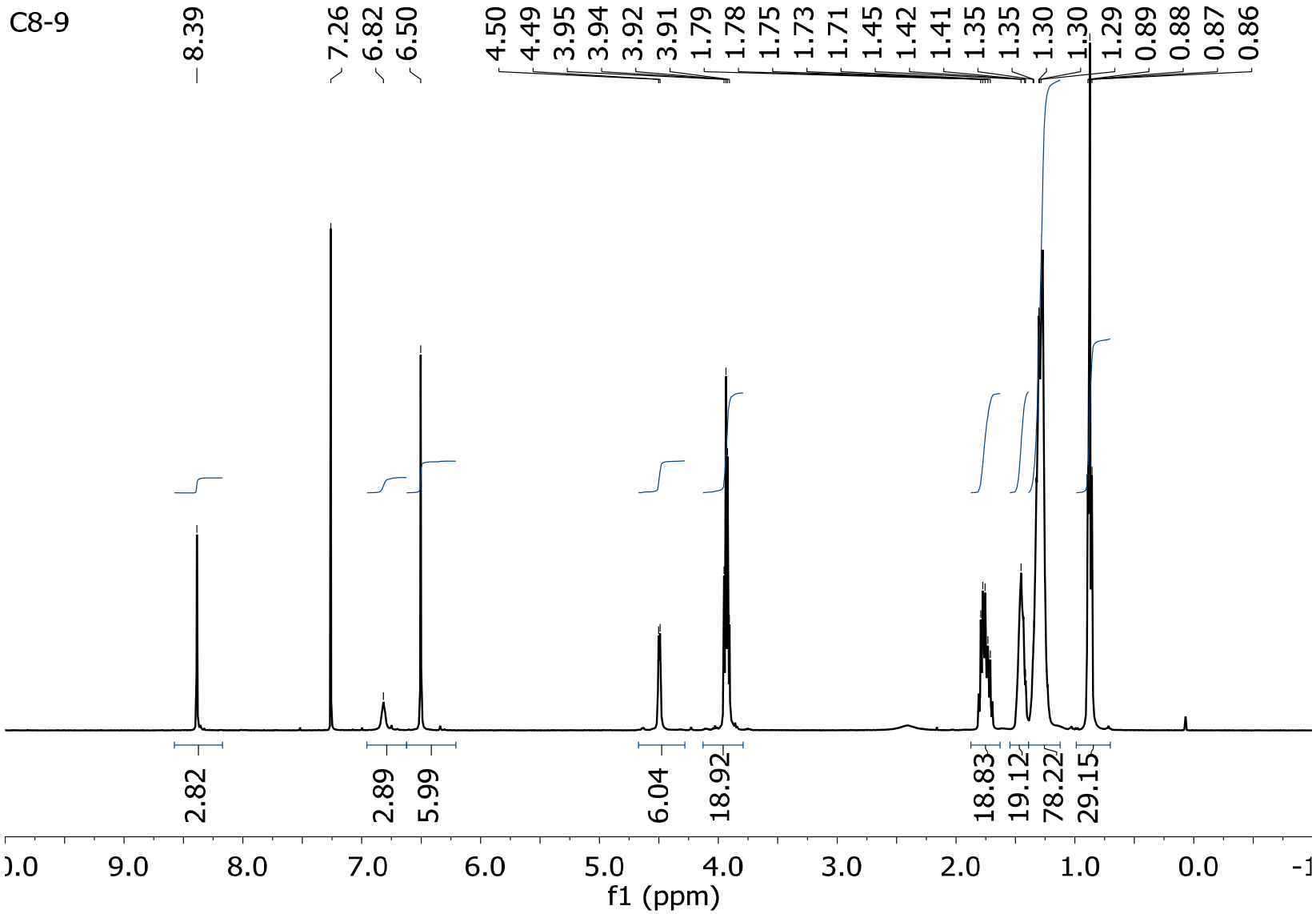
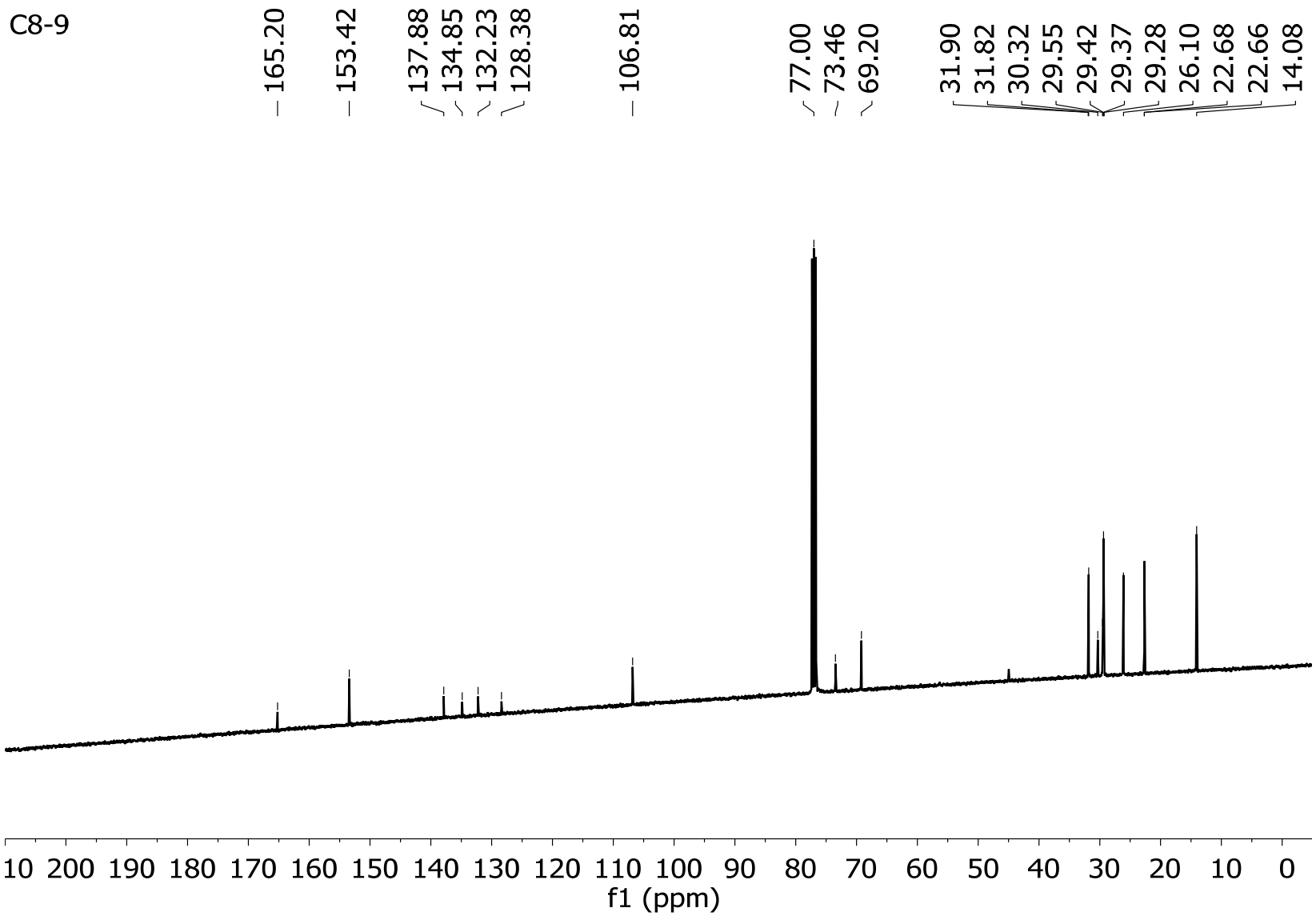
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


Cit-6
165.13
149.45
148.88
135.04
129.91
128.24
120.65
114.01
113.95
77.32
77.00
67.76
67.68
39.26
37.38
37.35
36.30
36.24
29.91
27.98
24.71
22.70
22.60
19.67
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


C8-9
8.39
7.26
6.82
6.50
4.50
4.49
3.95
3.94
3.92
3.91
1.79
1.78
1.75
1.73
1.71
1.45
1.42
1.41
1.35
1.35
1.30
1.30
1.29
0.89
0.88
0.87
0.86
2.82
2.89
5.99
6.04
18.92
18.83
19.12
78.22
29.15
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


C8-9
165.20
153.42
137.88
134.85
132.23
128.38
106.81
77.00
73.46
69.20
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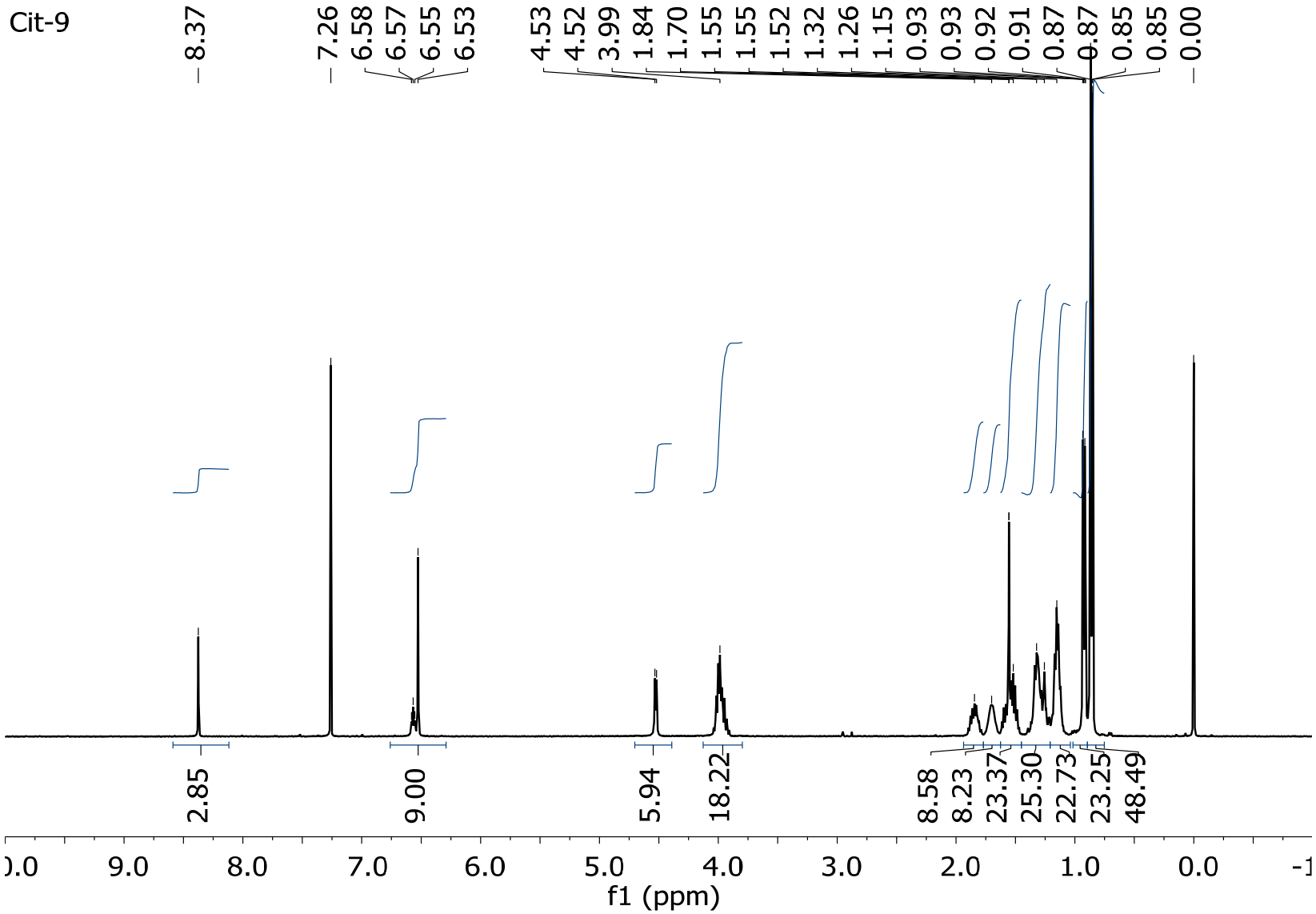
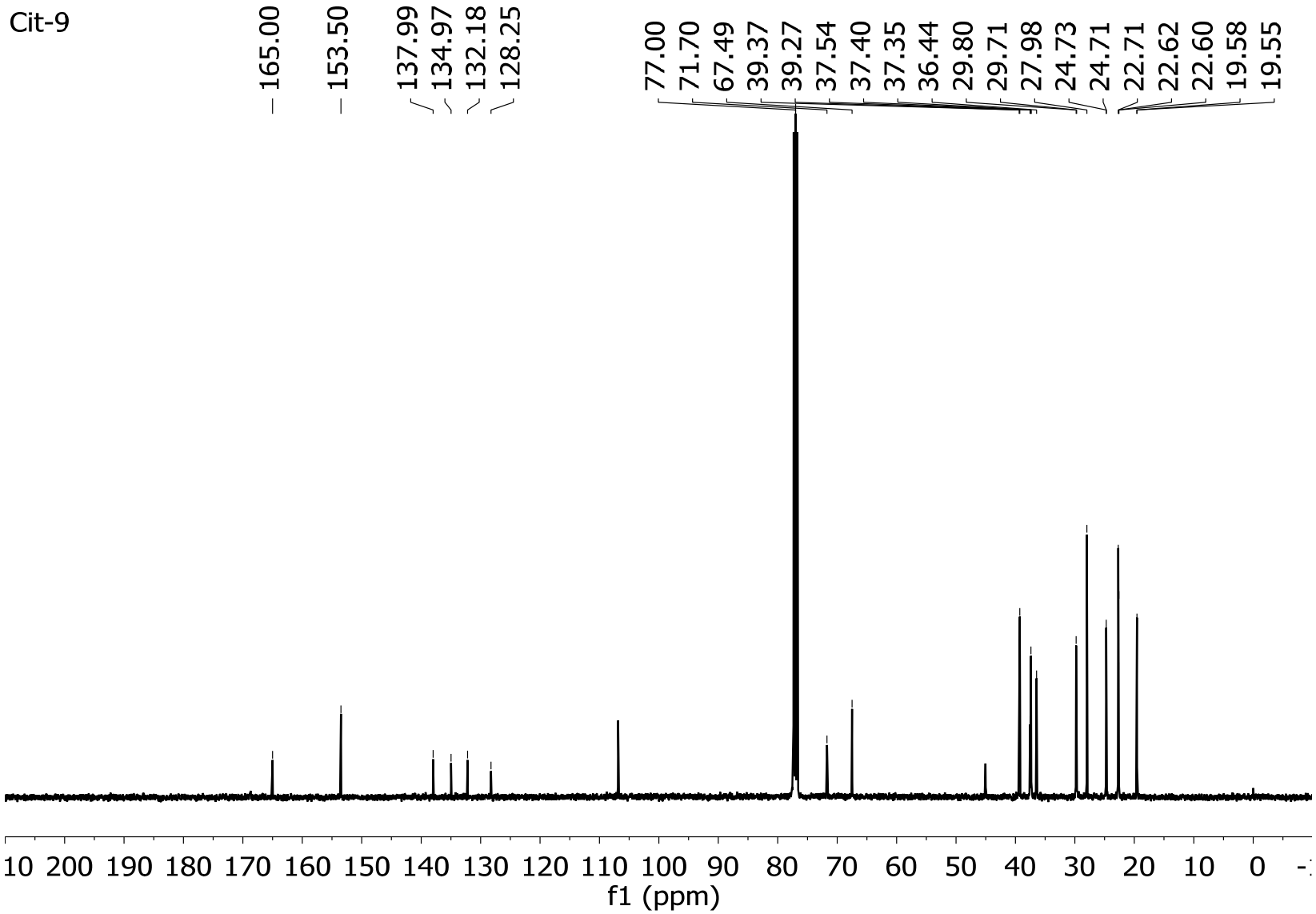
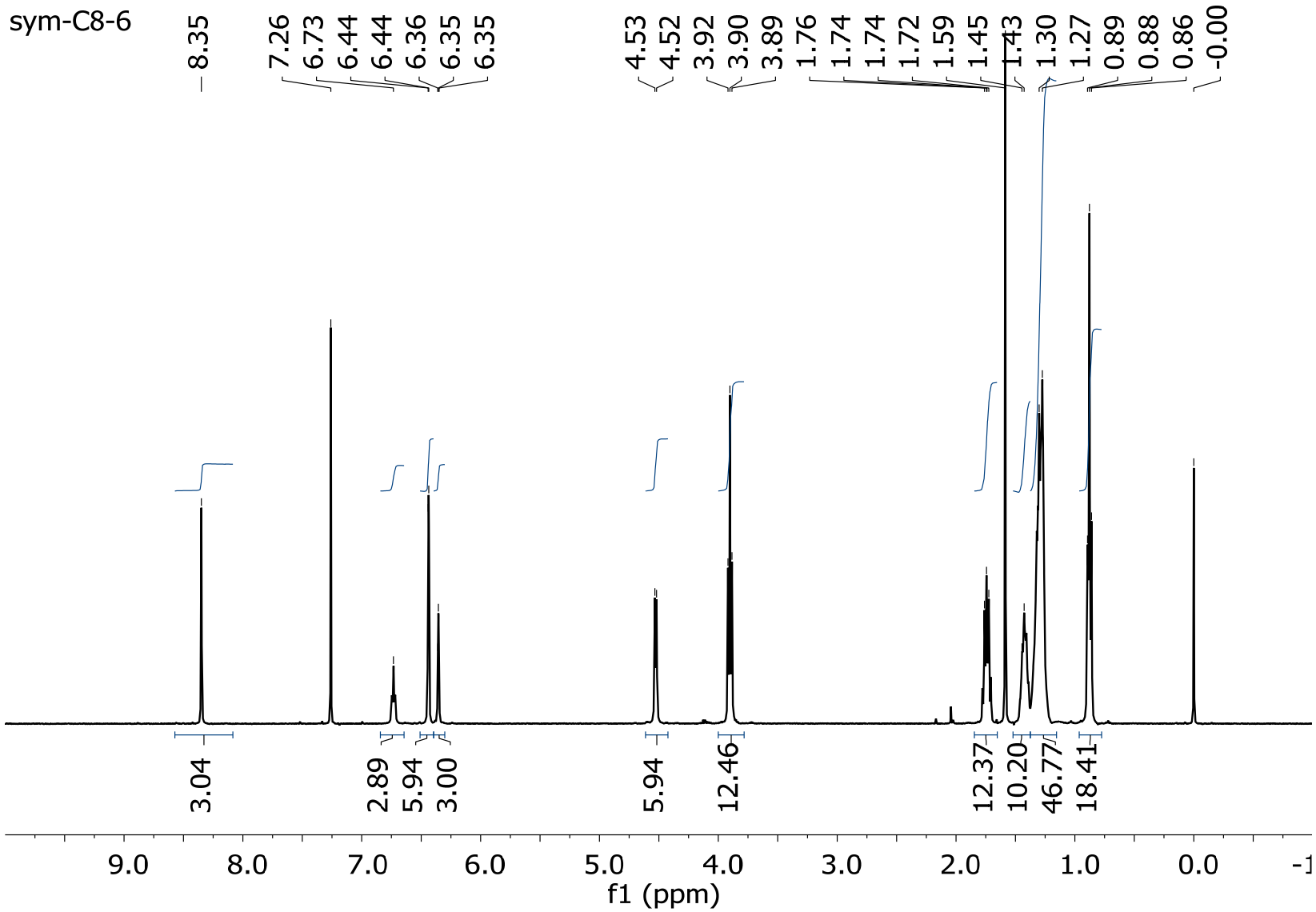
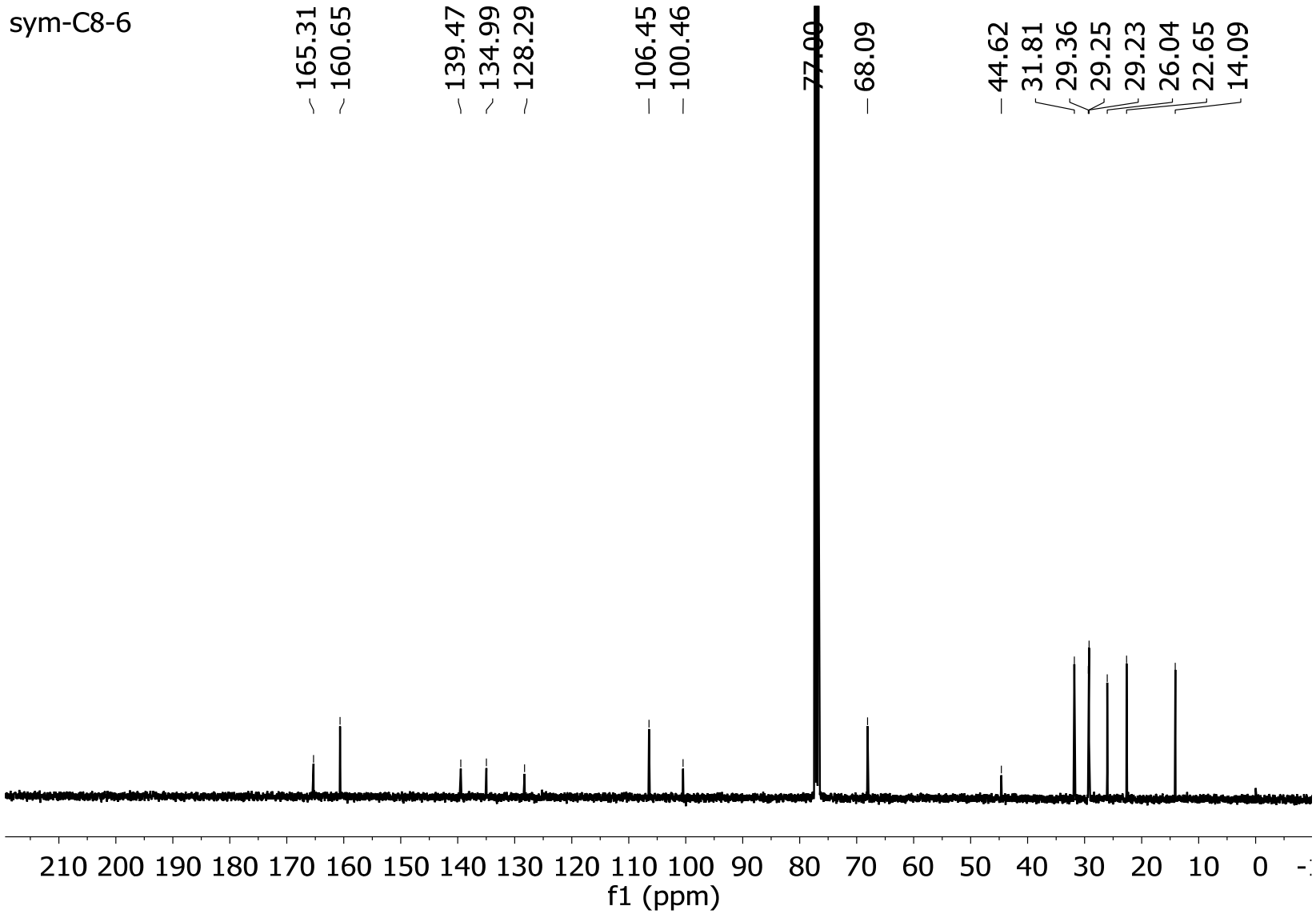
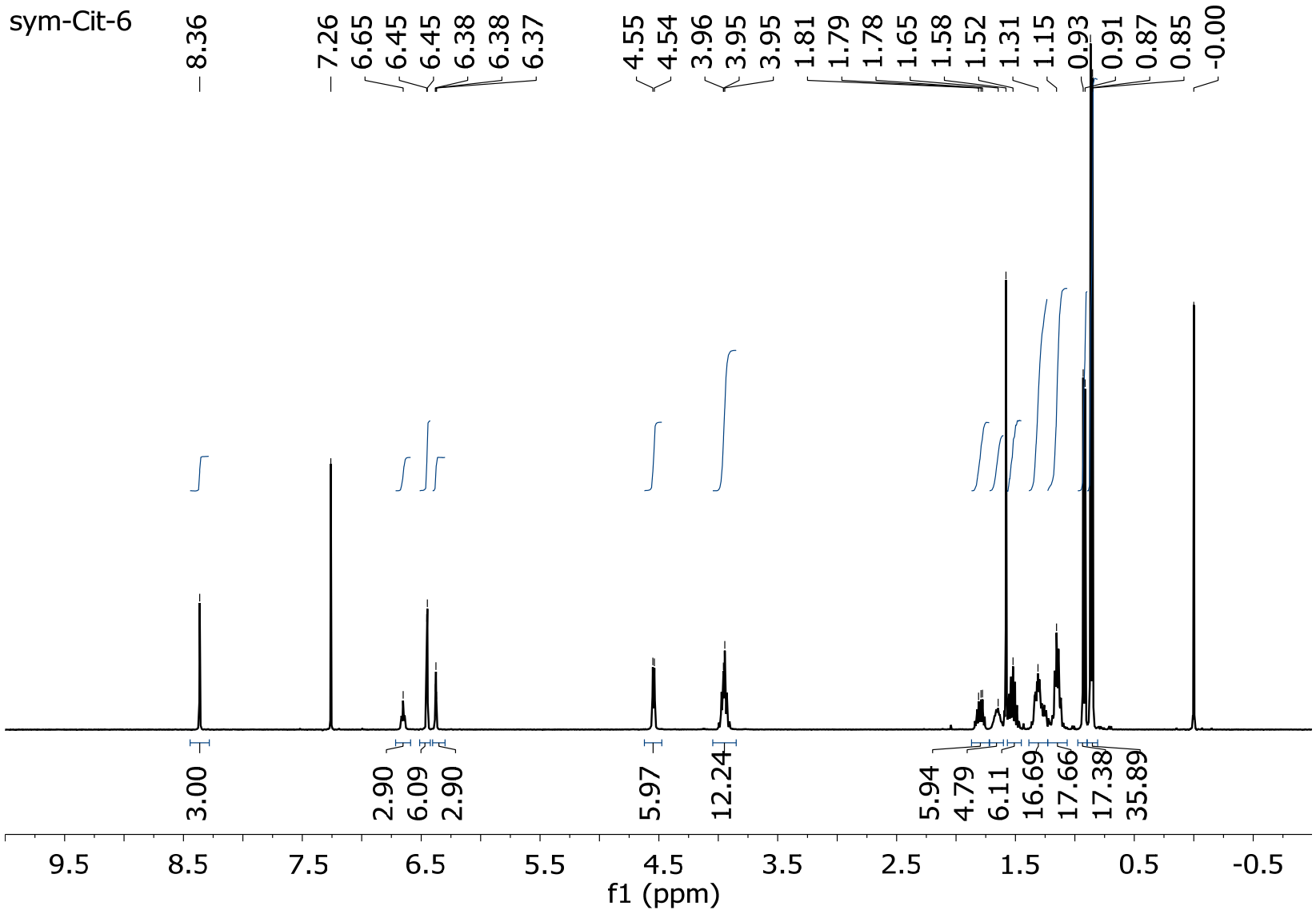
31.82
30.32
29.55
29.42
29.37
29.28
26.10
22.68
22.66
14.08
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

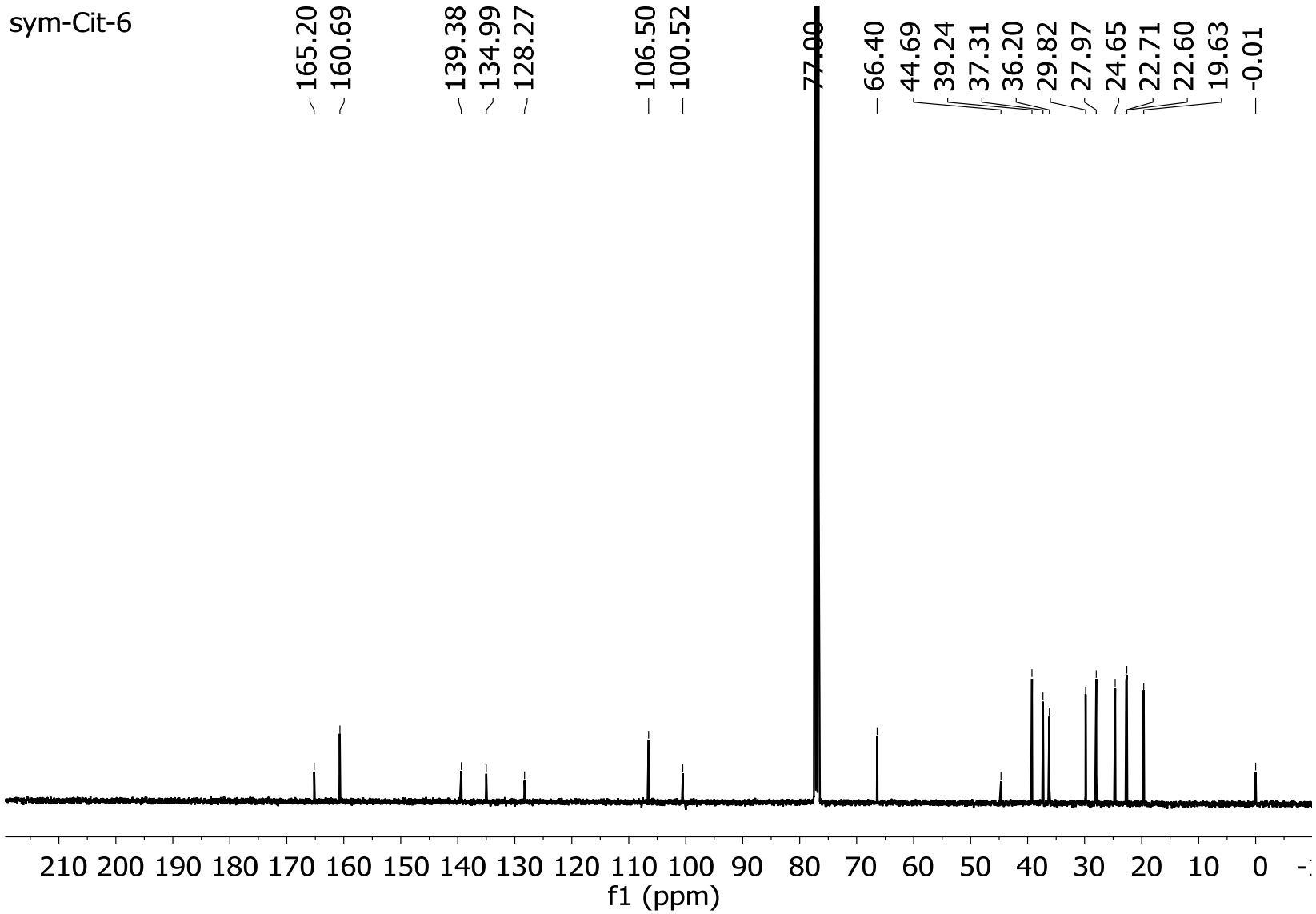

Cit-9
8.37
7.26
6.58
6.57
6.55
6.53
4.53
4.52
3.99
1.84
1.70
1.55
1.55
1.52
1.32
1.26
1.15
0.93
0.93
0.92
0.91
0.87
0.87
0.85
0.85
0.00
2.85
9.00
5.94
18.22
8.58
8.23
23.37
25.30
22.73
23.25
48.49
f1 (ppm)


Cit-9
165.00
153.50
137.99
134.97
132.18
128.25
77.00
71.70
67.49
39.37
39.27
37.54
37.40
37.35
36.44
29.80
29.71
27.98
24.73
24.71
22.71
22.62
22.60
19.58
19.55
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


sym-C8-6
8.35
7.26
6.73
6.44
6.44
6.36
6.35
6.35
4.53
4.52
3.92
3.90
3.89
1.76
1.74
1.74
1.72
1.59
1.45
1.43
1.30
1.27
0.89
0.88
0.86
-0.00
3.04
2.89
5.94
3.00
5.94
12.46
12.37
10.20
46.77
18.41
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

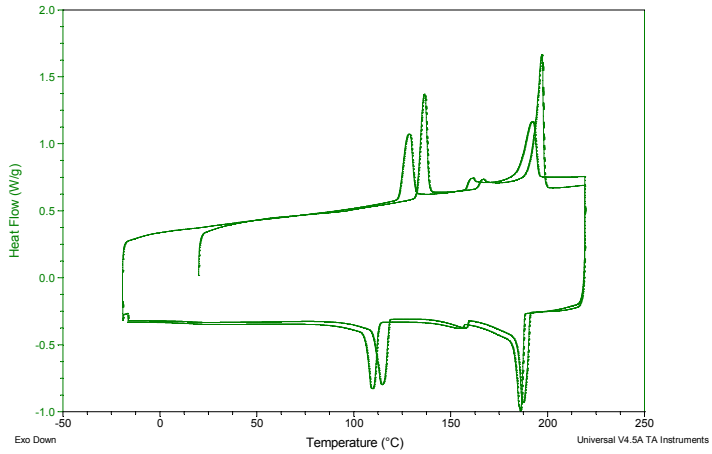

sym-C8-6
165.31
160.65
139.47
134.99
128.29
106.45
100.46
77.00
68.09
44.62
31.81
29.36
29.25
29.23
26.04
22.65
14.09
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


sym-Cit-6
8.36
7.26
6.65
6.45
6.45
6.38
6.38
6.37
4.55
4.54
3.96
3.95
3.95
1.81
1.79
1.78
1.65
1.58
1.52
1.31
1.15
0.93
0.91
0.87
0.85
-0.00
3.00
2.90
6.09
2.90
5.97
12.24
5.94
4.79
6.11
16.69
17.66
17.38
35.89
9.5
8.5
7.5
6.5
5.5
4.5
3.5
2.5
1.5
0.5
-0.5
f1 (ppm)

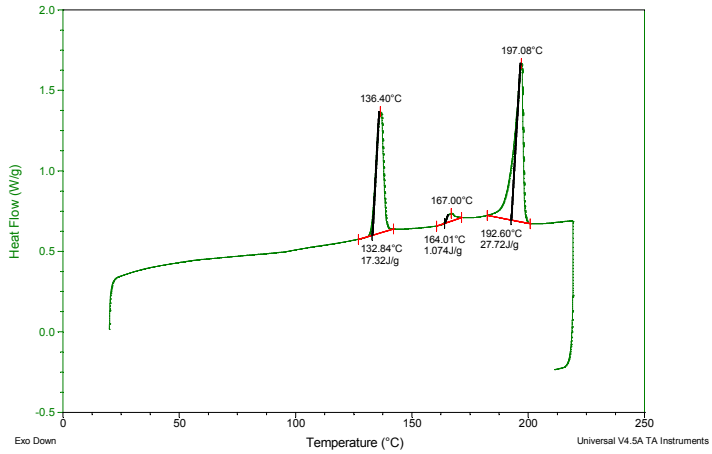

sym-Cit-6
165.20
160.69
139.38
134.99
128.27
106.50
100.52
77.00
66.40
44.69
39.24
37.31
36.20
29.82
27.97
24.65
22.71
22.60
19.63
-0.01
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

DSC thermograms of the BTA derivatives

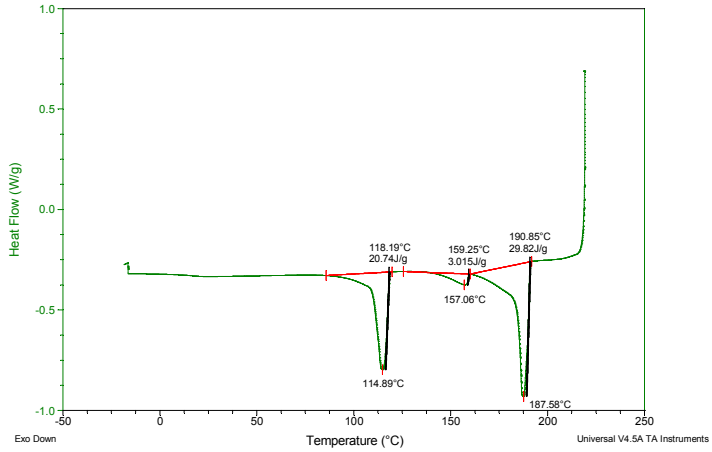
C8-3



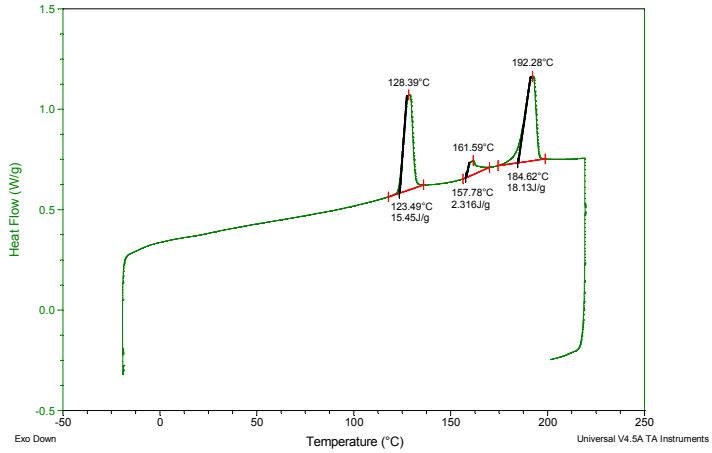
C8-3 1st heating scan



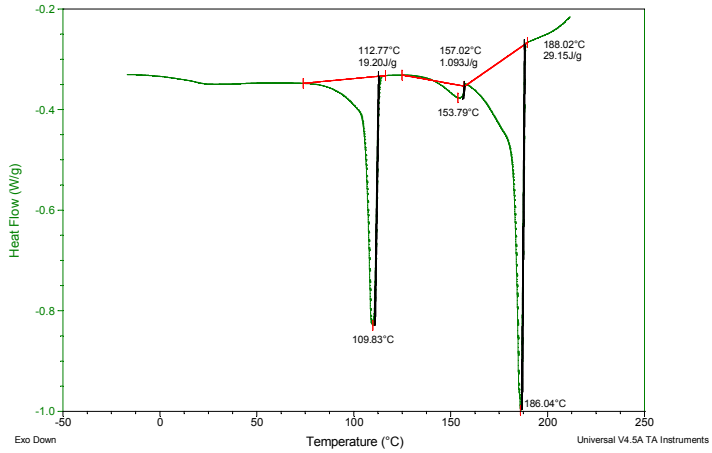
C8-3 1st cooling scan



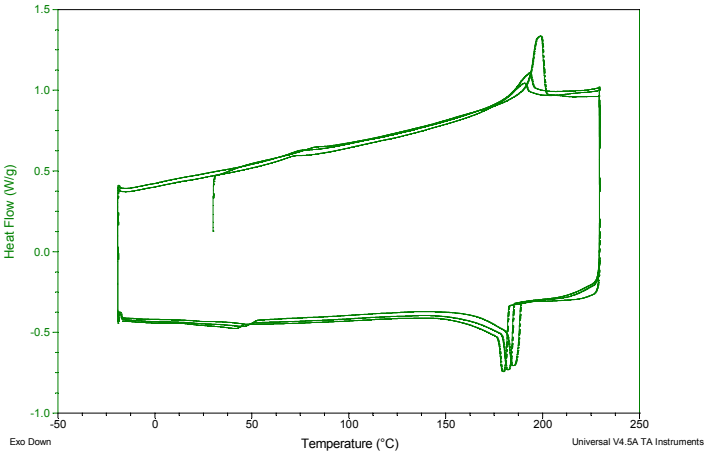
C8-3 2nd heating scan



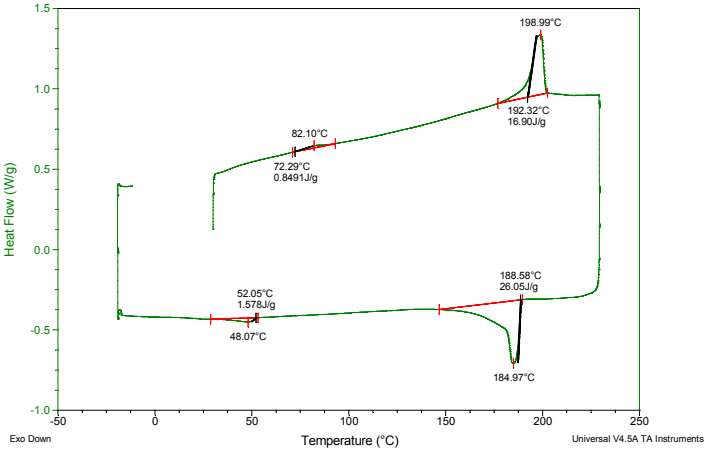
C8-3 2nd cooling scan



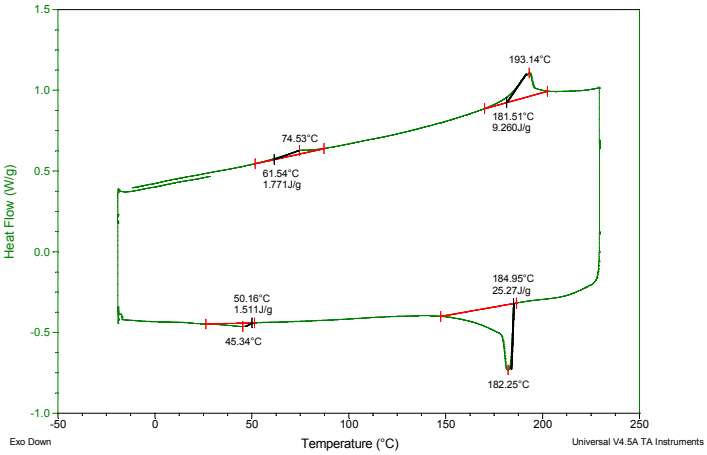
Cit-3



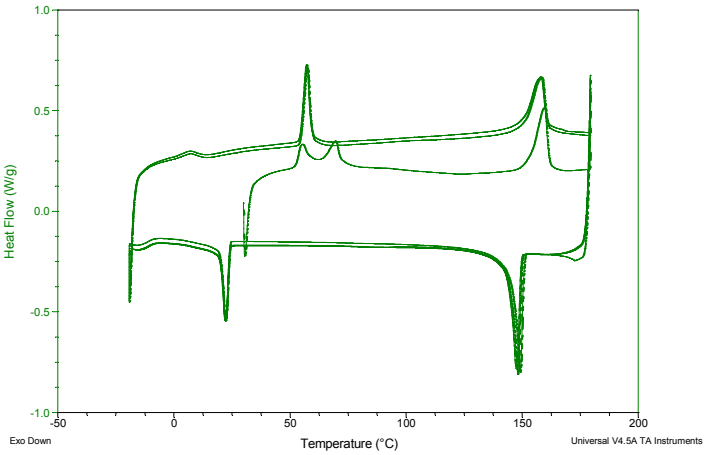
Cit-3 1st heating scan + 1st cooling scan



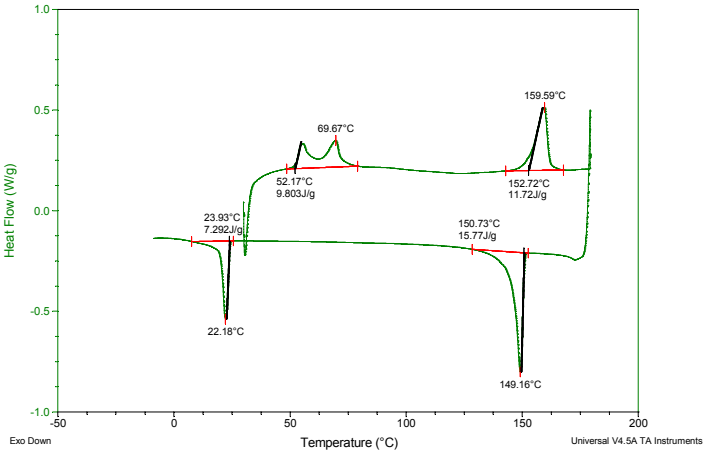
Cit-3 2nd heating scan + 2nd cooling scan



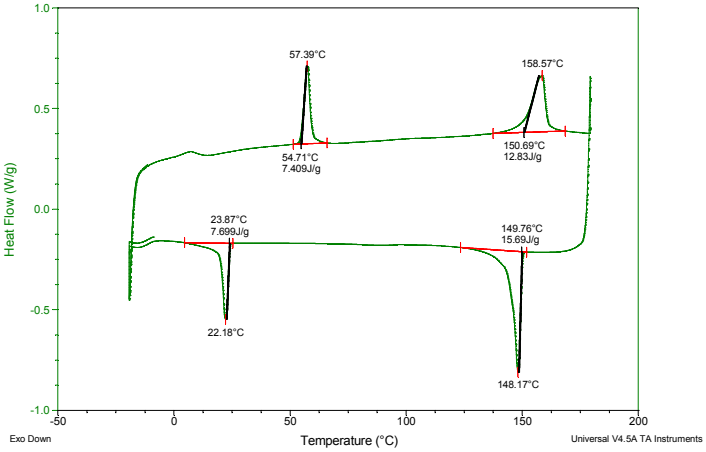
C8-6



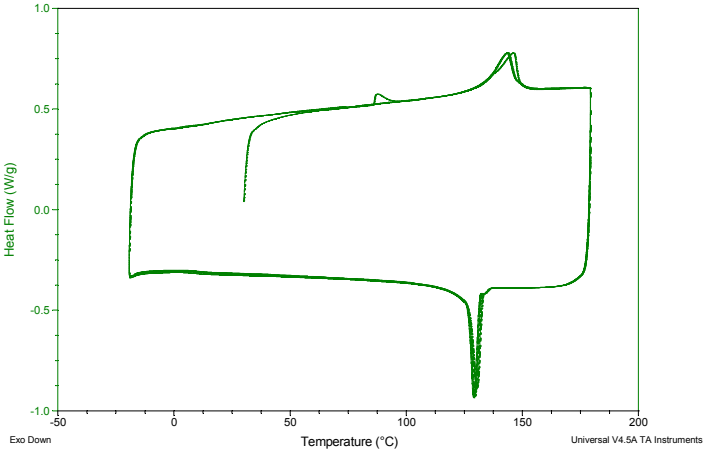
C8-6 1st heating and 1st cooling scan



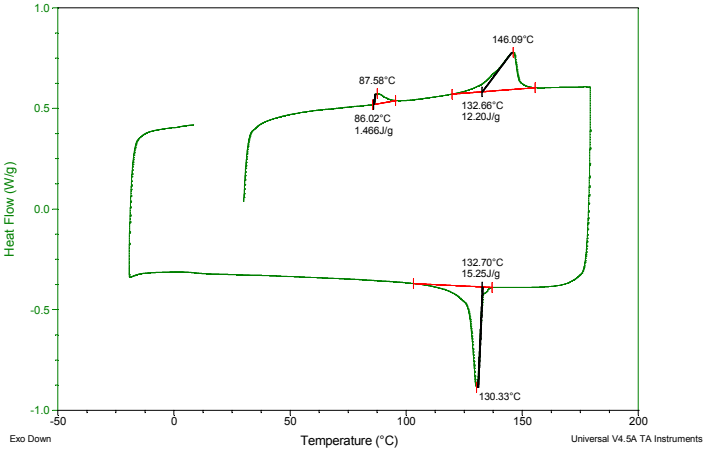
C8-6 2nd heating and 2nd cooling scan



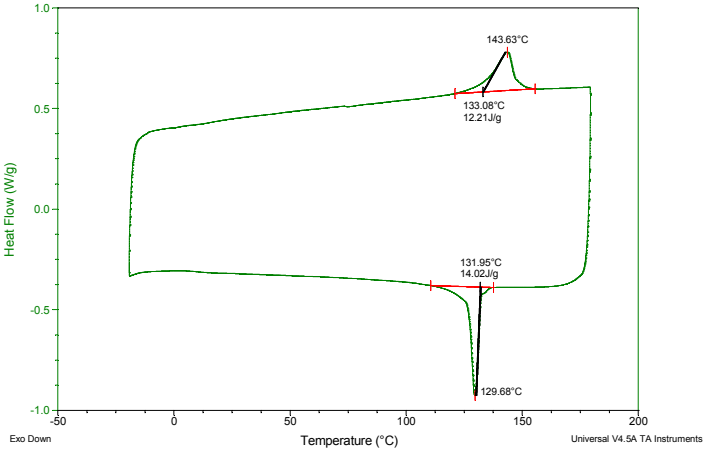
Cit-6



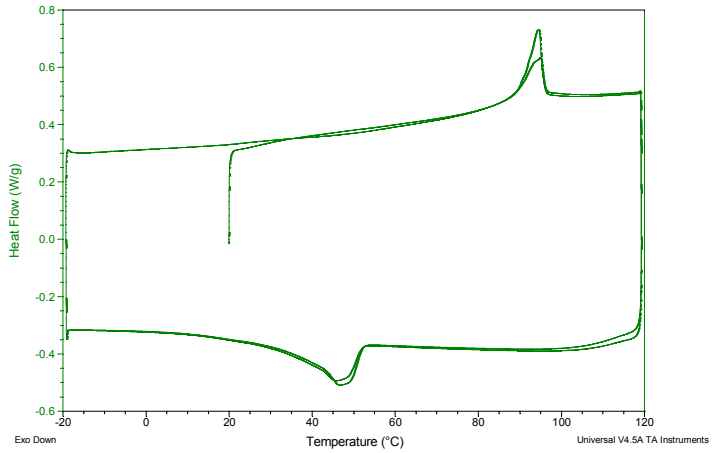
Cit-6 1st heating and 1st cooling scan



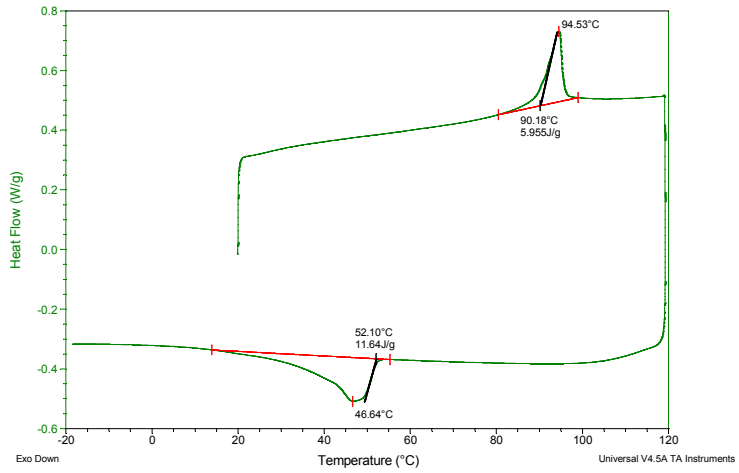
Cit-6 2nd heating and 2nd cooling scan



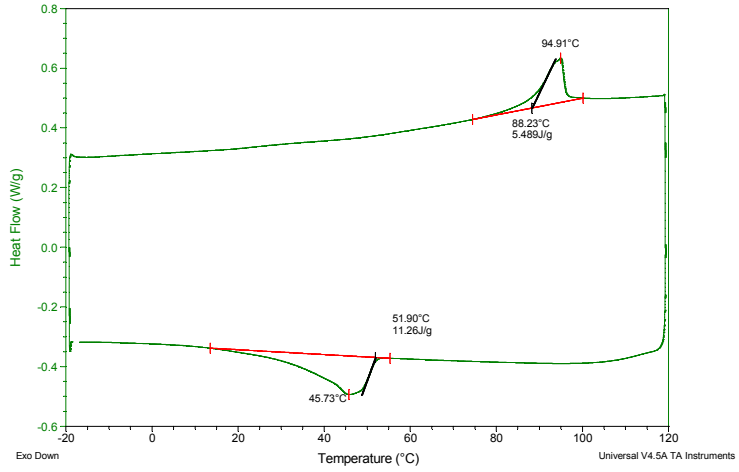
C8-9



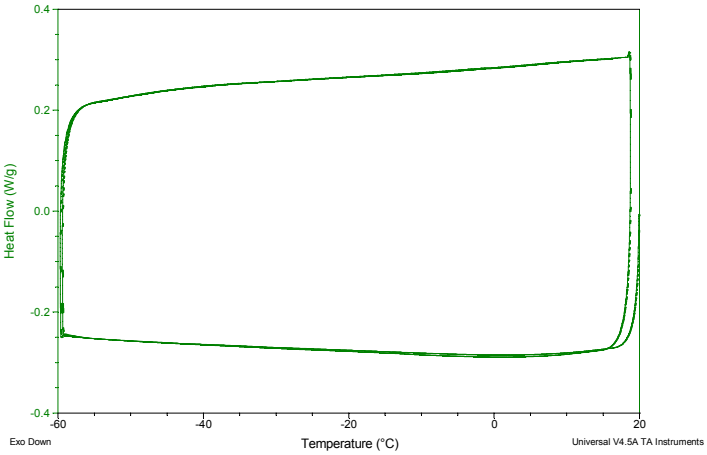
C8-9 1st heating scan and 1st cooling scan



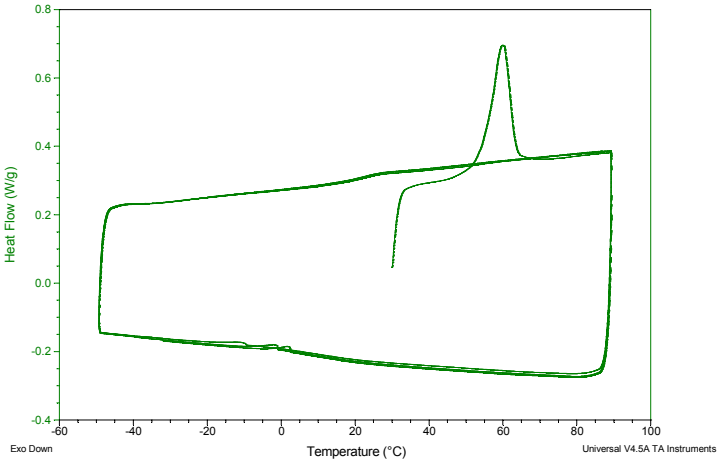
C8-9 2nd heating scan and 2nd cooling scan



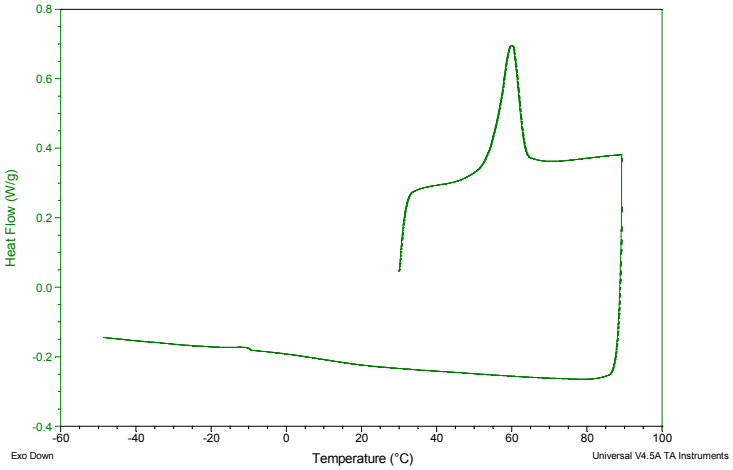
Cit-9


0.4
0.2
0.0
-0.2
-0.4
Heat Flow (W/g)
-60
-40
-20
0
20
Temperature (°C)
Exo Down
Universal V4.5A TA Instruments

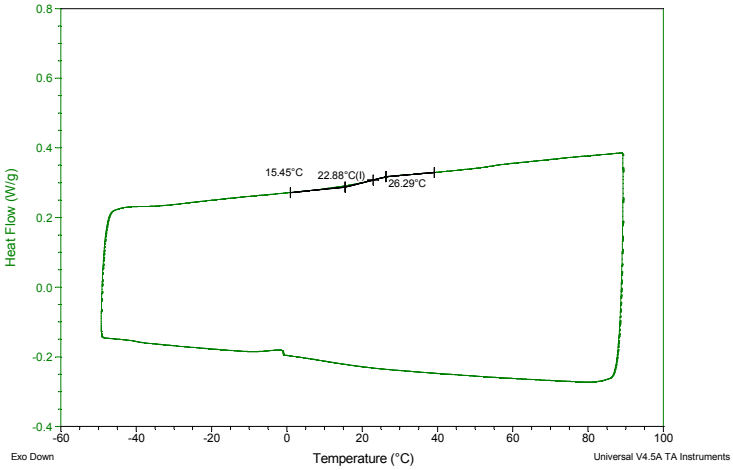
Sym-C8-6



Sym-C8-6 1st heating and 1st cooling scan



Sym-C8-6 2nd heating and 2nd cooling scan



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