# Catalyst-free Hydrodefluorination of Perfluoroarenes with $NaBH_4$

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## Supporting Information

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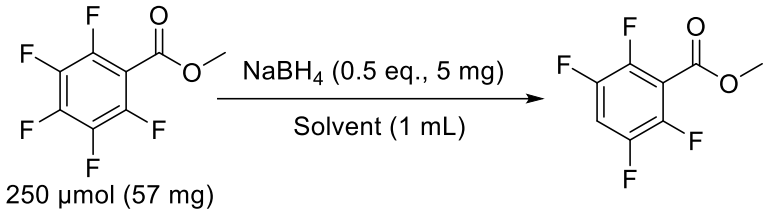
**General Experimental** : - All reagents were obtained from commercial suppliers (Aldrich, VWR, TCI chemicals, Oakwood chemicals, Alfa Aesar) and used without further purification unless otherwise noted. Reactions were monitored by thin layer chromatography (TLC), obtained from sorbent technology Silica XHL TLC Plates, w/UV254, glass backed, 250 µm, 20 x 20 cm visualized with ultraviolet light, and GC-MS (QP 2010S, Shimadzu equipped with auto sampler), also by aliquots subjected to $^{19}F$ NMR described below. Contrathermodynamic isomerization was set up in a light bath equipped with a linear vertical array of 1 W 447 nm LEDs. Solvents were used as received, stored over 4 Å molecular sieves except DMSO and THF, which were first distilled from $CaH_2$ and Na metal respectively and stored under argon. Flash chromatography was carried out with Merck 60 Å, mesh 230-400 silica gel; all compounds that were purified by flash chromatography utilized a gradient of hexanes and ethyl acetate (or DCM) unless otherwise noted. NMR spectra were obtained on 400 MHz Bruker Avance III spectrometer or a Bruker NEO 600 MHz spectrometer equipped with BBO BBF-H-D-05 SmartProbe. $^{1}H$, $^{19}F$ and $^{13}C$ NMR chemical shifts are reported in ppm relative to the residual proteo solvent peak (with $^{19}F$ spectra referencing the residual solvent indirectly using the tabulated IUPAC standard ratio, Ξ, derived from $CFCl_3$).[1] Fluorescence spectroscopy was performed with a Cary Eclipse Fluorescence Spectrophotometer and UV-vis absorbance spectroscopy was performed with a Shimadzu UV-2600 UV-vis spectrophotometer. HRMS was obtained with a Thermo Scientific Orbitrap Fusion Tribrid Mass Spectrometer, utilizing the quadrupole mass analyzer.

**Initial Optimizations**

**Scheme 1. Solvent Optimization**

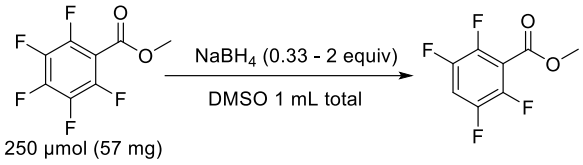



6 NMR tubes were each charged with a benzene $d^6$ capillary, 125 µmol (5 mg) of $NaBH_4$, and 1 mL of methanol, ethanol, 1,2-dimethoxyethane, tetrahydrofuran, dimethylsulfoxide, or dimethylformamide respectively. Each tube was agitated under sonication until it became a homogeneous solution of $NaBH_4$; however, tetrahydrofuran and 1,2-dimethoxyethane did not completely dissolve and remained suspensions. To each tube was then carefully added 250 µmol (57 mg) of methyl pentafluorobenzoate (MPFB), which caused some effervescence in the samples with methanol and to a lesser degree, ethanol. The tubes were left sitting at room temperature for 10 hours before the addition to each of fluorobenzene (10 µL, 106 µmol) as an internal standard for subsequent $^{19}FNMR$ spectra to quantify residual MPFB for NMR conversion and to quantify the product methyl 2,3,5,6-tetrafluorobenzoate for NMR yield.

**Table 1. Solvent Optimization**

| entry | Equiv. $NaBH_4$ | Solvent | Time (hours) | % NMR Yield | % Conversion MPFB |
|---|---|---|---|---|---|
| 1 | 0.50 | MeOH | 10 | 0 | ~100 |
| 2 | 0.50 | EtOH | 10 | 6 | 72 |
| 3 | 0.50 | THF | 10 | <2 | <2 |
| 4 | 0.50 | DME | 10 | 46 | 46 |
| 5 | 0.50 | DMSO | 10 | 97 | 98 |
| 6 | 0.50 | DMF | 10 | 70 | 72 |

**Scheme 2. $NaBH_4$ loading variation**




4 NMR tubes were each charged with a benzene-$d^6$ filled capillary and 57 mg (250 µmol) MPFB. A 0.5 M stock solution of $NaBH_4$ in dimethylsulfoxide was prepared by dissolving 1 mmol (38 mg) $NaBH_4$ in 2 mL dimethylsulfoxide. This stock solution along with pure dimethylsulfoxide was dispensed into the 4 NMR tubes according to **table 2** (below) such that each tube contained a total of 1 mL of solution. The tubes were allowed to sit at room temperature for 2 hours before being charged with 10 µL (106 µmol) fluorobenzene internal standard and having their $^{19}$FNMR spectra collected for methyl 2,3,5,6-tetrafluorobenzoate quantitation (% NMR yield).

**Table 2. $NaBH_4$ Loading Variation**

| entry | Volume 0.5 M stock solution of $NaBH_4$ | Volume DMSO | Eq. $NaBH_4$ | % NMR Yield |
|---|---|---|---|---|
| 1 | 165 µL | 835 µL | 0.33 | 23 |
| 2 | 330 µL | 660 µL | 0.66 | 43 |
| 3 | 500 µL | 500 µL | 1.00 | 99 |
| 4 | 1000 µL | 0 µL | 2.00 | 99 |

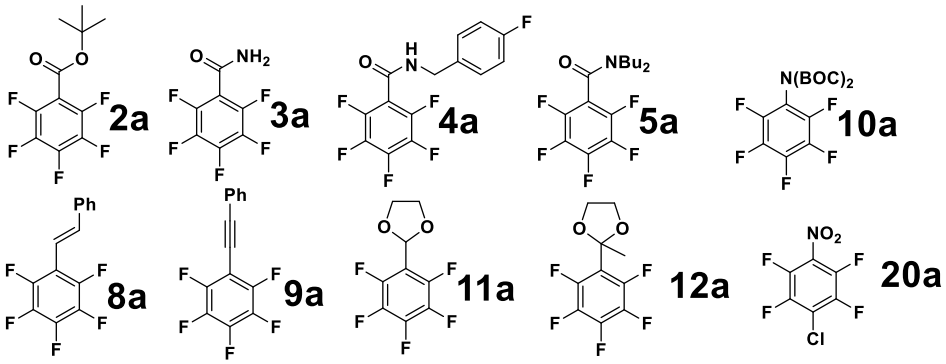
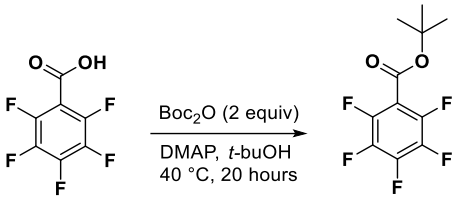



**Figure 1. Substrates above were prepared for HDF.**

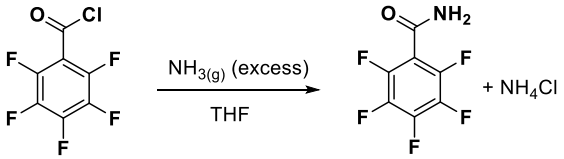
***Synthesis of tert-butyl pentafluorobenzoate 2a***




**2a**

Into a 100 mL round-bottom flask equipped with a magnetic stir bar was loaded pentafluorobenzoic acid (2 g, 9.4 mmol), di-*tert*-butyl dicarbonate (4.1 g, 18.9 mmol), 4-(dimethylamino)pyridine (116 mg, 0.95 mmol), and 30 mL of *tert*-butanol. The flask was heated to 40 °C for 20 hours with stirring before being quenched with 1 M HCl (20 mL) followed by subsequent extraction with EtoAc ( 3x 20 mL). The combined organic layers were washed with saturated sodium carbonate solution and then brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by silica gel chromatography using 2% EtoAC in Hexanes as eluent to afford the desired product (1.9 g, 76% yield). The $^{1}H$ NMR, $^{19}F$ NMR and mass spectra match the literature.[2]

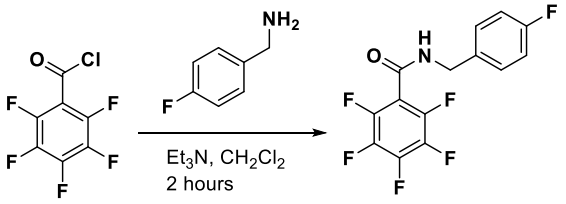
***Synthesis of pentafluorobenzamide 3a***




**3a**

Into a dry 125 mL Erlenmeyer flask is added pentafluorobenzoyl chloride (647 mg, 2.8 mmol) in 30 mL THF. Using a glass diffuser connected by rubber tubing to a separate vessel of ammonium chloride and NaOH pellets, a large excess of ammonia gas is bubbled through the THF solution over 2 minutes, or until the exotherm subsides (determined by touching the outside of the flask). The THF solution containing the product is then eluted through a silica plug, thoroughly rinsing the precipitated ammonium chloride with more THF (2 x 20 mL). The THF filtrate was concentrated under reduced pressure, and the resulting white solid (434 mg, 73 % yield) was used without further purification. The mass spectrum was found to match the literature.[3] 19F NMR (376 MHz, $CDCl_3$) δ -139.63 – -139.73 (m, 2F), -149.54 (tt, J = 20.1, 3.5 Hz, 1F), -159.7 – -159.84 (m, 2F). 1H NMR (400 MHz, $CDCl_3$) δ 6.37 – 6.05 (brs, 1H), 6.18 – 5.84 (brs, 1H).

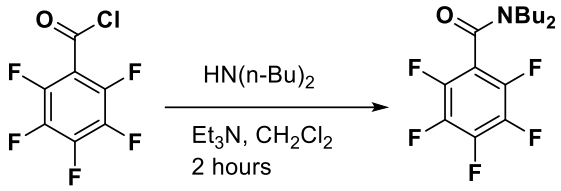
***Synthesis of N-(4-fluorobenzyl)pentafluorobenzamide 4a***




**4a**

To an ice-cooled solution of parafluorobenzylamine (0.35 mL, 3.05 mmol) in $CH_2Cl_2$ (10 mL) is added dropwise a solution of pentafluorobenzoyl chloride (640 mg, 2.77 mmol) in $CH_2Cl_2$ (2 mL) followed by triethylamine (1.2 mL, 8.31 mmol). The ice bath was removed after 30 minutes and the reaction was allowed to continue for 2 hours before being quenched with cold water and diluted with $CH_2Cl_2$ (60 mL). The organic layer was washed with water and subsequently brine, dried over $MgSO_4$. Removal of solvent and purification by silica gel flash chromatography (Hexane : EtOAc ramp) afforded **4a** as pale orange-white needles (726 mg, 82% yield). The mp 156-157 °C; 19F NMR (376 MHz, $C_6D_6$) δ -114.13 (tt, J = 8.6, 5.2 Hz, 1F), -140.27 – -140.41 (m, 2F), -150.26 (tt, J = 20.8, 3.2 Hz, 1F), -159.73 – -159.84 (m, 2F). 1H NMR (400 MHz, $CDCl_3$) δ 7.35-7.28 (m, 2H), 7.09-7.02 (m, 2H), 6.34 – 6.09 (brs, 1H), 4.62 (d, J = 5.7 Hz, 2H). $^{13}$C NMR (151 MHz, Acetone-$d_6$) δ 163.8, 162.2, 157.9, 144.8 (dddt, *J* = 249.0, 12.6, 8.5, 4.1 Hz), 142.7(dtt, *J* = 253.2, 12.9, 4.9 Hz), 138.4 (dddd, *J* = 250.3, 17.2, 12.4, 4.8 Hz), 135.4 (d, *J* = 3.2 Hz), 130.4 (d, *J* = 8.1 Hz), 116.07 (d, *J* = 21.6 Hz), 43.6. Calculated HRMS(ESI) for (C14H7F6NO (M+H) + is 320.0510 observed 320.0512.

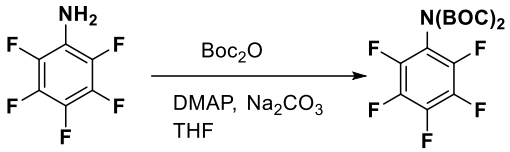
***Synthesis of N,N-di-n-butylpentafluorobenzamide 5a***




**5a**

Into a stirring ice-cooled solution of *N,N*-di-*n*-butylamine (0.51 mL, 3.05 mmol) in DCM (10 mL) is added dropwise a solution of pentafluorobenzoyl chloride (640 mg 2.77 mmol) in DCM (1 mL) and then triethylamine (1.2 mL, 8.31 mmol). The cooling bath was removed after 30 minutes and the stirring continued for 2 hours before quenching with cold water. The quenched reaction was diluted with DCM (60 mL) and washed with water (20 mL) and then brine (20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* prior to silica gel column purification using EtOAc : hexane ramp to afford the desired product (843 mg, 94 % yield). 19F NMR (376 MHz, Chloroform-d) δ -140.94 – -141.10 (m, 2F), -152.64 – -152.85 (m, 1F), -159.94 – -160.17 (m, 2F). 1H NMR (400 MHz, Chloroform-d) 3.56 – 3.48 (m, 2H), 3.16 – 3.10 (m, 2H), 1.69 – 1.58 (m, 2H), 1.53 – 1.44 (m, 2H), 1.38 (sext, J = 7.3, 2H), 1.19 (sext, J = 7.3, 2H), 0.96 (t, J = 7.3, 3H), 0.83 (t, J = 7.3, 3H). $^{13}$C NMR (101 MHz, Chloroform -d) δ 158.3, 142.8 (dddt, J = 249.4, 12.4, 8.4, 4.0 Hz), 141.7 (dtt, J = 256.3, 13.3, 4.7), 137.8 (d, J = 253.3 Hz), 112.3 (t, J = 22.1 Hz), 48.6, 45.0, 30.6, 29.4, 20.2, 19.8, 13.9, 13.7. GC/MS (m/z, relative intensity) 323 (M+, 10), 304 (4), 294 (5), 280 (13), 195 (100). Calculated HRMS(ESI) for (C15H18F5NO (M+H) + is 324.1387 observed 324.1379

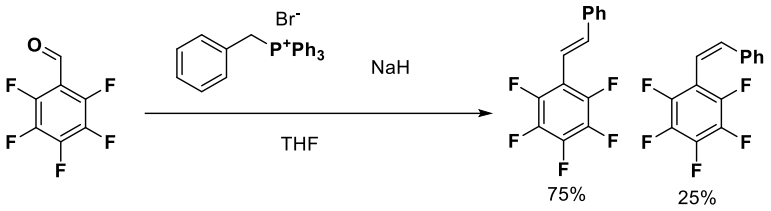
***Synthesis of di-BOC-pentafluorobenzamide 10a***




**10a**

The procedure reported by Bissember et al.[4] was followed scaled to 500 mg of pentafluoroaniline, ultimately affording a 48 % yield of **10a** as a colorless solid.

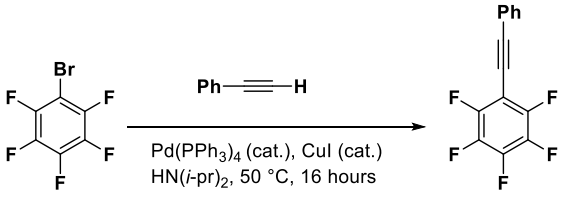
***Synthesis of E-styrylpentafluorobenzene 8a***




**8a**

To a stirring suspension of sodium hydride (111 mg of 60 % paraffin dispersion, 2.77 mmol) in 5 mL THF at 0 °C is added benzyltriphenylphosphonium bromide (1 g, 2.315 mmol) in THF (5 mL). The solution was allowed to gradually warm to room temperature and then stir for 2 hours. To the solution is then added pentafluorobenzaldehyde (0.285 mL, 2.315 mmol) which is then allowed to continue stirring overnight prior to a quench with minimal ice water. The solution was concentrated *in vacuo* and the residue diluted with EtOAc before being washed sequentially with water and then brine. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue is subjected to silica gel column chromatography with 100% hexane to afford the desired product as a 3:1 mixture of E- and Z-isomers (930 mg, 74% yield). $^1$H NMR, $^{19}$F NMR, and mass spectra match the literature.[5]

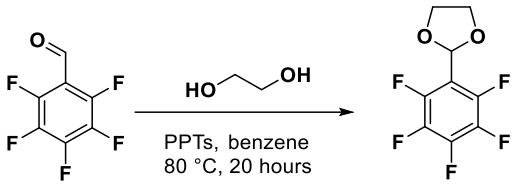
***Synthesis of pentafluoro(phenylethynyl)benzene 9a***




**9a**

To a deaerated, stirring solution of bromopentafluorobenzene (0.88 mL, 6.82 mmol) and phenylacetylene (465 mg, 4.55 mmol) in diisopropylamine (20 mL) is added CuI (43 mg, 227 µmol) and $Pd(PPh)_3$ (262 mg, 227 µmol). The mixture is heated to 50 °C and left overnight under an argon atmosphere. The mixture was then cooled to room temperature and diluted with diethyl ether before filtering through celite and concentrating in vacuo. The residue was subjected to silica column chromatography in pure hexane to afford the desired product (400 mg, 33% yield). Melting point, $^1$H NMR and $^{19}$F NMR match the literature.[6] GC/MS (m/z, relative intensity) 268 (M+, 5), 253 (5), 252 (40), 224 (5), 210 (100).

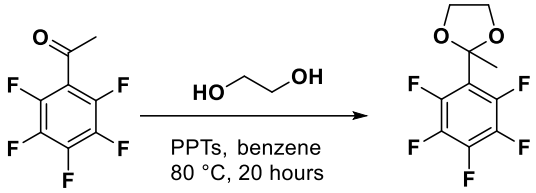
***Synthesis of 2-(perfluorophenyl)-1,3-dioxolane 11a***




**11a**

The procedure reported by Kambe et al.[7] was followed and scaled to 500 mg (2.55 mmol) of pentafluorobenzaldehyde, affording an 83 % yield of desired product. 19F NMR (376 MHz, $CDCl_3$) δ -143.80 – -144.06 (m, 2F), -152.56 – -152.88 (t, J = 20.9 Hz, 1F), -161.92 – -162.27 (m, 2F). 1H NMR (400 MHz, $CDCl_3$) δ 6.21 – 6.18 (s, 1H), 4.25 – 4.15 (m, 2H), 4.09 – 3.99 (m, 2H).

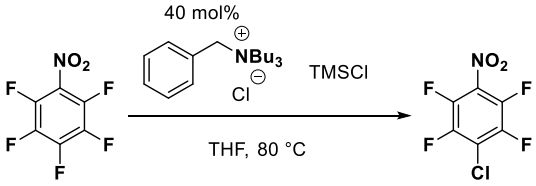
***Synthesis of 2-methyl-2-(perfluorophenyl)-1,3-dioxolane 12a***




**12a**

The procedure reported by Kambe et al.[7] was followed and scaled to 500 mg (2.38 mmol) of pentafluoroacetophenone. An additional step was required at the end. Namely, the product residue was dissolved in 0 °C EtOH (6 mL) with $NaBH_4$ (45 mg, 1.19 mmol), and allowed to stir for 2 hours to convert residual pentafluoroacetophenone to a more easily separated alcohol. The solution was quenched with cold water, extracted with EtOAc, the organic layer washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Silica column chromatography using a ramp of EtOAc : hexane afforded the desired product (375 mg, 62% yield) as a colorless liquid. $^{19}F$ NMR (376 MHz, Chloroform-d) δ -142.10 – -142.29 (m, 2F), -155.02 (tt, J = 21.4, 3.0, 1F), -161.90 – -162.08 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 64.18 – 4.15 (m, 2H), 3.95-3.83 (m, 2H), 1.83 – 1.77 (s, 3H). $^{13}C$ NMR (101 MHz, Chloroform-d) δ 144.6 (dddd, J = 252.0, 11.8, 7.9, 4.0 Hz), 140.8 (dtt, J = 254.6, 13.5, 5.2 Hz), 137.9 (m, $J_{C-F}$ = 252.5 Hz), 116.7 (tdt, J = 13.9, 4.6, 2.9 Hz), 107.5, 65.0, 26.7 (t, J = 1.9 Hz)

***Synthesis of p-chloro-tetrafluoronitrobenzene 20a***

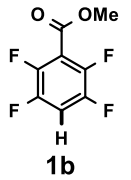



**20a**

The procedure described by Weaver et al. was followed.[8] Pentafluoronitrobenzene (426 mg, 2 mmol), benzyltributylammonium chloride (250 mg, 0.8 mmol), TMSCl (261 mg, 2.4 mmol), and 3 mL THF are added to a microwave vial charged with a magnetic stir bar and sealed. The reaction was heated in an oil bath at 80 °C overnight before concentration *in vacuo* and subjection to silica column chromatography with hexane to afford the desired product **20a** (365 mg, 80%) yield.

**General Procedure A for HDF of Perfluoroarenes**

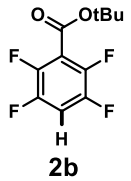
To stirring a solution of fluoroarene in dimethylsulfoxide (0.2 M) was slowly added $NaBH_4$ dissolved in equal volume of DMSO. **CAUTION**: some of the reactions effervesce hydrogen gas, especially when the solvent is not dry! Care should be taken to use dry DMSO and ensure that the gas can safely escape the reaction vessel! The reactions were monitored by removing aliquots and subjecting them to $^{19}FNMR$. When complete, the mixtures were diluted with ethyl acetate (10-fold) and carefully quenched with aqueous brine solution over 10 minutes. The organic layers were washed five times with brine to remove the DMSO, dried over $MgSO_4$, then concentrated *in vacuo* to afford the desired products without any further purification. If NMR yields were to be obtained (for products too volatile for concentration *in vacuo*), 20 microliters (213 μmol) fluorobenzene internal standard would be added to aliquots of crude reaction mixture in lieu of dilution with ethyl acetate and workup. This procedure was used on 0.1 – 22.1 mmol scale, including 1.0 mmol. See **18b** and **19b** for details.



**1b**

***methyl 2,3,5,6-tetrafluorobenzoate 1b***

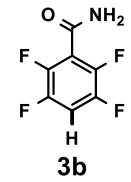
**General Procedure A** was followed using methyl pentafluorobenzoate (90 mg, 400 µmol) and 1 equiv $NaBH_4$ (16 mg, 400 micromol) in 2 mL DMSO. The desired product **1b** was obtained as a colorless oil (72 mg, 87% yield). A known compound, characteristic NMR spectra match the literature.[8] $^{19}F$ NMR (376 MHz, Chloroform-d) δ -137.45 – -137.60 (m, 2F), -139.48 – -139.63 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.20 (tt, J = 9.4, 7.2 Hz, 1H), 4.00-3.97 (s, 3H)



**2b**

***tert-butyl 2,3,5,6-tetrafluorobenzoate 2b***

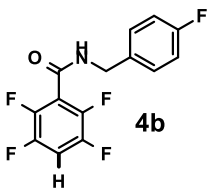
**General Procedure A** was followed using *tert*-butyl pentafluorobenzoate (54 mg, 200 µmol) and $NaBH_4$ (8 mg, 200 µmol) in 2 mL DMSO. The desired product **2b** was obtained as a colorless oil (42 mg, 85% yield). A known compound, characteristic NMR spectra match the literature.[8] $^{19}F$ NMR (376 MHz, Chloroform-d) δ -137.82 – -138.03 (m, 2F), -141.07 – -141.23 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.13 (tt, J = 9.5, 7.2 Hz, 1H), 1.61 – 1.58 (s, 9H).



**3b**

***2,3,5,6-tetrafluorobenzamide 3b***

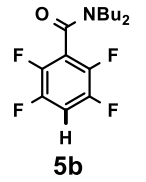
**General Procedure A** was followed using pentafluorobenzamide (40 mg, 190 µmol) and $NaBH_4$ (5 mg, 190 µmol) in 1 mL DMSO. The desired product **3b** was obtained as a white powder (30 mg, 88% yield). A known compound, $^{19}F$ NMR spectrum and melting point are in accord with the literature.[9] $^{19}F$ NMR (564 MHz, DMSO-$d_6$) δ -138.51 – -138.78 (m), -142.97 – -143.12 (m). $^{1}H$ NMR (599 MHz, DMSO-$d_6$) δ 8.32 (s, 1H), 8.14 (s, 1H), 7.96 (tt, *J* = 10.4, 7.5 Hz, 1H). $^{13}C$ NMR (151 MHz, DMSO-$d_6$) δ 159.2 (t, *J* = 1.8 Hz), 145.2 (dddd, *J* = 246.6, 14.2, 10.3, 3.7 Hz), 142.3 (dddd, *J* = 247.2, 15.1, 6.5, 3.9 Hz), 118.3 (t, *J* = 21.5 Hz), 107.4 (t, *J* = 23.4 Hz). GC/MS (m/z, relative intensity) 193 (M+, 95), 177 (100), 150 (36), 149 (89), 99 (80).



**4b**

***2,3,5,6-tetrafluoro-N-(4-fluorobenzyl)benzamide 4b***

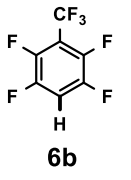
**General Procedure A** was followed using pentafluoro-N-(4-fluorobenzyl)benzamide (64 mg, 200 µmol) and $NaBH_4$ (8 mg, 200 µmol) in 2 mL DMSO. The desired product **4b** was obtained as a white, crystalline solid (60 mg, 99% yield). The mp 135-136 °C $^{19}F$ NMR (376 MHz, Chloroform-d) δ -114.20 – -114.31 (m, 1F), -136.86 – -137.09 (m, 2F), -141.10 – -141.31 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.27 – 7.21 (m, 2H), 7.06 (tt, J = 9.4, 7.3 Hz, 1H), 7.01 – 6.93 (m, 2H), 6.38 – 6.20 (brs, 1H), 4.56 – 4.51 (d, J = 5.75 Hz, 2H).



**5b**

***N,N-dibutyl-2,3,5,6-tetrafluorobenzamide 5b***

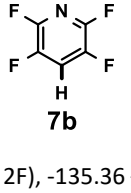
**General Procedure A** was followed using N,N-dibutyl-pentafluorobenzamide **5a** (32 mg, 100 µmol) and $NaBH_4$ (8 mg, 200 µmol) in 1 mL DMSO. The desired product **5b** was obtained as a colorless oil (29 mg, 85% yield). $^{19}F$ NMR (376 MHz, Chloroform-d) δ -137.18 – -137.48 (m, 2F), -141.60 – -141.88 (m, 2F) . $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.09 (tt, J = 9.5, 7.2 Hz, 1H), 3.56 – 3.50 (m, 2H), 3.16 – 3.10 (m, 2H), 1.69 – 1.60 (m, 2H), 1.53 – 1.44 (m, 2H), 1.39 (sext, J = 7.3 Hz, 2H), 1.18 (sext, J = 7.3 Hz, 2H), 0.97 (t, J = 7.3 Hz, 3H), 0.81 (t, J = 7.3 Hz, 3H) GC/MS (m/z, relative intensity) 305 (M+, 9), 287 (5), 276 (6), 262 (15), 177 (100).



**6b**

***1,2,4,5-tetrafluoro-3-(trifluoromethyl)benzene 6b***

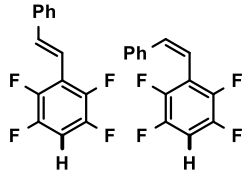
**General Procedure A** was followed using octafluorotoluene (100 mg, 466 µmol) and $NaBH_4$ (16 mg, 470 µmol) in 5 mL DMSO. When the reaction was complete, 500 µL of reaction mixture (10% of the total volume) was taken into an NMR tube charged with a benzene-$d^6$ capillary and fluorobenzene (20 µL, 213 µmol) as internal standard. The aliquot was calculated to contain 44 µmol of **6b** corresponding to a 93% yield. Mass spectrum was found consistent with literature.[8] $^{19}F$ NMR (376 MHz, DMSO) δ -55.15 – -55.30 (td, J = 21.6, 3.1 Hz, 3F), -136.29 – -136.47 (m, 2F), -141.12 – -141.49 (m, 2F). $^{1}H$ NMR (400 MHz, DMSO) δ 8.37 – 8.24 (m, 1H).



**7b**

***2,3,5,6-tetrafluoropyridine 7b***

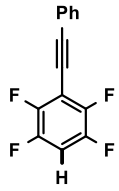
**General Procedure A** was followed using pentafluoropyridine (100 mg, 592 µmol) and $NaBH_4$ (23 mg, 600 µmol) in 5 mL DMSO. When the reaction was complete, 500 µL of reaction mixture (10% of the total volume) was taken into an NMR tube charged with a benzene-$d^6$ capillary and fluorobenzene (20 µL, 213 µmol) as internal standard. The aliquot was calculated to contain 54 µmol of **7b** corresponding to an 89% yield. Mass spectrum was found consistent with the literature.[8] $^{19}F$ NMR (376 MHz, Chloroform-d) δ -87.95 – -88.26 (m, 2F), -135.36 – 135.60 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 8.67 – 8.55 (m, 1H).




**8b** (3:1 E:Z)

***1,2,4,5-tetrafluoro-3-styrylbenzene 8b***

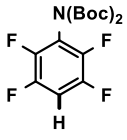
To a stirring solution of **8a** (50 mg, 185 µmol, 3:1 E:Z isomeric mix) in THF (500 µL) is added $NaBH_4$ (7 mg, 185 µmol) in DMSO (500 µL). The reaction mixture is left to stir 24 hours before it is quenched by dilution with EtOAc (5 mL) and 5 consecutive washes with saturated brine solution (1 mL each). The organic layer is dried over $MgSO_4$ and concentrated *in vacuo* to afford the product **8b** as a white solid (40 mg, 86% yield)**.** Melting point matches that found by Stephens et.al.[10] $^{13}C$ NMR and mass spectra were found to match the literature.[5] $^{1}H$ NMR (599 MHz, Chloroform-d) δ E: 7.58 (m, 2H), 7.53 (d, J = 16.8 Hz, 1H), 7.43 (m, 2H), 7.37 (m, 1H), 7.11 (d, J = 16.8 Hz, 1H), 6.97 (tt, J = 9.5, 7.5 Hz, 1H). Z: 7.43 (m, 1H), 7.27 (m,2H), 7.17 (m, 2H), 7.01 (m, 2H), 6.35 (d, J = 12.1 Hz, 1H).




**9b**

***1,2,4,5-tetrafluoro-3-(phenylethynyl)benzene 9b***

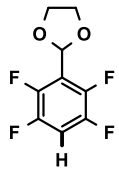
Aryl alkyne **9a** (53 mg, 197 µmol) was added to a stirring suspension of $NaBH_4$ (7 mg, 200 µmol) in 1 mL of 1,2-dimethoxyethane and left to stir overnight. The reaction was worked up by dilution with ethyl acetate (10 mL) and quenching with brine (1.5 mL). The organic layer was washed with brine (3 x 1 mL) and dried over $MgSO_4$ before being concentrated *in vacuo* to afford **9b** as a white solid (49 mg, 99 % yield). The melting point, $^{1}H$, $^{13}C$, and $^{19}F$ NMR match with the literature.[11] $^{19}F$ NMR (376.48 MHz, Chloroform-d) δ -136.63 – -136.77 (m, 2F), -138.96 – -139.11 (m ,2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.63 – 7.55 (m, 2H), 7.44 – 7.35 (m, 3H), 7.10 – 6.99 (tt, J = 9.8, 7.3 Hz, 1H). $^{13}C$ NMR (151 MHz, Chloroform-*d*) δ 146.8 (ddt, *J* = 251.9, 14.3, 3.3 Hz), 145.9 (dddd, *J* = 248.1, 13.6, 10.8, 4.2 Hz), 132.1, 129.8, 128.7, 121.8, 106.2 (t, *J* = 22.8 Hz), 105.6 (tt, *J* = 17.6, 2.6 Hz), 102.0 (t, *J* = 3.8 Hz), 74.5 (t, *J* = 4.4 Hz). GC/MS (m/z, relative intensity) 250 (M+, 100)




**10b**

***tert-butyl (tert-butoxycarbonyl)(2,3,5,6-tetrafluorophenyl)carbamate 10b***

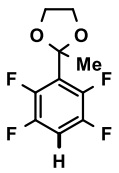
**General Procedure A** was followed using *tert*-butyl (*tert*-butoxycarbonyl)(pentafluorophenyl)carbamate (192 mg, 500 µmol) and $NaBH_4$ (57 mg, 1.5 mmol). The starting substrate was dissolved in 1.5 mL THF rather than DMSO since it was only sparing soluble in pure DMSO. The $NaBH_4$ was still added as a solution in 1.5 mL DMSO. The reaction was heated to 60 °C after the reagents were all mixed. The desired product **10b** was obtained as a white solid (173 mg, 95% yield). The mp 56-57 °C; $^{19}F$ NMR (376 MHz, Chloroform-d) δ -139.45 – -139.70 (m, 2F), -146.25 – 146.50 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.15 – 7.03 (tt, J = 9.8, 7.2, 1H), 1.45 – 1.43 (s, 18H). Mass spectrum obtained following conversion to 2,3,5,6-tetrafluoroaniline via trifluoroacetic acid (S12) is consistent with the literature.[3]




**11b**

***2-(2,3,5,6-tetrafluorophenyl)-1,3-dioxolane 11b***

**General Procedure A** was followed using 2-(pentafluorophenyl)-1,3-dioxolane (46 mg, 200 µmol) and $NaBH_4$ (20 mg, 530 µmol) in 2 mL DMSO heated to 50 °C. A known compound,[12] the desired product **11b** was obtained as a colorless oil (35 mg, 82% yield). $^{19}F$ NMR (376 MHz, Chloroform-d) δ -138.99 – -139.15 (m, 2F), -144.43 – -144.60 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.12 – 7.03 (tt, J = 9.5, 7.2, 1H), 6.26 – 6.23 (s, 1H), 4.26 – 4.17 (m, 2H), 4.10 – 4.00 (m, 2H). GC/MS (m/z, relative intensity) 222 (M+, 55), 221 (M-$H^{\cdot}$, 80), 203 (40), 177 (90), 162 (100).



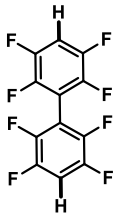

**12b**

***2-methyl-2-(2,3,5,6-tetrafluorophenyl)-1,3-dioxolane 12b***

**General Procedure A** was followed using 2-methyl-2-(pentafluorophenyl)-1,3-dioxolane (51 mg, 200 µmol) and $NaBH_4$ (16 mg, 420 µmol) in DMSO (2 mL) heated to 50 °C. The desired product **12b** was obtained as a colorless oil (38 mg, 80% yield). $^{19}F$ NMR (376 MHz, Chloroform-d) δ -138.75 – -138.90 (m, 2F), -142.62 – -142.77 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.06 – 6.97 (tt, J = 9.5, 7.2, 1H), 4.17 – 4.07 (m, 2H), 3.95 – 3.86 (m, 2H), 1.84 – 1.80 (s, 3H). GC/MS (m/z, relative intensity) 221 (M-·$CH_3$, 100), 187 (11), 177 (100), 149 (23), 99 (22).


***3,5-dichloro-2,6-difluoropyridine 13b***

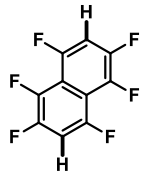
**General Procedure A** was followed using 3,5-dichloro-2,4,6-trifluoropyridine (101 mg, 500 µmol) and $NaBH_4$ (19 mg, 500 µmol) in 3 mL DMSO. Product **13b** was obtained as a pale-yellow, high-vapor-pressure solid (62 mg, 75% yield – some mass was lost under high vacuum). NMR spectra collected were a match for the literature.[13] $^{19}F$ NMR (376 MHz, Chloroform-d) δ -72.00 – -72.26 (d, J = 7.5, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.98 – 7.92 (t, J = 7.5, 1H).



14b

***2,2',3,3',5,5',6,6'-octafluoro-1,1'-biphenyl 14b***

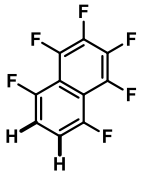
**General Procedure A** was followed using decafluorobiphenyl (67 mg, 200 µmol) and $NaBH_4$ (23 mg, 600 µmol) in 1 mL DMSO heated to 45 °C. The desired product 1**4b** was obtained as a white powder (60 mg, 84% yield). Melting point, $^{13}C$ and mass spectrum matched the literature.[14,15] $^{19}F$ NMR (376 MHz, Chloroform-d) δ -137.68 – -137.92 (m, 4F), -138.24 – -138.45 (m, 4F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.44 – 7.35 (m, 2H).



15b

***1,2,4,5,6,8-hexafluoronaphthalene 15b***

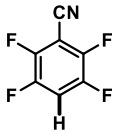
Octafluoronaphthalene (544 mg, 2 mmol) was taken into 8 mL THF and set stirring in a 50 mL round-bottom flask. To this was added $NaBH_4$ (182 mg, 4.8 mmol) in 12 mL of DMSO. The reaction mixture was heated to 45°C and continued to stir for 2 hours. The reaction mix was diluted with 180 mL EtOAc and quenched with brine. The organic layer was separated and washed five times with brine before being dried over $MgSO_4$ and concentrated under reduced pressure. The residue was subjected to silica gel flash chromatography eluting with pure hexane to afford an intractable mixture of **15b** and **15c** with a relative ratio of 8:1 respectively, for a combined yield of 423 mg (90%), corresponding to an 80% yield **15b** and 10% yield **15c**. The melting point, mass, $^{19}F$ NMR and $^{1}H$ NMR spectra match the literature.[14,16,17] $^{19}F$ NMR (564 MHz, Chloroform-d) δ -117.02 – -117.24 (m, 2F), -135.84 – -135.98 (m, 2F), -148.46 – -148.73 (m, 2F). $^{1}H$ NMR (599 MHz, Chloroform-d) δ 7.24 – 7.16 (m, 2H).



15c

***1,2,3,4,5,8-hexafluoronaphthalene 15c***

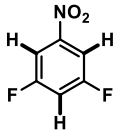
See entry for **15b** for procedure. $^{19}F$ NMR (564 MHz, Chloroform-d) δ -115.19 – -115.28 (m, 2F), -132.88 – -132.97 (m, 2F), -150.10 – -150.21 (m, 2F). $^{1}H$ NMR (599 MHz, Chloroform-d) δ 7.14 – 7.08 (m, 2H).



16b

***2,3,5,6-tetrafluorobenzonitrile 16b***

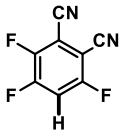
Into a reaction vial is placed pentafluorobenzonitrile (97 mg, 500 µmol) and $NaBH_4$ (19 mg, 500 µmol) suspended in 2 mL of THF, set stirring with a magnetic stir bar. When the reaction was found to be complete by $^{19}F$ NMR the THF was removed under reduced pressure and the residue extracted with hexanes, affording **16b** as a colorless oil (77 mg, 88% yield). Mass spectrum matched the literature,[18] as well as the $^{13}C$ NMR.[14] $^{19}F$ NMR (376 MHz, Chloroform-d) δ -131.77 – -131.92 (m, 2F), -134.81 – -134.99 (m, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.45 – 7.35 (tt, J = 9.4, 7.3, 1H).



17b

***1,3-difluoro-5-nitrobenzene 17b***

To a stirring suspension of $NaBH_4$ (34 mg, 900 µmol) in 3 mL of THF, cooled to 0 °C, is added $H_2O$ (15 mg, 900 µmol) and pentafluoronitrobenzene (64 mg, 300 µmol). The reaction mixture is allowed to gradually warm to room temperature and is carefully monitored by $^{19}F$ NMR. When complete, the reaction is quenched by dilution with EtOAc, which precipitates the reactive salts, and the solution is decanted into a round-bottom flask. The decanted solution is dry loaded onto silica and subjected to silica gel flash chromatography to afford the product **17b** as a yellow oil (38 mg). $^{1}H$ and $^{19}F$ NMR suggested trace contamination of 10 mol% trifluoroaniline isomers and 3 mol% ethyl acetate, making the isolated yield 71%. $^{19}F$ NMR (376.48 MHz, Chloroform-d) δ -105.08 (dd, J = 8.1, 6.5 Hz, 2F). $^{1}H$ NMR (400 MHz, Chloroform-d) δ 7.83 – 7.77 (dd, J = 6.5, 2.3 Hz, 2H), 7.22 – 7.17 (tt, J = 8.1, 2.3, 1H). GC/MS (m/z, relative intensity) 159 (M+, 60), 129 (7), 113 (100), 101 (19).

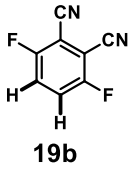


18b

***3,4,6-trifluorophthalonitrile 18b***

To a stirring suspension of $NaBH_4$ (38 mg, 1 mmol) and $H_2O$ (20 mg, 1.1 mmol) in THF (20 mL) at 0 °C is added tetrafluorophthalonitrile (200 mg, 1 mmol). This mixture is stirred for 30 minutes before quenching with trifluoroacetic acid (200 µL) and concentrating under reduced pressure onto silica for flash chromatography using hexane/DCM for elution. Product **18b** was obtained as a pale-yellow oil (133 mg, 73% yield). Yield for this substrate was found to be highly time-dependent, with the product being highly prone to subsequent chemistry if left for longer than 30 minutes; moreover, it does not store well (highly moisture-

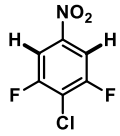
sensitive). $^{19}$F NMR (564 MHz, Chloroform-d) δ -101.71 (ddd, J = 12.9, 9.3, 8.0 Hz, 1F), -117.02 (dt, J = 20.9, 9.0 Hz, 1F), -128.85 (ddd, J = 20.9, 12.9, 6.3 Hz, 1F). $^{1}$H NMR (599 MHz, Chloroform-d) δ 7.45 (td, J = 8.4, 6.3 Hz, 1H). $^{13}$C NMR (151 MHz, Chloroform-d) δ 159.7 (ddd, J = 263.4, 10.9, 3.3 Hz), 153.8 (dt, J = 266.5, 12.6 Hz), 149.4 (ddd, 264.6, 15.5, 4.0 Hz), 112.5 (dd, J = 25.6, 21.3 Hz), 109.3 (t, J = 2.4 Hz), 109.0 (t, J = 3.7 Hz), 106.7 (dt, J = 16.1, 3.4 Hz), 100.8 (dd, J = 20.2, 4.8 Hz). GC/MS (m/z, relative intensity) 182 (M+, 100).



**19b**

***3,6-difluorophthalonitrile 19b***

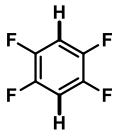
To a stirring suspension of $NaBH_4$ (82 mg, 2.2 mmol) in THF (10 mL) cooled to 0 °C is added $H_2O$ (40 mg, 2.2 mmol) and subsequently tetrafluorophthalonitrile (200 mg, 1 mmol) as a solution in THF (20 mL, 0 °C). The reaction mixture warmed to room temperature and is monitored by $^{19}$F NMR. After 3 hours, the reaction is complete and concentrated onto silica for flash column chromatography using $CH_2Cl_2$: hexane (ramp) for elution to afford **19b** (95 mg, 58% yield). Similar to **18b**, this reaction product degrades readily under ambient laboratory conditions (moisture-sensitive) and stores poorly. $^{13}$C NMR was found to match the literature.[14] $^{19}$F NMR (376 MHz, Chloroform-d) δ -106.57 – -106.62 (m, 2F). $^{1}$H NMR (400 MHz, Chloroform-d) δ 7.58 – 7.54 (m, 2H). GC/MS (m/z, relative intensity) 164 (M+, 100).



**20b**

***2-chloro-1,3-difluoro-5-nitrobenzene 20b***

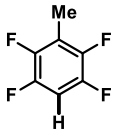
To a stirring suspension of $NaBH_4$ (28 mg, 740 µmol) in 3 mL of THF is added 1-chloro-2,3,5,6-tetrafluoro-4-nitrobenzene **20a** (92 mg, 400 µmol). When the reaction was deemed complete by $^{19}$F NMR, the mixture was concentrated *in vacuo* and quenched by dilution with pentane, which precipitated out insoluble species. The remaining solution was filtered and concentrated *in vacuo* to afford the product **20b** as an orange oil (65 mg, 77% yield). Product appears to be moisture sensitive. $^{19}$F NMR (376 MHz, Chloroform-d) δ -107.10 – 107.16 (m, 2F). $^{1}$H NMR (400 MHz, Chloroform-d) δ 7.94 – 7.88 (m, 2H). GC/MS (m/z, relative intensity) 195 (M+2, 13), 193 (M+, 40).



**21b**

***1,2,4,5-tetrafluorobenzene 21b***

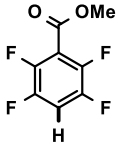
**General Procedure A** was followed using hexafluorobenzene (100 mg, 537 µmol) and $NaBH_4$ (100 mg, 2.6 mmol) in 5 mL of DMSO. When the reaction was complete, 1 mL of reaction mixture (20% of the total volume) was taken into an NMR tube charged with a benzene-d$^6$ capillary and fluorobenzene (20 µL, 213 µmol) as internal standard. The aliquot was calculated to contain 87 µmol of **7b** corresponding to an 81% yield. Mass spectrum was found to be in accord with the literature.[3] $^{19}$F NMR (564 MHz, DMSO) δ -134.78 – 134.84 (t, J = 9.0, 4F).



**22b**

***1,2,4,5-tetrafluoro-3-methylbenzene 22b***

**General Procedure A** was followed using 1,2,3,4,5-pentafluoro-6-methylbenzene (100 mg, 550 µmol) and $NaBH_4$ (104 mg, 2.6 mmol) in 5 mL of DMSO heated to 80 °C. When the reaction was complete, 500 µL of reaction mixture was taken into an NMR tube charged with a benzene-d$^6$ capillary and fluorobenzene (20 µL, 213 µmol) as internal standard. The aliquot was calculated to contain 39 µmol of **22b** corresponding to a 72% yield. The mass spectrum was a match for the literature.[3] $^{19}$F NMR (564 MHz, DMSO) δ -140.03 (m, 2F), -143.23 (m, 2F).



**1b**

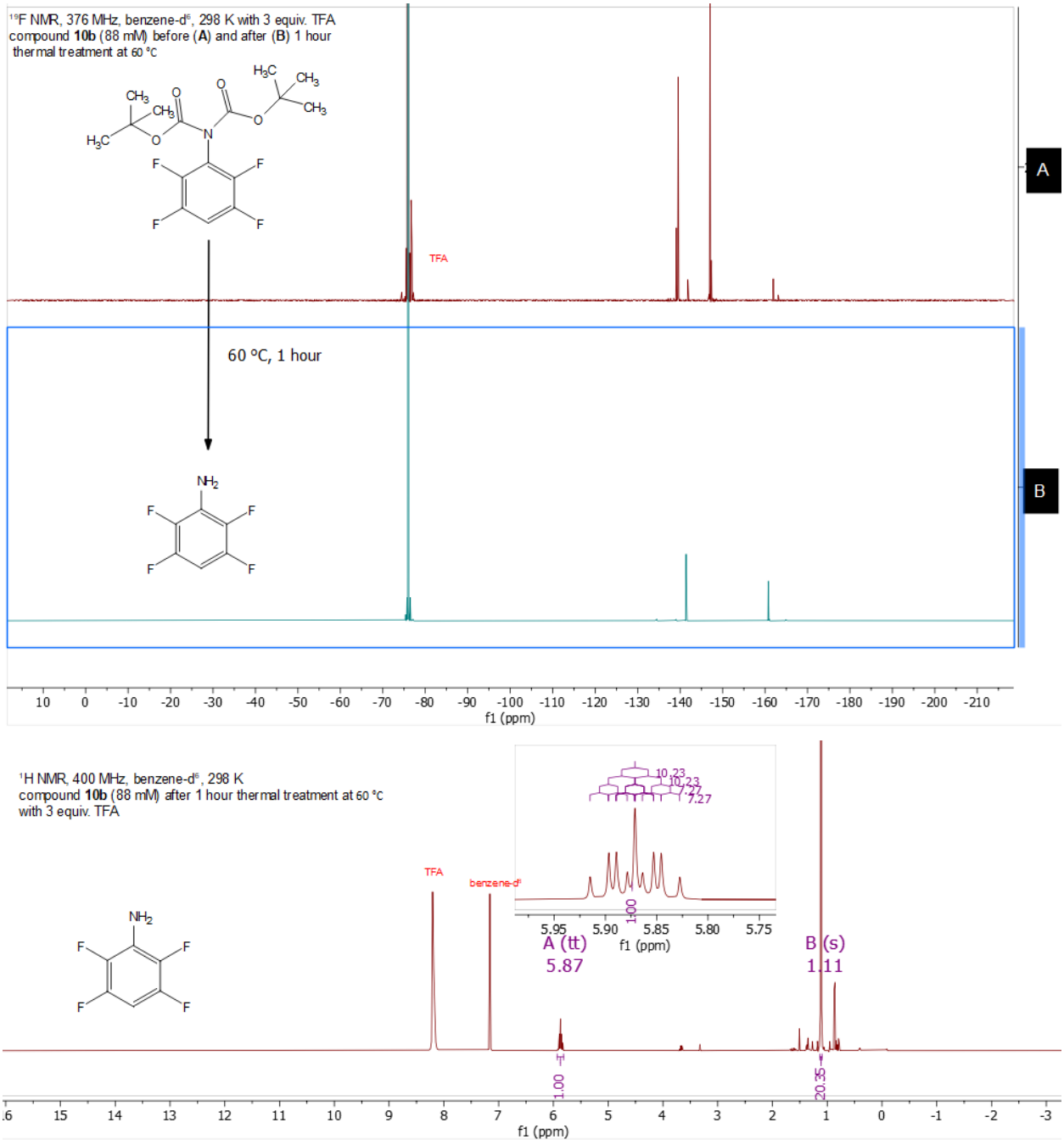
***methyl 2,3,5,6-tetrafluorobenzoate 1b (5 g scale)***

**General Procedure A** was followed using methyl pentafluorobenzoate (5.00 g, 22.1 mmol) and 1 equiv $NaBH_4$ (837 mg, 22.1 mmol) in 75 mL DMSO. The desired product **1b** was obtained as a colorless oil (4.15 g, 90% yield). A known compound, characteristic NMR spectra match the literature.[8] $^{19}$F NMR (376 MHz, Chloroform-d) δ -137.45 – -137.60 (m, 2F), -139.48 – -139.63 (m, 2F). $^{1}$H NMR (400 MHz, Chloroform-d) δ 7.20 (tt, J = 9.4, 7.2 Hz, 1H), 4.00-3.97 (s, 3H)

## NMR Demonstration of Deprotection of N,N-(boc)$_2$-tetrafluoroaniline 10b

To demonstrate the facility of converting **10b** to the corresponding 2,3,5,6-tetrafluoroaniline, 16 mg (44 µmol) of **10b** were taken into an NMR tube charged with benzene-d$^6$ (500 µL) and trifluoroacetic acid (15 mg, 132 µmol). NMR spectra collected prior to and following a one-hour thermal treatment at 60 °C showed complete conversion to 2,3,5,6-tetrafluoroaniline (**Figure 2**), consistent with the literature spectrum in benzene-d$^6$.[19]

**Figure 2. NMR Spectra of 10b Before and After Heating in TFA Solution**

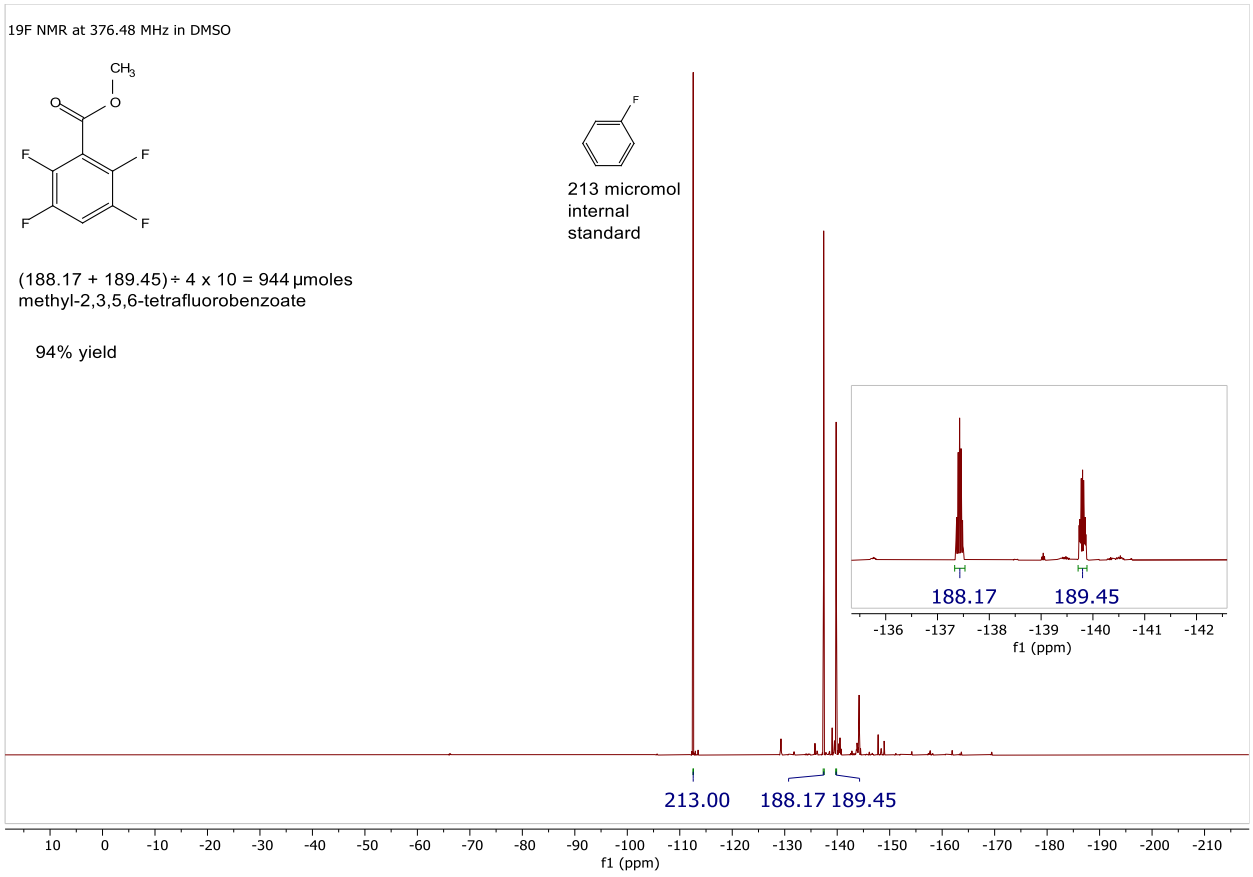


**Stability Test Using Methyl Pentafluorobenzoate**

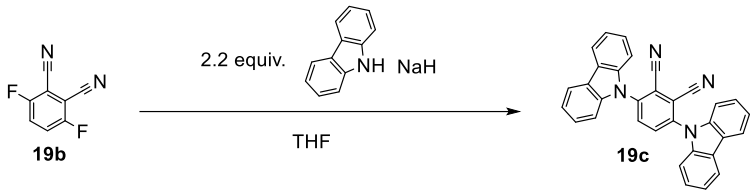
In order to make a statement regarding the stability of substrates like **1b** under reaction conditions over extended periods, a 1 mmol scale synthesis of **1b** was set up according to General Procedure A (in 5.00 mL of DMSO) and left to stir for a period of time in excess of 40 hours. Periodic monitoring of the reaction by GCMS indicated complete consumption of the starting material within 4 hours, and no evidence for the formation of undesired side-products. After approximately 40 hours, aliquots subjected to GCMS still showed primarily methyl 2,3,5,6-tetrafluorobenzoate.

Finally, a 1/10 volume sample from the reaction mixture was taken into an NMR tube charged with a benzene-$d^6$ capillary and fluorobenzene as an internal standard (20 microliters, 213 micromoles) for an expedient $^{19}F$ NMR yield of 94%. No attempt was made to characterize any trace side products or the fate of the remaining 3 equivalents of hydrides, although a distinct odor of dimethylsulfide suggested that the complex hydride side products preferentially react with the solvent over the methyl 1,3,5,6-tetrafluorobenzoate.

It is important to note that several of the other tested substrates were very much less stable under reaction conditions, requiring careful monitoring and timely workup to mitigate subsequent functional group reduction (**17b**, **18b**, **19b**, and **20b**)

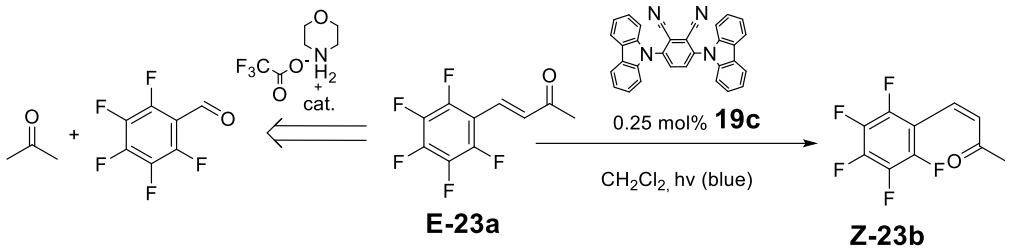


***Synthesis of 3,6-di(9H-carbazol-9-yl)phthalonitrile 19c***



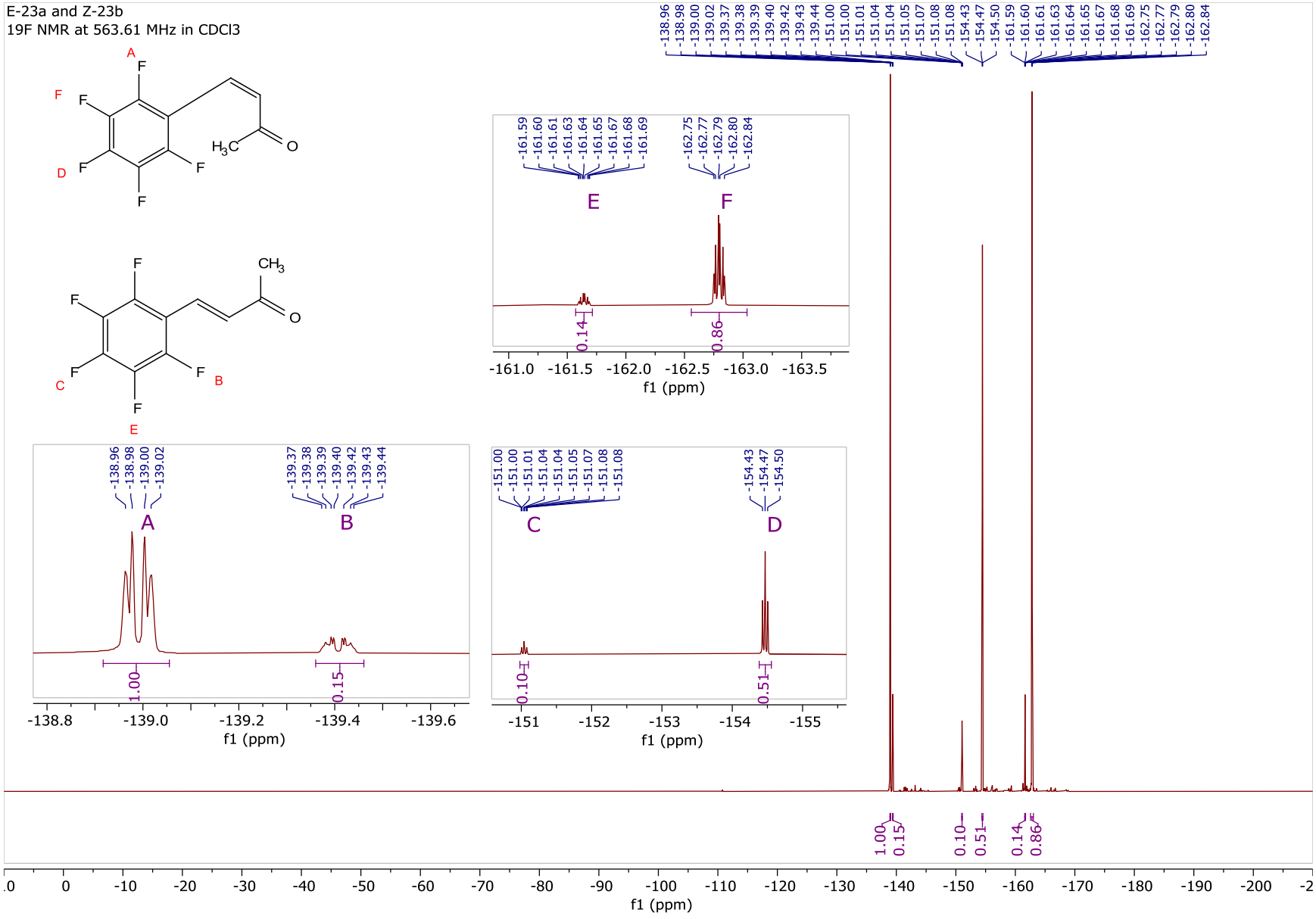

Following the procedure of Adachi et al.,[20] NaH (110 mg 60% paraffin dispersion, 2.7 mmol) was added portion-wise to a stirring solution of carbazole (450 mg, 2.7 mmol) in dry THF (3 mL) under argon. The stirring was continued until the exotherm and effervescence had entirely subsided, then the suspension was carefully transferred via syringe to another stirring 3 mL THF solution of 3,6-difluorophthalonitrile **19b** (200 mg, 1.22 mmol). The $S_NAr$ reaction was essentially diffusion controlled but allowed to stir for 30 minutes before being quenched in ice water and extracted with $CH_2Cl_2$ until the extractions no longer fluoresced under 365 nm irradiation. The organic layer was dried over $MgSO_4$ and subjected to silica gel flash chromatography eluting with 60% $CH_2Cl_2$ 40% hexane affording 455 mg of **19c** (81% yield) as a bright yellow, fluorescent powder. $^1$H NMR (599 MHz, Benzene-$d_6$) δ 7.97 (d, *J* = 7.7 Hz, 4H), 7.36 (t, *J* = 7.6 Hz, 6H), 7.27 (t, *J* = 7.4 Hz, 4H), 7.03 (d, *J* = 8.1 Hz, 4H), 6.72 (s, 2H). $^{13}$C NMR (151 MHz, Benzene-$d_6$) δ 140.86, 140.51, 134.48, 126.89, 124.87, 122.18, 121.26, 117.81, 113.10, 110.07

## Scheme 3. Contrathermodynamic Isomerization of E-23a




***19c – Photocatalyzed Synthesis of (Z)-4-(perfluorophenyl)but-3-en-2-one (Z-23b)***

The procedure reported by Sun et al.[21] was followed scaled to 980 mg of pentafluorobenzaldehyde, affording **E-23a** in 80% yield. 100 mg (424 μmol) of **E-23a** was placed into glass culture tube charged with **19c** in $CH_2Cl_2$ (4 mL, 280 μM), which was subsequently placed in the 447 nm light bath described in the general experimental at 0 °C for 1 hour. The solution was concentrated *in vacuo* and subjected to silica gel chromatography with hexane/EtOAc to afford **Z-23b** (70 mg combined, 70% combined yield as a mixture of 8 : 1 **Z-23b** : **E-23a**). $^{19}$F NMR (564 MHz, chloroform-d) δ -138.99 (m, 2F), -154.47 (t, J = 20.7 Hz, 1F), -162.78 (m, 2F). $^1$H NMR (599 MHz, chloroform-d) δ 6.58 (d, J = 11.9 Hz, 1H), 6.49 (dq, J = 11.9, 1.5 Hz, 1H), 2.27 (s, 3H). $^{13}$C NMR (151 MHz, chloroform-d) δ 197.72 (s), 144.12 (dddt, J = 249.0, 11.2, 7.4, 3.8 Hz,), 141.22 (dtt, J = 255.6, 13.9, 5.4 Hz), 137.37 (m, $J_{C\text{-}F}$ = 251.2 Hz), 133.96 (s, 1C), 122.65 (s), 110.98 (td, J = 17.7, 4.1 Hz), 30.63 (s).


E-23a and Z-23b
19F NMR at 563.61 MHz in CDCl3
A
F
F
F
F
F
D
H3C
O
F
CH3
F
F
F
C
B
O
F
E
-138.96
-138.98
-139.00
-139.02
-139.37
-139.38
-139.39
-139.40
-139.42
-139.43
-139.44
-151.00
-151.00
-151.01
-151.04
-151.04
-151.05
-151.07
-151.08
-151.08
-154.43
-154.47
-154.50
-161.59
-161.60
-161.61
-161.63
-161.64
-161.65
-161.67
-161.68
-161.69
-162.75
-162.77
-162.79
-162.80
-162.84
E
F
0.14
0.86
-161.0
-161.5
-162.0
-162.5
-163.0
-163.5
f1 (ppm)
A
B
1.00
0.15
-138.8
-139.0
-139.2
-139.4
-139.6
f1 (ppm)
C
D
0.10
0.51
-151
-152
-153
-154
-155
f1 (ppm)
1.00
0.15
0.10
0.51
0.14
0.86
.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
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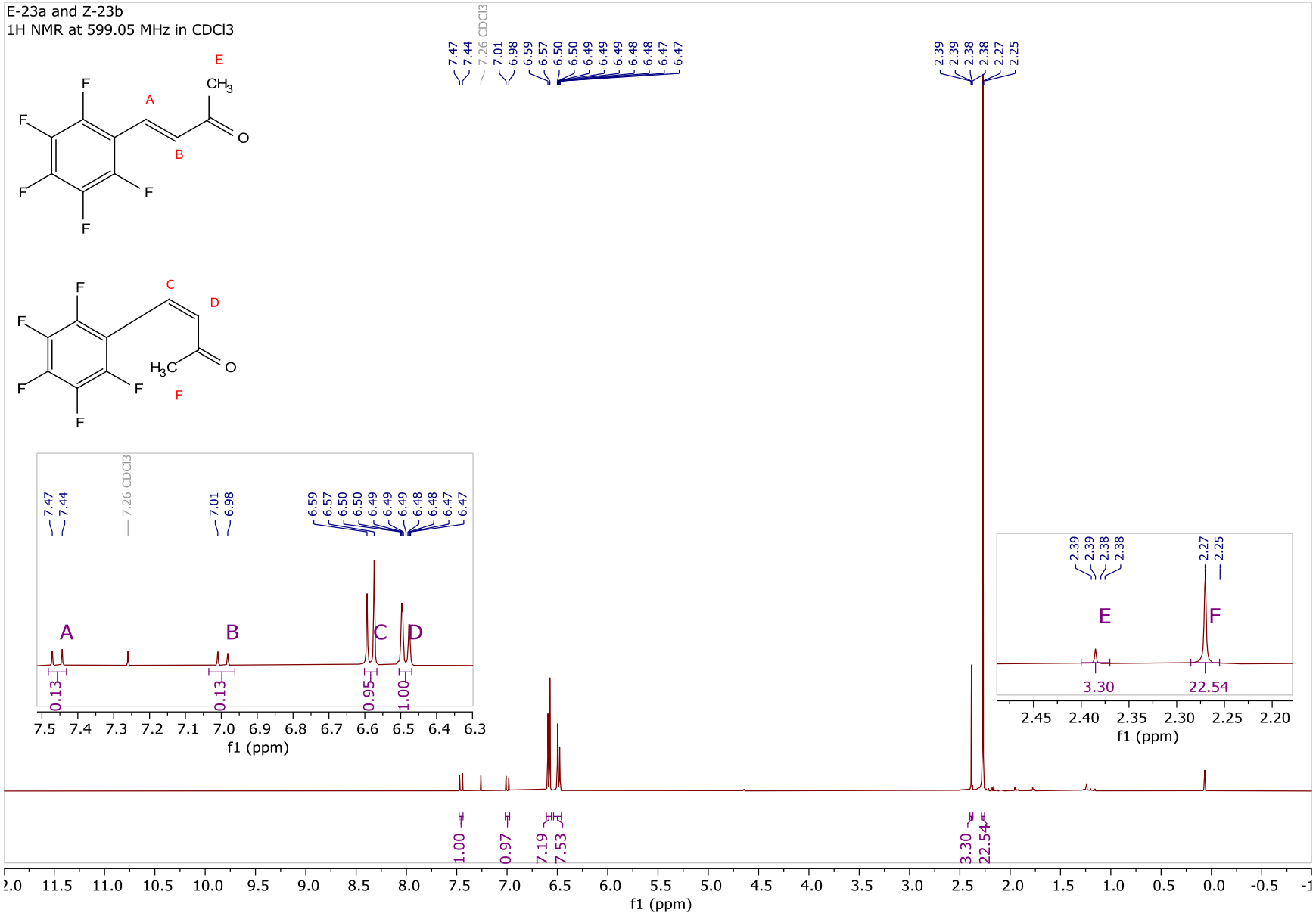
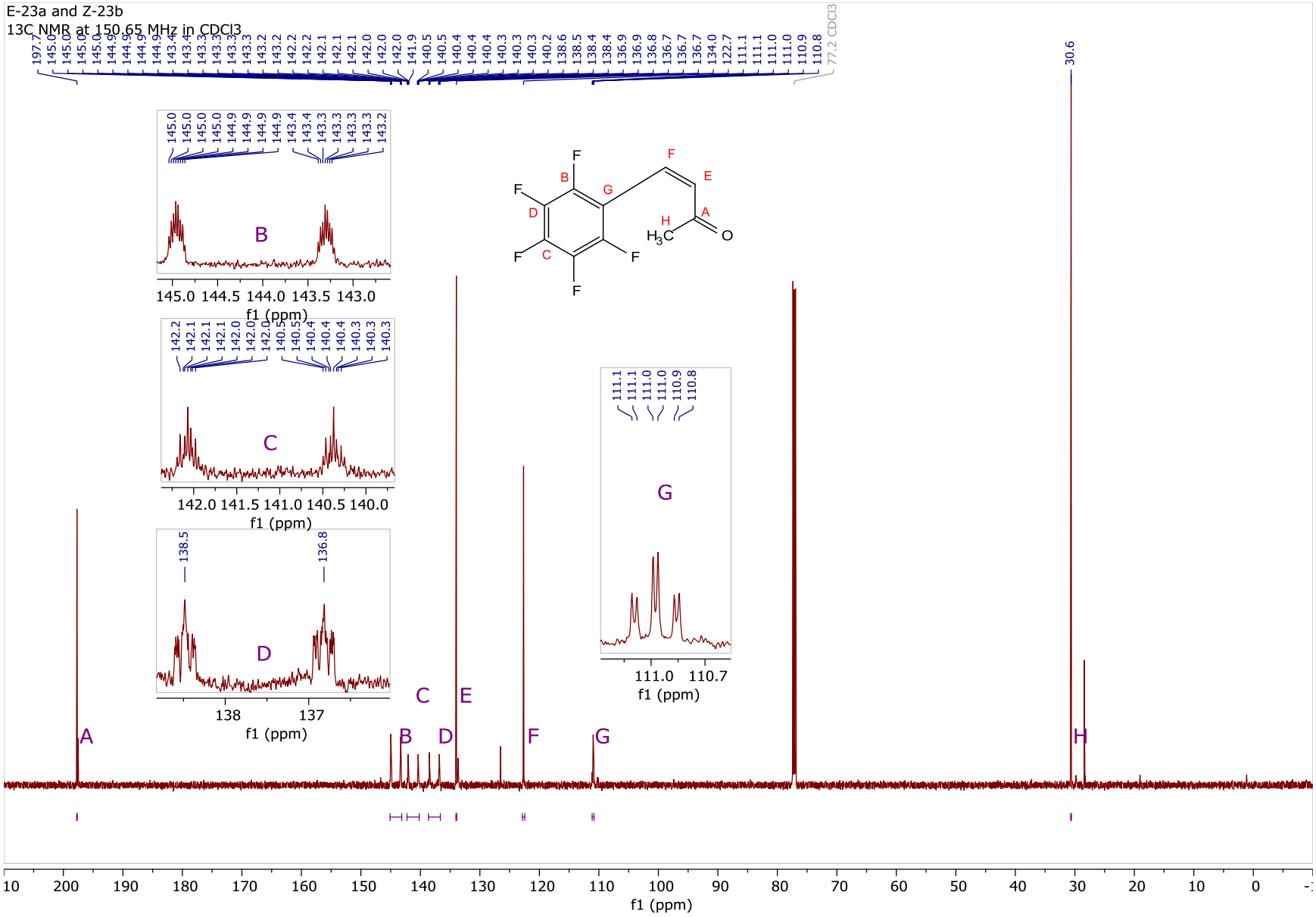
-160
-170
-180
-190
-200
-2
f1 (ppm)


E-23a and Z-23b
1H NMR at 599.05 MHz in CDCl3
E
CH3
A
B
F
C
D
H3C
O
7.47
7.44
7.26 CDCl3
7.01
6.98
6.59
6.57
6.50
6.50
6.49
6.49
6.48
6.48
6.47
6.47
2.39
2.39
2.38
2.38
2.27
2.25
A
B
C
D
0.13
0.13
0.95
1.00
E
F
3.30
22.54
f1 (ppm)
1.00
0.97
7.19
7.53
3.30
22.54


E-23a and Z-23b
13C NMR at 150.65 MHz in CDCl3
77.2 CDCl3
30.6
B
C
D
G
A
B
C
D
E
F
G
H
f1 (ppm)

## REFERENCES


(1) Harris, R.; Becker, E. D.; Cabral de Menezes, S. M.; Goodfellow, R.; Granger, P. NMR Nomenclature. Nuclear Spin Properties and Conventions for Chemical Shifts. *Pure Appl. Chem.* **2001**, *73* (11), 1795–1818.

(2) Davies, L. C.; Friedlos, F.; Hedley, D.; Martin, J.; Ogilvie, L. M.; Scanlon, I. J.; Springer, C. J. Novel Fluorinated Prodrugs for Activation by Carboxypeptidase G2 Showing Good in Vivo Antitumor Activity in Gene-Directed Enzyme Prodrug Therapy. *J. Med. Chem.* **2005**, *48* (16), 5321–5328. https://doi.org/10.1021/jm0502182.

(3) Wallace, W. E.; NIST Mass Spectrometry Data Center. "Mass Spectra." In *NIST Chemistry WebBook, NIST Standard Reference Database Number 69*; Linstrom, P. J., Mallard, W. G., Eds.; National Institute of Standards and Technology: Gaithersburg MD, 20899, 2018. https://doi.org/10.18434/T4D303.

(4) Nicholls, T. P.; Robertson, J. C.; Gardiner, M. G.; Bissember, A. C. Identifying the Potential of Pulsed LED Irradiation in Synthesis: Copper-Photocatalysed C-F Functionalisation †. *Chem. Commun* **2018**, *54*, 4589. https://doi.org/10.1039/c8cc02244e.

(5) Zhang, X.; Fan, S.; He, C.-Y.; Wan, X.; Min, Q.-Q.; Yang, J.; Jiang, Z.-X. Pd(OAc) 2 Catalyzed Olefination of Highly Electron-Deficient Perfluoroarenes. *J. Am. Chem. Soc.* **2010**, *132* (13), 4506–4507. https://doi.org/10.1021/ja908434e.

(6) Matsuyama, N.; Kitahara, M.; Hirano, K.; Satoh, T.; Miura, M. Nickel- and Copper-Catalyzed Direct Alkynylation of Azoles and Polyfluoroarenes with Terminal Alkynes under O2 or Atmospheric Conditions. *Org. Lett.* **2010**, *12* (10), 2358–2361. https://doi.org/10.1021/ol100699g.

(7) Iwasaki, T.; Min, X.; Fukuoka, A.; Zhu, L.; Qiu, R.; Yang, T.; Ehara, M.; Sudalai, A.; Kambe, N. Ni-Catalyzed Dimerization and Hydroperfluoroarylation of 1,3-Dienes. *J. Org. Chem.* **2018**, *83*, 9267. https://doi.org/10.1021/acs.joc.8b01266.

(8) Senaweera, S. M.; Singh, A.; Weaver, J. D. Photocatalytic Hydrodefluorination: Facile Access to Partially Fluorinated Aromatics. *J. Am. Chem. Soc.* **2014**, *136*, 3002. https://doi.org/10.1021/ja500031m.

(9) Laev, S. S.; Shteingarts, V. D. Reductive Dehalogenation of Polyfluoroarenes by Zinc in Aqueous Ammonia. *J. Fluor. Chem.* **1999**, *96* (2), 175–185. https://doi.org/10.1016/S0022-1139(99)00082-2.

(10) Aroskar, E. V.; Brown, P. J. N.; Plevey, R. G.; Stephens, R. Aromatic Polyfluoro-Compounds. PArt XLI.1 Some Reactions of Pentafluorobenzaldehyde. *J. Chem. Soc. C* **1966**, 1569–1575. https://doi.org/10.1039/J39680001569.

(11) Wiles, M. R.; Massey, A. G. Synthesis of 1-Phenylethynyl- 4-Substituted Tetrafluorobenzenes. *Tetrahedron Lett.* **1967**, *8* (51), 5137–5138. https://doi.org/10.1016/S0040-4039(01)89629-5.

(12) Krebs, F. C.; Jensen, T. Fluorinated Molecules Relevant to Conducting Polymer Research. *J. Fluor. Chem.* **2003**, *120* (1), 77–84. https://doi.org/10.1016/S0022-1139(02)00289-0.

(13) Chambers, R. D.; Hall, C. W.; Hutchinson, J.; Millar, R. W. Polyhalogenated Heterocyclic Compounds. Part 42. Fluorinated Nitrogen Heterocycles with Unusual Substitution Patterns. *J. Chem. Soc. - Perkin Trans. 1* **1998**, No. 10, 1705–1713. https://doi.org/10.1039/a709291a.

(14) Kikushima, K.; Grellier, M.; Ohashi, M.; Ogoshi, S. Transition-Metal-Free Catalytic Hydrodefluorination of Polyfluoroarenes by Concerted Nucleophilic Aromatic Substitution with a Hydrosilicate. *Angew. Chemie - Int. Ed.* **2017**, *56* (51), 16191–16196. https://doi.org/10.1002/anie.201708003.

(15) Deacon, G. B.; Phillips, R. J. Organothallium Compounds. XIV. Thermal Decomposition of Some Polyfluorobenzoatobis(Polyfluorophenyl)-Thallium(III) Compounds. *Aust. J. Chem* **1978**, *31*, 1709–1724. https://doi.org/10.1071/CH9781709.

(16) Facundo, A. A.; Aré, A.; Fundora-Galano, G.; Flores-A ´lamo, M.; Orgaz, E.; Garcí, J. J. Hydrodefluorination of Functionalized Fluoroaromatics with Triethylphosphine: A Theoretical and Experimental Study †. *New J. Chem* **2019**, *43*, 6897. https://doi.org/10.1039/c9nj00721k.

(17) Yow, S.; Gates, S. J.; White, A. J. P.; Crimmin, M. R. Zirconocene Dichloride Catalyzed Hydrodefluorination of C Sp 2–F Bonds. *Angew. Chemie Int. Ed.* **2012**, *51* (50), 12559–12563. https://doi.org/10.1002/anie.201207036.

(18) Senaweera, S. M.; Singh, A.; Weaver, J. D. *Photocatalytic Hydrodefluorination; Facile Access to Partially Fluorinated Aromatics-SI*; 2014.

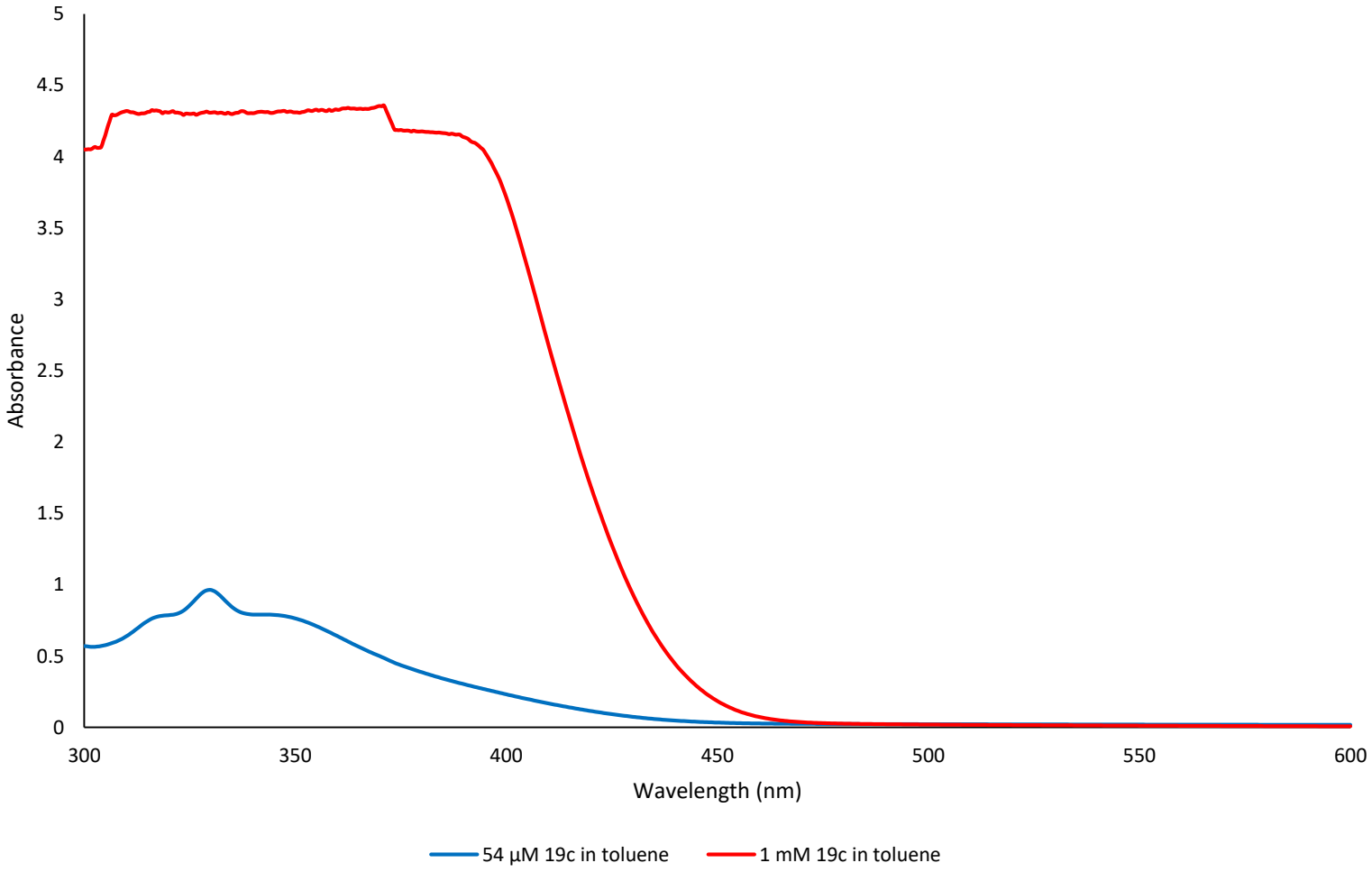
(19) Andreevskaya, O. I.; Furin, G. G.; Yakobson, G. G. AROMATIC FLUORO-SUBSTITUTED DERIVATIVES. LXXV. BENZIDINE REARRANGEMENT OF 2,2′,3,3′,5,5′,6,6′-OCTAFLUOROHYDRAZOBENZENE AND WALLACH REARRANGEMENT OF 2,2′,3,3′,5,5′,6,6′-OCTAFLUOROAZOXYBENZENE IN ULTRASTRONG ACIDS. *Zhurnal Org. Khimii* **1977**, *13*, 1648–1693. https://doi.org/10.1002/chin.197748097.

(20) Uoyama, H.; Goushi, K.; Shizu, K.; Nomura, H.; Adachi, C. Highly Efficient Organic Light-Emitting Diodes from Delayed Fluorescence. *Nature* **2012**, *492* (7428), 234–238. https://doi.org/10.1038/nature11687.

(21) Song, X.; Zhu, X.; Li, T.; Liang, C.; Zhang, M.; Shao, Y.; Tao, J.; Sun, R. Dehydrozingerone Inspired Discovery of Potential Broad-Spectrum Fungicidal Agents as Ergosterol Biosynthesis Inhibitors. *J. Agric. Food Chem.* **2019**, *67* (41), 11354–11363. https://doi.org/10.1021/acs.jafc.9b04231.

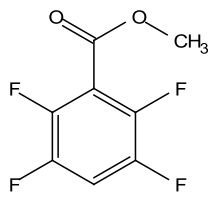
UV-Vis absorption spectra were collected at reaction concentration (approximately 1 mM) and at 54 µM for the organodye **19c** as part of the substance characterization.

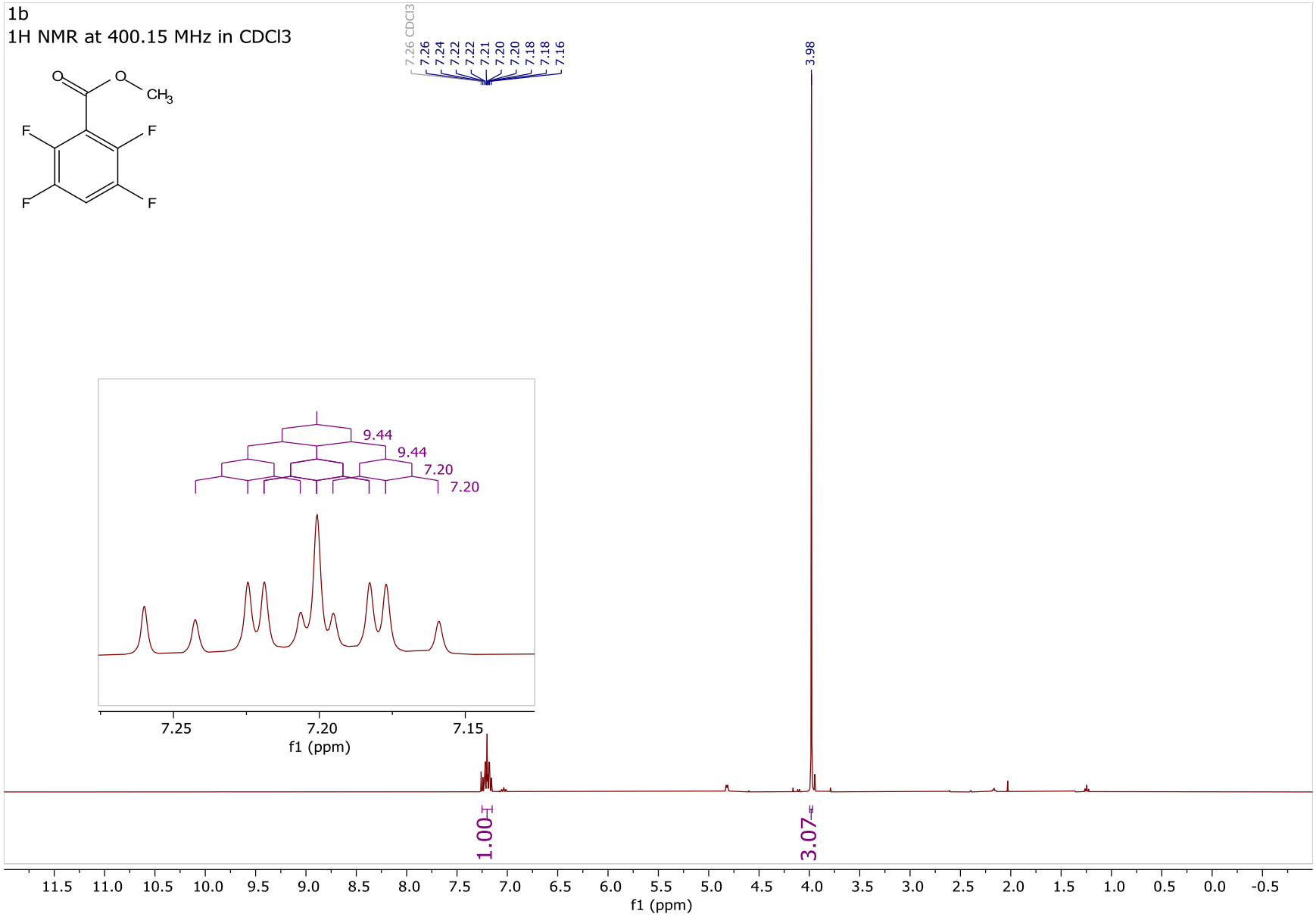
**Figure 4. UV-Vis Absorption Spectrum for organodye *19c***



1b

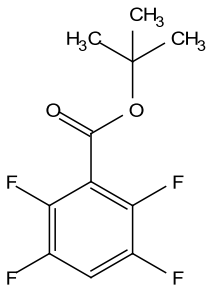
19F NMR at 376.48 MHz in CDCl3

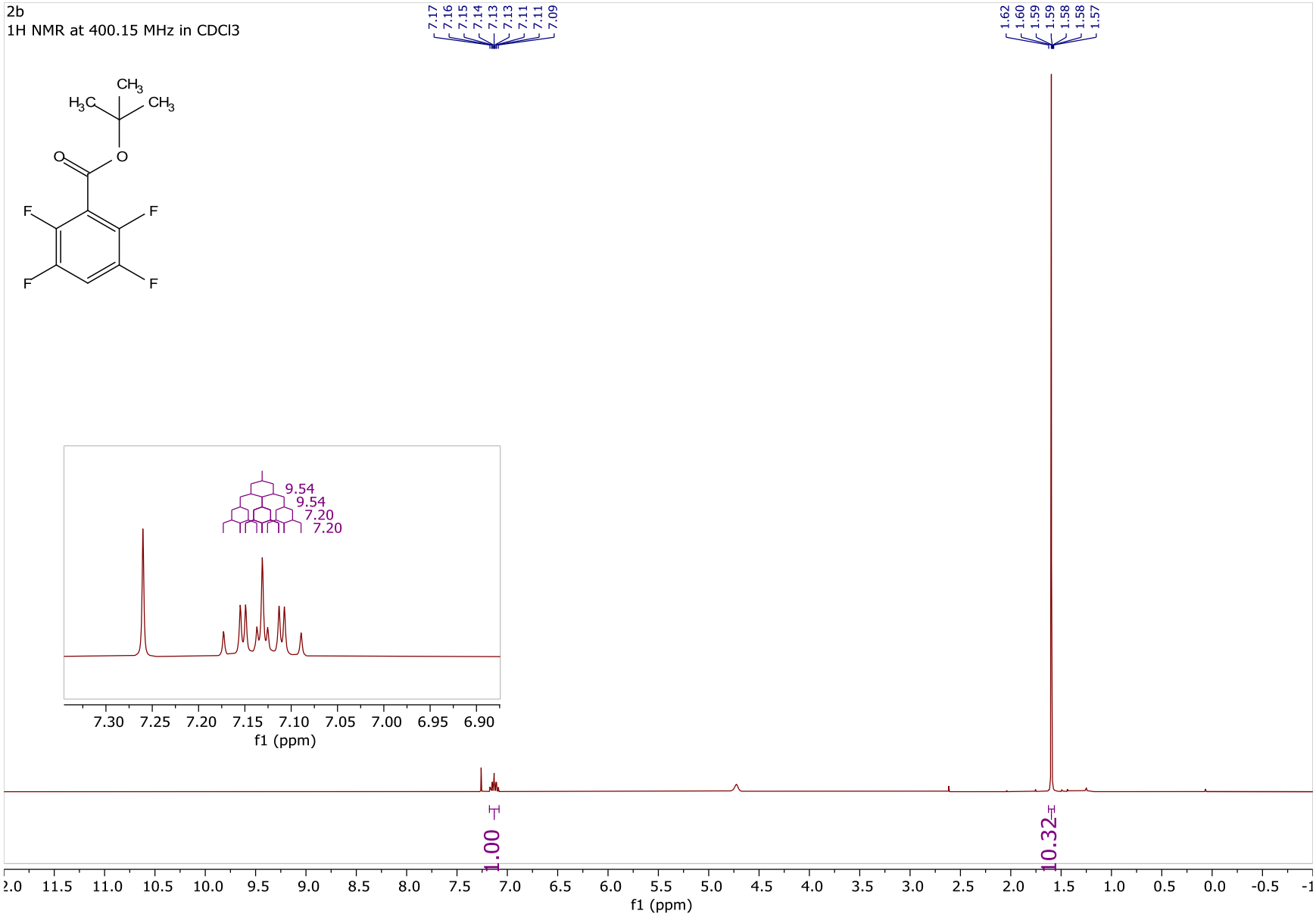


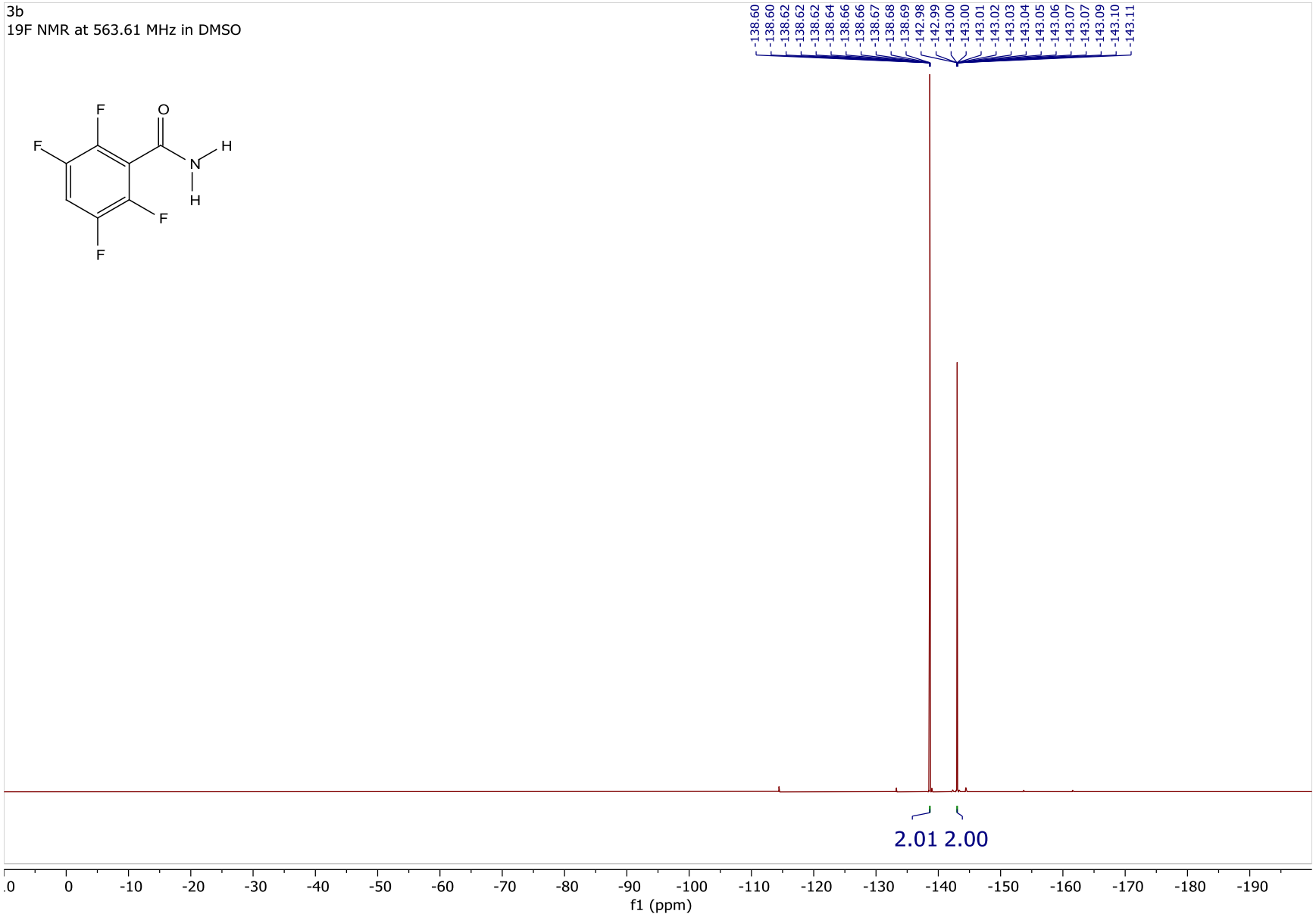

1b
1H NMR at 400.15 MHz in CDCl3
7.26 CDCl3
7.26
7.24
7.22
7.22
7.21
7.20
7.20
7.18
7.18
7.16
3.98
O
O
CH3
F
F
F
F
9.44
9.44
7.20
7.20
7.25
7.20
7.15
f1 (ppm)
1.00
3.07
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

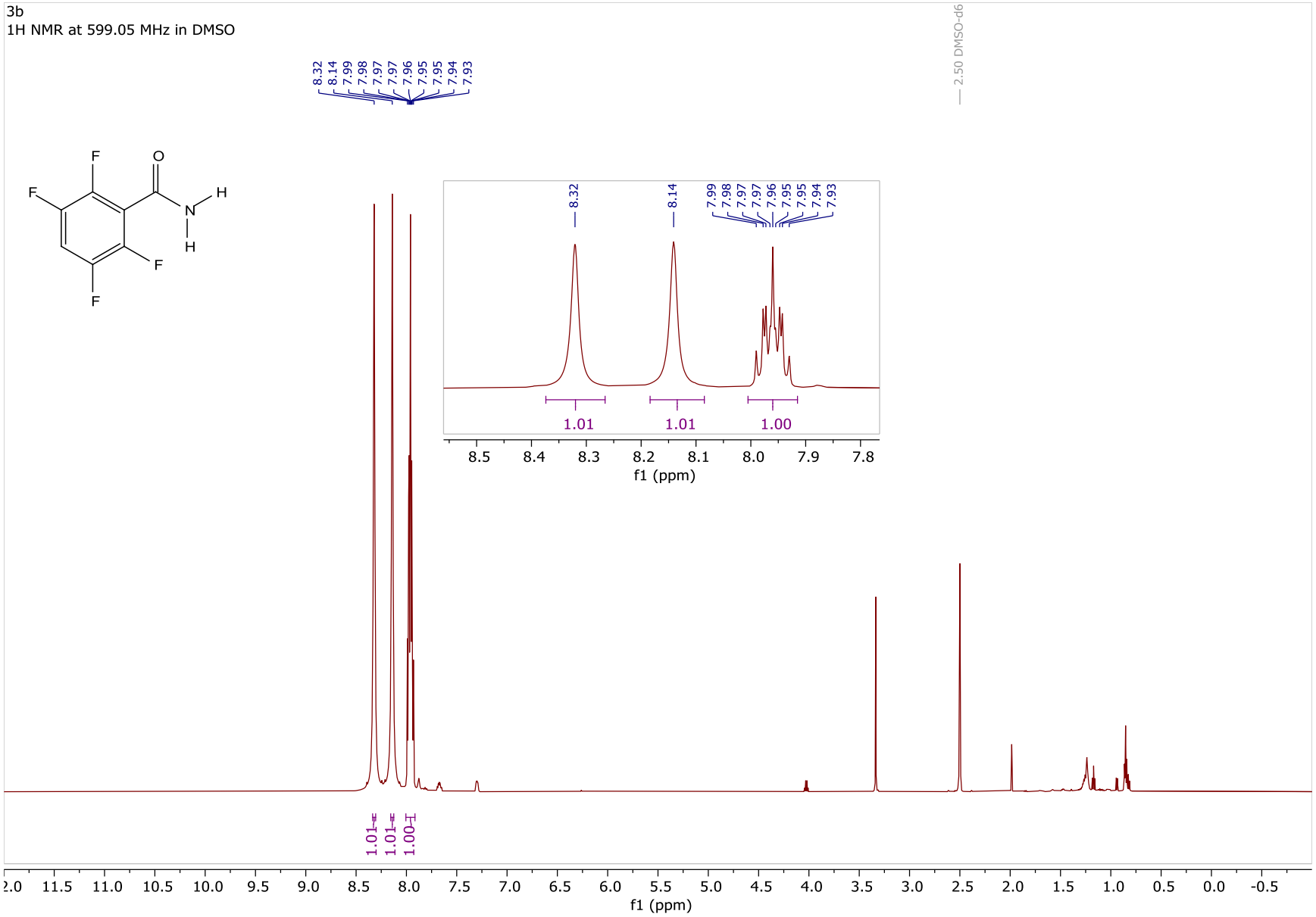
2b

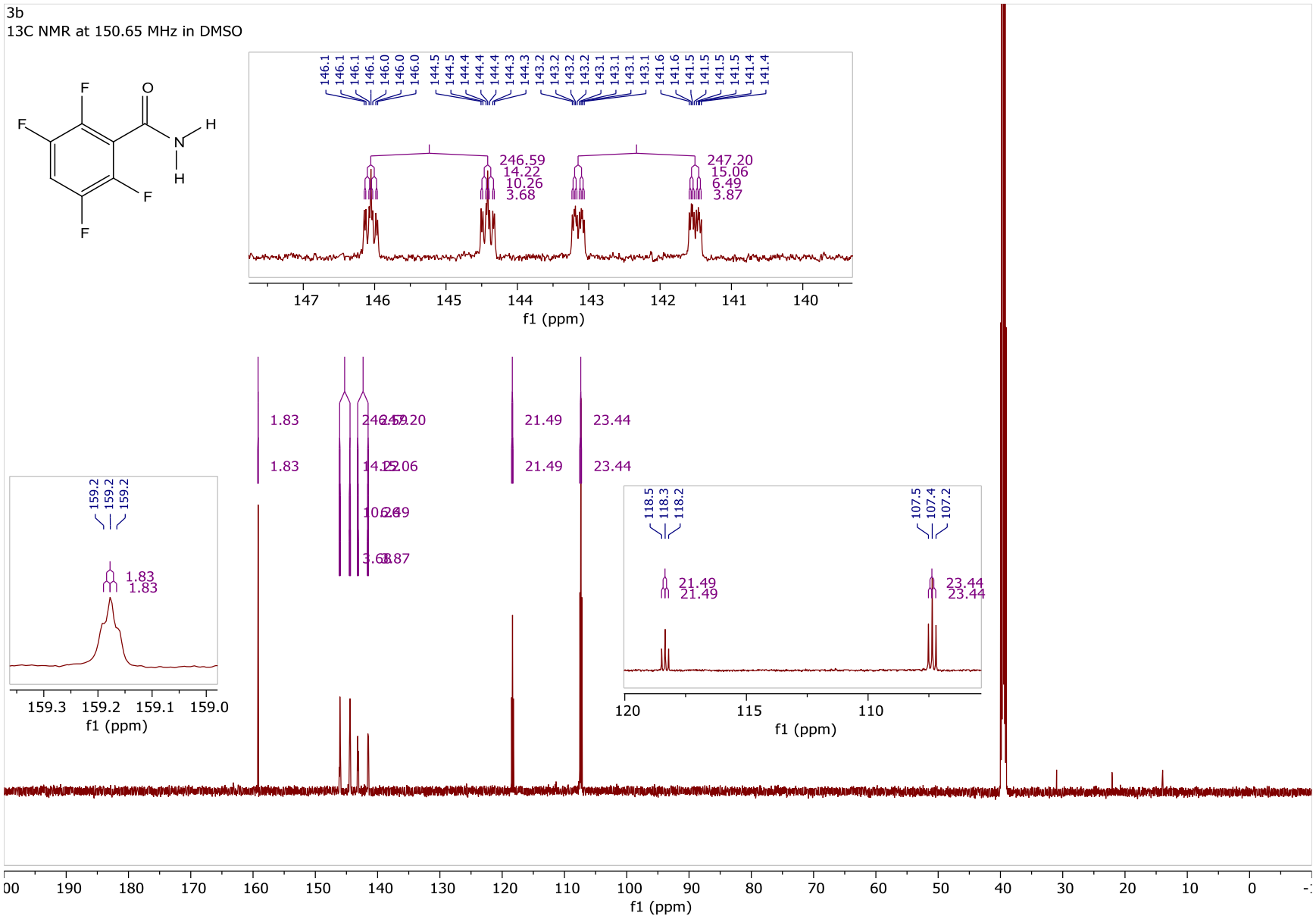
19F NMR at 376.48 MHz in CDCl3

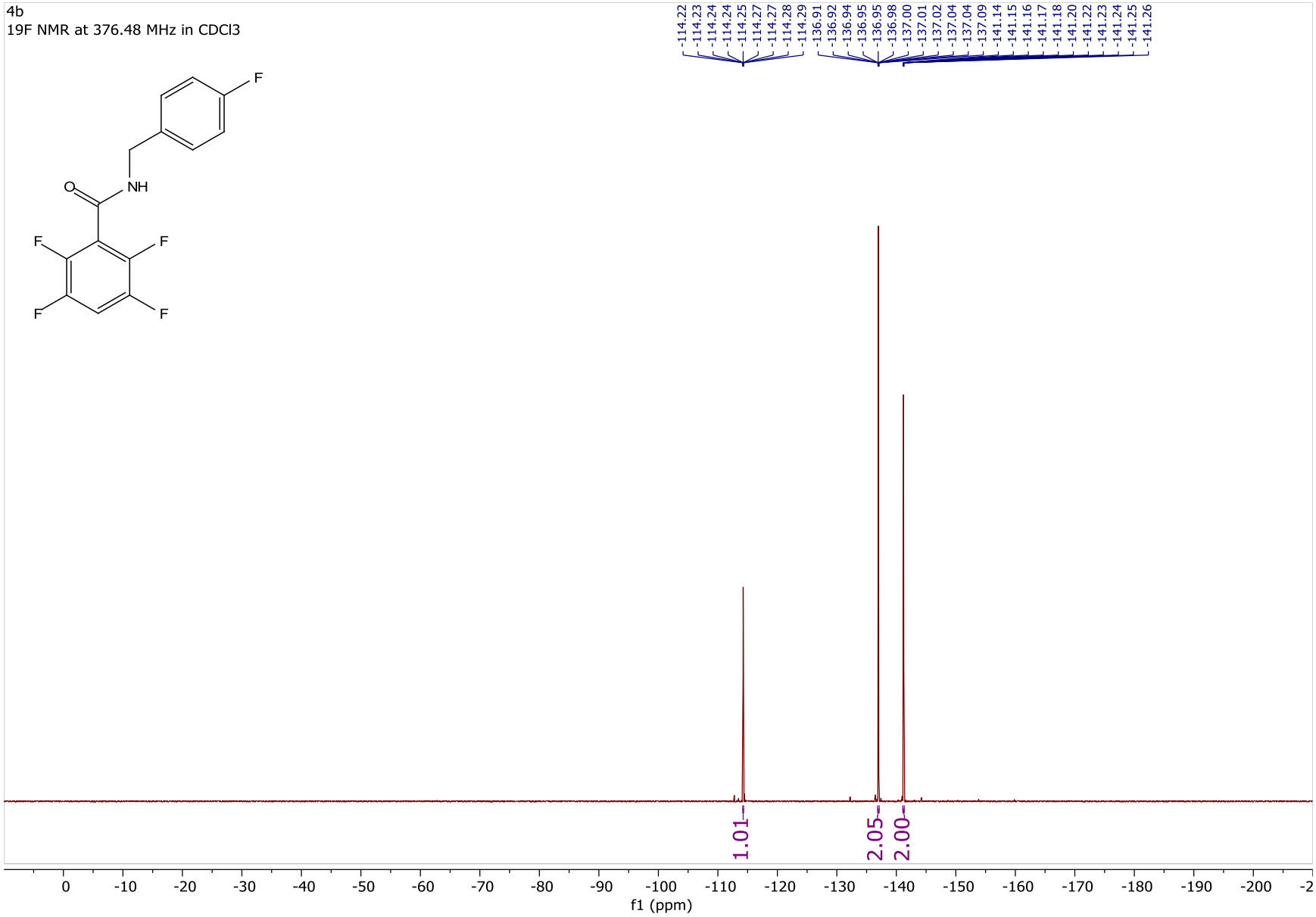


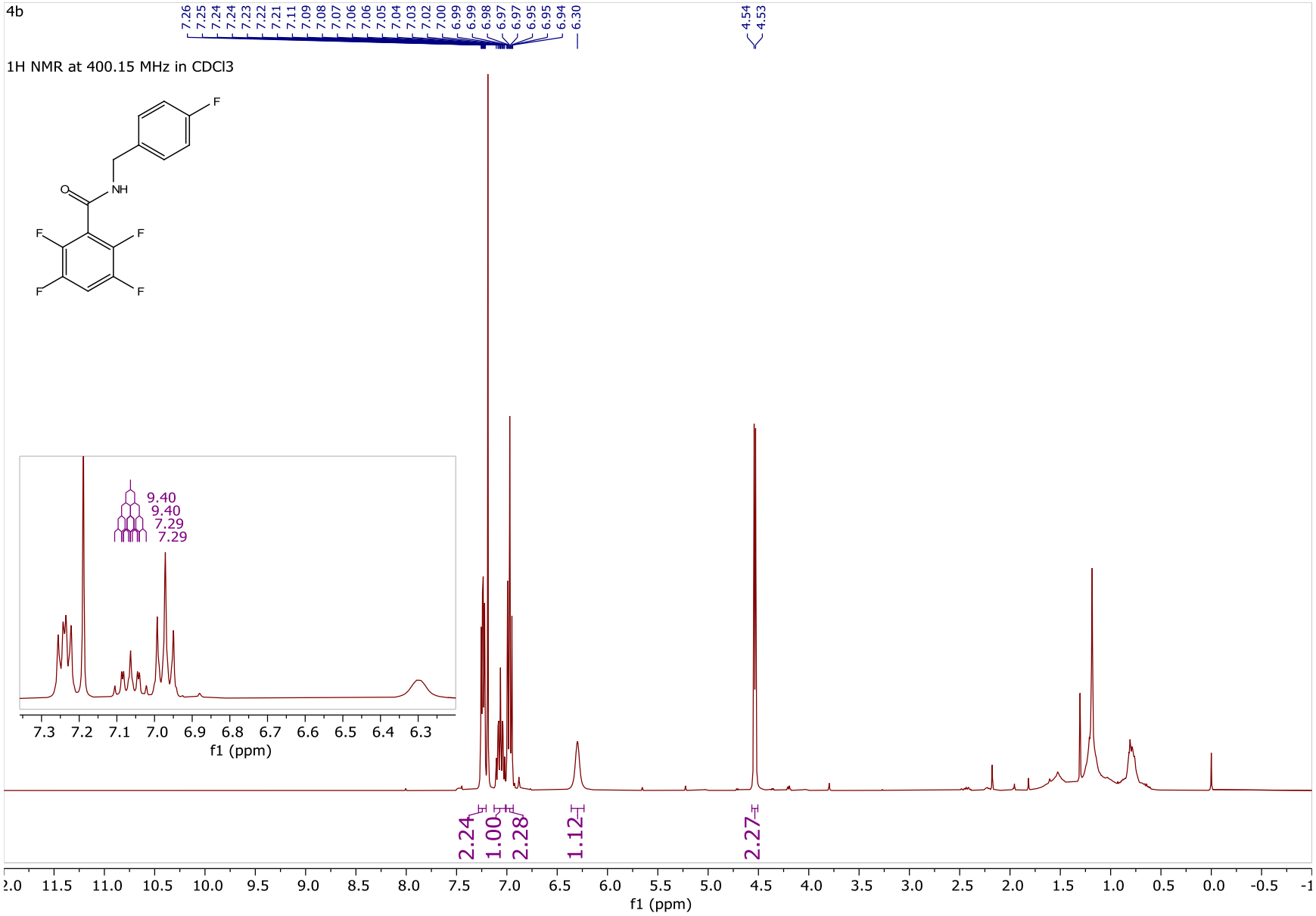

2b
1H NMR at 400.15 MHz in CDCl3
7.17
7.16
7.15
7.14
7.13
7.13
7.11
7.11
7.09
1.62
1.60
1.59
1.59
1.58
1.58
1.57
CH3
H3C
CH3
O
O
F
F
F
F
9.54
9.54
7.20
7.20
7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95 6.90
f1 (ppm)
1.00
10.32
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


3b
19F NMR at 563.61 MHz in DMSO
F
O
F
N
H
H
F
F
-138.60
-138.60
-138.62
-138.62
-138.62
-138.64
-138.66
-138.66
-138.67
-138.68
-138.69
-142.98
-142.99
-143.00
-143.00
-143.01
-143.02
-143.03
-143.04
-143.05
-143.06
-143.07
-143.07
-143.09
-143.10
-143.11
2.01 2.00
.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

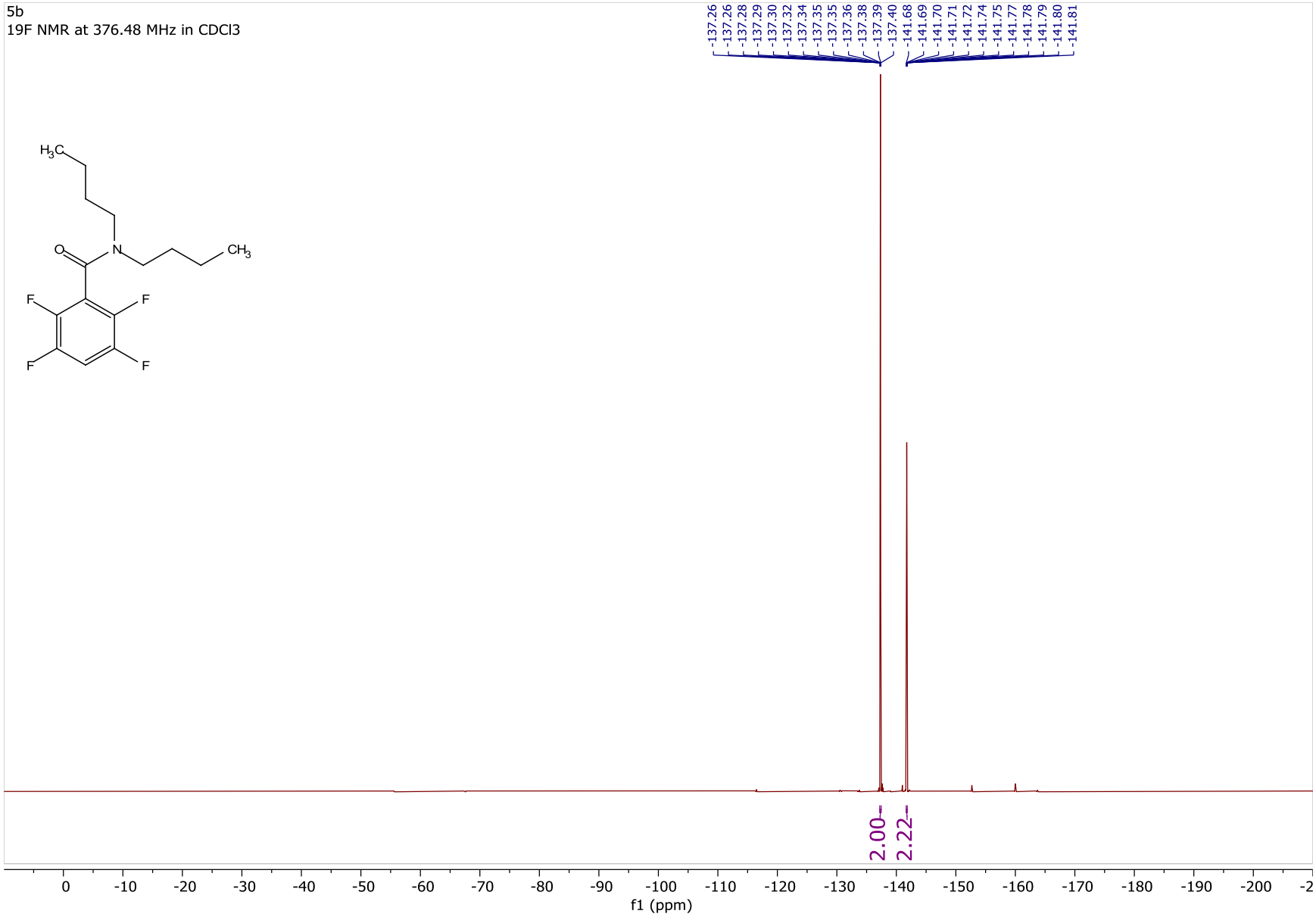

3b
1H NMR at 599.05 MHz in DMSO
8.32
8.14
7.99
7.98
7.97
7.97
7.96
7.95
7.95
7.94
7.93
2.50 DMSO-d6
F
O
F
N
H
H
F
F
1.01
1.01
1.00
f1 (ppm)
f1 (ppm)


3b
13C NMR at 150.65 MHz in DMSO
F
O
F
H
N
H
F
F
146.1
146.1
146.1
146.0
146.0
146.0
144.5
144.5
144.4
144.4
144.4
144.3
144.3
143.2
143.2
143.2
143.2
143.1
143.1
143.1
143.1
141.6
141.6
141.5
141.5
141.5
141.5
141.4
141.4
246.59
14.22
10.26
3.68
247.20
15.06
6.49
3.87
147
146
145
144
143
142
141
140
f1 (ppm)
1.83
1.83
21.49
21.49
23.44
23.44
159.2
159.2
159.2
1.83
1.83
159.3
159.2
159.1
159.0
f1 (ppm)
118.5
118.3
118.2
107.5
107.4
107.2
21.49
21.49
23.44
23.44
120
115
110
f1 (ppm)
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

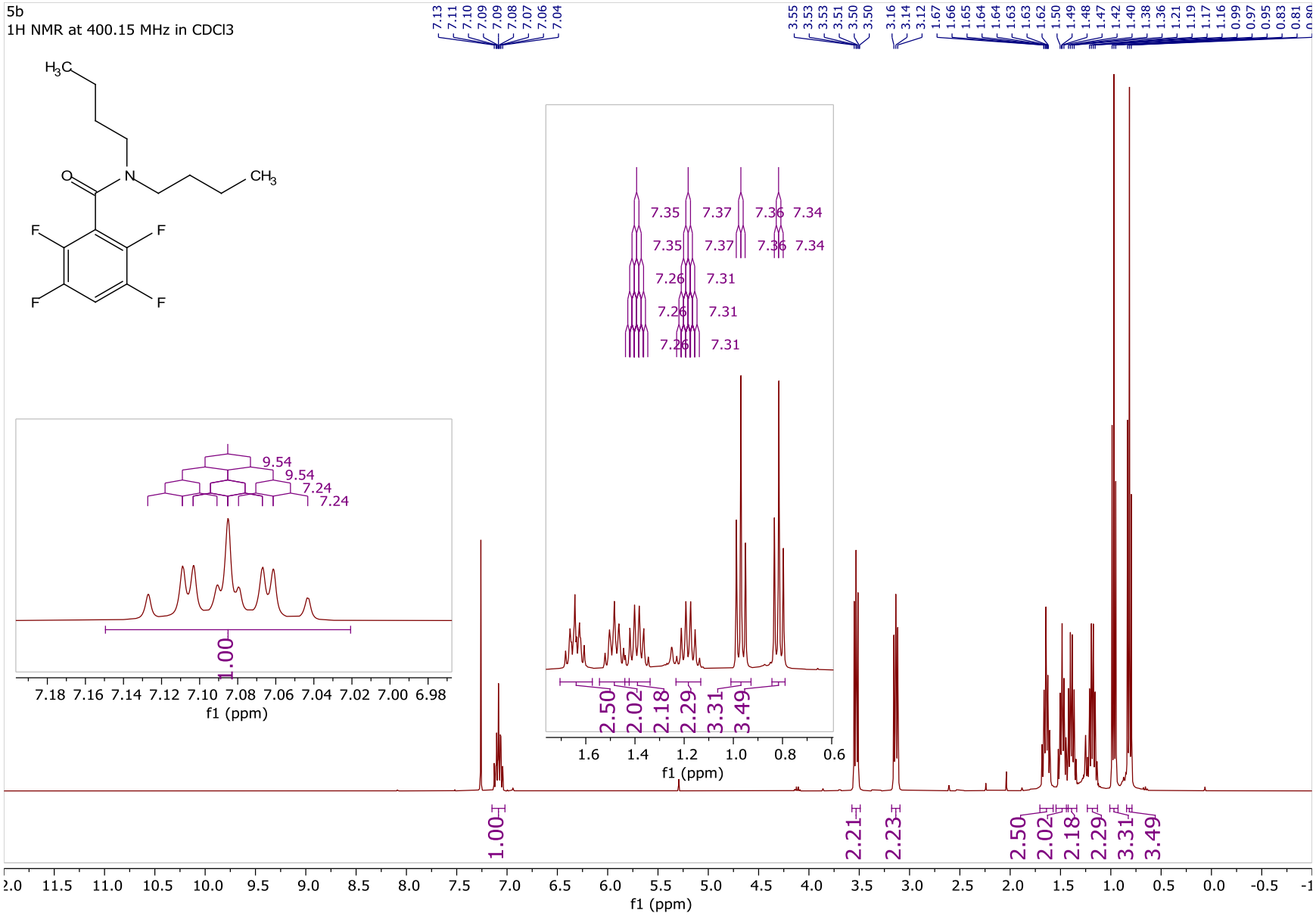

4b
19F NMR at 376.48 MHz in CDCl3
F
O
NH
F
F
F
F
-114.22
-114.23
-114.24
-114.24
-114.25
-114.27
-114.27
-114.28
-114.29
-136.91
-136.92
-136.94
-136.95
-136.95
-136.98
-137.00
-137.01
-137.02
-137.04
-137.04
-137.09
-141.14
-141.15
-141.16
-141.17
-141.18
-141.20
-141.22
-141.23
-141.24
-141.25
-141.26
1.01
2.05
2.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

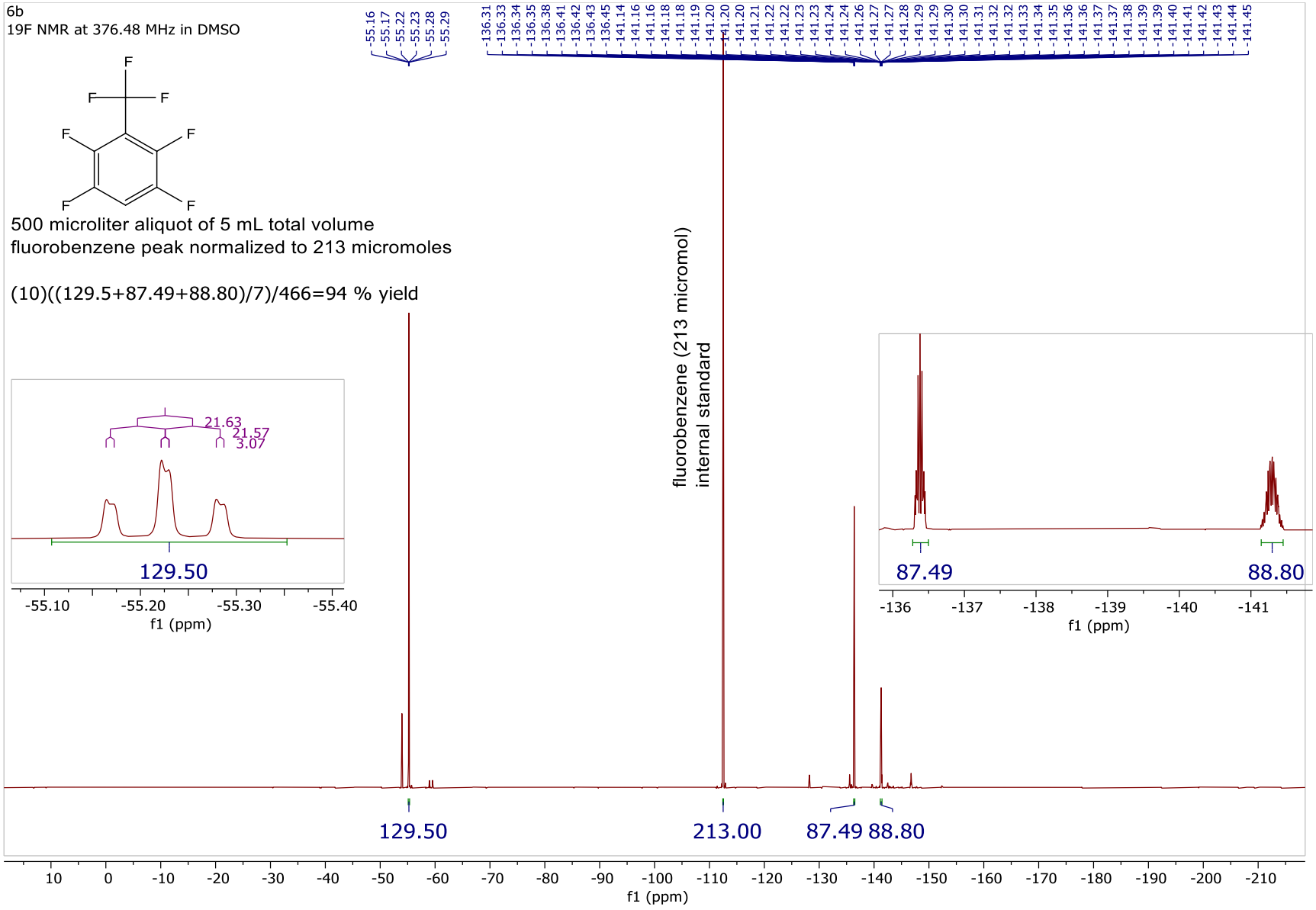

4b
7.26 7.25 7.24 7.24 7.23 7.22 7.21 7.11 7.09 7.08 7.07 7.06 7.06 7.05 7.04 7.03 7.02 7.00 6.99 6.99 6.98 6.97 6.97 6.95 6.95 6.94 6.30
4.54 4.53
1H NMR at 400.15 MHz in CDCl3
F
NH
O
F
F
F
F
9.40
9.40
7.29
7.29
7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 6.4 6.3
f1 (ppm)
2.24
1.00
2.28
1.12
2.27
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

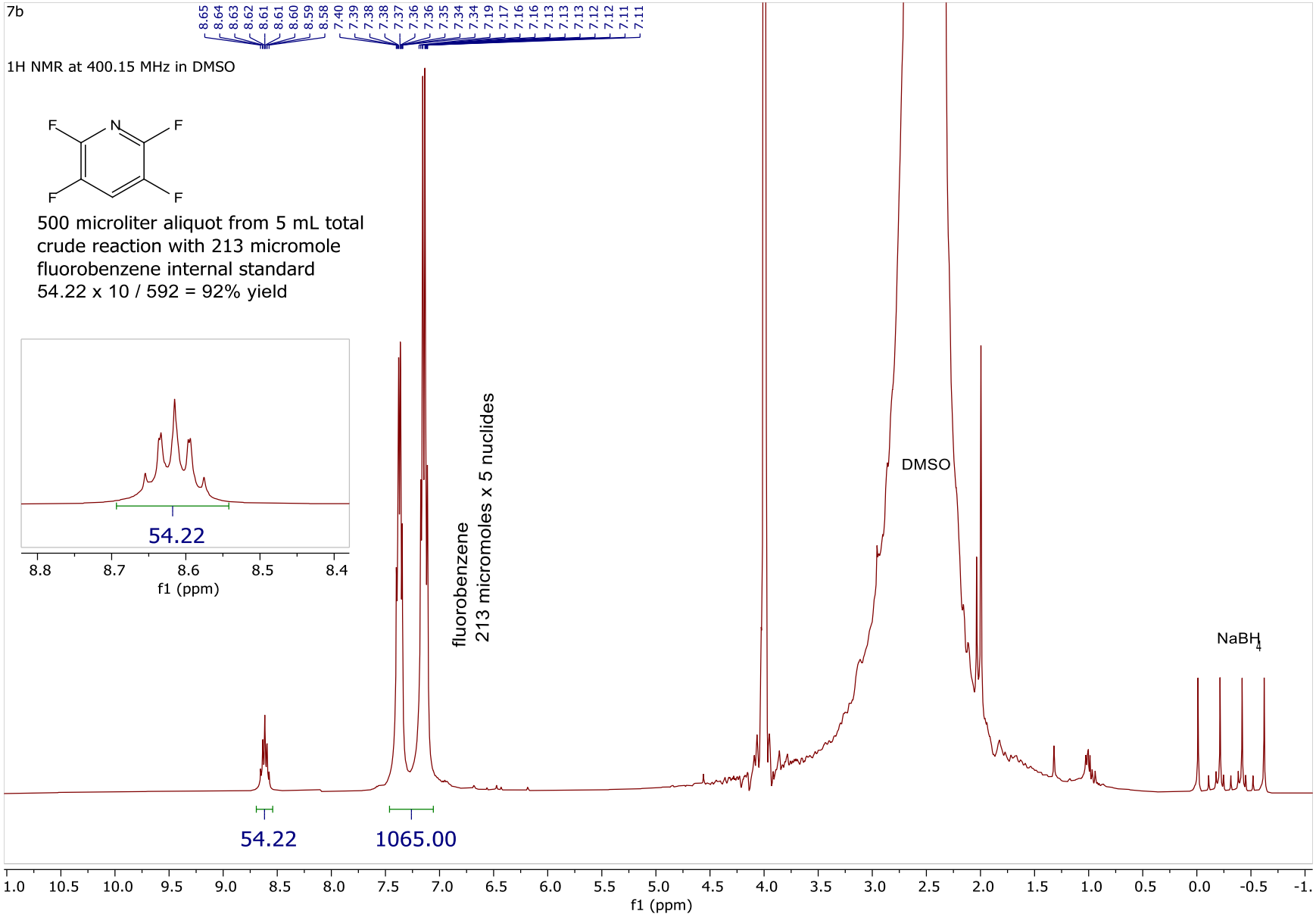
m

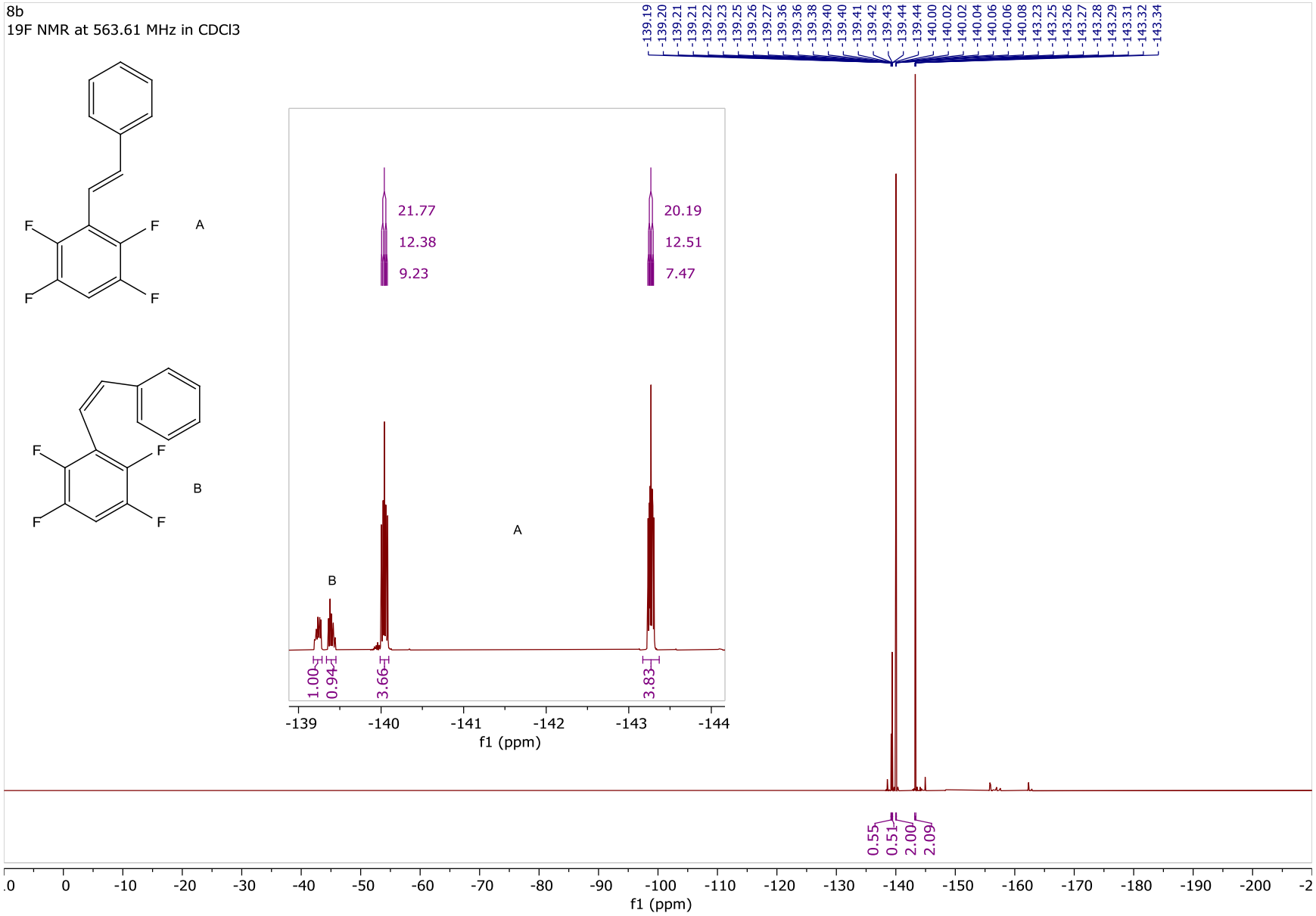

5b
19F NMR at 376.48 MHz in CDCl3
-137.26
-137.26
-137.28
-137.29
-137.30
-137.32
-137.34
-137.35
-137.35
-137.36
-137.38
-137.39
-137.40
-141.68
-141.69
-141.70
-141.71
-141.72
-141.74
-141.75
-141.77
-141.78
-141.79
-141.80
-141.81
H3C
O
N
CH3
F
F
F
F
2.00
2.22
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

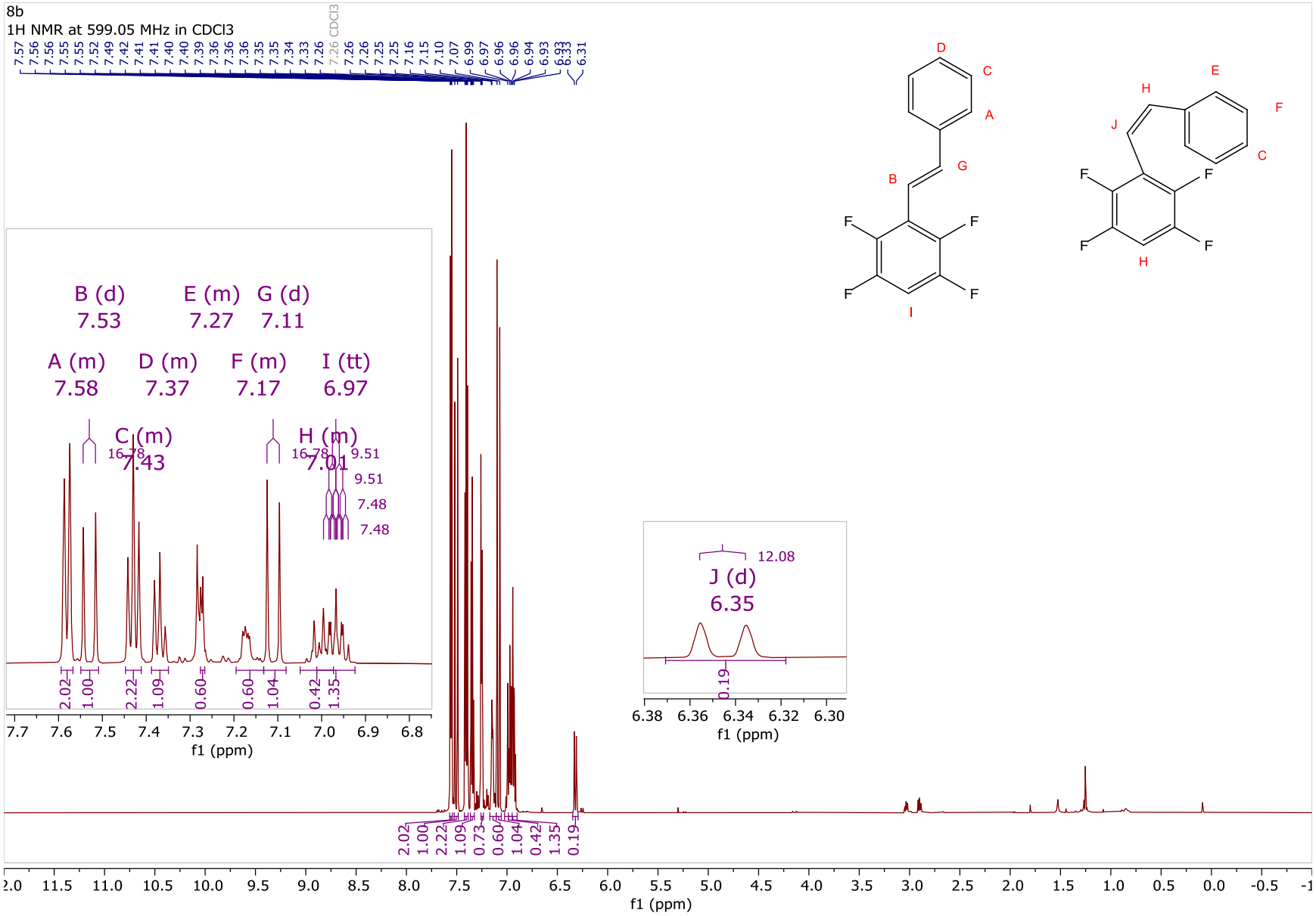
m

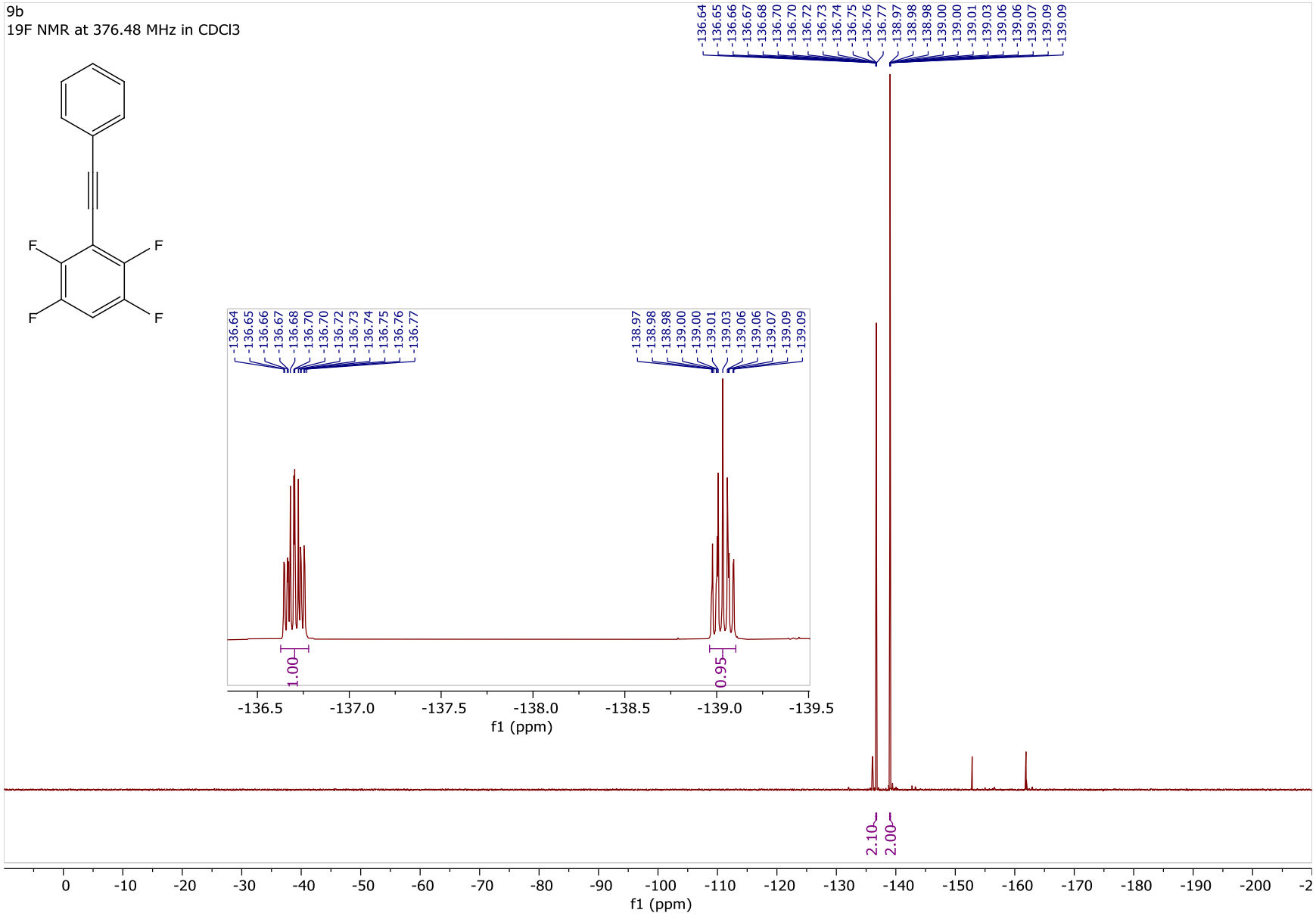

5b
1H NMR at 400.15 MHz in CDCl3
f1 (ppm)

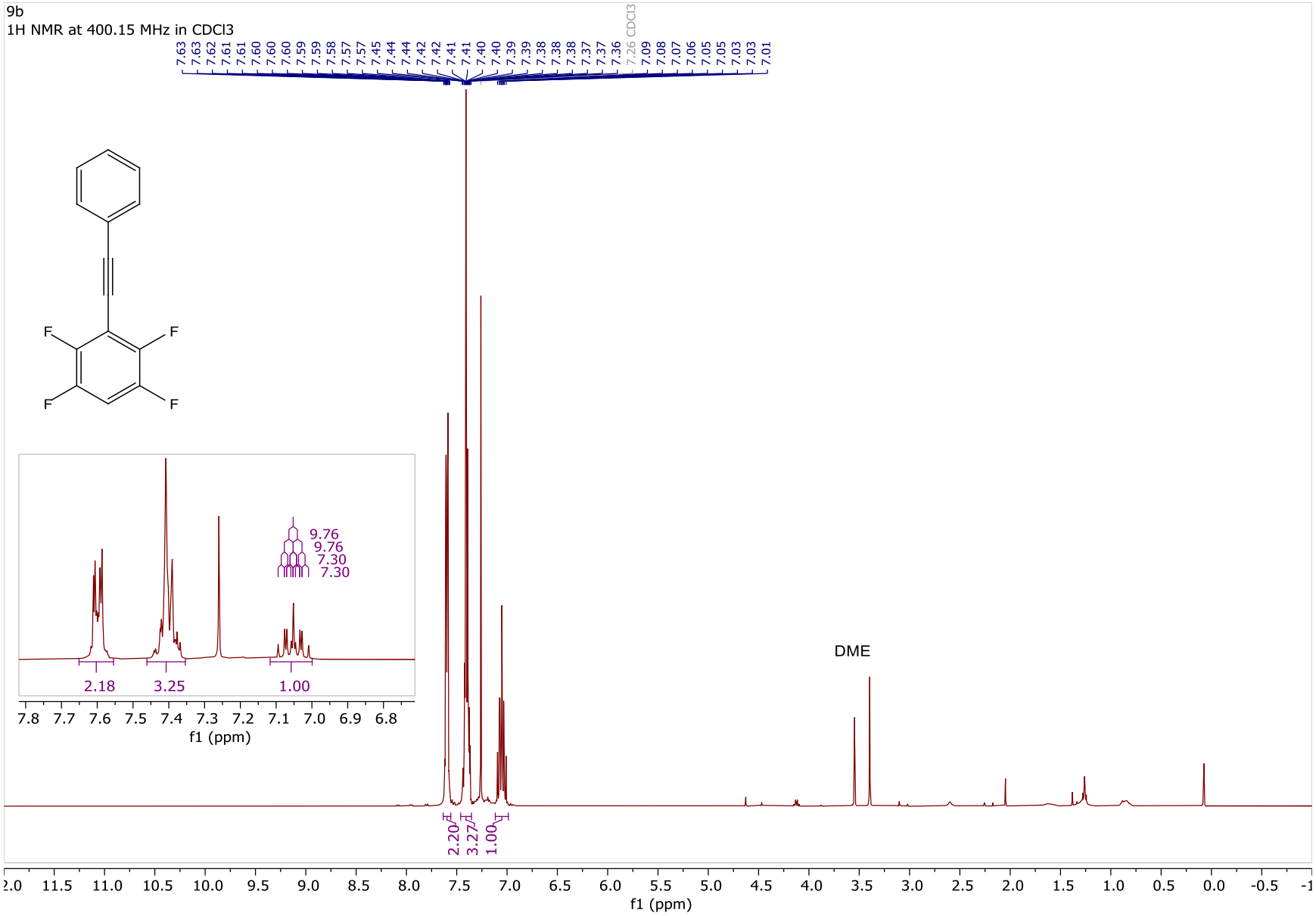

6b
19F NMR at 376.48 MHz in DMSO
F
F
F
F
F
F
500 microliter aliquot of 5 mL total volume
fluorobenzene peak normalized to 213 micromoles
(10)((129.5+87.49+88.80)/7)/466=94 % yield
fluorobenzene (213 micromol)
internal standard
21.63
21.57
3.07
129.50
-55.10
-55.20
-55.30
-55.40
f1 (ppm)
87.49
88.80
-136
-137
-138
-139
-140
-141
f1 (ppm)
129.50
213.00
87.49
88.80
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

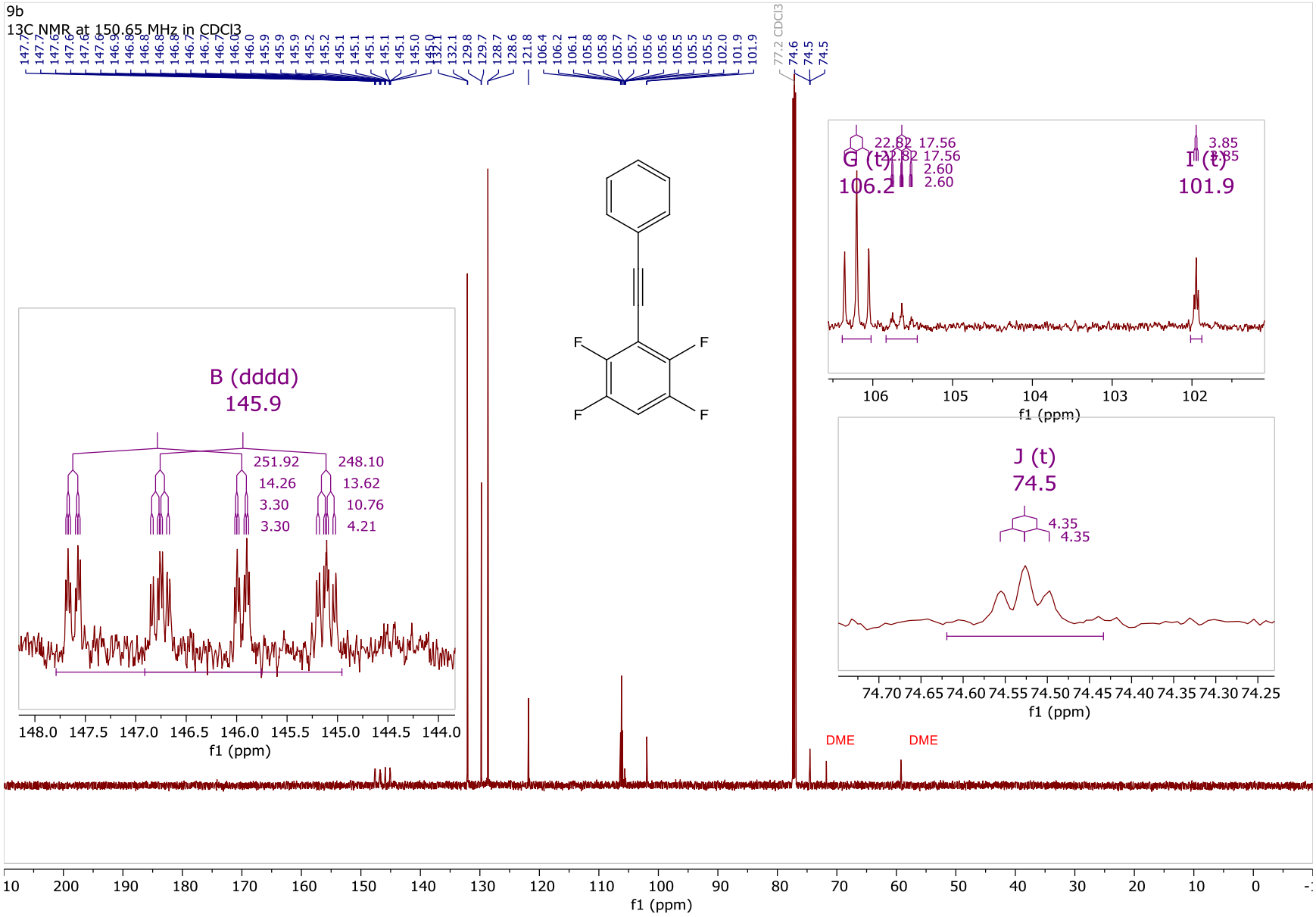

7b
8.65 8.64 8.63 8.62 8.61 8.61 8.60 8.59 8.58 7.40 7.39 7.38 7.38 7.37 7.36 7.36 7.35 7.34 7.34 7.19 7.17 7.16 7.16 7.13 7.13 7.13 7.12 7.12 7.11 7.11
1H NMR at 400.15 MHz in DMSO
F
N
F
F
F
500 microliter aliquot from 5 mL total crude reaction with 213 micromole fluorobenzene internal standard
54.22 x 10 / 592 = 92% yield
54.22
8.8 8.7 8.6 8.5 8.4
f1 (ppm)
fluorobenzene
213 micromoles x 5 nuclides
DMSO
NaBH4
54.22
1065.00
1.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

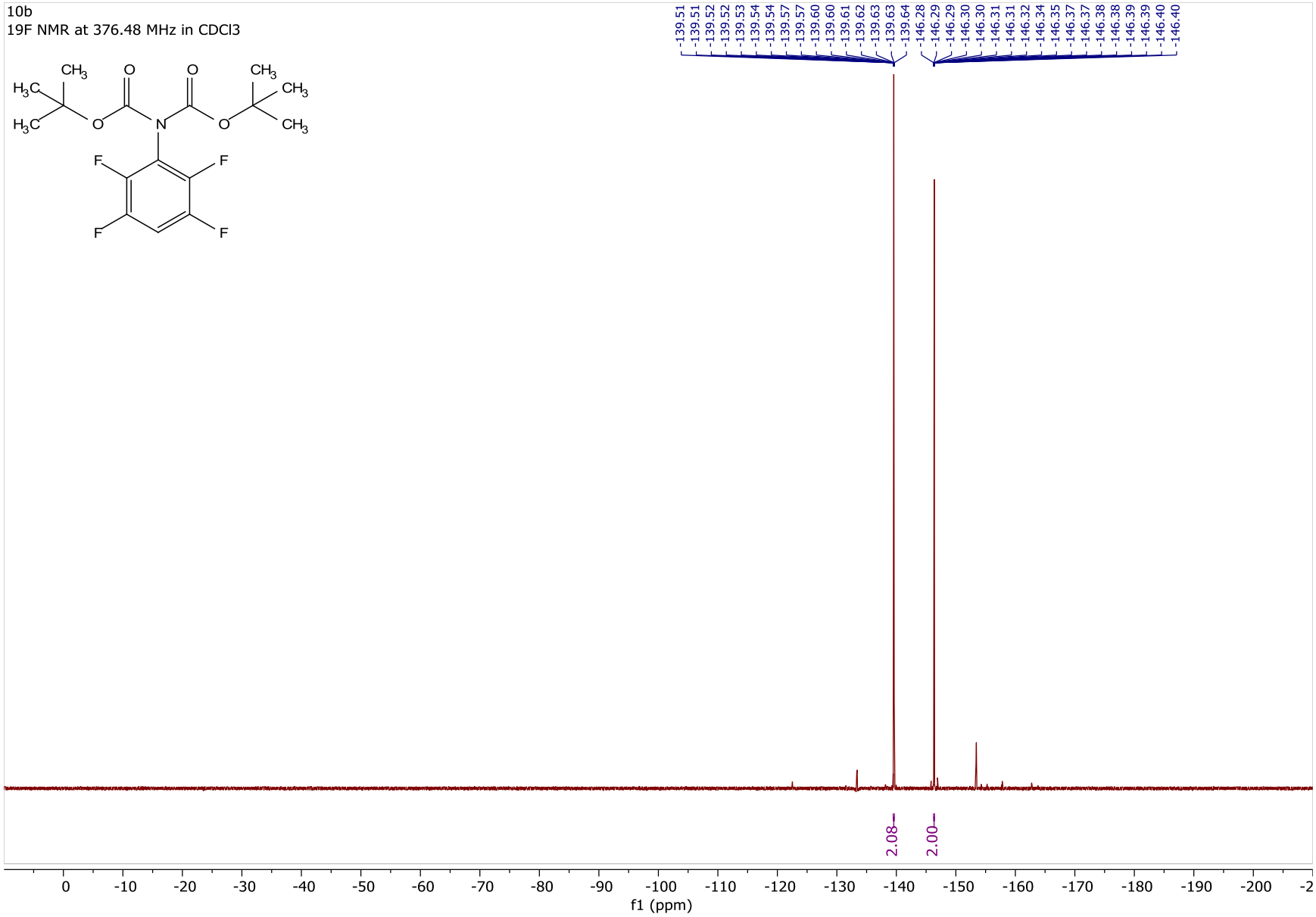

8b
19F NMR at 563.61 MHz in CDCl3
A
B
21.77
12.38
9.23
20.19
12.51
7.47
1.00
0.94
3.66
3.83
0.55
0.51
2.00
2.09
f1 (ppm)

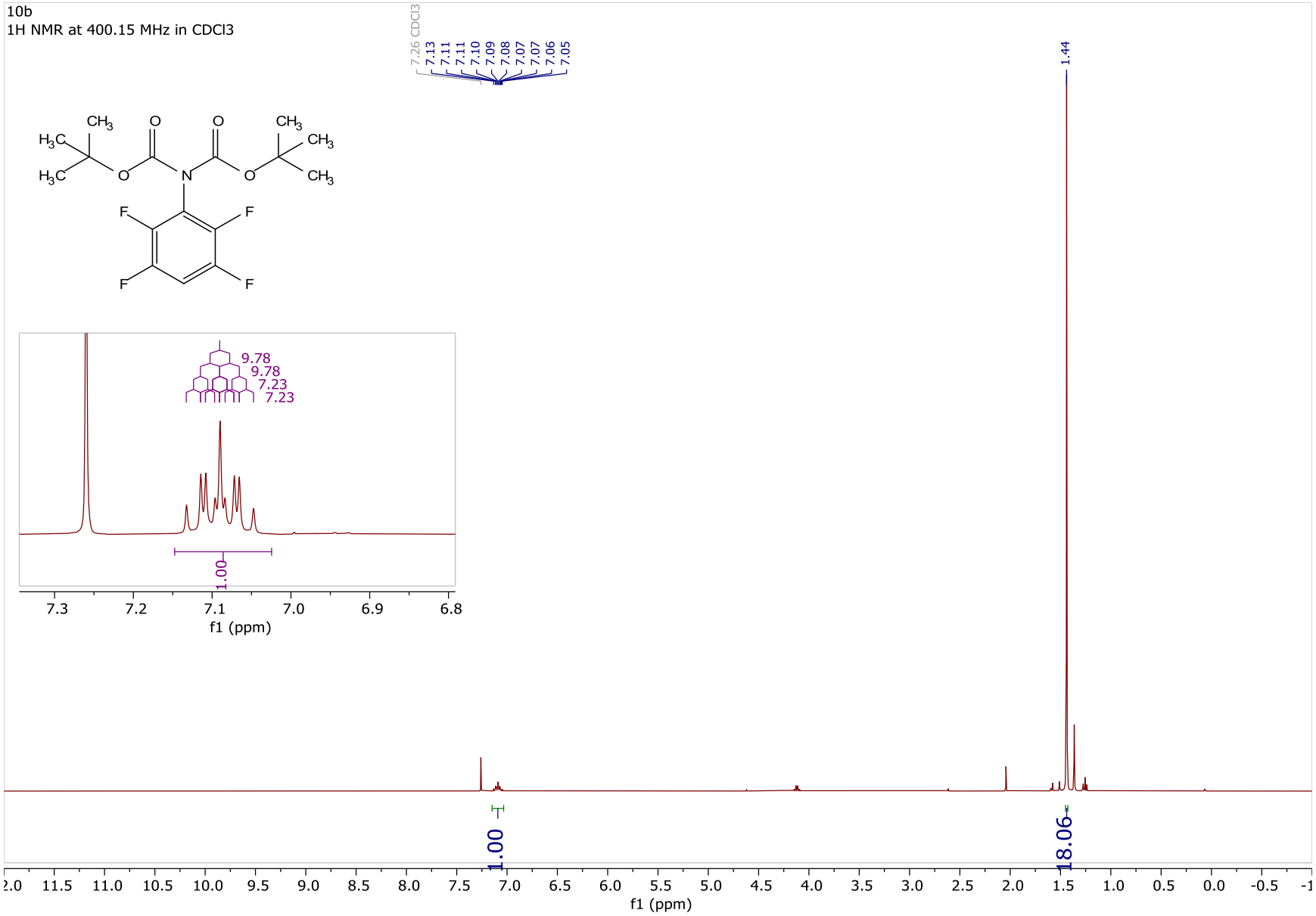

8b
1H NMR at 599.05 MHz in CDCl3
B (d) 7.53
E (m) 7.27
G (d) 7.11
A (m) 7.58
D (m) 7.37
F (m) 7.17
I (tt) 6.97
C (m) 7.43
H (m) 7.01
J (d) 6.35
f1 (ppm)

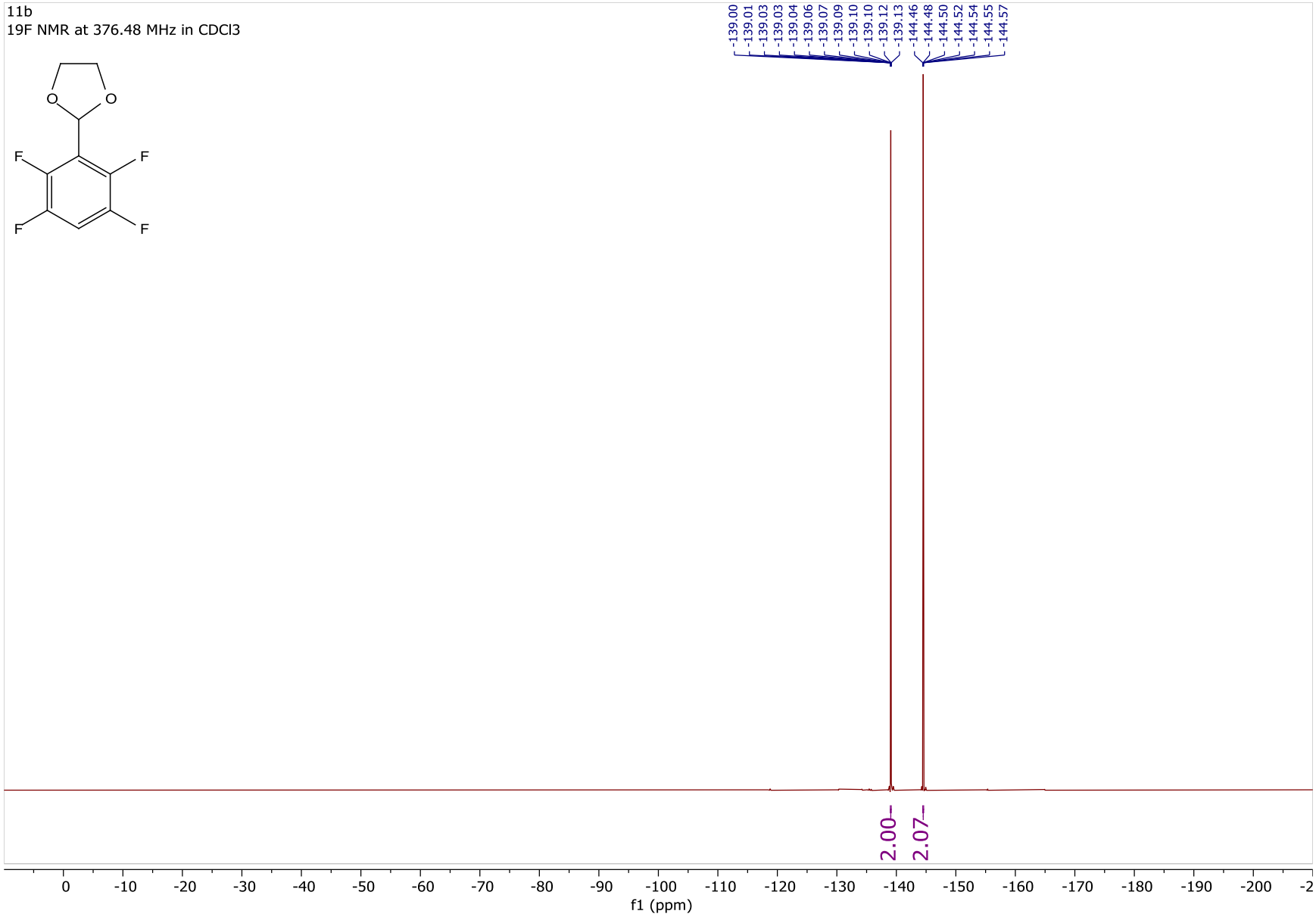

9b
19F NMR at 376.48 MHz in CDCl3
F
F
F
F
-136.64
-136.65
-136.66
-136.67
-136.68
-136.70
-136.70
-136.72
-136.73
-136.74
-136.75
-136.76
-136.77
-138.97
-138.98
-138.98
-139.00
-139.00
-139.01
-139.03
-139.06
-139.06
-139.07
-139.09
-139.09
1.00
0.95
-136.5
-137.0
-137.5
-138.0
-138.5
-139.0
-139.5
f1 (ppm)
2.10
2.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

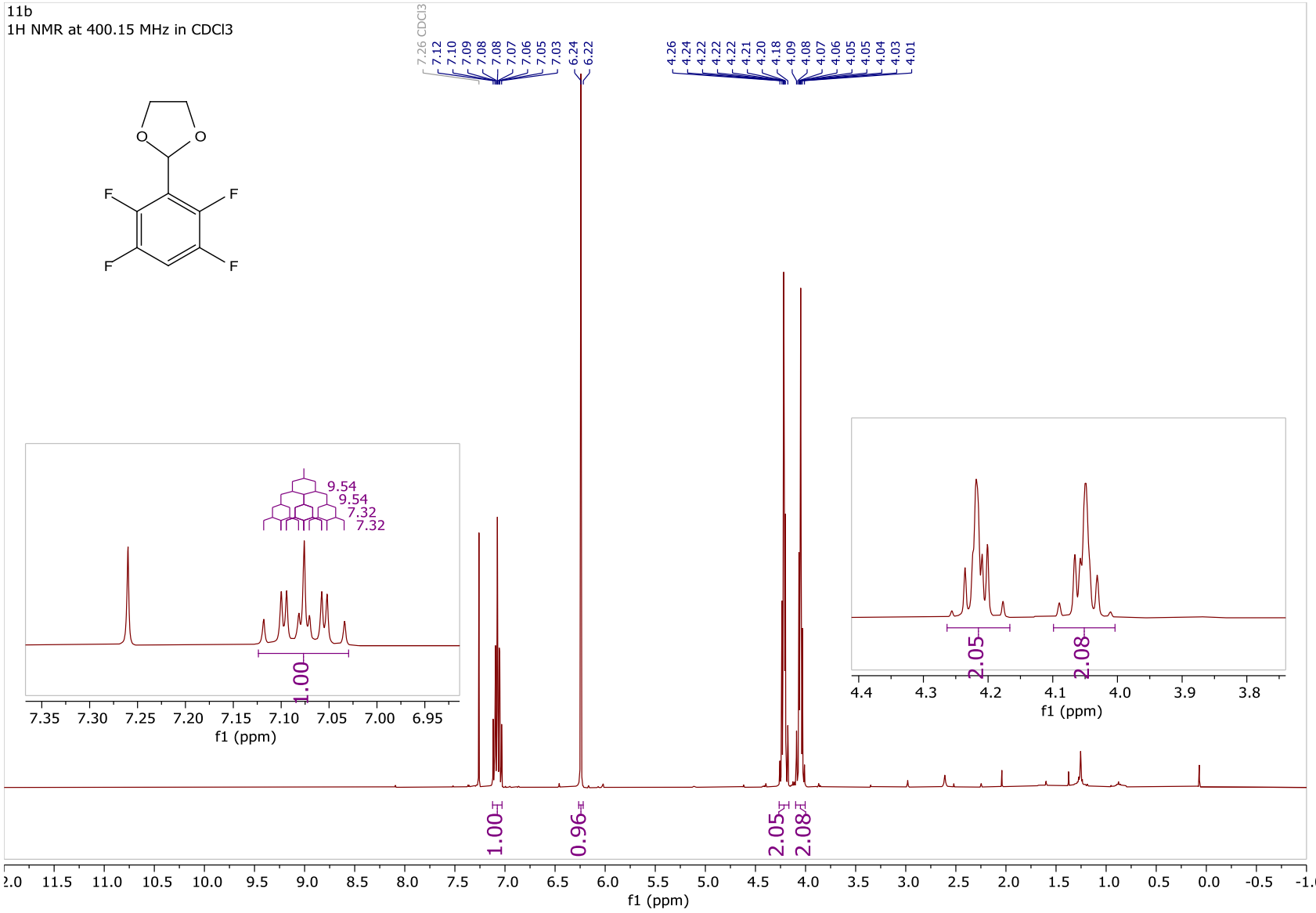

9b
1H NMR at 400.15 MHz in CDCl3
7.63 7.63 7.62 7.61 7.61 7.60 7.60 7.60 7.59 7.59 7.58 7.57 7.57 7.45 7.44 7.44 7.42 7.42 7.41 7.41 7.40 7.40 7.39 7.39 7.38 7.38 7.37 7.37 7.36 7.26 CDCl3 7.09 7.08 7.07 7.06 7.05 7.05 7.03 7.03 7.01
F
F
F
F
9.76
9.76
7.30
7.30
2.18
3.25
1.00
7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
DME
2.20
3.27
1.00
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)


9b
13C NMR at 150.65 MHz in CDCl3
77.2 CDCl3
74.6
74.5
74.5
B (dddd)
145.9
251.92
14.26
3.30
3.30
248.10
13.62
10.76
4.21
148.0 147.5 147.0 146.5 146.0 145.5 145.0 144.5 144.0
f1 (ppm)
G (t)
106.2
22.82 17.56
22.82 17.56
2.60
2.60
I (t)
101.9
3.85
3.85
106 105 104 103 102
f1 (ppm)
J (t)
74.5
4.35
4.35
74.70 74.65 74.60 74.55 74.50 74.45 74.40 74.35 74.30 74.25
f1 (ppm)
F
F
F
F
DME
DME
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

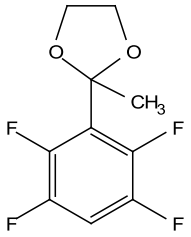

10b
19F NMR at 376.48 MHz in CDCl3
-139.51
-139.51
-139.52
-139.52
-139.53
-139.54
-139.54
-139.57
-139.57
-139.60
-139.60
-139.61
-139.62
-139.63
-139.63
-139.64
-146.28
-146.29
-146.29
-146.30
-146.30
-146.31
-146.31
-146.32
-146.34
-146.35
-146.37
-146.37
-146.38
-146.38
-146.39
-146.39
-146.40
-146.40
2.08
2.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

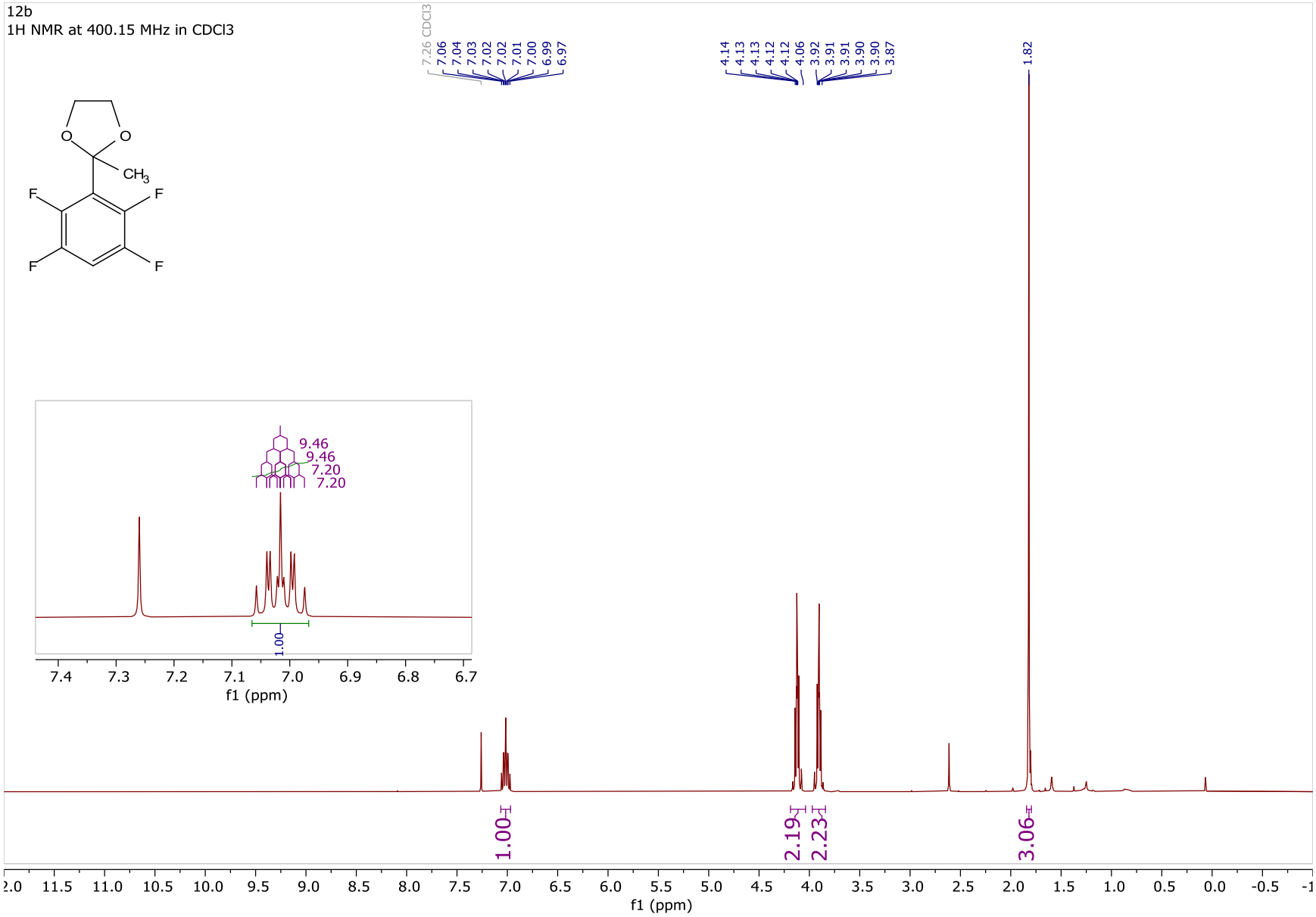

10b
1H NMR at 400.15 MHz in CDCl3
7.26 CDCl3
7.13
7.11
7.11
7.10
7.09
7.08
7.07
7.07
7.06
7.05
1.44
9.78
9.78
7.23
7.23
1.00
7.3
7.2
7.1
7.0
6.9
6.8
f1 (ppm)
1.00
18.06
f1 (ppm)

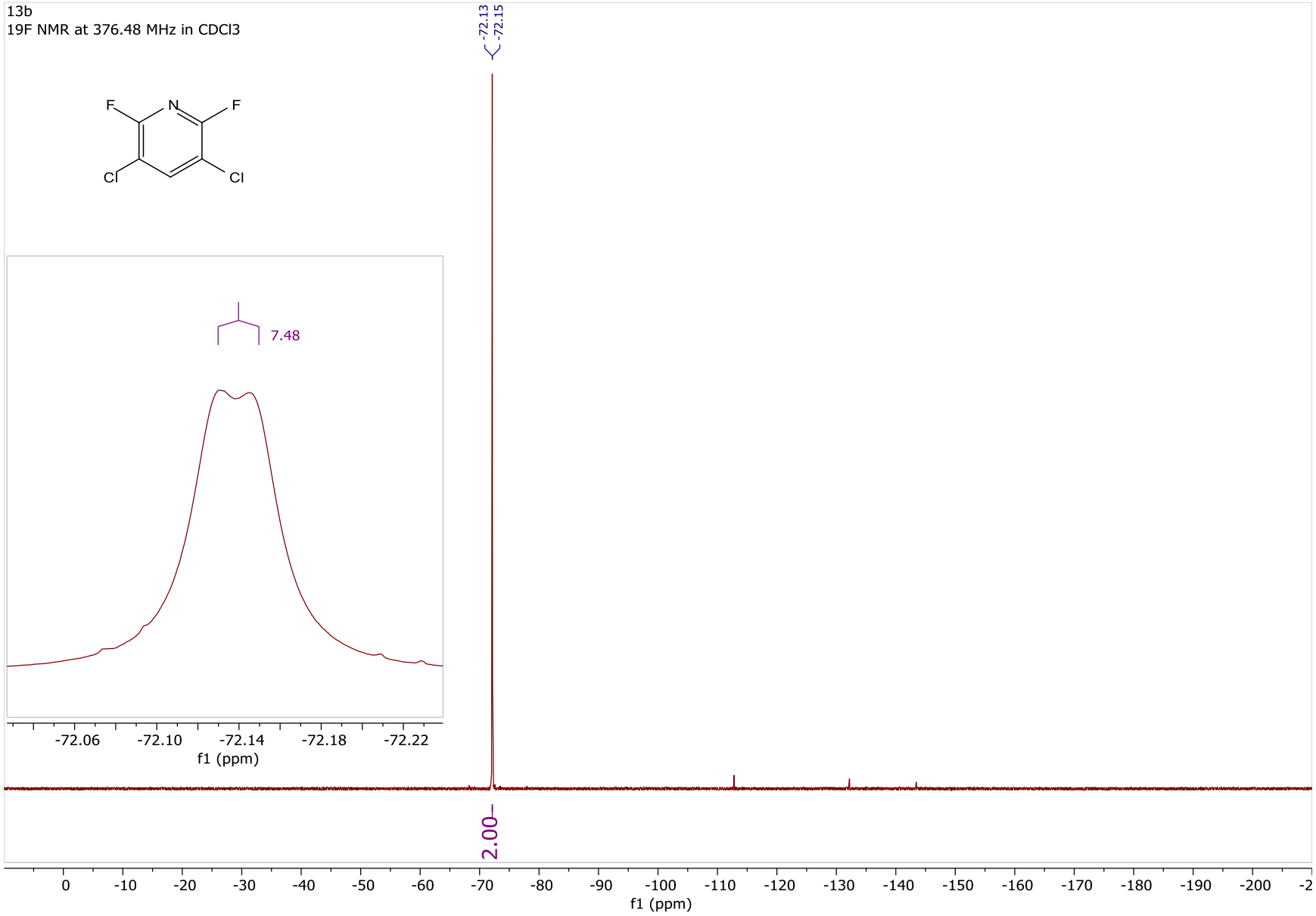

11b
19F NMR at 376.48 MHz in CDCl3
-139.00
-139.01
-139.03
-139.03
-139.04
-139.06
-139.07
-139.09
-139.10
-139.10
-139.12
-139.13
-144.46
-144.48
-144.50
-144.52
-144.54
-144.55
-144.57
O
O
F
F
F
F
2.00
2.07
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

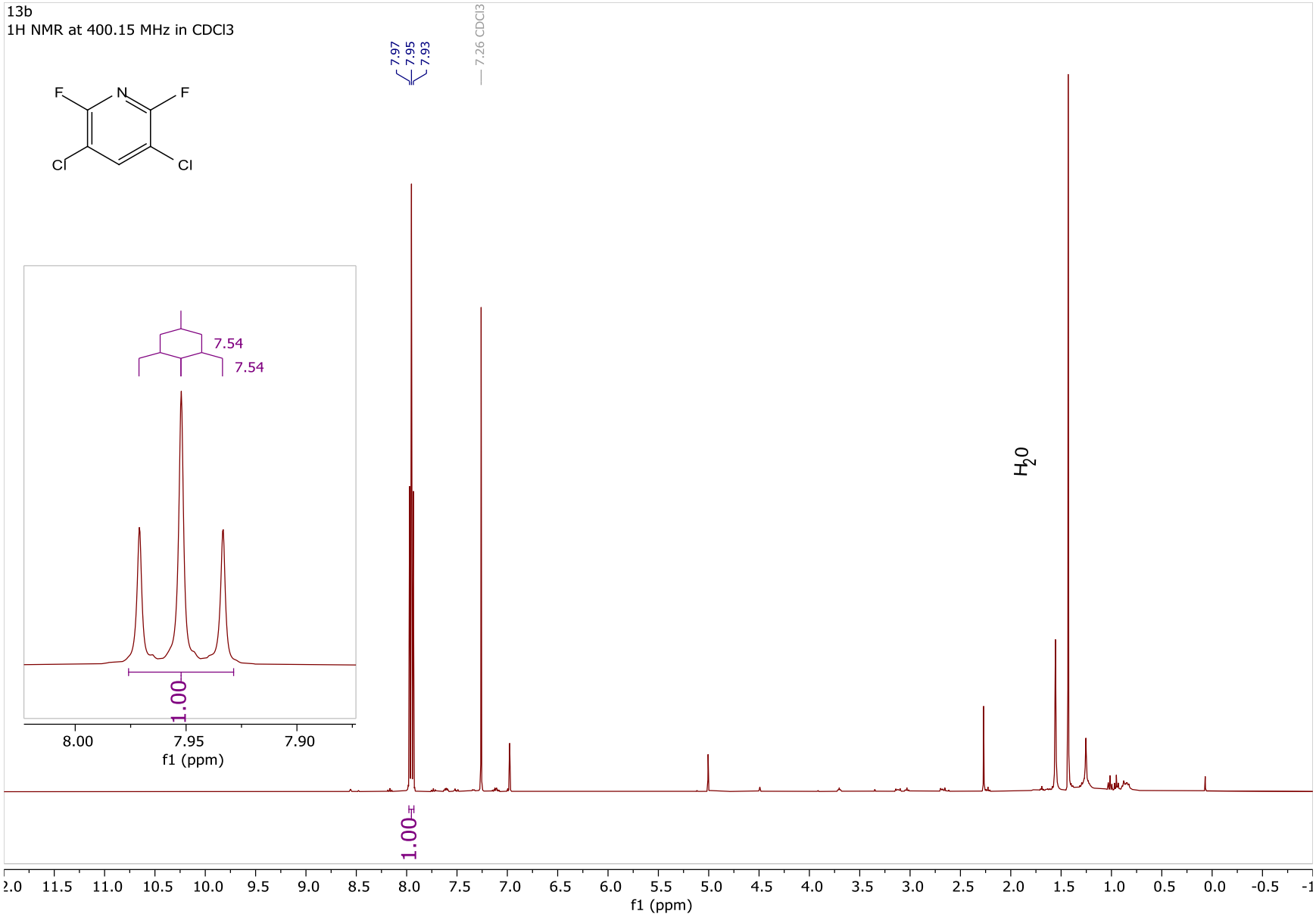

11b
1H NMR at 400.15 MHz in CDCl3
7.26 CDCl3
7.12
7.10
7.09
7.08
7.08
7.07
7.06
7.05
7.03
6.24
6.22
4.26
4.24
4.22
4.22
4.22
4.21
4.20
4.18
4.09
4.08
4.07
4.06
4.05
4.05
4.04
4.03
4.01
O
O
F
F
F
F
9.54
9.54
7.32
7.32
1.00
7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95
f1 (ppm)
2.05
2.08
4.4 4.3 4.2 4.1 4.0 3.9 3.8
f1 (ppm)
1.00
0.96
2.05
2.08
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)

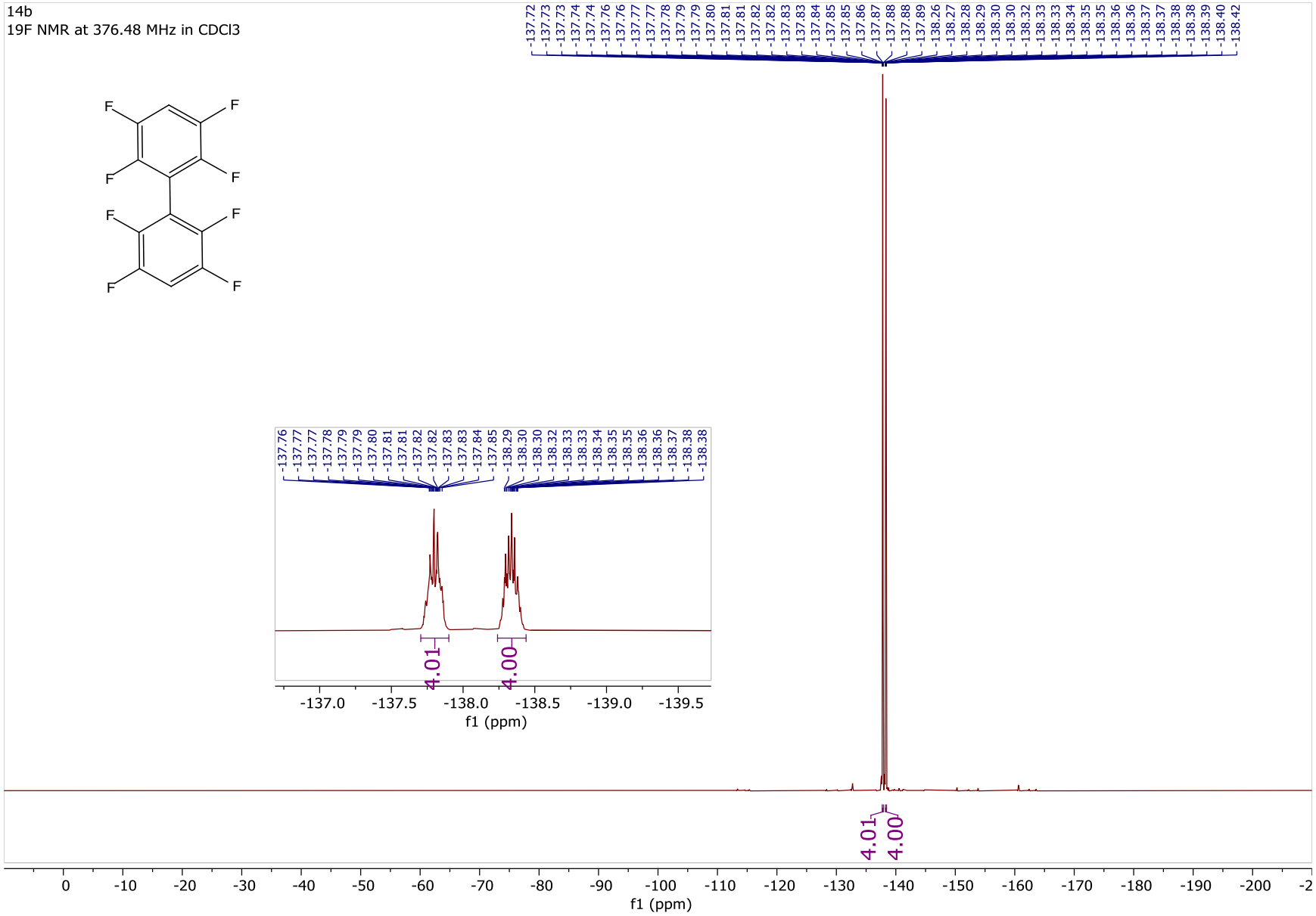
12b
19F NMR at 376.48 MHz in CDCl3

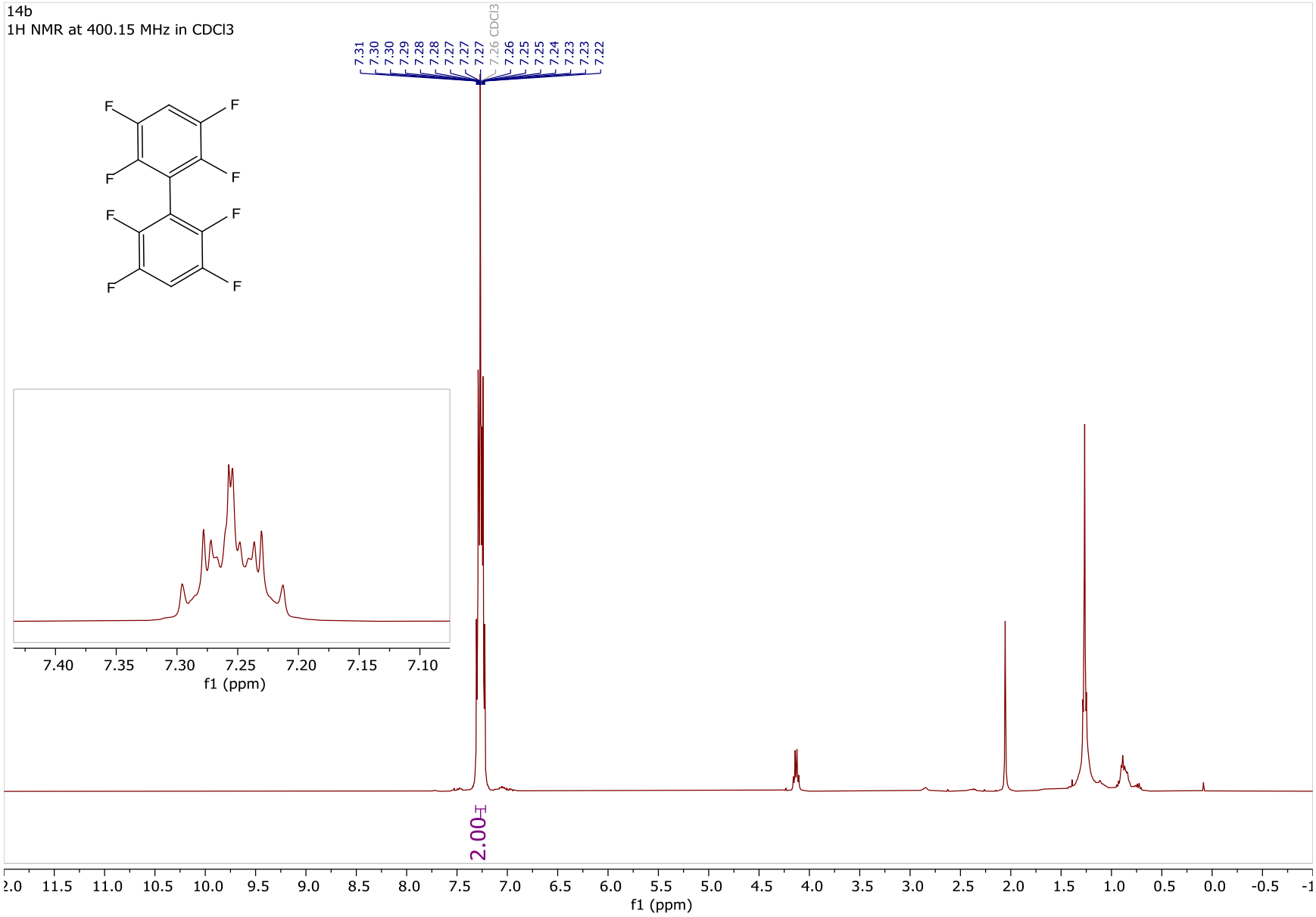


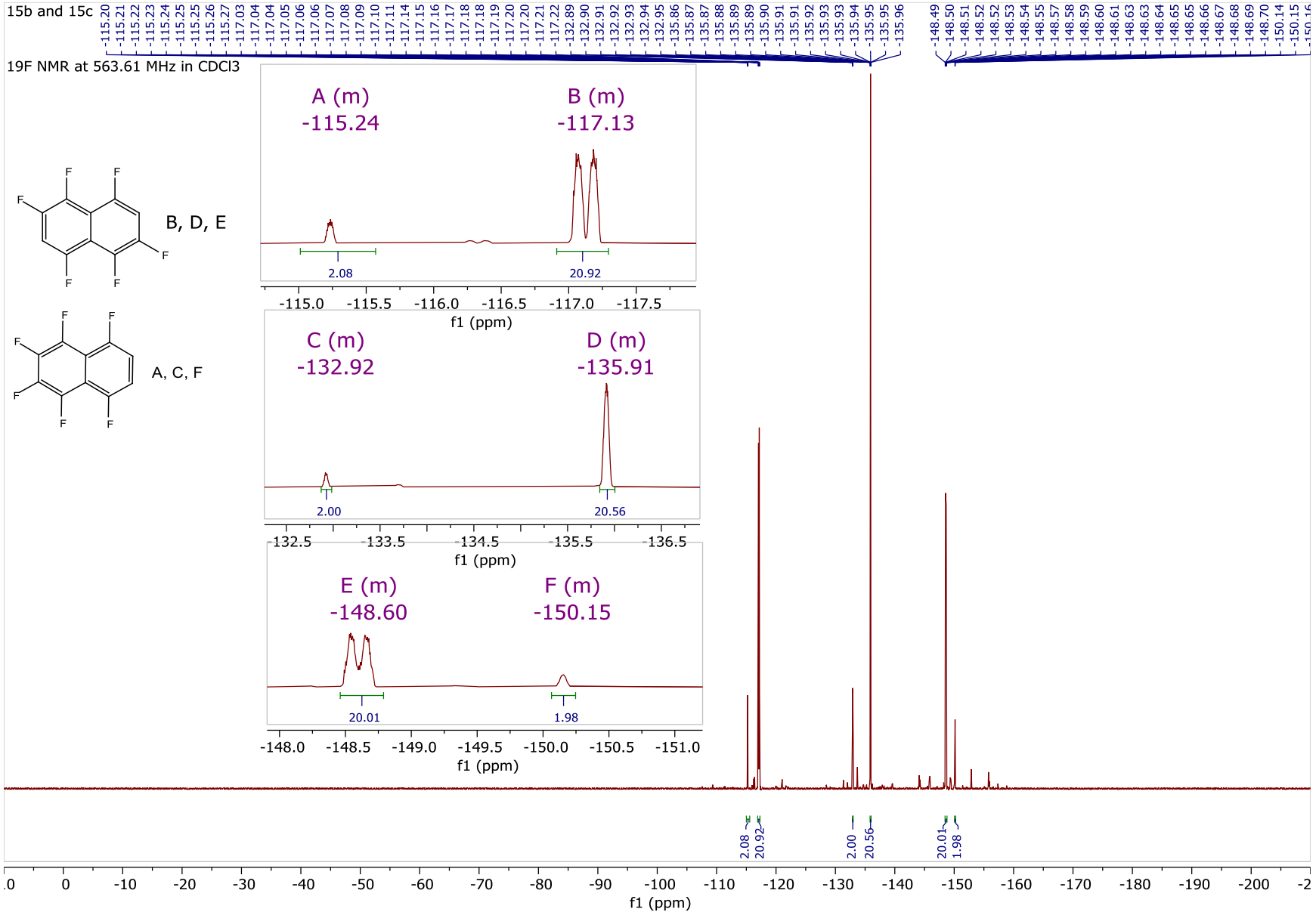

12b
1H NMR at 400.15 MHz in CDCl3
7.26 CDCl3
7.06
7.04
7.03
7.02
7.02
7.01
7.00
6.99
6.97
4.14
4.13
4.13
4.12
4.12
4.06
3.92
3.91
3.91
3.90
3.90
3.87
1.82
O
O
CH3
F
F
F
F
9.46
9.46
7.20
7.20
1.00
7.4
7.3
7.2
7.1
7.0
6.9
6.8
6.7
f1 (ppm)
1.00
2.19
2.23
3.06
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

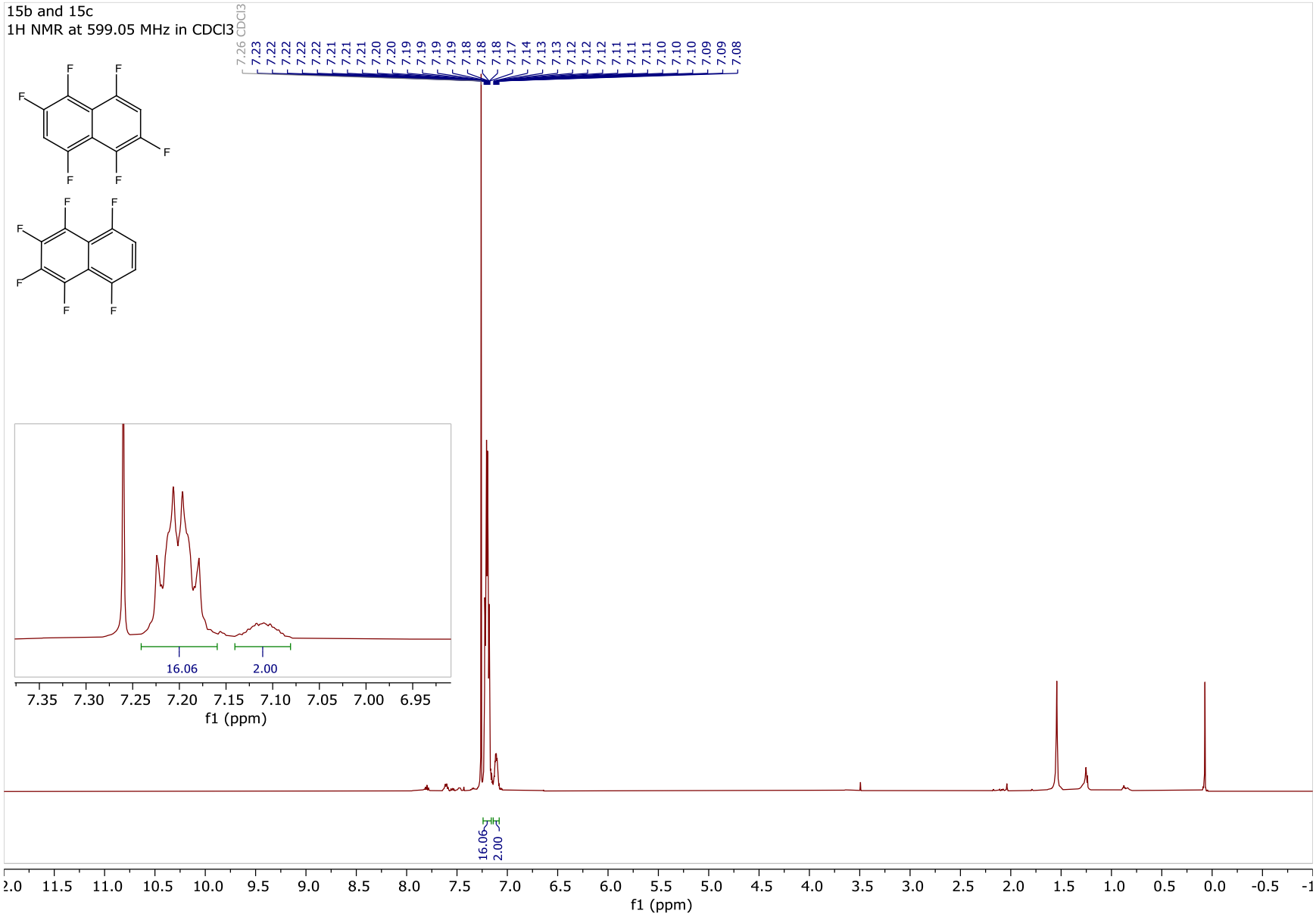

13b
19F NMR at 376.48 MHz in CDCl3
F
N
F
Cl
Cl
-72.13
-72.15
7.48
-72.06
-72.10
-72.14
-72.18
-72.22
f1 (ppm)
2.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

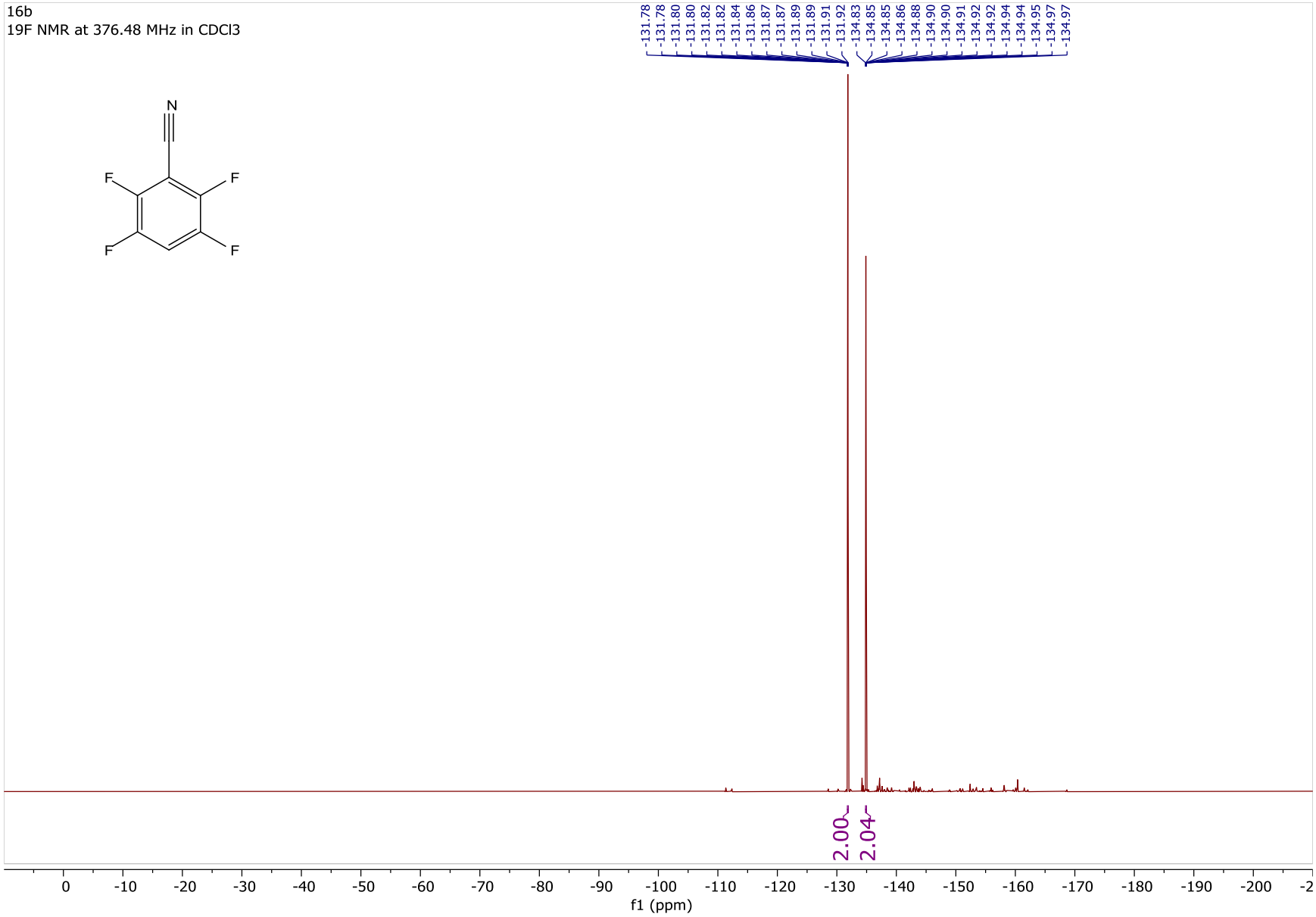

13b
1H NMR at 400.15 MHz in CDCl3
F
N
F
Cl
Cl
7.97
7.95
7.93
7.26 CDCl3
7.54
7.54
1.00
8.00
7.95
7.90
f1 (ppm)
H2O
1.00
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

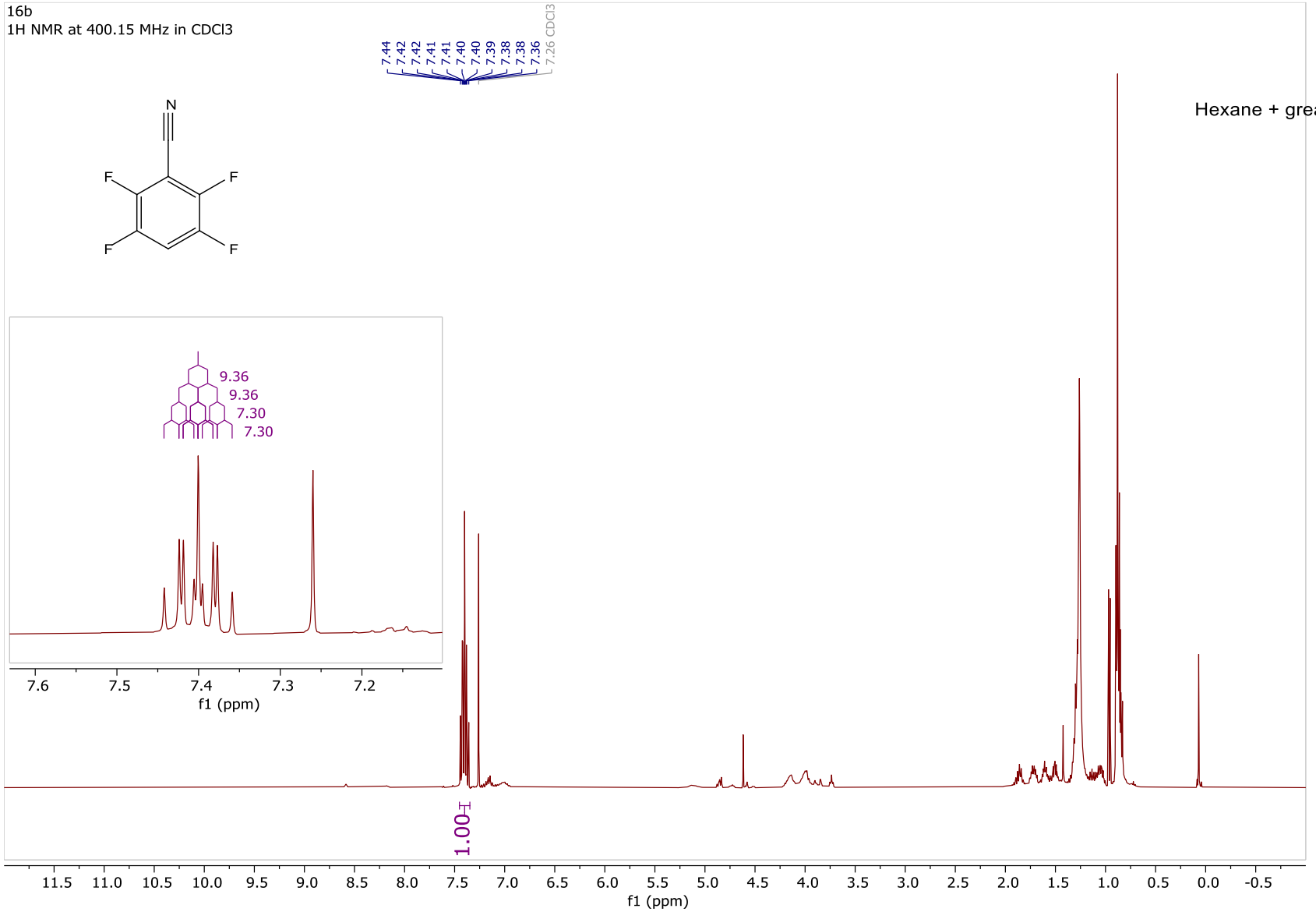

14b
19F NMR at 376.48 MHz in CDCl3
F
F
F
F
F
F
F
F
-137.72
-137.73
-137.73
-137.74
-137.74
-137.76
-137.76
-137.77
-137.77
-137.78
-137.79
-137.79
-137.80
-137.81
-137.81
-137.82
-137.82
-137.83
-137.83
-137.84
-137.85
-137.85
-137.86
-137.87
-137.88
-137.88
-137.89
-138.26
-138.27
-138.28
-138.29
-138.30
-138.30
-138.32
-138.33
-138.33
-138.34
-138.35
-138.35
-138.36
-138.36
-138.37
-138.37
-138.38
-138.38
-138.39
-138.40
-138.42
-137.76
-137.77
-137.77
-137.78
-137.79
-137.79
-137.80
-137.81
-137.81
-137.82
-137.82
-137.83
-137.83
-137.84
-137.85
-138.29
-138.30
-138.30
-138.32
-138.33
-138.33
-138.34
-138.35
-138.35
-138.36
-138.36
-138.37
-138.38
-138.38
4.01
4.00
-137.0
-137.5
-138.0
-138.5
-139.0
-139.5
f1 (ppm)
4.01
4.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

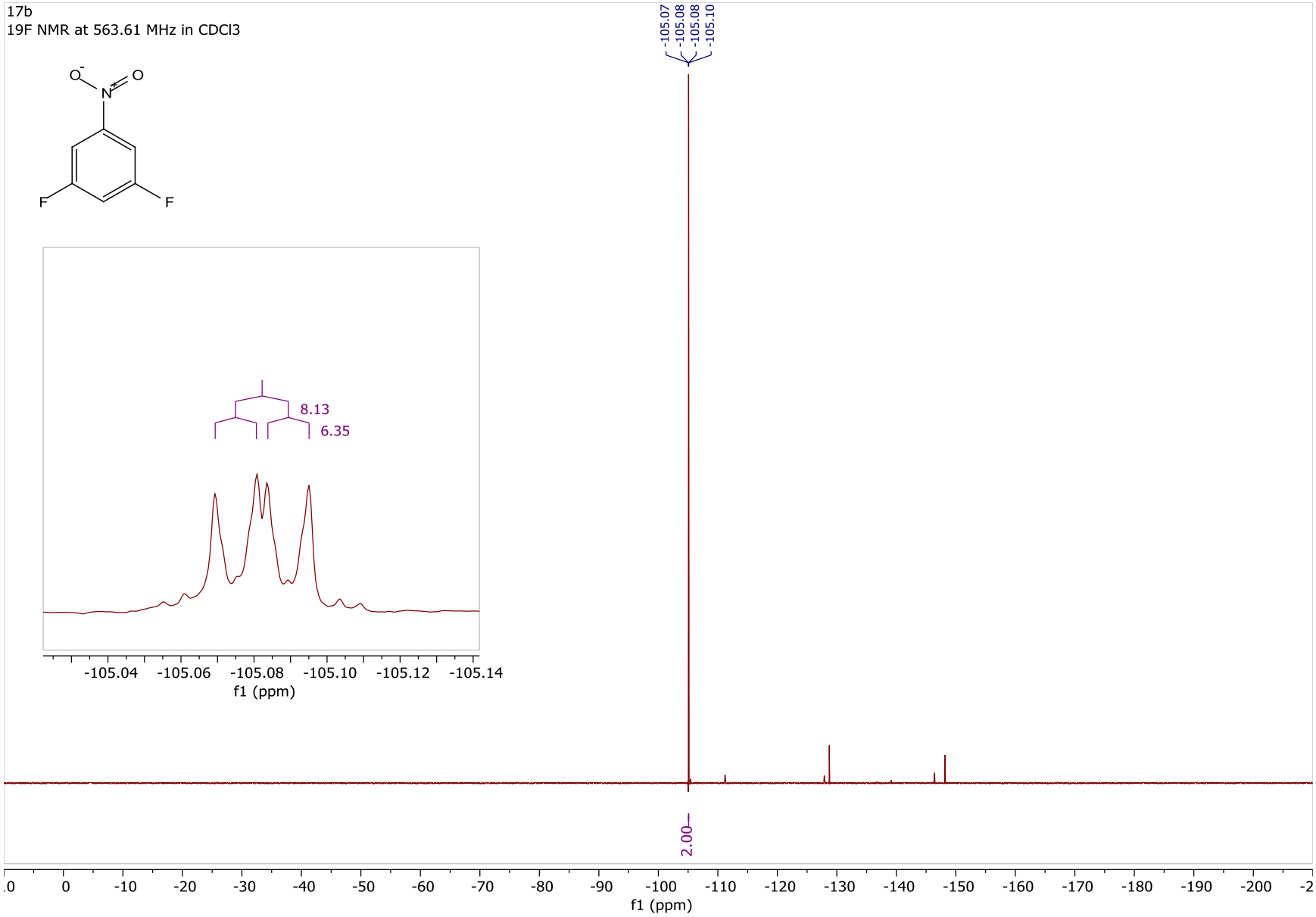

14b
1H NMR at 400.15 MHz in CDCl3
7.31
7.30
7.30
7.29
7.28
7.28
7.27
7.27
7.27
7.26 CDCl3
7.26
7.25
7.25
7.24
7.23
7.23
7.22
F
F
F
F
F
F
F
F
7.40
7.35
7.30
7.25
7.20
7.15
7.10
f1 (ppm)
2.00
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)

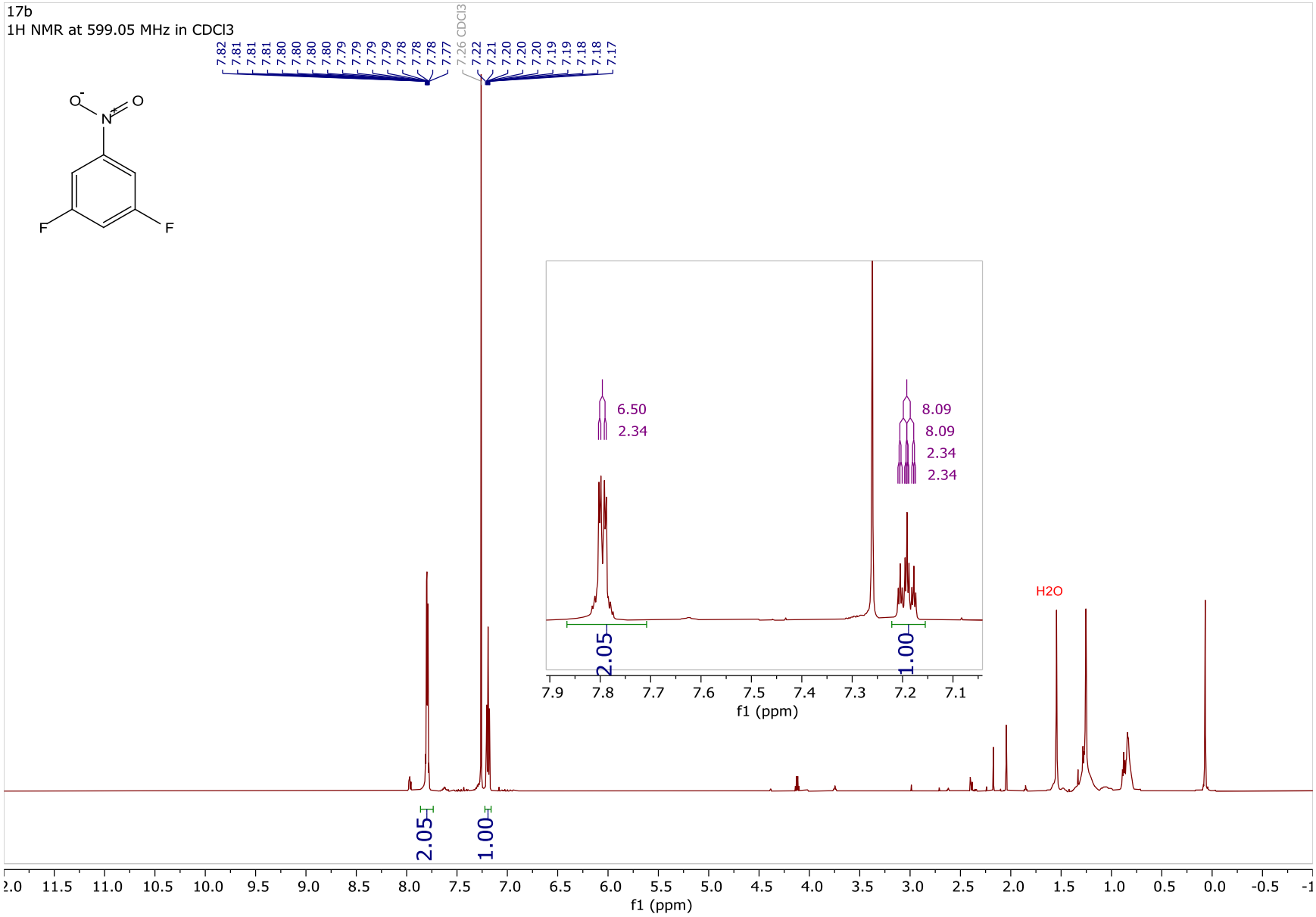

15b and 15c
19F NMR at 563.61 MHz in CDCl3
A (m)
-115.24
B (m)
-117.13
2.08
20.92
f1 (ppm)
B, D, E
C (m)
-132.92
D (m)
-135.91
2.00
20.56
f1 (ppm)
A, C, F
E (m)
-148.60
F (m)
-150.15
20.01
1.98
f1 (ppm)
2.08
20.92
2.00
20.56
20.01
1.98
f1 (ppm)

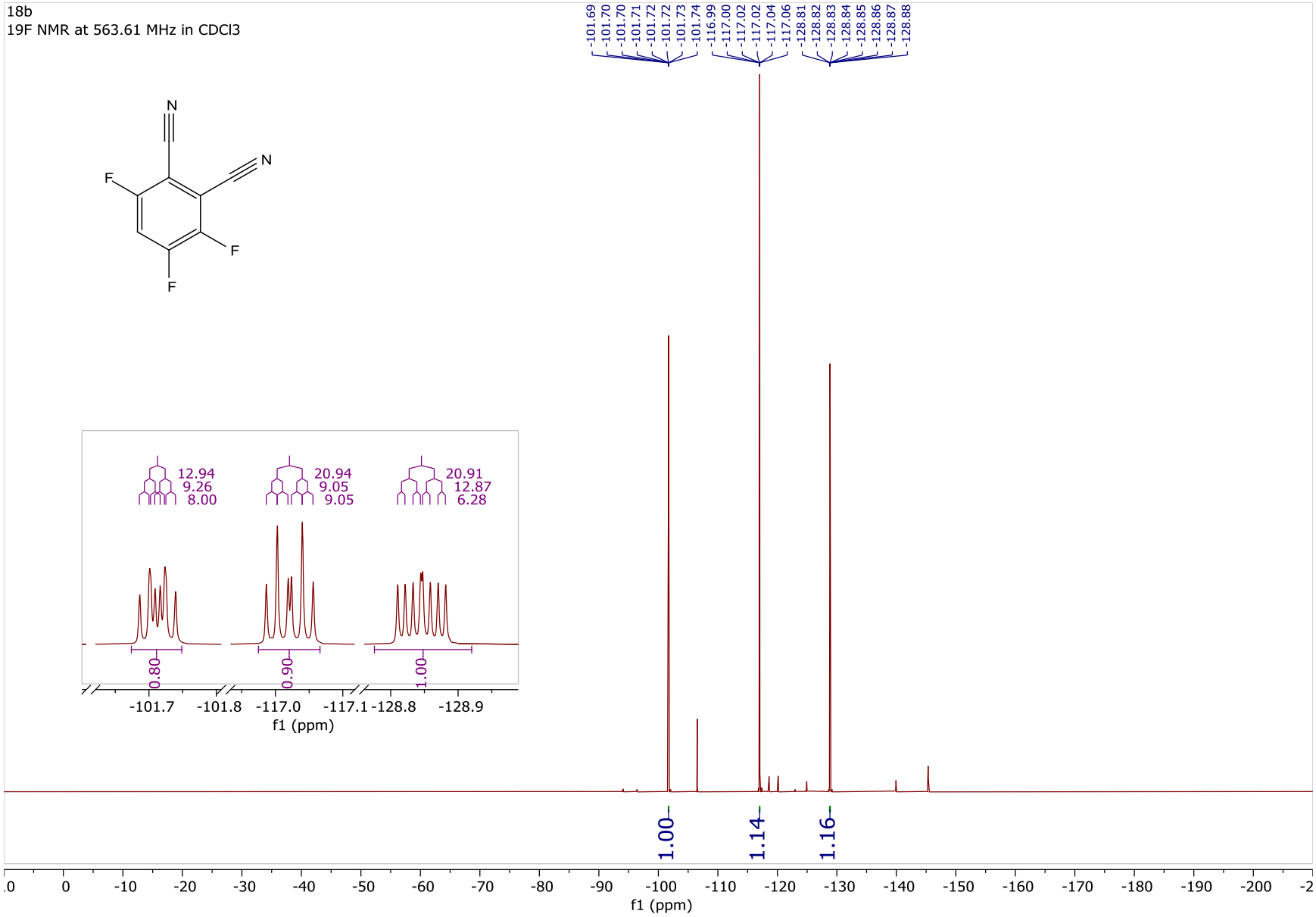

15b and 15c
1H NMR at 599.05 MHz in CDCl3
7.26 CDCl3
7.23 7.22 7.22 7.22 7.22 7.21 7.21 7.21 7.20 7.19 7.19 7.19 7.19 7.18 7.18 7.18 7.17 7.14 7.13 7.13 7.12 7.12 7.12 7.11 7.11 7.11 7.10 7.10 7.10 7.09 7.09 7.08
F
F
F
F
F
F
F
F
F
F
16.06
2.00
7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95
f1 (ppm)
16.06
2.00
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

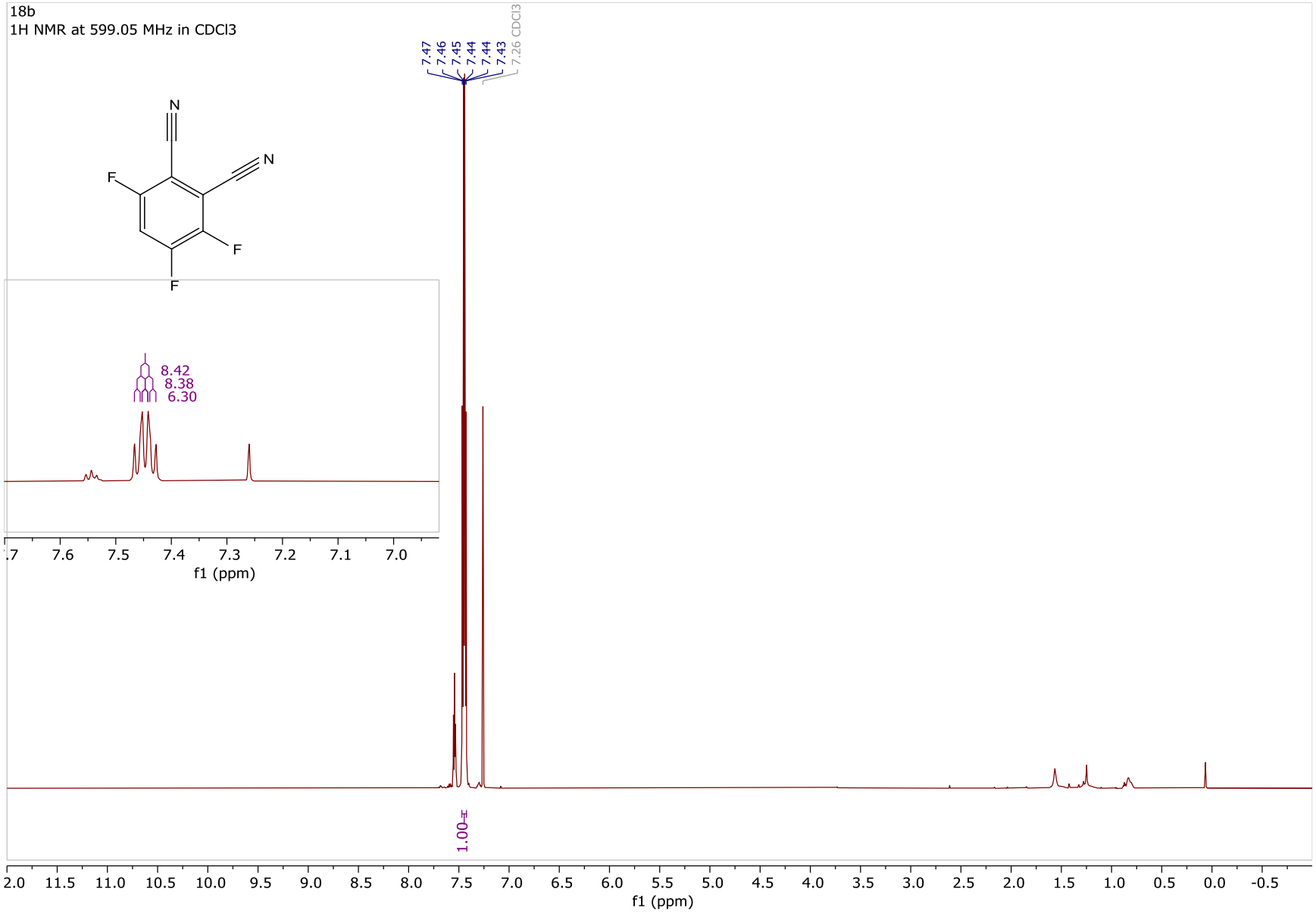

16b
19F NMR at 376.48 MHz in CDCl3
N
F
F
F
F
-131.78
-131.78
-131.80
-131.80
-131.82
-131.82
-131.84
-131.86
-131.87
-131.87
-131.89
-131.89
-131.91
-131.92
-134.83
-134.85
-134.85
-134.86
-134.88
-134.90
-134.90
-134.91
-134.92
-134.92
-134.94
-134.94
-134.95
-134.97
-134.97
2.00
2.04
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

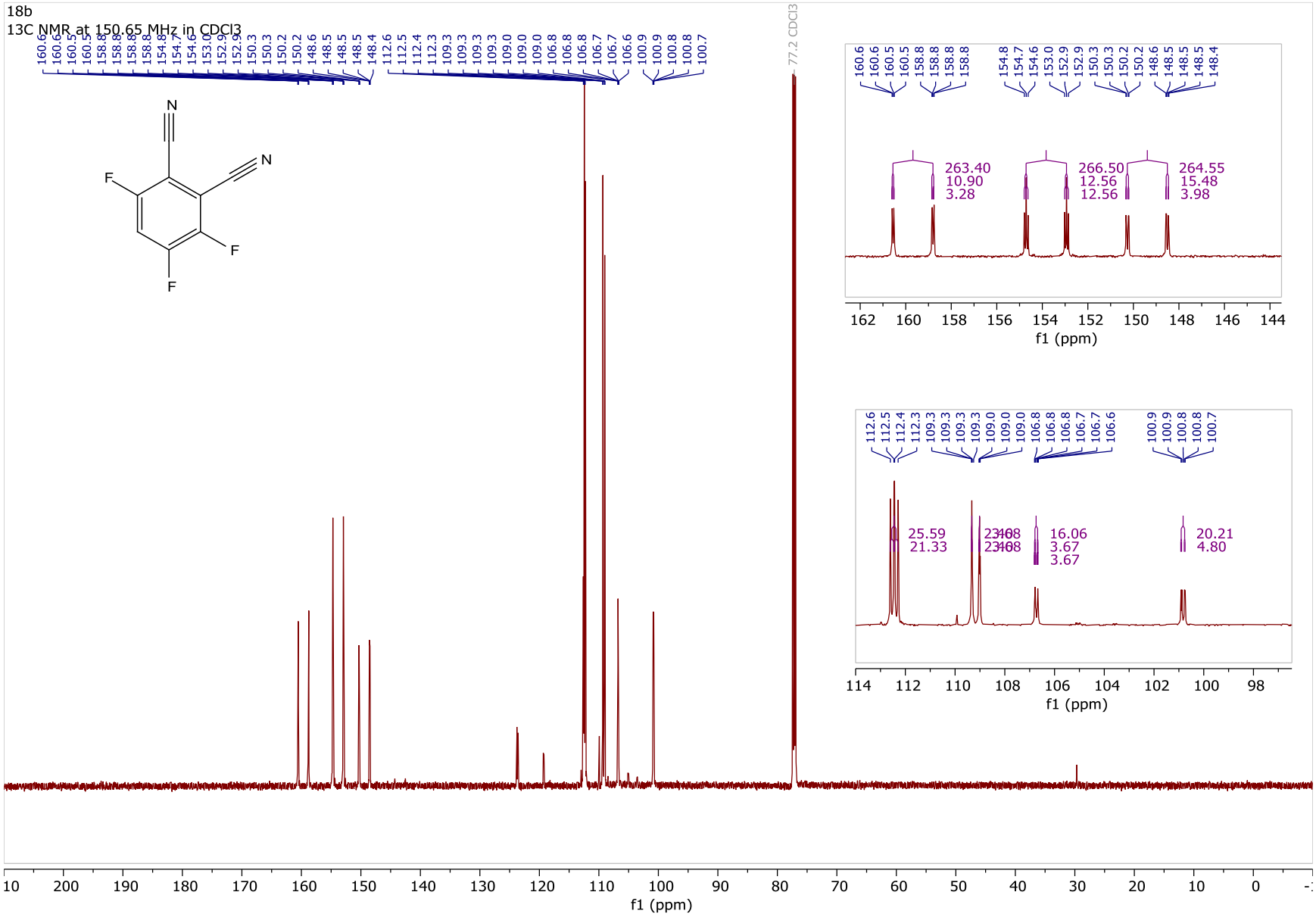

16b
1H NMR at 400.15 MHz in CDCl3
7.44
7.42
7.42
7.41
7.41
7.40
7.40
7.39
7.38
7.38
7.36
7.26 CDCl3
N
F
F
F
F
Hexane + grease
9.36
9.36
7.30
7.30
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
1.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

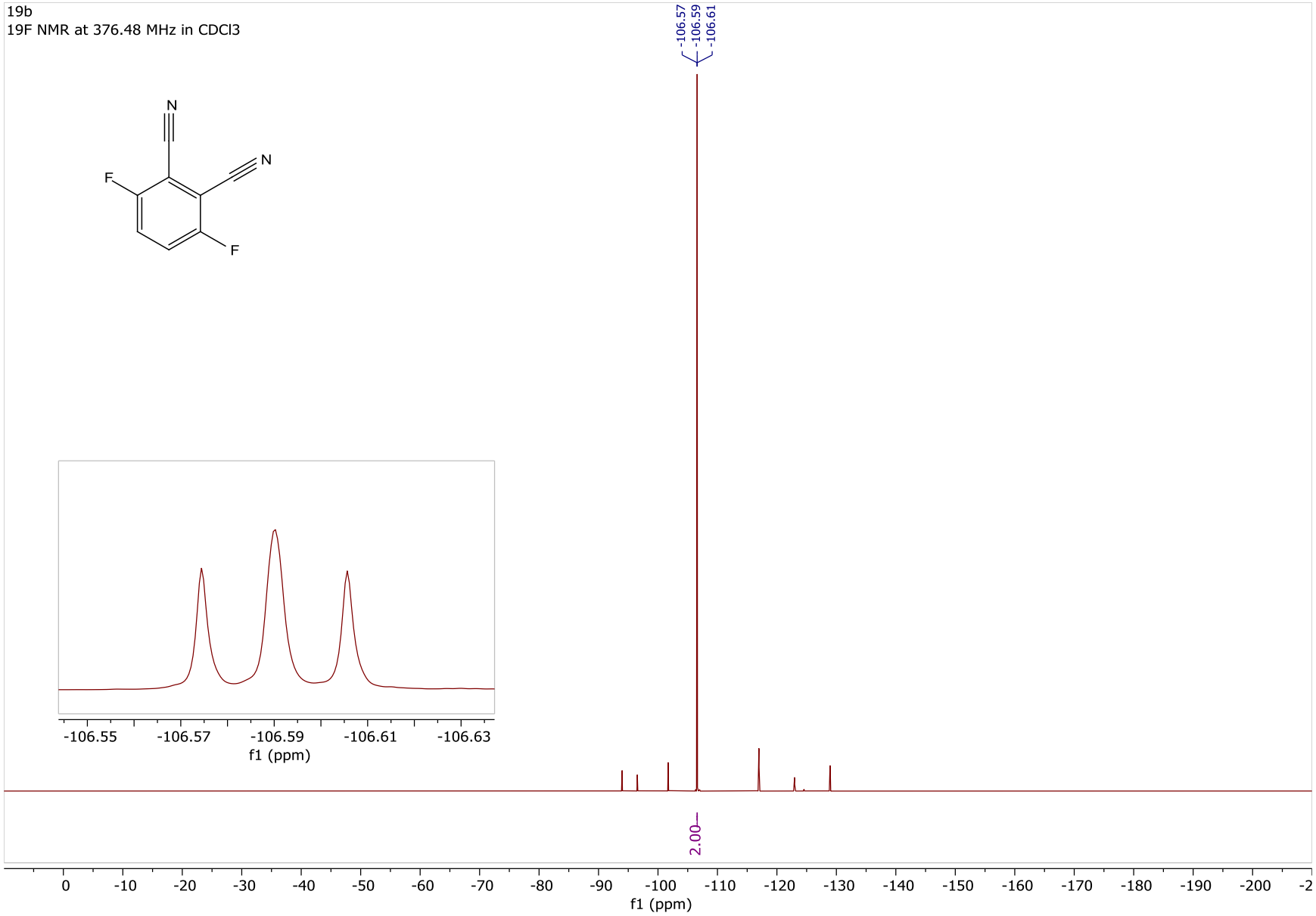

17b
19F NMR at 563.61 MHz in CDCl3
-105.07
-105.08
-105.08
-105.10
O
N
O
F
F
8.13
6.35
-105.04
-105.06
-105.08
-105.10
-105.12
-105.14
f1 (ppm)
2.00
.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

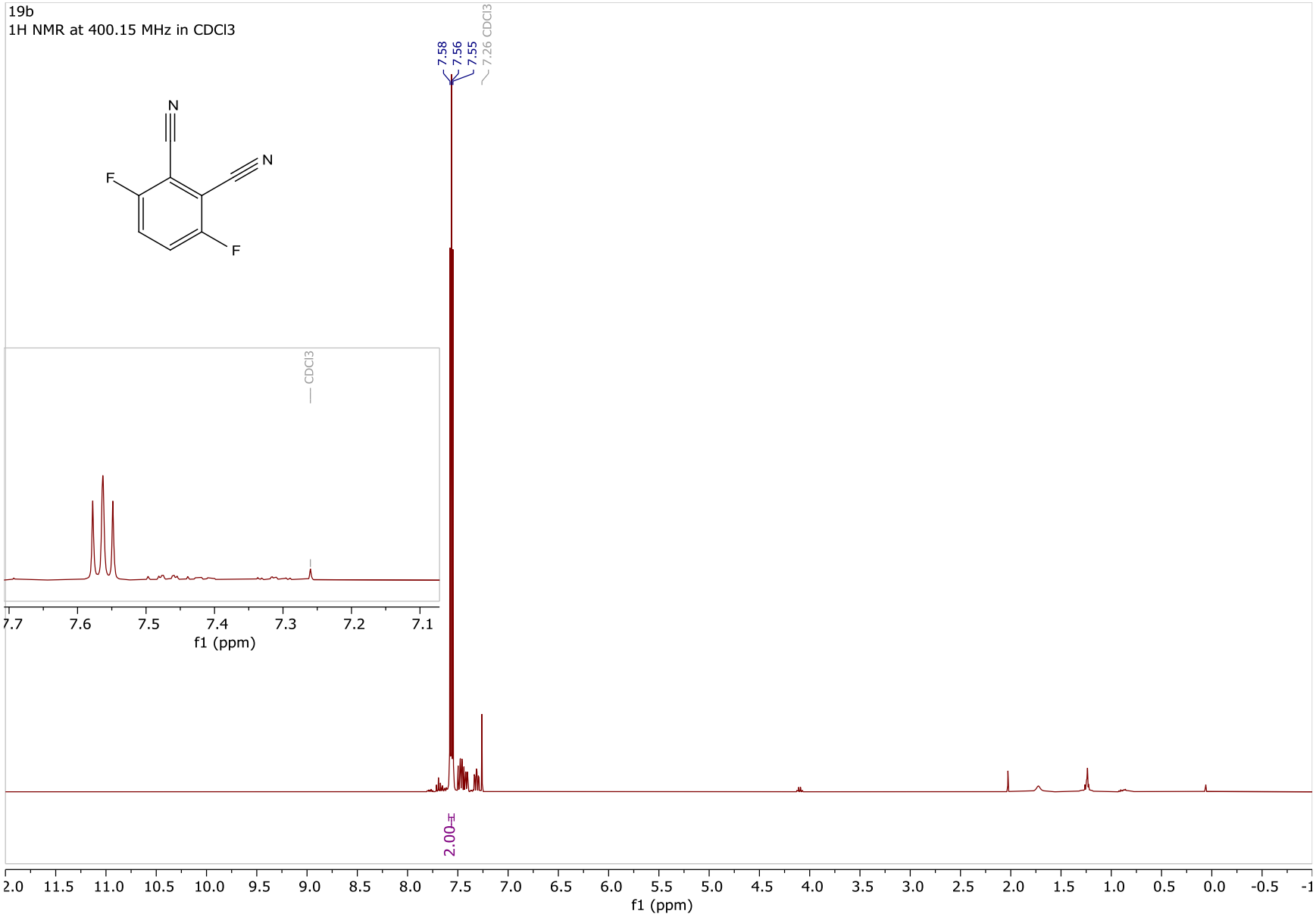

17b
1H NMR at 599.05 MHz in CDCl3
7.82 7.81 7.81 7.81 7.80 7.80 7.80 7.80 7.79 7.79 7.79 7.79 7.78 7.78 7.78 7.77
7.26 CDCl3
7.22 7.21 7.20 7.20 7.20 7.19 7.19 7.18 7.18 7.17
O
N
O
F
F
6.50
2.34
8.09
8.09
2.34
2.34
2.05
1.00
7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1
f1 (ppm)
H2O
2.05
1.00
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

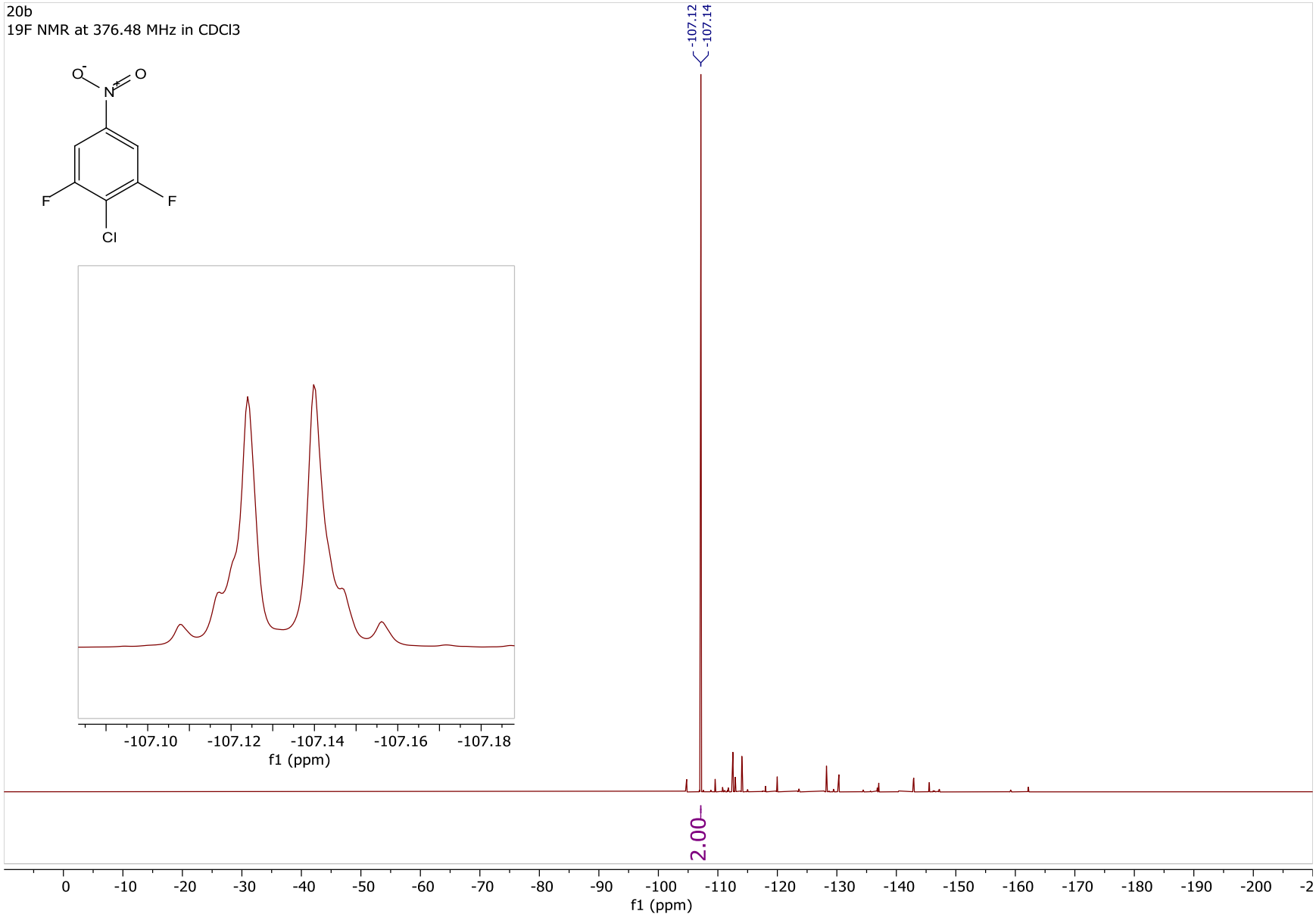

18b
19F NMR at 563.61 MHz in CDCl3
-101.69
-101.70
-101.70
-101.71
-101.72
-101.72
-101.73
-101.74
-116.99
-117.00
-117.02
-117.02
-117.04
-117.06
-128.81
-128.82
-128.83
-128.84
-128.85
-128.86
-128.87
-128.88
N
N
F
F
F
12.94
9.26
8.00
20.94
9.05
9.05
20.91
12.87
6.28
0.80
0.90
1.00
-101.7
-101.8
-117.0
-117.1
-128.8
-128.9
f1 (ppm)
1.00
1.14
1.16
f1 (ppm)

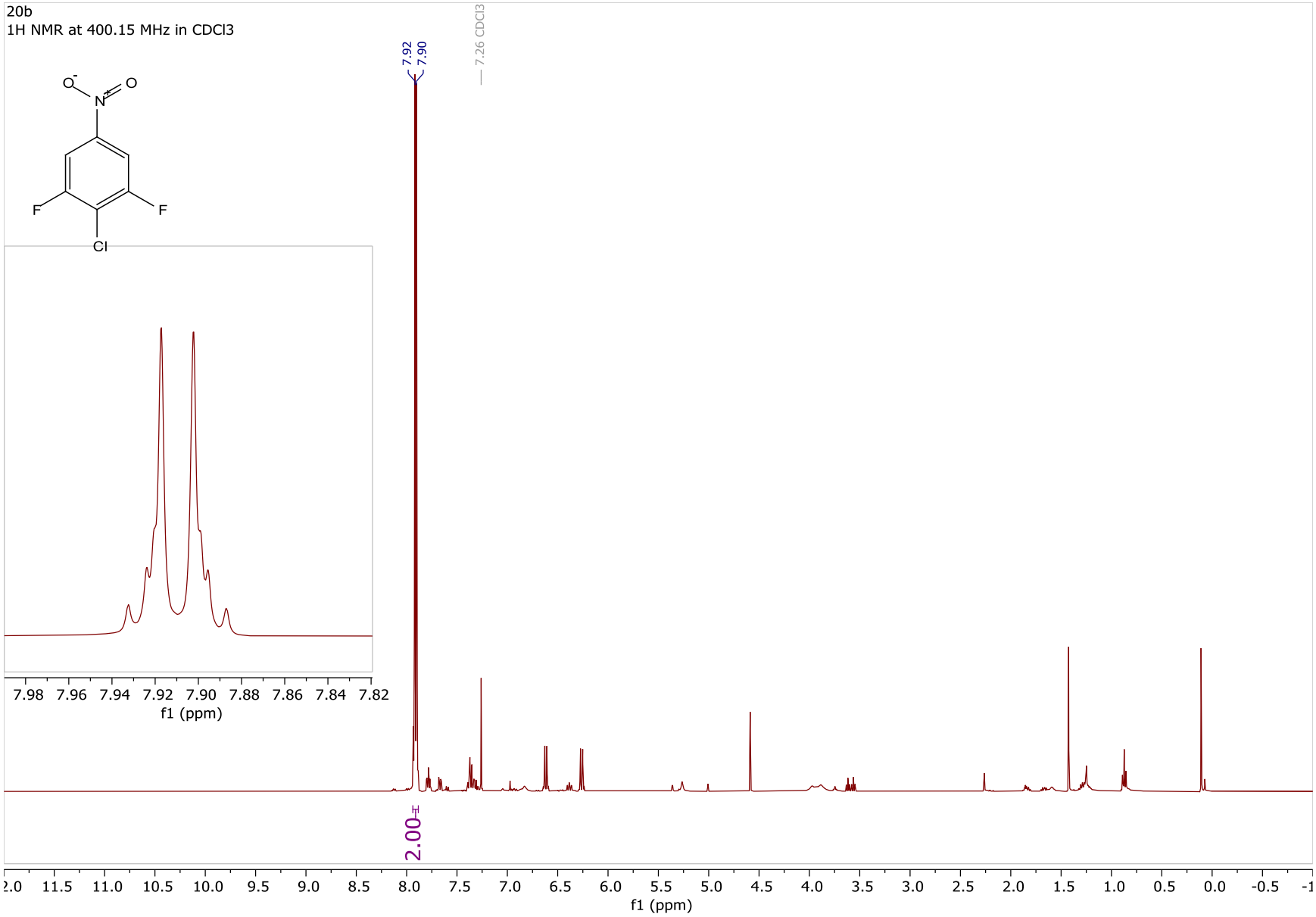

18b
1H NMR at 599.05 MHz in CDCl3
7.47
7.46
7.45
7.44
7.44
7.43
7.26 CDCl3
N
N
F
F
F
8.42
8.38
6.30
7.7
7.6
7.5
7.4
7.3
7.2
7.1
7.0
f1 (ppm)
1.00
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

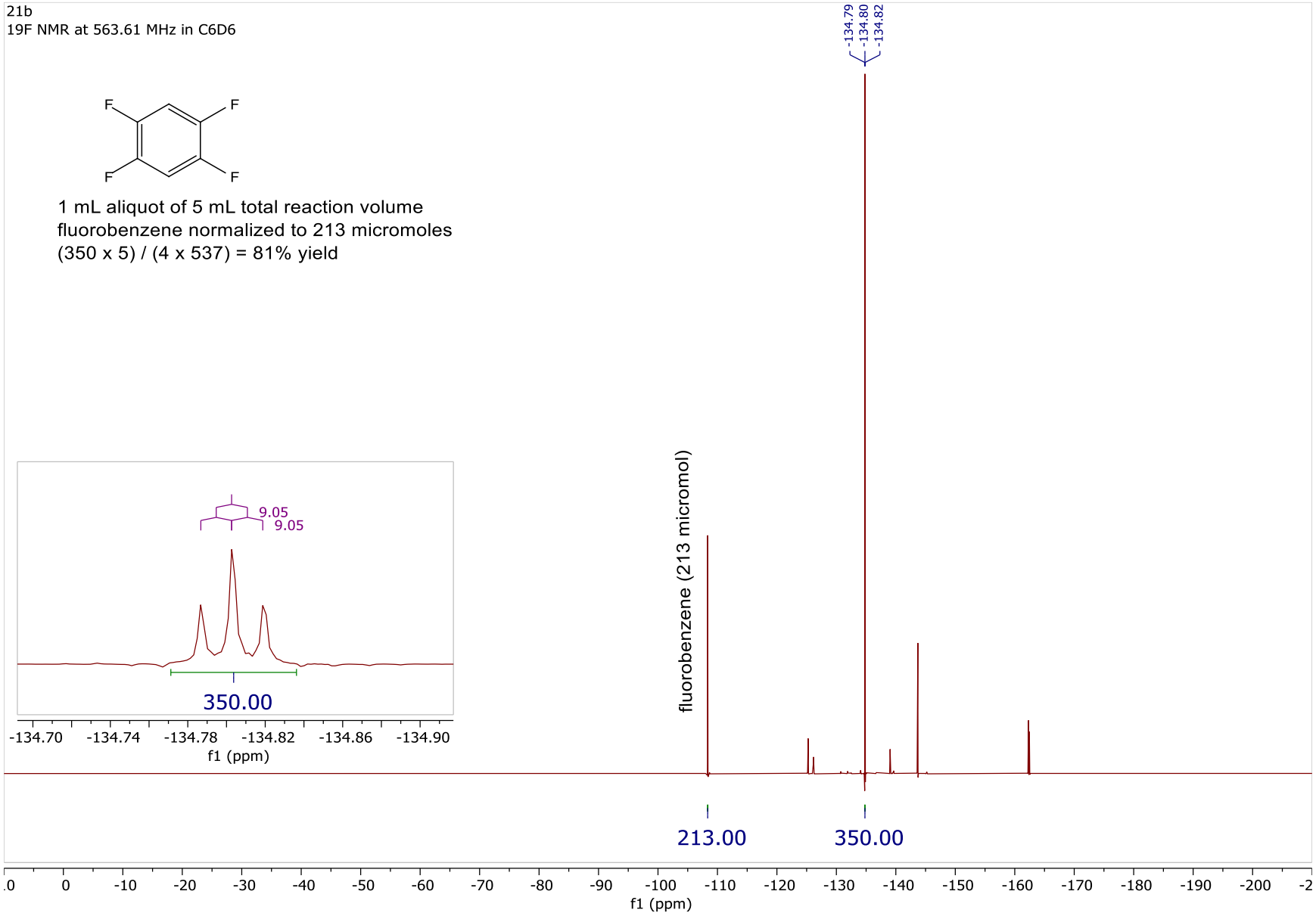

18b
13C NMR at 150.65 MHz in CDCl3
77.2 CDCl3
263.40
10.90
3.28
266.50
12.56
12.56
264.55
15.48
3.98
25.59
21.33
16.06
3.67
3.67
20.21
4.80
f1 (ppm)


19b
19F NMR at 376.48 MHz in CDCl3
N
N
F
F
-106.57
-106.59
-106.61
-106.55
-106.57
-106.59
-106.61
-106.63
f1 (ppm)
2.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

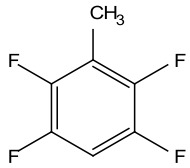

19b
1H NMR at 400.15 MHz in CDCl3
7.58
7.56
7.55
7.26 CDCl3
N
N
F
F
CDCl3
7.7
7.6
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
2.00
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


20b
19F NMR at 376.48 MHz in CDCl3
O
N
O
F
F
Cl
-107.12
-107.14
-107.10
-107.12
-107.14
-107.16
-107.18
f1 (ppm)
2.00
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)

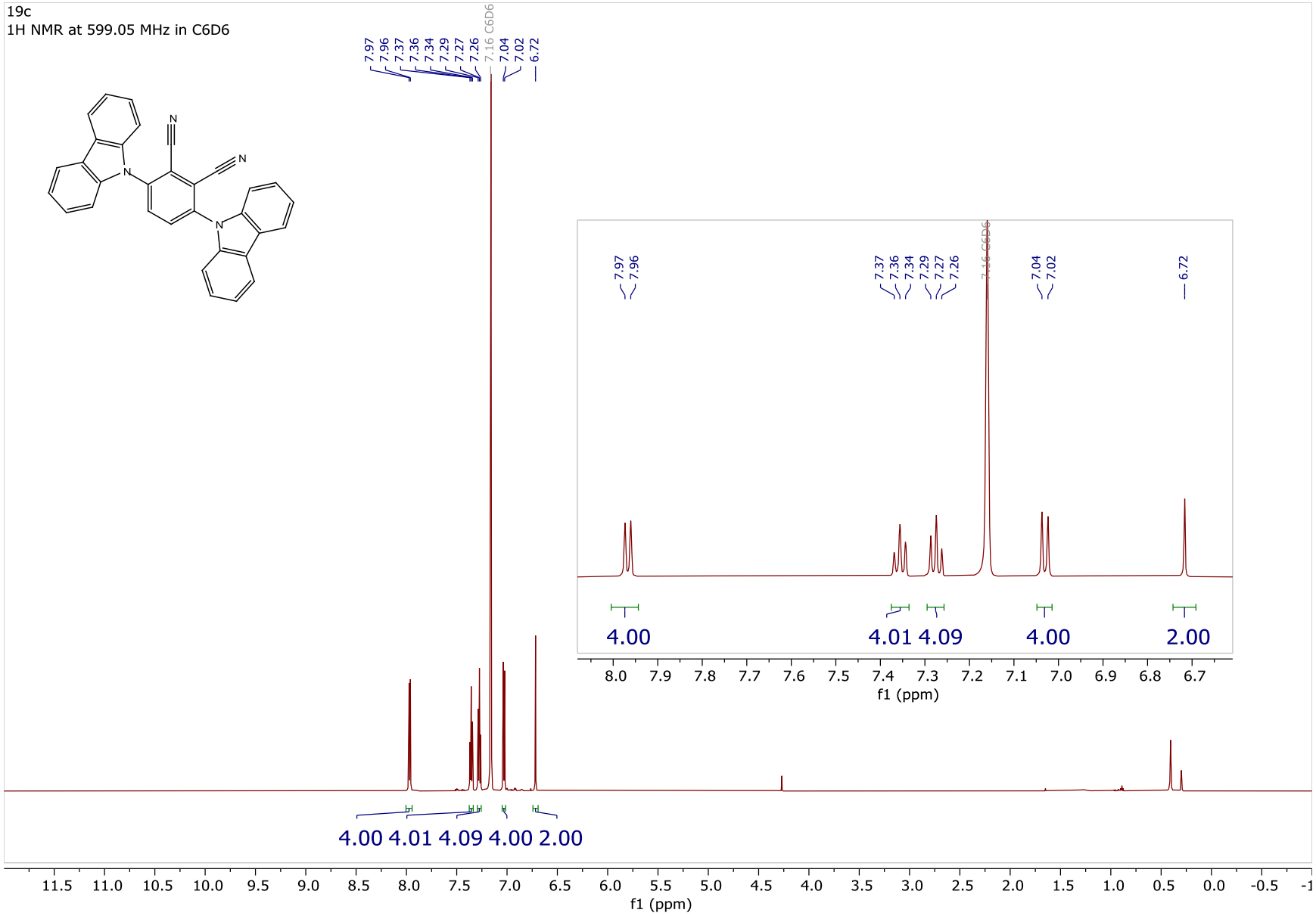

20b
1H NMR at 400.15 MHz in CDCl3
7.92
7.90
7.26 CDCl3
O
N
O
F
F
Cl
7.98 7.96 7.94 7.92 7.90 7.88 7.86 7.84 7.82
f1 (ppm)
2.00
f1 (ppm)

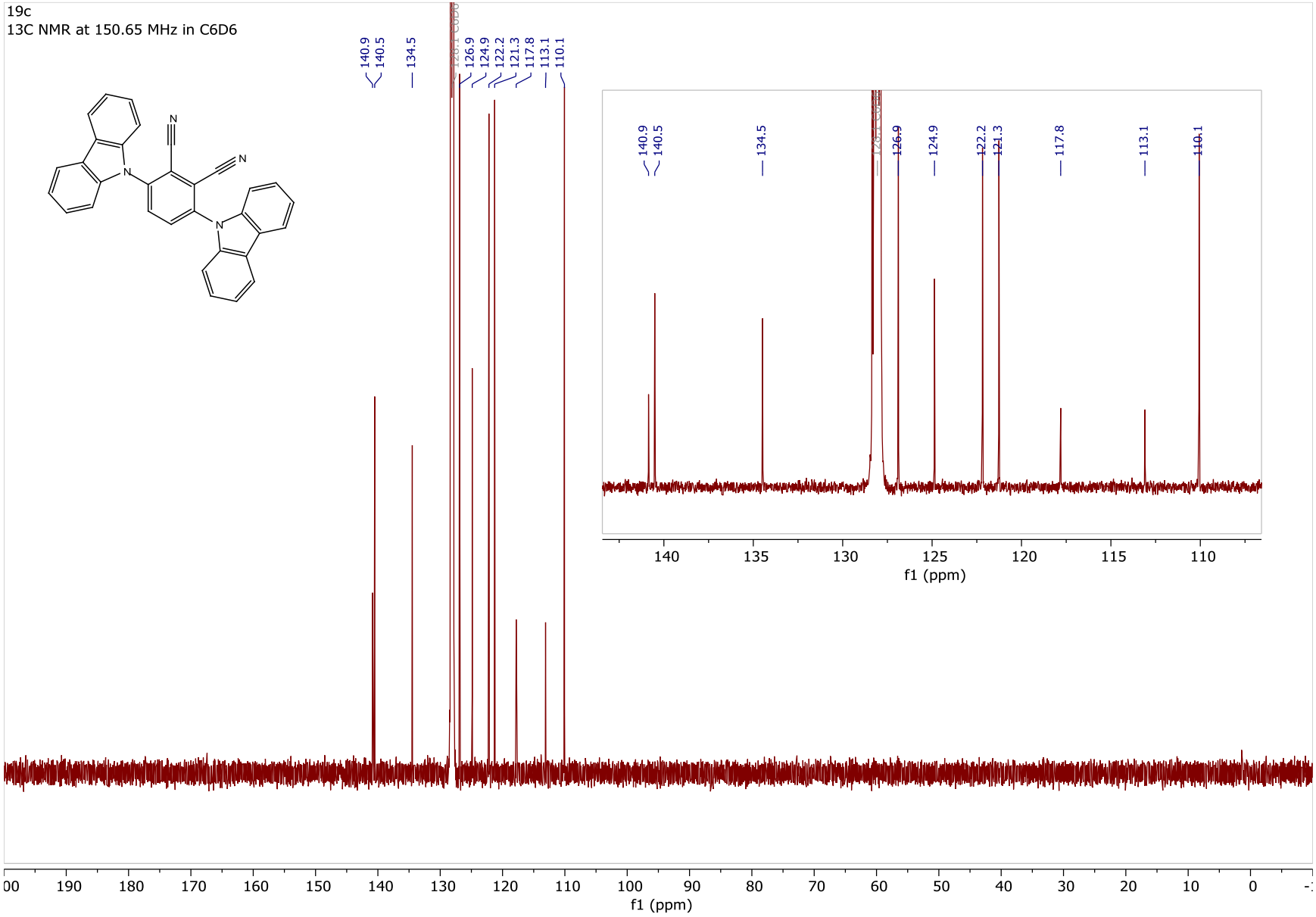

21b
19F NMR at 563.61 MHz in C6D6
F
F
F
F
1 mL aliquot of 5 mL total reaction volume
fluorobenzene normalized to 213 micromoles
(350 x 5) / (4 x 537) = 81% yield
-134.79
-134.80
-134.82
9.05
9.05
350.00
-134.70
-134.74
-134.78
-134.82
-134.86
-134.90
f1 (ppm)
fluorobenzene (213 micromol)
213.00
350.00
.0
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-2
f1 (ppm)

22b
19F NMR at 376.48 MHz in DMSO




500 microliter aliquot from 5 mL total reaction volume
fluorobenzene normalized to 213 micromoles
(10 x (78.32 + 78.95)/(4 x 550) = 72% yield


19c
1H NMR at 599.05 MHz in C6D6
7.97
7.96
7.37
7.36
7.34
7.29
7.27
7.26
7.16 C6D6
7.04
7.02
6.72
N
N
N
4.00 4.01 4.09 4.00 2.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)
4.00
4.01 4.09
4.00
2.00
8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)


19c
13C NMR at 150.65 MHz in C6D6
140.9
140.5
134.5
126.9
124.9
122.2
121.3
117.8
113.1
110.1
N
N
N
f1 (ppm)