Targeting Stat3 anti-apoptosis pathways with organic and hybrid organic–inorganic inhibitors.

*Matthew B. Minus[4], Haopei Wang[1], Jaime O. Munoz[2], Alexandra M. Stevens[2], Alicia E. Mangubat-Medina[1], Michael J. Krueger[2], Wei Liu[2], Moses M. Kasembeli[3], Julian C. Cooper[1], Mikhail I. Kolosov[5], David J. Tweardy[3,6], Michele S. Redell[2], Zachary T. Ball[1] **

[1]Department of Chemistry, Rice University, Houston, TX 77005 (USA).

[2]Baylor College of Medicine, Texas Children's Cancer Center, Houston, TX 77030 (USA).

[3]Department of Infectious Diseases, Infection Control and Employee Health and [6]Department of Molecule and Cellular Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030 (USA).

[5]Department of Medicine, Baylor College of Medicine, Houston, TX 77030 (USA)

[4]Prairieview A&M University, Prairie View, TX, 77446 (USA)

* Corresponding Author

Supporting information

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Experimental

1.1. General Methods:

Flash chromatography: was performed with 40-63-µm particle size silica gel.

NMR Spectroscopy: NMR data was acquired with Bruker Avance 400, Bruker Avance 500 MHz or, Bruker Avance 600 instrument. ^1H and ^{13}C NMR spectra were referenced relative to residual solvent or TMS. ^{19}F NMR chemical shifts were determined relative to C_6H_5F in corresponding solvents.

Mass spectroscopy: ESI-MS was performed on Bruker Daltonics micro-TOF instrument.

Chemicals: The following chemicals were purchased and used as received: thiophenol (Aldrich), 4-hydroxythiophenol, 2-hydroxythiophenol, 4-tertbutylthiophenol, 2-naphthol, 4-nitronaphthylamine, 1,5-dintitronaphthalene, 1-naphthol, 4-amino-1-naphthol hydrochloride (TCI), pentafluorobenzene sulfonyl chloride (Sigma), diisopropylethylamine (Fisher), $Rh_2(OAc)_4$ (Pressure Chemical), 2,2,2-trifluoroethanol (Aldrich), iodobenzene diacetate (Aldrich), butyric acid (Acros), 2-bromo-4-nitro-1-naphthylamine, 2,4-dibromo-1-naphthylamine(Aldrich), 2,4-dibromo-1-naphthol(Aldrich), 2,4-dibromo-1-naphthol (compound **14**, TCI), 2,4-dibromonaphthalen-1-amine (compound **15**, Sigma), 2-Bromo-4-nitro-1-naphthalenamine (compound **16**, AmBeed), Na_2SO_4 (Fisher), and $MgSO_4$ (Fisher).

Solvents: All solvents were reagent grade. Solvents used in inert atmosphere reactions were purified and degassed by the glass contour solvent system from SG waters USA.

Synthesis of known compounds: $Rh_2(OAc)_3(tfa)$,[1] *cis*- $Rh_2(OAc)_2(tfa)_2$,[1] $Rh_2(tfa)_4$,[2] methyl 4-(chlorosulfonyl)butanoate,[3] methyl 5-(chlorosulfonyl)-2-hydroxybenzoate,[4] 3-(chlorosulfonyl)benzoic acid,[5] methyl 2-(4-(chlorosulfonyl)phenoxy)acetate,[6] compound **1a**,[7] compound **1b**,[8] compound **1c**,[7] compound**3aa**,[7] compound **4a**,[7] compound **5**,[9] compound **6**,[10] compound **S2**,[7] compound **13ab**,[7] compound **13ac**,[11] and 1,8-difluoronaphthalene,[9] were prepared according to previously reported protocols.

STAT3 expression: The dimeric (pSTAT3) and monomeric (STAT3) recombinant core fragments of STAT3 (AA 127-722) were expressed, purified, and analyzed according to a previously described method.[12]

HPLC: HPLC was performed on a Shimadzu CBM-20A instrument with Phenomenex Jupiter 4 μ Proteo 90A (250 mm × 15 μm) and Phenomenex Jupiter 4 μ Proteo 90A (250 mm × 4.6 μm) columns. Flow rates of 8 mL/min and 1 mL/min were used for preparative and analytical columns, respectively. Analytical and preparative HPLC were performed with gradients of acetonitrile and water (no 2,2,2-trifluoroacetic acid). All samples were run on a gradient of increasing (40% → 90%) MeCN/H_2O from 2-22 min unless otherwise noted in the synthesis section. The absorbance was monitored at 320 nm during each run unless otherwise noted in the synthesis section.

Surface plasmon resonance (SPR) inhibition measurements:

a) Phosphopeptide binding. The ability of molecules to inhibit STAT3 binding to phosphopeptide (P1068) was assessed by SPR analysis on a Biacore 3000 instrument as previously described.[13]

Preparation of aqueous NMR samples for decomposition analysis

DSMO-*d*$_6$ was purged with nitrogen for 0.5 h. Potassium Phosphate buffer (pH 6.8) was prepared by dissolving KH_2PO_4 and K_2HPO_4 in D_2O (10 mL). C188-9 (100 μL, 10 mM in DMSO-*d*$_6$) and DSMO-*d*$_6$ (100 μL) were added to deuterated potassium phosphate buffer (800 μL). The final concentration of C188-9 (1 mM) is similar to previously reported *in vivo* dosing concentration. Air was bubbled through samples for 15 min. Samples were then incubated at 38 °C until analyzed by NMR and ESI-MS.

STAT3 phosphorylation assay

Cells were added in a 24-well plate ($1x10^5$ cells/well). Inhibitor was incubated with the cells for 1 h. After 1 h, Granulocyte-colony stimulating factor (G-CSF) (1 μL, 100 ng/μL) was added into each well and incubated for 15 min. Paraformaldehyde was then added into eppendorf tubes to creating a 2% paraformaldehyde suspension. The cells were spun down, aspirated, and resuspended in phospho-flow buffer (500 μL). The rinsing was repeated 2 more times. The resulting pellet was evenly mixed in phospho-flow buffer. Then 1 mL of ice-cold methanol was immediately added to the eppendorf tube. The tube was placed on ice for 30 min. To remove the methanol the eppendorf tube was spun and the supernatant was aspirated. The cells were resuspended into 500 μL phospho-flow buffer. This step was repeated in order to remove trace amounts of methanol. Antibody solution (4 μL p-stat3 antibody + 46 μL phospho-flow buffer) was added to the eppendorf tube. The tube was allowed to rest at rt for 30 min in the dark. Phospho-flow buffer (500 μL)was then added to cellular suspension. The eppendorf tube was spun and the supernatant was aspirated. The resulting cellular pellet was suspended in phospho-flow buffer (300 μL). The suspension was transferred to a 5 mL flow tube through a strainer for further analysis.

- Cells were centrifuged at 200 rpm for 5 min.
- Phospho-flow buffer: 450 mL H_2O, 50 mL 10x PBS, 1 g BSA, 450 mg Na Azide

Cellular apoptosis

The human AML cells were grown in RPMI medium (ATCC) supplemented with 10% FBS and 1% penicillin-streptomycin. They were grown in a humidified 37 °C incubator with 5% CO_2. AML cells were plated in growth medium and exposed to drug or vehicle for 24 h. Apoptosis was quantified based on Annexin V-FITC and propidium iodide using an LSRII flow cytometer and data were analyzed using FCS Express software

Oxidative decay of C-188-9

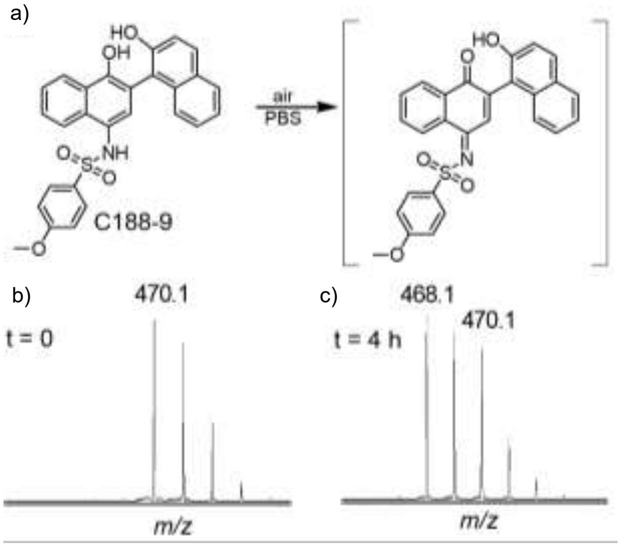


Figure S1. (a) Oxidation of C188-9 in PBS at 37°C, based on ESI-MS results. (b) ESI-MS spectrum (negative mode) of C188-9 before aqueous incubation. (c) ESI-MS spectrum (negative mode) of c188-9 after 4h of aqueous incubation.

Oxiativ decay of 4-hydroxynaphthylsulfonamdies in aqueous buffer

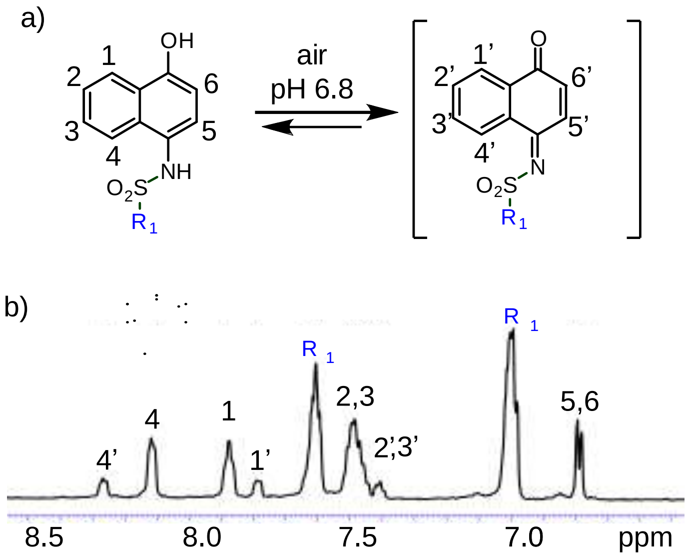
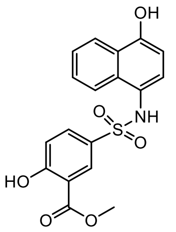


Figure S2. (a) Oxidation of 4-hydroxynaphthylsulfonamides in aqueous buffer (b) NMR spectrum of **1b** after 4 h of incubation (1 mM, 20% DMSO, 1x PBS, 38 °C).

1.2. **Chemical synthesis and characterization**

The general N-sulfonylation procedure

Synthesis of sulfonamide compound 1e

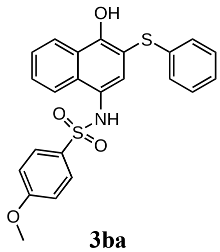


1e

Solid 4-amino-1-naphthol hydrochloride (971 mg, 4.9 mmol) and methyl 5-(chlorosulfonyl)-2-hydroxybenzoate (500 mg, 2 mmol) were placed in a round-bottomed flask containing $MgSO_4$ (1.00 g) and a stir bar. The reaction vessel was evacuated and back-filled with nitrogen (3×). Both pyridine (10 mL) and acetonitrile (1 mL) were added by syringe to the round-bottomed flask. The reaction was monitored by TLC and was complete after 3 h. Upon completion, the reaction mixture was taken up in CH_2Cl_2 and washed with aq HCl (3 × 20 mL, 2 M). The organic layer was dried with Na_2SO_4, and filtered through cotton. Nitrogen gas was bubbled through the organic layer for 15 min. Then the organic layer was evaporated under vacuum. The resulting product was used without further purificaiton (971 mg, 83%).

The general procedure for the oxidative coupling of thiols

Synthesis of compound 3ba

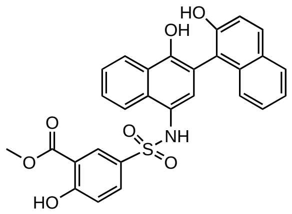


3ba

The naphtholsulfonamide **1b** (700 mg, 2.12 mmol) was dissolved into acetone (10 mL). Iodobenzene diacetate (750 mg, 2.3 mmol) was added to the reaction. After 1 h, the oxidation was complete by TLC (1:1 EtOAc/hexanes). Thiophenol (972 mg, 8.83 mmol) was added to the reaction mixture along with formic acid (1 mL). After 2 h, the reaction mixture was extracted with chloroform and washed thrice with 1M aq HCl. The organic layer was dried with Na_2SO_4, filtered through cotton, and dried onto silica gel. The crude was purified by silica gel chromatography (1:3 Et_2O/hexanes) to afford **3ba** (350 mg, 37%).

The general procedure for the oxidative coupling of 2-naphthol

Synthesis of compound 4d



4d

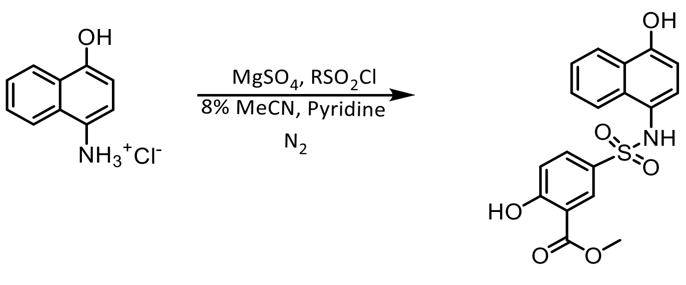
i) Oxidation

Naphthalene derivative **1e** (373 mg, 1 mmol) was placed in a 20-mL vial. Aq MeCN (10 mL, 50%) was added to the reaction vessel. The oxidant $PhI(OAc)_2$ (395 mg, 1.21 mmol) was added to the resulting solution. The solution was stirred with a magnetic stir bar for 0.5 h. The solution turned a deep red. The reaction was complete by TLC (1:1 EtOAc/hexanes). The reaction mixture was extracted thrice with CH_2Cl_2. The combined organic extracts were washed twice with water, dried with Na_2SO_4, and filtered through cotton. The solvent was evaporated under vacuum to yield a brown solid crude which was taken to the next step without purification.

ii) Oxidative addition

The 2-naphthol (1.00 g, 6.9 mmol) was added to the crude solid from part *i)* along with a magnetic stir bar. The flask was evacuated, and backfilled with nitrogen thrice. The dry solvent CH_2Cl_2 (7 mL) was added to the reaction. $BF_3 \cdot Et_2O$ (1.0 mL, 8.1 mmol) was added to the reaction mixture. The reaction was stirred at rt under nitrogen for 14 h. Once the quinone-imine intermediate was no longer visible by TLC (1:1 EtOAc/hexanes), the reaction was taken up in CH_2Cl_2. The organic solution was washed thrice with 1 M HCl, dried with Na_2SO_4, and filtered through cotton. Toluene was added to the solution. The solution was purged with nitrogen. The solvent was evaporated under vacuum. The dried crude was purified by silica gel chromatography (1:1 EtOAc/hexanes) to yield **4d** (237 mg, 46% over 2 steps).

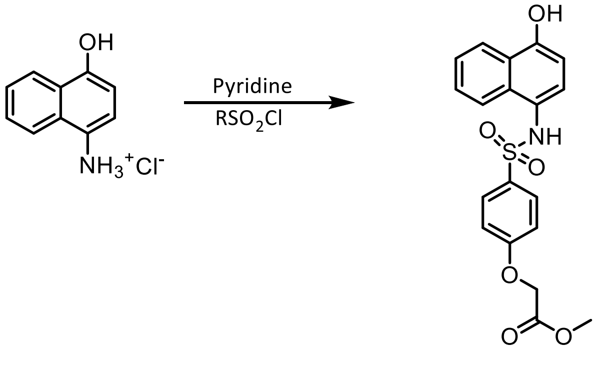
methyl 2-hydroxy-4-(N-(4-hydroxynaphthalen-1-yl)sulfamoyl)benzoate, 1e



1e

Product **1e** was sufficiently pure after extraction. (971 mg, 83%). ^{1}H NMR (600 MHz, acetonitrile-*d*$_3$) δ 10.98 (s, 1H), 8.05 (dd, *J* = 6.7, 2.8 Hz, 1H), 7.94 (d, *J* = 2.6 Hz, 1H), 7.81 – 7.77 (m, 1H), 7.76 (s, 1H), 7.65 – 7.58 (m, 2H), 7.41 – 7.30 (m, 3H), 6.91 (d, *J* = 8.9 Hz, 1H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.66 (d, *J* = 8.1 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR (151 MHz, acetonitrile-*d*$_3$) δ 170.3, 165.2, 153.5, 135.1, 132.8, 131.6, 130.9, 127.6, 127.3, 126.2, 126.0, 124.4, 123.9, 123.0, 119.2, 113.4, 108.3, 53.6. MS (ESI) m/z [M-H] $^-$ calcd for $C_{18}H_{15}NO_6S^-$ 372.05, found 372.03. HPLC *t*$_R$: 6.7 min

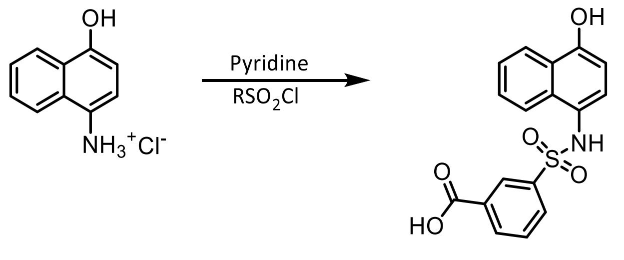
methyl 2-(4-(N-(4-hydroxynaphthalen-1-yl)sulfamoyl)phenoxy)acetate,1d



1d

Sulfonamide **1d** was synthesized with the general N-sulfonylation procedure. Instead of column chromatography, the crude solid was dissolved in CH_2Cl_2. The product was precipitated by adding hexanes to the solution. The solid was filtered and dried to afford **1d** (281 mg, 48%). ^{1}H NMR (600 MHz, acetonitrile-*d*$_3$) δ 8.15 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.80 (s, 1H), 7.63 – 7.58 (m, 3H), 7.46 (q, *J* = 7.0 Hz, 2H), 6.95 (dd, *J* = 14.3, 8.2 Hz, 3H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.73 (s, 2H), 3.76 (s, 3H). ^{13}C NMR (151 MHz, acetonitrile-*d*$_3$) δ 170.0, 162.5, 153.7, 133.9, 133.2, 130.8, 127.97, 127.4, 126.6, 126.4, 125.1, 124.4, 123.4, 116.1, 108.7, 66.4, 53.2. MS (ESI) m/z [M-H] $^-$ calcd for $C_{19}H_{16}NO_6S^-$ 386.07, found 386.04. HPLC *t*$_R$: 6.4 min

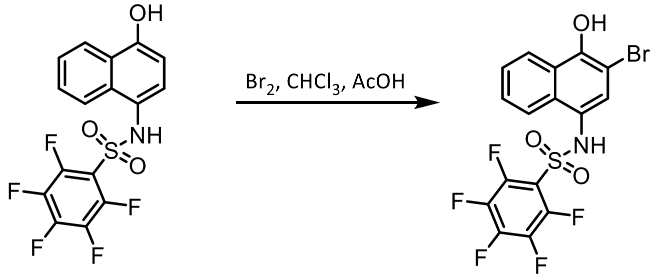
3-(N-(4-hydroxynaphthalen-1-yl)sulfamoyl)benzoic acid, 1f



1f

Sulfonamide **1f** was synthesized with the general N-sulfonylation procedure. Instead of column chromatography, the crude solid was dissolved in CH_2Cl_2. The product was precipitated by adding hexanes to the solution. The solid was filtered and dried to afford **1f** (600 mg, 32%). ^{1}H NMR (500 MHz, acetone-*d*$_6$) δ 8.39 (t, *J* = 1.8 Hz, 1H), 8.19 (dt, *J* = 8.0, 1.2 Hz, 2H), 8.05 – 7.96 (m, 1H), 7.86 – 7.78 (m, 1H), 7.57 (t, *J* = 7.8 Hz, 1H), 7.47 – 7.34 (m, 2H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H). ^{13}C NMR (151 MHz, acetone-*d*$_6$) δ 171.5, 152.9, 139.6, 139.4, 133.7, 132.3, 129.0, 128.6, 127.9, 126.8, 126.3, 125.5, 125.3, 123.5, 123.4, 122.3, 107.5. MS (ESI) m/z [M-H] $^-$ calcd for $C_{17}H_{12}NO_5S^-$ 342.04, found 342.1. HPLC t_R:5.9 min

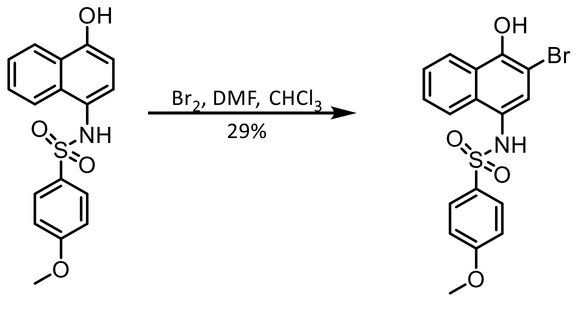
2-bromo-4-((perfluorophenyl)sulfonamido)naphthalen-1-olate, 2a



1a **2a**

Sulfonamide **1a** (28 mg, 0.70 mmol) was placed in a scintillation vial and then dissolved in $CHCl_3$(1 mL).The vial was wrapped in foil and chilled to 0 °C. A solution of Br_2 (44 µL, 9% in AcOH, 0.86 mmol) was added dropwise to the reaction mixture. After 0.5h, the reaction was complete by TLC. The reaction was washed thrice with water and once with $Na_2S_2SO_3$. The resulting organic layer was dried with Na_2SO_4 and filtered through cotton. The organic solution was dried. The crude material was purified by silica gel chromatography (1:4, EtOAc/hexanes) to afford **2a** (22 mg, 66%).^{1}H NMR (600 MHz, acetone-*d*$_6$) δ 8.68 (s, 0H), 8.23 (dd, *J* = 16.6, 7.8 Hz, 2H), 7.93 (t, *J* = 7.5 Hz, 1H), 7.87 (t, *J* = 7.9 Hz, 1H).^{13}C NMR (151 MHz, acetone-*d*$_6$) δ 177.2, 164.1, 141.4, 135.6, 135.1, 134.2, 133.3, 132.3, 128.6, 127.8. MS (ESI) m/z [M-H] $^-$ calcd for $C_{16}H_6BrF_5NO_3S^-$ 465.9, found 466.1.

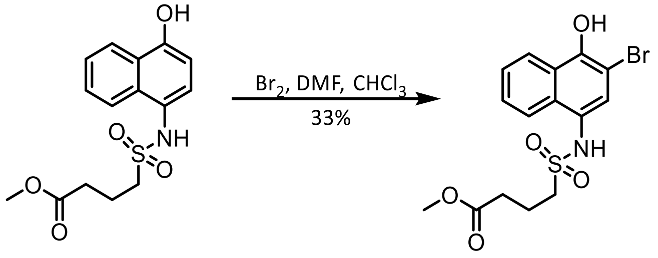
N-(3-bromo-4-hydroxynaphthalen-1-yl)-4-methoxybenzenesulfonamide, 2b



1b **2b**

Compound **1b** (50 mg, 0.15 mmol) was charged into a 4-ml vial with a stir bar. DMF (500 μL) was added to dissolve compound. Bromine (16 μL, 0.30 mmol) was diluted in 500 μL of $CHCl_3$, and then added slowly to the 4-ml vial at 0 °C. The reaction mixture was allowed to warm to rt, and stirred in the dark for 5 h. The crude reaction mixture was diluted in EtOAc (3.0 mL), and washed with saturated $Na_2S_2O_3$, water and brine. The organic layer was dried with Na_2SO_4, and filtered with filter paper. The solvent was removed with a stream of N_2 gas. The crude mixture was purified with preparative HPLC (gradient: 40% → 90% MeCN with 0.1 % TFA from 4 to 29 min, absorbance 320 nm) to yield a bright yellow solid **2b** (18 mg, 29%). The product oxidized during synthesis, so all the characterizations were done for the oxidized product. ^{1}H NMR (acetone-*d*$_6$) δ 3.96 (s, 1H), 7.21- 7.23 (m, 2H), 7.82- 7.88 (m, 2H), 8.04- 8.05 (m, 2H), 8.17 (m, 2H), 8.94 (s, 1H). ^{13}C NMR (acetone-*d*$_6$) δ 56.83, 115.97, 127.77, 127.91, 128.62, 128.95, 131.10, 132.72, 133.47, 134.55, 135.31, 135.54, 135.84, 140.01, 141.80, 161.59, 165.35, 178.11. MS (ESI) m/z $[M+H]^+$ calcd for $C_{17}H_{12}BrNO_4S^+$ (oxidized compound **2b**) 406.0, found 406.0.

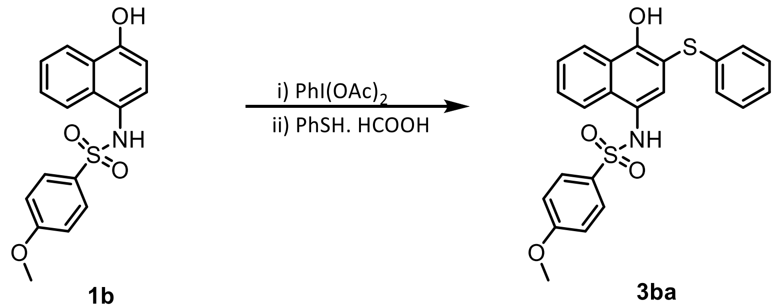
methyl 4-(N-(3-bromo-4-hydroxynaphthalen-1-yl)sulfamoyl)butanoate, 2c



1c **2c**

Compound **1c** (20 mg, 0.062 mmol) was charged into a 4-ml vial with a stir bar. DMF (500 μL) was added to dissolve compound **3**. Bromine (3.0 μL, 0.059 mmol) was diluted in 500 μL of $CHCl_3$, and then added slowly to the 4-mL vial. The reaction mixture was stirred at rt in the dark for 16 h. The crude reaction mixture was diluted in EtOAc (3.0 mL), and washed with saturated $Na_2S_2O_3$, water and brine. The organic layer was dried with Na_2SO_4, and filtered with filter paper. The solvent was removed with a stream of N_2 gas. The crude mixture was purified with preparative HPLC (gradient: 40% → 90% MeCN with 0.1% TFA from 4 to 29 min, absorbance 320 nm) to yield a dark green solid **2c** (8.3 mg, 33%). ^{1}H NMR (acetone-*d*$_6$) δ 2.29 (q, *J*= 7.5 Hz, 2H), 2.65 (t, *J*= 7.3 Hz, 2H), 3.59 (m, 2H), 3.67 (s, 3H), 7.90 (m, 2H), 8.19 (m, 1H), 8.35 (m, 1H), 8.66 (s, 1H). ^{13}C NMR (acetone-*d*$_6$) δ 20.65, 32.81, 52.39, 55.28, 127.92, 129.05, 132.80, 134.48, 135.09, 135.47, 135.66, 139.89, 162.87, 173.84, 178.10. MS (ESI) m/z $[M-H]^-$ calcd for $C_{15}H_{16}BrNO_5S^-$ 401.3, found 401.2.

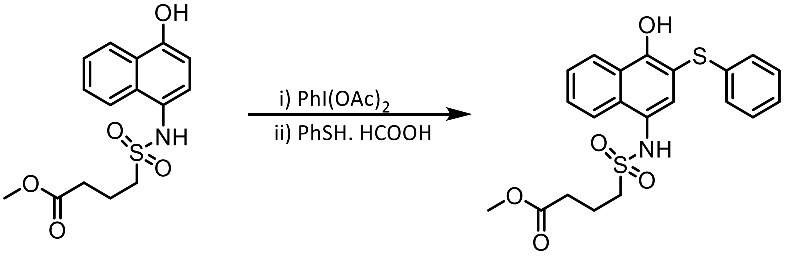
N-(4-hydroxy-3-(phenylthio)naphthalen-1-yl)-4-methoxybenzenesulfonamide, 3ba



1b **3ba**

The thioether **3ba** was synthesized from **2** using the general oxidative coupling to thiols procedure. Tan solid (350 mg, 37%). ^{1}H NMR (500 MHz, acetone-d_6) δ 8.79 (s, 1H), 8.64 (s, 1H), 8.29 (dd, *J* = 7.8, 1.9 Hz, 1H), 8.27 – 8.21 (m, 1H), 7.64 – 7.53 (m, 4H), 7.30 (t, *J* = 7.7 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 7.08 (s, 1H), 7.02 (d, *J* = 7.7 Hz, 2H), 6.91 – 6.84 (m, 2H), 3.76 (s, 3H).^{13}C NMR (126 MHz, acetone-d_6) δ 166.7, 158.2, 140.3, 136.9, 135.3, 135.1, 133.3, 133.0, 131.5, 130.8, 129.9, 129.3, 128.9, 127.7, 126.8, 117.8, 112.4, 59.0. MS (ESI) m/z [M-H] $^-$ calcd for $C_{23}H_{18}NO_4S_2^-$ 437.1, found 437.0

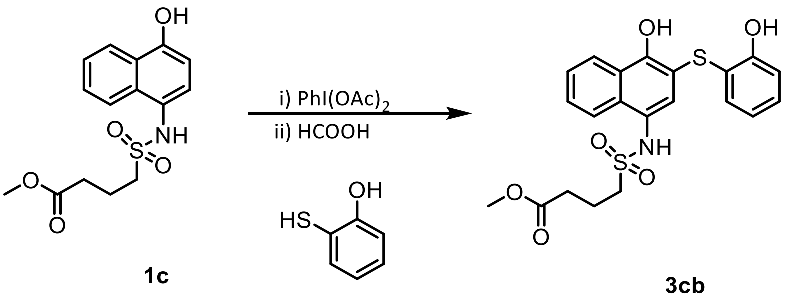
methyl 4-(N-(4-hydroxy-3-(phenylthio)naphthalen-1-yl)sulfamoyl)butanoate, 3ca



1c **3ca**

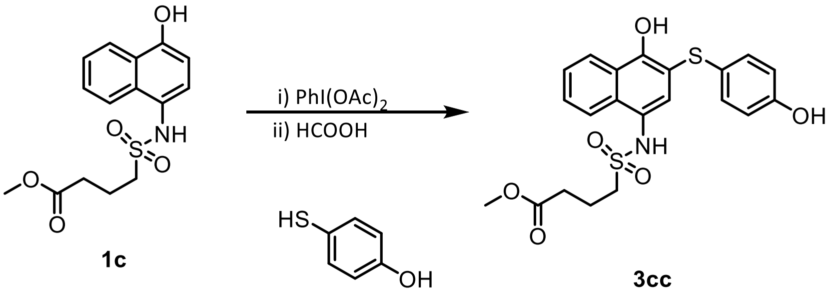
The naphthol sulfonamide **1c** (375 mg, 1.16 mmol) was dissolved into acetone. Iodobenzene diacetate (358 mg, 1.1 mmol) was subsequently added to the reaction. After 1 h, the reaction was complete by TLC (1:4 EtOAc/hexanes). The thiophenol (200 mg, 1.8 mmol) was added to the reaction mixture. The formic acid was subsequently added to the reaction mixture. After 2 h, the reaction mixture was extracted with chloroform and washed thrice with 1 M aq HCl. The organic layer was dried with $MgSO_4$ and degassed with nitrogen. After degassing the solvent was evaporated under vacuum. The crude material was purified by silica gel chromatography (1:4, EtOAc/hexanes) to afford **3ca** (50 mg, 26%).^{1}H NMR (600 MHz, acetonitrile-d_3) δ 8.28 (d, 1H, J = 8.4 Hz), 8.21 (d, 1H, J = 8.4 Hz), 7.69 (t, 1H, J = 7.7 Hz), 7.62 (t, 1H, J = 7.7 Hz), 7.54 (s, 1H), 7.28 (t, 2H, J = 7.7 Hz), 7.20 (t, 1H, J = 7.4 Hz), 7.15 (d, 2H, J = 8.0 Hz), 3.57 (s, 3H), 3.13-3.10 (m, 2H), 2.38 (t, 2H, J = 7.2 Hz), 2.04-1.99 (m, 2H). ^{13}C NMR (151 MHz, acetonitrile-d_3) δ 173.6, 155.1, 137.3, 133.7, 131.8, 130.3, 129.3, 128.3, 127.5, 127.3, 126.1, 125.7, 124.5, 124.1, 118.3, 110.3, 52.1, 51.6, 32.4, 20.0. MS (ESI) m/z [M-H]$^-$ calcd for $C_{21}H_{20}NO_5S_2^-$ 430.1, found 430.1. HPLC t_R: 12.2 min

methyl 4-(N-(4-hydroxy-3-((2-hydroxyphenyl)thio)naphthalen-1-yl)sulfamoyl)butanoate, 3cb



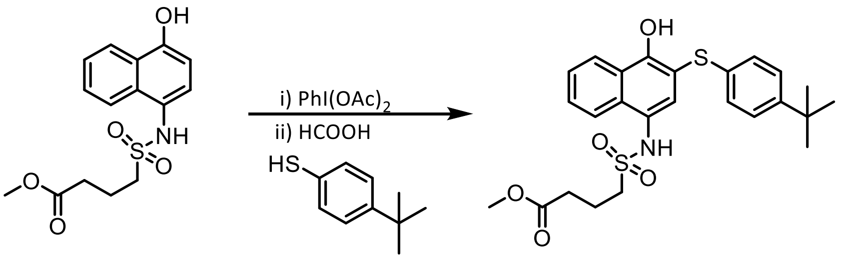
Sulfonamide **1c** was subjected to the general oxidative coupling of thiols procedure. The resulting crude material was purified by silica gel chromatography (Et_2O/hexanes, 1:3) to afford **3cb** (20 mg, 50%).^{1}H NMR (600 MHz, acetone-d_6) δ 8.39 – 8.25 (m, 2H), 7.71 – 7.62 (m, 2H), 7.62 – 7.54 (m, 1H), 7.22 – 7.07 (m, 2H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.80 (t, *J* = 7.5 Hz, 1H), 3.61 (s, 3H), 3.28 – 3.11 (m, 2H), 2.49 (t, *J* = 7.3 Hz, 2H), 2.15 – 2.09 (m, 2H). ^{13}C NMR (151 MHz, acetone-d_6) δ 174.2, 157.3, 155.6, 134.4, 133.6, 132.3, 130.78, 129.4, 127.9, 126.9, 125.5, 124.7, 123.2, 122.5, 117.3, 112.7, 52.7, 52.3, 33.3, 21.0. MS (ESI) m/z [M-H] $^-$ calcd for $C_{21}H_{20}NO_6S_2^-$ 446.1, found 446.1. HPLC t_R:8.3 min

methyl 4-(N-(4-hydroxy-3-((4-hydroxyphenyl)thio)naphthalen-1-yl)sulfamoyl)butanoate, 3cc



Sulfonamide **1c** was subjected to the general oxidative coupling of thiols procedure. The resulting crude material was purified by silica gel chromatography (Et_2O/hexanes, 1:4) to afford **3cc** (6 mg, 36%).^{1}H NMR (600 MHz, acetonitrile-d_3) δ 8.24 (d, *J* = 8.4 Hz, 1H), 8.16 (d, *J* = 8.4 Hz, 1H), 7.72 (s, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.61 – 7.55 (m, 2H), 7.47 (s, 1H), 7.41 (s, 1H), 7.20 (d, *J* = 8.6 Hz, 2H), 7.08 (s, 1H), 6.76 (d, *J* = 8.7 Hz, 2H), 3.59 (s, 3H), 3.14 – 3.03 (m, 2H), 2.38 (t, *J* = 7.2 Hz, 2H), 2.06 – 1.97 (m, 2H).^{13}C NMR (151 MHz, acetonitrile-d_3) δ 173.3, 157.2, 153.3, 132.8, 132.3, 130.4, 128.4, 127.0, 125.5, 125.4, 125.2, 124.1, 123.4, 116.9, 113.1, 51.7, 51.1, 32.0, 19.5. MS (ESI) m/z [M-H] $^-$ calcd for $C_{21}H_{20}NO_6S_2^-$ 446.1, found 446.1. HPLC t_R:8.3 min

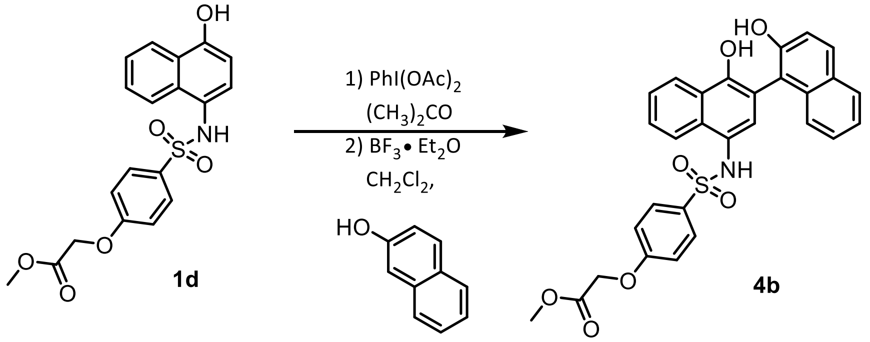
methyl 4-(N-(3-((4-(tert-butyl)phenyl)thio)-4-hydroxynaphthalen-1-yl)sulfamoyl)butanoate, 3cd



1c **3cd**

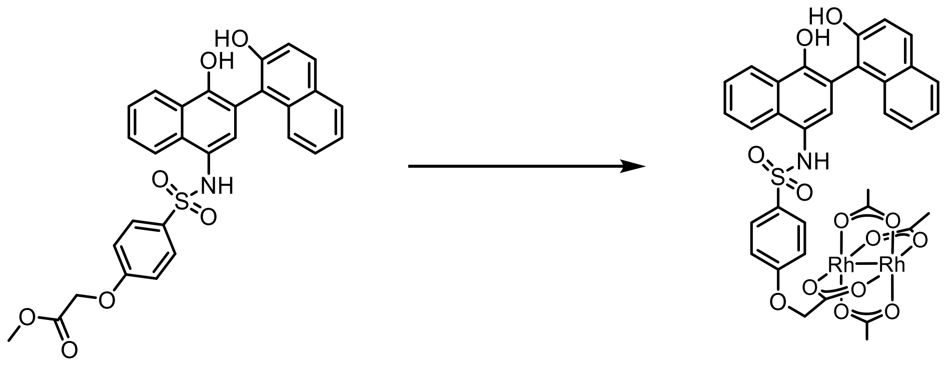
Sulfonamide **1c** was subjected to the general oxidative coupling of thiols procedure. The resulting crude material was purified by silica gel chromatography (Et_2O/hexanes, 1:10) to afford **3cd** (50 mg, 35%).^{1}H NMR (500 MHz, chloroform-*d*) δ 8.25 (dd, J = 8.3, 1.2 Hz, 1H), 8.09 – 8.01 (m, 1H), 7.64 – 7.58 (m, 2H), 7.52 (ddd, J = 8.2, 6.8, 1.2 Hz, 1H), 7.23 (s, 1H), 7.18 (t, J = 4.3 Hz, 2H), 7.00 (d, J = 8.5 Hz, 2H), 6.43 (s, 1H), 3.55 (s, 3H), 3.19 – 3.05 (m, 2H), 2.40 (t, J = 7.0 Hz, 2H), 2.11 (dq, J = 9.0, 7.0 Hz, 2H), 1.18 (s, 9H).^{13}C NMR (126 MHz, chloroform-*d*) δ 172.8, 154.4, 149.9, 132.5, 130.9, 128.9, 127.4, 126.6, 126.4, 124.3, 123.9, 123.9, 122.3, 109.4, 51.8, 51.1, 34.5, 31.9, 31.2, 19.1. MS (ESI) m/z [M-H]$^-$ calcd for $C_{25}H_{28}NO_5S_2^-$ 486.1, found 486.2. HPLC t_R:7.5 min

methyl 2-(4-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)phenoxy)acetate, 4b



Sulfonamide **1d** was subjected to the general oxidative coupling of 2-naphthol procedure. The resulting crude material was purified by silica gel chromatography (Et_2O/hexanes, 1:2) to afford **4b** (60 mg, 61%).^{1}H NMR (500 MHz, acetone-d_6) δ 8.32 (dd, *J* = 15.1, 8.6 Hz, 2H), 7.86 (t, *J* = 8.1 Hz, 3H), 7.82 – 7.76 (m, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.56 (p, *J* = 7.1 Hz, 2H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 8.9 Hz, 1H), 7.19 (d, *J* = 8.3 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 6.85 (s, 1H), 4.67 (s, 2H), 3.74 (s, 3H). HPLC t_R: 11 min

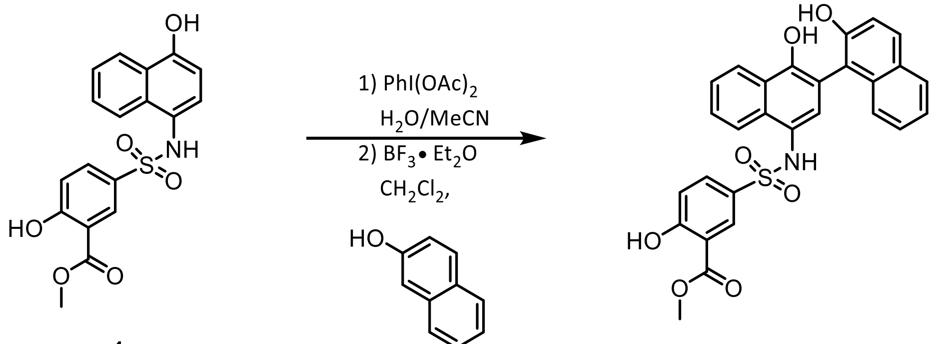
Rhodium conjugate,13b



4b **13b**

Ester **4b** (10 mg, 0.018 mmol), was hydrolyzed according to procedures described in literature.[7] The metal complex $Rh_2(OAc)_3(tfa)$ (6 mg, 0.012 mmol), the carboxylic acid of ester **4b**, and a stir bar were placed in a vial. The solid mixture was dissolved into 2,2,2-trifluoroethanol (1 mL). The resulting solution was purged with nitrogen for 15 min. $^{i}Pr_2EtN$ (1.5 mg, 0.012 mmol) was added to the reaction and it was heated for 4 h at 50 °C while stirring. After 4 h, the reaction was complete by TLC (1:3, EtOAc/hexanes). The crude reaction mixture was evaporated onto silica and purified by silica gel chromatography (1:3, EtOAc/hexanes) to yield **13b** as a blue solid (4 mg, 37%). ^{1}H NMR (500 MHz, acetone-d_6) δ 8.36 – 8.25 (m, 2H), 7.84 (dd, *J* = 9.4, 6.5 Hz, 2H), 7.65 – 7.59 (m, 2H), 7.59 – 7.49 (m, 2H), 7.37 – 7.29 (m, 2H), 7.25 (dd, *J* = 13.3, 8.2 Hz, 2H), 7.21 – 7.11 (m, 2H), 6.82 (s, 1H), 6.62 (d, *J* = 8.9 Hz, 1H), 4.28 – 4.17 (m, 2H), 1.70 (s, 9H). MS (ESI) m/z [M-H]$^-$ calcd for $[C_{34}H_{28}NO_{13}Rh_2S]^-$ 895.9, found 896.1

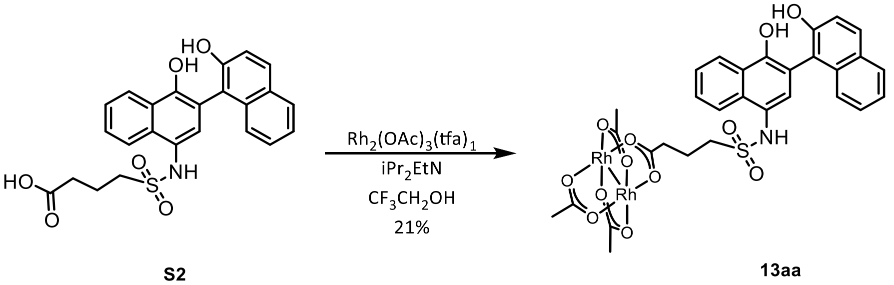
methyl 5-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)-2-hydroxybenzoate, 4d



1e **4d**

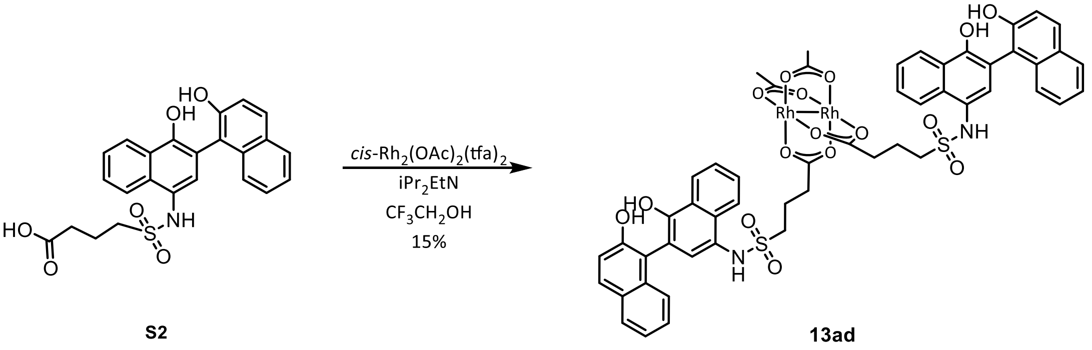
Synthesis of **4d** was described in the general synthetic procedures section. White solid (240 mg, 46%). ^{1}H NMR (600 MHz, acetonitrile-d_3) δ 8.26 (d, *J* = 8.1 Hz, 1H), 8.19 (d, *J* = 8.3 Hz, 1H), 8.10 (d, *J* = 2.4 Hz, 1H), 7.88 (dd, *J* = 11.4, 8.4 Hz, 2H), 7.79 (dd, *J* = 8.8, 2.5 Hz, 1H), 7.72 (s, 1H), 7.58 (dt, *J* = 18.8, 7.2 Hz, 2H), 7.32 (dt, *J* = 24.8, 7.2 Hz, 3H), 7.23 (d, *J* = 8.9 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 8.8 Hz, 1H), 6.79 (s, 1H), 6.75 (s, 1H), 6.69 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (151 MHz, acetonitrile-d_3) δ 169.9, 164.7, 153.6, 151.3, 134.9, 134.5, 132.7, 131.0, 130.8, 130.6, 129.7, 128.6, 127.4, 127.3, 126.4, 126.3, 124.6, 124.4, 124.1, 123.8, 123.1, 118.9, 118.9, 115.3, 114.5, 113.0, 53.3. MS (ESI) m/z [M-H] $^-$ calcd for $[C_{28}H_{21}NO_7S]^-$ 514.1, found 516.0. HPLC t_R: 12.5 min

Rhodium conjugate, 13aa



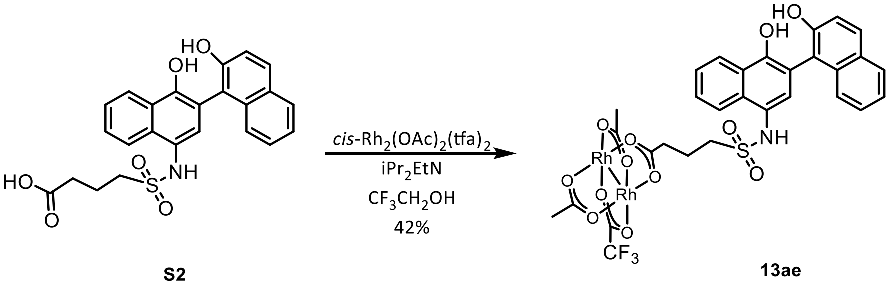
The metal complex $Rh_2(OAc)_3(tfa)_1$ (1.4 mg, 0.0028 mmol), compound **S2** (1.4 mg, 0.0031 mmol), and a stir bar were placed in a vial. The solid mixture was dissolved into 2,2,2-trifluoroethanol (1.4 mL). The resulting solution was purged with nitrogen for 15 min. $^iPr_2EtN$ (0.4 mg, 0.0031 mmol) was added to the reaction and it was heated at 40 °C for 22 h while stirring. After 22 h, the reaction was purified by HPLC to yield **13aa** as a blue solid (0.5 mg, 21%). ^1H NMR (500 MHz, acetone-d_6) δ 8.45-8.37 (m, 3H), 7.87 (d, 2H, J = 8.3, Hz), 7.67-7.63 (m, 1H), 7.60-7.57 (m, 1H), 7.44 (m, 1H), 7.40-7.30 (m, 4H), 3.31-3.25 (m, 2H), 2.49-2.46 (m, 2H), 1.81-1.80 (m, 8H). MS (ESI), [M-H]- calcd for $[C_{30}H_{28}NO_{12}Rh_2S]^-$ 831.9, found 831.7.

Rhodium conjugate,13ad



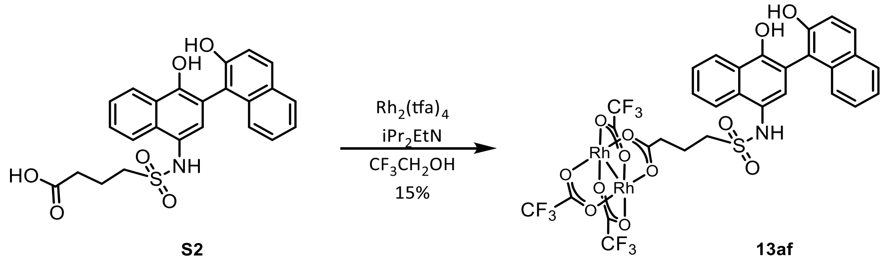
The metal complex *cis*-$Rh_2(OAc)_2(tfa)_2$ (86 mg, 0.16 mmol), compound **S2** (80 mg, 0.18 mmol), and a stir bar were placed in a vial. The solid mixture was dissolved into 2,2,2-trifluoroethanol (5 mL). The resulting solution was purged with nitrogen for 15 min. $^iPr_2EtN$ (18.5 mg, 0.14 mmol) was added to the reaction and it was heated for 4 h at 50 °C while stirring. After 4 h, the reaction was complete by TLC (1:3, EtOAc/hexanes). The crude reaction mixture was evaporated onto silica and purified by silica gel chromatography (1:3, EtOAc/hexanes) to yield **13ad** as a blue solid (30 mg, 15%). ^1H NMR (600 MHz, DMSO-d_6) δ 9.96 (s, 1H), 8.63 (d, *J* = 8.3 Hz, 1H), 8.49 (s, 1H), 8.44 (d, *J* = 8.1 Hz, 1H), 8.37 (d, *J* = 8.4 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 1H), 8.12 (d, *J* = 9.0 Hz, 1H), 8.07 (d, *J* = 8.9 Hz, 1H), 7.82 (t, *J* = 7.5 Hz, 1H), 7.76 (t, *J* = 7.5 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 2.99 – 2.96 (m, 2H), 2.17 (t, *J* = 7.2 Hz, 2H), 1.81 – 1.76 (m, 2H), 1.64 (s, 3H). MS (ESI), [M-H]- calcd for $[C_{52}H_{45}N_2O_{16}Rh_2S_2]^-$ 1223.0, found 1223.1.

Rhodium conjugate,13ae



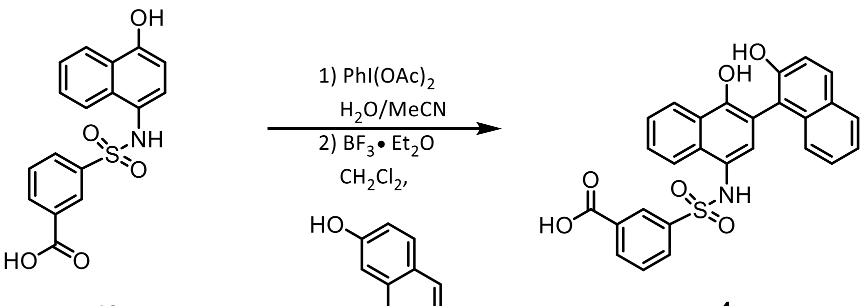
The metal complex cis-Rh$_2$(OAc)$_2$(tfa)$_2$ (86 mg, 0.16 mmol), compound **S2** (80 mg, 0.18 mmol), and a stir bar were placed in a vial. The solid mixture was dissolved into 2,2,2-trifluoroethanol (5 mL). The resulting solution was purged with nitrogen for 15 min. ^{i}Pr$_2$EtN (18.5 mg, 0.14 mmol) was added to the reaction and it was heated for 4 h at 50 °C while stirring. After 4 h, the reaction was complete by TLC (1:3, EtOAc/hexanes). The crude reaction mixture was evaporated onto silica and purified by silica gel chromatography (1:3, EtOAc/hexanes) to yield **13ae** as a blue solid (60 mg, 42%).^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ 8.27 (d, J = 8.1 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 7.85 (t, J = 8.1 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.32 – 7.21 (m, 4H), 7.11 (s, 1H), 2.89 (t, J = 7.7 Hz, 2H), 2.24 (d, J = 8.1 Hz, 2H), 1.91 – 1.68 (m, 8H) ^{13}C NMR (151 MHz, DMSO-*d*$_6$) δ 193.5, 193.1, 192.4, 172.7 (q, J = 38.4 Hz), 153.5, 150.2, 134.1, 131.6, 129.6, 129.5, 128.6, 128.4, 126.6, 126.5, 126.4, 125.5, 124.7, 124.0, 123.1, 122.8, 119.1, 117.1, 116.8, 110.9 (q, J = 285.9 Hz), 79.6, 50.1, 35.2, 30.1, 23.9 (d, J = 29.5 Hz)., 20.1.MS (ESI), [M-H]- calcd for [$C_{30}H_{25}F_3NO_{12}Rh_2S$]$^-$ 885.9, found 885.9. HPLC (10% → 90% MeCN-20min, absorbance 254 nm) t$_R$:16.9 min

Rhodium conjugate, 13af



N,N-Diisopropylethylamine (8.7 μL, 0.050 mmol) was added to a solution of **S2** (22.6 mg, 0.050 mmol) and Rh$_2$(tfa)$_4$ (32.9 mg, 0.050 mmol) in 2,2,2-trifluoroethanol (0.5 mL) and stirred at 50 °C for 18 h. The crude reaction mixture was evaporated onto silica and purified using flash chromatography (EtOAc/hexanes ,1:5) to obtain **13af** as a green solid (7.3 mg, 15%). ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.47 (d, *J* = 8.3 Hz, 1H), 8.28 (d, *J* = 8.6 Hz, 1H), 8.03 (d, *J* = 9.0 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.6 Hz, 1H), 7.67 (d, *J* = 9.0 Hz, 1H), 7.56 – 7.35 (m, 5H), 3.61 (m, 1.5H), 3.57 – 3.48 (m, 1.5H), 3.22 (m, 0.5H), 3.12 (m, 0.5H), 2.44 (dd, *J* = 7.4, 4.8 Hz, 2H), 2.06 (s, 1H), 1.35 – 1.24 (m, 2H). MS (ESI), [M-H]$^-$ calcd for [$C_{30}H_{19}F_9NO_{12}Rh_2S$]$^-$ 993.86 found 993.84

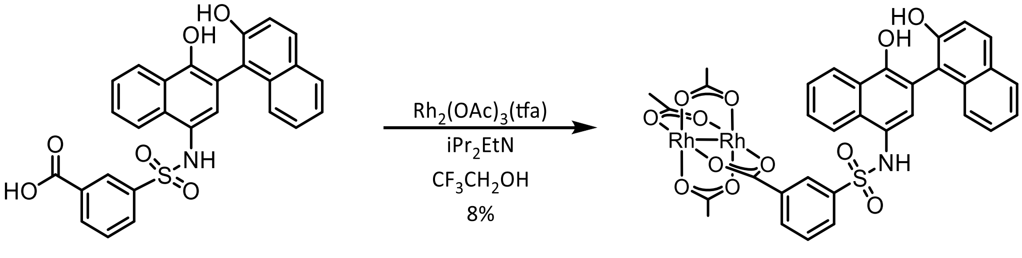
3-(N-(1',2-dihydroxy-[1,2'-binaphthalen]-4'-yl)sulfamoyl)benzoic acid, 4c



1f **4c**

Sulfonamide **1f** was subjected to the general oxidative coupling of 2-naphthol procedure. The resulting crude material was purified by silica gel chromatography (Et2O/hexanes, 1:19) to afford **4c** (145 mg, 30%).^{1}H NMR (600 MHz, DMSO-d_6) δ 10.04 (s, 1H), 8.37 (s, 0H), 8.26 (d, *J* = 11.7 Hz, 2H), 8.12 (d, *J* = 8.6 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 1H), 7.86 (t, *J* = 8.7 Hz, 2H), 7.63 – 7.58 (m, 1H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.30 (t, *J* = 8.0 Hz, 3H), 7.01 (d, *J* = 8.2 Hz, 1H), 6.71 (s, 1H).^{13}C NMR (151 MHz, DMSO-d_6) δ 166.4, 153.4, 150.4, 140.6, 134.2, 133.5, 131.9, 131.5, 131.4, 130.0, 129.7, 129.5, 128.4, 128.3, 128.0, 126.5, 126.4, 126.2, 125.5, 124.3, 123.9, 123.3, 123.0, 122.8, 118.9, 116.7, 116.6, 79.6. MS (ESI) m/z [M-H] $^-$ calcd for $[C_{27}H_{18}NO_6S]^-$ 484.1, found 485.9. HPLC t_R: 8.9 min.

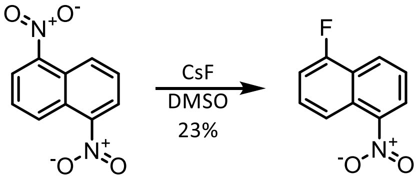
Rhodium conjugate, 13c



4c **13c**

The metal complex Rh$_2$(OAc)$_3$(tfa) (0.3 mg, 0.0006 mmol), compound **18** (0.6 mg, 0.0012 mmol)**,** and a stir bar were placed in a vial. The solid mixture was dissolved into 2,2,2-trifluoroethanol (124 µL) that had been purged with nitrogen for 15min. A solution of ^{i}Pr$_2$EtN (24 µL, 0.0006 mmol, 25 mM in 2,2,2-trifluoroethanol) was subsequently added to this vial. The reaction was heated for 4 h at 40 °C with stirring. After 4 h, the reaction was purified by analytical HPLC to yield **13c** (0.04 mg, 8%). MS (ESI) m/z [M-H] $^-$ calcd for $[C_{33}H_{26}NO_{12}Rh_2S]^-$ 865.9, found 865.9. HPLC t_R: 14.4 min.

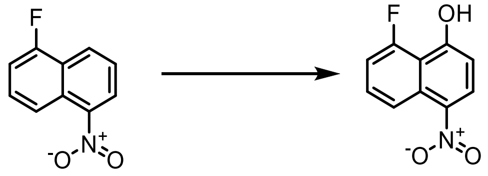
1-fluoro-5-nitronaphthalene,6



6

The aromatic compound 1,5-dinitronaphthalene (10 g, 45.9 mmol) was placed in a 20-mL vial in a nitrogen-atmosphere glovebox. Cesium fluoride (21 g, 139 mmol) and dry DMSO (70 mL, Sigma-Aldrich Sureseal) were added to the vial. The vial was then sealed and then taken out of the glovebox and heated at 100 °C for 4 h. The reaction vessel was then allowed to cool to rt. The mixture was diluted with water and washed thrice with ether. The organic layer were combined and washed once with water and once more with brine. The ether layer was dried with Na_2SO_4 and filtered through cotton. The resulting solution was evaporated onto silica and purified using flash chromatography (CH_2Cl_2/hexanes, 1:4) to afford a yellow solid **6** (2 g, 23%). ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.43 (d, J = 8.4 Hz, 1H), 8.35 (d, J = 8.8 Hz, 1H), 8.29 (d, J = 7.6 Hz, 1H), 7.66 – 7.60 (m, 2H), 7.30 (dd, J_{FH}= 9.9 Hz, J_{HH}= 7.8 Hz, 1H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 158.8 (d, J_{CF} = 253.7 Hz), 146.5 (d, J_{CF} = 2.6 Hz), 129.6 (d, J_{CF} = 8.7 Hz), 127.3 (d, J_{CF} = 6.6 Hz), 126.5 (d, J_{CF} = 3.8 Hz), 125.1, 125.1 (d, J_{CF} = 17.5 Hz), 124.8, 119.3 (d, J_{CF} = 4.4 Hz), 111.3 (d, J_{CF} = 19.8 Hz). ^{19}F NMR (565 MHz, chloroform-*d*) δ -119.9 (dd, J_{FH} = 9.9, 6.0 Hz). MS (GC) m/z $[M^{\cdot}]^+$ calcd for $[C_{10}H_6FNO_2]^+$ 191.04, found 191.04

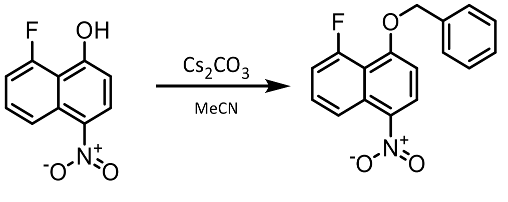
8-fluoro-4-nitronaphthalen-1-ol, 7



6 **7**

Liquid ammonia (30 mL) was added to a chilled round-bottomed flask (-78 °C). The fluorinated naphthalene **6** (750 mg, 3.9 mmol in 5 mL of THF) was added to the round bottomed flask, followed by addition of NaOH (1.00 g, 25.0 mmol) and 70% tBuOOH (1.5 mL, 987 mg, 11.0 mmol). The round-bottomed flask was removed from the dry ice/acetone bath. The reaction mixture was refluxed with a dry ice/ acetone coldfinger (-78 °C) to condense the liquid ammonia. After 2 h, the reaction was complete by TLC (1:1, CH_2Cl_2/hexanes). The coldfinger was removed to allow the ammonia to evaporate. Once at rt, the reaction was quenched with 2 N HCl and extracted with ether. The ether extract was washed with 2 N HCl thrice. The organic layer was dried onto silica and purified by silica gel chromatography (1:1, CH_2Cl_2/hexanes) to afford **7** (450 mg, 55%). Yellow solid. ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.63 (d, J = 8.8 Hz, 1H), 8.39 (d, J = 8.7 Hz, 1H), 7.78 (d, J = 31.4 Hz, 1H), 7.65 (td, J = 8.4, 6.1 Hz, 1H), 7.29 (dd, J = 15.2, 7.9 Hz, 1H), 7.01 (d, J = 8.7 Hz, 1H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 159.7 (d, J_{CF} = 243.5 Hz), 157.6, 139.1, 130.0 (d, J_{CF} = 10.9 Hz), 129.4 (d, J_{CF} = 2.1 Hz), 129, 121.1 (d, J_{CF} = 4.4 Hz), 113.9 (d, J_{CF} = 7.0 Hz), 111.6 (d, J_{CF} = 23.0 Hz), 110.6 (d, J_{CF} = 2.2 Hz). ^{19}F NMR (565 MHz, chloroform-*d*) δ -120.6 (s).MS (GC) m/z $[M^{\cdot}]^+$ calcd for $C_{10}H_6FNO_3^+$ 207.0, found 207.0

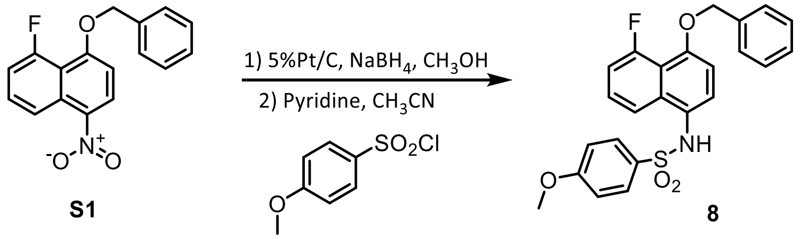
4-(benzyloxy)-5-fluoro-1-nitronaphthalene, S1



7 **S1**

The aromatic molecule **7** (150 mg, 0.72 mmol) was placed in a round bottomed flask along with Cs_2CO_3 (600 mg, 1.84 mmol) and a magnetic stir bar. The air in the vial was evacuated and backfilled with nitrogen thrice. Acetonitrile (7 mL) was added to the reaction vessel. Benzyl bromide (1 mL, 8.42 mmol) was subsequently added to the vial. The reaction vessel was heated to 70 °C. After 14 h, the reaction was complete by TLC (1:2, CH_2Cl_2/hexanes). The reaction mixture was dried onto silica and purified by silica gel chromatography (1:2, CH_2Cl_2/hexanes) to yield **S1** (183 mg, 85%). ^1H NMR (600 MHz, acetone-d_6) δ 8.40 (d, J = 8.8 Hz, 2H), 7.78 (ddd, J_{HH}= 8.2, 8.2, J_{FH} = 5.1 Hz, 1H), 7.63 (d, J = 7.6 Hz, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.41 – 7.35 (m, 2H), 7.29 (d, J = 8.8 Hz, 1H), 5.49 (s, 2H). ^{13}C NMR (151 MHz, acetone-d_6) δ 160.5 (d, J_{CF} = 4.3 Hz), 160.3 (d, J_{CF} = 260.4 Hz), 140.5 (d, J_{CF} = 3.3 Hz), 137.2, 131.2 (d, J_{CF} = 9.8 Hz), 129.9 (d, J_{CF} = 3.2 Hz), 129.5, 129.0, 128.6, 128.2, 119.8 (d, J_{CF} = 4.4 Hz), 116.7 (d, J_{CF} = 10.9 Hz), 113.7(d, J_{CF} = 22.4 Hz), 106.3, 71.9. ^{19}F NMR (565 MHz, acetone-d_6) δ -109.3 (dd, J_{FH} = 14.1, 5.9 Hz). MS (GC) m/z $[M^{\cdot}]^+$ calcd for $C_{17}H_{12}FNO_3^+$ 297.08, found 297.08

N-(4-(benzyloxy)-5-fluoronaphthalen-1-yl)-4-methoxybenzenesulfonamide, 8



Nitro reduction

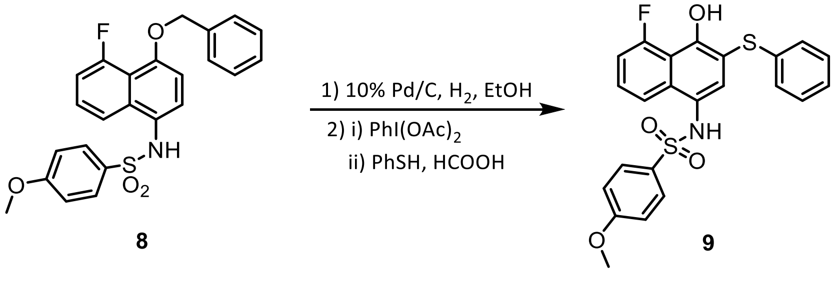
Molecule **S1** (70 mg, 0.24 mmol) was placed in scintillation vial along with 5% Pt/C (70 mg, 0.018 mmol). Methanol (4 mL) was added to the reaction vessel. The resulting slurry was degassed with nitrogen for 15 min. The reductant $NaBH_4$ (50 mg, 1.35 mmol) was added to the reaction vessel. After 1h, the reaction was complete by TLC (1:2 EtOAc/hexanes). The crude reaction was filtered through celite. The resulting solution was purged with nitrogen, and the volatiles were removed under vacuum. The crude residue was taken to the next step without further purification.

N-sulfonylation

The crude sludge was already in a round-bottomed flask. The 4-methoxybenzenesulfonyl chloride (56 mg,0.21 mmol) was added to the flask. The reaction vessel was evacuated and back-filled with nitrogen three times. A mixture of pyridine (4 mL) and acetonitrile (1 mL) was chilled in dry ice for 15 min and then transferred by syringe to the round-bottomed flask. The reaction was monitored by TLC (1:2 EtOAc/hexanes) and was complete after 2 h. The reaction mixture was taken up in CH_2Cl_2 and washed with aq HCl (3 × 20 mL, 2 M). The organic layer was purge with nitrogen gas. Compound was dry loaded and purified by silica gel chromatography (1:2, EtOAc/hexanes). The product fractions were collected and dried to yield **8** (78 mg, 46%). White solid. ^1H NMR (600 MHz, acetone-d_6) δ 7.90 (d, J = 8.6 Hz, 1H), 7.65 – 7.55 (m, 4H), 7.45 – 7.37 (m, 3H), 7.35 (d, J = 7.4 Hz, 1H), 7.16 (dd, J = 13.6, 7.9 Hz, 2H), 7.02 (d, J = 8.4 Hz, 1H), 7.00 – 6.94 (m, 2H), 5.29 (s, 2H), 3.85 (s, 3H). ^{13}C NMR (151 MHz, acetone-d_6) δ 163.9, 160.0 (d, J_{CF} = 258.2 Hz), 154.7 (d, J_{CF} = 4.1 Hz), 138.1, 135.5 (d, J_{CF} = 3.3 Hz), 132.9, 130.3, 129.3, 128.6, 128.6 (d, J_{CF} = 4.4 Hz), 128, 127.6, 127.5 (d, J_{CF} = 8.7 Hz), 120.5 (d, J_{CF} = 4.8 Hz), 117.1

(d, J_{CF} = 9.8 Hz), 114.9, 112.3 (d, J_{CF} = 23.0 Hz), 107.5 (d, J_{CF} = 2.2 Hz), 71.1, 56.1. . ^{19}F NMR (565 MHz, acetone-d_6) δ -111.9 (dd, J_{FH} = 12.3, 4.1 Hz). HPLC t_R:16.9 min

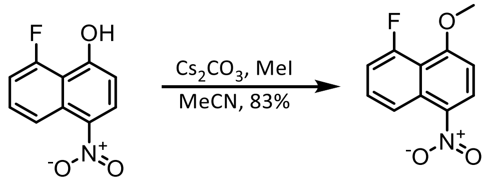
N-(5-fluoro-4-hydroxy-3-(phenylthio)naphthalen-1-yl)-4-methoxybenzenesulfonamide, 9



deprotection
The benzylether **8** (22 mg, 0.05 mmol) and 10% Pd/C (16 mg) were added to a scintillation vial. Ethanol (3 mL) was added to the vial. The vial was sealed and flushed with hydrogen gas. The solution was stirred overnight under hydrogen atmosphere (1 atm). The resulting mixture was filtered through celite. The organic solvent was evaporated under vacuum. The resulting crude was used directly in the next step.

oxidative coupling
The resulting crude solid was subjected to the general oxidative coupling to thiols procedure and then purified by silica gel chromatography (7:3, Et_2O/Hex) to afford **9** (6 mg, 44% over 2 steps).^{1}H NMR (600 MHz, benzene-d_6) δ 7.78 (d, J = 8.6 Hz, 1H), 7.48 (d, J = 8.6 Hz, 2H), 6.97 – 6.76 (m, 7H), 6.71 (dd, J = 12.9, 7.7 Hz, 1H), 6.27 (d, J = 8.6 Hz, 2H), 2.97 (s, 3H). ^{13}C NMR (151 MHz, benzene-d_6) δ 162.7, 159.2 (d, J_{CF} = 212.8 Hz), 153.1, 135.6, 134.9, 132.0, 131.1, 129.6, 129.1, 128.0, 127.6, 127.3, 127.2, 126.4, 124.7, 120.0, 113.7, 111.7 (d, J_{CF} = 18.1 Hz), 54.5. MS (ESI) m/z [M-H] $^-$calcd for $C_{23}H_{17}FNO_4S_2^-$ 454.1, found 455.7

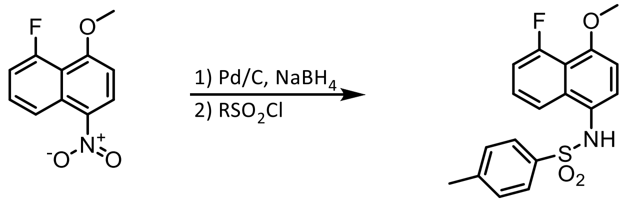
5-fluoro-4-methoxy-1-nitronaphthalene, 10



The aromatic molecule **7** (49.7 mg, 0.24 mmol) was placed in a round bottomed flask along with K_2CO_3 (132 mg, 0.96 mmol) and a magnetic stir bar. The air in the vial was evacuated and backfilled with nitrogen thrice. DMF (5 mL) was added to the reaction vessel. Iodomethane (0.3 mL, 4.8 mmol) was subsequently added to the vial. The reaction vessel was stirred at rt. After 14 h, the reaction was quenched by adding saturated sodium thiosulfate aqueous solution and HCl. The reaction mixture was then diluted with 100 mL of H_2O and extracted with ether (3 × 30 mL). The organic layer was dried with $MgSO_4$, filtered, and the solvent was removed in vacuo to yield **10** (61.9 mg, 84%). Characterization was in agreement with the literature.[9] ^{1}H NMR (600 MHz, chloroform-d) δ 8.46 (d, 1H, J = 8.8 Hz), 8.32 (d, 1H, J = 8.8 Hz), 7.60 (ddd, J_{FH} =4.2 , J_{HH} =

8.7, 7.9 Hz, 1H), 7.21 (dd, 1H, J_{FH} = 12.3, J_{HH} = 7.8 Hz), 6.81 (d, 1H, J =8.8 Hz), 4.06 (s, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 161.2 (d, J_{CF} = 5.5 Hz), 159.7 (d, J_{CF} = 260.9 Hz), 139.5 (d, J_{CF} = 4.3 Hz), 130.3 (d, J_{CF} = 9.8 Hz), 129.3 (d, J_{CF} = 3.3 Hz), 128.0, 119.4 (d, J_{CF} = 5.5 Hz), 116.1 (d, J_{CF} = 10.4 Hz), 113.0 (d, J_{CF} = 22.3 Hz), 103.4 (d, J_{CF} = 2.2 Hz), 56.7. ^{19}F NMR (565 MHz, chloroform-*d*) δ -109.2 (dd, J_{FH} = 12.3, 4.2). HPLC t_R:13.6 min.

N-(5-fluoro-4-methoxynaphthalen-1-yl)-4-methylbenzenesulfonamide, 11a



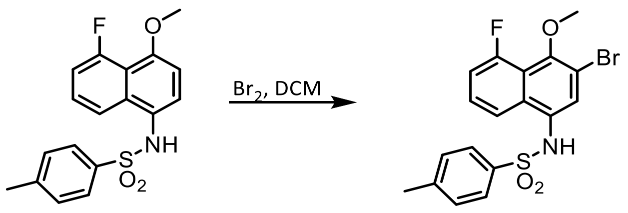
10 **11a**

The aromatic compound **10** (60 mg, 0.27 mmol) was placed in a round bottomed flask along with 10% Pd/ C (35 mg, 0.03 mmol). Methanol (25 mL) was added to the reaction vessel. The resulting slurry was degassed with nitrogen for 15 min. The reductant $NaBH_4$ (50 mg, 1.32 mmol) was added to the reaction vessel. After 1 h, the reaction was complete by TLC (1:2 EtOAc/hexanes). A purple spot formed when the product was stained with ninhydrin. The crude reaction was filtered through celite. The resulting solution was purged with nitrogen and then condensed in a round bottom flask. The crude sludge was taken to the next step without further purification.

N-sulfonylation

The crude sludge was already in a round-bottomed flask. The electrophile para-toluenesulfonylchloride (57 mg, 0.31 mmol) was added to the flask. The reaction vessel was evacuated and back-filled with nitrogen three times. A mixture of pyridine (5 mL) and acetonitrile (5 mL) was chilled in dry ice for 15 min and then transferred by syringe to the round-bottomed flask. The reaction was monitored by TLC (1:2 EtOAc/hexanes) and was complete after 2 h. The reaction mixture was taken up in CH_2Cl_2 and washed with aq HCl (3 × 20 mL, 2 M). The organic layer was purged with nitrogen gas. Compound was dry loaded and purified by silica gel chromatography (1:2, EtOAc/hexanes). The product fractions were collected and dried to yield **11a** (43 mg, 46%). ^{1}H NMR (600 MHz, acetonitrile-d_3) δ 7.72 (d, 1H, J = 8.4 Hz), 7.69 (s, 1H), 7.54 (d, 2H, J = 8.4 Hz), 7.35 (ddd, J_{FH} =5.5 , J_{HH} = 8.7, 8.7 Hz, 1H), 7.25 (d, 2H, J = 8.1 Hz), 7.10 (dd, 1H, J_{FH} = 13.6, J_{HH} = 8.3 Hz), 7.05 (d, 1H, J = 8.3 Hz), 6.78 (d, 1H, J = 8.4 Hz), 3.89 (s, 3H), 2.35 (s, 3H).
^{13}C NMR (151 MHz, acetonitrile-d_3) δ 160.0 (d, J_{CF} = 255.1 Hz), 156.1 (d, J_{CF} = 5.4 Hz), 144.9, 137.8, 135.3 (d, J_{CF} = 3.3 Hz), 130.5, 128.2, 127.9, 127.8 (d, J_{CF} = 9.3 Hz), 125.2 (d, J_{CF} = 3.4 Hz), 120.3 (d, J_{CF} = 4.4 Hz), 116.8 (d, J_{CF} = 10.9 Hz), 112.4 (d, J_{CF} = 22.7 Hz), 106.0 (d, J_{CF} = 2.1 Hz), 56.7, 21.5. ^{19}F NMR (565 MHz, acetonitirile-d_3) δ -112.6 (dd, J_{FH}=13.6, 5.5 Hz). White solid. HPLC t_R:18.4 min

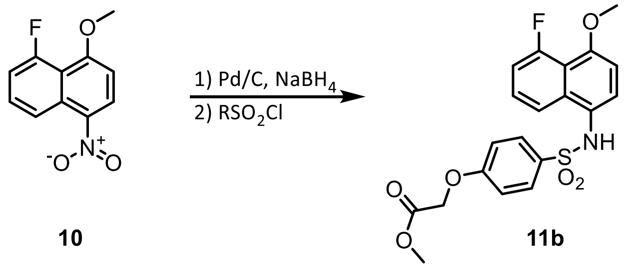
N-(3-bromo-5-fluoro-4-methoxynaphthalen-1-yl)-4-methylbenzenesulfonamide, 12a



11a **12a**

Molecule **11a** (10 mg, 0.024 mmol) was placed in a round bottomed flask and dissolved in CH_2Cl_2 (1 mL). A 10% solution of Br_2 in CH_2Cl_2 was added to the reaction vessel (12.4 µL, 0.024 mmol), The reaction was stirred in the dark for 3 h. The resulting solution was taken up into ether. The ethereal layer was washed thrice with NaS_2O_3 (aq) and then once with brine. The ether extract was dried with Na_2SO_4, filtered through cotton and dried onto silica gel. The dried crude with silica was loaded onto a silica gel column and purified by flash chromatography (1:3 Et_2O/hexanes) to yield **12a** (8 mg, 75%), a white solid. ^{1}H NMR (600 MHz, acetonitrile-d_3) δ 7.95 (s, 1H), 7.77 (d, J = 8.6 Hz, 1H), 7.60 (d, J = 8.1 Hz, 2H), 7.45 (ddd, J_{FH} =5.4 , J_{HH} = 8.2, 4.8 Hz, 1H), 7.35 (s, 1H), 7.33 – 7.24 (m, 3H), 3.91 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (151 MHz, acetonitrile-d_3) δ 158.3 (d, J_{CF} = 250.3 Hz), 152.0 (d, J_{CF} = 3.9 Hz), 145.4, 137.2, 134.1 (d, J_{CF} = 2.1 Hz), 130.7, 130.3, 130.2 (d, J_{CF} = 3.9 Hz), 128.3, 128.2 (d, J_{CF} = 9.3 Hz), 121.0 (d, J_{CF} = 3.8 Hz), 120.5 (d, J_{CF} = 9.9 Hz), 114.6, 114.0 (d, J_{CF} = 21.8 Hz), 62.5, 21.5. ^{19}F NMR (565 MHz, acetonitrile-d_3) δ -118.0 (dd, J_{FH} = 13.2, 5.4 Hz).

methyl 2-(4-(N-(5-fluoro-4-methoxynaphthalen-1-yl)sulfamoyl)phenoxy)acetate, 11b



10 **11b**

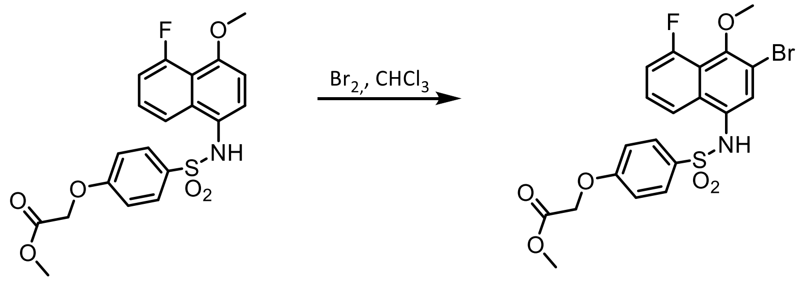
Reduction

The aromatic compound **10** (40 mg, 0.18 mmol) was placed in a round bottomed flask along with 10% Pd/ C (15 mg, 0.01 mmol). Ethanol (4 mL) was added to the reaction vessel. The resulting slurry was degassed with nitrogen for 15 min. The reductant $NaBH_4$ (37 mg, 1 mmol) was added to the reaction vessel. After 1 h, the reaction was complete by TLC (1:2 EtOAc/hexanes). A purple spot formed when the product was stained with ninhydrin. The crude reaction was filtered through celite. The resulting solution was purged with nitrogen and then condensed in a round bottom flask. The crude sludge was taken to the next step without further purification.

N-sulfonylation

The crude sludge was already in a round-bottomed flask. Methyl 2-(4-(chlorosulfonyl)phenoxy)acetate (56 mg,0.21 mmol) was added to the flask. The reaction vessel was evacuated and back-filled with nitrogen three times. Both pyridine (4 mL) and acetonitrile (1 mL) were transferred by syringe to the round-bottomed flask. The reaction was monitored by TLC (1:2 EtOAc/hexanes) and was complete after 2 h. The reaction mixture was taken up in CH_2Cl_2 and washed with 1 M HCl thrice. The organic layer was purge with nitrogen gas. Compound was dry loaded and purified on a silica gel column (10% Et_2O/toluene). The product fractions were collected and dried to yield (35 mg, 46%) of **11b**. ^{1}H NMR (600 MHz, acetone-d_6) δ 7.85 (d, J = 8.6 Hz, 1H), 7.62 (d, J = 8.5 Hz, 2H), 7.38 (ddd, J_{FH} =4.1 , J_{HH} = 8.1, 4.8 Hz, 1H), 7.21 – 7.07 (m, 2H), 7.03 – 6.98 (m, 2H), 6.90 (d, J = 8.4 Hz, 1H), 4.82 (s, 2H), 3.95 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (151 MHz, acetone-d_6) δ 169.3, 162.2, 160.0 (d, J_{CF} = 260.9 Hz), 155.9 (d, J_{CF} = 5.0 Hz), 135.4 (d, J_{CF} = 2.9 Hz), 133.8, 130.3, 127.8, 127.5 (d, J_{CF} = 8.9 Hz), 125.8 (d, J_{CF} = 5.7 Hz), 120.4 (d, J_{CF} = 4.4 Hz), 116.8 (d, J_{CF} = 10.3 Hz), 115.6, 112.2 (d, J_{CF} = 21.7 Hz), 105.9 (d, J_{CF} = 2.2 Hz), 65.7, 56.3, 52.4. ^{19}F NMR (565 MHz, acetone-d_6) δ -112.3 (dd, J_{FH} = 14.0, 4.1 Hz). HPLC t_R:13.5 min

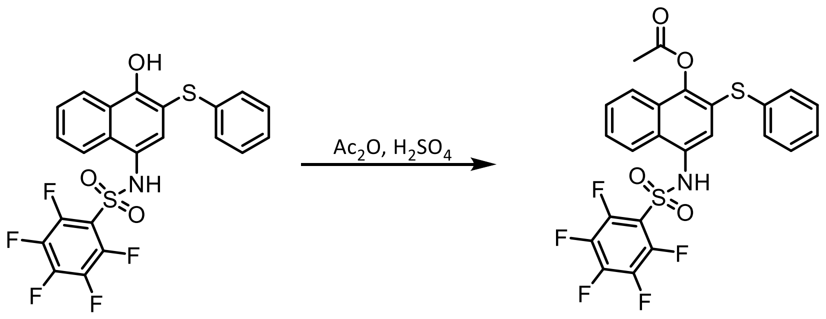
methyl 2-(4-(N-(3-bromo-5-fluoro-4-methoxynaphthalen-1-yl)sulfamoyl)phenoxy)acetate, 12b



11b **12b**

Molecule **12b** was synthesized with the same bromination process that yielded **12a.** The crude material was purified by flash chromatography (1:4, EtOAc/hexanes) and the preparative HPLC to afford a white solid **29** (9 mg, 19%). ^{1}H NMR (600 MHz, chloroform-d) δ 7.72 – 7.65 (m, 2H), 7.59 (d, J = 8.5 Hz, 1H), 7.48 (s, 1H), 7.38 (td, J = 8.1, 4.7 Hz, 1H), 7.18 (dd, J = 12.7, 7.7 Hz, 1H), 6.89 (d, J = 8.9 Hz, 2H), 6.55 (s, 1H), 4.66 (s, 2H), 3.93 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (151 MHz, chloroform-d) δ 168.2, 161.4, 157.7 (d, J_{CF} = 213.0 Hz), 151.4, 132.6, 131.7, 129.6, 129.5, 128.1, 127.3 (d, J_{CF} = 7.9 Hz), 119.8 (d, J_{CF} = 8.1 Hz), 118.6, 114.9 (d, J_{CF} = 8.2 Hz), 113.6 (d, J_{CF} = 18.8 Hz), 112.9, 65.2, 61.9, 52.5.

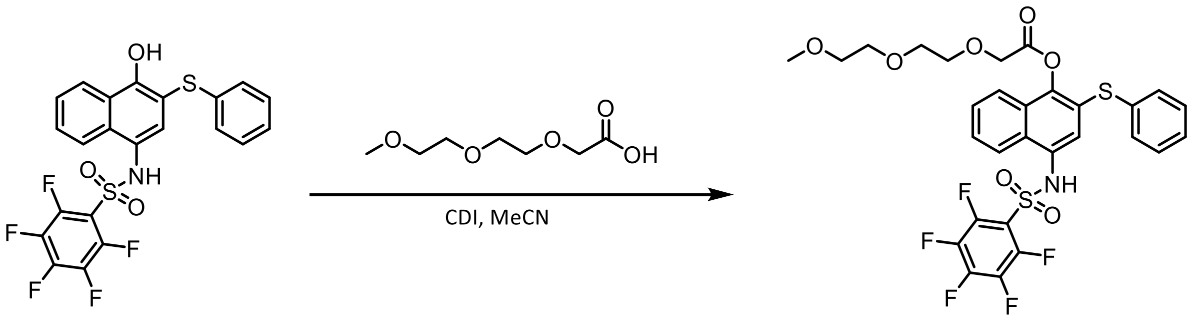
4-((perfluorophenyl)sulfonamido)-2-(phenylthio)naphthalen-1-yl acetates, 17



3aa **17**

The STAT3 inhibitor **3aa** was placed in a vial (10 mg, 0.020 mmol). A solution of 10% acetic anhydride in sulfuric acid (2 mL) was subsequently added to this vial. After 30 minutes , the reaction was complete by TLC (1:10 EtOAc/hexanes). The reaction mixture was taken up into ether and washed thrice with water. The solution was dried with Na_2SO_4, filtered through cotton , and dried under vacuum to yield **17** (5.6 mg, 52%). Product was used without further purification. ^{1}H NMR (600 MHz, methanol-*d*$_4$) δ 8.15 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.66 – 7.56 (m, 2H), 7.37 – 7.29 (m, 6H), 6.92 (s, 1H), 2.47 (s, 2H), 2.05 (s, 1H).^{13}C NMR (151 MHz, methanol-*d*$_4$) δ 169.1, 144.1, 132.9, 132.2, 130.2, 130.1, 129.1, 128.1, 127.9, 127.7, 126.9, 126.0, 124.7, 123.1, 121.3, 19.1. Due to extensive ^{19}F splitting, ^{13}C peaks in the perfluorophenyl region were not identified. ^{19}F NMR (565 MHz, methanol-*d*$_4$) δ -138.3 (m), -148.5 (s), -161.6 (m). HPLC *t*$_R$:17.2 min

4-((perfluorophenyl)sulfonamido)-2-(phenylthio)naphthalen-1-yl 2-(2-(2-methoxyethoxy)ethoxy)acetate, 18

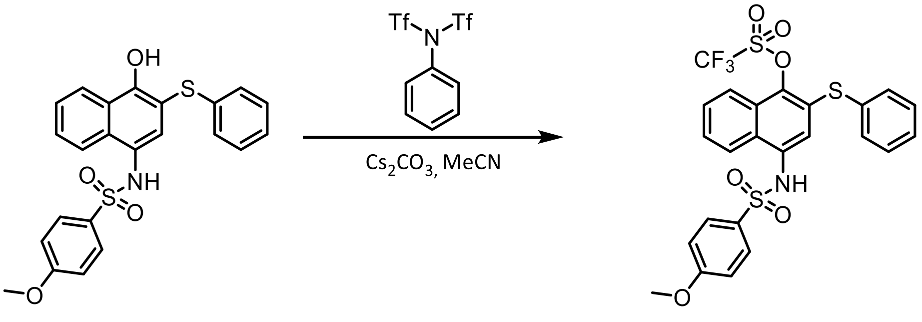


3aa **18**

The coupling agent carbonyl diimdazole was taken out of the glovebox in a sealed 20-mL vial. The liquid 2-(2-(2-methoxyethoxy)ethoxy)acetic acid was added to the sealed flask while under nitrogen from a manifold. Gas bubbled from the reaction. After 10 min, a solution of **3aa** (100 mg, 0.20 mmol) in dry acetonitrile was added to the vial (4 mL). The reaction was complete by TLC after 30 min (1:5 EtOAc/hexanes). The reaction mixture was then taken up into ether and washed thrice with water. The organic layer was dried with Na_2SO_4 and filtered through cotton. After filtration, the organic solution was dried onto silica and loaded onto a silica gel column where it was purified by elution on solvent (1:9 EtOAc/hexanes) to yield **18** (70 mg, 50%), a yellow oil.^{1}H NMR (600 MHz, chloroform-*d*) δ 8.03 – 7.97 (m, 1H), 7.83 – 7.76 (m, 1H), 7.62 – 7.56 (m, 2H), 7.39 – 7.28 (m, 5H), 7.26 (s, 1H), 6.98 (s, 1H), 4.65 (s, 2H), 3.93 – 3.87 (m, 2H), 3.74 (dd, *J* = 5.7, 3.7 Hz, 2H), 3.69 – 3.62 (m, 2H), 3.58 – 3.50 (m, 2H), 3.37 (s, 2H).^{13}C NMR

(151 MHz, chloroform-*d*) δ 168.6, 144.0, 132.7, 132.6, 129.4, 129.1, 128.6, 128.3, 128.3, 128.1, 127.9, 126.6, 124.2, 122.0, 121.9, 71.9, 70.7, 70.6, 68.4, 59.1, 22.5. Due to extensive ^{19}F splitting, ^{13}C peaks in the perfluorophenyl region were not identified.

4-((perfluorophenyl)sulfonamido)-2-(phenylthio)naphthalen-1-yl trifluoromethanesulfonate, 19

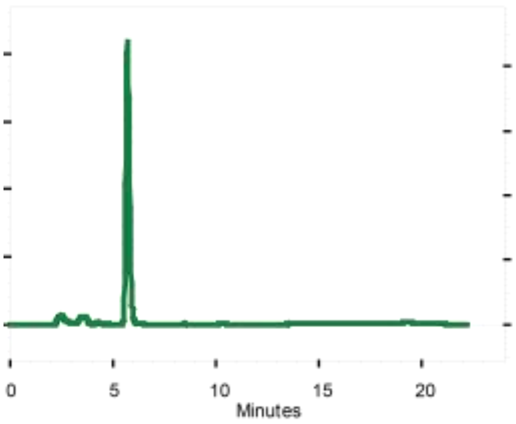


3ba **19**

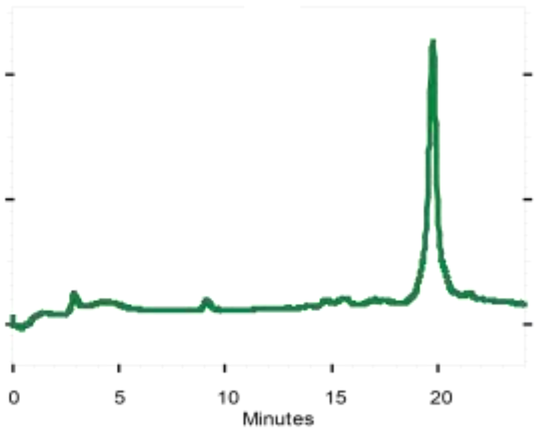
The sulfonamide **3ba** (50 mg, 0.11 mmol) was placed in a scintillation vial along N-Phenyl-bis(trifluoromethanesulfonimide) (50 mg, 0.14 mmol) and Cs_2CO_3 (50 mg, 0.15 mmol). The air in the vial was evacuated and the vial was backfilled with nitrogen. Degassed MeCN (2 mL) from the solvent purification system was added to the sealed reaction vessel. The reaction was allowed to stir at rt. After 2 h, no starting material remained by TLC (1:2, EtOAc/hexanes). The reaction mixture was taken up into toluene and washed thrice with brine. The resulting organic layer was dried with Na_2SO_4 and filtered through cotton. Solvent was removed to afford a crude orange solid. This material was purified by flash chromatography (1:4, EtOAc/hexanes) to afford a yellow solid **19,** (40 mg, 50%).^{1}H NMR (600 MHz, chloroform-*d*) δ 8.16 (d, *J* = 7.4 Hz, 1H), 8.12 (d, *J* = 7.1 Hz, 1H), 7.78 – 7.72 (m, 2H), 7.62 (s, 7H), 7.48 (s, 1H), 6.94 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (151 MHz, chloroform-*d*) δ 181.4, 163.5, 160.5, 156.1, 136.1, 134.3, 134.2, 133.3, 133.0, 132.0, 131.2, 130.8, 129.8, 127.5, 127.4, 127.2, 122.0, 114.4, 56.0. Due to extensive ^{19}F splitting, ^{13}C peak for CF_3 was not identified.

1.3. **HPLC**

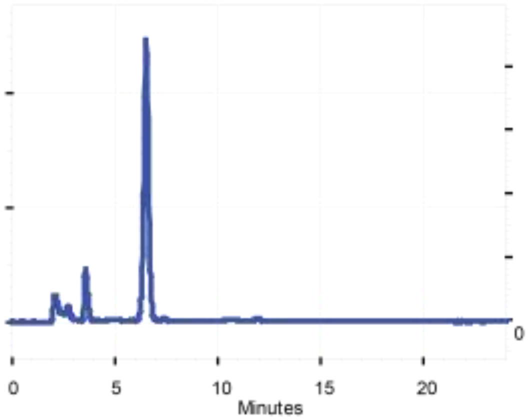
1d



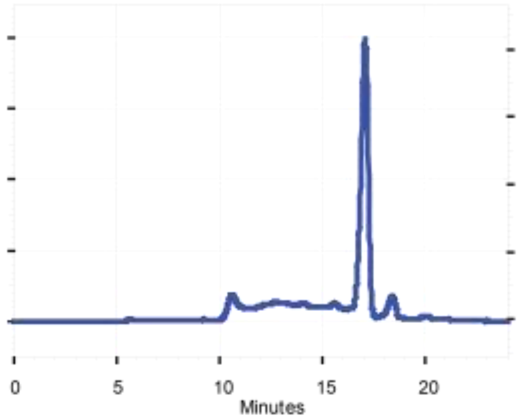
1f



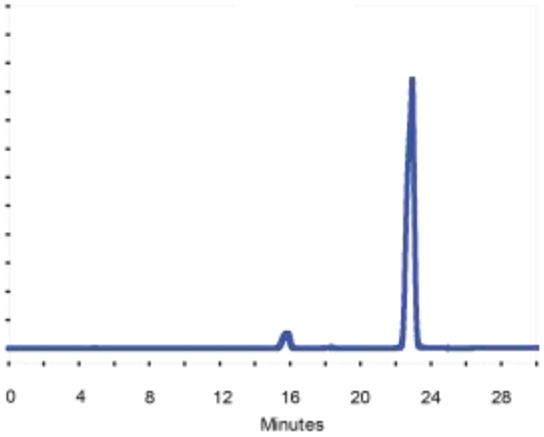
1c



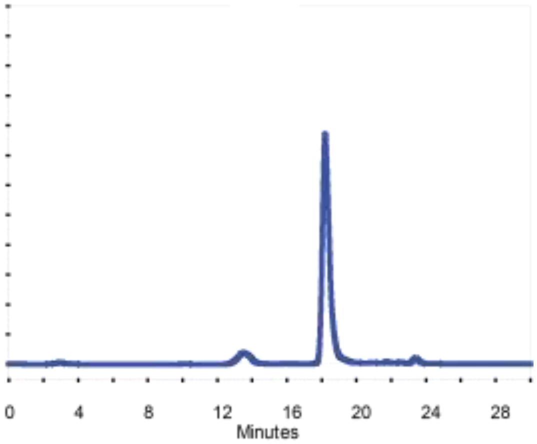
2a



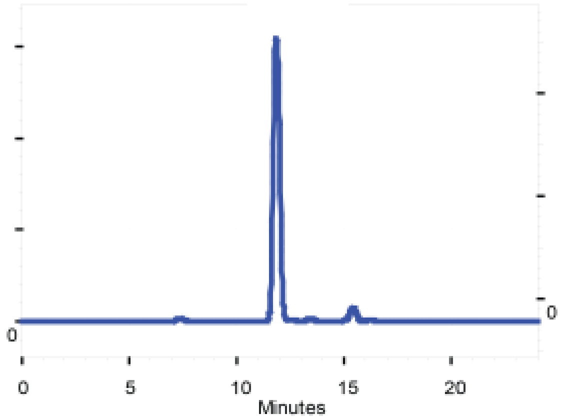
2b*



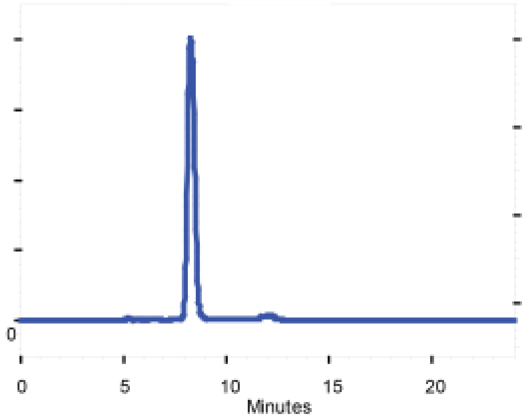
2c



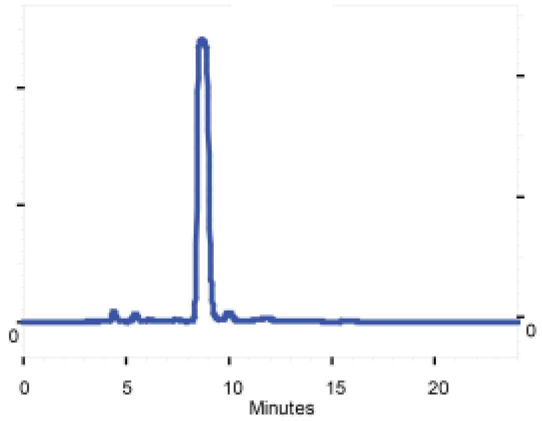
3ca



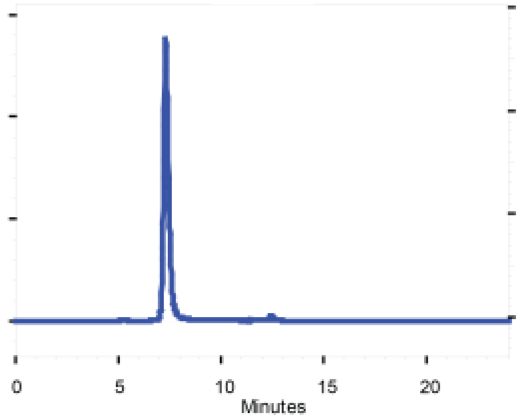
3cb



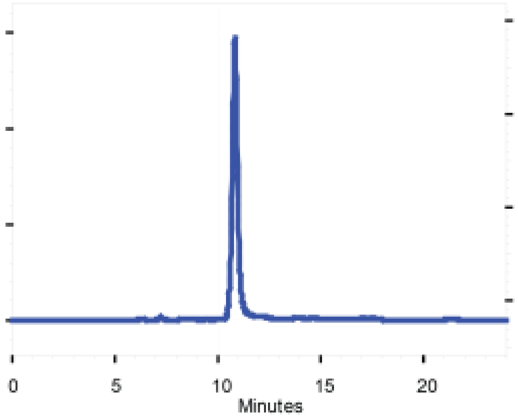
3cc



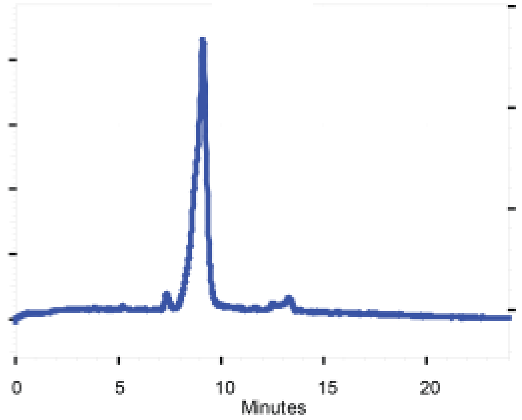
3cd



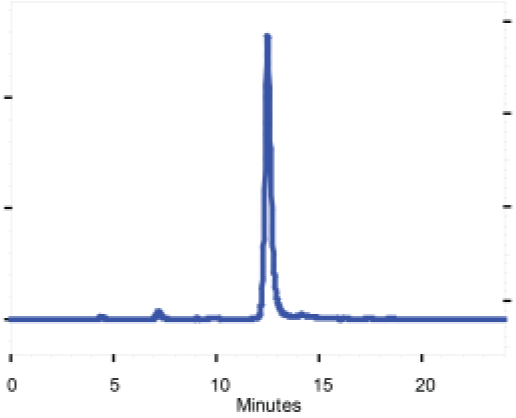
4b



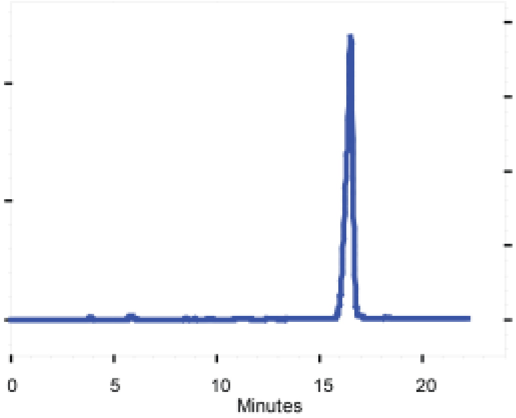
4c



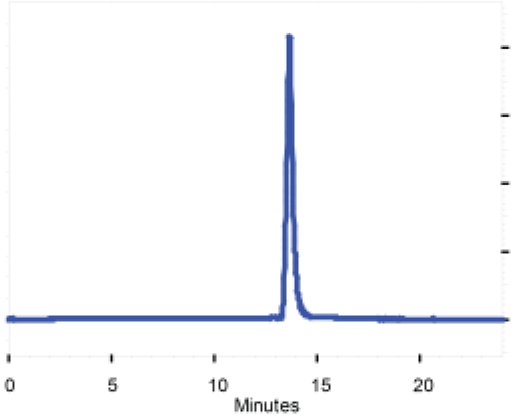
4d



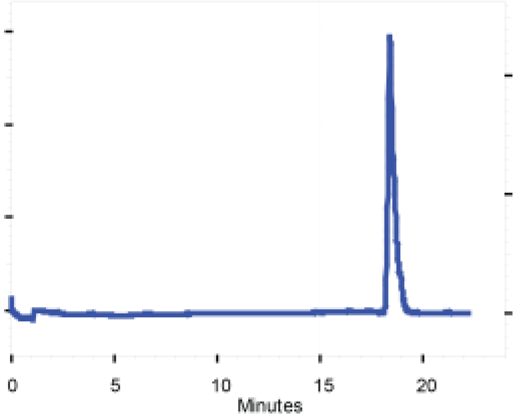
8



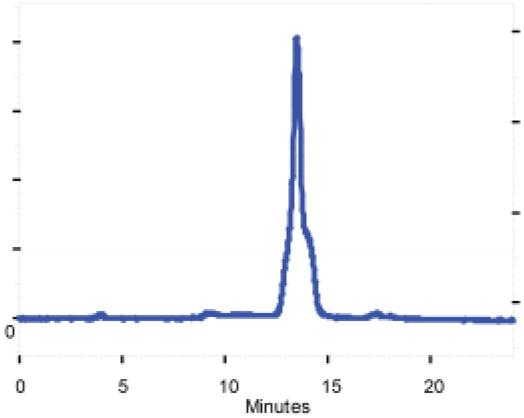
10



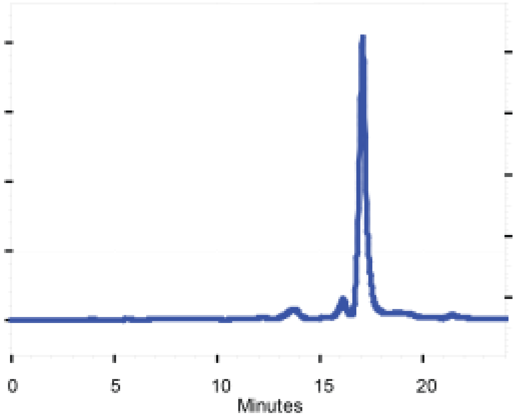
11a



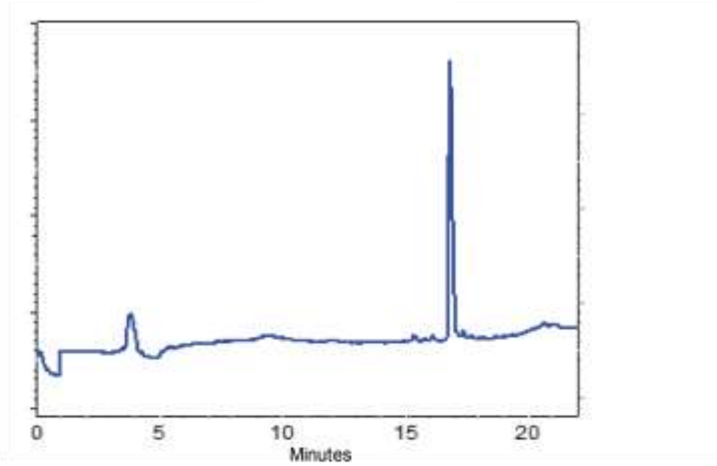
11b



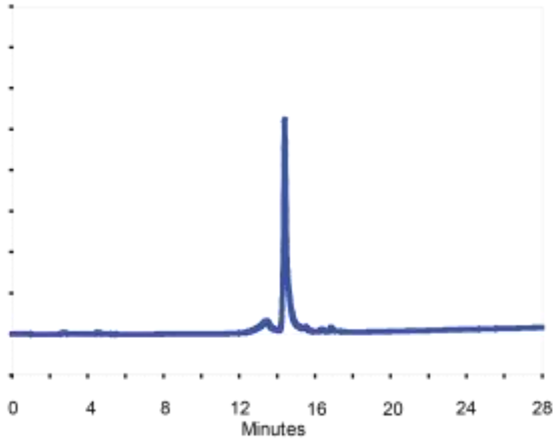
17



13ae

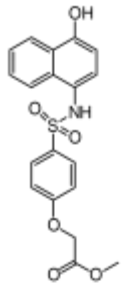


13c

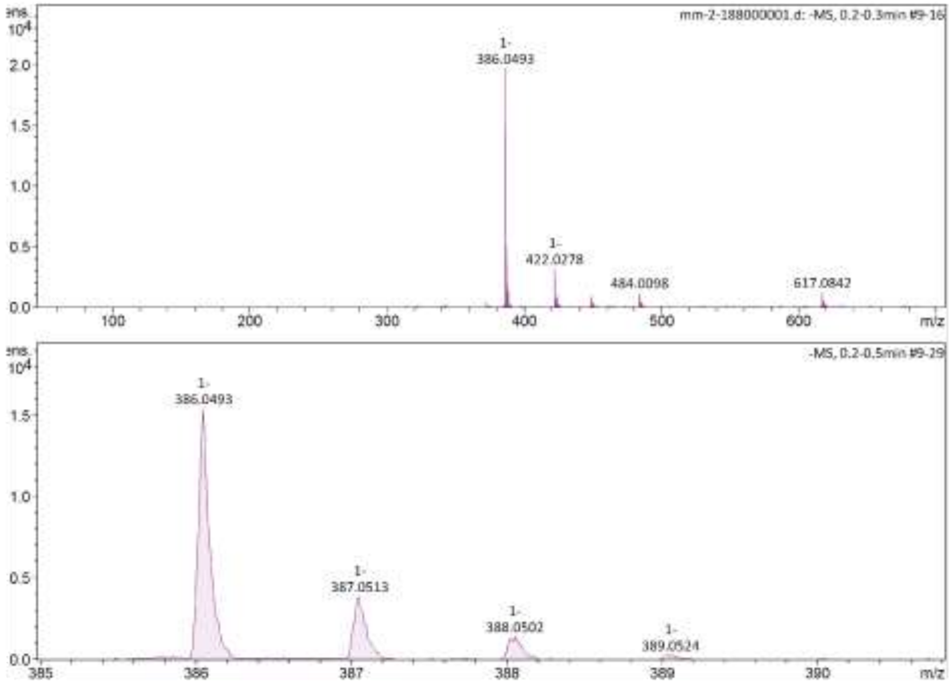


1.4. **ESI-MS**

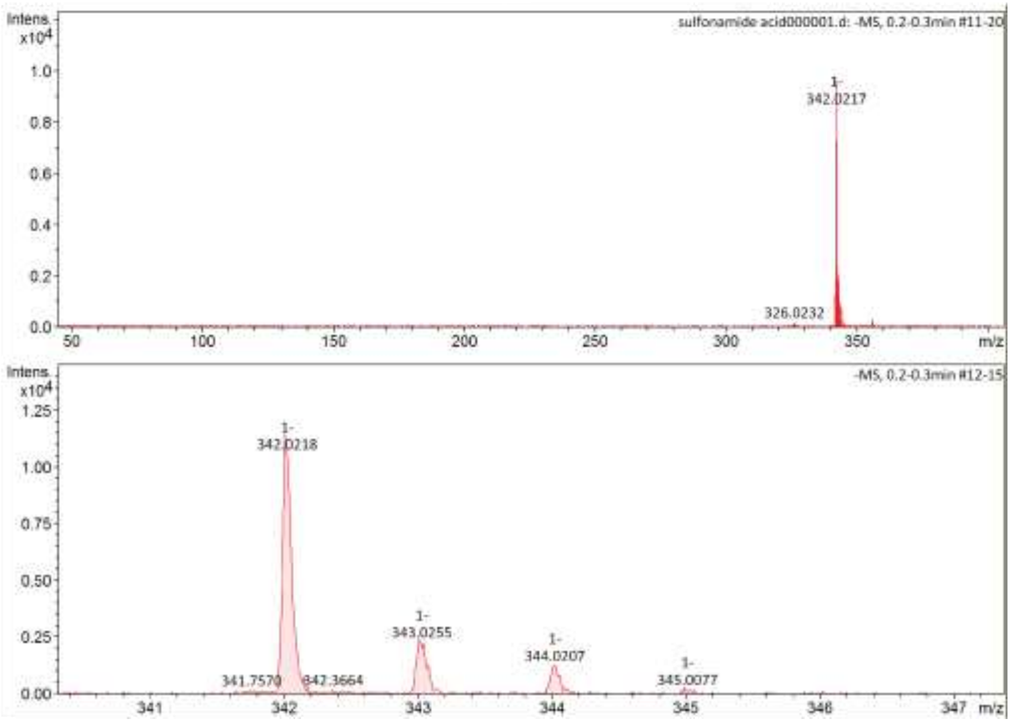
1d

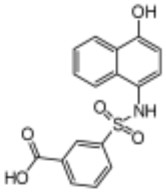


1d



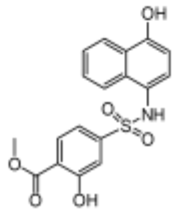
1f



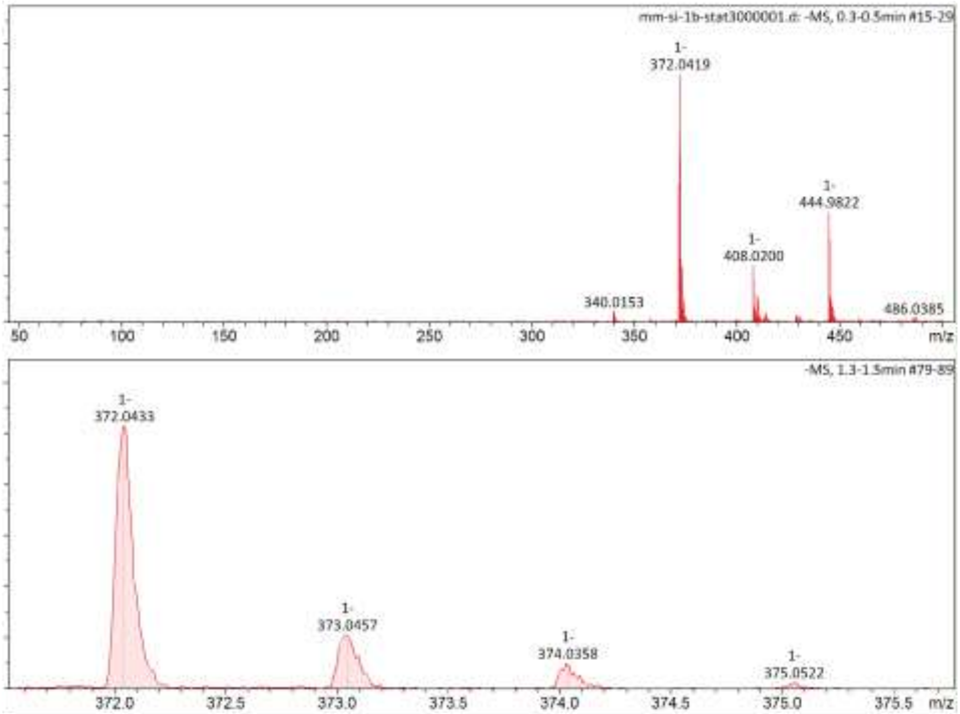


1f

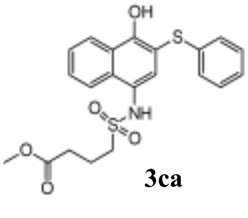
1c


OH
NH
O
S
O
O
O
OH

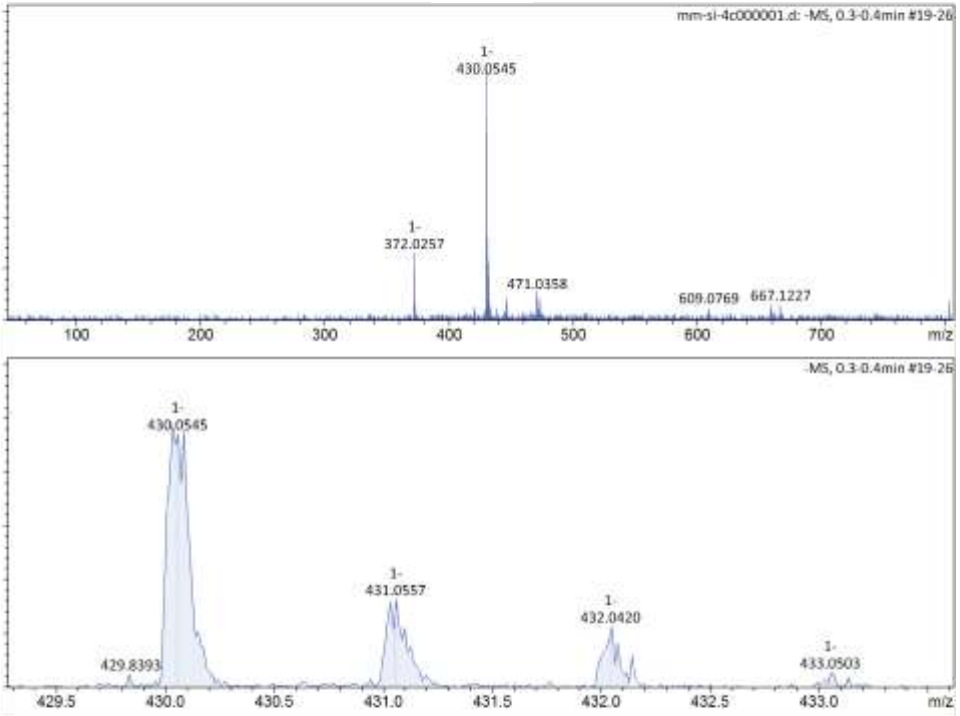
1c


mm-si-1b-stat3000001.d: -MS, 0.3-0.5min #15-29
1-
372.0419
1-
444.9822
1-
408.0200
340.0153
486.0385
50
100
150
200
250
300
350
400
450
m/z
-MS, 1.3-1.5min #79-89
1-
372.0433
1-
373.0457
1-
374.0358
1-
375.0522
372.0
372.5
373.0
373.5
374.0
374.5
375.0
375.5
m/z

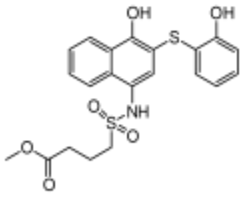
3ca


OH
S
NH
O
S
O
O
O

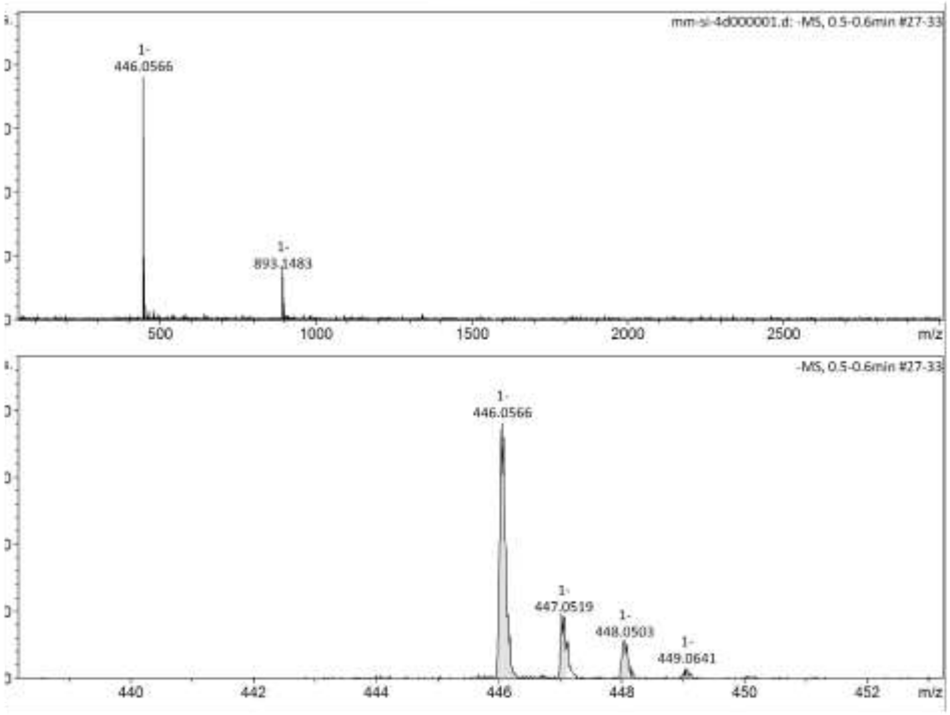
3ca


mm-si-4c000001.d: -MS, 0.3-0.4min #19-26
1-
430.0545
1-
372.0257
471.0358
609.0769
667.1227
100
200
300
400
500
600
700
m/z
-MS, 0.3-0.4min #19-26
1-
430.0545
1-
431.0557
1-
432.0420
1-
433.0503
429.8393
429.5
430.0
430.5
431.0
431.5
432.0
432.5
433.0
m/z

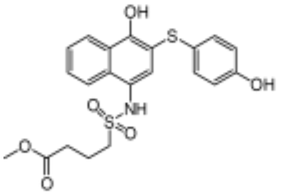
3cb



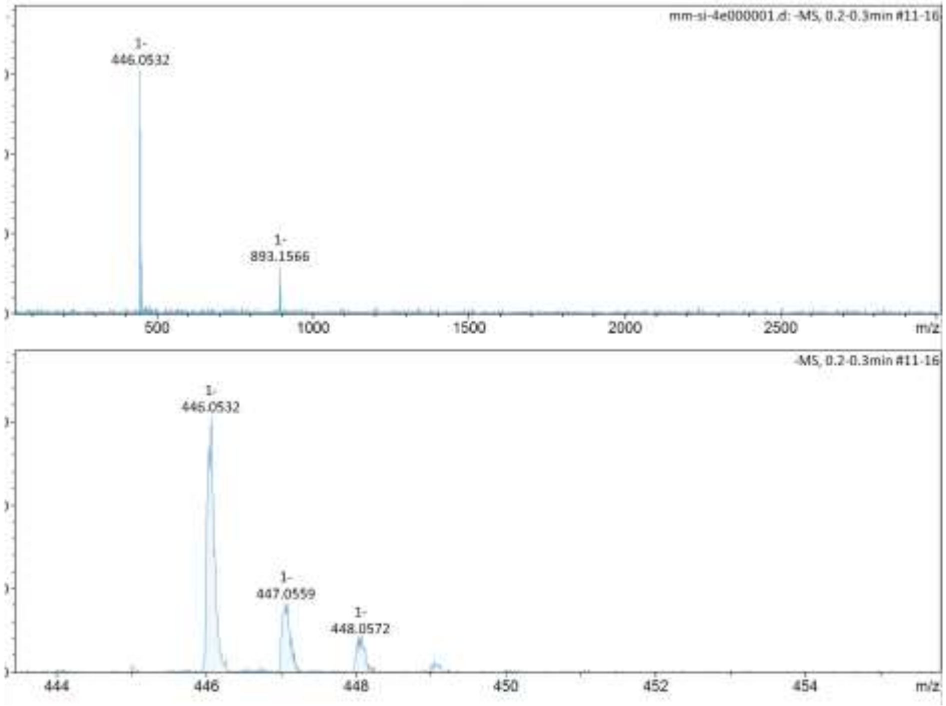
3cb



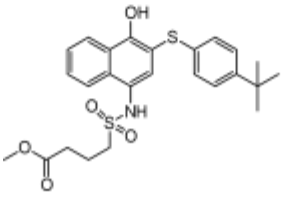
3cc



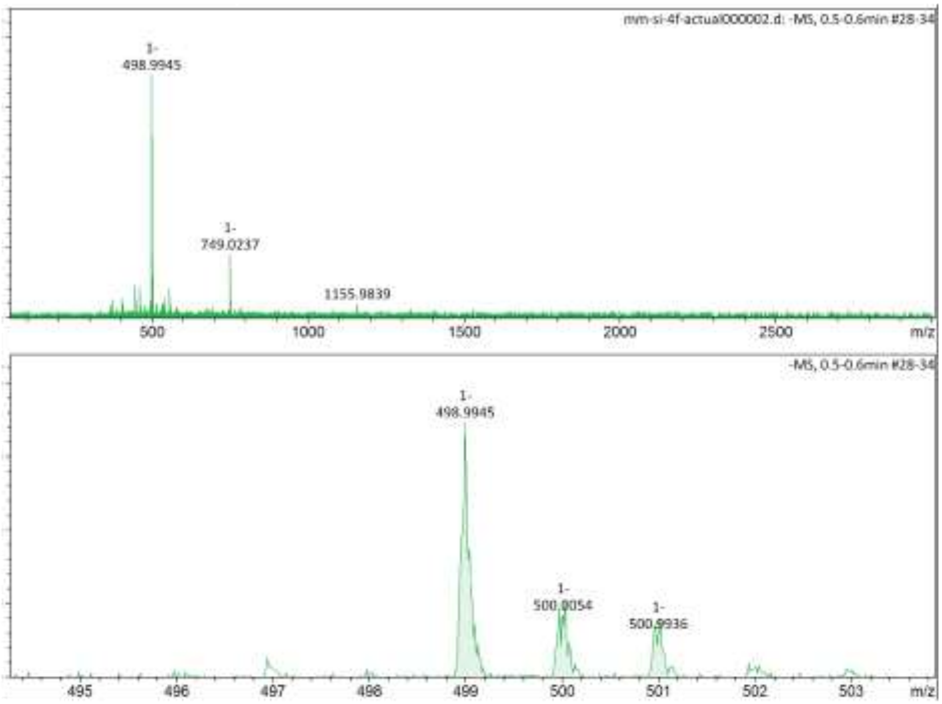
3cc



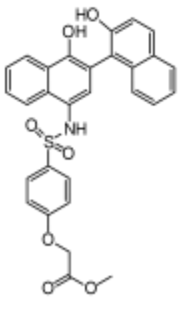
3cd


OH
S
NH
O
S
O
O
O

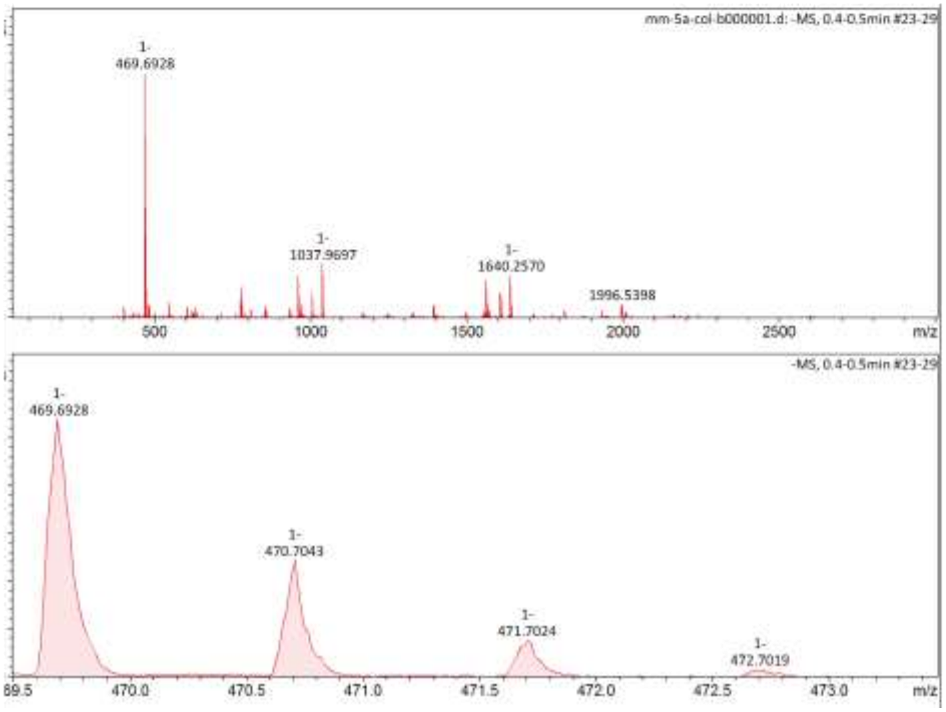
3cd


mm-si-4f-actual000002.d: -MS, 0.5-0.6min #28-34
1-
498.9945
1-
749.0237
1155.9839
500
1000
1500
2000
2500
m/z
-MS, 0.5-0.6min #28-34
1-
498.9945
1-
500.0054
1-
500.9936
495
496
497
498
499
500
501
502
503
m/z

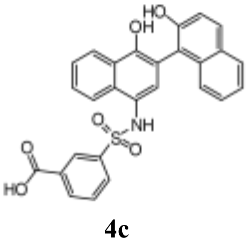
4b


HO
OH
NH
O
S
O
O
O
O

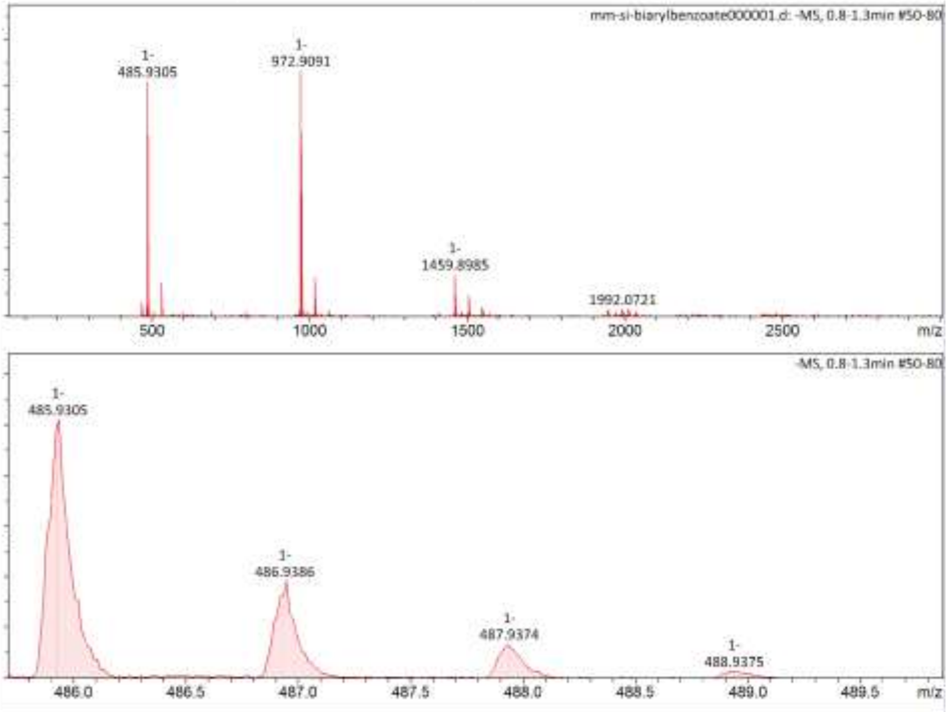
4b


mm-5a-col-b000001.d: -MS, 0.4-0.5min #23-29
1-
469.6928
1-
1037.9697
1-
1640.2570
1996.5398
500
1000
1500
2000
2500
m/z
-MS, 0.4-0.5min #23-29
1-
469.6928
1-
470.7043
1-
471.7024
1-
472.7019
89.5
470.0
470.5
471.0
471.5
472.0
472.5
473.0
m/z

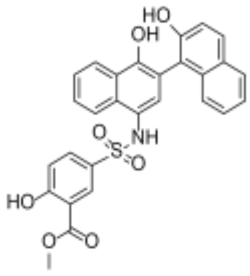
4c


HO
OH
NH
O
S
O
O
HO

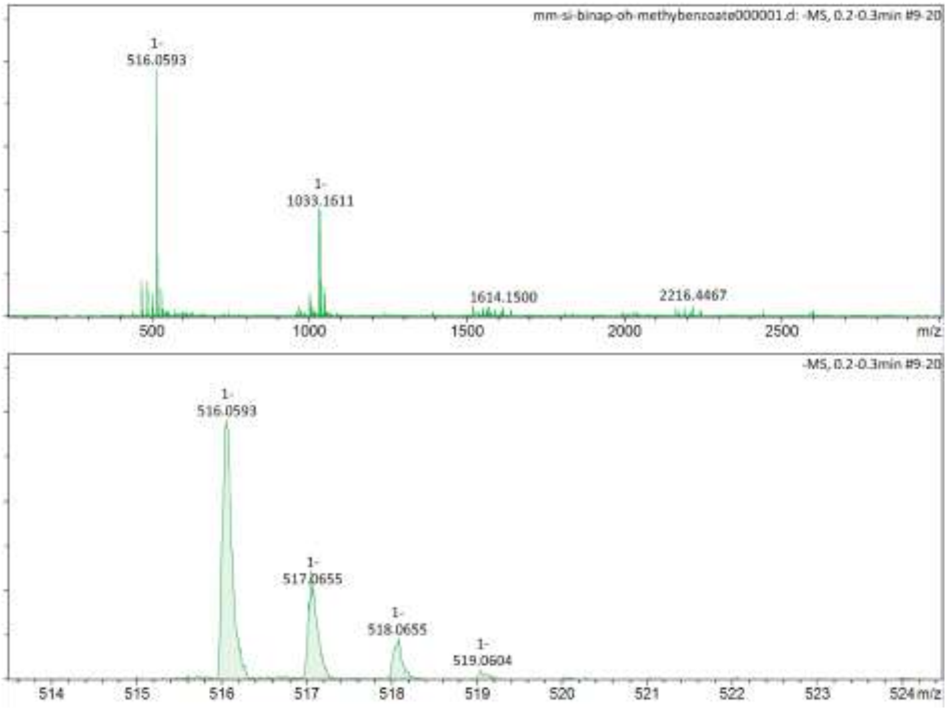
4c


mm-si-biarylbenzoate000001.d: -MS, 0.8-1.3min #50-80
1-
485.9305
1-
972.9091
1-
1459.8985
1992.0721
500
1000
1500
2000
2500
m/z
-MS, 0.8-1.3min #50-80
1-
485.9305
1-
486.9386
1-
487.9374
1-
488.9375
486.0
486.5
487.0
487.5
488.0
488.5
489.0
489.5
m/z

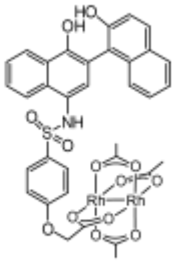
4d


HO
OH
O
S
NH
O
HO
O
O

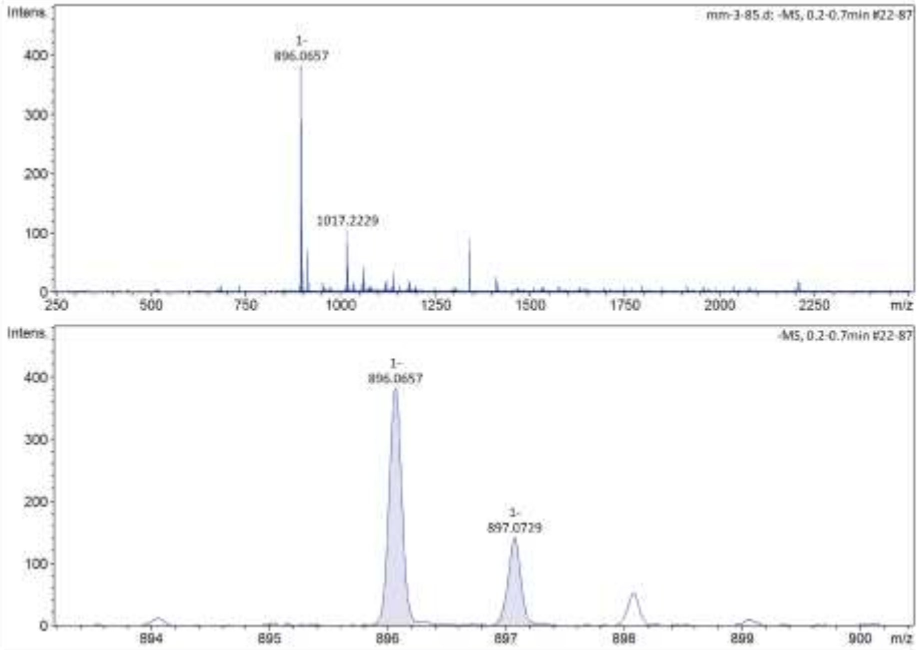
4d


mm-si-binap-oh-methybenzoate000001.d: -MS, 0.2-0.3min #9-20
1-
516.0593
1-
1033.1611
1614.1500
2216.4467
500
1000
1500
2000
2500
m/z
-MS, 0.2-0.3min #9-20
1-
516.0593
1-
517.0655
1-
518.0655
1-
519.0604
514
515
516
517
518
519
520
521
522
523
524
m/z

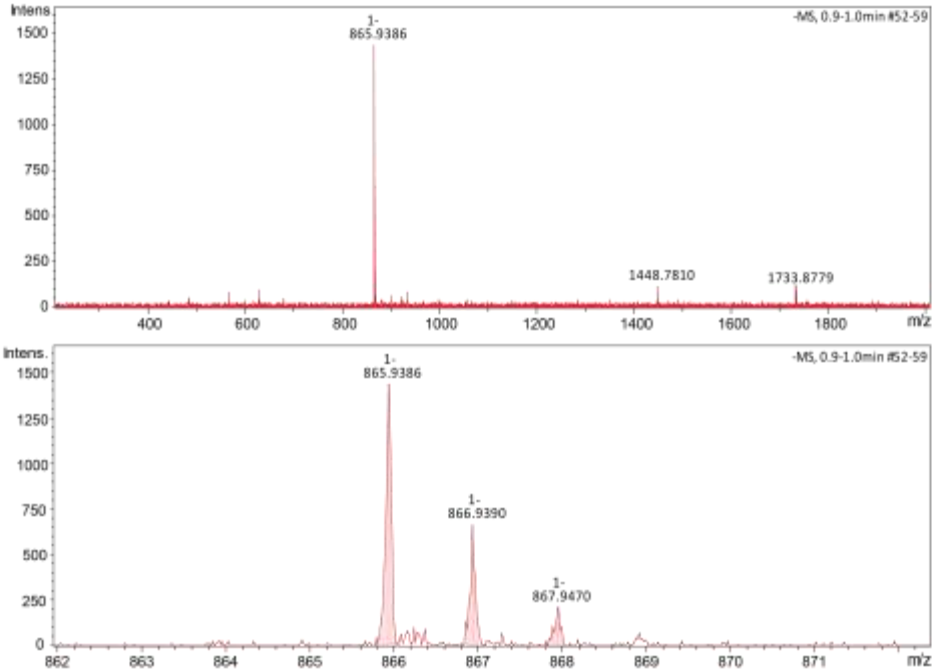
13b

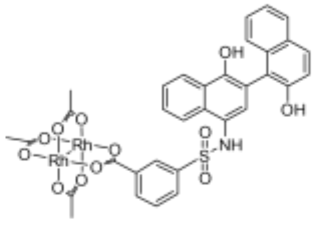


13b



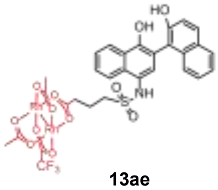
13c



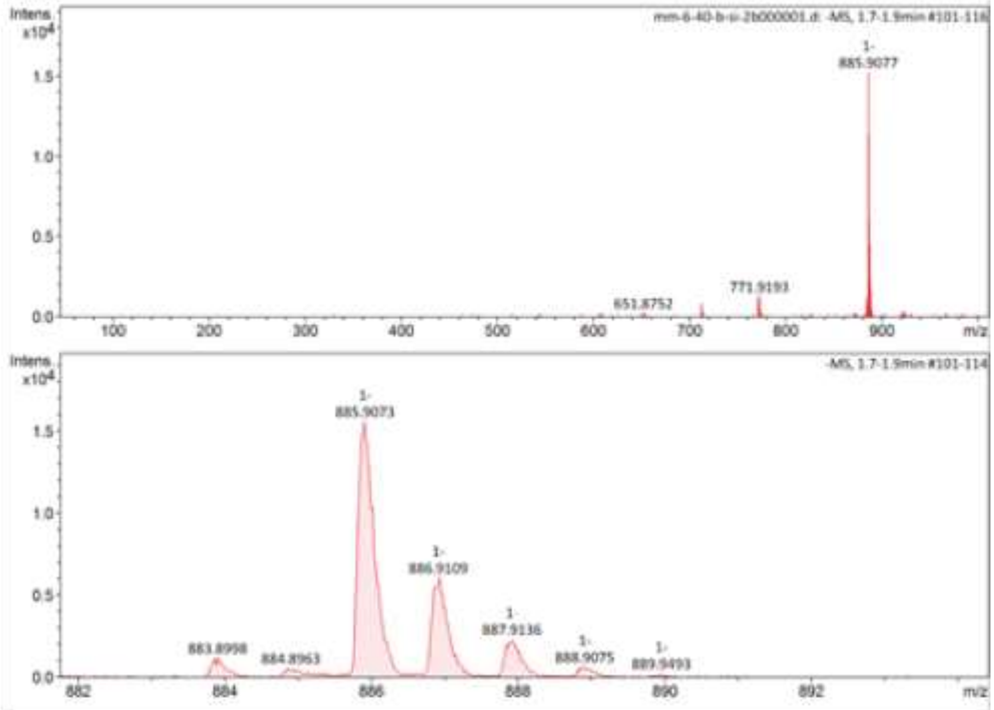


13c

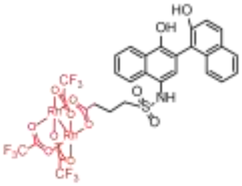
13ae



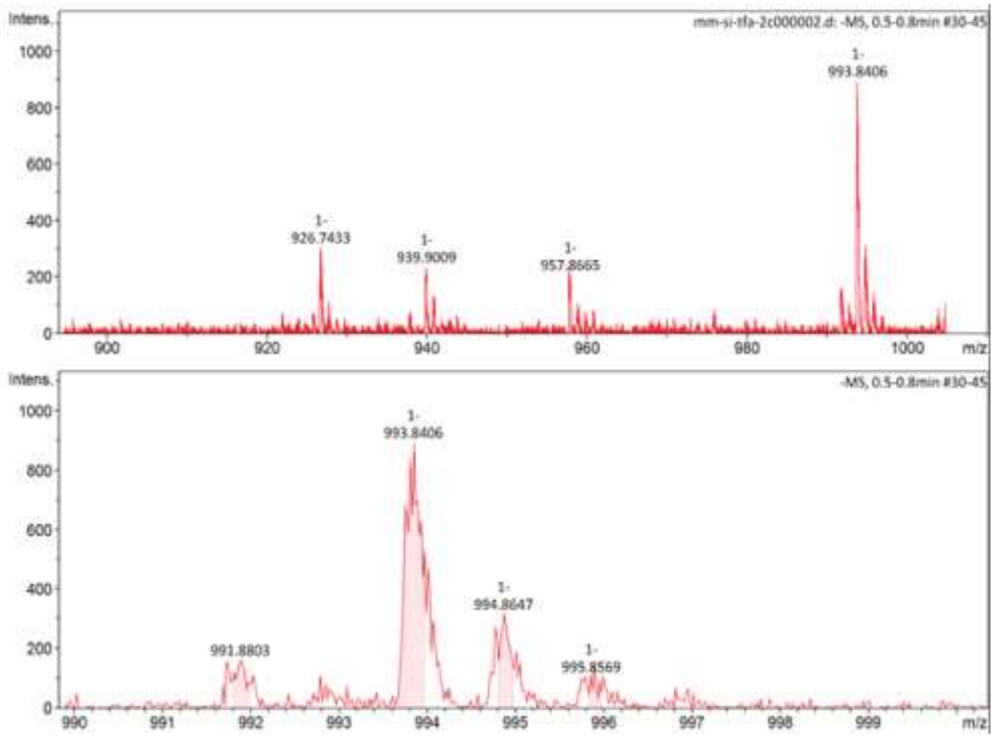
13ae



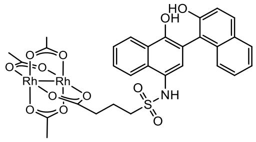
13af



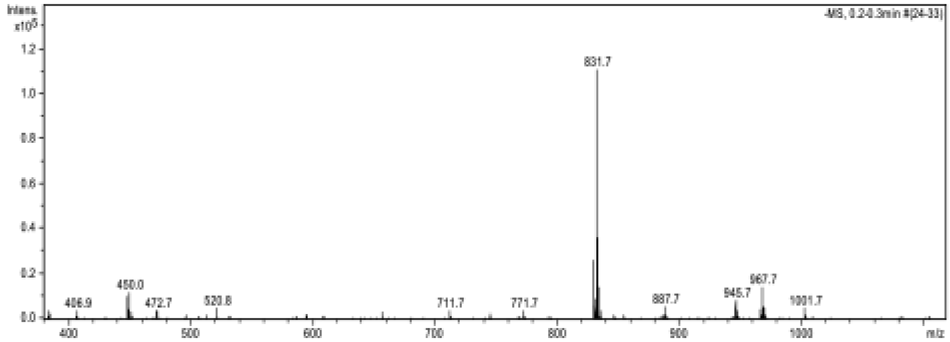
13af



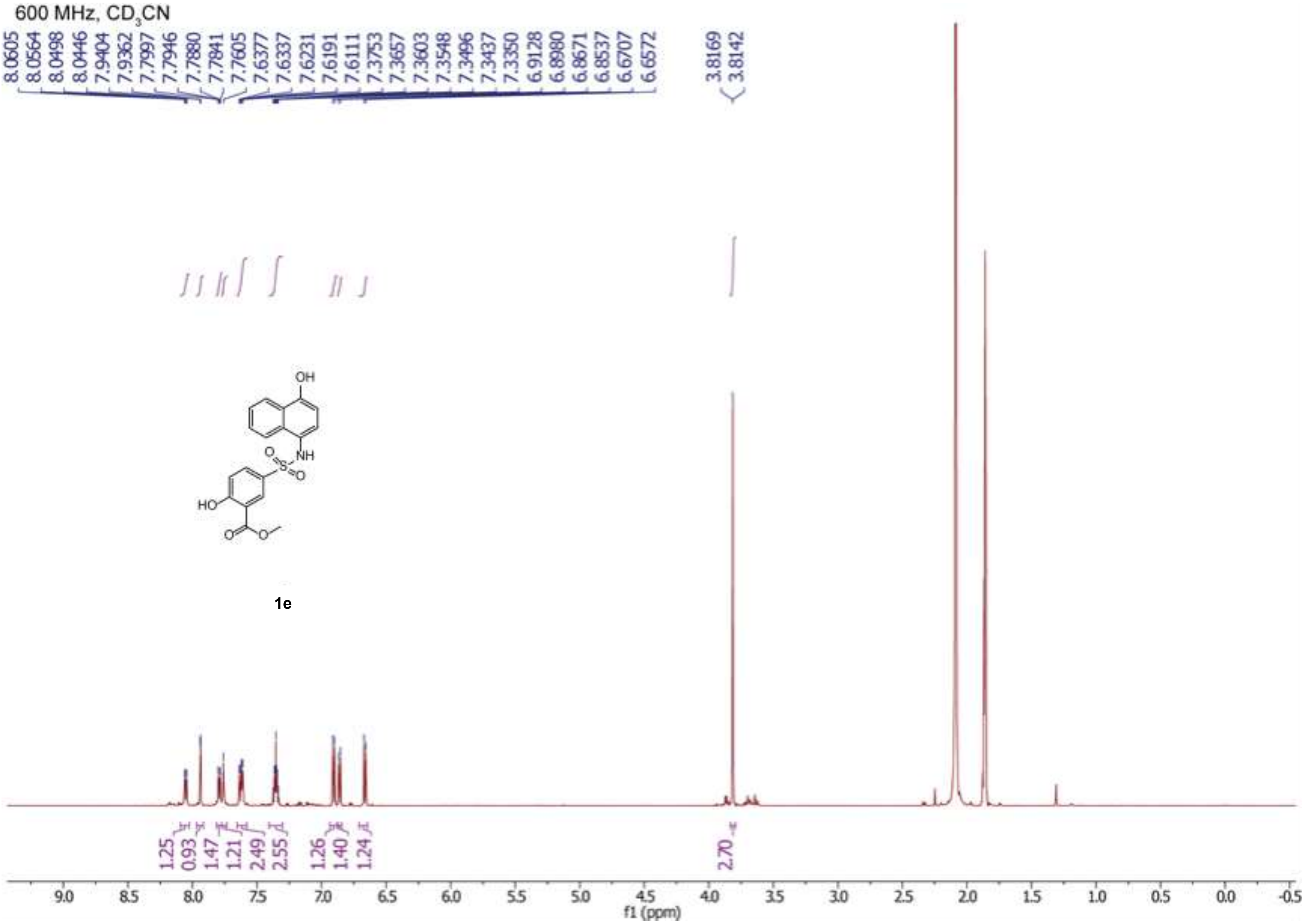
13aa

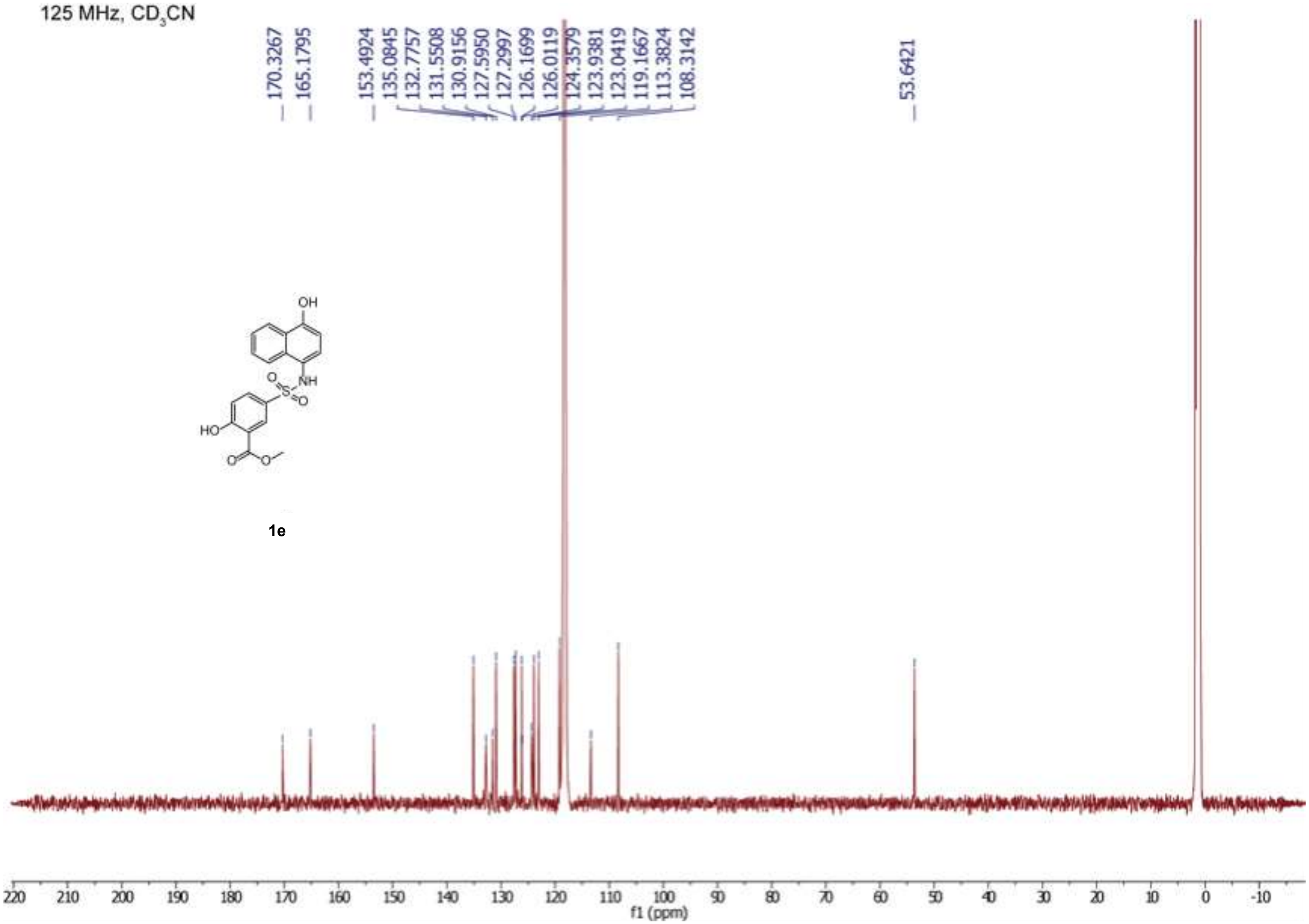

HO
OH
Rh
Rh
O
S
NH

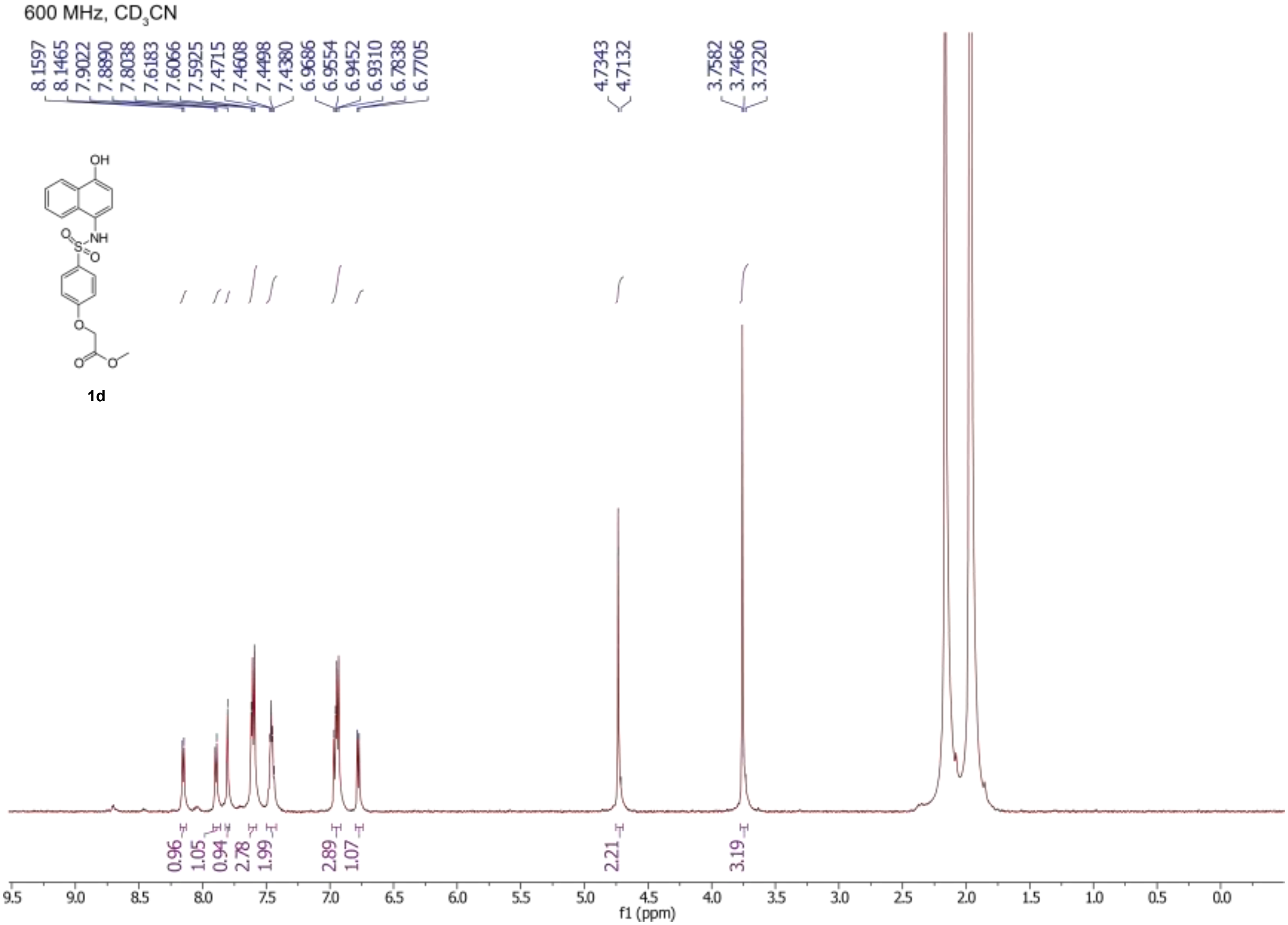
13aa

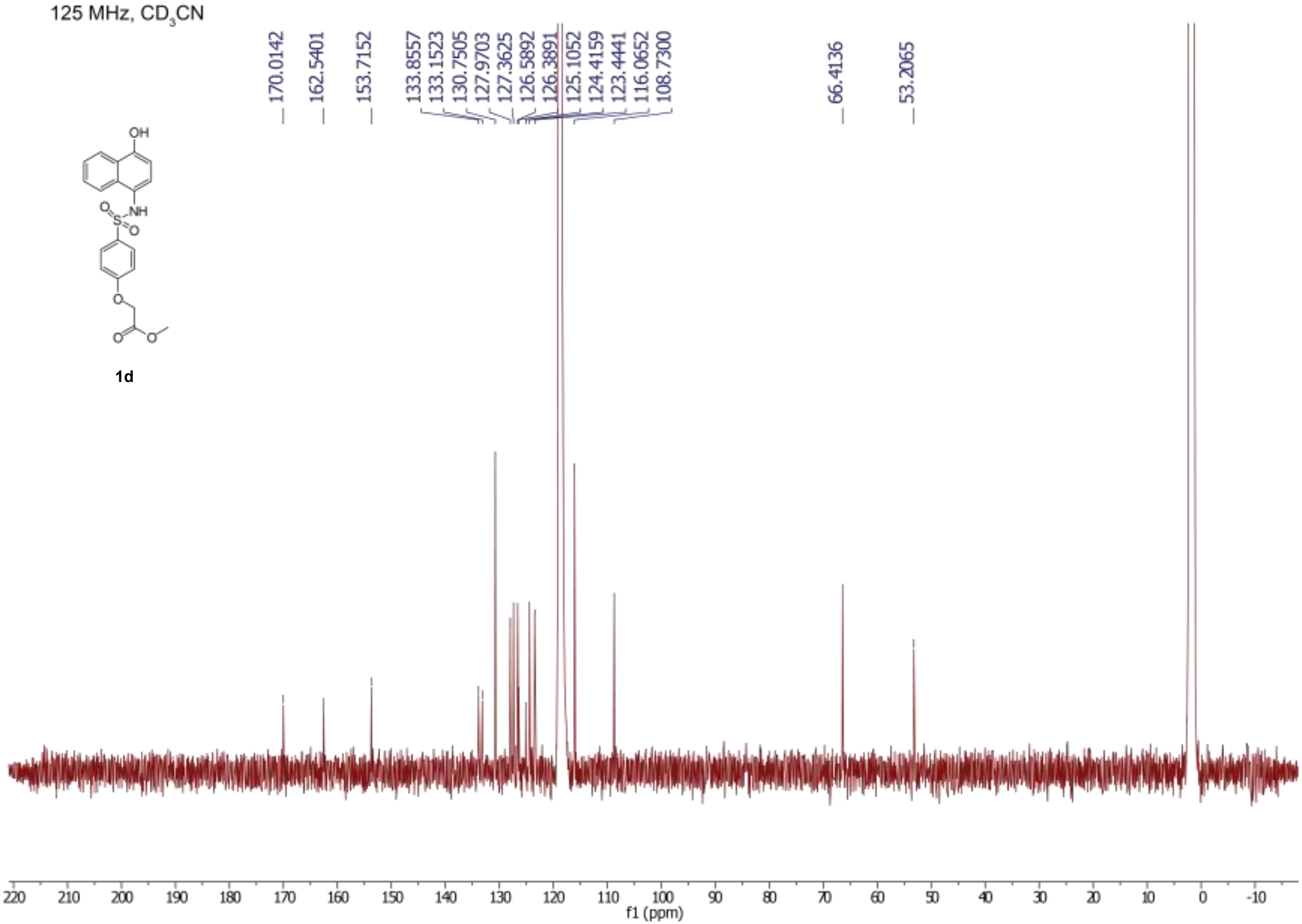

Intens.
x10^5
1.2
1.0
0.8
0.6
0.4
0.2
0.0
-MS, 0.2-0.3min #(24-33)
831.7
406.9
450.0
472.7
520.8
711.7
771.7
887.7
945.7
967.7
1001.7
400
500
600
700
800
900
1000
m/z

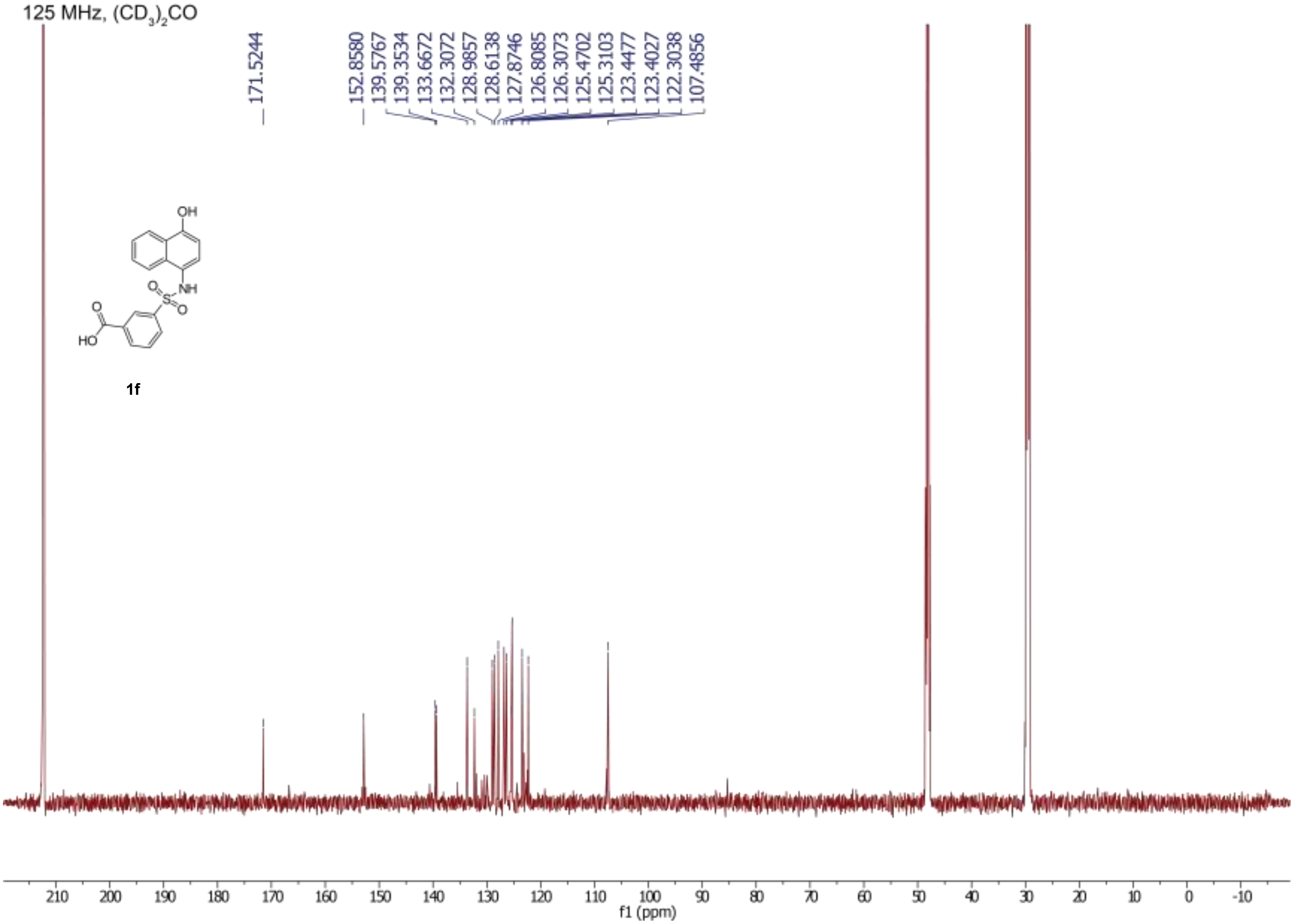
1.5. **NMR Spectrum**

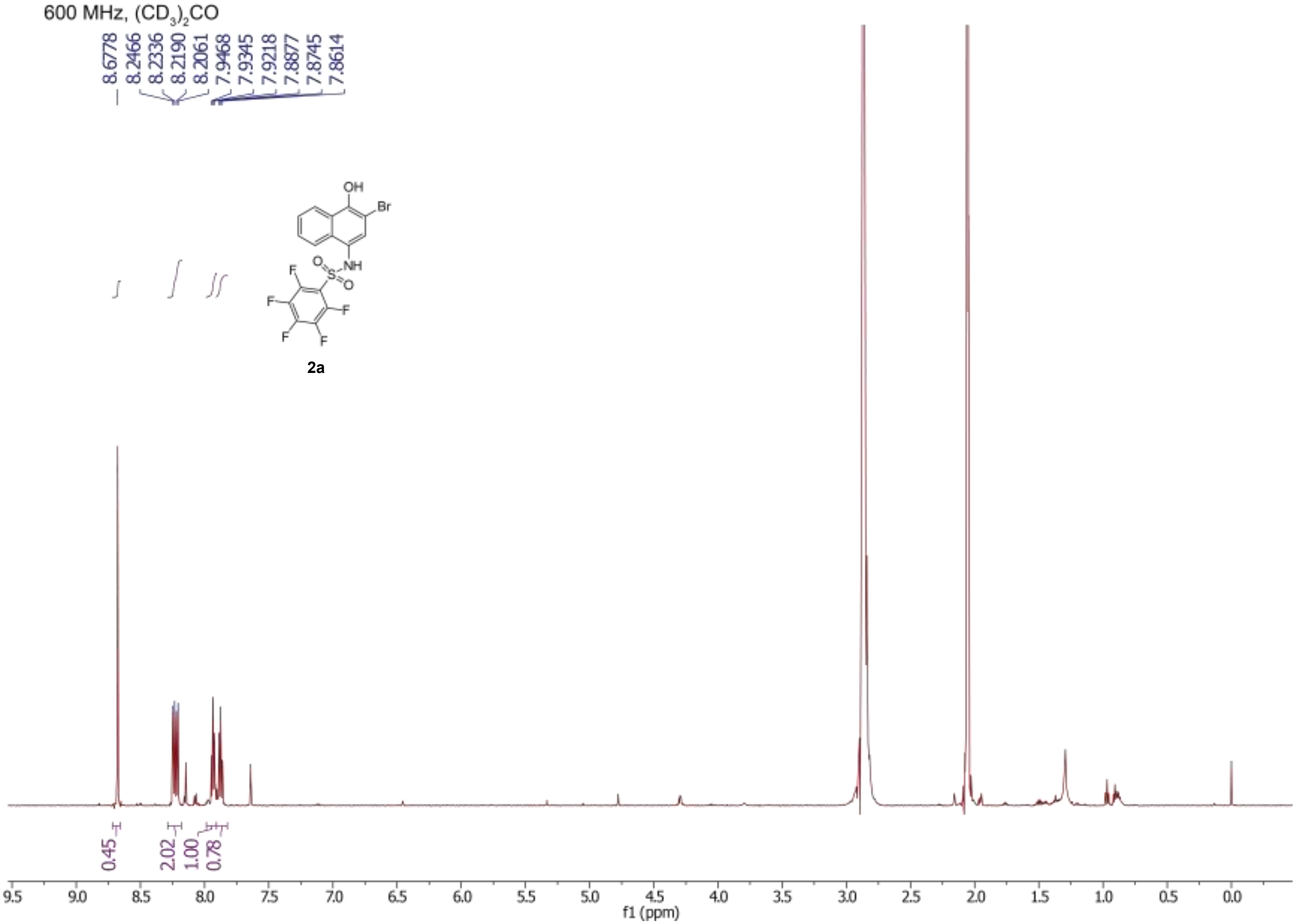

600 MHz, CD_3CN
8.0605
8.0564
8.0498
8.0446
7.9404
7.9362
7.7997
7.7946
7.7880
7.7841
7.7605
7.6377
7.6337
7.6231
7.6191
7.6111
7.3753
7.3657
7.3603
7.3548
7.3496
7.3437
7.3350
6.9128
6.8980
6.8671
6.8537
6.6707
6.6572
3.8169
3.8142
OH
NH
O
S
O
HO
O
O
1e
1.25
0.93
1.47
1.21
2.49
2.55
1.26
1.40
1.24
2.70
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

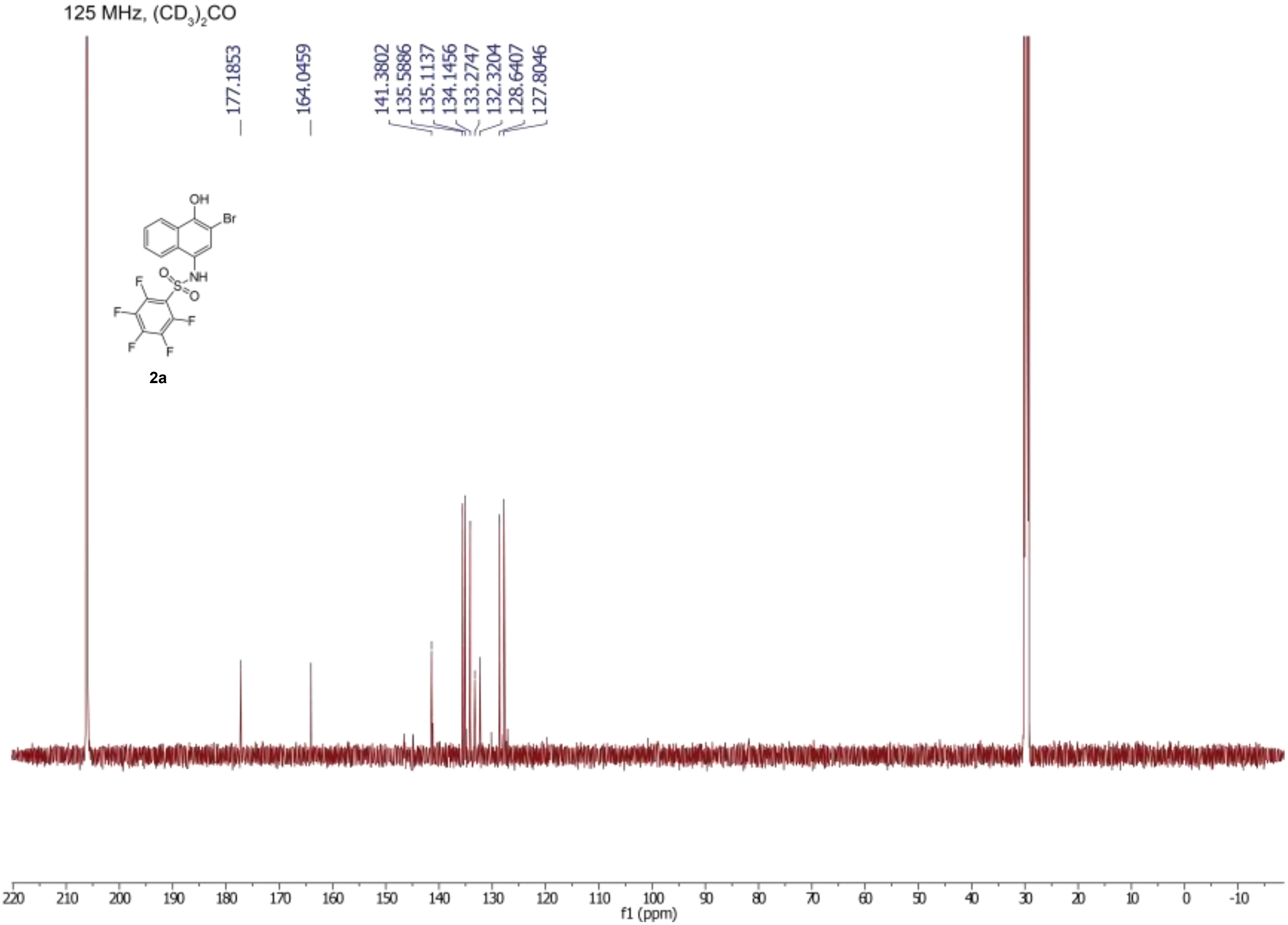

125 MHz, CD_3CN
170.3267
165.1795
153.4924
135.0845
132.7757
131.5508
130.9156
127.5950
127.2997
126.1699
126.0119
124.3579
123.9381
123.0419
119.1667
113.3824
108.3142
53.6421
OH
NH
O
S
O
HO
O
O
1e
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


600 MHz, CD_3CN
8.1597
8.1465
7.9022
7.8890
7.8038
7.6183
7.6066
7.5925
7.4715
7.4608
7.4498
7.4380
6.9686
6.9554
6.9452
6.9310
6.7838
6.7705
4.7343
4.7132
3.7582
3.7466
3.7320
OH
NH
S
O
O
O
O
O
1d
0.96
1.05
0.94
2.78
1.99
2.89
1.07
2.21
3.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

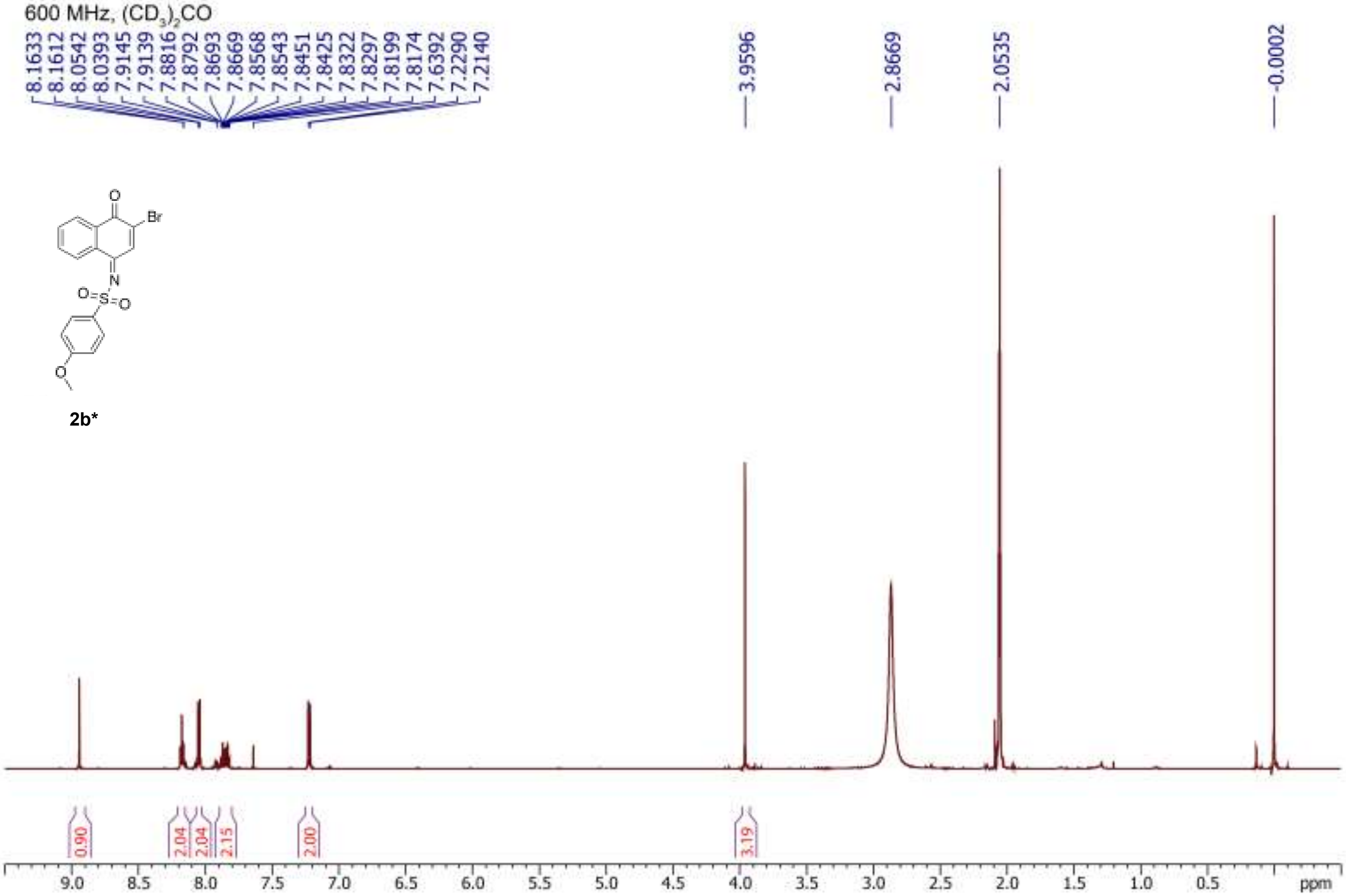

125 MHz, CD_3CN
170.0142
162.5401
153.7152
133.8557
133.1523
130.7505
127.9703
127.3625
126.5892
126.3891
125.1052
124.4159
123.4441
116.0652
108.7300
66.4136
53.2065
OH
NH
O
S
O
O
O
O
1d
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

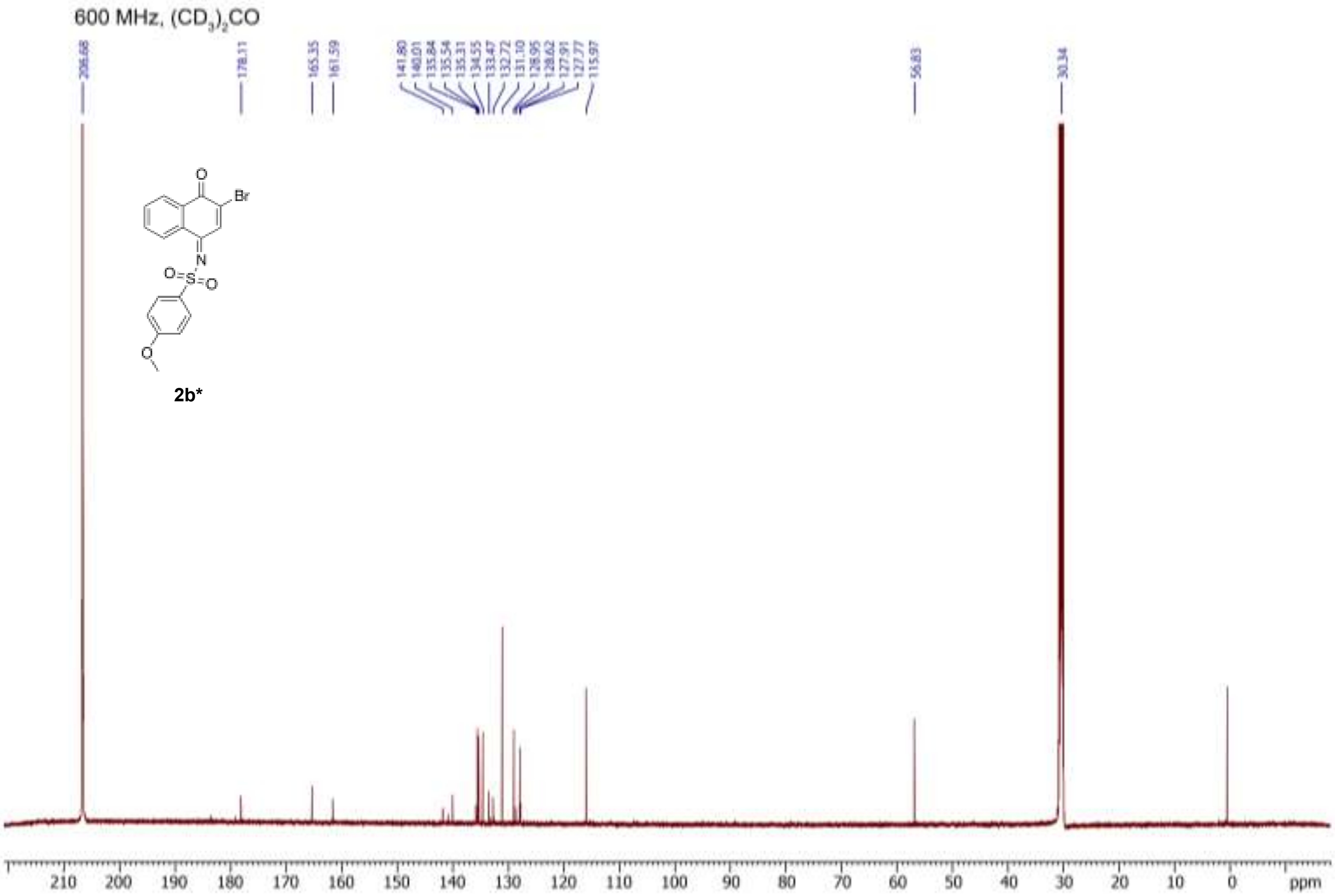

125 MHz, $(CD_3)_2CO$
171.5244
152.8580
139.5767
139.3534
133.6672
132.3072
128.9857
128.6138
127.8746
126.8085
126.3073
125.4702
125.3103
123.4477
123.4027
122.3038
107.4856
OH
NH
O
S
O
O
HO
1f
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

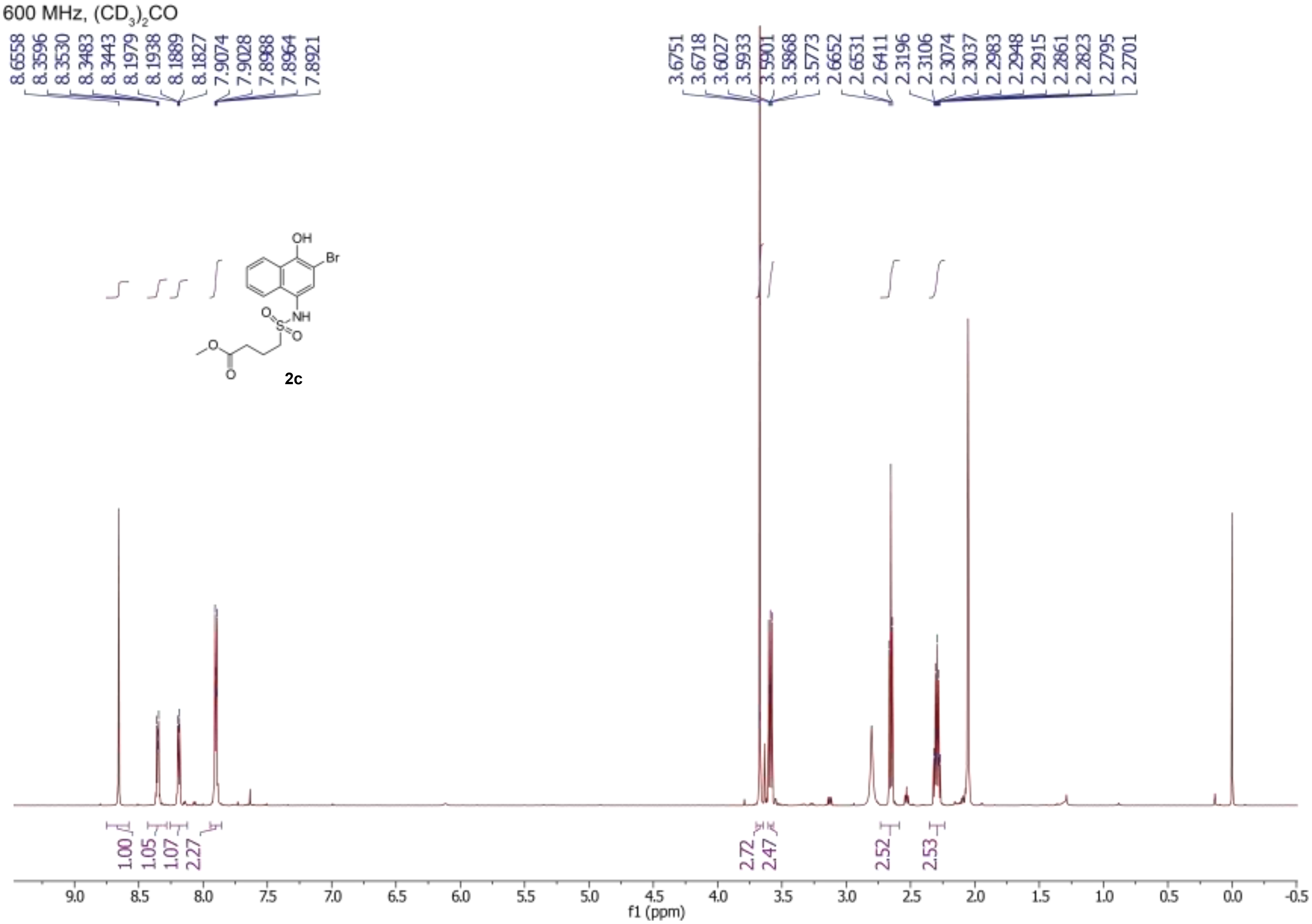

600 MHz, $(CD_3)_2CO$
8.6778
8.2466
8.2336
8.2190
8.2061
7.9468
7.9345
7.9218
7.8877
7.8745
7.8614
OH
Br
NH
O
S
O
F
F
F
F
F
2a
0.45
2.02
1.00
0.78
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

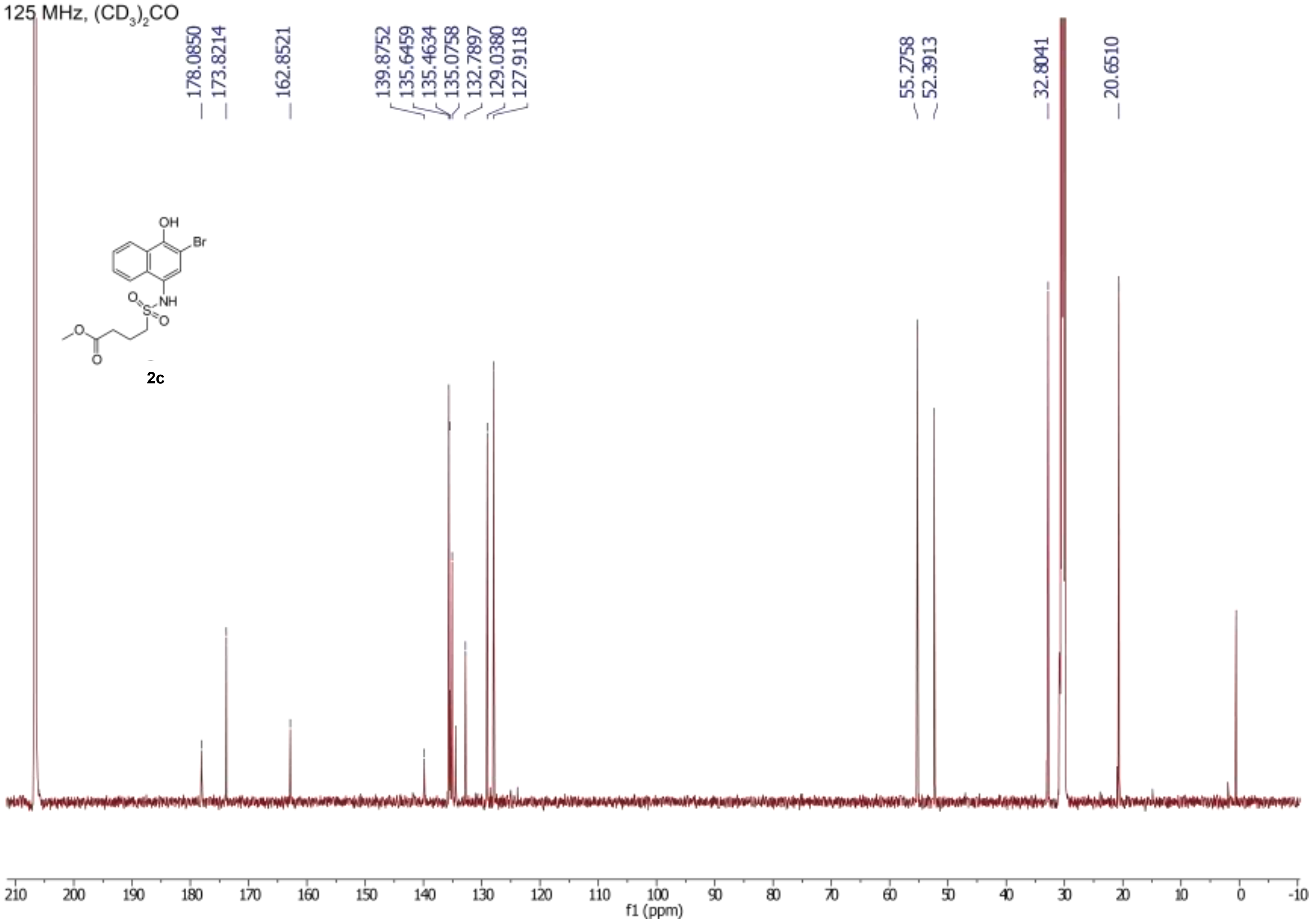

125 MHz, $(CD_3)_2CO$
177.1853
164.0459
141.3802
135.5886
135.1137
134.1456
133.2747
132.3204
128.6407
127.8046
OH
Br
NH
O
S
O
F
F
F
F
F
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

2a

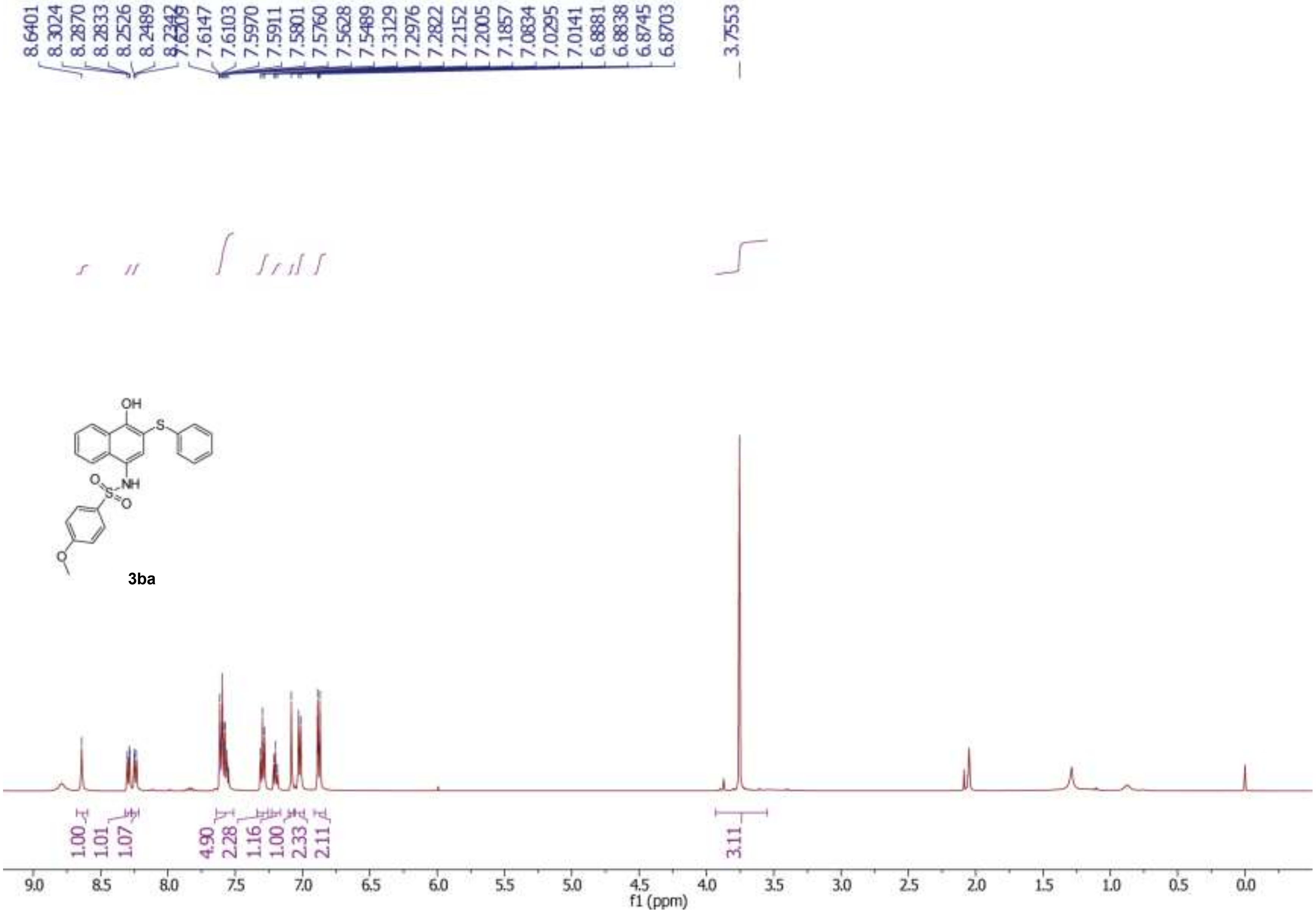

600 MHz, (CD3)2CO
8.1633
8.1612
8.0542
8.0393
7.9145
7.9139
7.8816
7.8792
7.8693
7.8669
7.8568
7.8543
7.8451
7.8425
7.8322
7.8297
7.8199
7.8174
7.6392
7.2290
7.2140
3.9596
2.8669
2.0535
-0.0002
O
Br
N
O
S
O
O
2b*
0.90
2.04
2.04
2.15
2.00
3.19
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


600 MHz, $(CD_3)_2CO$
206.68
178.11
165.35
161.59
141.80
140.01
135.84
135.54
135.31
134.55
133.47
132.72
131.10
128.95
128.62
127.91
127.77
115.97
56.83
30.34
O
Br
N
O=S=O
O
2b*
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

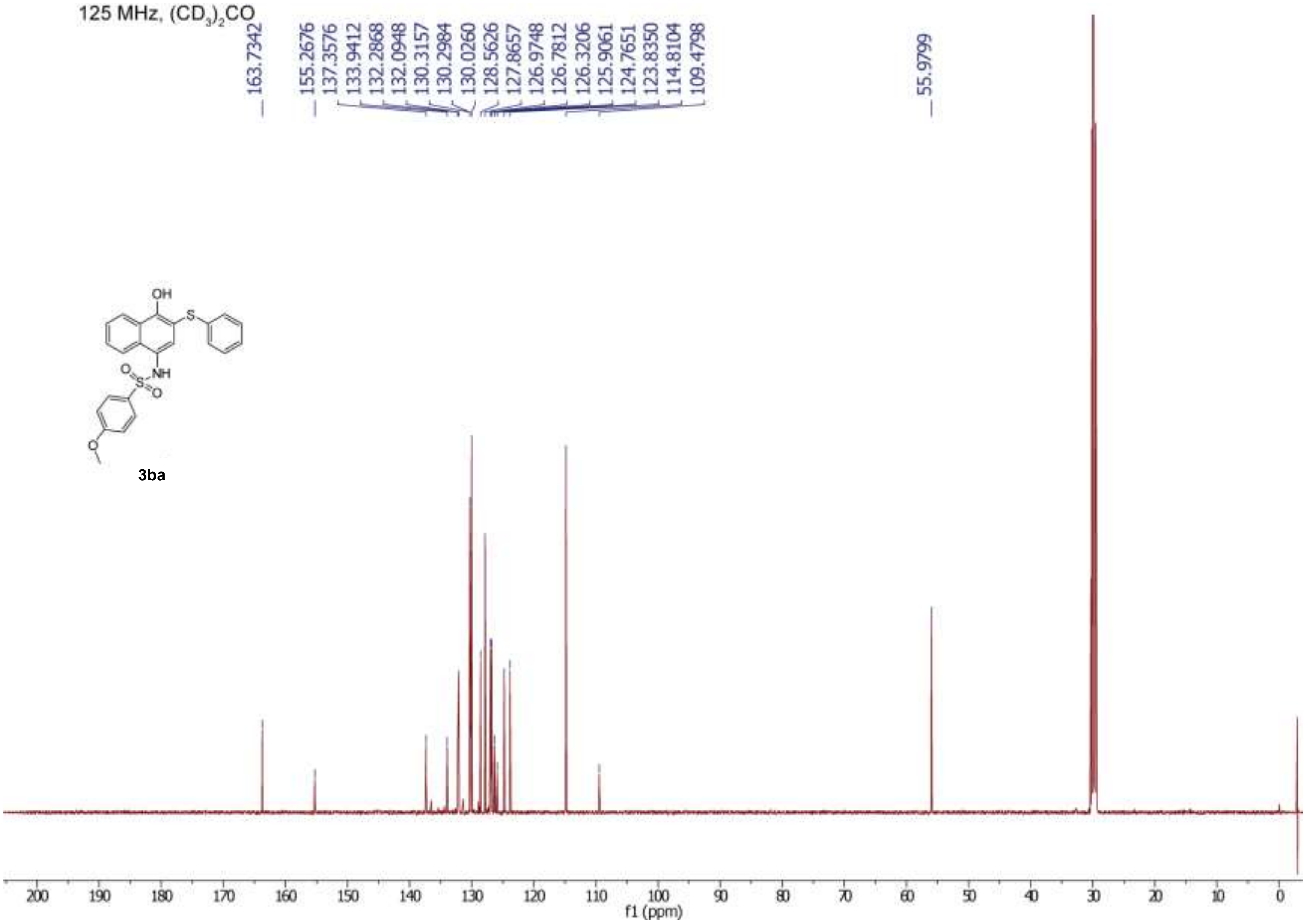

600 MHz, $(CD_3)_2CO$
8.6558
8.3596
8.3530
8.3483
8.3443
8.1979
8.1938
8.1889
8.1827
7.9074
7.9028
7.8988
7.8964
7.8921
3.6751
3.6718
3.6027
3.5933
3.5901
3.5868
3.5773
2.6652
2.6531
2.6411
2.3196
2.3106
2.3074
2.3037
2.2983
2.2948
2.2915
2.2861
2.2823
2.2795
2.2701
OH
Br
NH
O
S
O
O
O
2c
1.00
1.05
1.07
2.27
2.72
2.47
2.52
2.53
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

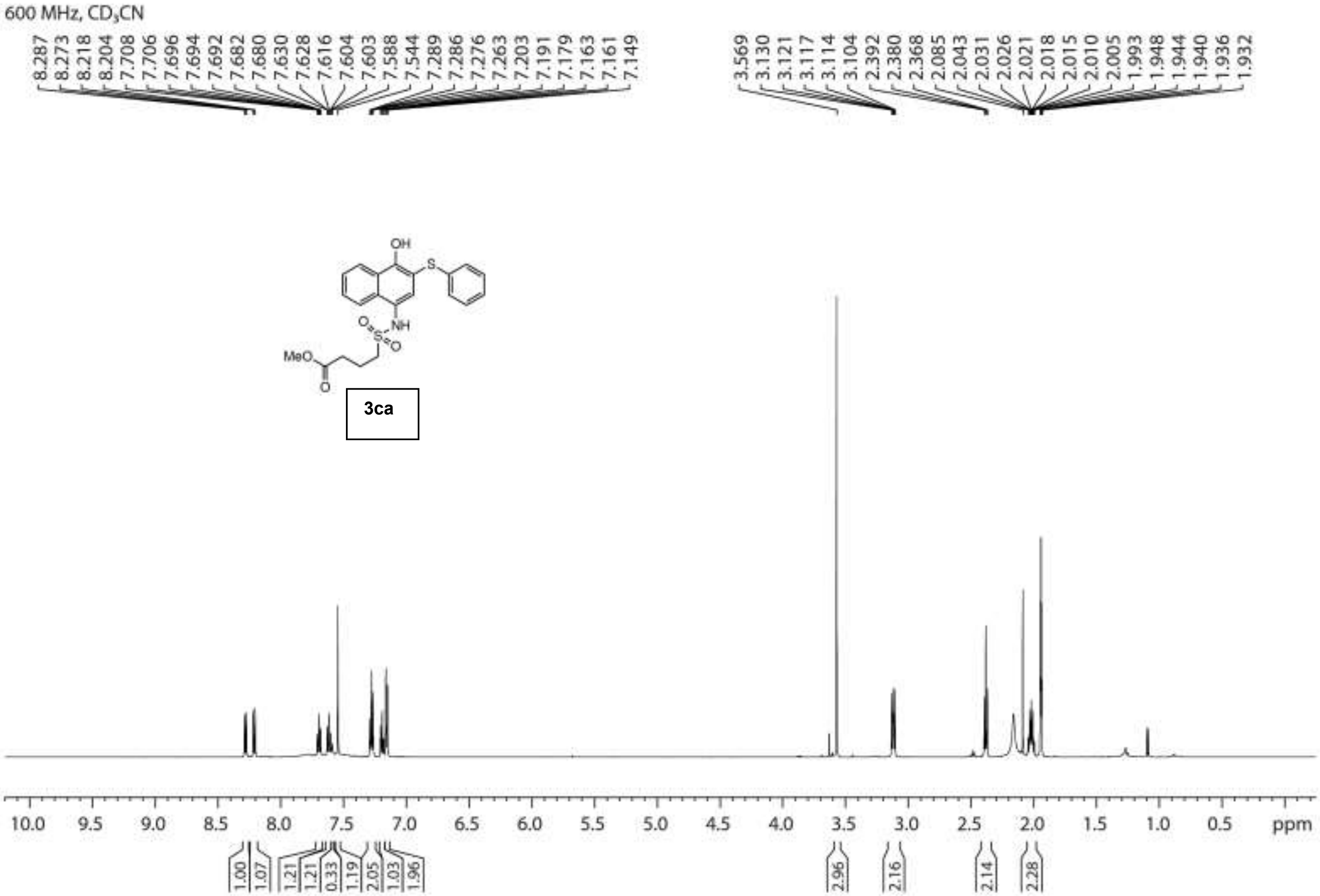

125 MHz, (CD$_3$)$_2$CO
178.0850
173.8214
162.8521
139.8752
135.6459
135.4634
135.0758
132.7897
129.0380
127.9118
55.2758
52.3913
32.8041
20.6510
OH
Br
NH
O
S
O
O
O
2c
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

600 MHz, $(CD_3)_2CO$

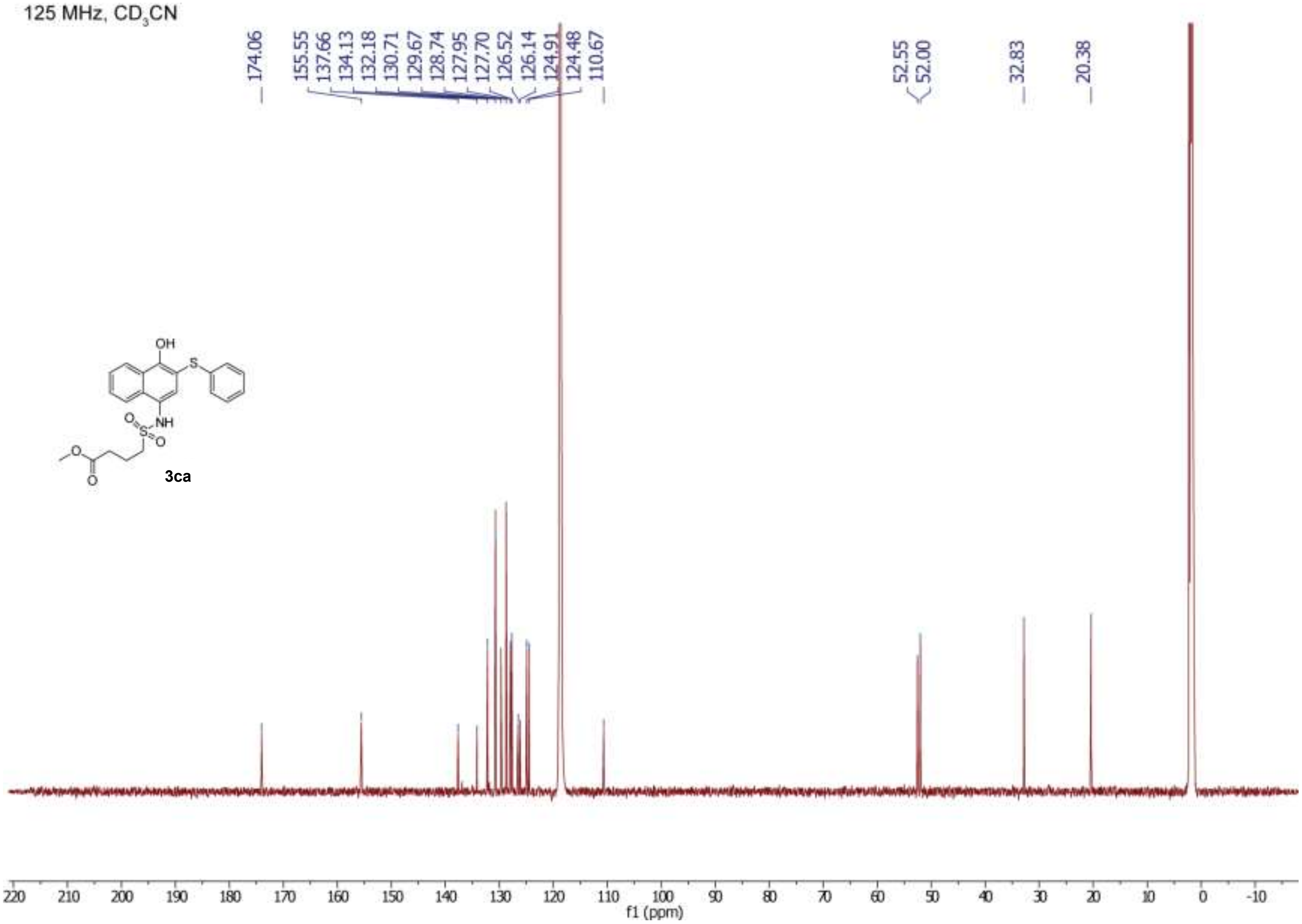


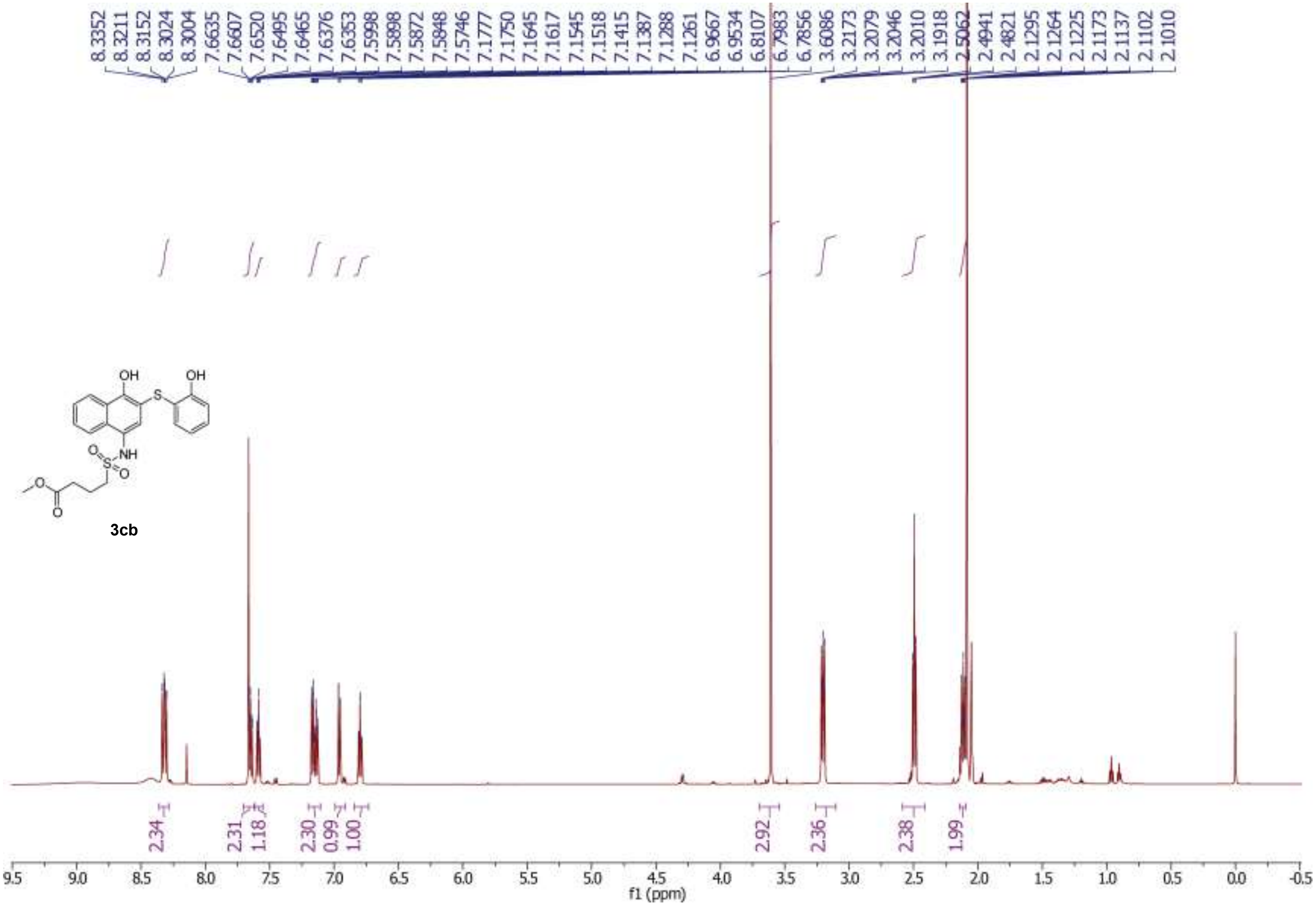
3ba

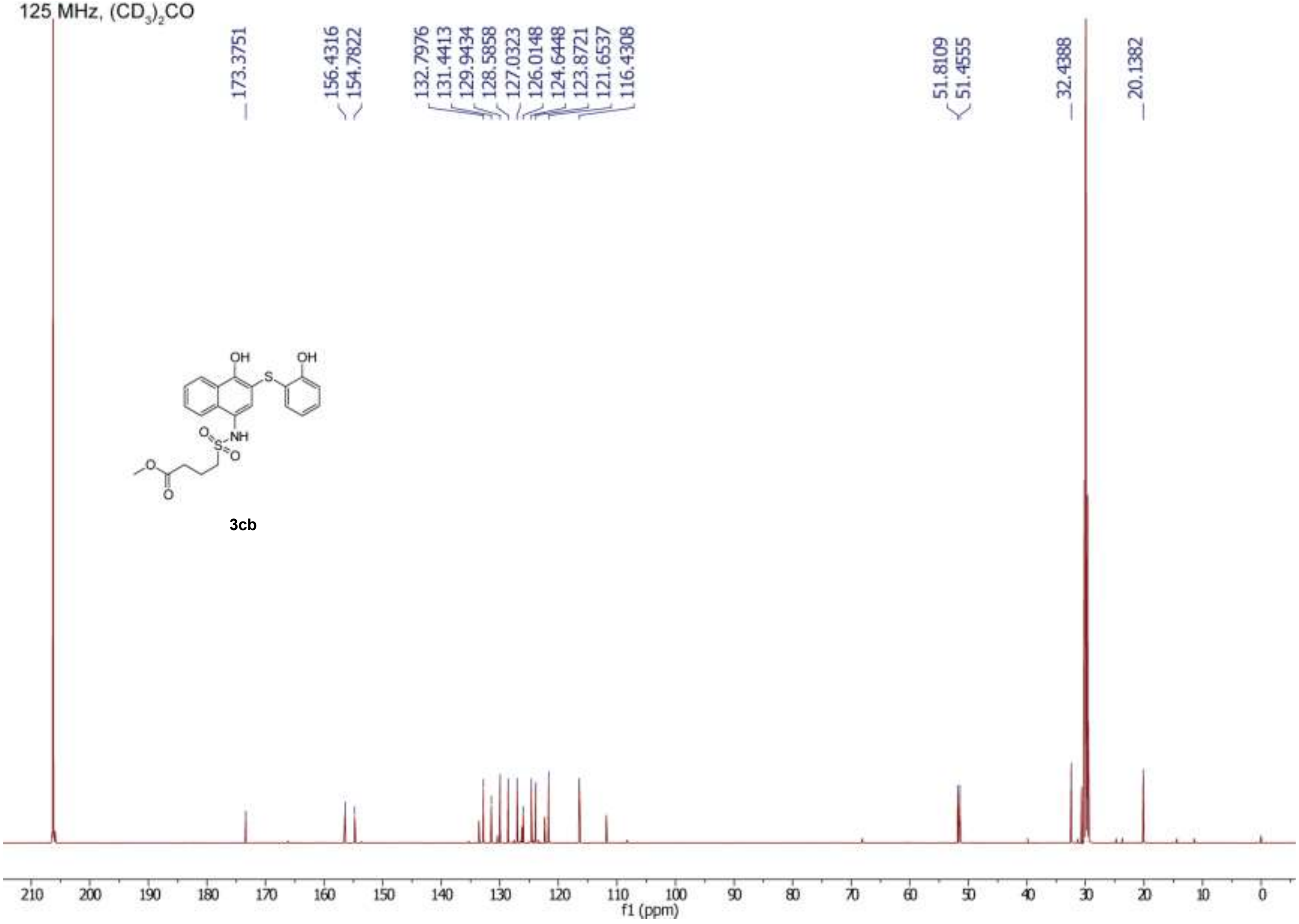

125 MHz, $(CD_3)_2CO$
163.7342
155.2676
137.3576
133.9412
132.2868
132.0948
130.3157
130.2984
130.0260
128.5626
127.8657
126.9748
126.7812
126.3206
125.9061
124.7651
123.8350
114.8104
109.4798
55.9799
OH
S
NH
O
S
O
O
3ba
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

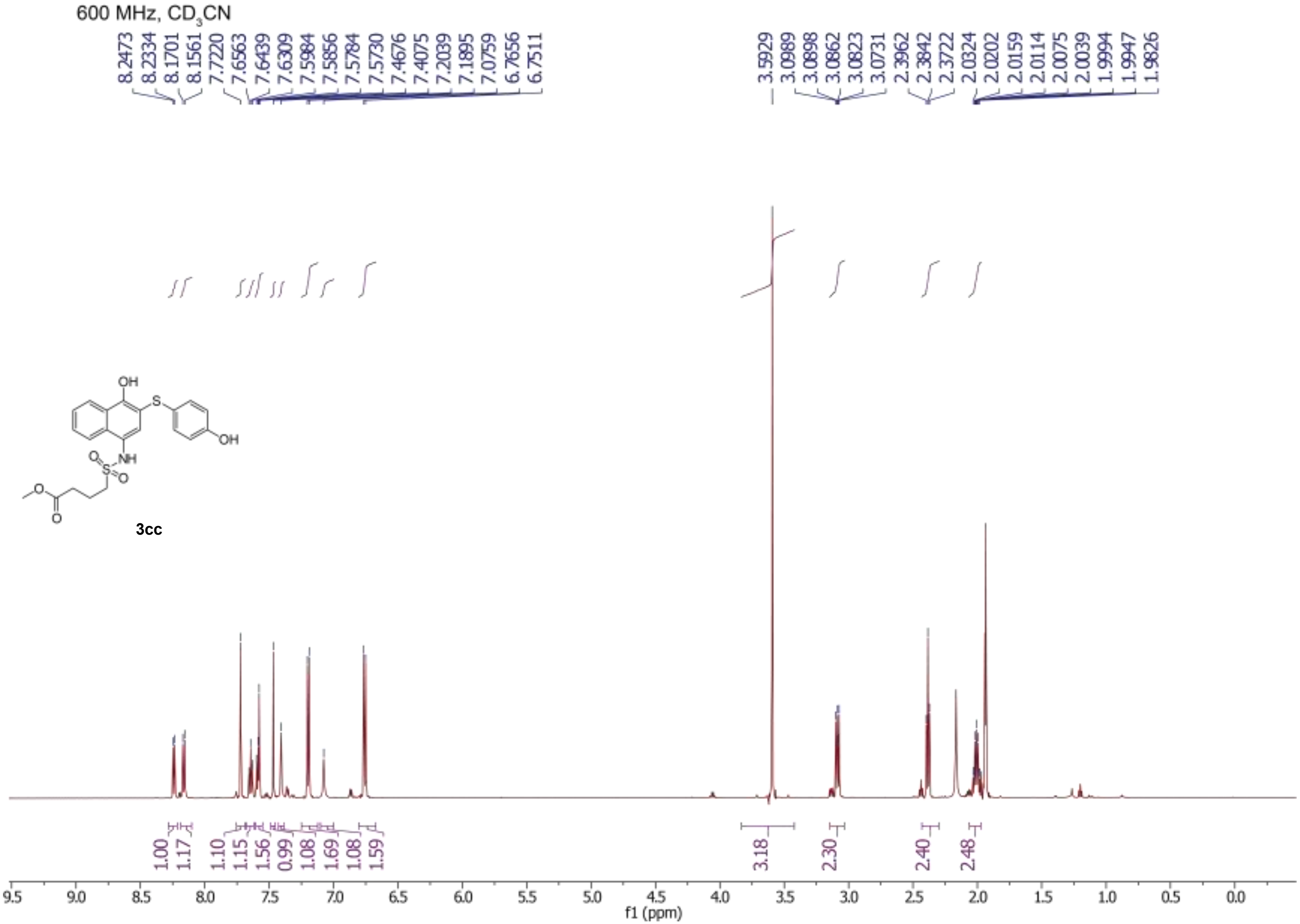

600 MHz, CD$_3$CN
8.287
8.273
8.218
8.204
7.708
7.706
7.696
7.694
7.692
7.682
7.680
7.630
7.628
7.616
7.604
7.603
7.588
7.544
7.289
7.286
7.276
7.263
7.203
7.191
7.179
7.163
7.161
7.149
3.569
3.130
3.121
3.117
3.114
3.104
2.392
2.380
2.368
2.085
2.043
2.031
2.026
2.021
2.018
2.015
2.010
2.005
1.993
1.948
1.944
1.940
1.936
1.932
OH
S
NH
O
S
O
MeO
O
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.07
1.21
1.21
0.33
1.19
2.05
1.03
1.96
2.96
2.16
2.14
2.28

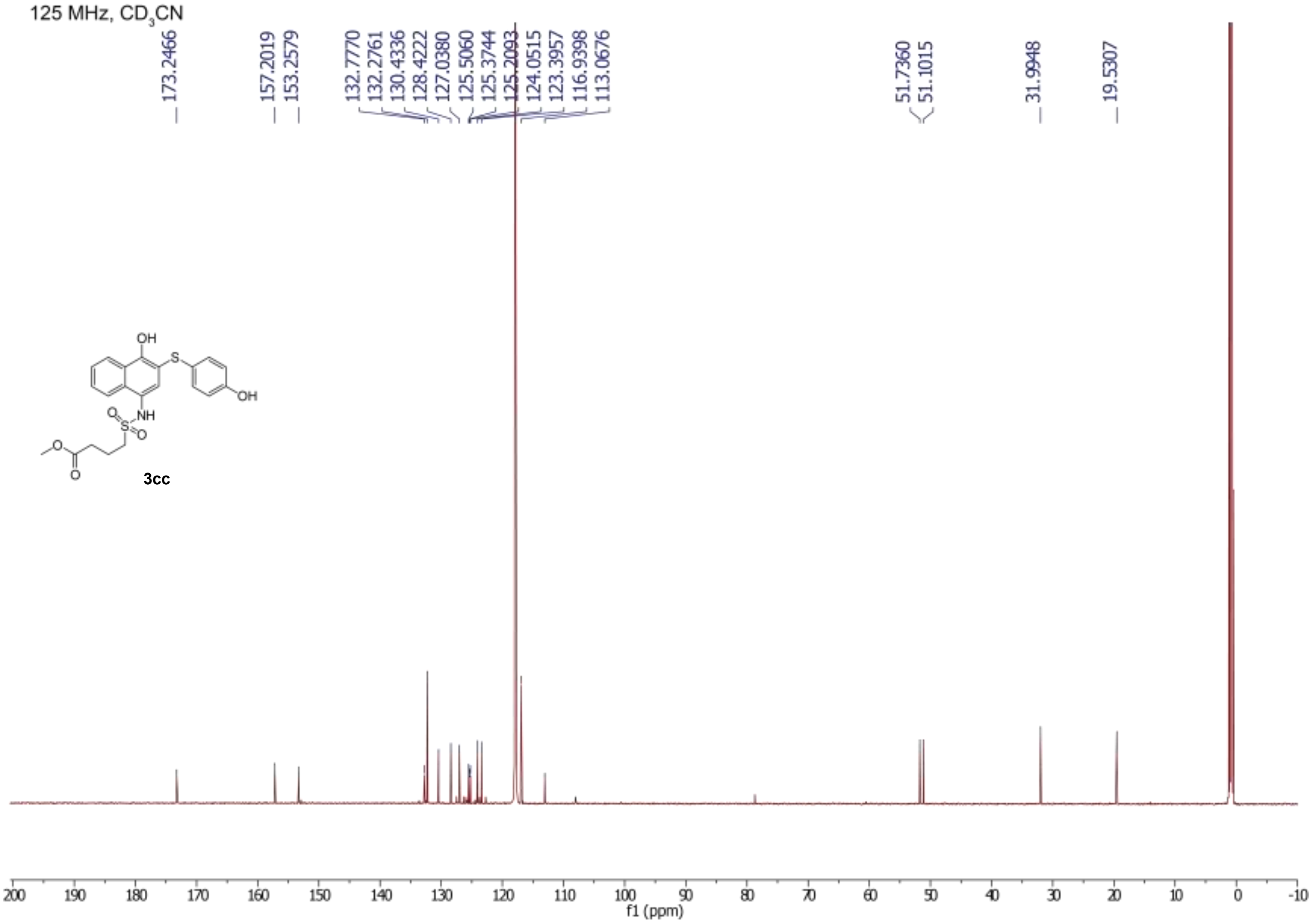
3ca

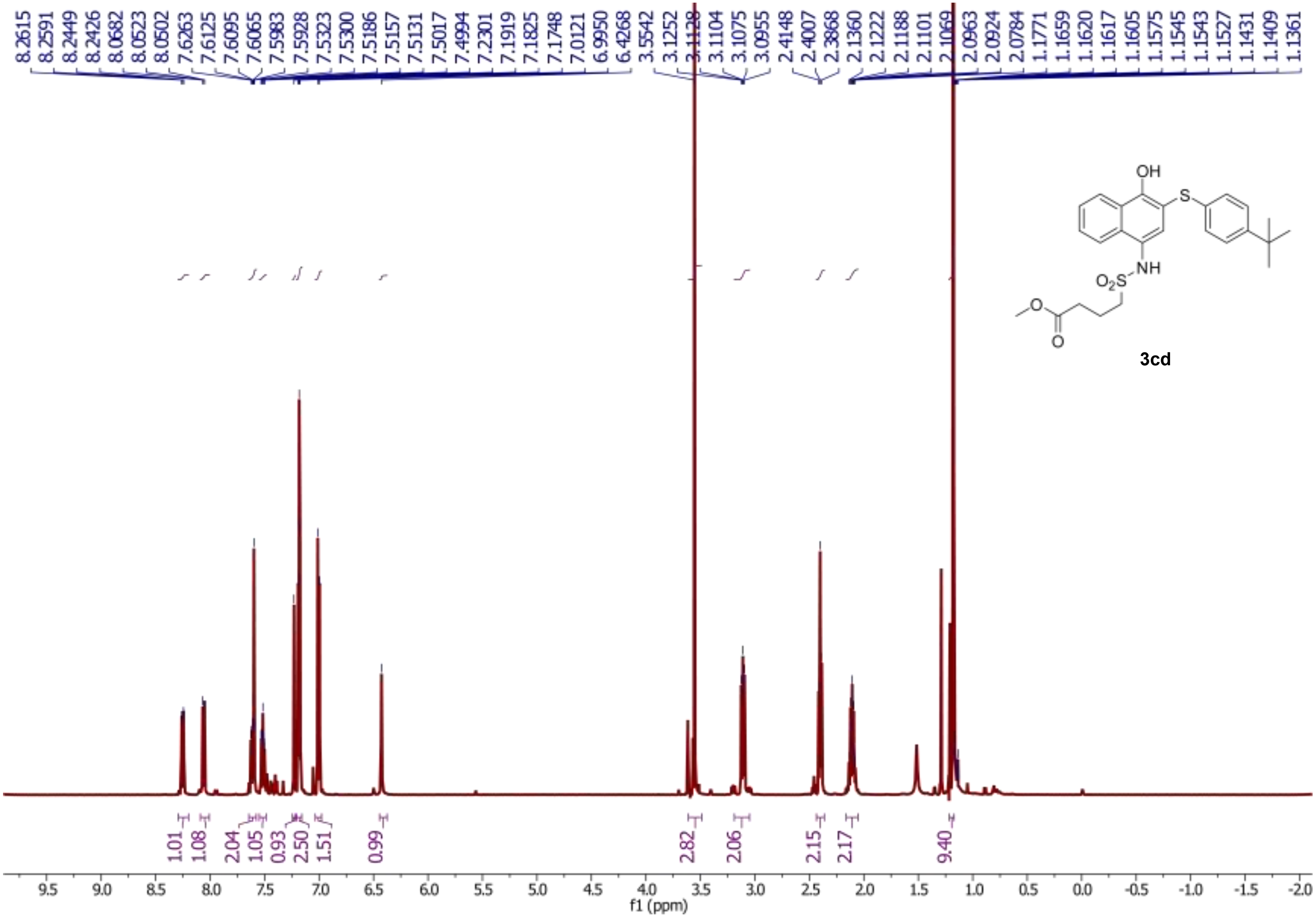

125 MHz, CD$_3$CN
174.06
155.55
137.66
134.13
132.18
130.71
129.67
128.74
127.95
127.70
126.52
126.14
124.91
124.48
110.67
52.55
52.00
32.83
20.38
OH
S
NH
O
S
O
O
O
3ca
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.3352
8.3211
8.3152
8.3024
8.3004
7.6635
7.6607
7.6520
7.6495
7.6465
7.6376
7.6353
7.5998
7.5898
7.5872
7.5848
7.5746
7.1777
7.1750
7.1645
7.1617
7.1545
7.1518
7.1415
7.1387
7.1288
7.1261
6.9667
6.9534
6.8107
6.7983
6.7856
3.6086
3.2173
3.2079
3.2046
3.2010
3.1918
2.5062
2.4941
2.4821
2.1295
2.1264
2.1225
2.1173
2.1137
2.1102
2.1010
OH
OH
S
NH
O
S
O
O
O
3cb
2.34
2.31
1.18
2.30
0.99
1.00
2.92
2.36
2.38
1.99
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

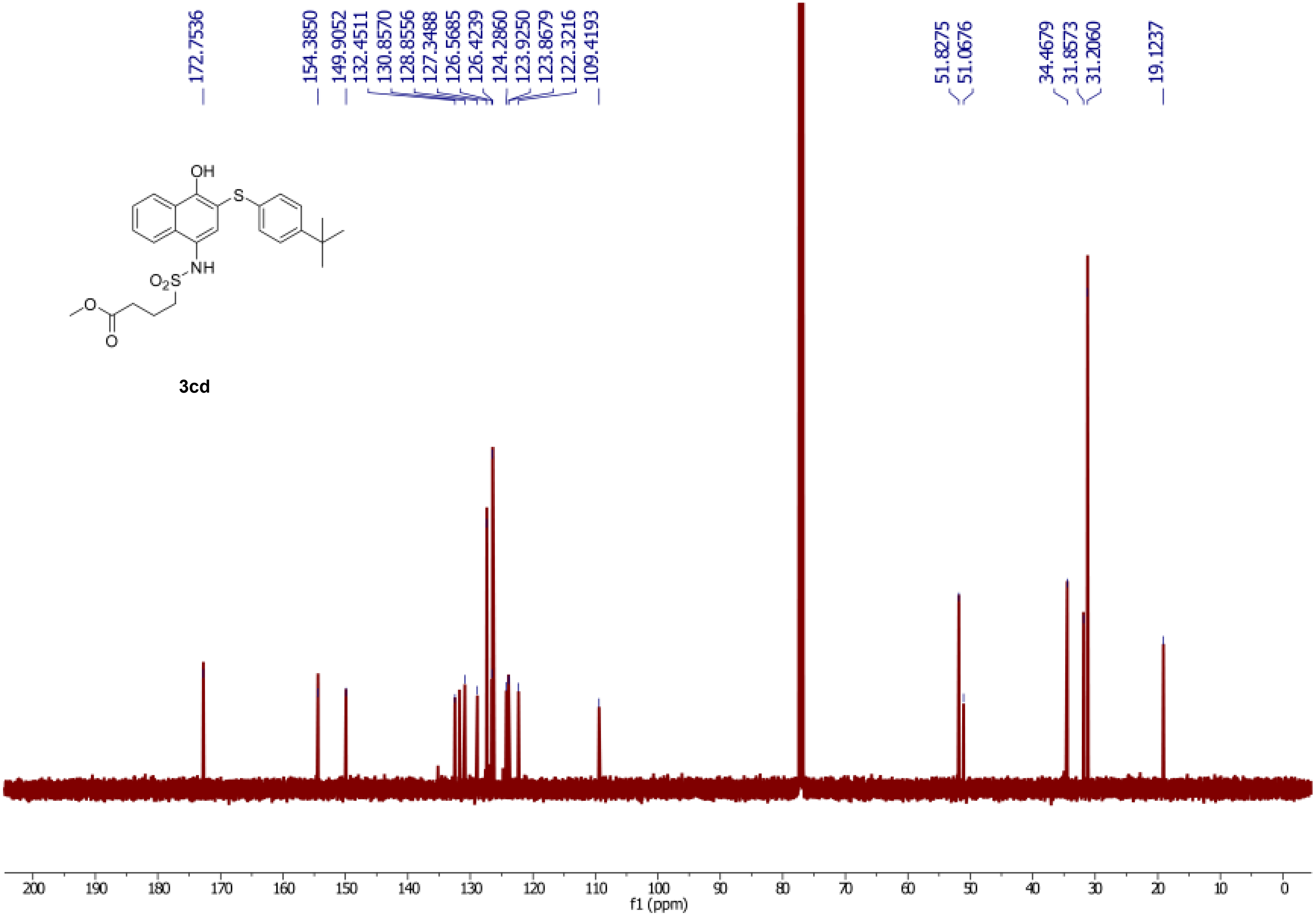

125 MHz, (CD$_3$)$_2$CO
173.3751
156.4316
154.7822
132.7976
131.4413
129.9434
128.5858
127.0323
126.0148
124.6448
123.8721
121.6537
116.4308
51.8109
51.4555
32.4388
20.1382
OH
OH
S
NH
O
S
O
O
O
3cb
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


600 MHz, CD_3CN
8.2473
8.2334
8.1701
8.1561
7.7220
7.6563
7.6439
7.6309
7.5984
7.5856
7.5784
7.5730
7.4676
7.4075
7.2039
7.1895
7.0759
6.7656
6.7511
3.5929
3.0989
3.0898
3.0862
3.0823
3.0731
2.3962
2.3842
2.3722
2.0324
2.0202
2.0159
2.0114
2.0075
2.0039
1.9994
1.9947
1.9826
OH
S
OH
NH
O
S
O
O
O
3cc
1.00
1.17
1.10
1.15
1.56
0.99
1.08
1.69
1.08
1.59
3.18
2.30
2.40
2.48
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

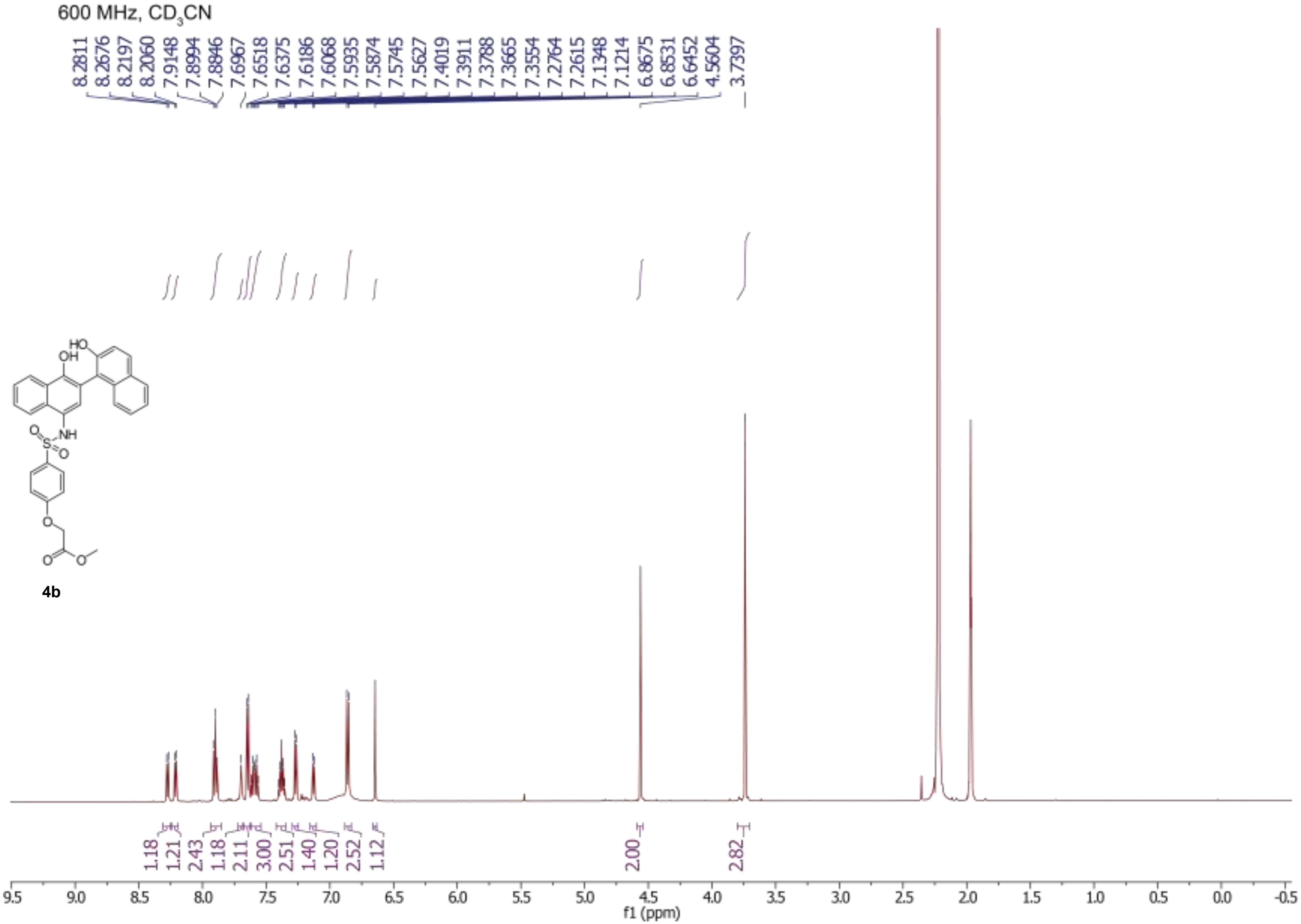

125 MHz, CD$_3$CN
173.2466
157.2019
153.2579
132.7770
132.2761
130.4336
128.4222
127.0380
125.5060
125.3744
125.2093
124.0515
123.3957
116.9398
113.0676
51.7360
51.1015
31.9948
19.5307
OH
S
OH
NH
O
S
O
O
O
O
3cc
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.2615
8.2591
8.2449
8.2426
8.0682
8.0523
8.0502
7.6263
7.6125
7.6095
7.6065
7.5983
7.5928
7.5323
7.5300
7.5186
7.5157
7.5131
7.5017
7.4994
7.2301
7.1919
7.1825
7.1748
7.0121
6.9950
6.4268
3.5542
3.1252
3.1128
3.1104
3.1075
3.0955
2.4148
2.4007
2.3868
2.1360
2.1222
2.1188
2.1101
2.1069
2.0963
2.0924
2.0784
1.1771
1.1659
1.1620
1.1617
1.1605
1.1575
1.1545
1.1543
1.1527
1.1431
1.1409
1.1361
OH
S
NH
O_2S
O
O
1.01
1.08
2.04
1.05
0.93
2.50
1.51
0.99
2.82
2.06
2.15
2.17
9.40
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
-2.0
f1 (ppm)

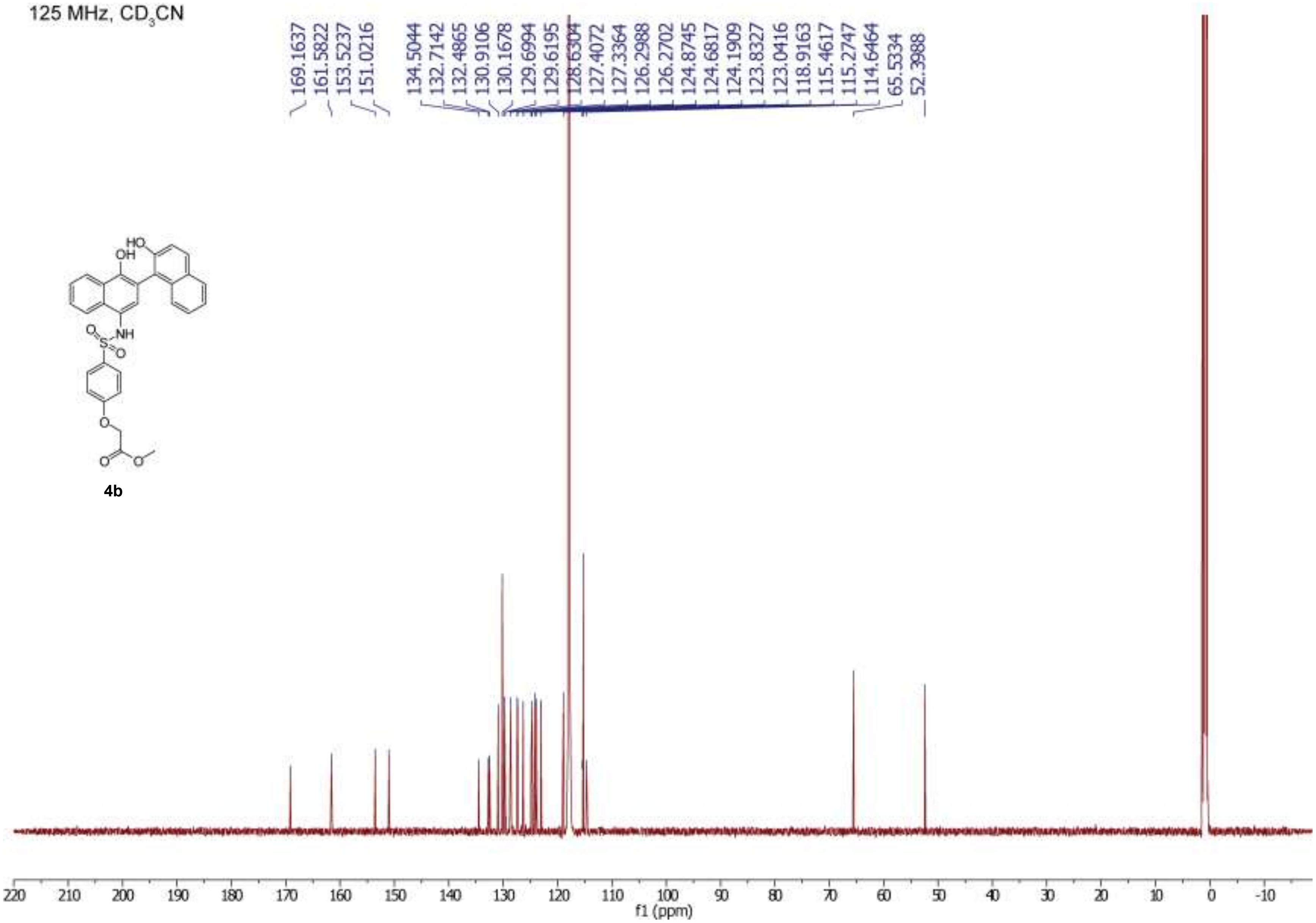
3cd


3cd

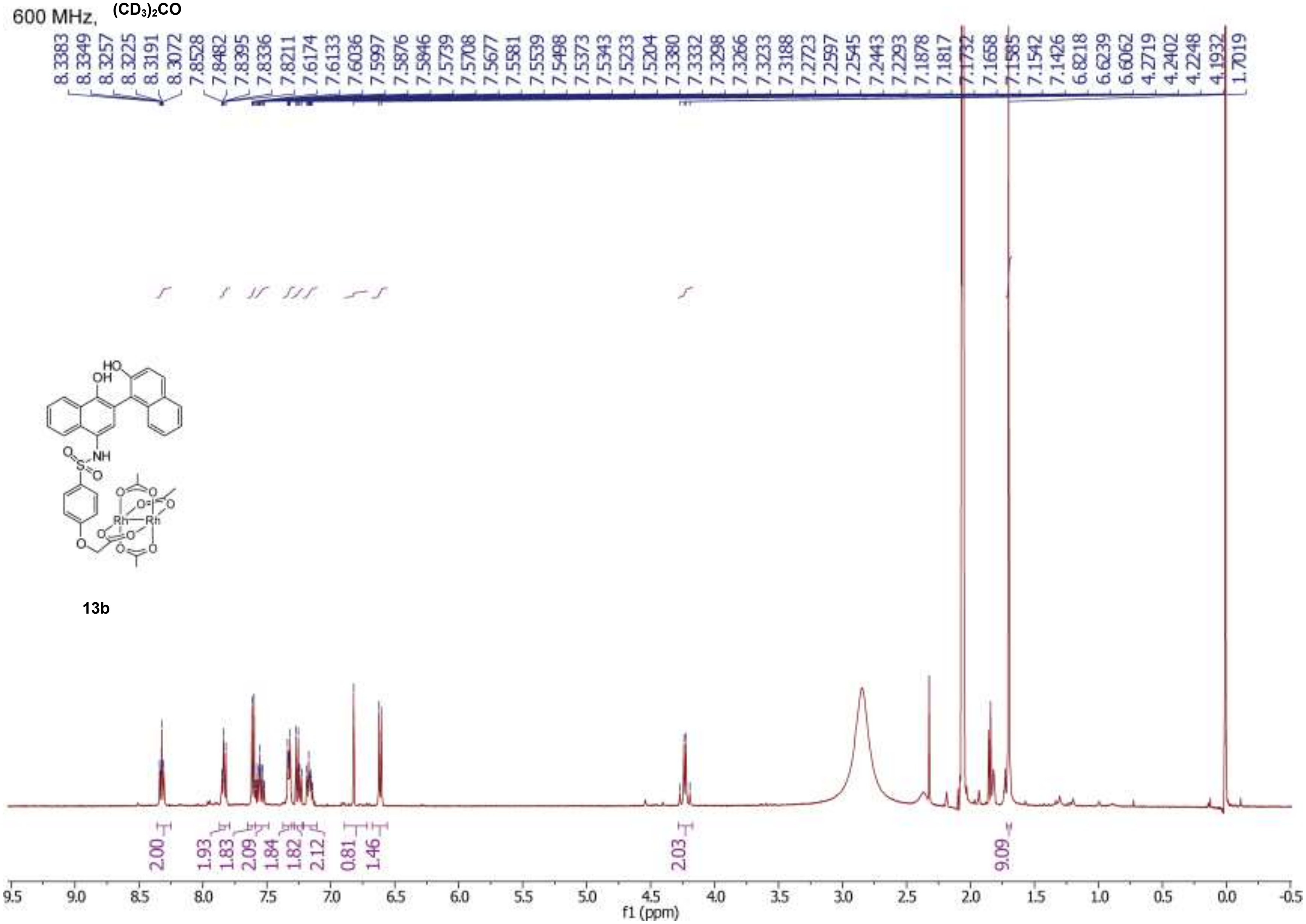
172.7536
154.3850
149.9052
132.4511
130.8570
128.8556
127.3488
126.5685
126.4239
124.2860
123.9250
123.8679
122.3216
109.4193
51.8275
51.0676
34.4679
31.8573
31.2060
19.1237
OH
S
NH
O2S
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


600 MHz, CD_3CN
8.2811
8.2676
8.2197
8.2060
7.9148
7.8994
7.8846
7.6967
7.6518
7.6375
7.6186
7.6068
7.5935
7.5874
7.5745
7.5627
7.4019
7.3911
7.3788
7.3665
7.3554
7.2764
7.2615
7.1348
7.1214
6.8675
6.8531
6.6452
4.5604
3.7397
HO
OH
NH
O
S
O
O
O
O
1.18
1.21
2.43
1.18
2.11
3.00
2.51
1.40
1.20
2.52
1.12
2.00
2.82
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

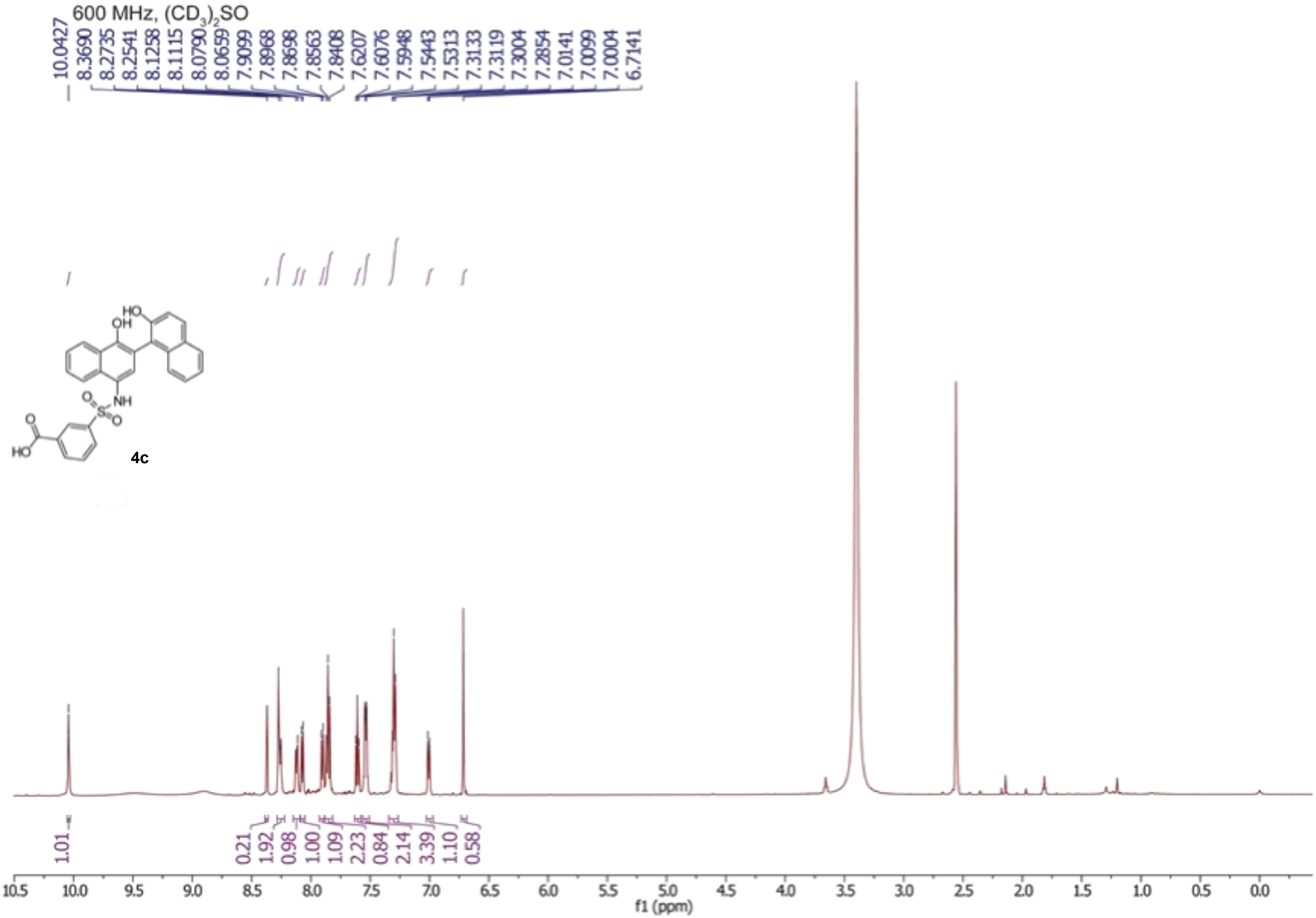
4b

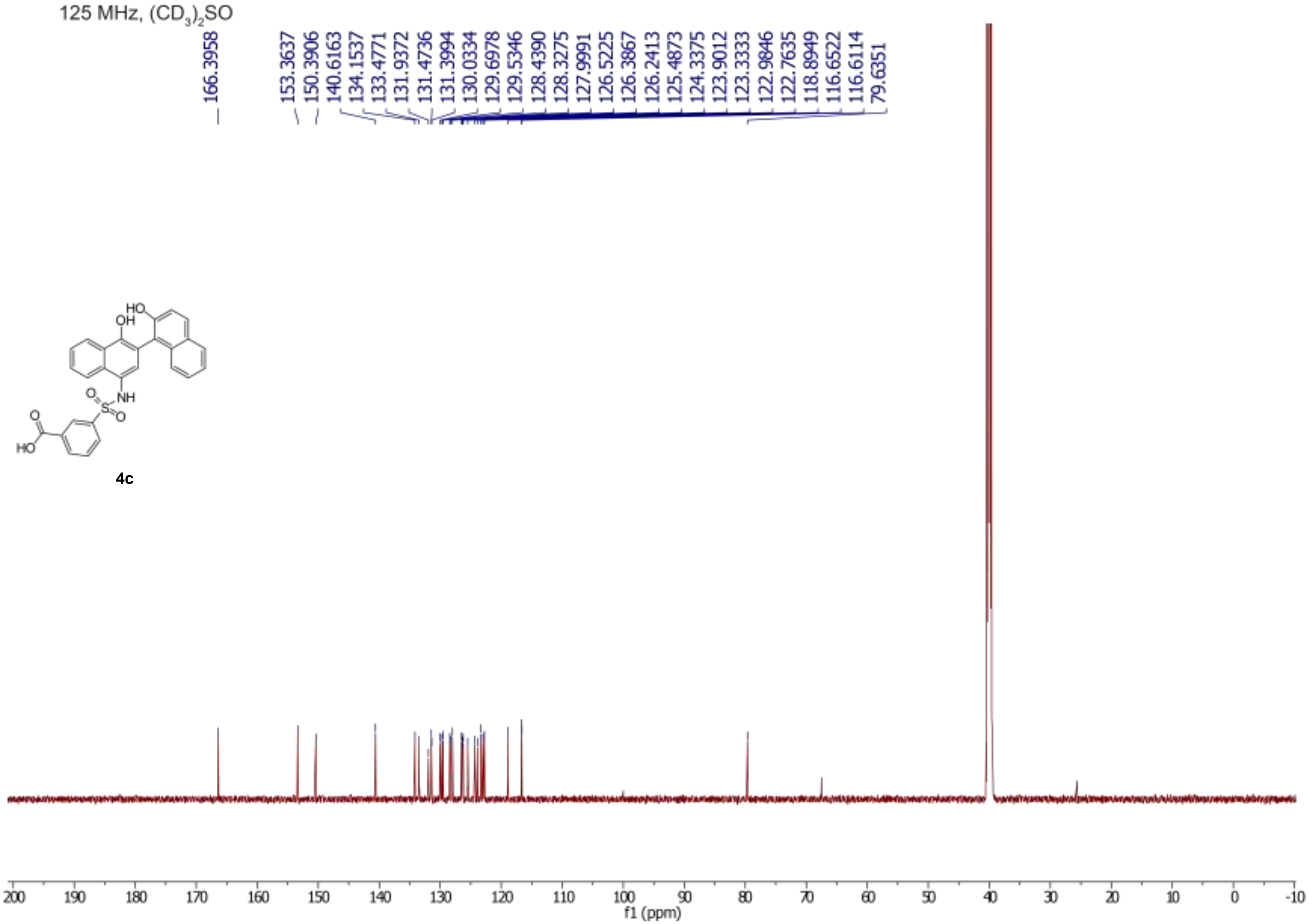

125 MHz, CD_3CN
169.1637
161.5822
153.5237
151.0216
134.5044
132.7142
132.4865
130.9106
130.1678
129.6994
129.6195
128.6304
127.4072
127.3364
126.2988
126.2702
124.8745
124.6817
124.1909
123.8327
123.0416
118.9163
115.4617
115.2747
114.6464
65.5334
52.3988
HO
OH
NH
O
S
O
O
O
O
4b
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

600 MHz, $(CD_3)_2CO$

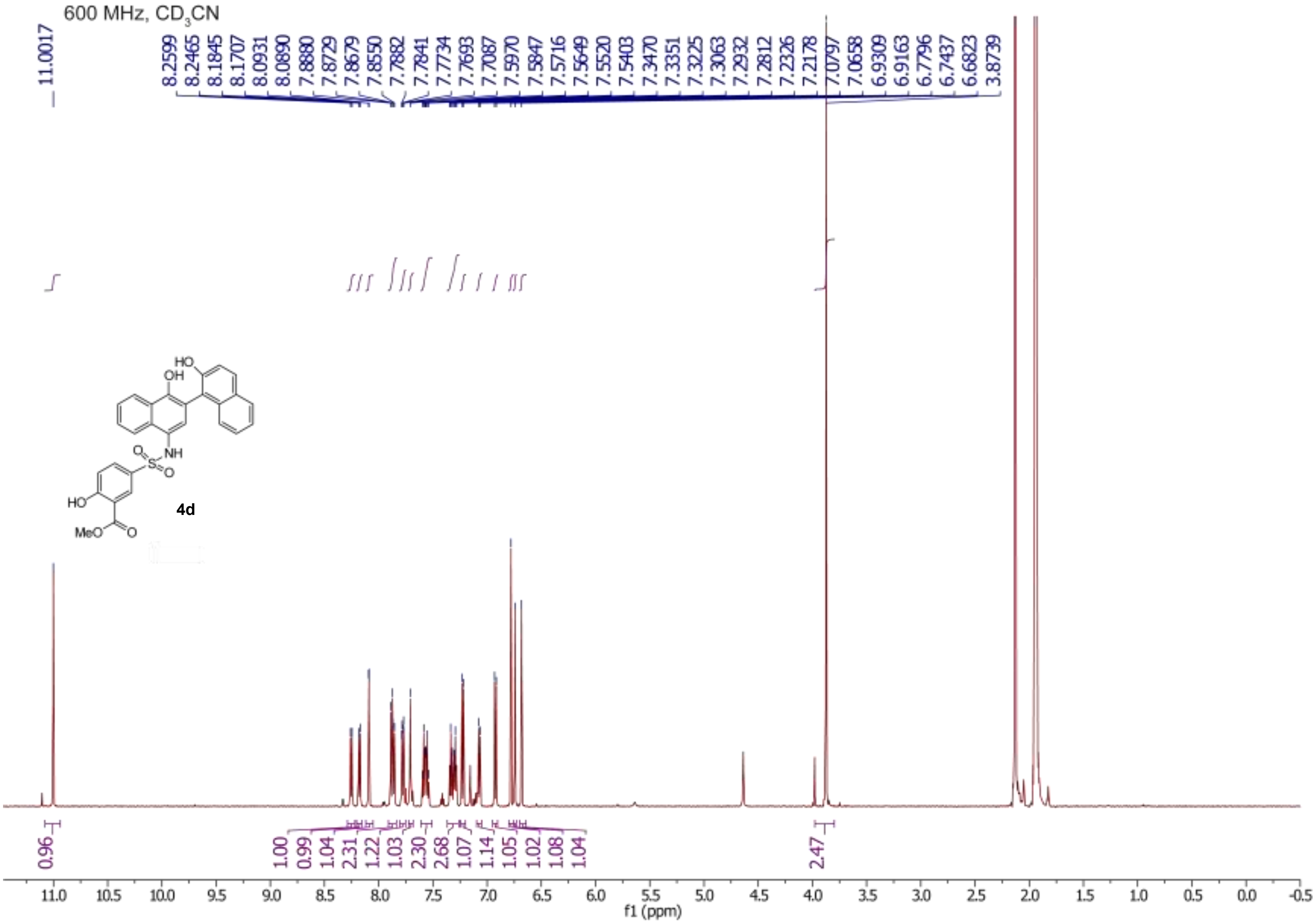


13b

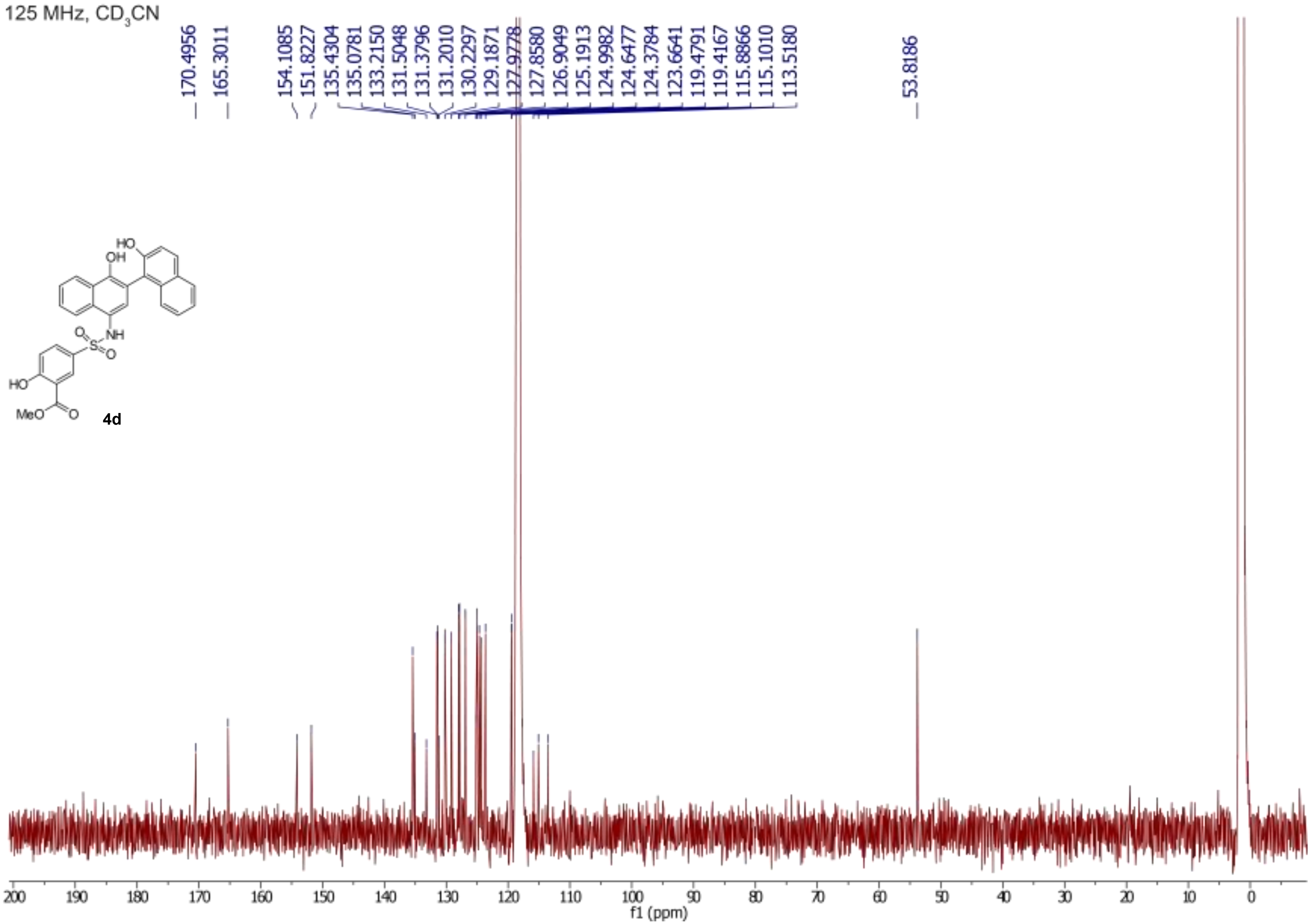

600 MHz, $(CD_3)_2SO$
10.0427
8.3690
8.2735
8.2541
8.1258
8.1115
8.0790
8.0659
7.9099
7.8968
7.8698
7.8563
7.8408
7.6207
7.6076
7.5948
7.5443
7.5313
7.3133
7.3119
7.3004
7.2854
7.0141
7.0099
7.0004
6.7141
HO
OH
NH
O
S
O
HO
4c
1.01
0.21
1.92
0.98
1.00
1.09
2.23
0.84
2.14
3.39
1.10
0.58
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

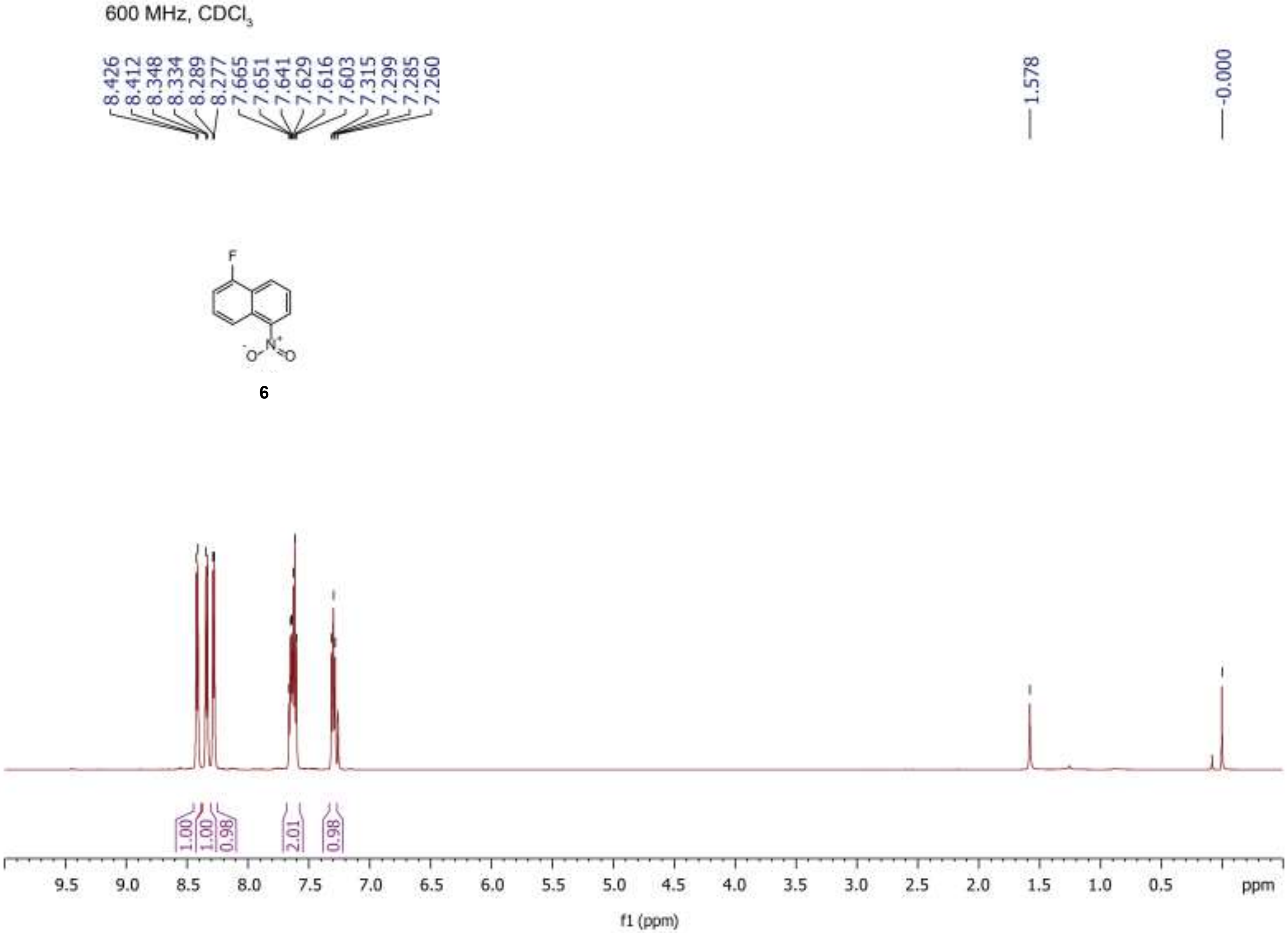

125 MHz, $(CD_3)_2SO$
166.3958
153.3637
150.3906
140.6163
134.1537
133.4771
131.9372
131.4736
131.3994
130.0334
129.6978
129.5346
128.4390
128.3275
127.9991
126.5225
126.3867
126.2413
125.4873
124.3375
123.9012
123.3333
122.9846
122.7635
118.8949
116.6522
116.6114
79.6351
HO
OH
NH
O
S
O
O
HO
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

4c

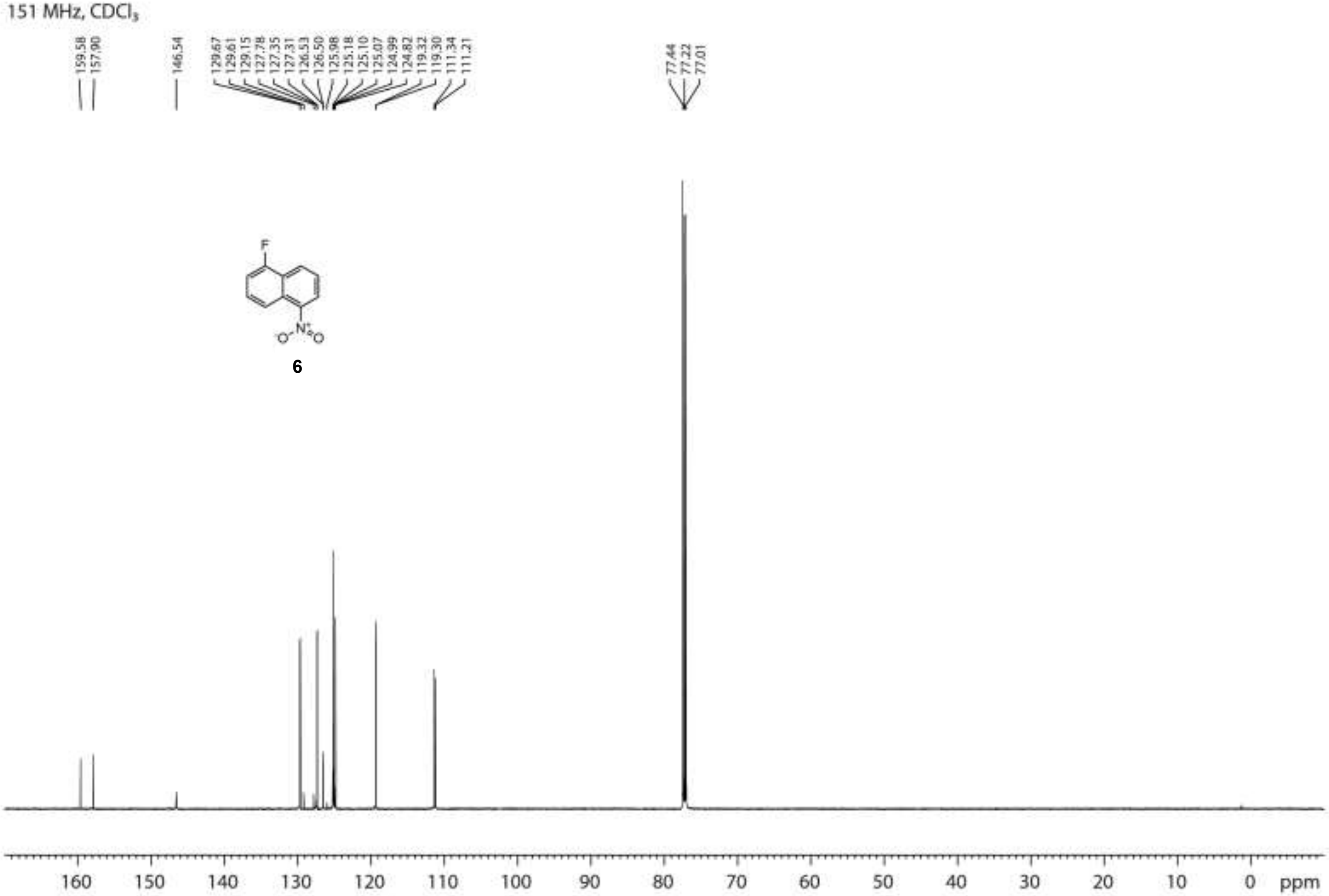

600 MHz, CD_3CN
11.0017
8.2599
8.2465
8.1845
8.1707
8.0931
8.0890
7.8880
7.8729
7.8679
7.8550
7.7882
7.7841
7.7734
7.7693
7.7087
7.5970
7.5847
7.5716
7.5649
7.5520
7.5403
7.3470
7.3351
7.3225
7.3063
7.2932
7.2812
7.2326
7.2178
7.0797
7.0658
6.9309
6.9163
6.7796
6.7437
6.6823
3.8739
HO
OH
NH
O
S
O
HO
MeO
O
0.96
1.00
0.99
1.04
2.31
1.22
1.03
2.30
2.68
1.07
1.14
1.05
1.02
1.08
1.04
2.47
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

4d


125 MHz, CD_3CN
170.4956
165.3011
154.1085
151.8227
135.4304
135.0781
133.2150
131.5048
131.3796
131.2010
130.2297
129.1871
127.9778
127.8580
126.9049
125.1913
124.9982
124.6477
124.3784
123.6641
119.4791
119.4167
115.8866
115.1010
113.5180
53.8186
HO
OH
NH
O
S
O
HO
MeO
O
4d
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

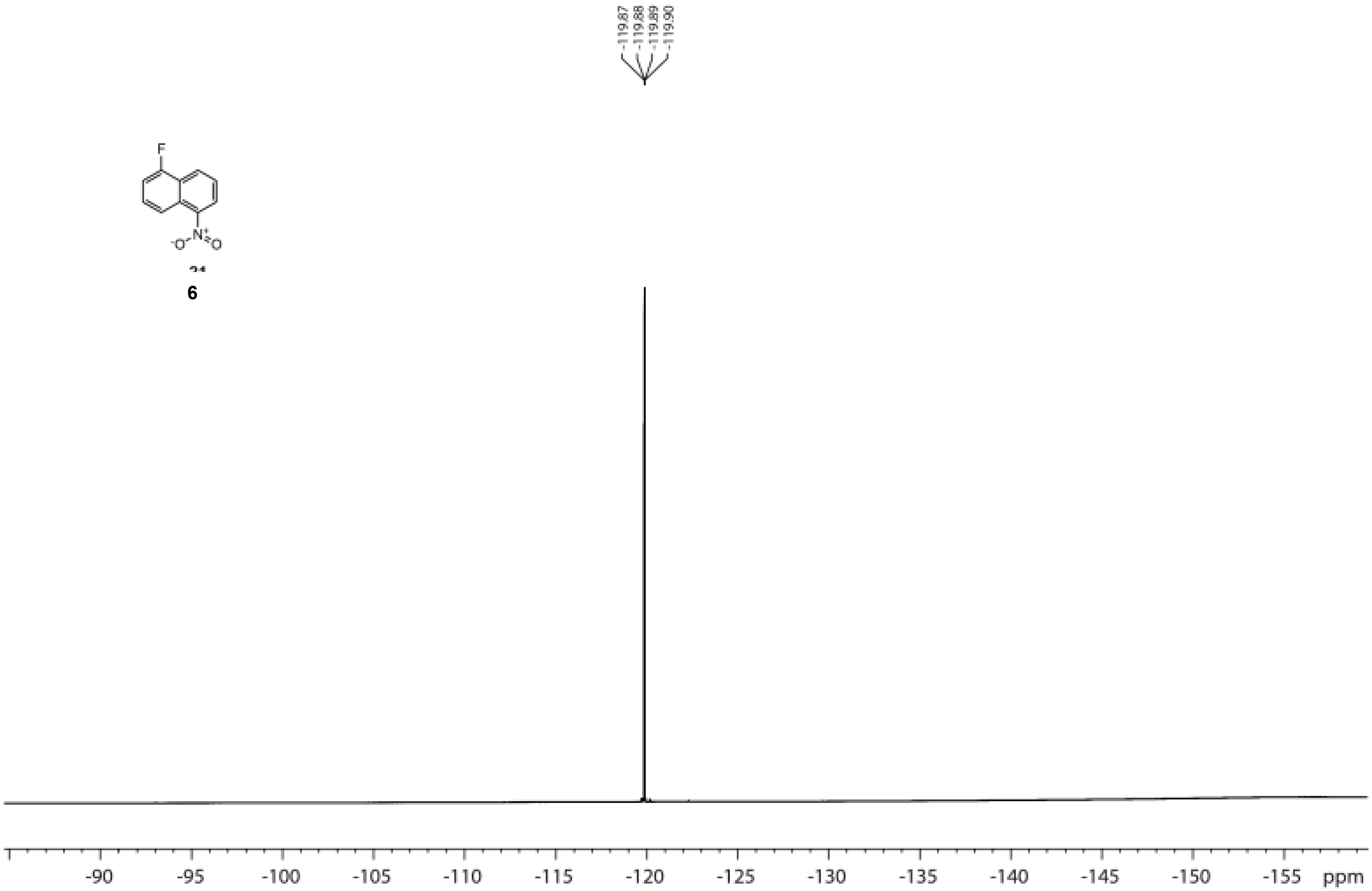

600 MHz, $CDCl_3$
8.426
8.412
8.348
8.334
8.289
8.277
7.665
7.651
7.641
7.629
7.616
7.603
7.315
7.299
7.285
7.260
1.578
-0.000
F
N^+
O^-
O
1.00
1.00
0.98
2.01
0.98
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
f1 (ppm)

6

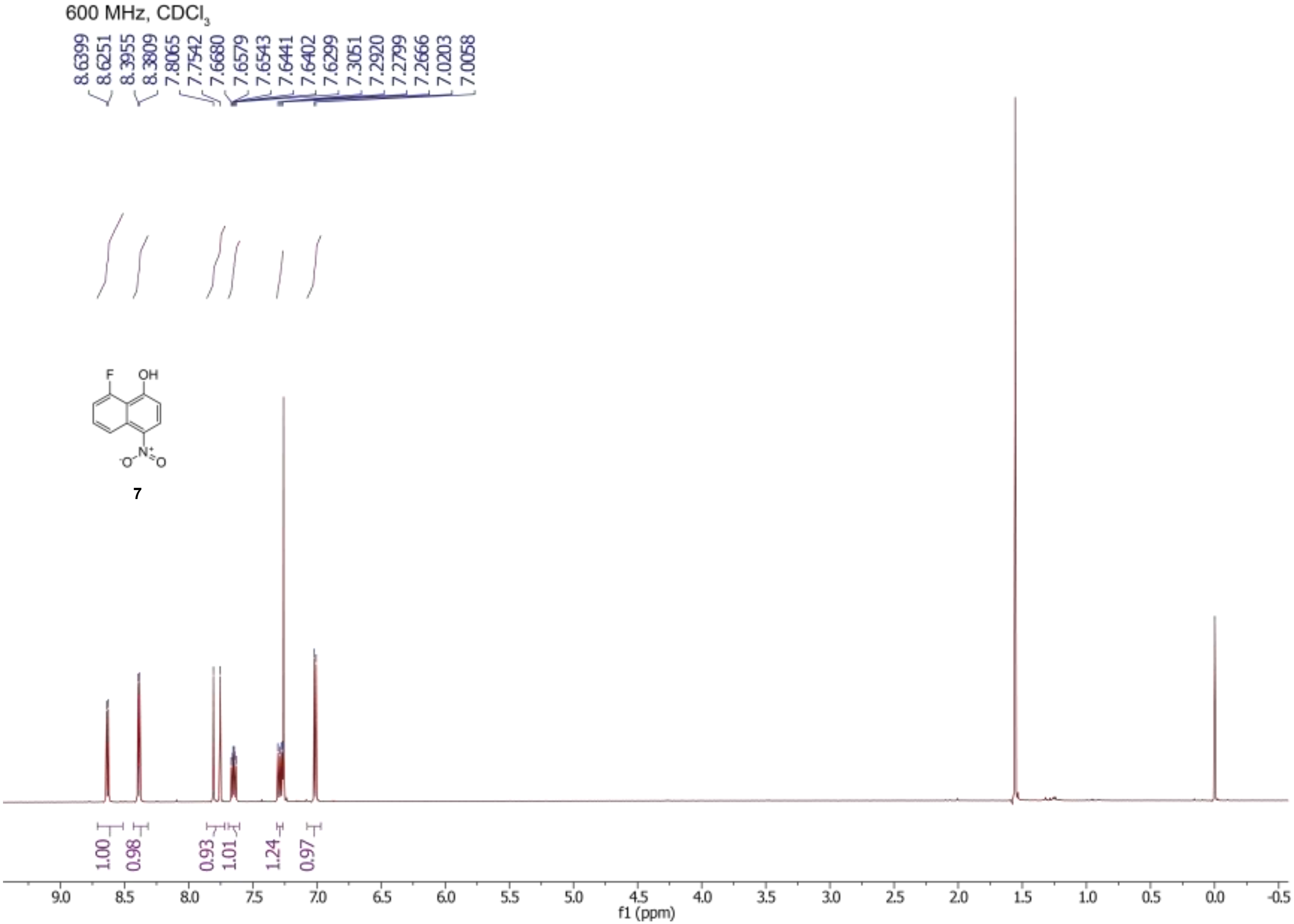

151 MHz, $CDCl_3$
159.58
157.90
146.54
129.67
129.61
129.15
127.78
127.35
127.31
126.53
126.50
125.98
125.18
125.10
125.07
124.99
124.82
119.32
119.30
111.34
111.21
77.44
77.22
77.01
F
N
O
O
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

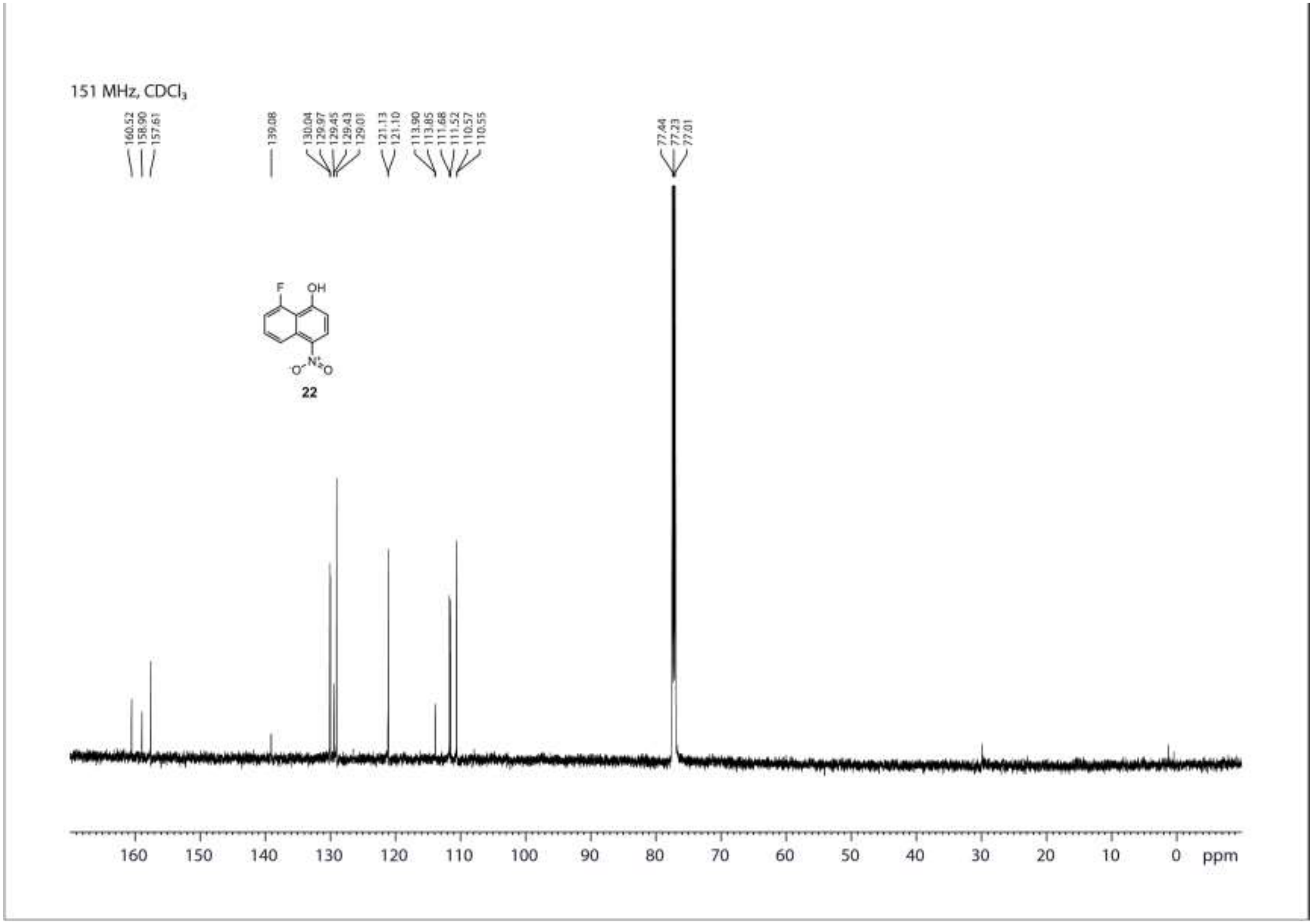
6

565 MHz, $CDCl_3$

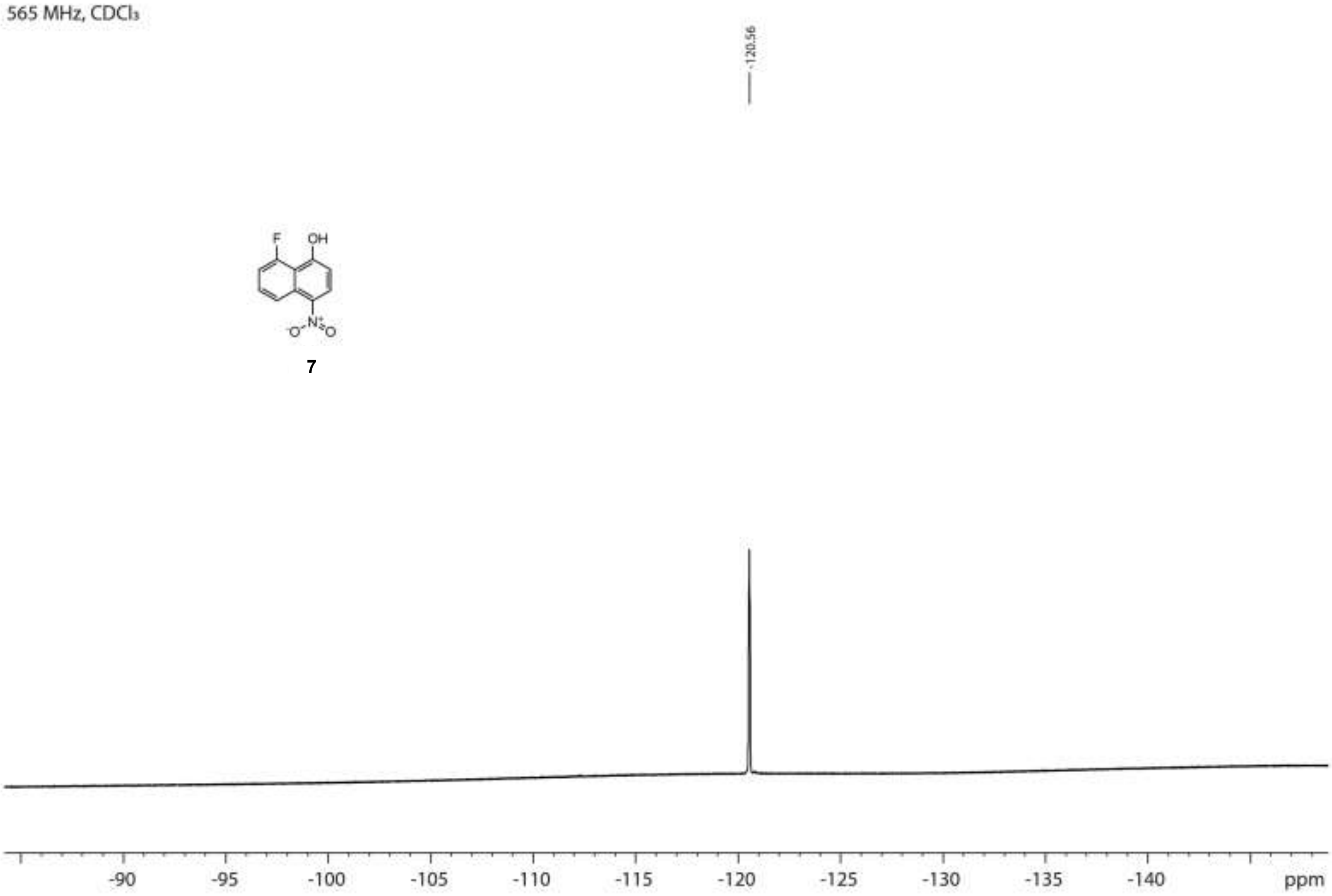


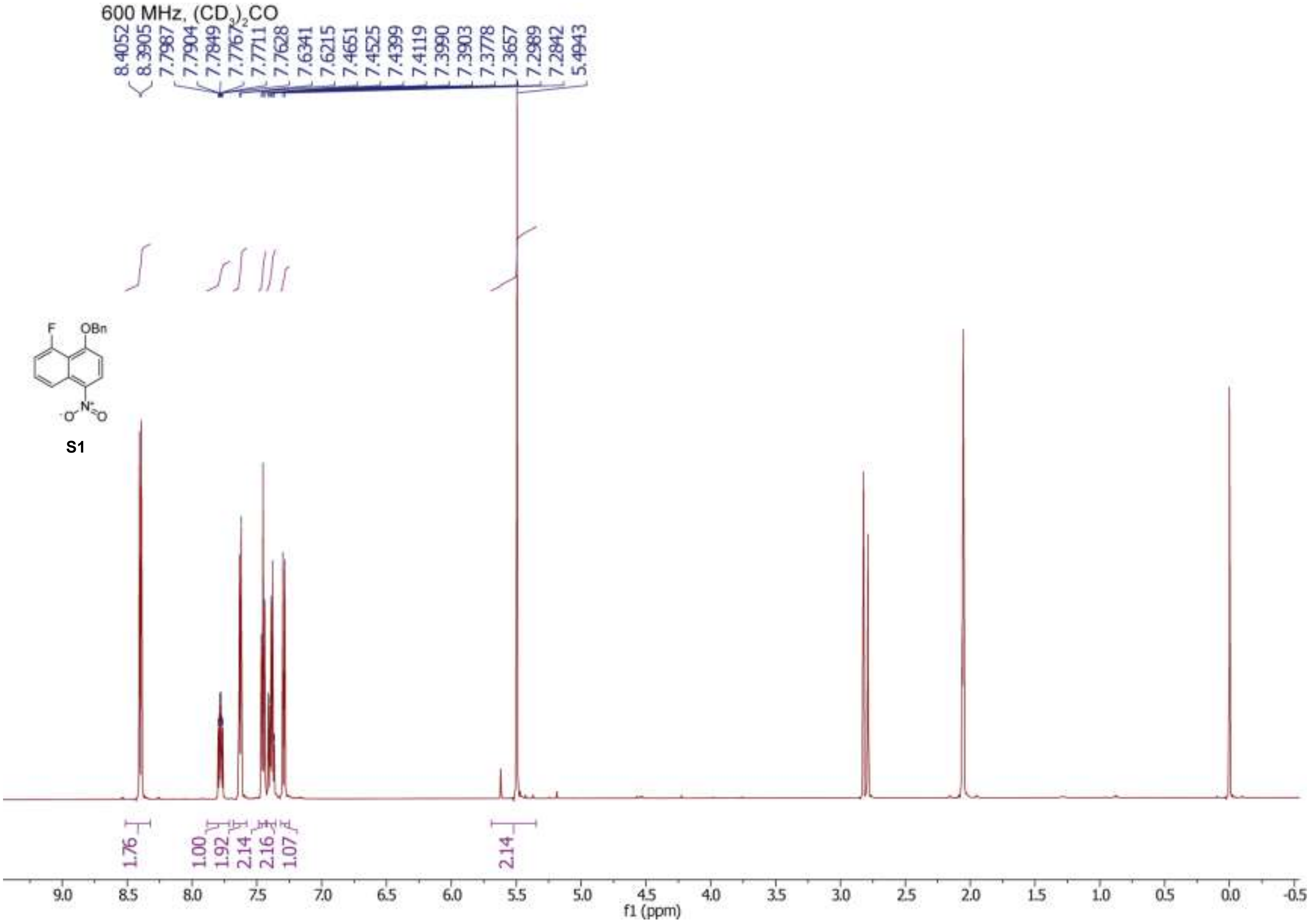
6


600 MHz, CDCl$_3$
8.6399
8.6251
8.3955
8.3809
7.8065
7.7542
7.6680
7.6579
7.6543
7.6441
7.6402
7.6299
7.3051
7.2920
7.2799
7.2666
7.0203
7.0058
F
OH
$^{-}$O
N^{+}
O
7
1.00
0.98
0.93
1.01
1.24
0.97
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

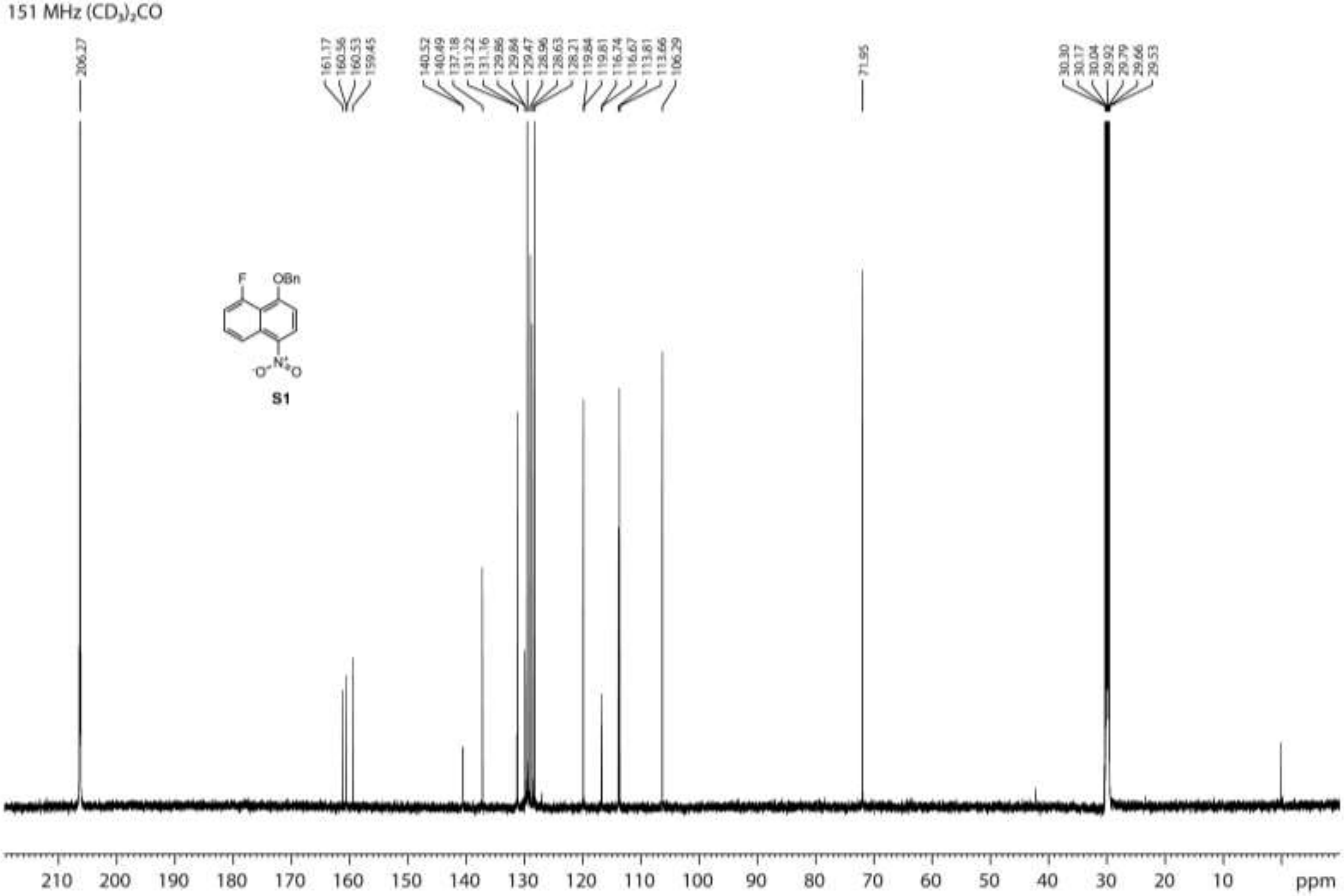


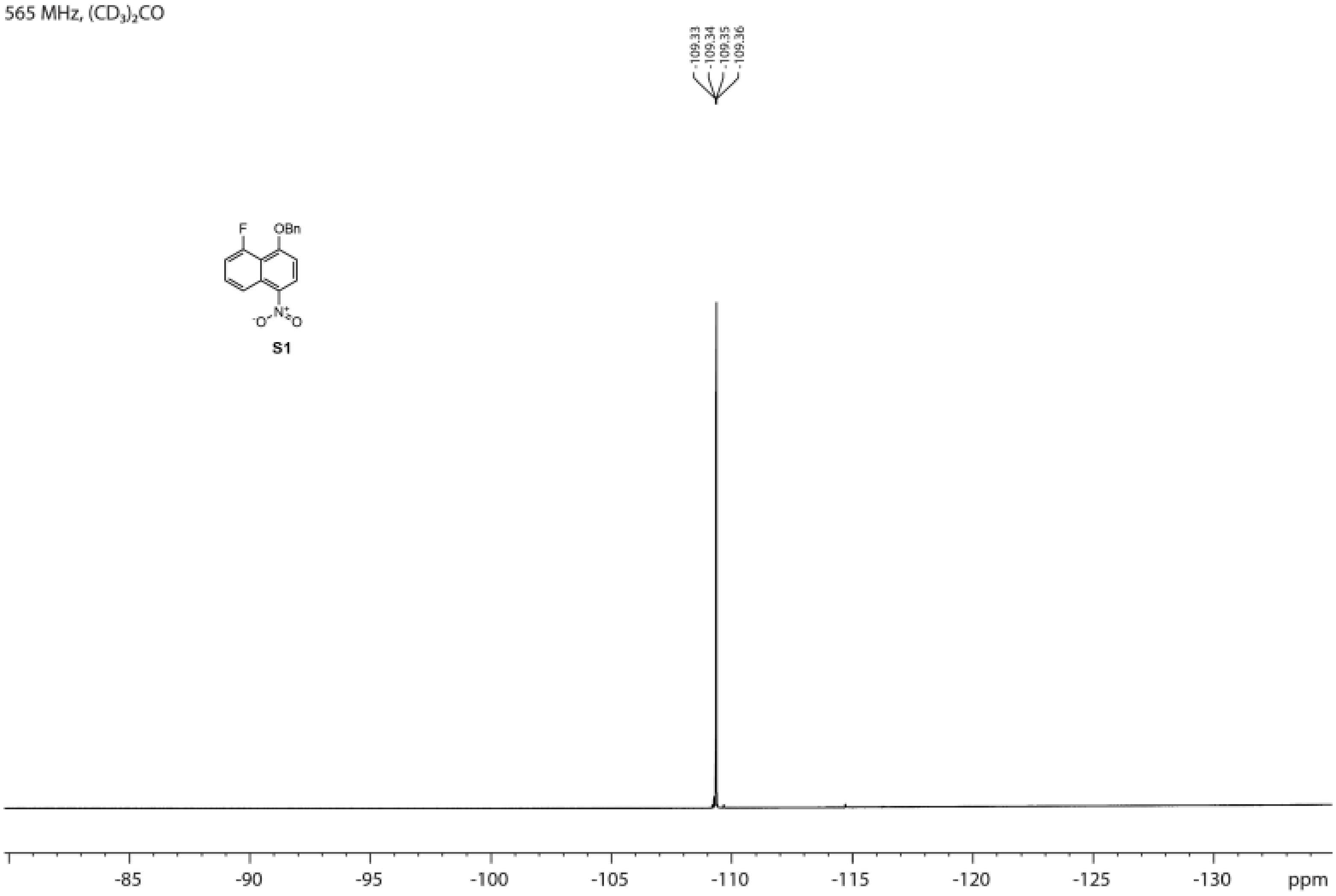
151 MHz, CDCl₃
160.52
158.90
157.61
139.08
130.04
129.97
129.45
129.43
129.01
121.13
121.10
113.90
113.85
111.68
111.52
110.57
110.55
77.44
77.23
77.01
F
OH
N⁺
⁻O
O
22
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

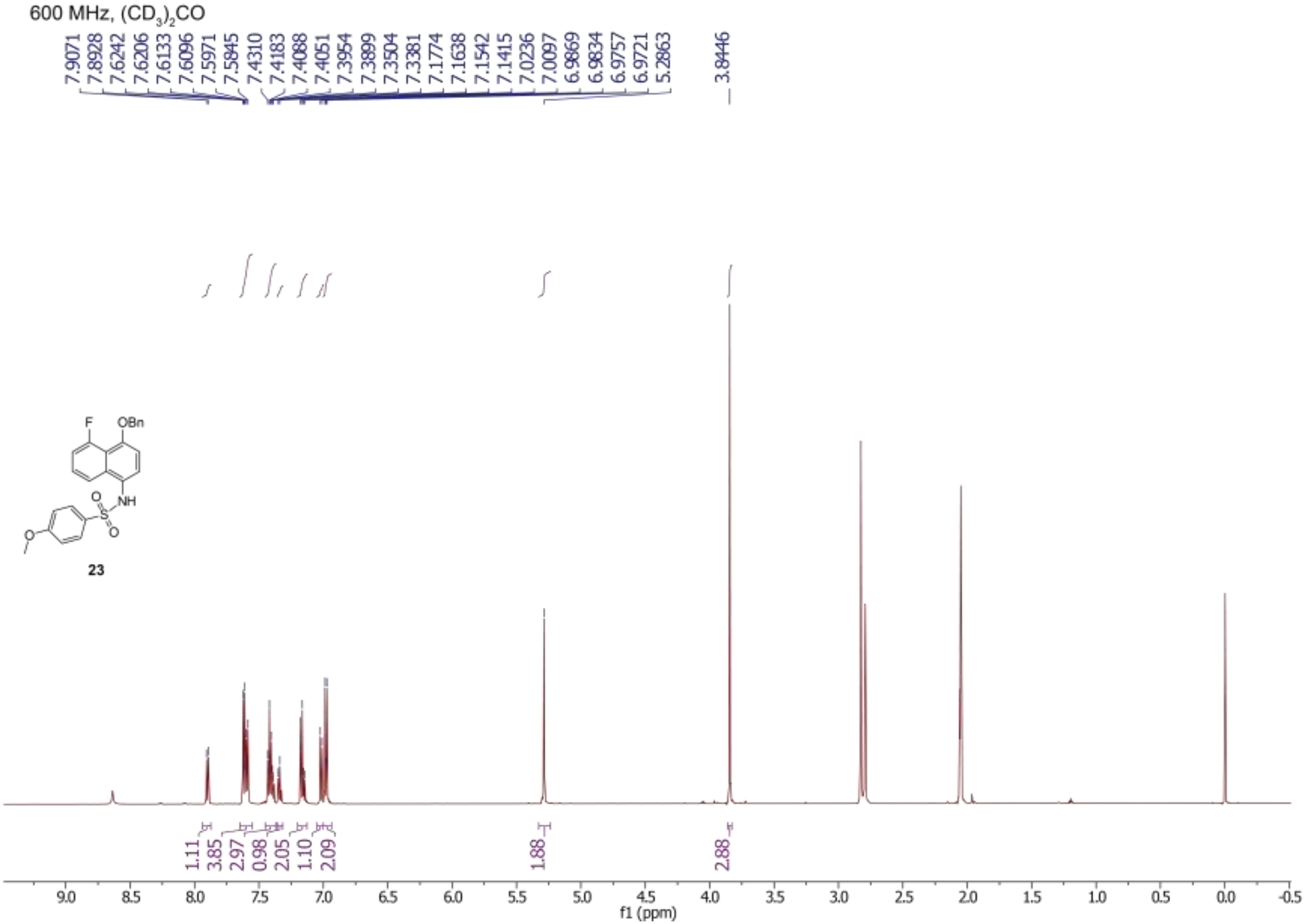

565 MHz, CDCl₃
-120.56
F
OH
$^{-}$O
N^{+}
O
7
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
ppm


600 MHz, $(CD_3)_2CO$
8.4052
8.3905
7.7987
7.7904
7.7849
7.7767
7.7711
7.7628
7.6341
7.6215
7.4651
7.4525
7.4399
7.4119
7.3990
7.3903
7.3778
7.3657
7.2989
7.2842
5.4943
F
OBn
N^+
^-O
O
1.76
1.00
1.92
2.14
2.16
1.07
2.14
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

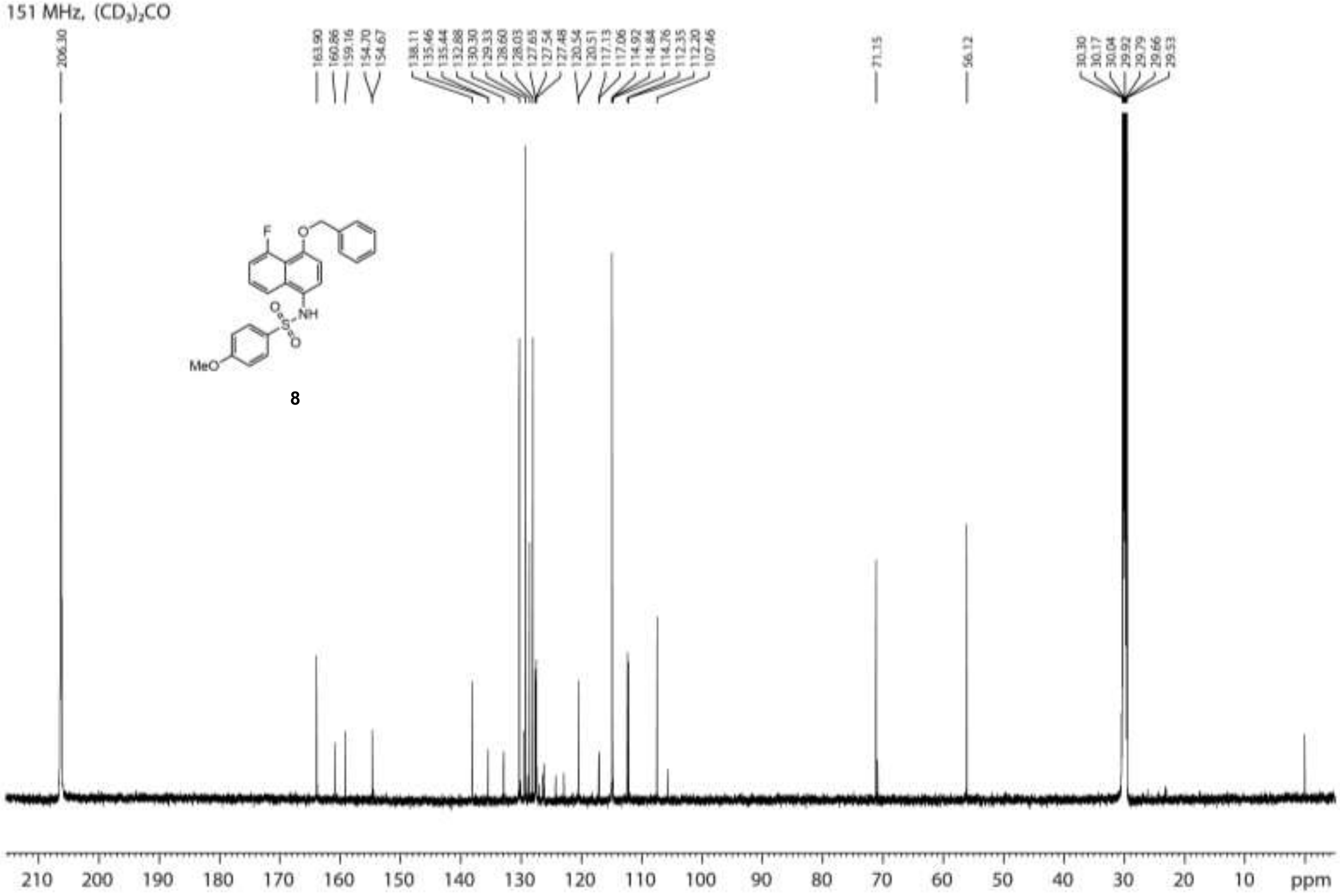
S1


151 MHz (CD$_3$)$_2$CO
206.27
161.17
160.56
160.53
159.45
140.52
140.49
137.18
131.22
131.16
129.86
129.84
129.47
128.96
128.63
128.21
119.84
119.81
116.74
116.67
113.81
113.66
106.29
71.95
30.30
30.17
30.04
29.92
29.79
29.66
29.53
F
OBn
$^-$O
N$^+$
O
S1
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

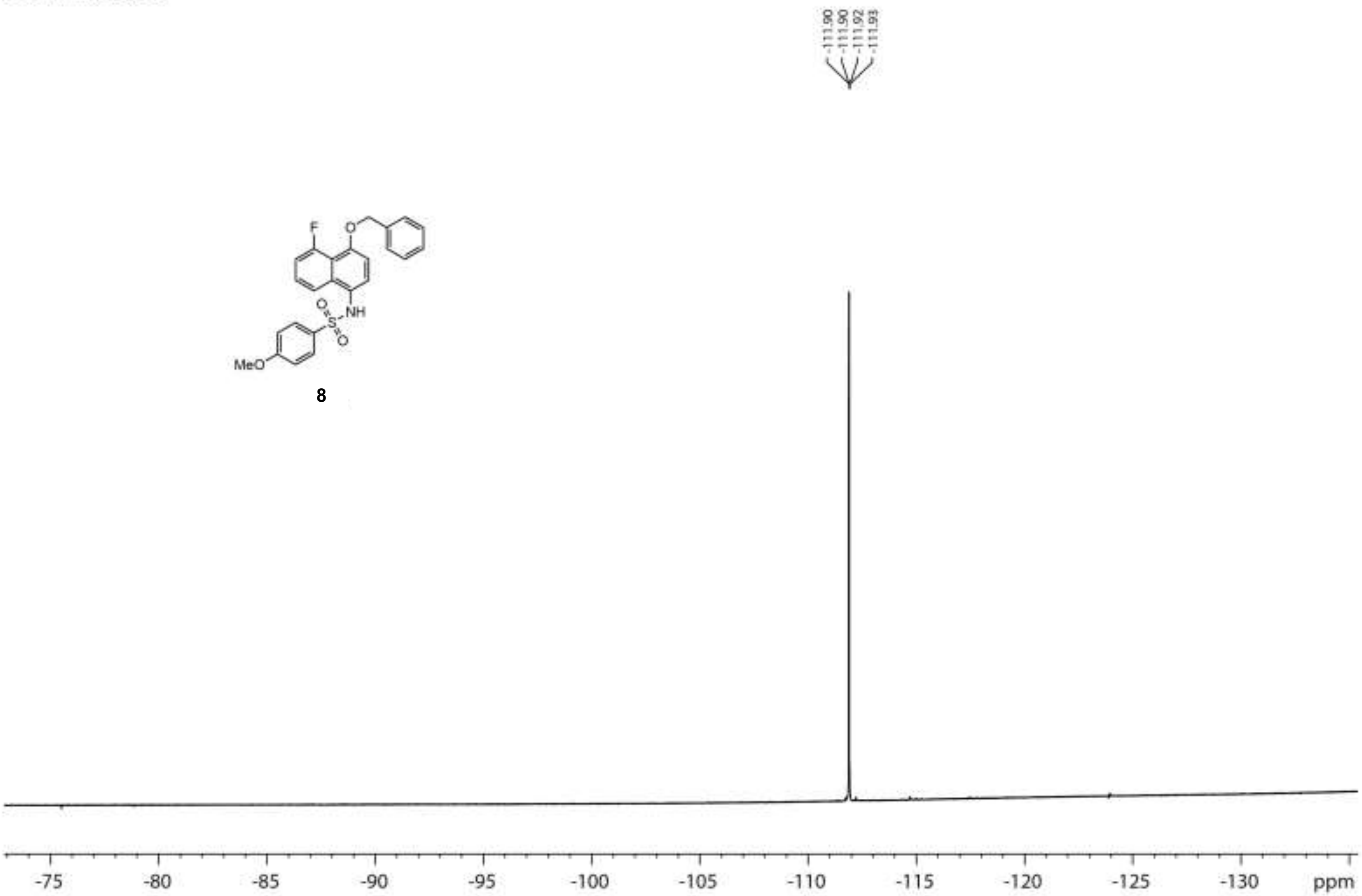

565 MHz, $(CD_3)_2CO$
-109.33
-109.34
-109.35
-109.36
F
OBn
^-O
N^+
O
S1
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
ppm


600 MHz, (CD$_3$)$_2$CO
7.9071
7.8928
7.6242
7.6206
7.6133
7.6096
7.5971
7.5845
7.4310
7.4183
7.4088
7.4051
7.3954
7.3899
7.3504
7.3381
7.1774
7.1638
7.1542
7.1415
7.0236
7.0097
6.9869
6.9834
6.9757
6.9721
5.2863
3.8446
F
OBn
NH
O
S
O
O
1.11
3.85
2.97
0.98
2.05
1.10
2.09
1.88
2.88
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

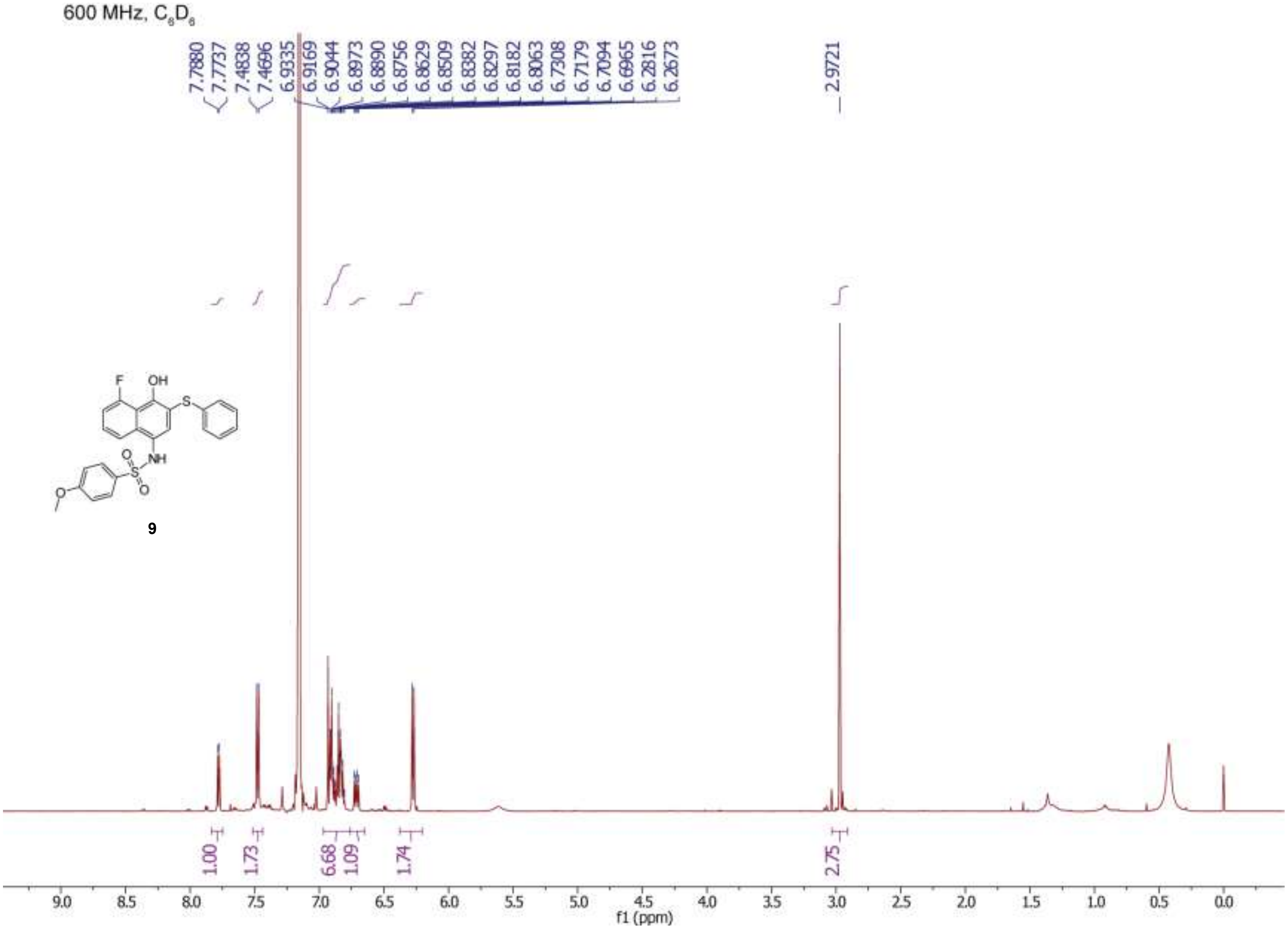
23


151 MHz, (CD₃)₂CO
206.30
163.90
160.86
159.16
154.70
154.67
138.11
135.46
135.44
132.88
130.30
129.33
128.60
128.03
127.65
127.54
127.48
120.54
120.51
117.13
117.06
114.92
114.84
114.76
112.35
112.20
107.46
71.15
56.12
30.30
30.17
30.04
29.92
29.79
29.66
29.53
F
O
NH
O
S
O
MeO
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

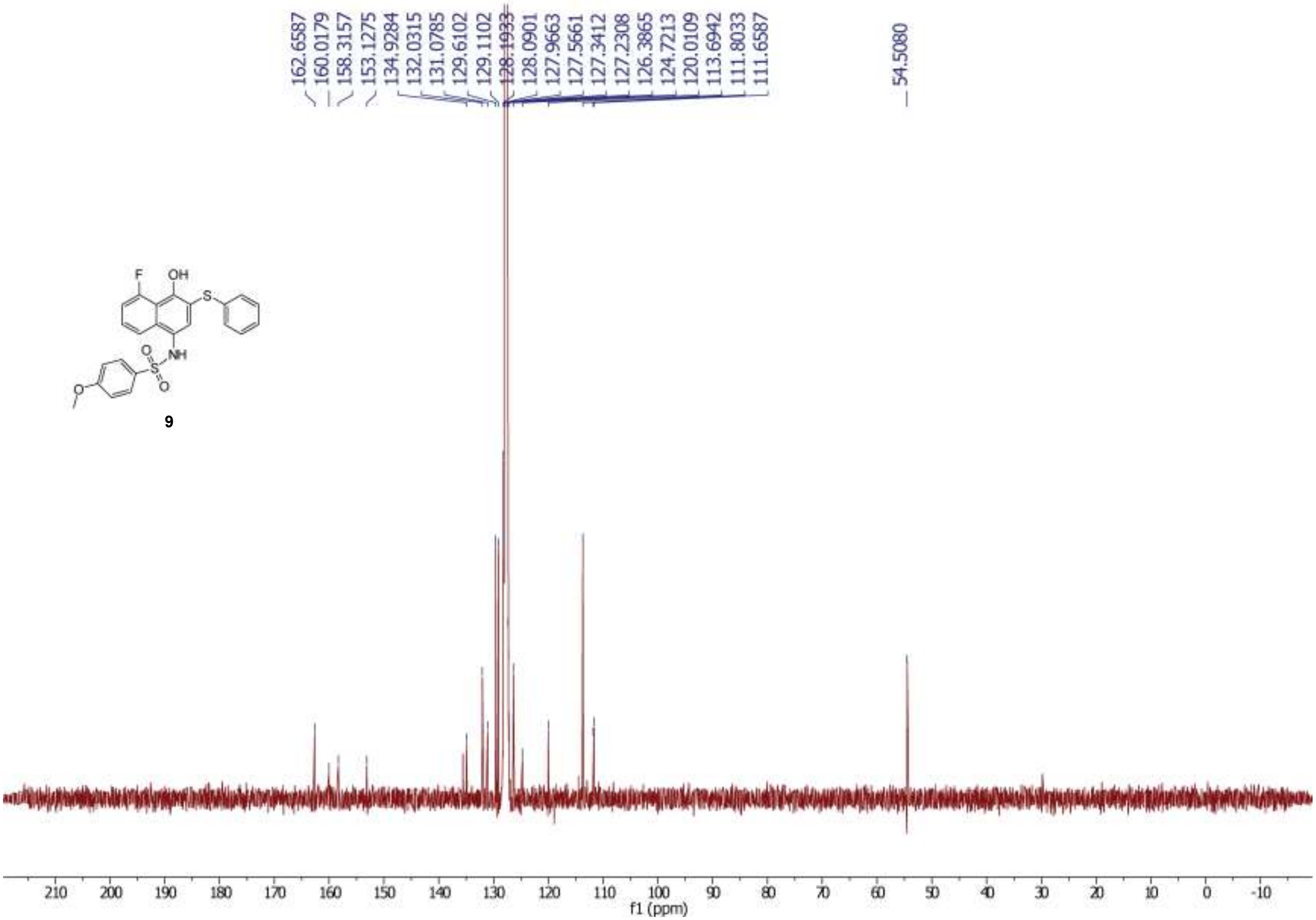
565 MHz, $(CD_3)_2CO$

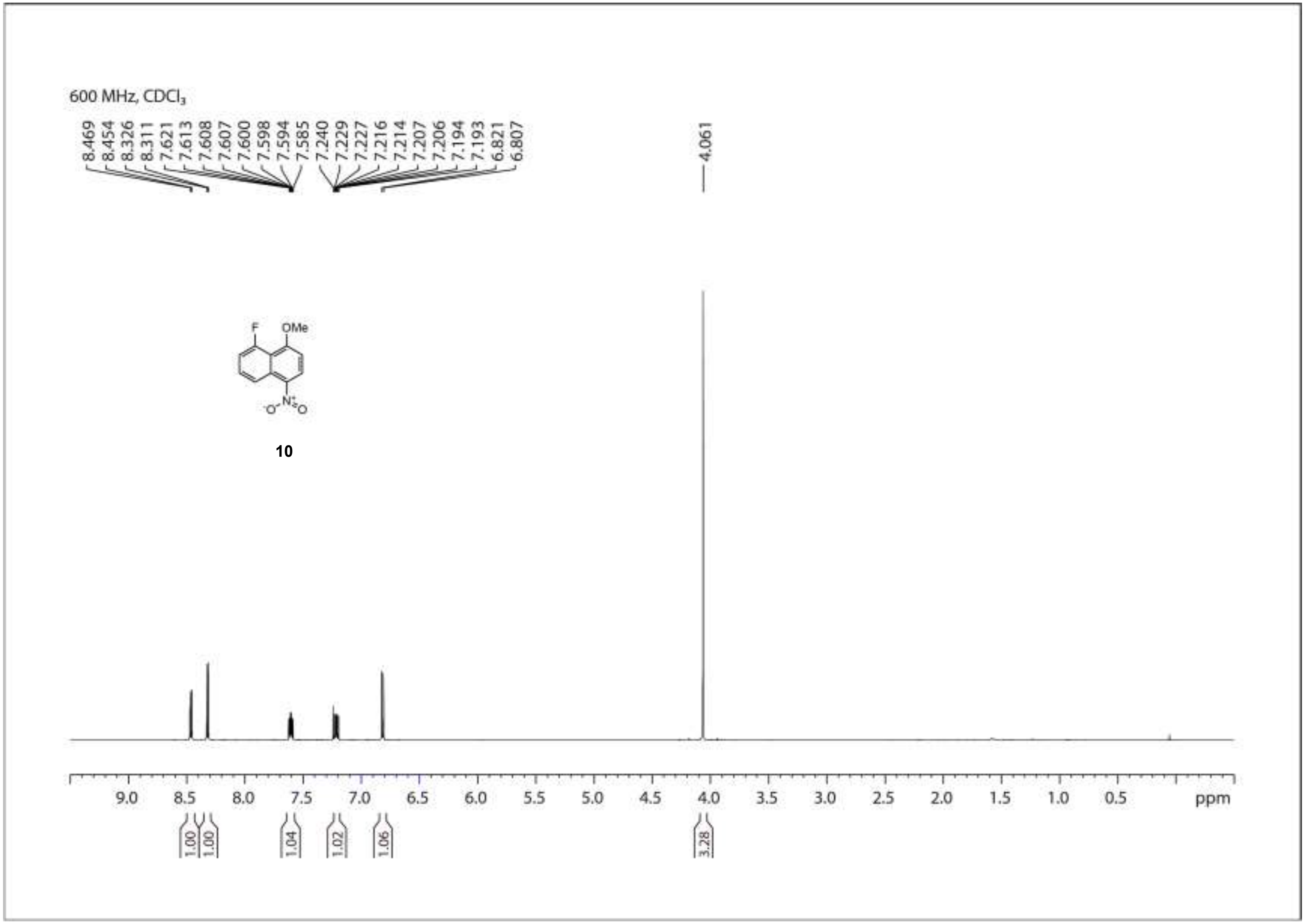


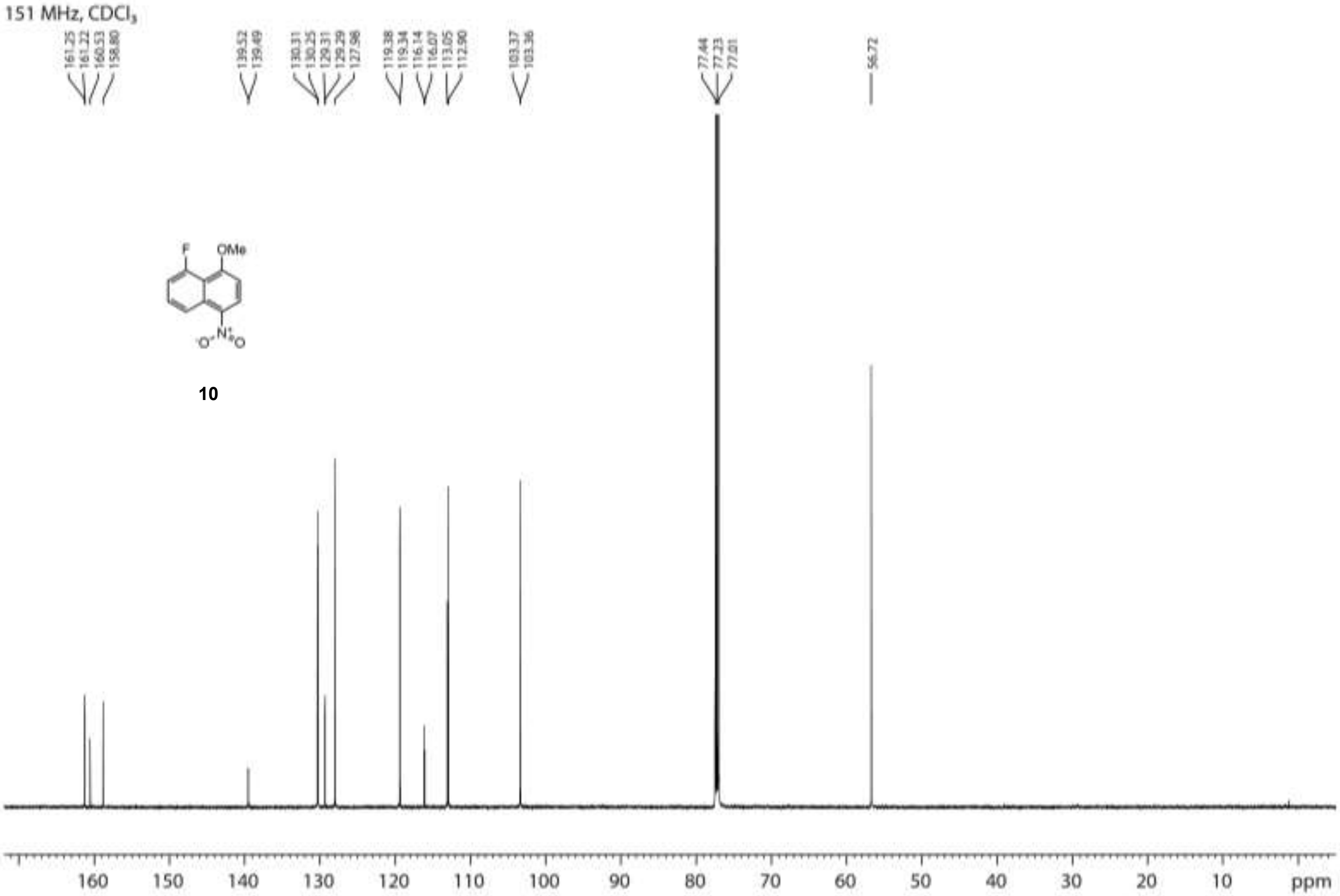
8

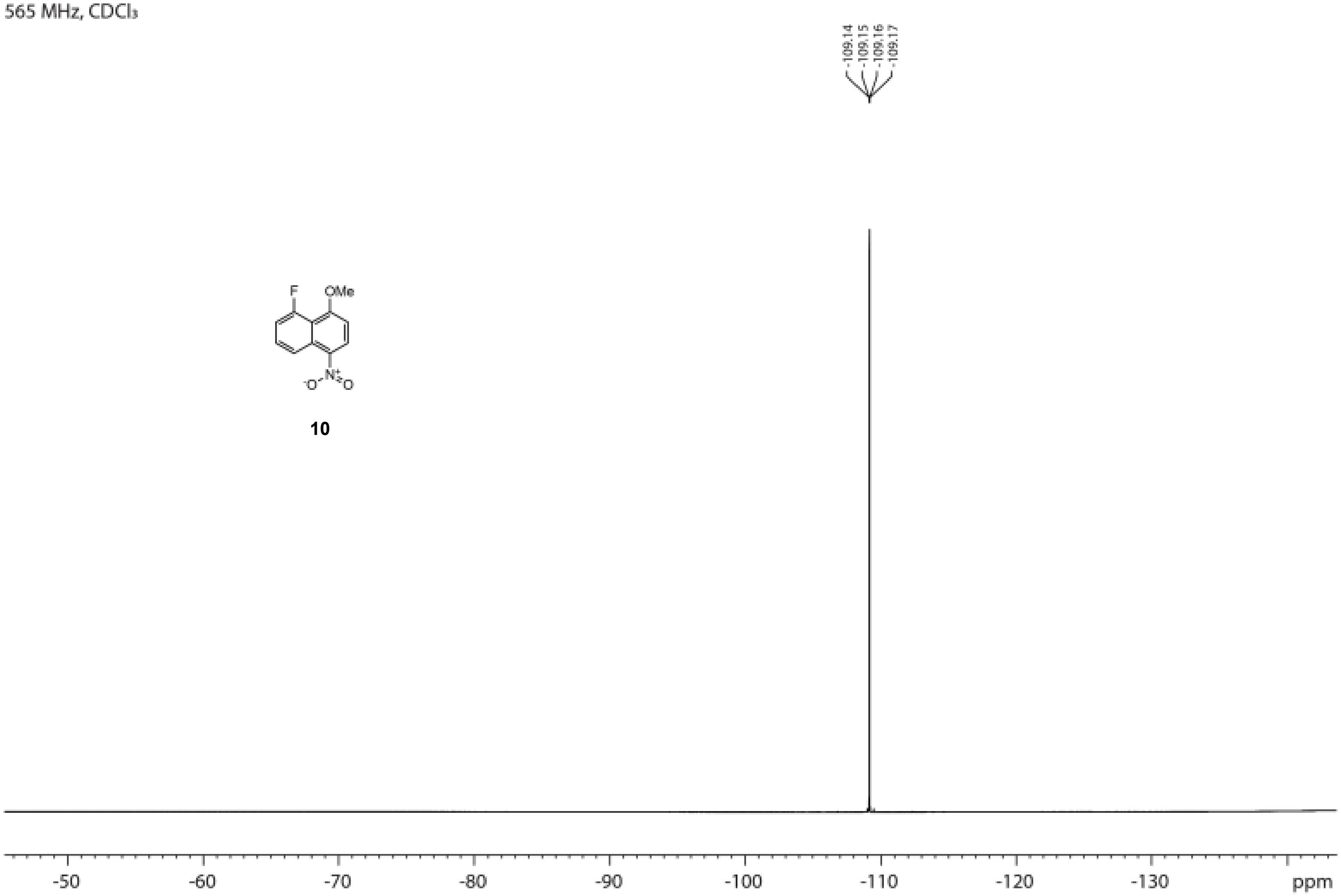

600 MHz, C_6D_6
7.7880
7.7737
7.4838
7.4696
6.9335
6.9169
6.9044
6.8973
6.8890
6.8756
6.8629
6.8509
6.8382
6.8297
6.8182
6.8063
6.7308
6.7179
6.7094
6.6965
6.2816
6.2673
2.9721
F
OH
S
NH
O
S
O
O
9
1.00
1.73
6.68
1.09
1.74
2.75
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

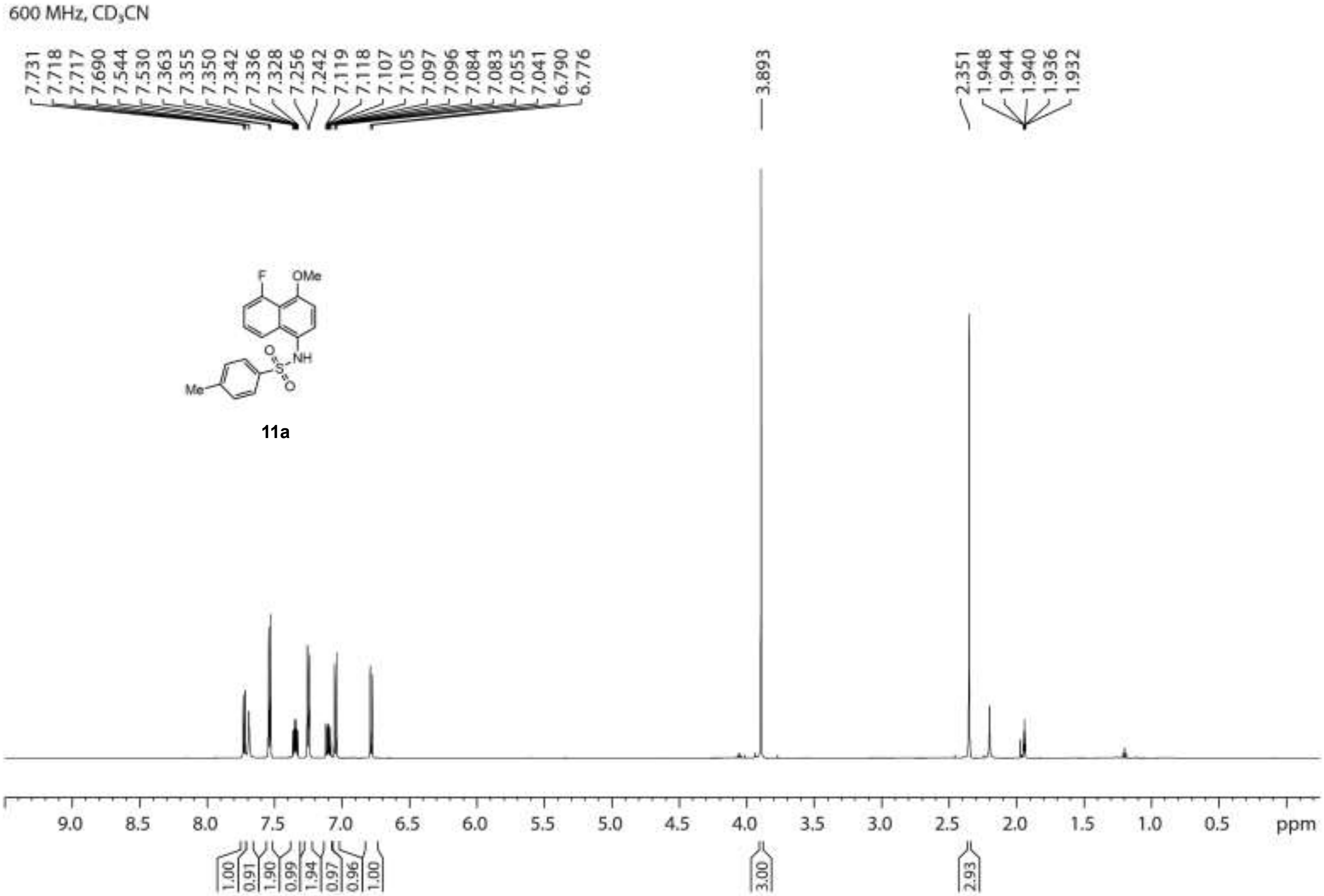
125 MHz, C_6D_6


9

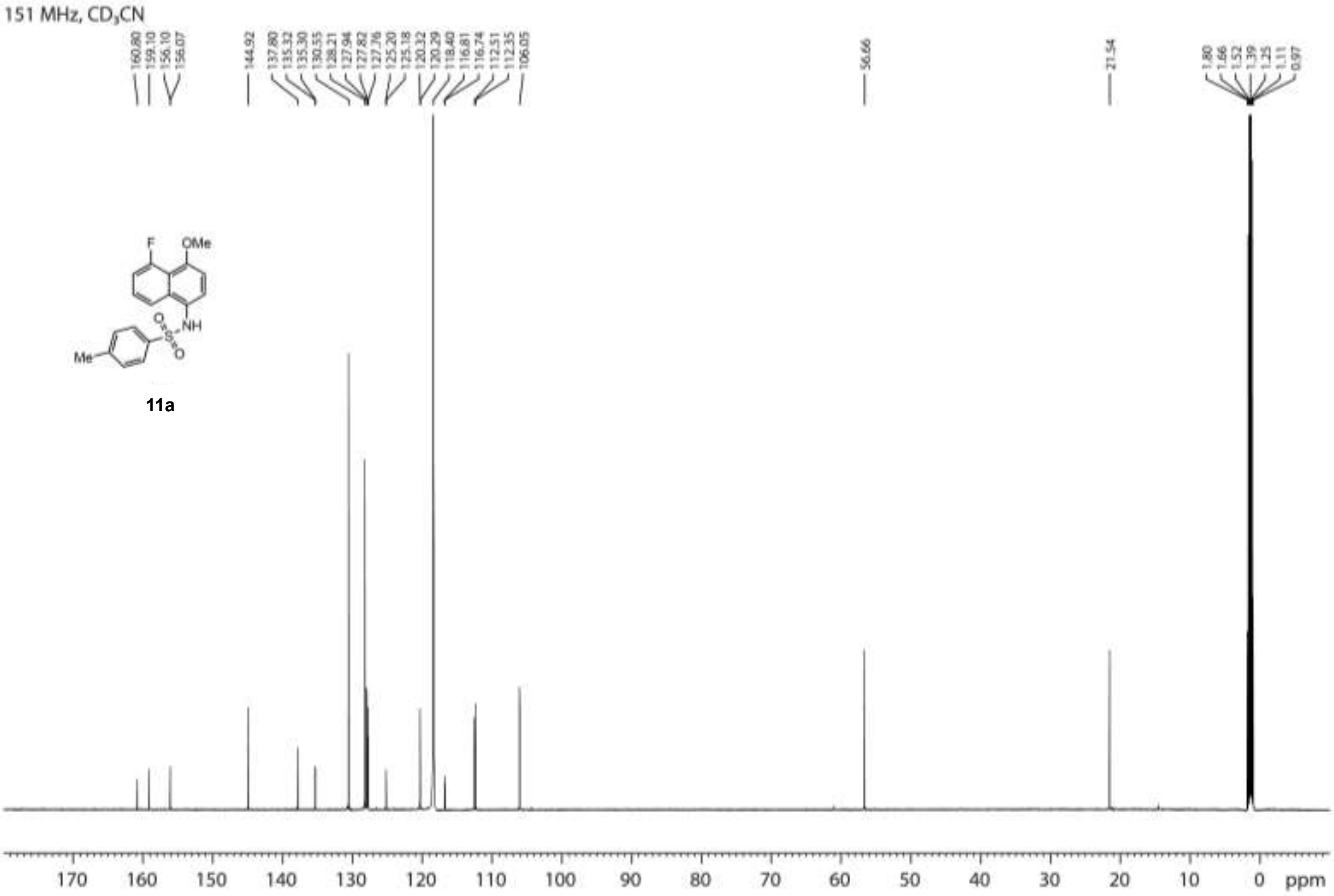

600 MHz, CDCl₃
8.469
8.454
8.326
8.311
7.621
7.613
7.608
7.607
7.600
7.598
7.594
7.585
7.240
7.229
7.227
7.216
7.214
7.207
7.206
7.194
7.193
6.821
6.807
4.061
F
OMe
N
O
O
10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.00
1.04
1.02
1.06
3.28


151 MHz, CDCl3
161.25
161.22
160.53
158.80
139.52
139.49
130.31
130.25
129.31
129.29
127.98
119.38
119.34
116.14
116.07
113.05
112.90
103.37
103.36
77.44
77.23
77.01
56.72
F
OMe
N+
-O
O
10
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

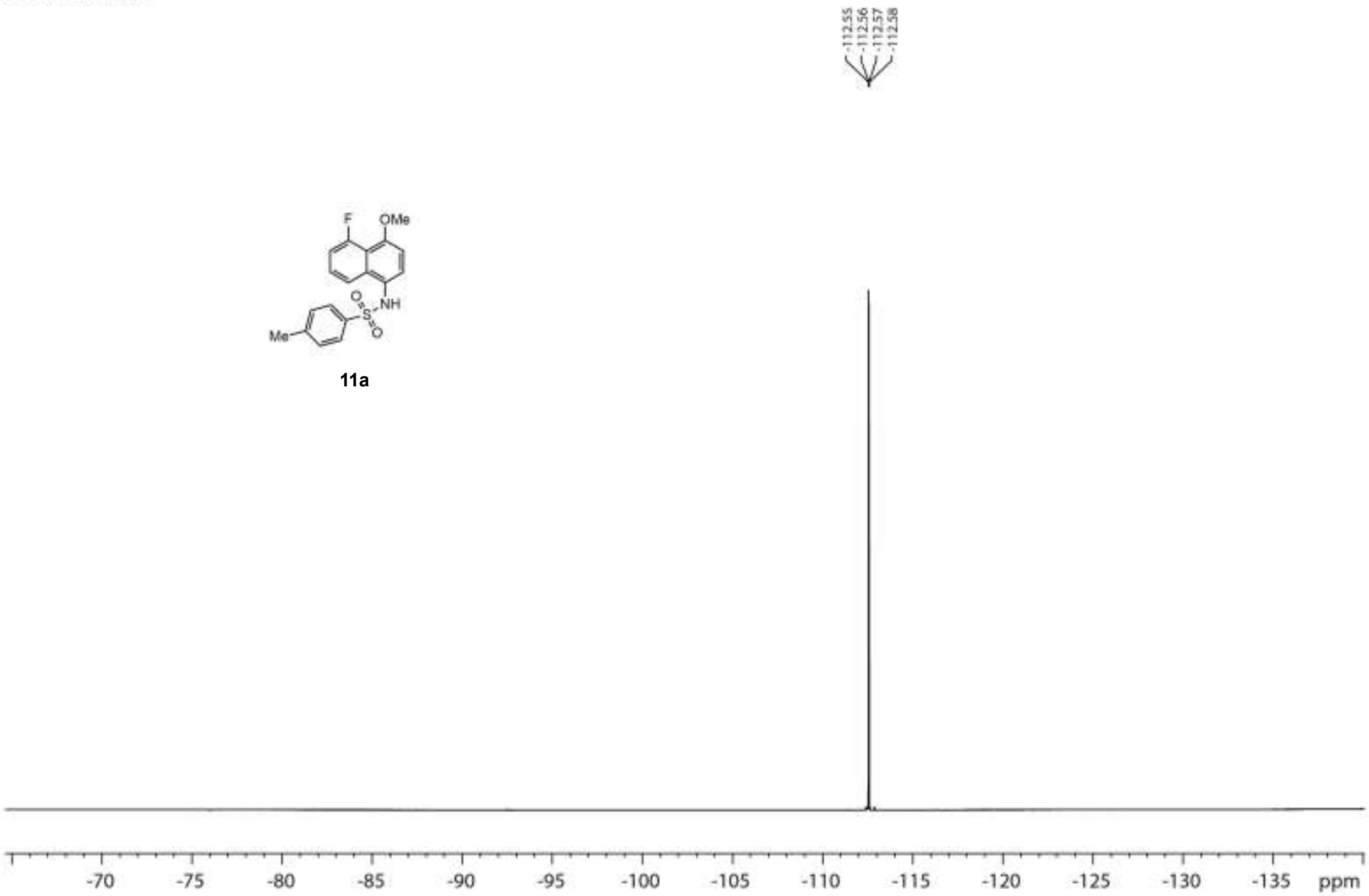

565 MHz, CDCl₃
-109.14
-109.15
-109.16
-109.17
F
OMe
N+
-O
O
10
-50
-60
-70
-80
-90
-100
-110
-120
-130
ppm

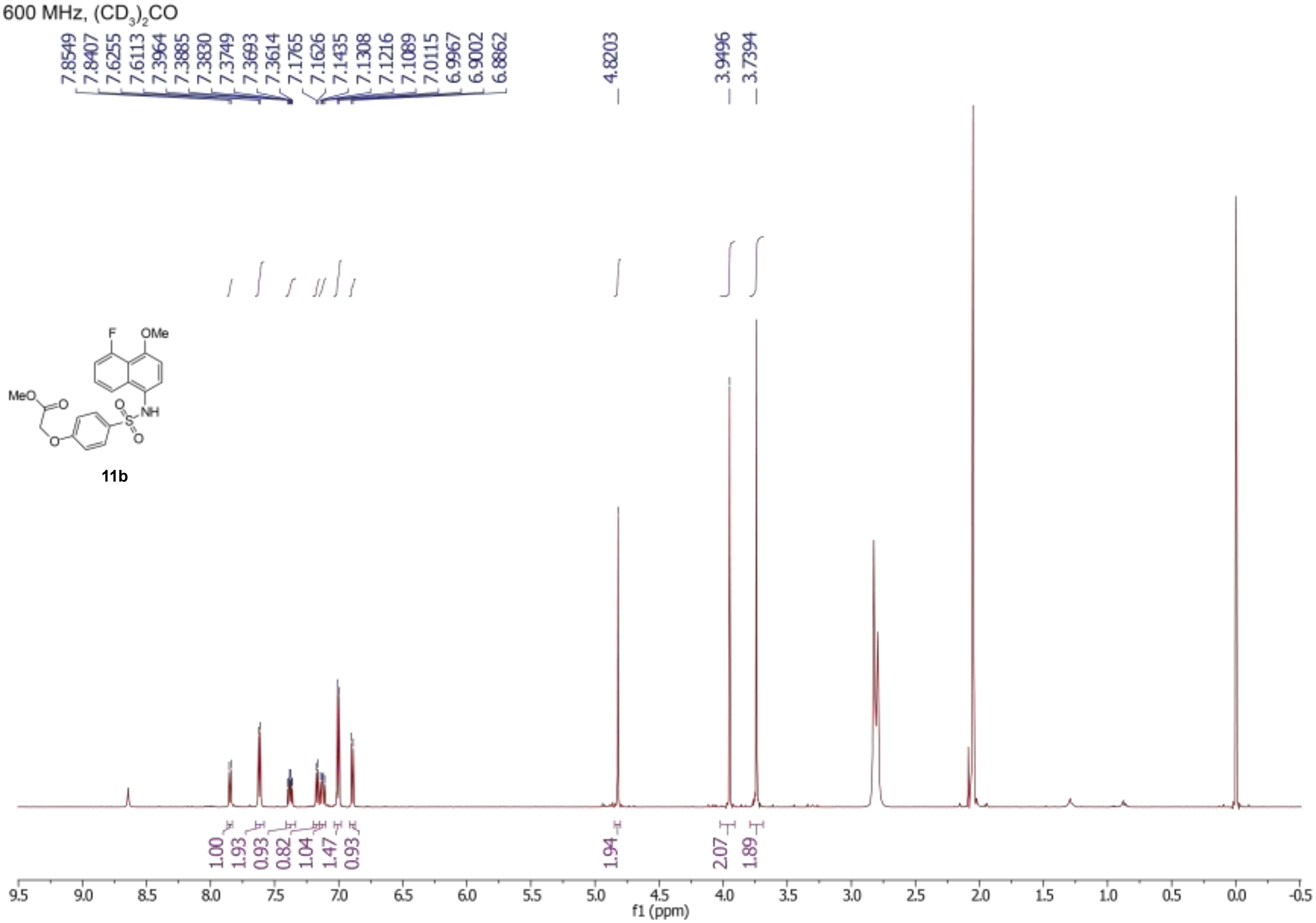

600 MHz, CD_3CN
7.731
7.718
7.717
7.690
7.544
7.530
7.363
7.355
7.350
7.342
7.336
7.328
7.256
7.242
7.119
7.118
7.107
7.105
7.097
7.096
7.084
7.083
7.055
7.041
6.790
6.776
3.893
2.351
1.948
1.944
1.940
1.936
1.932
F
OMe
NH
O
S
O
Me
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
0.91
1.90
0.99
1.94
0.97
0.96
1.00
3.00
2.93

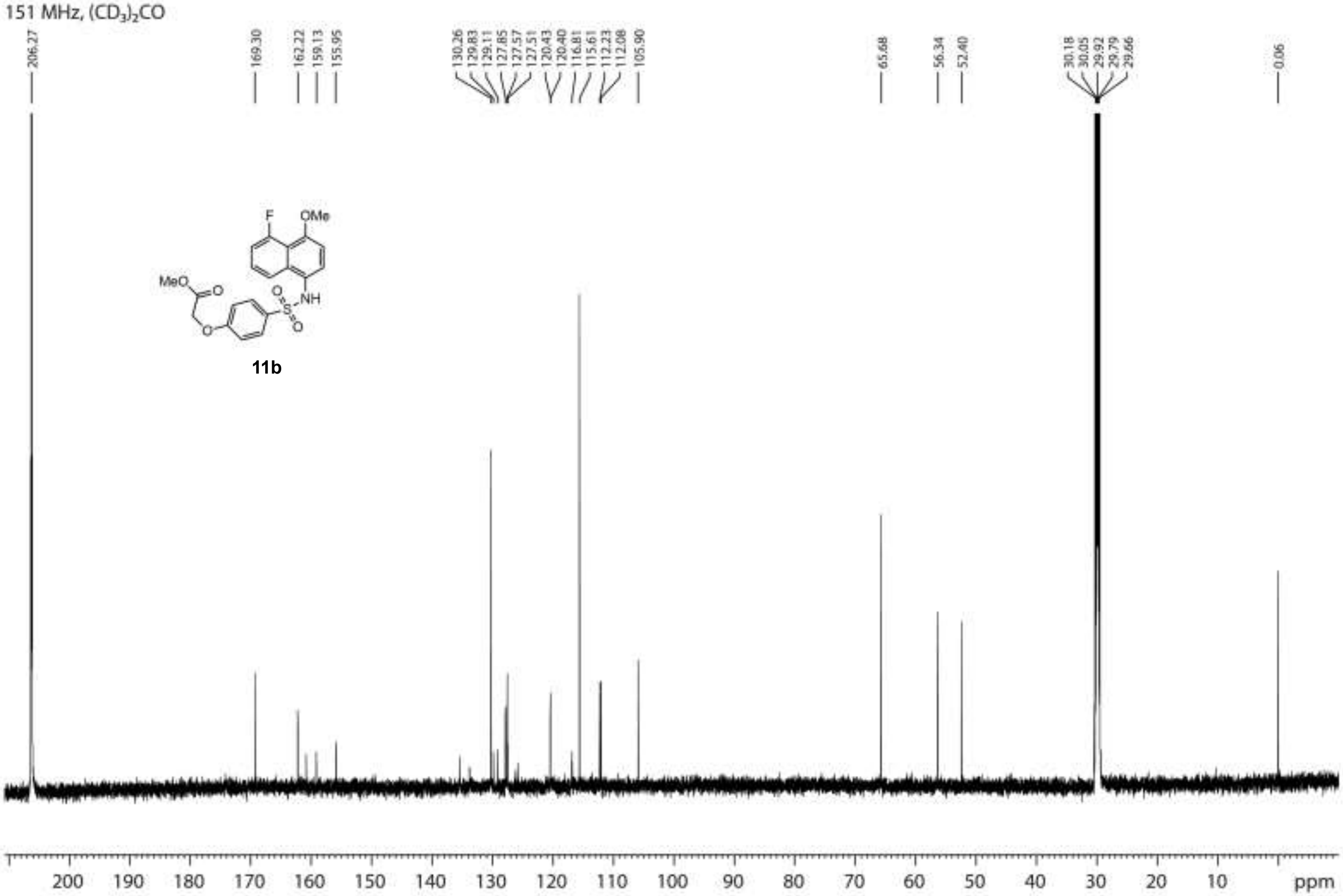
11a


151 MHz, CD$_3$CN
160.80
159.10
156.10
156.07
144.92
137.80
135.32
135.30
130.55
128.21
127.94
127.82
127.76
125.20
125.18
120.32
120.29
118.40
116.81
116.74
112.51
112.35
106.05
56.66
21.54
1.80
1.66
1.52
1.39
1.25
1.11
0.97
F
OMe
NH
O
S
O
Me
11a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

565 MHz, CD3CN

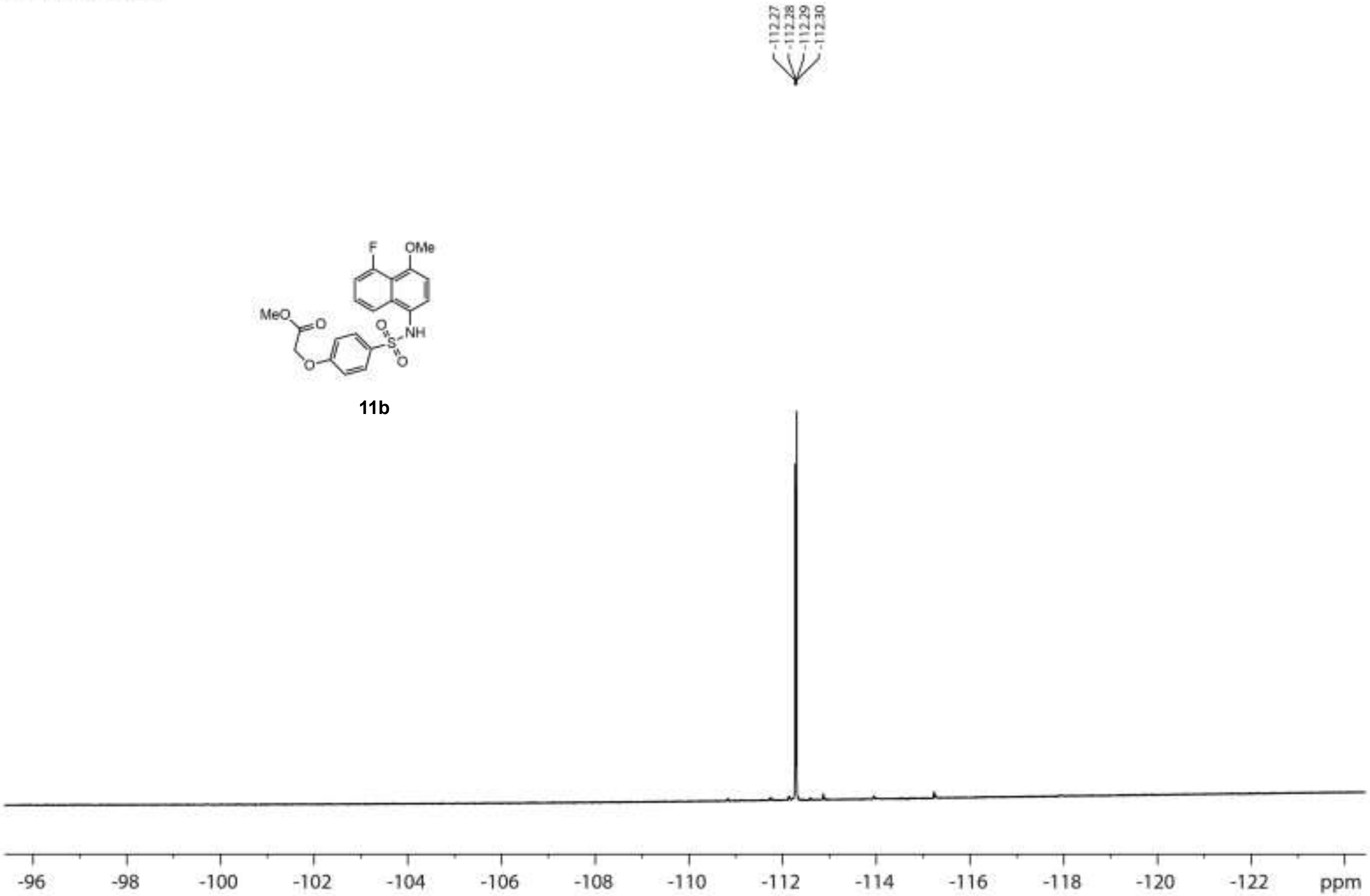


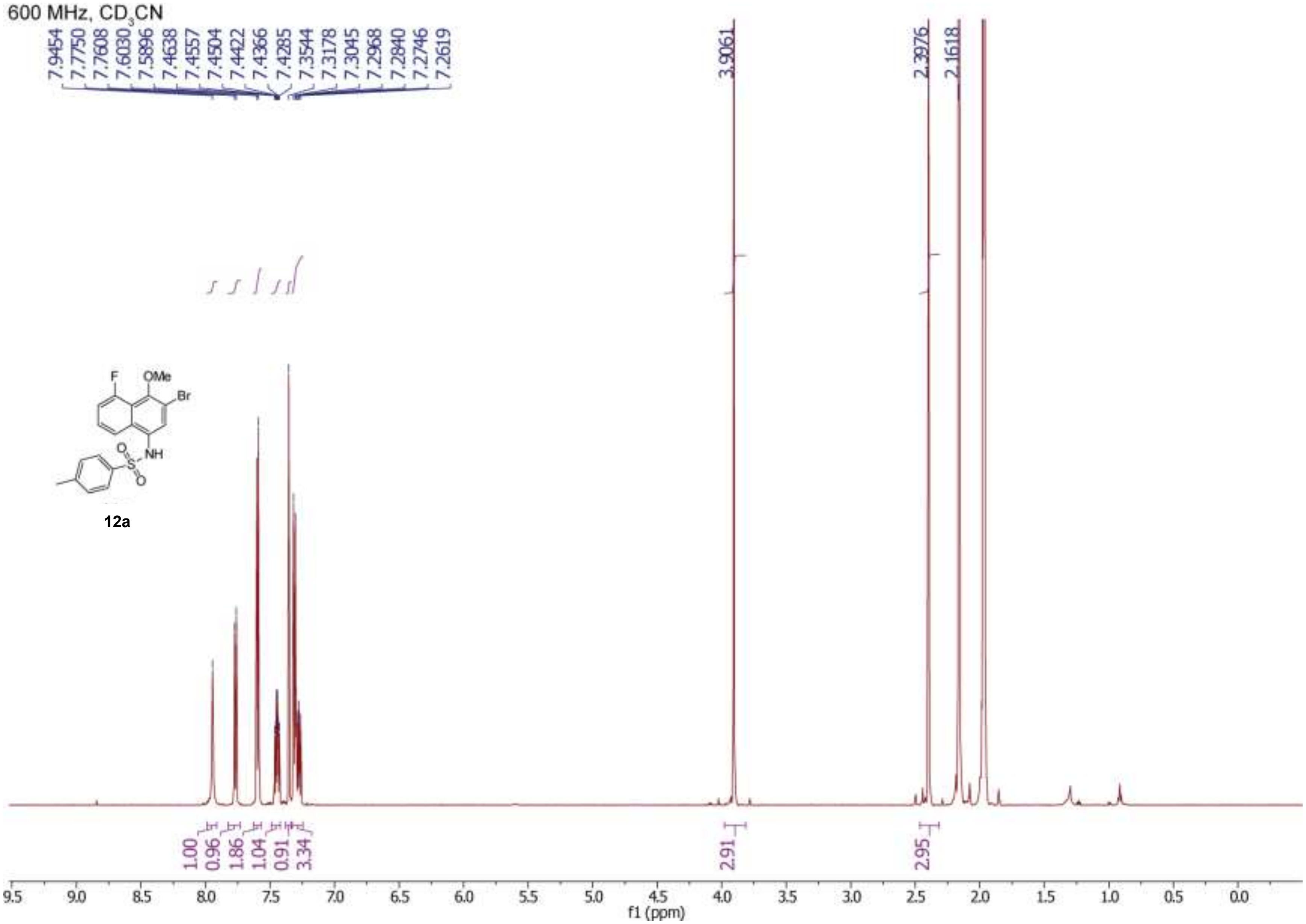

600 MHz, $(CD_3)_2CO$
7.8549
7.8407
7.6255
7.6113
7.3964
7.3885
7.3830
7.3749
7.3693
7.3614
7.1765
7.1626
7.1435
7.1308
7.1216
7.1089
7.0115
6.9967
6.9002
6.8862
4.8203
3.9496
3.7394
F
OMe
MeO
O
NH
S
O
O
O
11b
1.00
1.93
0.93
0.82
1.04
1.47
0.93
1.94
2.07
1.89
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

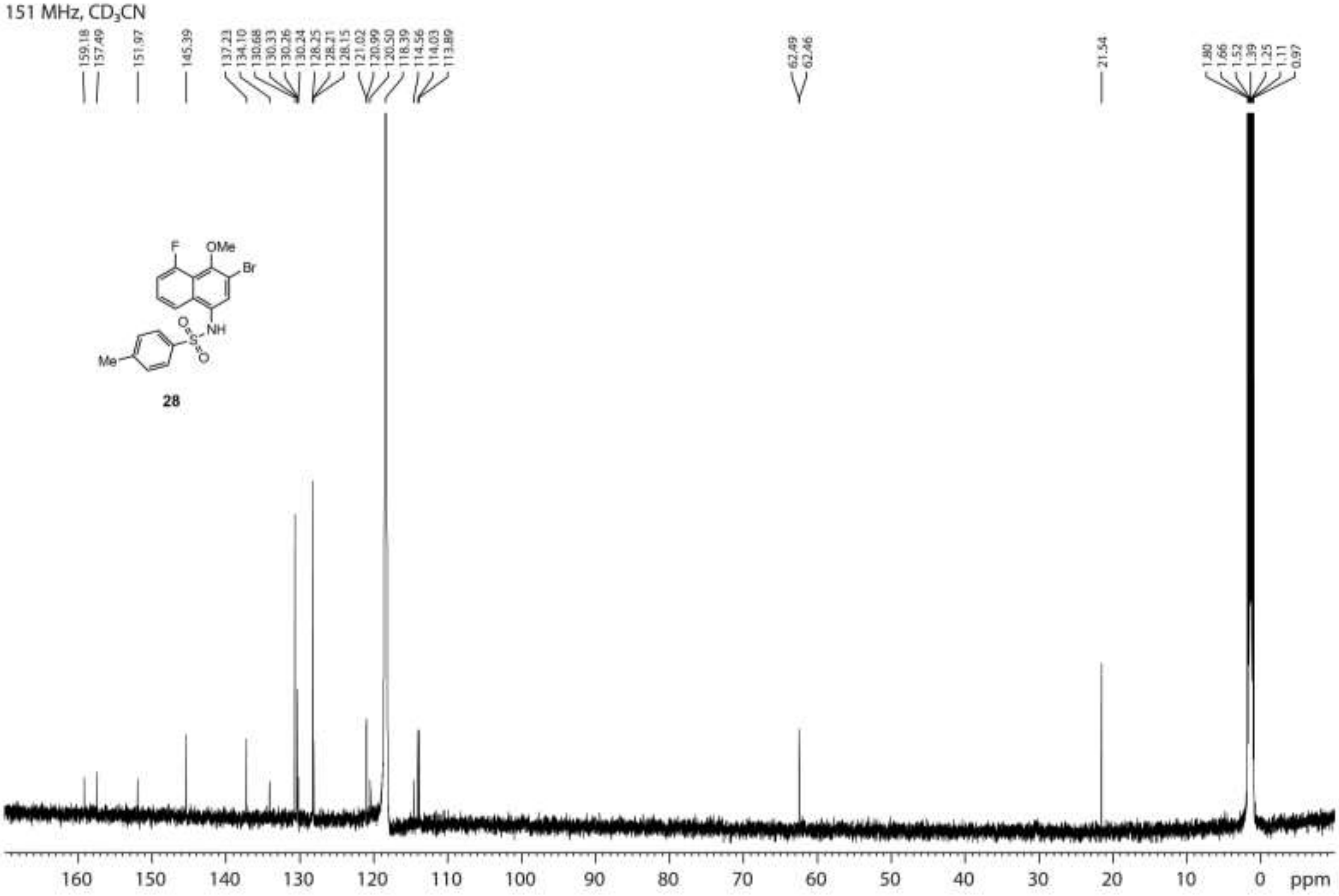

151 MHz, $(CD_3)_2CO$
206.27
169.30
162.22
159.13
155.95
130.26
129.83
129.11
127.85
127.57
127.51
120.43
120.40
116.81
115.61
112.23
112.08
105.90
65.68
56.34
52.40
30.18
30.05
29.92
29.79
29.66
0.06
F
OMe
MeO
O
NH
S
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

11b

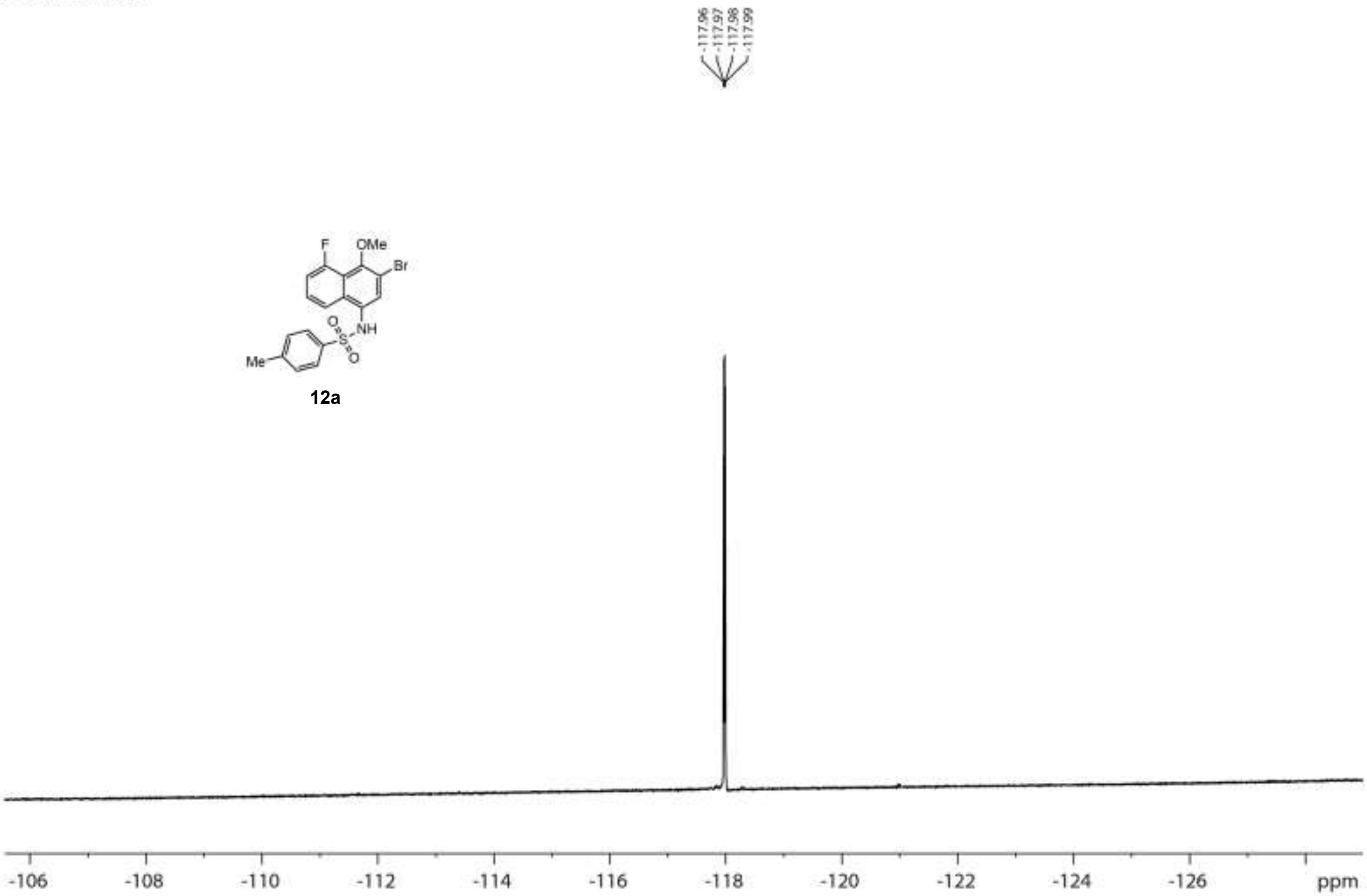
565 MHz, $(CD_3)_2CO$

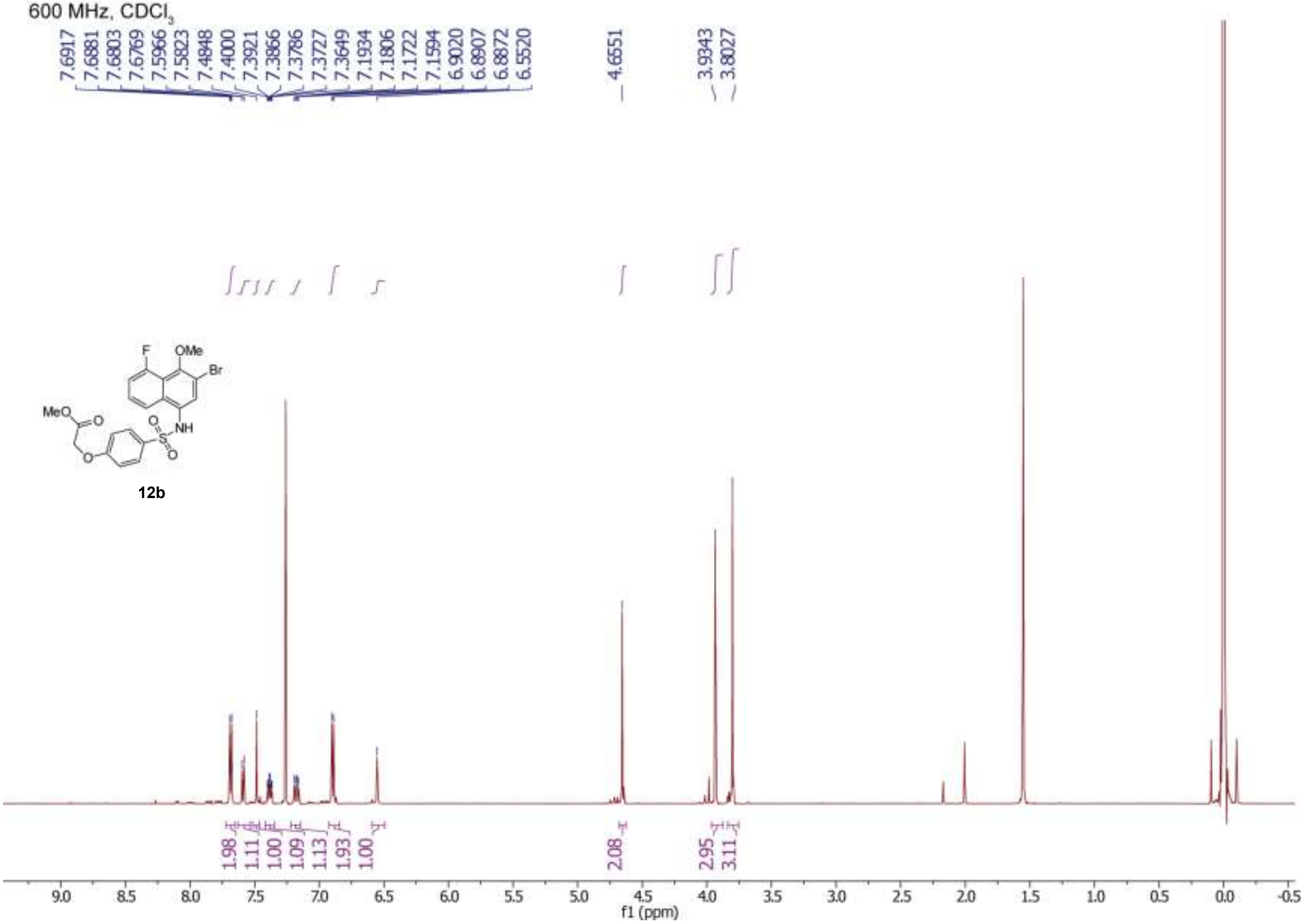


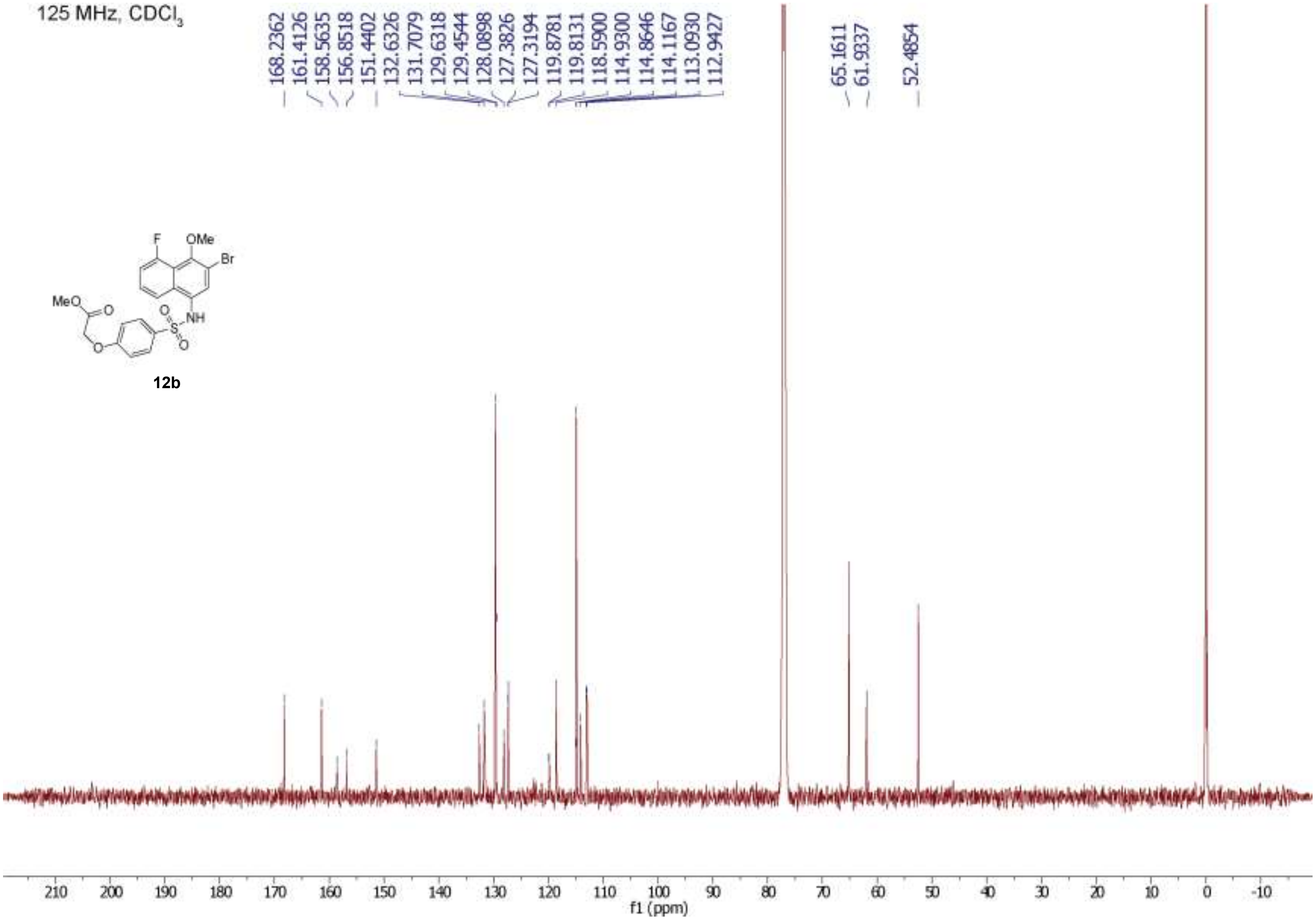

600 MHz, CD$_3$CN
7.9454
7.7750
7.7608
7.6030
7.5896
7.4638
7.4557
7.4504
7.4422
7.4366
7.4285
7.3544
7.3178
7.3045
7.2968
7.2840
7.2746
7.2619
3.9061
2.3976
2.1618
F
OMe
Br
NH
S
O
O
12a
1.00
0.96
1.86
1.04
0.91
3.34
2.91
2.95
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


151 MHz, CD_3CN
159.18
157.49
151.97
145.39
137.23
134.10
130.68
130.33
130.26
130.24
128.25
128.21
128.15
121.02
120.99
120.50
118.39
114.56
114.03
113.89
62.49
62.46
21.54
1.80
1.66
1.52
1.39
1.25
1.11
0.97
F
OMe
Br
NH
S
O
O
Me
28
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

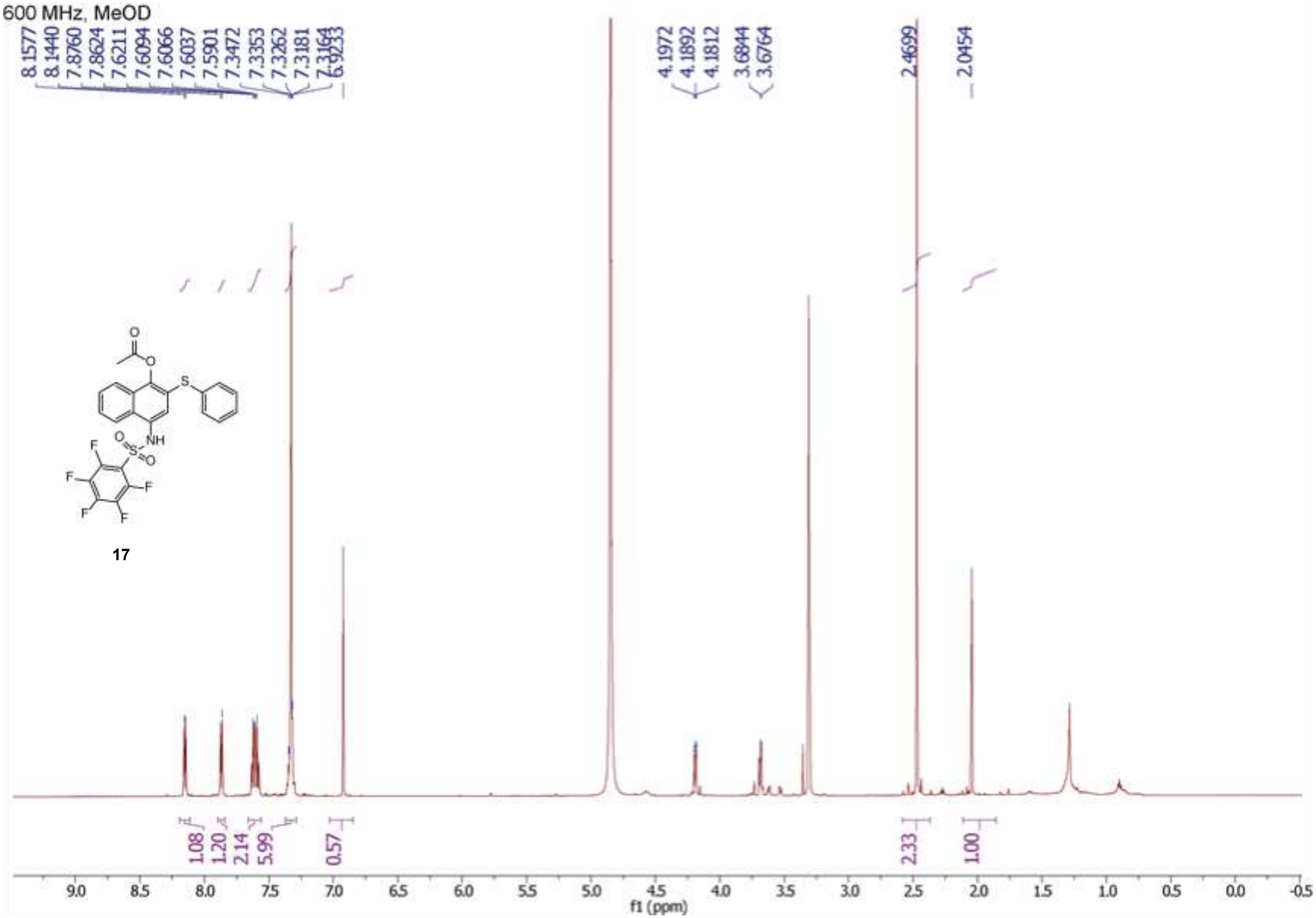
565 MHz, CD_3CN



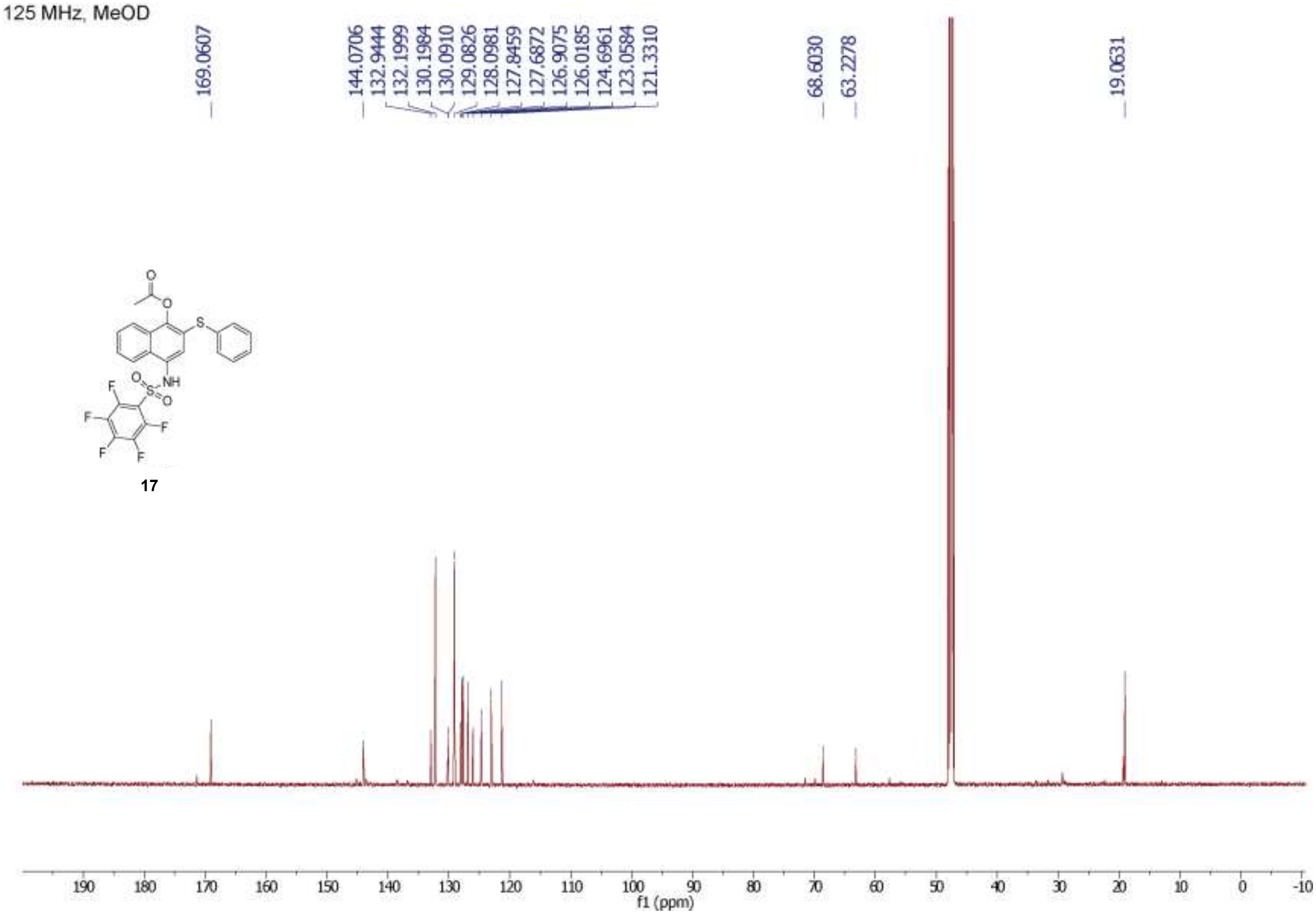

600 MHz, $CDCl_3$
7.6917
7.6881
7.6803
7.6769
7.5966
7.5823
7.4848
7.4000
7.3921
7.3866
7.3786
7.3727
7.3649
7.1934
7.1806
7.1722
7.1594
6.9020
6.8907
6.8872
6.5520
4.6551
3.9343
3.8027
F
OMe
Br
MeO
O
NH
S
O
O
O
12b
1.98
1.11
1.00
1.09
1.13
1.93
1.00
2.08
2.95
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

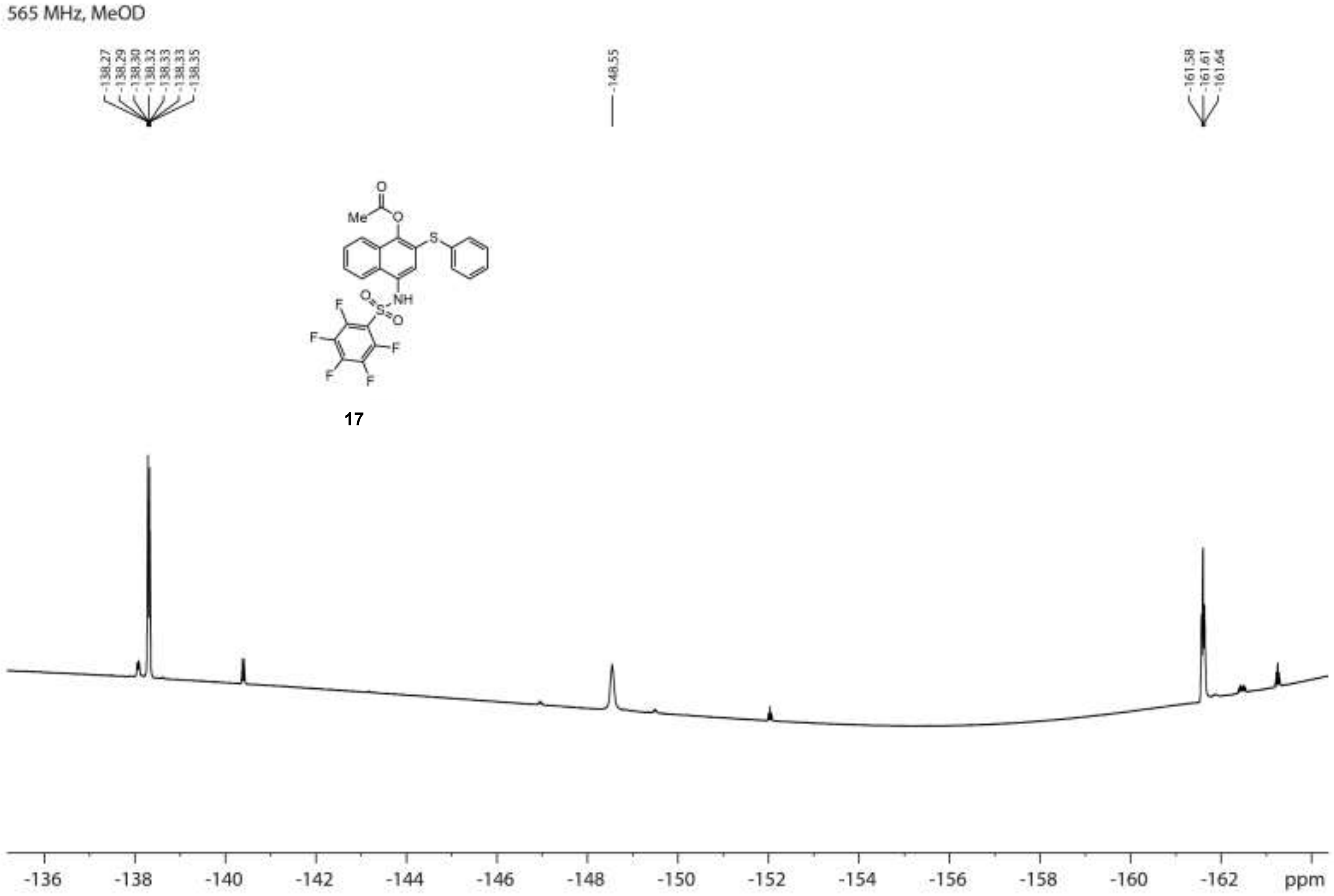

125 MHz, CDCl3
168.2362
161.4126
158.5635
156.8518
151.4402
132.6326
131.7079
129.6318
129.4544
128.0898
127.3826
127.3194
119.8781
119.8131
118.5900
114.9300
114.8646
114.1167
113.0930
112.9427
65.1611
61.9337
52.4854
F
OMe
Br
MeO
O
NH
O
S
O
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

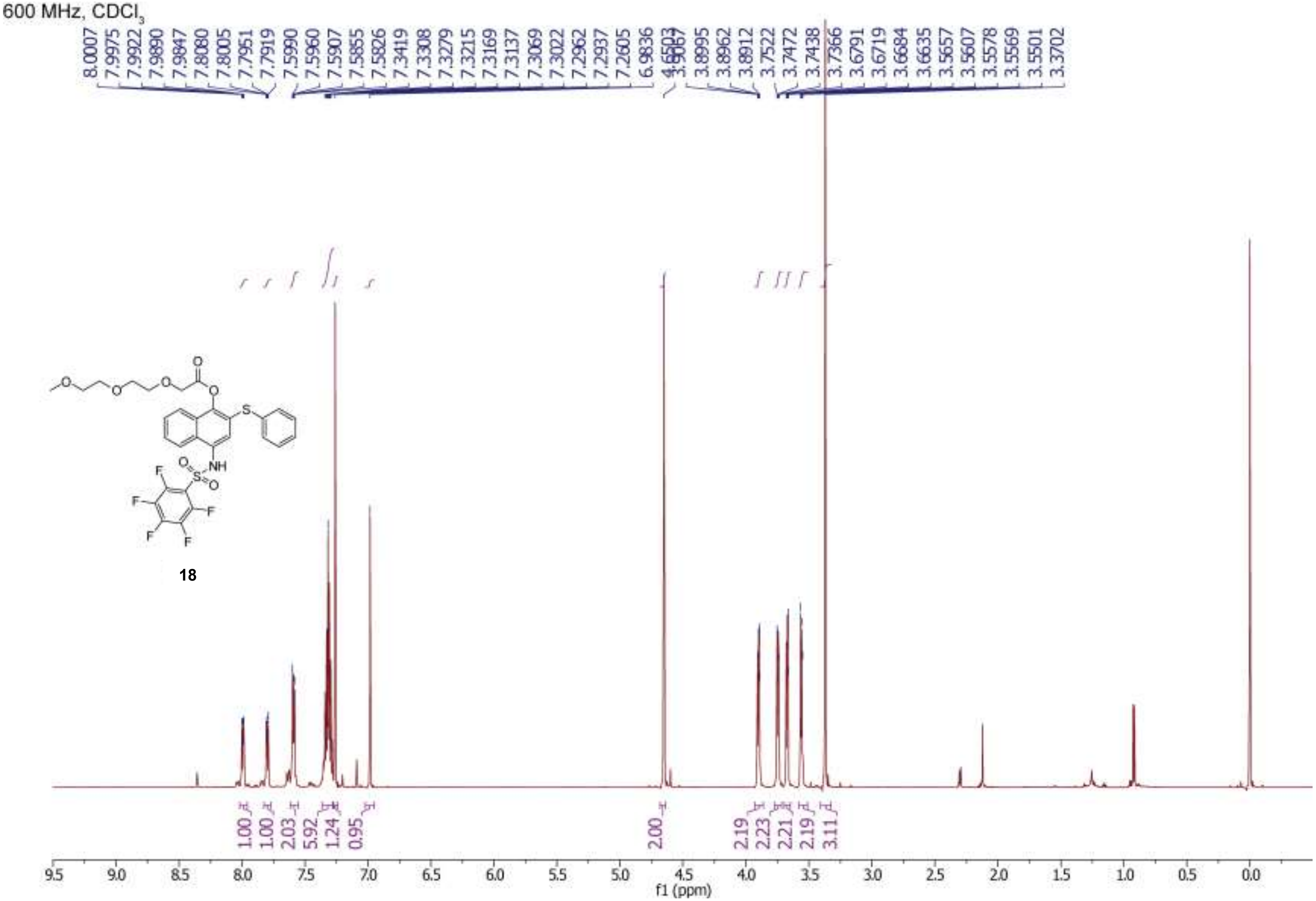
12b

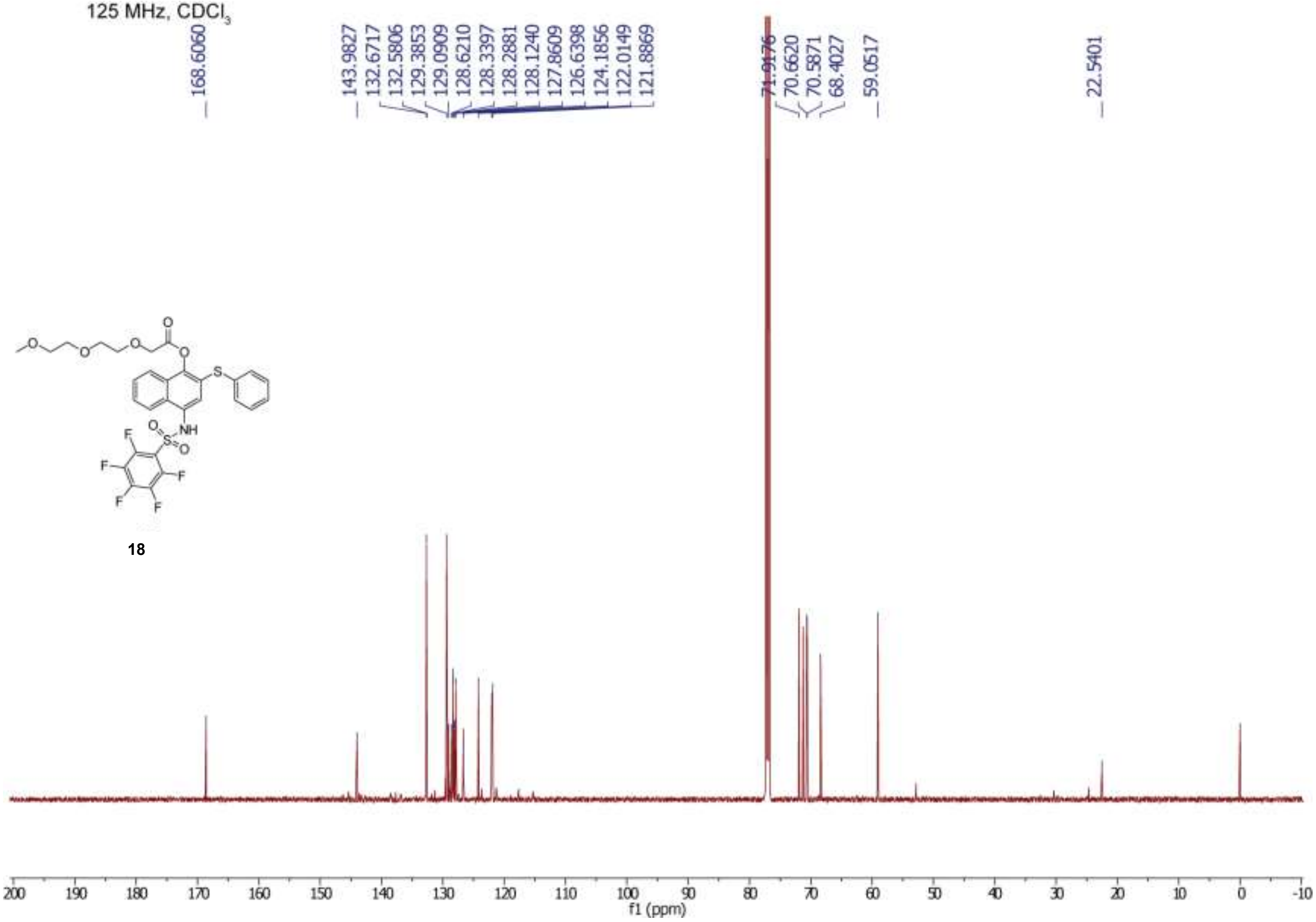

600 MHz, MeOD
8.1577
8.1440
7.8760
7.8624
7.6211
7.6094
7.6066
7.6037
7.5901
7.3472
7.3353
7.3262
7.3181
7.3164
6.9233
4.1972
4.1892
4.1812
3.6844
3.6764
2.4699
2.0454
O
O
S
NH
O
S
O
F
F
F
F
F
1.08
1.20
2.14
5.99
0.57
2.33
1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

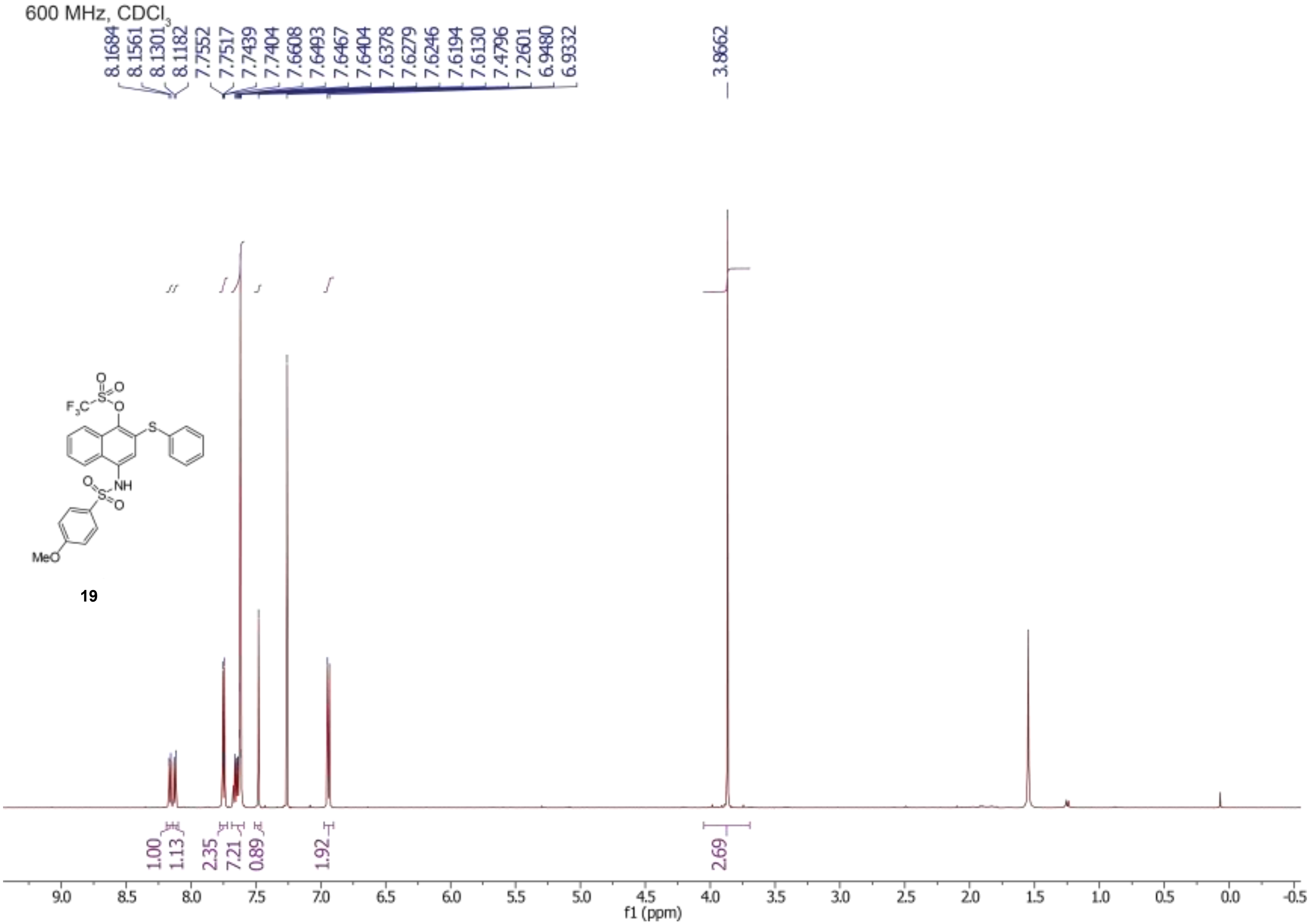
17


125 MHz, MeOD
169.0607
144.0706
132.9444
132.1999
130.1984
130.0910
129.0826
128.0981
127.8459
127.6872
126.9075
126.0185
124.6961
123.0584
121.3310
68.6030
63.2278
19.0631
O
O
S
NH
O
S
O
F
F
F
F
F
17
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

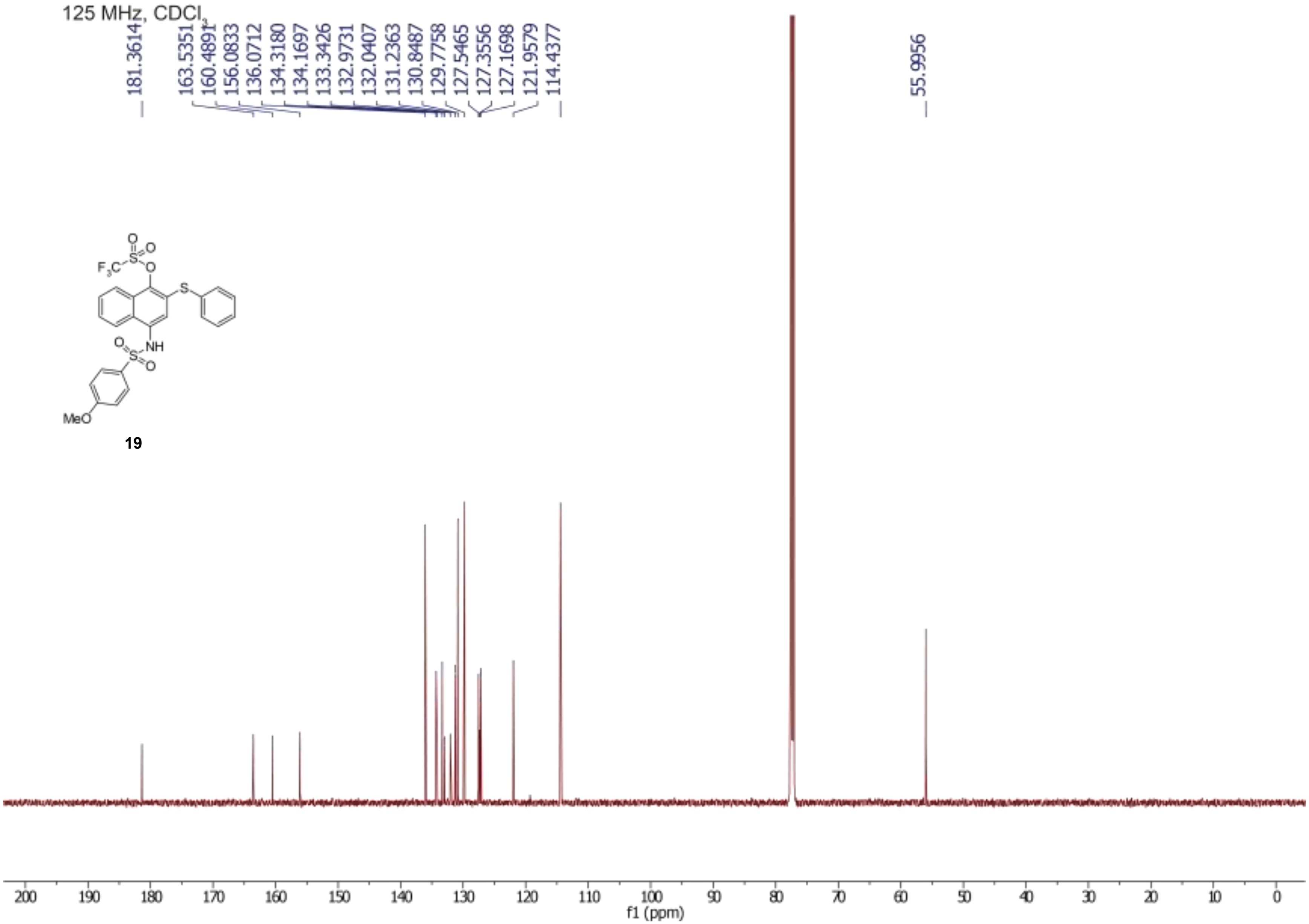

565 MHz, MeOD
-138.27
-138.29
-138.30
-138.32
-138.33
-138.33
-138.35
-148.55
-161.58
-161.61
-161.64
Me
O
O
S
NH
O
S
O
F
F
F
F
F
17
-136
-138
-140
-142
-144
-146
-148
-150
-152
-154
-156
-158
-160
-162
ppm


600 MHz, $CDCl_3$
8.0007
7.9975
7.9922
7.9880
7.9847
7.8080
7.8005
7.7951
7.7919
7.5990
7.5960
7.5907
7.5855
7.5826
7.3419
7.3308
7.3279
7.3215
7.3169
7.3137
7.3069
7.3022
7.2962
7.2937
7.2605
6.9836
4.6503
3.9067
3.8995
3.8962
3.8912
3.7522
3.7472
3.7438
3.7366
3.6791
3.6719
3.6684
3.6635
3.5657
3.5607
3.5578
3.5569
3.5501
3.3702
O
O
O
O
O
S
NH
S
O
O
F
F
F
F
F
18
1.00
1.00
2.03
5.92
1.24
0.95
2.00
2.19
2.23
2.21
2.19
3.11
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

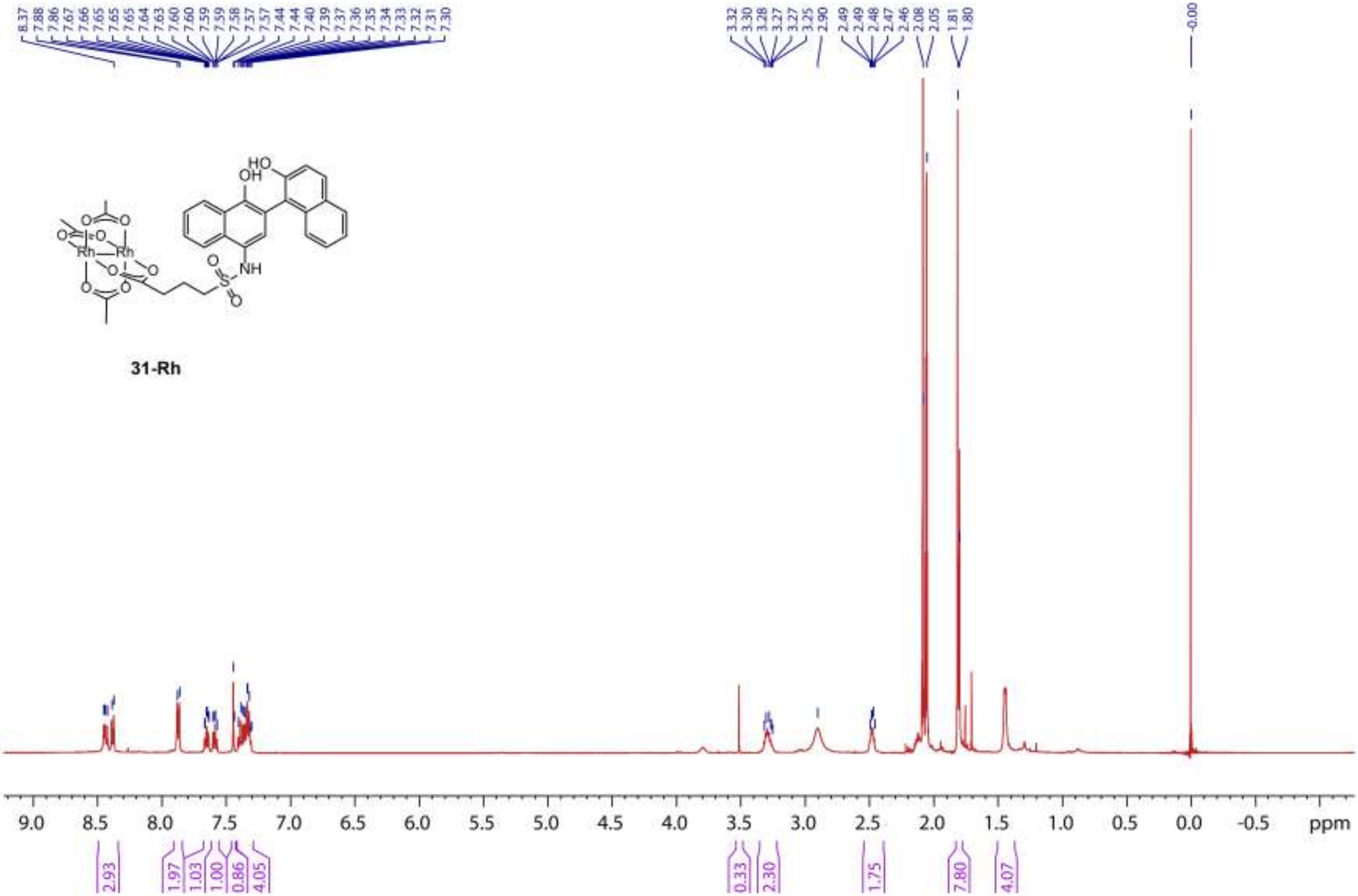

125 MHz, CDCl3
168.6060
143.9827
132.6717
132.5806
129.3853
129.0909
128.6210
128.3397
128.2881
128.1240
127.8609
126.6398
124.1856
122.0149
121.8869
71.9176
70.6620
70.5871
68.4027
59.0517
22.5401
O
O
O
O
O
S
NH
O
S
O
F
F
F
F
F
18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


600 MHz, CDCl$_3$
8.1684
8.1561
8.1301
8.1182
7.7552
7.7517
7.7439
7.7404
7.6608
7.6493
7.6467
7.6404
7.6378
7.6279
7.6246
7.6194
7.6130
7.4796
7.2601
6.9480
6.9332
3.8662
F$_3$C
S
O
O
O
S
NH
O
S
O
MeO
1.00
1.13
2.35
7.21
0.89
1.92
2.69
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

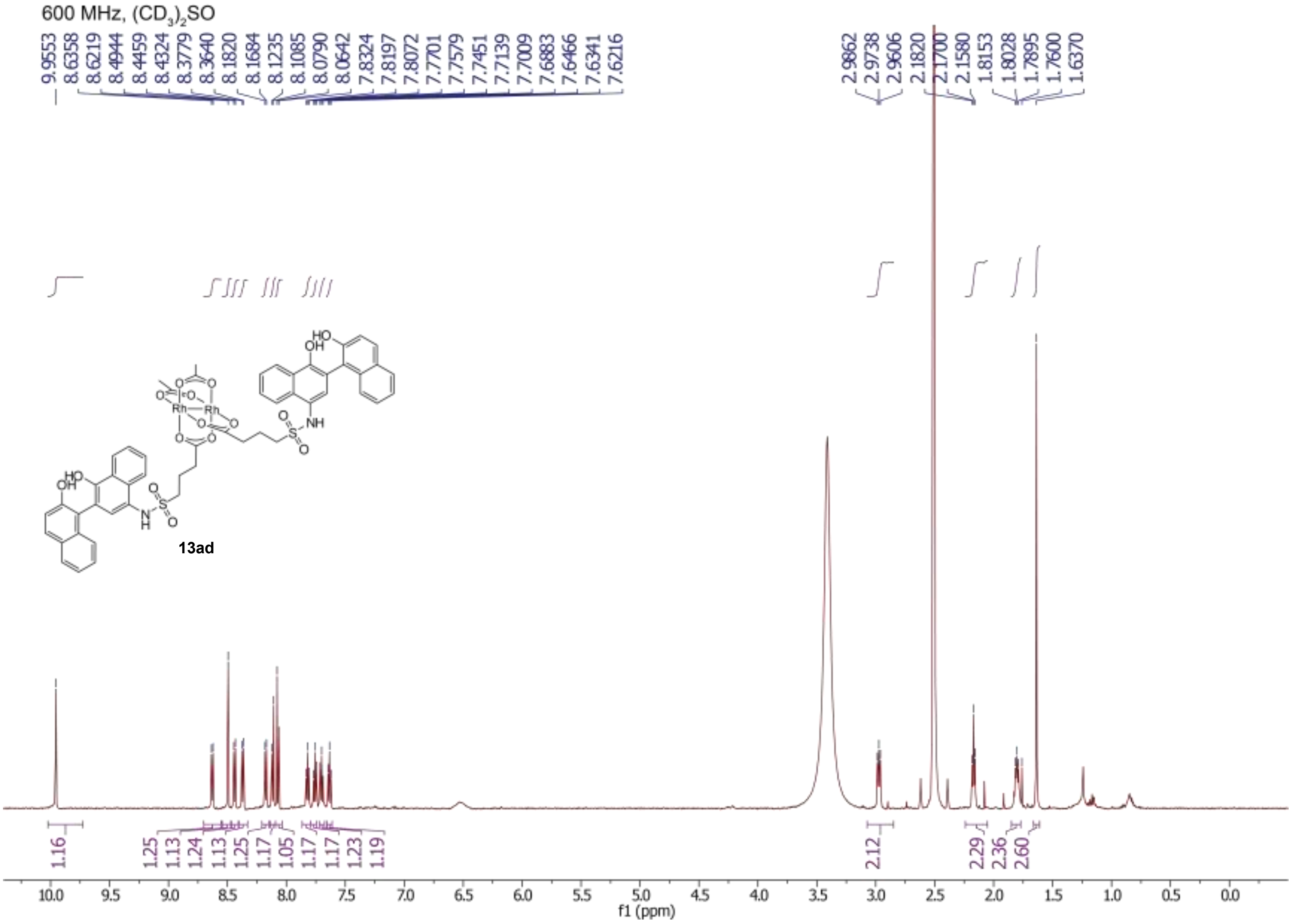
19


125 MHz, CDCl$_3$
181.3614
163.5351
160.4891
156.0833
136.0712
134.3180
134.1697
133.3426
132.9731
132.0407
131.2363
130.8487
129.7758
127.5465
127.3556
127.1698
121.9579
114.4377
55.9956
F$_3$C
S
O
O
O
S
NH
O
S
O
MeO
19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

¹H NMR, ((CD$_3$)$_2$CO, 500 MHz)

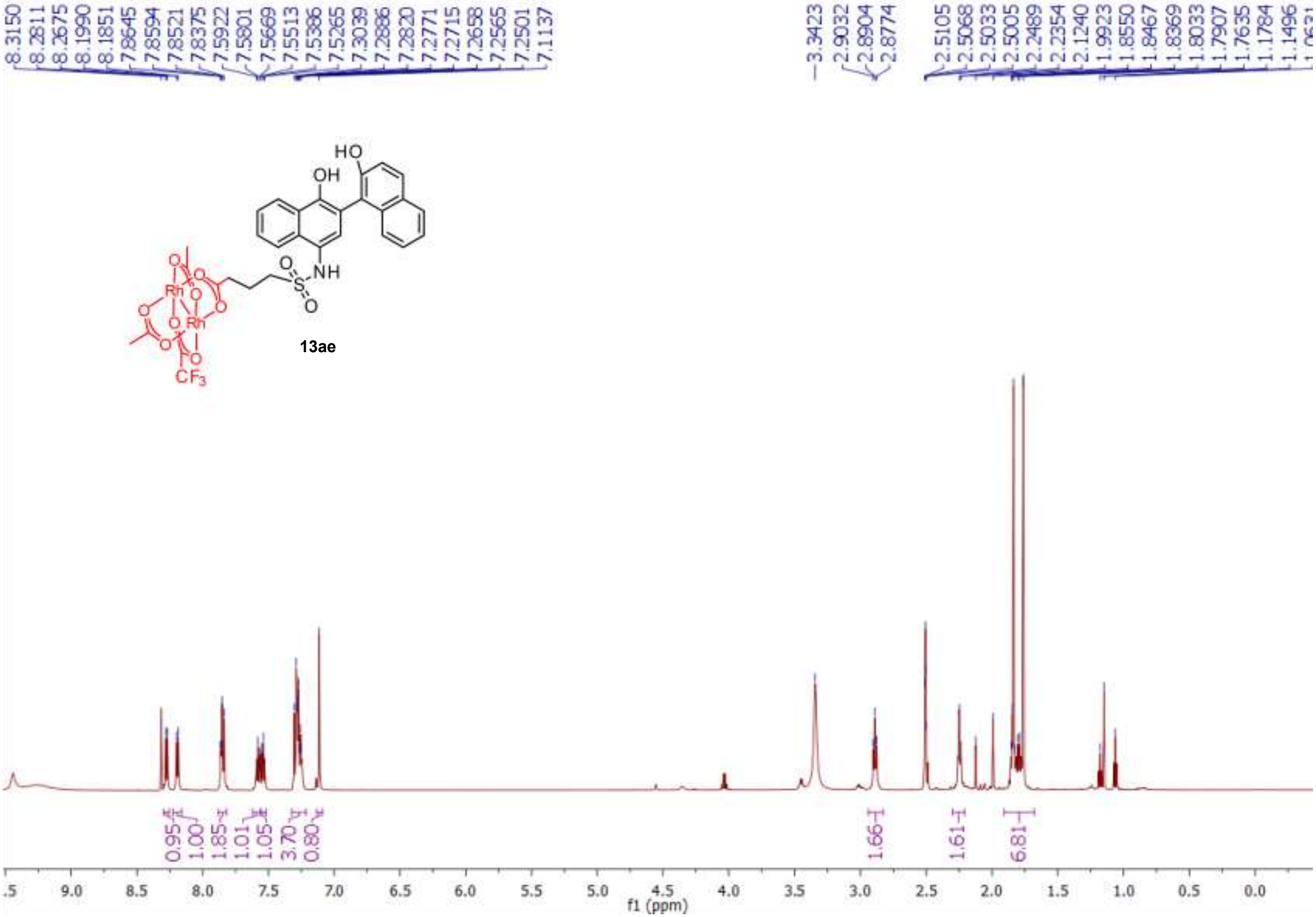


31-Rh


600 MHz, $(CD_3)_2SO$
9.9553
8.6358
8.6219
8.4944
8.4459
8.4324
8.3779
8.3640
8.1820
8.1684
8.1235
8.1085
8.0790
8.0642
7.8324
7.8197
7.8072
7.7701
7.7579
7.7451
7.7139
7.7009
7.6883
7.6466
7.6341
7.6216
2.9862
2.9738
2.9606
2.1820
2.1700
2.1580
1.8153
1.8028
1.7895
1.7600
1.6370
1.16
1.25
1.13
1.24
1.13
1.25
1.17
1.05
1.17
1.17
1.23
1.19
2.12
2.29
2.36
2.60
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
HO
OH
Rh
Rh
NH
H
N
S
O

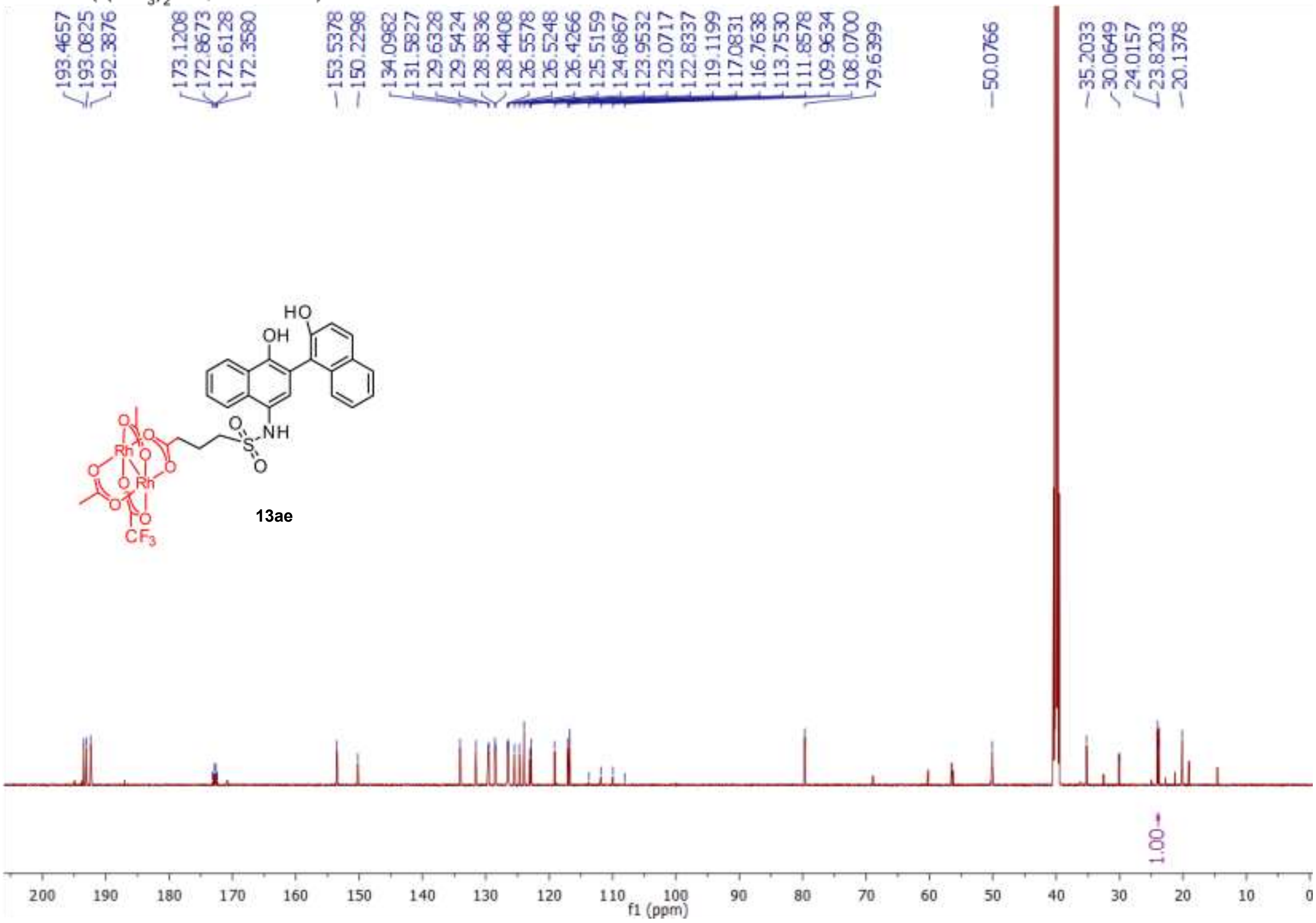
13ad

^{1}H NMR ($(CD_3)_2SO$, 600 MHz)

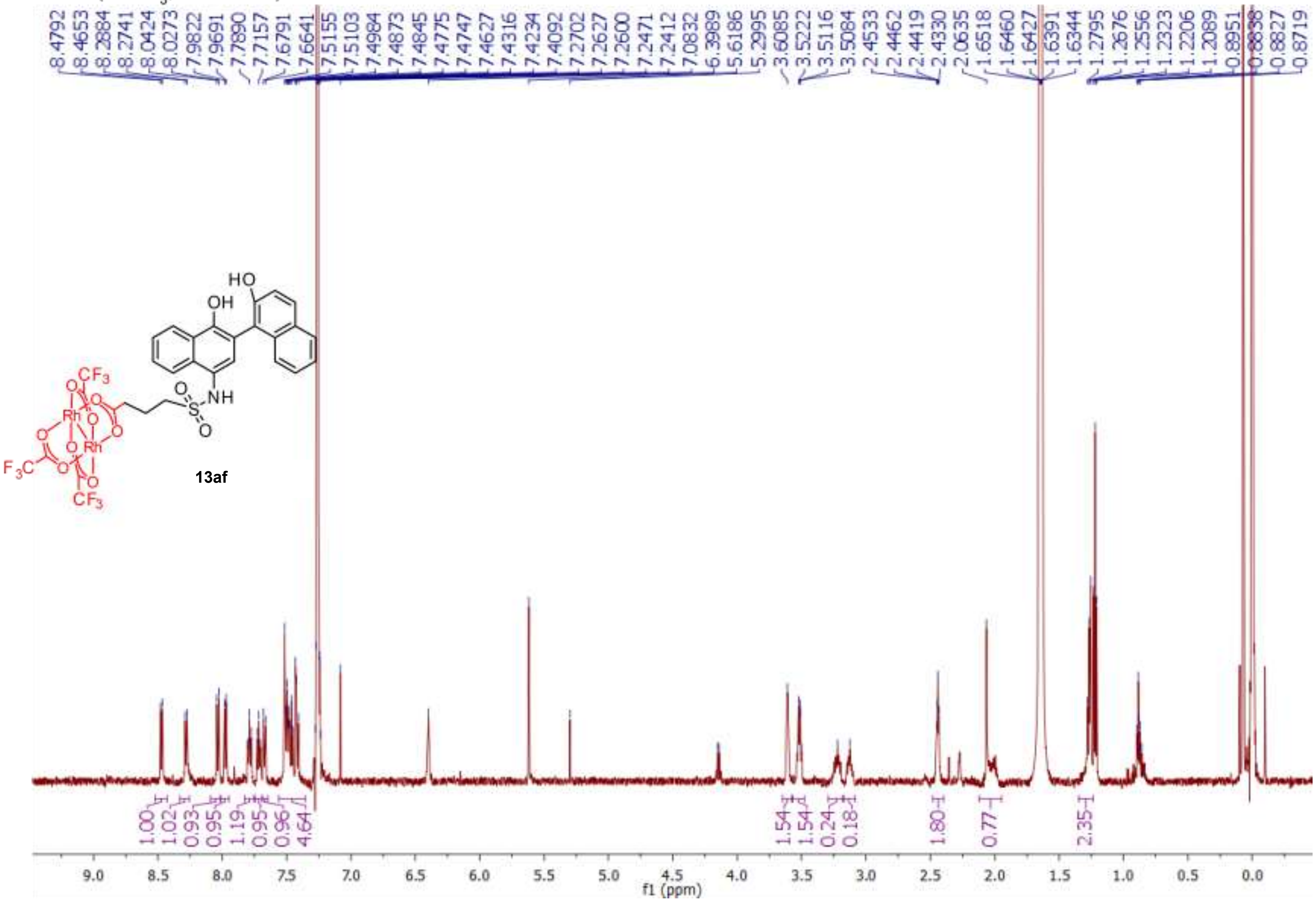


Lorem ipsum

^{13}C NMR ($(CD_3)_2SO$, 150 MHz)



¹H NMR ($CDCl_3$, 600 MHz)



13af

1.6. **References**

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