Supporting Information for

Direct Synthesis of Acyl Fluorides from Carboxylic Acids with the Bench-Stable Solid Reagent $(Me_4N)SCF_3$

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1. General experimental details

Reagents. $(Me_4N)SCF_3$ was prepared according to the corresponding literature procedure.[1] Anhydrous tetramethylammonium fluoride and (trifluoromethyl)trimethylsilane were purchased from ABCR and sulfur from Sigma Aldrich. Unless otherwise stated, all starting materials were commercially available and used as received.

Solvents. CH_2Cl_2 and pentane were of technical grade.

Characterization. All ^1H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at ambient temperature either on Varian V-NMRS 600 or Varian V-NMRS 400 spectrometers. Chemical shifts (δ) are quoted in parts per million (ppm) and were referenced to the residual solvent peak in the case of ^1H and ^{13}C NMR spectra. Coupling constants (J) are given in Hz. The resonance multiplicity is described as s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sex (sextet), hept (heptet), m (multiplet), dd (doublet of doublets) and br (broad). ^{19}F NMR spectra were recorded using the F-H decoupled pulse sequence from the Varian program library. The peak observed at 83.3 ppm in ^{13}C NMR measured at 151 MHz is an artifact from the instrument.

High Resolution Mass Spectrometric analysis were performed on a Thermo Scientific LTQ Orbitrap XL (ESI), and on a Finnigan SSQ 7000, EI: 70 eV (EI). IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum 100 using ATR-Unit. Optical rotations were measured on a Perkin-Elmer 241 polarimeter.

Reactions were followed with an Agilent Technologies 5975 series MSD mass spectrometer coupled with an Agilent Technologies 7820A gas chromatograph (with an Agilent 19091s-433 HP-SMS column (30 m x 0.250 µm x 0.25 µm)).

(GC-MS Conditions: Front inlet mode: split; Temperature: 250°C; Pressure: 10.42 psi; Total flow 22.7 ml/min; Split ratio: 20:1; Split flow: 20 ml/min; Run time: 25.5 min; Oven Program: 60°C for 0.5 min then 10°C/min to 280°C for 3 min; Flow 1.2 ml/min.)

2. General experimental procedures and compound characterization data

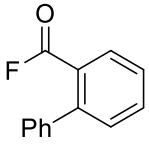
General procedure for the synthesis of compounds from Scheme 1 and Figure 2 (top and middle):

Under air atmosphere, the carboxylic acid (0.2 mmol, 1 equiv.) and the $(Me_4N)SCF_3$ salt (39 mg, 0.22 mmol, 1.1 equiv.) were mixed in CH_2Cl_2 (1.5 mL) at room temperature. After the indicated time, pentane (1.5 mL) was added to the reaction mixture which was then filtered through a pad of silica (3 cm). Subsequent wash of the silica pad with a 1/1 mixture of CH_2Cl_2 / pentane (1.5 mL) was performed. The filtrate was then concentrated under reduced pressure to afford the expected product. Unless otherwise stated no further purification was necessary.

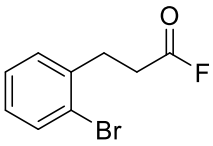
Procedure for the synthesis of the *N*-protected amino acid fluorides from Figure 2 (bottom):

Under air atmosphere, the protected amino acid (0.2 mmol, 1 equiv) was dissolved in CH_2Cl_2 (1 mL) and was added at once to the $(Me_4N)SCF_3$ reagent (0.22 mmol, 39 mg, 1.1 equiv) at room temperature. After stirring for 5 minutes, pentane (1 mL) was added to the reaction mixture which was then filtered through a pad of celite (3 cm). Subsequent wash of the celite pad with a 1/1 mixture of CH_2Cl_2 / pentane (1 mL) was performed. The filtrate was then concentrated at 20 °C under reduced pressure to afford the expected product.

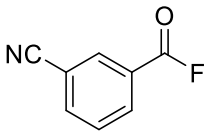
Compounds from Scheme 1:



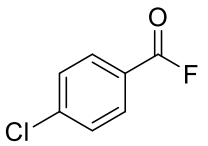
[1,1'-Biphenyl]-2-carbonyl fluoride 1 : The title compound was obtained as a colorless liquid after 1.5 hours in 91% yield (36.3 mg) using [1,1'-biphenyl]-2-carboxylic acid after column chromatography on silica gel with pentane / CH_2Cl_2 (10/1, R_f = 0.27) following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.69 – 7.63 (m, 1H), 7.53 – 7.46 (m, 1H), 7.45 – 7.37 (m, 4H), 7.35 – 7.29 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 35.0. ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.5 (d, *J* = 348.1 Hz), 145.5 (d, *J* = 2.4 Hz), 140.1, 133.9, 132.2 (d, *J* = 2.7 Hz), 131.7 (d, *J* = 2.4 Hz), 128.4, 128.2, 127.9, 127.6, 124.2 (d, *J* = 56.8 Hz). HRMS (EI) calculated for $C_{13}H_9OF$: 200.0632 $[M]^+$, Found: 200.0631.



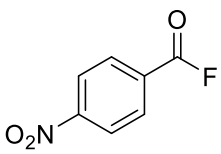
3-(2-bromophenyl)propanoyl fluoride 2 : The title compound was obtained as an orange liquid after 30 minutes in 93% yield (42.8 mg) using 3-(2-bromophenyl)propanoic acid after filtration over silica following the general procedure. ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.57 (d, *J* = 7.9 Hz, 1H), 7.32 – 7.26 (m, 2H), 7.16 – 7.11 (m, 1H), 3.11 (t, *J* = 7.6 Hz, 2H), 2.88 (t, *J* = 7.6 Hz, 2H). ^{19}F NMR (376 MHz, CD_2Cl_2) δ 44.3. ^{13}C NMR (101 MHz, CD_2Cl_2) δ 162.6 (d, *J* = 359.8 Hz), 138.2, 132.9, 130.6, 128.6, 127.8, 124.1, 31.9 (d, *J* = 50.9 Hz), 30.4 (d, *J* = 2.5 Hz). HRMS (EI) calculated for $C_9H_8O^{79}BrF$: 229.9743 $[M]^+$, Found: 229.9737.



3-Cyanobenzoyl fluoride 3 : The title compound was obtained as a light yellow solid after 1 hour in 75% yield (22.4 mg) using 3-cyanobenzoic acid after filtration over silica following the general procedure. M.p. = 75-76 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 – 8.29 (m, 1H), 8.29 – 8.24 (m, 1H), 8.00 – 7.95 (m, 1H), 7.72 – 7.66 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 19.4. ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4 (d, *J* = 345.2 Hz), 138.2, 135.2 (d, *J* = 3.7 Hz), 134.8 (d, *J* = 3.3 Hz), 130.3, 126.4 (d, *J* = 64.1 Hz), 117.0, 114.0. HRMS (EI) calculated for C_8H_4ONF: 149.0271 $[M]^+$, Found: 149.0271.

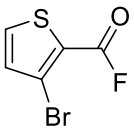


4-Chlorobenzoyl fluoride 4 : The title compound was obtained as a light yellow solid after 30 minutes in 84% yield (26.7 mg) using 4-chlorobenzoic acid after filtration over silica following the general procedure. M.p. = 55-56 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.92 (m, 2H), 7.54 – 7.45 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 18.4. ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.6 (d, *J* = 343.5 Hz), 142.2, 132.7 (d, *J* = 3.8 Hz), 129.5, 123.3 (d, *J* = 62.6 Hz). HRMS (EI) calculated for $C_7H_4O^{35}ClF$: 157.9929 $[M]^+$, Found: 157.9931. The analytical data are in agreement with those reported previously in the literature.[2]

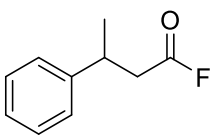


4-Nitrobenzoyl fluoride 5 : The title compound was obtained as a yellow solid after 3 hours in 93% yield (31.5 mg) using 4-nitrobenzoic acid after filtration over silica following the general procedure. M.p. = 144-145 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 – 8.33 (m, 2H), 8.27 – 8.20 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 21.3. ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4 (d, *J* = 346.4 Hz), 151.8, 132.6 (d, *J* = 3.5 Hz), 130.2 (d, *J* = 63.4 Hz),

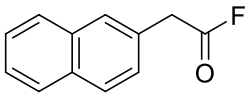
124.1. HRMS (EI) calculated for $C_7H_4O_3NF$: 169.0170 $[M]^+$, Found: 169.0166. The analytical data are in agreement with those reported previously in the literature.[3]



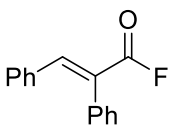
3-Bromothiophene-2-carbonyl fluoride 6 : The title compound was obtained as an off-white solid after 1 hour in 92% yield (38.5 mg) using 3-bromothiophene-2-carboxylic acid after filtration over silica following the general procedure. M.p. = 33-34 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, *J* = 5.2 Hz, 1H), 7.21 (dd, *J* = 5.2, 3.1 Hz, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 33.1. ^{13}C NMR (151 MHz, $CDCl_3$) δ 150.6 (d, *J* = 329.5 Hz), 135.2, 133.8 (d, *J* = 4.2 Hz), 122.6 (d, *J* = 7.1 Hz), 121.8 (d, *J* = 73.9 Hz). HRMS (EI) calculated for $C_5H_2O^{81}BrF^{32}S$: 209.8968 $[M]^+$, Found: 209.8965.



3-Phenylbutanoyl fluoride 7 : The title compound was obtained as a yellow liquid after 30 minutes in 87% yield (29.0 mg) using 3-phenylbutanoic acid after filtration over silica following the general procedure. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 2H), 7.27 – 7.19 (m, 3H), 3.34 – 3.21 (sex, *J* = 7.1 Hz, 1H), 2.86 – 2.69 (m, 2H), 1.37 (d, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 47.2. ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.1 (d, *J* = 361.2 Hz), 144.2, 128.8, 127.0, 126.6, 40.7 (d, *J* = 48.5 Hz), 35.7, 21.6. HRMS (EI) calculated for $C_{10}H_{11}OF$: 166.0788 [M]+, Found: 166.0791.

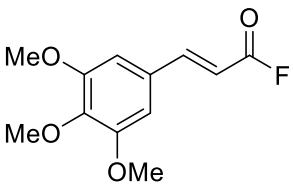


2-(Naphthalen-2-yl)acetyl fluoride 8 : The title compound was obtained as a light yellow solid after 30 minutes in 89% yield (33.5 mg) using 2-(naphthalen-2-yl)acetic acid after filtration over silica following the general procedure. M.p. = 72-73 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 – 7.80 (m, 3H), 7.76 (s, 1H), 7.55 – 7.49 (m, 2H), 7.39 (dd, *J* = 8.4, 1.4 Hz, 1H), 3.98 (d, *J* = 2.1 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 45.2. ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.4 (d, *J* = 362.0 Hz), 133.3, 132.8, 128.8, 128.4, 128.1 (d, *J* = 2.3 Hz), 127.7 (d, *J* = 1.5 Hz), 126.8, 126.6, 126.4, 126.1, 39.1 (d, *J* = 54.7 Hz). HRMS (EI) calculated for $C_{12}H_9OF$: 188.0632 $[M]^+$, Found: 188.0631.

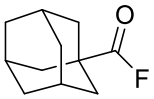


(*E*)-2,3-Diphenylacryloyl fluoride 9 : The title compound was obtained as an off-white solid after 1.5 hours in 98% yield (44.6 mg) using (*E*)-2,3-diphenylacrylic acid after filtration over silica following the general procedure. M.p. = 52-53 °C. ^{1}H NMR (400 MHz,

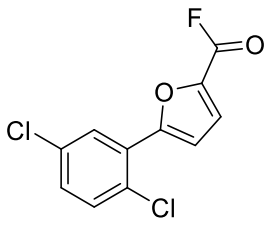
$CDCl_3$) δ 7.93 (s, 1H), 7.47 – 7.35 (m, 3H), 7.32 – 7.23 (m, 3H), 7.23 – 7.16 (m, 2H), 7.09 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 18.9. ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.2 (d, *J* = 346.4 Hz), 146.4, 133.8, 133.4, 131.1, 130.5, 129.6, 129.1, 128.7, 128.5, 127.4 (d, *J* = 55.4 Hz). HRMS (EI) calculated for $C_{15}H_{11}OF$: 226.0788 $[M]^+$, Found: 226.0790.



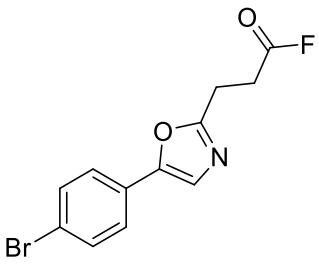
(*E*)-3-(3,4,5-Trimethoxyphenyl)acryloyl fluoride 10 : The title compound was obtained as a white solid after 1.5 hours in 85% yield (40.7 mg) using (*E*)-3-(3,4,5-trimethoxyphenyl)acrylic acid after filtration over silica following the general procedure. M.p. = 102-103 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 15.9 Hz, 1H), 6.76 (s, 2H), 6.24 (dd, *J* = 15.9, 7.3 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 25.2 (d, *J* = 7.3 Hz). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.1 (d, *J* = 337.7 Hz), 153.5, 151.3 (d, *J* = 4.9 Hz), 141.4, 128.5, 111.1 (d, *J* = 67.2 Hz), 105.9, 61.0 (d, *J* = 2.4 Hz), 56.2 (d, *J* = 2.4 Hz). HRMS (EI) calculated for $C_{12}H_{13}O_4F$: 240.0792 $[M]^+$, Found: 240.0796. The analytical data are in agreement with those reported previously in the literature.[4]



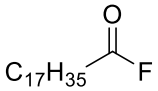
1-Adamantanecarbonyl fluoride 11 : The title compound was obtained as a colorless oil after 30 minutes in 89% yield (32.4 mg) using 1-adamantanecarboxylic acid after filtration over silica following the general procedure. ^1H NMR (400 MHz, $CDCl_3$) δ 2.07 – 2.03 (m, 3H), 1.95 (d, *J* = 2.7 Hz, 6H), 1.76 – 1.69 (m, 6H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 23.8. ^{13}C NMR (151 MHz, $CDCl_3$) δ 167.1 (d, *J* = 371.7 Hz), 40.6 (d, *J* = 44.7 Hz), 37.8, 36.1, 27.3. *m/z* (EI) 182 (M, 3), 135 (100). The analytical data are in agreement with those reported previously in the literature.[2]



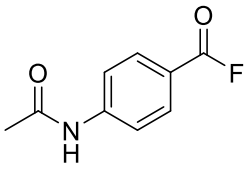
5-(2,5-Dichlorophenyl)furan-2-carbonyl fluoride 12 : The title compound was obtained as a yellow solid after 1 hour in 98% yield (50.6 mg) using 5-(2,5-dichlorophenyl)furan-2-carboxylic acid after filtration over silica following the general procedure. M.p. = 119-120 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 2.5 Hz, 1H), 7.50 (d, *J* = 3.8 Hz, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.34 – 7.27 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 15.4. ^{13}C NMR (151 MHz, $CDCl_3$) δ 155.4 (d, *J* = 2.6 Hz), 148.2 (d, *J* = 327.2 Hz), 138.2 (d, *J* = 91.4 Hz), 133.5, 132.1, 130.4, 129.6, 128.7, 128.4, 124.8, 113.7. HRMS (EI) calculated for $C_{11}H_5O_2{}^{35}Cl_2F$: 257.9645 $[M]^+$, Found: 257.9645.



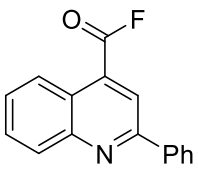
3-(5-(4-Bromophenyl)oxazol-2-yl)propanoyl fluoride 13 : The title compound was obtained as an off-white solid after 30 minutes in 77% yield (46.0 mg) using 3-(5-(4-bromophenyl)oxazol-2-yl)propanoic acid after filtration over celite following the general procedure. M.p. = 88-89 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.55 – 7.52 (m, 2H), 7.48 – 7.45 (m, 2H), 7.24 (s, 1H), 3.20 (t, *J* = 7.1 Hz, 2H), 3.09 (t, *J* = 7.1 Hz, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 44.3. ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.2 (d, *J* = 358.7 Hz), 161.4, 150.8, 132.1, 126.6, 125.5, 122.4, 122.3, 29.0 (d, *J* = 55.7 Hz), 22.8 (d, *J* = 3.4 Hz). HRMS (EI) calculated for $C_{12}H_9O_2N^{79}BrF$: 296.9795 $[M]^+$, Found: 296.9793.



Stearoyl fluoride 14 : The title compound was obtained as a white solid after 30 minutes in 95% yield (54.3 mg) using stearic acid after filtration over silica following the general procedure. M.p. = 33-34 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (t, *J* = 7.4 Hz, 2H), 1.65 (p, *J* = 7.4 Hz, 2H), 1.36 – 1.21 (m, 28H), 0.86 (t, *J* = 6.8 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 45.4. ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.6 (d, *J* = 360.8 Hz), 32.1 (d, *J* = 50.0 Hz), 31.9 , 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.4, 29.3, 29.1, 28.7, 23.9, 23.9, 22.7, 14.1. HRMS (EI) calculated for $C_{18}H_{35}OF$: 286.2667 $[M]^+$, Found: 286.2664. The analytical data are in agreement with those reported previously in the literature.[5]

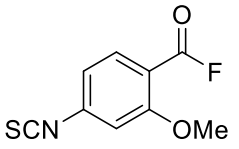


4-Acetamidobenzoyl fluoride 15 : The title compound was obtained as a white solid after 1.5 hours in 96% yield (34.7 mg) using 4-acetamidobenzoic acid after filtration over silica. The reaction was performed in acetonitrile following the general procedure. M.p. = 186-187°C. ^{1}H NMR (400 MHz, CD_3CN) δ 8.70 (brs, 1H), 8.02 – 7.95 (m, 2H), 7.80 – 7.74 (m, 2H), 2.11 (s, 3H). ^{19}F NMR (376 MHz, CD_3CN) δ 14.6. ^{13}C NMR (151 MHz, CD_3CN) δ 174.6, 162.3 (d, *J* = 339.7 Hz), 151.0, 138.0, 123.9, 122.6, 28.9. HRMS (EI) calculated for $C_9H_8O_2NF$: 181.0534 $[M]^+$, Found: 181.0534.

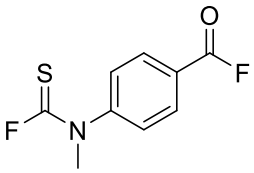


2-Phenylquinoline-4-carbonyl fluoride 16 : The title compound was obtained as a white solid after 1 hour in 89% yield (45.0 mg) using 2-phenylquinoline-4-carboxylic acid after filtration over silica following the general procedure. M.p. = 91-92 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (d, *J* = 8.6 Hz, 1H), 8.51 (s, 1H), 8.28 (d, *J* = 8.4 Hz,

1H), 8.22 – 8.19 (m, 2H), 7.86 – 7.82 (m, 1H), 7.74 – 7.70 (m, 1H), 7.58 – 7.54 (m, 2H), 7.54 – 7.50 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 32.4. ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.7, 155.5 (d, *J* = 349.3 Hz), 149.4 (d, *J* = 3.4 Hz), 138.0, 130.7, 130.6, 130.2, 129.1, 129.1 (d, *J* = 58.6 Hz), 127.4, 124.6, 123.8 (d, *J* = 6.0 Hz), 122.4. HRMS (EI) calculated for $C_{16}H_{10}ONF$: 251.0741 $[M]^+$, Found: 251.0741.

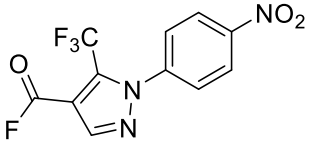


4-Isothiocyanato-2-methoxybenzoyl fluoride 17 : The title compound was obtained as a white solid after 1 hour in 69% yield (29.1 mg) using 4-amino-2-methoxybenzoic acid and 2.2 equiv. of the $(Me_4N)SCF_3$ salt (78 mg, 0.44 mmol) after filtration over silica following the general procedure. M.p. = 116-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 1H), 6.87 (dd, *J* = 8.4, 1.5 Hz, 1H), 6.80 (s, 1H), 3.93 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 31.7. ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4 (d, *J* = 4.0 Hz), 154.0 (d, *J* = 341.7 Hz), 139.3, 139.2, 135.1 (d, *J* = 2.3 Hz), 117.8, 111.9 (d, *J* = 60.5 Hz), 109.4 (d, *J* = 2.6 Hz), 56.4. HRMS (EI) calculated for $C_9H_6O_2NF^{32}S$: 211.0098 $[M]^+$, Found: 211.0088.



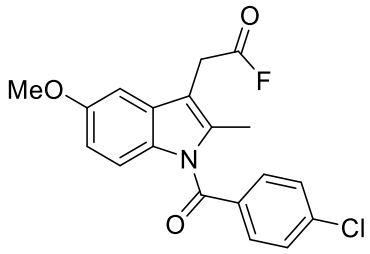
4-((Fluorocarbonothioyl)(methyl)amino)benzoyl fluoride 18 : The title compound was obtained as an off-white solid after 1 hour in 92% yield (39.6 mg) using 4-(methylamino)benzoic acid and 2.2 equiv. of the $(Me_4N)SCF_3$ salt (78 mg, 0.44 mmol) after filtration over silica following the general procedure. M.p. = 72-73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J* = 8.5 Hz, 2H), 7.45 (brs, 2H), 3.82 – 3.47 (brs, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 22.9, 19.0. ^{13}C NMR (151 MHz, $CDCl_3$) δ 179.7 (d, *J* = 320.9 Hz), 156.1 (d, *J* = 344.4 Hz), 146.7, 132.8, 125.6, 124.6 (d, *J* = 63.7 Hz), 44.4. HRMS (EI) calculated for $C_9H_7ONF_2{}^{32}S$: 215.0211 $[M]^+$, Found: 215.0210.

Compounds from Figure 2:

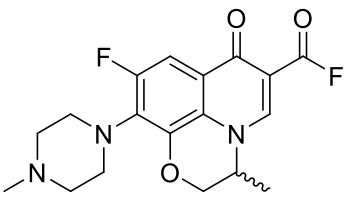


1-(4-Nitrophenyl)-5-(trifluoromethyl)-1H-pyrazole-4-carbonyl fluoride 19 : The title compound was obtained as an orange solid after 1.5 hours in 83% yield (50.3 mg) using 1-(4-nitrophenyl)-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid after filtration over silica following the general procedure. M.p. = 76-77 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 – 8.37 (m, 2H), 8.26 (s, 1H), 7.69 – 7.63 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 35.7

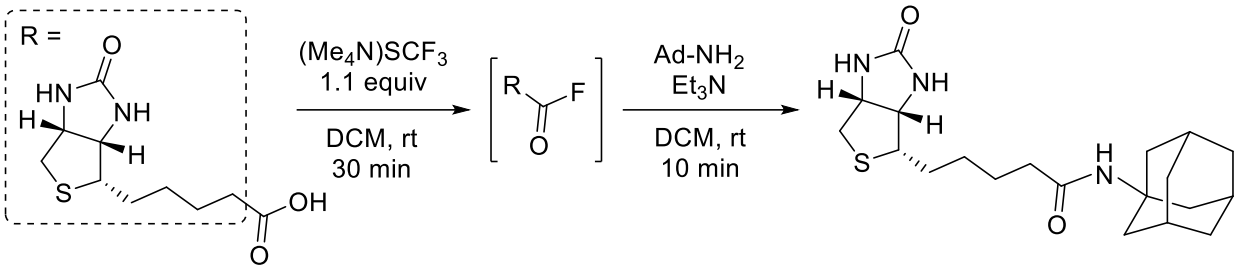
(q, J = 8.6 Hz), -55.6 (d, J = 8.6 Hz). ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.9 (d, J = 332.9 Hz), 148.6, 144.3, 143.1, 126.9, 124.8, 118.3 (q, J = 272.6 Hz), 111.9, 111.4. HRMS (EI) calculated for $C_{11}H_5O_3N_3F_4$: 303.0262 $[M]^+$, Found: 303.0261.

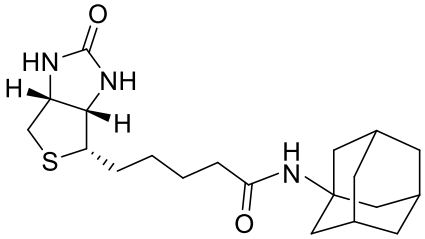


2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1H-indol-3-yl)acetyl fluoride 20 : The title compound was obtained as an off-white solid after 30 minutes in 94% yield (68.0 mg) using indomethacin after filtration over silica following the general procedure. M.p. = 149-150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 2H), 7.50 – 7.44 (m, 2H), 6.87 (d, J = 2.5 Hz, 1H), 6.83 (d, J = 9.0 Hz, 1H), 6.68 (dd, J = 9.0, 2.5 Hz, 1H), 3.85 (d, J = 2.5 Hz, 2H), 3.82 (s, 3H), 2.39 (s, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 44.4. ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.2, 160.5 (d, J = 363.7 Hz), 156.2, 139.6, 136.7, 133.5, 131.2, 130.7, 129.8, 129.2, 115.1, 112.1, 109.2 (d, J = 1.8 Hz), 100.6, 55.7, 28.2 (d, J = 58.0 Hz), 13.2. HRMS (EI) calculated for $C_{19}H_{15}O_3N^{35}ClF$: 359.0719 $[M]^+$, Found: 359.0721.

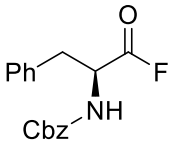


9-Fluoro-3-methyl-10-(4-methylpiperazin-1-yl)-7-oxo-2,3-dihydro-7H-[1,4]oxazino[2,3,4-ij]quinoline-6-carbonyl fluoride 21 : The title compound was obtained as a pale yellow solid after 1 hour in 92% yield (66.9 mg) using ofloxacin after washing the organic phase with saturated $NaHCO_3$ aqueous solution following the general procedure. M.p. = 247-249 °C (dec.). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.83 (s, 1H), 7.42 (d, J = 12.7 Hz, 1H), 4.77 – 4.71 (m, 1H), 4.50 (d, J = 11.3 Hz, 1H), 4.30 (d, J = 11.3 Hz, 1H), 3.26 – 3.18 (m, 4H), 2.43 – 2.35 (m, 4H), 2.21 (s, 3H), 1.39 (d, J = 6.9 Hz, 3H). ^{19}F NMR (376 MHz, DMSO-d_6) δ 24.1, -121.5 (d, J = 12.7 Hz). ^{13}C NMR (151 MHz, DMSO-d_6) δ 172.2, 156.7, 155.1, 154.5 (d, J = 335.3 Hz), 149.9, 141.0 (d, J = 6.7 Hz), 131.9 (d, J = 13.8 Hz), 123.9, 122.8 (d, J = 10.1 Hz), 104.5 (d, J = 23.8 Hz), 68.5, 55.7, 54.9, 50.5, 46.4, 18.1. HRMS (ESI) calculated for $C_{18}H_{20}O_3N_3F_2$: 364.1467 $[M+H]^+$, Found: 364.1469.

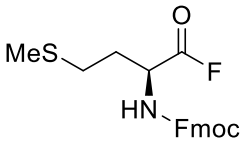




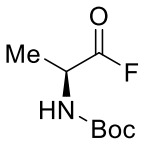
***N*-(adamantan-1-yl)-5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanamide 22 :** Under air atmosphere, vitamin B7 (49 mg, 0.2 mmol, 1 equiv.) and the $(Me_4N)SCF_3$ salt (39 mg, 0.22 mmol, 1.1 equiv.) were mixed in MeCN (1.5 mL) at room temperature. After 30 minutes, a solution of 1-adamantanamine (36 mg, 0.24 mmol, 1.2 equiv.), triethylamine (42 μL, 0.3 mmol, 1.5 equiv.) in DCM (0.5 mL) was added at room temperature to the acid fluoride intermediate formed in the first step. After 10 minutes, DCM was added (10 mL), water (20 mL) and the two phases were separated. The organic phase was washed with water (5 mL) and then brine (5 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The crude material obtained was purified by column chromatography with CH_2Cl_2 / MeOH (90/10, R_f = 0.13) to afford the title compound as a white solid in 84% yield (63.4 mg). M.p. = 135-137 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.36 (s, 1H), 5.72 (s, 1H), 5.45 (s, 1H), 4.48 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.27 (dd, *J* = 7.8, 4.4 Hz, 1H), 3.15 – 3.09 (m, 1H), 2.87 (dd, *J* = 12.8, 4.8 Hz, 1H), 2.71 (d, *J* = 12.8 Hz, 1H), 2.11 – 2.06 (m, 2H), 2.02 (brs, 3H), 1.97 – 1.93 (m, 6H), 1.74 – 1.56 (m, 10H), 1.44 – 1.35 (m, 2H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 172.3, 164.0, 61.8, 60.2, 55.6, 51.7, 41.6, 40.6, 37.0, 36.4, 29.4, 28.2, 28.1, 25.7. HRMS (ESI) calculated for $C_{20}H_{31}O_2N_3NaS$: 400.2029 $[M+Na]^+$, Found: 400.2021.



Benzyl (*S*)-(1-fluoro-1-oxo-3-phenylpropan-2-yl)carbamate 23: The title compound was obtained as an off-white solid in 94% yield (56.6 mg) using Cbz-*L*-Phe-OH after filtration over celite following the procedure for *N*-protected amino acid fluorides. M.p. = 83-85 °C. IR (ATR) $\bar{\upsilon}$ = 1829 cm $^{-1}$. $[\alpha]_D$ = -30.1 (c = 0.575, EtOAc, 26 °C).[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 8H), 7.15 (d, *J* = 6.8 Hz, 2H), 5.11 (s, 2H), 5.08 (d, *J* = 7.8 Hz, 1H), 4.86 – 4.81 (m, 1H), 3.23 – 3.15 (m, 2H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 30.7. ^{13}C NMR (151 MHz, $CDCl_3$) δ 161.8 (d, *J* = 369.6 Hz), 155.5, 135.7, 134.1, 129.2, 129.1, 128.6, 128.4, 128.2, 127.8, 67.5, 53.7 (d, *J* = 60.4 Hz), 36.8.



(9H-Fluoren-9-yl)methyl (*S*)-(1-fluoro-4-(methylthio)-1-oxobutan-2-yl)carbamate 24: The title compound was obtained as an off-white solid in 92% yield (68.6 mg) using Fmoc-*L*-Met-OH after filtration over celite following the procedure for *N*-protected amino acid fluorides. M.p. = 131-133 °C. IR (ATR) $\bar{\upsilon}$ = 1841 cm $^{-1}$. $[\alpha]_D$ = -10.2 (c = 0.55, EtOAc, 26 °C).[6] ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.6 Hz, 2H), 7.59 (d, *J* = 6.3 Hz, 2H), 7.44 – 7.38 (m, 2H), 7.35 – 7.30 (m, 2H), 5.36 (d, *J* = 8.0 Hz, 1H), 4.76 – 4.67 (m, 1H), 4.48 (dd, *J* = 6.4, 2.5 Hz, 1H), 4.23 (t, *J* = 6.7 Hz, 1H), 2.64 – 2.58 (m, 1H), 2.58 – 2.52 (m, 1H), 2.28 – 2.20 (m, 1H), 2.11 (s, 3H), 2.10 – 2.03 (m, 1H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 29.9. ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4 (d, *J* = 369.7 Hz), 155.7, 143.6, 143.4, 141.3, 127.8, 127.1, 124.9, 120.0, 120.0, 67.3, 51.8 (d, *J* = 59.8 Hz), 47.1, 30.1, 29.8, 15.4.



***tert*-Butyl (*S*)-(1-fluoro-1-oxopropan-2-yl)carbamate 25:** Pyridine (16 μL, 0.2 mmol, 1 equiv) was added to the solution of Boc-*L*-Ala-OH before addition to the $(Me_4N)SCF_3$ reagent. The title compound was obtained as an pale yellow solid in 84% yield (32.1 mg) using Boc-*L*-Ala-OH after filtration over celite following the procedure for *N*-protected amino acid fluorides. M.p. = 57-59 °C. IR (ATR) $\bar{\upsilon}$ = 1841 cm $^{-1}$. $[\alpha]_D$ = -18.0 (c = 0.4, EtOAc, 26 °C).[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.90 (s, 1H), 4.44 (s, 1H), 1.48 (d, *J* = 7.4 Hz, 3H), 1.44 (s, 9H). ^{19}F NMR (376 MHz, $CDCl_3$) δ 27.7. ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.4 (d, *J* = 370.5 Hz), 154.8, 80.8, 48.1 (d, *J* = 62.4 Hz), 28.2, 17.1.

3. ReactIR® experiments

Experiments were performed on a Mettler Toledo ReactIR® 15 apparatus equipped with a 6.3 mm probe. Absorbance profiles of starting material and product in solution in DCM were obtained at room temperature. Due to the limited solubility of 4-chlorobenzoic acid and 4-nitrobenzoic acid in DCM, the signals of these starting materials could not be followed. See Figures S1-4 for the 3 different reactions.

Procedure for the 5 mmol scale reaction and temperature monitoring. Under air atmosphere, 1-adamantanecarboxylic acid (901 mg, 5 mmol, 1 equiv.) was dissolved in CH_2Cl_2 (25 mL) at room temperature. The probe was immerged in the solution and temperature was recorded (see Figure S5). The $(Me_4N)SCF_3$ salt (965 mg, 5.5 mmol, 1.1 equiv.) was added to the solution in one portion. After 1h, pentane (25 mL) was added to the reaction mixture which was then filtered through a pad of silica. Subsequent wash of the silica pad with a 1/1 mixture of CH_2Cl_2 / pentane (2 x 10 mL) was performed. The filtrate was then

concentrated under reduced pressure to afford 829 mg of the desired product (91% yield) as a pale yellow oil.

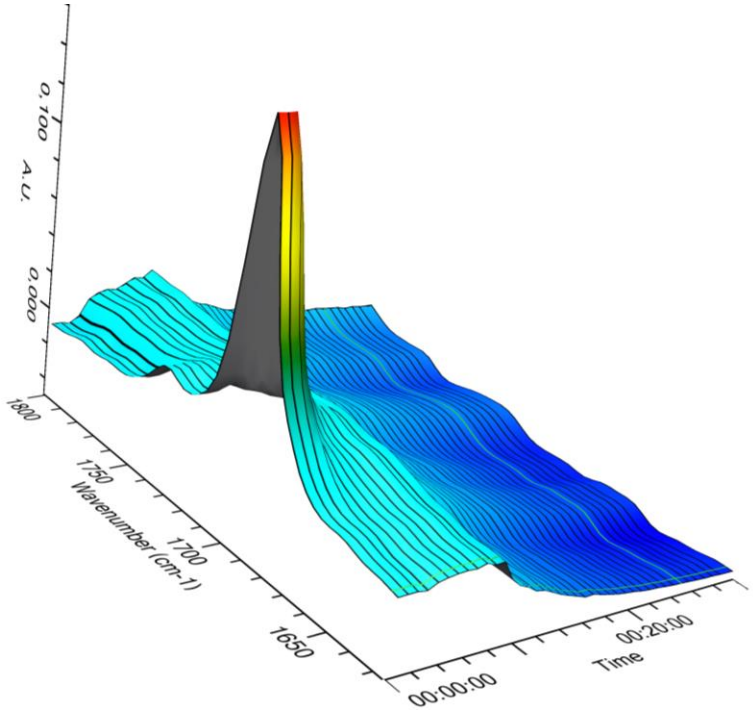


Figure S1. 1-Adamantanecarboxylic acid (characteristic absorption band at 1697 cm^{-1}) monitored consumption over time.

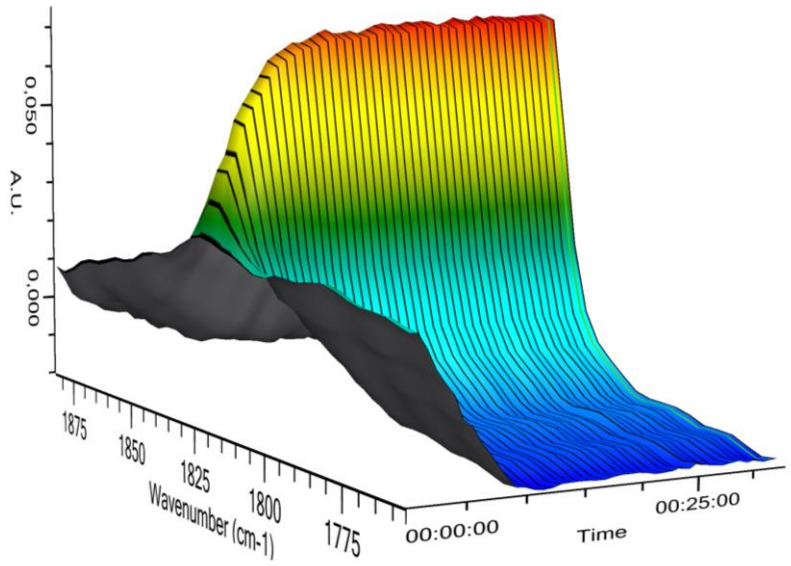


Figure S2. 1-Adamantanecarbonyl fluoride (characteristic absorption band at 1824 cm^{-1}) monitored formation over time.

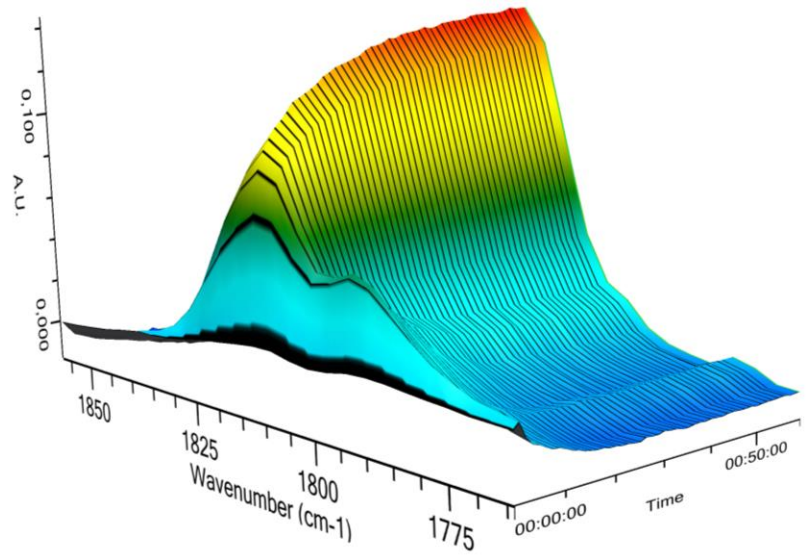


Figure S3. 4-Chlorobenzoyl fluoride (characteristic absorption band at 1812 cm^{-1}) monitored formation over time.

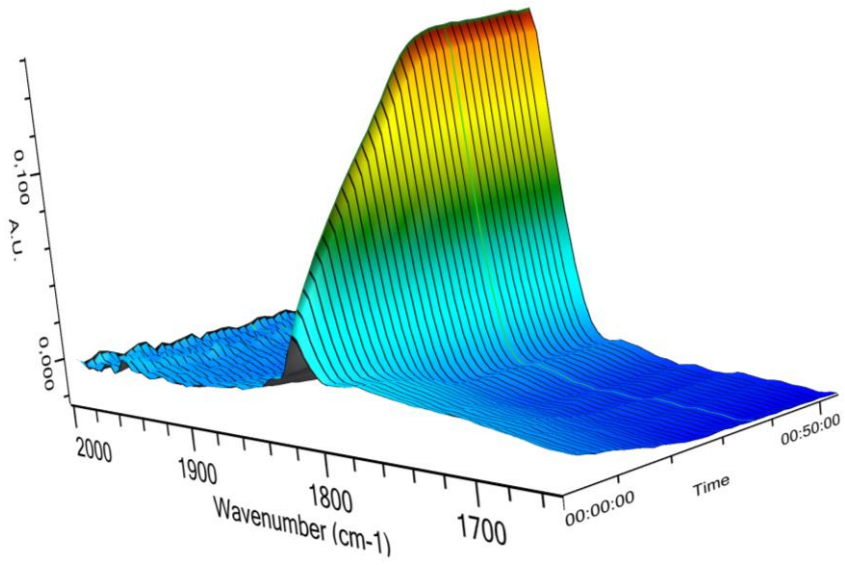


Figure S4. 4-Nitrobenzoyl fluoride (characteristic absorption band at 1824 cm^{-1}) monitored formation over time.

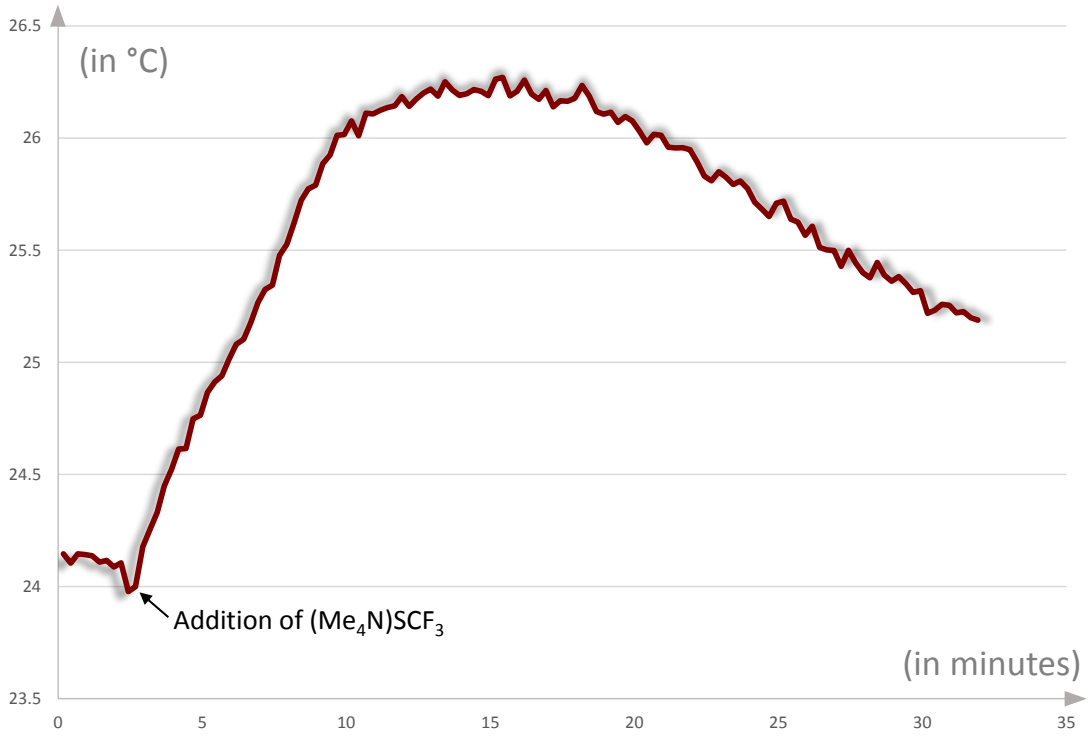


Figure S5. Temperature monitoring of the 5 mmol scale reaction with 1-adamantanecarboxylic acid.

4. References

1. Yin, G.; Kalvet, I.; Schoenebeck, F. *Angew. Chem. Int. Ed.* **2015,** *54*, 6809.
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3. Ochiai, M.; Yoshimura, A.; Hoque, M. M.; Okubo, T.; Saito, M.; Miyamoto, K. *Org. Lett.* **2011,** *13*, 5568.
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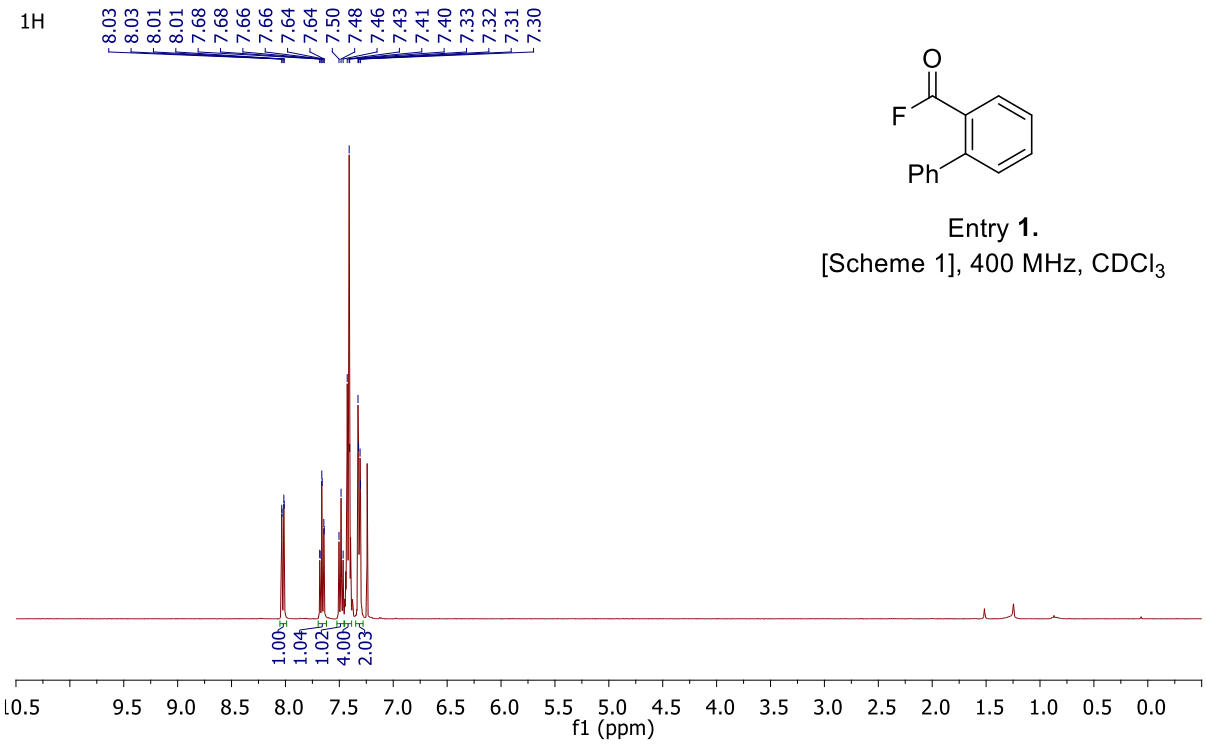
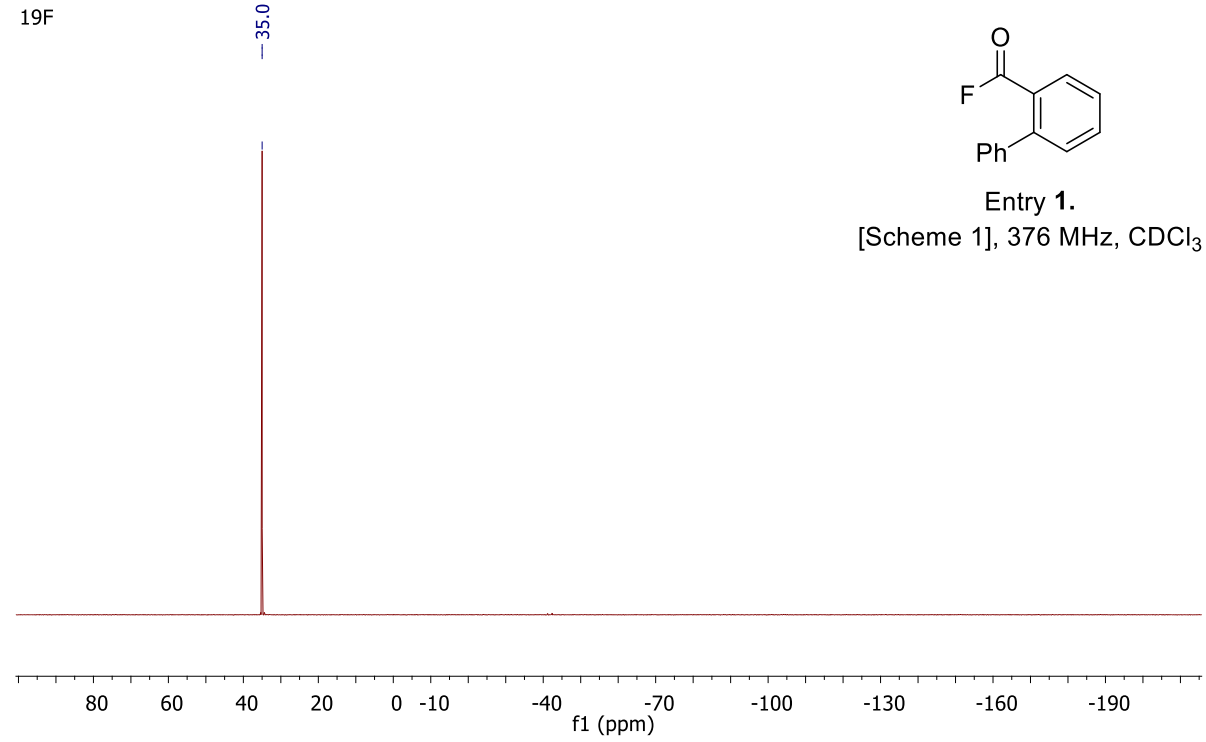
5. NMR spectra

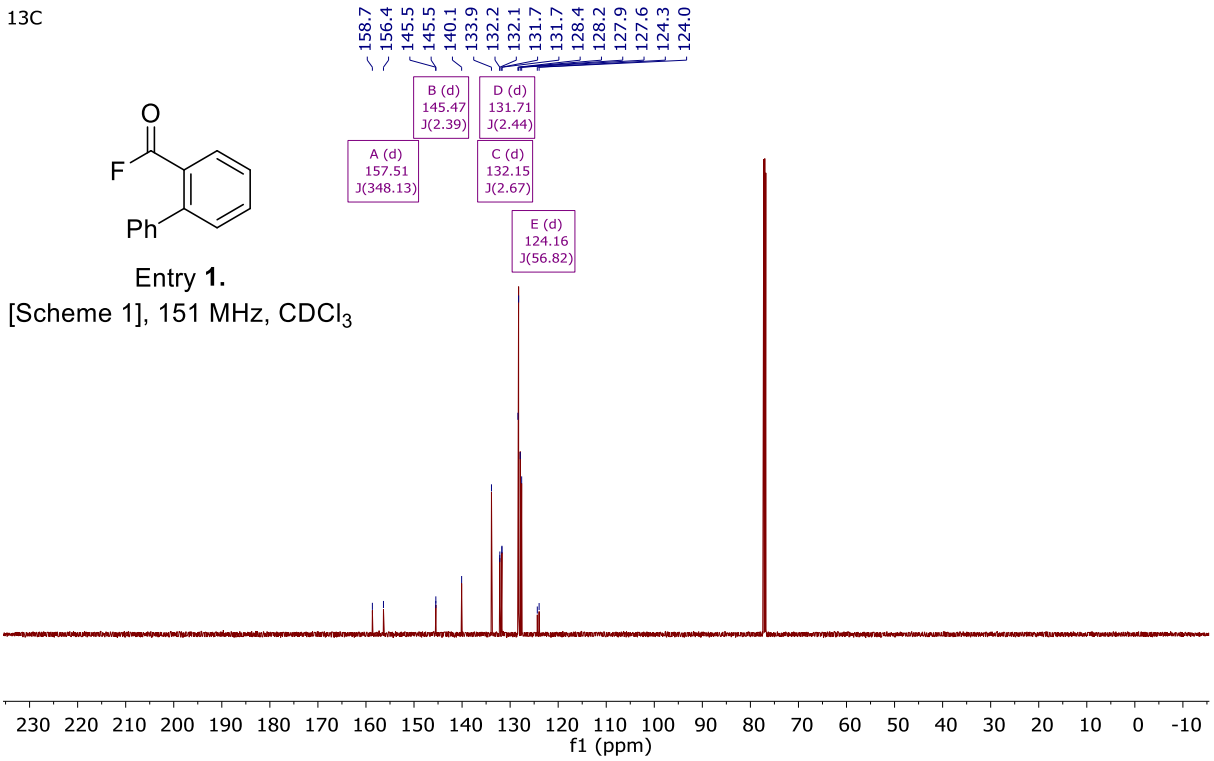


Entry **1.**
[Scheme 1], 400 MHz, $CDCl_3$



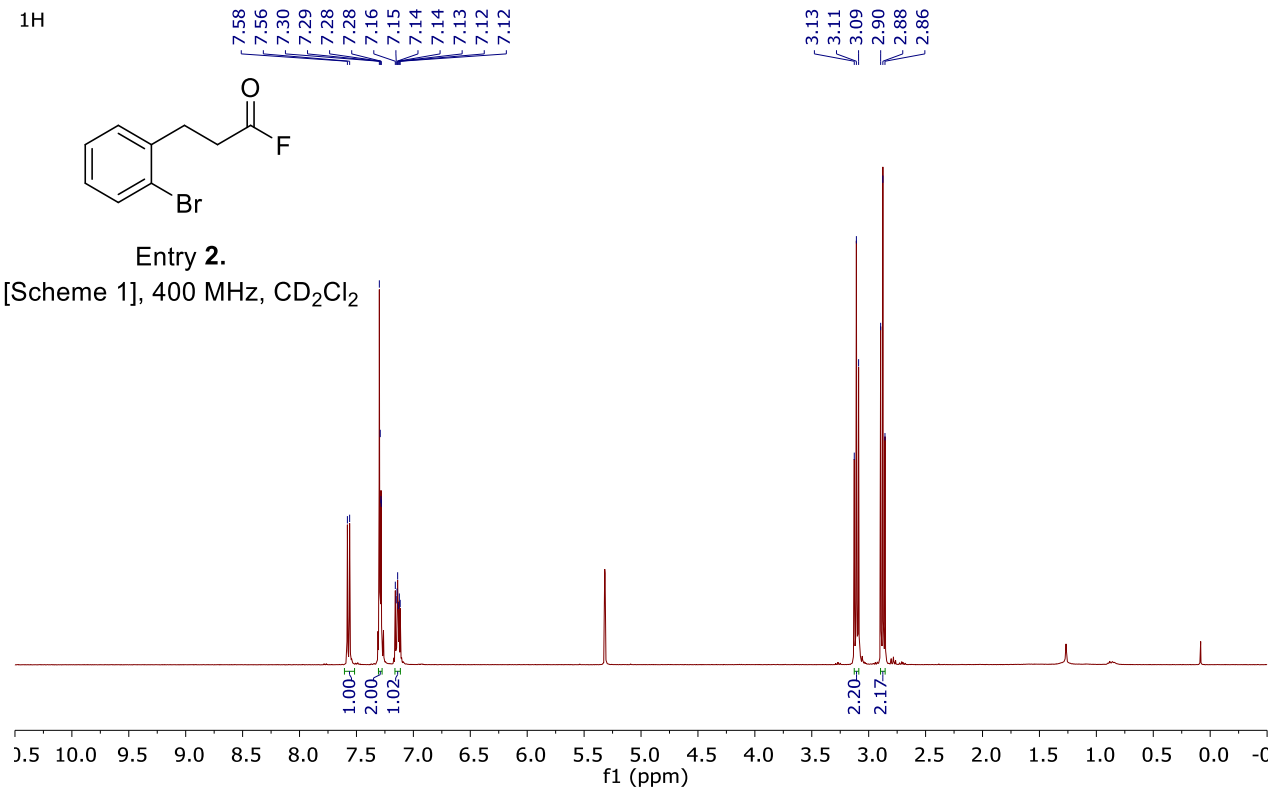
Entry **1.**
[Scheme 1], 376 MHz, $CDCl_3$

13C



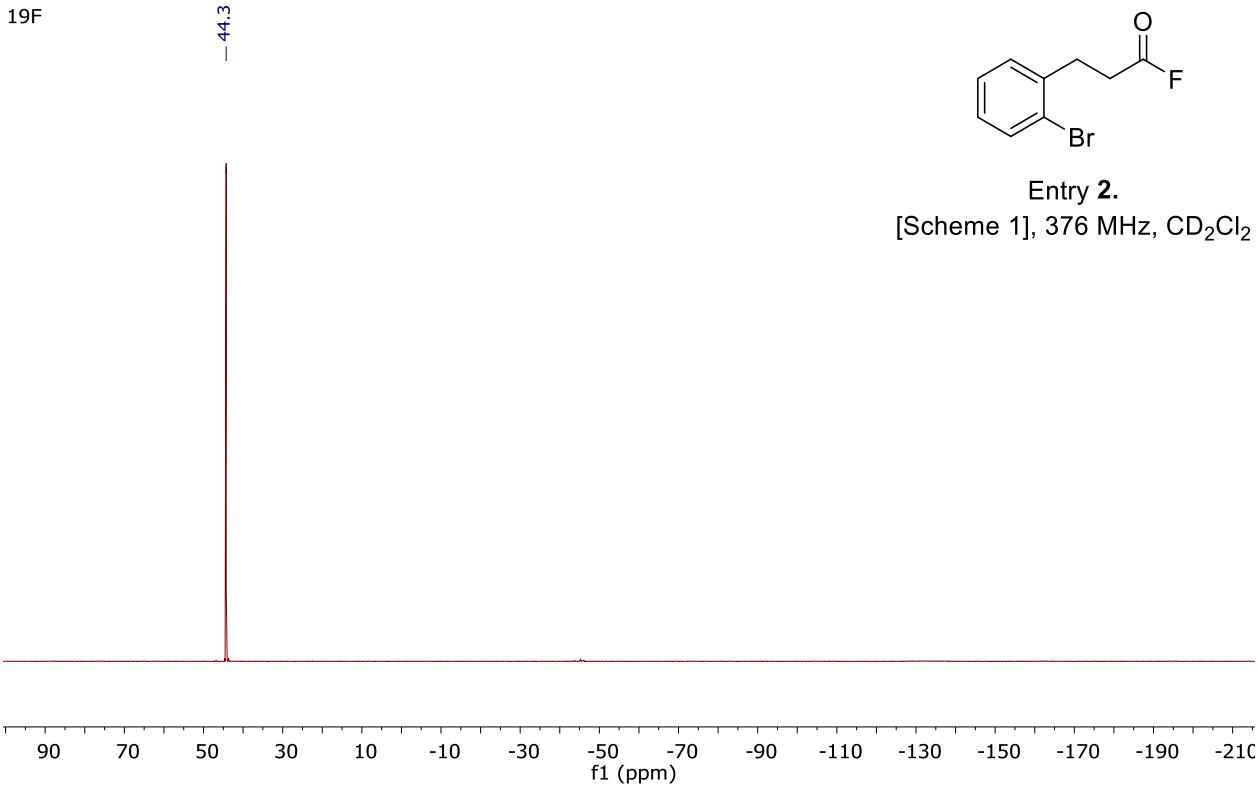
Entry **1.**
[Scheme 1], 151 MHz, $CDCl_3$

1H



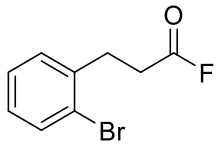
Entry **2.**
[Scheme 1], 400 MHz, CD_2Cl_2

19F

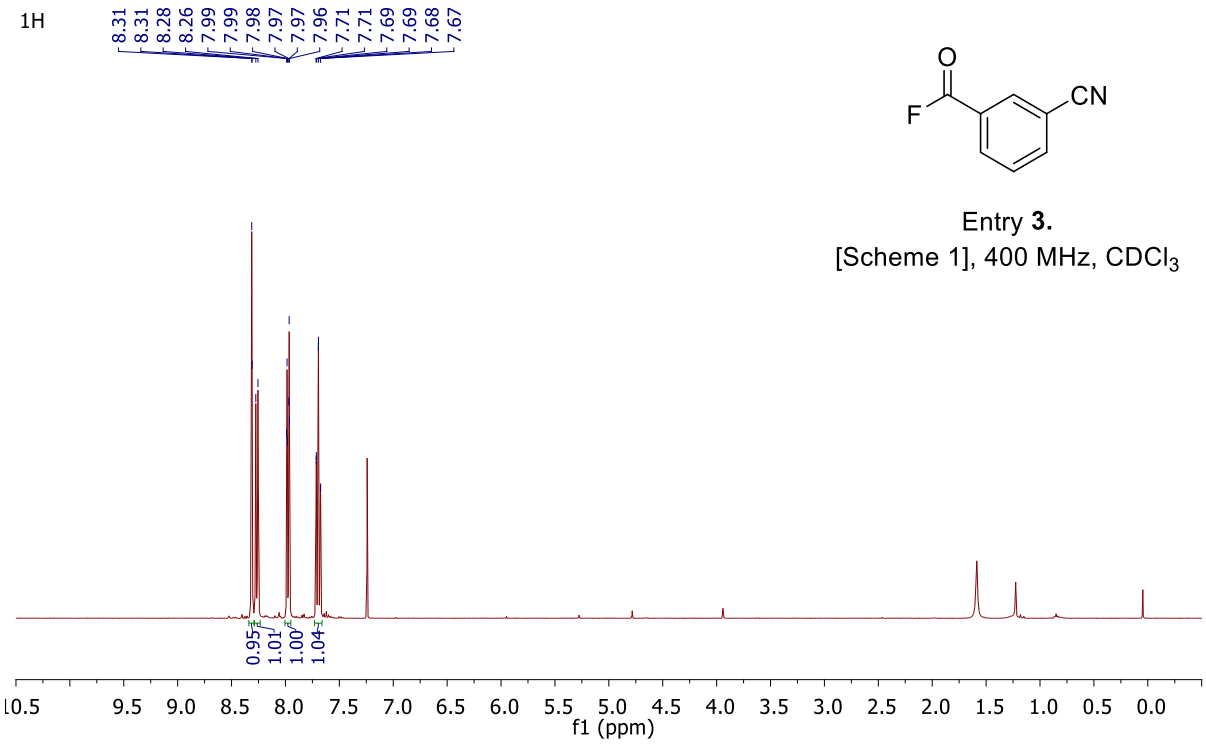


Entry **2.**
[Scheme 1], 376 MHz, CD_2Cl_2

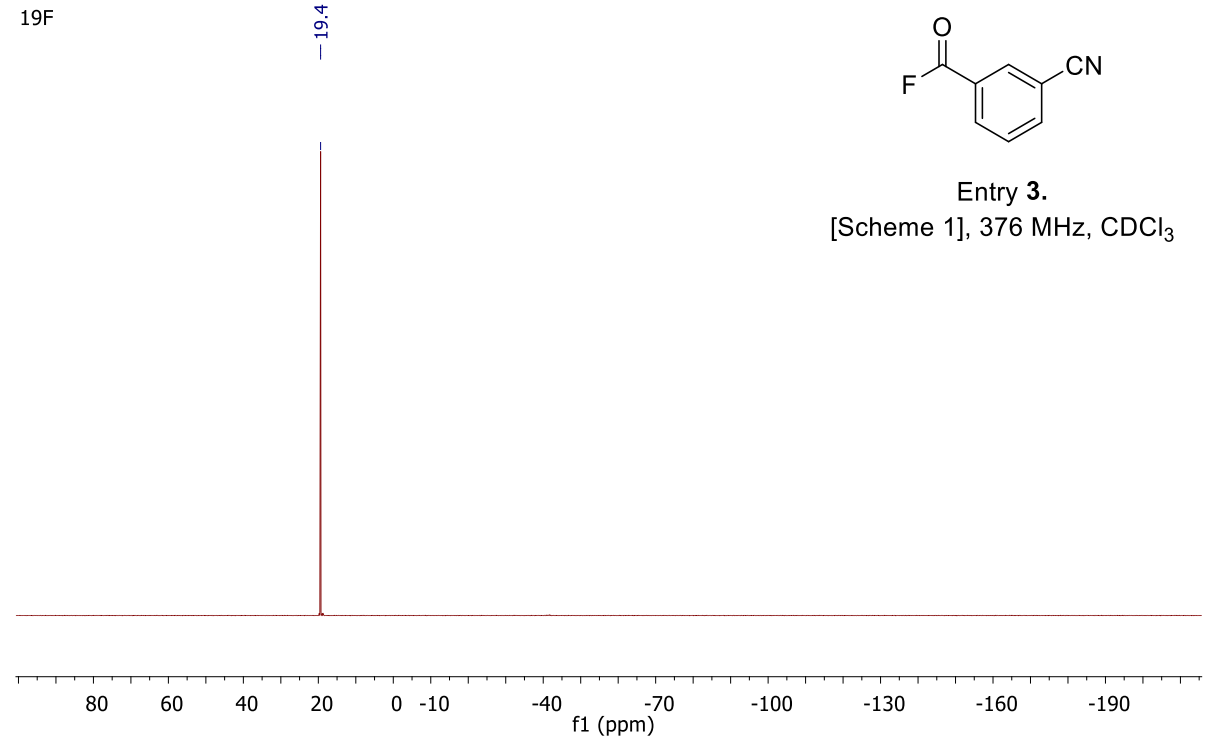
13C



Entry **2.**
[Scheme 1], 101 MHz, CD_2Cl_2

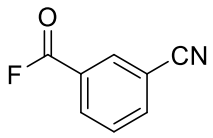


Entry **3.**
[Scheme 1], 400 MHz, $CDCl_3$



Entry **3.**
[Scheme 1], 376 MHz, $CDCl_3$

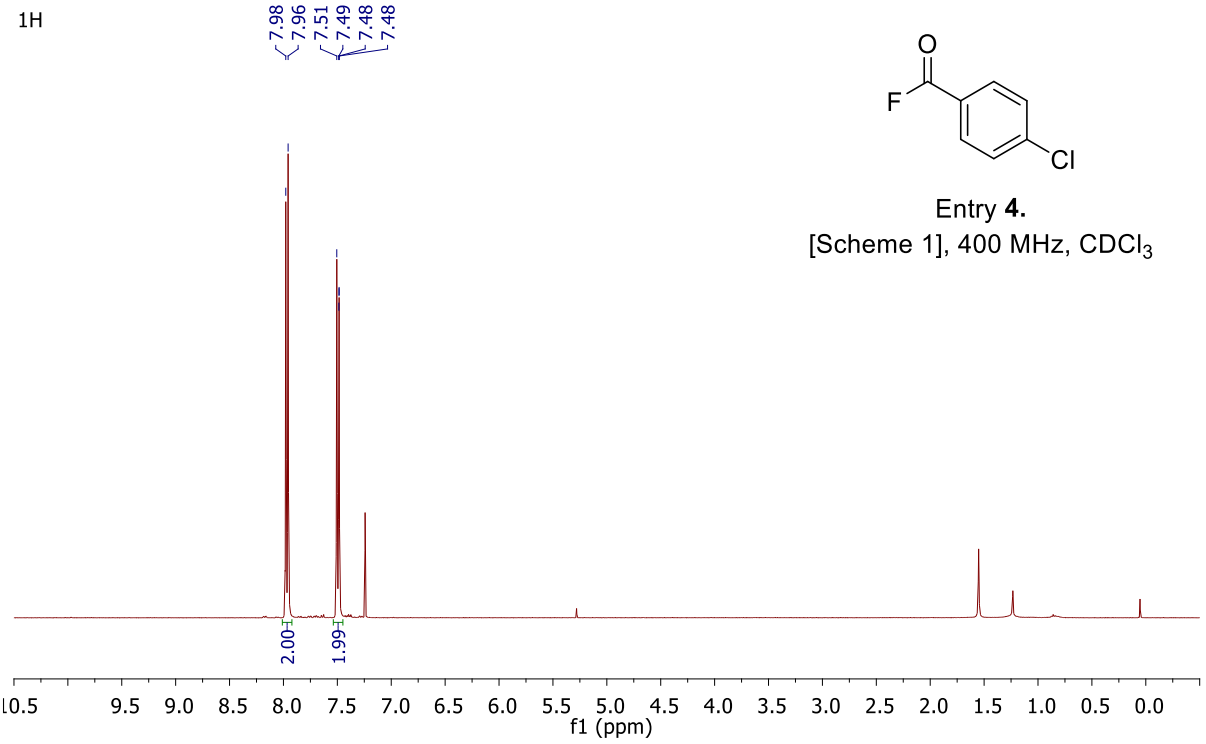
13C



Entry **3.**
[Scheme 1], 151 MHz, $CDCl_3$

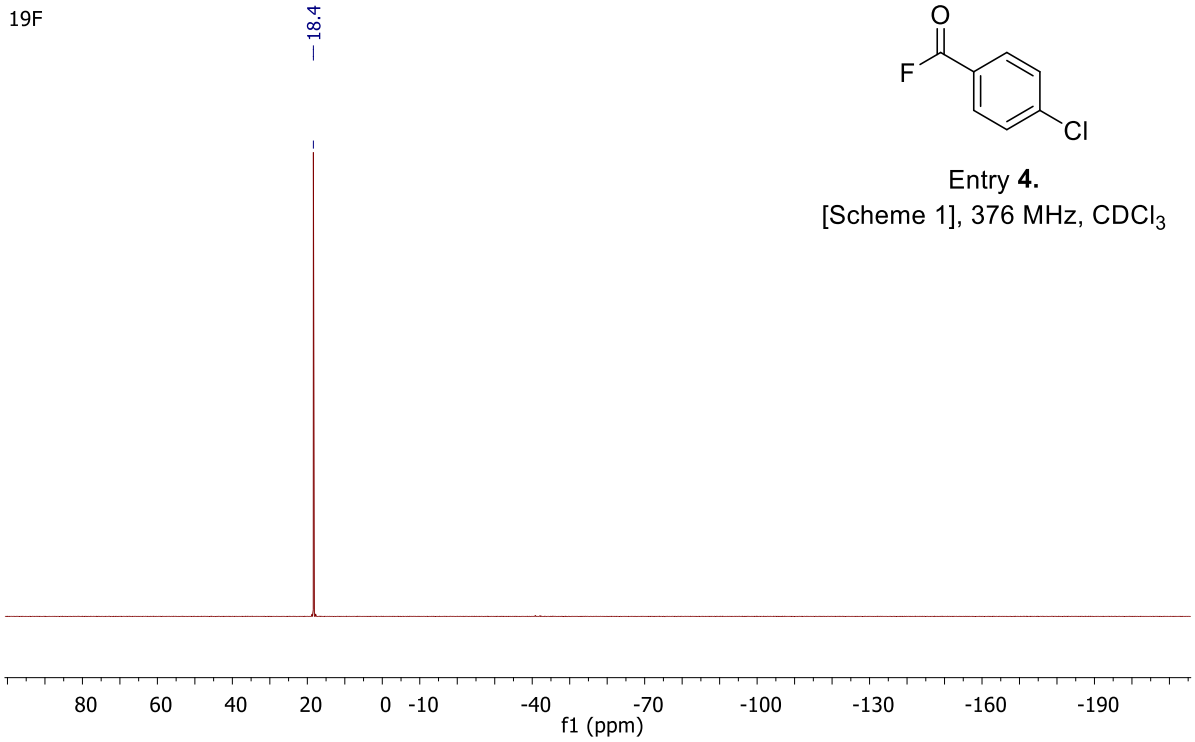
*peak at 83.3 ppm is an artifact of the instrument.

1H



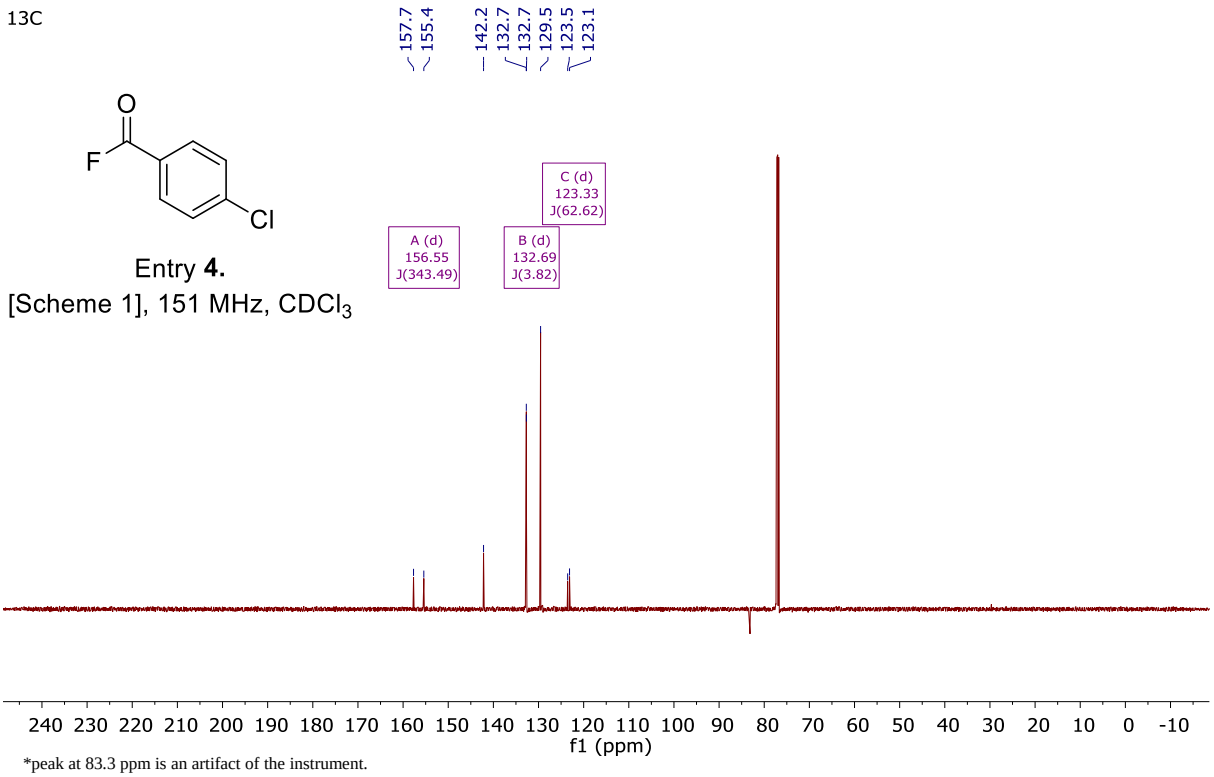
Entry **4.**
[Scheme 1], 400 MHz, $CDCl_3$

19F



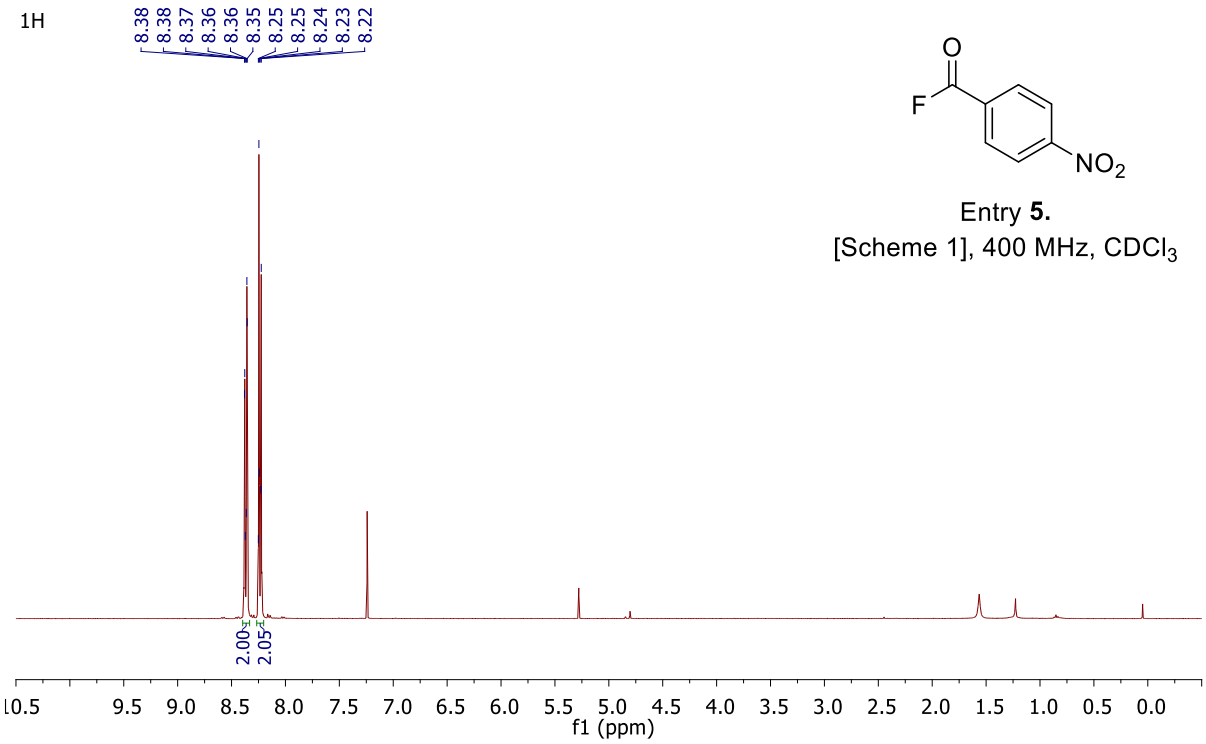
Entry **4.**
[Scheme 1], 376 MHz, $CDCl_3$

13C

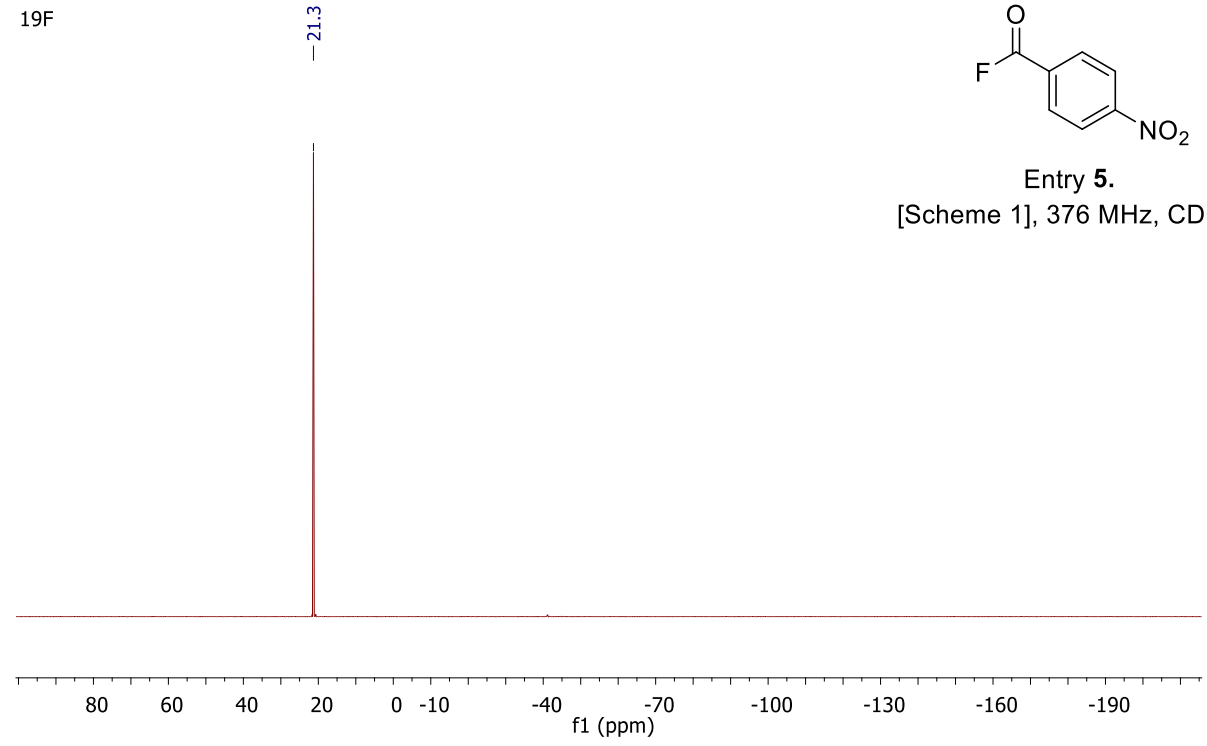


Entry **4.**
[Scheme 1], 151 MHz, $CDCl_3$

*peak at 83.3 ppm is an artifact of the instrument.

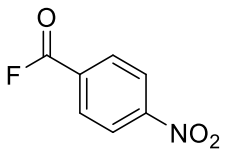


Entry **5.**
[Scheme 1], 400 MHz, $CDCl_3$



Entry **5.**
[Scheme 1], 376 MHz, $CDCl_3$

13C

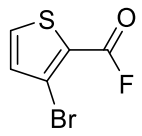


Entry **5.**

[Scheme 1], 151 MHz, $CDCl_3$

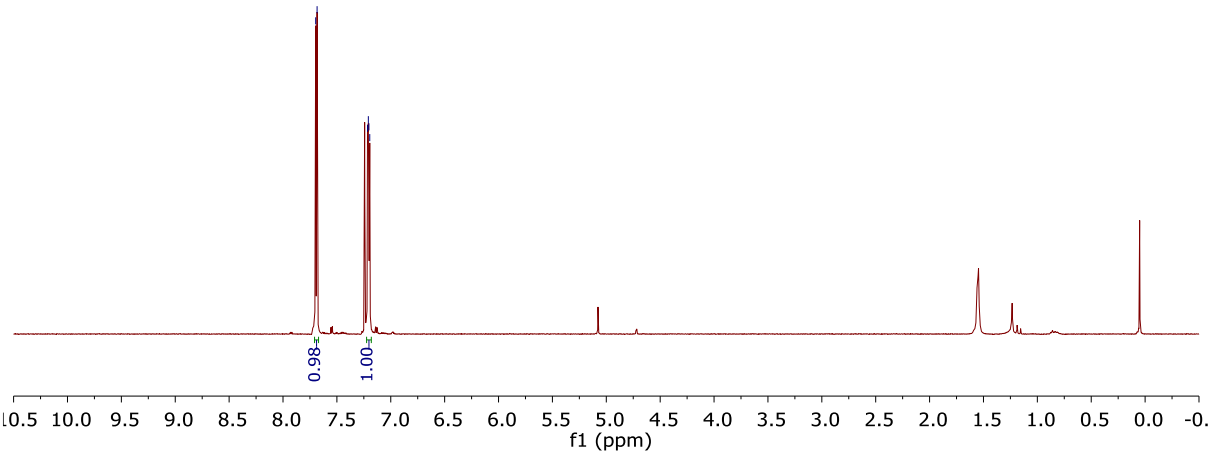
*peak at 83.3 ppm is an artifact of the instrument.

1H

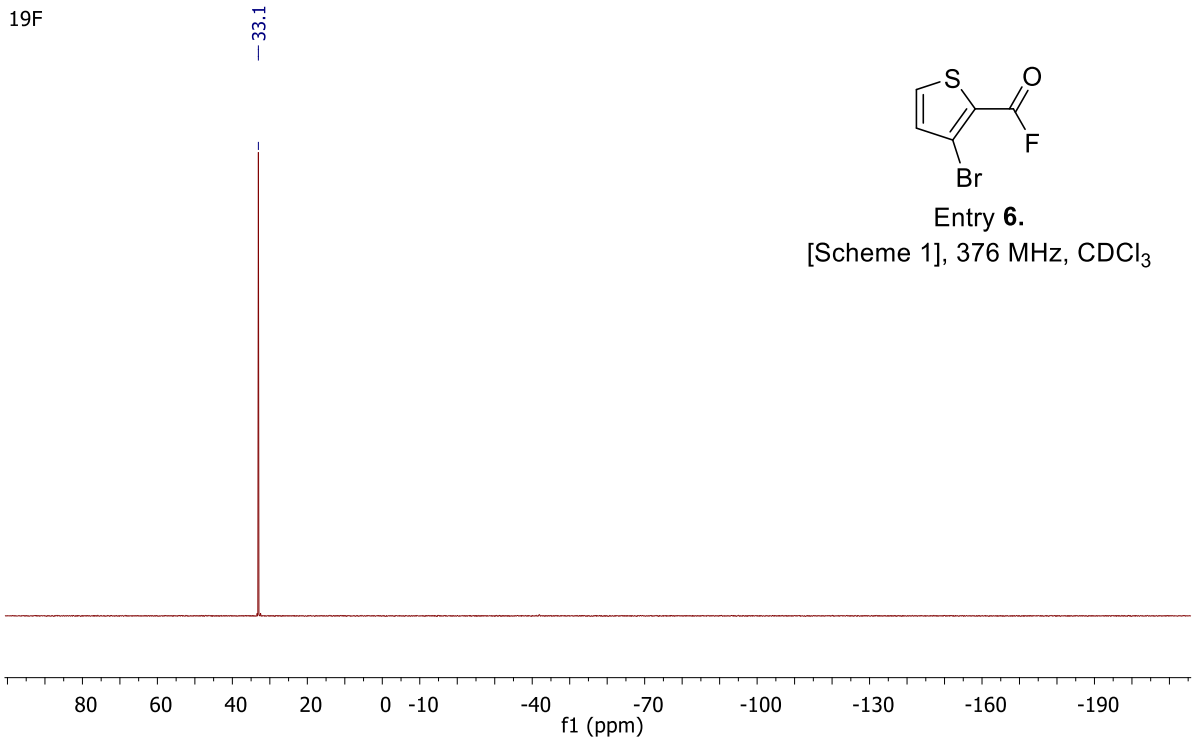


Entry **6.**

[Scheme 1], 400 MHz, $CDCl_3$



19F

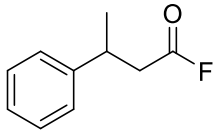


Entry **6.**
[Scheme 1], 376 MHz, $CDCl_3$

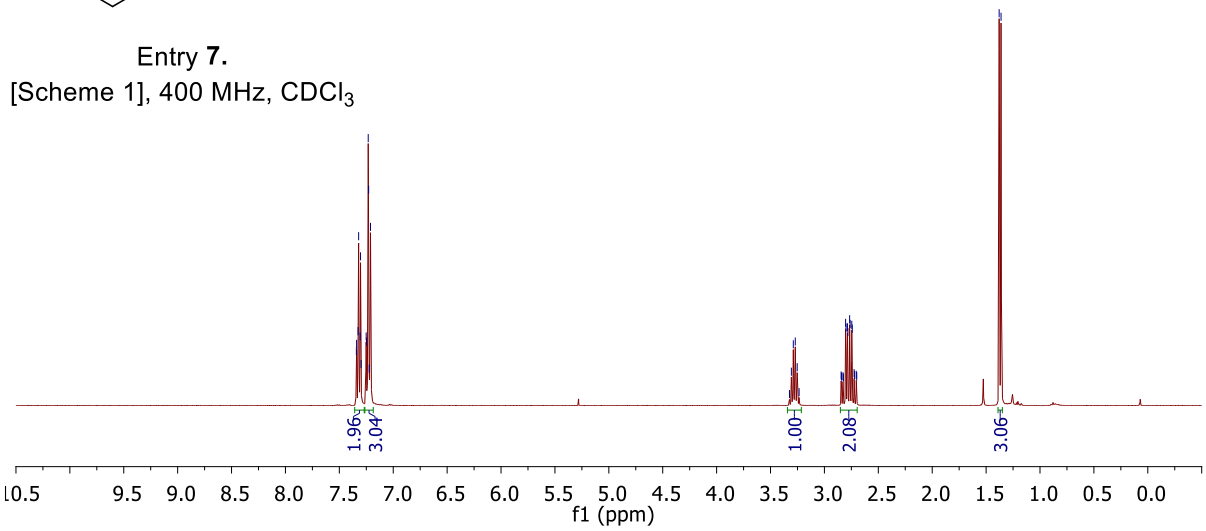
13C

Entry **6.**
[Scheme 1], 151 MHz, $CDCl_3$

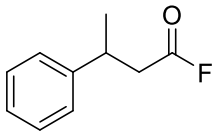
1H



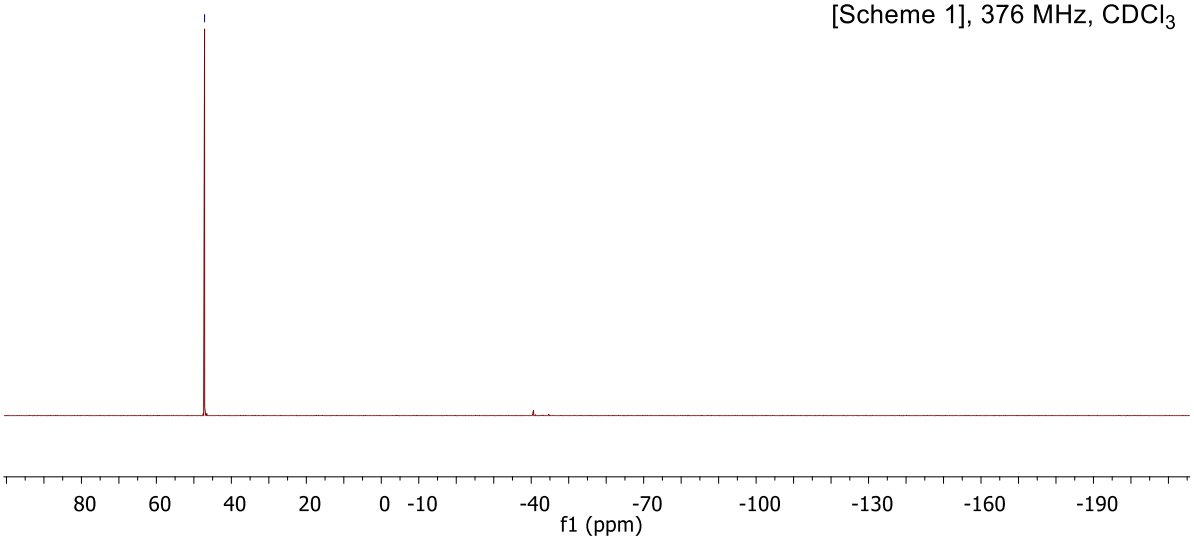
Entry **7.**
[Scheme 1], 400 MHz, $CDCl_3$

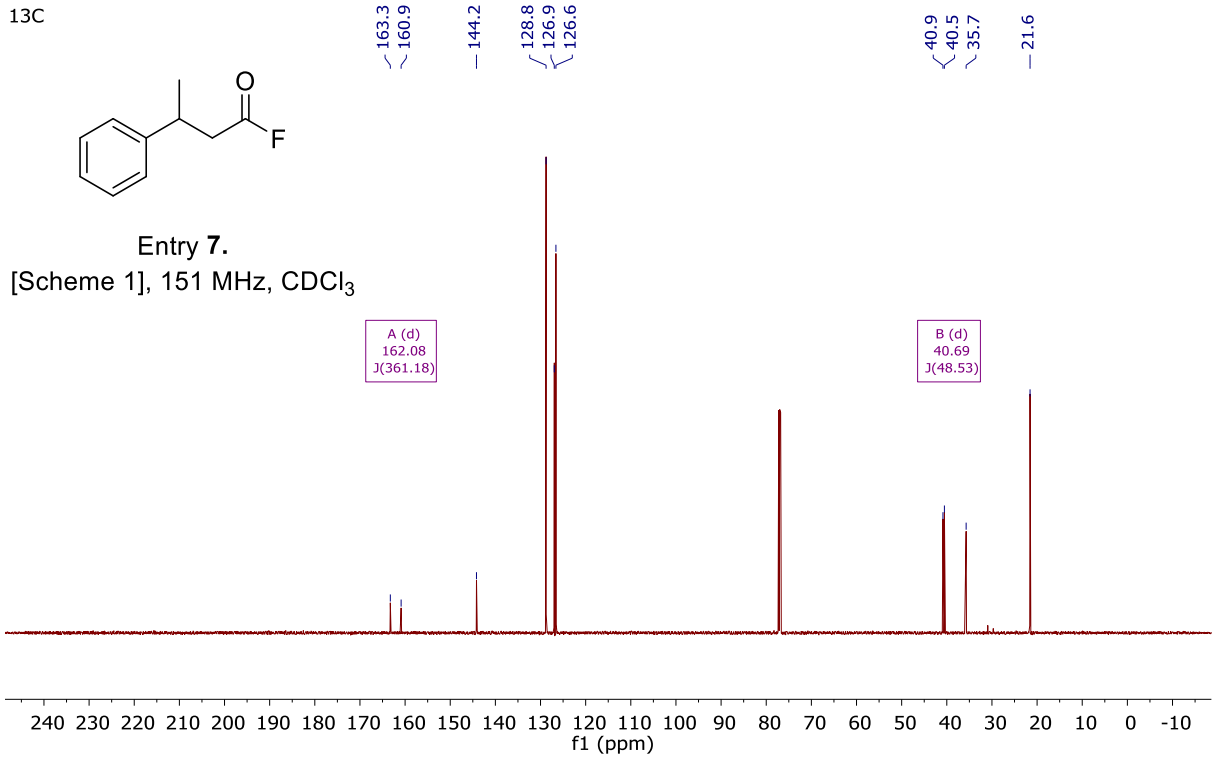


19F

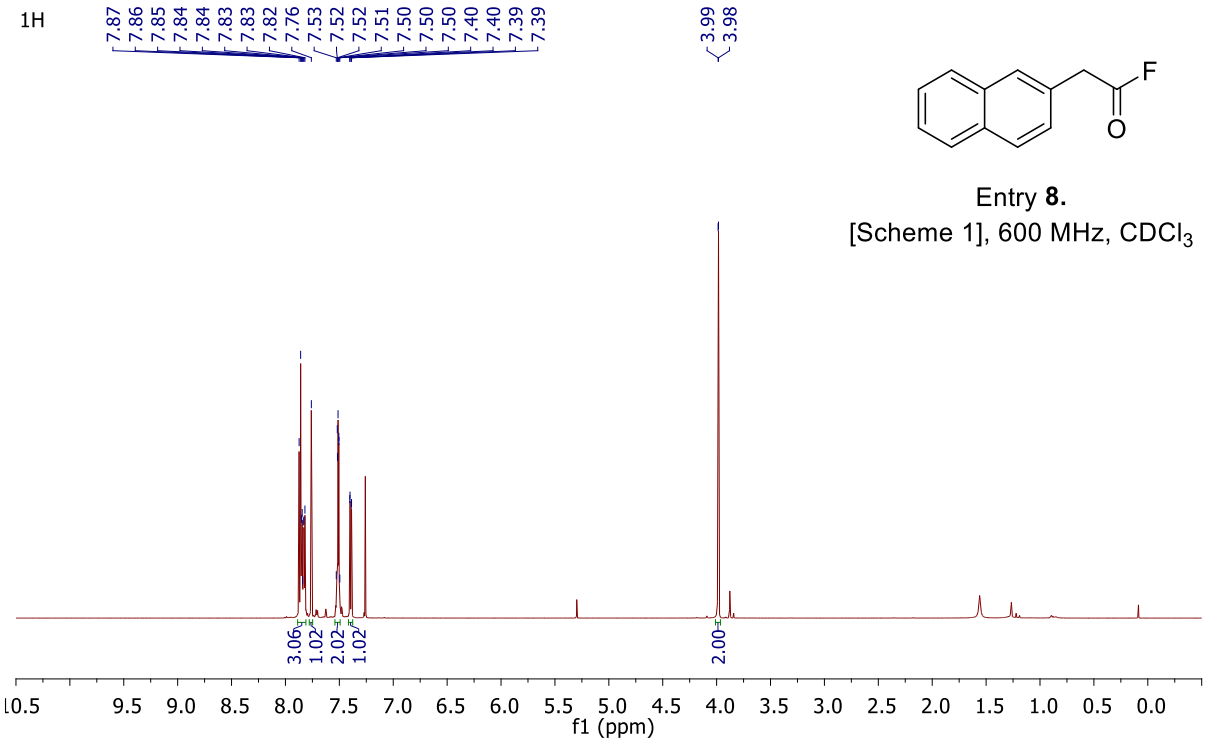


Entry **7.**
[Scheme 1], 376 MHz, $CDCl_3$



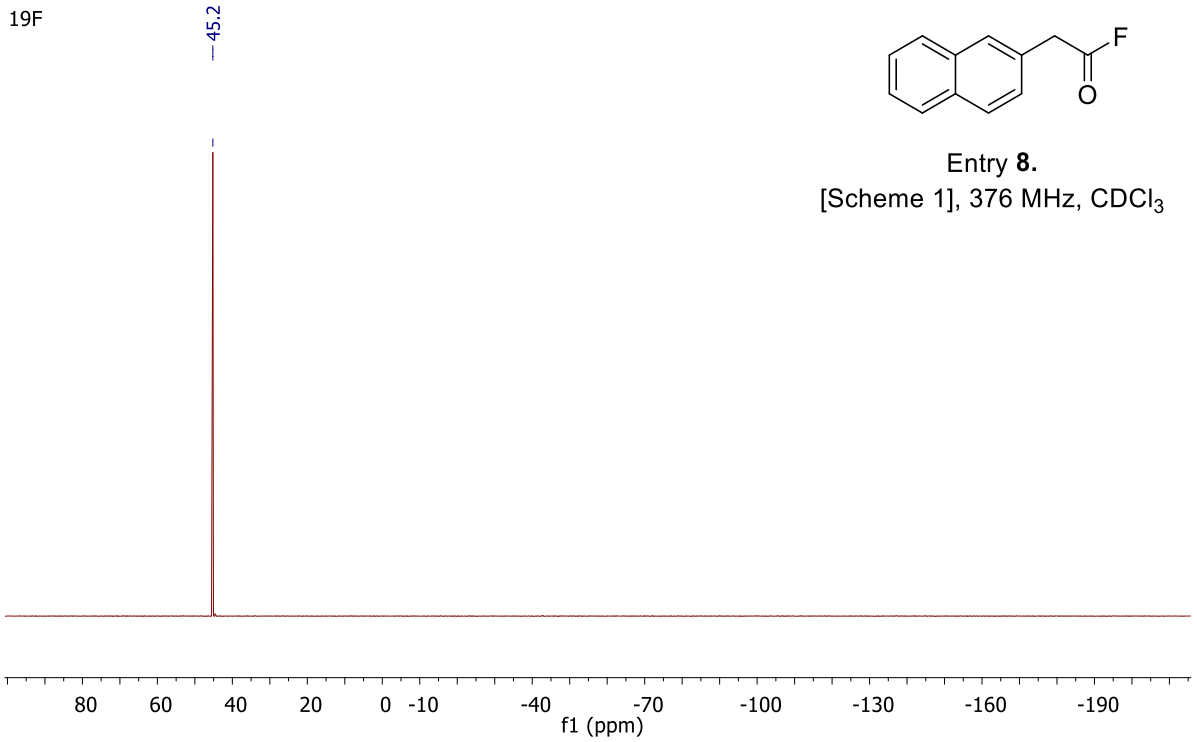


Entry **7.**
[Scheme 1], 151 MHz, $CDCl_3$



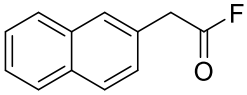
Entry **8.**
[Scheme 1], 600 MHz, $CDCl_3$

19F



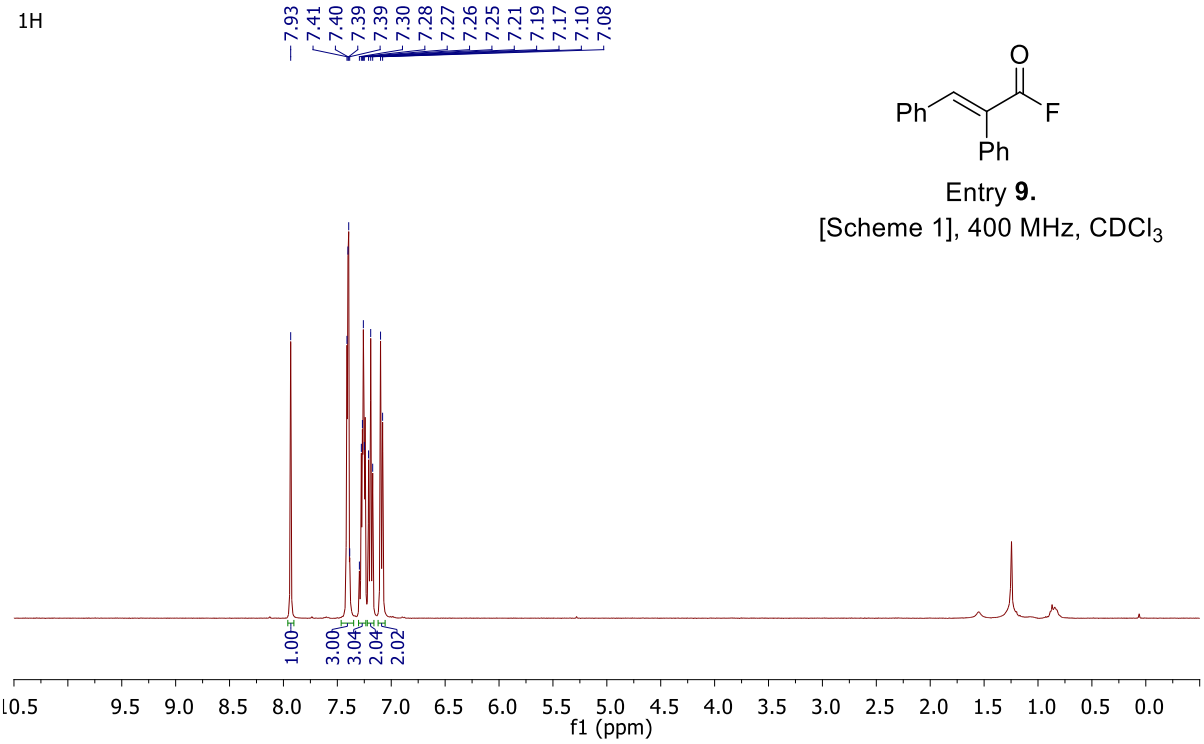
Entry **8.**
[Scheme 1], 376 MHz, $CDCl_3$

13C



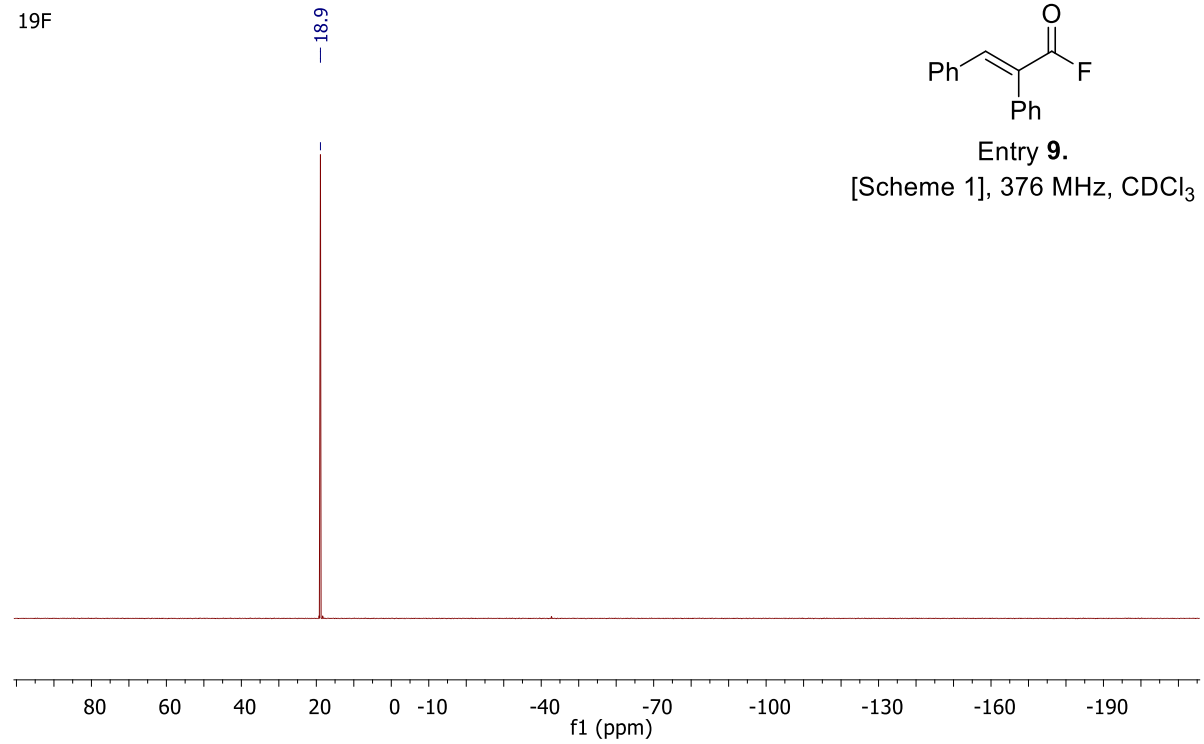
Entry **8.**
[Scheme 1], 151 MHz, $CDCl_3$

1H



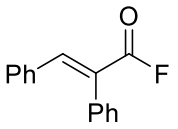
Entry **9.**
[Scheme 1], 400 MHz, $CDCl_3$

19F



Entry **9.**
[Scheme 1], 376 MHz, $CDCl_3$

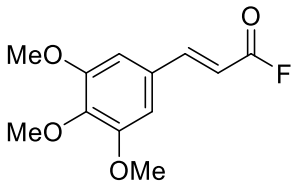
13C



Entry **9.**

[Scheme 1], 151 MHz, $CDCl_3$

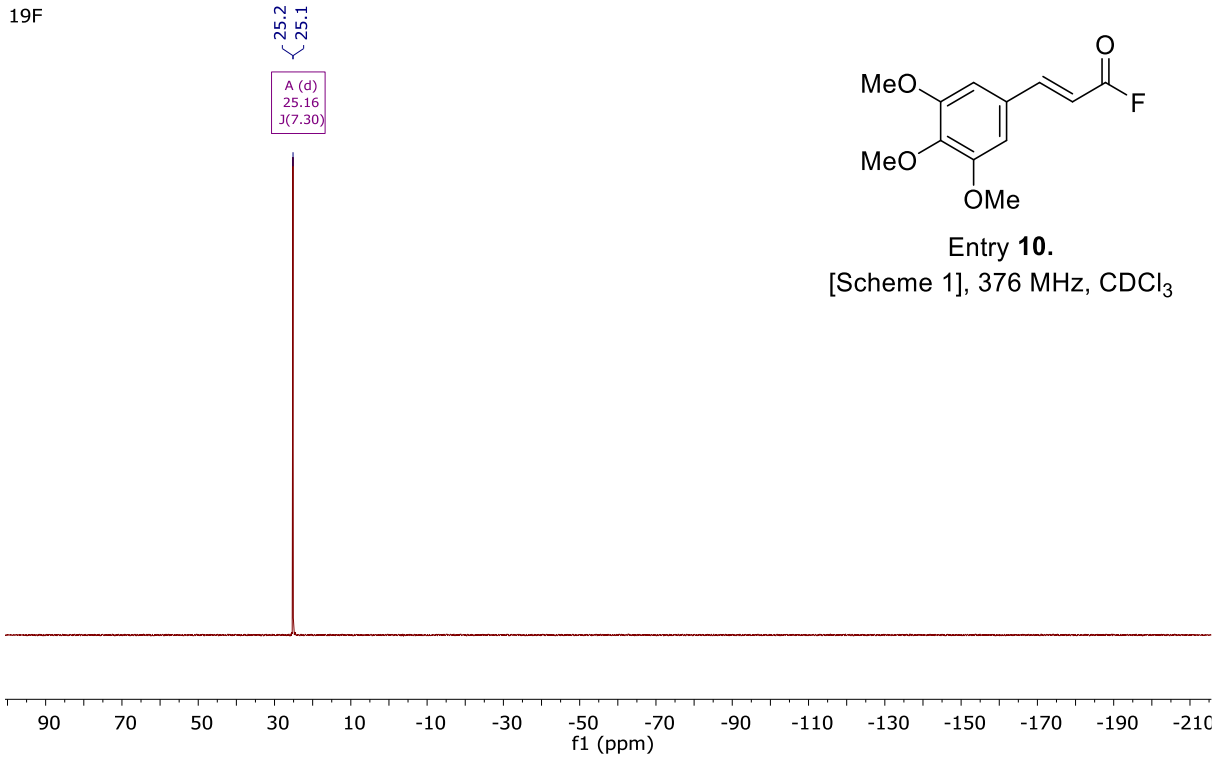
1H



Entry **10.**

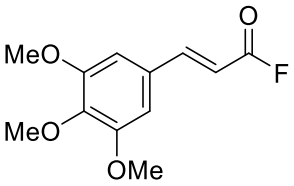
[Scheme 1], 400 MHz, $CDCl_3$

19F



Entry **10.**
[Scheme 1], 376 MHz, $CDCl_3$

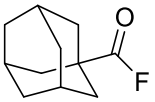
13C



Entry **10.**
[Scheme 1], 151 MHz, $CDCl_3$

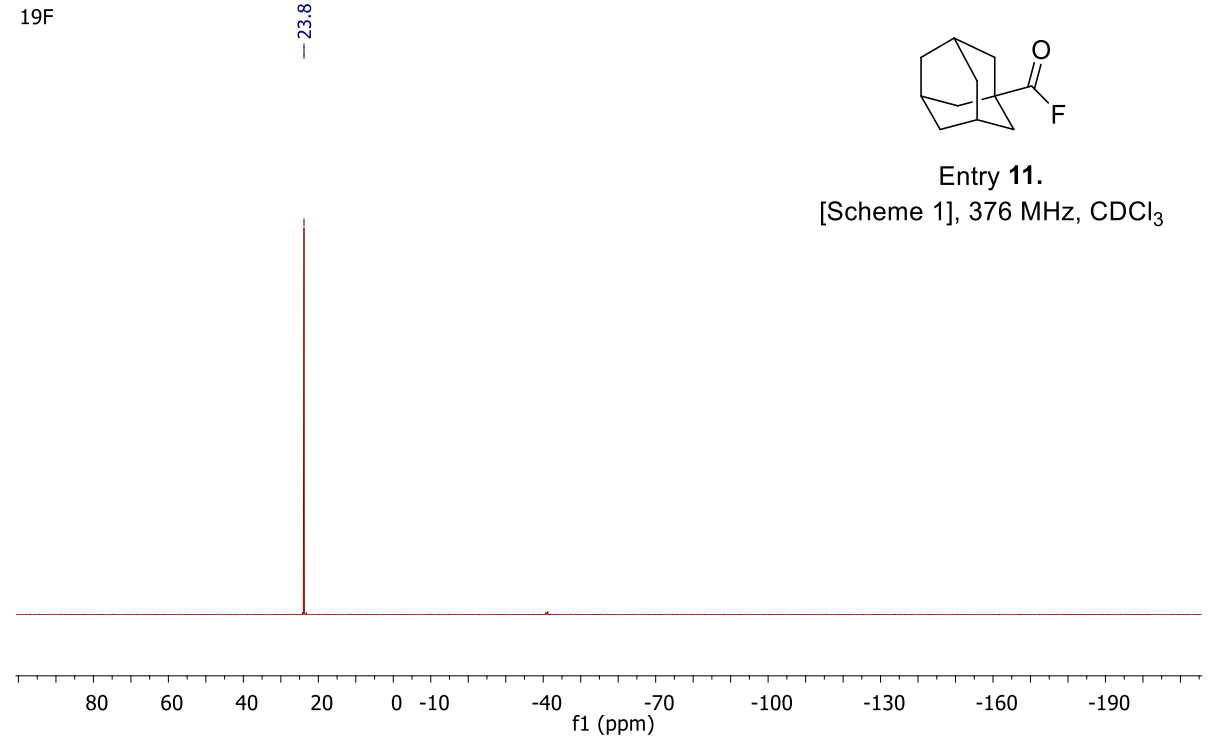
*peak at 83.3 ppm is an artifact of the instrument.

1H



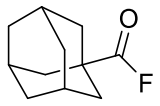
Entry **11.**
[Scheme 1], 400 MHz, $CDCl_3$

19F



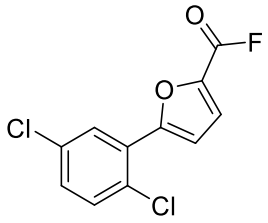
Entry **11.**
[Scheme 1], 376 MHz, $CDCl_3$

13C

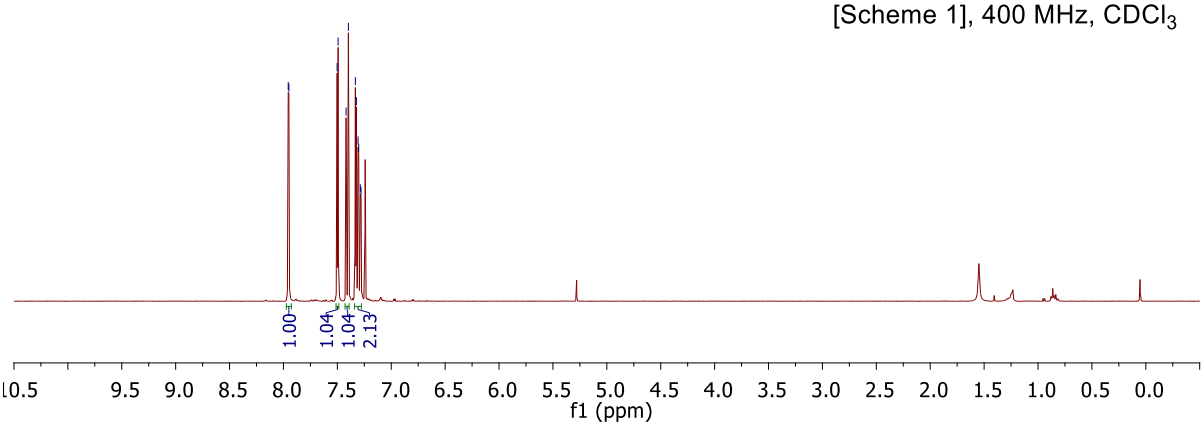


Entry **11.**
[Scheme 1], 151 MHz, $CDCl_3$

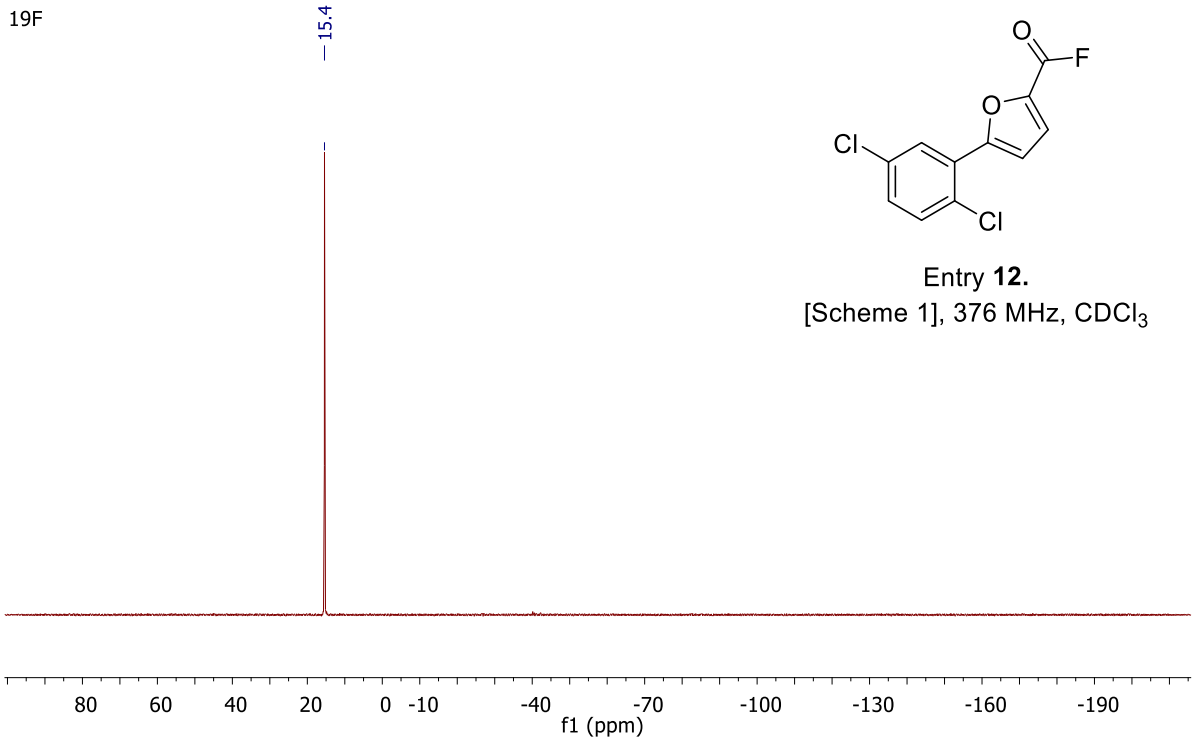
1H



Entry **12.**
[Scheme 1], 400 MHz, $CDCl_3$

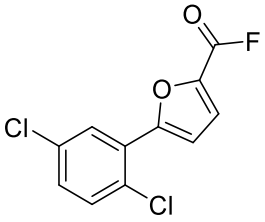


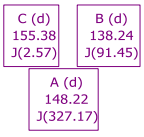
19F



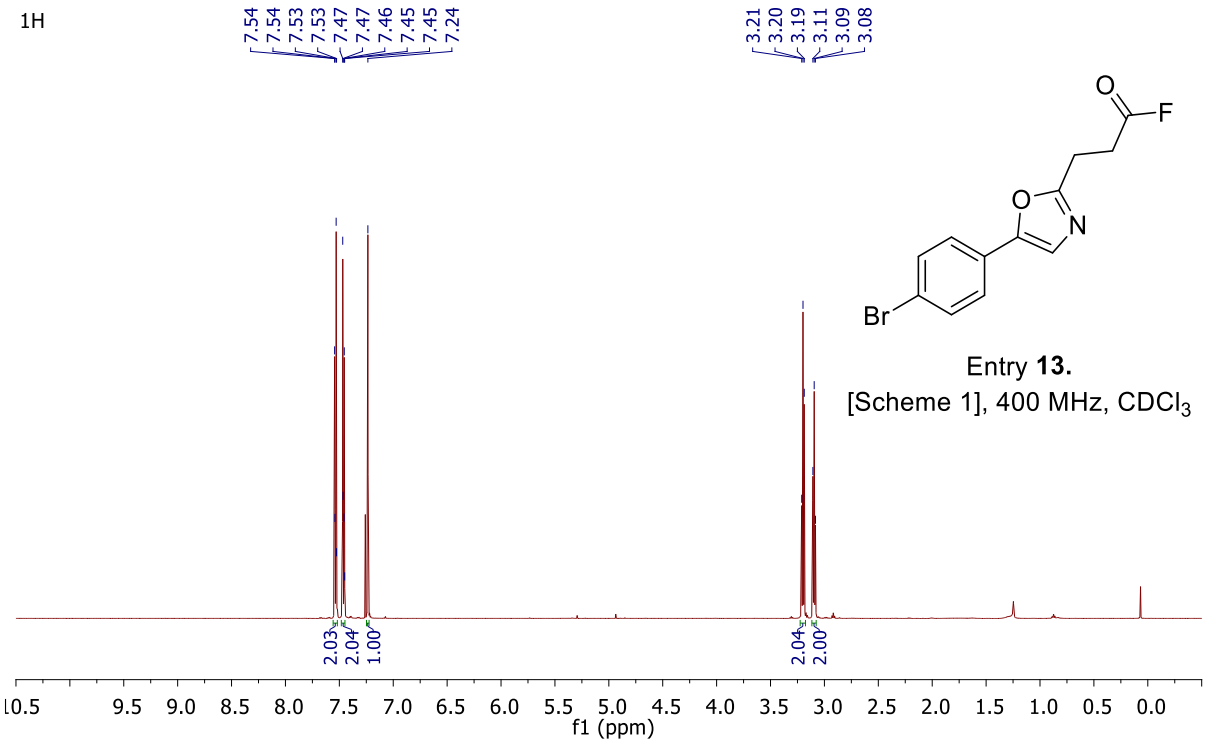
Entry **12.**
[Scheme 1], 376 MHz, $CDCl_3$

13C

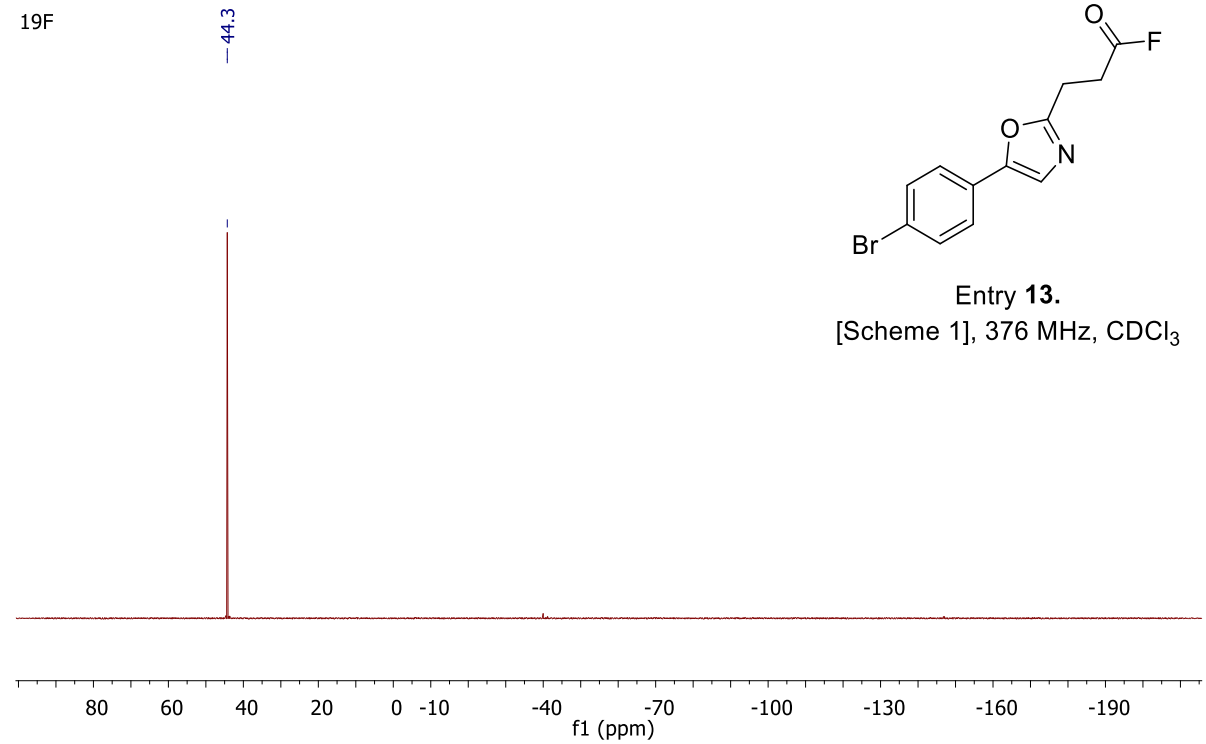




Entry **12.**
[Scheme 1], 151 MHz, $CDCl_3$

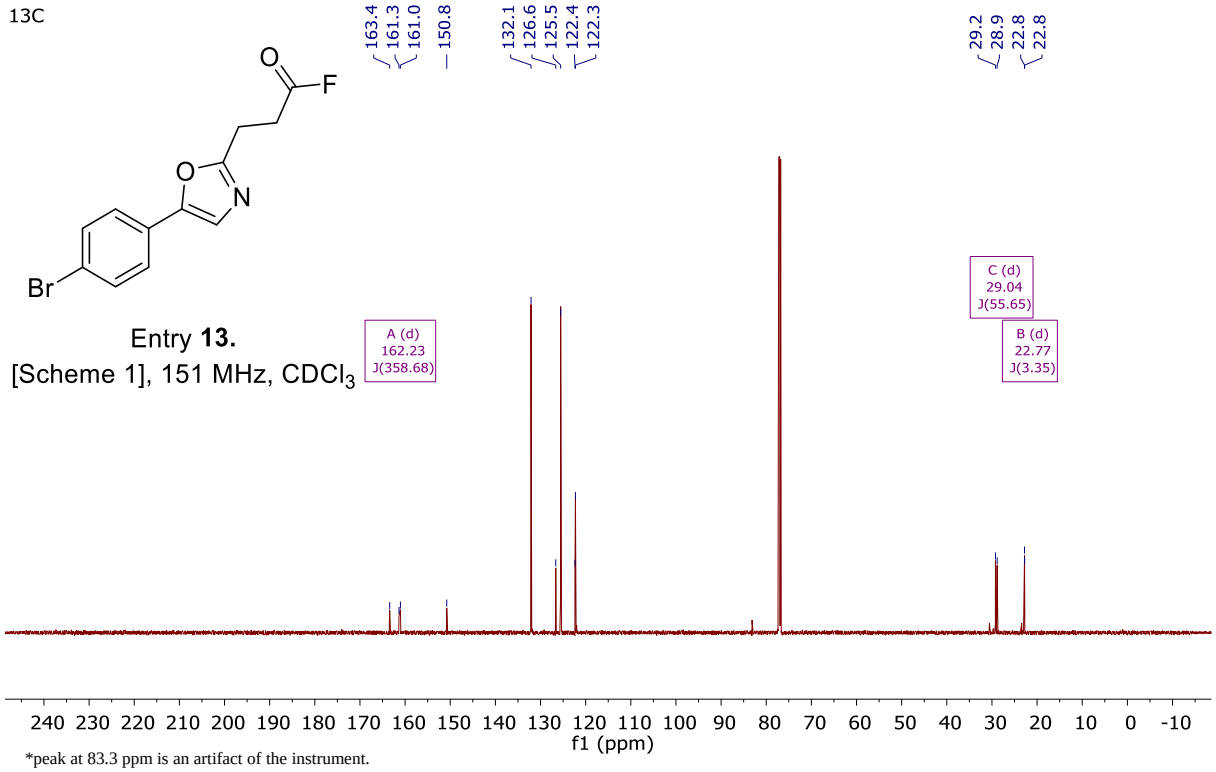


Entry **13.**
[Scheme 1], 400 MHz, $CDCl_3$



Entry **13.**
[Scheme 1], 376 MHz, $CDCl_3$

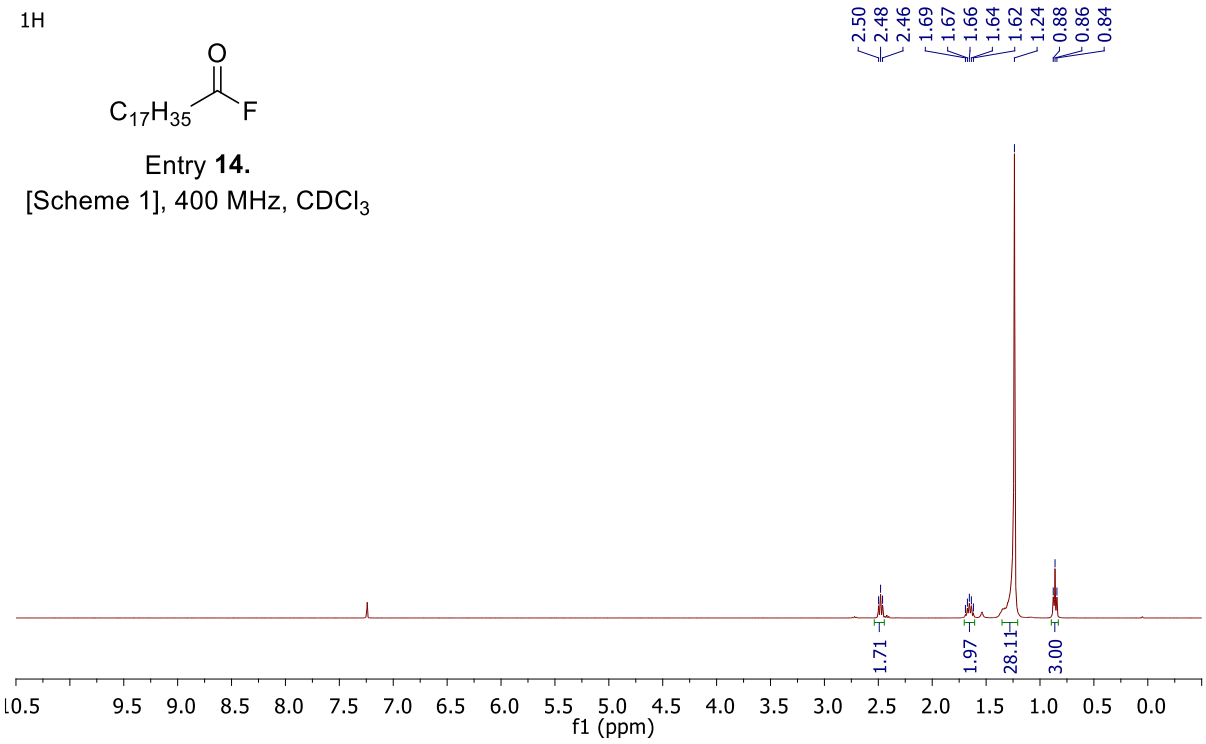
13C



Entry **13.**
[Scheme 1], 151 MHz, $CDCl_3$

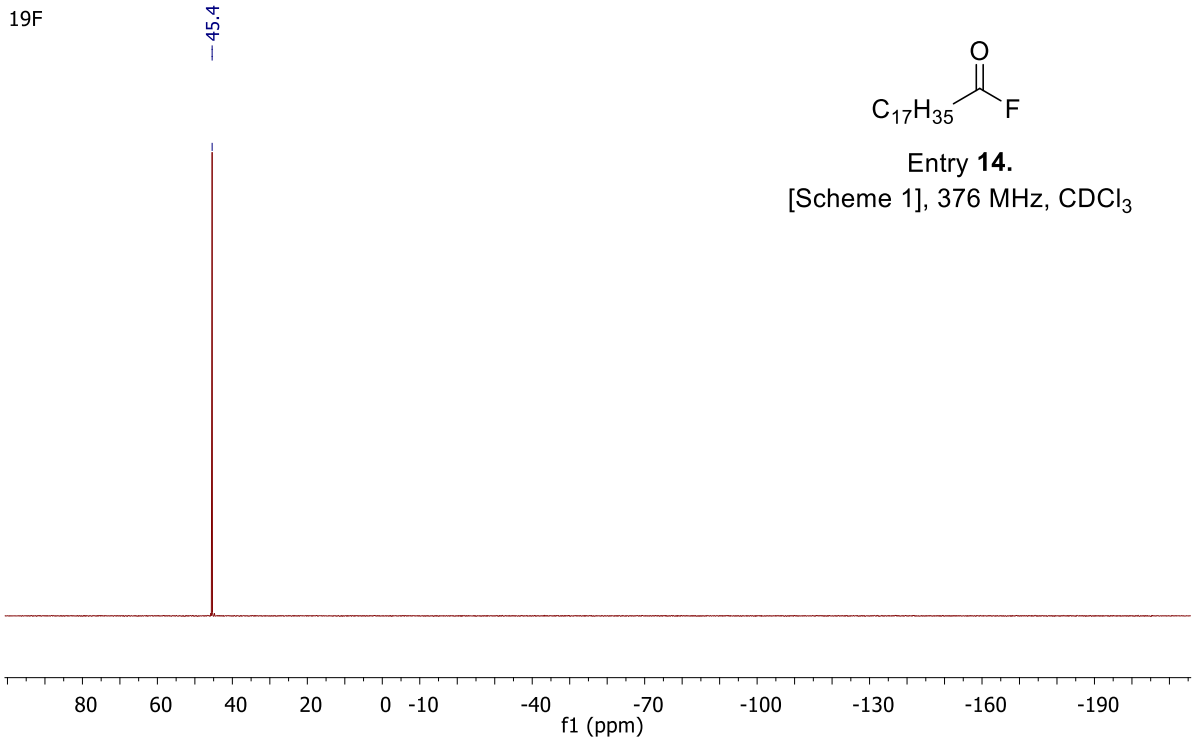
*peak at 83.3 ppm is an artifact of the instrument.

1H



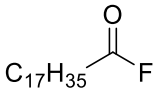
Entry **14.**
[Scheme 1], 400 MHz, $CDCl_3$

19F



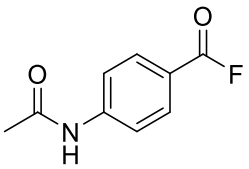
Entry **14.**
[Scheme 1], 376 MHz, $CDCl_3$

13C

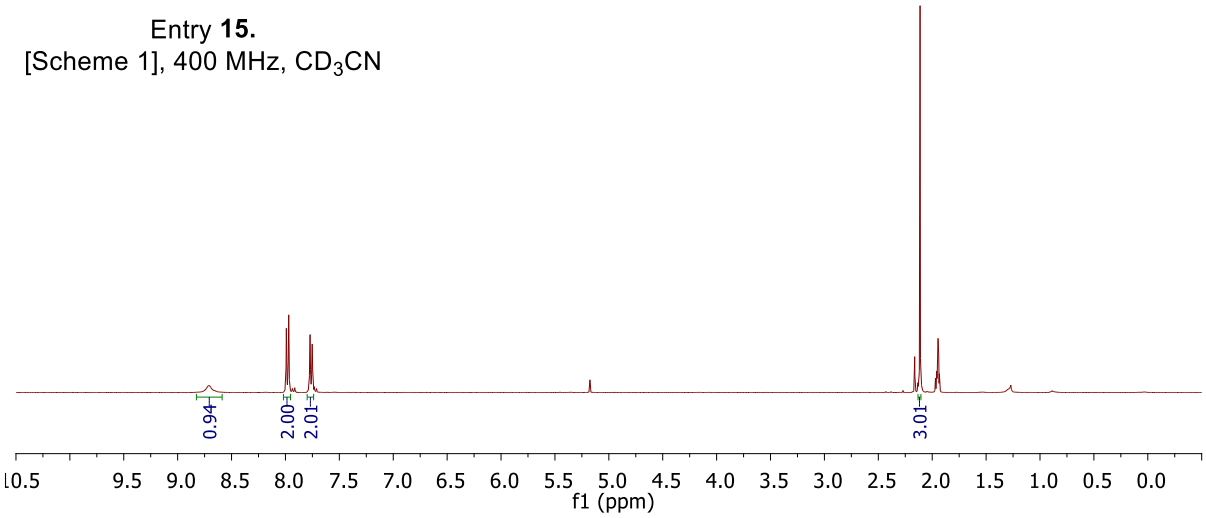


Entry **14.**
[Scheme 1], 151 MHz, $CDCl_3$

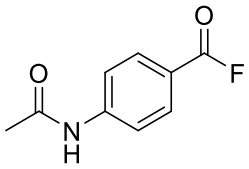
1H



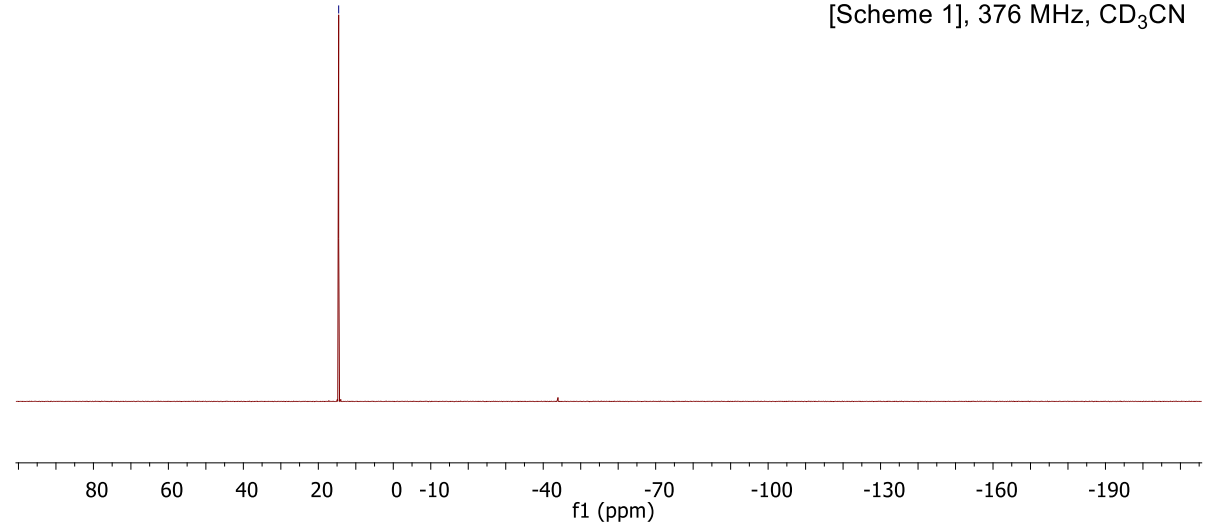
Entry **15.**
[Scheme 1], 400 MHz, CD_3CN

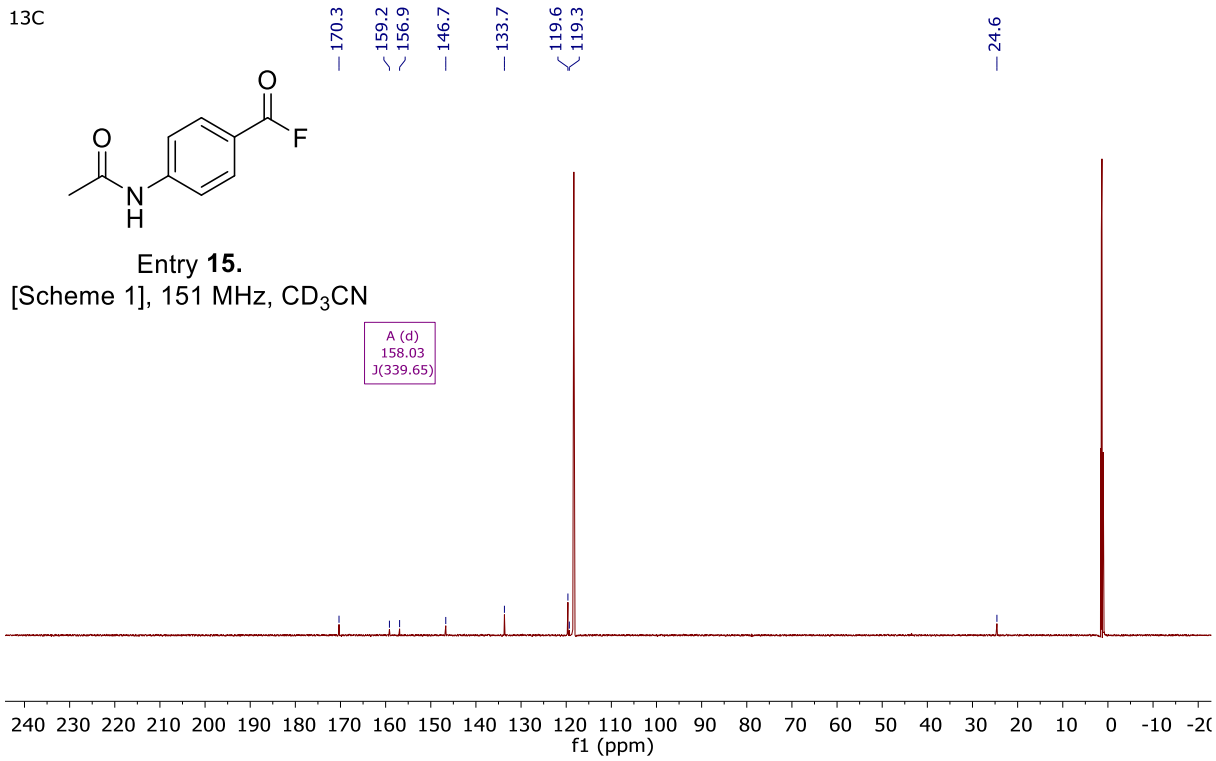


19F

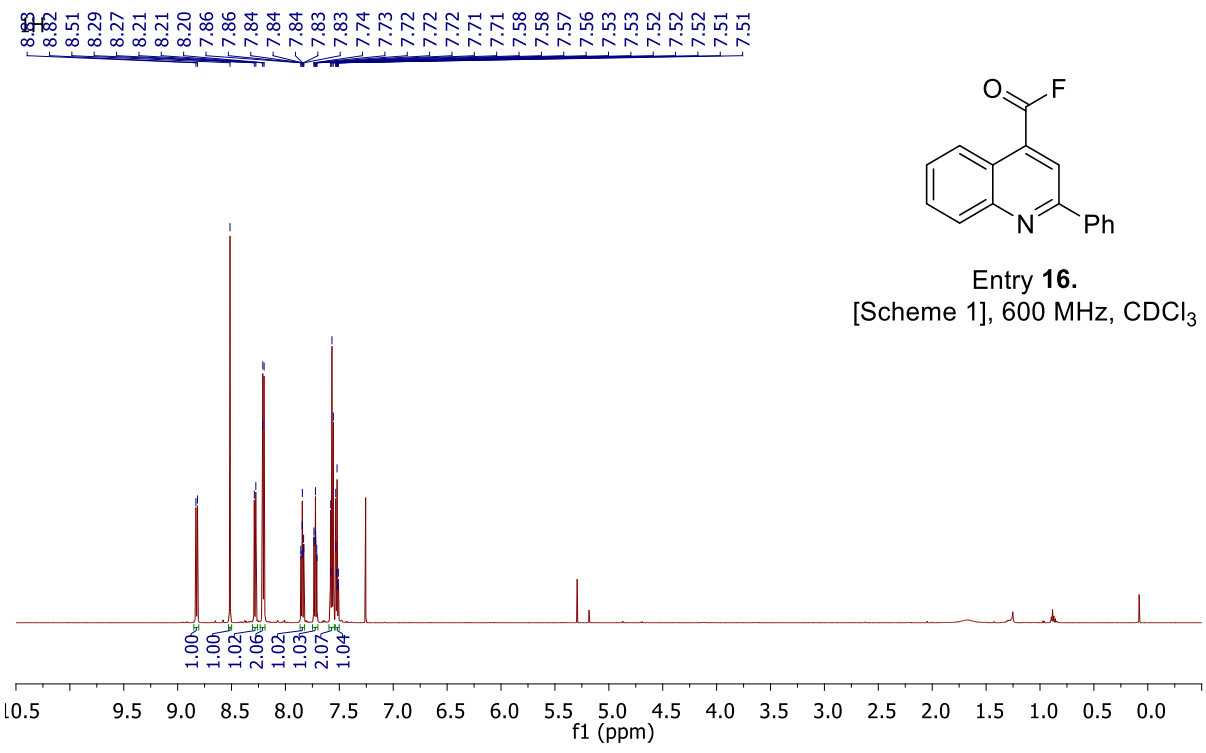


Entry **15.**
[Scheme 1], 376 MHz, CD_3CN



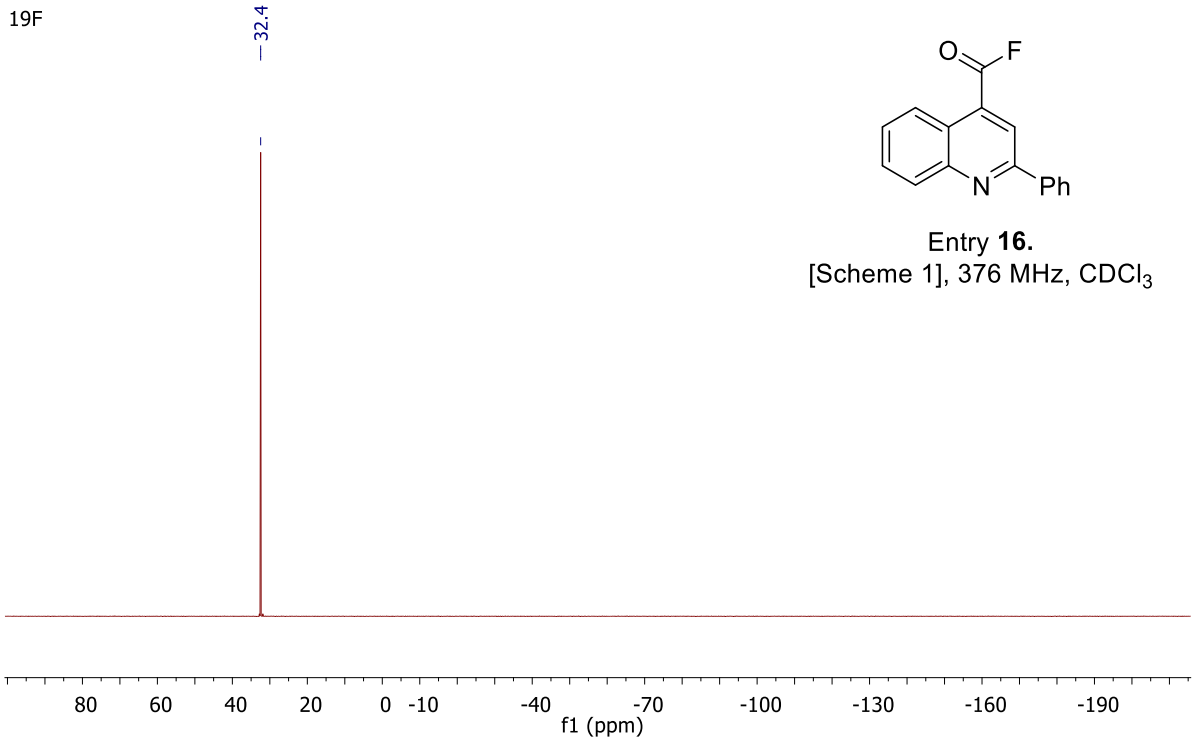


Entry **15.**
[Scheme 1], 151 MHz, CD_3CN



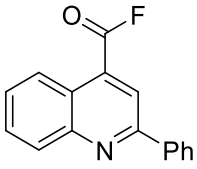
Entry **16.**
[Scheme 1], 600 MHz, $CDCl_3$

19F



Entry **16.**
[Scheme 1], 376 MHz, $CDCl_3$

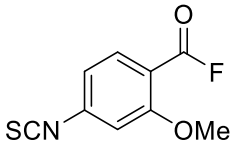
13C



Entry **16.**
[Scheme 1], 151 MHz, $CDCl_3$

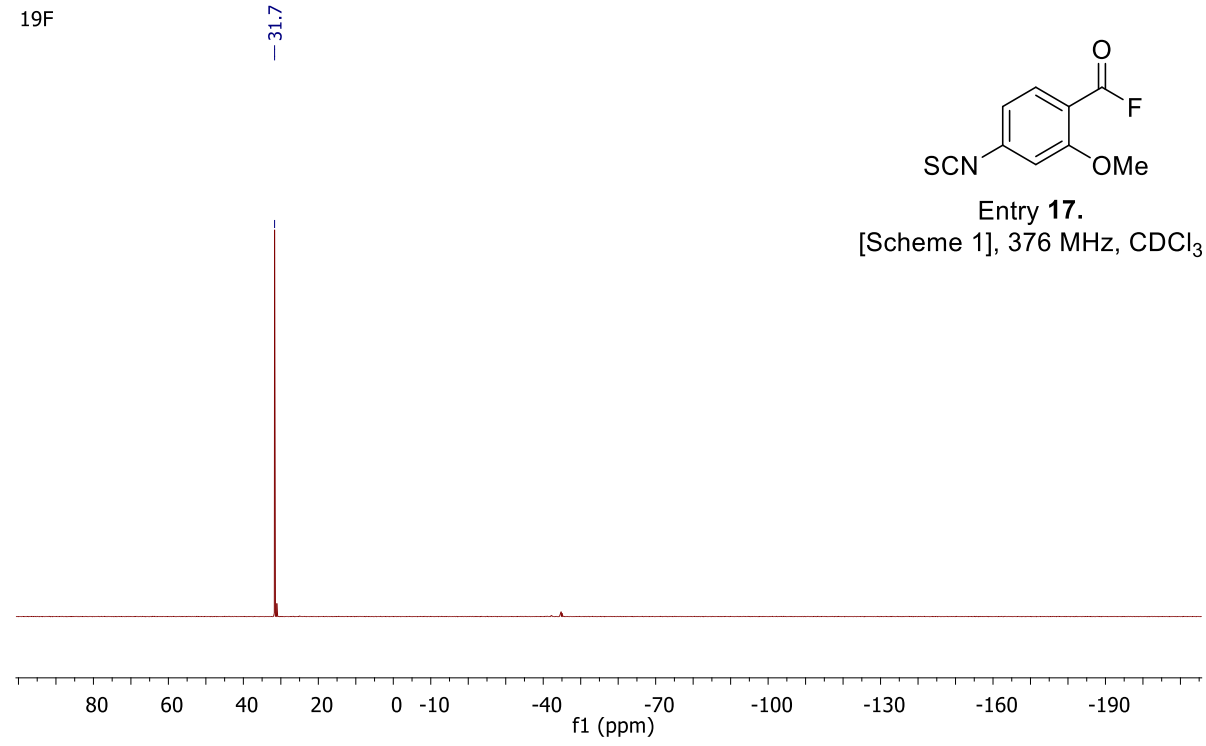
*peak at 83.3 ppm is an artifact of the instrument.

1H



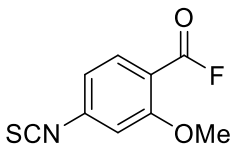
Entry **17.**
[Scheme 1], 400 MHz, $CDCl_3$

19F



Entry **17.**
[Scheme 1], 376 MHz, $CDCl_3$

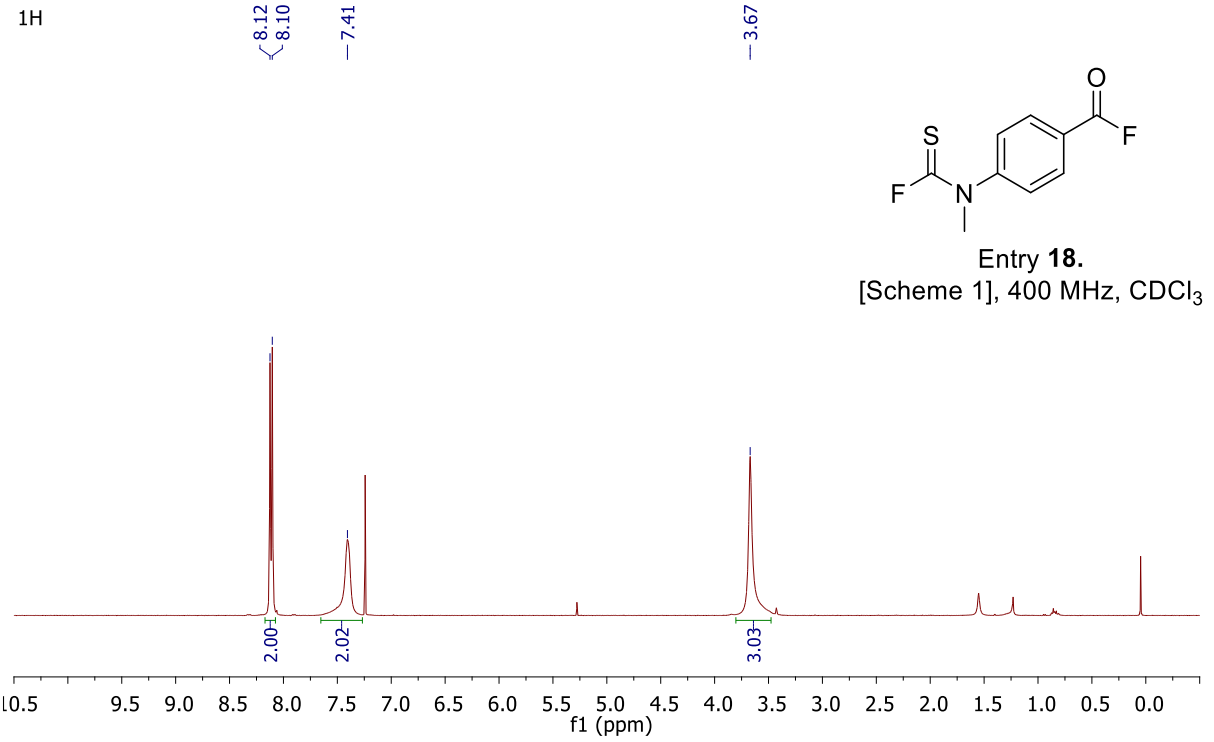
13C



Entry **17.**
[Scheme 1], 151 MHz, $CDCl_3$

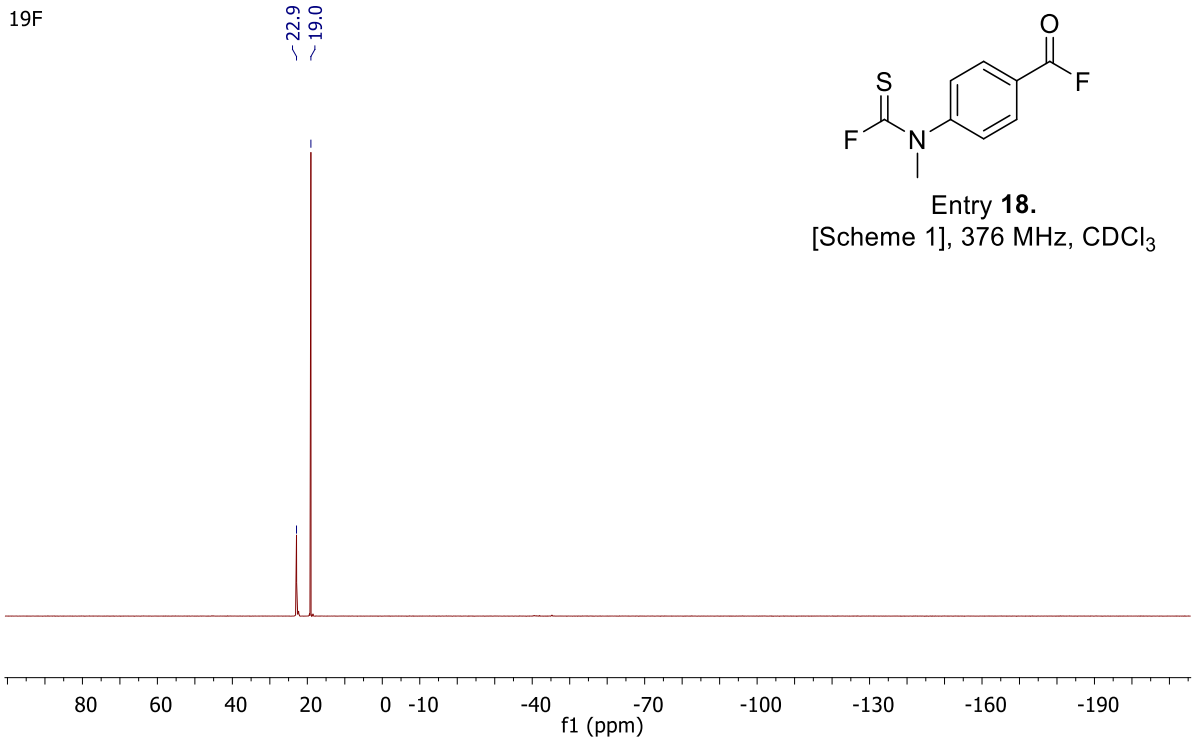
*peak at 83.3 ppm is an artifact of the instrument.

1H



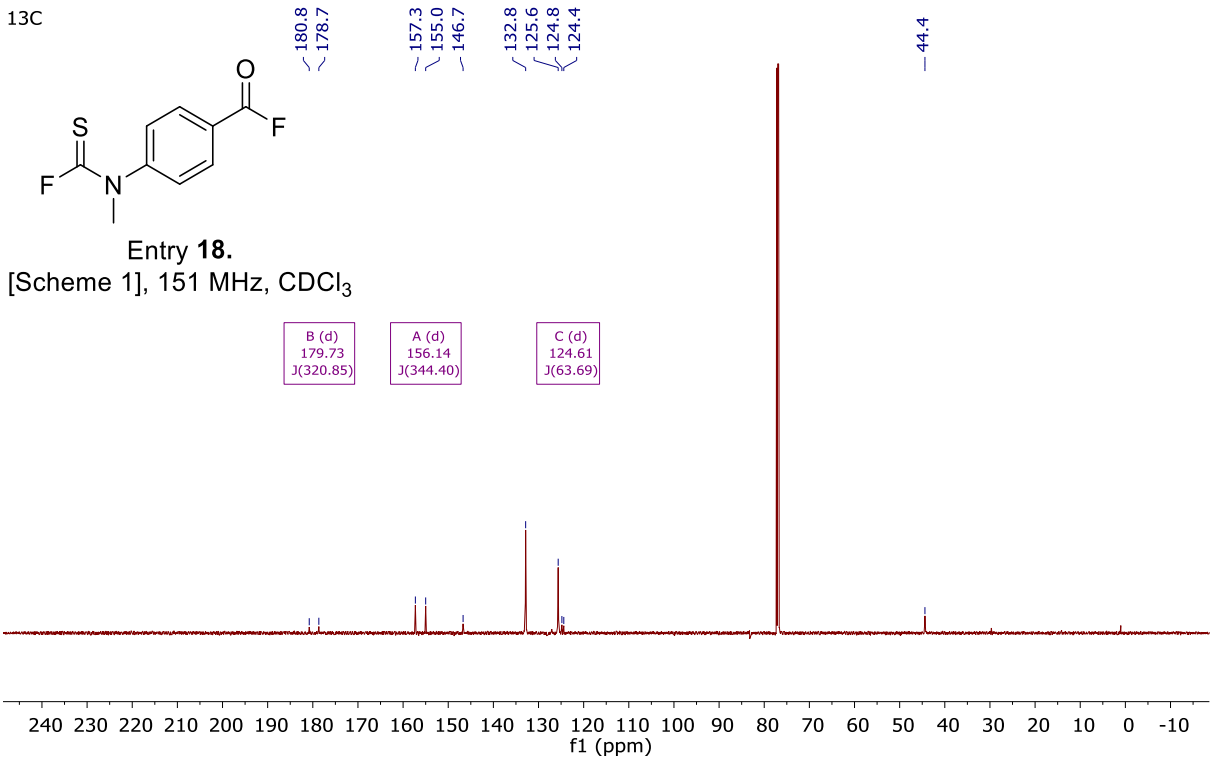
Entry **18.**
[Scheme 1], 400 MHz, $CDCl_3$

19F

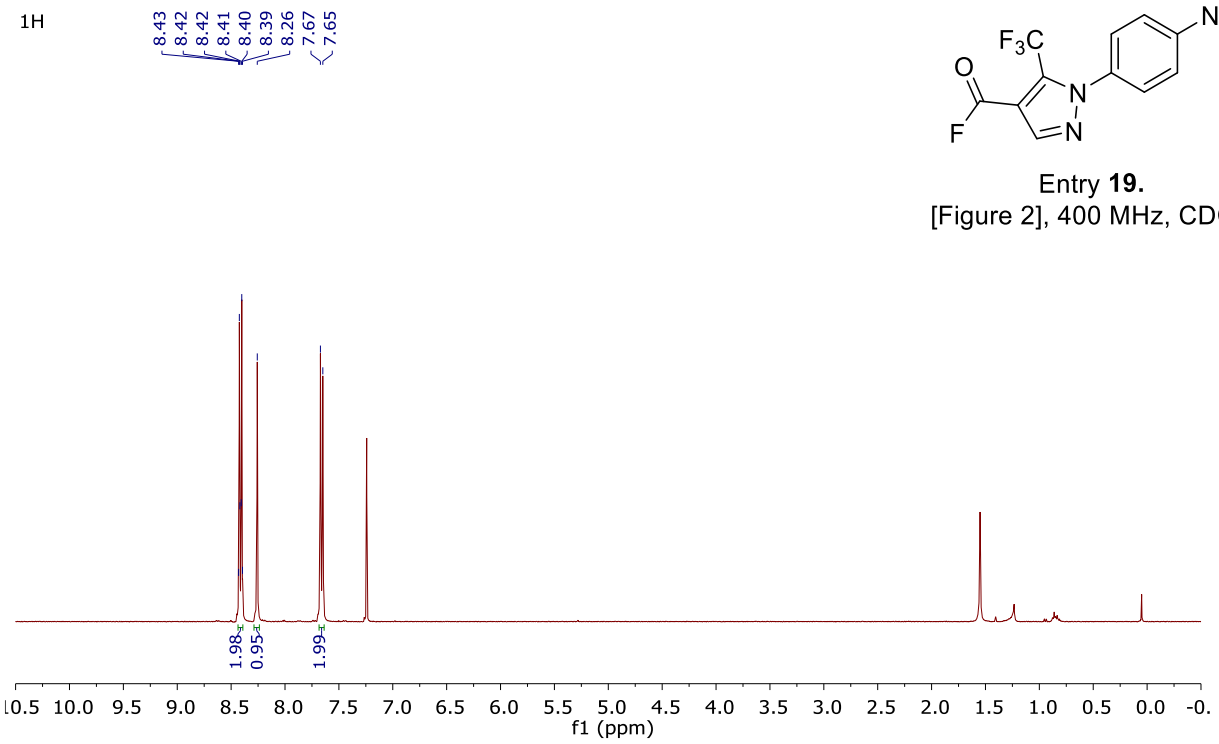


Entry **18.**
[Scheme 1], 376 MHz, $CDCl_3$

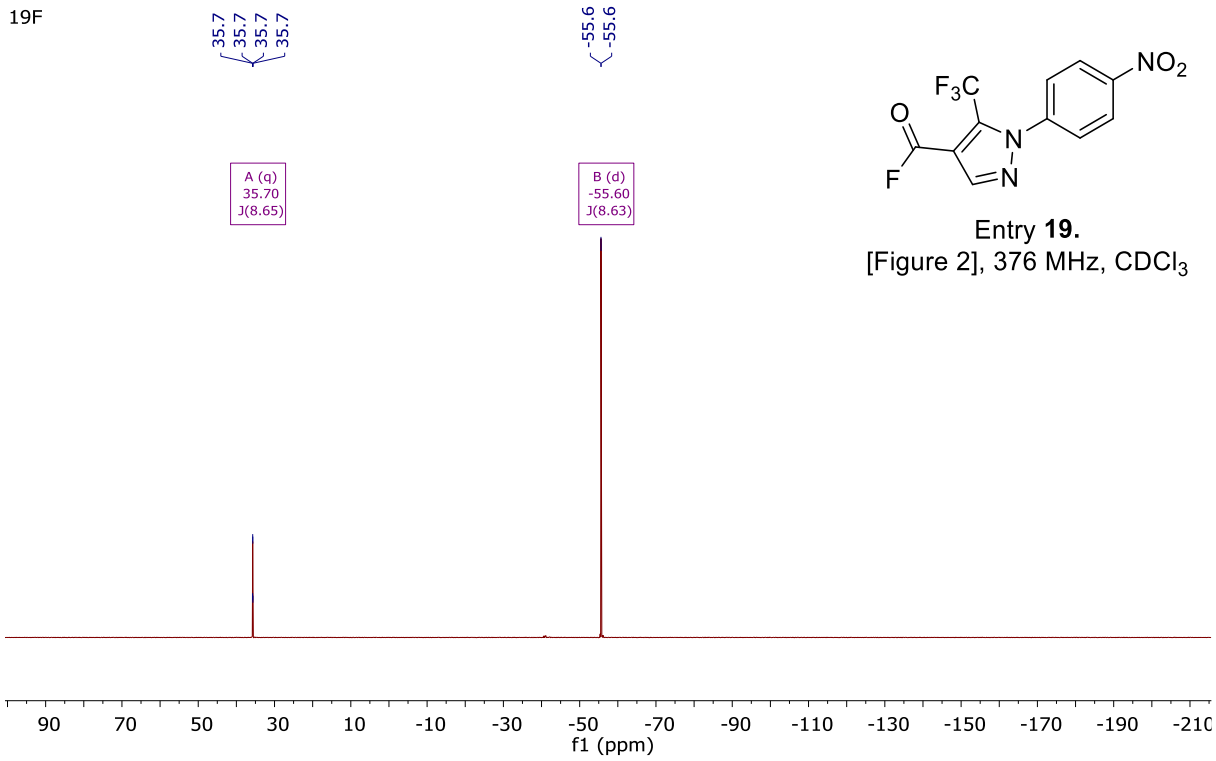
13C



Entry **18.**
[Scheme 1], 151 MHz, $CDCl_3$

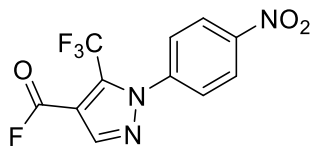


Entry **19.**
[Figure 2], 400 MHz, $CDCl_3$



Entry **19.**
[Figure 2], 376 MHz, $CDCl_3$

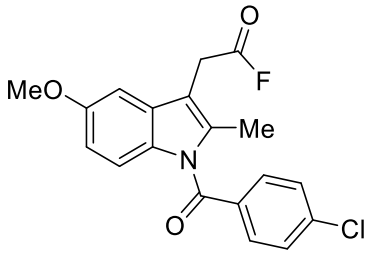
13C



Entry **19.**
[Figure 2], 151 MHz, $CDCl_3$

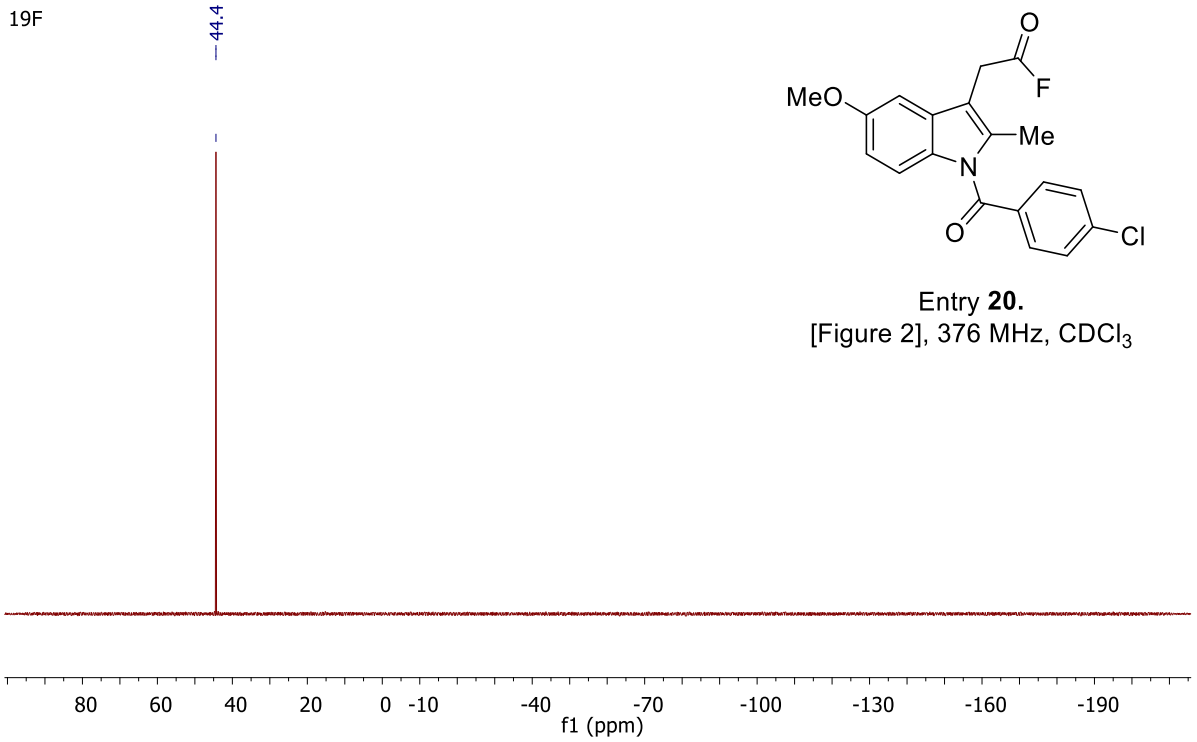
*peak at 83.3 ppm is an artifact of the instrument.

1H



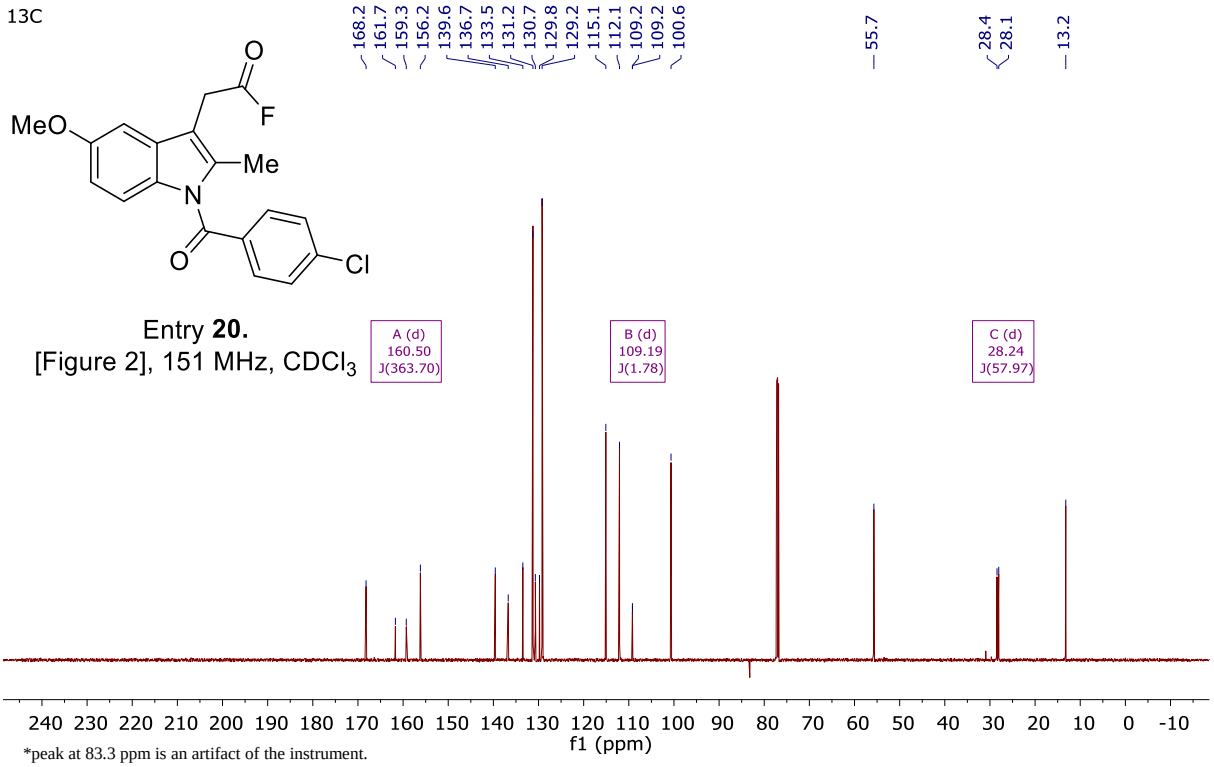
Entry **20.**
[Figure 2], 400 MHz, $CDCl_3$

19F



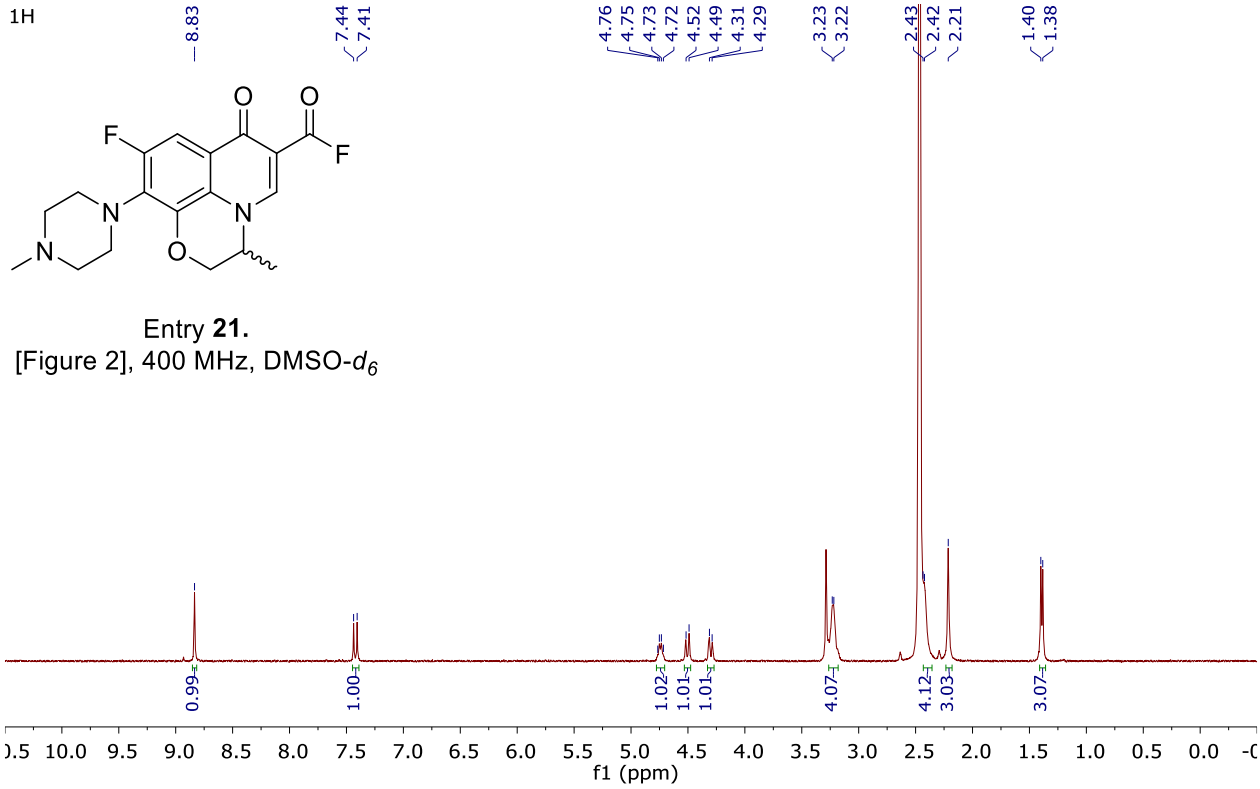
Entry **20.**
[Figure 2], 376 MHz, $CDCl_3$

13C

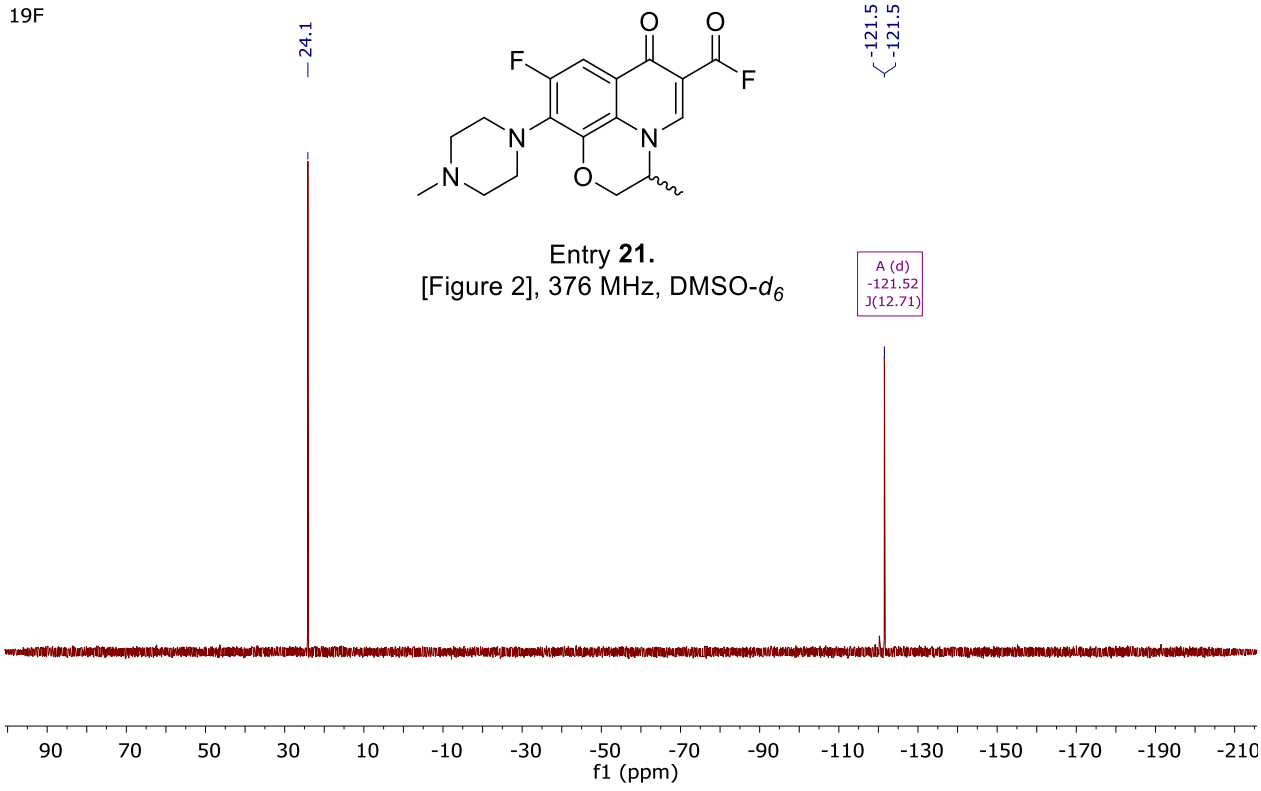


Entry **20.**
[Figure 2], 151 MHz, $CDCl_3$

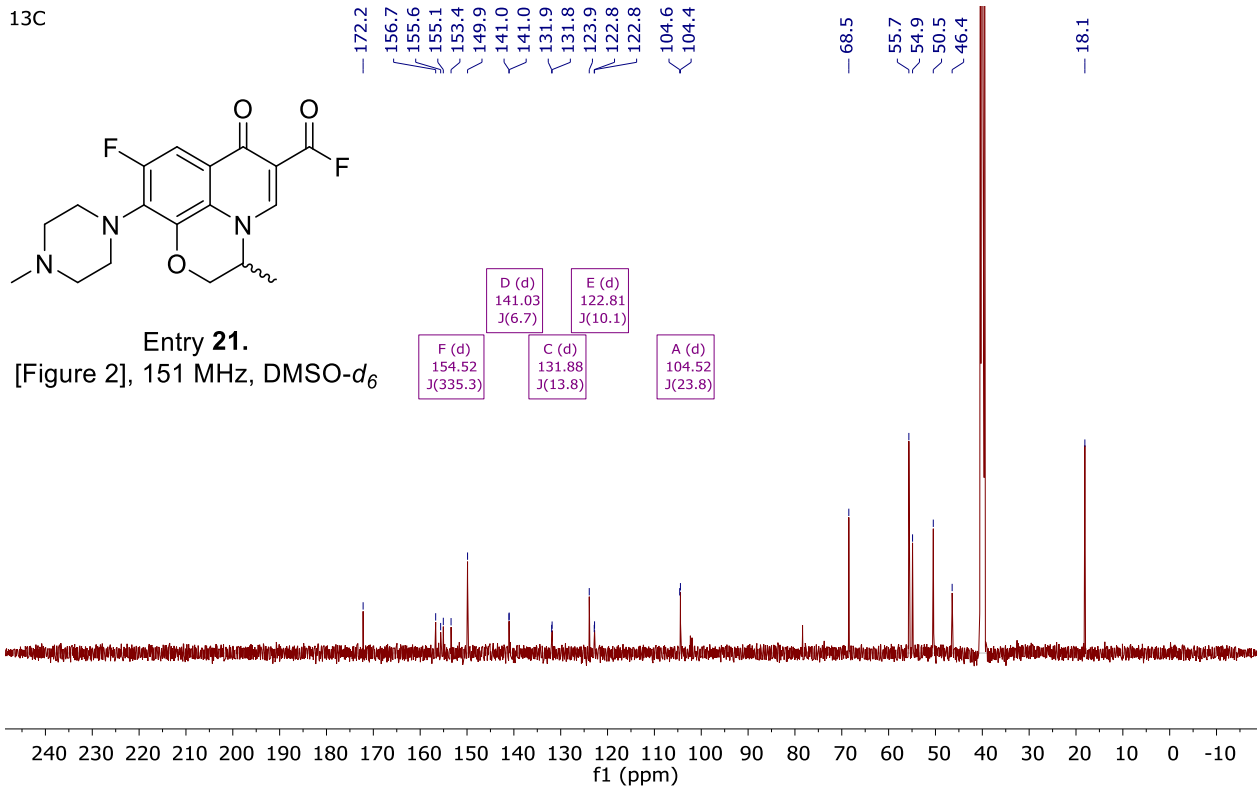
*peak at 83.3 ppm is an artifact of the instrument.



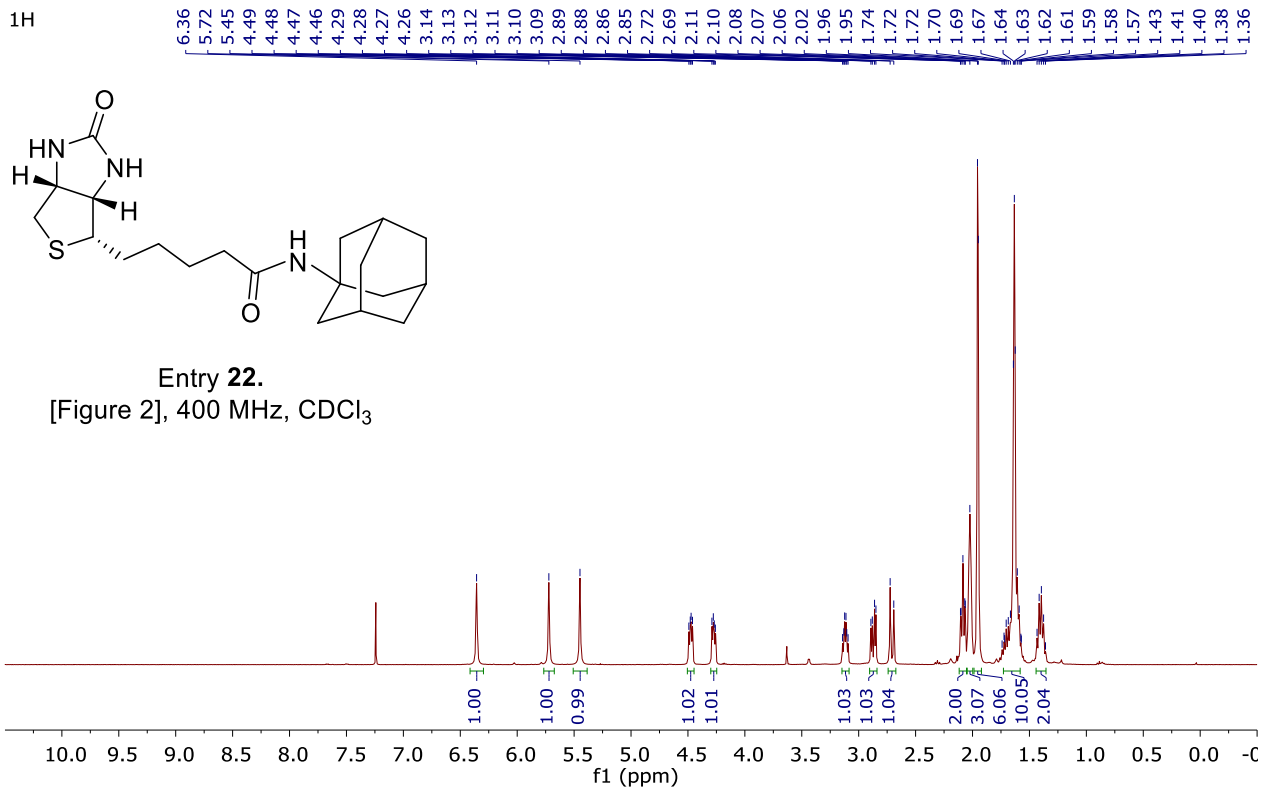
Entry **21.**
[Figure 2], 400 MHz, DMSO-d_6



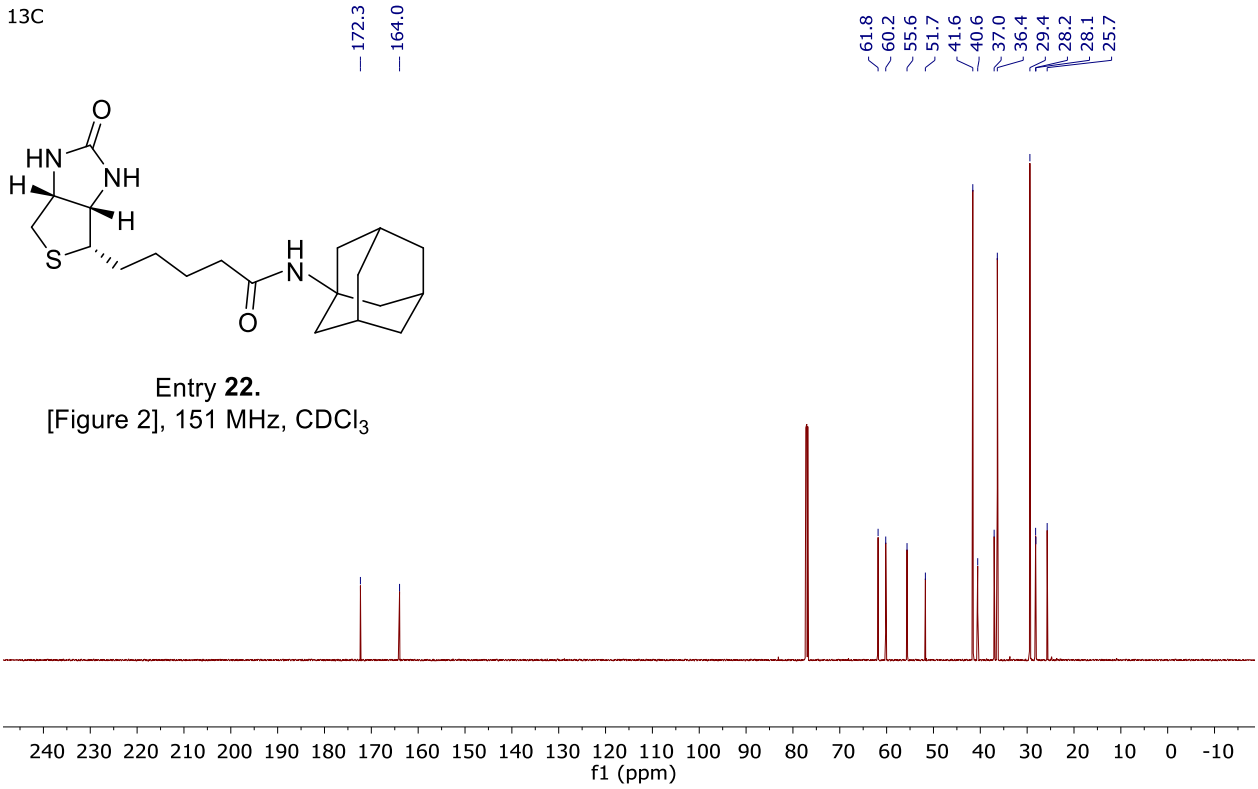
Entry **21.**
[Figure 2], 376 MHz, DMSO-d_6



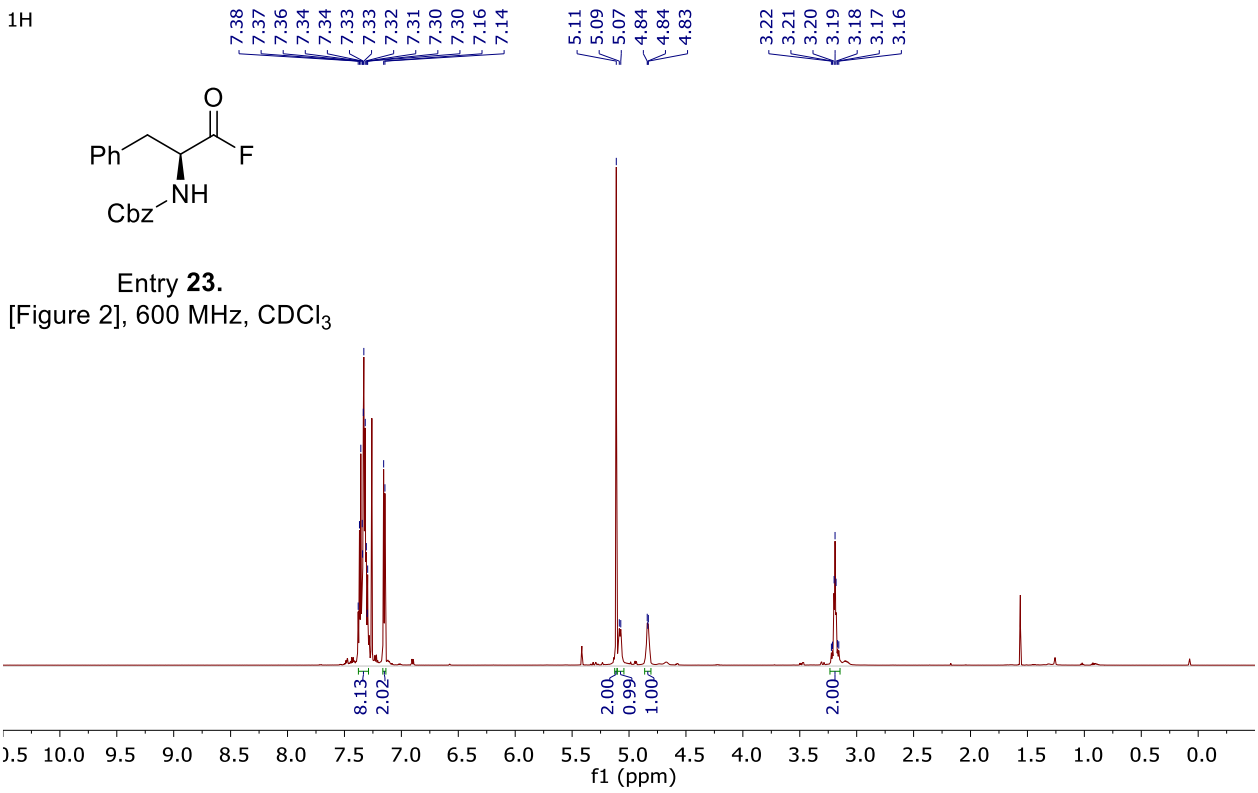
Entry **21.**
[Figure 2], 151 MHz, DMSO-d_6



Entry **22.**
[Figure 2], 400 MHz, $CDCl_3$

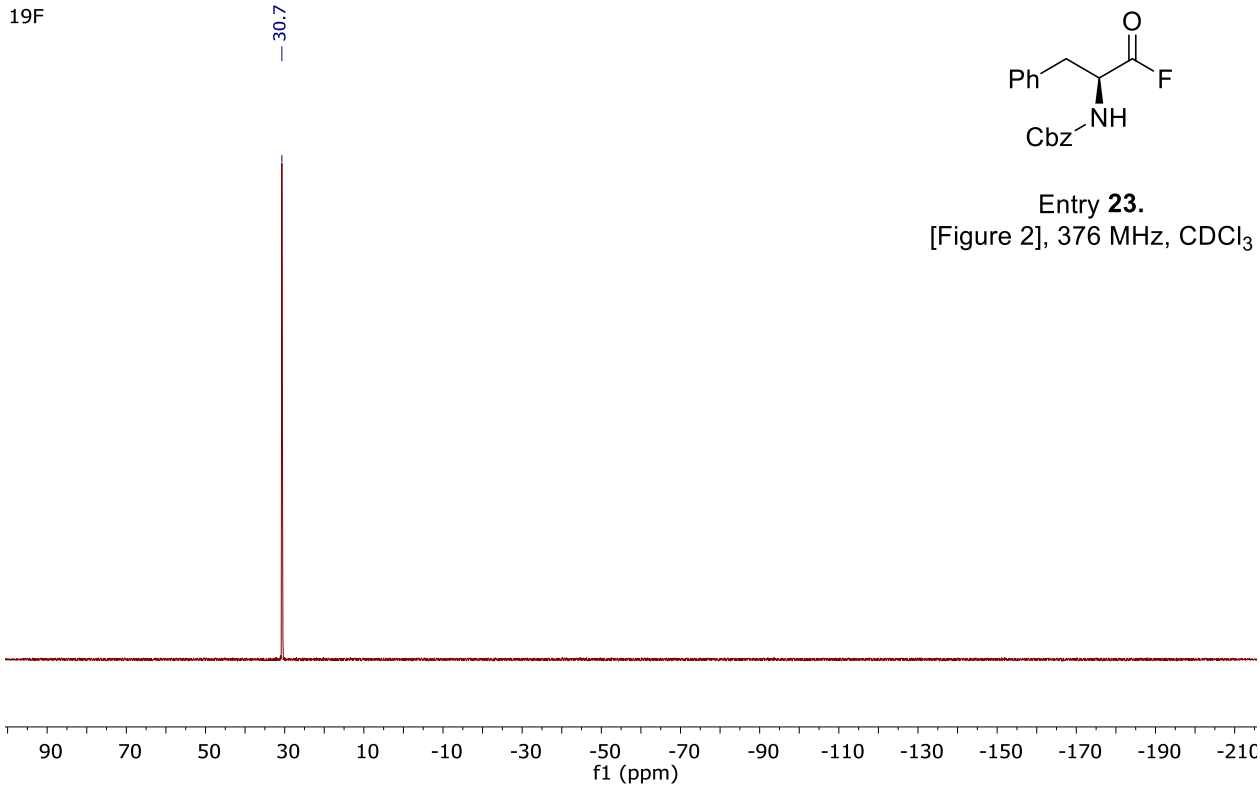


Entry **22.**
[Figure 2], 151 MHz, $CDCl_3$



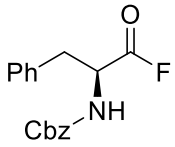
Entry **23.**
[Figure 2], 600 MHz, $CDCl_3$

19F

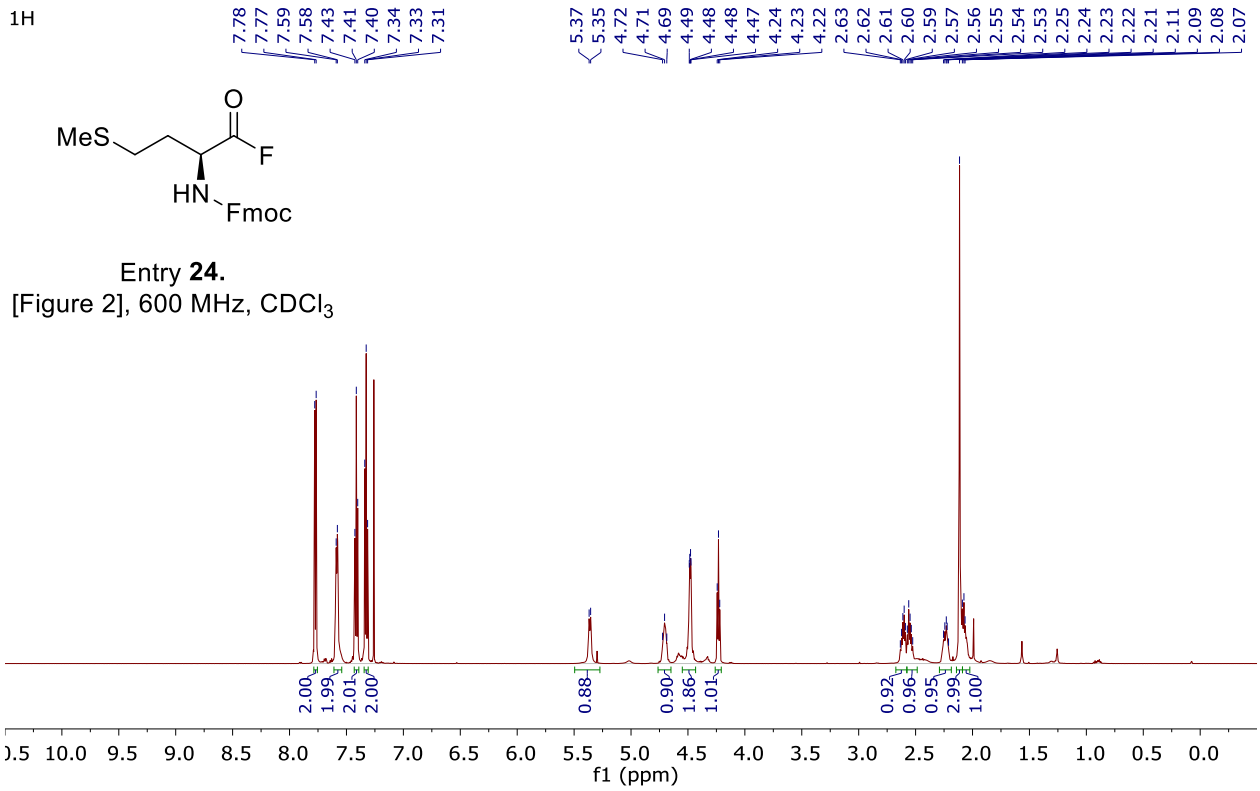


Entry **23.**
[Figure 2], 376 MHz, $CDCl_3$

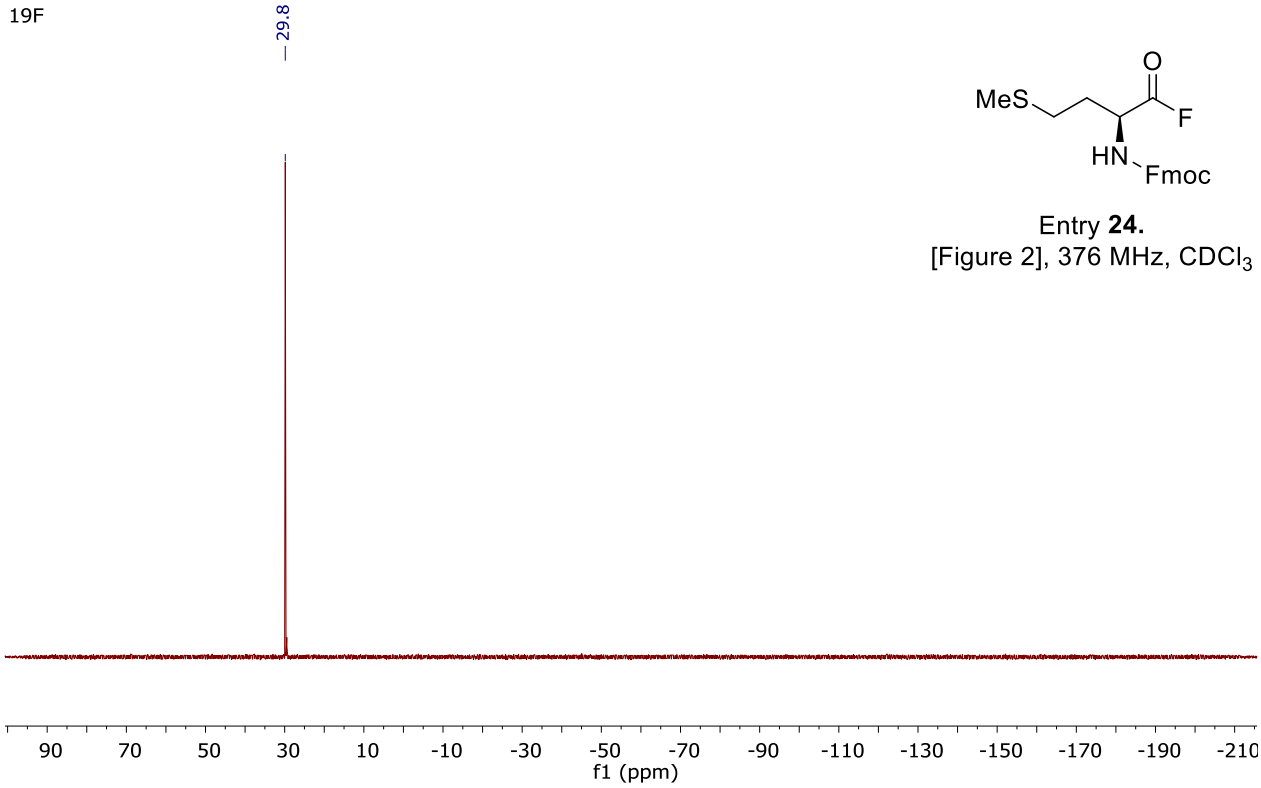
13C



Entry **23.**
[Figure 2], 151 MHz, $CDCl_3$

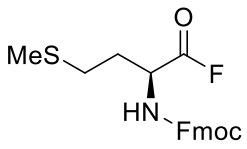


Entry **24.**
[Figure 2], 600 MHz, $CDCl_3$



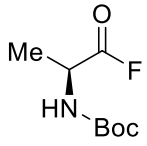
Entry **24.**
[Figure 2], 376 MHz, $CDCl_3$

13C



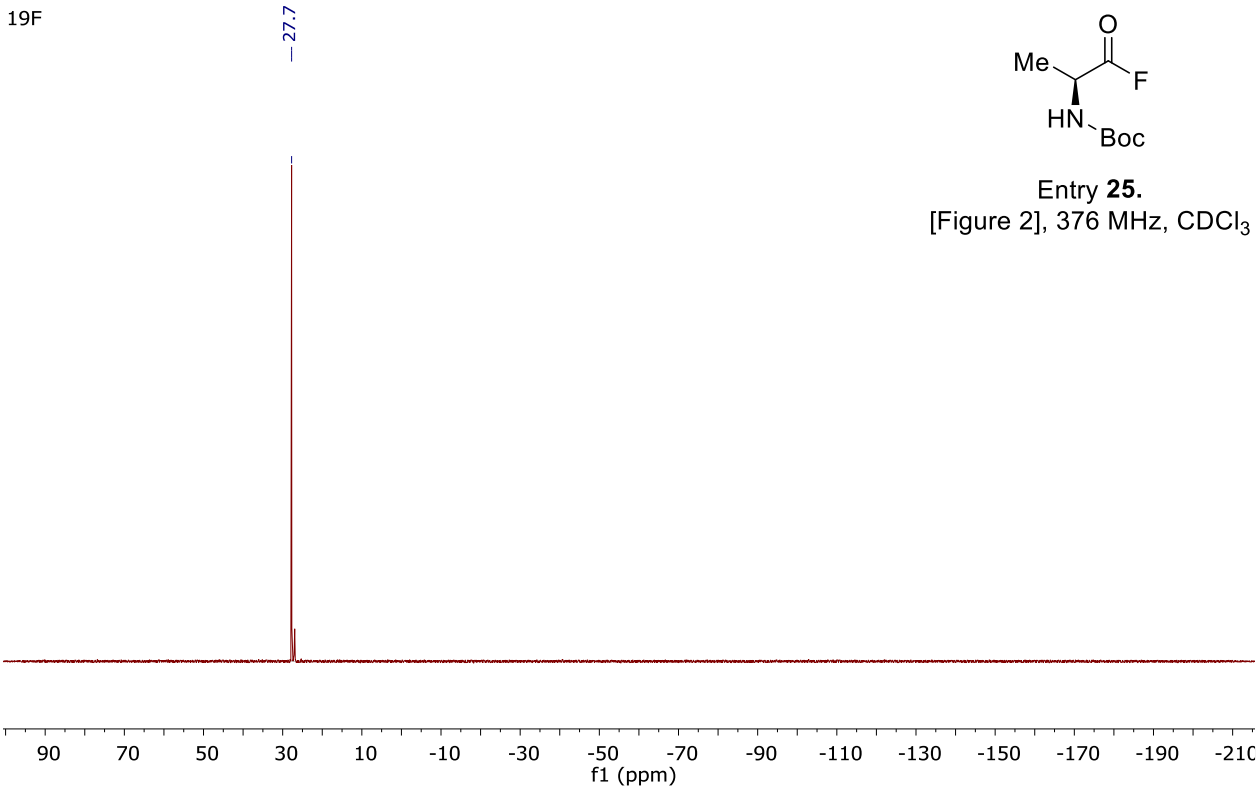
Entry **24.**
[Figure 2], 151 MHz, $CDCl_3$

1H



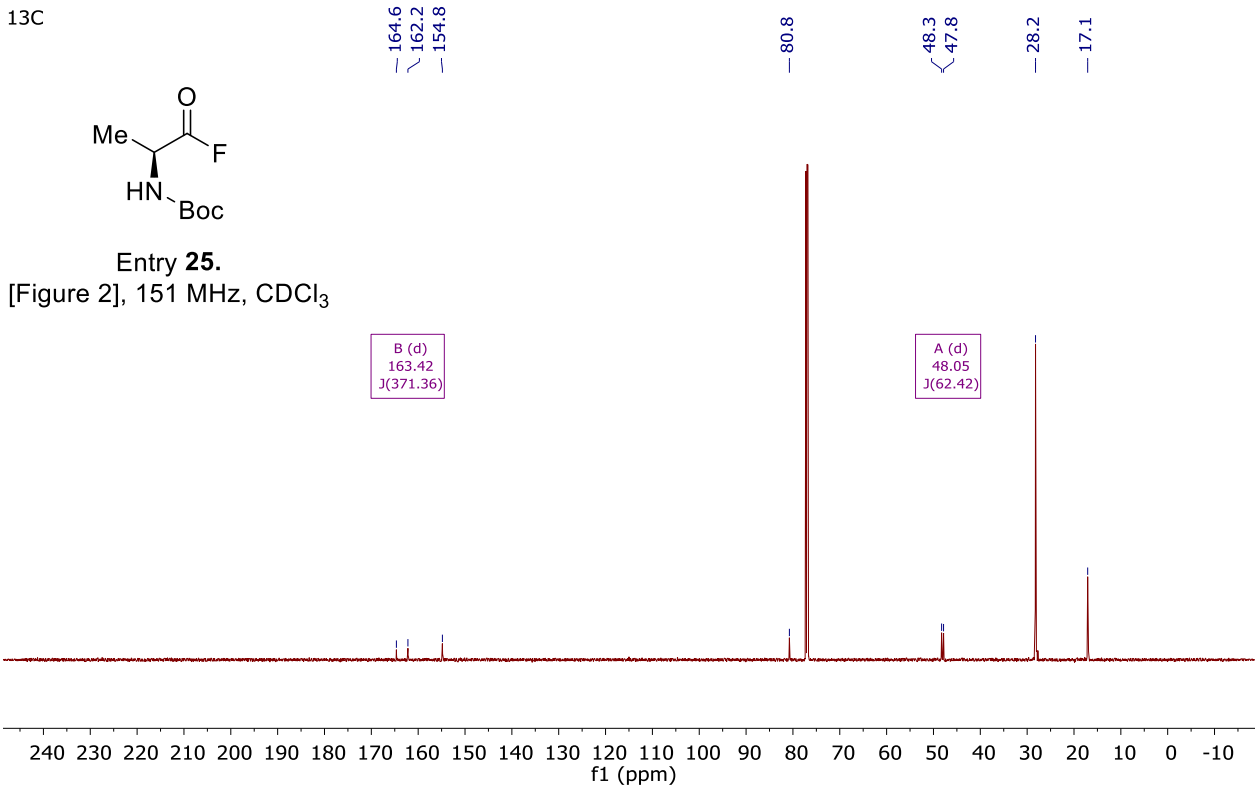
Entry **25.**
[Figure 2], 400 MHz, $CDCl_3$

19F



Entry **25.**
[Figure 2], 376 MHz, $CDCl_3$

13C



Entry **25.**
[Figure 2], 151 MHz, $CDCl_3$