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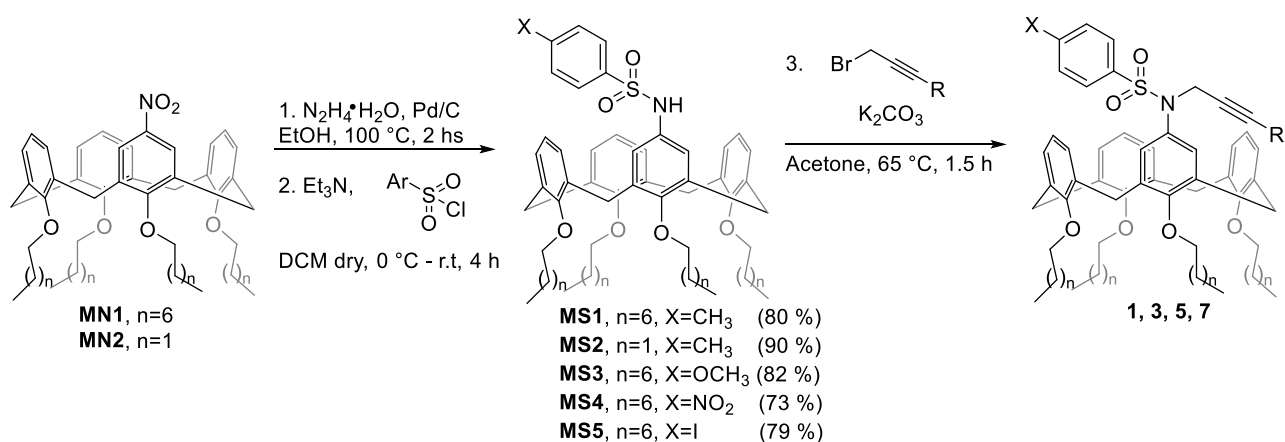
- **General remarks and materials**

All chemicals those syntheses are not reported hereafter were purchased from commercial sources and used as received. Solvents were dried and stored over molecular sieves previously activated in an oven (450 °C overnight). Anhydrous CH₂Cl₂ for catalytic reactions was supplied by Fluka in Sureseal® bottles and used without any further purification. Melting points were measured with an Electrothermal apparatus and are uncorrected. Column chromatography was performed on silica gel 60 (70-230 mesh). NMR spectra were recorded on a Bruker 400 MHz and JEOL 600 MHz using solvents as internal standards (7.26 ppm for ¹H NMR and 77.00 ppm for ¹³C NMR for CDCl₃). The terms m, s, d, t, q and quint represent multiplet, singlet, doublet, triplet, quadruplet and quintuplet, respectively, and the term br means a broad signal. ¹³C DEPTQ NMR spectra are reported for substrates and corresponding products. Exact masses were recorded on an LTQ ORBITRAP XL Thermo Mass Spectrometer (ESI source).

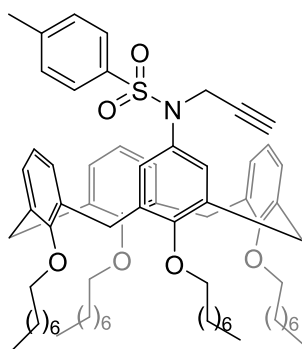
Materials: **MN1** and **MN2** derivatives were synthesized according to known procedures.^[1] Substituted propargyl bromide derivatives were synthesized in variable yields (72-86%) from propargyl alcohol and commercially available aryl iodides following typical protocols. *Step 1:* Propargyl alcohol/aryl iodide/Bis-(triphenylphosphine)-palladium(II) chloride/CuI (1.1/1.0/0.02/0.04 equiv.), TEA (0.2 M), r.t., 4 hs;^[2] *Step 2:* substituted propargyl alcohol derivative/PPh₃/CBr₄ (1.0/1.5/1.5 eq.), CH₂Cl₂ (0.2 M), r.t., 2 hs.^[3]

- Synthesis and characterisation of substrates

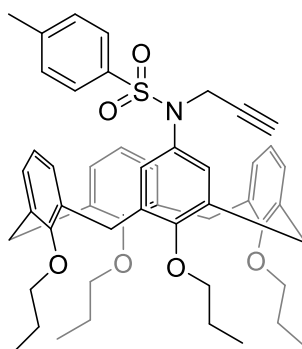
General procedure:



In a two-necked round bottom flask, under nitrogen atmosphere, Pd/C (cat. amount) and hydrazine monohydrate (60 eq.) were added to a suspension of **MN** (200 mg, 0.22 mmol) in EtOH (20 mL). The reaction was heated to 100 °C and let react under reflux for 2 hrs. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, the mixture was cooled to r.t. and filtered through celite and the solvent removed under low pressure. Water and DCM were added to the residue and the organic phase was recovered, washed with water (2 x 30 mL) and brine (30 mL), dried over Na_2SO_4 , filtered and the solvent removed under low pressure. The crude was used in the next step without further purification. The mono-ammino derivative was then dissolved in dry DCM, under nitrogen atmosphere, and Et_3N (3 eq.) and the respective sulphonyl chloride (1 eq.) were added at 0 °C. The mixture was let warm up at r.t. and stirred for 4 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na_2SO_4 and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1). Finally, the **MS** intermediate was dissolved in Acetone (10 mL) along with K_2CO_3 (2.5 eq.) and the respective propargyl bromide derivative (1.5 eq.). The mixture was warmed to 65 °C and stirred for 1.5 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na_2SO_4 and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1), obtaining the desired substrate.

1a

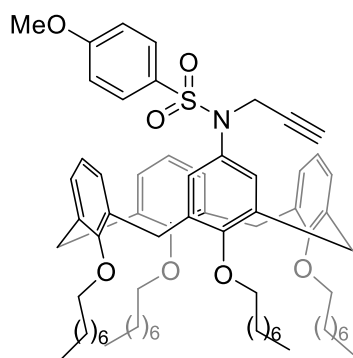
General procedure was followed using **MS1** (229 mg, 0.22 mmol) and propargyl bromide (36 μ L, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **1a** (204 mg, 86 %) as a white solid, **M.p.** = 111 – 112 °C. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.61 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 2H), 6.75 (d, *J* = 7.4 Hz, 2H), 6.66 – 6.47 (m, 7H), 6.40 (dd, *J* = 7.5 Hz, 1.8 Hz, 2H), 4.45 (d, *J* = 13.2 Hz, 2H), 4.40 (d, *J* = 13.2 Hz, 2H), 4.17 (d, *J* = 2.5 Hz, 2H), 3.94 – 3.83 (m, 8H), 3.16 (d, *J* = 13.3 Hz, 2H), 3.06 (d, *J* = 13.3 Hz, 2H), 2.45 (s, 3H), 2.06 (t, *J* = 2.4 Hz, 1H), 1.96 – 1.89 (m, 8H), 1.49 – 1.31 (m, 40H), 0.94 – 0.90 (m, 12H). **¹³C NMR** (101 MHz, CDCl₃) δ = 156.8 (C_q), 156.7 (C_q), 156.3 (C_q), 143.3 (C_q), 136.2 (C_q), 136.0 (C_q), 135.3 (C_q), 134.9 (C_q), 134.3 (C_q), 133.0 (C_q), 129.0 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 122.0 (CH), 121.9 (CH), 77.3 (CH), 75.4 (CH₂), 75.3 (CH₂), 75.2 (CH₂), 73.5 (C_q), 41.5 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.6 (CH₂), 29.6 (CH₂), 26.4 (CH₂), 26.3 (CH₂), 26.3 (CH₂), 22.7 (CH₂), 21.6 (CH₃), 14.1 (CH₃). **LC-MS:** *m/z* [M+NH₄]⁺ calculated for C₇₀H₁₀₁N₂O₆S: 1097.74; found: 1097.42. **HR-MS** (ESI) *m/z*: [M+H]⁺ calcd. for C₇₀H₉₈NO₆S 1080.7155; found 1080.7160.

1b

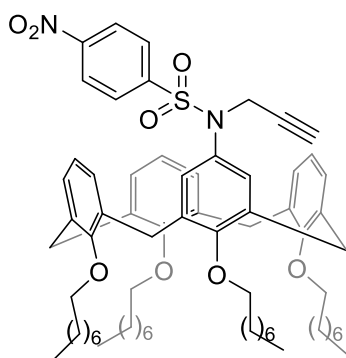
General procedure was followed using **MS2** (236 mg, 0.31 mmol) and propargyl bromide (50 μ L, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **1b** (193 mg, 78 %) as a white solid, **M.p.** = 115-115 °C. **¹H NMR:** (400 MHz, CDCl₃) δ = 8.28 (d, *J* = 8.4 Hz, 2H), 8.01 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 7.2 Hz, 2H), 6.64 (t, *J* = 8.4 Hz, 3H), 6.57–6.49 (m, 4H), 6.39 (dd, *J* = 7.6 Hz, 2.0 Hz, 2H), 4.46 (d, *J* = 13.3 Hz, 2H), 4.41 (d, *J* = 13.3 Hz, 2H), 4.17 (d, *J* = 2.4 Hz, 2H), 3.91 – 3.80 (m, 8H), 3.17 (d, *J* = 13.2 Hz, 2H), 3.07 (d, *J* = 13.2 Hz, 2H), 2.46 (s, 3H), 2.07 (t, *J* = 2.4 Hz, 1H), 1.99 – 1.89 (m, 8H), 1.04 – 0.97 (m, 12H). **¹³C NMR:** (101 MHz, CDCl₃) δ = 156.8 (C_q), 156.7 (C_q), 156.2 (C_q), 143.3 (C_q), 136.2 (C_q), 135.9 (C_q), 135.9 (C_q),

134.8 (C_q), 134.2 (C_q), 133.0 (C_q), 129.0 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 122.0 (CH), 121.9 (CH), 77.2 (CH), 76.9 (CH₂), 76.8 (CH₂), 76.7 (CH₂), 73.6 (C_q), 41.5 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 23.3 (CH₂), 23.2 (CH₂), 21.6 (CH₂), 10.8 (CH₃), 10.3 (CH₃), 10.2 (CH₃). **LC-MS:** m/z [M+NH₄]⁺ calculated for C₅₀H₆₁N₂O₆S: 817.43; found: 818.03. **HR-MS** (ESI) m/z : [M+H]⁺ calcd. for C₅₀H₅₈NO₆S 800.3985; found 800.3991.

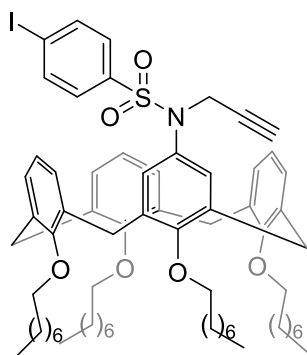
1c



General procedure was followed using **MS3** (233 mg, 0.22 mmol) and propargyl bromide (36 μ L, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **1c** (174 mg, 72 %) as a colourless oil. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.66 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 6.74 (d, J = 7.4 Hz, 2H), 6.63 – 6.58 (m, 5H), 6.53 (t, J = 7.4 Hz, 2H), 6.46 – 6.41 (m, 2H), 4.45 (d, J = 13.2 Hz, 2H), 4.41 (d, J = 13.2 Hz, 2H), 4.16 (d, J = 2.5 Hz, 2H), 3.94 – 3.85 (m, 11H), 3.17 (d, J = 13.3 Hz, 2H), 3.07 (d, J = 13.3 Hz, 2H), 2.07 (t, J = 2.5 Hz, 1H), 1.97 – 1.90 (m, 8H), 1.42 – 1.32 (m, 40H), 0.95 – 0.91 (m, 12H). **¹³C NMR:** (101 MHz, CDCl₃) δ = 162.9 (C_q), 156.8 (C_q), 156.7 (C_q), 156.3 (C_q), 135.9 (C_q), 135.2 (C_q), 135.0 (C_q), 134.4 (C_q), 133.2 (C_q), 130.9 (C_q), 130.4 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 122.0 (CH), 121.9 (CH), 113.5 (CH), 77.4 (CH), 75.4 (CH₂), 75.3 (CH₂), 75.2 (CH₂), 73.5 (C_q), 35.6 (CH₃), 41.5 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.7 (CH₂), 26.5 (CH₂), 26.4 (CH₂), 26.3 (CH₂), 22.7 (CH₂), 14.2 (CH₃). **LC-MS:** m/z [M+Na]⁺ calculated for C₇₀H₉₇NNaO₇S: 1118.69; found: 1118.17. **HR-MS** (ESI) m/z : [M+H]⁺ calcd. for C₇₀H₉₈NO₇S 1096.7064; found 1096.7060.

1d

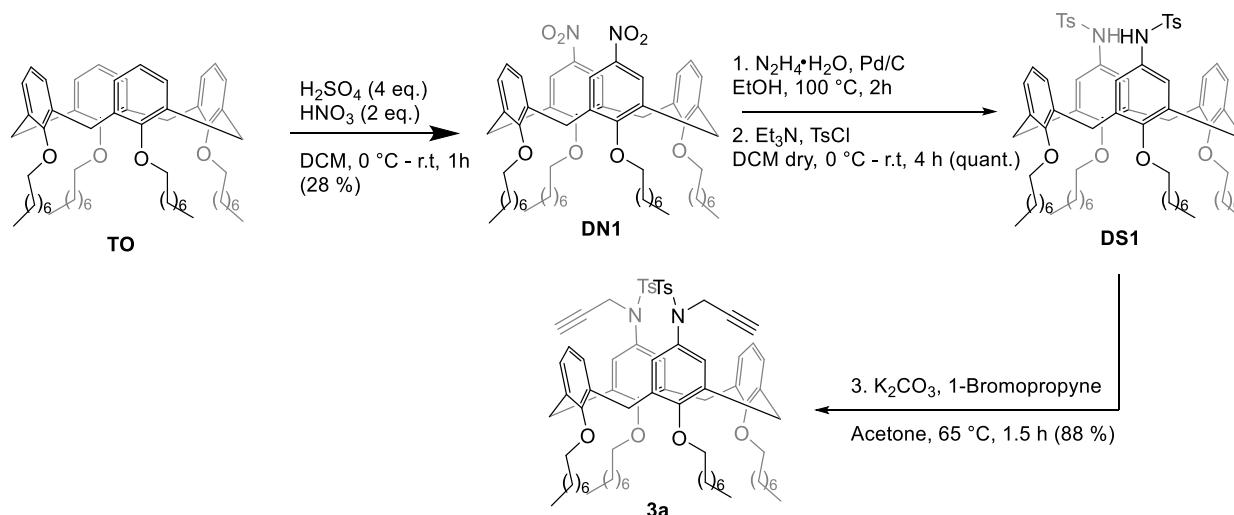
General procedure was followed using **MS4** (236 mg, 0.22 mmol) and propargyl bromide (36 μ L, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **1d** (203 mg, 83 %) as a yellowish oil. $^1\text{H NMR}$: (400 MHz, CDCl_3) δ = 8.28 (d, J = 8.8 Hz, 2H), 7.81 (d, J = 8.8 Hz, 2H), 6.82 (dd, J = 7.4 Hz, 1.9 Hz, 2H), 6.69 – 6.57 (m, 6H), 6.48 – 6.44 (m, 3H), 4.46 (d, J = 12.7 Hz, 2H), 4.42 (d, J = 12.7 Hz, 2H), 4.07 (d, J = 2.5 Hz, 2H), 4.02 – 3.92 (m, 4H), 3.84 (dt, J = 14.9 Hz, 7.2 Hz, 4H), 3.18 (d, J = 13.2 Hz, 2H), 3.08 (d, J = 13.2 Hz, 2H), 2.01 (t, J = 2.4 Hz, 1H), 1.97 – 1.90 (m, 8H), 1.47 – 1.28 (m, 40H), 0.94 – 0.90 (m, 12H). $^{13}\text{C NMR}$: (101 MHz, CDCl_3) δ = 156.8 (C_q), 156.7 (C_q), 156.3 (C_q), 149.9 (C_q), 145.2 (C_q), 135.8 (C_q), 135.8 (C_q), 134.9 (C_q), 134.4 (C_q), 132.6 (C_q), 129.4 (CH), 128.7 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 123.5 (CH), 122.1 (CH), 121.9 (CH), 77.2 (CH), 75.6 (CH_2), 75.5 (CH_2), 75.2 (CH_2), 74.2 (C_q), 41.9 (CH_2), 32.0 (CH_2), 31.0 (CH_2), 30.9 (CH_2), 30.5 (CH_2), 30.2 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 22.7 (CH_2), 14.1 (CH_3). **LC-MS**: m/z [$\text{M}+\text{K}$] $^+$ calculated for $\text{C}_{69}\text{H}_{94}\text{KN}_2\text{O}_8\text{S}$: 1149.64; found: 1149.37. **HR-MS** (ESI) m/z : [$\text{M}+\text{H}$] $^+$ calcd. for $\text{C}_{69}\text{H}_{95}\text{N}_2\text{O}_8\text{S}$ 1111.6809; found 1111.6802.

1e

General procedure was followed using **MS5** (254 mg, 0.22 mmol) and propargyl bromide (36 μ L, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **1e** (207 mg, 79 %) as a colourless oil. $^1\text{H NMR}$: (400 MHz, CDCl_3) δ = 7.82 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.5 Hz, 2H), 6.72 – 6.59 (m, 6H), 6.57 – 6.52 (m, 5H), 4.46 (d, J = 13.1 Hz, 2H), 4.42 (d, J = 13.2 Hz, 2H), 4.11 (d, J = 2.5 Hz, 2H), 3.96 – 3.85 (m, 8H), 3.18 (d, J = 13.3 Hz, 2H), 3.08 (d, J = 13.3 Hz, 2H), 2.06 (t, J = 2.5 Hz, 1H), 1.97 – 1.90 (m, 8H), 1.42 – 1.29 (m, 40H), 0.96 – 0.91 (m, 12H). $^{13}\text{C NMR}$: (101 MHz, CDCl_3) δ = 156.6 (C_q), 156.6 (C_q), 138.9 (C_q), 137.6 (CH), 135.8 (C_q), 135.3 (C_q), 134.9 (C_q), 134.6 (C_q), 132.8 (C_q), 129.7 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH),

122.1 (CH), 121.9 (CH), 99.92 (C_q), 77.2 (CH), 75.4 (CH₂), 75.3 (CH₂), 75.2 (CH₂), 74.0 (C_q), 41.7 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 30.4 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 26.4 (CH₂), 26.4 (CH₂), 22.8 (CH₂), 14.1 (CH₃). **LC-MS**: *m/z* [M+NH₄]⁺ calculated for C₆₉H₉₈IN₂O₆S: 1209.62; found: 1209.05. **HR-MS** (ESI) *m/z*: [M+H]⁺ calcd. for C₆₉H₉₅INO₆S 1192.5925; found 1192.5919.

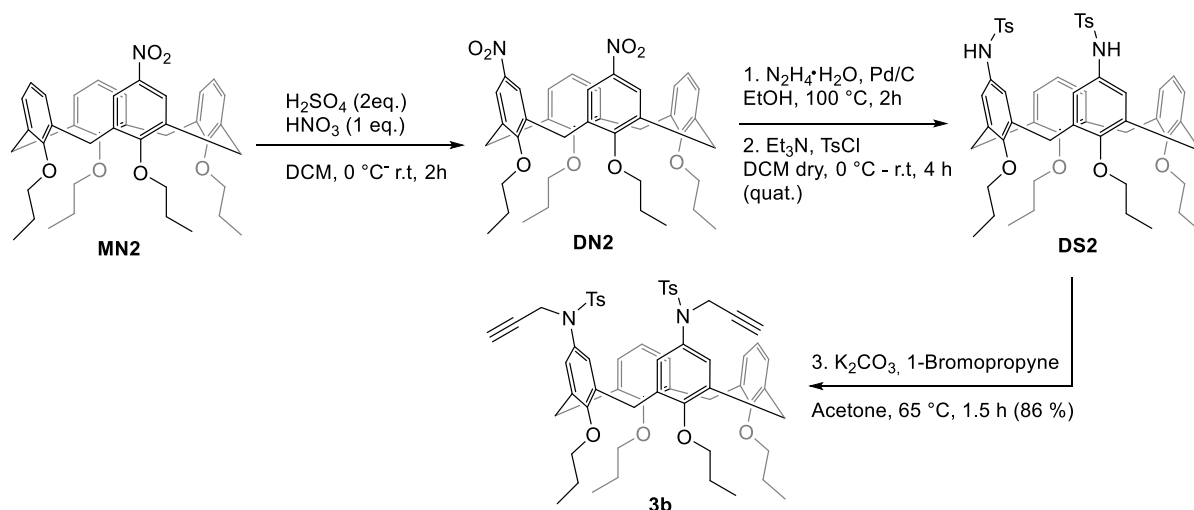
3a



Into a round bottom flask, H₂SO₄ (375 μL, 4 eq.) and HNO₃ (235 μL, 2 eq.) were added to a solution of **TO** (1 g, 1.69 mmol) in DCM (100 mL) at 0 °C. After 5 minutes the mixture was allowed to warm up to r.t and left under magnetic stirring for 1h. The reaction was monitored by TLC (*n*-hexane/EtOAc 95:5). Upon complete conversion of the starting material, the reaction was quenched with water (50 mL). The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dehydrated with Na₂SO₄ and filtered. The crude was purified by column chromatography on silica gel (*n*-hexane/EtOAc 95:5) yielding **DN1** (350 mg, 28%) as a red waxy solid. Into a two-necked round bottom flask, under nitrogen atmosphere, Pd/C (cat. amount) and hydrazine monohydrate (940 μL, 60 eq.) were added to a suspension of **DN1** (200 mg, 0.21 mmol) in EtOH (20 mL). The reaction was heated to 100 °C and let react under reflux for 2 h. The reaction was monitored by TLC (*n*-Hex:EtOAc 9:1). Once the reaction was completed, the mixture was cooled to r.t. and filtered through celite and the solvent removed under low pressure. Water and DCM were added to the residue and the organic phase was recovered, washed with water (2 x 30 mL) and brine (30 mL), dehydrated with Na₂SO₄, filtered and the solvent removed under low pressure. The crude was used in the next step without further purification. The di-ammino derivative was then dissolved in dry DCM, under nitrogen atmosphere, and Et₃N (4 eq.) and *p*-toluensulfonyl chloride (2 eq.) were added at 0 °C. The mixture was let warm up at r.t. and stirred for 4 h. The reaction was monitored by TLC (*n*-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (*n*-Hex:EtOAc 9:1). Finally, the **DS1** intermediate was dissolved in Acetone (10mL) along with K₂CO₃ (116 mg, 4 eq.) and propargyl bromide (70 μL, 3 eq.). The

mixture was warmed to 65 °C and stirred for 1.5 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1), yielding **3a** (249 mg, 88 %) as a colourless oil. ¹H NMR: (400 MHz, CDCl₃) δ = 7.70 (d, *J* = 8.3 Hz, 4H), 7.31 (d, *J* = 8.3 Hz, 4H), 7.04 (s, 4H), 6.24 (t, *J* = 7.6 Hz, 2H), 5.99 (d, *J* = 7.6 Hz, 4H), 4.52 (d, *J* = 2.5 Hz, 4H), 4.37 (d, *J* = 13.4 Hz, 4H), 4.10 – 4.02 (m, 4), 3.65 (t, *J* = 6.6 Hz, 4H), 3.04 (d, *J* = 13.4 Hz, 4H), 2.45 (s, 6H), 2.26 (t, *J* = 2.5 Hz, 2H), 1.99 – 1.79 (m, 8H), 1.60 – 1.49 (m, 4H), 1.42 – 1.20 (m, 36H), 0.96 – 0.88 (m, 12H). ¹³C NMR: (101 MHz, CDCl₃) δ = 157.8 (C_q), 155.2 (C_q), 143.5 (C_q), 137.5 (2C_q), 135.9 (C_q), 132.7 (2C_q), 132.6 (C_q), 129.2 (CH), 128.9 (CH), 128.2 (CH), 127.5 (CH), 121.9 (CH), 77.2 (CH), 75.4 (CH₂), 75.1 (CH₂), 73.6 (C_q), 41.4 (CH₂), 32.0 (CH₂), 30.9 (CH₂), 30.5 (CH₂), 30.2 (CH₂), 30.1 (CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.5 (CH₂), 26.7 (CH₂), 26.0 (CH₂), 22.8 (CH₂), 22.7 (CH₂), 21.7 (CH₃), 14.1 (CH₃). **LC-MS**: *m/z* [M+Na]⁺ calculated for C₈₀H₁₀₆N₂NaO₈S₂: 1309.73; found: 1309.26. **HR-MS** (ESI) *m/z*: [M+H]⁺ calcd. for C₈₀H₁₀₇N₂O₈S₂ 1287.7469; found 1287.7466.

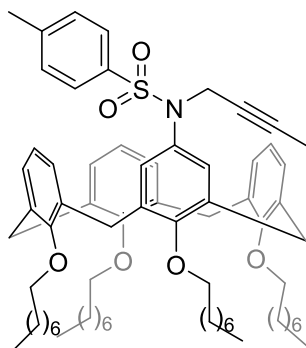
3b



Into a round bottom flask, H₂SO₄ (175 μL, 2 eq.) and HNO₃ (110 μL, 1 eq.) were added to a solution of **MN2** (1 g, 1.57 mmol) in DCM (100 mL) at 0 °C. After 5 minutes the mixture was allowed to warm up to r.t and left under magnetic stirring for 1h. The reaction was monitored by TLC (n-hexane/EtOAc 95:5). Upon complete conversion of the starting material, the reaction was quenched with water (50 mL). The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and filtered. The crude was purified by column chromatography on silica gel (n-hexane/EtOAc 95:5) yielding **DN2** (343 mg, 32%) as a red waxy solid. Into a two-necked round bottom flask, under nitrogen atmosphere, Pd/C (cat. amount) and hydrazine monohydrate (1300 μL, 60 eq.) were added to a suspension of **DN2** (200 mg, 0.29 mmol) in EtOH (20 mL). The reaction was heated to 100 °C and let react under reflux for 2 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, the mixture was cooled to r.t. and filtered through

celite and the solvent removed under low pressure. Water and DCM were added to the residue and the organic phase was recovered, washed with water (2 x 30 mL) and brine (30 mL), dehydrated with Na₂SO₄, filtered and the solvent removed under low pressure. The crude was used in the next step without further purification. The di-ammino derivative was then dissolved in dry DCM, under nitrogen atmosphere, and Et₃N (4 eq.) and p-toluensulphonyl chloride (2 eq.) were added at 0 °C. The mixture was let warm up at r.t. and stirred for 4 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1). Finally, the **DS2** intermediate was dissolved in Acetone (10mL) along with K₂CO₃ (116 mg, 4 eq.) and 1-bromopropyne (70 μL, 3 eq.). The mixture was warmed to 65 °C and stirred for 1.5 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1), yielding **3b** (251 mg, 86 %) as a colourless oil. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.59 (d, *J* = 8.4 Hz, 4H), 7.32 (d, *J* = 8.1 Hz, 4H), 6.68 (dd, *J* = 6.8 Hz, 2.4 Hz, 2H), 6.57 – 6.49 (m, 8H), 4.44 (d, *J* = 13.1 Hz, 1H), 4.40 (d, *J* = 13.1 Hz, 2H), 4.36 (d, *J* = 13.1 Hz, 1H), 4.24 (dd, *J* = 17.6 Hz, 2.5 Hz, 2H), 3.96 (dd, *J* = 17.7 Hz, 2.5 Hz, 2H), 3.89 – 3.81 (m, 8H), 3.15 (d, *J* = 13.2 Hz, 1H), 3.06 – 3.01 (m, 3H), 2.49 (s, 6H) 2.11 (t, *J* = 2.4 Hz, 2H), 1.98 – 1.91 (m, 8H), 1.04 – 0.98 (m, 12H). **¹³C NMR:** (101 MHz, CDCl₃) δ = 156.4 (C_q), 143.6 (2C_q), 136.1 (C_q), 135.6 (C_q), 135.2 (C_q), 134.9 (C_q), 134.4 (C_q), 133.3 (C_q), 129.2 (CH), 128.8 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH), 122.1 (CH), 77.2 (CH), 76.9 (CH₂), 76.8 (CH₂), 74.0 (C_q), 41.7 (CH₂), 30.9 (CH₂), 30.9 (CH₂), 30.8 (CH₂), 23.2 (CH₂), 21.6 (CH₃), 10.3 (CH₃). **LC-MS:** *m/z* [M+Na]⁺ calculated for C₈₀H₁₀₆N₂NaO₈S₂: 1309.73; found: 1309.87. **HR-MS** (ESI) *m/z*: [M+H]⁺ calcd. for C₈₀H₁₀₇N₂O₈S₂ 1287.7469; found 1287.7474.

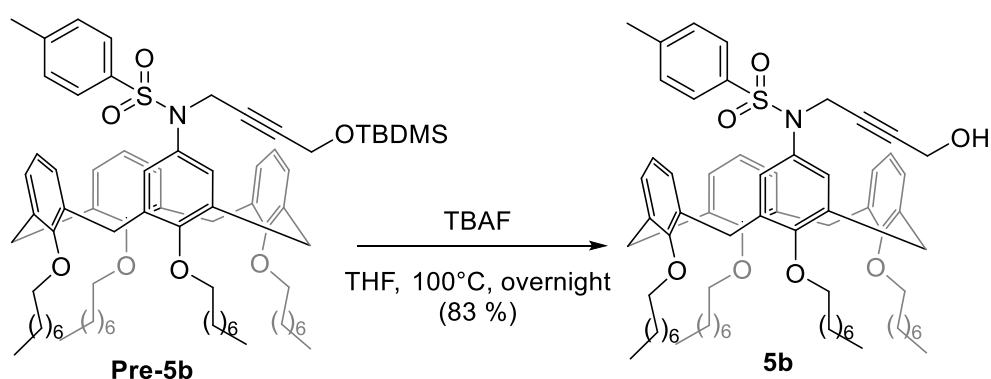
5a



General procedure was followed using **MS1** (229 mg, 0.22 mmol) and 1-bromo-2-butyne (29 μL, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5a** (207 mg, 86 %) as a white solid, **M.p.** = 97 – 98 °C. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.60 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 2H),

6.80 (d, $J = 7.4$ Hz, 2H), 6.69 (m, 3H), 6.54 – 6.44 (m, 4H), 6.36 (dd, $J = 7.2$ Hz, 2.0 Hz, 2H), 4.46 (d, $J = 13.3$ Hz, 2H), 4.41 (d, $J = 13.3$ Hz, 2H), 4.16 (d, $J = 2.7$ Hz, 2H), 3.96 (m, 4H), 3.84 (m, 4H), 3.16 (d, $J = 13.4$ Hz, 2H), 3.07 (d, $J = 13.4$ Hz, 2H), 2.45 (s, 3H), 1.93 (m, 8H), 1.69 (s, 3H), 1.54 – 1.23 (m, 40H), 0.95 – 0.91 (m, 12H). ^{13}C NMR: (101 MHz, CDCl_3) $\delta = 157.0$ (C_q), 156.7 (C_q), 156.1 (C_q), 143.0 (C_q), 136.4 (C_q), 136.0 (C_q), 135.6 (C_q), 134.7 (C_q), 134.2 (C_q), 133.5 (C_q), 128.8 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 122.0 (CH), 121.9 (CH), 81.1 (C_q), 75.3 (CH_2), 75.2 (CH_2), 75.1 (CH_2), 73.9 (C_q), 42.0 (CH_2), 32.0 (CH_2), 31.0 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.3 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 26.5 (CH_2), 26.3 (CH_2), 26.3 (CH_2), 22.7 (CH_2), 21.6 (CH_3), 14.1 (CH_3), 3.6 (CH_3). **LC-MS:** m/z $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{71}\text{H}_{99}\text{NNaO}_6\text{S}$: 1116.71; found: 1116.22. **HR-MS** (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{71}\text{H}_{100}\text{NO}_6\text{S}$ 1094.7271; found 1094.7277.

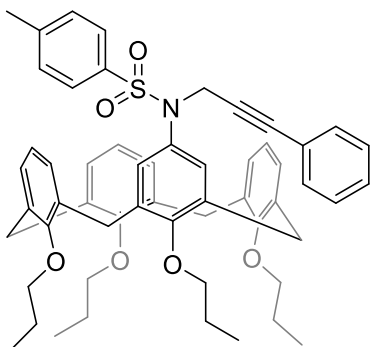
5b



General procedure was followed using **MS1** (229 mg, 0.22 mmol) and [(4-bromobut-2-yn-1-yl)oxy][(t-butyl)dimethylsilane] (75.3 mg, 1.3 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **Pre-5b** (205 mg, 76 %) as a colourless oil. Then the intermediate, under nitrogen atmosphere, was dissolved in THF (4 mL) and TBAF (44 mg, 1.5 eq.) was finally added. The mixture was heated to 100 °C and let stirring overnight. The reaction was monitored by TLC (*n*-Hex:EtOAc 8:2). Once the reaction was completed, water and EtOAc were added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na_2SO_4 and filtered. The crude was purified by column chromatography on silica gel (*n*-Hex:EtOAc 8:2) obtaining the desired product **5b** (157 mg, 83 %) as a colourless oil. ^1H NMR: (400 MHz, CDCl_3) $\delta = 7.59$ (d, $J = 8.3$ Hz, 2H), 7.27 (d, $J = 8.3$ Hz, 2H), 6.71 (d, $J = 7.4$ Hz, 2H), 6.65 – 6.57 (m, 5H), 6.55 (t, $J = 7.4$ Hz, 2H), 6.46 (dd, $J = 7.4$ Hz, 1.8 Hz, 2H), 4.45 (d, $J = 13.2$ Hz, 2H), 4.41 (d, $J = 13.2$ Hz, 2H), 4.17 (s, 2H), 4.10 (s, 2H), 3.96 – 3.83 (m, 8H), 3.17 (d, $J = 13.3$ Hz, 2H), 3.07 (d, $J = 13.3$ Hz, 2H), 2.46 (s, 3H), 1.99 – 1.86 (m, 8H), 1.61 (bs, 1H), 1.47 – 1.23 (m, 40H), 0.97 – 0.87 (m, 12H). ^{13}C NMR: (101 MHz, CDCl_3) $\delta = 156.8$ (C_q), 156.6 (C_q), 156.4 (C_q), 143.3 (C_q), 136.4 (C_q), 135.8 (C_q), 135.2 (C_q), 135.1 (C_q), 134.5 (C_q), 133.4 (C_q), 128.9 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 127.9 (CH), 122.0 (CH), 83.2 (C_q), 80.7 (C_q), 75.4 (CH_2), 75.3 (CH_2), 75.2 (CH_2), 51.0 (CH_2), 41.8 (CH_2), 32.0 (CH_2), 31.0 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.3 (CH_2), 29.9 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 26.4 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 22.7 (CH_2),

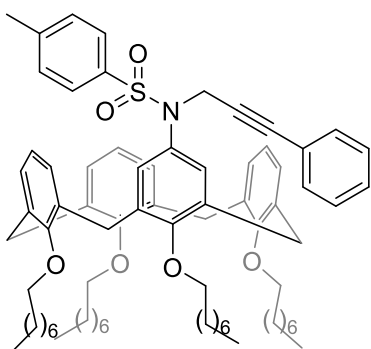
21.6 (CH₃), 14.1 (CH₃). **LC-MS:** m/z [M+Na]⁺ calculated for C₇₁H₉₉NNaO₇S: 1132.70 ; found: 1132.16. **HR-MS** (ESI) m/z : [M+H]⁺ calcd. for C₇₁H₁₀₀NO₇S 1110.7221; found 1110.7216.

5c



General procedure was followed using **MS2** (236 mg, 0.31 mmol) and (3-bromo-1-propynyl)benzene (91 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5c** (230 mg, 85 %) as a colourless oil. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.64 (d, J = 8.3 Hz, 2H), 7.40 – 7.28 (m, 3H), 7.27 – 7.18 (m, 4H), 6.86 – 6.79 (m, 4H), 6.72 (dd, J = 8.1, 6.8 Hz, 1H), 6.49 (dd, J = 7.2, 2.2 Hz, 2H), 6.40 – 6.35 (m, 3H), 6.33 (d, J = 7.4 Hz, 1H), 4.52 – 4.39 (m, 6H), 3.99 – 3.88 (m, 4H), 3.87 – 3.77 (m, 4H), 3.18 (d, J = 13.3 Hz, 2H), 3.10 (d, J = 13.3 Hz, 2H), 2.42 (s, 3H), 2.04 – 1.88 (m, 8H), 1.13 – 0.96 (m, 12H). **¹³C NMR:** (101 MHz, CDCl₃) δ = 157.0 (C_q), 156.8 (C_q), 156.0 (C_q), 143.2 (C_q), 136.3 (C_q), 136.1 (C_q), 135.6 (C_q), 134.6 (C_q), 134.0 (C_q), 133.5 (C_q), 131.5 (CH), 129.1 (CH), 128.4 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 122.8 (C_q), 122.2 (CH), 121.9 (CH), 85.2 (C_q), 84.2 (C_q), 76.9 (CH₂), 76.8 (CH₂), 76.7 (CH₂), 42.2 (CH₂), 31.0 (4CH₂), 23.3 (2CH₂), 23.2 (CH₂), 21.6 (CH₃), 10.5 (CH₃), 10.3 (CH₃), 10.2 (CH₃). **LC-MS:** m/z [M+Na]⁺ calculated for C₅₆H₆₁NNaO₆S: 898.41; found: 898.12. **HR-MS** (ESI) m/z : [M+H]⁺ calcd. for C₅₆H₆₂NO₆S 876.4298; found 876.4294.

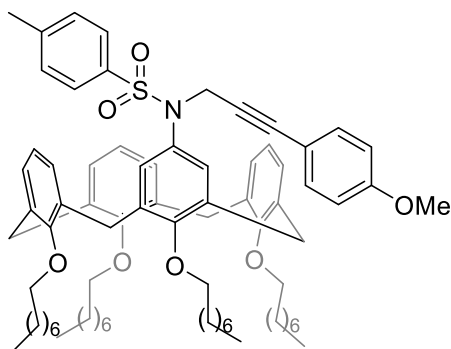
5d



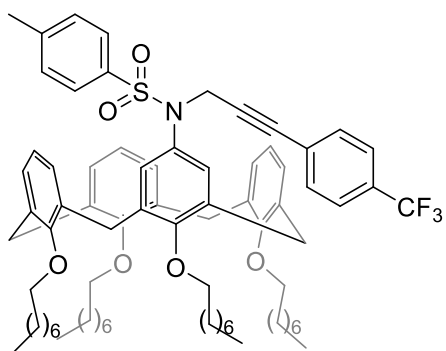
General procedure was followed using **MS1** (229 mg, 0.22 mmol) and (3-bromo-1-propynyl)benzene (64 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5d** (211 mg, 83 %) as a colourless oil. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.65 (d, J = 8.3 Hz, 2H), 7.37 – 7.31 (m, 3H), 7.24 – 7.21 (m, 4H), 6.83 (m, 4H), 6.73 (dd, J = 8.0 Hz, 6.8 Hz, 1H), 6.52 (dd, J = 7.2 Hz, 2.1 Hz, 2H), 6.40 (dd, J = 7.7 Hz, 2.2

Hz, 2H), 6.35 (t, $J = 7.2$ Hz, 2H), 4.54 – 4.40 (m, 6H), 4.03 – 3.92 (m, 4H), 3.90 – 3.86 (m, 4H), 3.19 (d, $J = 13.3$ Hz, 2H), 3.11 (d, $J = 13.3$ Hz, 2H), 2.42 (s, 3H), 2.00 – 1.94 (m, 8H), 1.62 – 1.50 (m, 4H), 1.43 – 1.35 (m, 36H), 0.97 – 0.94 (m, 12H). **^{13}C NMR:** (101 MHz, CDCl_3) $\delta = 157.0$ (C_q), 156.8 (C_q), 156.1 (C_q), 143.2 (C_q), 136.4 (C_q), 136.1 (C_q), 135.6 (C_q), 134.7 (C_q), 134.1 (C_q), 133.6 (C_q), 131.5 (CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 122.8 (C_q), 122.2 (CH), 122.0 (CH), 85.3 (C_q), 84.2 (C_q), 75.4 (CH_2), 75.3 (CH_2), 42.2 (CH_2), 32.1 (CH_2), 31.0 (CH_2), 30.4 (3 CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (2 CH_2), 26.5 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 22.6 (CH_2), 21.6 (CH_3), 14.3 (CH_3). **LC-MS:** m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{76}\text{H}_{101}\text{NO}_6\text{S}^+$: 1157.75 ; found: 1157.70. **HR-MS (ESI)** m/z : $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{76}\text{H}_{102}\text{NO}_6\text{S}$ 1156.7428; found 1156.7422.

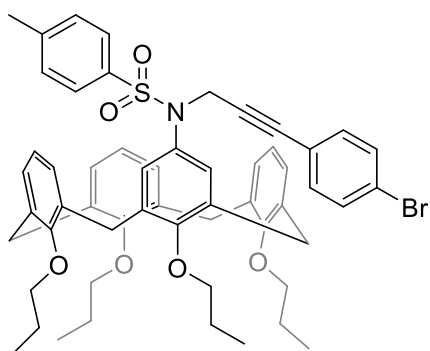
5e



General procedure was followed using **MS1** (229 mg, 0.22 mmol) and (3-bromo-1-propynyl)4-methoxybenzene (74 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5e** (217 mg, 83 %) as a yellowish oil. **^1H NMR:** (400 MHz, CDCl_3) $\delta = 7.62$ (d, $J = 8.3$ Hz, 2H), 7.20 (d, $J = 8.3$ Hz, 2H), 7.14 (d, $J = 8.8$ Hz, 2H), 6.87 – 6.79 (m, 6H), 6.75 – 6.67 (m, 1H), 6.46 (t, $J = 4.4$ Hz, 2H), 6.33 (d, $J = 5.0$ Hz, 4H), 4.49 – 4.36 (m, 6H), 4.02 – 3.88 (m, 4H), 3.87 – 3.78 (m, 7H), 3.16 (d, $J = 13.4$ Hz, 2H), 3.07 (d, $J = 13.4$ Hz, 2H), 2.40 (s, 3H), 2.00 – 1.84 (m, 8H), 1.50 – 1.25 (m, 40H), 0.99 – 0.87 (m, 12H). **^{13}C NMR:** (101 MHz, CDCl_3) $\delta = 159.6$ (C_q), 157.0 (C_q), 156.8 (C_q), 156.0 (C_q), 143.0 (C_q), 136.3 (C_q), 136.1 (C_q), 135.7 (C_q), 134.6 (C_q), 134.0 (C_q), 133.5 (C_q), 133.0 (CH), 129.0 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.8 (CH), 122.1 (CH), 121.9 (CH), 114.9 (C_q), 113.8 (CH), 85.1 (C_q), 82.7 (C_q), 75.3 (CH_2), 75.2 (CH_2), 75.2 (CH_2), 55.3 (CH_3), 42.3 (CH_2), 32.0 (CH_2), 31.0 (CH_2), 30.9 (CH_2), 30.4 (CH_2), 30.3 (2 CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 26.5 (CH_2), 26.3 (CH_2), 22.8 (CH_2), 21.6 (CH_3), 14.1 (CH_3). **LC-MS:** m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{77}\text{H}_{106}\text{NO}_7\text{S}$: 1186.76 ; found: 1186.54. **HR-MS (ESI)** m/z : $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{77}\text{H}_{104}\text{NO}_7\text{S}$ 1186.7534; found 1186.7539.

5f

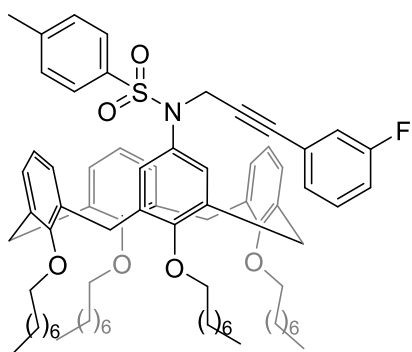
General procedure was followed using **MS1** (229 mg, 0.22 mmol) and (3-bromo-1-propynyl)4-(trifluoromethyl)benzene (87 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5f** (202 mg, 75 %) as a colourless oil. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.61 (d, *J* = 8.3 Hz, 2H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 2H), 6.76 (d, *J* = 7.5 Hz, 2H), 6.72 (s, 2H), 6.69 – 6.63 (m, 1H), 6.53 (dd, *J* = 7.4 Hz, 1.8 Hz, 2H), 6.40 (dd, *J* = 7.4 Hz, 1.8 Hz, 2H), 6.34 (t, *J* = 7.5 Hz, 2H), 4.50 – 4.38 (m, 6H), 3.99 – 3.80 (m, 8H), 3.16 (d, *J* = 13.3 Hz, 2H), 3.08 (d, *J* = 13.3 Hz, 2H), 2.41 (s, 3H), 2.00 – 1.86 (m, 8H), 1.48 – 1.26 (m, 40 H), 0.99 – 0.86 (m, 12H). **¹³C NMR:** (101 MHz, CDCl₃) δ = 156.9 (C_q), 156.7 (C_q), 156.2 (C_q), 143.2 (C_q), 136.4 (C_q), 136.0 (C_q), 135.4 (C_q), 134.9 (C_q), 134.2 (C_q), 133.5 (C_q), 131.8 (CH), 129.9 (C_q), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 126.5 (C_q), 125.1 (q, *J*_{C-F} = 3.8 Hz, CH), 124.0 (d, *J*_{C-F} = 272 Hz, C_q), 122.1 (CH), 121.9 (CH), 86.9 (C_q), 83.8 (C_q), 75.4 (CH₂), 75.3 (CH₂), 42.2 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.0 (2CH₂), 29.9 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 26.4 (CH₂), 26.3 (CH₂), 22.7 (CH₂), 21.6 (CH₃), 14.1 (CH₃). **¹⁹F NMR:** (565 MHz, CDCl₃) δ = - 62.7. **ESI-MS:** *m/z* [M+H₃O]⁺ calculated for C₇₇H₁₀₃F₃NO₇S: 1242.74; found: 1242.86. **HR-MS (ESI) *m/z*:** [M+H]⁺ calcd. for C₇₇H₁₀₁F₃NO₆S 1224.7302; found 1224.7309.

5g

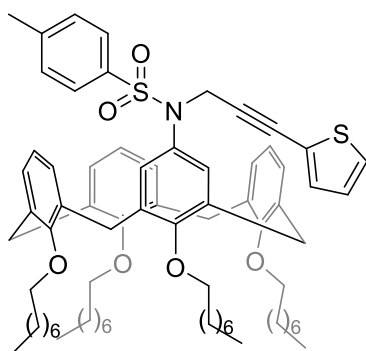
General procedure was followed using **MS2** (236 mg, 0.31 mmol) and 1-bromo-4-(3-bromoprop-1-yn-1-yl)benzene (129 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5g** (243 mg, 82 %) as a yellowish solid, **M.p.** = 94 – 95 °C. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.60 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.78 (d, *J* = 7.2 Hz, 2H), 6.72 (s, 2H), 6.71 – 6.63 (m, 1H), 6.51 (dd, *J* = 7.0 Hz, 2.4 Hz, 2H), 6.39 – 6.30 (m, 4H), 4.50 – 4.35 (m, 6H), 3.95

– 3.76 (m, 8H), 3.16 (d, $J = 13.3$ Hz, 2H), 3.07 (d, $J = 13.3$ Hz, 2H), 2.41 (s, 3H), 2.02 – 1.86 (m, 8H), 1.06 – 0.94 (m, 12H). $^{13}\text{C NMR}$: (101 MHz, CDCl_3) $\delta = 156.9$ (C_q), 156.7 (C_q), 156.1 (C_q), 143.2 (C_q), 136.3 (C_q), 136.0 (C_q), 135.5 (C_q), 134.8 (C_q), 134.1 (C_q), 133.4 (C_q), 132.9 (CH), 131.4 (CH), 129.1 (CH), 128.3 (2CH), 128.1 (CH), 128.1 (CH), 127.8 (CH), 122.5 (C_q), 122.1 (CH), 121.9 (CH), 121.7 (C_q), 85.4 (C_q), 84.1 (C_q), 76.8 (CH_2), 76.8 (2 CH_2), 76.8 (CH_2), 42.2 (CH_2), 31.0 (4 CH_2), 23.3 (CH_2), 23.2 (2 CH_2), 21.6 (CH_3), 10.4 (CH_3), 10.3 (CH_3), 10.2 (CH_3). **LC-MS**: m/z [$\text{M}+\text{NH}_4$] $^+$ calculated for $\text{C}_{56}\text{H}_{64}\text{BrN}_2\text{O}_6\text{S}$: 973.36; found: 973.56. **HR-MS**: m/z [$\text{M}+\text{H}$] $^+$ calculated for $\text{C}_{56}\text{H}_{61}\text{BrNO}_6\text{S}$: 954.3403; found: 954.3397.

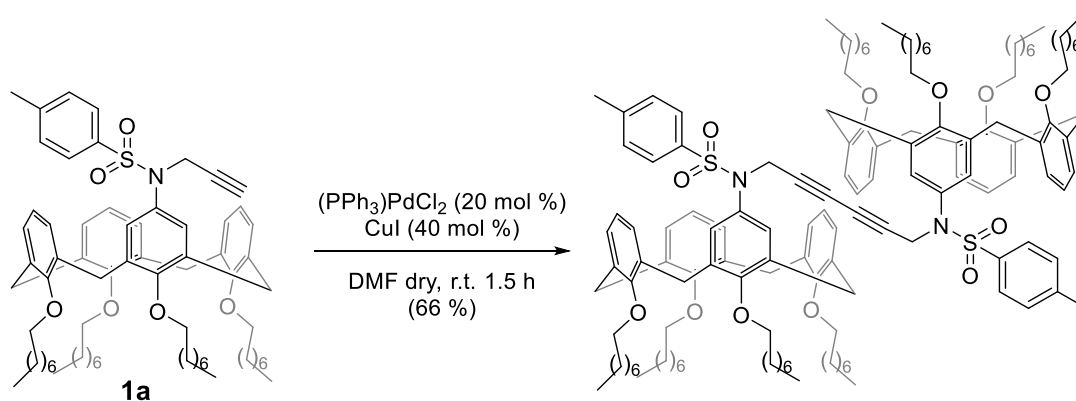
5h



General procedure was followed using **MS1** (229 mg, 0.22 mmol) and (3-bromo-1-propynyl)3-fluorobenzene (70 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5h** (207 mg, 80 %) as a colourless oil. $^1\text{H NMR}$: (400 MHz, CDCl_3) $\delta = 7.60$ (d, $J = 8.3$ Hz, 2H), 7.28 – 7.26 (m, 1H), 7.22 (d, $J = 8.3$ Hz, 2H), 7.05 (td, $J = 8.4$ Hz, 2.8 Hz, 1H), 6.98 (d, $J = 7.7$ Hz, 1H), 6.81 (dt, $J = 9.4$ Hz, 1.5 Hz, 1H), 6.73 (d, $J = 7.3$ Hz, 2H), 6.70 (s, 2H), 6.67 – 6.61 (m, 1H), 6.55 (d, $J = 7.3$ Hz, 2H), 6.42 (d, $J = 7.5$ Hz, 2H), 6.37 (t, $J = 7.3$ Hz, 2H), 4.50 – 4.35 (m, 6H), 3.98 – 3.81 (m, 8H), 3.16 (d, $J = 13.3$ Hz, 2H), 3.08 (d, $J = 13.3$ Hz, 2H), 2.42 (s, 3H), 2.01 – 1.84 (m, 8H), 1.48 – 1.25 (m, 40H), 0.99 – 0.86 (m, 12H). $^{13}\text{C NMR}$: (101 MHz, CDCl_3) $\delta = 162.4$ (d, $J_{\text{C-F}} = 247$ Hz, C_q), 156.8 (C_q), 156.7 (C_q), 156.3 (C_q), 143.3 (C_q), 136.4 (C_q), 135.9 (C_q), 135.3 (C_q), 135.0 (C_q), 134.3 (C_q), 133.6 (C_q), 129.7 (d, $J_{\text{C-F}} = 8.4$ Hz, CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.3 (d, $J_{\text{C-F}} = 3.3$ Hz, CH), 124.6 (d, $J_{\text{C-F}} = 9.8$ Hz, C_q), 122.1 (CH), 121.9 (CH), 118.3 (d, $J_{\text{C-F}} = 23.0$ Hz, CH), 118.6 (d, $J_{\text{C-F}} = 21.2$ Hz, CH), 85.2 (C_q), 83.9 (d, $J_{\text{C-F}} = 3.3$ Hz, C_q), 75.4 (CH_2), 75.3 (CH_2), 75.2 (CH_2), 42.1 (CH_2), 32.0 (CH_2), 31.0 (CH_2), 30.4 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.7 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 26.3 (CH_2), 22.7 (CH_2), 21.5 (CH_3), 14.1 (CH_3). $^{19}\text{F NMR}$: (565 MHz, CDCl_3) $\delta = -62.5$. **LC-MS**: m/z [$\text{M}+\text{Na}$] $^+$ calculated for $\text{C}_{76}\text{H}_{100}\text{FNNaO}_6\text{S}$: 1196.72; found: 1196.45. **HR-MS** (ESI) m/z : [$\text{M}+\text{H}$] $^+$ calcd. for $\text{C}_{76}\text{H}_{101}\text{FNO}_6\text{S}$ 1174.7334; found 1174.7338.

5i

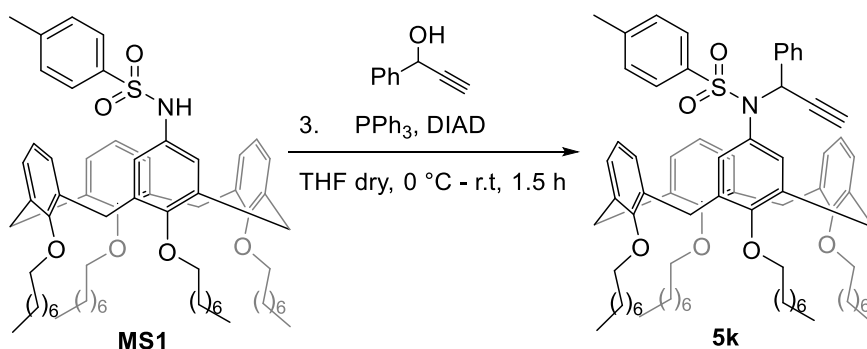
General procedure was followed using **MS1** (229 mg, 0.22 mmol) and 2-(3-bromo-1-propynyl)thiophene (66 mg, 1.5 eq.). Purification by column chromatography on silica gel (*n*-hexane/EtOAc 9:1) yielded **5i** (194 mg, 76 %) as a yellowish solid, **M.p.** = 122 – 123 °C. **¹H NMR:** (400 MHz, CDCl₃) δ = 7.61 (d, *J* = 8.3 Hz, 2H), 7.26 (dd, *J* = 5.1 Hz, 1.6 Hz, 1H), 7.22 (d, *J* = 8.3 Hz, 2H), 7.05 (dd, *J* = 3.6 Hz, 1.4 Hz, 1H), 6.99 (dd, *J* = 5.1 Hz, 3.5 Hz, 1H), 6.80 (d, *J* = 7.5 Hz, 2H), 6.74 (s, 2H), 6.71 – 6.65 (m, 1H), 6.53 – 6.47 (m, 2H), 6.42 – 6.35 (m, 4H), 4.50 – 4.36 (m, 6H), 3.99 – 3.89 (m, 4H), 3.88 – 3.79 (m, 4H), 3.16 (d, *J* = 13.3 Hz, 2H), 3.08 (d, *J* = 13.3 Hz, 2H), 2.40 (s, 3H), 2.00 – 1.85 (m, 8H), 1.49 – 1.26 (m, 40H), 0.98 – 0.88 (m, 12H). **¹³C NMR:** (101 MHz, CDCl₃) δ = 157.0 (C_q), 156.8 (C_q), 156.1 (C_q), 143.2 (C_q), 136.2 (C_q), 136.1 (C_q), 135.6 (C_q), 134.7 (C_q), 134.1 (C_q), 133.5 (C_q), 132.0 (CH), 129.1 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 128.1 (CH), 127.9 (CH), 127.0 (CH), 126.8 (CH), 122.7 (C_q), 122.1 (CH), 121.9 (CH), 88.1 (C_q), 78.5 (C_q), 75.3 (CH₂), 75.2 (CH₂), 42.4 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 30.4 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 26.5 (CH₂), 26.3 (CH₂), 26.3 (CH₂), 22.7 (CH₂), 21.6 (CH₃), 14.1 (CH₃). **LC-MS:** *m/z* [M+NH₄]⁺ calculated for C₇₄H₁₀₃N₂O₆S₂: 1179.73; found: 1179.52. **HR-MS** (ESI) *m/z*: [M+H]⁺ calcd. for C₇₄H₁₀₀NO₆S₂ 1162.6992; found 1162.6988.

5j

In a two-necked round-bottom flask, under nitrogen atmosphere, bis(triphenylphosphine)Pd(II) dichloride (0.2 eq.), CuI (0.4 eq.) Et₃N (1.5 eq.) were added to a solution of **1a** (100 mg, 0.093 mmol) in DMF (4 mL). The was le stirring at r.t. for 1.5 h. The reaction was monitored by TLC (*n*-Hex:EtOAc 9:1). Once the reaction was completed, water and EtOAc were added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and filtered. Purified by column chromatography on

silica gel (n-Hex:EtOAc 9:1), yielded **5j** (132 mg, 66 %) as a colourless oil. **¹H NMR**: (400 MHz, CDCl₃) δ = 7.59 (d, *J* = 8.1 Hz, 4H), 7.28 (d, *J* = 8.2 Hz, 4H), 6.79 (d, *J* = 7.5 Hz, 4H), 6.70 – 6.61 (m, 6H), 6.58 – 6.48 (m, 8H), 6.36 (dd, *J* = 7.2, 2.1 Hz, 4H), 4.45 (d, *J* = 13.2 Hz, 4H), 4.40 (d, *J* = 13.2 Hz, 4H), 4.31 (s, 4H), 3.97 – 3.77 (m, 16H), 3.16 (d, *J* = 13.3 Hz, 4H), 3.07 (d, *J* = 13.3 Hz, 4H), 2.44 (s, 6H), 1.99 – 1.88 (m, 16H), 1.48 – 1.25 (m, 80H), 0.99 – 0.88 (m, 24H). **¹³C NMR**: (101 MHz, CDCl₃) δ = 156.9 (C_q), 156.8 (C_q), 156.1 (C_q), 143.6 (C_q), 136.3 (C_q), 135.8 (C_q), 135.6 (C_q), 134.7 (C_q), 134.00 (C_q), 133.1 (C_q), 129.2 (CH), 128.3 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 122.2 (CH), 121.9 (CH), 75.4 (CH₂), 75.3 (CH₂), 73.8 (C_q), 69.5 (C_q), 42.3 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.9 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.7 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 26.5 (CH₂), 26.3 (CH₂), 26.2 (CH₂), 22.7 (CH₂), 21.6 (CH₃), 14.1 (CH₃). **LC-MS**: *m/z* [M+2K]²⁺ calculated for C₁₄₀H₁₉₂K₂N₂O₁₂S₂: 1117.65; found: 1117.47. **HR-MS** (ESI) *m/z*: [M+2K]⁺ calcd. for C₁₄₀H₁₉₂K₂N₂O₁₂S₂: 1117.6595; found: 1117.6590.

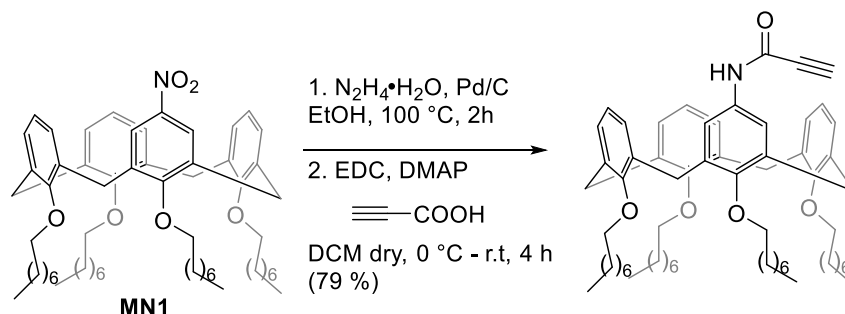
5k



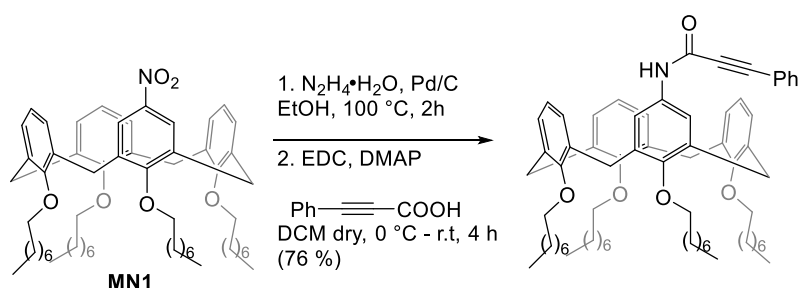
MS1 (229 mg, 0.22 mmol) was dissolved in dry THF (2mL) along with PPh₃ (69 mg, 1.2 eq.), DIAD (53 mg, 1.2 eq.) and 1-phenylprop-2-yn-1-ol (34 mg, 1.2 eq.). The mixture was let stirring at r.t. for 2.5 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water and EtOAc was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dehydrated with Na₂SO₄ and the solvent removed under low pressure. Purification by column chromatography on silica gel (n-Hex:EtOAc 97:3), yielded **5k** (221 mg, 87 %) as a white solid. **M.p.** = 104 – 105 °C. **¹H NMR**: (400 MHz, CDCl₃) δ = 7.77 (d, *J* = 8.3 Hz, 2H), 7.52 – 7.45 (m, 2H), 7.36 – 7.29 (m, 5H), 7.11 – 7.04 (m, 2H), 6.88 (t, *J* = 7.3 Hz, 1H), 6.83 (d, *J* = 2.6 Hz, 1H), 6.56 – 6.50 (m, 2H), 6.27 (t, *J* = 7.4 Hz, 1H), 6.20– 6.14 (m, 3H), 6.05 (dd, *J* = 7.6 Hz, 2.0 Hz, 1H), 5.30 (t, *J* = 4.4 Hz, 1H), 4.46 – 4.38 (m, 2H), 4.30 (d, *J* = 13.3 Hz, 1H), 4.25 (d, *J* = 13.3 Hz, 1H), 4.05 – 3.95 (m, 4H), 3.73 – 3.59 (m, 4H), 3.13 (d, *J* = 13.3 Hz, 2H), 2.90 (d, *J* = 13.3 Hz, 1H), 2.86 (d, *J* = 13.3 Hz, 1H), 2.48 (m, 4H), 1.99 – 1.77 (m, 8H), 1.56 – 1.48 (m, 4H), 1.44 – 1.18 (m, 36H), 0.99 – 0.86 (m, 12H). **¹³C NMR**: (101 MHz, CDCl₃) δ = 158.0 (C_q), 157.7 (C_q), 155.2 (C_q), 143.3 (C_q), 137.0 (C_q), 136.9 (C_q), 136.8 (C_q), 136.7 (C_q), 136.4 (C_q), 135.9 (C_q), 133.5 (C_q), 133.3 (C_q), 133.0 (CH), 132.9 (C_q), 132.7 (C_q), 130.7 (CH), 129.1 (CH), 128.8 (CH), 128.8 (CH), 128.7 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.5 (CH), 127.4 (CH), 127.3 (CH), 122.0 (CH), 121.9 (CH), 121.8 (CH), 77.2 (CH), 75.3 (C_q + CH₂), 75.2 (CH₂), 75.1 (CH₂), 75.0 (CH₂), 54.9 (CH), 32.1 (CH₂), 32.0 (CH₂), 31.0 (CH₂), 30.7 (CH₂), 30.6 (CH₂), 30.5 (CH₂), 30.4 (CH₂), 30.2 (CH₂),

30.1 (CH₂), 30.0 (CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.5 (CH₂), 26.6 (CH₂), 26.5 (CH₂), 26.1 (CH₂), 22.8 (CH₂), 22.7 (CH₂), 22.7 (CH₂), 21.7 (CH₃), 14.1 (CH₃). **ESI-MS**: m/z [M+NH₄]⁺ calculated for C₇₆H₁₀₅N₂O₆S: 1173.77; found: 1173.64. **HR-MS** (ESI) m/z : [M+H]⁺ calcd. for C₇₆H₁₀₂NO₆S₂ 1156.7428; found 1156.7422.

7a



In a two-necked round bottom flask, under nitrogen atmosphere, Pd/C (cat. amount) and hydrazine monohydrate (60 eq.) were added to a suspension of **MN1** (200 mg, 0.22 mmol) in EtOH (20 mL). The reaction was heated to 100 °C and let react under reflux for 2 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, the mixture was cooled to r.t. and filtered through celite and the solvent removed under low pressure. Water and DCM were added to the residue and the organic phase was recovered, washed with water (2 x 30 mL) and brine (30 mL), dried over Na₂SO₄, filtered and the solvent removed under low pressure. The crude was used in the next step without further purification. The mono-ammino derivative was then dissolved in dry DCM, under nitrogen atmosphere, and EDC (1.3 eq.), DMAP (cat.) and 3-propionic acid (1.3 eq.) were added at 0 °C. The mixture was let warm up at r.t. and stirred for 4 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dried over Na₂SO₄ and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1), obtaining the desired substrate **7a** (163 mg, 79 %) as a colourless oil. **¹H NMR**: (400 MHz, CDCl₃) δ = 7.00 (s, 1H), 6.84 – 6.77 (m, 4H), 6.72 (t, *J* = 7.4 Hz, 2H), 6.52 (s, 2H), 6.47 (s, 3H), 4.46 (d, *J* = 13.3 Hz, 2H), 4.44 (d, *J* = 13.3 Hz, 2H), 3.97 – 3.94 (m, 2H), 3.82 (q, *J* = 7.0 Hz, 4H), 3.18 (d, *J* = 13.2 Hz, 2H), 3.14 (d, *J* = 13.2 Hz, 2H), 2.84 (s, 1H), 1.97 – 1.84 (m, 8H), 1.55 – 1.24 (m, 40H), 0.96 – 0.88 (m, 12H). **¹³C NMR**: (101 MHz, CDCl₃) δ = 157.1 (C_q), 156.3 (C_q), 153.9 (C_q), 149.0 (C_q), 135.9 (C_q), 135.5 (C_q), 135.4 (C_q), 134.6 (C_q), 130.5 (C_q), 128.6 (CH), 128.4 (CH), 127.8 (CH), 122.0 (CH), 121.4 (CH), 120.1 (CH), 76.8 (CH), 75.2 (CH₂), 75.2 (CH₂), 75.2 (CH₂), 73.3 (C_q), 32.0 (CH₂), 31.1 (CH₂), 31.0 (CH₂), 30.4 (CH₂), 30.3 (CH₂), 30.3 (CH₂), 30.0 (CH₂), 29.9 (CH₂), 29.9 (CH₂), 29.7 (CH₂), 29.6 (CH₂), 29.6 (CH₂), 26.5 (CH₂), 26.4 (CH₂), 26.2 (CH₂), 22.7 (CH₂), 22.7 (CH₂), 14.1 (CH₃). **LC-MS**: m/z [M+NH₄]⁺ calculated for C₆₃H₉₃N₂O₅: 957.71; found: 957.45. **HR-MS** (ESI) m/z : [M+H]⁺ calcd. for C₆₃H₉₀NO₅ 940.6819; found 940.6816.

7b

In a two-necked round bottom flask, under nitrogen atmosphere, Pd/C (cat. amount) and hydrazine monohydrate (60 eq.) were added to a suspension of **MN1** (200 mg, 0.22 mmol) in EtOH (20 mL). The reaction was heated to 100 °C and let react under reflux for 2 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, the mixture was cooled to r.t. and filtered through celite and the solvent removed under low pressure. Water and DCM were added to the residue and the organic phase was recovered, washed with water (2 x 30 mL) and brine (30 mL), dehydrated with Na_2SO_4 , filtered and the solvent removed under low pressure. The crude was used in the next step without further purification. The mono-ammino derivative was then dissolved in dry DCM, under nitrogen atmosphere, and EDC (1.3 eq.), DMAP (cat.) and 3-phenylpropionic acid (1.3 eq.) were added at 0 °C. The mixture was let warm up at r.t. and stirred for 4 h. The reaction was monitored by TLC (n-Hex:EtOAc 9:1). Once the reaction was completed, water was added to the mixture. The organic phase was separated and washed with water (2x 30 mL) and brine (30 mL), dehydrated with Na_2SO_4 and the solvent removed under low pressure. The crude was purified by column chromatography on silica gel (n-Hex:EtOAc 9:1), obtaining the desired substrate **7b** (170 mg, 76 %) as a colourless oil. **$^1\text{H NMR}$** : (400 MHz, CDCl_3) δ = 7.61 – 7.54 (m, 2H), 7.49 – 7.30 (m, 3H), 7.08 (s, 1H), 6.85 – 6.77 (m, 3H), 6.72 (t, J = 7.4 Hz, 2H), 6.59 (s, 2H), 6.55 – 6.45 (m, 2H), 4.47 (d, J = 13.3 Hz, 2H), 4.45 (d, J = 13.3 Hz, 2H), 4.00 – 3.89 (m, 4H), 3.89 – 3.79 (m, 4H), 3.18 (d, J = 13.4 Hz, 2H), 3.17 (d, J = 13.4 Hz, 2H), 1.99 – 1.84 (m, 8H), 1.48 – 1.23 (m, 40H), 0.96 – 0.88 (m, 12H). **$^{13}\text{C NMR}$** : (101 MHz, CDCl_3) δ = 157.1 (C_q), 156.4 (C_q), 153.8 (C_q), 150.4 (C_q), 135.9 (C_q), 135.5 (C_q), 135.4 (C_q), 134.7 (C_q), 132.6 (CH), 131.0 (C_q), 130.1 (CH), 128.6 (CH), 128.4 (CH), 127.9 (CH), 122.0 (CH), 121.5 (CH), 120.2 (C_q), 120.1 (CH), 85.0 (C_q), 83.7 (C_q), 75.2 (CH_2), 75.1 (CH_2), 32.0 (CH_2), 31.1 (CH_2), 31.0 (CH_2), 30.4 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 30.0 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 26.5 (CH_2), 26.4 (CH_2), 26.3 (CH_2), 22.7 (CH_2), 14.1 (CH_3). **LC-MS**: m/z $[\text{M}+\text{NH}_4]^+$ calculated for $\text{C}_{69}\text{H}_{97}\text{N}_2\text{O}_5$: 1033.74; found: 1033.46. **HR-MS** (ESI) m/z : $[\text{M}+\text{H}]^+$ calcd. for $\text{C}_{69}\text{H}_{94}\text{NO}_5$ 1016.7132; found 1016.7128.

- NMR analysis of **4b'**

Figure 1. 2D-ROESY NMR of **4b'** (CDCl₃, 400 MHz).

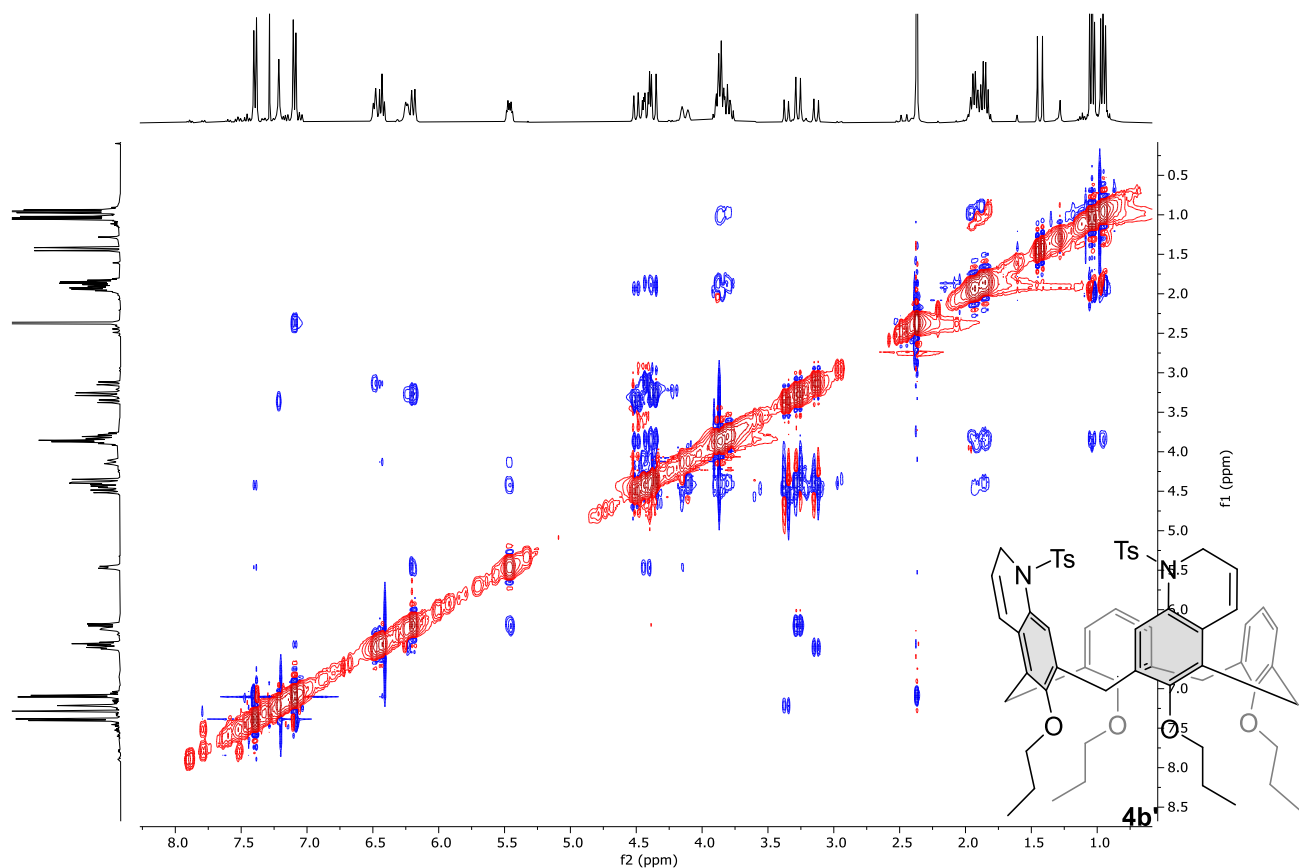
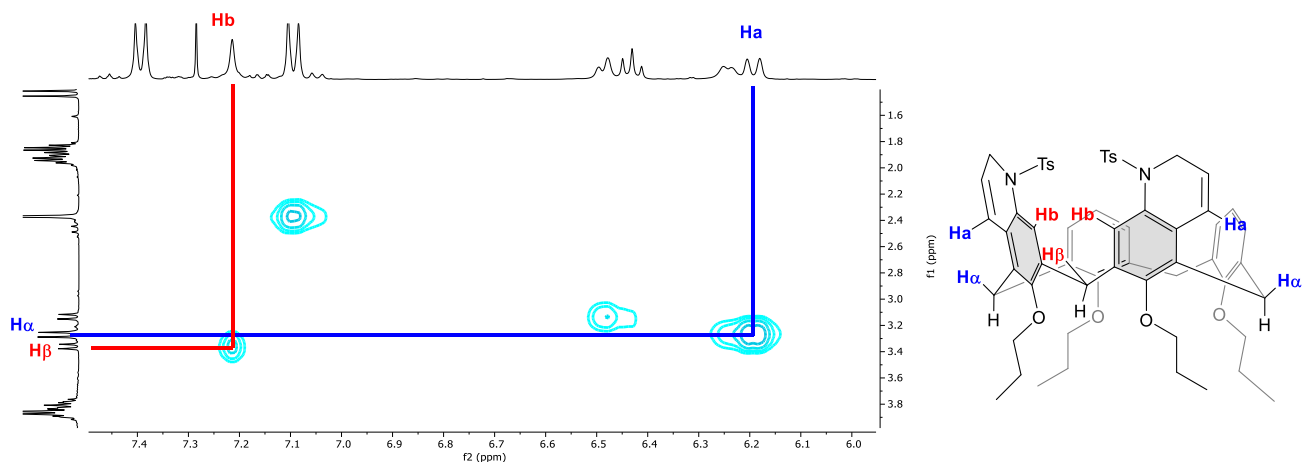
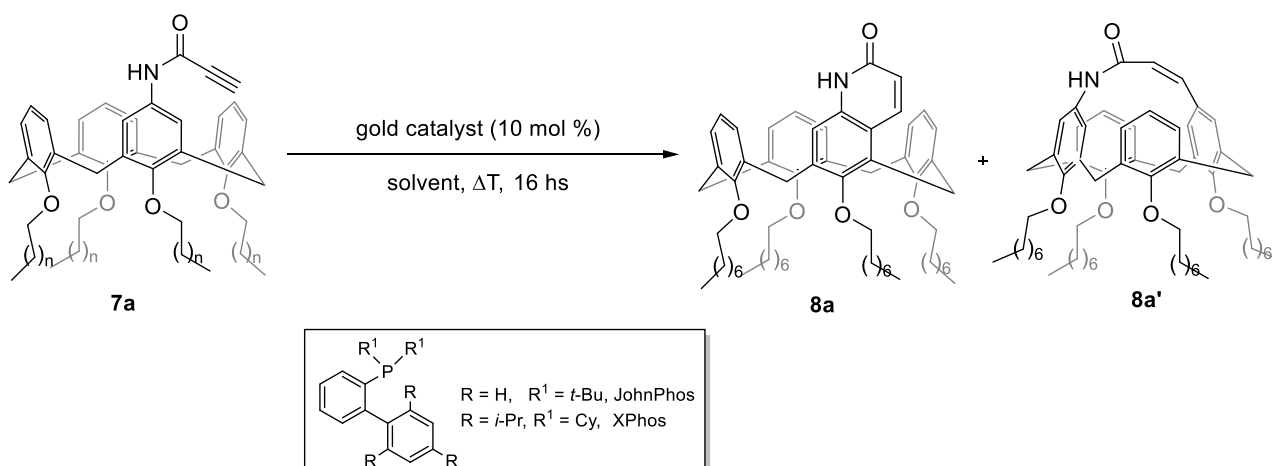


Figure 2. Low-field expanded region of the 2D-ROESY NMR of **4b'** (CDCl₃, 400 MHz, spin-lock = 200 ms) showing the dipolar correlation of:

- Olefinic proton α with equatorial methylene protons α (blue)
- Aromatic CH proton with equatorial methylene proton β (red)



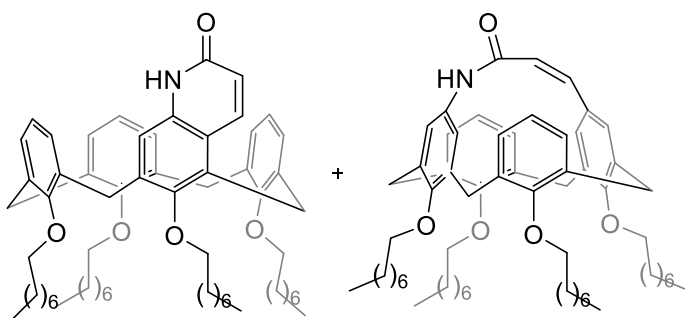
• **Reactivity with substrate 7a**



Into a Schlenk flask, under nitrogen atmosphere, **7a** (50.0 mg) and a gold catalyst (10 mol %) were dissolved in a dry solvent (1.0 mL) and the mixture stirred at the desired temperature for 16 hrs. After completion, the mixture was diluted with CH_2Cl_2 (10 ml) and filtered through a pad of celite that was washed with additional 20 ml of CH_2Cl_2 . The solvent was removed under low pressure and the crude was purified by column chromatography on silica gel (n-Hex: EtOAc 95:5), obtaining the **8a** and **8a'** as an inseparable mixture.*

Entry	[Au] (10 mol %)	Solvent	T [°C]	Yield [%]	8a+8a'
1	[JohnPhosAu(I)ACN] ⁺ SbF ₆ ⁻	CH ₂ Cl ₂	25	40	1:1.1
2	XPhosAuCl/AgSbF ₆	CH ₂ Cl ₂	25	25	1.1: 1
3	[JohnPhosAu(I)ACN] ⁺ SbF ₆ ⁻	toluene	50	45	1:1
4	[JohnPhosAu(I)ACN] ⁺ SbF ₆ ⁻	DCE	80	75	1:1.1
5	XPhosAuCl/AgSbF ₆	toluene	100	67	1:1.2
6	PPh ₃ AuCl/AgSbF ₆	toluene	100	52	1:1.2
7	[JohnPhosAu(I)ACN] ⁺ SbF ₆ ⁻	toluene	100°C	96	1:1.2

* Several unsuccessful attempts were made to separate these compounds by preparative TLC. Further, we also attempted chemical modifications by basic hydrolysis (NaOH in EtOH at reflux) or reduction ($\text{BH}_3 \cdot \text{SMe}_2$, THF, 80 °C). Unfortunately, low and partial conversions prevented fruitful separations.

8a + 8a'

Representative procedure was followed using **7a** (50.0 mg, 0.053 mmol), [JohnPhosAu(I)ACN]⁺SbF₆⁻ (10 mol %), toluene (1.0 ml) as the solvent and stirring the reaction at 100 °C. Purification by column chromatography on silica gel (n-Hexane/EtOAc 95:5) yielded **8a + 8a'** (47.8 mg, 96%, **8a/8a'** 1:1.2) as a colourless oil.

8a: ¹H NMR (400 MHz, CDCl₃) δ = 8.52 (d, *J* = 9.1 Hz, 1H), 8.43 (s, 1H), 7.58 (s, 1H), 6.92 (d, *J* = 9.0 Hz, 1H), 6.88 – 6.85 (m, 2H), 6.83 – 6.78 (m, 1H), 6.67 (t, *J* = 7.4 Hz, 1H), 6.43 (s, 2H), 6.34 – 6.27 (m, 2H), 6.13 (d, *J* = 6.7 Hz, 1H), 4.79 – 4.61 (m, 2H), 4.51 – 4.41 (m, 2H), 4.18 (td, *J* = 10.5, 5.7 Hz, 1H), 4.10 – 3.99 (m, 3H), 3.99 – 3.88 (m, 1H), 3.88 – 3.76 (m, 3H), 3.42 (d, *J* = 13.3 Hz, 1H), 3.24 – 3.12 (m, 3H), 2.10 – 1.84 (m, 8H), 1.65 – 1.25 (m, 40H), 0.97 – 0.84 (m, 12H). ¹³C NMR (101 MHz, CDCl₃) δ = 157.5 (C_q), 157.2 (C_q), 156.0 (C_q), 155.7 (C_q), 153.1 (C_q), 142.5 (C_q), 142.1 (C_q), 136.9 (CH), 136.5 (C_q), 136.4 (C_q), 135.7 (C_q), 134.3 (C_q), 134.2 (C_q), 133.2 (C_q), 131.9 (C_q), 128.6 (CH), 128.4 (CH), 127.8 (CH), 127.6 (CH), 127.2 (CH), 127.0 (CH), 122.2 (CH), 122.2 (CH), 121.8 (CH), 121.8 (CH), 110.0 (CH), 75.6 (CH₂), 75.4 (CH₂), 75.3 (CH₂), 75.0 (CH₂), 32.0 (CH₂), 32.0 (CH₂), 31.6 (CH₂), 31.1 (CH₂), 30.6 (CH₂), 30.5 (CH₂), 30.4 (CH₂), 30.4 (CH₂), 30.1 (CH₂), 30.0 (CH₂), 30.0 (CH₂), 29.6 (CH₂), 29.6 (CH₂), 29.6 (CH₂), 29.5 (CH₂), 26.6 (CH₂), 26.6 (CH₂), 26.5 (CH₂), 26.5 (CH₂), 25.2 (CH₂), 22.7 (CH₂), 14.1 (CH₃).

8a': ¹H NMR (400 MHz, CDCl₃) δ = 8.26 (d, *J* = 7.4 Hz, 1H), 6.92 (s, 1H), 6.83 – 6.78 (m, 2H), 6.76 (t, *J* = 7.3 Hz, 2H), 6.64 – 6.61 (m, 2H), 6.43 (s, 1H), 6.34 – 6.27 (m, 3H), 5.37 (d, *J* = 7.4 Hz, 1H), 4.51 – 4.41 (m, 4H), 3.99 – 3.88 (m, 4H), 3.88 – 3.76 (m, 4H), 3.24 – 3.12 (m, 4H), 2.10 – 1.84 (m, 8H), 1.65 – 1.25 (m, 40H), 0.97 – 0.84 (m, 12H). ¹³C NMR (101 MHz, CDCl₃) δ = 162.3 (C_q), 156.3 (C_q), 155.9 (C_q), 155.4 (C_q), 142.9 (CH), 142.5 (C_q), 136.4 (C_q), 135.9 (C_q), 135.3 (C_q), 134.7 (C_q), 128.7 (CH), 128.4 (CH), 128.0 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 125.6 (C_q), 121.9 (CH), 121.6 (CH), 120.0 (CH), 113.7 (C_q), 106.7 (CH), 75.2 (CH₂), 75.1 (CH₂), 75.1 (CH₂), 65.9 (C_q), 64.9 (C_q), 32.0 (CH₂), 31.0 (CH₂), 30.3 (CH₂), 30.3 (2CH₂), 30.2 (CH₂), 29.9 (CH₂), 29.9 (CH₂), 29.8 (CH₂), 29.8 (CH₂), 29.7 (CH₂), 29.7 (CH₂), 26.3 (CH₂), 26.2 (CH₂), 26.2 (CH₂), 22.7 (CH₂), 14.1 (CH₃).

LC-MS of the mixture: *m/z* [M+K]⁺ calculated for C₆₃H₈₉KNO₅: 978.64; found: 978.75.

Figure 3. Detailed low-field expanded region of $^1\text{H-NMR}$ of **8a+8a'** mixture (CDCl_3 , 400 MHz) showing the $^1\text{H-NMR}$ resonances of olefinic protons. *Noteworthy, olefinic protons of 8a' are upfield shifted, with respect to their analogues in 8a, because of their proximity to the macrocyclic cavity.*

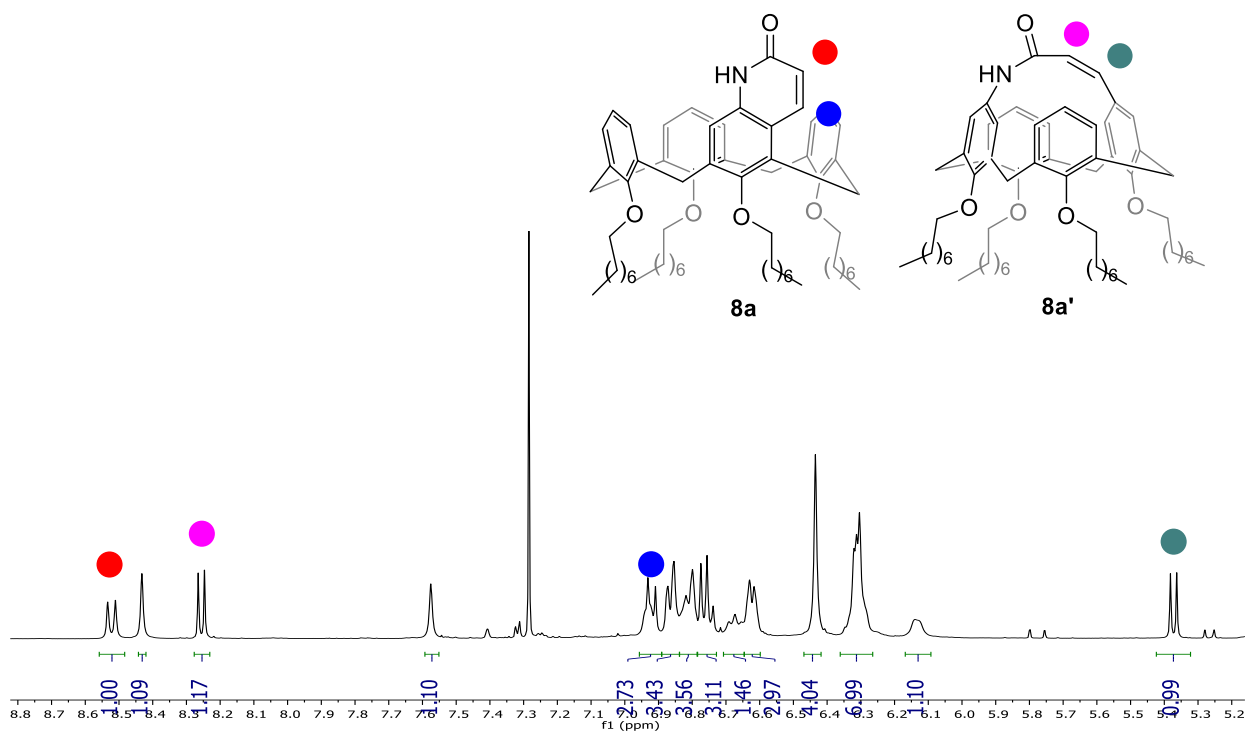
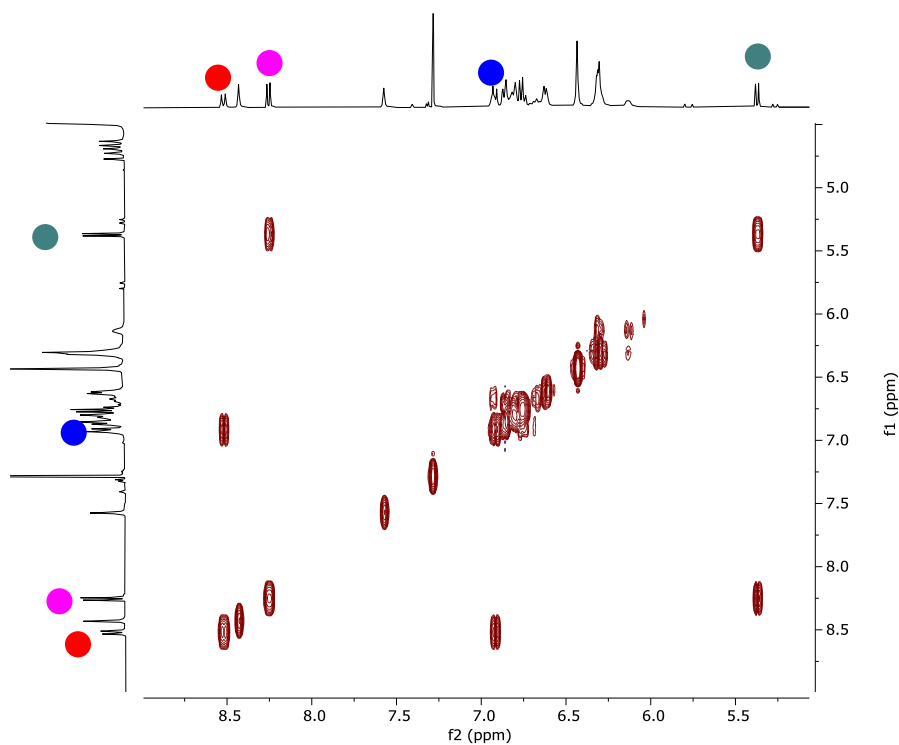
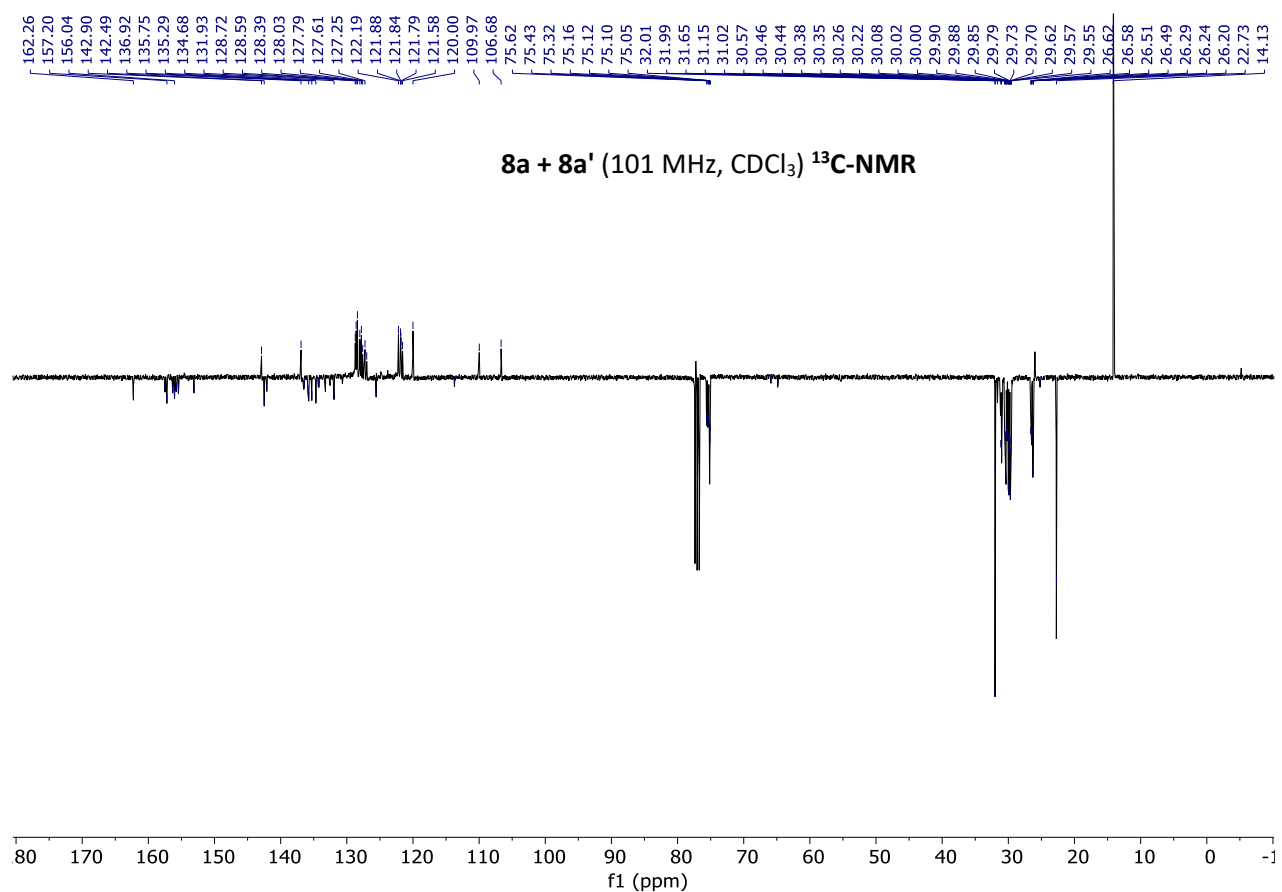
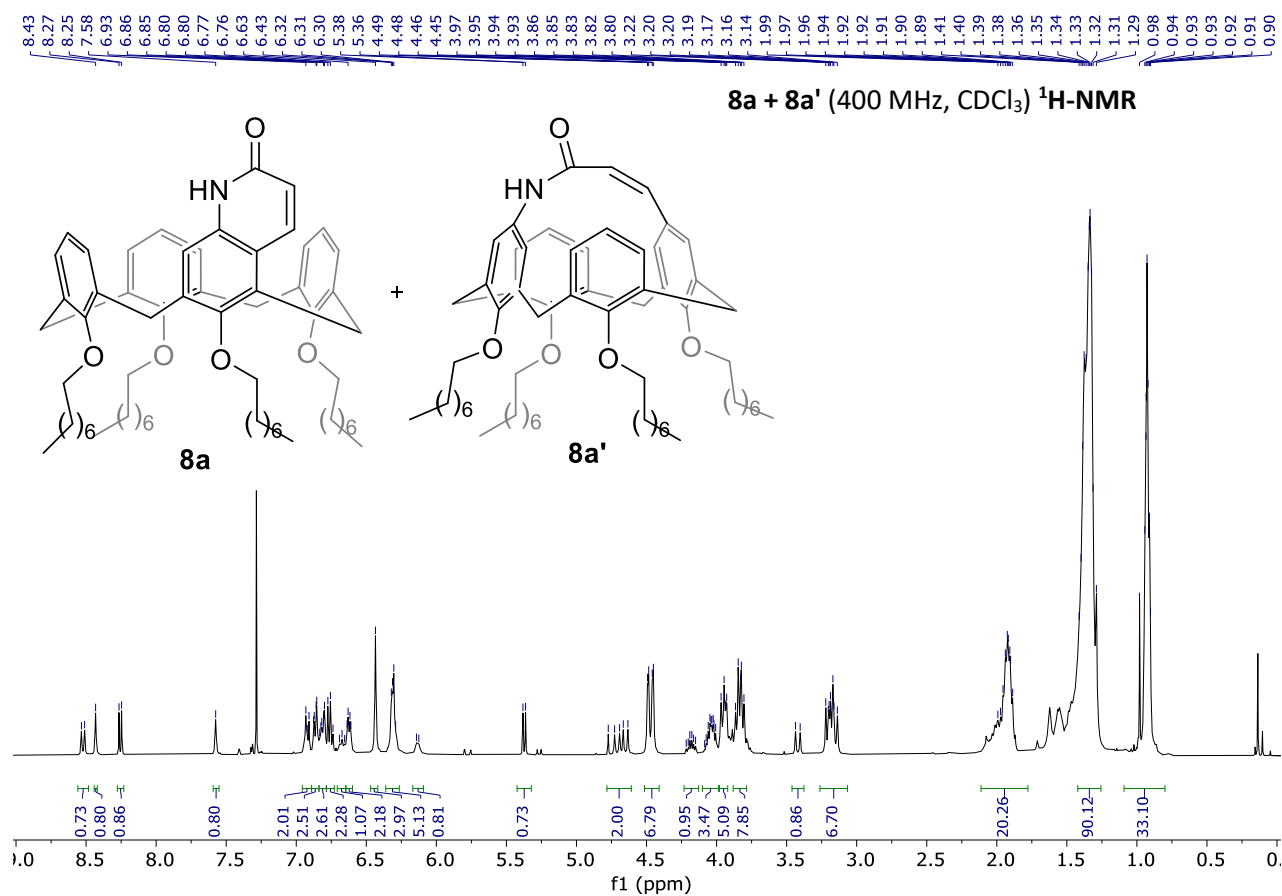
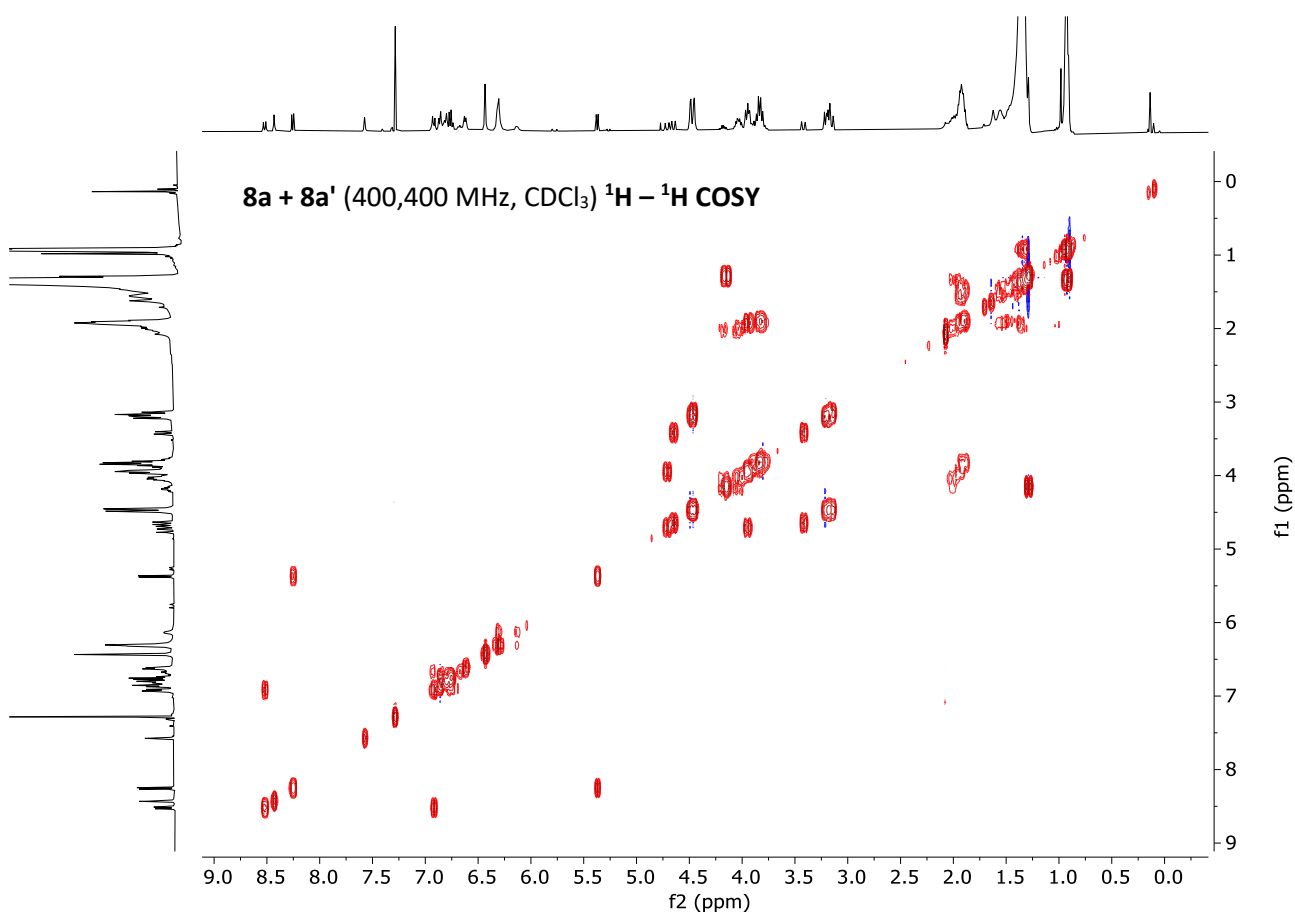
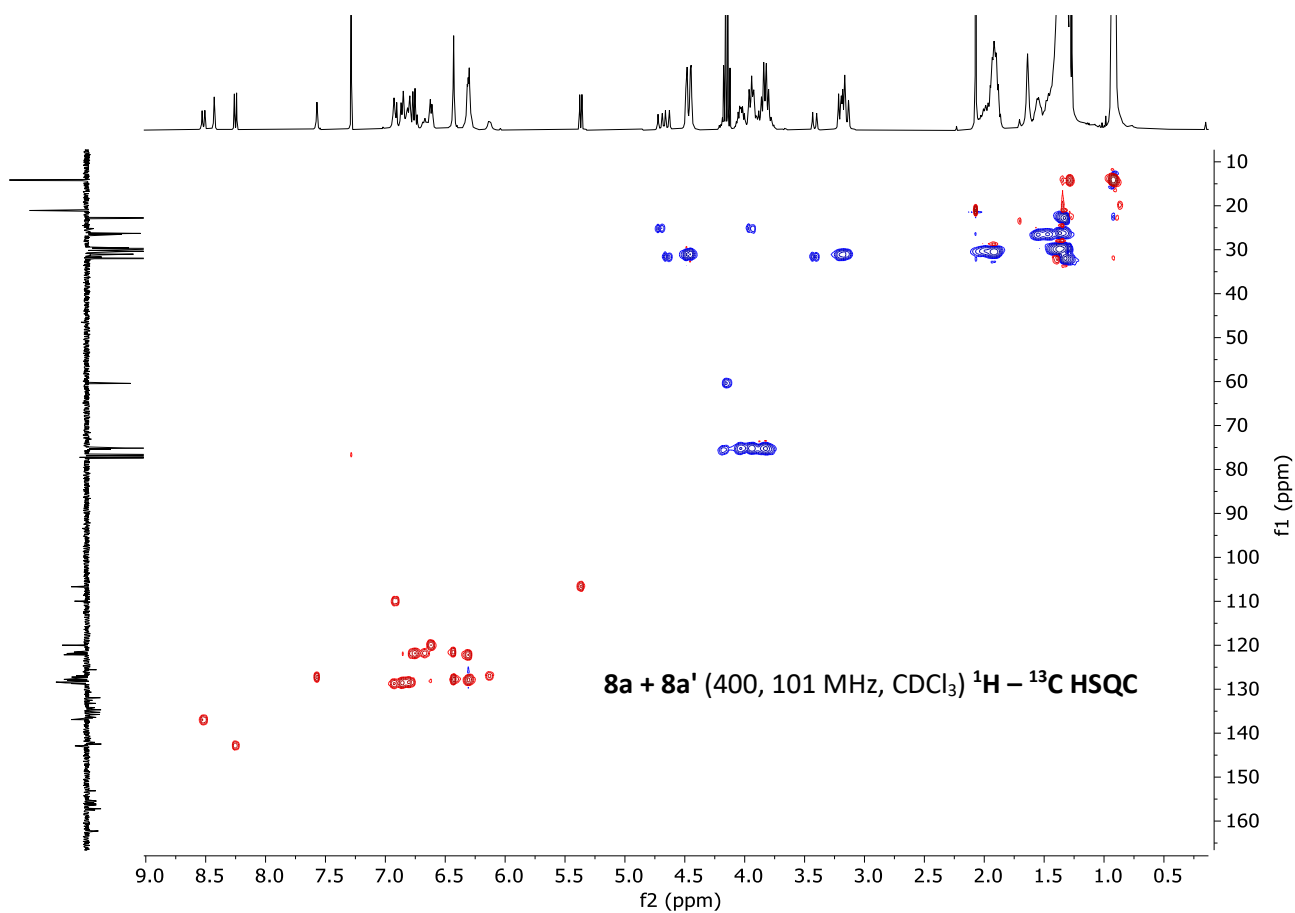


Figure 4. Detailed low-field expanded region of 2D $^1\text{H}^1\text{H}$ COSY NMR (CDCl_3 , 400 MHz) spectrum of **8a+8a'** mixture showing the J -coupling correlation of olefinic protons.

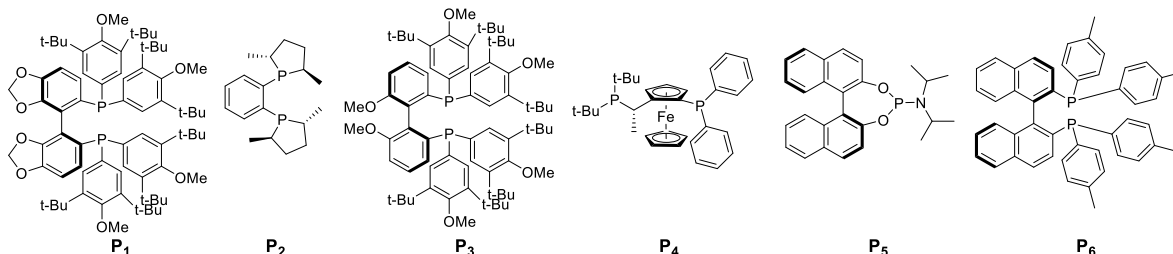
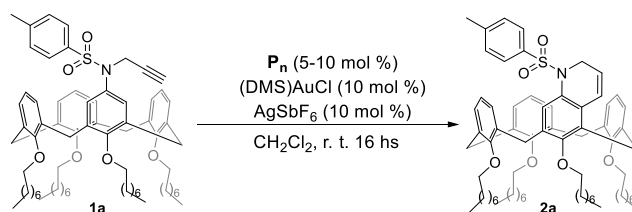


NMR spectra of 8a+8a':





• Preliminary enantioselective studies:

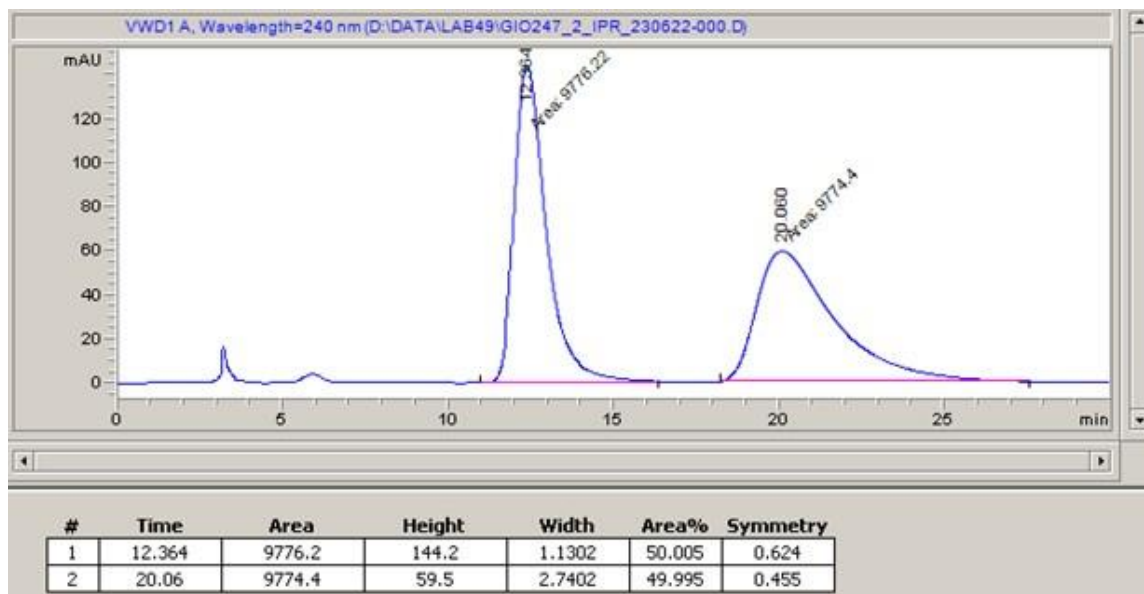


In a two-necked round-bottom flask, under nitrogen atmosphere, (DMS)AuCl (1.6 mg, 0.0056 mmol, 10 mol %) was added to a solution of the appropriate chiral phosphine P_n (5 or 10 mol % depending on the nature of the phosphine ligand) in dry CH₂Cl₂, at 0 °C. The mixture was left stirring for 30 minutes in an iced bath, then allowed to warm up to r.t. and left stirring for an additional 30 minutes. Then, the solvent was removed under reduced pressure and the residue was left under high vacuum for 3 hours. Once the gold complex was formed, dry CH₂Cl₂ (1 mL) was added along with AgSbF₆ (1.9 mg, 0.0056 mmol, 10 mol %) and the flask was covered with aluminium foil. Finally, the model substrate **1a** (60 mg, 0.056 mmol) was added and the mixture was left stirring at r.t. for 16 h. The reaction was monitored by TLC (n-Hex:EtOAc 98:2). Once the reaction was completed, the mixture was diluted with DCM (10 ml) and filtered through celite. The crude was purified by column chromatography on silica gel (n-Hex: EtOAc 95:5), yielding **2a**.

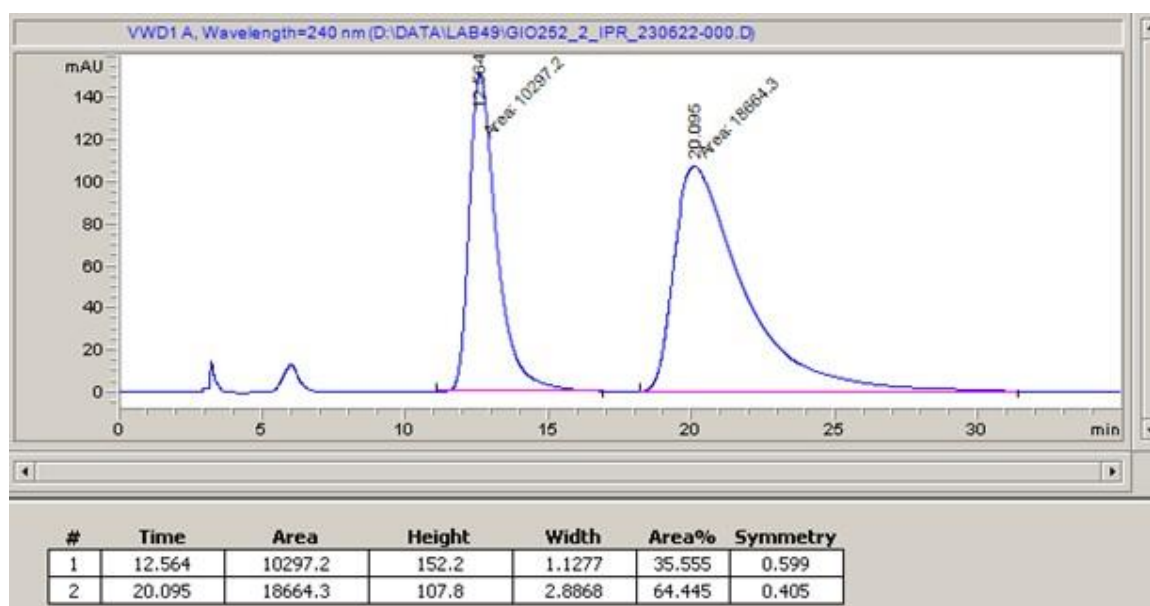
Entry	P_n	Conversion (%)	Yield 2a (%)	e.r. ^a
1	P₁ (5 mol %)	100	84	49:51
2	P₂ (5 mol %)	15	11	44:56
3	P₃ (5 mol %)	100	82	45:55
4	P₄ (5 mol %)	30	26	47:53
5	P₅ (10 mol %)	100	98	36:64
6	P₆ (5 mol %)	59	46	45:55

a) Enantiomeric excess was determined by HPLC analysis using Lux[®] 5 μm Cellulose 2, eluent: n-Hex:i-PrOH 98:2, flux: 1 ml/min.

Catalysis with [JohnPhosAu(I)ACN]SbF₆:

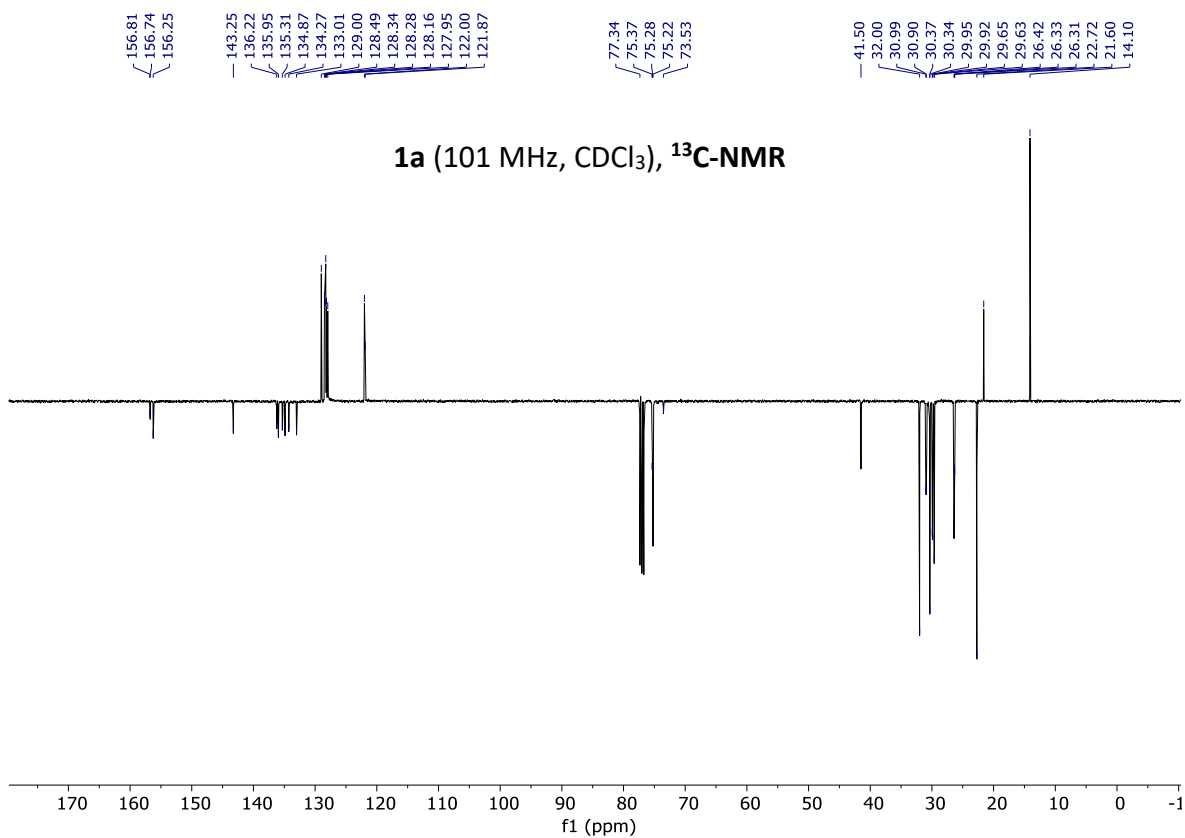
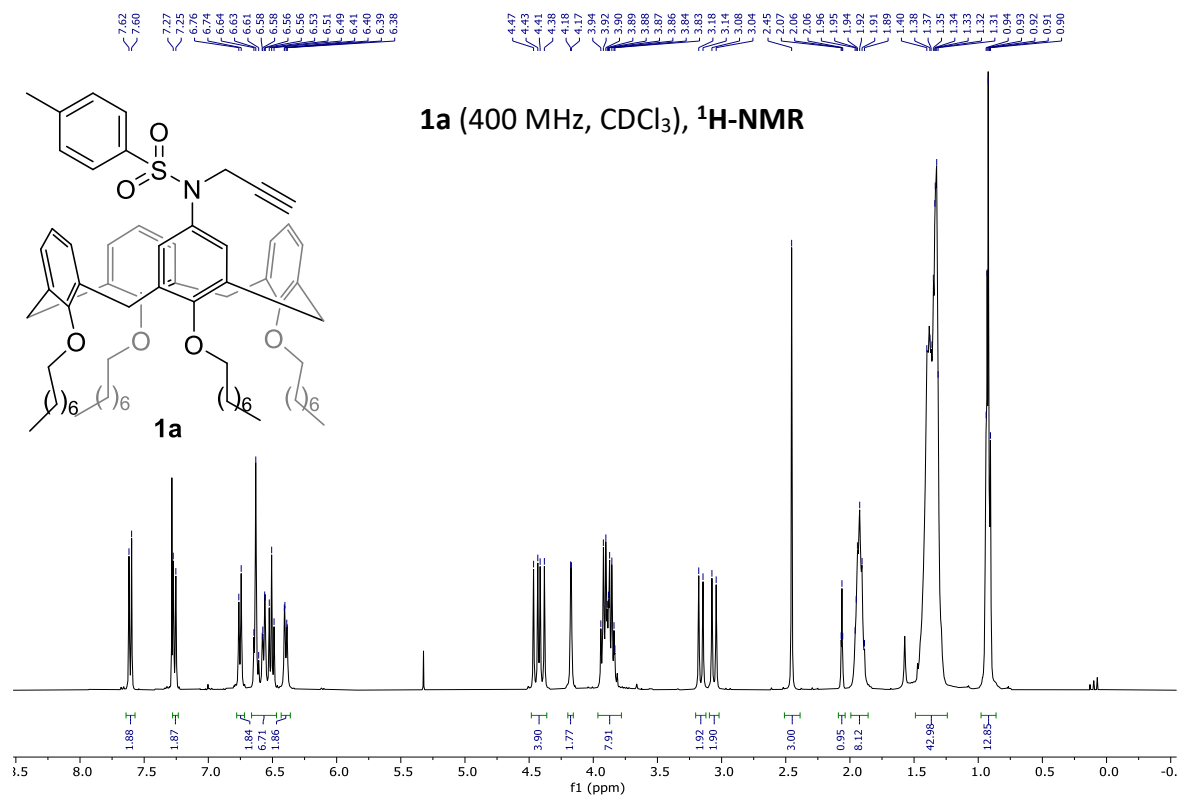


Catalysis with ligand P5:

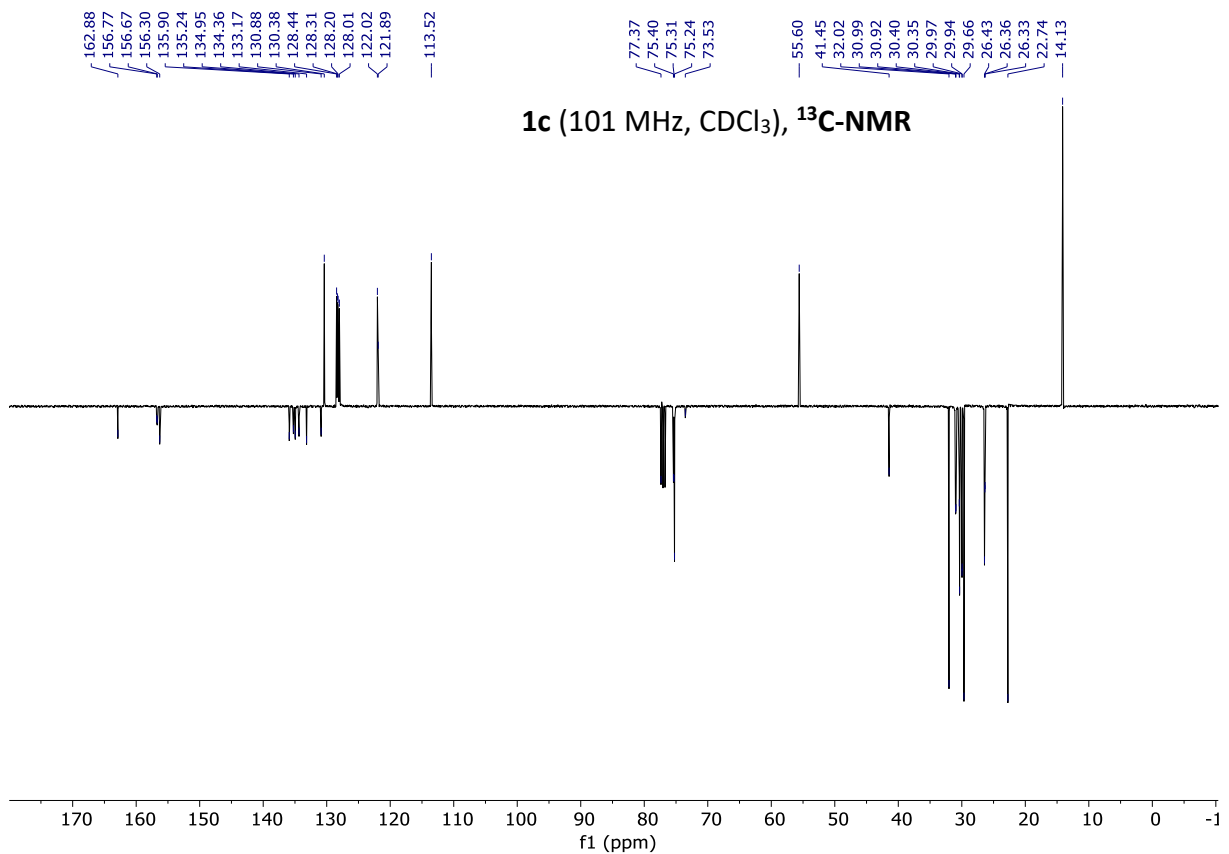
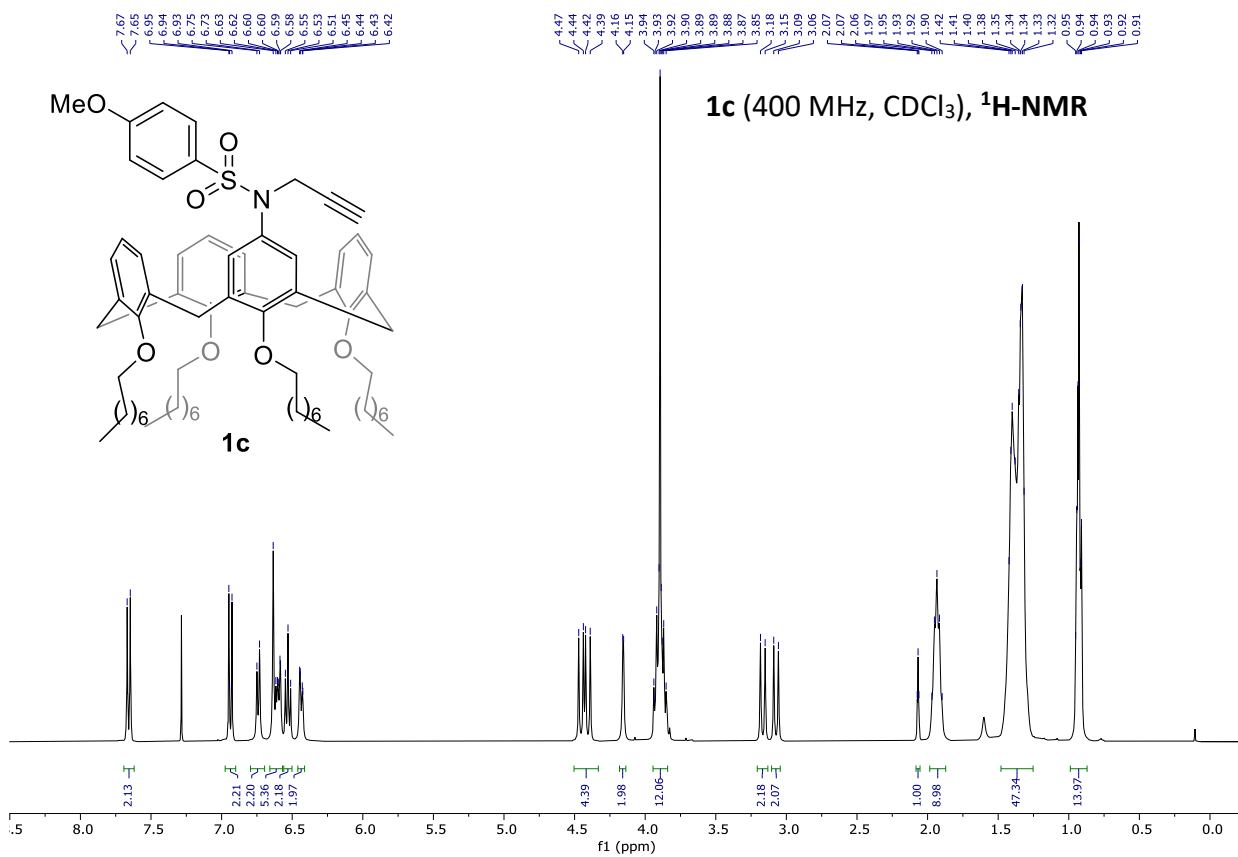


- NMR spectra of reagents:

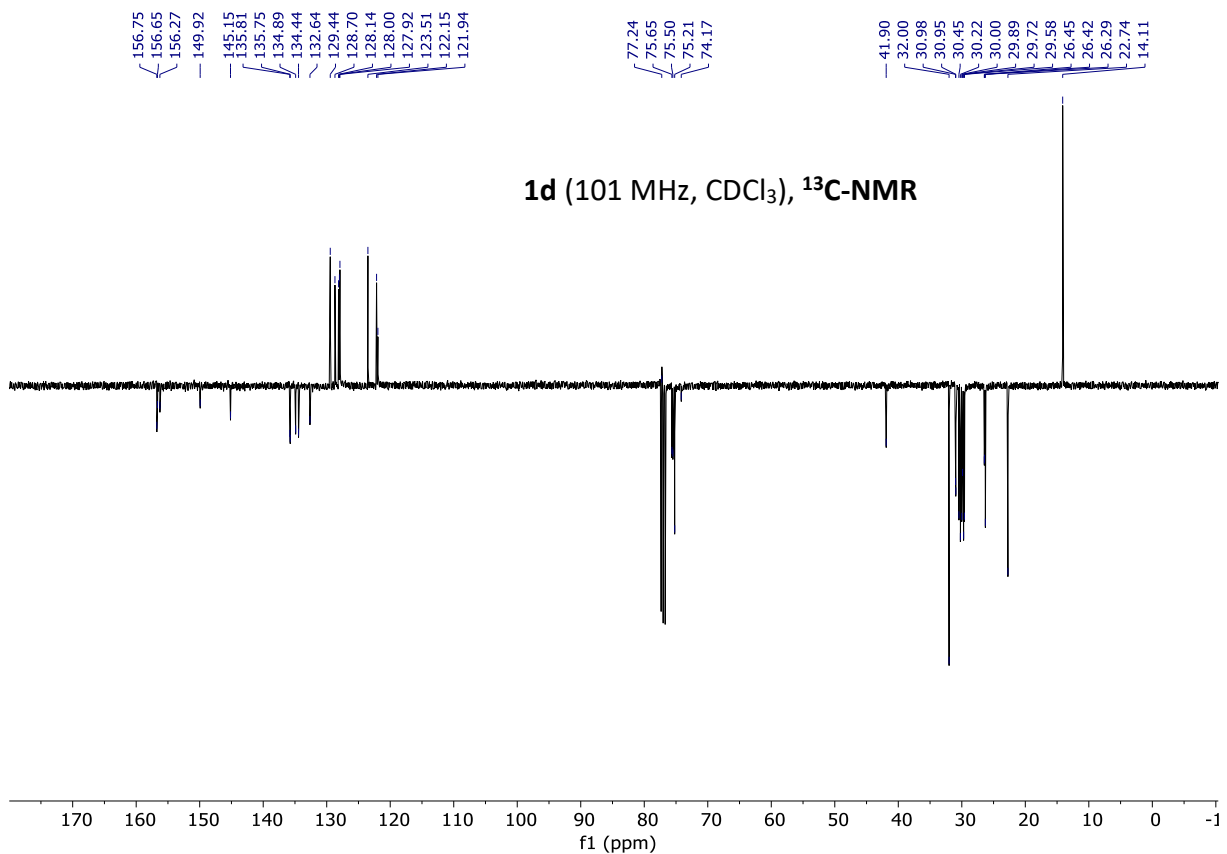
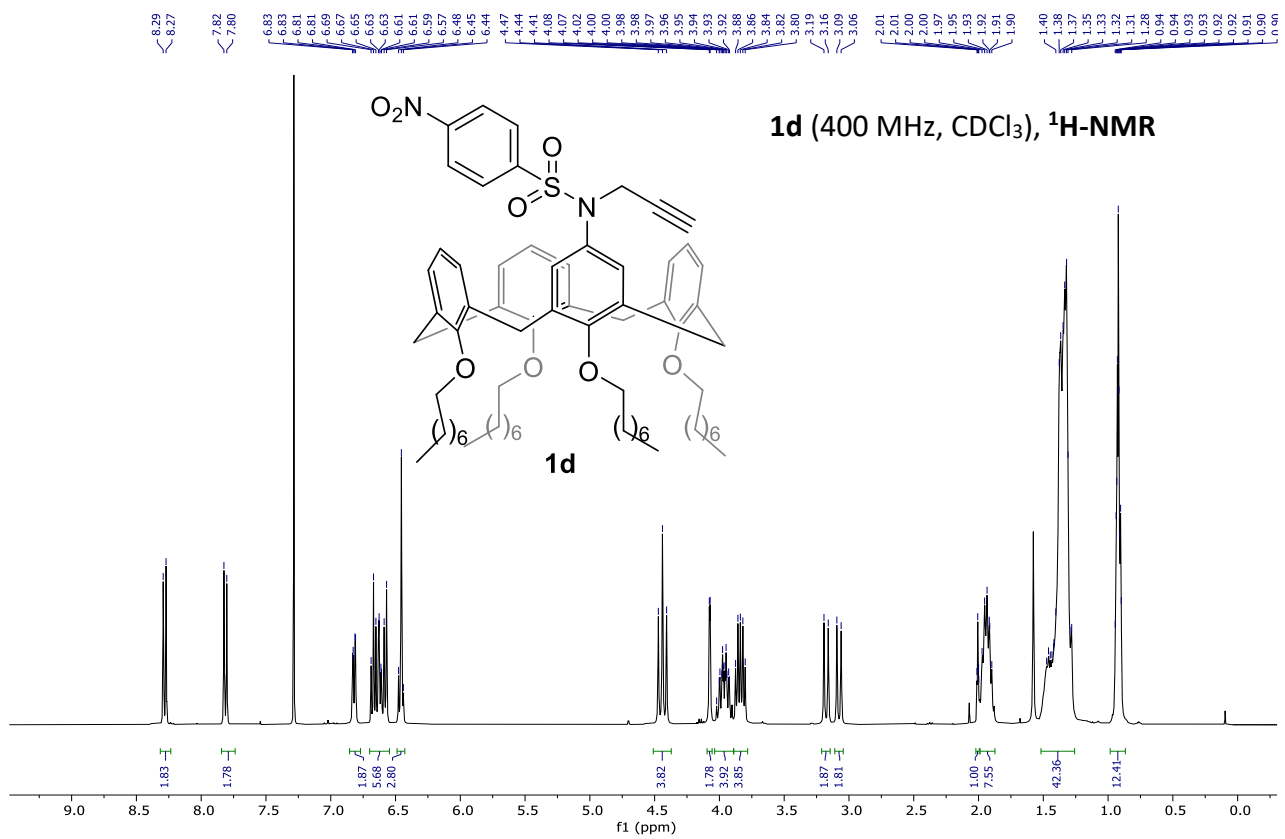
Substrate 1a:



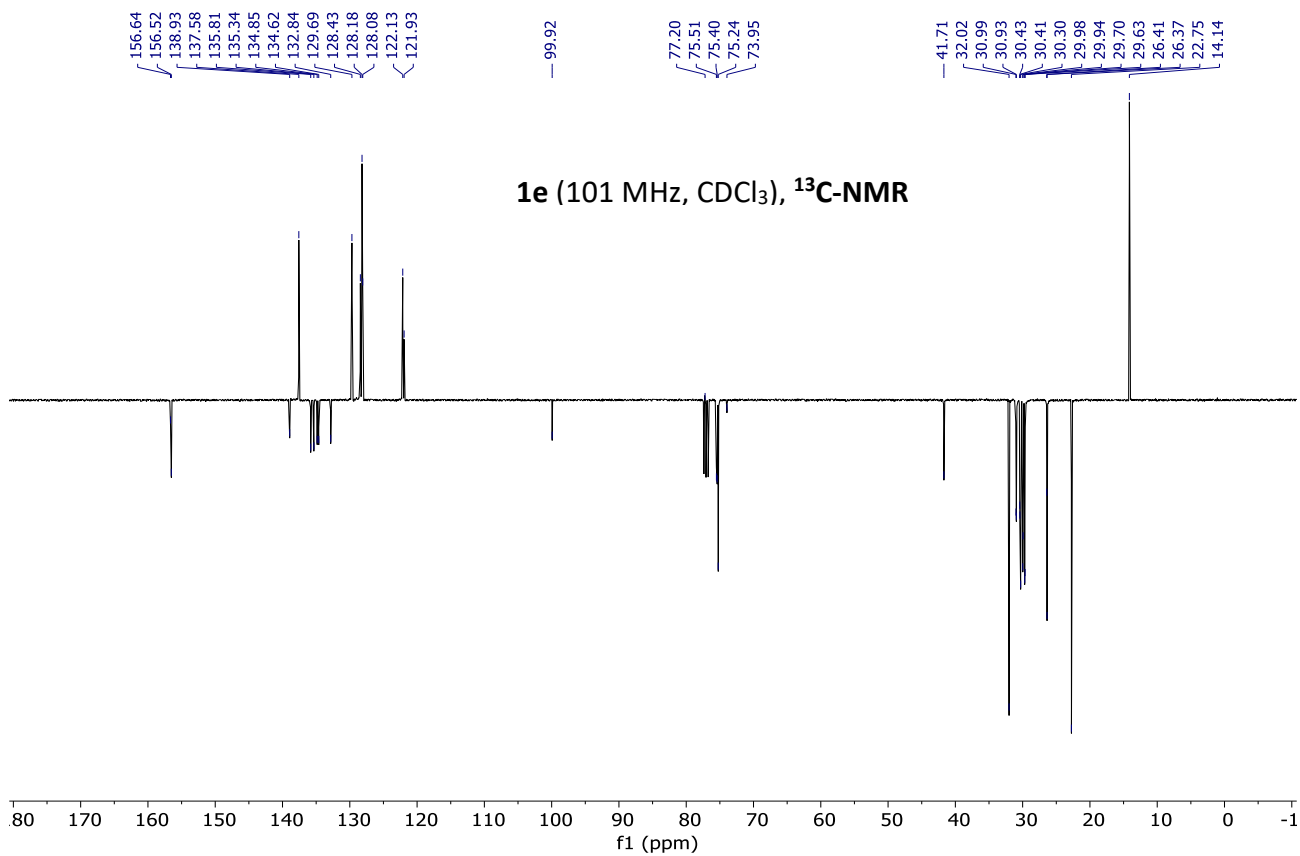
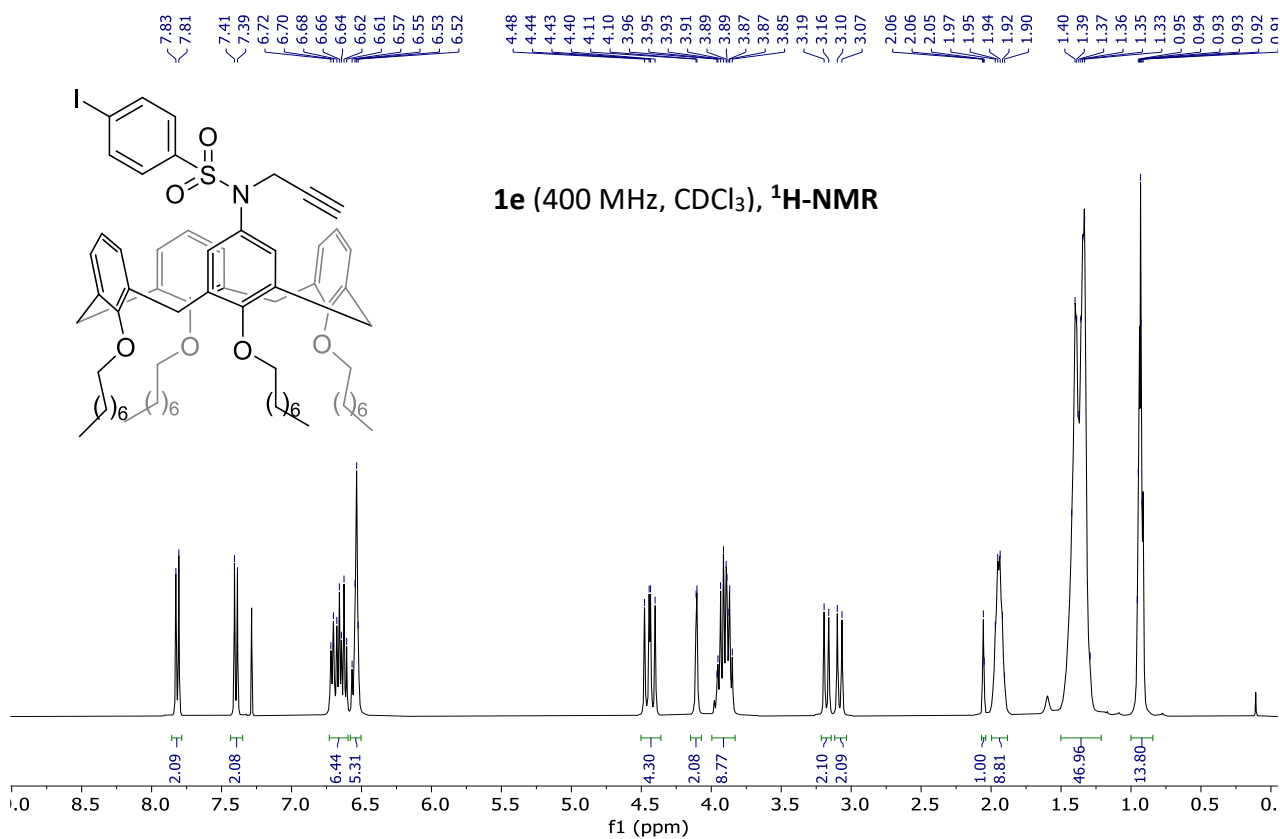
Substrate 1c:



Substrate 1d:

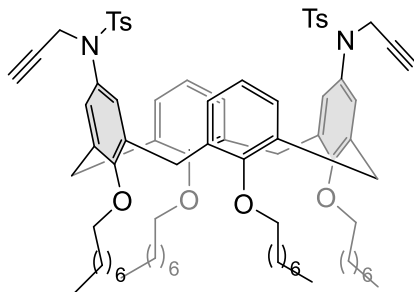


Substrate 1e:



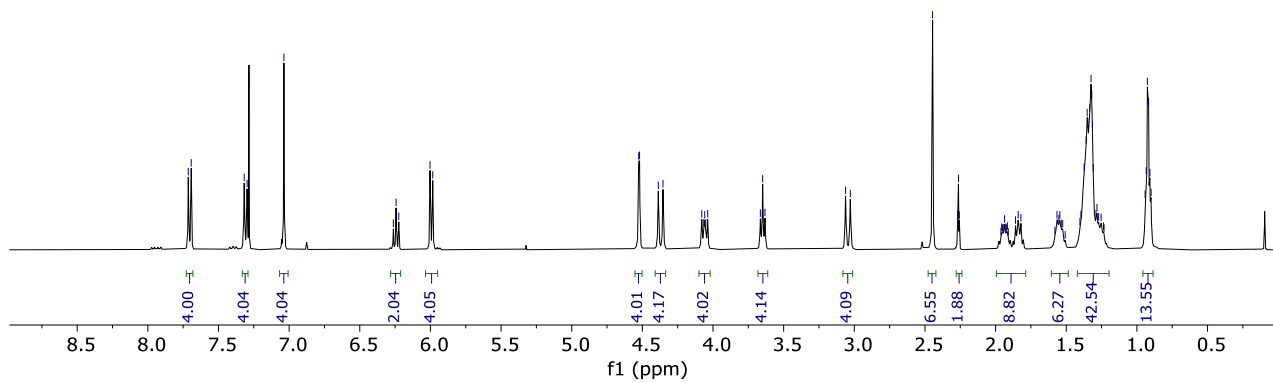
Substrate 3a:

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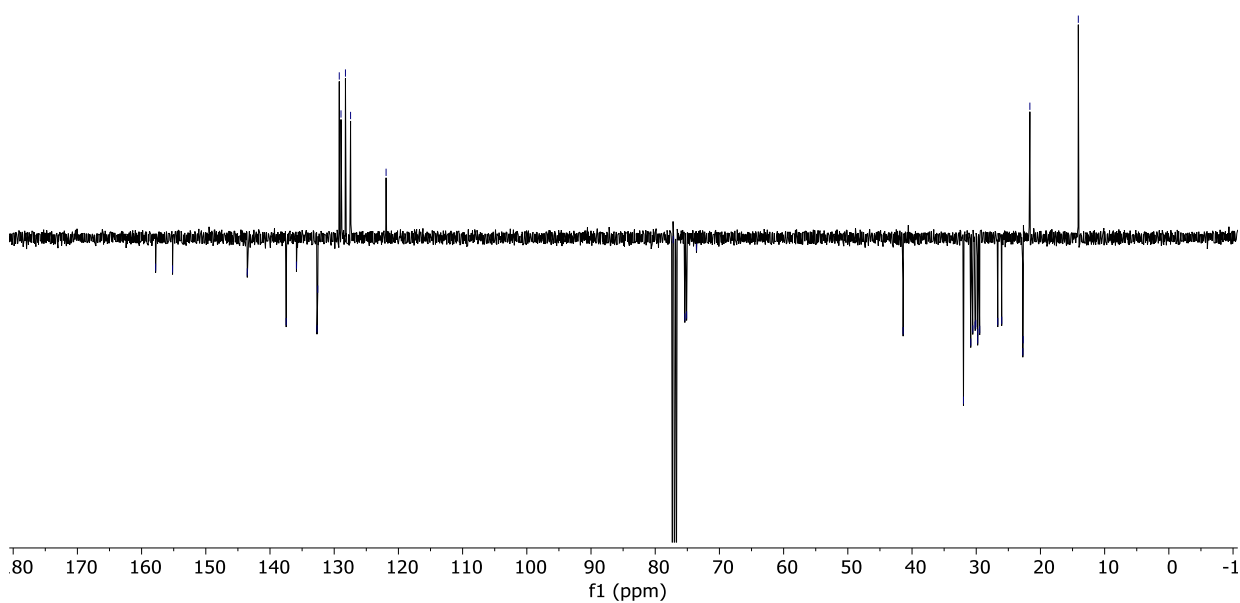
3a

3a (400 MHz, CDCl₃), ¹H-NMR

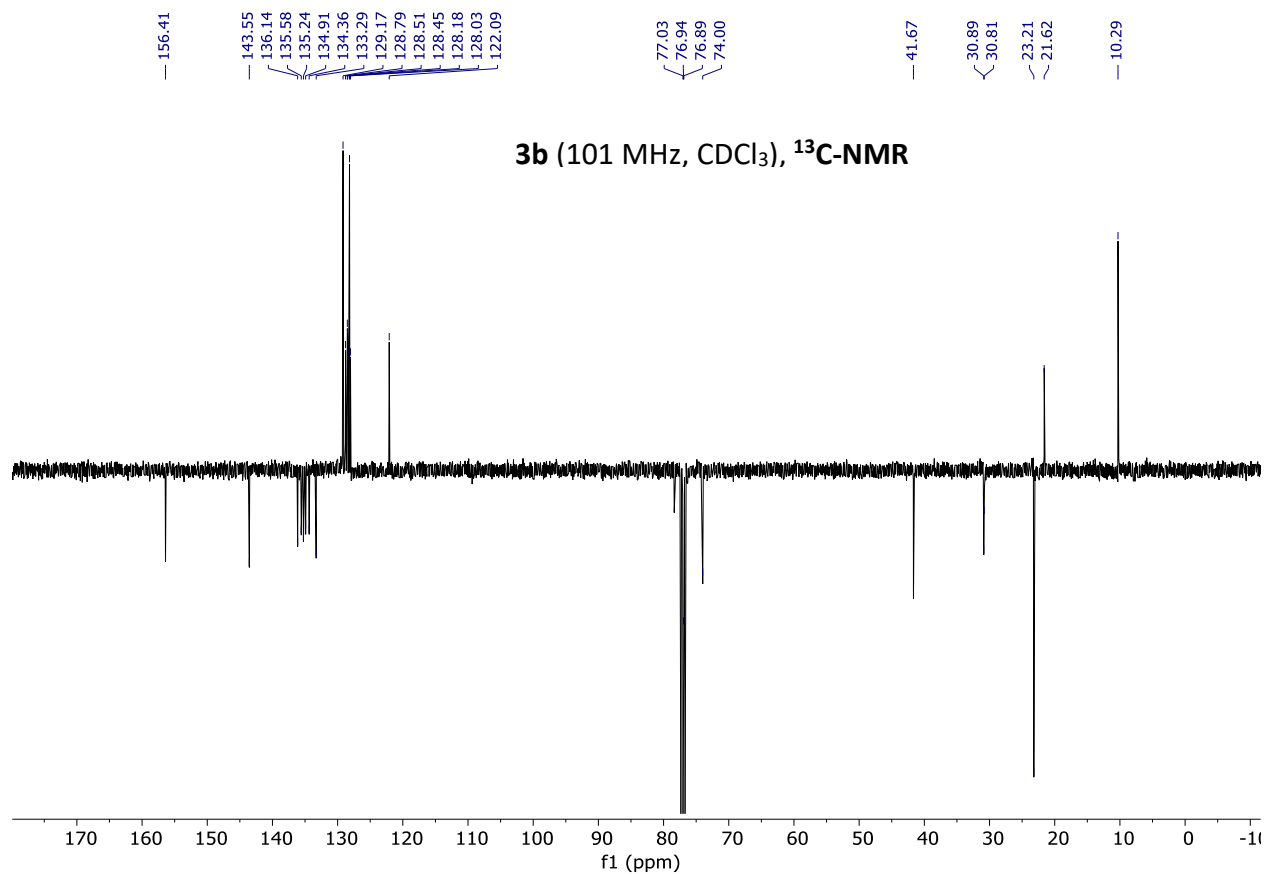
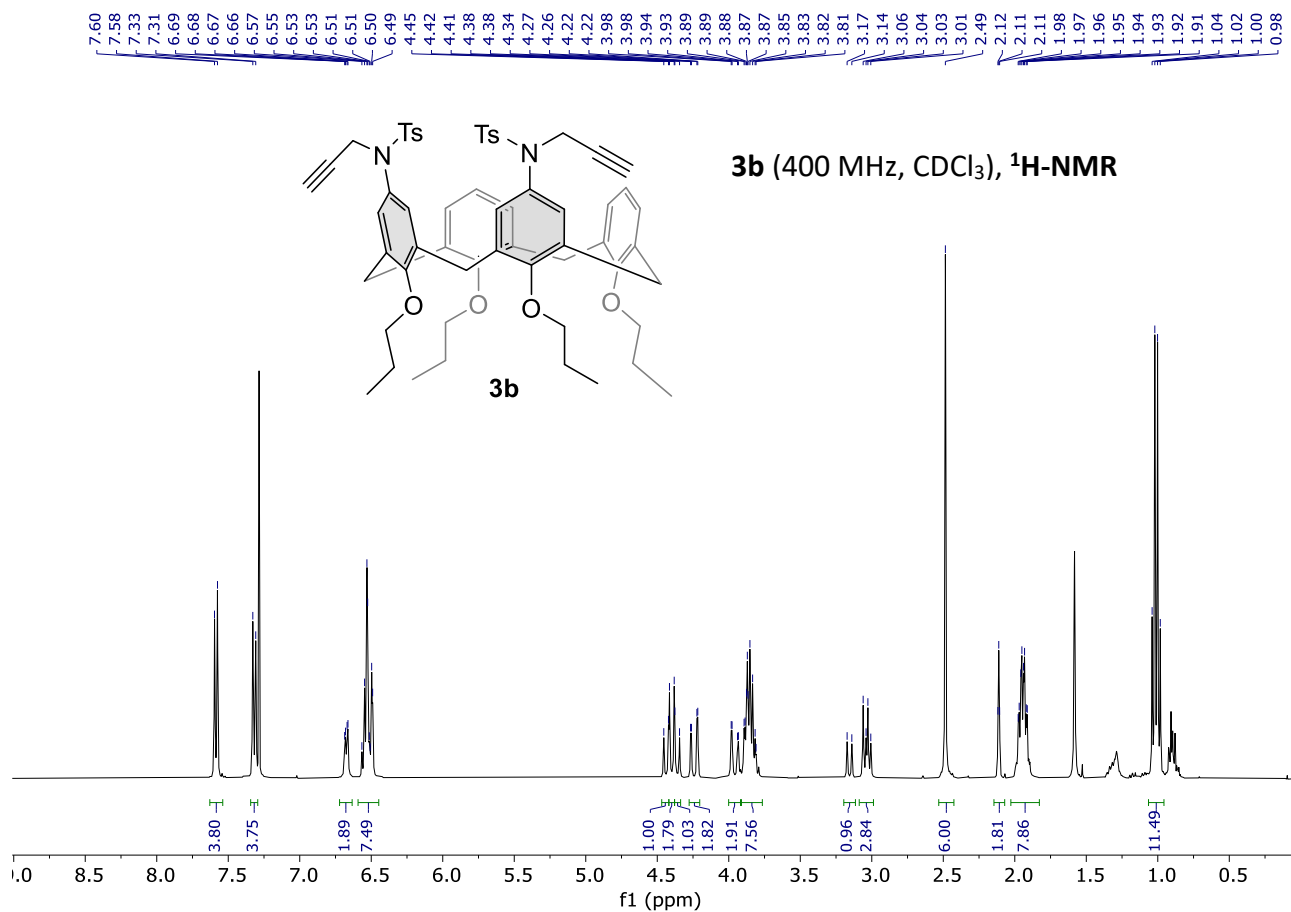


157.82 155.18 143.54 137.48 135.88 132.68 132.56 129.21 128.94 128.25 127.45 121.92 77.20 75.38 75.11 73.58 41.39 31.99 30.85 30.54 30.18 30.07 29.77 29.76 29.46 26.65 26.03 22.74 22.69 21.65 14.10

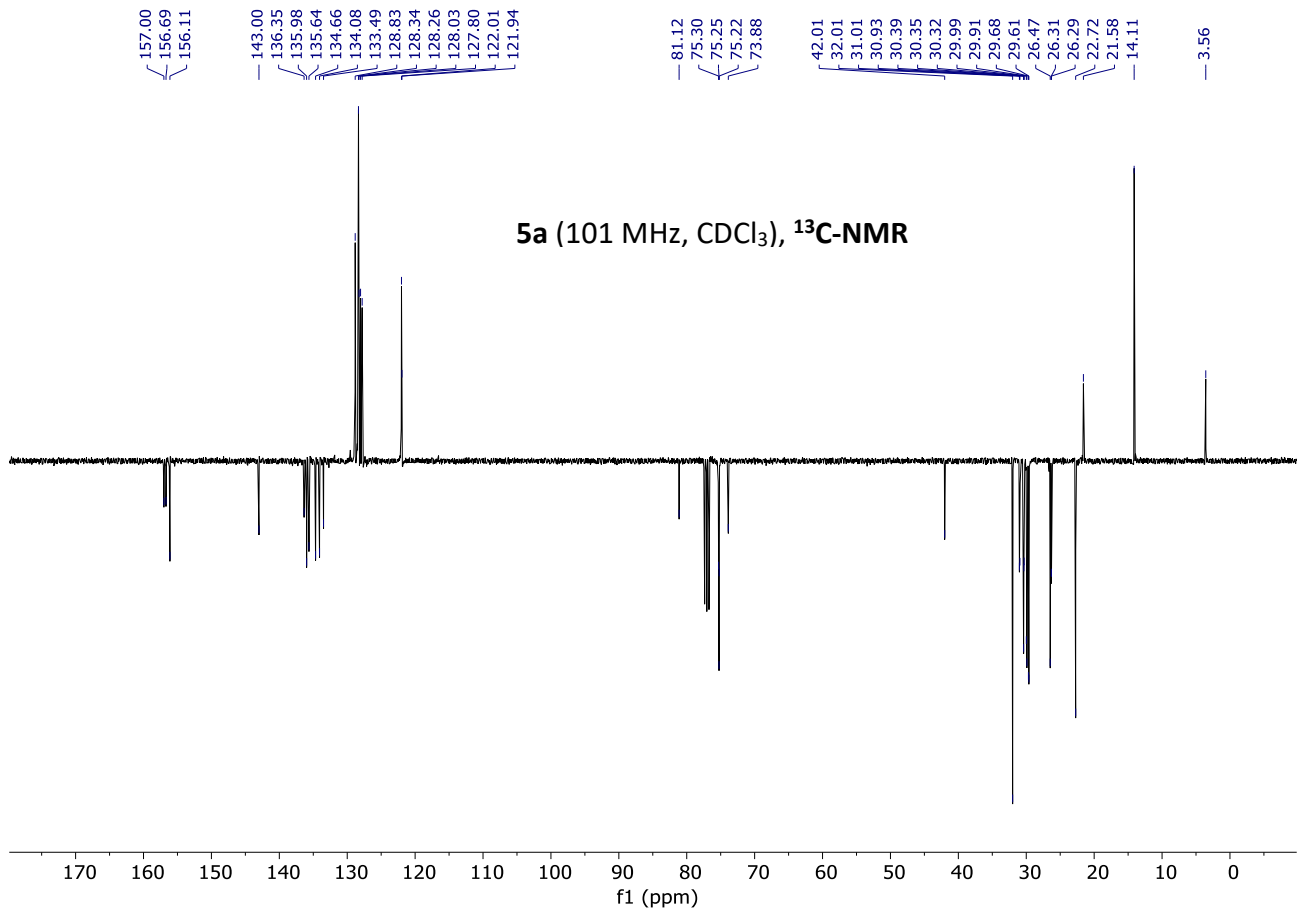
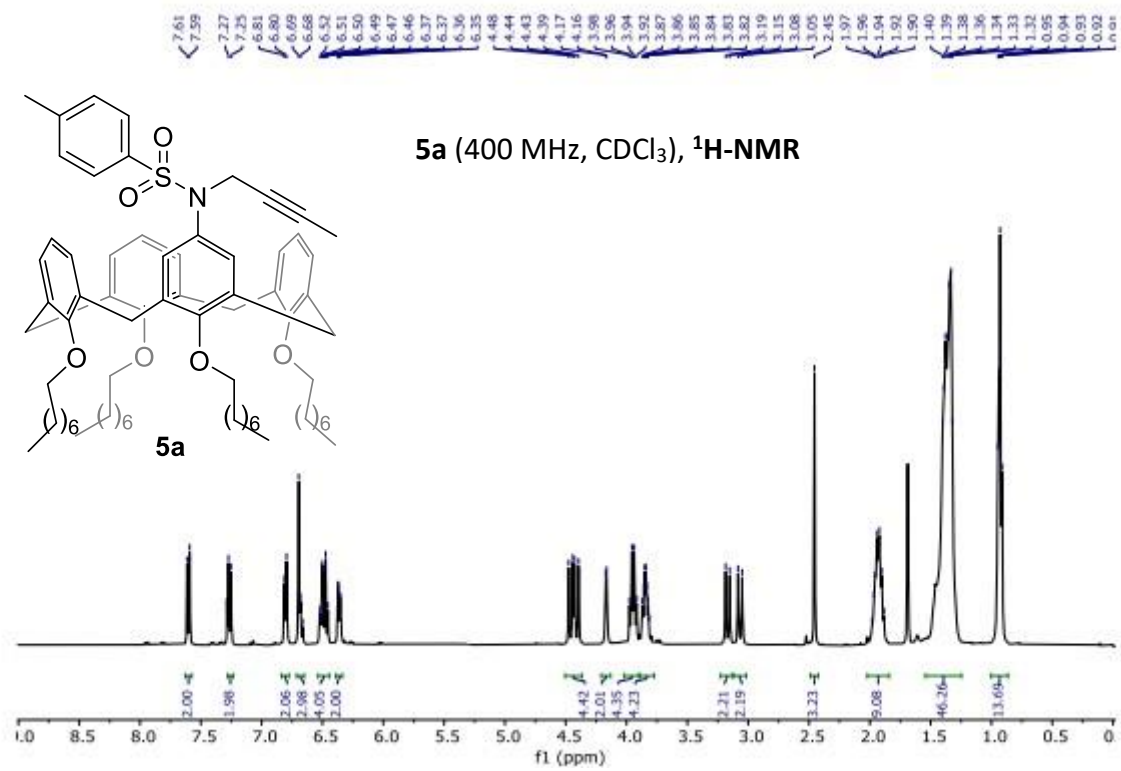
3a (101 MHz, CDCl₃), ¹³C-NMR



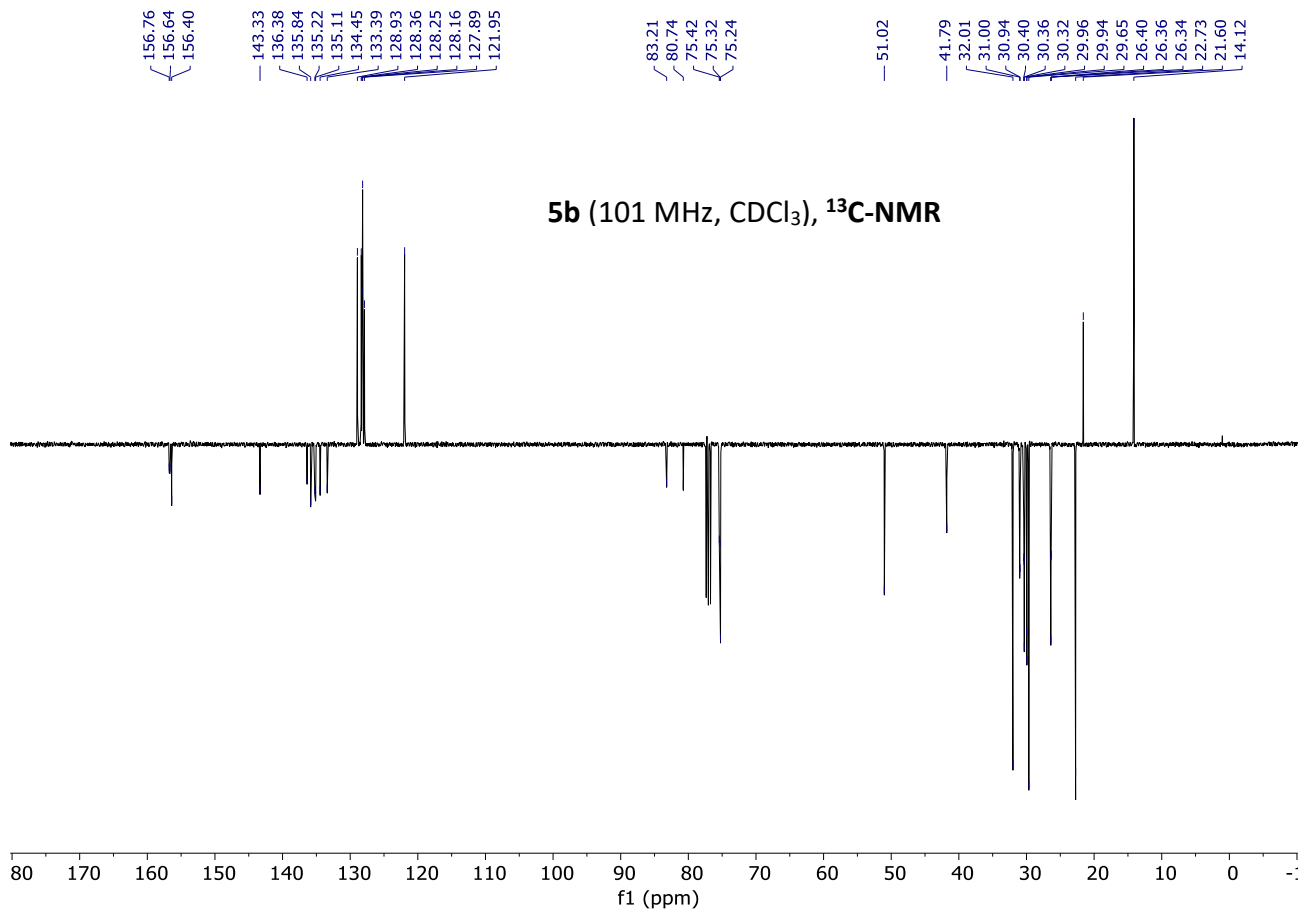
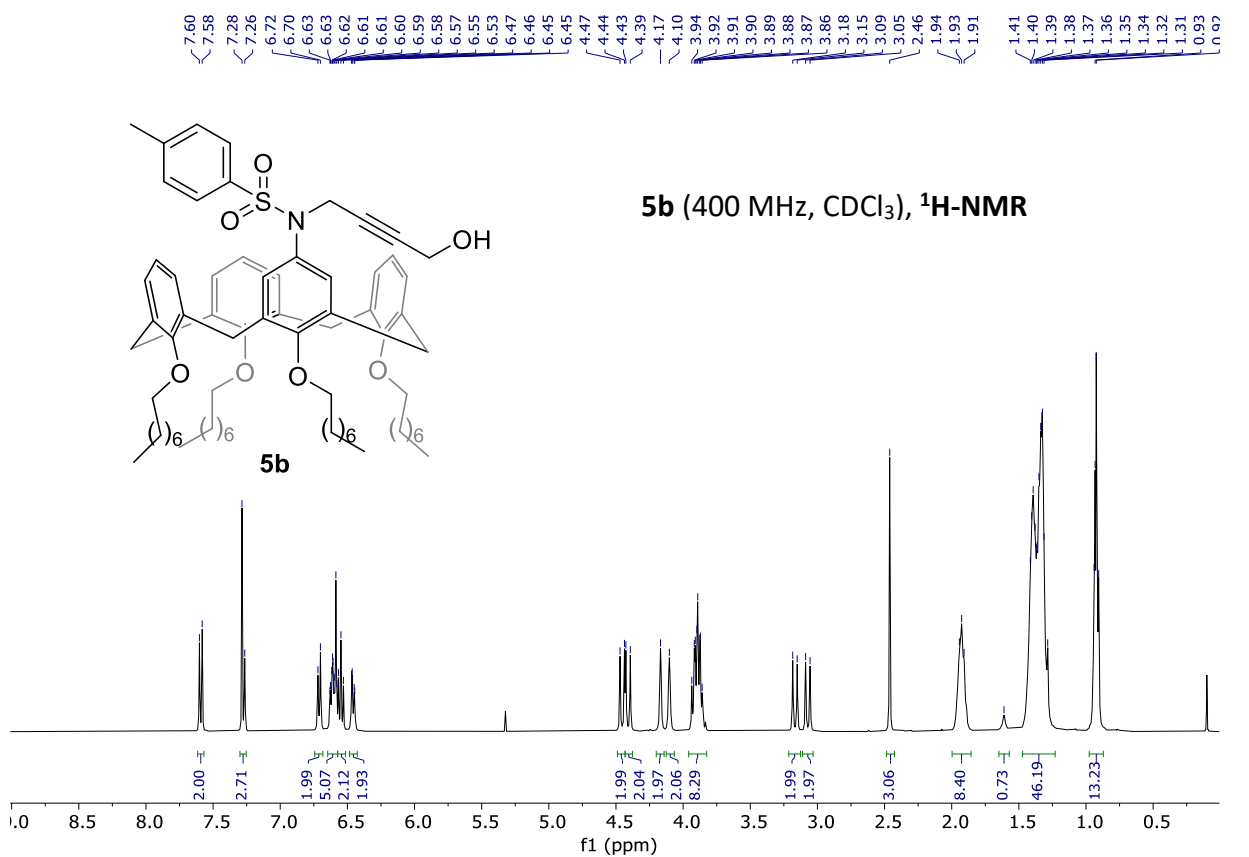
Substrate 3b:



Substrate 5a:

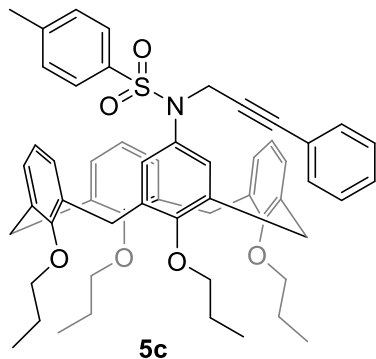


Substrate 5b:

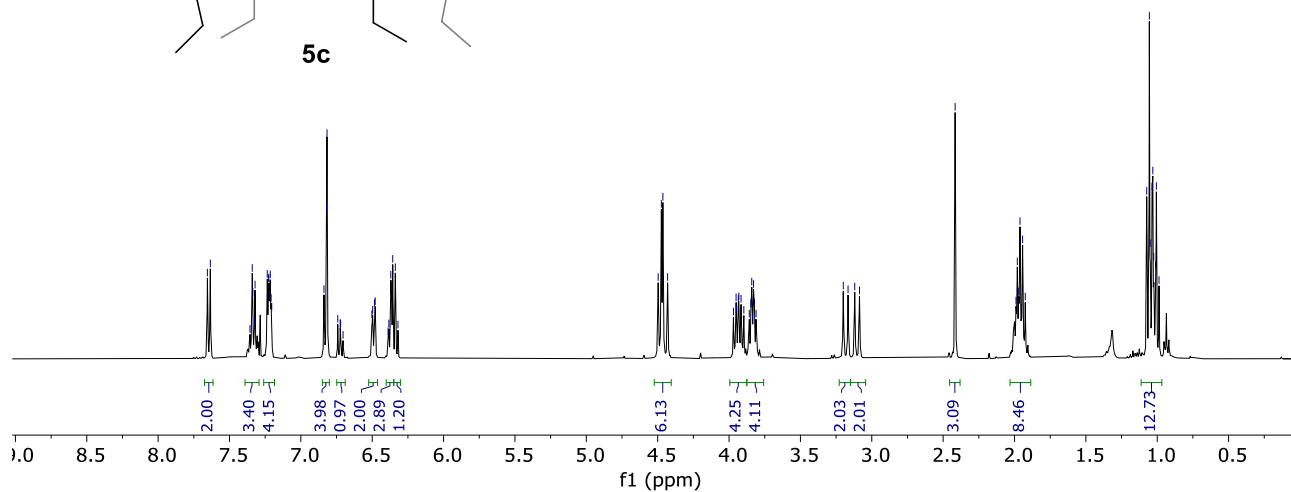


Substrate 5c:

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7.63
7.35
7.34
7.34
7.32
7.24
7.23
7.22
7.22
7.21
7.21
7.20
6.84
6.82
6.74
6.50
6.50
6.48
6.48
6.37
6.36
6.36
6.34
4.50
4.47
4.46
4.43
3.97
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3.95
3.93
3.93
3.92
3.91
3.90
3.86
3.85
3.84
3.84
3.83
3.82
3.81
3.20
3.17
3.12
3.09
2.42
1.99
1.98
1.97
1.96
1.95
1.94
1.92
1.07
1.06
1.05
1.04
1.03
1.02
1.01
1.01
0.99

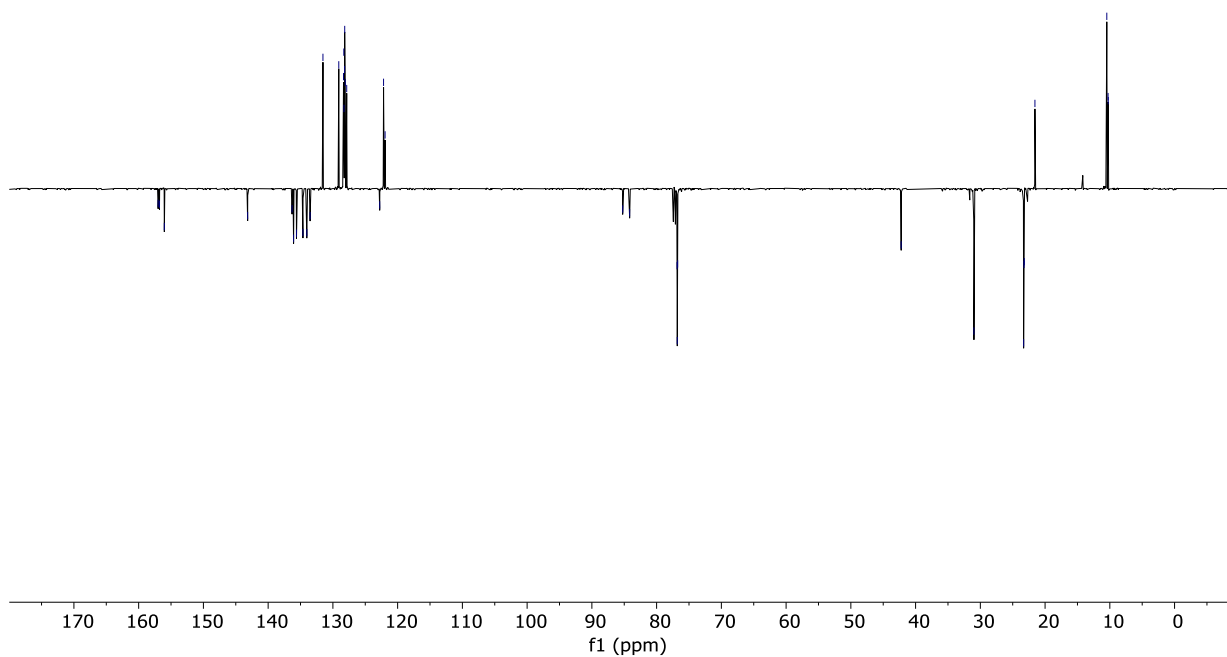


5c (400 MHz, CDCl₃), ¹H NMR

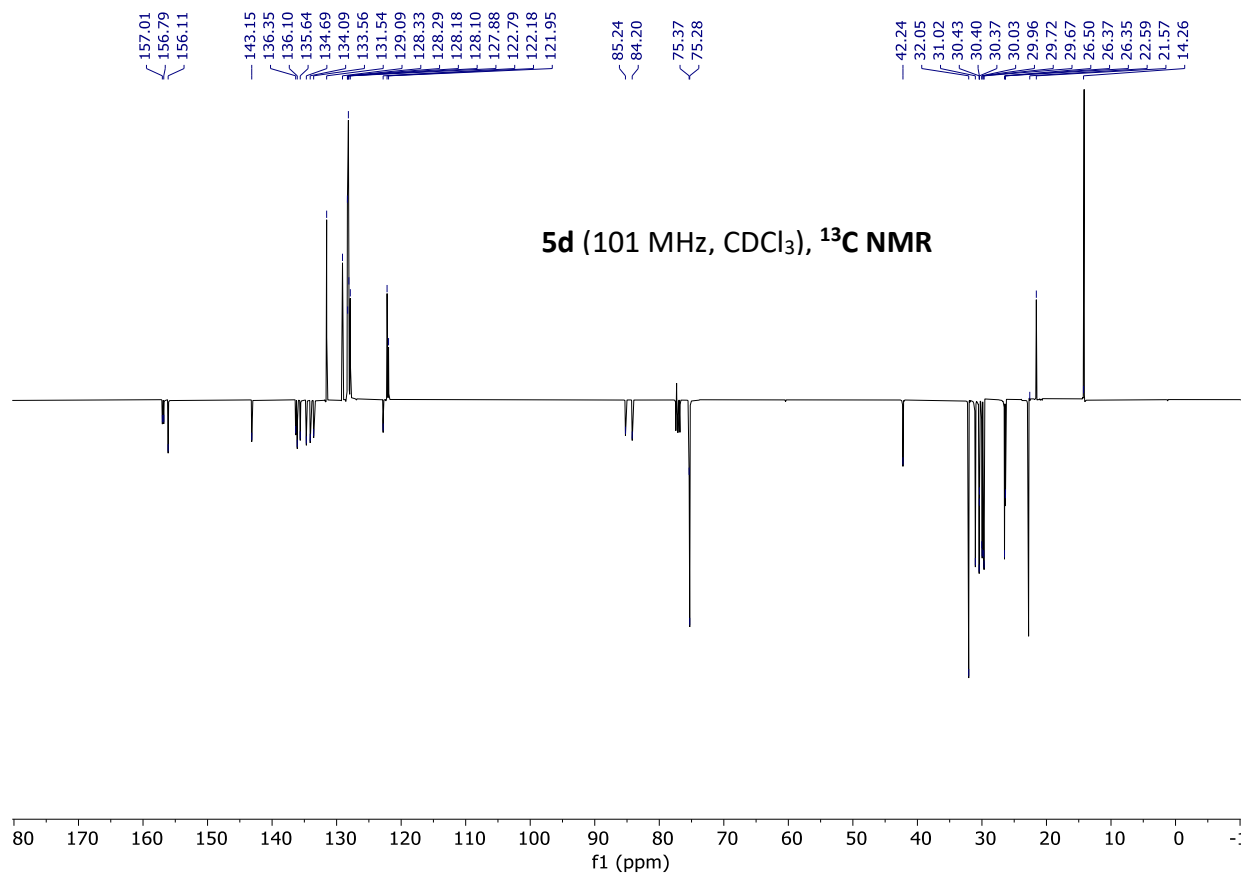
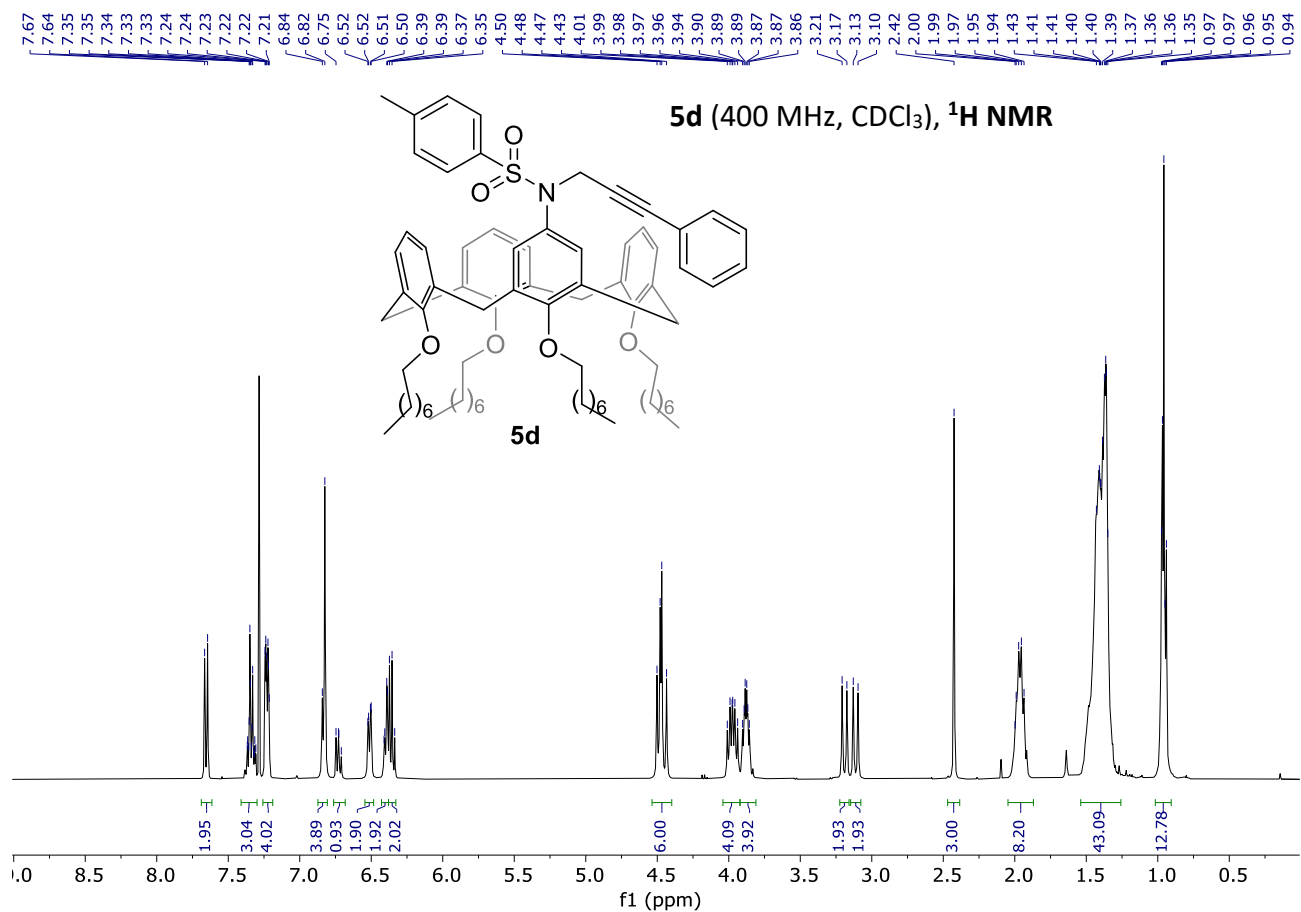


157.00
156.79
156.03
143.17
136.31
136.07
135.63
134.63
134.03
133.52
131.54
129.09
128.36
128.31
128.29
128.19
128.18
128.09
127.86
122.77
122.17
121.94
85.24
84.17
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23.21
21.57
10.47
10.27
10.24

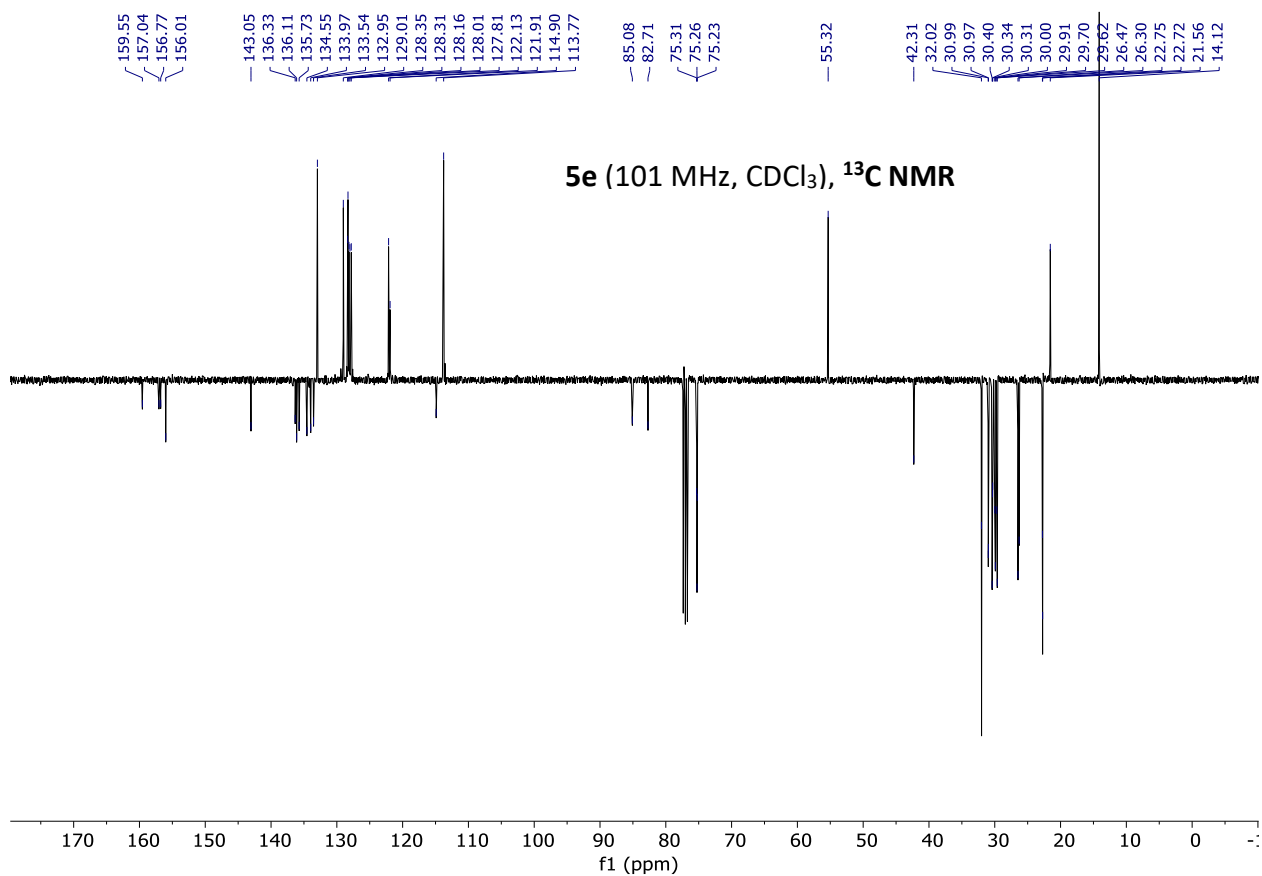
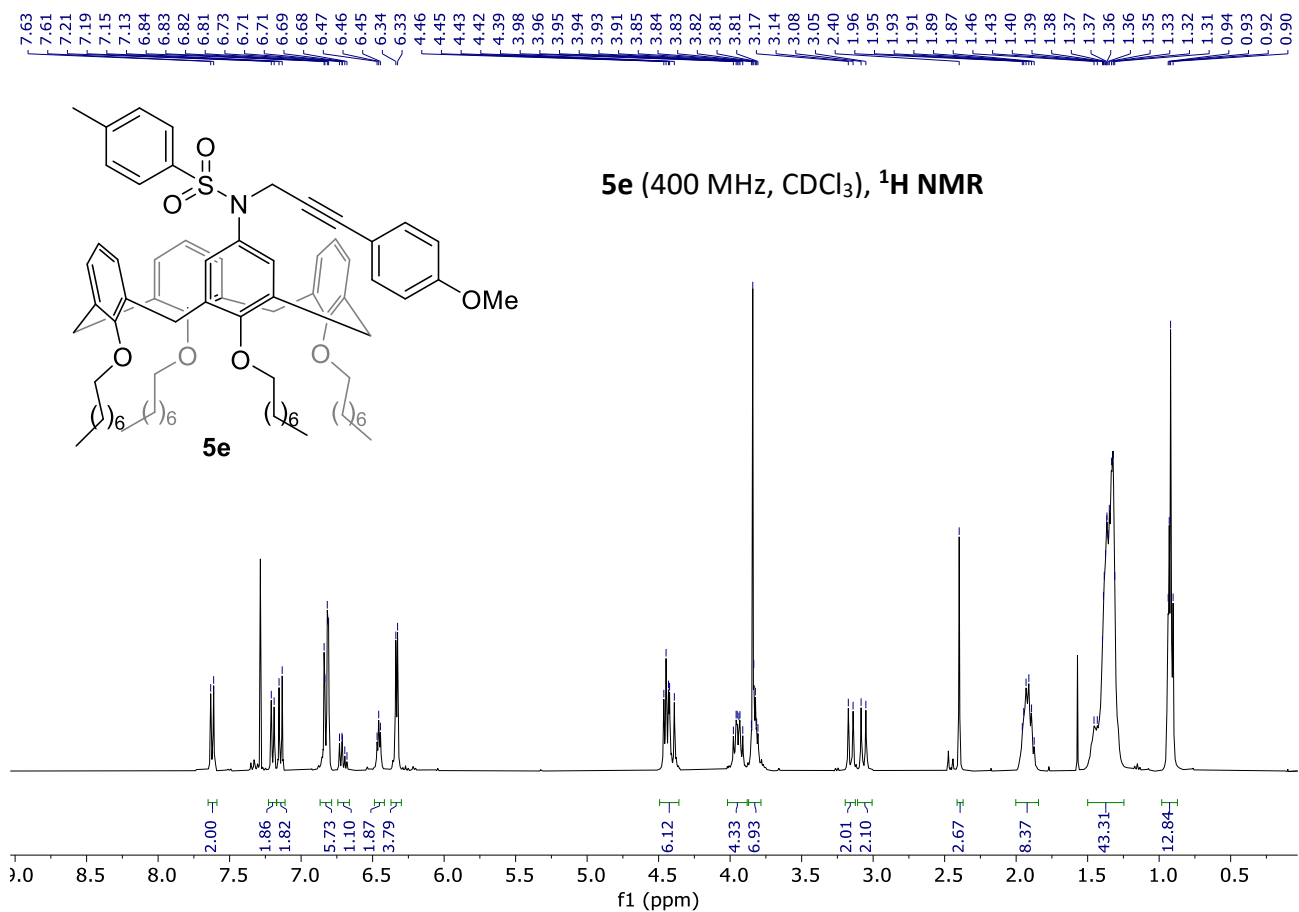
5c (101 MHz, CDCl₃), ¹³C NMR



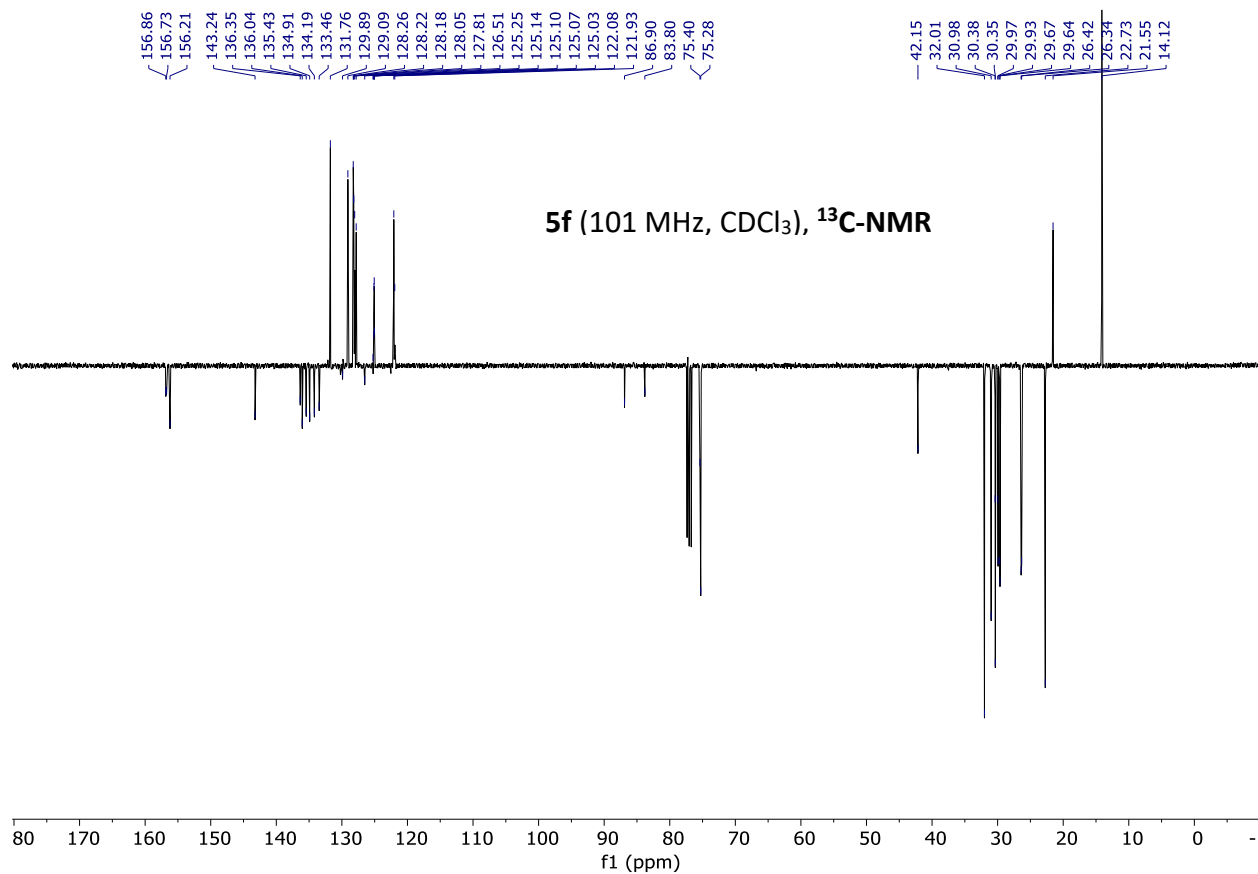
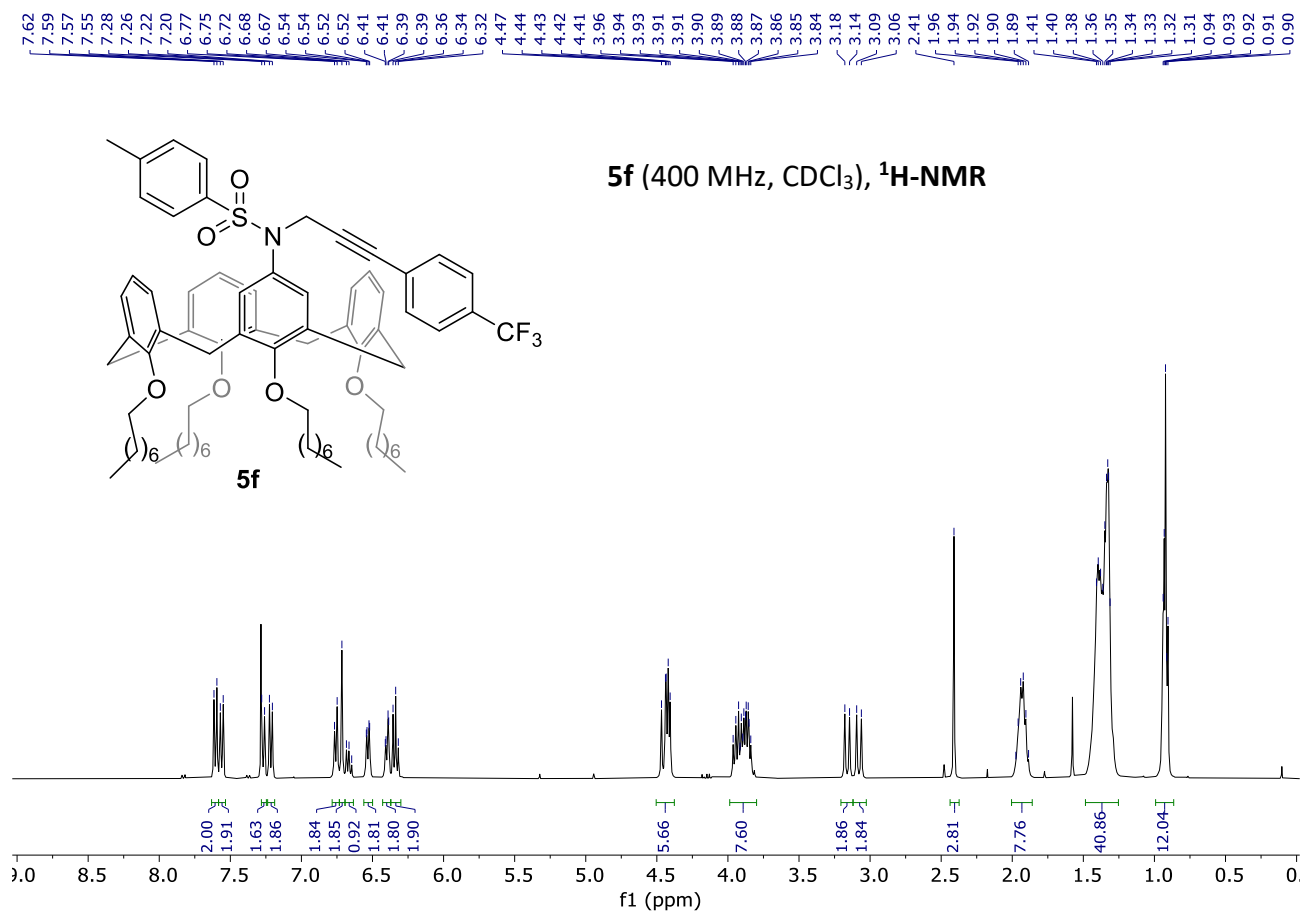
Substrate 5d:



Substrate 5e:

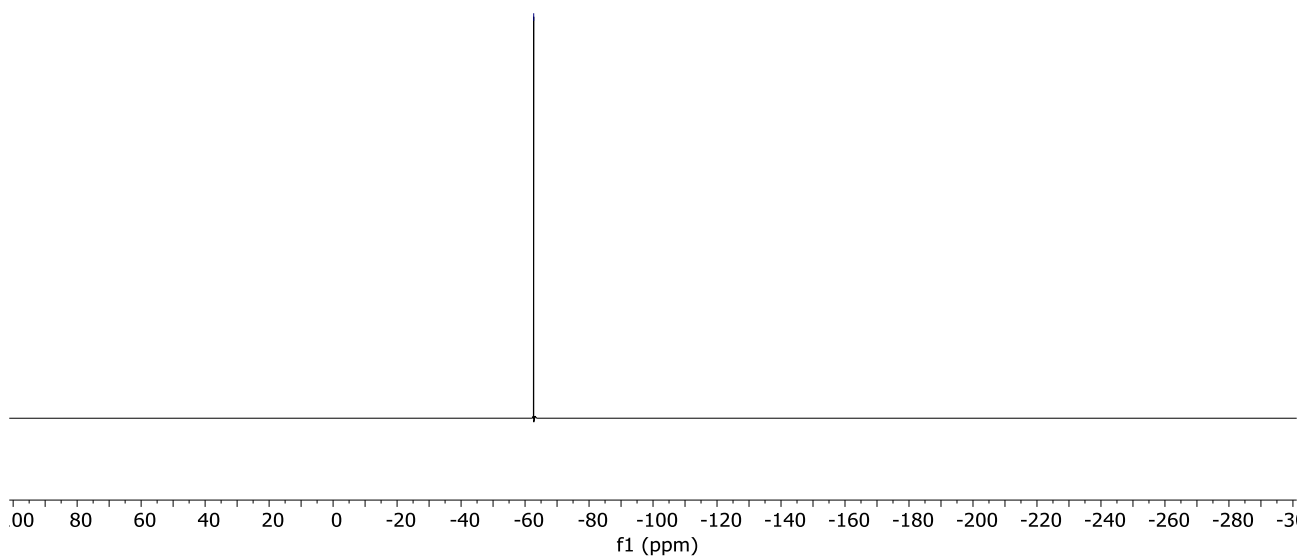


Substrate 5f:



-62.70

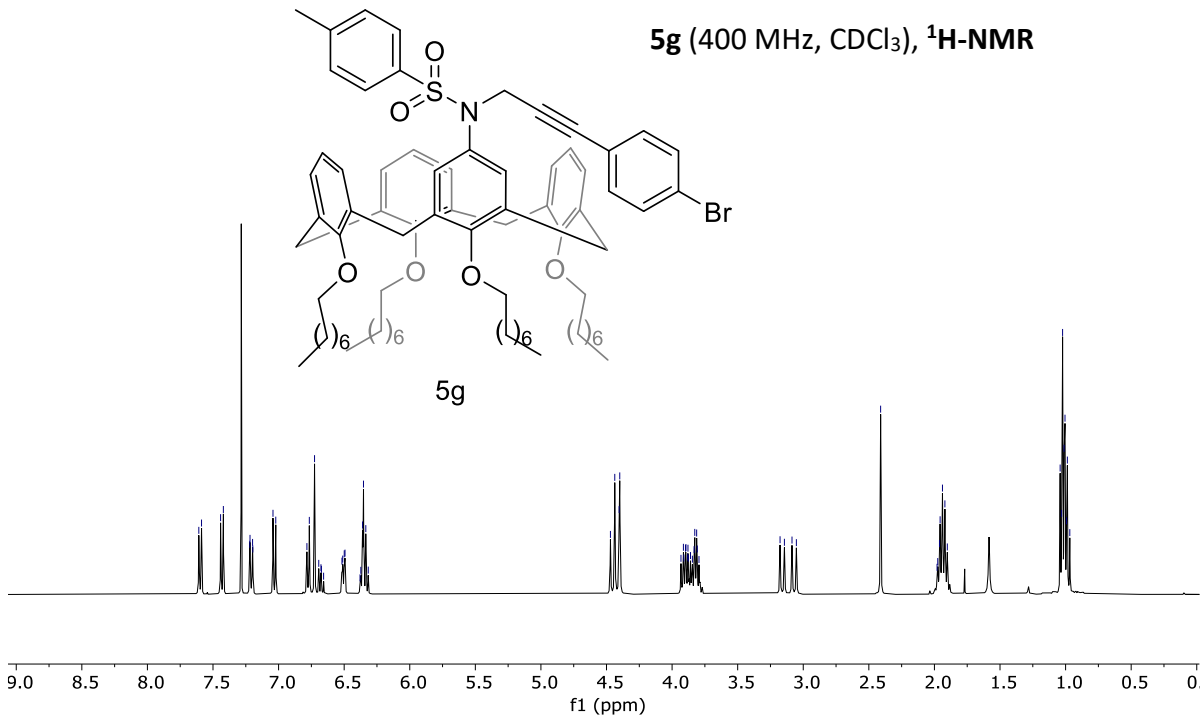
5f (565 MHz, CDCl₃), ¹⁹F-NMR



Substrate 5g:

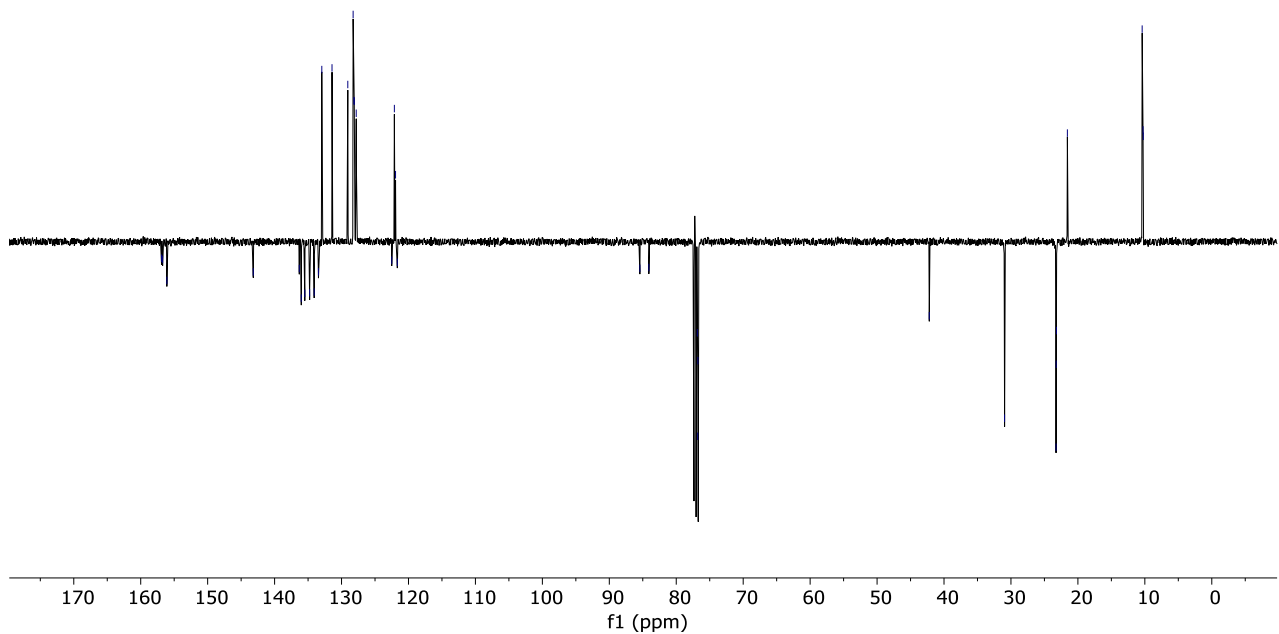
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5g (400 MHz, CDCl₃), ¹H-NMR

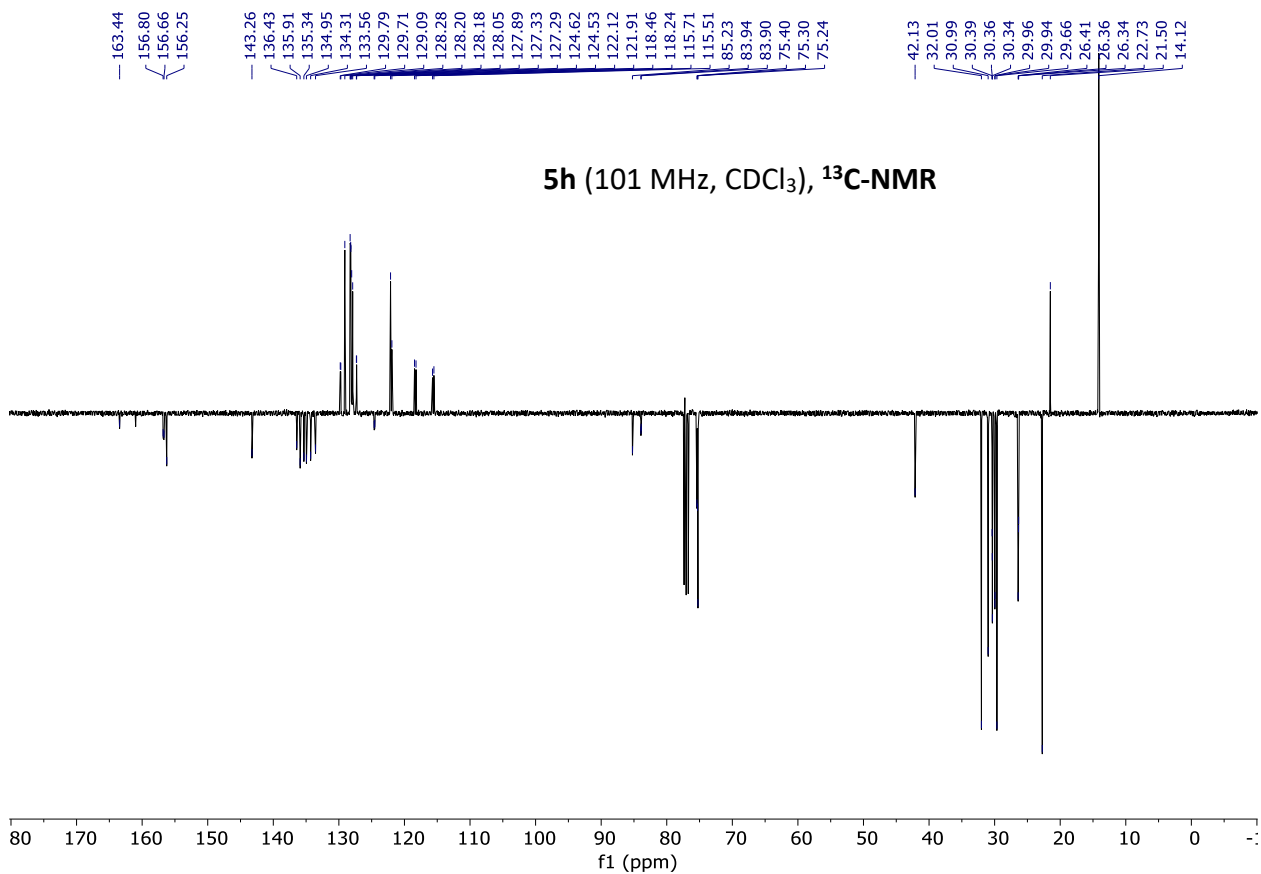
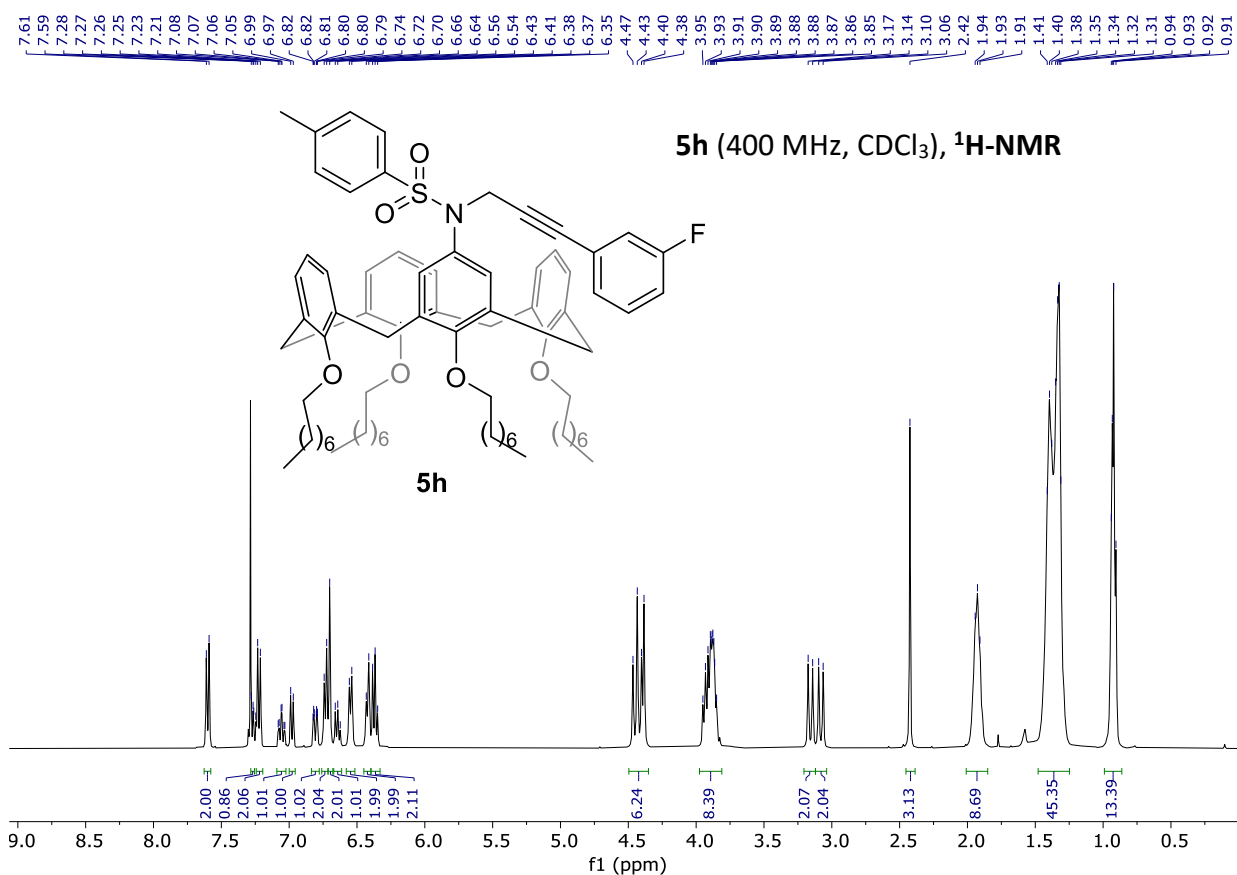


156.89, 156.73, 156.10, 143.19, 136.31, 135.49, 134.77, 134.09, 133.45, 132.95, 131.42, 129.06, 128.27, 128.14, 128.10, 127.81, 122.50, 122.11, 121.93, 121.67, 85.44, 84.09, 76.85, 76.79, 76.76, 42.20, 30.96, 23.26, 23.25, 23.20, 21.57, 10.40, 10.27, 10.23

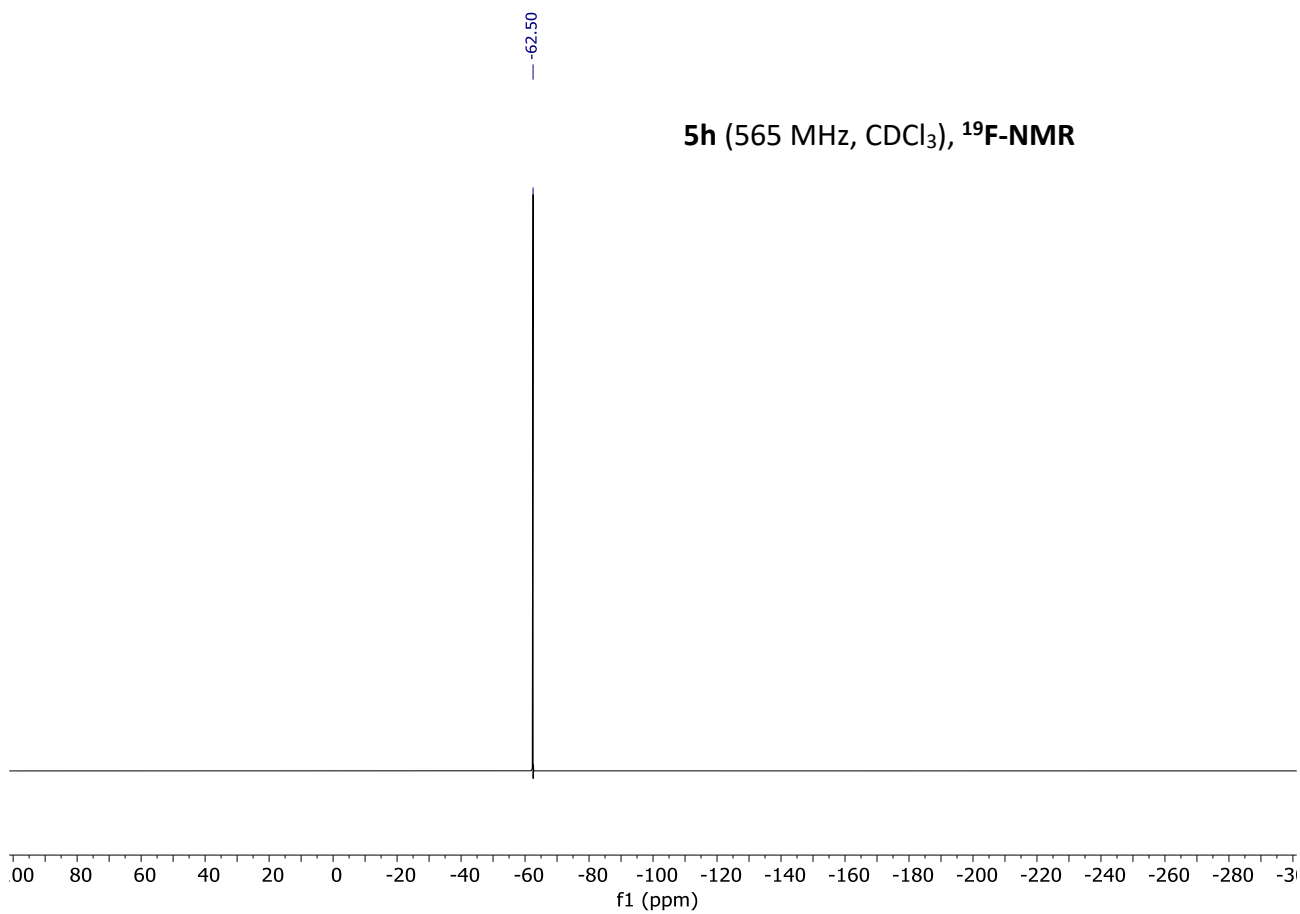
5g (101 MHz, CDCl₃), ¹³C-NMR



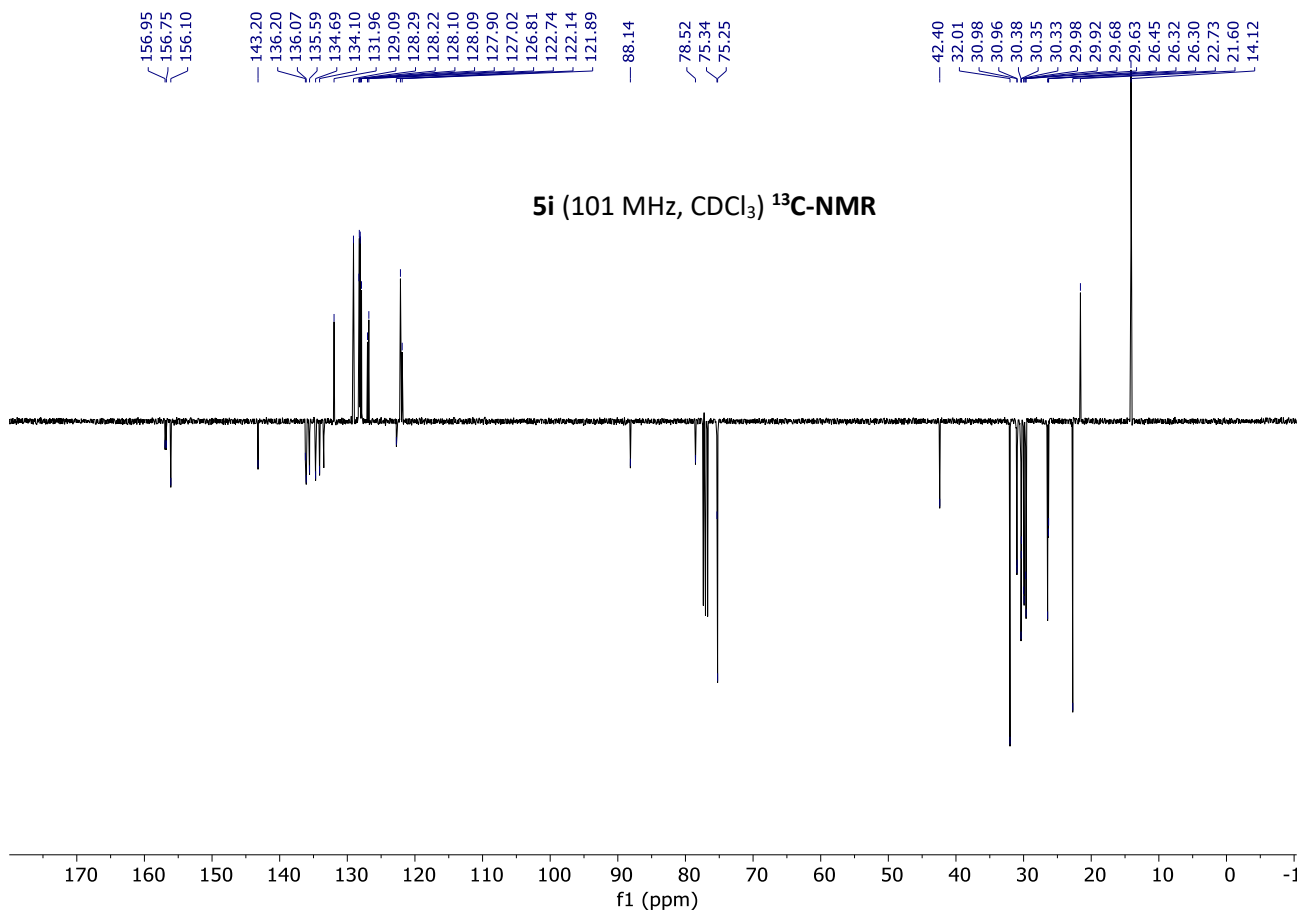
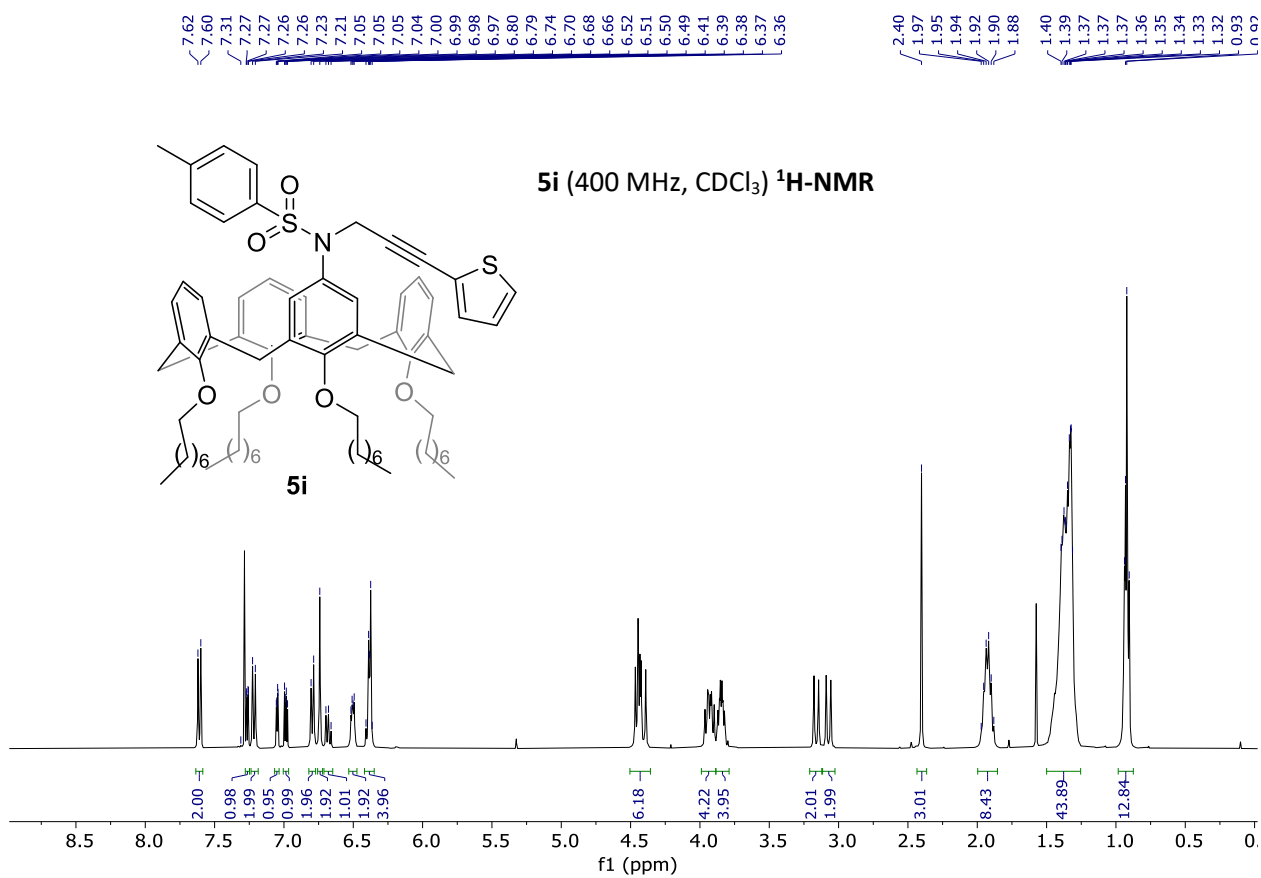
Substrate 5h:



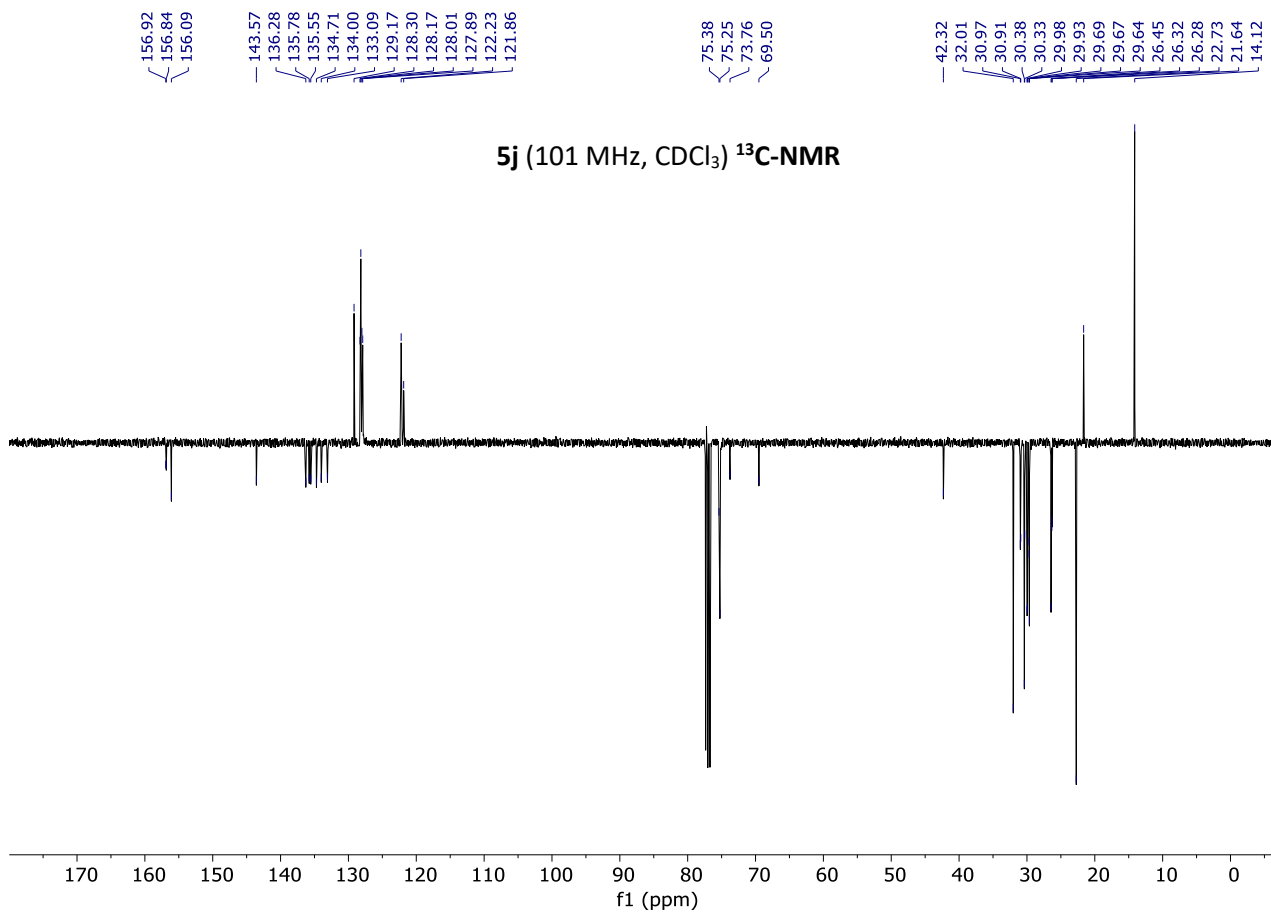
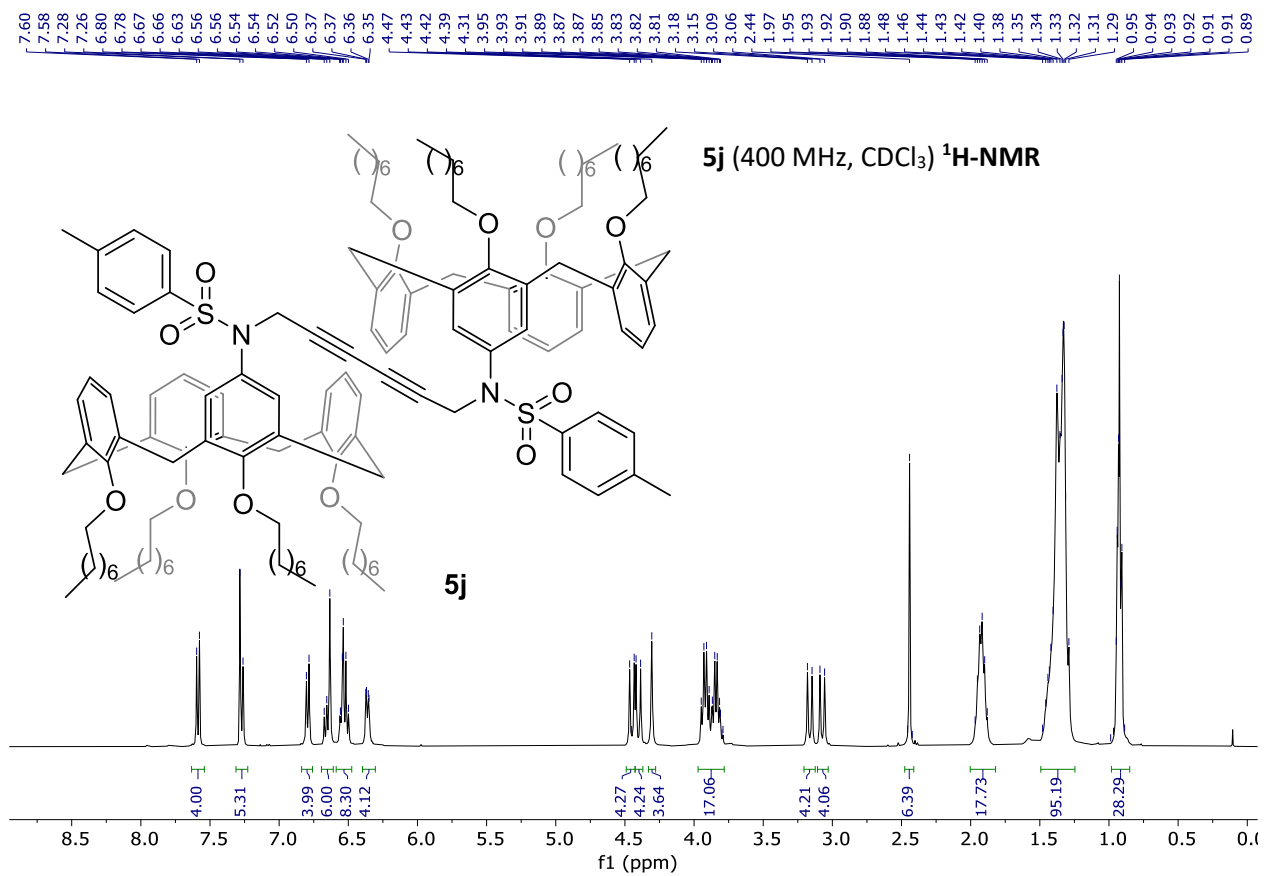
5h (565 MHz, CDCl₃), ¹⁹F-NMR



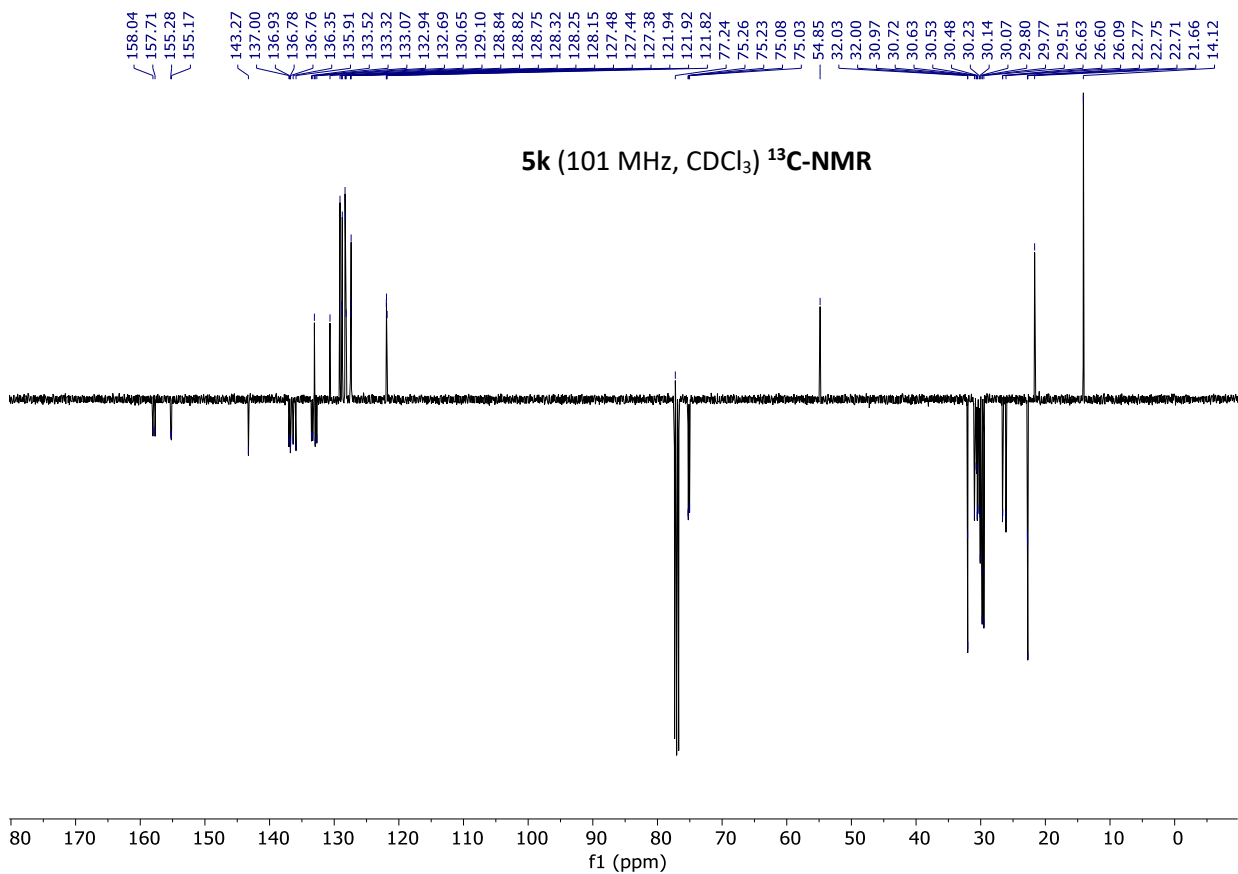
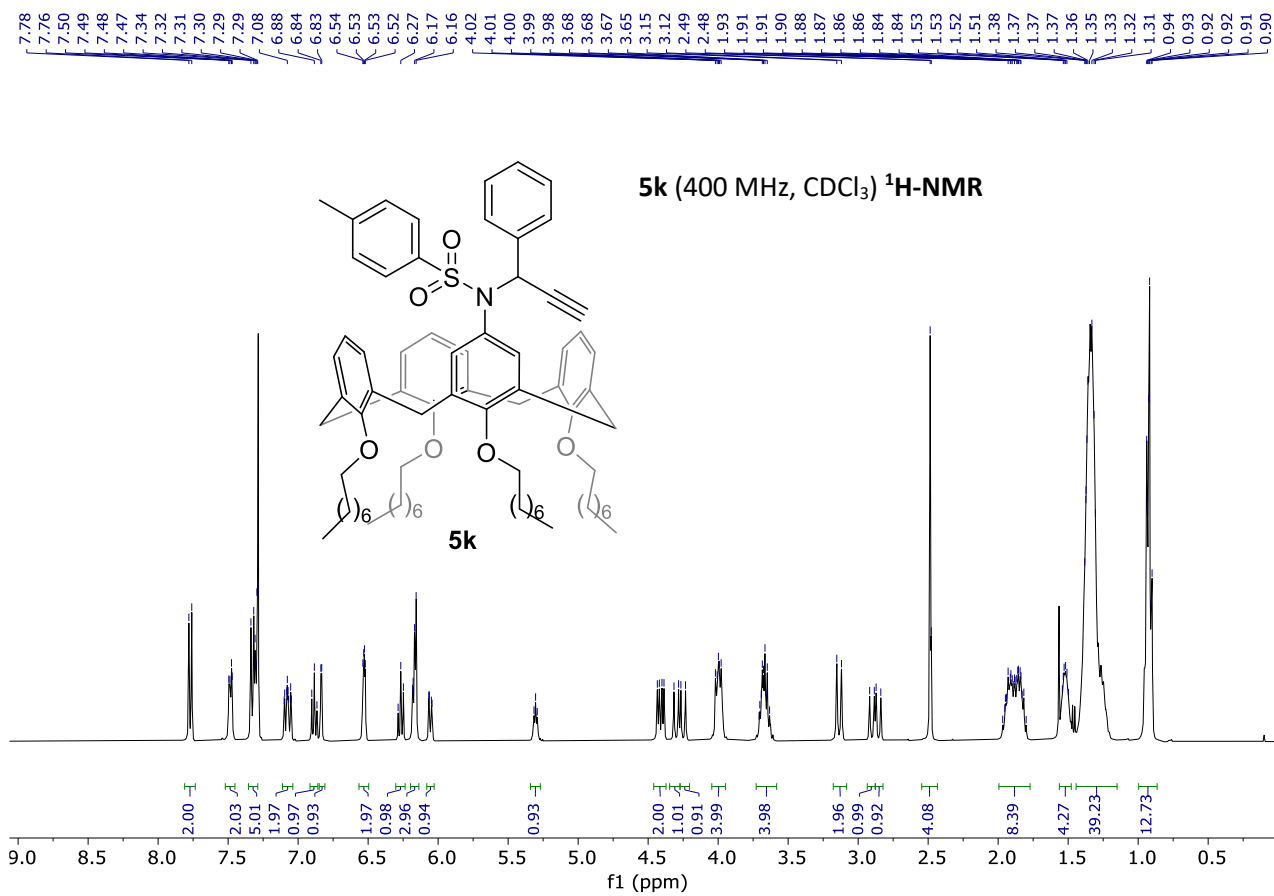
Substrate 5i:



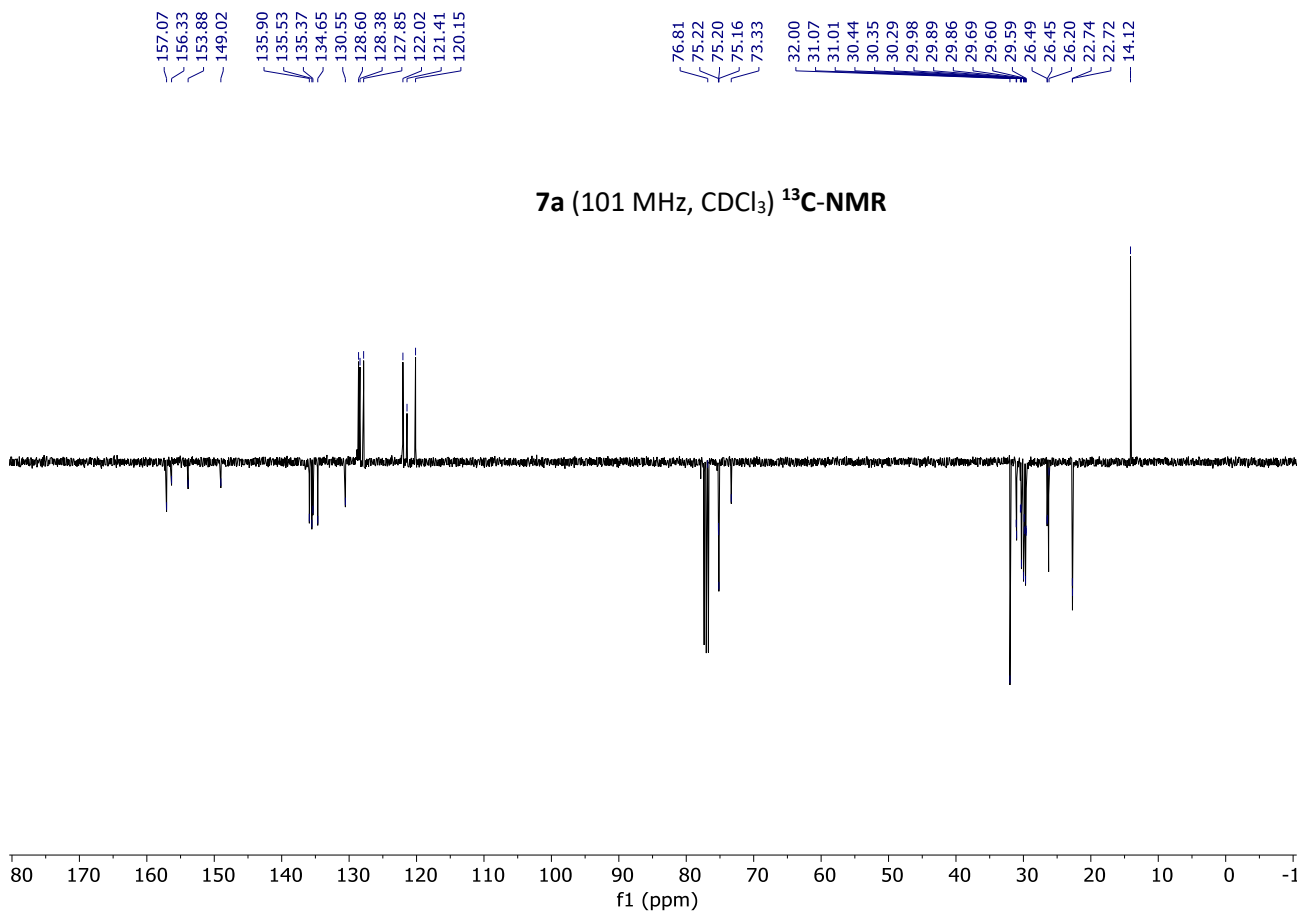
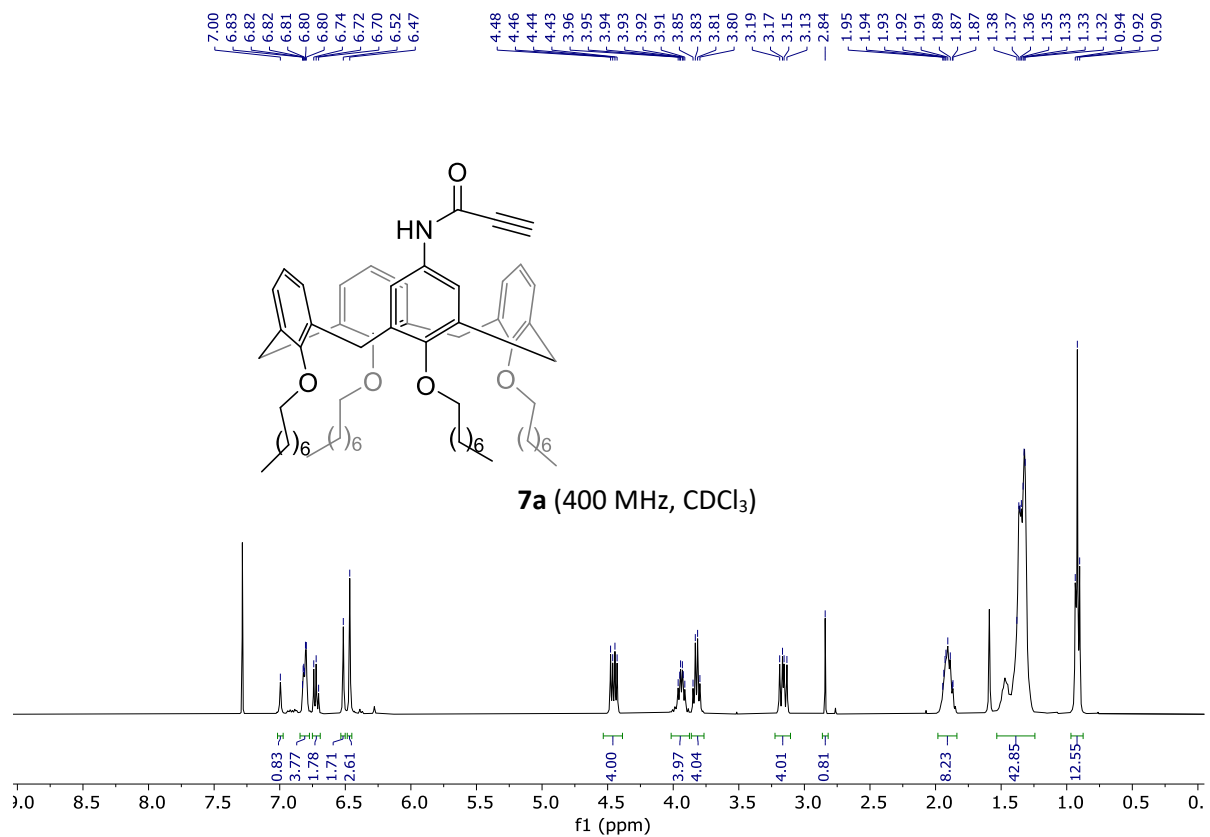
Substrate 5j:



Substrate 5k:

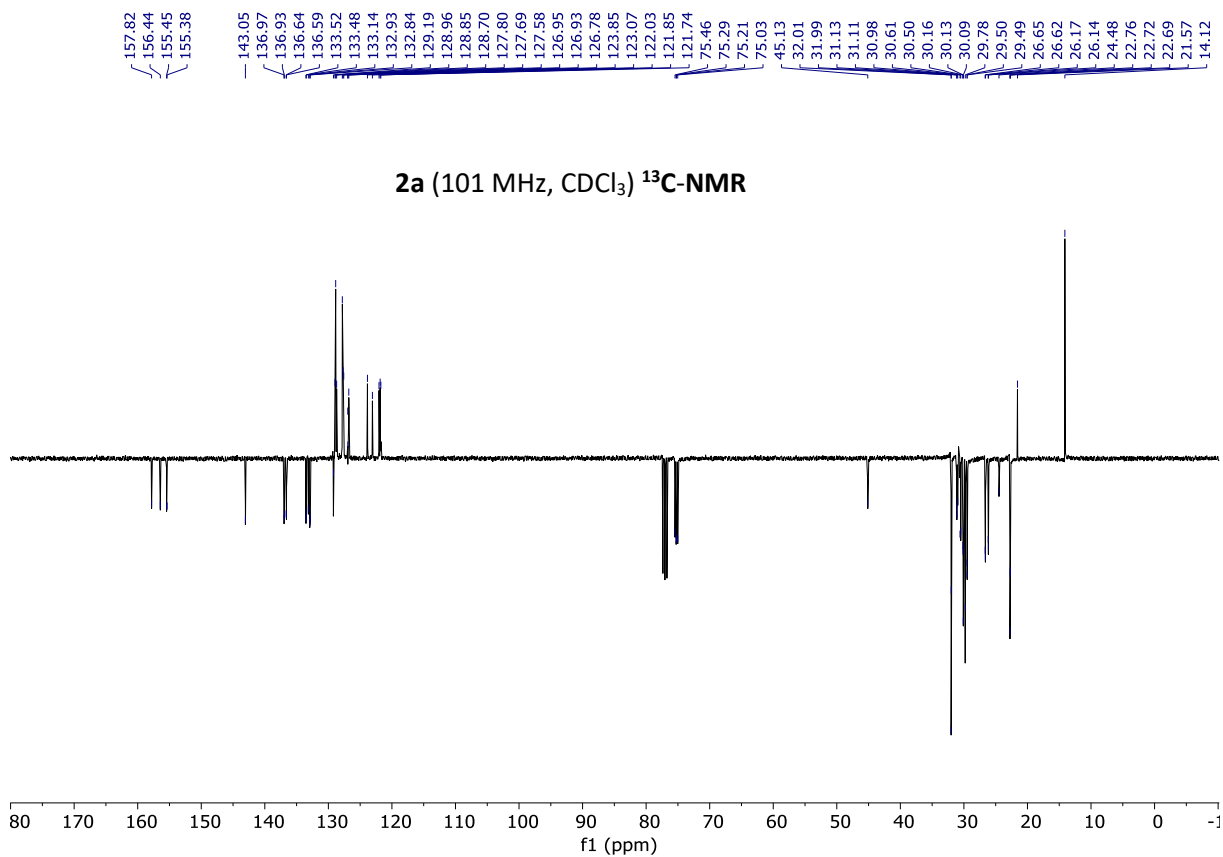
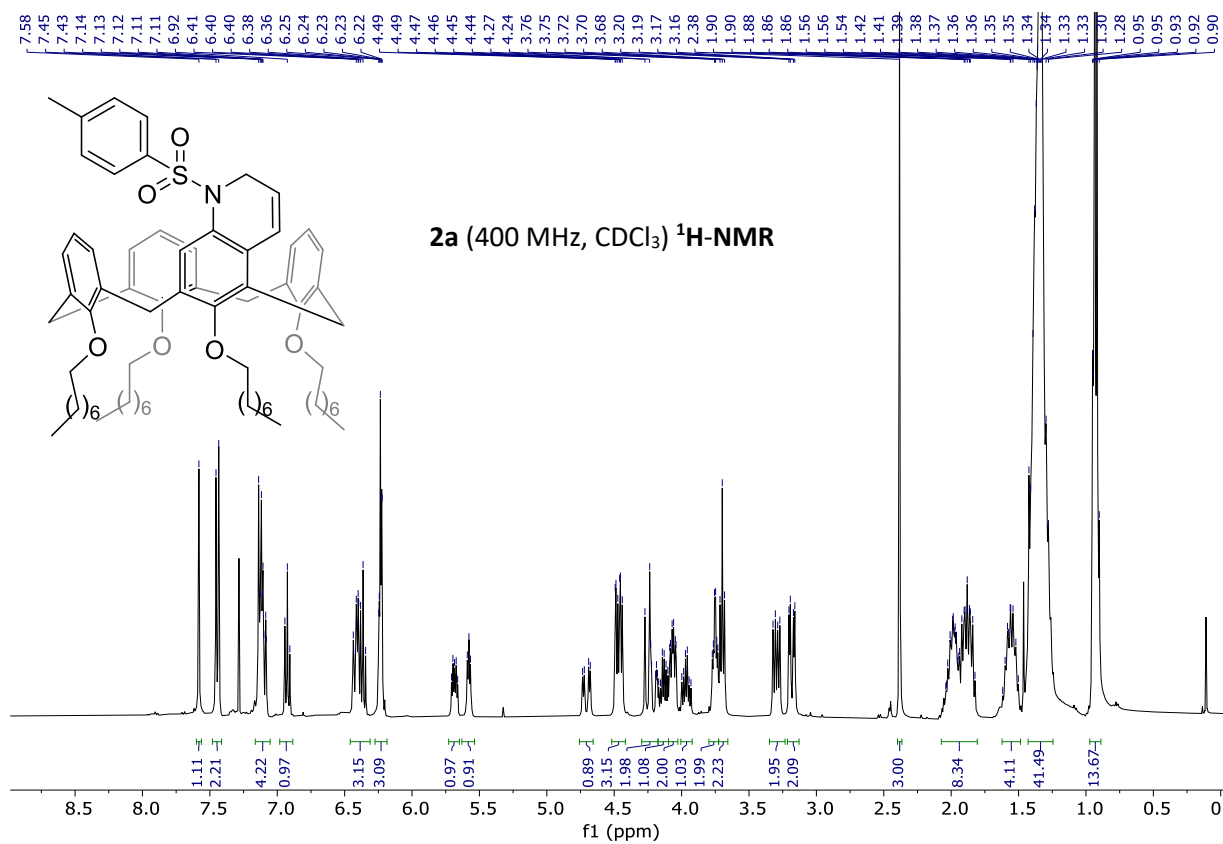


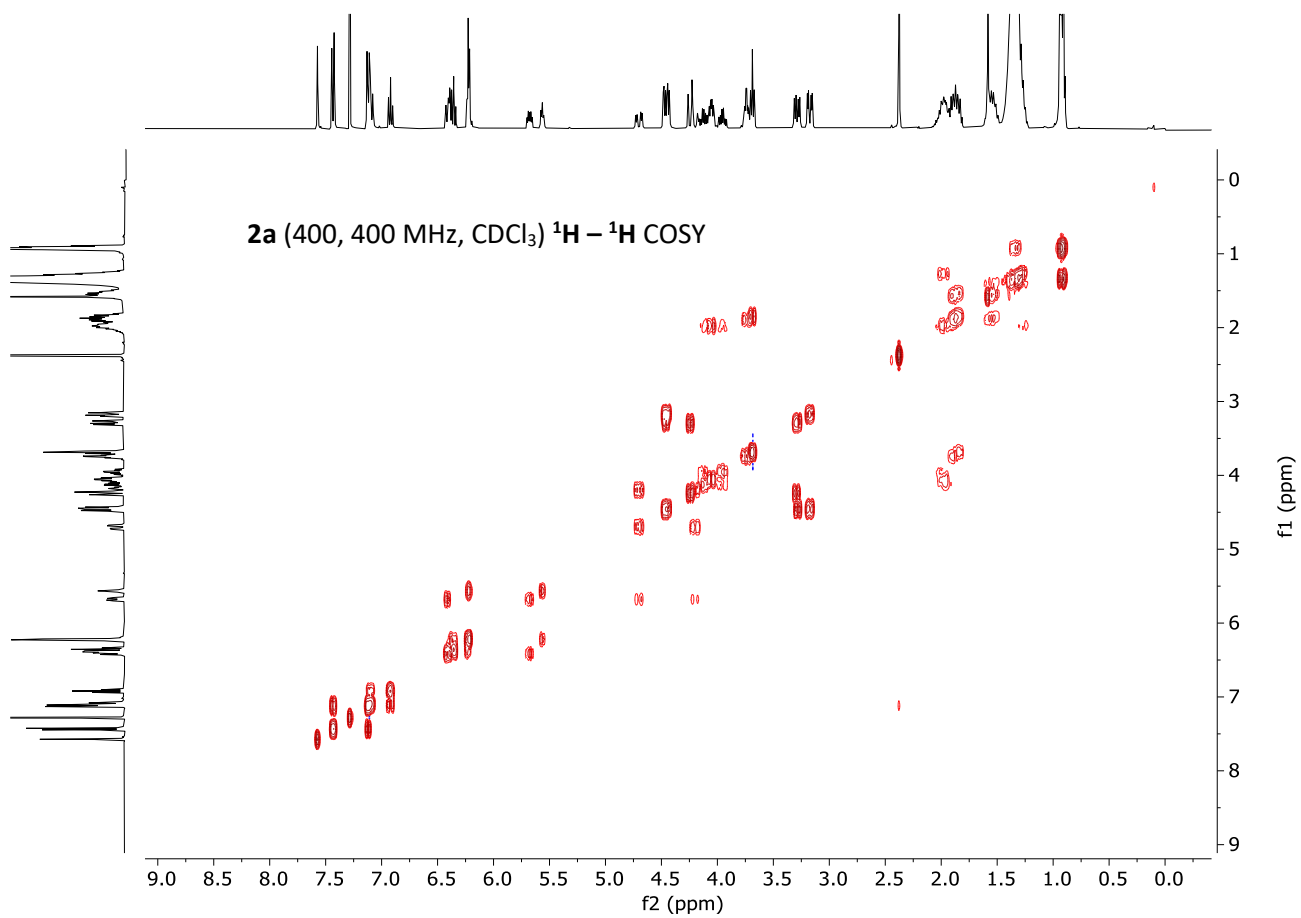
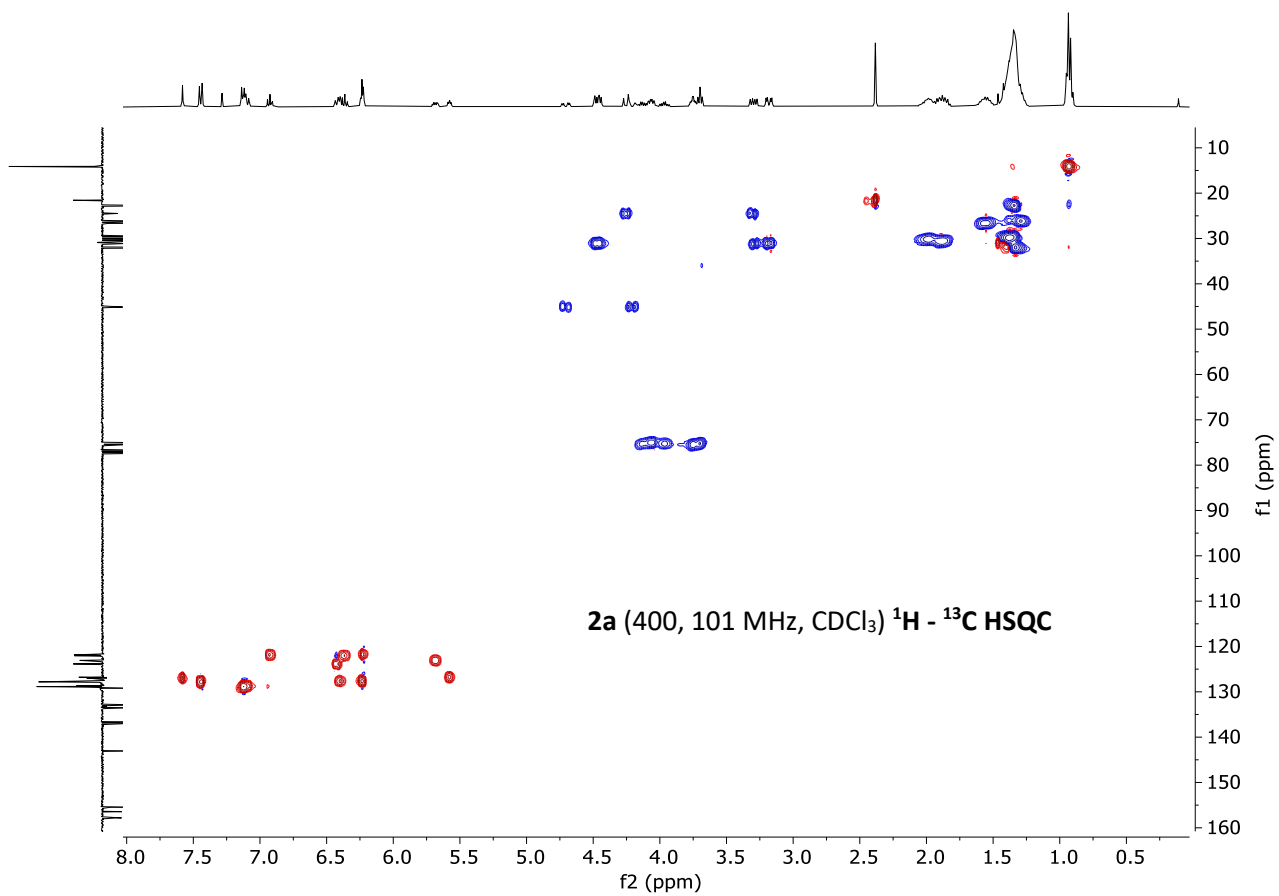
Substrate 7a:

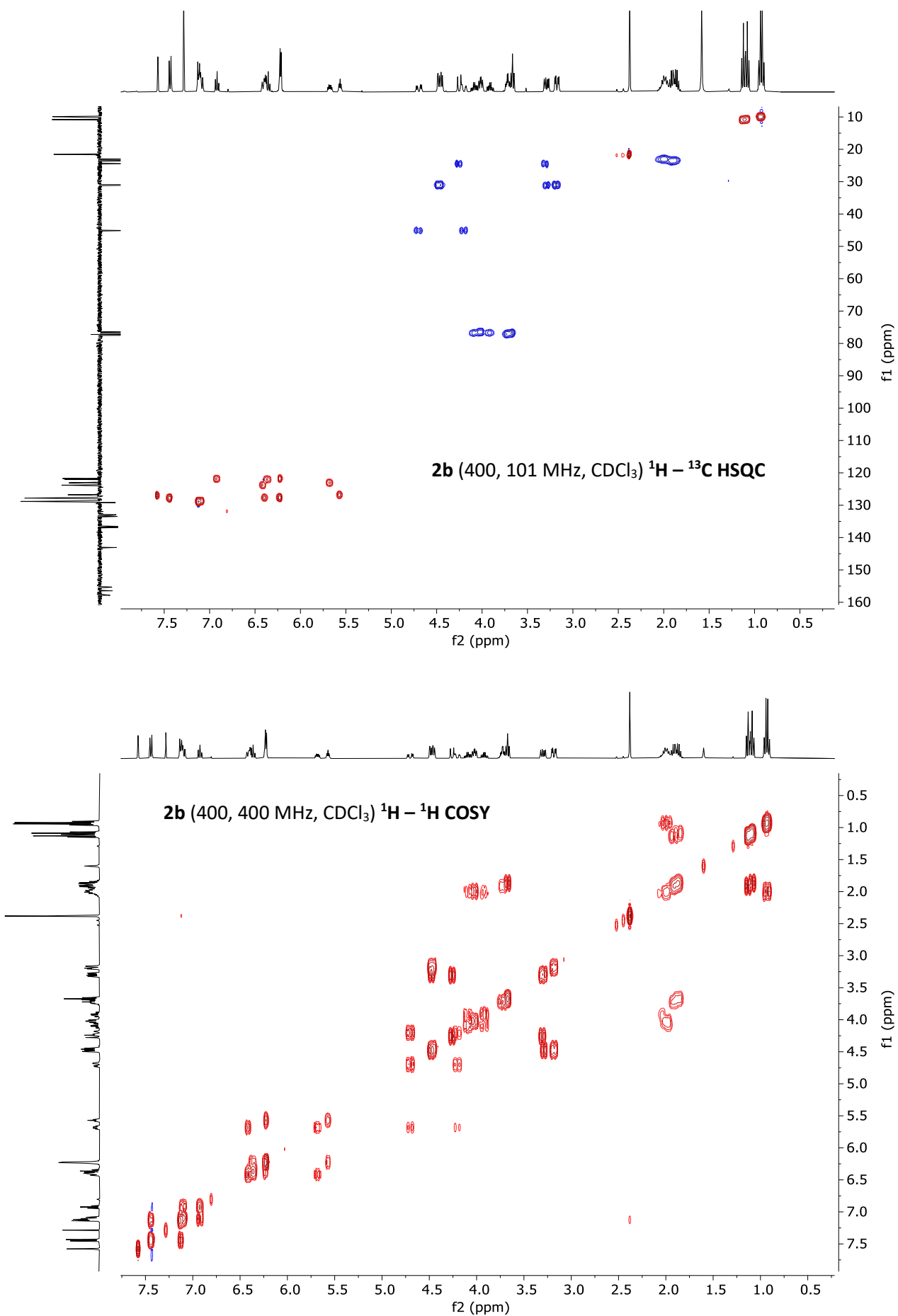


- NMR spectra of products:

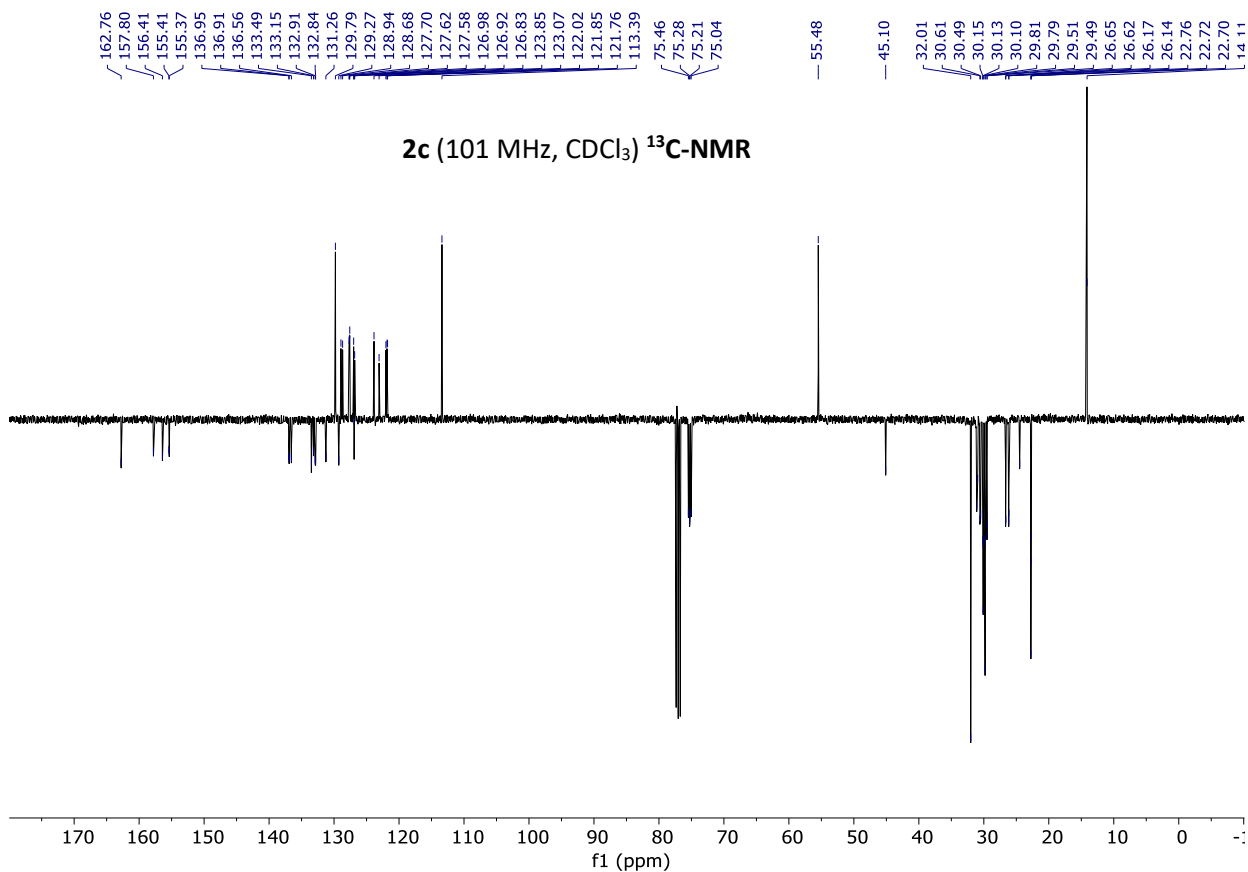
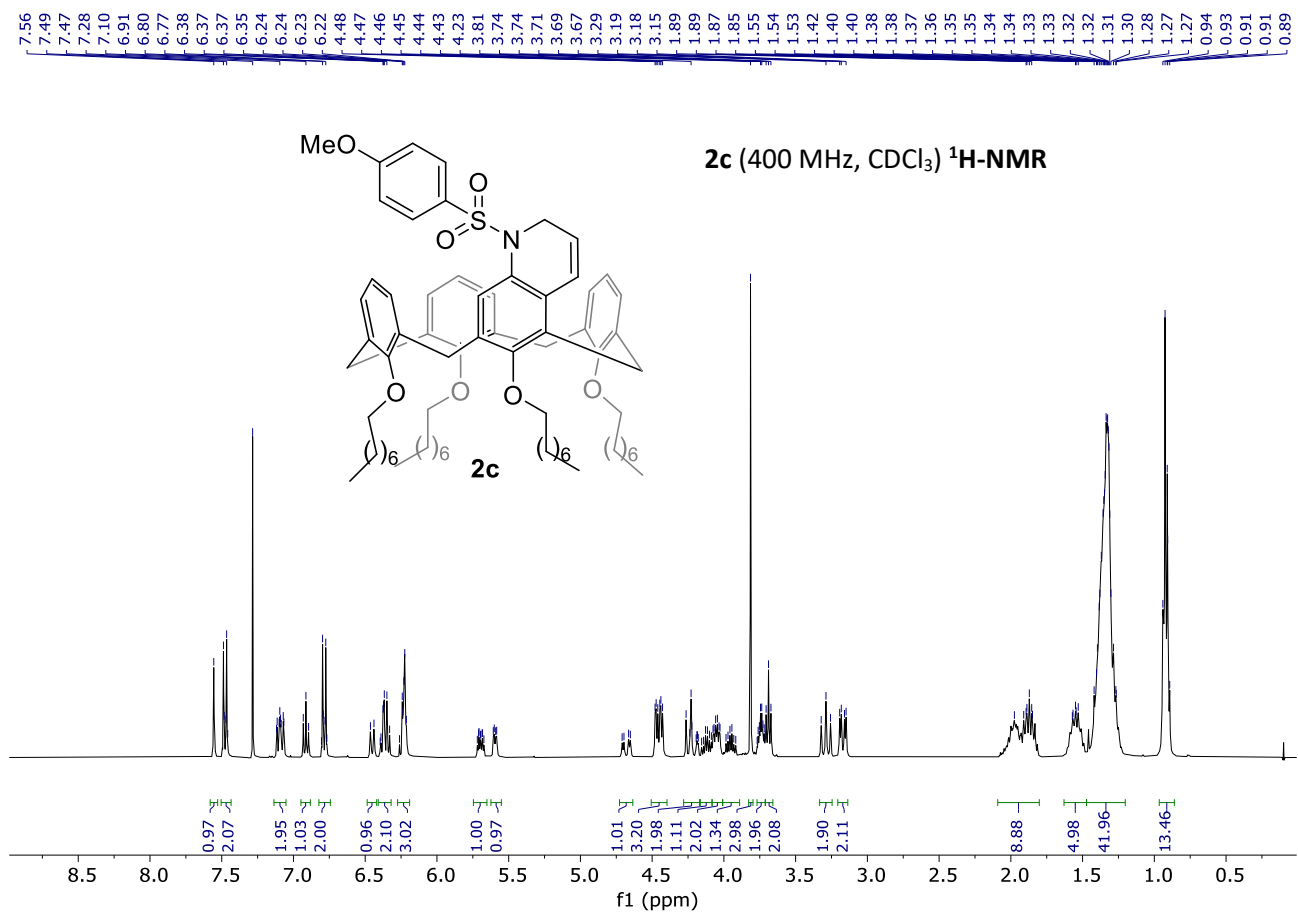
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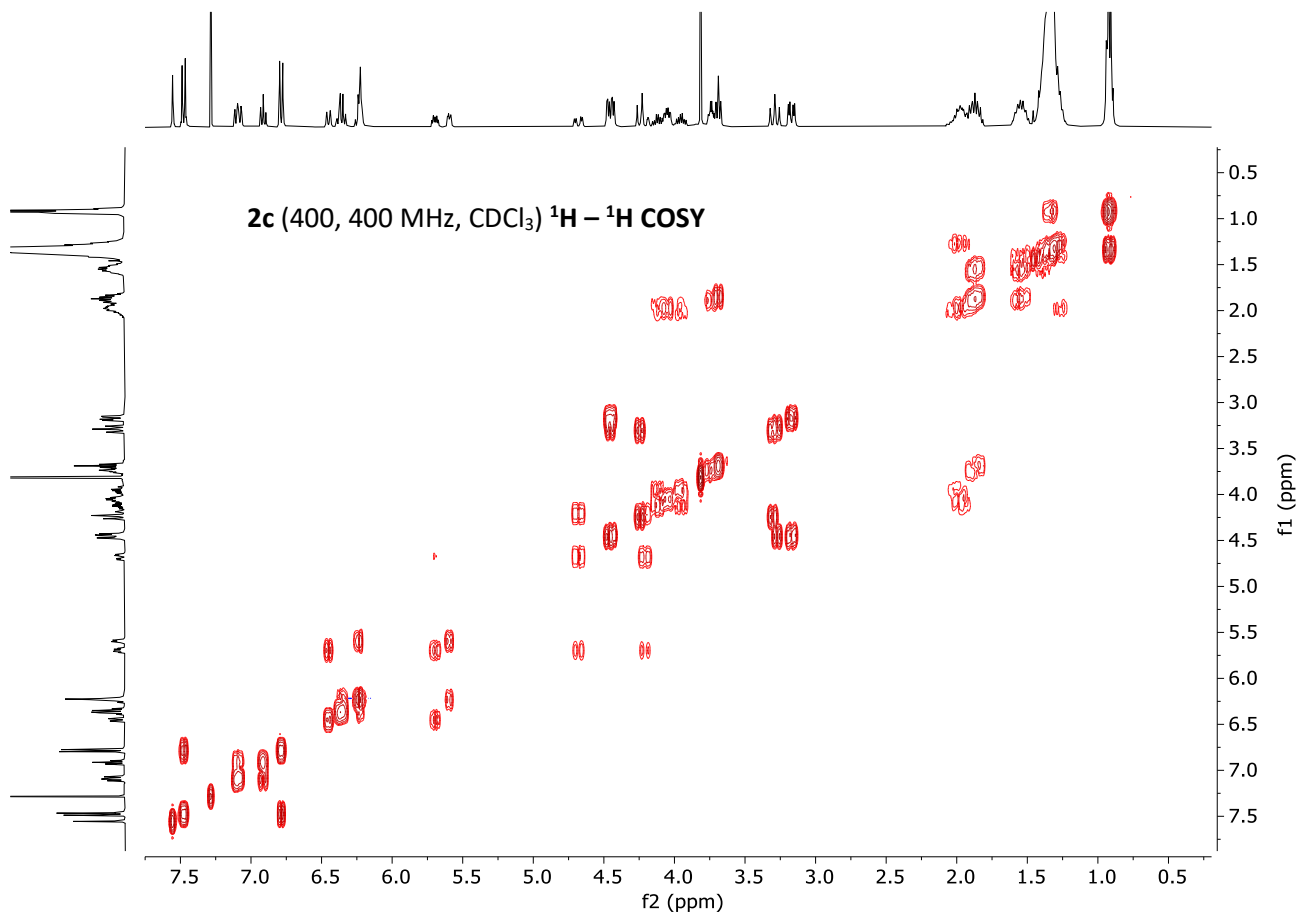
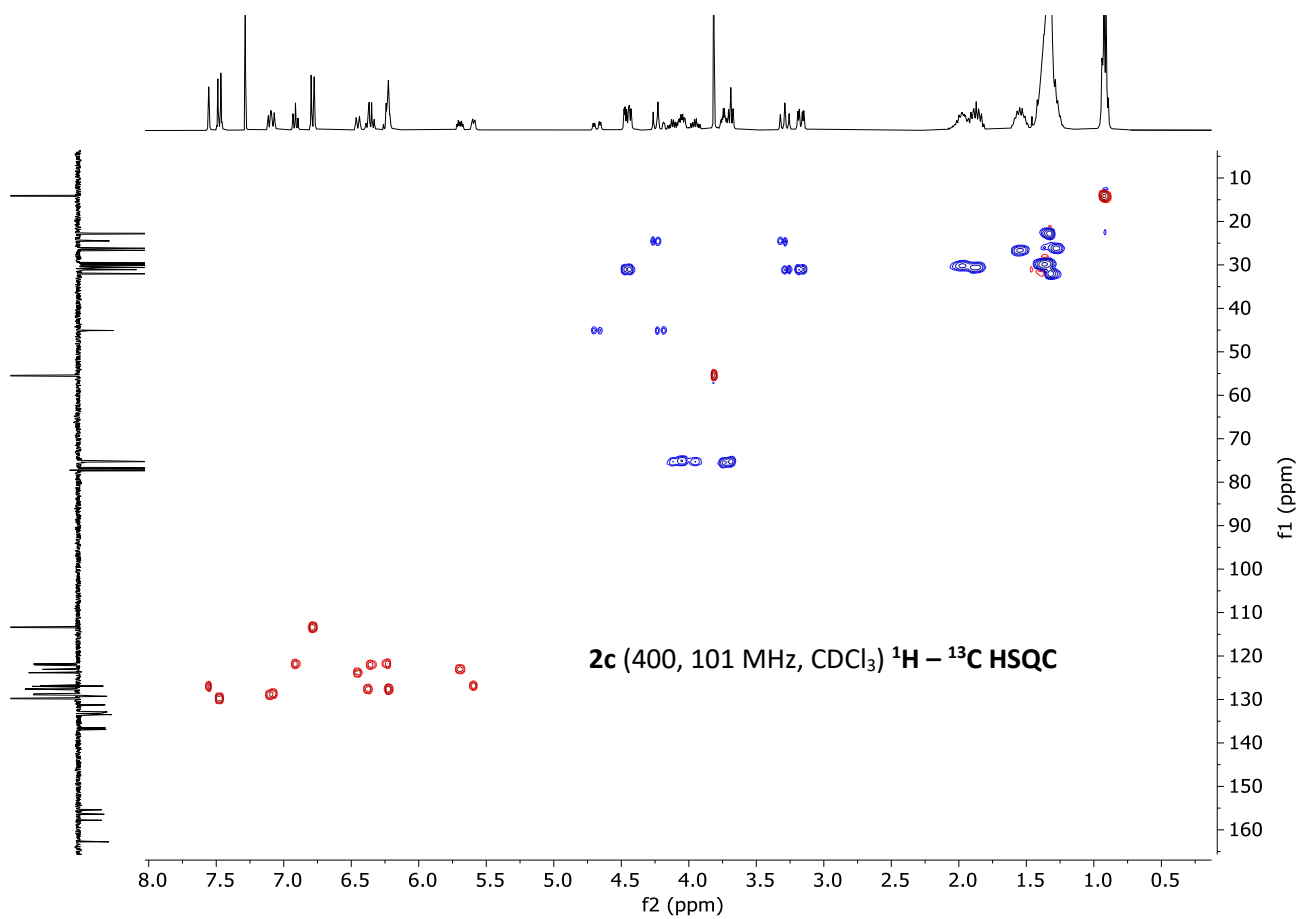




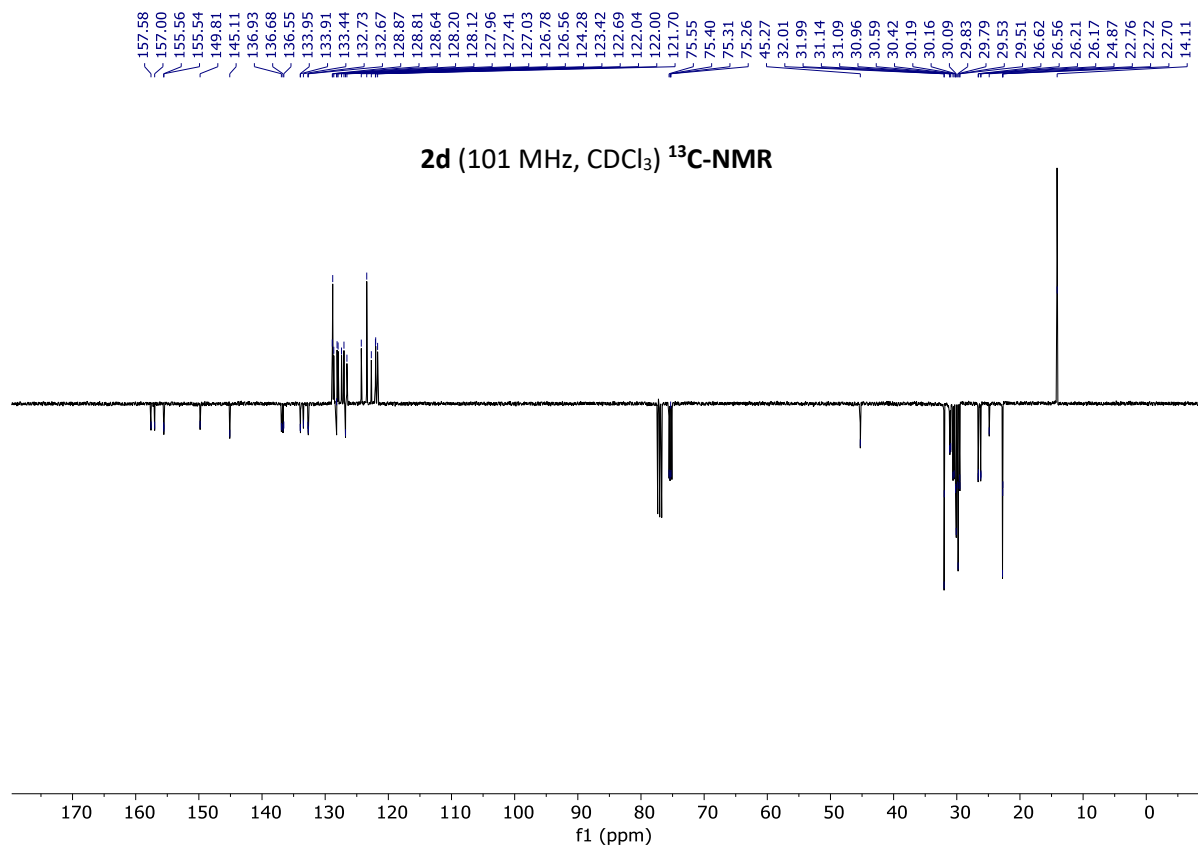
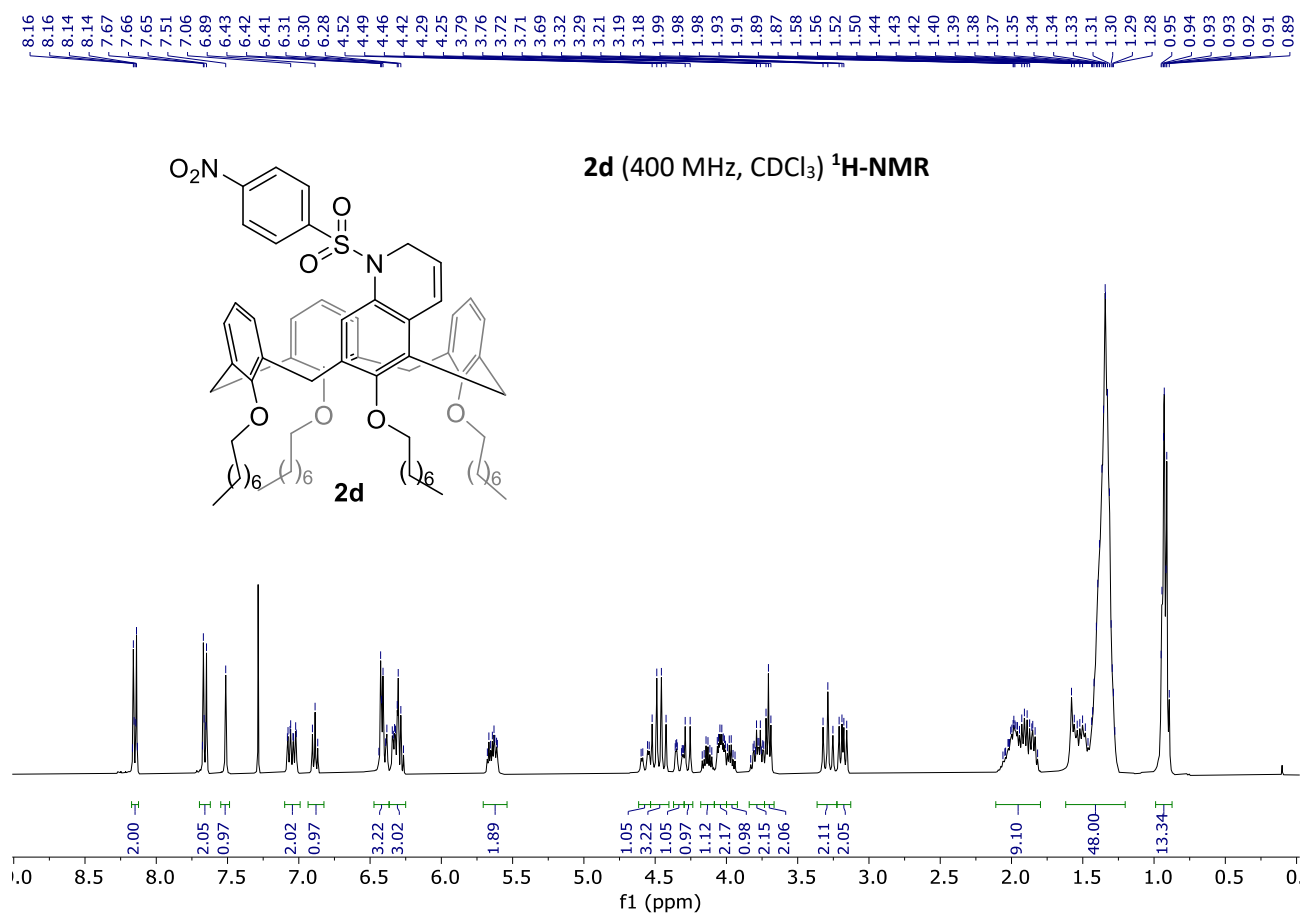


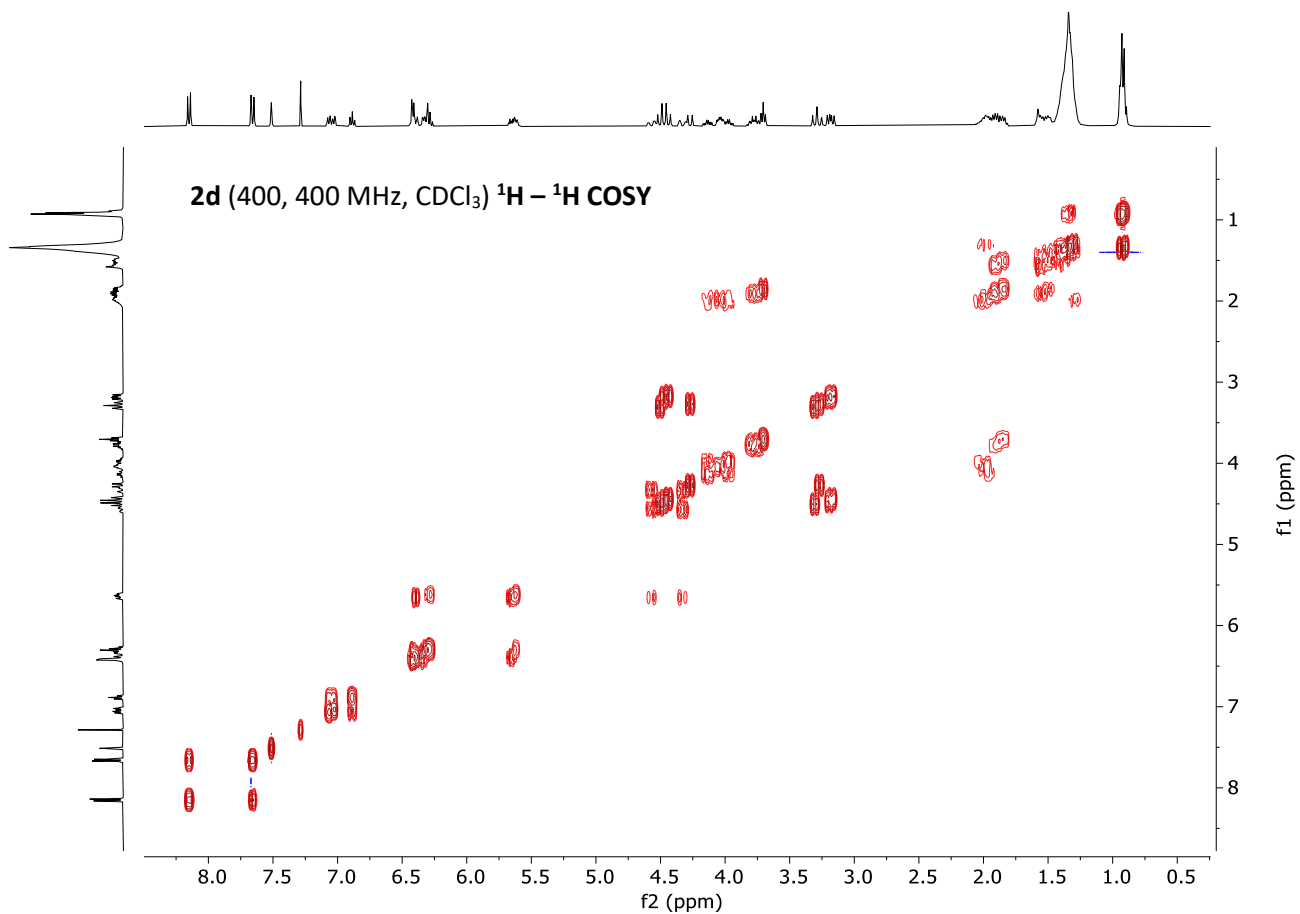
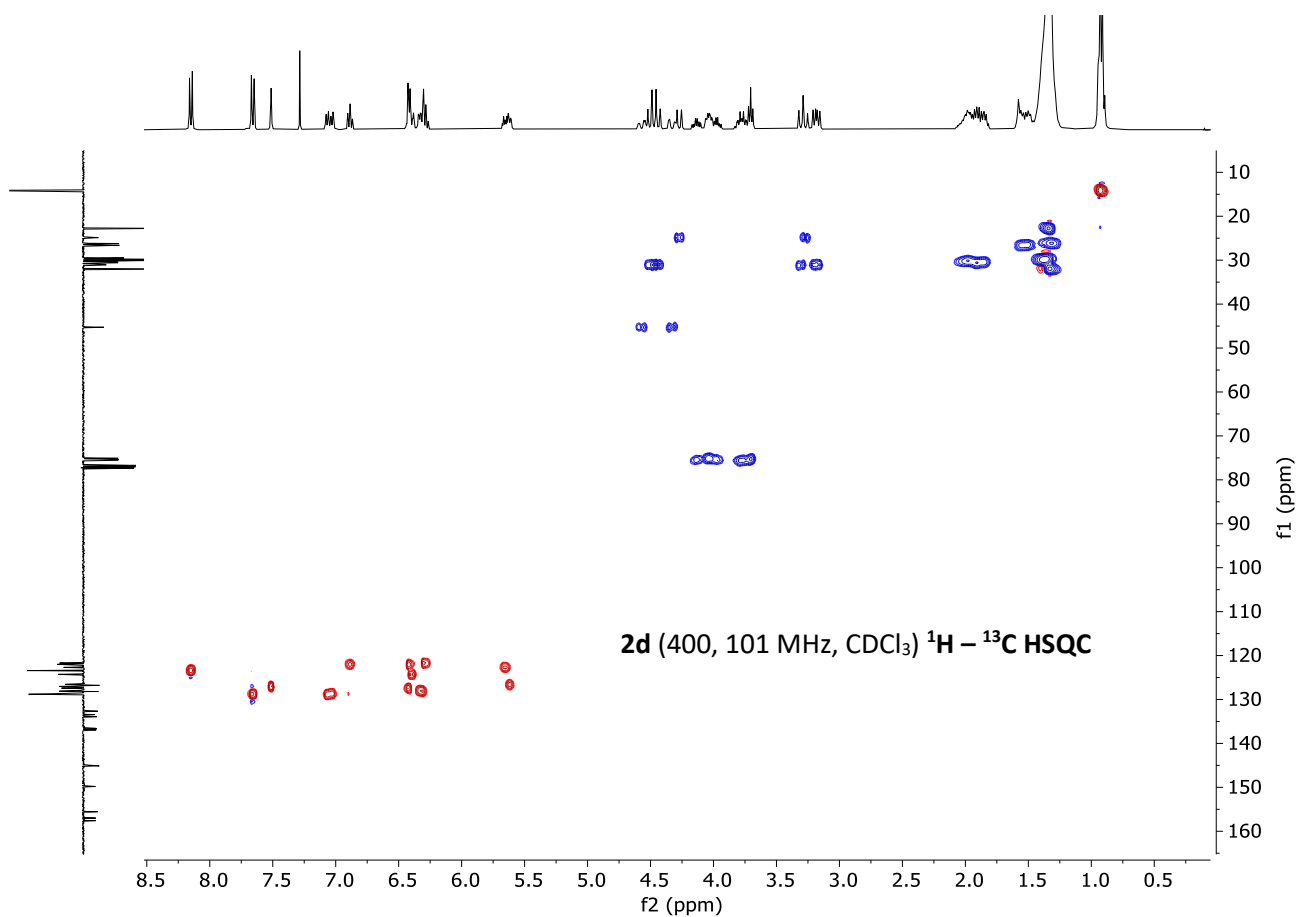
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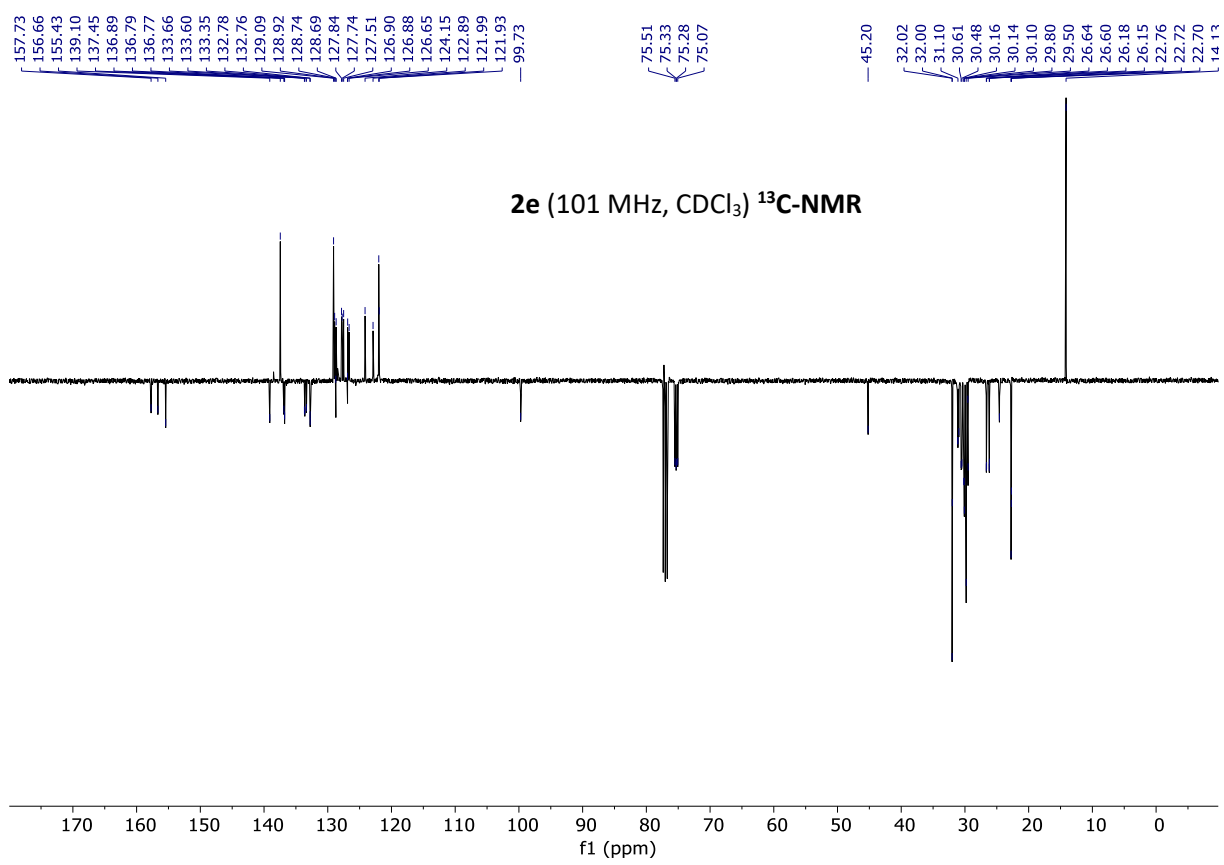
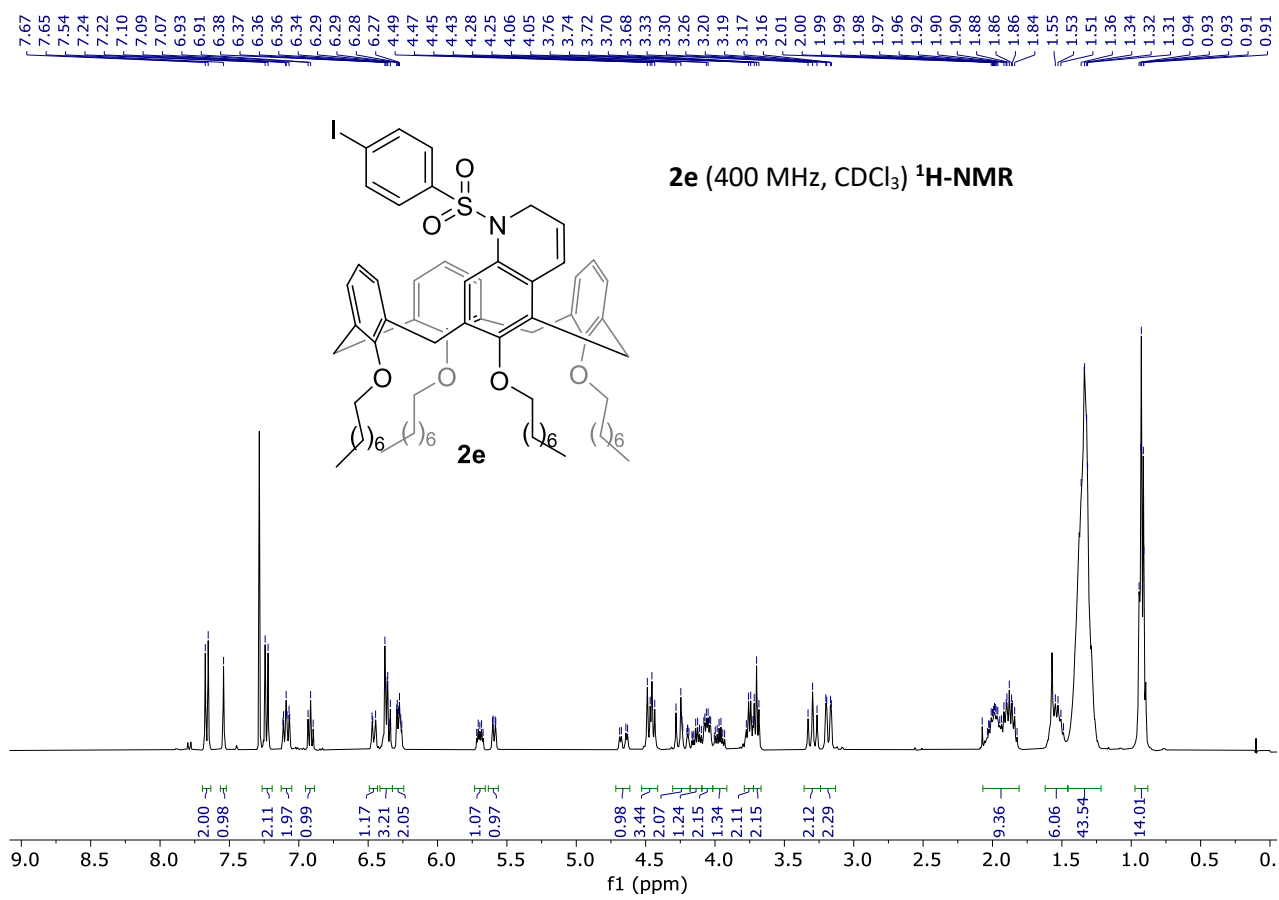


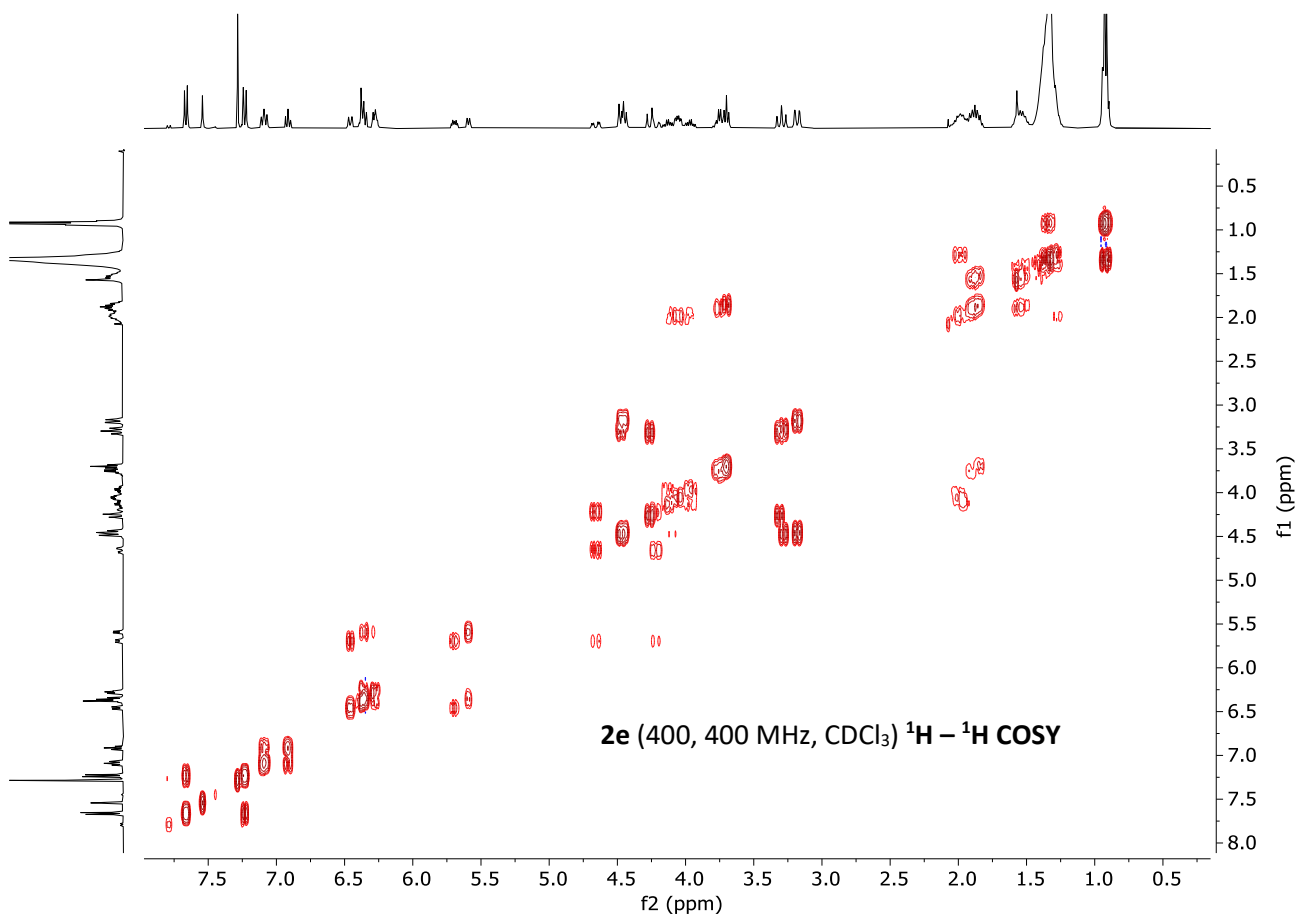
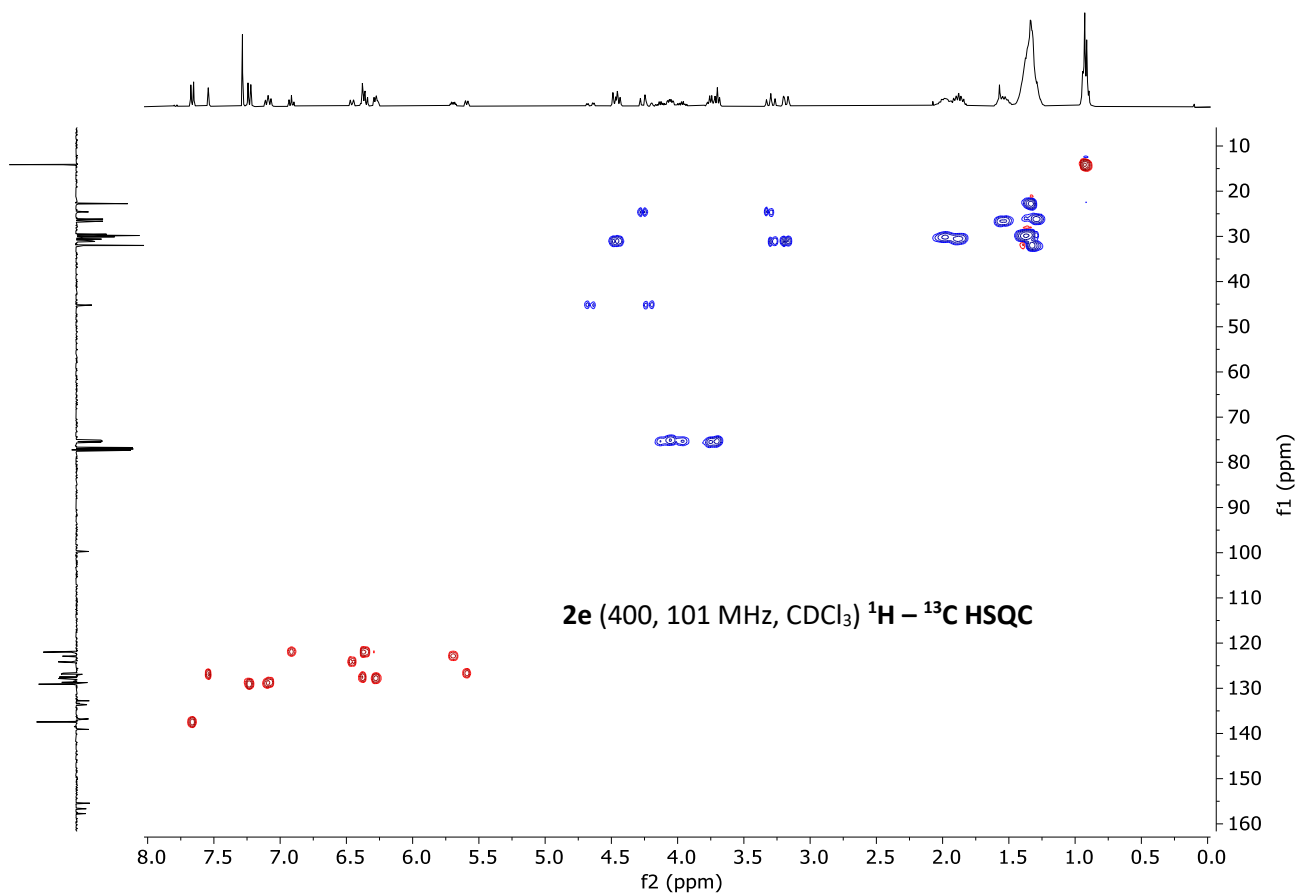
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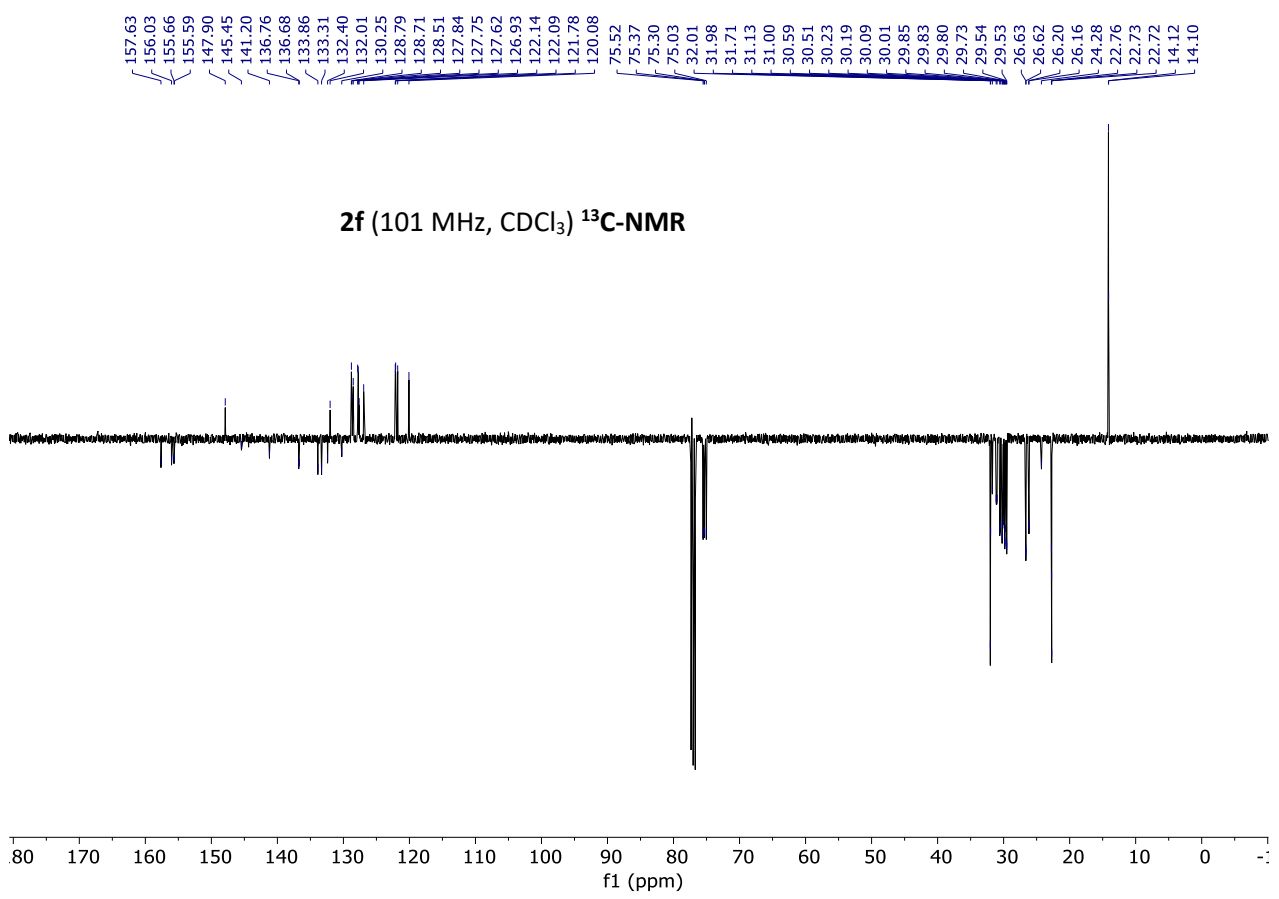
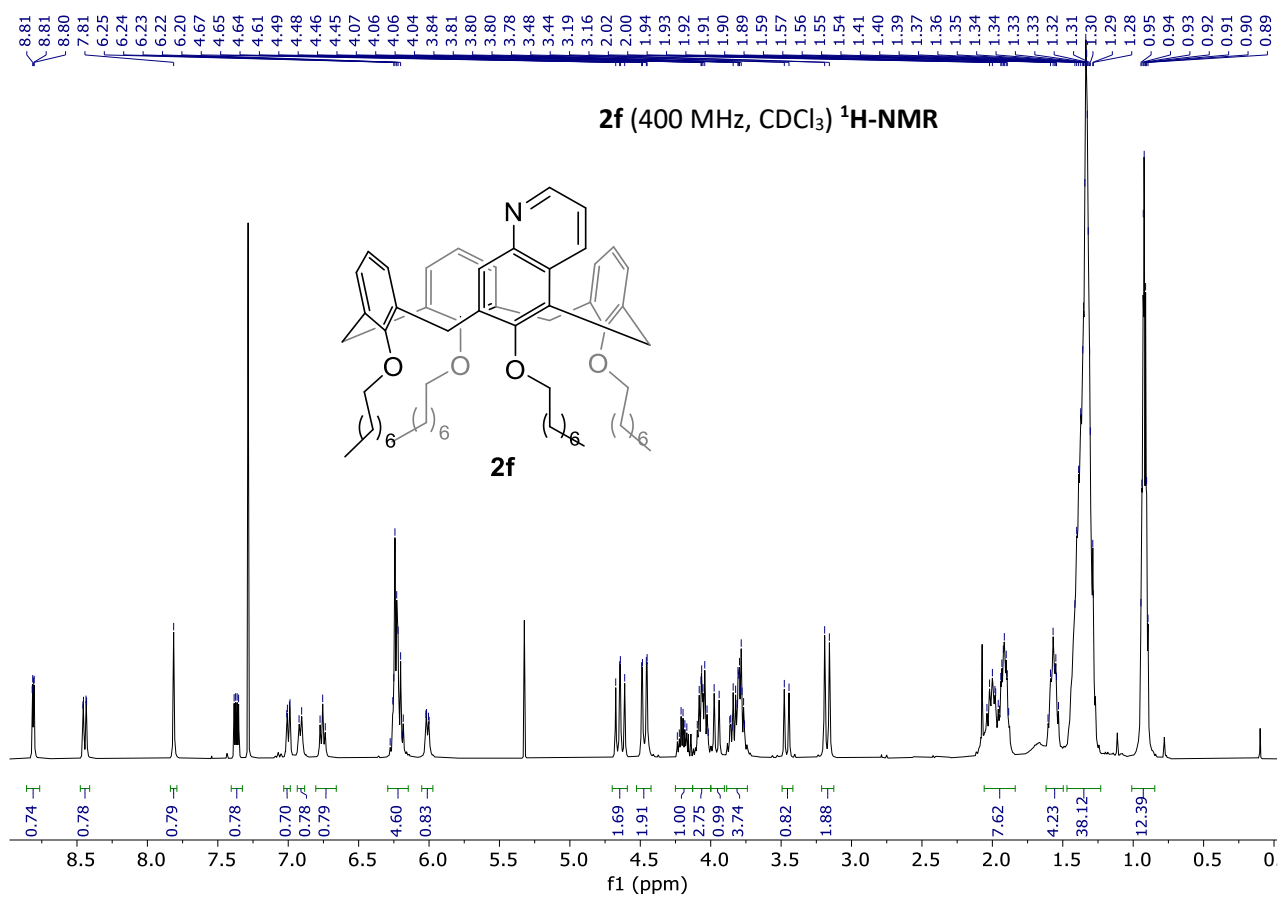


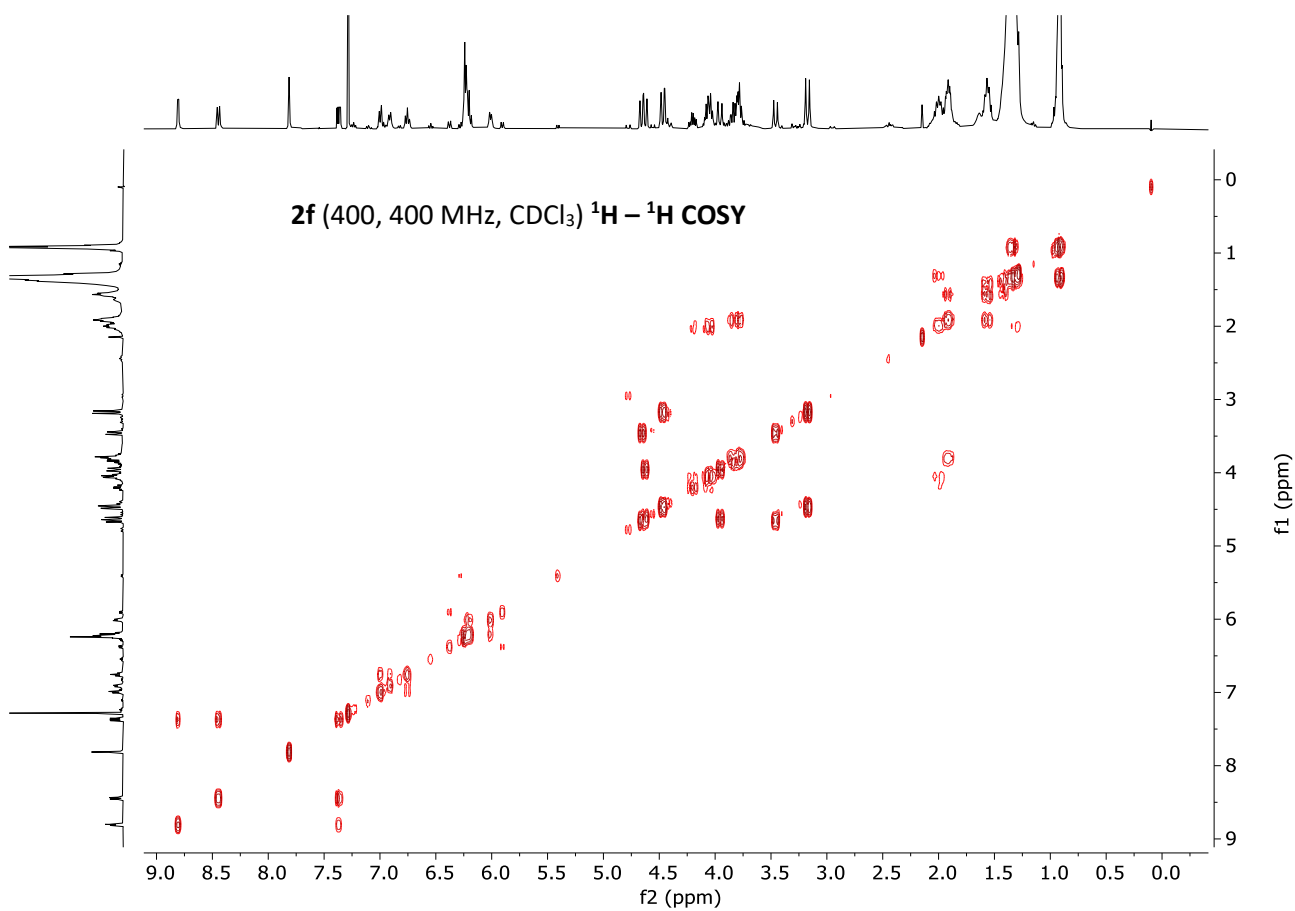
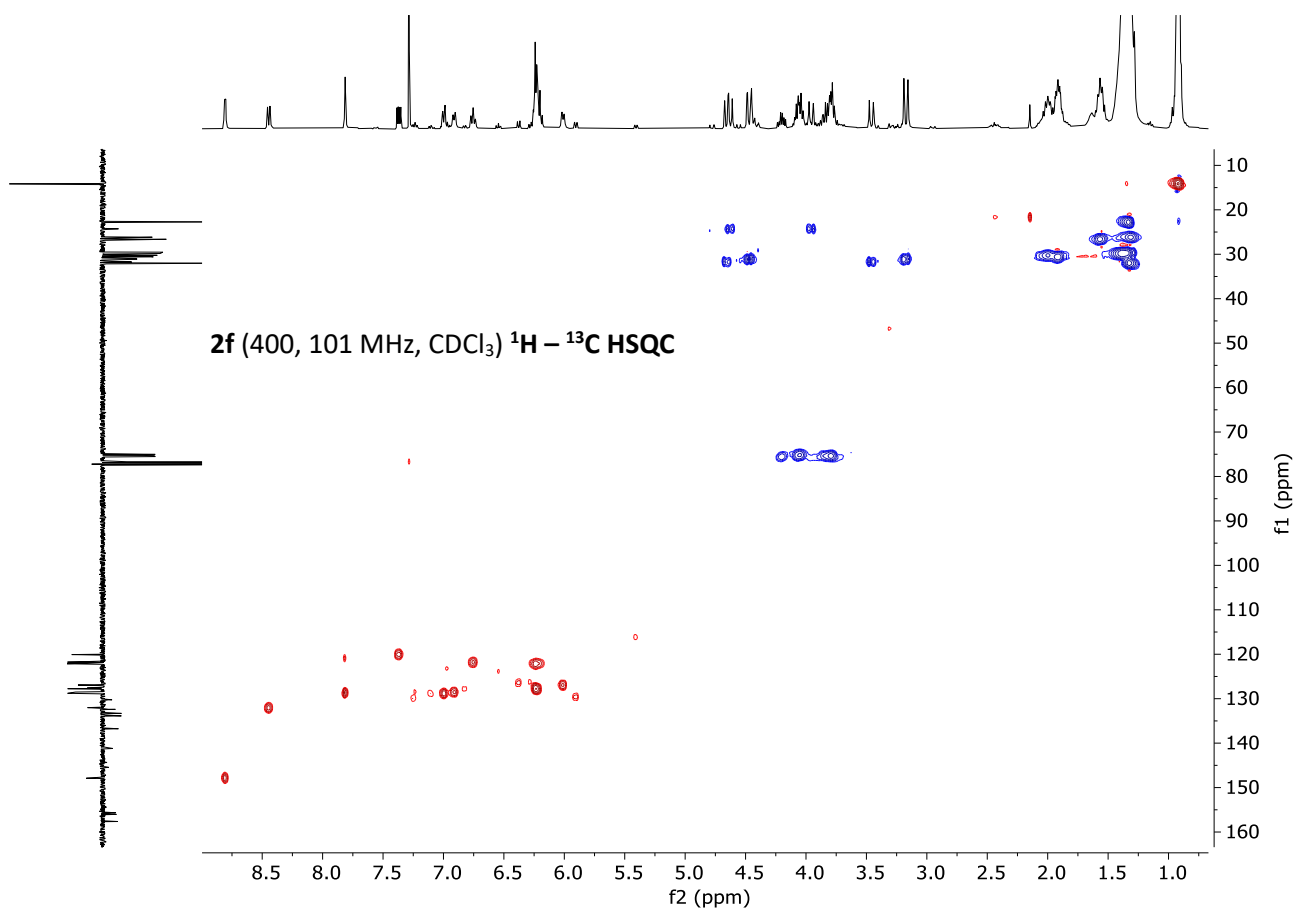
Product 2e:



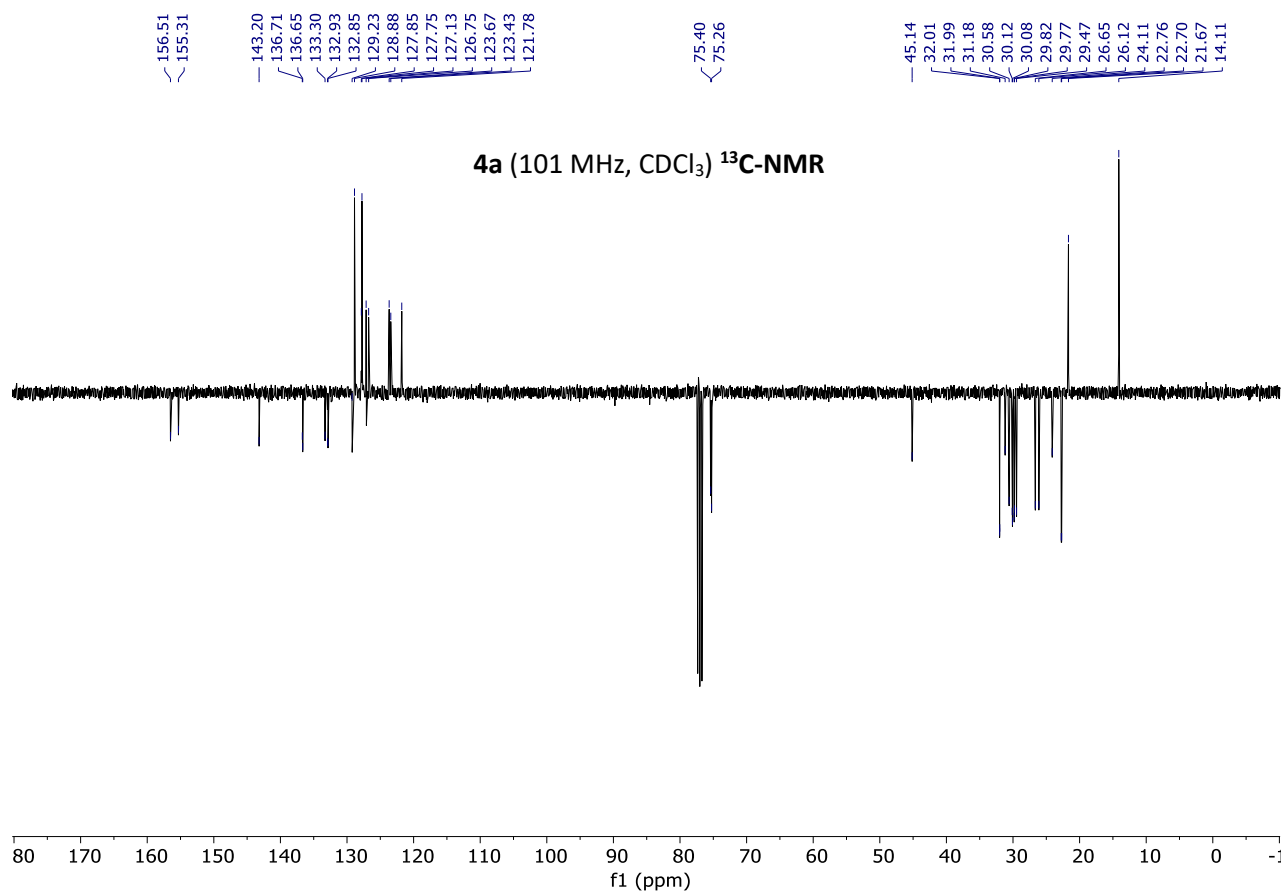
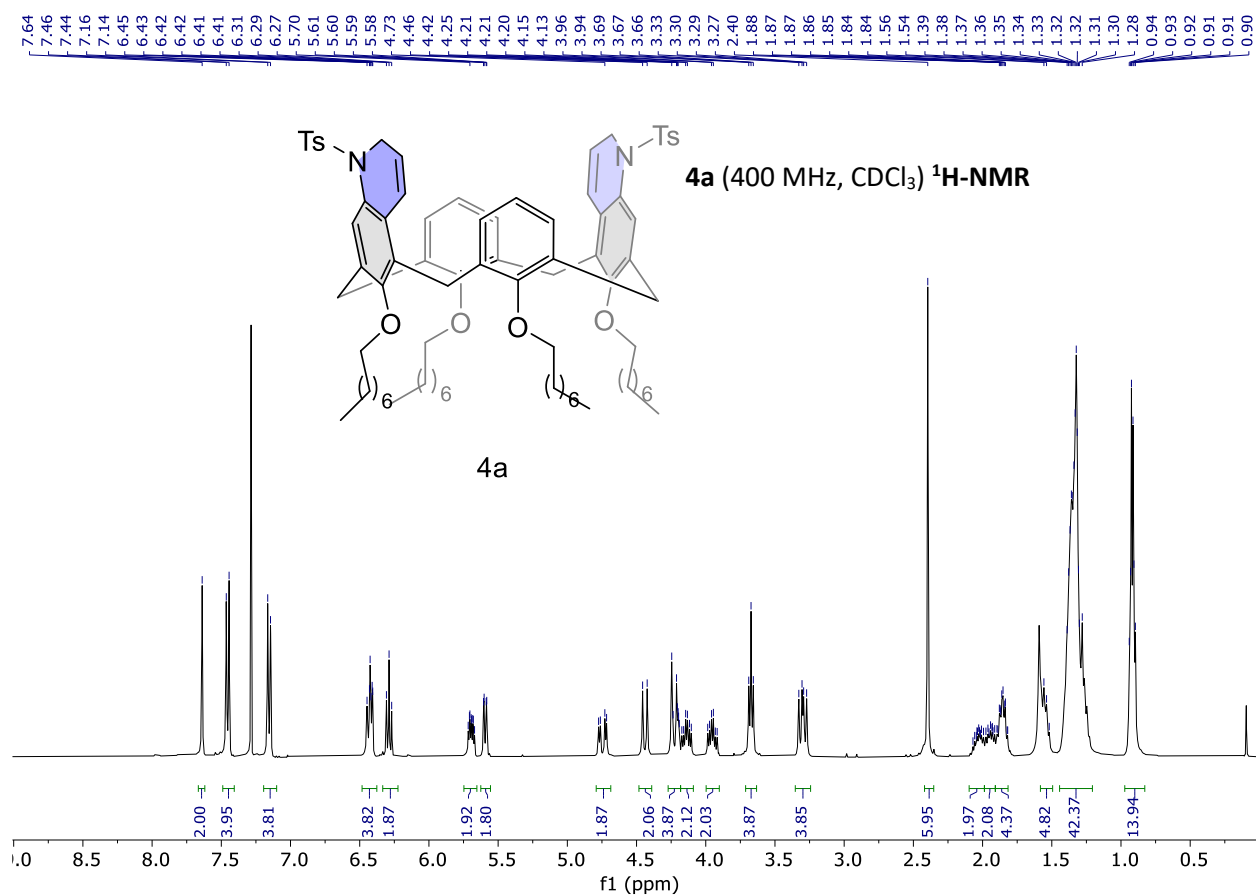


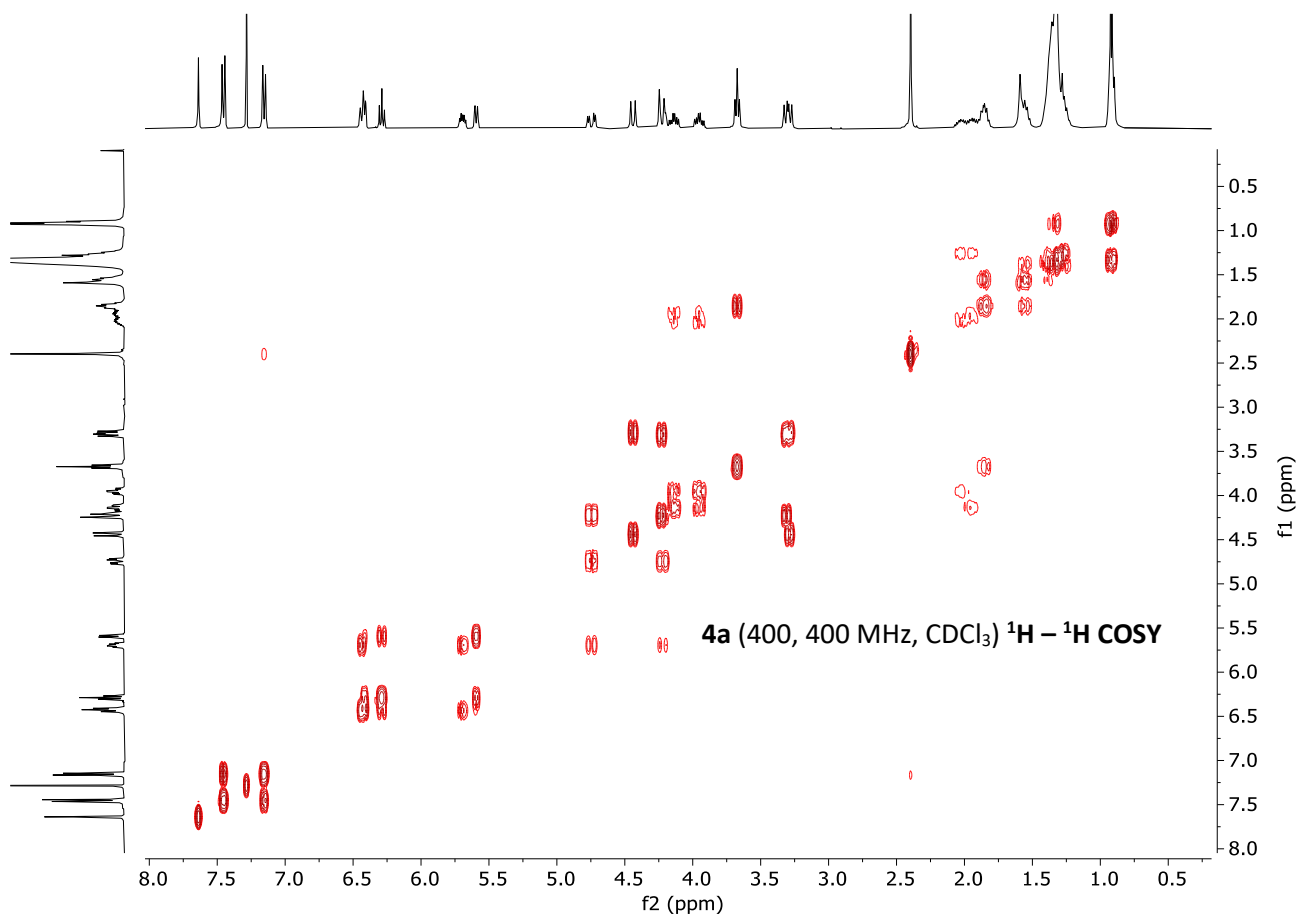
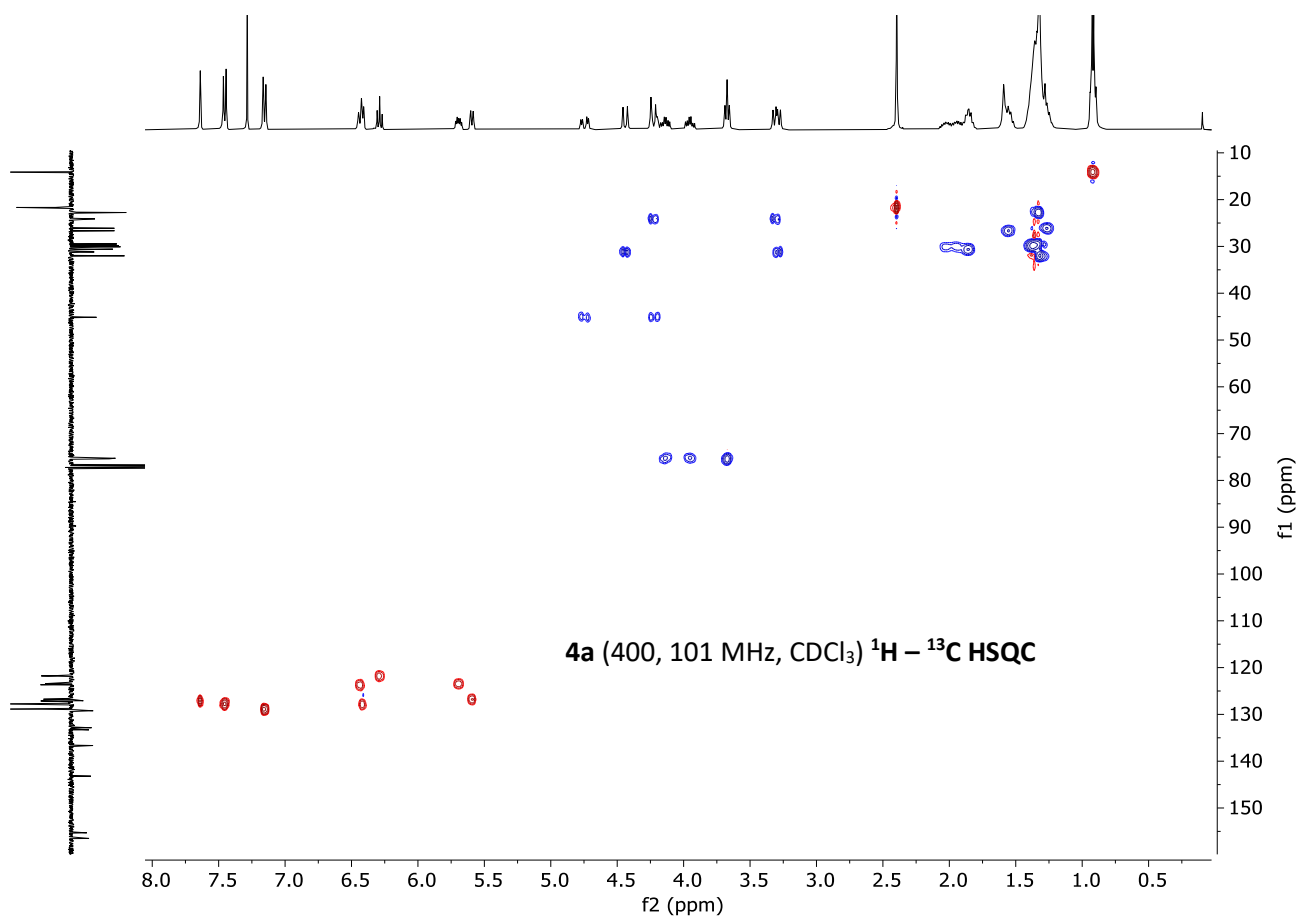
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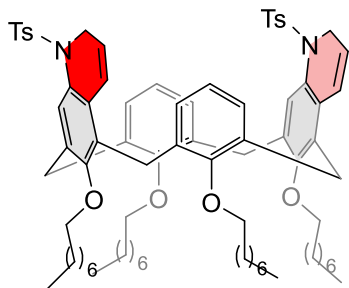


Product 4a:

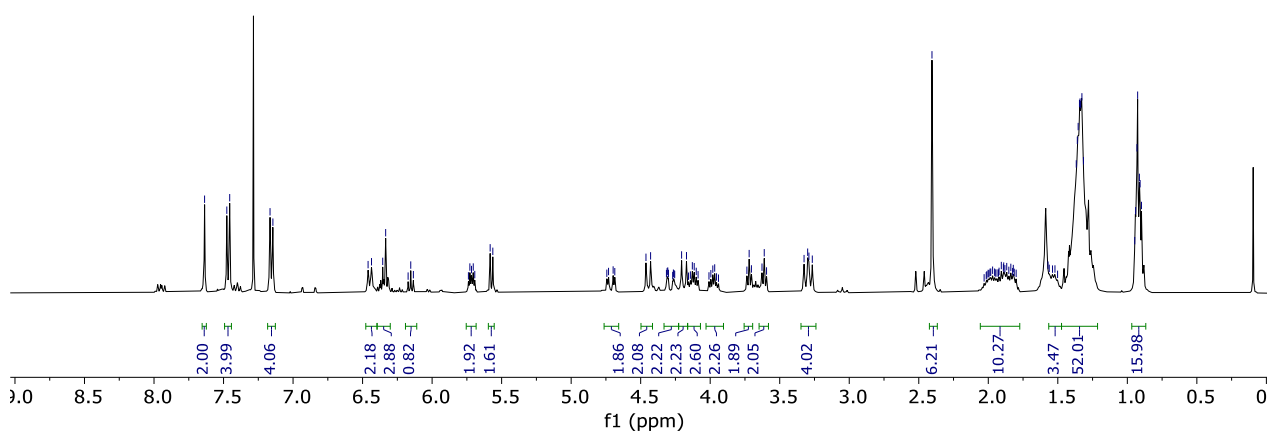




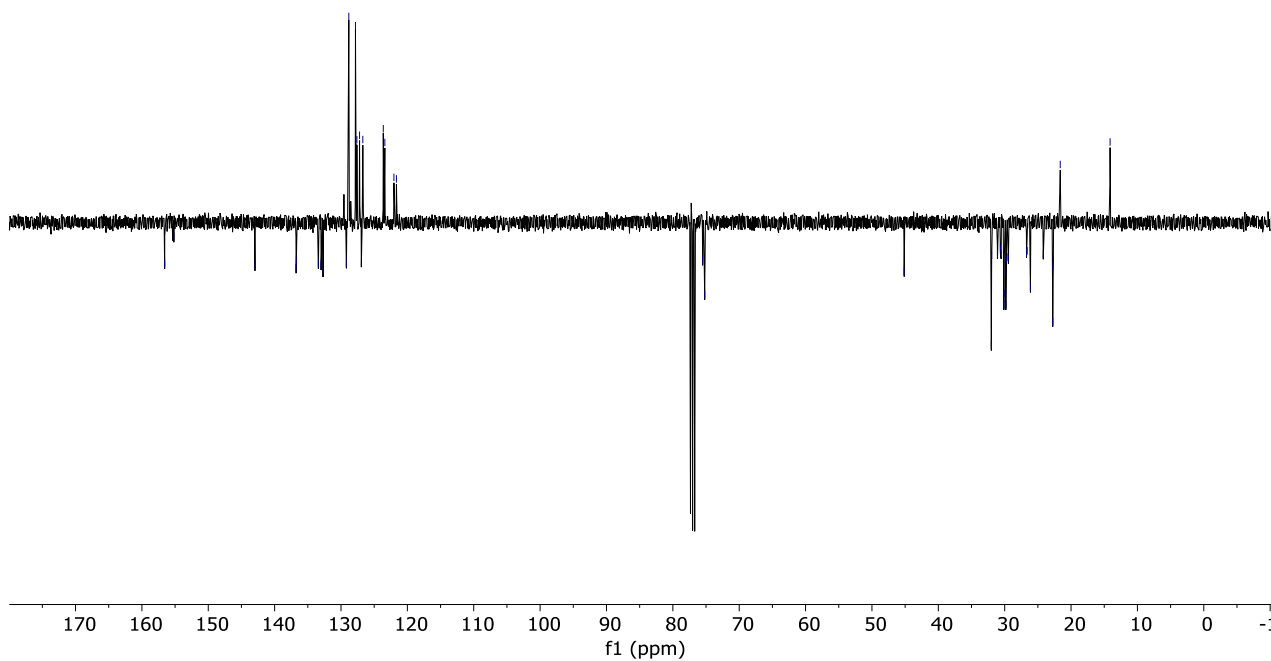
Product 4a':

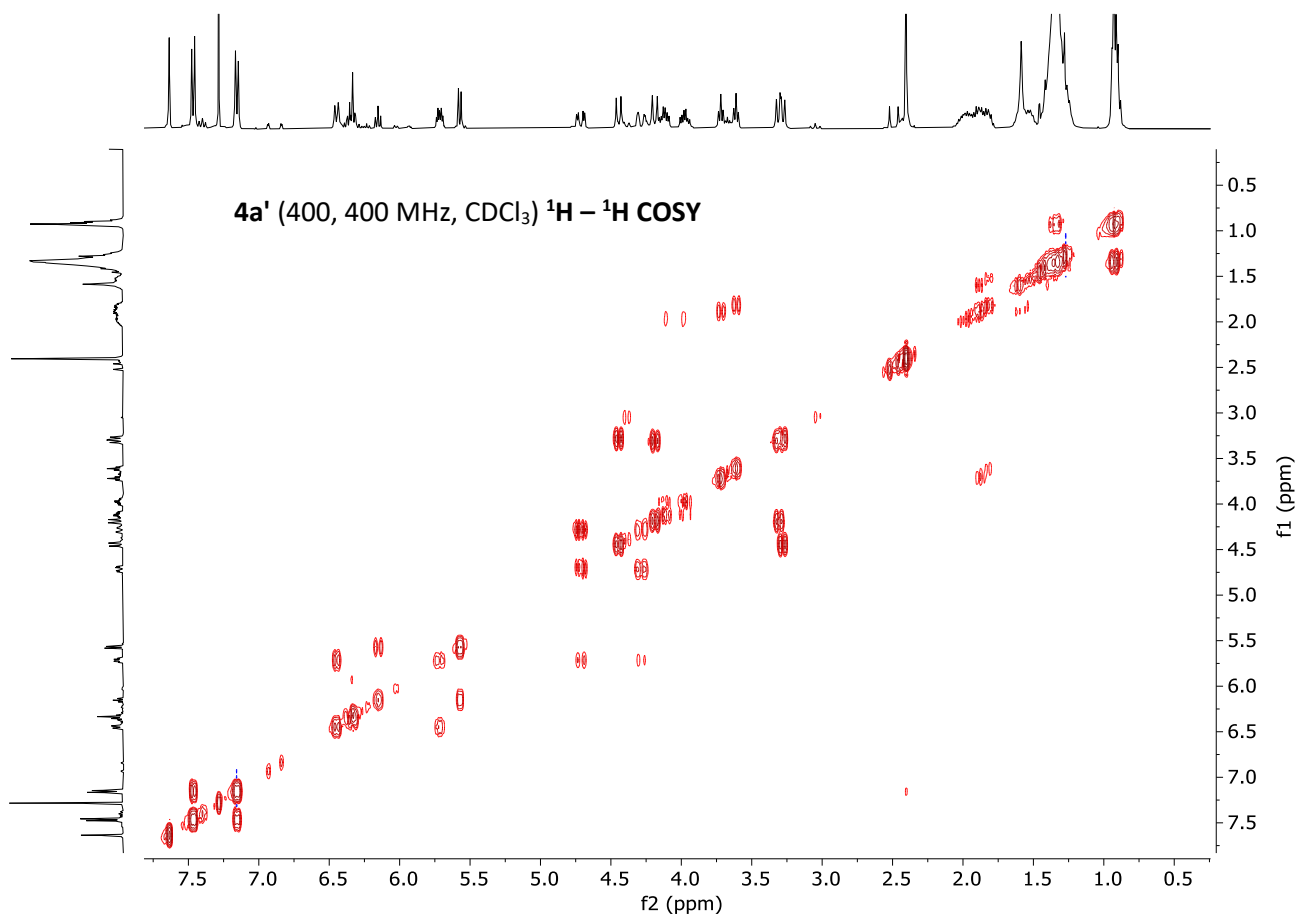
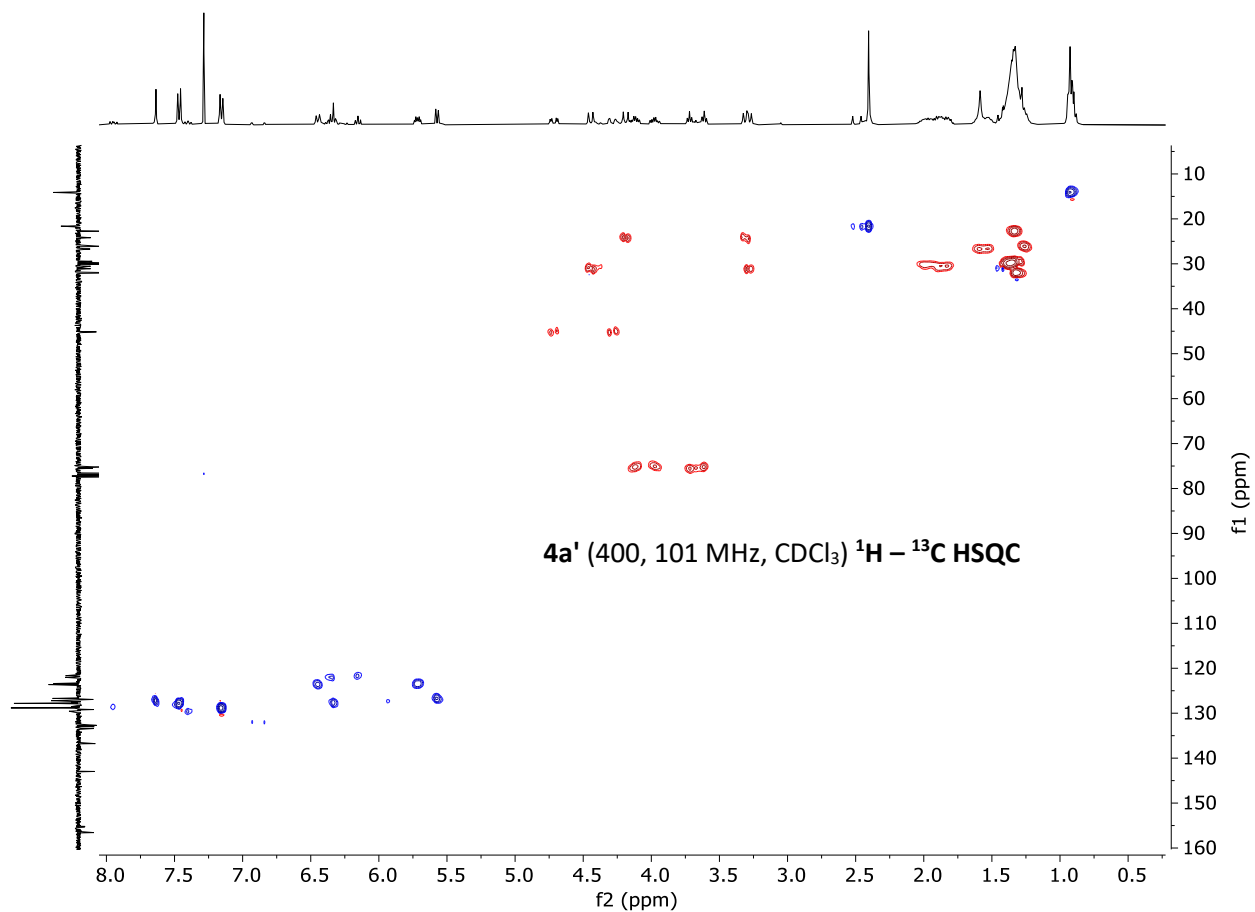


4a' (400 MHz, CDCl₃) ¹H-NMR



4a' (101 MHz, CDCl₃) ¹³C-NMR

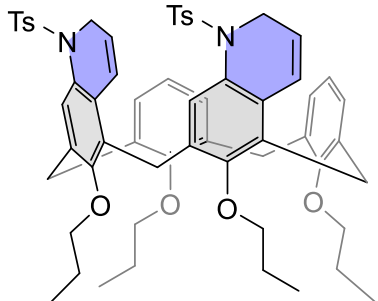




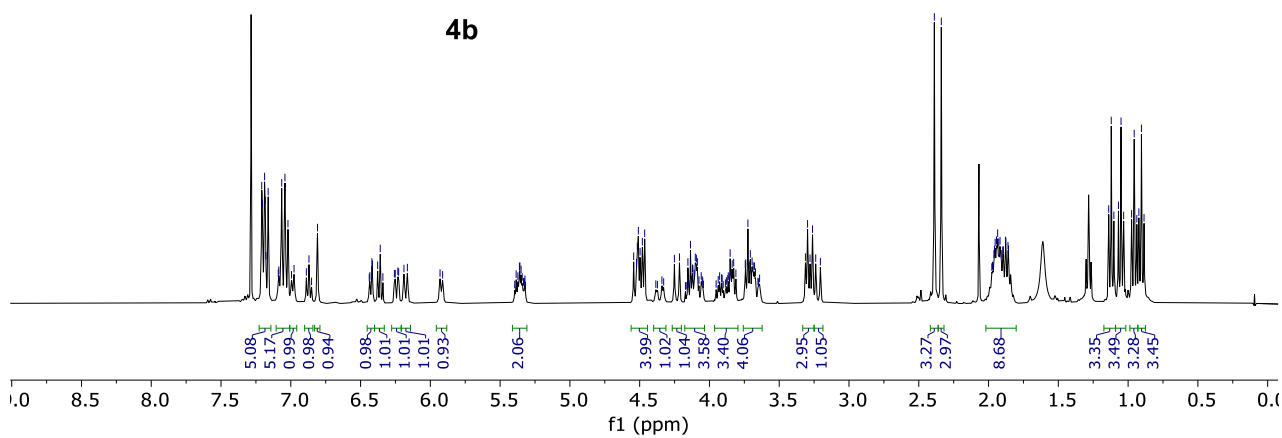
Product 4b:



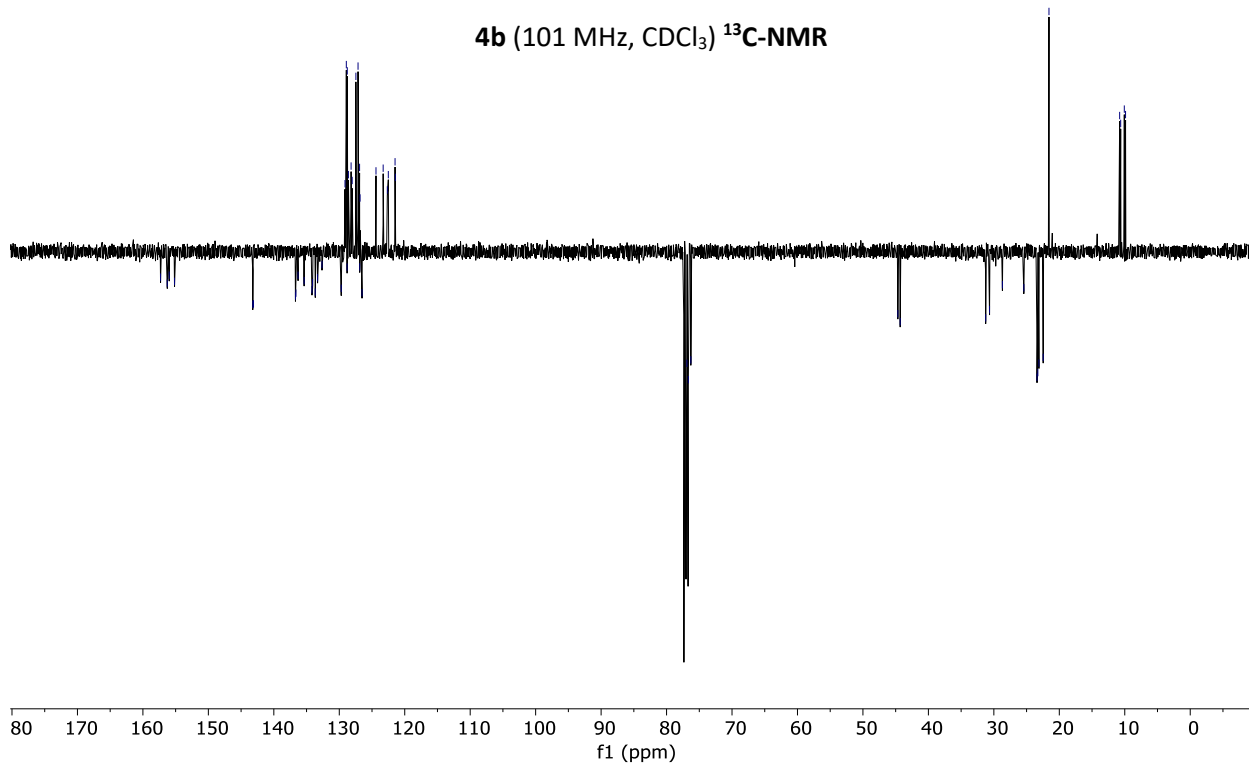
4b (400 MHz, CDCl₃) ¹H-NMR

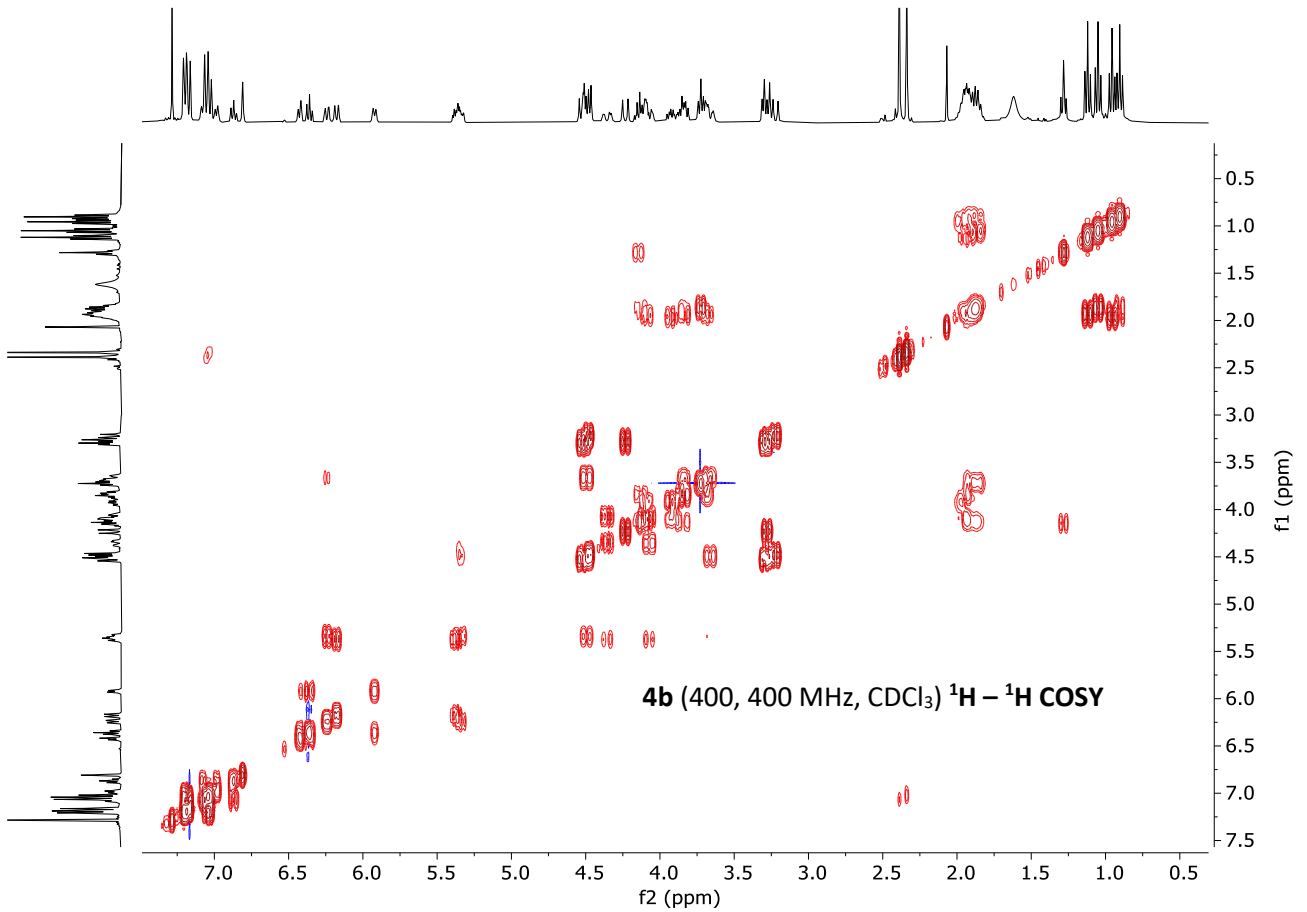
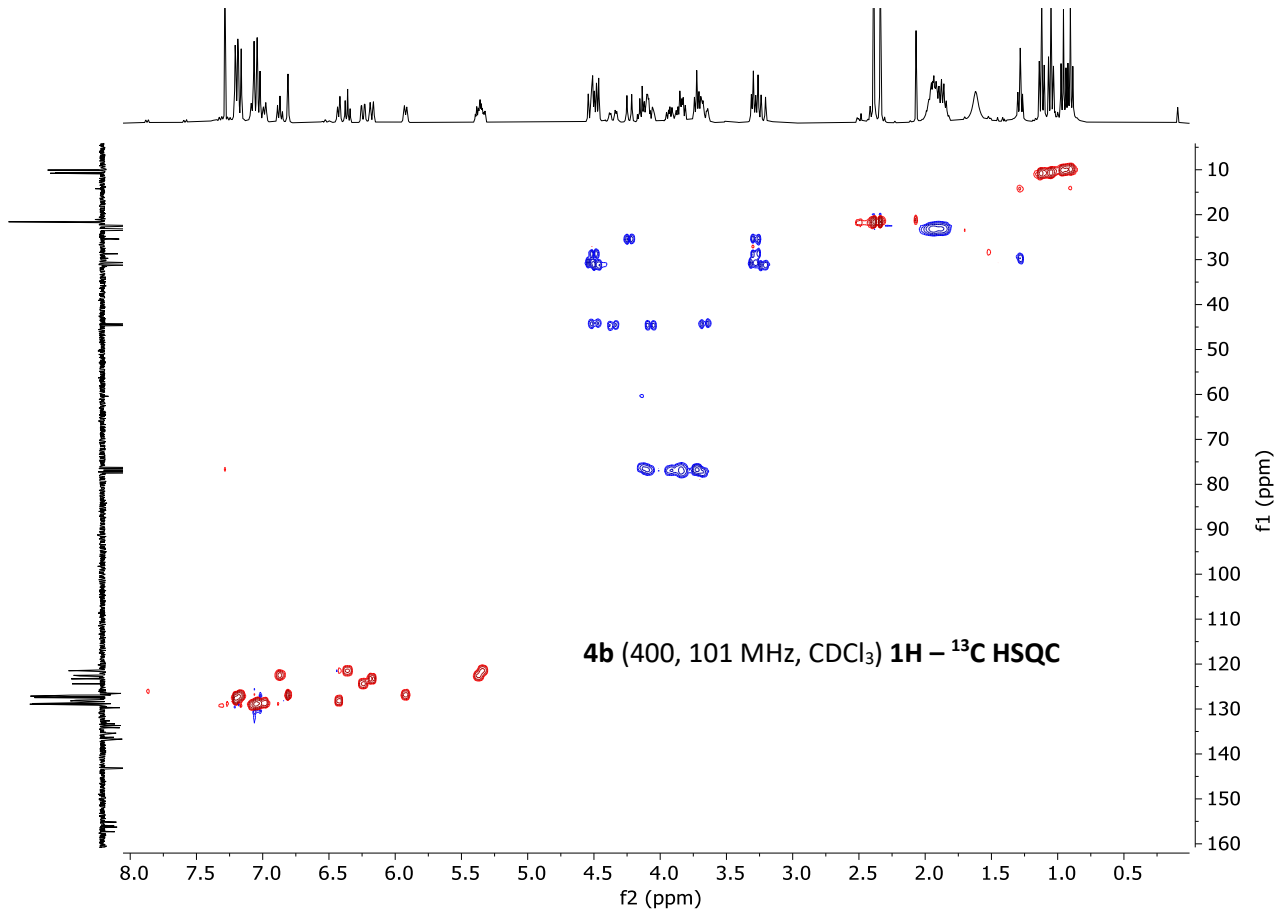


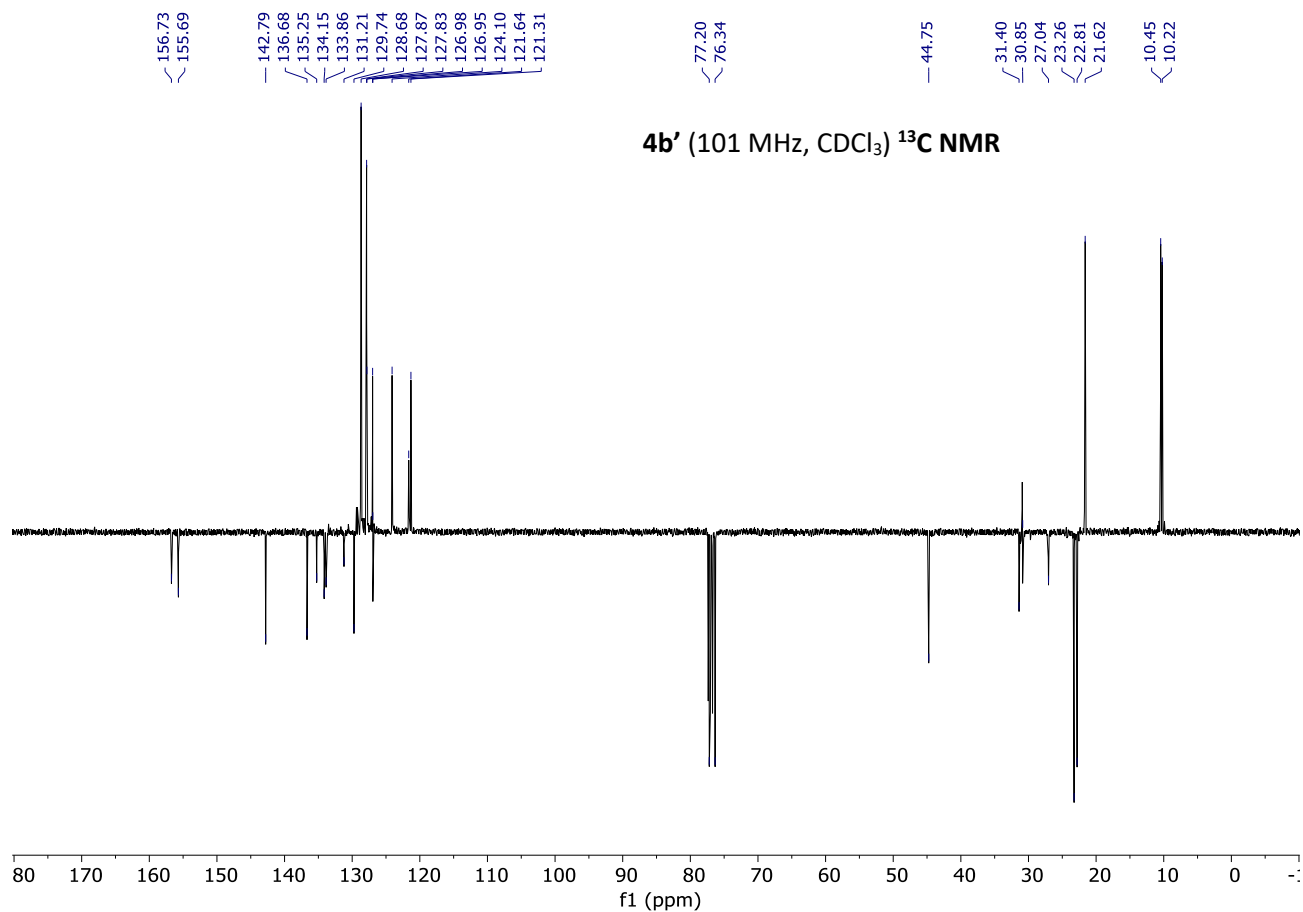
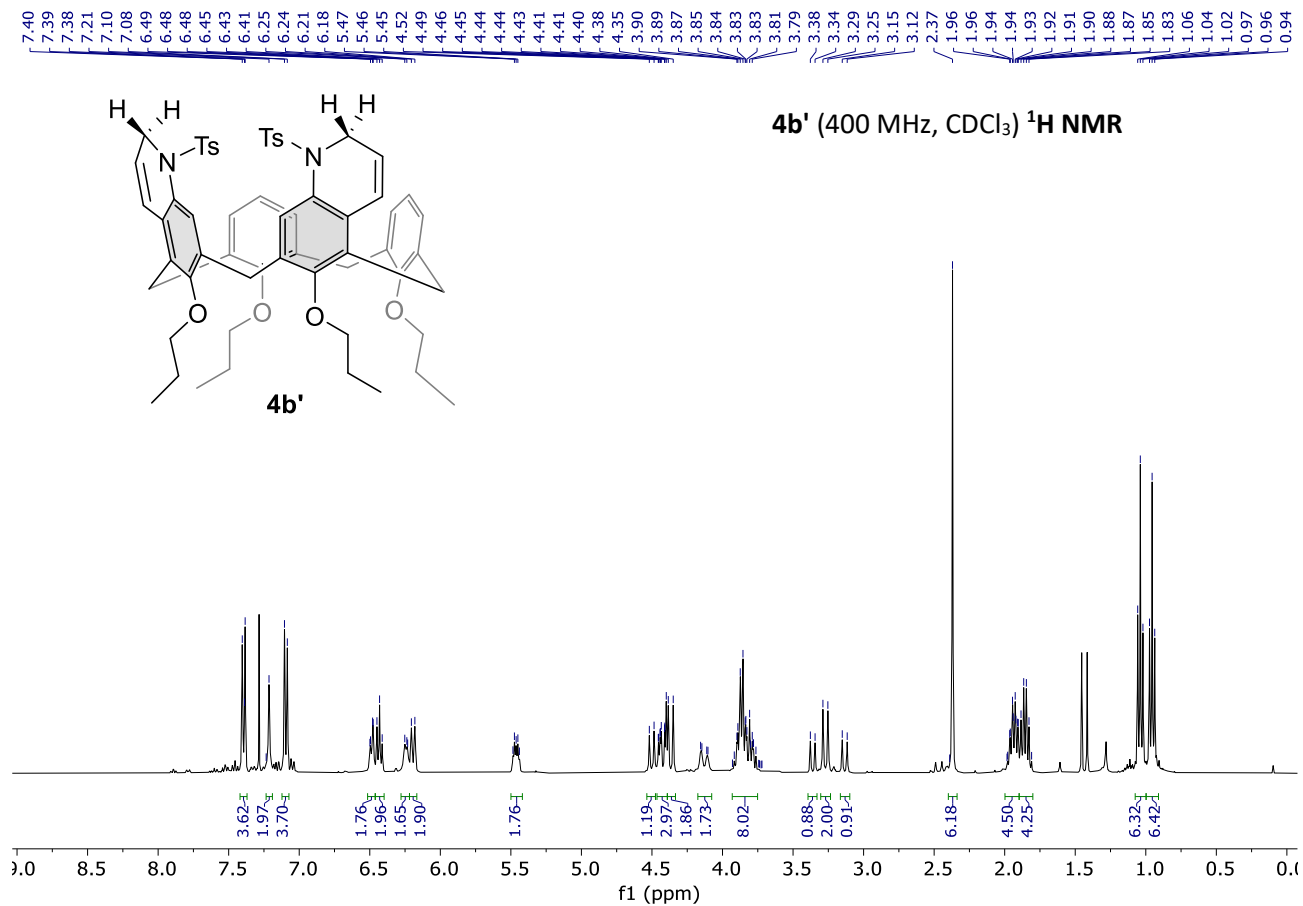
4b

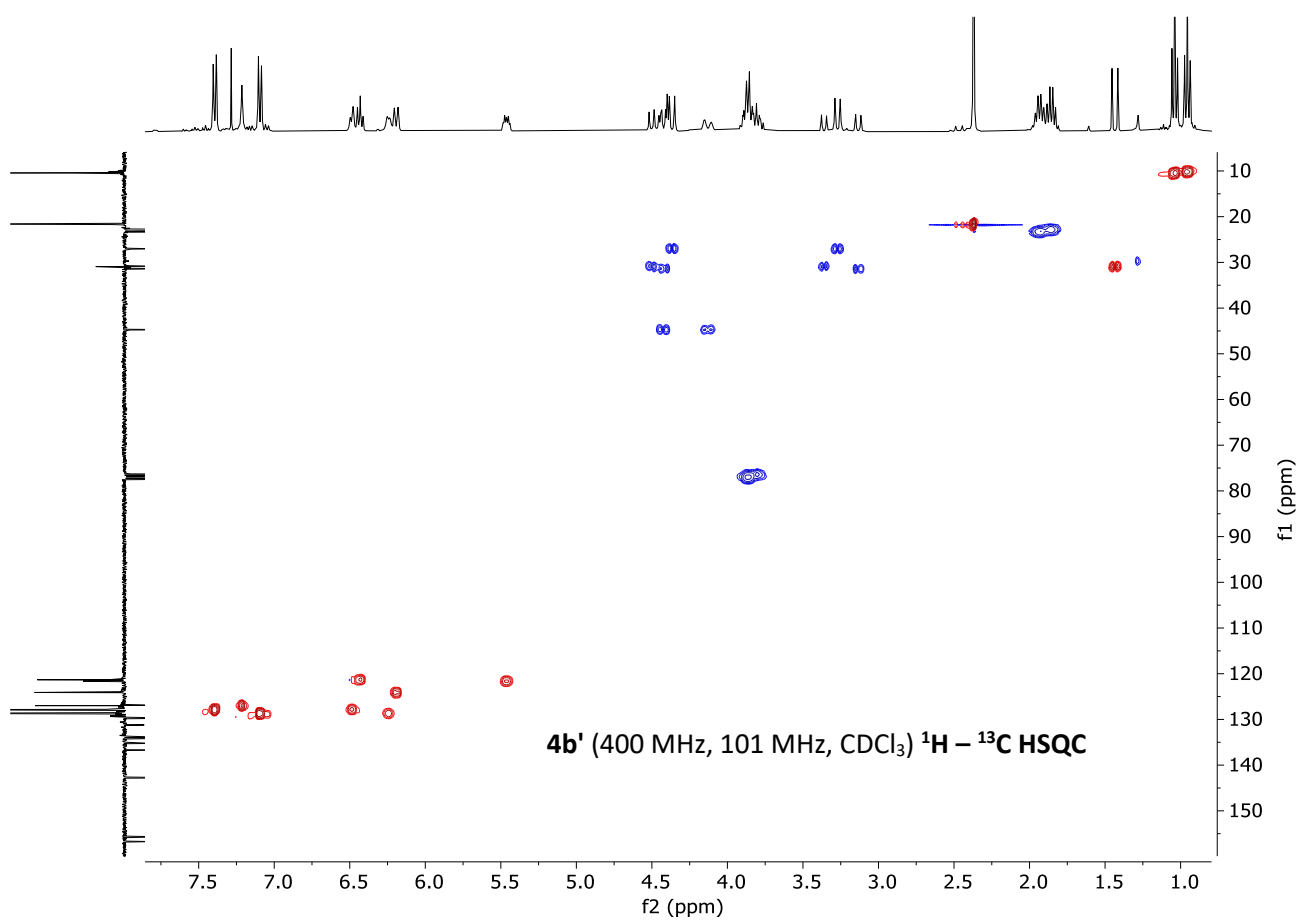
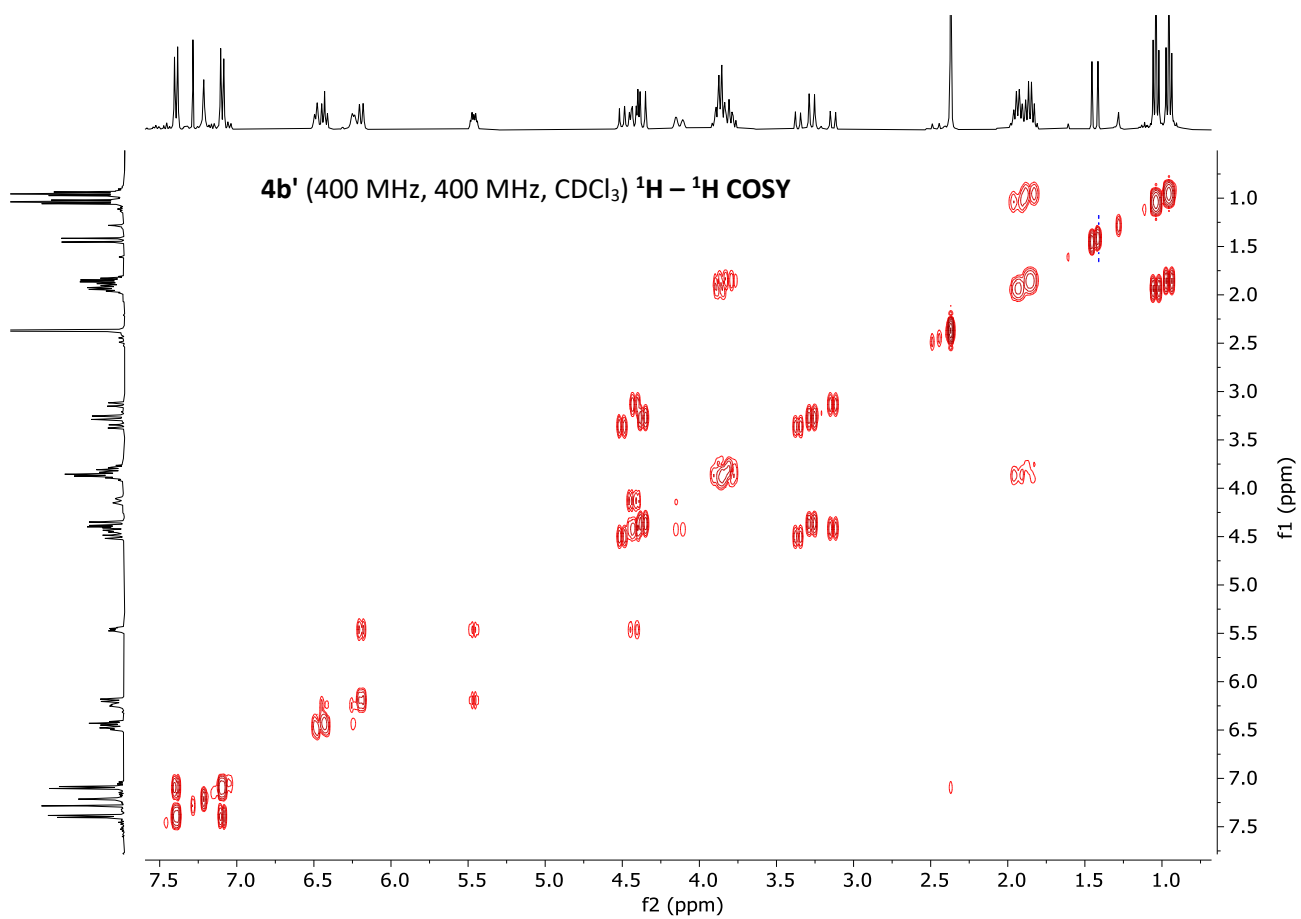


4b (101 MHz, CDCl₃) ¹³C-NMR

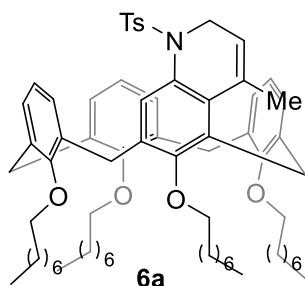




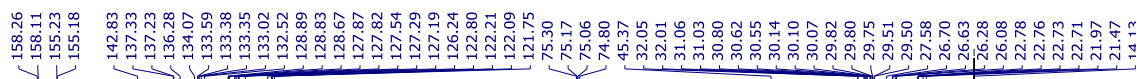
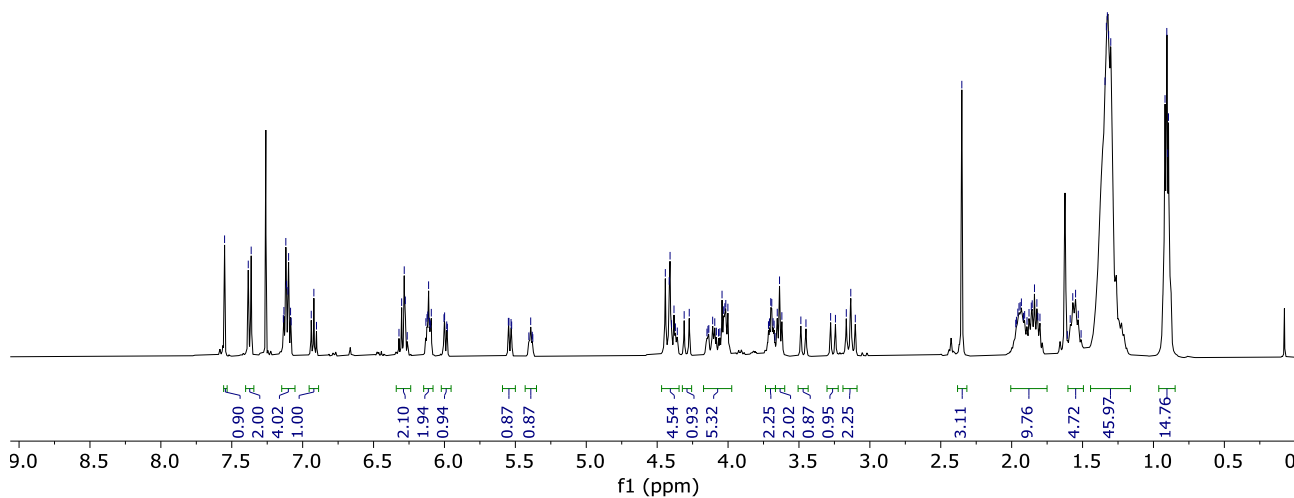




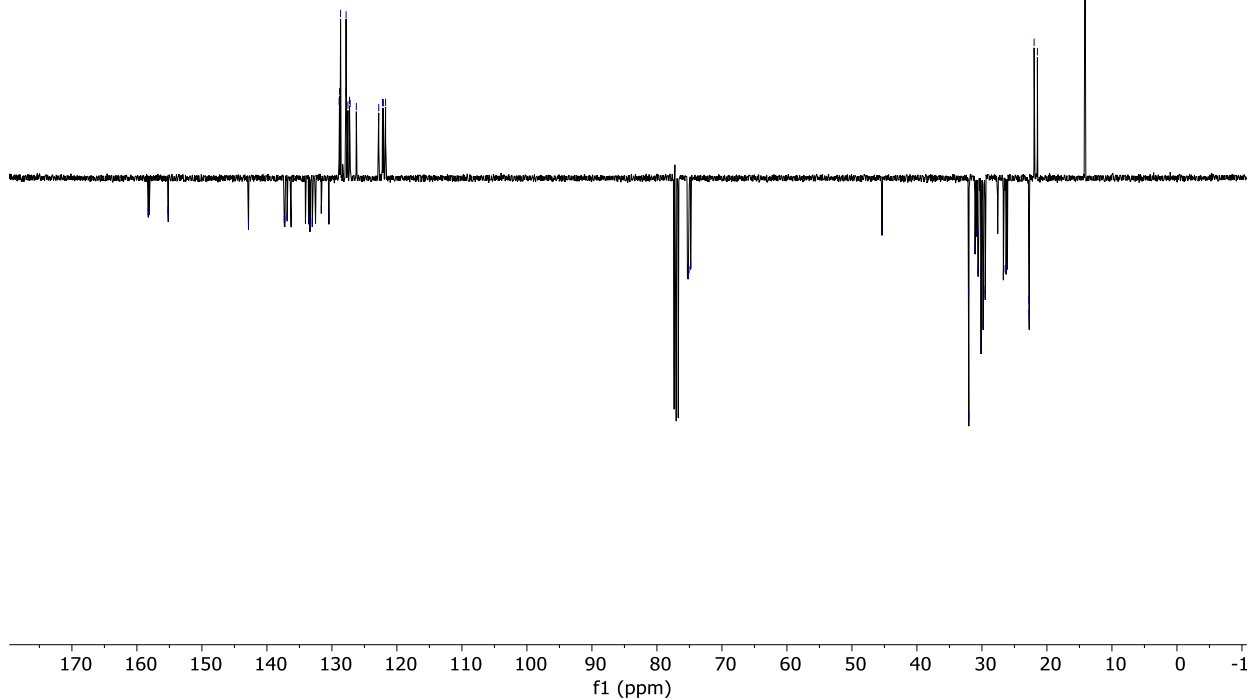
Product 6a:

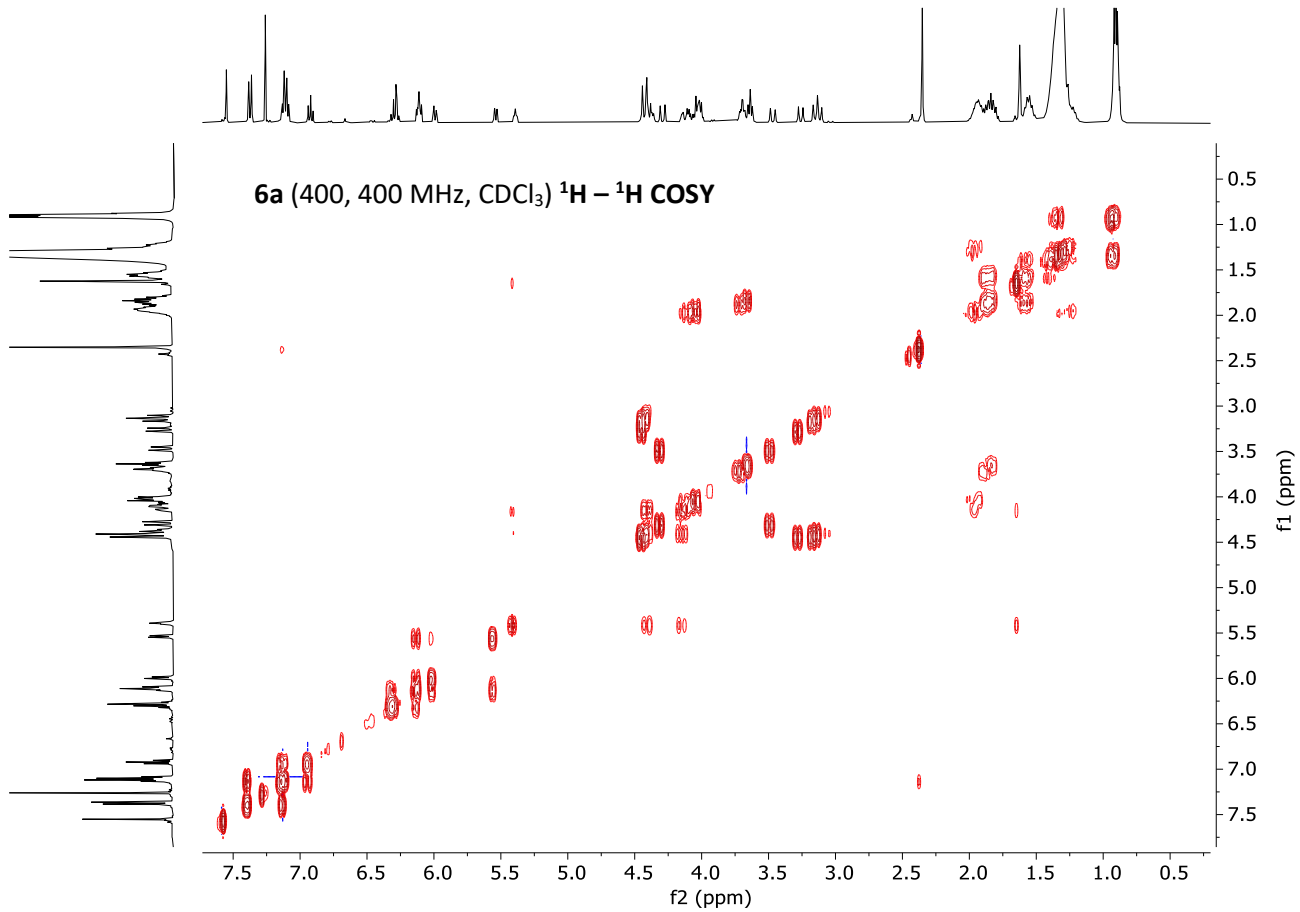
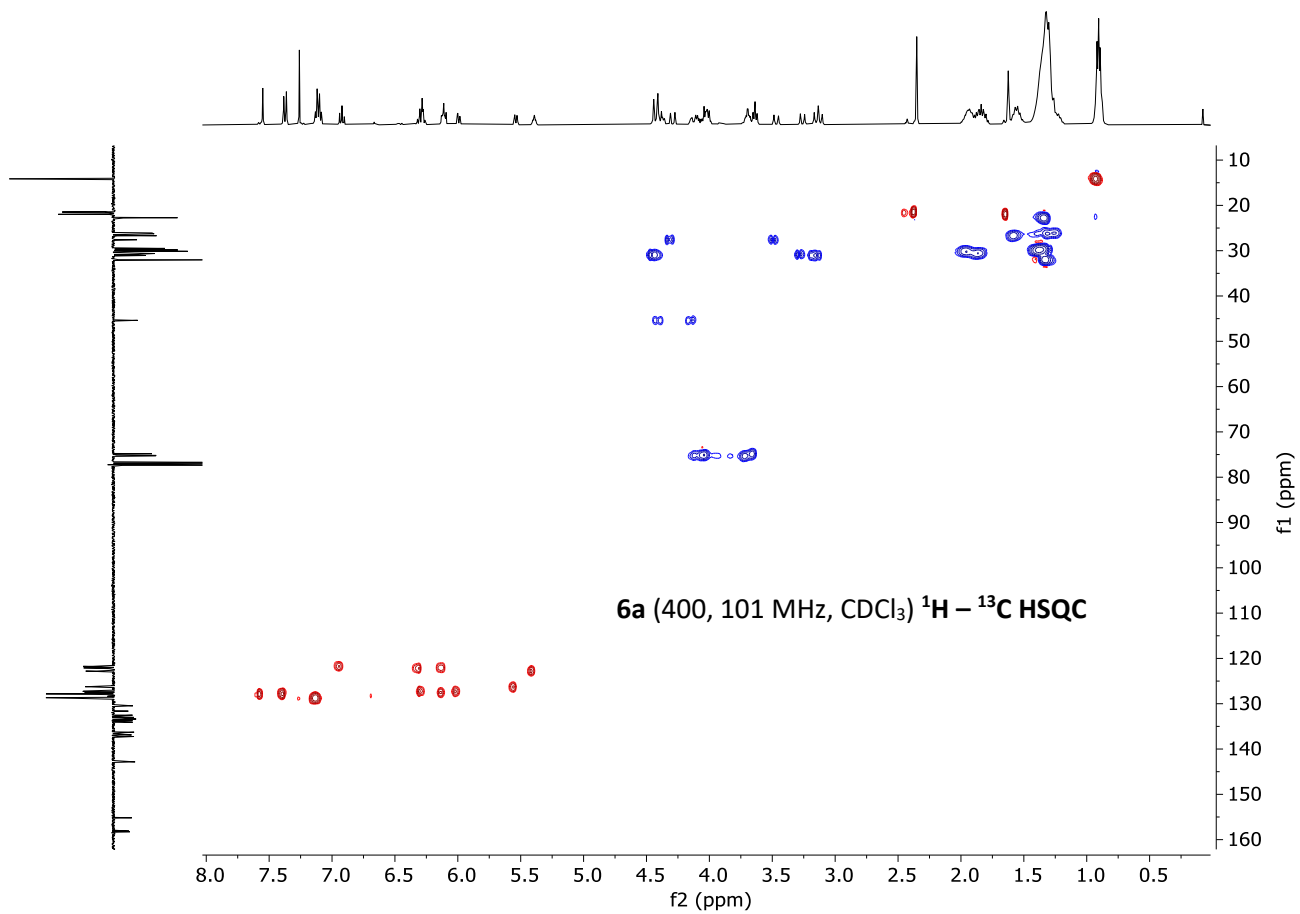


6a (400 MHz, CDCl₃) ¹H-NMR

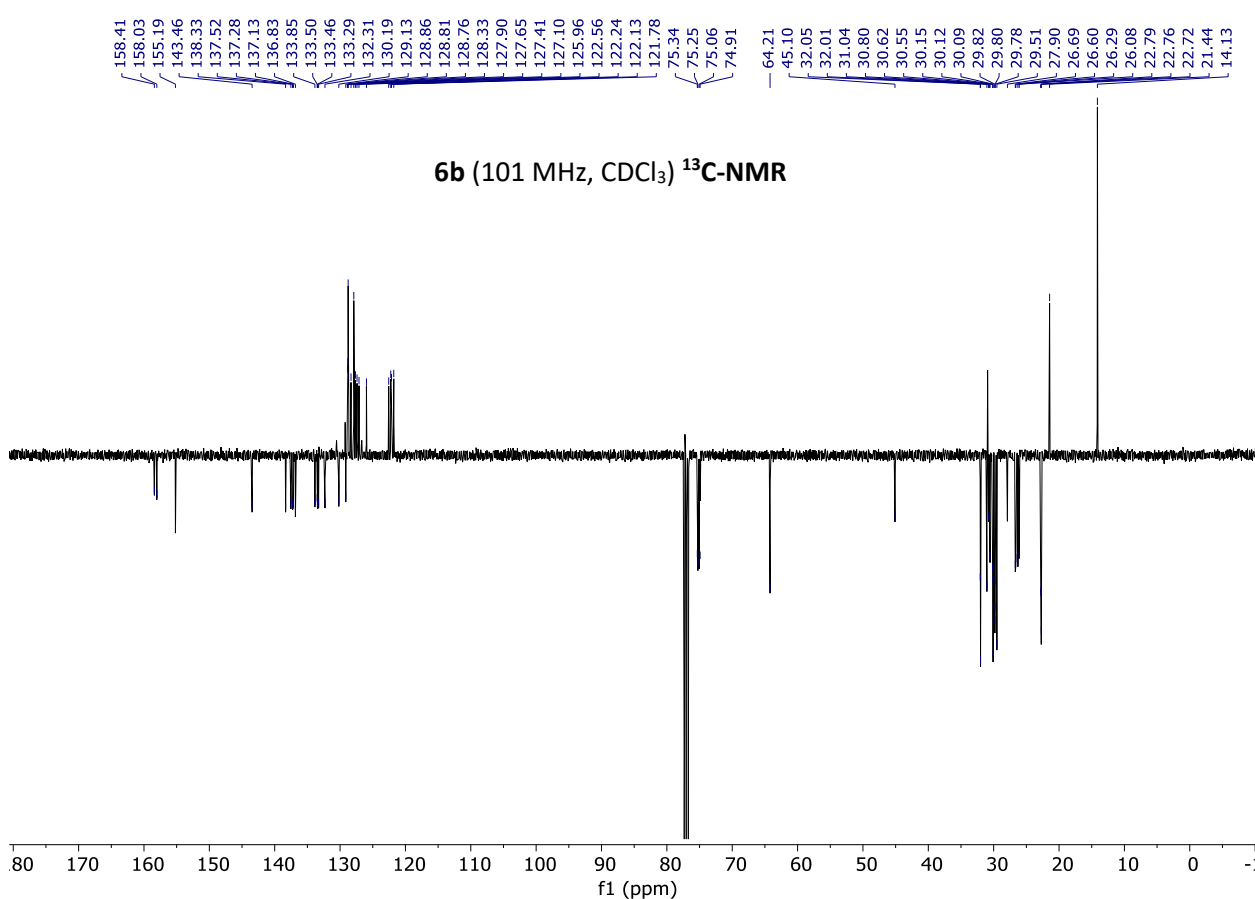
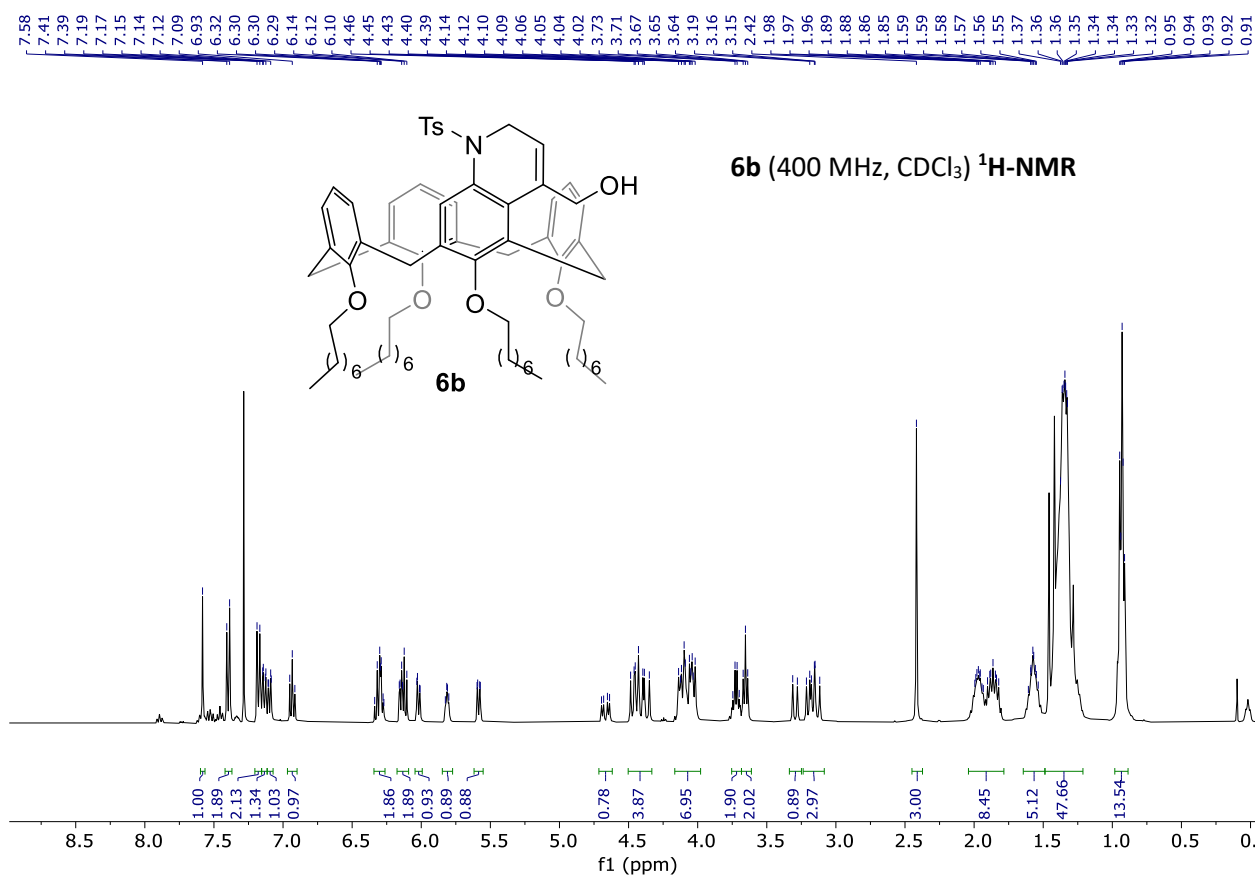


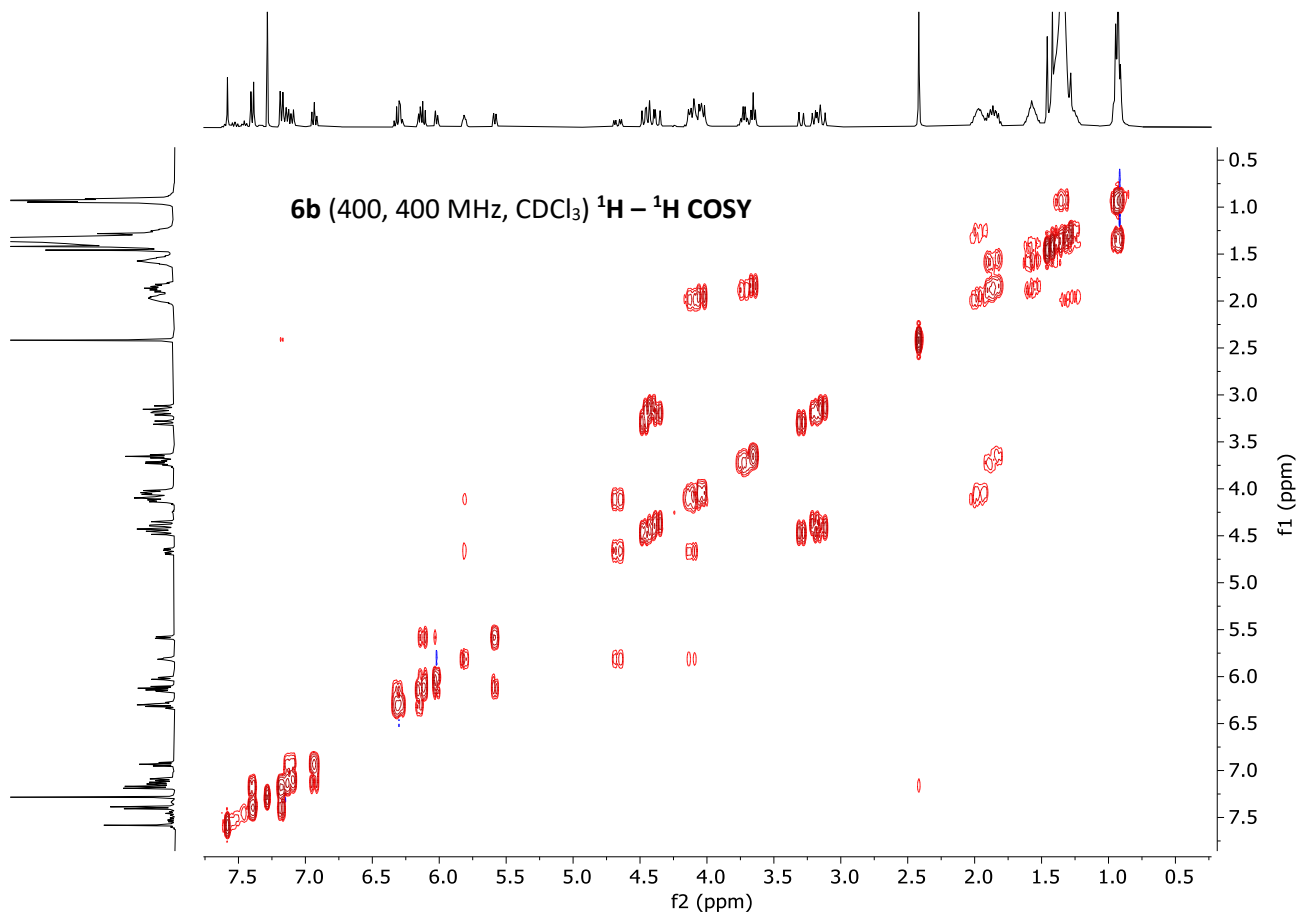
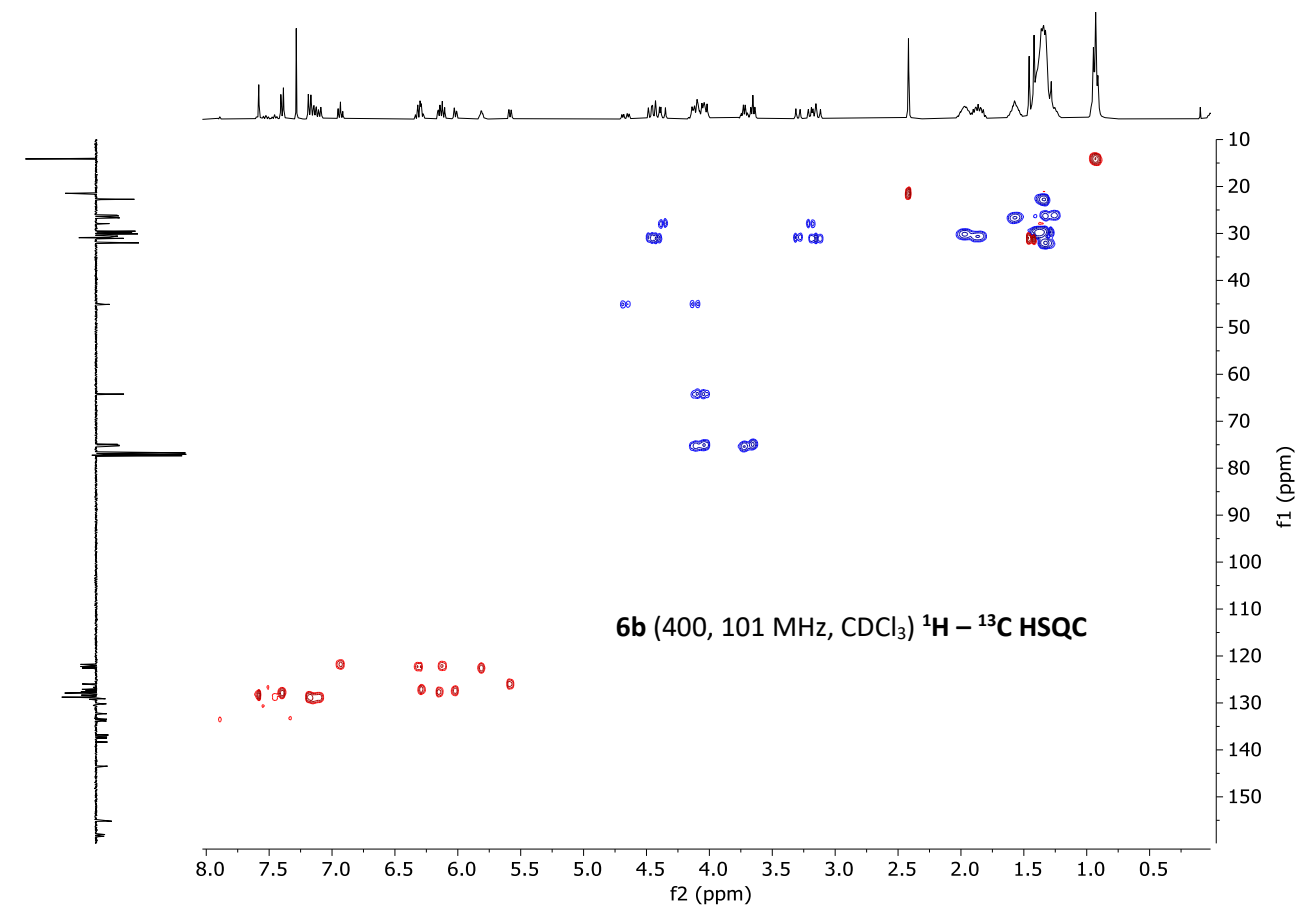
6a (101 MHz, CDCl₃) ¹³C-NMR

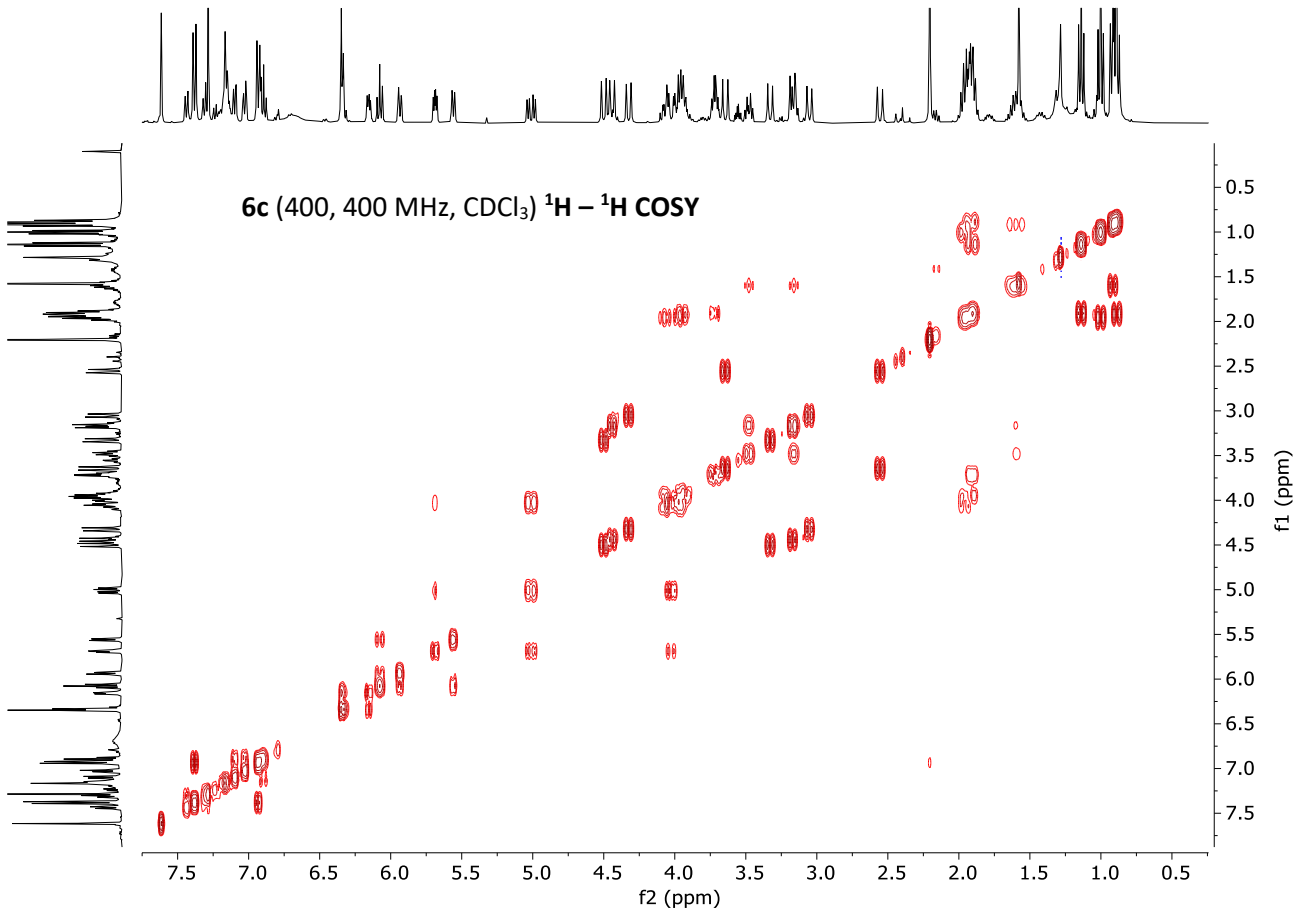
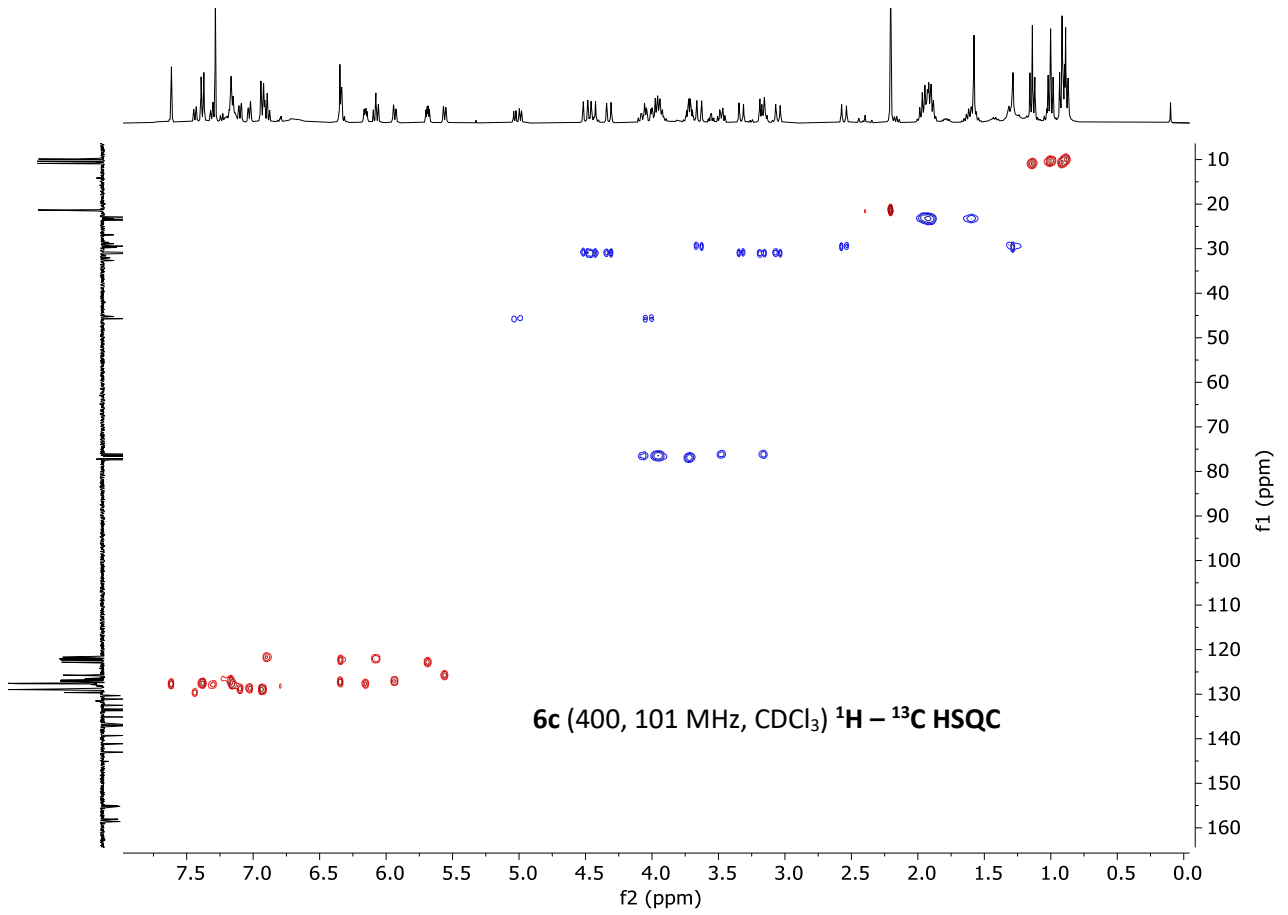




Product 6b:



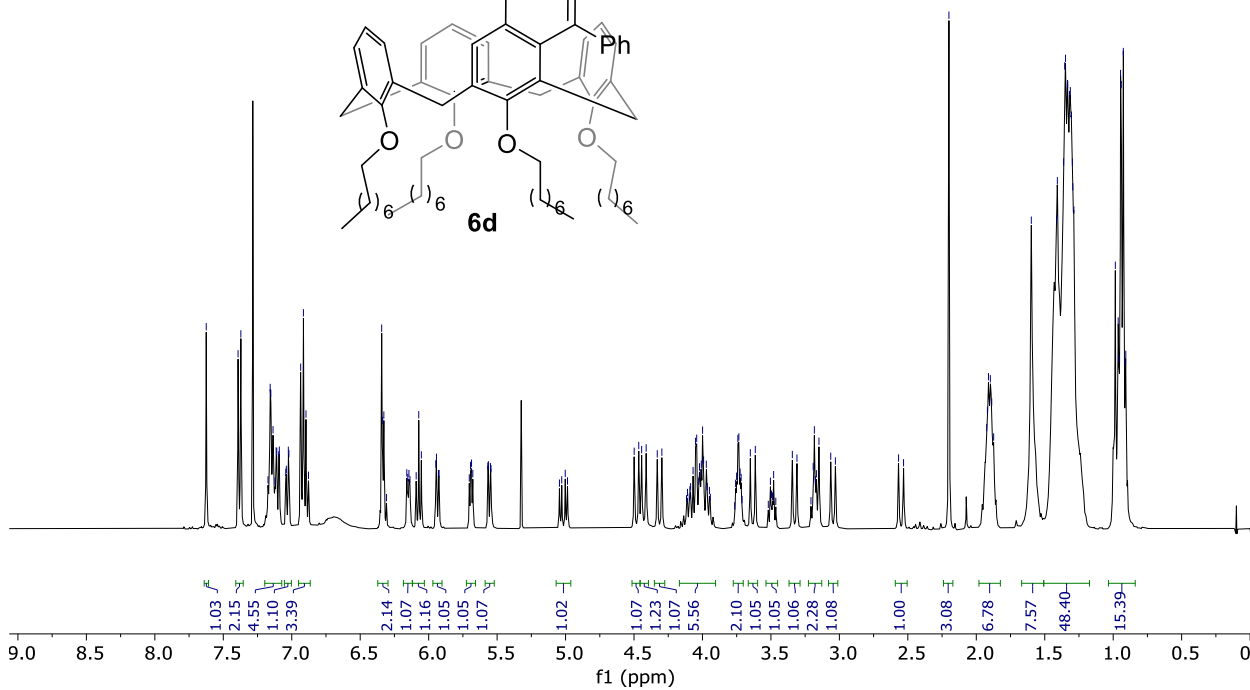
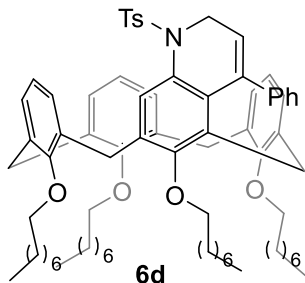




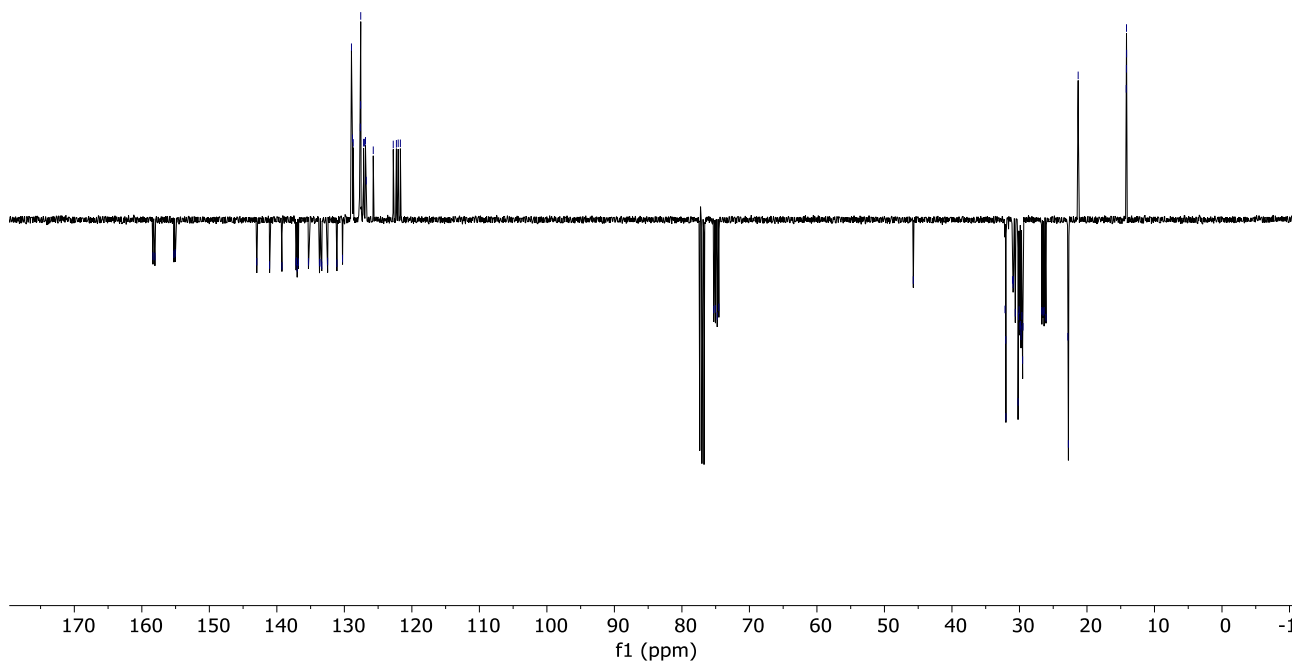
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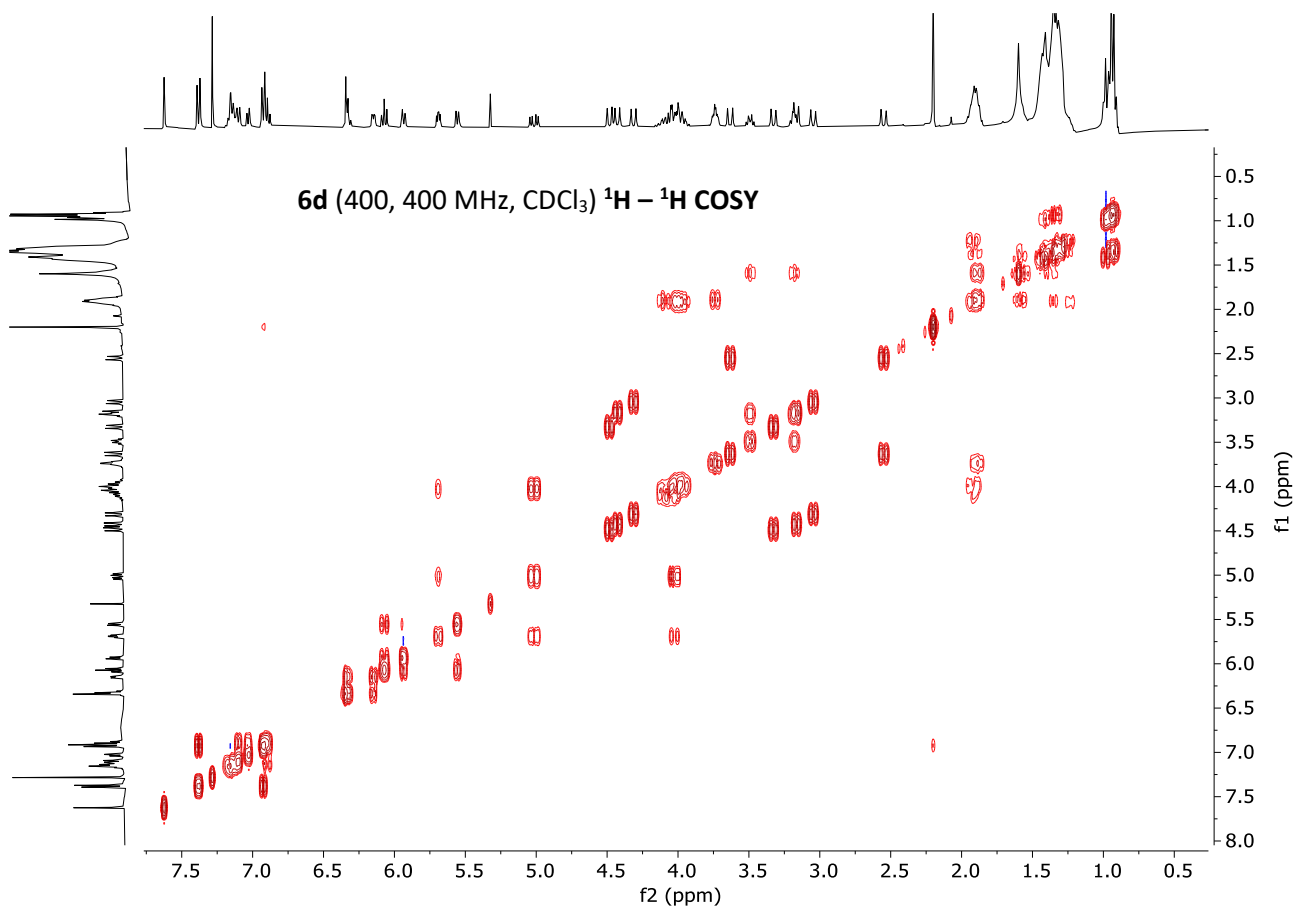
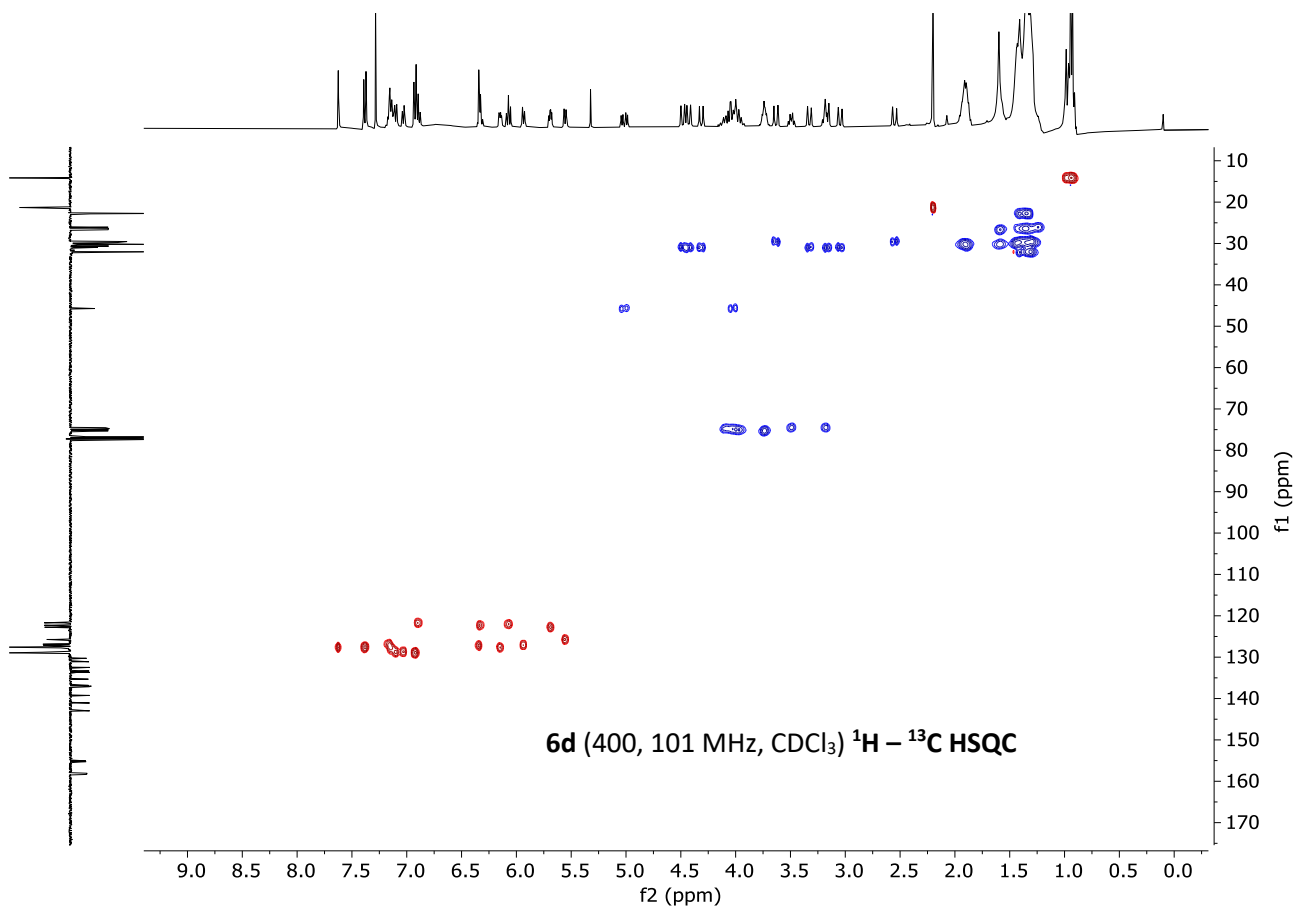


6d (400 MHz, CDCl₃) ¹H-NMR

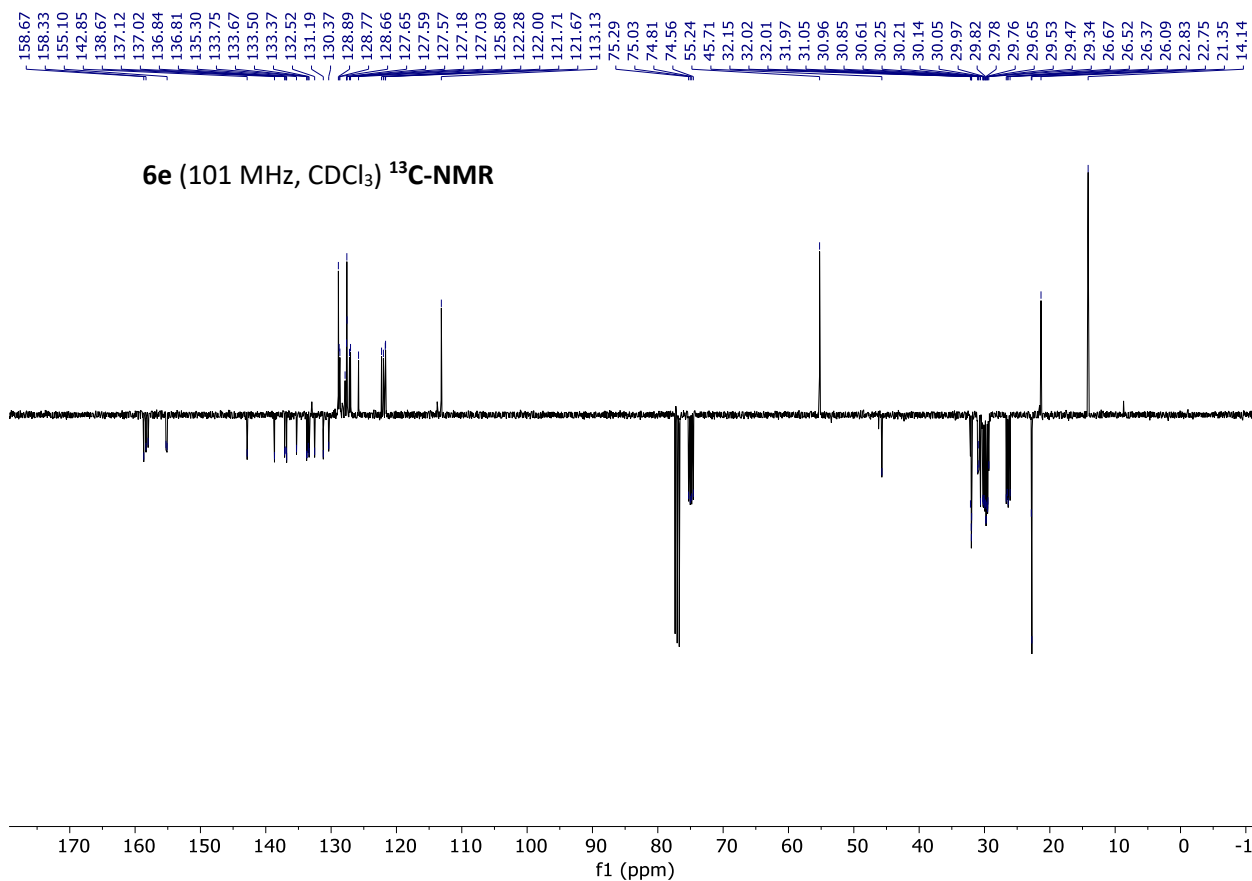
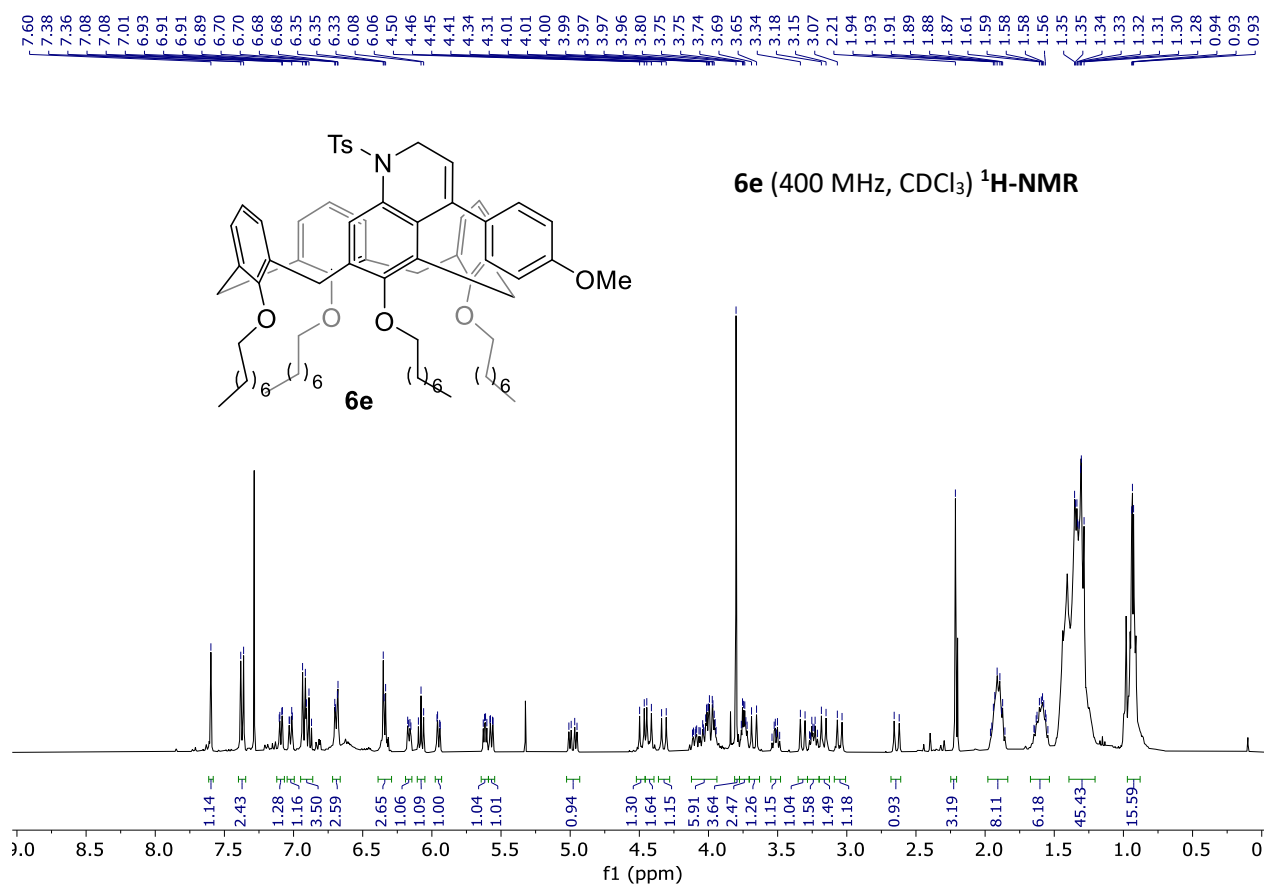


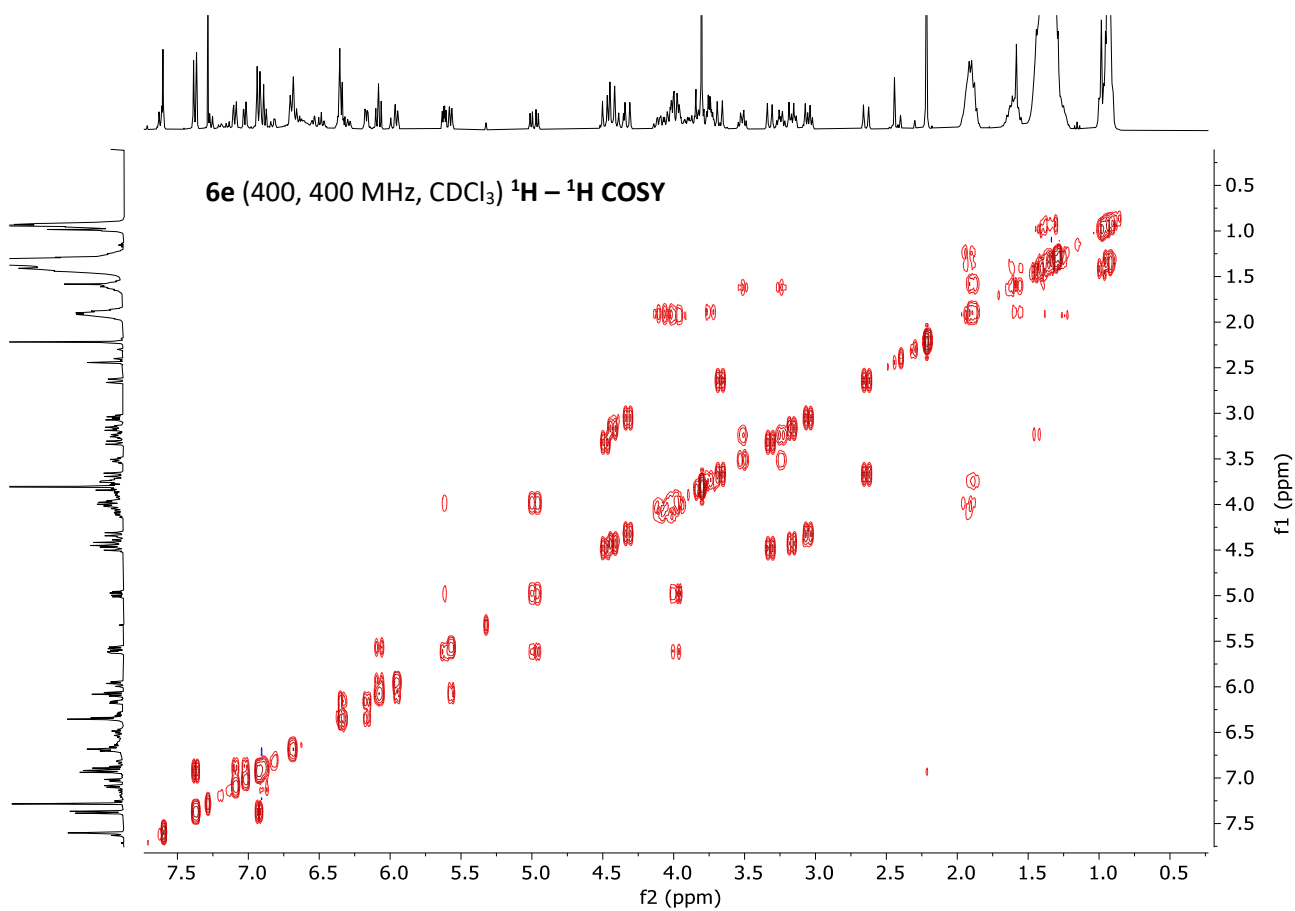
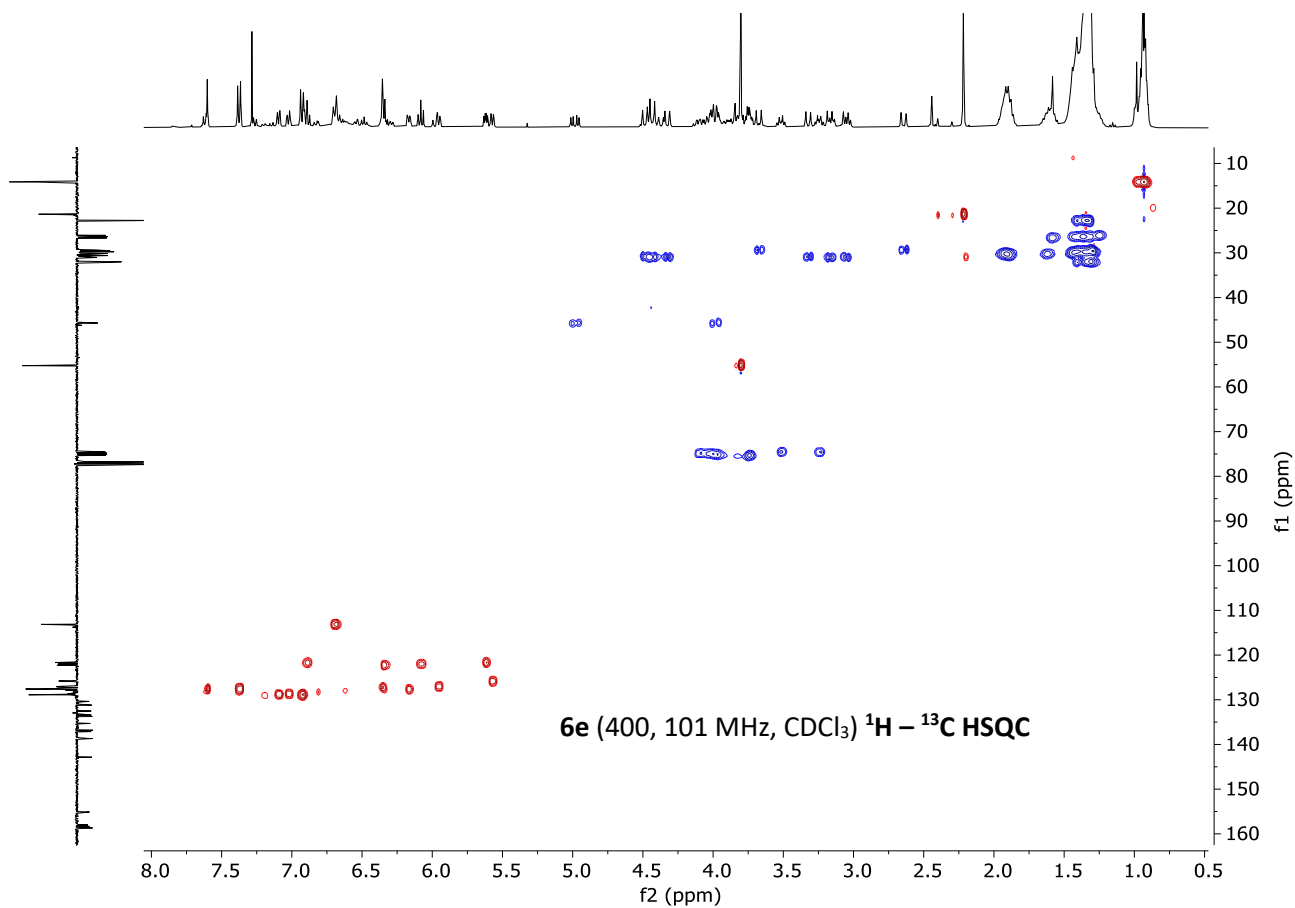
6d (101 MHz, CDCl₃) ¹³C-NMR





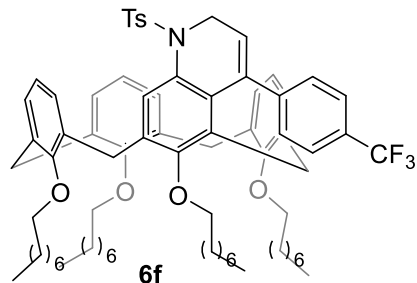
Product 6e:



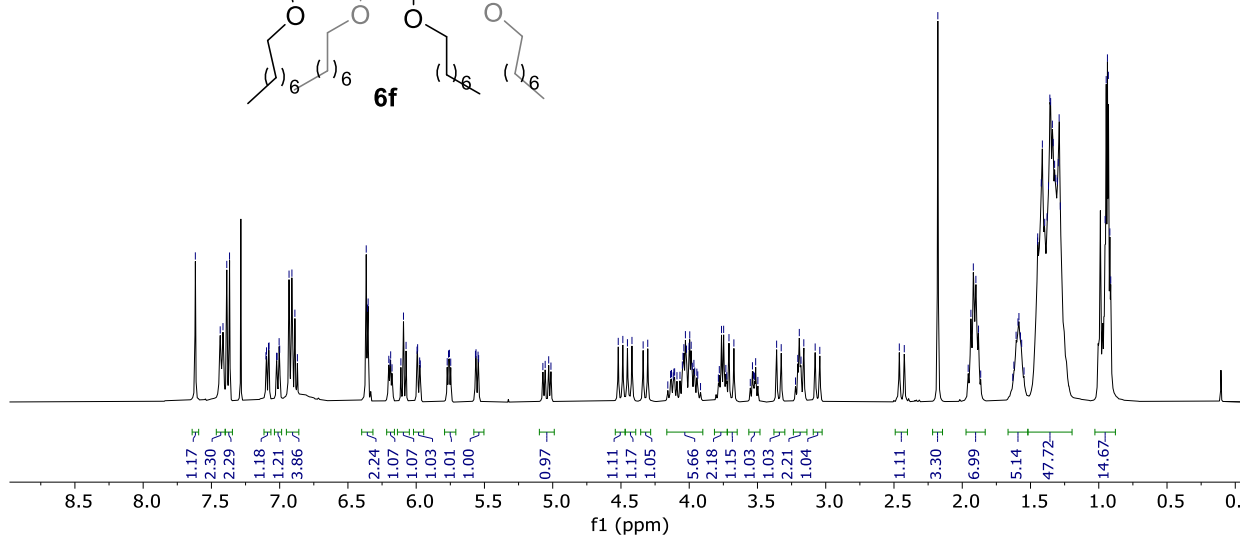


Product 6f:

7.62
7.44
7.42
7.39
7.37
7.08
7.00
6.93
6.91
6.89
6.37
6.36
6.35
6.09
6.07
4.52
4.49
4.45
4.42
4.34
4.30
4.03
4.00
3.99
3.76
3.75
3.71
3.67
3.36
3.19
3.16
2.18
1.94
1.92
1.90
1.88
1.61
1.59
1.58
1.57
1.56
1.45
1.45
1.42
1.41
1.40
1.38
1.37
1.36
1.35
1.34
1.33
1.32
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1.30
1.30
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1.28
0.95
0.95
0.94
0.93
0.92
0.91

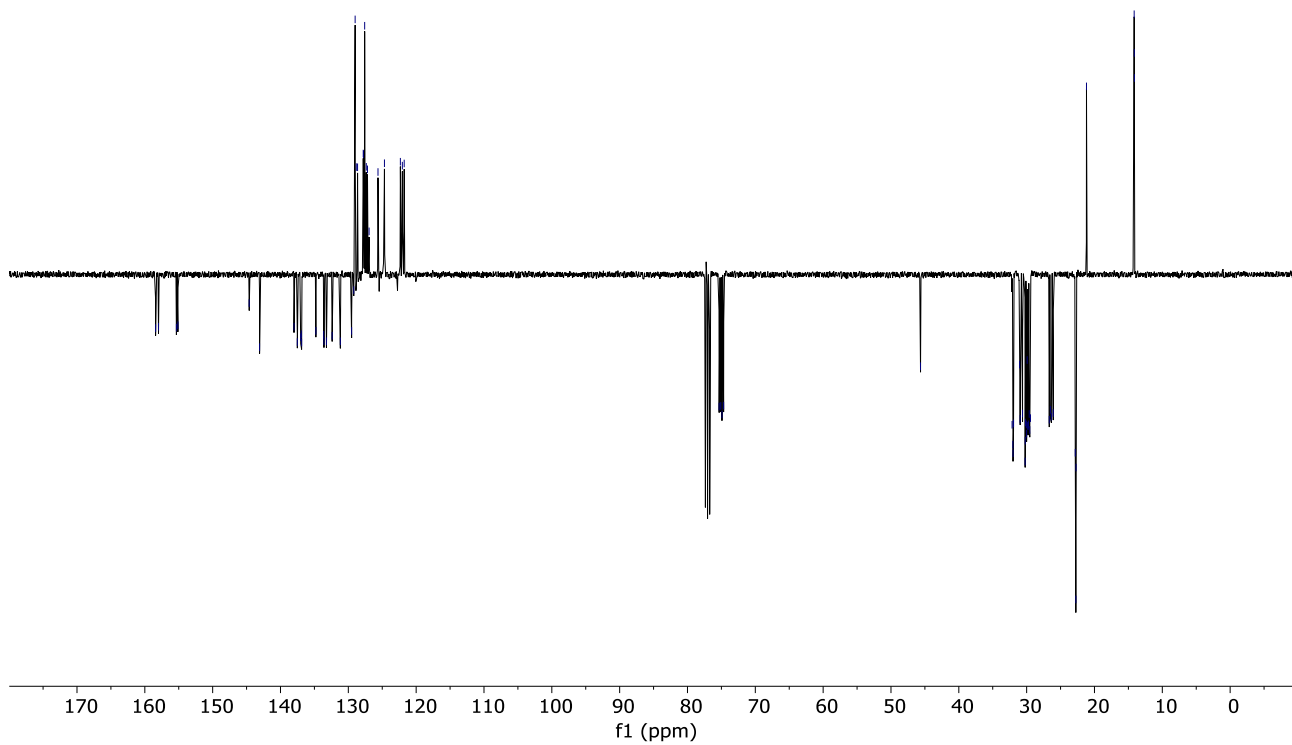


6f (400 MHz, CDCl₃) ¹H-NMR



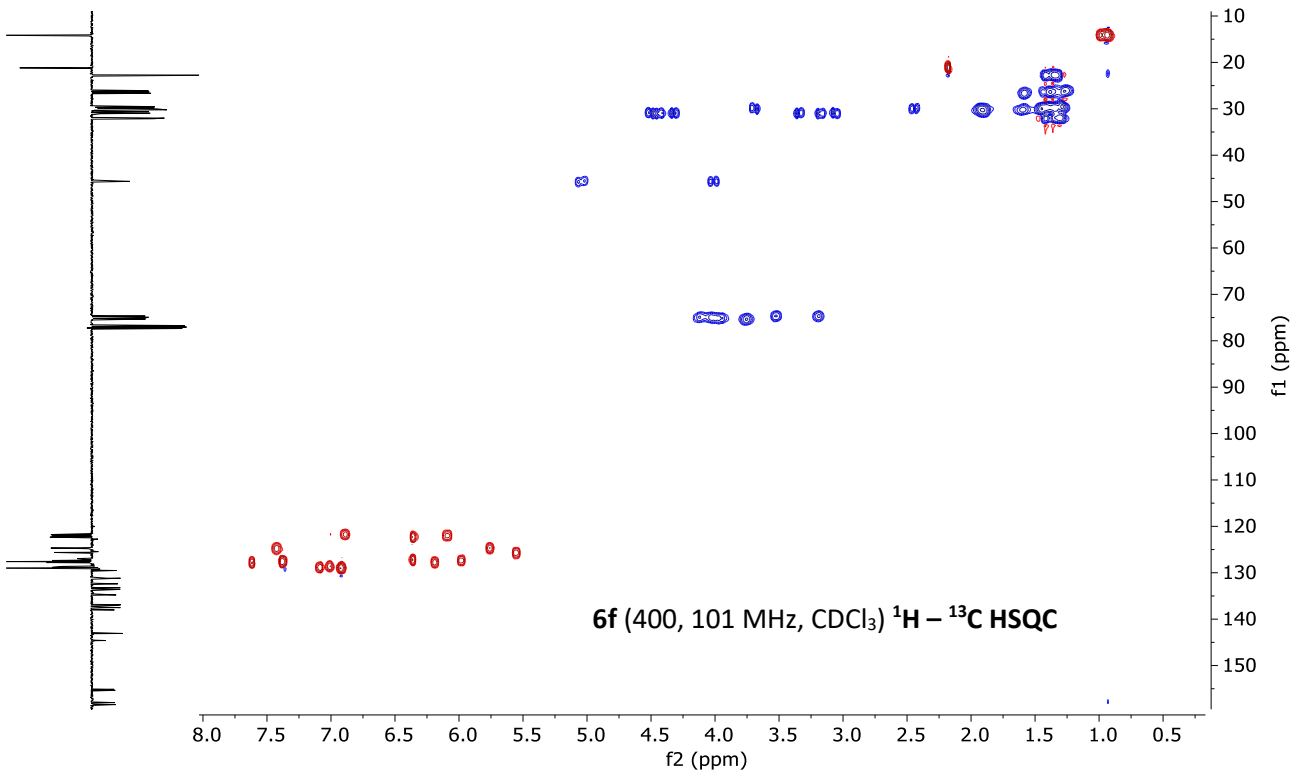
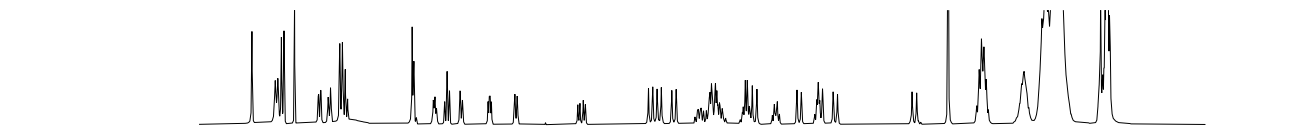
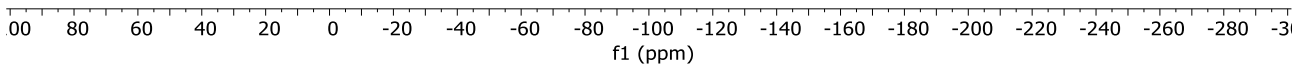
158.41
157.98
155.34
155.12
143.09
138.01
137.52
137.02
136.93
136.88
134.78
133.63
133.59
133.22
132.39
131.18
129.51
129.00
128.83
128.64
127.80
127.76
127.59
127.35
127.18
125.63
124.67
122.33
122.03
121.76
75.34
75.09
74.91
74.67
45.65
32.15
32.03
32.01
31.93
31.04
30.96
30.61
30.22
30.21
30.17
30.05
30.01
29.92
29.83
29.78
29.74
29.62
29.54
29.43
26.67
26.50
26.36
26.08
22.83
22.75
22.72
21.18
14.15
14.11

6f (101 MHz, CDCl₃) ¹³C-NMR

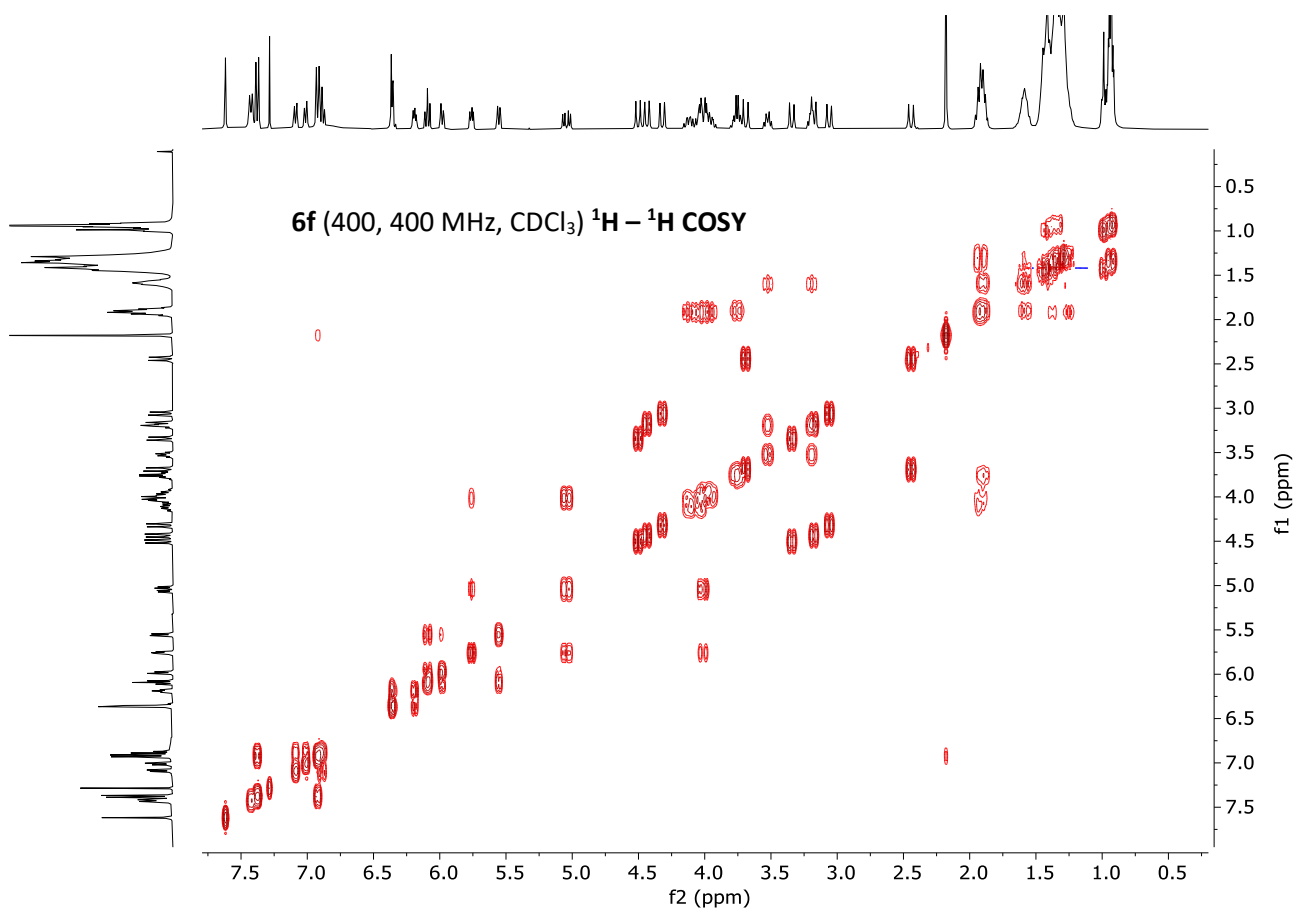


-62.50

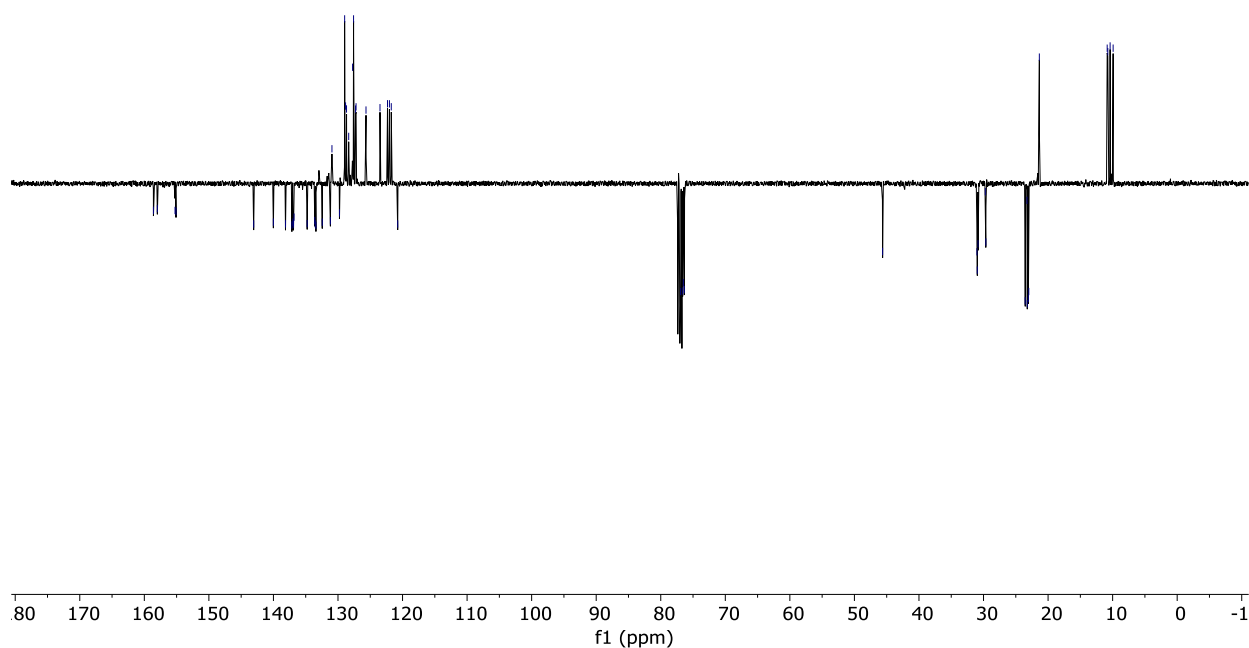
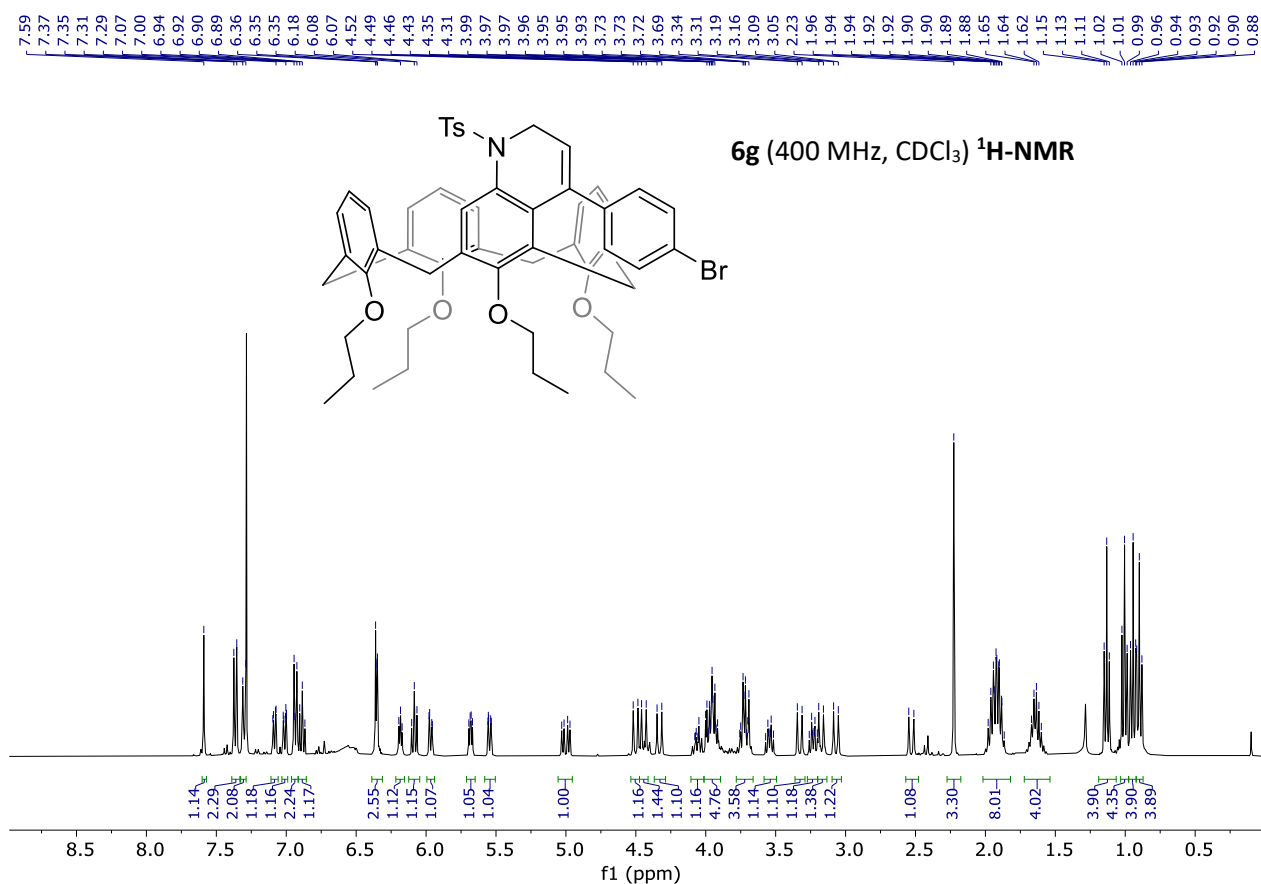
6f (565 MHz, CDCl₃) ¹⁹F-NMR

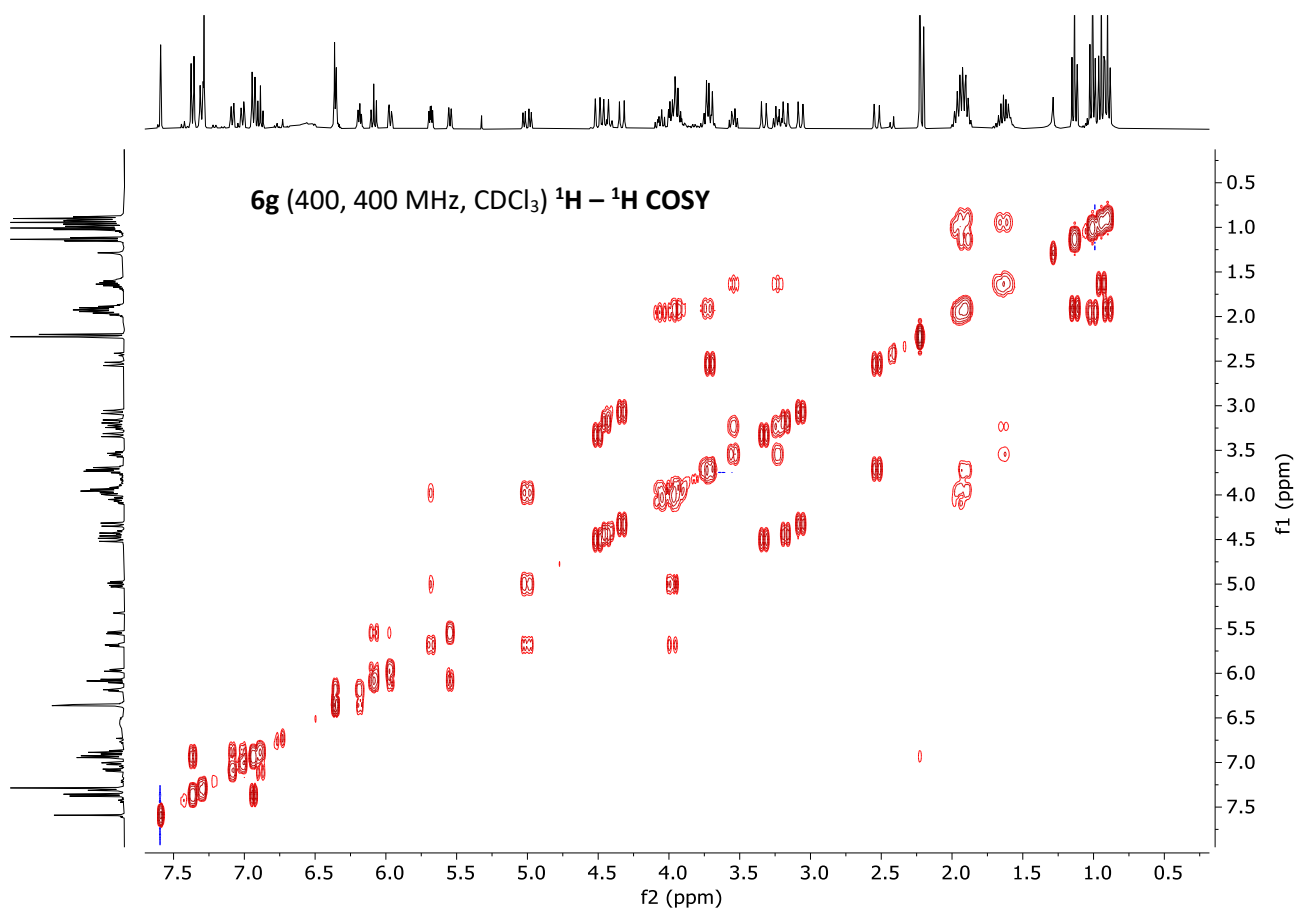
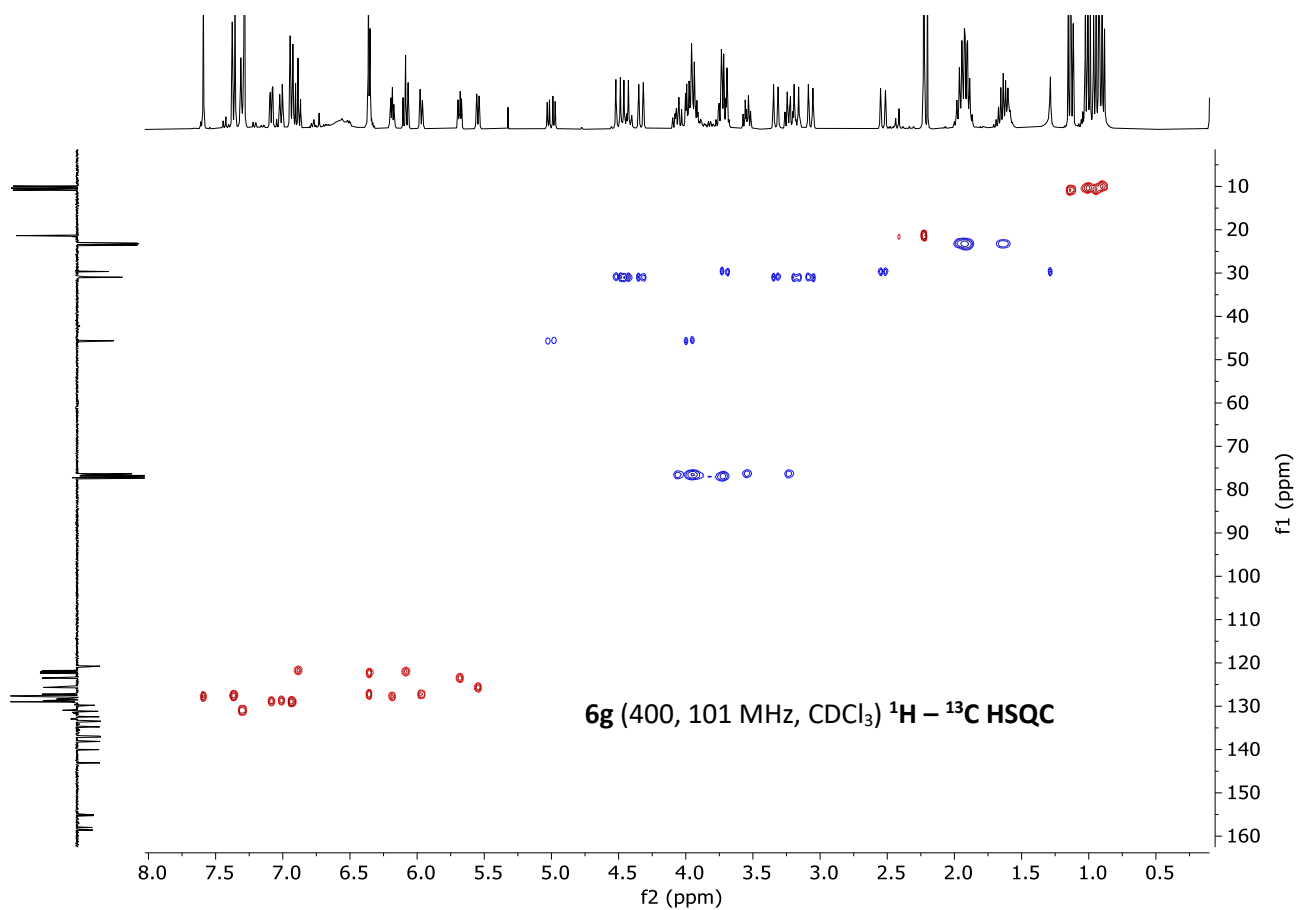


6f (400, 101 MHz, CDCl₃) ¹H - ¹³C HSQC

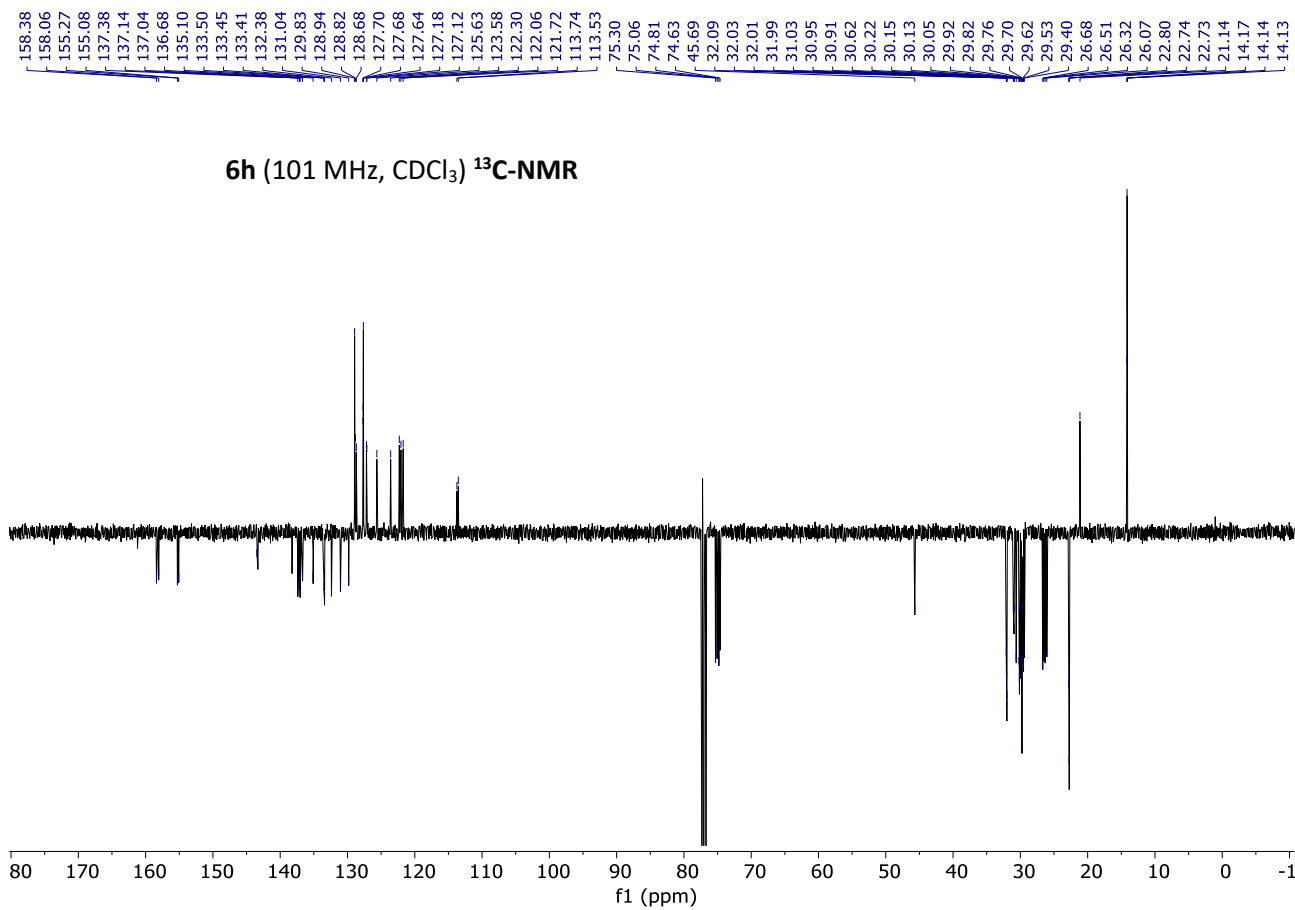
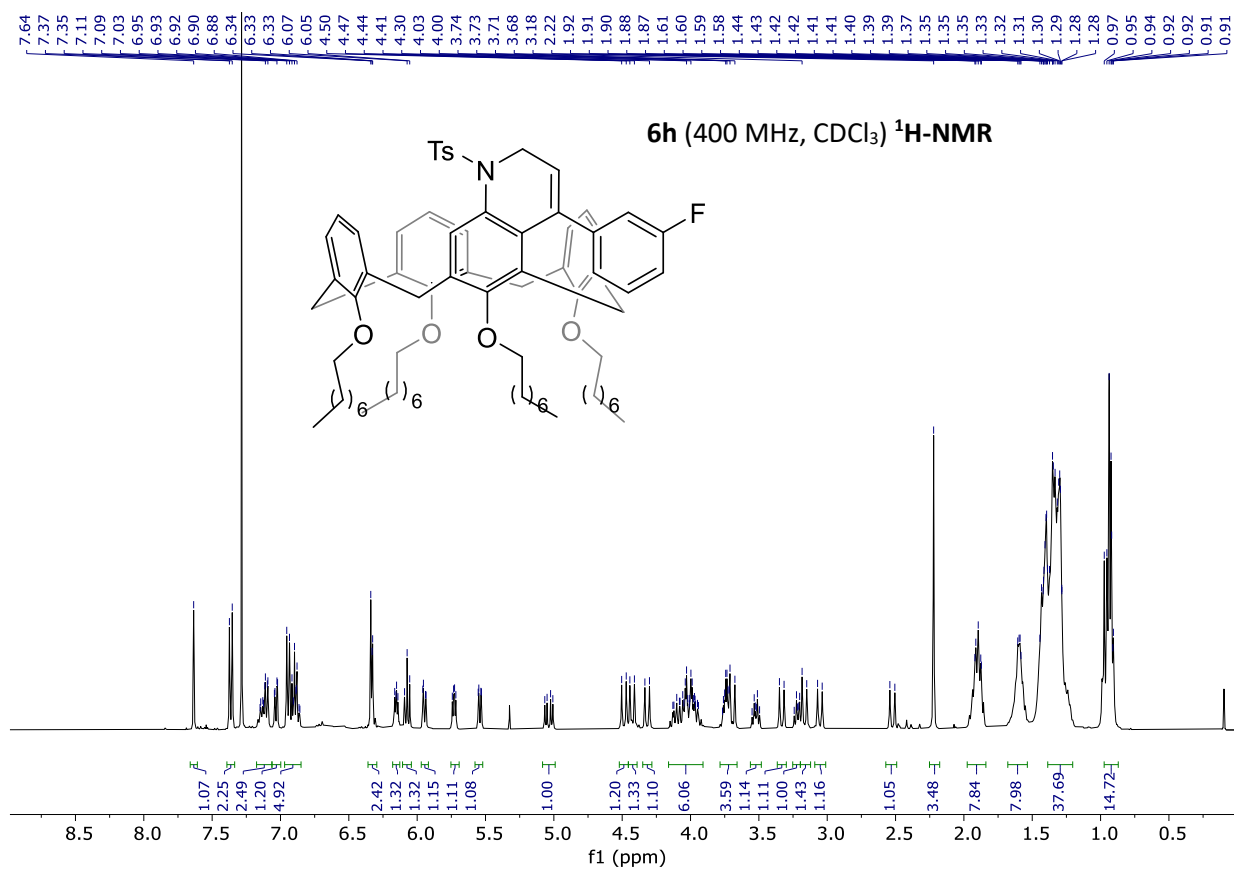


Product 6g:

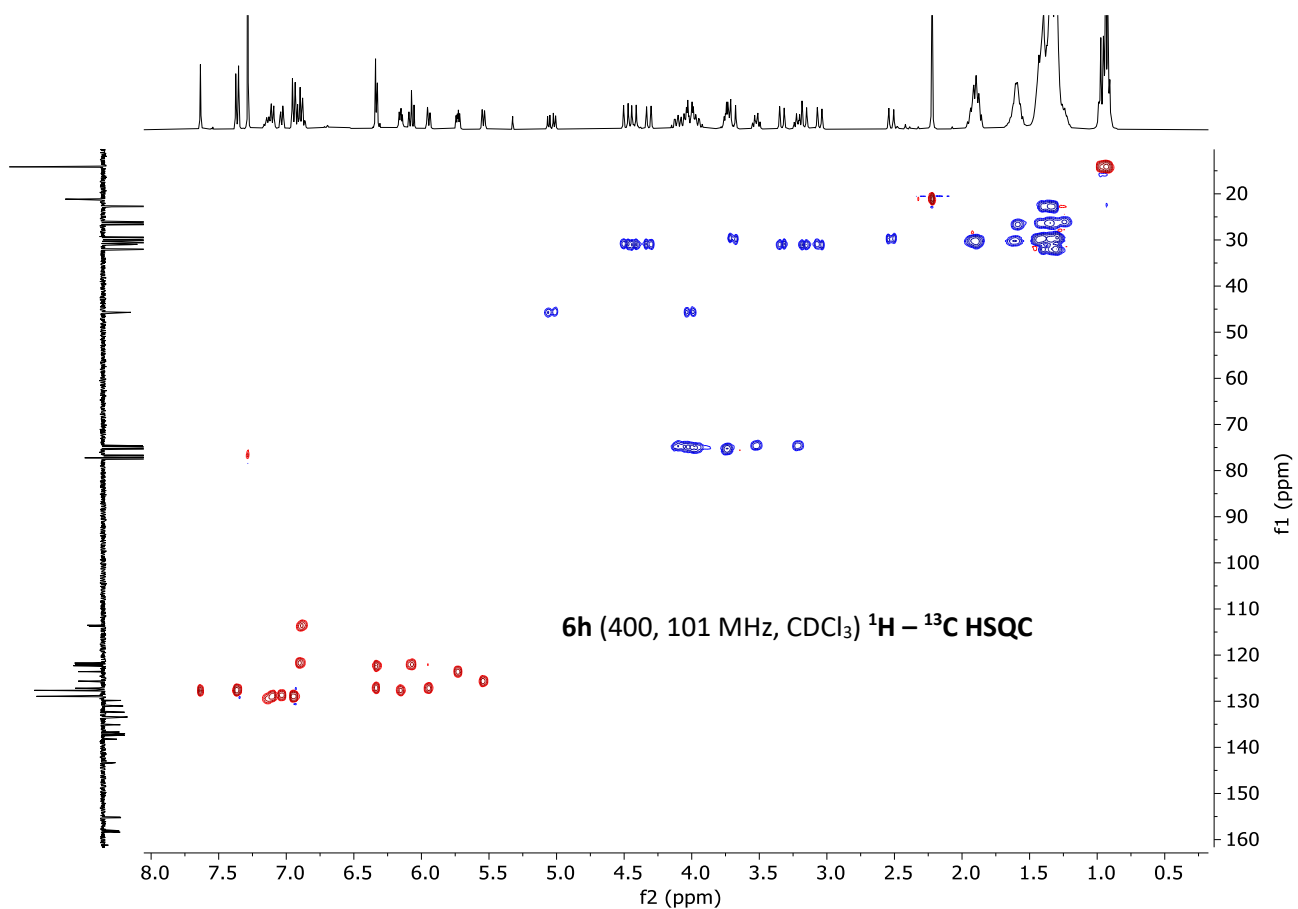
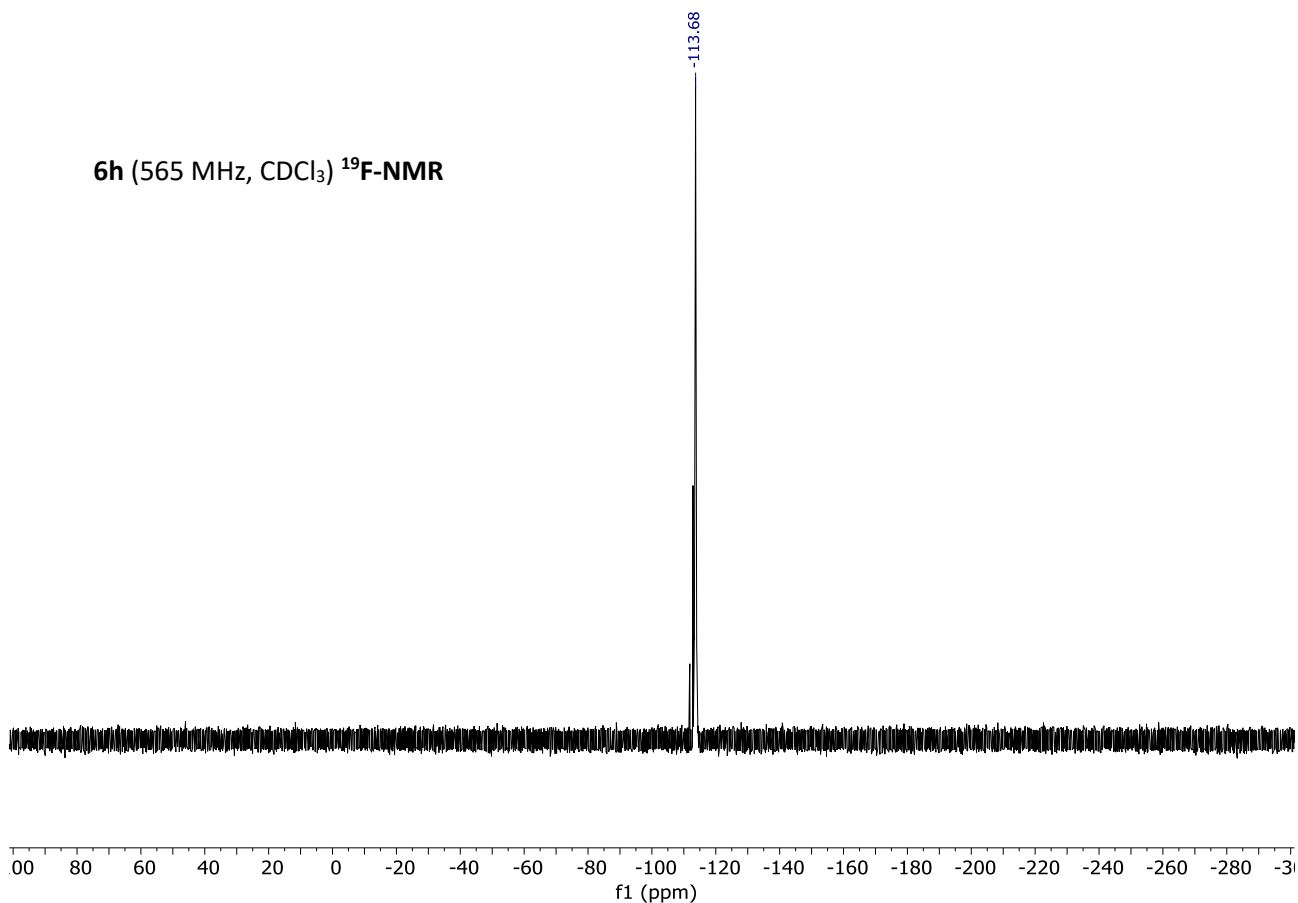


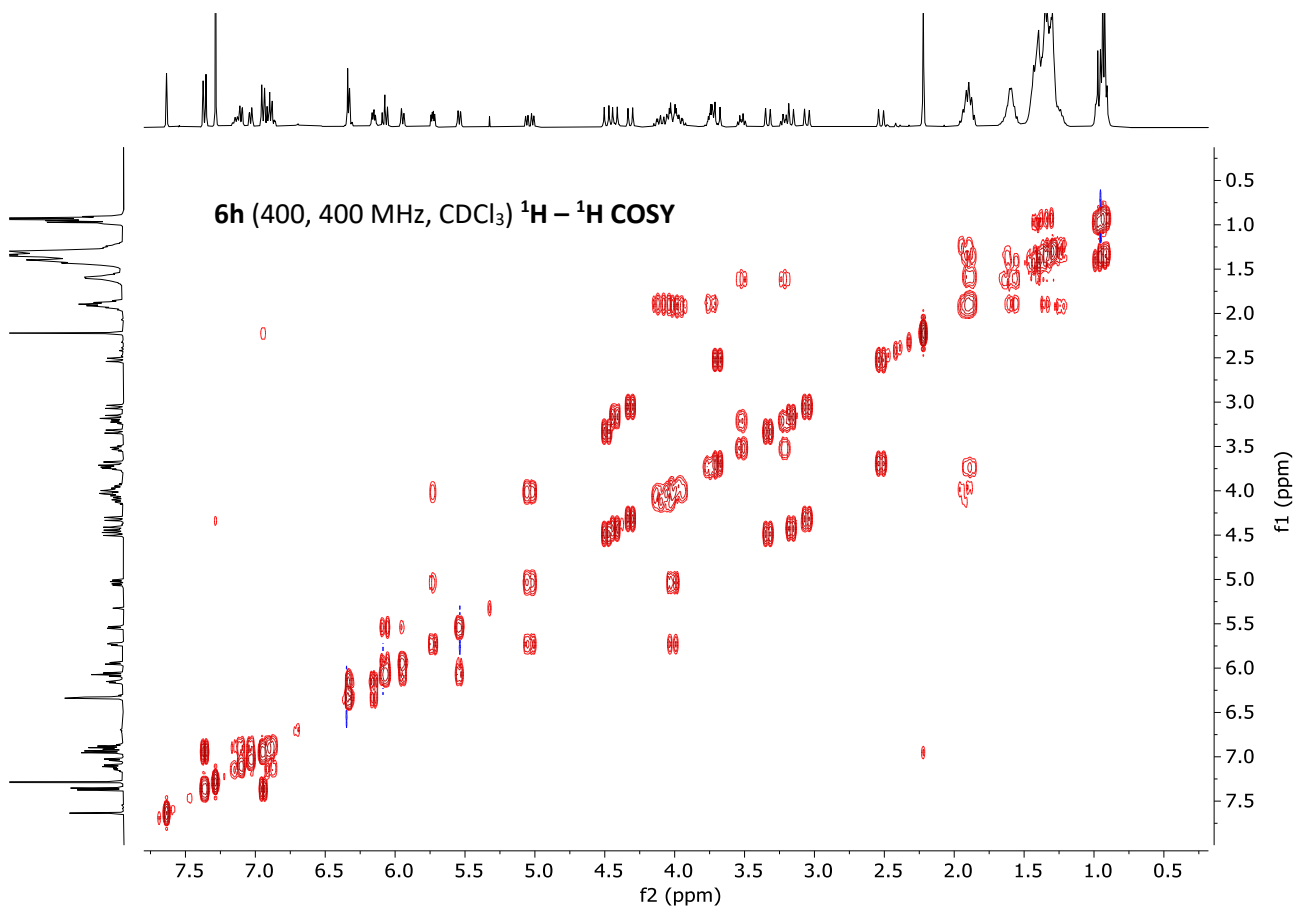


Product 6h:



6h (565 MHz, CDCl₃) ¹⁹F-NMR

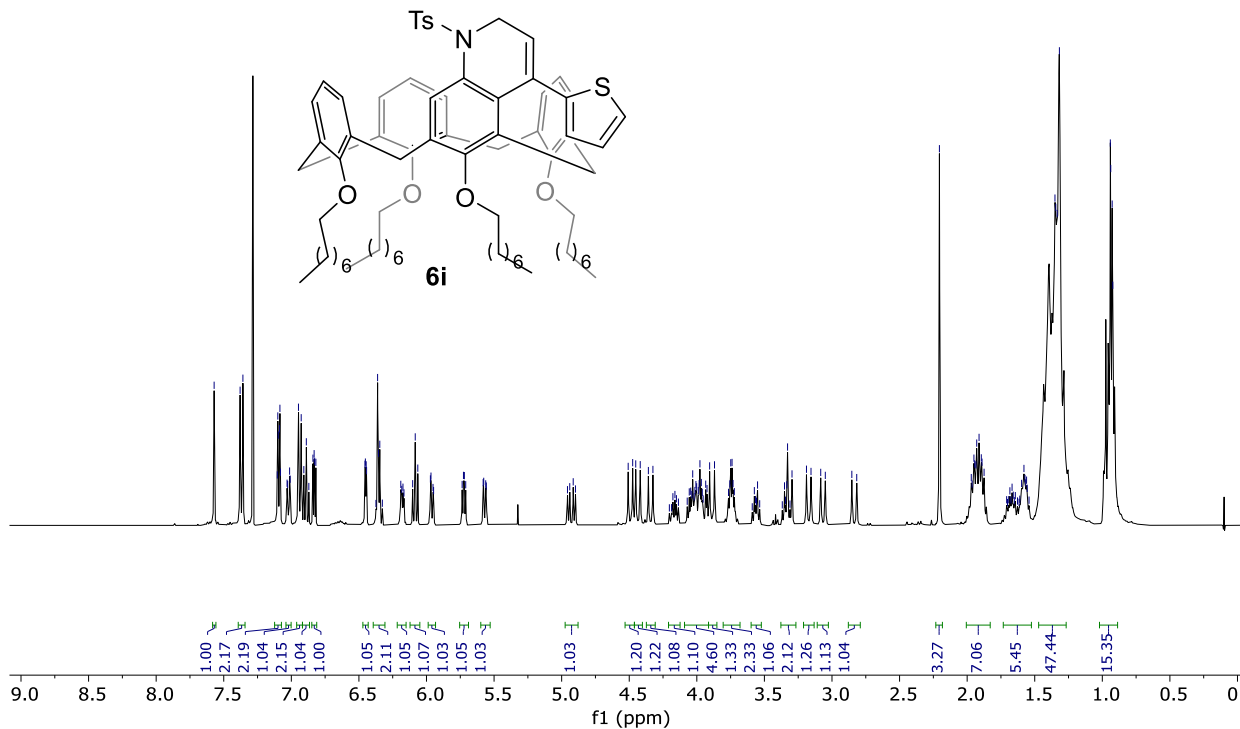




Product 6i:

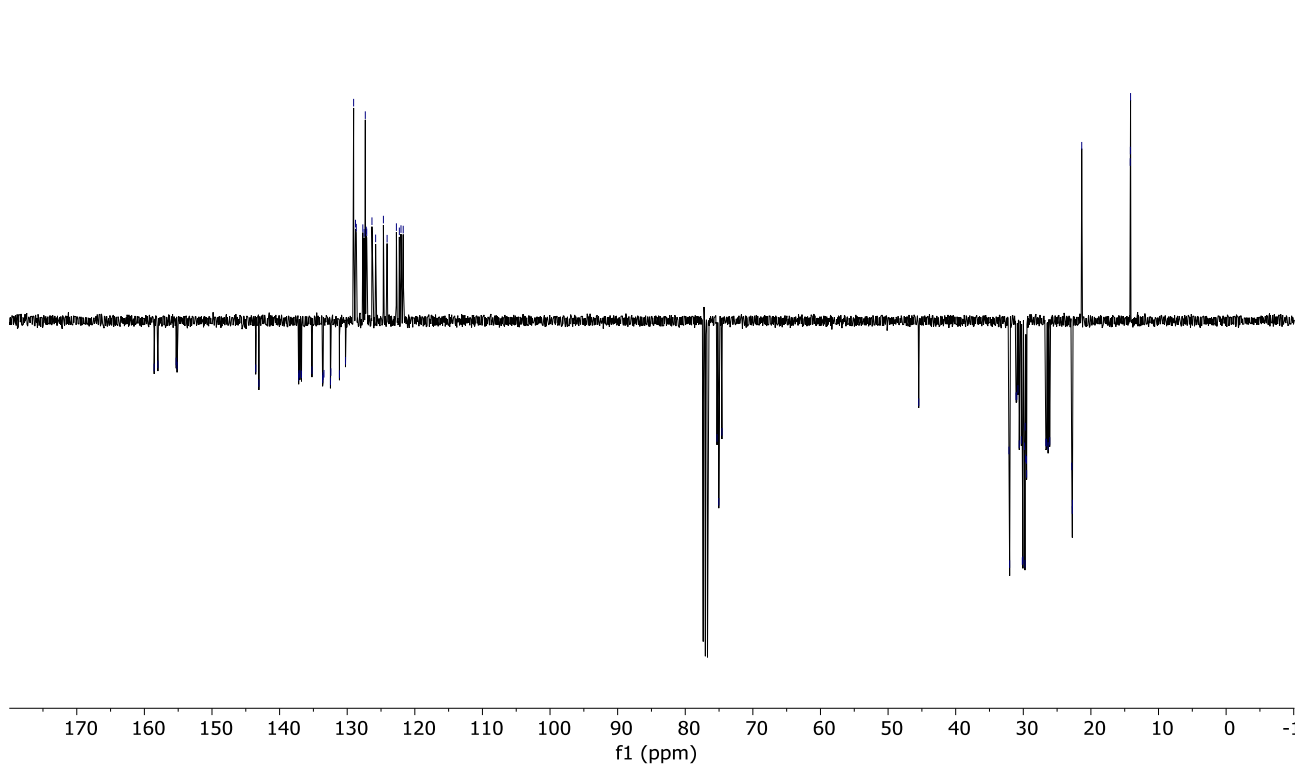
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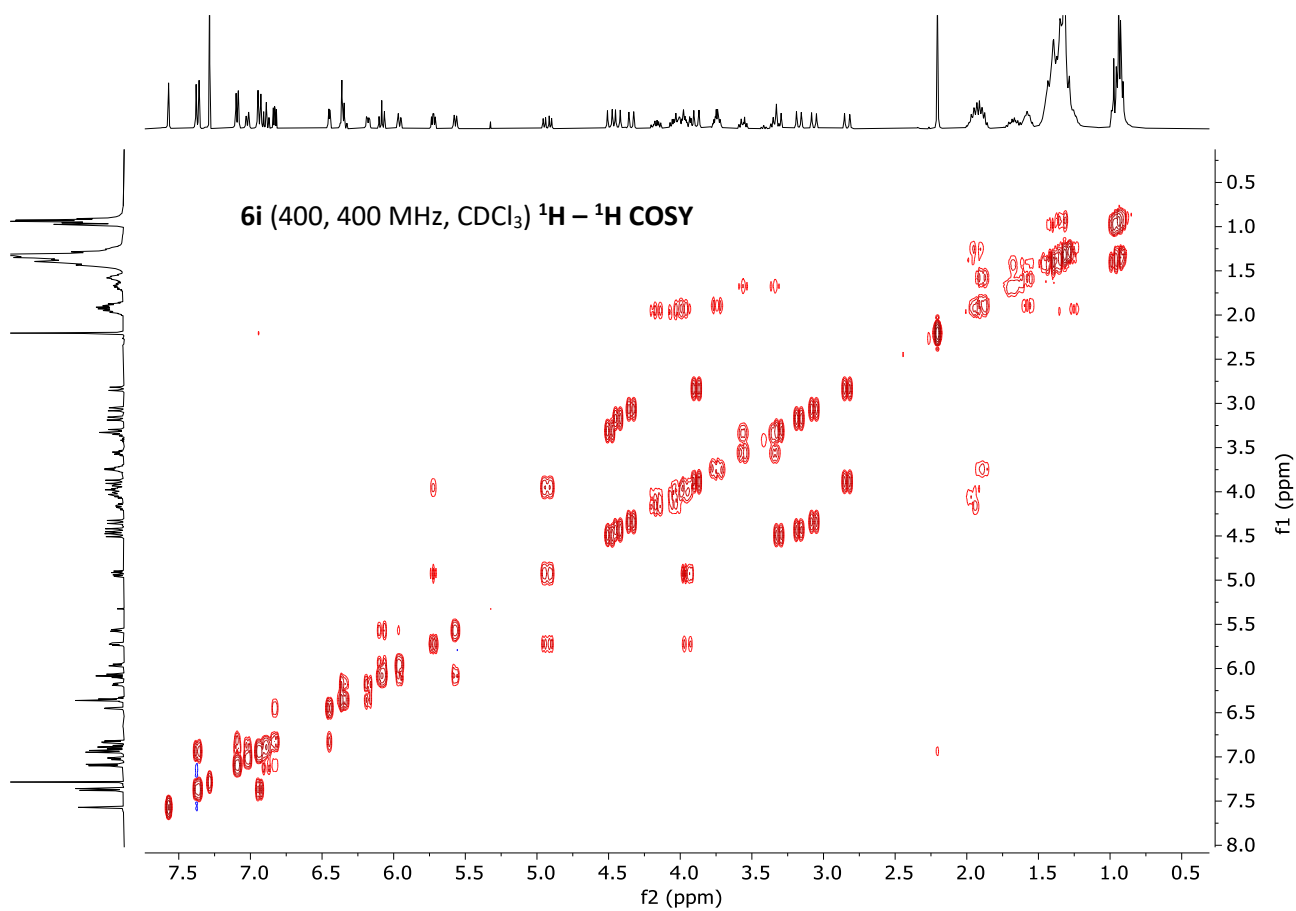
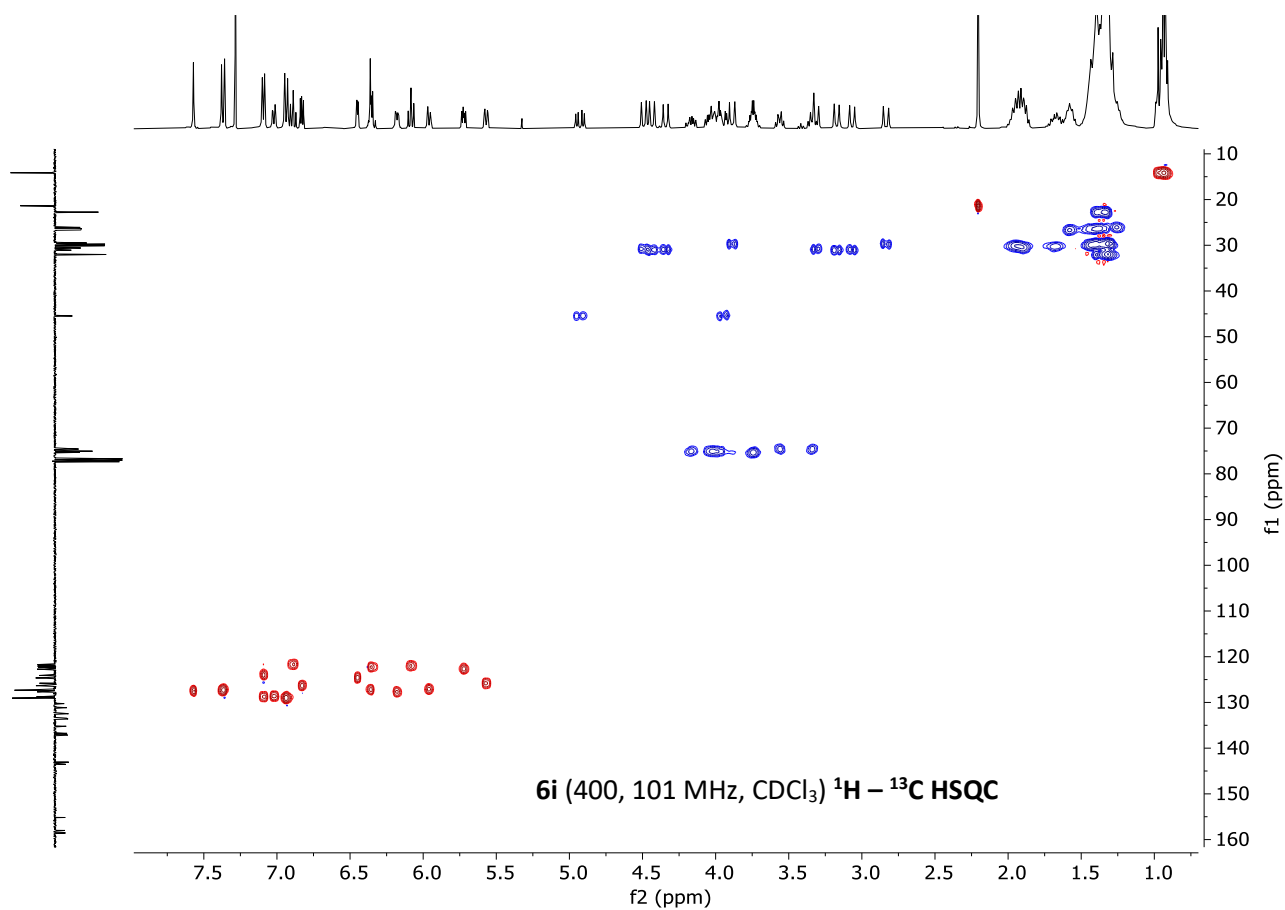
6i (400 MHz, CDCl₃) ¹H-NMR



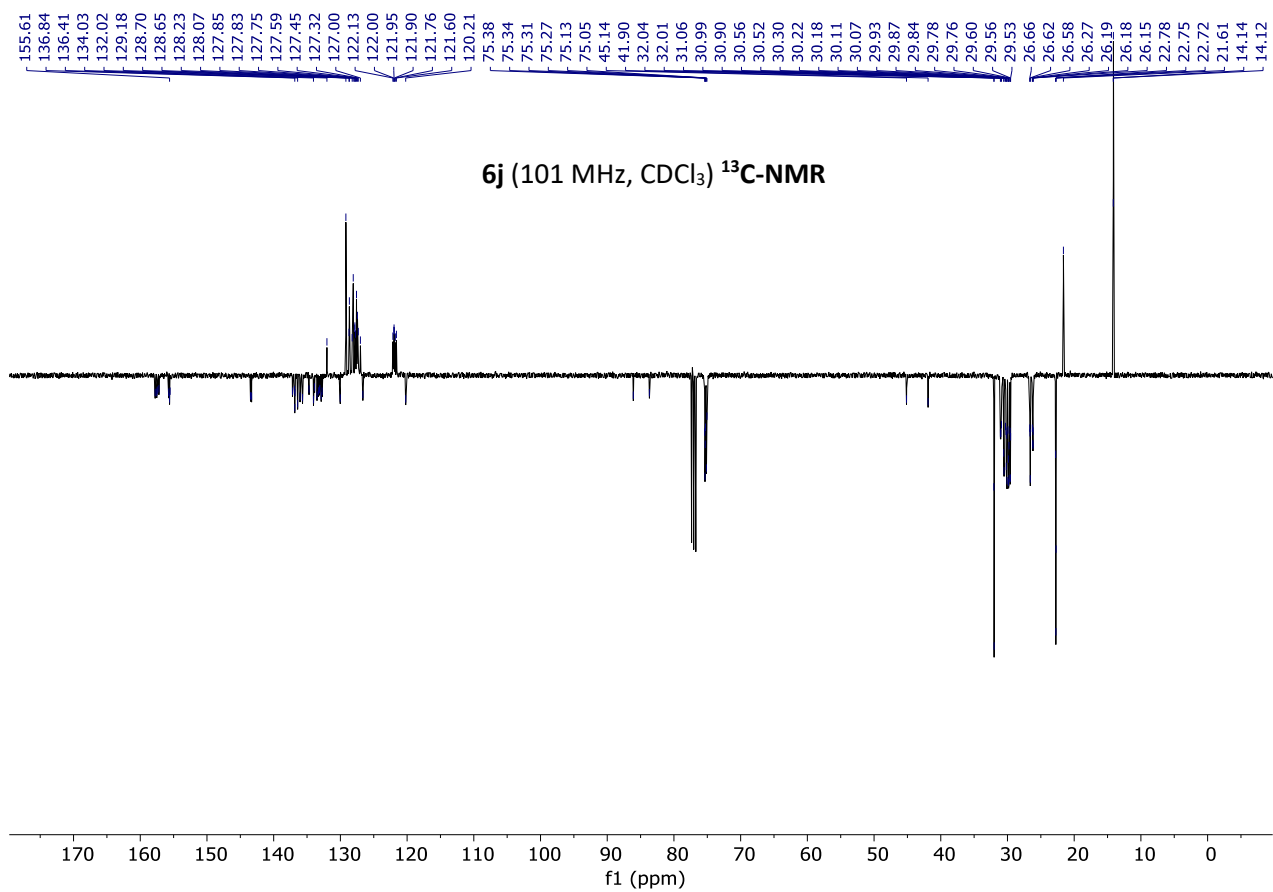
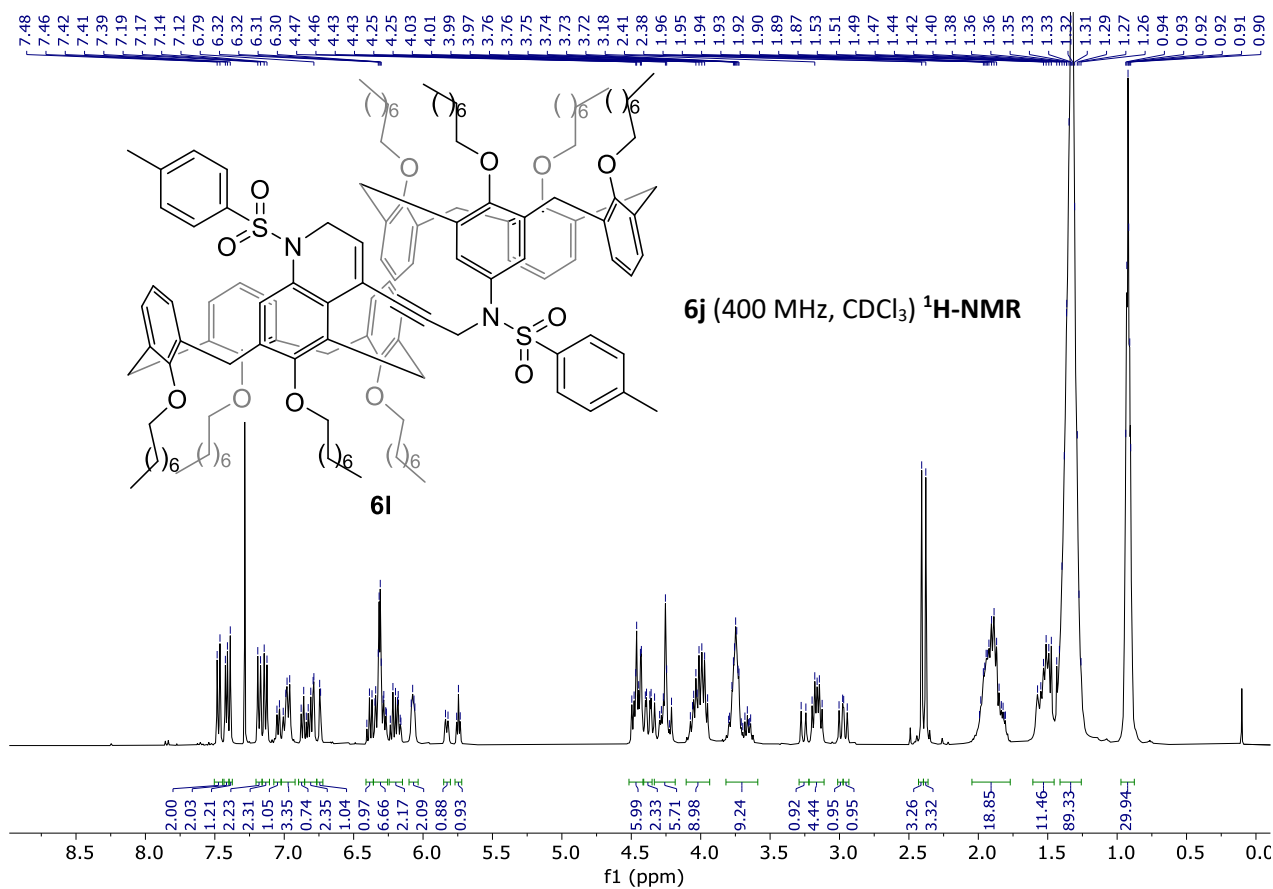
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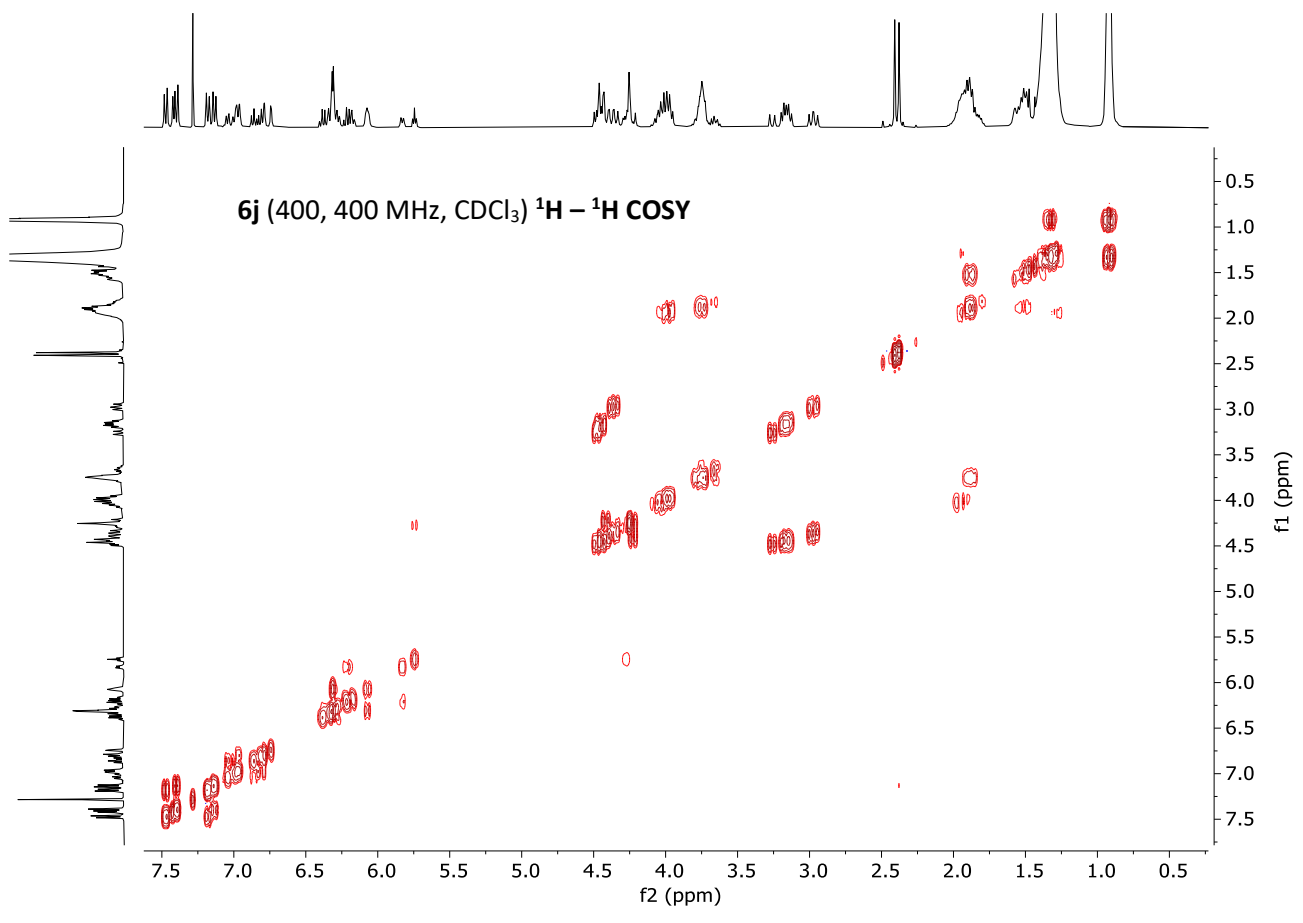
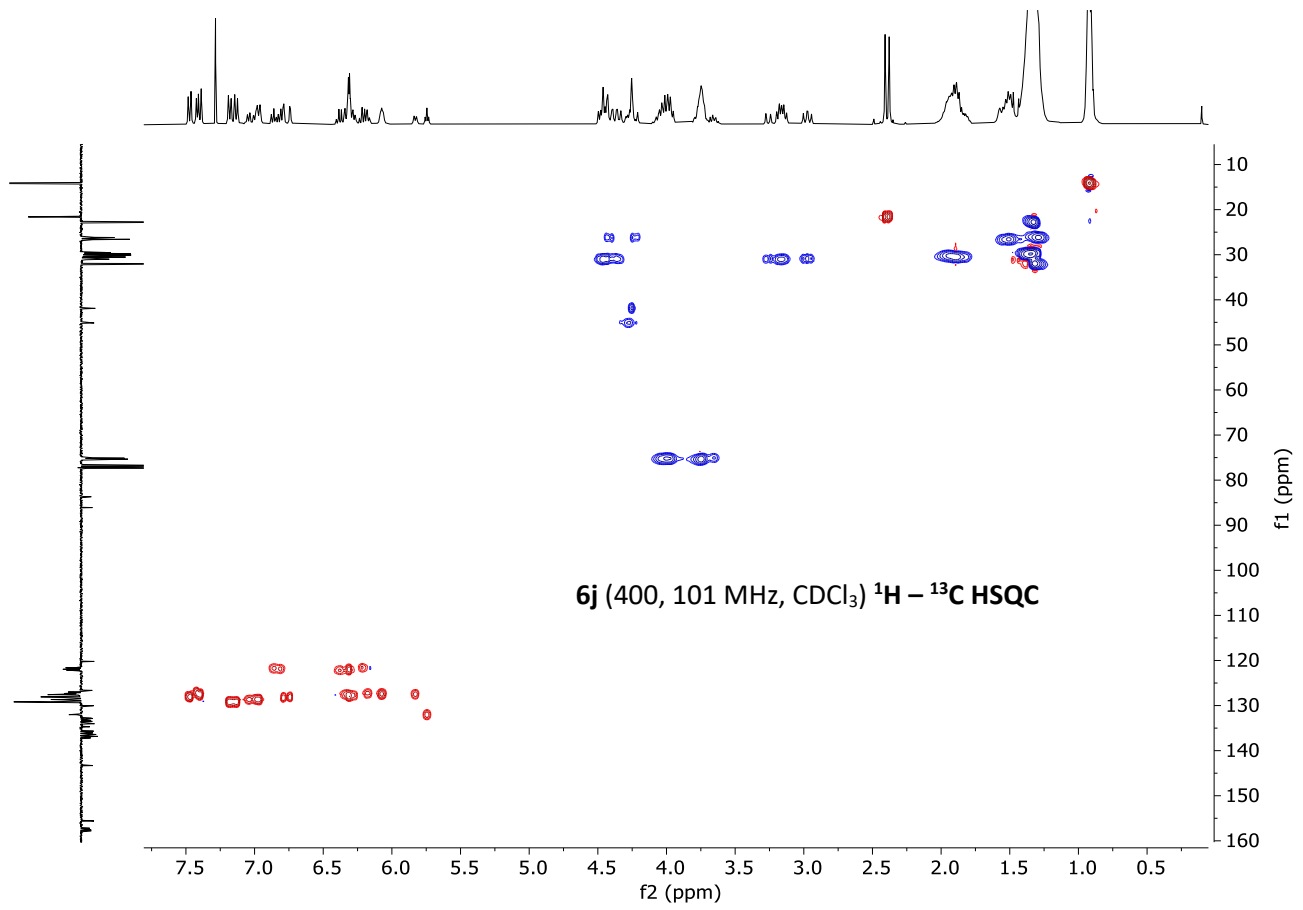
6i (101 MHz, CDCl₃) ¹³C-NMR



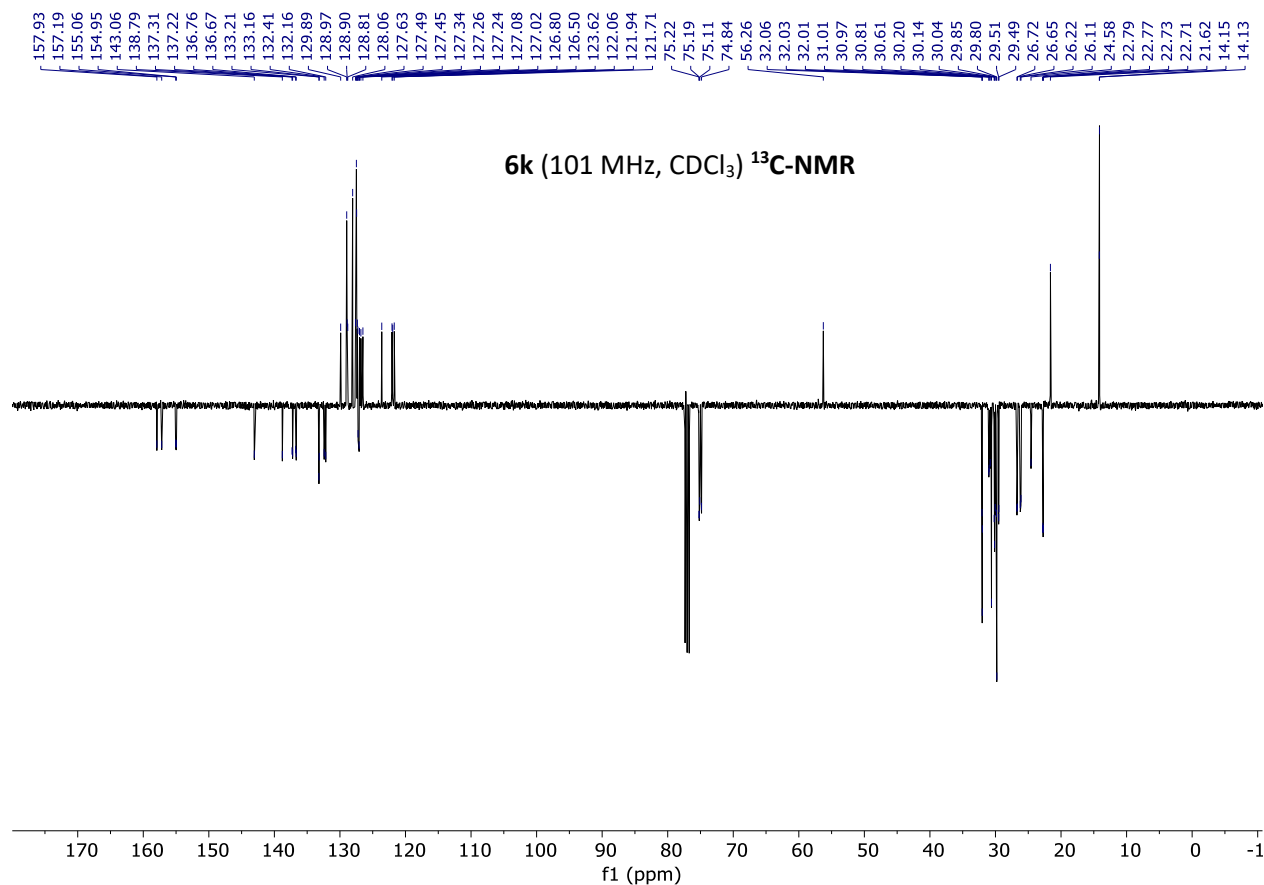
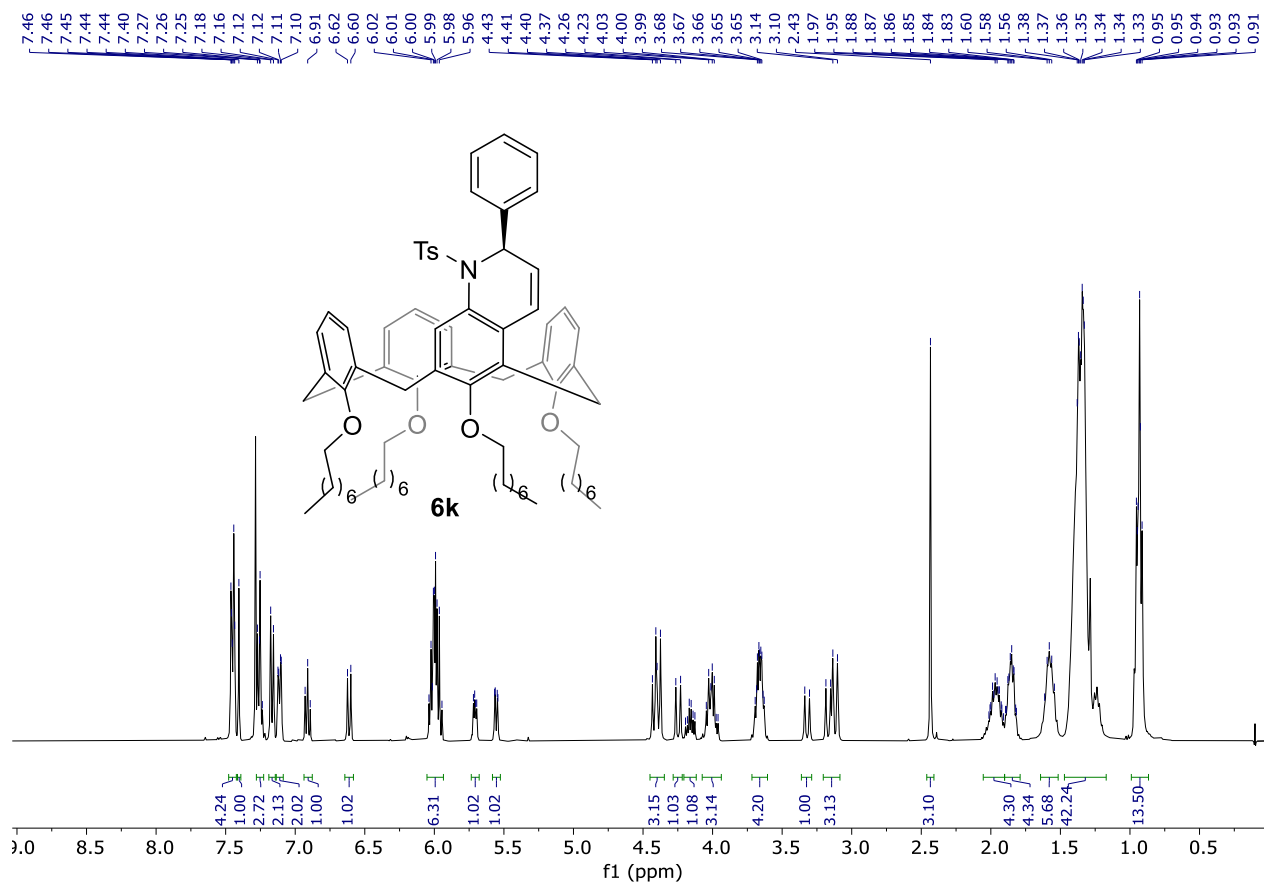


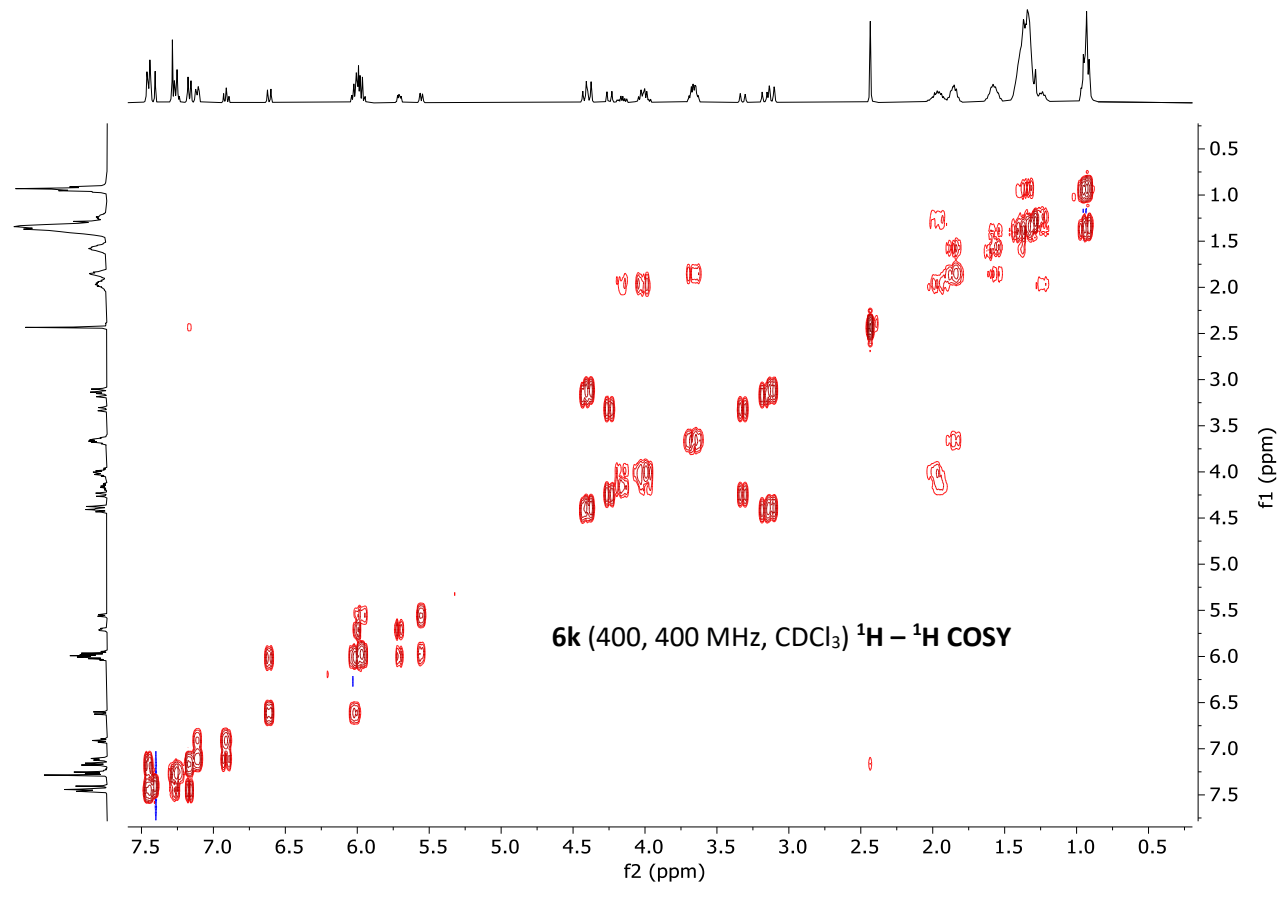
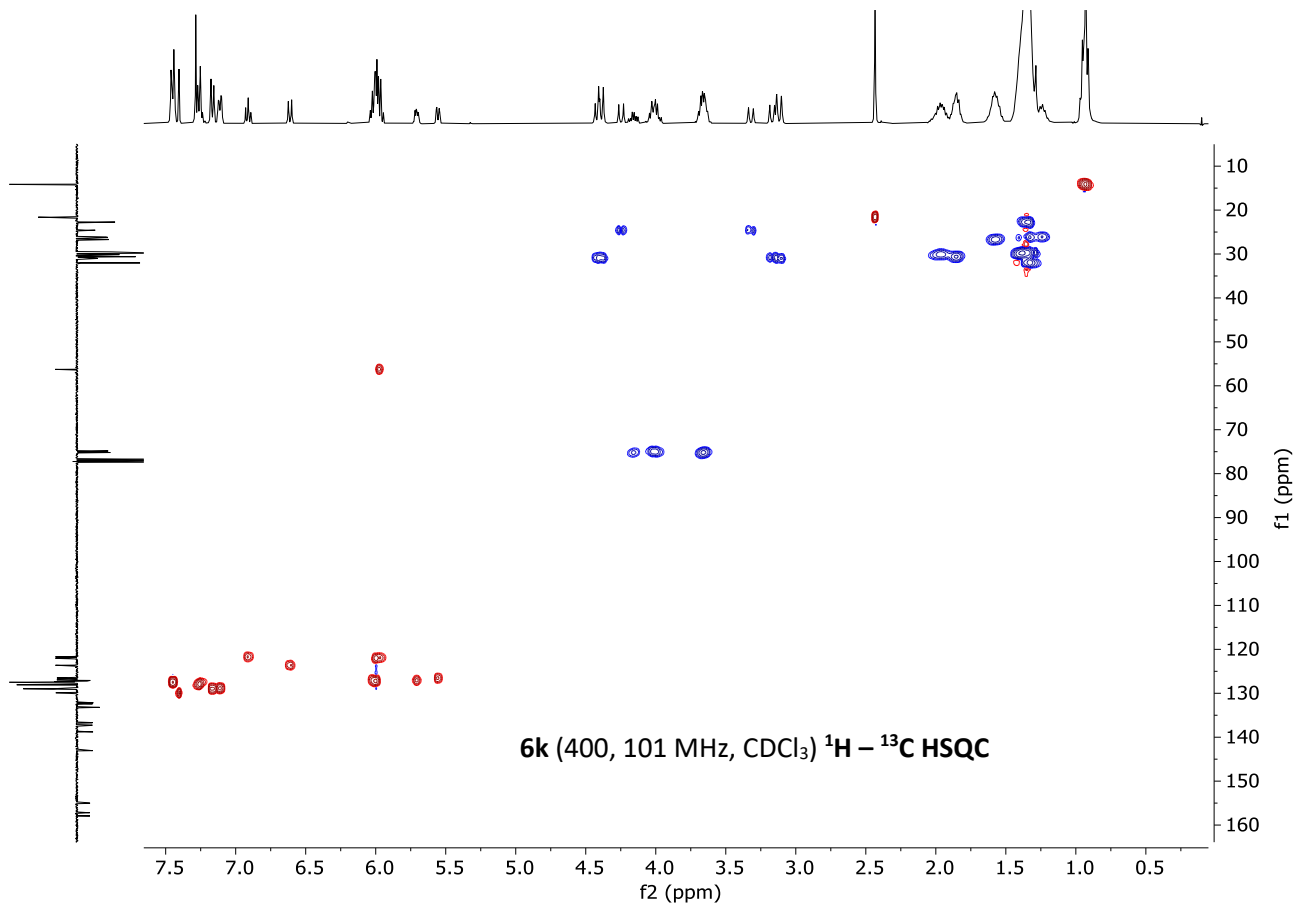
Product 6j:



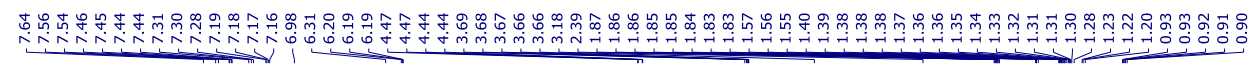


Product 6k:

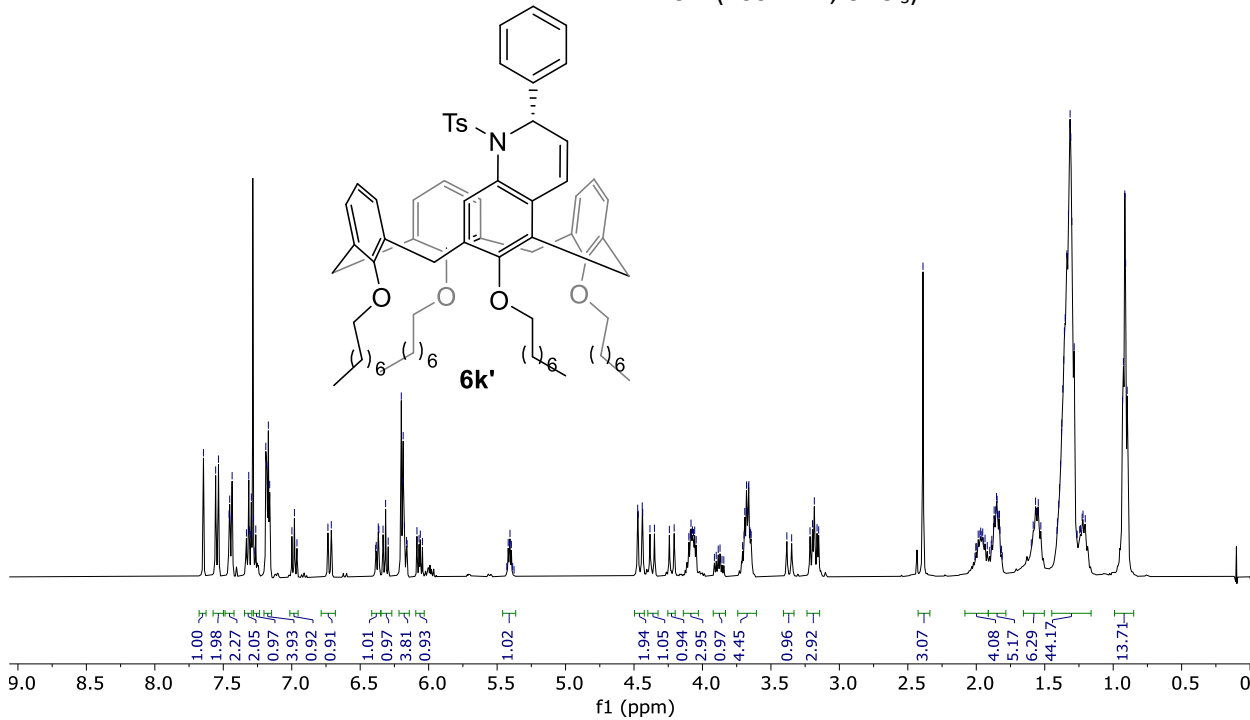




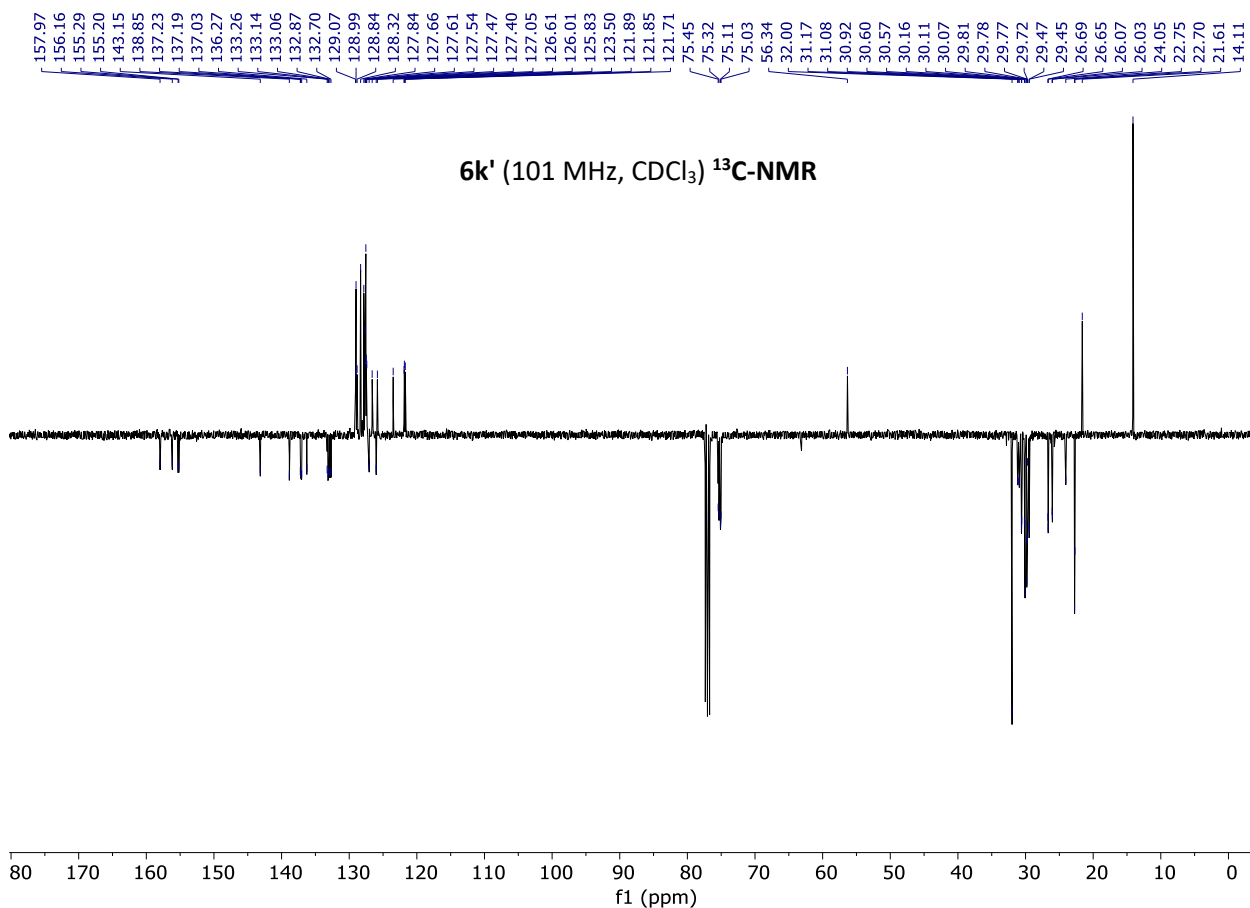
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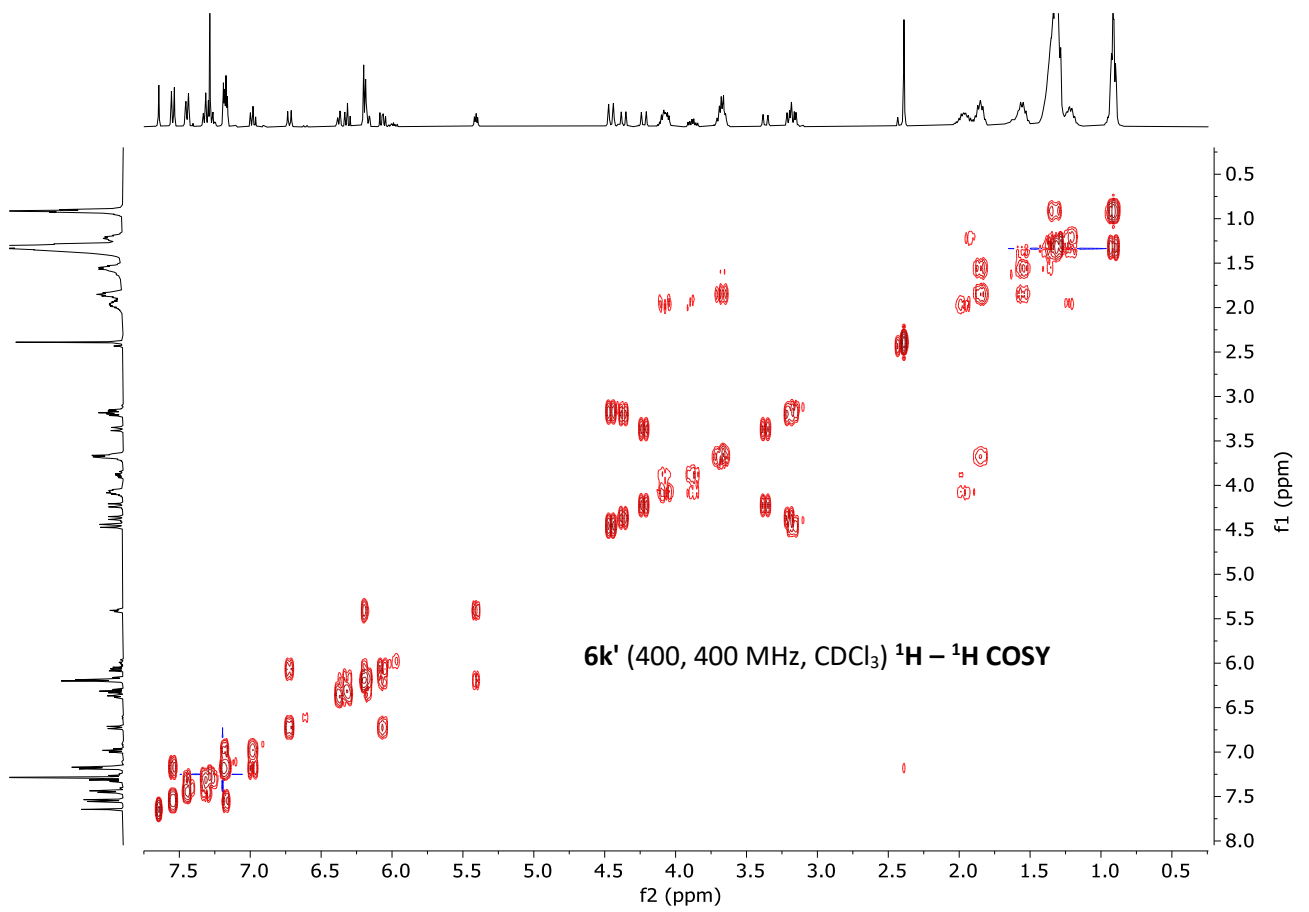
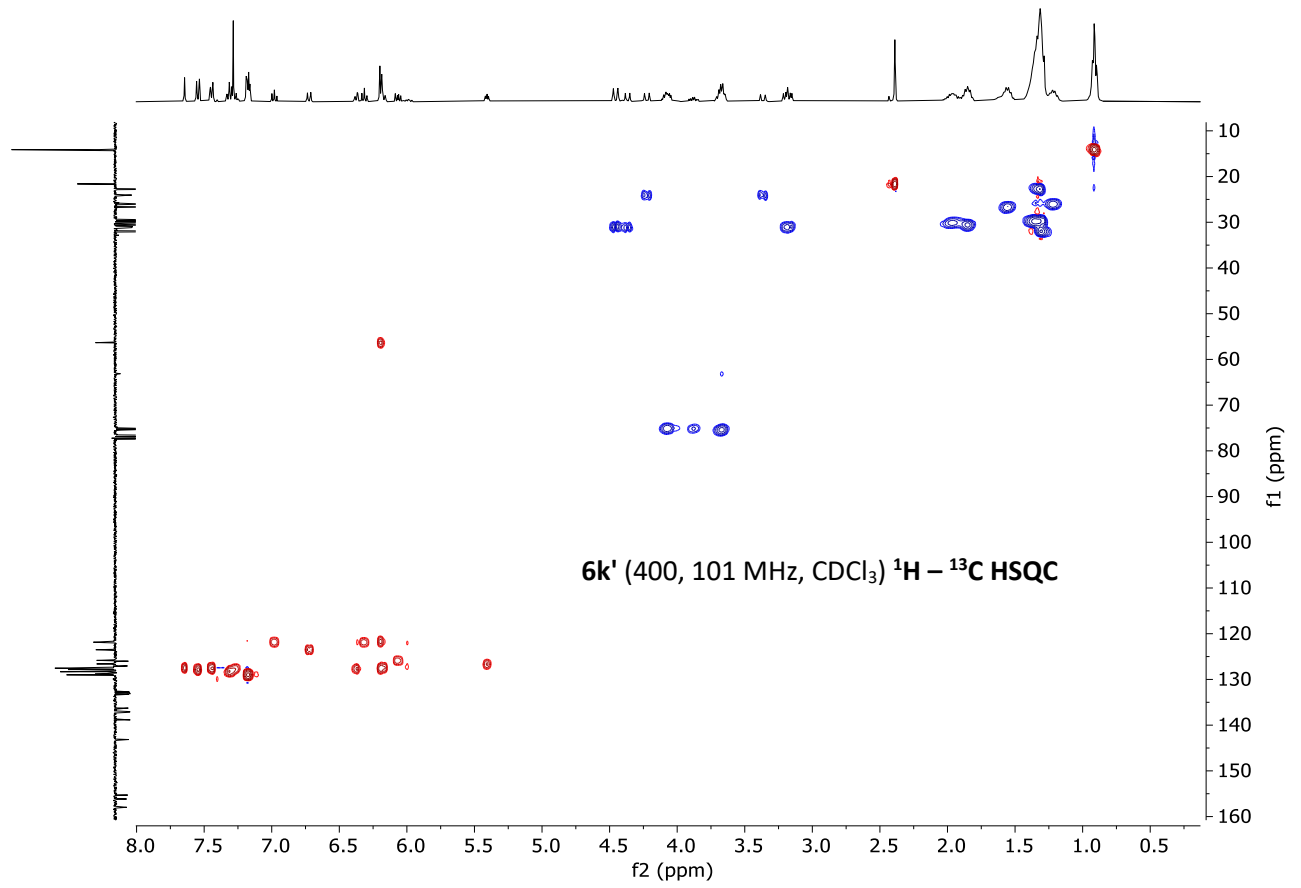


6k' (400 MHz, CDCl₃) ¹H-NMR

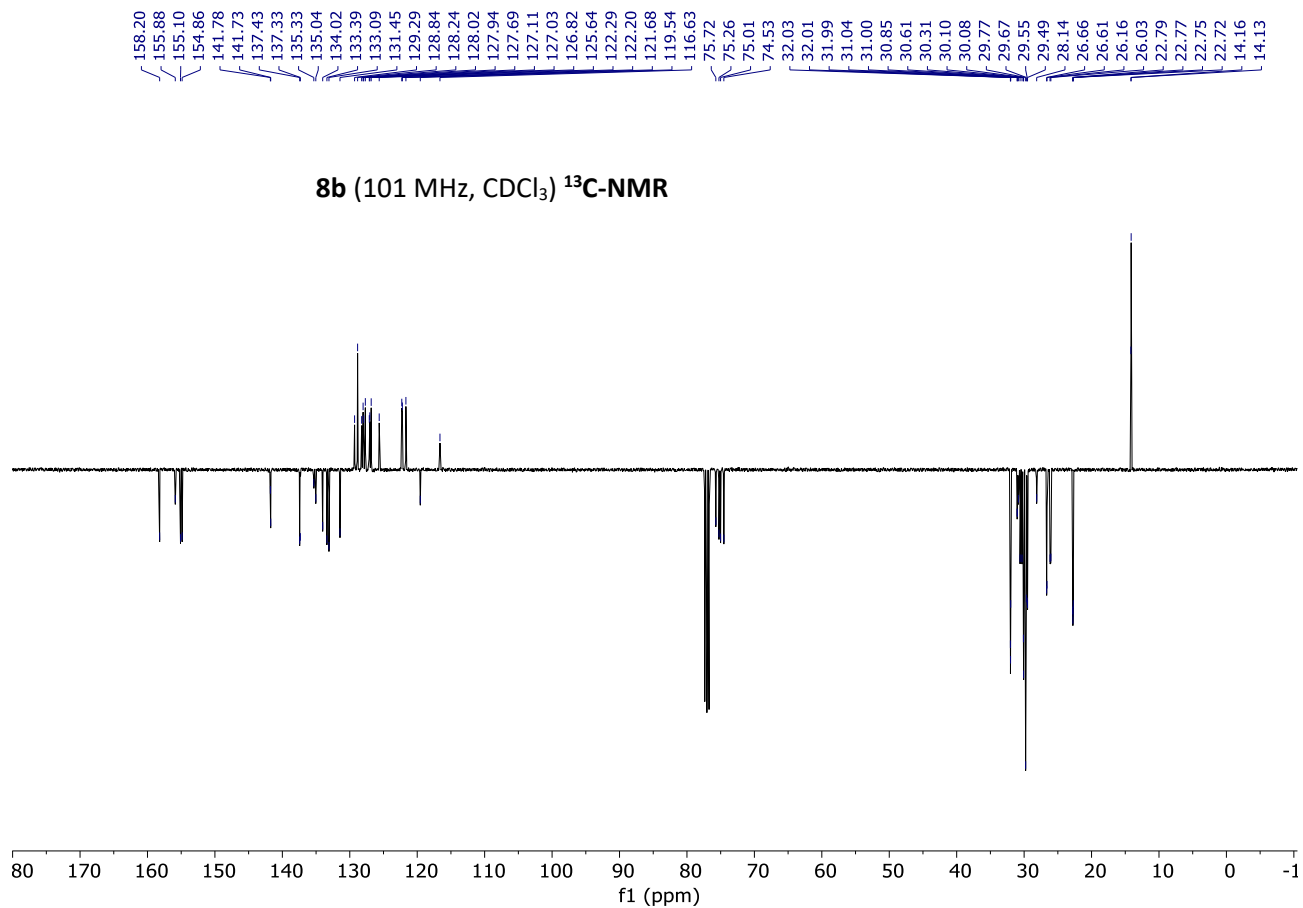
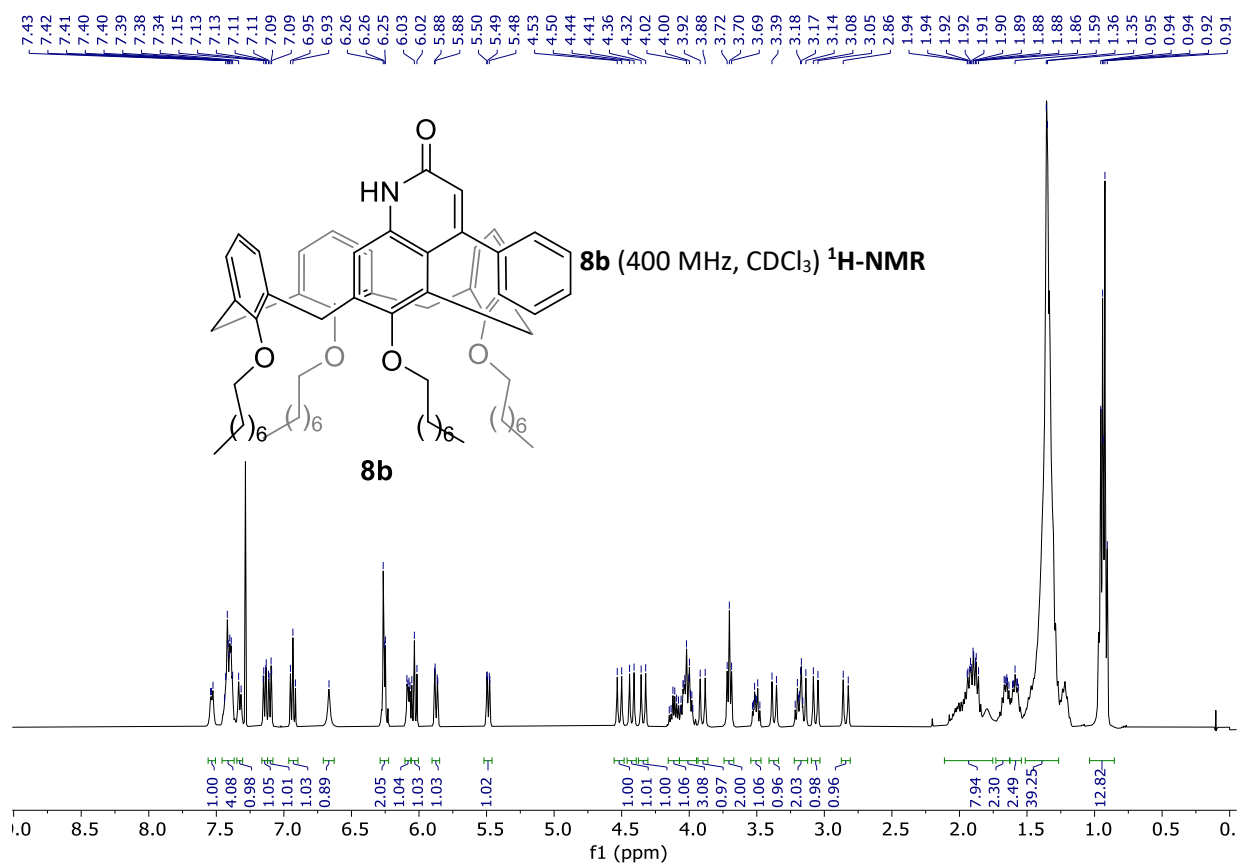


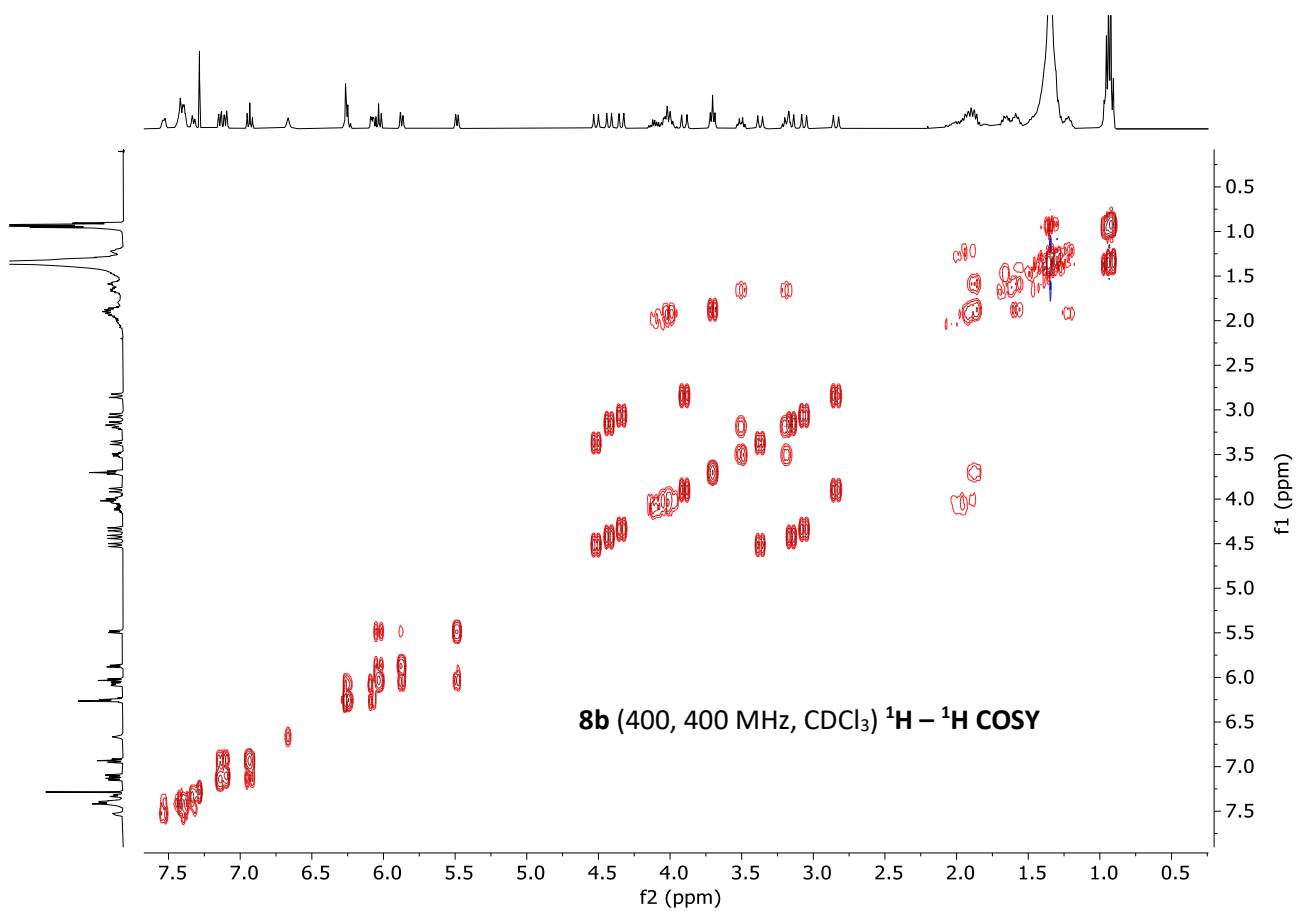
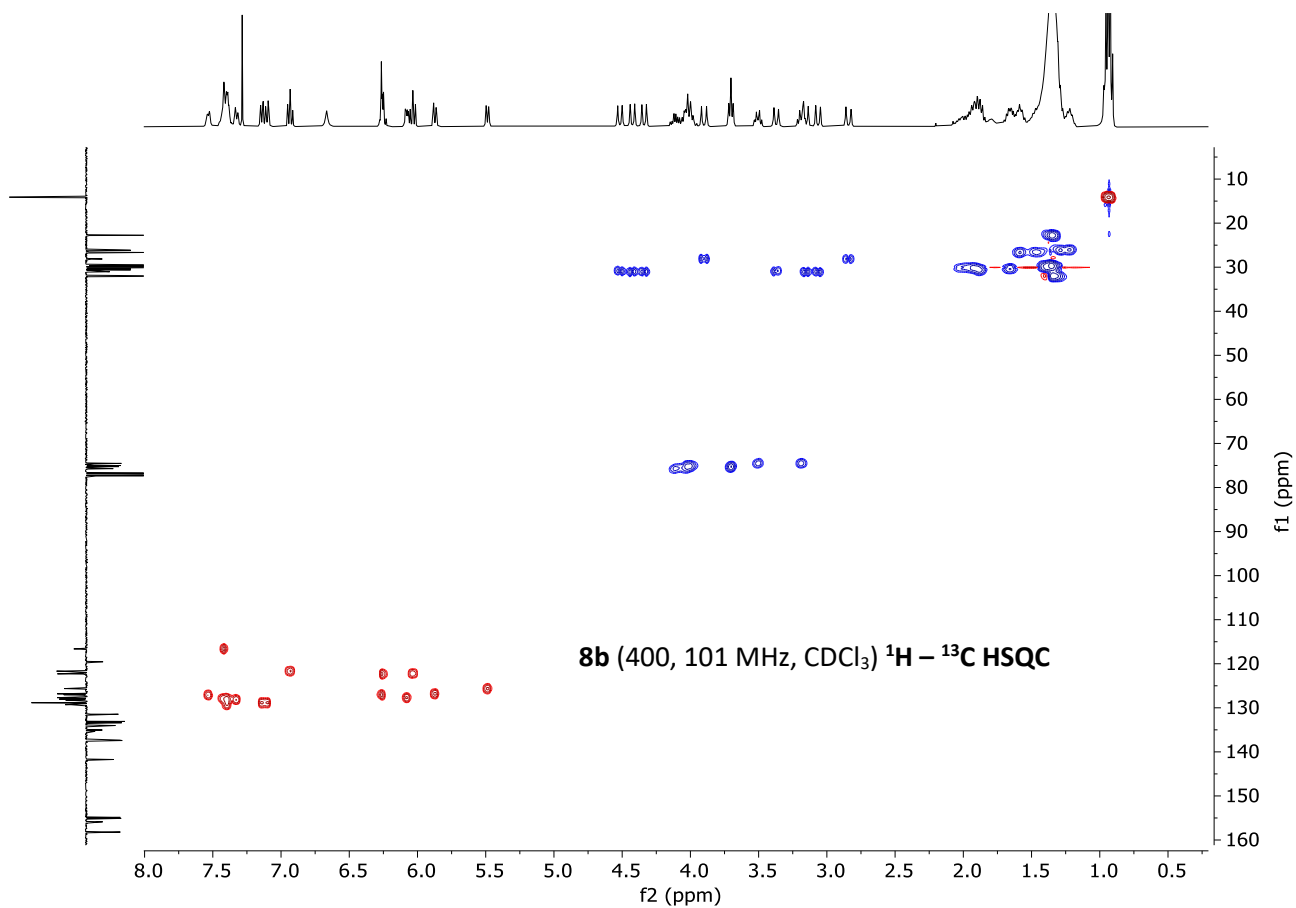
6k' (101 MHz, CDCl₃) ¹³C-NMR





Product 8b:





- **References**

[1] C. D. Jurisch, and G. E. Arnott, *Beilstein J. Org. Chem.* 2019, **15**, 1996–2002.

[2] Z. Chen, P. Liang, F. Xu, Z. Deng, L. Long, G. Luo and M. Ye, *J. Org. Chem.* 2019, **84**, 12639–12647.

[3] D. Lim and S. B. Park, *Chem. Eur. J.*, 2013, **19**, 7100 – 7108.