Supporting Information

Efficient Enantioselective Synthesis of CF_2H-Containing Dispiro [benzo [*b*] thiophene – oxindole - pyrrolidine]s *via* Organocatalytic Cycloaddition

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1. General Information

Reactions were monitored by thin layer chromatography (TLC), and compounds were visualized with a UV light at 254 nm and 365 nm. Column chromatography purifications were carried out using silica gel. ^{1}H, $^{13}C\{^{1}H\}$ and ^{19}F NMR spectra were recorded on a Bruker (300 MHz or 400 MHz) spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as internal standard. Data are presented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constant in Hertz (Hz). Mass peaks are identified by the corresponding *m/z* values. The ee values determination was carried out using chiral high-performance liquid chromatography (HPLC) with Daicel Chiralpak (IA, IB, IA-3) and Daicel Chiralcel OD-H column. (Note: The mobile phase of all I series chiral columns is added with 5% DCM to help dissolve) Optical rotations were measured on a digital polarimeter and are reported as follows: $[\alpha]D^{T}$ (1 g/100 mL, $CHCl_3$).

All solvents were obtained from commercial sources and were purified according to standard procedures. The starting material methyleneindolinone[1] and difluoromethyl imine[2] was synthesized by literature method. The derivative 7a was synthesized by literature method [3].

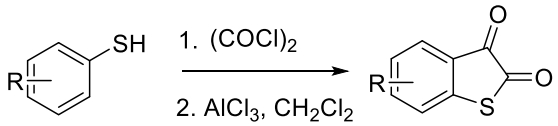
2. Reference

[1] Cao, S.-H.; Zhang, X.-C.; Wei, Y.; Shi, M. Chemoselective Reduction of Isatin-Derived Electron-Deficient Alkenes Using Alkylphosphanes as Reduction Reagents, *Eur. J. Org. Chem.* **2011**, *14*, 2668-2672.

[2] Gao, F.-Y.; Guo, Y.-F.; Sun, M.-M.; Wang, Y-L.; Yang, C-Y.; Wang, Y.-Q.; Wang K.-R.; and Yan, W.-J. Catalytic Asymmetric Construction of Tertiary Carbon Centers Featuring an *α*-Difluoromethyl Group with CF_2H-CH_2-NH_2 as the "Building Block", *Org. Lett.* **2021**, *23*, 2584-2589.

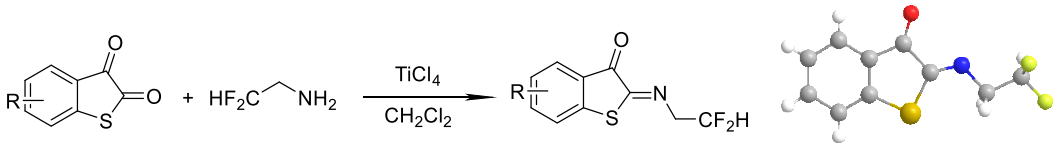
[3] Nandakumar, M.; Karunakaran, J.; Mohanakrishnan, A. K. Diels–Alder Reaction of 1,3-Diarylbenzo[*c*]furans with Thiophene *S*,*S*-Dioxide/Indenone Derivatives: A Facile Preparation of Substituted Dibenzothiophene *S*,*S*-Dioxides and Fluorenones, *Org. Lett.* **2014**, *16*, 3068-3071.

3. General procedures for substrates difluoromethyl imines



Oxalyl chloride (1.1 equiv., 10.7 mmol) was added dropwise to a solution of thiophenol with different substituents (1 equiv., 9.7 mmol) in anhydrous Et_2O (30 mL) at 0 ℃ under a N_2 atmosphere, and the reaction stirred for 1.5 hours, warming to room temperature. The reaction mixture was concentratedin vacuo and the residue dissolved

in anhydrous CH_2Cl_2 (40 mL). Aluminium chloride (3.6 equiv., 35 mmol) was added portionwise at 0 °Cand the reaction mixture then stirred for 16 hours, slowly warming to room temperature. Upon completion, an ice/1M HCl mixture was added dropwise until the reaction turned clear and was then stirred for a further hour. The phases were separated and the aqueous layer extracted with CH_2Cl_2 (3 x 25 mL). the organic phases were combined, dried (Na_2SO_4), filtered and concentrated in vacuo to give the crude product, which was recrystallized from ethyl acetate to give benzo[*b*]thiophene-2,3-dione with different substituents.(yield: 50-83%).

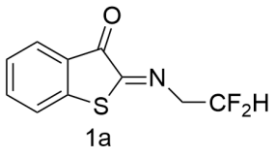


x-ray of **1a** (**CCDC:2120999**)

In a 100 mL round-bottom flask, 2,2-difluoroethan-1-amine (9.0 mmol, 1.5equiv.) and Benzo[*b*]thiophene-2,3-dione with different substituents (6.0 mmol, 1.0 equiv.) were dissolved with 60 mL DCM was added to the solution. Then the mixture was cooled to 0 °C, and then titanium tetrachloride (7.2 mmol,1.2 equiv.) was added dropwise to the solution and the reaction mixture was stirred at room temperature until TLC revealed complete conversion of benzo[*b*]thiophene-2,3-dione with different substituents. After the reaction completed, the mixture was quenched by 10% NaOH solution and filtered. The organic layer was washed with saturated $NaHCO_3$, saturated NaCl, and dried over Na_2SO_4. Organic layer was concentrated under reduced pressure, the crude mixture was purified by silica-gel column chromatography to obtain the target product (yield:45-70%).

4. Physical and chemical data of the substrate difluoromethyl imines

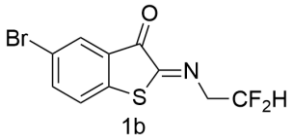
(*Z*)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one



1a

Brown yellow solid, Mp. = 65-66 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ7.95 – 7.87 (m, 1H), 7.72 – 7.60 (m, 1H), 7.44 (s, 1H), 7.36 (td, J = 7.6, 0.9 Hz, 1H), 6.34 (tt, J = 55.6, 4.5 Hz, 1H), 3.94 (td, J = 14.3, 4.5 Hz, 2H). ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$) δ 184.6, 161.3, 142.4, 137.4, 128.0, 127.9, 127.1, 125.1, 114.5 (t, $J_{C\text{-}F}$ = 180.0 Hz), 60.5 (t, $J_{C\text{-}F}$ = 20.6 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ -120.50. HRMS (ESI) *m/z* calcd for $C_{10}H_7F_2NOSNa$ $[M+Na]^+$: 250.0109, found 250.0096.

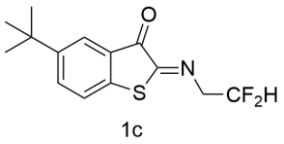
(*Z*)-5-bromo-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one



1b

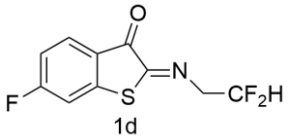
Brown solid, Mp. = 78-79 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 1.8 Hz, 1H), 7.77 (dd, J = 8.3, 1.9 Hz, 1H), 7.35 (d, J = 8.3 Hz, 1H), 6.33 (tt, J = 55.5, 4.4 Hz, 1H), 3.94 (td, J = 14.2, 4.4 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 183.4, 160.5, 141.1, 140.0, 130.6, 129.3, 129.2, 126.4, 121.0, 114.4 (t, $J_{C\text{-}F}$ = 242.4 Hz), 60.5 (t, $J_{C\text{-}F}$ = 27.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{10}H_7BrF_2NOS$ $[M+H]^+$: 327.9214, found 327.9199.

(*Z*)-5-(tert-butyl)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one


1c

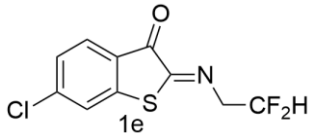
Red solid, Mp. = 50-51 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.0 Hz, 1H), 7.71 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.37 (d, *J* = 8.3 Hz, 1H), 6.34 (tt, *J* = 55.6, 4.5 Hz, 1H), 3.93 (td, *J* = 14.3, 4.5 Hz, 2H), 1.35 (s, 9H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.9, 162.1, 151.0, 139.4, 135.2, 127.8, 124.7, 124.6, 114.6 (t, $J_{C\text{-}F}$ = 241.9 Hz), 60.4 (t, $J_{C\text{-}F}$ = 25.3 Hz), 34.9, 31.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{14}H_{15}F_2NOSNa$ $[M+Na]^+$: 306.0735, found 306.0735.

(*Z*)-2-((2,2-difluoroethyl)imino)-6-fluorobenzo[*b*]thiophen-3(2H)-one


1d

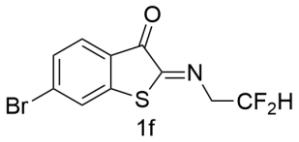
Yellow solid, Mp. = 70-71 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.5, 5.4 Hz, 1H), 7.17 (dd, *J* = 7.9, 2.2 Hz, 1H), 7.06 (td, *J* = 8.5, 2.2 Hz, 1H), 6.33 (tt, *J* = 55.5, 4.5 Hz, 1H), 3.95 (td, *J* = 14.2, 4.5 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 182.6, 169.3, 166.6, 160.5, 145.4, 145.3, 130.3, 130.2, 124.6, 124.6, 112.0, 115.2, 115.0, 114.4 (t, $J_{C\text{-}F}$ = 242.4 Hz), 112.7, 112.4, 60.4 (t, $J_{C\text{-}F}$ = 27.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -95.7, -120.5. HRMS (ESI) *m/z* calcd for $C_{10}H_6F_3NOSNa$ $[M+Na]^+$: 268.0014, found 268.0003.

(Z)-6-chloro-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one


1e

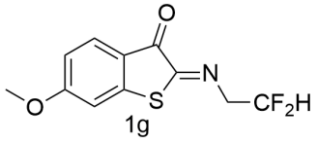
Yellow solid, Mp. = 132-133 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (t, *J* = 7.9 Hz, 1H), 7.38 – 7.24 (m, 2H), 6.33 (tt, *J* = 55.6, 4.4 Hz, 1H), 3.93 (td, *J* = 14.3, 4.4 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 181.5, 160.3, 144.7, 136.9, 136.8, 129.4, 124.0, 123.5, 114.5 (t, $J_{C\text{-}F}$ = 325.0 Hz), 60.4 (t, $J_{C\text{-}F}$ = 37.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{10}H_6ClF_2NOSNa$ $[M+Na]^+$: 283.9719, found 283.9720.

(*Z*)-6-bromo-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one


1f

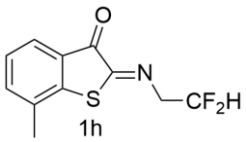
Pink solid, Mp. = 81-82 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.47 – 7.39 (m, 2H), 6.33 (tt, *J* = 55.6, 4.5 Hz, 1H), 3.94 (td, *J* = 14.2, 4.5 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 181.8, 160.4, 145.3, 136.9, 132.7, 125.2, 124.6, 124.1, 114.5 (t, $J_{C\text{-}F}$ = 241.9 Hz), 60.3 (t, $J_{C\text{-}F}$ = 27.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{10}H_6BrF_2NOSNa$ $[M+Na]^+$: 327.9219, found 327.9213.

(Z)-2-((2,2-difluoroethyl)imino)-6-methoxybenzo[*b*]thiophen-3(2H)-one


1g

Red solid, Mp. = 123-124 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (dd, *J* = 24.7, 8.6 Hz, 1H), 6.89 (d, *J* = 2.2 Hz, 1H), 6.83 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.33 (tt, *J* = 55.6, 4.5 Hz, 1H), 4.03 – 3.90 (m, 4H), 3.89 (d, *J* = 4.5 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 182.7, 167.0, 161.9, 145.4, 129.9, 121.8, 117.0, 114.6, 113.8, 112.2 (t, $J_{C\text{-}F}$ = 186.8 Hz), 109.6, 60.4 (t, $J_{C\text{-}F}$ = 37.0 Hz), 56.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{11}H_9BrF_2NO_2SNa$ $[M+Na]^+$: 280.0214, found 280.0216.

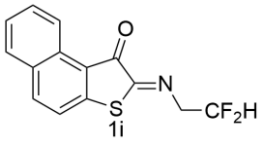
(*Z*)-2-((2,2-difluoroethyl)imino)-7-methylbenzo[*b*]thiophen-3(2H)-one



1h

Orange solid, Mp. = 49-50℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 1H), 6.34 (tt, *J* = 55.6, 4.5 Hz, 1H), 3.98 (td, *J* = 14.3, 4.5 Hz, 2H), 2.36 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 185.2, 161.7, 142.2, 138.0, 133.9, 128.0, 126.9, 125.2, 114.6 (t, J_{C-F} = 241.9 Hz), 60.5 (t, J_{C-F} = 27.3 Hz), 18.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{11}H_9F_2NOSNa$ [M+Na]$^{+}$: 264.0265, found 264.0257.

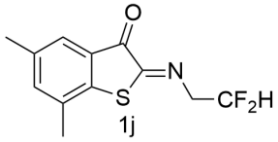
(Z)-2-((2,2-difluoroethyl)imino)naphtho[2,1-*b*]thiophen-1(2H)-one



1i

Red solid, Mp. = 70-71 ℃. ^{1}H NMR (400 MHz, CDCl3) δ 9.16 (d, *J* = 8.5 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.77 – 7.70 (m, 1H), 7.56 (t, *J* = 4.1 Hz, 1H), 7.47 (d, *J* = 8.5 Hz, 1H), 6.37 (tt, *J* = 55.6, 4.5 Hz, 1H), 4.00 (td, *J* = 14.3, 4.5 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.6, 161.2, 146.9, 139.7, 138.6, 132.3, 131.6, 131.0, 130.9, 129.3, 128.9, 127.5, 127.2, 123.3, 123.0, 122.8, 122.2, 121.6, 114.6 (t, J_{C-F} = 325.0 Hz), 60.5 (t, J_{C-F} = 37.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.4. HRMS (ESI) *m/z* calcd for $C_{14}H_9F_2NOSNa$ [M+Na]$^{+}$: 300.0265, found 300.0266.

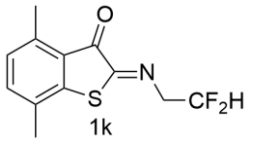
(Z)-2-((2,2-difluoroethyl)imino)-5,7-dimethylbenzo[*b*]thiophen-3(2H)-one



1j

Red solid, Mp. = 93-94 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 35.0 Hz, 1H), 7.32 (d, *J* = 11.8 Hz, 1H), 6.34 (tt, *J* = 55.6, 4.5 Hz, 1H), 3.95 (td, *J* = 14.3, 4.5 Hz, 2H), 2.36 (s, 3H), 2.31 (s, 3H), 2.29 – 2.16 (m, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 185.3, 162.2, 140.3, 139.2, 139.1, 137.1, 133.6, 128.0, 126.1, 125.5, 114.6 (t, J_{C-F} = 324.8 Hz), 60.4 (t, J_{C-F} = 37.0 Hz), 20.7, 18.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{12}H_{11}F_2NOSNa$ [M+Na]$^{+}$: 278.0422, found 278.0422.

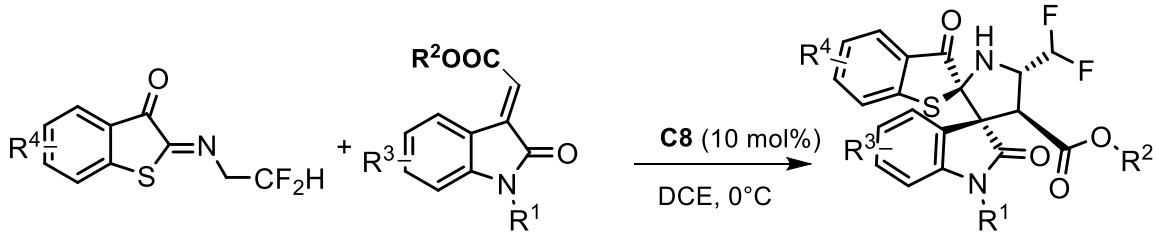
(Z)-2-((2,2-difluoroethyl)imino)-4,7-dimethylbenzo[*b*]thiophen-3(2H)-one



1k

Orange solid, Mp. = 95-96 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 7.7 Hz, 1H), 7.03 (d, *J* = 7.7 Hz, 1H), 6.33 (tt, *J* = 55.7, 4.5 Hz, 1H), 3.95 (td, *J* = 14.4, 4.5 Hz, 2H), 2.65 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 185.8, 161.6, 142.6, 140.5, 137.0, 131.0, 129.4, 125.5, 114.7 (t, J_{C-F} = 324.7 Hz), 60.3 (t, J_{C-F} = 37.0 Hz), 18.7, 18.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.5. HRMS (ESI) *m/z* calcd for $C_{12}H_{11}F_2NOSNa$ [M+Na]$^{+}$: 278.0422, found 278.0422.

5. General Procedure for the Synthesis of 3aa–3ka

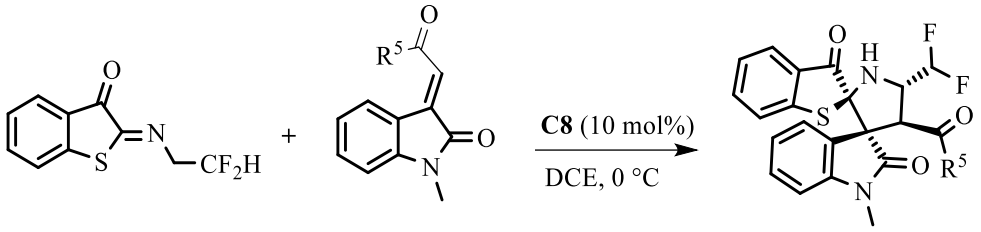


(Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** (0.1 mmol) was added to a solution of catalyst **C8** (0.01 mmol, 10 mol%) and methyleneindolinone **2** (0.12 mmol) in anhydrous DCE (1.0 mL) at 0 ℃, After completion (monitored by TLC), the

reaction mixture was directly purified by flash column chromatography on silica gel (EA:PE = 1:7(v/v)) to obtain the title compounds **3aa-3ka**.

Racemates were prepared following the general procedure with 10 mol% DABCO or a combination of equivalent cinchonidine-derived squaramide and cinchonine-derived squaramide.

6. General Procedure for the Synthesis of 5aa–5ak



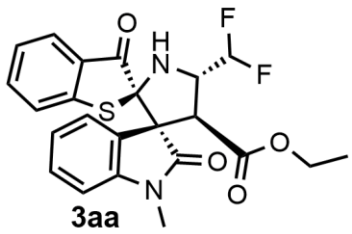
1a 4 5

(Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** (0.1 mmol) was added to a solution of catalyst **C8** (0.01 mmol, 10 mol%) and methyleneindolinone **4** (0.12 mmol) in anhydrous DCE (1.0 mL) at 0 ℃, After completion (monitored by TLC), the reaction mixture was directly purified by flash column chromatography on silica gel (EA:PE = 1:10(v/v)) to obtain the title compounds **5aa-5ak**.

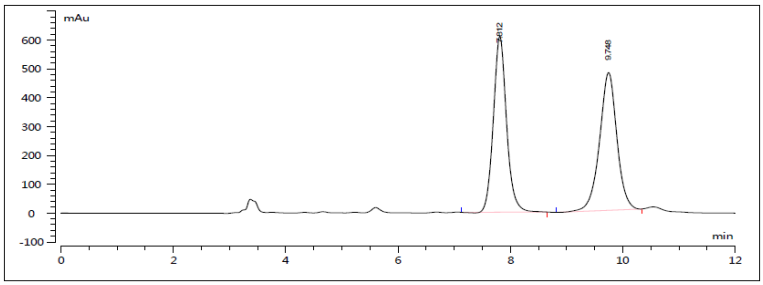
Racemates were prepared following the general procedure with 10 mol% DABCO.

7. Analytical Data and HPLC Chromatogram of the Products

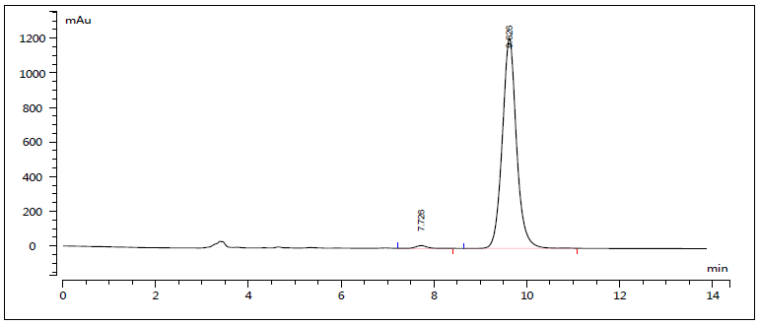
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 43.5 mg (95% yield) of compound **3aa** was obtained as a white solid, [α] D ^{24} = -372 (*c* = 1.0, $CHCl_3$), Mp. = 184-185 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 9.6 min, t_{minor} = 7.7 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.49 – 7.32 (m, 3H), 7.22 – 7.08 (m, 2H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.59 (ddd, *J* = 58.2, 56.7, 7.1 Hz, 1H), 4.75 – 4.42 (m, 1H), 4.30 (d, *J* = 8.1 Hz, 1H), 3.80 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.69 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.10 (s, 3H), 2.75 (s, 1H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.4, 171.5, 167.6, 147.8, 144.1, 136.4, 129.9, 128.8, 128.4, 127.3, 125.6, 124.2, 123.2, 123.2, 117.5 (dd, J_{C-F} = 330.9, 323.6 Hz), 108.1, 86.6, 62.5, 61.0, 59.6 (dd, J_{C-F} = 38.2, 32.5 Hz), 49.8, 49.7, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 296.3 Hz, 1F), -123.0 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{20}F_2N_2NaO_4S$ $[M+Na]^+$: 481.1004, found 481.1004.

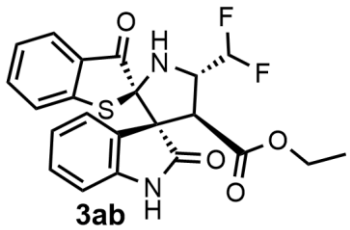


No	Retention Time	Area	% Area	Int Type
1	7.812	9940.090	49.301	BB
2	9.748	10221.984	50.699	BB



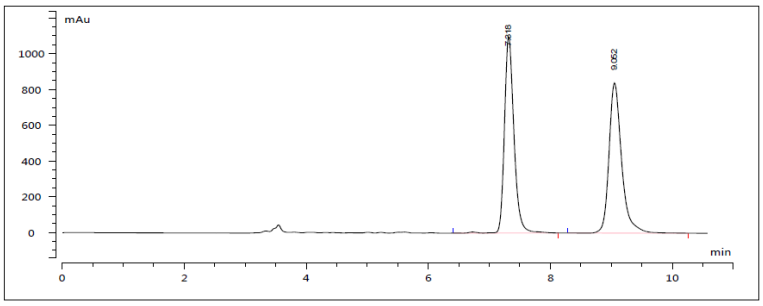
No	Retention Time	Area	% Area	Int Type
1	7.726	256.961	0.987	BB
2	9.626	25769.543	99.013	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

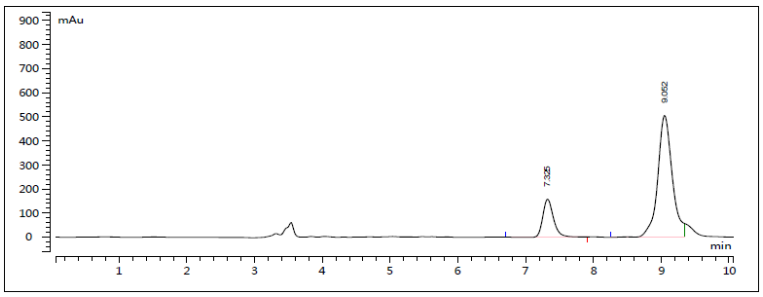


3ab

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 26.0 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2b**, 35.5 mg (80% yield) of compound **3ab** was obtained as a red solid, [α] D ^{24} = -372 (*c* = 1.0, $CHCl_3$), Mp. = 148-149 °C. Dr (> 20:1) was determined by HPLC analysis. 64% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 9.1 min, t_{minor} = 7.3 min. ^{1}H NMR (400 MHz, DMSO) δ 10.70 (s, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.61 – 7.51 (m, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.27 (ddd, *J* = 15.7, 11.0, 4.2 Hz, 3H), 7.07 – 6.99 (m, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.42 (td, *J* = 57.6, 7.0 Hz, 1H), 5.00 (d, *J* = 5.3 Hz, 1H), 4.39 (d, *J* = 7.3 Hz, 1H), 4.08 (d, *J* = 8.3 Hz, 1H), 3.77 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.65 (dq, *J* = 10.9, 7.1 Hz, 1H), 0.64 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, DMSO) δ 201.6, 172.7, 167.5, 147.6, 142.5, 136.5, 129.6, 128.6, 128.6, 126.5, 125.4, 124.2, 123.5, 121.8, 117.80 (t, J_{C-F} = 325.9 Hz), 109.6, 85.7, 79.1, 62.9, 60.6, 59.9, 59.6, 59.4, 49.7, 49.6, 13.1. ^{19}F NMR (376 MHz, DMSO) δ -117.0 (d, *J* = 287.2 Hz, 1F), -122.0 (d, *J* = 287.2 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{22}H_{18}F_2N_2NaO_4S$ $[M+Na]^+$: 467.0848, found 467.0848.

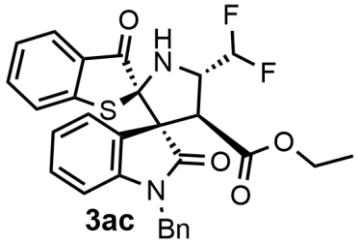


No	Retention Time	Area	% Area	Int Type
1	7.318	11834.406	49.528	BB
2	9.052	12060.157	50.472	BB



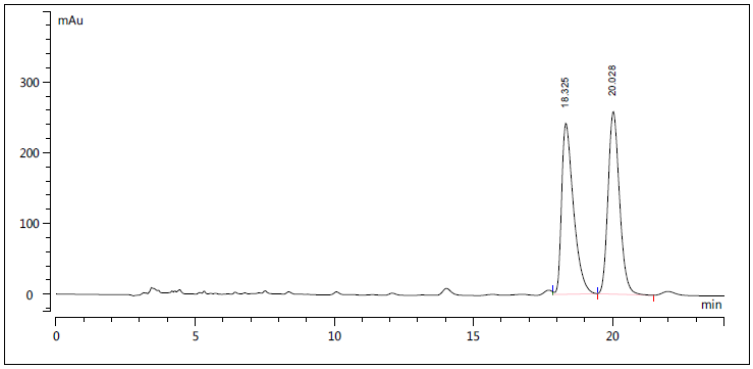
No	Retention Time	Area	% Area	Int Type
1	7.325	1665.017	18.132	BB
2	9.052	7517.907	81.868	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-1''-benzyl-5'-(difluoromethyl)-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

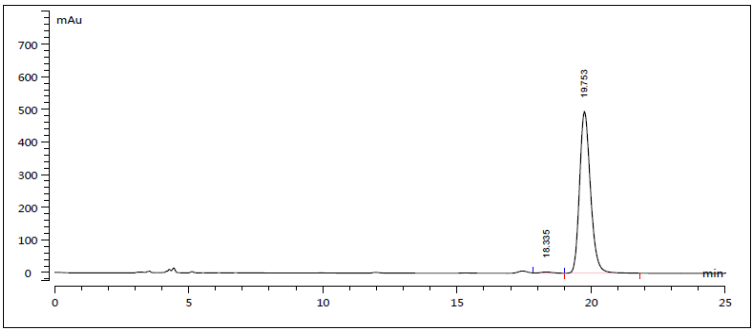


From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2c**, 44.3 mg (83% yield) of compound **3ac** was obtained as a yellow solid, [α] D ^{25} = - 456 (*c* = 1.0, $CHCl_3$), Mp. = 189-190 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 60:40, 1.0 mL/min). Retention time: t_{major} = 19.8 min, t_{minor} = 18.3 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.7 Hz, 1H), 7.54 – 7.44 (m, 1H), 7.39 (d, *J* = 7.4 Hz, 1H), 7.30 – 7.22 (m, 1H), 7.20 – 7.04 (m, 5H), 7.01 (dd, *J* = 6.9, 4.8 Hz, 3H), 6.82 – 6.45 (m, 2H), 5.03 (d, *J* = 15.5 Hz, 1H), 4.66 – 4.52 (m, 1H), 4.38 (dd, *J* = 71.2, 11.8 Hz, 1H), 3.78 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.60 (dq, *J* = 10.8, 7.1 Hz, 1H), 2.76 (s, 1H), 0.59 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.6, 171.7, 167.6, 147.6, 143.3, 136.3, 135.3, 129.8, 129.0, 128.6, 128.6, 127.6, 127.4, 127.3, 125.7, 124.2, 123.2, 123.1, 117.61 (dd, J_{C-F} = 331.0, 323.6 Hz), 109.0, 87.4, 62.5, 61.1, 59.72 (dd, J_{C-F} = 38.1, 32.5 Hz), 49.5, 49.5, 44.1, 13.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.4 (d, *J* = 295.9 Hz, 1F), -123.1 (d,

J = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{29}H_{24}F_2N_2NaO_4S$ $[M+Na]^+$: 557.1317, found 557.1317.

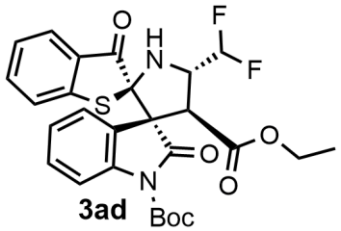


No	Retention Time	Area	% Area	Int Type
1	18.325	7152.158	49.157	BB
2	20.028	7397.369	50.843	BB



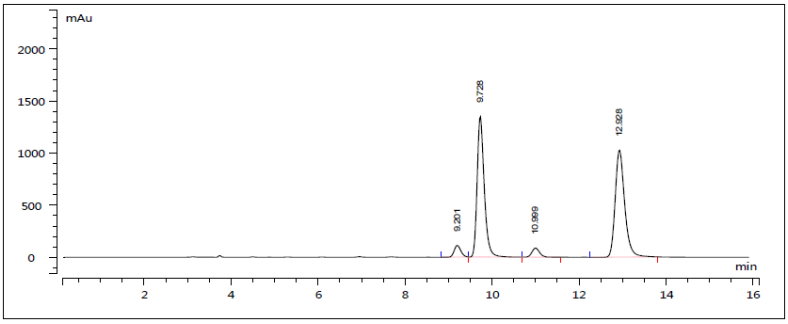
No	Retention Time	Area	% Area	Int Type
1	18.335	85.225	0.606	BB
2	19.753	13983.541	99.394	BB

1''-(tert-butyl) 4'-ethyl (2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-1'',4'-dicarboxylate



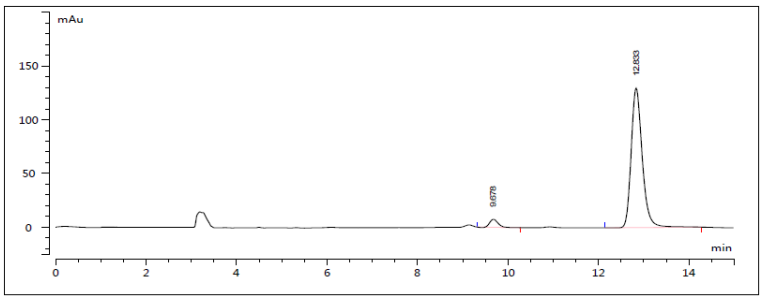
From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 38.0 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2d**, 45.7 mg (84% yield) of compound **3ad** was obtained as a yellow solid, [α] D ^{25} = - 221 (*c* = 1.0, $CHCl_3$), Mp. = 65-66 °C. Dr (> 20:1) was determined by HPLC analysis. 92% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 10:90, 1.0 mL/min). Retention time: t_{major} = 12.8 min, t_{minor} = 9.7 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.1 Hz, 1H), 7.72 (d, *J* = 7.6 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.29 – 7.15 (m, 2H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.60 (td, *J* = 57.9, 7.0 Hz, 1H), 4.57 – 4.45 (m, 1H), 4.30 (d, *J* = 8.1 Hz, 1H), 3.84 – 3.76 (m, 1H), 3.72 (ddd, *J* = 14.3, 10.7, 7.1 Hz, 1H), 2.75 (s, 1H), 1.49 (s, 9H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.1, 170.3, 167.3, 148.6, 147.9, 140.3, 136.4,

130.1, 128.7, 127.5, 127.2, 125.6, 125.0, 123.9, 123.3, 117.3 (dd, J_{C-F} = 331.3, 323.7 Hz), 114.9, 87.3, 84.6, 62.9, 61.3, 59.4 (dd, J_{C-F} = 38.4, 32.9 Hz), 50.6, 50.5, 27.9, 13.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, J = 296.7 Hz, 1F), -123.0 (d, J = 296.7 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{26}F_2N_2NaO_6S$ $[M+Na]^+$: 567.1372, found 567.1372.



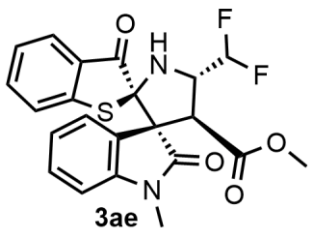
No	Retention Time	Area	% Area	Int Type
1	9.201	1180.207	3.582	BB
2	9.728	15242.273	46.266	BB
3	10.999	1056.738	3.208	BB
4	12.928	15465.998	46.945	BB

No	Retention Time	Area	% Area	Int Type
1	9.728	15242.273	49.636	BB
2	12.928	15465.998	50.364	BB



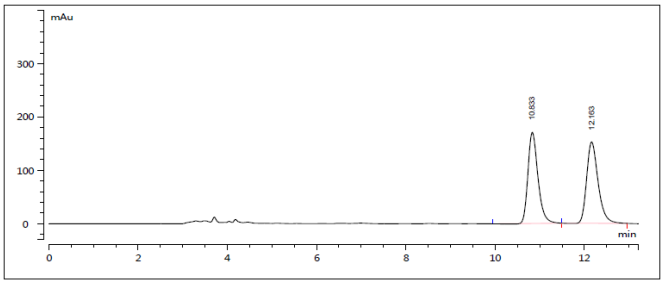
No	Retention Time	Area	% Area	Int Type
1	9.678	91.502	3.985	BB
2	12.833	2204.886	96.015	BB

Methyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

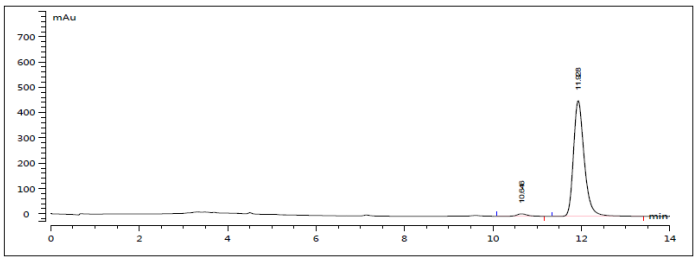


From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 26.0 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2e**, 37.3 mg (84% yield) of compound **3ae** was obtained as a white solid, [α] D ^{25} = -181 (*c* = 1.0, $CHCl_3$), Mp. = 181-182 °C. Dr (> 20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 60:40, 1.0

mL/min). Retention time: t_{major} = 11.9 min, t_{minor} = 10.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.7 Hz, 1H), 7.42 (qd, *J* = 7.7, 1.1 Hz, 3H), 7.23 – 7.07 (m, 2H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.58 (ddd, *J* = 58.1, 56.7, 7.1 Hz, 1H), 4.68 – 4.39 (m, 1H), 4.30 (d, *J* = 8.1 Hz, 1H), 3.25 (s, 3H), 3.11 (s, 3H), 2.76 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.4, 171.4, 168.2, 147.8, 143.9, 136.4, 130.0, 128.8, 128.3, 127.3, 125.6, 124.2, 123.2, 123.2, 117.4(dd, J_{C-F} = 330.7, 323.9 Hz), 108.1, 86.4, 62.6, 59.6(dd, J_{C-F} = 38.4, 32.5 Hz), 52.2, 50.0, 49.9, 26.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 296.3 Hz, 1F), -123.0 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{22}H_{18}F_2N_2NaO_4S$ $[M+Na]^+$: 467.0848, found 467.0848.

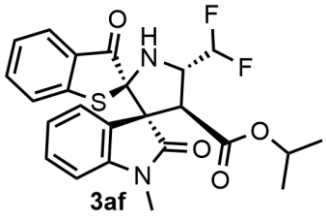


No	Retention Time	Area	% Area	Int Type
1	10.833	2652.156	49.459	BB
2	12.163	2710.222	50.541	BB



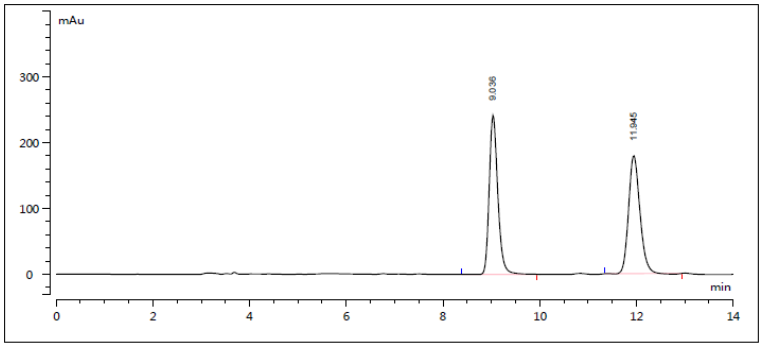
No	Retention Time	Area	% Area	Int Type
1	10.646	148.374	1.893	BB
2	11.928	7688.807	98.107	BB

Iso-propyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

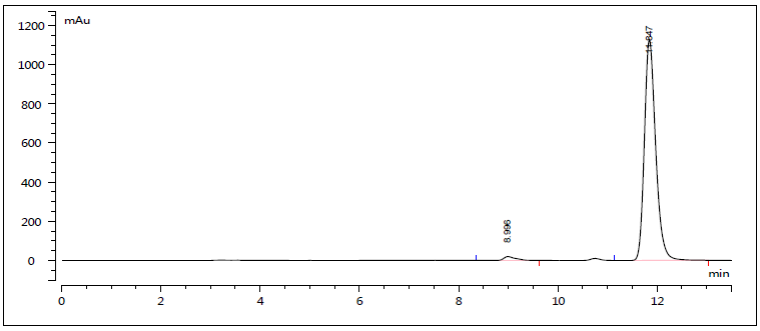


From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 29.4 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2f**, 40.6 mg (86% yield) of compound **3af** was obtained as a white solid, [α] D ^{24} = - 366 (*c* = 1.0, $CHCl_3$), Mp. = 86-87 °C. Dr (> 20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 60:40, 1.0 mL/min). Retention time: t_{major} = 11.8 min, t_{minor} = 9.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.55 – 7.31 (m, 3H), 7.15 (ddd, *J* = 15.1, 7.7, 0.8 Hz, 2H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.59 (ddd, *J* = 58.2, 56.7, 7.1 Hz, 1H), 4.61 (dt, J = 12.5, 6.3 Hz, 1H), 4.53 (dt, *J* = 16.3, 6.0 Hz, 1H), 4.28 (d, *J* = 8.1 Hz,

1H), 3.10 (s, 3H), 2.74 (s, 1H), 0.97 (d, J = 6.3 Hz, 3H), 0.56 (d, J = 6.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 202.4, 171.5, 167.0, 147.8, 144.3, 136.3, 129.9, 128.9, 128.5, 127.3, 125.6, 124.2, 123.2, 123.1, 117.5 (dd, J_{C-F} = 331.3, 323.5 Hz), 115.1, 108.1, 86.6, 68.7, 62.4, 59.6 (dd, J_{C-F} = 38.2, 32.3 Hz), 49.8, 49.7, 26.6 , 21.5, 20.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, J = 295.9 Hz, 1F), -123.0 (d, J = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 495.1161, found 495.1161.

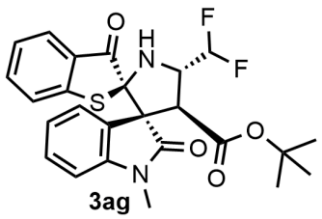


No	Retention Time	Area	% Area	Int Type
1	9.036	2981.291	50.749	BB
2	11.945	2893.305	49.251	BB



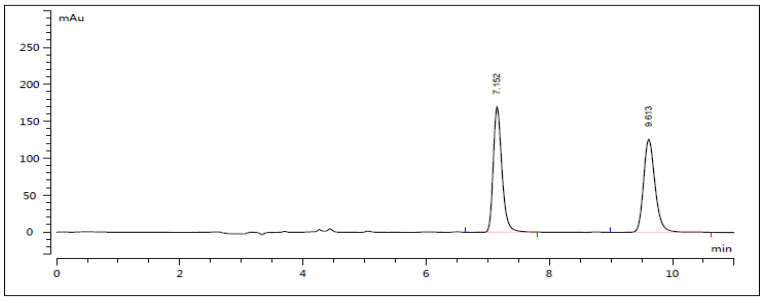
No	Retention Time	Area	% Area	Int Type
1	8.996	319.077	1.760	BB
2	11.847	17810.752	98.240	BB

Tert-buty-(2_S_,3'_S_,4'_S_,5'_S_)-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[_b_]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

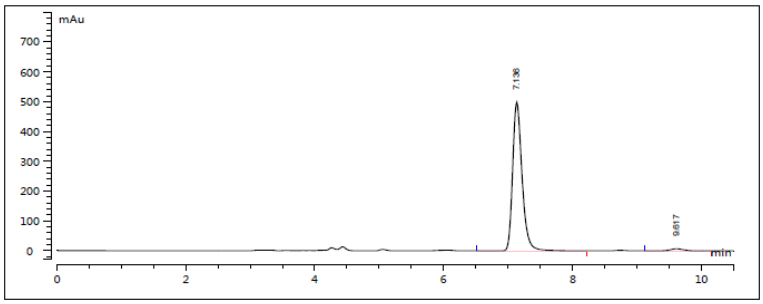


From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 31.0 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2g**, 41.3 mg (85% yield) of compound **3ag** was obtained as a yellow solid, [α] D ^{24} = - 338 (*c* = 1.0, $CHCl_3$), Mp. = 207-208 °C. Dr (> 20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2-propanol 60:40, 1.0 mL/min). Retention time: t_{major} = 7.1 min, t_{minor} = 9.6 min. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, J = 7.7, 0.6 Hz, 1H), 7.56 – 7.28 (m, 3H), 7.22 – 7.08 (m, 2H), 7.00 (d, J = 7.9 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 6.59 (ddd, J = 58.3, 56.7, 7.1 Hz, 1H), 4.49 (td, J = 12.2, 7.1 Hz, 1H), 4.24 (d, J = 8.1 Hz, 1H), 3.10 (s, 3H), 2.72

(s, 1H), 0.97 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 202.4, 171.6, 166.5, 147.8, 144.3, 136.3, 129.8, 128.9, 128.9, 127.3, 125.6, 124.2, 123.2, 123.1, 119.9, 117.5(dd, J_{C-F} = 331.3, 323.1 Hz) 107.9, 86.8, 81.7, 62.4, 59.6 (dd, J_{C-F} = 38.2, 32.1 Hz), 50.2, 50.2, 26.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, J = 295.2 Hz, 1F), -123.0 (d, J = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{25}H_{24}F_2N_2NaO_4S$ $[M+Na]^+$: 509.1317, found 509.1317.

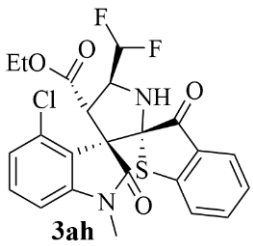


No	Retention Time	Area	% Area	Int Type
1	7.152	1658.059	50.394	BB
2	9.613	1632.158	49.606	BB



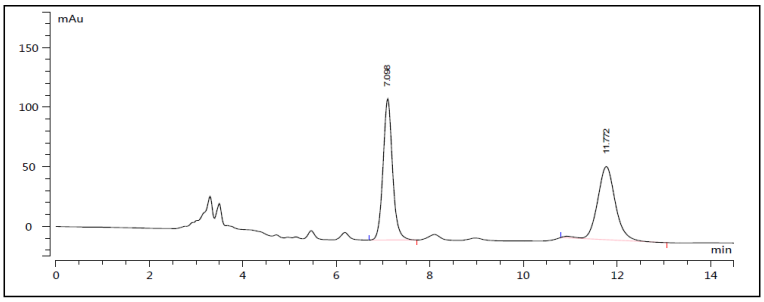
No	Retention Time	Area	% Area	Int Type
1	7.136	5059.279	98.056	BB
2	9.617	100.277	1.944	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-4''-chloro-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

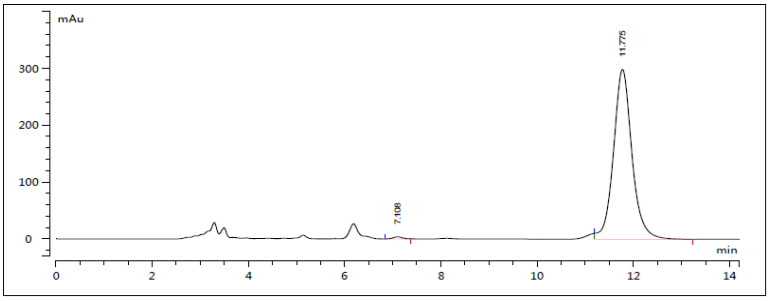


From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 40.1 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2h**, 40.3 mg (82% yield) of compound **3ah** was obtained as a white solid, [α] D ^{24} = - 374 (*c* = 1.0, $CHCl_3$), Mp. = 92-93 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 11.8 min, t_{minor} = 7.1 min. ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 1H), 7.52 – 7.42 (m, 1H), 7.35 (d, J = 8.0 Hz, 1H), 7.18 (t, J = 7.5 Hz, 1H), 7.11 (dd, J = 8.0, 1.7 Hz, 1H), 7.02 (d, J = 7.9 Hz, 1H), 6.85 (d, J = 1.6 Hz, 1H), 6.76 – 6.39 (m, 1H), 4.59 – 4.42 (m, 1H), 4.28 (d, J = 8.1 Hz, 1H), 3.83

(dq, J = 10.9, 7.1 Hz, 1H), 3.74 (dq, J = 10.8, 7.1 Hz, 1H), 3.08 (s, 3H), 2.74 (s, 1H), 0.81 (t, J = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 202.2, 171.5, 167.4, 147.6, 145.3, 136.5, 135.9, 128.7, 127.3, 126.7, 125.7, 125.2, 123.3, 123.0, 117.3 (dd, J_{C-F} = 331.3, 323.7 Hz), 108.9, 86.4, 62.2, 61.2, 59.46 (dd, J_{C-F} = 38.2, 32.6 Hz), 49.6, 49.6, 26.8, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, J = 296.7 Hz, 1F), -122.9 (d, J = 297.1 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}ClF_2N_2NaO_4S$ $[M+Na]^+$: 515.0614, found 515.0614.

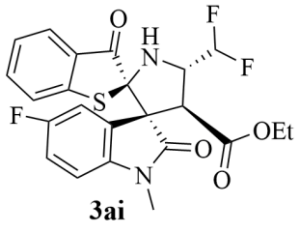


No	Retention Time	Area	% Area	Int Type
1	7.098	1670.867	50.924	BB
2	11.772	1610.211	49.076	BB



No	Retention Time	Area	% Area	Int Type
1	7.108	47.384	0.592	BB
2	11.775	7956.463	99.408	BB

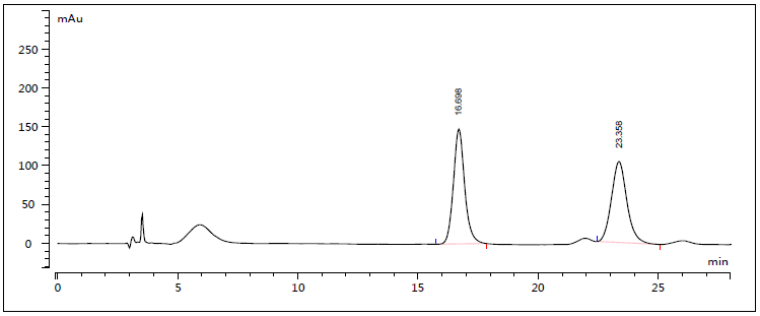
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-5''-fluoro-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



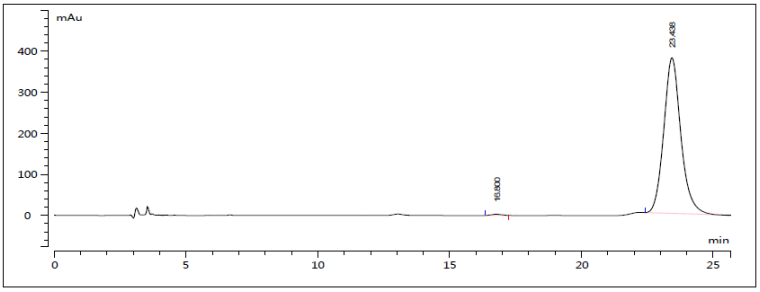
3ai

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 29.9 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2i**, 41.8 mg (88% yield) of compound **3ai** was obtained as a white solid, [α] D ^{24} = - 373 (*c* = 1.0, $CHCl_3$), Mp. = 138-139 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 84:16, 1.0 mL/min). Retention time: t_{major} = 23.4 min, t_{minor} = 16.8 min. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 7.7, 0.7 Hz, 1H), 7.45 (td, J = 7.9, 1.3 Hz, 1H), 7.24 – 7.15 (m, 2H), 7.10 (td, J = 8.8, 2.6 Hz, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.78 (dd, J = 8.5, 4.1 Hz, 1H), 6.60 (ddd, J = 58.2, 56.7, 7.1 Hz, 1H), 4.57 – 4.43 (m, 1H), 4.29 (d, J = 8.1 Hz, 1H), 3.84

(dq, J = 10.8, 7.1 Hz, 1H), 3.74 (dq, J = 10.8, 7.1 Hz, 1H), 3.09 (s, 3H), 2.72 (s, 1H), 0.79 (t, J = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 202.2, 171.2, 167.4, 160.4, 158.0, 147.6, 140.2, 140.2, 136.5, 129.7, 129.7, 128.8, 127.3, 125.7, 117.3 (dd, J_{C-F} = 331.4, 323.6 Hz), 116.3, 116.0, 112.9, 112.6, 108.6, 108.5, 86.3, 62.8, 61.1, 59.4 (dd, J_{C-F} = 38.4, 32.7 Hz), 49.6, 49.5, 26.8, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ - 118.8, -119.3 (d, J = 297.1 Hz, 1F), -122.9 (d, J = 297.1 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}F_3N_2NaO_4S$ $[M+Na]^+$: 499.0910, found 499.0910.

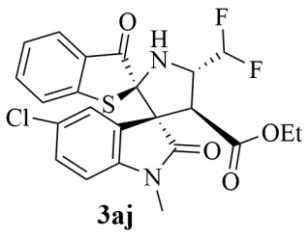


No	Retention Time	Area	% Area	Int Type
1	16.698	4805.330	50.825	BB
2	23.358	4649.321	49.175	BB



No	Retention Time	Area	% Area	Int Type
1	16.800	79.255	0.463	BB
2	23.438	17042.738	99.537	BB

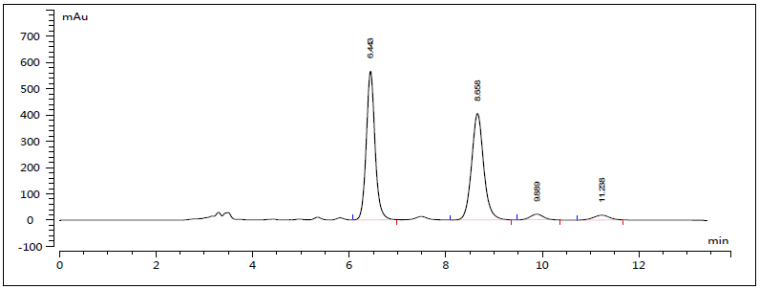
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5''-chloro-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



3aj

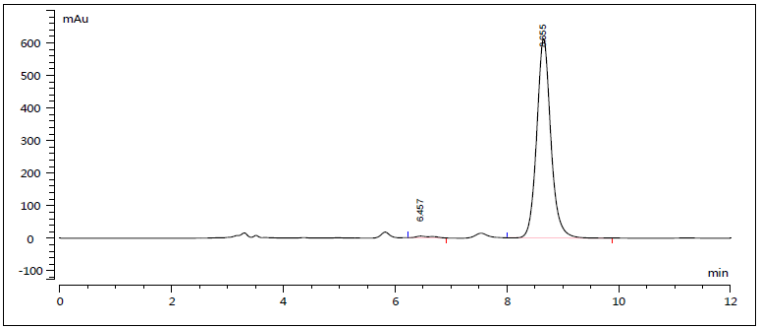
From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 31.8 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2j**, 48.1 mg (98% yield) of compound **3aj** was obtained as a white solid, [α] D ^{24} = - 455 (*c* = 1.0, $CHCl_3$), Mp. = 68-69 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 8.7 min, t_{minor} = 6.5 min. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, J = 7.7, 0.7 Hz, 1H), 7.50 – 7.40 (m, 2H), 7.37 (dd, J = 8.3, 2.1 Hz, 1H), 7.22 – 7.13 (m, 1H), 7.03 (d, J = 7.9 Hz, 1H), 6.78 (d, J = 8.3 Hz, 1H), 6.59 (ddd, J =

58.2, 56.6, 7.1 Hz, 1H), 4.55 – 4.45 (m, 1H), 4.28 (d, J = 8.1 Hz, 1H), 3.85 (dq, J = 10.8, 7.1 Hz, 1H), 3.75 (dq, J = 10.8, 7.1 Hz, 1H), 3.09 (s, 3H), 2.73 (s, 1H), 0.79 (t, J = 7.1 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 202.1, 171.1, 167.3, 147.6, 142.8, 136.5, 129.9, 129.8, 128.8, 128.5, 127.3, 125.7, 124.6, 123.3, 117.3 (dd, J_{C-F} = 331.4, 323.7 Hz), 109.0, 86.3, 62.6, 61.2, 59.4 (dd, J_{C-F} = 38.4, 32.7 Hz), 49.7, 49.6, 26.8, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, J = 296.7 Hz, 1F), -122.9 (d, J = 297.1 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}ClF_2N_2NaO_4S$ $[M+Na]^+$: 515.0614, found 515.0614.



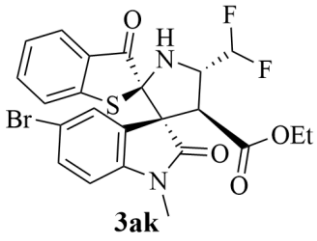
No	Retention Time	Area	% Area	Int Type
1	6.443	7124.814	47.353	BB
2	8.658	7073.348	47.011	BB
3	9.889	430.159	2.859	BB
4	11.238	417.970	2.778	BB

No	Retention Time	Area	% Area	Int Type
1	6.443	7124.814	50.181	BB
2	8.658	7073.348	49.819	BB



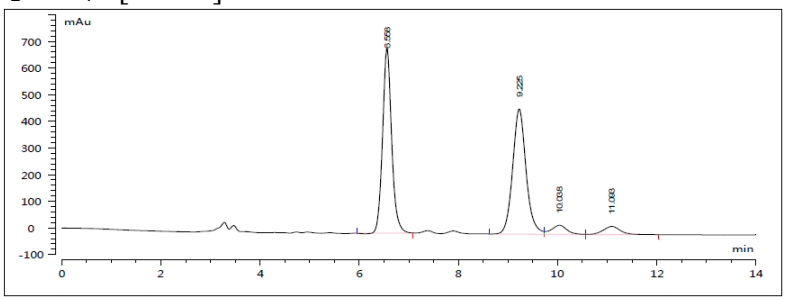
No	Retention Time	Area	% Area	Int Type
1	6.457	104.585	0.970	BB
2	8.655	10675.497	99.030	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5''-bromo-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



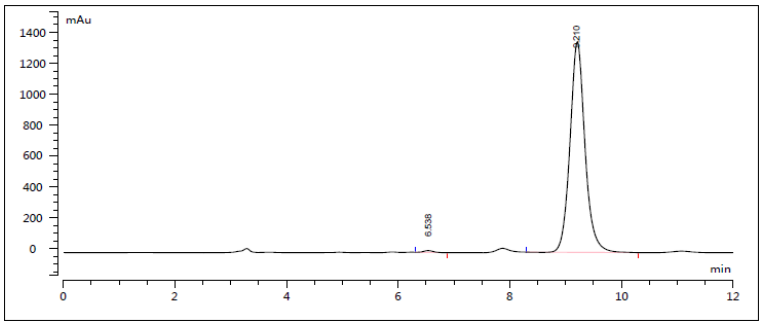
3ak

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 37.1 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2k**, 43.5 mg (83% yield) of compound **3ak** was obtained as a yellow solid, [α] D ^{24} = - 35 (*c* = 1.0, $CHCl_3$), Mp. = 72-73 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2-propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 9.2 min, t_{minor} = 6.5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.67 (m, 1H), 7.60 – 7.50 (m, 2H), 7.45 (td, *J* = 7.9, 1.3 Hz, 1H), 7.22 – 7.12 (m, 1H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.76 – 6.40 (m, 2H), 4.61 – 4.38 (m, 1H), 4.27 (d, *J* = 8.1 Hz, 1H), 3.85 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.75 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.08 (s, 3H), 2.74 (s, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.1, 171.0, 167.3, 147.6, 143.3, 136.5, 132.8, 130.3, 128.7, 127.3, 127.3, 125.7, 123.3, 117.3 (dd, J_{C-F} = 331.3, 323.7 Hz), 115.7, 109.5, 86.3, 62.5, 61.2, 59.4 (dd, J_{C-F} = 38.4, 32.6 Hz), 49.7, 49.6, 26.8, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.2 (d, *J* = 297.1 Hz, 1F), -122.8 (d, *J* = 296.7 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}BrF_2N_2NaO_4S$ $[M+Na]^+$: 559.0109 found 559.0109.



No	Retention Time	Area	% Area	Int Type
1	6.558	8807.048	46.218	BB
2	9.225	8810.980	46.238	BB
3	10.038	719.871	3.778	BB
4	11.093	717.695	3.766	BB

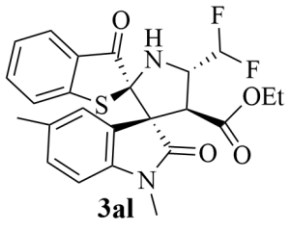
No	Retention Time	Area	% Area	Int Type
1	6.558	8807.048	49.989	BB
2	9.225	8810.980	50.011	BB



No	Retention Time	Area	% Area	Int Type

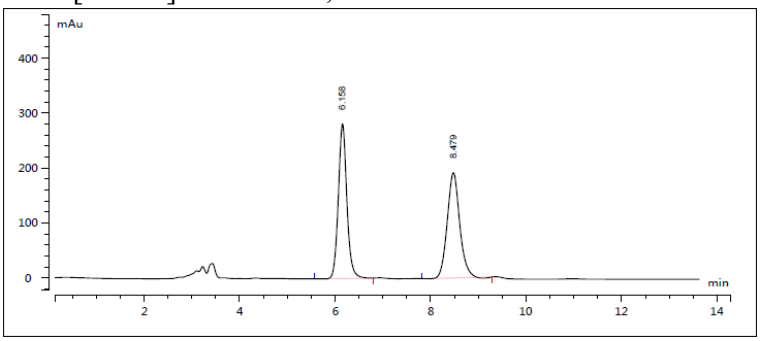
1	6.538	135.886	0.530	BB
2	9.210	25486.011	99.470	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1'',5''-dimethyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

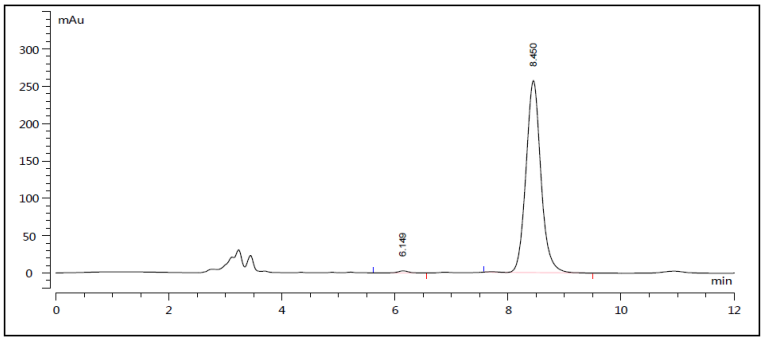


3al

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 29.4 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2l**, 43.5 mg (89% yield) of compound **3al** was obtained as a white solid, [α] D ^{24} = - 429 (*c* = 1.0, $CHCl_3$), Mp. = 106-107 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 8.5 min, t_{minor} = 6.1 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.43 (td, *J* = 7.9, 1.3 Hz, 1H), 7.25 – 7.09 (m, 3H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.78 – 6.36 (m, 2H), 4.54 (ddd, *J* = 11.8, 7.3, 3.4 Hz, 1H), 4.28 (d, *J* = 8.1 Hz, 1H), 3.81 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.71 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.08 (s, 3H), 2.72 (s, 1H), 2.39 (s, 3H), 0.75 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.5, 171.4, 167.6, 147.8, 141.8, 136.3, 132.8, 130.2, 128.9, 128.4, 127.3, 125.6, 124.9, 123.2, 117.5 (dd, J_{C-F} = 330.9, 323.6 Hz), 107.8, 86.6, 62.6, 60.9, 59.6 (dd, J_{C-F} = 38.2, 32.3 Hz), 49.8, 49.7, 26.7, 21.3, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 295.9 Hz, 1F), -123.0 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 495.1161, found 495.1161.

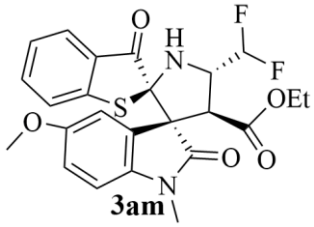


No	Retention Time	Area	% Area	Int Type
1	6.158	3495.106	50.331	BB
2	8.479	3449.153	49.669	BB

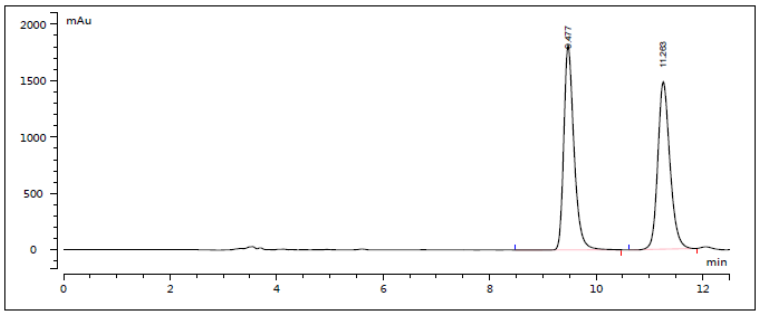


No	Retention Time	Area	% Area	Int Type
1	6.149	33.249	0.702	BB
2	8.450	4703.165	99.298	BB

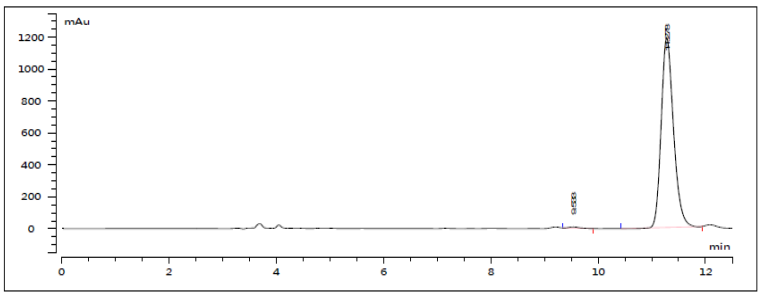
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-5''-methoxy-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 31.3 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2m**, 43.5 mg (99% yield) of compound **3am** was obtained as a white solid, [α] D ^{24} = - 400 (*c* = 1.0, $CHCl_3$), Mp. = 83-84 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 11.3 min, t_{minor} = 9.5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.2 Hz, 1H), 7.53 – 7.36 (m, 1H), 7.17 (dd, *J* = 11.1, 3.9 Hz, 1H), 7.03 (dd, *J* = 16.1, 5.2 Hz, 2H), 6.90 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.78 – 6.41 (m, 2H), 4.52 (td, *J* = 12.1, 5.2 Hz, 1H), 4.28 (d, *J* = 8.1 Hz, 1H), 3.95 – 3.77 (m, 4H), 3.75 – 3.67 (m, 1H), 3.07 (s, 3H), 2.72 (s, 1H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.5, 171.1, 167.5, 156.2, 147.8, 137.6, 136.3, 129.5, 128.9, 127.3, 125.6, 123.2, 117.5 (dd, J_{C-F} = 331.0, 323.6 Hz), 113.9, 111.8, 108.4, 86.5, 62.9, 61.0, 59.5 (dd, J_{C-F} = 38.2, 32.5 Hz), 55.9, 49.7, 49.6, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 295.9 Hz, 1F), -123.0 (d, *J* = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_5S$ $[M+Na]^+$: 511.1110, found 511.1110.

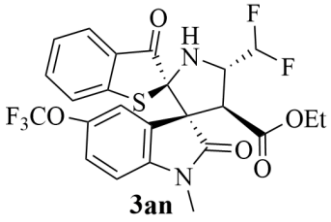


No	Retention Time	Area	% Area	Int Type
1	9.477	23985.411	50.555	BB
2	11.263	23458.680	49.445	BB



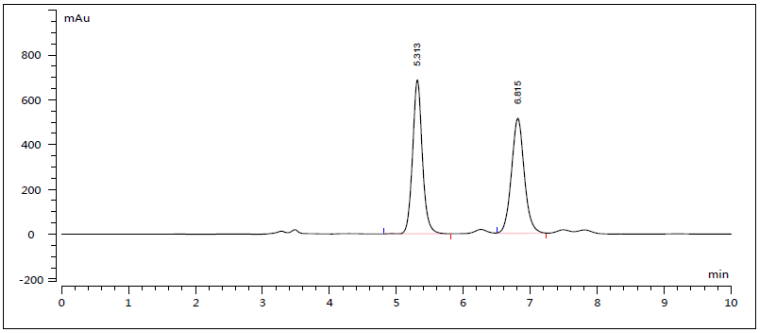
No	Retention Time	Area	% Area	Int Type
1	9.533	88.763	0.468	BB
2	11.278	18871.331	99.532	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-5''-(trifluoromethoxy)-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

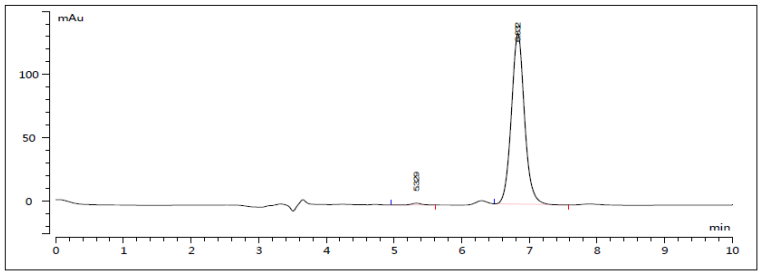


3an

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 37.8 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2n**, 47.9 mg (89% yield) of compound **3an** was obtained as a white solid, [α] D ^{24} = - 356 (*c* = 1.0, $CHCl_3$), Mp. = 86-87 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2-propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 6.8 min, t_{minor} = 5.3 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.60 (m, 1H), 7.46 (td, *J* = 7.9, 1.3 Hz, 1H), 7.34 (d, *J* = 1.6 Hz, 1H), 7.28 (dd, *J* = 6.5, 5.1 Hz, 1H), 7.18 (dd, *J* = 11.1, 4.0 Hz, 1H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 1H), 6.60 (ddd, *J* = 58.1, 56.7, 7.0 Hz, 1H), 4.58 – 4.43 (m, 1H), 4.28 (d, *J* = 8.0 Hz, 1H), 3.85 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.78 – 3.64 (m, 1H), 3.11 (s, 3H), 2.73 (s, 1H), 0.78 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.1, 171.3, 167.3, 147.6, 144.8, 144.8, 142.9, 136.5, 129.7, 128.7, 127.3, 125.7, 123.3, 123.0, 121.8, 119.3, 118.6, 117.3 (dd, $J_{C\text{-}F}$ = 331.4, 323.6 Hz), 108.5, 86.3, 62.6, 61.2, 59.3 (dd, $J_{C\text{-}F}$ = 38.4, 32.7 Hz), 49.7, 49.6, 26.8, 13.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ - 58.4, -119.3 (d, *J* = 297.1 Hz, 1F), -123.0 (d, *J* = 297.5 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{19}F_5N_2NaO_5S$ $[M+Na]^+$: 565.0827, found 565.0827.

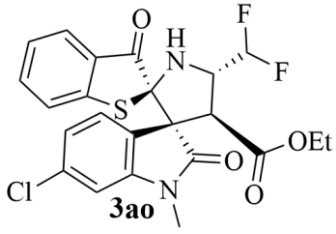


No	Retention Time	Area	% Area	Int Type
1	5.313	6982.515	50.493	BB
2	6.815	6846.061	49.507	BB

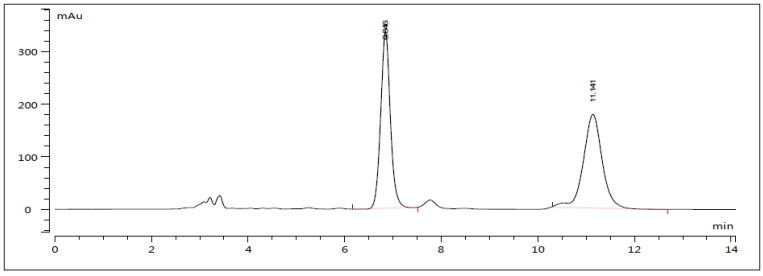


No	Retention Time	Area	% Area	Int Type
1	5.329	12.265	0.671	BB
2	6.832	1816.784	99.329	BB

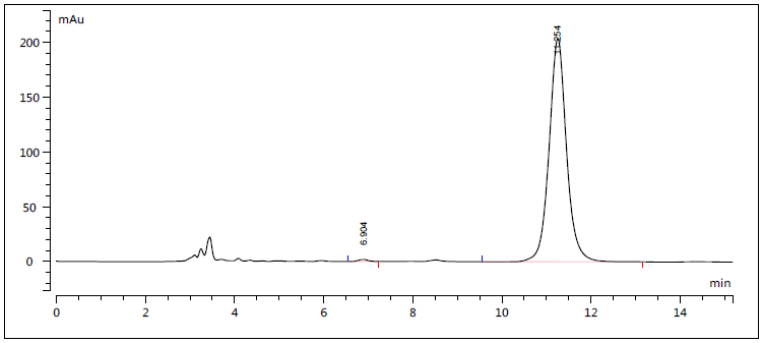
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-6''-chloro-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 31.8 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2o**, 47.0 mg (96% yield) of compound **3ao** was obtained as a white solid, [α] D ^{25} = - 393 (*c* = 1.0, $CHCl_3$), Mp. = 175-176 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 11.3 min, t_{minor} = 6.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.7 Hz, 1H), 7.52 – 7.41 (m, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 11.1, 3.9 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.85 (d, *J* = 1.7 Hz, 1H), 6.75 – 6.41 (m, 1H), 4.57 – 4.40 (m, 1H), 4.28 (d, *J* = 8.1 Hz, 1H), 3.83 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.74 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.08 (s, 3H), 2.74 (s, 1H), 0.81 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.1, 171.5, 167.4, 147.6, 145.3, 136.5, 135.9, 128.8, 127.3, 126.7, 125.7, 125.2, 123.3, 123.0, 117.3 (dd, J_{C-F} = 331.1, 323.7 Hz), 108.9, 86.4, 62.2, 61.2, 59.5 (dd, J_{C-F} = 38.4, 32.6 Hz), 49.7, 49.6, 26.8, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 297.1 Hz, 1F), -122.9 (d, *J* = 296.7 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}ClF_2N_2NaO_4S$ $[M+Na]^+$: 515.0614, found 515.0614.

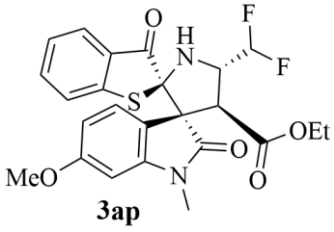


No	Retention Time	Area	% Area	Int Type
1	6.846	4662.004	49.157	BB
2	11.141	4821.956	50.843	BB



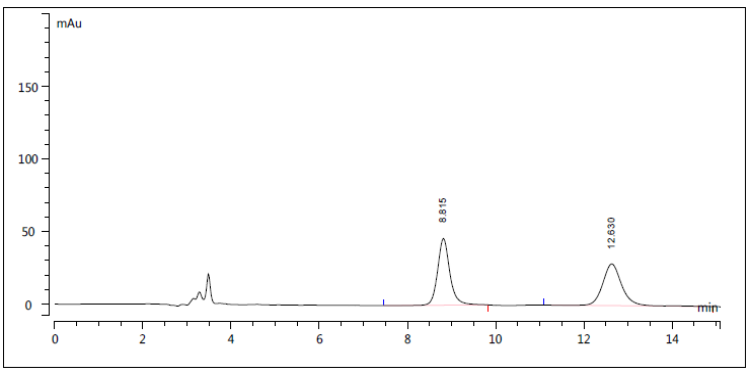
No	Retention Time	Area	% Area	Int Type
1	6.904	28.535	0.513	BB
2	11.254	5530.655	99.487	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-6''-methoxy-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



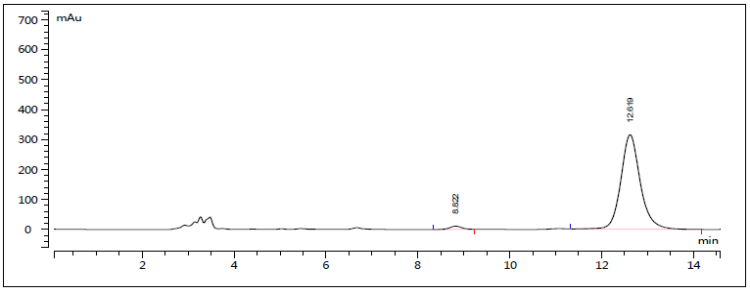
3ap

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 31.3 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2p**, 36.0 mg (74% yield) of compound **3ap** was obtained as a pink solid, [α] D ^{25} = - 360 (*c* = 1.0, $CHCl_3$), Mp. = 179-180 °C. Dr (> 20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2-propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 12.6 min, t_{minor} = 8.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.38 (m, 1H), 7.32 (d, *J* = 8.3 Hz, 1H), 7.16 (dd, *J* = 11.1, 3.9 Hz, 1H), 7.02 (d, *J* = 7.9 Hz, 1H), 6.80 – 6.23 (m, 3H), 4.51 (dt, *J* = 11.8, 5.8 Hz, 1H), 4.27 (d, *J* = 8.1 Hz, 1H), 3.97 – 3.77 (m, 4H), 3.77 – 3.60 (m, 1H), 3.07 (s, 3H), 2.71 (s, 1H), 0.80 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.4, 172.0, 167.7, 161.4, 147.9, 145.5, 136.3, 128.9, 127.3, 125.6, 125.1, 123.2, 120.4, 117.5 (dd, J_{C-F} = 331.3, 323.7 Hz), 106.2, 96.4, 87.0, 62.2, 61.0, 59.6 (dd, J_{C-F} = 38.2, 32.3 Hz), 55.5, 49.8, 49.7, 26.7, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.4 (d, *J* = 295.9 Hz, 1F), -123.0 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_5S$ $[M+Na]^+$: 511.1110, found 511.1110.



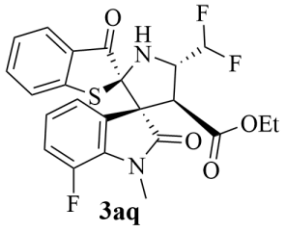
No	Retention Time	Area	% Area	Int Type

1	8.815	880.012	50.886	BB
2	12.630	849.368	49.114	BB



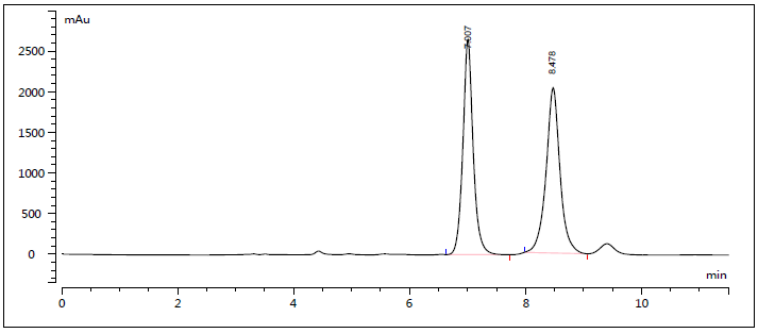
No	Retention Time	Area	% Area	Int Type
1	8.822	191.958	2.033	BB
2	12.619	9251.770	97.967	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-7''-fluoro-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

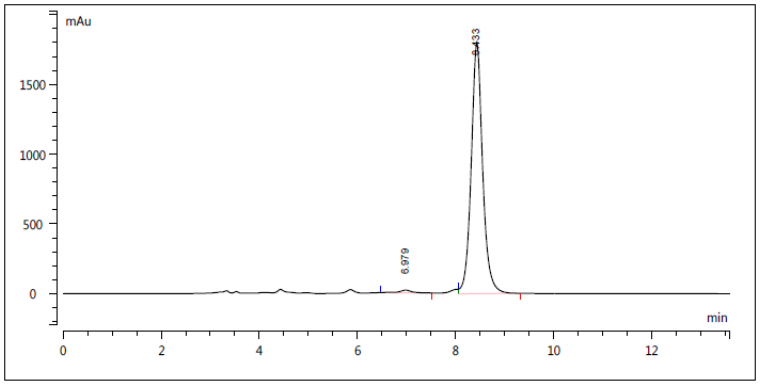


3aq

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 29.9 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2q**, 45.0 mg (89% yield) of compound **3aq** was obtained as a white solid, [α] D ^{24} = - 393 (*c* = 1.0, $CHCl_3$), Mp. = 165-166 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 8.4 min, t_{minor} = 7.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.46 (td, *J* = 7.9, 1.3 Hz, 1H), 7.31 – 6.99 (m, 5H), 6.59 (ddd, *J* = 58.2, 56.6, 7.1 Hz, 1H), 4.62 – 4.38 (m, 1H), 4.27 (d, *J* = 8.1 Hz, 1H), 3.88 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.74 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.30 (d, *J* = 2.7 Hz, 3H), 2.74 (s, 1H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.2, 171.2, 167.4, 148.7, 147.6, 146.3, 136.5, 131.1, 131.1, 130.9, 130.8, 128.7, 127.3, 125.7, 123.8, 123.7, 123.3, 120.1, 120.1, 119.8, 118.0, 117.4 (dd, $J_{C\text{-}F}$ = 331.3, 323.7 Hz) 86.5, 62.7, 61.1, 59.5(dd, $J_{C\text{-}F}$ = 38.4, 32.6 Hz) 49.9, 49.8, 29.2, 29.2, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 296.3 Hz, 1F), -123.0 (d, *J* = 296.7 Hz, 1F), - 136.2. HRMS (ESI) *m/z* calcd for $C_{23}H_{19}F_3N_2NaO_4S$ $[M+Na]^+$: 499.0910, found 499.0910.

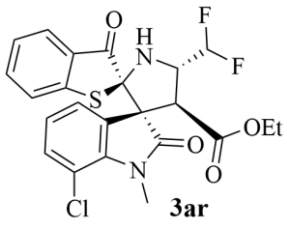


No	Retention Time	Area	% Area	Int Type
1	7.007	32735.616	49.059	BB
2	8.478	33991.362	50.941	BB



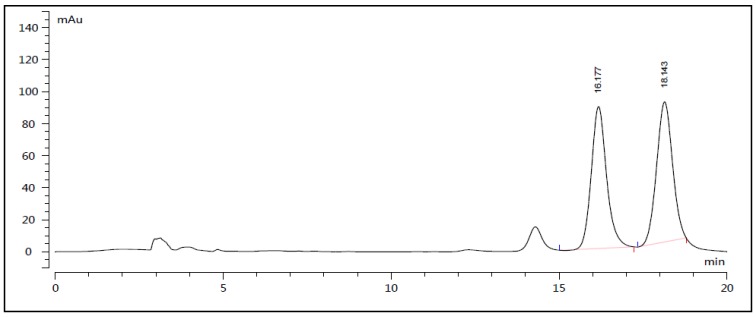
No	Retention Time	Area	% Area	Int Type
1	6.979	302.800	1.027	BB
2	8.433	29176.251	98.973	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-7''-chloro-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

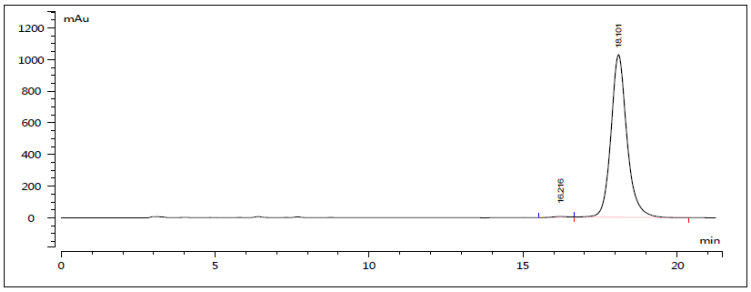


3ar

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 31.8 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2r**, 47.0 mg (96% yield) of compound **3ar** was obtained as a white solid, [α] D ^{24} = - 376 (*c* = 1.0, $CHCl_3$), Mp. = 75-76 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 18.1 min, t_{minor} = 16.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.3 Hz, 1H), 7.55 – 7.40 (m, 1H), 7.39 – 7.29 (m, 2H), 7.18 (t, J = 7.4 Hz, 1H), 7.05 (t, J = 7.7 Hz, 2H), 6.60 (ddd, J = 58.1, 56.8, 7.1 Hz, 1H), 4.62 – 4.39 (m, 1H), 4.26 (d, J = 8.1 Hz, 1H), 3.90 (dq, J = 10.8, 7.1 Hz, 1H), 3.72 (dq, J = 10.8, 7.1 Hz, 1H), 3.45 (s, 3H), 2.72 (s, 1H), 0.82 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.2, 171.9, 167.4, 147.6, 140.1, 136.5, 132.2, 131.1, 128.7, 127.3, 125.7, 123.9, 123.3, 122.8, 117.4 (dd, J_{C-F} = 331.4, 323.5 Hz), 86.6, 62.1, 61.2, 59.5(dd, J_{C-F} = 38.4, 32.7 Hz), 50.0, 50.0, 30.2, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.2 (d, *J* = 297.1 Hz, 1F), -123.0 (d, *J* = 297.1 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}ClF_2N_2NaO_4S$ $[M+Na]^+$: 515.0614, found 515.0614.

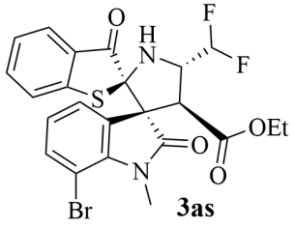


No	Retention Time	Area	% Area	Int Type
1	16.177	2802.172	49.292	BB
2	18.143	2882.641	50.708	BB



No	Retention Time	Area	% Area	Int Type
1	16.216	130.951	0.352	BB
2	18.101	37068.727	99.648	BB

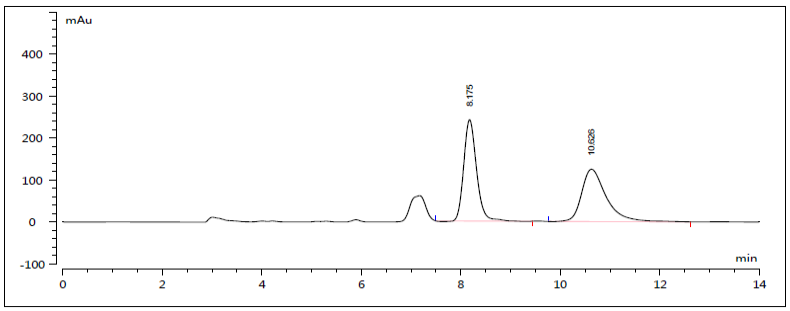
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-7''-bromo-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



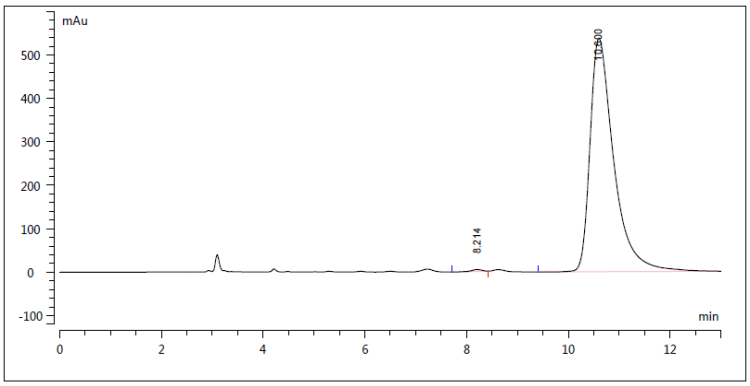
3as

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 37.1 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2s**, 50.0 mg (93% yield) of compound **3as** was obtained as a yellow solid, [α] D ^{24} = - 363 (*c* = 1.0, $CHCl_3$), Mp. = 76-77 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 10.6 min, t_{minor} = 8.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.4 Hz, 1H), 7.48 (ddd, *J* = 18.4, 11.7, 4.8 Hz, 2H), 7.39 (dd, *J* = 7.4, 0.9 Hz, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 7.01 – 6.93 (m, 1H), 6.61 (ddd, *J* = 58.1, 56.7, 7.1 Hz, 1H), 4.58 – 4.42 (m, 1H), 4.25 (d, *J* = 8.0 Hz, 1H), 3.90 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.72 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.47 (s, 3H), 2.72 (s, 1H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.2, 172.1, 167.3, 147.6, 141.5, 136.5, 135.5, 131.4, 128.7, 127.3, 125.7, 124.3, 123.3, 123.3, 117.4 (dd, J_{C-F} = 331.4, 323.6 Hz), 102.5, 86.6, 62.1, 61.2, 59.5 (dd, J_{C-F} = 38.4, 32.6 Hz), 50.1, 50.0, 30.4, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.2 (d, *J* = 296.7 Hz, 1F), -123.0 (d, *J* = 297.5 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}BrF_2N_2NaO_4S$ $[M+Na]^+$: 559.0109, found

559.0109.

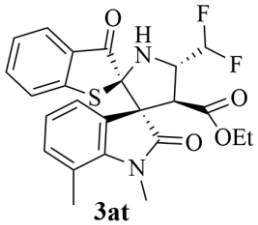


No	Retention Time	Area	% Area	Int Type
1	8.175	4279.940	49.986	BB
2	10.626	4282.407	50.014	BB



No	Retention Time	Area	% Area	Int Type
1	8.214	61.312	0.351	BB
2	10.600	17393.858	99.649	BB

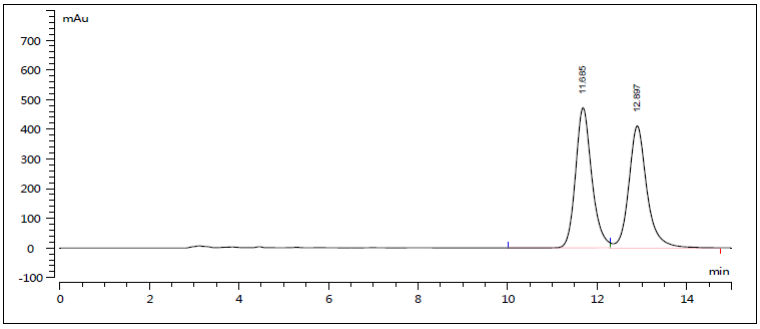
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1'',7''-dimethyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



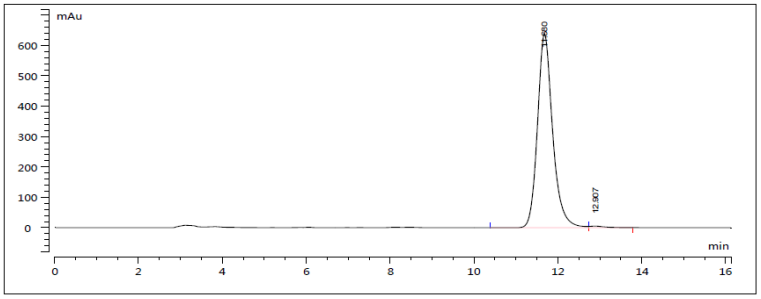
3at

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 29.4 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2t**, 43.0 mg (91% yield) of compound **3at** was obtained as a white solid, [α] D ^{24} = - 404 (*c* = 1.0, $CHCl_3$), Mp. = 71-72 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 11.7 min, t_{minor} = 12.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.44 (td, *J* = 7.9, 1.3 Hz, 1H), 7.28 (d, *J* = 8.9 Hz, 1H), 7.20 – 7.08 (m, 2H), 7.01 (t, *J* = 7.5 Hz, 2H), 6.59 (ddd, *J* = 58.2, 56.7, 7.1 Hz, 1H), 4.63 – 4.44 (m, 1H), 4.26 (d, *J* = 8.1 Hz, 1H), 3.87 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.70 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.36 (s, 3H), 2.72 (s, 1H), 2.56 (s, 3H), 0.78 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.6, 172.3, 167.6, 147.8, 141.9, 136.3, 133.7,

129.0, 128.9, 127.3, 125.6, 123.2, 123.1, 122.1, 119.6, 117.5 (dd, $J_{C\text{-}F}$ = 330.9, 323.6 Hz) 86.8, 61.9, 60.9, 59.6 (dd, $J_{C\text{-}F}$ = 38.2, 32.3 Hz), 50.2, 50.1, 30.1, 19.2, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.2 (d, J = 295.9 Hz, 1F), -123.1 (d, J = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 495.1161, found 495.1161.

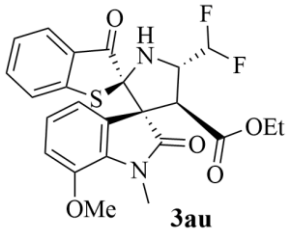


No	Retention Time	Area	% Area	Int Type
1	11.685	11887.717	50.702	BB
2	12.897	11558.688	49.298	BB



No	Retention Time	Area	% Area	Int Type
1	11.680	16004.794	99.312	BB
2	12.907	110.828	0.688	BB

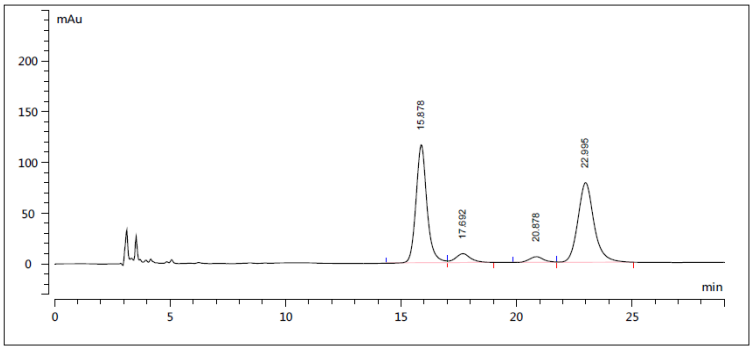
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-7''-methoxy-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



3au

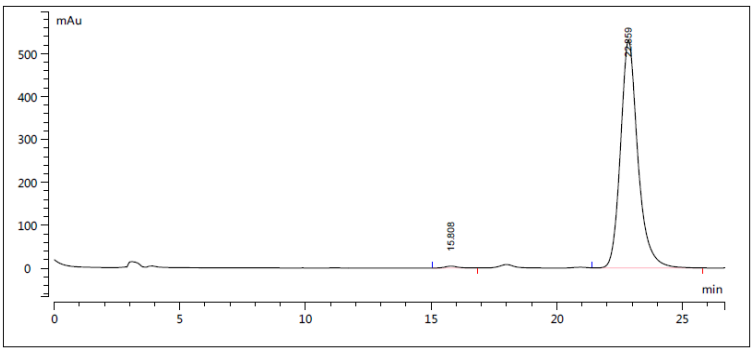
From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 31.3 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2u**, 45.0 mg (92% yield) of compound **3au** was obtained as a white solid, [α] D ^{24} = - 470 (*c* = 1.0, $CHCl_3$), Mp. = 178-179 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 22.9 min, t_{minor} = 15.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, J = 7.7, 0.7 Hz, 1H), 7.43 (td, J = 7.9, 1.3 Hz, 1H), 7.21 – 7.11 (m, 1H), 7.10 – 6.92 (m, 4H), 6.58 (ddd, J = 58.2, 56.7, 7.1 Hz, 1H), 4.60 – 4.41 (m, 1H), 4.25 (d, J = 8.1 Hz, 1H), 3.92 – 3.80 (m, 4H), 3.72 (tt, J = 10.7, 7.0 Hz, 1H), 3.35 (s, 3H), 2.72 (d, J = 1.7 Hz, 1H), 0.80 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.5,

171.6, 167.6, 147.8, 145.2, 136.3, 132.0, 129.8, 128.9, 127.3, 125.6, 123.7, 123.2, 117.5 (dd, $J_{C\text{-}F}$ = 330.9, 323.6 Hz) 116.7, 113.6, 86.6, 62.6, 62.6, 60.9, 59.56 (dd, $J_{C\text{-}F}$ = 38.2, 32.3 Hz) 55.9, 50.1, 50.0, 30.1, 13.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, J = 295.6 Hz, 1F), -123.1 (d, J = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_5S$ $[M+Na]^+$: 511.1110, found 511.1110.



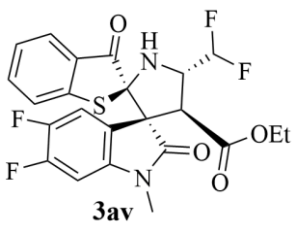
No	Retention Time	Area	% Area	Int Type
1	15.878	3799.750	46.100	BB
2	17.692	388.967	4.719	BB
3	20.878	243.088	2.949	BB
4	22.995	3810.651	46.232	BB

No	Retention Time	Area	% Area	Int Type
1	15.878	3799.750	49.980	BB
2	22.995	3810.651	50.232	BB

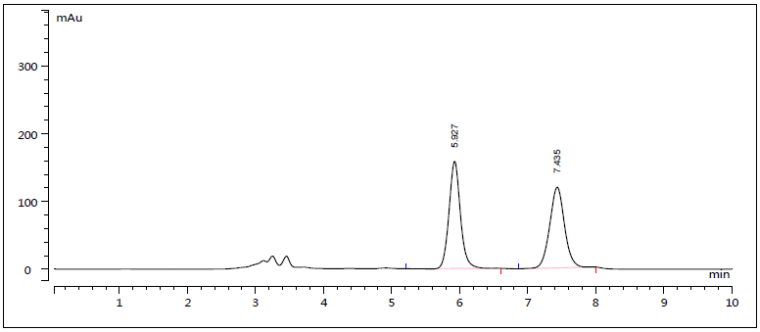


No	Retention Time	Area	% Area	Int Type
1	15.808	138.953	0.544	BB
2	22.859	25391.618	99.456	BB

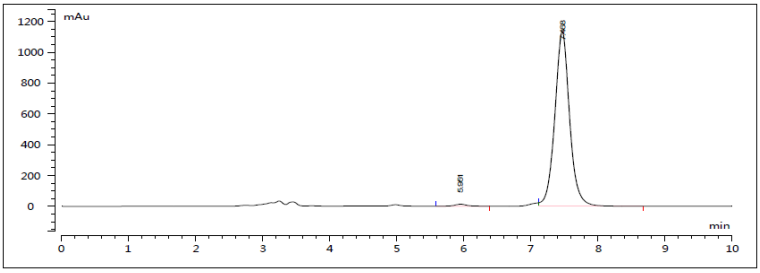
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-5'',6''-difluoro-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 32.0 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2v**, 42.2 mg (86% yield) of compound **3av** was obtained as a white solid, [α] D ^{25} = - 375 (*c* = 1.0, $CHCl_3$), Mp. = 80-81 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 7.5 min, t_{minor} = 6.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.64 (m, 1H), 7.47 (td, *J* = 7.9, 1.3 Hz, 1H), 7.34 (dd, *J* = 9.2, 7.7 Hz, 1H), 7.23 – 7.14 (m, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 6.78 – 6.37 (m, 2H), 4.58 – 4.34 (m, 1H), 4.27 (d, *J* = 8.1 Hz, 1H), 3.87 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.77 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.07 (s, 3H), 2.73 (s, 1H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.1, 171.3, 167.3, 152.7, 152.6, 150.3, 150.1, 147.8, 147.7, 147.5, 145.4, 145.3, 140.8, 140.7, 140.7, 140.6, 136.6, 128.7, 127.3, 125.8, 123.6, 123.6, 123.6, 123.5, 123.3, 117.2 (dd, $J_{C\text{-}F}$ = 331.4, 323.6 Hz), 114.6, 114.4, 98.6, 98.3, 86.4, 62.4, 61.2, 59.24 (dd, $J_{C\text{-}F}$ = 38.4, 32.7 Hz), 49.5, 49.4, 26.9, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 297.7 Hz, 1F), -122.8 (d, *J* = 297.5 Hz, 1F), -133.6 (d, *J* = 37.6 Hz, 1F), -144.1 (d, *J* = 37.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{18}F_4N_2NaO_4S$ $[M+Na]^+$: 517.0816, found 517.0816.



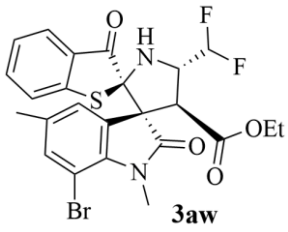
No	Retention Time	Area	% Area	Int Type
1	5.927	1835.977	50.465	BB
2	7.435	1802.113	49.535	BB



No	Retention Time	Area	% Area	Int Type
1	5.951	161.553	0.919	BB
2	7.468	17409.294	99.081	BB

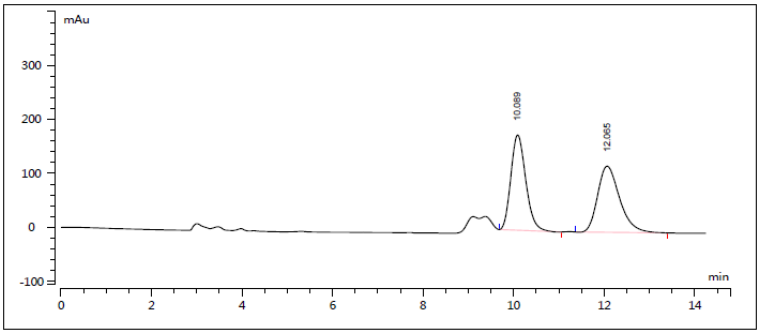
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-7''-bromo-5'-(difluoromethyl)-1'',5''-dimethyl-2'',3-dioxo-

3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

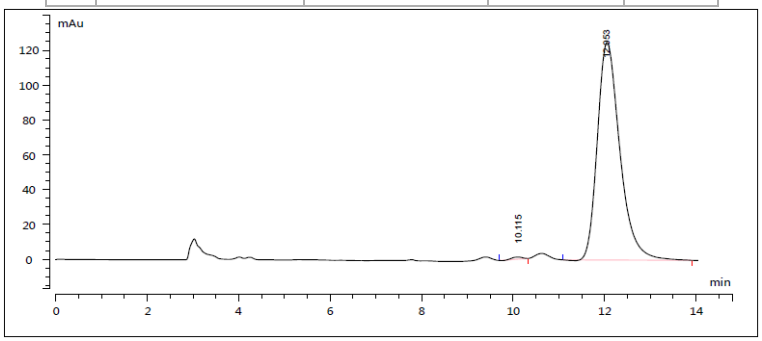


3aw

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 38.8 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2w**, 53.6 mg (97% yield) of compound **3aw** was obtained as a yellow solid, [α] D ^{25} = - 400 (*c* = 1.0, $CHCl_3$), Mp. = 79-80 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralcel OD-H column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 12.1 min, t_{minor} = 10.1 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.61 (m, 1H), 7.44 (ddd, *J* = 15.8, 11.2, 1.5 Hz, 2H), 7.28 (s, 1H), 7.24 – 7.11 (m, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 6.59 (ddd, *J* = 58.1, 56.8, 7.1 Hz, 1H), 4.58 – 4.36 (m, 1H), 4.24 (d, *J* = 8.1 Hz, 1H), 3.91 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.77 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.34 (s, 3H), 2.70 (s, 1H), 2.53 (s, 3H), 0.83 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.3, 171.8, 167.3, 147.6, 141.1, 136.4, 136.1, 130.8, 128.8, 127.3, 125.7, 125.0, 123.3, 121.5, 117.4 (dd, J_{C-F} = 331.3, 323.7 Hz), 115.4, 86.5, 62.0, 61.1, 59.3 (dd, J_{C-F} = 38.4, 32.6 Hz), 50.0, 49.9, 30.1, 18.9, 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.2 (d, *J* = 297.1 Hz, 1F), -123.0 (d, *J* = 297.1 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{21}BrF_2N_2NaO_4S$ $[M+Na]^+$: 573.0266, found 573.0266.



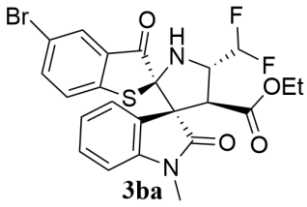
No	Retention Time	Area	% Area	Int Type
1	10.089	4041.165	49.447	BB
2	12.065	4131.477	50.553	BB



No	Retention Time	Area	% Area	Int Type
1	10.115	18.181	0.424	BB
2	12.053	4274.499	99.576	BB

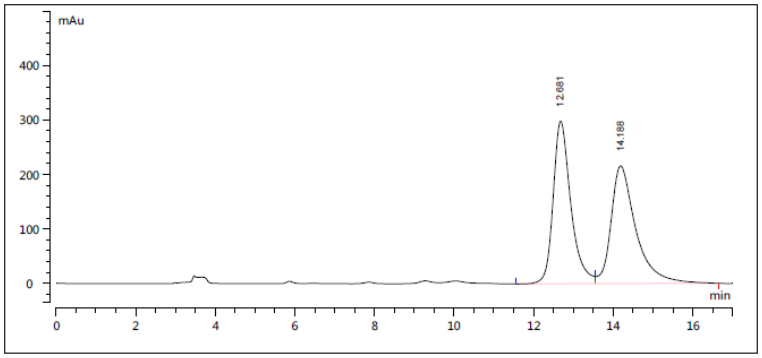
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5-bromo-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-

dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

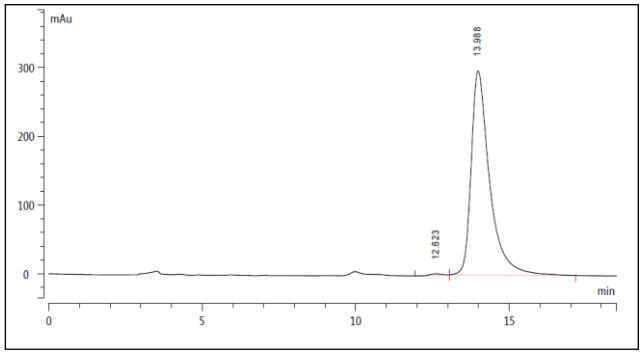


3ba

From 30.5 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1b** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 42.8 mg (80% yield) of compound **3ba** was obtained as a yellow solid, [α] D ^{25} = - 409 (*c* = 1.0, $CHCl_3$), Mp. = 191-192 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 75:25, 1.0 mL/min). Retention time: t_{major} = 14.0 min, t_{minor} = 12.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 2.0 Hz, 1H), 7.52 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.40 (dd, *J* = 12.1, 4.4 Hz, 2H), 7.18 – 7.07 (m, 1H), 6.87 (dd, *J* = 14.1, 8.0 Hz, 2H), 6.55 (ddd, *J* = 58.1, 56.6, 7.1 Hz, 1H), 4.61 – 4.44 (m, 1H), 4.23 (d, *J* = 8.1 Hz, 1H), 3.80 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.69 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.12 (s, 3H), 2.77 (s, 1H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 201.4, 171.4, 167.4, 146.5, 144.1, 139.0, 130.4, 130.1, 129.9, 128.2, 124.6, 124.2, 123.3, 119.8, 117.3 (dd, J_{C-F} = 331.1, 323.7 Hz), 108.2, 87.3, 62.6, 61.1, 59.57 (dd, J_{C-F} = 38.4, 32.5 Hz), 49.7, 49.6, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 296.7 Hz, 1F), -123.0 (d, *J* = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}BrF_2N_2NaO_4S$ $[M+Na]^+$: 559.0109, found 559.0109.

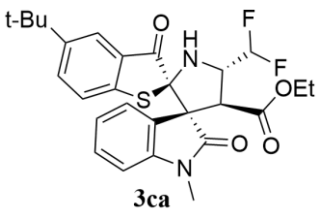


No	Retention Time	Area	% Area	Int Type
1	12.681	9226.288	49.665	BB
2	14.188	9350.868	50.335	BB



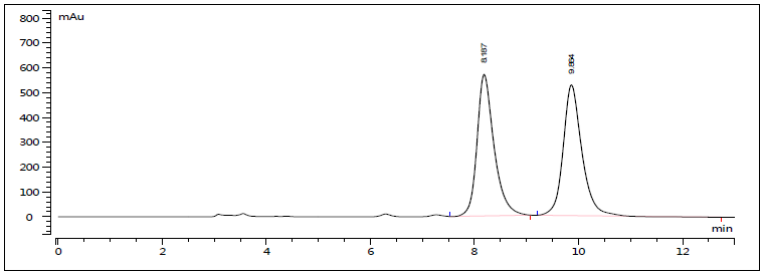
No	Retention Time	Area	% Area	Int Type
1	12.623	45.536	0.366	BB
2	13.988	12401.307	99.634	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5-(tert-butyl)-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

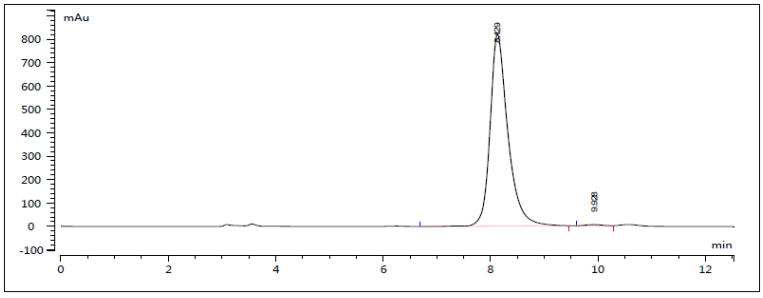


3ca

From 28.3 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1c** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 49.0 mg (95% yield) of compound **3ca** was obtained as a white solid, [α] D ^{25} = - 368 (*c* = 1.0, $CHCl_3$), Mp. = 214-215 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2-propanol 87:13, 1.0 mL/min). Retention time: t_{major} = 8.1 min, t_{minor} = 9.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 2.0 Hz, 1H), 7.52 (dd, *J* = 8.3, 2.1 Hz, 1H), 7.47 – 7.35 (m, 2H), 7.20 – 7.05 (m, 1H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.55 (ddd, *J* = 58.2, 56.8, 7.1 Hz, 1H), 4.65 – 4.47 (m, 1H), 4.37 (d, *J* = 8.0 Hz, 1H), 3.80 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.70 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.13 (s, 3H), 2.76 (s, 1H), 1.30 (s, 9H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.3, 171.5, 167.7, 149.1, 145.2, 144.1, 134.5, 129.9, 128.5, 128.5, 124.2, 123.8, 123.1, 122.9, 117.4 (dd, J_{C-F} = 330.6, 323.9 Hz), 108.0, 86.7, 62.2, 61.0, 59.8 (dd, J_{C-F} = 38.2, 32.3 Hz), 50.0, 49.9, 34.6, 31.1, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.4 (d, *J* = 295.2 Hz, 1F), -123.0 (d, *J* = 295.2 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{28}F_2N_2NaO_4S$ $[M+Na]^+$: 537.1630, found 537.1630.



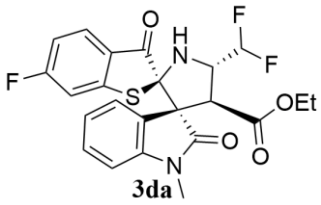
No	Retention Time	Area	% Area	Int Type
1	8.187	12923.523	49.731	BB
2	9.864	13063.206	50.269	BB



No	Retention Time	Area	% Area	Int Type
1	8.129	18856.281	99.532	BB
2	9.928	88.682	0.468	BB

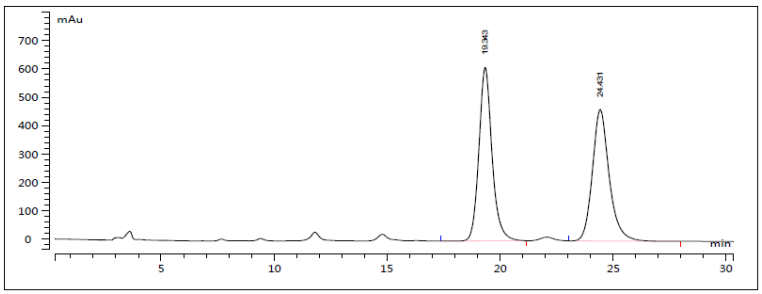
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-6-fluoro-1''-methyl-2'',3-dioxo-3H-

dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

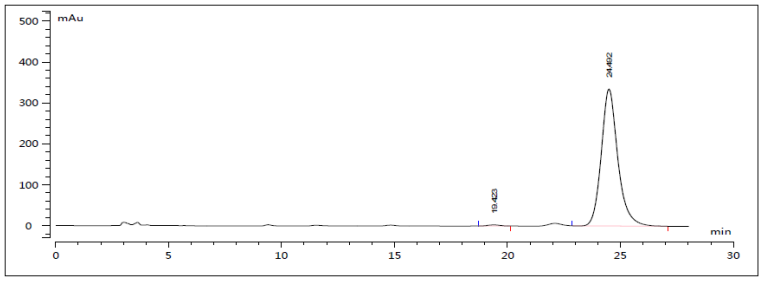


3da

From 24.5 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1d** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 43.5 mg (90% yield) of compound **3da** was obtained as a white solid, [α] D ^{25} = - 381 (*c* = 1.0, $CHCl_3$), Mp. = 184-185 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IA-3 column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 24.5 min, t_{minor} = 19.4 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 8.5, 5.5 Hz, 1H), 7.41 (ddd, *J* = 8.8, 6.1, 2.2 Hz, 2H), 7.13 (dd, *J* = 11.1, 4.1 Hz, 1H), 6.89 – 6.81 (m, 2H), 6.74 – 6.39 (m, 2H), 4.54 (td, *J* = 12.0, 7.0 Hz, 1H), 4.26 (d, *J* = 8.1 Hz, 1H), 3.80 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.69 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.12 (s, 3H), 2.78 (s, 1H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 200.5, 171.4, 169.2, 167.5, 166.7, 150.7, 150.6, 144.1, 130.1, 129.7, 129.6, 128.2, 125.3, 125.3, 124.2, 123.3, 117.4 (dd, J_{C-F} = 331.0, 323.7 Hz), 114.0, 113.7, 110.5, 110.2, 108.1, 87.4, 62.5, 61.0, 59.6 (dd, J_{C-F} = 38.4, 32.5 Hz), 49.7, 49.6, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ - 99.1, -119.0 (d, *J* = 295.6 Hz, 1F), -123.0 (d, *J* = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}F_3N_2NaO_4S$ $[M+Na]^+$: 499.0910, found 499.0910.

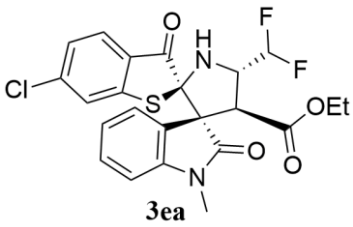


No	Retention Time	Area	% Area	Int Type
1	19.343	24682.401	50.724	BB
2	24.431	23977.865	49.276	BB



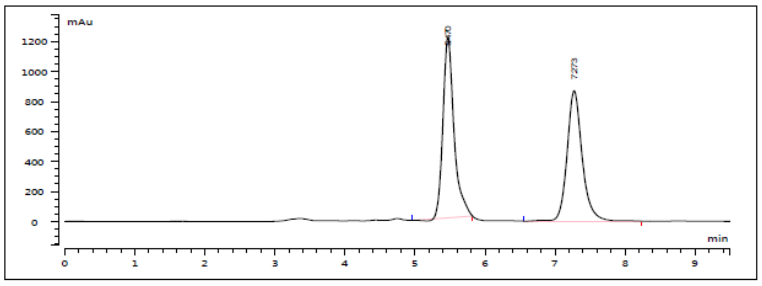
No	Retention Time	Area	% Area	Int Type
1	19.423	98.808	0.575	BB
2	24.492	17082.092	99.425	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-6-chloro-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

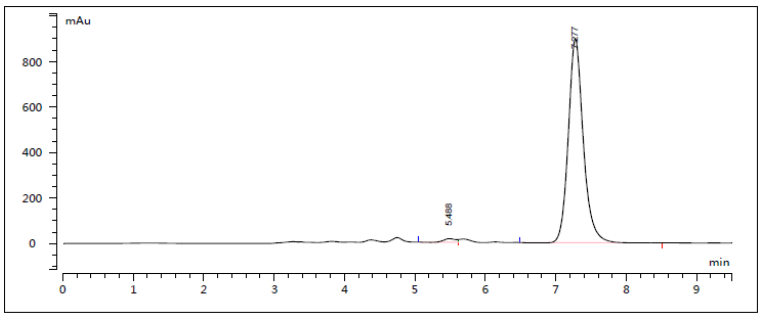


3ea

From 26.1 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1e** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 42.3 mg (86% yield) of compound **3ea** was obtained as a white solid, [α] D ^{25} = - 510 (*c* = 1.0, $CHCl_3$), Mp. = 167-168 °C. Dr (> 20:1) was determined by HPLC analysis. 97% ee was determined by HPLC analysis (Daicel Chiralpak IA-3 column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 7.3 min, t_{minor} = 5.5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (ddd, *J* = 13.0, 6.4, 2.4 Hz, 2H), 7.32 (t, *J* = 7.9 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 2H), 6.94 – 6.87 (m, 1H), 6.87 – 6.51 (m, 2H), 4.53 (ddd, *J* = 11.9, 9.6, 6.4 Hz, 1H), 4.21 (d, *J* = 8.2 Hz, 1H), 3.77 (ddd, *J* = 10.6, 9.0, 5.3 Hz, 1H), 3.70 (ddd, *J* = 17.9, 8.9, 5.3 Hz, 1H), 3.09 (s, 3H), 2.69 (s, 1H), 0.75 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 200.7, 171.5, 167.4, 149.5, 144.2, 135.9, 135.0, 130.0, 128.0, 127.6, 124.7, 124.4, 123.3, 121.7, 117.5 (dd, J_{C-F} = 331.3, 323.6 Hz), 108.1, 87.0, 63.0, 61.0, 59.46 (dd, J_{C-F} = 38.4, 32.5 Hz), 49.6, 49.5, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.1 (d, *J* = 297.5 Hz, 1F), -122.7 (d, *J* = 298.0 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}ClF_2N_2NaO_4S$ $[M+Na]^+$: 515.0614, found 515.0614.

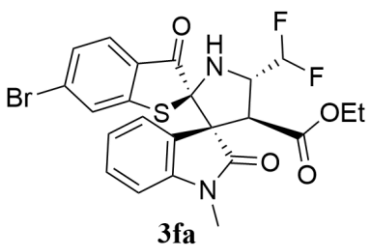


No	Retention Time	Area	% Area	Int Type
1	5.470	13177.002	50.291	BB
2	7.273	13024.760	49.709	BB



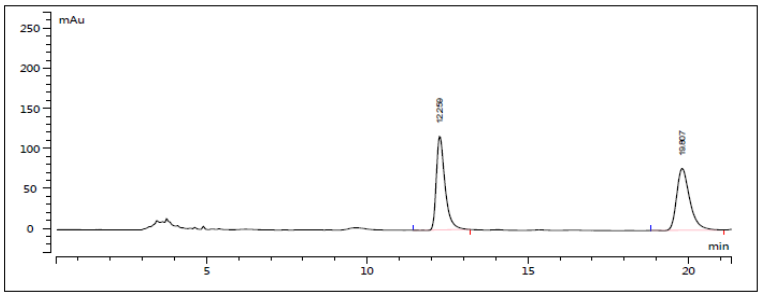
No	Retention Time	Area	% Area	Int Type
1	5.488	172.437	1.290	BB
2	7.277	13194.459	98.710	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-6-bromo-5'-(difluoromethyl)-1''-methyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

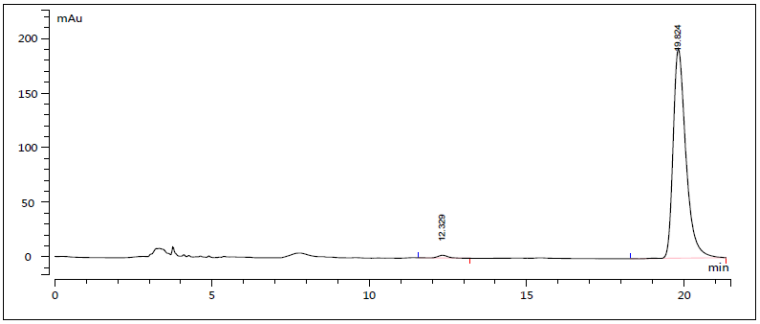


3fa

From 30.5 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1f** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 47.7 mg (89% yield) of compound **3fa** was obtained as a yellow solid, [α] D ^{25} = - 544 (*c* = 1.0, $CHCl_3$), Mp. = 207-208 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IA-3 column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 19.8 min, t_{minor} = 12.3 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.31 (m, 3H), 7.24 (dd, *J* = 16.2, 8.4 Hz, 1H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.89 – 6.49 (m, 2H), 4.59 – 4.46 (m, 1H), 4.21 (d, *J* = 8.2 Hz, 1H), 3.83 – 3.73 (m, 1H), 3.69 (ddd, *J* = 14.3, 8.5, 4.9 Hz, 1H), 3.09 (s, 3H), 2.71 (s, 1H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 201.0, 171.5, 167.4, 150.0, 144.2, 136.0, 130.9, 130.0, 128.0, 125.9, 124.4, 123.3, 123.0, 122.3, 117.54 (dd, J_{C-F} = 331.3, 323.6 Hz), 108.1, 87.1, 68.5, 63.1, 61.0, 59.44 (dd, J_{C-F} = 38.2, 32.5 Hz), 49.6, 49.5, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.1 (d, *J* = 298.0 Hz, 1F), -122.7 (d, *J* = 298.0 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{19}BrF_2N_2NaO_4S$ $[M+Na]^+$: 560.0109, found 561.0109.



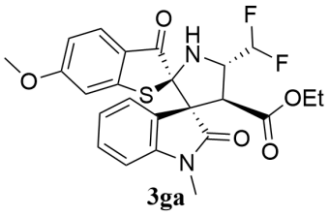
No	Retention Time	Area	% Area	Int Type
1	12.259	2188.295	50.009	BB
2	19.807	2187.504	49.991	BB



No	Retention Time	Area	% Area	Int Type
1	12.329	54.159	0.995	BB
2	19.824	5391.182	99.005	BB

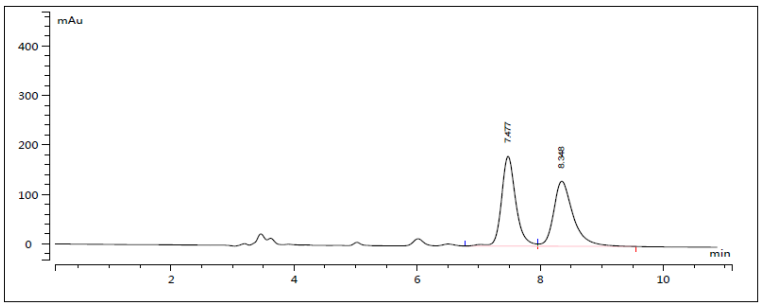
Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-6-methoxy-1''-methyl-2'',3-dioxo-3H-

dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

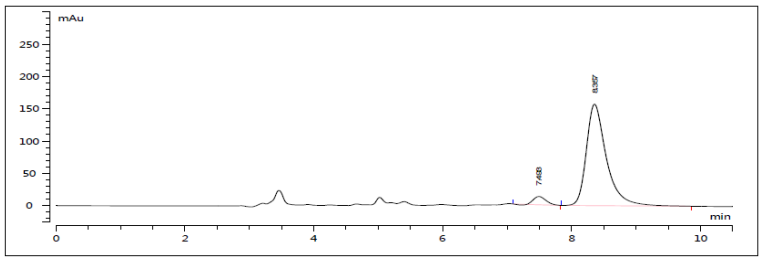


3ga

From 25.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1g** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 34.2 mg (70% yield) of compound **3ga** was obtained as a white solid, [α] D ^{25} = - 300 (*c* = 1.0, $CHCl_3$), Mp. = 177-178 °C. Dr (> 20:1) was determined by HPLC analysis. 90% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 8.4 min, t_{minor} = 7.5 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.6 Hz, 1H), 7.46 – 7.34 (m, 2H), 7.13 (t, *J* = 7.3 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 6.78 – 6.30 (m, 3H), 4.65 – 4.45 (m, 1H), 4.32 (d, *J* = 8.0 Hz, 1H), 3.91 – 3.53 (m, 5H), 3.12 (s, 3H), 2.75 (s, 1H), 0.73 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 199.9, 171.4, 167.7, 166.5, 150.8, 144.1, 129.9, 129.0, 128.5, 124.2, 123.1, 121.9, 117.5 (dd, J_{C-F} = 331.0, 323.5 Hz), 113.3, 108.0, 107.1, 87.3, 62.3, 60.9, 59.6 (dd, J_{C-F} = 38.1, 32.5 Hz), 55.8, 49.8, 49.7, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.4 (d, *J* = 298.0 Hz, 1F), -123.1 (d, *J* = 298.0 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_5S$ $[M+Na]^+$: 511.1110, found 511.1110.

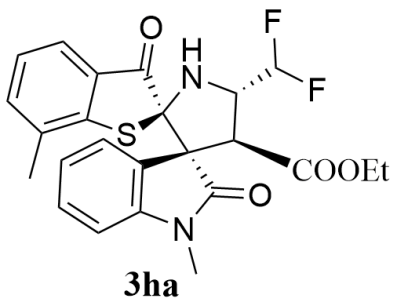


No	Retention Time	Area	% Area	Int Type
1	7.477	2929.285	50.234	BB
2	8.348	2902.035	49.766	BB



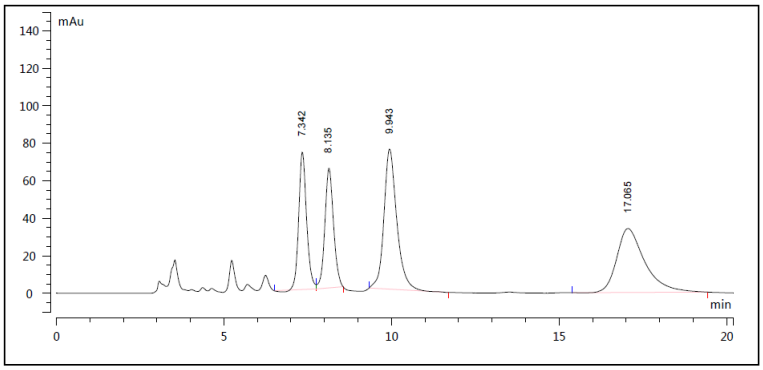
No	Retention Time	Area	% Area	Int Type
1	7.493	163.913	4.613	BB
2	8.357	3389.025	95.387	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1'',7-dimethyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate



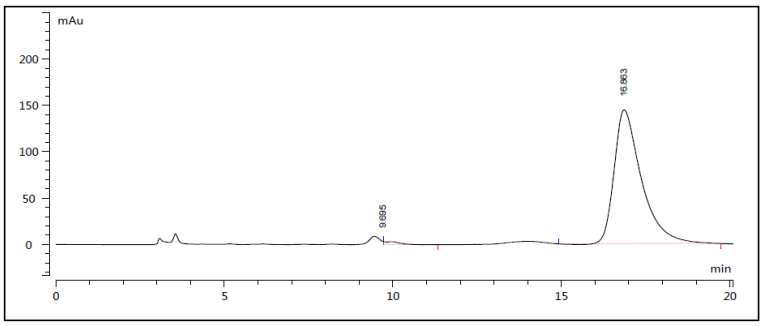
3ha

From 24.1 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1h** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 46.0 mg (97% yield) of compound **3ha** was obtained as a white solid, [α] D ^{25} = - 402 (*c* = 1.0, $CHCl_3$), Mp. = 184-185 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 87:13, 1.0 mL/min). Retention time: t_{major} = 16.9 min, t_{minor} = 9.7 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.6 Hz, 1H), 7.48 – 7.36 (m, 2H), 7.30 – 7.24 (m, 1H), 7.12 (dt, *J* = 15.3, 7.5 Hz, 2H), 6.84 (d, *J* = 7.8 Hz, 1H), 6.73 – 6.41 (m, 1H), 4.62 – 4.50 (m, 1H), 4.35 (d, *J* = 8.1 Hz, 1H), 3.79 (dq, *J* = 10.9, 7.1 Hz, 1H), 3.69 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.11 (s, 3H), 2.76 (s, 1H), 2.04 (s, 3H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.7, 171.5, 167.7, 147.6, 144.1, 136.6, 132.4, 129.9, 128.7, 128.3, 125.7, 124.7, 124.2, 123.1, 117.41 (dd, J_{C-F} = 330.7, 323.7 Hz), 108.1, 86.4, 62.4, 61.0, 59.68 (dd, J_{C-F} = 38.4, 32.5 Hz), 50.0, 49.9, 26.7, 18.5, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.4 (d, *J* = 295.6 Hz, 1F), -123.0 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 495.1161, found 495.1161.



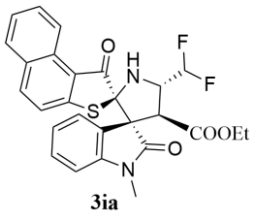
No	Retention Time	Area	% Area	Int Type
1	7.342	1191.394	18.842	BB
2	8.135	1156.156	18.285	BB
3	9.943	1993.866	31.533	BB
4	17.065	1981.684	31.340	BB

No	Retention Time	Area	% Area	Int Type
1	9.943	1993.866	50.153	BB
2	17.065	1981.684	49.847	BB



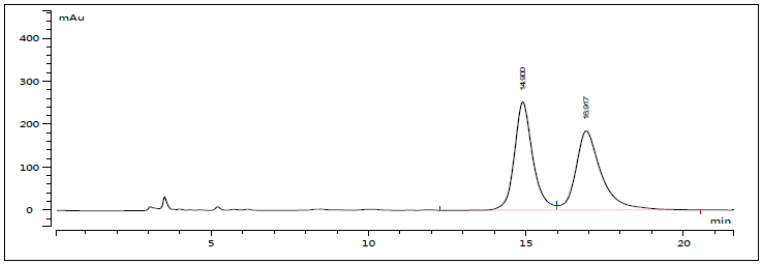
No	Retention Time	Area	% Area	Int Type
1	9.695	78.394	0.955	BB
2	16.863	8134.695	99.045	BB

Ethyl-(2'*S*,3*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1-methyl-1'',2-dioxo-1''H-dispiro[indoline-3,3'-pyrrolidine-2',2''-naphtho[2,1-*b*]thiophene]-4'-carboxylate

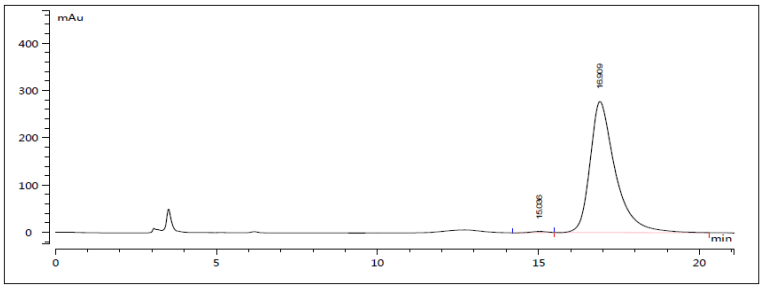


3ia

From 27.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1i** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 45.7 mg (90% yield) of compound **3ia** was obtained as a yellow solid, [α] D ^{25} = - 673 (*c* = 1.0, $CHCl_3$), Mp. = 140-141 °C. Dr (> 20:1) was determined by HPLC analysis. 99% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 87:13, 1.0 mL/min). Retention time: t_{major} = 16.9 min, t_{minor} = 15.0 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.6 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.73 – 7.60 (m, 1H), 7.54 – 7.44 (m, 2H), 7.40 (td, *J* = 7.8, 1.0 Hz, 1H), 7.15 (dd, *J* = 11.1, 4.1 Hz, 1H), 7.06 (d, *J* = 8.6 Hz, 1H), 6.93 – 6.56 (m, 2H), 4.58 (ddd, *J* = 11.9, 9.5, 6.4 Hz, 1H), 4.40 (d, *J* = 8.1 Hz, 1H), 3.85 – 3.65 (m, 2H), 3.04 (s, 3H), 2.74 (s, 1H), 0.75 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 203.3, 171.6, 167.7, 152.7, 144.1, 137.4, 131.5, 130.8, 130.3, 129.9, 128.6, 128.5, 126.4, 124.3, 123.2, 123.1, 121.3, 121.1, 117.7 (dd, J_{C-F} = 331.0, 323.5 Hz), 108.1, 86.7, 62.6, 61.0, 59.69 (dd, J_{C-F} = 38.2, 32.3 Hz), 49.7, 49.6, 26.7, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.2 (d, *J* = 296.3 Hz, 1F), -123.0 (d, *J* = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 531.1161, found 531.1162.

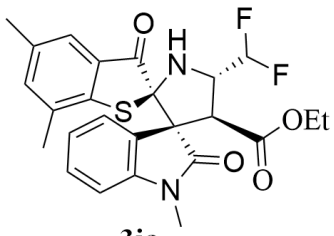


No	Retention Time	Area	% Area	Int Type
1	14.900	10203.736	49.504	BB
2	16.917	10408.120	50.496	BB



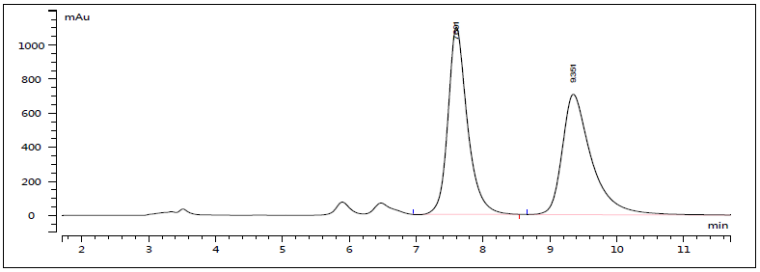
No	Retention Time	Area	% Area	Int Type
1	15.036	77.263	0.509	BB
2	16.909	15087.223	99.491	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1'',5,7-trimethyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

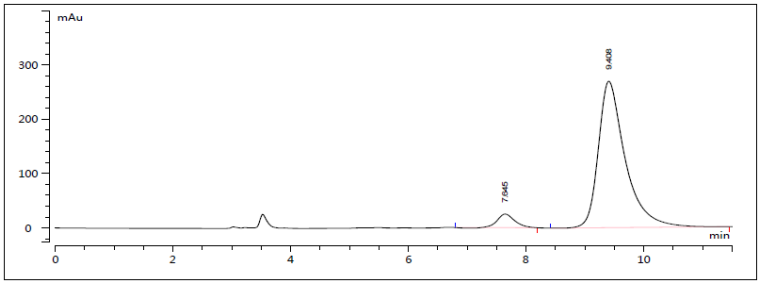


3ja

From 25.5 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1j** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 37.5 mg (78% yield) of compound **3ja** was obtained as a white solid, [α] D ^{25} = - 318 (*c* = 1.0, $CHCl_3$), Mp. = 184-185 °C. Dr (> 20:1) was determined by HPLC analysis. 88% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 9.4 min, t_{minor} = 7.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.34 (m, 3H), 7.13 (dd, *J* = 13.6, 5.8 Hz, 2H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.58 (ddd, *J* = 58.2, 56.8, 7.1 Hz, 1H), 4.64 – 4.49 (m, 1H), 4.36 (d, *J* = 8.1 Hz, 1H), 3.79 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.70 (dq, *J* = 10.8, 7.1 Hz, 1H), 3.12 (s, 3H), 2.72 (s, 1H), 2.29 (s, 3H), 2.01 (s, 3H), 0.75 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.8, 171.6, 167.7, 144.6, 144.1, 138.1, 135.7, 132.1, 129.9, 128.6, 128.4, 124.8, 124.2, 123.1, 117.4 (dd, J_{C-F} = 329.5, 324.7 Hz), 108.0, 86.6, 62.4, 60.9, 59.7 (t, J_{C-F} = 38.2, 32.1 Hz), 50.0, 50.0, 29.7, 26.7, 20.7, 18.4, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 295.2 Hz, 1F), -123.0 (d, *J* = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{25}H_{24}F_2N_2NaO_4S$ $[M+Na]^+$: 509.1317, found 509.1317.

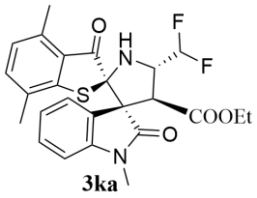


No	Retention Time	Area	% Area	Int Type
1	7.601	22159.113	50.790	BB
2	9.351	21469.988	49.210	BB



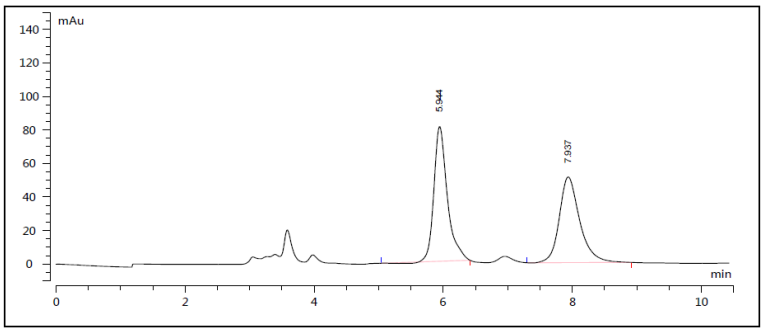
No	Retention Time	Area	% Area	Int Type
1	7.645	509.130	5.617	BB
2	9.408	8555.285	94.383	BB

Ethyl-(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1'',4,7-trimethyl-2'',3-dioxo-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-4'-carboxylate

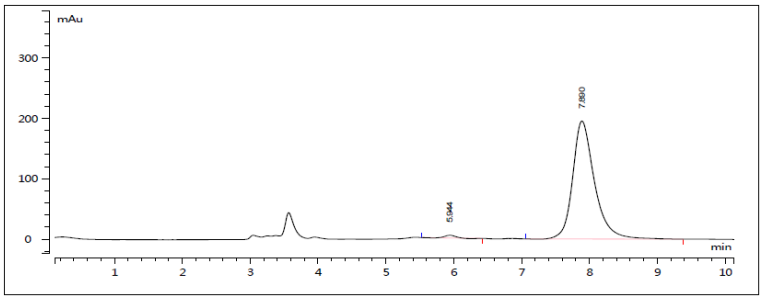


3ka

From 25.5 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1k** and 27.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **2a**, 45.0 mg (88% yield) of compound **3ka** was obtained as a white solid, [α] D ^{25} = - 408 (*c* = 1.0, $CHCl_3$), Mp. = 218-219 °C. Dr (> 20:1) was determined by HPLC analysis. 98% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 7.9 min, t_{minor} = 5.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (ddd, *J* = 11.9, 8.8, 4.2 Hz, 2H), 7.18 – 7.06 (m, 2H), 6.88 – 6.47 (m, 3H), 4.62 – 4.48 (m, 1H), 4.30 (d, *J* = 8.2 Hz, 1H), 3.82 – 3.64 (m, 2H), 3.08 (s, 3H), 2.70 (s, 1H), 2.61 (s, 3H), 1.98 (s, 3H), 0.74 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 203.8, 171.8, 167.7, 147.6, 144.1, 139.4, 135.5, 129.8, 129.5, 128.3, 127.8, 126.0, 124.3, 123.1, 117.6 (dd, J_{C-F} = 330.7, 323.5 Hz), 108.0, 85.5, 62.7, 60.9, 59.57 (dd, J_{C-F} = 38.1, 32.3 Hz), 49.9, 49.8, 26.7, 18.8, 18.1, 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.3 (d, *J* = 295.9 Hz, 1F), -123.0 (d, *J* = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{25}H_{24}F_2N_2NaO_4S$ $[M+Na]^+$: 509.1317, found 509.1317.

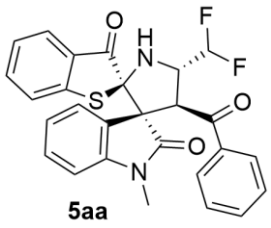


No	Retention Time	Area	% Area	Int Type
1	5.944	1155.980	50.669	BB
2	7.937	1125.464	49.331	BB



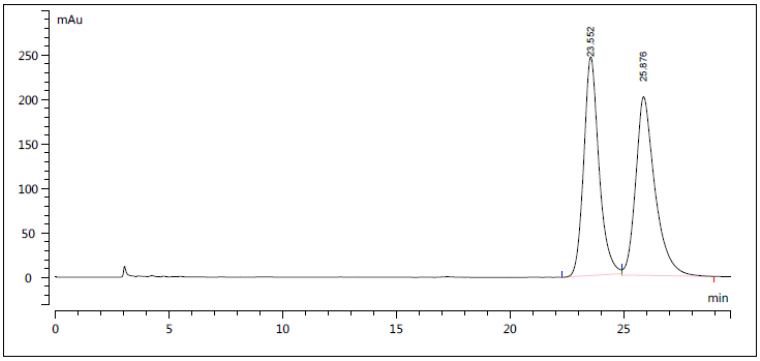
No	Retention Time	Area	% Area	Int Type
1	5.944	39.973	0.909	BB
2	7.890	4359.383	99.091	BB

(2*S*,3'*S*,4'*S*,5'*S*)-4'-benzoyl-5'-(difluoromethyl)-1''-methyl-3H-dispiro [benzo [*b*] thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

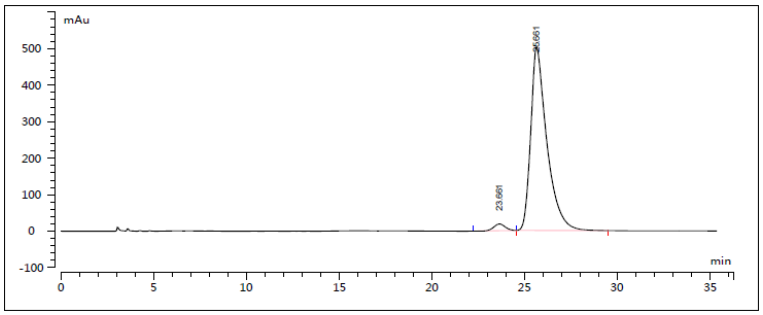


5aa

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 31.6 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4a**, 43.6 mg (89% yield) of compound **5aa** was obtained as a white solid, [α] D ^{24} = - 36 (*c* = 1.0, $CHCl_3$), Mp. = 98-99 °C. Dr (> 20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 91:9, 1.0 mL/min). Retention time: t_{major} = 25.7 min, t_{minor} = 23.7 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.46 – 7.39 (m, 3H), 7.39 – 7.34 (m, 2H), 7.31 (td, *J* = 7.8, 1.2 Hz, 1H), 7.27 – 7.22 (m, 2H), 7.21 – 7.11 (m, 2H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.68 (ddd, *J* = 58.6, 56.7, 7.2 Hz, 1H), 6.49 (d, *J* = 7.7 Hz, 1H), 5.15 (d, *J* = 7.7 Hz, 1H), 4.95 (dd, *J* = 12.4, 6.8 Hz, 1H), 2.84 (s, 1H), 2.46 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.8, 194.5, 171.4, 147.7, 143.1, 136.5, 136.4, 133.0, 129.8, 129.1, 128.1, 128.1, 127.4, 127.2, 125.6, 125.3, 123.4, 123.3, 117.7 (dd, J_{C-F} = 329.1, 324.7 Hz), 108.1, 87.0, 63.8, 59.43 (dd, J_{C-F} = 38.9, 32.5 Hz), 52.7, 52.7, 26.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.9 (d, *J* = 295.6 Hz, 1F), -123.4 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{20}F_2N_2NaO_3S$ $[M+Na]^+$: 513.1055, found 513.1055.

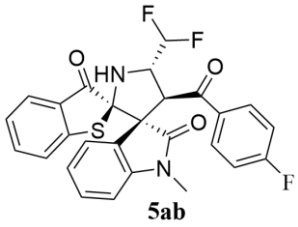


No	Retention Time	Area	% Area	Int Type
1	23.552	11407.605	49.083	BB
2	25.876	11834.052	50.917	BB



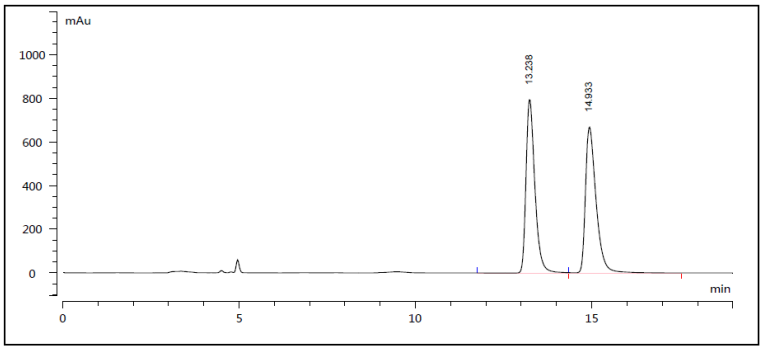
No	Retention Time	Area	% Area	Int Type
1	23.661	776.830	2.496	BB
2	25.661	30350.267	97.504	BB

(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-4'-(4-fluorobenzoyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

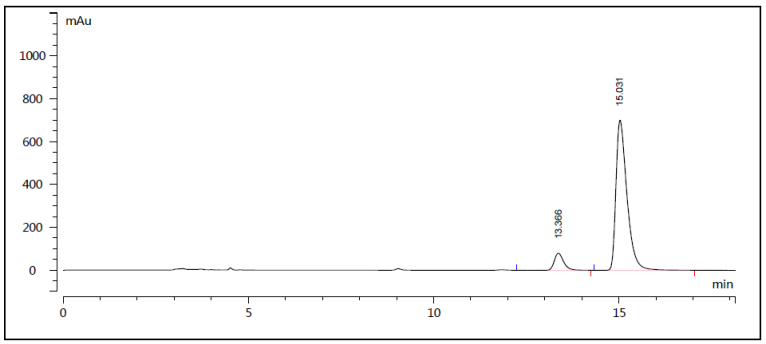


5ab

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 33.7 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4b**, 43.5 mg (86% yield) of compound **5ab** was obtained as a white solid, [α] D ^{25} = - 227 (*c* = 1.0, $CHCl_3$), Mp. = 88-89 °C. Dr (> 20:1) was determined by HPLC analysis. 82% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 15.0 min, t_{minor} = 13.4 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.3 Hz, 1H), 7.53 – 7.39 (m, 4H), 7.32 (td, *J* = 7.8, 1.0 Hz, 1H), 7.24 – 7.13 (m, 2H), 7.05 – 6.89 (m, 3H), 6.87 – 6.44 (m, 2H), 5.14 (d, *J* = 7.8 Hz, 1H), 4.94 (td, *J* = 12.1, 7.3 Hz, 1H), 2.85 (s, 1H), 2.57 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.6, 192.7, 171.4, 166.9, 164.4, 147.7, 143.0, 136.4, 132.7, 132.7, 131.0, 131.0, 129.9, 129.0, 127.3, 127.2, 125.7, 125.4, 123.5, 123.3, 117.6 (dd, J_{C-F} = 329.9, 243.5 Hz), 115.2, 115.1, 108.1, 87.1, 63.8, 59.6 (dd, J_{C-F} = 38.9, 32.6 Hz), 52.4, 52.3, 26.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.5, -118.9 (d, *J* = 295.9 Hz, 1F), -123.4 (d, *J* = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{19}F_3N_2NaO_3S$ $[M+Na]^+$: 531.0961, found 531.0961.

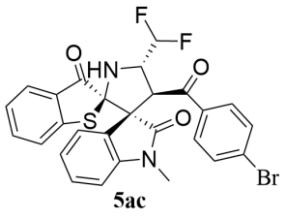


No	Retention Time	Area	% Area	Int Type
1	13.238	13860.165	49.754	BB
2	14.933	13996.972	50.246	BB



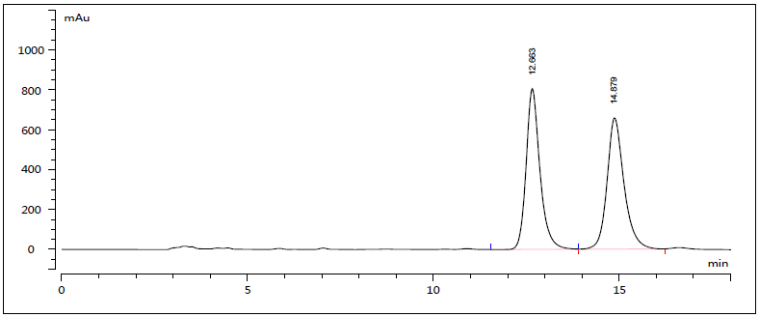
No	Retention Time	Area	% Area	Int Type
1	13.366	1387.920	8.778	BB
2	15.031	14424.224	91.222	BB

(2*S*,3'*S*,4'*S*,5'*S*)-4'-(4-bromobenzoyl)-5'-(difluoromethyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

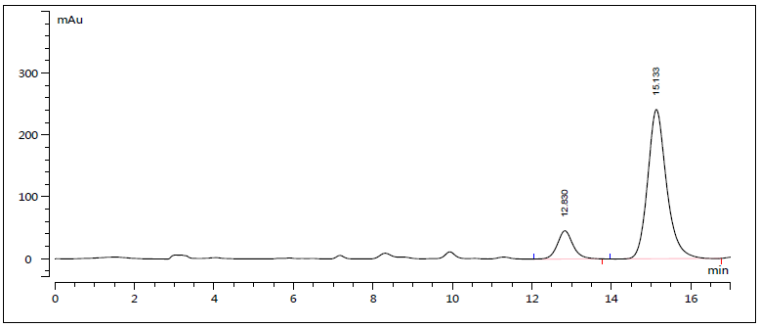


5ac

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 40.9 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4c**, 48.2 mg (85% yield) of compound **5ac** was obtained as a yellow solid, [α] D ^{25} = - 347 (*c* = 1.0, $CHCl_3$), Mp. = 56-57 °C. Dr (> 20:1) was determined by HPLC analysis. 73% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 15.1 min, t_{minor} = 12.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 1H), 7.50 – 7.37 (m, 4H), 7.32 (td, *J* = 7.8, 1.0 Hz, 1H), 7.26 (t, *J* = 4.3 Hz, 2H), 7.18 (dt, *J* = 14.9, 7.5 Hz, 2H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.83 – 6.49 (m, 2H), 5.11 (d, *J* = 7.7 Hz, 1H), 4.92 (dd, *J* = 12.0, 4.7 Hz, 1H), 2.84 (s, 1H), 2.56 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.6, 193.5, 171.3, 147.7, 143.0, 136.5, 135.1, 131.4, 129.9, 129.7, 129.0, 128.3, 127.2, 125.7, 125.4, 123.5, 123.3, 117.6 (dd, J_{C-F} = 329.9, 242.4 Hz), 108.2, 87.0, 63.7, 59.6 (dd, J_{C-F} = 38.1, 32.5 Hz), 52.6, 52.5, 29.7, 26.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 296.3 Hz, 1F), -123.4 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{19}BrF_2N_2NaO_3S$ $[M+Na]^+$: 591.0160, found 591.0160.

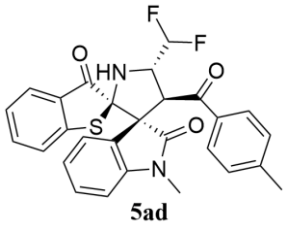


No	Retention Time	Area	% Area	Int Type
1	12.663	20825.106	49.984	BB
2	14.879	20838.087	50.016	BB



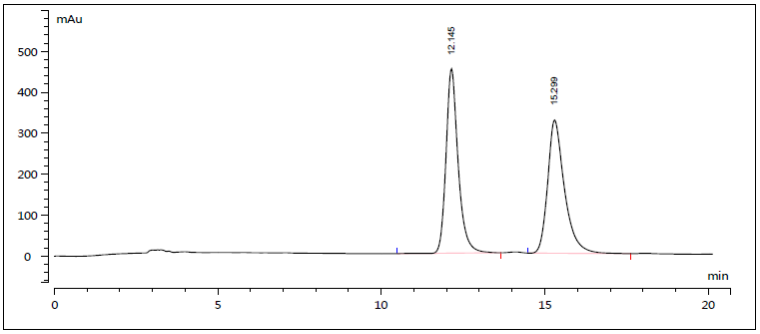
No	Retention Time	Area	% Area	Int Type
1	12.830	1245.913	13.556	BB
2	15.133	7944.936	86.444	BB

(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-4'-(4-methylbenzoyl)-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

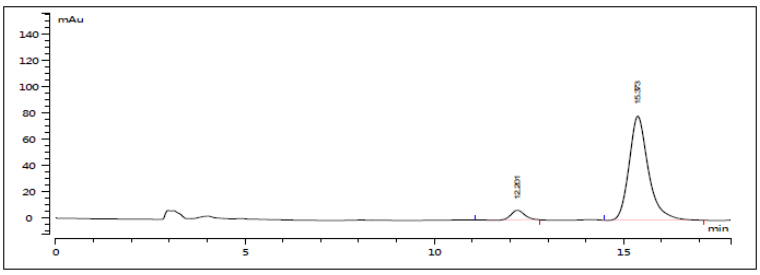


5ad

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 33.2 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4d**, 43.5 mg (86% yield) of compound **5ad** was obtained as a white solid, [α] D ^{25} = - 365 (*c* = 1.0, $CHCl_3$), Mp. = 148-149 °C. Dr (> 20:1) was determined by HPLC analysis. 88% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 15.4 min, t_{minor} = 12.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.3 Hz, 1H), 7.43 (dd, *J* = 10.6, 4.4 Hz, 2H), 7.30 (td, *J* = 8.6, 1.4 Hz, 3H), 7.22 – 7.11 (m, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.87 – 6.40 (m, 1H), 5.13 (d, *J* = 7.7 Hz, 1H), 4.94 (d, *J* = 5.4 Hz, 1H), 2.84 (s, 1H), 2.50 (s, 3H), 2.31 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.8, 193.8, 171.5, 147.7, 143.9, 143.1, 136.3, 133.9, 129.7, 129.1, 128.7, 128.4, 127.5, 127.2, 125.6, 125.4, 123.3, 123.3, 117.7(dd, J_{C-F} = 329.9, 323.7 Hz), 108.0, 87.1, 64.0, 59.60 (dd, J_{C-F} = 38.9, 32.2 Hz), 52.5, 52.4, 26.0, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.9 (d, *J* = 158.5 Hz, 1F), -123.4 (d, *J* = 164.5 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{28}H_{22}F_2N_2NaO_3S$ $[M+Na]^+$: 527.1211, found 527.1211.

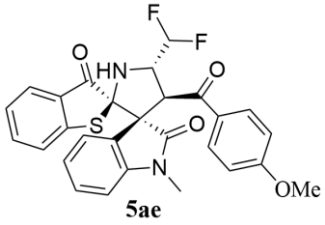


No	Retention Time	Area	% Area	Int Type
1	12.145	11605.150	50.026	BB
2	15.299	11593.218	49.974	BB



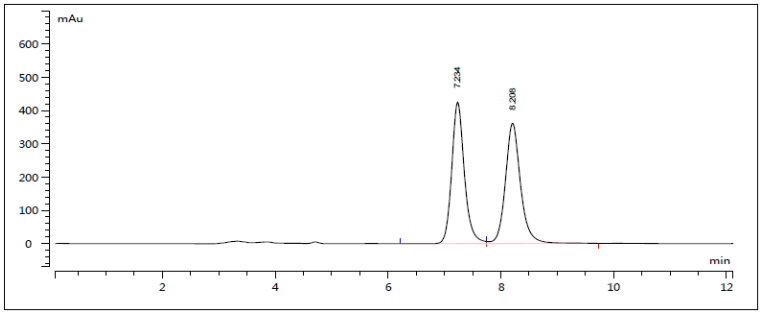
No	Retention Time	Area	% Area	Int Type
1	12.201	171.850	5.781	BB
2	15.373	2800.862	94.219	BB

(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-4'-(4-methoxybenzoyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

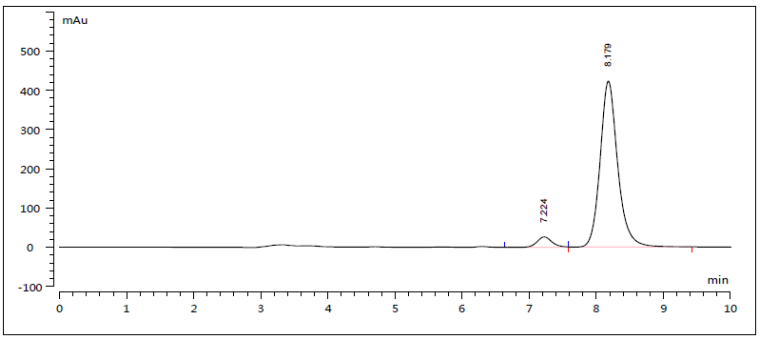


5ae

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino)benzo[*b*]thiophen-3(2H)-one **1a** and 35.2 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4e**, 42.0 mg (81% yield) of compound **5ae** was obtained as a white solid, [α] D ^{25} = - 183 (*c* = 1.0, $CHCl_3$), Mp. = 75-76 °C. Dr (> 20:1) was determined by HPLC analysis. 90% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2-propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 8.2 min, t_{minor} = 7.2 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.53 – 7.39 (m, 4H), 7.35 – 7.23 (m, 1H), 7.17 (dt, *J* = 12.4, 7.5 Hz, 2H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.82 – 6.42 (m, 4H), 5.14 (d, *J* = 7.8 Hz, 1H), 4.95 (td, *J* = 12.1, 7.2 Hz, 1H), 3.79 (s, 3H), 2.86 (s, 1H), 2.58 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.7, 192.3, 171.6, 163.6, 147.7, 143.0, 136.3, 130.7, 129.7, 129.2, 129.1, 127.5, 127.1, 125.6, 125.5, 123.3, 123.3, 117.8 (dd, J_{C-F} = 330.6, 323.9 Hz), 113.3, 108.0, 87.2, 64.2, 59.78 (dd, J_{C-F} = 38.8, 32.2 Hz), 55.5, 51.9, 51.9, 26.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 295.6 Hz, 1F), -123.4 (d, *J* = 295.2 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{28}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 543.1161, found 543.1161.

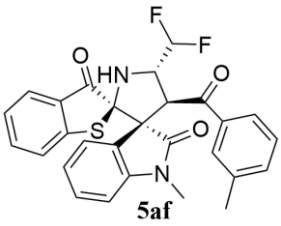


No	Retention Time	Area	% Area	Int Type
1	7.234	6621.987	49.434	BB
2	8.208	6773.551	50.566	BB



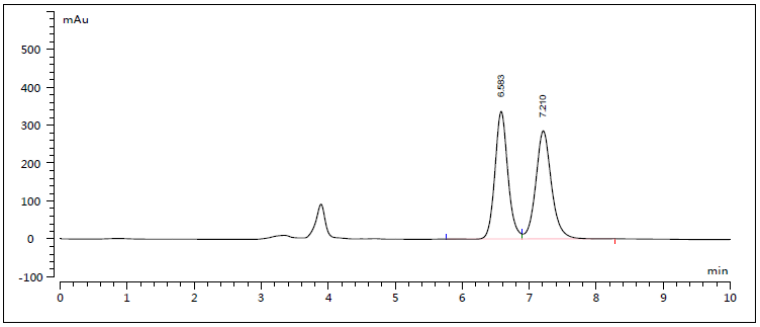
No	Retention Time	Area	% Area	Int Type
1	7.224	400.057	4.937	BB
2	8.179	7702.609	95.063	BB

(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-4'-(3-methylbenzoyl)-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione



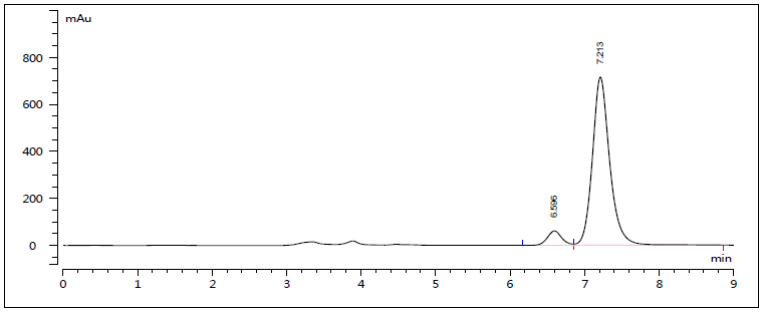
5af

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 33.2 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4f**, 43.0 mg (85% yield) of compound **5af** was obtained as a white solid, [α] D ^{25} = - 326 (*c* = 1.0, $CHCl_3$), Mp. = 79-80 °C. Dr (> 20:1) was determined by HPLC analysis. 87% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 7.2 min, t_{minor} = 6.6 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.73 (m, 1H), 7.53 – 7.35 (m, 2H), 7.30 (td, *J* = 7.8, 1.1 Hz, 1H), 7.25 – 7.06 (m, 6H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.69 (ddd, *J* = 58.6, 56.8, 7.2 Hz, 1H), 6.48 (d, *J* = 7.8 Hz, 1H), 5.10 (d, *J* = 7.6 Hz, 1H), 4.95 (td, *J* = 12.2, 7.2 Hz, 1H), 2.82 (s, 1H), 2.48 (s, 3H), 2.27 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.7, 194.7, 171.5, 147.7, 143.2, 137.9, 136.5, 136.3, 133.7, 129.7, 129.1, 128.6, 128.0, 127.5, 127.2, 125.6, 125.3, 125.3, 123.3, 123.3, 117.7 (dd, J_{C-F} = 329.0, 324.4 Hz), 107.9, 87.1, 63.8, 59.4 (dd, J_{C-F} = 38.8, 32.3 Hz), 53.0, 52.9, 25.9, 21.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.9 (d, *J* = 295.6 Hz, 1F), -123.5 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{28}H_{22}F_2N_2NaO_3S$ $[M+Na]^+$: 527.1211, found 527.1211.



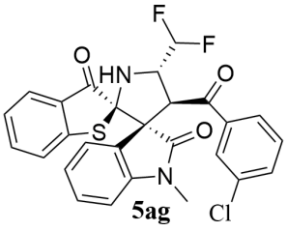
No	Retention Time	Area	% Area	Int Type
1	6.583	4489.656	49.245	BB

2	7.210	4627.348	50.755	BB



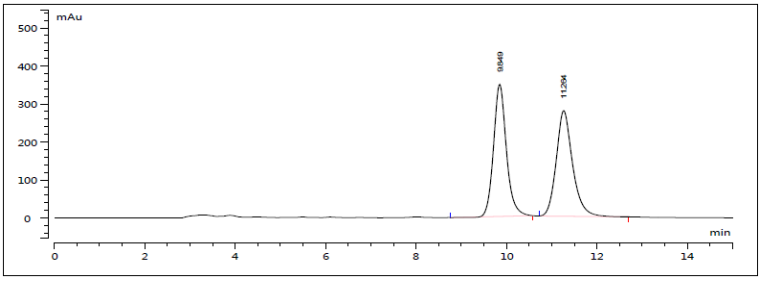
No	Retention Time	Area	% Area	Int Type
1	6.596	808.492	6.554	BB
2	7.213	11527.329	93.446	BB

(2*S*,3'*S*,4'*S*,5'*S*)-4'-(3-chlorobenzoyl)-5'-(difluoromethyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

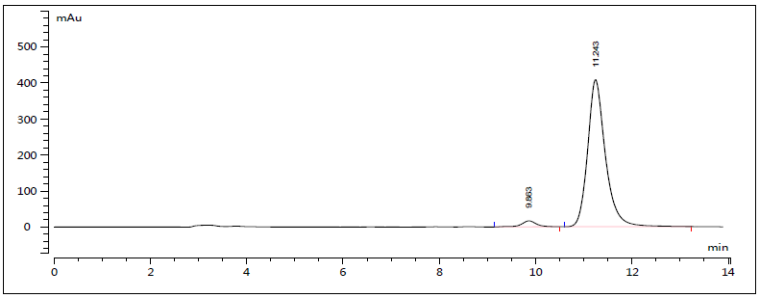


5ag

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 35.6 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4g**, 45.6 mg (87% yield) of compound **5ag** was obtained as a white solid, [α] D ^{25} = - 340 (*c* = 1.0, $CHCl_3$), Mp. = 65-66 °C. Dr (> 20:1) was determined by HPLC analysis. 93% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 70:30, 1.0 mL/min). Retention time: t_{major} = 11.2 min, t_{minor} = 9.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.73 (m, 1H), 7.49 – 7.28 (m, 5H), 7.26 – 7.21 (m, 2H), 7.21 – 7.12 (m, 3H), 6.99 (d, *J* = 7.9 Hz, 1H), 6.85 – 6.50 (m, 2H), 5.08 (d, *J* = 7.7 Hz, 1H), 4.93 (td, *J* = 12.0, 7.1 Hz, 1H), 2.84 (s, 1H), 2.55 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.6, 193.4, 171.4, 147.6, 143.1, 138.0, 136.4, 134.5, 132.9, 130.0, 129.4, 129.0, 129.0, 128.2, 128.0, 127.2, 127.2, 126.3, 125.7, 125.3, 123.5, 123.3, 117.6 (dd, $J_{C\text{-}F}$ = 329.9, 323.2 Hz), 108.1, 87.0, 63.6, 59.47 (dd, $J_{C\text{-}F}$ = 38.9, 32.6 Hz), 53.0, 52.9, 29.7, 26.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 296.3 Hz, 1F), -123.4 (d, *J* = 296.3 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{27}H_{19}ClF_2N_2NaO_3S$ $[M+Na]^+$: 547.0665, found 547.0665.

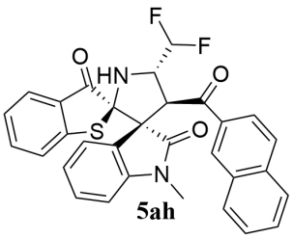


No	Retention Time	Area	% Area	Int Type
1	9.849	6860.491	49.593	BB
2	11.264	6973.031	50.407	BB

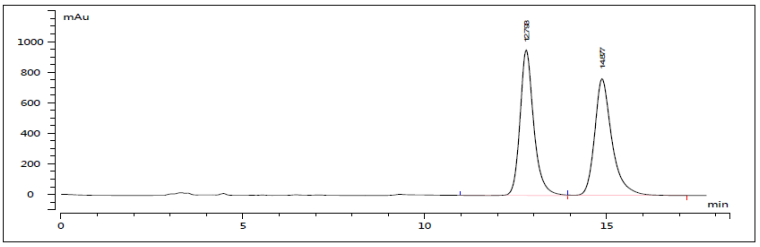


No	Retention Time	Area	% Area	Int Type
1	9.863	359.821	3.324	BB
2	11.243	10463.568	96.676	BB

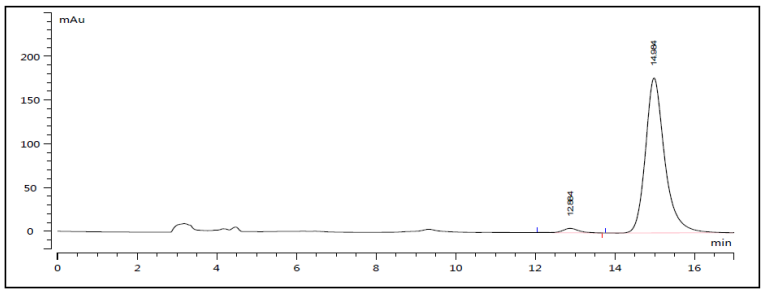
(2*S*,3'*S*,4'*S*,5'*S*)-4'-(2-naphthoyl)-5'-(difluoromethyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 37.6 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4h**, 48.0 mg (89% yield) of compound **5ah** was obtained as a white solid, [α] D ^{25} = - 246 (*c* = 1.0, $CHCl_3$), Mp. = 116-117 °C. Dr (> 20:1) was determined by HPLC analysis. 95% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 15.0 min, t_{minor} = 12.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 7.2 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 7.58 – 7.52 (m, 1H), 7.49 (dd, *J* = 11.5, 4.5 Hz, 1H), 7.46 – 7.35 (m, 2H), 7.27 (dt, *J* = 7.6, 3.1 Hz, 2H), 7.21 – 7.12 (m, 2H), 6.97 (d, *J* = 7.9 Hz, 1H), 6.75 (ddd, *J* = 58.5, 56.9, 7.2 Hz, 1H), 6.35 (d, *J* = 7.7 Hz, 1H), 5.28 (d, *J* = 7.7 Hz, 1H), 5.04 (d, *J* = 5.5 Hz, 1H), 2.87 (s, 1H), 2.11 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.8, 194.3, 171.7, 147.7, 143.0, 136.4, 135.3, 133.5, 131.9, 130.0, 129.8, 129.7, 129.1, 128.7, 127.9, 127.5, 127.5, 127.2, 126.8, 125.6, 125.3, 123.8, 123.4, 123.3, 117.7(dd, J_{C-F} = 329.9, 323.7 Hz), 108.1, 87.2, 63.8, 59.56 (dd, J_{C-F} = 39.1, 32.5 Hz), 53.1, 53.0, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 295.6 Hz, 1F), -123.4 (d, *J* = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{31}H_{22}F_2N_2NaO_3S$ $[M+Na]^+$: 563.1211, found 563.1211.

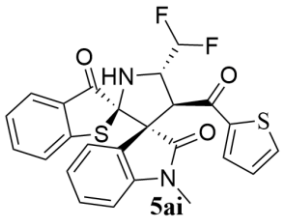


No	Retention Time	Area	% Area	Int Type
1	12.793	24901.451	49.666	BB
2	14.877	25236.485	50.334	BB



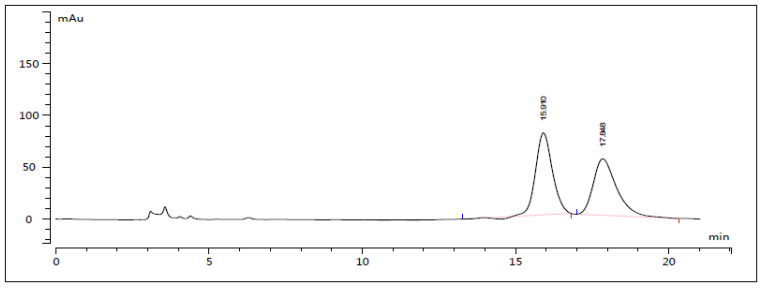
No	Retention Time	Area	% Area	Int Type
1	12.884	135.380	2.226	BB
2	14.984	5947.134	97.774	BB

(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-1''-methyl-4'-(thiophene-2-carbonyl)-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione

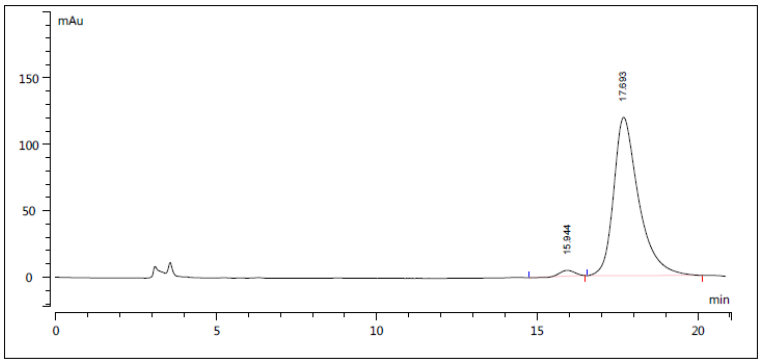


5ai

From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 32.2 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4i**, 43.2 mg (87% yield) of compound **5ai** was obtained as a pink solid, [α] D ^{25} = - 433 (*c* = 1.0, $CHCl_3$), Mp. = 62-63 °C. Dr (> 20:1) was determined by HPLC analysis. 96% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 87:13, 1.0 mL/min). Retention time: t_{major} = 17.7 min, t_{minor} =15.9 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.67 (dd, *J* = 3.9, 0.9 Hz, 1H), 7.60 – 7.37 (m, 3H), 7.32 (td, *J* = 7.8, 1.1 Hz, 1H), 7.23 – 7.11 (m, 2H), 7.01 (dd, *J* = 8.2, 3.2 Hz, 2H), 6.81 – 6.43 (m, 2H), 5.06 (d, *J* = 8.0 Hz, 1H), 4.97 – 4.82 (m, 1H), 2.88 (s, 1H), 2.73 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.5, 185.6, 171.7, 147.7, 143.0, 143.0, 136.4, 135.0, 133.3, 129.9, 129.1, 127.9, 127.3, 127.2, 125.7, 125.5, 123.5, 123.3, 117.6 (t, J_{C-F} = 329.9, 242.4 Hz), 108.2, 87.2, 68.5, 64.6, 59.9 (dd, J_{C-F} = 38.9, 32.3 Hz), 52.9, 52.8, 27.8, 26.3, 22.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 295.6 Hz, 1F), -123.3 (d, *J* = 295.9 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{25}H_{18}F_2N_2NaO_3S_2$ $[M+Na]^+$: 519.0619, found 519.0619.

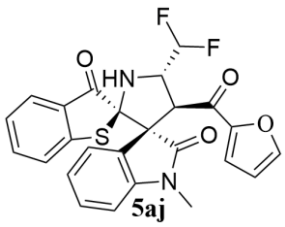


No	Retention Time	Area	% Area	Int Type
1	15.910	2981.669	50.930	BB
2	17.848	2872.812	49.070	BB

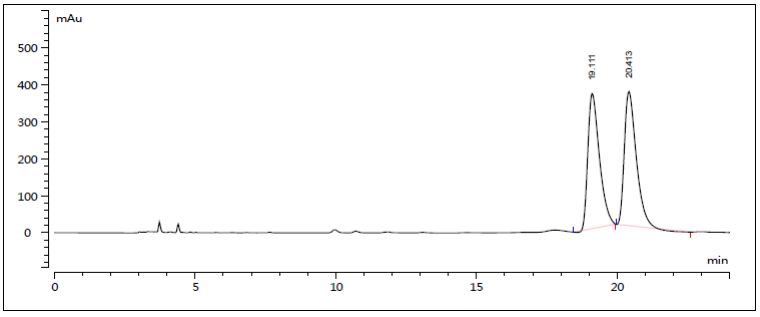


No	Retention Time	Area	% Area	Int Type
1	15.944	129.402	1.967	BB
2	17.693	6450.332	98.033	BB

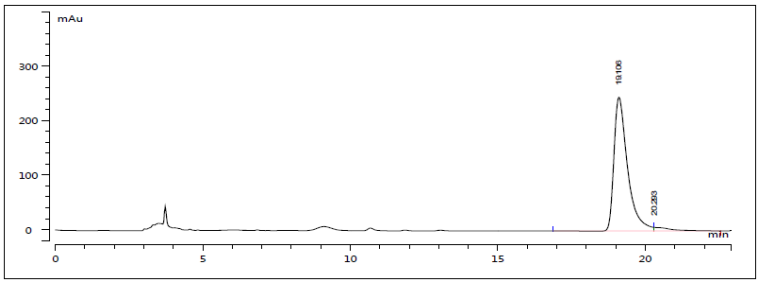
(2*S*,3'*S*,4'*S*,5'*S*)-5'-(difluoromethyl)-4'-(furan-2-carbonyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 30.4 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4j**, 42.2 mg (88% yield) of compound **5aj** was obtained as a white solid, [α] D ^{25} = - 382 (*c* = 1.0, $CHCl_3$), Mp. = 76-77 °C. Dr (> 20:1) was determined by HPLC analysis. 93% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 19.1 min, t_{minor} = 20.3 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.7 Hz, 1H), 7.52 – 7.39 (m, 3H), 7.31 (td, *J* = 7.8, 1.1 Hz, 1H), 7.23 – 7.10 (m, 3H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.78 – 6.43 (m, 2H), 6.41 (dd, *J* = 3.6, 1.6 Hz, 1H), 5.02 – 4.80 (m, 2H), 2.87 (d, *J* = 17.8 Hz, 4H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.4, 180.8, 177.7, 171.6, 151.2, 147.7, 147.5, 143.0, 136.4, 129.9, 129.1, 127.2, 127.2, 125.6, 125.5, 123.5, 123.3, 119.5, 117.6 (t, J_{C-F} = 329.9, 243.9 Hz), 112.2, 108.2, 87.4, 68.5, 64.3, 59.6 (dd, J_{C-F} = 38.9, 32.3 Hz), 52.1, 52.0, 27.8, 26.4, 22.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.9 (d, *J* = 295.6 Hz, 1F), -123.3 (d, *J* = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{25}H_{18}F_2N_2NaO_4S$ $[M+Na]^+$: 503.0848, found 503.0848.

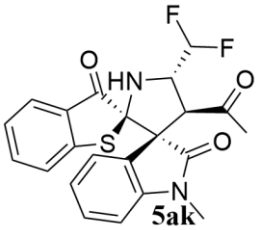


No	Retention Time	Area	% Area	Int Type
1	19.111	10417.963	49.552	BB
2	20.413	10606.287	50.448	BB

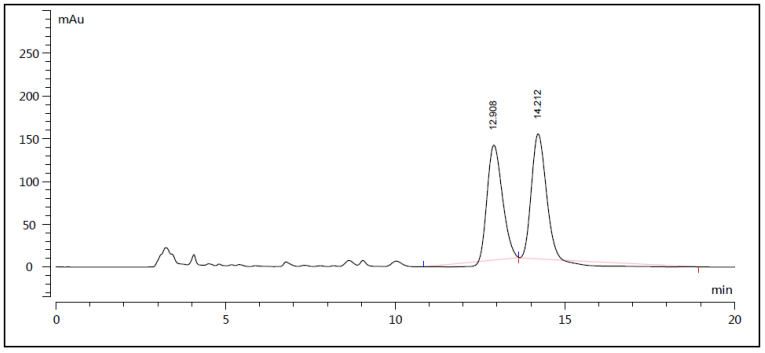


No	Retention Time	Area	% Area	Int Type
1	19.106	7846.068	96.787	BB
2	20.293	260.471	3.213	BB

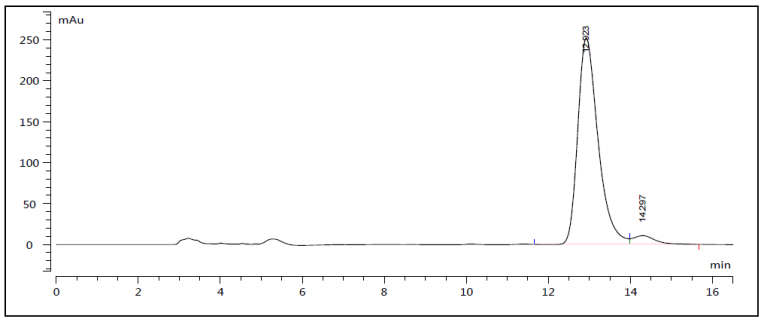
(2*S*,3'*S*,4'*S*,5'*S*)-4'-acetyl-5'-(difluoromethyl)-1''-methyl-3H-dispiro[benzo[*b*]thiophene-2,2'-pyrrolidine-3',3''-indoline]-2'',3-dione



From 22.7 mg (0.1 mmol) of (Z)-2-((2,2-difluoroethyl)imino) benzo[*b*]thiophen-3(2H)-one **1a** and 24.1 mg (0.12 mmol, 1.2 equiv) of methyleneindolinone **4k**, 34.2 mg (80% yield) of compound **5ak** was obtained as a white solid, [α] D ^{25} = - 350 (*c* = 1.0, $CHCl_3$), Mp. = 89-90 °C. Dr (> 20:1) was determined by HPLC analysis. 91% ee was determined by HPLC analysis (Daicel Chiralcel OD-H column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 12.9 min, t_{minor} = 14.3 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.53 – 7.32 (m, 3H), 7.22 – 7.09 (m, 2H), 7.01 (d, *J* = 7.9 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.53 (ddd, *J* = 58.3, 56.7, 7.1 Hz, 1H), 4.70 – 4.55 (m, 1H), 4.42 (d, *J* = 8.1 Hz, 1H), 3.13 (s, 3H), 2.78 (s, 1H), 1.75 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 202.1, 200.5, 171.7, 147.7, 143.4, 136.4, 130.1, 128.8, 127.6, 127.3, 125.7, 124.9, 123.7, 123.2, 117.6 (dd, J_{C-F} = 329.5, 324.7 Hz), 108.5, 87.4, 62.6, 59.0 (dd, J_{C-F} = 38.2, 32.1 Hz), 56.9, 56.8, 29.1, 26.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.0 (d, *J* = 295.2 Hz, 1F), -123.0 (d, *J* = 295.6 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{22}H_{18}F_2N_2NaO_3S$ $[M+Na]^+$: 451.1025, found 451.1025.

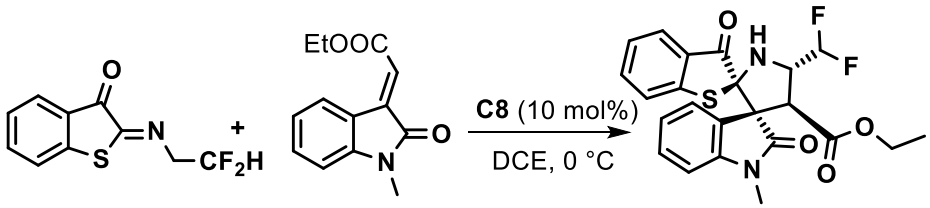


No	Retention Time	Area	% Area	Int Type
1	12.908	3916.171	50.768	BB
2	14.212	3797.694	49.232	BB



No	Retention Time	Area	% Area	Int Type
1	12.923	8676.302	95.622	BB
2	14.297	397.282	4.378	BB

8. Gram-scale asymmetric cycloaddition for the synthesis of 3aa

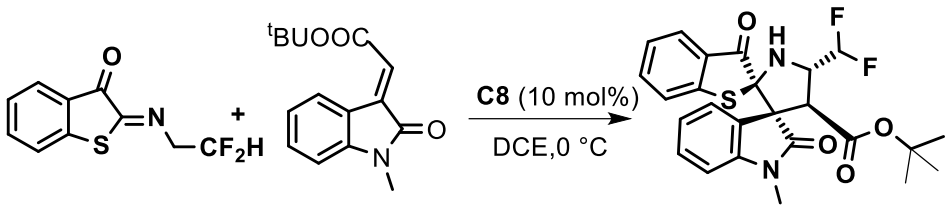


1a **2a** **3aa**

2.5 mmol 3.0 mmol 1.05 g, 92% yield
0.567 g 0.693 g > 20:1 dr, 96% ee

To a dried 50 mL bottle were added **1a** (2.5 mmol, 0.567 g), **2a** (3.0 mmol, 0.693g) and catalyst **C8** (157.6 mg, 0.25 mmol, 10 mol %) in 25 mL dry 1,2-dichloroethane (DCE). After stirring at 0℃ for 4.5 h, the **1a** was completely consumped as detected by TLC analysis (petroleum ether / EtOAc = 4:1). Product **3aa** was obtained by silica gel column chromatography (petroleum ether / EtOAc = 4:1), as a white solid (1.05 g, 92% yield) with >20:1 dr and 96% ee.

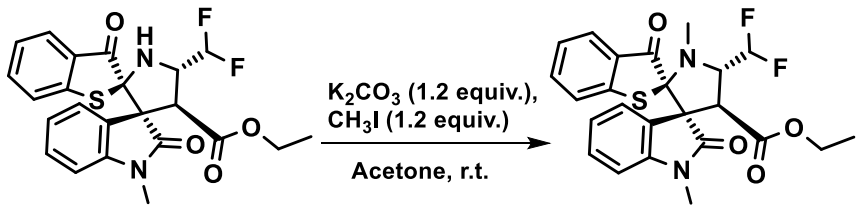
9. Gram-scale asymmetric cycloaddition for the synthesis of 3ag



1a **2g** **3ag**

To a dried 50 mL bottle were added **1a** (2.5 mmol, 0.567 g), **2g** (3.0 mmol, 0.777g) and catalyst **C8** (157.6 mg, 0.25 mmol, 10 mol %) in 25 mL dry 1,2-dichloroethane (DCE). After stirring at 0℃ for 8 h, the **1a** was completely consumped as detected by TLC analysis (petroleum ether / EtOAc = 10:1). Product **3ag** was obtained by silica gel column chromatography (petroleum ether / EtOAc = 10:1), as a white solid (1.21 g, 83% yield) with >20:1 dr and 96% ee.

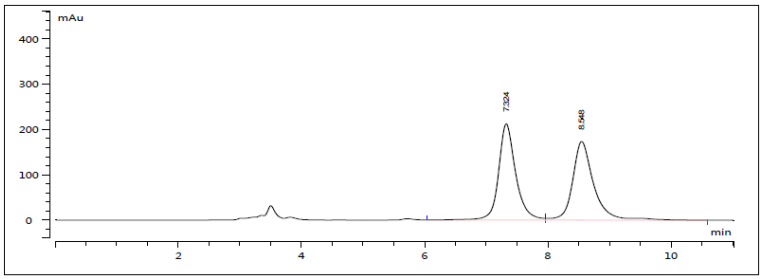
10. Synthetic transformation of 3aa



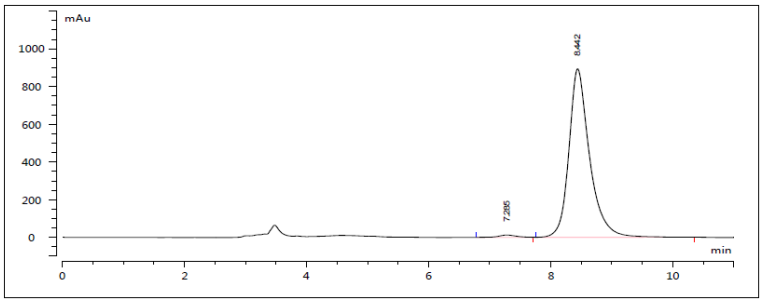
3aa — 0.1 mmol, 96% ee

6a — 24 h, 95% yield, > 20:1, 97% ee

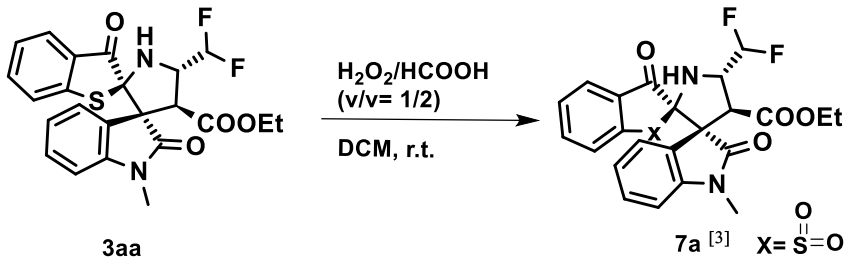
To a dried 5 mL bottle were added **3aa** (0.1 mmol, 45.8 mg) and K_2CO_3 (16.6 mg, 0.12 mmol, 1.2e) in 1 mL dry Acetone. The mixture was stirred at room temperature for 30 min, and Iodomethane (CH_3I) (17.0 mg, 0.12 mmol, 1.2e) was then added. After stirring at room temperature for 24 h, the **3aa** was completely consumped as detected by TLC analysis (petroleum ether / EtOAc = 5:1). Product **6a** was obtained by silica gel column chromatography (petroleum ether / EtOAc = 5:1), as a yellow solid (44.8 mg, 95% yield) with >20:1 dr and 97% ee. [α] D ^{25} = +19 (*c* = 1.0, $CHCl_3$), Mp. = 50-51 °C. Dr (> 20:1) was determined by HPLC analysis. 97% ee was determined by HPLC analysis (Daicel Chiralpak IB column, 230 nm, hexane/2 -propanol 80:20, 1.0 mL/min). Retention time: t_{major} = 8.4 min, t_{minor} = 7.3 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.64 – 7.37 (m, 1H), 7.36 – 7.23 (m, 2H), 7.23 – 7.14 (m, 1H), 7.04 – 6.94 (m, 2H), 6.88 (d, *J* = 7.8 Hz, 1H), 6.29 (td, *J* = 55.2, 3.5 Hz, 1H), 5.41 (dtd, *J* = 15.9, 8.9, 3.5 Hz, 1H), 4.03 (d, *J* = 8.4 Hz, 1H), 3.85 – 3.59 (m, 2H), 3.35 (s, 3H), 2.33 (s, 3H), 0.69 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 187.7, 173.9, 171.1, 168.1, 144.5, 142.8, 133.2, 132.8, 130.0, 126.2, 124.6, 123.9, 123.6, 122.6, 114.3 (t, $J_{C\text{-}F}$ = 329.4 Hz), 108.7, 76.1, 75.8, 75.6, 66.9, 61.3, 51.4, 27.0, 16.4, 13.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.0 (d, *J* = 288.8 Hz, 1F), -127.1 (d, *J* = 301.7 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{24}H_{22}F_2N_2NaO_4S$ $[M+Na]^+$: 495.1147, found 495.1147.



No	Retention Time	Area	% Area	Int Type
1	7.324	4098.591	49.817	BB
2	8.548	4128.723	50.183	BB



No	Retention Time	Area	% Area	Int Type
1	7.285	240.712	1.134	BB
2	8.442	20981.486	98.866	BB



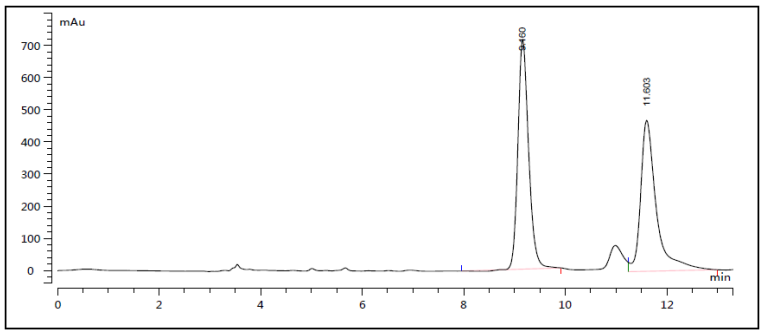
3aa

0.2 mmol, 96% ee

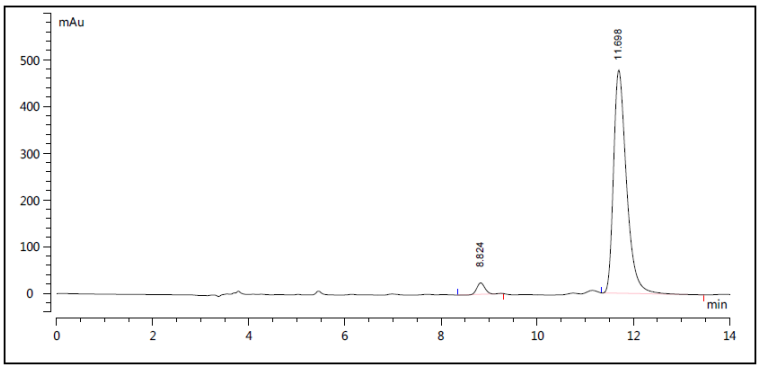
7a [3]

3 h, 50% yield
>20:1 dr, 94% ee

To a solution of **3aa** (0.2 mmol, 91.6 mg) in CH_2Cl_2 (1.5 mL), mixture of 33% H_2O_2 (0.2 ml) and HCO_2H (0.4 mL) was added at 5-10 ℃ with vigorous stirring. Then it was stirred at room temperature for 3 h. Then, the reaction mixture was poured into saturated aqueous solution of $NaHCO_3$ (3 mL) and extracted with CH_2Cl_2 (3 x 3 mL) and dried (Na_2SO_4). Removal of solvent followed by column chromatographic purification (silica gel; 50% ethyl acetate in hexane) furnished **7a** as a colorless solid (49.1 mg, 50% yield) with >20:1 dr and 94% ee. [α] D ^{25} = -305 (*c* = 1.0, $CHCl_3$), Mp. = 90-91 °C. Dr (> 20:1) was determined by HPLC analysis. 94% ee was determined by HPLC analysis (Daicel Chiralpak IA column, 230 nm, hexane/2-propanol 50:50, 1.0 mL/min). Retention time: t_{major} = 11.7 min, t_{minor} = 8.8 min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 3.9 Hz, 2H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.51 – 7.43 (m, 1H), 7.19 (td, *J* = 7.7, 1.4 Hz, 1H), 6.85 (d, *J* = 7.8 Hz, 1H), 6.70 – 6.32 (m, 3H), 6.04 (s, 1H), 5.09 (dtd, *J* = 13.4, 6.7, 3.3 Hz, 1H), 3.97 (d, *J* = 6.3 Hz, 1H), 3.80 – 3.63 (m, 2H), 3.39 (s, 3H), 0.66 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 189.1, 174.0, 166.9, 146.3, 143.9, 135.3, 132.3, 130.2, 128.5, 127.4, 125.5, 124.1, 122.9, 122.7, 116.6 (t, J_{C-F} = 235.4 Hz), 108.8, 92.5, 64.7, 64.5, 64.4, 64.2, 61.6, 59.3, 49.1, 49.0, 27.0, 13.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.4 (d, *J* = 297.1 Hz, 1F), -123.7 (d, *J* = 297.1 Hz, 1F). HRMS (ESI) *m/z* calcd for $C_{23}H_{20}F_2N_2NaO_6S$ $[M+Na]^+$: 513.0902, found 513.0902.

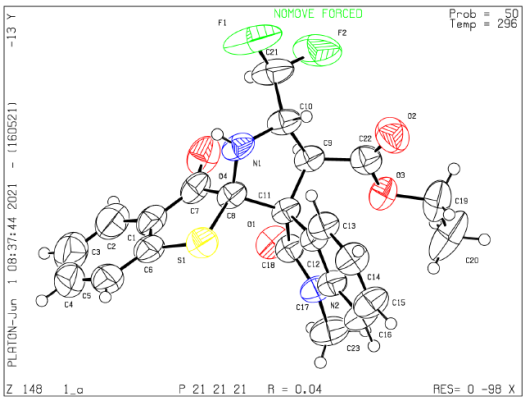


No	Retention Time	Area	% Area	Int Type
1	9.160	10410.138	50.888	BB
2	11.603	10046.984	49.112	BB

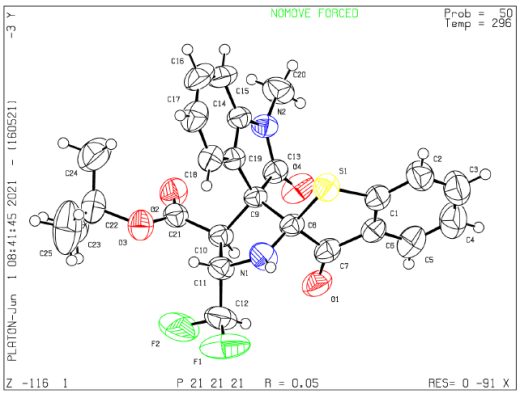


No	Retention Time	Area	% Area	Int Type
1	8.824	274.723	2.979	BB
2	11.698	8948.205	97.021	BB

11. X-ray Structures of Compounds 3aa and 3ag

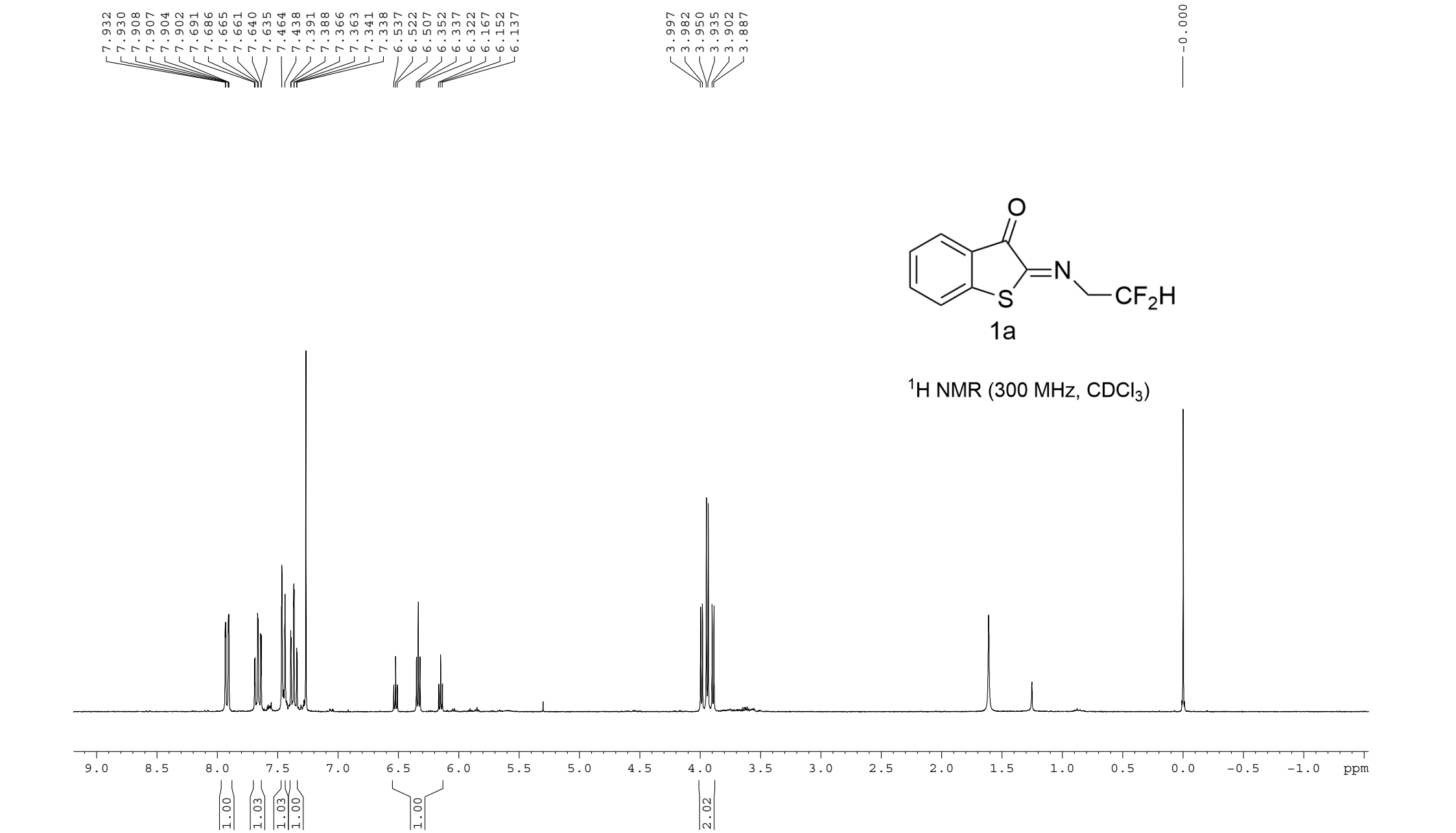


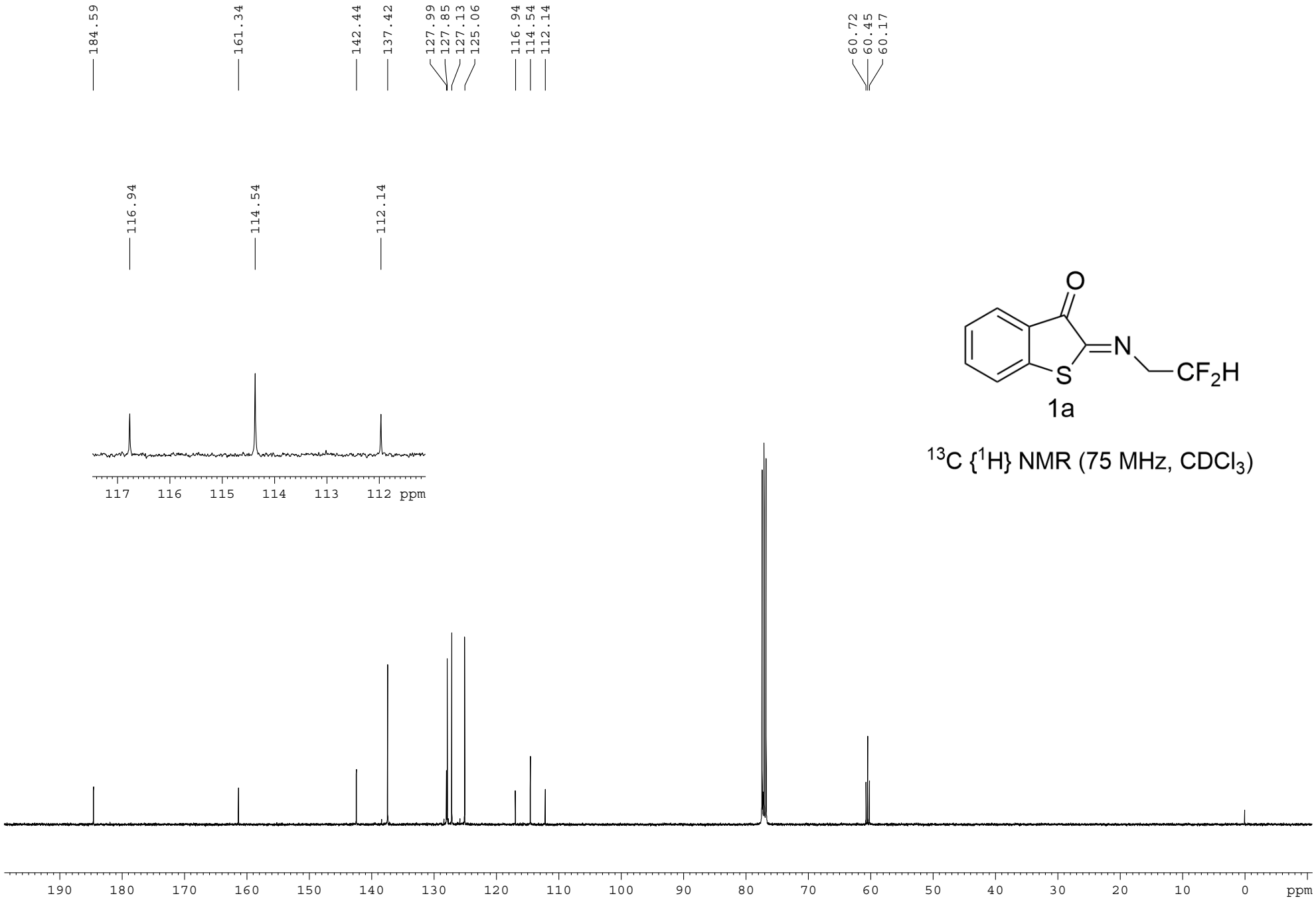
3aa

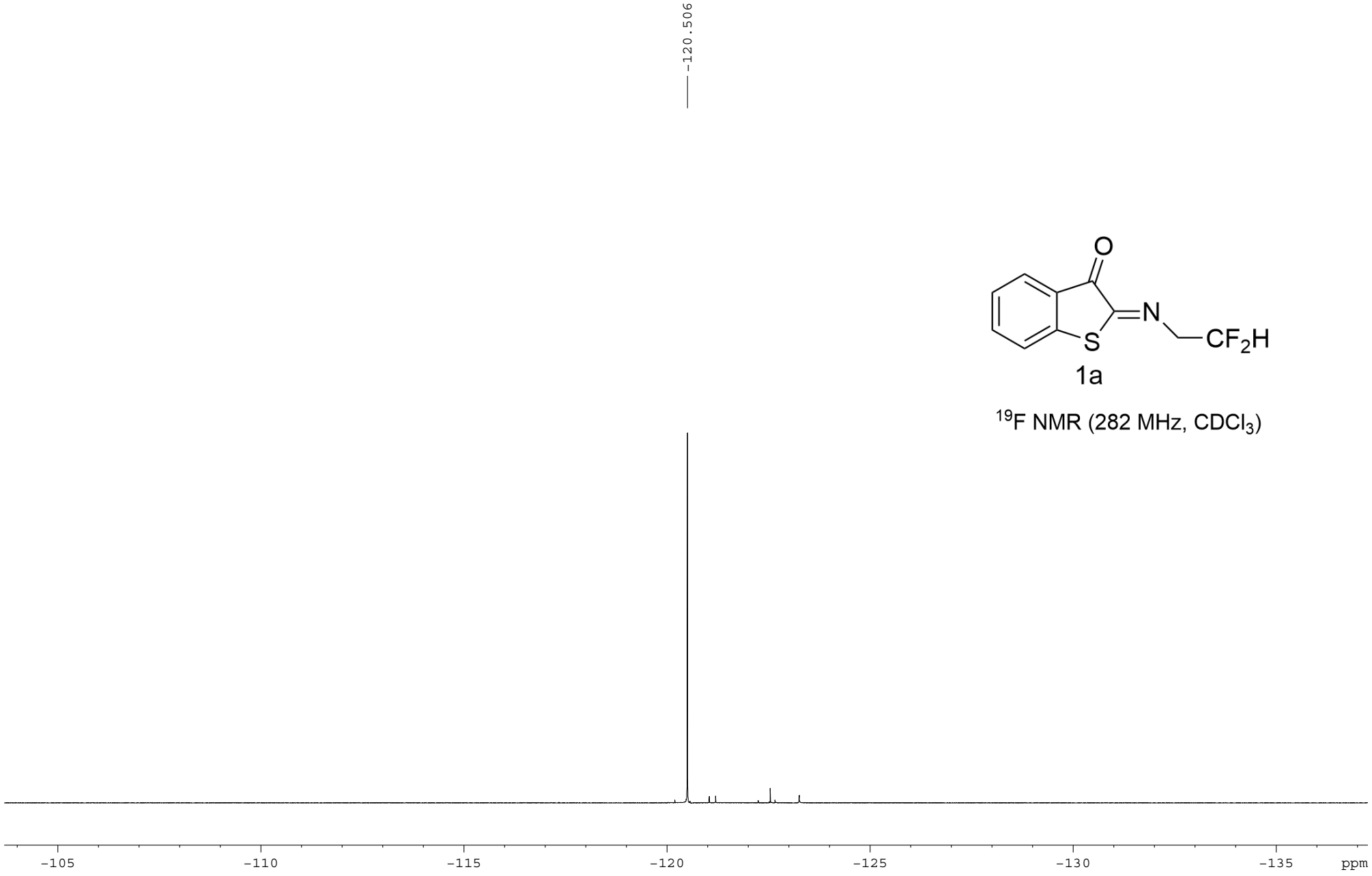


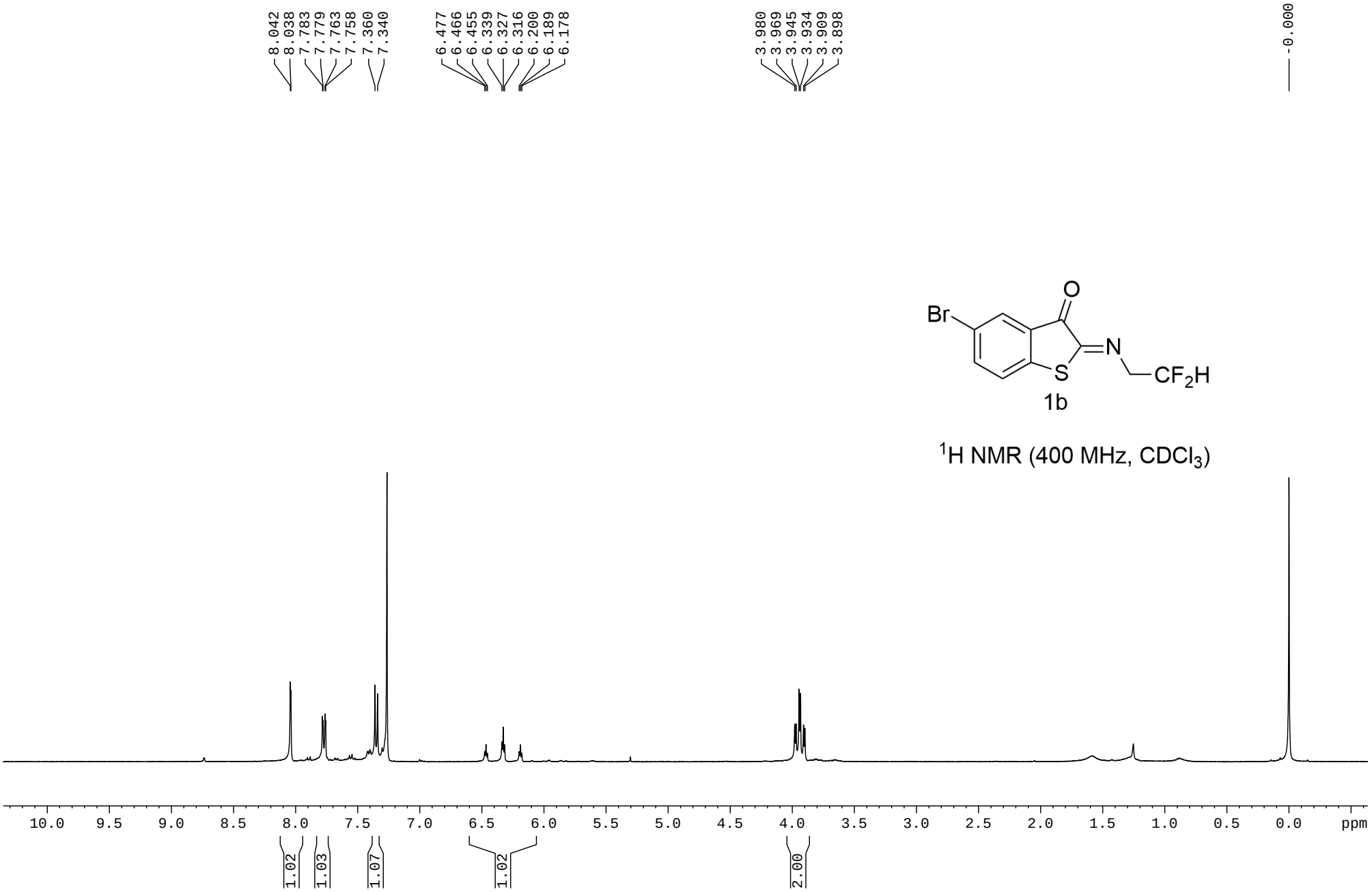
3ag

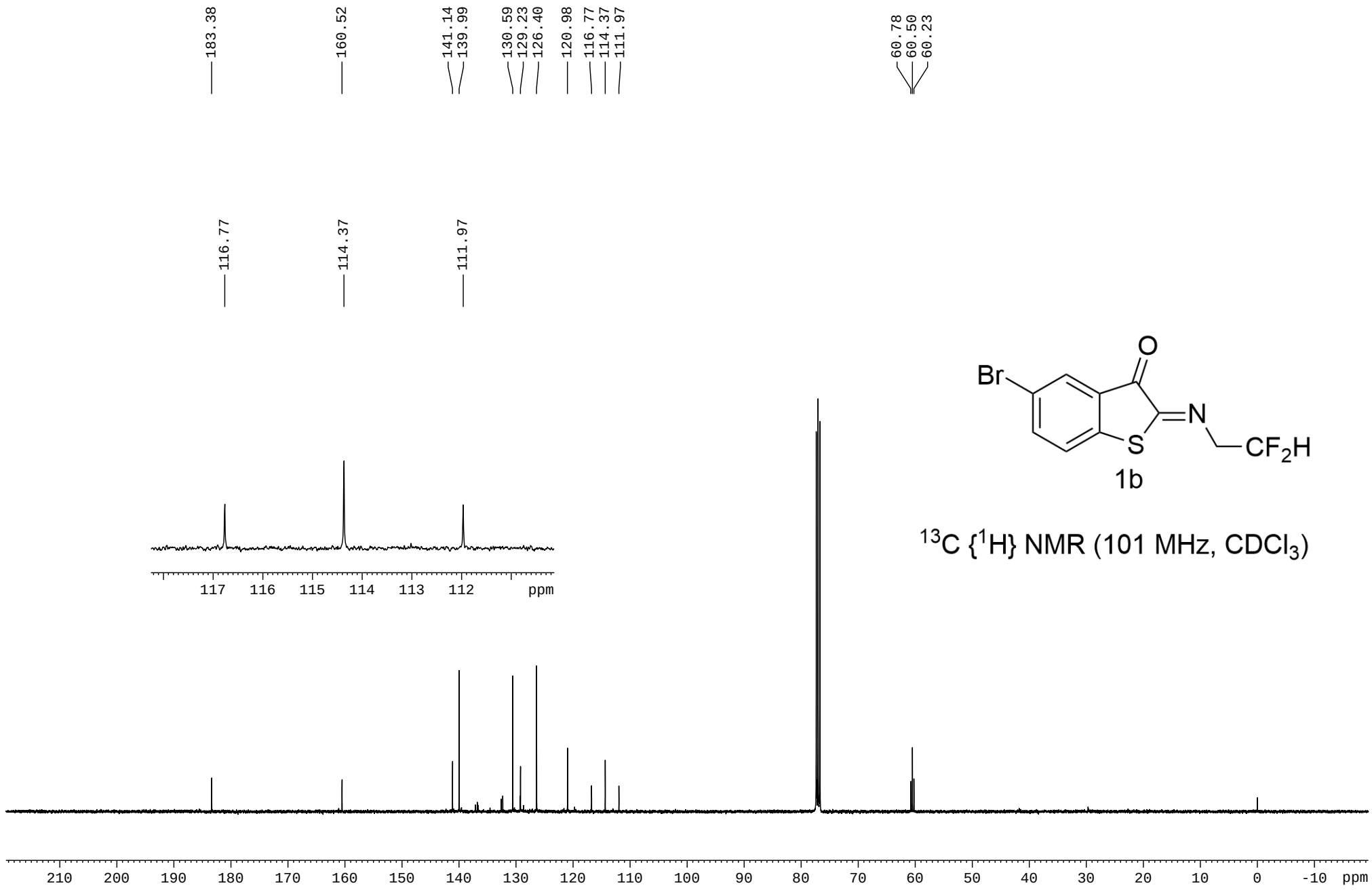
12. Copies of ^{1}H, ^{19}F and $^{13}C\{^{1}H\}$ NMR Spectra

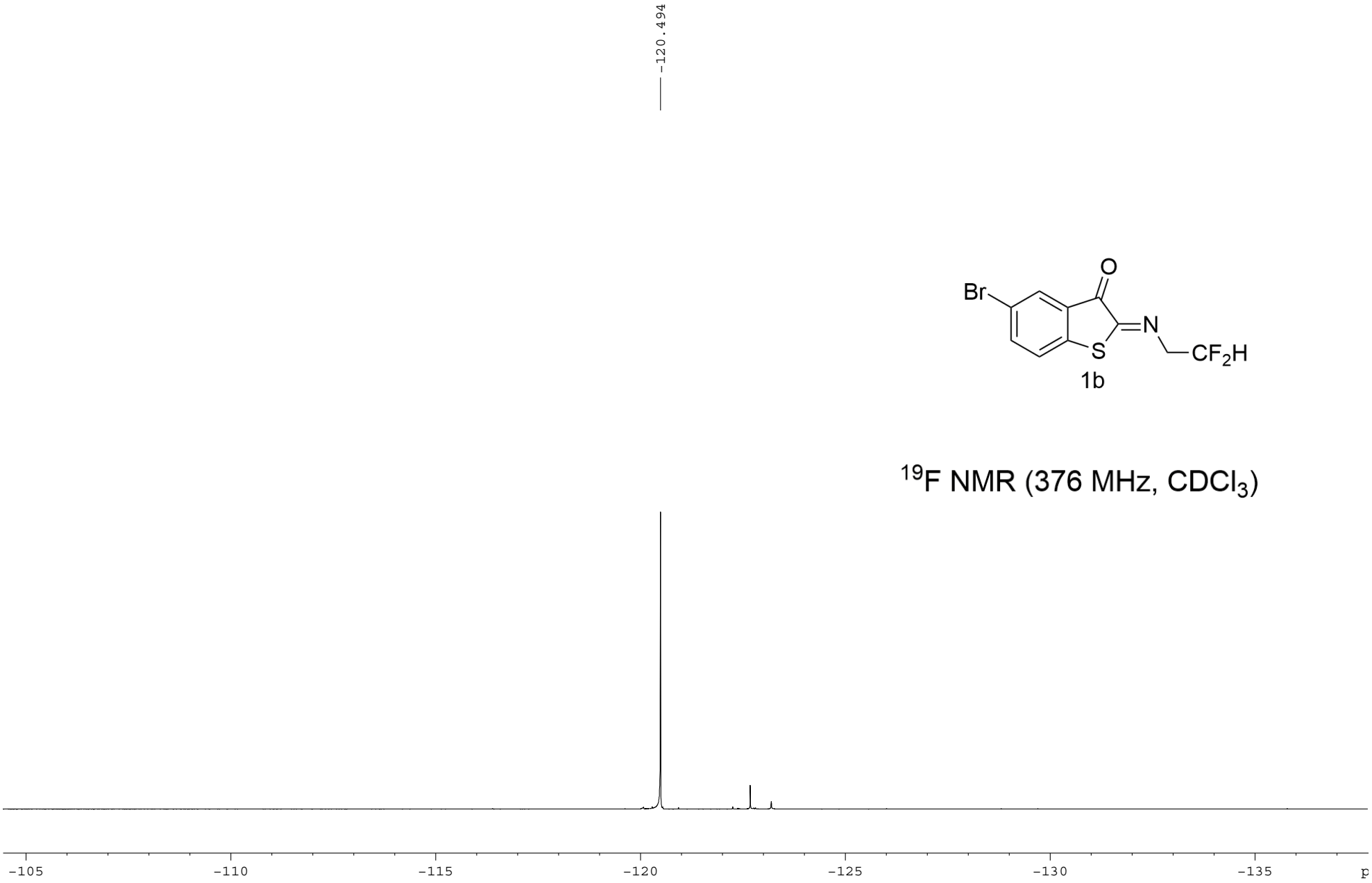

7.932
7.930
7.908
7.907
7.904
7.902
7.691
7.686
7.665
7.661
7.640
7.635
7.464
7.438
7.391
7.388
7.366
7.363
7.341
7.338
6.537
6.522
6.507
6.352
6.337
6.322
6.167
6.152
6.137
3.997
3.982
3.950
3.935
3.902
3.887
-0.000
O
N
S
CF2H
1a
1H NMR (300 MHz, CDCl3)
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
ppm
1.00
1.03
1.03
1.00
1.00
2.02

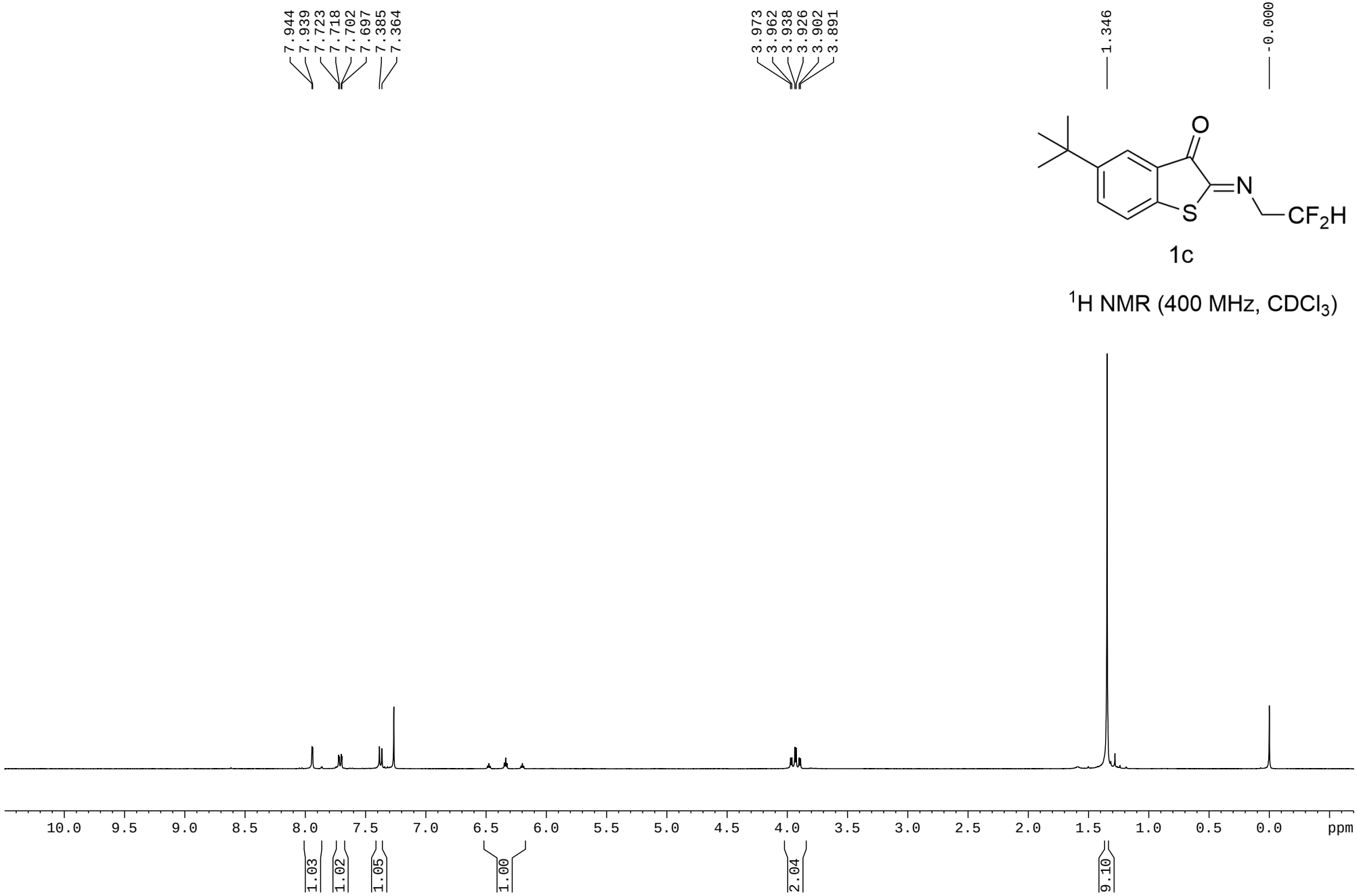

184.59
161.34
142.44
137.42
127.99
127.85
127.13
125.06
116.94
114.54
112.14
60.72
60.45
60.17
116.94
114.54
112.14
117 116 115 114 113 112 ppm
O
N
S
CF2H
1a
13C {1H} NMR (75 MHz, CDCl3)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

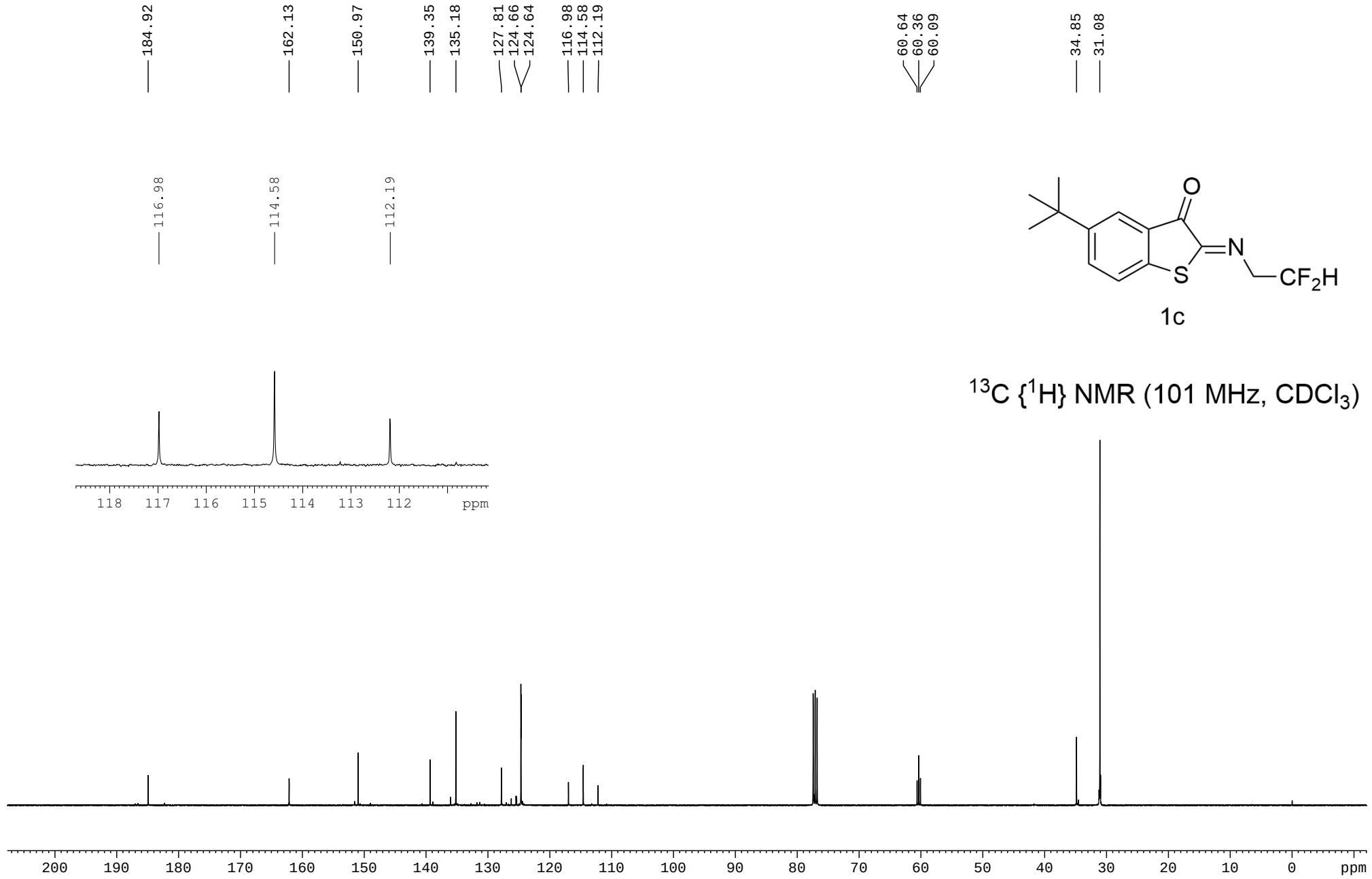

-120.506
O
N
S
CF2H
1a
19F NMR (282 MHz, CDCl3)
-105
-110
-115
-120
-125
-130
-135
ppm

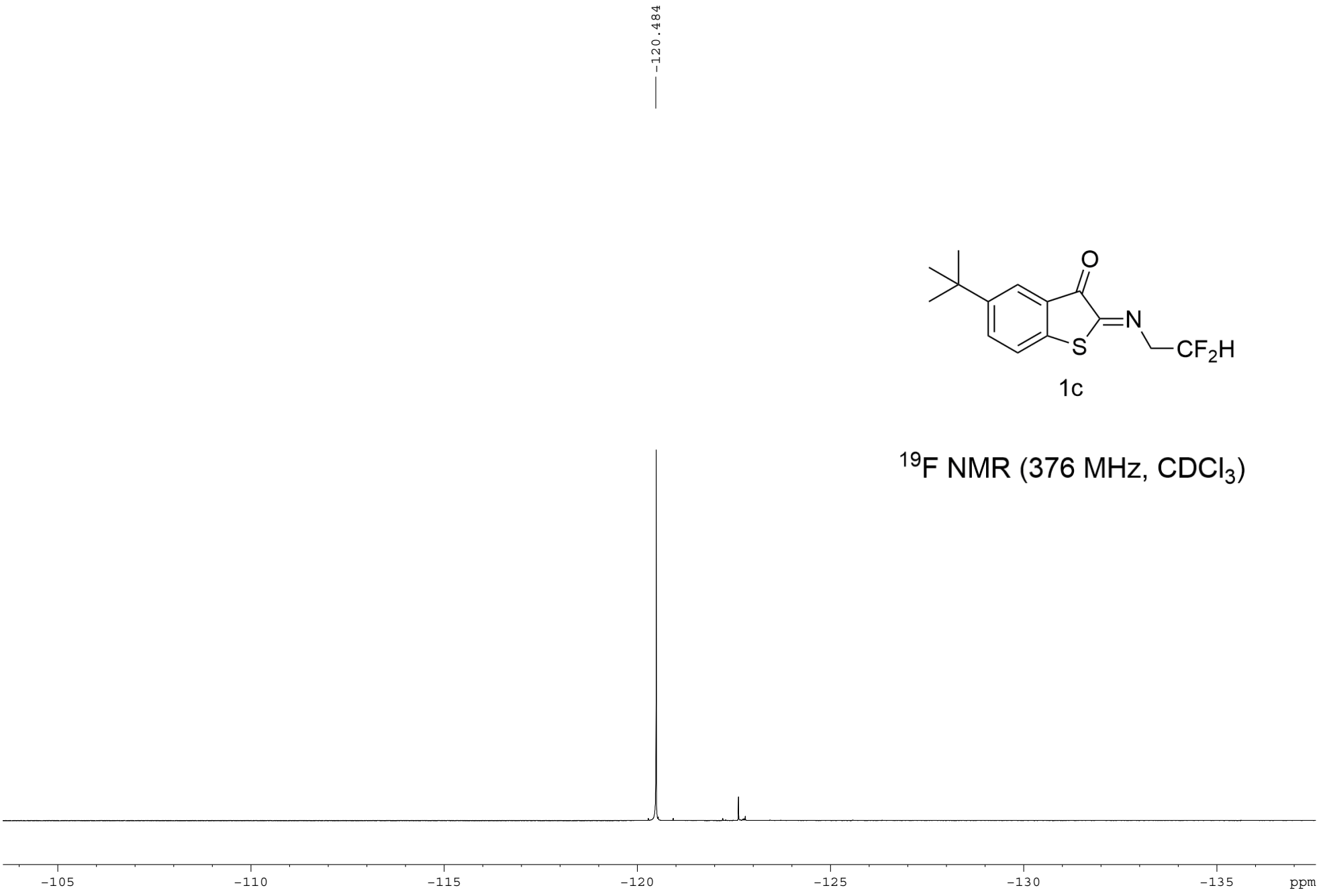

8.042
8.038
7.783
7.779
7.763
7.758
7.360
7.340
6.477
6.466
6.455
6.339
6.327
6.316
6.200
6.189
6.178
3.980
3.969
3.945
3.934
3.909
3.898
-0.000
Br
O
N
S
CF2H
1b
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.02
1.03
1.07
1.02
2.00

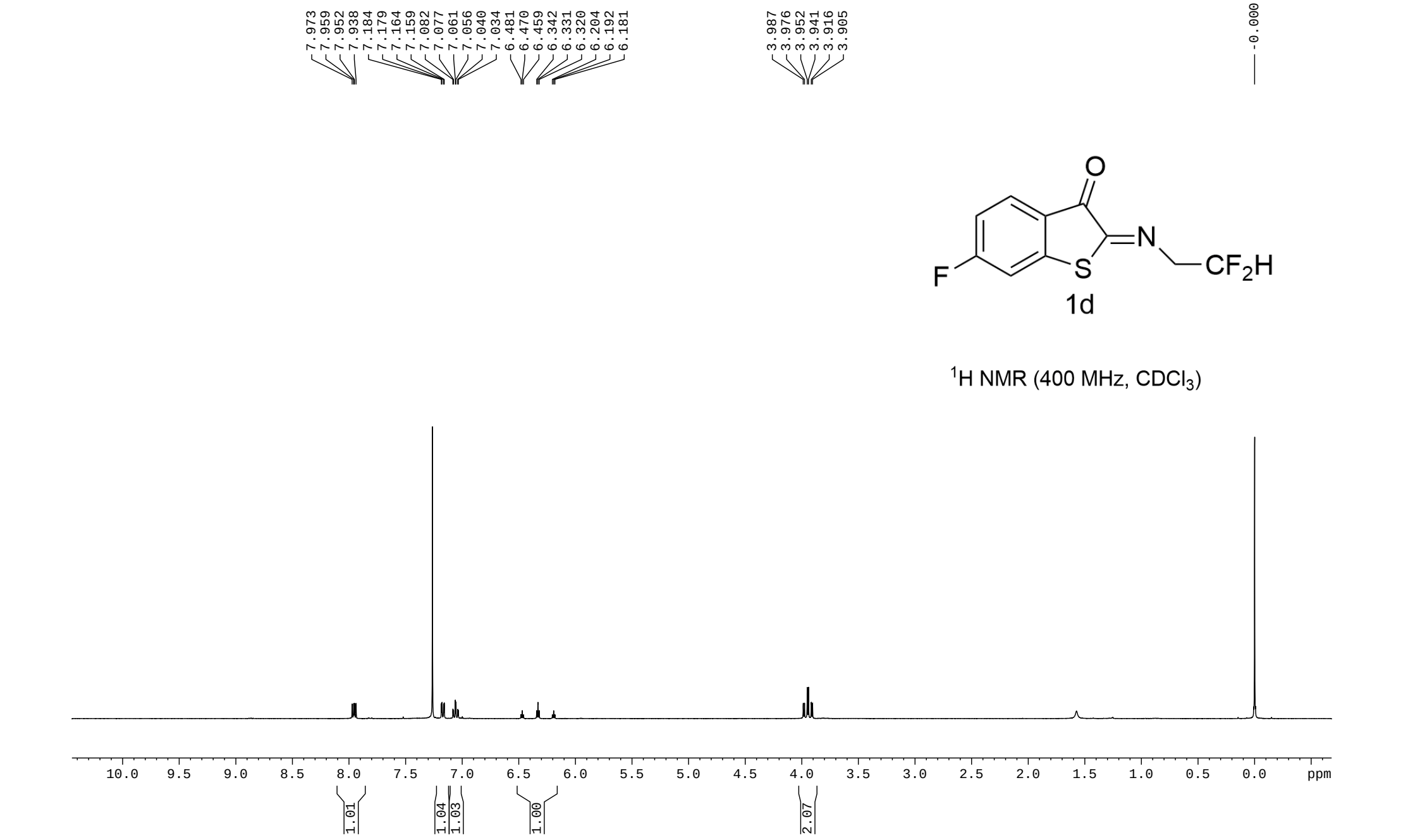

183.38
160.52
141.14
139.99
130.59
129.23
126.40
120.98
116.77
114.37
111.97
60.78
60.50
60.23
116.77
114.37
111.97
117 116 115 114 113 112 ppm
Br
O
N
S
CF2H
1b
13C {1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 ppm

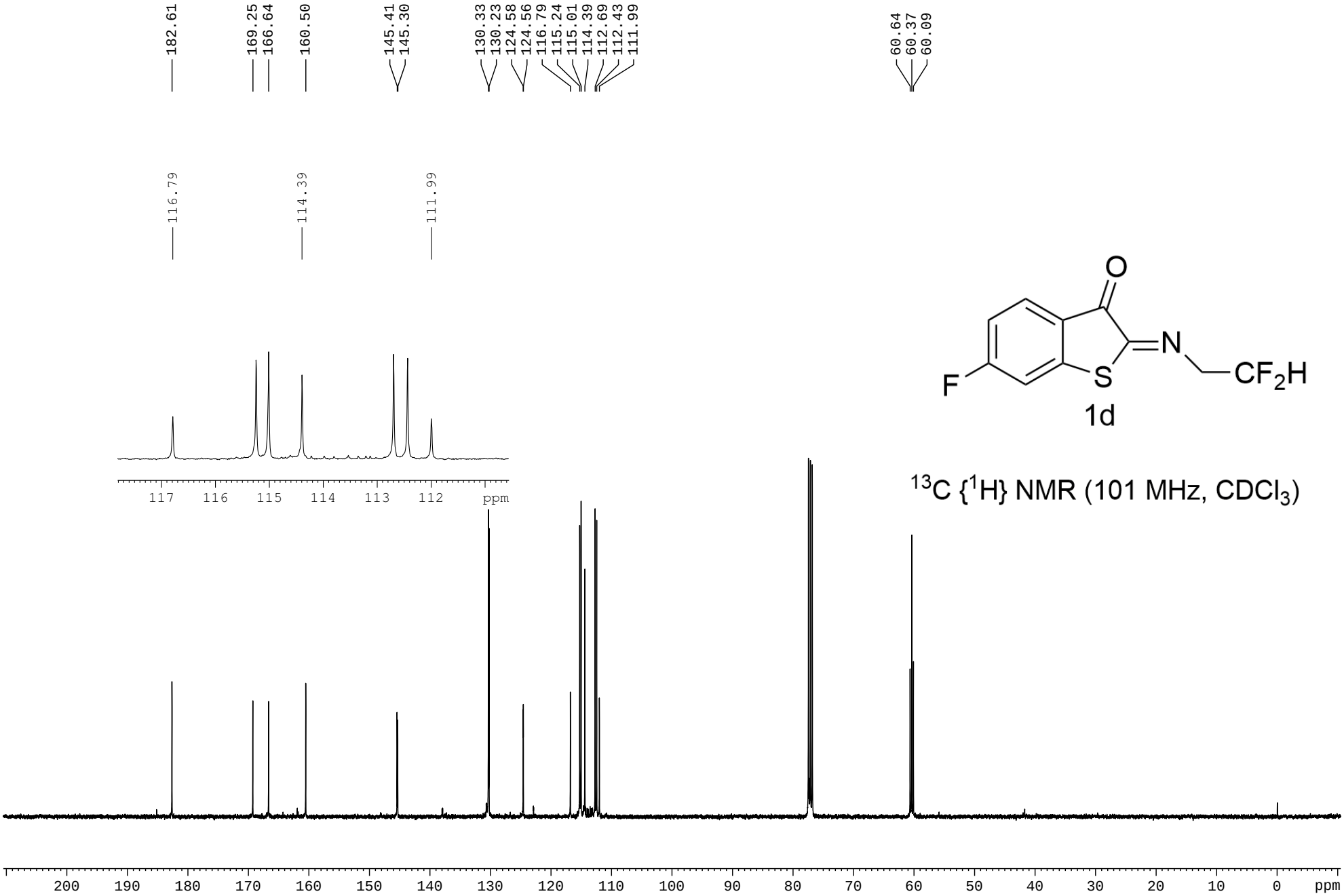

-120.494
Br
O
N
S
CF2H
1b
19F NMR (376 MHz, CDCl3)
-105
-110
-115
-120
-125
-130
-135

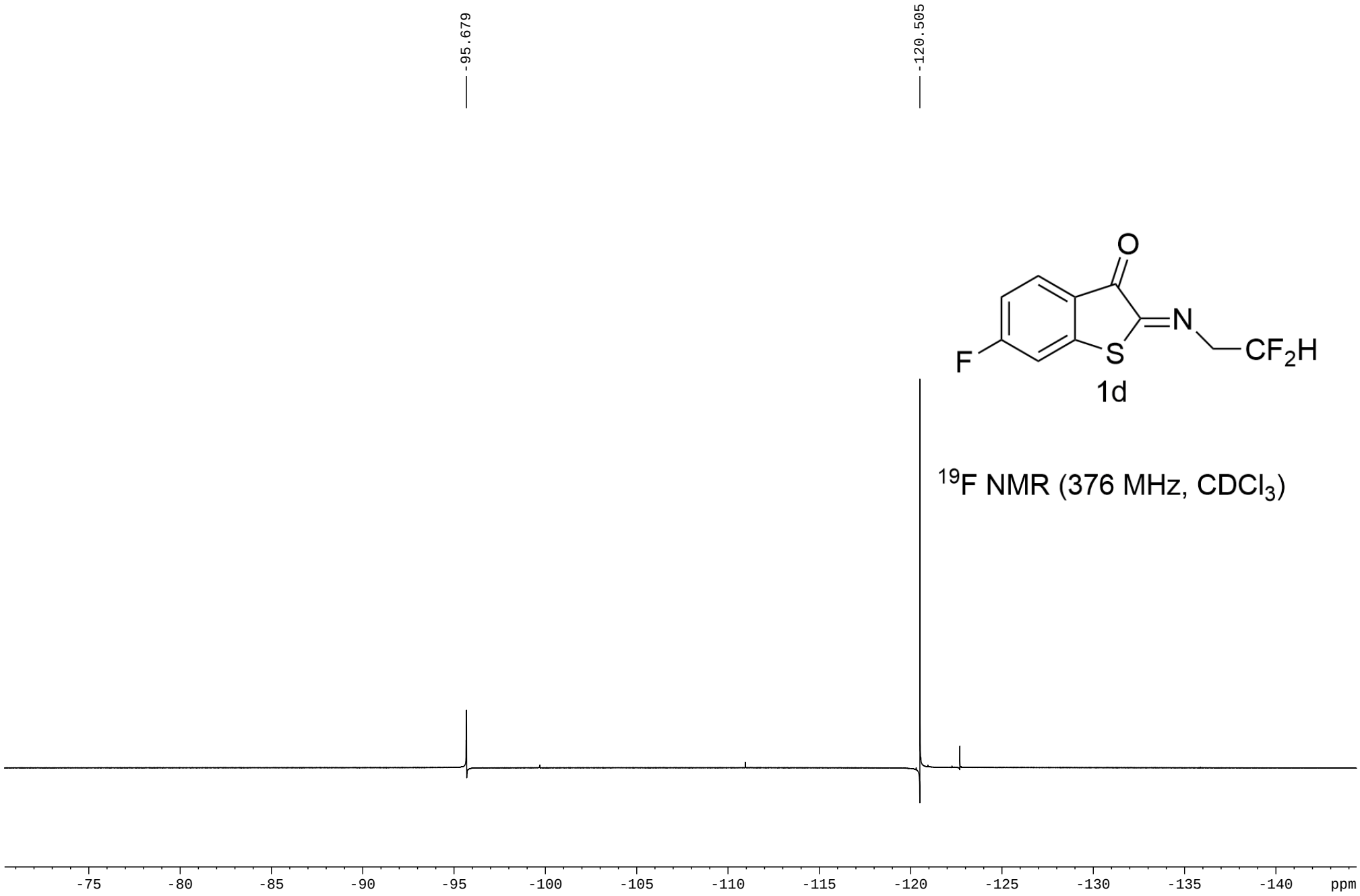

7.944
7.939
7.723
7.718
7.702
7.697
7.385
7.364
3.973
3.962
3.938
3.926
3.902
3.891
1.346
-0.000
O
N
S
CF2H
1c
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.03
1.02
1.05
1.00
2.04
9.10

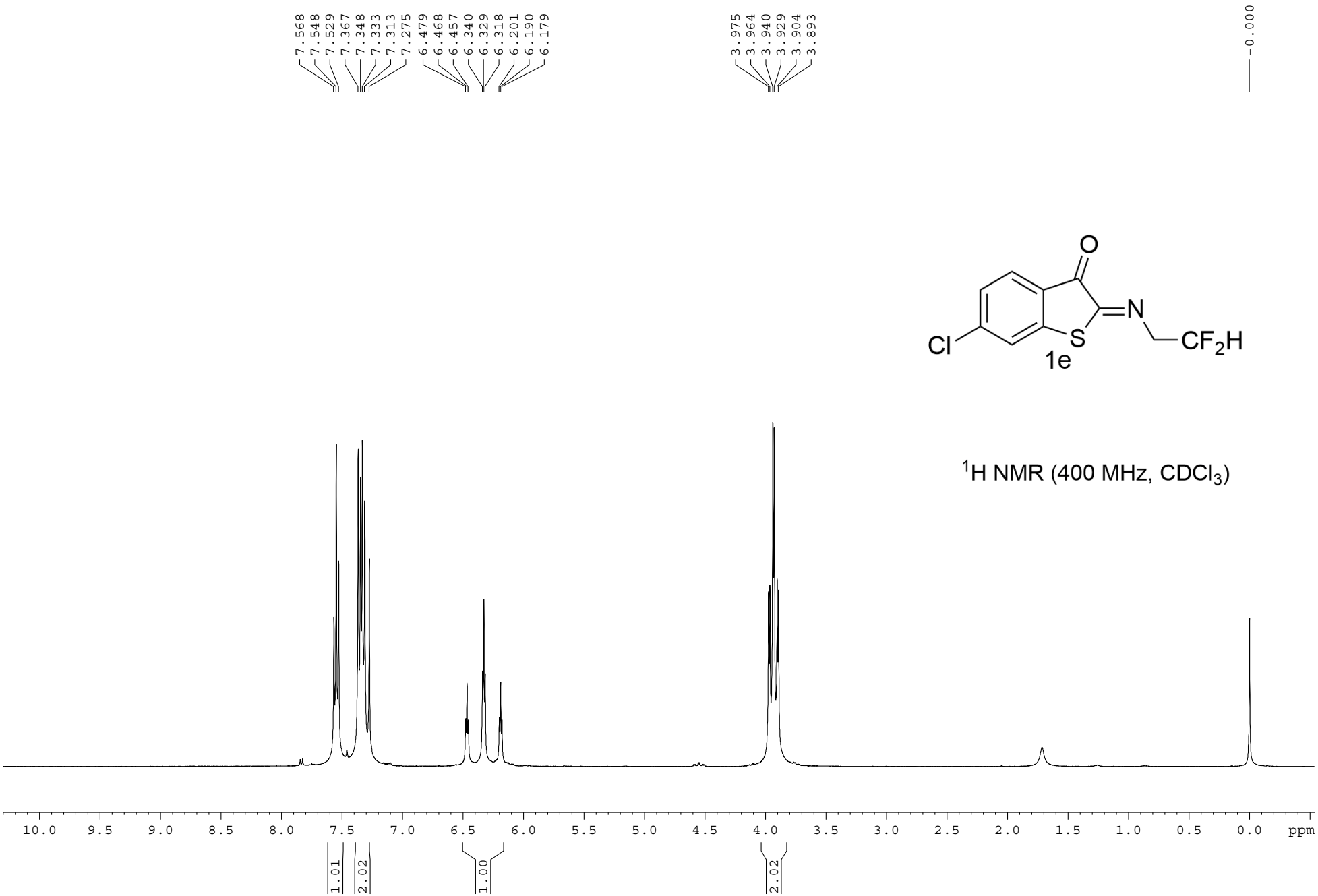

184.92
162.13
150.97
139.35
135.18
127.81
124.66
124.64
116.98
114.58
112.19
60.64
60.36
60.09
34.85
31.08
O
N
S
CF2H
1c
13C {1H} NMR (101 MHz, CDCl3)
118
117
116
115
114
113
112
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

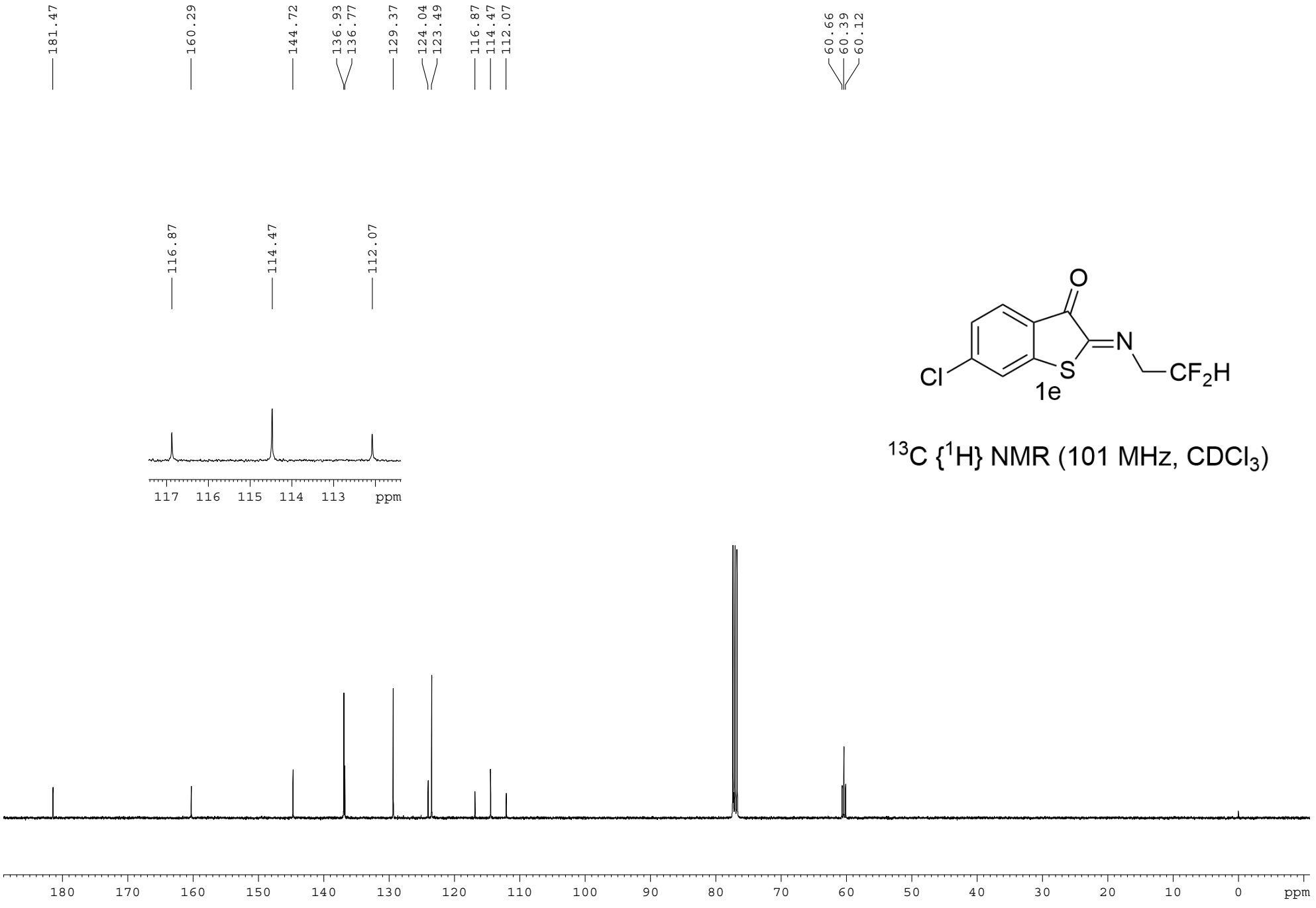

-120.484
O
N
S
CF2H
1c
19F NMR (376 MHz, CDCl3)
-105
-110
-115
-120
-125
-130
-135
ppm

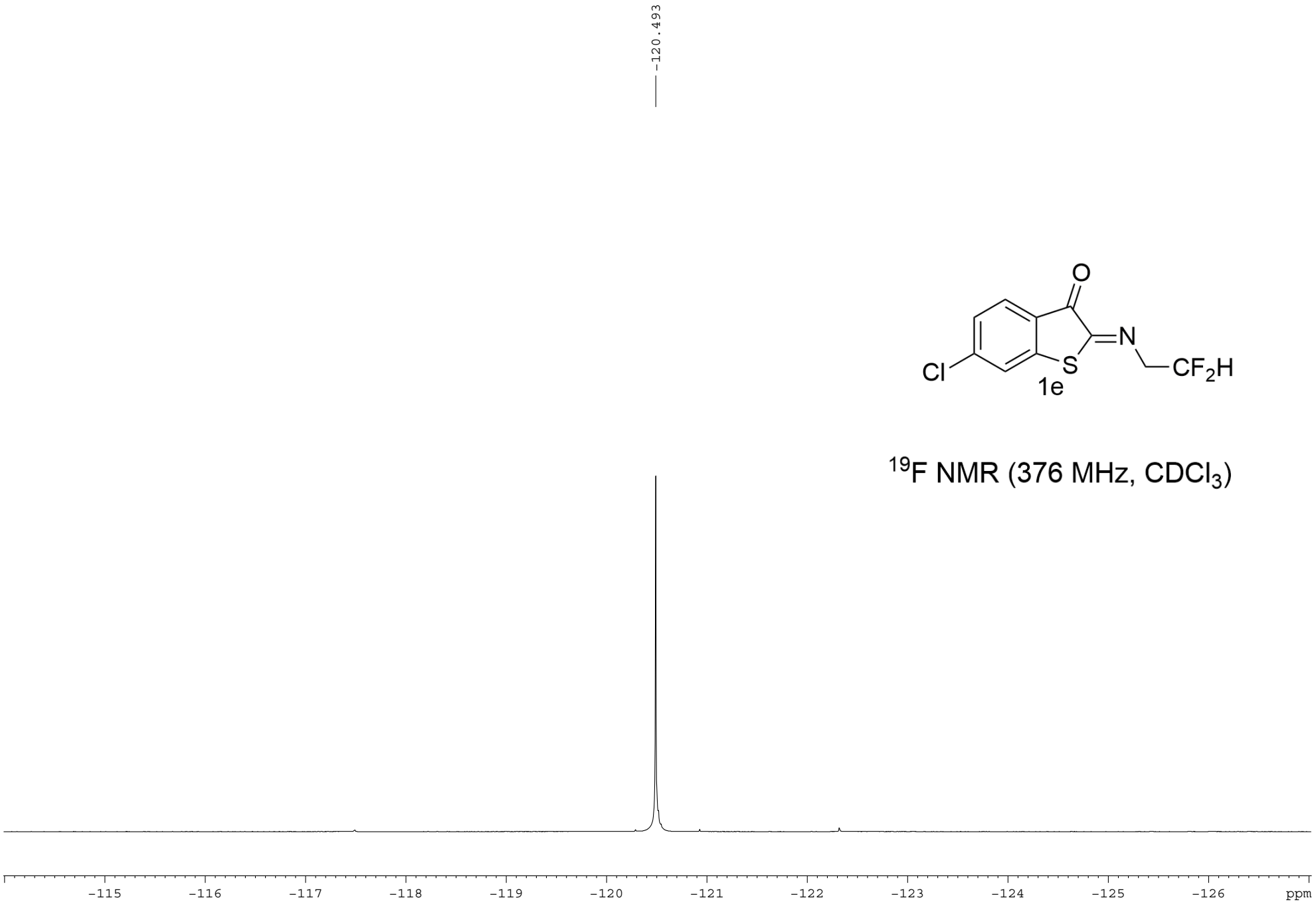

7.973
7.959
7.952
7.938
7.184
7.179
7.164
7.159
7.082
7.077
7.061
7.056
7.040
7.034
6.481
6.470
6.459
6.342
6.331
6.320
6.204
6.192
6.181
3.987
3.976
3.952
3.941
3.916
3.905
-0.000
O
N
S
F
CF2H
1d
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.01
1.04
1.03
1.00
2.07

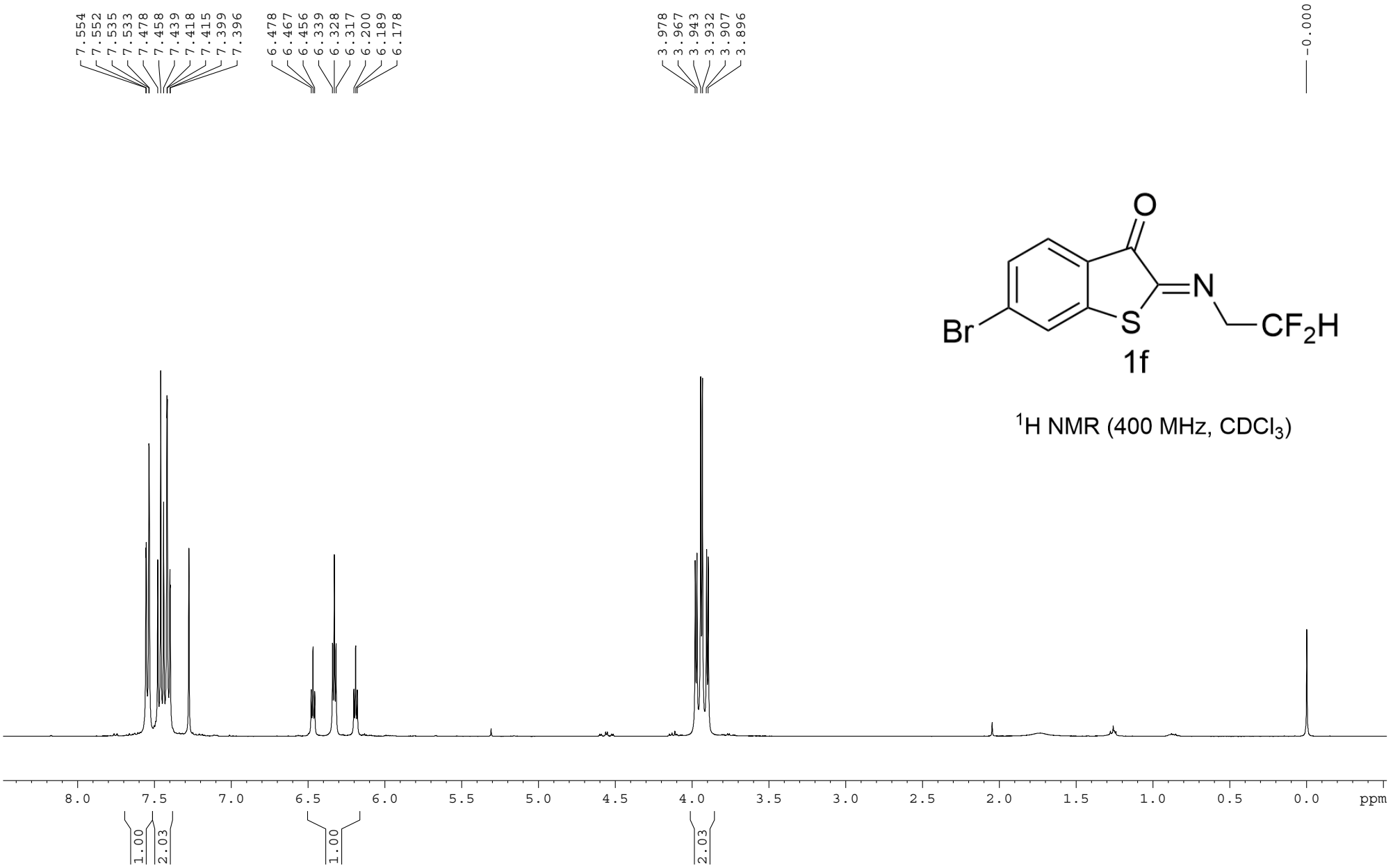

182.61
169.25
166.64
160.50
145.41
145.30
130.33
130.23
124.58
124.56
116.79
115.24
115.01
114.39
112.69
112.43
111.99
60.64
60.37
60.09
116.79
114.39
111.99
117
116
115
114
113
112
ppm
O
N
S
F
CF2H
1d
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

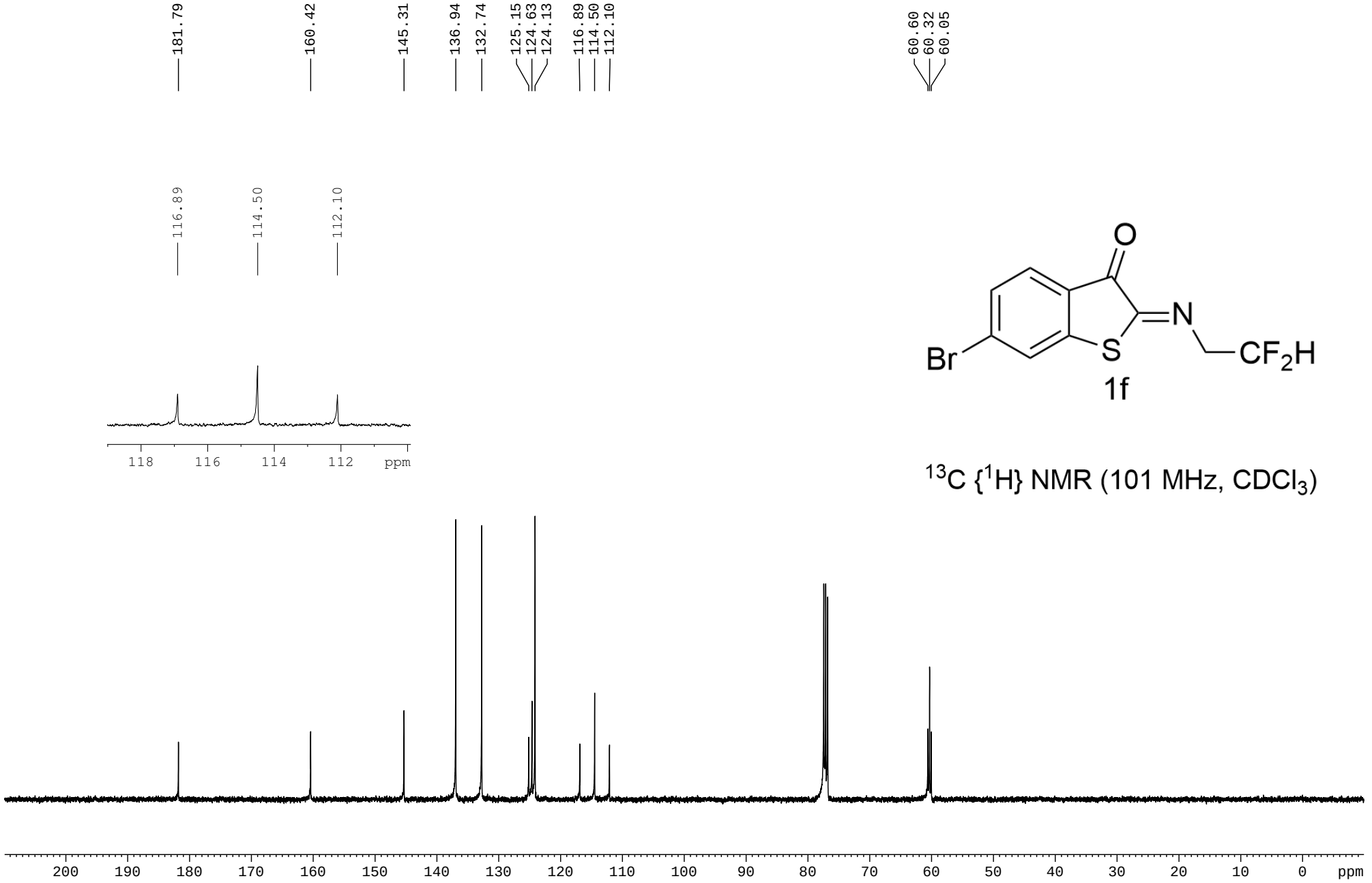

-95.679
-120.505
O
N
F
S
CF2H
1d
19F NMR (376 MHz, CDCl3)
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
ppm

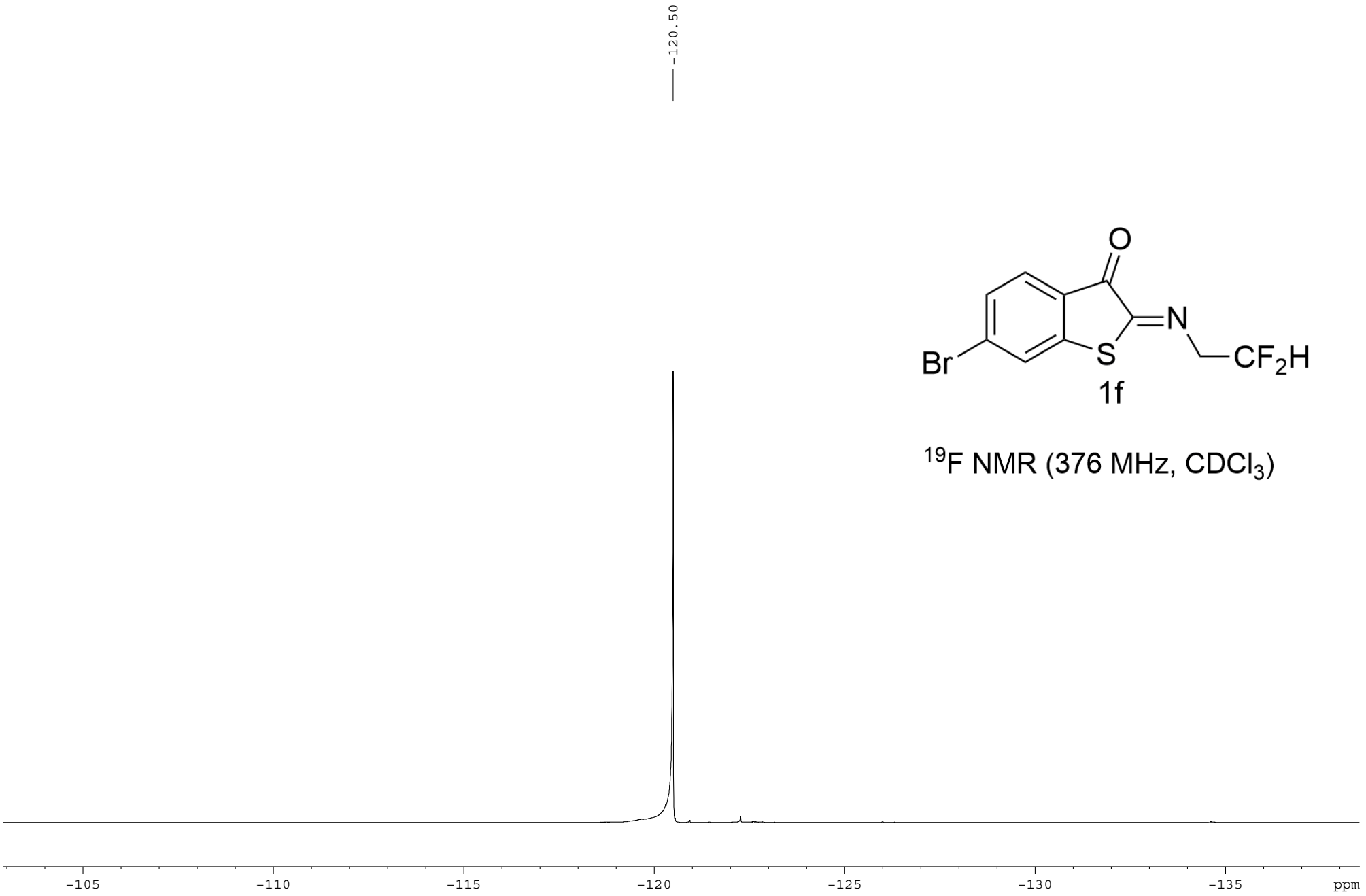

7.568
7.548
7.529
7.367
7.348
7.333
7.313
7.275
6.479
6.468
6.457
6.340
6.329
6.318
6.201
6.190
6.179
3.975
3.964
3.940
3.929
3.904
3.893
-0.000
O
N
S
Cl
CF2H
1e
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.01
2.02
1.00
2.02


181.47
160.29
144.72
136.93
136.77
129.37
124.04
123.49
116.87
114.47
112.07
60.66
60.39
60.12
116.87
114.47
112.07
117 116 115 114 113 ppm
O
N
Cl
S
CF2H
1e
13C {1H} NMR (101 MHz, CDCl3)
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


-120.493
O
N
Cl
S
CF2H
1e
19F NMR (376 MHz, CDCl3)
-115
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

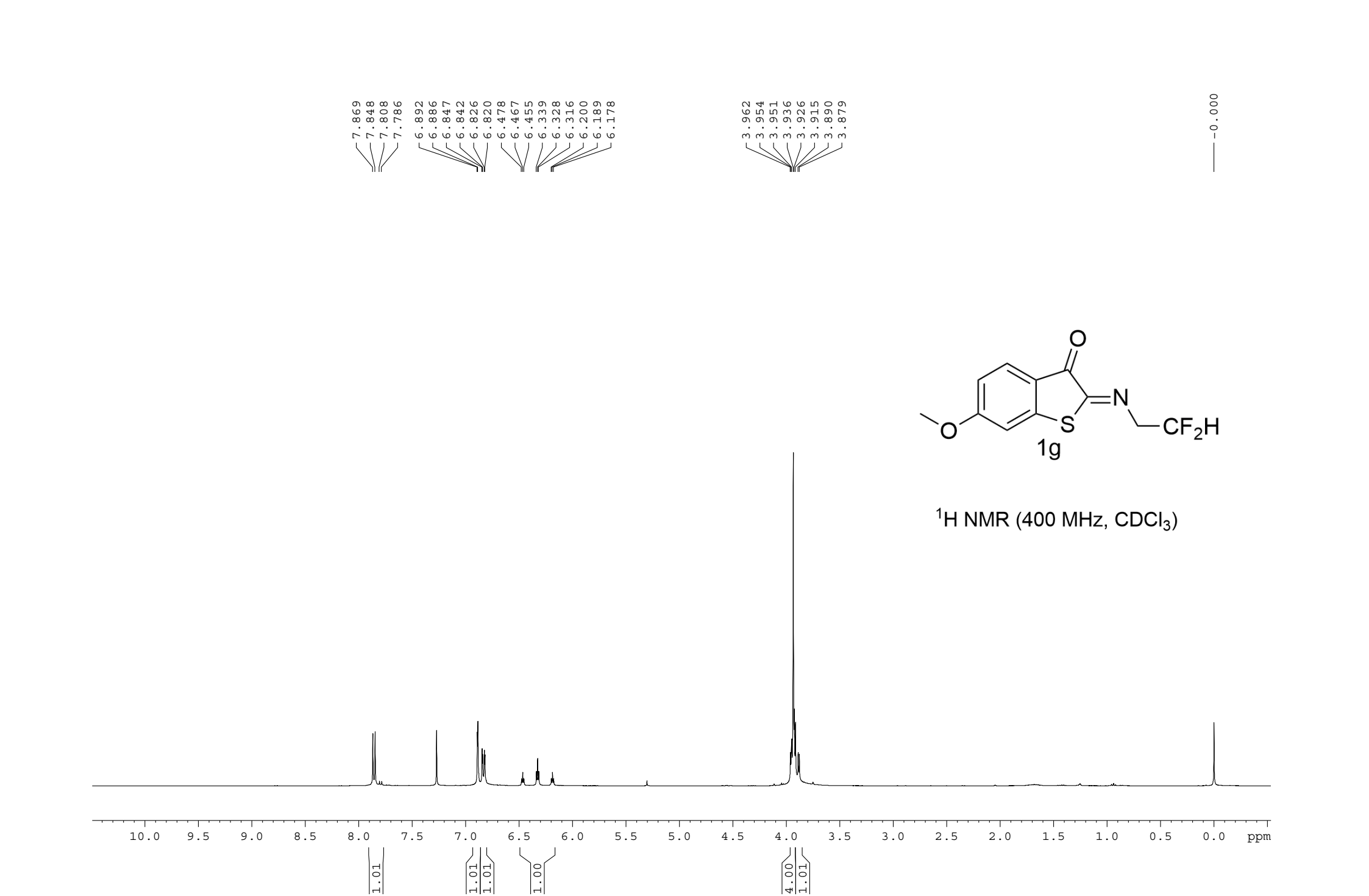

7.554
7.552
7.535
7.533
7.478
7.458
7.439
7.418
7.415
7.399
7.396
6.478
6.467
6.456
6.339
6.328
6.317
6.200
6.189
6.178
3.978
3.967
3.943
3.932
3.907
3.896
-0.000
O
N
S
Br
CF2H
1f
1H NMR (400 MHz, CDCl3)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
2.03
1.00
2.03

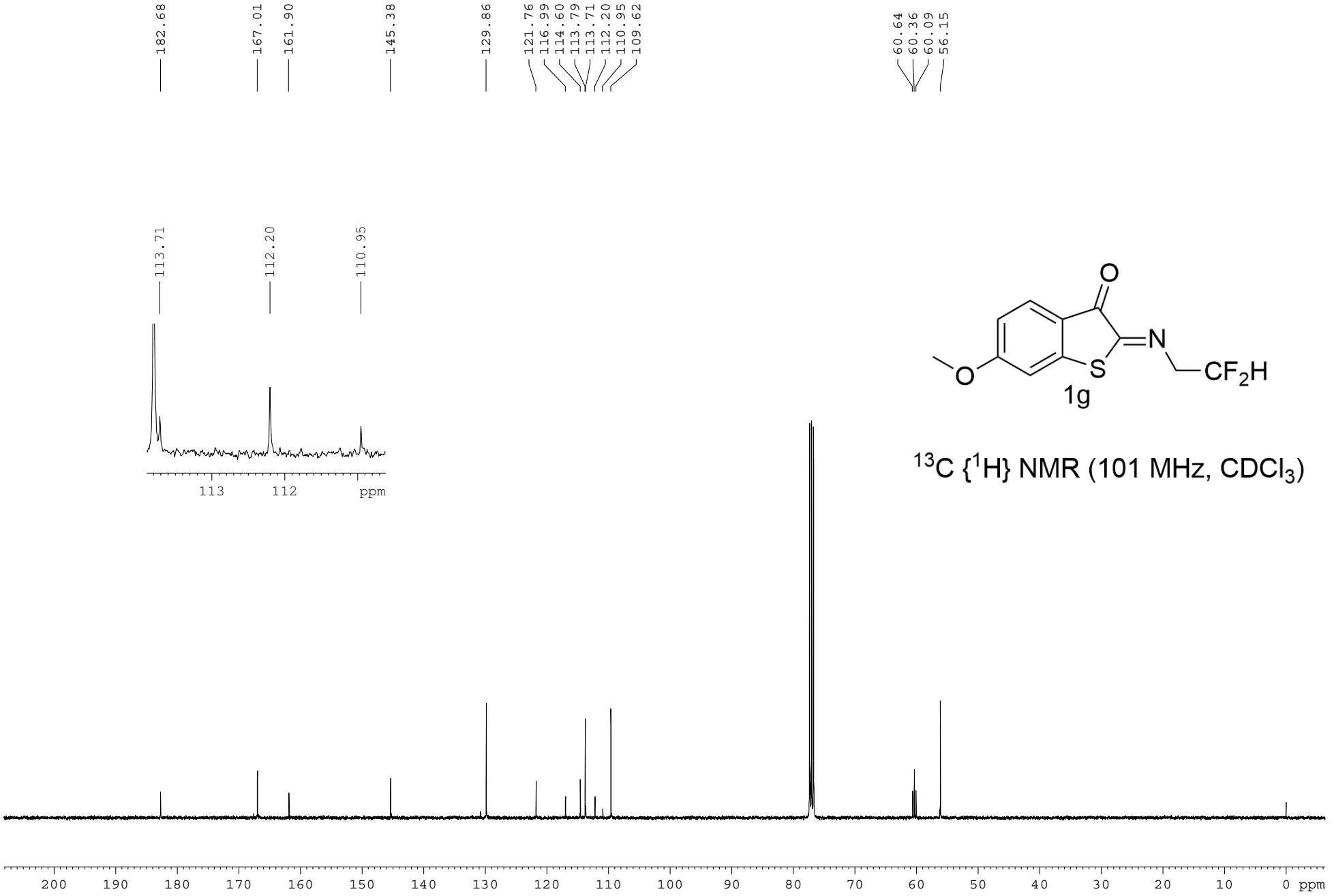

181.79
160.42
145.31
136.94
132.74
125.15
124.63
124.13
116.89
114.50
112.10
60.60
60.32
60.05
O
N
Br
S
CF2H
1f
13C {1H} NMR (101 MHz, CDCl3)
118
116
114
112
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

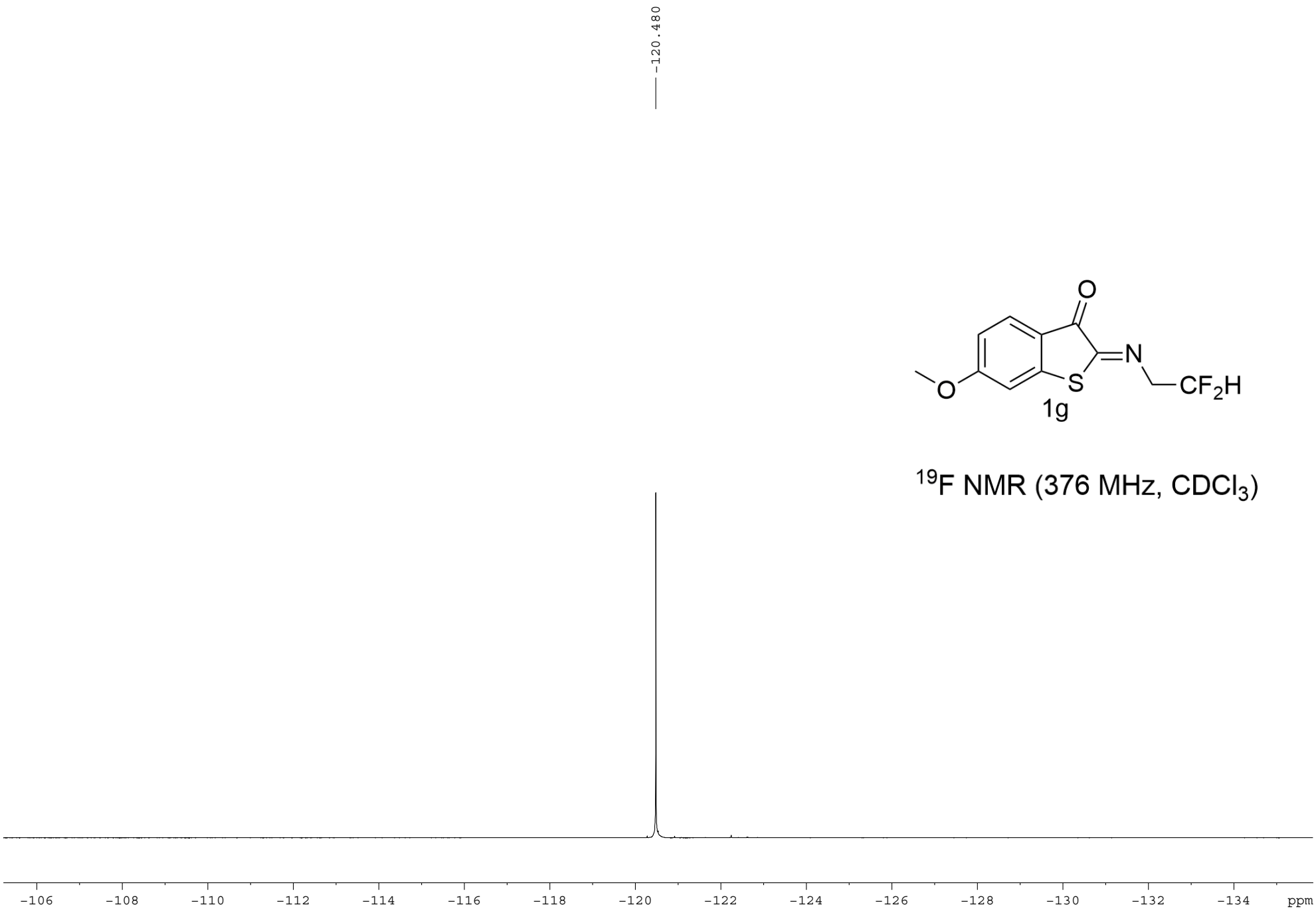


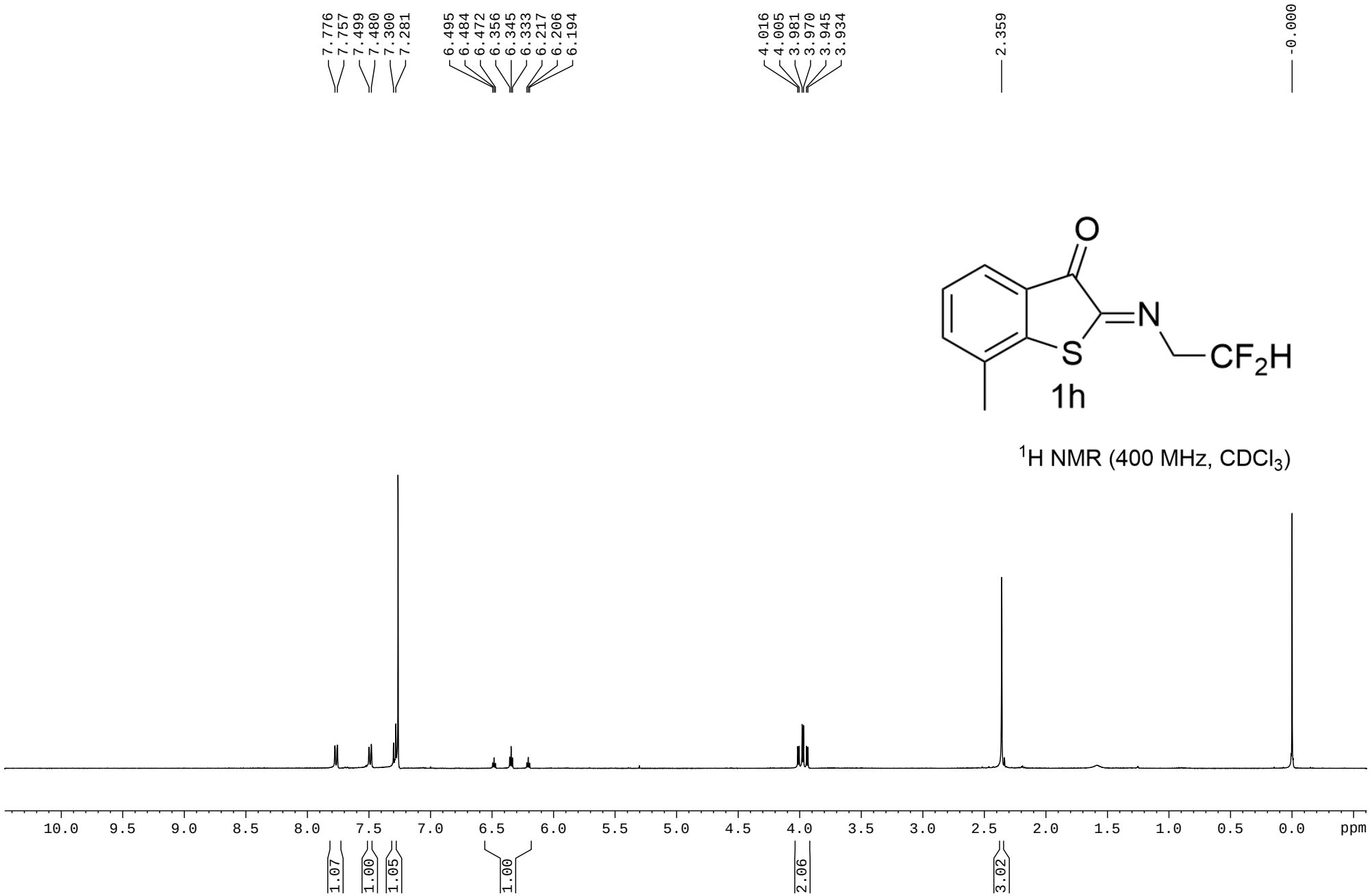
1f

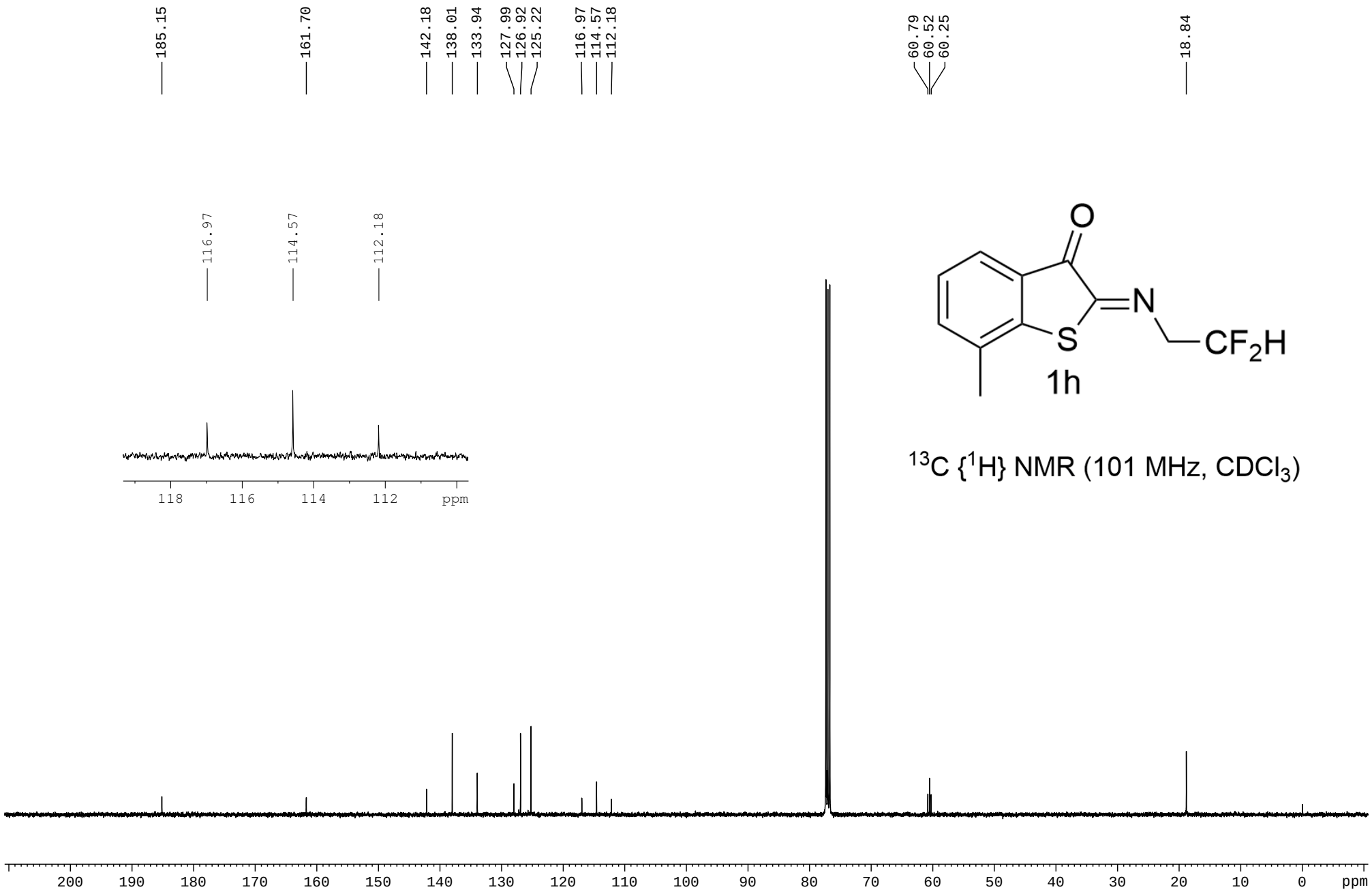
^{19}F NMR (376 MHz, $CDCl_3$)

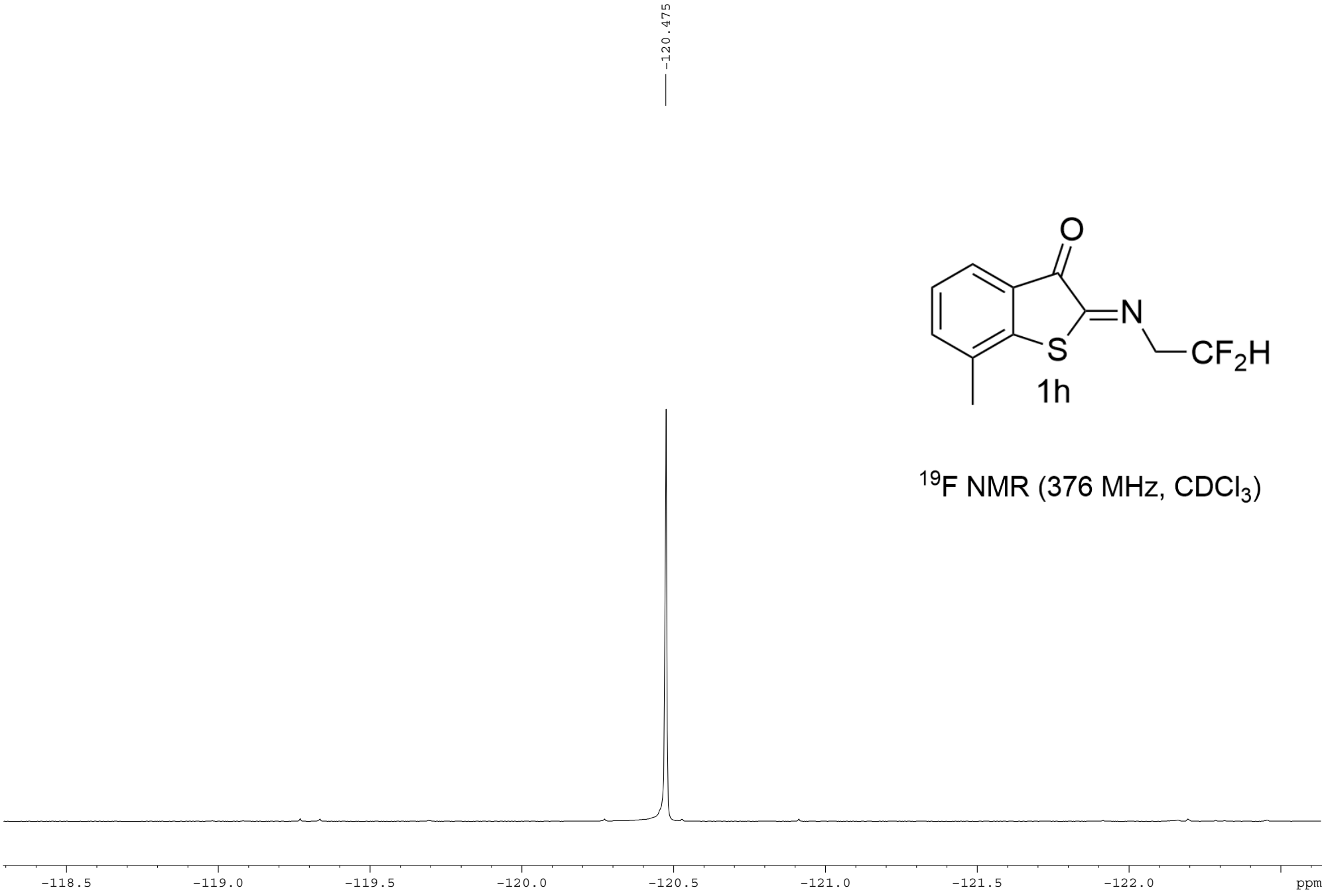

7.869
7.848
7.808
7.786
6.892
6.886
6.847
6.842
6.826
6.820
6.478
6.467
6.455
6.339
6.328
6.316
6.200
6.189
6.178
3.962
3.954
3.951
3.936
3.926
3.915
3.890
3.879
0.000
O
N
S
O
CF2H
1g
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.01
1.01
1.01
1.00
4.00
1.01

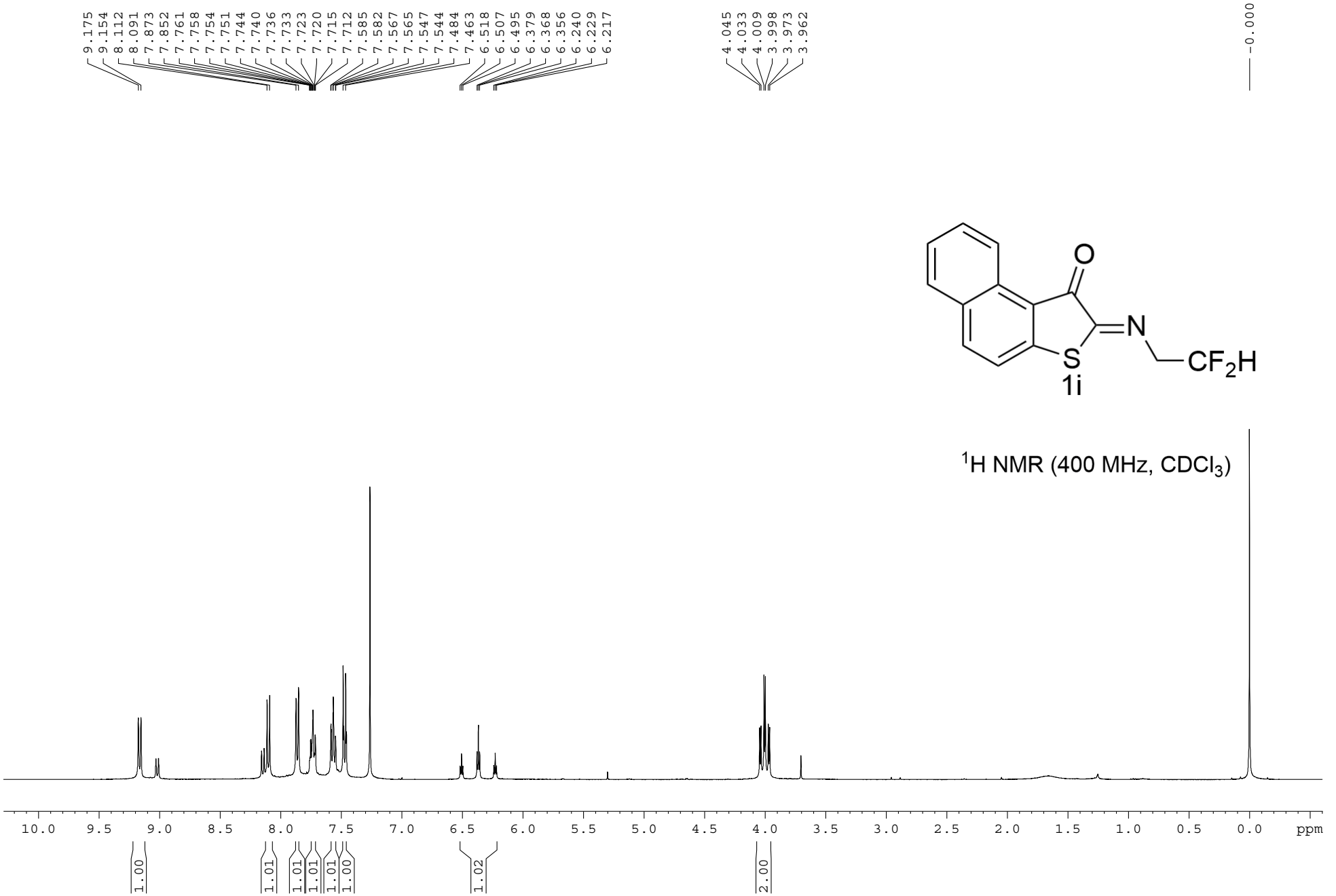

182.68
167.01
161.90
145.38
129.86
121.76
116.99
114.60
113.79
113.71
112.20
110.95
109.62
60.64
60.36
60.09
56.15
113.71
112.20
110.95
113
112
ppm
O
N
S
O
CF2H
1g
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0 ppm

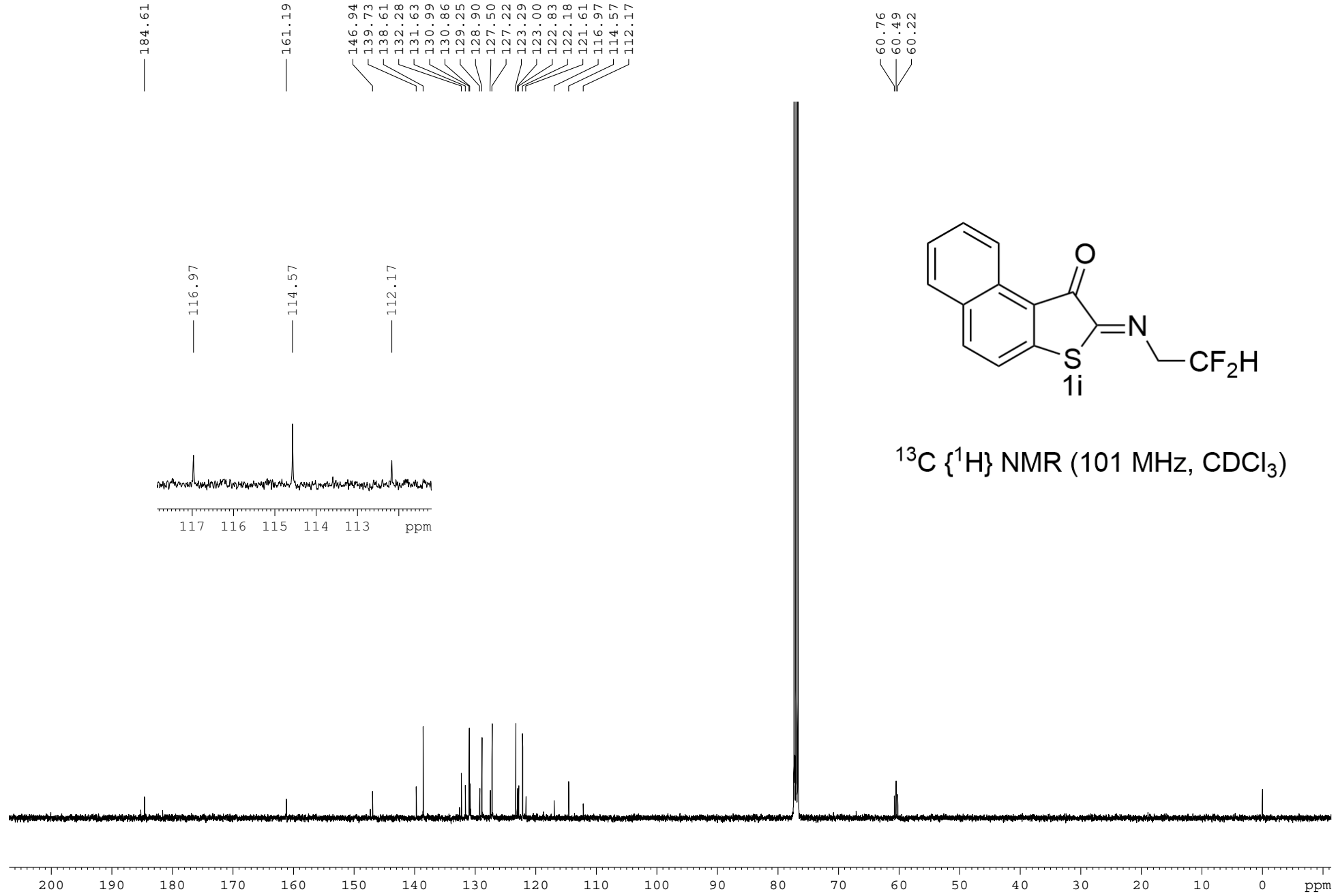

-120.480
O
N
O
S
CF2H
1g
19F NMR (376 MHz, CDCl3)
-106
-108
-110
-112
-114
-116
-118
-120
-122
-124
-126
-128
-130
-132
-134
ppm

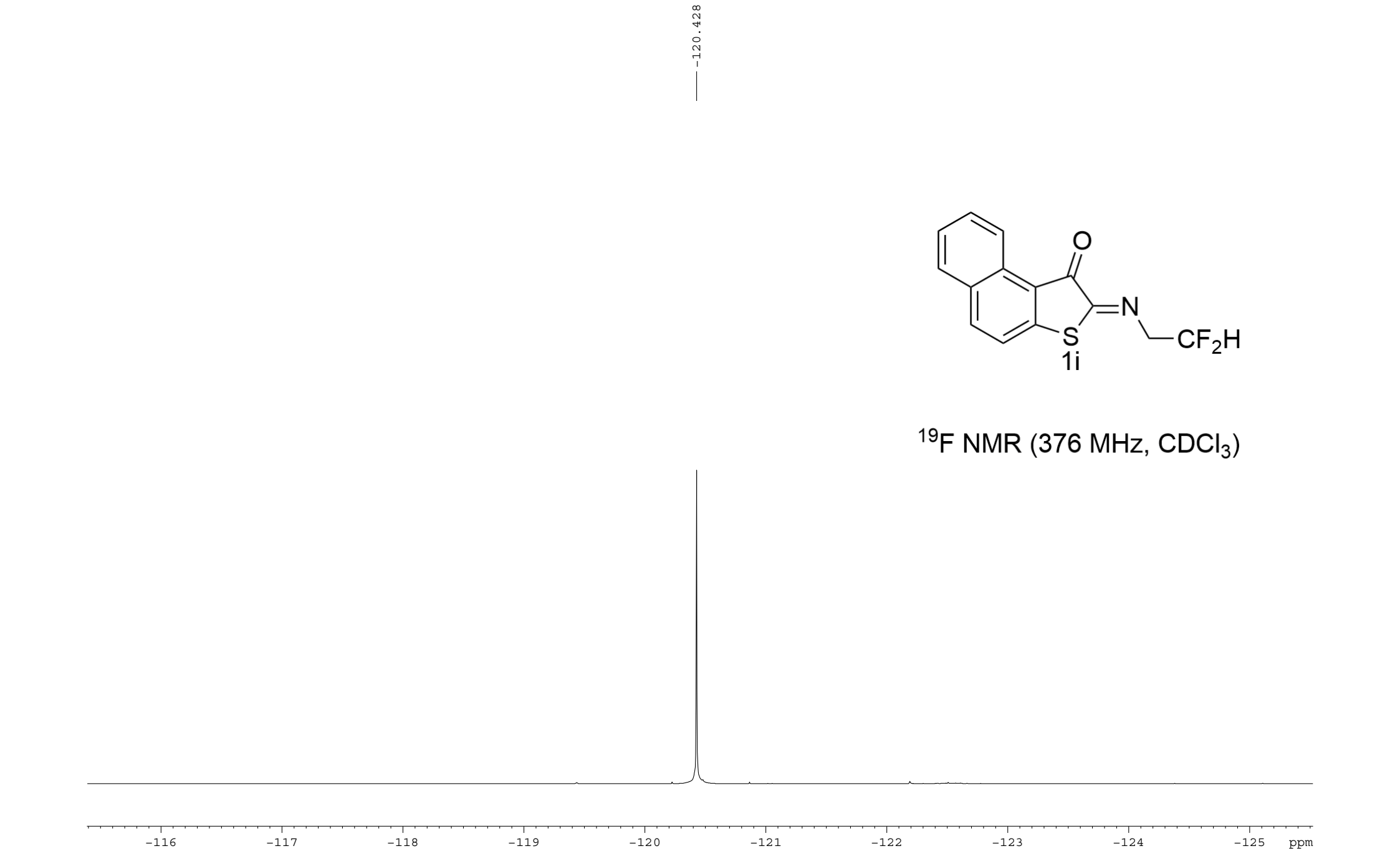

7.776
7.757
7.499
7.480
7.300
7.281
6.495
6.484
6.472
6.356
6.345
6.333
6.217
6.206
6.194
4.016
4.005
3.981
3.970
3.945
3.934
2.359
-0.000
O
N
S
CF2H
1h
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.07
1.00
1.05
1.00
2.06
3.02

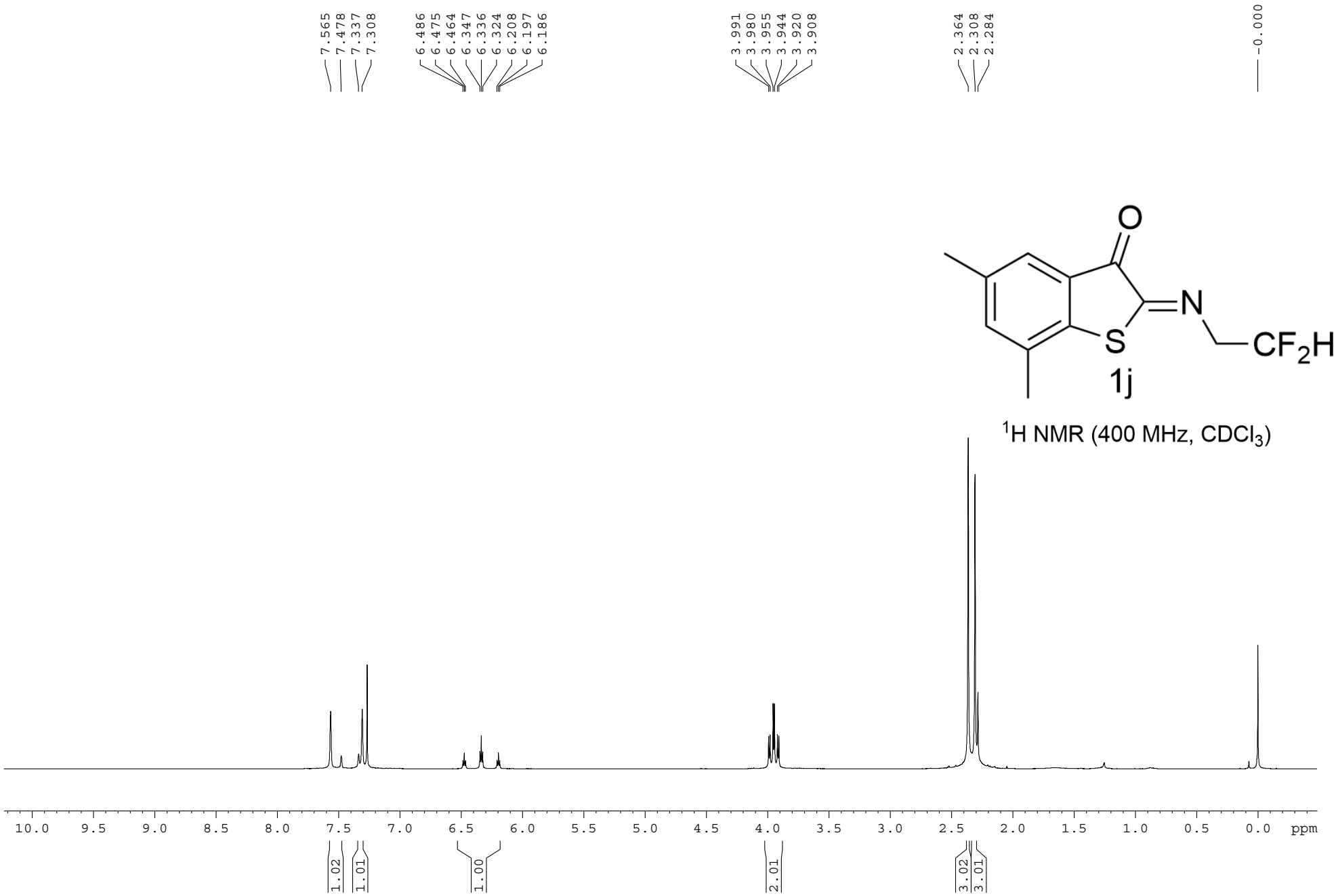

185.15
161.70
142.18
138.01
133.94
127.99
126.92
125.22
116.97
114.57
112.18
60.79
60.52
60.25
18.84
116.97
114.57
112.18
118
116
114
112
ppm
O
N
S
CF2H
1h
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

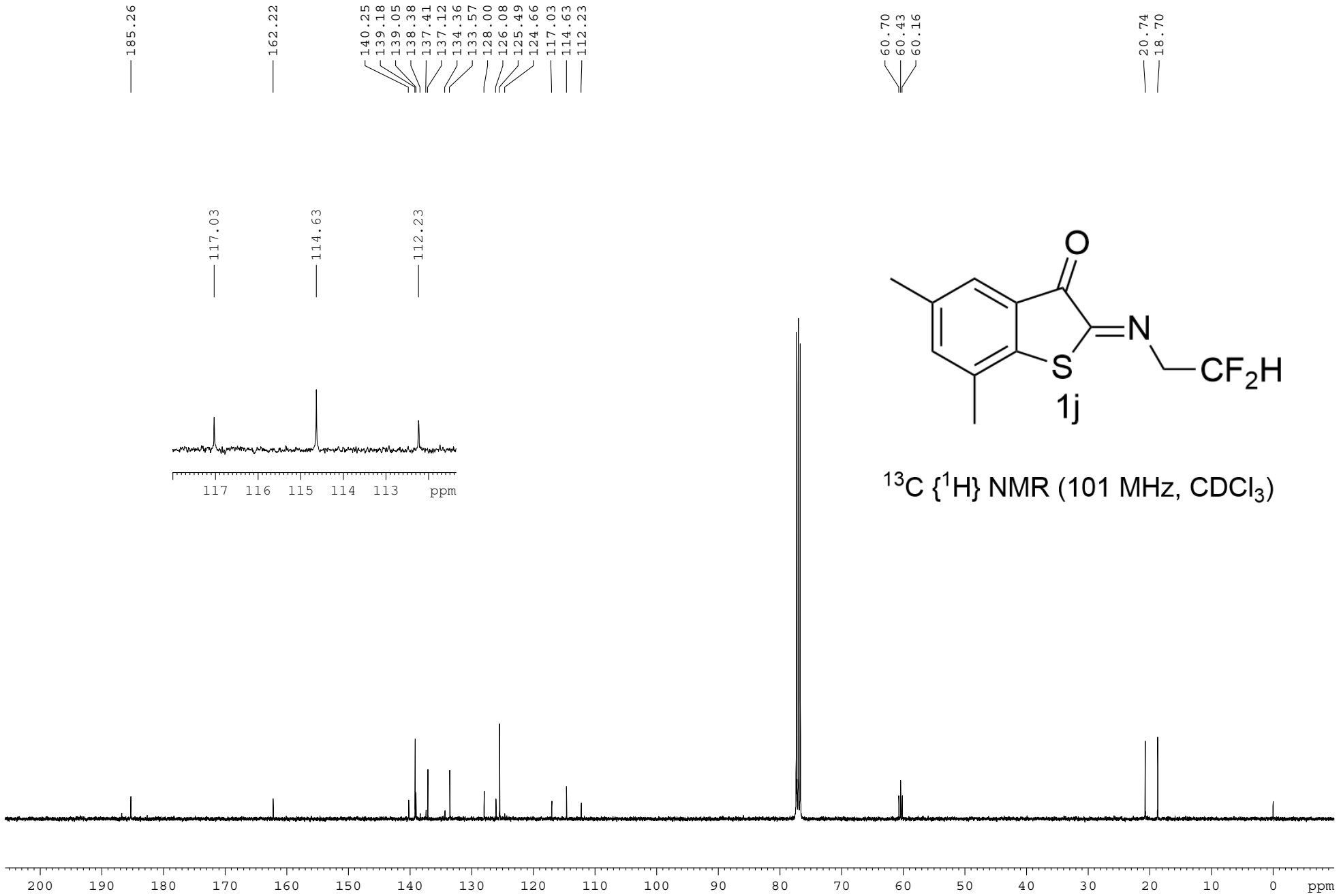

-120.475
O
N
S
CF_2H
1h
^{19}F NMR (376 MHz, $CDCl_3$)
-118.5
-119.0
-119.5
-120.0
-120.5
-121.0
-121.5
-122.0
ppm

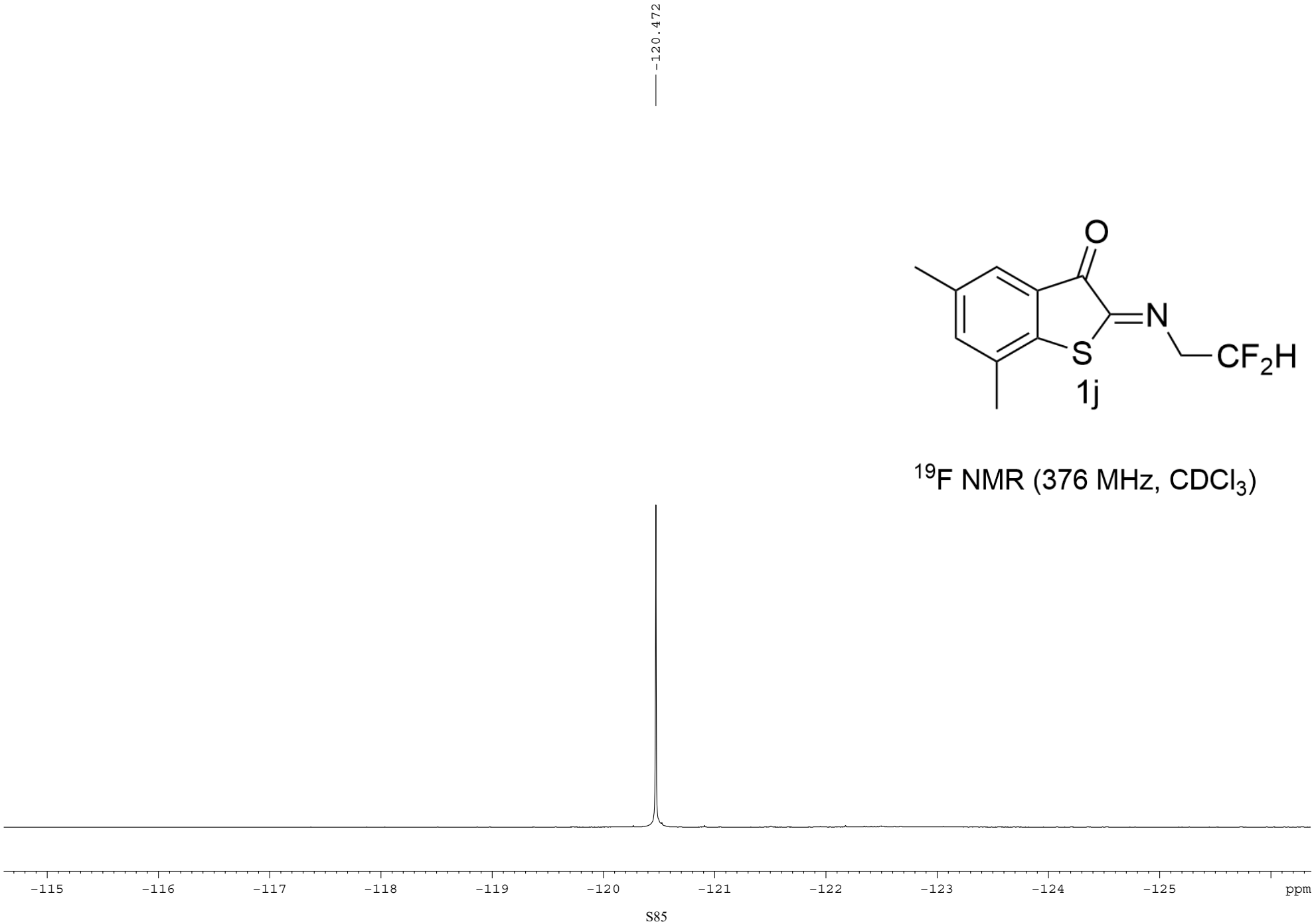

9.175
9.154
8.112
8.091
7.873
7.852
7.761
7.758
7.754
7.751
7.744
7.740
7.736
7.733
7.723
7.720
7.715
7.712
7.585
7.582
7.567
7.565
7.547
7.544
7.484
7.463
6.518
6.507
6.495
6.379
6.368
6.356
6.240
6.229
6.217
4.045
4.033
4.009
3.998
3.973
3.962
-0.000
O
N
S
CF2H
1i
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
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
ppm
1.00
1.01
1.01
1.01
1.01
1.00
1.02
2.00

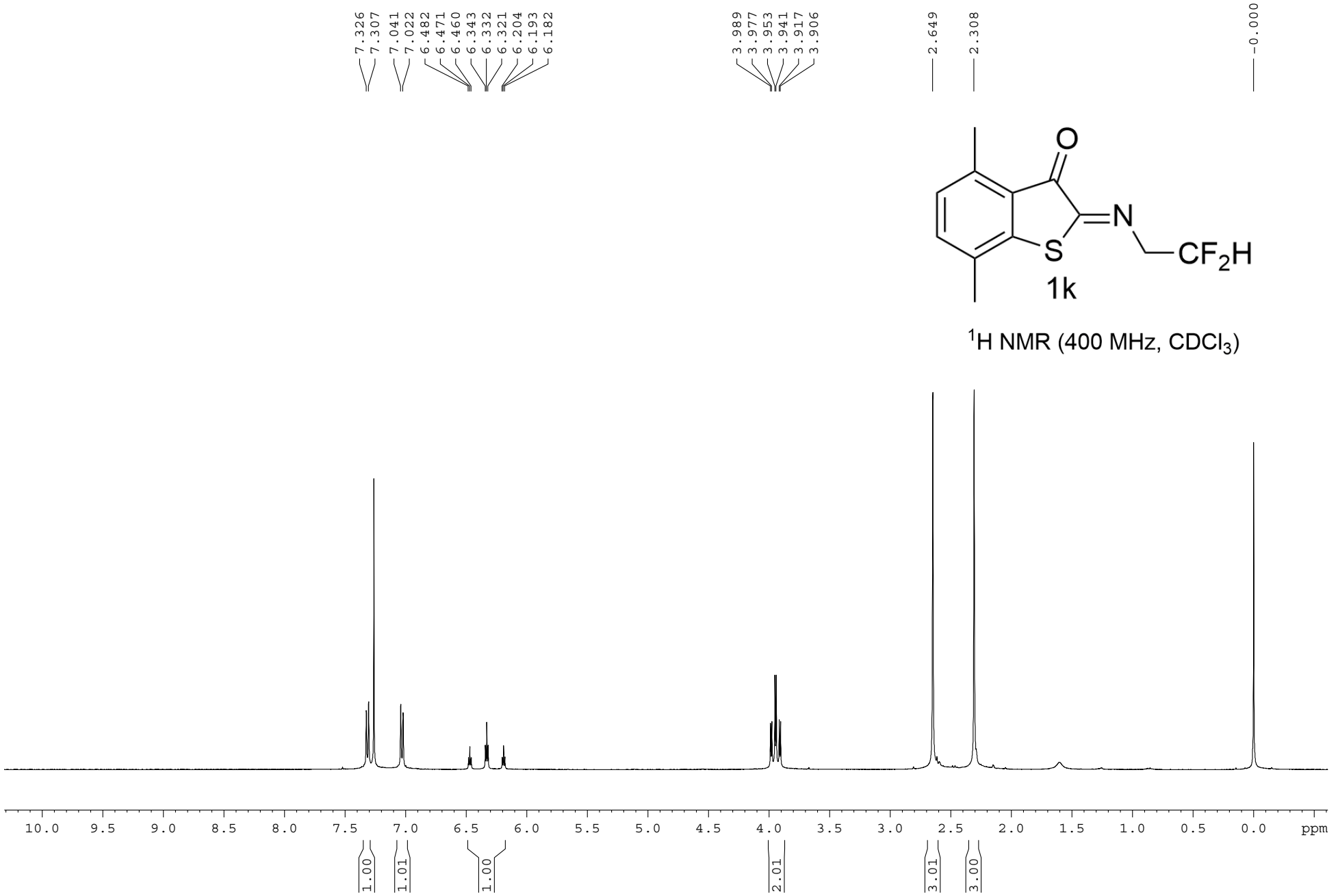

184.61
161.19
146.94
139.73
138.61
132.28
131.63
130.99
130.86
129.25
128.90
127.50
127.22
123.29
123.00
122.83
122.18
121.61
116.97
114.57
112.17
60.76
60.49
60.22
116.97
114.57
112.17
117 116 115 114 113 ppm
O
N
S
CF2H
1i
13C {1H} NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

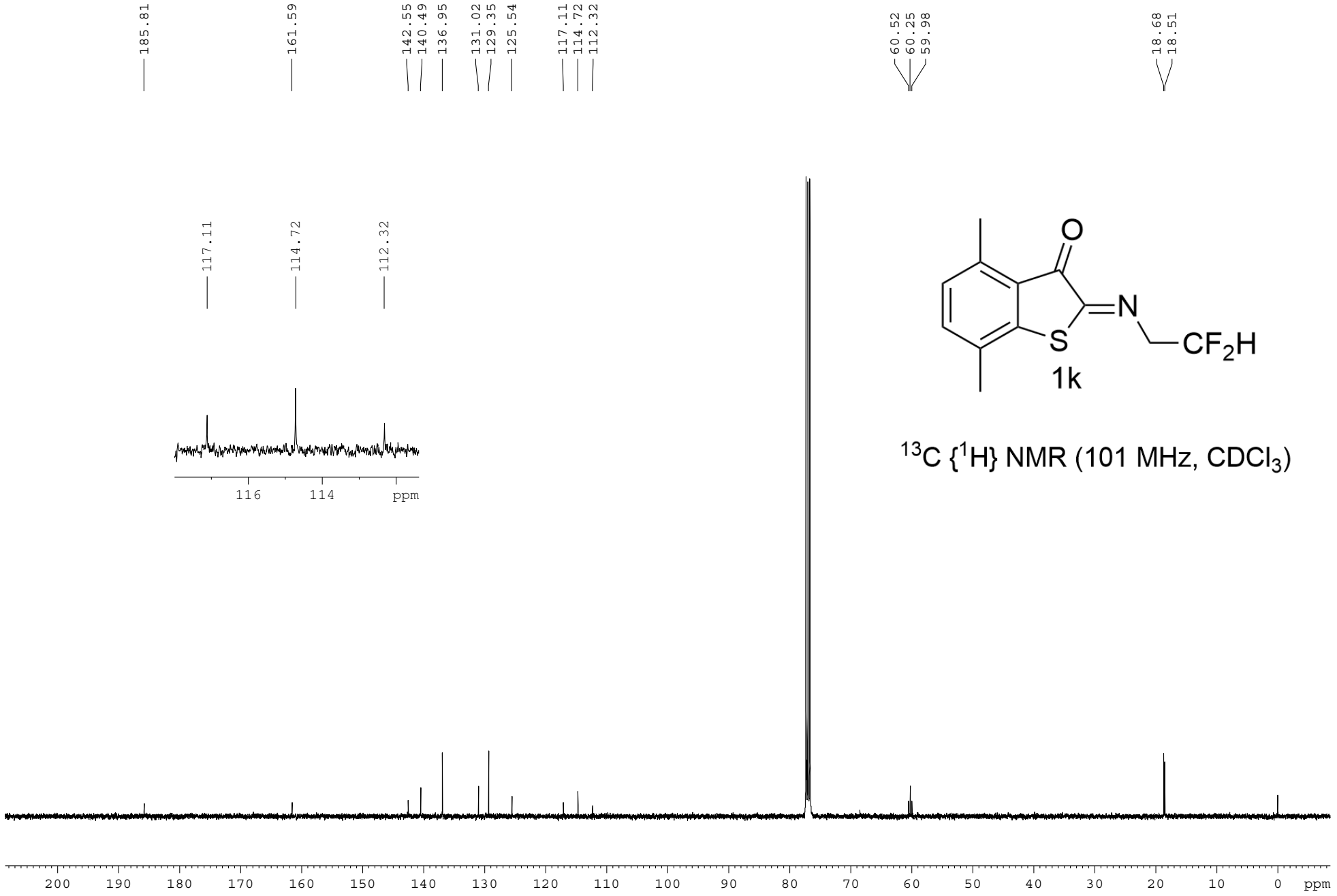

-120.428
O
N
S
CF2H
1i
19F NMR (376 MHz, CDCl3)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
ppm

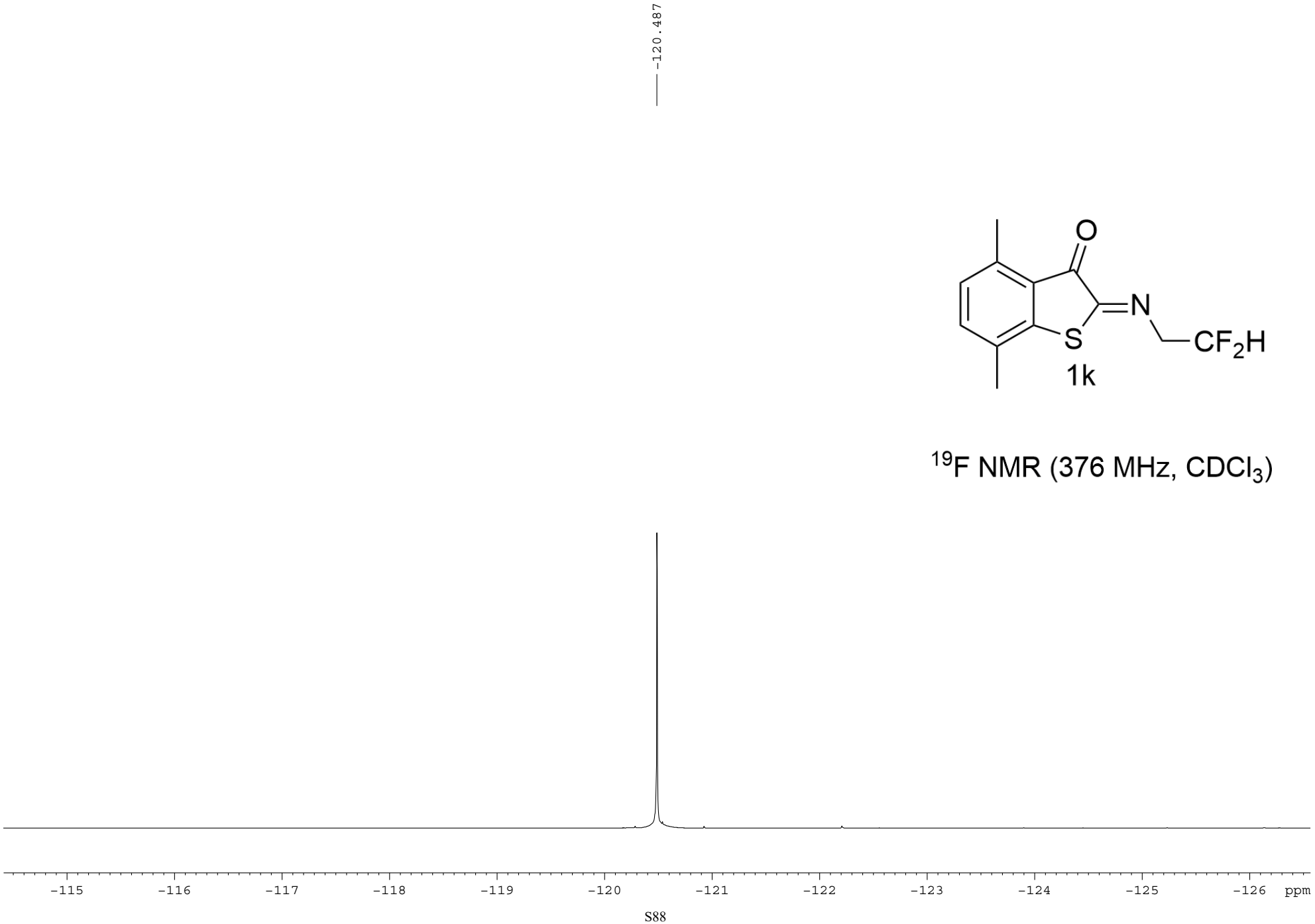

7.565
7.478
7.337
7.308
6.486
6.475
6.464
6.347
6.336
6.324
6.208
6.197
6.186
3.991
3.980
3.955
3.944
3.920
3.908
2.364
2.308
2.284
0.000
O
N
S
CF2H
1j
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.02
1.01
1.00
2.01
3.02
3.01

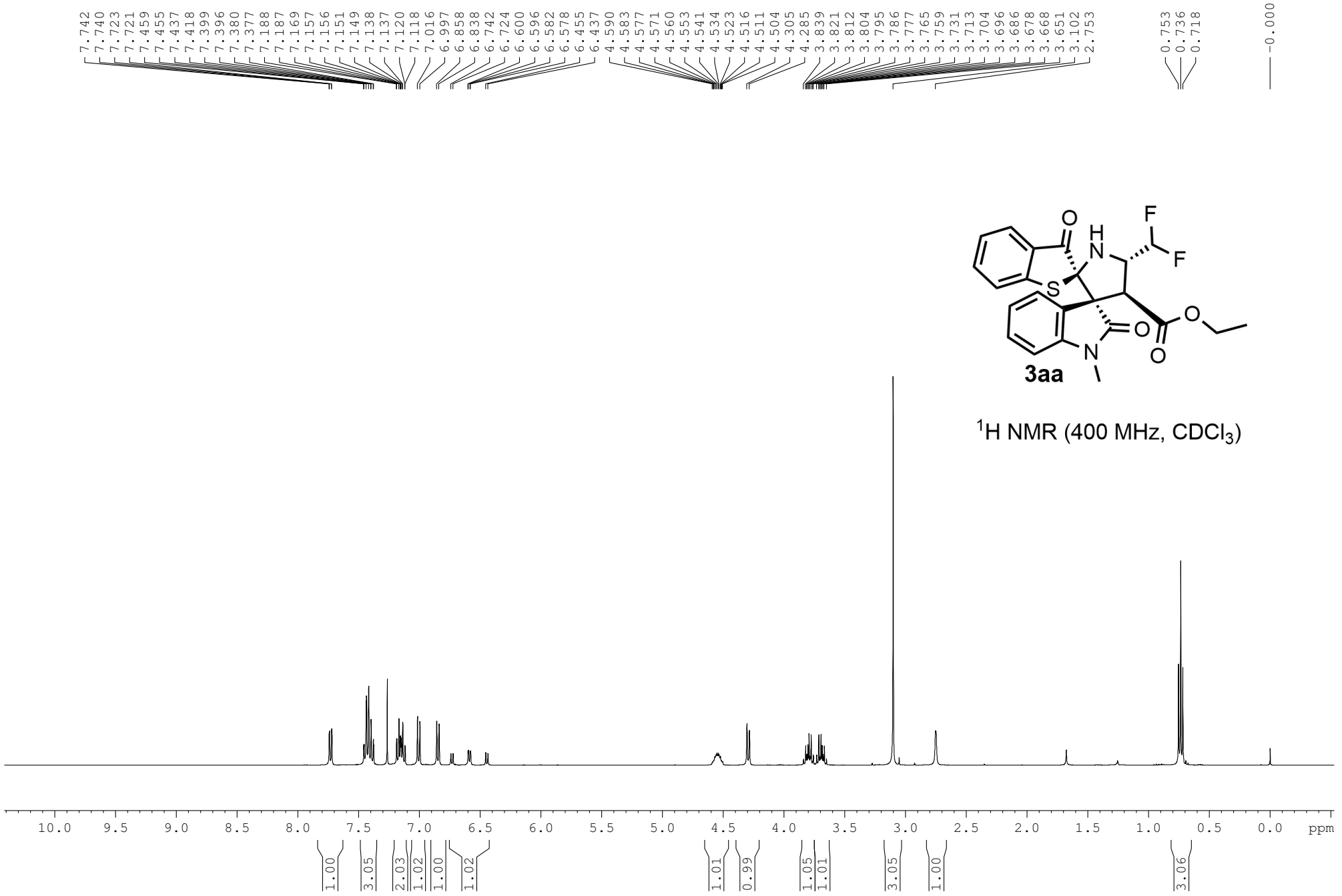

185.26
162.22
140.25
139.18
139.05
138.38
137.41
137.12
134.36
133.57
128.00
126.08
125.49
124.66
117.03
114.63
112.23
60.70
60.43
60.16
20.74
18.70
117.03
114.63
112.23
117 116 115 114 113 ppm
O
N
S
CF2H
1j
13C {1H} NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

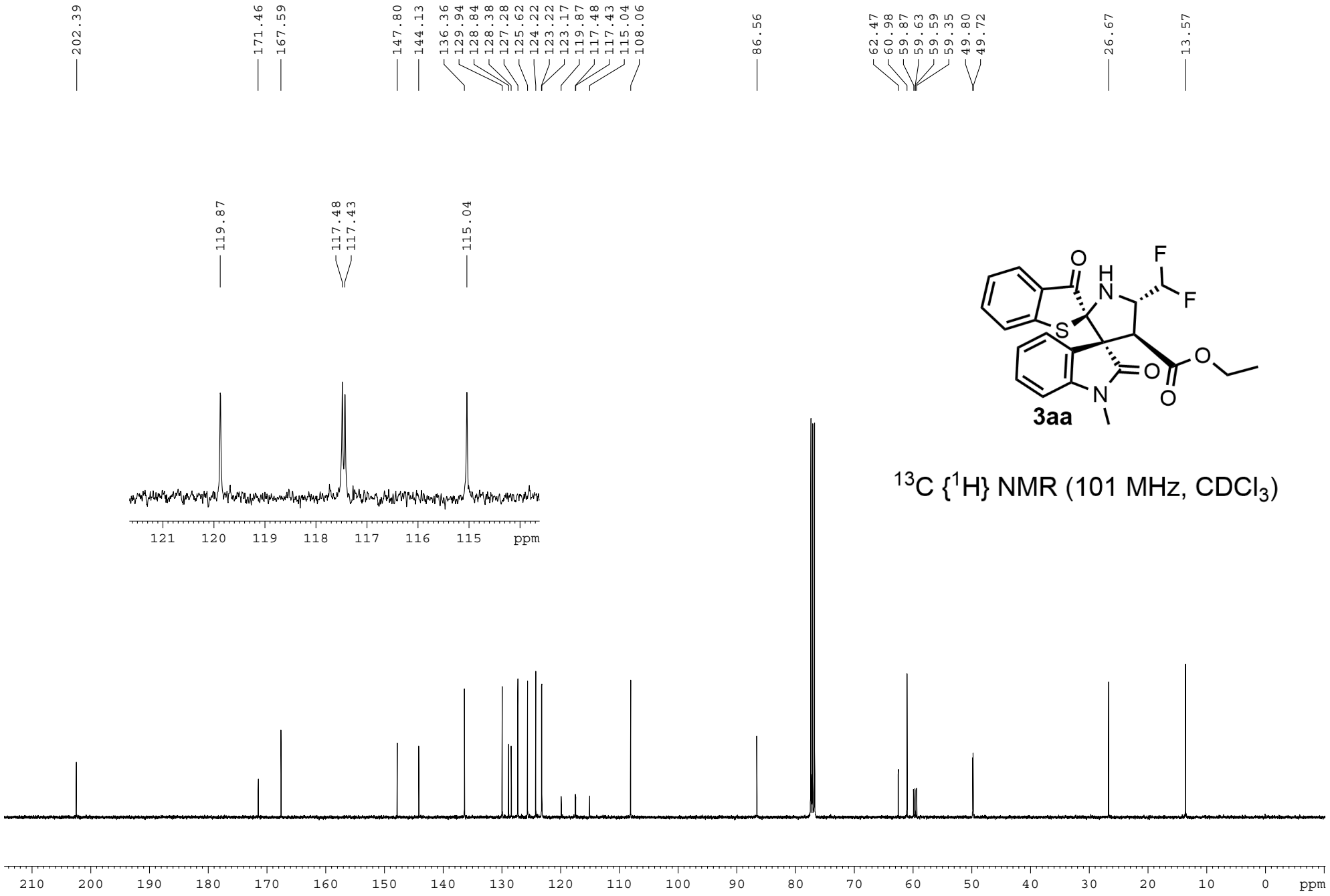

-120.472
O
N
S
CF2H
1j
19F NMR (376 MHz, CDCl3)
-115
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
ppm

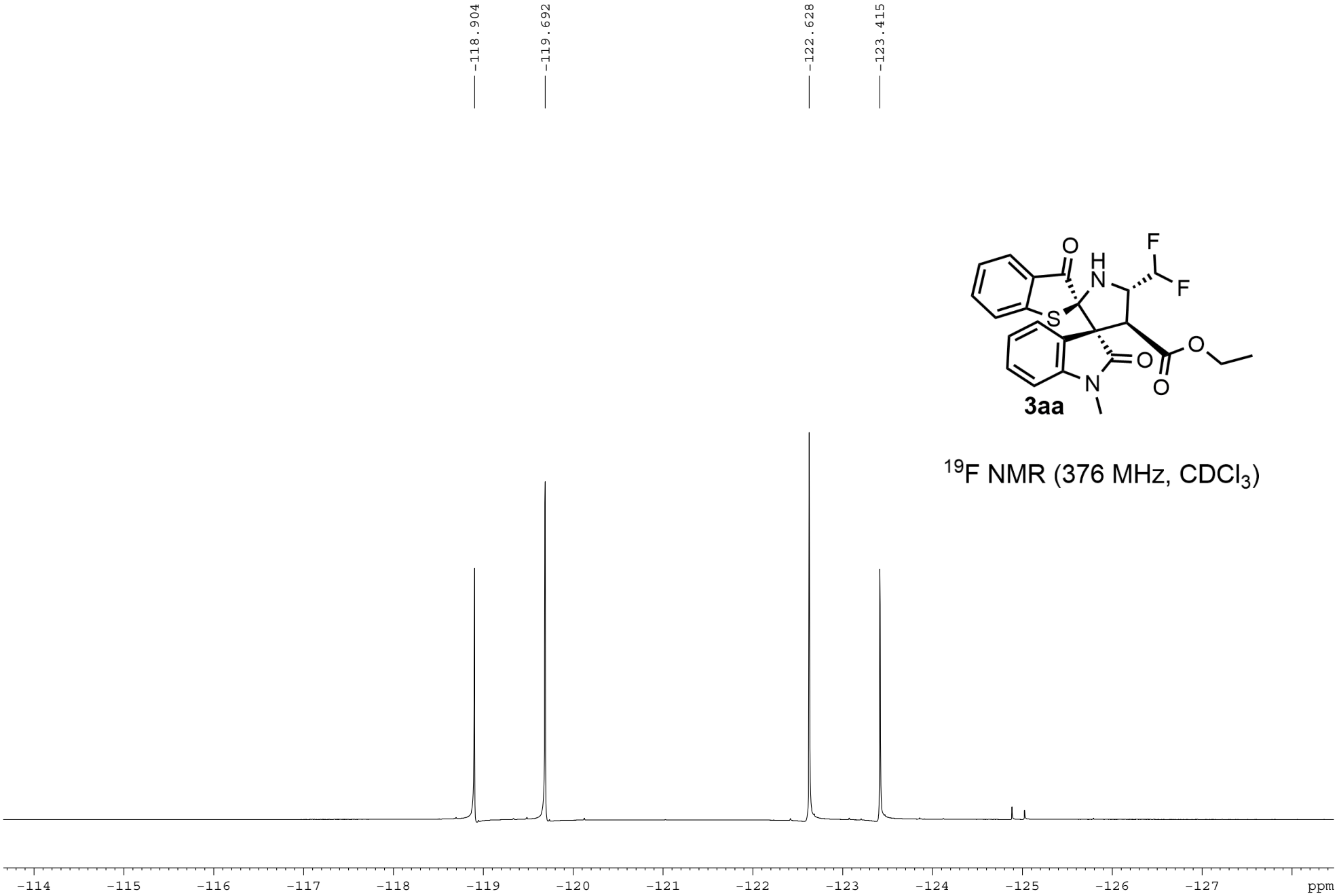

7.326
7.307
7.041
7.022
6.482
6.471
6.460
6.343
6.332
6.321
6.204
6.193
6.182
3.989
3.977
3.953
3.941
3.917
3.906
2.649
2.308
-0.000
O
N
S
CF2H
1k
1H NMR (400 MHz, CDCl3)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
1.00
1.01
1.00
2.01
3.01
3.00

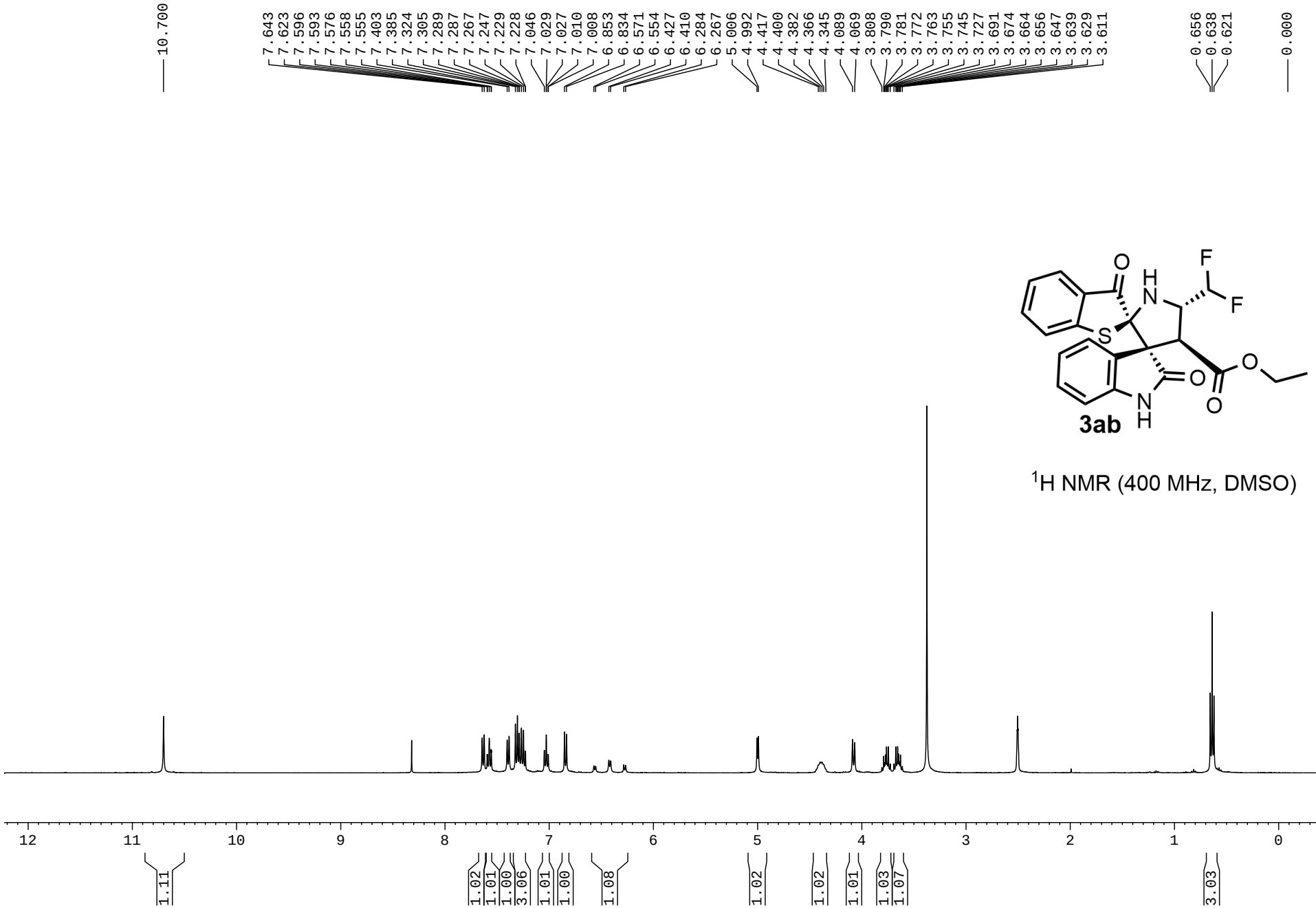

185.81
161.59
142.55
140.49
136.95
131.02
129.35
125.54
117.11
114.72
112.32
60.52
60.25
59.98
18.68
18.51
117.11
114.72
112.32
116
114
ppm
O
N
S
CF2H
1k
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

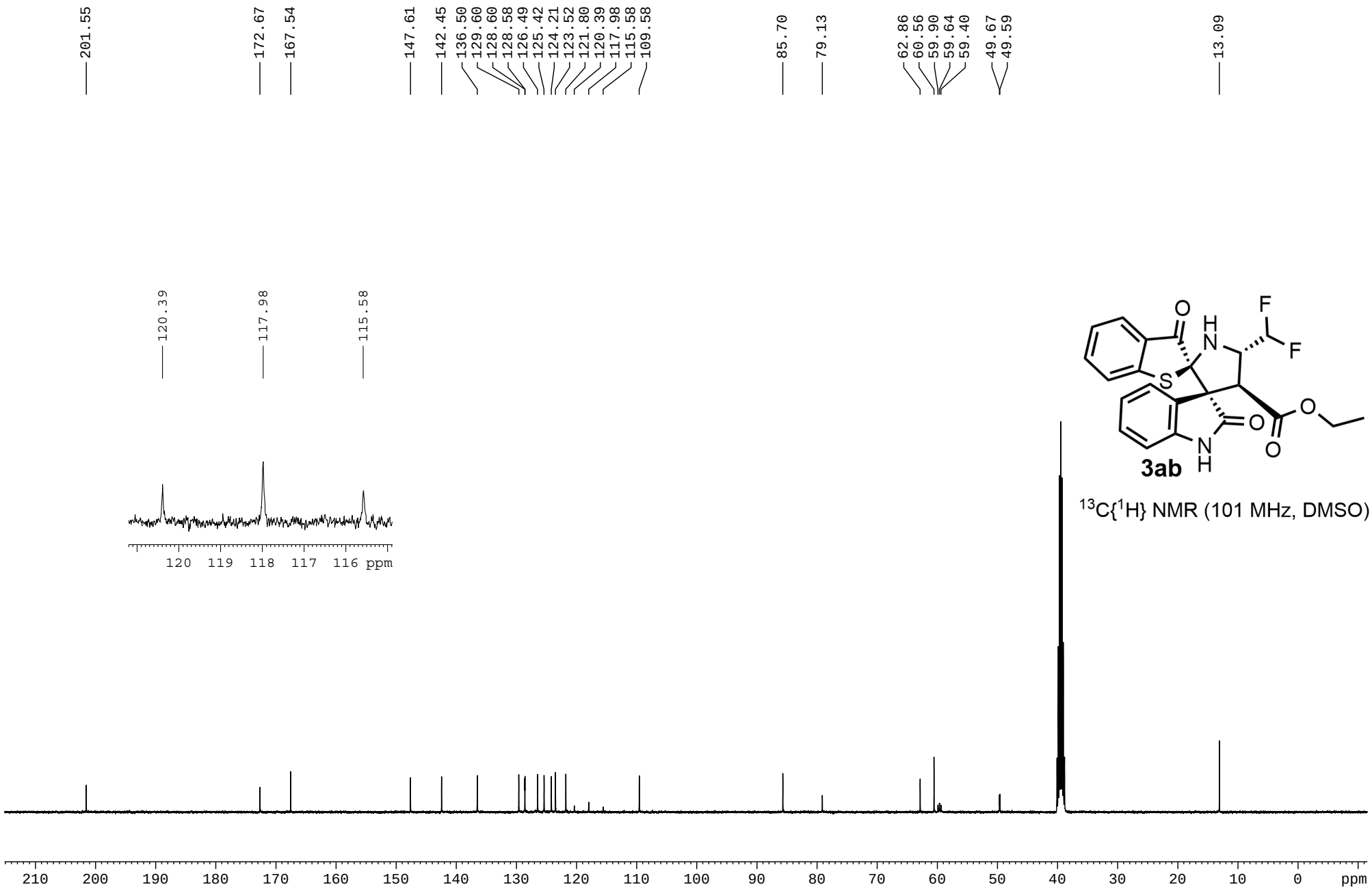

-120.487
O
N
S
CF2H
1k
19F NMR (376 MHz, CDCl3)
-115
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

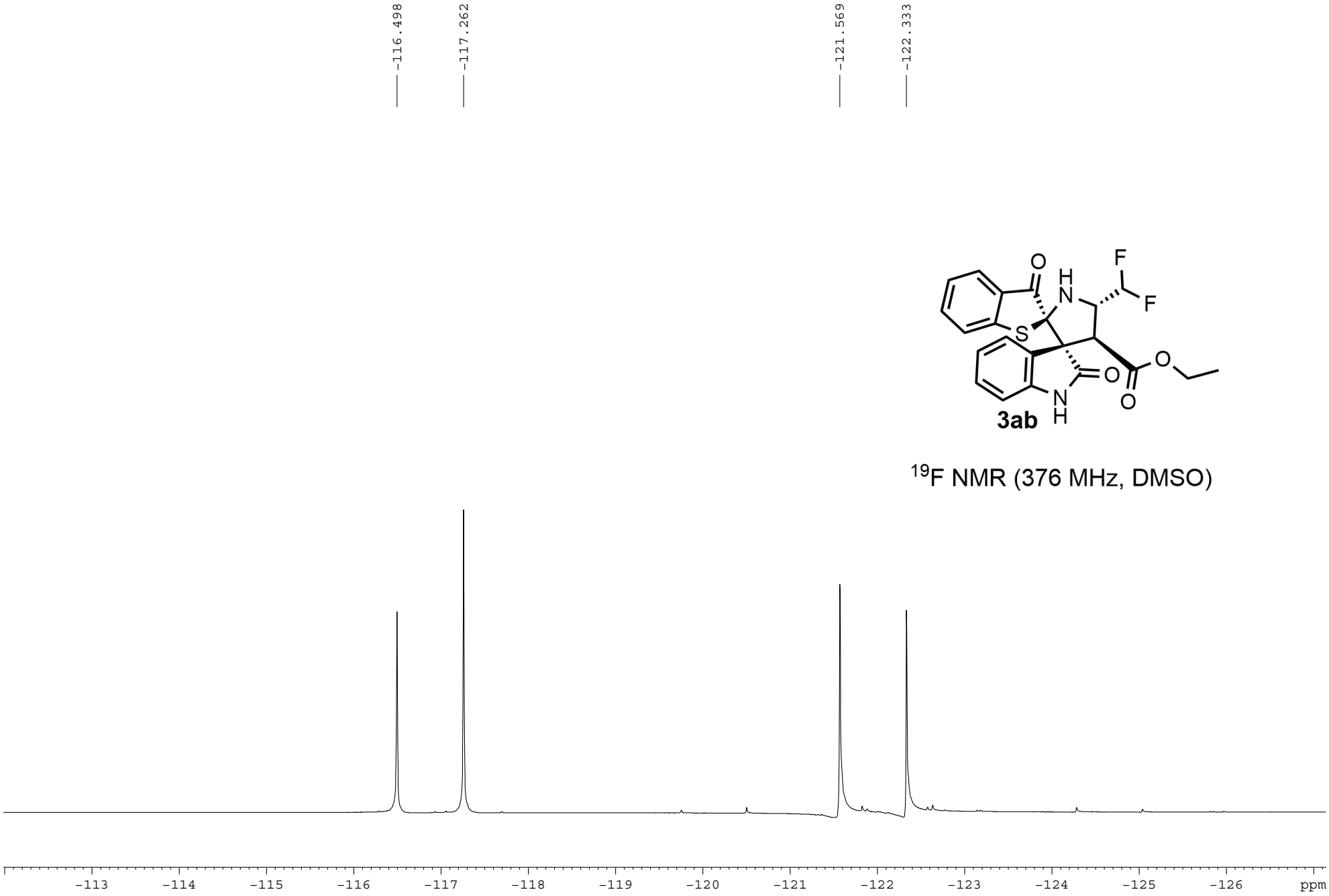

7.742
7.740
7.723
7.721
7.459
7.455
7.437
7.418
7.399
7.396
7.380
7.377
7.188
7.187
7.169
7.157
7.156
7.151
7.149
7.138
7.137
7.120
7.118
7.016
6.997
6.858
6.838
6.742
6.724
6.600
6.596
6.582
6.578
6.455
6.437
4.590
4.583
4.577
4.571
4.560
4.553
4.541
4.534
4.523
4.516
4.511
4.504
4.305
4.285
3.839
3.821
3.812
3.804
3.795
3.786
3.777
3.765
3.759
3.731
3.713
3.704
3.696
3.686
3.678
3.668
3.651
3.102
2.753
0.753
0.736
0.718
-0.000
O
H
N
F
F
S
O
O
O
N
3aa
^{1}H NMR (400 MHz, $CDCl_3$)
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
ppm
1.00
3.05
2.03
1.02
1.00
1.02
1.01
0.99
1.05
1.01
3.05
1.00
3.06

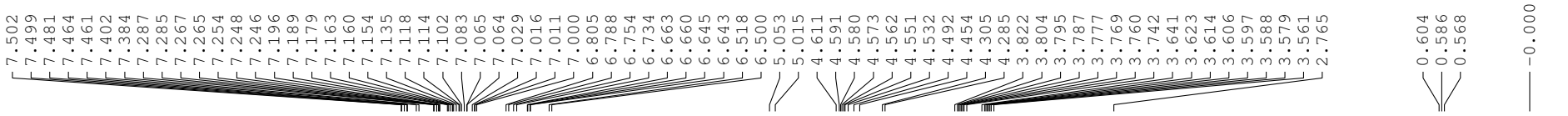

202.39
171.46
167.59
147.80
144.13
136.36
129.94
128.84
128.38
127.28
125.62
124.22
123.22
123.17
119.87
117.48
117.43
115.04
108.06
86.56
62.47
60.98
59.87
59.63
59.59
59.35
49.80
49.72
26.67
13.57
119.87
117.48
117.43
115.04
121
120
119
118
117
116
115
ppm
O
H
N
F
F
S
O
O
O
N
3aa
13C {1H} NMR (101 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

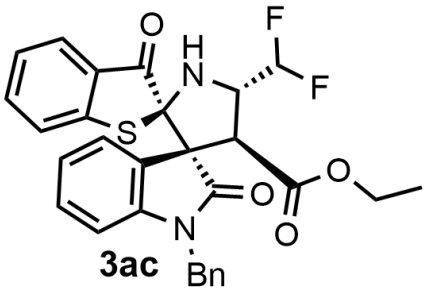

-118.904
-119.692
-122.628
-123.415
O
H
N
F
F
S
O
O
O
N
3aa
^{19}F NMR (376 MHz, $CDCl_3$)
-114
-115
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
-127
ppm


10.700
7.643
7.623
7.596
7.593
7.576
7.558
7.555
7.403
7.385
7.324
7.305
7.289
7.287
7.267
7.247
7.229
7.228
7.046
7.029
7.027
7.010
7.008
6.853
6.834
6.571
6.554
6.427
6.410
6.284
6.267
5.006
4.992
4.417
4.400
4.382
4.366
4.345
4.089
4.069
3.808
3.790
3.781
3.772
3.763
3.755
3.745
3.727
3.691
3.674
3.664
3.656
3.647
3.639
3.629
3.611
0.656
0.638
0.621
0.000
O
H
N
F
F
S
O
O
O
N
H
3ab
1H NMR (400 MHz, DMSO)
12
11
10
9
8
7
6
5
4
3
2
1
0
ppm
1.11
1.02
1.01
1.00
3.06
1.01
1.00
1.08
1.02
1.02
1.01
1.03
1.07
3.03


201.55
172.67
167.54
147.61
142.45
136.50
129.60
128.60
128.58
126.49
125.42
124.21
123.52
121.80
120.39
117.98
115.58
109.58
85.70
79.13
62.86
60.56
59.90
59.64
59.40
49.67
49.59
13.09
120.39
117.98
115.58
120 119 118 117 116 ppm
3ab
13C{1H} NMR (101 MHz, DMSO)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

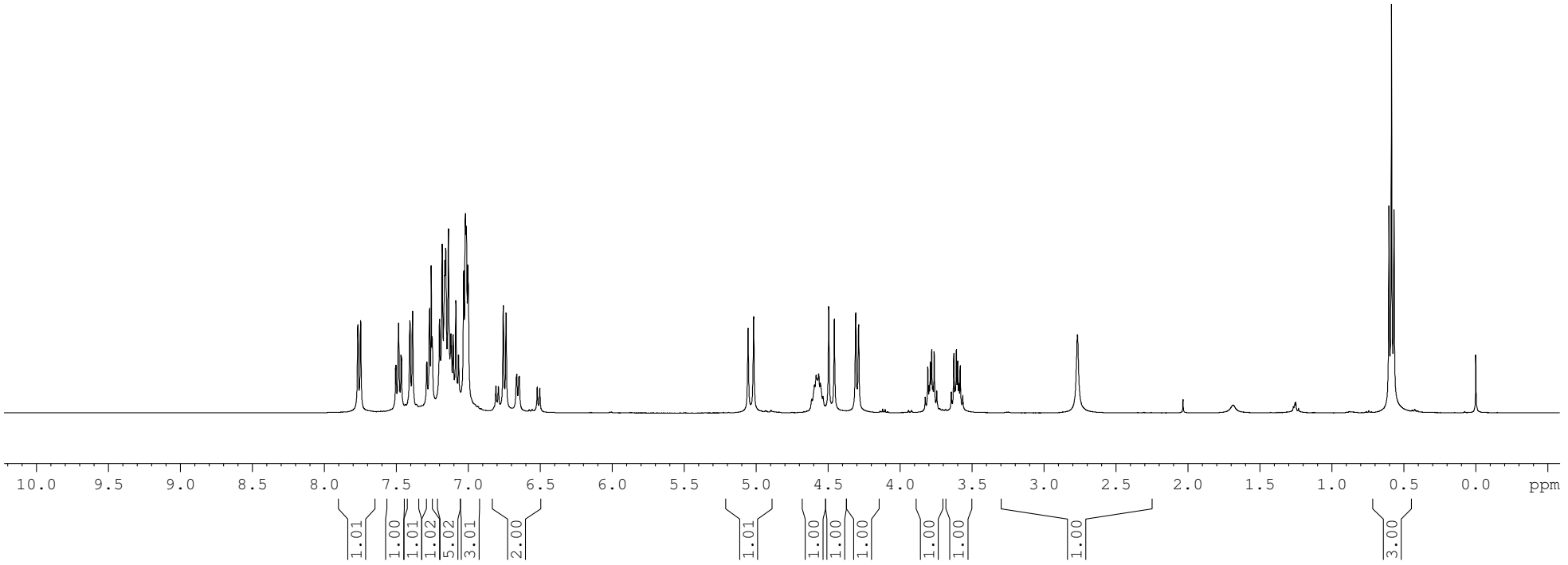

-116.498
-117.262
-121.569
-122.333
O
H
N
F
F
S
O
O
O
N
H
3ab
^{19}F NMR (376 MHz, DMSO)
-113
-114
-115
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

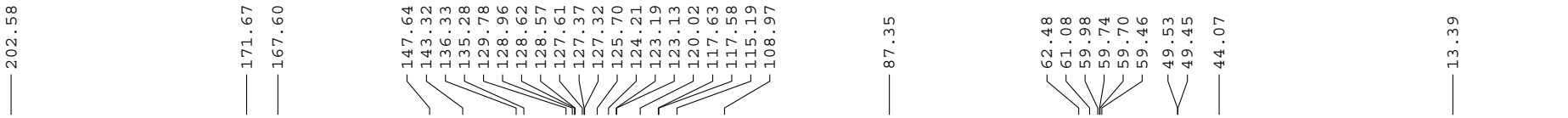


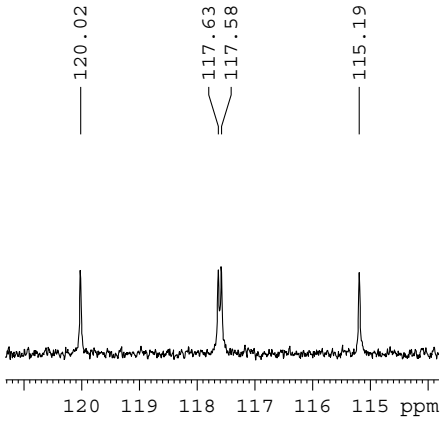


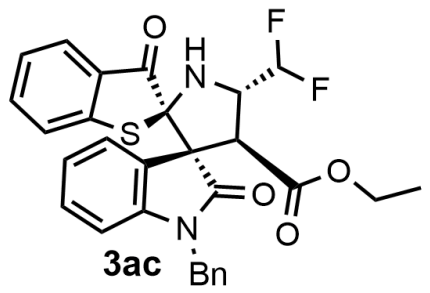
3ac

^{1}H NMR (400 MHz, $CDCl_3$)



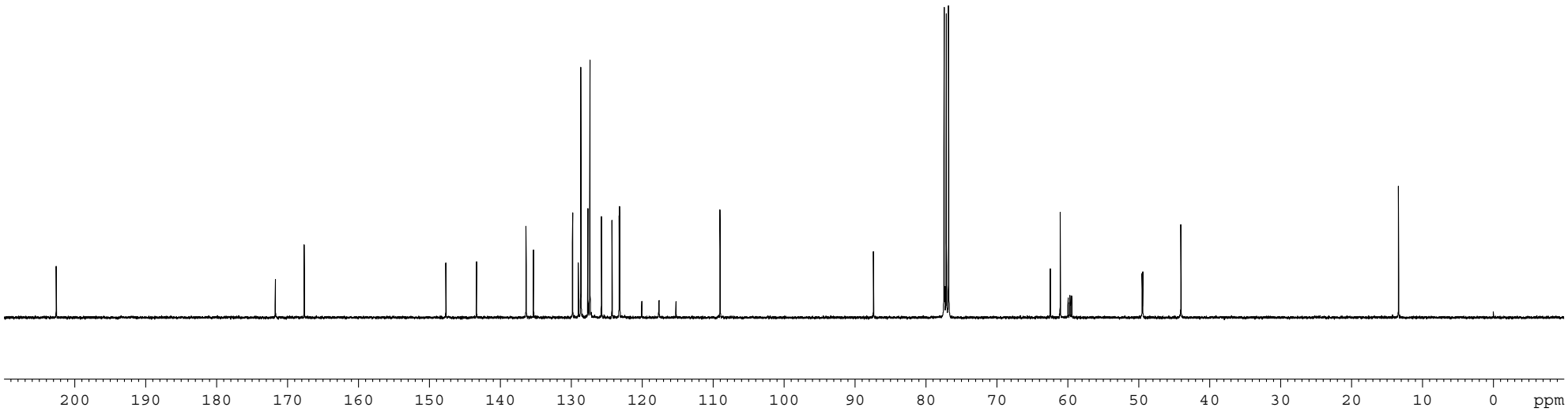


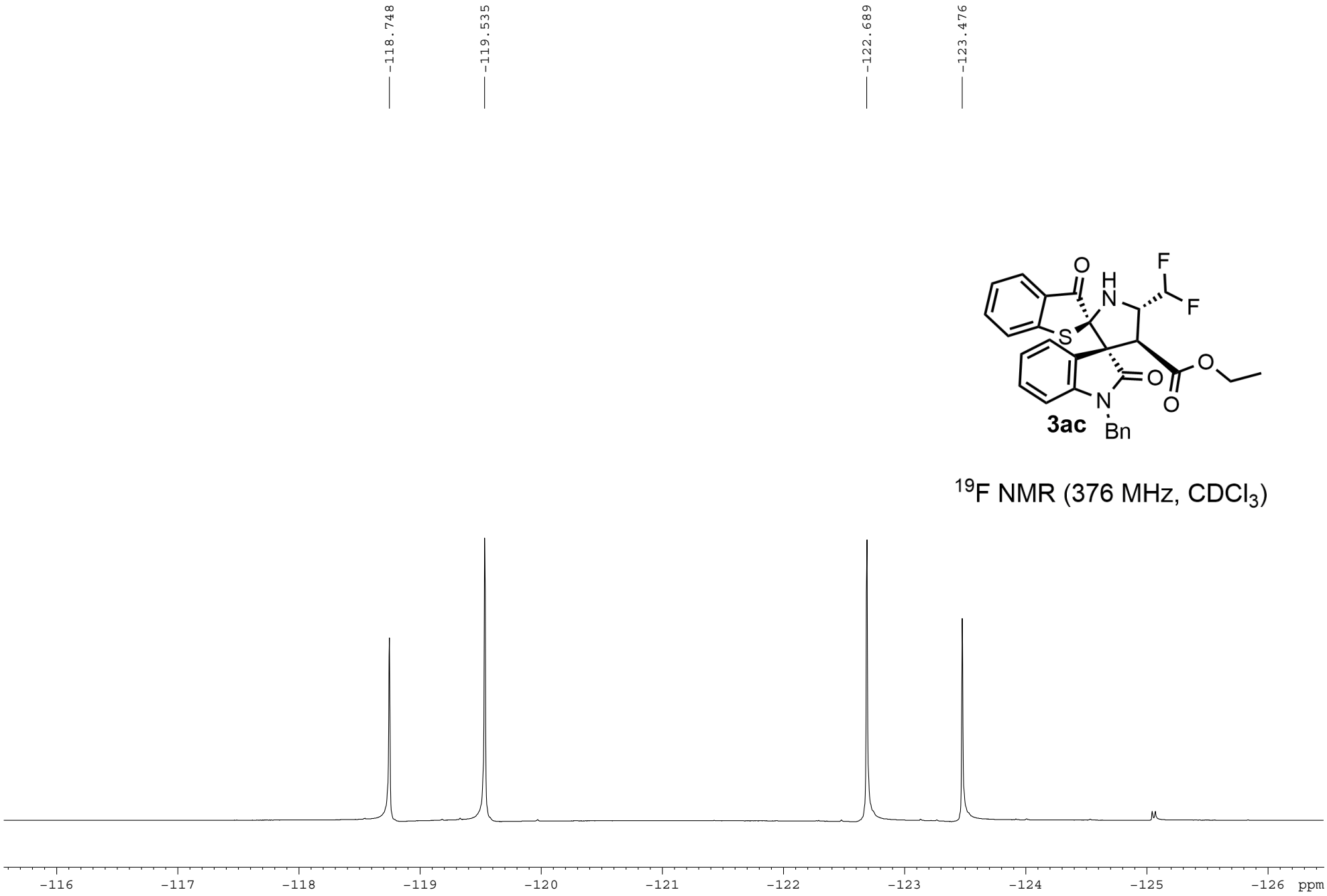


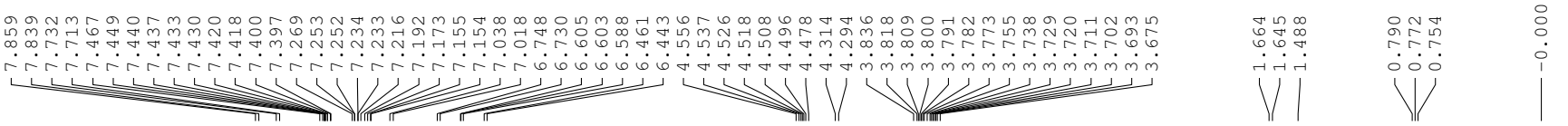


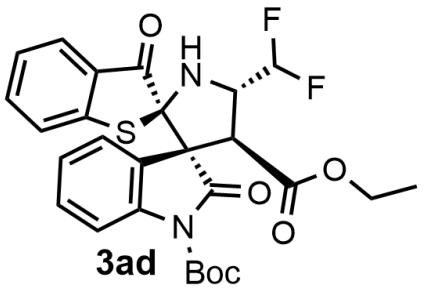
3ac

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)



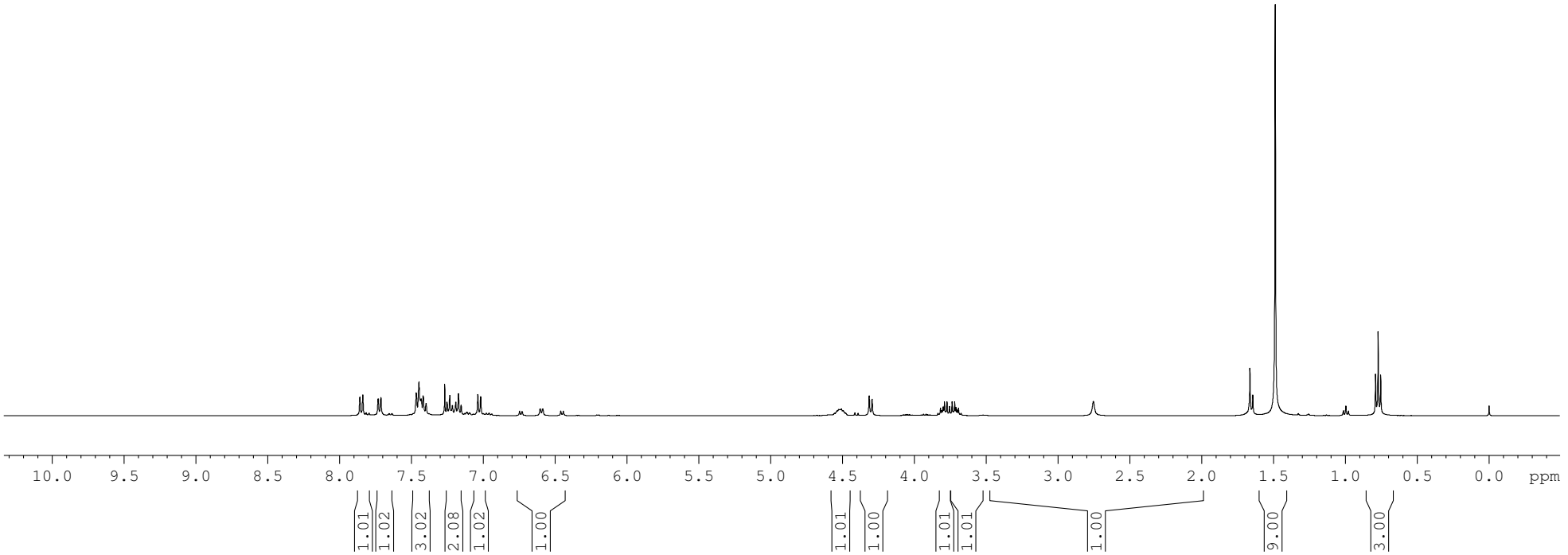

-118.748
-119.535
-122.689
-123.476
O
H
N
F
F
S
O
O
O
N
Bn
3ac
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

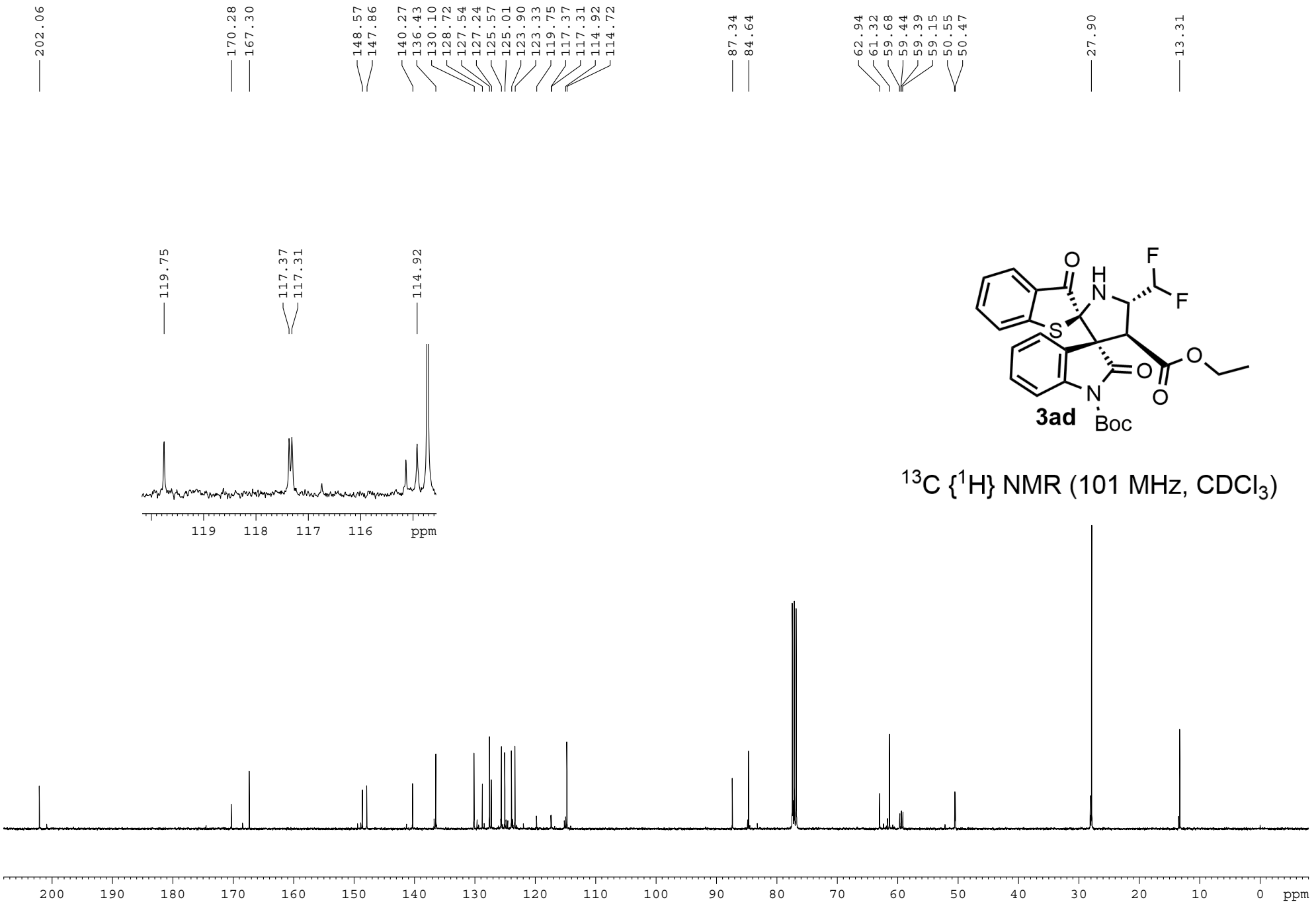


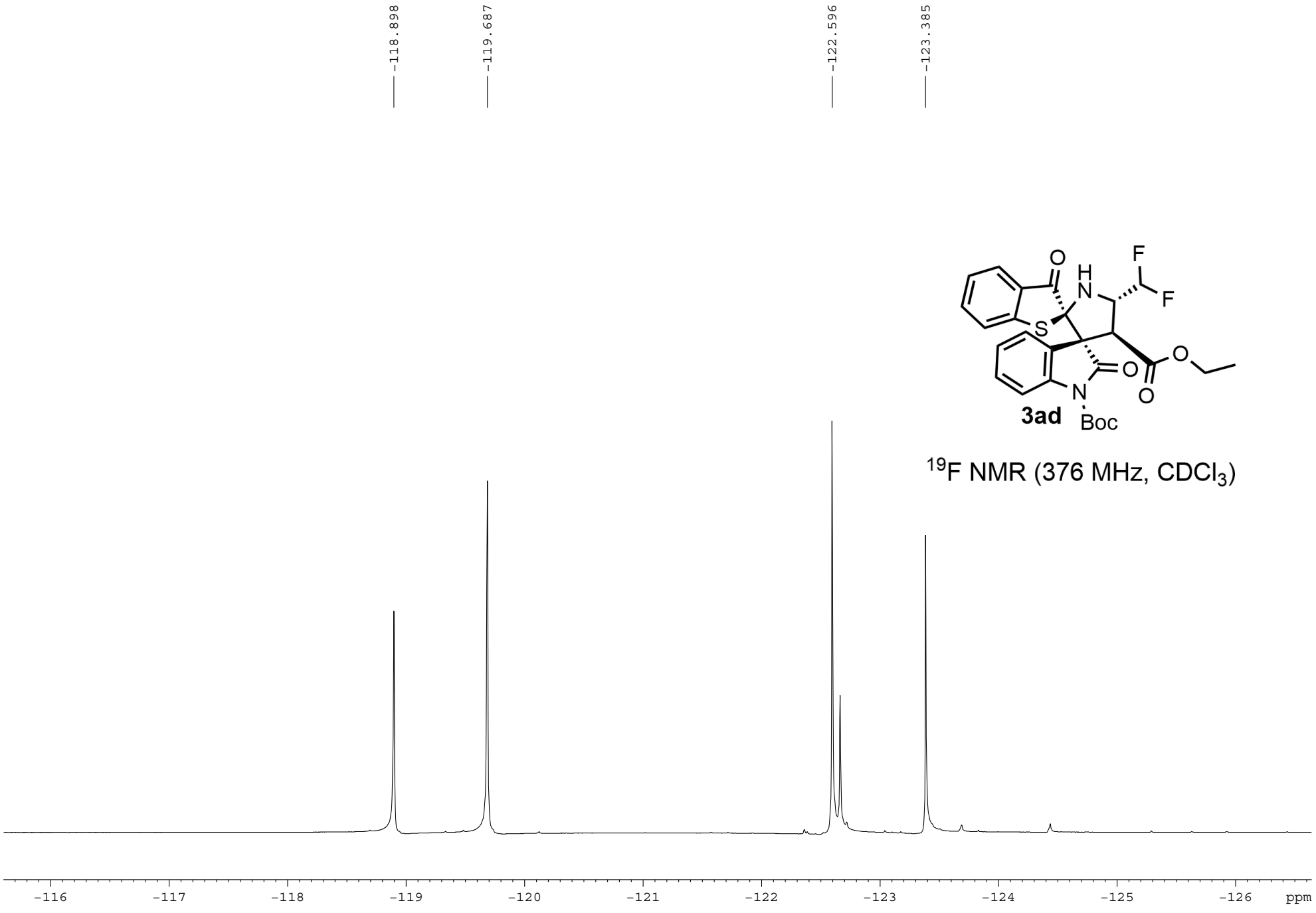


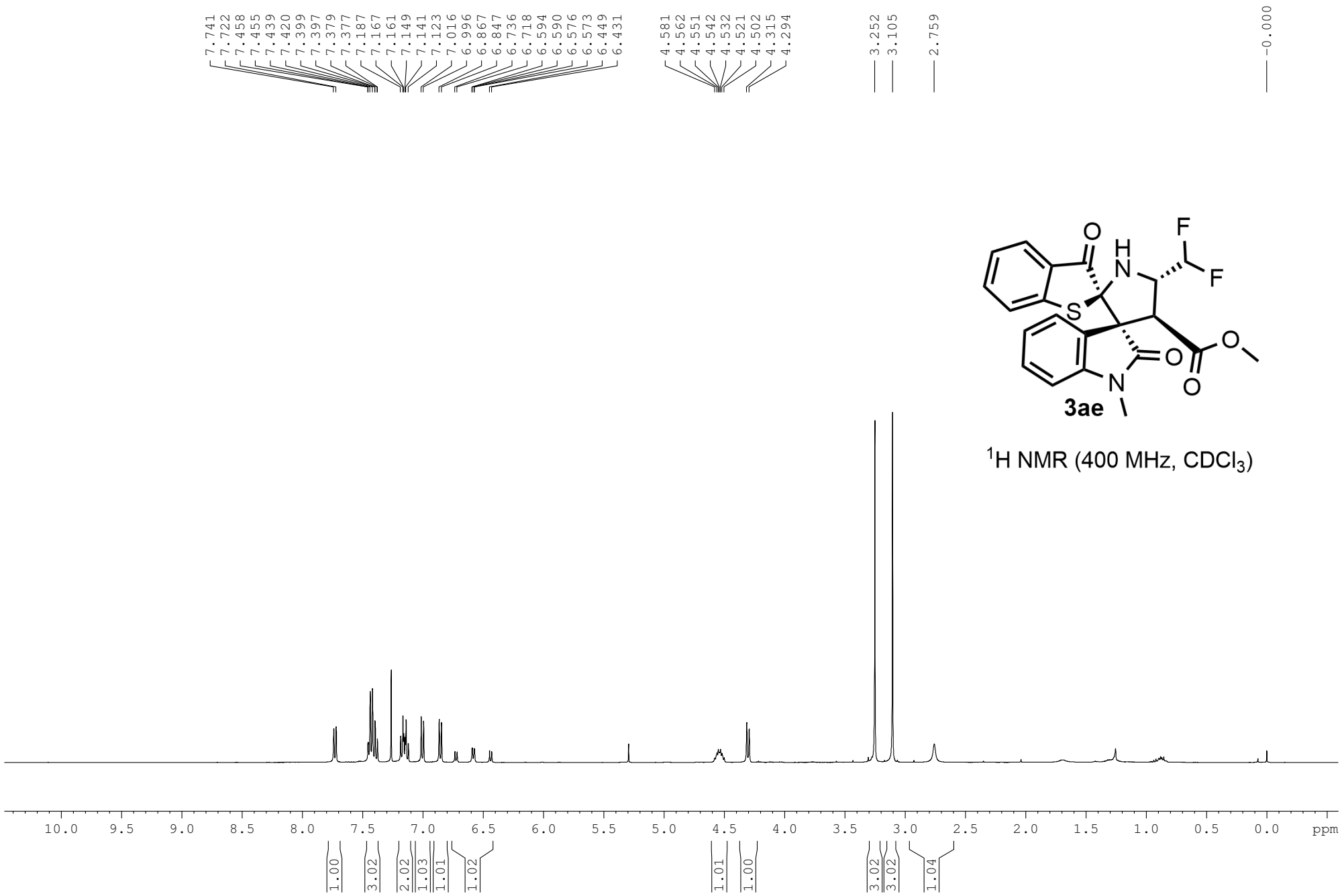
3ad

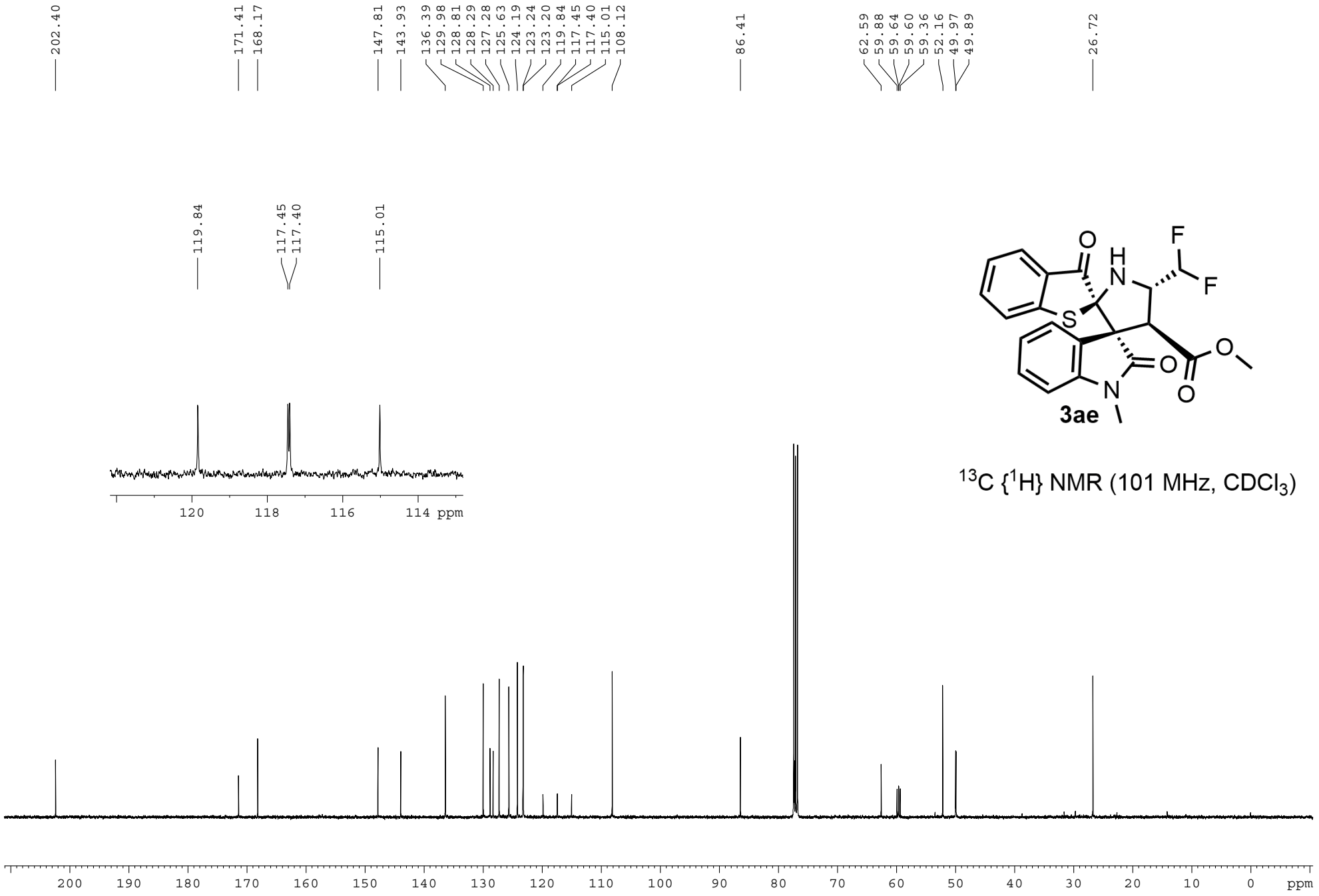
^{1}H NMR (400 MHz, $CDCl_3$)

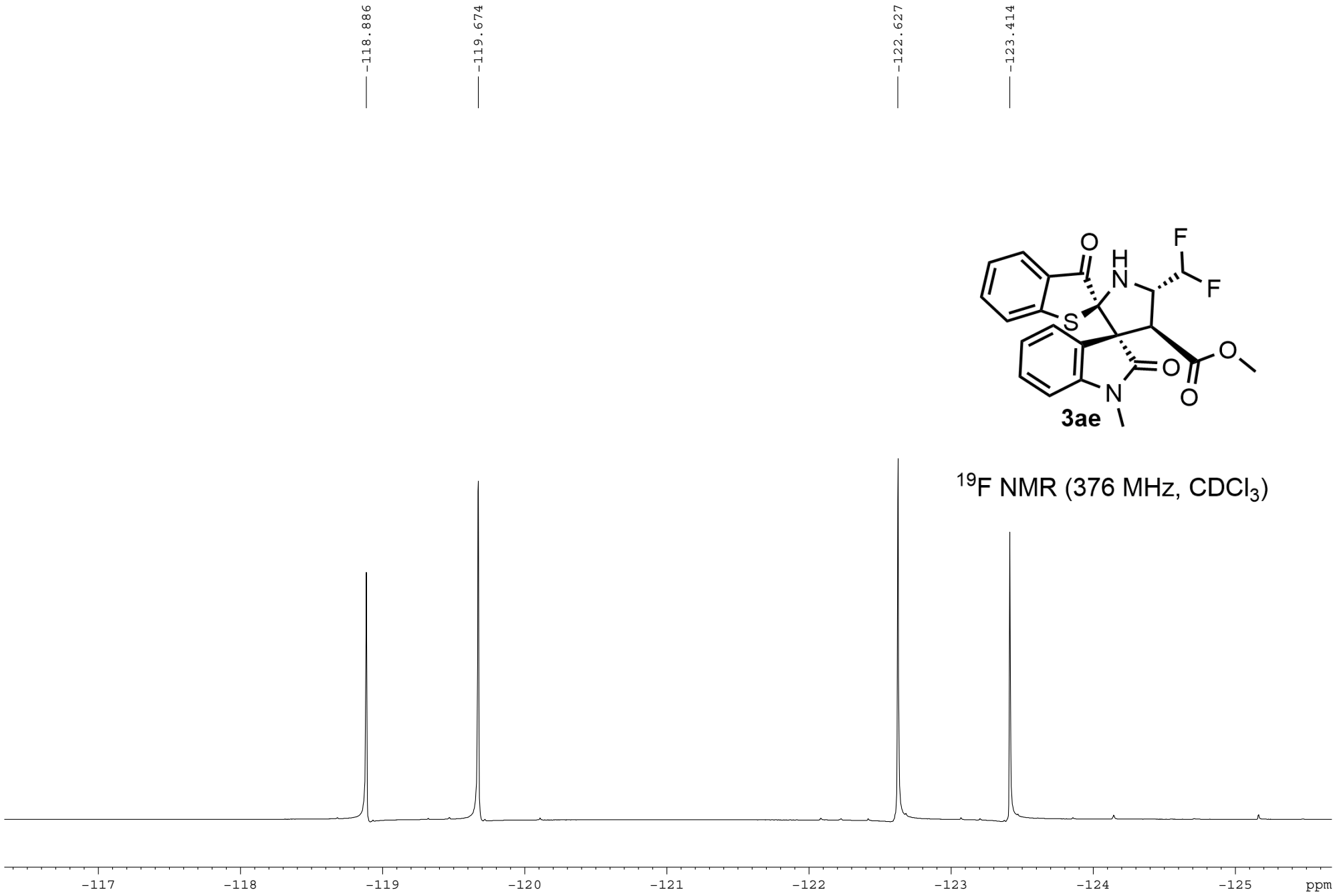


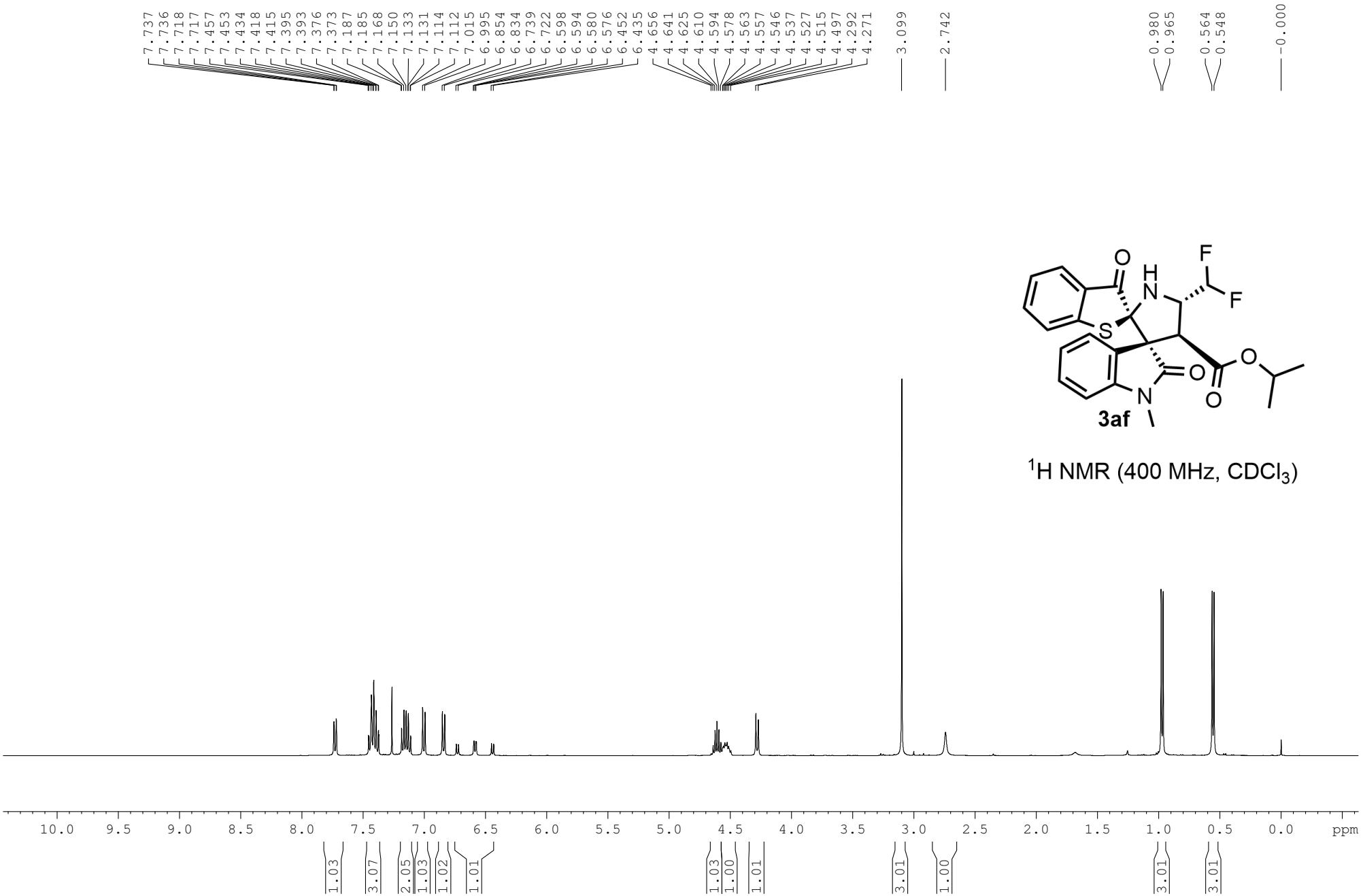

202.06
170.28
167.30
148.57
147.86
140.27
136.43
130.10
128.72
127.54
127.24
125.57
125.01
123.90
123.33
119.75
117.37
117.31
114.92
114.72
87.34
84.64
62.94
61.32
59.68
59.44
59.39
59.15
50.55
50.47
27.90
13.31
119.75
117.37
117.31
114.92
119
118
117
116
ppm
O
H
N
F
F
S
O
O
O
N
Boc
3ad
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

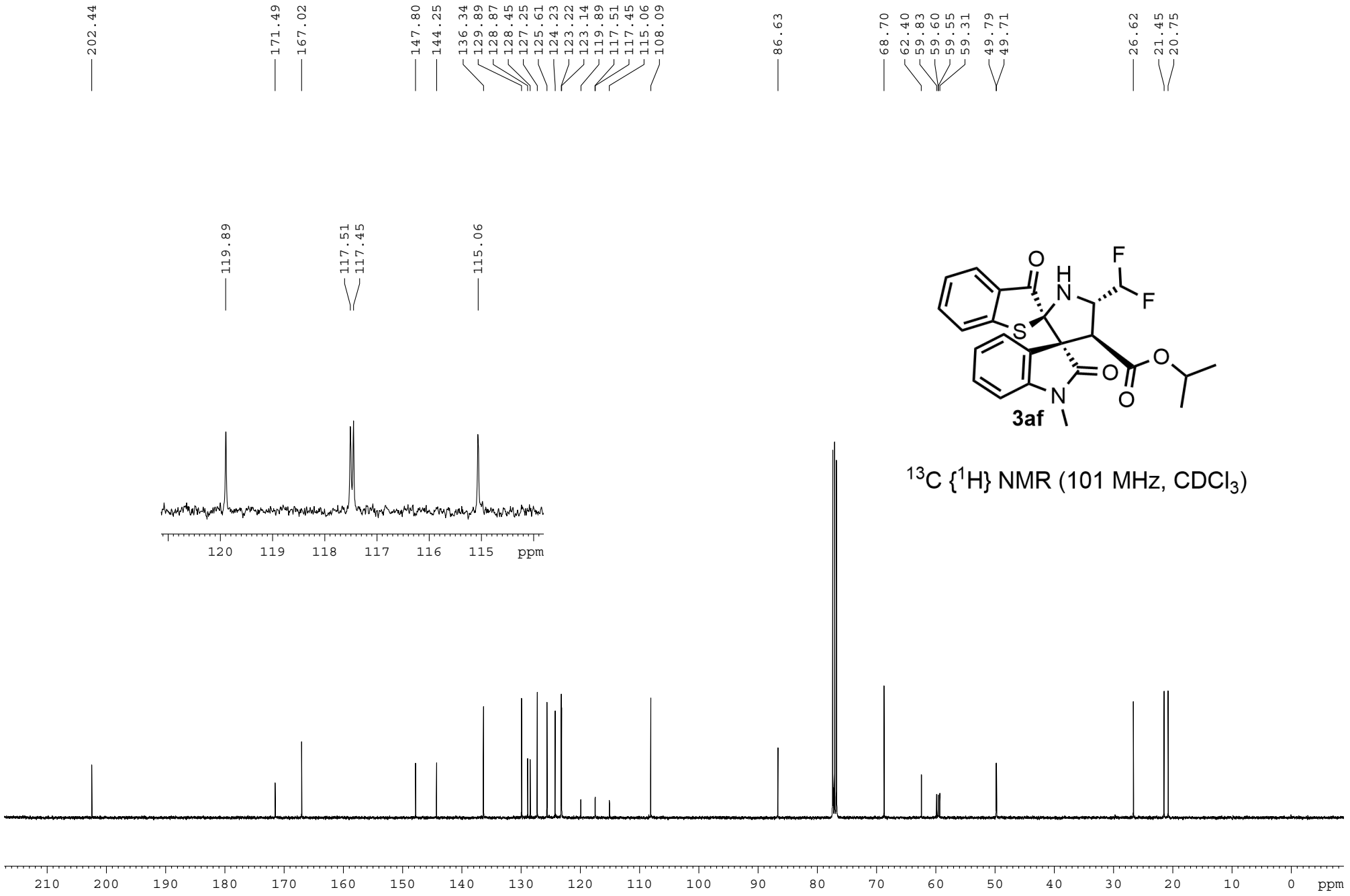

-118.898
-119.687
-122.596
-123.385
O
H
N
F
F
S
O
O
O
N
Boc
3ad
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

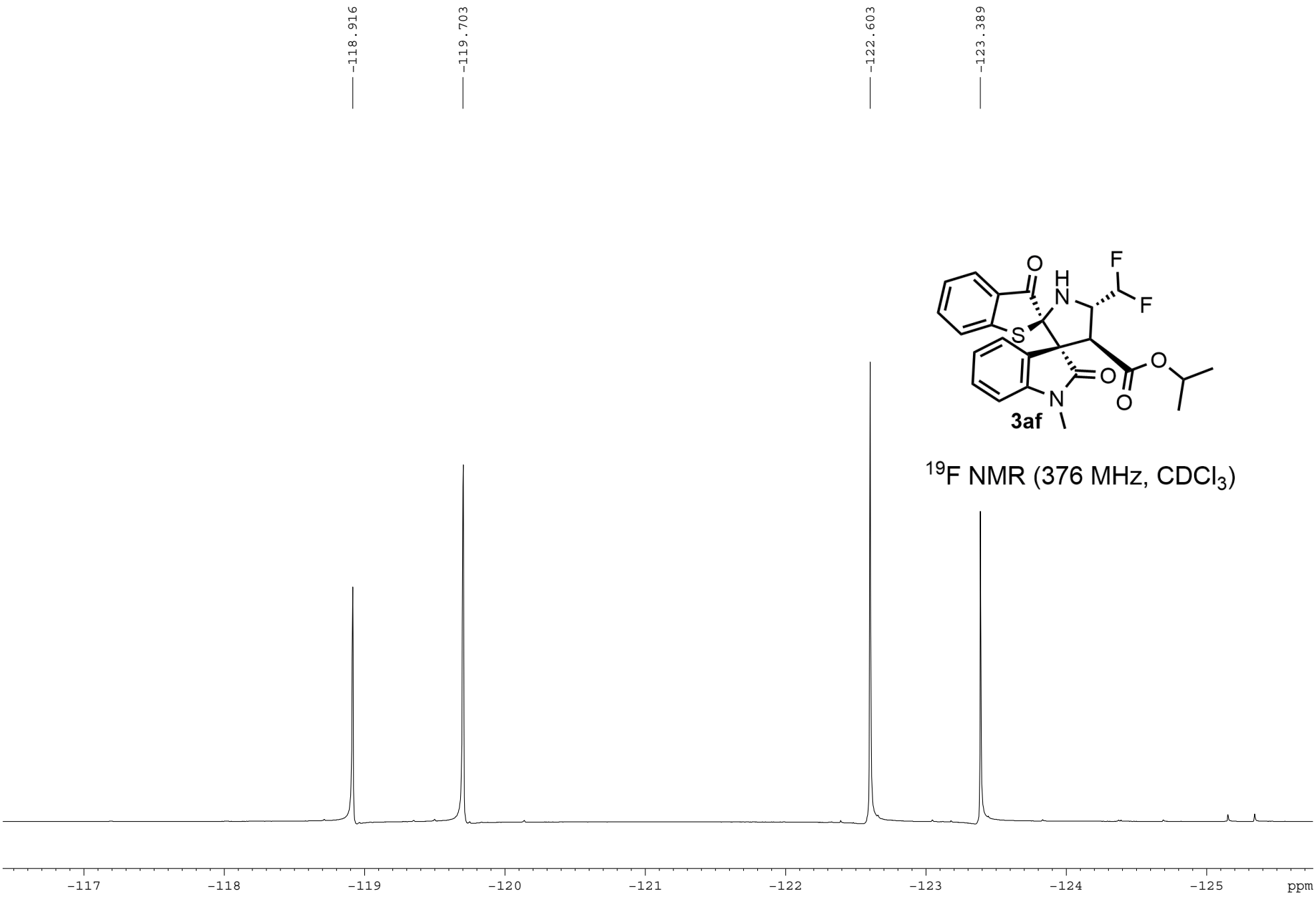

7.741
7.722
7.458
7.455
7.439
7.420
7.399
7.397
7.379
7.377
7.187
7.167
7.161
7.149
7.141
7.123
7.016
6.996
6.867
6.847
6.736
6.718
6.594
6.590
6.576
6.573
6.449
6.431
4.581
4.562
4.551
4.542
4.532
4.521
4.502
4.315
4.294
3.252
3.105
2.759
0.000
O
H
N
F
F
S
O
O
O
N
3ae
^{1}H NMR (400 MHz, $CDCl_3$)
10.0
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
ppm
1.00
3.02
2.02
1.03
1.01
1.02
1.01
1.00
3.02
3.02
1.04

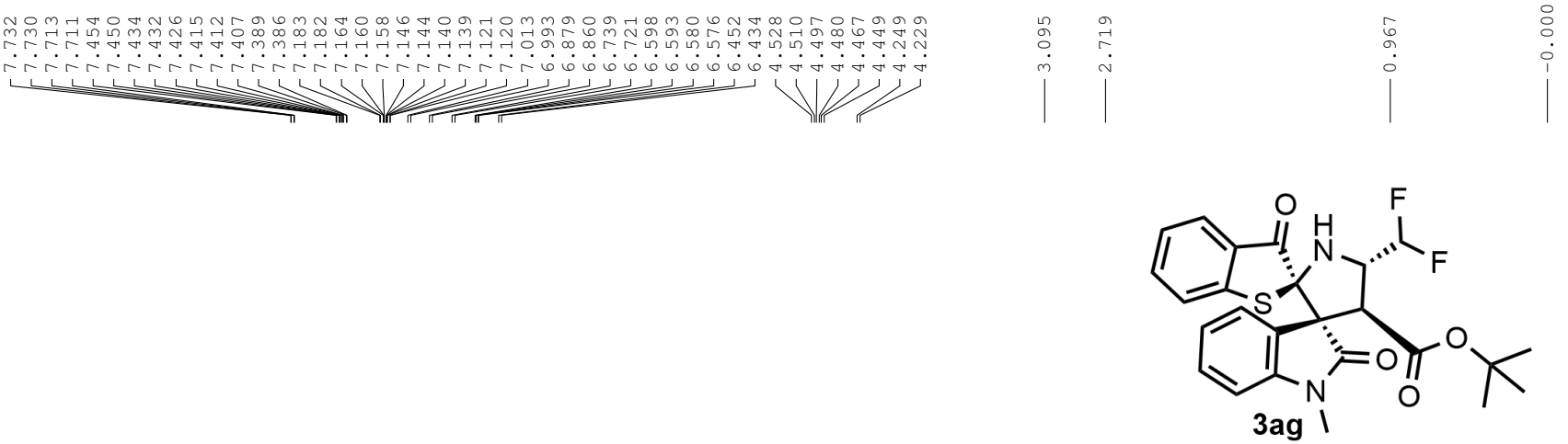

202.40
171.41
168.17
147.81
143.93
136.39
129.98
128.81
128.29
127.28
125.63
124.19
123.24
123.20
119.84
117.45
117.40
115.01
108.12
86.41
62.59
59.88
59.64
59.60
59.36
52.16
49.97
49.89
26.72
119.84
117.45
117.40
115.01
120
118
116
114 ppm
O
H
N
F
F
S
O
O
O
N
3ae
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


-118.886
-119.674
-122.627
-123.414
O
H
N
F
F
S
O
O
O
N
3ae
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
ppm

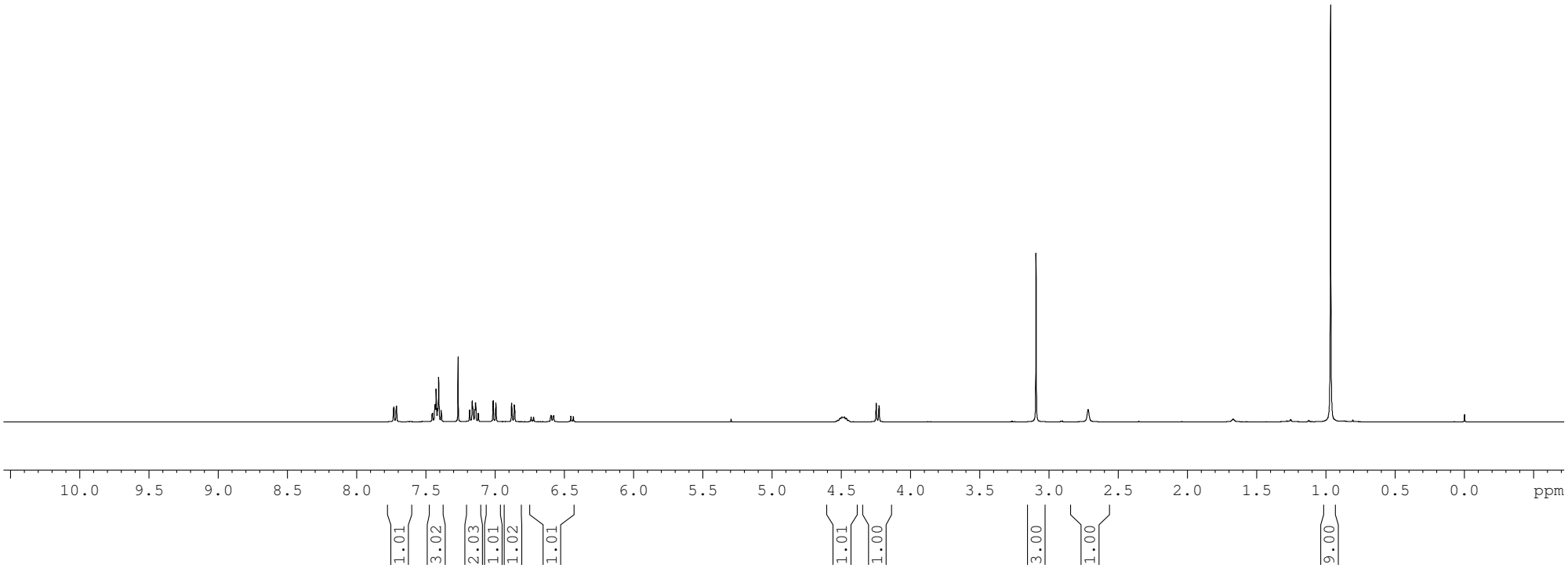

7.737
7.736
7.718
7.717
7.457
7.453
7.434
7.418
7.415
7.395
7.393
7.376
7.373
7.187
7.185
7.168
7.150
7.133
7.131
7.114
7.112
7.015
6.995
6.854
6.834
6.739
6.722
6.598
6.594
6.580
6.576
6.452
6.435
4.656
4.641
4.625
4.610
4.594
4.578
4.563
4.557
4.546
4.537
4.527
4.515
4.497
4.292
4.271
3.099
2.742
0.980
0.965
0.564
0.548
-0.000
O
H
N
F
F
S
O
O
O
N
3af
1H NMR (400 MHz, CDCl3)
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
ppm
1.03
3.07
2.05
1.03
1.02
1.01
1.03
1.00
1.01
3.01
1.00
3.01
3.01

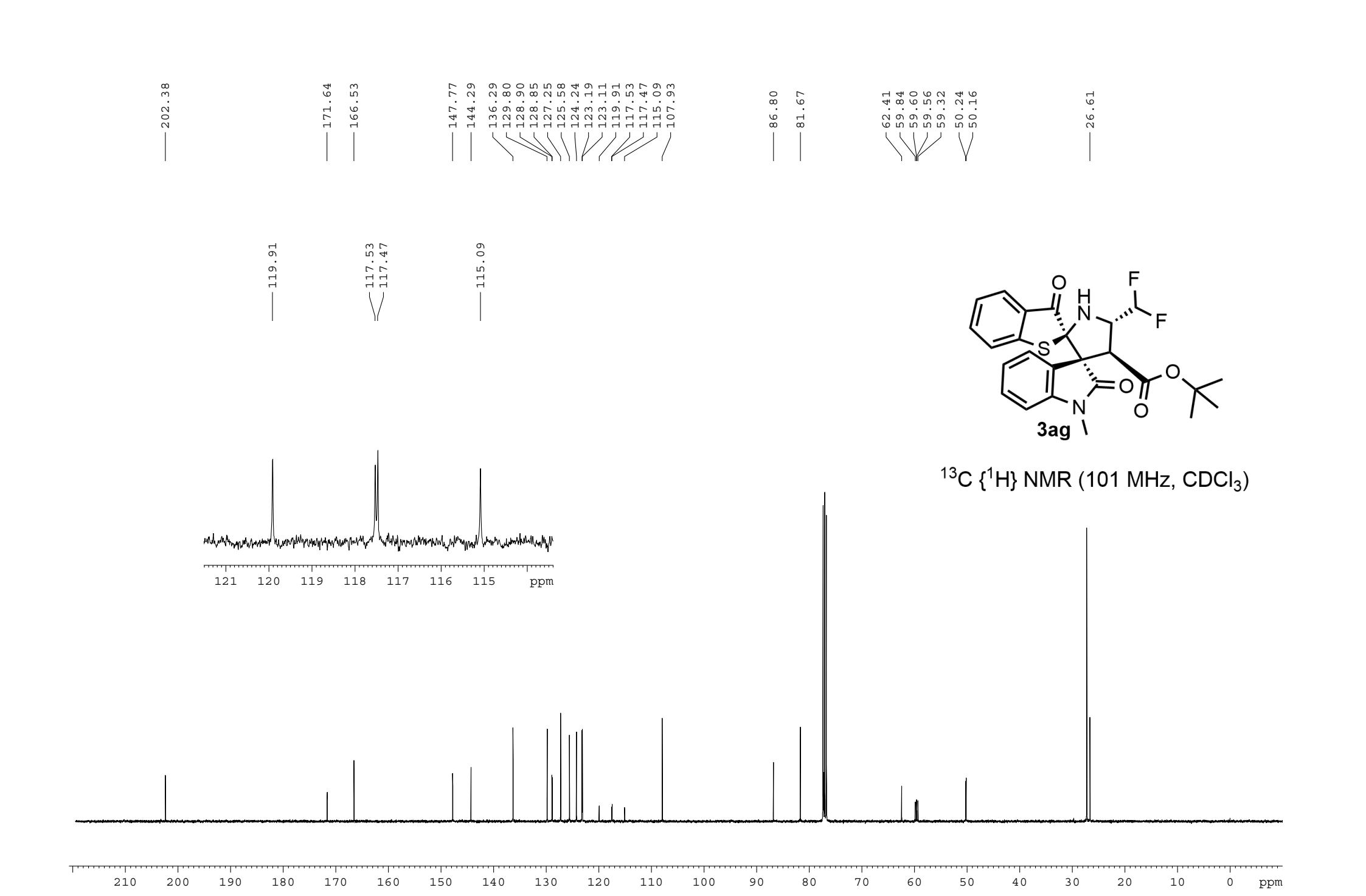

202.44
171.49
167.02
147.80
144.25
136.34
129.89
128.87
128.45
127.25
125.61
124.23
123.22
123.14
119.89
117.51
117.45
115.06
108.09
86.63
68.70
62.40
59.83
59.60
59.55
59.31
49.79
49.71
26.62
21.45
20.75
119.89
117.51
117.45
115.06
120
119
118
117
116
115
ppm
O
H
N
F
F
S
O
O
O
N
O
3af
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

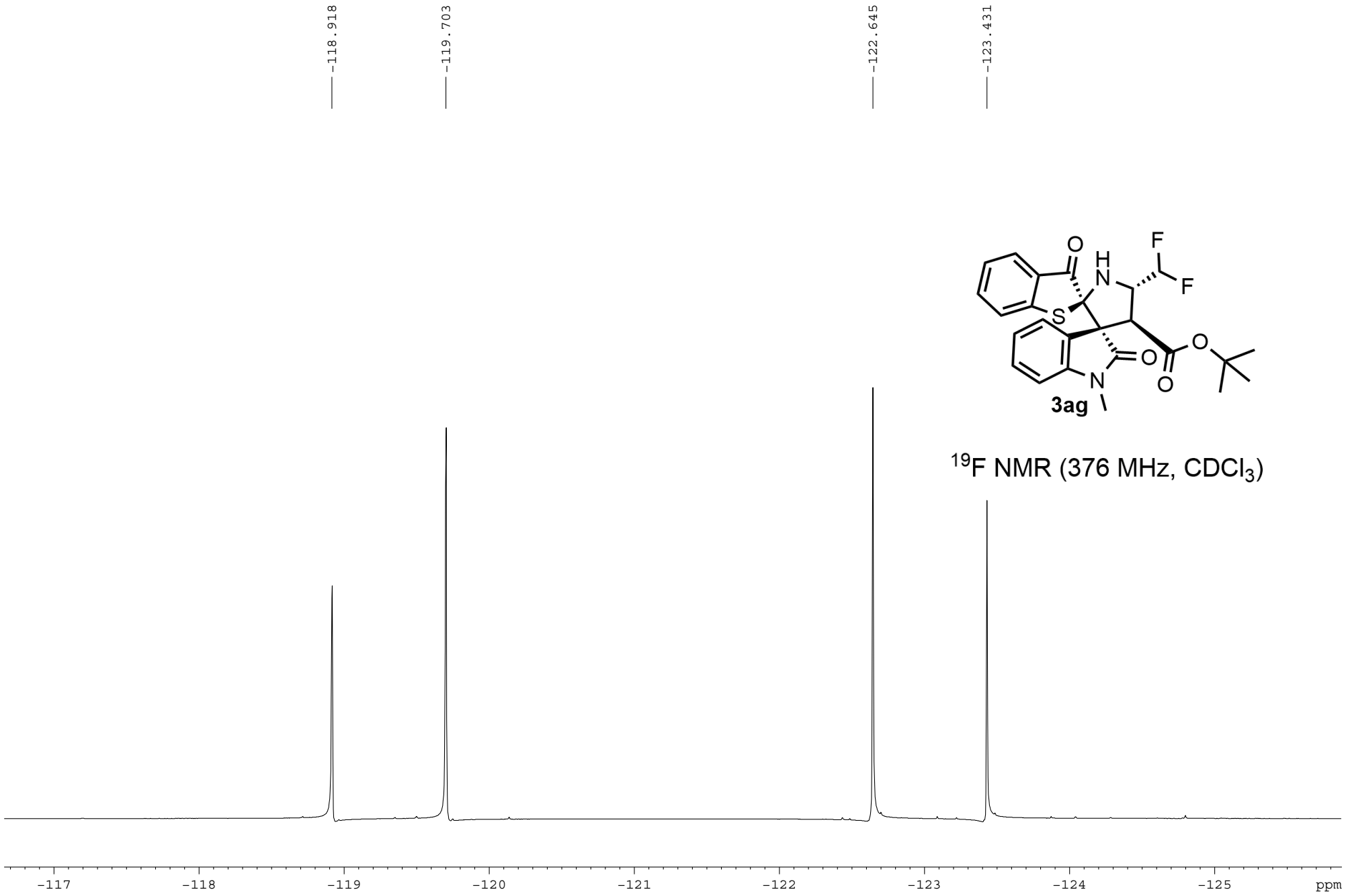

-118.916
-119.703
-122.603
-123.389
O
H
N
F
F
S
O
O
O
N
3af
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
ppm

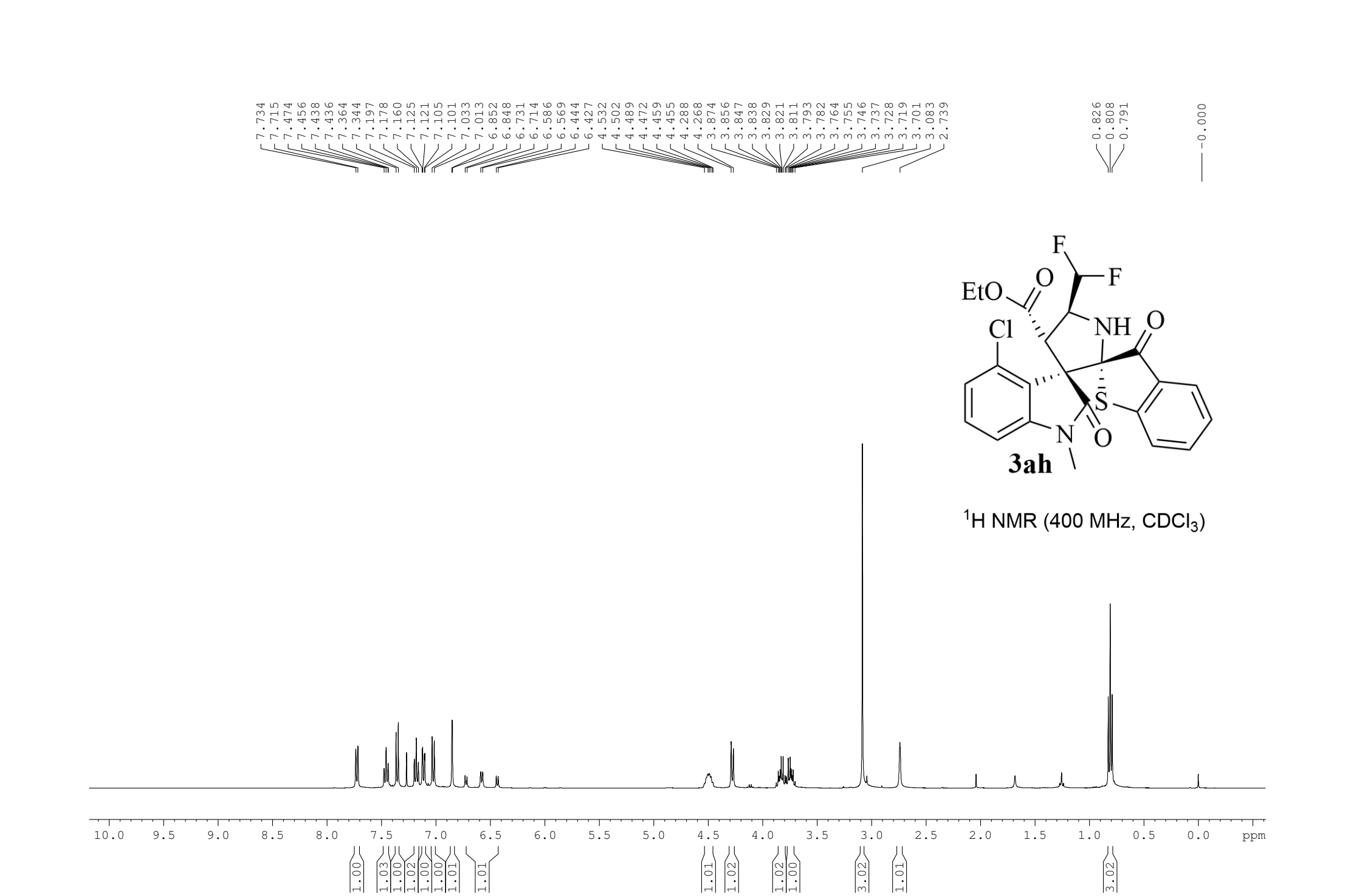


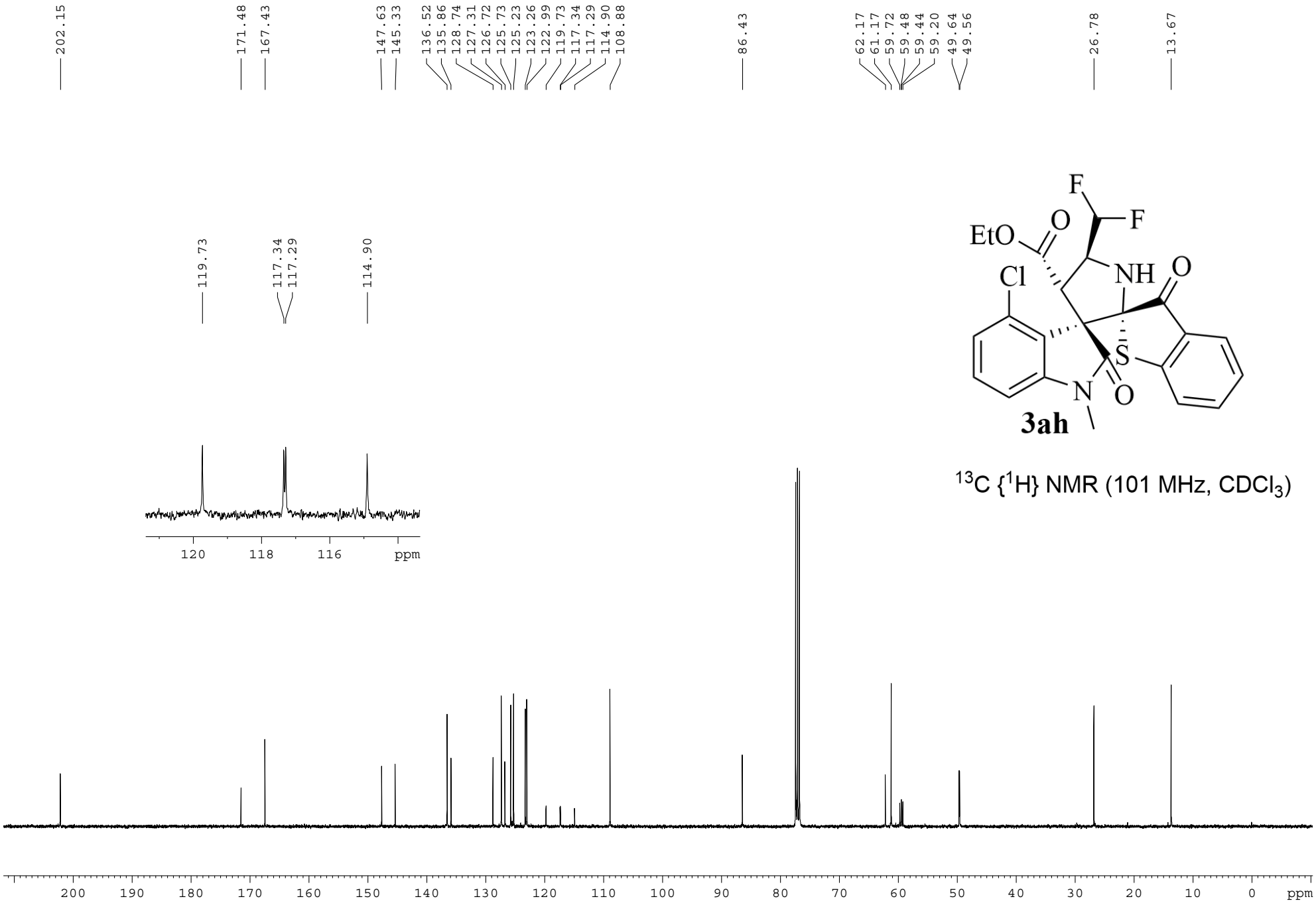
^{1}H NMR (400 MHz, $CDCl_3$)

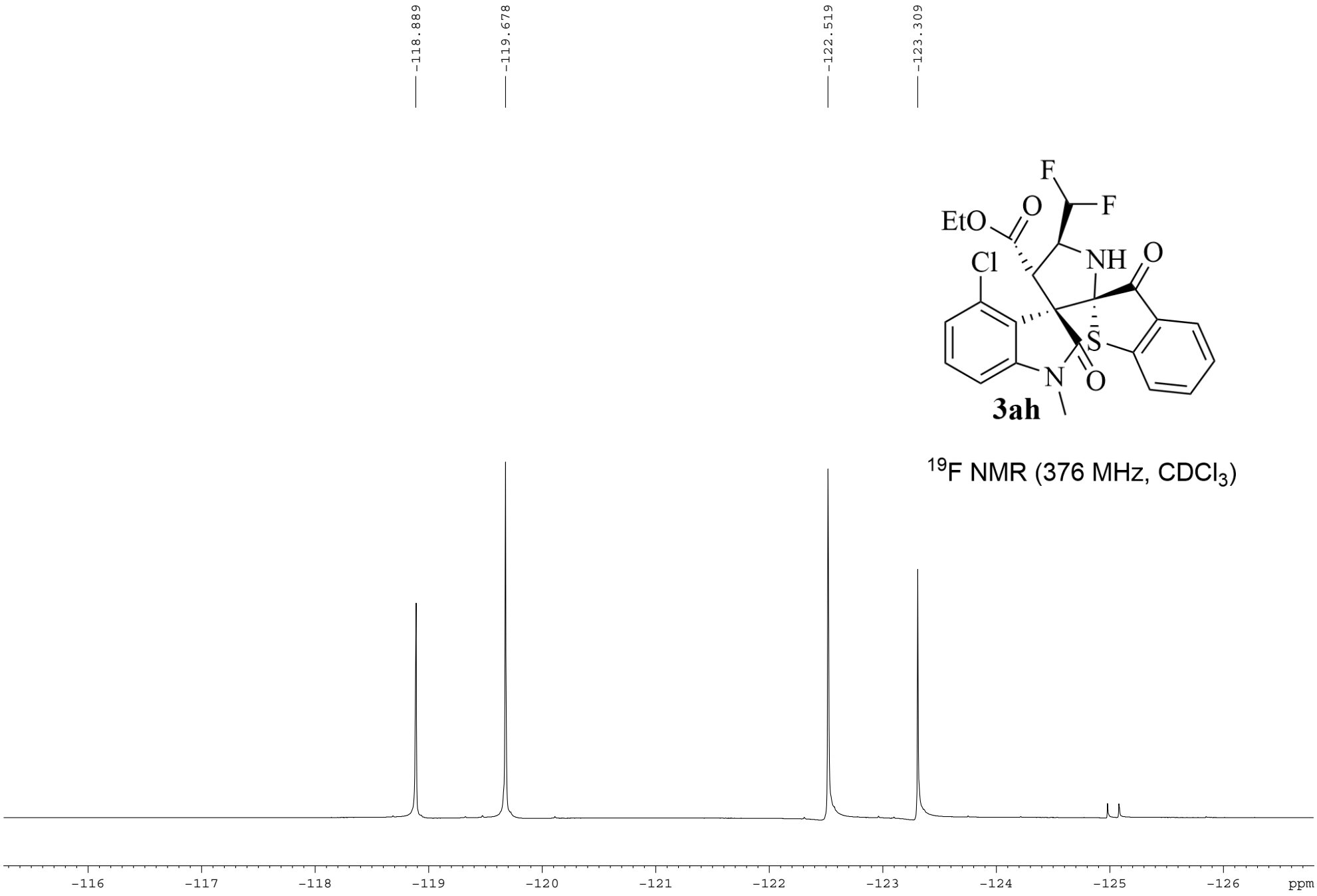


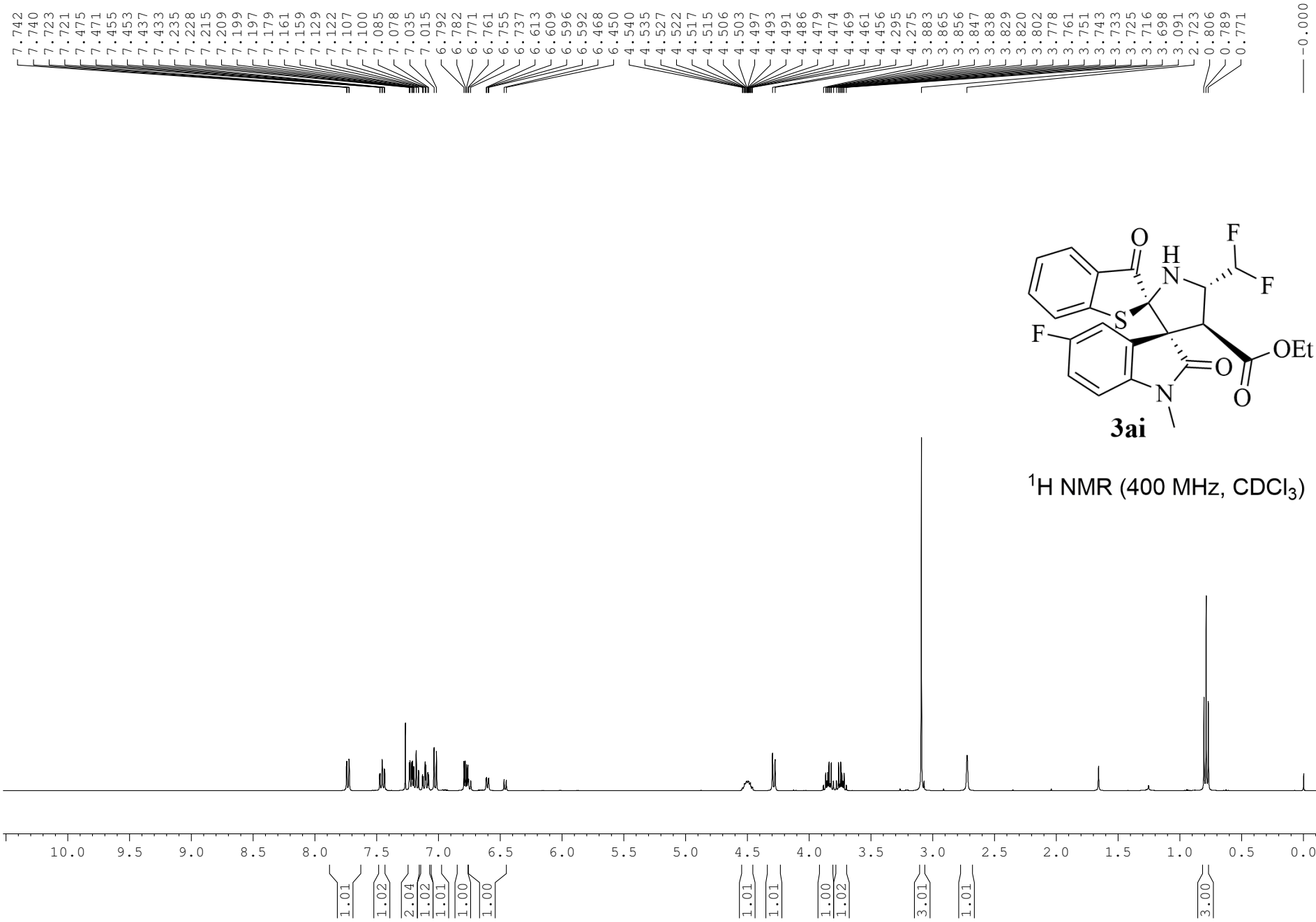

202.38
171.64
166.53
147.77
144.29
136.29
129.80
128.90
128.85
127.25
125.58
124.24
123.19
123.11
119.91
117.53
117.47
115.09
107.93
86.80
81.67
62.41
59.84
59.60
59.56
59.32
50.24
50.16
26.61
119.91
117.53
117.47
115.09
121 120 119 118 117 116 115 ppm
O
H
N
F
F
S
O
O
O
N
3ag
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

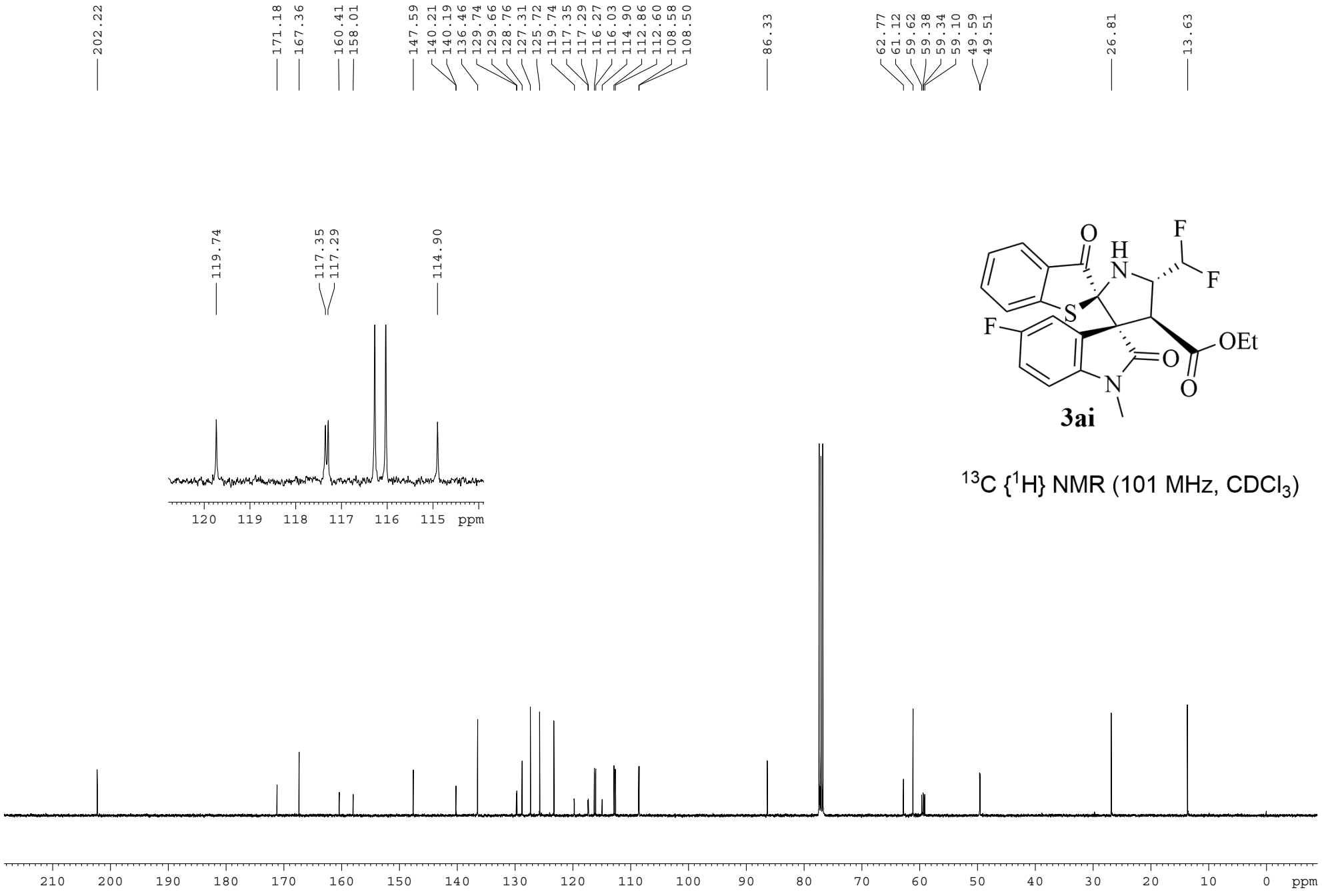

-118.918
-119.703
-122.645
-123.431
O
H
N
F
F
S
O
O
O
N
3ag
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
ppm

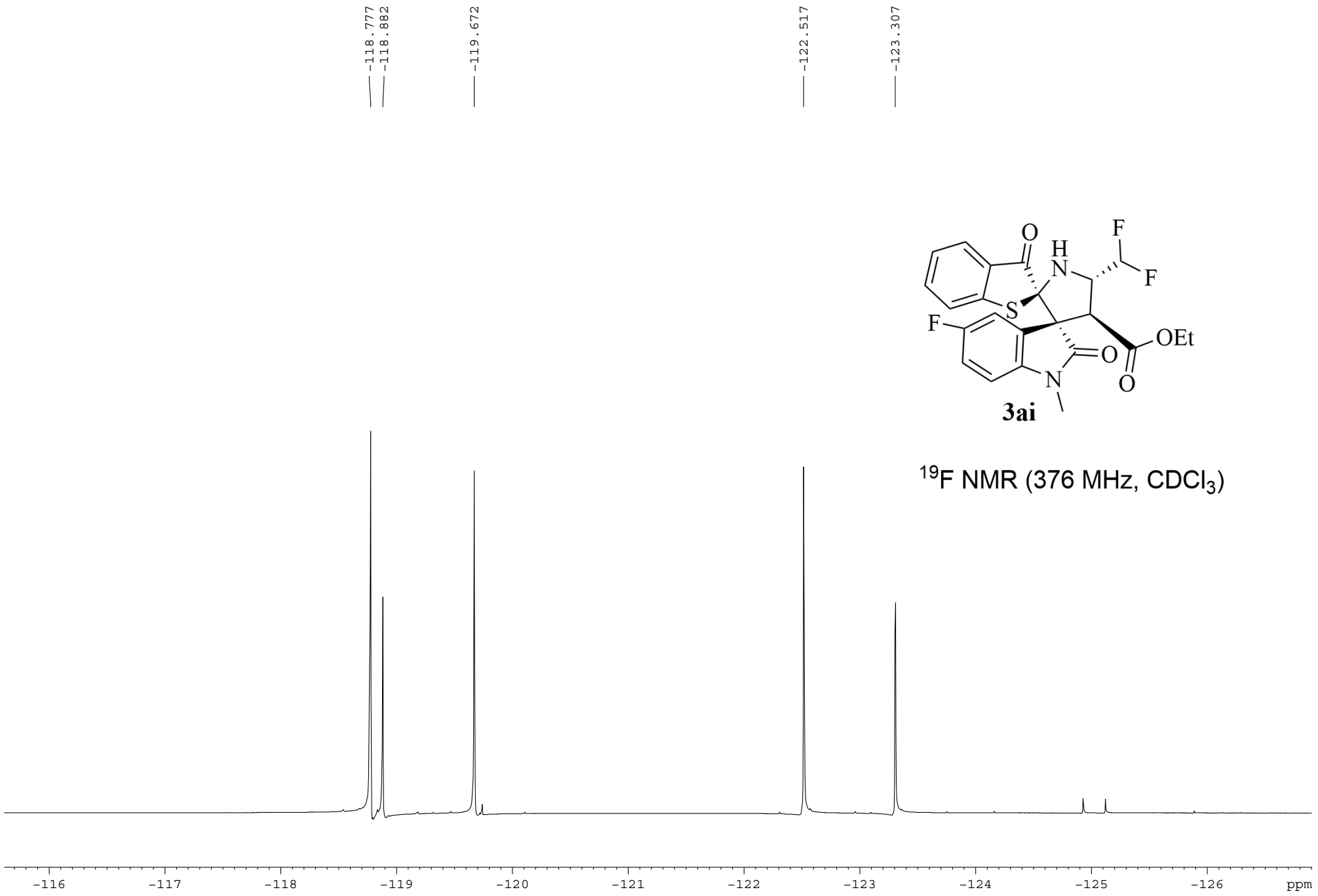

7.734
7.715
7.474
7.456
7.438
7.436
7.364
7.344
7.197
7.178
7.160
7.125
7.121
7.105
7.101
7.033
7.013
6.852
6.848
6.731
6.714
6.586
6.569
6.444
6.427
4.532
4.502
4.489
4.472
4.459
4.455
4.288
4.268
3.874
3.856
3.847
3.838
3.829
3.821
3.811
3.793
3.782
3.764
3.755
3.746
3.737
3.728
3.719
3.701
3.083
2.739
0.826
0.808
0.791
0.000
F
F
EtO
O
Cl
NH
O
S
N
O
3ah
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
1.03
1.00
1.02
1.00
1.00
1.01
1.01
1.01
1.02
1.02
1.00
3.02
1.01
3.02


202.15
171.48
167.43
147.63
145.33
136.52
135.86
128.74
127.31
126.72
125.73
125.23
123.26
122.99
119.73
117.34
117.29
114.90
108.88
86.43
62.17
61.17
59.72
59.48
59.44
59.20
49.64
49.56
26.78
13.67
119.73
117.34
117.29
114.90
120
118
116
ppm
F
F
EtO
O
Cl
NH
O
S
N
O
3ah
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


-118.889
-119.678
-122.519
-123.309
F
F
EtO
O
Cl
NH
O
S
N
O
3ah
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

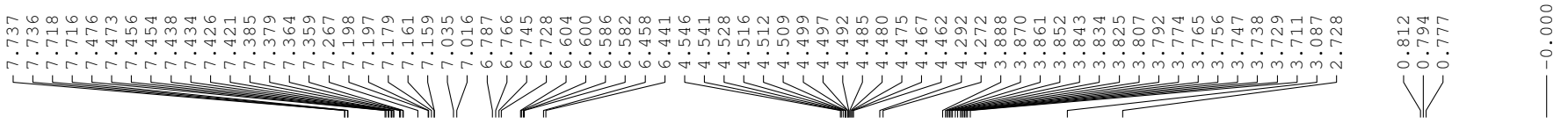

7.742
7.740
7.723
7.721
7.475
7.471
7.455
7.453
7.437
7.433
7.235
7.228
7.215
7.209
7.199
7.197
7.179
7.161
7.159
7.129
7.122
7.107
7.100
7.085
7.078
7.035
7.015
6.792
6.782
6.771
6.761
6.755
6.737
6.613
6.609
6.596
6.592
6.468
6.450
4.540
4.535
4.527
4.522
4.517
4.515
4.506
4.503
4.497
4.493
4.491
4.486
4.479
4.474
4.469
4.461
4.456
4.295
4.275
3.883
3.865
3.856
3.847
3.838
3.829
3.820
3.802
3.778
3.761
3.751
3.743
3.733
3.725
3.716
3.698
3.091
2.723
0.806
0.789
0.771
-0.000
O
H
N
F
F
S
F
OEt
O
O
N
3ai
1H NMR (400 MHz, CDCl3)
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
ppm
1.01
1.02
2.04
1.02
1.01
1.00
1.00
1.01
1.01
1.00
1.02
3.01
1.01
3.00

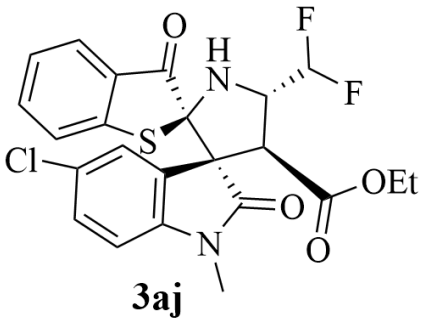

202.22
171.18
167.36
160.41
158.01
147.59
140.21
140.19
136.46
129.74
129.66
128.76
127.31
125.72
119.74
117.35
117.29
116.27
116.03
114.90
112.86
112.60
108.58
108.50
86.33
62.77
61.12
59.62
59.38
59.34
59.10
49.59
49.51
26.81
13.63
119.74
117.35
117.29
114.90
120 119 118 117 116 115 ppm
O
H
N
F
F
S
F
OEt
O
O
N
3ai
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



3ai

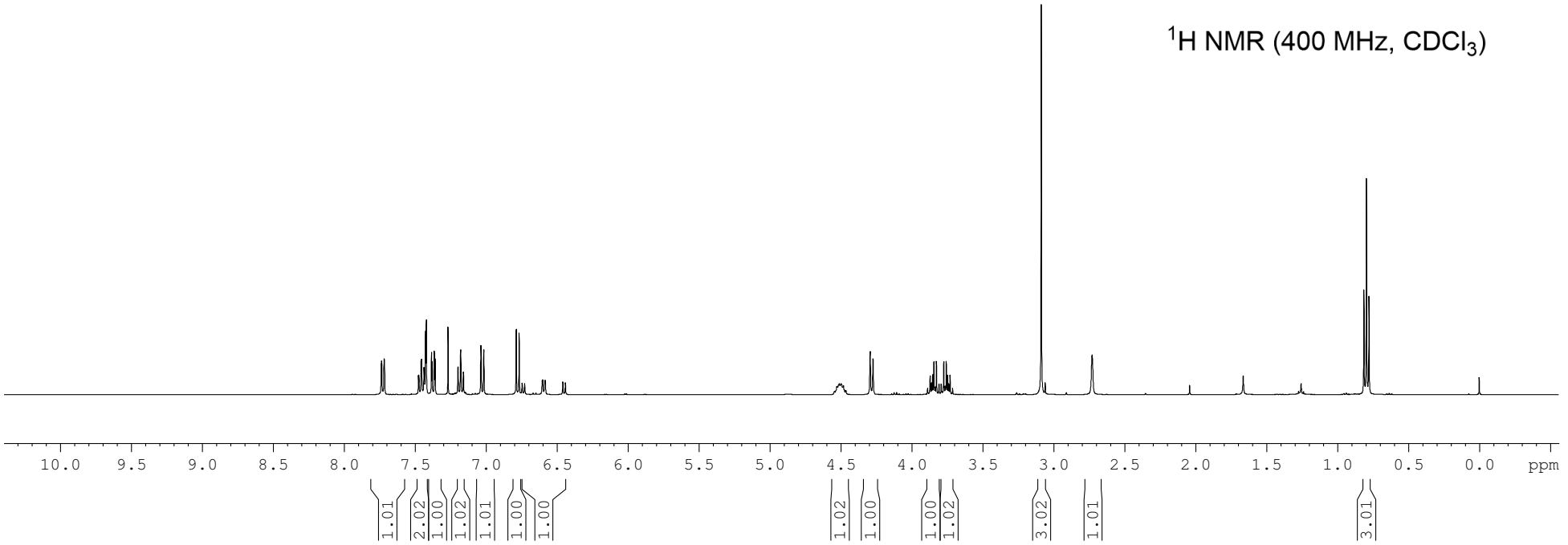
^{19}F NMR (376 MHz, $CDCl_3$)

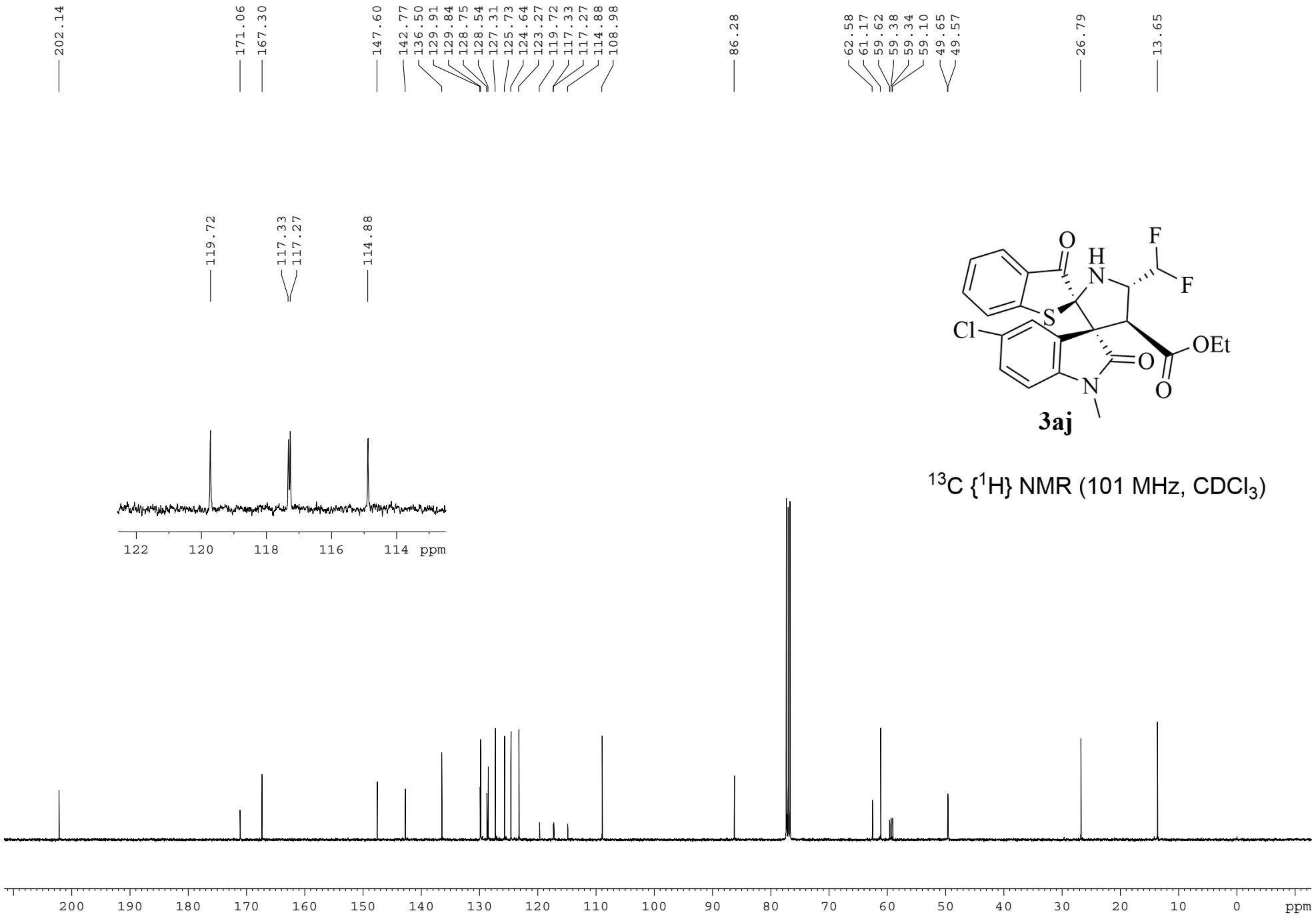


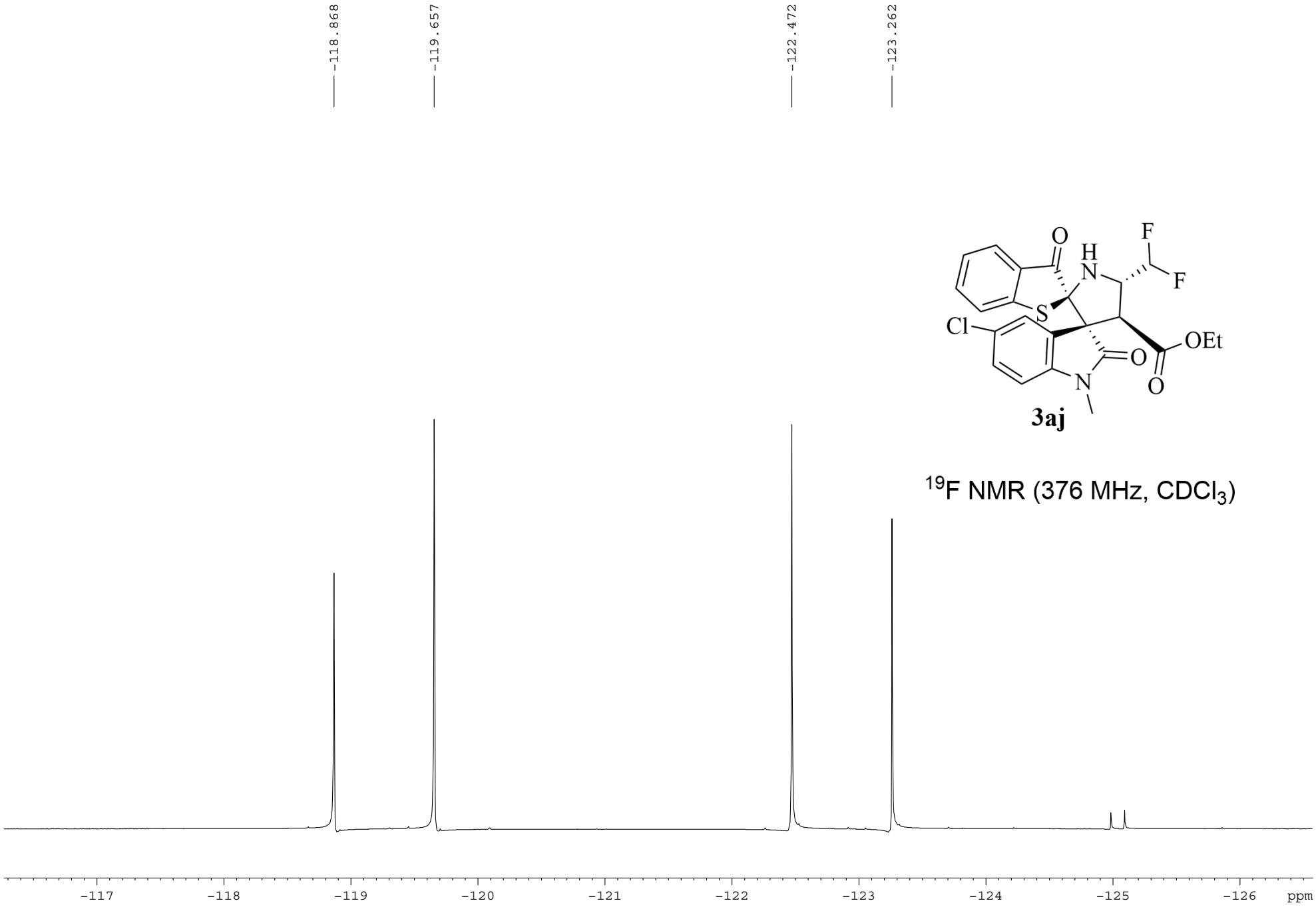


3aj

^{1}H NMR (400 MHz, $CDCl_3$)

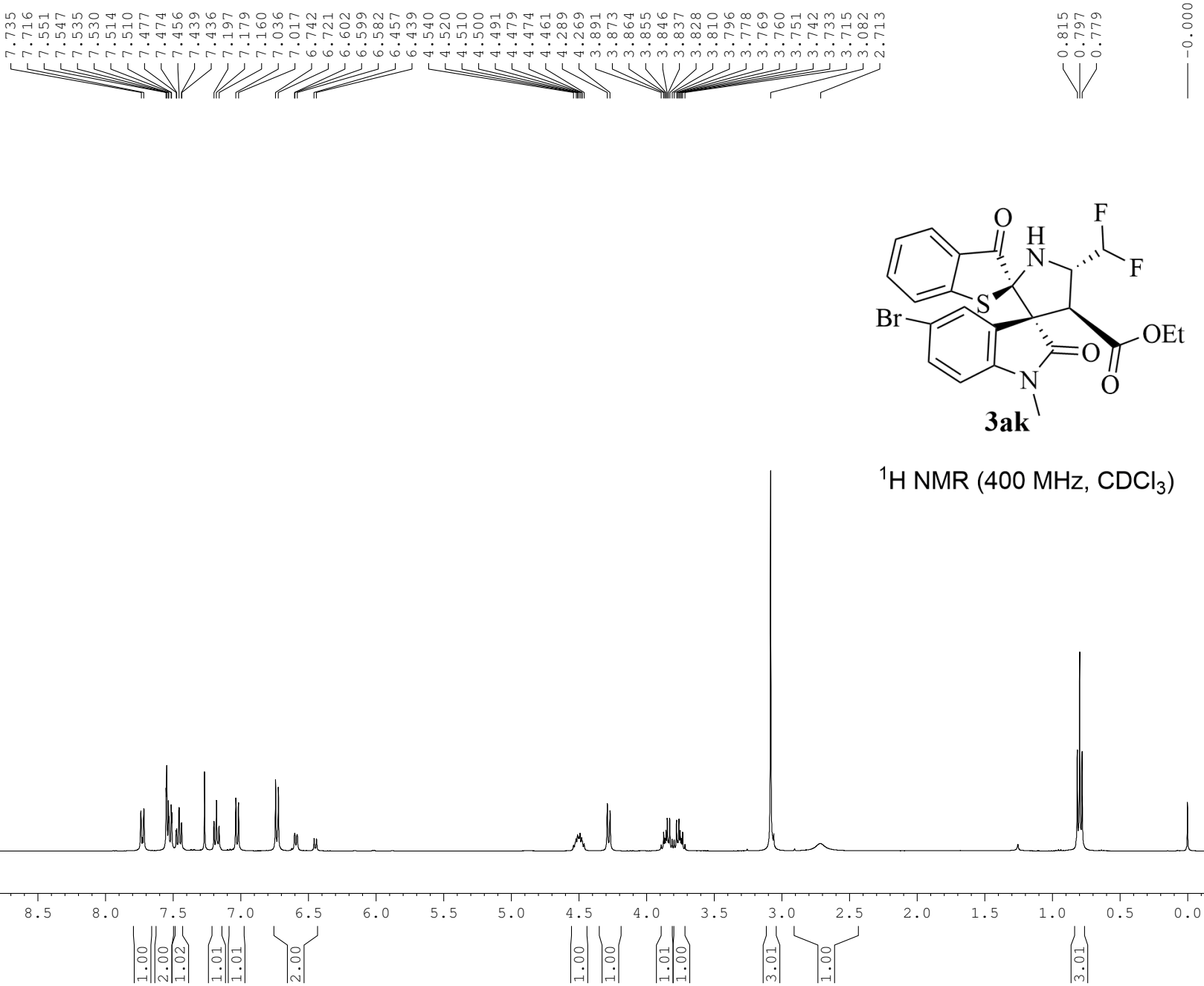


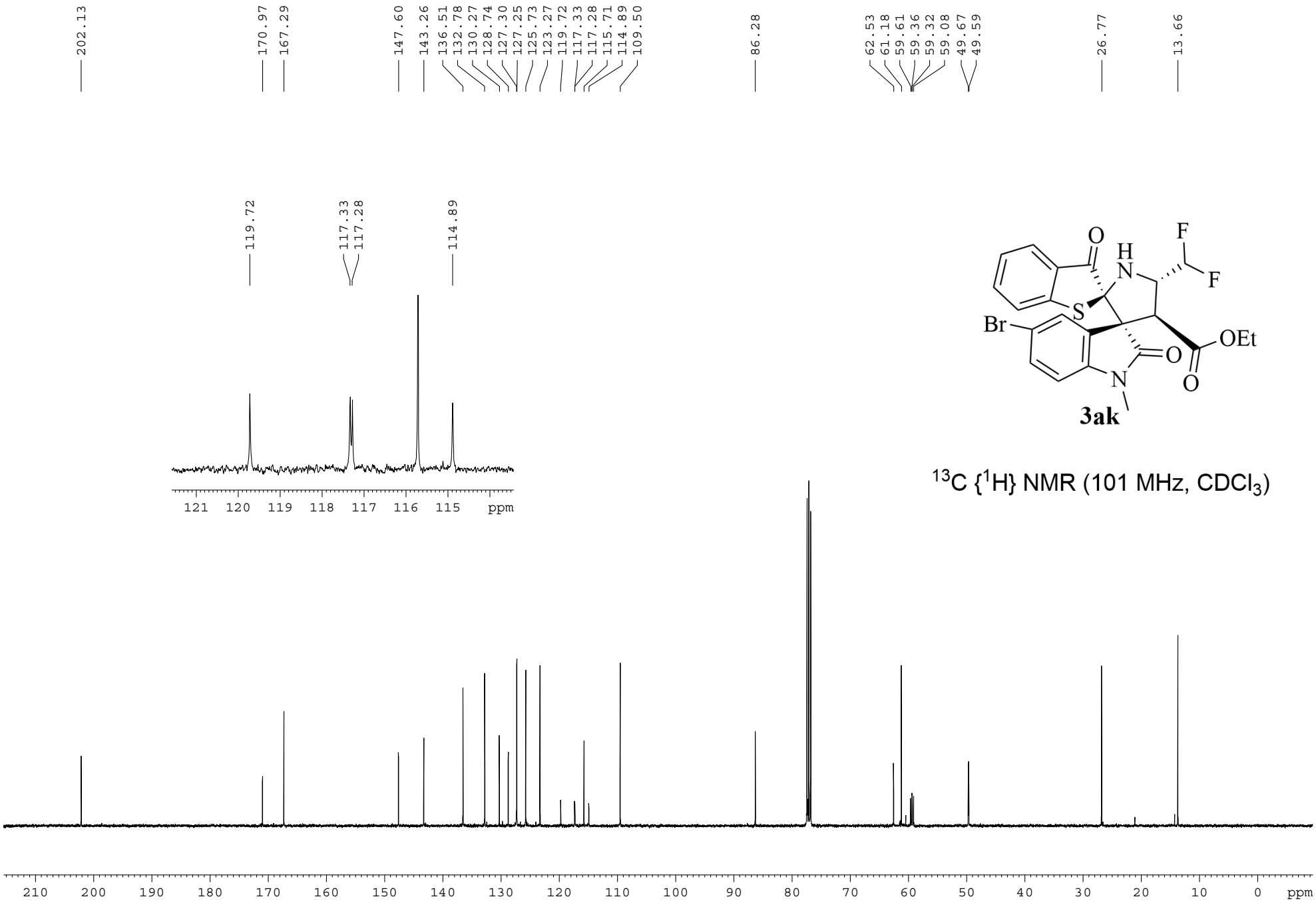

202.14
171.06
167.30
147.60
142.77
136.50
129.91
129.84
128.75
128.54
127.31
125.73
124.64
123.27
119.72
117.33
117.27
114.88
108.98
86.28
62.58
61.17
59.62
59.38
59.34
59.10
49.65
49.57
26.79
13.65
119.72
117.33
117.27
114.88
122
120
118
116
114
ppm
O
H
N
F
F
S
Cl
OEt
O
O
N
3aj
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

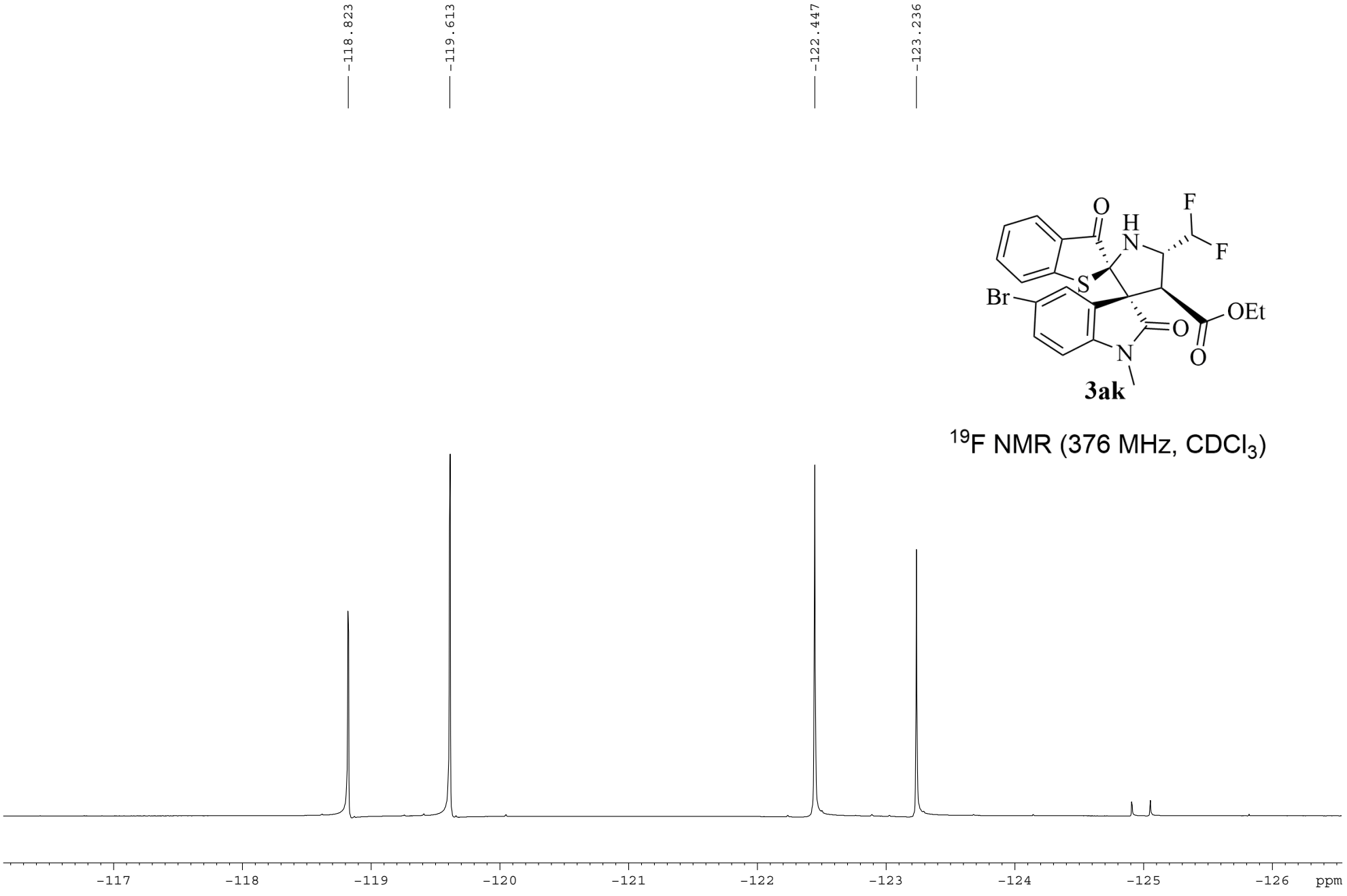


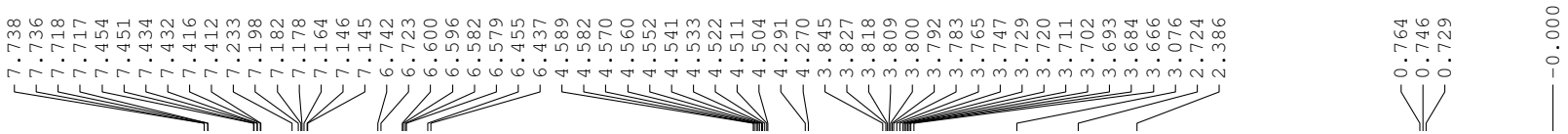
3aj

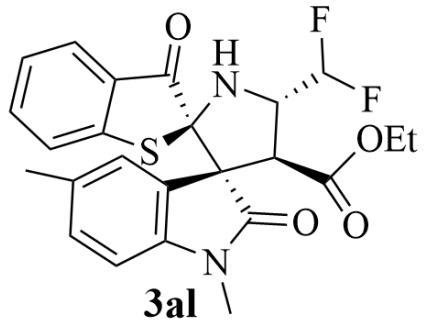
^{19}F NMR (376 MHz, $CDCl_3$)


7.735
7.716
7.551
7.547
7.535
7.530
7.514
7.510
7.477
7.474
7.456
7.439
7.436
7.197
7.179
7.160
7.036
7.017
6.742
6.721
6.602
6.599
6.582
6.457
6.439
4.540
4.520
4.510
4.500
4.491
4.479
4.474
4.461
4.289
4.269
3.891
3.873
3.864
3.855
3.846
3.837
3.828
3.810
3.796
3.778
3.769
3.760
3.751
3.742
3.733
3.715
3.082
2.713
0.815
0.797
0.779
0.000
O
H
N
F
F
S
Br
OEt
O
O
N
3ak
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
2.00
1.02
1.01
1.01
2.00
1.00
1.00
1.01
1.00
3.01
1.00
3.01


202.13
170.97
167.29
147.60
143.26
136.51
132.78
130.27
128.74
127.30
127.25
125.73
123.27
119.72
117.33
117.28
115.71
114.89
109.50
86.28
62.53
61.18
59.61
59.36
59.32
59.08
49.67
49.59
26.77
13.66
119.72
117.33
117.28
114.89
121 120 119 118 117 116 115 ppm
O
H
N
F
F
S
Br
OEt
O
O
N
O
3ak
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

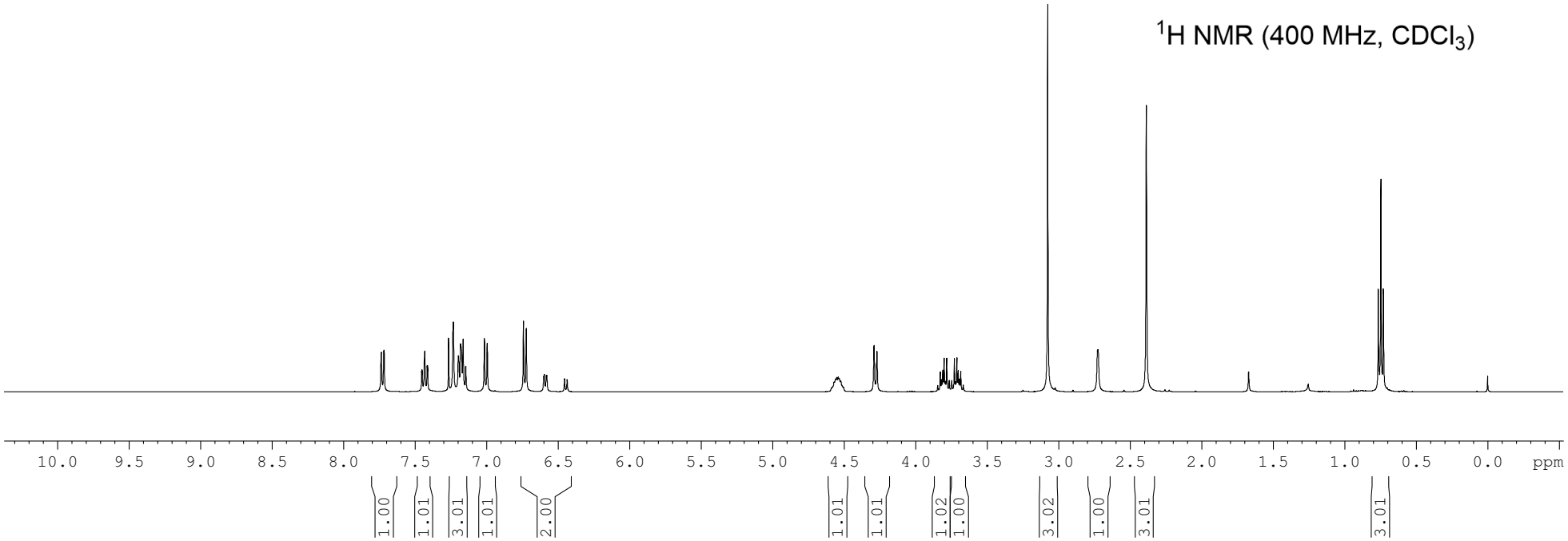

-118.823
-119.613
-122.447
-123.236
O
H
N
F
F
S
Br
OEt
O
O
N
3ak
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

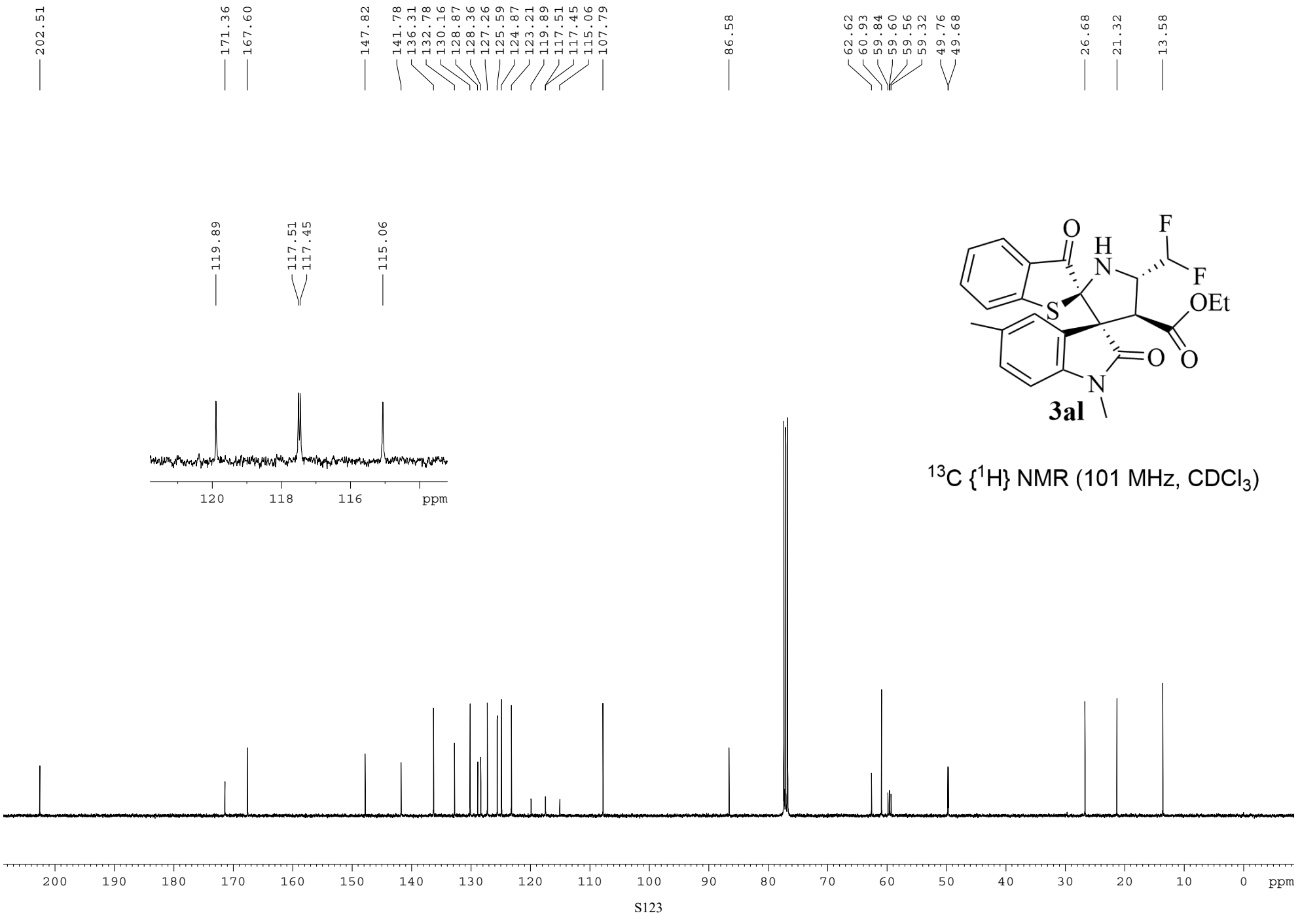


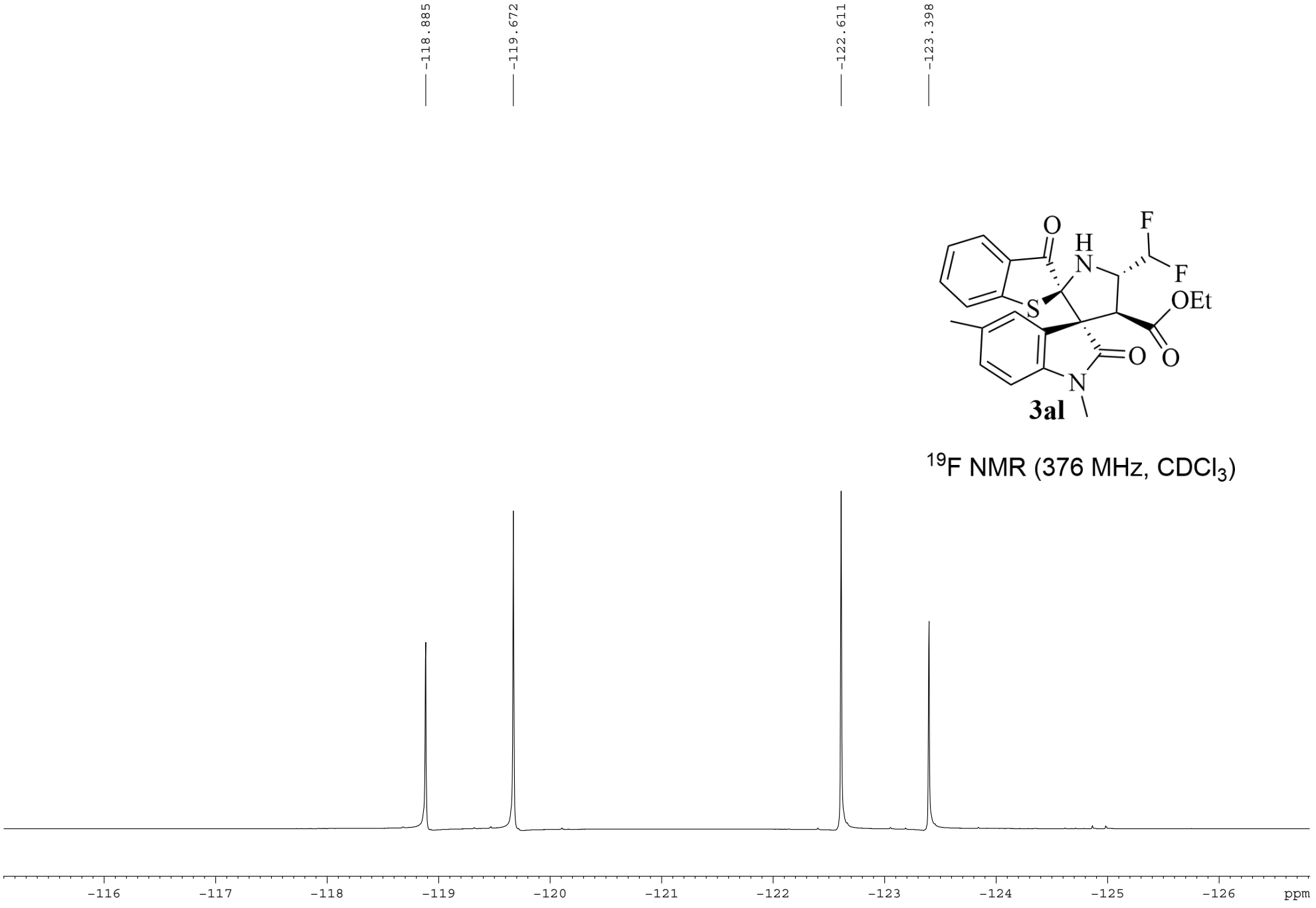


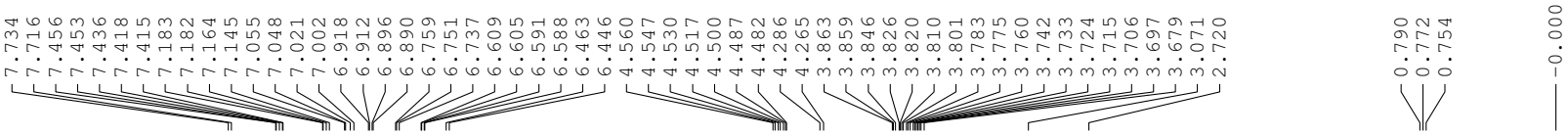
3al

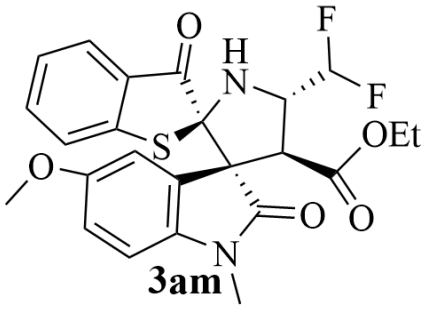
^{1}H NMR (400 MHz, $CDCl_3$)




202.51
171.36
167.60
147.82
141.78
136.31
132.78
130.16
128.87
128.36
127.26
125.59
124.87
123.21
119.89
117.51
117.45
115.06
107.79
86.58
62.62
60.93
59.84
59.60
59.56
59.32
49.76
49.68
26.68
21.32
13.58
119.89
117.51
117.45
115.06
120
118
116
ppm
O
H
N
F
F
S
OEt
O
O
O
N
3al
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

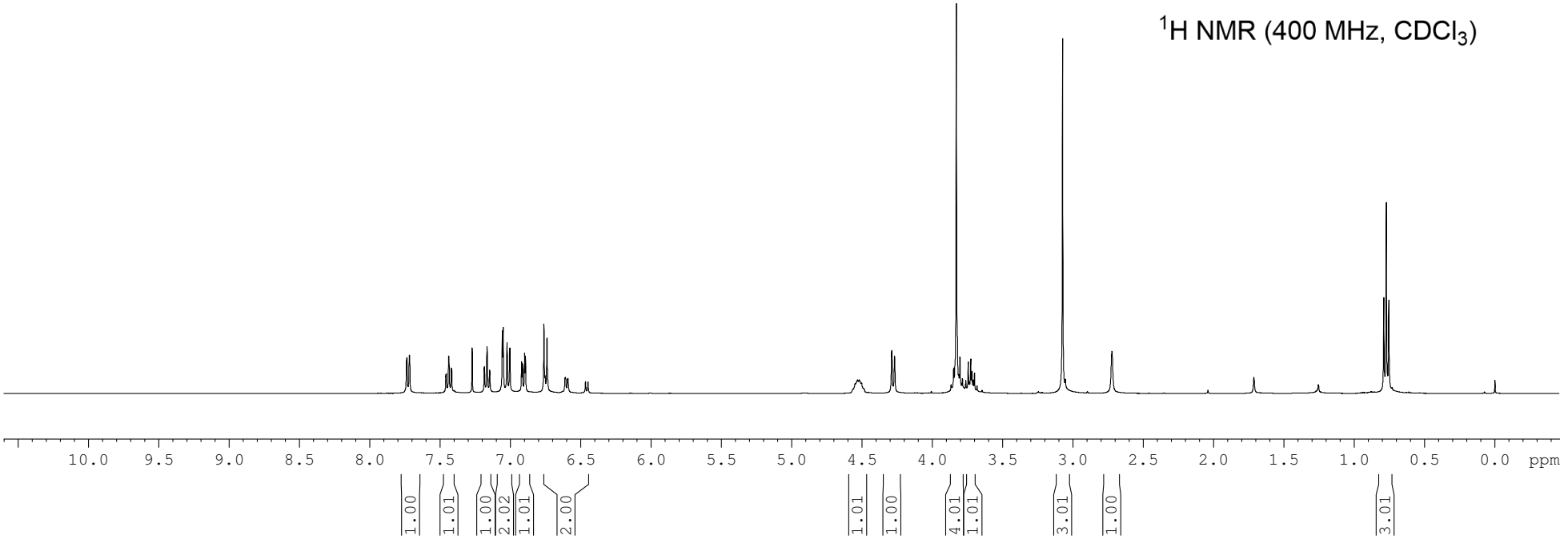

-118.885
-119.672
-122.611
-123.398
O
H
N
F
F
OEt
S
O
O
N
3al
19F NMR (376 MHz, CDCl3)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

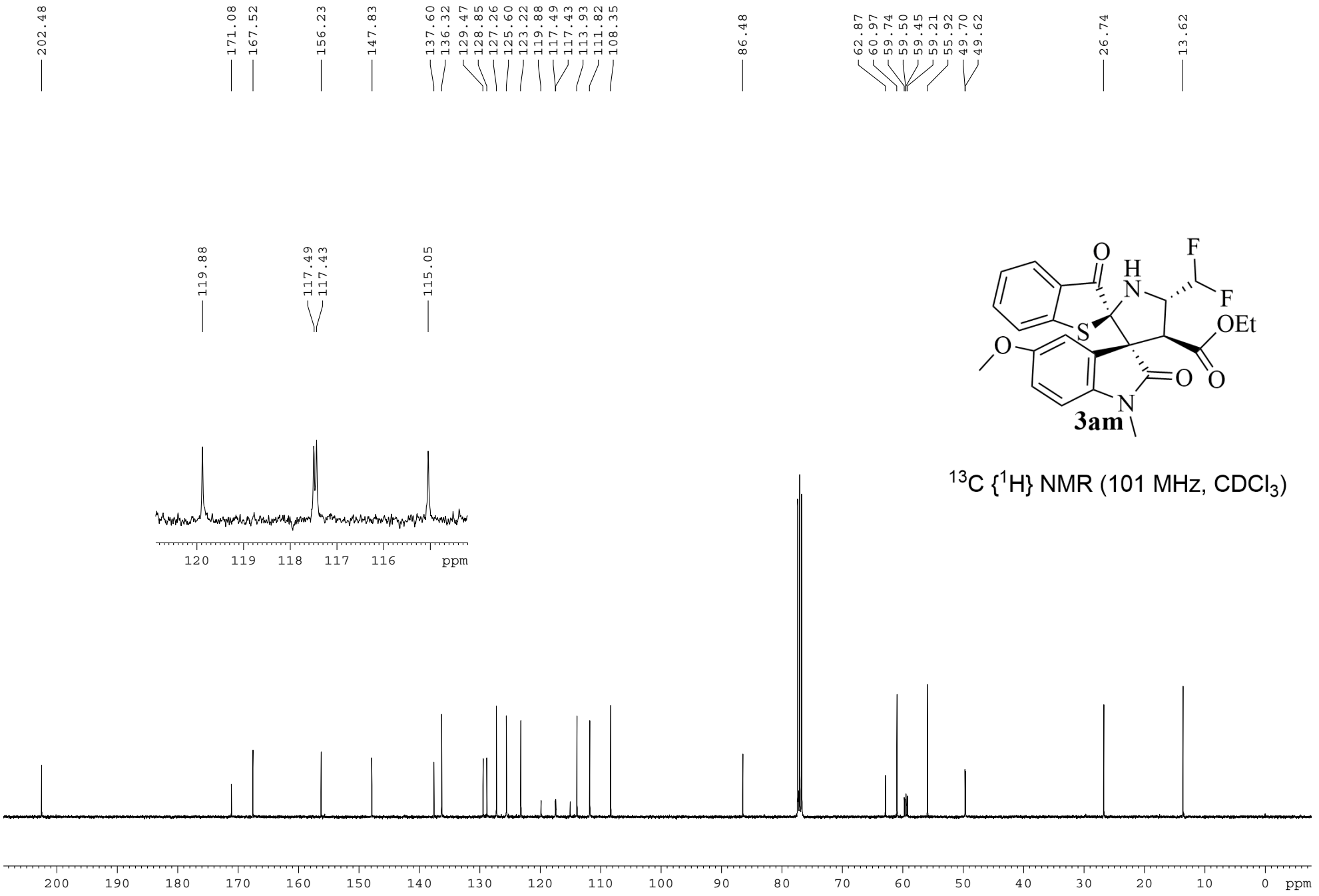


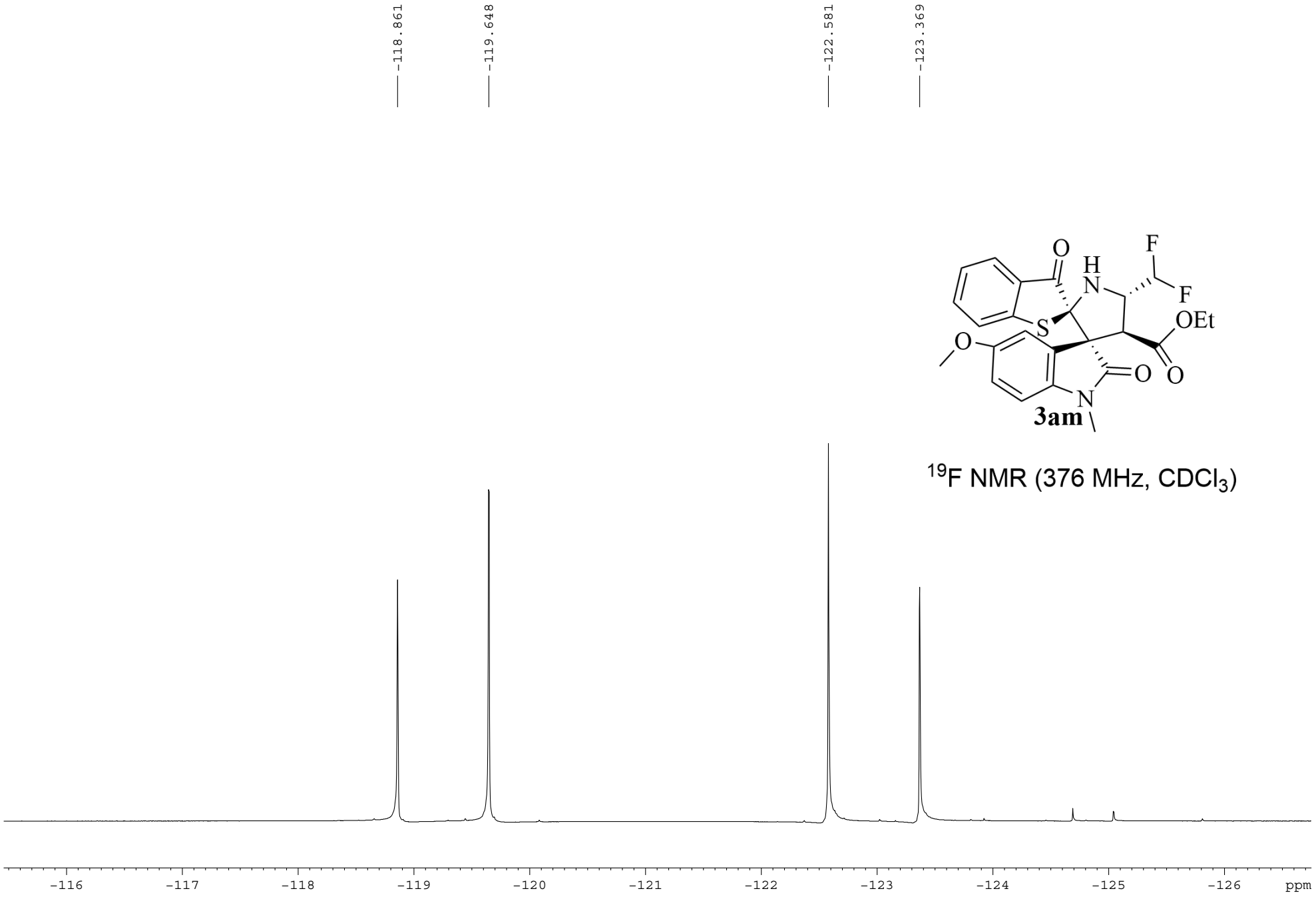


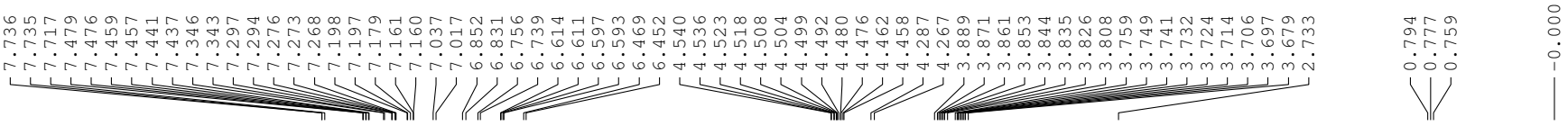
3am

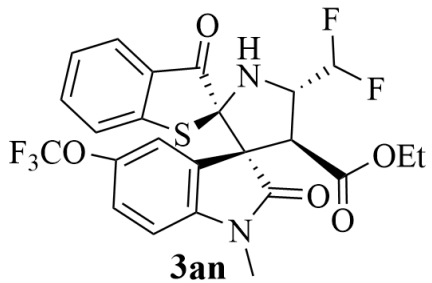
^{1}H NMR (400 MHz, $CDCl_3$)




202.48
171.08
167.52
156.23
147.83
137.60
136.32
129.47
128.85
127.26
125.60
123.22
119.88
117.49
117.43
113.93
111.82
108.35
86.48
62.87
60.97
59.74
59.50
59.45
59.21
55.92
49.70
49.62
26.74
13.62
119.88
117.49
117.43
115.05
120
119
118
117
116
ppm
O
H
N
F
F
S
OEt
O
O
O
N
3am
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

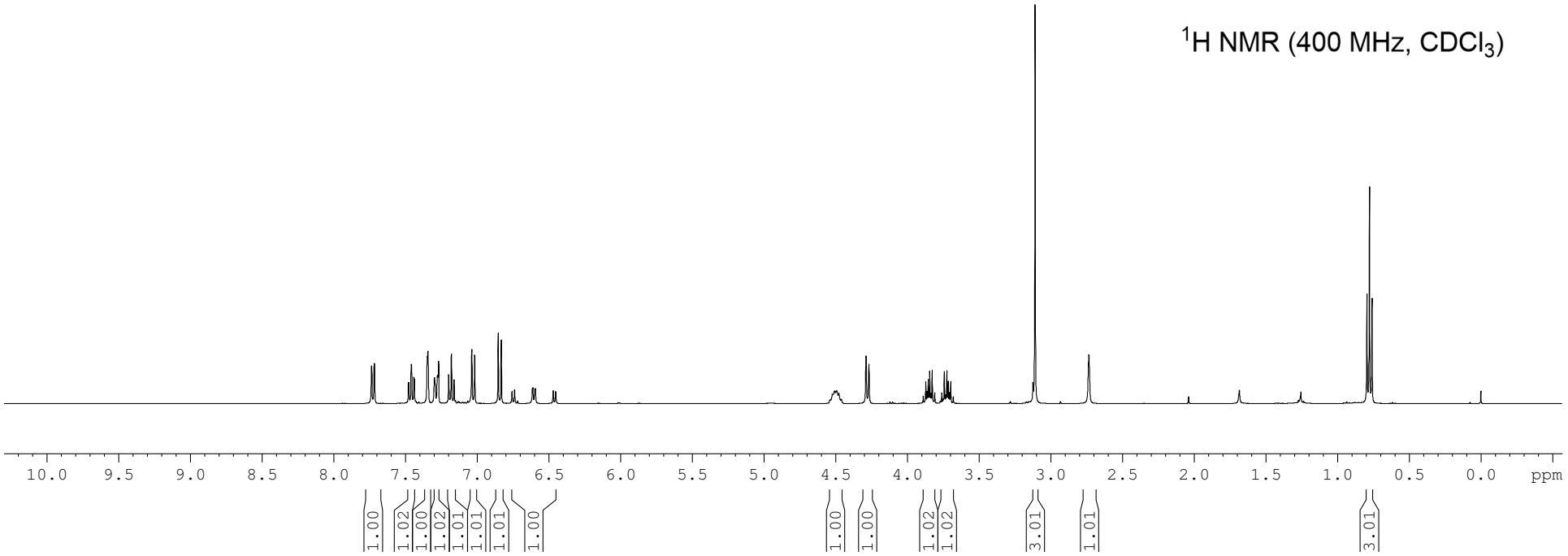

-118.861
-119.648
-122.581
-123.369
O
H
N
F
F
OEt
S
O
O
O
N
3am
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

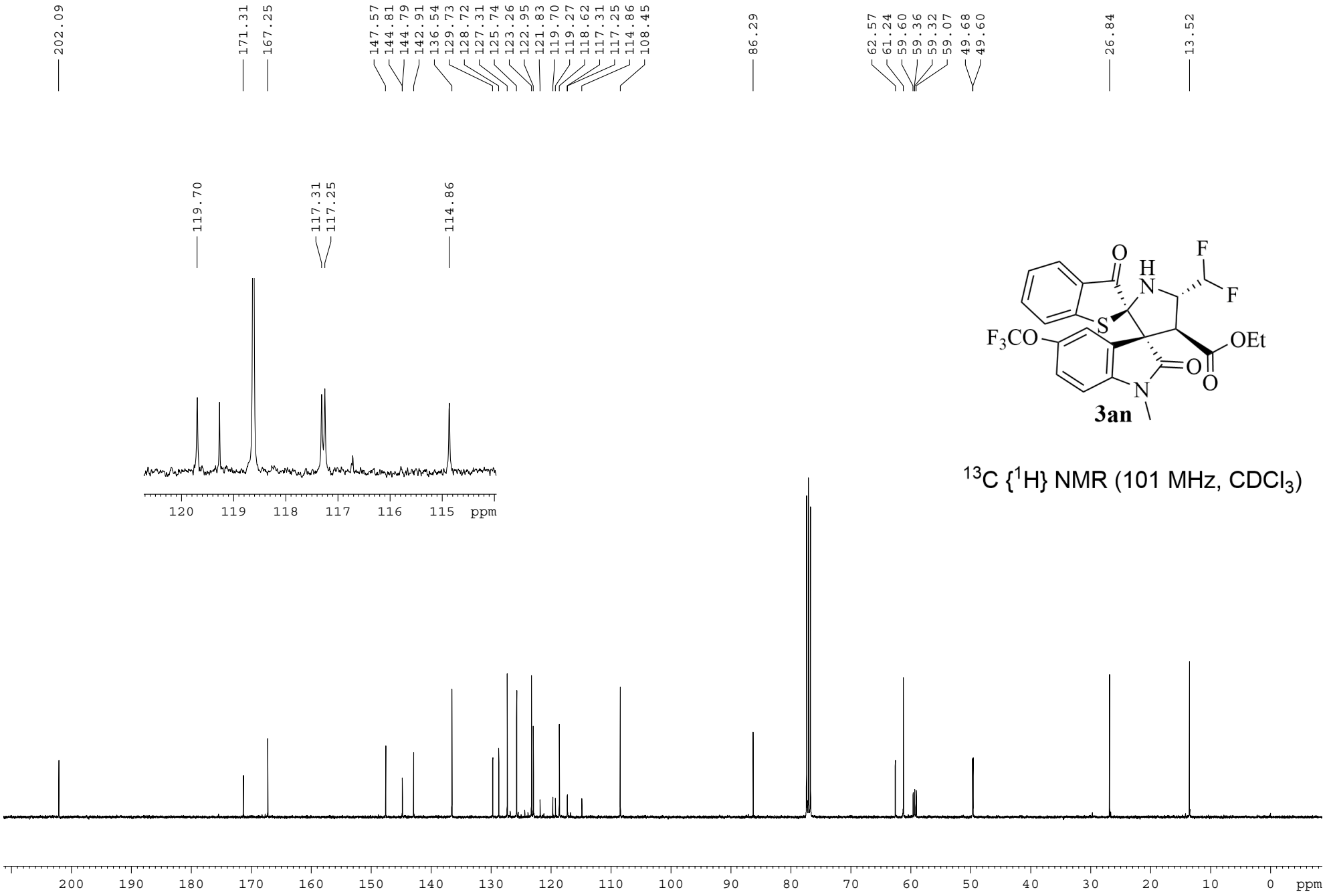


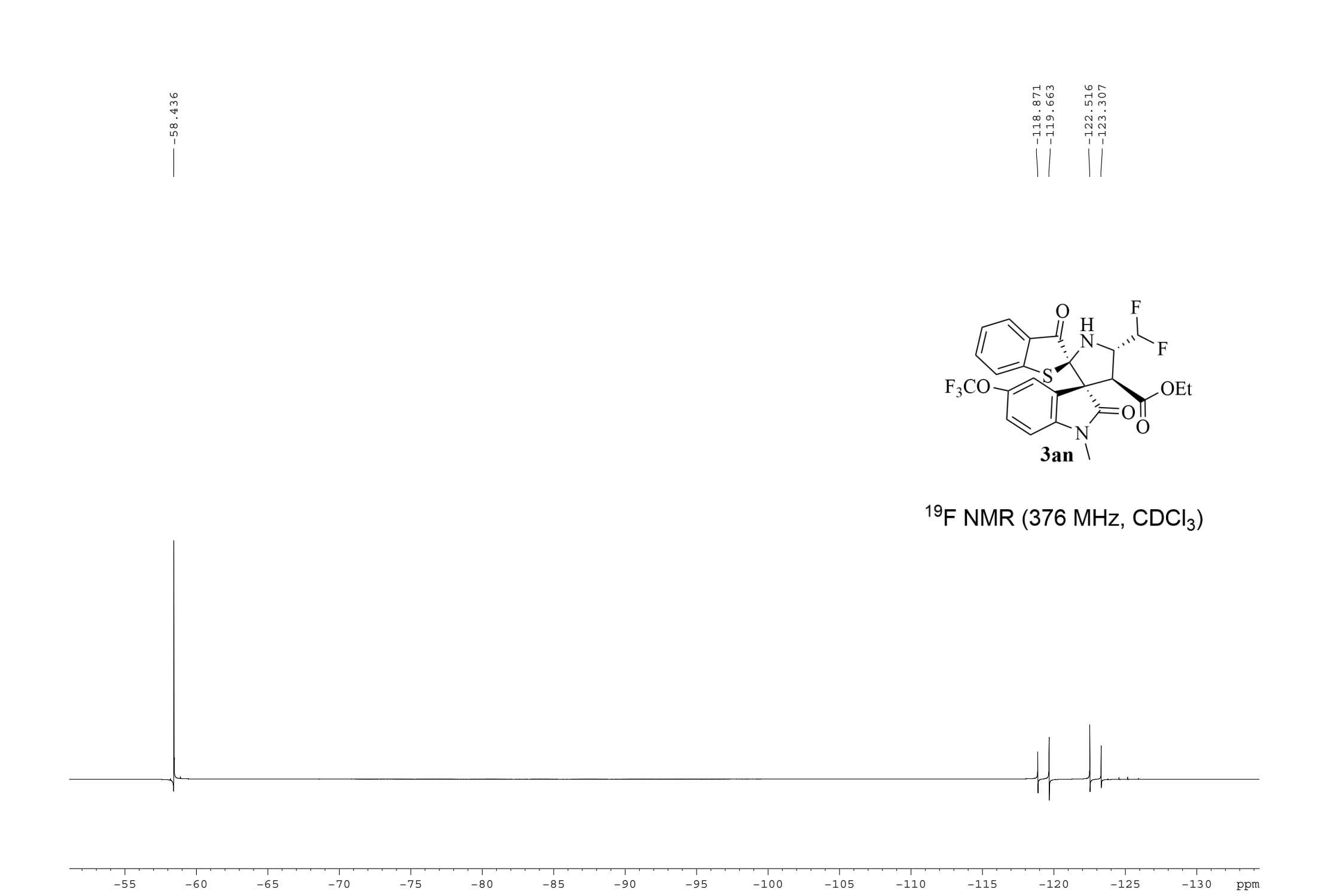


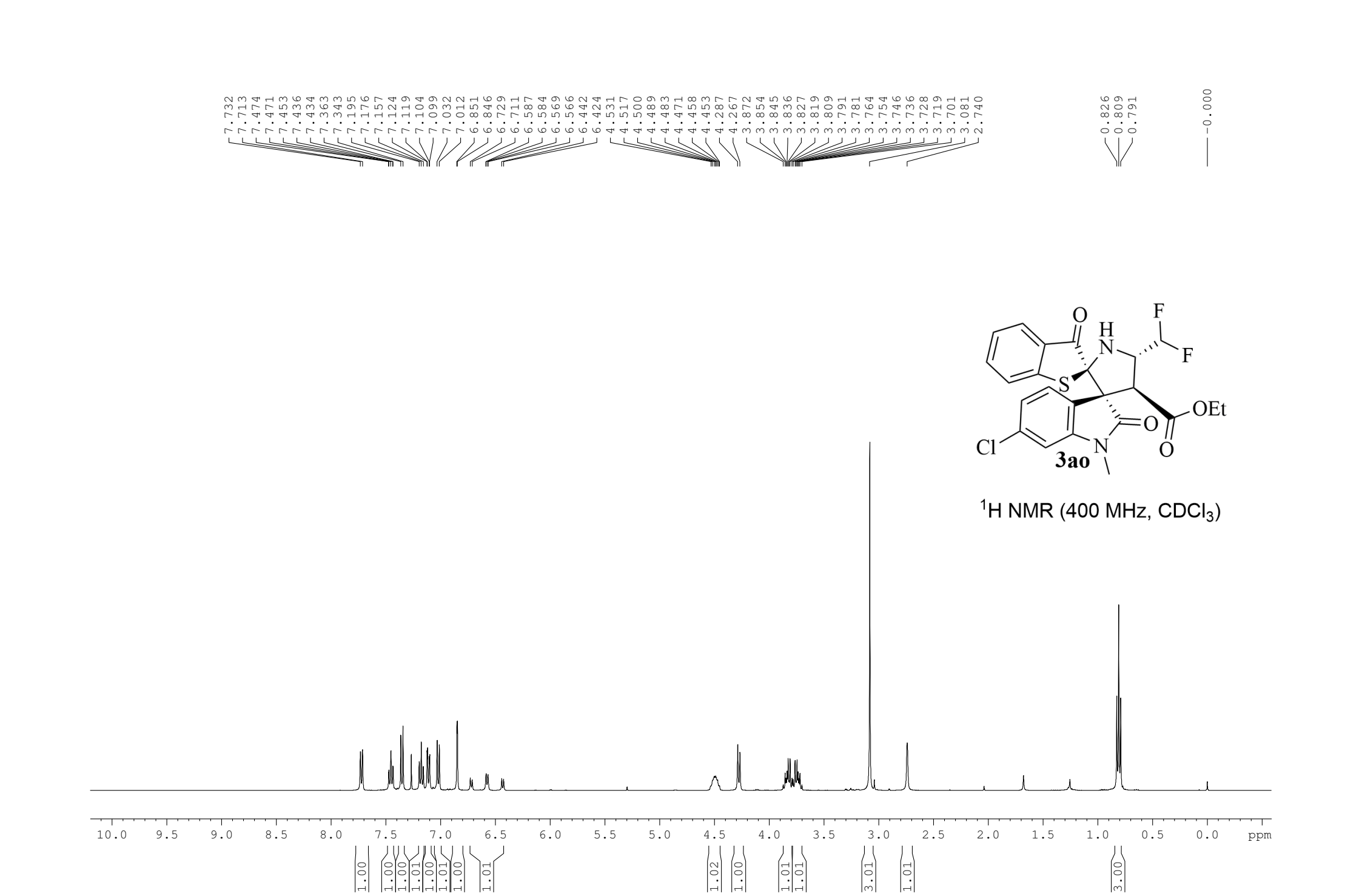
3an

^{1}H NMR (400 MHz, $CDCl_3$)

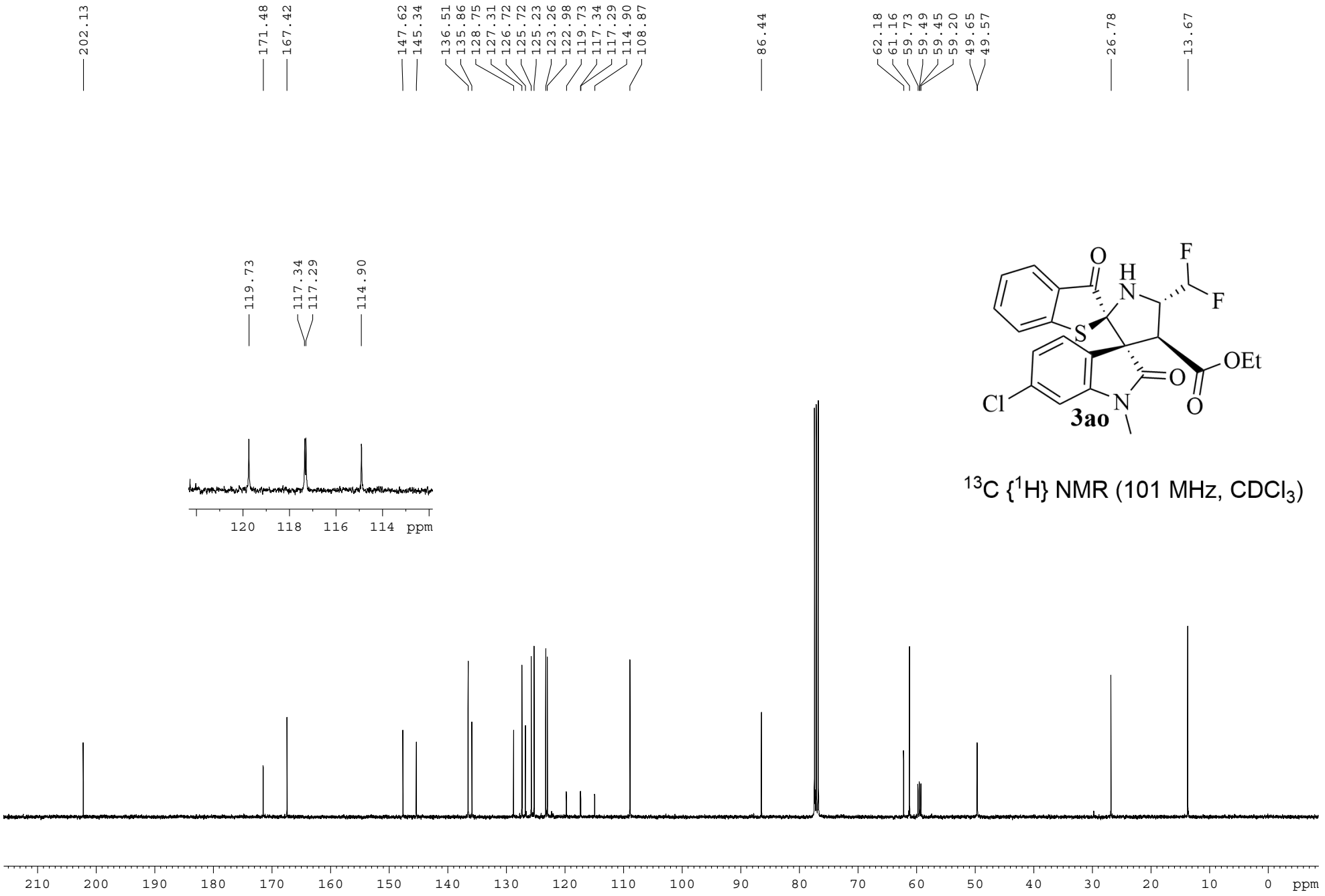



202.09
171.31
167.25
147.57
144.81
144.79
142.91
136.54
129.73
128.72
127.31
125.74
123.26
122.95
121.83
119.70
119.27
118.62
117.31
117.25
114.86
108.45
86.29
62.57
61.24
59.60
59.36
59.32
59.07
49.68
49.60
26.84
13.52
119.70
117.31
117.25
114.86
120
119
118
117
116
115
ppm
O
H
N
F
F
S
F3CO
OEt
O
O
N
3an
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

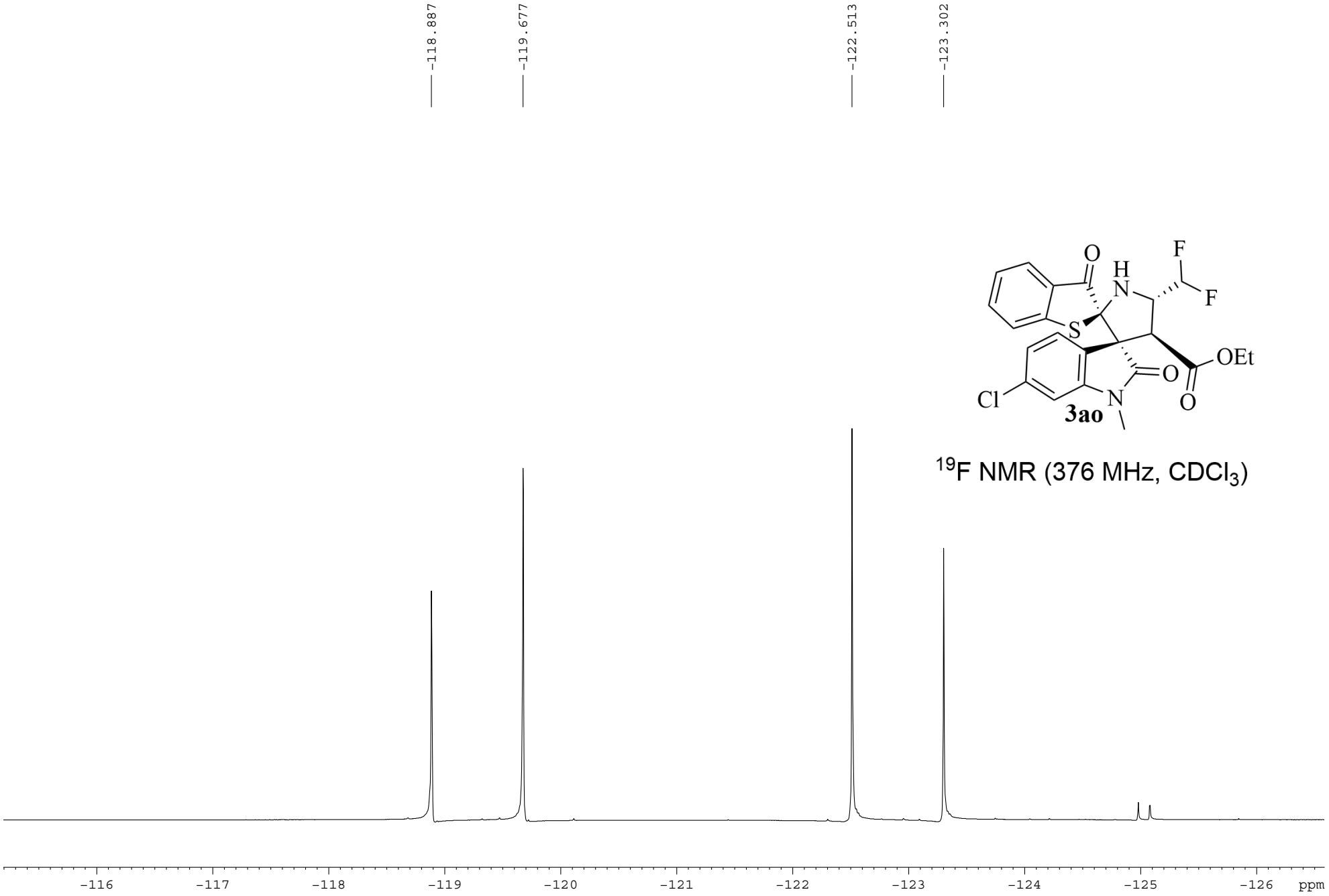

-58.436
-118.871
-119.663
-122.516
-123.307
O
H
N
F
F
S
F3CO
OEt
O
O
N
3an
19F NMR (376 MHz, CDCl3)
-55
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125
-130
ppm

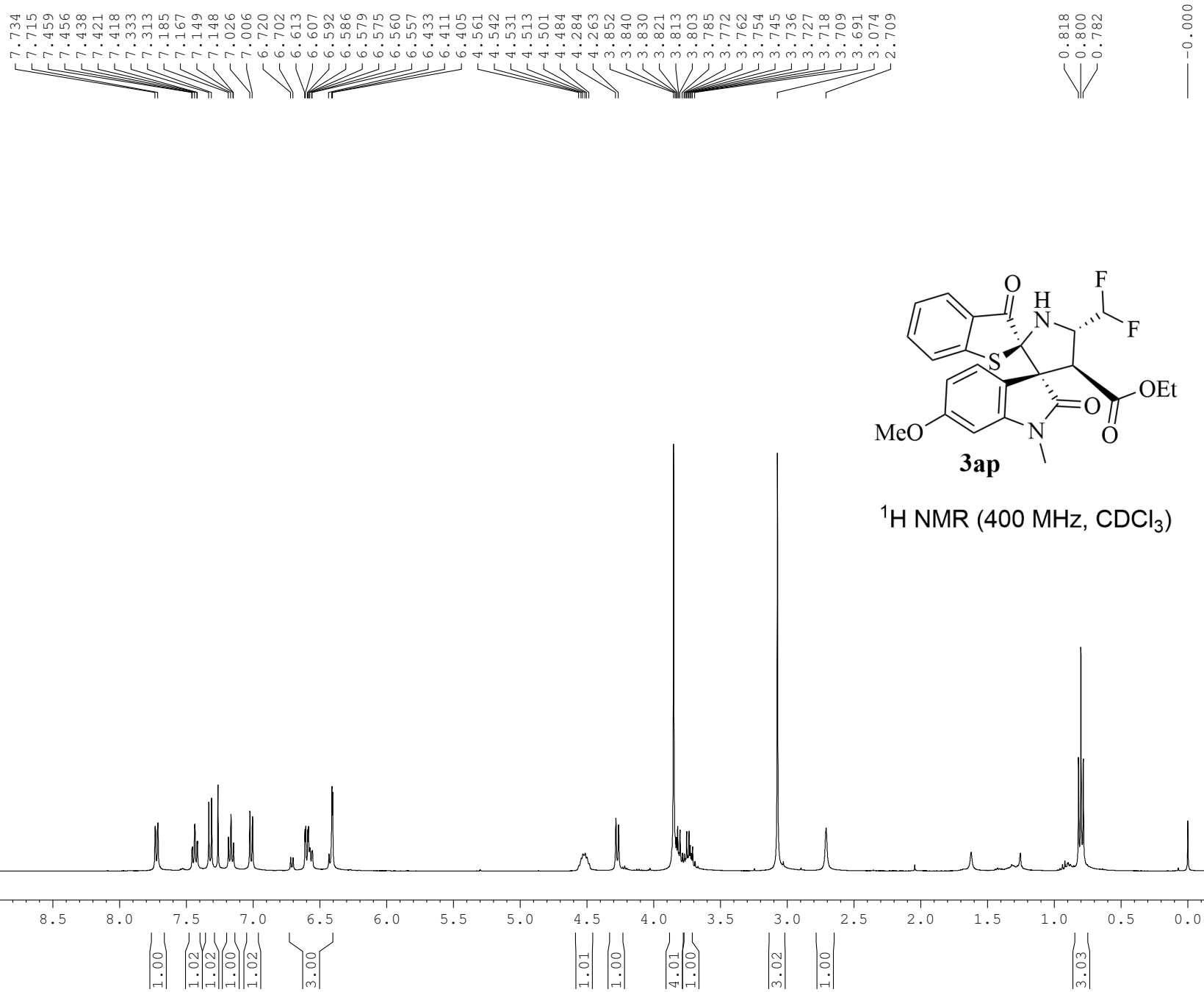


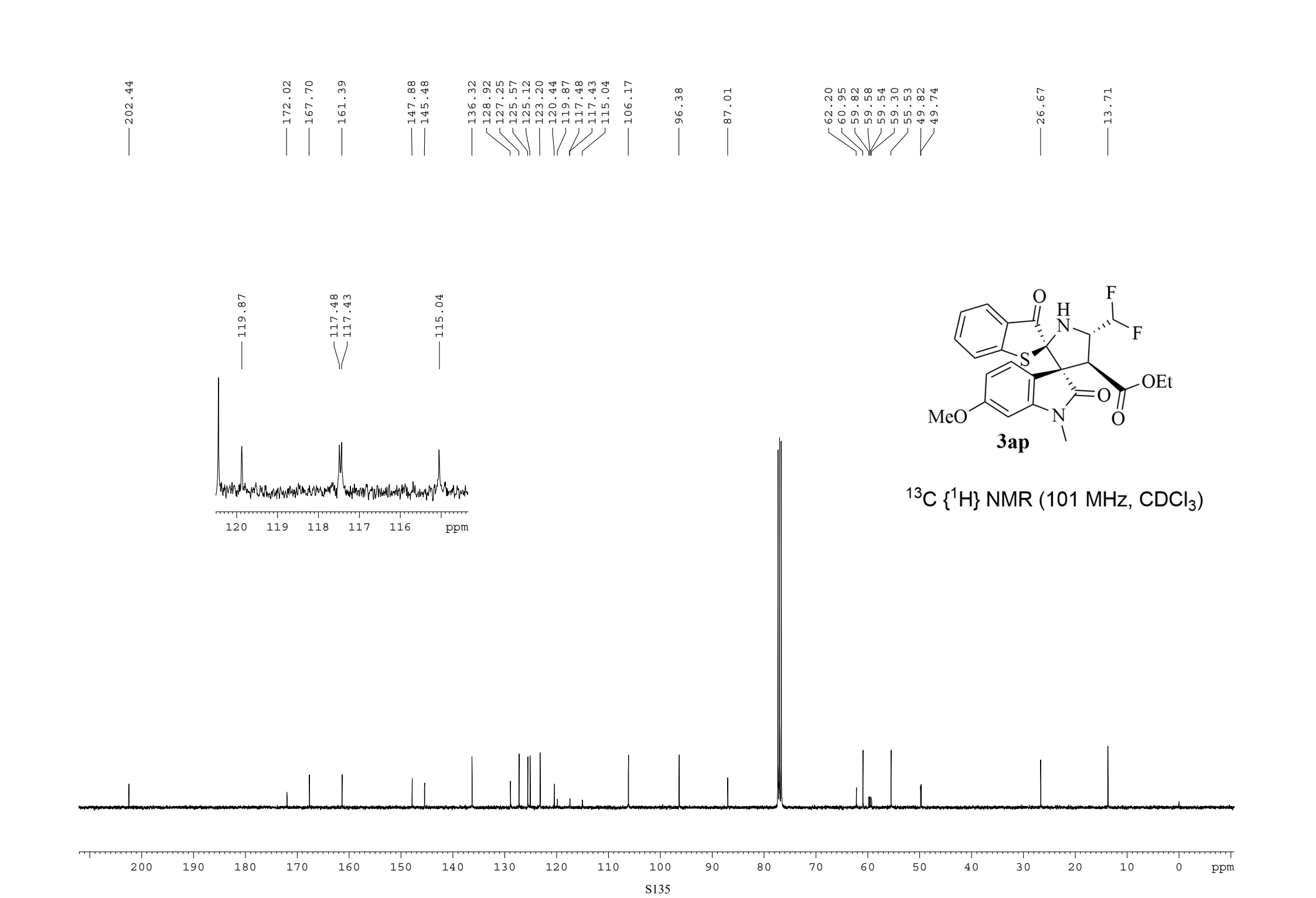
^{1}H NMR (400 MHz, $CDCl_3$)

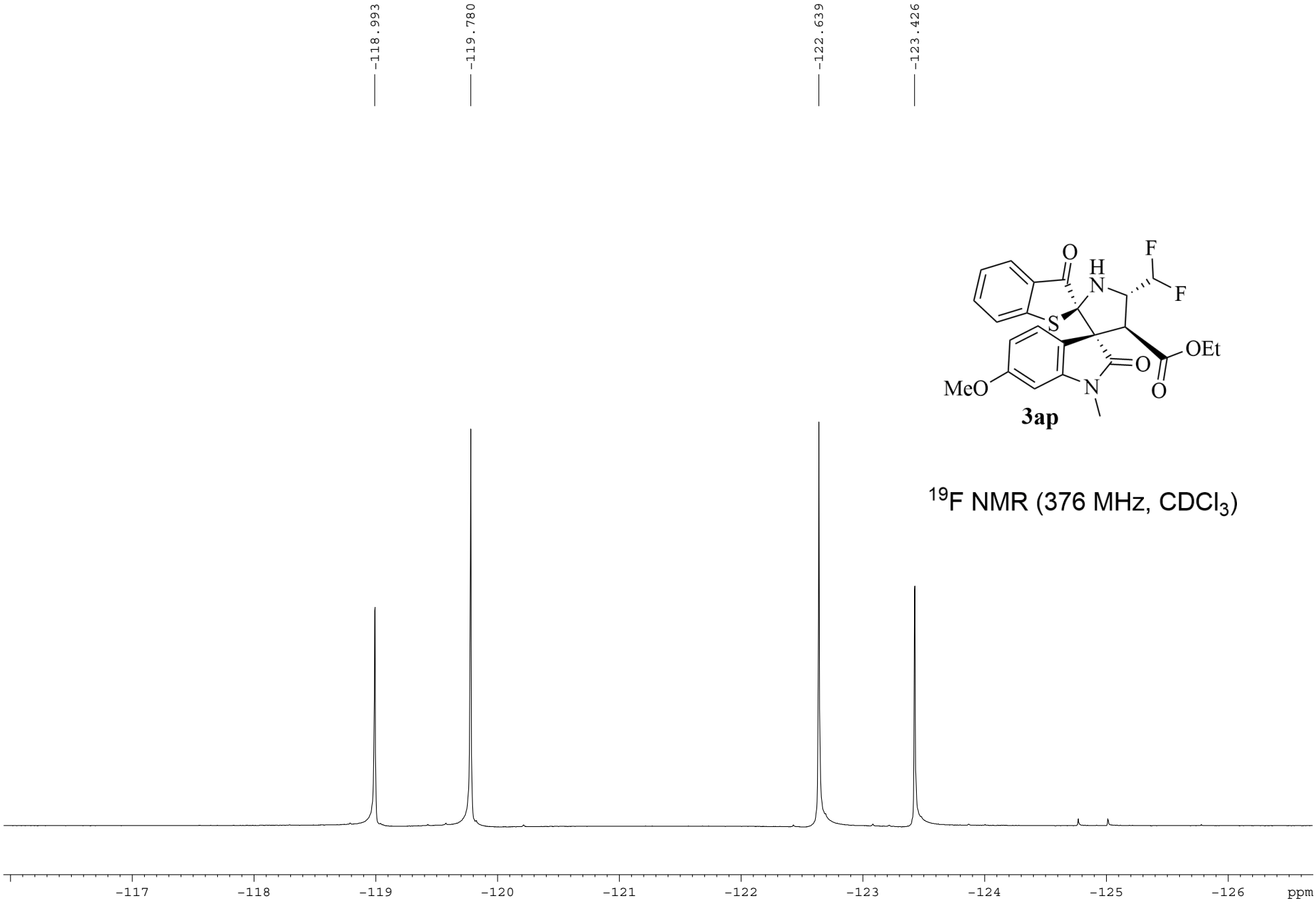


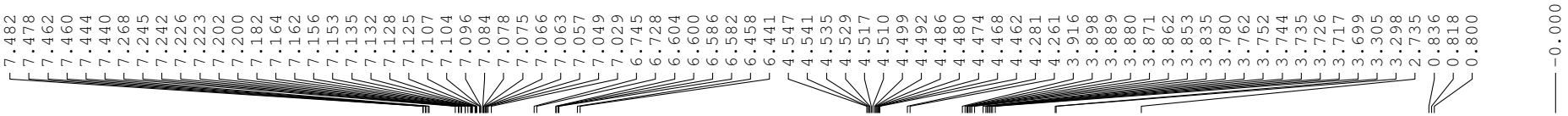
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

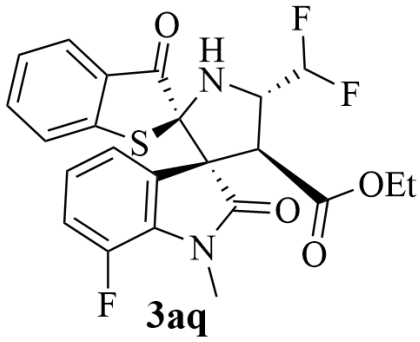

-118.887
-119.677
-122.513
-123.302
O
H
N
F
F
S
OEt
O
O
Cl
N
O
3ao
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.734
7.715
7.459
7.456
7.438
7.421
7.418
7.333
7.313
7.185
7.167
7.149
7.148
7.026
7.006
6.720
6.702
6.613
6.607
6.592
6.586
6.579
6.575
6.560
6.557
6.433
6.411
6.405
4.561
4.542
4.531
4.513
4.501
4.484
4.284
4.263
3.852
3.840
3.830
3.821
3.813
3.803
3.785
3.772
3.762
3.754
3.745
3.736
3.727
3.718
3.709
3.691
3.074
2.709
0.818
0.800
0.782
0.000
O
H
N
F
F
S
OEt
O
O
MeO
N
O
3ap
^{1}H NMR (400 MHz, $CDCl_3$)
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
ppm
1.00
1.02
1.02
1.00
1.02
3.00
1.01
1.00
4.01
1.00
3.02
1.00
3.03


202.44
172.02
167.70
161.39
147.88
145.48
136.32
128.92
127.25
125.57
125.12
123.20
120.44
119.87
117.48
117.43
115.04
106.17
96.38
87.01
62.20
60.95
59.82
59.58
59.54
59.30
55.53
49.82
49.74
26.67
13.71
119.87
117.48
117.43
115.04
120
119
118
117
116
ppm
O
H
N
F
F
S
OEt
O
O
MeO
N
3ap
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

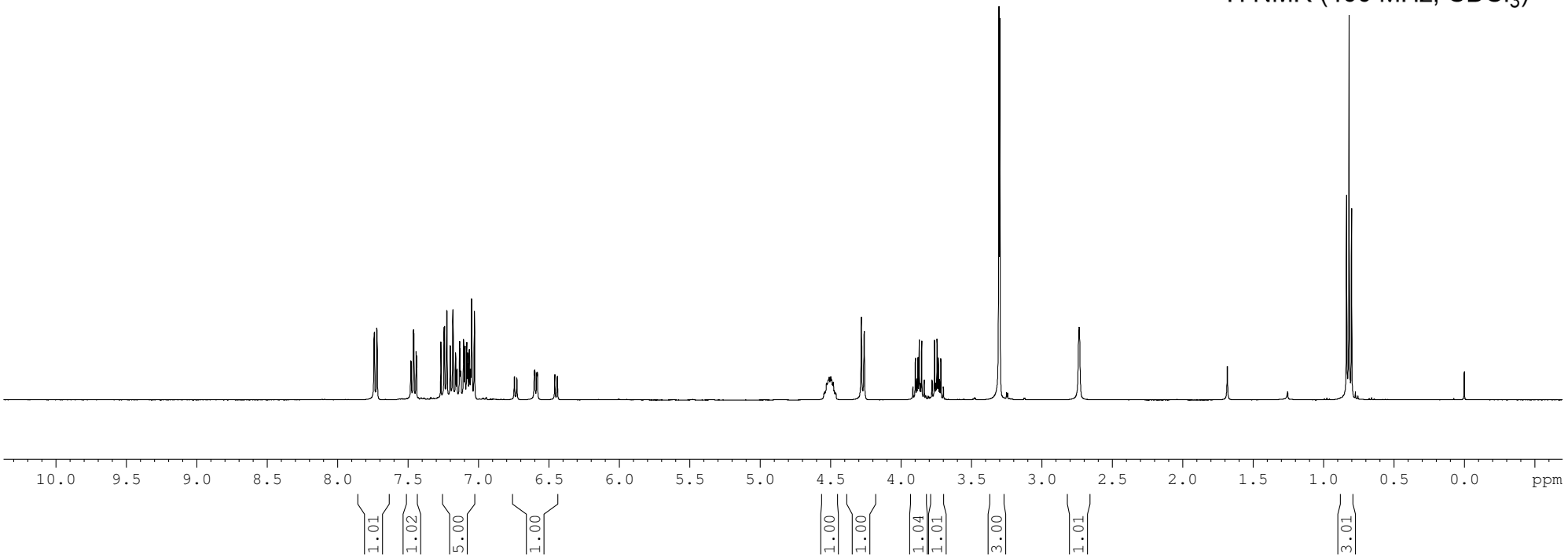

-118.993
-119.780
-122.639
-123.426
O
H
N
F
F
S
OEt
O
O
MeO
N
3ap
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

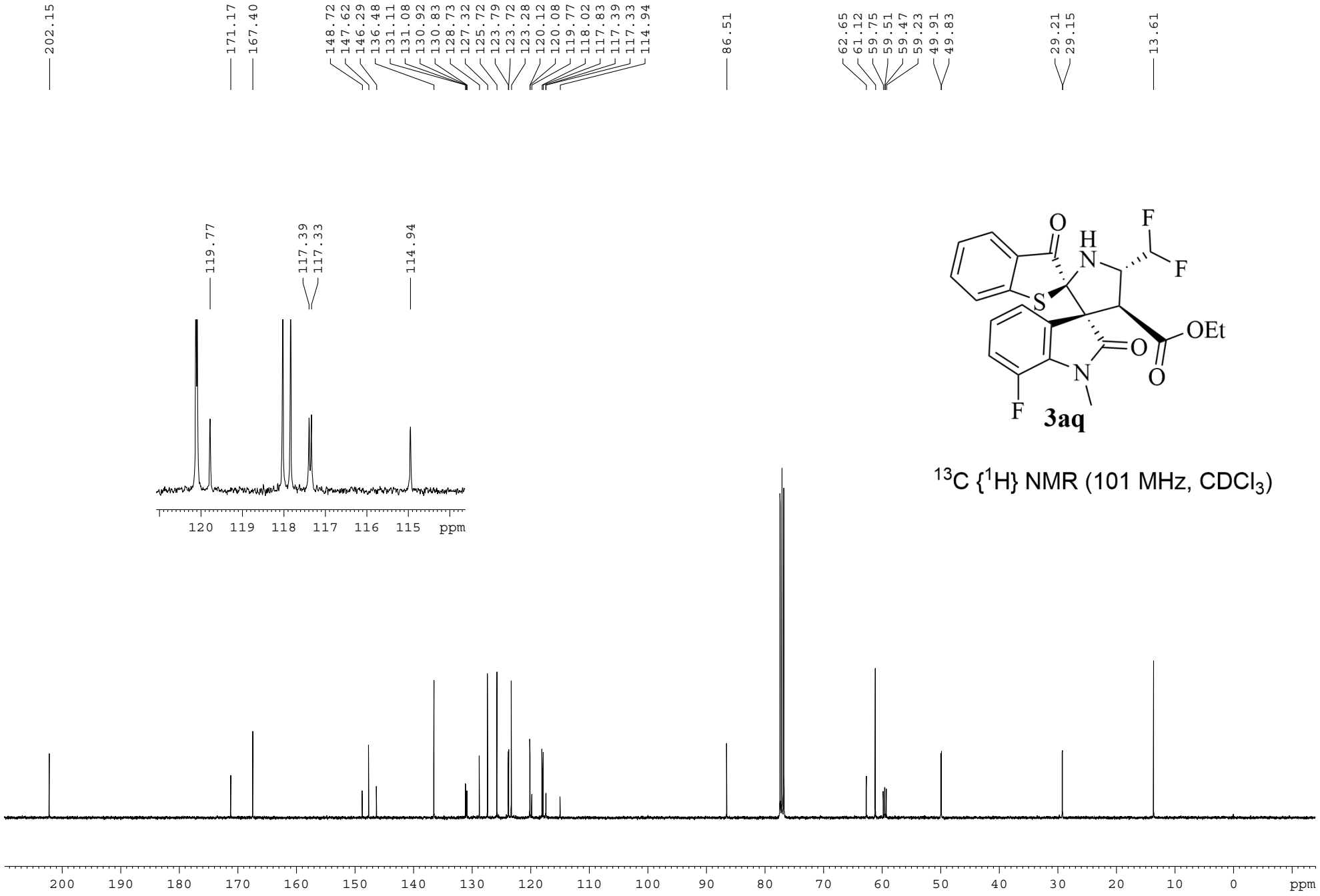


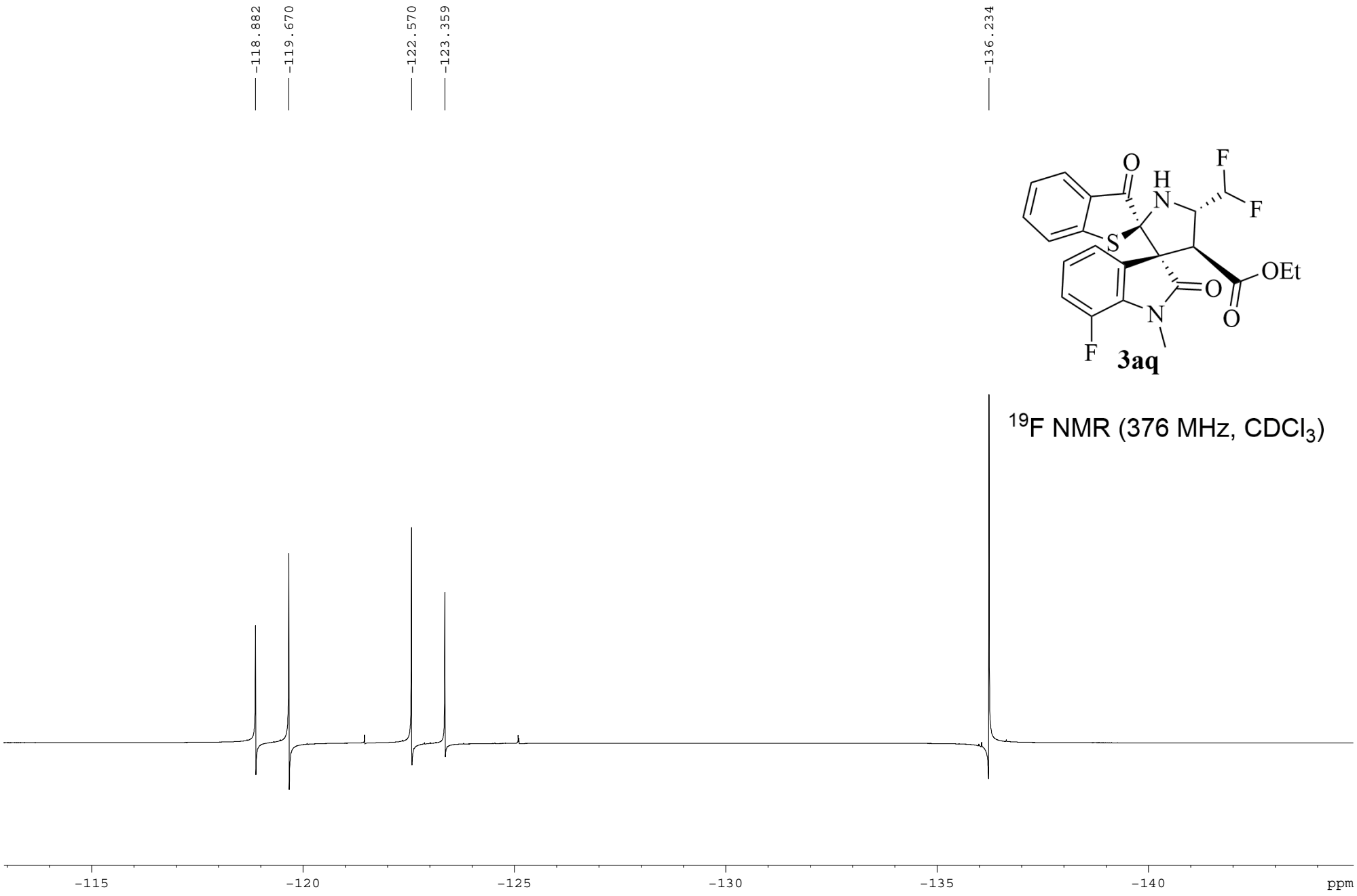


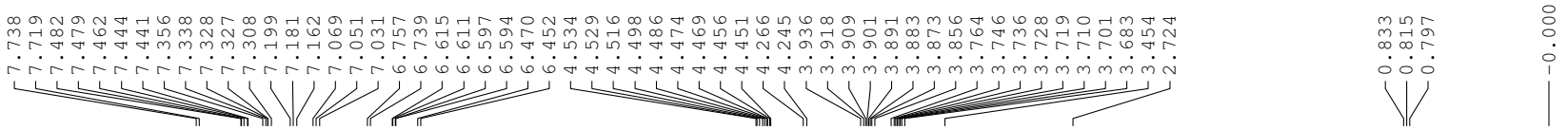
3aq

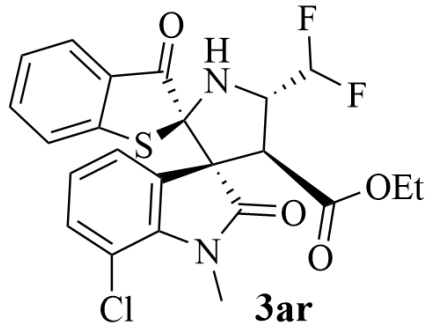
^{1}H NMR (400 MHz, $CDCl_3$)




202.15
171.17
167.40
148.72
147.62
146.29
136.48
131.11
131.08
130.92
130.83
128.73
127.32
125.72
123.79
123.72
123.28
120.12
120.08
119.77
118.02
117.83
117.39
117.33
114.94
86.51
62.65
61.12
59.75
59.51
59.47
59.23
49.91
49.83
29.21
29.15
13.61
119.77
117.39
117.33
114.94
120 119 118 117 116 115 ppm
O
H
N
F
F
S
OEt
O
O
N
F
3aq
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

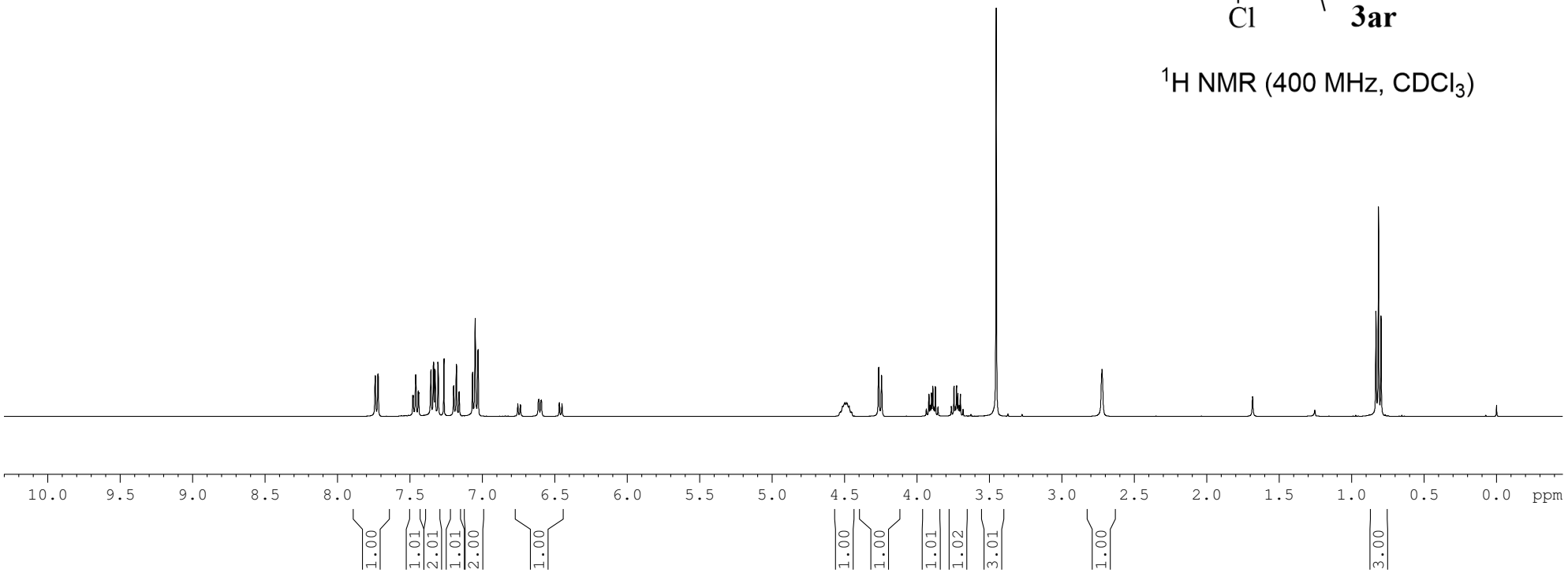

-118.882
-119.670
-122.570
-123.359
-136.234
O
H
N
F
F
S
OEt
O
O
N
F
3aq
^{19}F NMR (376 MHz, $CDCl_3$)
-115
-120
-125
-130
-135
-140
ppm

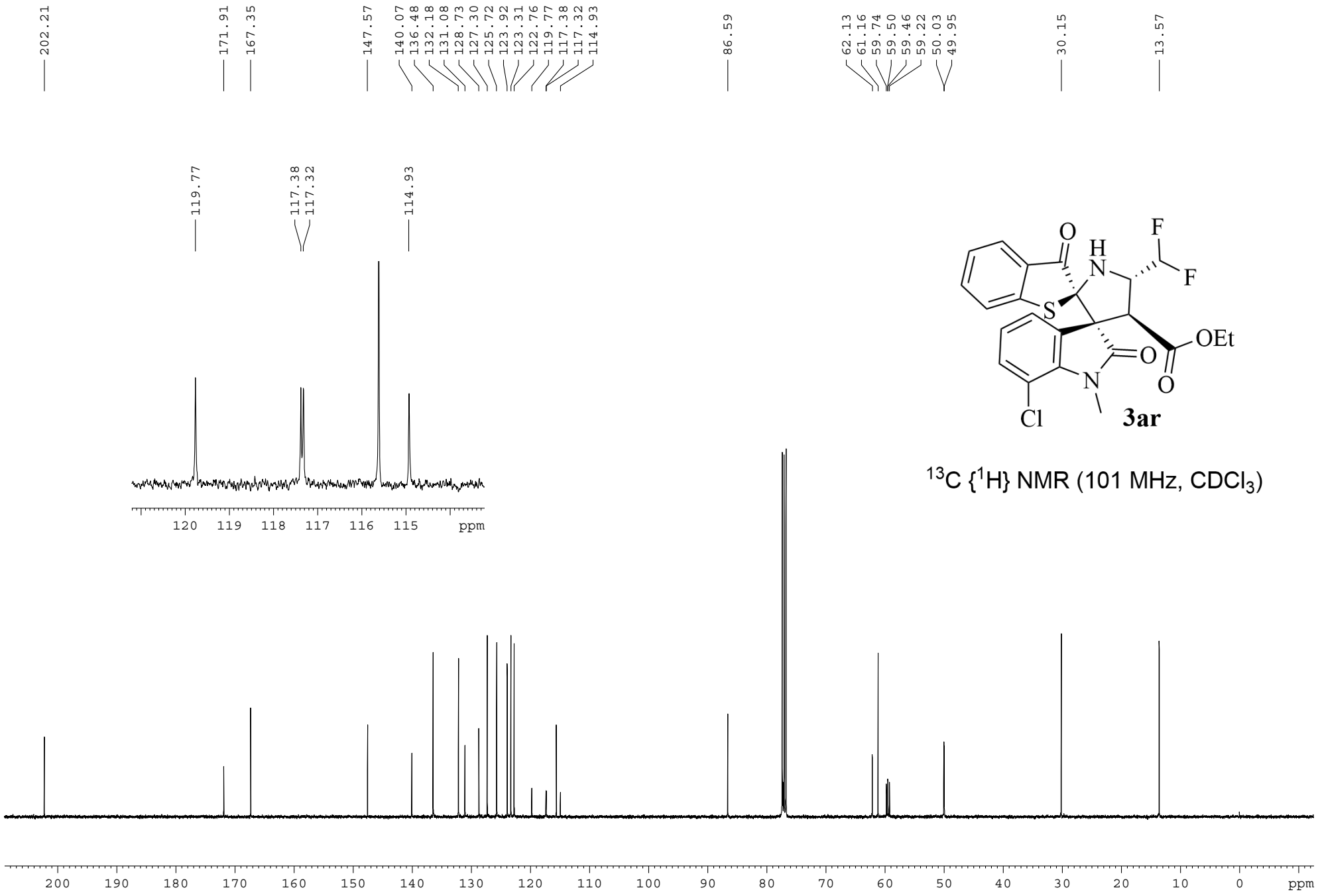


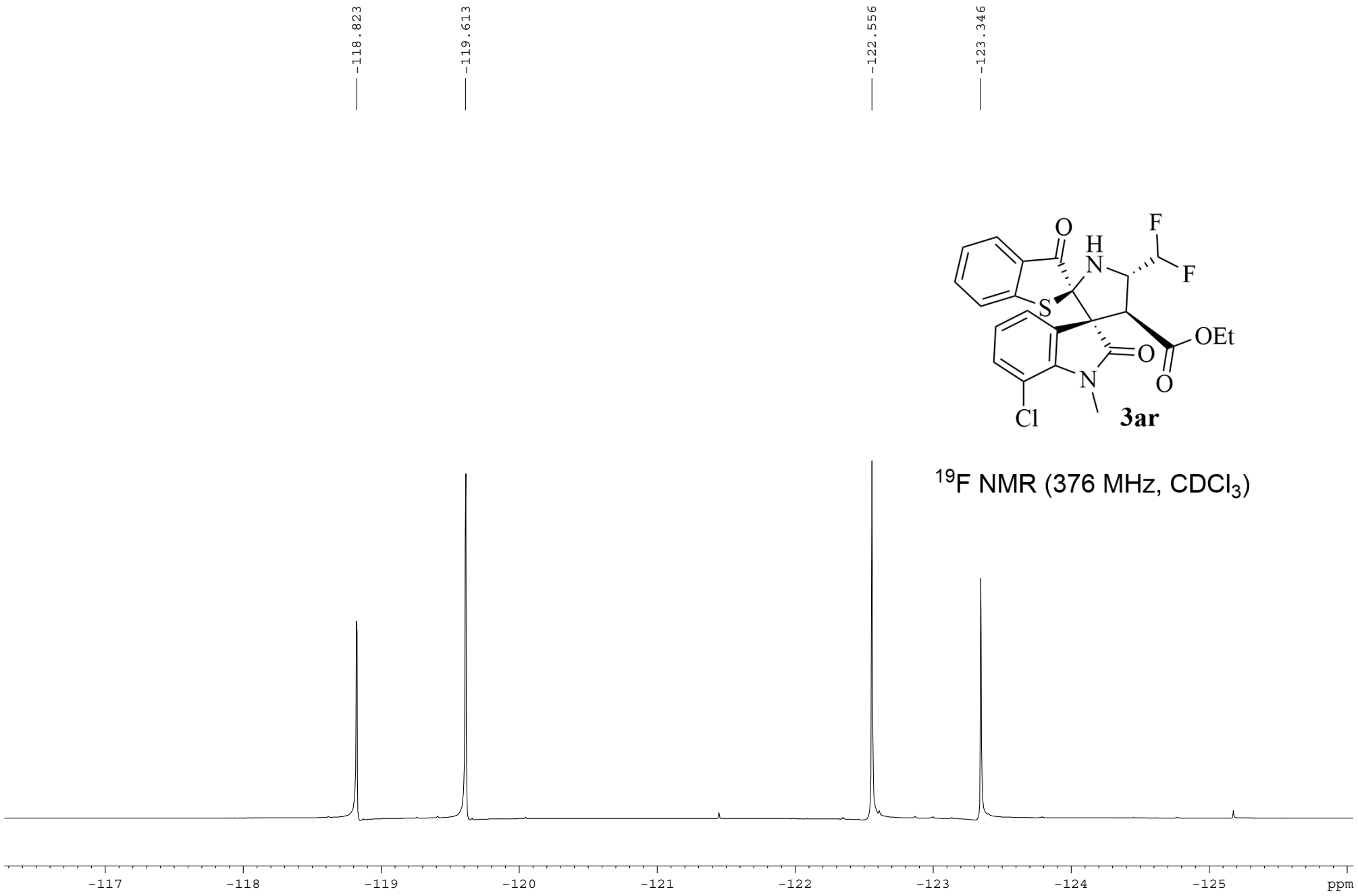


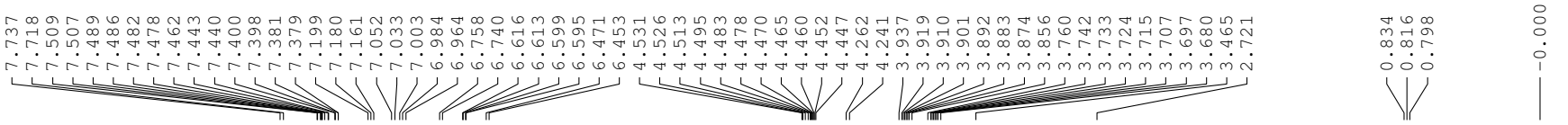
3ar

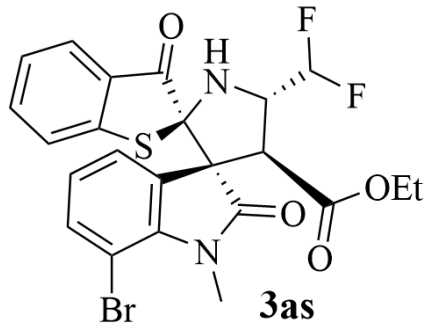
^{1}H NMR (400 MHz, $CDCl_3$)




202.21
171.91
167.35
147.57
140.07
136.48
132.18
131.08
128.73
127.30
125.72
123.92
123.31
122.76
119.77
117.38
117.32
114.93
86.59
62.13
61.16
59.74
59.50
59.46
59.22
50.03
49.95
30.15
13.57
119.77
117.38
117.32
114.93
120 119 118 117 116 115 ppm
O
H
N
F
F
S
OEt
O
O
N
Cl
3ar
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

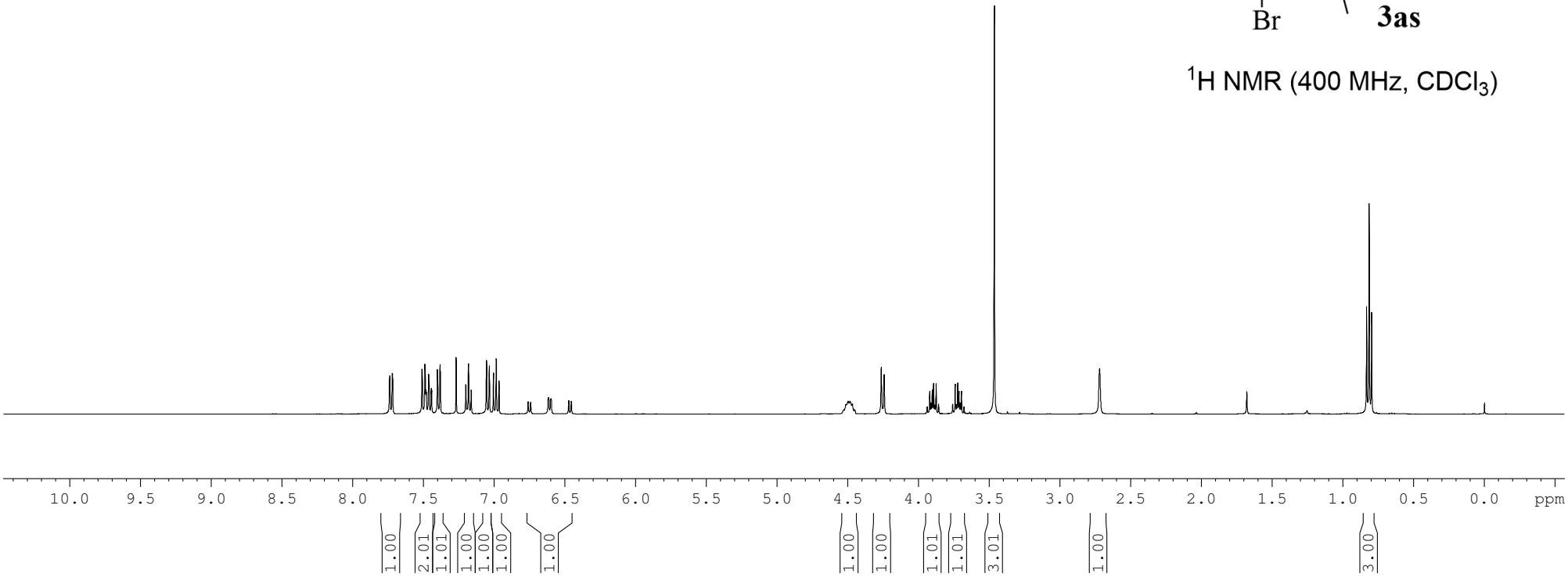

-118.823
-119.613
-122.556
-123.346
O
H
N
F
F
S
OEt
O
O
N
Cl
3ar
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
ppm

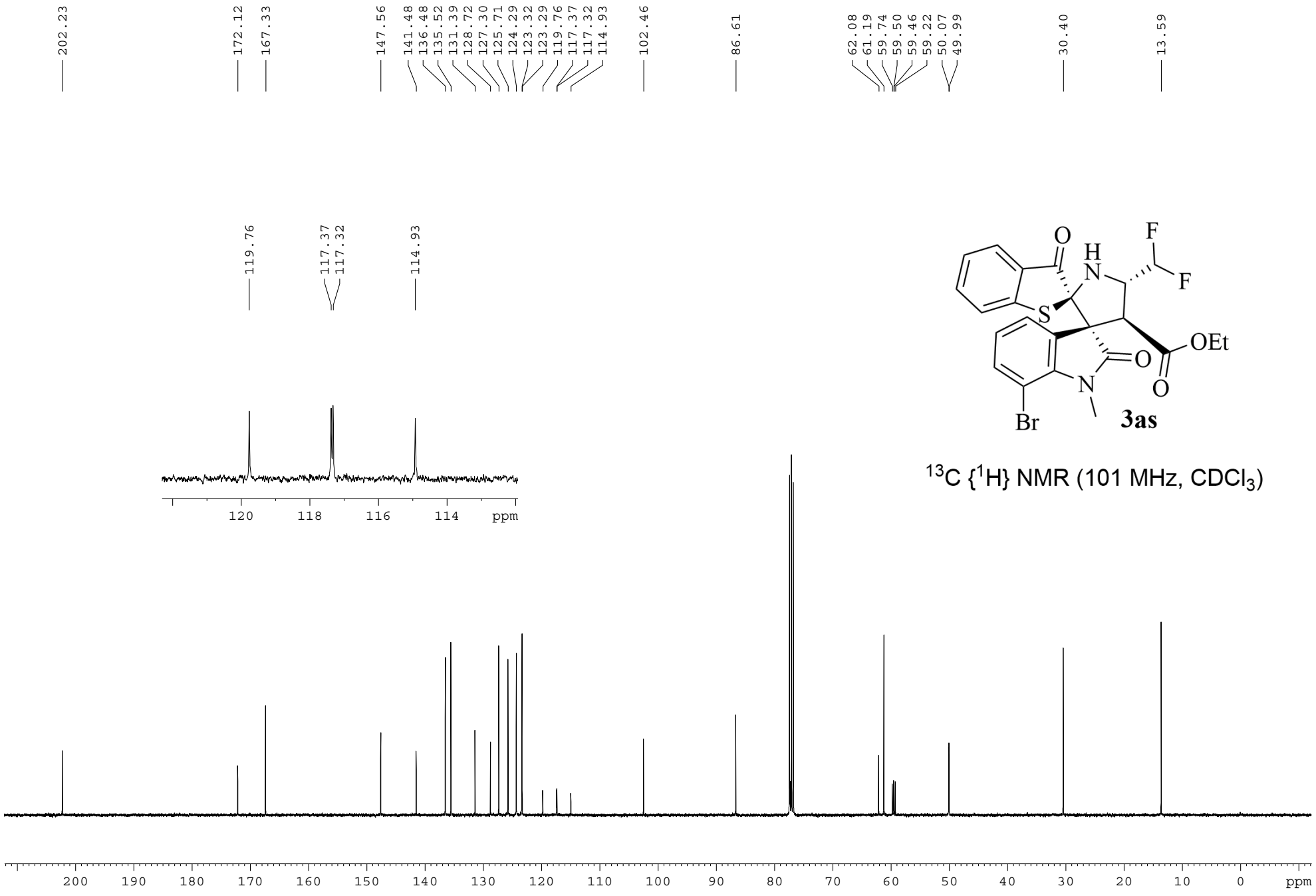


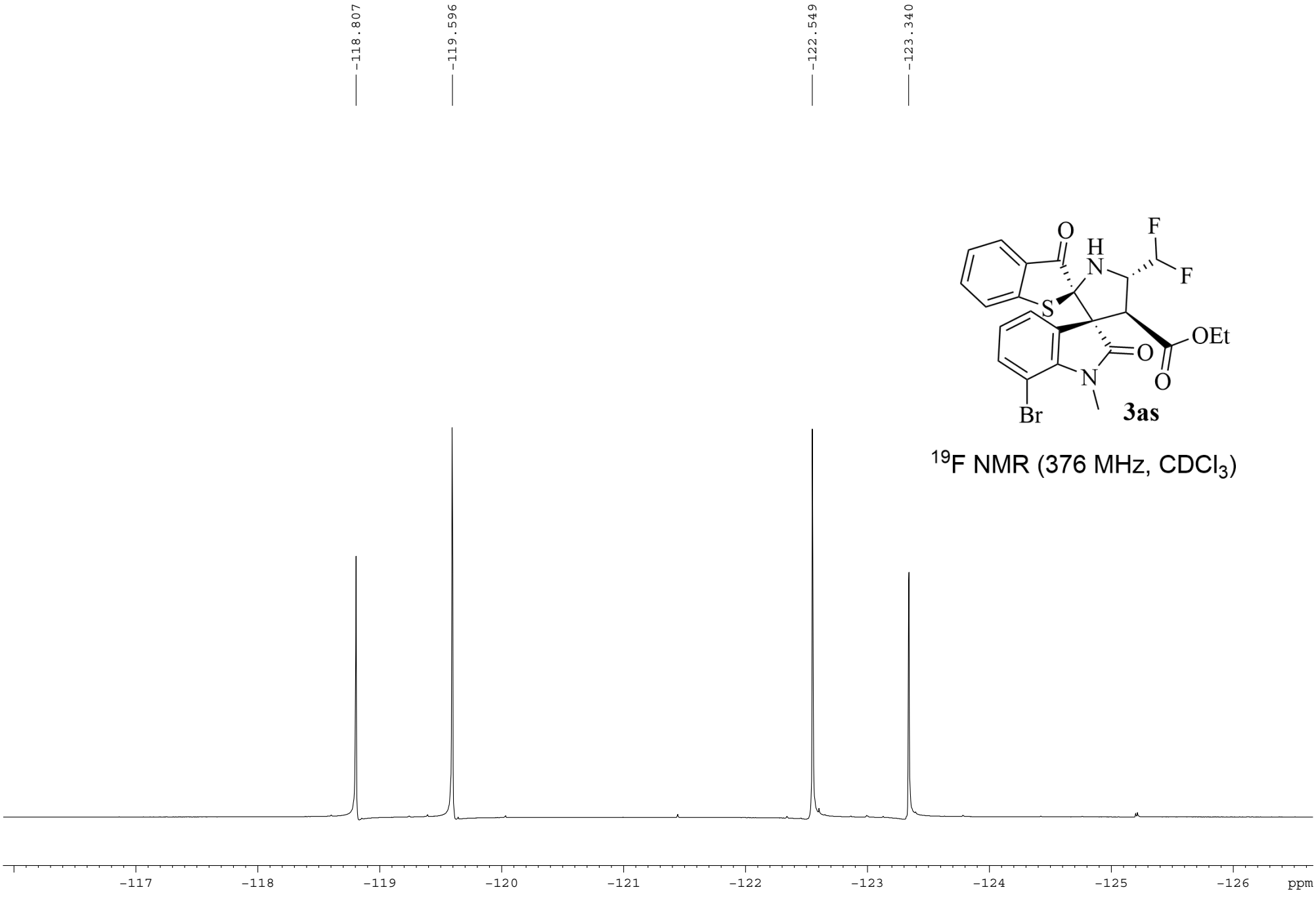


3as

^{1}H NMR (400 MHz, $CDCl_3$)

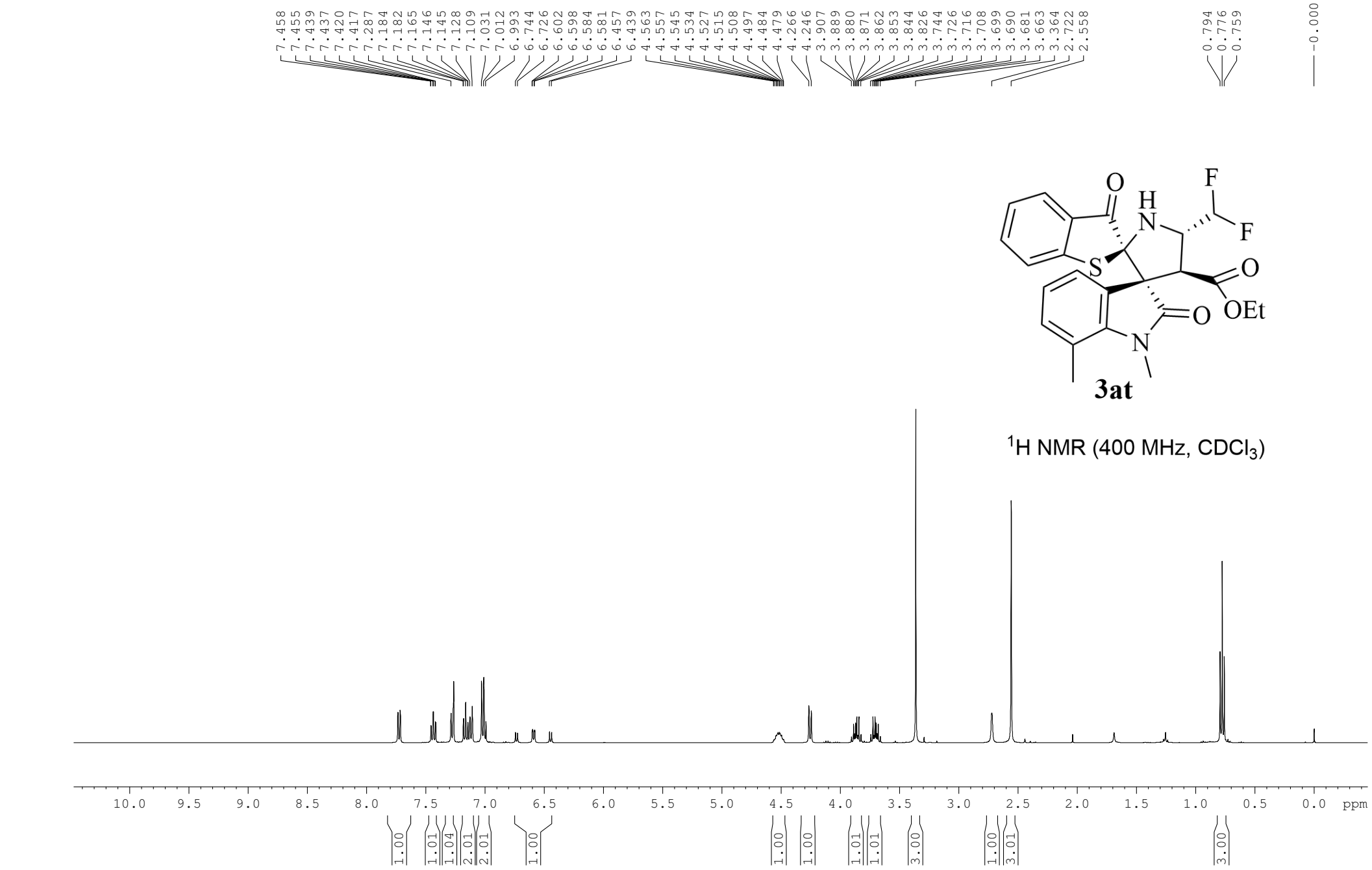


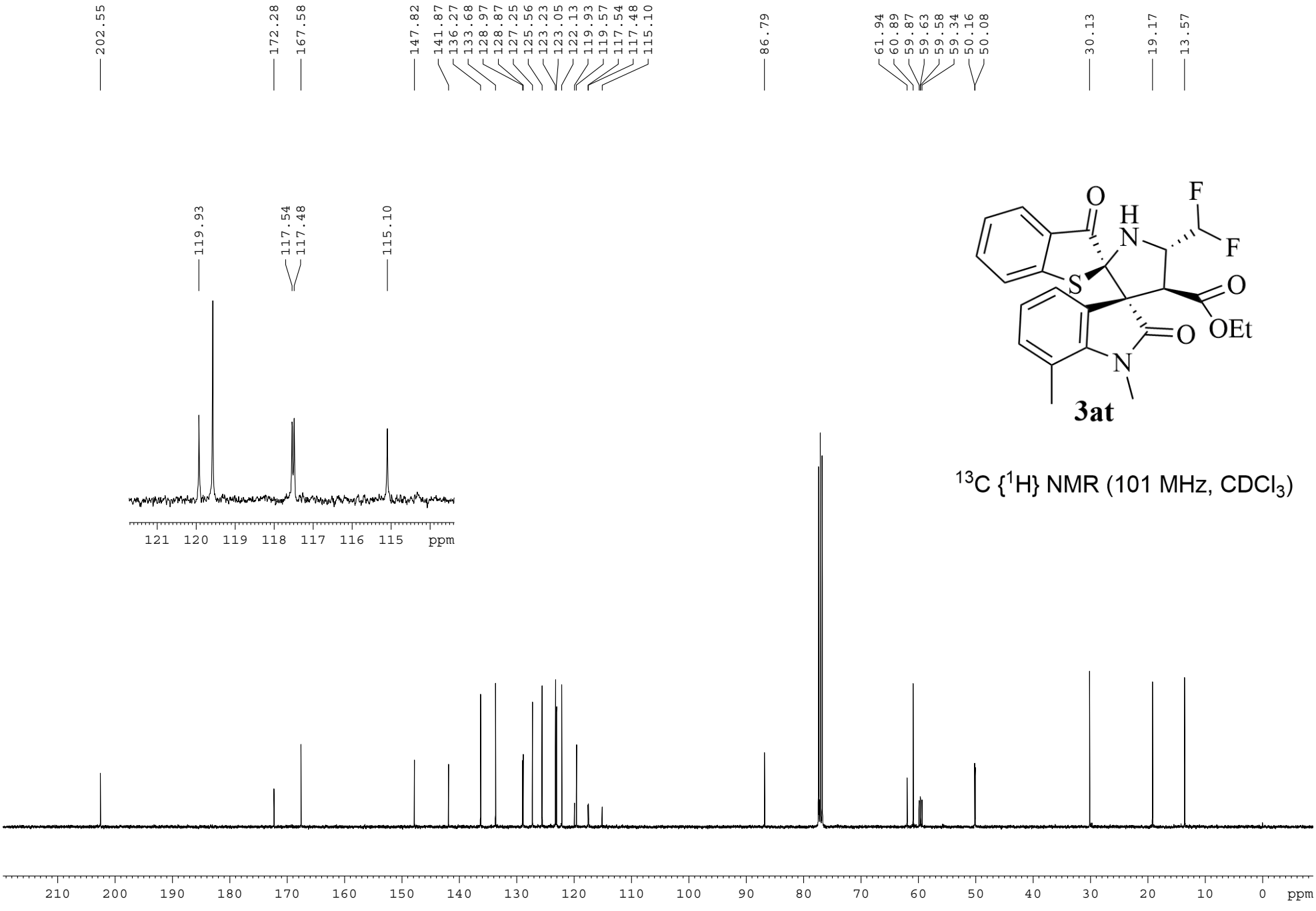

202.23
172.12
167.33
147.56
141.48
136.48
135.52
131.39
128.72
127.30
125.71
124.29
123.32
123.29
119.76
117.37
117.32
114.93
102.46
86.61
62.08
61.19
59.74
59.50
59.46
59.22
50.07
49.99
30.40
13.59
120
118
116
114
ppm
O
H
N
F
F
S
OEt
O
O
N
Br
3as
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

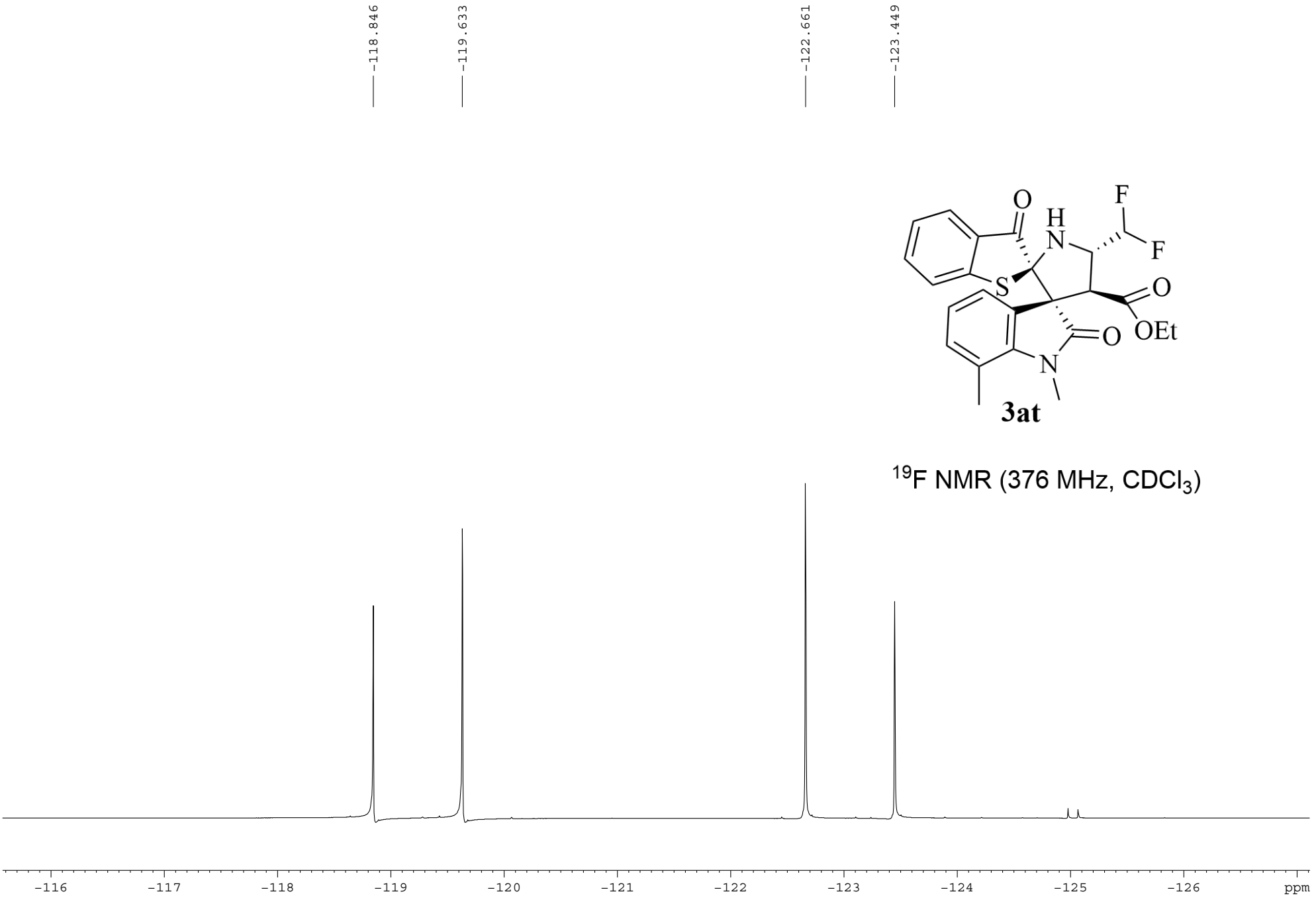


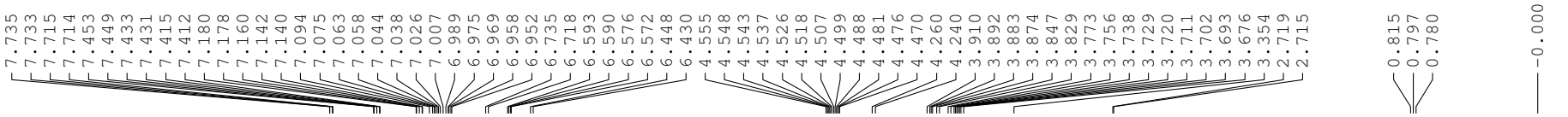
3as

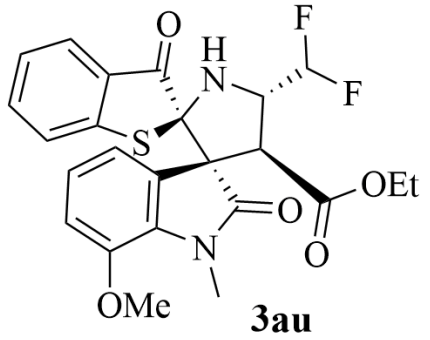
^{19}F NMR (376 MHz, $CDCl_3$)


7.458
7.455
7.439
7.437
7.420
7.417
7.287
7.184
7.182
7.165
7.146
7.145
7.128
7.109
7.031
7.012
6.993
6.744
6.726
6.602
6.598
6.584
6.581
6.457
6.439
4.563
4.557
4.545
4.534
4.527
4.515
4.508
4.497
4.484
4.479
4.266
4.246
3.907
3.889
3.880
3.871
3.862
3.853
3.844
3.826
3.744
3.726
3.716
3.708
3.699
3.690
3.681
3.663
3.364
2.722
2.558
0.794
0.776
0.759
-0.000
O
H
N
F
F
S
O
O
OEt
O
N
3at
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
1.01
1.04
2.01
2.01
1.00
1.00
1.00
1.01
1.01
3.00
1.00
3.01
3.00


202.55
172.28
167.58
147.82
141.87
136.27
133.68
128.97
128.87
127.25
125.56
123.23
123.05
122.13
119.93
119.57
117.54
117.48
115.10
86.79
61.94
60.89
59.87
59.63
59.58
59.34
50.16
50.08
30.13
19.17
13.57
119.93
117.54
117.48
115.10
121 120 119 118 117 116 115 ppm
O
H
N
F
F
S
O
O
OEt
O
N
3at
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

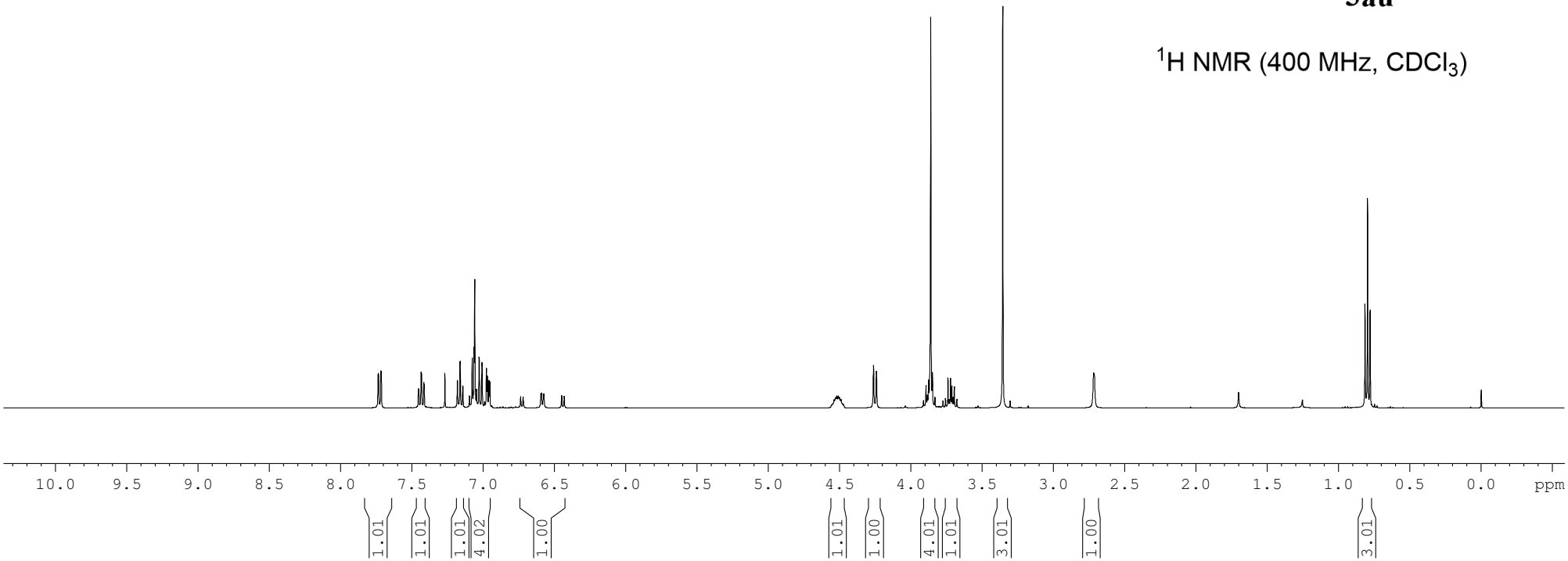

-118.846
-119.633
-122.661
-123.449
O
H
N
F
F
S
O
O
OEt
O
N
3at
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

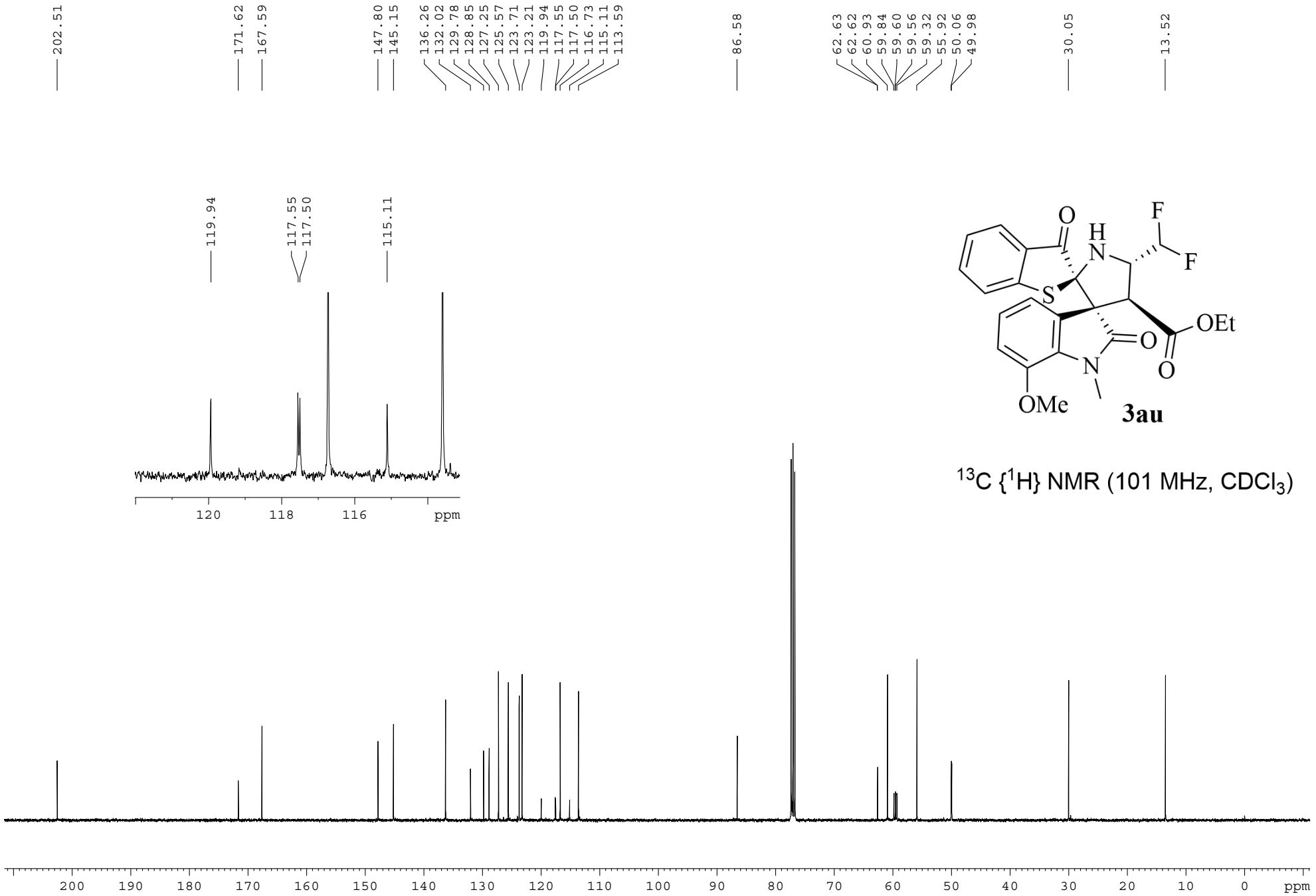


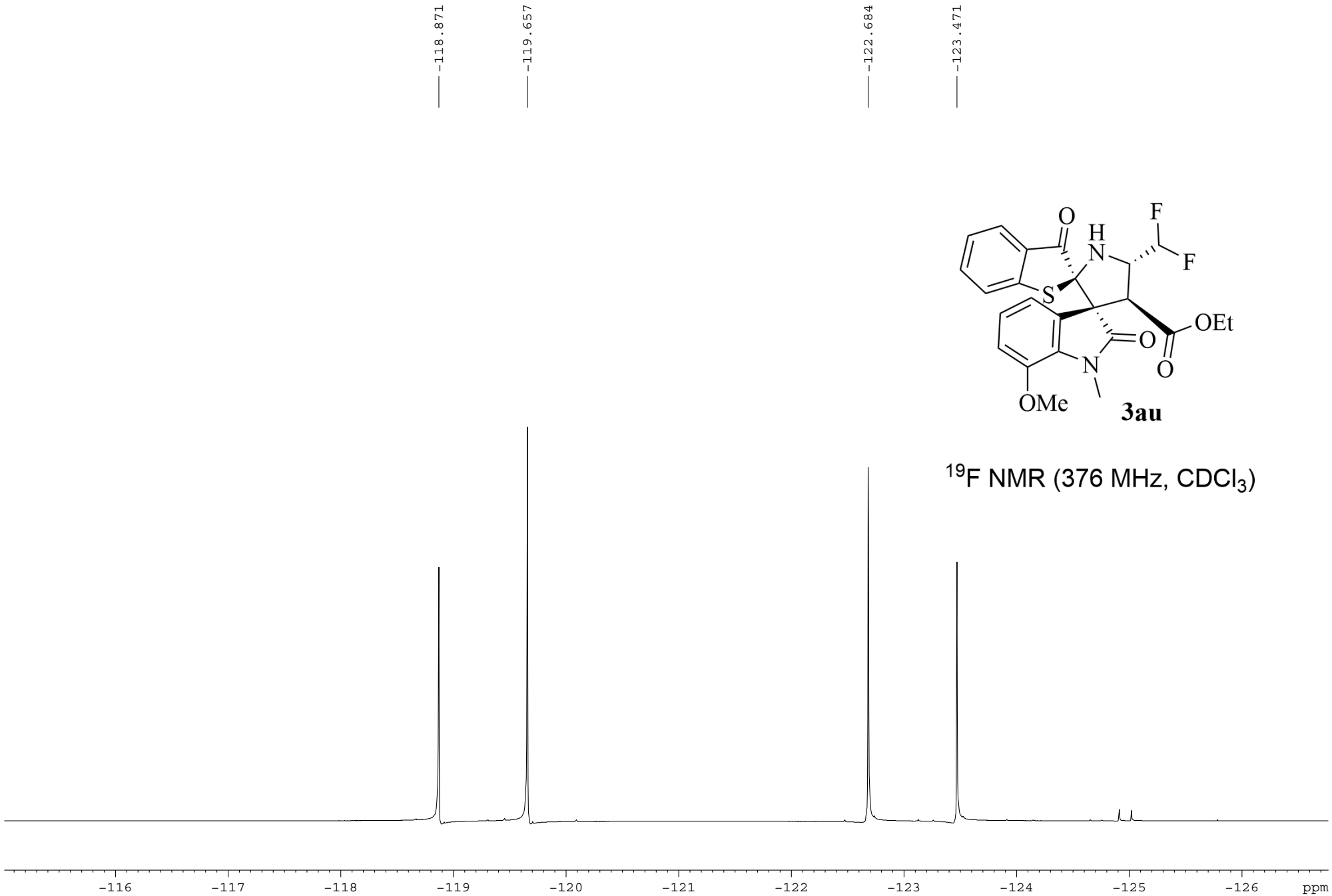


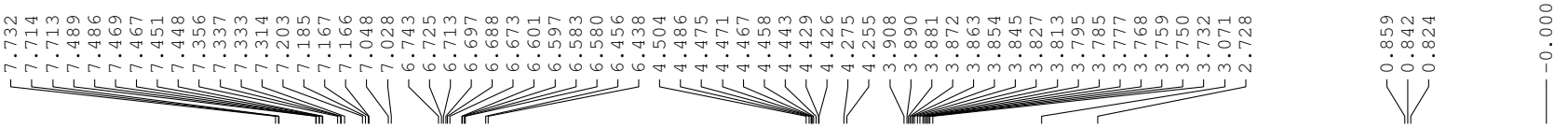
3au

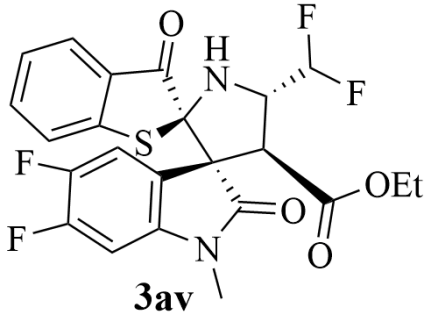
^{1}H NMR (400 MHz, $CDCl_3$)




202.51
171.62
167.59
147.80
145.15
136.26
132.02
129.78
128.85
127.25
125.57
123.71
123.21
119.94
117.55
117.50
116.73
115.11
113.59
86.58
62.63
62.62
60.93
59.84
59.60
59.56
59.32
55.92
50.06
49.98
30.05
13.52
119.94
117.55
117.50
115.11
120
118
116
ppm
O
H
N
F
F
S
OEt
O
O
N
OMe
3au
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

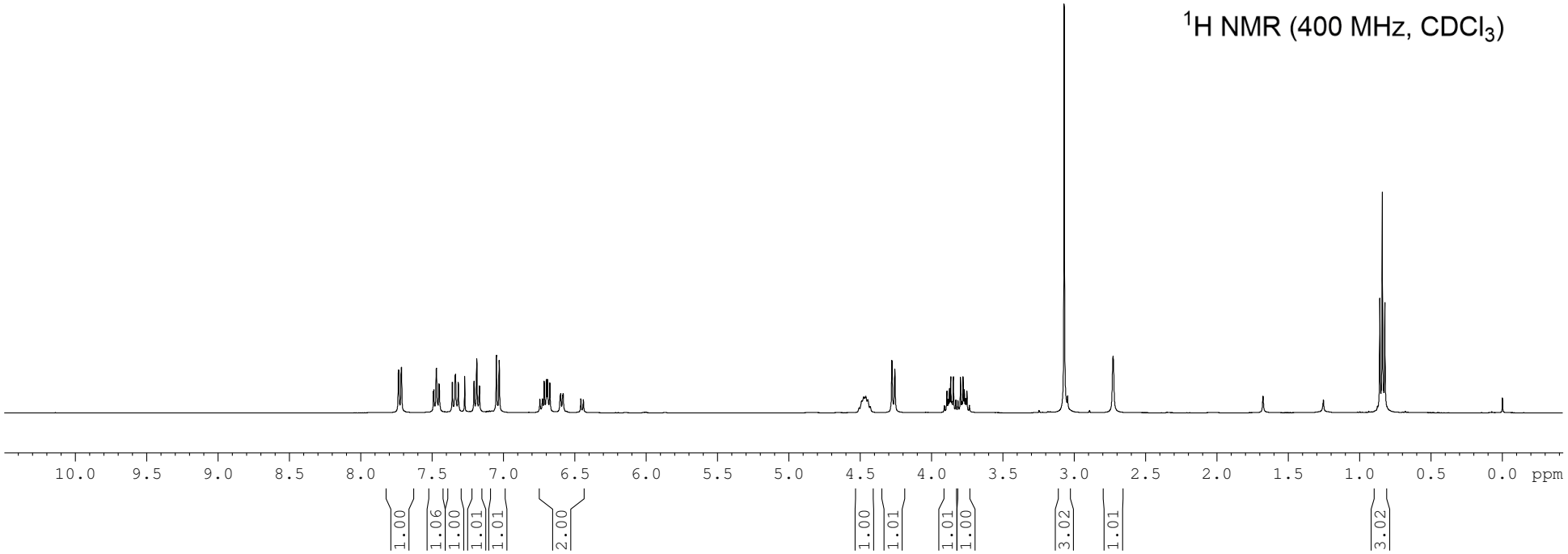

-118.871
-119.657
-122.684
-123.471
O
H
N
F
F
S
OEt
O
O
N
OMe
3au
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

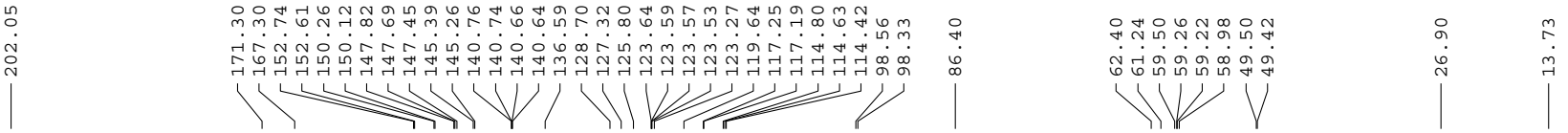


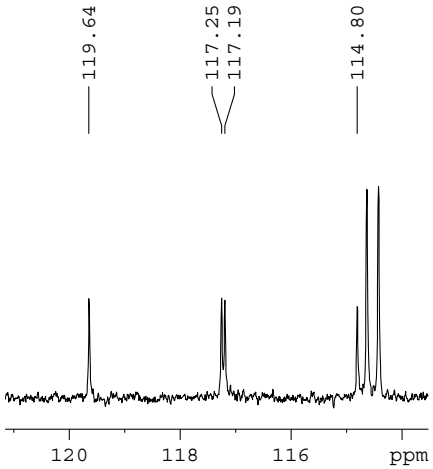


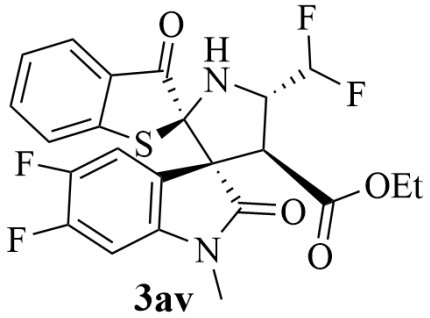
3av

^{1}H NMR (400 MHz, $CDCl_3$)



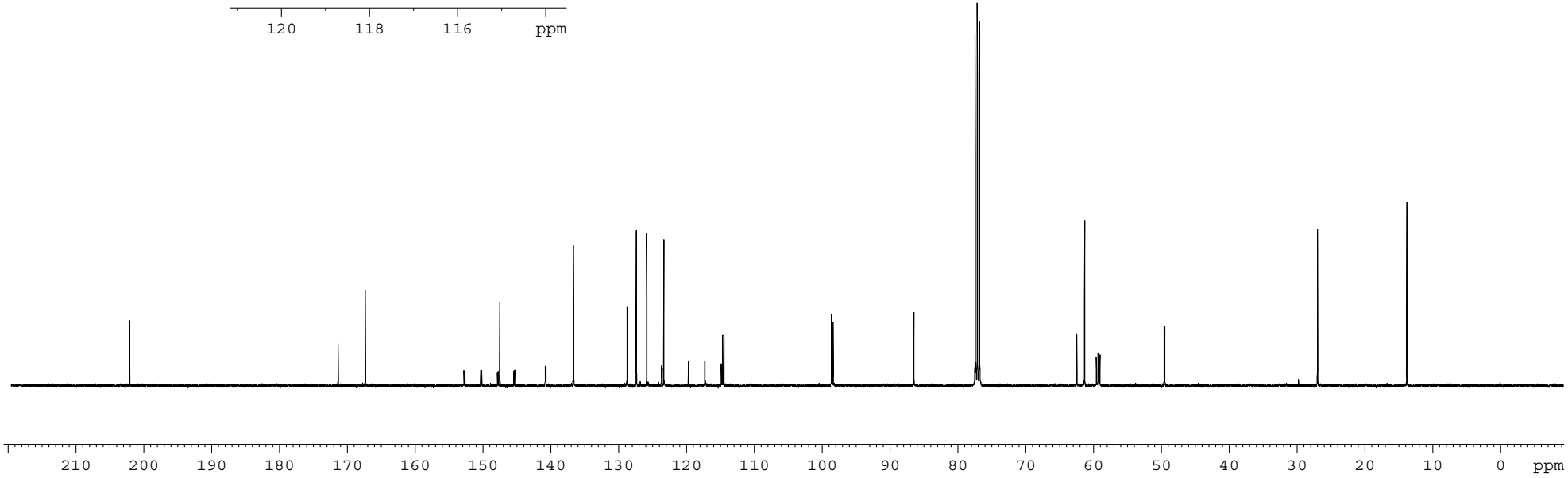


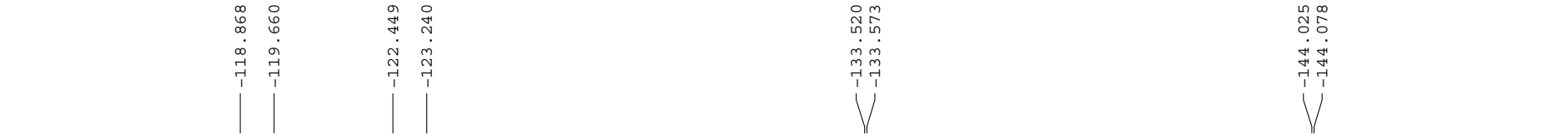


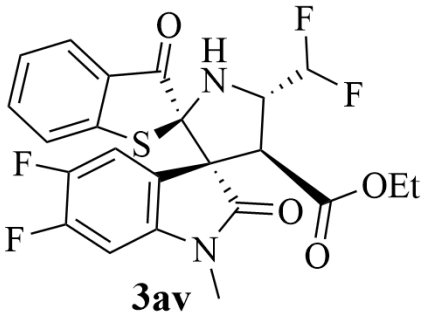


3av

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)

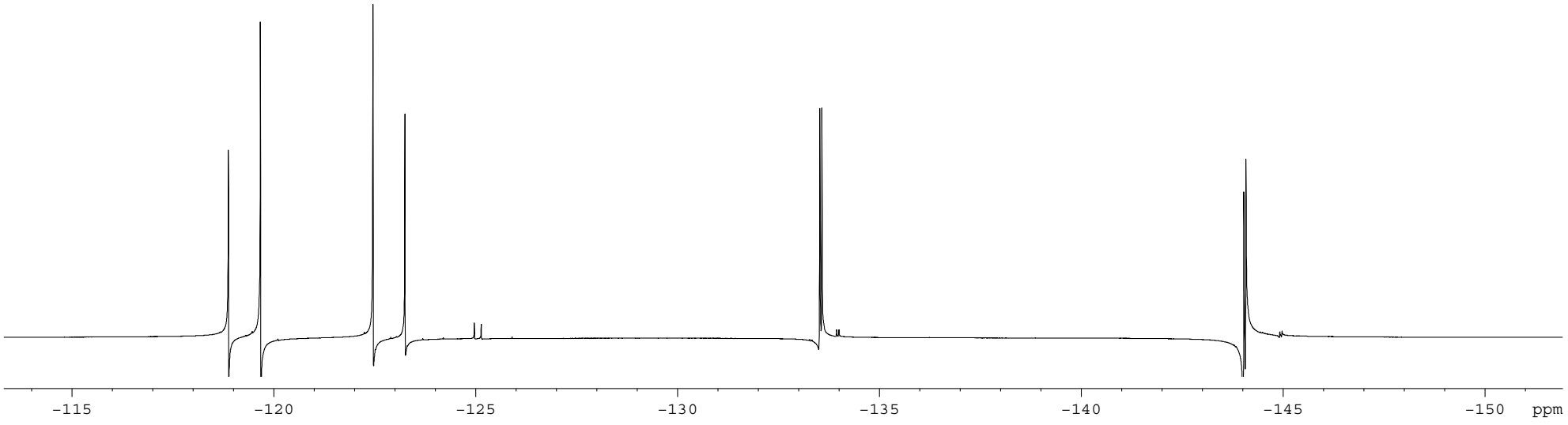


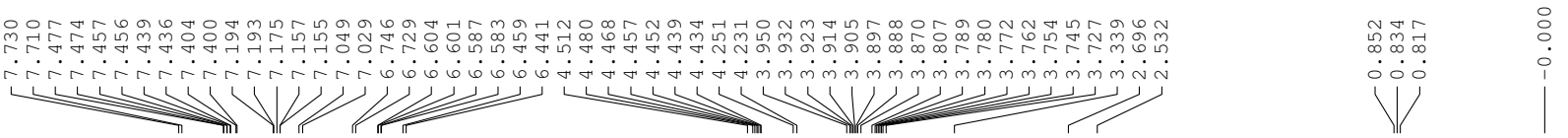


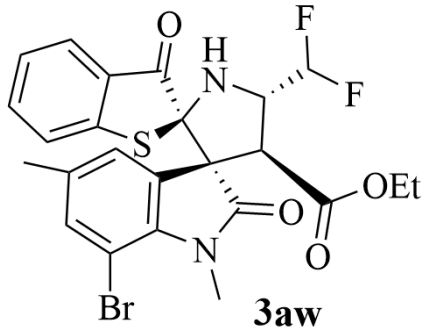


3av

^{19}F NMR (376 MHz, $CDCl_3$)

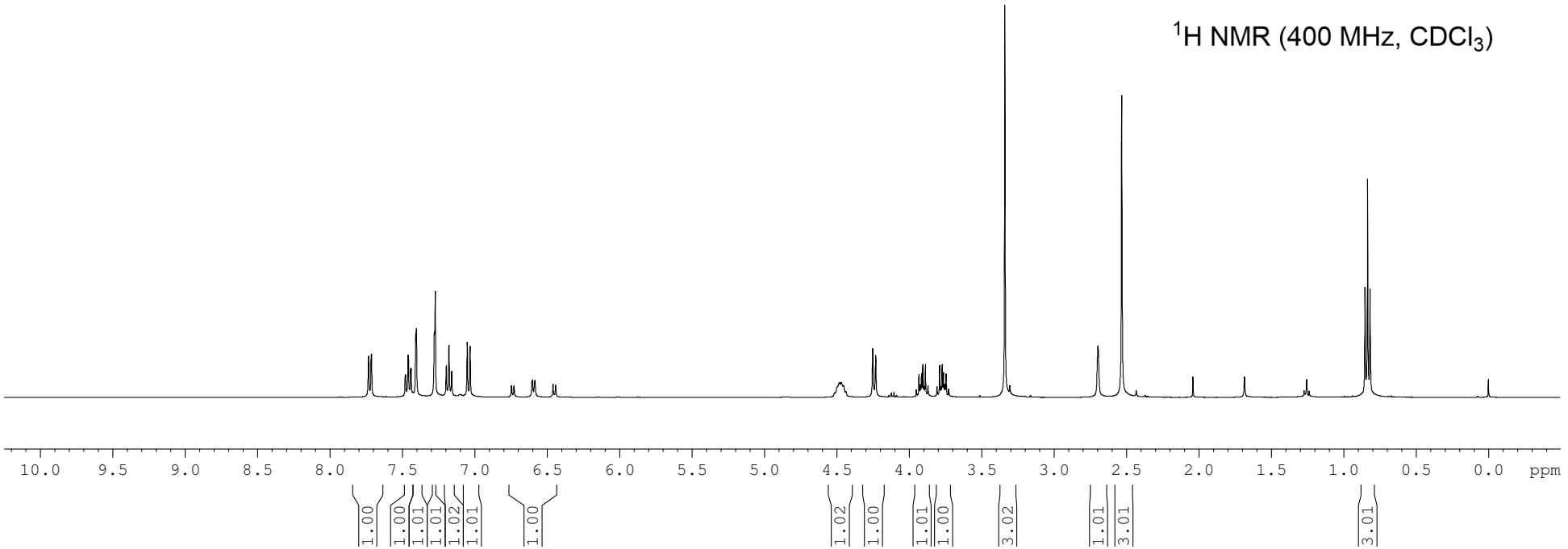


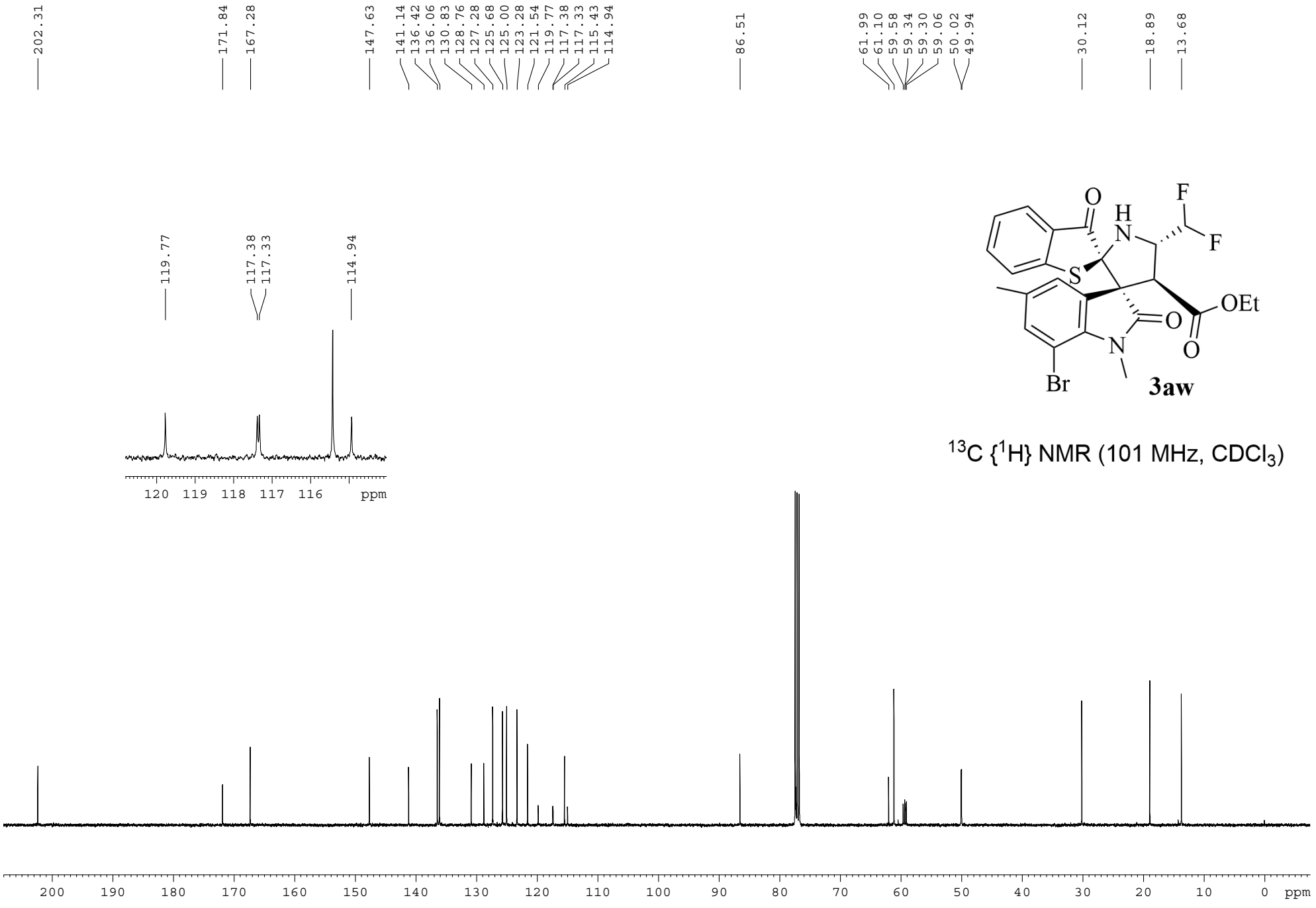


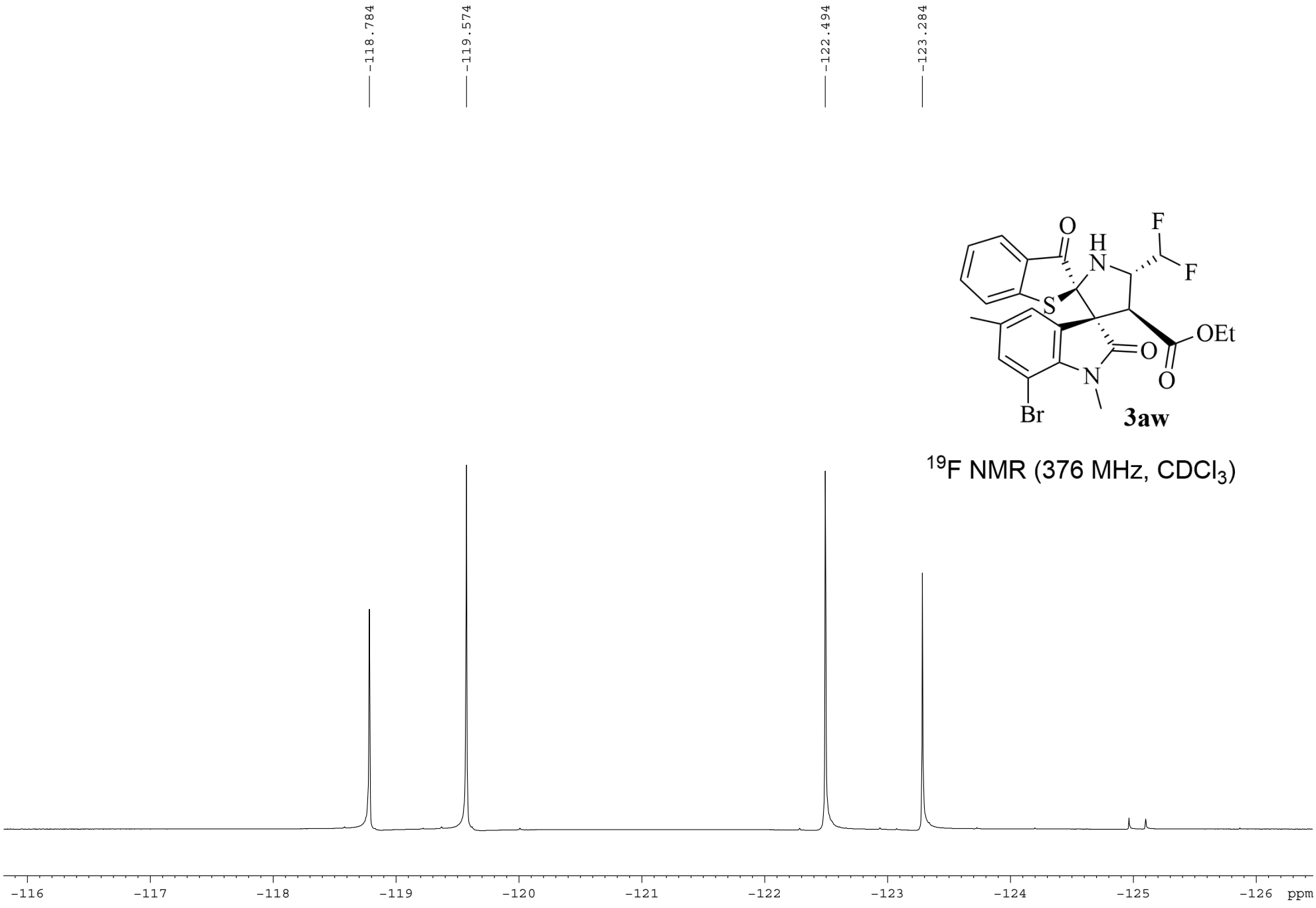


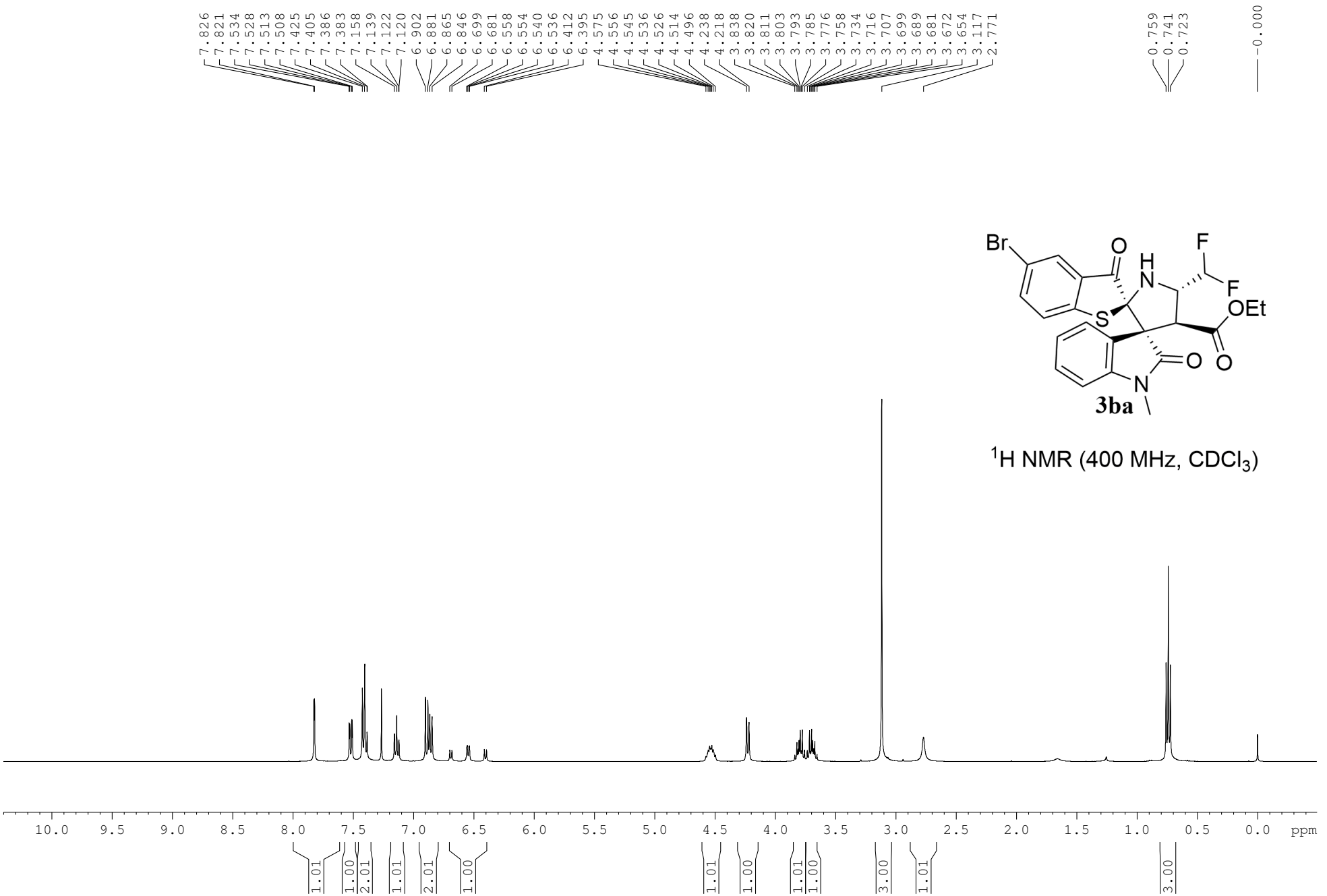
3aw

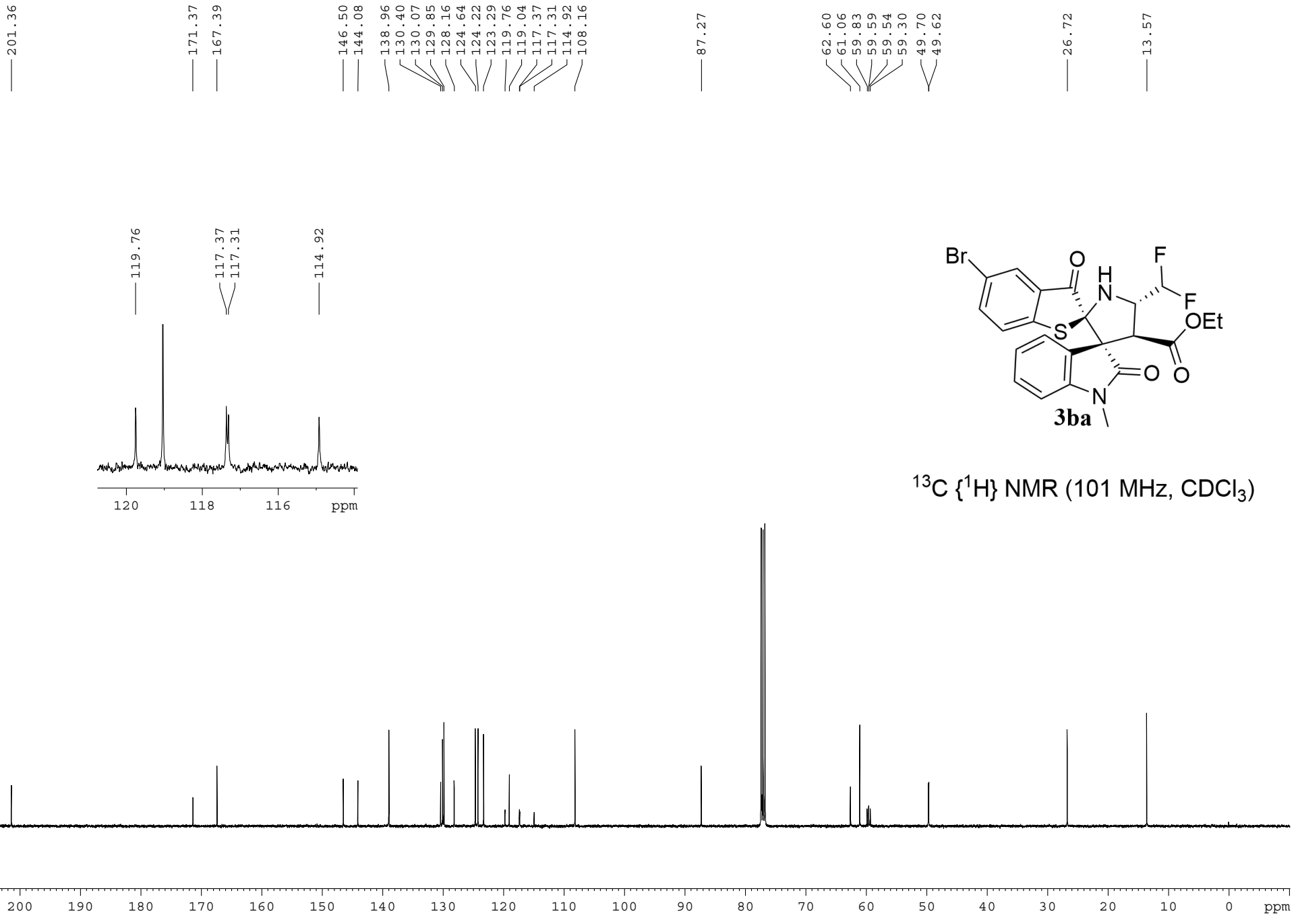
^{1}H NMR (400 MHz, $CDCl_3$)

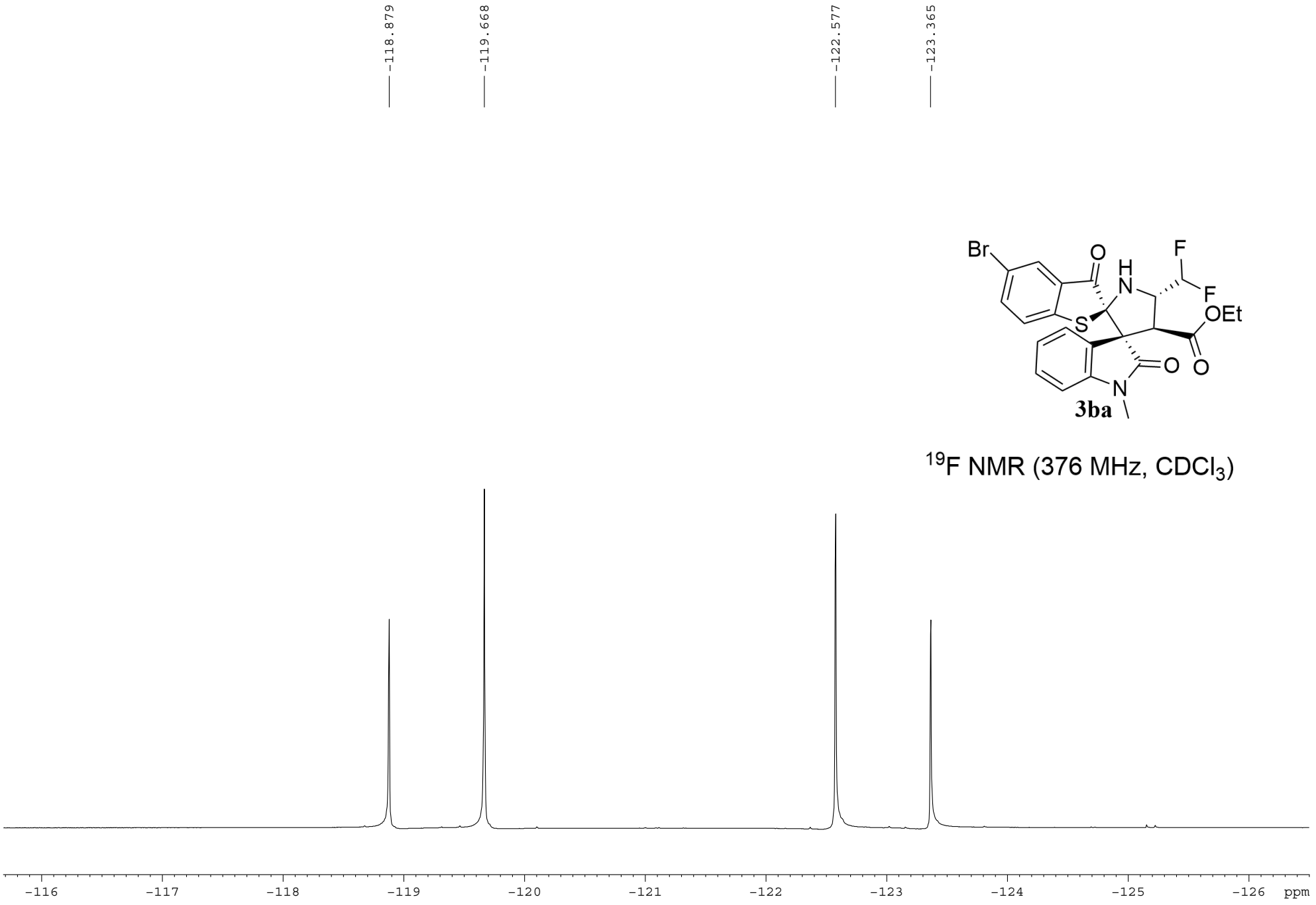


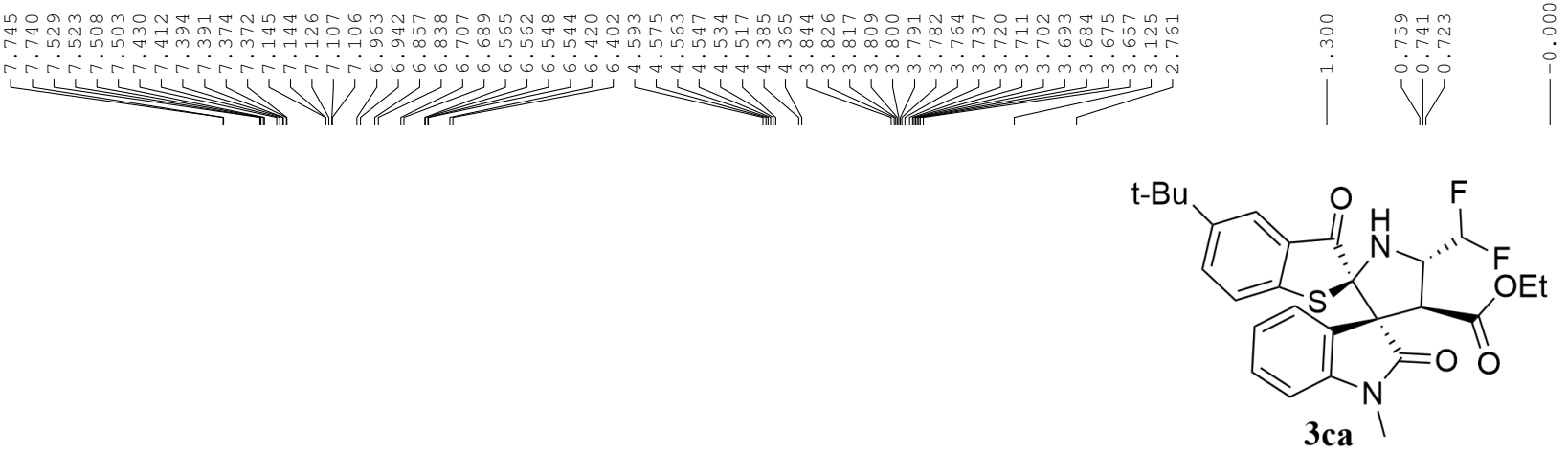

202.31
171.84
167.28
147.63
141.14
136.42
136.06
130.83
128.76
127.28
125.68
125.00
123.28
121.54
119.77
117.38
117.33
115.43
114.94
86.51
61.99
61.10
59.58
59.34
59.30
59.06
50.02
49.94
30.12
18.89
13.68
119.77
117.38
117.33
114.94
120 119 118 117 116 ppm
O
H
N
F
F
S
OEt
O
O
N
O
Br
3aw
13C {1H} NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


-118.784
-119.574
-122.494
-123.284
O
H
N
F
F
S
OEt
O
O
N
Br
3aw
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

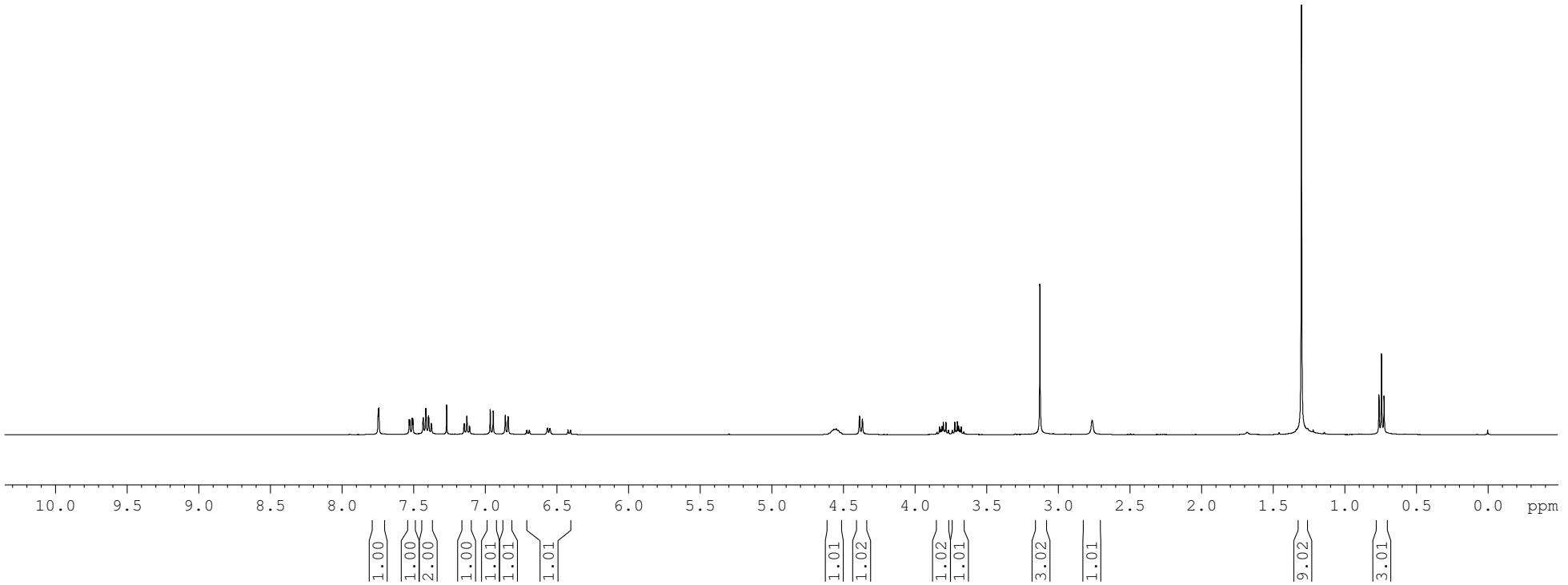

7.826
7.821
7.534
7.528
7.513
7.508
7.425
7.405
7.386
7.383
7.158
7.139
7.122
7.120
6.902
6.881
6.865
6.846
6.699
6.681
6.558
6.554
6.540
6.536
6.412
6.395
4.575
4.556
4.545
4.536
4.526
4.514
4.496
4.238
4.218
3.838
3.820
3.811
3.803
3.793
3.785
3.776
3.758
3.734
3.716
3.707
3.699
3.689
3.681
3.672
3.654
3.117
2.771
0.759
0.741
0.723
0.000
Br
O
H
N
F
F
OEt
S
O
O
O
N
3ba
^{1}H NMR (400 MHz, $CDCl_3$)
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
ppm
1.01
1.00
2.01
1.01
2.01
1.00
1.01
1.00
1.01
1.00
3.00
1.01
3.00

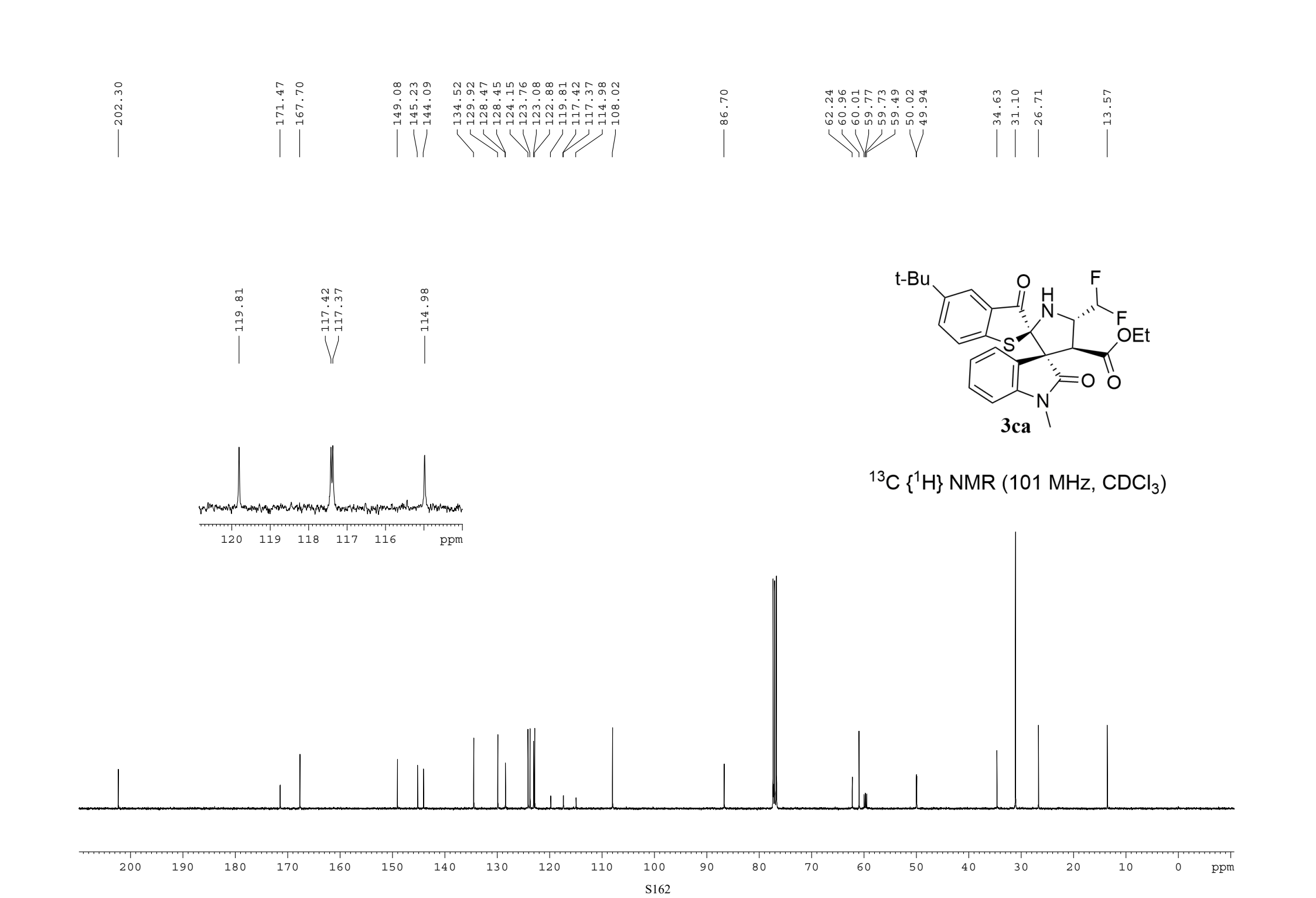

201.36
171.37
167.39
146.50
144.08
138.96
130.40
130.07
129.85
128.16
124.64
124.22
123.29
119.76
119.04
117.37
117.31
114.92
108.16
87.27
62.60
61.06
59.83
59.59
59.54
59.30
49.70
49.62
26.72
13.57
119.76
117.37
117.31
114.92
120
118
116
ppm
Br
O
H
N
F
F
OEt
S
O
O
O
N
3ba
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

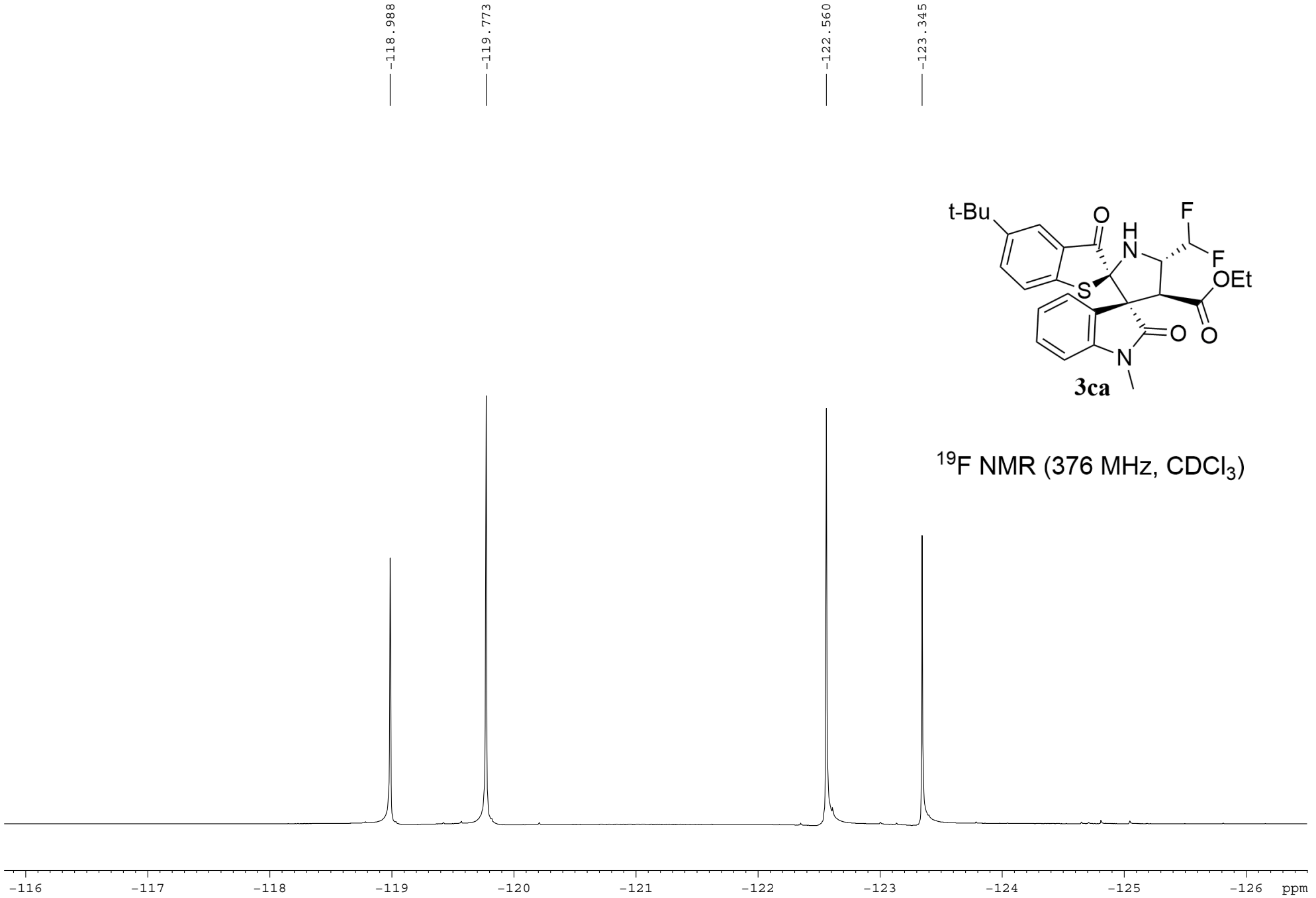

-118.879
-119.668
-122.577
-123.365
Br
O
H
N
F
F
OEt
S
O
O
O
N
3ba
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

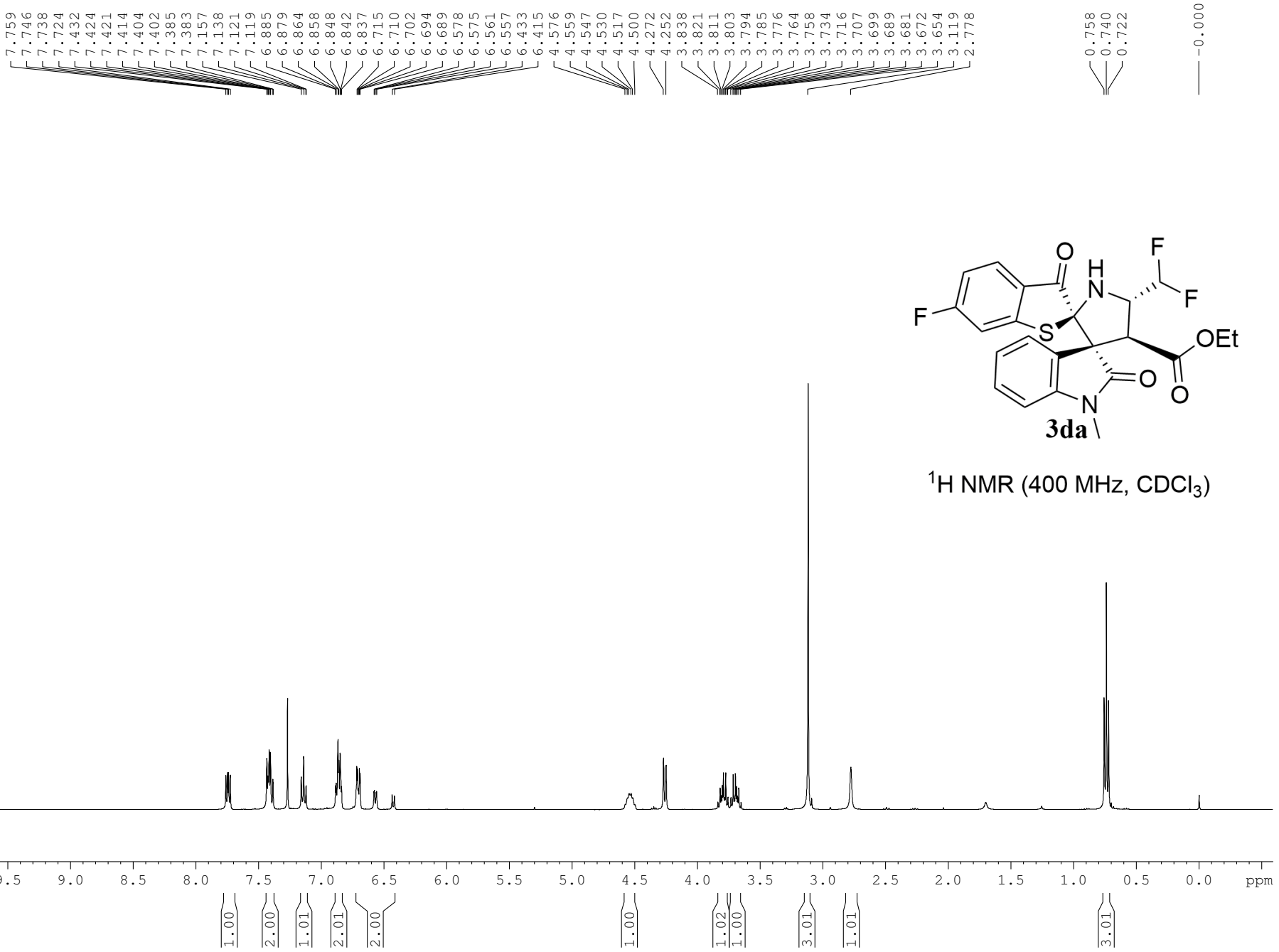


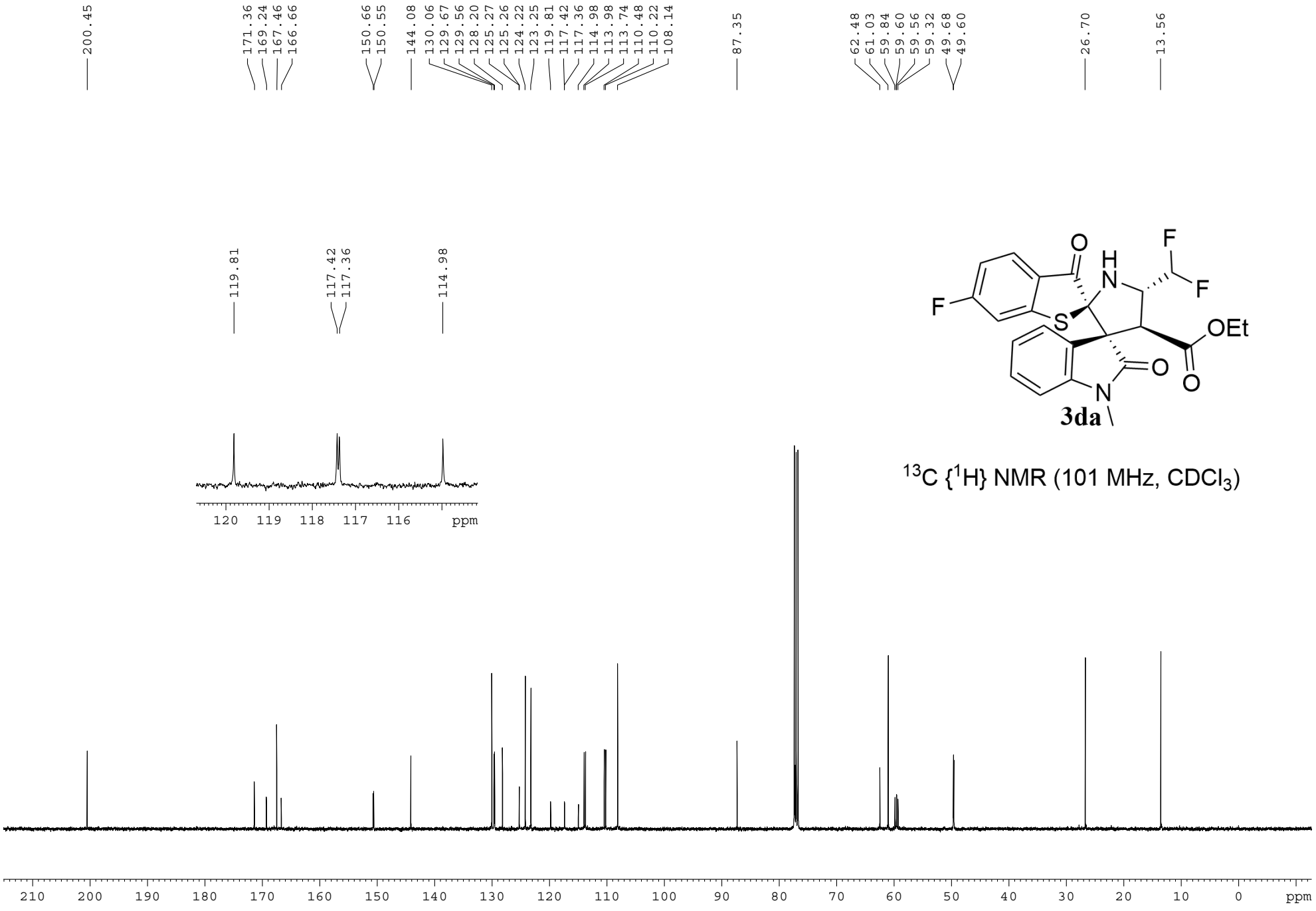
^{1}H NMR (400 MHz, $CDCl_3$)



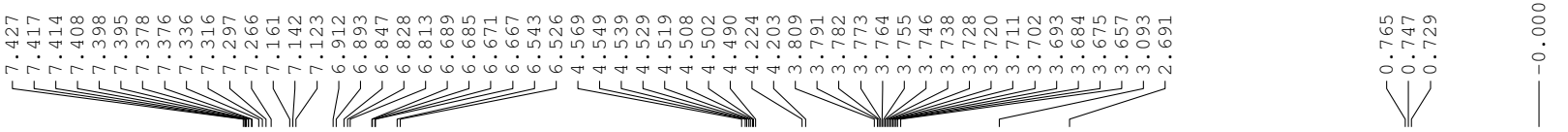

202.30
171.47
167.70
149.08
145.23
144.09
134.52
129.92
128.47
128.45
124.15
123.76
123.08
122.88
119.81
117.42
117.37
114.98
108.02
86.70
62.24
60.96
60.01
59.77
59.73
59.49
50.02
49.94
34.63
31.10
26.71
13.57
119.81
117.42
117.37
114.98
120
119
118
117
116
ppm
t-Bu
O
H
N
F
F
OEt
S
O
O
O
N
3ca
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

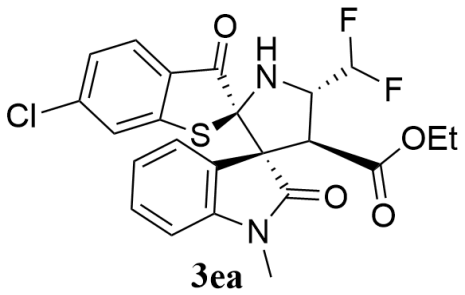

-118.988
-119.773
-122.560
-123.345
t-Bu
O
H
N
F
F
OEt
S
O
O
O
N
3ca
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.759
7.746
7.738
7.724
7.432
7.424
7.421
7.414
7.404
7.402
7.385
7.383
7.157
7.138
7.121
7.119
6.885
6.879
6.864
6.858
6.848
6.842
6.837
6.715
6.710
6.702
6.694
6.689
6.578
6.575
6.561
6.557
6.433
6.415
4.576
4.559
4.547
4.530
4.517
4.500
4.272
4.252
3.838
3.821
3.811
3.803
3.794
3.785
3.776
3.764
3.758
3.734
3.716
3.707
3.699
3.689
3.681
3.672
3.654
3.119
2.778
0.758
0.740
0.722
0.000
O
H
N
F
F
F
S
OEt
O
O
O
N
3da
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
2.00
1.01
2.01
2.00
1.00
1.02
1.00
3.01
1.01
3.01


200.45
171.36
169.24
167.46
166.66
150.66
150.55
144.08
130.06
129.67
129.56
128.20
125.27
125.26
124.22
123.25
119.81
117.42
117.36
114.98
113.98
113.74
110.48
110.22
108.14
87.35
62.48
61.03
59.84
59.60
59.56
59.32
49.68
49.60
26.70
13.56
119.81
117.42
117.36
114.98
120 119 118 117 116 ppm
O
H
N
F
F
F
S
OEt
O
O
O
N
3da
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

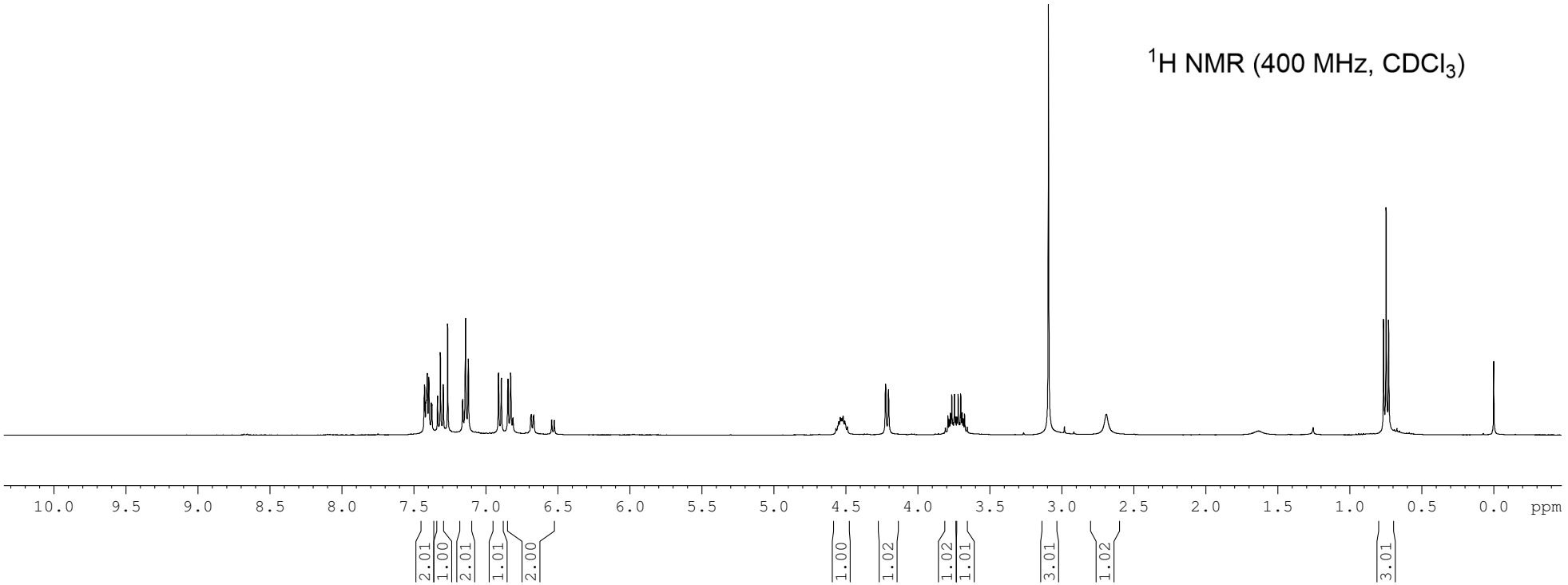
^{19}F NMR (376 MHz, $CDCl_3$)

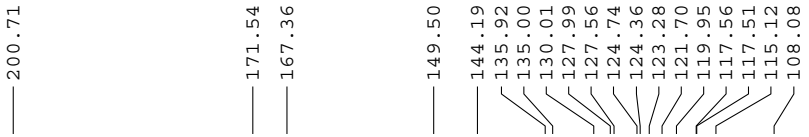


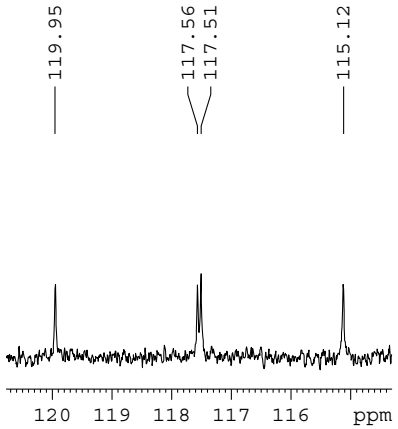


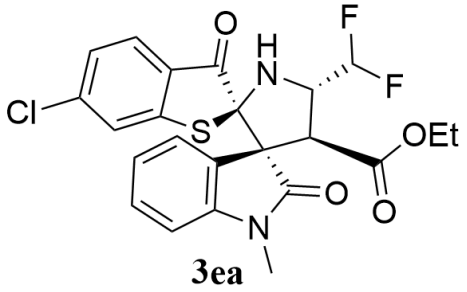
3ea

^{1}H NMR (400 MHz, $CDCl_3$)



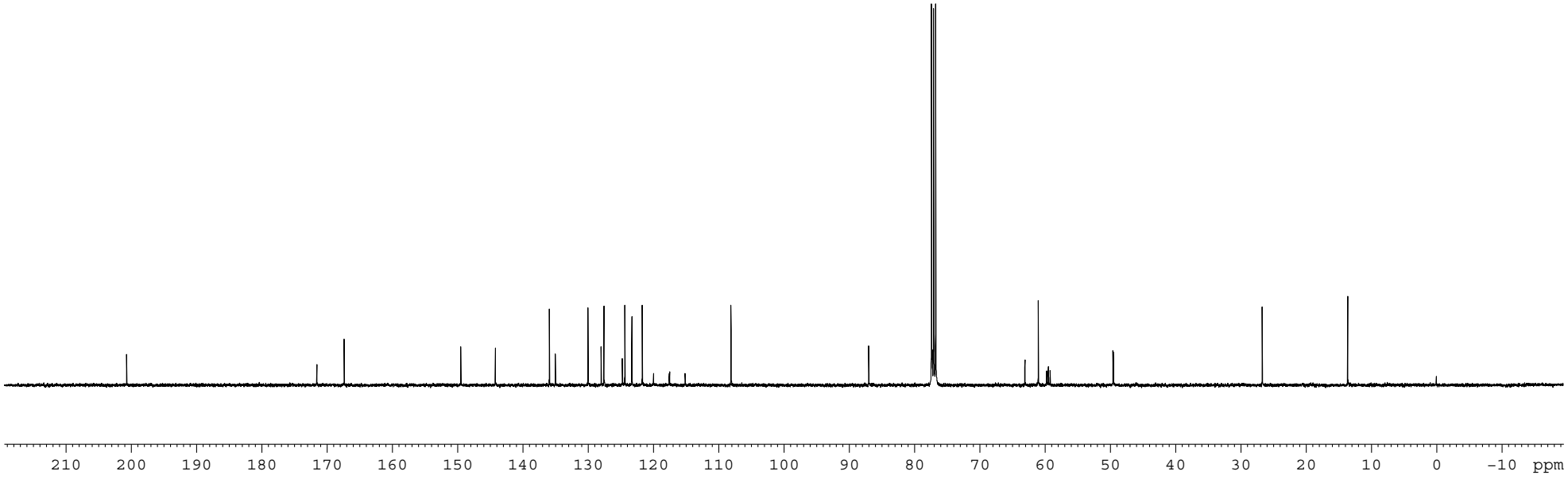


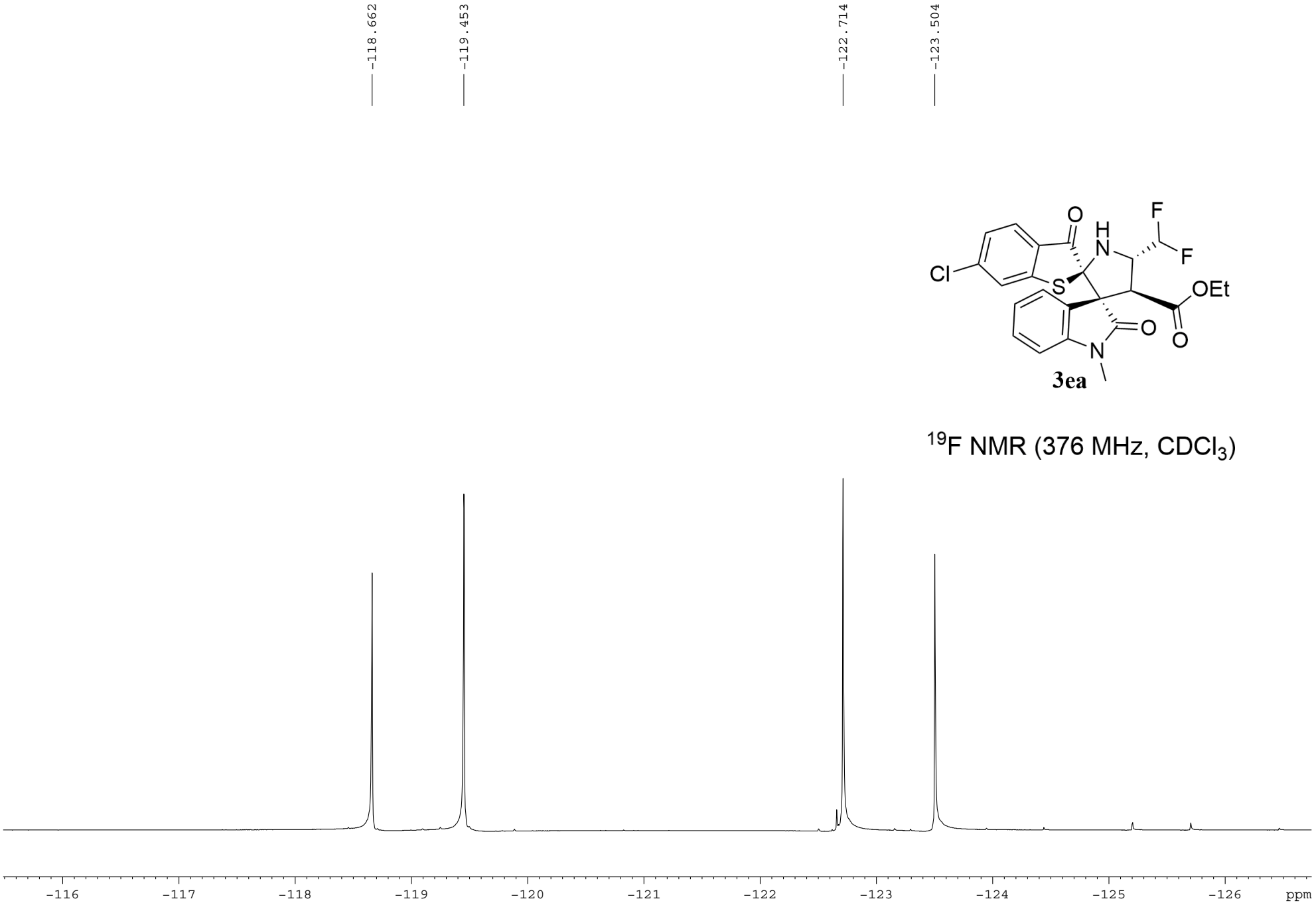


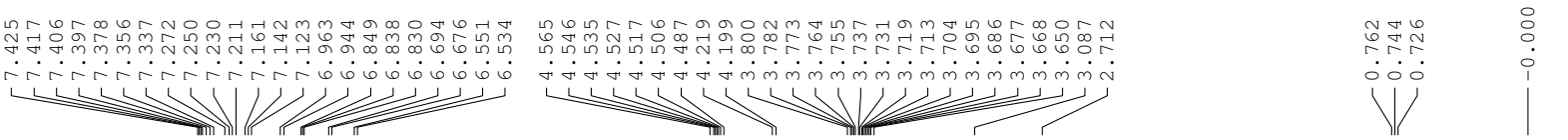


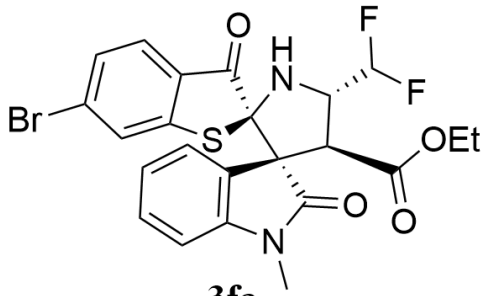
3ea

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)



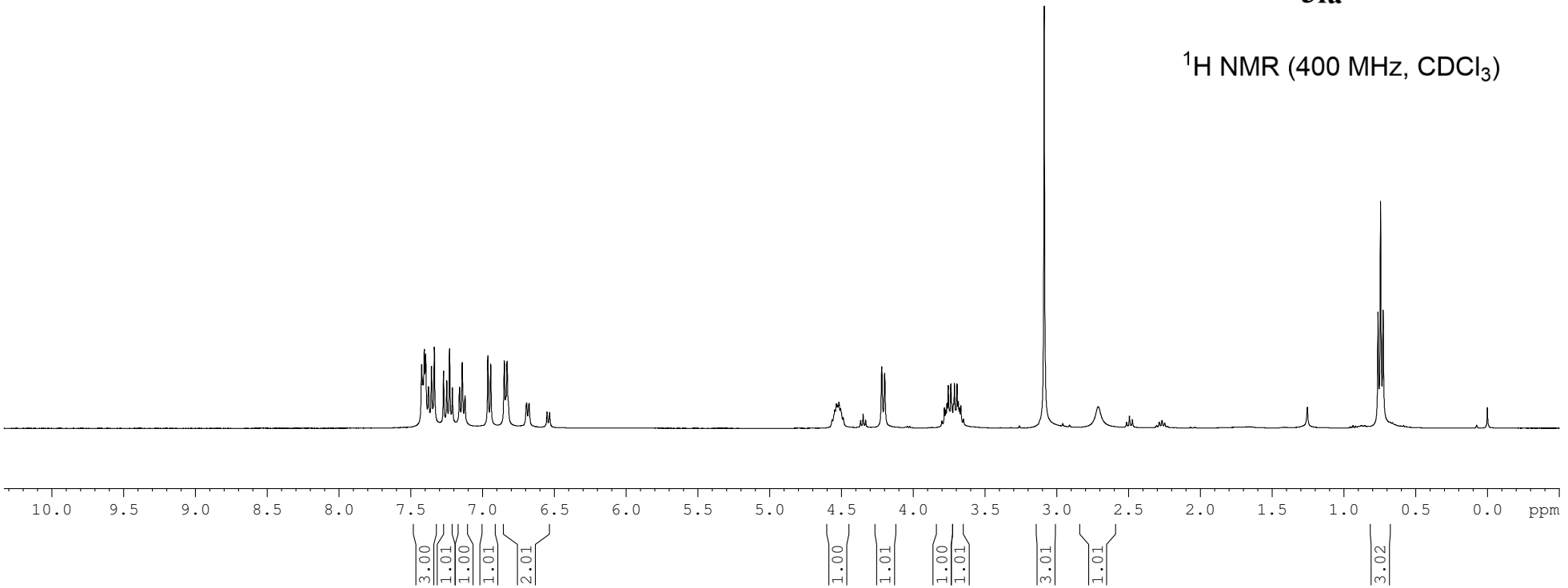

-118.662
-119.453
-122.714
-123.504
O
H
N
F
F
Cl
S
OEt
O
O
N
3ea
19F NMR (376 MHz, CDCl3)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

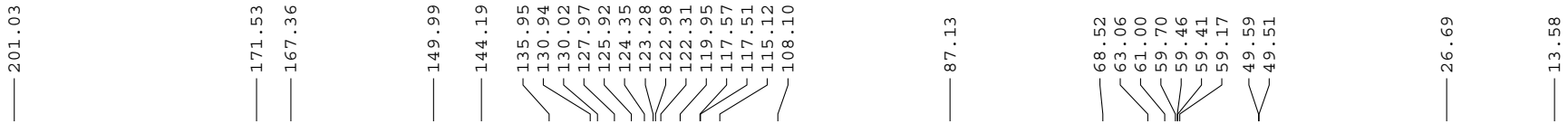


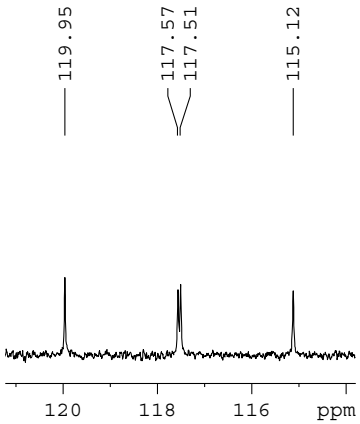


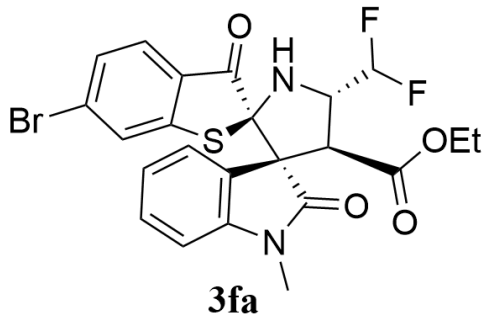
3fa

^{1}H NMR (400 MHz, $CDCl_3$)



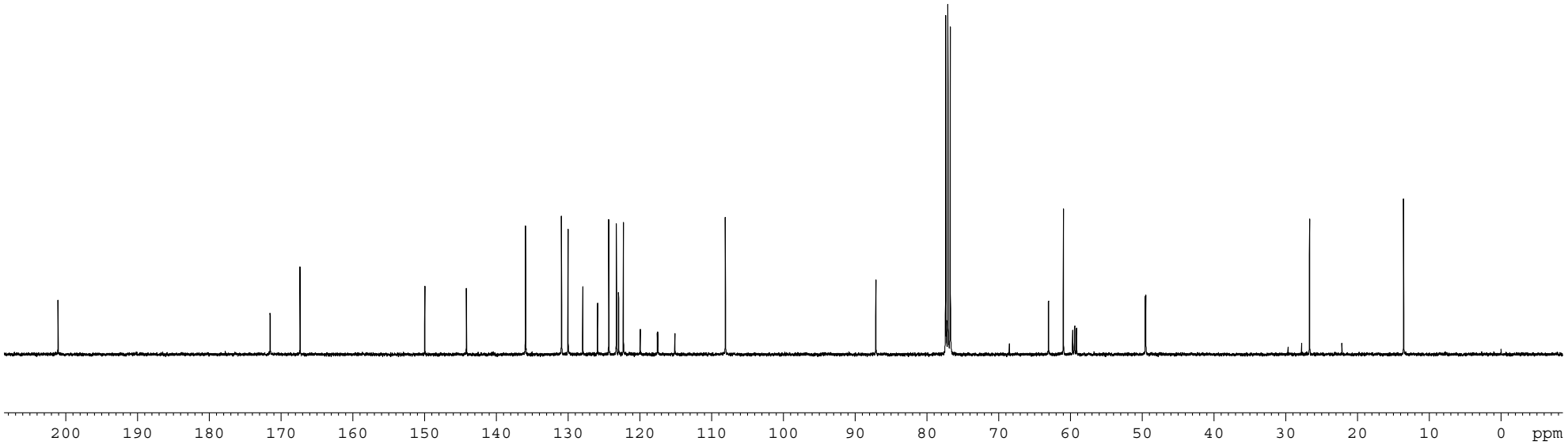


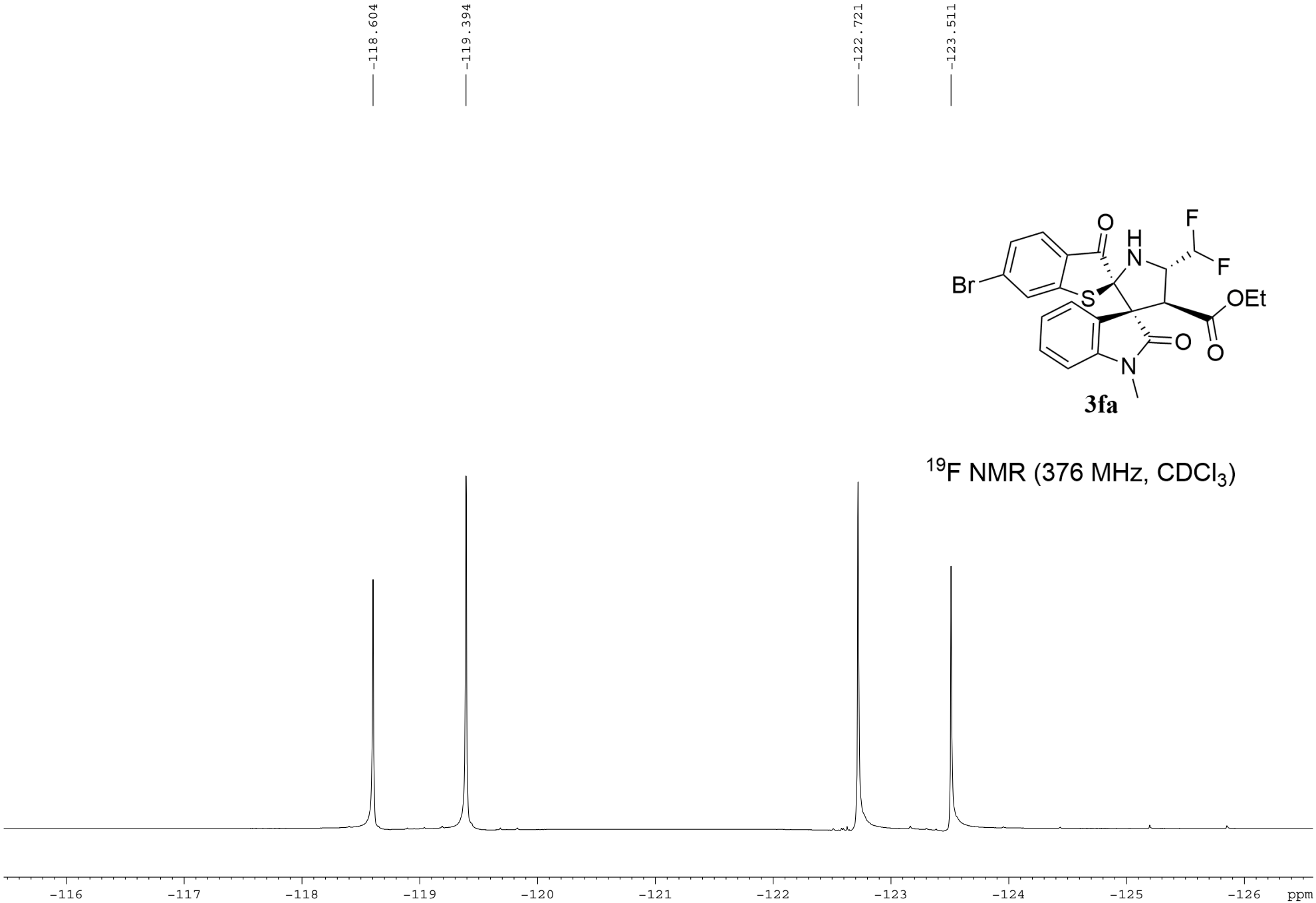




3fa

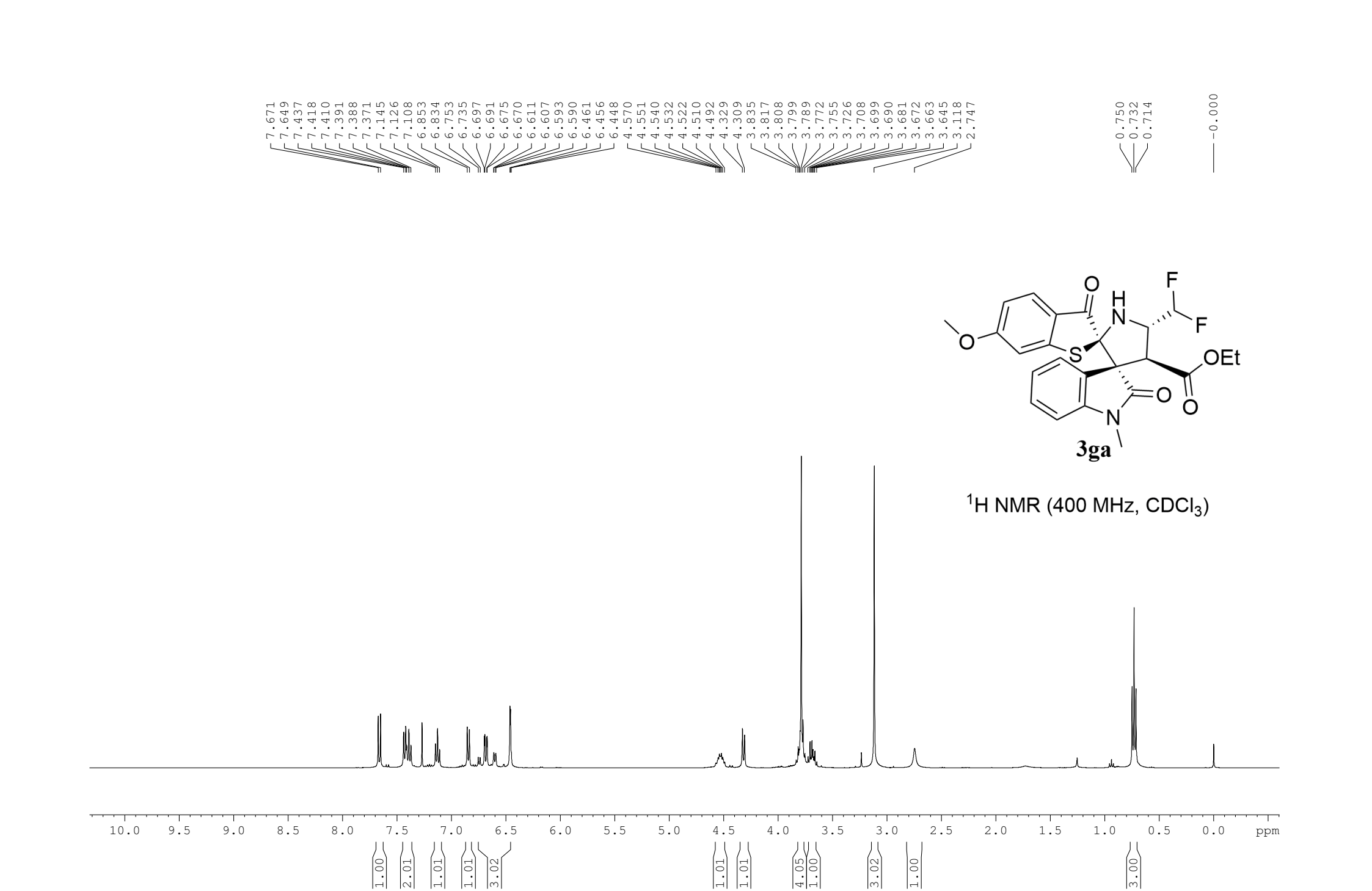
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)

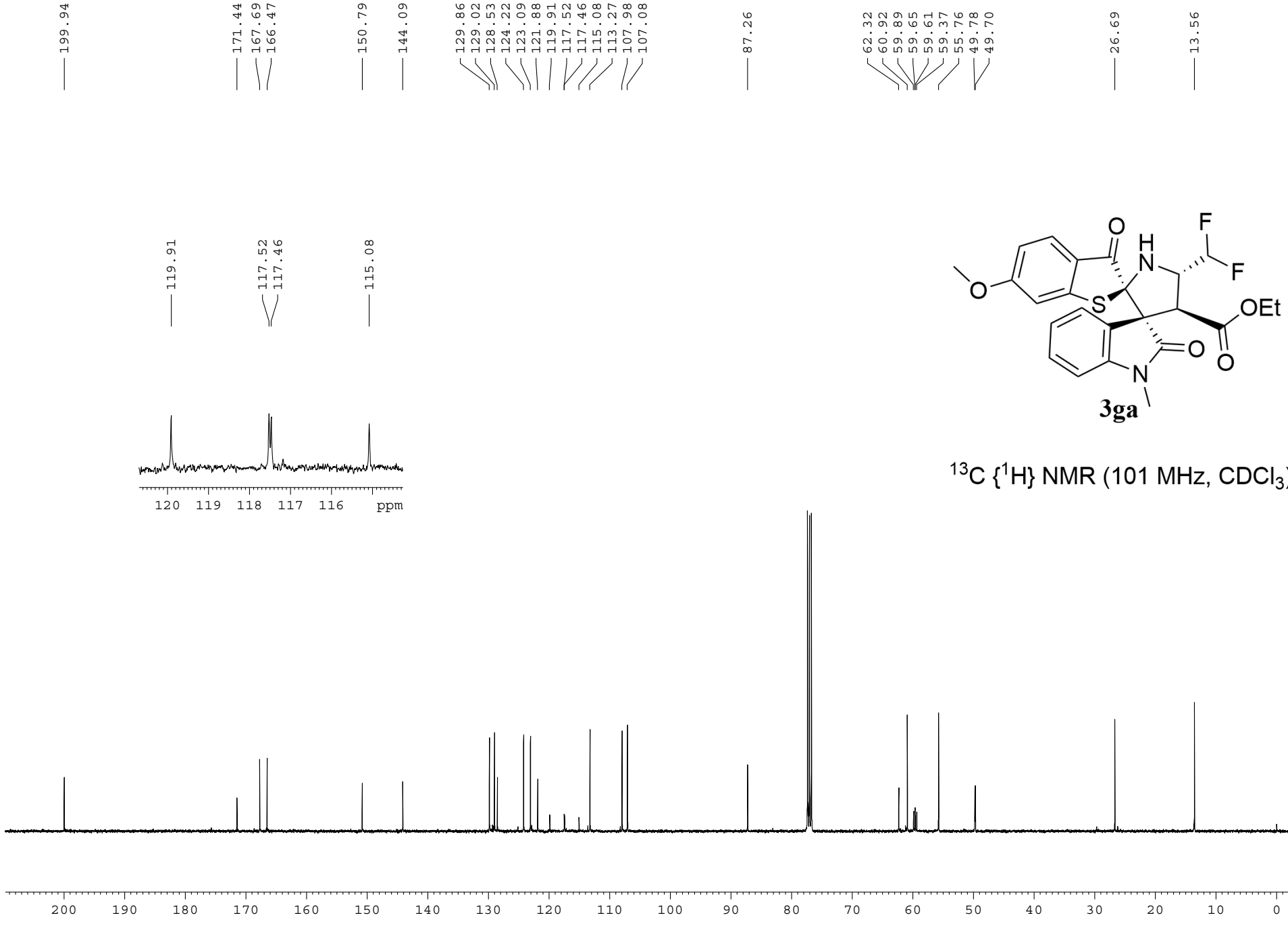


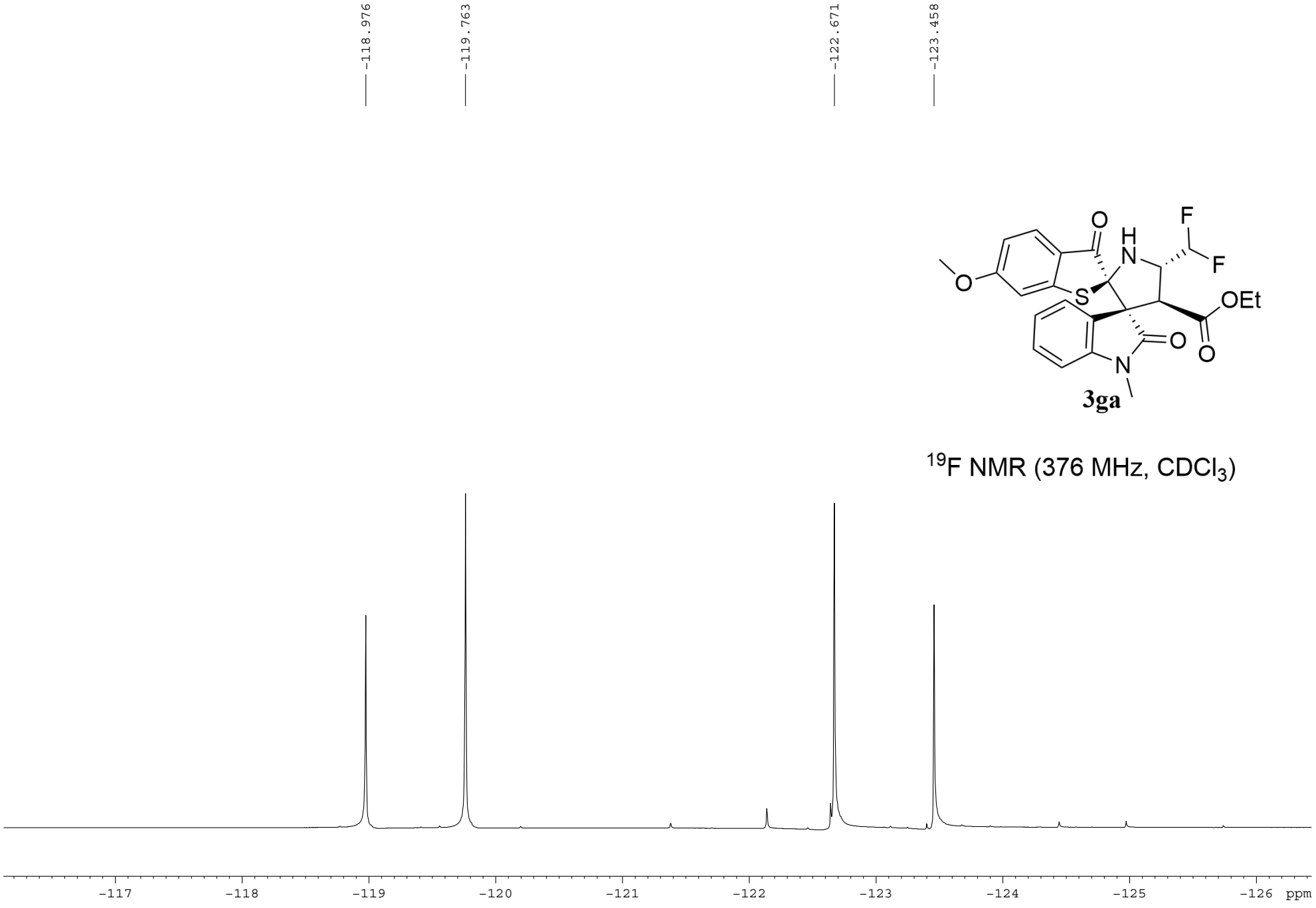


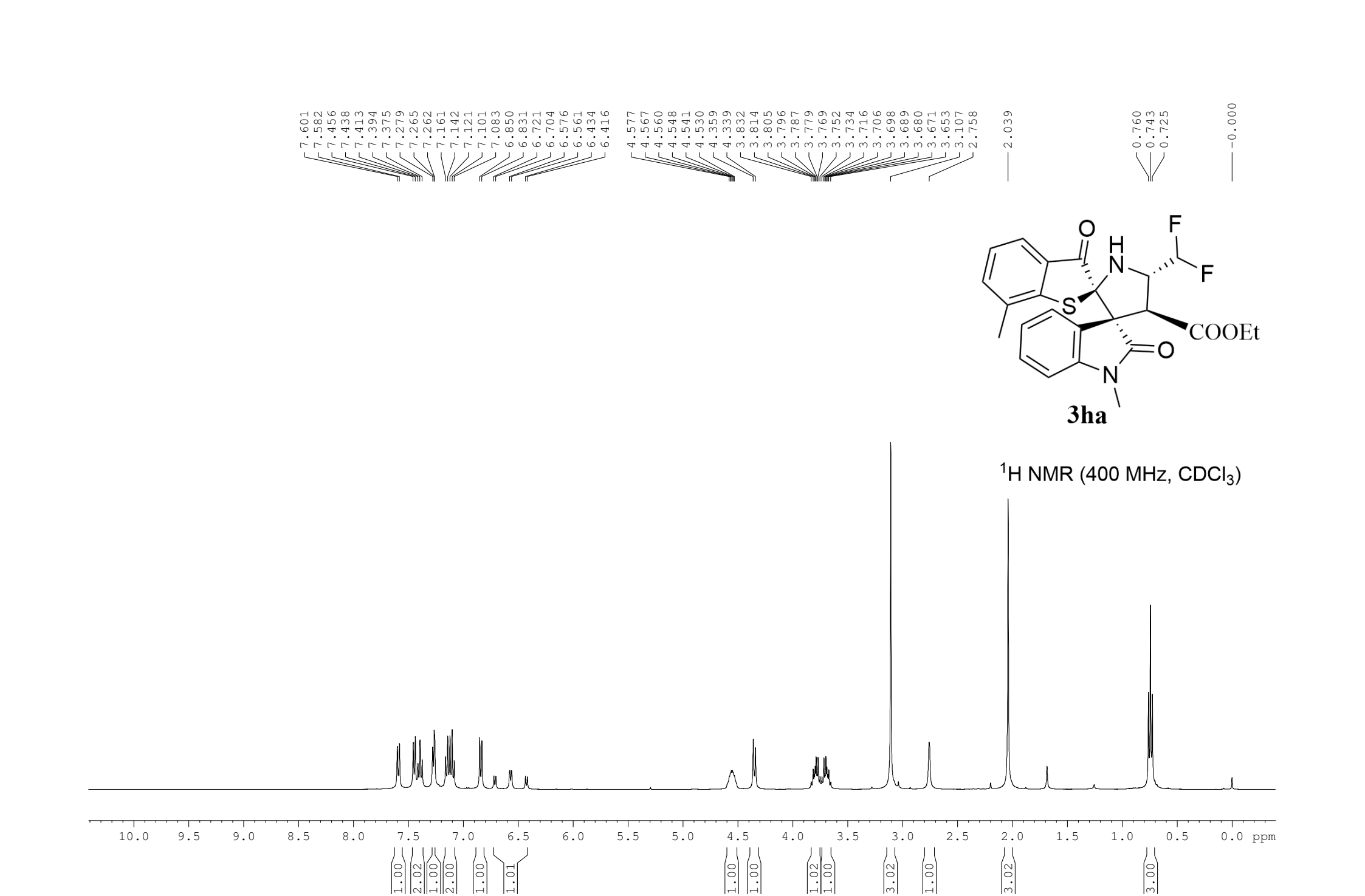
3fa

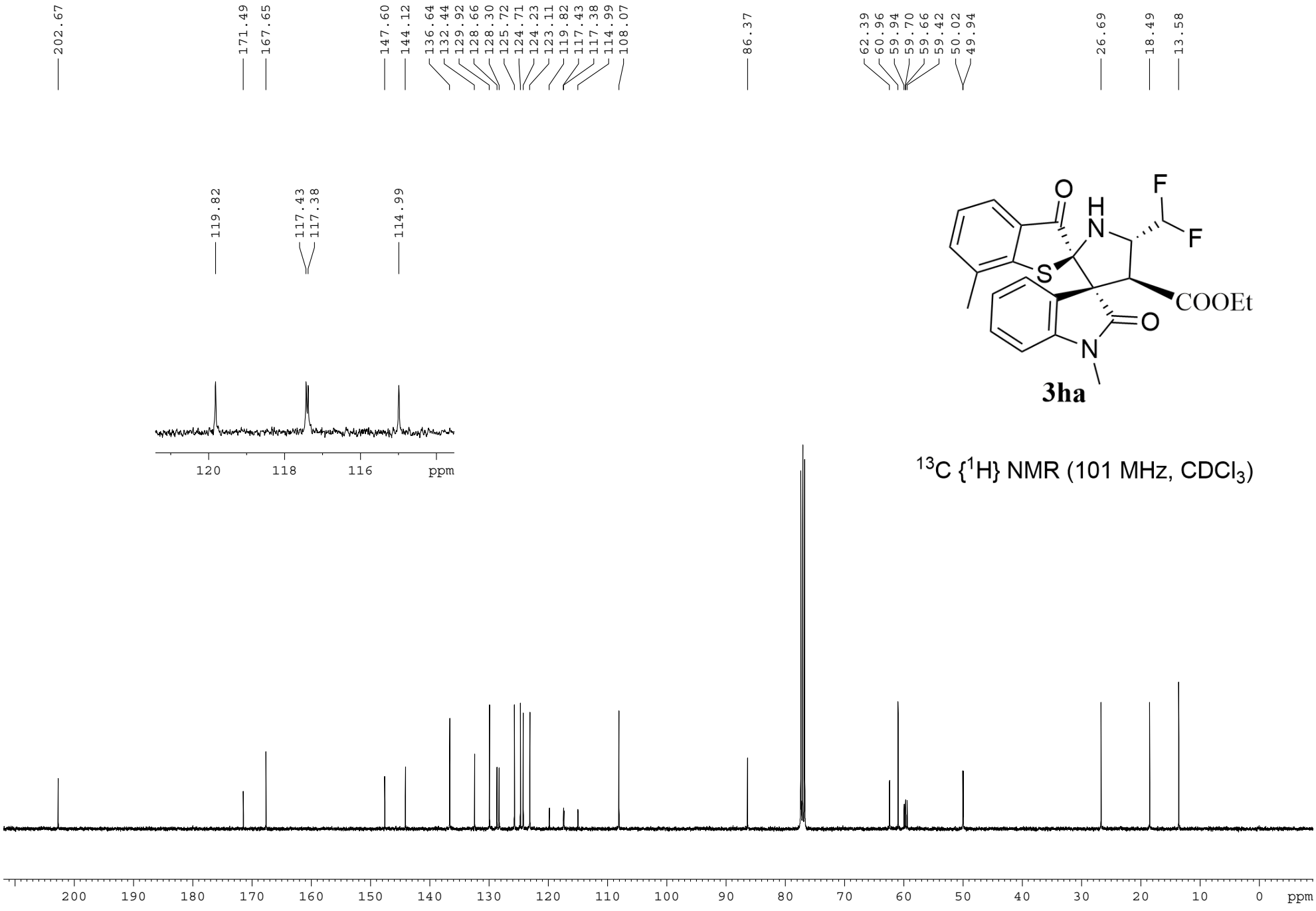
^{19}F NMR (376 MHz, $CDCl_3$)

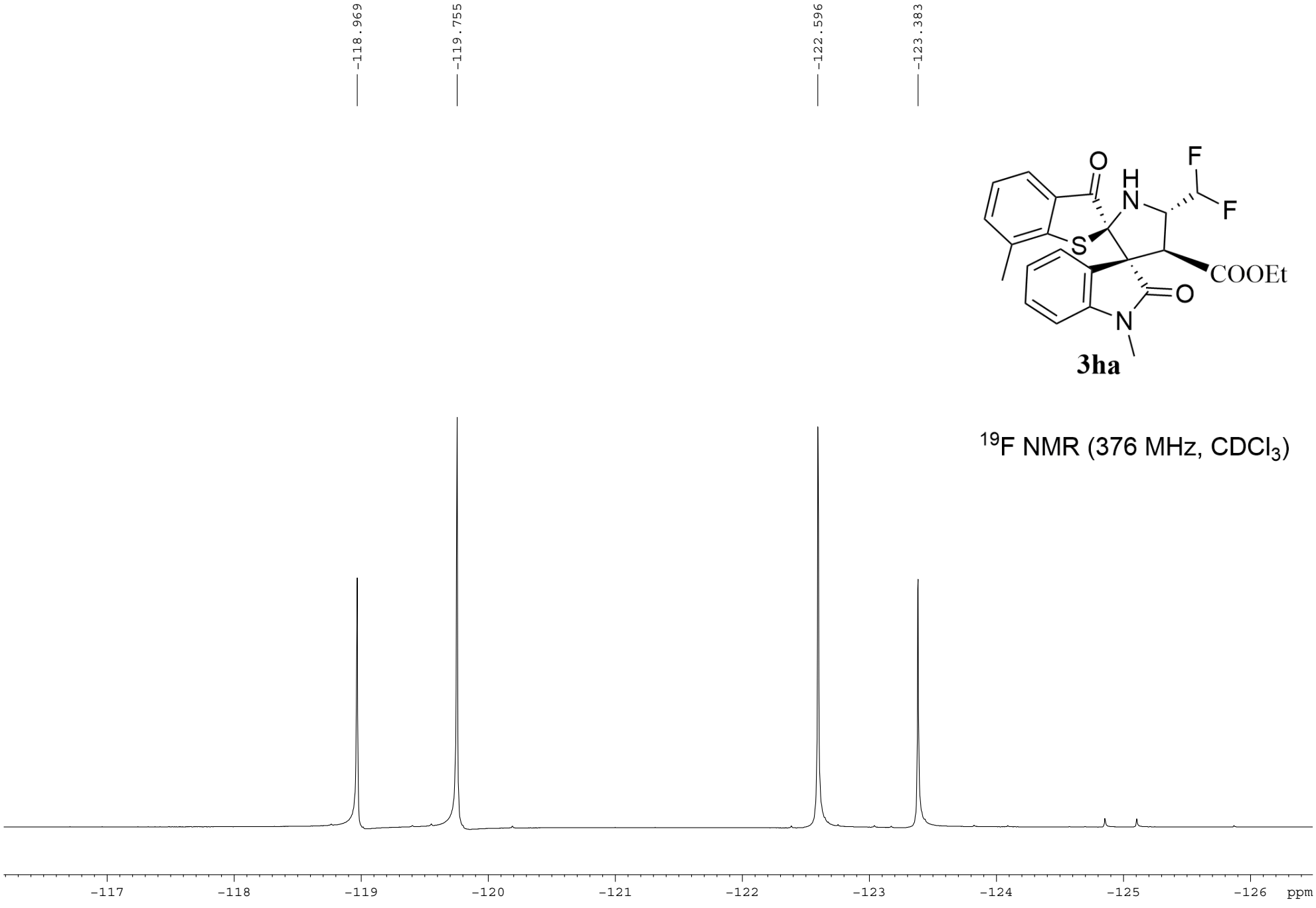

7.671
7.649
7.437
7.418
7.410
7.391
7.388
7.371
7.145
7.126
7.108
6.853
6.834
6.753
6.735
6.697
6.691
6.675
6.670
6.611
6.607
6.593
6.590
6.461
6.456
6.448
4.570
4.551
4.540
4.532
4.522
4.510
4.492
4.329
4.309
3.835
3.817
3.808
3.799
3.789
3.772
3.755
3.726
3.708
3.699
3.690
3.681
3.672
3.663
3.645
3.118
2.747
0.750
0.732
0.714
-0.000
O
H
N
F
F
O
S
OEt
O
O
N
3ga
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
2.01
1.01
1.01
3.02
1.01
1.01
4.05
1.00
3.02
1.00
3.00

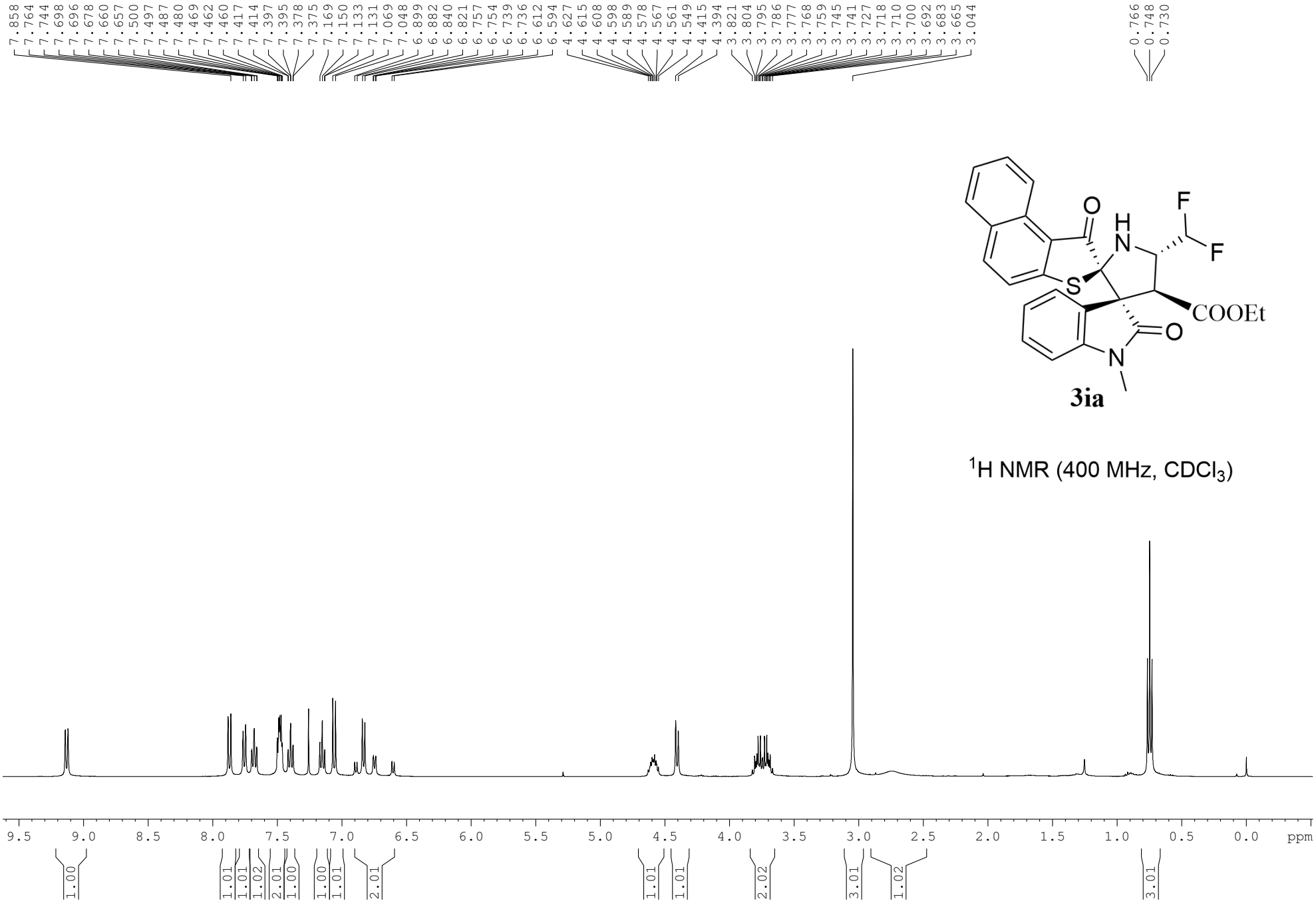

199.94
171.44
167.69
166.47
150.79
144.09
129.86
129.02
128.53
124.22
123.09
121.88
119.91
117.52
117.46
115.08
113.27
107.98
107.08
87.26
62.32
60.92
59.89
59.65
59.61
59.37
55.76
49.78
49.70
26.69
13.56
119.91
117.52
117.46
115.08
120 119 118 117 116 ppm
O
H
N
F
F
O
S
OEt
O
O
N
3ga
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

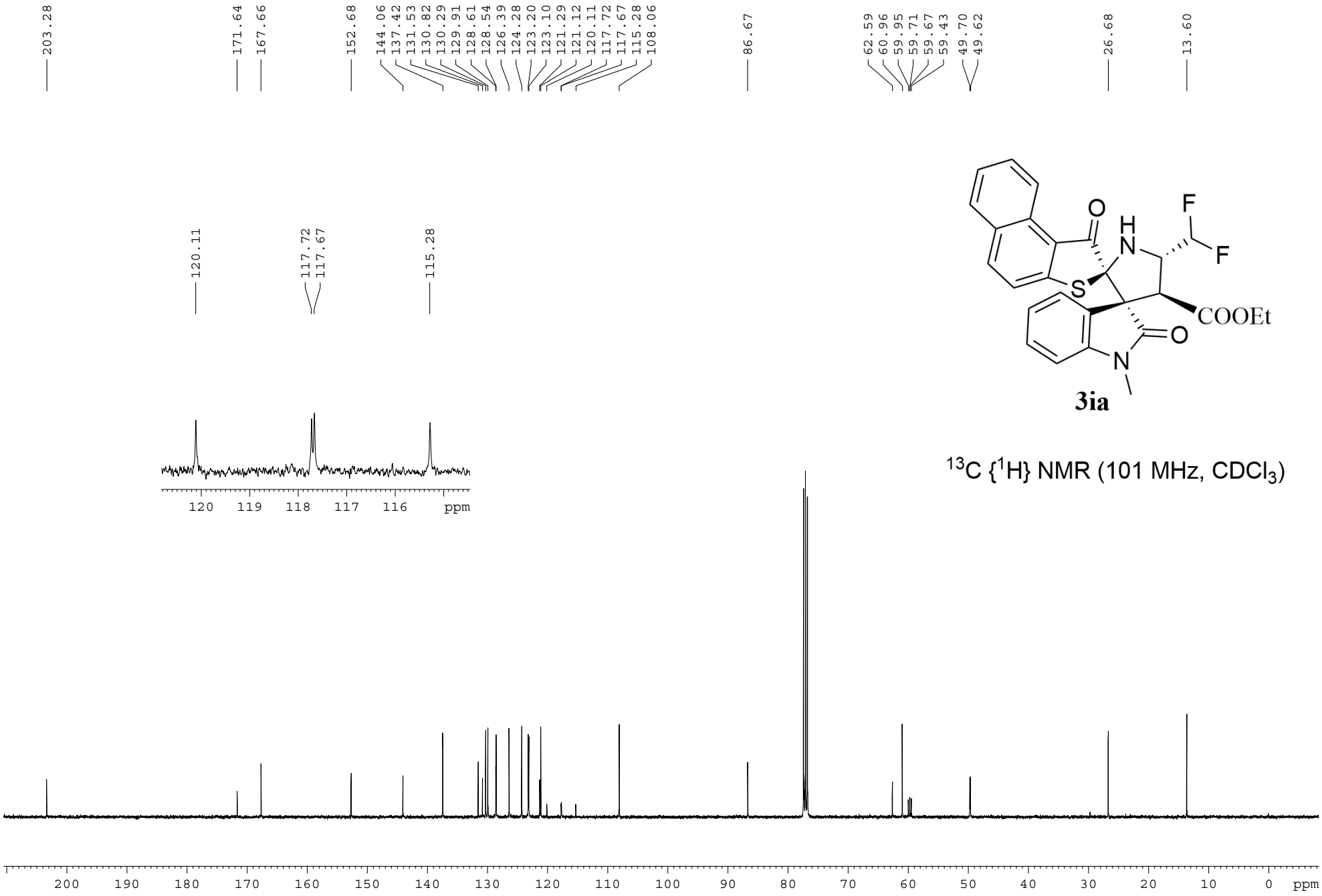

-118.976
-119.763
-122.671
-123.458
O
H
N
F
F
O
S
OEt
O
O
N
3ga
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

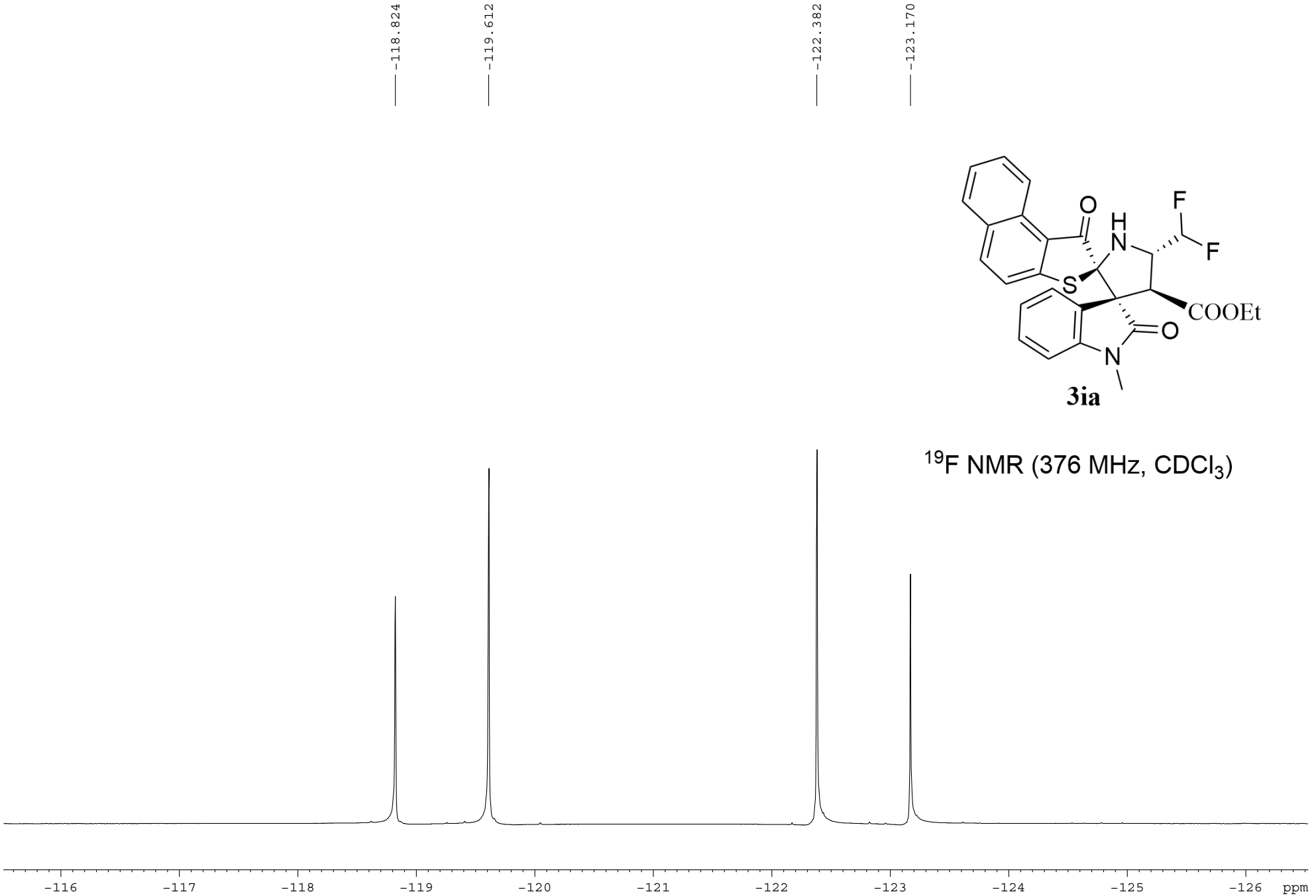

7.601
7.582
7.456
7.438
7.413
7.394
7.375
7.279
7.265
7.262
7.161
7.142
7.121
7.101
7.083
6.850
6.831
6.721
6.704
6.576
6.561
6.434
6.416
4.577
4.567
4.560
4.548
4.541
4.530
4.359
4.339
3.832
3.814
3.805
3.796
3.787
3.779
3.769
3.752
3.734
3.716
3.706
3.698
3.689
3.680
3.671
3.653
3.107
2.758
2.039
0.760
0.743
0.725
-0.000
O
H
N
F
F
S
COOEt
O
N
3ha
1H NMR (400 MHz, CDCl3)
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 ppm
1.00
2.02
1.00
2.00
1.00
1.01
1.00
1.00
1.02
1.00
3.02
1.00
3.02
3.00

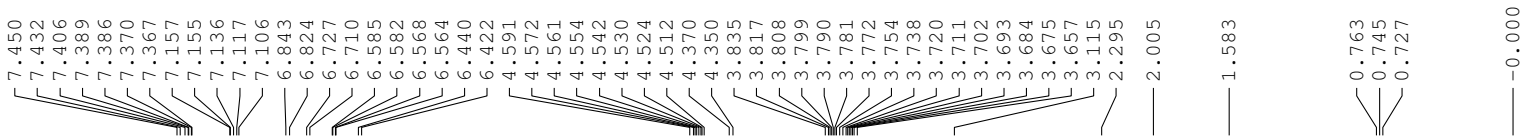

202.67
171.49
167.65
147.60
144.12
136.64
132.44
129.92
128.66
128.30
125.72
124.71
124.23
123.11
119.82
117.43
117.38
114.99
108.07
86.37
62.39
60.96
59.94
59.70
59.66
59.42
50.02
49.94
26.69
18.49
13.58
119.82
117.43
117.38
114.99
120
118
116
ppm
O
H
N
F
F
S
COOEt
O
N
3ha
13C {1H} NMR (101 MHz, CDCl3)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

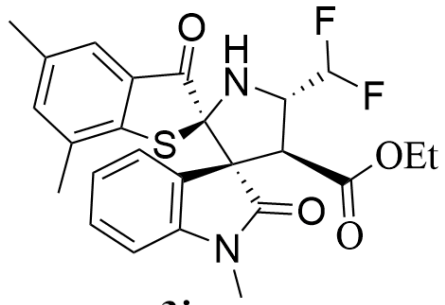

-118.969
-119.755
-122.596
-123.383
O
H
N
F
F
S
COOEt
O
N
3ha
19F NMR (376 MHz, CDCl3)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.858
7.764
7.744
7.698
7.696
7.678
7.660
7.657
7.500
7.497
7.487
7.480
7.469
7.462
7.460
7.417
7.414
7.397
7.395
7.378
7.375
7.169
7.150
7.133
7.131
7.069
7.048
6.899
6.882
6.840
6.821
6.757
6.754
6.739
6.736
6.612
6.594
4.627
4.615
4.608
4.598
4.589
4.578
4.567
4.561
4.549
4.415
4.394
3.821
3.804
3.795
3.786
3.777
3.768
3.759
3.745
3.741
3.727
3.718
3.710
3.700
3.692
3.683
3.665
3.044
0.766
0.748
0.730
O
H
N
F
F
S
COOEt
O
N
3ia
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
1.01
1.01
1.02
2.01
1.00
1.00
1.01
2.01
1.01
1.01
2.02
3.01
1.02
3.01


203.28
171.64
167.66
152.68
144.06
137.42
131.53
130.82
130.29
129.91
128.61
128.54
126.39
124.28
123.20
123.10
121.29
121.12
120.11
117.72
117.67
115.28
108.06
86.67
62.59
60.96
59.95
59.71
59.67
59.43
49.70
49.62
26.68
13.60
120.11
117.72
117.67
115.28
120
119
118
117
116
ppm
O
H
N
F
F
S
COOEt
O
N
3ia
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

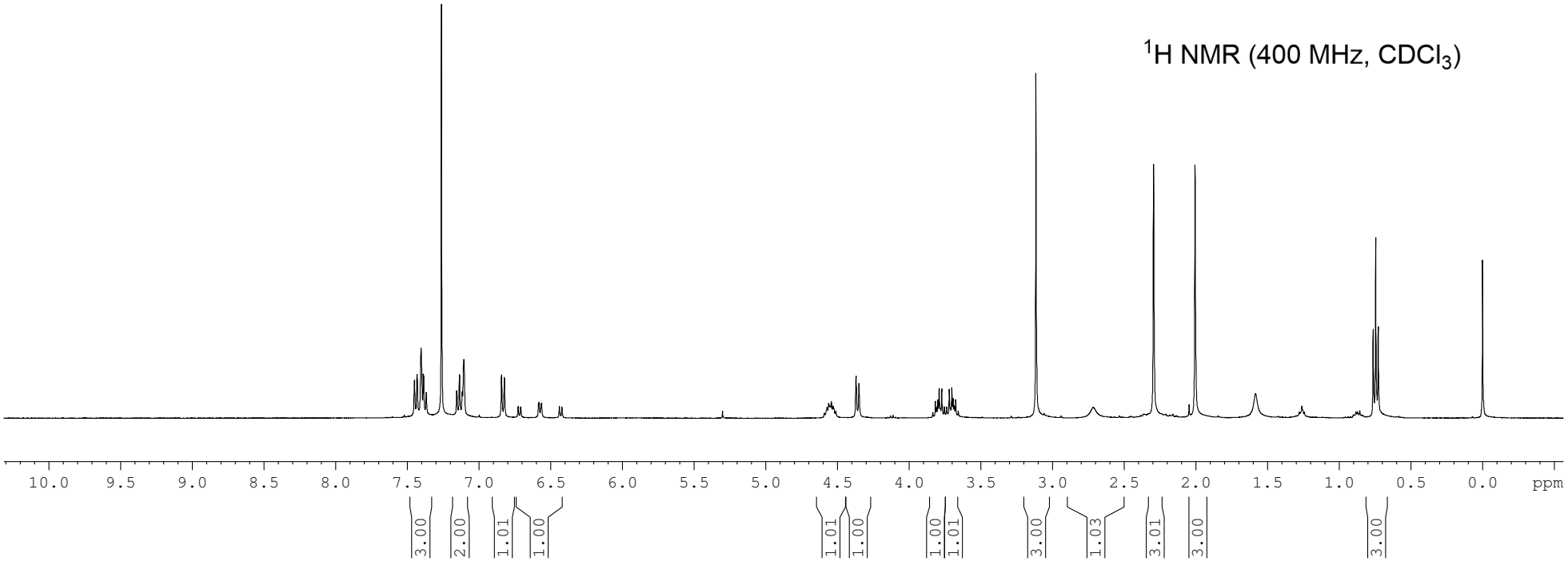

-118.824
-119.612
-122.382
-123.170
O
H
N
F
F
S
COOEt
O
N
3ia
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

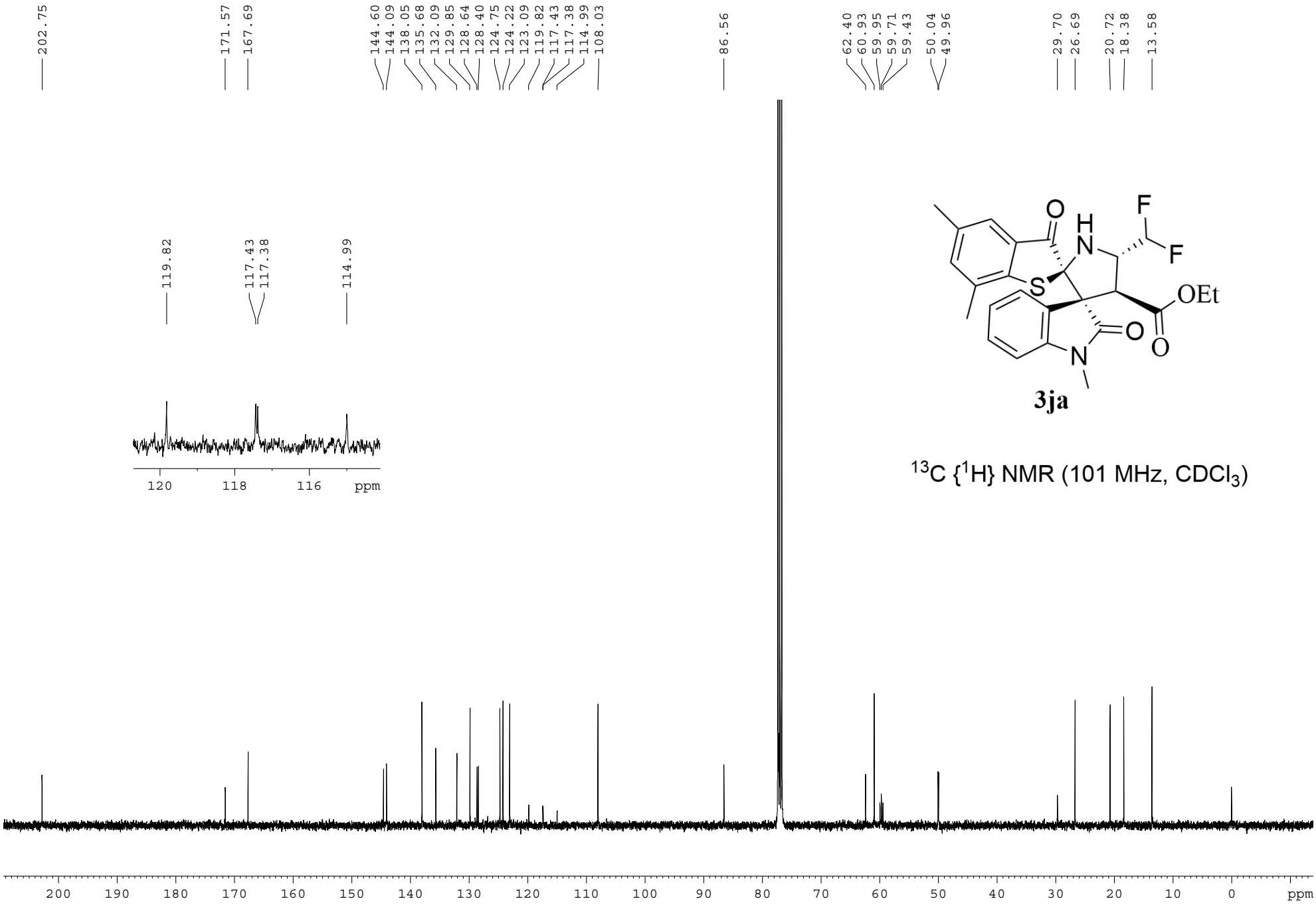


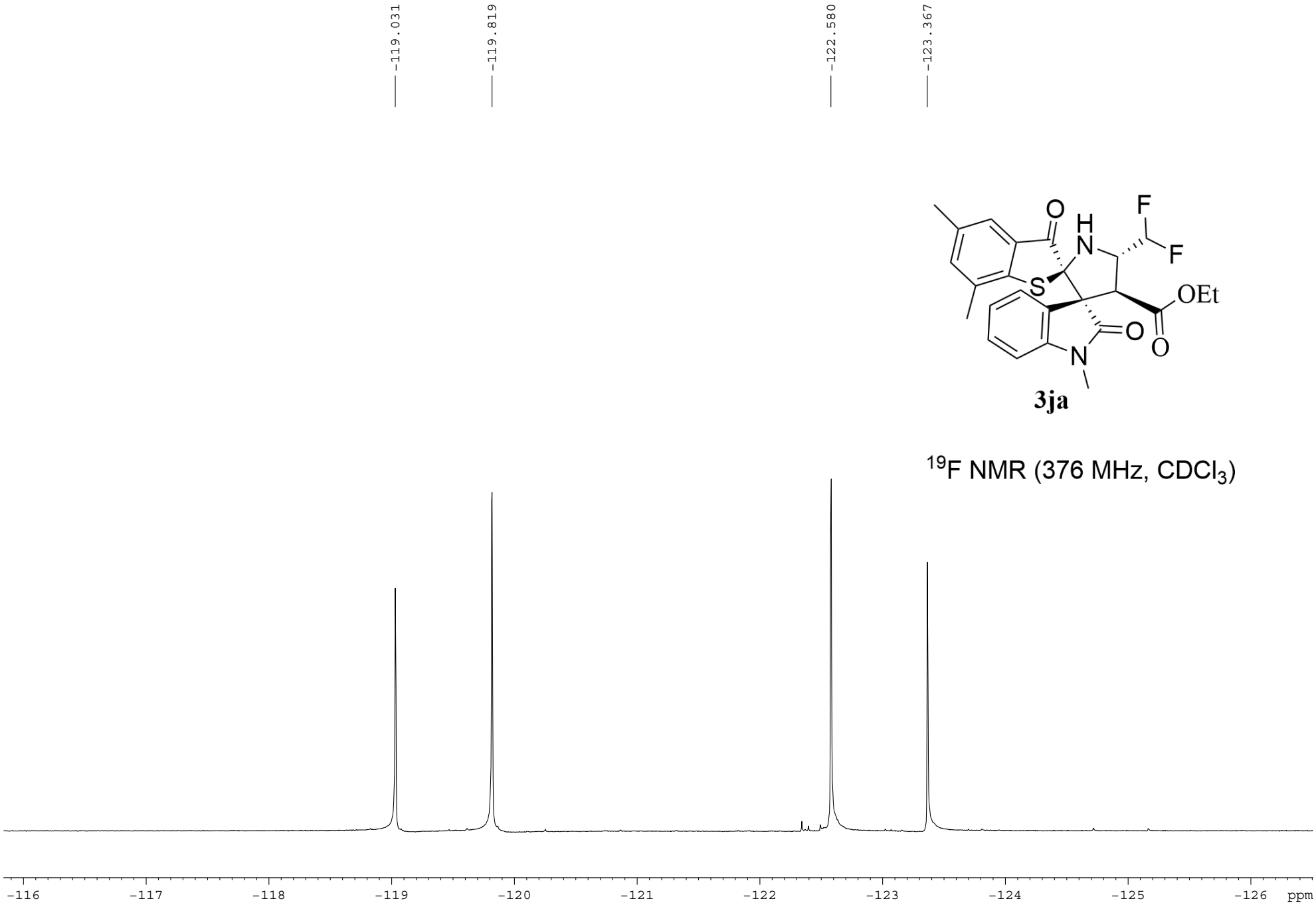


3ja

^{1}H NMR (400 MHz, $CDCl_3$)

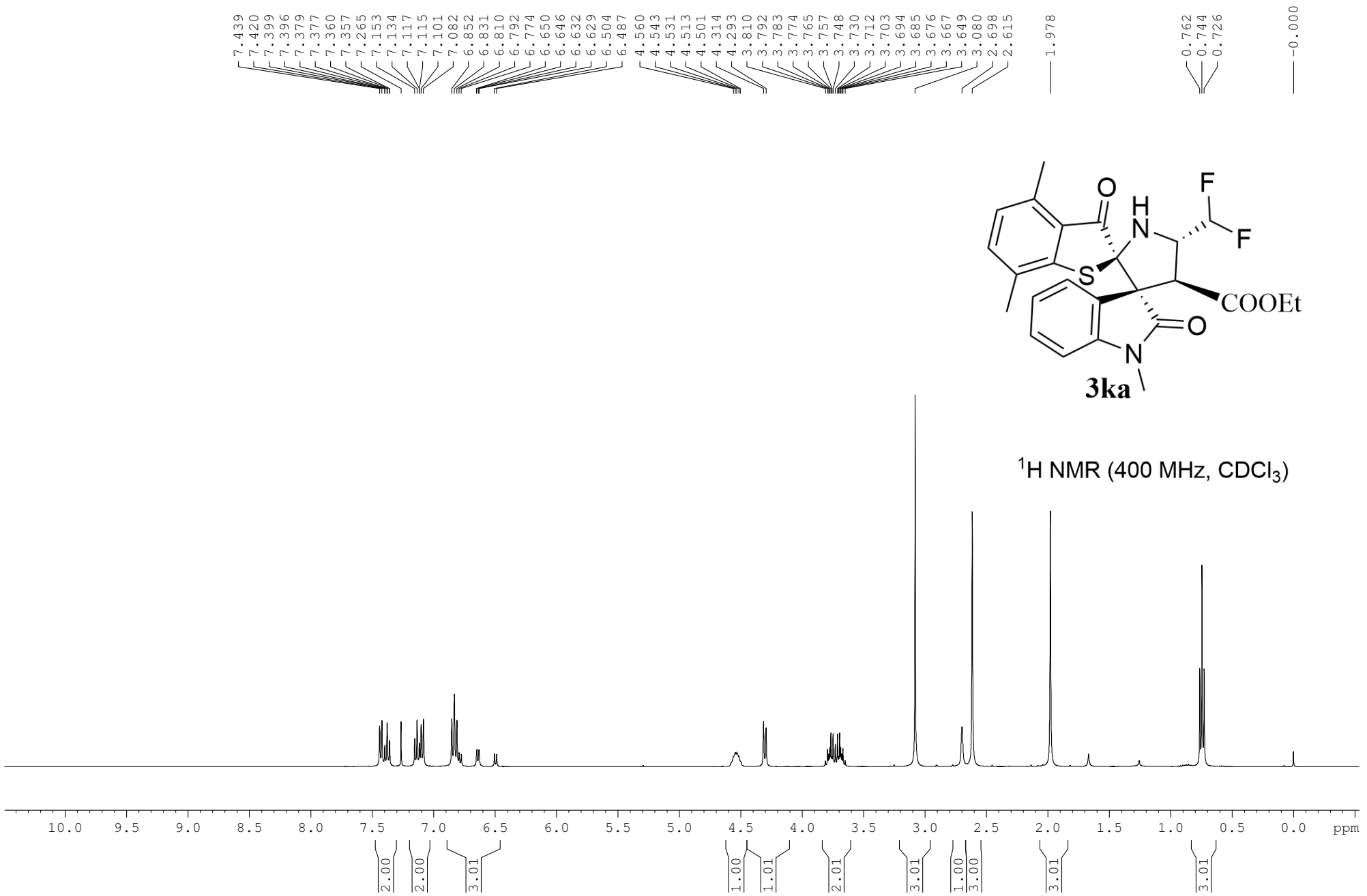


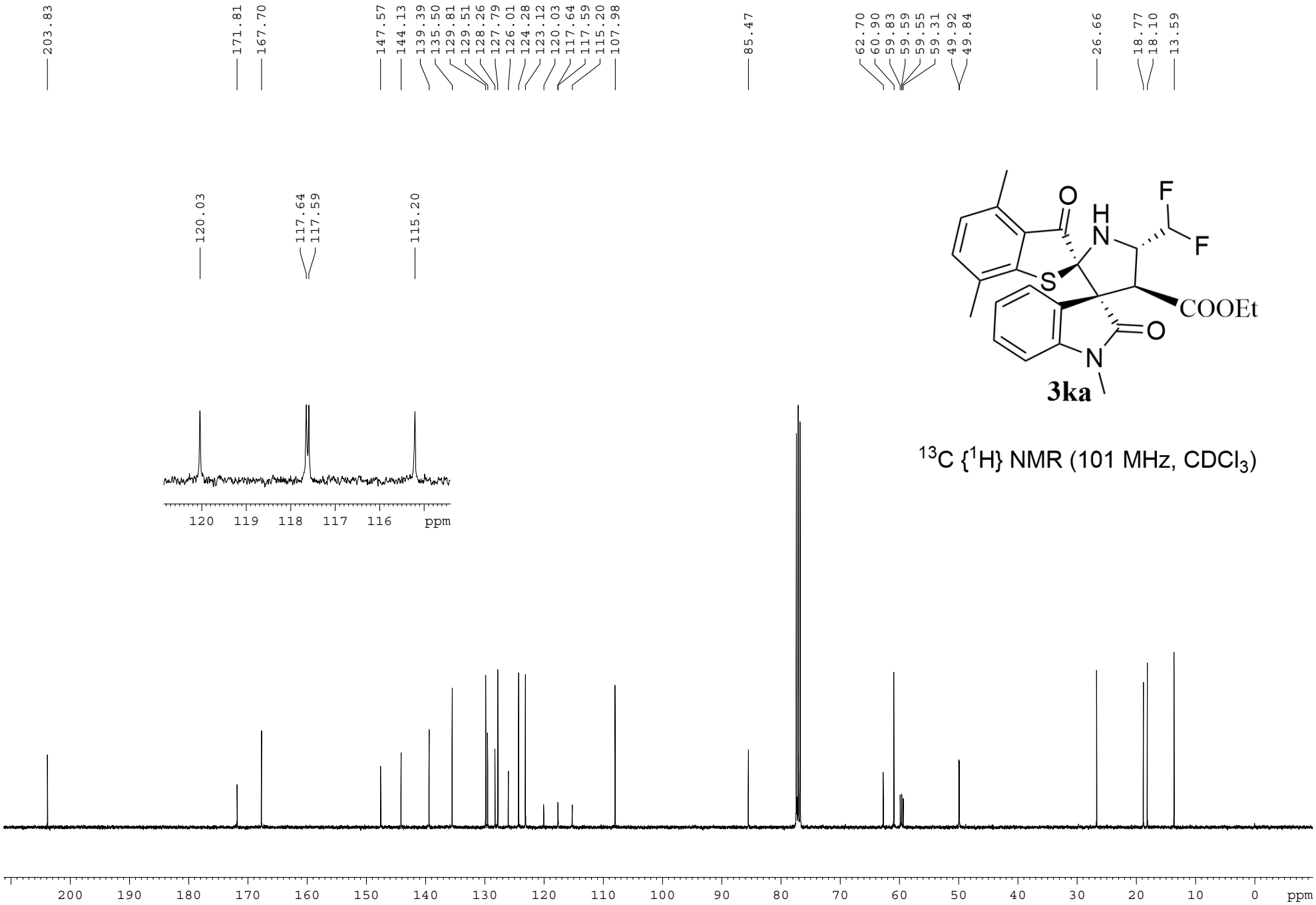

202.75
171.57
167.69
144.60
144.09
138.05
135.68
132.09
129.85
128.64
128.40
124.75
124.22
123.09
119.82
117.43
117.38
114.99
108.03
86.56
62.40
60.93
59.95
59.71
59.43
50.04
49.96
29.70
26.69
20.72
18.38
13.58
119.82
117.43
117.38
114.99
120
118
116
ppm
O
H
N
F
F
S
OEt
O
O
N
3ja
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

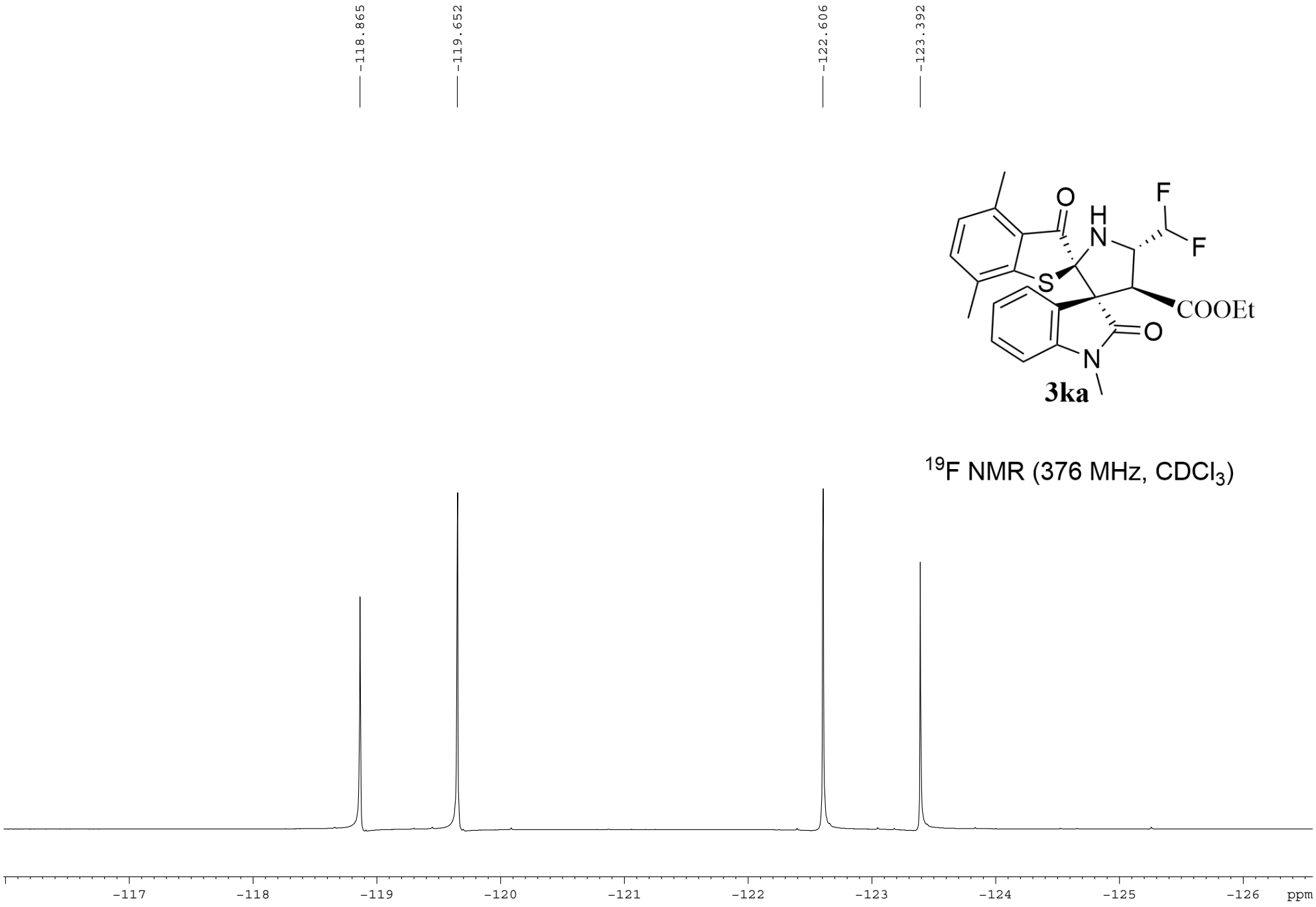


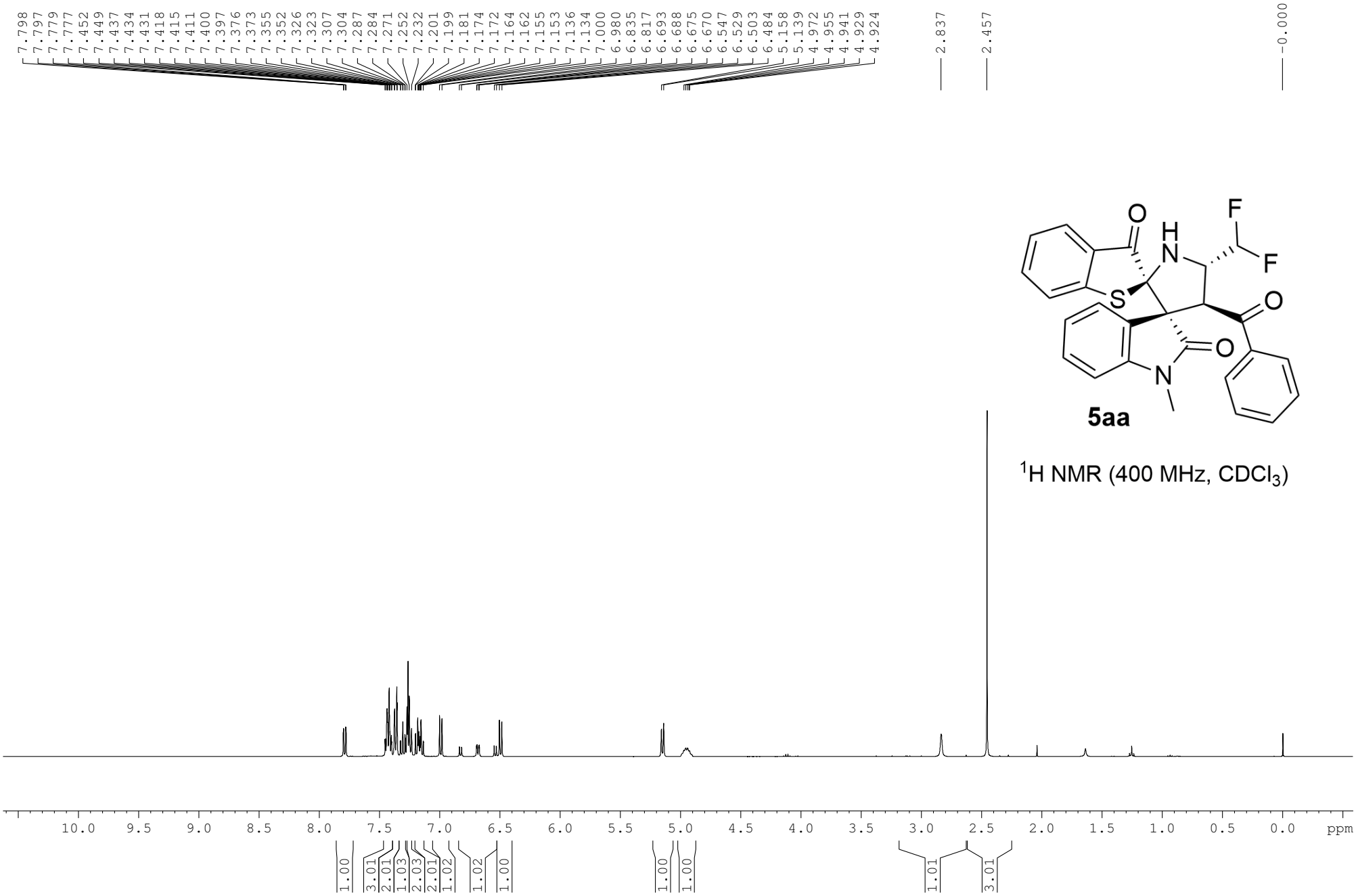
3ja

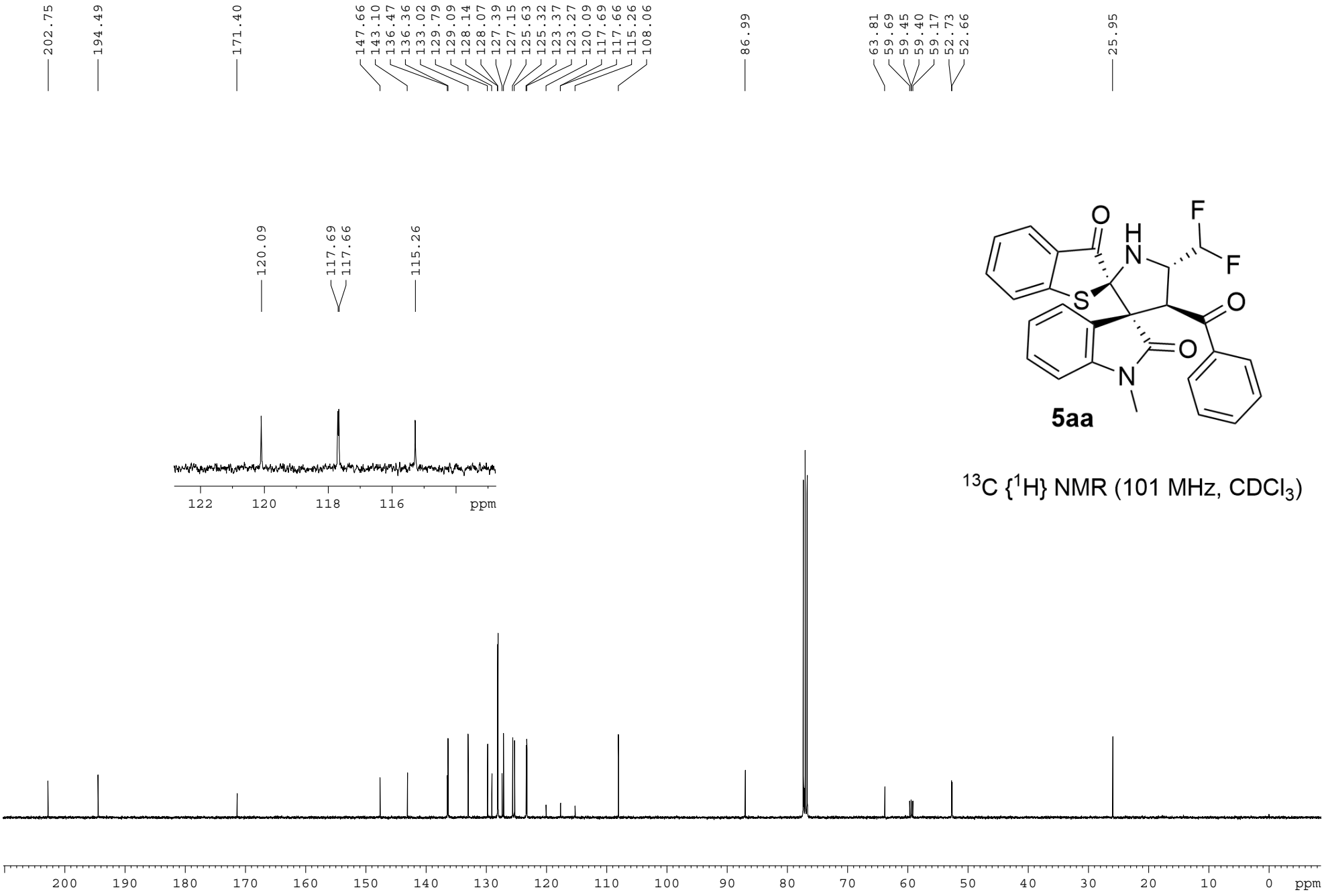
^{19}F NMR (376 MHz, $CDCl_3$)

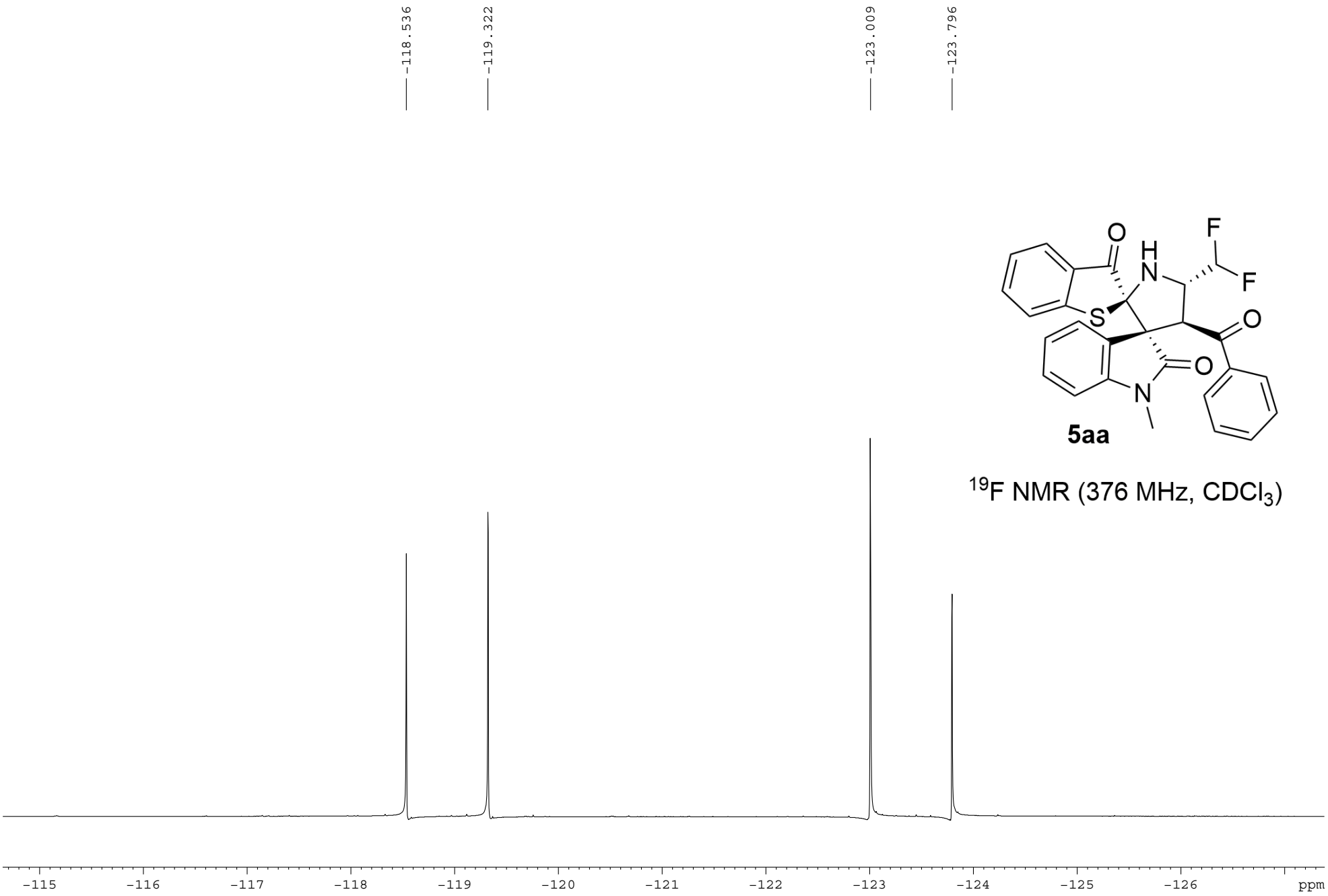

7.439
7.420
7.399
7.396
7.379
7.377
7.360
7.357
7.265
7.153
7.134
7.117
7.115
7.101
7.082
6.852
6.831
6.810
6.792
6.774
6.650
6.646
6.632
6.629
6.504
6.487
4.560
4.543
4.531
4.513
4.501
4.314
4.293
3.810
3.792
3.783
3.774
3.765
3.757
3.748
3.730
3.712
3.703
3.694
3.685
3.676
3.667
3.649
3.080
2.698
2.615
1.978
0.762
0.744
0.726
-0.000
O
H
N
F
F
S
COOEt
O
N
3ka
1H NMR (400 MHz, CDCl3)
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
ppm
2.00
2.00
3.01
1.00
1.01
2.01
3.01
1.00
3.00
3.01
3.01

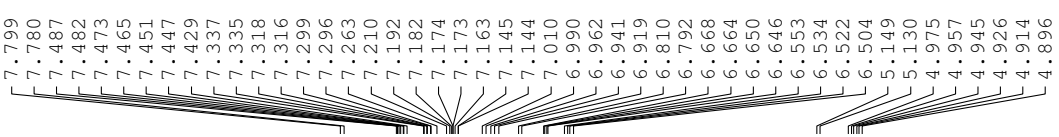

203.83
171.81
167.70
147.57
144.13
139.39
135.50
129.81
129.51
128.26
127.79
126.01
124.28
123.12
120.03
117.64
117.59
115.20
107.98
85.47
62.70
60.90
59.83
59.59
59.55
59.31
49.92
49.84
26.66
18.77
18.10
13.59
O
H
N
F
F
S
COOEt
O
N
3ka
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
120
119
118
117
116
ppm
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

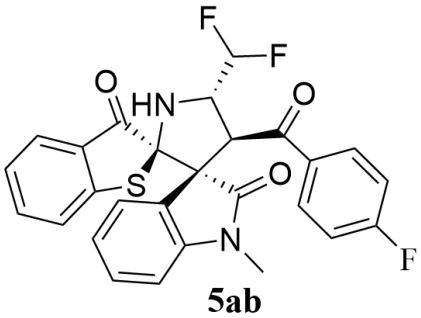

-118.865
-119.652
-122.606
-123.392
O
H
N
F
F
S
COOEt
O
N
3ka
19F NMR (376 MHz, CDCl3)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.798
7.797
7.779
7.777
7.452
7.449
7.437
7.434
7.431
7.418
7.415
7.411
7.400
7.397
7.376
7.373
7.355
7.352
7.326
7.323
7.307
7.304
7.287
7.284
7.271
7.252
7.232
7.201
7.199
7.181
7.174
7.172
7.164
7.162
7.155
7.153
7.136
7.134
7.000
6.980
6.835
6.817
6.693
6.688
6.675
6.670
6.547
6.529
6.503
6.484
5.158
5.139
4.972
4.955
4.941
4.929
4.924
2.837
2.457
-0.000
O
H
N
F
F
S
O
O
N
5aa
^{1}H NMR (400 MHz, $CDCl_3$)
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
ppm
1.00
3.01
2.01
1.03
2.03
2.01
1.02
1.02
1.00
1.00
1.00
1.01
3.01


202.75
194.49
171.40
147.66
143.10
136.47
136.36
133.02
129.79
129.09
128.14
128.07
127.39
127.15
125.63
125.32
123.37
123.27
120.09
117.69
117.66
115.26
108.06
86.99
63.81
59.69
59.45
59.40
59.17
52.73
52.66
25.95
120.09
117.69
117.66
115.26
122
120
118
116
ppm
O
H
N
F
F
S
O
O
N
5aa
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

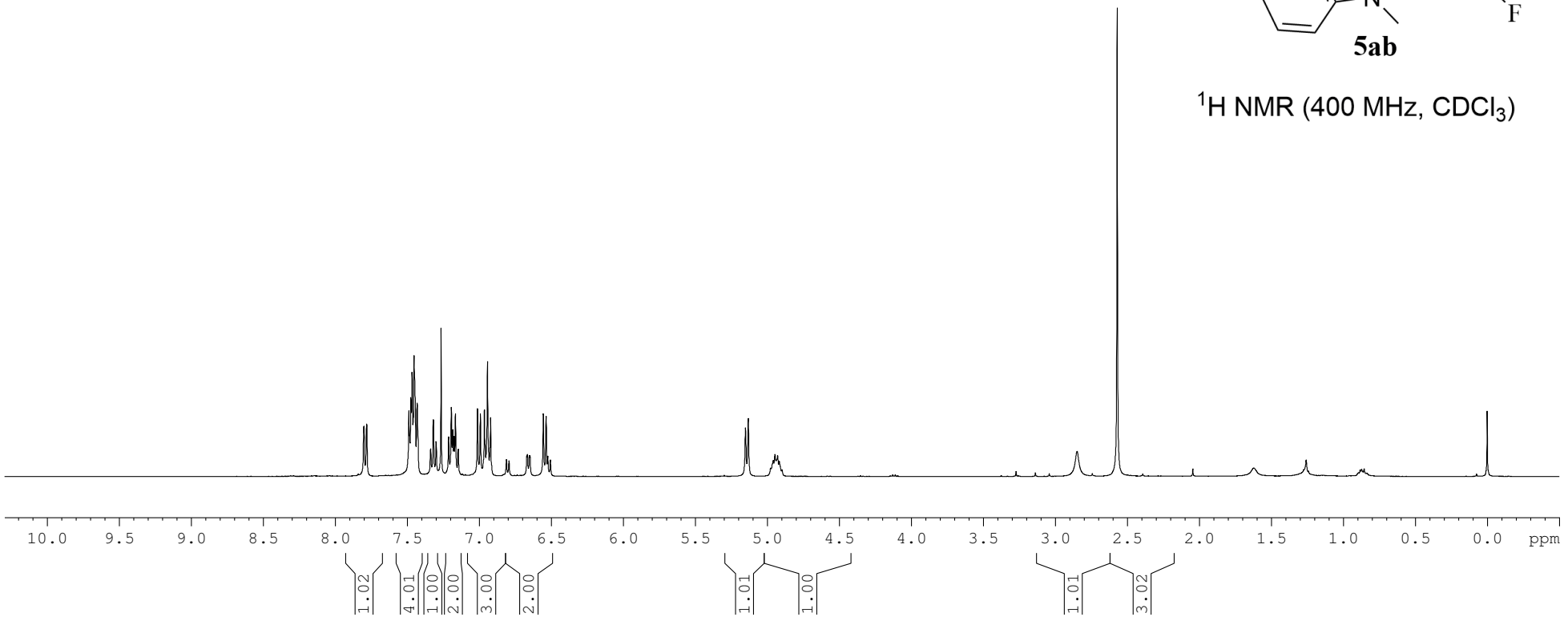

-118.536
-119.322
-123.009
-123.796
O
H
N
F
F
S
O
O
N
5aa
^{19}F NMR (376 MHz, $CDCl_3$)
-115
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

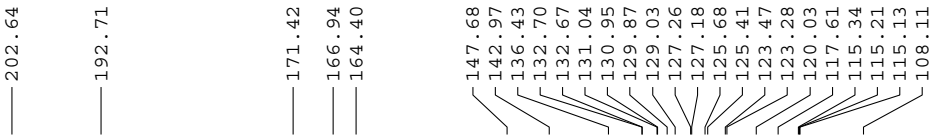


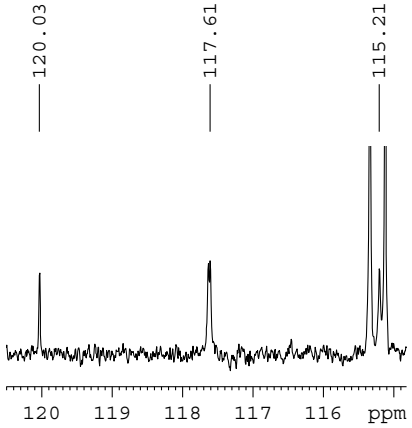


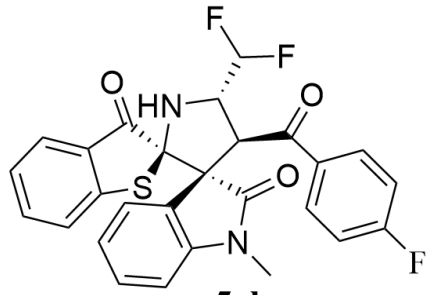
5ab

^{1}H NMR (400 MHz, $CDCl_3$)



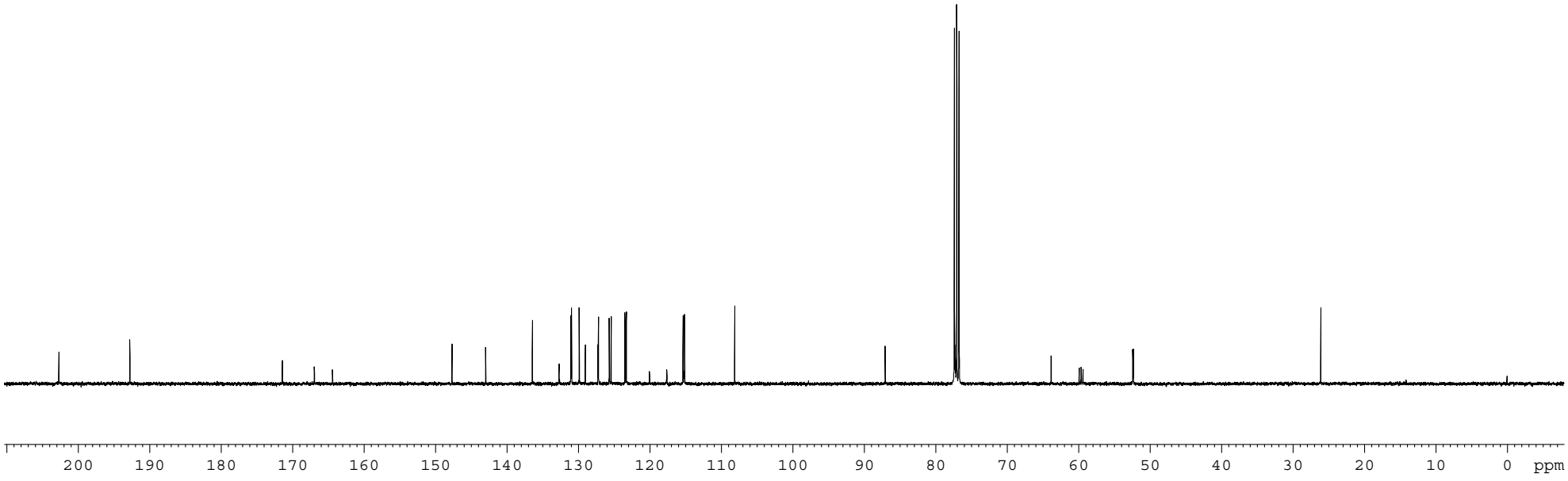






5ab

^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)



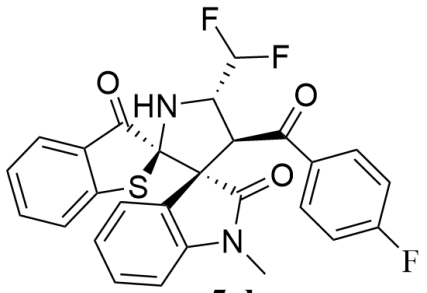
-104.490

-118.541

-119.328

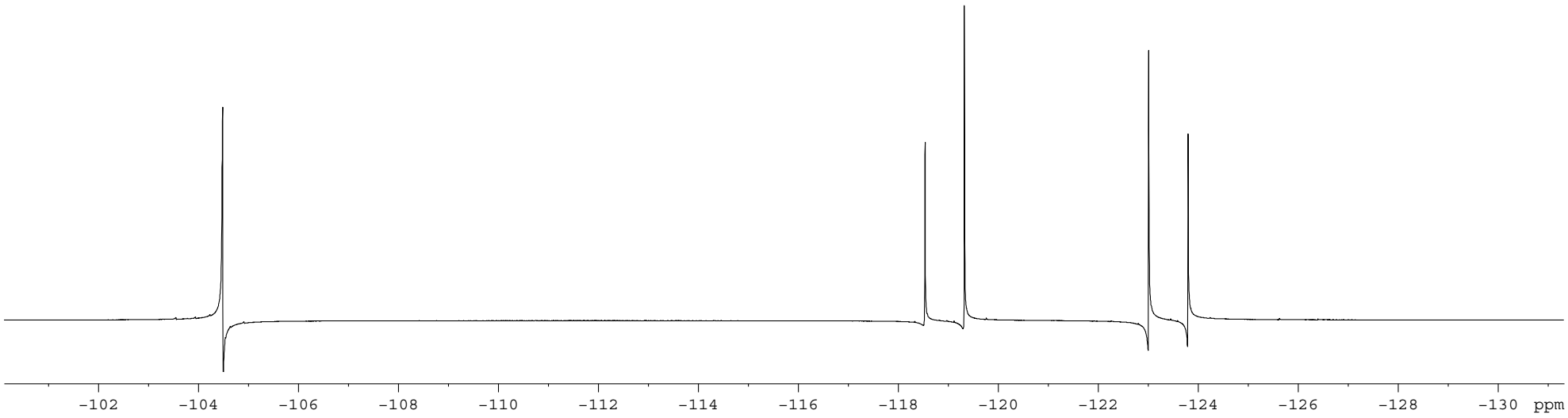
-123.016

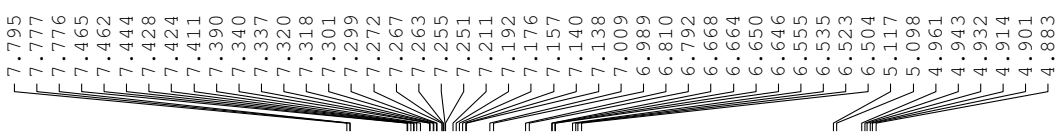
-123.804

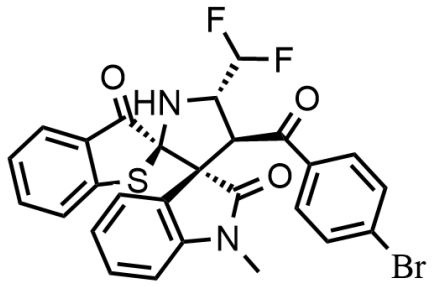


5ab

^{19}F NMR (376 MHz, $CDCl_3$)

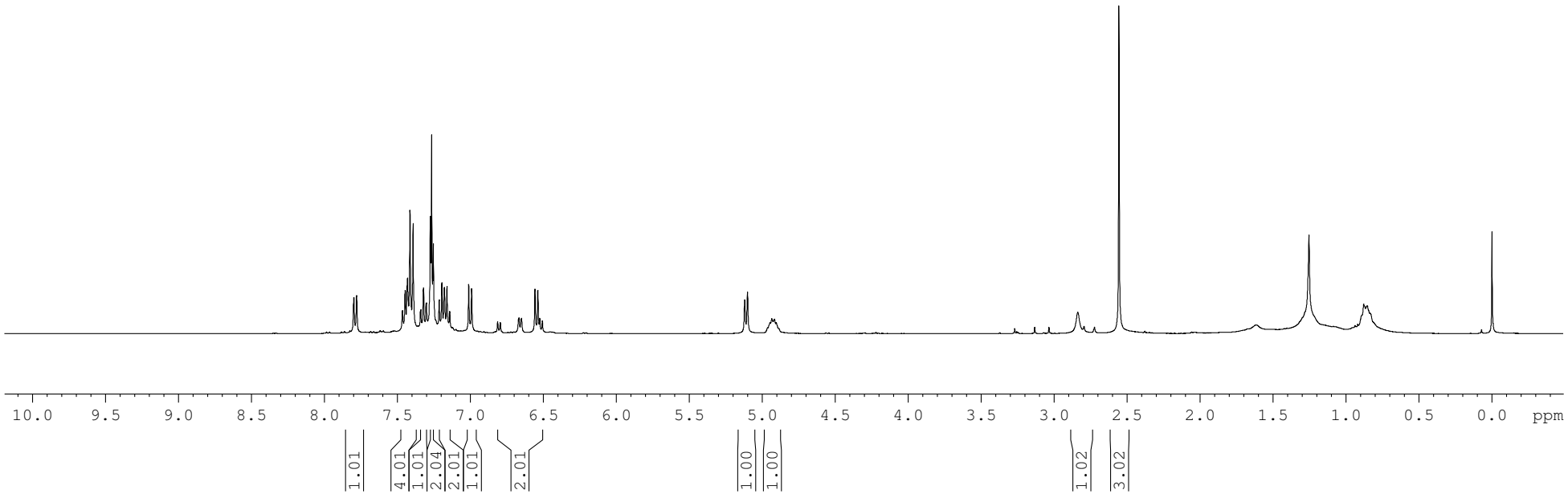


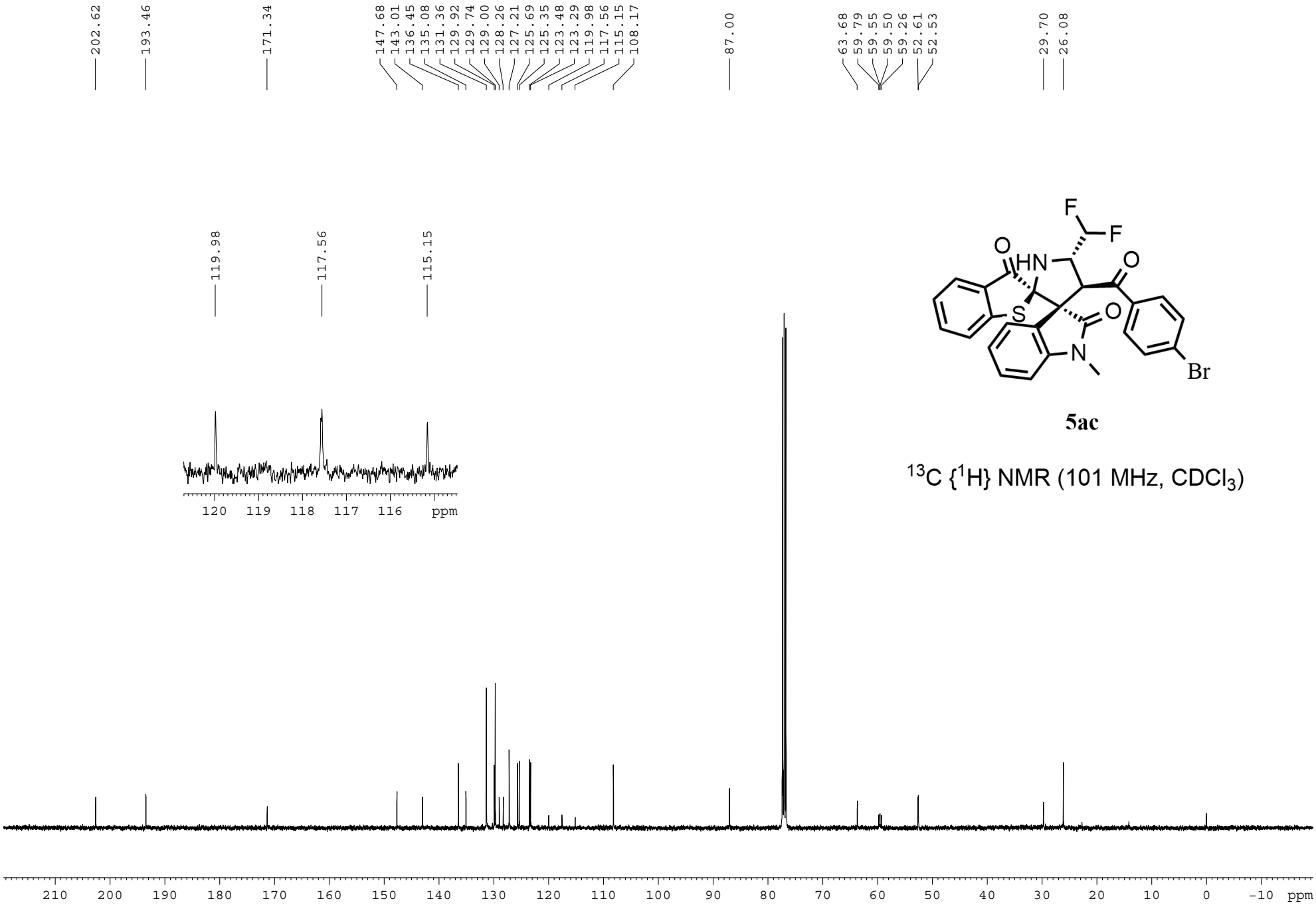


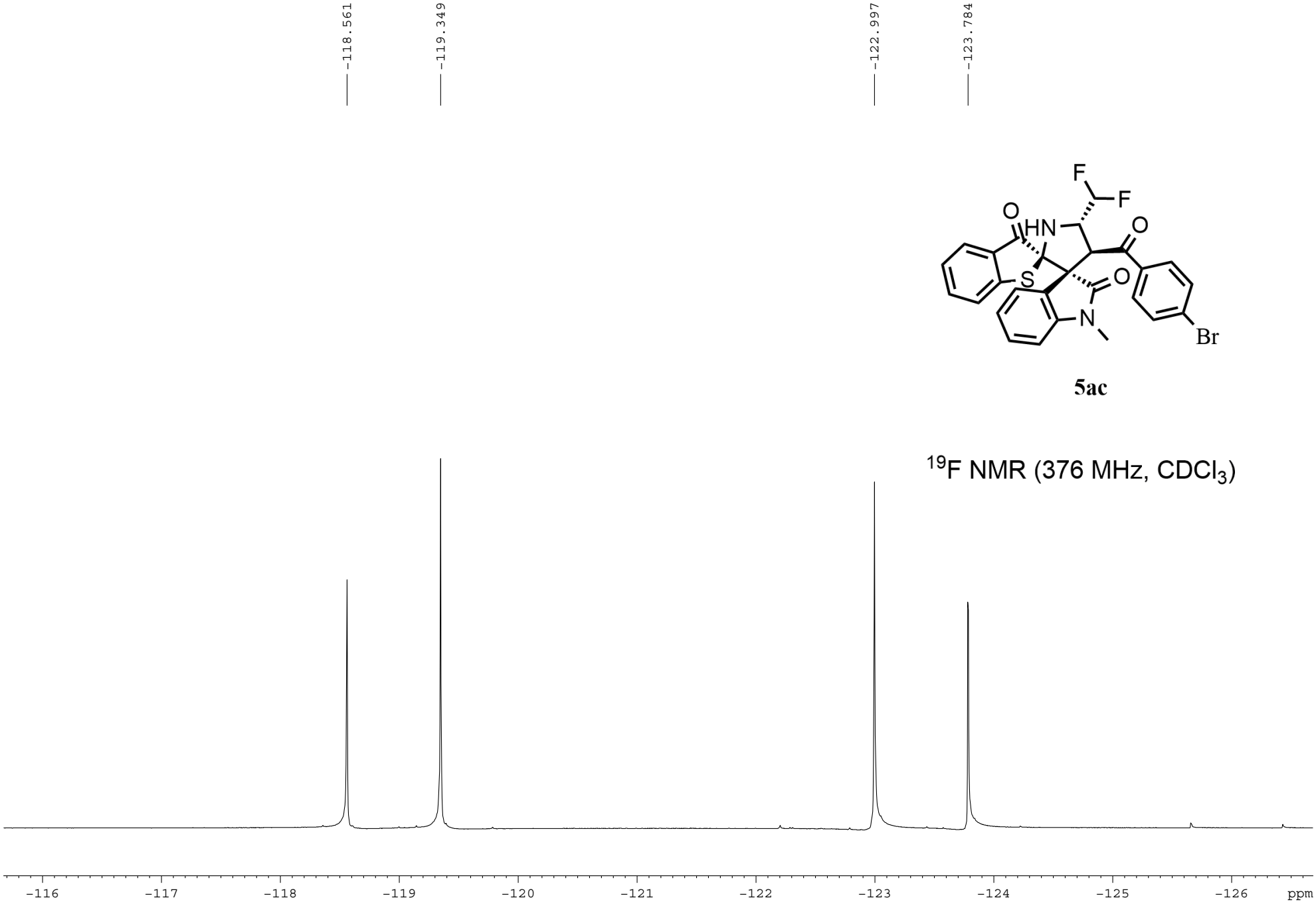


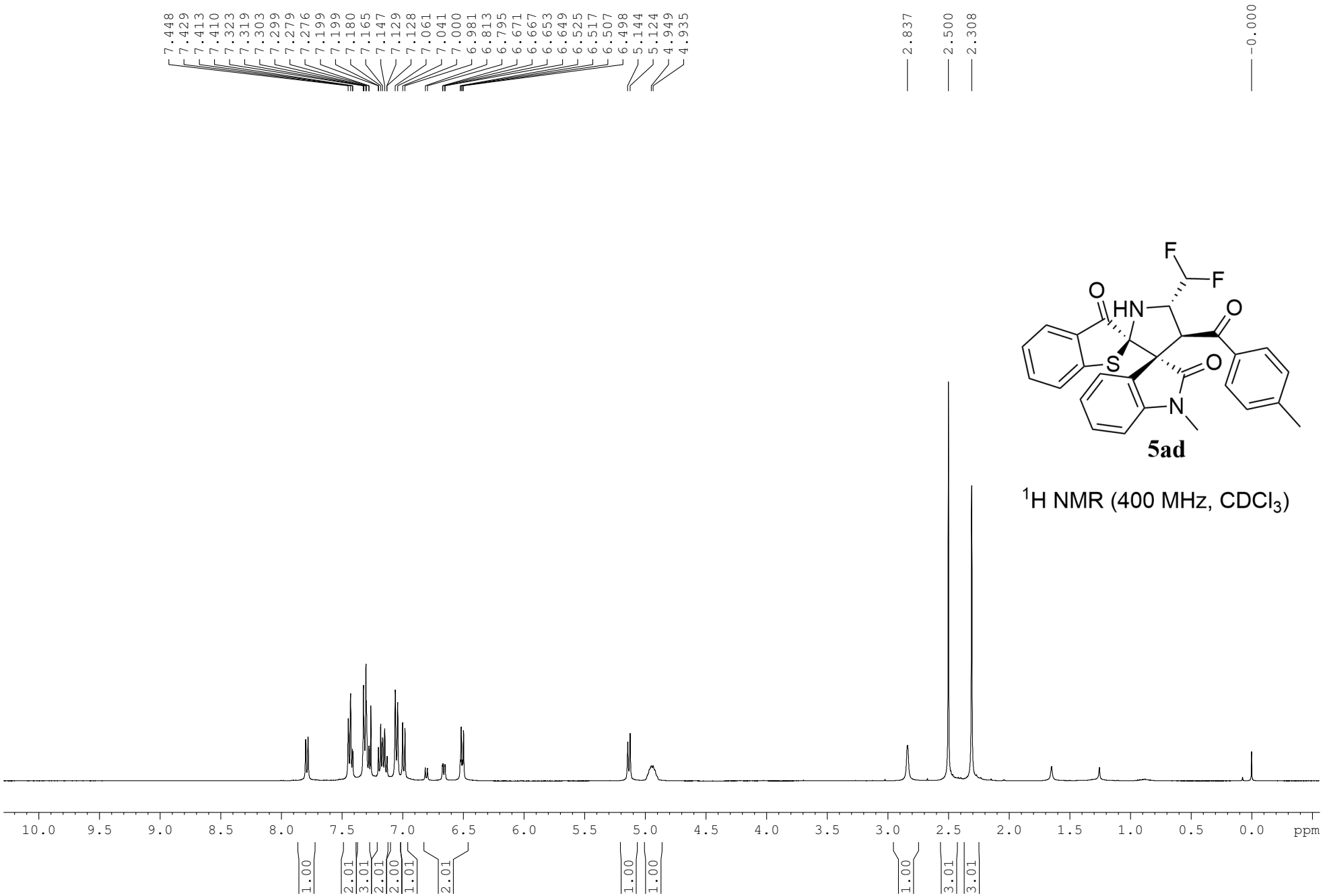
5ac

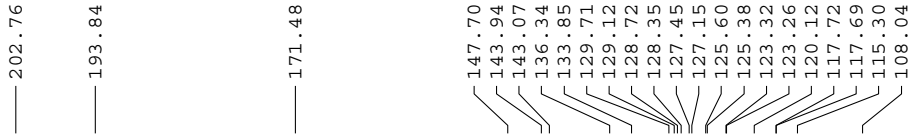
^{1}H NMR (400 MHz, $CDCl_3$)

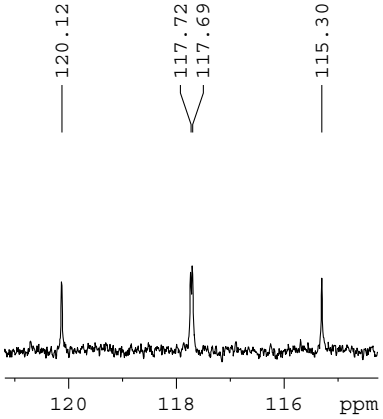


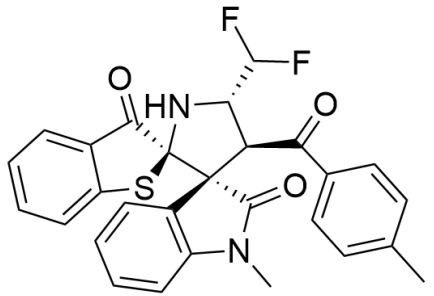

202.62
193.46
171.34
147.68
143.01
136.45
135.08
131.36
129.92
129.74
129.00
128.26
127.21
125.69
125.35
123.48
123.29
119.98
117.56
115.15
108.17
87.00
63.68
59.79
59.55
59.50
59.26
52.61
52.53
29.70
26.08
119.98
117.56
115.15
120 119 118 117 116 ppm
F
F
O
HN
O
S
O
N
Br
5ac
13C {1H} NMR (101 MHz, CDCl3)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 ppm


-118.561
-119.349
-122.997
-123.784
F
F
O
HN
O
S
O
N
Br
5ac
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.448
7.429
7.413
7.410
7.323
7.319
7.303
7.299
7.279
7.276
7.199
7.199
7.180
7.165
7.147
7.129
7.128
7.061
7.041
7.000
6.981
6.813
6.795
6.671
6.667
6.653
6.649
6.525
6.517
6.507
6.498
5.144
5.124
4.949
4.935
2.837
2.500
2.308
0.000
F
F
O
HN
O
S
O
N
5ad
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
2.01
3.01
2.01
2.00
1.01
2.01
1.00
1.00
1.00
3.01
3.01

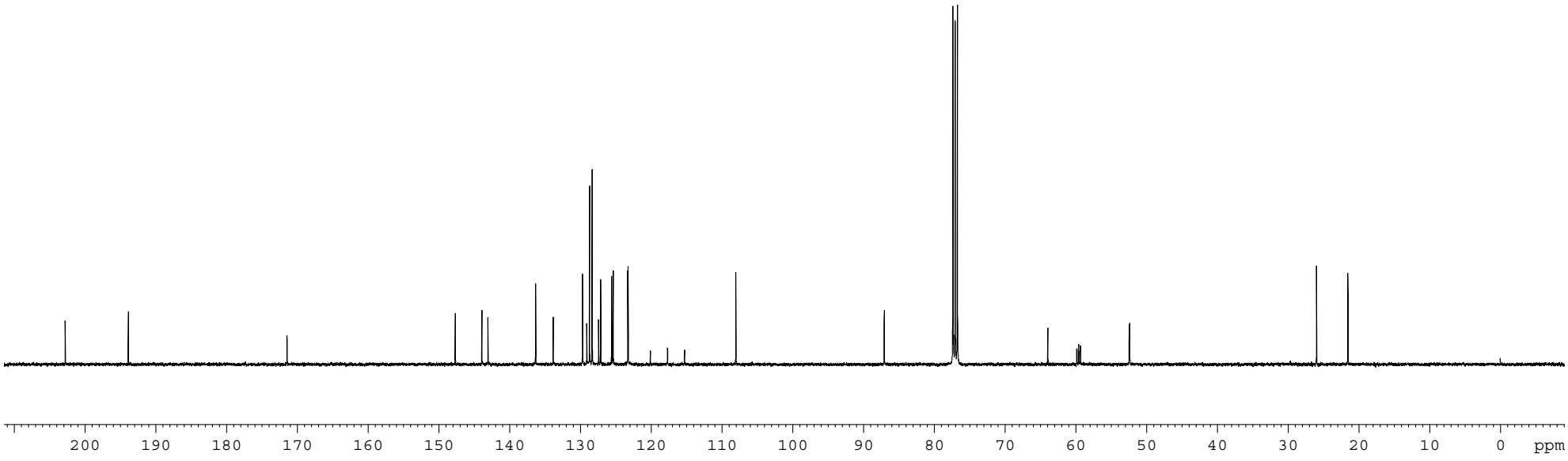


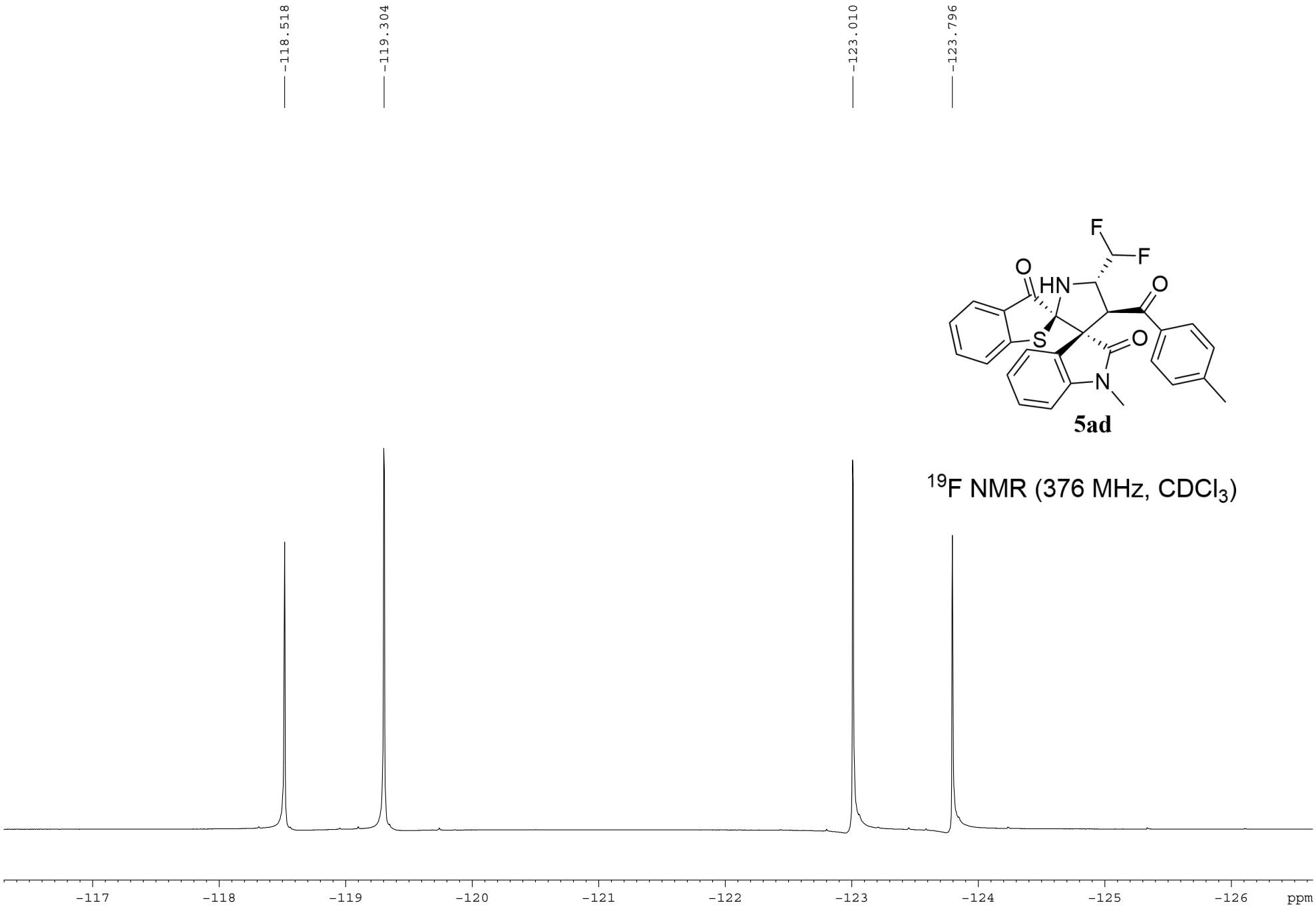


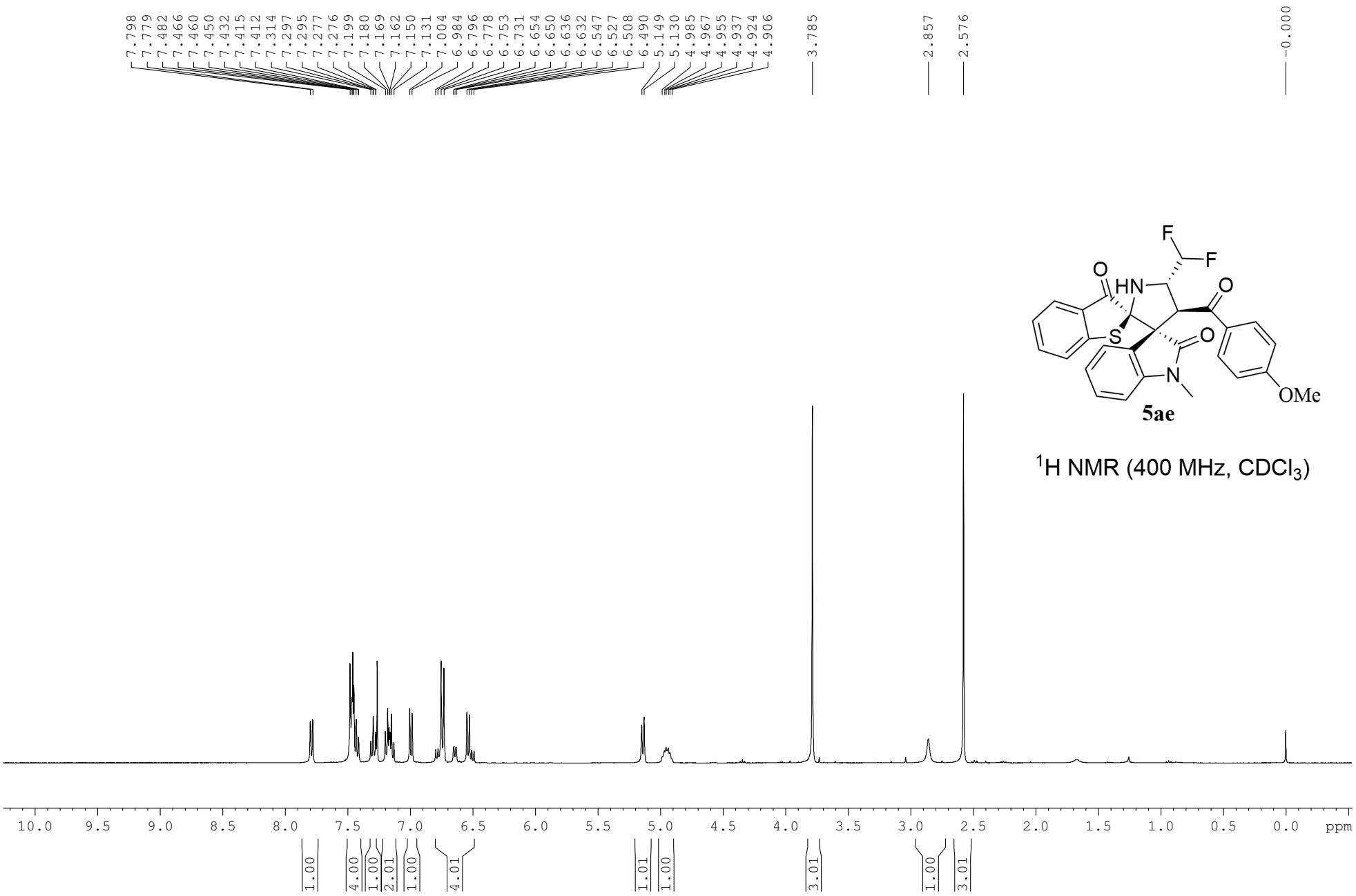


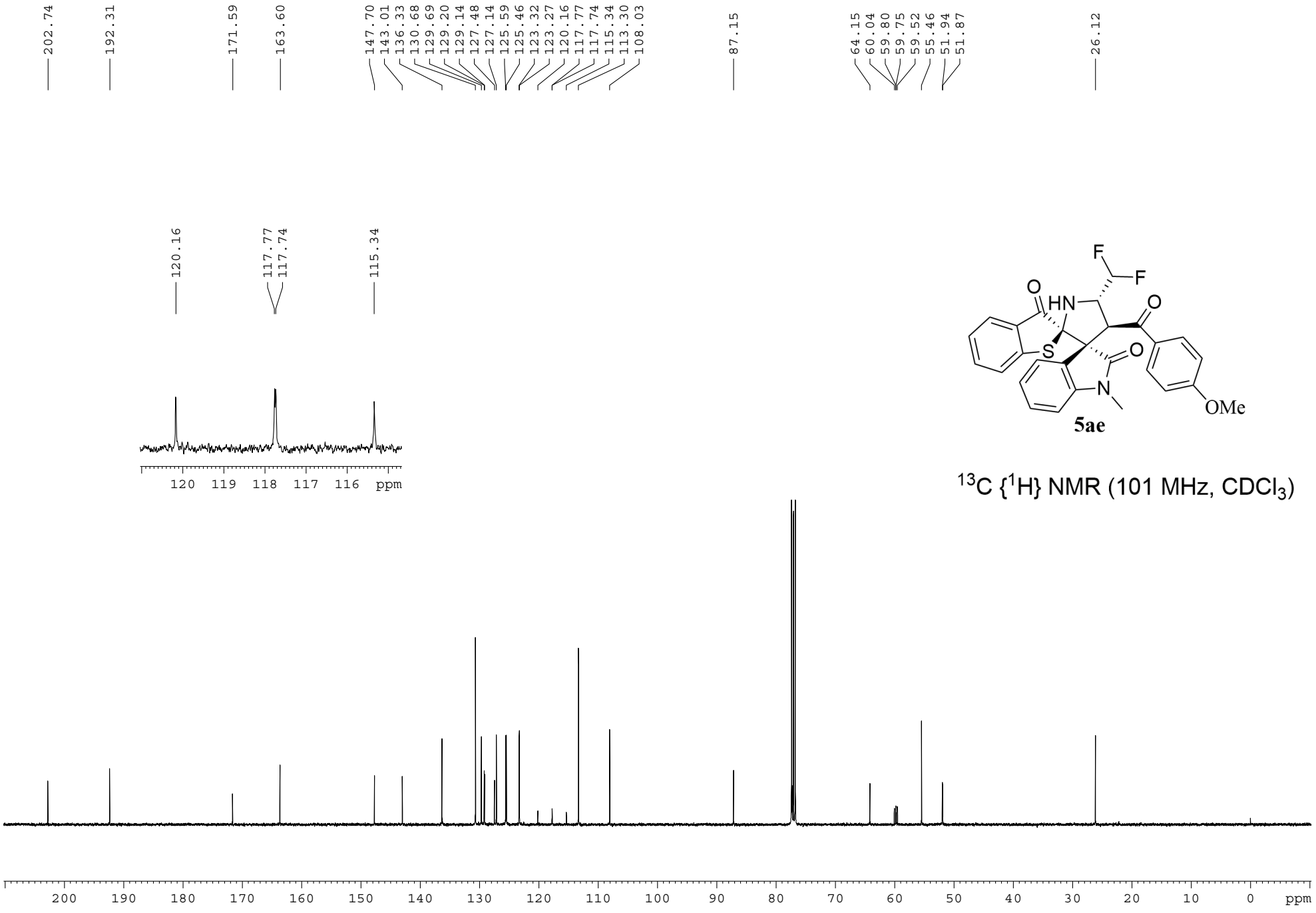
5ad

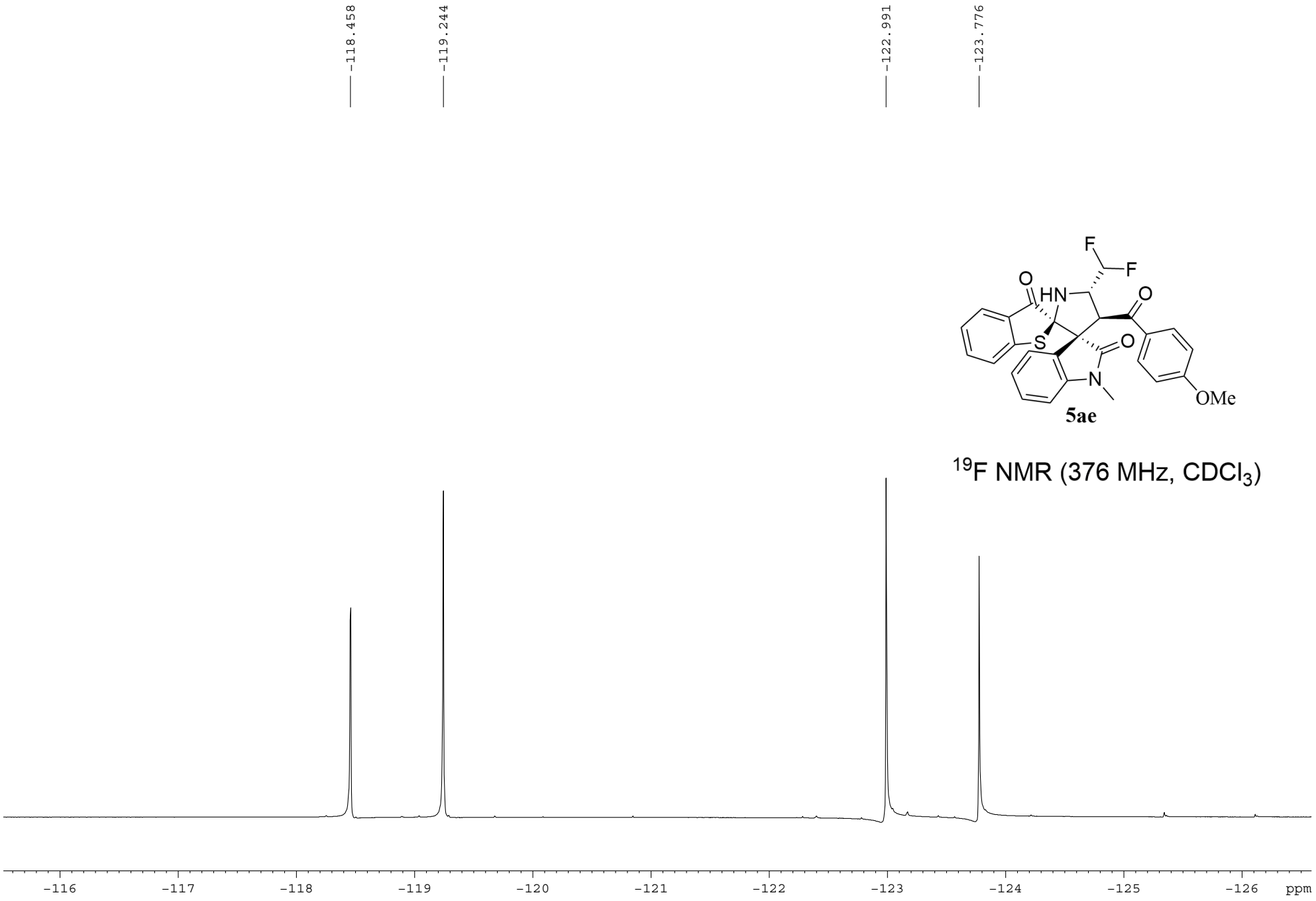
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

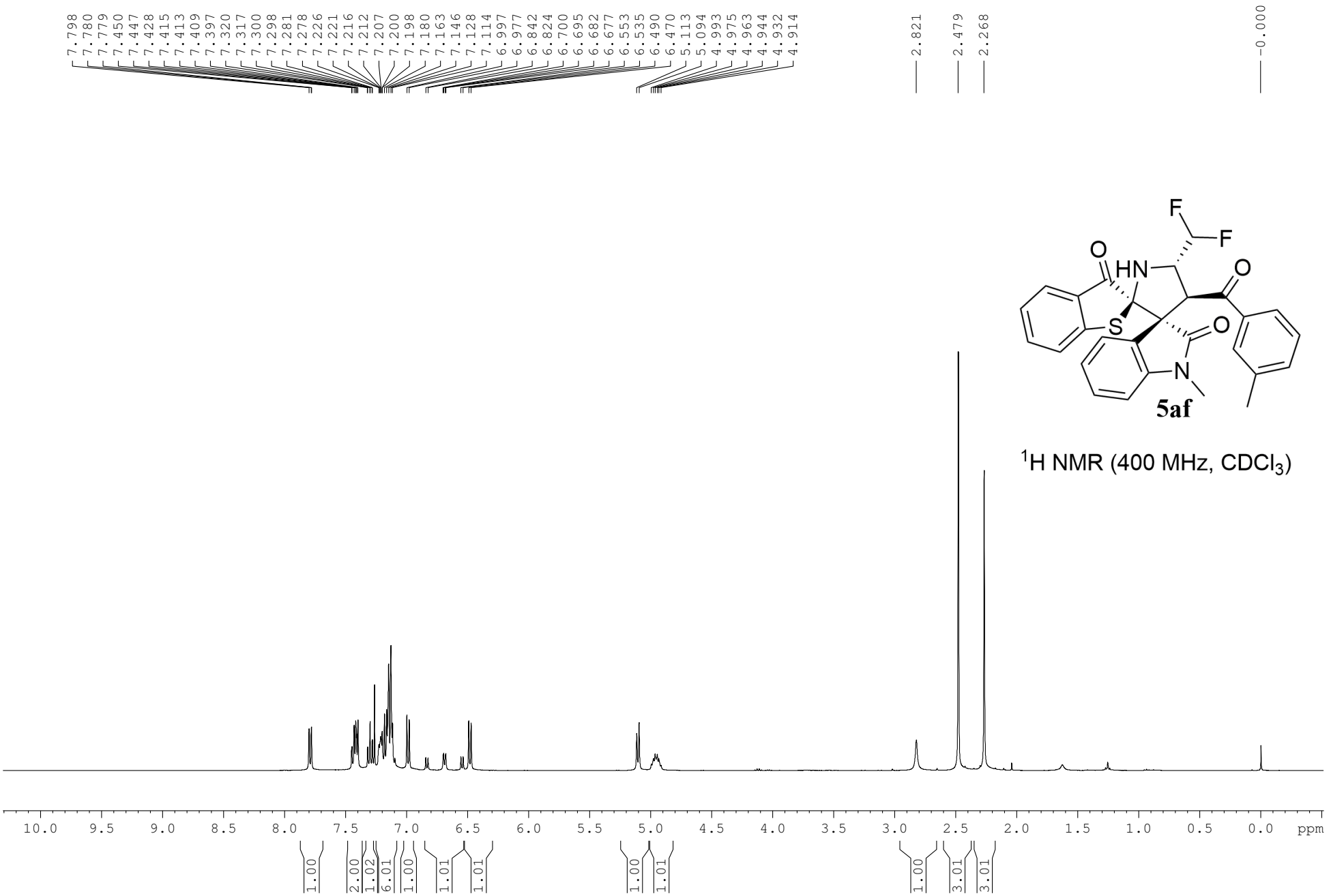


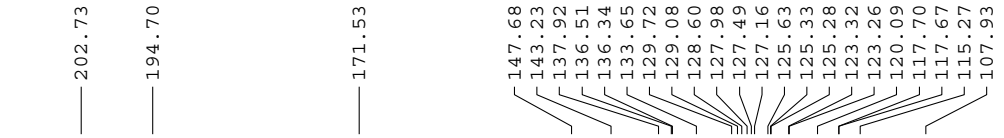

-118.518
-119.304
-123.010
-123.796
F
F
O
HN
O
S
O
N
5ad
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

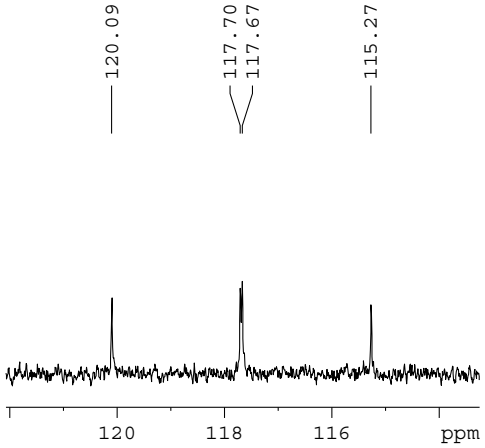

7.798
7.779
7.482
7.466
7.460
7.450
7.432
7.415
7.412
7.314
7.297
7.295
7.277
7.276
7.199
7.180
7.169
7.162
7.150
7.131
7.004
6.984
6.796
6.778
6.753
6.731
6.654
6.650
6.636
6.632
6.547
6.527
6.508
6.490
5.149
5.130
4.985
4.967
4.955
4.937
4.924
4.906
3.785
2.857
2.576
0.000
F
F
O
HN
O
S
O
N
OMe
5ae
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
4.00
1.00
2.01
1.00
4.01
1.01
1.00
3.01
1.00
3.01

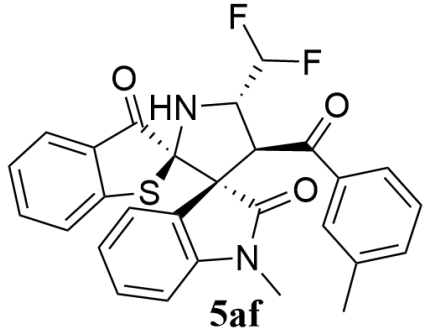

202.74
192.31
171.59
163.60
147.70
143.01
136.33
130.68
129.69
129.20
129.14
127.48
127.14
125.59
125.46
123.32
123.27
120.16
117.77
117.74
115.34
108.03
87.15
64.15
60.04
59.80
59.75
59.52
55.46
51.94
51.87
26.12
120.16
117.77
117.74
115.34
120 119 118 117 116 ppm
F
F
O
HN
O
S
O
N
OMe
5ae
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


-118.458
-119.244
-122.991
-123.776
F
F
O
HN
O
S
O
N
OMe
5ae
19F NMR (376 MHz, CDCl3)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.798
7.780
7.779
7.450
7.447
7.428
7.415
7.413
7.409
7.397
7.320
7.317
7.300
7.298
7.281
7.278
7.226
7.221
7.216
7.212
7.207
7.200
7.198
7.180
7.163
7.146
7.128
7.114
6.997
6.977
6.842
6.824
6.700
6.695
6.682
6.677
6.553
6.535
6.490
6.470
5.113
5.094
4.993
4.975
4.963
4.944
4.932
4.914
2.821
2.479
2.268
-0.000
F
F
O
HN
O
S
O
N
5af
^{1}H NMR (400 MHz, $CDCl_3$)
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
ppm
1.00
2.00
1.02
6.01
1.00
1.01
1.01
1.00
1.01
1.00
3.01
3.01

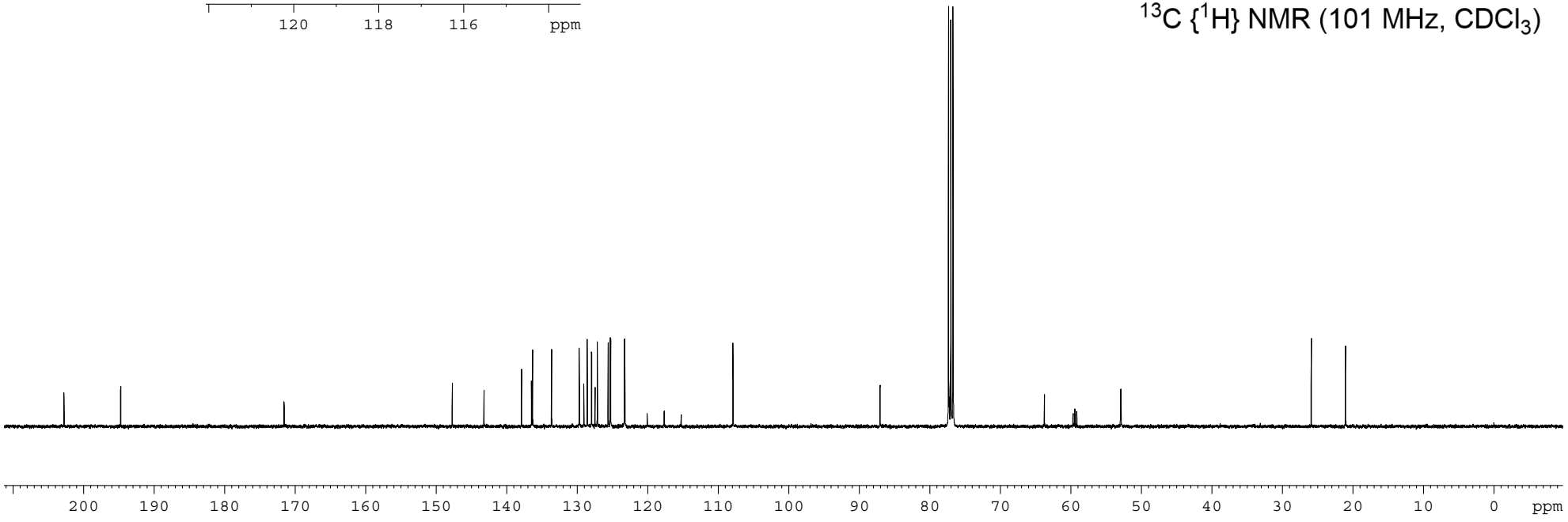


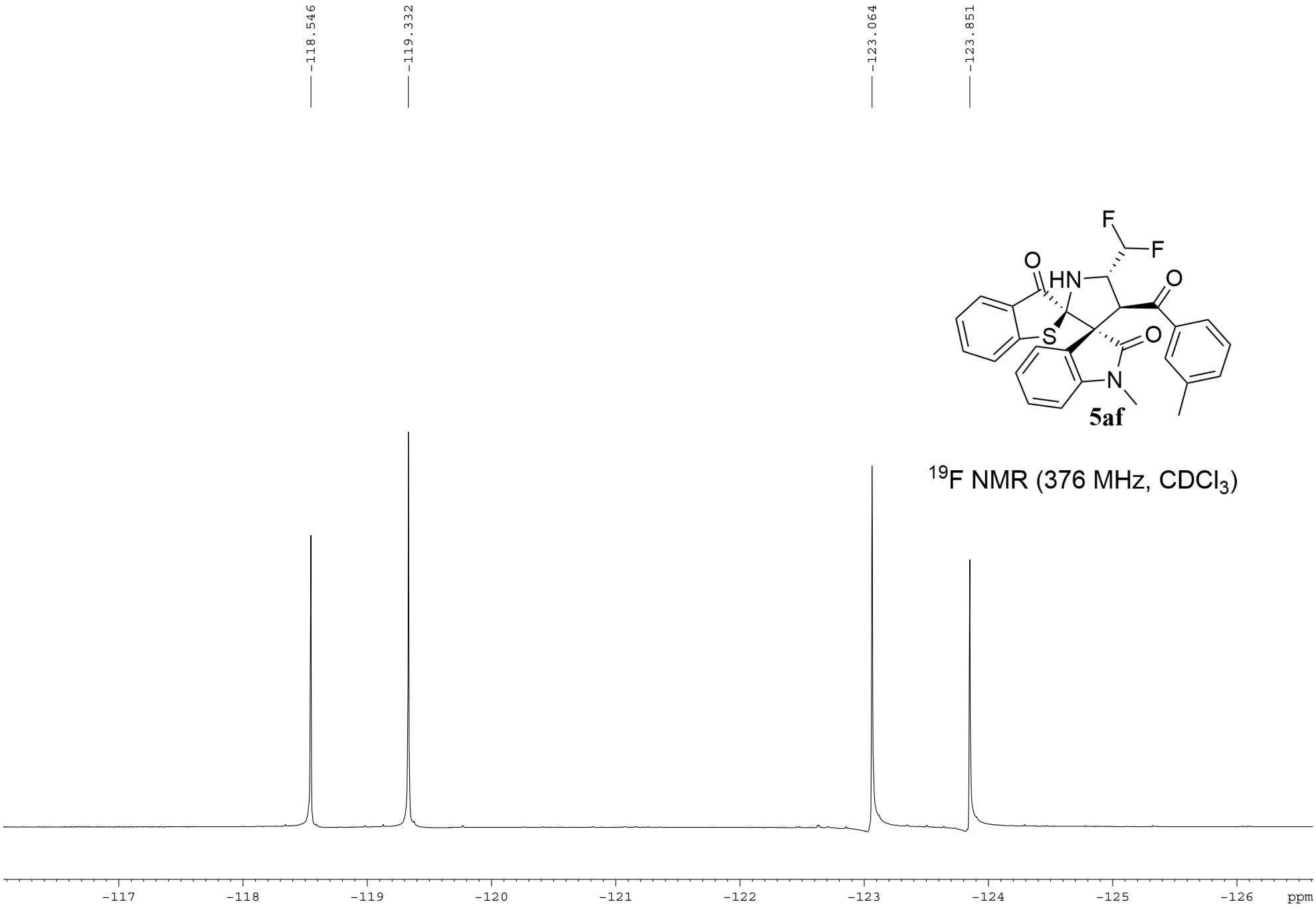


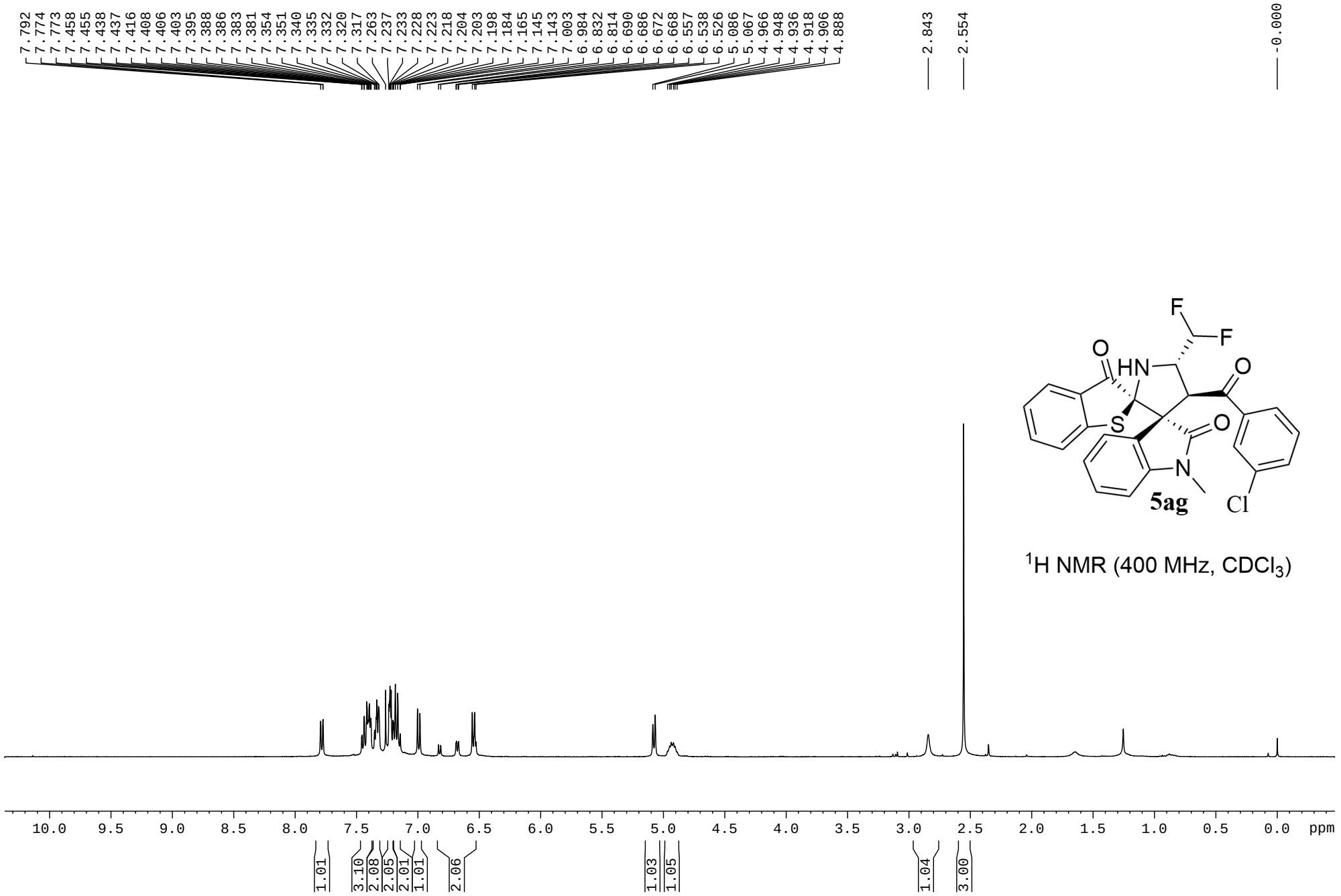


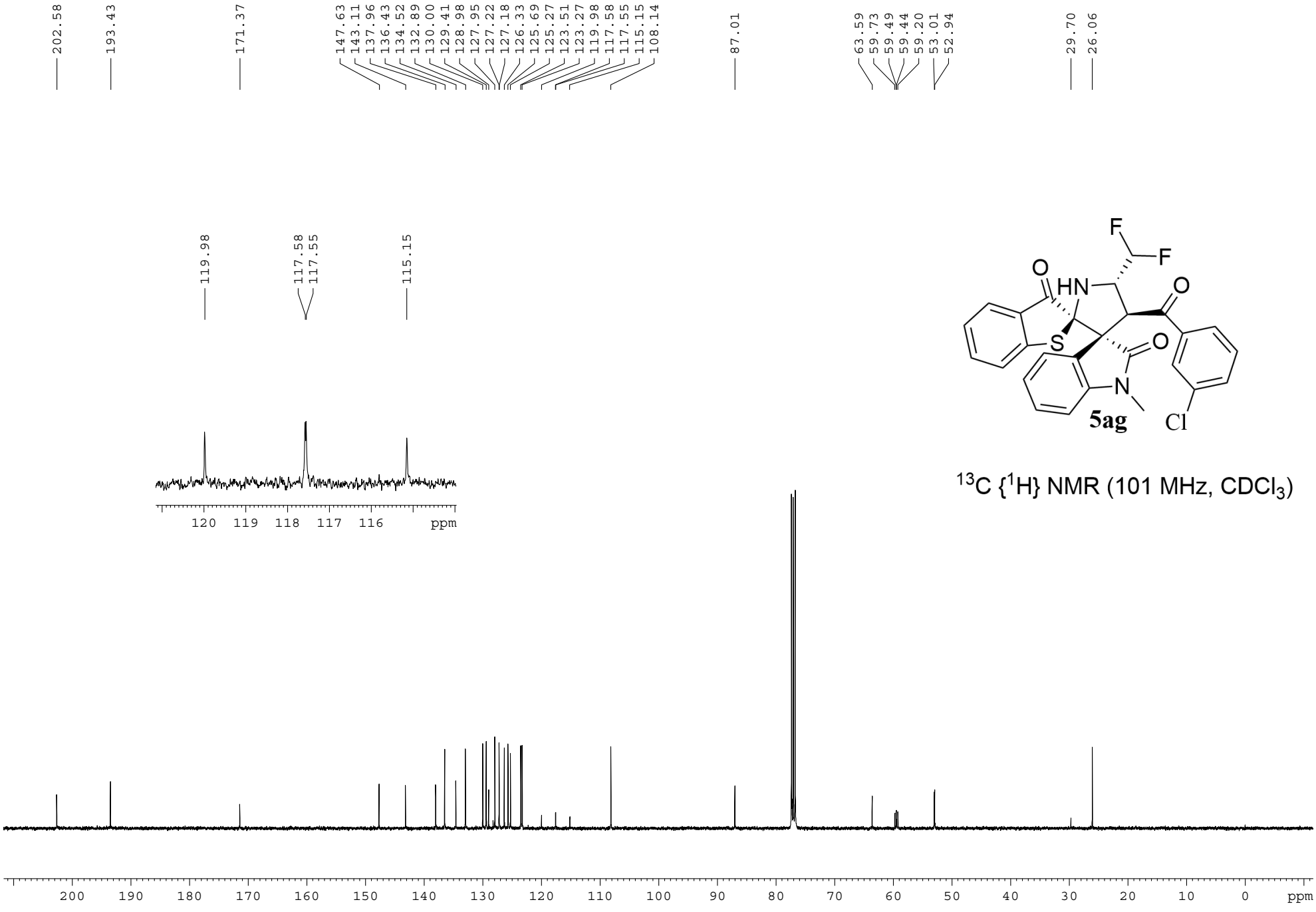
5af

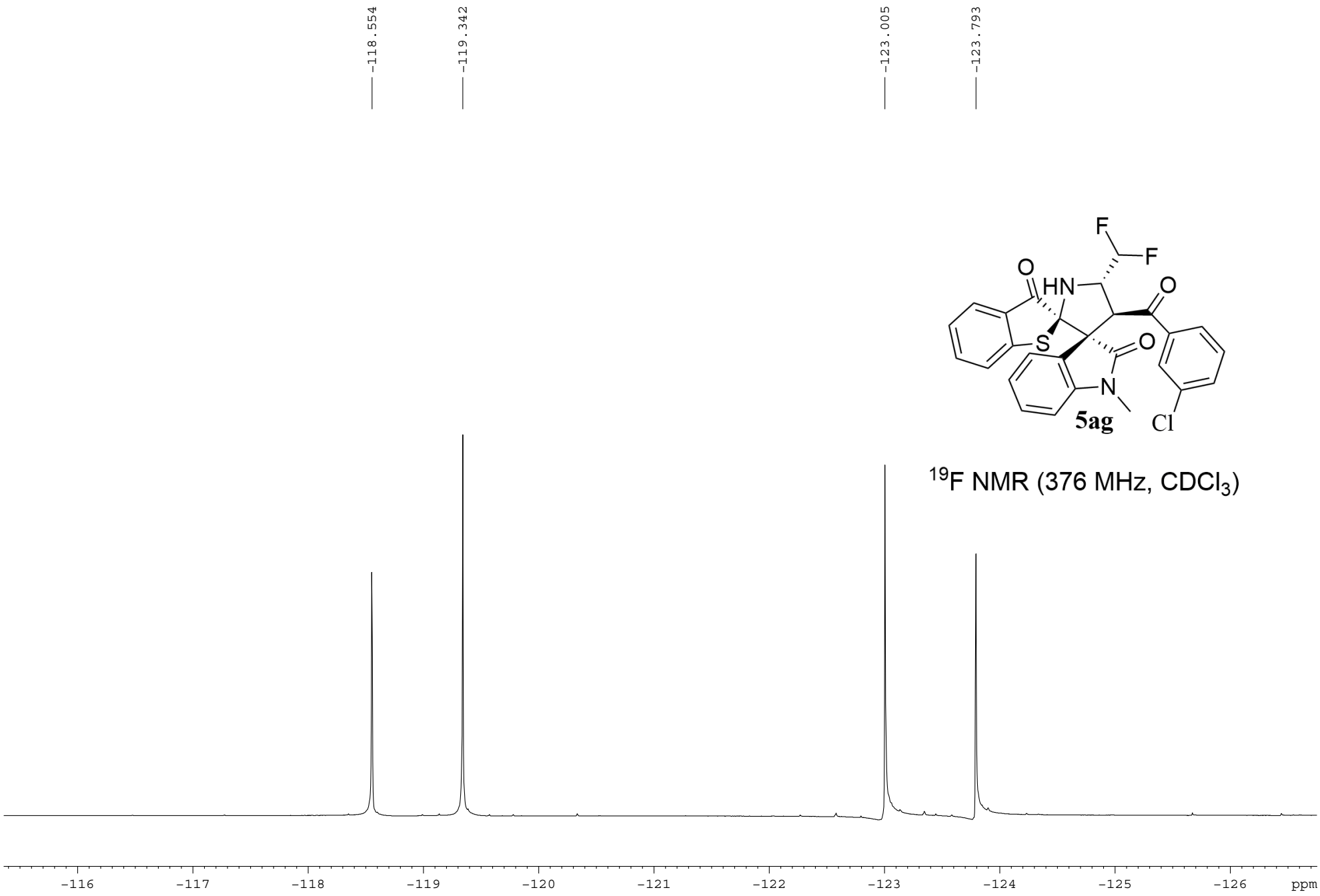
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)

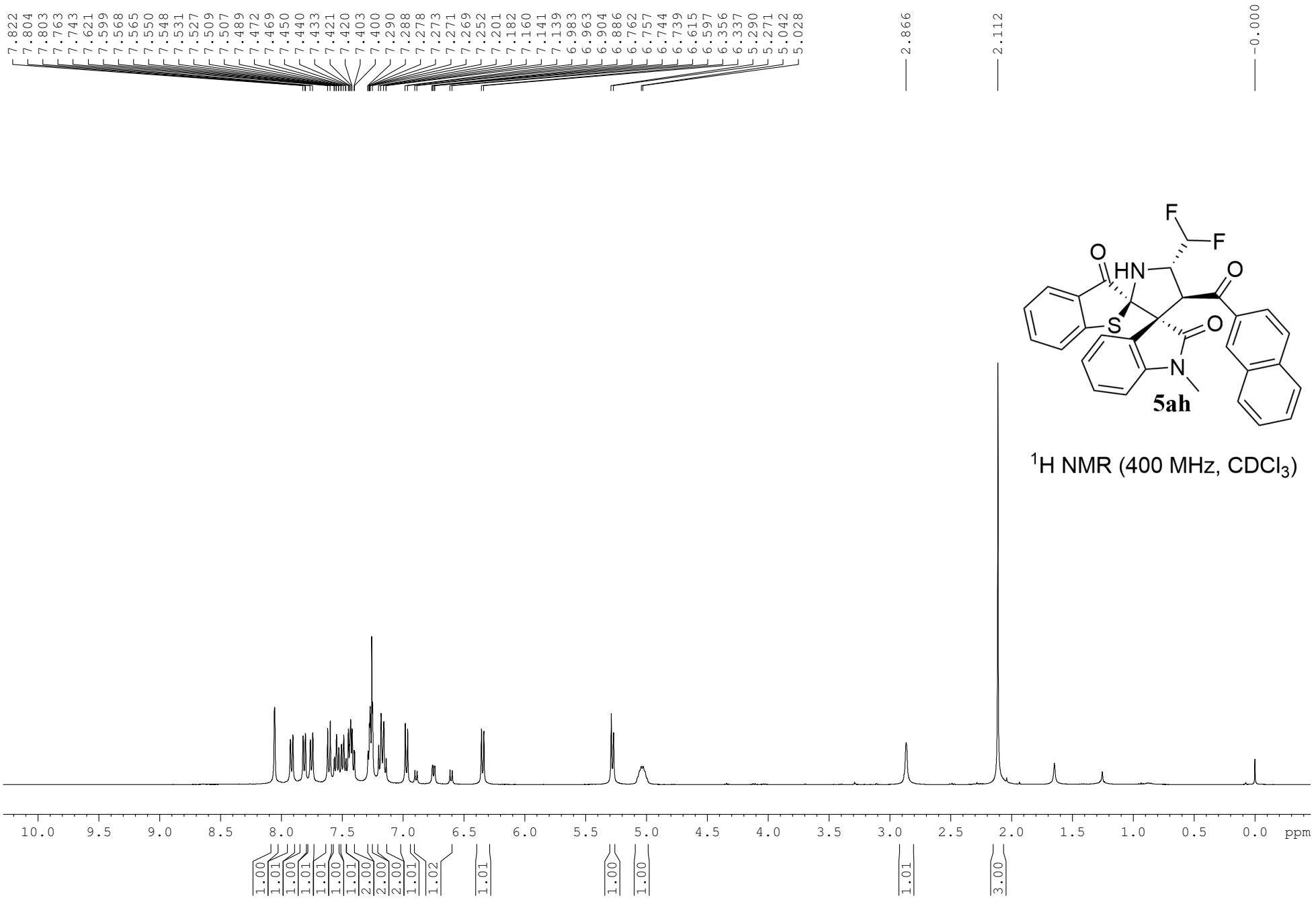


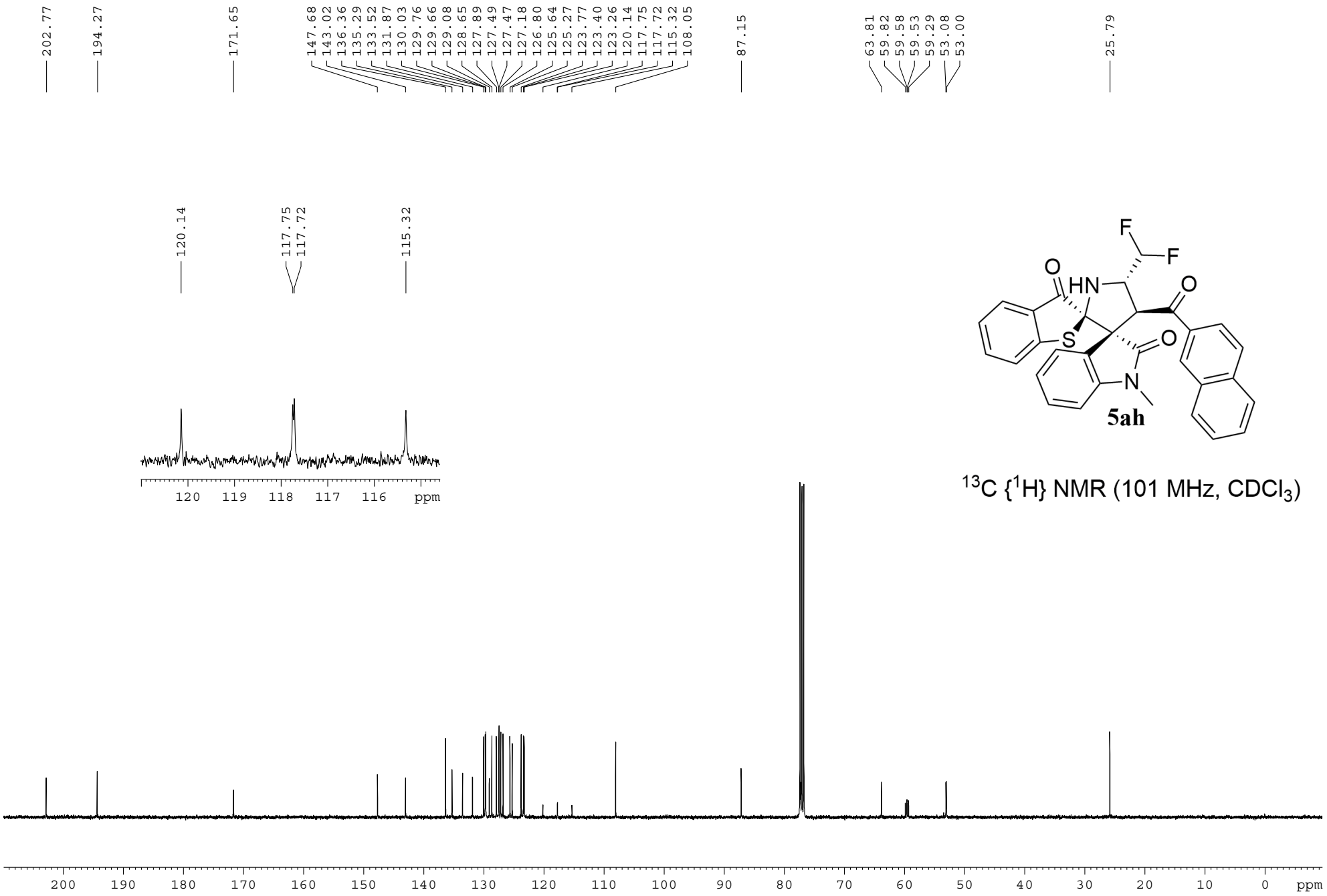

-118.546
-119.332
-123.064
-123.851
F
F
O
HN
O
S
O
N
5af
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

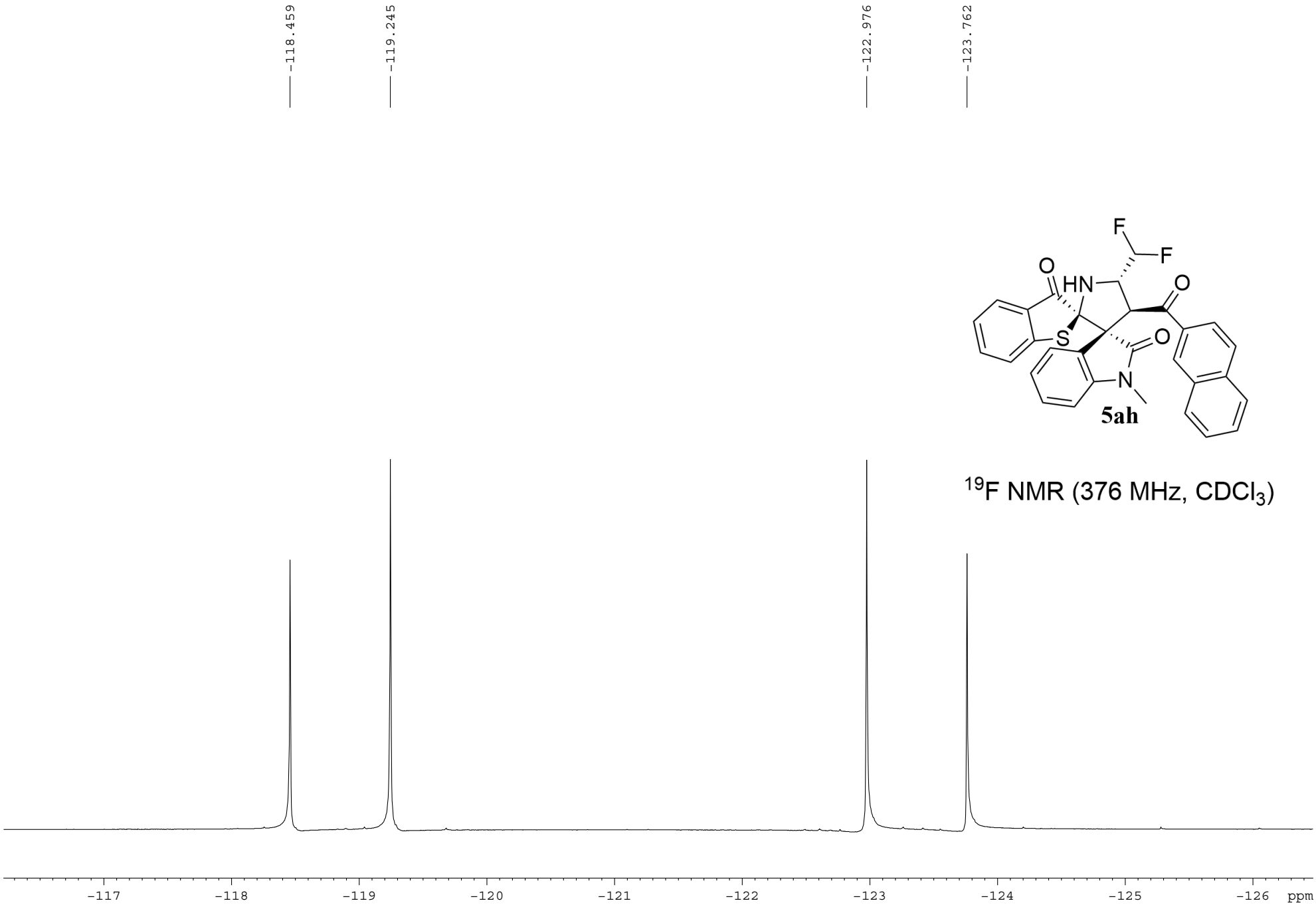

7.792
7.774
7.773
7.458
7.455
7.438
7.437
7.416
7.408
7.406
7.403
7.395
7.388
7.386
7.383
7.381
7.354
7.351
7.340
7.335
7.332
7.320
7.317
7.263
7.237
7.233
7.228
7.223
7.218
7.204
7.203
7.198
7.184
7.165
7.145
7.143
7.003
6.984
6.832
6.814
6.690
6.686
6.672
6.668
6.557
6.538
6.526
5.086
5.067
4.966
4.948
4.936
4.918
4.906
4.888
2.843
2.554
-0.000
F
F
O
HN
O
S
O
N
Cl
5ag
^{1}H NMR (400 MHz, $CDCl_3$)
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
ppm
1.01
3.10
2.08
2.05
2.01
1.01
2.06
1.03
1.05
1.04
3.00

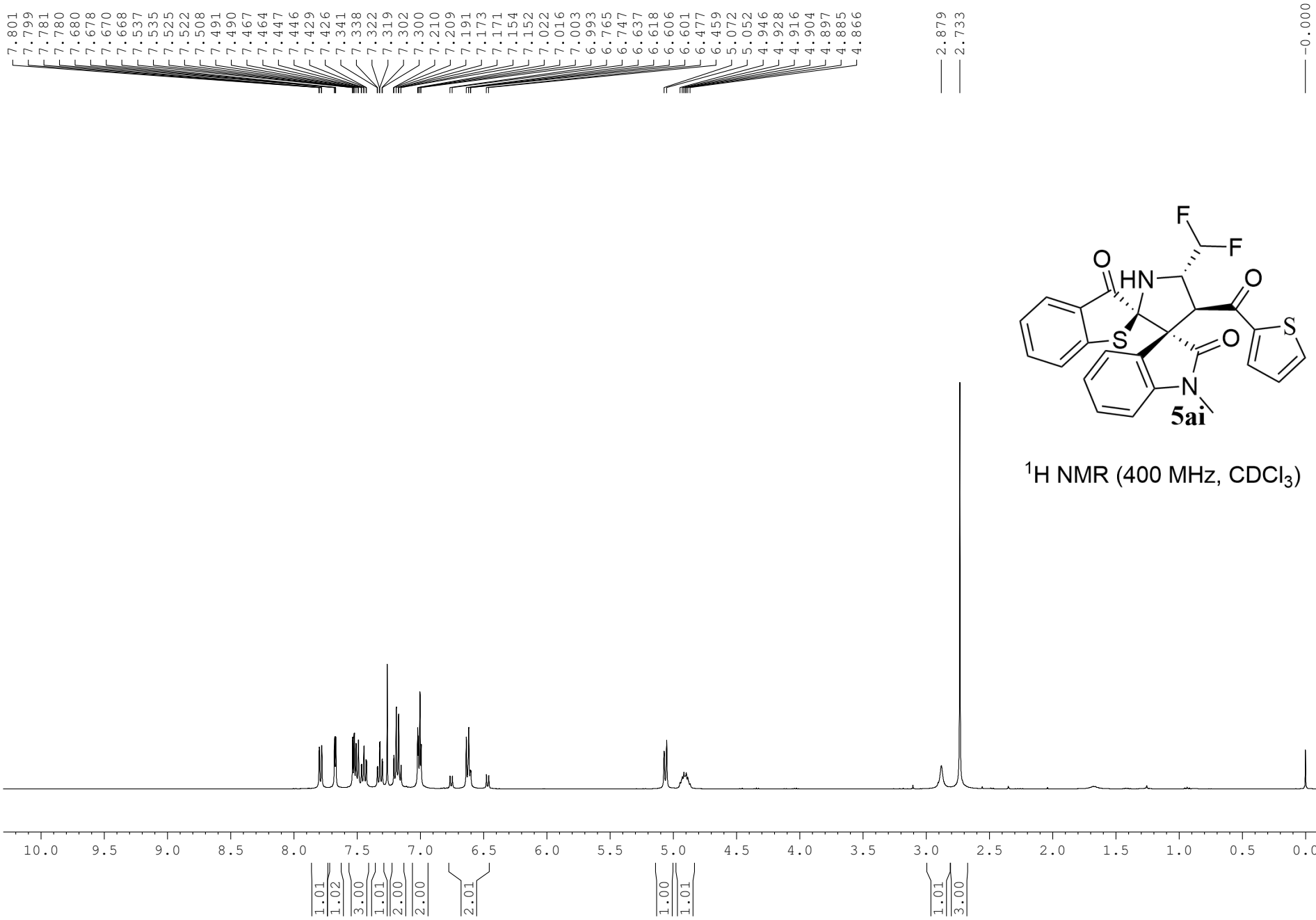

202.58
193.43
171.37
147.63
143.11
137.96
136.43
134.52
132.89
130.00
129.41
128.98
127.95
127.22
127.18
126.33
125.69
125.27
123.51
123.27
119.98
117.58
117.55
115.15
115.14
108.14
87.01
63.59
59.73
59.49
59.44
59.20
53.01
52.94
29.70
26.06
119.98
117.58
117.55
115.15
120 119 118 117 116 ppm
F
F
O
HN
O
S
O
N
Cl
5ag
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

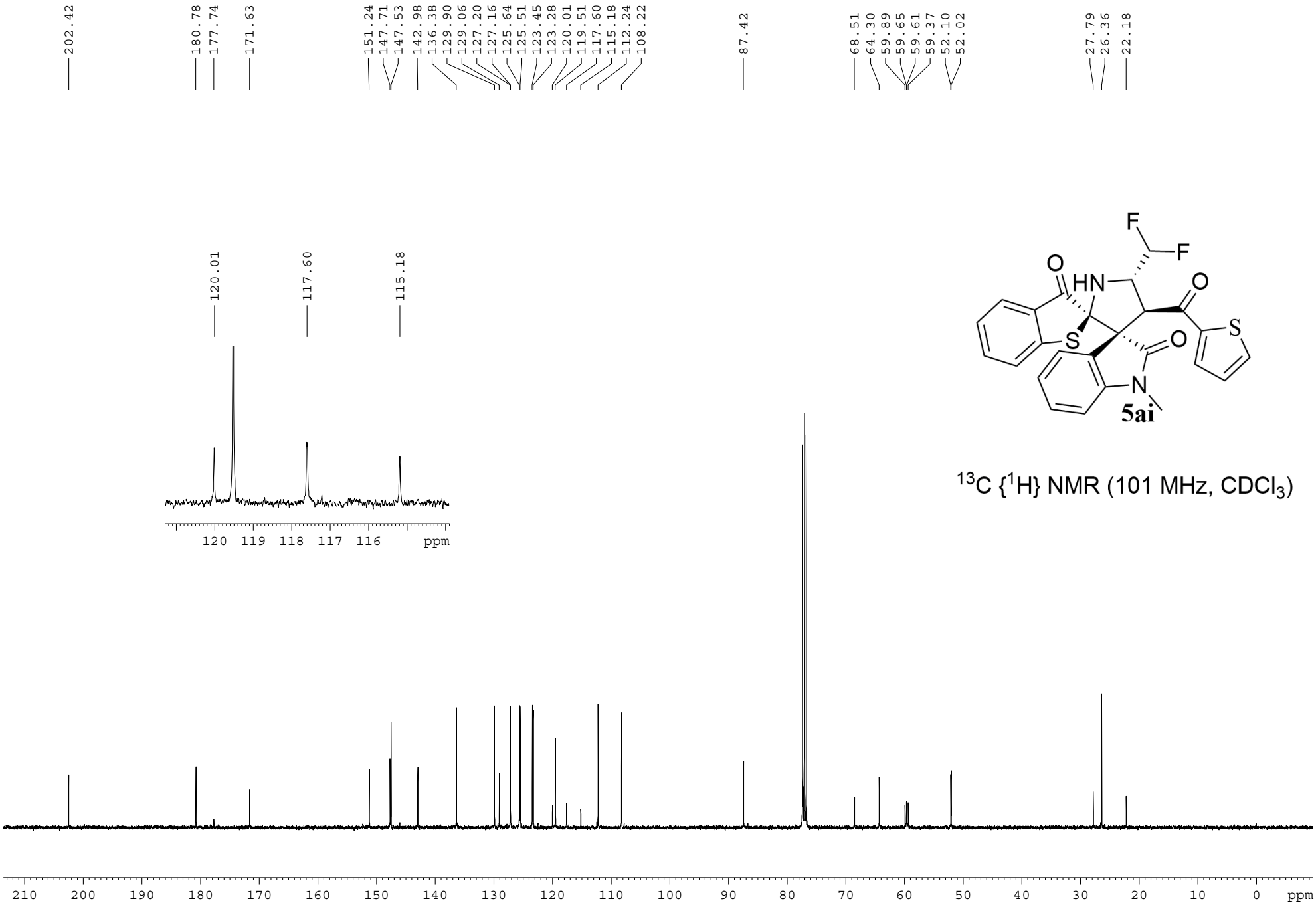

-118.554
-119.342
-123.005
-123.793
F
F
O
HN
O
S
O
N
Cl
5ag
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

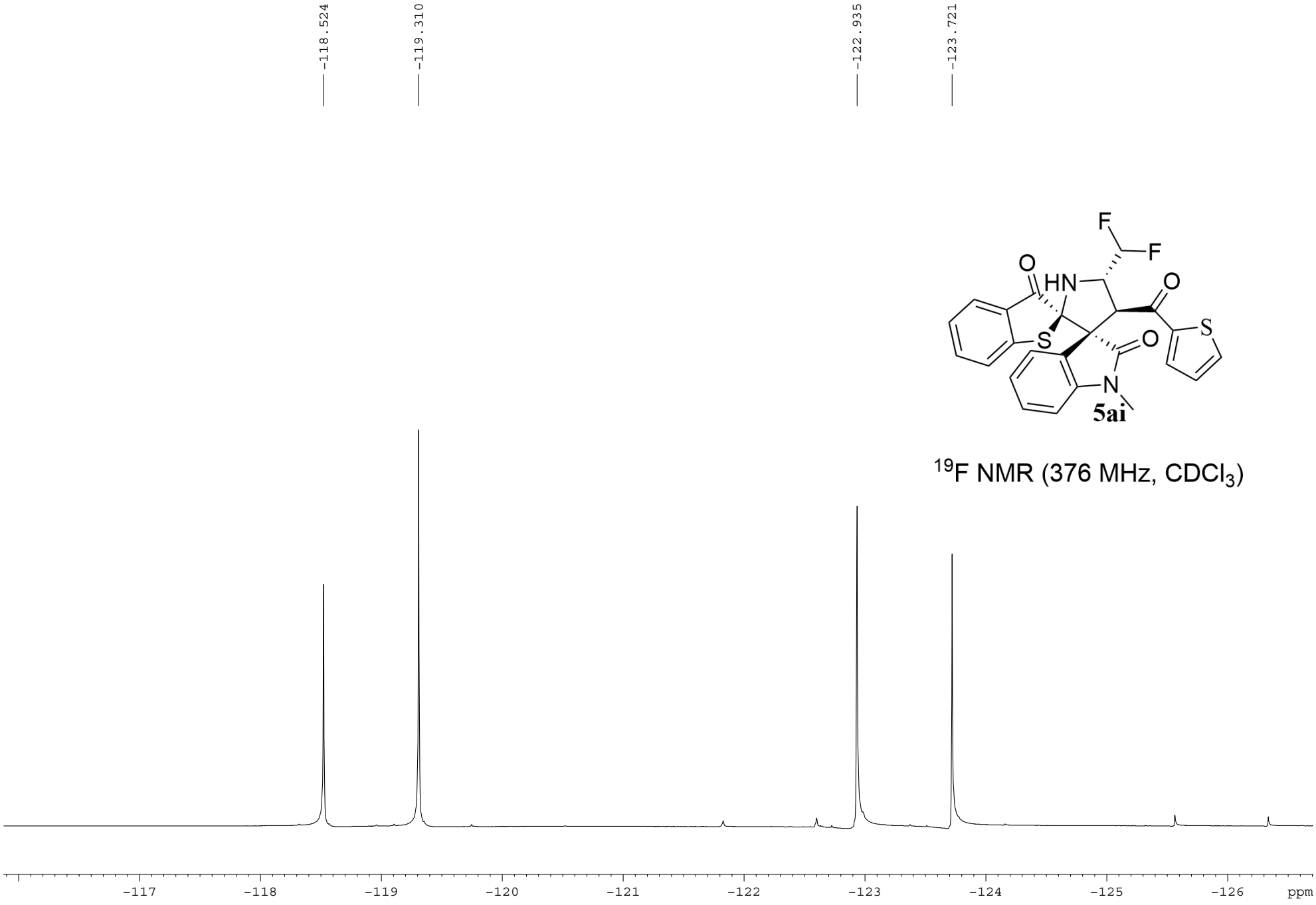

7.822
7.804
7.803
7.763
7.743
7.621
7.599
7.568
7.565
7.550
7.548
7.531
7.527
7.509
7.507
7.489
7.472
7.469
7.450
7.440
7.433
7.421
7.420
7.403
7.400
7.290
7.288
7.278
7.273
7.271
7.269
7.252
7.201
7.182
7.160
7.141
7.139
6.983
6.963
6.904
6.886
6.762
6.757
6.744
6.739
6.615
6.597
6.356
6.337
5.290
5.271
5.042
5.028
2.866
2.112
0.000
F
F
O
HN
O
S
O
N
5ah
1H NMR (400 MHz, CDCl3)
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
ppm
1.00
1.01
1.00
1.01
1.01
1.00
1.01
2.00
2.00
2.00
1.01
1.02
1.01
1.00
1.00
1.01
3.00

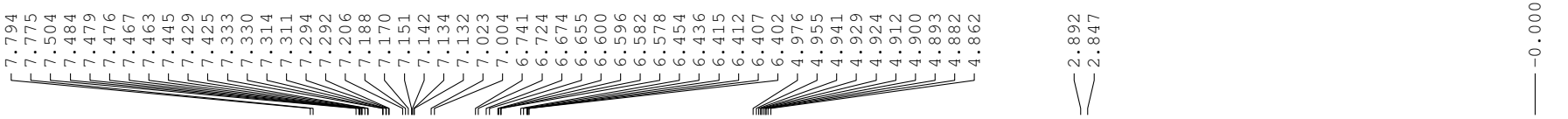

202.77
194.27
171.65
147.68
143.02
136.36
135.29
133.52
131.87
130.03
129.76
129.66
129.08
128.65
127.89
127.49
127.47
127.18
126.80
125.64
125.27
123.77
123.40
123.26
120.14
117.75
117.72
115.32
108.05
87.15
63.81
59.82
59.58
59.53
59.29
53.08
53.00
25.79
120.14
117.75
117.72
115.32
120 119 118 117 116 ppm
F
F
O
HN
O
S
O
N
5ah
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

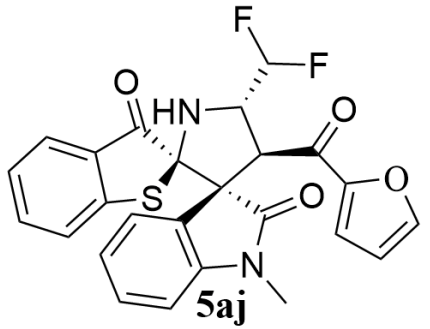

-118.459
-119.245
-122.976
-123.762
F
F
O
HN
O
S
O
N
5ah
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.801
7.799
7.781
7.780
7.680
7.678
7.670
7.668
7.537
7.535
7.525
7.522
7.508
7.491
7.490
7.467
7.464
7.447
7.446
7.429
7.426
7.341
7.338
7.322
7.319
7.302
7.300
7.210
7.209
7.191
7.173
7.171
7.154
7.152
7.022
7.016
7.003
6.993
6.765
6.747
6.637
6.618
6.606
6.601
6.477
6.459
5.072
5.052
4.946
4.928
4.916
4.904
4.897
4.885
4.866
2.879
2.733
0.000
F
F
O
HN
O
S
O
S
N
5ai
1H NMR (400 MHz, CDCl3)
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
ppm
1.01
1.02
3.00
1.01
2.00
2.00
2.01
1.00
1.01
1.01
3.00


202.42
180.78
177.74
171.63
151.24
147.71
147.53
142.98
136.38
129.90
129.06
127.20
127.16
125.64
125.51
123.45
123.28
120.01
119.51
117.60
115.18
112.24
108.22
87.42
68.51
64.30
59.89
59.65
59.61
59.37
52.10
52.02
27.79
26.36
22.18
120.01
117.60
115.18
120 119 118 117 116 ppm
F
F
O
HN
O
S
O
S
N
5ai
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

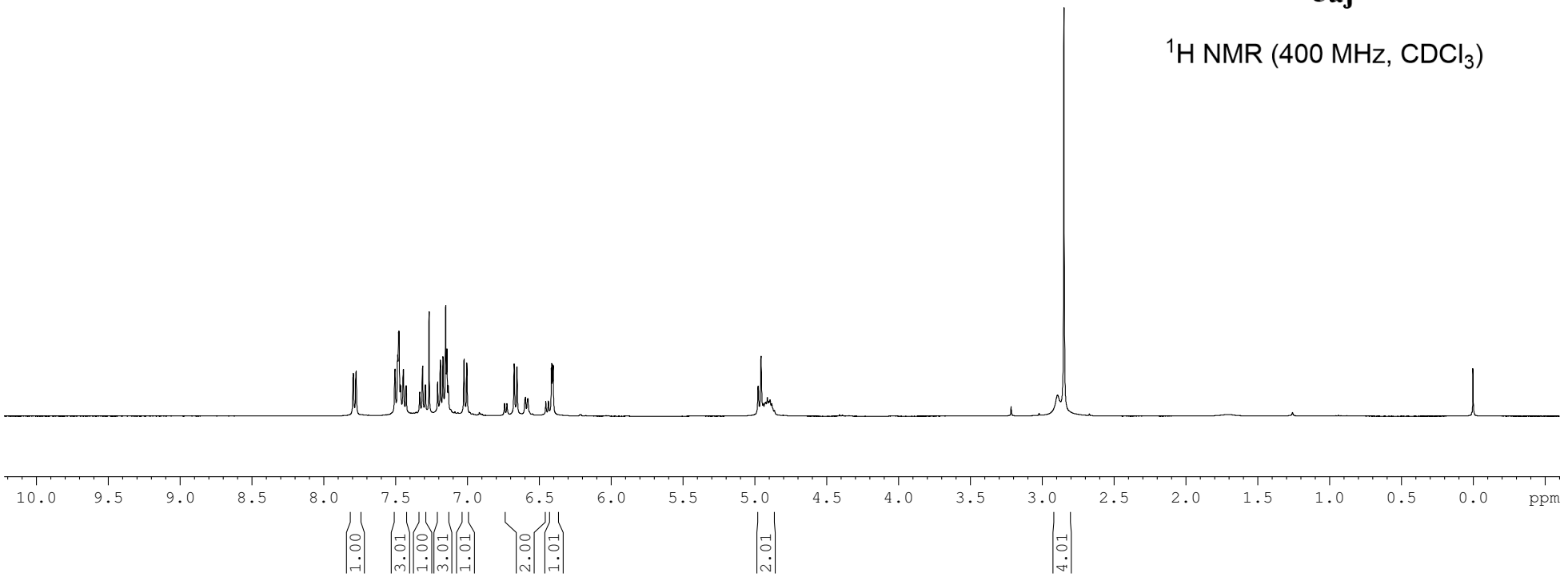

-118.524
-119.310
-122.935
-123.721
F
F
O
HN
O
S
O
S
N
5ai
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

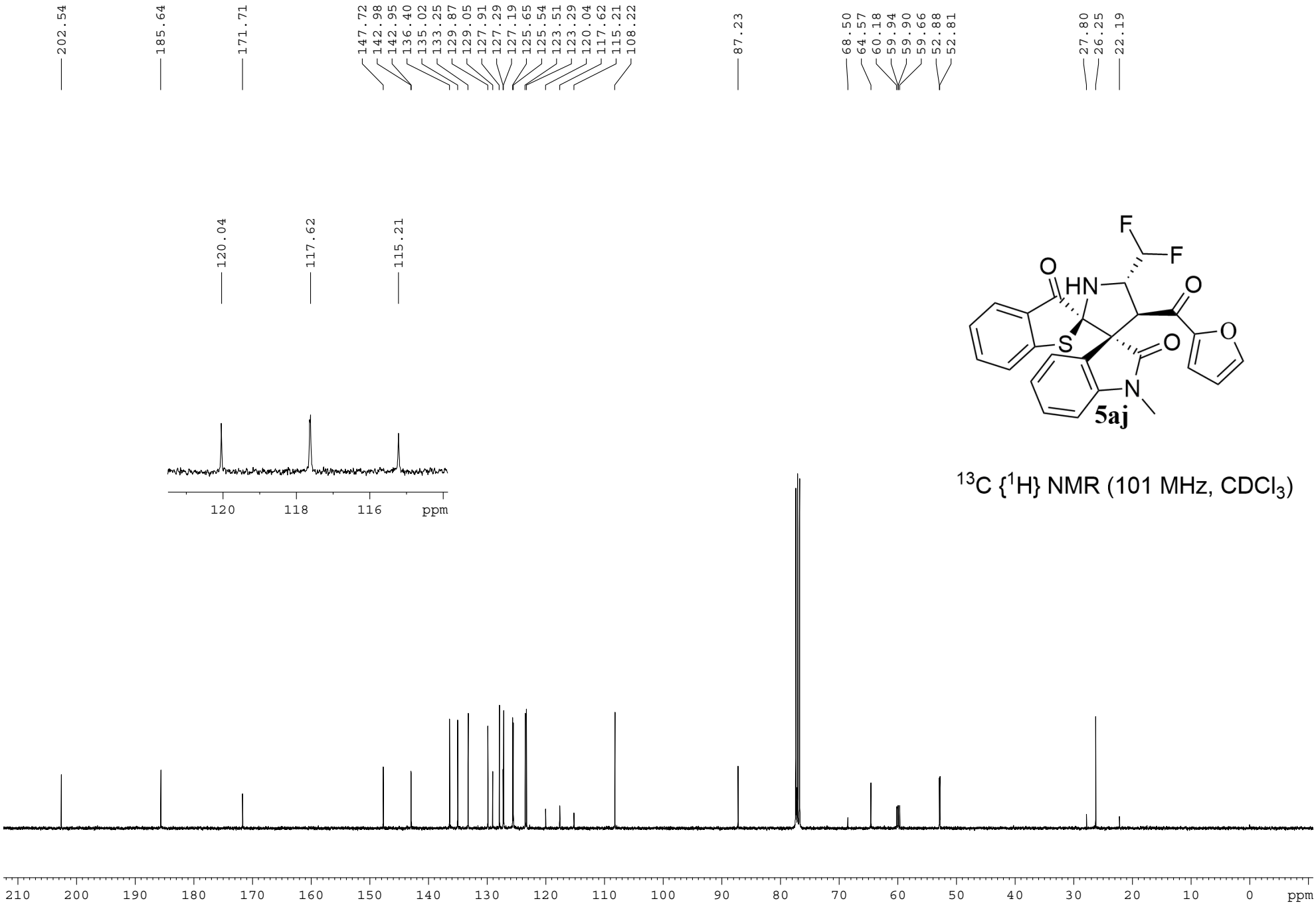


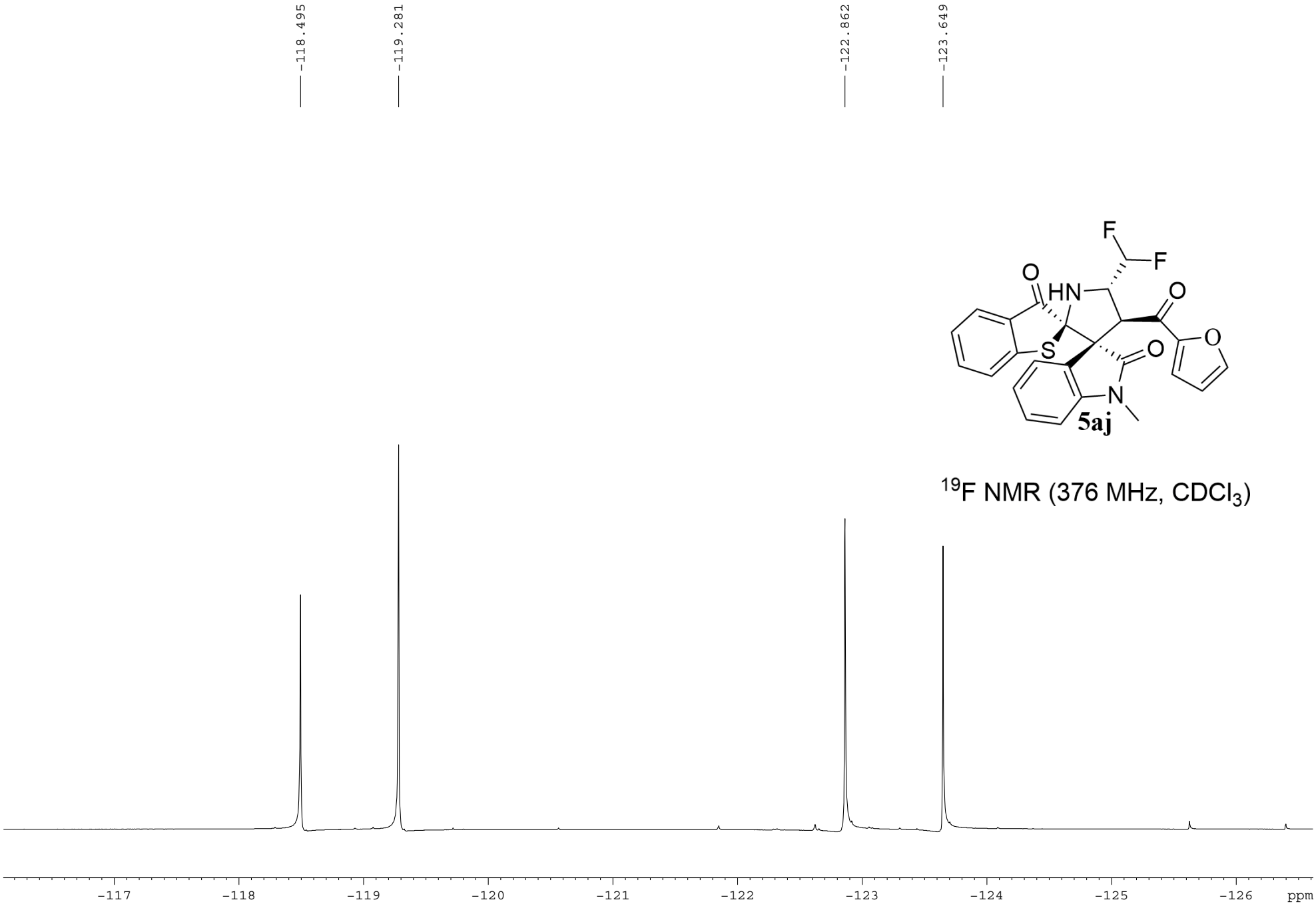


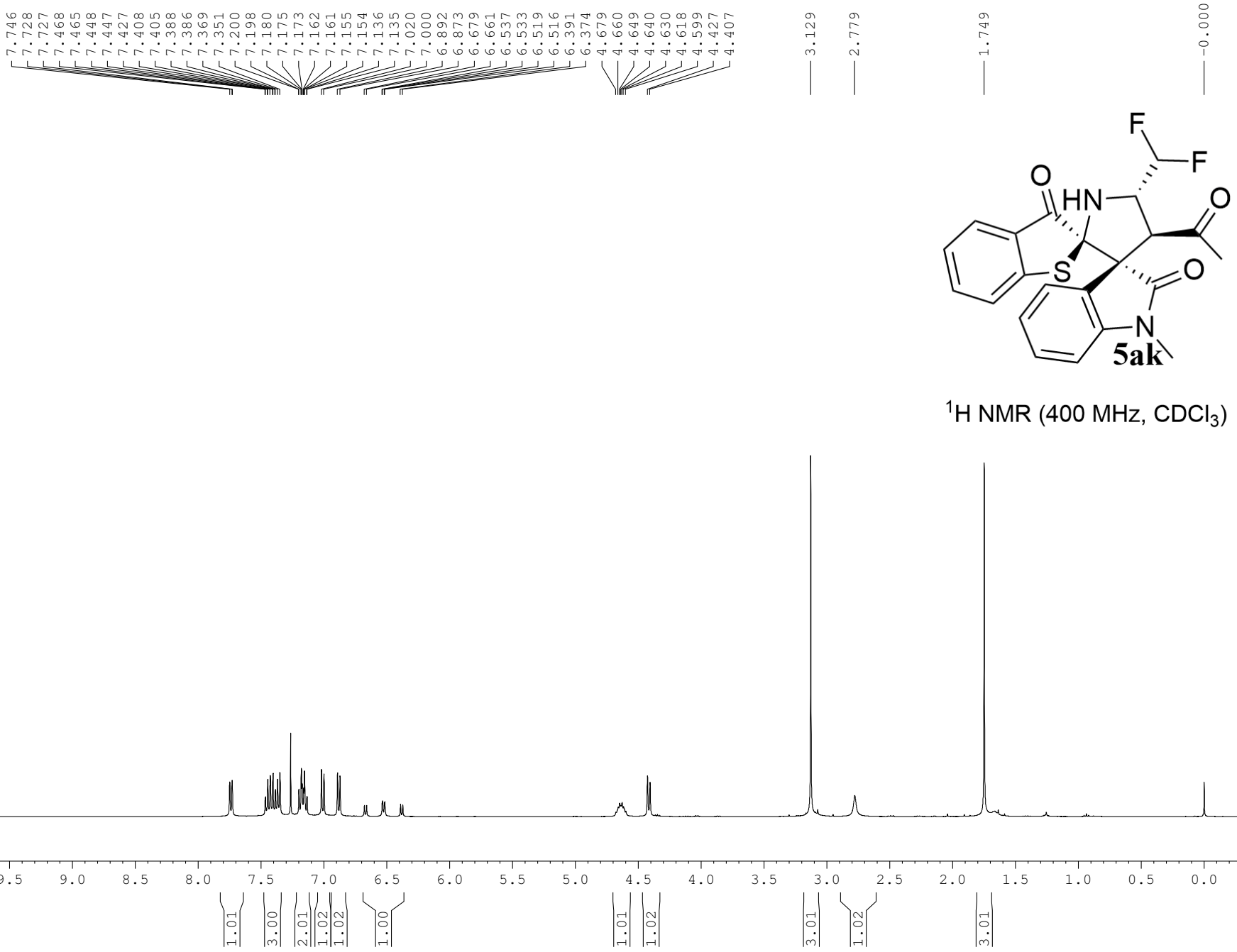
5aj

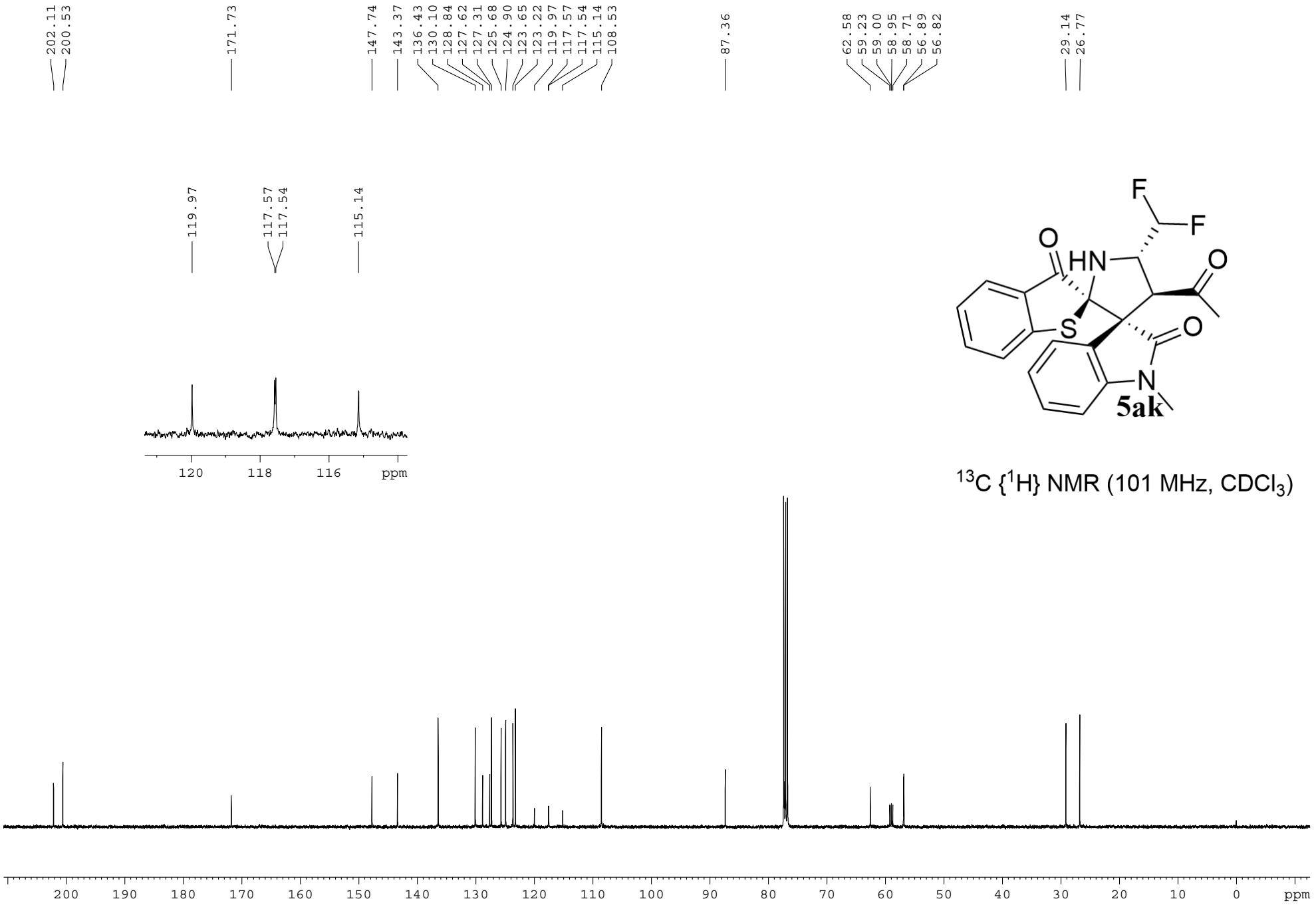
^{1}H NMR (400 MHz, $CDCl_3$)

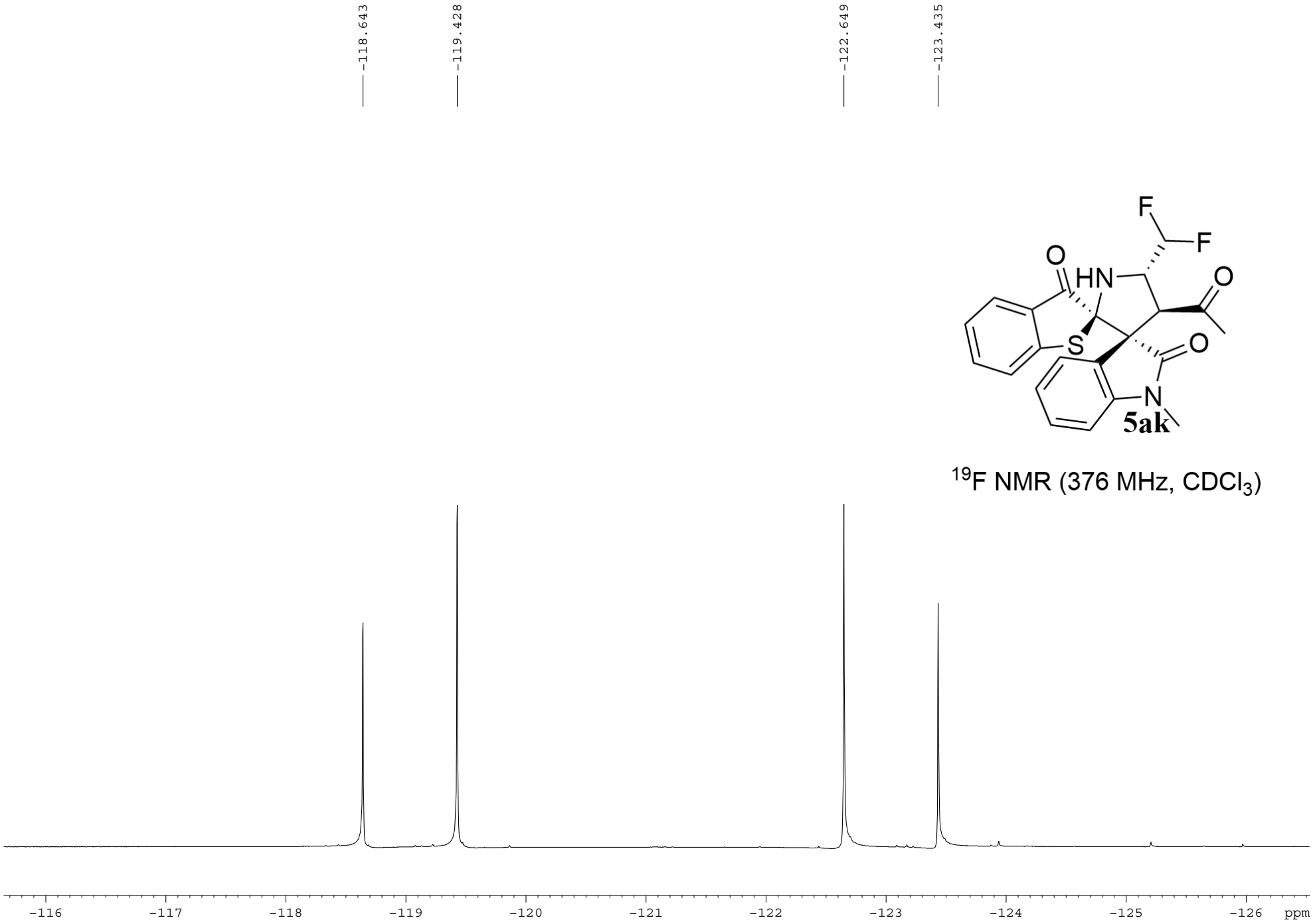


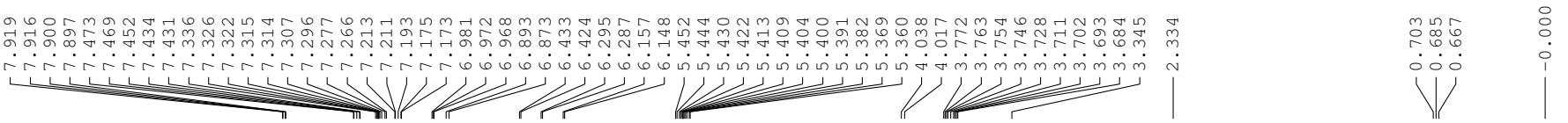

202.54
185.64
171.71
147.72
142.98
142.95
136.40
135.02
133.25
129.87
129.05
127.91
127.29
127.19
125.65
125.54
123.51
123.29
120.04
117.62
115.21
108.22
87.23
68.50
64.57
60.18
59.94
59.90
59.66
52.88
52.81
27.80
26.25
22.19
120.04
117.62
115.21
120
118
116
ppm
F
F
O
HN
O
S
O
O
N
5aj
13C {1H} NMR (101 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

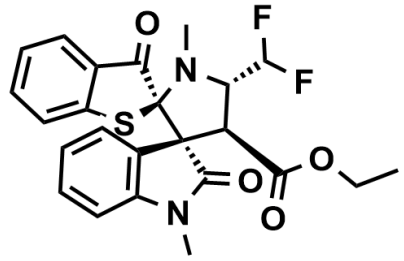

-118.495
-119.281
-122.862
-123.649
F
F
O
HN
O
S
O
O
N
5aj
^{19}F NMR (376 MHz, $CDCl_3$)
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm


7.746
7.728
7.727
7.468
7.465
7.448
7.447
7.427
7.408
7.405
7.388
7.386
7.369
7.351
7.200
7.198
7.180
7.175
7.173
7.162
7.161
7.155
7.154
7.136
7.135
7.020
7.000
6.892
6.873
6.679
6.661
6.537
6.533
6.519
6.516
6.391
6.374
4.679
4.660
4.649
4.640
4.630
4.618
4.599
4.427
4.407
3.129
2.779
1.749
-0.000
F
F
O
HN
O
S
O
N
5ak
1H NMR (400 MHz, CDCl3)
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
ppm
1.01
3.00
2.01
1.02
1.02
1.00
1.01
1.02
3.01
1.02
3.01


202.11
200.53
171.73
147.74
143.37
136.43
130.10
128.84
127.62
127.31
125.68
124.90
123.65
123.22
119.97
117.57
117.54
115.14
108.53
87.36
62.58
59.23
59.00
58.95
58.71
56.89
56.82
29.14
26.77
119.97
117.57
117.54
115.14
120
118
116
ppm
F
F
O
HN
O
S
O
N
5ak
$^{13}C\ \{^{1}H\}$ NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

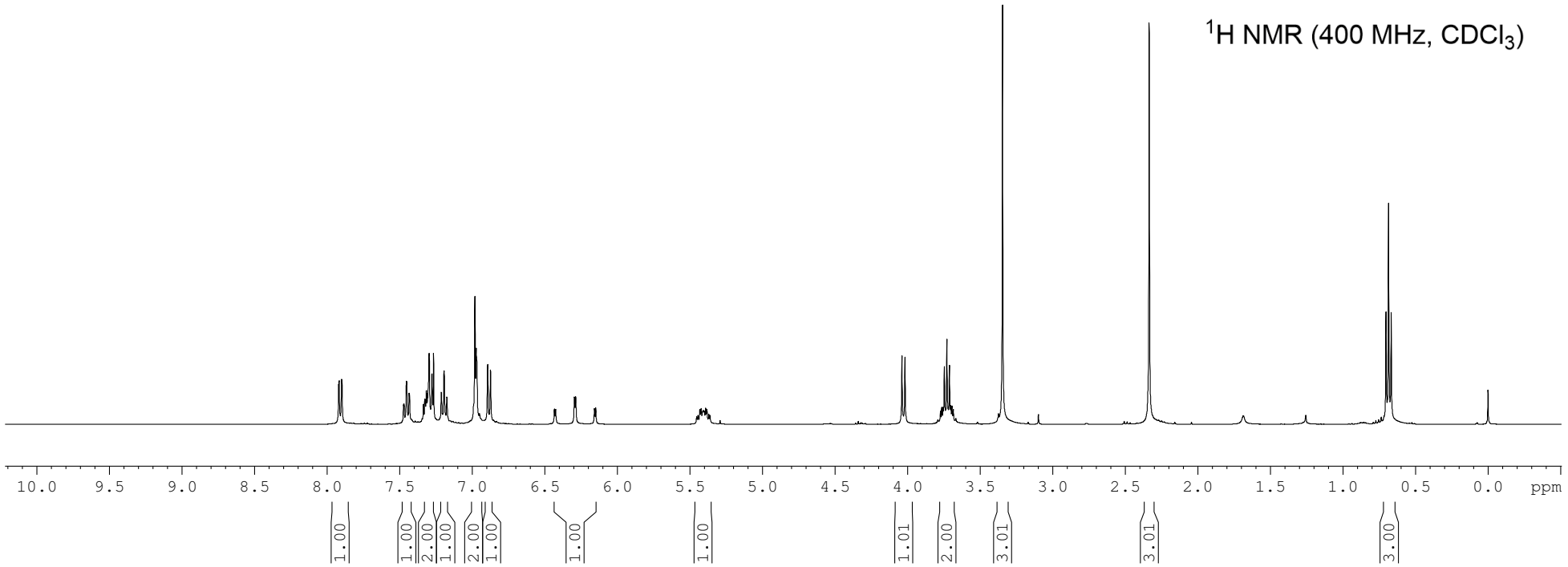

-118.643
-119.428
-122.649
-123.435
F
F
O
HN
O
S
O
N
5ak
^{19}F NMR (376 MHz, $CDCl_3$)
-116
-117
-118
-119
-120
-121
-122
-123
-124
-125
-126
ppm

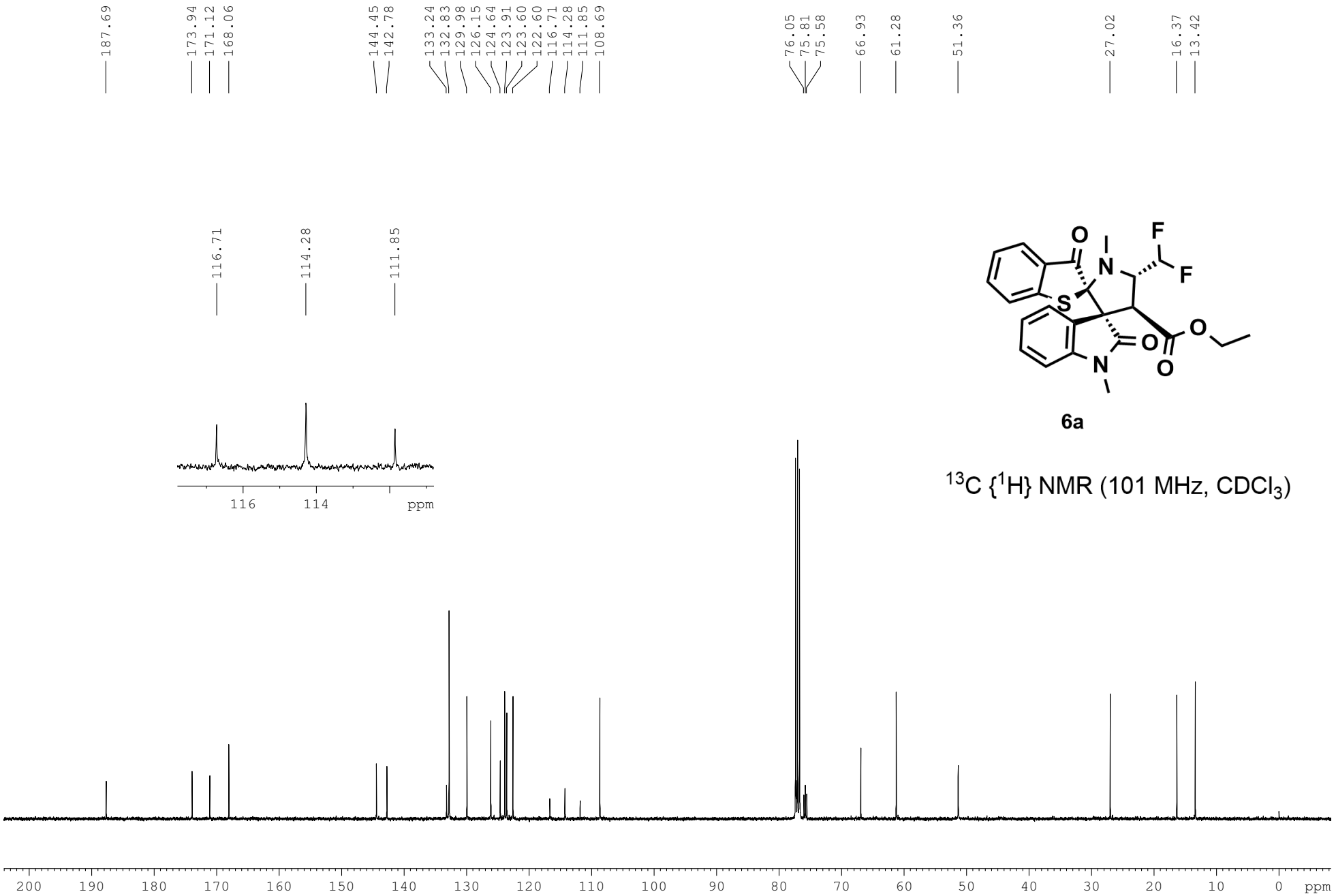


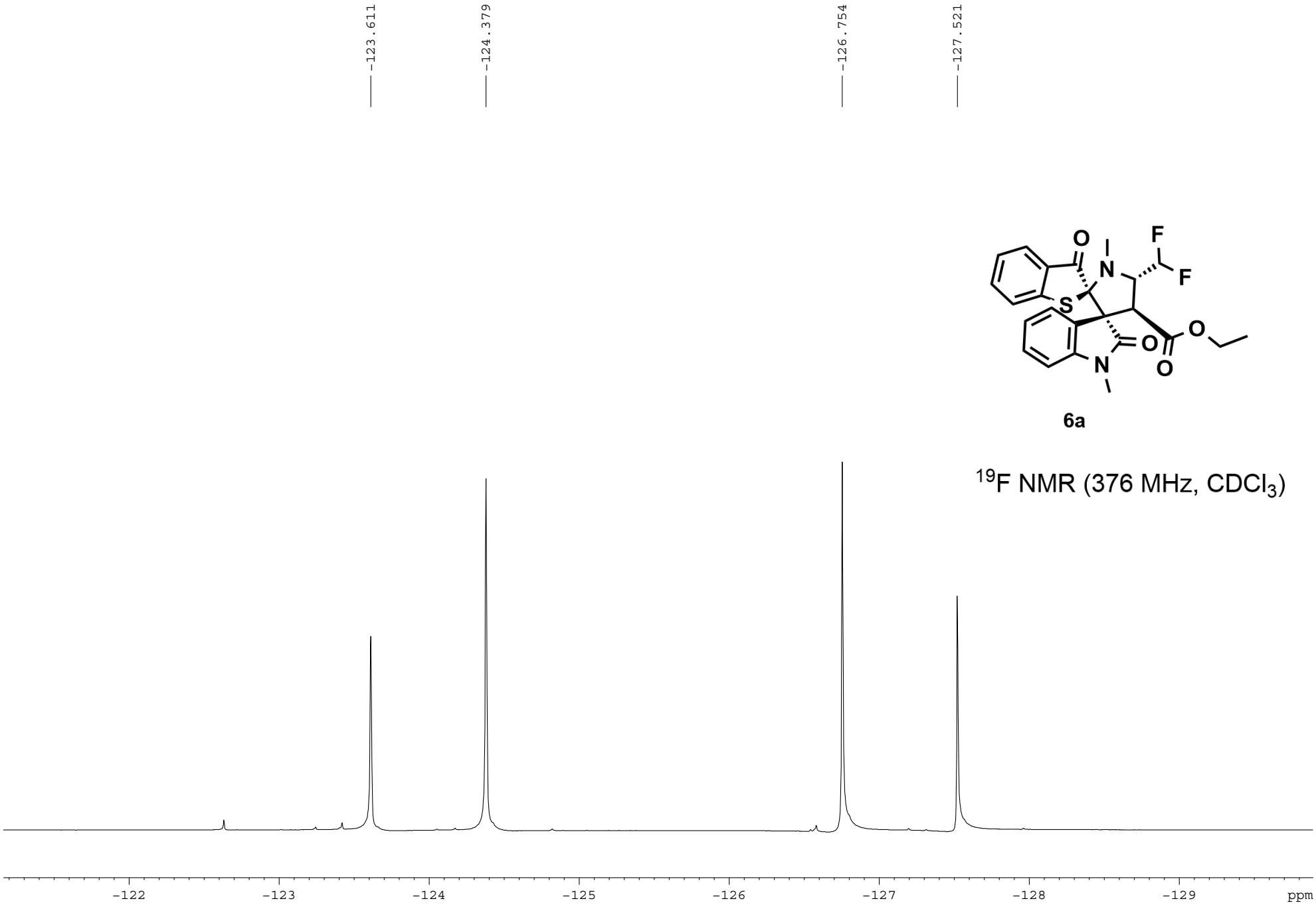


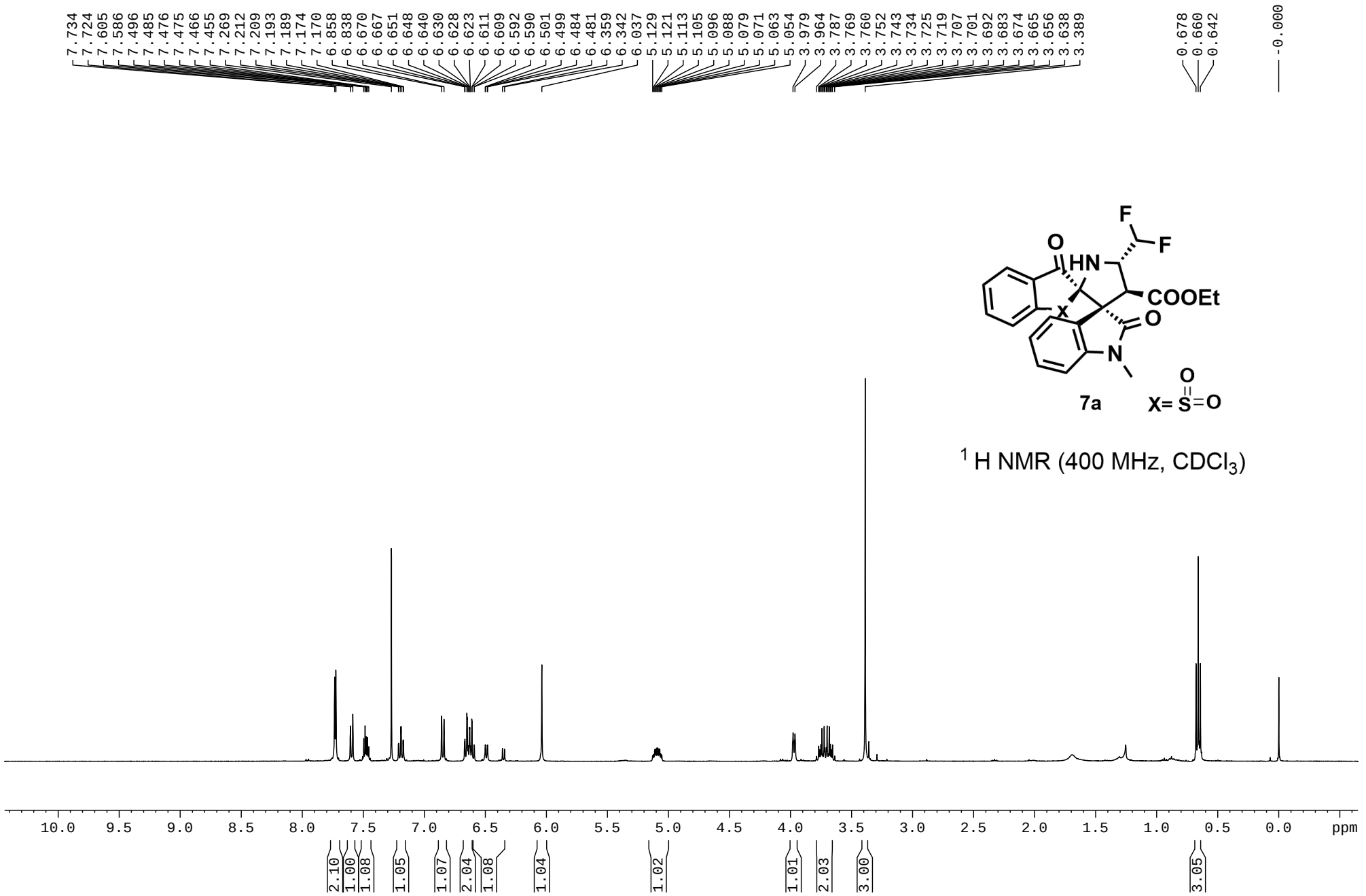
6a

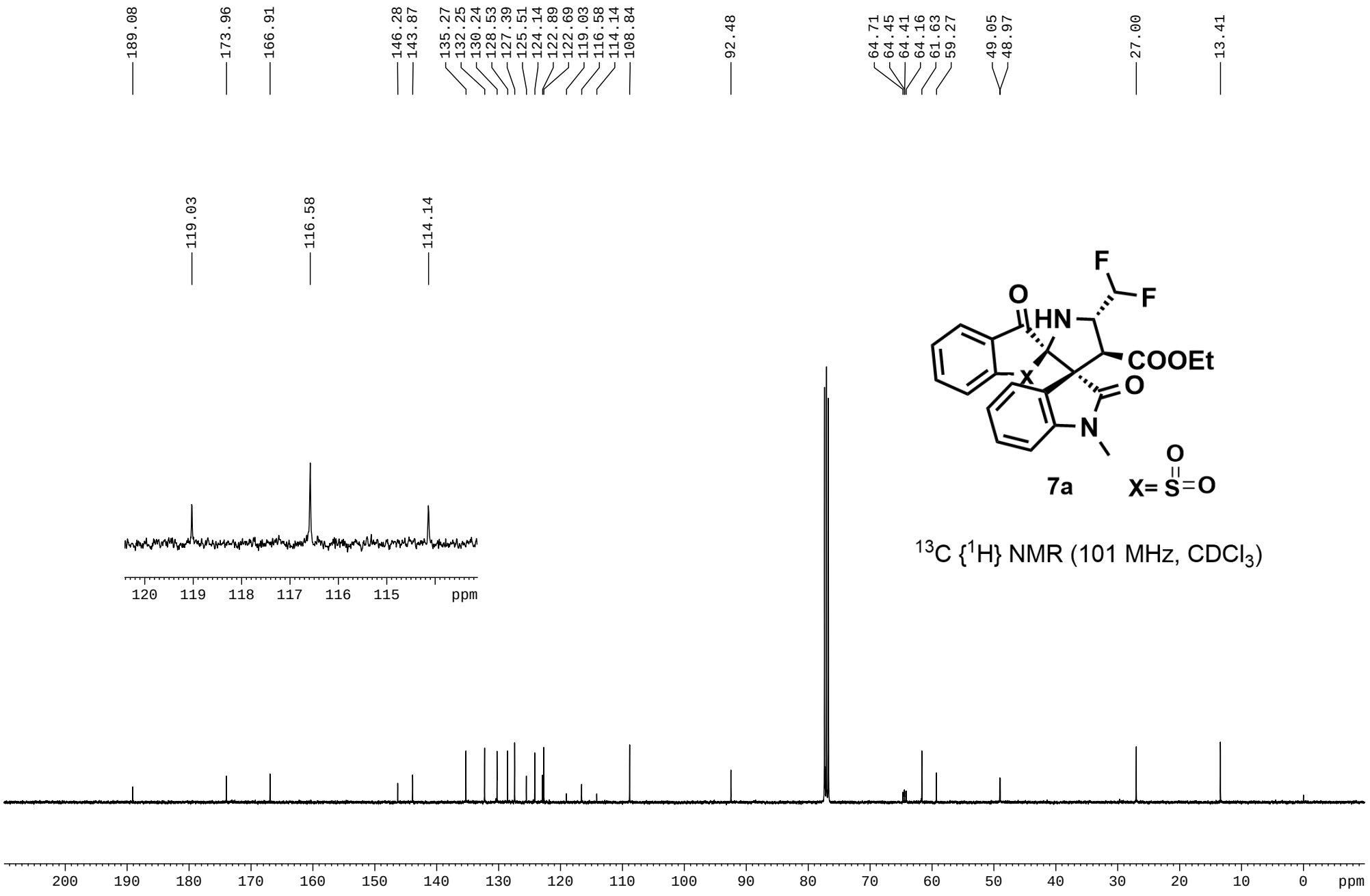
^{1}H NMR (400 MHz, $CDCl_3$)

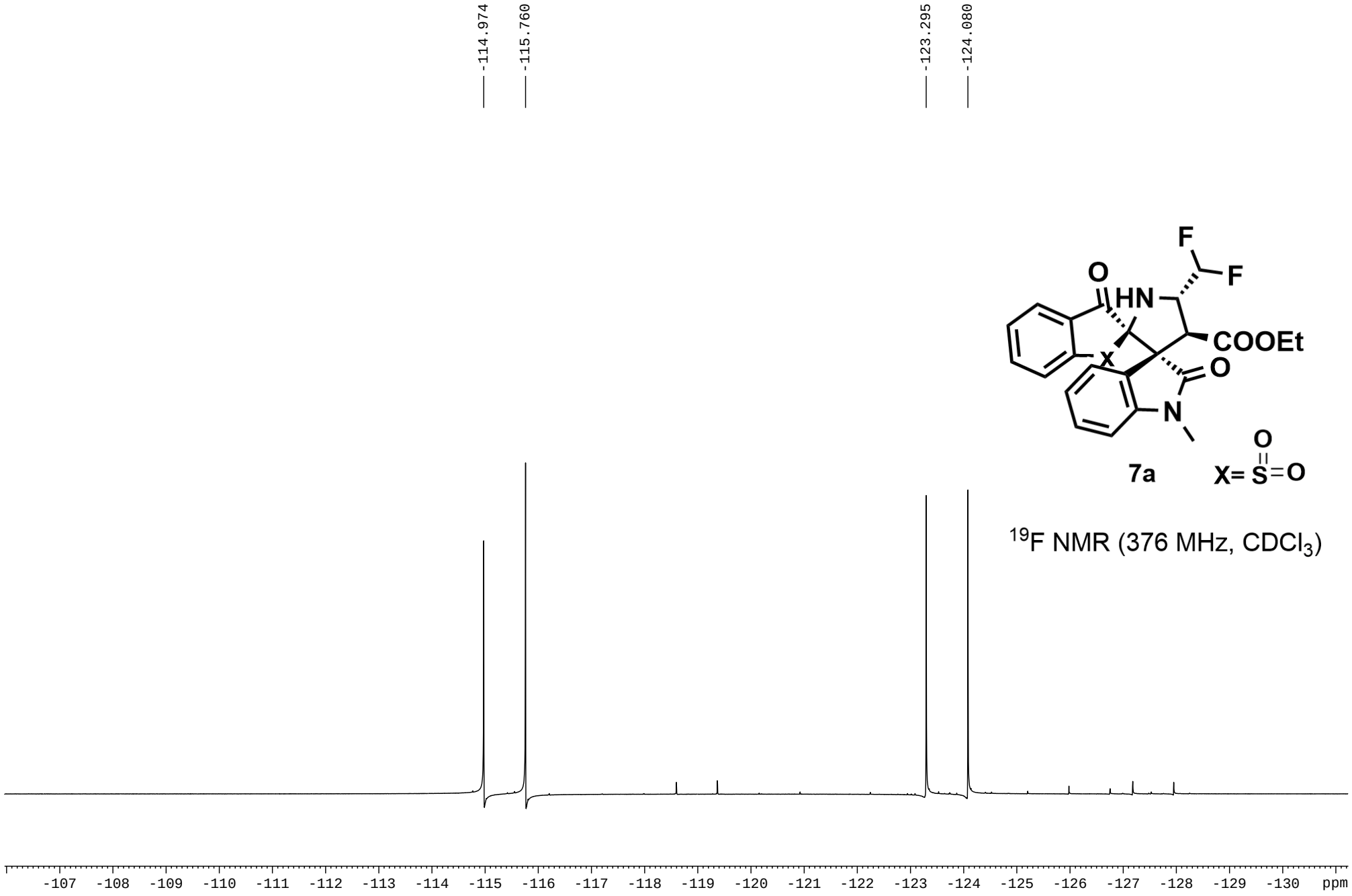



187.69
173.94
171.12
168.06
144.45
142.78
133.24
132.83
129.98
126.15
124.64
123.91
123.60
122.60
116.71
114.28
111.85
108.69
76.05
75.81
75.58
66.93
61.28
51.36
27.02
16.37
13.42
116.71
114.28
111.85
116
114
ppm
O
N
F
F
S
O
O
O
N
O
6a
^{13}C {^{1}H} NMR (101 MHz, $CDCl_3$)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


-123.611
-124.379
-126.754
-127.521
O
N
F
F
S
O
O
O
N
6a
^{19}F NMR (376 MHz, $CDCl_3$)
-122
-123
-124
-125
-126
-127
-128
-129
ppm


7.734
7.724
7.605
7.586
7.496
7.485
7.476
7.475
7.466
7.455
7.269
7.212
7.209
7.193
7.189
7.174
7.170
6.858
6.838
6.670
6.667
6.651
6.648
6.640
6.630
6.628
6.623
6.611
6.609
6.592
6.590
6.501
6.499
6.484
6.481
6.359
6.342
6.037
5.129
5.121
5.113
5.105
5.096
5.088
5.079
5.071
5.063
5.054
3.979
3.964
3.787
3.769
3.760
3.752
3.743
3.734
3.725
3.719
3.707
3.701
3.692
3.683
3.674
3.665
3.656
3.638
3.389
0.678
0.660
0.642
-0.000
F
F
O
HN
COOEt
X
O
N
O
X= S=O
7a
1 H NMR (400 MHz, CDCl3)
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
ppm
2.10
1.00
1.08
1.05
1.07
2.04
1.08
1.04
1.02
1.01
2.03
3.00
3.05


189.08
173.96
166.91
146.28
143.87
135.27
132.25
130.24
128.53
127.39
125.51
124.14
122.89
122.69
119.03
116.58
114.14
108.84
92.48
64.71
64.45
64.41
64.16
61.63
59.27
49.05
48.97
27.00
13.41
119.03
116.58
114.14
120 119 118 117 116 115 ppm
F
F
O
HN
COOEt
O
X
N
O
S
O
7a
X=
^{13}C {^{1}H} NMR (101 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


-114.974
-115.760
-123.295
-124.080
F
F
O
HN
COOEt
X
O
N
O
X= S=O
7a
^{19}F NMR (376 MHz, $CDCl_3$)
-107 -108 -109 -110 -111 -112 -113 -114 -115 -116 -117 -118 -119 -120 -121 -122 -123 -124 -125 -126 -127 -128 -129 -130 ppm