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Room Temperature Deoxofluorination of Aromatic Aldehydes with XtalFluor-E under Highly Concentrated Conditions

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1. General information

The following includes general experimental procedures, specific details for representative reactions, isolation and spectroscopic information for the compounds prepared. Solvents were used as purchased unless stated as dry. CH_3CN, CH_2Cl_2, and toluene were purified using a Vacuum Atmospheres Inc. solvent purification system. All air and water sensitive reactions were carried out under an argon atmosphere. Reactions were monitored by TLC on precoated plates (SiliCycle, silica gel 60 Å F254 230-240 mesh), and products were visualized under 254 nm UV light followed, if necessary, by staining with $KMnO_4$ or phosphomolybdic acid (PMA) NMR spectra were recorded on an Agilent DD2 500 spectrometer in the indicated deuterated solvent at 298 K. Chemical shifts are reported on the delta scale in ppm. For ^1H and ^{13}C spectra, chemical shifts are referenced to residual solvent references or internal TMS reference. For ^{19}F spectra, calibration was performed using a unified scale.[1] Resonances are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, p = pentaplet, m = multiplet, or a combination of the above), coupling constant (Hz), integration. High-resolution mass (HRMS) spectra were recorded on a LC/MS-TOF Agilent 6210 using electrospray ionization (ESI) in positive mode. GC–MS analyses were performed on a Thermo Trace ULTRA GCMS equipped with an Agilent J&W HP-5 capillary column, an ITQ 900 mass selective detector using Electron impact Ionization (EI) with the following method: 45 °C for 1 min then 25 °C/min until 250 °C. Infrared spectra (IR) were recorded on an ABB MB 3000 FT-IR spectrometer and on a Thermo Scientific Nicolet 380 FT-IR spectrometer. Absorptions are reported in cm^{-1}. Melting points were measured on a Stanford Research System OptiMelt MPA100 automated melting point apparatus.

2. Aldehydes

All the aldehydes (except 4-(chloromethyl)benzaldehyde) were obtained from commercial sources or were prepared according to methods in the literature.

4-(Chloromethyl)benzaldehyde was prepared as follows: DMSO (0.34 mL, 4.8 mmol, 2.4 equiv) was added to a solution of oxalyl chloride (0.21 mL, 2.4 mmol, 1.2 equiv) in dichloromethane (18 mL) at −78 °C and stirred for 15 min. The reaction vessel was wrapped in aluminum foil before (4-(chloromethyl)phenyl)methanol (312.2 mg, 2.0 mmol) in dichloromethane (2 mL) was added and the reaction mixture stirred for a further 15 min at −78 °C. Triethylamine (1.67 mL, 12.0 mmol, 6

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[1] Harris, R. K.; 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*, 1795–1818, DOI: 10.1351/pac200173111795.

equiv) was added and the reaction mixture was allowed to warm to room temperature while stirring for 18 h. The reaction mixture was quenched using a saturated aqueous solution of sodium bicarbonate and stirred for 30 min. The phases were then separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The light-sensitive aldehyde was isolated as a white solid (224.8 mg, 73%) after purification by flash chromatography (20% EtOAc in hexanes). Mp = 71.5–73.7 °C. FT-IR (ν/cm^{-1}): 2858, 2756, 1684, 1607, 1580, 1392, 1165, 831, 775, 735. ^{1}H NMR (500 MHz, $CDCl_3$): δ 10.03 (s, 1H), 7.89 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.1 Hz, 2H), 4.64 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 191.6, 143.8, 136.2, 130.1, 129.1, 45.3. HRMS (ESI-TOF), *m/z*: [M + H]$^+$ calcd for C_8H_7ClO, 155.0258; found, 155.0262.

3. General procedure for deoxofluorination of aldehydes

To a dried, argon flushed polytetrafluoroethylene (PTFE) conical tube were added the aldehyde (1.0 mmol), $Et_3N \cdot 3HF$ (0.49 mL, 3.0 mmol, 3 equiv) and XtalFluor-E (343.5 mg, 1.5 mmol, 1.5 equiv). The mixture was stirred for 18 hours at room temperature under an argon atmosphere. The reaction mixture was quenched using a saturated aqueous solution of sodium bicarbonate. The phases were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried over anhydrous $MgSO_4$, filtered and concentrated in vacuo. The crude mixture was purified by flash chromatography on silica gel.

4. Robustness screen

Following the general procedure 3, additive (1 equiv) was added with the aldehyde (1 equiv). NMR yields were calculated with ^{19}F NMR using 2-fluoro-4-nitrotoluene as internal standard.

Using benzoic acid as additive (0.5 mmol, 62.6 mg) **2a** was observed in a 12% yield as well as benzoyl fluoride[2] in a 16% yield using 2-fluoro-4-nitrotoluene as internal standard.

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[2] L'Heureux, A. Aminodifluorosulfinium Salts: Selective Fluorination Reagents with Enhanced Thermal Stability and Ease of Handling *J. Org. Chem.* **2010,** 75, 3401–3411, DOI: 10.1021/jo100504x.

Using benzyl alcohol as additive (0.5 mmol, 54.2 mg) **2a** was observed in a 32% yield as well as benzyl fluoride[3] in a 16% yield using 2-fluoro-4-nitrotoluene as internal standard.

Using acetophenone as additive (0.5 mmol, 60.1 mg) **2a** was observed in a 66% yield using 2-fluoro-4-nitrotoluene as internal standard.

Using benzamide as additive (0.5 mmol, 61.2 mg) **2a** was observed in a 37% yield using 2-fluoro-4-nitrotoluene as internal standard.

Using *N*-(naphthalen-2-yl)formamide as additive (0.5 mmol. 85.5 mg) 2a was observed in a 17% yield using 2-fluoro-4-nitrotoluene as internal standard.NMR spectra

5. Deoxofluorination of aromatic aldehydes

*1-Bromo-4-(difluoromethyl)benzene (**2a**).* According to a general procedure starting with 4-bromobenzaldehyde (1.0 mmol, 185 mg), **2a** was observed in 85% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a clear liquid (162.4 mg, 78%) after purification by flash chromatography using pentane as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.6 (d, J = 8.3 Hz, 2H), 7.38 (d, J = 8.4 Hz, 2H), 6.61 (t, J = 56.3 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ − 111.1 (d, J = 56.3 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*1-Iodo-4-(difluoromethyl)benzene (**2b**).* According to a general procedure starting with 4-iodobenzaldehyde (1.0 mmol, 232 mg), **2b** was observed in 88% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a white solid (175.6 mg, 69%) after purification by flash chromatography using hexanes as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82–7.79 (m, 2H), 7.26–7.23 (m, 2H), 6.59 (t, J = 56.3 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ − 111.4 (d, J = 56.3 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

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[3] Makosza, M. Cocatalysis in phase-transfer-catalyzed fluorination of alkyl halides and sulfonates. *J. Fluorine Chem.* **2005**, 126, 209-216, DOI: 10.1016/j.jfluchem.2004.12.003.

[4] Melvin, P. R.; Ferguson, D. M.; Schimler, S. D.; Bland, D. C.; Sanford, M. S. Room Temperature Deoxyfluorination of Benzaldehydes and α-Ketoesters with Sulfuryl Fluoride and Tetramethylammonium Fluoride, *Org. Lett.* **2019**, *21*, 1350−1353, 10.1021/acs.orglett.9b00054.

*4-(Difluoromethyl)-1,1'-biphenyl (**2c**).* According to a general procedure starting with biphenyl-4-carboxaldehyde (1.0 mmol, 182.2 mg), **2c** was observed in 85% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a white solid (171.7 mg, 84%) after purification by flash chromatography (10% toluene in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68–7.66 (m, 2H), 7.61–7.57 (m, 4H), 7.48–7.44 (m, 2H), 7.40–7.37 (m, 1H), 6.69 (t, *J* = 56.5 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 110.3 (d, *J* = 56.7 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*1-(tert-Butyl)-4-(difluoromethyl)benzene (**2d**).* According to a general procedure starting with 4-*tert*-butylbenzaldehyde (1.0 mmol, 162.2 mg), **2d** was observed in 68% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a clear liquid (91.2 mg, 50%) after purification by flash chromatography using hexanes as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.43 (m, 4H), 6.63 (t, *J* = 56.7 Hz, 1H), 1.34 (s, 9H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 109.9 (d, *J* = 56.7 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*1-(Difluoromethyl)-4-methoxybenzene (**2e**).* According to a general procedure starting with 4-methoxybenzaldehyde (1.0 mmol, 136.2 mg), **2e** was observed in 65% ^{19}F NMR yield using 1-bromo-4-(trifluoromethyl)benzene as an internal standard and was isolated as a yellow liquid (96.4 mg, 61%) after purification by flash chromatography (2% Et_2O in pentane). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45–7.42 (m, 2H), 6.97–6.94 (m, 2H), 6.60 (t, *J* = 56.8 Hz, 1H) 3.84 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 108.2 (d, *J* = 56.8 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[5]

*1-(Difluoromethyl)-4-nitrobenzene (**2f**).* According to a general procedure starting with 4-nitrobenzaldehyde (1.0 mmol, 151.1 mg), **2f** was observed in 89% ^{19}F NMR yield

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[5] Motohashi, H.; Kato, M.; Mikami, K. Ligand-Less Iron-Catalyzed Aromatic Cross-Coupling Difluoromethylation of Grignard Reagents with Difluoroiodomethane. *J. Org. Chem.* **2019**, *84*, 6483–6490, DOI: 10.1021/acs.joc.9b00585.

using 4-bromobenzotrifluoride as an internal standard and was isolated as a yellow liquid (145.8 mg, 84%) after purification by flash chromatography (15% EtOAc in hexanes). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.35–8.32 (m, 2H), 7.74–7.71 (m, 2H), 6.75 (t, *J* = 55.8 Hz, 1H). ^{19}F NMR (470 MHz, CDCl$_3$) δ − 113.0 (d, *J* = 55.7 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[6]

*4-(Difluoromethyl)benzonitrile (**2g**).* According to a general procedure starting with 4-cyanobenzaldehyde (1.0 mmol, 131.1 mg), **2g** was observed in 86% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a clear liquid (127.1 mg, 83%) after purification by flash chromatography (25 to 50% Et$_2$O in hexanes). ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.78–7.76 (m, 2H), 7.65–7.63 (m, 2H), 6.69 (t, *J* = 55.8 Hz, 1H). ^{19}F NMR (470 MHz, CDCl$_3$) δ − 113.2 (d, *J* = 55.7 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*Methyl 4-(difluoromethyl)benzoate (**2h**).* According to a general procedure starting with methyl 4-formylbenzoate (1.0 mmol, 164.2 mg), **2h** was observed in 88% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as an off-white solid (156 mg, 84%) after purification by flash chromatography (10% Et$_2$O in hexanes). ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.14–8.12 (m, 2H), 7.60–7.56 (m, 2H), 6.69 (t, *J* = 56.1 Hz, 1H), 3.95 (s, 3H). ^{19}F NMR (470 MHz, CDCl$_3$) δ − 112.2 (d, *J* = 56.2 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*1-(Chloromethyl)-4-(difluoromethyl)benzene (**2i**).* According to a general procedure starting with 4-(chloromethyl)benzaldehyde (1.0 mmol, 154.6 mg), **2i** was observed in 79% ^{19}F NMR yield using 1-bromo-4-(trifluoromethyl)benzene as an internal standard and was isolated as a yellow liquid (137.3 mg, 78%) after purification by flash chromatography (0-10% EtOAc in hexanes). FT-IR (ν/cm^{-1}): 2966, 1925, 1620, 1425, 1377, 1267, 1221, 1072, 1020, 835, 787, 733, 683. ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.52–

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[6] Motohashi, H.; Mikami, K. Nickel-Catalyzed Aromatic Cross-Coupling Difluoromethylation of Grignard Reagents with Difluoroiodomethane. *Org. Lett.* **2018**, *20*, 5340–5343, DOI: 10.1021/acs.orglett.8b02264.

7.47 (m, 4H), 6.65 (t, $J = 56.4$ Hz, 1H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 140.1 (t, $J_{C\text{–}F} = 2.0$ Hz), 134.4 (t, $J_{C\text{–}F} = 22.5$ Hz), 128.9, 126.0 (t, $J_{C\text{–}F} = 6.2$ Hz), 114.4 (t, $J_{C\text{–}F} = 239.2$ Hz), 45.4. ^{19}F NMR (470 MHz, CDCl$_3$) δ – 110.9 (d, $J = 56.4$ Hz, 2F). GC-MS (EI): m/z calcd for $C_8H_7ClF_2$ [M]$^+$ 176.02 found 176.02. Under all the conditions tested for HRMS analysis (ESI-TOF or APPI-TOF with or without additives), no significant ions could be detected.

*5-(Difluoromethyl)benzo[d][1,3]dioxole (**2j**).* According to a general procedure starting with benzo[d][1,3]dioxole-5-carbaldehyde (1.0 mmol, 150.1 mg), **2j** was observed in 62% ^{19}F NMR yield using 1-bromo-4-(trifluoromethyl)benzene as an internal standard and was isolated as a pale yellow liquid (100.3 mg, 58%) after purification by flash chromatography (20% EtOAc in hexanes). ^{1}H NMR (500 MHz, CDCl$_3$) δ 6.99–6.96 (m, 2H), 6.86–6.84 (m, 1H), 6.54 (t, $J = 56.6$ Hz, 1H), 6.02 (s, 2H). ^{19}F NMR (470 MHz, CDCl$_3$) δ – 107.9 (d, $J = 56.6$ Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[5]

*Methyl 3-(difluoromethyl)benzoate (**2k**).* According to a general procedure starting with methyl 3-formylbenzoate (1.0 mmol, 164.2 mg), **2k** was observed in 89% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a pale yellow liquid (151.5 mg, 81%) after purification by flash chromatography (10% Et$_2$O in hexanes). FT-IR (ν/cm^{-1}): 2957, 1720, 1435, 1373, 1286, 1207, 1026, 924, 754, 708. ^{1}H NMR (500 MHz, CDCl$_3$) δ 8.19–8.18 (m, 1H), 8.17–8.15 (m, 1H), 7.73–7.70 (m, 1H), 7.57–7.54 (m, 1H), 6.69 (t, $J = 56.2$ Hz, 1H), 3.95 (s, 3H). ^{13}C NMR (126 MHz, CDCl$_3$): δ 166.2, 134.8 (t, $J_{C\text{–}F} = 22.9$ Hz), 131.8 (t, $J_{C\text{–}F} = 1.7$ Hz), 130.8, 129.8 (t, $J_{C\text{–}F} = 5.8$ Hz), 129.0, 126.9 (t, $J_{C\text{–}F} = 6.2$ Hz), 114.1 (t, $J_{C\text{–}F} = 239.6$ Hz), 52.4. ^{19}F NMR (470 MHz, CDCl$_3$) δ – 111.2 (d, $J = 56.2$ Hz, 2F). HRMS (ESI-TOF), *m/z*: [M + H]$^+$ calcd for $C_9H_8F_2O_2$, 187.0565; found, 187.0567.

*1-(Difluoromethyl)-3,5-dimethoxybenzene (**2l**).* According to a general procedure starting with 3,5-dimethoxybenzaldehyde (1.0 mmol, 166.2 mg), **2l** was observed in 73% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a yellow liquid (127.1 mg, 68%) after purification by flash chromatography (6% Et$_2$O in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.65–6.64 (m, 2H), 6.56 (t, *J* = 56.5 Hz, 1H), 6.54–6.53 (m, 1H), 3.82 (s, 6H). ^{19}F NMR (470 MHz, $CDCl_3$) δ − 110.9 (d, *J* = 56.4 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[5]

*1-(Difluoromethyl)-3,5-bis(trifluoromethyl)benzene (**2m**).* According to a general procedure starting with 3,5-bis(trifluoromethyl)benzaldehyde (1.0 mmol, 242.1 mg), **2m** was observed in 74% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard.[7]

*1-(Difluoromethyl)-2-methylbenzene (**2n**).* According to a general procedure starting with 2-methylbenzaldehyde (1.0 mmol, 120.2 mg), **2n** was observed in 59% ^{19}F NMR yield using 1-bromo-4-(trifluoromethyl)benzene as an internal standard and was isolated as a clear liquid (29.3 mg, 21%) after purification by flash chromatography using pentane as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51–7.49 (m, 1H), 7.38–7.34 (m, 1H), 7.28–7.22 (m, 2H), 6.75 (t, *J* = 55.5 Hz, 1H) 2.44 (s, 3H). ^{19}F NMR (470 MHz, $CDCl_3$) δ − 113.1 (d, *J* = 55.5 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*2-(Difluoromethyl)-1,1'-biphenyl (**2o**).* According to a general procedure starting with biphenyl-2-carboxaldehyde (1.0 mmol, 182.2 mg), **2o** was observed in 75% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a pale yellow liquid (148.7 mg, 73%) after purification by flash chromatography (10% toluene in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80–7.78 (m, 1H), 7.53–7.48 (m, 2H), 7.47–7.39 (m, 3H), 7.37–7.33 (m, 3H), 6.53 (t, *J* = 54.8 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ − 107.4 (d, *J* = 54.8 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*1-(Difluoromethyl)naphthalene (**2p**).* According to a general procedure starting with 1-naphtaldehyde (1.0 mmol, 156.2 mg), **2p** was observed in 74% ^{19}F NMR yield using

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[7] Lalloo, N.; Malapit, C. A.; Taimoory, S. M.; Brigham, C. E.; Sandford, M. S. Decarbonylative Fluoroalkylation at Palladium(II): From Fundamental Organometallic Studies to Catalysis. *J. Am. Chem. Soc.* **2021**, *143*, 18617−18625, DOI: 10.1021/jacs.1c08551.

2-fluoro-4-nitrotoluene as an internal standard and was isolated as a clear liquid (116.8 mg, 66%) after purification by flash chromatography using hexanes as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18–8.15 (m, 1H), 7.97–7.95 (m, 1H), 7.92–7.90 (m, 1H), 7.70–7.68 (m, 1H), 7.61–7.54 (m, 2H), 7.52–7.48 (m, 1H), 7.13 (t, *J* = 55.2 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 110.8 (d, *J* = 55.1 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[5]

*2-(Difluoromethyl)naphthalene (**2q**).* According to a general procedure starting with 2-naphtaldehyde (1.0 mmol, 156.2 mg), **2q** was observed in 85% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a white solid (141.4 mg, 79%) after purification by flash chromatography using hexanes as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97–7.96 (m, 1H), 7.94–7.87 (m, 3H), 7.61–7.53 (m, 3H), 6.80 (t, *J* = 56.4 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 109.8 (d, *J* = 56.4 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[5]

*1-(4-(Difluoromethyl)phenyl)ethan-1-one (**2r**).* According to a general procedure starting with 4-acetylbenzaldehyde (0.94 mmol, 139.2 mg), **2r** was observed in 63% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a yellow oil (89.8 mg, 56%) after purification by flash chromatography (100% hexanes then 10% Et_2O in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = Hz, 2H), 7.62 (d, *J* = 8.1 Hz, 2H), 6.70 (t, *J* = 56.0 Hz, 1H), 2.64 (s, 3H); ^{19}F (470 MHz, $CDCl_3$) δ – 112.3 (d, *J* = 56.3, 2F). The analytical data are in agreement with those previously reported in the literature.[8]

*9-(Difluoromethyl)anthracene (**2s**).* According to a general procedure starting with anthracene-9-carbaldehyde (1.0 mmol, 206.2 mg), **2s** was observed in 81% ^{19}F NMR yield

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[8] Prakash, G. K. S.; Ganesh, S. K.; Jones, J.-P.; Kulkarni, A.; Masood, K.; Swabeck, J. K.; Olah, G. A. Copper-Mediated Difluoromethylation of (Hetero)aryl Iodides and β-Styryl Halides with Tributyl(difluoromethyl)stannane. *Angew. Chem. Int. Ed.*, **2012**, 51, 12090-12094, DOI: 10.1002/anie.201205850.

using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a yellow solid (180.7 mg, 79%) after purification by flash chromatography (20% toluene in hexanes). Mp = 69.4–72.6 °C. FT-IR (ν/cm^{-1}): 3034, 1950, 1817, 1796, 1626, 1452, 1261, 1161, 1099, 1009, 930, 899, 876, 731, 719. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (s, 1H), 8.47–8.44 (m, 2H), 8.04–8.02 (m, 2H), 7.99 (t, J = 53.7 Hz, 1H), 7.60–7.57 (m, 2H), 7.52–7.48 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 131.5 (t, $J_{C–F}$ = 2.0 Hz), 131.1, 129.6 (t, $J_{C–F}$ = 3.6 Hz), 129.2, 127.3, 125.2, 123.3 (t, $J_{C–F}$ = 2.2 Hz), 123.2 (t, $J_{C–F}$ = 20.4 Hz), 114.0 (t, $J_{C–F}$ = 236.1 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 106.6 (d, J = 53.7 Hz, 2F). GC-MS (EI): m/z calcd for $C_{15}H_{10}F_2$ $[M]^+$ 228.07 found 228.08. Under all the conditions tested for HRMS analysis (ESI-TOF or APPI-TOF with or without additives), no significant ions could be detected.

*2-(4-(Difluoromethyl)phenyl)pyridine (**2t**).* According to a general procedure starting with 4-(2-pyridyl)benzaldehyde (1.0 mmol, 183.2 mg), **2t** was observed in 94% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as an off-white solid (178.0 mg, 87%) after purification by flash chromatography (30% Et_2O in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72–8.71 (m, 1H), 8.09–8.07 (m, 2H), 7.79–7.73 (m, 2H), 7.62–7.60 (m, 2H), 7.28–7.25 (m, 1H), 6.70 (t, J = 56.4 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 110.9 (d, J = 56.5 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*4-(Difluoromethyl)quinoline (**2u**).* According to a general procedure starting with 4-quinolinecarboxaldehyde (1.0 mmol, 157.2 mg), **2u** was observed in 92% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a yellow solid (153.8 mg, 86%) after purification by flash chromatography (20 to 40% EtOAc in hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03–9.02 (m, 1H), 8.22–8.20 (m, 1H), 8.11–8.08 (m, 1H), 7.82–7.78 (m, 1H), 7.68–7.65 (m, 1H), 7.60–7.59 (m, 1H), 7.16 (t, J = 54.5 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ −115.09 (d, J = 54.7 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*2-(Difluoromethyl)quinoline (**2v**).* According to a general procedure starting with 2-quinolinecarboxaldehyde (1.0 mmol, 157.2 mg), **2v** was observed in 86% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a pale yellow liquid (139.6 mg, 78%) after purification by flash chromatography using toluene as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, J = 8.5 Hz, 1H), 8.15 (d, J = 8.5 Hz, 1H), 7.88 (dd, J = 8.2, 1.4 Hz, 1H), 7.79 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.63 (dd, J = 8.0, 6.9 Hz, 1H), 6.79 (t, J = 55.3 Hz, 1H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 114.2 (d, J = 55.5 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[4]

*2-(Difluoromethyl)-1-methyl-1H-imidazole (**2w**).* According to a general procedure starting with 1-Methyl-2-imidazolecarboxaldehyde (1.0 mmol, 110.1 mg), **2w** was observed in 30% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard.

6. Deoxofluorination of aliphatic aldehydes

*(3,3-Difluoropropyl)benzene (**3a**).* According to a general procedure starting with 3-phenylpropionaldehyde (1.0 mmol, 134.2 mg), **3a** was observed in 79% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a colorless liquid (92.1 mg, 59%) after purification by flash chromatography using pentane as the eluent. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33–7.29 (m, 2H), 7.25–7.19 (m, 3H), 5.80 (tt, J = 56.7, 4.5 Hz, 1H), 2.80–2.77 (m, 2H) 2.21–2.10 (m, 2H). ^{19}F NMR (470 MHz, $CDCl_3$) δ – 117.1 (dt, J = 56.8, 17.1 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[9]

*1-Benzoyloxy-4,4-difluorobutane (**3b**).* According to a general procedure starting with 4-oxobutyl benzoate (0.76 mmol, 146.2 mg), **3b** was observed in 61% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard and was isolated as a colorless liquid (126.4 mg, 59%) after purification by flash chromatography (10% EtOAc in hexanes). ^{1}H

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[9] Beaulieu, F.; Beauregard, L.-P.; Courchesne, G.; Couturier, M.; LaFlamme, F.; L'Heureux, A. Aminodifluorosulfinium Tetrafluoroborate Salts as Stable and Crystalline Deoxofluorinating Reagents. *Org. Lett.* **2009**, 11, 21, 5050–5053, DOI:10.1021/ol902039q.

NMR (500 MHz, $CDCl_3$) δ 8.05–8.03 (m, 2H), 7.59–7.56 (m, 1H), 7.47–7.43 (m, 2H), 5.91 (tt, *J* = 56.5, 4.1 Hz, 1H), 4.39–4.37 (m, 2H) 2.08–1.93 (m, 4H). ^{19}F NMR (470 MHz, $CDCl_3$) δ − 116.3 (dt, *J* = 56.6, 17.1 Hz, 2F). The analytical data are in agreement with those previously reported in the literature.[10]

*(Difluoromethyl)cyclohexane (**3c**).* According to a general procedure starting with cyclohexanecarbaldehyde (1.0 mmol, 112.2 mg), **3c** was observed in 67% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard. The analytical data are in agreement with those previously reported in the literature.[11]

*tert-Butyl 4-(difluoromethyl)piperidine-1-carboxylate (**3d**).* According to a general procedure starting with tert-butyl 4-formylpiperidine-1-carboxylate, **3d** was observed in 42% ^{19}F NMR yield using 2-fluoro-4-nitrotoluene as an internal standard. The analytical data are in agreement with those previously reported in the literature.[12]

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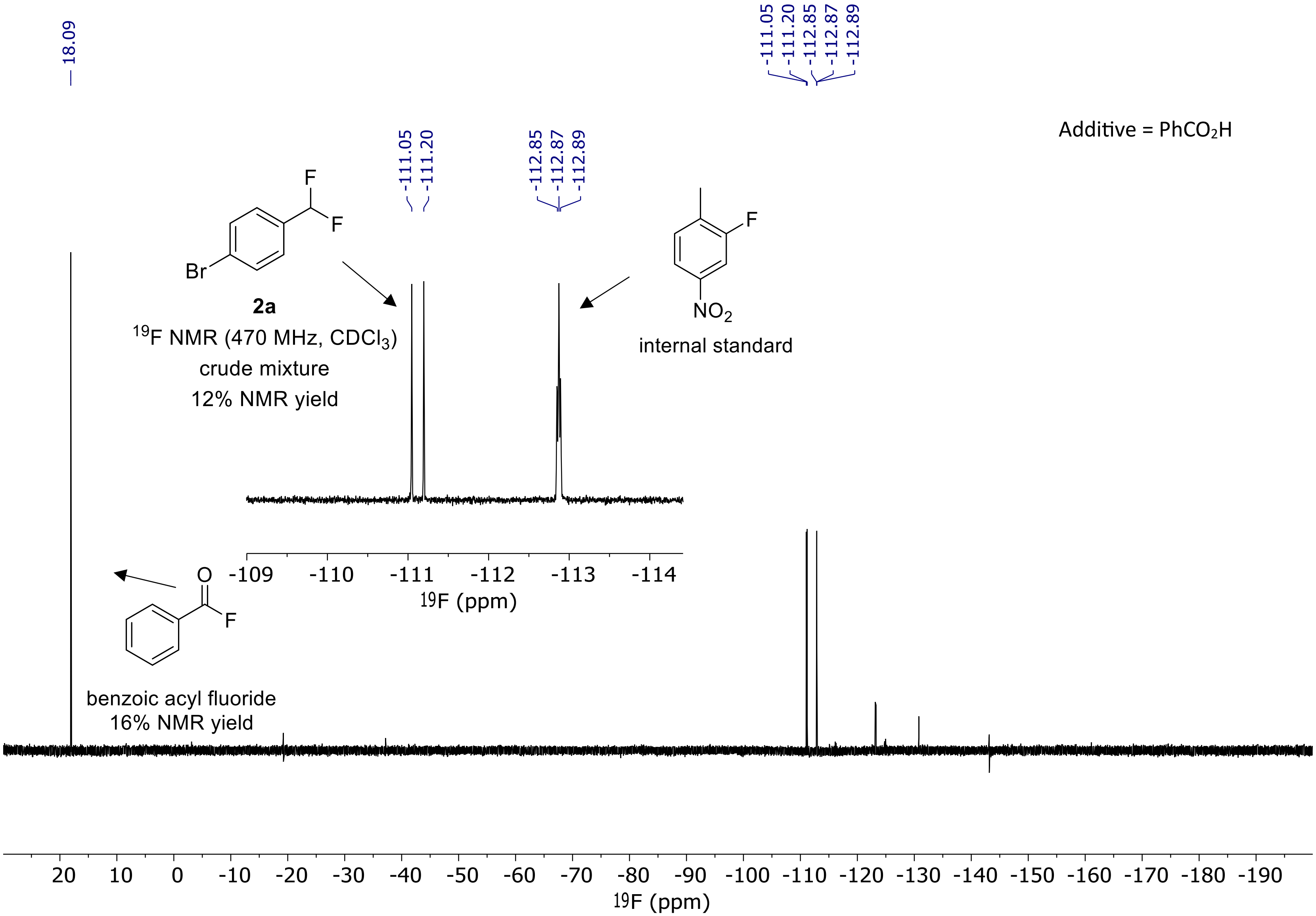
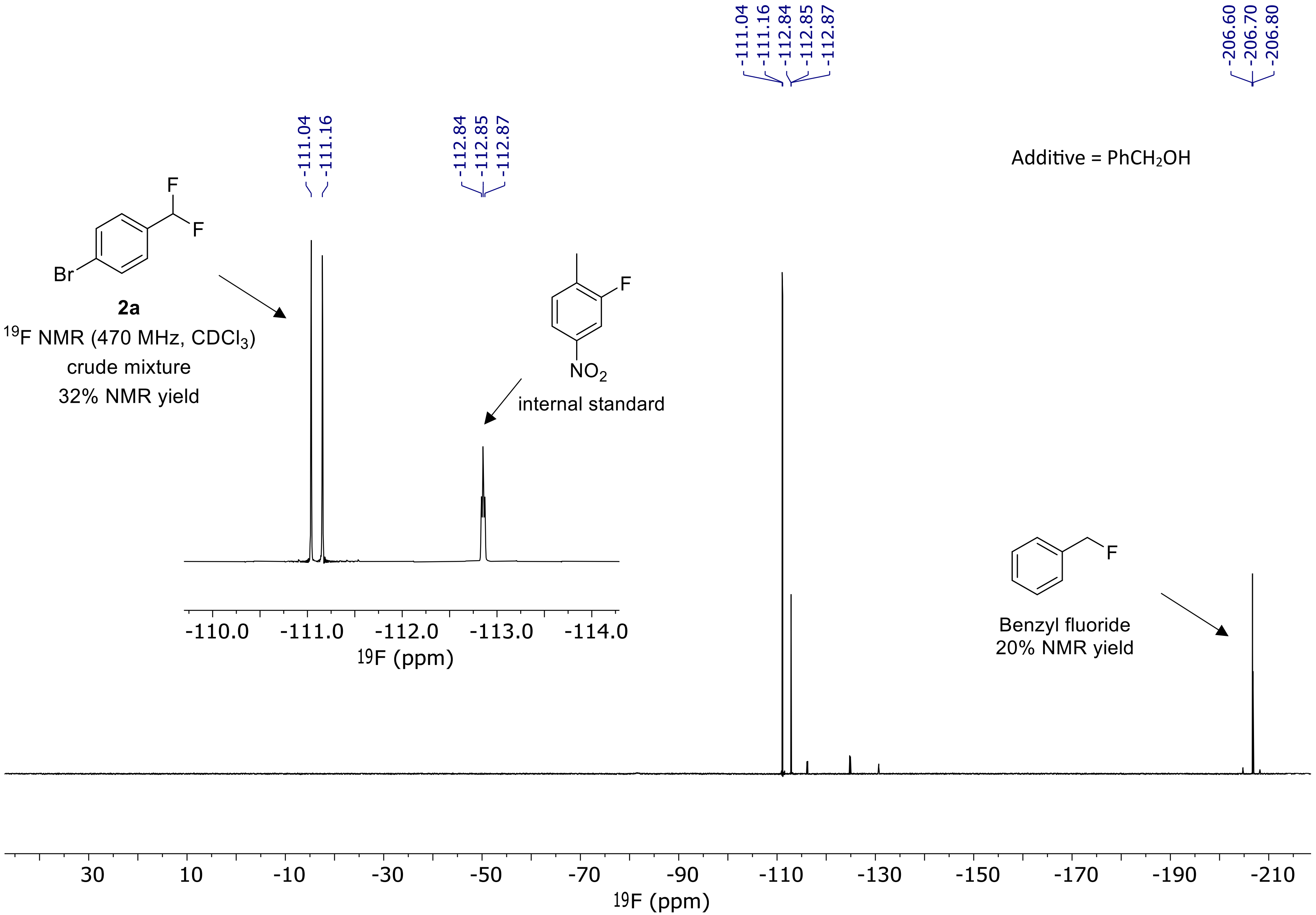
[10] Vorberg, R.; Trapp, N.; Zimmerli, D.; Wagner, B.; Fischer, H.; Kratochwil, N. A.; Kansy, M.; Carreira, E. M.; Müller, K. Effect of Partially Fluorinated N-Alkyl-Substituted Piperidine-2-carboxamides on Pharmacologically Relevant Properties. *ChemMedChem* **2016**, 11, 2216-2239, DOI:10.1002/cmdc.201600325.

[11] Bujok, R.; Makosza, M. Synthesis of 1,1-Difluoroalkanes via Phase Transfer Catalysed Reaction of 1,1-*bis*-Triflates with KF in the Presence of Cocatalyst – Ph_3SnF. *Synlett* **2002**, 1285-1286, DOI: 10.1055/s-2002-32959.

[12] Zeng, X.; Yan, W.; Zacate, S. B.; Cai, A.; Wang, Y.; Yang, D.; Yang, K.; Liu, W. Copper-Catalyzed Deaminative Difluoromethylation. *Angew. Chem. Int. Ed.* **2020**, *59*, 16398-16403. DOI: 10.1002/anie.202006048.

7. NMR spectra





Additive = $PhCH_2OH$

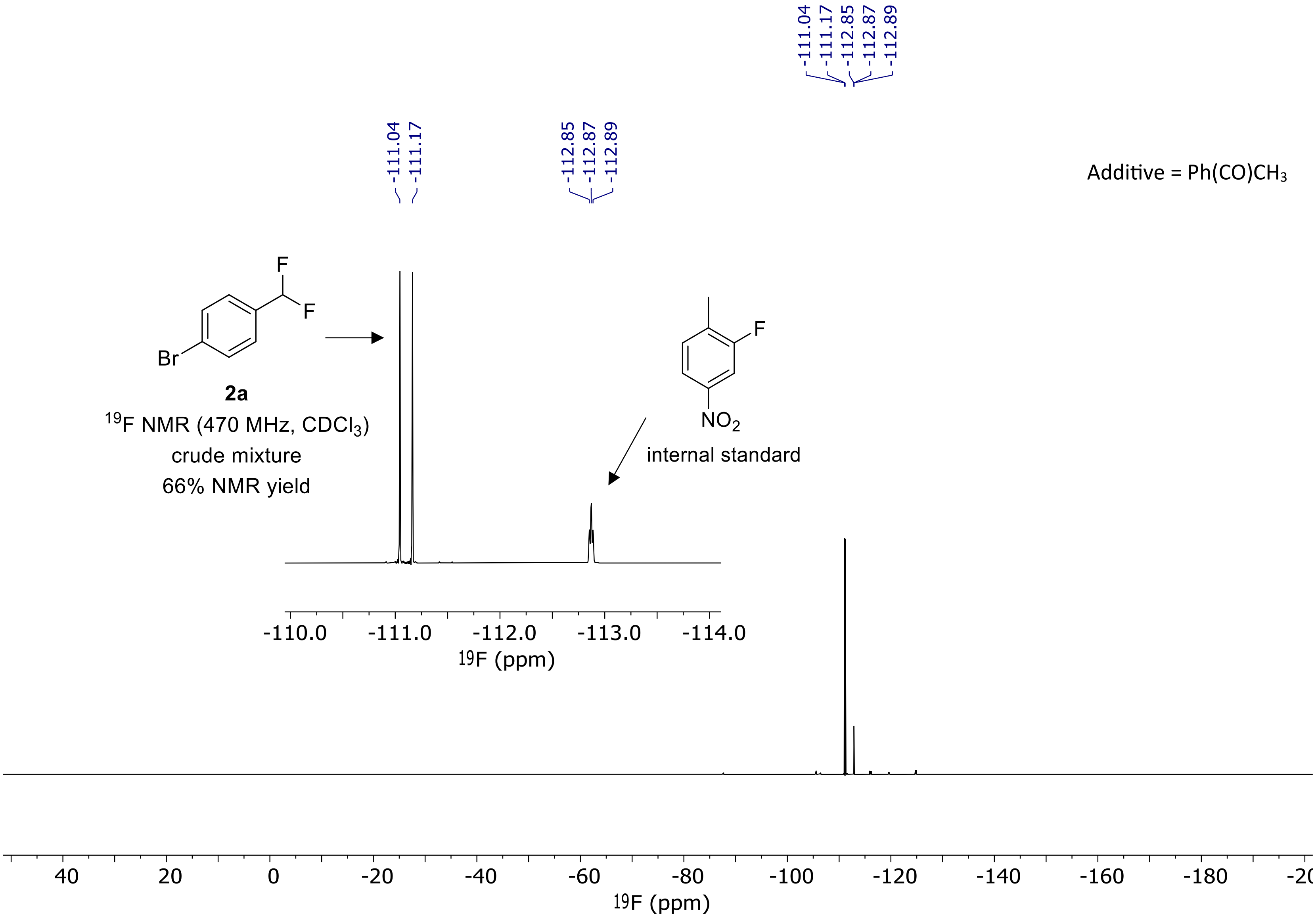
2a

^{19}F NMR (470 MHz, $CDCl_3$)
crude mixture
32% NMR yield

internal standard

Benzyl fluoride
20% NMR yield

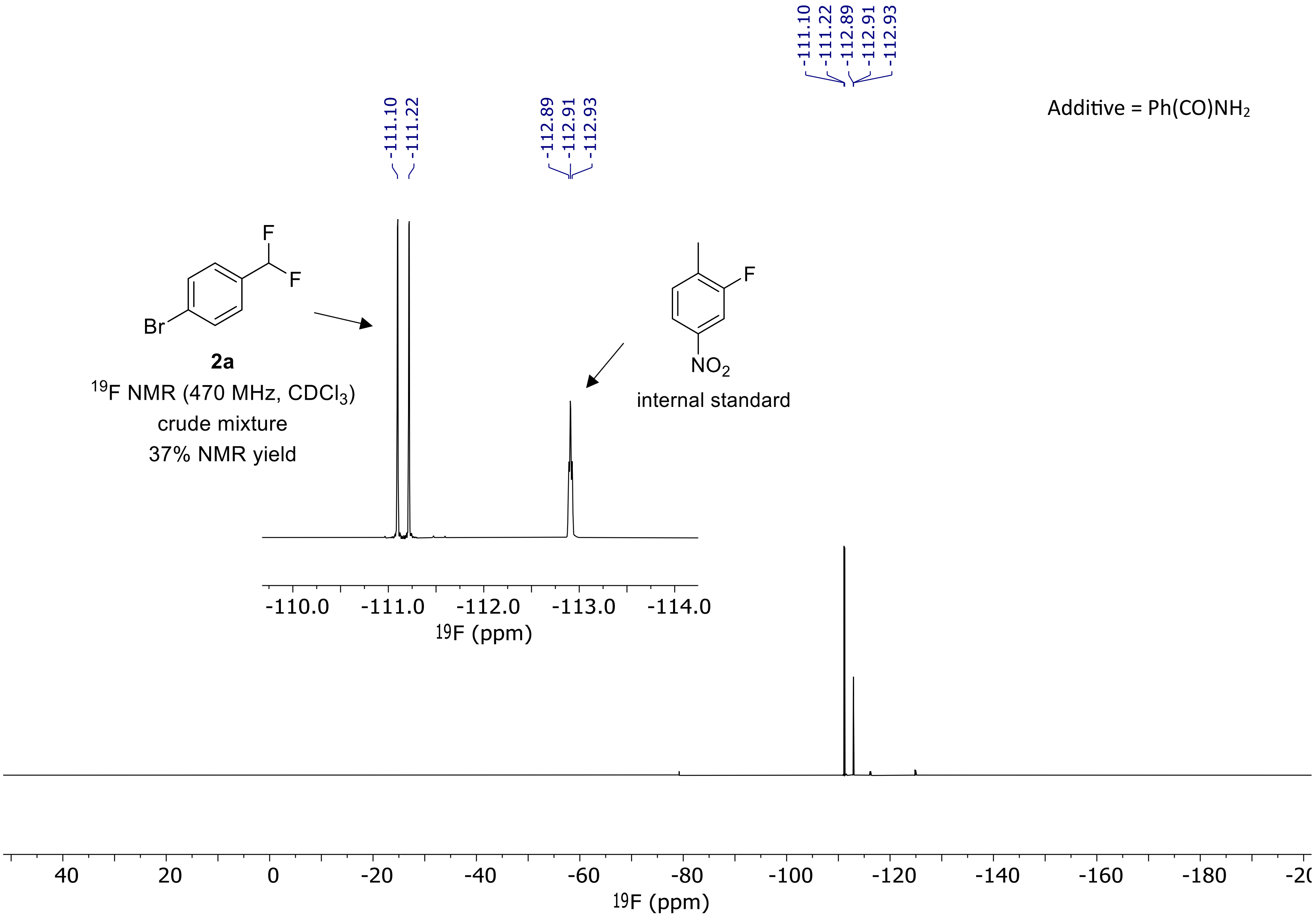
Additive = Ph(CO)CH_3

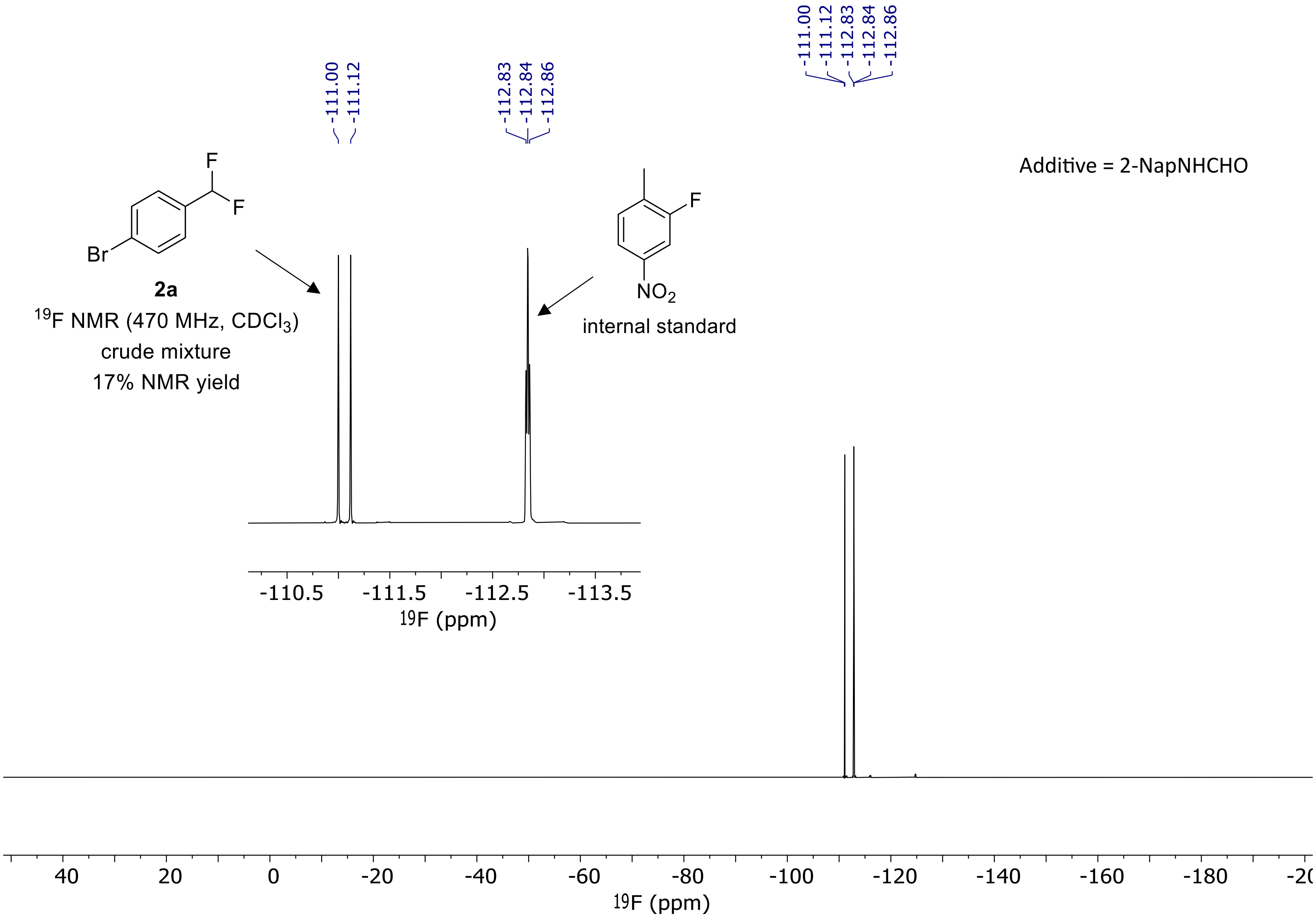

2a

^{19}F NMR (470 MHz, $CDCl_3$)

crude mixture

66% NMR yield


Additive = Ph(CO)NH$_2$
-111.10
-111.22
-112.89
-112.91
-112.93
2a
^{19}F NMR (470 MHz, CDCl$_3$)
crude mixture
37% NMR yield
F
F
Br
F
NO$_2$
internal standard
-110.0
-111.0
-112.0
-113.0
-114.0
^{19}F (ppm)
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
^{19}F (ppm)



Additive = 2-NapNHCHO

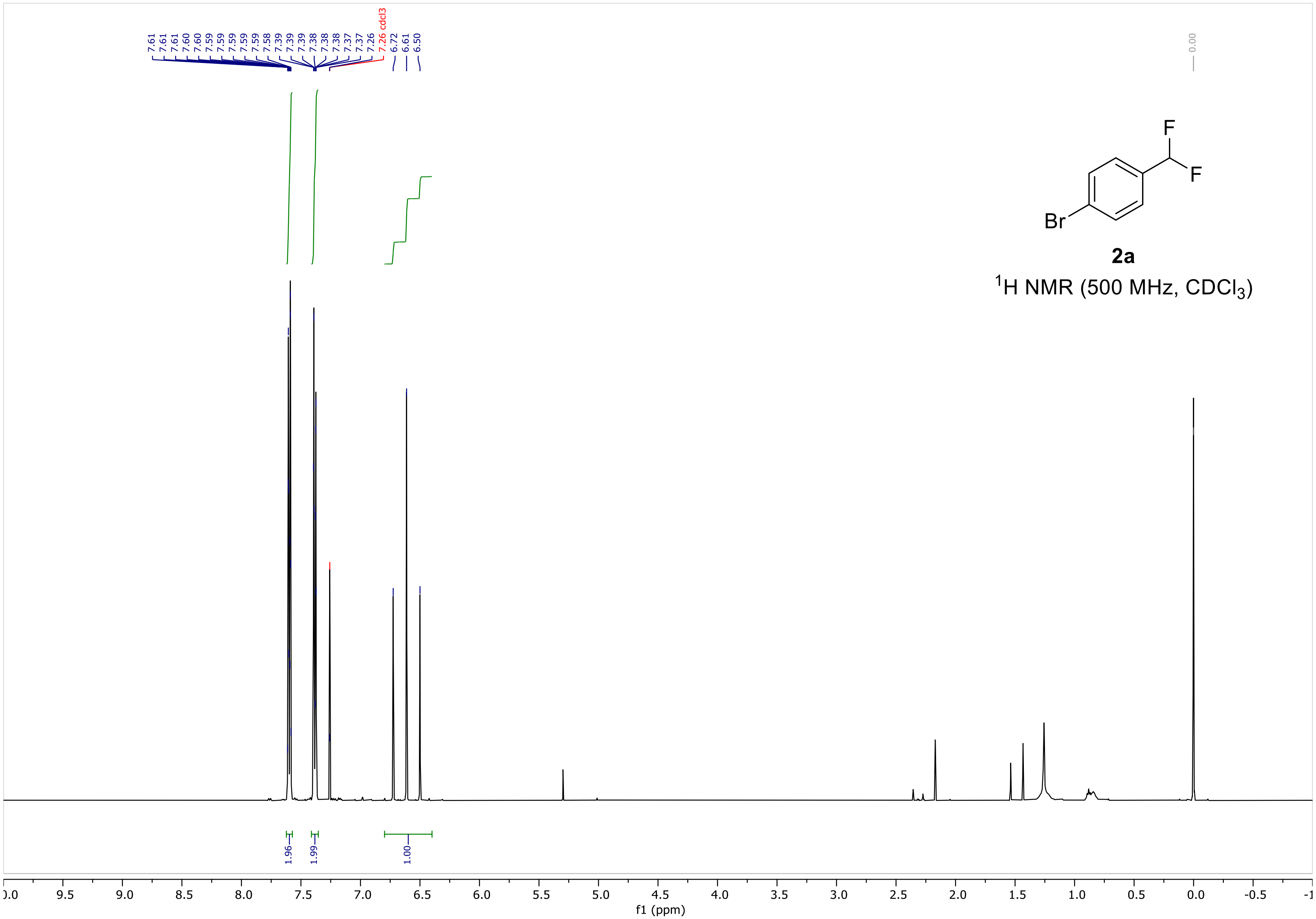
2a

^{19}F NMR (470 MHz, CDCl$_3$)

crude mixture

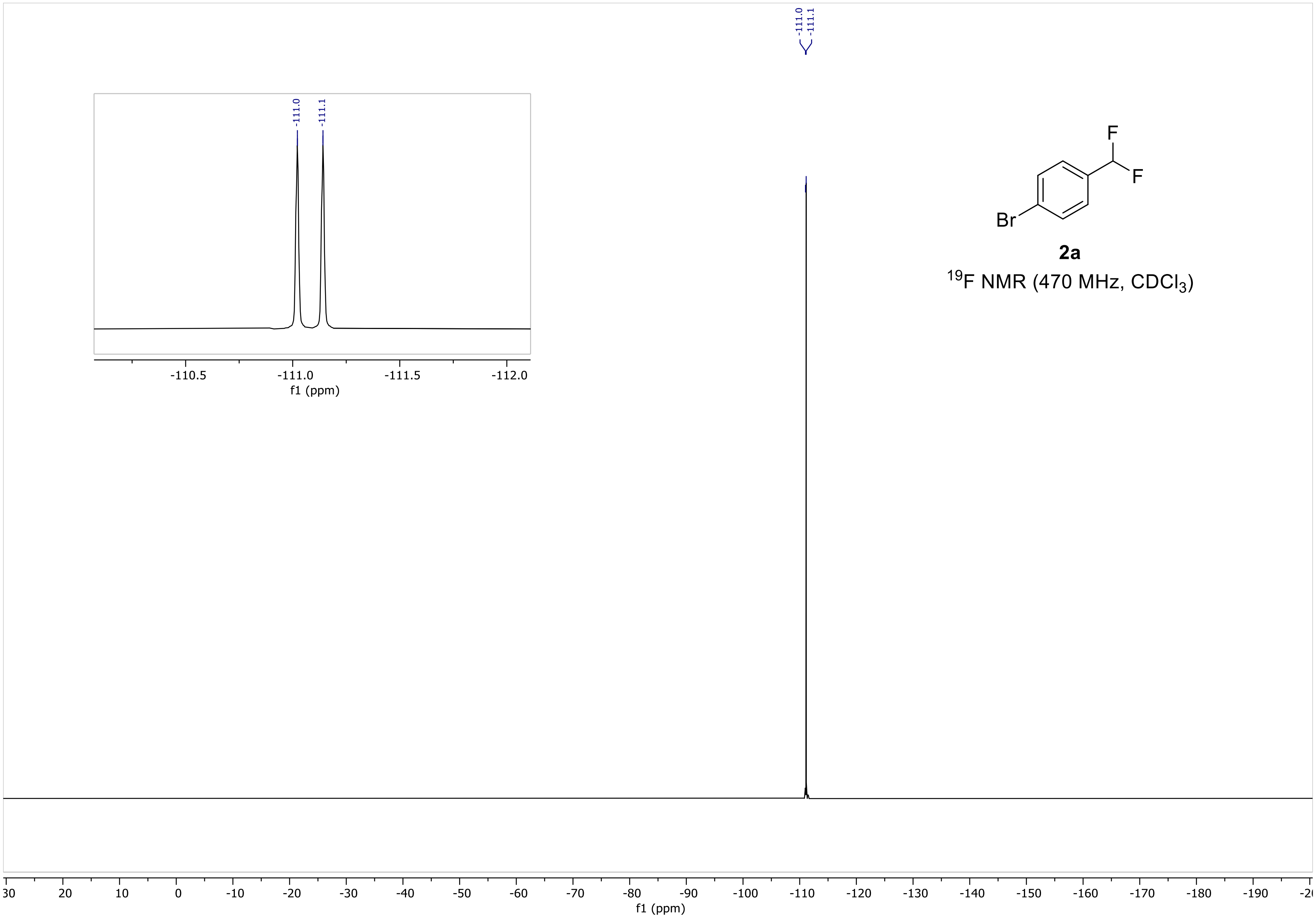
17% NMR yield

internal standard



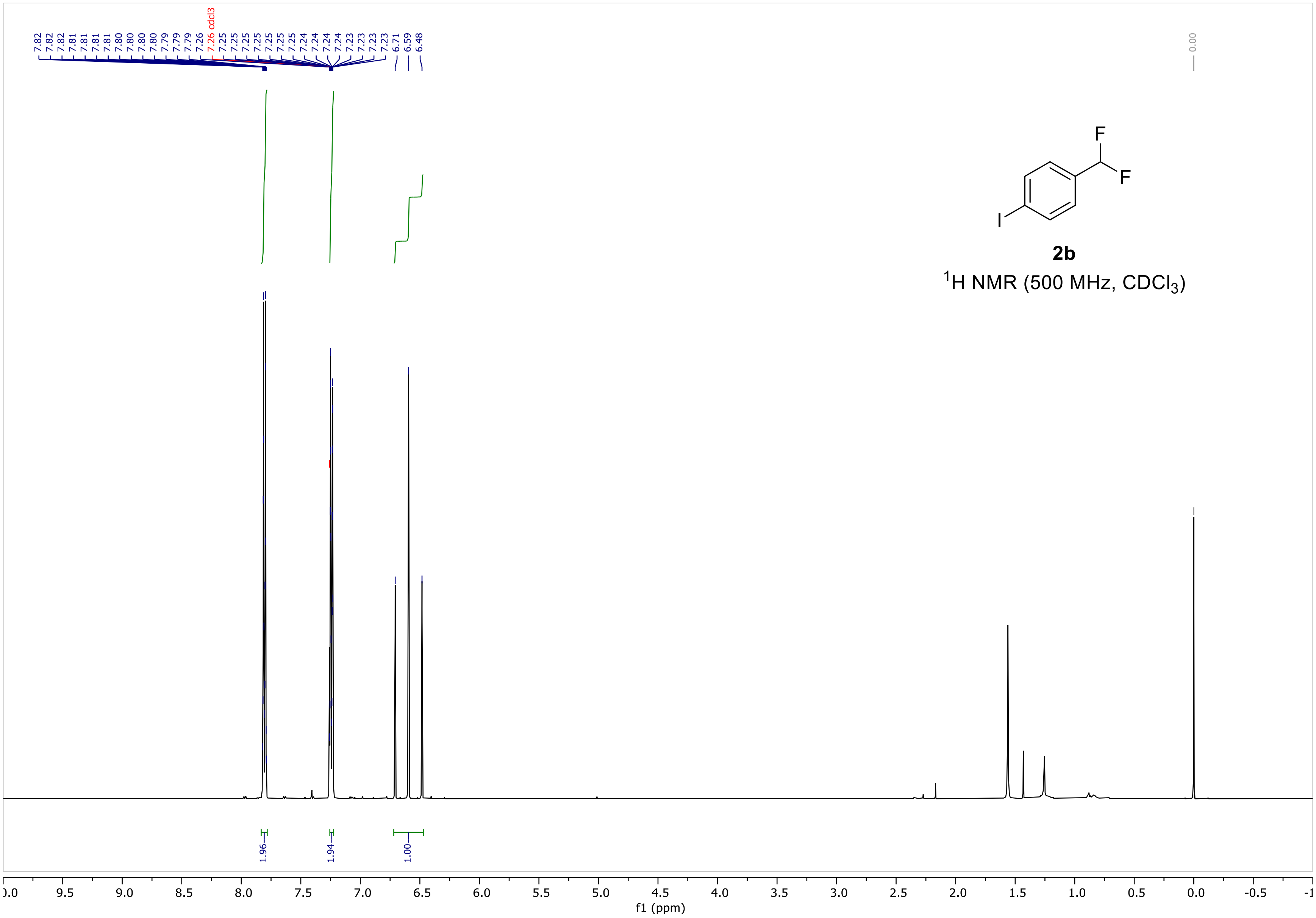
2a

^1H NMR (500 MHz, $CDCl_3$)



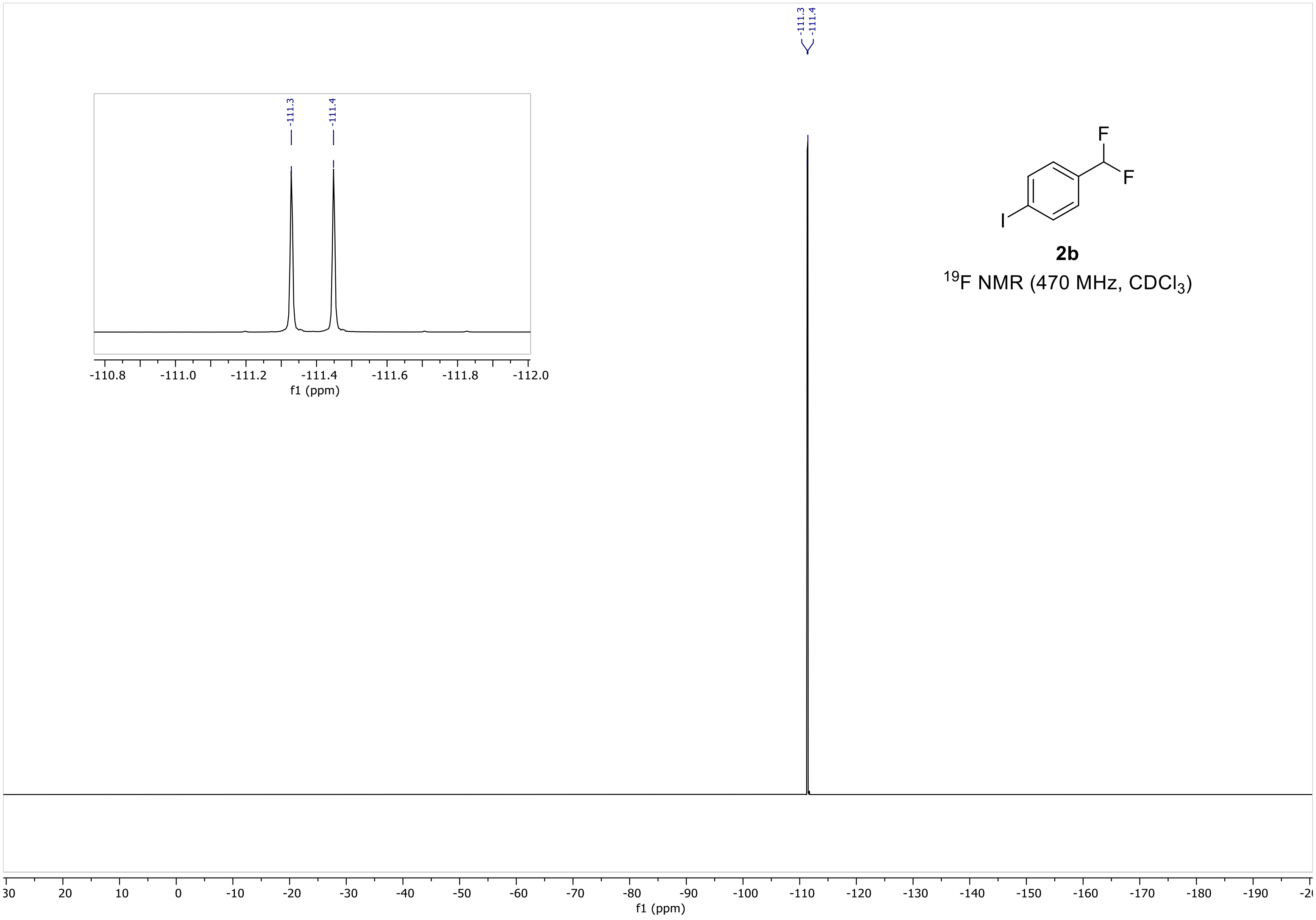
2a

^{19}F NMR (470 MHz, CDCl$_3$)



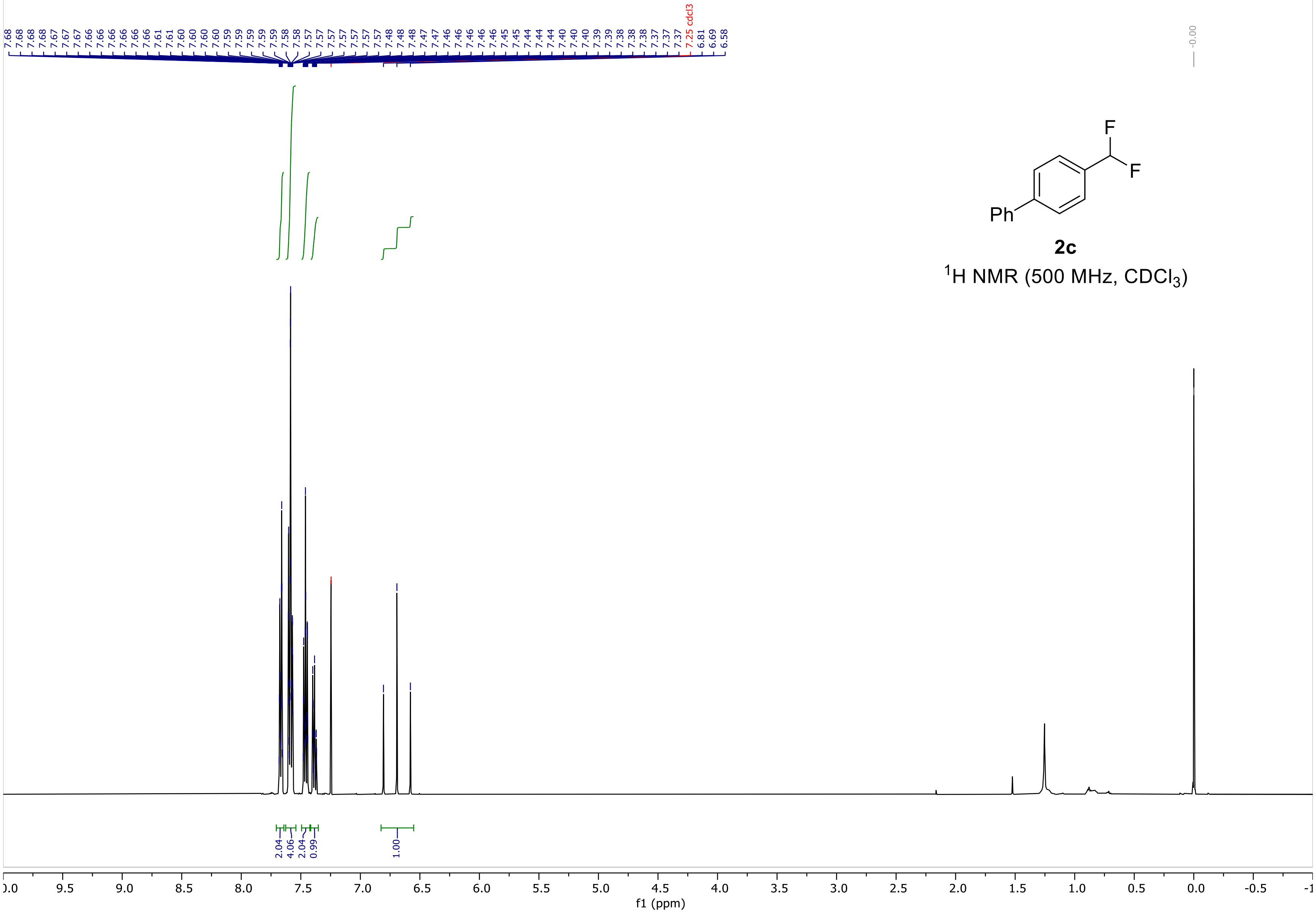
2b

^{1}H NMR (500 MHz, CDCl$_3$)



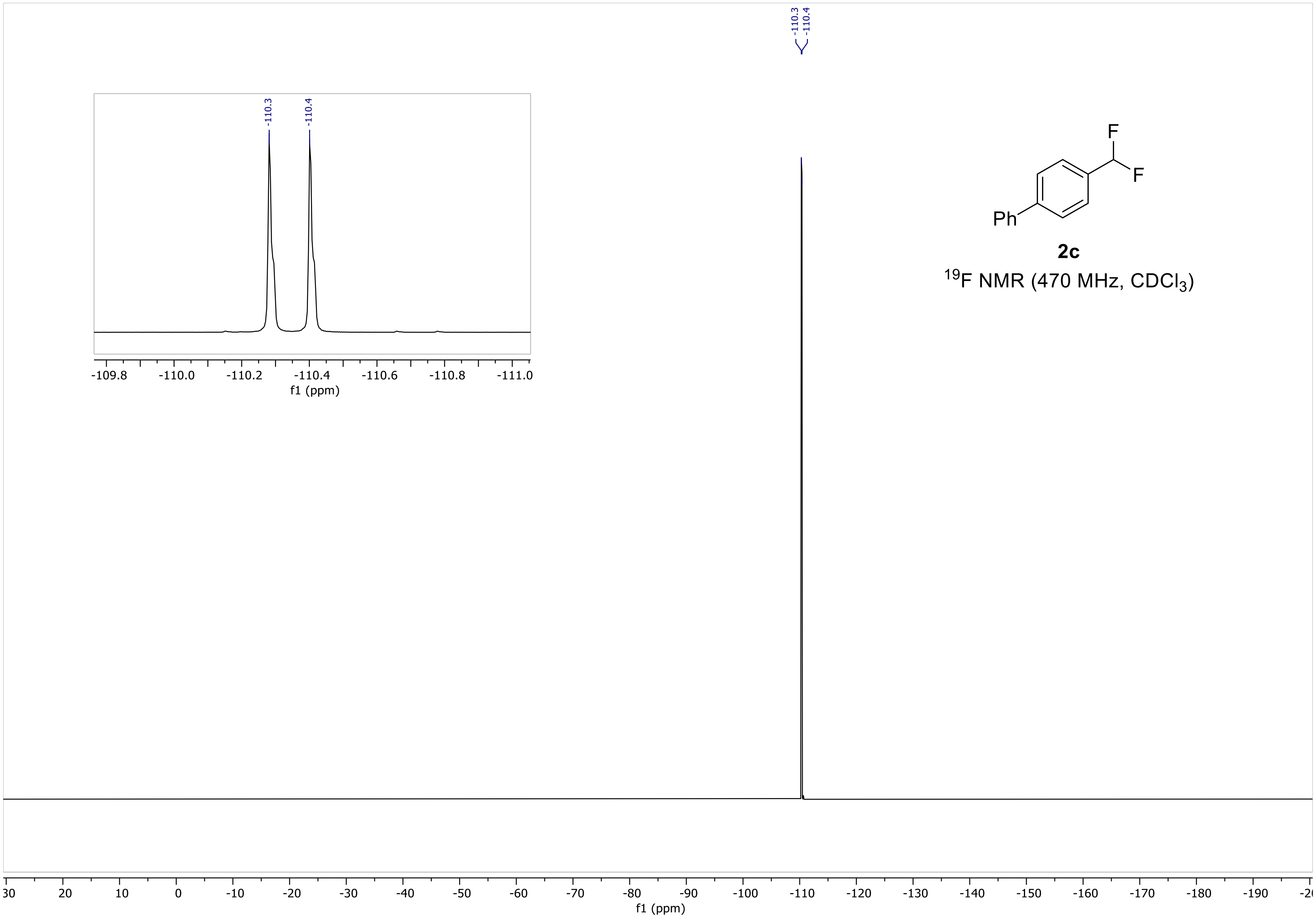
2b

^{19}F NMR (470 MHz, $CDCl_3$)



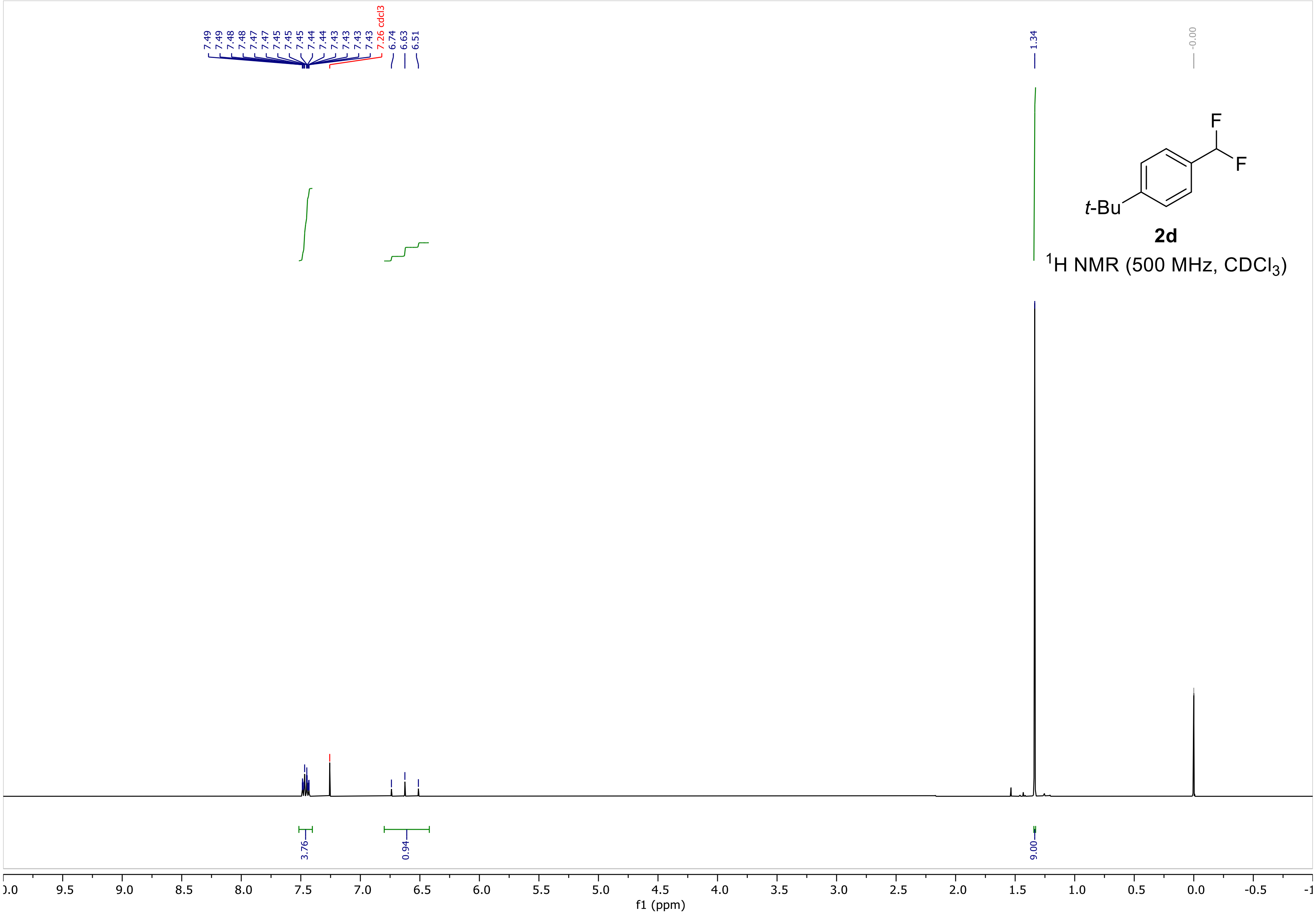
2c

^{1}H NMR (500 MHz, CDCl$_3$)



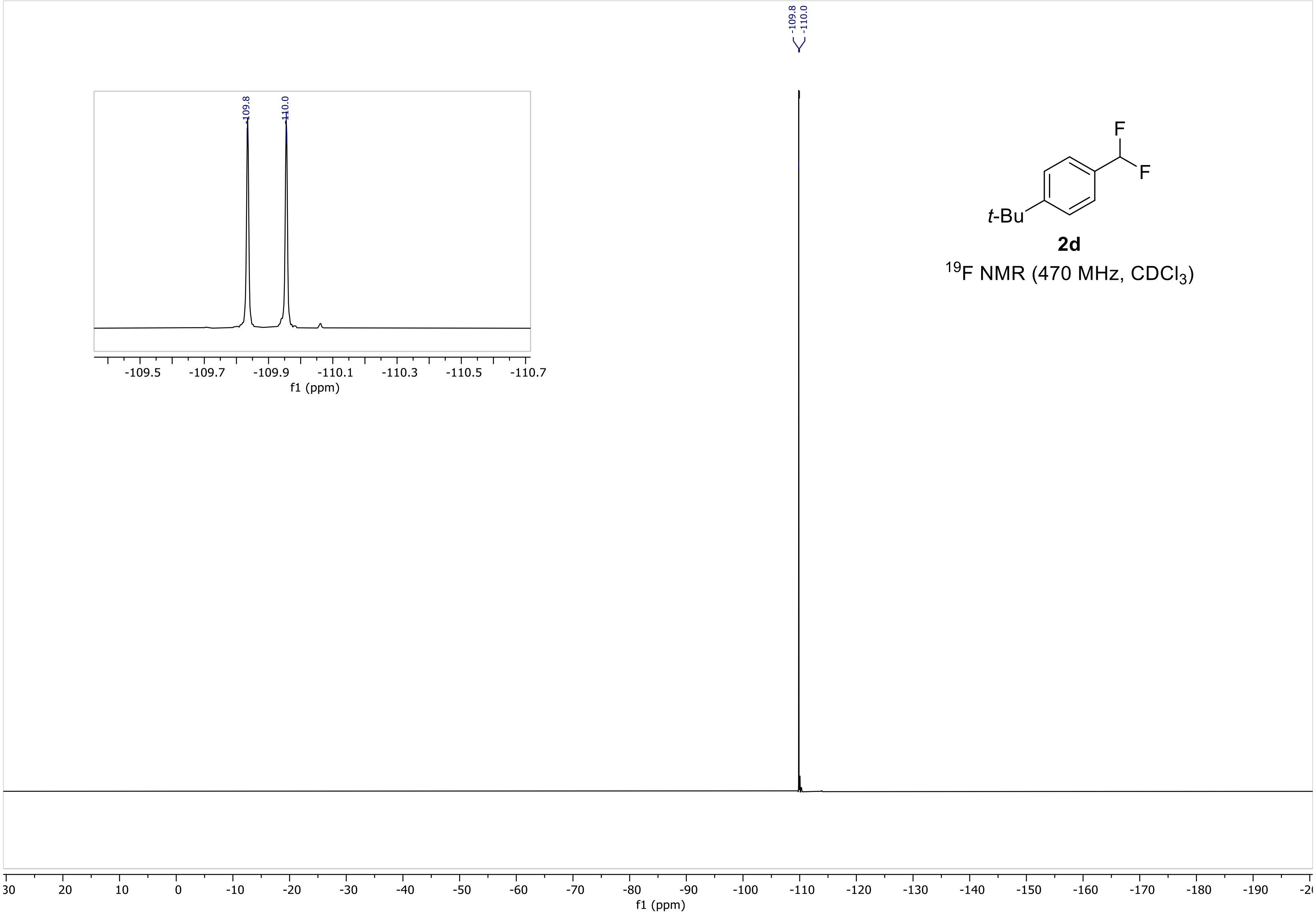
2c

^{19}F NMR (470 MHz, $CDCl_3$)



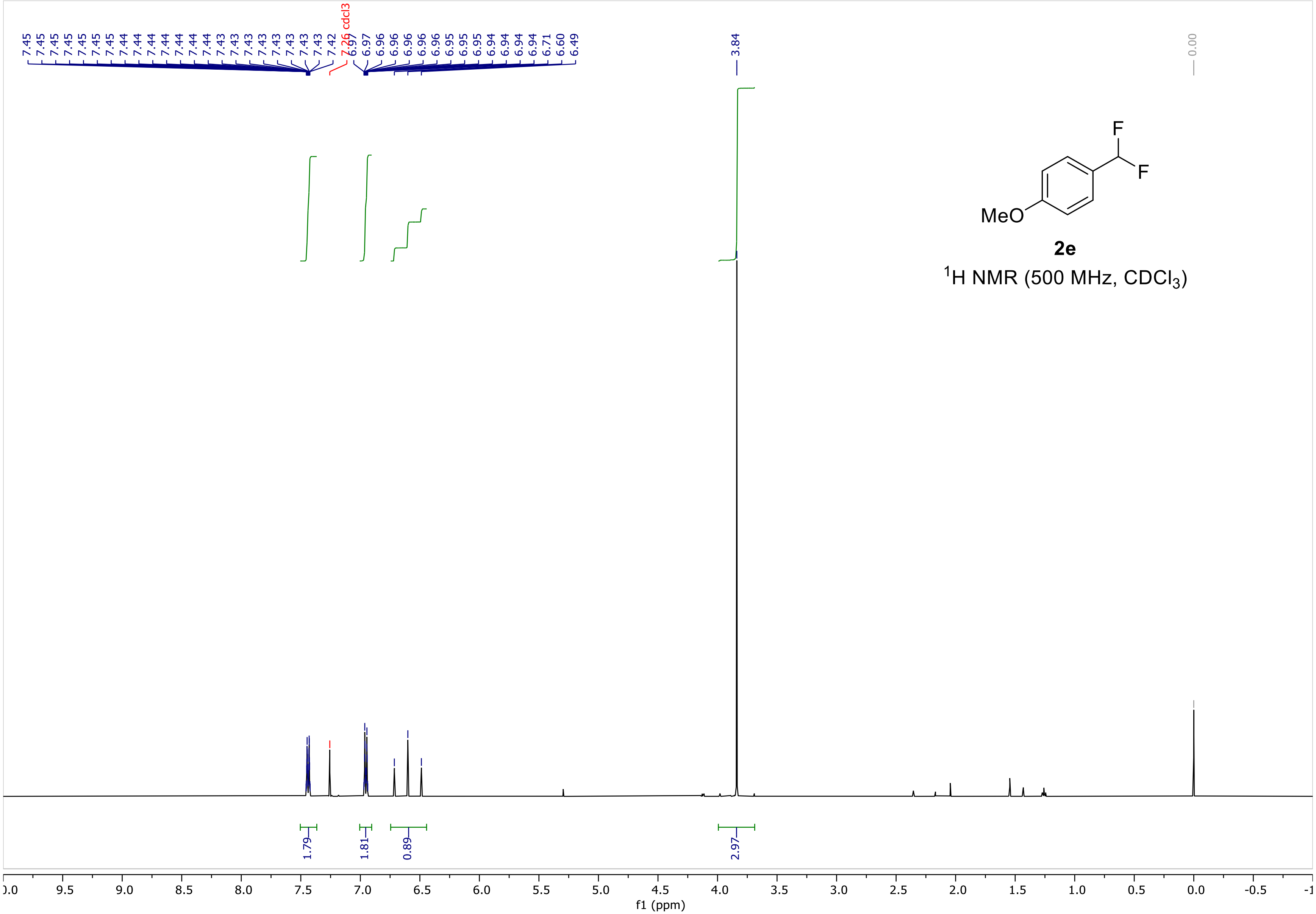
2d

^{1}H NMR (500 MHz, $CDCl_3$)



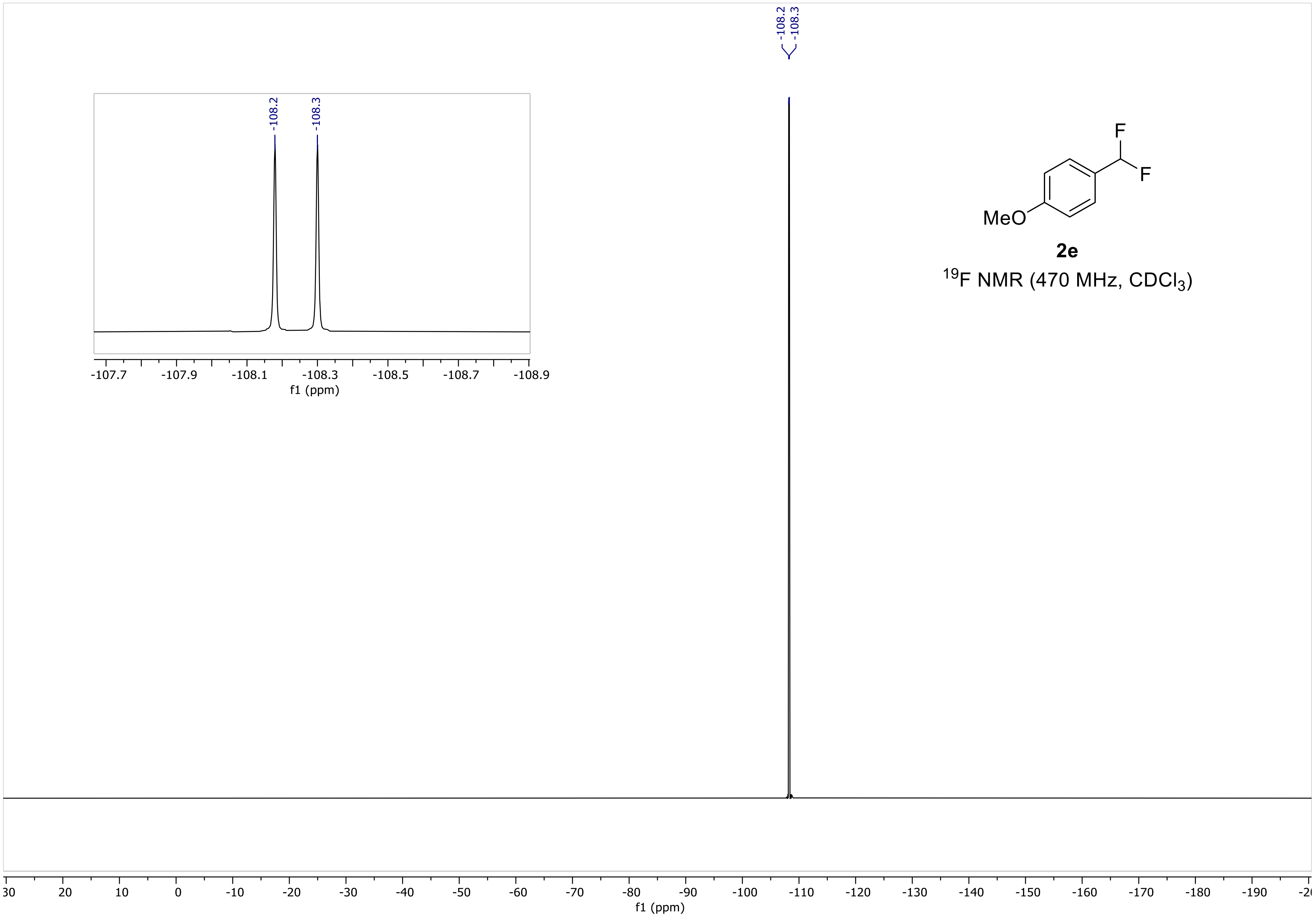
2d

^{19}F NMR (470 MHz, $CDCl_3$)



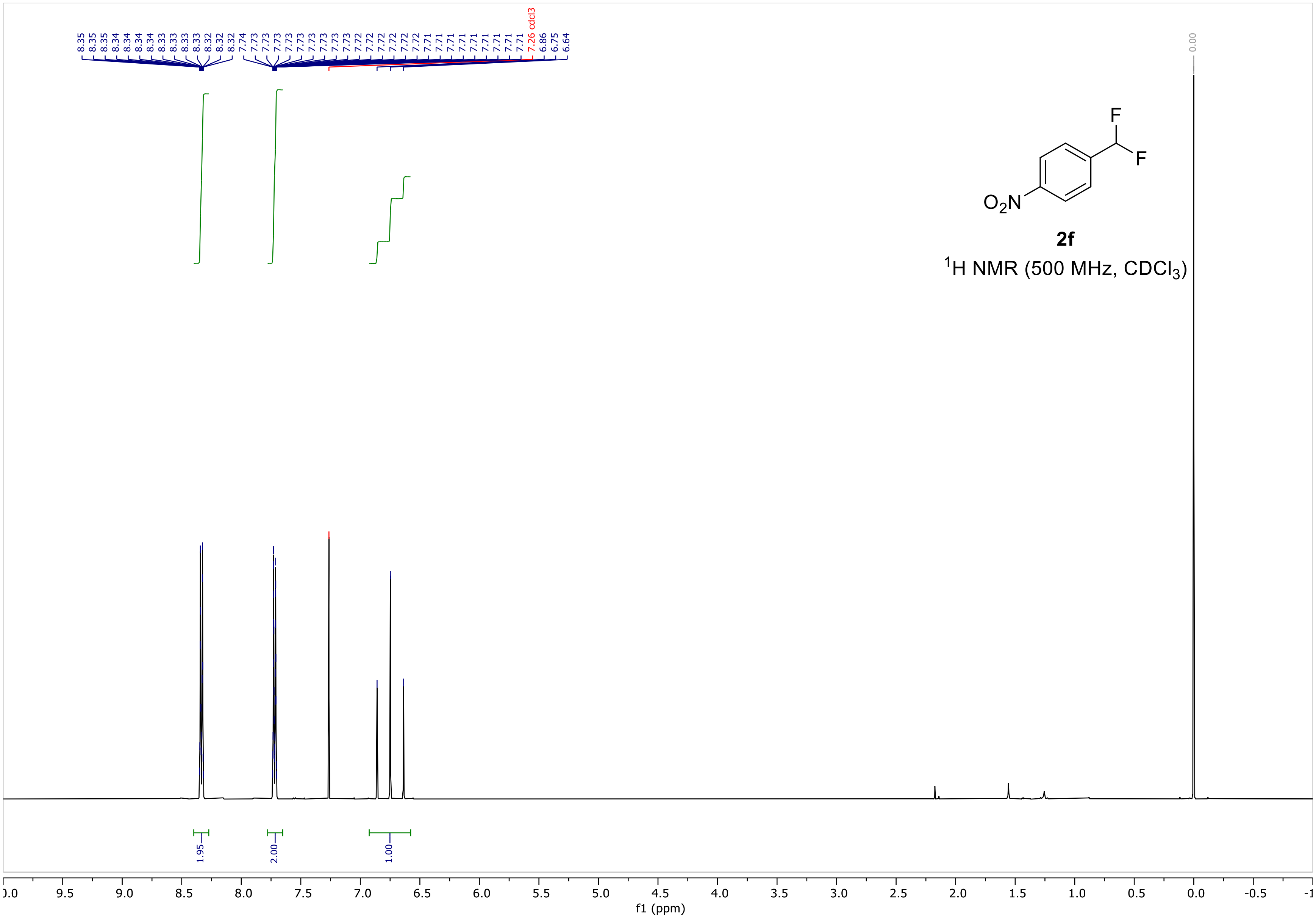
2e

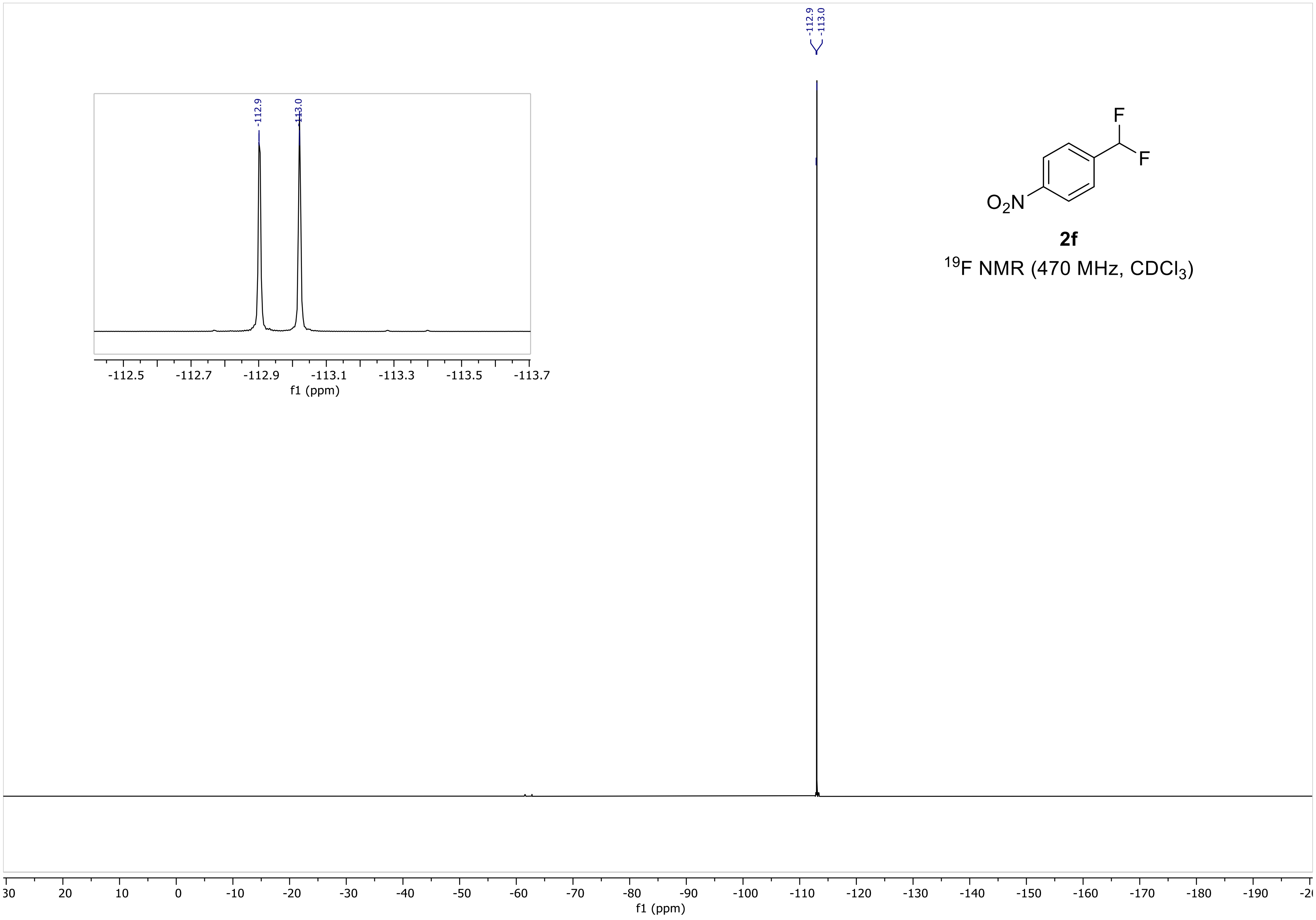
^{1}H NMR (500 MHz, CDCl$_3$)



2e

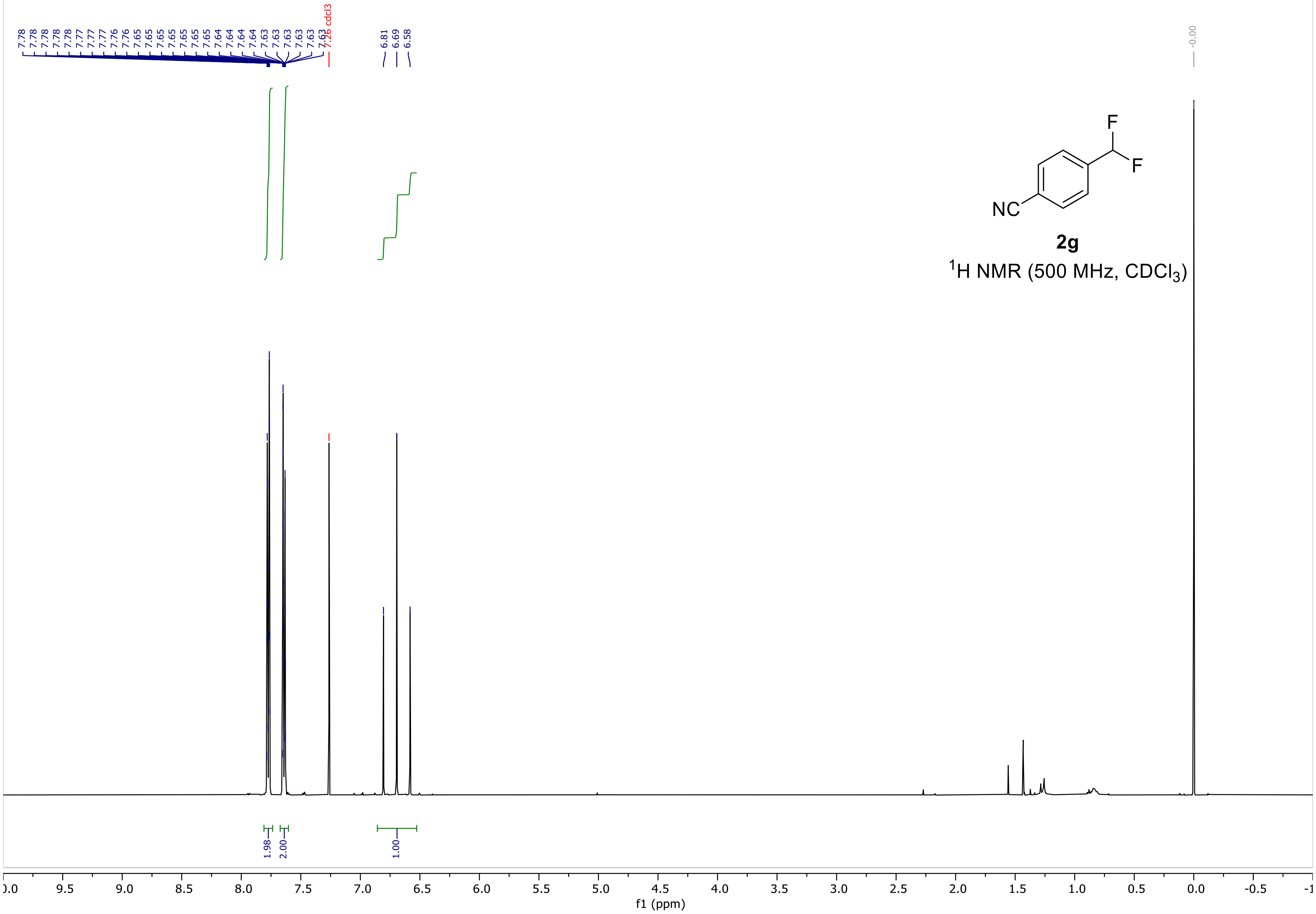
^{19}F NMR (470 MHz, CDCl$_3$)


8.35
8.35
8.35
8.34
8.34
8.34
8.34
8.33
8.33
8.33
8.33
8.32
8.32
8.32
7.74
7.73
7.73
7.73
7.73
7.73
7.73
7.73
7.73
7.73
7.72
7.72
7.72
7.72
7.72
7.72
7.71
7.71
7.71
7.71
7.71
7.71
7.71
7.71
7.71
7.26 cdcl3
6.86
6.75
6.64
0.00
F
F
O2N
2f
1H NMR (500 MHz, CDCl3)
1.95
2.00
1.00
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)



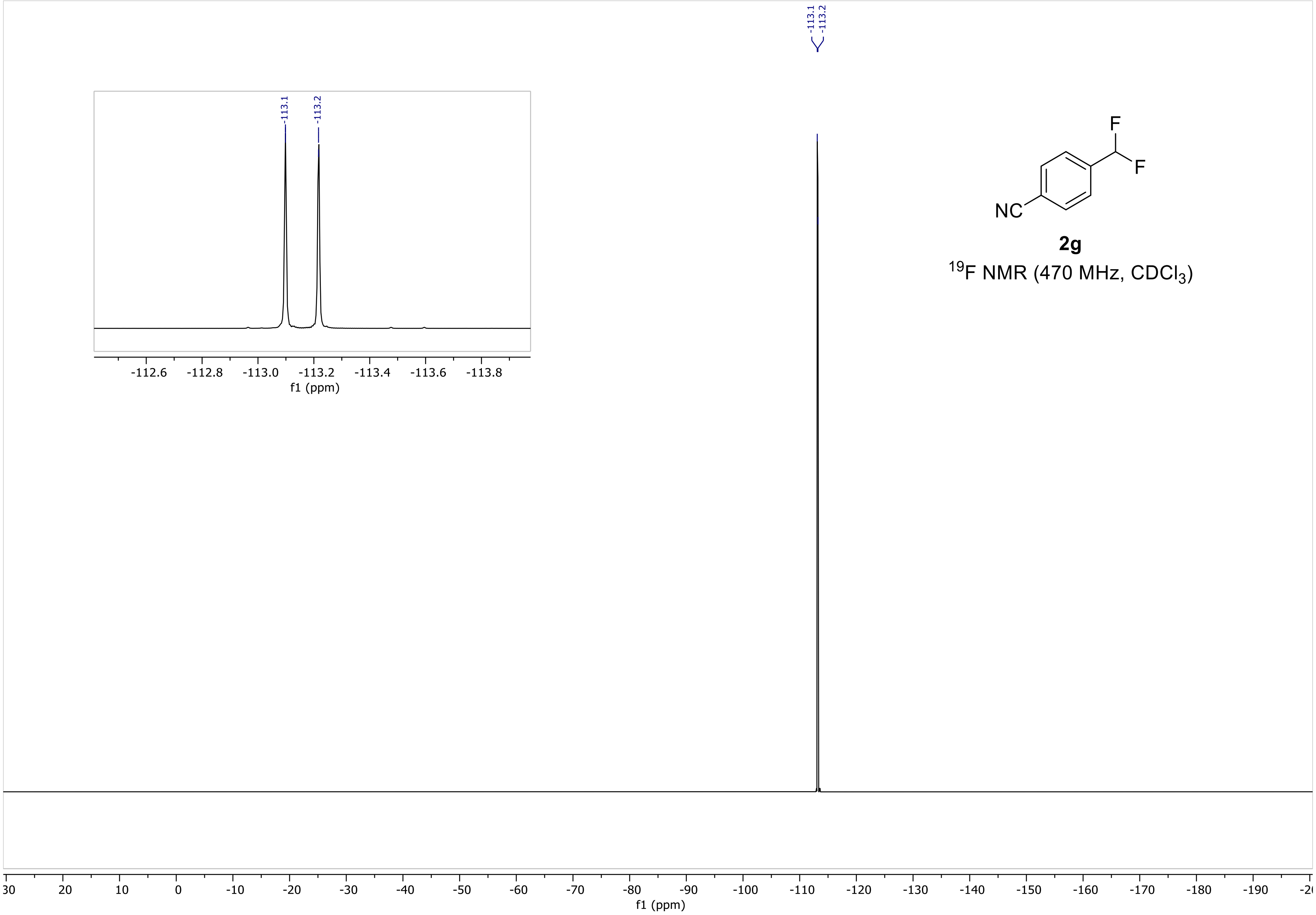
2f

^{19}F NMR (470 MHz, CDCl$_3$)



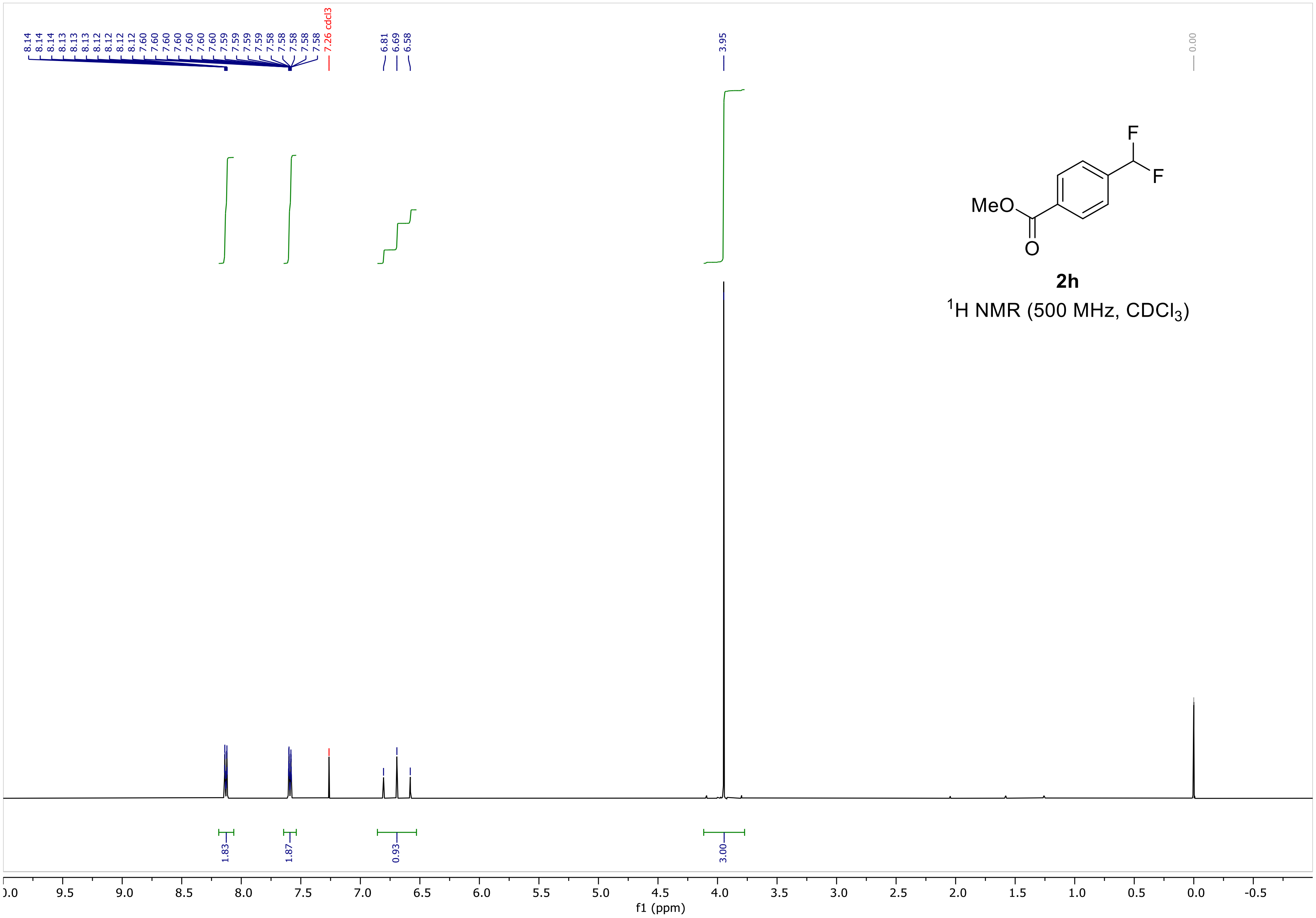
2g

^{1}H NMR (500 MHz, CDCl$_3$)



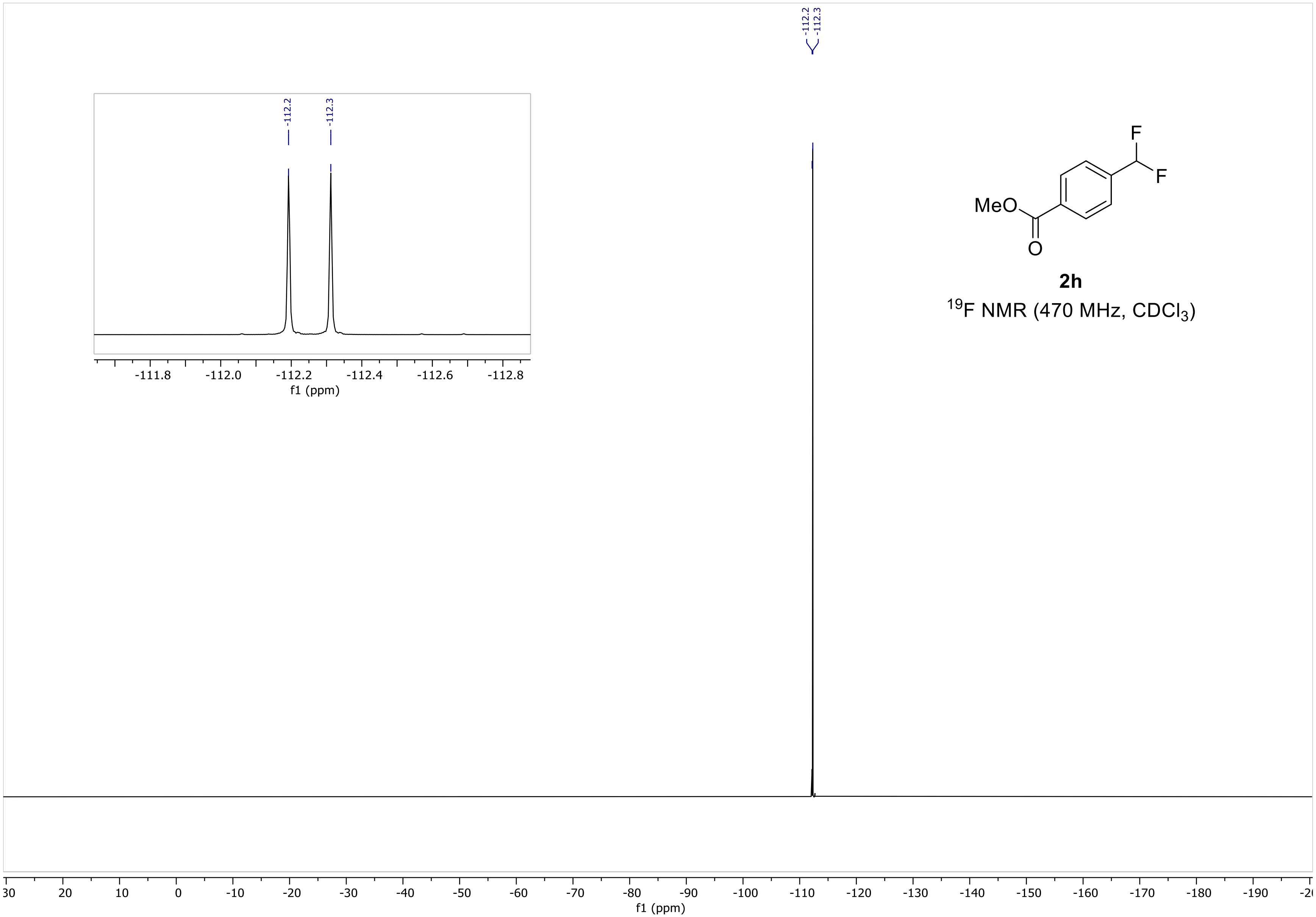
2g

^{19}F NMR (470 MHz, CDCl$_3$)



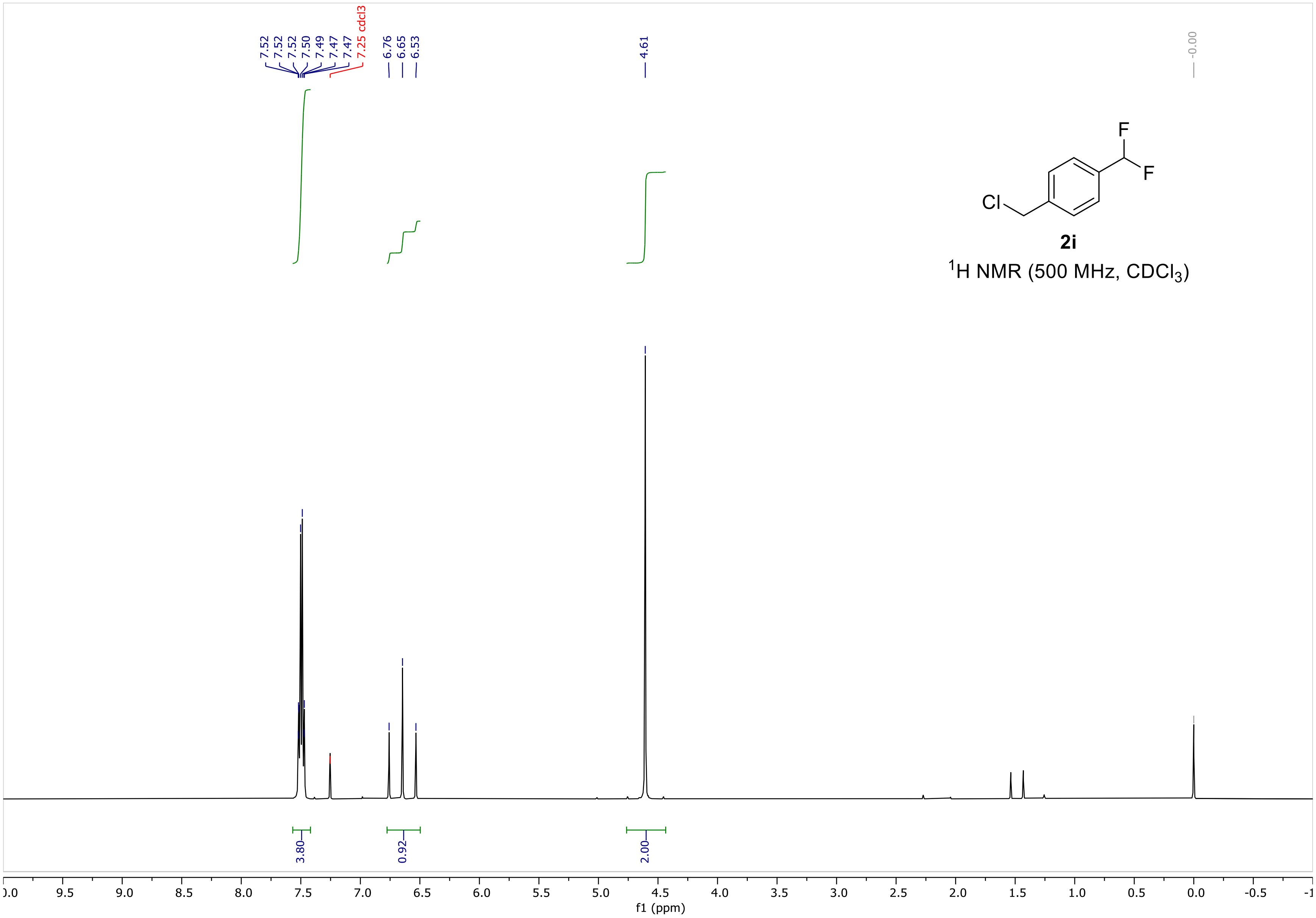
2h

^{1}H NMR (500 MHz, $CDCl_3$)



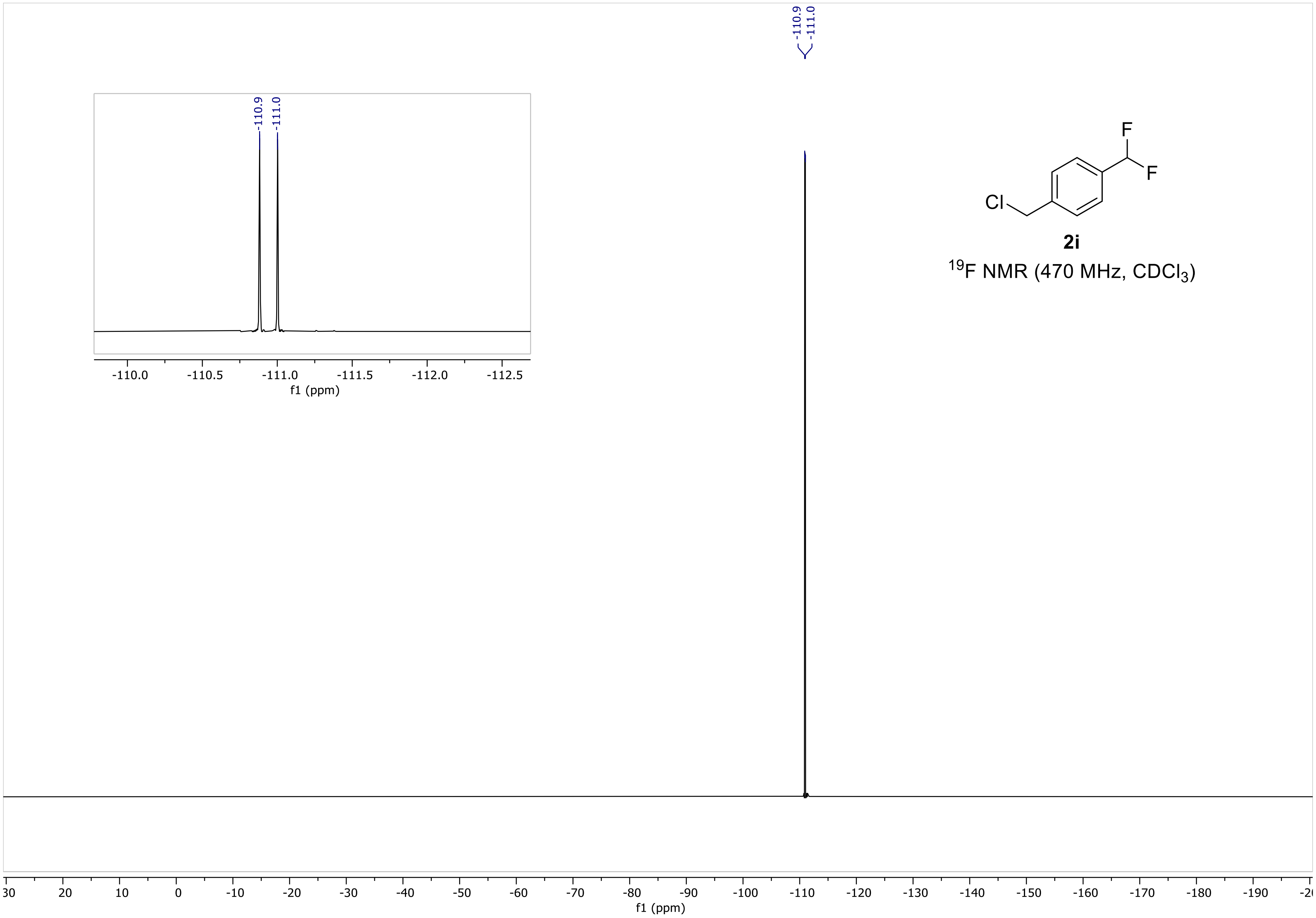
2h

^{19}F NMR (470 MHz, CDCl$_3$)



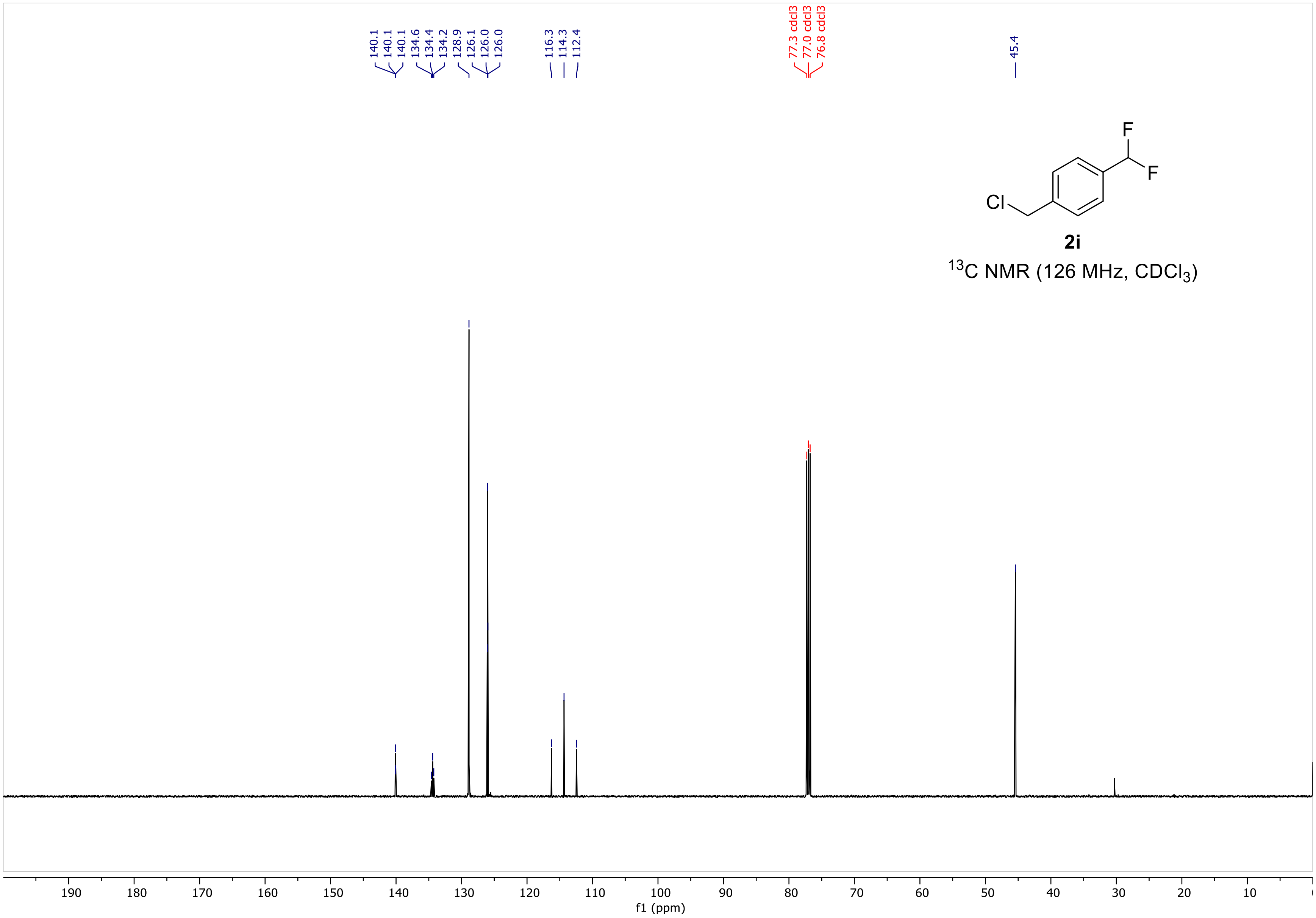
2i

^{1}H NMR (500 MHz, CDCl$_3$)



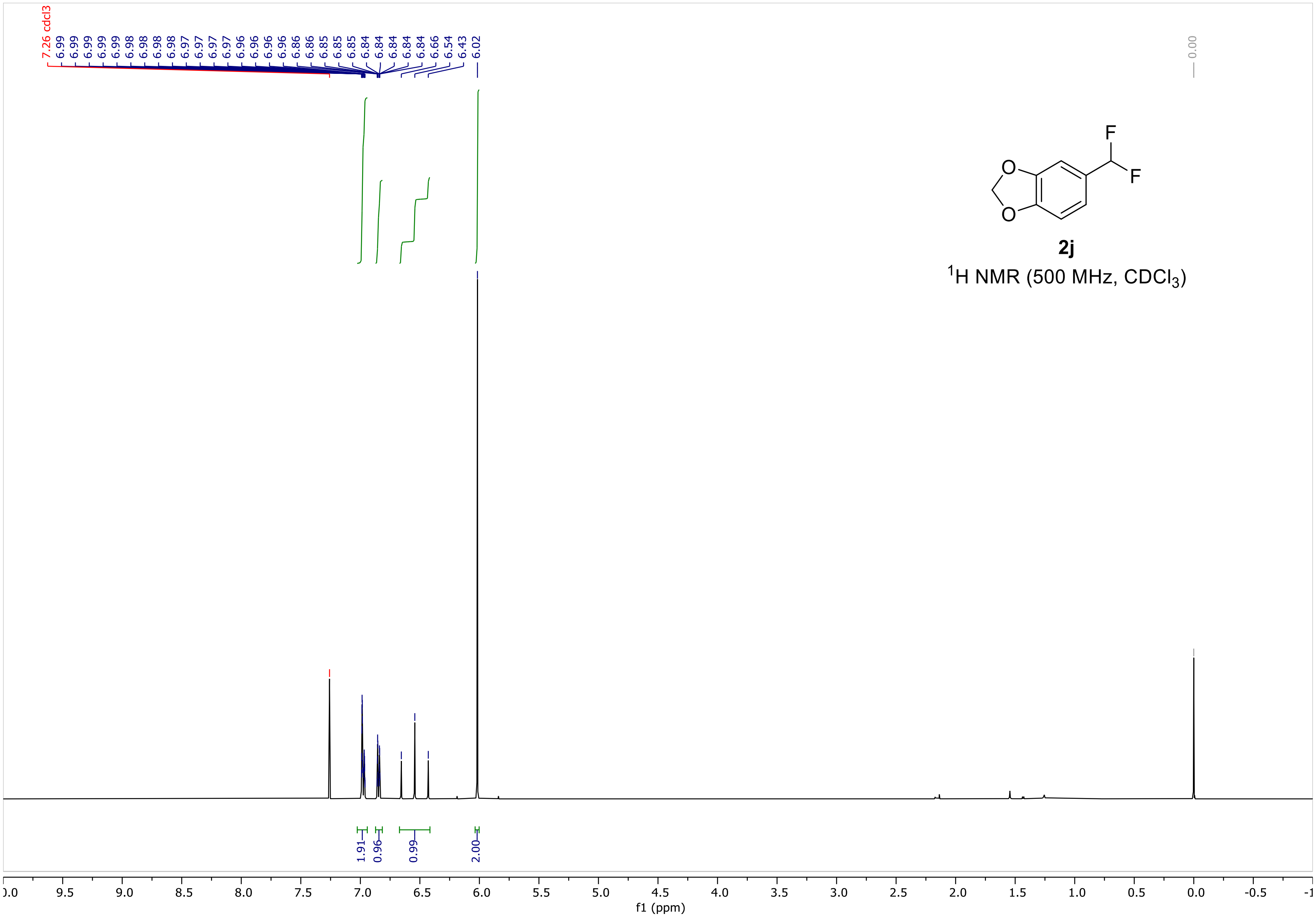
2i

^{19}F NMR (470 MHz, CDCl$_3$)



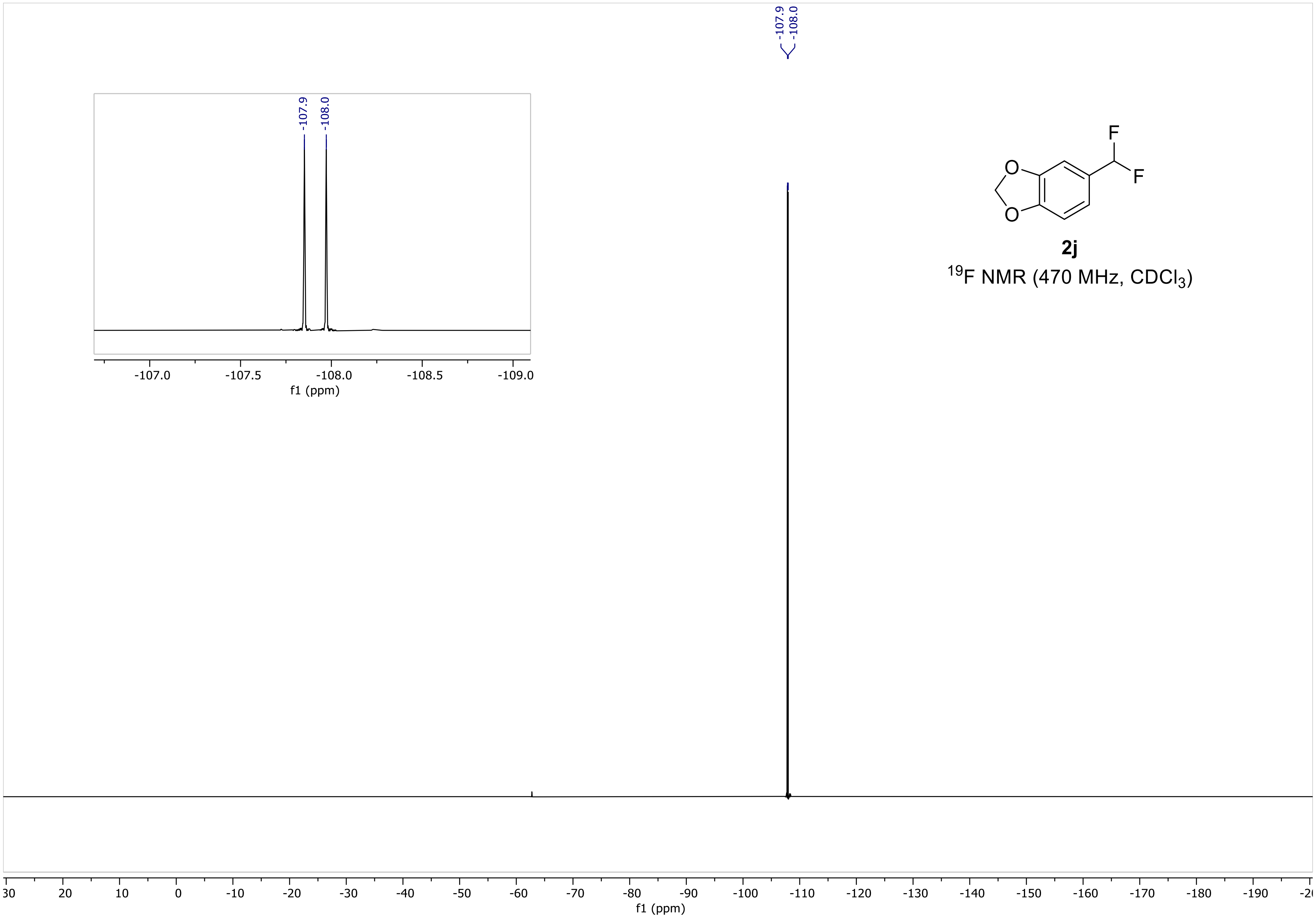
2i

^{13}C NMR (126 MHz, $CDCl_3$)



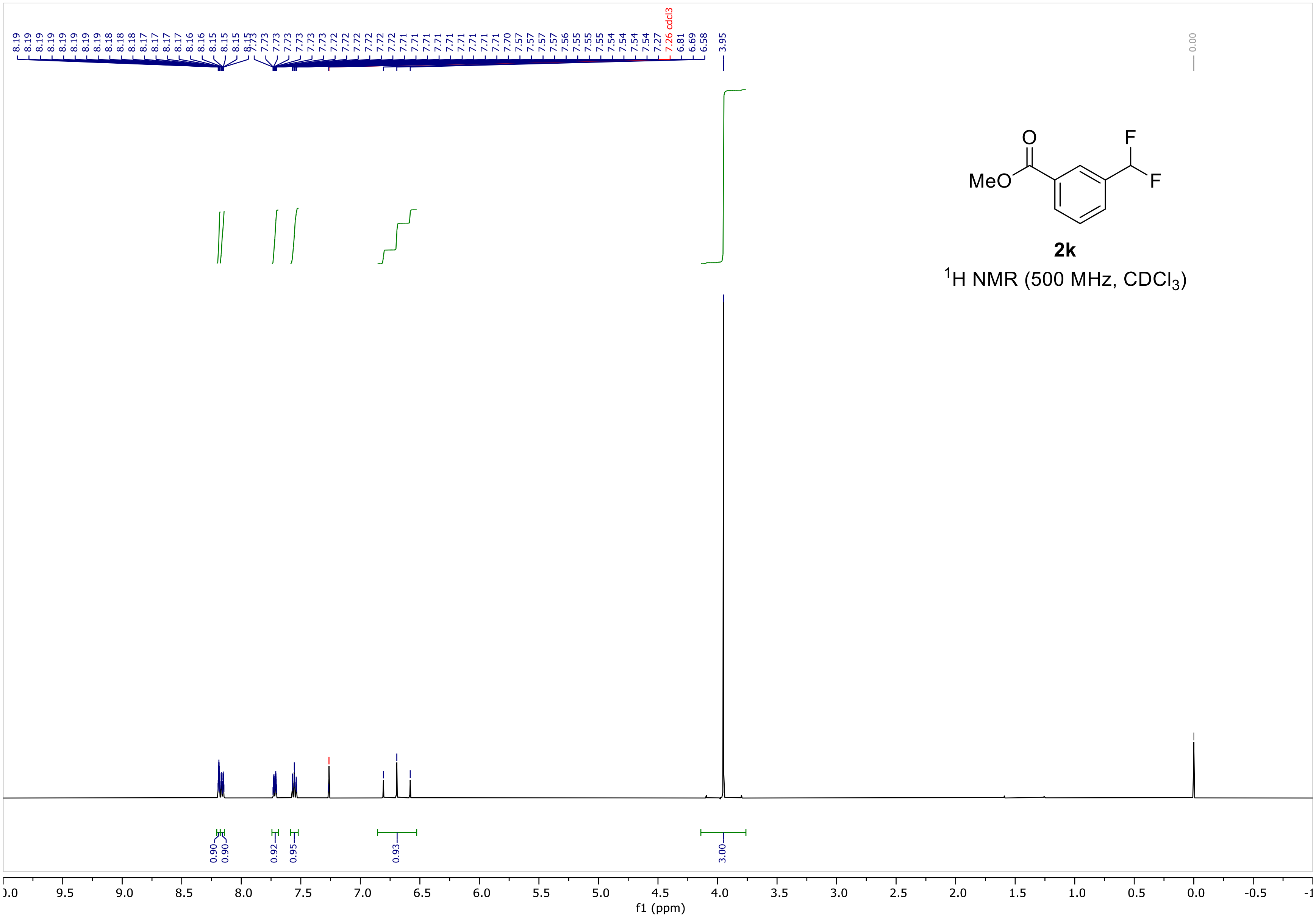
2j

^{1}H NMR (500 MHz, CDCl$_3$)



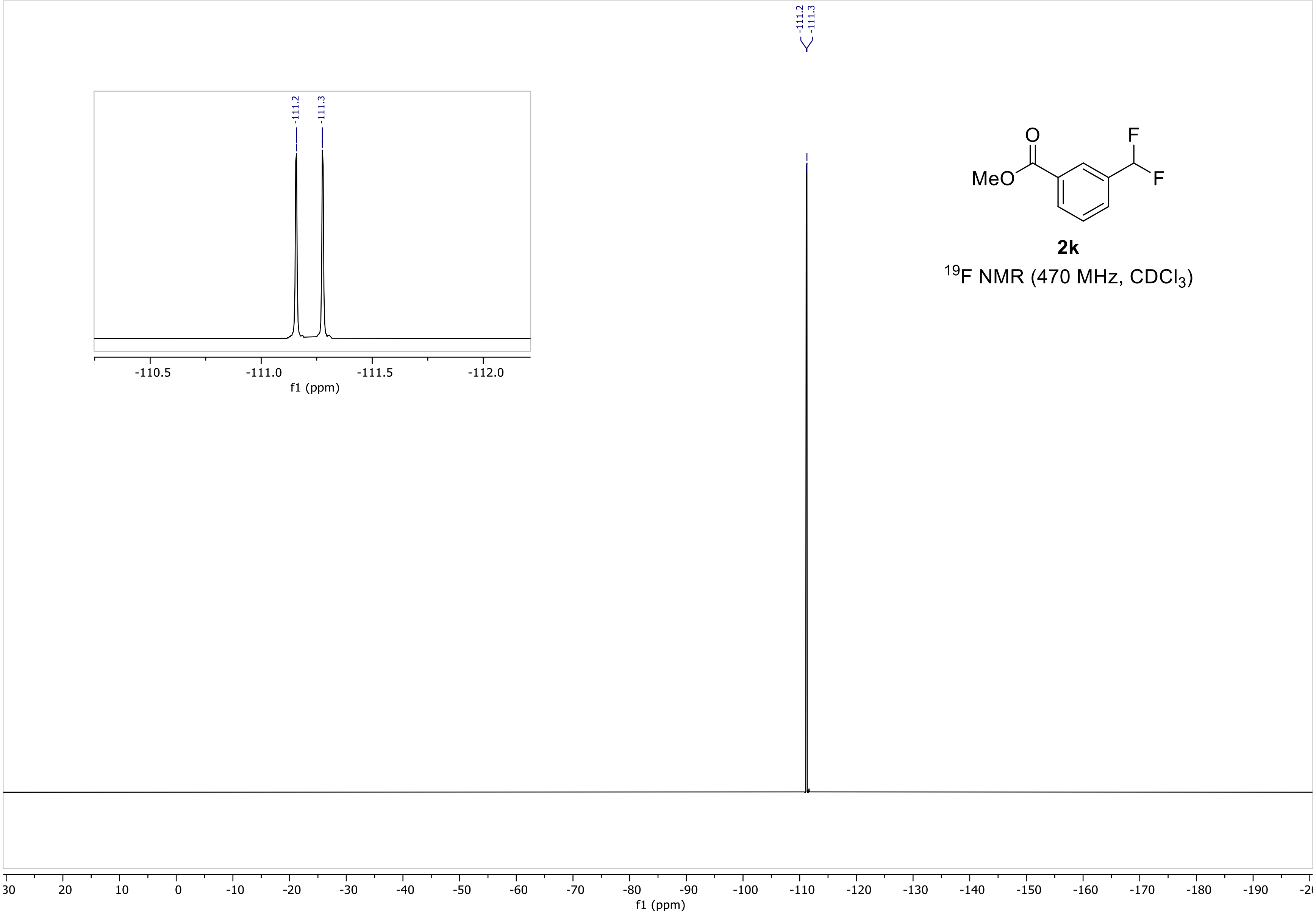
2j

^{19}F NMR (470 MHz, CDCl$_3$)



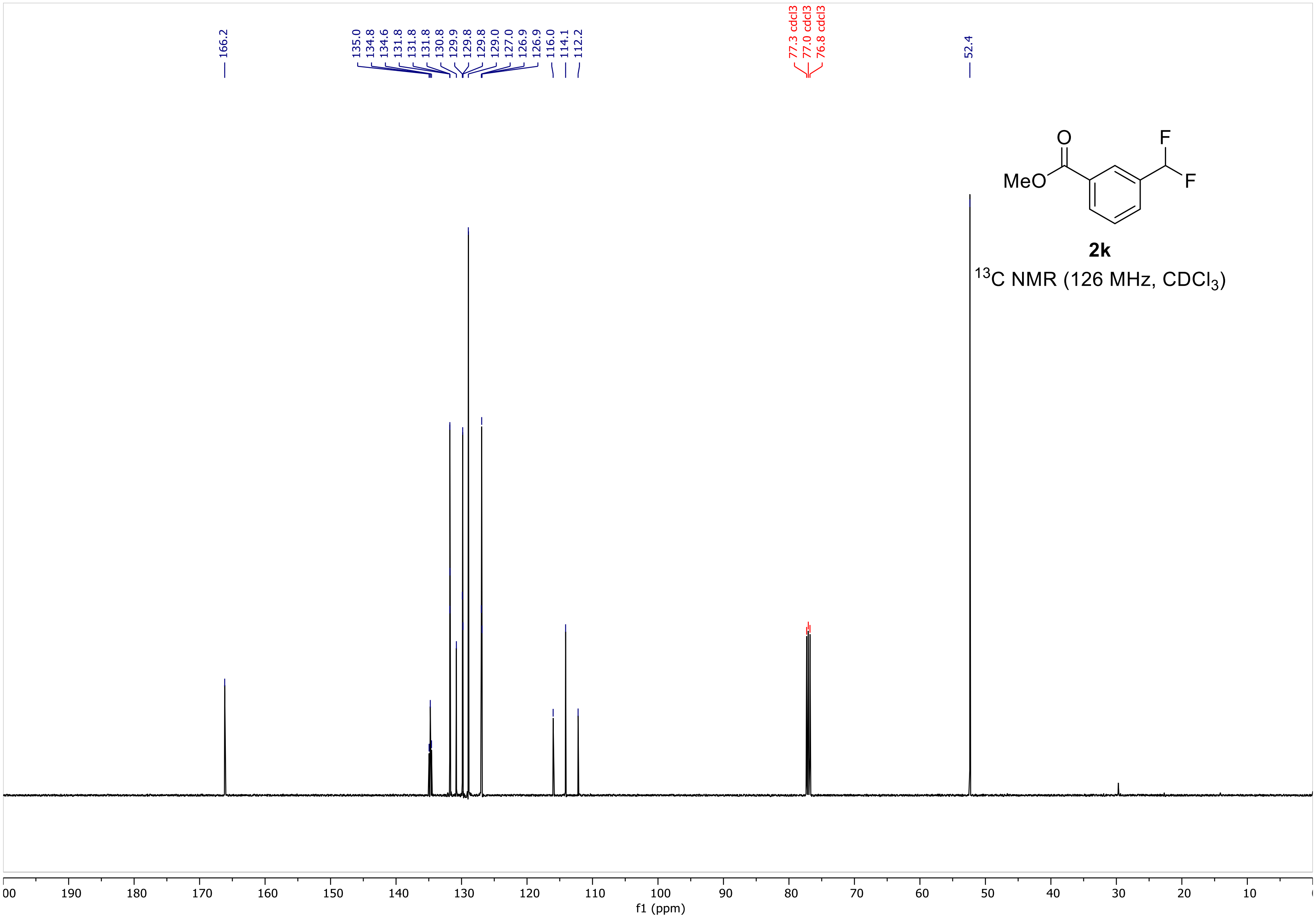
2k

^{1}H NMR (500 MHz, CDCl$_3$)



2k

^{19}F NMR (470 MHz, $CDCl_3$)



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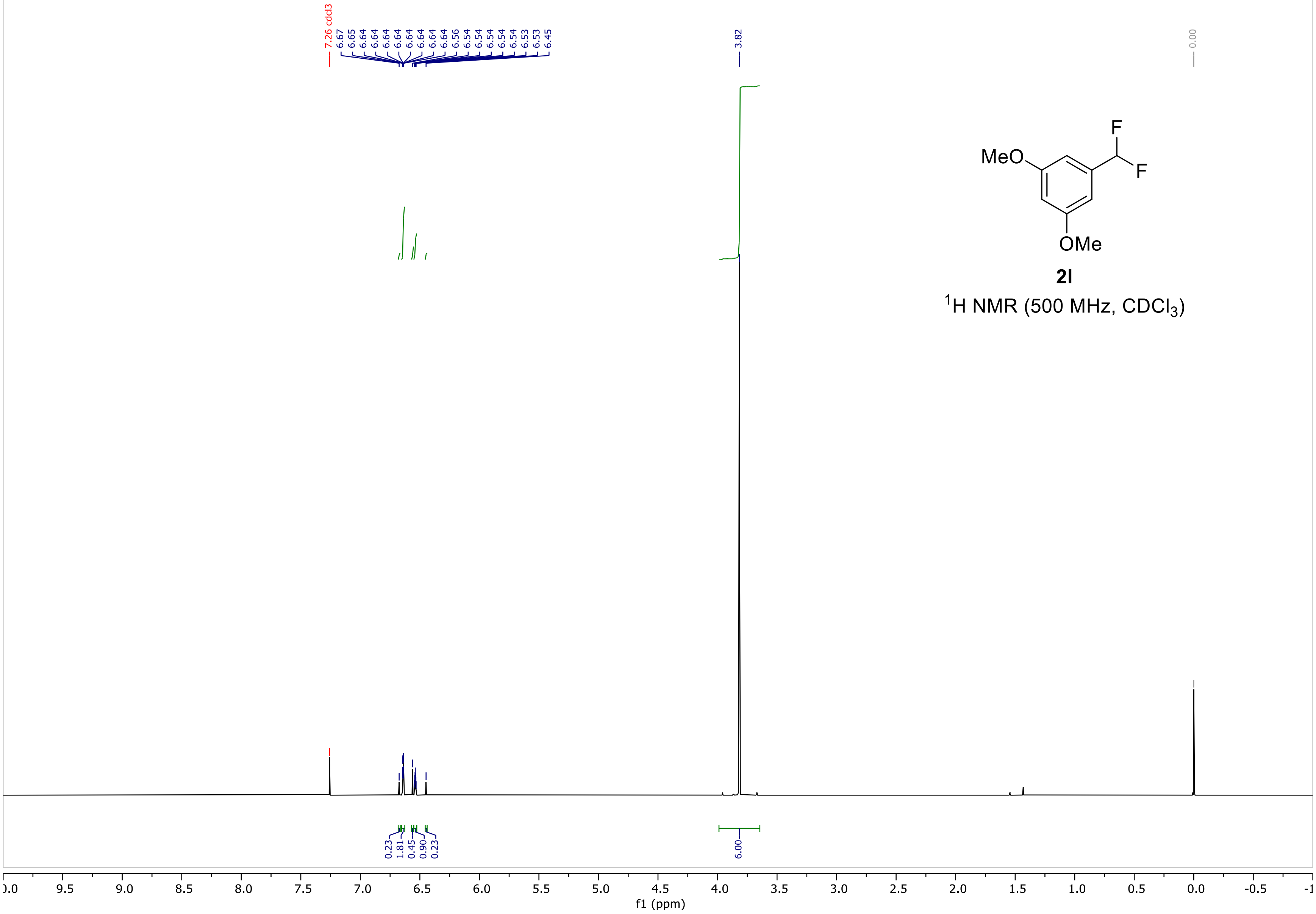
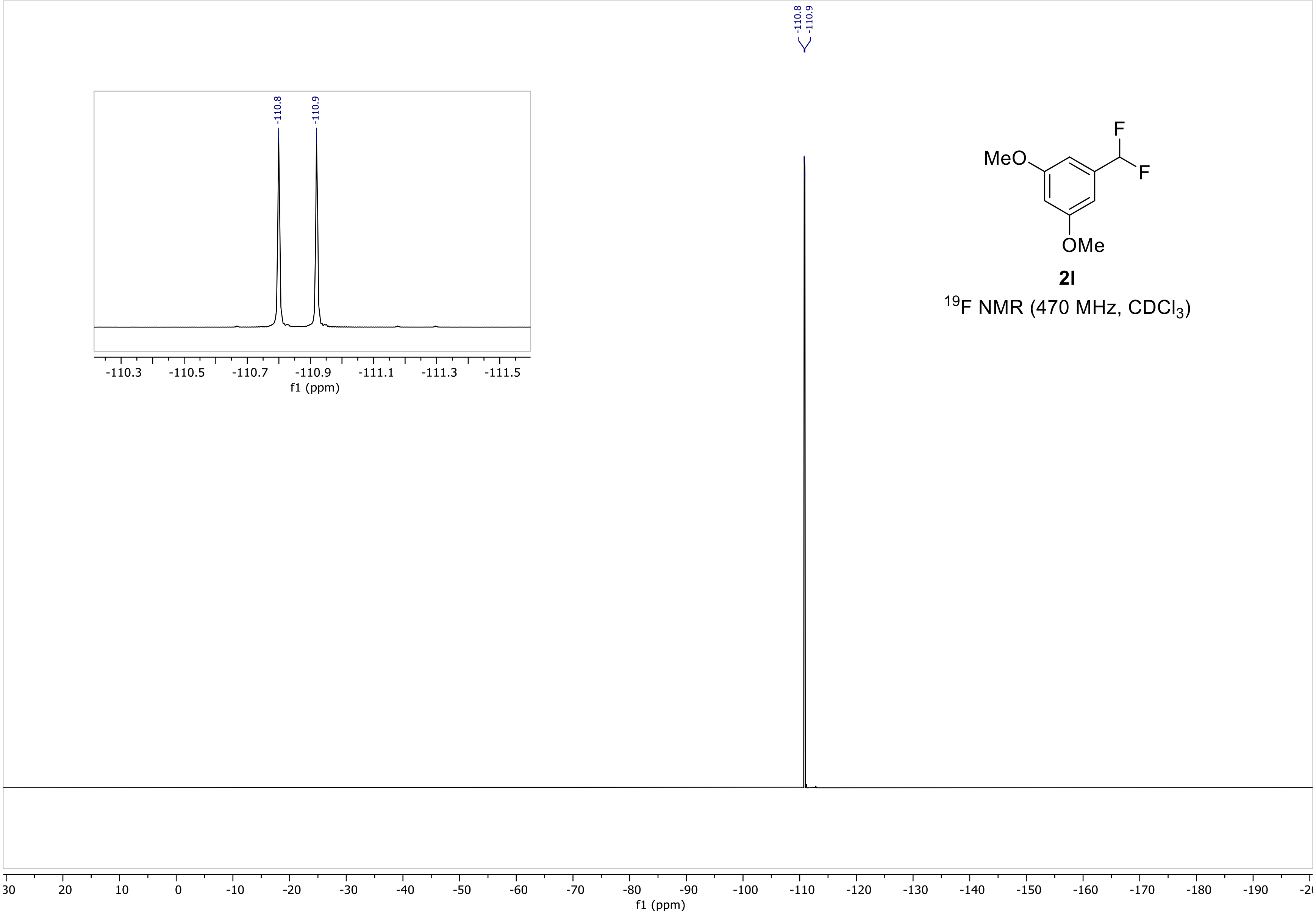
^{13}C NMR (126 MHz, CDCl$_3$)



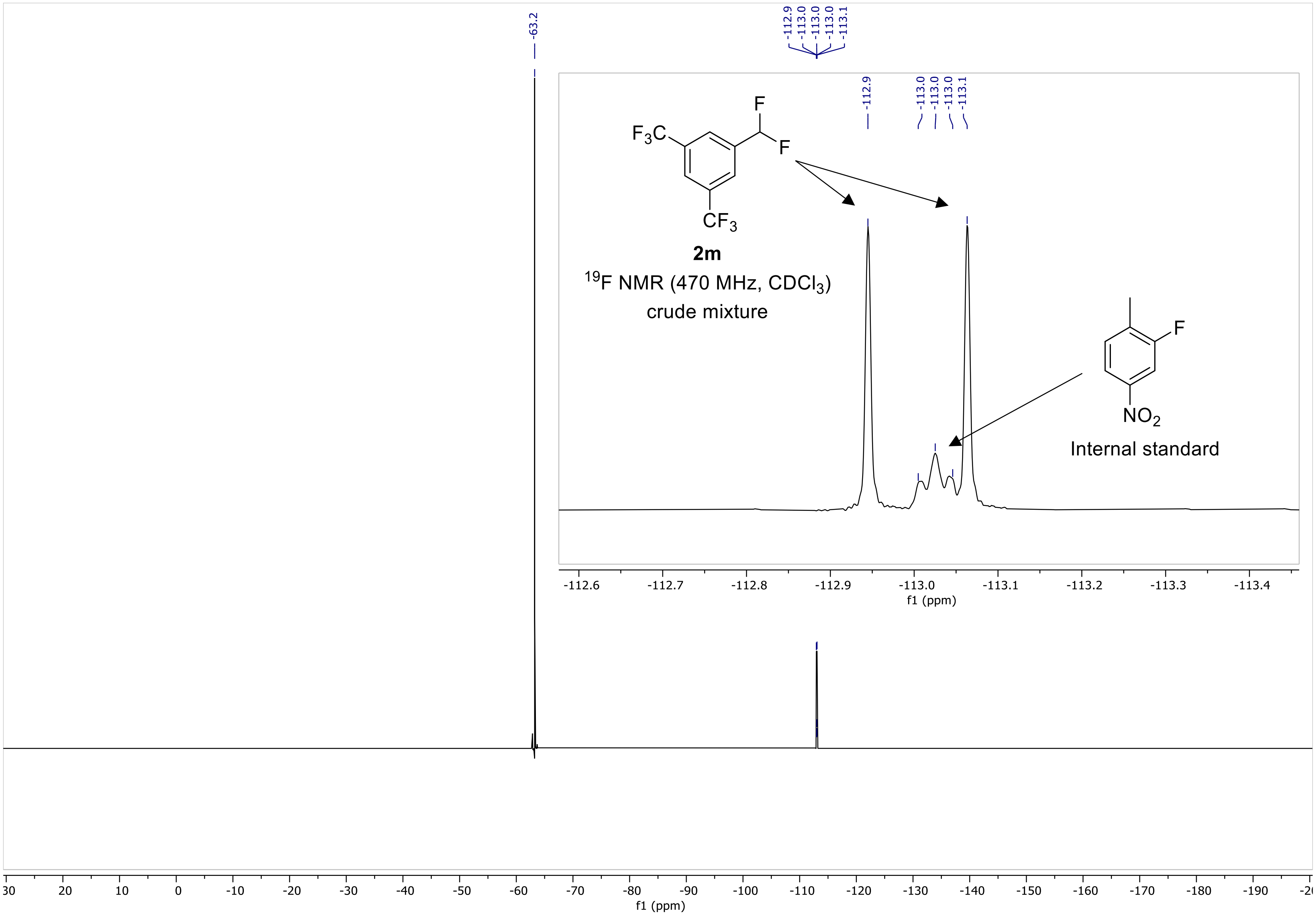
2l

^{1}H NMR (500 MHz, $CDCl_3$)



2l

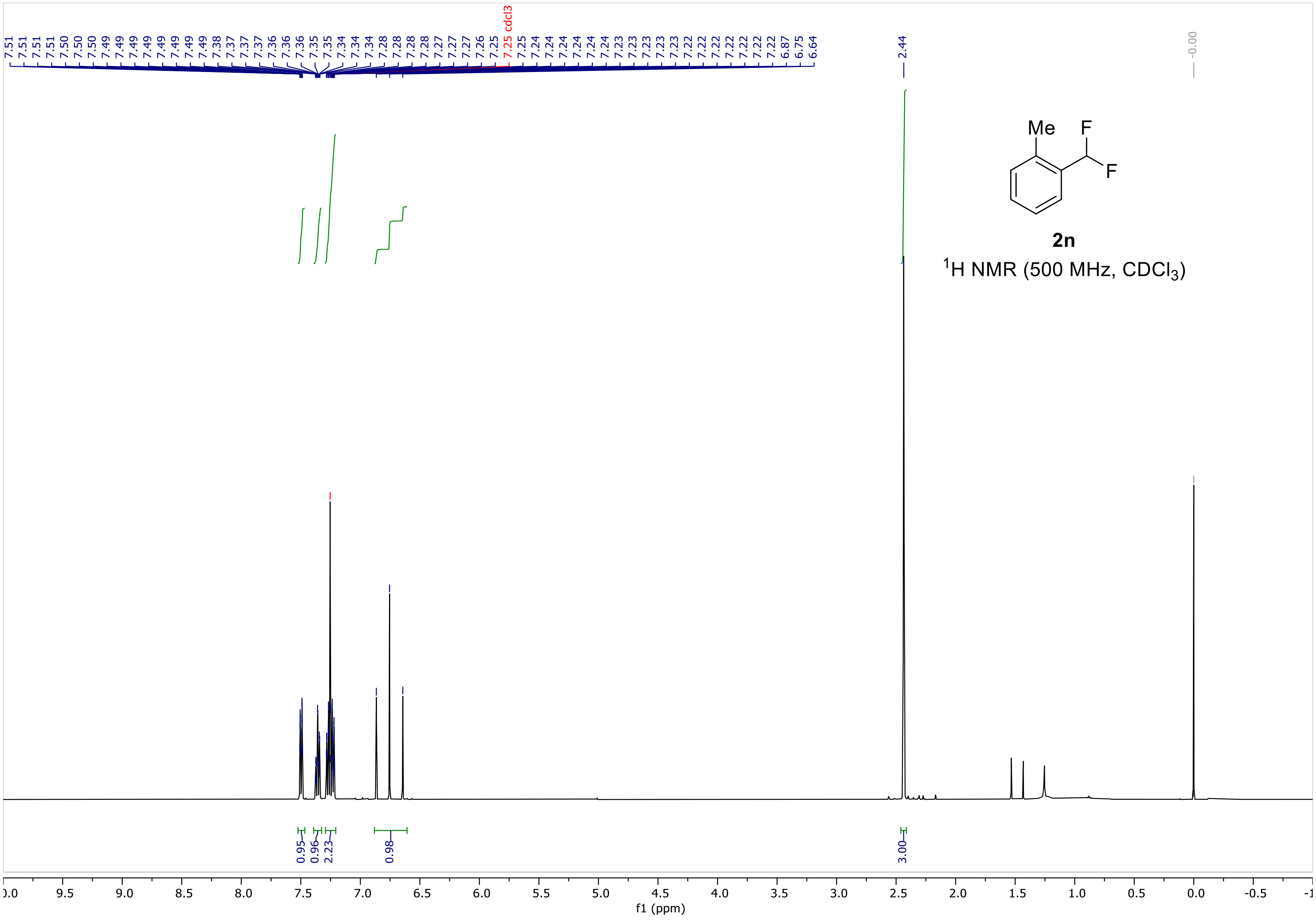
^{19}F NMR (470 MHz, CDCl$_3$)



2m

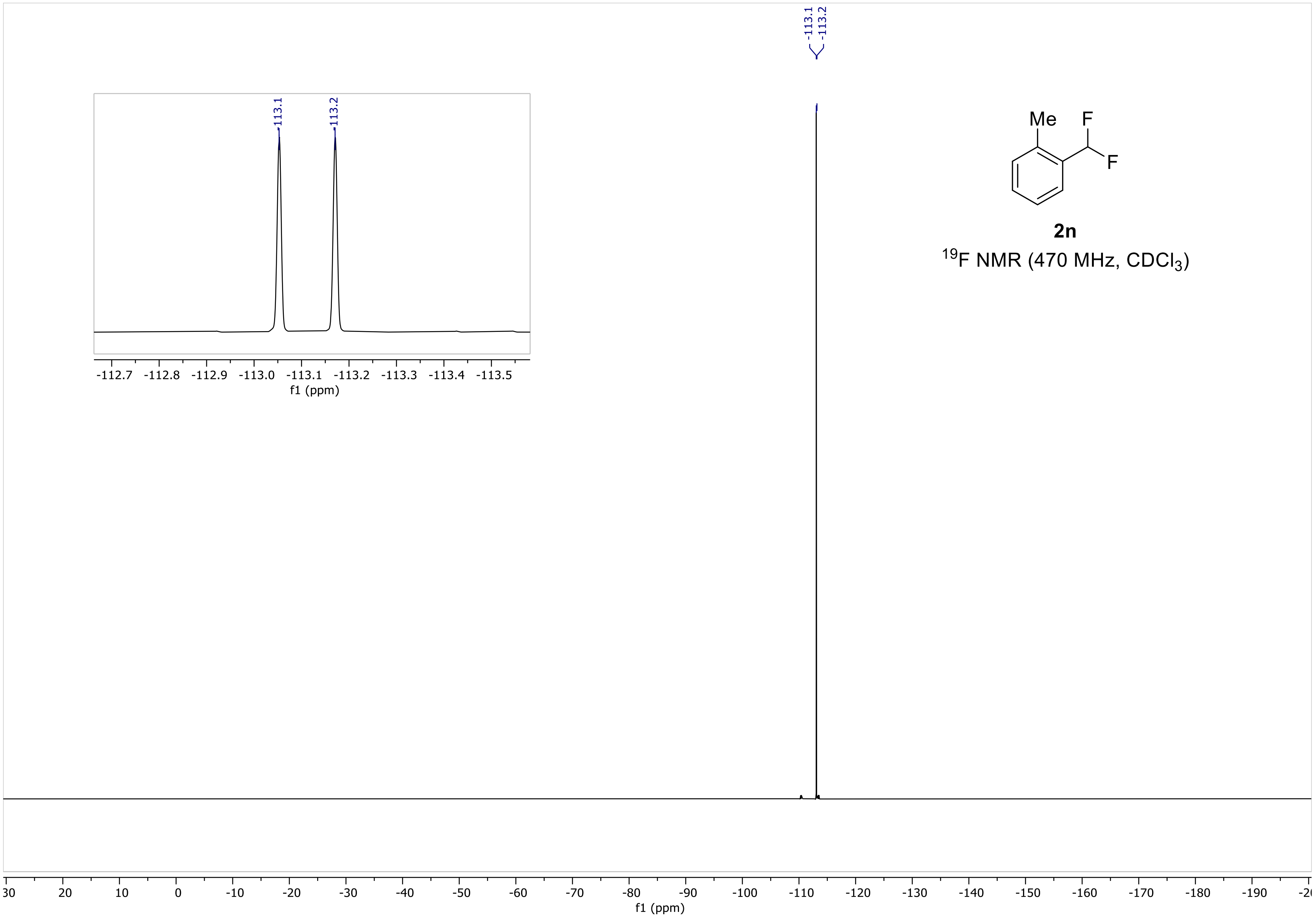
^{19}F NMR (470 MHz, $CDCl_3$)
crude mixture

Internal standard



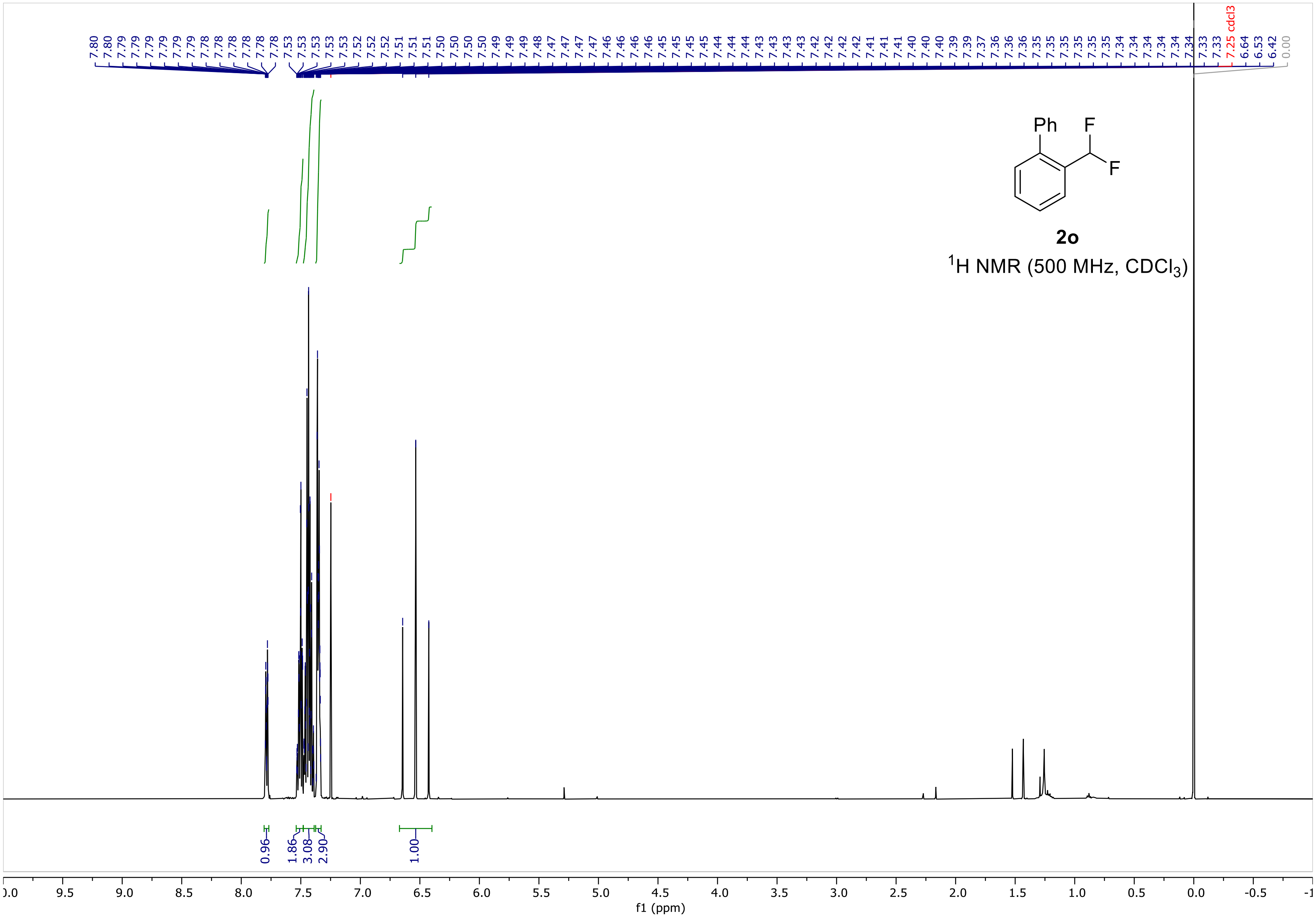
2n

^{1}H NMR (500 MHz, CDCl$_3$)



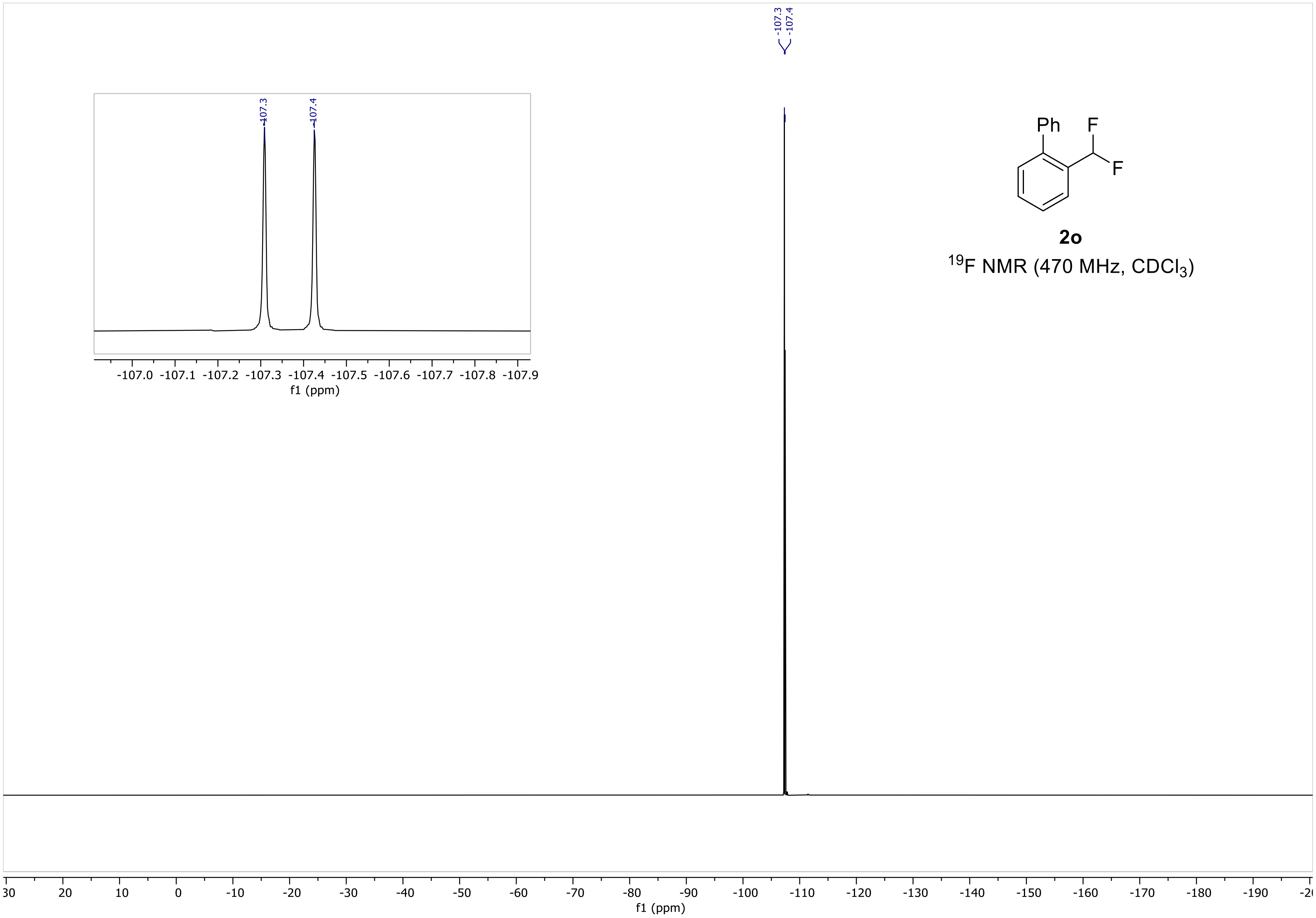
2n

^{19}F NMR (470 MHz, CDCl$_3$)



2o

^{1}H NMR (500 MHz, $CDCl_3$)



2o

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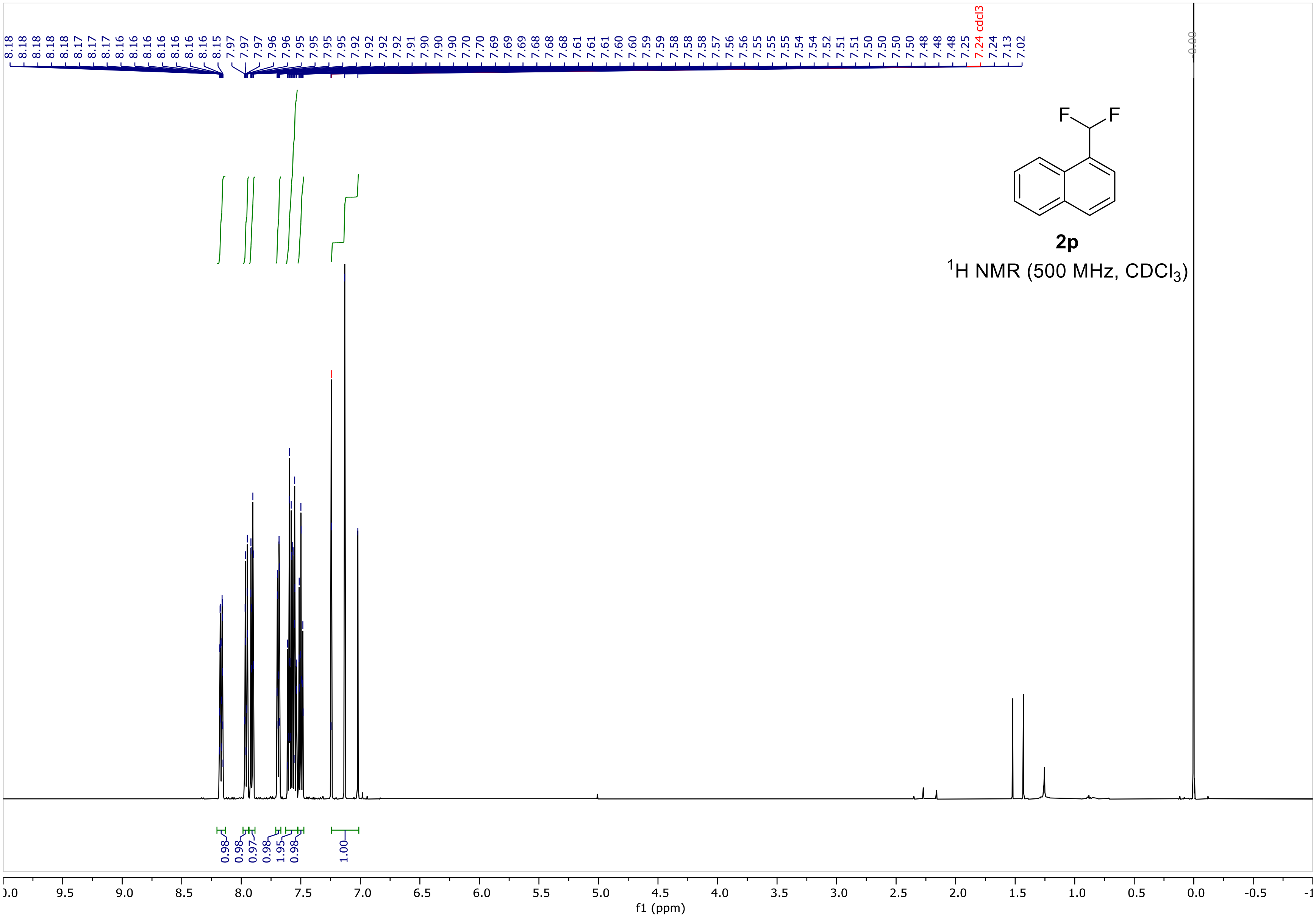
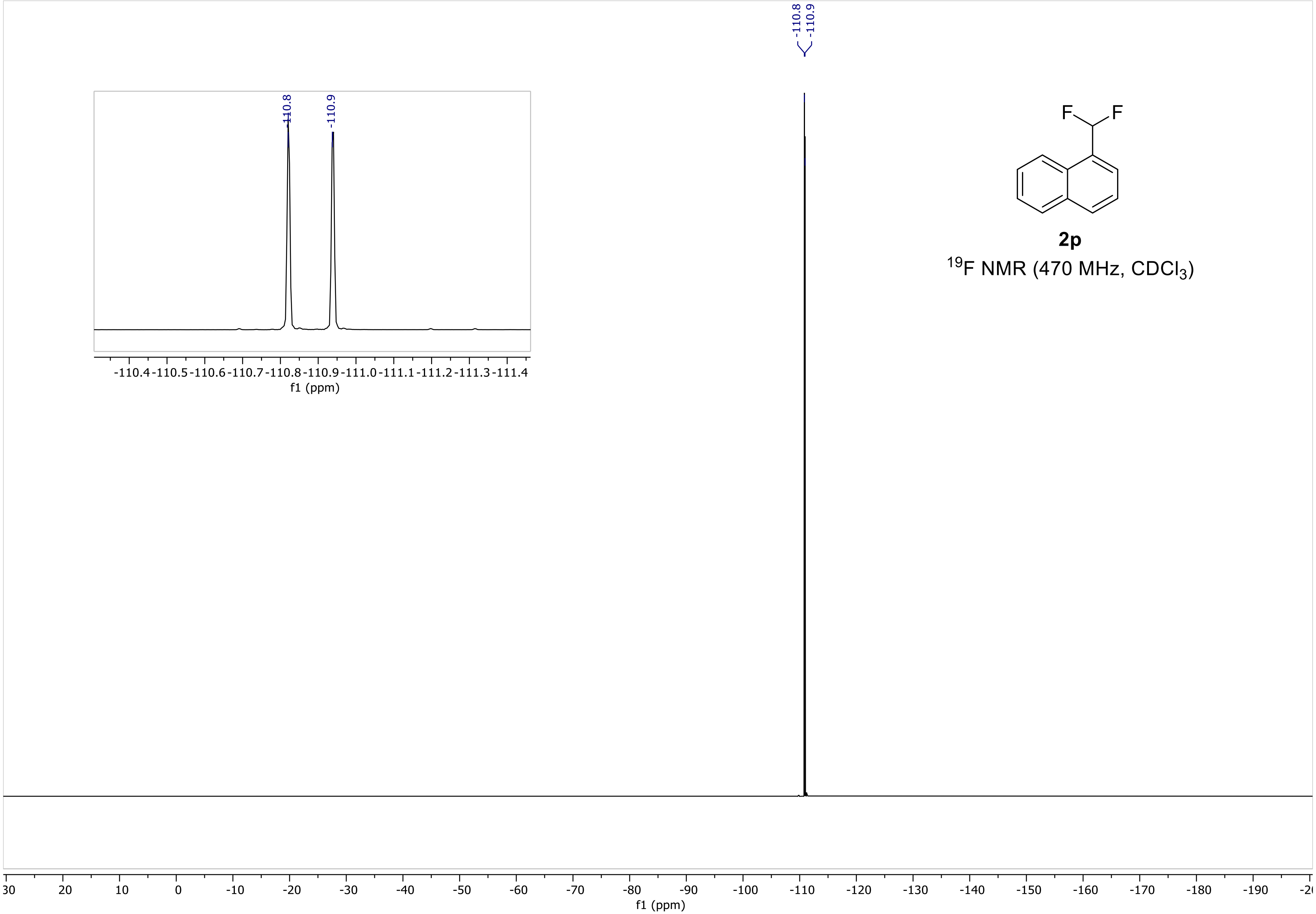


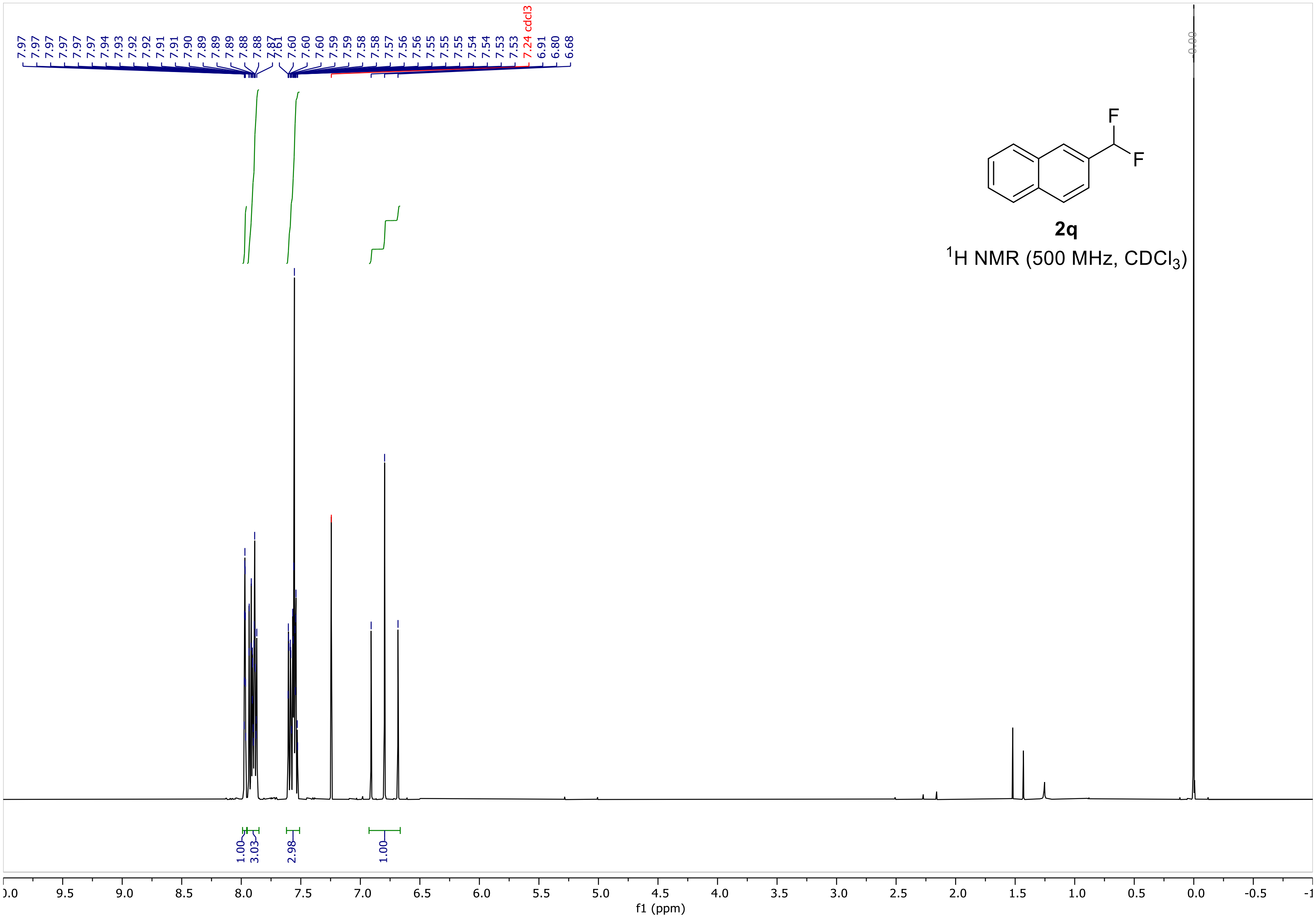
2p

^{1}H NMR (500 MHz, CDCl$_3$)



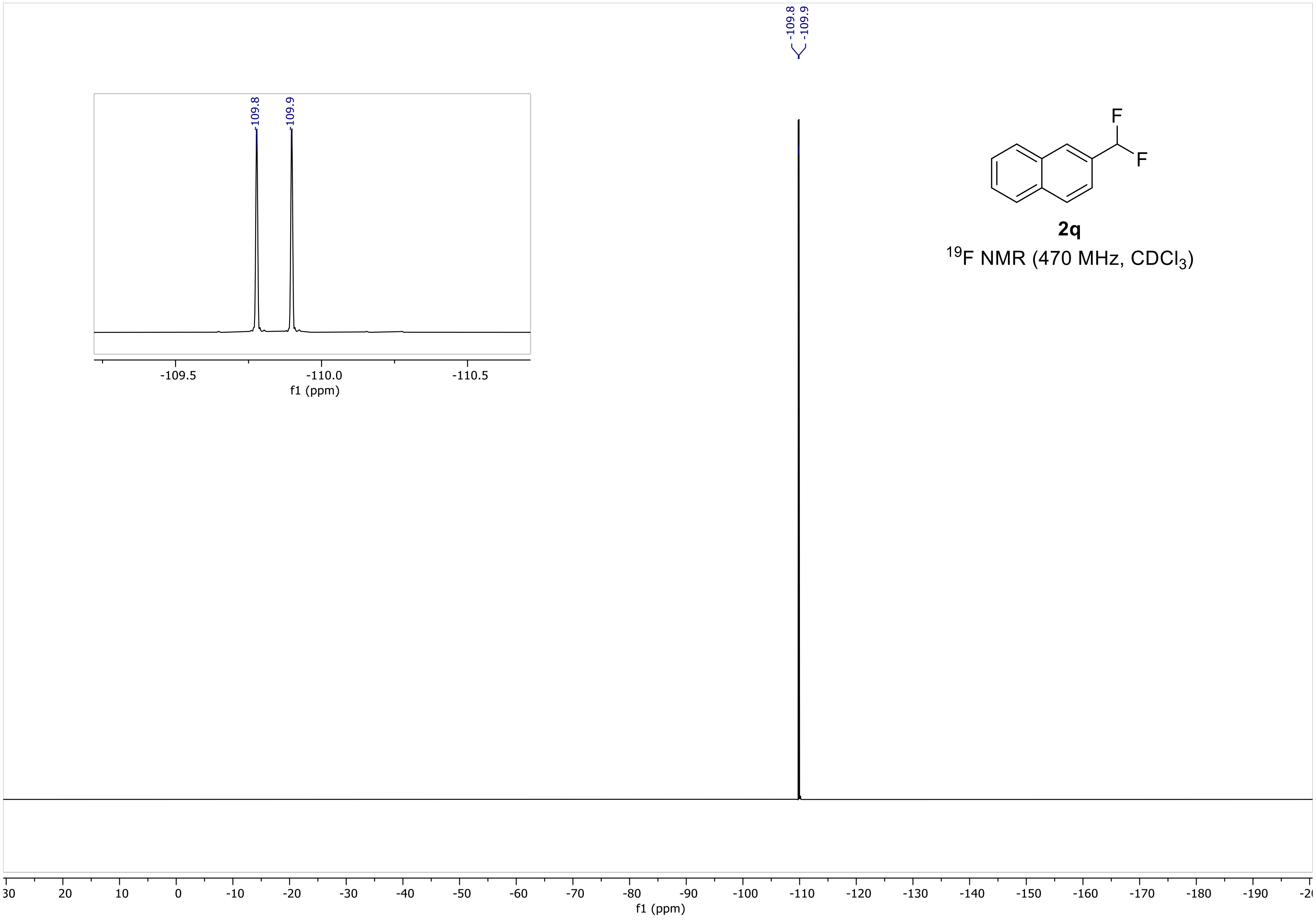
2p

^{19}F NMR (470 MHz, $CDCl_3$)



2q

^{1}H NMR (500 MHz, CDCl$_3$)



2q

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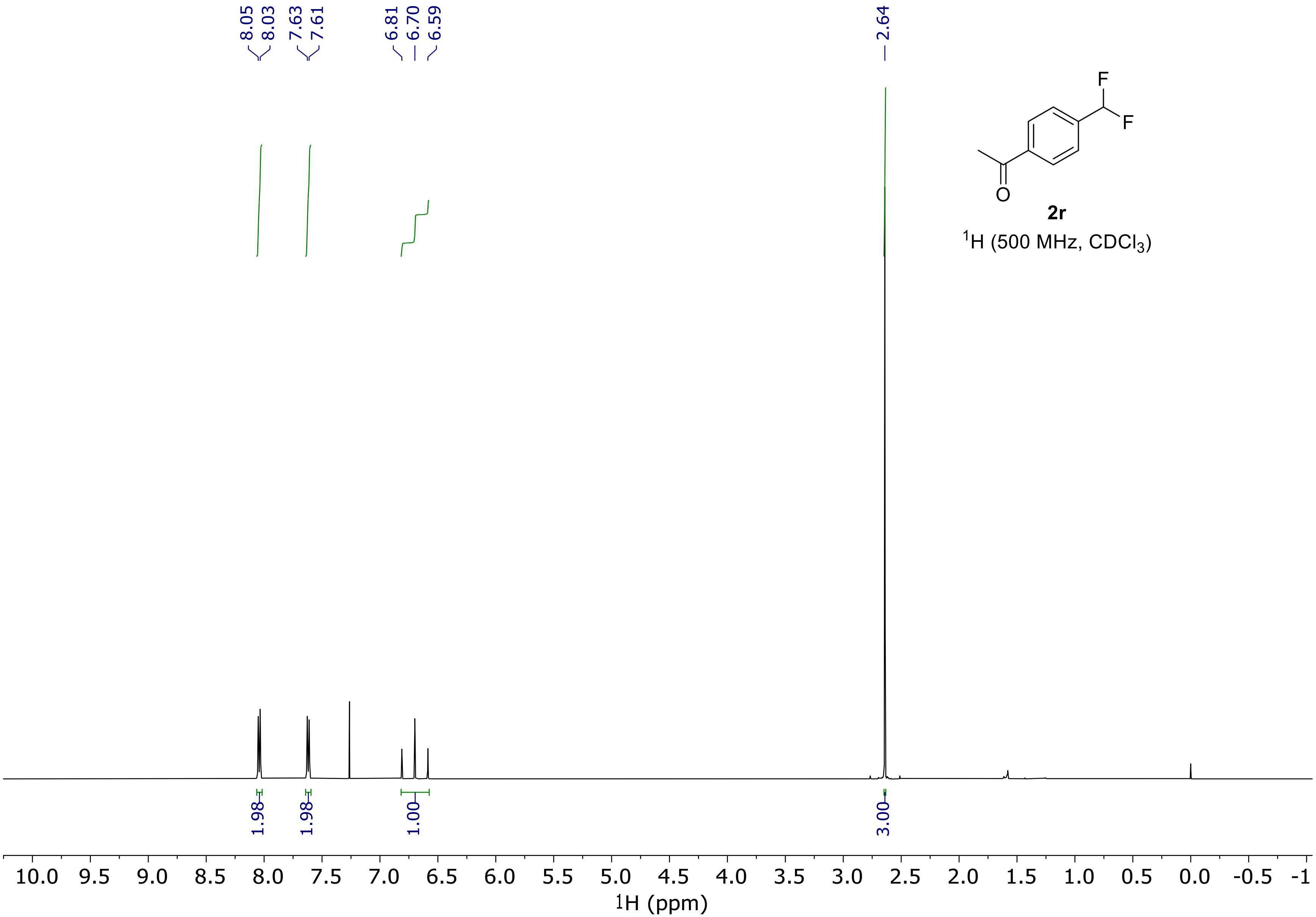
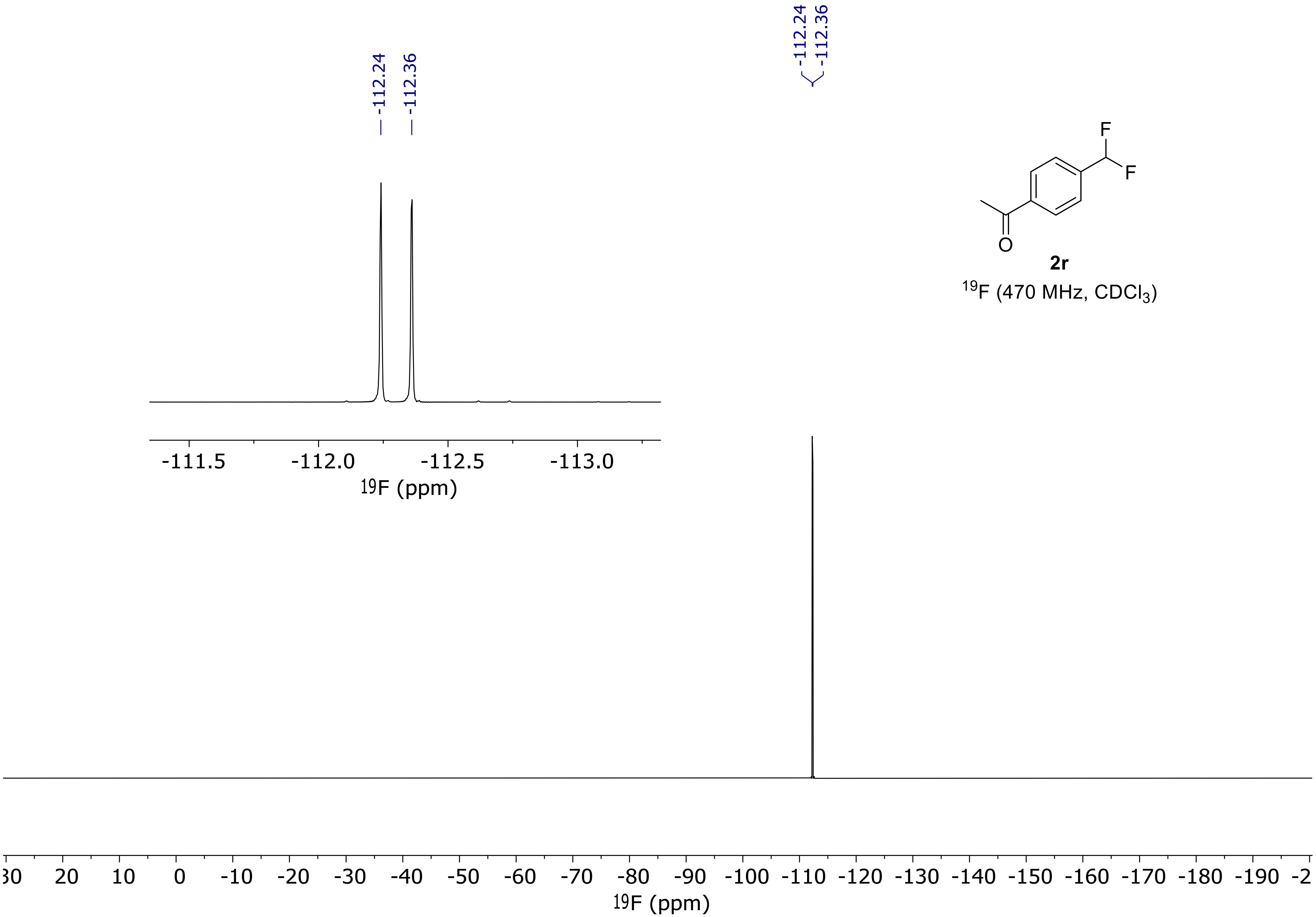


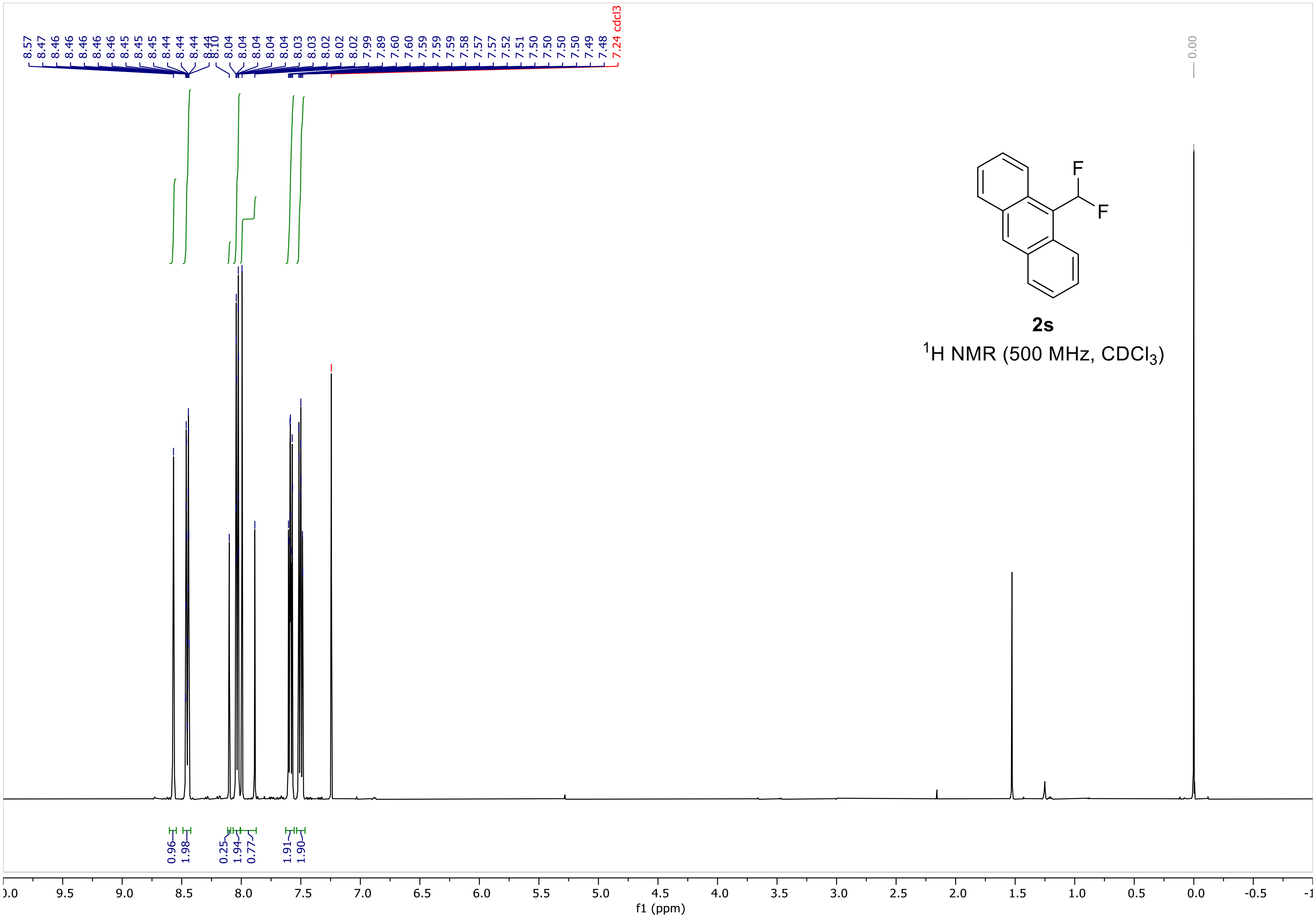
2r

^{1}H (500 MHz, CDCl$_3$)



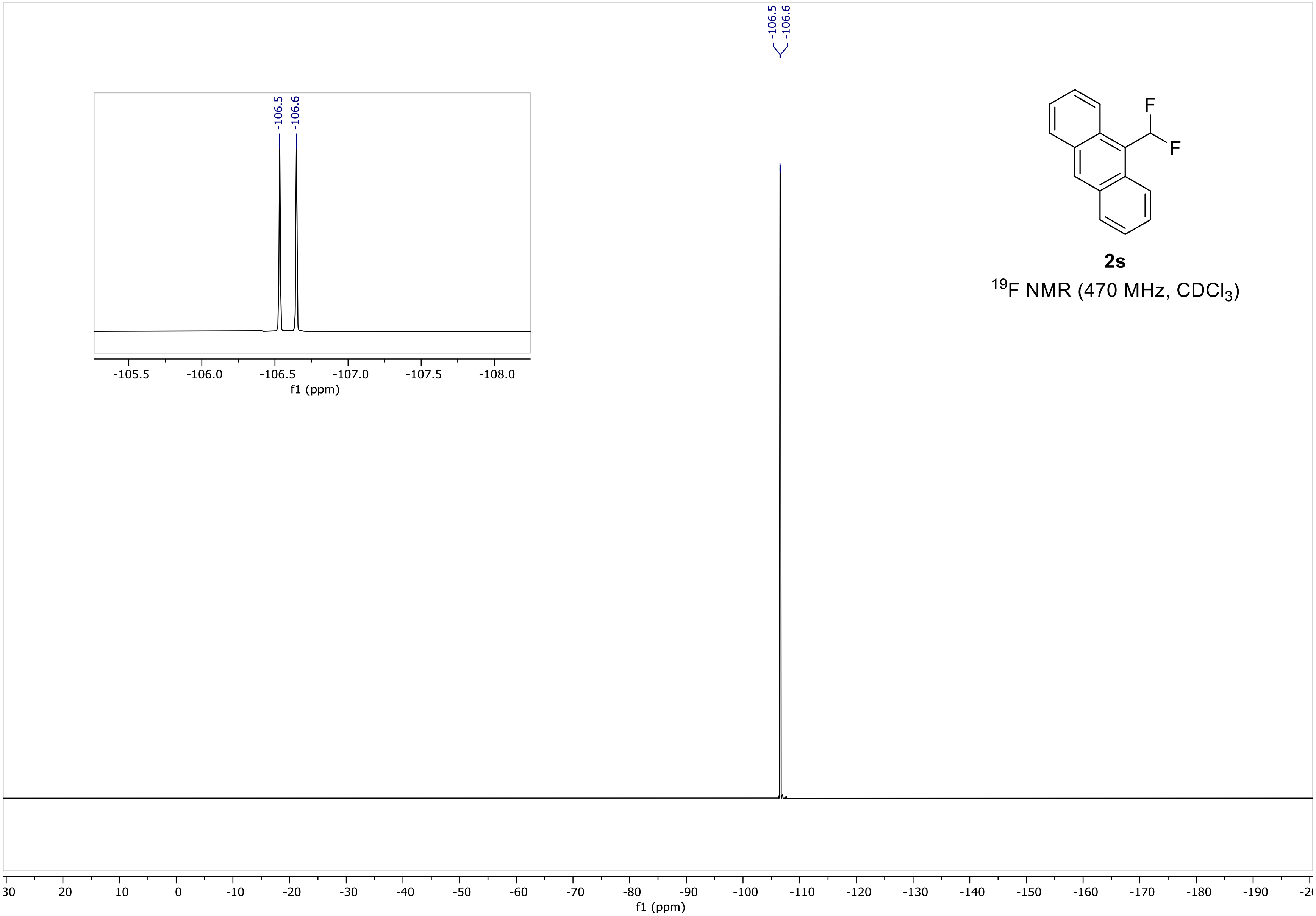
2r

^{19}F (470 MHz, CDCl$_3$)



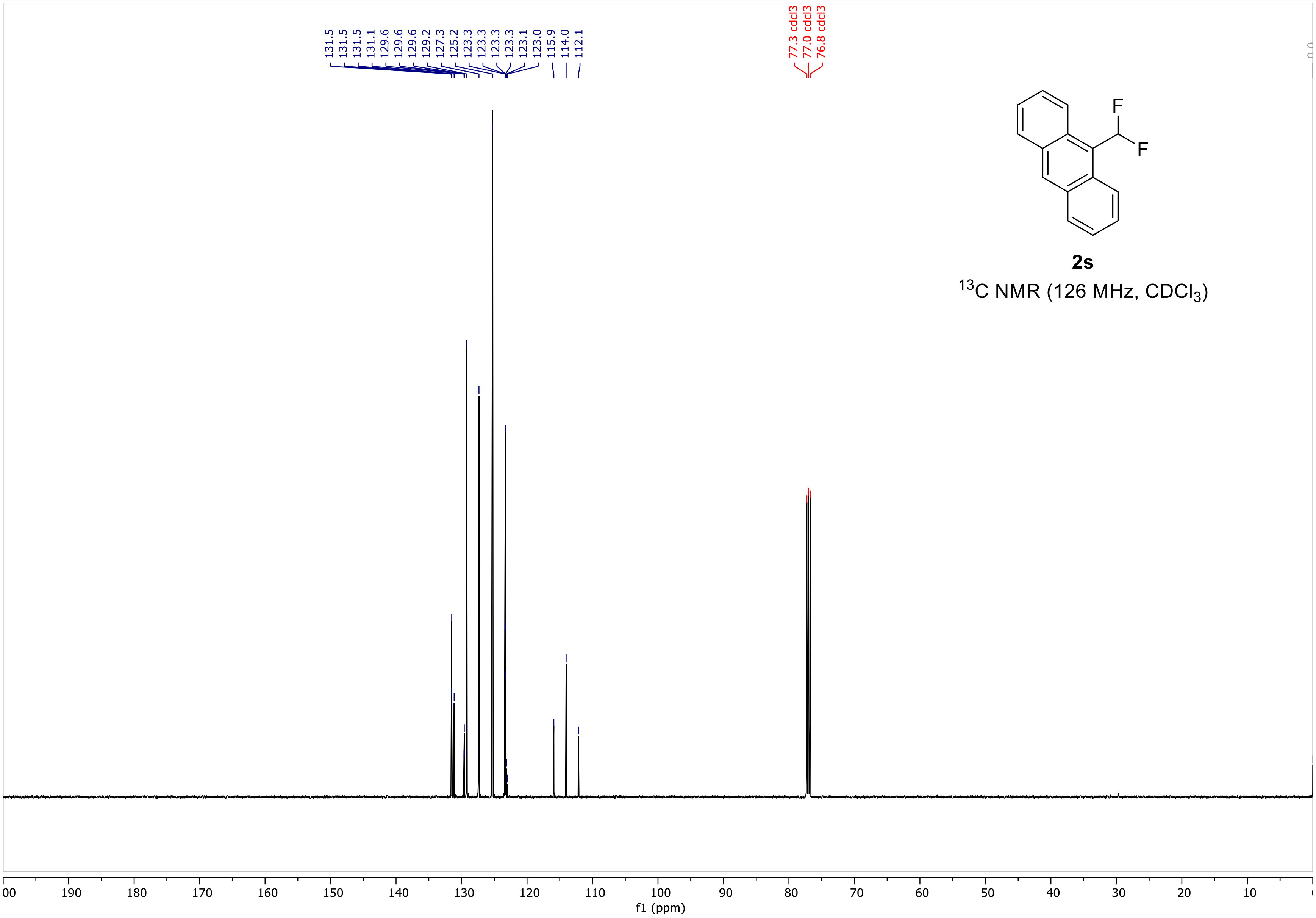
2s

^{1}H NMR (500 MHz, CDCl$_3$)



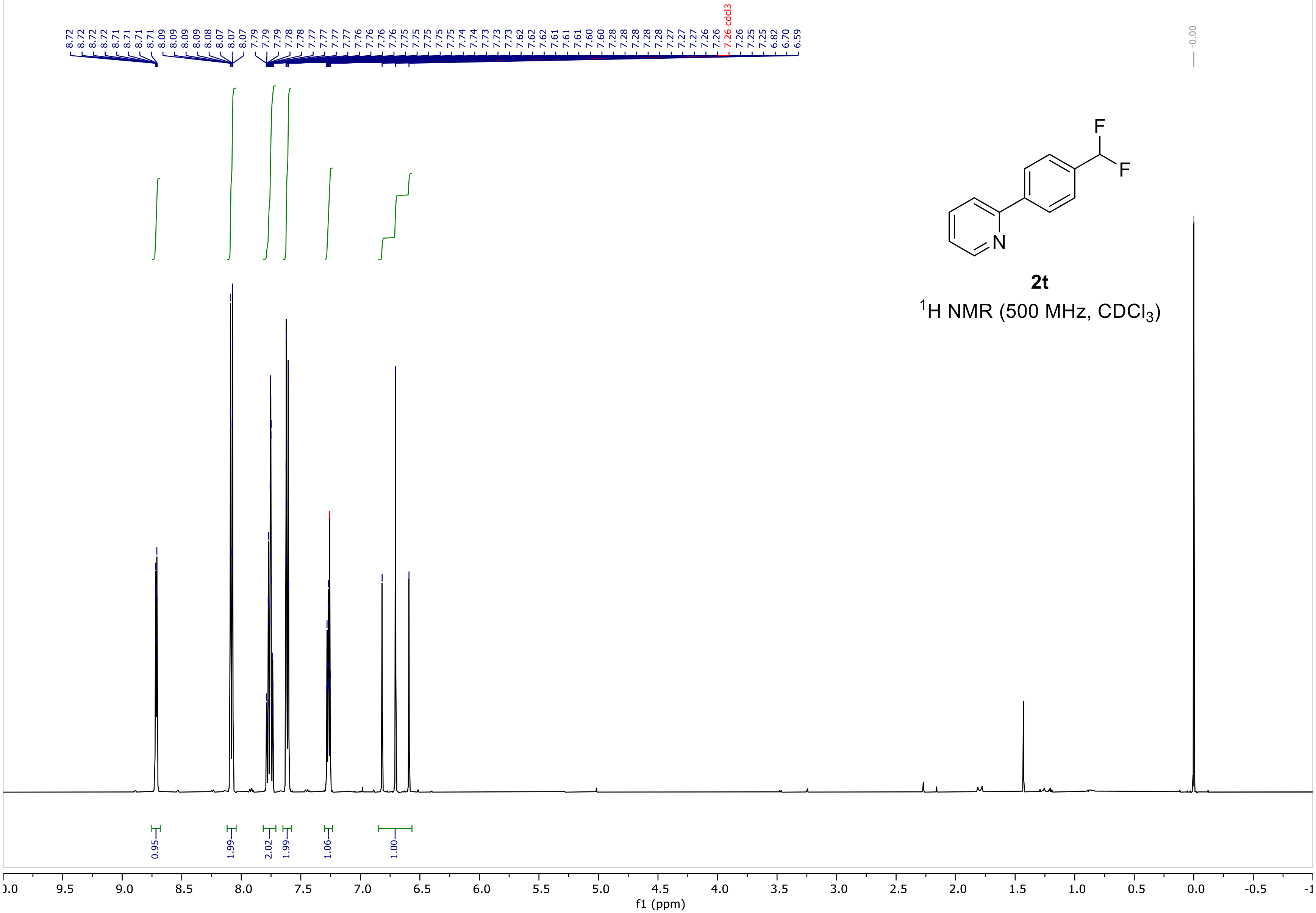
2s

^{19}F NMR (470 MHz, CDCl$_3$)



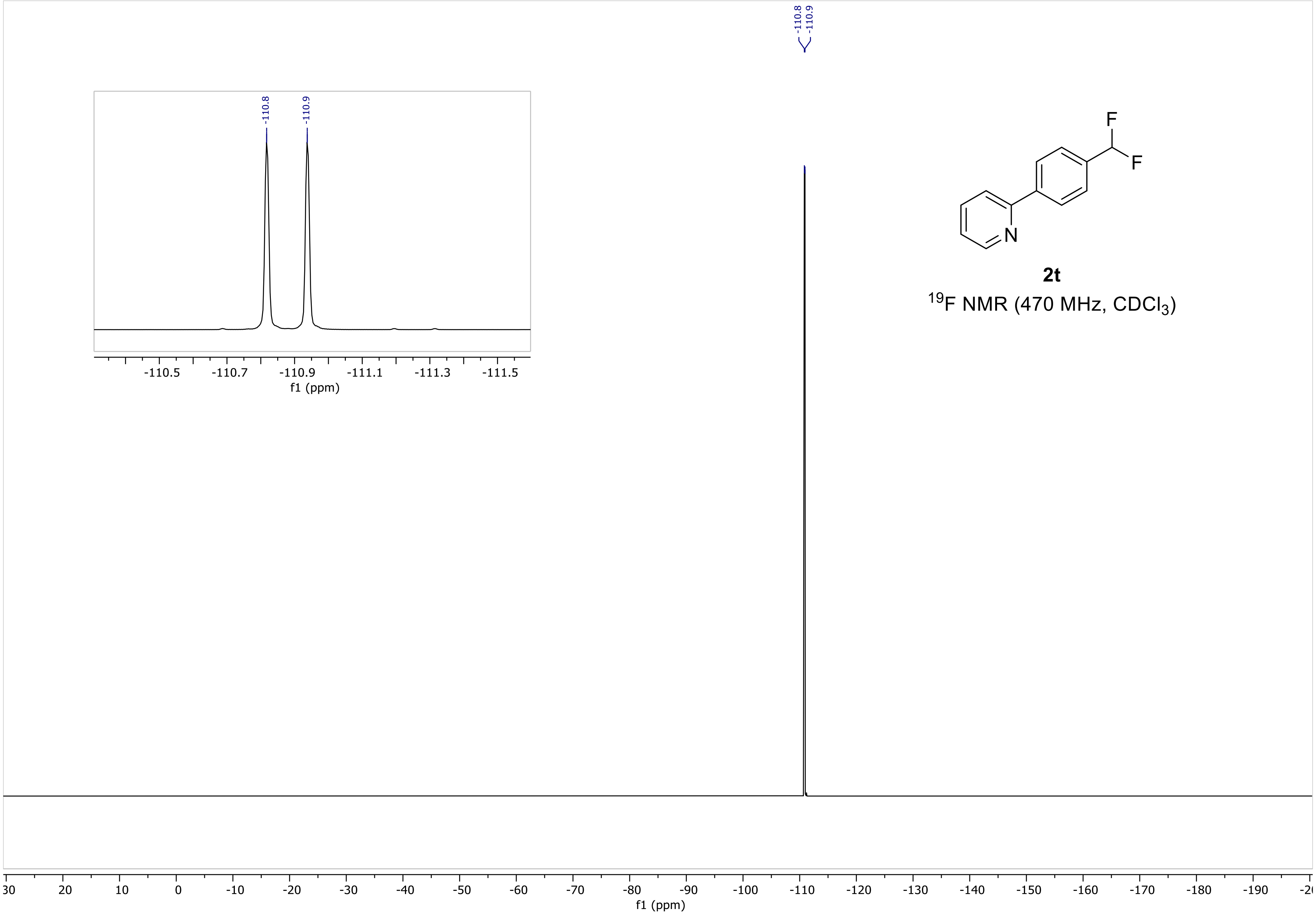
2s

^{13}C NMR (126 MHz, CDCl$_3$)



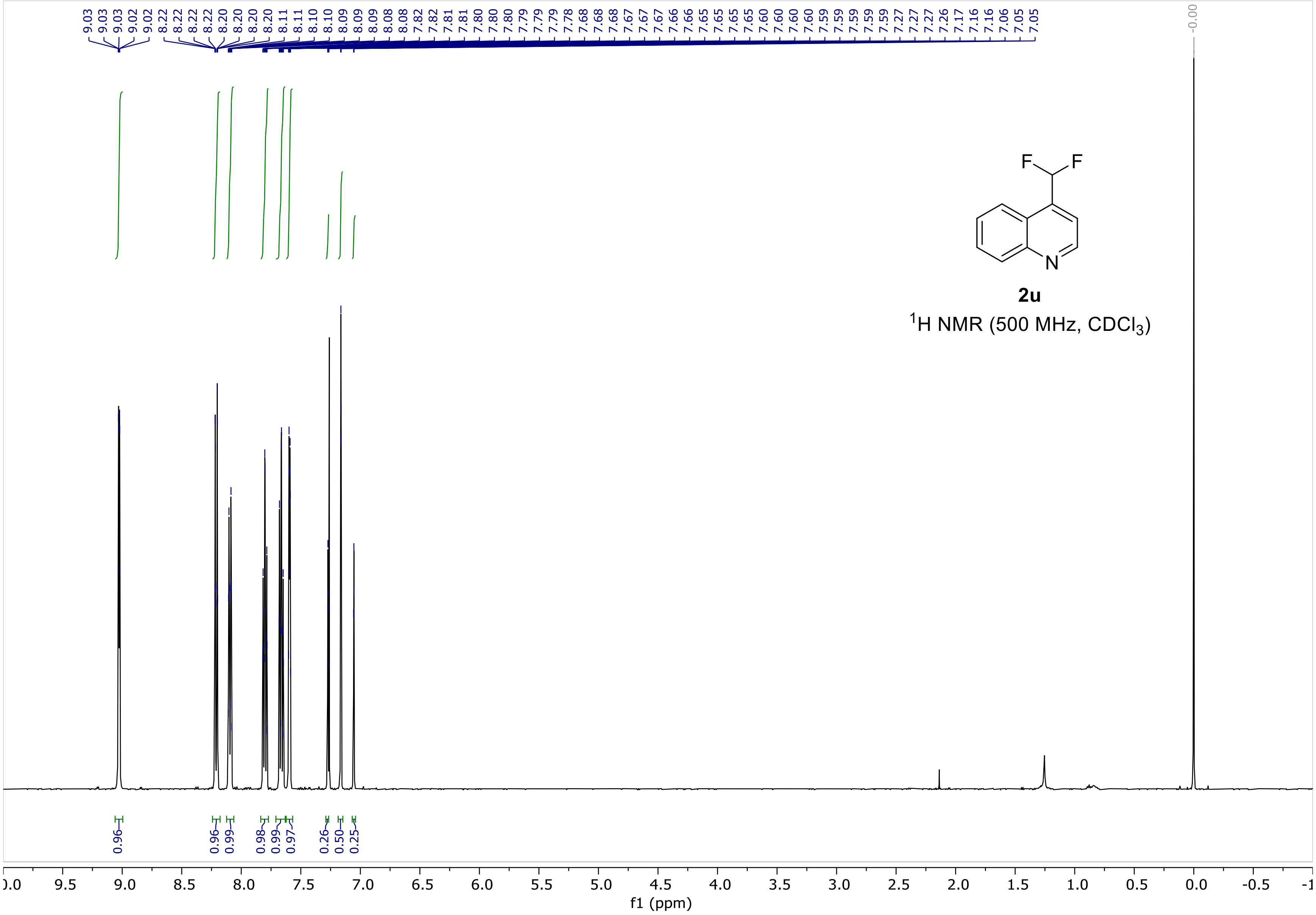
2t

^{1}H NMR (500 MHz, CDCl$_3$)



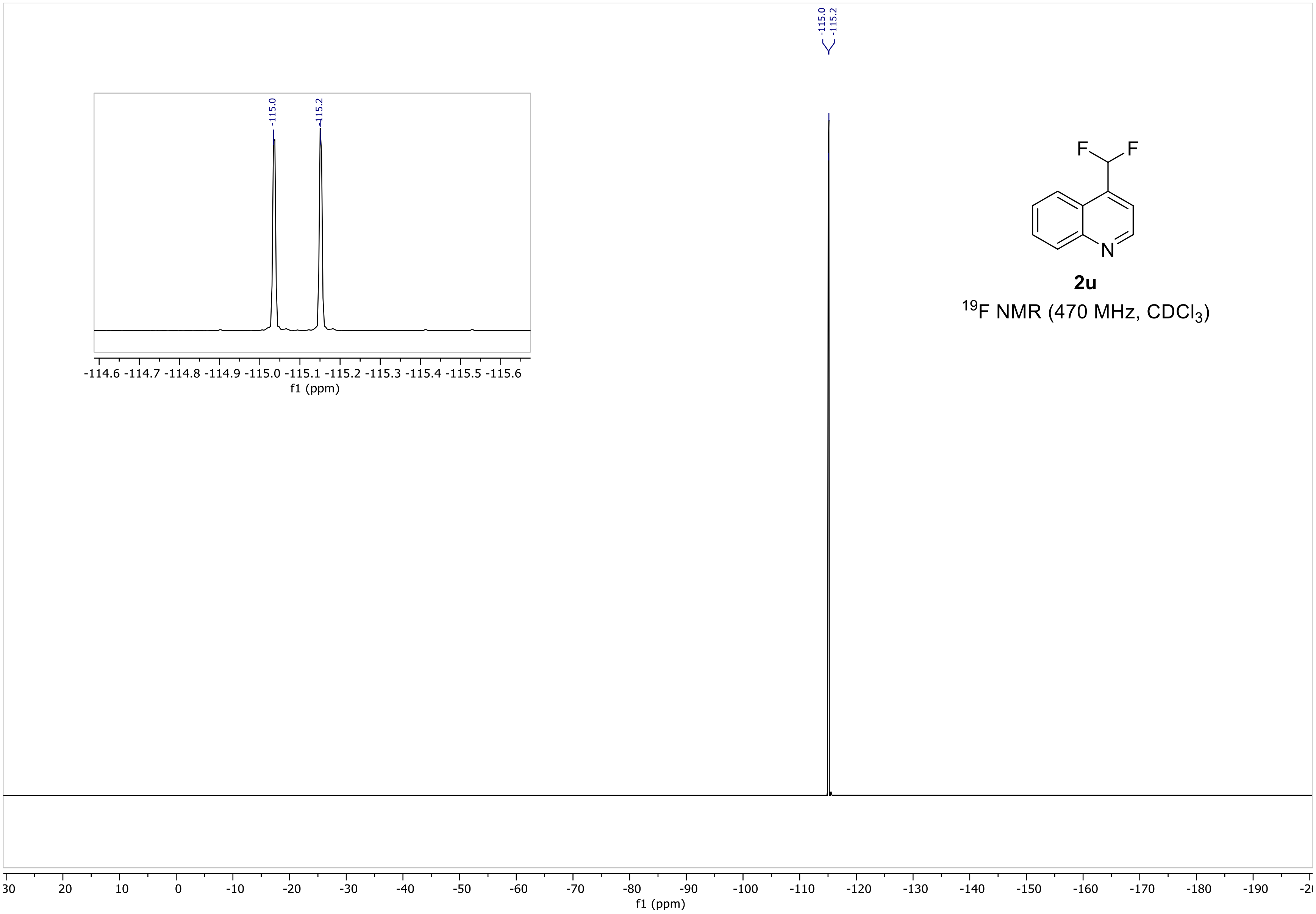
2t

^{19}F NMR (470 MHz, CDCl$_3$)



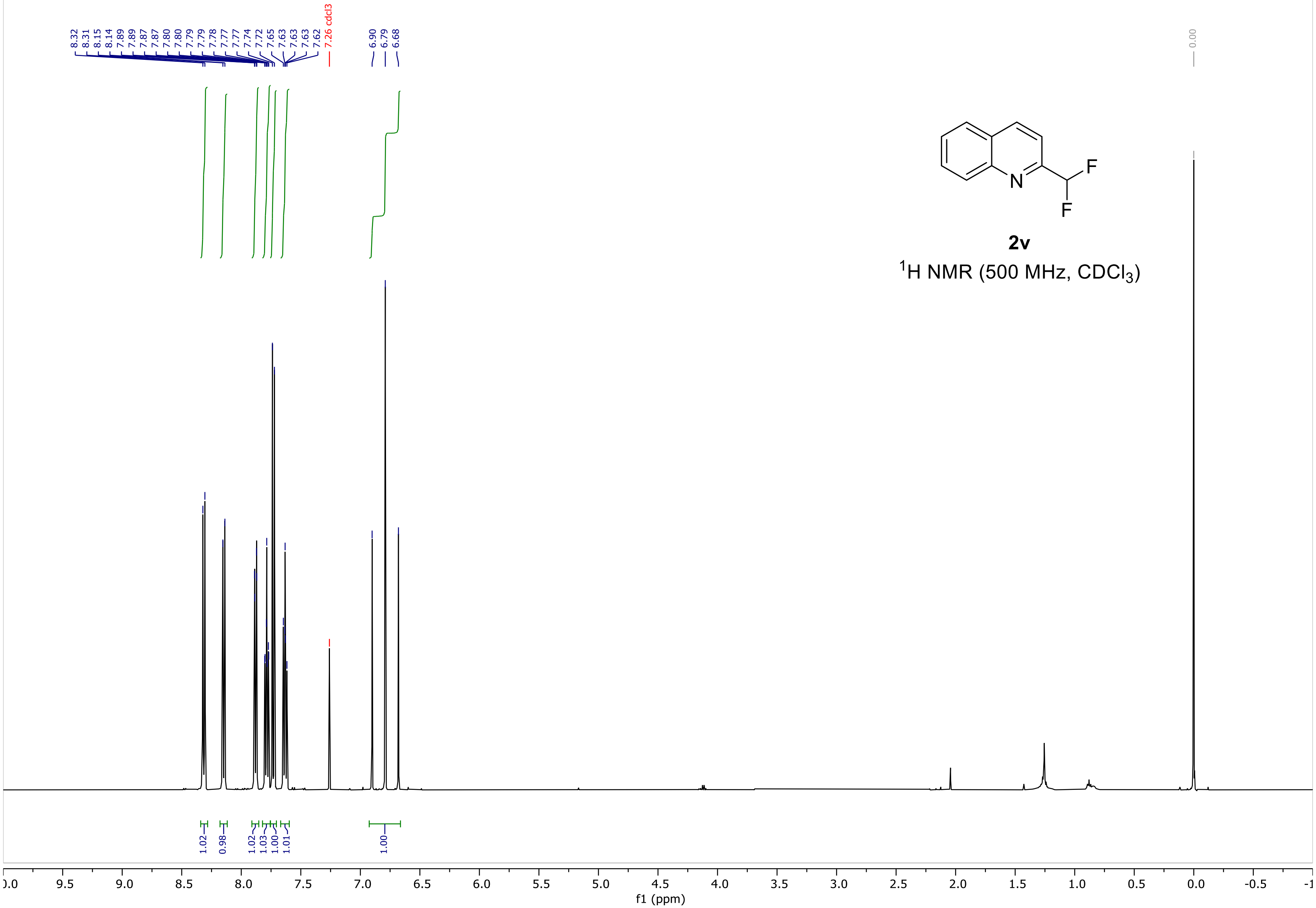
2u

^{1}H NMR (500 MHz, $CDCl_3$)



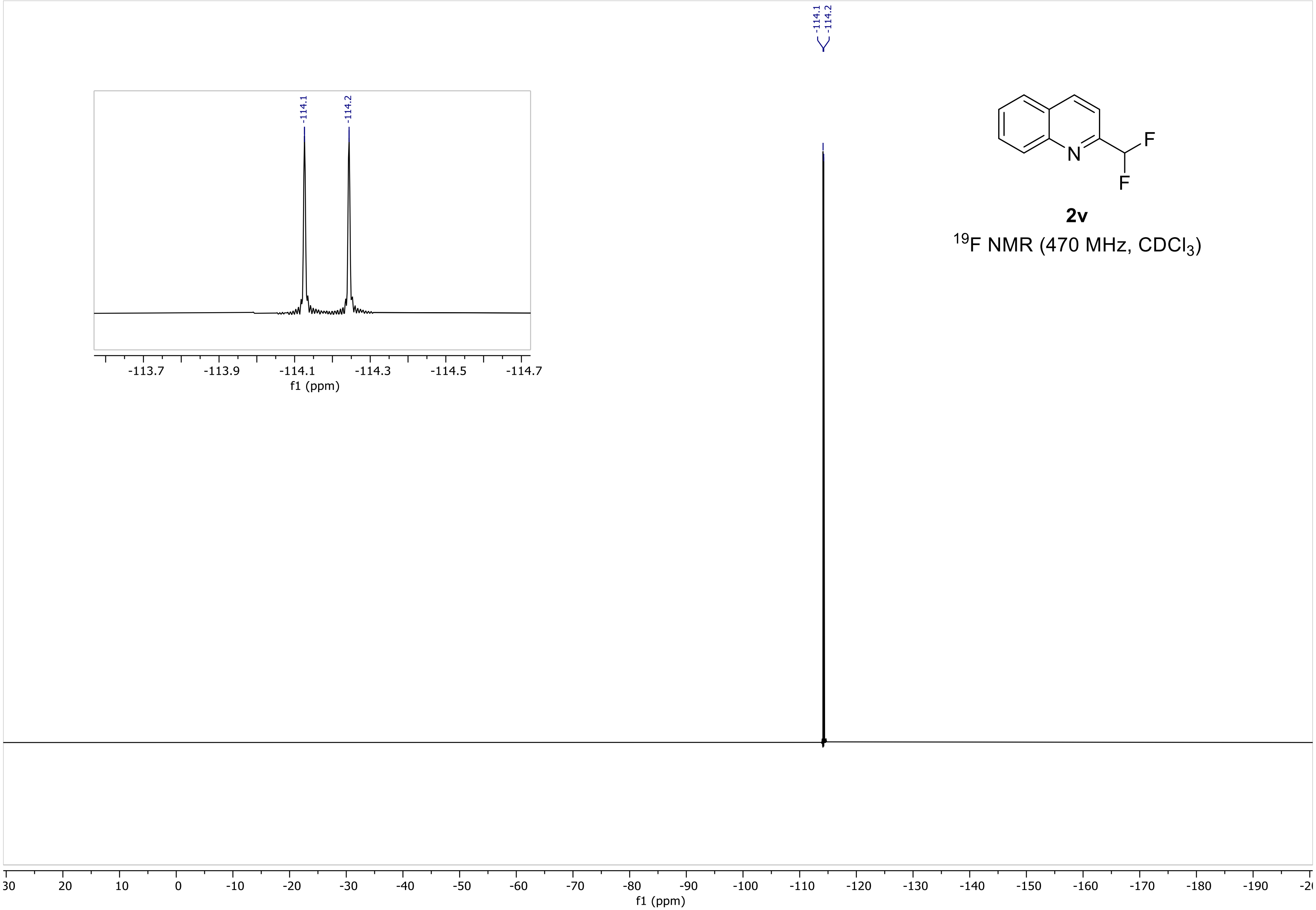
2u

^{19}F NMR (470 MHz, $CDCl_3$)



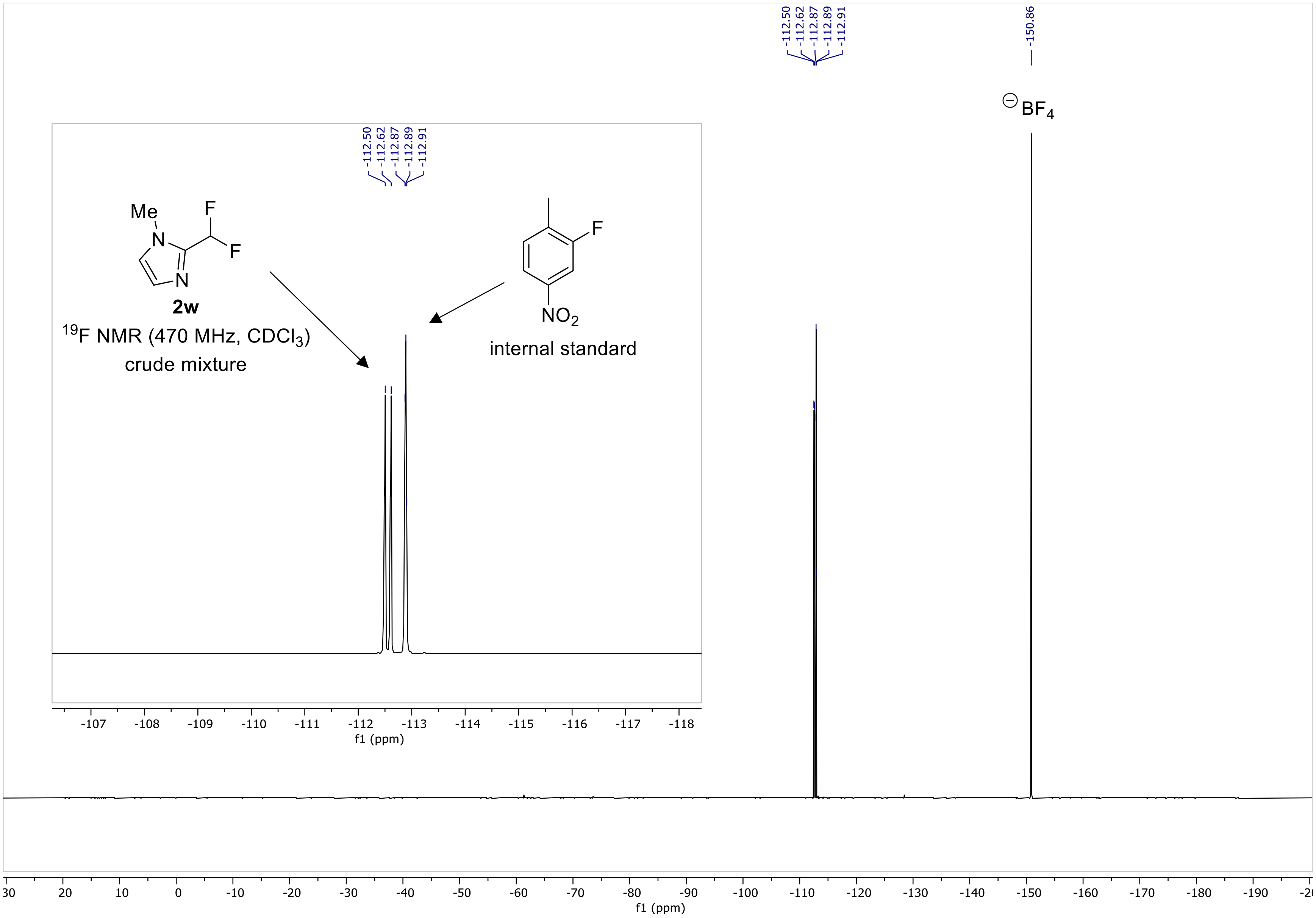
2v

^{1}H NMR (500 MHz, $CDCl_3$)

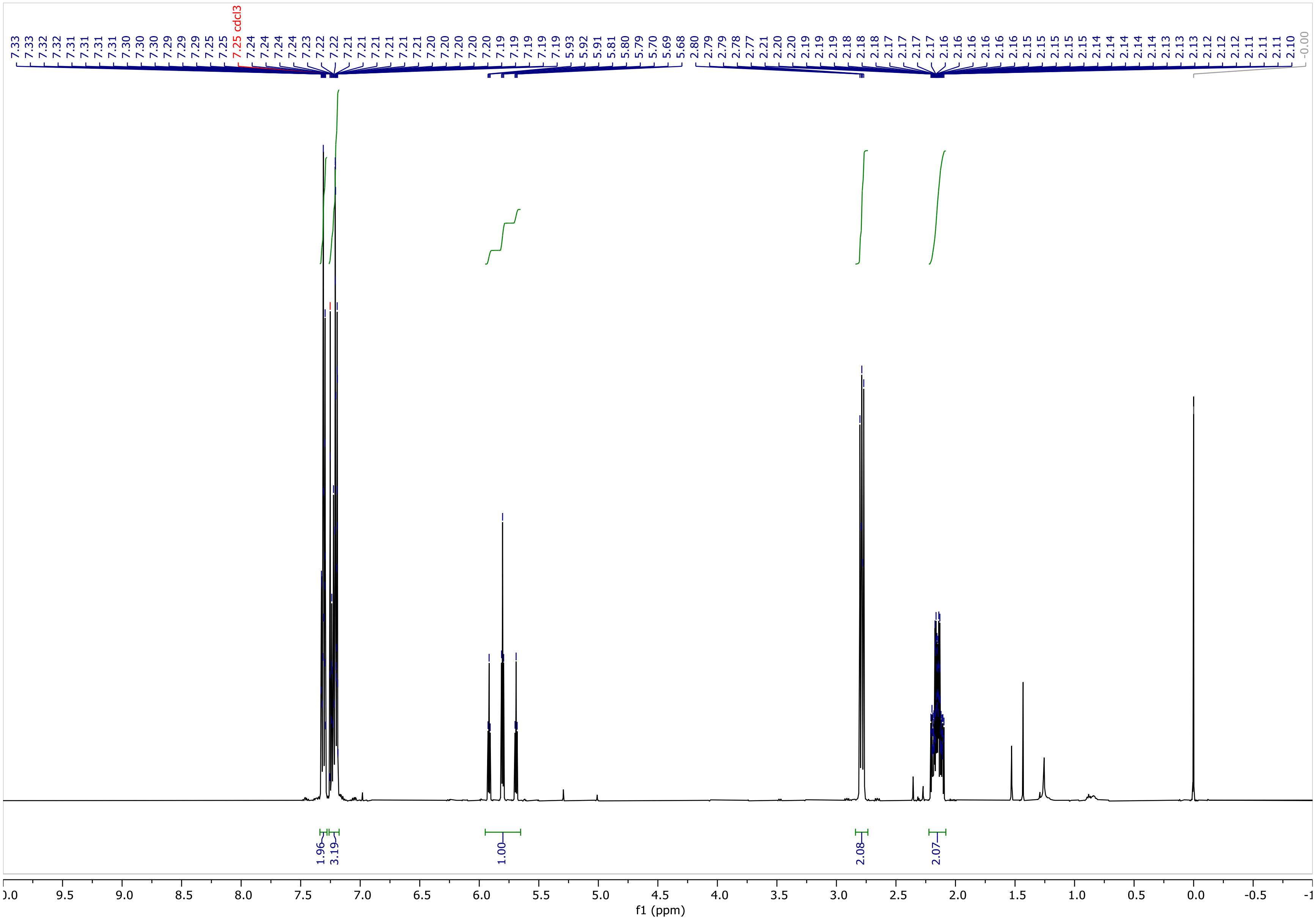


2v

^{19}F NMR (470 MHz, $CDCl_3$)



-112.50
-112.62
-112.87
-112.89
-112.91
-150.86
⊖BF$_4$
Me
N
F
F
N
2w
^{19}F NMR (470 MHz, CDCl$_3$)
crude mixture
F
NO$_2$
internal standard
-107
-108
-109
-110
-111
-112
-113
-114
-115
-116
-117
-118
f1 (ppm)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)



7.33
7.33
7.32
7.32
7.31
7.31
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7.29
7.29
7.25
7.25
7.25 cdcl3
7.24
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7.22
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7.21
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7.19
7.19
7.19
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7.19
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5.92
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5.81
5.80
5.79
5.70
5.69
5.68
2.80
2.79
2.79
2.78
2.77
2.21
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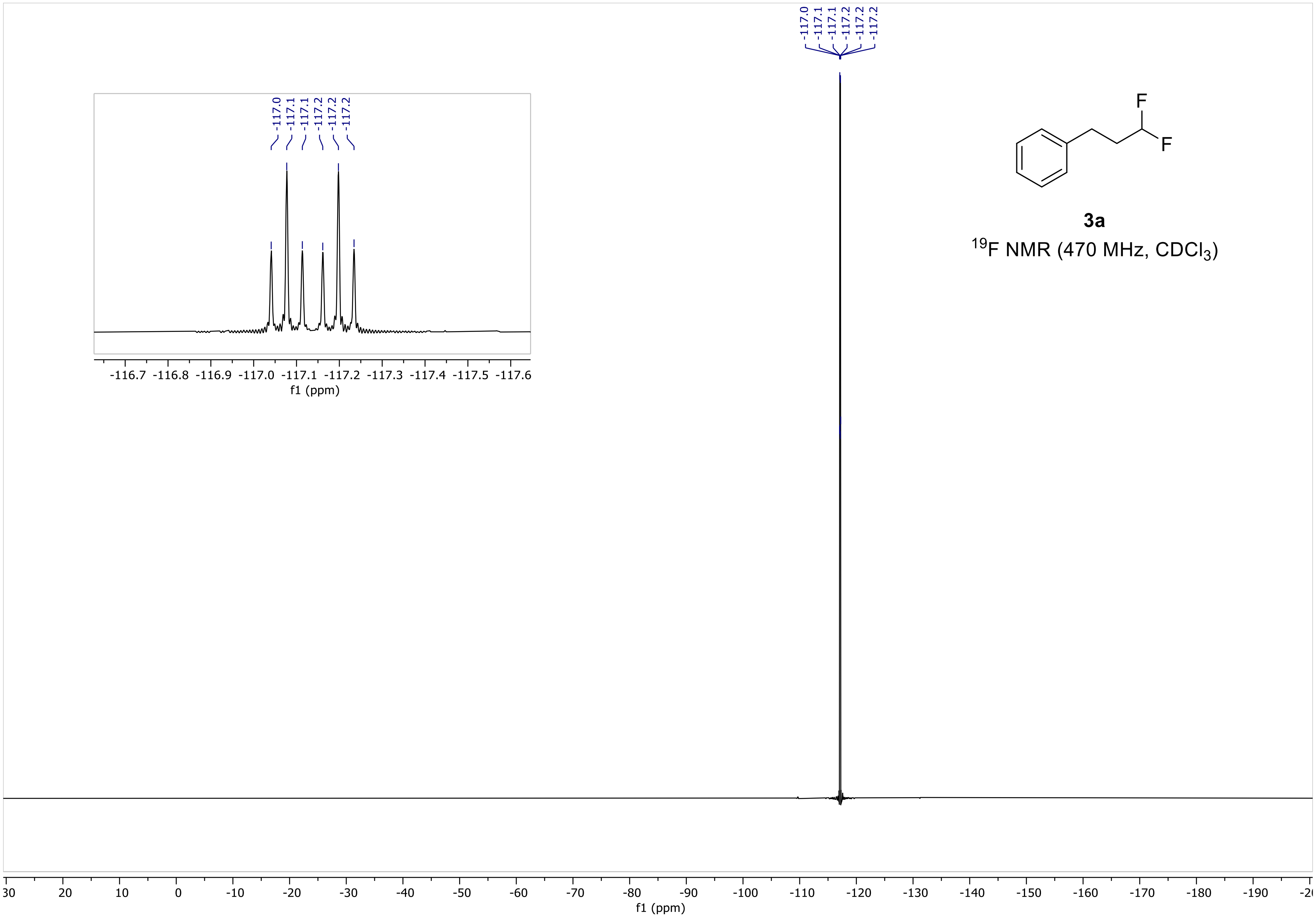
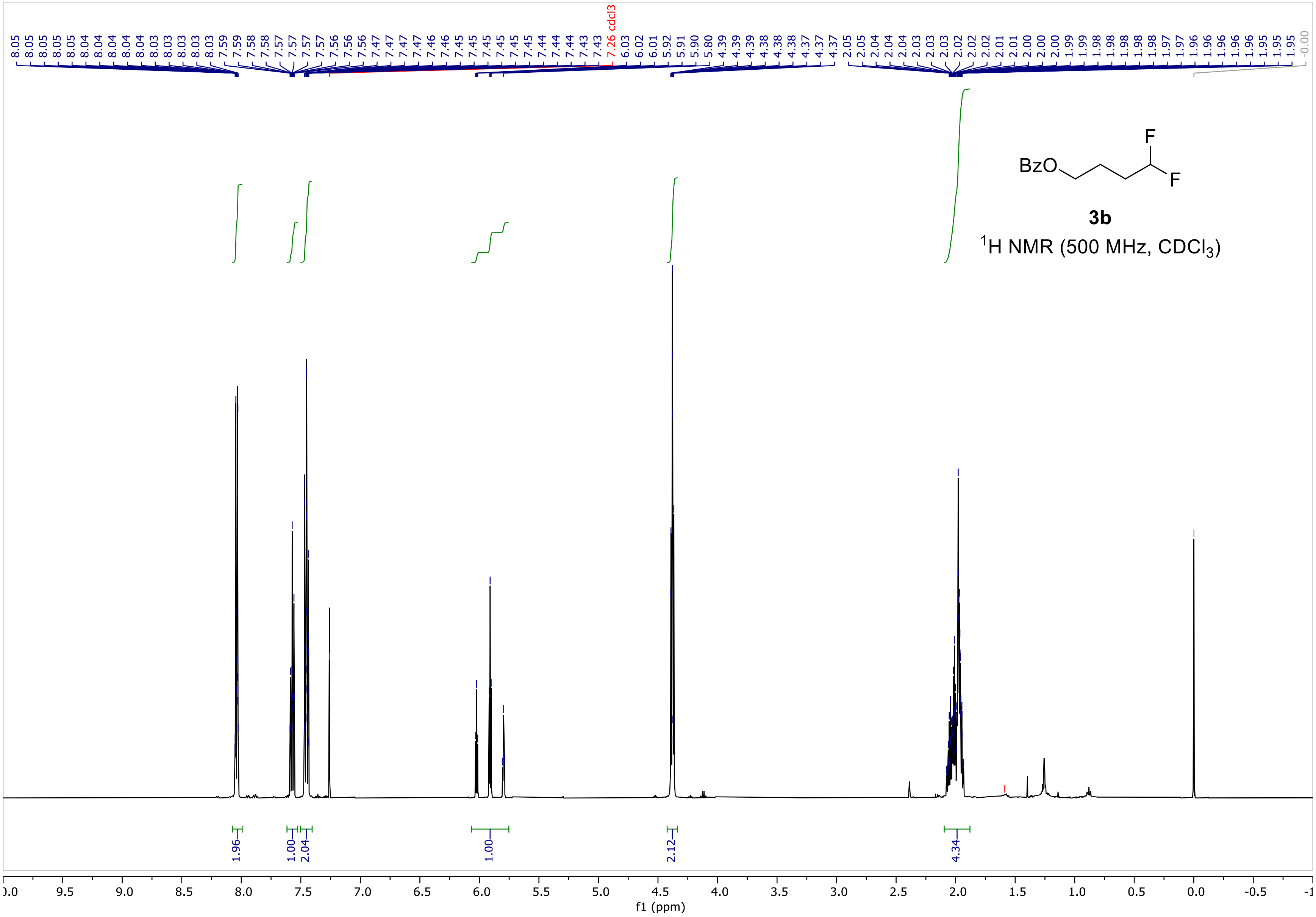
2.13
2.13
2.13
2.12
2.12
2.12
2.11
2.11
2.11
2.10
-0.00
1.96
3.19
1.00
2.08
2.07
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)



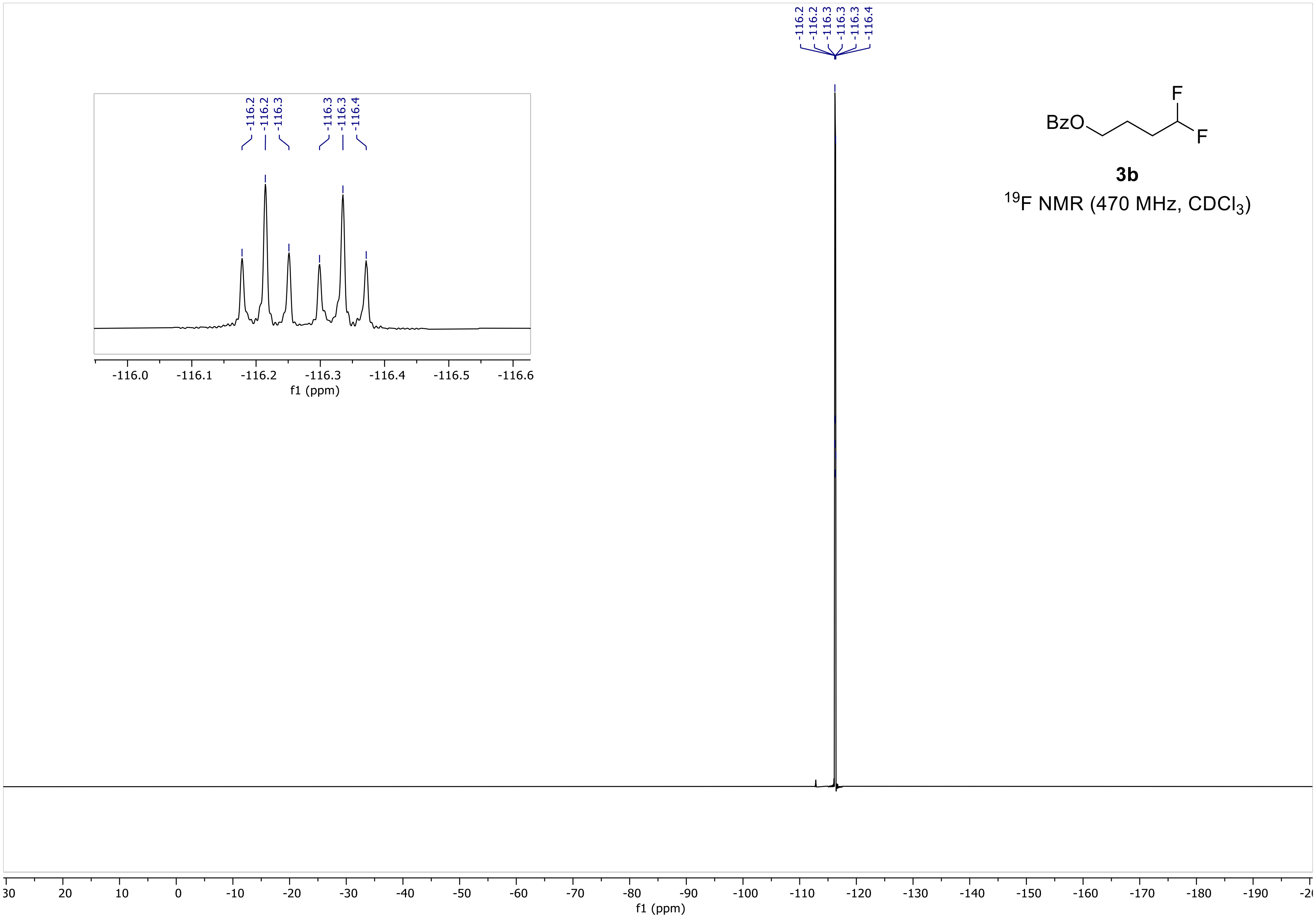
3a

^{19}F NMR (470 MHz, CDCl$_3$)



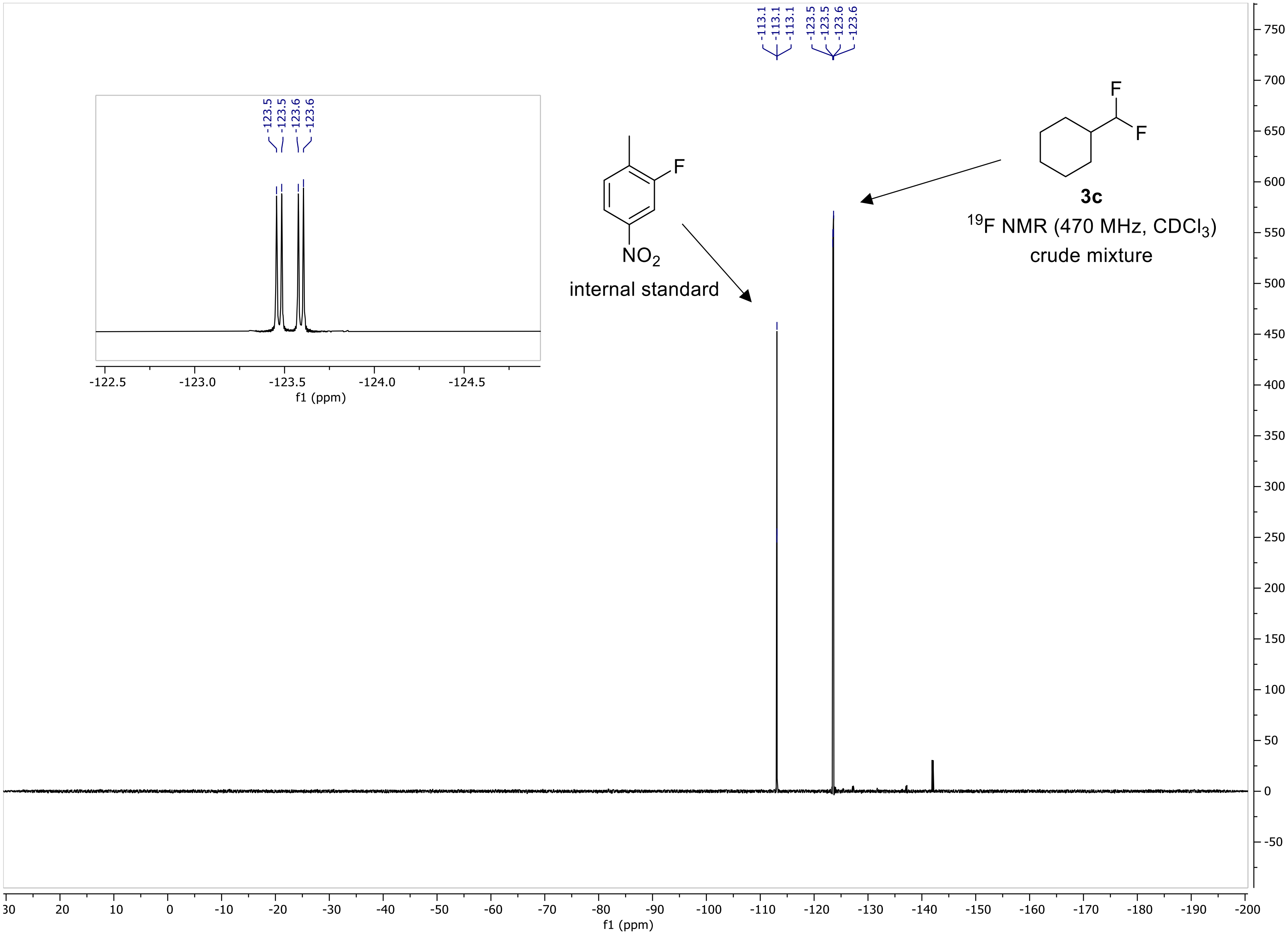
3b

^{1}H NMR (500 MHz, CDCl$_3$)

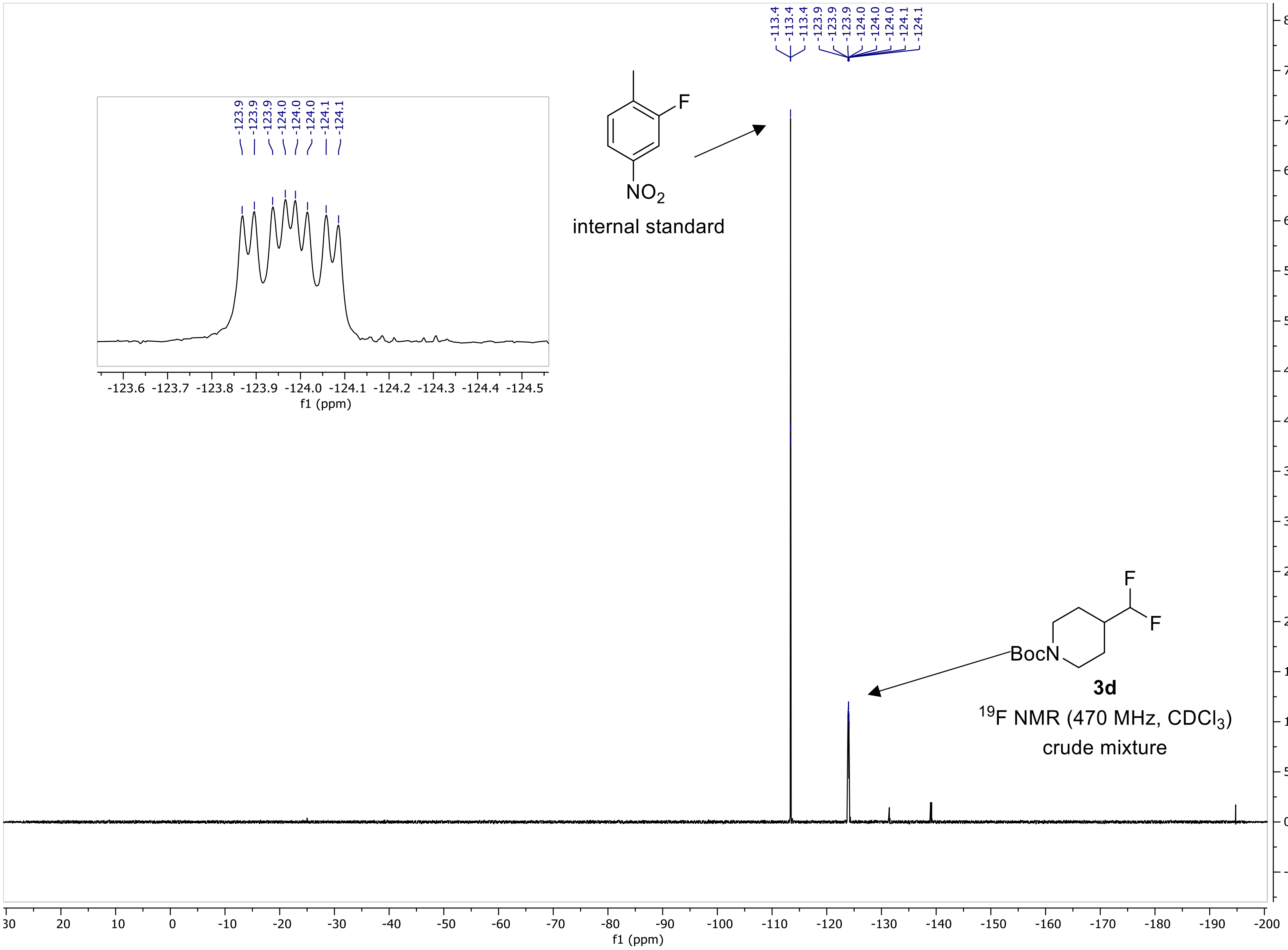


3b

^{19}F NMR (470 MHz, $CDCl_3$)



^{19}F NMR (470 MHz, CDCl$_3$)
crude mixture



3d

^{19}F NMR (470 MHz, CDCl$_3$)

crude mixture