Electronic Supporting Information

for

Highly chemoselective difluoromethylative homologation of iso(thio)cyanates: expeditious access to unprecedented α,α-difluoro(thio)amides

Margherita Miele,[a] Rosarita D'Orsi,[a, b] Vellaisamy Sridharan,[c] Wolfgang Holzer[a] and Vittorio Pace*[a]

[a] University of Vienna, Department of Pharmaceutical Chemistry, Althanstrasse 14, 1090 Vienna, Austria.

[b] University of Basilicata – Department of Sciences. Via dell'Ateneo Lucano, 10, 85100 Potenza, Italy.

[c] Department of Chemistry and Chemical Sciences, Central University of Jammu, Rahya-Suchani (Bagla), 181143, India.

** e-mail: vittorio.pace@univie.ac.at; Website: drugsynthesis.univie.ac.at*

Table of contents

1. Materials and Methods

Melting Points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV) and on a Bruker maXis 4G instrument (ESI-TOF, HRMS). ^{1}H, ^{13}C, ^{15}N and ^{19}F NMR spectra were recorded on a Bruker Avance III 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 40 MHz for ^{15}N, 376 MHz for ^{19}F) at 297 K using a directly detecting broadband observe (BBFO) probe. The centre of the solvent signal was used as an internal standard which was related to TMS with δ 7.26 ppm (^{1}H in $CDCl_3$), δ 77.00 ppm (^{13}C in $CDCl_3$). ^{15}N spectra (gsHMBC) were referenced against neat, external nitromethane, ^{19}F NMR spectra by absolute referencing via *Ξ* ratio. Spin-spin coupling constants (*J*) are given in Hz.

In nearly all cases, full and unambiguous assignment of all resonances was performed by combined application of standard NMR techniques, such as APT, HSQC, HMBC, COSY and NOESY experiments.

All the reactions were carried out under inert atmosphere of argon. THF was distilled over Na/benzophenone. Chemicals were purchased from Sigma-Aldrich, Acros, Alfa Aesar and TCI Europe. Solutions were evaporated under reduced pressure with a rotary evaporator.

TLC was carried out on aluminium sheets precoated with silica gel 60F254 (Merchery-Nagel, Merk); the spots were visualised under UV light (λ = 254 nm).

2. General Procedures

2.1 General Procedure A for the synthesis of α,α-difluoromethyl thioamides.

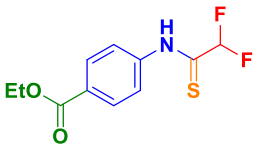
Difluoromethyltrimethylsilane (1.5 equiv) was added under an inert atmosphere to a solution of isothiocyanate (1 equiv) in dry THF and the mixture was cooled down to 0 °C. Then potassium *tert*-amylate solution (0.9 M in THF, 1.2 equiv) was added dropwise over a period of 30 minutes. Then the mixture was stirred at 0°C for 1 hour and then quenched with aqueous NH_4Cl solution. The reaction mixture was then extracted with Et_2O (x 3) , washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The resulting reaction crudes were purified through column chromatography as indicated.

2.2 General Procedure B for the synthesis of α,α-difluoromethyl amides.

Difluoromethyltrimethylsilane (1.5 equiv) was added under an inert atmosphere to a solution of isocyanate (1 equiv) in dry THF and the mixture was cooled down to 0 °C. Then potassium *tert*-amylate solution (0.9 M in THF, 1.2 equiv) was added dropwise over a period of 30 minutes. Then the mixture was stirred at 0°C for 1 hour and then quenched with aqueous NH_4Cl solution. The reaction mixture was then extracted with Et_2O (x 3), washed with brine, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The resulting reaction crudes were purified through column chromatography as indicated.

3. Characterization and Spectral Data.

ethyl 4-[(2,2-difluoroethanethioyl)amino]benzoate (2)



By following General Procedure A, starting from ethyl 4-isothiocyanatobenzoate (0.207 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **2** was obtained in 83% yield (0.215 g) as yellow solid (mp 71-74°C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.33 (br s, 1H, NH), 8.13 (m, 2H, Ph H-2,6), 7.99 (m, 2H, Ph H-3,5), 6.27 (t, $^2J_{H,F}$ = 56.5 Hz, 1H, CHF_2), 4.39 (q, ^3J =7.1 Hz, 2H, OCH_2), 1.41 (t, ^3J = 7.1 Hz, 3H, CH_3).

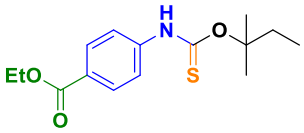
^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5 (CO), 140.6 (Ph C-4), 130.8 (Ph C-2,6), 129.2 (Ph C-1), 121.7 (Ph C-3,5), 112.9 (t, $^1J_{C,F}$ = 258.3 Hz, CHF_2), 61.2 (OCH_2), 14.3 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -291.0 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.9 (dd, $^2J_{H,F}$ = 56.5 Hz, $^nJ_{H,F}$ = 3.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{11}H_{12}F_2NO_2S^+$: 260.0551 $[M+H]^+$; found: 260.0546.

ethyl 4-[(((2-methyl-2-butanyl)oxy)carbothioyl)amino]benzoate (2b)

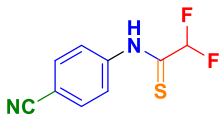


^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (m, 2H, Ph H-2,6), 7.42 (m, 2H, Ph H-3,5), 6.69 (br s, 1H, NH), 4.35 (q, ^3J =7.1 Hz, 2H, OCH_2), 1.84 (q, ^3J =7.5 Hz, 2H, CH_2), 1.49 (s, 6H, CH_3), 1.38 (t, ^3J = 7.1 Hz, 3H, OCH_2CH_3), 0.93 (t, ^3J =7.5 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3 (CO), 152.1 (C=S), 142.6 (Ph C-4), 130.8 (Ph C-2,6), 124.7 (Ph C-1), 117.3 (Ph C-3,5), 83.7 ($C(CH_3)_2$), 60.7 (OCH_2), 33.6 (CH_2), 25.7 (2C, CH_3), 14.3 (OCH_2CH_3), 8.2 (CH_3).

HRMS (ESI), *m/z*: calcd. for $C_{15}H_{21}NO_3S^+$: 296.1315 $[M+H]^+$; found: 296.1319.

***N*-(4-cyanophenyl)-2,2-difluoroethanethioamide (3)**



By following General Procedure A, starting from 4-isothiocyanatobenzonitrile (0.160 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **3** was obtained in 93% yield (0.197 g) as pale yellow solid (mp 155-158 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1),.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.33 (br s, 1H, NH), 8.07 (m, 2H, Ph H-2,6), 7.74 (m, 2H, Ph H-3,5), 6.27 (t, $^{2}J_{H,F}$ = 56.4 Hz, 1H, CHF_2).

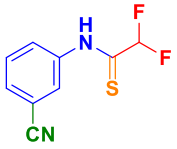
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.4 (t, $^{2}J_{C,F}$ =20.3 Hz, C=S), 140.6 (Ph C-1), 133.3 (Ph C-3,5), 122.4 (Ph C-2,6), 118.0 (CN), 112.8 (t, $^{1}J_{C,F}$ = 258.8 Hz, CHF_2), 110.7 (Ph C-4).

^{15}N NMR (40 MHz, $CDCl_3$): δ -292.4 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.9 (dd, $^{2}J_{H,F}$ = 56.4 Hz, $^{n}J_{H,F}$ = 3.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_6F_2N_2NaS$: 235.0112 $[M+Na]^+$; found: 235.0109.

***N*-(3-cyanophenyl)-2,2-difluoroethanethioamide (4)**



By following General Procedure A, starting from 3-isothiocyanatobenzonitrile (0.160 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **4** was obtained in 86% yield (0.182 g) as yellow solid (mp 112-115°C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.34 (br s, 1H, NH), 8.31 (m, 1H, Ph H-2), 8.02 (m, 1H, Ph H-6), 7.62 (m, 1H, Ph H-4), 7.57 (m, 1H, Ph H-5), 6.28 (t, $^{2}J_{H,F}$ = 56.3 Hz, 1H, CHF_2).

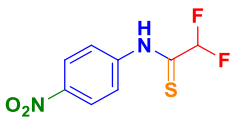
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.8 (t, $^{2}J_{C,F}$ =20.8 Hz, C=S), 137.7 (Ph C-1), 130.9 (Ph C-4), 130.2 (Ph C-5), 126.9 (Ph C-6), 125.8 (Ph C-2), 117.7 (CN), 113.4 (Ph C-3), 112.7 (t, $^{1}J_{C,F}$ = 258.4 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -294.1 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.3 Hz, $^{n}J_{H,F}$ = 3.2 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_6F_2N_2NaS$: 235.0112 $[M+Na]^+$; found: 235.0111.

2,2-difluoro-*N*-(4-nitrophenyl)ethanethioamide (5)



By following General Procedure A, starting from 1-isothiocyanato-4-nitrobenzene (0.180 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **5** was obtained in 85% yield (0.197 g) as brown solid (mp 60-63°C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 7:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.41 (br s, 1H, NH), 8.33 (m, 2H, Ph H-3,5), 8.14 (m, 2H, Ph H-2,6), 6.29 (t, $^{2}J_{H,F}$ = 56.3 Hz, 1H, CHF_2).

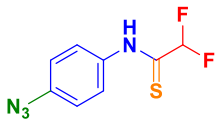
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.6 (t, $^{2}J_{C,F}$ =20.6 Hz, C=S), 145.7 (Ph C-4), 142.2 (Ph C-1), 125.0 (Ph C-3,5), 122.2 (Ph C-2,6), 112.8 (t, $^{1}J_{C,F}$ = 258.8 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -293.0 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.9 (dd, $^{2}J_{H,F}$ = 56.3 Hz, $^{n}J_{H,F}$ = 3.2 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_6F_2N_2NaO_2S$: 255.0010 $[M+Na]^+$; found: 255.0009.

***N*-(4-azidophenyl)-2,2-difluoroethanethioamide (6)**



By following General Procedure A, starting from 1-isothiocyanato-4-azidobenzene (0.176 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **6** was obtained in 88% yield (0.201 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.25 (br s, 1H, NH), 7.84 (m, 2H, Ph C-2,6), 7.10 (m, 2H, Ph C-3,5), 6.28 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

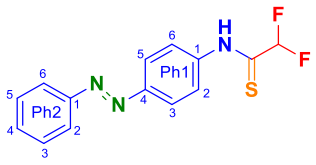
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.6 (t, $^{2}J_{C,F}$ =20.4 Hz, C=S), 133.6 (Ph C-1), 139.1 (Ph C-4), 124.2 (Ph C-2,6), 119.6 (Ph C-3,5), 112.8 (t, $^{1}J_{C,F}$ = 258.1 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -291.7 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.5 Hz, $^{n}J_{H,F}$ = 3.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_7F_2N_4S^+$: 229.0354 $[M+H]^+$; found: 229.0342.

2,2-difluoro-*N*-{4-[(*E*)-phenyldiazenyl]phenyl}ethanethioamide (7)



By following General Procedure A, starting from 1-(4-isothiocyanatophenyl)-2-phenyldiazene (0.239 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv), potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **7** was obtained in 90% yield (0.262 g) as orange solid (mp 83-86°C) after column chromatography on silica gel (*n*-hexane:diethyl ether 7:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.37 (br s, 1H, NH), 8.08 (m, 2H, Ph1 H-2,6), 8.02 (m, 2H, Ph1 H-3,5), 7.93 (m, 2H, Ph2 H-2,6), 7.54 (m, 2H, Ph H-3,5), 7.51 (m, 1H, Ph2 H-4), 6.30 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

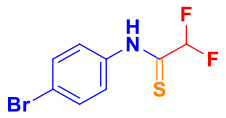
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.7 (C=S), 152.6 (Ph2 C-1), 151.0 (Ph1 C-4), 138.9 (Ph1 C-1), 131.4 (Ph2 C-4), 129.2 (Ph2 C-3,5), 123.9 (Ph1 C-3,5), 123.0 (Ph2 C-2,6), 122.7 (Ph1 C-2,6), 112.9 (t, $^{1}J_{C,F}$ = 258.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -290.6 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.9 (dd, $^{2}J_{H,F}$ = 56.5 Hz, $^{n}J_{H,F}$ = 3.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{12}F_2N_3S^+$: 292.0715 $[M+H]^+$; found: 292.0706.

***N*-(4-bromophenyl)-2,2-difluoroethanethioamide (8)**



By following General Procedure A, starting from 1-isothiocyanato-4-bromobenzene (0.214 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **8** was obtained in 91% yield (0.242 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

Reaction conducted on 10 mmol scale. By following General Procedure A, starting from 1-isothiocyanato-4-bromobenzene (2.14 g, 10 mmol, 1.0 equiv) in dry THF (80 mL), CHF_2SiMe_3 (1.85 g, 15 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (13 mL, 12 mmol, 1.2 equiv), compound **8** was obtained in 88% yield (2.34 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1). *Spectral and spectrometric data match with those reported for the compound obtained in the 1 mmol scale reaction.*

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (br s, 1H, NH), 7.75 (m, 2H, Ph H-2,6), 7.57 (m, 2H, Ph H-3,5), 6.27 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

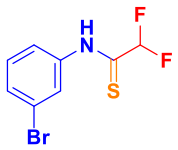
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.9 (t, $^{2}J_{C,F}$ =20.3 Hz, C=S), 135.9 (Ph C-1), 132.3 (Ph C-3,5), 124.1 (Ph C-2,6), 120.6 (Ph C-4), 112.8 (t, $^{1}J_{C,F}$ = 258.2 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -292.3 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.5 Hz, $^{2n}J_{H,F}$ = 3.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_7BrF_2NS^+$: 265.9445 $[M+H]^+$; found: 265.9438.

***N*-(3-bromophenyl)-2,2-difluoroethanethioamide (9)**



By following General Procedure A, starting from 1-isothiocyanato-3-bromobenzene (0.213 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **9** was obtained in 87% (0.230 g) as yellow oil after column chromatography on silica gel (*n*-heptane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (br s, 1H, NH), 8.10 (m, 1H, Ph H-2), 7.76 (m, 1H, Ph H-6), 7.47 (m, 1H, Ph H-4), 7.32 (m, 1H, Ph H-5), 6.27 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

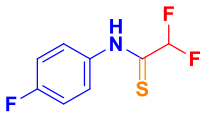
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.0 (C=S), 138.0 (Ph C-1), 130.6 (Ph C-4), 130.5 (Ph C-5), 125.5 (Ph C-2), 122.6 (Ph C-3), 121.3 (Ph C-6), 112.8 (t, $^{1}J_{C,F}$ = 258.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -292.9 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.5 Hz, $^{n}J_{H,F}$ = 3.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_7BrF_2NS^+$: 265.9445 $[M+H]^+$; found: 265.9421

2,2-difluoro-*N*-(4-fluorophenyl)ethanethioamide (10)



By following General Procedure A, starting from 1-isothiocyanato-4-fluorobenzene (0.153 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **10** was obtained in 95% yield (0.195 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.26 (br s, 1H, NH), 7.79 (m, 2H, Ph H-2,6), 7.14 (m, 2H, Ph H-3,5), 6.28 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

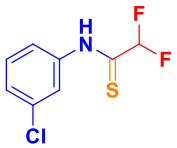
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1 (t, $^{2}J_{C,F}$ = 20.4 Hz, C=S), 161.1 (d, $^{1}J_{C,F}$ = 248.7 Hz, Ph C-4), 132.8 (d, $^{4}J_{C,F}$ = 3.0 Hz, Ph C-1), 124.9 (d, $^{3}J_{C,F}$ = 8.4 Hz, Ph C-2,6), 116.1 (d, $^{2}J_{C,F}$ = 23.0 Hz, Ph C-3,5), 112.8 (t, $^{1}J_{C,F}$ = 258.0 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -308.6 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.2 (dd, $^{2}J_{H,F}$ = 56.5 Hz, $^{n}J_{H,F}$ = 3.2 Hz, CHF_2), -112.4 (m, Ph-F).

HRMS (ESI), *m/z*: calcd. for $C_8H_7F_3NS^+$: 206.0246 $[M+H]^+$; found: 206.0233.

***N*-(3-chlorophenyl)-2,2-difluoroethanethioamide (11)**



By following General Procedure A, starting from 1-isothiocyanato-3-chlorobenzene (0.169 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **11** was obtained in 86% yield (0.190 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.21 (br s, 1H, NH), 7.98 (m, 1H, Ph H-2), 7.69 (m, 1H, Ph H-6), 7.38 (m, 1H, Ph H-5), 7.31 (m, 1H, Ph H-4), 6.27 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

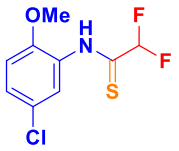
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.1 (t, $^{2}J_{C,F}$ = 20.8 Hz, C=S), 137.9 (Ph C-1), 134.9 (Ph C-3), 130.2 (Ph C-5), 127.7 (Ph C-4), 122.7 (Ph C-2), 120.7 (Ph C-6), 112.8 (t, $^{1}J_{C,F}$ = 258.4 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -292.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.4 Hz, $^{n}J_{H,F}$ = 3.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_6ClF_2NNaS$: 243.9770 $[M+Na]^+$; found: 243.9767.

***N*-(5-chloro-2-methoxyphenyl)-2,2-difluoroethanethioamide (12)**



By following General Procedure A, starting from ethyl 4-cloro-2-isothiocyanato-1-methoxybenzoate (0.199 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **12** was obtained in 83% yield (0.208 g) as brown solid (mp 70-72°C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 7:3).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.99 (br s, 1H, NH), 9.25 (d, $^{4}J_{H,H}$ =2.5 Hz, 1H, Ph H-6), 7.22 (dd, $^{3}J_{H,H}$ = 8.8 Hz, $^{4}J_{H,H}$ =2.5 Hz, 1H, Ph H-4), 6.90 (d, $^{3}J_{H,H}$ = 8.8 Hz, 1H, Ph H-3), 6.23 (t, $^{2}J_{H,F}$ = 56.6 Hz, 1H, CHF_2), 3.95 (s, 3H, OCH_3).

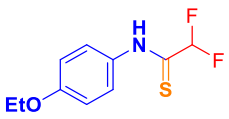
^{13}C NMR (100 MHz, $CDCl_3$): δ 185.1 (t, $^{2}J_{C,F}$ =20.4 Hz, C=S), 148.0 (Ph C-2), 127.6 (Ph C-1), 126.8 (Ph C-4), 125.6 (Ph C-5), 120.4 (Ph C-6), 113.0 (t, $^{1}J_{C,F}$ = 258.4 Hz, CHF_2), 111.2 (Ph C-3), 56.4 (OCH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -299.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.8 (dd, $^{2}J_{H,F}$ = 56.6 Hz, $^{2n}J_{H,F}$ = 3.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_9ClF_2NOS^+$: 252.0056 $[M+H]^+$; found: 252.0050.

***N*-(4-ethoxyphenyl)-2,2-difluoroethanethioamide (13)**



By following General Procedure A, starting from 1-isothiocyanato-4-ethoxybenzene (0.179 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **13** was obtained in 93% yield (0.214 g) as brown oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.20 (br s, 1H, NH), 7.72 (m, 2H, Ph H-2,6), 6.94 (m, 2H, Ph H-3,5), 6.28 (t, $^{2}J_{H,F}$ = 56.6 Hz, 1H, CHF_2), 4.06 (q, ^{3}J = 7.0 Hz, 2H, OCH_2), 1.43 (t, ^{3}J = 7.0 Hz, 3H, CH_3).

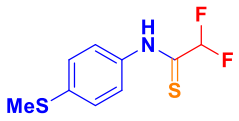
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.0 (t, $^{2}J_{C,F}$ =20.3 Hz, C=S), 158.0 (Ph C-4), 129.6 (Ph C-1), 124.3 (Ph C-2,6), 114.8 (Ph C-3,5), 112.8 (t, $^{1}J_{C,F}$ = 257.8 Hz, CHF_2), 63.8 (OCH_2), 14.7 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -290.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.6 Hz, $^{n}J_{H,F}$ = 3.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{10}H_{11}F_2NNaOS$: 254.0422 $[M+Na]^+$; found: 224.0420.

2,2-difluoro-*N*-[4-(methylsulfanyl)phenyl]ethanethioamide (14)



By following General Procedure A, starting from 1-isothiocyanato-4-methylsulfanylbenzene (0.181 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **14** was obtained in 88% yield (0.209 g) as yellow oil after column chromatography on silica gel (*n*-heptane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.22 (br s, 1H, NH), 7.77 (m, 2H, Ph H-2,6), 7.30 (m, 2H, Ph H-3,5), 6.27 (t, $^{2}J_{H,F}$ = 56.5 Hz, 1H, CHF_2), 2.51 (s, 3H, SCH_3).

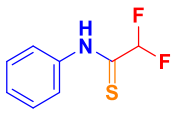
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.1 (t, $^{2}J_{C,F}$ =20.5 Hz, C=S), 138.4 (Ph C-4), 133.9 (Ph C-1), 126.7 (Ph C-3,5), 123.0 (Ph C-2,6), 112.8 (t, $^{1}J_{C,F}$ = 258.1 Hz, CHF_2), 15.7(SCH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -290.6 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.0 (dd, $^{2}J_{H,F}$ = 56.5 Hz, $^{n}J_{H,F}$ = 3.5 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_{10}F_2NS_2$: 234.0217 $[M+H]^+$; found: 234.0205.

2,2-difluoro-*N*-phenylethanethioamide (15)



By following General Procedure A, starting from isothiocyanatobenzene (0.135 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **15** was obtained in 91% yield (0.170 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 85:15).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.26 (br s, 1H, NH), 7.83 (m, 2H, Ph H-2,6), 7.45 (m, 2H, Ph H-3,5), 7.33 (m, 1H, Ph H-4) 6.28 (t, $^2J_{H,F}$ = 56.5 Hz, 1H, CHF_2).

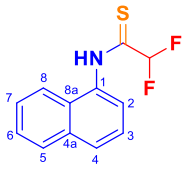
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.7 (t, $^2J_{C,F}$ =20.5 Hz, C=S), 136.8 (Ph C-1), 129.2 (Ph C-3,5), 127.7 (Ph C-4), 122.6 (Ph C-2,6), 112.9 (t, $^1J_{C,F}$ = 258.2 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -290.0 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^2J_{H,F}$ = 56.5 Hz, $^nJ_{H,F}$ = 3.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_8F_2NS^+$: 188.0340 $[M+H]^+$; found: 188.0342.

2,2-difluoro-*N*-(1-naphthyl)ethanethioamide (16)



By following General Procedure A, starting from 1-isothiocyanatonaphthalene (0.185 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **16** was obtained in 92% yield (0.218 g) as brown oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.52 (br s, 1H, NH), 7.93 (m, 2H, H-4,5), 7.91 (m, 1H, H-2), 7.80 (m, 1H, H-8), 7.58 (m, 1H, H-7), 7.57 (m, 1H, H-6), 7.55 (m, 1H, H-3), 6.45 (t, $^{2}J_{H,F}$ = 56.3 Hz, 1H, CHF_2).

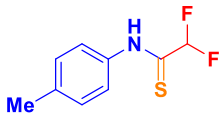
^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6 (t, $^{2}J_{C,F}$ = 20.7 Hz, C=S), 134.3 (napht C-1), 131.9 (napht C-4a), 129.0 (napht C-5), 128.9 (napht C-4), 128.0 (Ph C-9), 127.3 (napht C-7), 126.7 (napht C-6), 125.3 (napht C-3), 123.7 (napht C-2), 120.8 (napht C-8), 113.0 (t, $^{1}J_{C,F}$ = 257.4 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -297.2 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.9 (dd, $^{2}J_{H,F}$ = 56.3 Hz, $^{n}J_{H,F}$ = 3.0 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{12}H_9F_2NNaS$: 260.0316 $[M+Na]^+$; found: 260.0318.

2,2-difluoro-N-(4-methylphenyl)ethanethioamide (17)



By following General Procedure A, starting from 1-isothiocyanato-4-methylbenzene (0.149 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **17** was obtained in 90% yield (0.181 g) as brown oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.22 (br s, 1H, NH), 7.69 (m, 2H, Ph H-2,6), 7.25 (m, 2H, Ph H-3,5), 6.28 (t, $^{2}J_{H,F}$ = 56.6 Hz, 1H, CHF_2), 2.38 (s, 3H, CH_3).

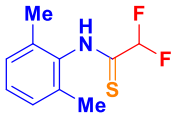
^{13}C NMR (100 MHz, $CDCl_3$): δ 186.4 (t, $^{2}J_{C,F}$ =20.2 Hz, C=S), 137.8 (Ph C-4), 134.3 (Ph C-1), 129.7 (Ph C-3,5), 122.6 (Ph C-2,6), 112.8 (t, $^{1}J_{C,F}$ = 258.0 Hz, CHF_2), 21.2 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -289.9 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.6 Hz, $^{n}J_{H,F}$ = 3.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_9F_2NNaS$: 224.0316 $[M+Na]^+$; found: 224.0310.

_N_-(2,6-dimethylphenyl)-2,2-difluoroethanethioamide (18)



By following General Procedure A, starting from 2-isothiocyanato-1,3-dimethylbenzene (0.163 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **18** was obtained in 90% yield (0.194 g) as brown oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.93 (br s, 1H, NH), 7.24 (m, 1H, Ph H-4), 7.15 (d, ^{3}J = 7.5 Hz, 2H, Ph H-3,5), 6.36 (t, $^{2}J_{H,F}$ = 56.2 Hz, 1H, CHF_2), 2.23 (s, 6H, CH_3).

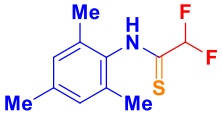
^{13}C NMR (100 MHz, $CDCl_3$): δ 189.7 (t, $^{2}J_{C,F}$ =20.9 Hz, C=S), 135.2 (Ph C-2,6), 133.6 (Ph C-1), 129.0 (Ph C-4), 128.6 (Ph C-3,5), 112.8 (t, $^{1}J_{C,F}$ = 256.8 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -295.8 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.1 (dd, $^{2}J_{H,F}$ = 56.2 Hz, $^{n}J_{H,F}$ = 2.7 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{10}H_{11}F_2NNaS$: 238.0472 $[M+Na]^+$; found: 238.0475.

2,2-difluoro-*N*-mesitylethanethioamide (19)



By following General Procedure A, starting from 2-isothiocyanato-1,3,5-trimethylbenzene (0.177 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **19** was obtained in 88% yield (0.202 g) as brown oil after column chromatography on silica gel (*n*-heptane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, C_6D_6): δ 7.83 (br s, 1H, NH), 6.64 (s, 2H, Ph H-3,5), 5.98 (t, $^{2}J_{H,F}$ = 56.3 Hz, 1H, CHF_2), 2.05 (s, 3H, Ph 4-CH_3), 1.92 (s, 6H, Ph 2,6-CH_3).

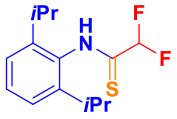
^{13}C NMR (100 MHz, C_6D_6): δ 189.8 (t, $^{2}J_{C,F}$ = 20.9 Hz, C=S), 138.3 (Ph C-4), 135.0 (Ph C-2,6), 132.0 (Ph C-1), 129.3 (Ph C-3,5), 113.6 (t, $^{1}J_{C,F}$ = 256.9 Hz, CHF_2), 21.0 (Ph 4-CH_3), 17.5 (Ph 2,6-CH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -232.2 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -115.7 (dd, $^{2}J_{H,F}$ = 56.3 Hz, $^{n}J_{H,F}$ = 2.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{11}H_{13}F_2NNaS$: 252.0629 $[M+Na]^+$; found: 252.0631.

***N*-(2,6-diisopropylphenyl)-2,2-difluoroethanethioamide (20)**



By following General Procedure A, starting from 1,3-diisopropyl-2-isothiocyanatobenzene (0.149 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **20** was obtained in 88% yield (0.238 g) as pale yellow solid (mp 96-99°C) after column chromatography on silica gel (*n*-hexane:DCM 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.88 (br s, 1H, NH), 7.25 (d, ^{3}J = 7.8 Hz, 2H, Ph H-3,5), 7.41 (t, ^{3}J = 7.8 Hz, 1H, Ph H-4), 6.39 (t, $^{2}J_{H,F}$ = 56.2 Hz, 1H, CHF_2), 2.92 (sept., ^{3}J = 6.85 Hz, 2H, C<u>H</u>$(CH_3)_2$), 1.24 (d, ^{3}J = 6.8 Hz, 6H, CH_3), 1.19 (d, ^{3}J = 6.9 Hz, 6H, CH_3).

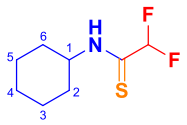
^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1 (t, $^{2}J_{C,F}$ =20.8 Hz, C=S), 145.6 (Ph C-2,6), 129.8 (Ph C-4), 130.9 (Ph C-1), 124.1 (Ph C-3,5), 112.9 (t, $^{1}J_{C,F}$ = 257.0 Hz, CHF_2), 28.7 (<u>C</u>H$(CH_3)_2$), 24.2 (CH_3), 23.2 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$): δ -297.9 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -116.2 (dd, $^{2}J_{H,F}$ = 56.2 Hz, $^{n}J_{H,F}$ = 2.6 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{19}F_2NNaS$: 294.1098 $[M+Na]^+$; found: 294.1103.

***N*-cyclohexyl-2,2-difluoroethanethioamide (21)**



By following General Procedure A, starting from isothiocyanatocyclohexane (0.141 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **21** was obtained in 85% yield (0.164 g) as brown oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (br s, 1H, NH), 6.15 (t, $^{2}J_{H,F}$ = 56.4 Hz, 1H, CHF_2), 4.33 (m, 1H, H-1), 2.10 (m, 2H, H-2,6), 1.78 (m, 2H, H-3,5), 1.68 (m, 1H, H-4), 1.43 (m, 2H, H-3,5), 1.30 (m, 2H, H-2,6), 1.25 (m, 1H, H-4).

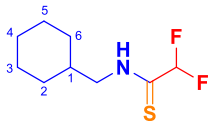
^{13}C NMR (100 MHz, $CDCl_3$): δ 187.9 (t, $^{2}J_{C,F}$ =20.9 Hz, C=S), 112.1 (t, $^{1}J_{C,F}$ = 255.9 Hz, CHF_2), 53.6 (C-1), 31.0 (C-2,6), 25.3 (C-4), 24.5 (C-3,5).

^{15}N NMR (40 MHz, $CDCl_3$): δ -281.1 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -117.5 (dd, $^{2}J_{H,F}$ = 56.4 Hz, $^{n}J_{H,F}$ = 2.5 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_{13}F_2NNaS$: 216.0629 $[M+Na]^+$; found: 216.0622.

***N*-(cyclohexylmethyl)-2,2-difluoroethanethioamide (22)**



By following General Procedure A, starting from (isothiocyanatomethyl)cyclohexane (0.155 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **22** was obtained in 83% yield (0.172 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (br s, 1H, NH), 6.19 (t, $^{2}J_{H,F}$ = 56.4 Hz, 1H, CHF_2), 3.55 (t, ^{3}J = 6.2 Hz, NCH_2), 1.76 (m, 4H, H-2,3,5,6), 1.74 (m, 1H, H-1), 1.69 (m, 1H, H-4), 1.26 (m, 2H, H-3,5), 1.19 (m, 1H, H-4), 1.03 (m, 2H, H-2,6).

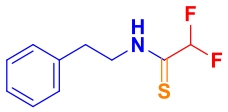
^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6 (t, $^{2}J_{C,F}$ = 21.0 Hz, C=S), 112.1 (t, $^{1}J_{C,F}$ = 255.7 Hz, CHF_2), 51.2 (NCH_2), 36.6 (C-1), 30.9 (C-2,6), 26.1 (C-4), 25.6 (C-3,5).

^{15}N NMR (40 MHz, $CDCl_3$): δ -297.3 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -117.2 (dd, $^{2}J_{H,F}$ = 56.4 Hz, $^{n}J_{H,F}$ = 2.7 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_{15}F_2NNaS$: 230.0785 $[M+Na]^+$; found: 230.0778.

2,2-difluoro-*N*-(2-phenylethyl)ethanethioamide (23)



By following General Procedure A, starting from (2-isothiocyanatoethyl)benzene (0.163 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **23** was obtained in 84% yield (0.181 g) as orange oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (br s, 1H, NH), 7.35 (m, 2H, Ph H-3,5), 7.28 (m, 1H, Ph H-4), 7.22 (m, 2H, Ph H-2,6), 6.15 (t, $^{2}J_{H,F}$ = 56.2 Hz, 1H, CHF_2), 3.96 (m, 2H, $C\underline{H}_2NH$), 3.01 (t, ^{3}J = 7.1 Hz, $C\underline{H}_2Ph$).

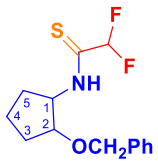
^{13}C NMR (100 MHz, $CDCl_3$): δ 189.7 (t, $^{2}J_{C,F}$ = 21.0 Hz, C=S), 137.4 (Ph C-1), 129.0 (Ph C-3,5), 128.6 (Ph C-2,6), 127.1 (Ph C-4), 112.0 (t, $^{1}J_{C,F}$ = 255.7 Hz, CHF_2), 46.0 (CH_2NH), 33.4 (CH_2Ph).

^{15}N NMR (40 MHz, $CDCl_3$): δ -297.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -117.4 (dd, $^{2}J_{H,F}$ = 56.2 Hz, $^{n}J_{H,F}$ = 2.7 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{10}H_{12}F_2NS^+$: 216.0653 $[M+H]^+$; found: 216.0650.

***N*-[2-(benzyloxy)cyclopentyl]-2,2-difluoroethanethioamide (24)**



By following General Procedure A, starting from (2-isothiocyanatocyclopentyloxy)methylbenzene (0.233 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **24** was obtained in 90% yield (0.257 g) as yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (br s, 1H, NH), 7.34 (m, 4H, Ph H-2,3,5,6), 7.29 (m, 1H, Ph H-4), 6.16 (t, $^{2}J_{H,F}$ = 56.4 Hz, 1H, CHF_2), 4.75 (m, 1H, H-1), 4.66 (A-part of an AB-system, $^{2}J_{AB}$= 12.2 Hz, 1H, OCH_2), 4.66 (B-part of an AB-system, $^{2}J_{AB}$= 12.2 Hz, 1H, OCH_2), 3.94 (m, 1H, H-2), 2.39 (m, 1H, H-5), 1.92 (m, 2H, H-4,3), 1.83 (m, 1H, H-3), 1.75 (m, 1H, H-4), 1.53 (m, 1H, H-5).

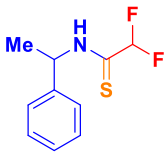
^{13}C NMR (100 MHz, $CDCl_3$): δ 188.9 (t, $^{2}J_{C,F}$ =21.0 Hz, C=S), 138.2 (Ph C-1), 128.4 (Ph C-3,5), 127.69 (Ph C-4) 127.66 (Ph C-2,6), 112.1 (t, $^{1}J_{C,F}$ = 256.0 Hz, CHF_2), 83.4 (C-2), 71.3 (OCH_2), 60.9 (C-1), 30.7 (C-3), 29.5 (C-5), 21.7 (C-4).

^{15}N NMR (40 MHz, $CDCl_3$): δ -287.3 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -117.1 (d, $^{2}J_{H,F}$ = 56.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{17}F_2NNaOS$: 308.0891 $[M+Na]^+$; found: 308.0889.

2,2-difluoro-N-(1-phenylethyl)ethanethioamide (25)



By following General Procedure A, starting from (1-isothiocyanatoethyl)benzene (0.163 g, 1 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.185 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.3 mL, 1.2 mmol, 1.2 equiv), compound **25** was obtained in 91% yield (0.196 g) as pale yellow oil after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99 (br s, 1H, NH), 7.39 (m, 2H, Ph H-3,5), 7.34 (m, 2H, Ph H-2,6), 7.33 (m, 1H, Ph H-4), 6.18 (t, $^{2}J_{H,F}$ = 56.3 Hz, 1H, CHF_2), 5.66 (m, 1H, NCH), 1.66 (d, ^{3}J = 6.9 Hz, 3H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ 188.3 (t, $^{2}J_{C,F}$ = 21.0 Hz, C=S), 140.1 (Ph C-1), 129.0 (Ph C-3,5), 128.3 (Ph C-4), 126.5 (Ph C-2,6), 112.1 (t, $^{1}J_{C,F}$ = 256.0 Hz, CHF_2), 54.0 (NCH), 19.8 (CH_3).

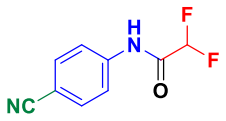
^{15}N NMR (40 MHz, $CDCl_3$): δ -281.6 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -117.2 (dd, $^{2}J_{H,F}$ = 56.3 Hz, $^{n}J_{H,F}$ = 2.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{10}H_{11}F_2NNaS$: 238.0467 $[M+Na]^+$; found: 238.0474.

4. Spectral and characterization data for α,α-difluoromethy-oxoamides

***N*-(4-cyanophenyl)-2,2-difluoroacetamide (26)**



By following General Procedure B, starting from 4-isocyanatobenzonitrile (0.144 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **26** was obtained in 90% yield (0.176 g) as yellow solid (mp 125-127 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (br s, 1H, NH), 7.74 (m, 2H, Ph H-2,6), 7.68 (m, 2H, Ph H-3,5), 6.04 (t, $^2J_{H,F}$ = 54.1 Hz, 1H, CHF_2).

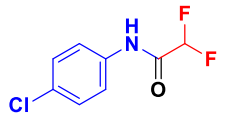
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.6 (t, $^2J_{C,F}$ =25.2 Hz, C=O), 139.7 (Ph C-1), 133.5 (Ph C-3,5), 120.3 (Ph C-2,6), 118.2 (CN), 109.1 (Ph C-4), 108.3 (t, $^1J_{C,F}$ = 254.6 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -258.6 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^2J_{H,F}$ = 54.1 Hz, $^nJ_{H,F}$ = 1.9 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_6F_2N_2NaO$: 219.0340 $[M+Na]^+$; found: 219.0339.

***N*-(4-chlorophenyl)-2,2-difluoroacetamide (27)**



By following General Procedure B, starting from 1-chloro-4-isocyanatobenzene (0.153 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **27** was obtained in 86% yield (0.177 g) as yellow solid (mp 101-103 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91 (br s, 1H, NH), 7.53 (m, 2H, Ph H-2,6), 7.34 (m, 2H, Ph H-3,5), 6.01 (t, $^{2}J_{H,F}$ = 54.3 Hz, 1H, CHF_2).

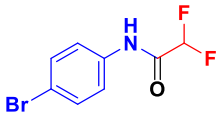
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (t, $^{2}J_{C,F}$ = 24.6 Hz, C=O), 134.2 (Ph C-1), 131.1 (Ph C-4), 129.4 (Ph C-3,5), 121.5 (Ph C-2,6), 108.4 (t, $^{1}J_{C,F}$ = 254.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -260.3 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^{2}J_{H,F}$ = 54.3 Hz, $^{n}J_{H,F}$ = 2.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_6ClF_2NNaO$: 227.9998 $[M+Na]^+$; found: 227.9999.

***N*-(4-bromophenyl)-2,2-difluoroacetamide (28)**



By following General Procedure B, starting from 1-bromo-4-isocyanatobenzene (0.198 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **28** was obtained in 91% yield (0.227 g) as brown solid (mp 114-116 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

Reaction conducted on 10 mmol scale. By following General Procedure B, starting from 1-bromo-4-isocyanatobenzene (1.98 g, 10 mmol, 1.0 equiv) in dry THF (80 mL), CHF_2SiMe_3 (1.86 g, 15 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (14 mL, 12 mmol, 1.2 equiv), compound **28** was obtained in 86% yield (2.15 g) as brown solid after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1). *Spectral and spectroscopic data match with those ones obtained when the product was prepared in 1 mmol scale.*

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (br s, 1H, NH), 7.49 ('s', 4H, Ph H-2,3,5,6), 6.01 (t, $^{2}J_{H,F}$ = 54.2 Hz, 1H, CHF_2).

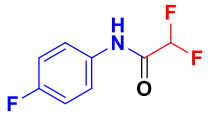
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (t, $^{2}J_{C,F}$ = 24.6 Hz, C=O), 134.7 (Ph C-1), 132.3 (Ph C-3,5), 121.8 (Ph C-2,6), 118.7 (Ph C-4), 108.4 (t, $^{1}J_{C,F}$ = 254.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -260.0 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.6 (dd, $^2J_{H,F}$ = 54.2 Hz, $^nJ_{H,F}$ = 1.2 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_6BrF_2NNaO$: 271.9493 $[M+Na]^+$; found: 271.9488.

2,2-difluoro-*N*-(4-fluorophenyl)acetamide (29)



By following General Procedure B, starting from 1-fluoro-4-isocyanatobenzene (0.137 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **29** was obtained in 87% yield (0.164 g) as white crystals (mp 91-93 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.86 (br s, 1H, NH), 7.55 (m, 2H, Ph H-2,6), 7.08 (m, 2H, Ph H-3,5), 6.02 (t, $^2J_{H,F}$ = 54.3 Hz, 1H, CHF_2).

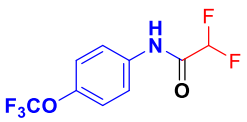
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (t, $^2J_{C,F}$ =24.4 Hz, C=O), 160.2 (d, $^1J_{C,F}$ = 245.8 Hz, Ph C-4), 131.6 (d, $^4J_{C,F}$ = 3.0 Hz, Ph C-1), 122.2 (d, $^3J_{C,F}$ = 8.1 Hz, Ph C-2,6), 116.1 ($^2J_{C,F}$ = 22.8 Hz, Ph C-3,5), 108.5 (t, $^1J_{C,F}$ = 254.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -261.1 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^2J_{H,F}$ = 54.3 Hz, $^nJ_{H,F}$ = 2.3 Hz, CHF_2), -115.6 (m, Ph 4-F).

HRMS (ESI), *m/z*: calcd. for $C_8H_6F_3NNaO$: 212.0294 $[M+Na]^+$; found: 212.0294.

2,2-difluoro-*N*-[4-trifluoromethoxy)phenyl]acetamide (30)



By following General Procedure B, starting from 1-isocyanato-4-(trifluoromethoxy)benzene (0.203 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **30** was obtained in 88% yield (0.224 g) as white needles (mp 105-107 °C) after column chromatography on silica gel (*n*-heptane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (br s, 1H, NH), 7.62 (m, 2H, Ph H-2,6), 7.24 (m, 2H, Ph H-3,5), 6.03 (t, $^2J_{H,F}$ = 54.4 Hz, 1H, CH).

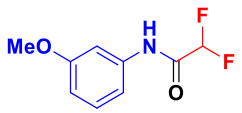
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (t, $^2J_{C,F}$ =24.6 Hz, C=O), 146.4 (Ph C-4), 134.2 (Ph C-1), 122.0 (Ph C-3,5), 121.6 (Ph C-2,6), 120.4 (q, $^1J_{C,F}$ = 257.5 Hz, CF_3), 108.4 (t, $^1J_{C,F}$ = 254.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -260.7 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^2J_{H,F}$ = 54.3 Hz, $^nJ_{H,F}$ = 2.3 Hz, CHF_2), -58.1 (s, CF_3).

HRMS (ESI), *m/z*: calcd. for $C_9H_6F_5NNaO_2^+$: 278.0211 $[M+Na]^+$; found: 278.0205.

2,2-difluoro-*N*-(3-methoxyphenyl)acetamide (31)



By following General Procedure B, starting from 1-isocyanato-3-methoxybenzene (0.149 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **31** was obtained in 90% yield (0.181 g) as brown solid (mp 67-69 °C) after column chromatography on silica gel (*n*-heptane:ethyl acetate 7:3).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (br s, 1H, NH), 7.30 (m, 1H, Ph H-2), 7.27 (m, 1H, Ph H-5), 7.05 (m, 1H, Ph H-6), 6.76 (m, 1H, Ph H-4), 6.01 (t, $^2J_{H,F}$ = 54.4 Hz, 1H, CHF_2), 3.81 (s, 3H, OCH_3).

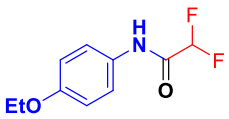
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (t, $^2J_{C,F}$ = 24.5 Hz, C=O), 160.3 (Ph C-3), 136.8 (Ph C-1), 130.0 (Ph C-5), 112.4 (Ph C-6), 111.6 (Ph C-4), 108.5 (t, $^1J_{C,F}$ = 254.3 Hz, CHF_2), 55.4 (OCH_3).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -258.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.6 (dd, $^2J_{H,F}$ = 54.4 Hz, $^nJ_{H,F}$ = 2.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_9F_2NaO_2$: 224.0494 $[M+Na]^+$; found: 224.0492.

***N*-(4-ethoxyphenyl)-2,2-difluoroacetamide (32)**



By following General Procedure B, starting from 1-ethoxy-4-isocyanatobezene (0.163 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **32** was obtained in 86% yield (0.185 g) as grey needles (mp 109-111 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (br s, 1H, NH), 7.46 (m, 2H, Ph H-2,6), 6.89 (m, 2H, Ph H-3,5), 6.00 (t, $^2J_{H,F}$ = 54.4 Hz, 1H, CHF_2), 4.02 (q, ^3J = 7.0 Hz, 2H, OCH_2), 1.41 (t, ^3J = 7.0 Hz, 3H, CH_3).

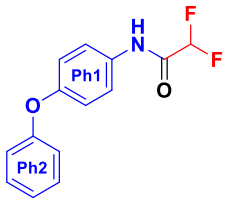
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.1 (t, $^2J_{C,F}$ =24.3 Hz, C=O), 156.8 (Ph C-4), 128.4 (Ph C-1), 122.0 (Ph C-2,6), 114.9 (Ph C-3,5), 108.6 (t, $^1J_{C,F}$ = 254.0 Hz, CHF_2), 63.7 (OCH_2), 14.8 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -260.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^2J_{H,F}$ = 54.4 Hz, $^nJ_{H,F}$ = 2.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{10}H_{11}F_2NaO$: 238.0650 $[M+Na]^+$; found: 238.0654.

2,2-difluoro-*N*-(4-phenoxyphenyl)acetamide (33)



By following General Procedure B, starting from 1-isocyanato-4-phenoxybenzene (0.211 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution

0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **33** was obtained in 90% yield (0.237 g) as white solid (mp 77-79 °C) after column chromatography on silica gel (*n*-heptane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (br s, 1H, NH), 7.53 (m, 2H, Ph1 H-2,6), 7.35 (m, 2H, Ph2 H-3,5), 7.12 (m, 1H, Ph2 H-4), 7.02 (m, 2H, Ph1 H-3,5), 7.01 (m, 2H, Ph2 H-2,6), 6.02 (t, $^{2}J_{H,F}$ = 54.4 Hz, 1H, CHF_2).

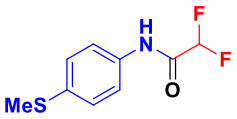
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.2 (t, $^{2}J_{C,F}$ =24.5 Hz, C=O), 157.0 (Ph2 C-1), 155.0 (Ph1 C-4), 130.8 (Ph1 C-1), 129.8 (Ph2 C-3,5), 123.5 (Ph2 C-4), 122.1 (Ph1 C-2,6), 119.5 (Ph1 C-3,5), 118.9 (Ph2 C-2,6), 108.6 (t, $^{1}J_{C,F}$ = 254.3 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -260.6 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^{2}J_{H,F}$ = 54.4 Hz, $^{n}J_{H,F}$ = 2.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{11}F_2NaO_2$: 286.0650 $[M+Na]^+$; found: 286.0654.

2,2-difluoro-*N*-[4-(methylsulfanyl)phenyl]acetamide (34)



By following General Procedure B, starting from 1-isocyanato-4-(methylsulfanyl)benzene (0.165 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **34** was obtained in 89% yield (0.193 g) as brown solid (mp 110-121 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (br s, 1H, NH), 7.50 (m, 2H, Ph H-2,6), 7.25 (m, 2H, Ph H-3,5), 6.01 (t, $^{2}J_{H,F}$ = 54.3 Hz, 1H, CHF_2), 2.48 (s, 3H, CH_3).

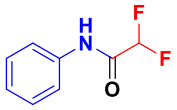
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.2 (t, $^{2}J_{C,F}$ =24.4 Hz, C=O), 135.8 (Ph C-4), 132.9 (Ph C-1), 127.5 (Ph C-3,5), 120.9 (Ph C-2,6), 108.5 (t, $^{1}J_{C,F}$ = 254.1 Hz, CHF_2), 16.1 (CH_3) .

^{15}N NMR (40 MHz, $CDCl_3$) δ: -259.4 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (d, $^{2}J_{H,F}$ = 54.3Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_9F_2NNaOS$: 240.0265 $[M+Na]^+$; found: 240.0262.

2,2-difluoro-*N*-phenylacetamide (35)



By following General Procedure B, starting from isocyanatobenzene (0.119 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **35** was obtained in 85% yield (0.145 g) as brown solid (mp 62 °C, lit.[1] 65 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (br s, 1H, NH), 7.58 (m, 2H, Ph H-2,6), 7.38 (m, 2H, Ph H-3,5), 7.21 (m, 1H, Ph H-4), 6.02 (t, $^{2}J_{H,F}$ = 54.4 Hz, 1H, CHF_2).

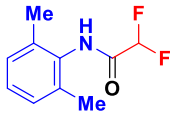
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.3 (t, $^{2}J_{C,F}$ =24.5 Hz, C=O), 135.6 (Ph C-1), 129.3 (Ph C-3,5), 125.8 (Ph C-4), 120.3 (Ph C-2,6), 108.5 (t, $^{1}J_{C,F}$ = 254.2 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -258.7 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^{2}J_{H,F}$ = 54.4 Hz, $^{n}J_{H,F}$ = 2.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_7F_2NNaO$: 194.0388 $[M+Na]^+$; found: 194.0386.

***N*-(2,6-dimethylphenyl)-2,2-difluoroacetamide (36)**



By following General Procedure B, starting from 2-isocyanato-1,3-dimethylbenzene (0.147 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **36** was obtained in 84% yield (0.167 g) as white needles (mp 110-112 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (br s, 1H, NH), 7.16 (m, 1H, Ph H-4), 7.10 (m, 2H, Ph H-3,5), 6.06 (t, $^{2}J_{H,F}$ = 54.2 Hz, 1H, CHF_2), 2.22 (s, 6H, CH_3).

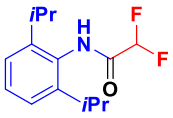
^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.0 (t, $^{2}J_{C,F}$ =24.7 Hz, C=O), 135.3 (Ph C-2,6), 131.1 (Ph C-1), 128.4 (Ph C-3,5), 128.2 (Ph C-4), 108.9 (t, $^{1}J_{C,F}$ = 253.4 Hz, CHF_2), 18.1 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -266.8 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -124.8 (dd, $^{2}J_{H,F}$ = 54.2 Hz, $^{n}J_{H,F}$ = 1.8 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{10}H_{11}F_2NNaO$: 222.0701 $[M+Na]^+$; found: 222.0703.

***N*-(2,6-dimethylphenyl)-2,2-difluoroacetamide (37)**



By following General Procedure B, starting from 2-isocyanato-1,3-diisopropylbenzene (0.203 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **37** was obtained in 80% yield (0.204 g) as white solid (mp 137-140 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54 (br s, 1H, NH), 7.35 (m, 1H, Ph H-4), 7.22 (d, $^{3}J_{H,H}$ = 7.7 Hz, 2H, Ph H-3,5), 6.08 (t, $^{2}J_{H,F}$ = 54.2 Hz, 1H, CHF_2), 3.01 (sept, $^{3}J_{H,H}$ = 6.9 Hz, 2H, CH), 1.21 (d, $^{3}J_{H,H}$ = 6.9 Hz, 12H, CH_3).

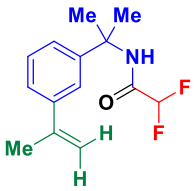
^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.1 (t, $^{2}J_{C,F}$ = 24.6 Hz, C=O), 146.0 (Ph C-2,6), 129.2 (Ph C-4), 128.3 (Ph C-1), 123.8 (Ph C-3,5), 109.0 (t, $^{1}J_{C,F}$ = 253.6 Hz, CHF_2), 28.7 ($\underline{C}HMe_2$), 23.5 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -270.1 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -124.7 (dd, $^{2}J_{H,F}$ = 54.2 Hz, $^{n}J_{H,F}$ = 2.1 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{19}F_2NNaO$: 278.1327 $[M+Na]^+$; found: 278.1330.

2,2-difluoro-*N*-[2-(3-isopropenylphenyl)-2-propanyl]acetamide (38)



By following General Procedure B, starting from 1-(2-isocyanato-2-propanyl)-3-isopropenylbenzene (0.201 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **38** was obtained in 81% yield (0.205 g) as pale yellow needles (mp 94-96 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (m, 1H, Ph H-2), 7.37 (m, 1H, Ph H-4), 7.33 (m, 1H, Ph H-5), 7.30 (m, 1H, Ph H-6), 6.51 (br s, 1H, NH), 5.81 (t, $^{2}J_{H,F}$ = 54.5 Hz, 1H, CHF_2), 5.35 (s, 1H, H_a), 5.11 (m, 1H, H_b), 2.16 (s, 3H, alkene-CH_3), 1.79 (s, 6H, CH_3).

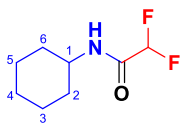
^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.4 (t, $^{2}J_{C,F}$ = 24.0 Hz, C=O), 145.3 (Ph C-1), 143.3 (H_2C=$\underline{C}$Me), 141.7 (Ph C-3), 128.5 (Ph C-5), 124.5 (Ph C-4), 123,7 (Ph C-6), 121.8 (Ph C-2), 112.8 ($H_2\underline{C}$=CMe), 108.7 (t, $^{1}J_{C,F}$ = 254.0 Hz, CHF_2), 56.6 (1C, $\underline{C}Me_2$), 28.6 (NC-CH_3), 21.8 (H_2C=C$\underline{C}H_3$).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -251.9 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.0 (dd, $^{2}J_{H,F}$ = 54.5Hz, $^{n}J_{H,F}$ = 1.7 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{17}F_2NNaO$: 276.1170 $[M+Na]^+$; found: 276.1170.

***N*-cyclohexyl-2,2-difluoroacetamide (39)**



By following General ProcedureB, starting from isocyanatocyclohexane (0.125 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in

THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **39**[2] was obtained in 83% yield (0.147 g) as volatile white solid (mp 65-67 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.14 (br s, 1H, NH), 5.86 (t, $^{2}J_{H,F}$ = 54.5 Hz, 1H, CHF_2), 3.80 (m, 1H, cyclohexyl H-1), 1.95 (m, 2H, cyclohexyl H-2,6), 1.74 (m, 2H, cyclohexyl H-3,5), 1.64 (m, 1H, cyclohexyl H-4), 1.38 (m, 2H, cyclohexyl H-3,5), 1.21 (m, 2H, cyclohexyl H-2,6), 1.19 (m, 2H, cyclohexyl H-4).

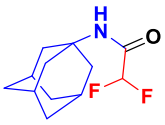
^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.6 (t, $^{2}J_{C,F}$ = 24.3 Hz, C=O), 108.5 (t, $^{1}J_{C,F}$ = 252.7 Hz, CHF_2), 48.4 (cyclohexyl C-1), 32.6 (cyclohexyl C-2,6), 25.3 (cyclohexyl C-4), 24.6 (cyclohexyl C-3,5).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -256.7 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -126.2 (dd, $^{2}J_{H,F}$ = 54.5 Hz, $^{n}J_{H,F}$ = 2.0 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_8H_{13}F_2NNaO$: 200.0857 $[M+Na]^+$; found: 200.0858.

***N*-(adamantan-1-yl)-2,2-difluoroacetamide (40)**



By following General Procedure B, starting from 1-isocyanatodamantane (0.177 g, 1.0 mmol, 1.0 equiv) in dry THF (10 mL), CHF_2SiMe_3 (0.186 g, 1.5 mmol, 1.5 equiv) and potassium *tert*-amylate solution 0.9 M in THF (1.4 mL, 1.2 mmol, 1.2 equiv), compound **40** was obtained in 85% yield (0.195 g) as white solid (mp 89-91 °C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 9:1).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.89 (br s, 1H, NH), 5.75 (t, $^{2}J_{H,F}$ = 54.7 Hz, 1H, CHF_2) , 2.11 (m, 3H, adamantyl H-3,5,7), 2.03 (m, 6H, adamantyl H-2,8,9), 1.70 (m, 6H, adamantyl H-4,6,10).

^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.3 (t, $^{2}J_{C,F}$ =23.5 Hz, C=O), 108.5 (t, $^{1}J_{C,F}$ = 254.0 Hz, CHF_2), 52.6 (adamantyl C-1), 41.2 (adamantyl C-2,8,9), 36.1 (adamantyl C-4,6,10), 29.3 (adamantyl C-3,5,7).

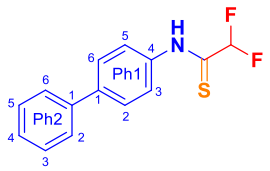
^{15}N NMR (40 MHz, $CDCl_3$) δ: -249.7 (NH).

^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.1 (dd, $^{2}J_{H,F}$ = 54.7 Hz, $^{n}J_{H,F}$ = 2.2 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{12}H_{17}F_2NNaO$: 252.1170 $[M+Na]^+$; found: 252.1169.

5. Synthetic manipulation of compounds (Scheme 3)

***N*-(biphenyl-4-yl)-2,2-difluoroacetamide (41)**



In a dry Schlenk flask $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 2.5 mol%) and P(*t*-Bu)$_3$ (0.4 mg, 0.002 mmol, 10 mol%) were added to anhydrous toluene. Then, difluoroamide **8** (0.38 mmol, 101 mg) was added to the mixture at -20 °C. Phenyllithium [1.9 M in *n*-dibutyl ether, 1.14 mmol, 0.6 mL) was diluted with toluene to reach a concentration of 0.6 M and TMEDA (0.46 mmol, 0.068 mL) was added to it; this solution was slowly added over 2 h *via* a syringe pump. After the addition was completed, $NaHCO_3$ (aq. 5%) was added and the mixture was extracted 3 times with diethyl ether. The organic phases were collected and concentrated under reduced pressure. The desired product **41** was obtained in 65% yield (65 mg) as pale yellow solid (mp 177-180°C) after column chromatography on silica gel (*n*-hexane:ethyl acetate 8:2).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (br s, 1H, NH), 7.66 (m, 2H, Ph1 C-3,5), 7.62 (m, 2H, Ph1 C-2,6), 7.58 (m, 2H, Ph2 C-2,6), 7.45 (m, 2H, Ph2 C-3,5), 7.35 (m, 1H, Ph2 C-4), 6.05 (t, $^2J_{H,F}$ = 54.4 Hz, 1H, CHF_2).

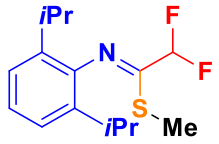
^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2 (m, C=O), 140.1 (Ph2 C-1), 138.8 (Ph1 C-1), 134.8 (Ph1 C-4), 127.9 (Ph1 C-2,6), 128.9 (Ph2 C-3,5), 127.5 (Ph2 C-4), 126.9 (Ph2 C-2,6), 120.6 (Ph1 C-3,5), 108.6 (t, $^1J_{C,F}$ = 254.8 Hz, CHF_2).

^{15}N NMR (40 MHz, $CDCl_3$): δ -295.5 (NH).

^{19}F NMR (376 MHz, $CDCl_3$): δ -125.4 (dd, $^2J_{H,F}$ = 54.4 Hz, $^nJ_{H,F}$ = 2.4 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_{14}H_{11}F_2NNaO$: 270.0701 $[M+Na]^+$; found: 270.0696.

Methyl (1*Z*)- *N*-(2,6-diisopropylphenyl)-2,2-difluoroethanimidothioate (42)



1,3-diisopropyl-2-isothiocyanatobenzene **20** (0.149 g, 0.55 mmol, 1.0 equiv) was dissolved in anhydrous acetone (5 mL) and, under argon, KOH (111 mg, 1.98 mmol, 3.6 equiv) and iodomethane (116 mg, 0.82 mmol, 1.5 equiv) were introduced. The resulting mixture was heated at 56 °C and the stirring was continued for 1 h. Upon completion of the reaction – as indicated by TLC analysis – the mixture was filtered on Celite. The corresponding filtrate – after evaporation of the solvent - was columned on silica gel (*n*-hexane:diethyl ether 9:1), giving compound **42** (115 mg, 73% yield) as a pale yellow oil.

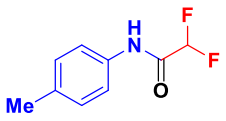
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.13 (m, 3H, Ph H-3,4,5), 6.38 (br m-t, CHF_2), 2.70 (sept., ^{3}J = 6.9 Hz, 2H, C<u>H</u>$(CH_3)_2$), 1.20 (br d, ^{3}J = 6.9 Hz, 6H, CH_3), 2.53 (s, 3H, SCH_3), 1.13 (d, ^{3}J = 6.9 Hz, 6H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ 160.5 (C=N), 143.7 (Ph C-1), 136.0 (Ph C-2,6), 125.0 (Ph C-4), 123.2 (Ph C-3,5), 28.1 (<u>C</u>H$(CH_3)_2$), 23.4 (CH_3), 23.0 (CH_3), 12.7 (SCH_3).

^{19}F NMR (376 MHz, $CDCl_3$): δ -114.3 (d, $^{2}J_{H,F}$ = 52 Hz).

HRMS (ESI), *m/z*: calcd. for $C_{15}H_{21}F_2NNaS$: 308.1255 $[M+Na]^+$; found: 308.1259.

2,2-difluoro-*N*-(4-methylphenyl)acetamide (43)



Bromo-oxamide **28** (125 mg, 0.5 mmol, 1.0 equiv) was dissolved in anhydrous toluene (5 mL) and, under argon, $Pd(PPh_3)_4$ (57 mg, 0.05 mmol, 0.10 equiv) and methyl stannatrane (274 mg, 1.0 mmol, 2.0 equiv) were introduced. The resulting mixture was heated at 90 °C and the stirring was continued for 4 h. Upon completion of the reaction – as indicated by TLC analysis – the mixture was filtered on Celite washing with Et_2O (15 mL). The corresponding filtrate – after evaporation of the solvent - was columned on silica gel (*n*-hexane:ethyl acetate 9:1), giving compound **43** (76 mg, 82% yield) as a pale yellow solid (mp 106-108 °C).

^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (br s, 1H, NH), 7.45 (m, 2H, Ph H-2,6), 7.18 (m, 2H, Ph H-3,5), 6.01 (t, $^{2}J_{H,F}$ = 54.4 Hz, 1H, CHF_2), 2.34 (s, 3H, CH_3).

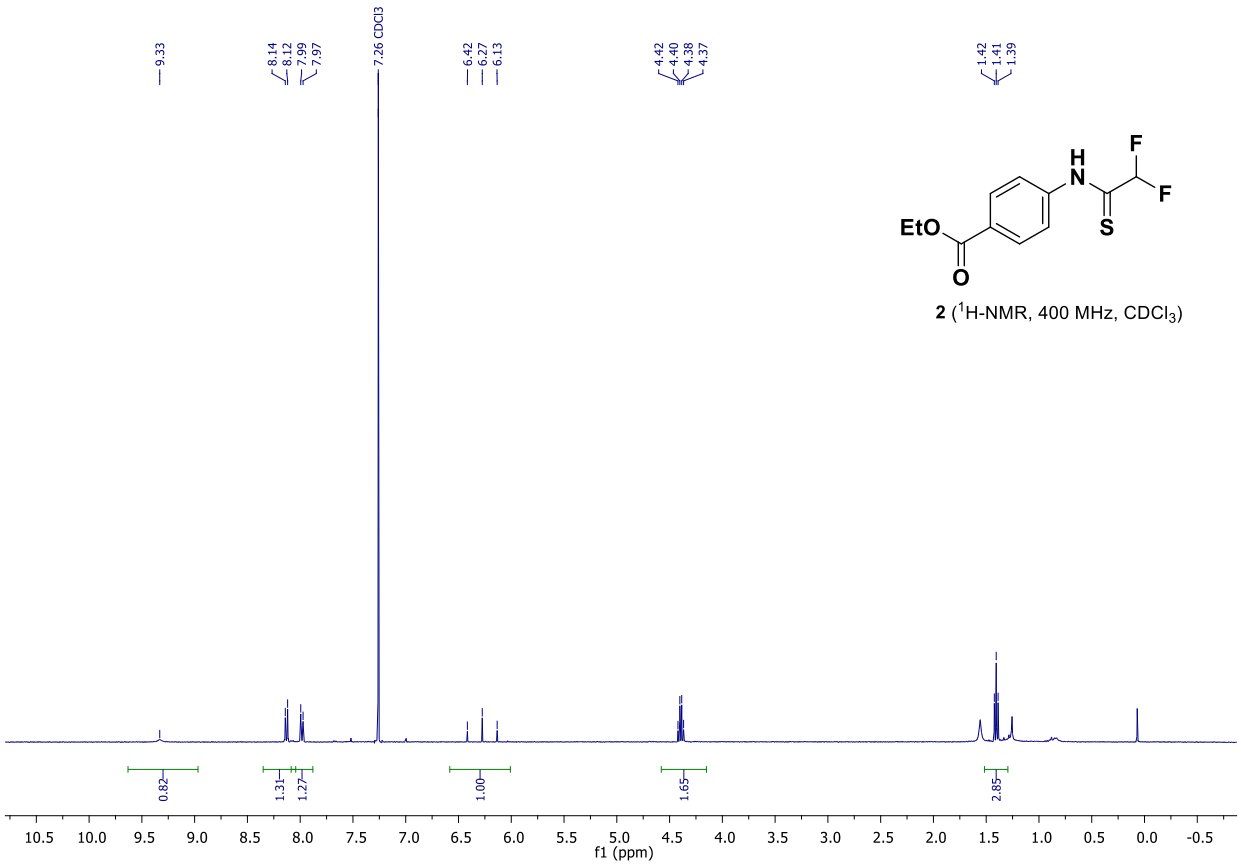
^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.1 (C=0), 135.7 (Ph C-4), 133.0 (Ph C-1), 129.8 (Ph C-3,5), 120.3 (Ph C-2,6), 108.6 (t, $^{1}J_{C,F}$ = 254.2 Hz, CHF_2), 20.9 (CH_3).

^{15}N NMR (40 MHz, $CDCl_3$) δ: -259.4 (NH).

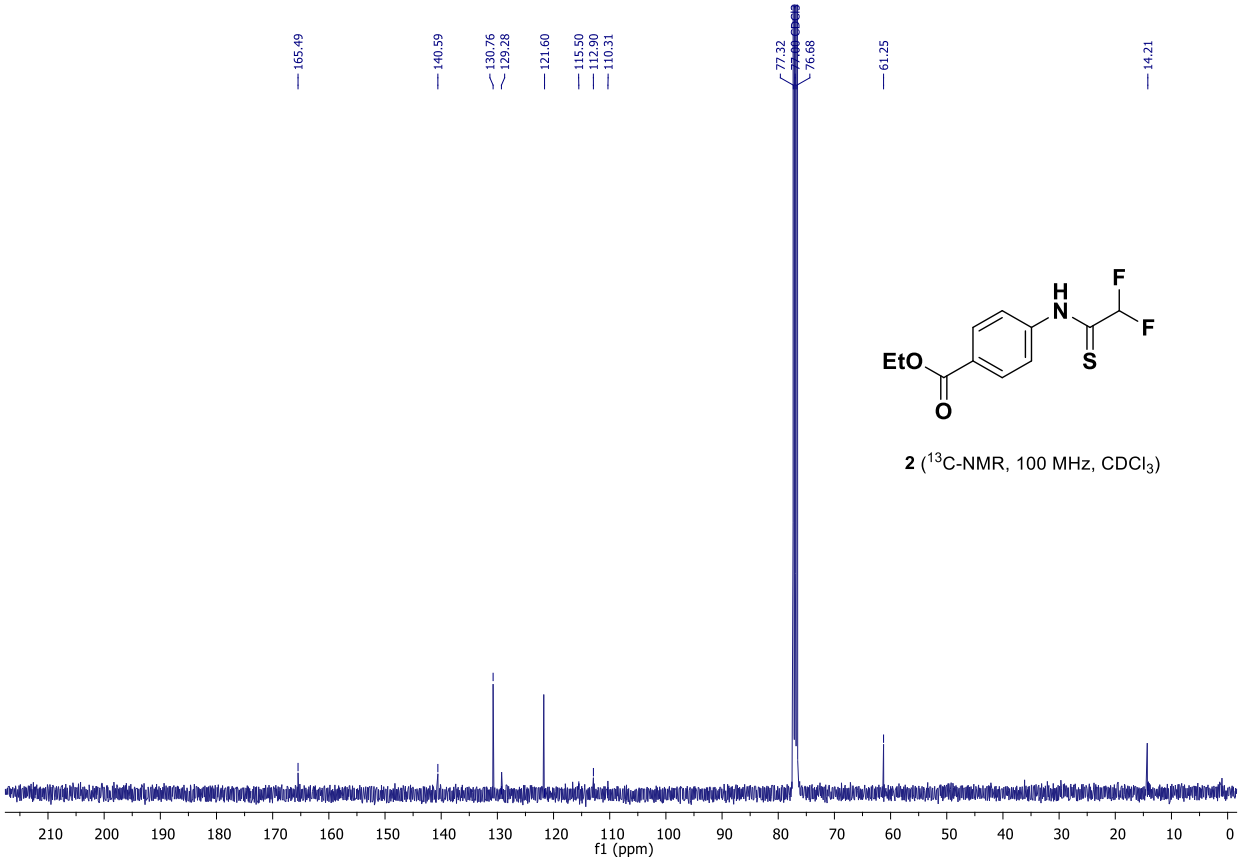
^{19}F NMR (376 MHz, $CDCl_3$) δ: -125.5 (dd, $^{2}J_{H,F}$ = 54.4 Hz, $^{n}J_{H,F}$ = 2.3 Hz, CHF_2).

HRMS (ESI), *m/z*: calcd. for $C_9H_9F_2NNaO$: 208.0544 $[M+Na]^+$; found: 208.0562.

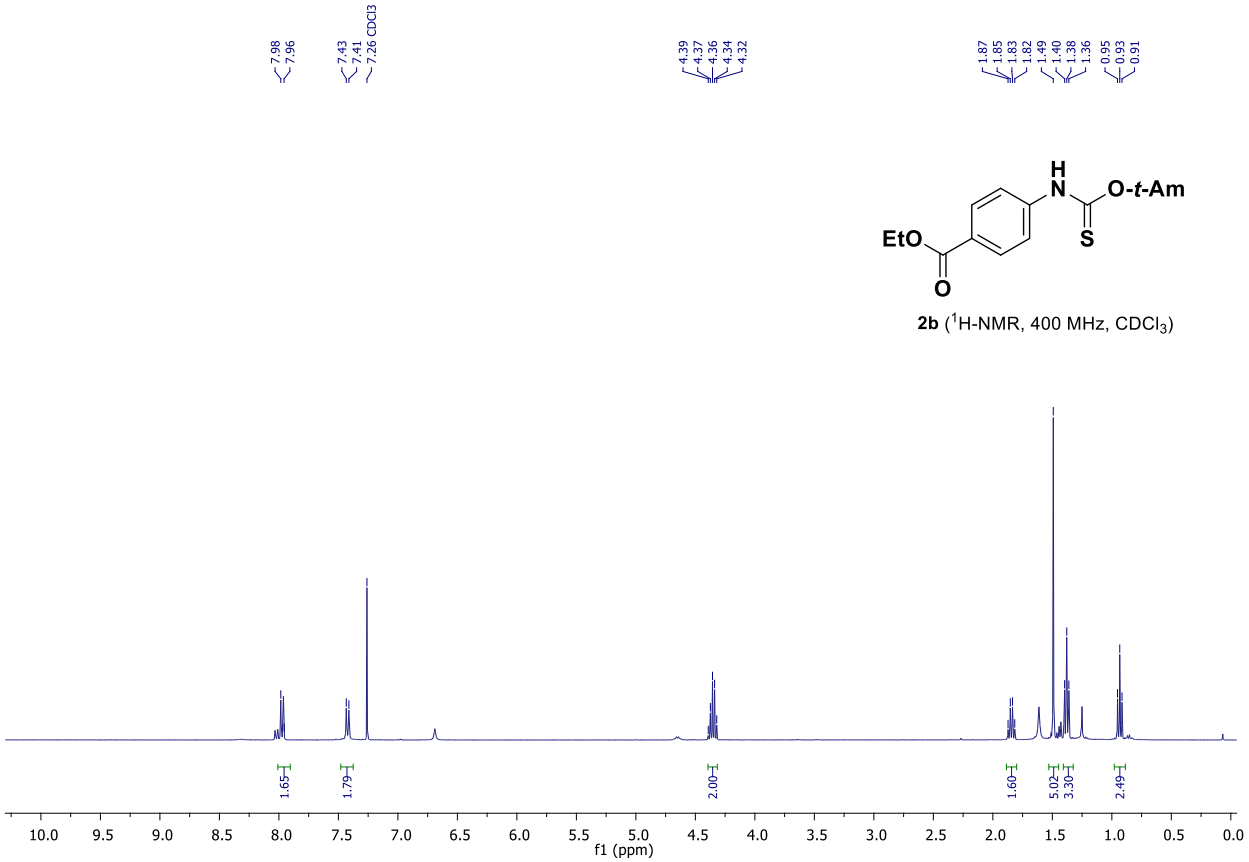
6. **^{1}H- and ^{13}C-NMR spectra.**



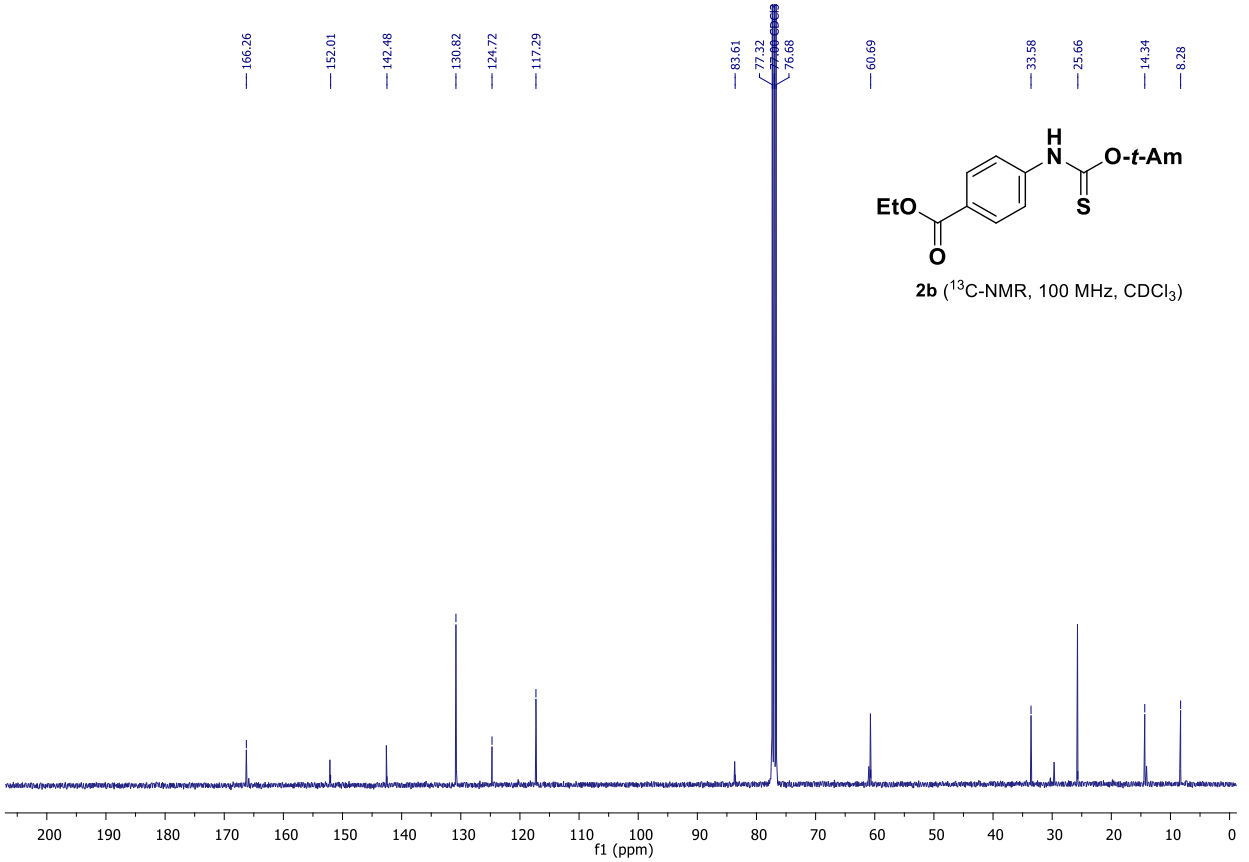
2 (^{1}H-NMR, 400 MHz, $CDCl_3$)



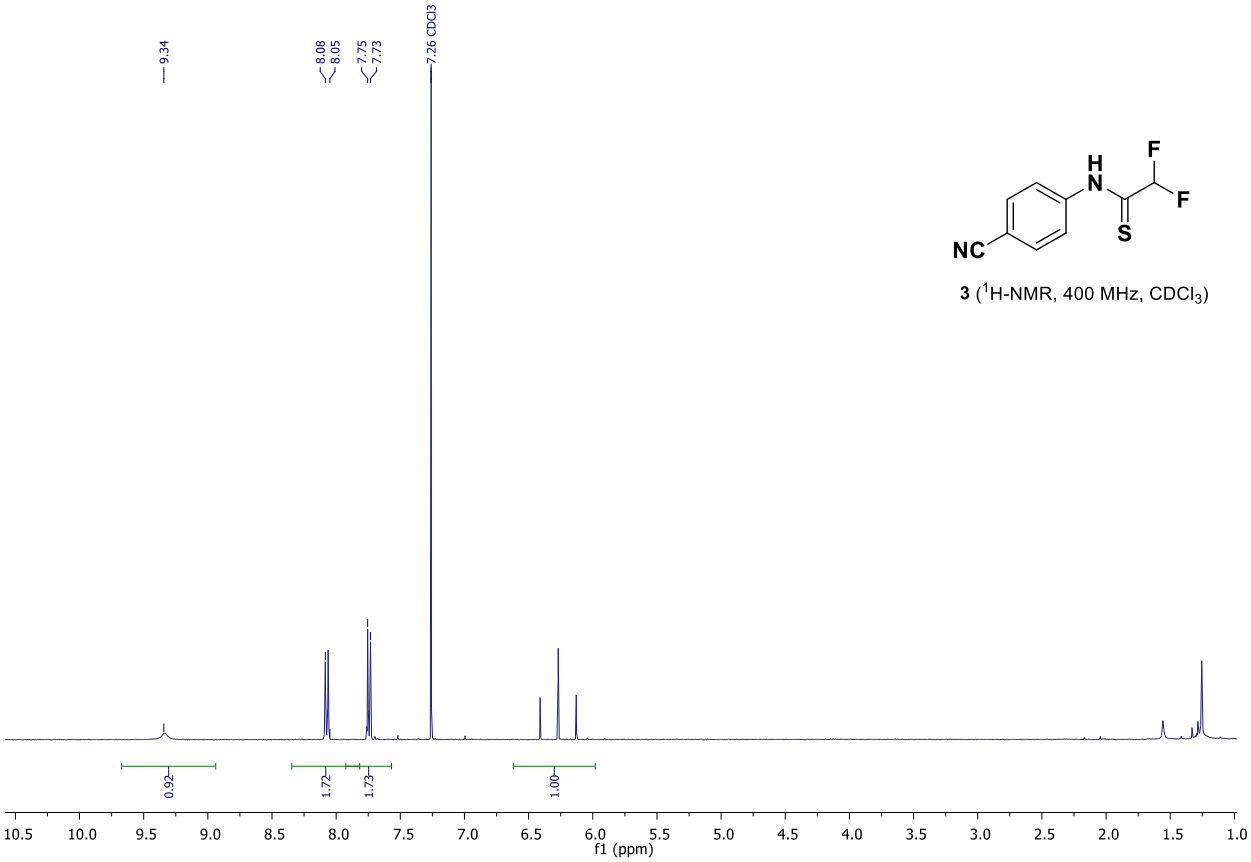
2 (^{13}C-NMR, 100 MHz, $CDCl_3$)



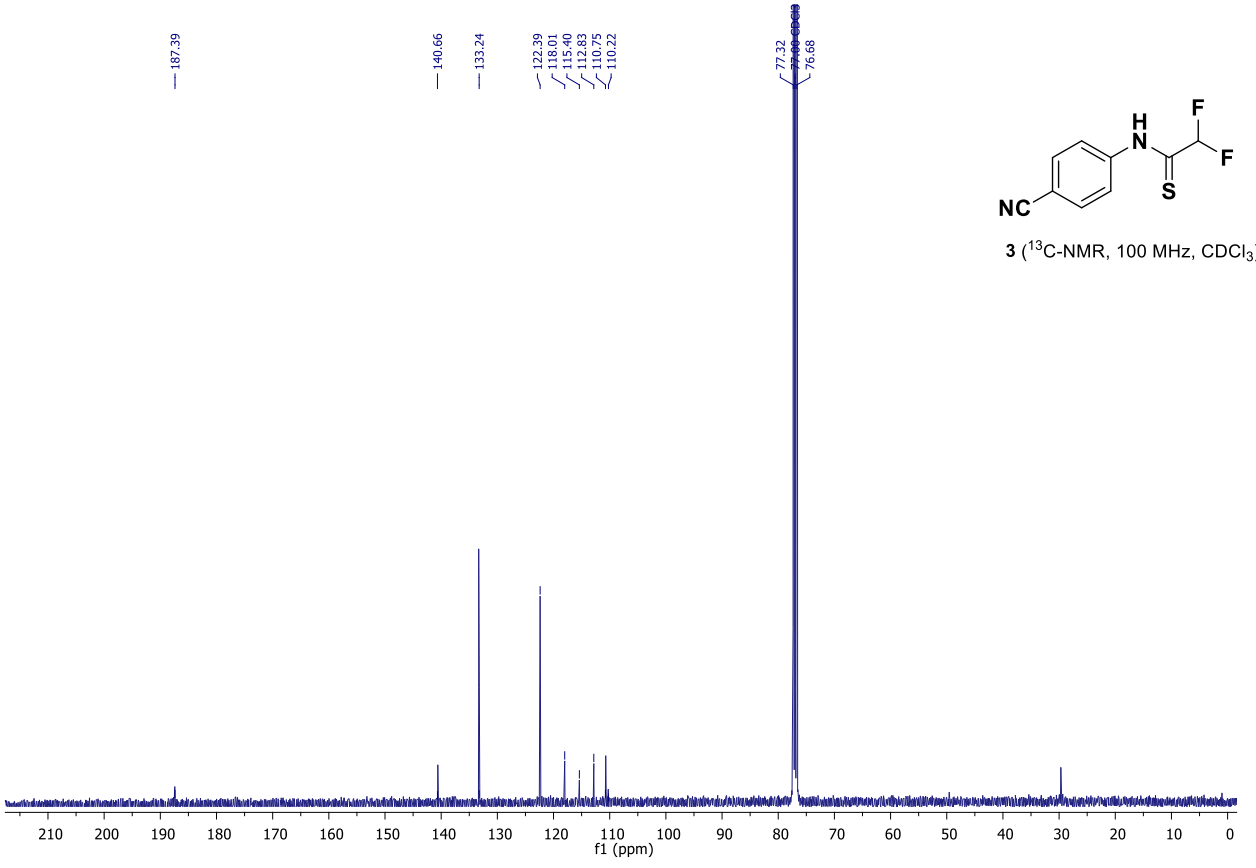
2b (^{1}H-NMR, 400 MHz, $CDCl_3$)



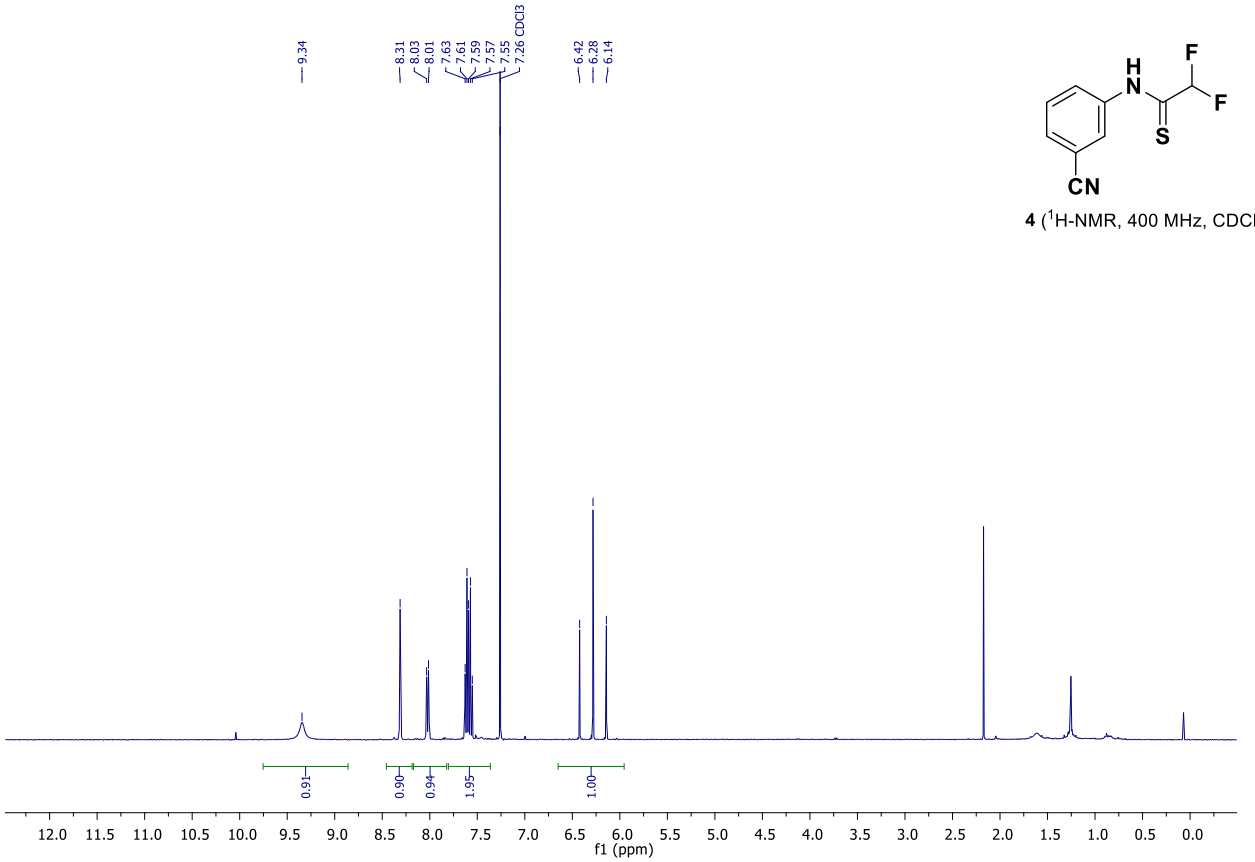
2b (^{13}C-NMR, 100 MHz, $CDCl_3$)



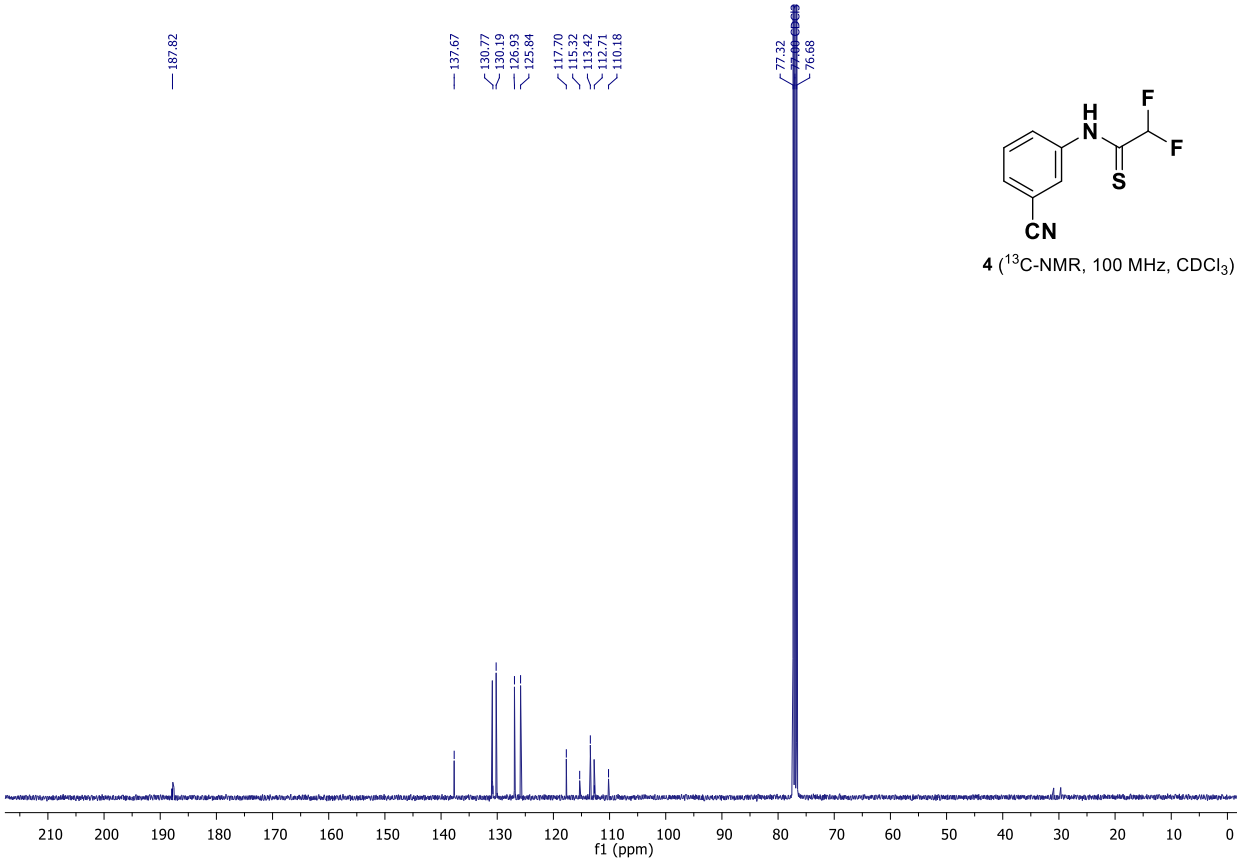
3 (^{1}H-NMR, 400 MHz, $CDCl_3$)



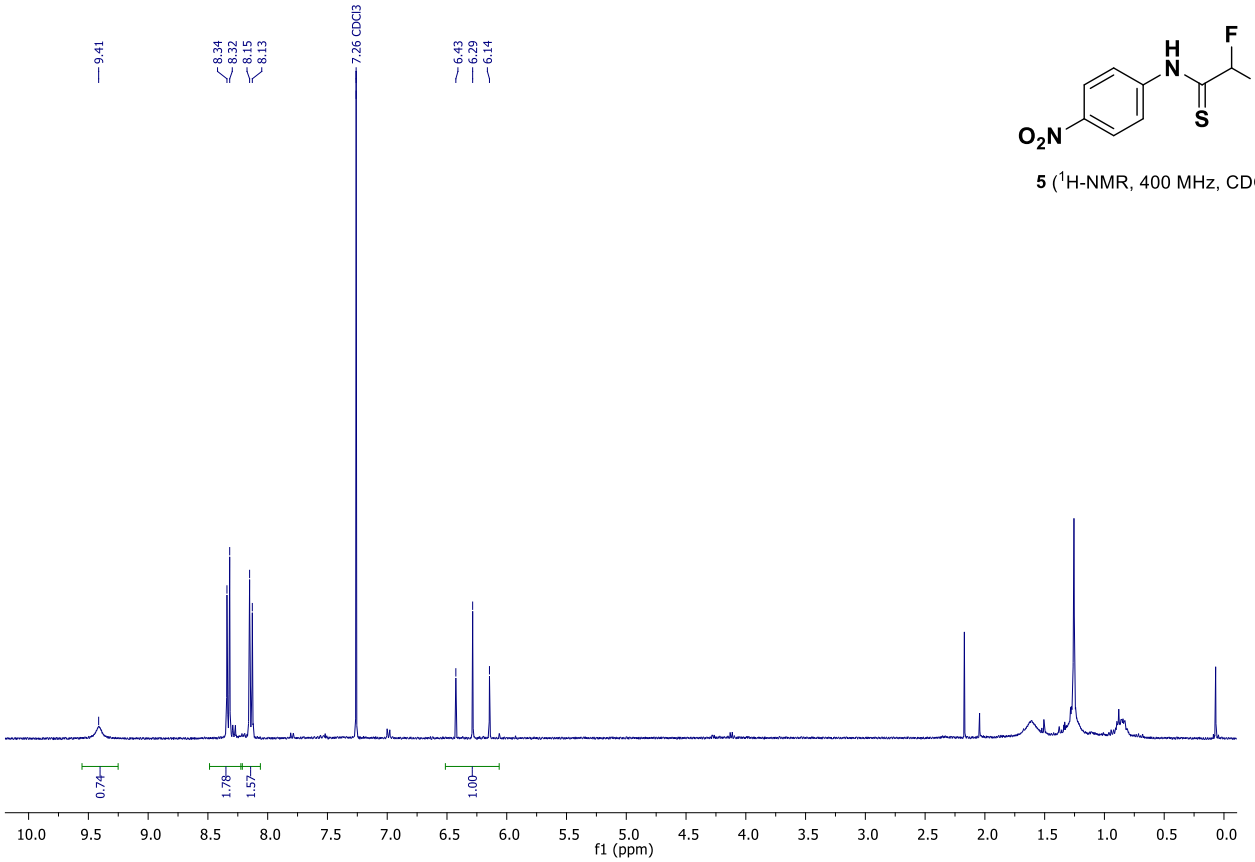
3 (^{13}C-NMR, 100 MHz, $CDCl_3$)



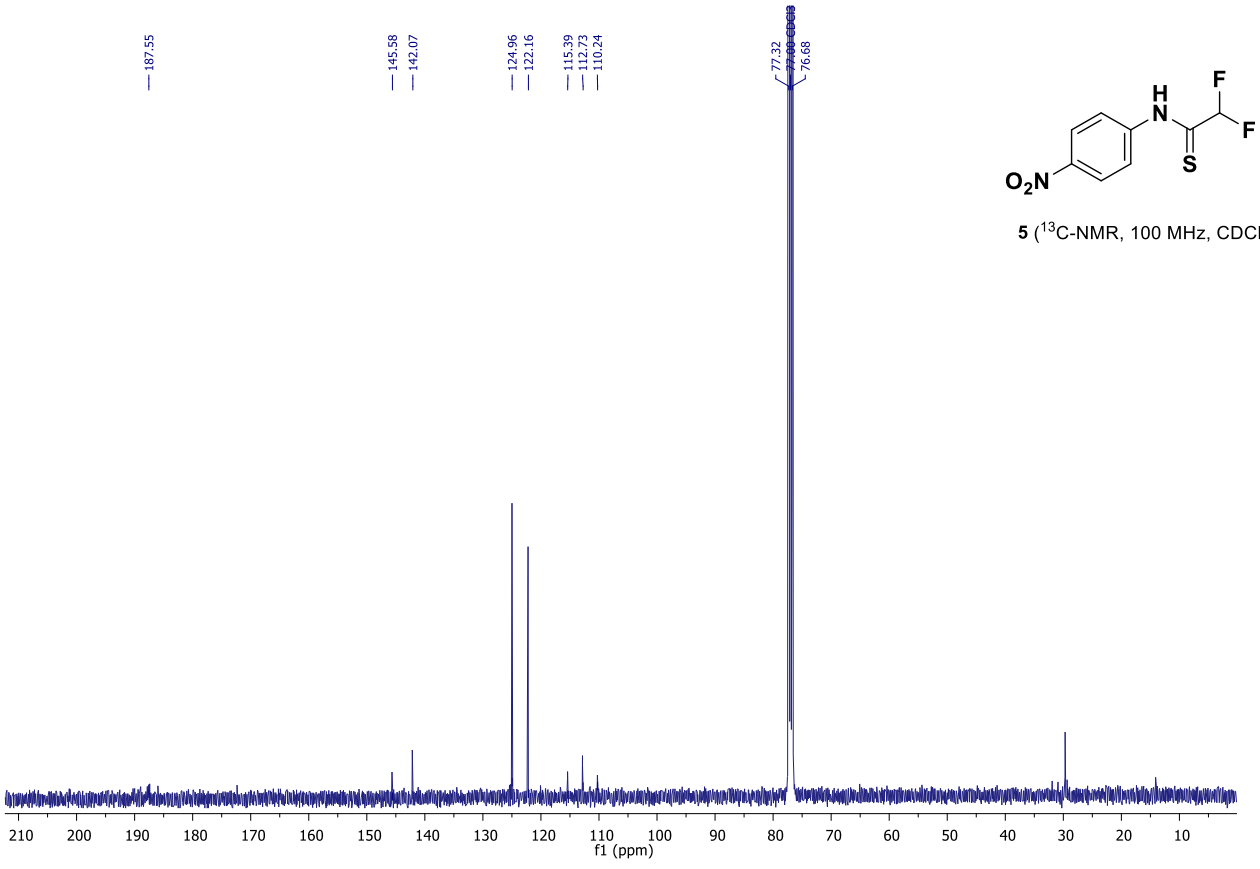
4 (^{1}H-NMR, 400 MHz, $CDCl_3$)



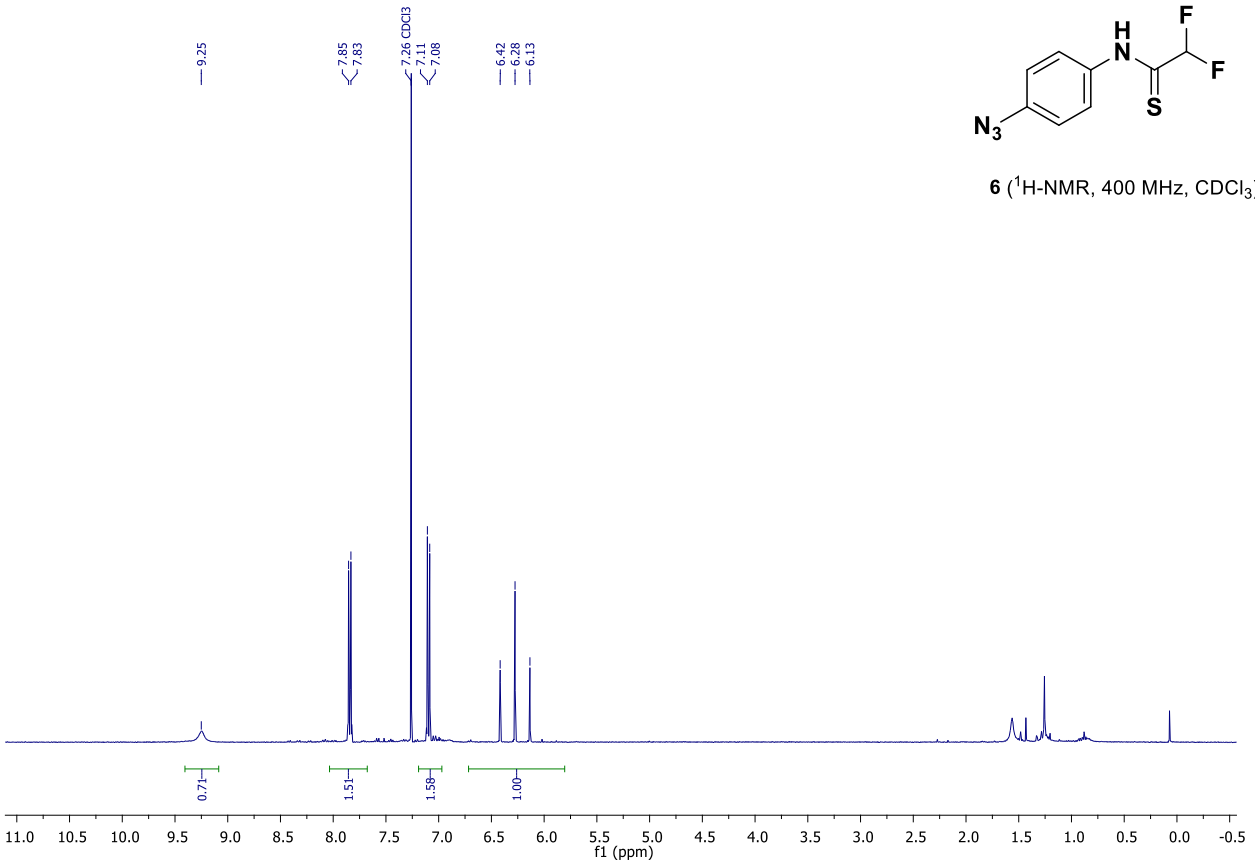
4 (^{13}C-NMR, 100 MHz, $CDCl_3$)



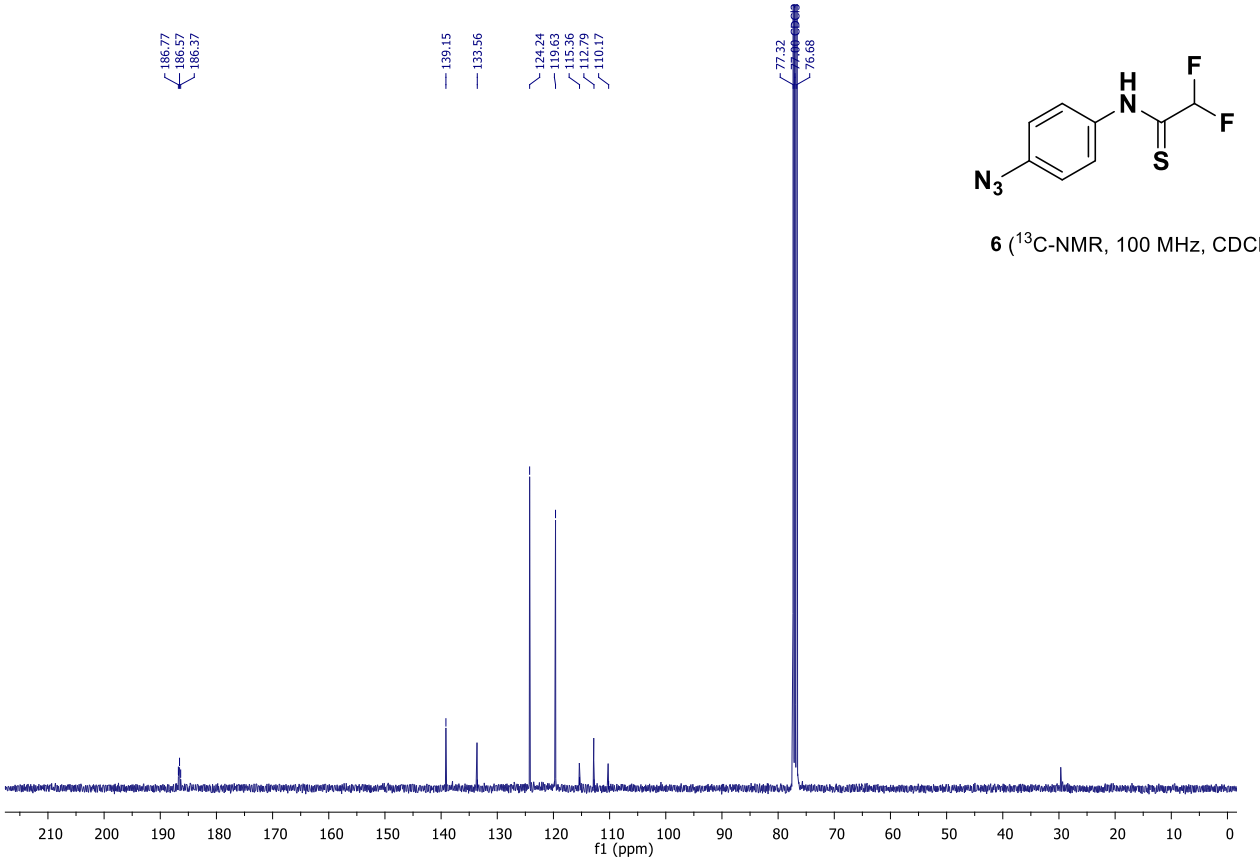
5 (^{1}H-NMR, 400 MHz, $CDCl_3$)



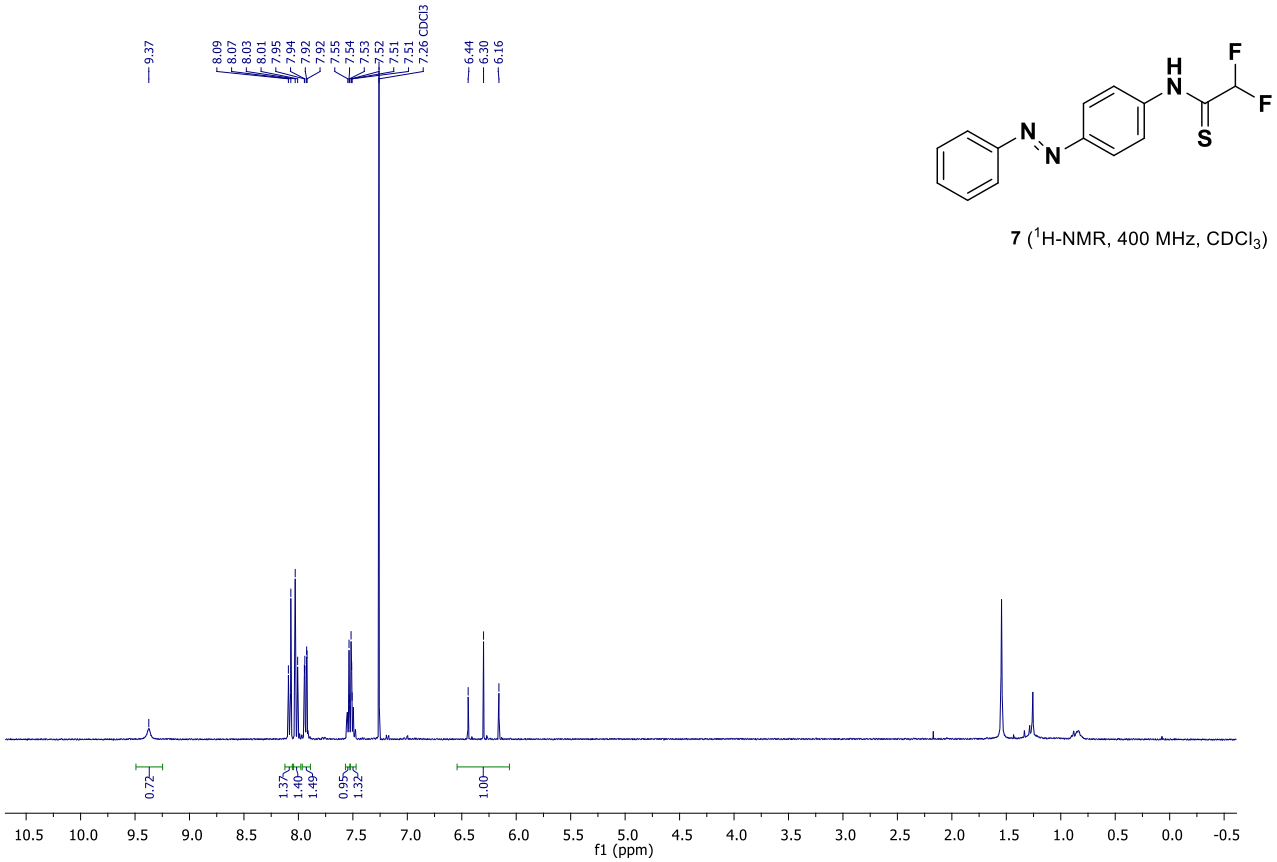
5 (^{13}C-NMR, 100 MHz, $CDCl_3$)



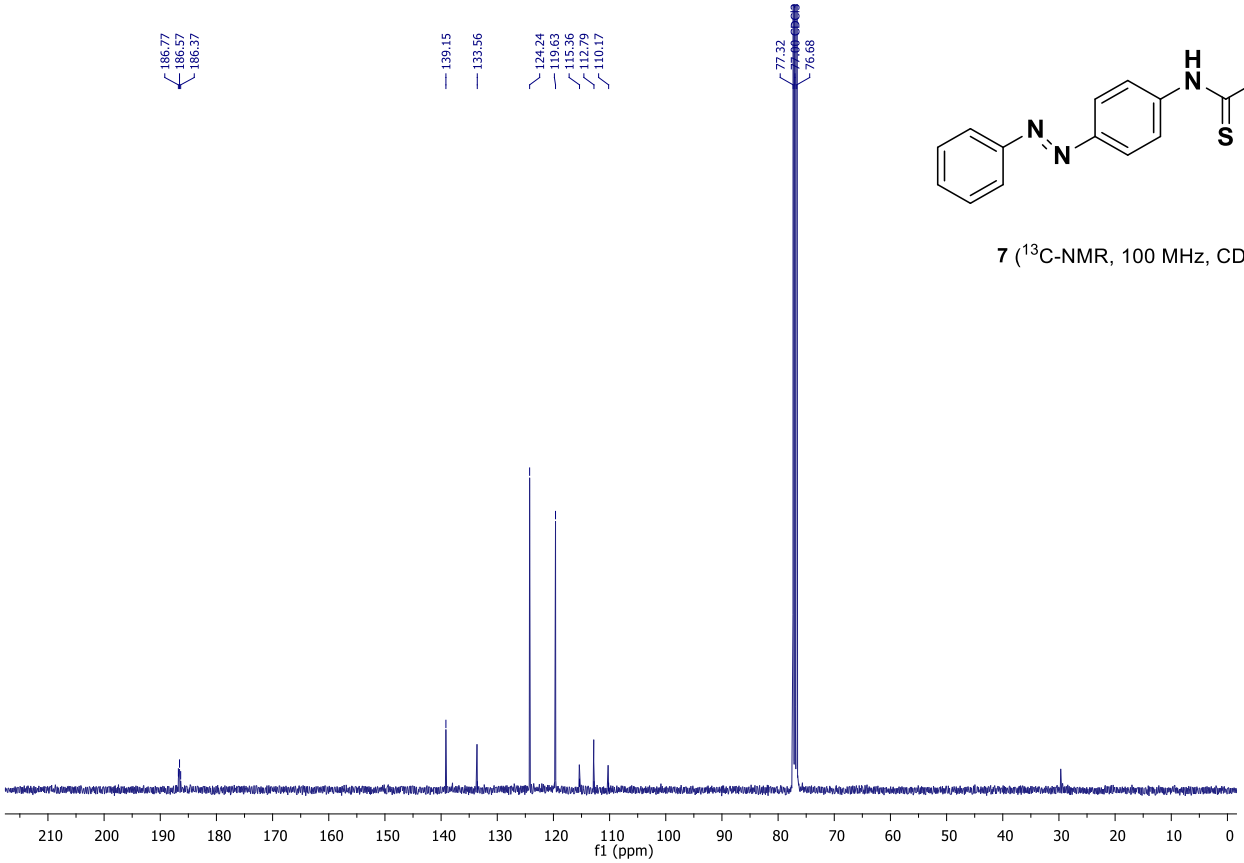
6 (^{1}H-NMR, 400 MHz, $CDCl_3$)



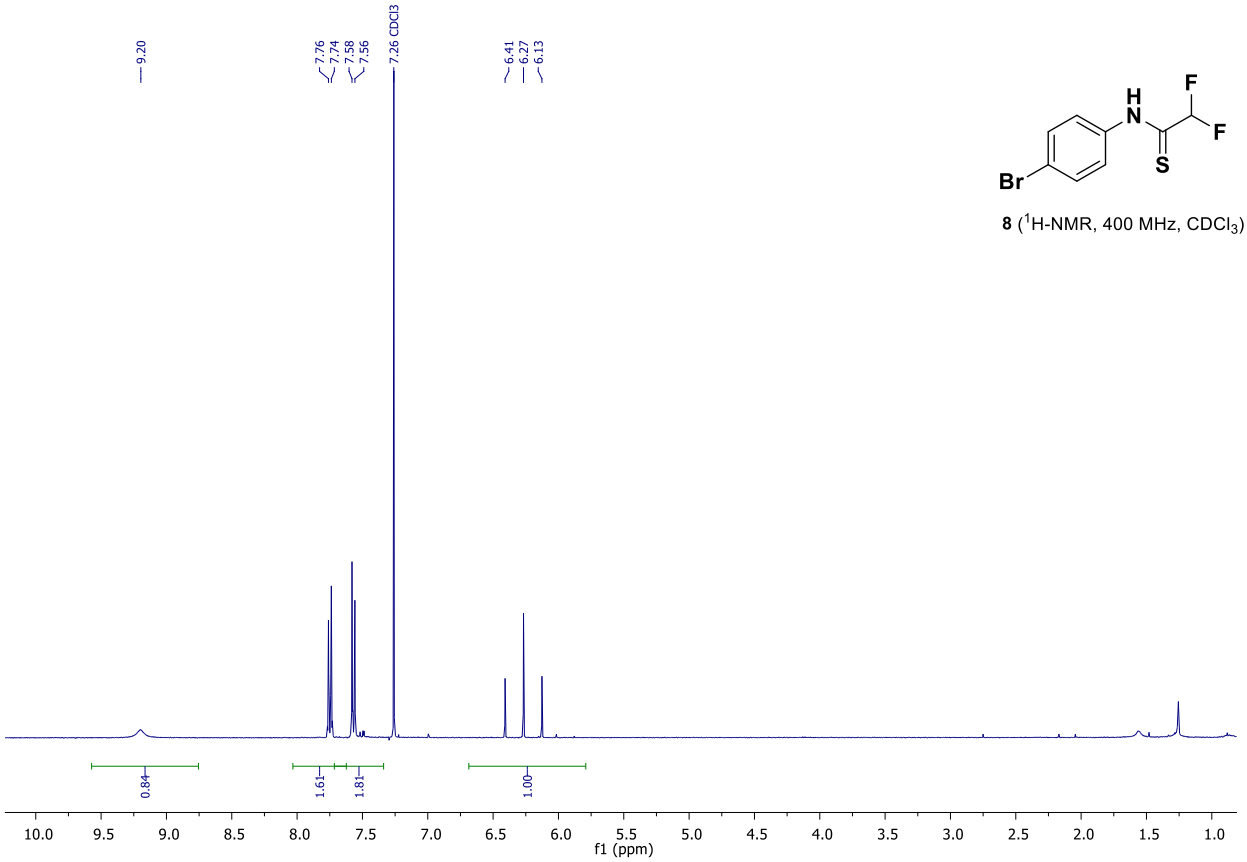
6 (^{13}C-NMR, 100 MHz, $CDCl_3$)



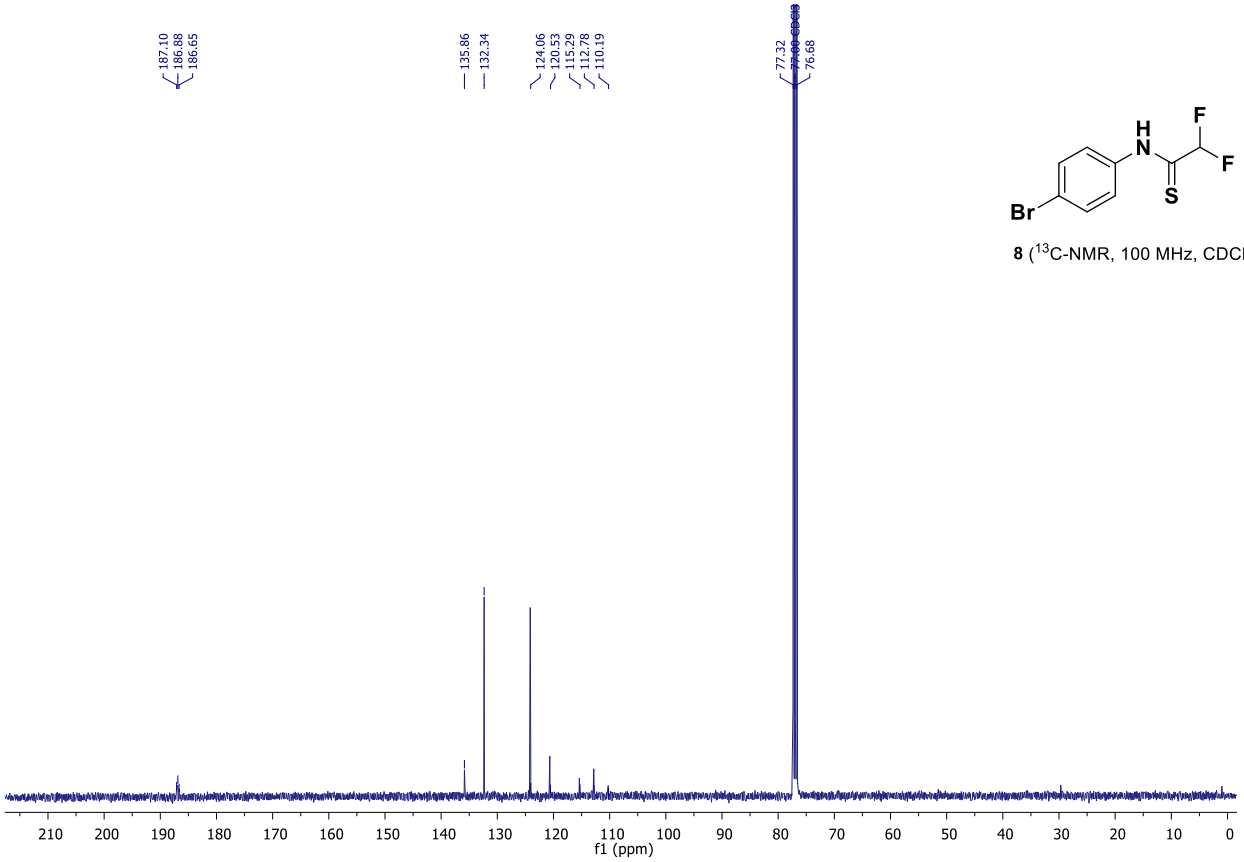
7 (^{1}H-NMR, 400 MHz, $CDCl_3$)



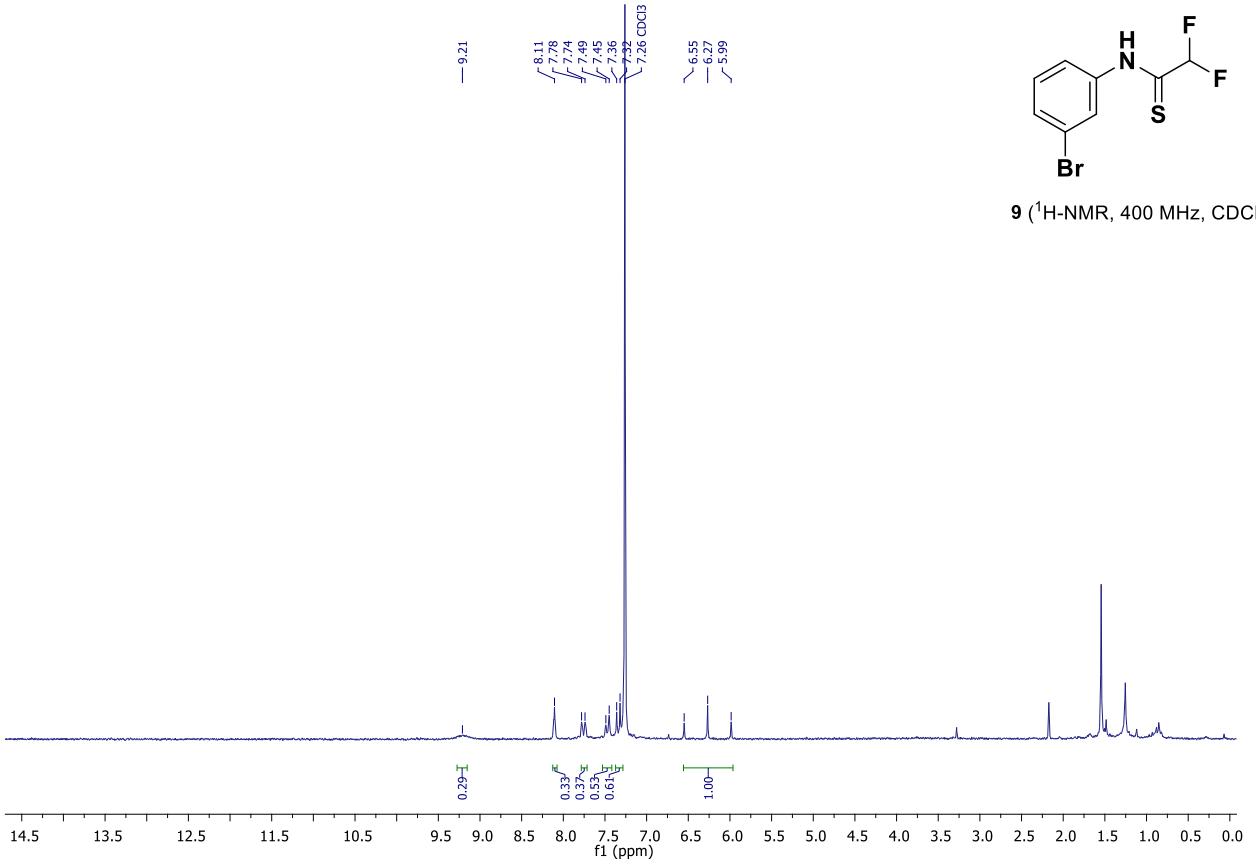
7 (^{13}C-NMR, 100 MHz, $CDCl_3$)



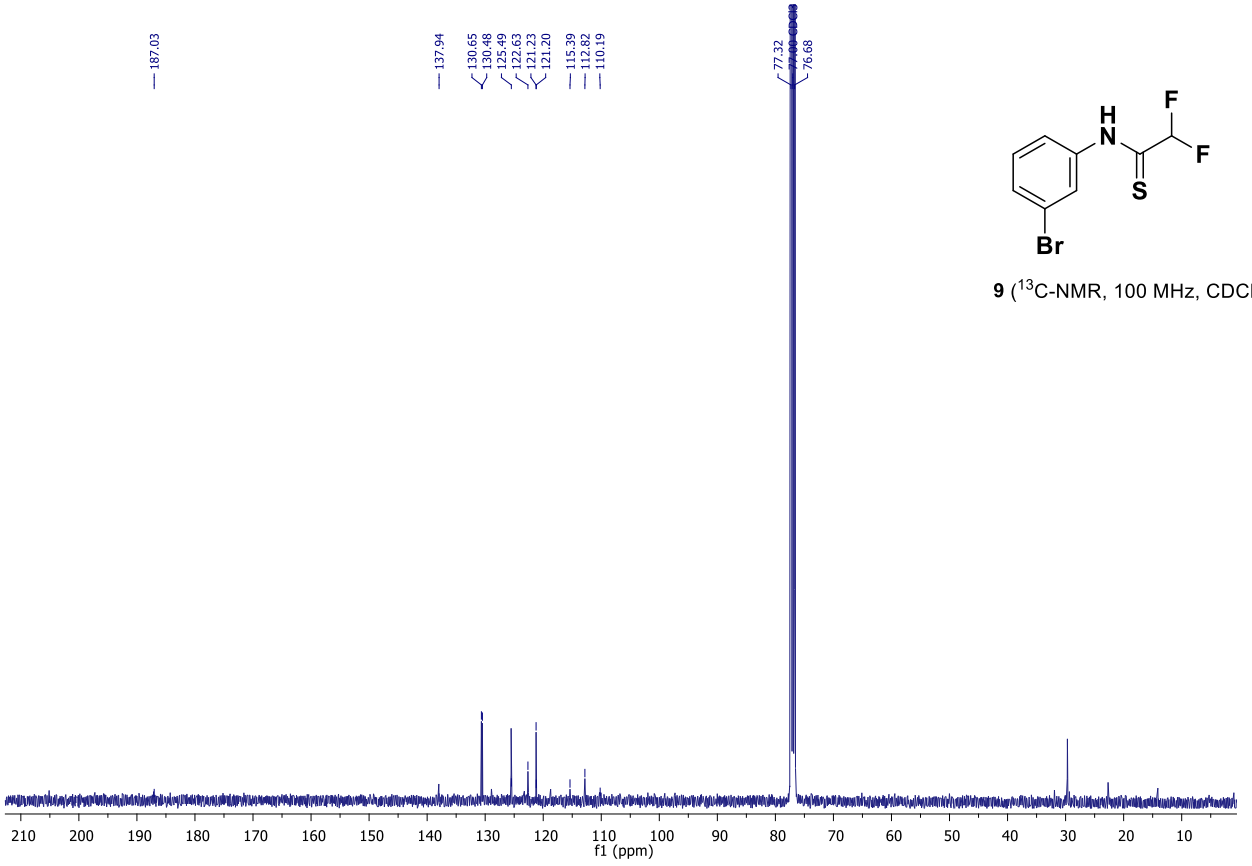
8 (^{1}H-NMR, 400 MHz, $CDCl_3$)



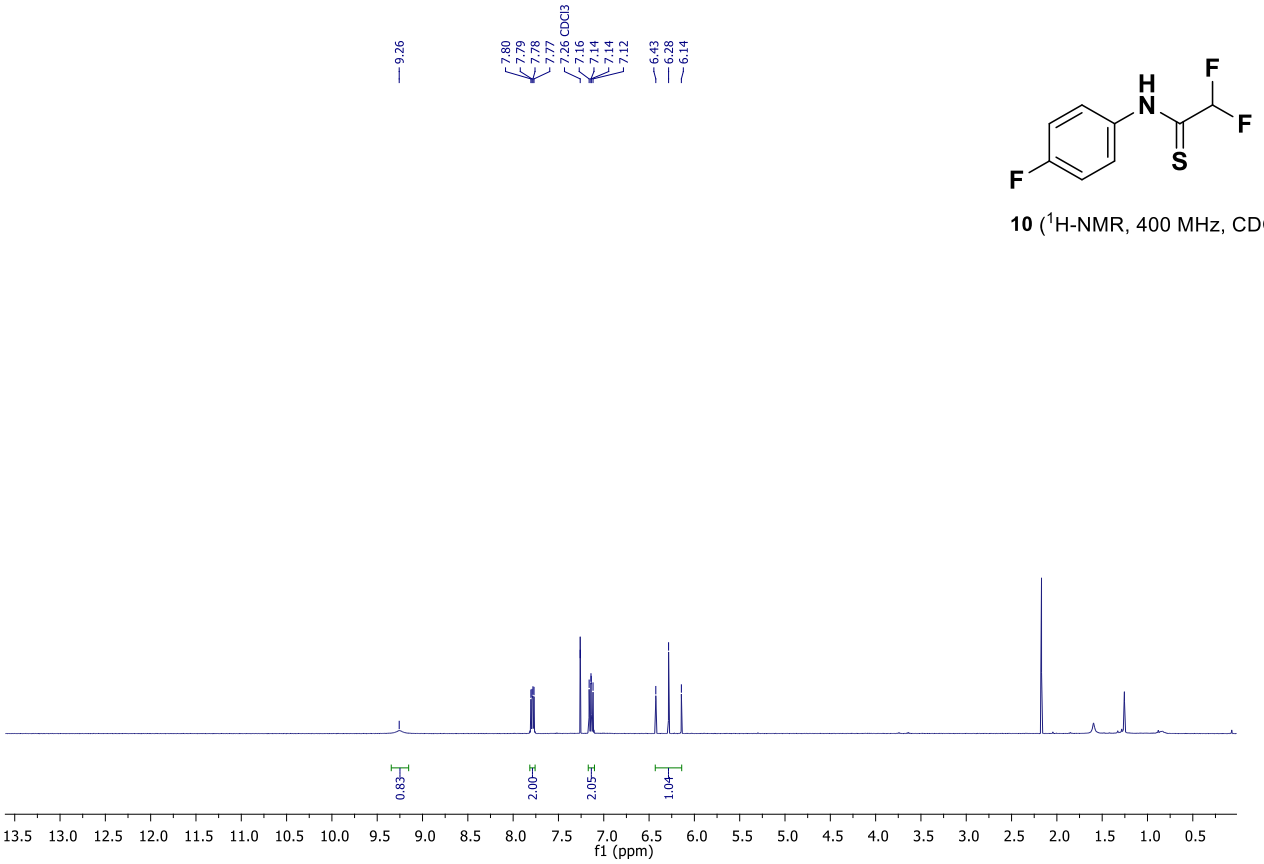
8 (^{13}C-NMR, 100 MHz, $CDCl_3$)



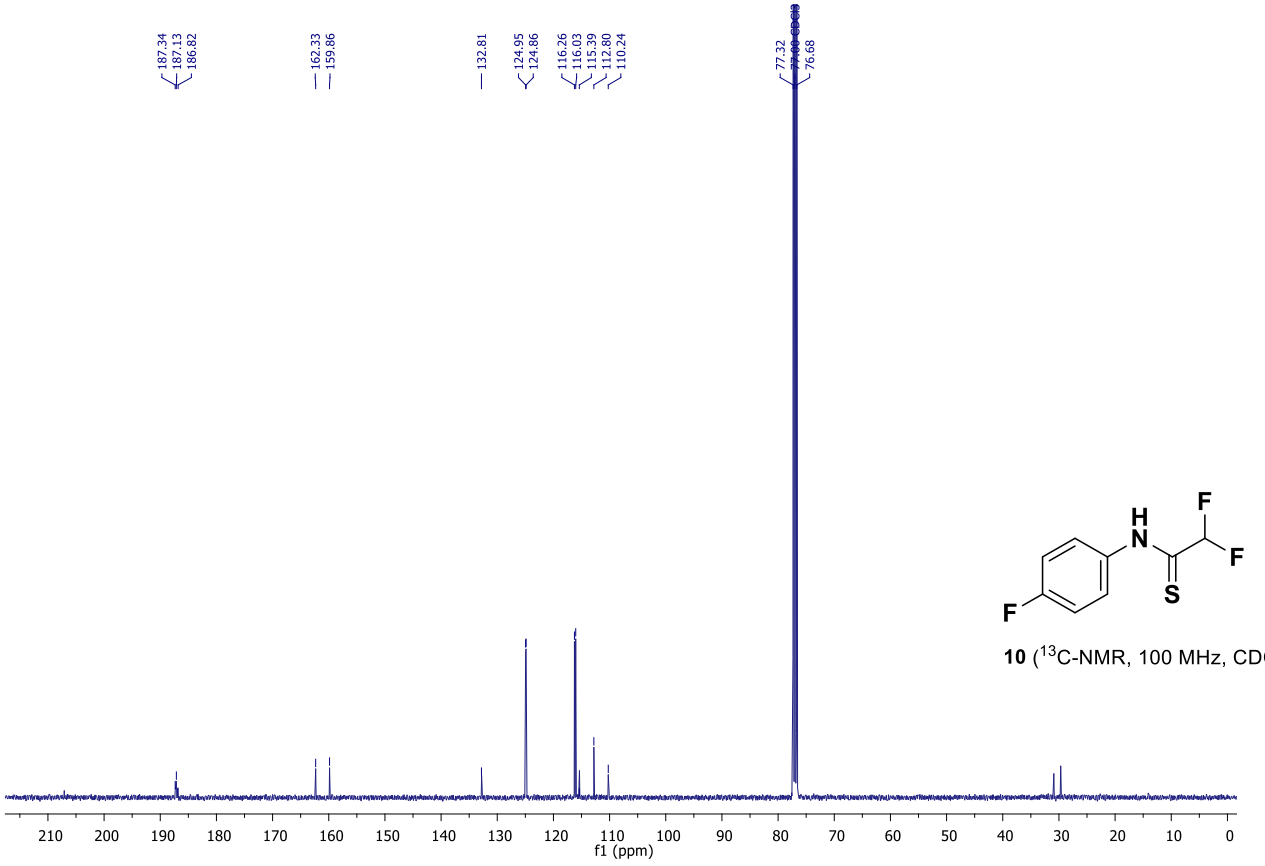
9 (^{1}H-NMR, 400 MHz, $CDCl_3$)



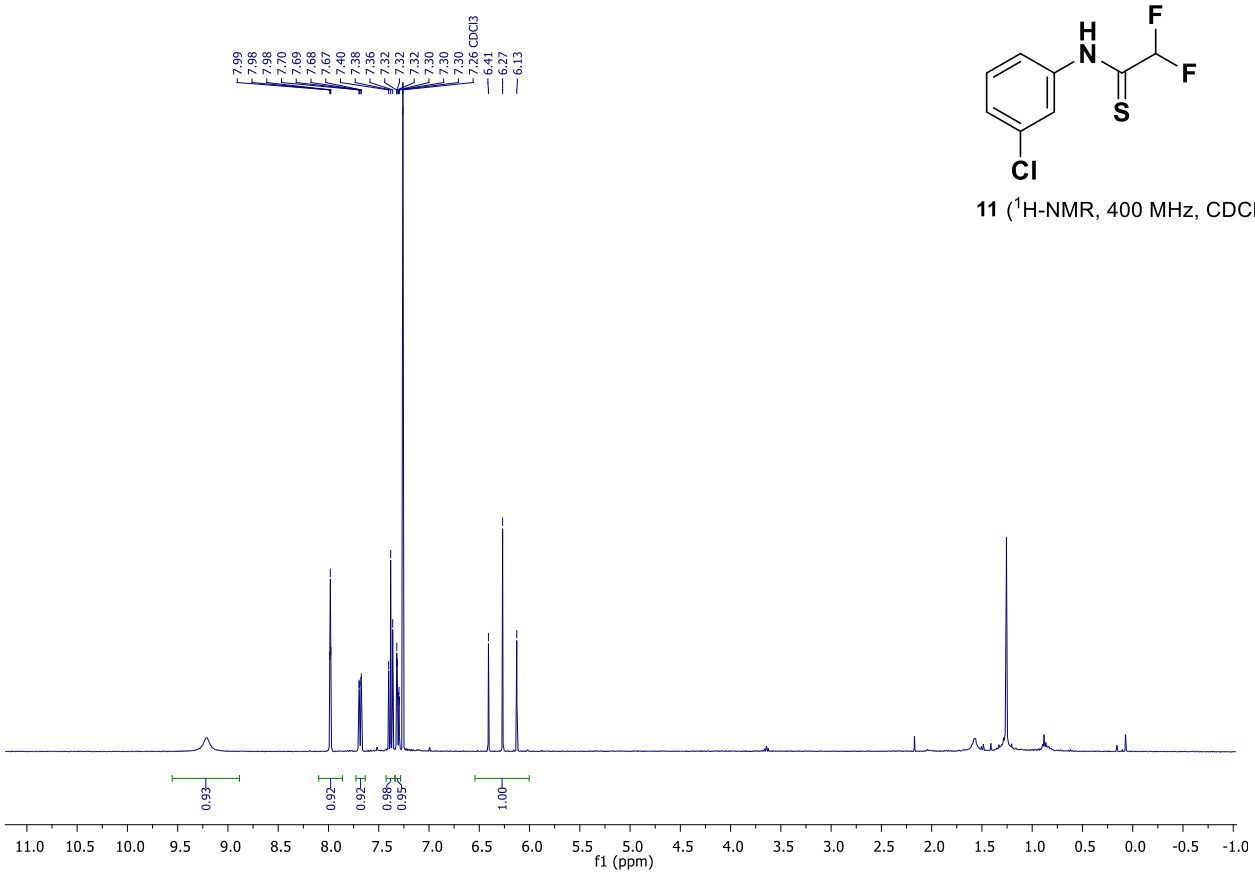
9 (^{13}C-NMR, 100 MHz, $CDCl_3$)



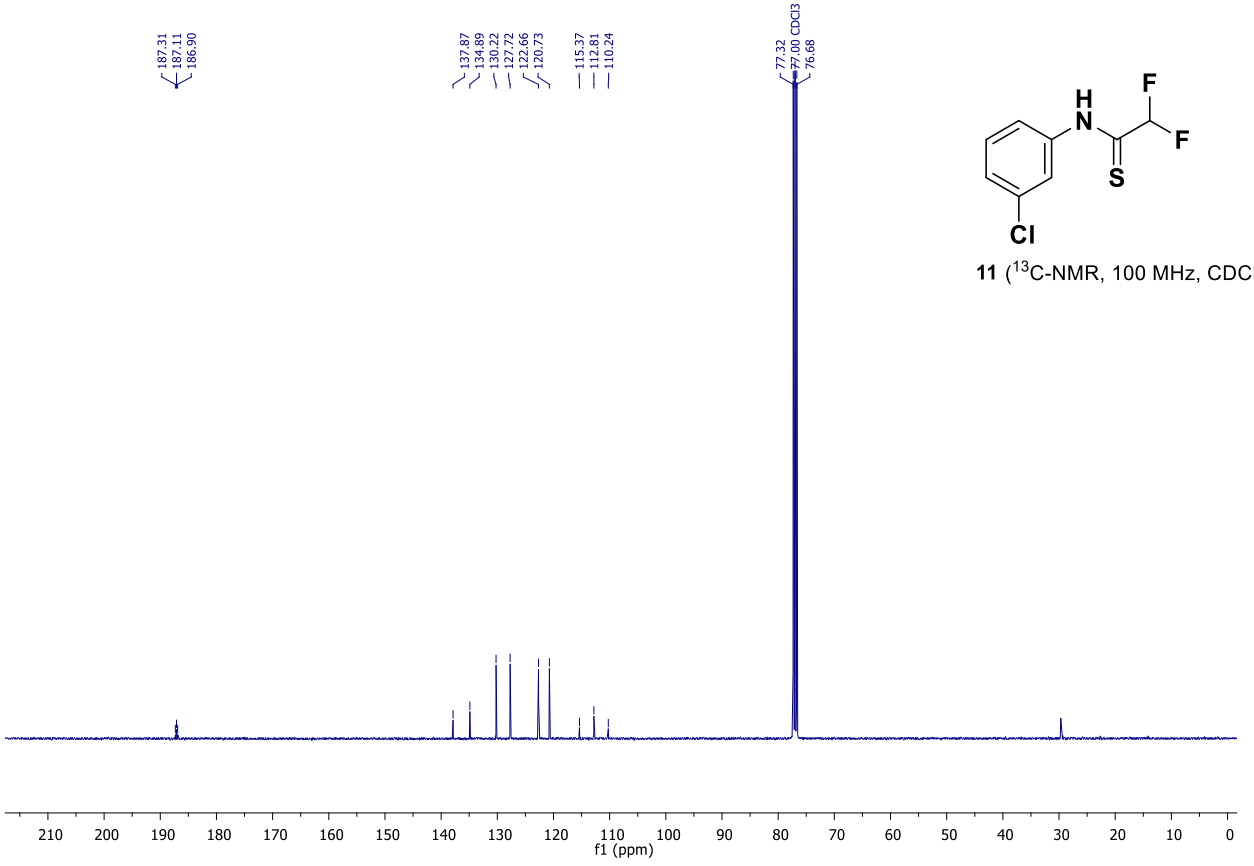
10 (^{1}H-NMR, 400 MHz, $CDCl_3$)



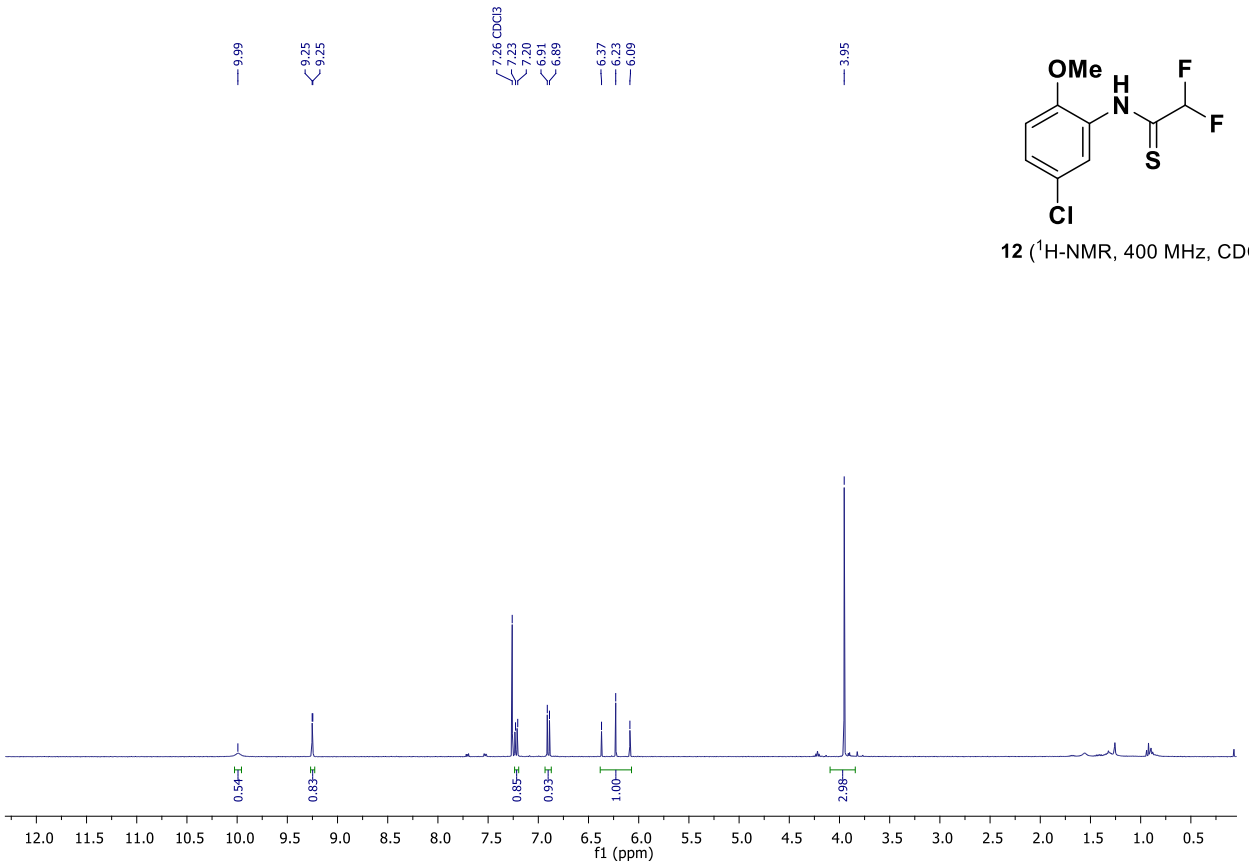
10 (^{13}C-NMR, 100 MHz, $CDCl_3$)



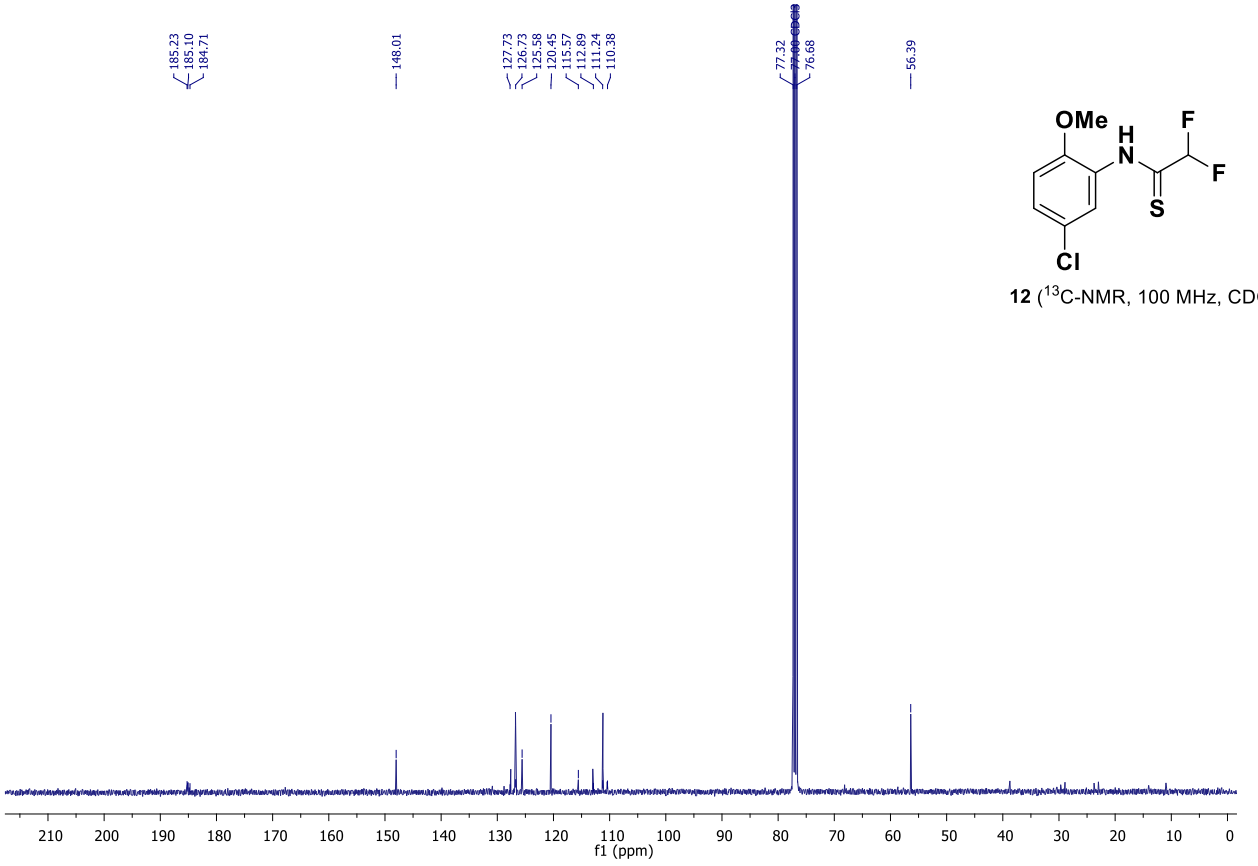
11 (^{1}H-NMR, 400 MHz, $CDCl_3$)



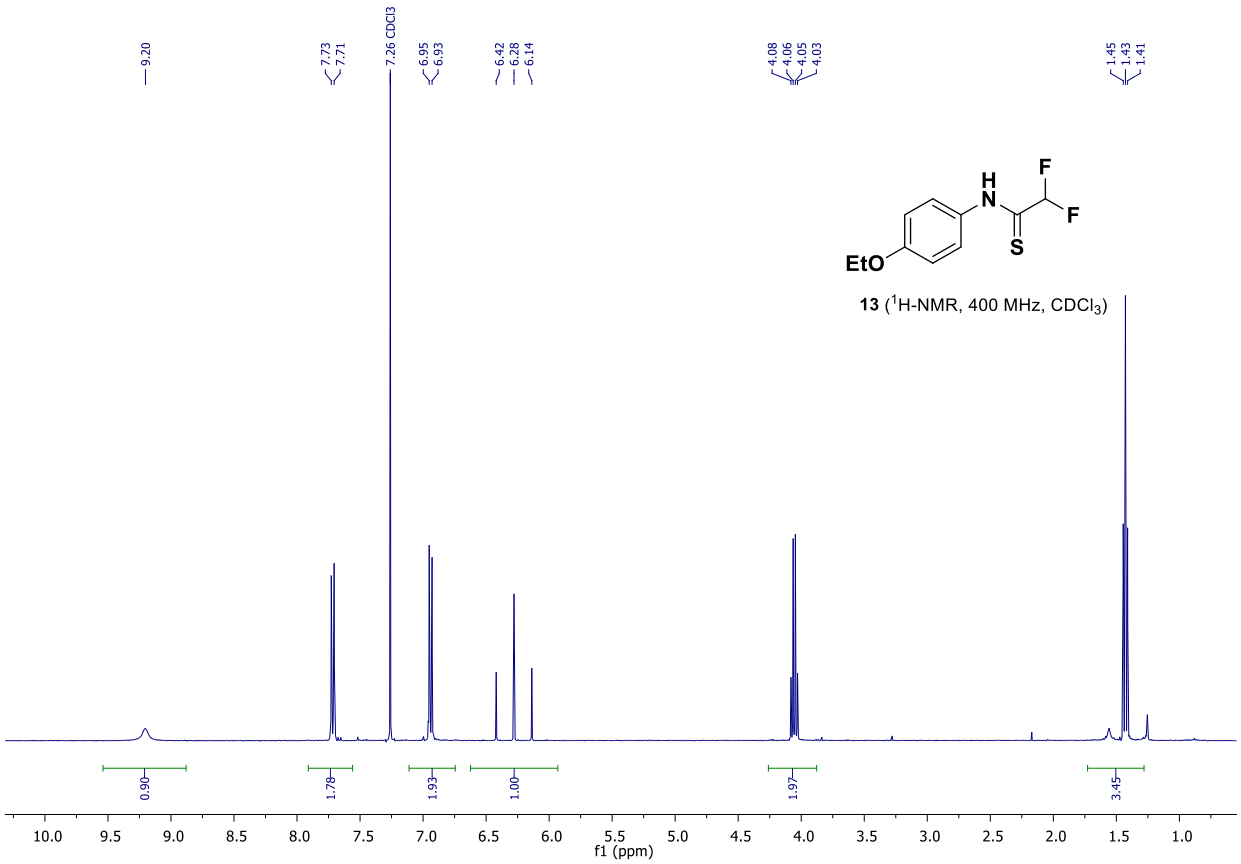
11 (^{13}C-NMR, 100 MHz, $CDCl_3$)



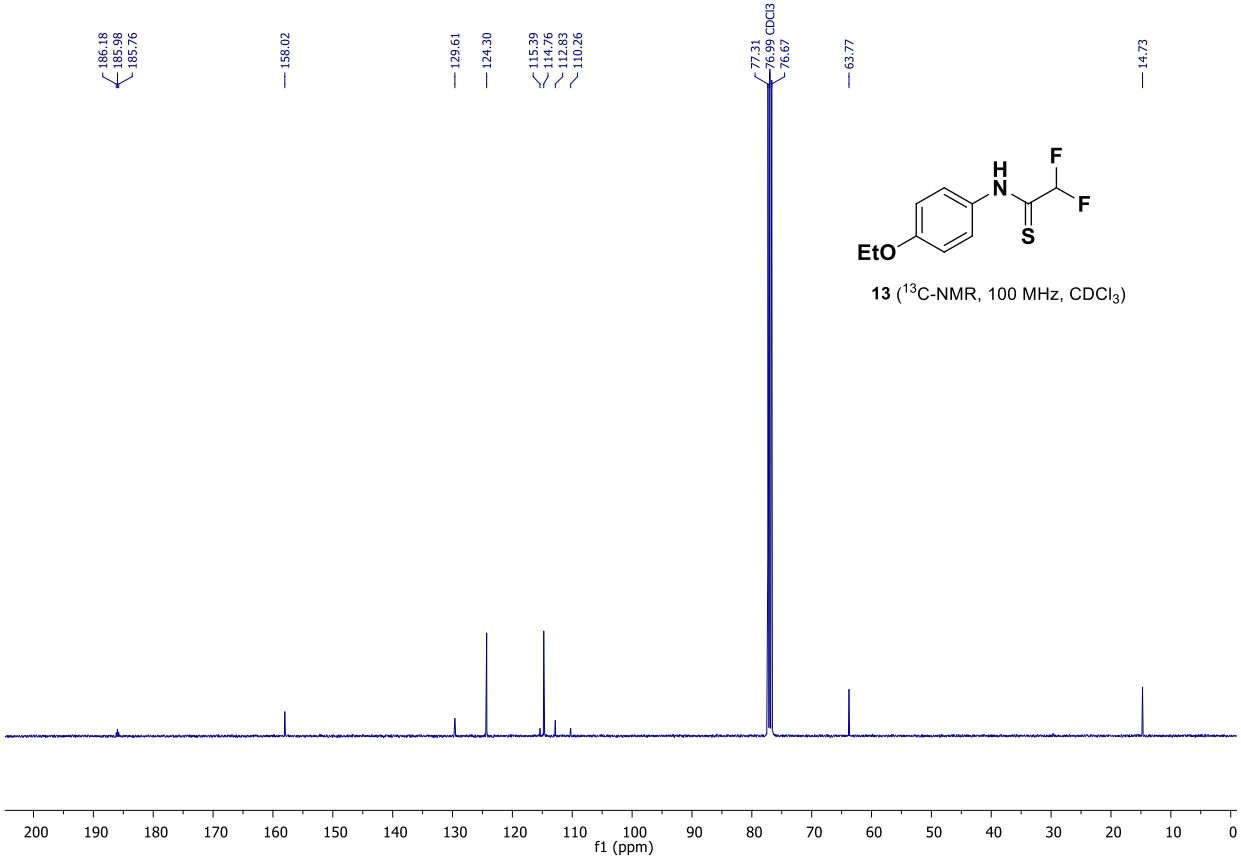
12 (^{1}H-NMR, 400 MHz, $CDCl_3$)



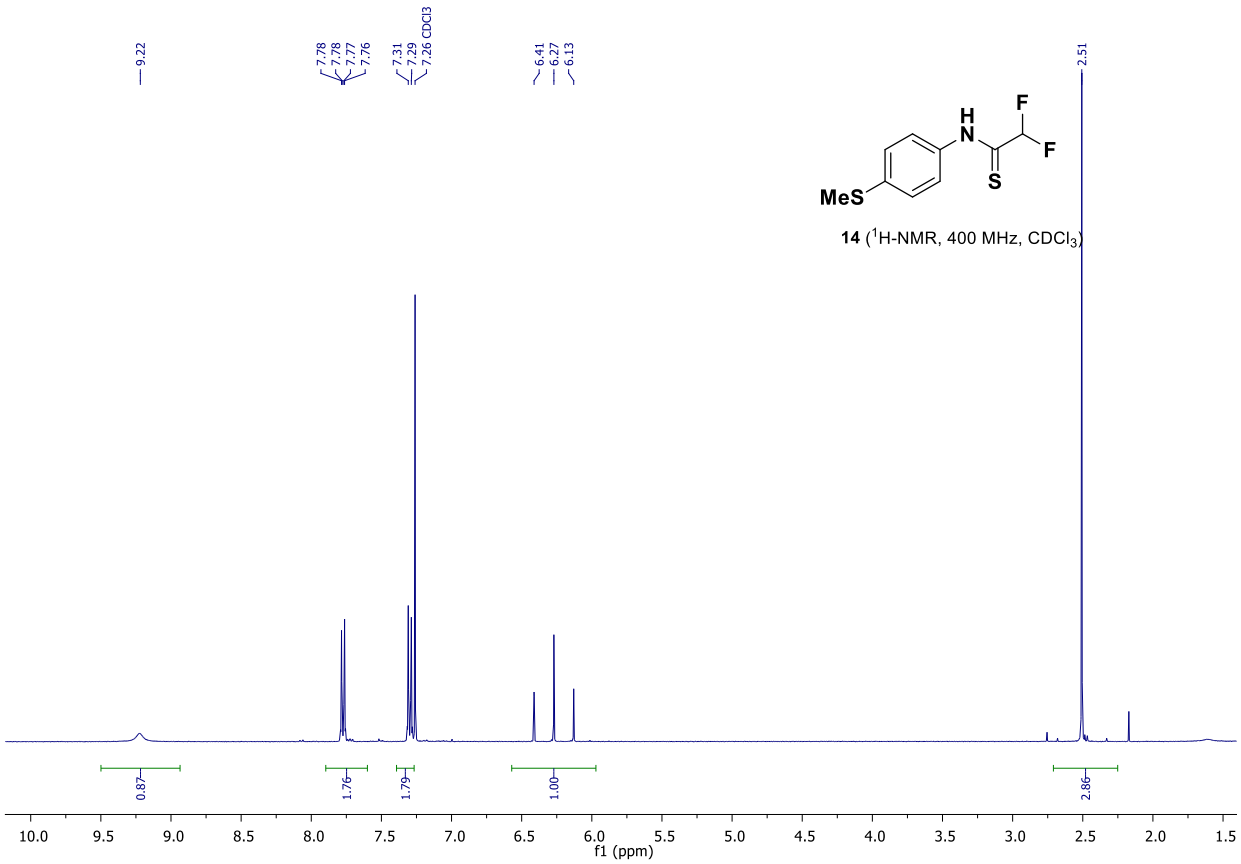
12 (^{13}C-NMR, 100 MHz, $CDCl_3$)



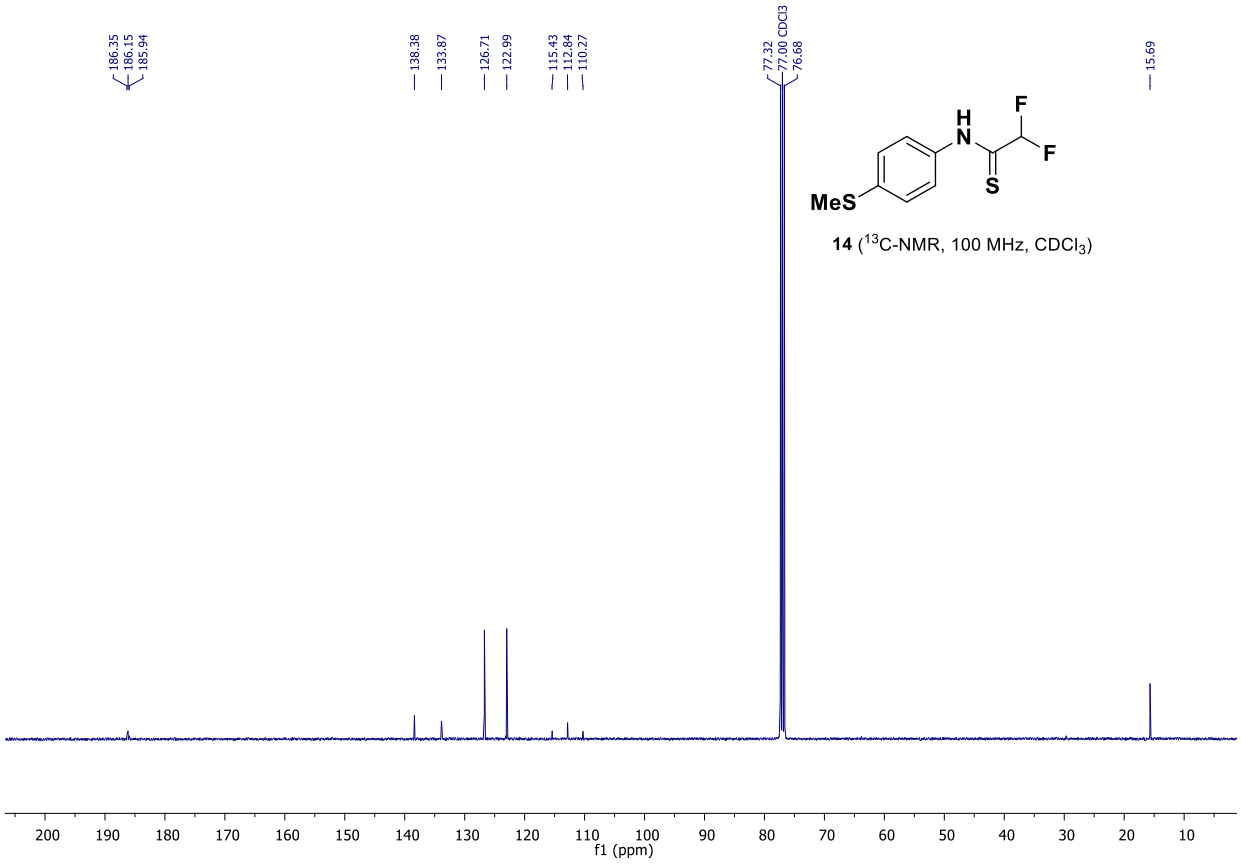
13 (^{1}H-NMR, 400 MHz, $CDCl_3$)



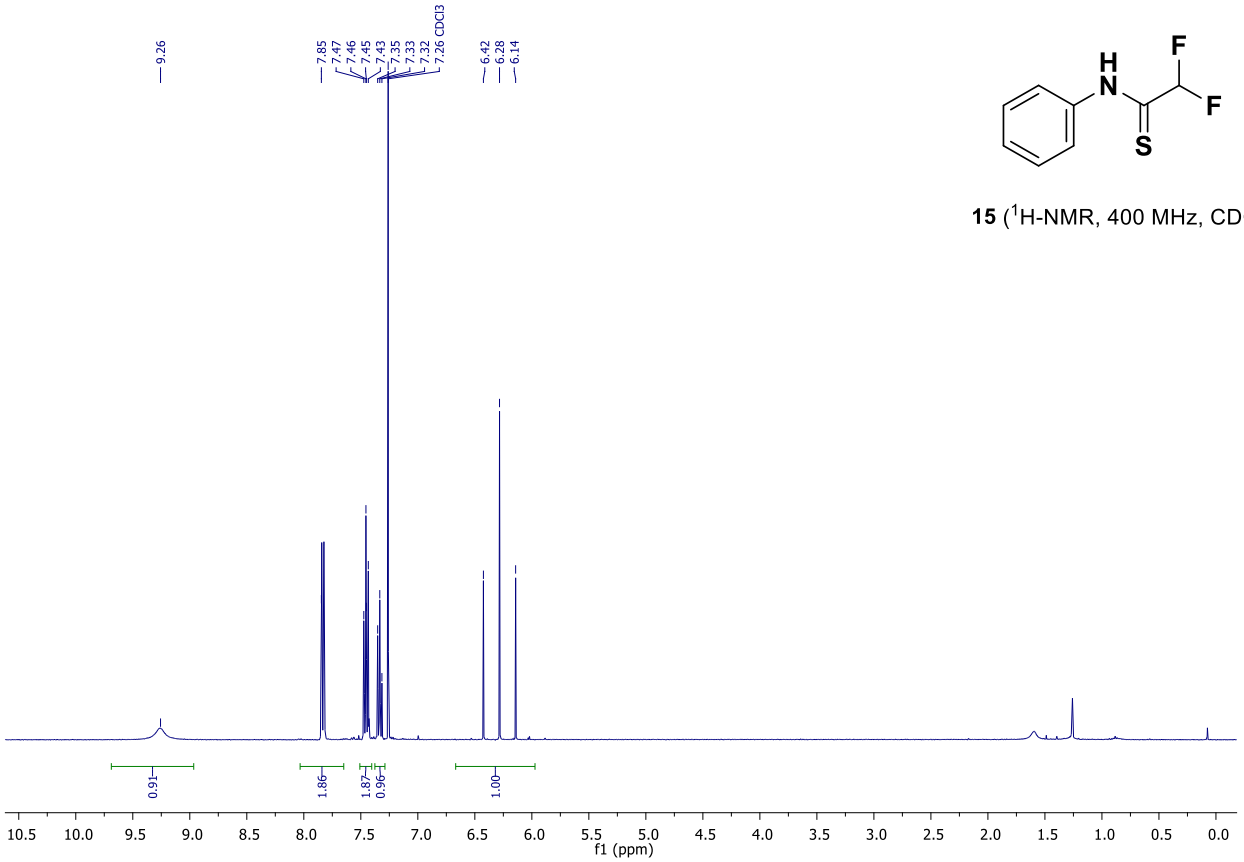
13 (^{13}C-NMR, 100 MHz, $CDCl_3$)



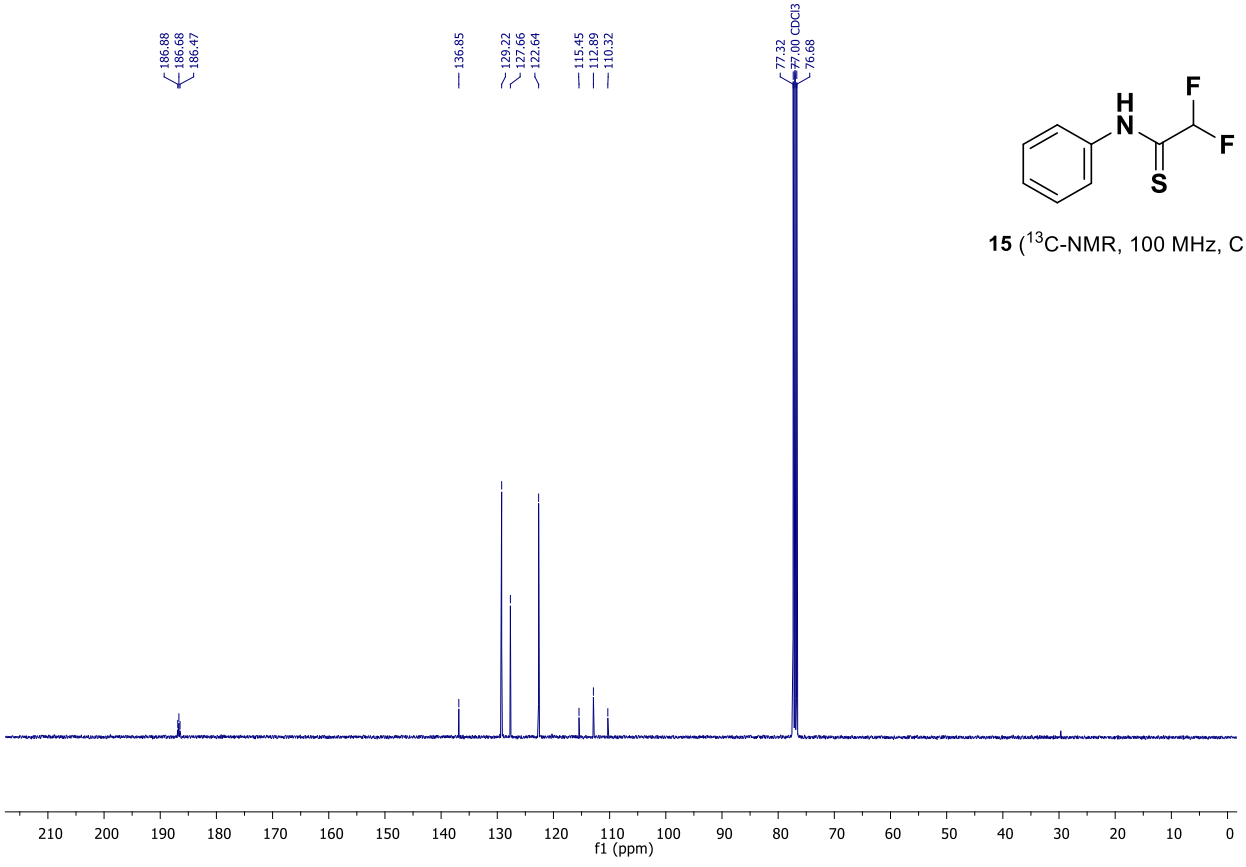
14 (^{1}H-NMR, 400 MHz, $CDCl_3$)



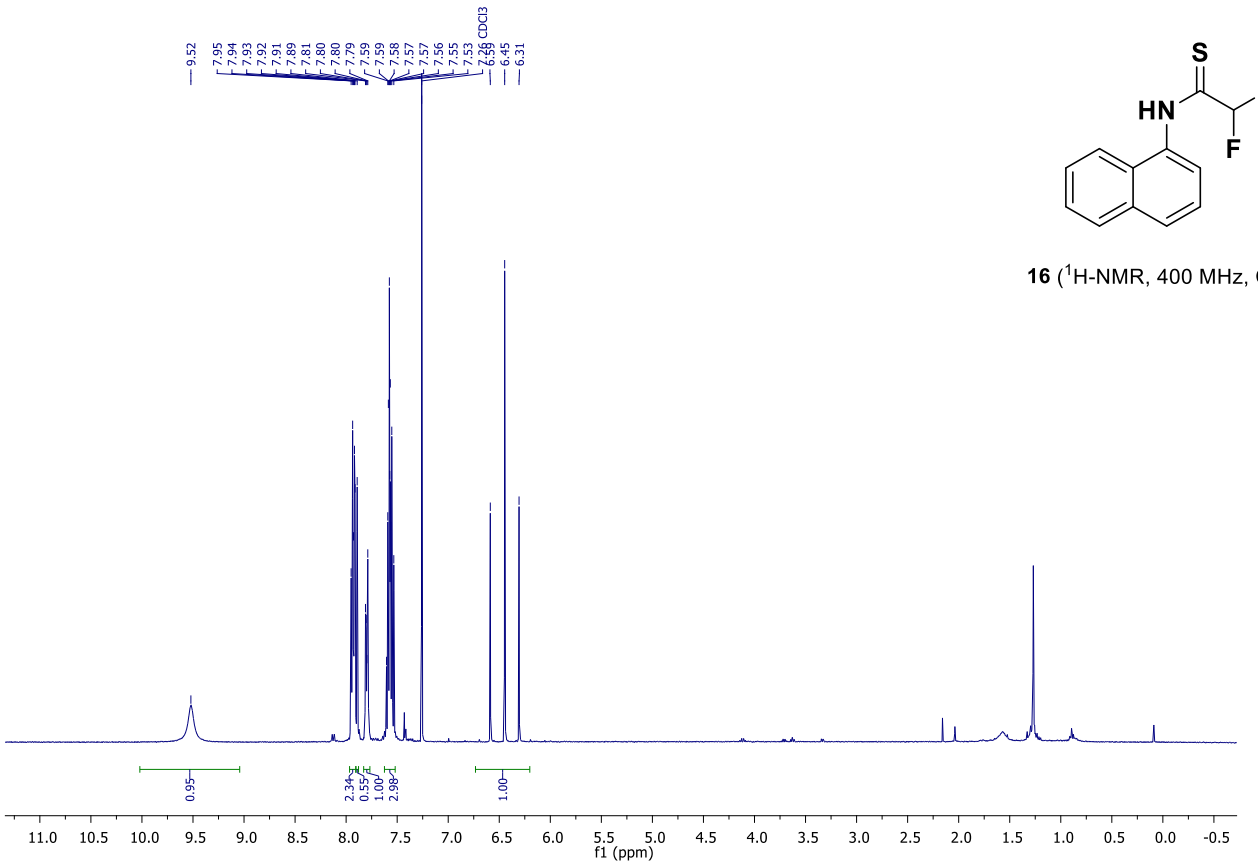
14 (^{13}C-NMR, 100 MHz, $CDCl_3$)



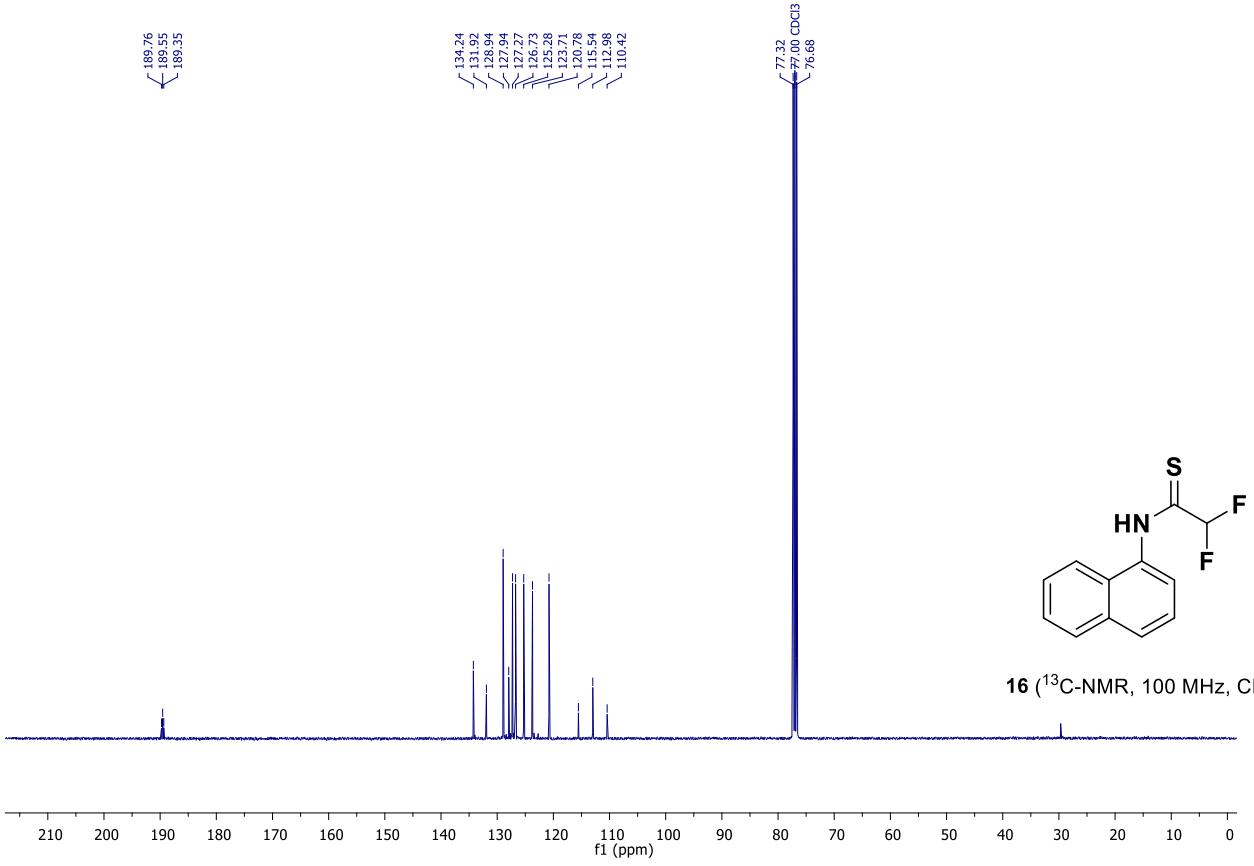
15 (^{1}H-NMR, 400 MHz, $CDCl_3$)



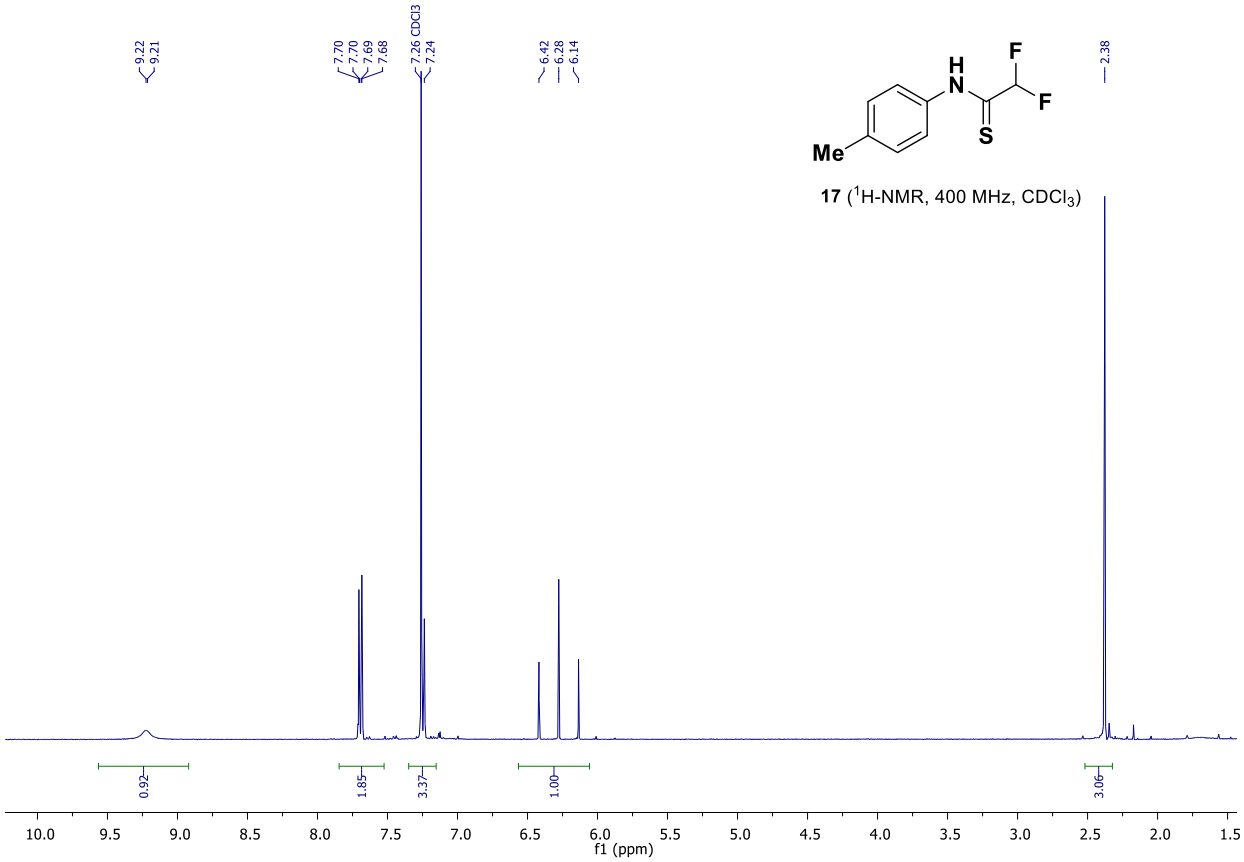
15 (^{13}C-NMR, 100 MHz, $CDCl_3$)



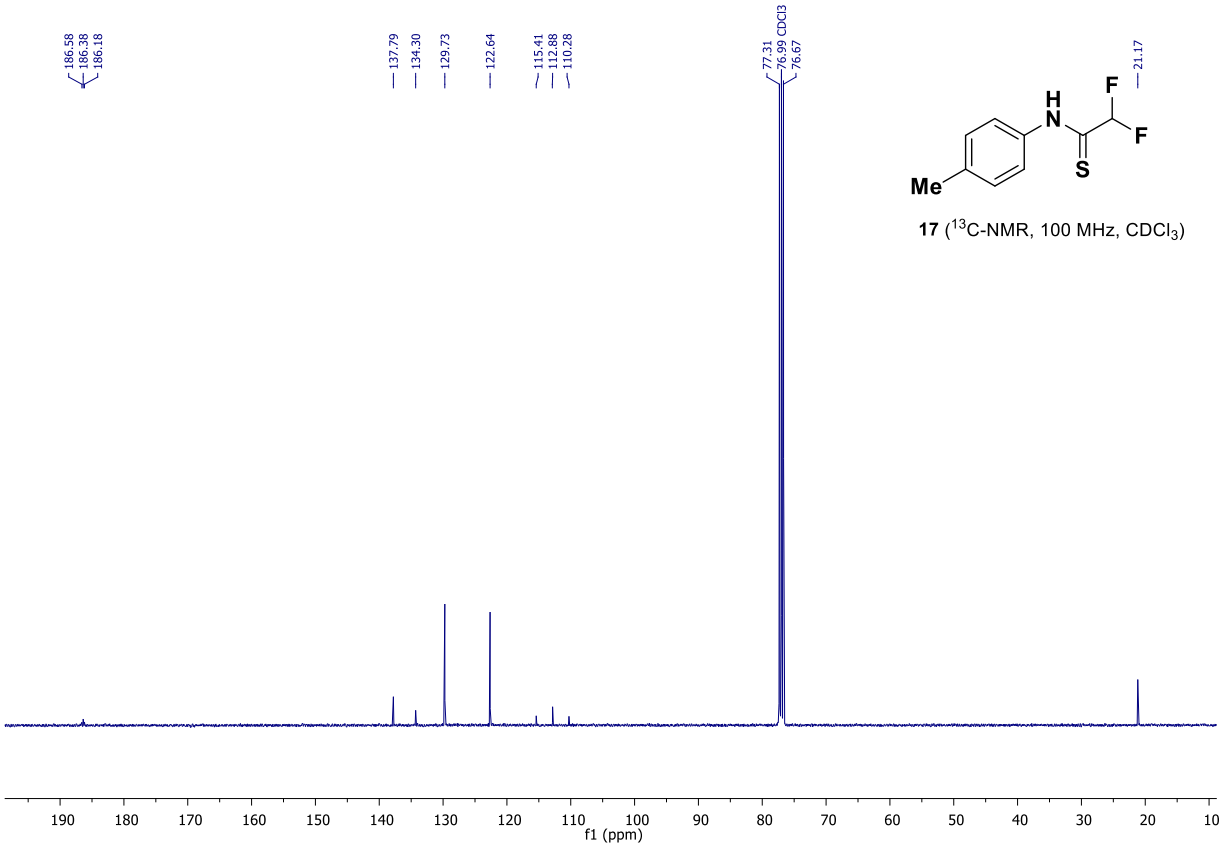
16 (^{1}H-NMR, 400 MHz, $CDCl_3$)



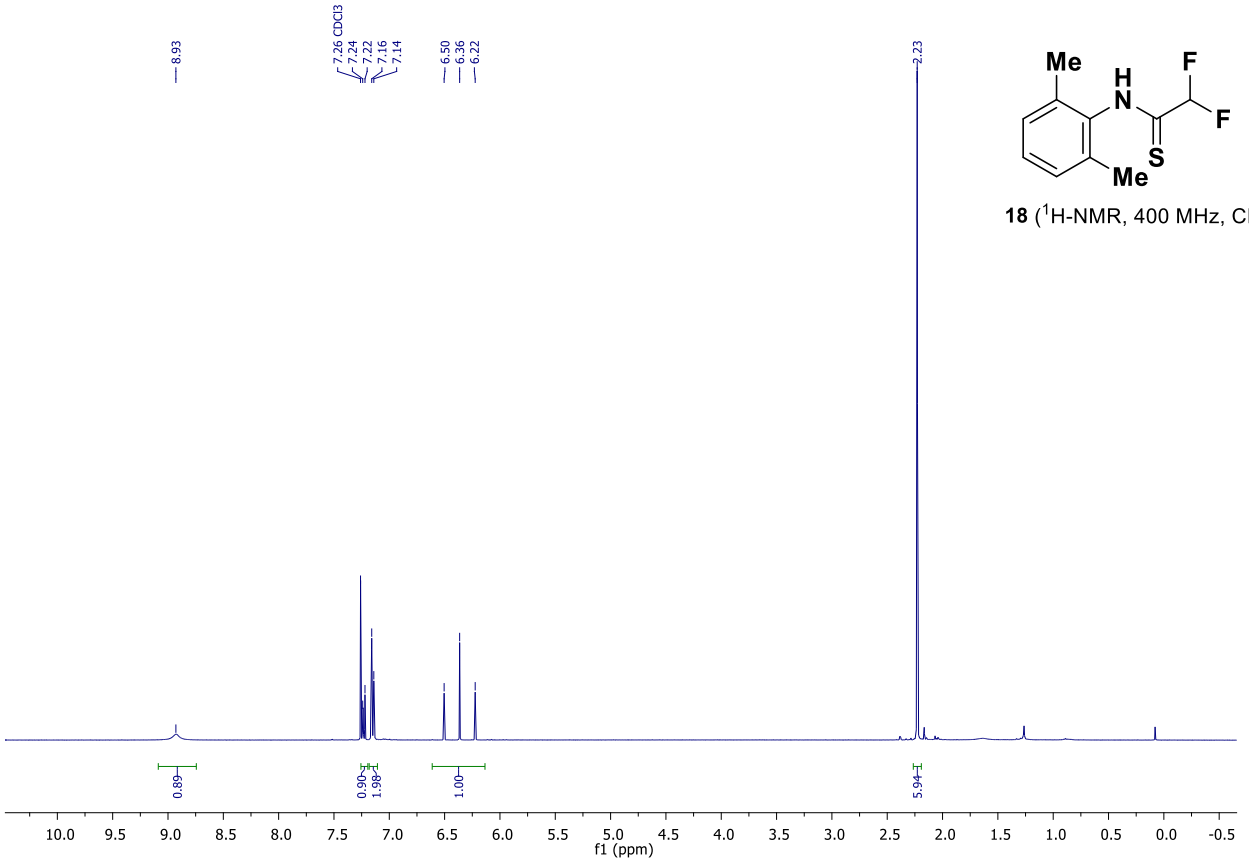
16 (^{13}C-NMR, 100 MHz, $CDCl_3$)



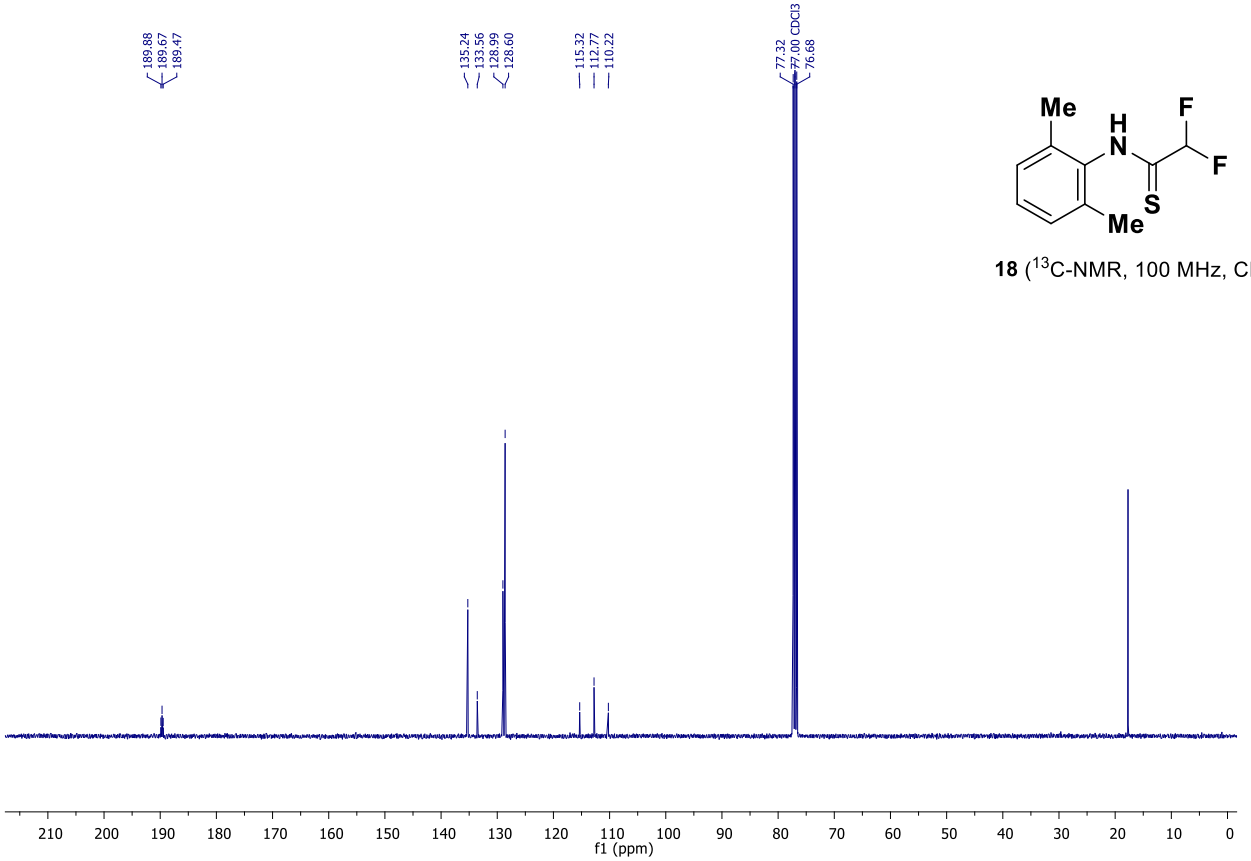
17 (^{1}H-NMR, 400 MHz, $CDCl_3$)



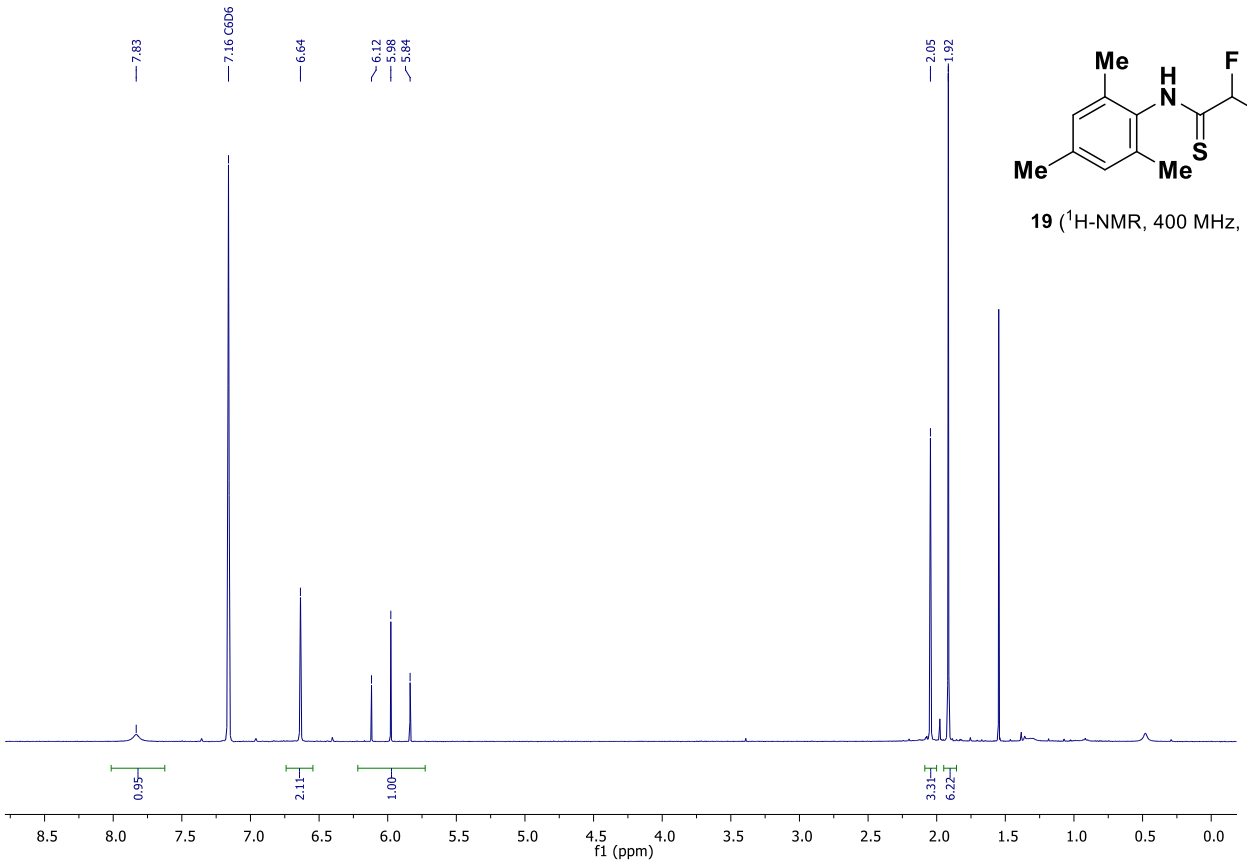
17 (^{13}C-NMR, 100 MHz, $CDCl_3$)



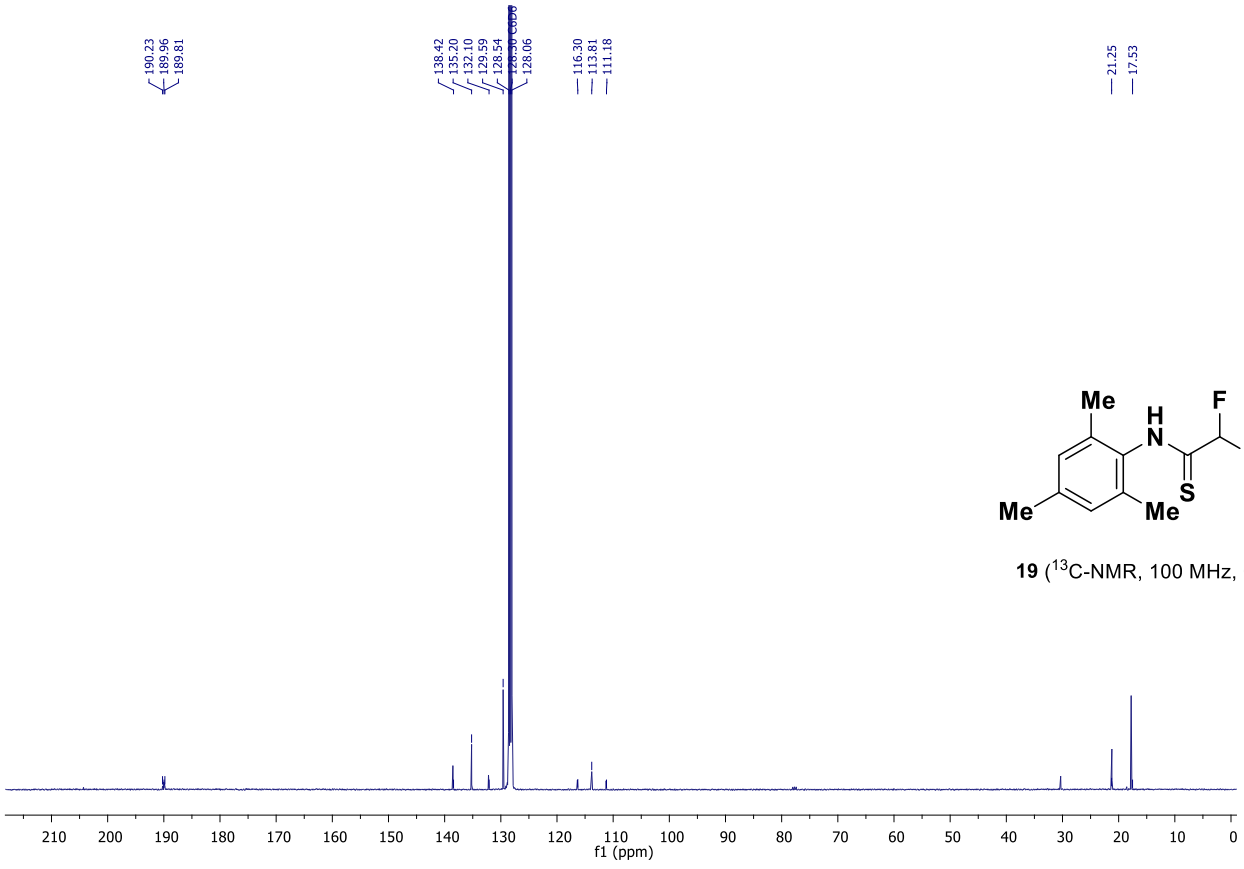
18 (^{1}H-NMR, 400 MHz, $CDCl_3$)



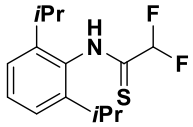
18 (^{13}C-NMR, 100 MHz, $CDCl_3$)



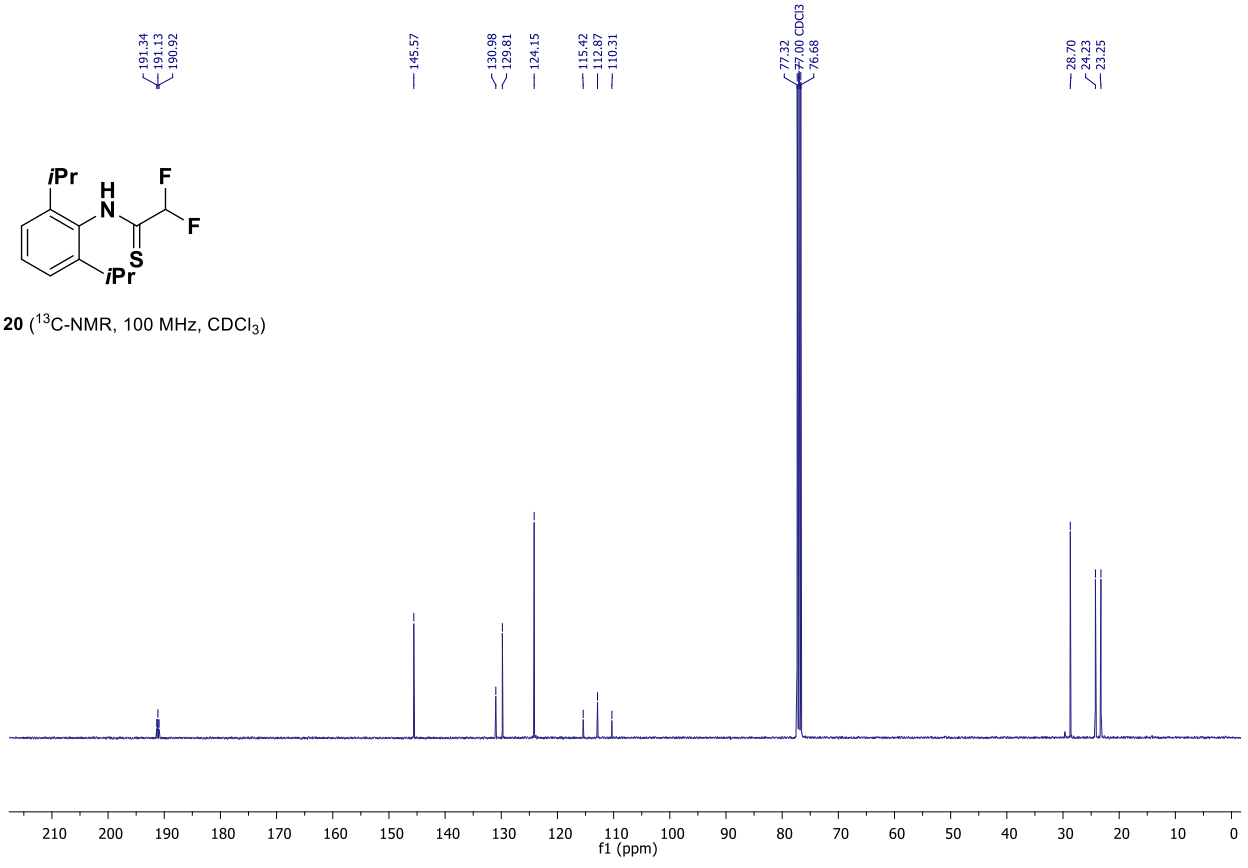
19 (^{1}H-NMR, 400 MHz, C_6D_6)



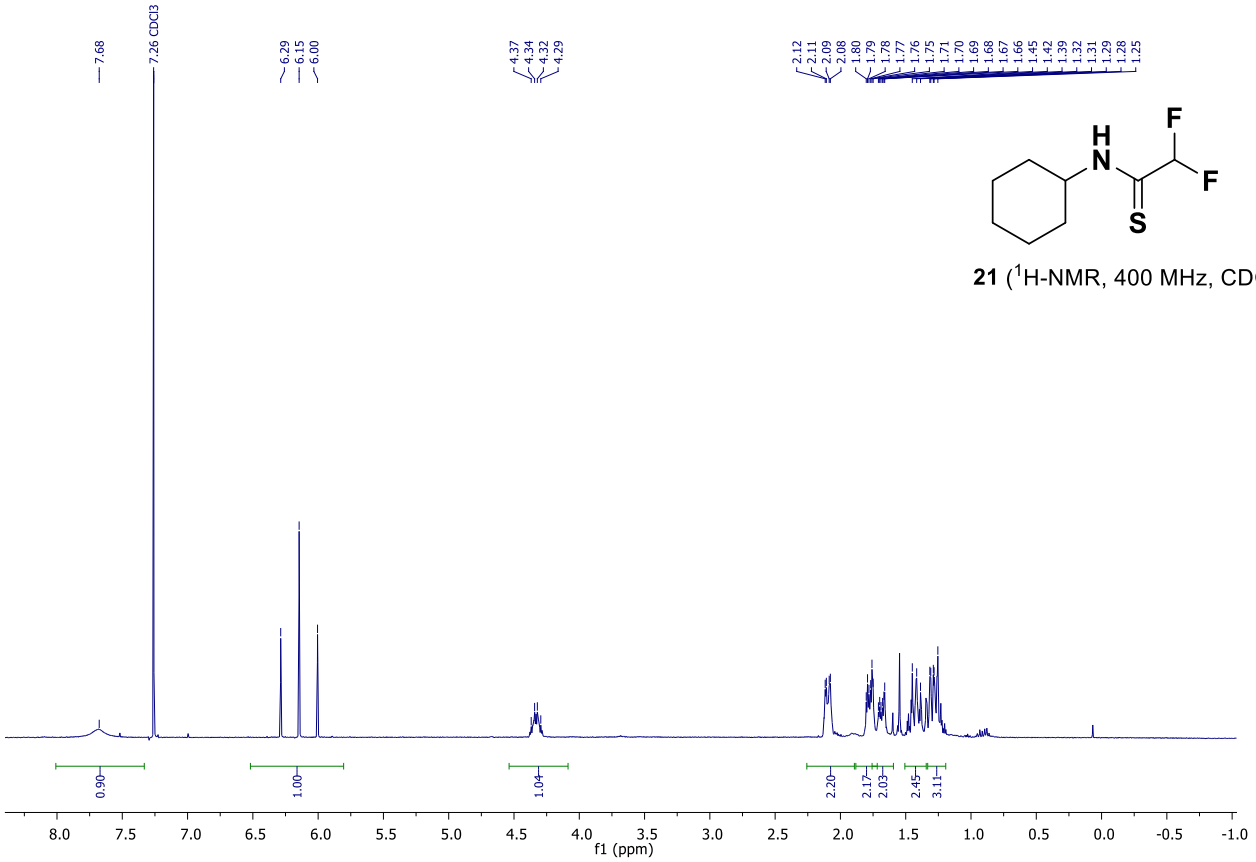
19 (^{13}C-NMR, 100 MHz, C_6D_6)



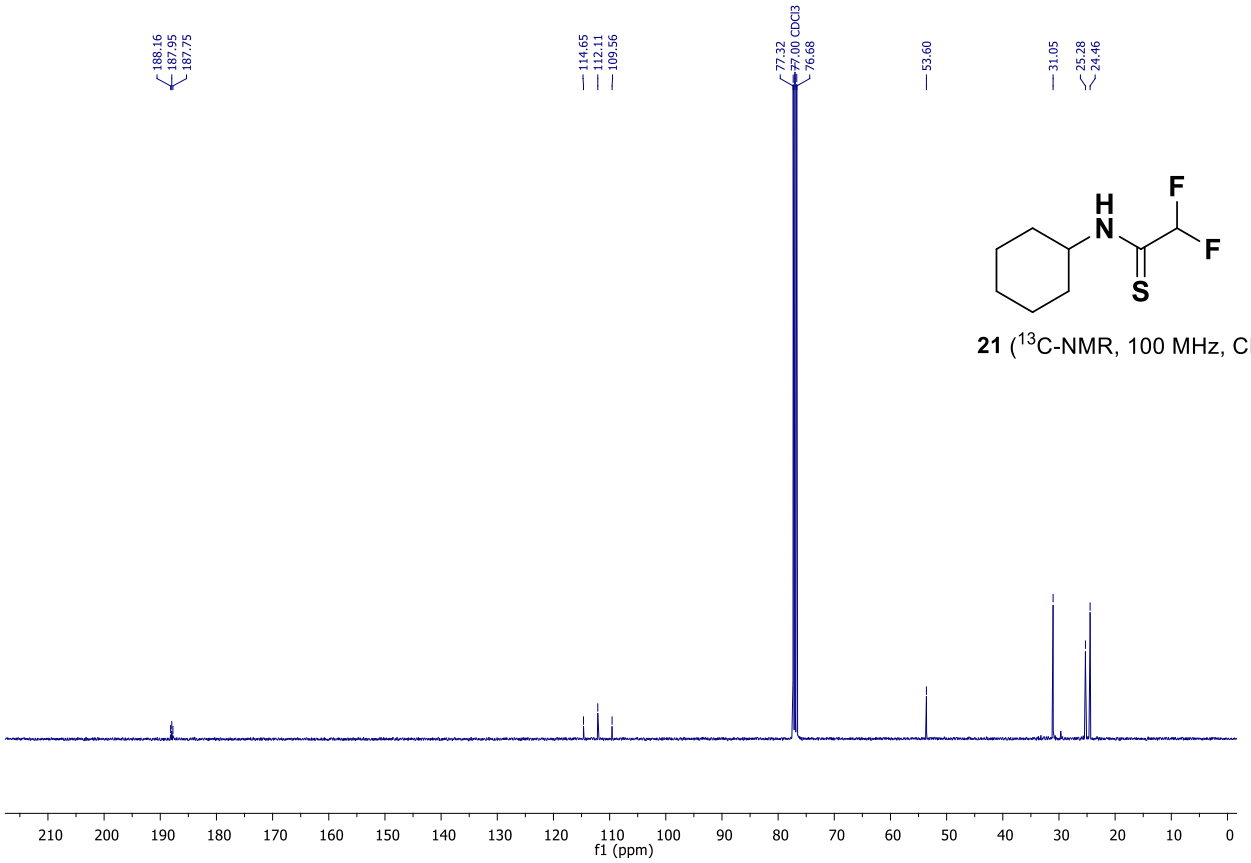
20 (^{1}H-NMR, 400 MHz, $CDCl_3$)



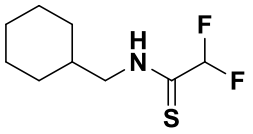
20 (^{13}C-NMR, 100 MHz, $CDCl_3$)



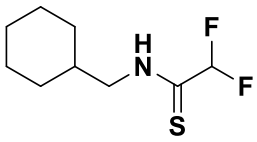
21 (^{1}H-NMR, 400 MHz, $CDCl_3$)



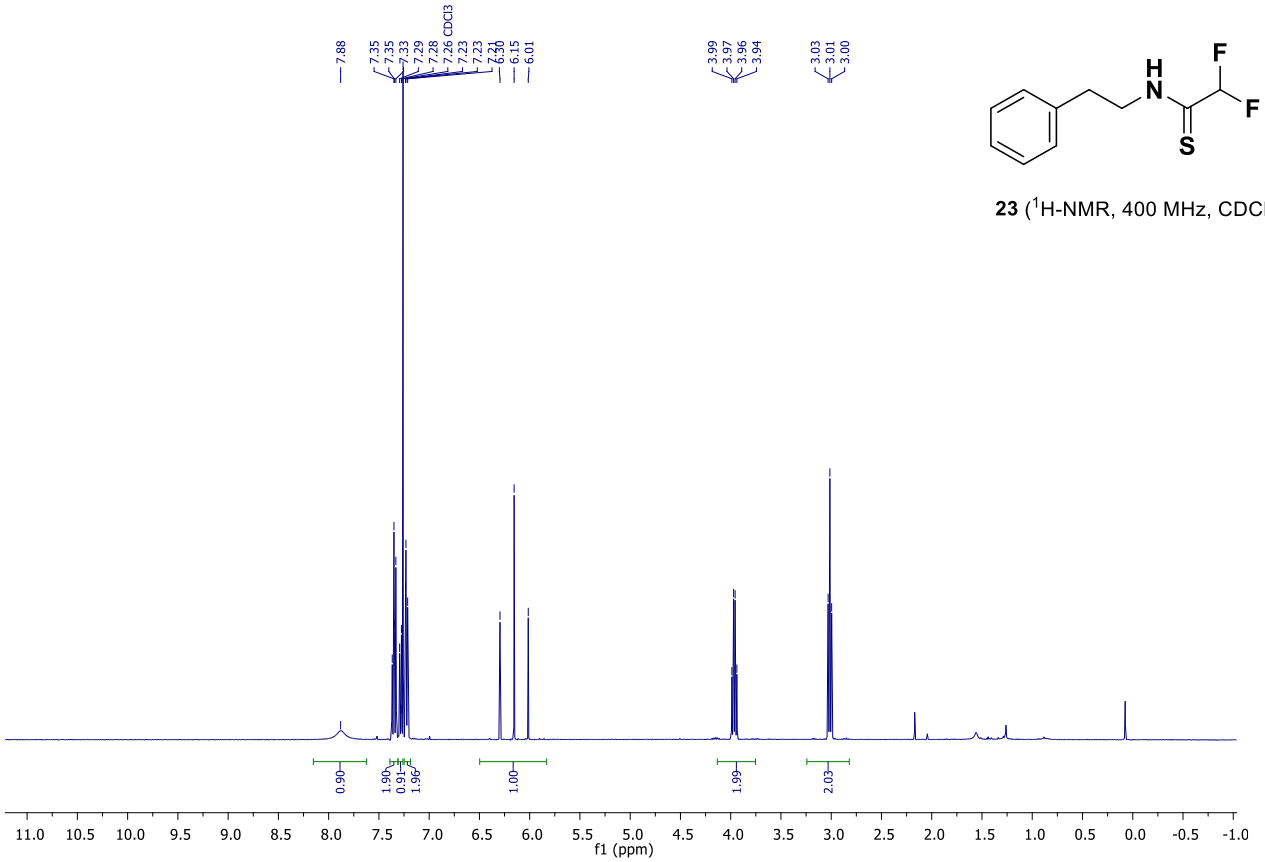
21 (^{13}C-NMR, 100 MHz, $CDCl_3$)



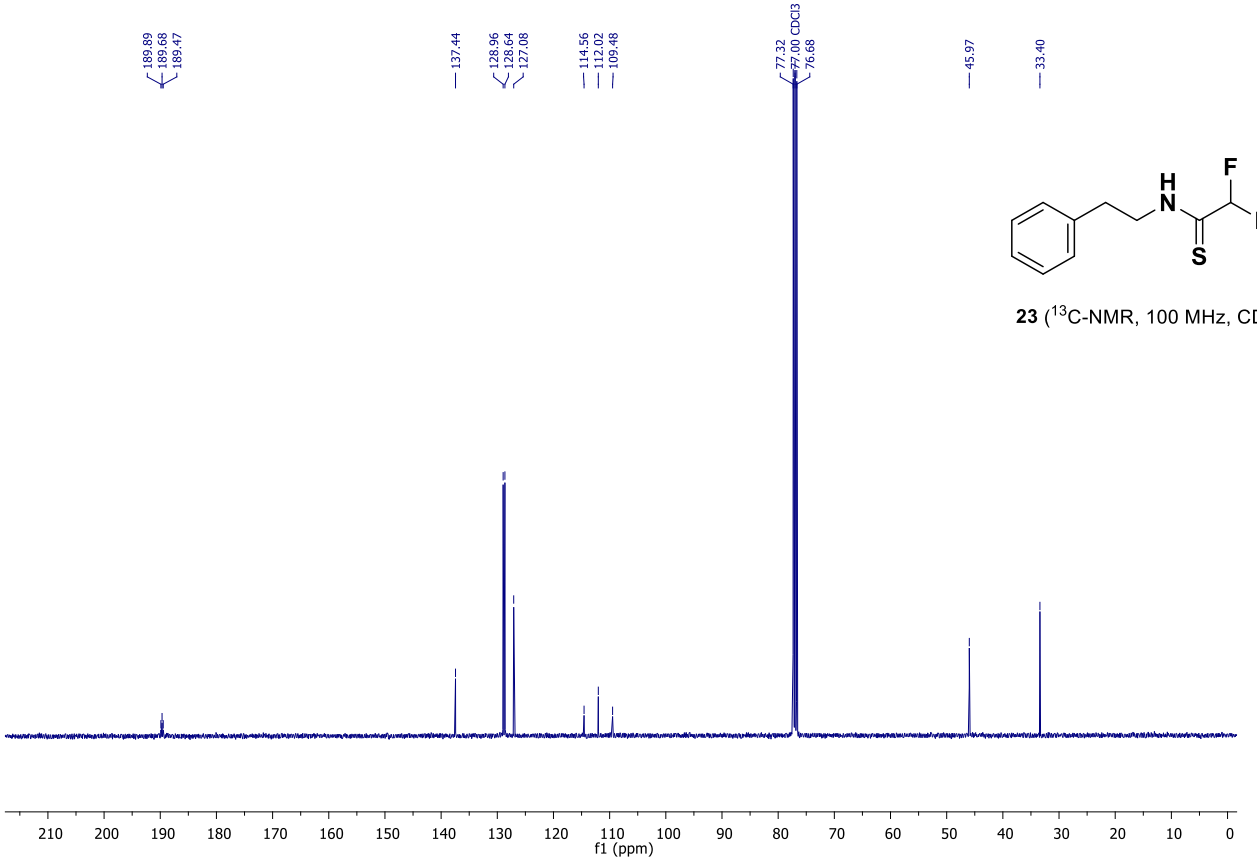
22 (^{1}H-NMR, 400 MHz, $CDCl_3$)



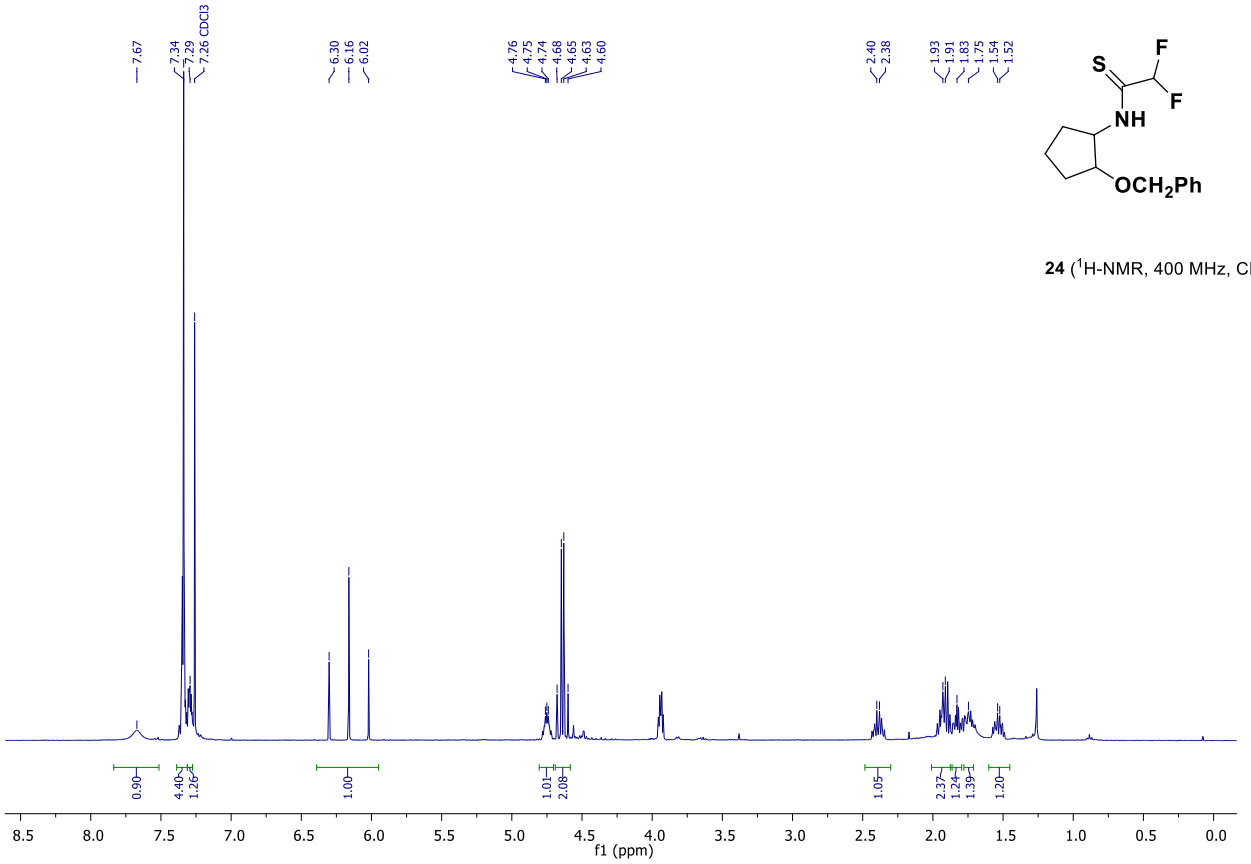
22 (^{13}C-NMR, 100 MHz, $CDCl_3$)



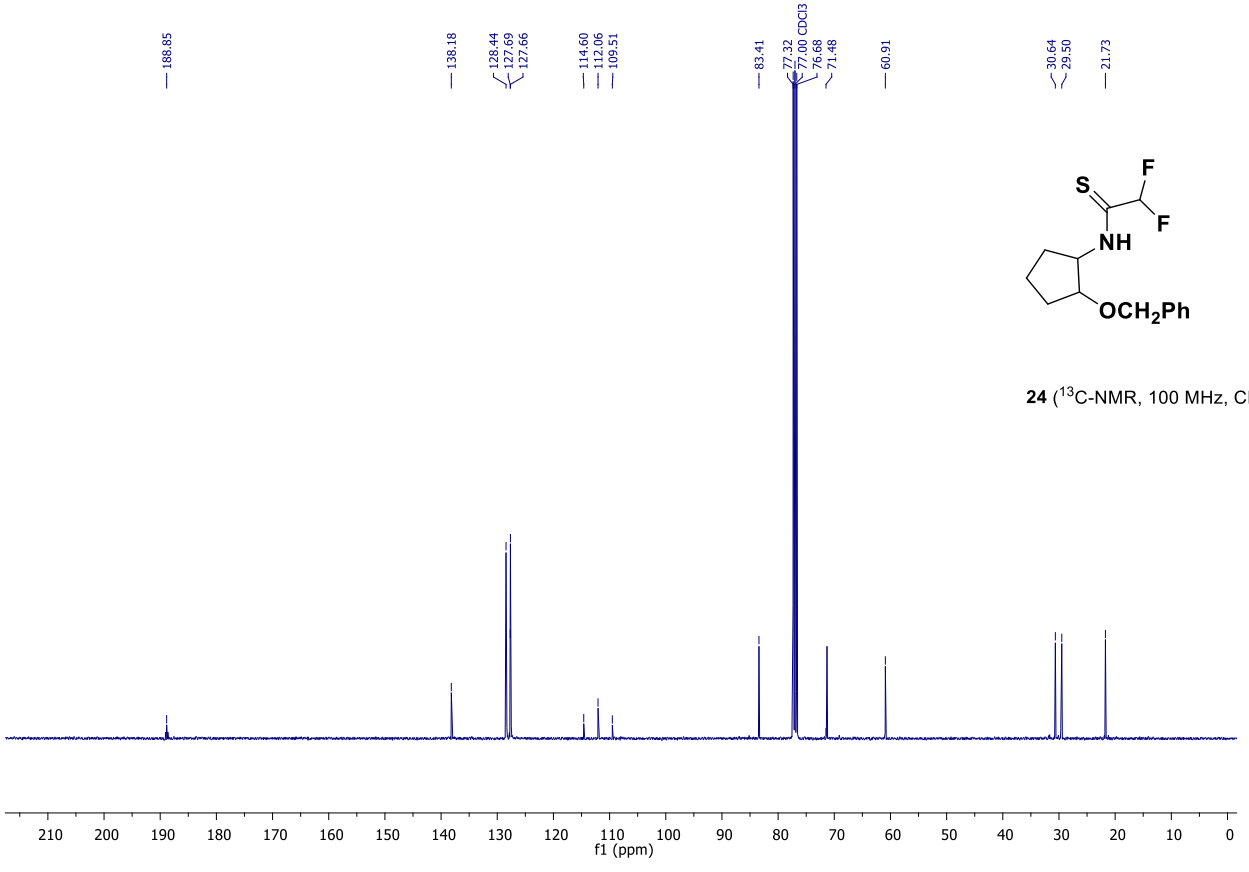
23 (^{1}H-NMR, 400 MHz, $CDCl_3$)



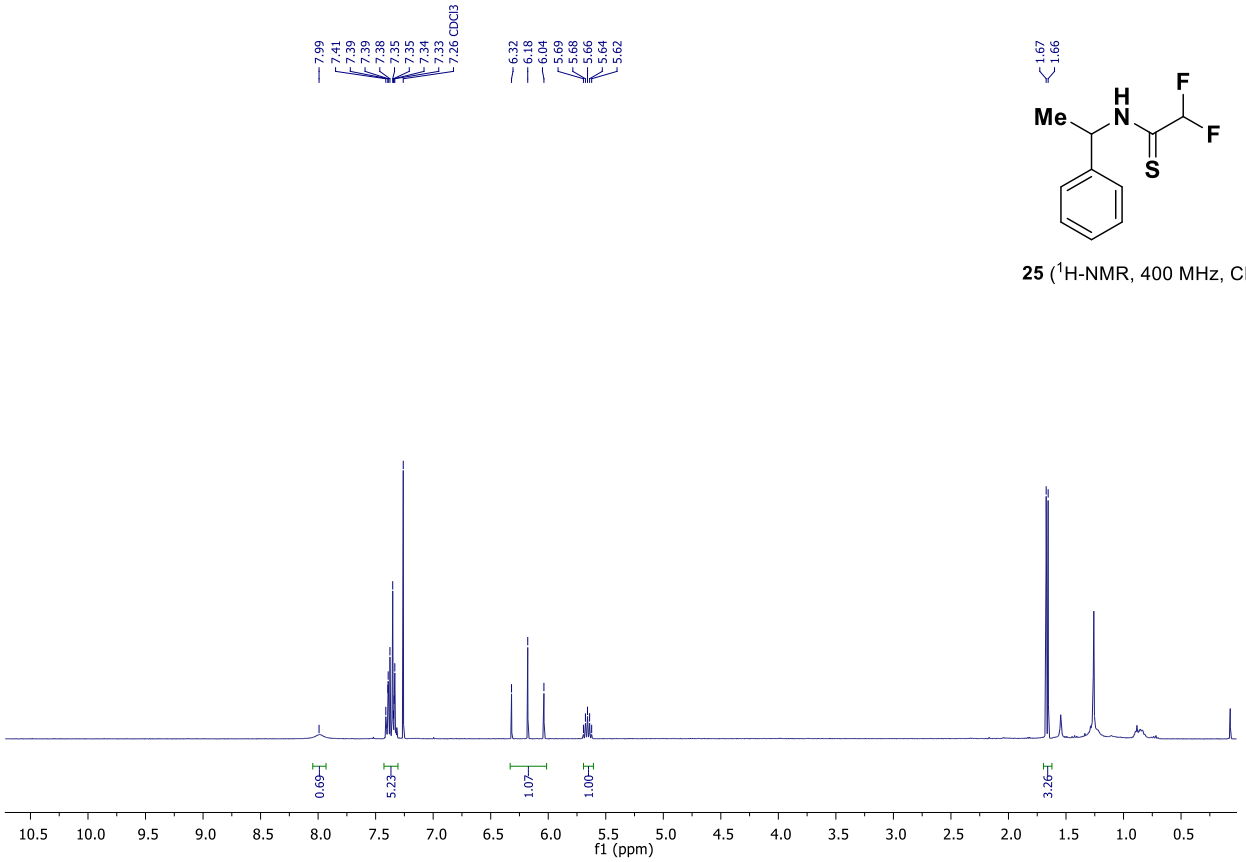
23 (^{13}C-NMR, 100 MHz, $CDCl_3$)



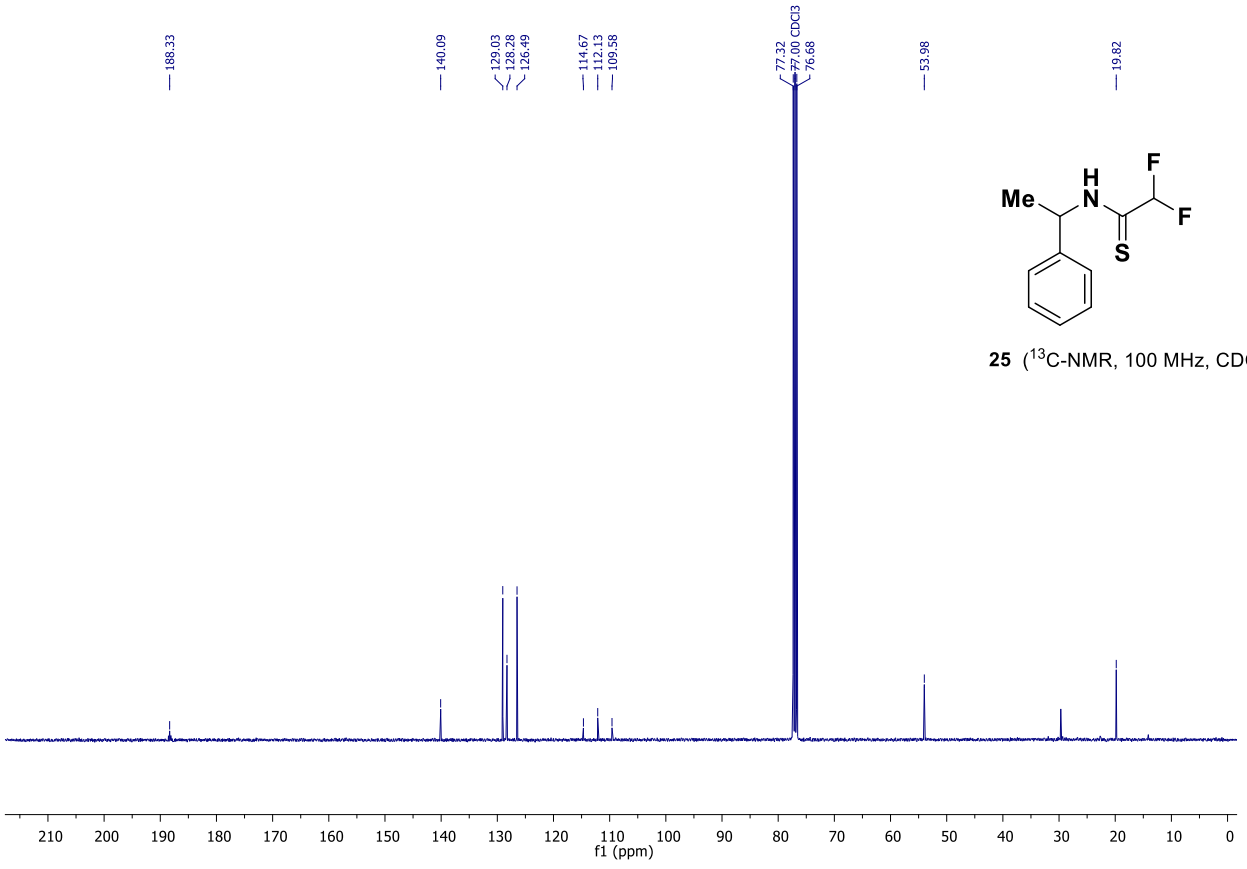
24 (^{1}H-NMR, 400 MHz, $CDCl_3$)



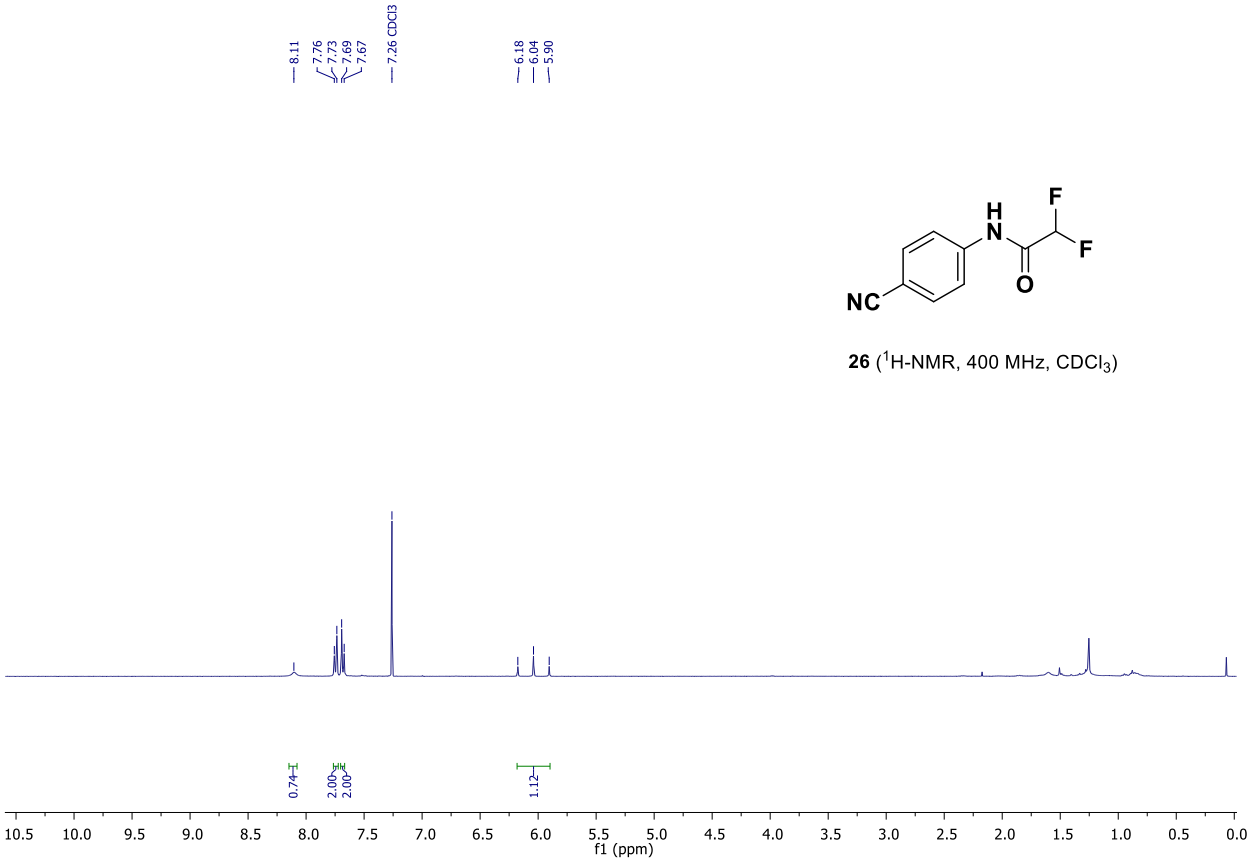
24 (^{13}C-NMR, 100 MHz, $CDCl_3$)



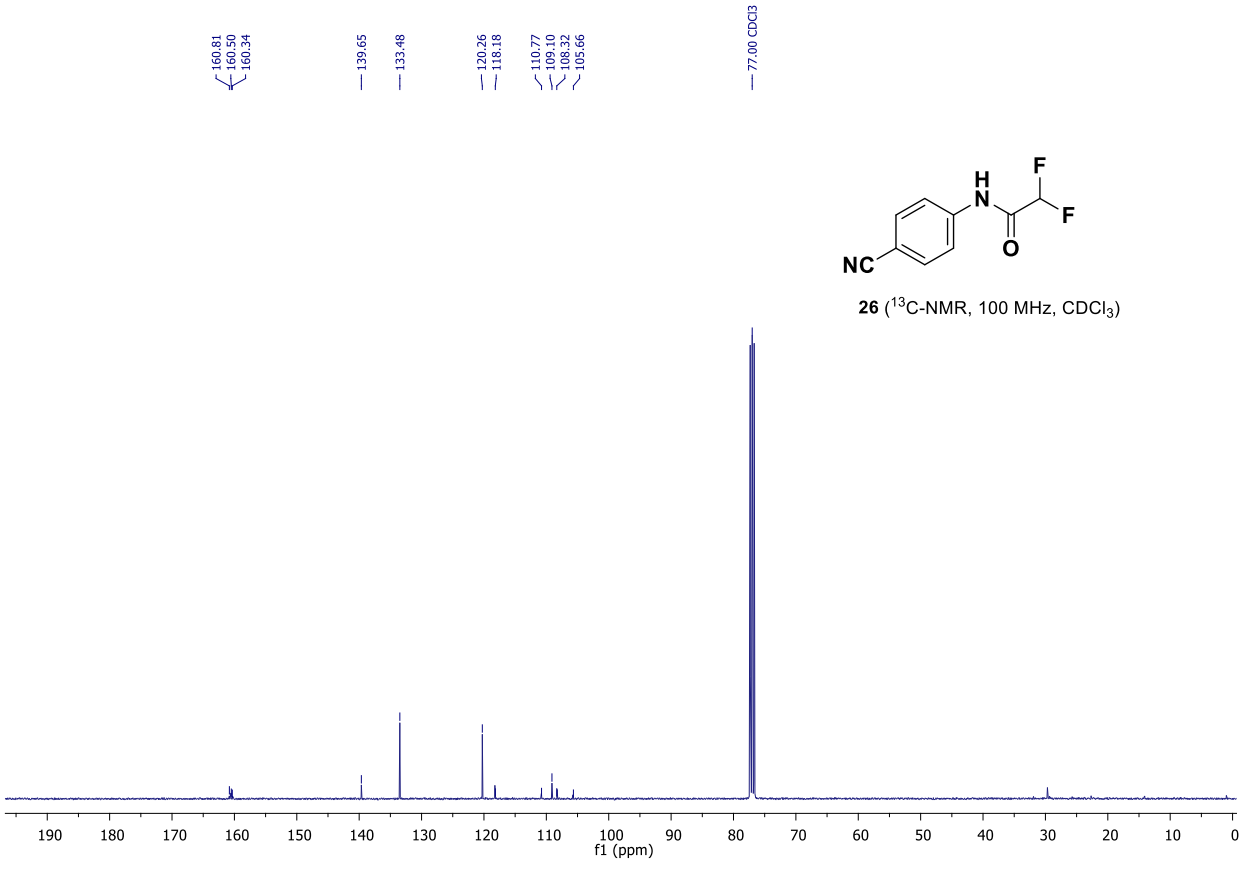
25 (^{1}H-NMR, 400 MHz, $CDCl_3$)



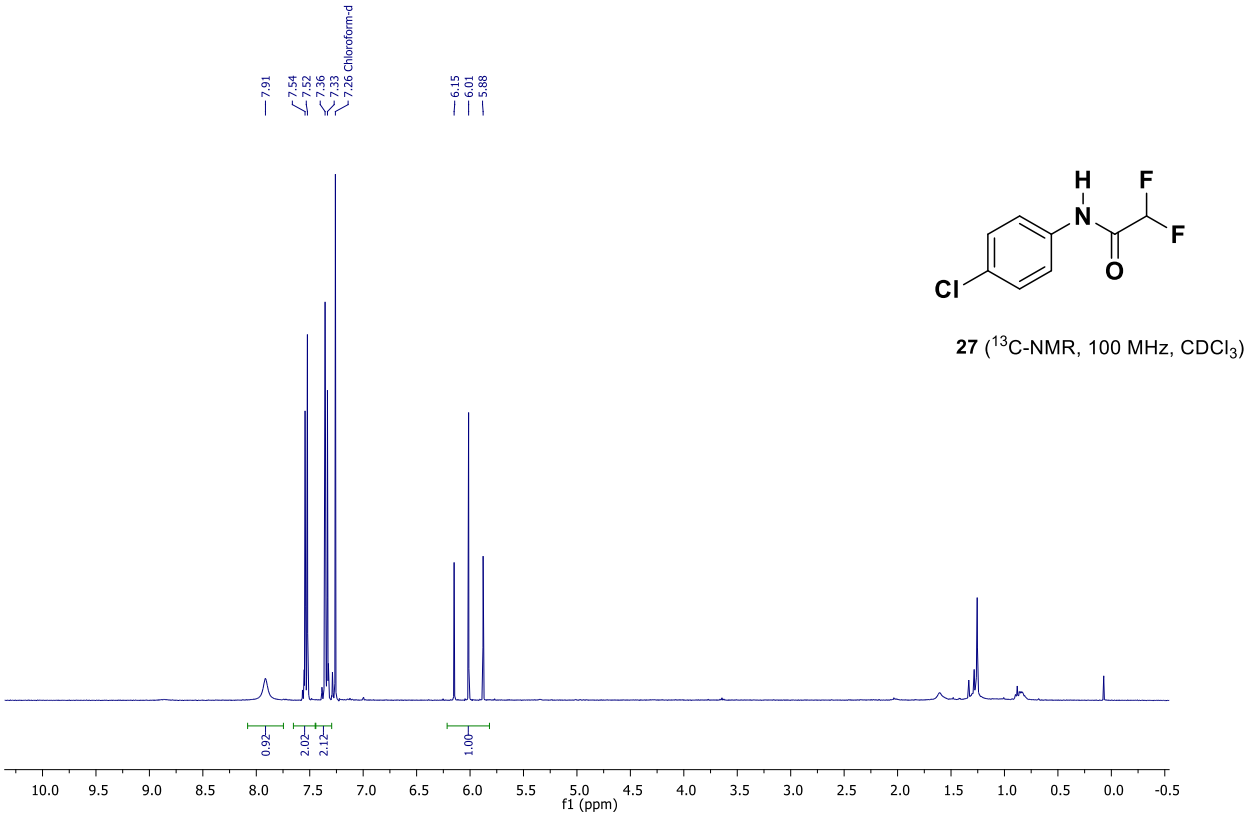
25 (^{13}C-NMR, 100 MHz, $CDCl_3$)



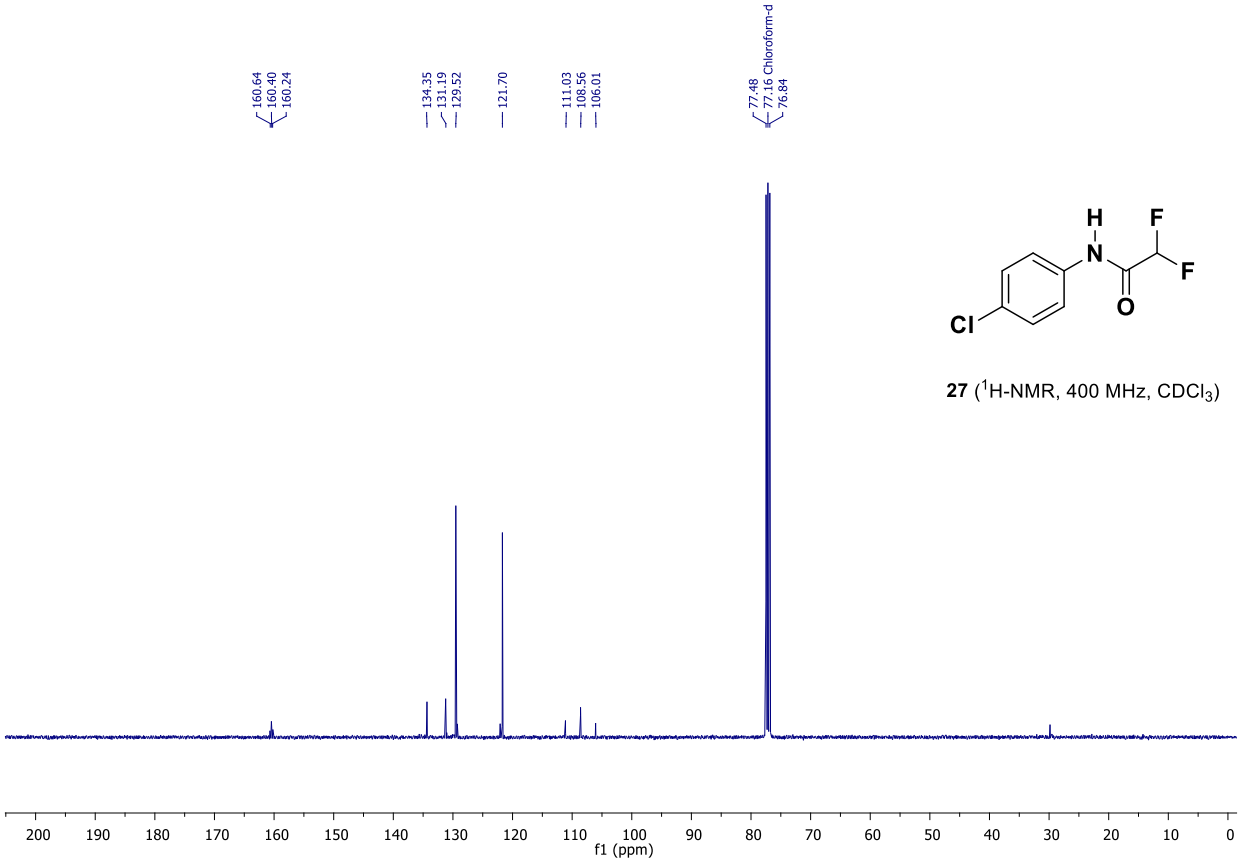
26 (^{1}H-NMR, 400 MHz, $CDCl_3$)



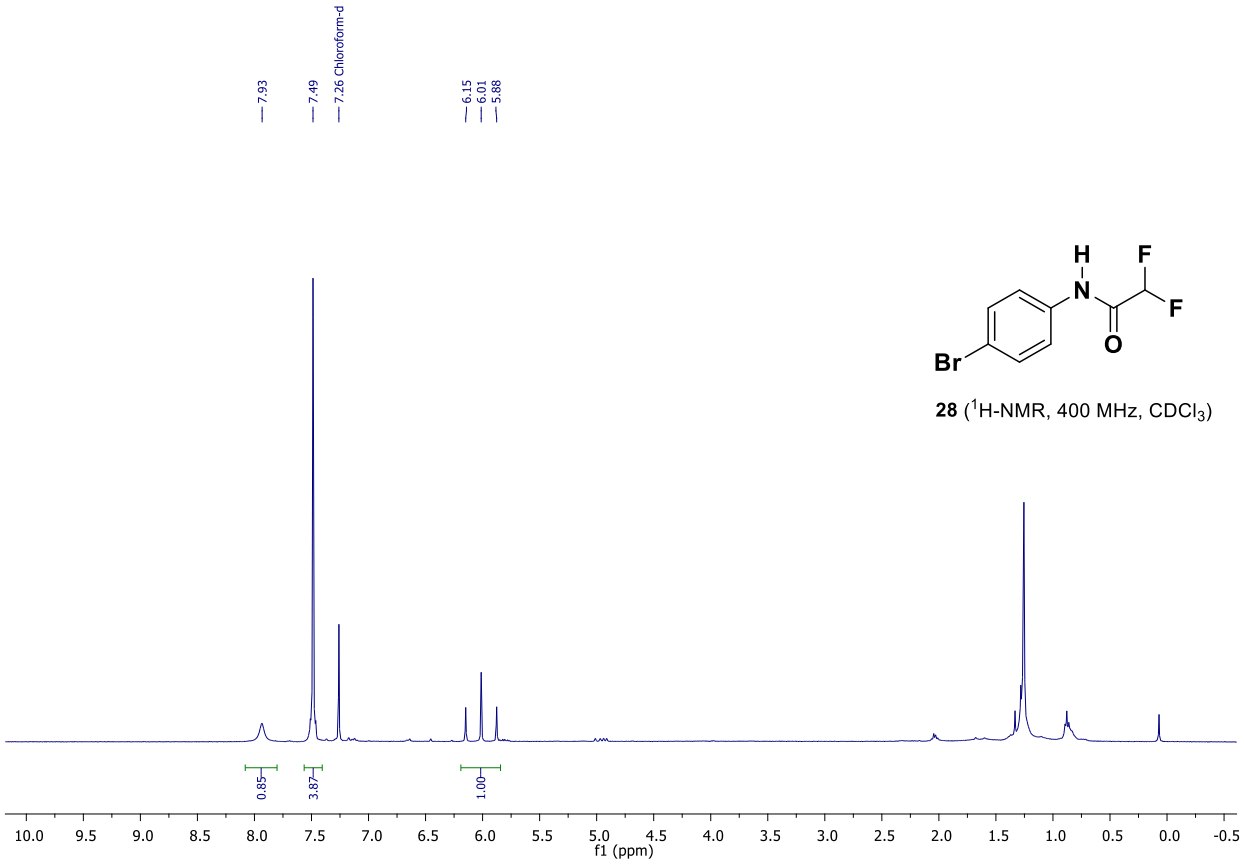
26 (^{13}C-NMR, 100 MHz, $CDCl_3$)



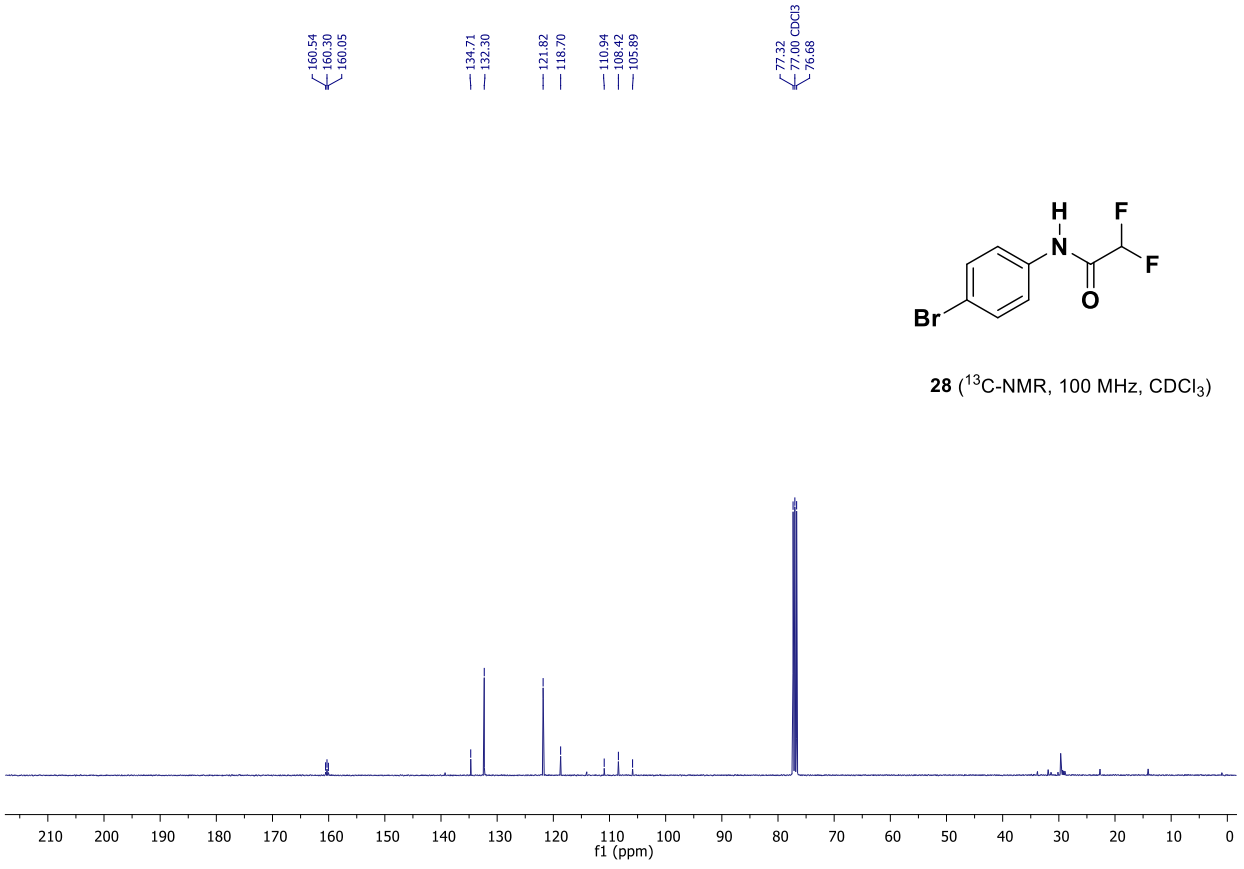
27 (^{13}C-NMR, 100 MHz, $CDCl_3$)



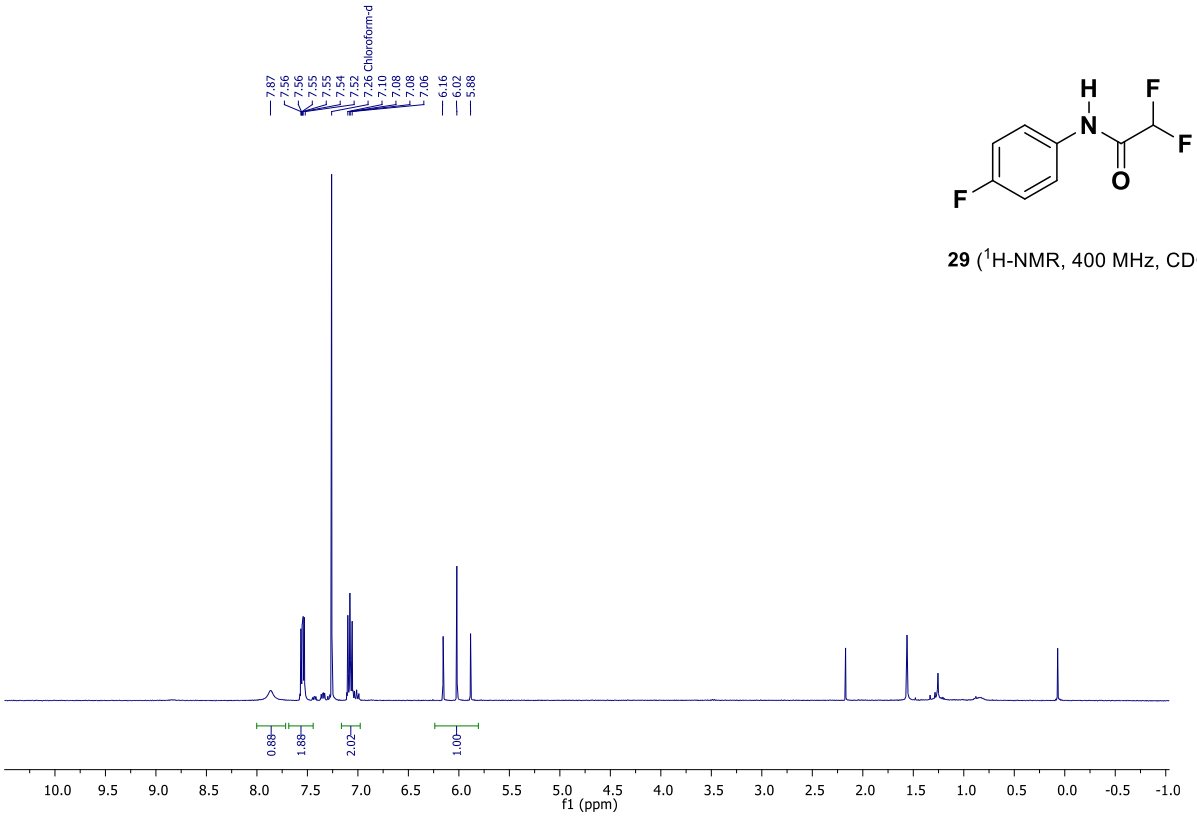
27 (^{1}H-NMR, 400 MHz, $CDCl_3$)



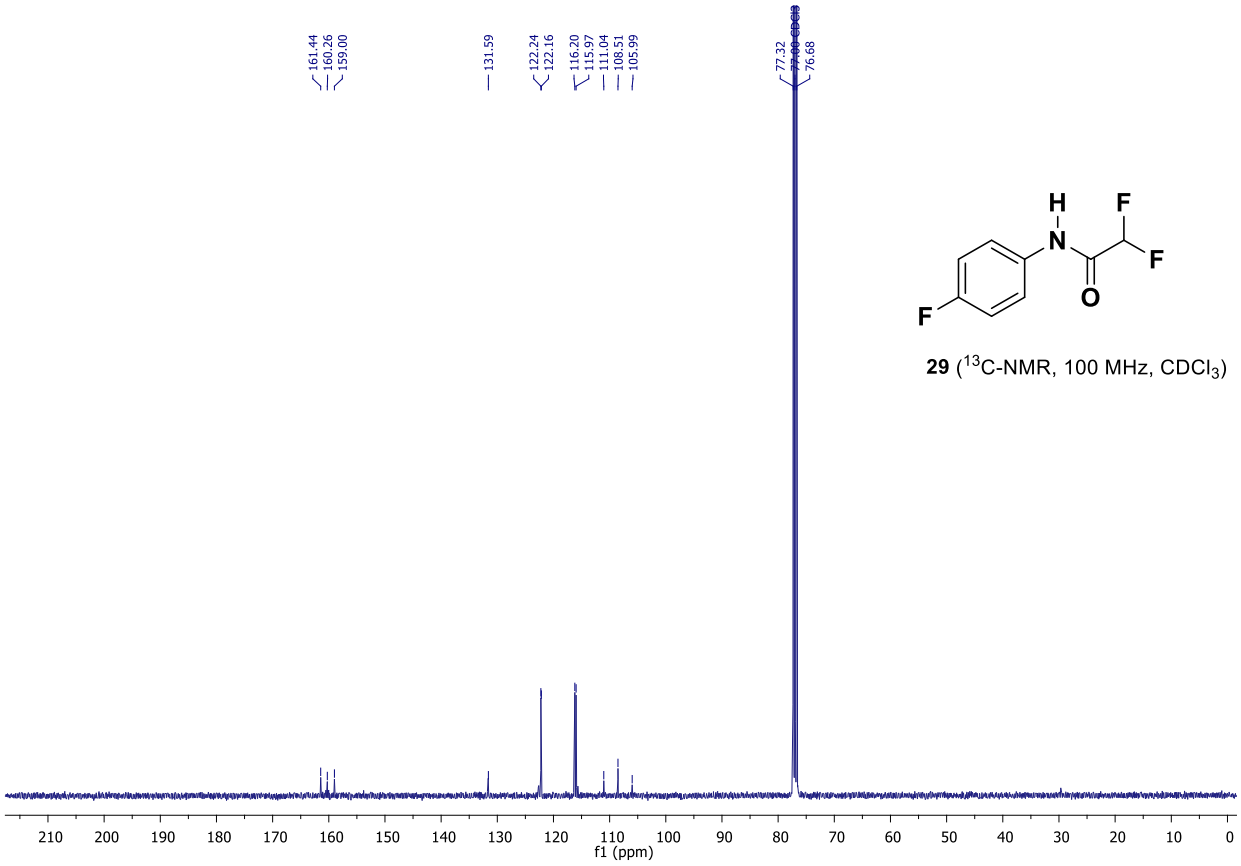
28 (^{1}H-NMR, 400 MHz, $CDCl_3$)



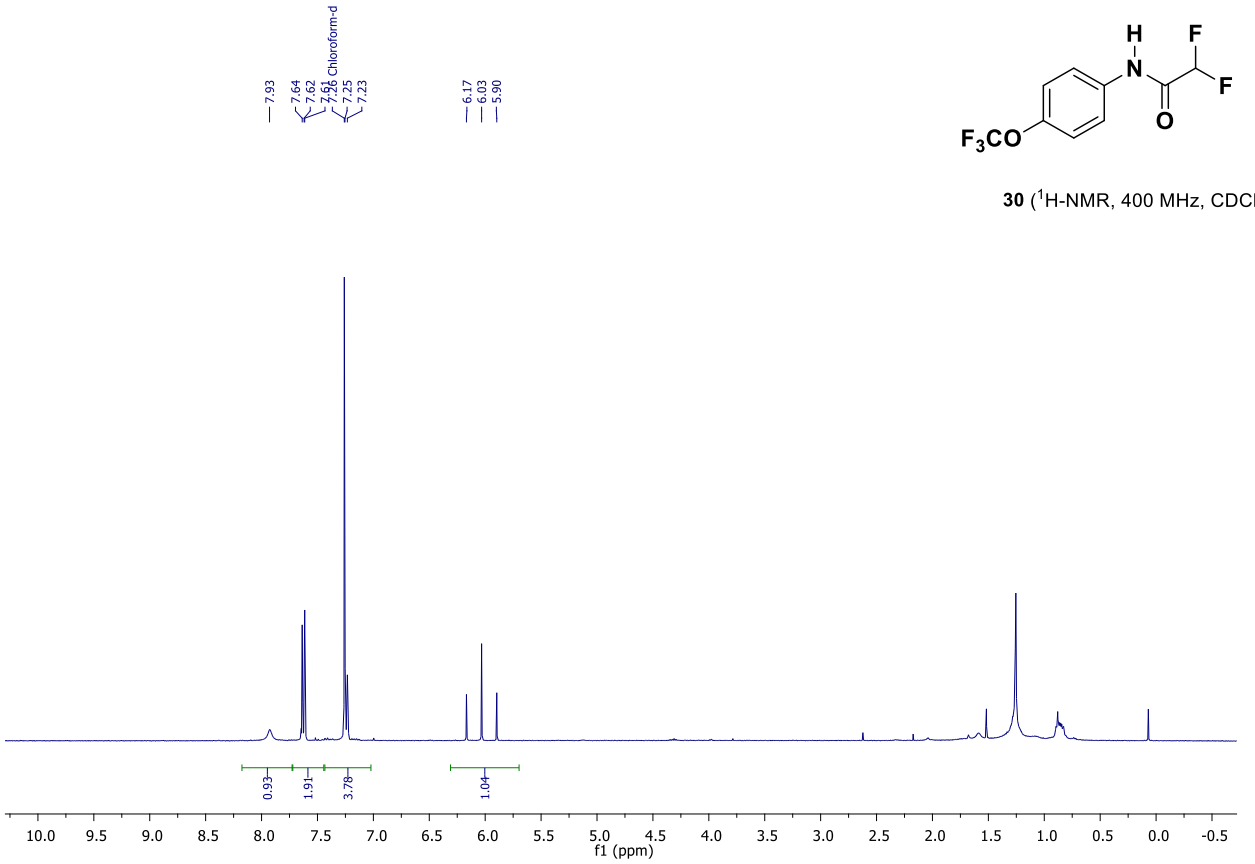
28 (^{13}C-NMR, 100 MHz, $CDCl_3$)



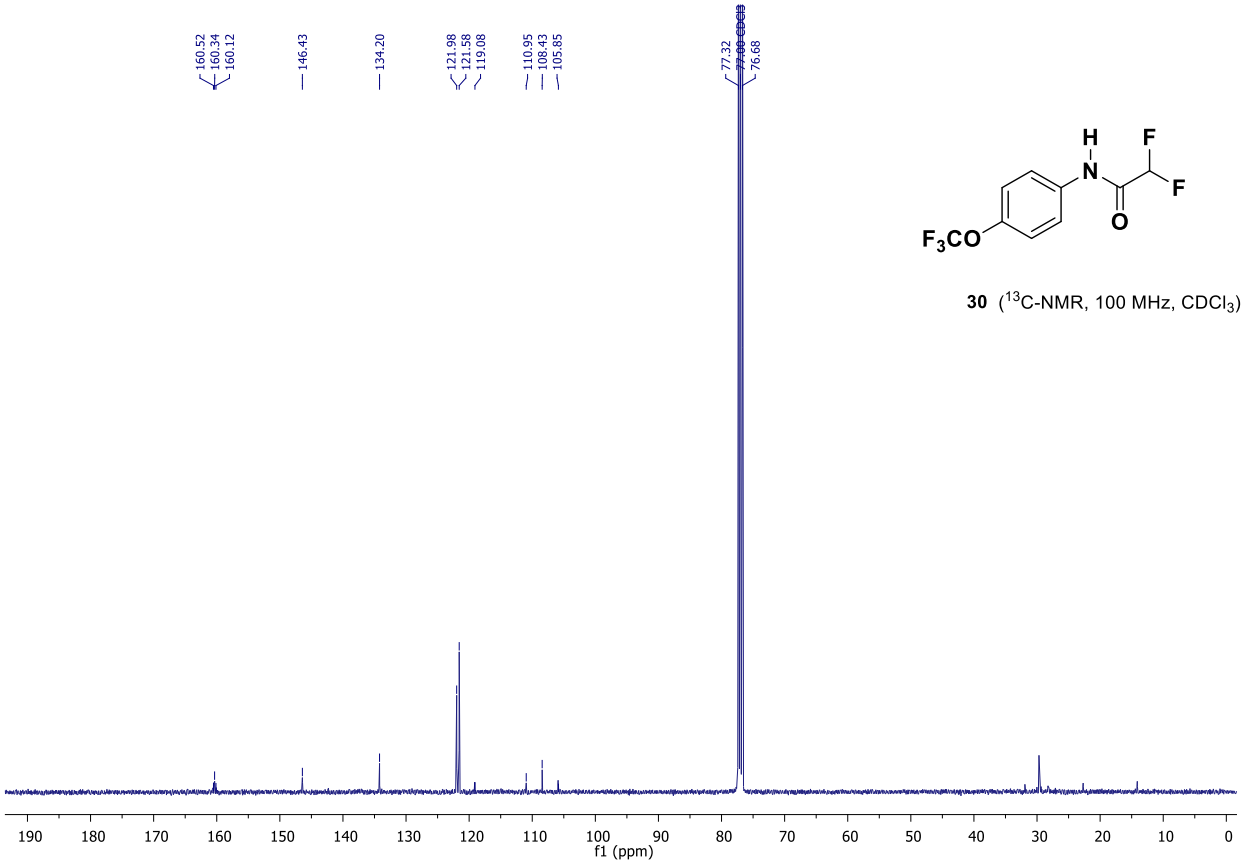
29 (^{1}H-NMR, 400 MHz, $CDCl_3$)



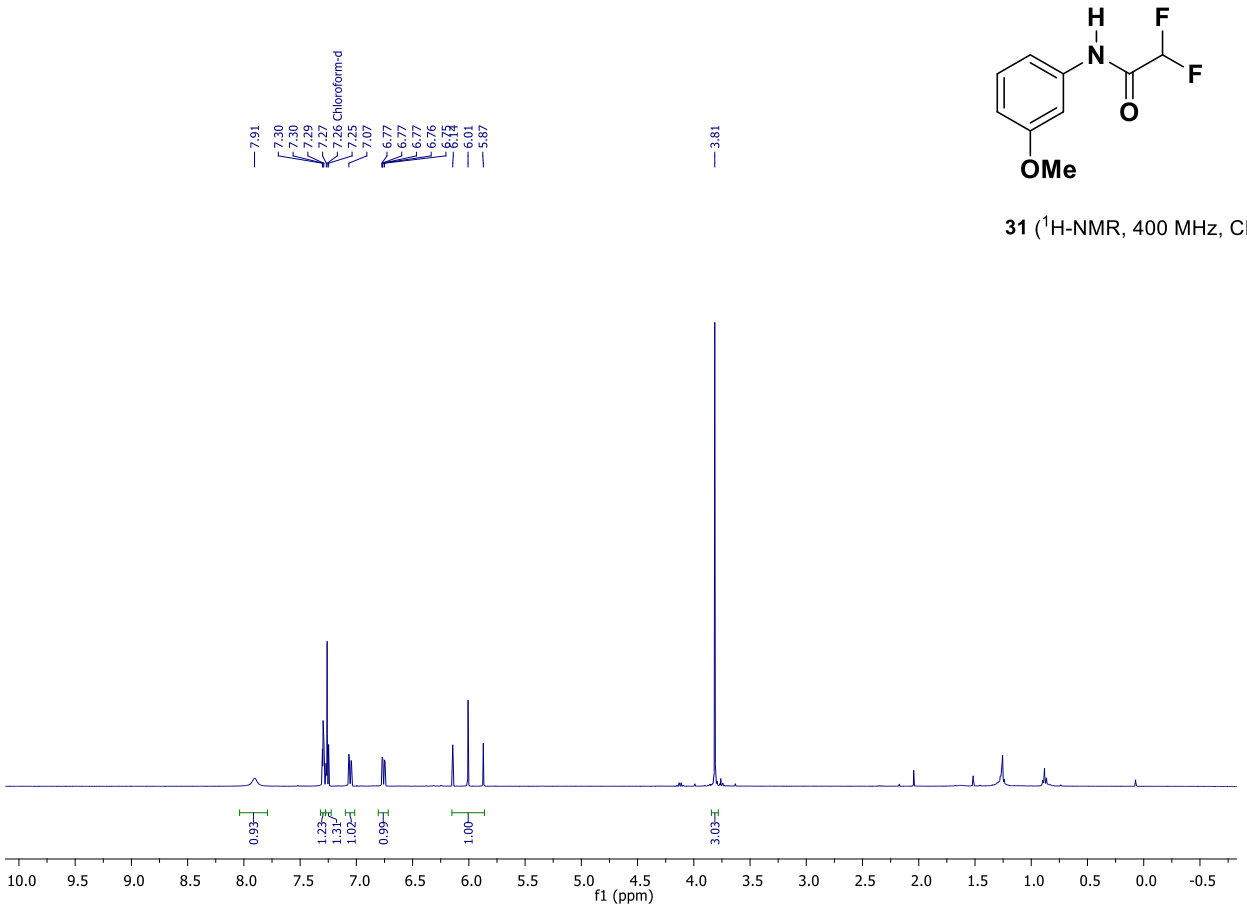
29 (^{13}C-NMR, 100 MHz, $CDCl_3$)



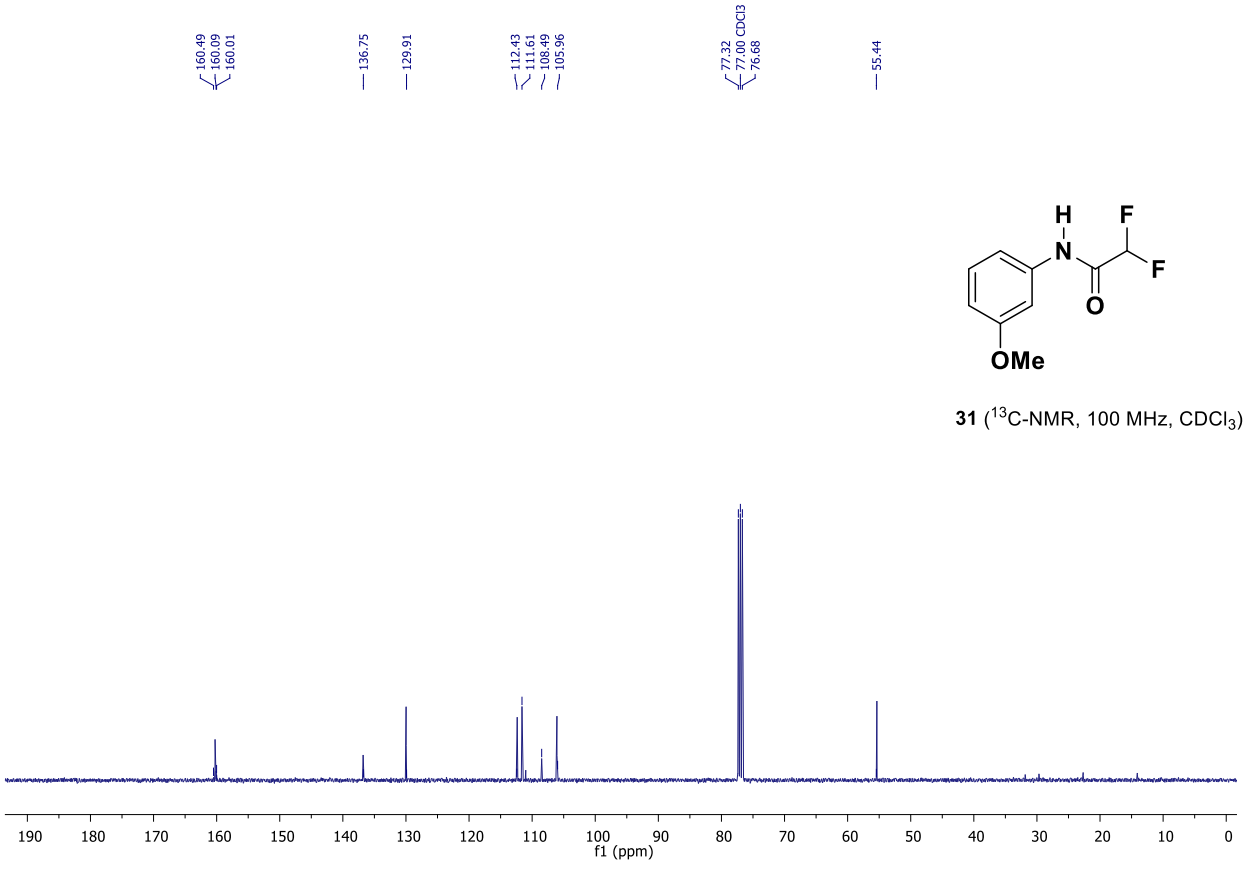
30 (^{1}H-NMR, 400 MHz, $CDCl_3$)



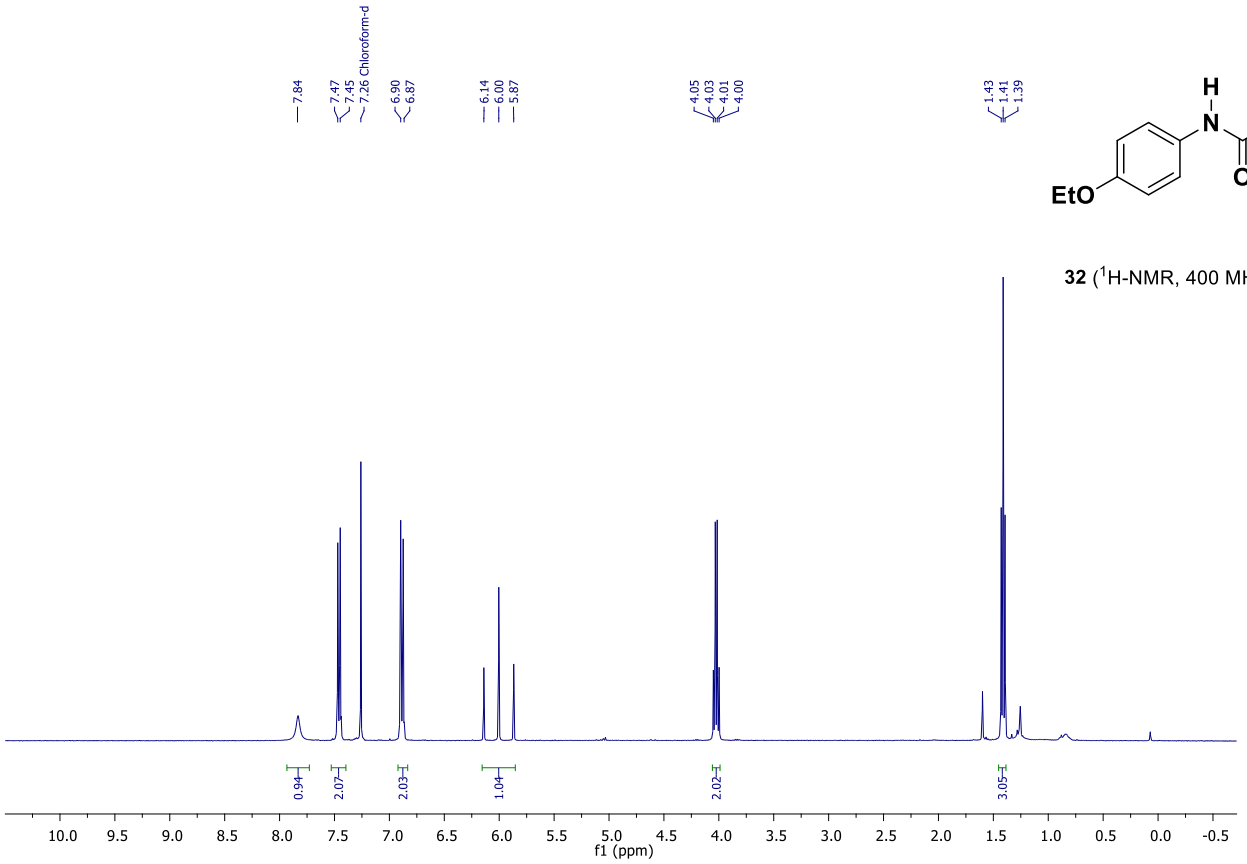
30 (^{13}C-NMR, 100 MHz, $CDCl_3$)



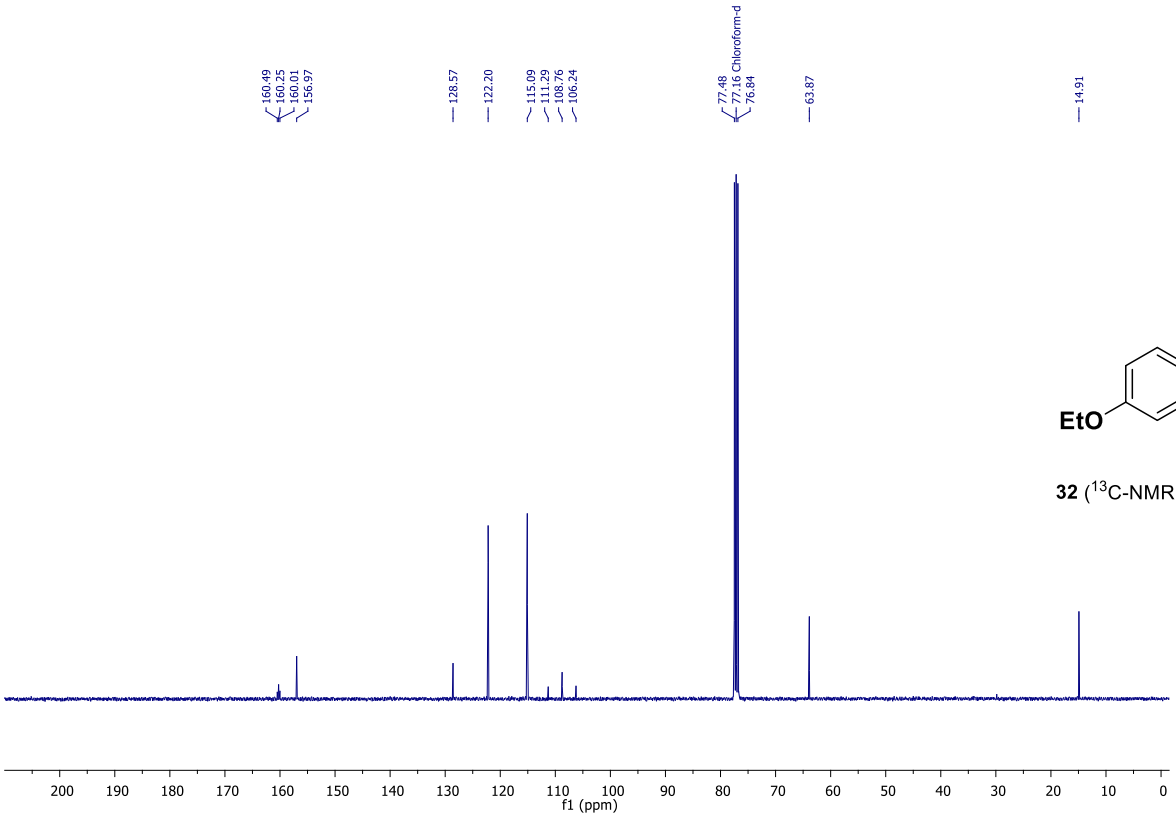
31 (^{1}H-NMR, 400 MHz, $CDCl_3$)

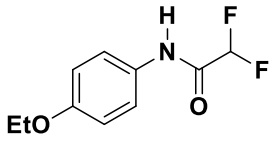


31 (^{13}C-NMR, 100 MHz, $CDCl_3$)

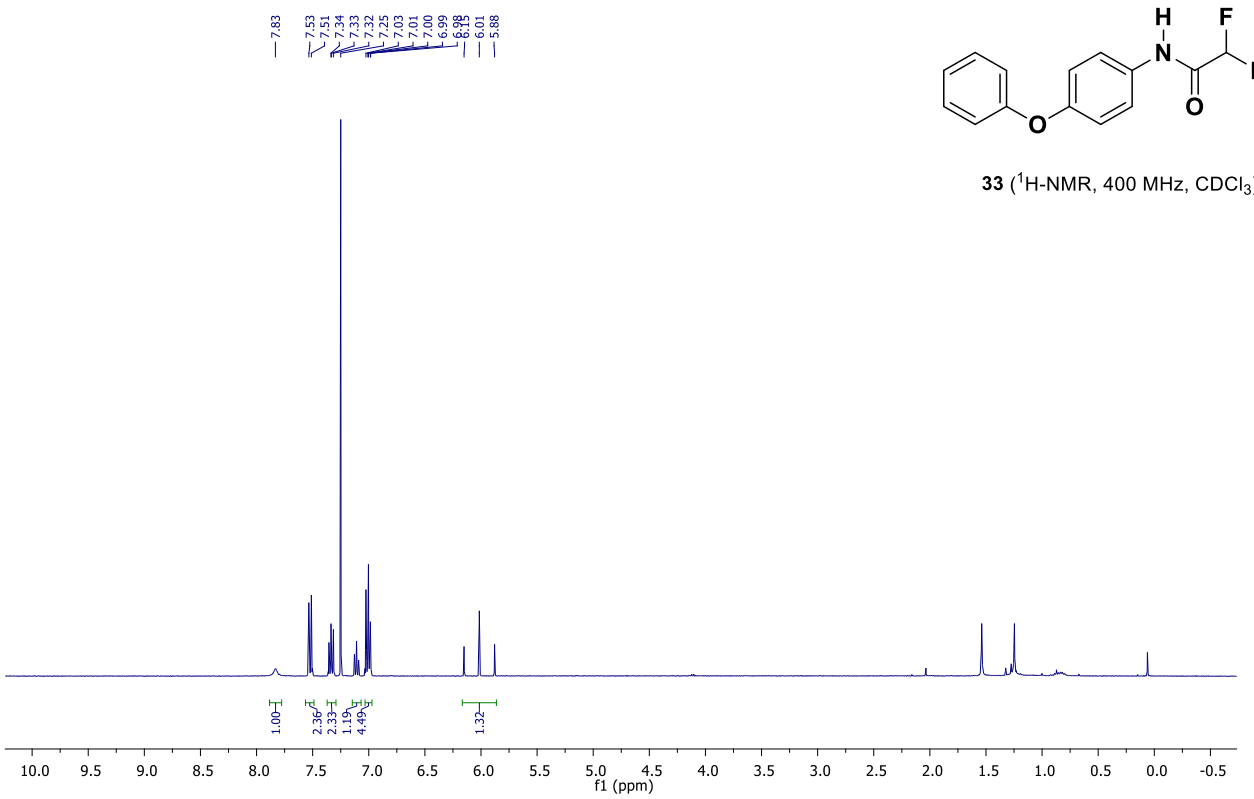


32 (^{1}H-NMR, 400 MHz, $CDCl_3$)

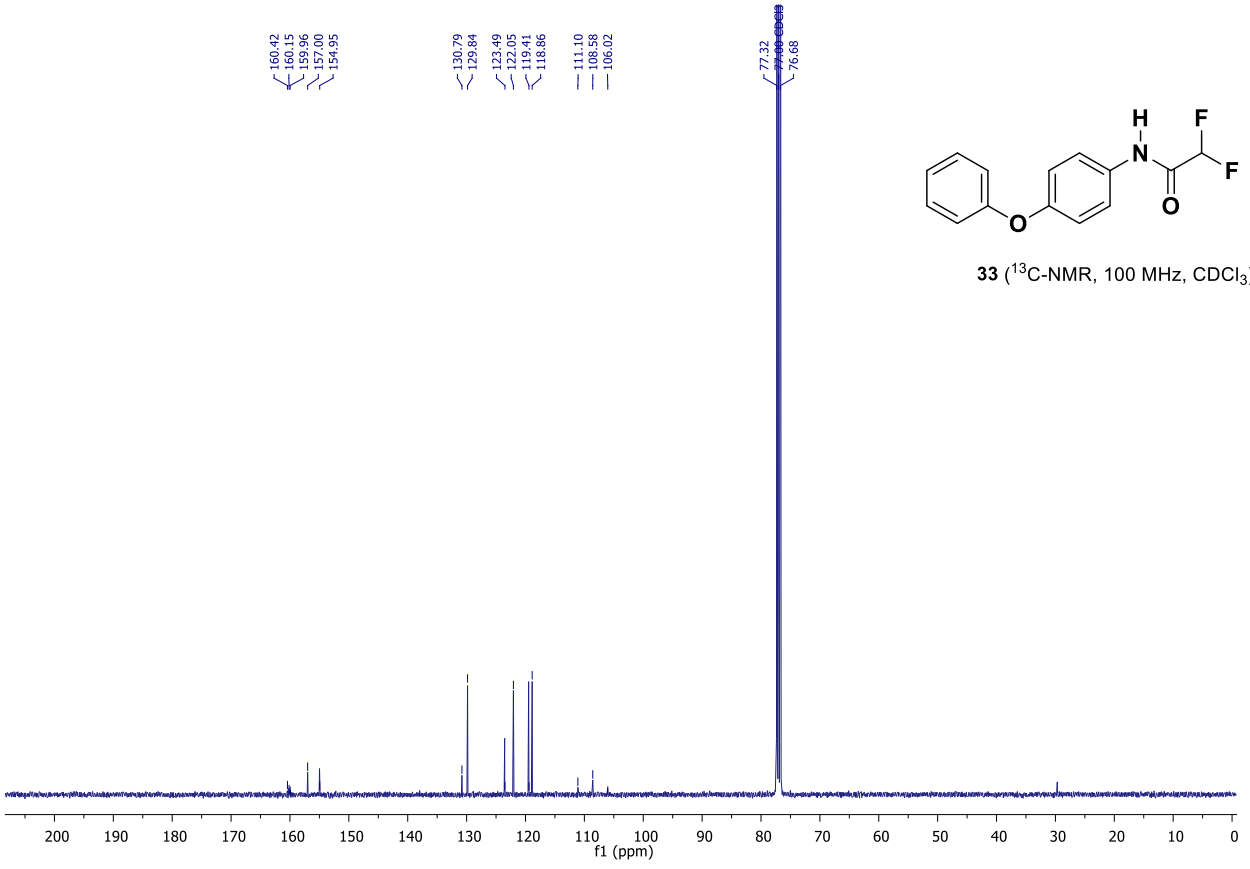




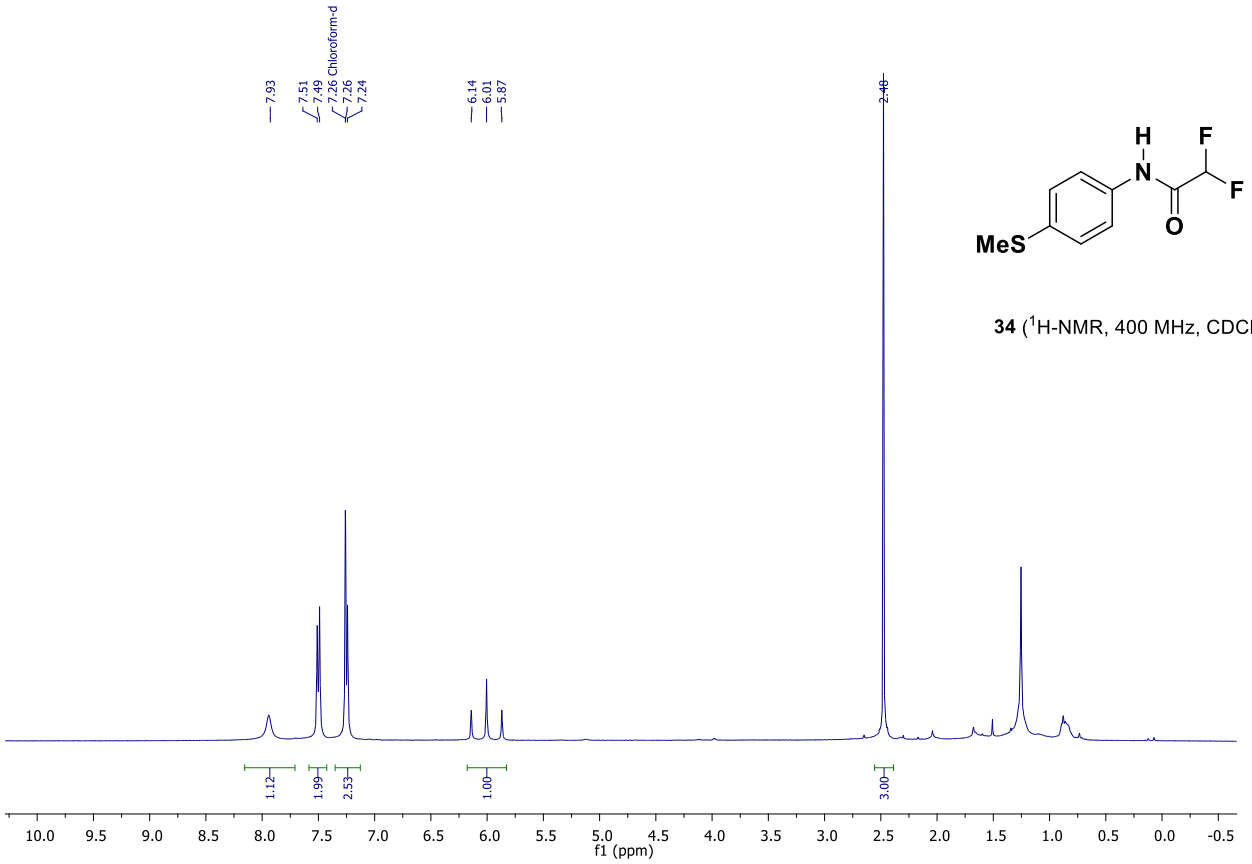
32 (^{13}C-NMR, 100 MHz, $CDCl_3$)



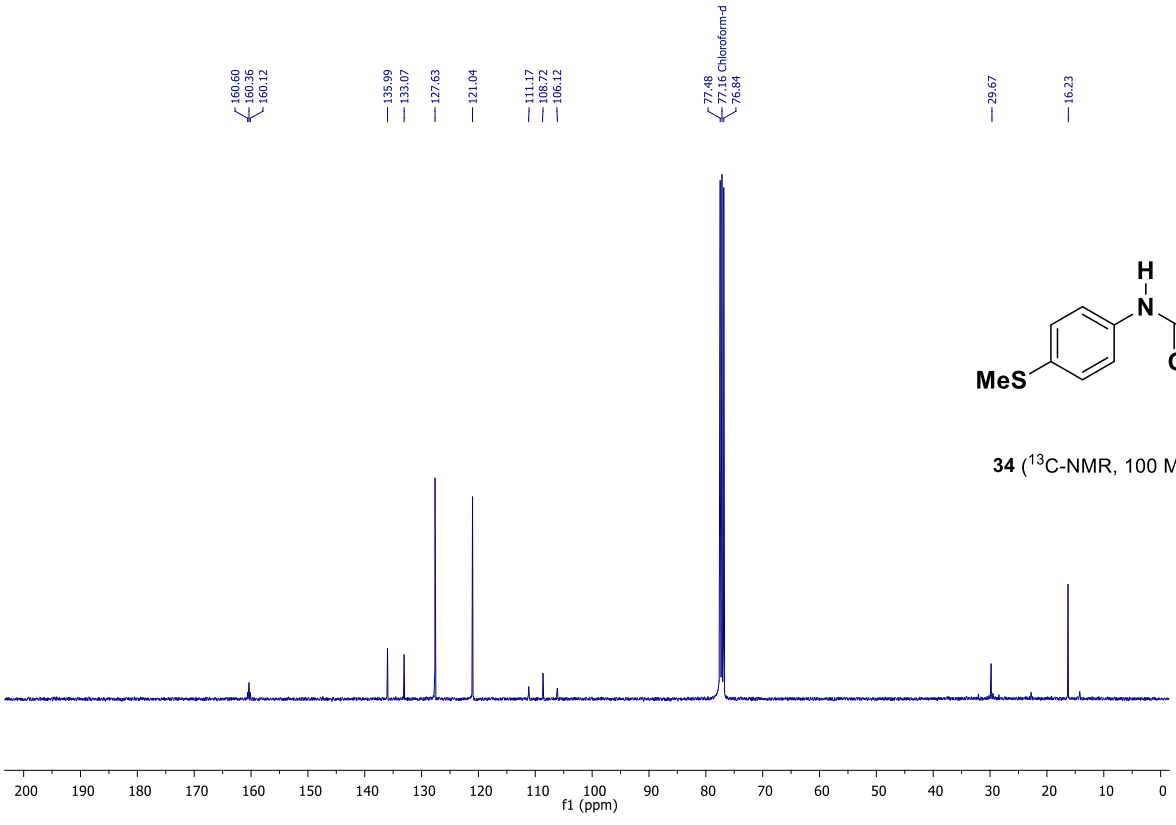
33 (^{1}H-NMR, 400 MHz, $CDCl_3$)



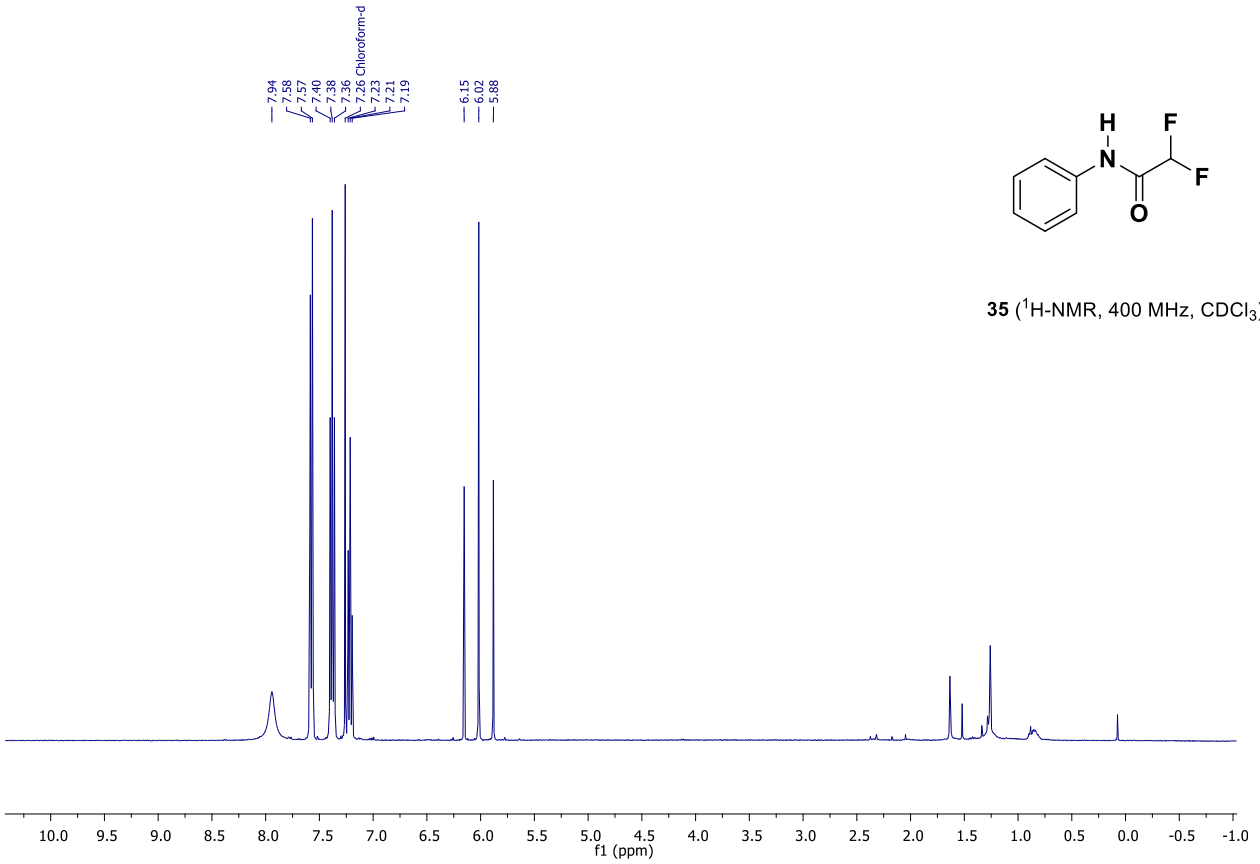
33 (^{13}C-NMR, 100 MHz, $CDCl_3$)



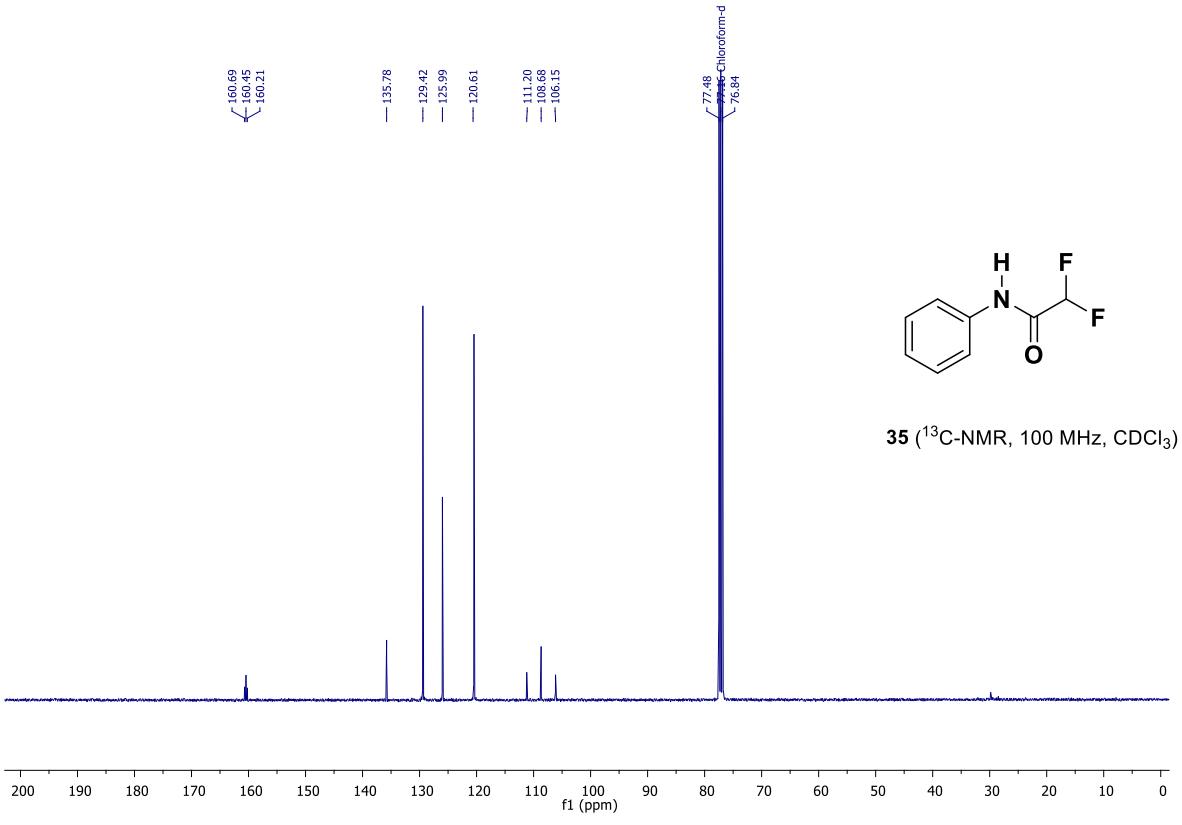
34 (^{1}H-NMR, 400 MHz, $CDCl_3$)



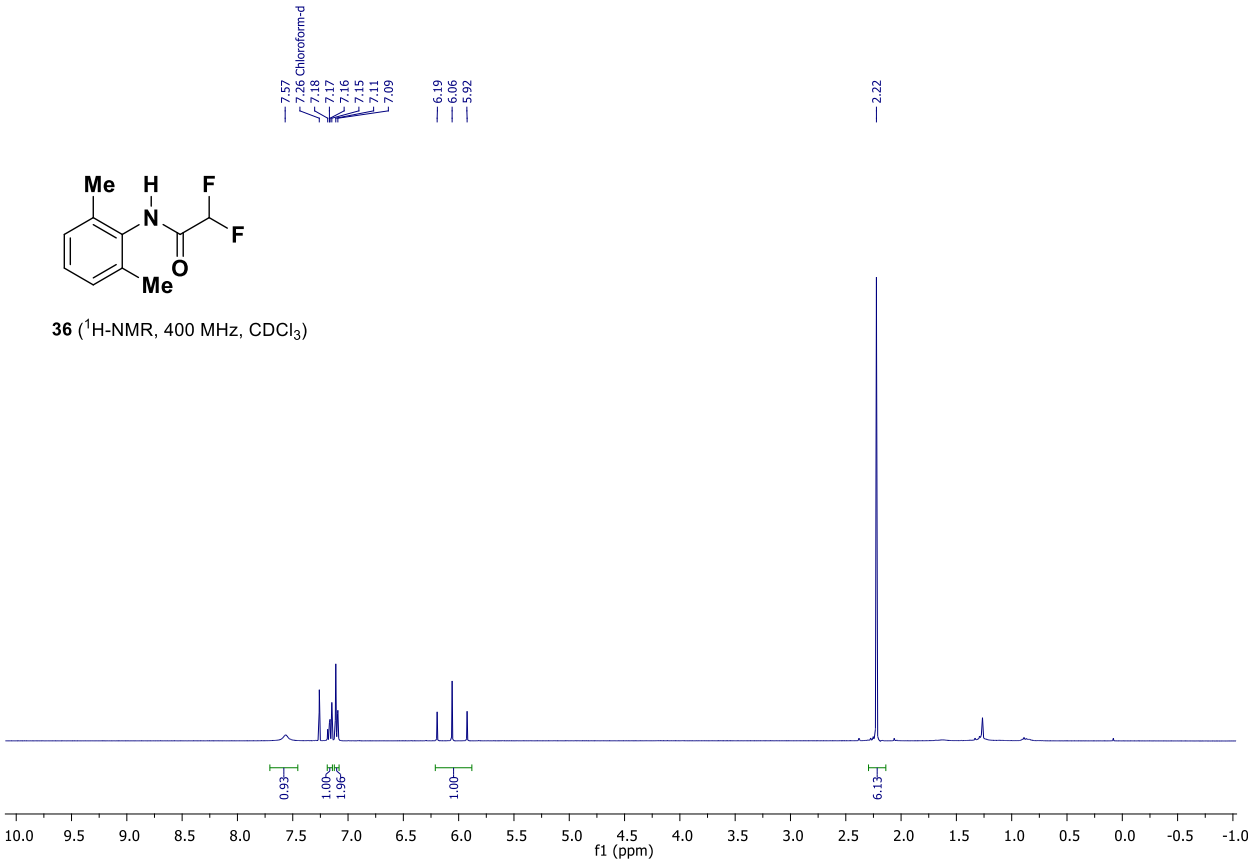
34 (^{13}C-NMR, 100 MHz, $CDCl_3$)



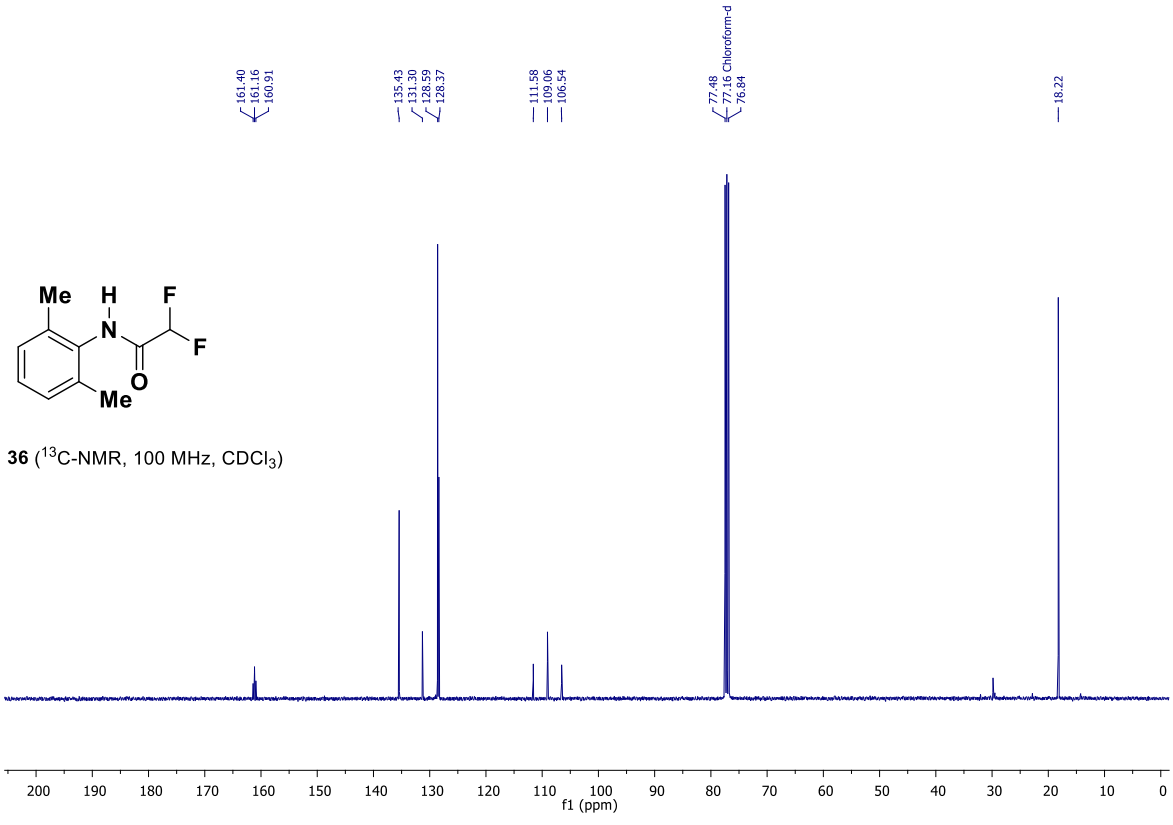
35 (^{1}H-NMR, 400 MHz, $CDCl_3$)



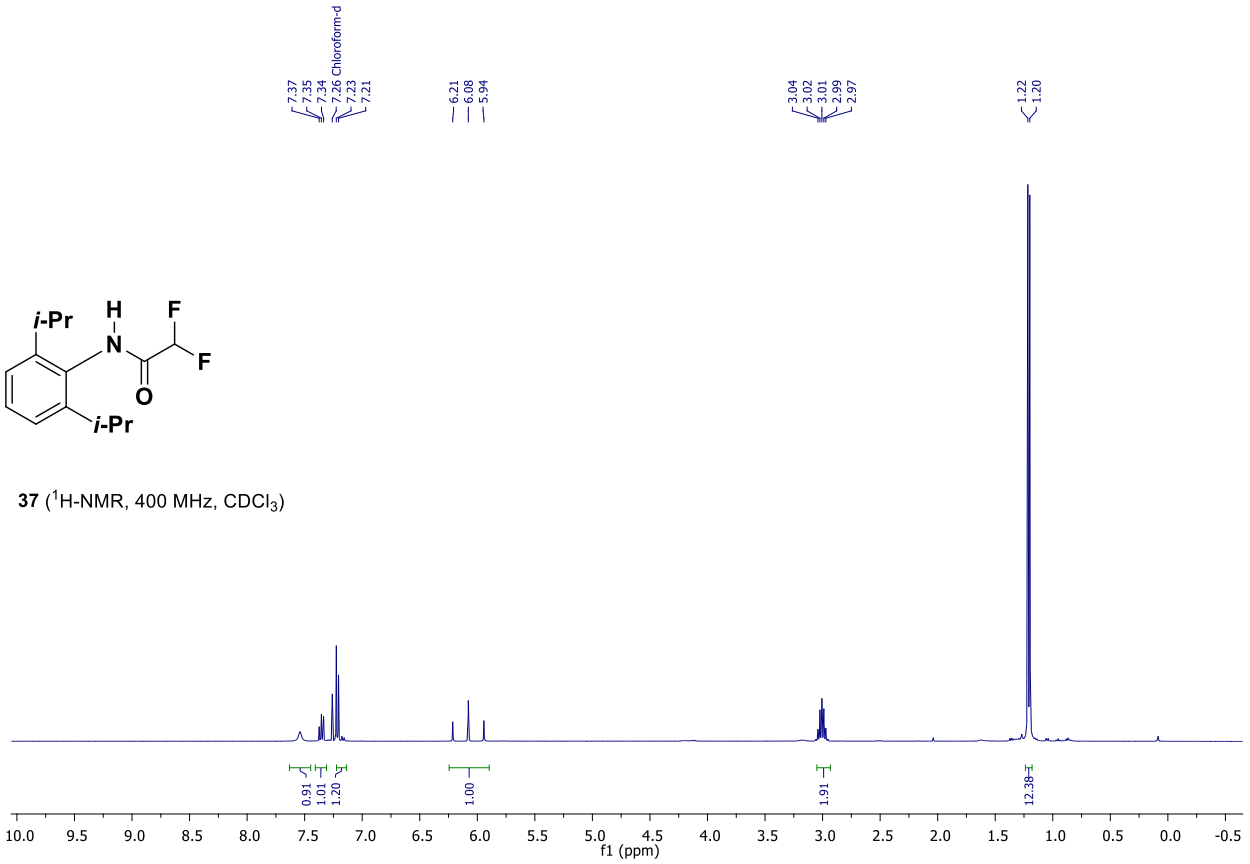
35 (^{13}C-NMR, 100 MHz, $CDCl_3$)



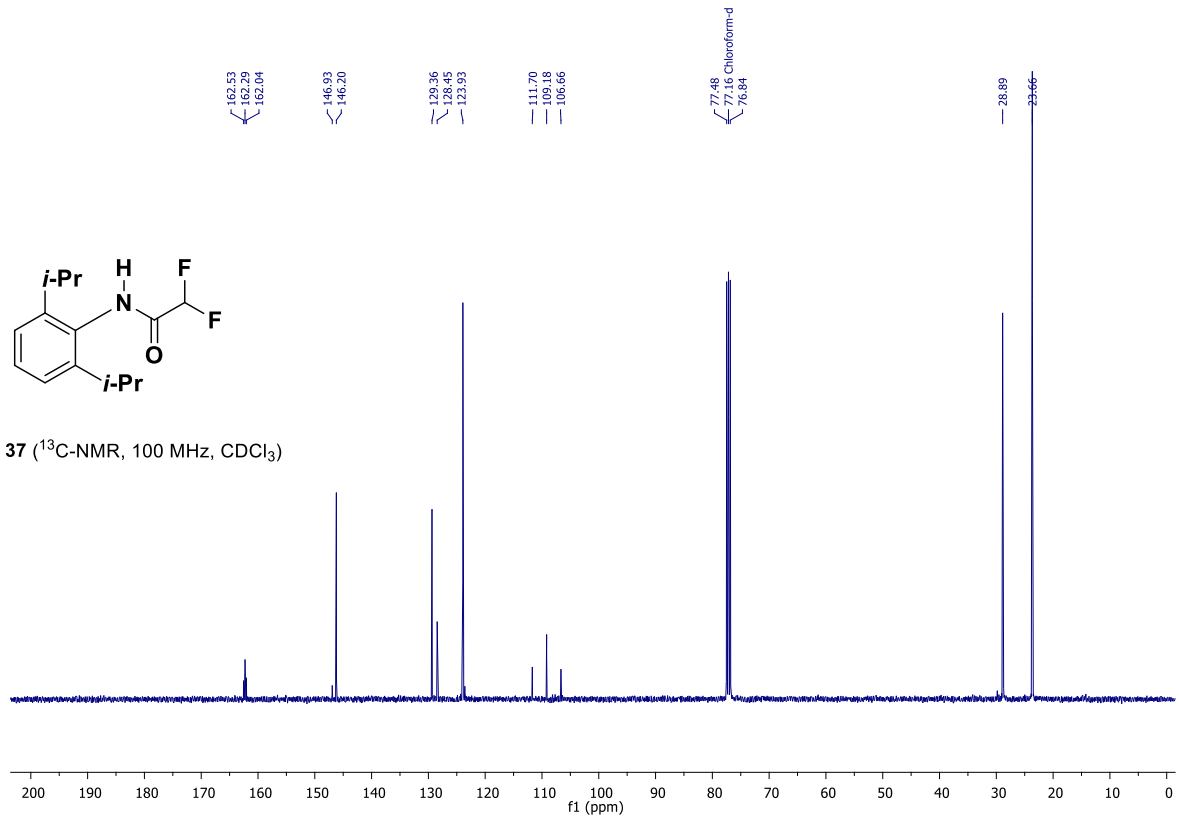
36 (^{1}H-NMR, 400 MHz, $CDCl_3$)



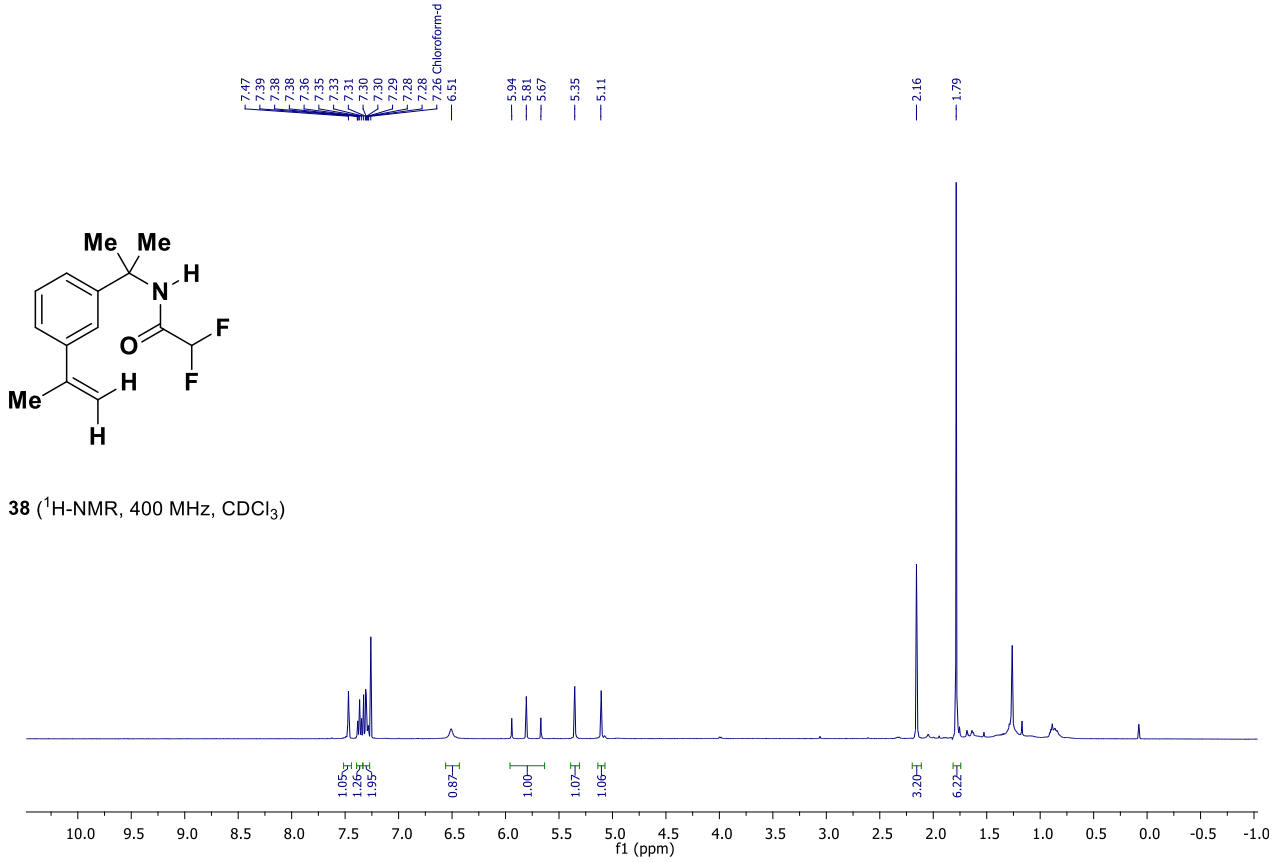
36 (^{13}C-NMR, 100 MHz, $CDCl_3$)



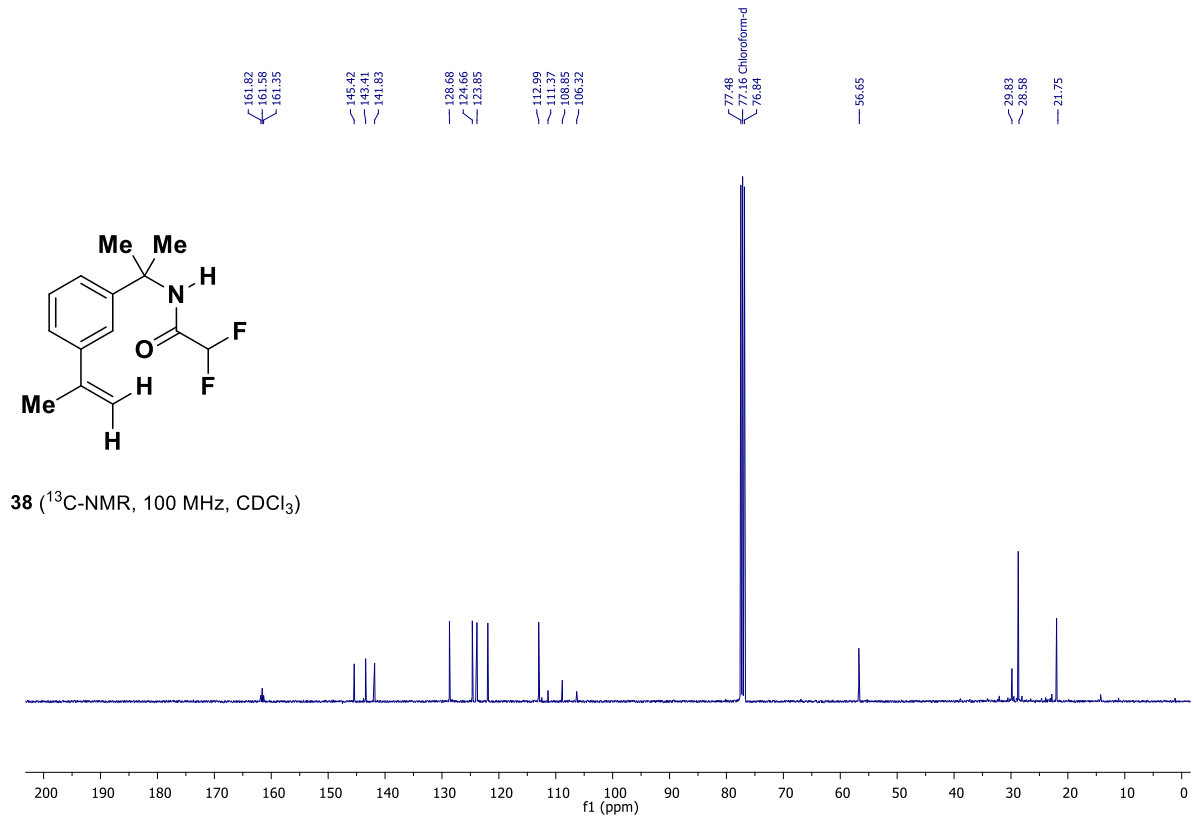
37 (^{1}H-NMR, 400 MHz, $CDCl_3$)



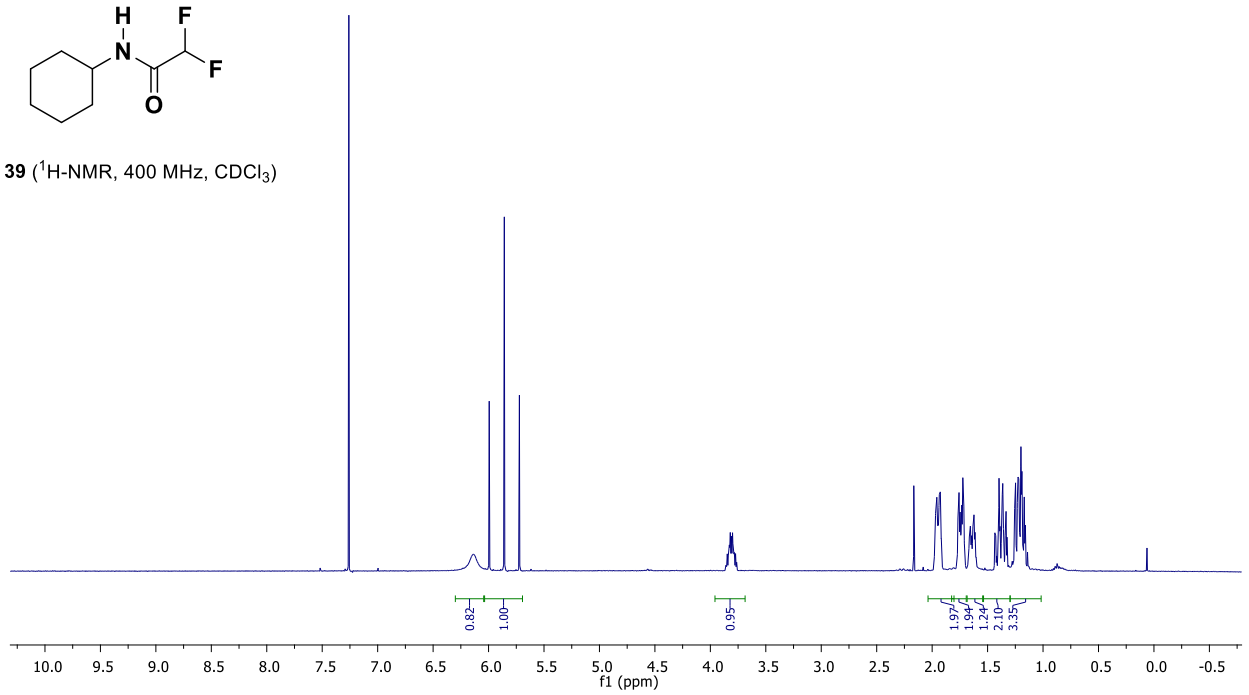
37 (^{13}C-NMR, 100 MHz, $CDCl_3$)



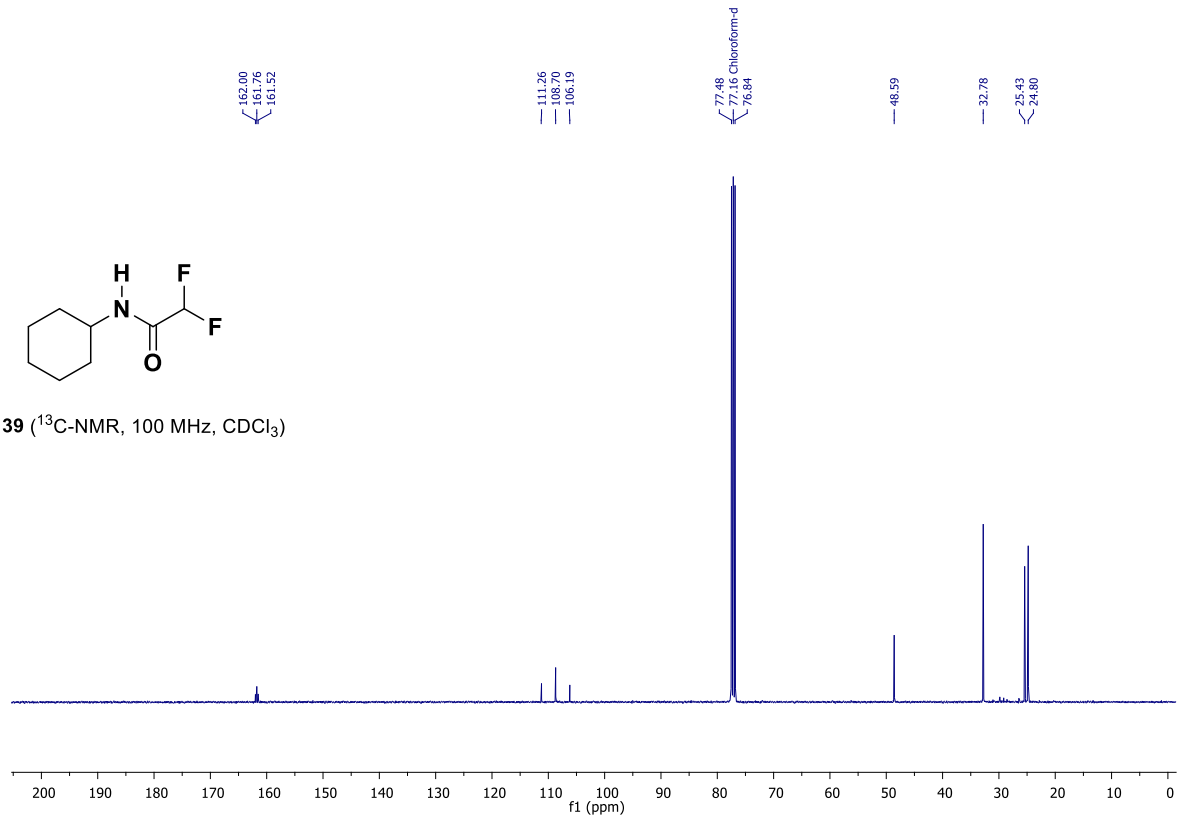
38 (^{1}H-NMR, 400 MHz, $CDCl_3$)



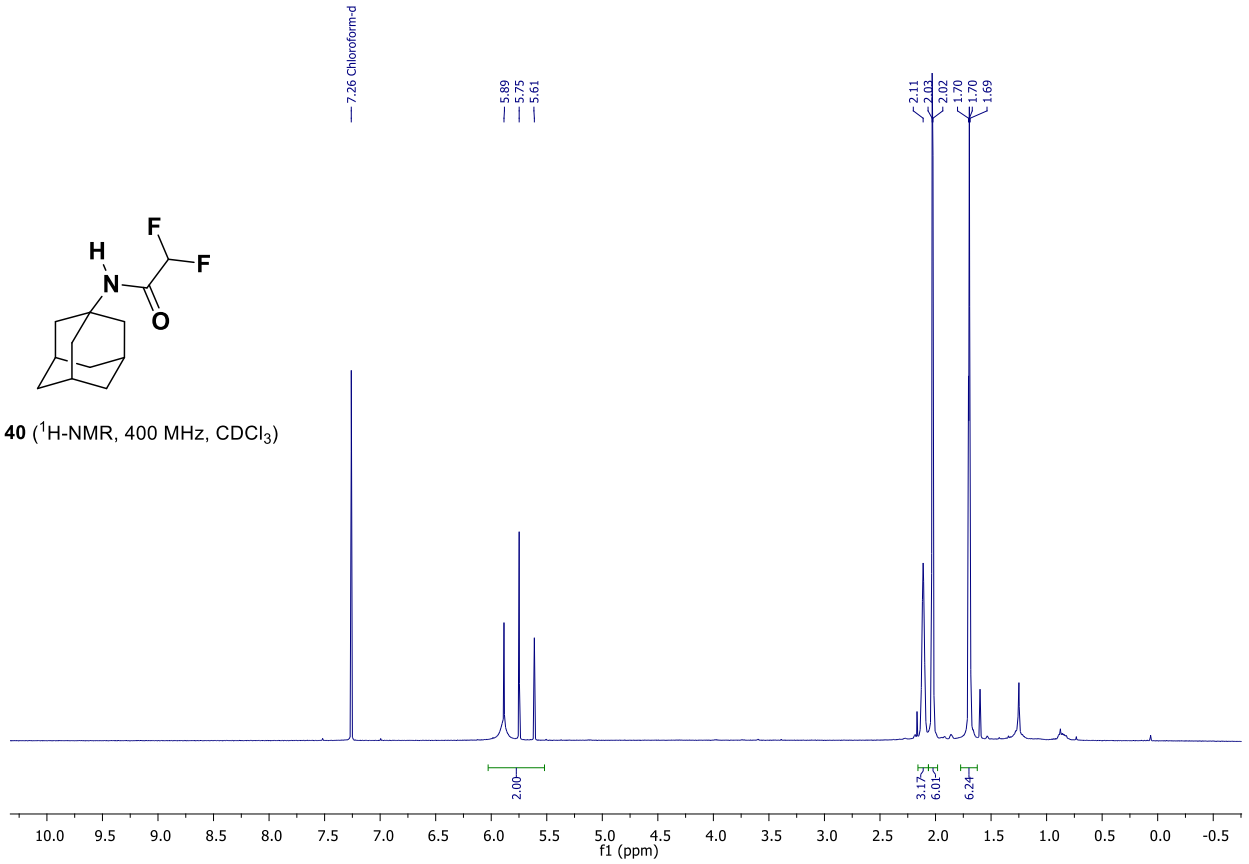
38 (^{13}C-NMR, 100 MHz, $CDCl_3$)



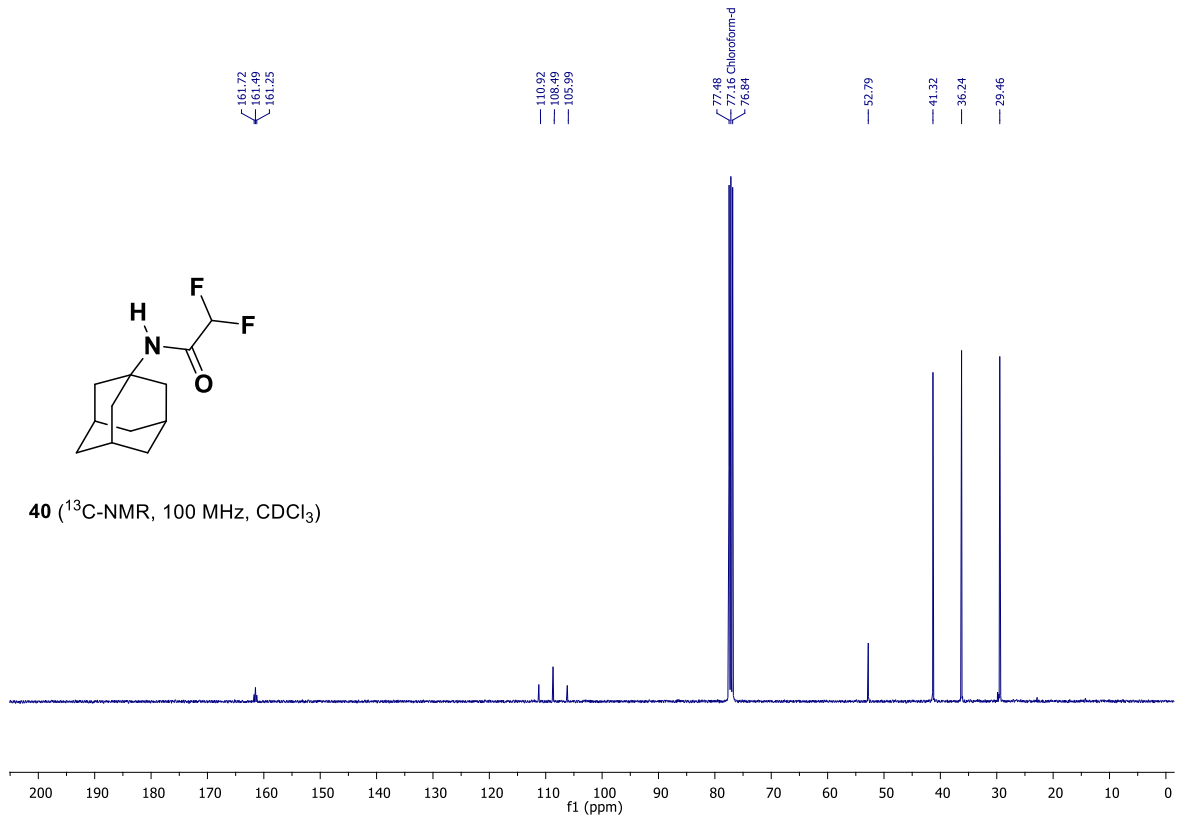
39 (^{1}H-NMR, 400 MHz, $CDCl_3$)



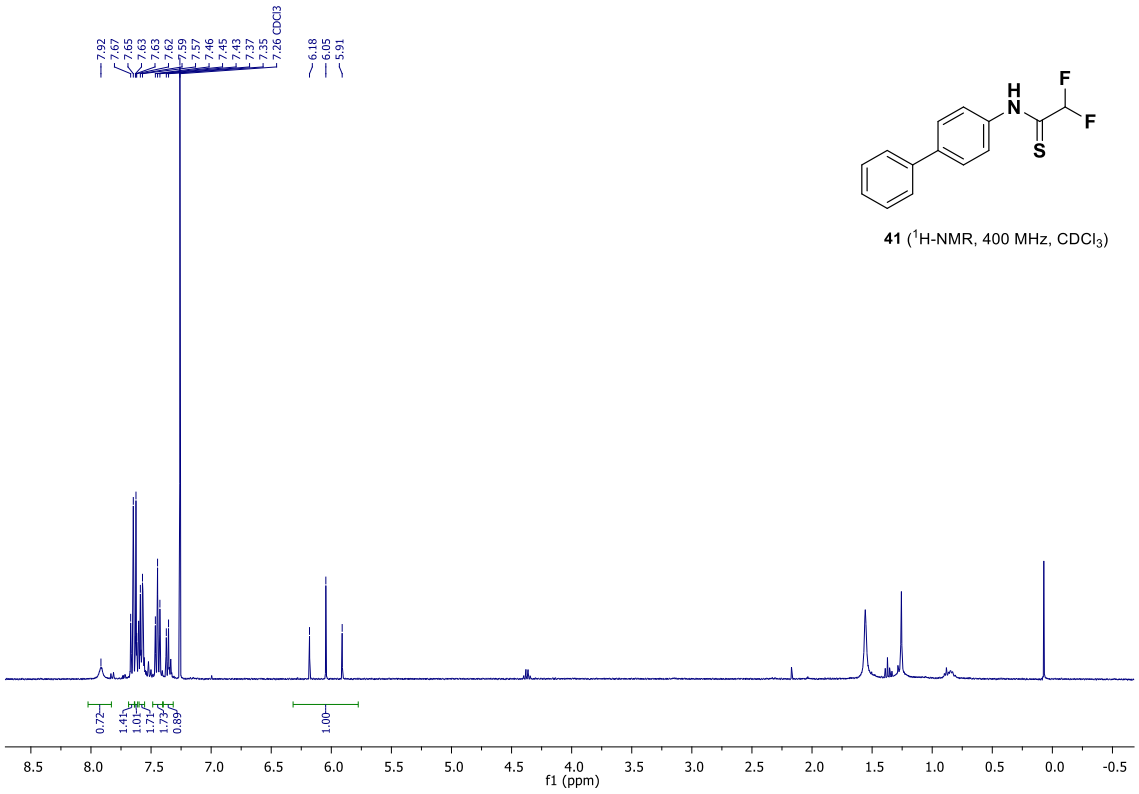
39 (^{13}C-NMR, 100 MHz, $CDCl_3$)



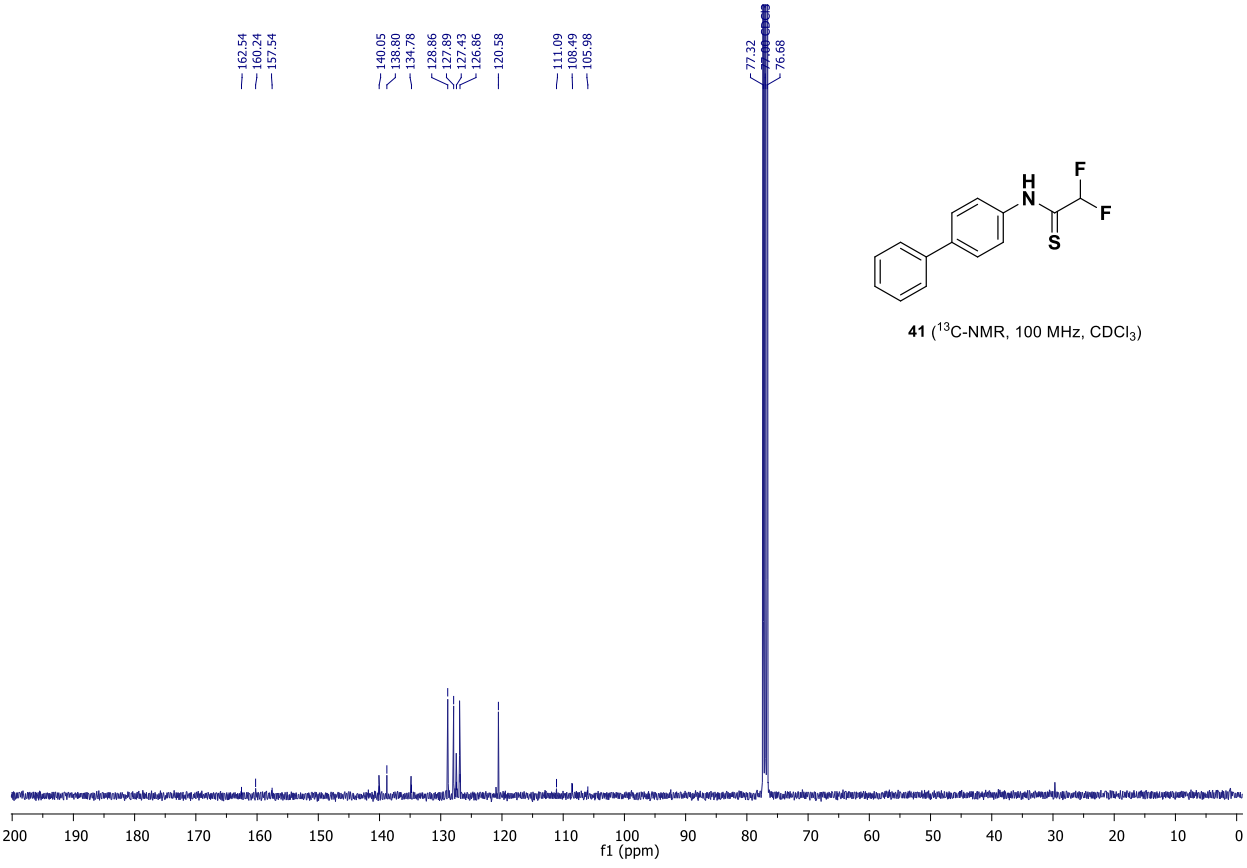
40 (^{1}H-NMR, 400 MHz, $CDCl_3$)



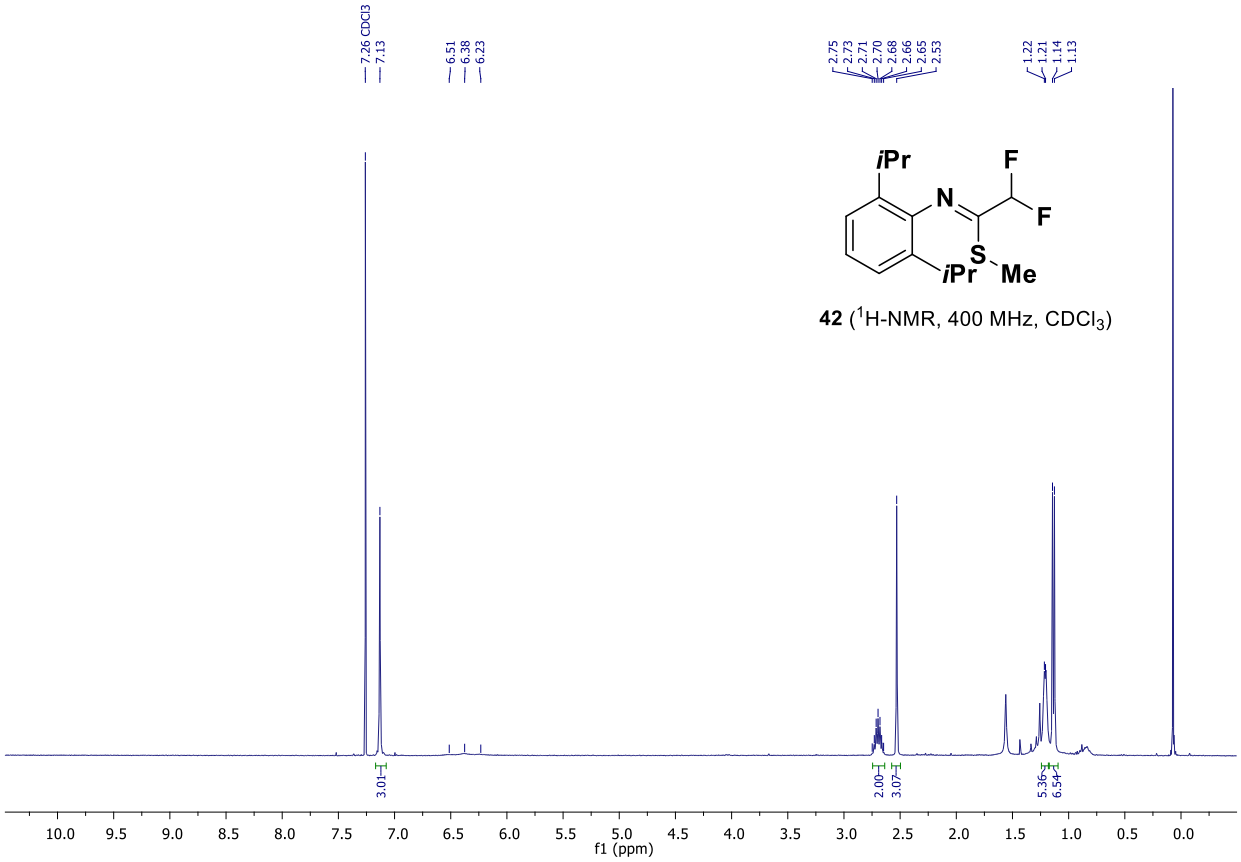
40 (^{13}C-NMR, 100 MHz, $CDCl_3$)



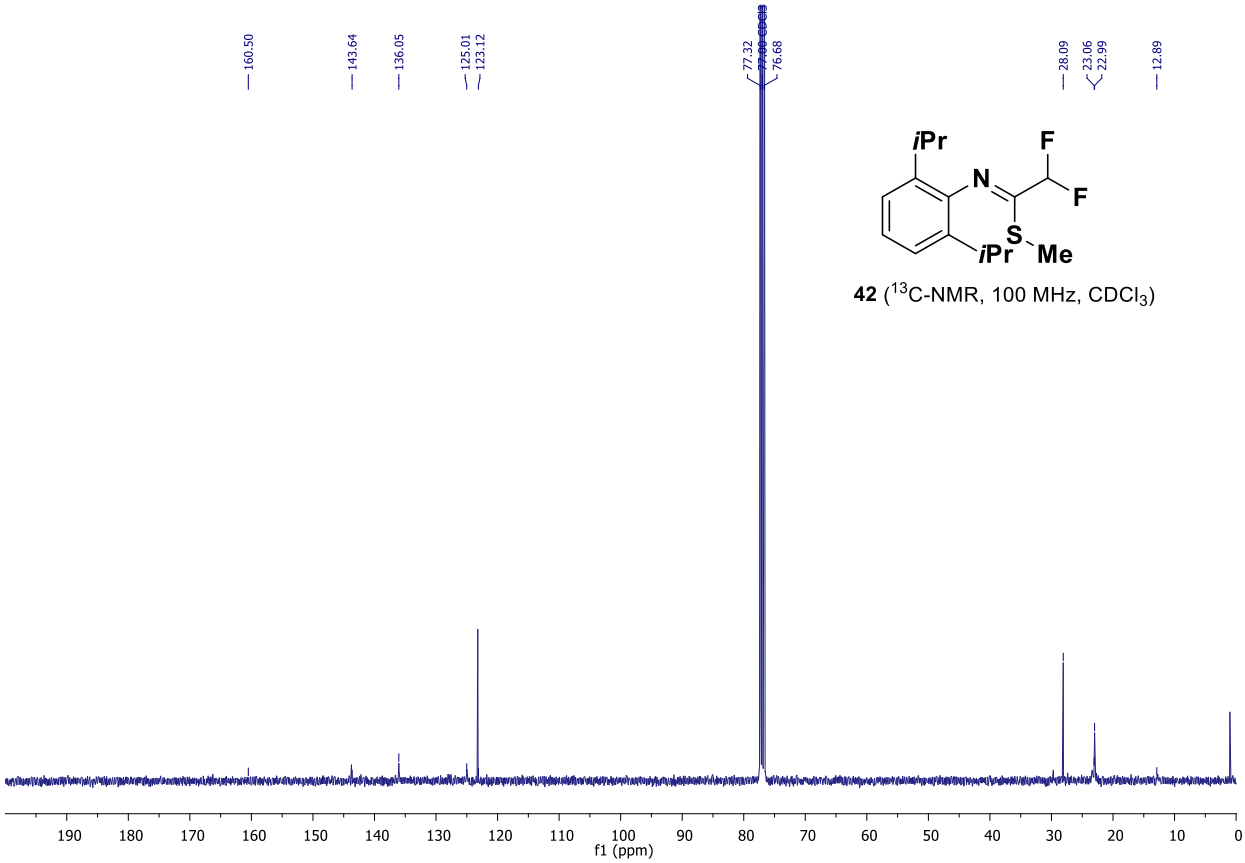
41 (^{1}H-NMR, 400 MHz, $CDCl_3$)



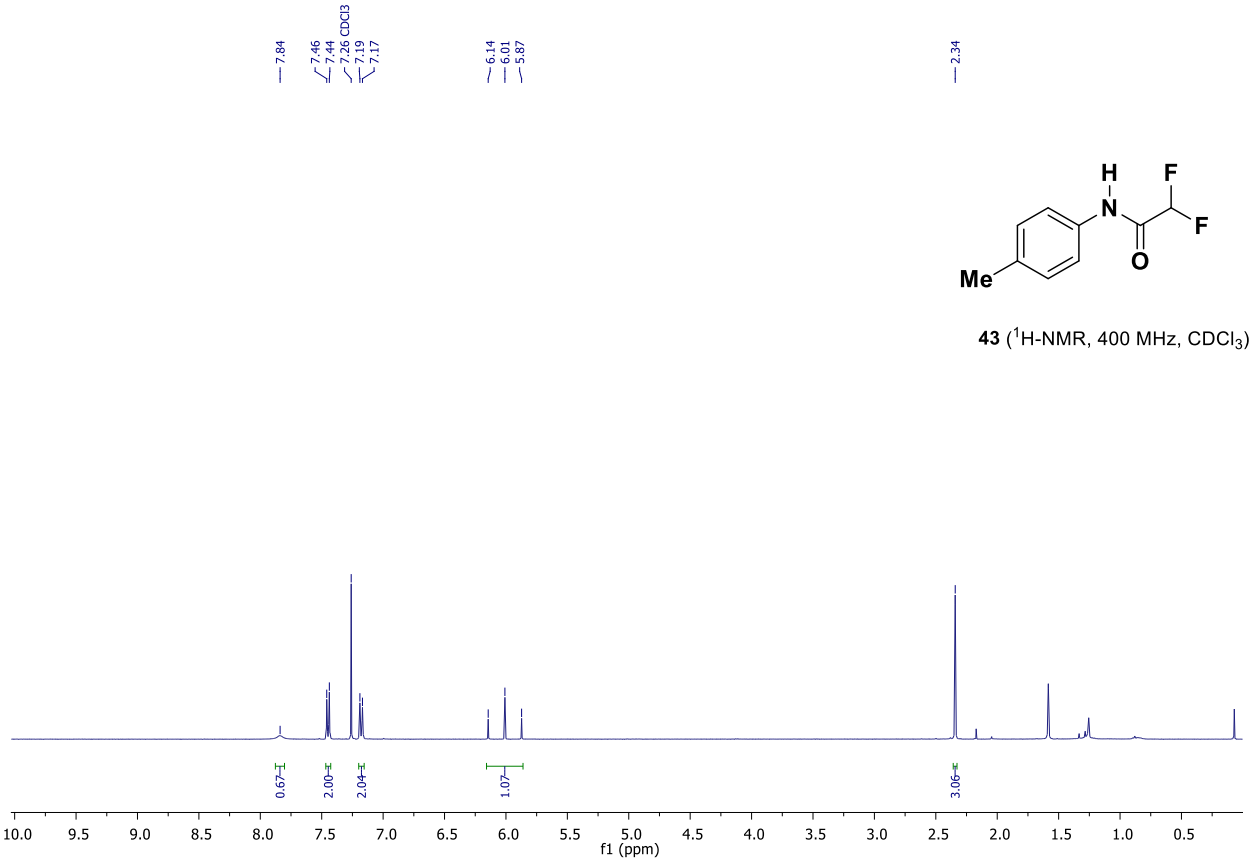
41 (^{13}C-NMR, 100 MHz, $CDCl_3$)



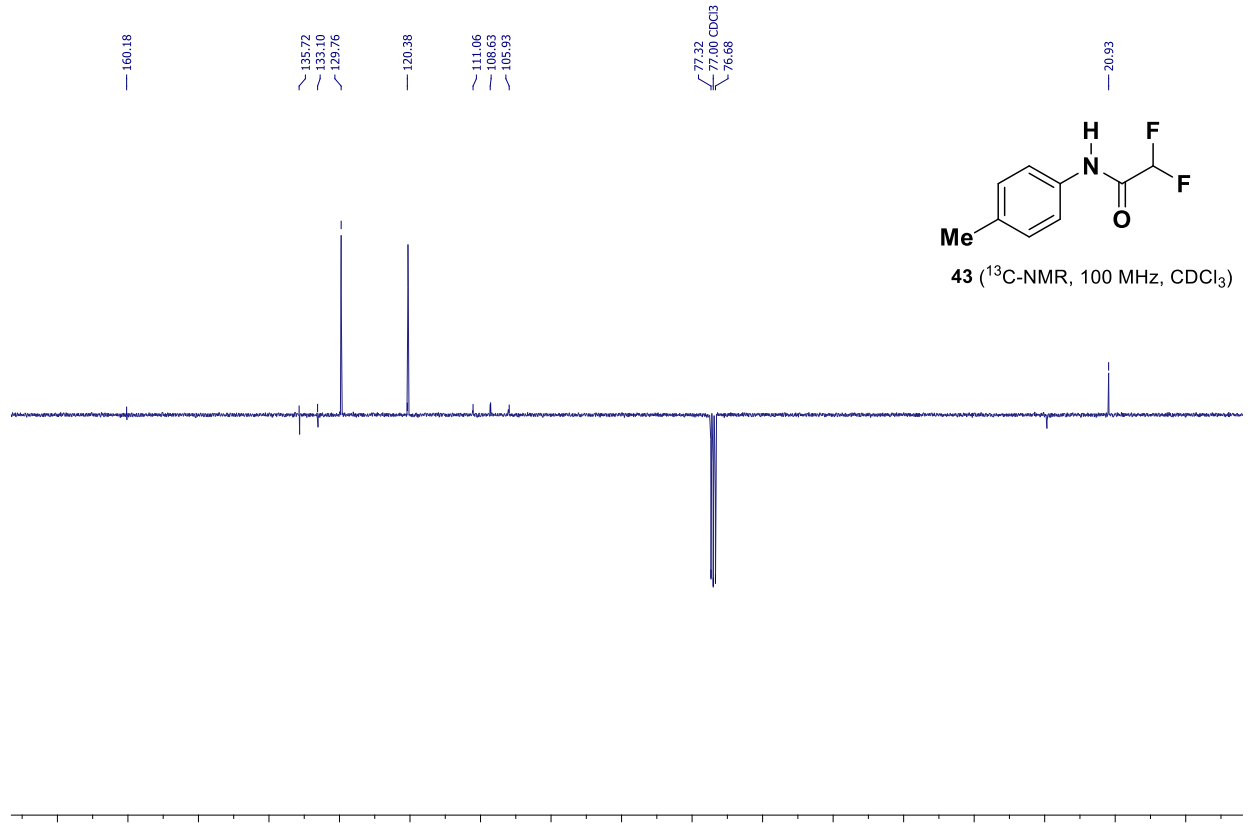
42 (^{1}H-NMR, 400 MHz, $CDCl_3$)



42 (^{13}C-NMR, 100 MHz, $CDCl_3$)

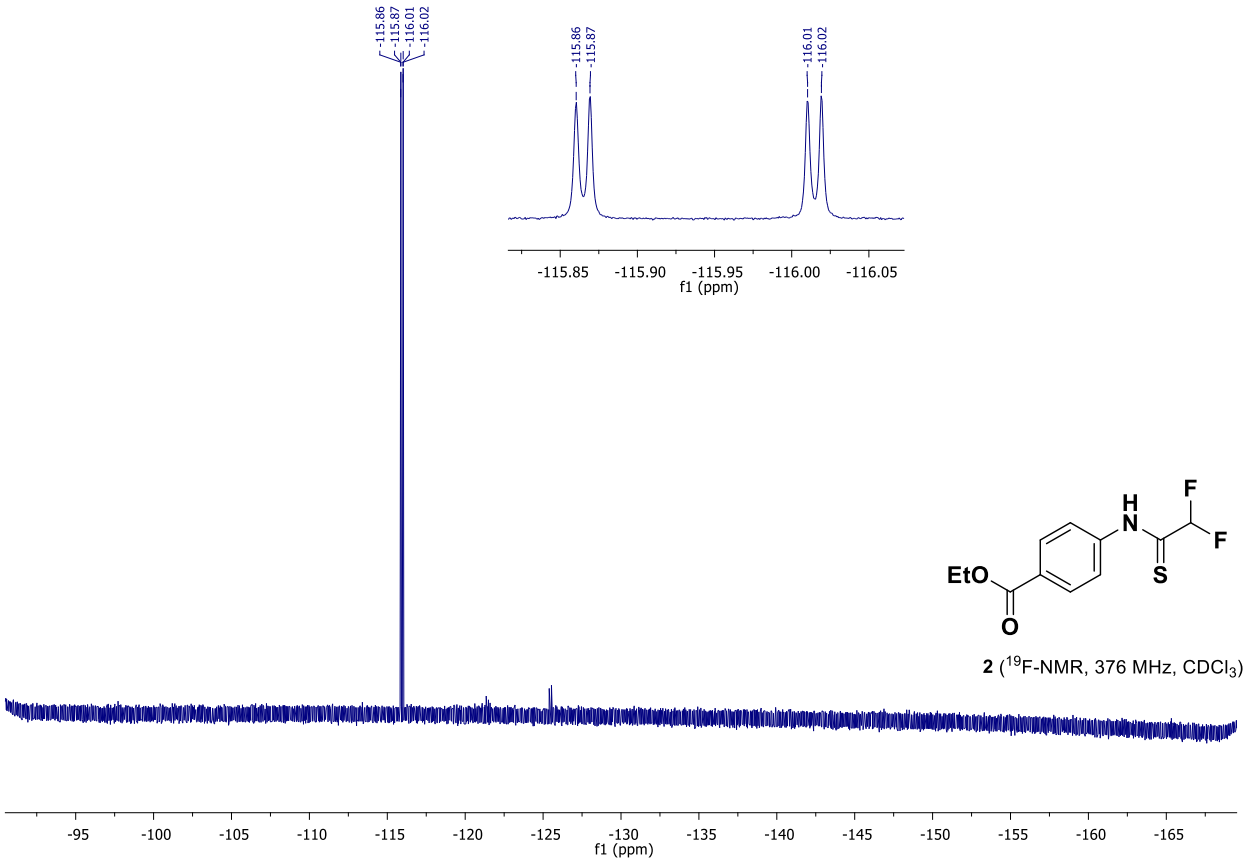


43 (^{1}H-NMR, 400 MHz, $CDCl_3$)

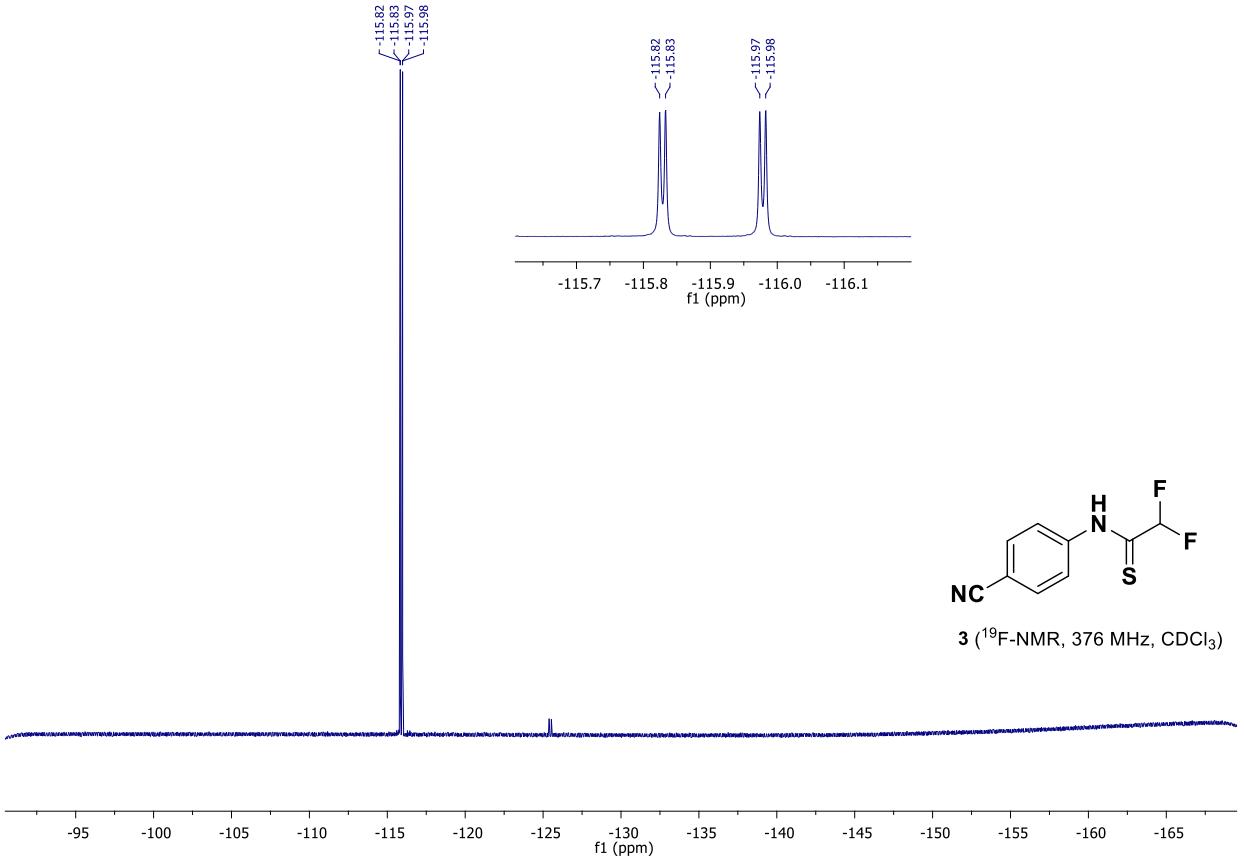


43 (^{13}C-NMR, 100 MHz, $CDCl_3$)

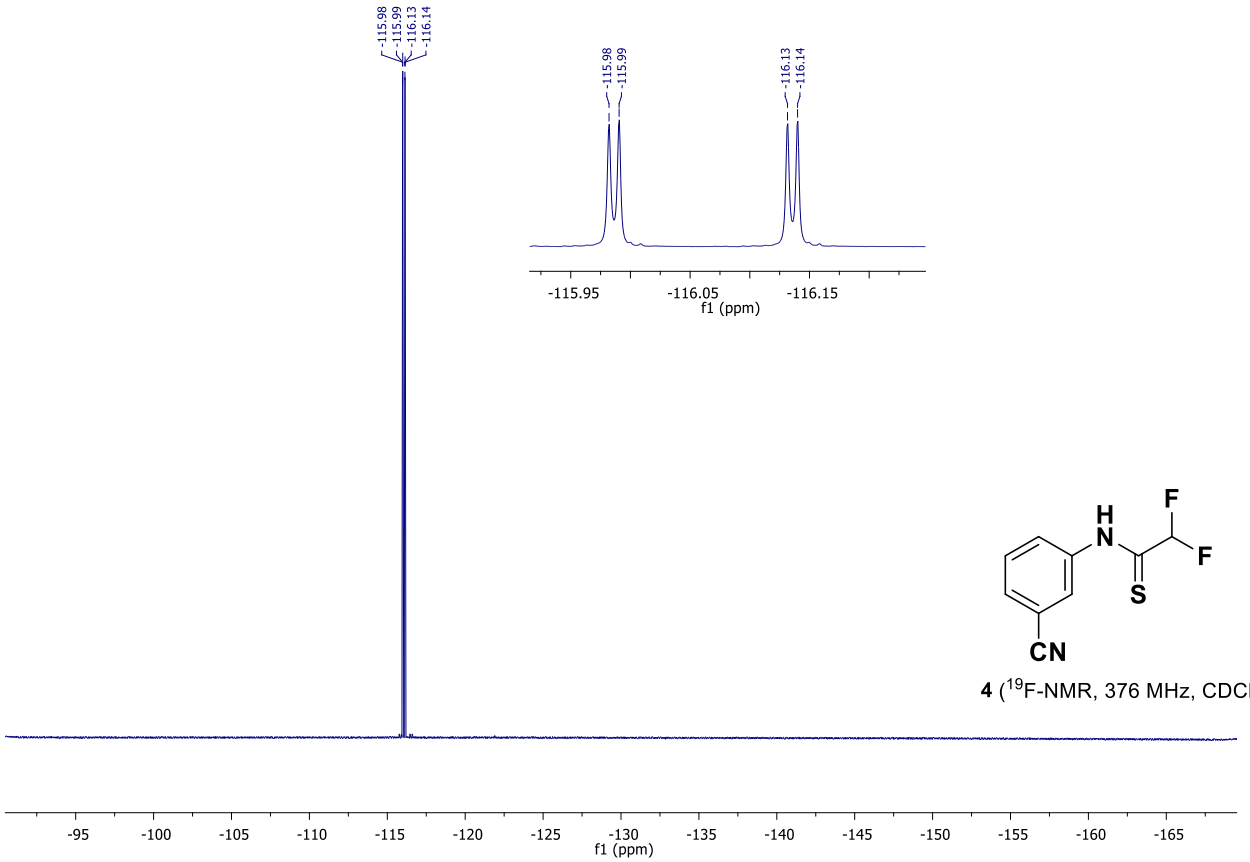
7. ^{19}F-NMR spectra.



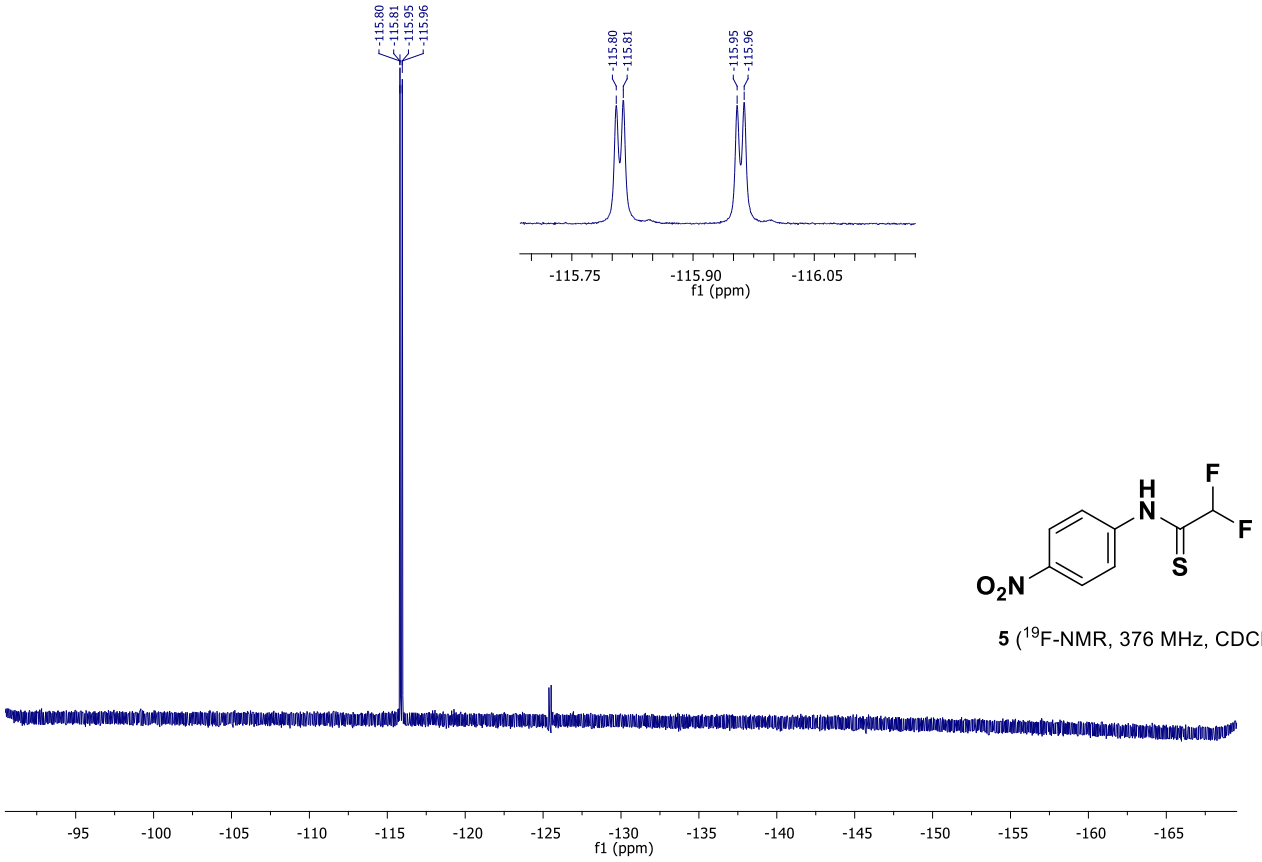
2 (^{19}F-NMR, 376 MHz, $CDCl_3$)



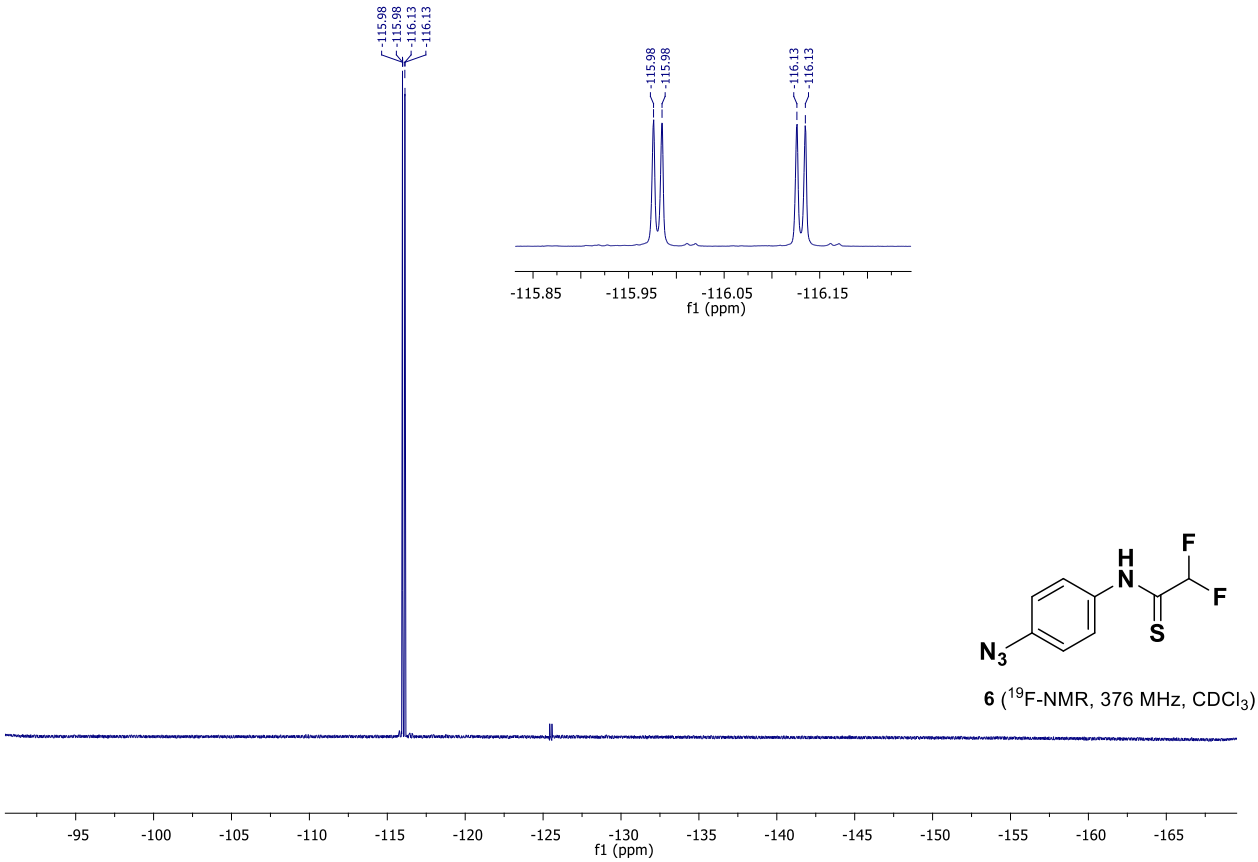
3 (^{19}F-NMR, 376 MHz, $CDCl_3$)



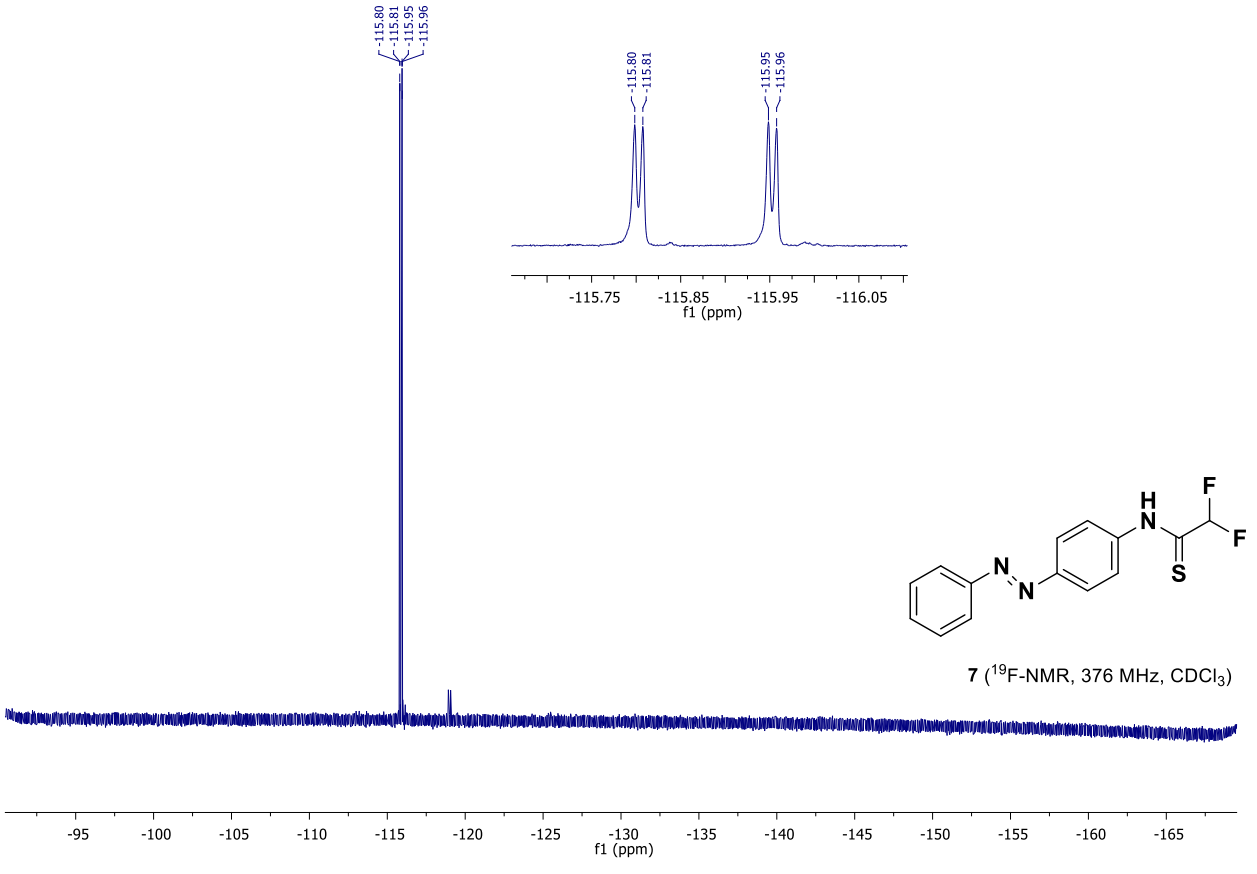
4 (^{19}F-NMR, 376 MHz, $CDCl_3$)



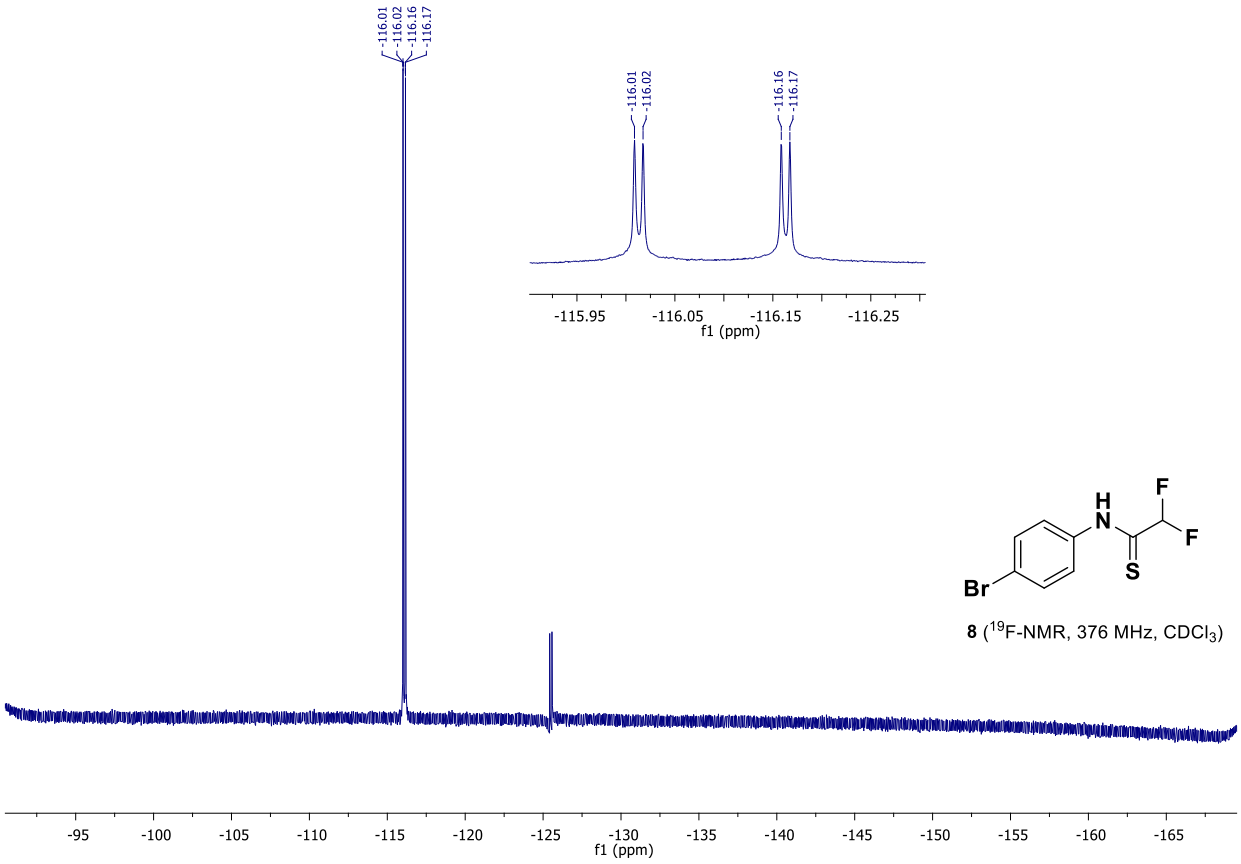
5 (^{19}F-NMR, 376 MHz, $CDCl_3$)



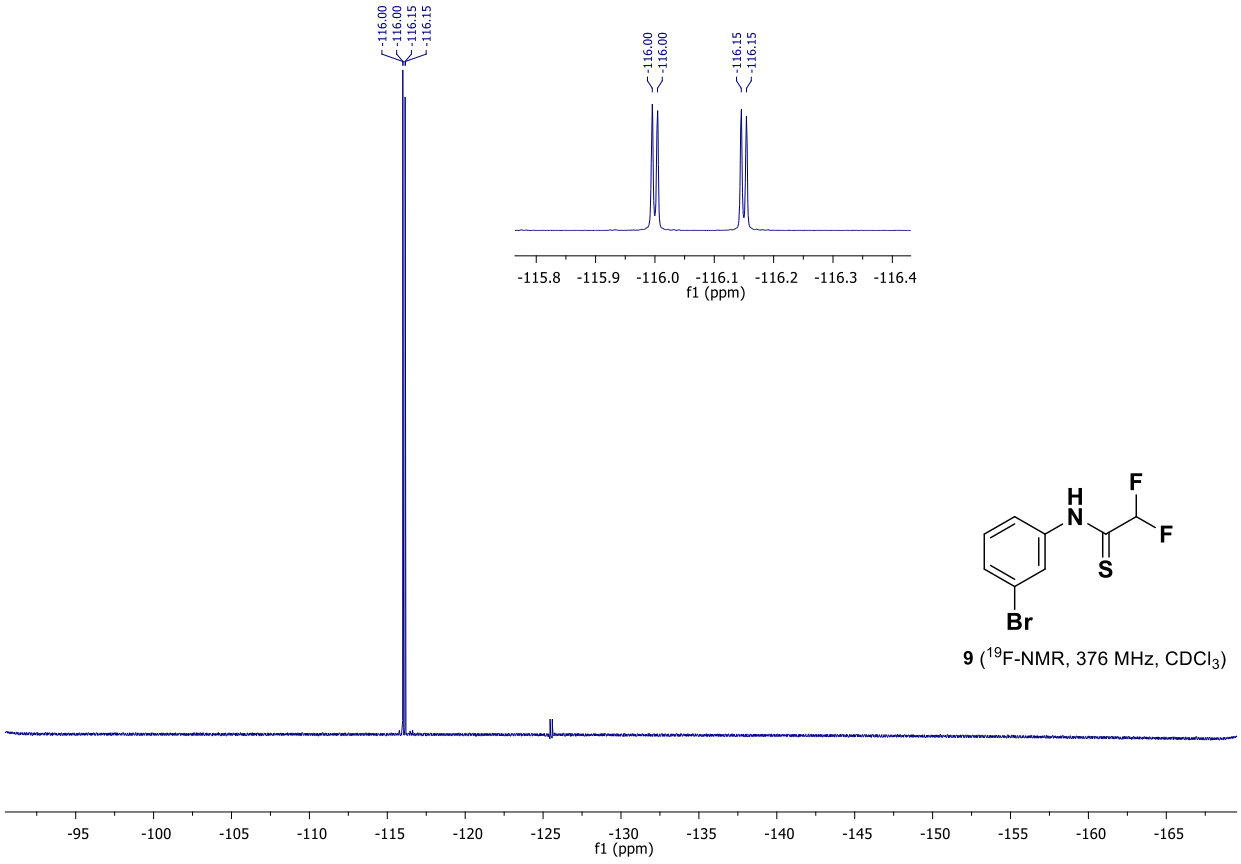
6 (^{19}F-NMR, 376 MHz, $CDCl_3$)



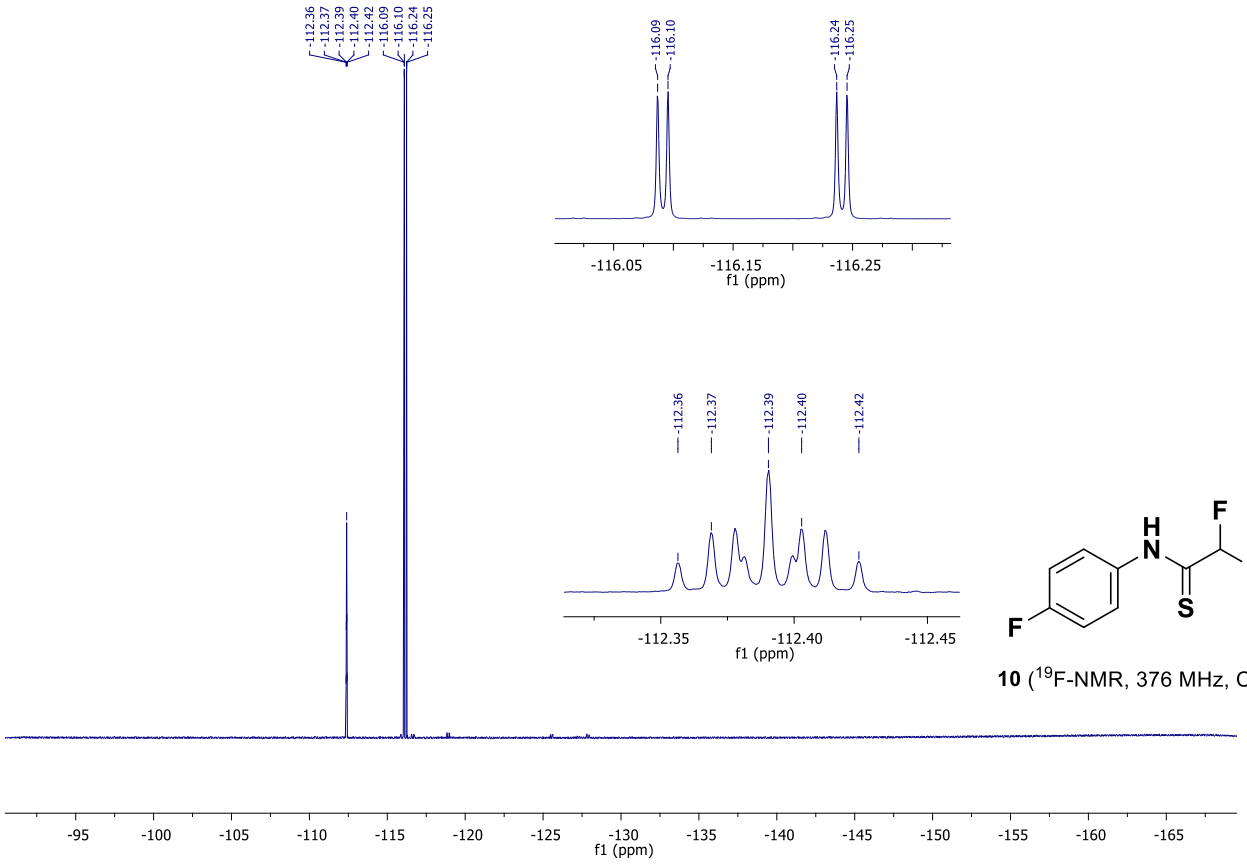
7 (^{19}F-NMR, 376 MHz, $CDCl_3$)



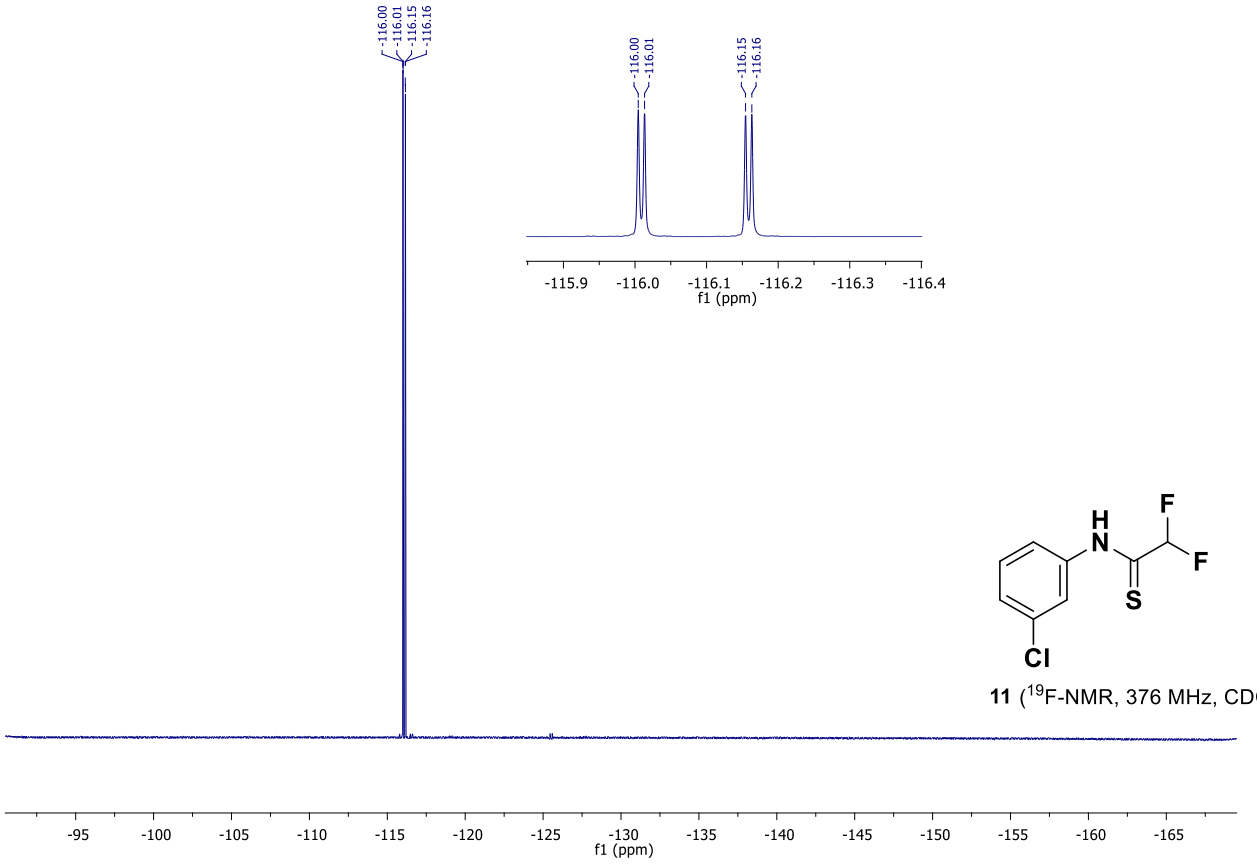
8 (^{19}F-NMR, 376 MHz, $CDCl_3$)



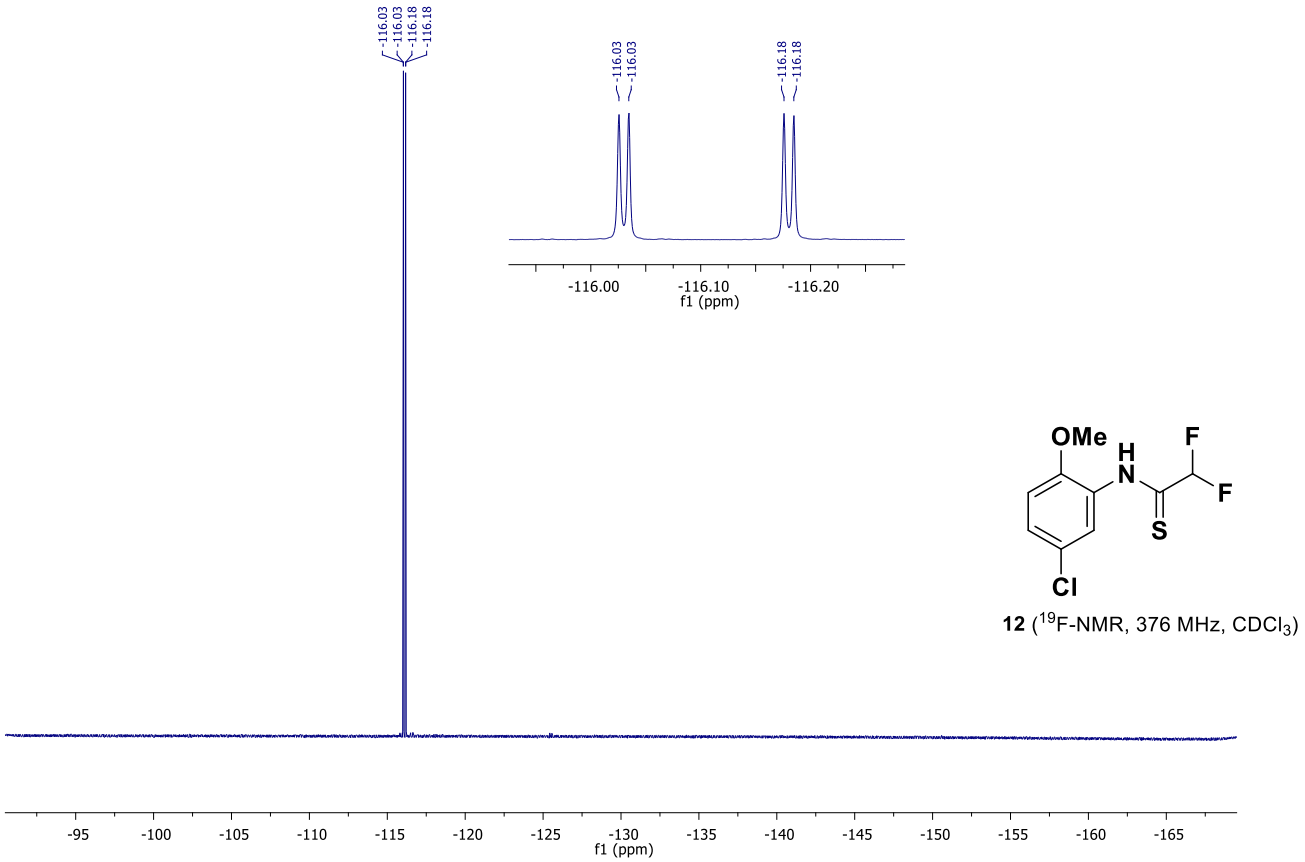
9 (^{19}F-NMR, 376 MHz, $CDCl_3$)



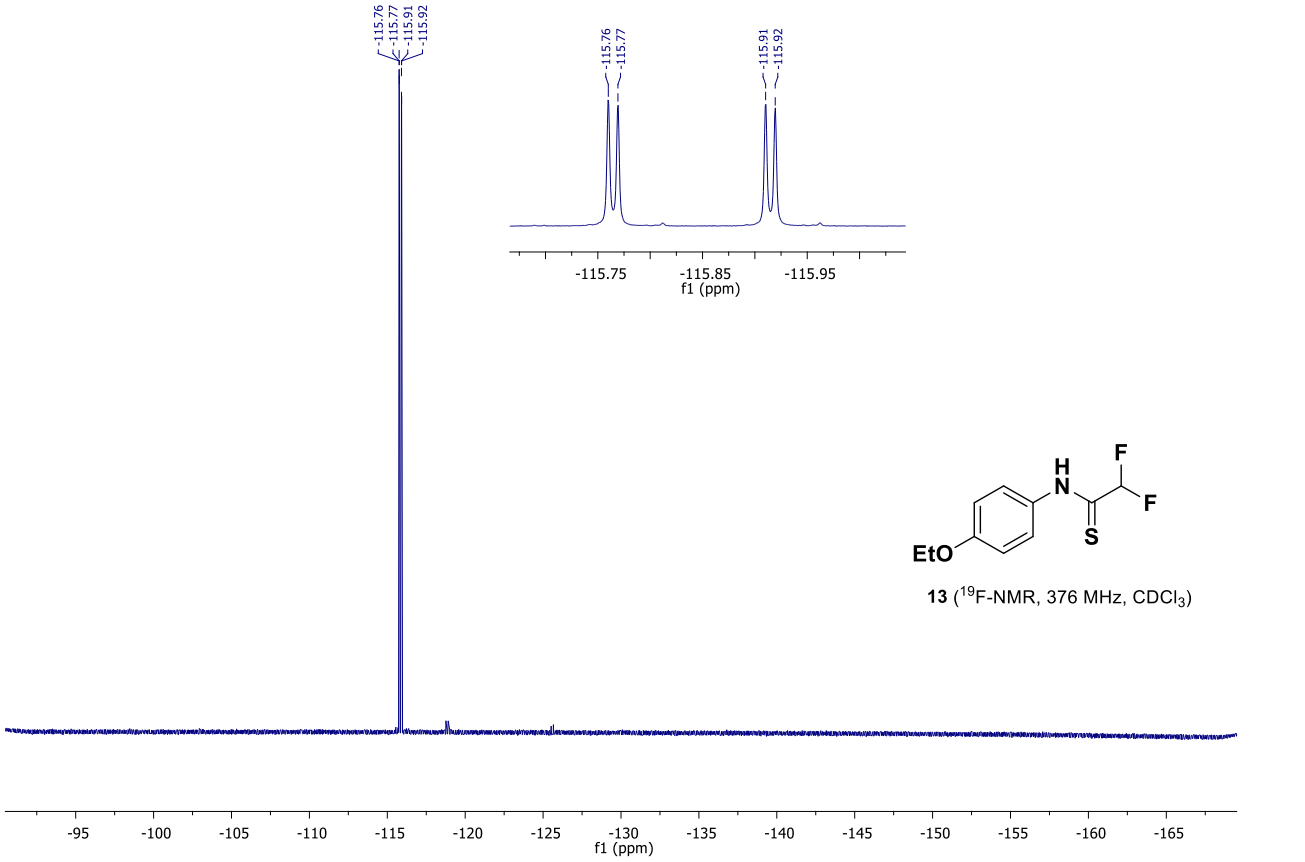
10 (^{19}F-NMR, 376 MHz, $CDCl_3$)



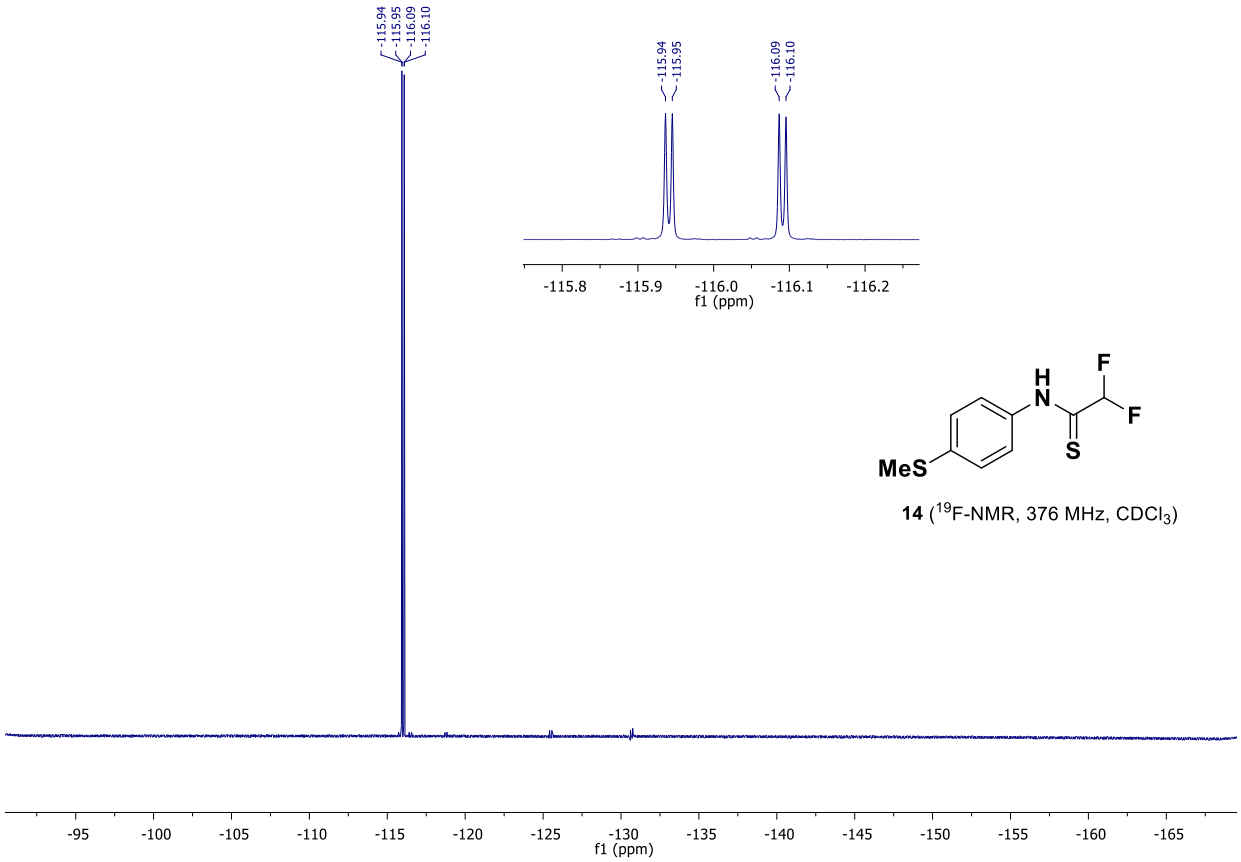
11 (^{19}F-NMR, 376 MHz, $CDCl_3$)



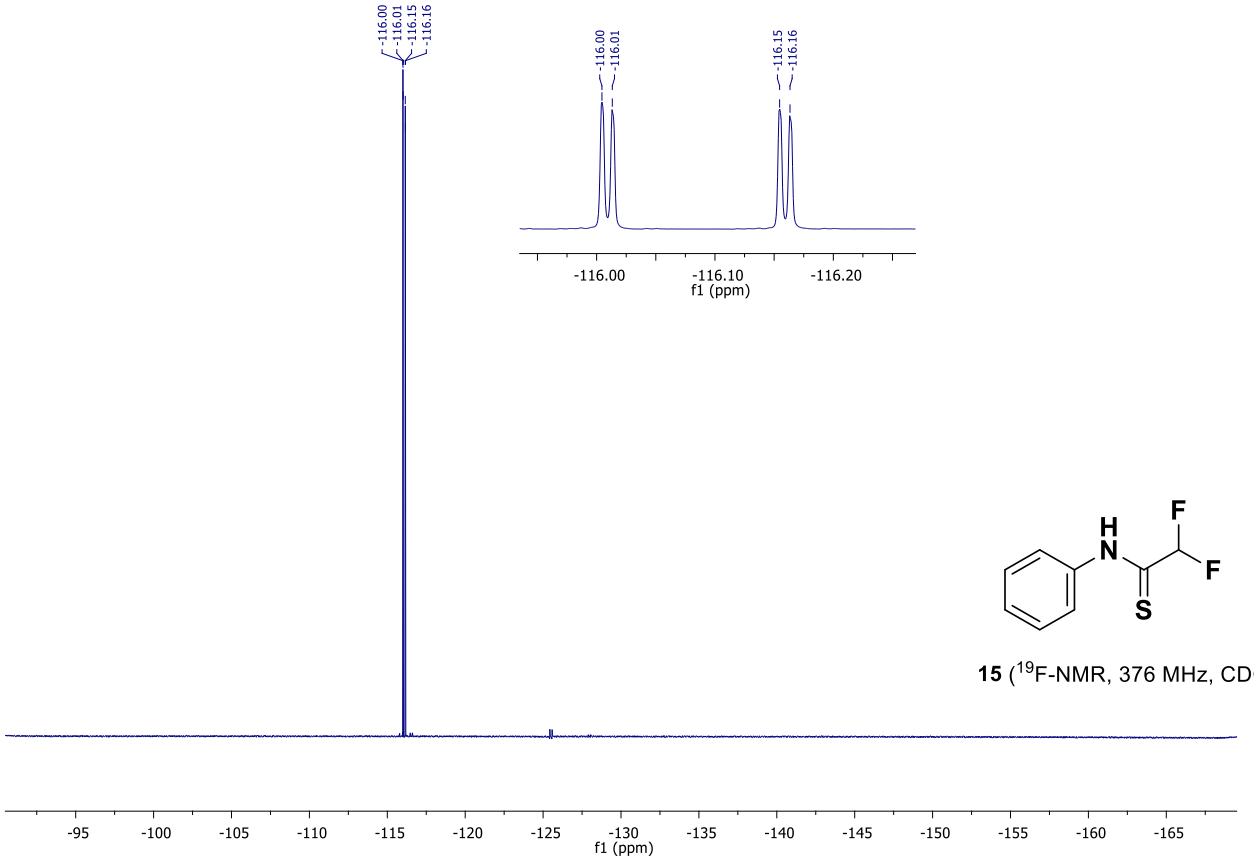
12 (^{19}F-NMR, 376 MHz, $CDCl_3$)



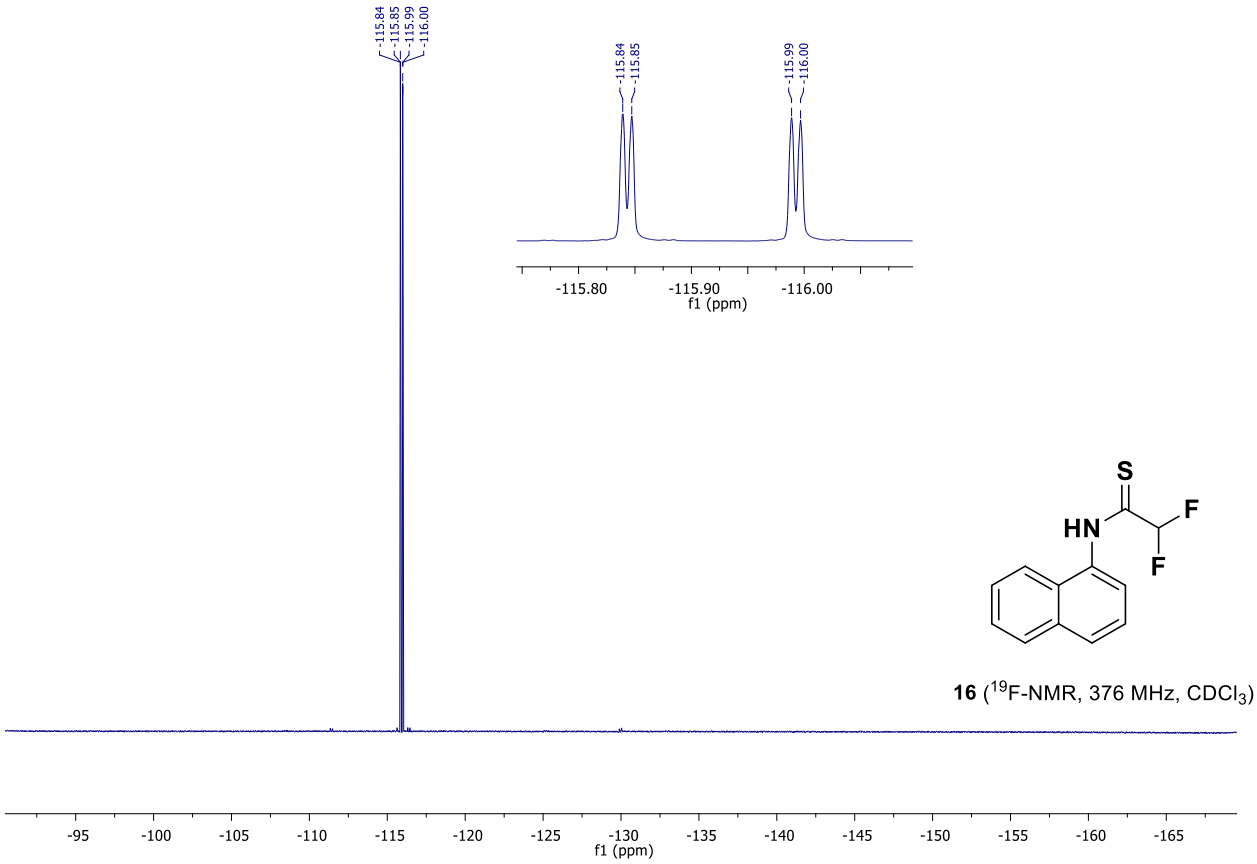
13 (^{19}F-NMR, 376 MHz, $CDCl_3$)



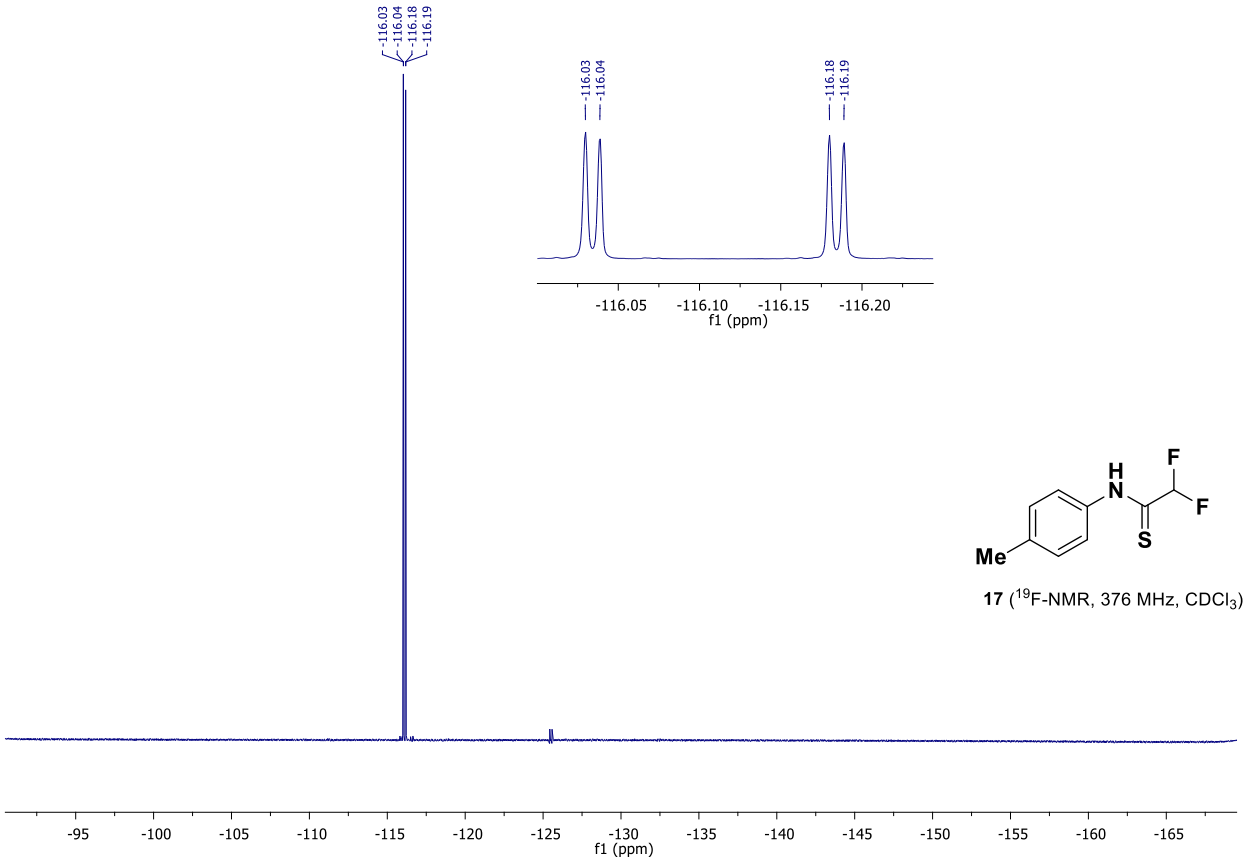
14 (^{19}F-NMR, 376 MHz, $CDCl_3$)



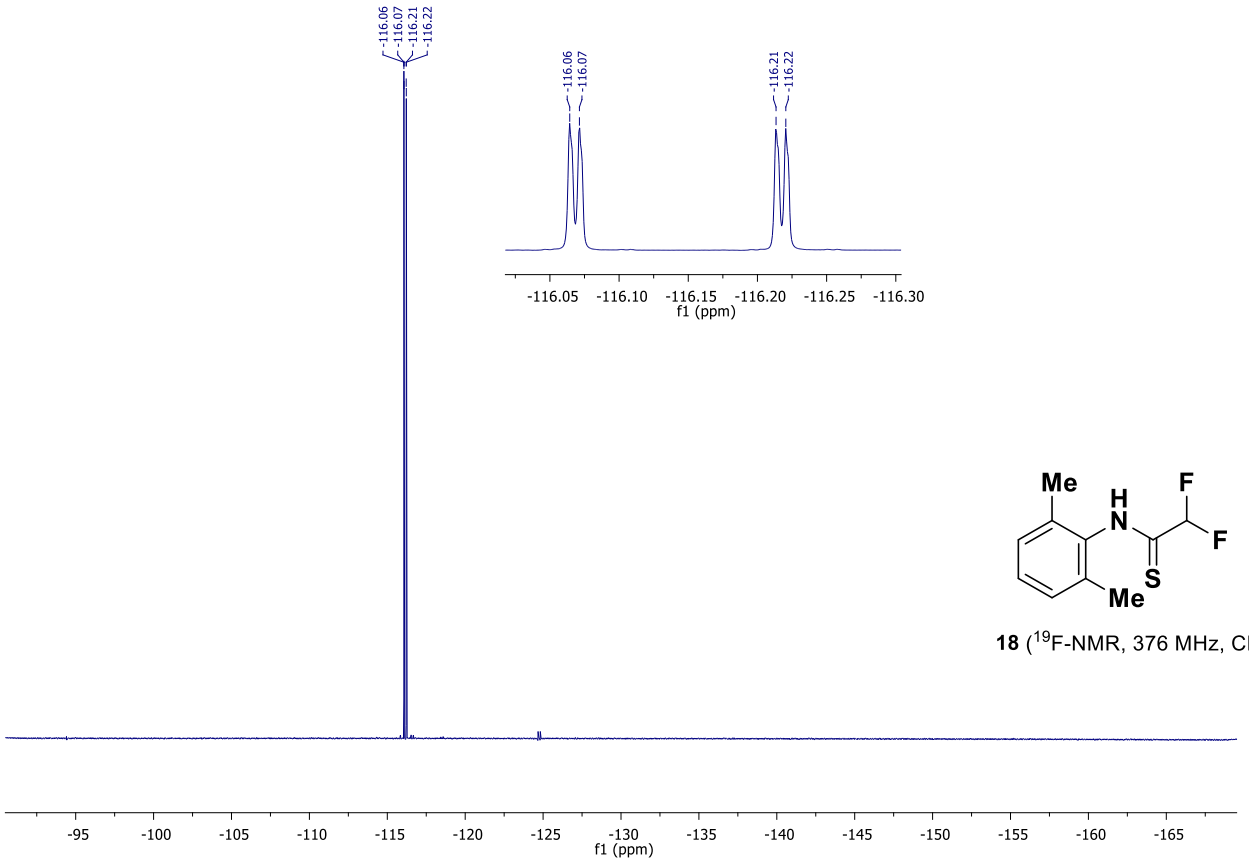
15 (^{19}F-NMR, 376 MHz, $CDCl_3$)



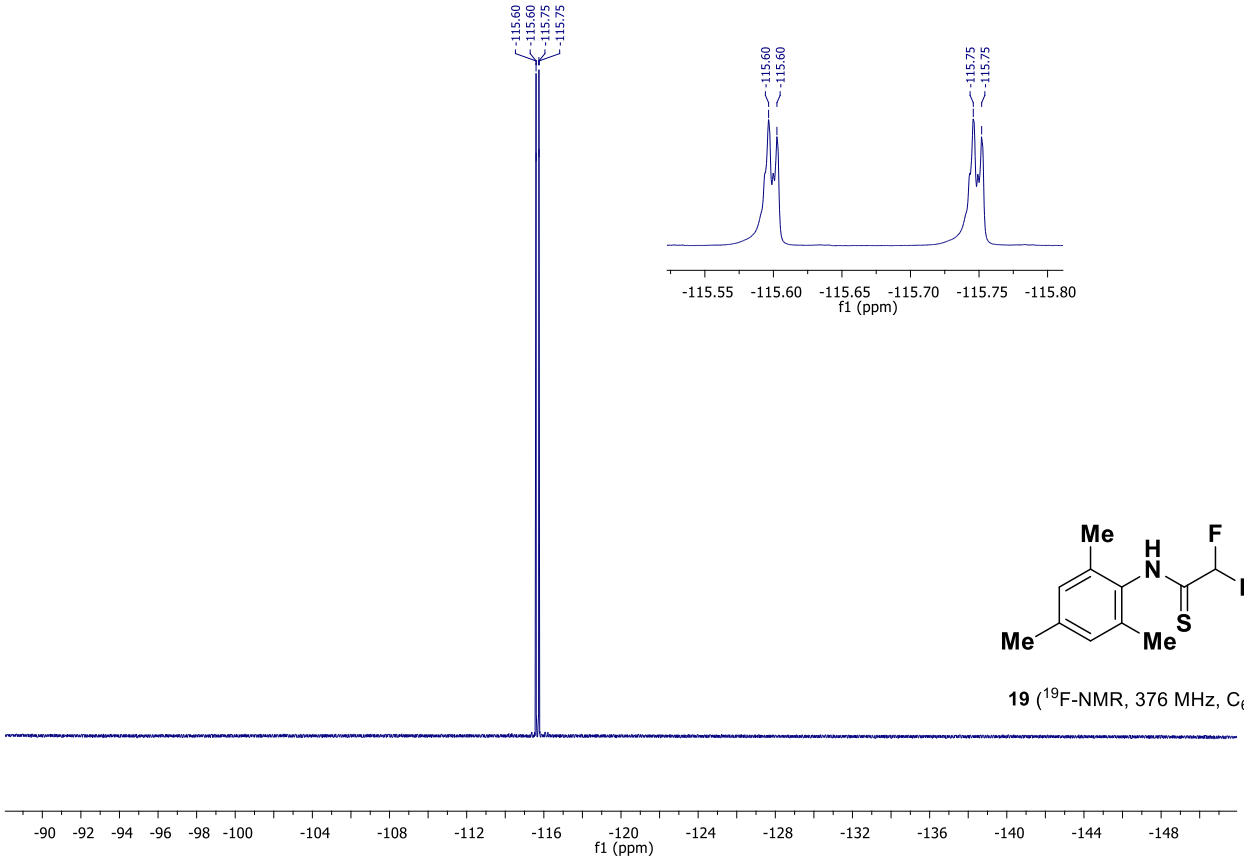
16 (^{19}F-NMR, 376 MHz, $CDCl_3$)



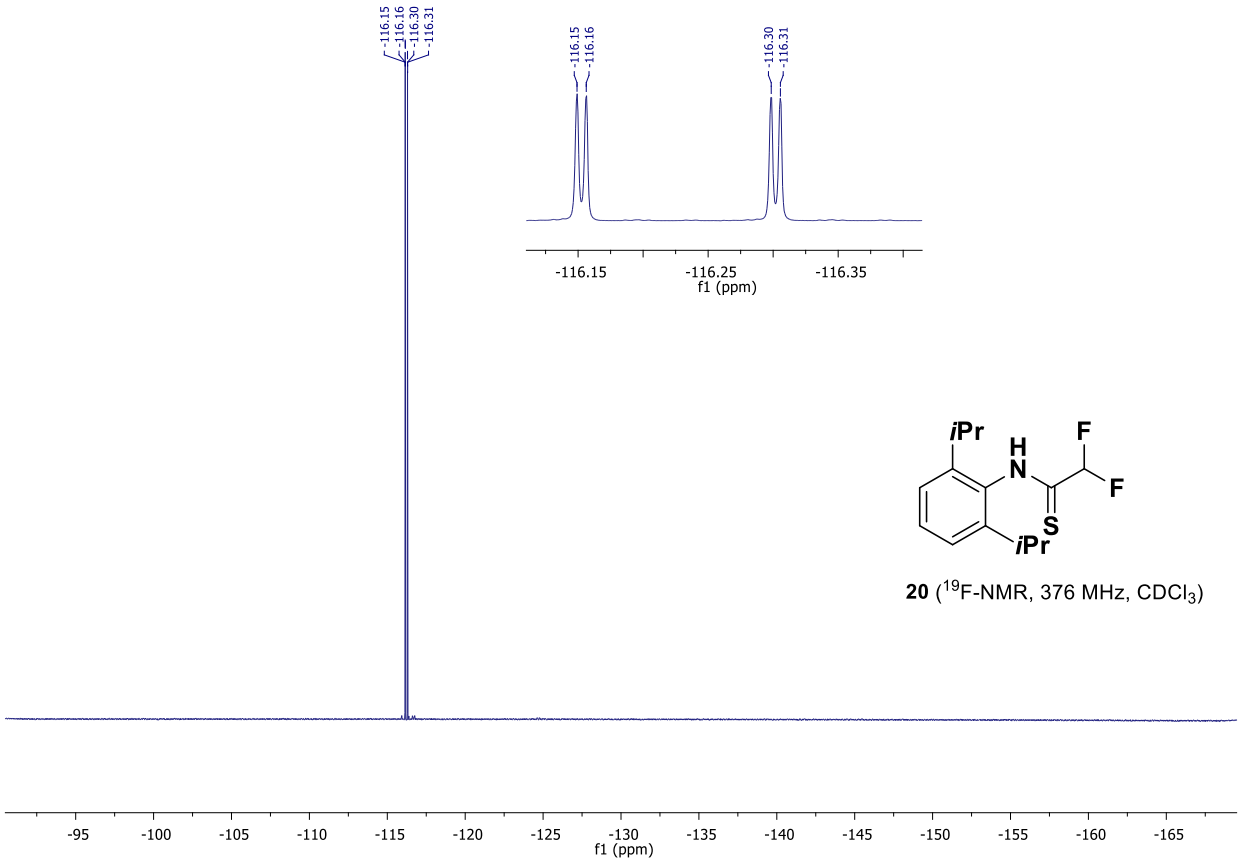
17 (^{19}F-NMR, 376 MHz, $CDCl_3$)



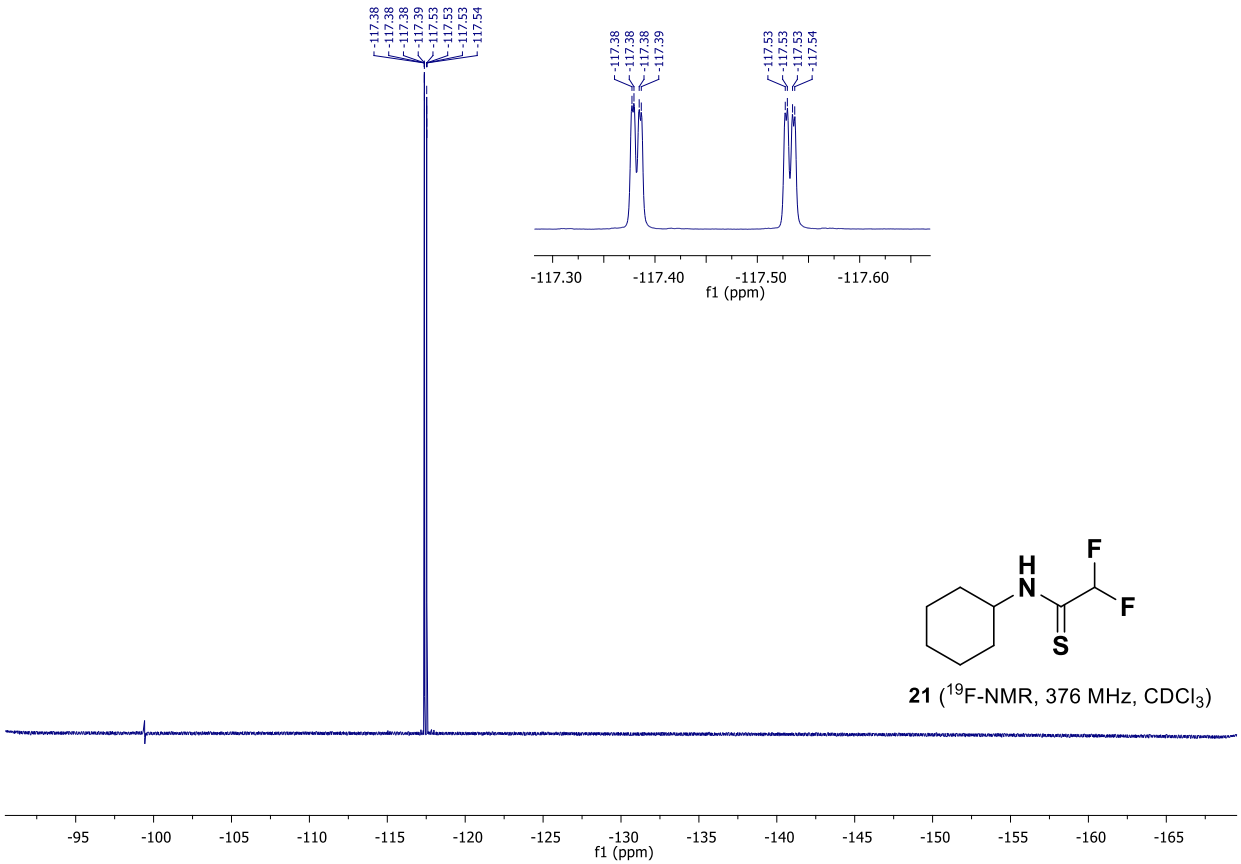
18 (^{19}F-NMR, 376 MHz, $CDCl_3$)



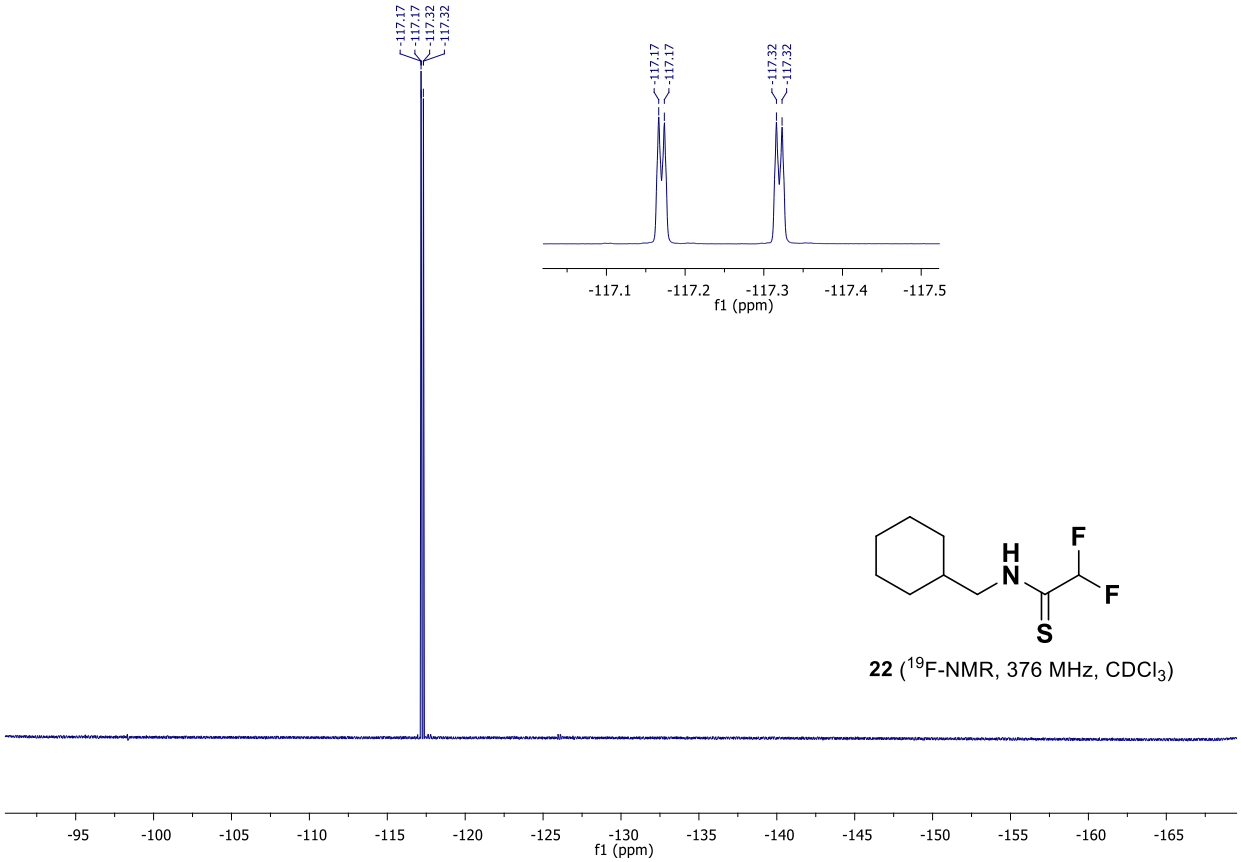
19 (^{19}F-NMR, 376 MHz, C_6D_6)



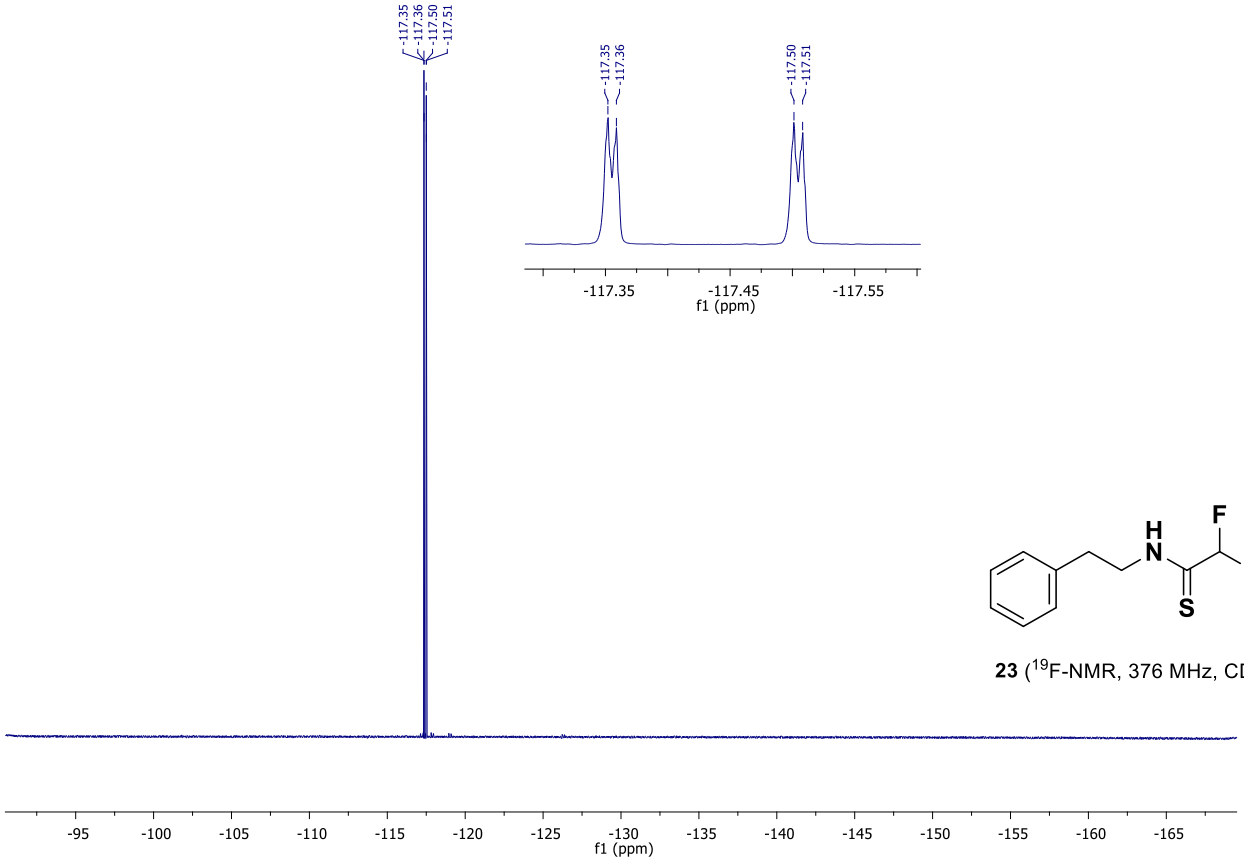
20 (^{19}F-NMR, 376 MHz, $CDCl_3$)



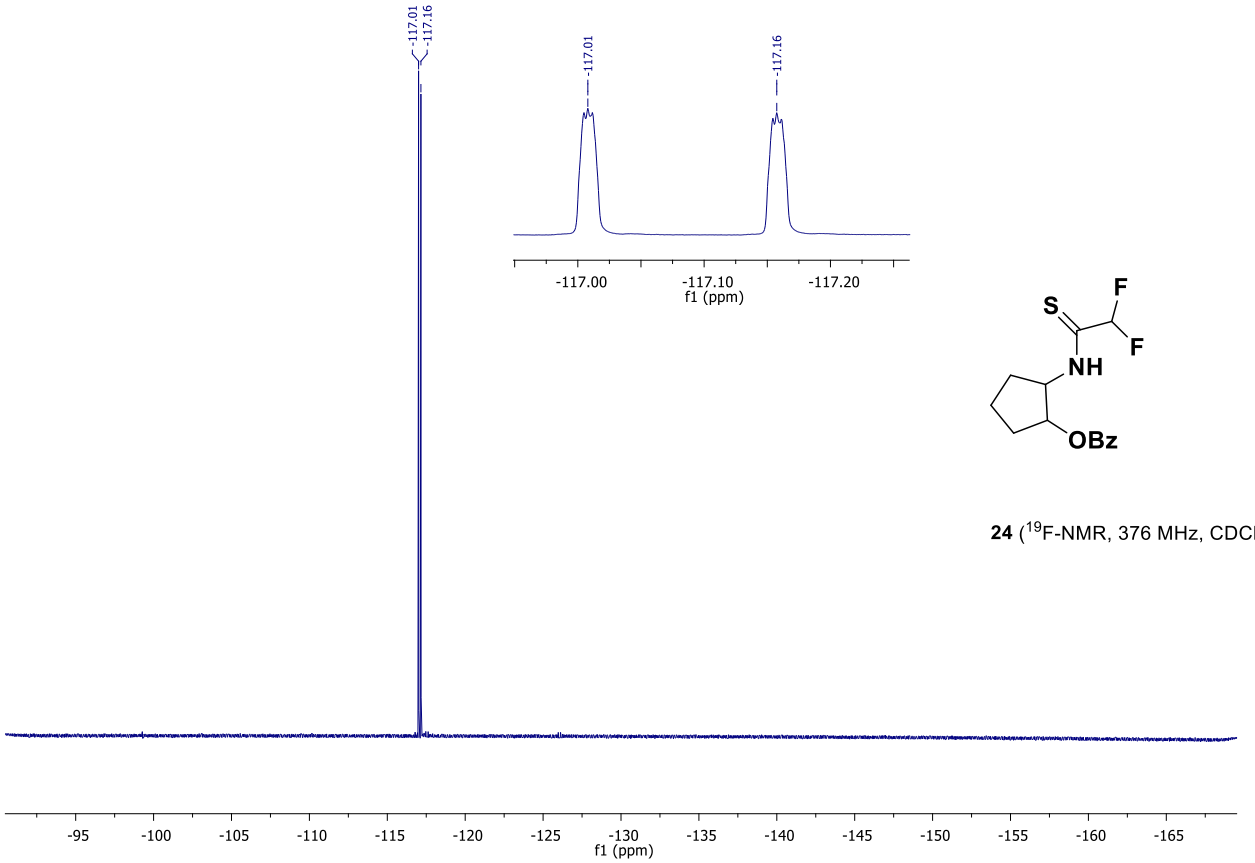
21 (^{19}F-NMR, 376 MHz, $CDCl_3$)



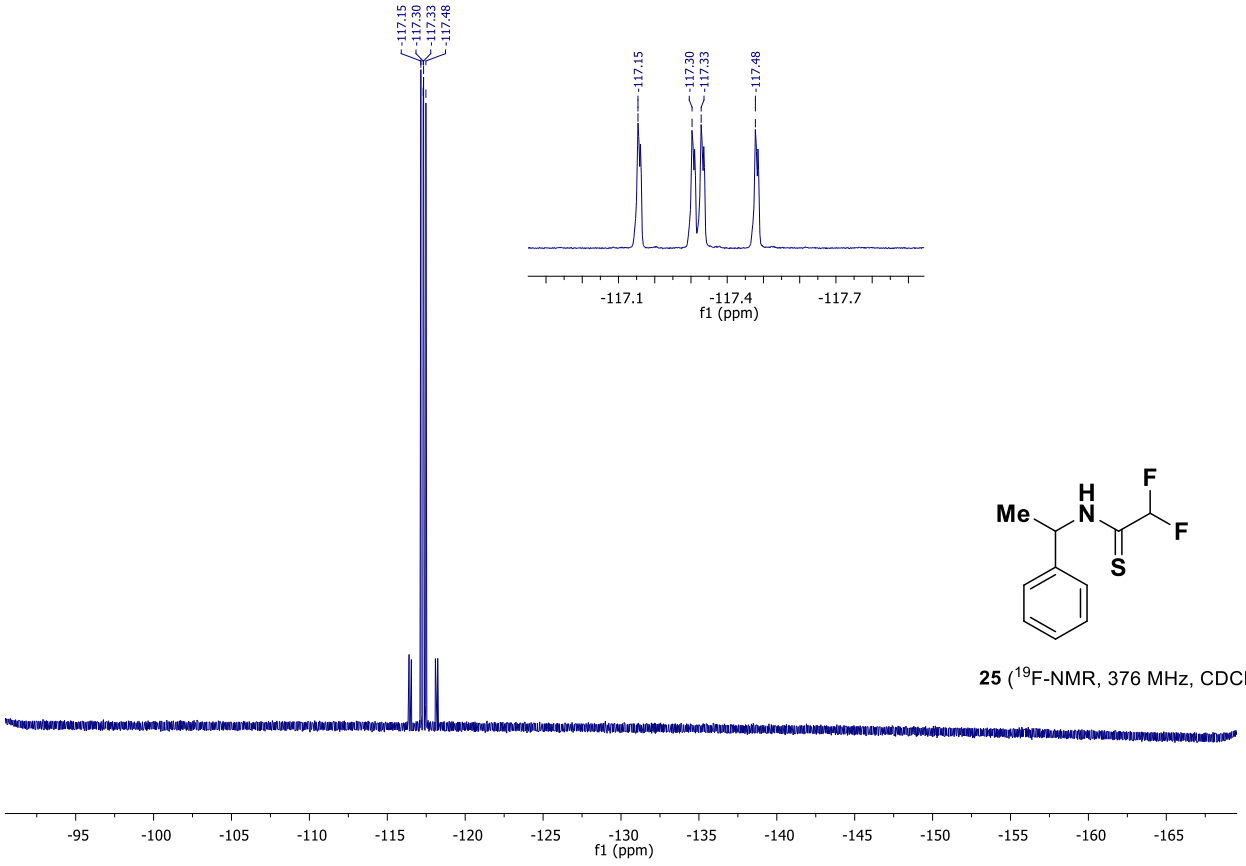
22 (^{19}F-NMR, 376 MHz, $CDCl_3$)



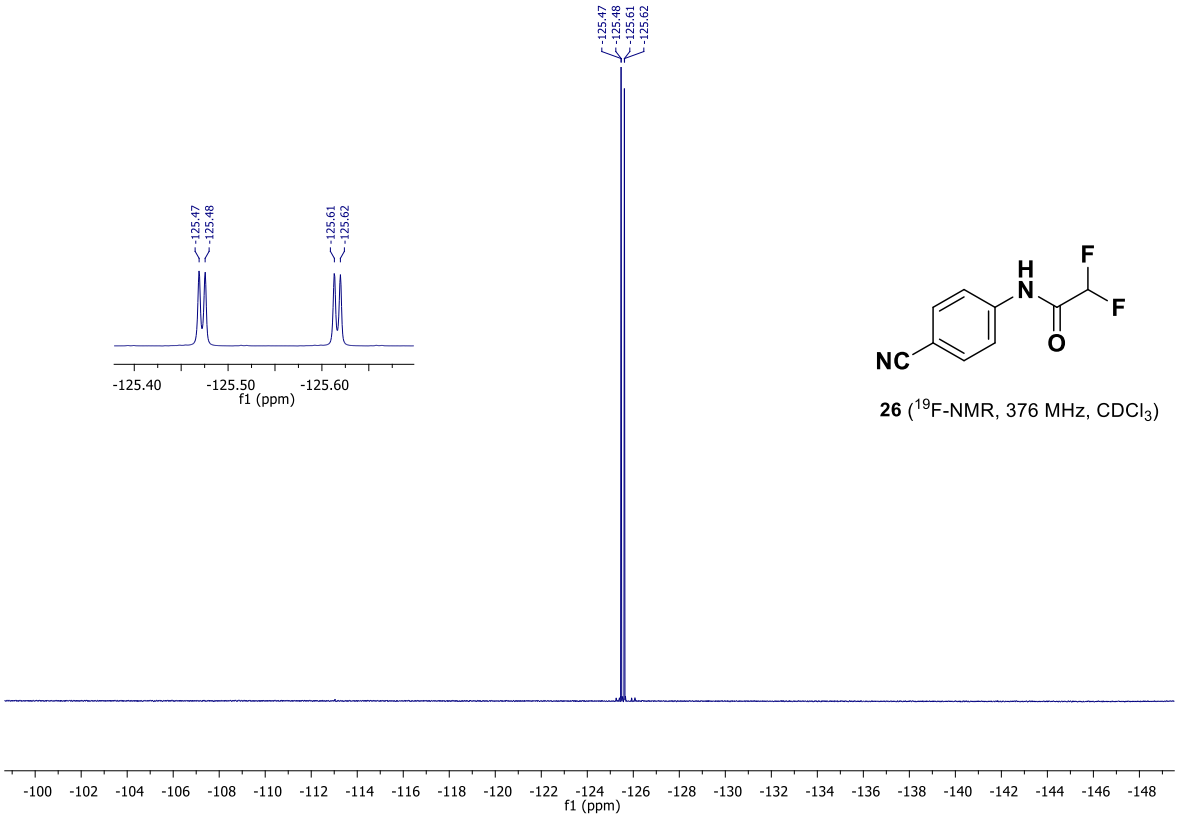
23 (^{19}F-NMR, 376 MHz, $CDCl_3$)



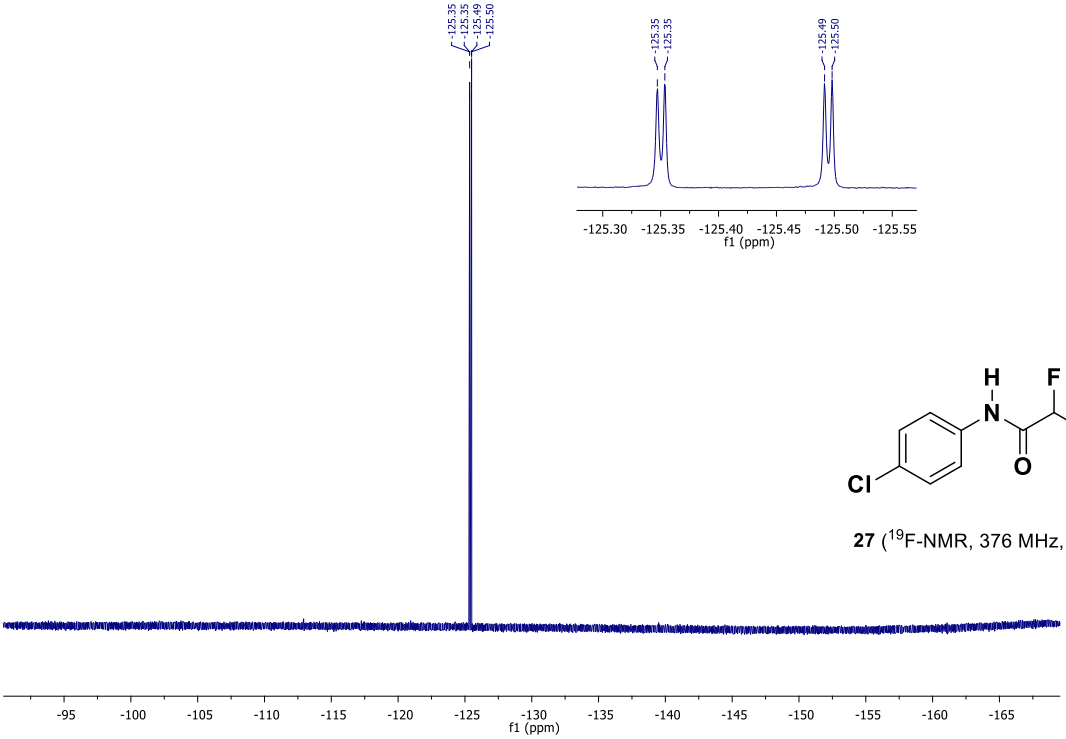
24 (^{19}F-NMR, 376 MHz, $CDCl_3$)



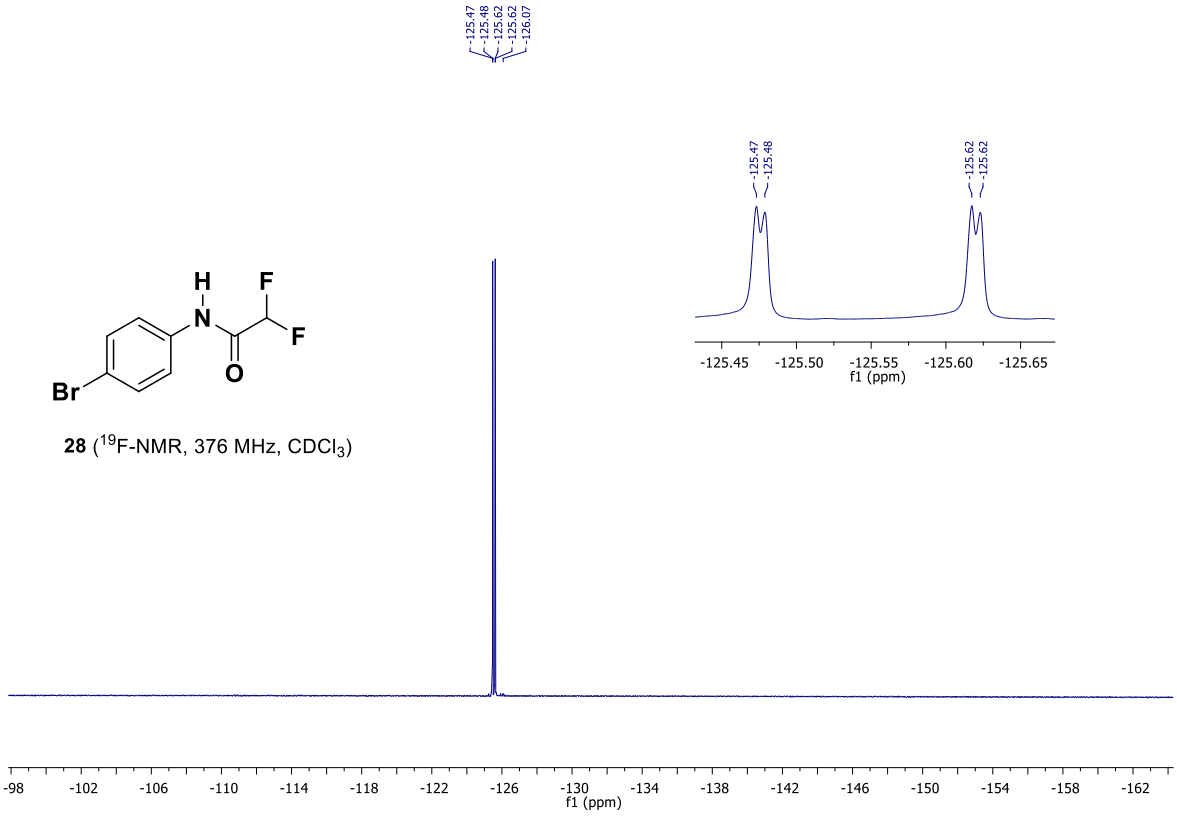
25 (^{19}F-NMR, 376 MHz, $CDCl_3$)



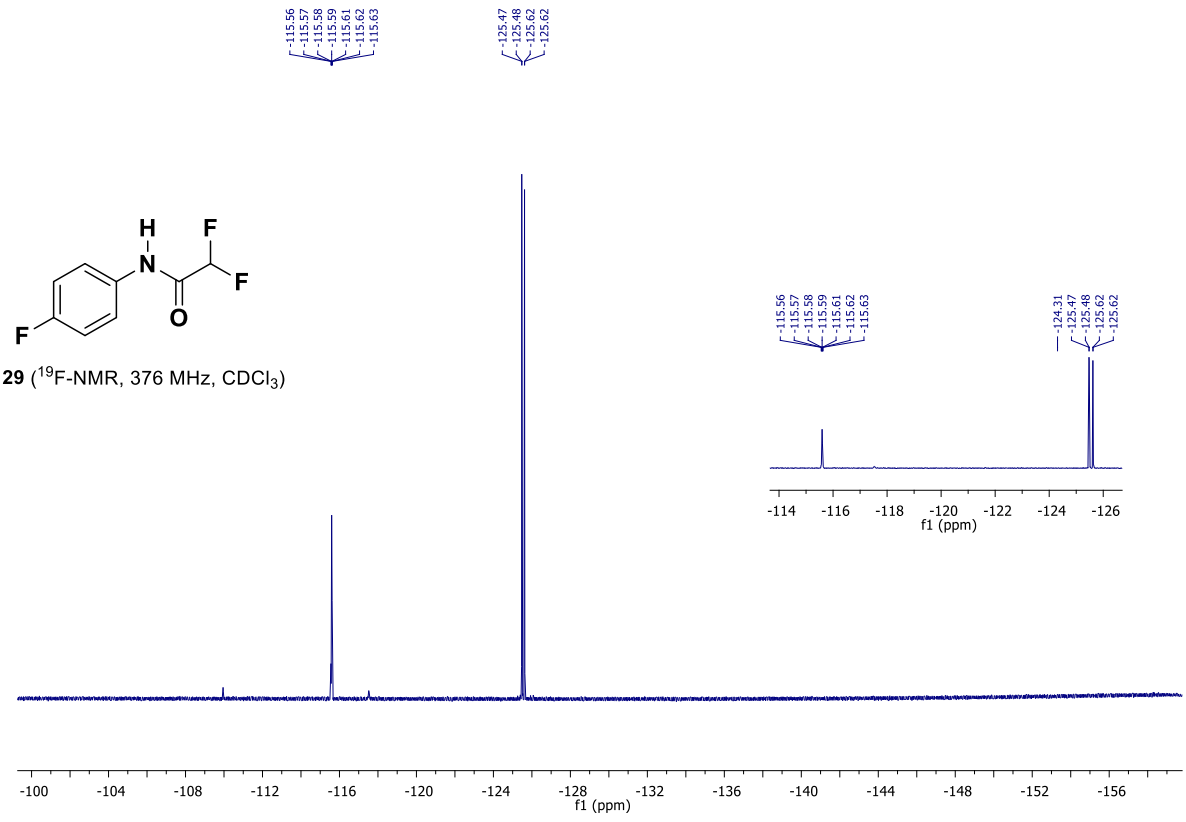
26 (^{19}F-NMR, 376 MHz, $CDCl_3$)



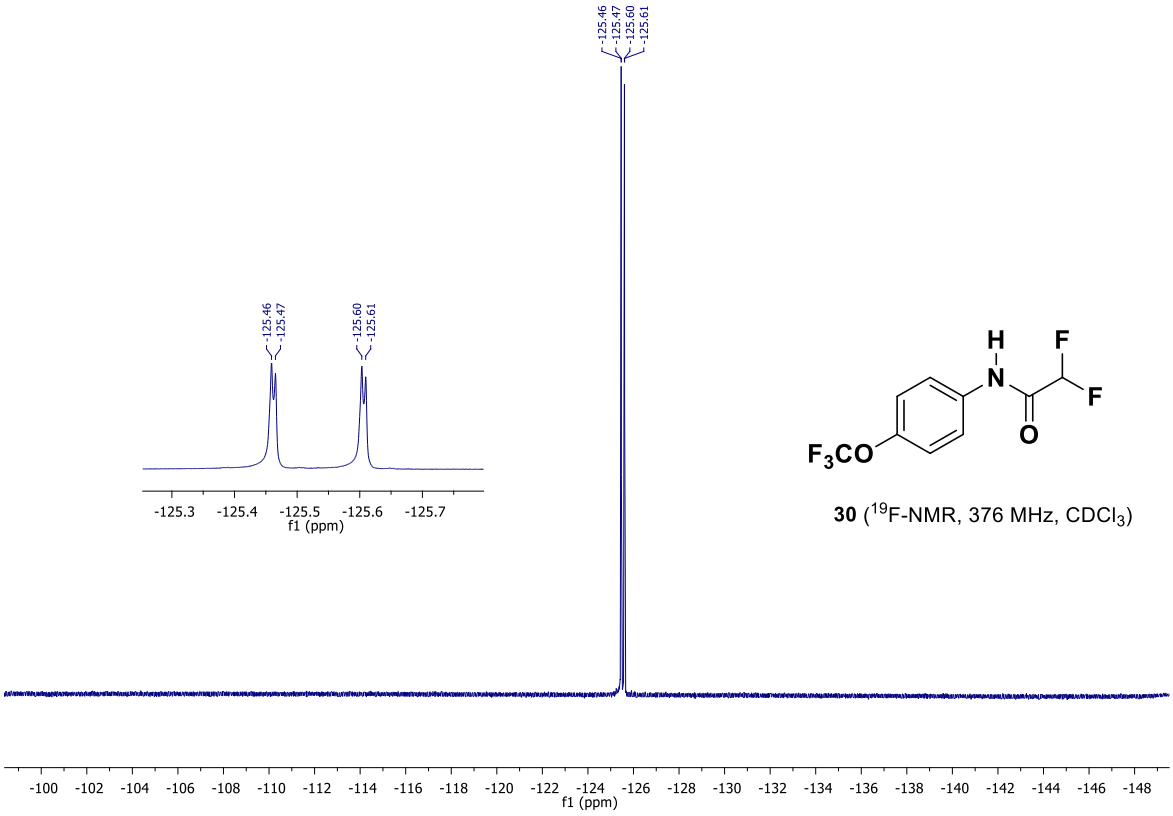
27 (^{19}F-NMR, 376 MHz, $CDCl_3$)



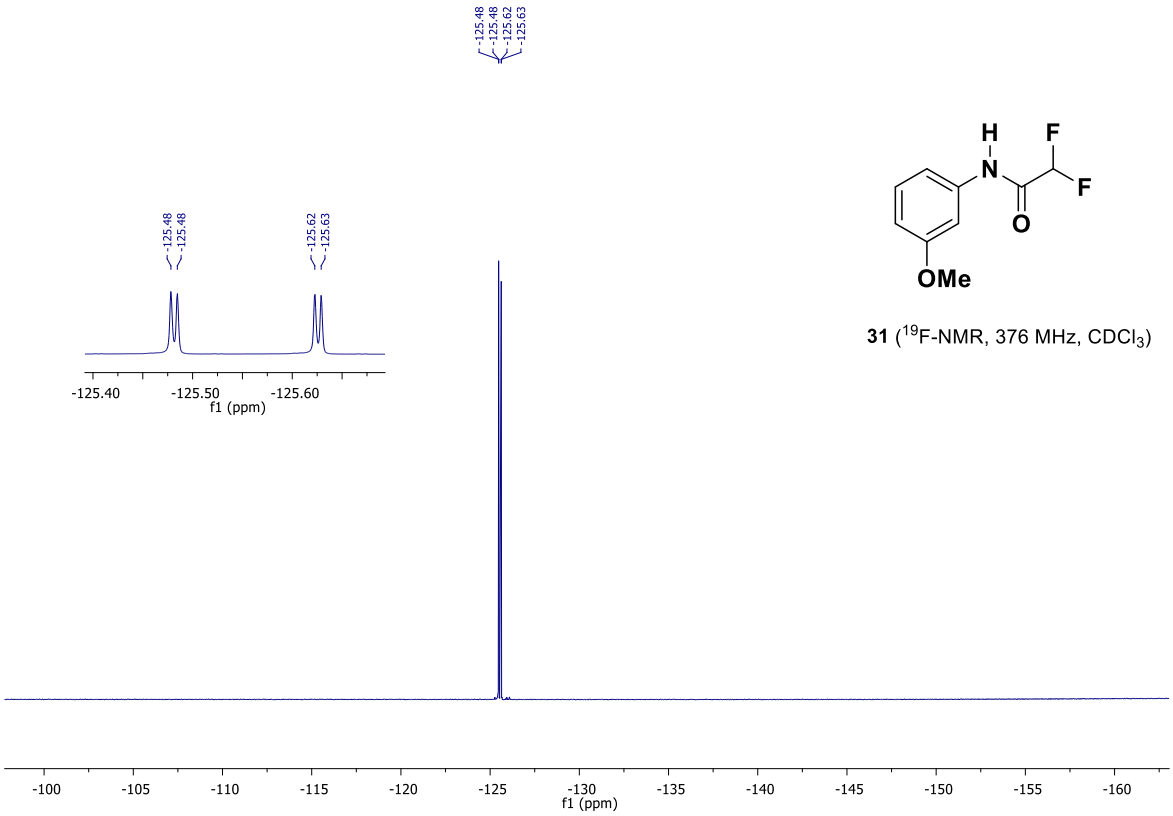
28 (^{19}F-NMR, 376 MHz, $CDCl_3$)



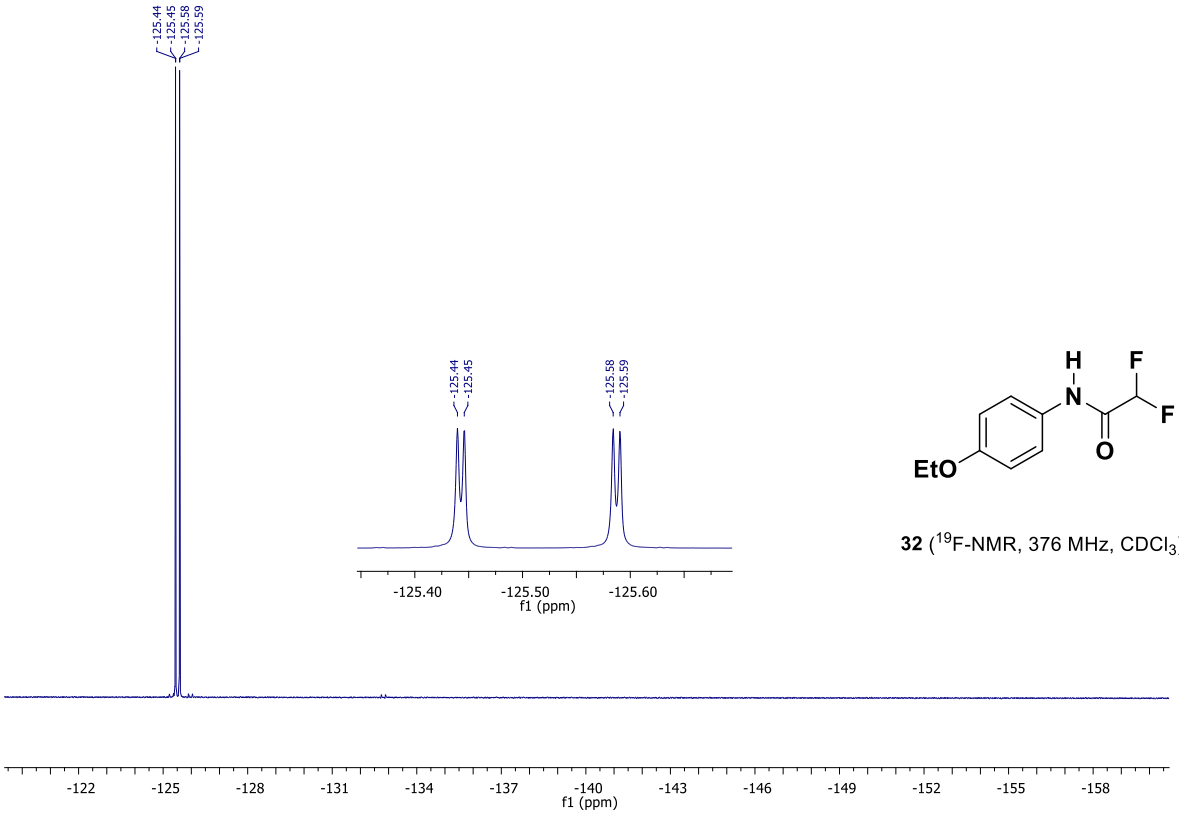
29 (^{19}F-NMR, 376 MHz, $CDCl_3$)



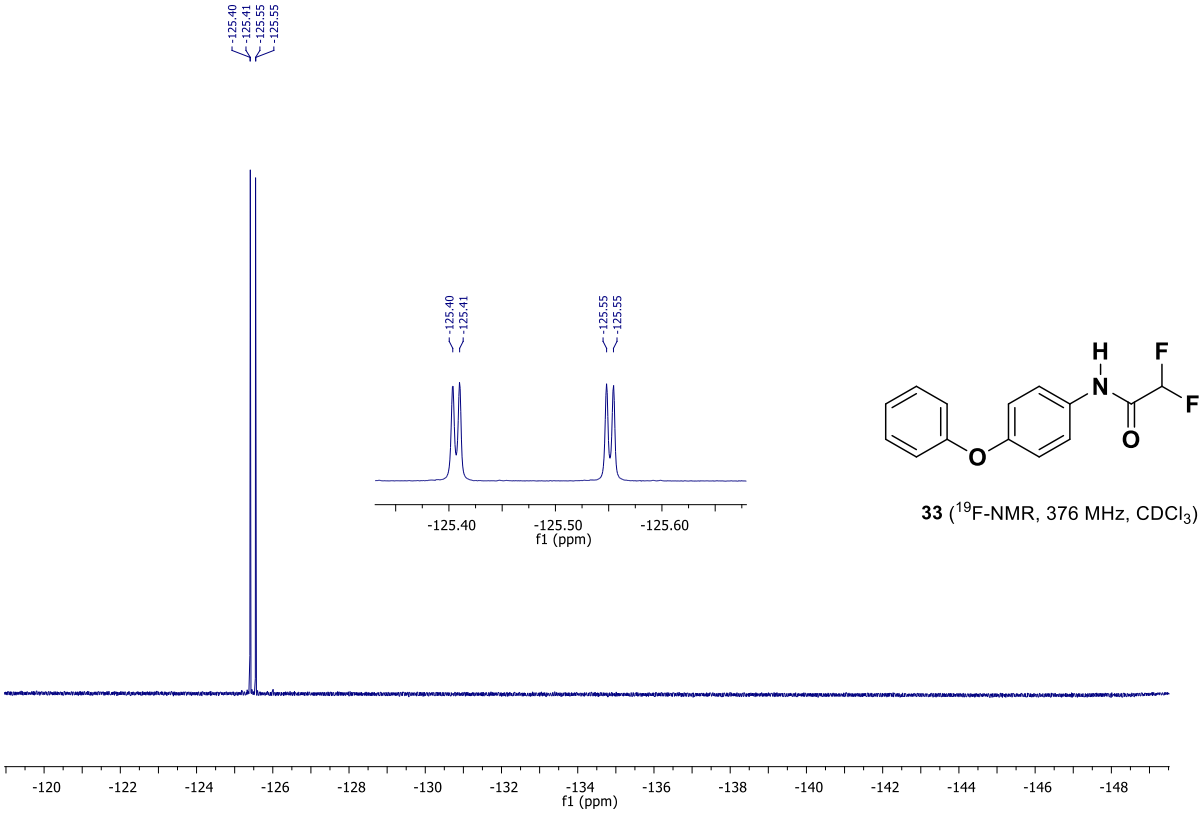
30 (^{19}F-NMR, 376 MHz, $CDCl_3$)



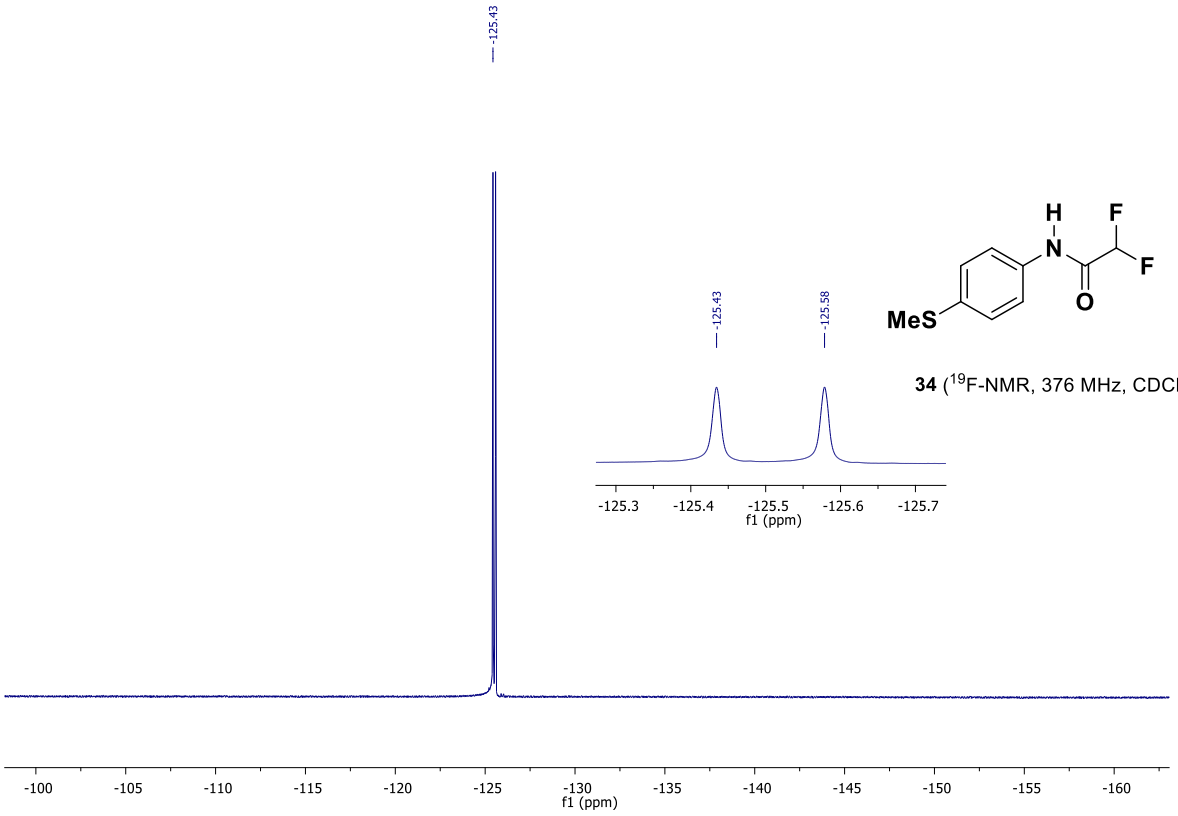
31 (^{19}F-NMR, 376 MHz, $CDCl_3$)



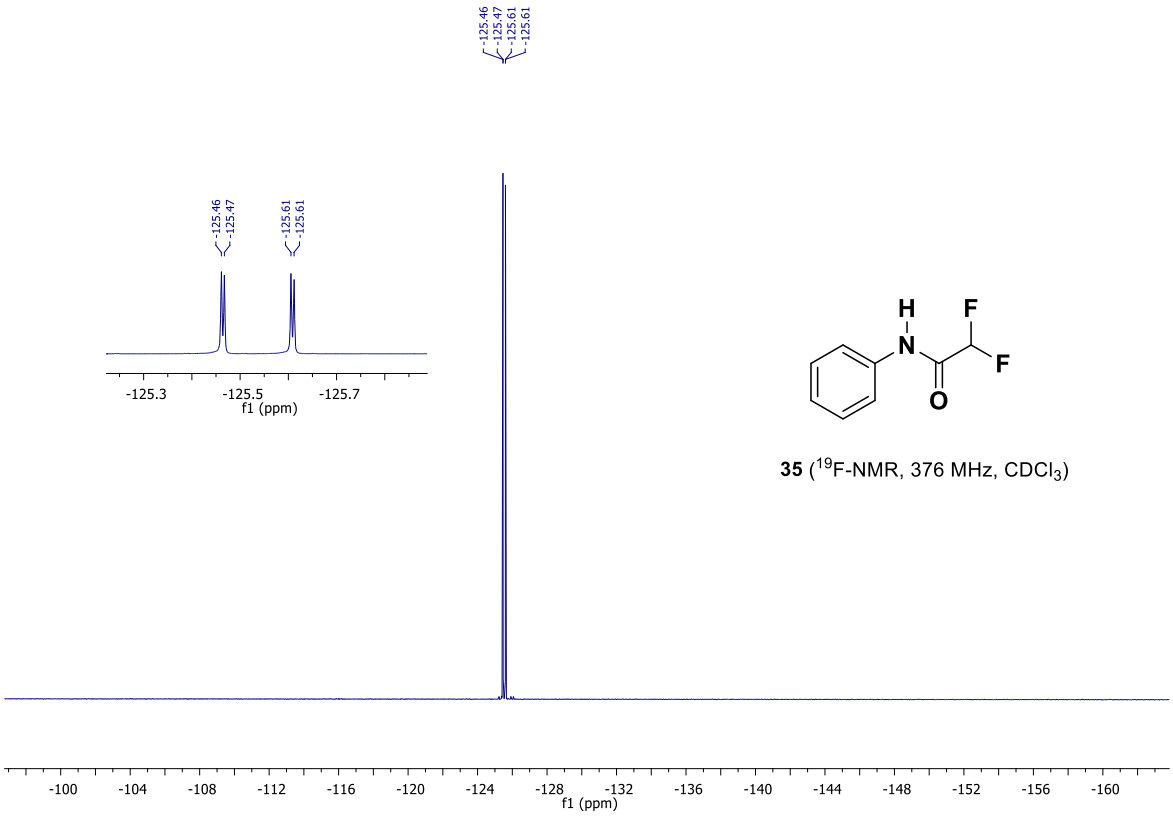
32 (^{19}F-NMR, 376 MHz, $CDCl_3$)



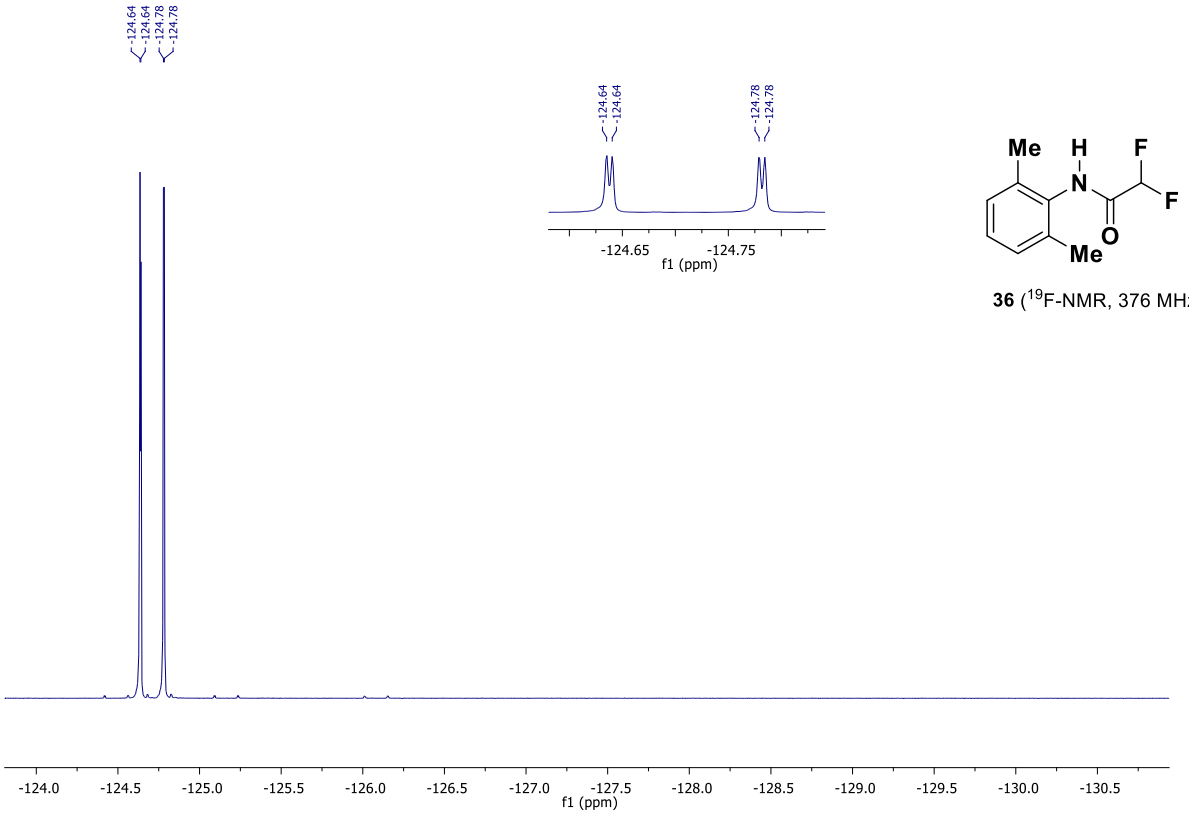
33 (^{19}F-NMR, 376 MHz, $CDCl_3$)



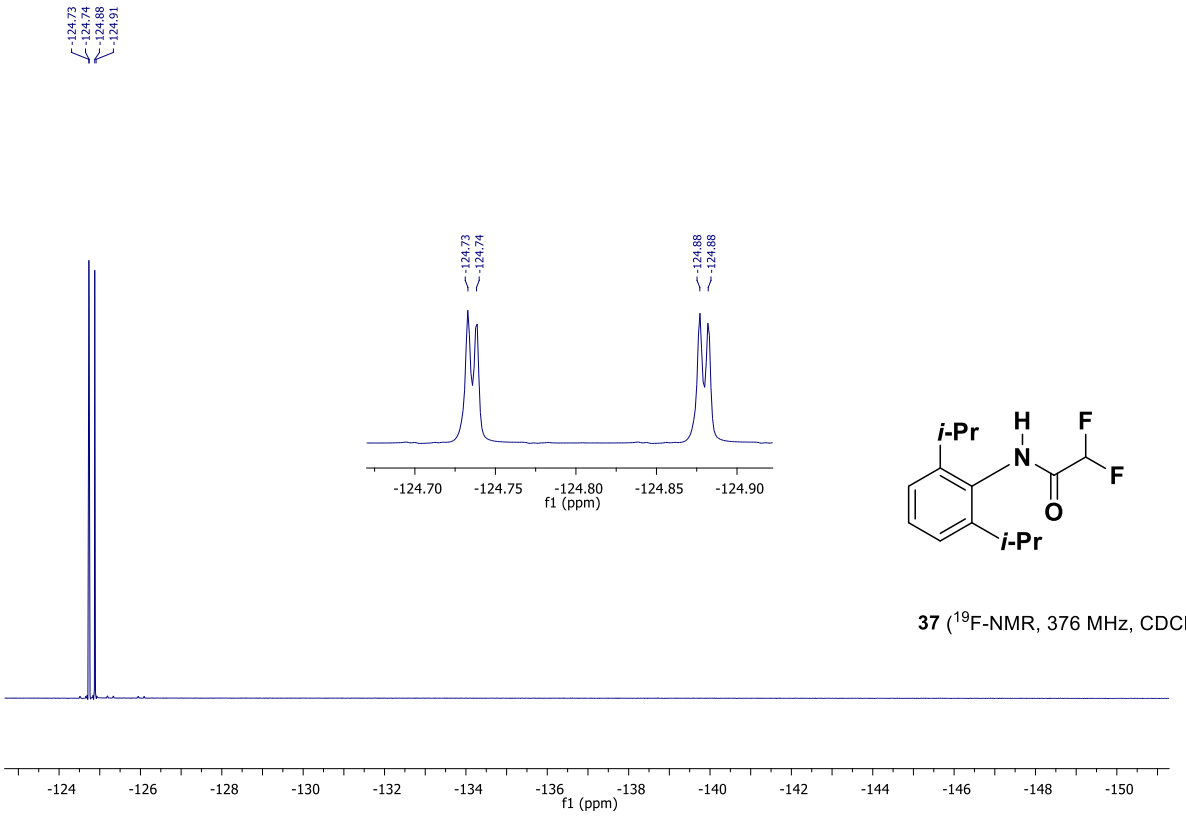
34 (^{19}F-NMR, 376 MHz, $CDCl_3$)



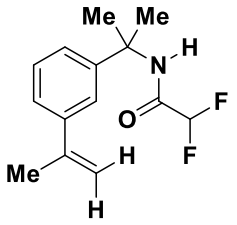
35 (^{19}F-NMR, 376 MHz, $CDCl_3$)



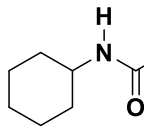
36 (^{19}F-NMR, 376 MHz, $CDCl_3$)



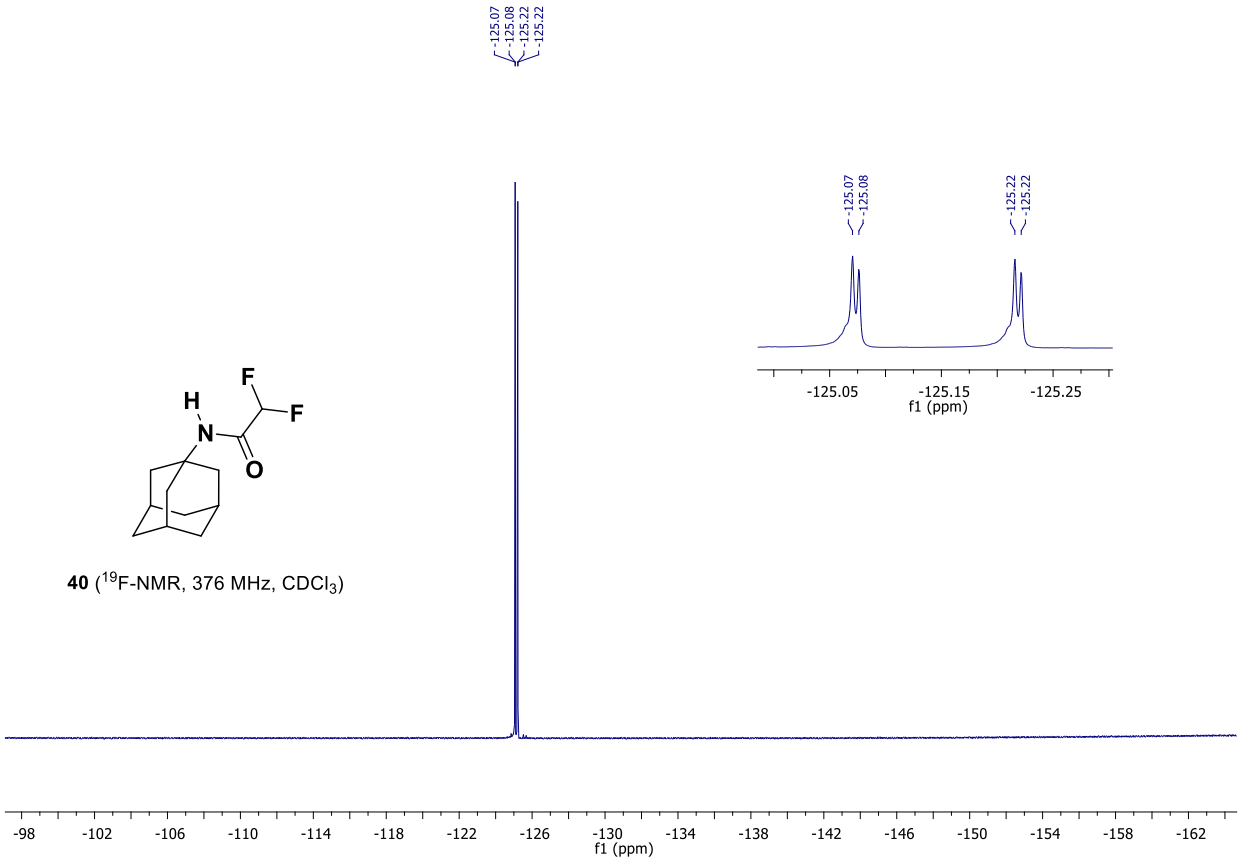
37 (^{19}F-NMR, 376 MHz, $CDCl_3$)



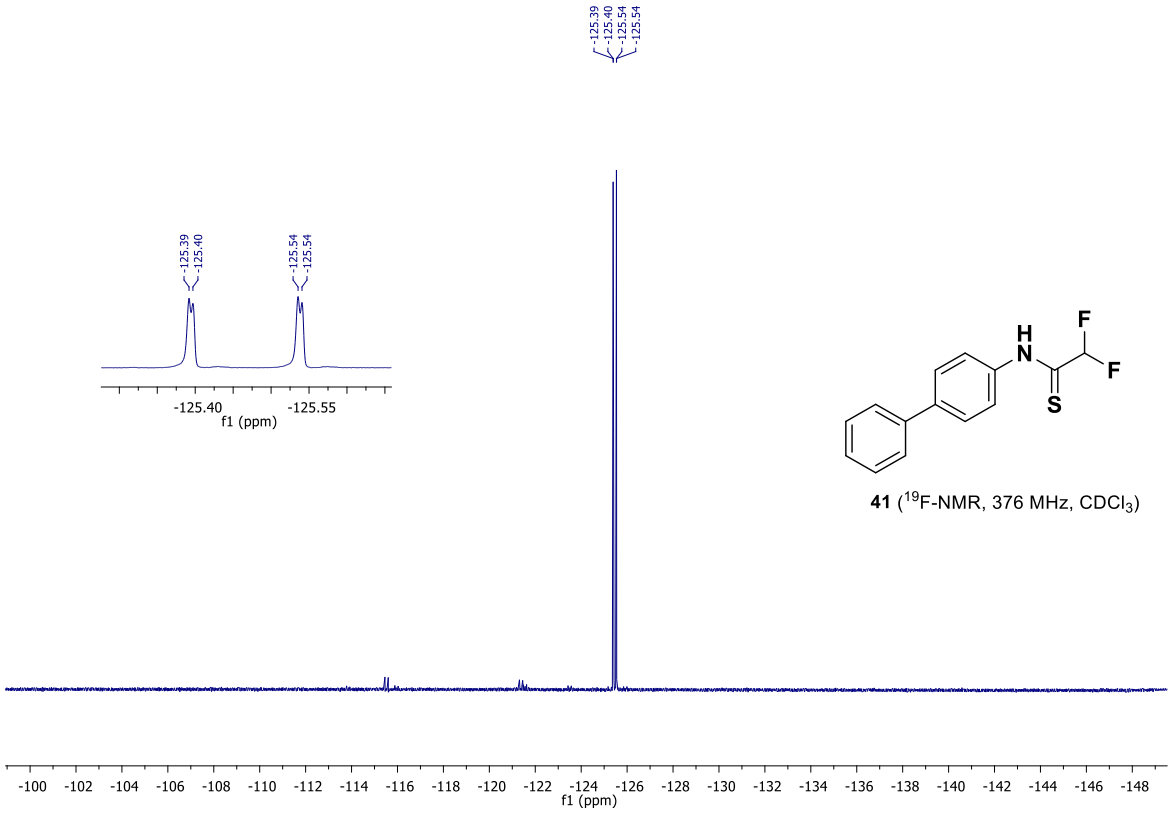
38 (^{19}F-NMR, 376 MHz, $CDCl_3$)



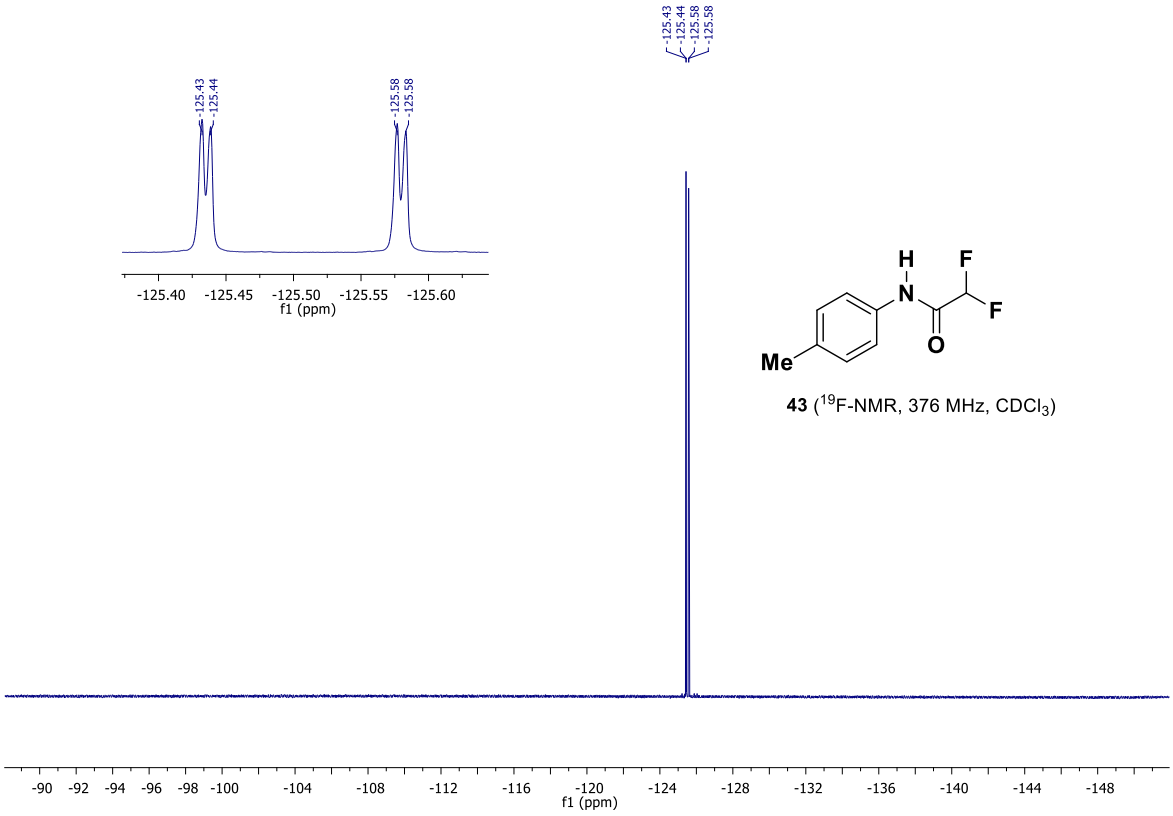
39 (^{19}F-NMR, 376 MHz, $CDCl_3$)



40 (^{19}F-NMR, 376 MHz, $CDCl_3$)



41 (^{19}F-NMR, 376 MHz, $CDCl_3$)



43 (^{19}F-NMR, 376 MHz, $CDCl_3$)

8. References

1. P. J. Czerwiński and B. Furman, *Chem. Commun.*, 2019, **55**, 9436.
2. D. C. England, L. R. Melby, M. A. Dietrich and R. V. Lindsey, *J. Am. Chem. Soc.*, 1960, **82**, 5116.