ELECTRONIC SUPPORTING INFORMATION

For

Chemoselective Synthesis of α-Fluoromethyl Amides *via* the Controlled Addition of $LiCH_2F$ to *N*-Aryl and *N*-Alkyl Isocyanates

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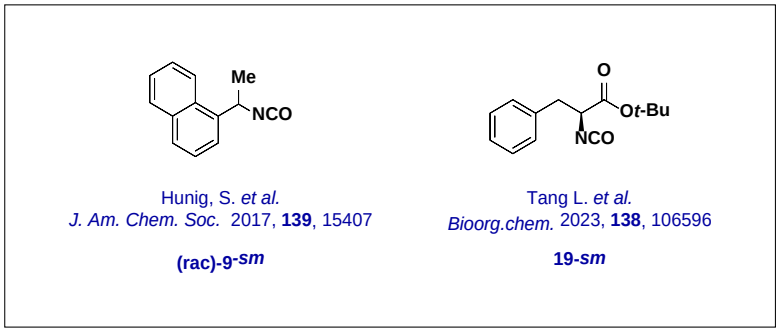
Instrumentation and General Analytical Methods

^{1}H- and ^{13}C-NMR spectra were recorded with a Bruker Avance Neo 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F) and a Jeol ECZR600 spectrometer (600 MHz for ^{1}H, 150 MHz for ^{13}C, 564 MHz for ^{19}F). The center of the (residual) solvent signal was used as internal standard which was related to TMS with δ 7.26 ppm (^{1}H in $CDCl_3$), δ 77.2 ppm (^{13}C in $CDCl_3$), δ 2.50 ppm (^{1}H) and δ 39.5 ppm (^{13}C) for DMSO-d_6. Spin-spin coupling constants (*J*) are given in Hz.

All reactions were performed under an inert atmosphere of argon by using standard schlenk techniques. THF and Et_2O were distilled over Na/benzophenone. Chemicals were purchased from SigmaAldrich, Acros, Alfa Aesar, Fluorochem and TCI Europe. Non-commercially available starting materials were prepared as detailed below and are indicated with the descriptor **nn-*sm***, being **nn** the corresponding final compound in the manuscript. Solutions were evaporated under reduced pressure with a rotary evaporator. For column chromatography, silica Gel 60 (0.04-0.063 mm) was used. TLC was carried out on aluminium sheets precoated with silica gel 60F254 (Merchery-Nagel, Merk); the spots were visualized under UV light (λ = 254 nm) and/or $KMnO_{4\ (aq.)}$ was used as revealing system.

Synthesis of starting materials

Most of isocyanates employed as starting materials are commercially available and were purchased from Thermofisher, VWR, Sigma-Aldrich, TCI and BLDPharm. Those which are not available were prepared as previously reported (see below). *All isocyanates were distilled or recrystallized prior to their use in order to eliminate traces of amines.*



Hunig, S. *et al.*
J. Am. Chem. Soc. 2017, **139**, 15407

(rac)-9-*sm*

Tang L. *et al.*
Bioorg.chem. 2023, **138**, 106596

19-*sm*

General procedures for the synthesis of α-fluoroacetamides

General procedure for 2-fluoroacetamides from *non*-sterically hindered aryl isocyanates (GP1)

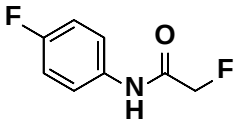
Under Ar atmosphere, to a solution of isocyanate (1.0 equiv) in dry THF/Et_2O 1:1 (20 mL) and fluoroiodomethane (5.2 equiv) cooled down to -78 °C, MeLi (1.6 M in Et_2O, 5 equiv) was quickly added and the mixture was immediately quenched (within 20 seconds) with a saturated solution of $NH_4Cl_{(aq.)}$ (3 mL). The organic phase was extracted with Et_2O (3 x 10 mL), washed with brine, dried over anhydrous Na_2SO_4 and the solvent was finally removed under reduced pressure. The final product was purified by column chromatography on silica gel as described below.

General procedure for 2-fluoroacetamides from alkyl- and sterically hindered aryl isocyanates (GP2)

Under Ar atmosphere, to a solution isocyanate (1.0 equiv) in dry THF/Et_2O 1:1 (5 mL) and fluoroiodomethane (3.0 equiv) cooled down to -78 °C, MeLi (1.6 M in Et_2O, 2.8 equiv) was added dropwise and the mixture was stirred for 5 minutes. Subsequently, a saturated solution of $NH_4Cl_{(aq.)}$ (3 mL) was added. The organic phase was extracted with Et_2O (3 x 10 mL), washed with brine, dried over anhydrous Na_2SO_4 and the solvent was finally removed under reduced pressure. The final product was purified by column chromatography on silica gel as described below.

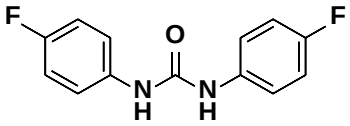
Characterization and spectral data of all products

2-fluoro-*N*-(4-fluorophenyl)acetamide (2)



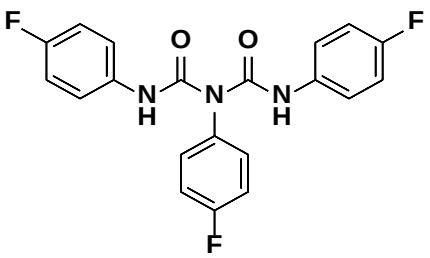
By following the general procedure 1 (GP1), starting from 4-fluorophenyl isocyanate (137.1 mg, 0.11 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (828.4 mg, 0.35 mL, 5.2 mmol, 5.2 equiv) and MeLi (3.12 mL of a solution 1.6 M in Et_2O, 5.0 mmol, 5.0 equiv) in dry THF/Et_2O (1:1 v/v, 20 mL), compound **2**[1] was obtained in 86% yield (147.1 mg) as a white solid (m.p.: 98 °C, lit[1] 99-100 °C) after chromatography on silica gel (7:3 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.90 (s, 1H), 7.59 – 7.49 (m, 2H), 7.06 (t, J = 8.6 Hz, 2H), 4.93 (d, J = 47.4 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.59 (d, J = 16.2 Hz), 160.01 (d, J = 244.6 Hz), 132.53 (d, J = 3.0 Hz), 122.10 (d, J = 8.0 Hz), 116.04 (d, J = 22.6 Hz), 80.33 (d, J = 187.5 Hz), 29.85.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -116.79 (dq, J = 8.2, 4.1 Hz), -222.38 (td, J = 47.2, 5.0 Hz).
HRMS (ESI), m/z: calc. for $C_8H_7F_2NOH^+$: 172,0568 $[M+H]^+$; found 172,0562.

1,3-bis(4-fluorophenyl)urea (2a)



Compound **2a**[2] was obtained as a by-product in yield up to 64% during the optimization tests, as a violet solid (m.p.: 261-262 °C, lit[3] 260-262 °C) after chromatography on silica gel (6:4 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (600 MHz, DMSO-d_6) δ: 8.68 (s, 2H), 7.46 (dt, J = 8.8, 3.9 Hz, 4H), 7.11 (t, J = 8.8 Hz, 4H).
^{13}C-NMR (150 MHz, DMSO-d_6) δ: 157.37 (d, J = 237.9 Hz), 152.75, 136.03 (d, J = 2.7 Hz), 120.03 (d, J = 7.8 Hz), 115.27 (d, J = 21.7 Hz).
^{19}F-NMR (376 MHz, DMSO-d_6) δ: -121.46 (m).
HRMS (ESI), m/z: calc. for $C_{13}H_{10}F_2N_2OH^+$: 249,0834 $[M+H]^+$; found 249,0838.

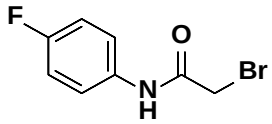
1,3,5-tris(4-fluorophenyl)biuret (2b)



Compound **2b**[4] was obtained as a by-product in yield up to 26% during the optimization tests, as a white solid (m.p.: 178 °C, lit[5] 175.5-179 °C) after chromatography on silica gel (6:4, v/v, petroleum ether/ethyl acetate).

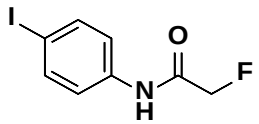
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.76 (s, 2H), 7.38 – 7.30 (m, 2H), 7.30 – 7.24 (m, 4H), 7.23 – 7.14 (m, 2H), 6.99 – 6.87 (m, 4H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 163.18 (d, J = 251.4 Hz), 159.83 (d, J = 244.2 Hz), 153.60, 133.08 (d, J = 2.9 Hz), 132.31 (d, J = 3.4 Hz), 131.85 (d, J = 9.0 Hz), 122.77 (d, J = 8.0 Hz), 117.76 (d, J = 22.9 Hz), 115.88 (d, J = 22.6 Hz).
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -109.97 (p, *J* = 7.6 Hz), -117.55 (br s).
HRMS (ESI), m/z: calc. for $C_{20}H_{14}F_3N_3O_2H^+$: 386,1111 $[M+H]^+$; found 386,1116.

2-bromo-*N*-(4-fluorophenyl)acetamide (2c)



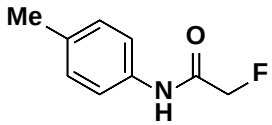
Compound **2c**[6] was obtained as a by-product in yield up to 18% during the optimization tests, as a white solid (m.p.: 138 °C, lit[7] 137-138) after chromatography on silica gel (7:3 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.17 (br, 1H), 7.53 – 7.44 (m, 2H), 7.10 – 6.99 (m, 2H), 4.01 (s, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 163.63, 160.04 (d, J = 244.9 Hz), 133.04 (d, J = 2.9 Hz), 122.18 (d, J = 8.0 Hz), 115.97 (d, J = 22.7 Hz), 29.47.
HRMS (ESI), m/z: calc. for $C_8H_7BrFNOH^+$: 231,9768 $[M+H]^+$; found 231,9761.

2-fluoro-*N*-(4-iodophenyl)acetamide (3)



By following the general procedure 1 (GP1), starting from 4-iodophenyl isocyanate (245.0 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (828.4 mg, 0.35 mL, 5.2 mmol, 5.2 equiv) and MeLi (3.12 mL of a solution 1.6 M in Et_2O, 5.0 mmol, 5.0 equiv) in dry THF/Et_2O (1:1 v/v, 20 mL), compound **3**[8] was obtained in 81% yield (225.8 mg) as white solid (m.p.: 157-158 °C) after chromatography on silica gel (75:25 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.88 (br, 1H), 7.67 (d, *J* = 8.7 Hz, 1H), 7.36 (d, *J* = 8.8 Hz, 1H), 4.92 (d, *J* = 47.4 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.5 (s), 138.3 (s), 136.3 (s), 122.0 (s), 88.7 (s), 80.3 (d, *J* = 187.9 Hz).
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.2 (td, *J* = 47.6, 5.3 Hz).
HRMS (ESI), m/z: calc. for $C_8H_7FINOH^+$: 279,9629 $[M+H]^+$; found 279,9632.

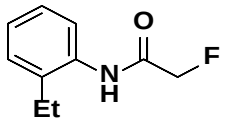
2-fluoro-*N*-(*p*-tolyl)acetamide (4)



By following the general procedure 1 (GP1), starting from *p*-tolyl isocyanate (133.2 mg, 0.13 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (828.4 mg, 0.35 mL, 5.2 mmol, 5.2 equiv) and MeLi (3.12 mL of a solution 1.6 M in Et_2O, 5.0 mmol, 5.0 equiv) in dry THF/Et_2O (1:1 v/v, 20 mL), compound **4**[9] was obtained in 86%

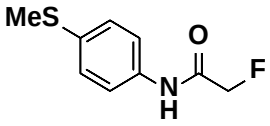
yield (143.8 mg) as white solid (m.p.: 112 °C, lit[1] 112-113 °C) after chromatography on silica gel (75:25 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.88 (br, 1H), 7.44 (d, *J* = 8.4 Hz, 1H), 7.16 (d, *J* = 8.2 Hz, 2H), 4.91 (d, *J* = 47.4 Hz, 2H), 2.33 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.5 (d, *J* = 16.3 Hz), 134.5 (d, *J* = 101.0 Hz), 129.8 (s), 120.3 (s), 80.3 (d, *J* = 187.8 Hz), 21.0 (s).
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.1 (td, *J* = 47.2, 5.1 Hz).
HRMS (ESI), m/z: calc. for $C_9H_{10}FNOH^+$: 168,0819 $[M+H]^+$; found 168,0813

***N*-(2-ethylphenyl)-2-fluoroacetamide (5)**



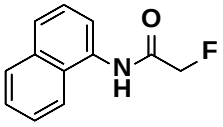
By following the general procedure 1 (GP1), starting from 2-ethylphenyl isocyanate (147,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (828.4 mg, 0.35 mL, 5.2 mmol, 5.2 equiv) and MeLi (3.12 mL of a solution 1.6 M in Et_2O, 5.0 mmol, 5.0 equiv) in dry THF/Et_2O (1:1 v/v, 20 mL), compound **5**[1] was obtained in 85% yield (154.0 mg) as white solid (m.p.: 63 °C, lit[1] 63-64 °C) after chromatography on silica gel (80:20 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.91 (br, 1H), 7.90 (dd, J = 8.5, 1.4 Hz, 1H), 7.27 – 7.23 (m, 1H), 7.20 – 7.16 (m, 1H), 4.97 (d, J = 47.4 Hz, 2H), 2.64 (q, J = 7.6 Hz, 2H), 1.26 (t, J = 7.6 Hz, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ: 165.8 (d, *J* = 16.1 Hz), 135.0 (s), 133.7 (s), 128.9 (s), 127.0 (s), 126.2 (s), 123.3 (s), 80.6 (d, *J* = 187.3 Hz), 24.3 (s), 14.0 (s).
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.1 (td, *J* = 47.2, 5.1 Hz).
HRMS (ESI), m/z: calc. for $C_{10}H_{13}FNOH^+$: 182,0976 $[M+H]^+$; found 182,0971.

2-fluoro-*N*-(4-(methylthio)phenyl)acetamide (6)



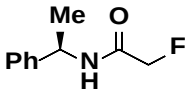
By following the general procedure 1 (GP1), starting from 4-(methylthio)phenyl isocyanate (165.2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (828.4 mg, 0.35 mL, 5.2 mmol, 5.2 equiv) and MeLi (3.12 mL of a solution 1.6 M in Et_2O, 5.0 mmol, 5.0 equiv) in dry THF/Et_2O (1:1 v/v, 20 mL), compound **6**[1] was obtained in 87% yield (173.3 mg) as white solid (m.p.: 96 °C, lit[1] 97-98 °C) after chromatography on silica gel (75:25 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.87 (br, 1H), 7.42 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.7 Hz, 2H), 4.83 (d, *J* = 47.4 Hz, 2H), 2.40 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.5 (d, *J* = 16.2 Hz), 134.5 (d, *J* = 88.8 Hz), 127.9 (s), 120.8 (s), 80.3 (d, *J* = 187.5 Hz), 16.5 (s).
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.2 (td, *J* = 47.8, 5.2 Hz).
HRMS (ESI), m/z: calc. for $C_9H_{10}FNOSH^+$: 200,0540 $[M+H]^+$; found 200,0534.

2-fluoro-*N*-(naphthalen-1-yl)acetamide (7)



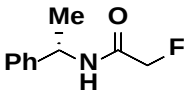
By following the general procedure 1 (GP1), starting from 1-naphthyl isocyanate (169.2 mg mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (828.4 mg, 0.35 mL, 5.2 mmol, 5.2 equiv) and MeLi (3.12 mL of a solution 1.6 M in Et_2O, 5.0 mmol, 5.0 equiv) in dry THF/Et_2O (1:1 v/v, 20 mL), compound **7**[10] was obtained in 84% yield (170.7 mg) as white solid (m.p.: 128 °C) after chromatography on silica gel (75:25 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.41 (br, 1H), 8.01 (d, *J* = 7.5 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 7.53 (m, *J* = 17.5, 7.5 Hz, 3H), 5.07 (d, *J* = 47.4 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.2 (d, *J* = 16.9 Hz), 134.2 (s), 130.8 (s), 129.0 (s), 127.0 (s), 126.7 (s), 126.5 (s), 126.3 (s), 125.8 (s), 120.9 (s), 120.3 (s), 80.76 (d, *J* = 187.3 Hz).
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.16 (td, *J* = 47.5, 5.2 Hz).
HRMS (ESI), m/z: calc. for $C_{12}H_{10}FNOH^+$: 204,0819 $[M+H]^+$; found 204,0822.

(*R*)-2-fluoro-*N*-(1-phenylethyl)acetamide ((*R*)-9)



By following the general procedure 2 (GP2), starting from (R)-1-phenylethylisocyanate (147,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(R)-9**[11] was obtained in 87% yield (157.5 mg) as white solid (m.p.: 78 °C, lit[11] 79-80 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.21 (m, 5H), 6.58 (br, 1H), 5.18 (p, 1H, J=7.0 Hz), 4.83 (dd, 1H, J=14.2, 8.6 Hz), 4.68 (dd, 1H, J=14.2, 8.6 Hz), 1.52 (d, J = 6.9 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.70 (d, J = 17.3 Hz), 142.52, 128.85, 127.70, 126.24, 80.33 (d, J = 185.9 Hz), 48.41, 21.77.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.42 (td, J = 47.6, 3.3 Hz).
HRMS (ESI), m/z: calc. for $C_{10}H_{12}FNOH^+$: 182,0976 $[M+H]^+$; found 182,0980.

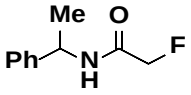
(*S*)-2-fluoro-*N*-(1-phenylethyl)acetamide ((*S*)-9)



By following the general procedure 2 (GP2), starting from (S)-1-phenylethylisocyanate (147,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(S)-9**[12] was obtained in 83% yield (151.5 mg) as white solid (m.p.: 77.5 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.21 (m, 5H), 6.58 (br, 1H), 5.18 (p, 1H, J=7.0 Hz), 4.83 (dd, 1H, J=14.2, 8.6 Hz), 4.68 (dd, 1H, J=14.2, 8.6 Hz), 1.52 (d, J = 6.9 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.70 (d, J = 17.3 Hz), 142.52, 128.85, 127.70, 126.24, 80.33 (d, J = 185.9 Hz), 48.41, 21.77.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.42 (td, J = 47.6, 3.3 Hz).

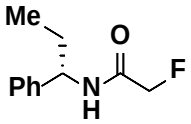
HRMS (ESI), m/z: calc. for $C_{10}H_{12}FNOH^+$: 182,0976 $[M+H]^+$; found 182,0973.

2-fluoro-*N*-(1-phenylethyl)acetamide ((*rac*)-9)



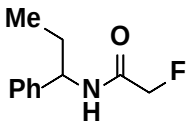
By following the general procedure 2 (GP2), starting from 1-phenylethylisocyanate (147,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(rac)-9**[13] was obtained in 84% yield (154.0 mg) as white solid (m.p.: 68-69 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.38 – 7.21 (m, 5H), 6.58 (br, 1H), 5.18 (p, 1H, J=7.0 Hz), 4.83 (dd, 1H, J=14.2, 8.6 Hz), 4.68 (dd, 1H, J=14.2, 8.6 Hz), 1.52 (d, J = 6.9 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.70 (d, J = 17.3 Hz), 142.52, 128.85, 127.70, 126.24, 80.33 (d, J = 185.9 Hz), 48.41, 21.77.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.42 (td, J = 47.6, 3.3 Hz).
HRMS (ESI), m/z: calc. for $C_{10}H_{12}FNOH^+$: 182,0976 $[M+H]^+$; found 182,0972.

(*S*)-2-fluoro-*N*-(1-phenylpropyl)acetamide ((*S*)-10)



By following the general procedure 2 (GP2), starting from (S)-1-phenylpropylisocyanate (147,2 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(S)-10** was obtained in 88% yield (171.8 mg) as white solid (m.p.: 81 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40 – 7.18 (m, 5H), 6.57 (br, 1H), 4.93 (q, J = 7.8 Hz, 1H), 4.89 – 4.58 (m, 2H), 1.94 – 1.80 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.90 (d, J = 17.1 Hz), 141.47, 128.81, 127.67, 126.70, 80.35 (d, J = 185.8 Hz), 54.53, 29.15, 10.76.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.28 (td, J = 47.3, 3.5 Hz).
HRMS (ESI), m/z: calc. for $C_{11}H_{14}FNOH^+$: 196,1132 $[M+H]^+$; found 196,1127.

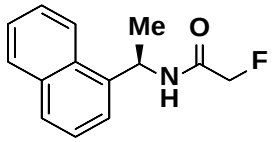
2-fluoro-*N*-(1-phenylpropyl)acetamide ((*rac*)-10)



By following the general procedure 2 (GP2), starting from (S)-1-phenylpropylisocyanate (147,2 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(rac)-10** was obtained in 89% yield (173.7 mg) as white solid (m.p.: 81 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.40 – 7.18 (m, 5H), 6.57 (br, 1H), 4.93 (q, J = 7.8 Hz, 1H), 4.89 – 4.58 (m, 2H), 1.94 – 1.80 (m, 2H), 0.89 (t, J = 7.4 Hz, 3H).

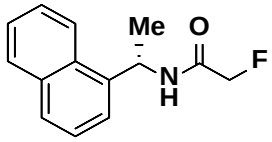
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.90 (d, J = 17.1 Hz), 141.47, 128.81, 127.67, 126.70, 80.35 (d, J = 185.8 Hz), 54.53, 29.15, 10.76.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.28 (td, J = 47.3, 3.5 Hz).
HRMS (ESI), m/z: calc. for $C_{11}H_{14}FNOH^+$: 196,1132 $[M+H]^+$; found 196,1138.

((*R*)-2-fluoro-*N*-(1-(naphthalen-1-yl)ethyl)acetamide ((*R*)-11)



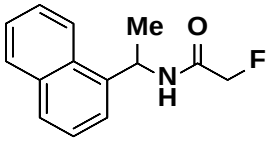
By following the general procedure 2 (GP2), starting from (R)-1-(1-naphtyl)ethylisocyanate (197.2 mg, 0.18 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(R)-11** was obtained in 82% yield (189.7 mg) as white solid (m.p.: 112 °C,) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J = 7.8 Hz, 1H), 7.89 (dd, J = 7.9, 1.8 Hz, 1H), 7.85 – 7.79 (m, 1H), 7.60 – 7.50 (m, 3H), 7.50 – 7.43 (m, 1H), 6.72 (br, 1H), 6.04 (p, J = 7.1 Hz, 1H), 4.86 (q, J = 17.6 Hz, 1H), 4.70 (q, 1H), 1.71 (d, J = 17.6 Hz, J = 6.8 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.49 (d, J = 17.4 Hz), 130.97, 128.90, 128.56, 126.66, 125.93, 125.23, 123.13, 122.65, 80.19 (d, J = 185.9 Hz), 20.92. J = 17.6 Hz
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.49 (td, J = 47.4, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_{14}H_{14}FNOH^+$: 232,1132 $[M+H]^+$; found 232,1135.

((*S*)-2-fluoro-*N*-(1-(naphthalen-1-yl)ethyl)acetamide ((*S*)-11)



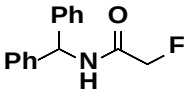
By following the general procedure 2 (GP2), starting from (S)-1-(1-naphtyl)ethylisocyanate (197.2 mg, 0.18 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(S)-11** was obtained in 84% yield (194.3 mg) as white solid (m.p.: 112.5 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
<u>Scale-up to 20 mmol:</u>
By following the general procedure 2 (GP2), starting from (S)-1-(1-naphtyl)ethylisocyanate (3944.0 mg, 3.6 mL, 20.0 mmol, 1.0 equiv), fluoroiodomethane (9596.0 mg, 4.0 mL, 60.0 mmol, 3.0 equiv) and MeLi (35.0 mL of a solution 1.6 M in Et_2O, 56.0 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 100 mL), compound **(S)-11** was obtained in 83% yield (3838 mg) as white solid (m.p.: 112.5 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J = 7.8 Hz, 1H), 7.89 (dd, J = 7.9, 1.8 Hz, 1H), 7.85 – 7.79 (m, 1H), 7.60 – 7.50 (m, 3H), 7.50 – 7.43 (m, 1H), 6.72 (br, 1H), 6.04 (p, J = 7.1 Hz, 1H), 4.86 (q, J = 17.6 Hz, 1H), 4.70 (q, 1H), 1.71 (d, J = 17.6 Hz, J = 6.8 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.49 (d, J = 17.4 Hz), 130.97, 128.90, 128.56, 126.66, 125.93, 125.23, 123.13, 122.65, 80.19 (d, J = 185.9 Hz), 20.92. J = 17.6 Hz
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.49 (td, J = 47.4, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_{14}H_{14}FNOH^+$: 232,1132 $[M+H]^+$; found 232,1138.

2-fluoro-*N*-(1-(naphthalen-1-yl)ethyl)acetamide ((*rac*)-11)



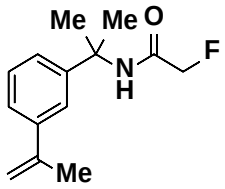
By following the general procedure 2 (GP2), starting from (S)-1-(1-naphtyl)ethylisocyanate (197.23 mg, 0.18 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **(rac)-11** was obtained in 86% yield (199.0 mg) as white solid (m.p.: 104 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (600 MHz, $CDCl_3$) δ: 8.13 (d, J = 7.8 Hz, 1H), 7.89 (dd, J = 7.9, 1.8 Hz, 1H), 7.85 – 7.79 (m, 1H), 7.60 – 7.50 (m, 3H), 7.50 – 7.43 (m, 1H), 6.72 (br, 1H), 6.04 (p, J = 7.1 Hz, 1H), 4.86 (q, J = 17.6 Hz, 1H), 4.70 (q, 1H), 1.71 (d, J = 17.6 Hz, J = 6.8 Hz, 3H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ: 166.49 (d, J = 17.4 Hz), 130.97, 128.90, 128.56, 126.66, 125.93, 125.23, 123.13, 122.65, 80.19 (d, J = 185.9 Hz), 20.92. J = 17.6 Hz
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.49 (td, J = 47.4, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_{14}H_{14}FNOH^+$: 232,1132 $[M+H]^+$; found 232,1127.

***N*-benzhydryl-2-fluoroacetamide (12)**



By following the general procedure 2 (GP2), starting from benzhydrylisocyanate (225.3 mg, 0.2 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **12**[14] was obtained in 90% yield (218.7 mg) as white solid (m.p.: 108 °C) after chromatography on silica gel (7:3 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.46 – 7.21 (m, 10H), 6.91 (br, 1H), 6.33 (d, J = 8.4 Hz, 1H), 4.87 (d, J = 47.4 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.91, 140.90, 128.91, 127.87, 127.49, 80.45 (d, J = 185.9 Hz), 56.40.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.67 (td, J = 47.4, 3.3 Hz).
HRMS (ESI), m/z: calc. for $C_{15}H_{14}FNOH^+$: 244,1132 $[M+H]^+$; found 244,1128.

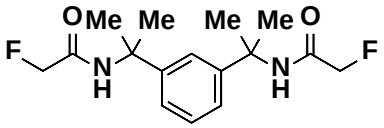
2-fluoro-*N*-(2-(3-(prop-1-en-2-yl)phenyl)propan-2-yl)acetamide (13)



By following the general procedure 2 (GP2), starting from 3-isopropenyl-α,α-dimethylbenzyl isocyanate (201.3 mg, 0.20 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **13** was obtained in 85% yield (200.0 mg) as white solid (m.p.: 98 °C) after chromatography on silica gel (85:15 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.50 (s, 1H), 7.40 – 7.27 (m, 3H), 6.55 (br, 1H), 5.36 (s, 1H), 5.10 (s, 1H), 4.72 (d, J = 47.6 Hz, 2H), 2.16 (s, 3H), 1.78 (s, 6H).

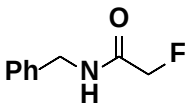
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.54 (d, J = 15.8 Hz), 146.23, 143.53, 141.68, 128.51, 124.40, 123.95, 122.03, 112.81, 80.48 (d, J = 187.1 Hz), 56.23, 29.08, 22.00.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -221.03 (td, J = 47.6, 4.0 Hz).
HRMS (ESI), m/z: calc. for $C_{14}H_{18}FNOH^+$: 236,1445 $[M+H]^+$; found 236,1451.

***N*,*N*'-(1,3-phenylenebis(propane-2,2-diyl))bis(2-fluoroacetamide) (14)**



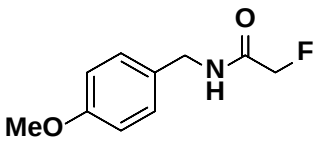
By following the general procedure 2 (GP2), starting from 1,3-bis(2-isocyanatopropan-2-yl)benzene (244.3 mg, 0.23 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (959.6 mg, 0.40 mL, 6.0 mmol, 3.0 equiv) and MeLi (3.50 mL of a solution 1.6 M in Et_2O, 5.6 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **14** was obtained in 81% yield (253.0 mg) as yellow solid (m.p.: 108 °C) after chromatography on silica gel (4:6 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.44 (t, J = 2.0 Hz, 1H), 7.37 – 7.24 (m, 3H), 6.53 (br, 2H), 4.70 (d, J = 47.6 Hz, 2H), 1.76 (s, 12H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.56 (d, J = 15.9 Hz), 146.49, 128.79, 123.52, 121.27, 80.43 (d, J = 187.1 Hz), 56.35, 29.06.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -221.01 (td, J = 47.7, 4.0 Hz).
HRMS (ESI), m/z: calc. for $C_{16}H_2F_2N_2O_2H^+$: 313,1722 $[M+H]^+$; found 313,1718.

***N*-benzyl-2-fluoroacetamide (15)**



By following the general procedure 2 (GP2), starting from benzylisocyanate (133.2 mg, 0.12 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **15**[15] was obtained in 88% yield (147.1 mg) as white solid (m.p.: 70-72 °C, lit[16] 71-72 °C) after chromatography on silica gel (7:3 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.41 – 7.25 (m, 5H), 6.70 (br, 1H), 4.82 (d, J = 47.4 Hz, 2H), 4.50 (d, J = 5.9 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.57 (d, J = 17.3 Hz), 137.51, 128.88, 127.93, 127.85, 80.35 (d, J = 186.0 Hz), 42.96.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.50 (td, J = 47.7, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_9H_{10}FNOH^+$: 168,0819 $[M+H]^+$; found 168,0824.

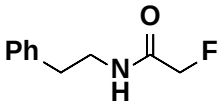
2-fluoro-*N*-(4-methoxybenzyl)acetamide (16)



By following the general procedure 2 (GP2), starting from 4-Methoxybenzyl isocyanate (163,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a

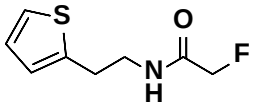
solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **16** was obtained in 81% yield (159.7 mg) as yellow solid (m.p.: 100-102 °C) after chromatography on silica gel (6:4 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.22 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.7 Hz, 2H), 6.61 (br, 1H), 4.80 (d, J = 47.4 Hz, 2H), 4.43 (d, J = 5.8 Hz, 2H), 3.79 (s, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.44 (d, J = 17.3 Hz), 159.32, 129.60, 129.34, 114.26, 80.35 (d, J = 185.9 Hz), 42.46.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.82 (td, J = 47.4, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_{10}H_{12}FNO_2H^+$: 198,0925 $[M+H]^+$; found 198,0928.

2-fluoro-*N*-phenethylacetamide (17)



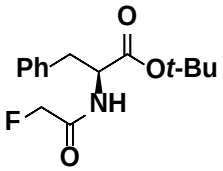
By following the general procedure 2 (GP2), starting from phenethyl isocyanate (147,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **17**[17] was obtained in 86% yield (155.8 mg) as white solid (m.p.: 56-58 °C, lit[13] 57-58 °C) after chromatography on silica gel (65:35 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.37 – 7.17 (m, 5H), 6.41 (br, 1H), 4.75 (d, J = 47.4 Hz, 2H), 3.60 (q, J = 6.8 Hz, 2H), 2.86 (t, J = 7.1 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.61 (d, J = 17.1 Hz), 138.44, 128.78, 128.75, 126.74, 80.31 (d, J = 185.9 Hz), 40.05, 35.67.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.67 (td, J = 47.2, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_{10}H_{12}FNOH^+$: 182,0976 $[M+H]^+$; found 182,0982.

2-fluoro-*N*-(2-(thiophen-2-yl)ethyl)acetamide (18)



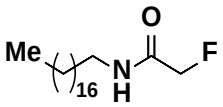
By following the general procedure 2 (GP2), starting from 2-(2-Thienyl)ethyl isocyanate (153.2 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **18** was obtained in 89% yield (166.6 mg) as yellow solid (m.p.: 72 °C) after chromatography on silica gel (65:35 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.15 (dd, J = 5.1, 1.2 Hz, 1H), 6.93 (dd, J = 5.1, 3.4 Hz, 1H), 6.84 (dt, J = 3.4, 1.0 Hz, 1H), 6.57 (br, 1H), 4.75 (d, J = 47.3 Hz, 2H), 3.59 (q, J = 6.6 Hz, 2H), 3.06 (t, J = 6.8 Hz, 2H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.69 (d, J = 17.1 Hz), 140.72, 127.14, 125.48, 124.13, 80.27 (d, J = 185.9 Hz), 40.21, 29.79.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.90 (td, J = 47.5, 3.4 Hz).
HRMS (ESI), m/z: calc. for $C_8H_{10}FNOSH^+$: 188,0540 $[M+H]^+$; found 188,0535.

(2-fluoroacetyl)-L-phenylalanine *tert*-butyl ester (19)



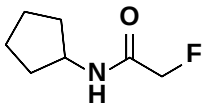
By following the general procedure 2 (GP2), starting from L-phenylalanine *tert*-butyl ester isocyanate (147,3 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **19** was obtained in 82% yield (230.4 mg) as white solid (m.p.: 187 °C) after chromatography on silica gel (7:3 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (600 MHz, $CDCl_3$) δ: δ 7.34 – 7.25 (m, 2H), 7.25 (m, 1H), 7.21 – 7.13 (m, 2H), 6.76 (br d, J = 7.8 Hz, 1H), 4.81 (qd, J = 6.2, 1.2 Hz, 1H), 4.78 (d, J = 47.3 Hz, 2H), 3.12 (d, J = 6.2 Hz, 2H), 1.41 (s, 9H).
^{13}C-NMR (150 MHz, $CDCl_3$) δ: 170.12, 167.23 (d, J = 17.4 Hz), 135.88, 129.57, 128.64, 127.28, 82.87, 80.20 (d, J = 186.2 Hz), 53.09, 38.32, 28.06.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.67 (td, J = 47.4, 3.3 Hz).
HRMS (ESI), m/z: calc. for $C_{15}H_{10}FNO_3H^+$: 282,1500 $[M+H]^+$; found 282,1506.

2-fluoro-*N*-octadecylacetamide (20)



By following the general procedure 2 (GP2), starting from octadecyl isocyanate (290.5 mg, 0.34 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **20**[18] was obtained in 91% yield (299.7 mg) as white solid (m.p.: 75-76 °C, lit[18] 73-75 °C) after chromatography on silica gel (78:22 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.31 (br, 1H), 4.77 (d, J = 47.6 Hz, 2H), 3.31 (q, J = 6.8 Hz, 2H), 1.53 (p, J = 7.1 Hz, 2H), 1.24 (s, 30H), 0.86 (t, J = 6.6 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.54 (d, J = 17.0 Hz), 80.41 (d, J = 185.9 Hz), 39.04, 32.04, 29.78 (br), 29.75 (br), 29.68, 29.63, 29.60, 29.48, 29.36, 26.95, 22.80, 14.21.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.00 (td, J = 47.7, 3.6 Hz).
HRMS (ESI), m/z: calc. for $C_{20}H_{40}FNOH^+$: 330,3167 $[M+H]^+$; found 330,3162.

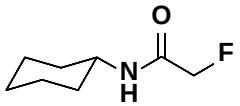
***N*-cyclopentyl-2-fluoroacetamide (21)**



By following the general procedure 2 (GP2), starting from cyclopentyl isocyanate (111.1 mg, 0.11 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **21**[13] was obtained in 89% yield (129.2 mg) as white solid (m.p.: 61 °C, lit[13] 60-31 °C) after chromatography on silica gel (95:5 v/v, DCM/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.22 (s, 1H), 4.74 (d, J = 47.4 Hz, 2H), 4.26 (h, J = 7.1 Hz, 1H), 2.00 (dtd, J = 12.0, 7.2, 2.8 Hz, 2H), 1.78 – 1.53 (m, 3H), 1.51 – 1.34 (m, 2H).

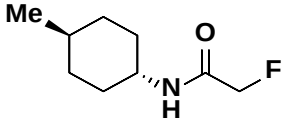
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.10 (d, J = 16.9 Hz), 80.39 (d, J = 185.9 Hz), 50.71, 33.10, 23.76.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.10 (td, J = 48.0, 3.5 Hz).
HRMS (ESI), m/z: calc. for $C_7H_{12}FNOH^+$: 146,0976 $[M+H]^+$; found 146,0980.

***N*-cyclohexyl-2-fluoroacetamide (22)**



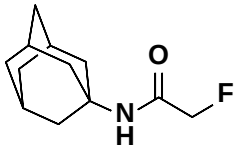
By following the general procedure 2 (GP2), starting from cyclohexyl isocyanate (125.2 mg, 0.13 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **22**[18] was obtained in 88% yield (140.1 mg) as white solid (m.p.: 101 °C, lit[18] 99-101 °C) after chromatography on silica gel (95:5 v/v, DCM/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.14 (br, 1H), 4.76 (d, J = 47.4 Hz, 2H), 3.92 – 3.77 (m, 1H), 1.99 – 1.88 (m, 2H), 1.81 – 1.69 (m, 2H), 1.63 (m, 1H), 1.46 – 1.31 (m, 2H), 1.20 (m, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.68 (d, J = 16.7 Hz), 80.42 (d, J = 186.0 Hz), 47.94, 33.15, 25.55, 24.92.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.00 (td, J = 47.8, 3.6 Hz).
HRMS (ESI), m/z: calc. for $C_8H_{14}FNOH^+$: 160,1132 $[M+H]^+$; found 160,1127.

2-fluoro-*N*-((1R,4R)-4-methylcyclohexyl)acetamide (23)



By following the general procedure 2 (GP2), starting from trans-4-methylcyclohexyl isocyanate (139.2 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **23** was obtained in 86% yield (148.9 mg) as white solid (m.p.: 131 °C) after chromatography on silica gel (95:5 v/v, DCM/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 6.07 (rb, 1H), 4.75 (d, J = 47.4 Hz, 2H), 3.78 (qdd, J = 11.7, 5.7, 2.5 Hz, 1H), 2.06 – 1.92 (m, 2H), 1.77 – 1.69 (m, 2H), 1.34 (tdq, J = 13.0, 6.5, 3.4 Hz, 1H), 1.25 – 0.97 (m, 4H), 0.89 (d, J = 6.5 Hz, 3H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.79 (d, J = 16.9 Hz), 80.41 (d, J = 186.0 Hz), 48.22, 33.86, 33.17, 31.99, 22.24.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -224.00 (td, J = 47.6, 3.2 Hz).
HRMS (ESI), m/z: calc. for $C_9H_{16}FNOH^+$: 174,1289 $[M+H]^+$; found 174,1281.

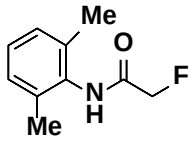
***N*-(adamantan-1-yl)-2-fluoroacetamide (24)**



By following the general procedure 2 (GP2), starting from 1-adamantyl isocyanate (177,2 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M

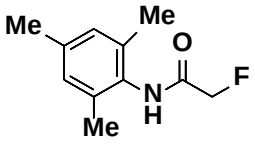
in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **24**[19] was obtained in 85% yield (179.6 mg) as white solid (m.p.: 178-179 °C) after chromatography on silica gel (82:18 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 5.91 (br, 1H), 4.64 (d, J = 47.7 Hz, 2H), 2.10 (s, 3H), 2.04 (s, 6H), 1.69 (s, 6H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.39 (d, J = 15.4 Hz), 80.20 (d, J = 187.5 Hz), 52.13, 41.61, 36.23, 29.42.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: δ -220.00 (td, J = 47.7, 4.1 Hz).
HRMS (ESI), m/z: calc. for $C_{12}H_{18}FNOH^+$: 212,1445 $[M+H]^+$; found 212,1452.

***N*-(2,6-dimethylphenyl)-2-fluoroacetamide (25)**



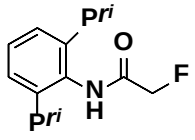
By following the general procedure 2 (GP2), starting from 2,6-dimethylphenyl isocyanate (147,2 mg, 0.14 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **25** was obtained in 88% yield (159.5 mg) as white solid (m.p.: 136 °C) after chromatography on silica gel (72:28 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.62 (br, 1H), 7.18 – 7.06 (m, 3H), 4.97 (d, J = 47.5 Hz, 2H), 2.23 (s, 6H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.06 (d, J = 16.9 Hz), 135.47, 132.19, 128.37, 127.84, 80.49 (d, J = 186.4 Hz), 18.32.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.56 (td, J = 47.7, 4.1 Hz).
HRMS (ESI), m/z: calc. for $C_{10}H_{12}FNOH^+$: 182,0976 $[M+H]^+$; found 182,0971.

***N*-(2,4,6-trimethylphenyl)-2-fluoroacetamide (26)**



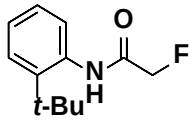
By following the general procedure 2 (GP2), starting from 2,4,6-trimethylphenyl isocyanate (161,2 mg, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **26**[20] was obtained in 87% yield (169.7 mg) as white solid (m.p.: 148 °C) after chromatography on silica gel (75:25 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.54 (br, 1H), 6.92 (s, 2H), 4.97 (d, J = 47.4 Hz, 2H), 2.29 (s, 3H), 2.19 (s, 6H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.21 (d, J = 16.8 Hz), 137.55, 135.17, 129.50, 129.10, 80.53 (d, J = 186.4 Hz), 20.95, 18.21.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.68 (td, J = 47.2, 4.1 Hz).
HRMS (ESI), m/z: calc. for $C_{11}H_{14}FNOH^+$: 196,1132 $[M+H]^+$; found 196,1138.

***N*-(2,6-diisopropylphenyl)-2-fluoroacetamide (27)**



By following the general procedure 2 (GP2), starting from 2,6-diisopropylphenyl isocyanate (203.3 mg, 0.21 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **27** was obtained in 91% yield (215.9 mg) as white solid (m.p.: 134 °C) after chromatography on silica gel (85:15 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 7.45 (br, 1H), 7.25 (t, J = 7.7 Hz, 1H), 7.12 (d, J = 7.7 Hz, 2H), 4.93 (d, J = 47.5 Hz, 2H), 2.97 (hept, J = 6.9 Hz, 2H), 1.14 (d, J = 7.0 Hz, 12H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.13 (d, J = 16.7 Hz), 146.28, 129.37, 128.96, 123.80, 80.69 (d, J = 186.4 Hz), 28.97, 23.70.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.49 (td, J = 47.6, 4.1 Hz).
HRMS (ESI), m/z: calc. for $C_{14}H_{20}FNOH^+$: 237,1529 $[M+H]^+$; found 237,1525.

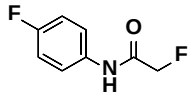
***N*-(2-(*tert*-butyl)phenyl)-2-fluoroacetamide (28)**



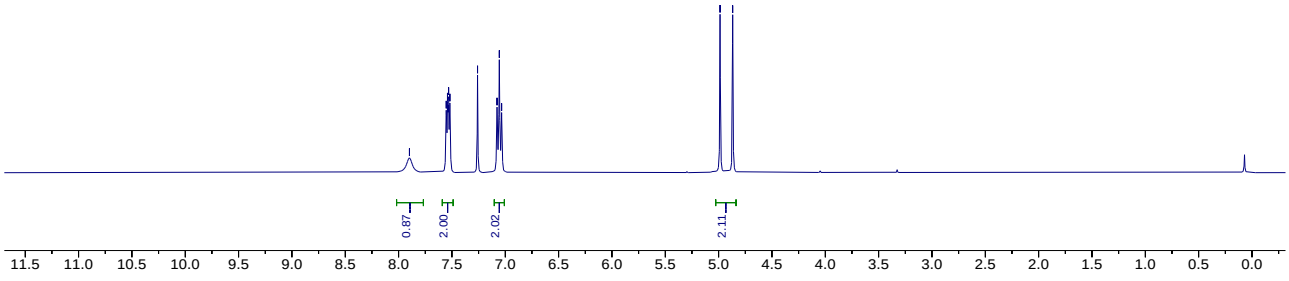
By following the general procedure 2 (GP2), starting from 2-(*tert*-butyl)phenylisocyanate (175,2 mg, 0.18 mL, 1.0 mmol, 1.0 equiv), fluoroiodomethane (479.8 mg, 0.20 mL, 3.0 mmol, 3.0 equiv) and MeLi (1.75 mL of a solution 1.6 M in Et_2O, 2.8 mmol, 2.8 equiv) in dry THF/Et_2O (1:1 v/v, 5 mL), compound **28** was obtained in 88% yield (167.3 mg) as white solid (m.p.: 123 °C) after chromatography on silica gel (80:20 v/v, petroleum ether/ethyl acetate).
^{1}H-NMR (400 MHz, $CDCl_3$) δ: 8.14 (br, 1H), 7.74 (dd, J = 7.9, 1.6 Hz, 1H), 7.40 (dd, J = 7.9, 1.7 Hz, 1H), 7.24 (td, J = 7.5, 1.7 Hz, 1H), 7.17 (td, J = 7.6, 1.6 Hz, 1H), 4.96 (d, J = 47.5 Hz, 2H), 1.41 (s, 9H).
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 165.58 (d, J = 16.2 Hz), 142.05, 133.86, 127.03, 126.79, 126.63, 126.49, 80.65 (d, J = 186.9 Hz), 34.58, 30.71.
^{19}F-NMR (376 MHz, $CDCl_3$) δ: -222.60 (td, J = 47.4, 5.1 Hz).
HRMS (ESI), m/z: calc. for $C_{12}H_{16}FNOH^+$: 210,1289 $[M+H]^+$; found 210,1285.

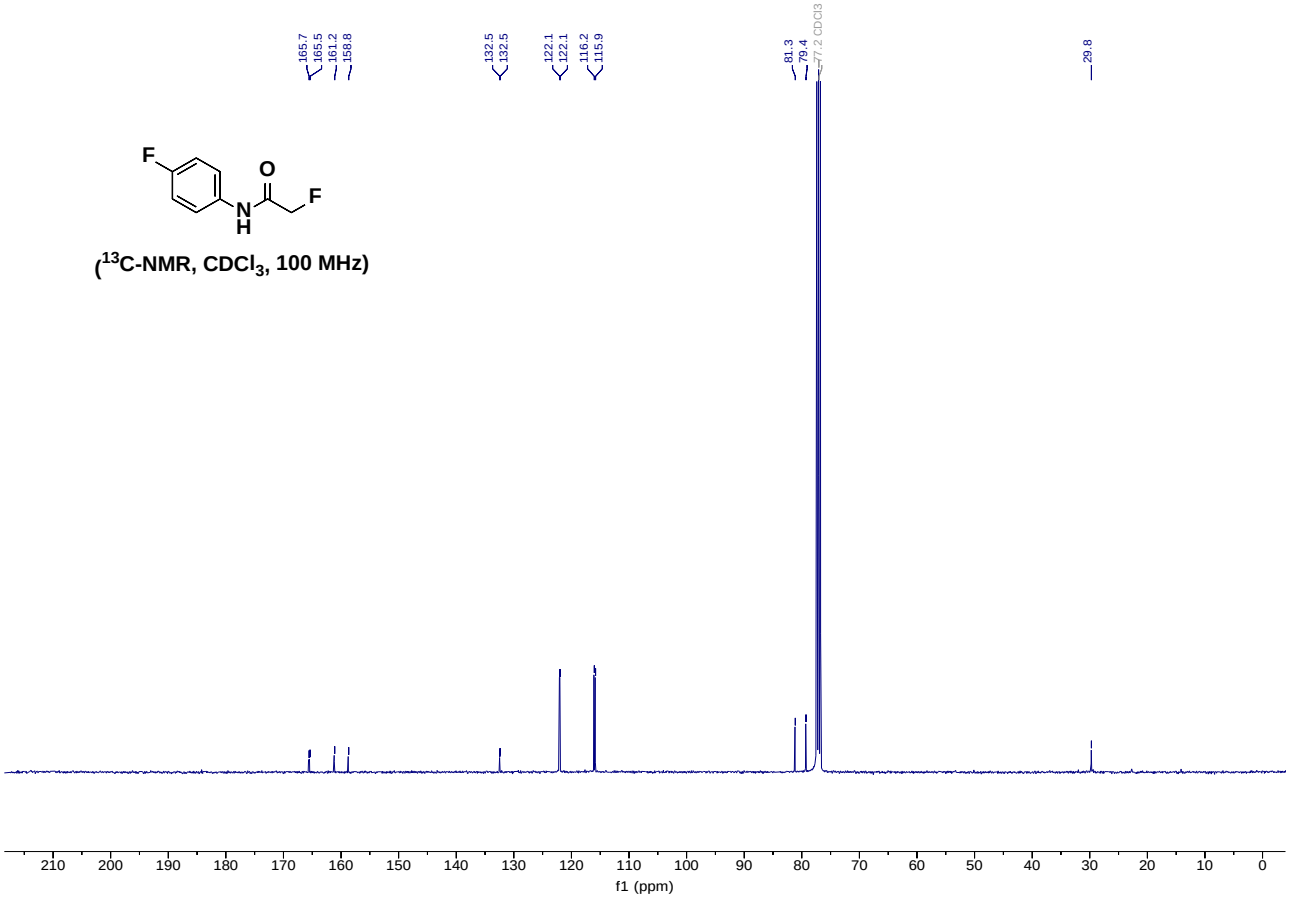
Copies of ^{1}H, ^{13}C and ^{19}F -NMR copies of all compounds

2-fluoro-*N*-(4-fluorophenyl)acetamide (2)



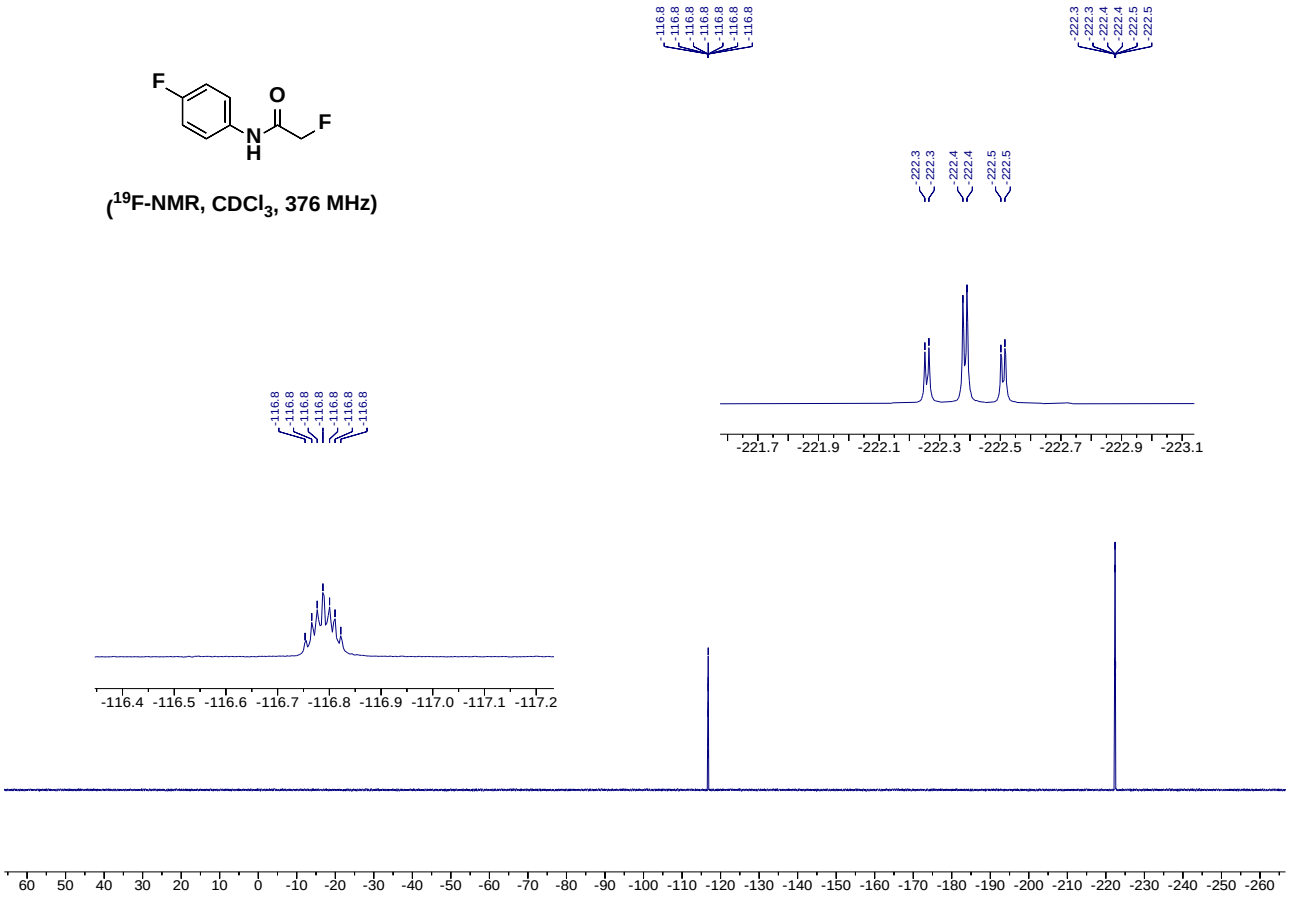
(^{1}H-NMR, $CDCl_3$, 400 MHz)



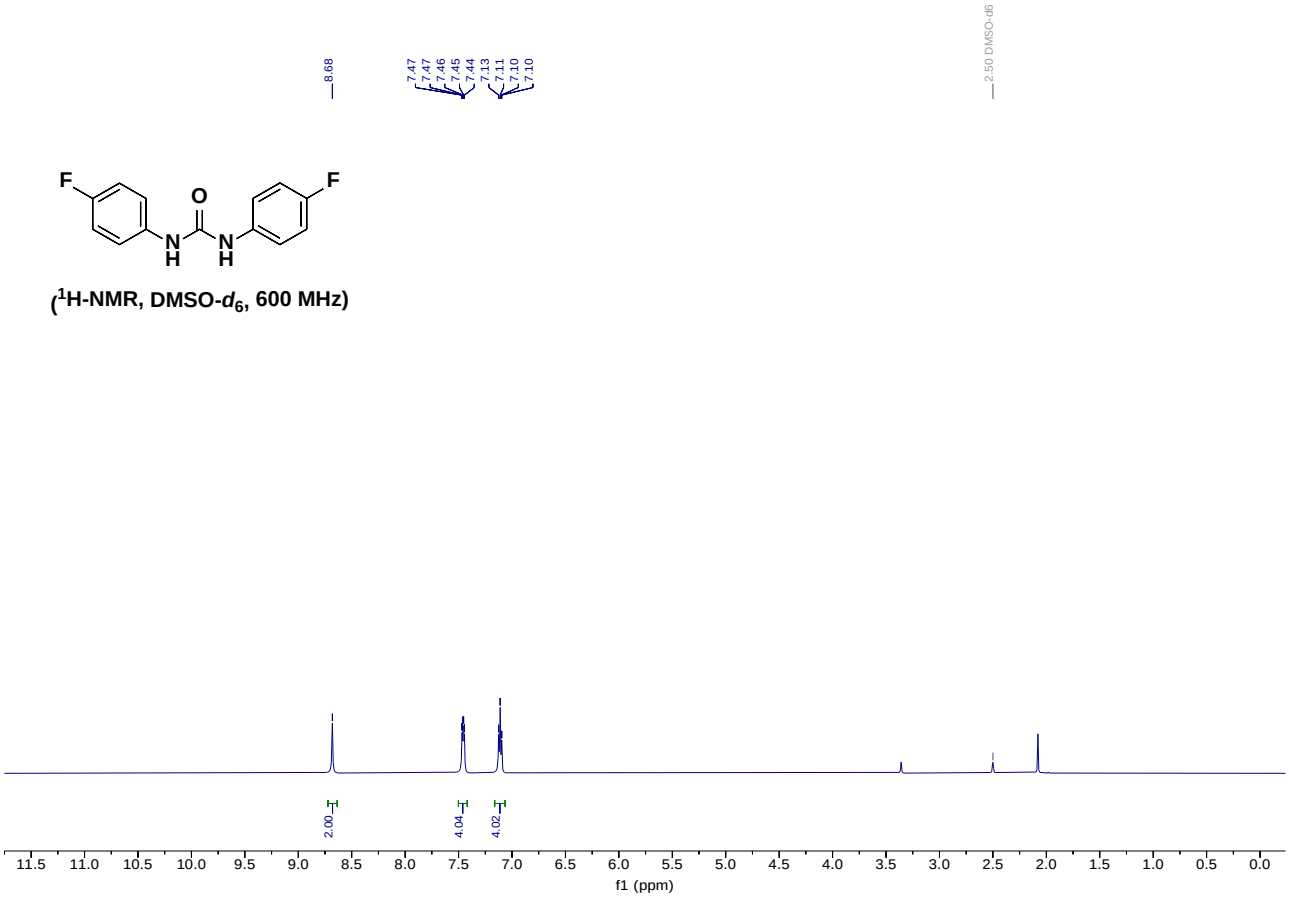


(^{13}C-NMR, $CDCl_3$, 100 MHz)

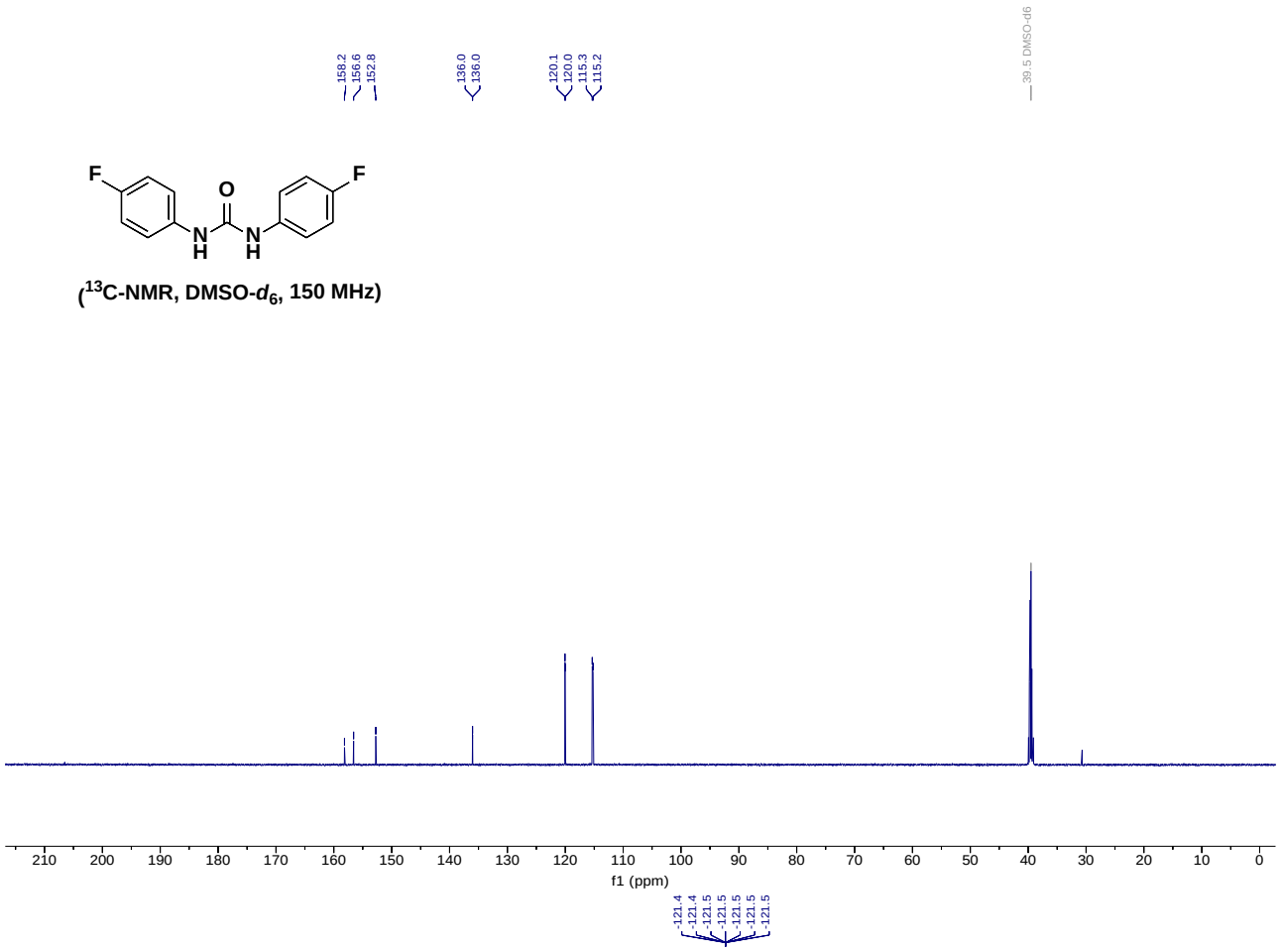
(¹⁹F-NMR, $CDCl_3$, 376 MHz)



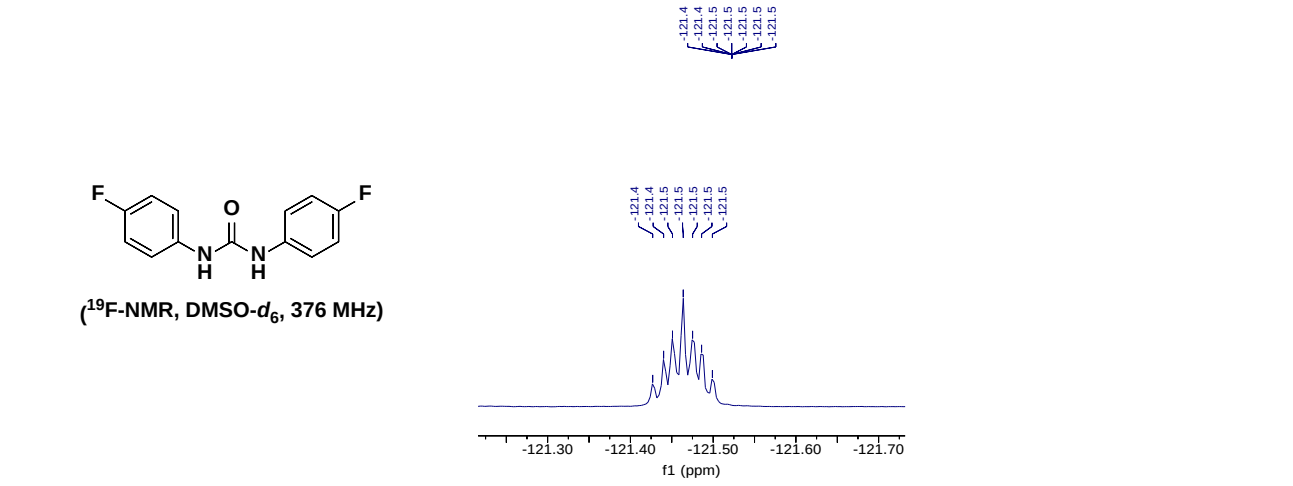
1,3-bis(4-fluorophenyl)urea (2a)



(¹H-NMR, DMSO-d_6, 600 MHz)

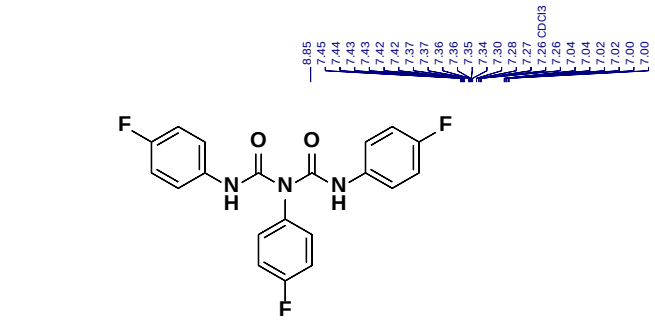


(¹³C-NMR, DMSO-d_6, 150 MHz)

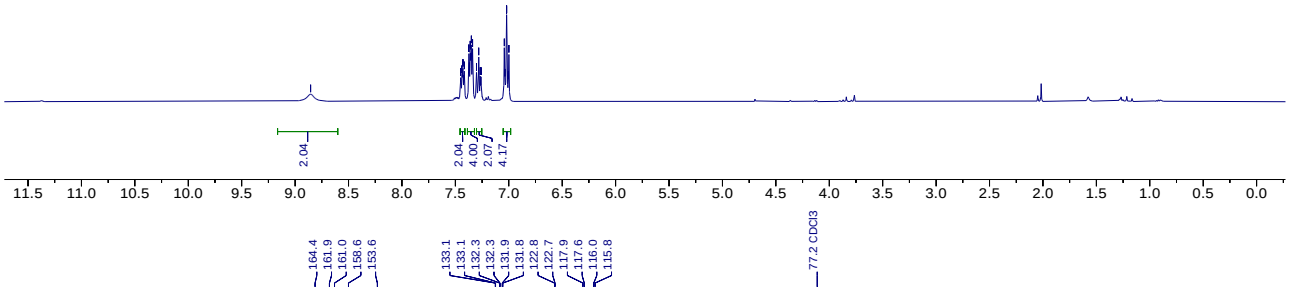


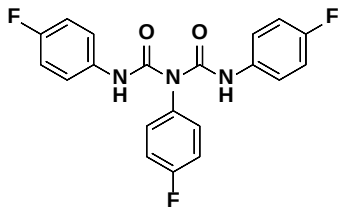
(¹⁹F-NMR, DMSO-d_6, 376 MHz)

1,3,5-tris(4-fluorophenyl)biuret (2b)

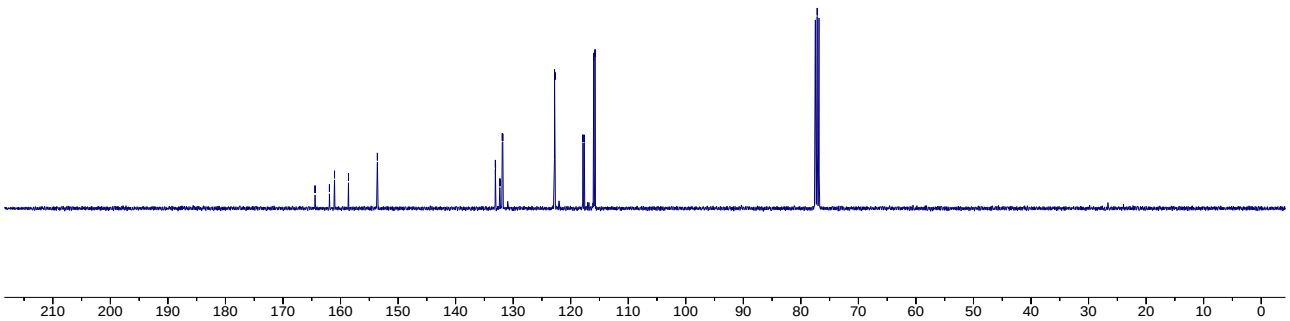


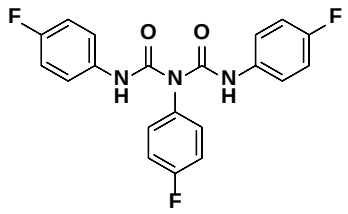
(^{1}H-NMR, $CDCl_3$, 400 MHz)

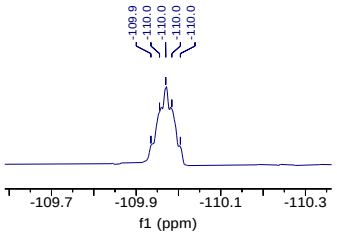




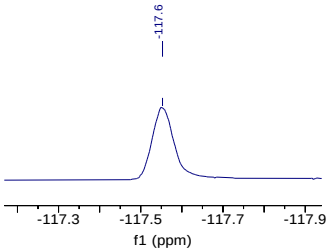
(^{13}C-NMR, $CDCl_3$, 100 MHz)

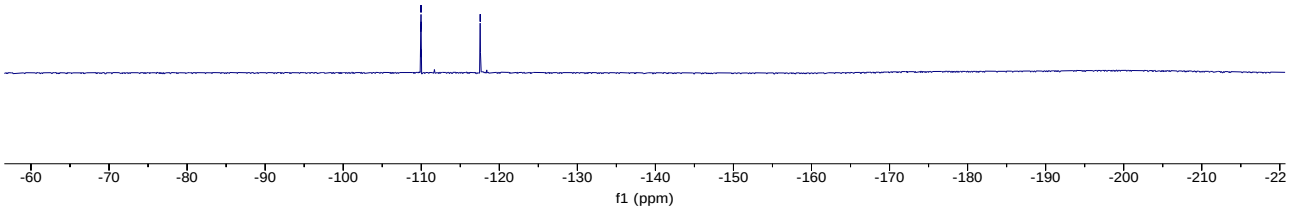




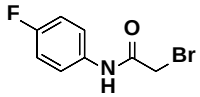


(¹⁹F-NMR, $CDCl_3$, 376 MHz)

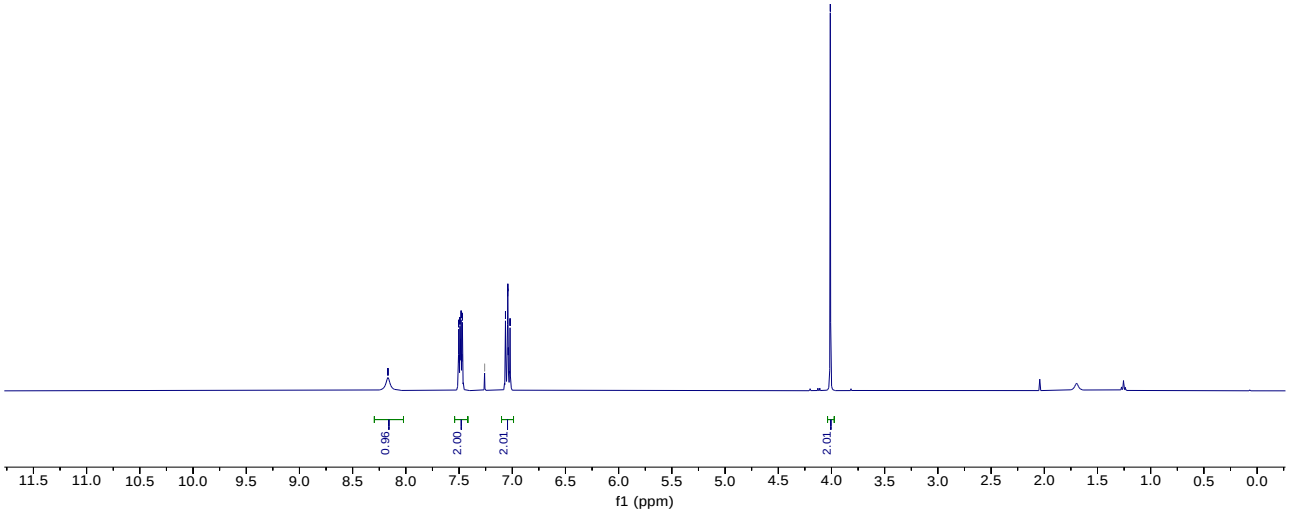


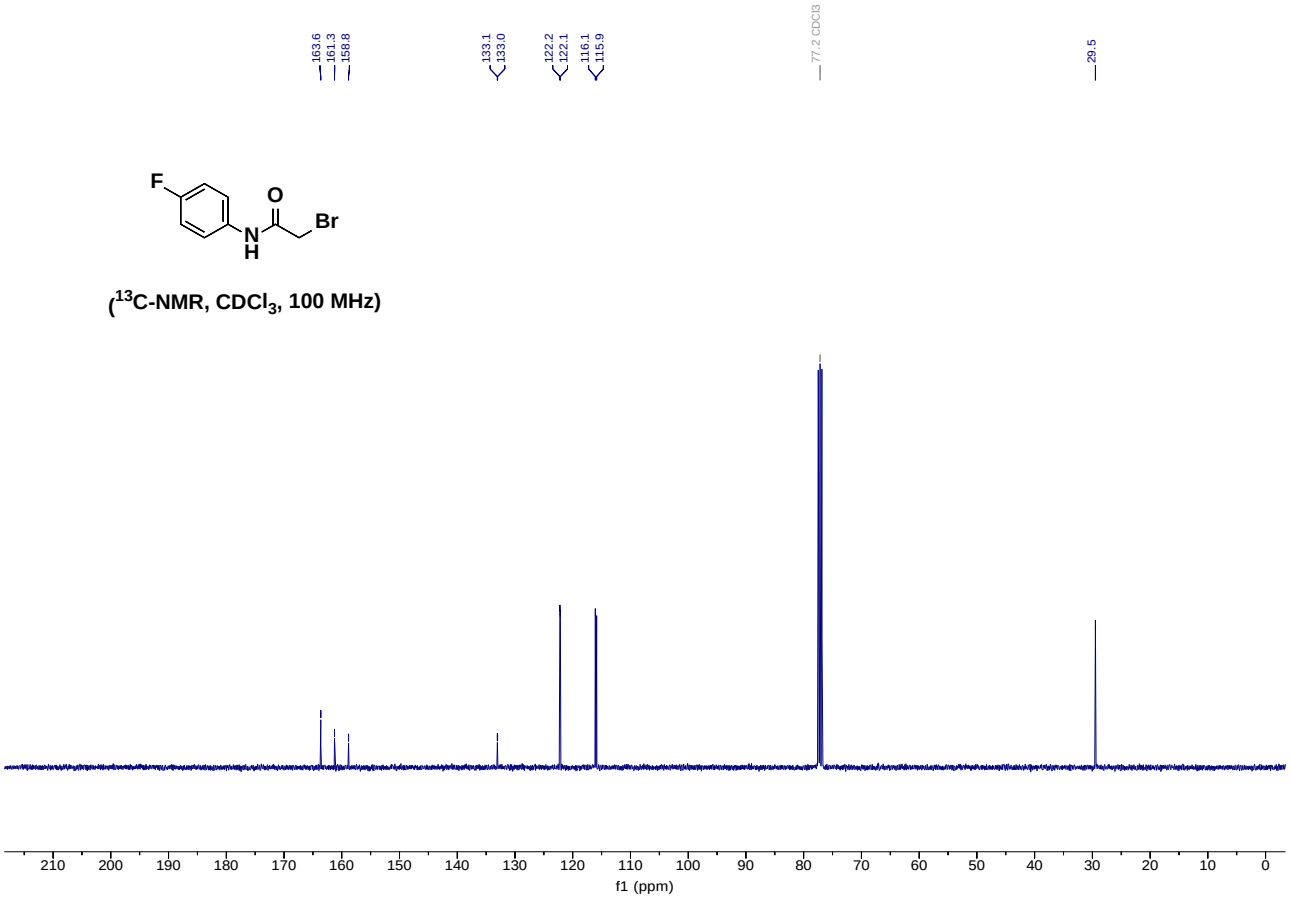


2-bromo-*N*-(4-fluorophenyl)acetamide (2c)



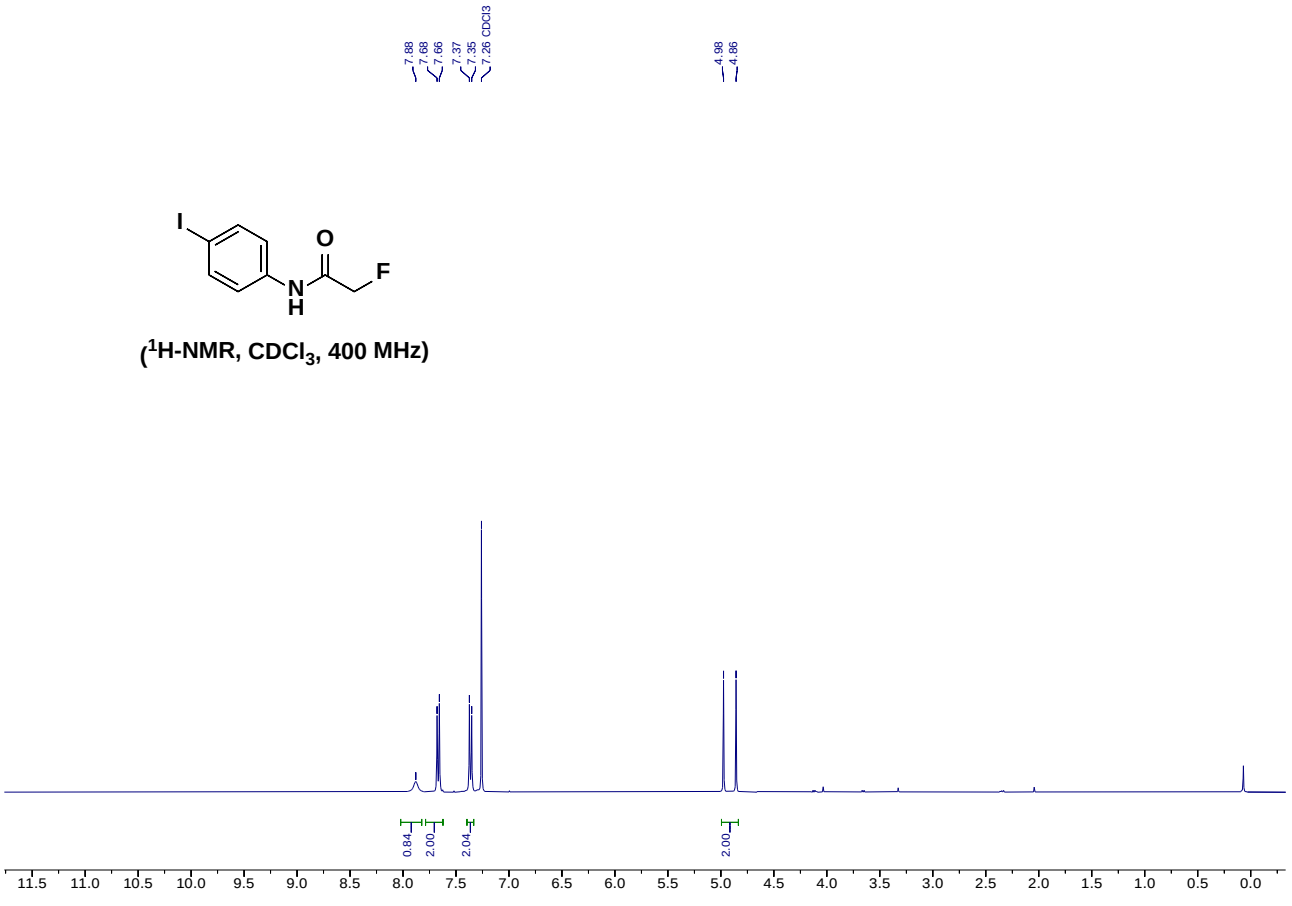
(¹H-NMR, $CDCl_3$, 400 MHz)





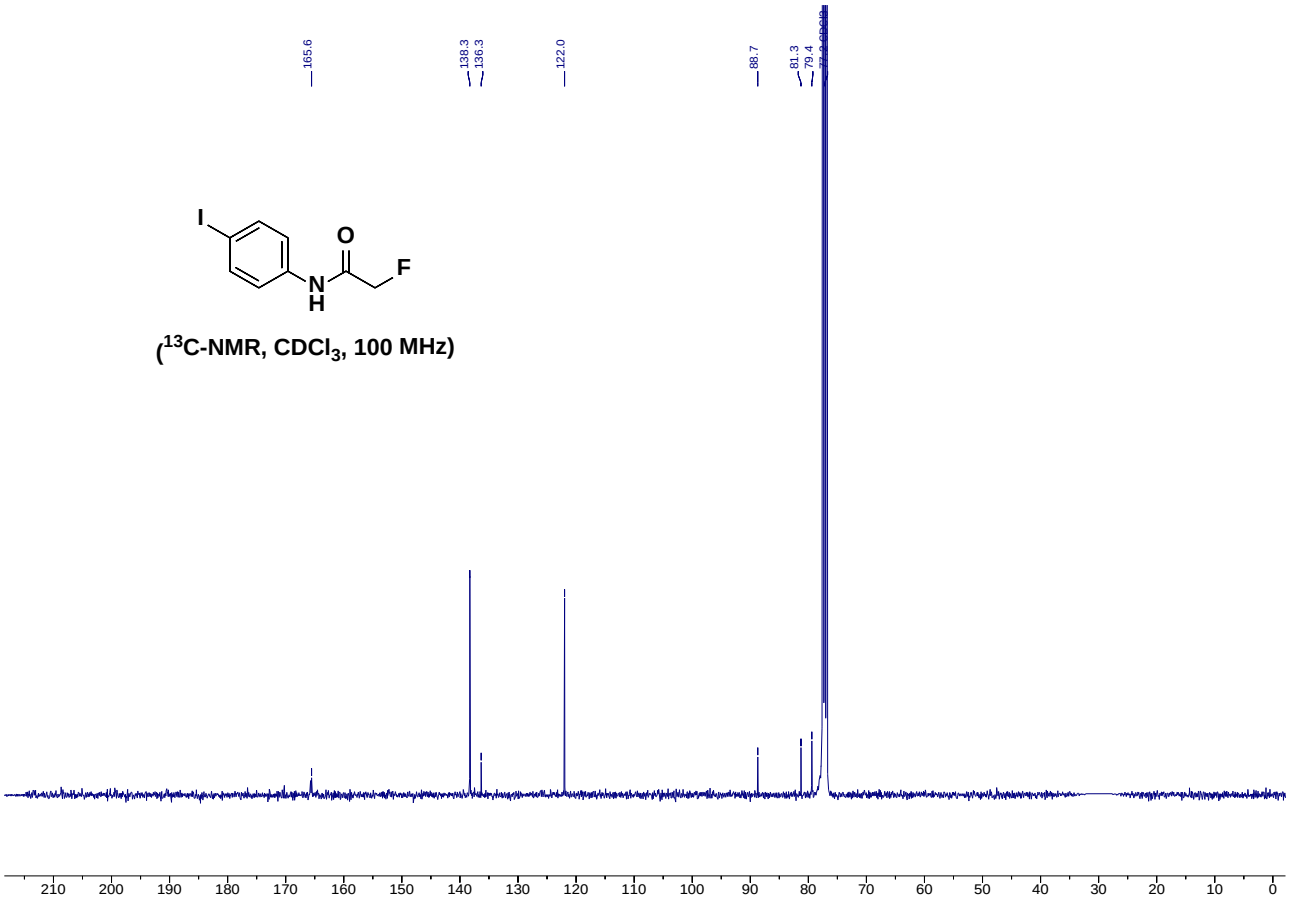
(^{13}C-NMR, $CDCl_3$, 100 MHz)

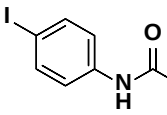
2-fluoro-*N*-(4-iodophenyl)acetamide (3)



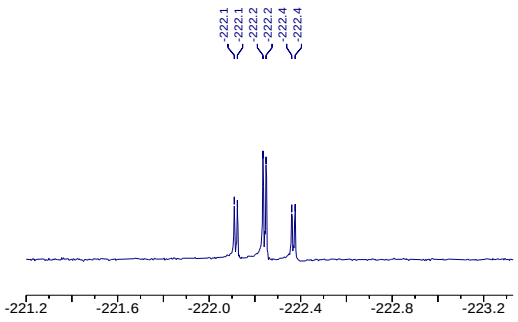
(^{1}H-NMR, $CDCl_3$, 400 MHz)

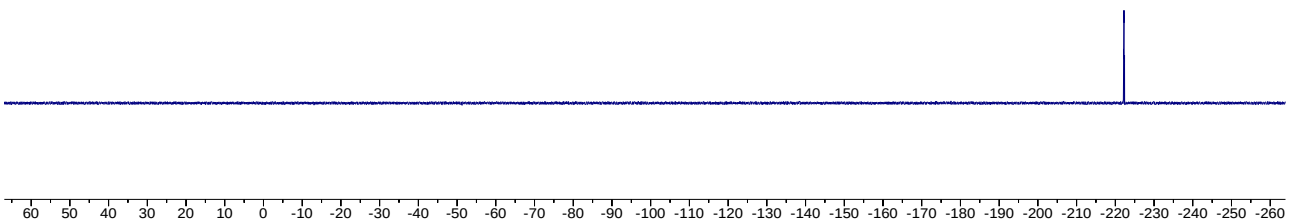
(^{13}C-NMR, $CDCl_3$, 100 MHz)



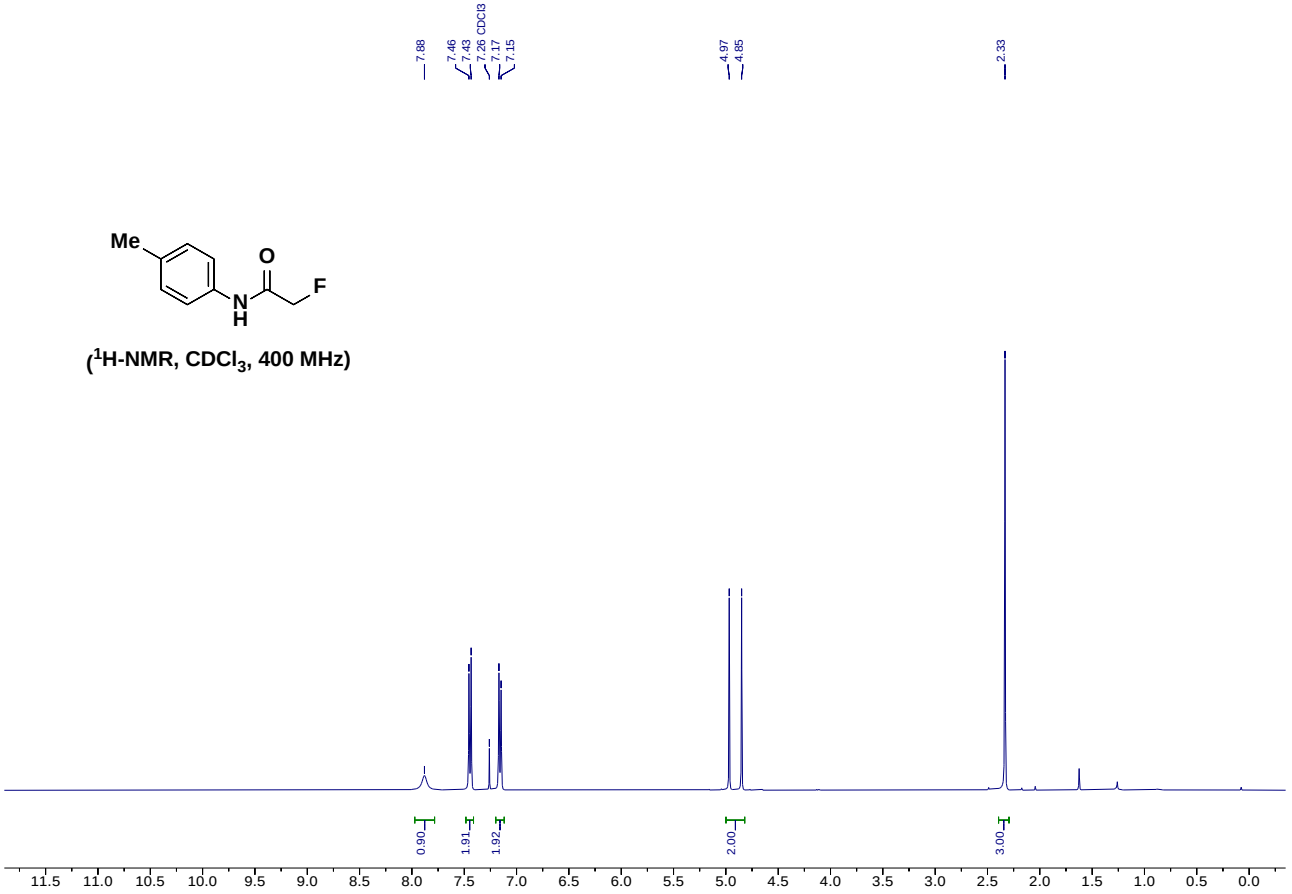


(^{19}F-NMR, $CDCl_3$, 376 MHz)

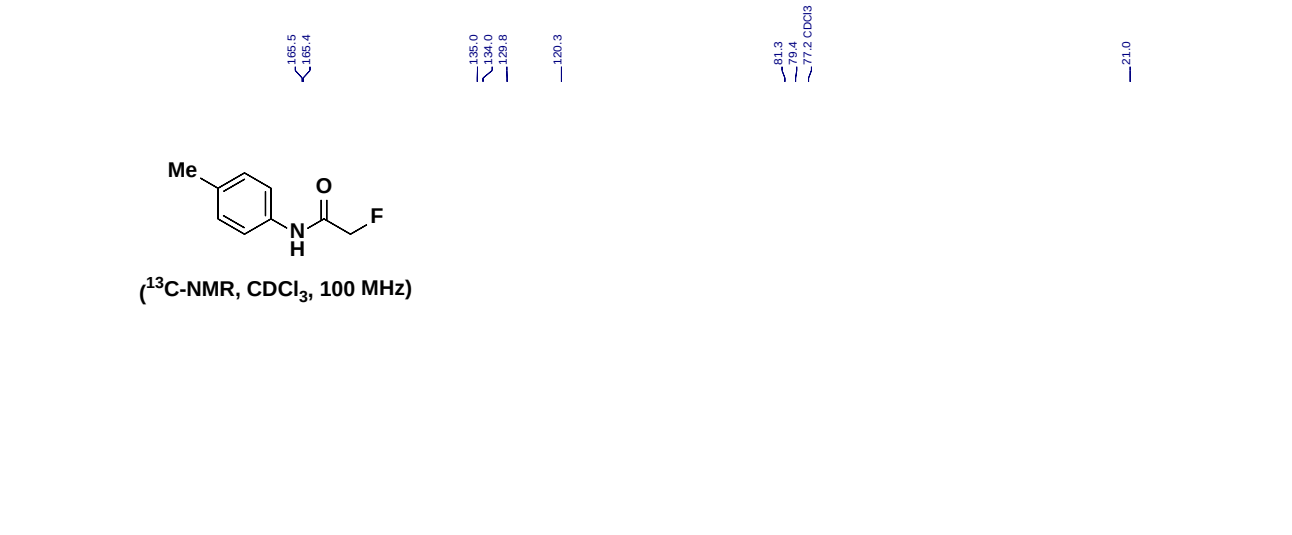




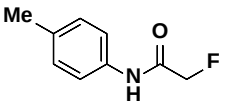
2-fluoro-*N*-(*p*-tolyl)acetamide (4)



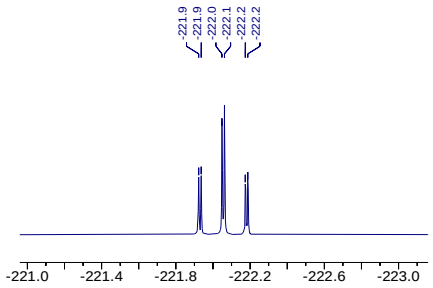
(^{1}H-NMR, $CDCl_3$, 400 MHz)

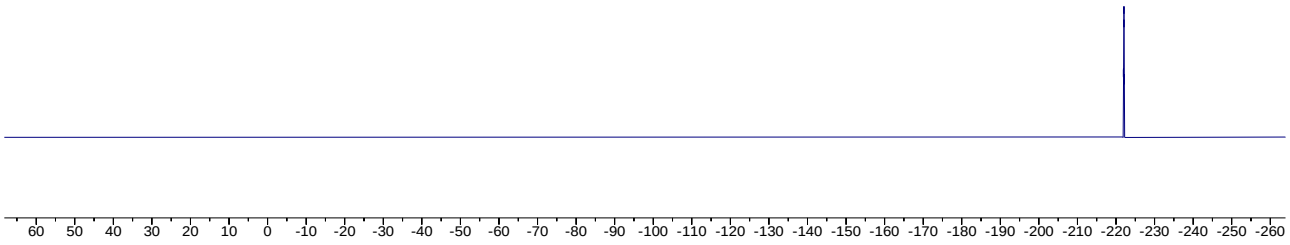


(^{13}C-NMR, $CDCl_3$, 100 MHz)

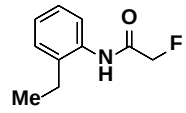


(¹⁹F-NMR, $CDCl_3$, 376 MHz)

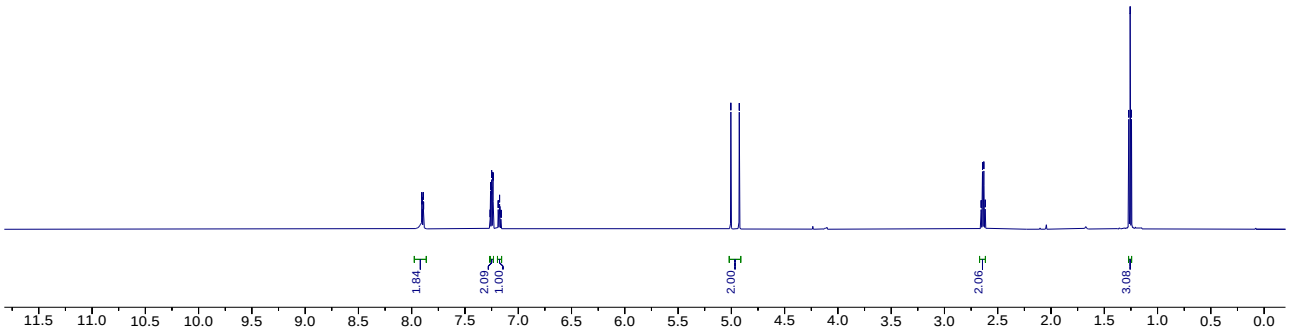


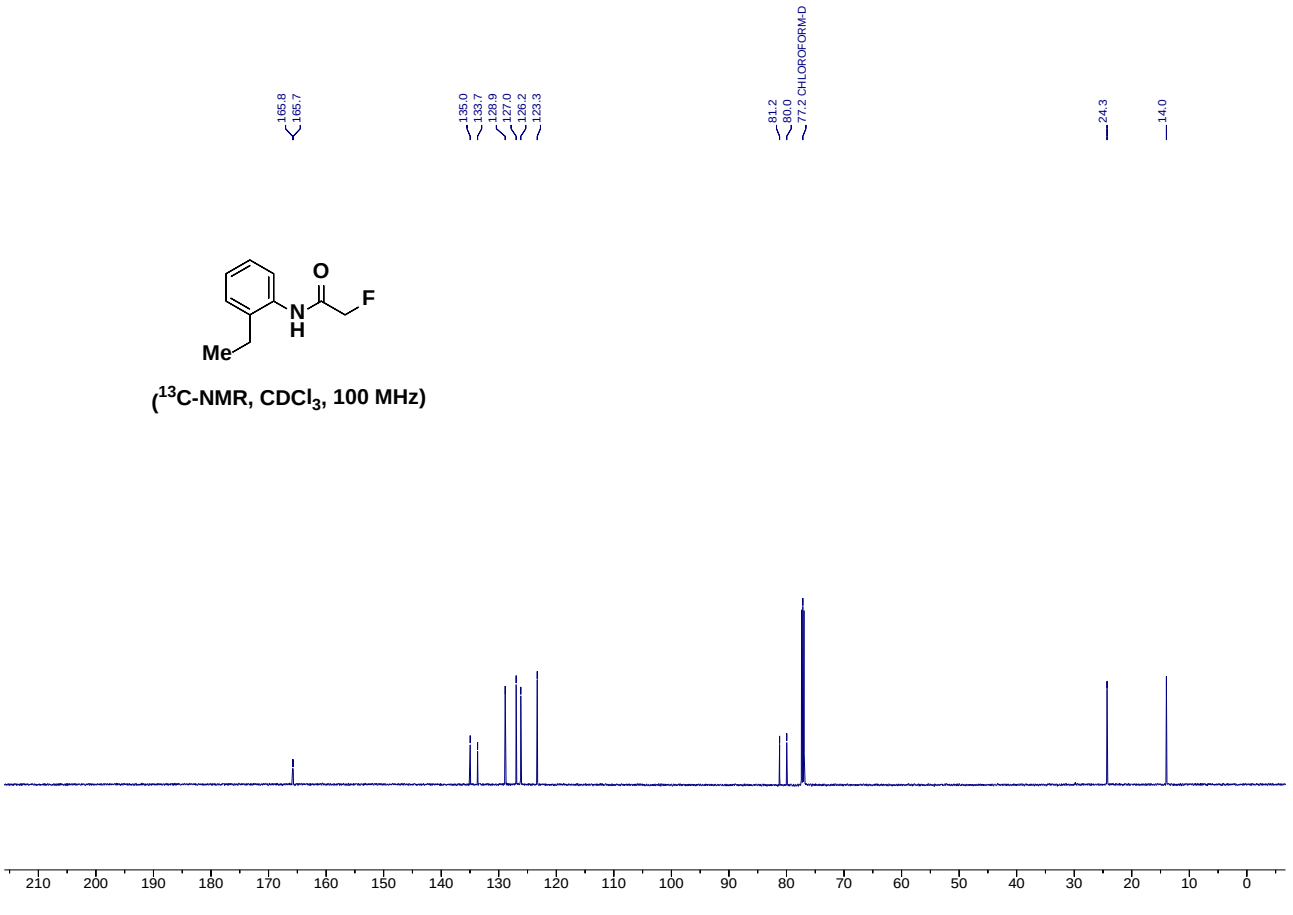


N-(2-ethylphenyl)-2-fluoroacetamide (5)

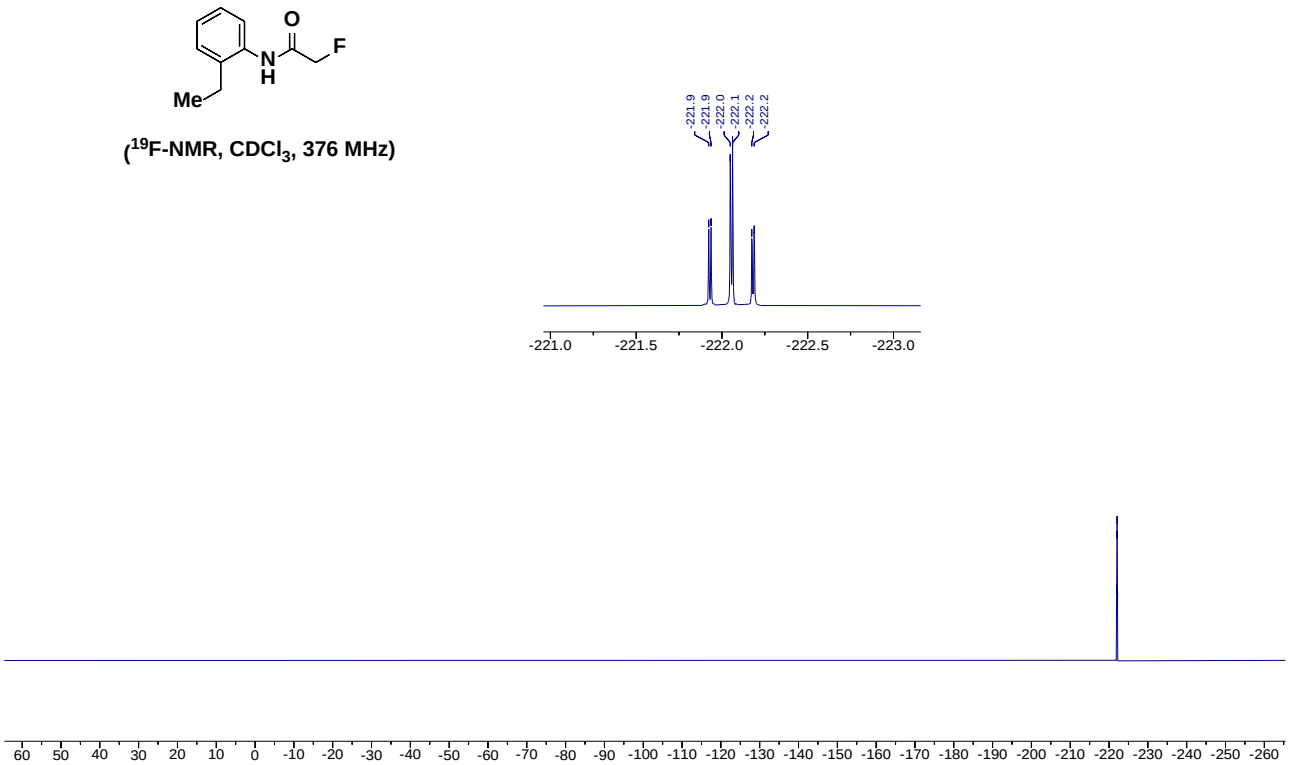


(¹H-NMR, $CDCl_3$, 400 MHz)





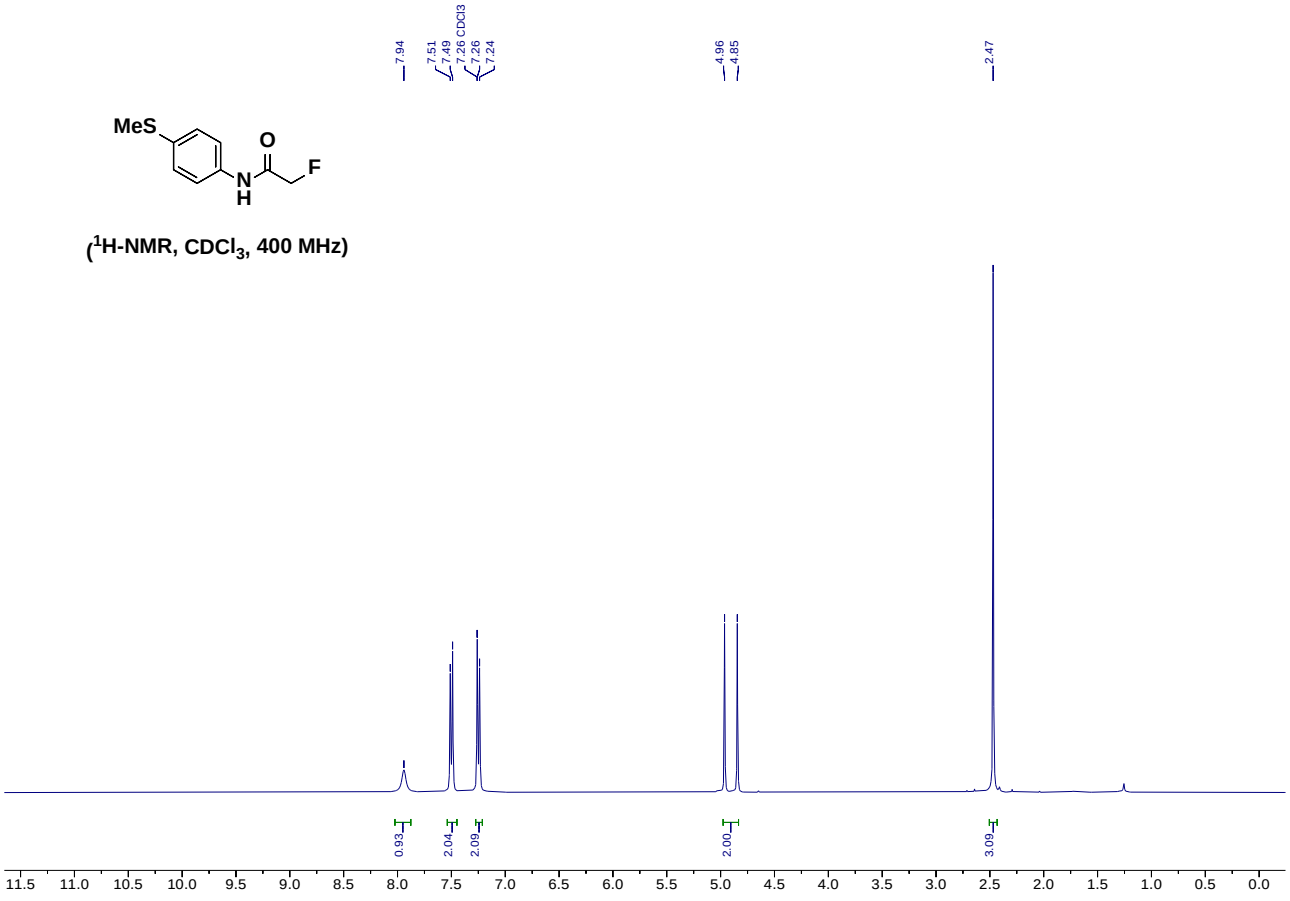
(¹³C-NMR, $CDCl_3$, 100 MHz)

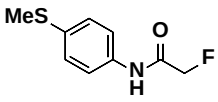


(¹⁹F-NMR, $CDCl_3$, 376 MHz)

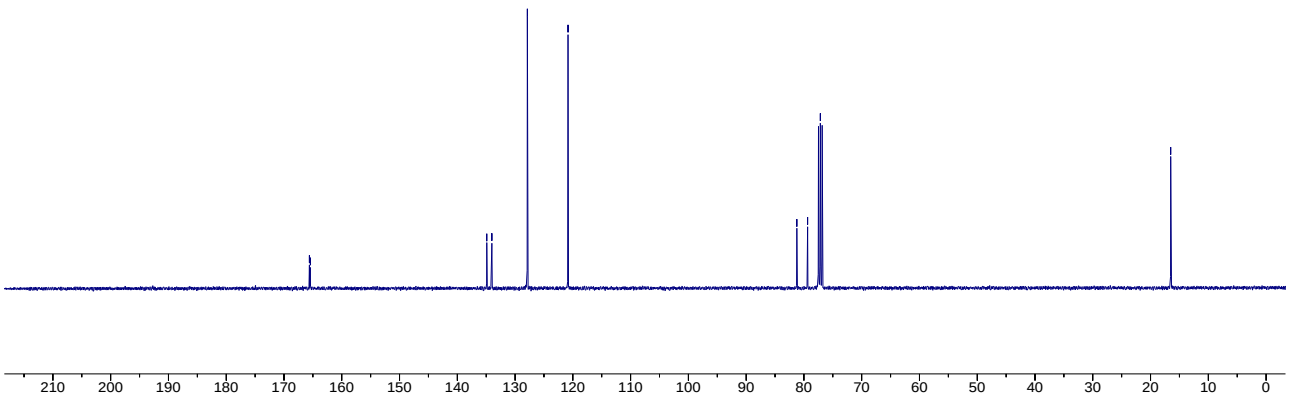
2-fluoro-*N*-(4-(methylthio)phenyl)acetamide (6)

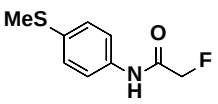
(^{1}H-NMR, $CDCl_3$, 400 MHz)



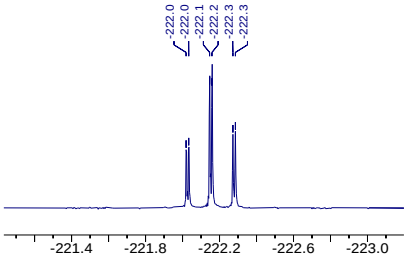


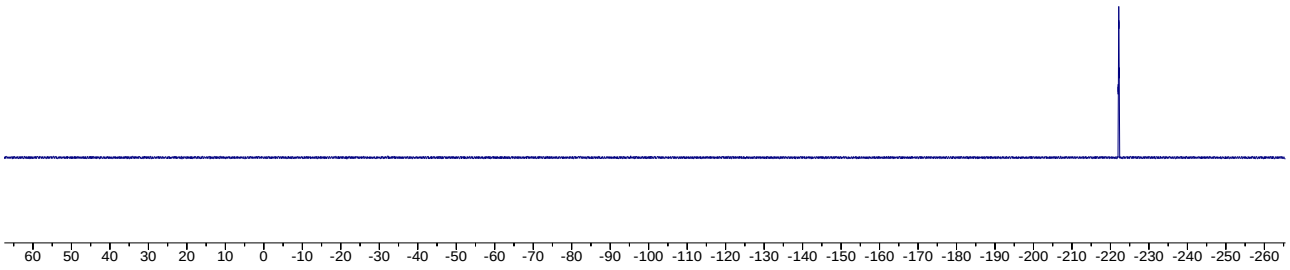
(^{13}C-NMR, $CDCl_3$, 100 MHz)



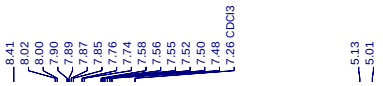


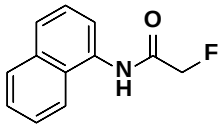
(¹⁹F-NMR, $CDCl_3$, 376 MHz)



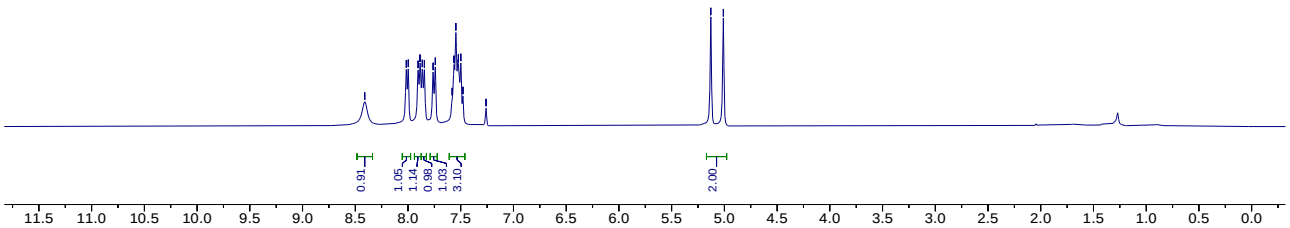


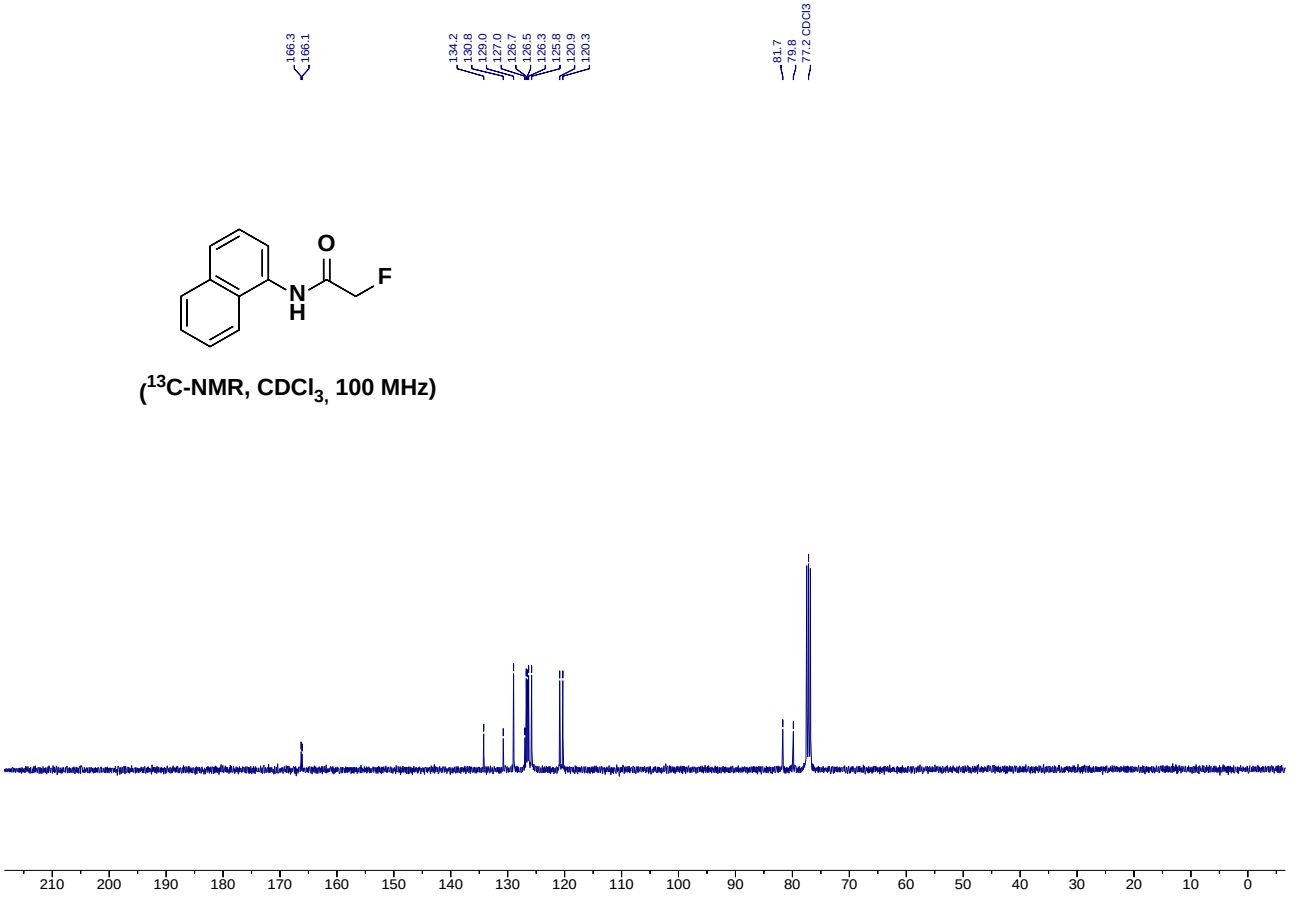
2-fluoro-*N*-(naphthalen-1-yl)acetamide (7)



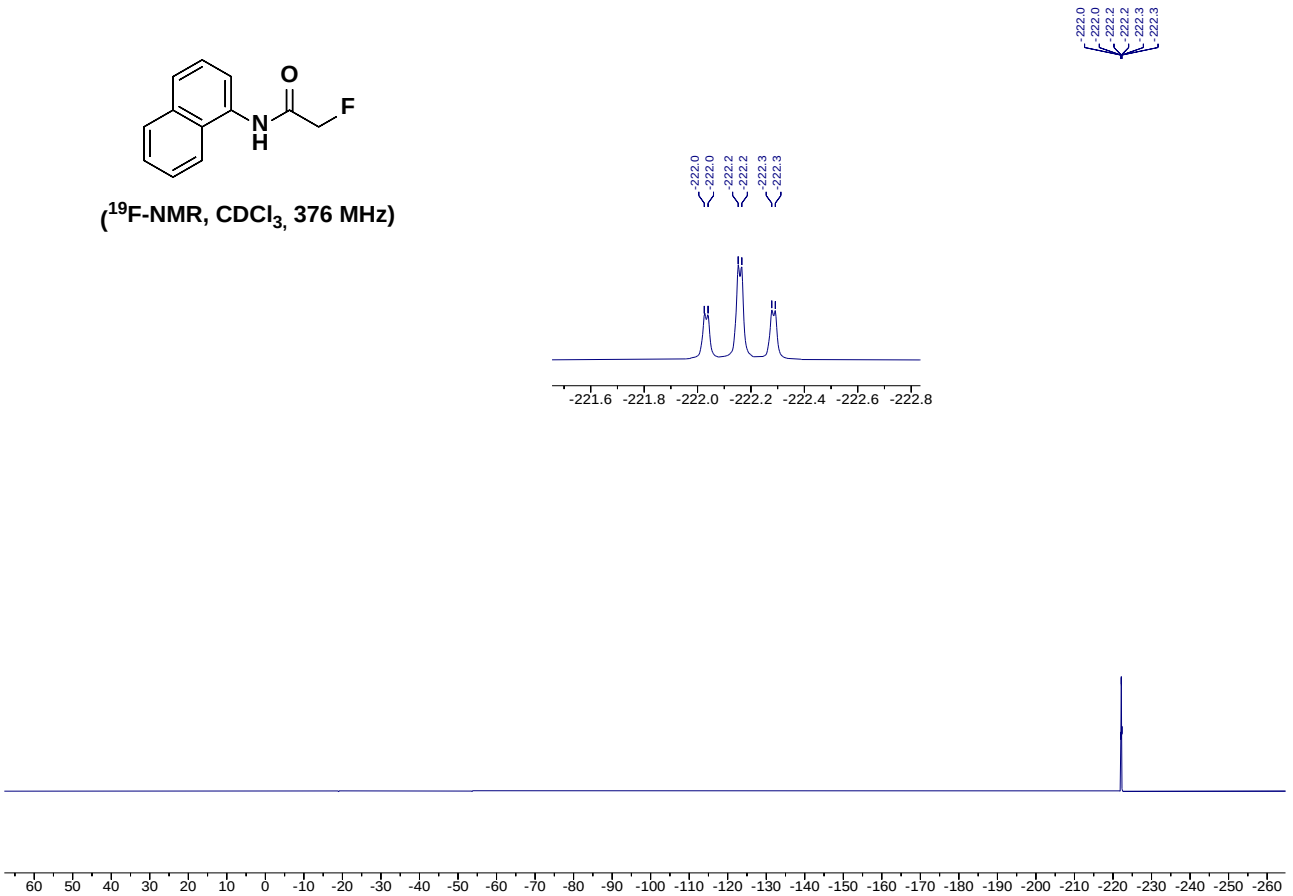


(¹H-NMR, $CDCl_3$, 400 MHz)



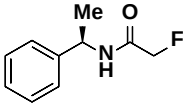


(^{13}C-NMR, $CDCl_3$, 100 MHz)

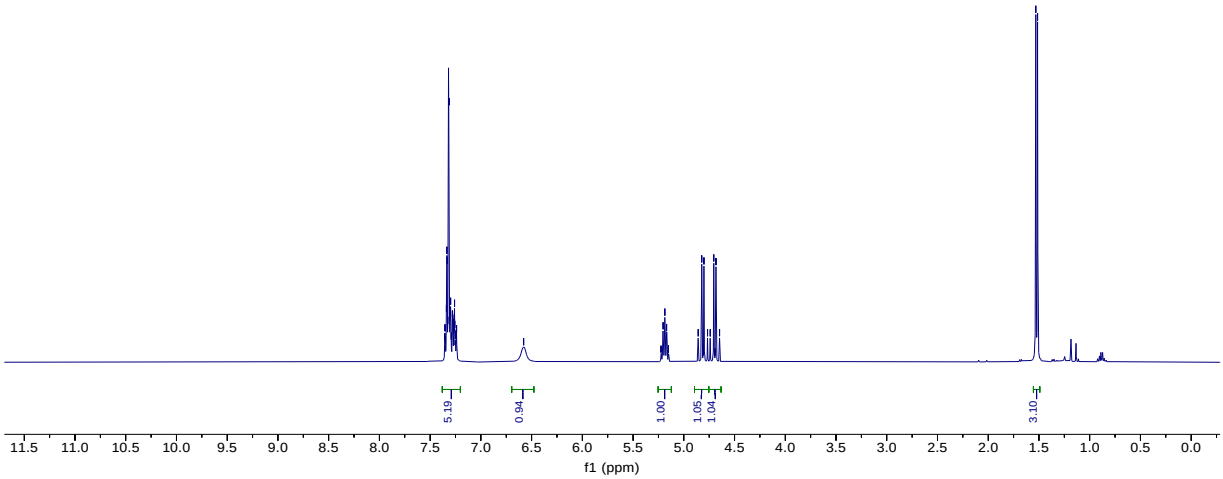


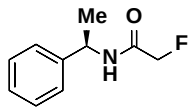
(^{19}F-NMR, $CDCl_3$, 376 MHz)

(R)-2-fluoro-N-(1-phenylethyl)acetamide ((R)-9)

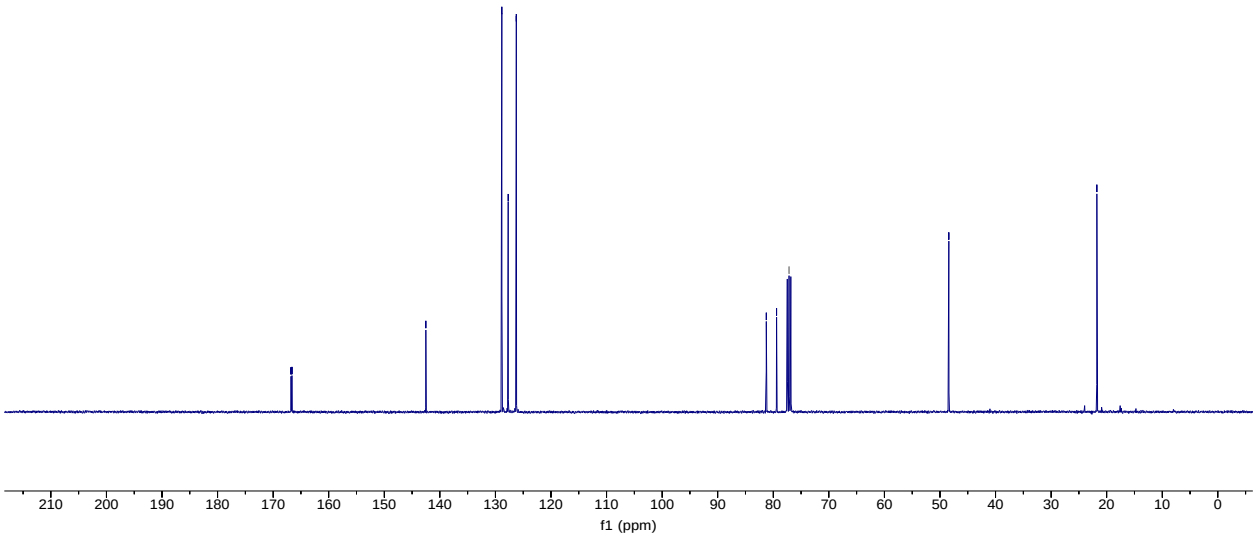


(^{1}H-NMR, $CDCl_3$, 400 MHz)

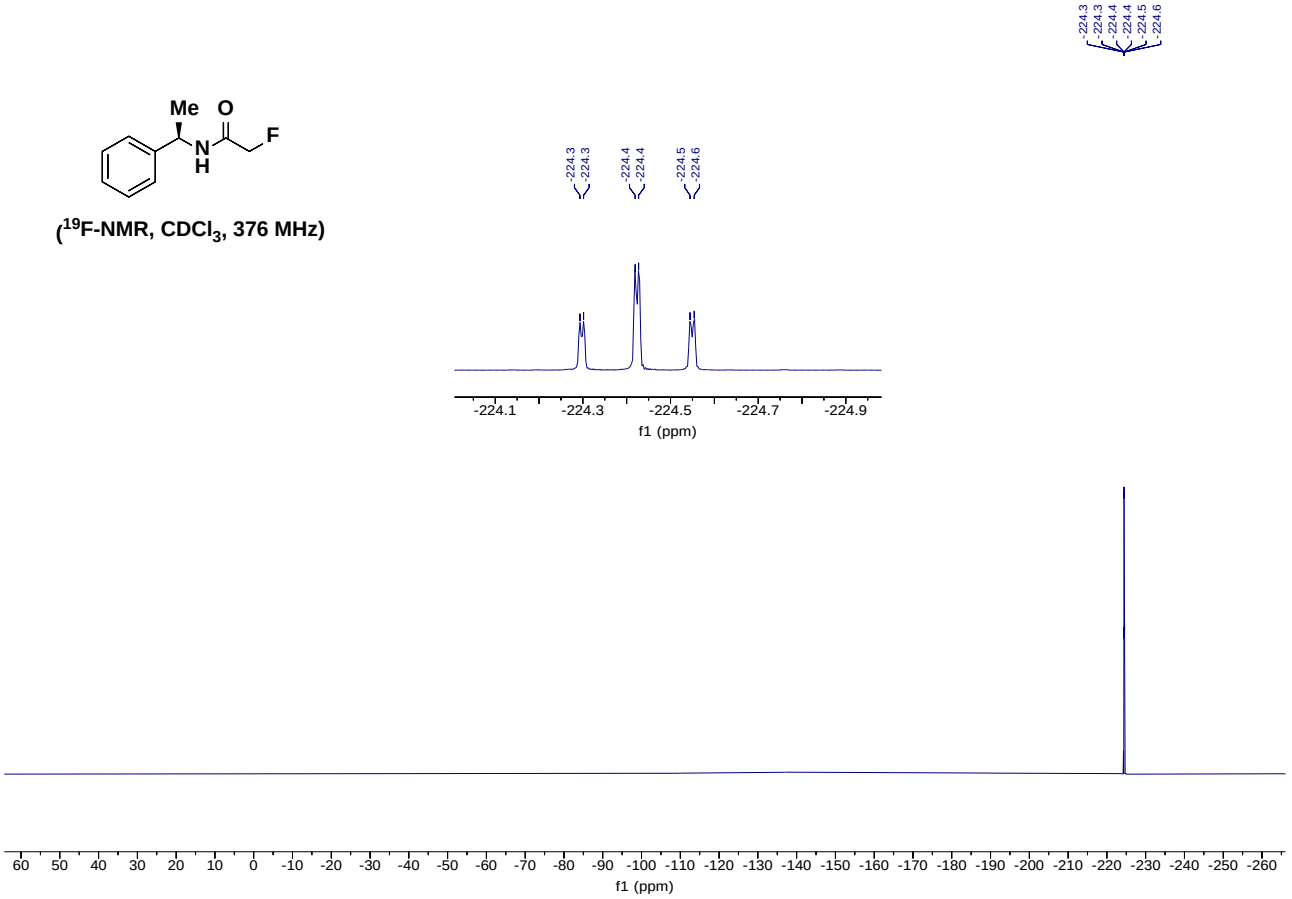




(^{13}C-NMR, $CDCl_3$, 100 MHz)

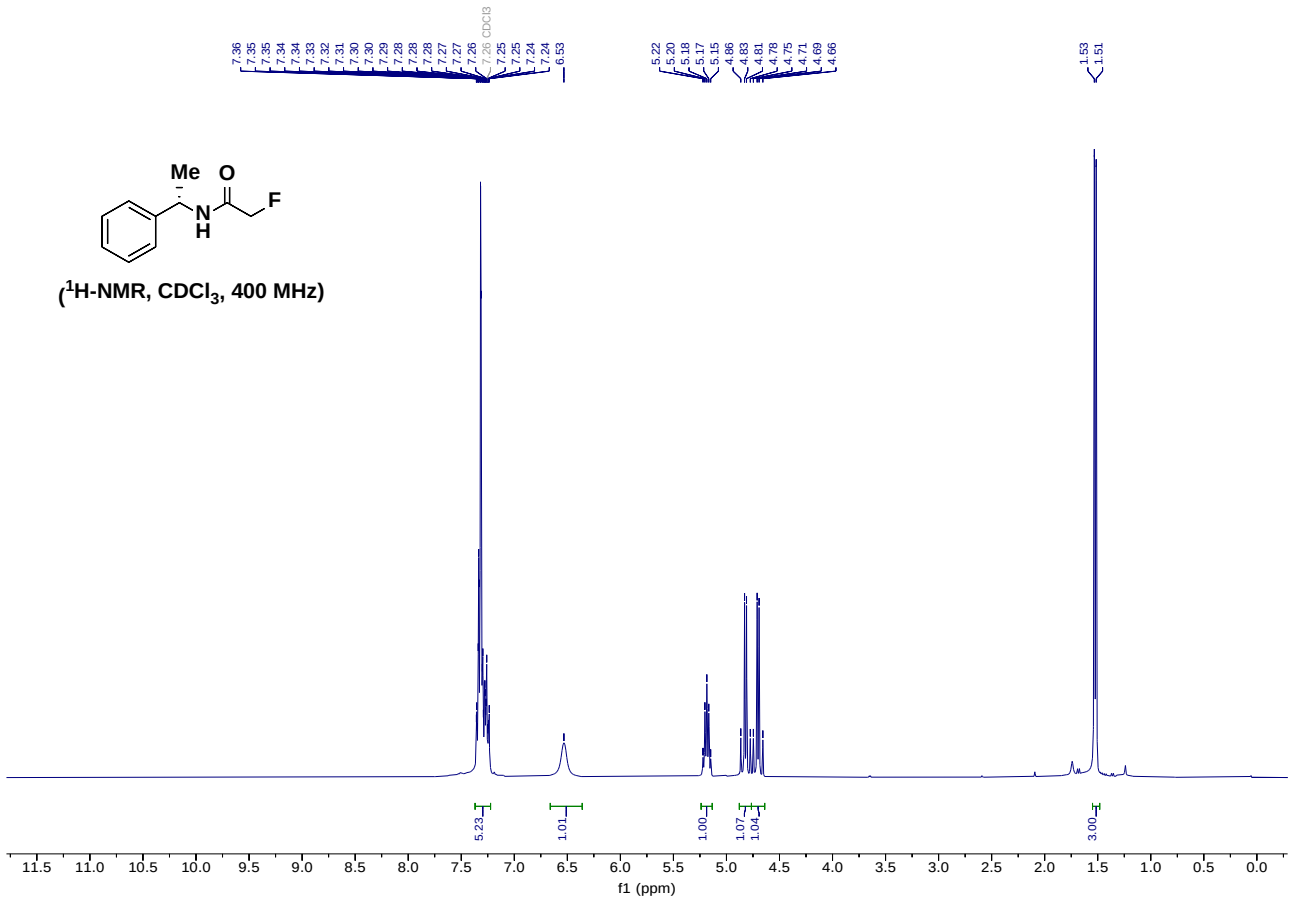


(¹⁹F-NMR, $CDCl_3$, 376 MHz)

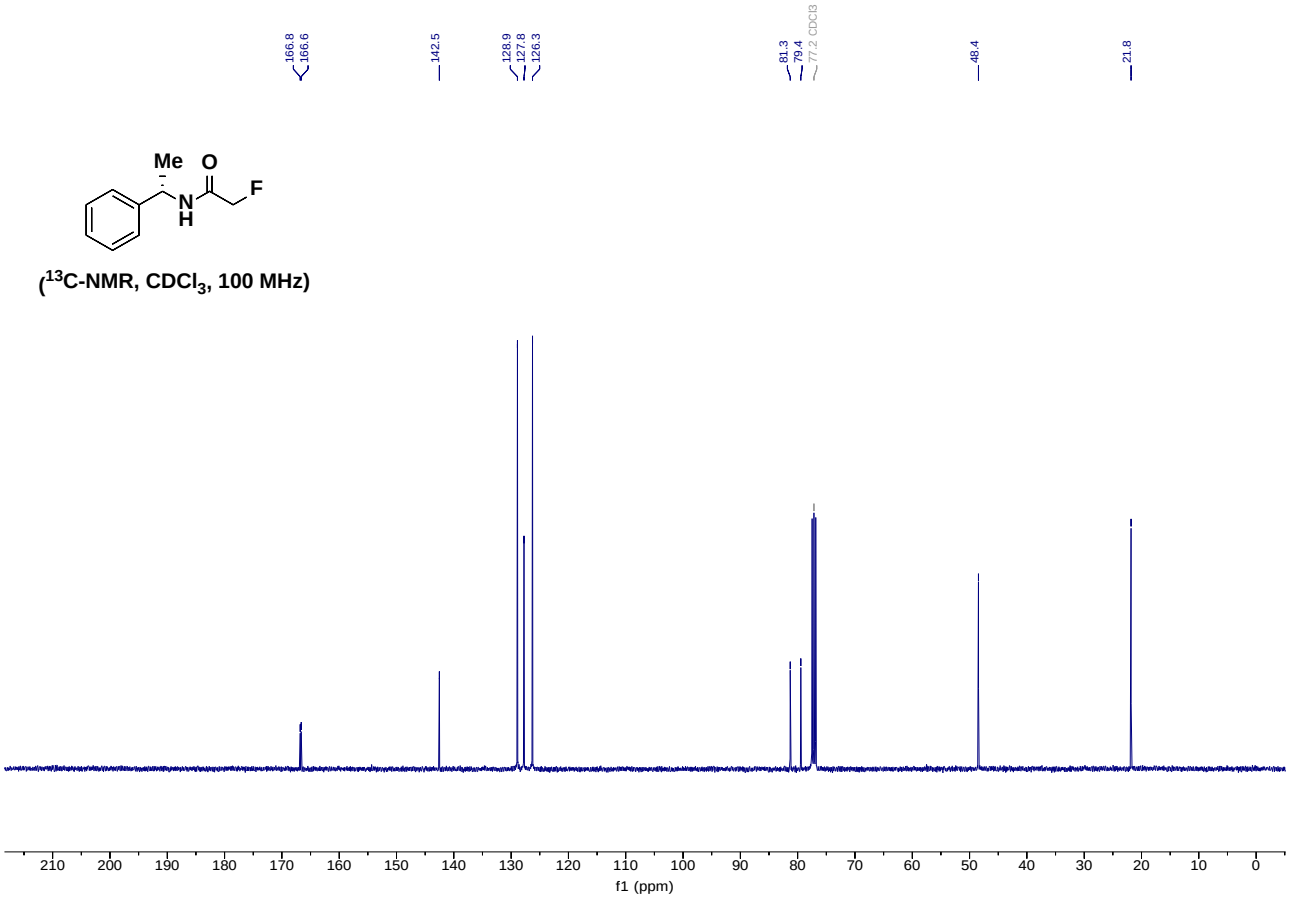


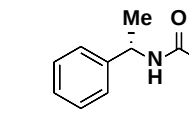
(S)-2-fluoro-*N*-(1-phenylethyl)acetamide ((S)-9)

(¹H-NMR, $CDCl_3$, 400 MHz)

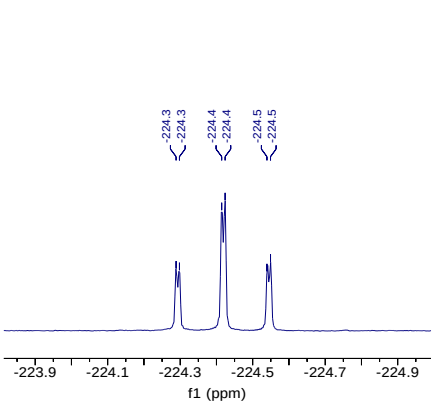


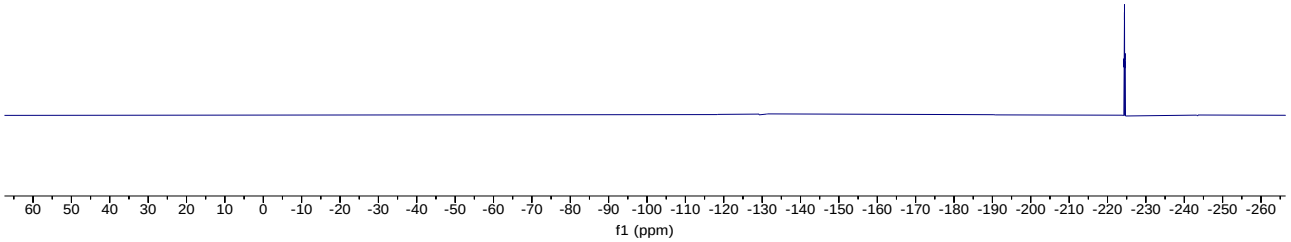
(^{13}C-NMR, $CDCl_3$, 100 MHz)



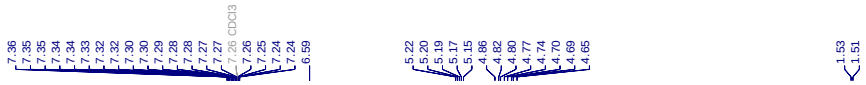


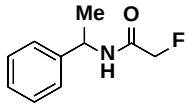
(^{19}F-NMR, $CDCl_3$, 376 MHz)



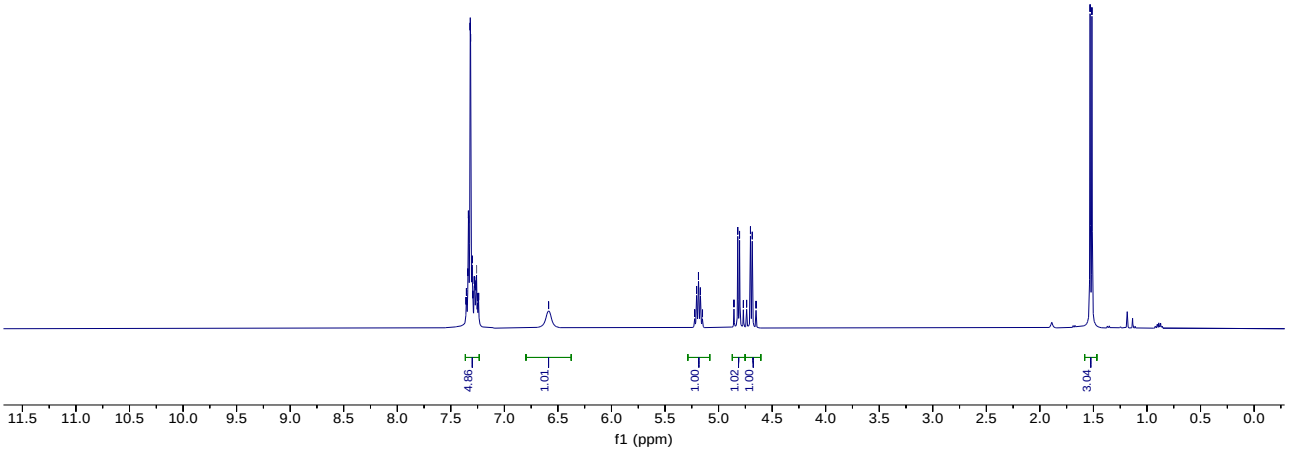


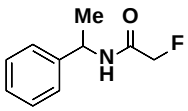
2-fluoro-*N*-(1-phenylethyl)acetamide ((rac)-9)



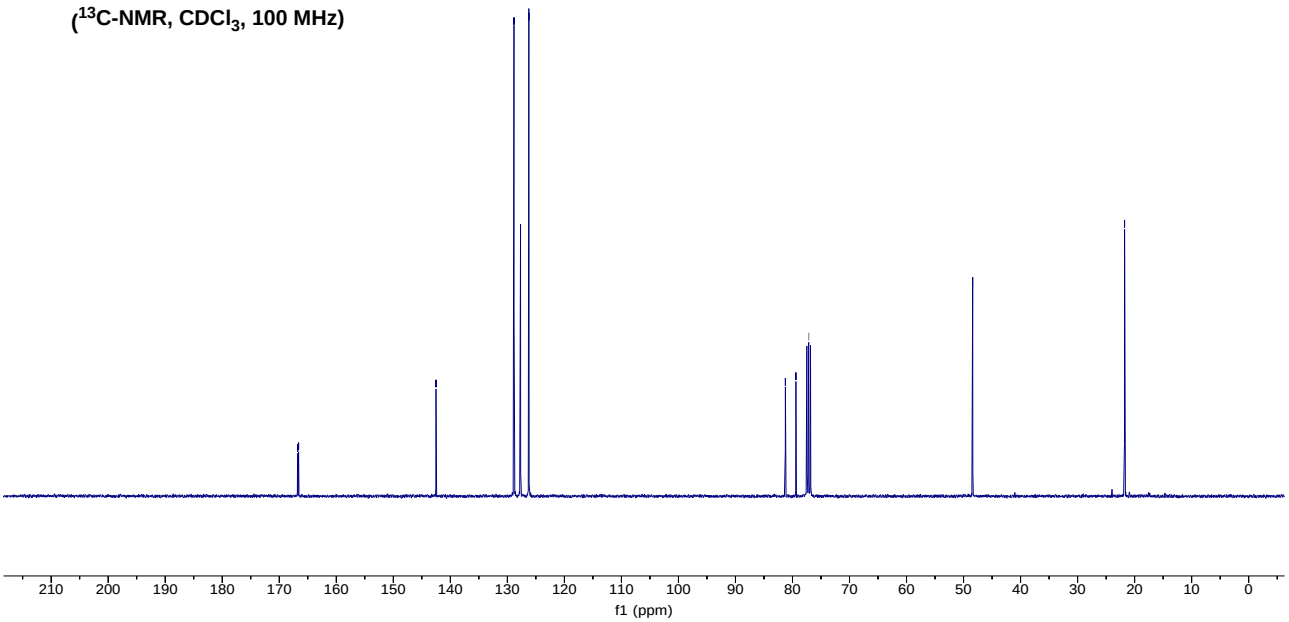


(^{1}H-NMR, $CDCl_3$, 400 MHz)



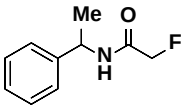


(^{13}C-NMR, $CDCl_3$, 100 MHz)



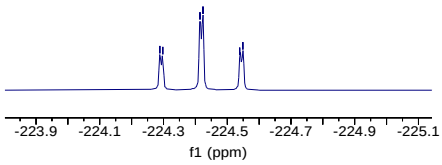
-224.3
-224.3
-224.4
-224.4
-224.5
-224.5

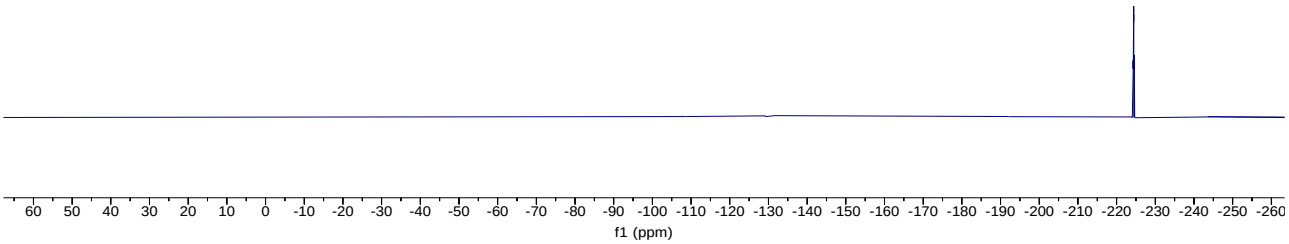
-



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

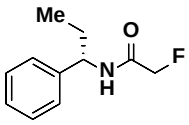
-224.3
-224.3
-224.4
-224.4
-224.5
-224.5



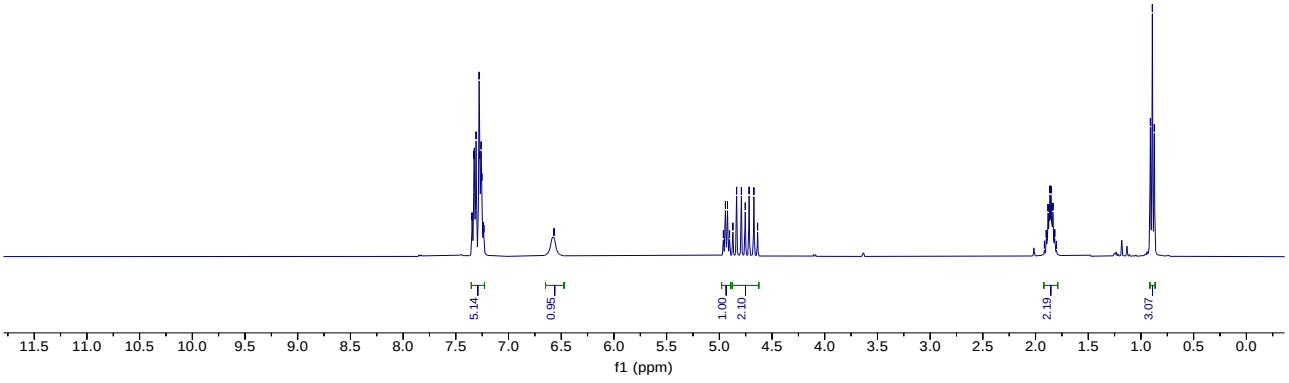


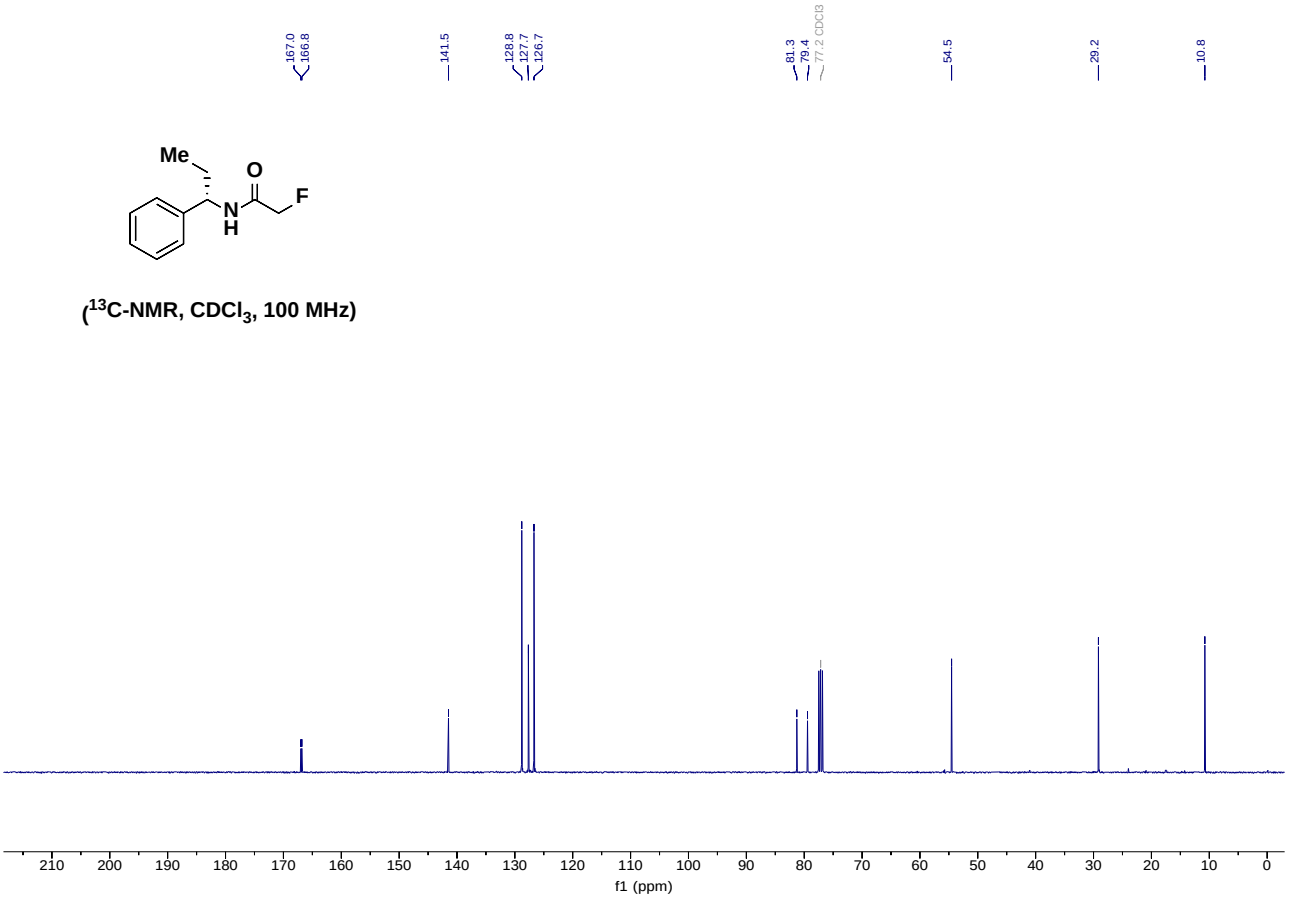
(S)-2-fluoro-*N*-(1-phenylpropyl)acetamide ((S)-10)

7.35
7.34
7.33
7.32
7.31
7.28
7.27
7.26
7.26 CDCl3
7.25
7.24
7.24
7.23
6.57
4.96
4.94
4.92
4.90
4.87
4.84
4.79
4.75
4.72
4.67
4.64
1.92
1.90
1.89
1.88
1.87
1.86
1.85
1.84
1.84
1.83
1.82
1.80
0.91
0.89
0.87

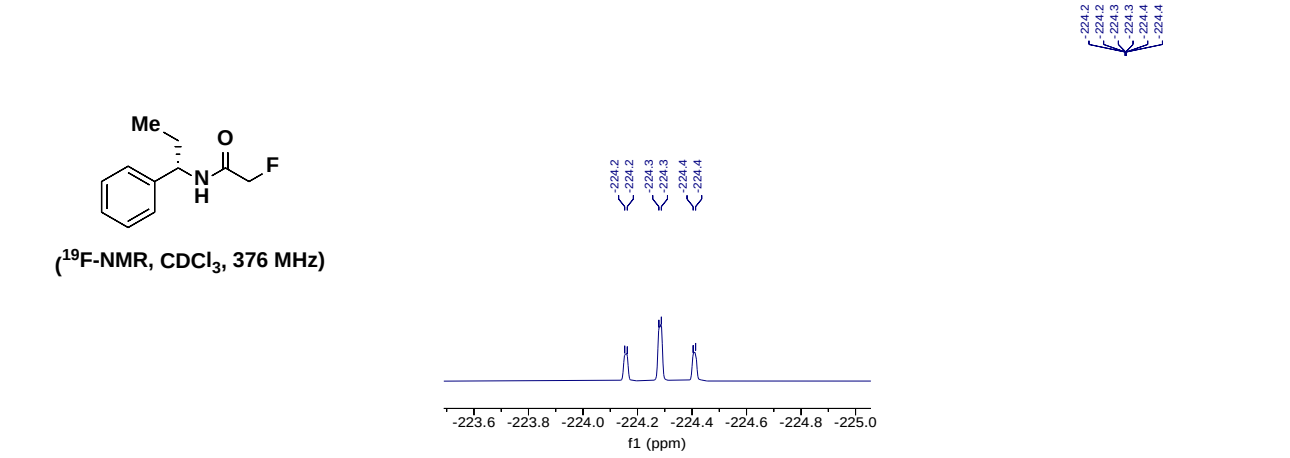


(**^{1}H-NMR, $CDCl_3$, 400 MHz**)

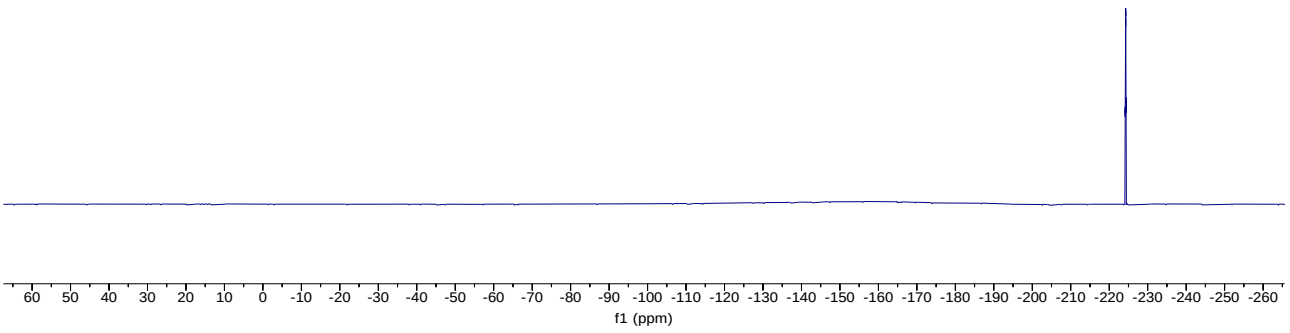




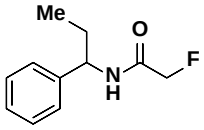
(¹³C-NMR, $CDCl_3$, 100 MHz)



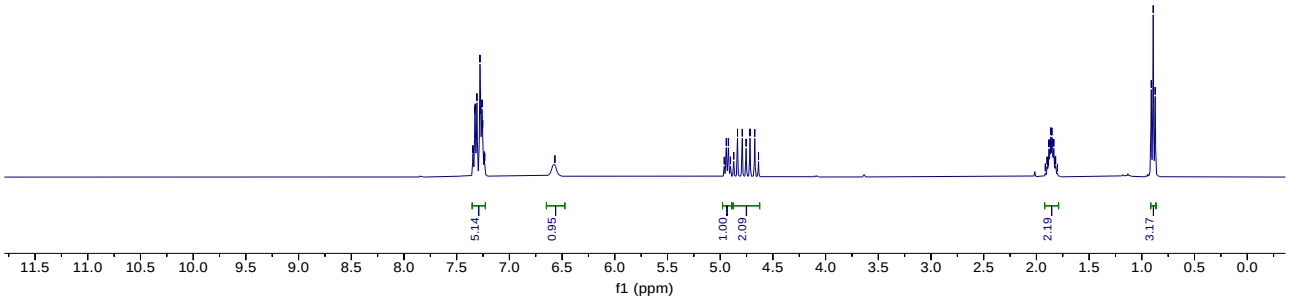
(¹⁹F-NMR, $CDCl_3$, 376 MHz)



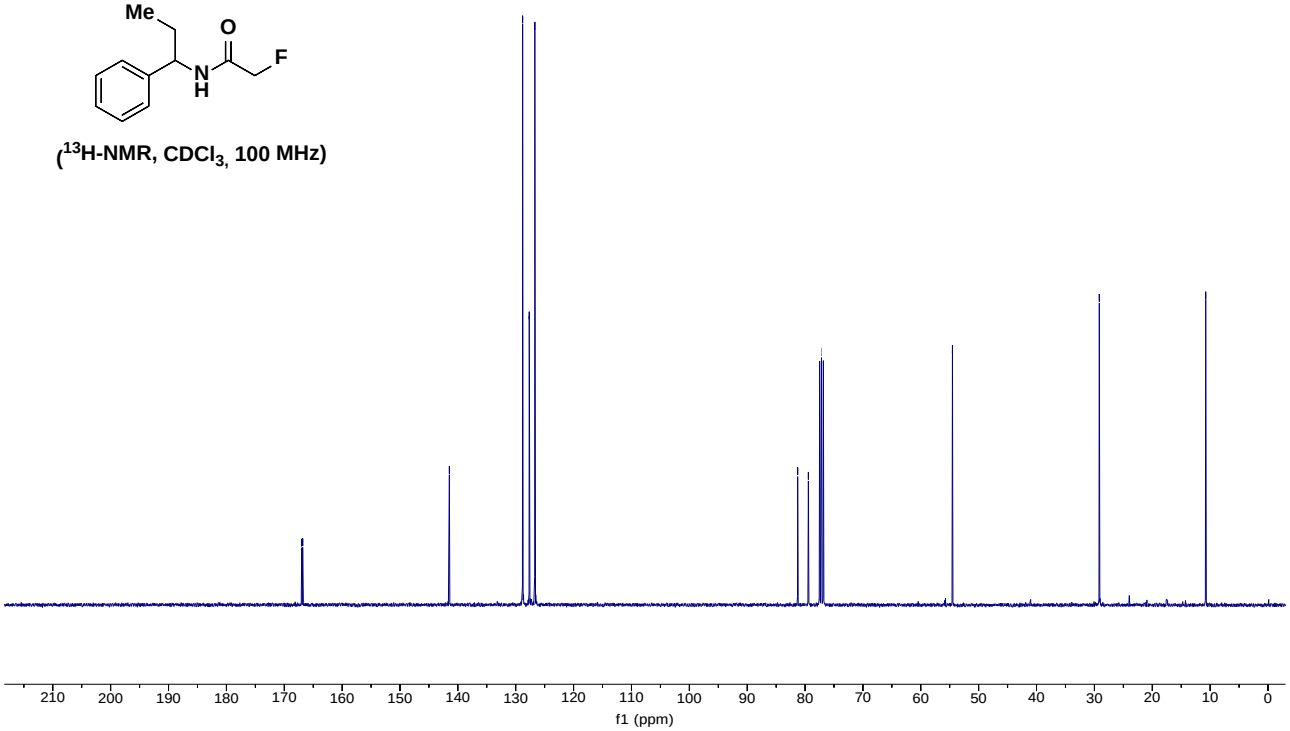
2-fluoro-*N*-(1-phenylpropyl)acetamide ((rac)-10)

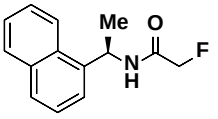


(^{1}H-NMR, $CDCl_3$, 400 MHz)

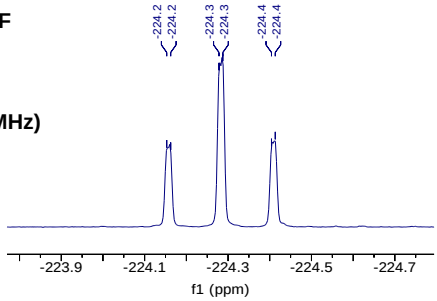


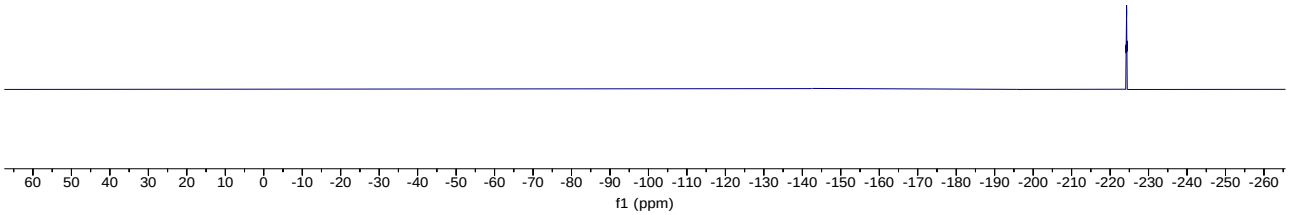
(^{13}H-NMR, $CDCl_3$, 100 MHz)



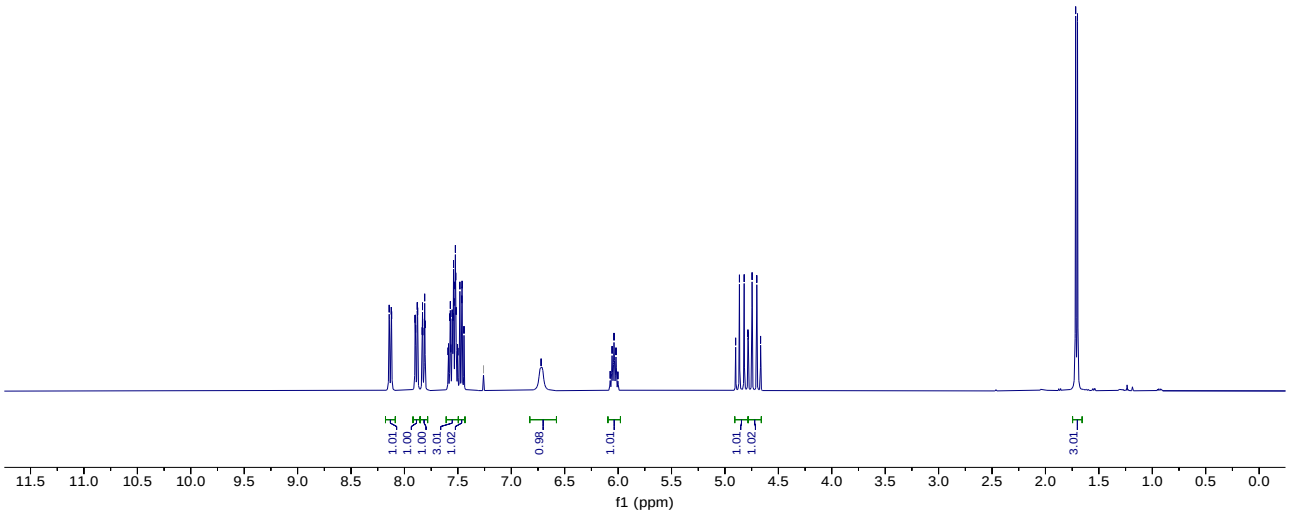


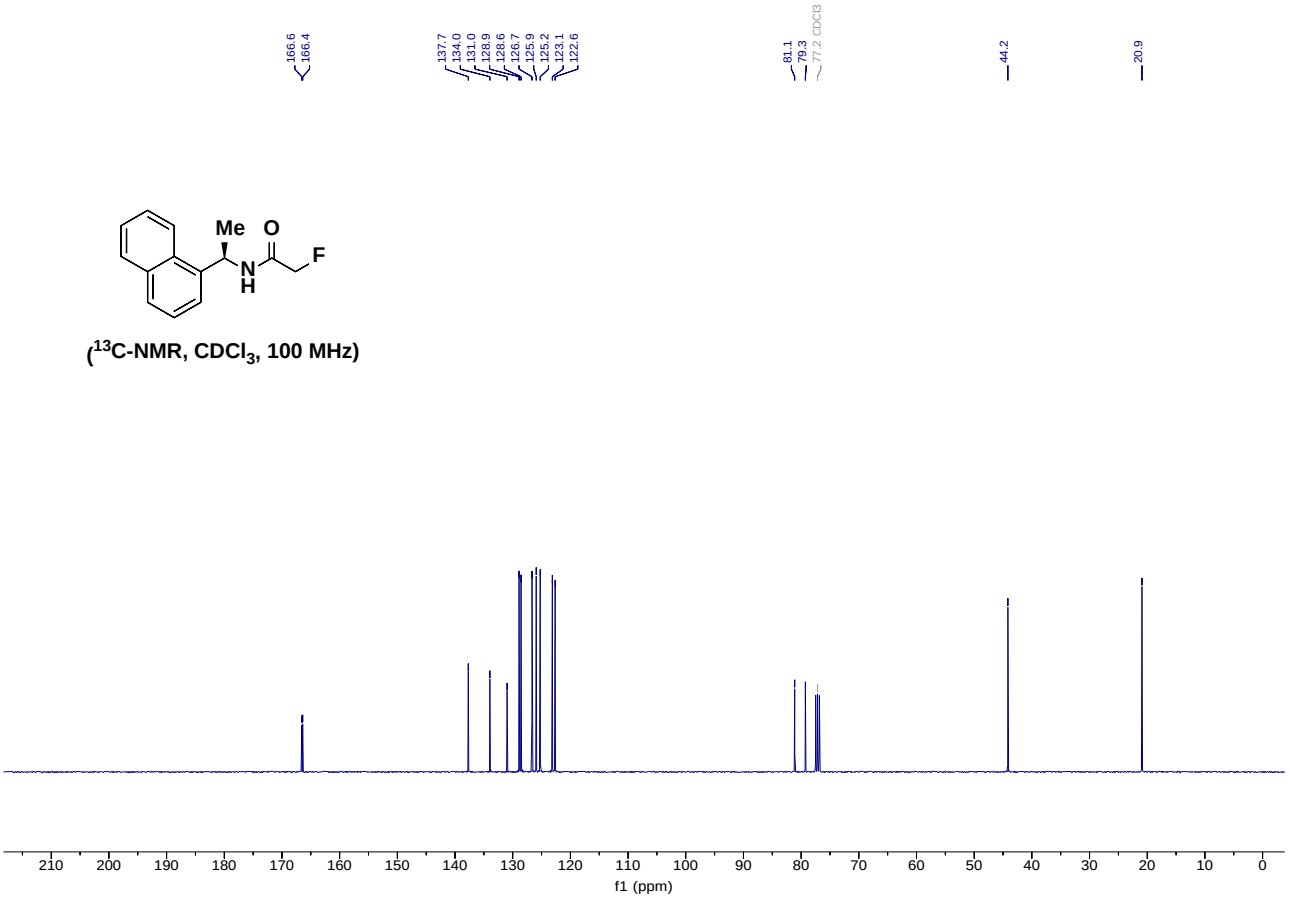
(**^{1}H-NMR, $CDCl_3$, 400 MHz**)



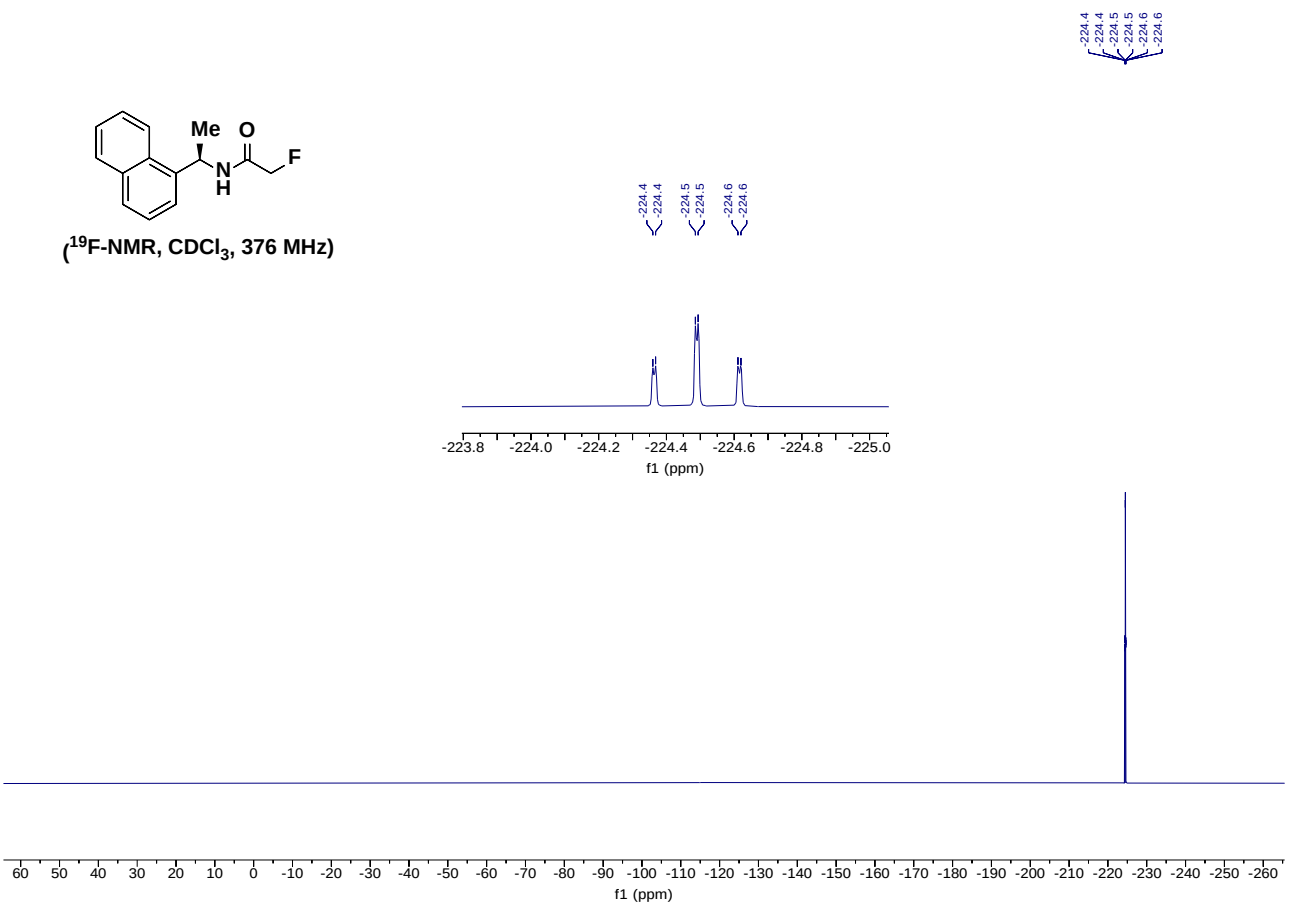


((R)-2-fluoro-*N*-(1-(naphthalen-1-yl)ethyl)acetamide ((R)-11)



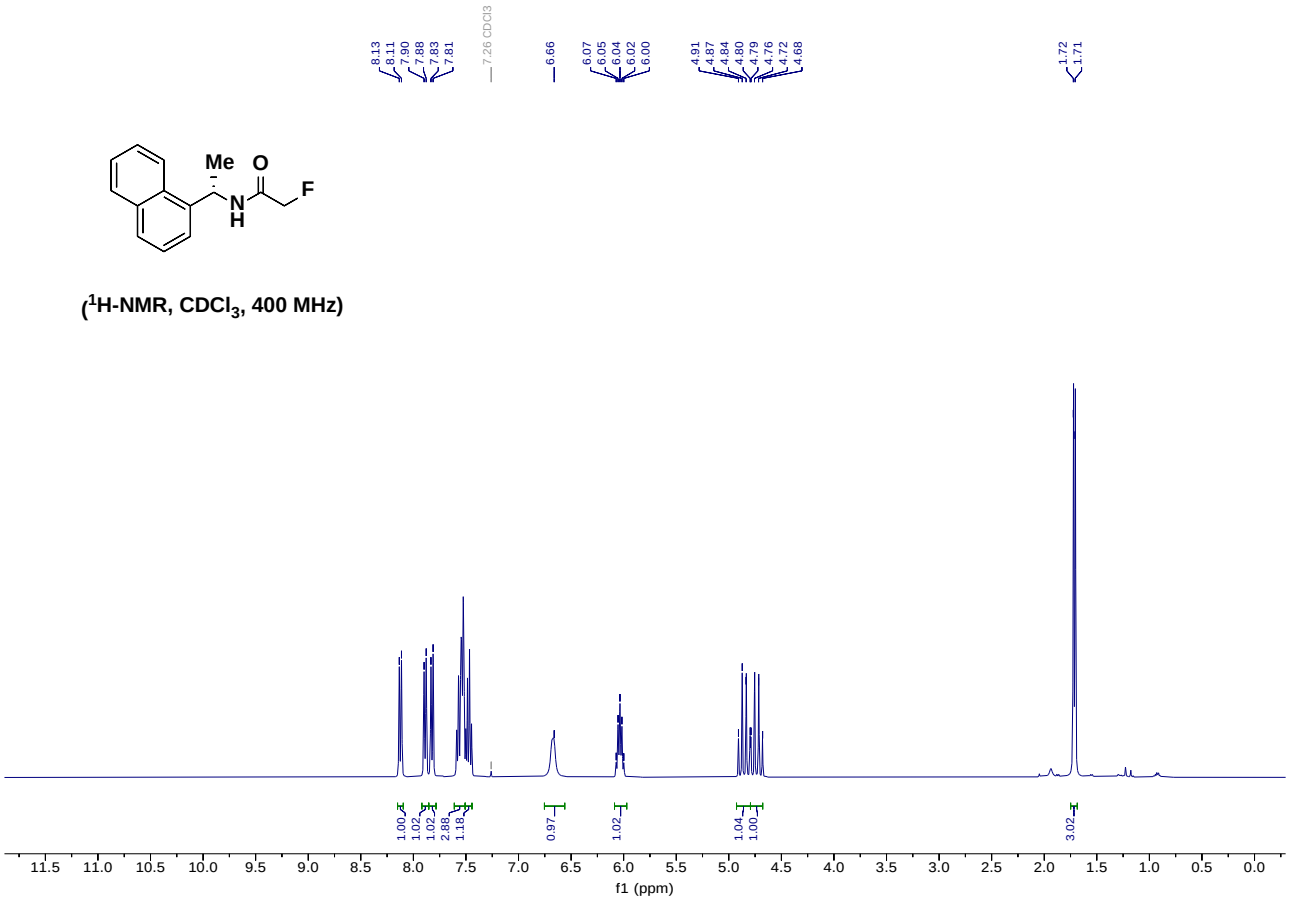


(^{13}C-NMR, $CDCl_3$, 100 MHz)

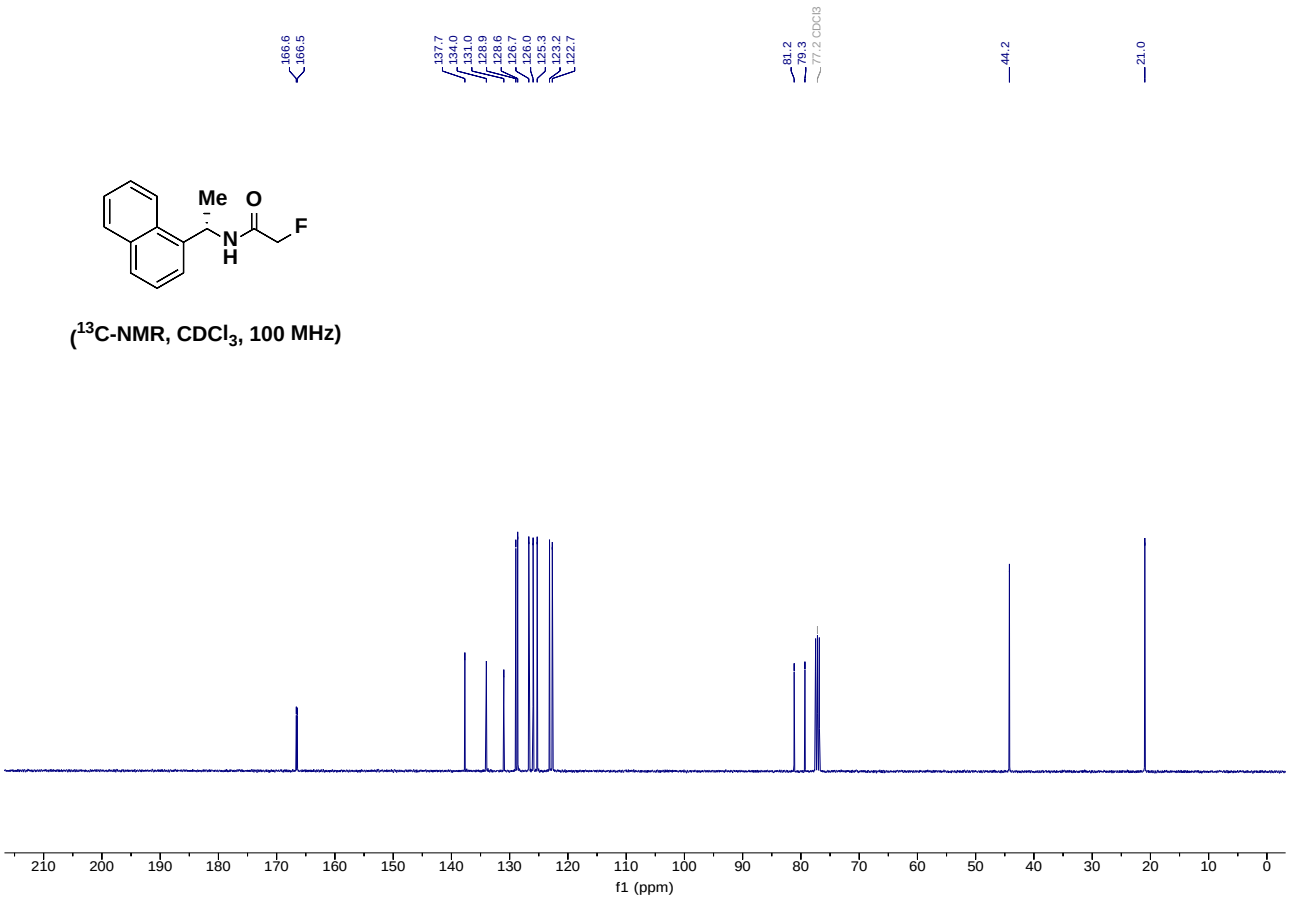


(^{19}F-NMR, $CDCl_3$, 376 MHz)

((S)-2-fluoro-*N*-(1-(naphthalen-1-yl)ethyl)acetamide ((S)-11)

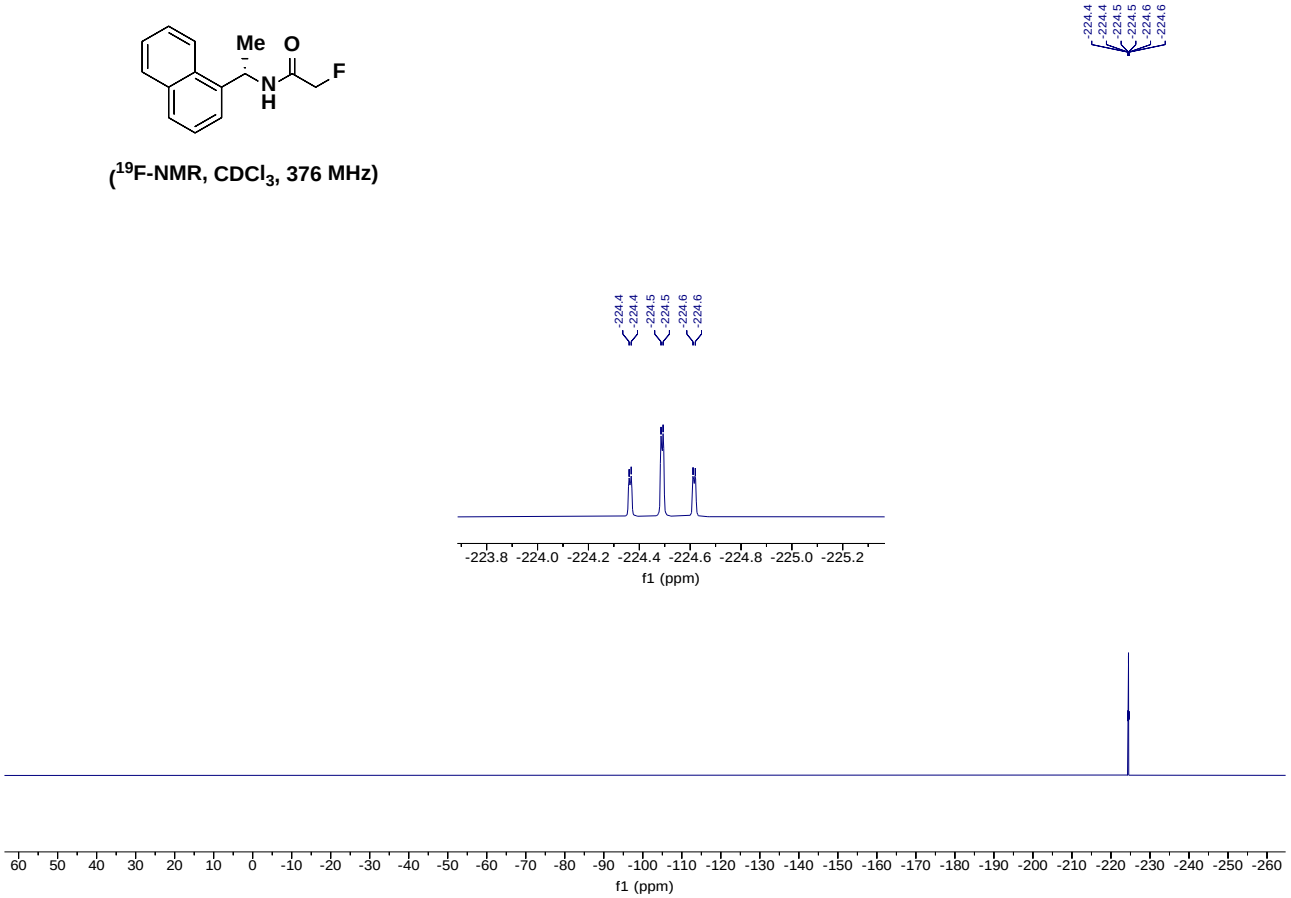


(¹H-NMR, $CDCl_3$, 400 MHz)

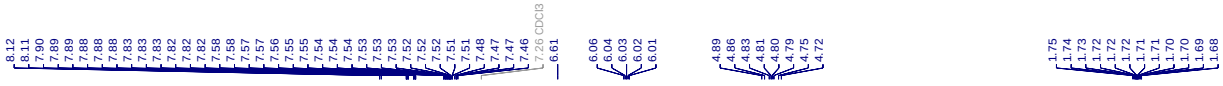


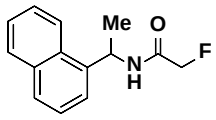
(¹³C-NMR, $CDCl_3$, 100 MHz)

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

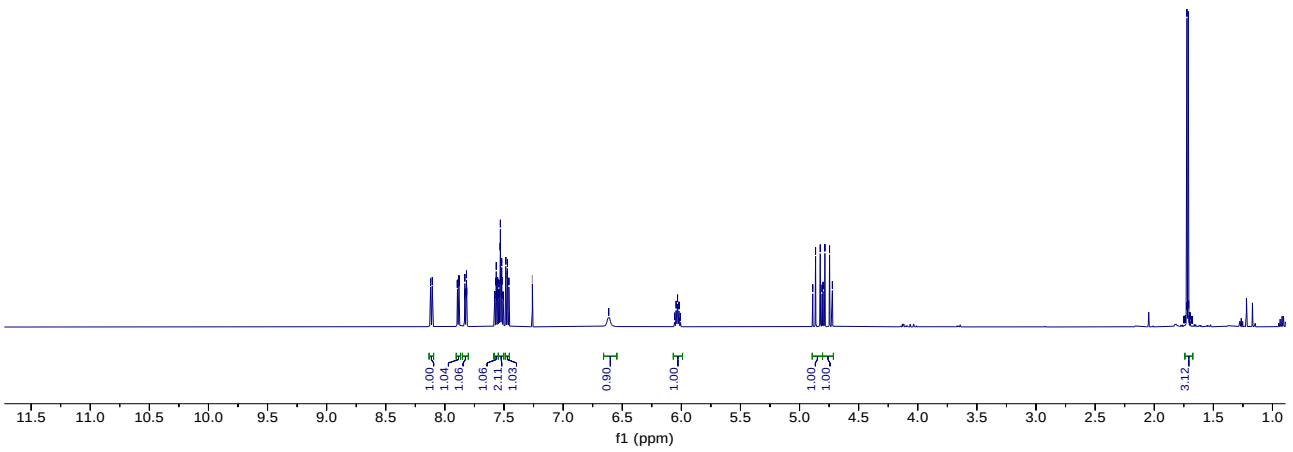


((rac)-2-fluoro-*N*-(1-(naphthalen-1-yl)ethyl)acetamide ((rac)-11)

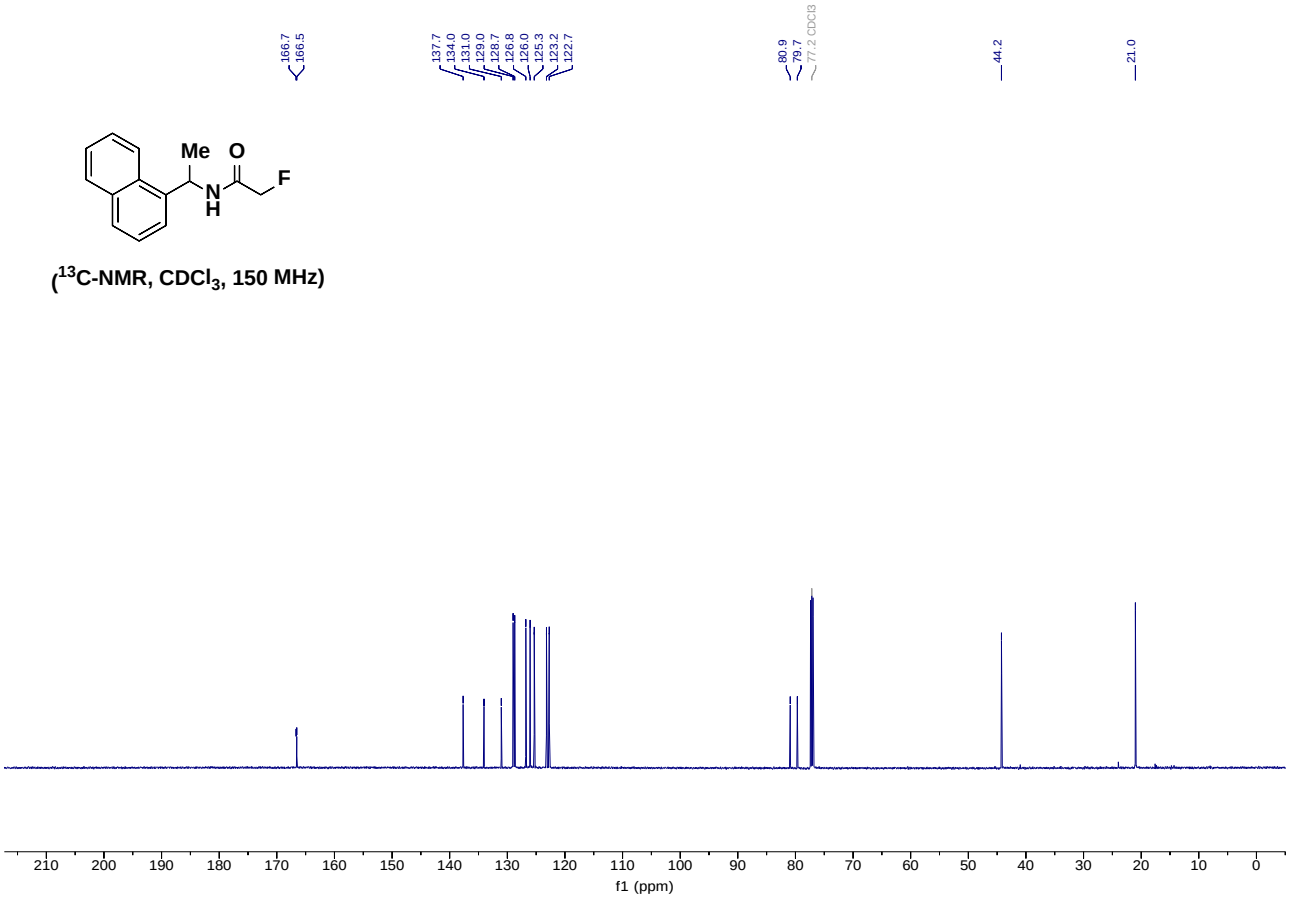




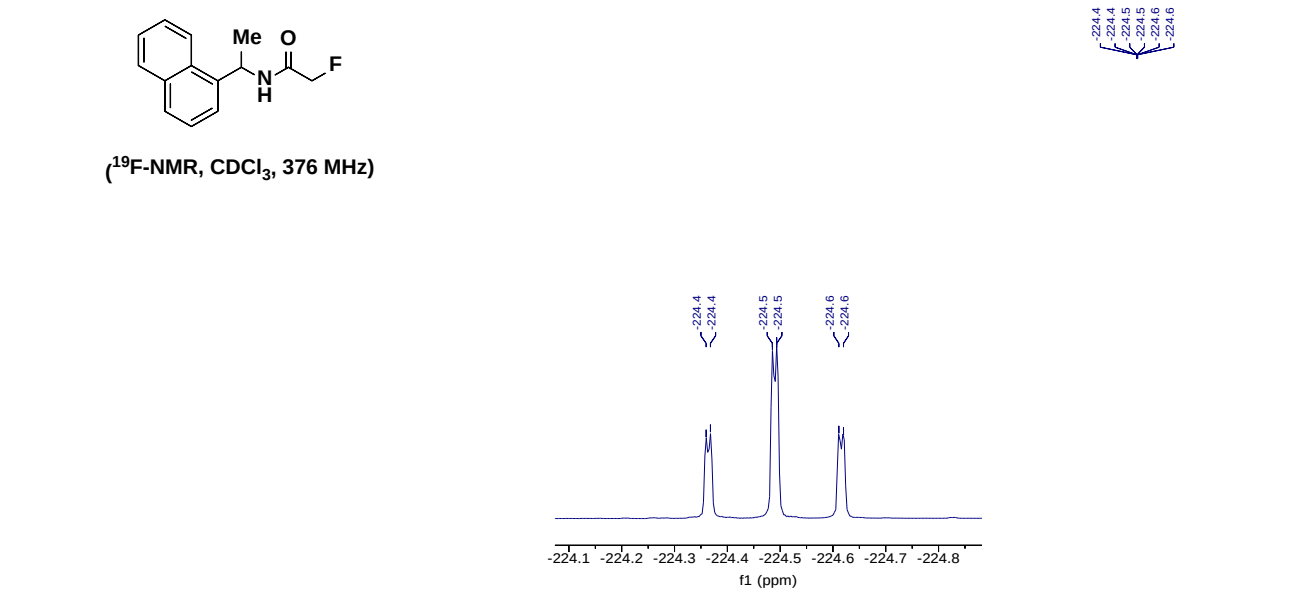
(**^{1}H-NMR, $CDCl_3$, 600 MHz)**

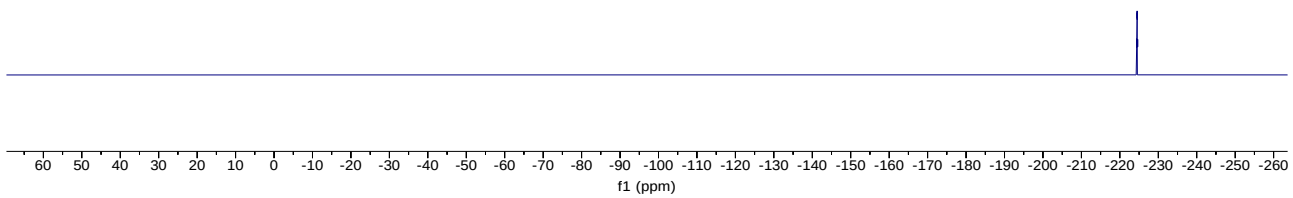


(^{13}C-NMR, $CDCl_3$, 150 MHz)



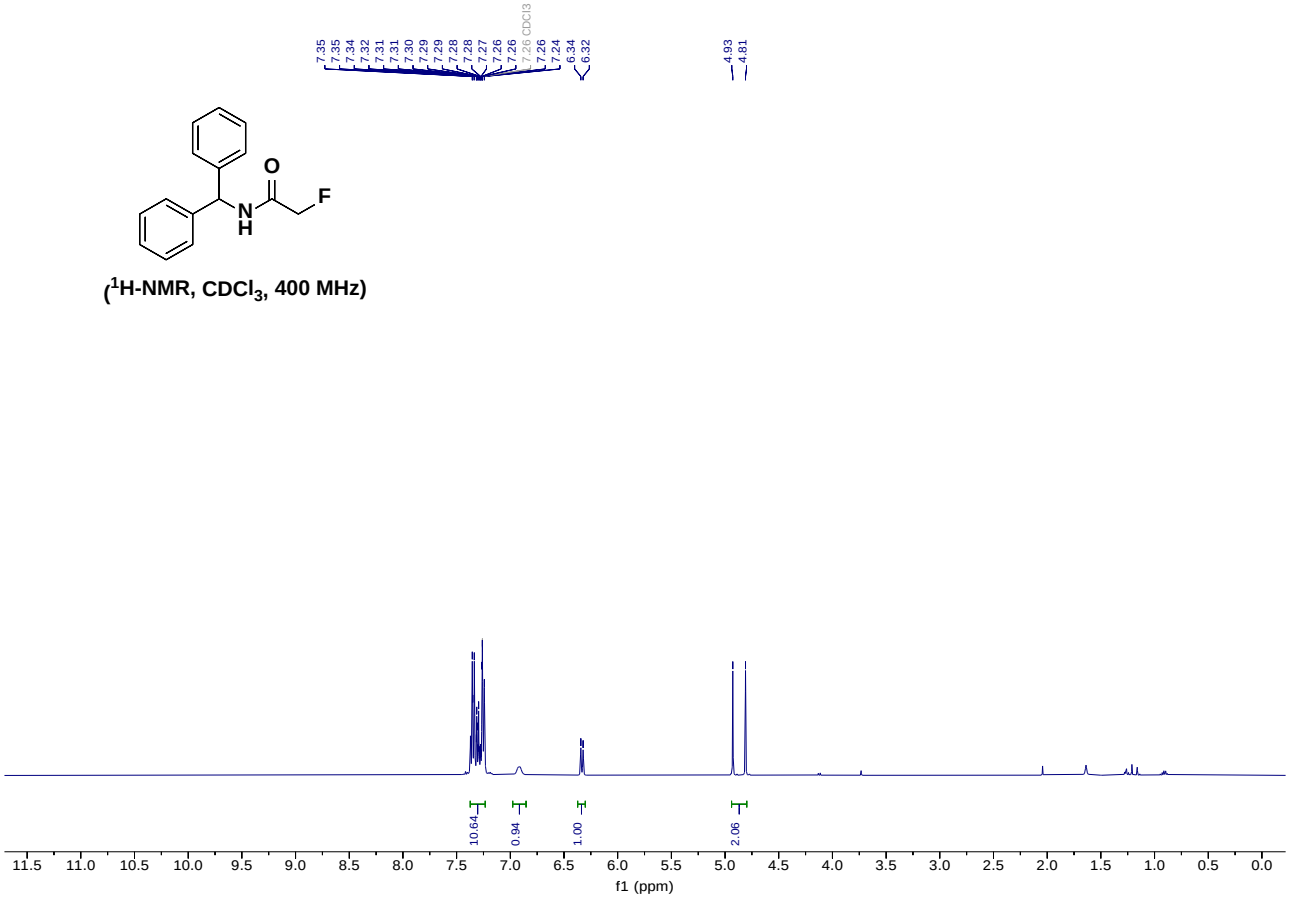
(^{19}F-NMR, $CDCl_3$, 376 MHz)



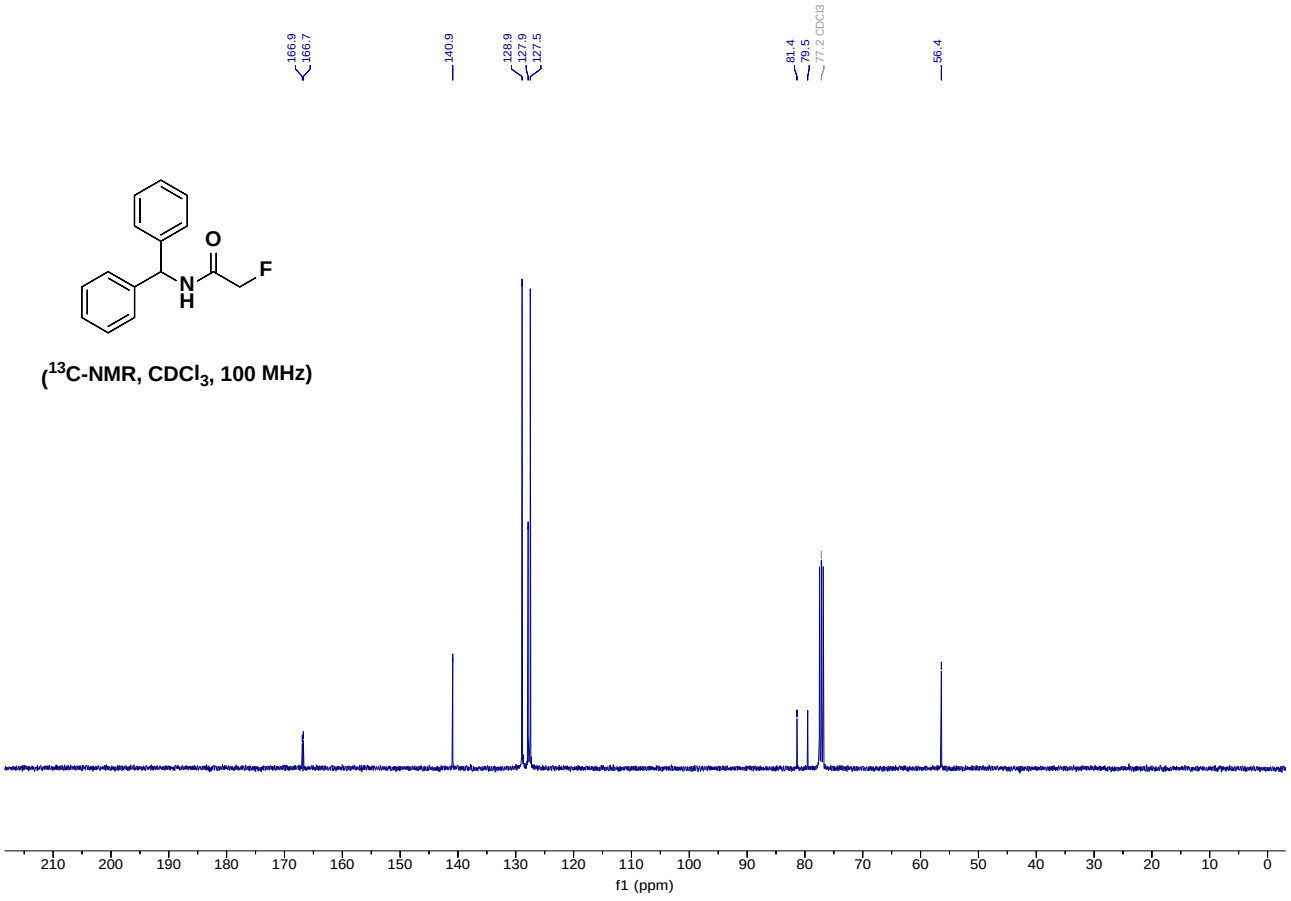


N-benzhydryl-2-fluoroacetamide (12)

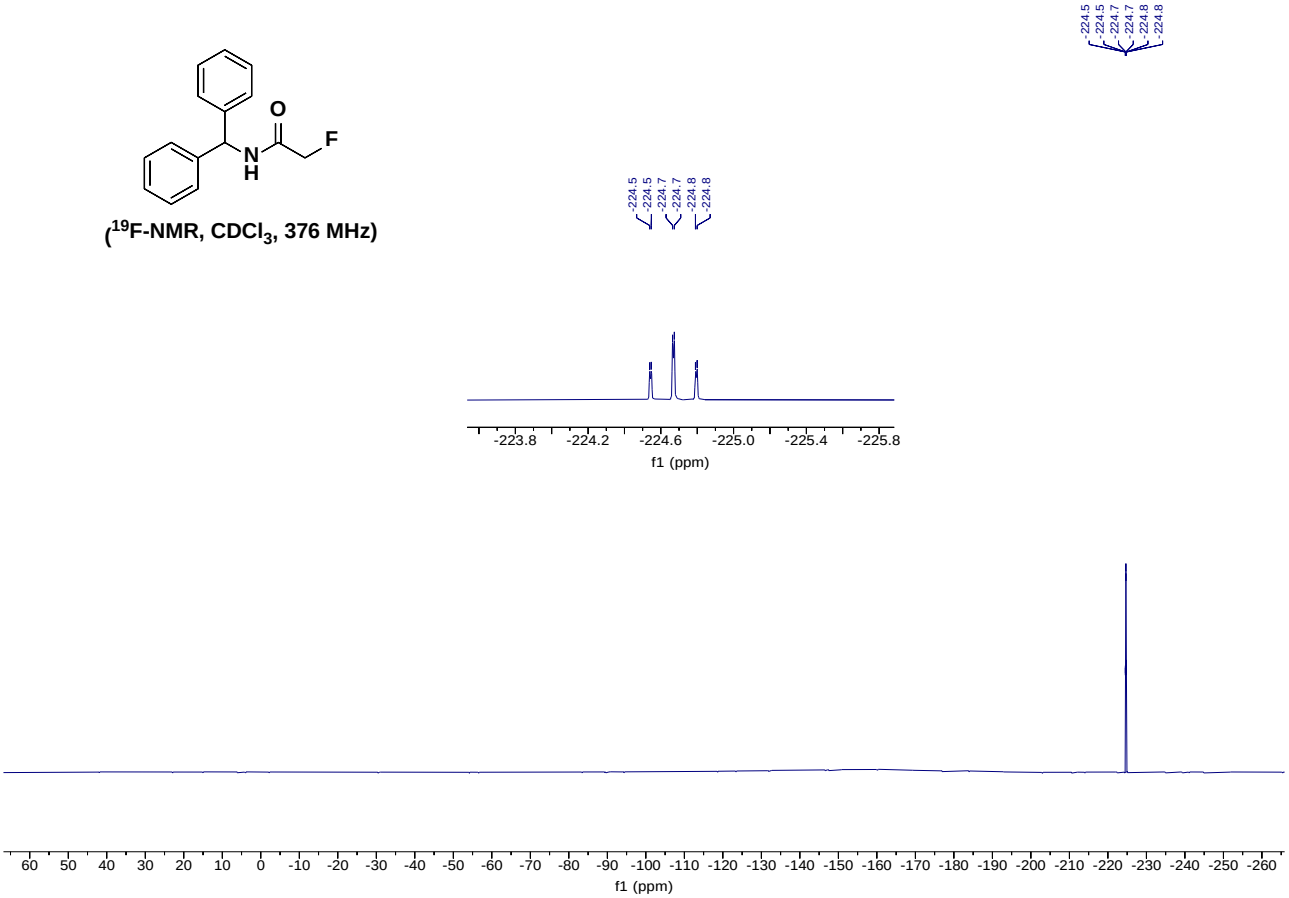
(^{1}H-NMR, $CDCl_3$, 400 MHz)



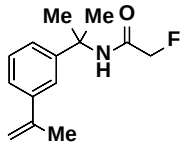
(^{13}C-NMR, $CDCl_3$, 100 MHz)



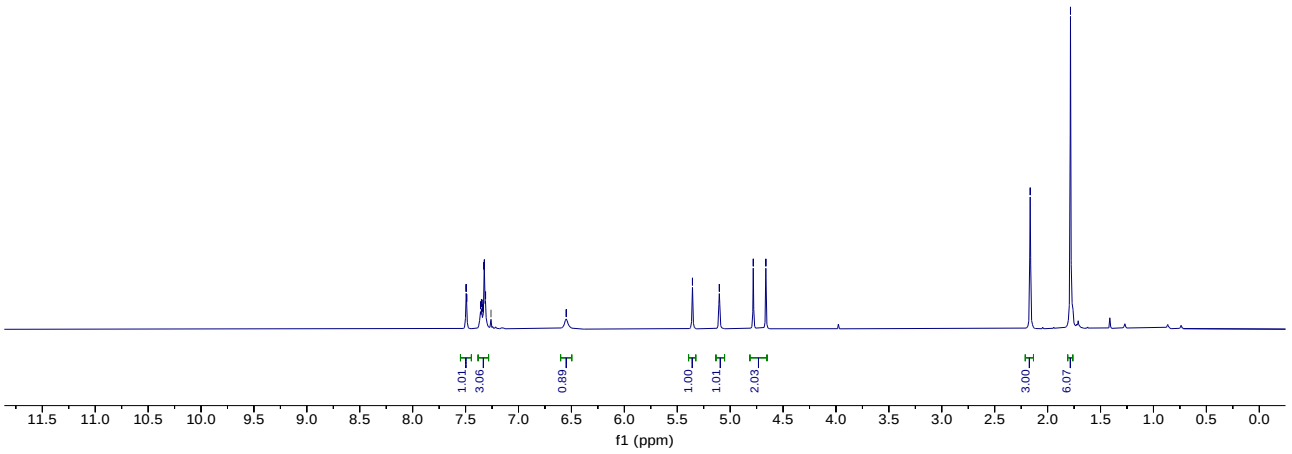
(¹⁹F-NMR, $CDCl_3$, 376 MHz)

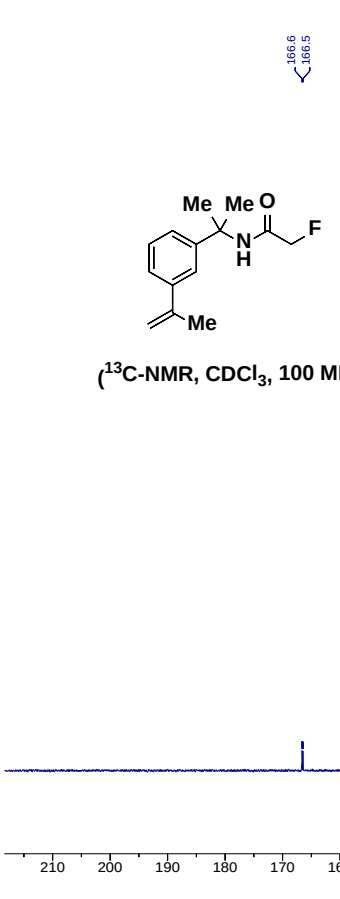


2-fluoro-*N*-(2-(3-(prop-1-en-2-yl)phenyl)propan-2-yl)acetamide (13)

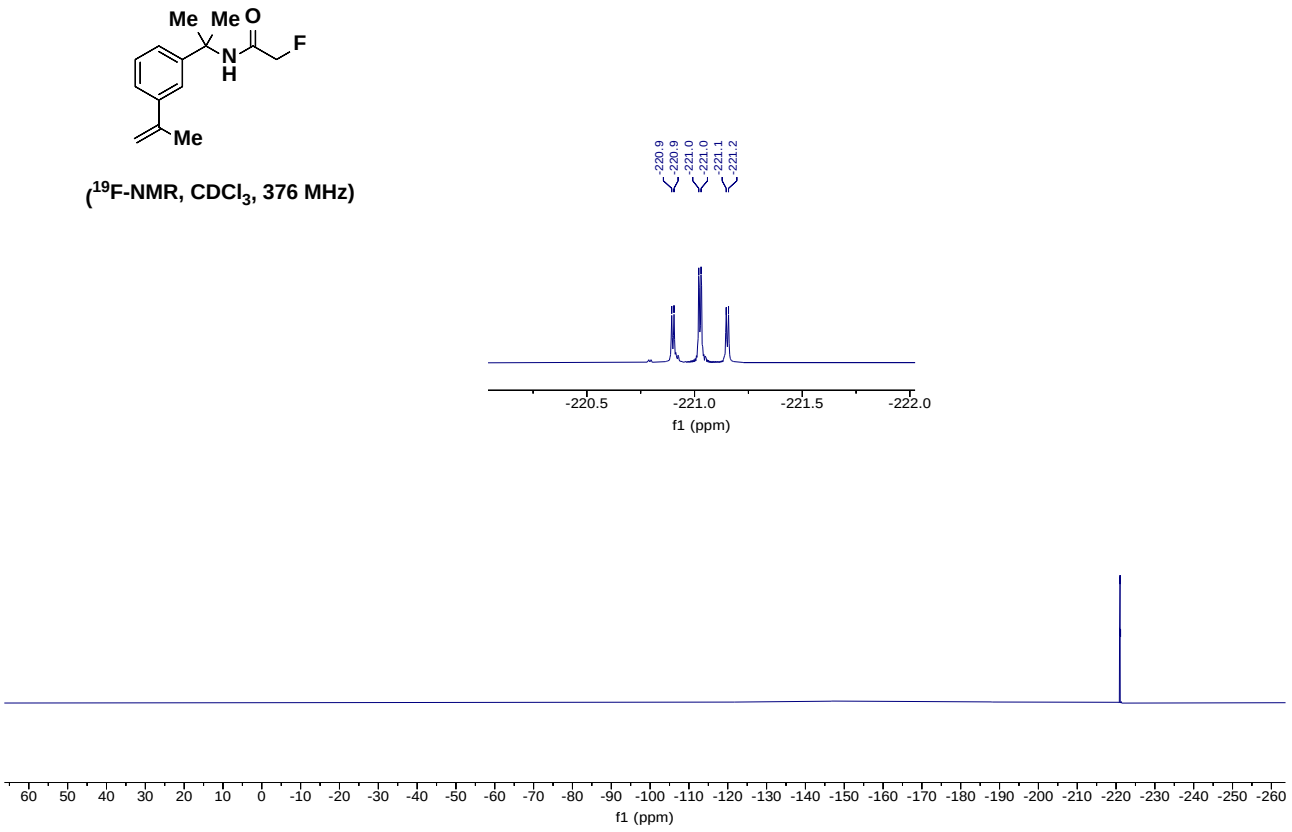


(¹H-NMR, $CDCl_3$, 400 MHz)



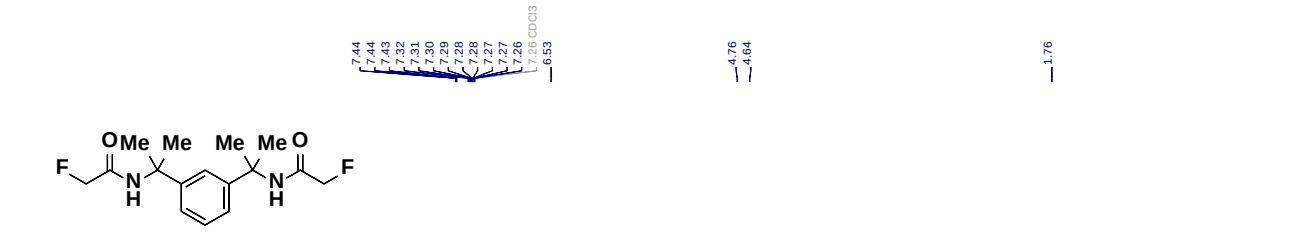


(^{13}C-NMR, $CDCl_3$, 100 MHz)

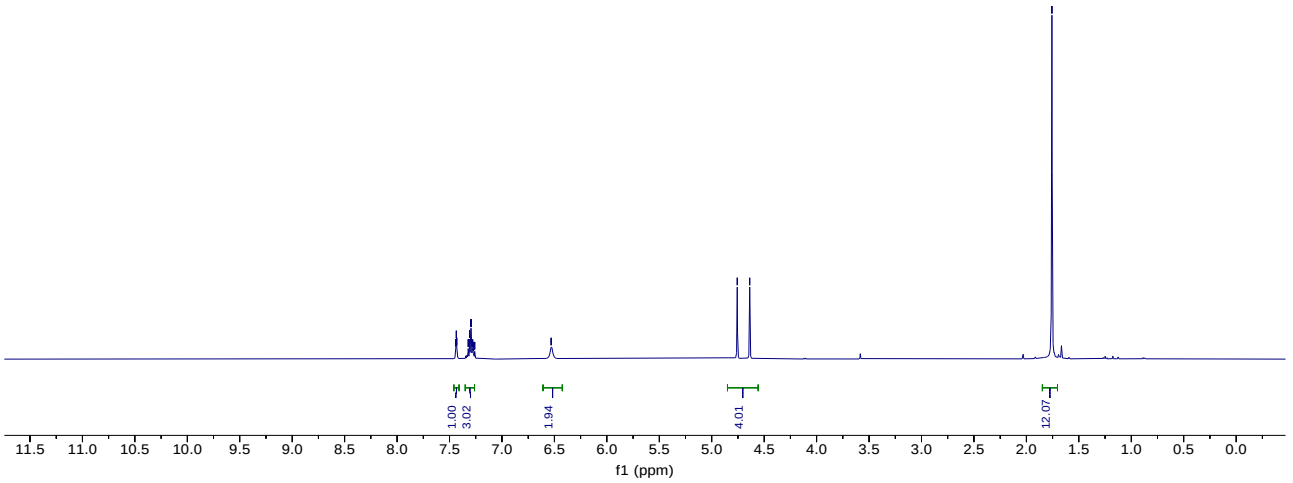


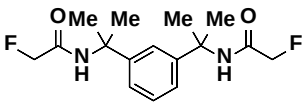
(^{19}F-NMR, $CDCl_3$, 376 MHz)

N,*N*'-(1,3-phenylenebis(propane-2,2-diyl))bis(2-fluoroacetamide) (14)

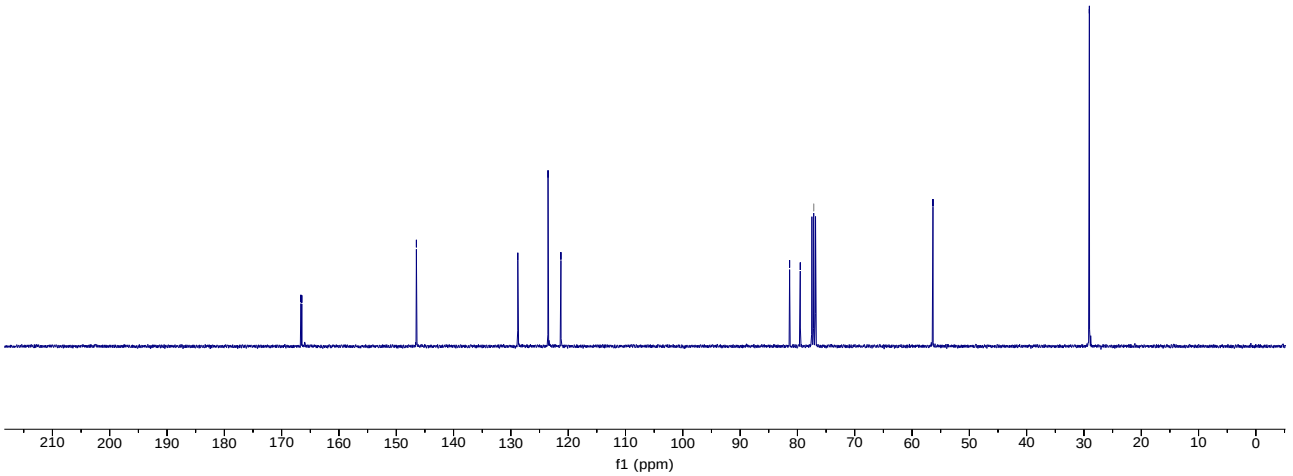


(¹H-NMR, $CDCl_3$, 400 MHz)

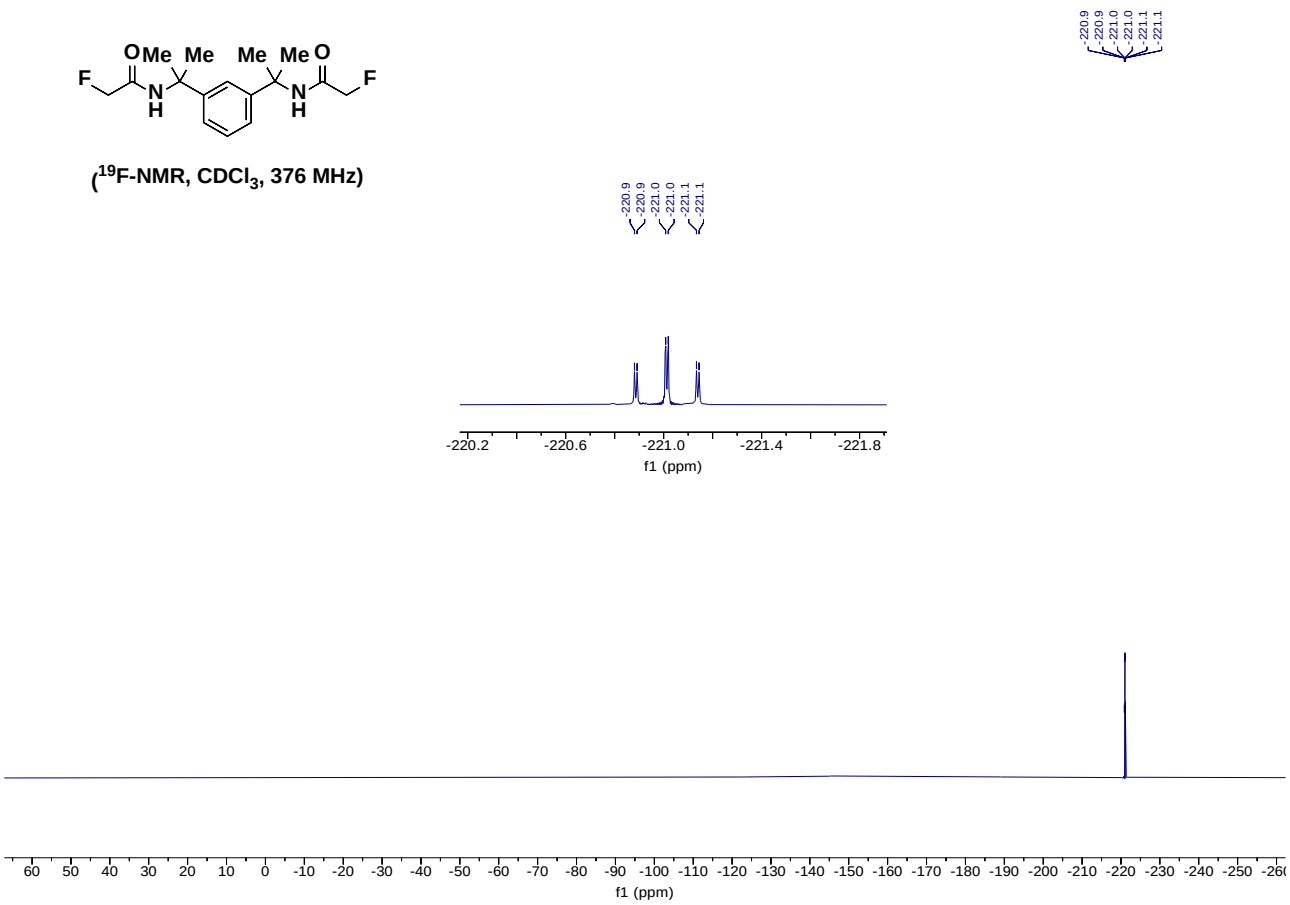




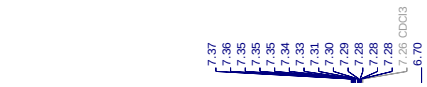
(¹³C-NMR, $CDCl_3$, 100 MHz)

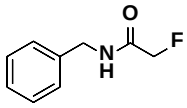


(¹⁹F-NMR, $CDCl_3$, 376 MHz)

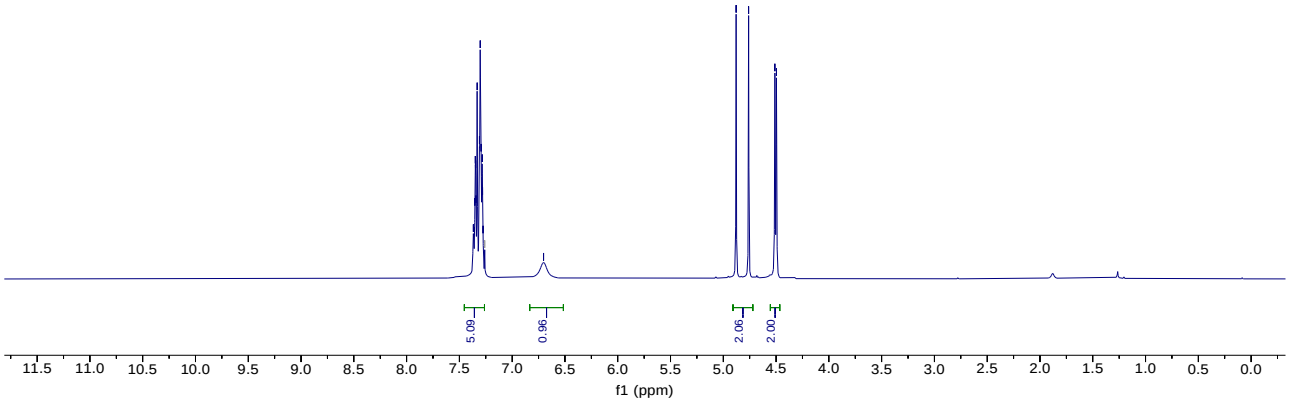


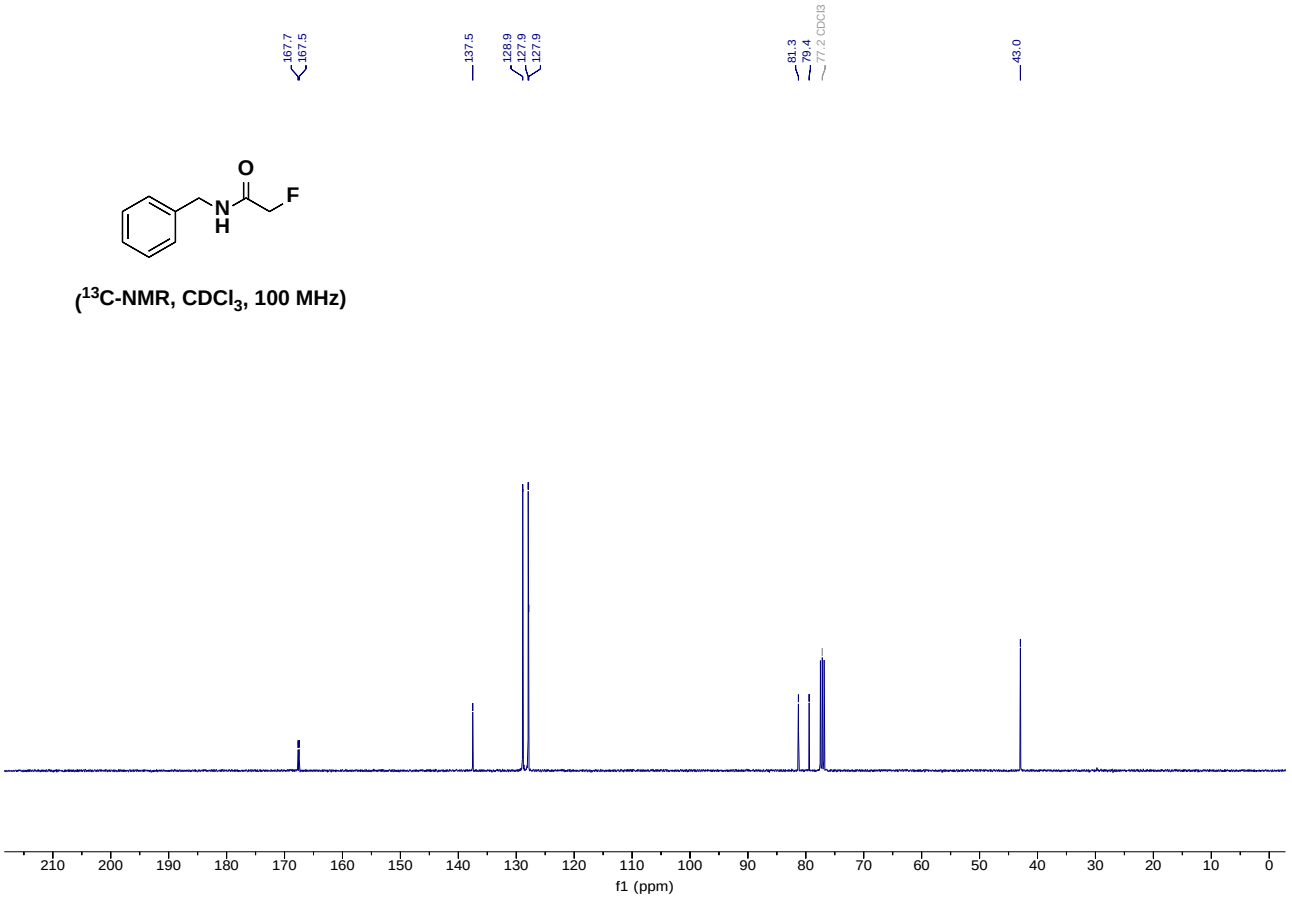
N-benzyl-2-fluoroacetamide (15)



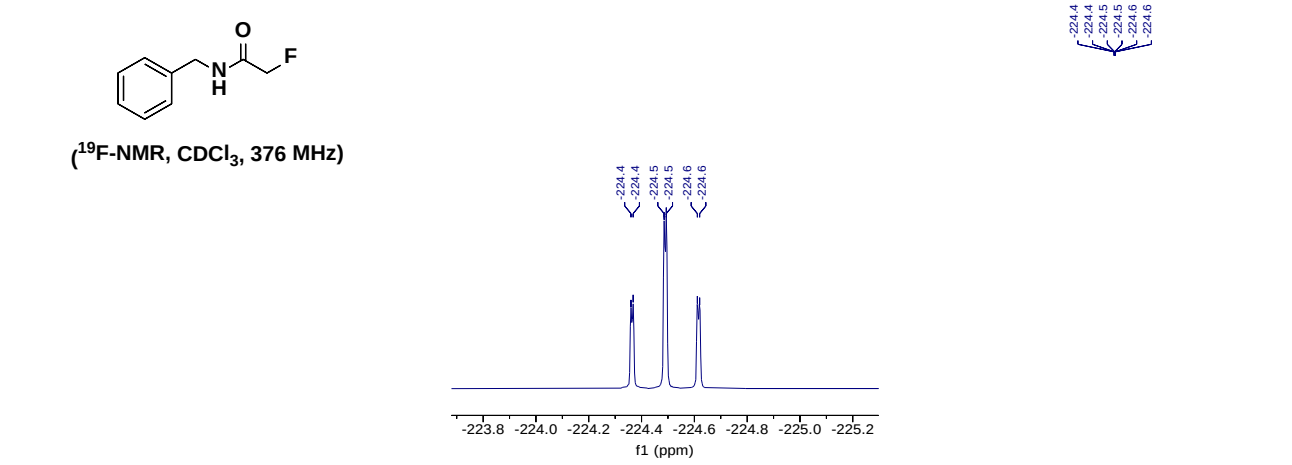


(¹H-NMR, $CDCl_3$, 400 MHz)

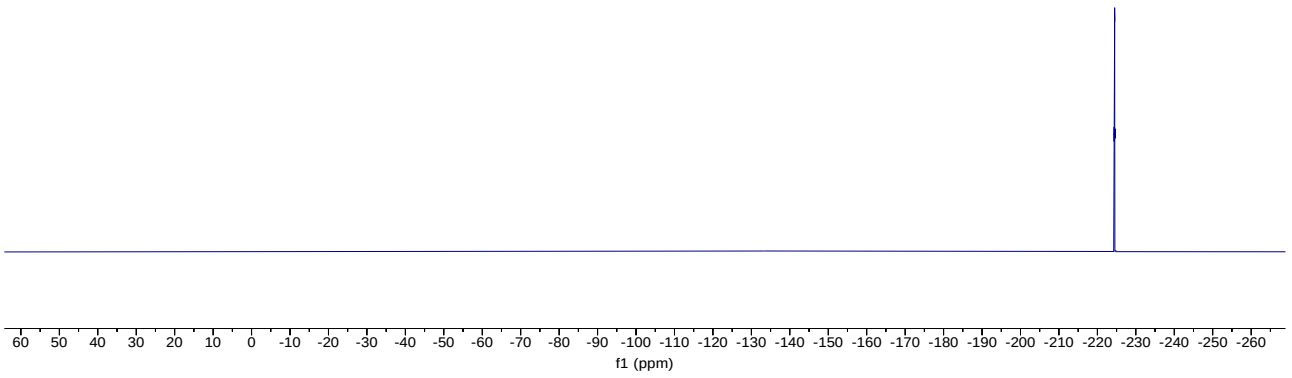




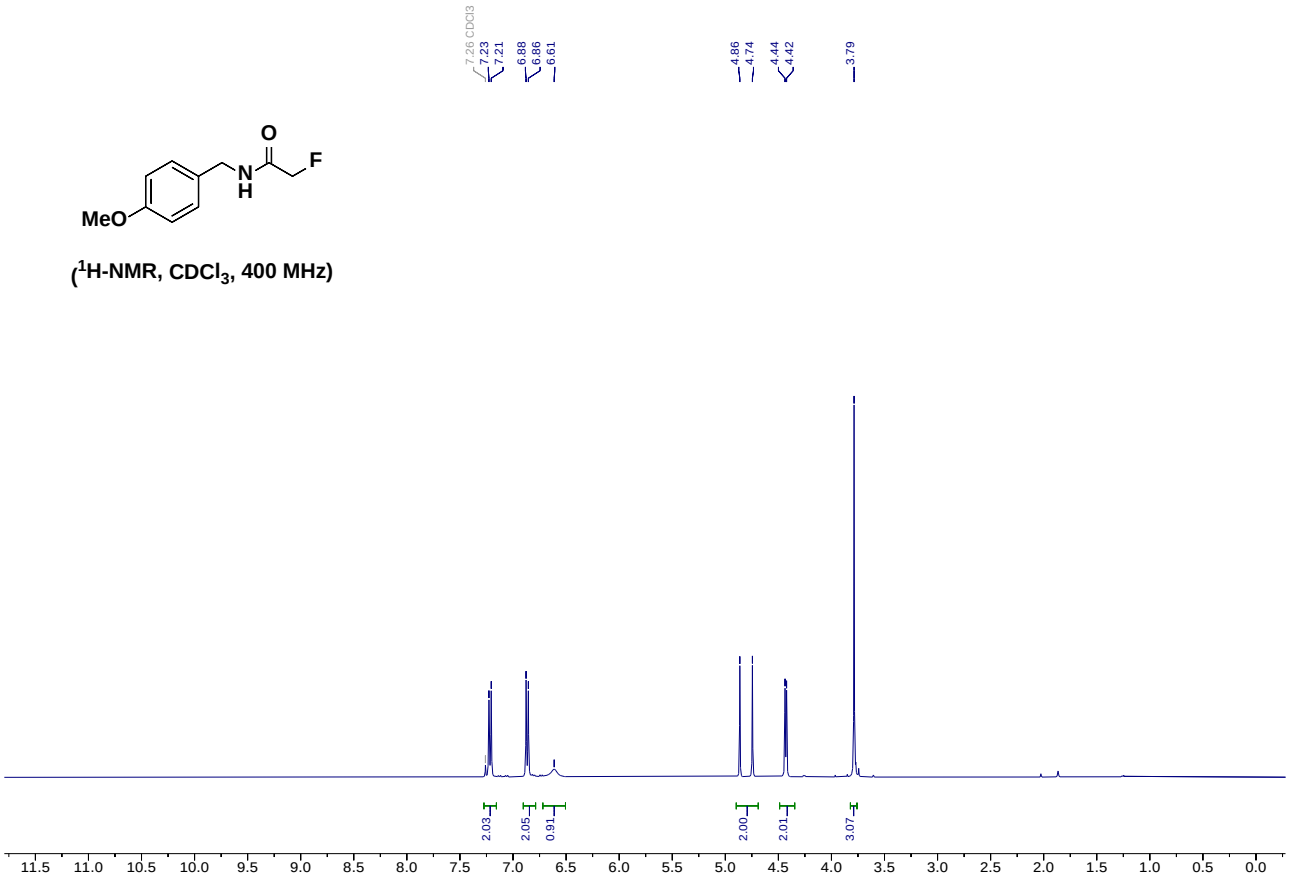
(^{13}C-NMR, $CDCl_3$, 100 MHz)



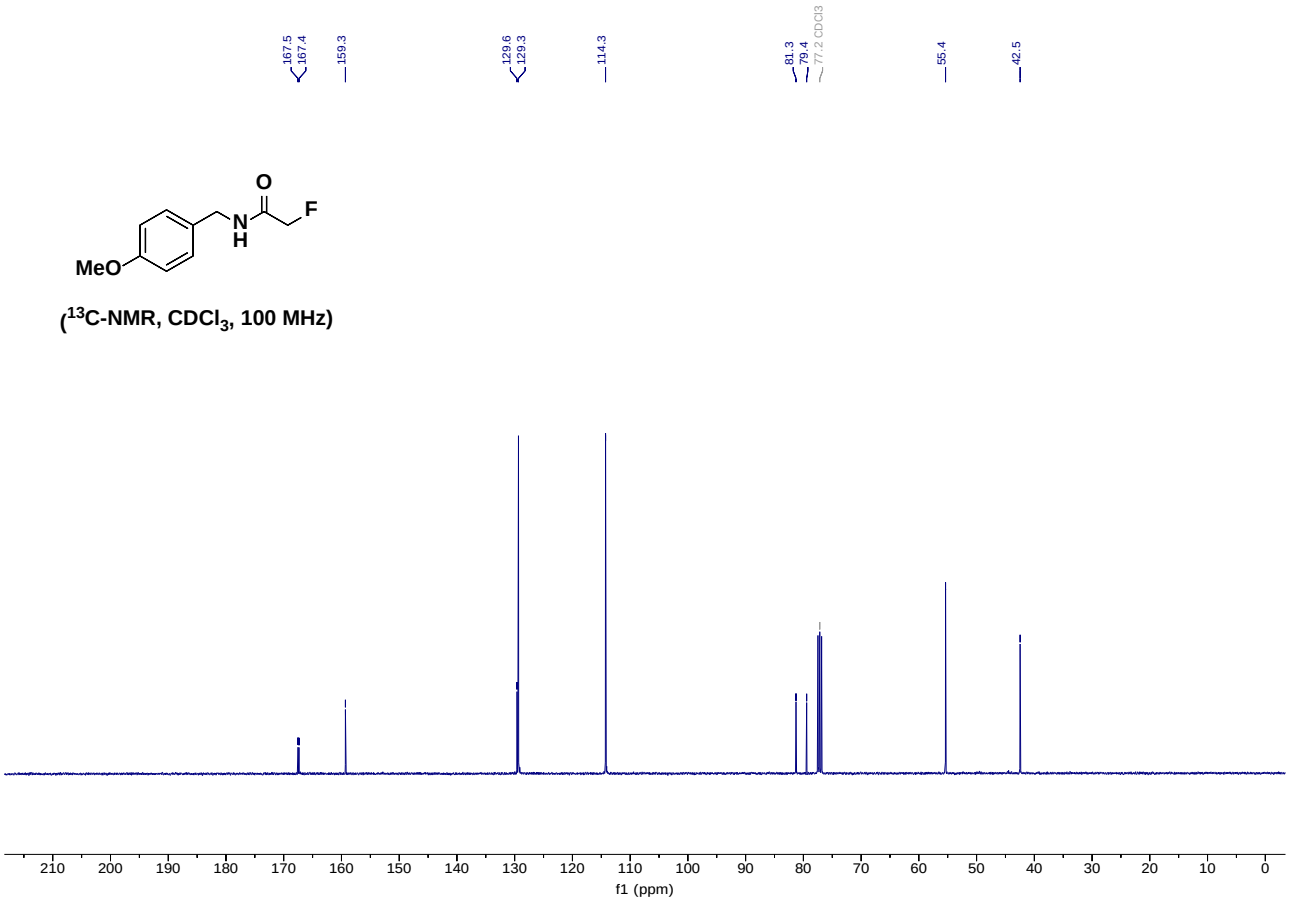
(^{19}F-NMR, $CDCl_3$, 376 MHz)



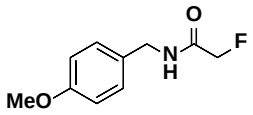
2-fluoro-*N*-(4-methoxybenzyl)acetamide (16)



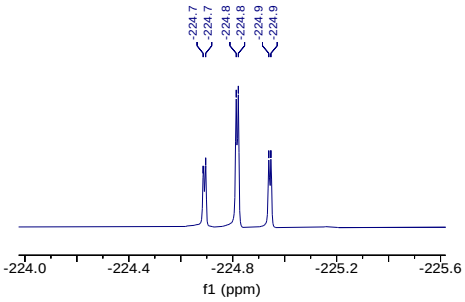
(¹H-NMR, $CDCl_3$, 400 MHz)

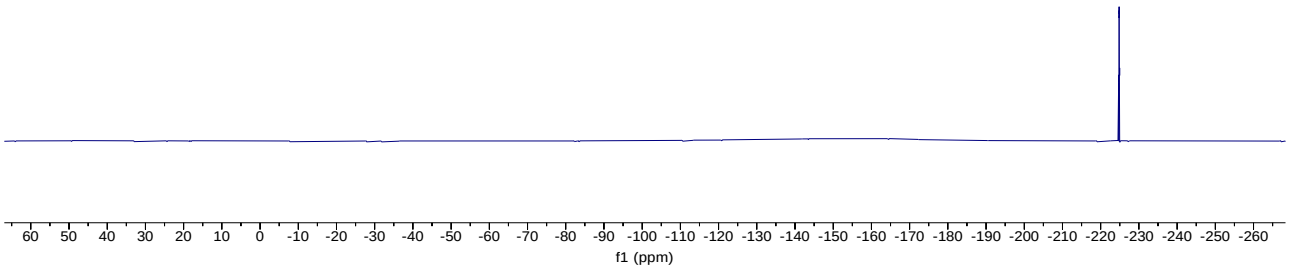


(¹³C-NMR, $CDCl_3$, 100 MHz)

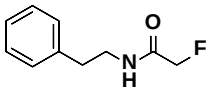


(¹⁹F-NMR, $CDCl_3$, 376 MHz)

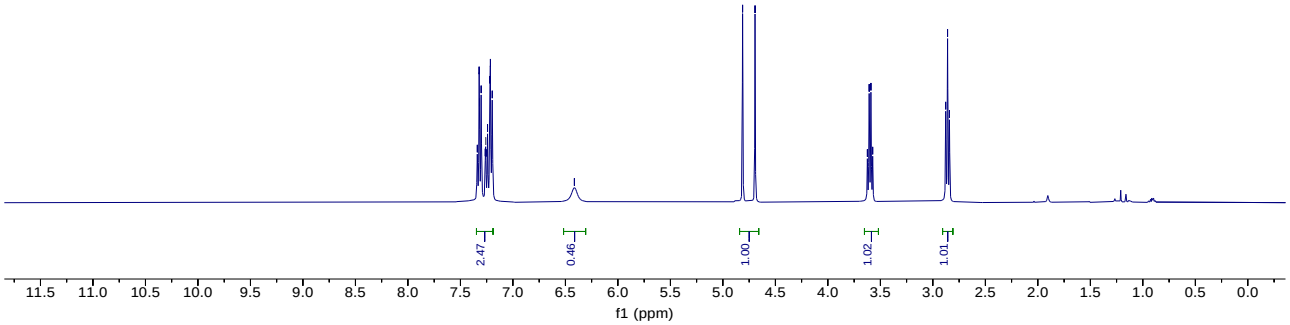


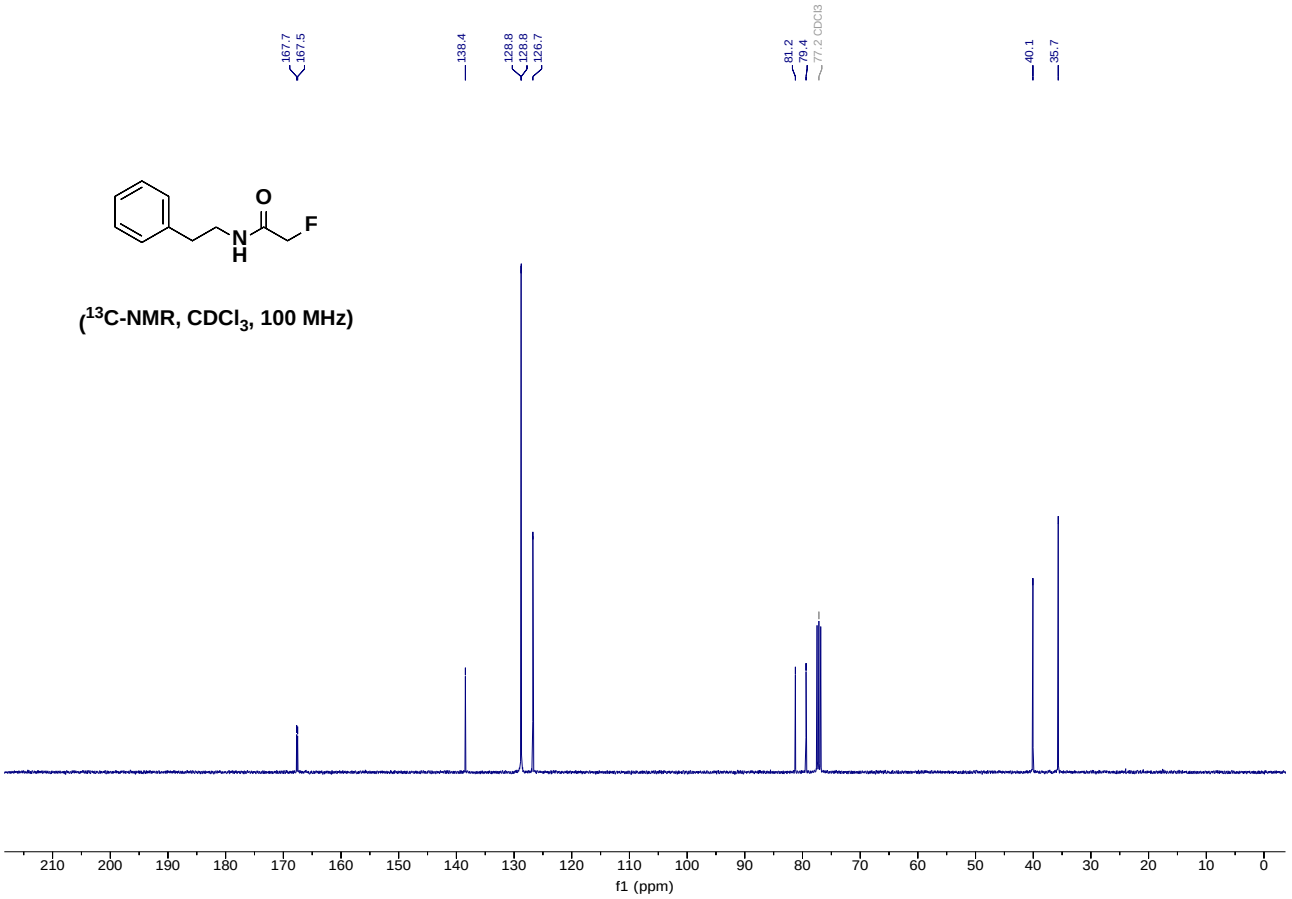


2-fluoro-*N*-phenethylacetamide (17)

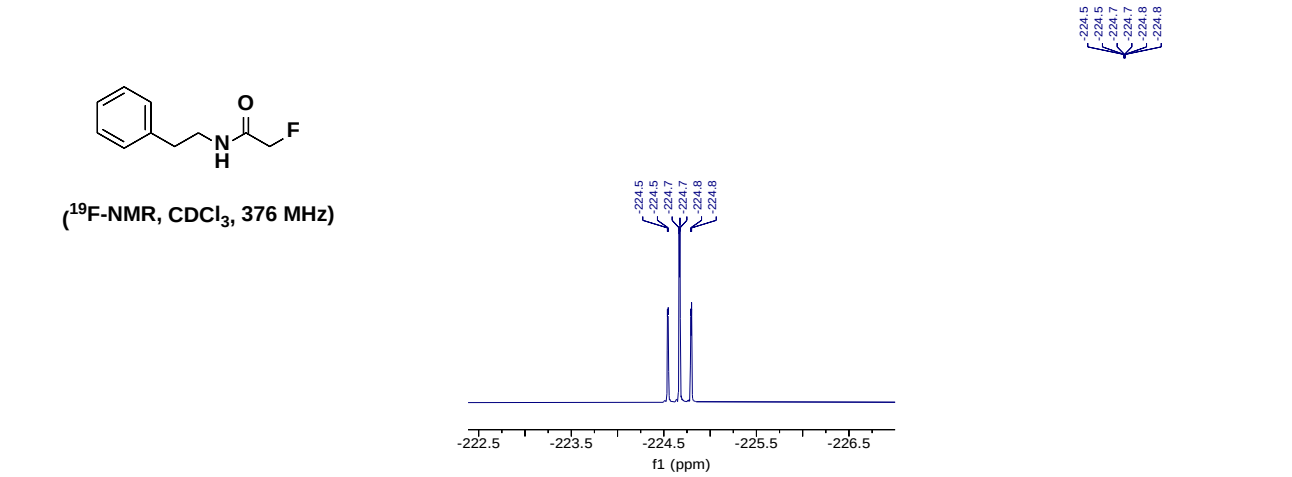


(¹H-NMR, $CDCl_3$, 400 MHz)

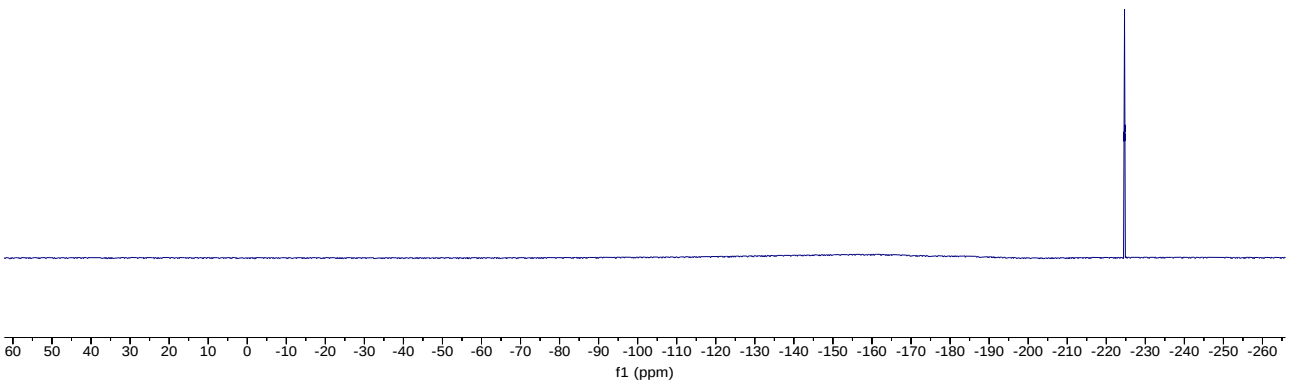




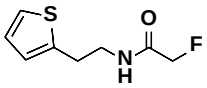
(^{13}C-NMR, $CDCl_3$, 100 MHz)



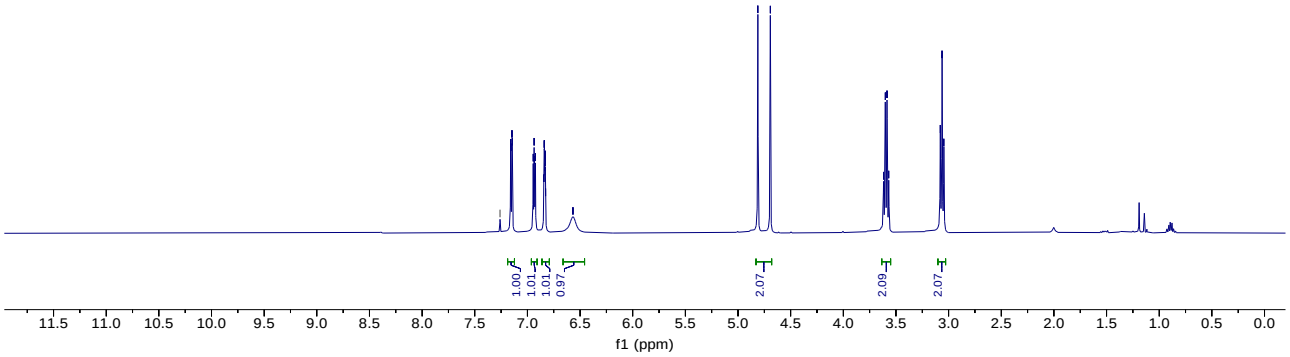
(^{19}F-NMR, $CDCl_3$, 376 MHz)

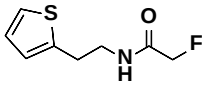


2-fluoro-*N*-(2-(thiophen-2-yl)ethyl)acetamide (18)

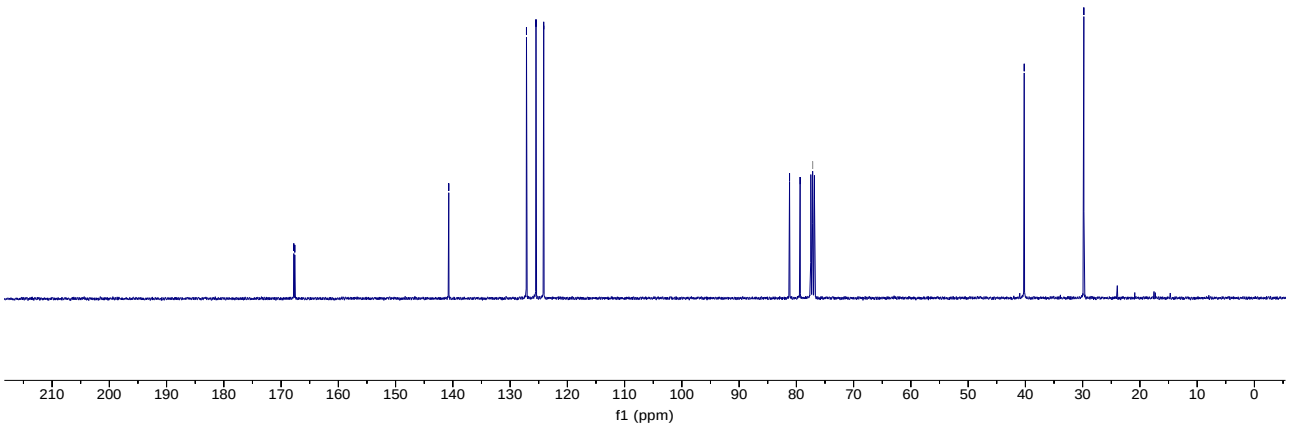


(^{1}H-NMR, $CDCl_3$, 400 MHz)

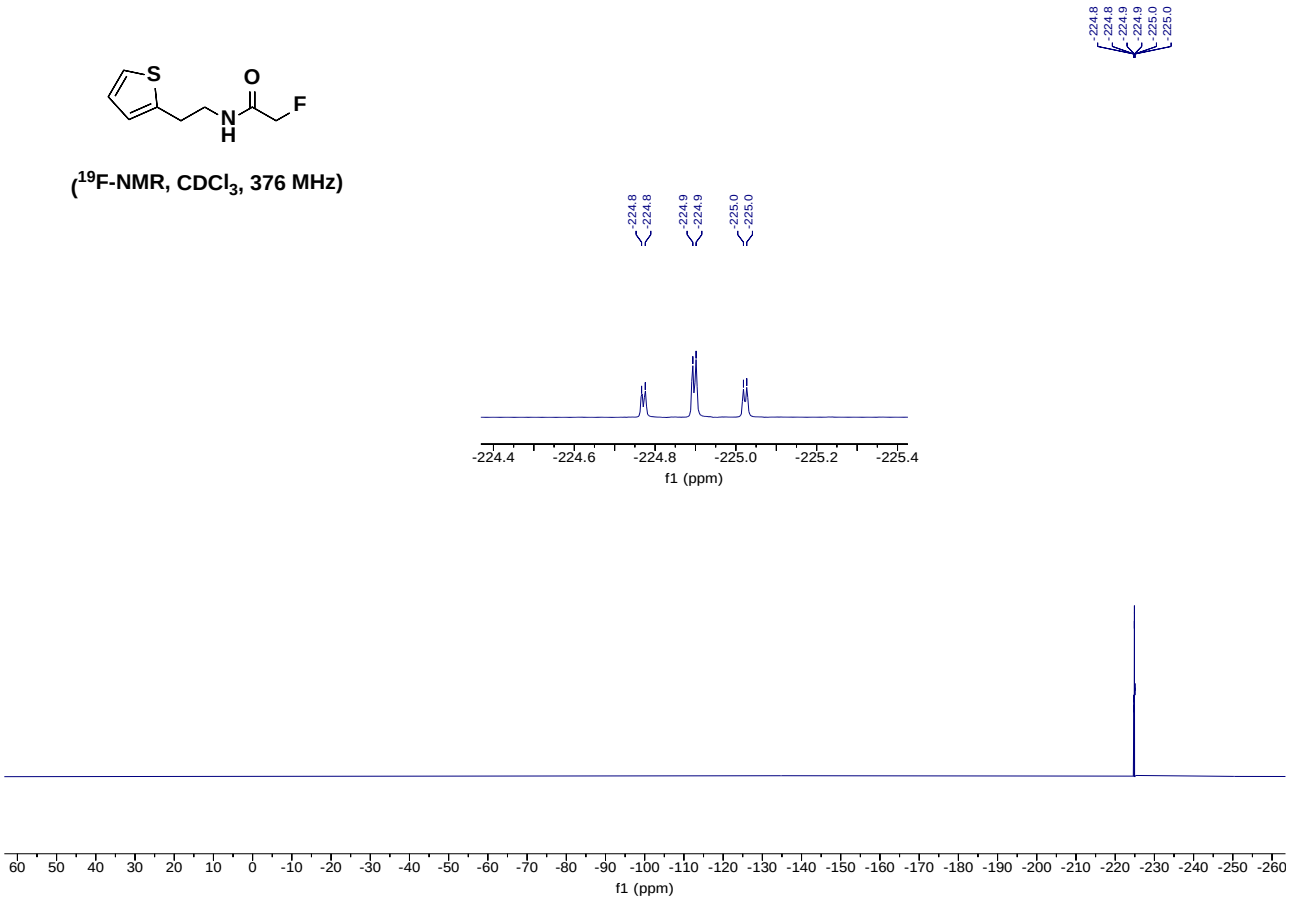




(^{13}C-NMR, $CDCl_3$, 100 MHz)

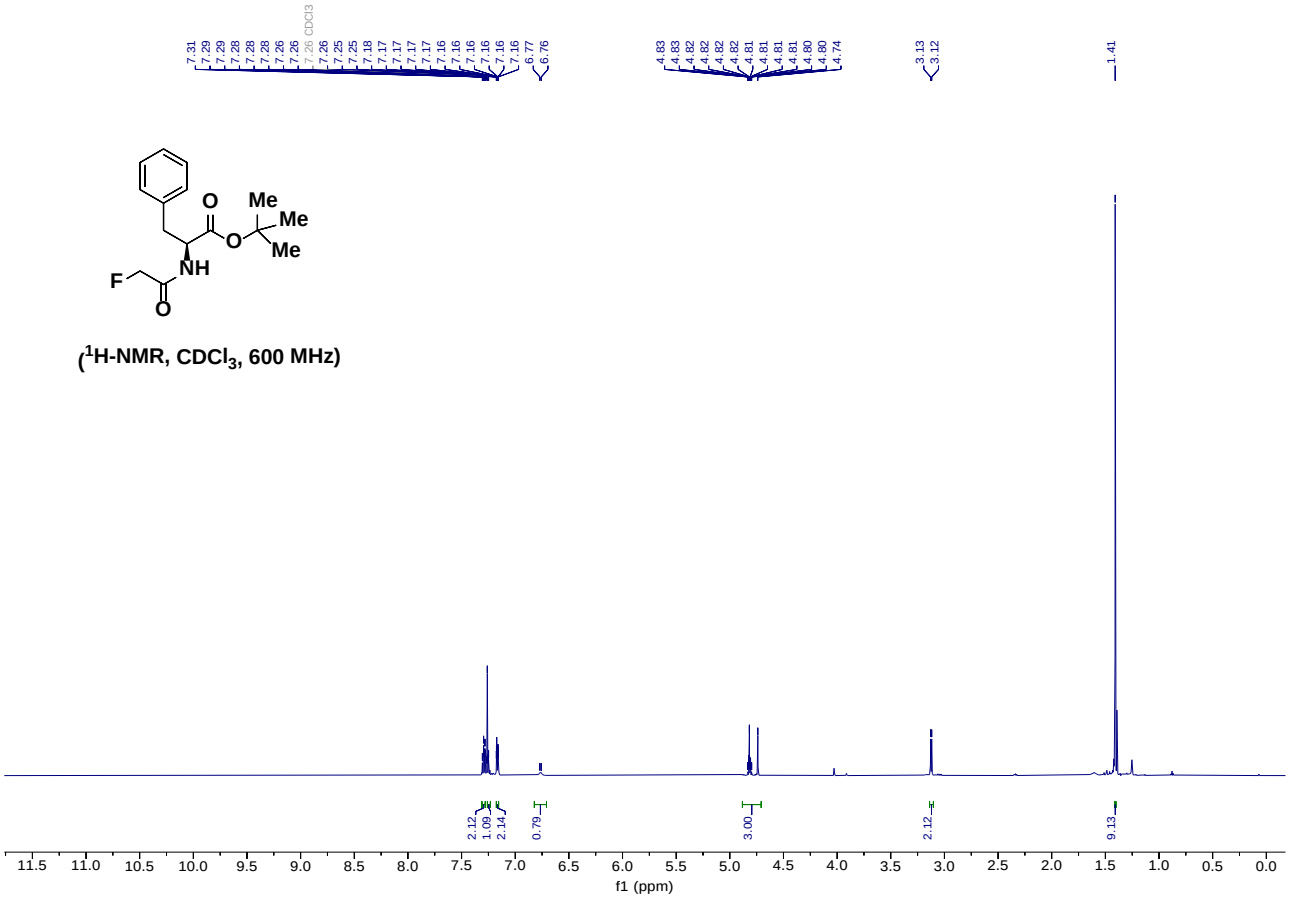


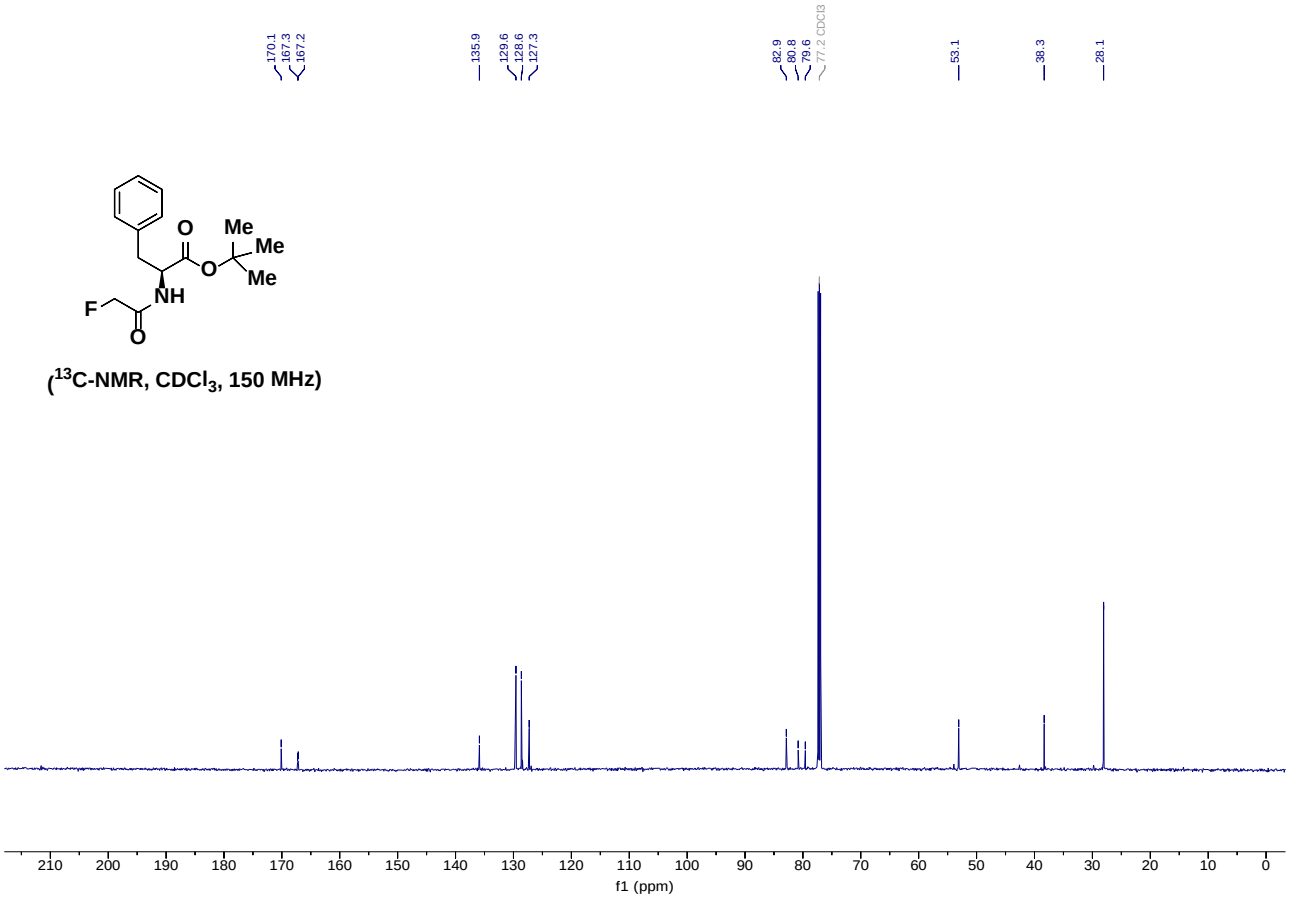
(¹⁹F-NMR, $CDCl_3$, 376 MHz)



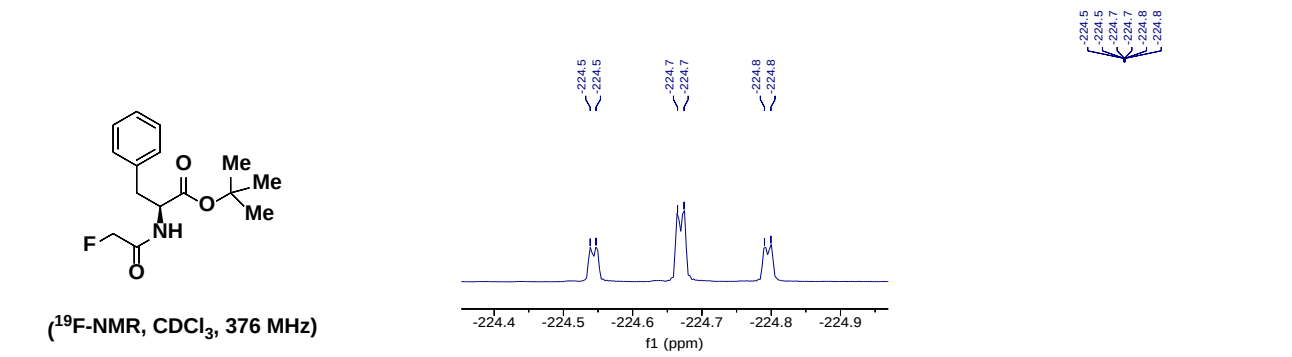
(2-fluoroacetyl)-L-phenylalanine *tert*-butyl ester (19)

(¹H-NMR, $CDCl_3$, 600 MHz)

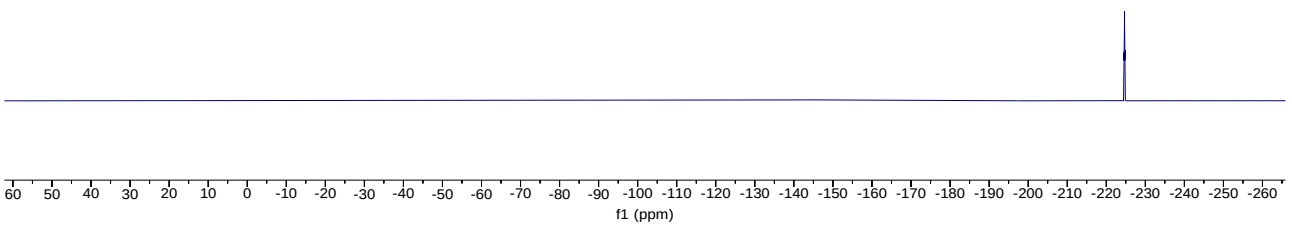




(^{13}C-NMR, $CDCl_3$, 150 MHz)

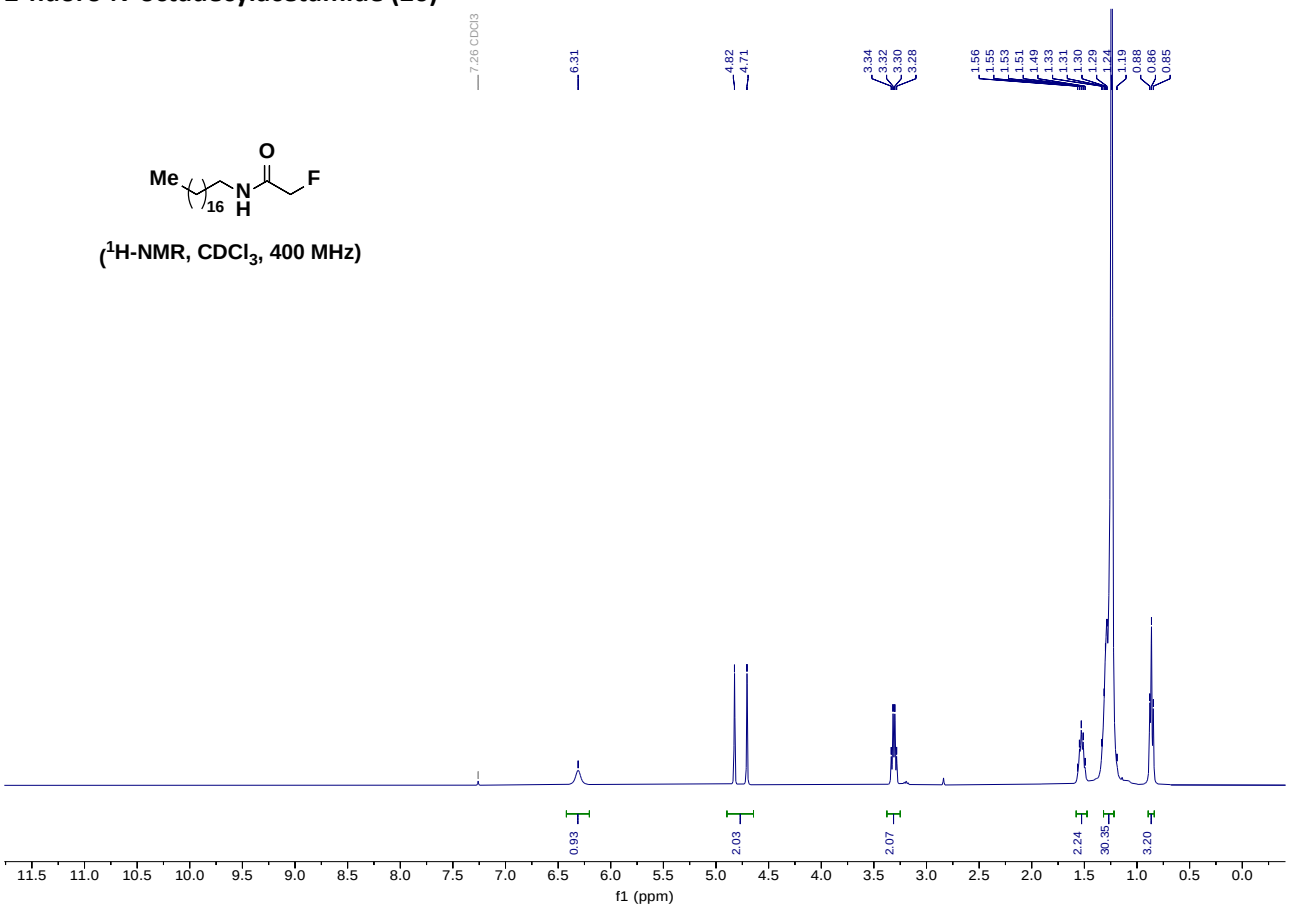


(^{19}F-NMR, $CDCl_3$, 376 MHz)

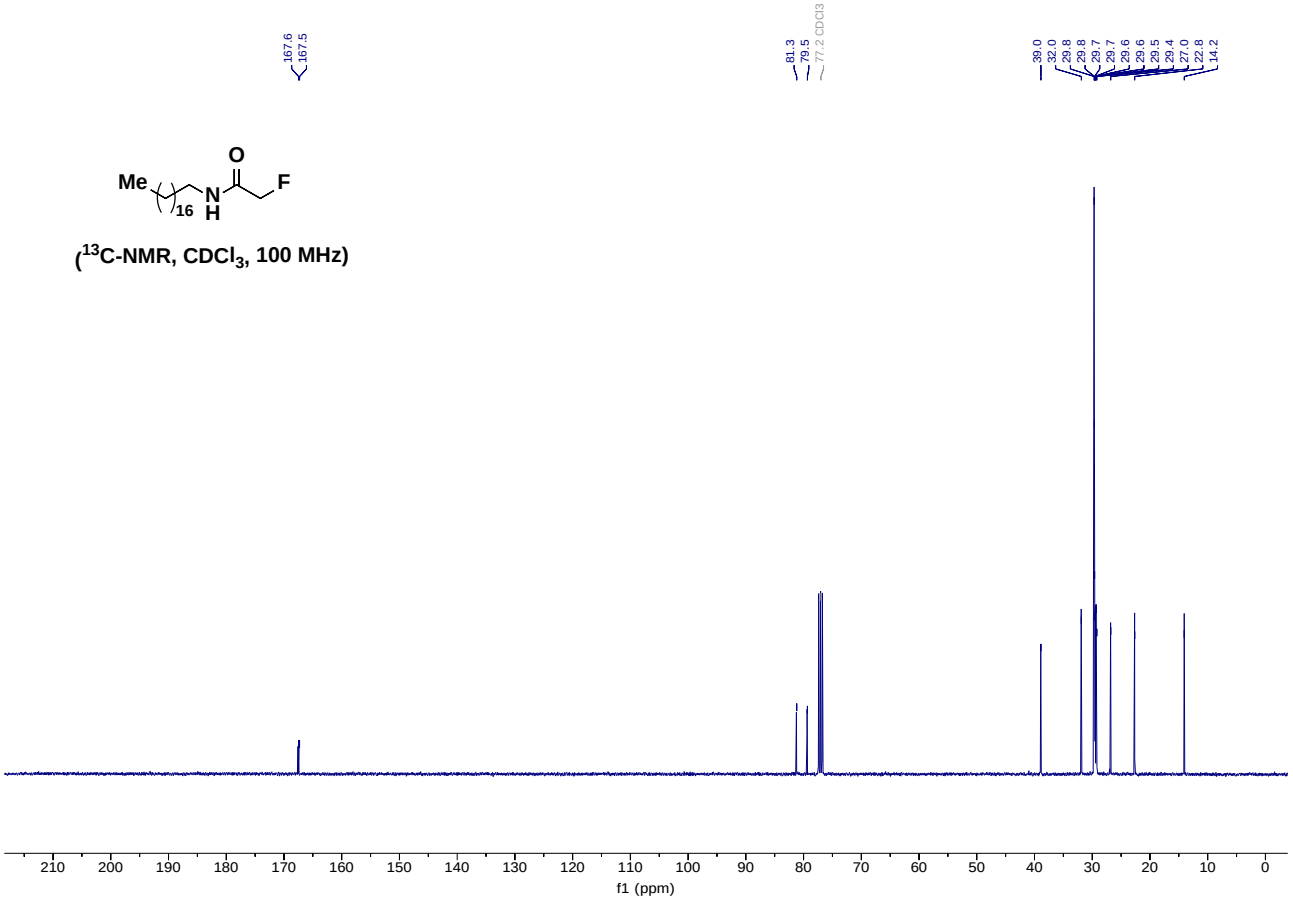


2-fluoro-*N*-octadecylacetamide (20)

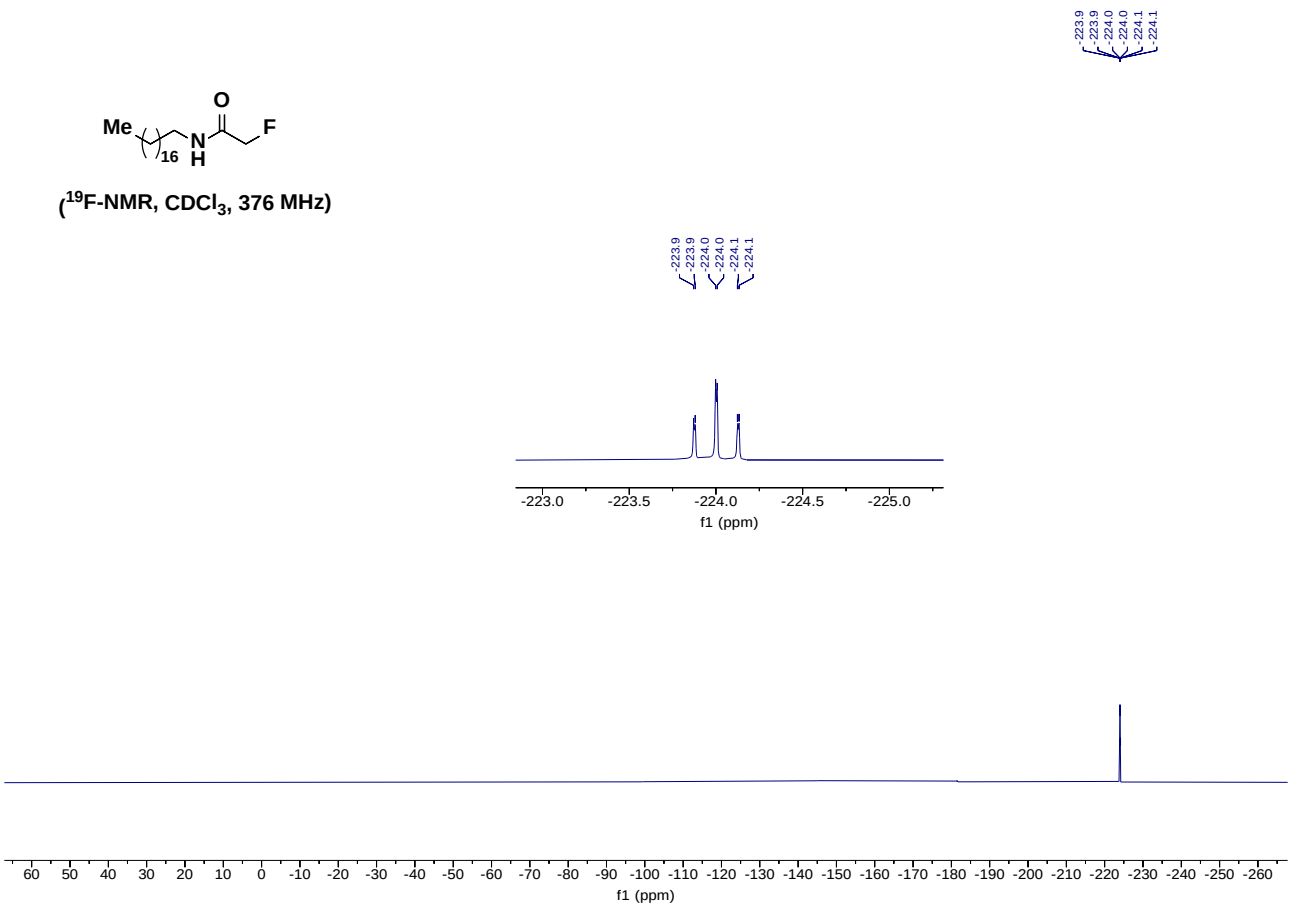
(^{1}H-NMR, $CDCl_3$, 400 MHz)



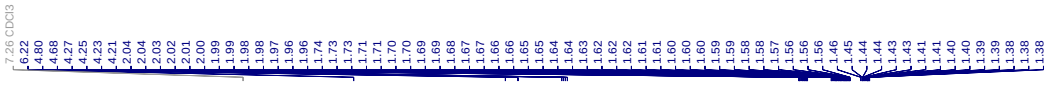
(^{13}C-NMR, $CDCl_3$, 100 MHz)

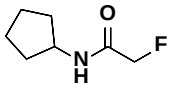


(**^{19}F-NMR, $CDCl_3$, 376 MHz**)

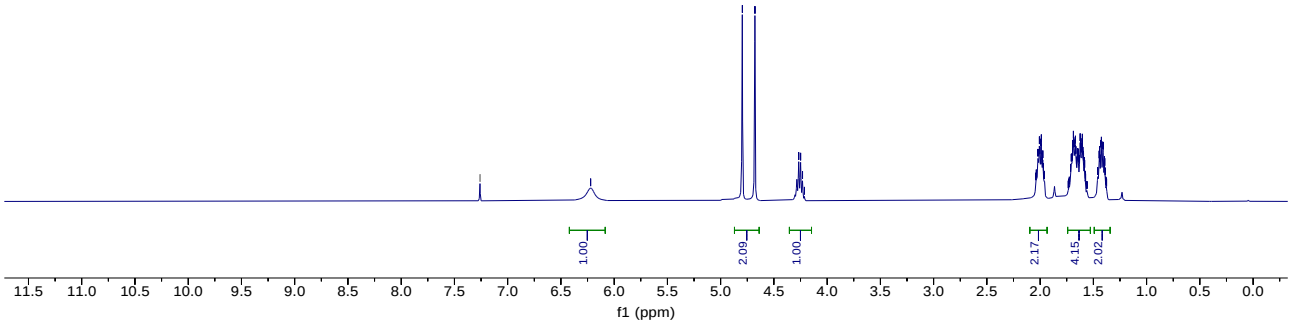


N-cyclopentyl-2-fluoroacetamide (21)

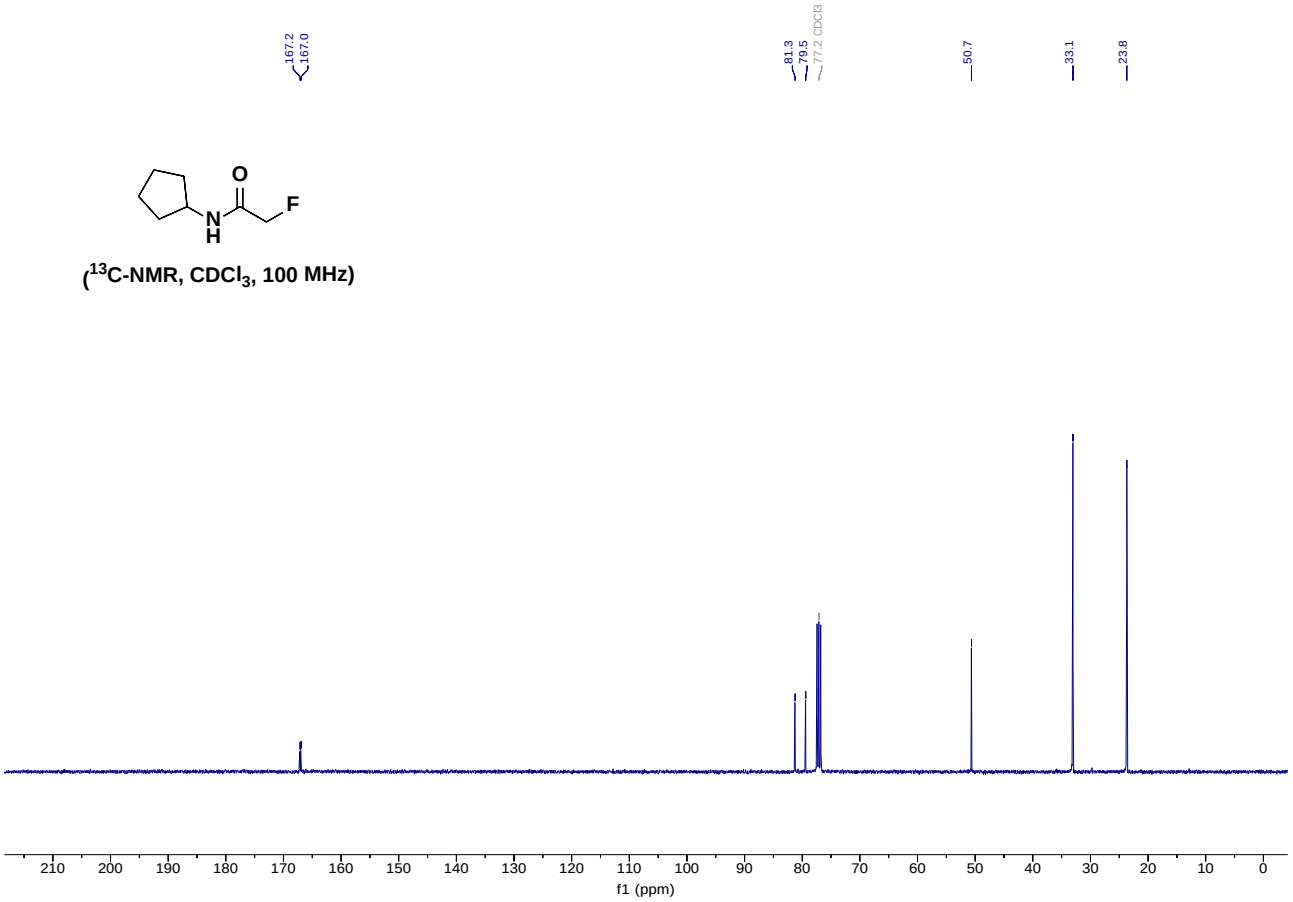




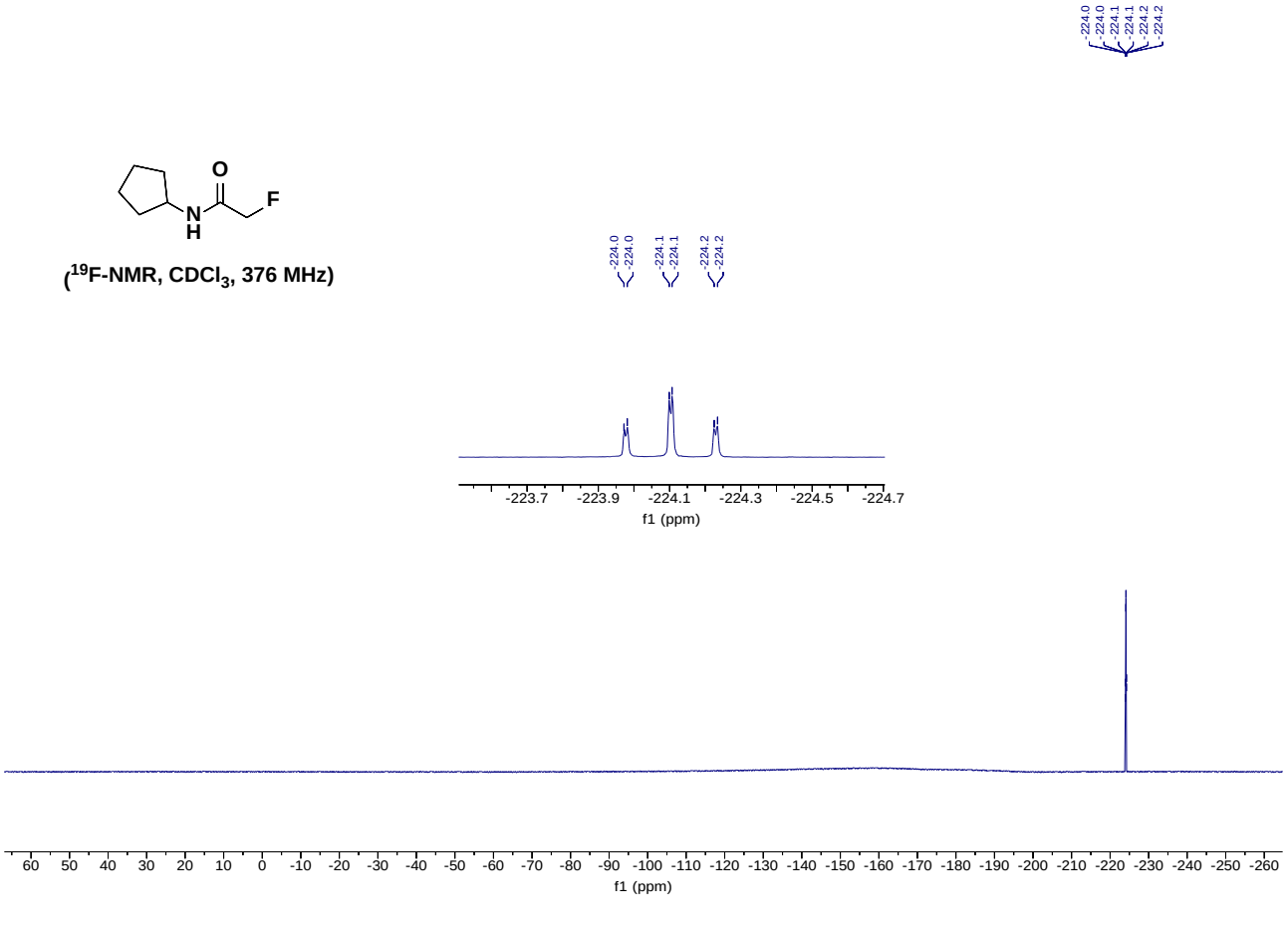
(**^{1}H-NMR, $CDCl_3$, 400 MHz**)



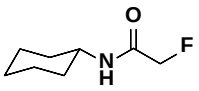
(^{13}C-NMR, $CDCl_3$, 100 MHz)



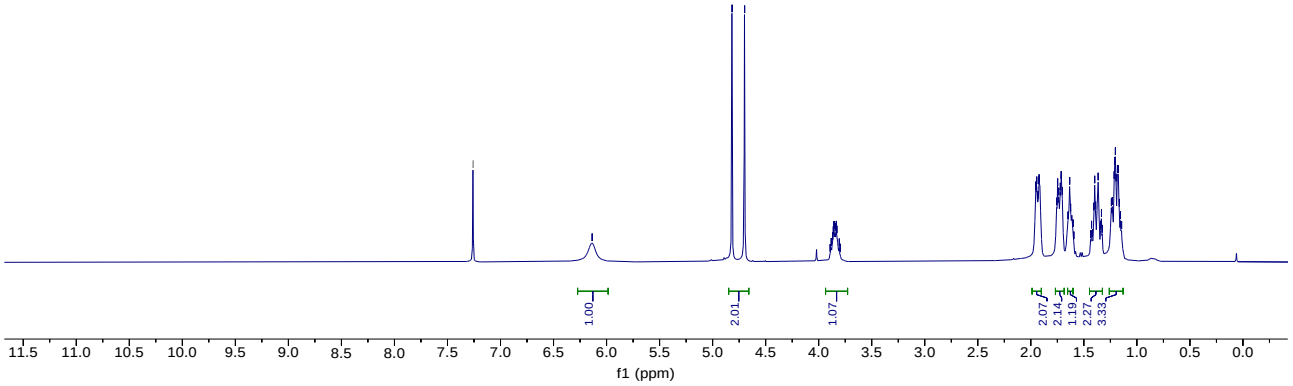
(^{19}F-NMR, $CDCl_3$, 376 MHz)

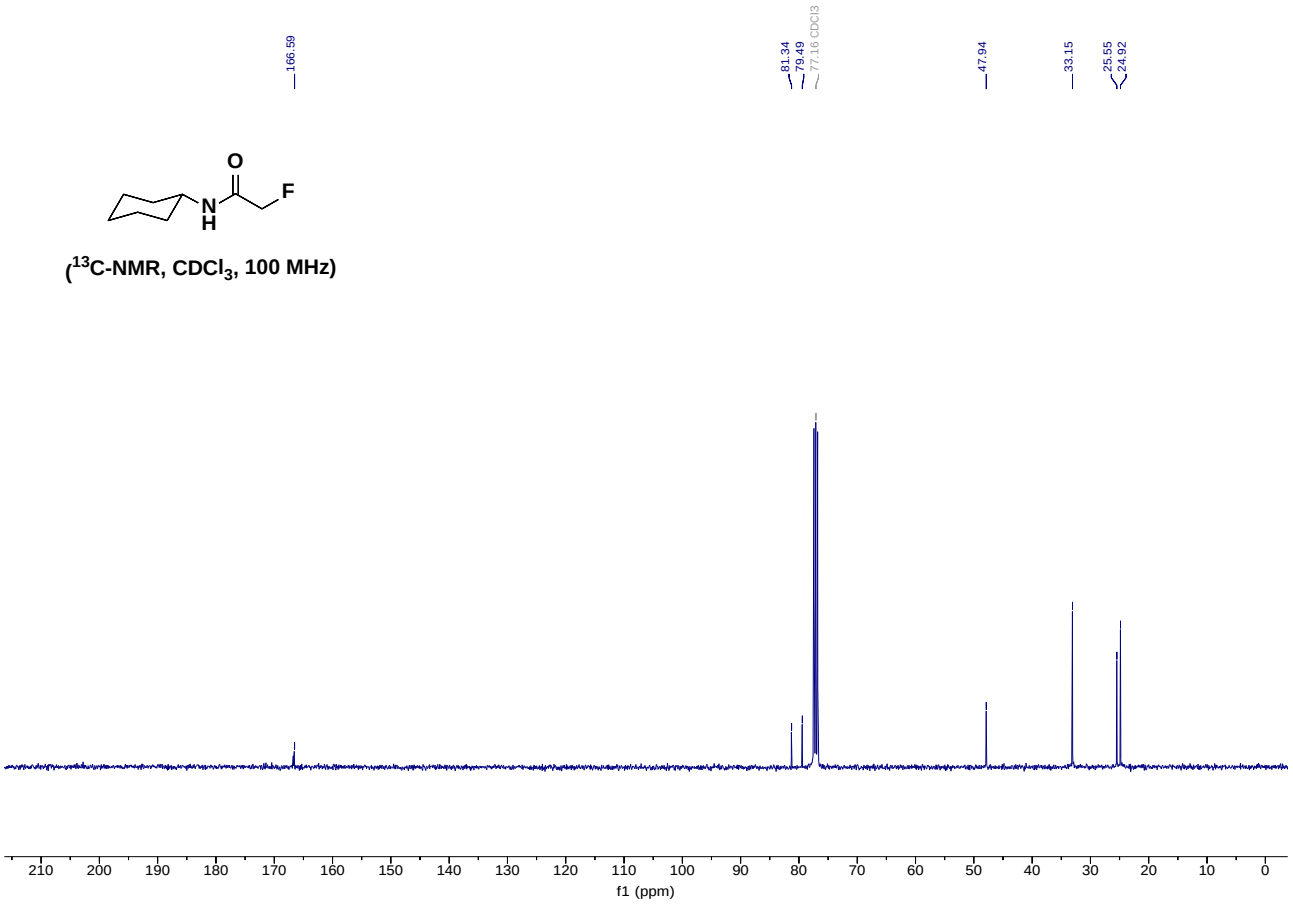


N-cyclohexyl-2-fluoroacetamide (22)

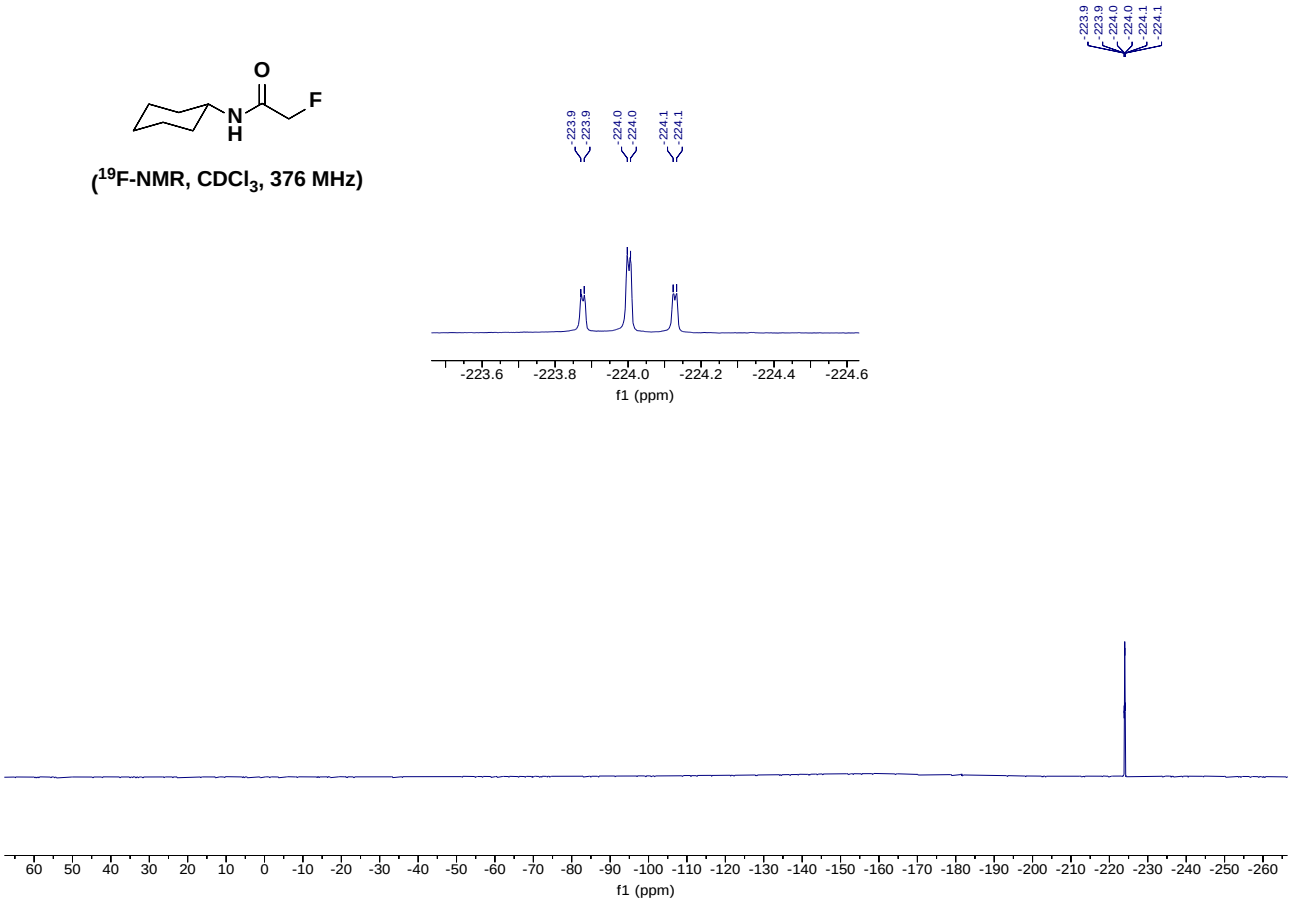


(**^{1}H-NMR, $CDCl_3$, 400 MHz**)



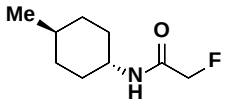


(^{13}C-NMR, $CDCl_3$, 100 MHz)

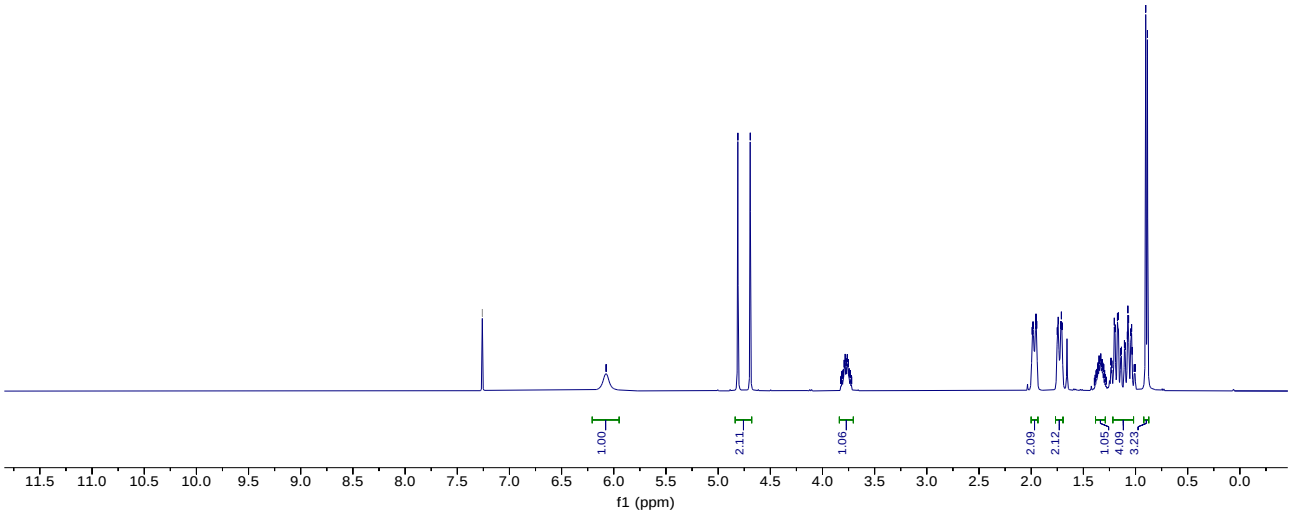


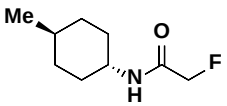
(^{19}F-NMR, $CDCl_3$, 376 MHz)

2-fluoro-*N*-((1R,4R)-4-methylcyclohexyl)acetamide (23)

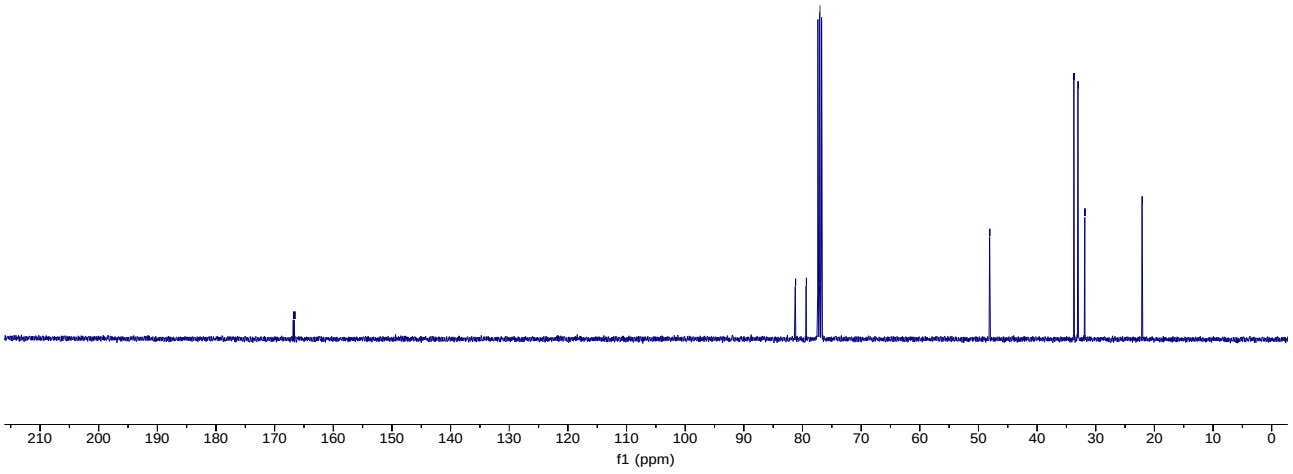


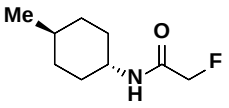
(^{1}H-NMR, $CDCl_3$, 400 MHz)



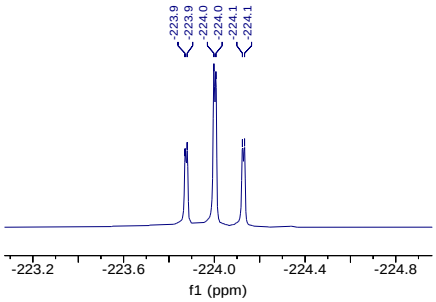


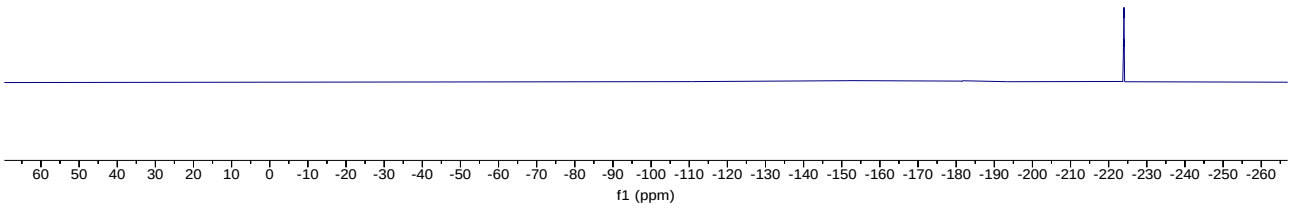
(^{13}C-NMR, $CDCl_3$, 100 MHz)





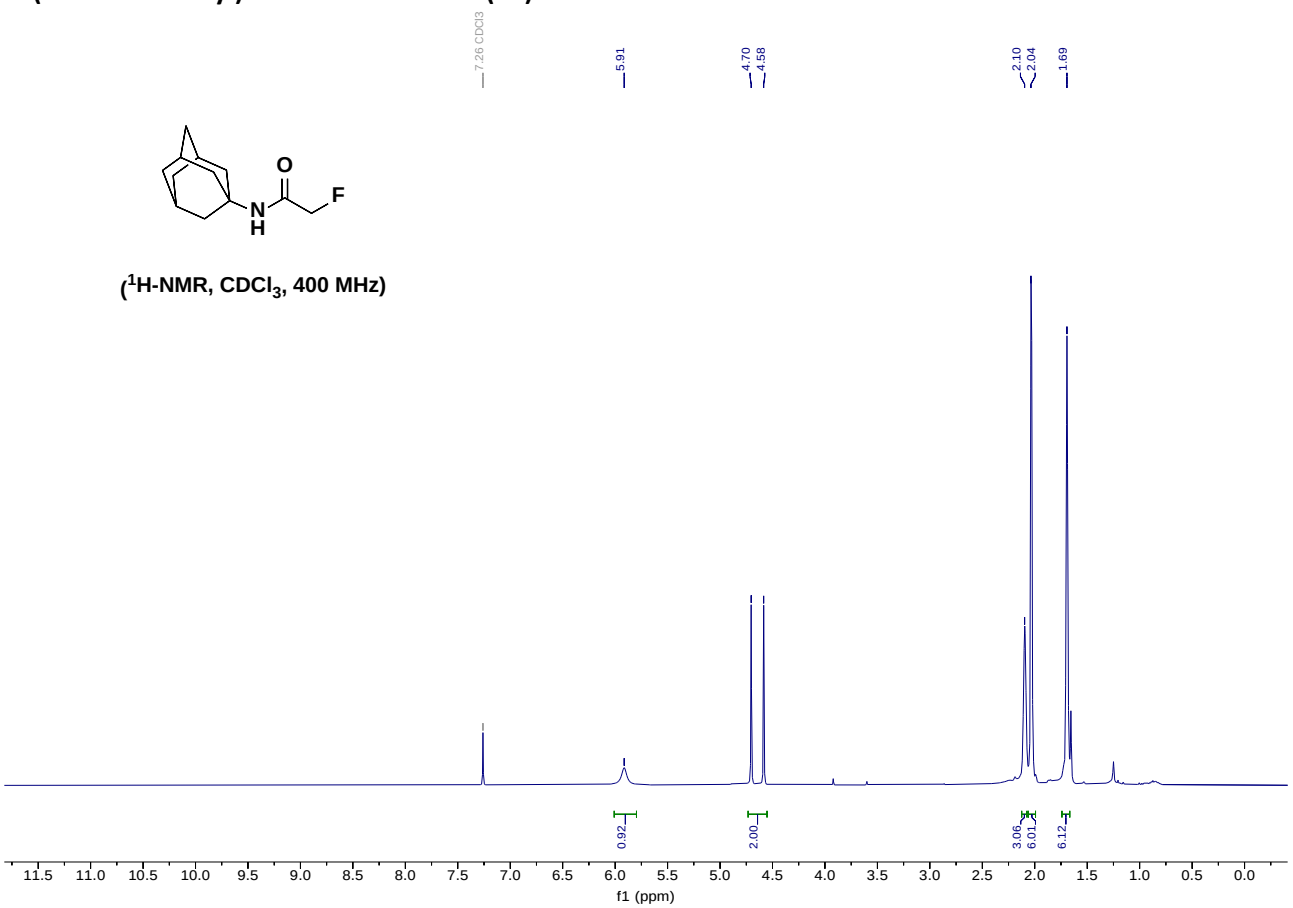
(¹⁹F-NMR, $CDCl_3$, 376 MHz)

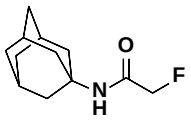




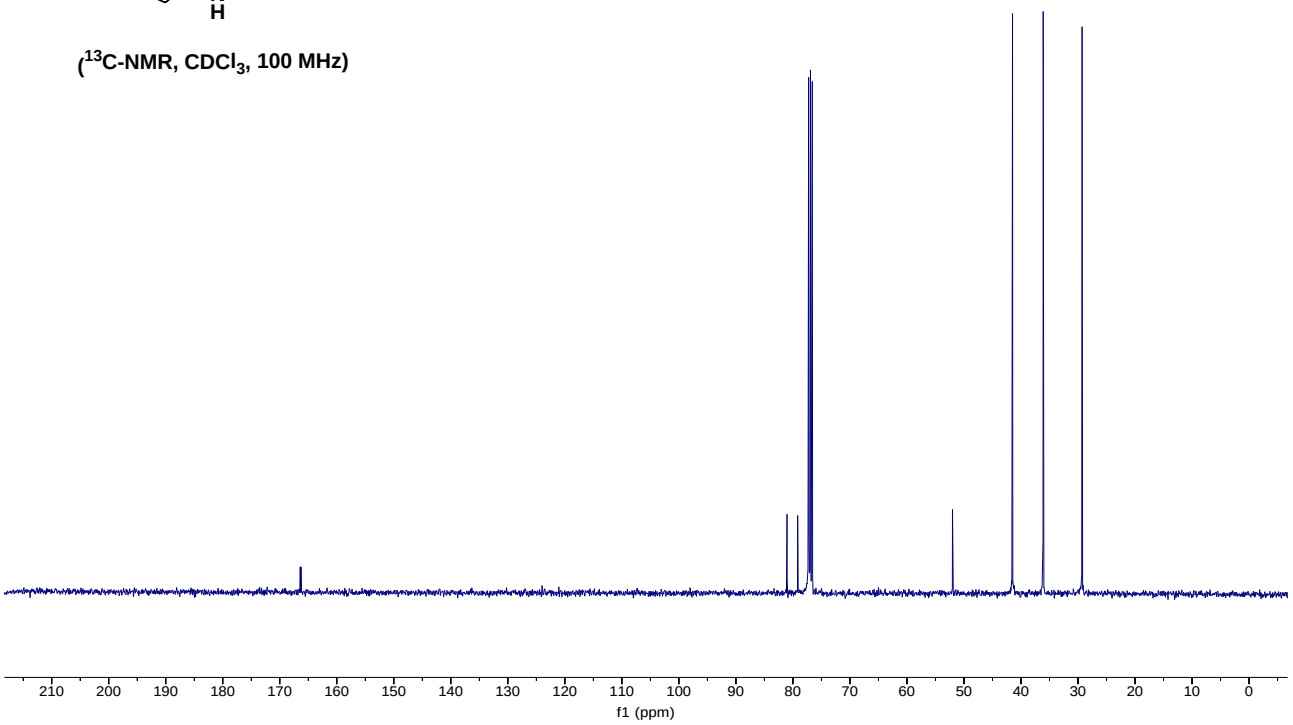
N-(adamantan-1-yl)-2-fluoroacetamide (24)

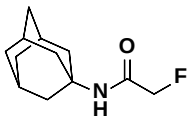
(¹H-NMR, $CDCl_3$, 400 MHz)



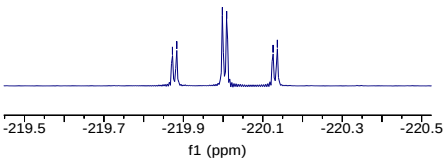


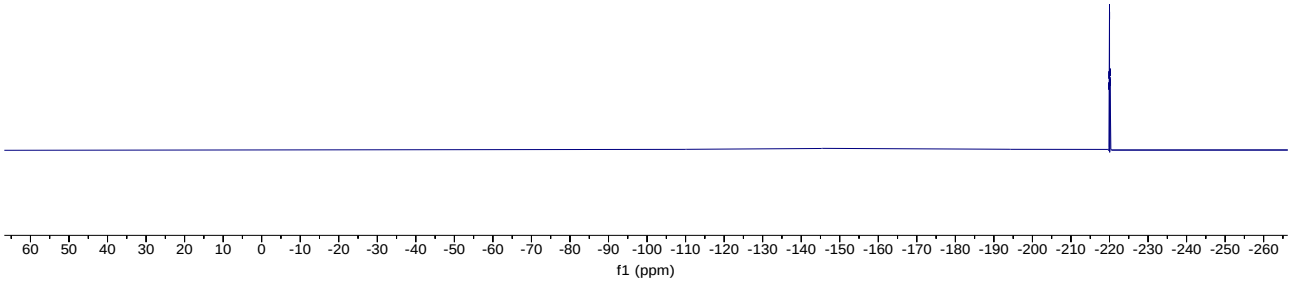
(^{13}C-NMR, $CDCl_3$, 100 MHz)





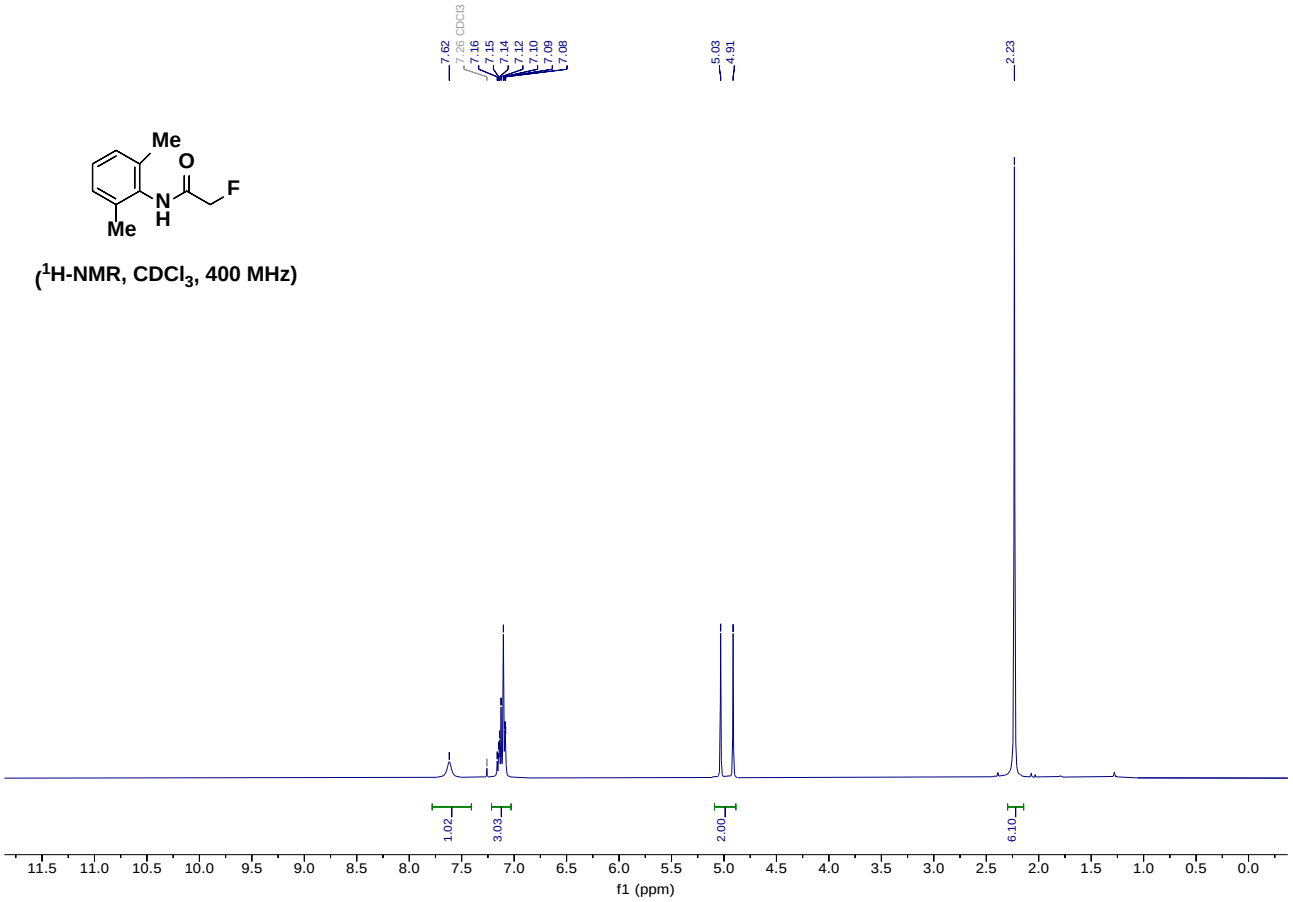
(^{19}F-NMR, $CDCl_3$, 376 MHz)

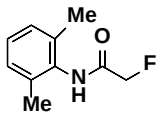




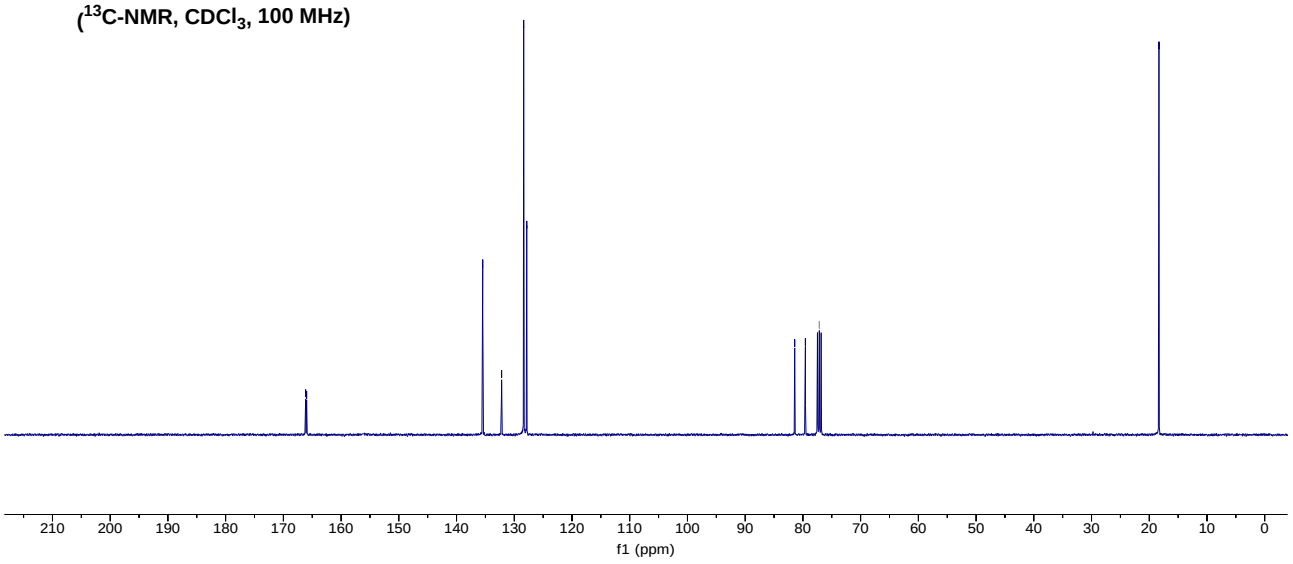
***N*-(2,6-dimethylphenyl)-2-fluoroacetamide (25)**

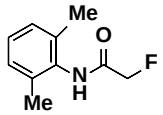
(^{1}H-NMR, $CDCl_3$, 400 MHz)



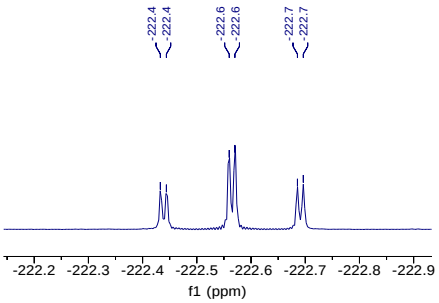


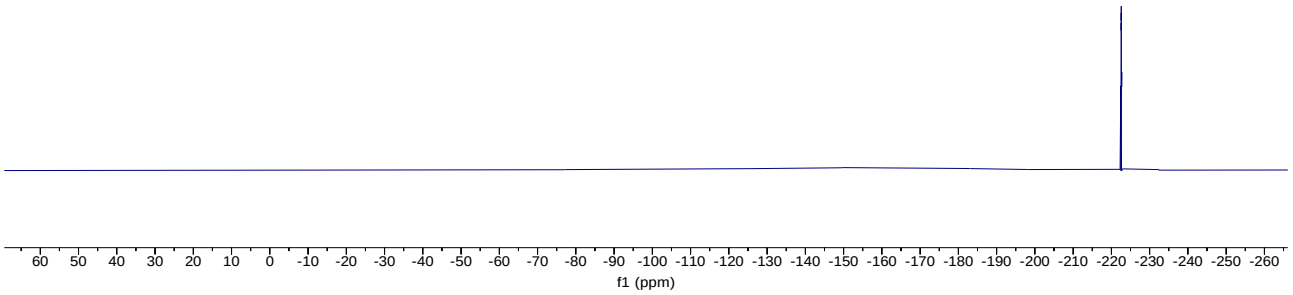
(^{13}C-NMR, $CDCl_3$, 100 MHz)





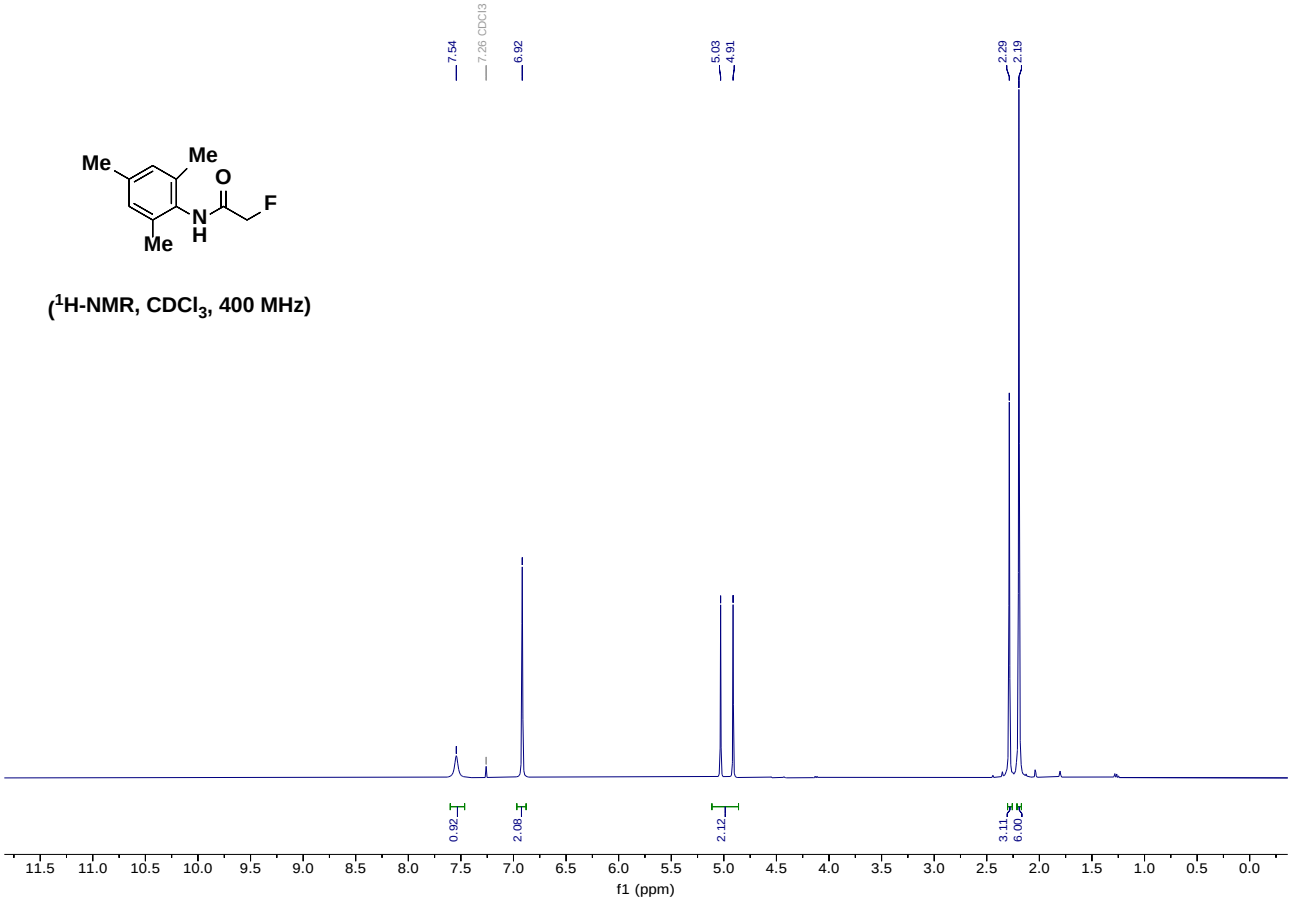
(**^{19}F-NMR, $CDCl_3$, 376 MHz)**



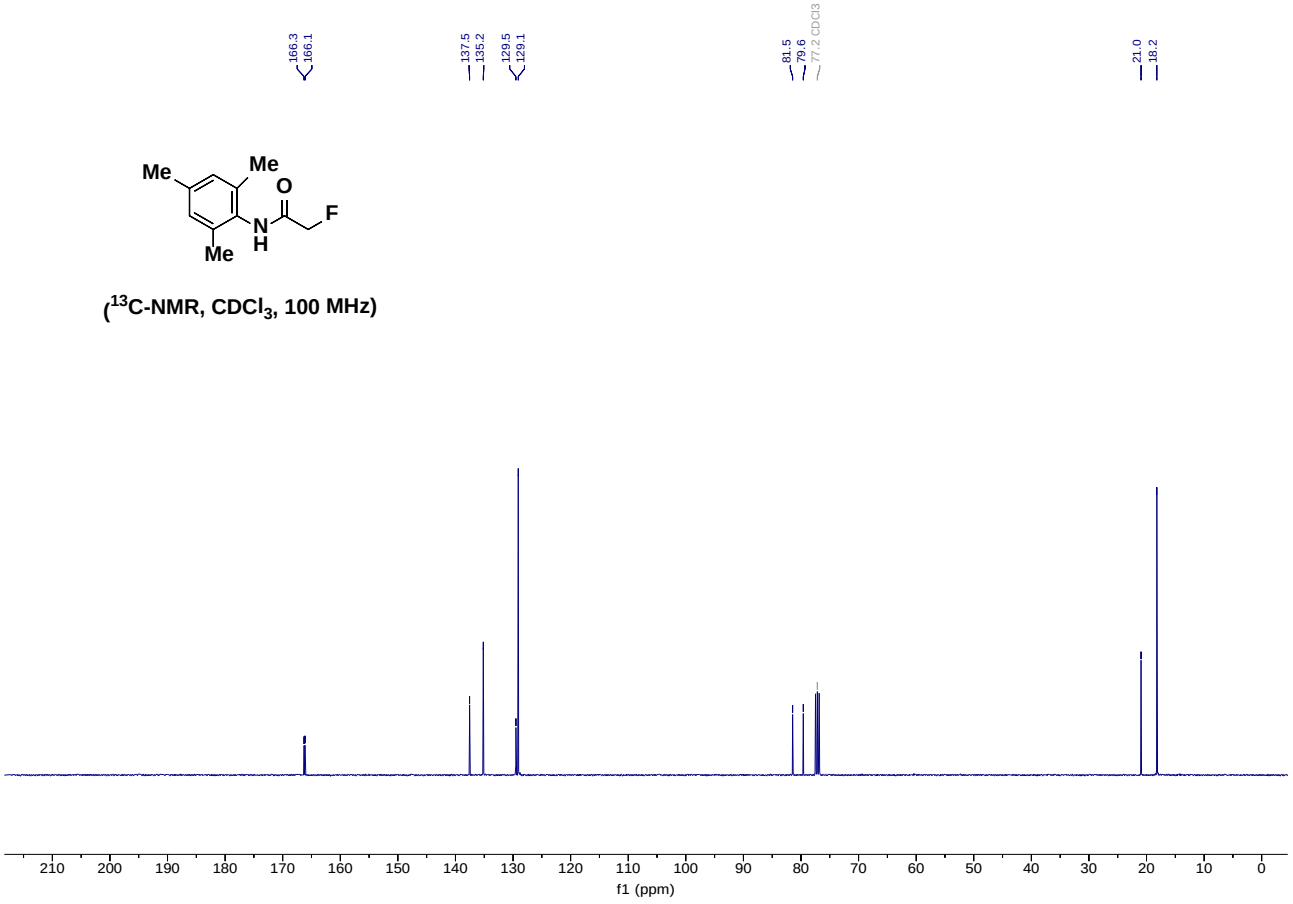


N-(2,4,6-trimethylphenyl)-2-fluoroacetamide (26)

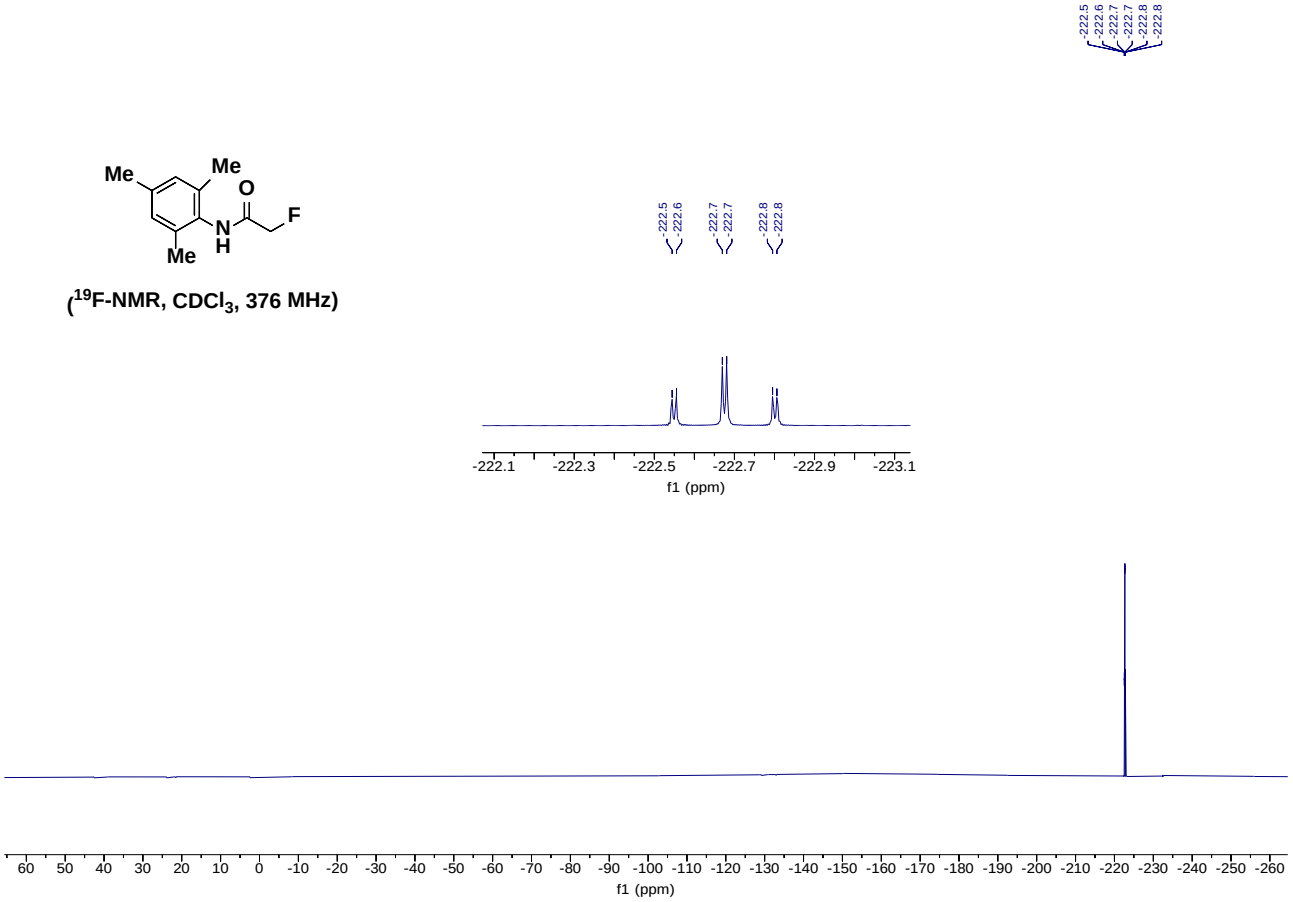
(¹H-NMR, $CDCl_3$, 400 MHz)



(¹³C-NMR, $CDCl_3$, 100 MHz)

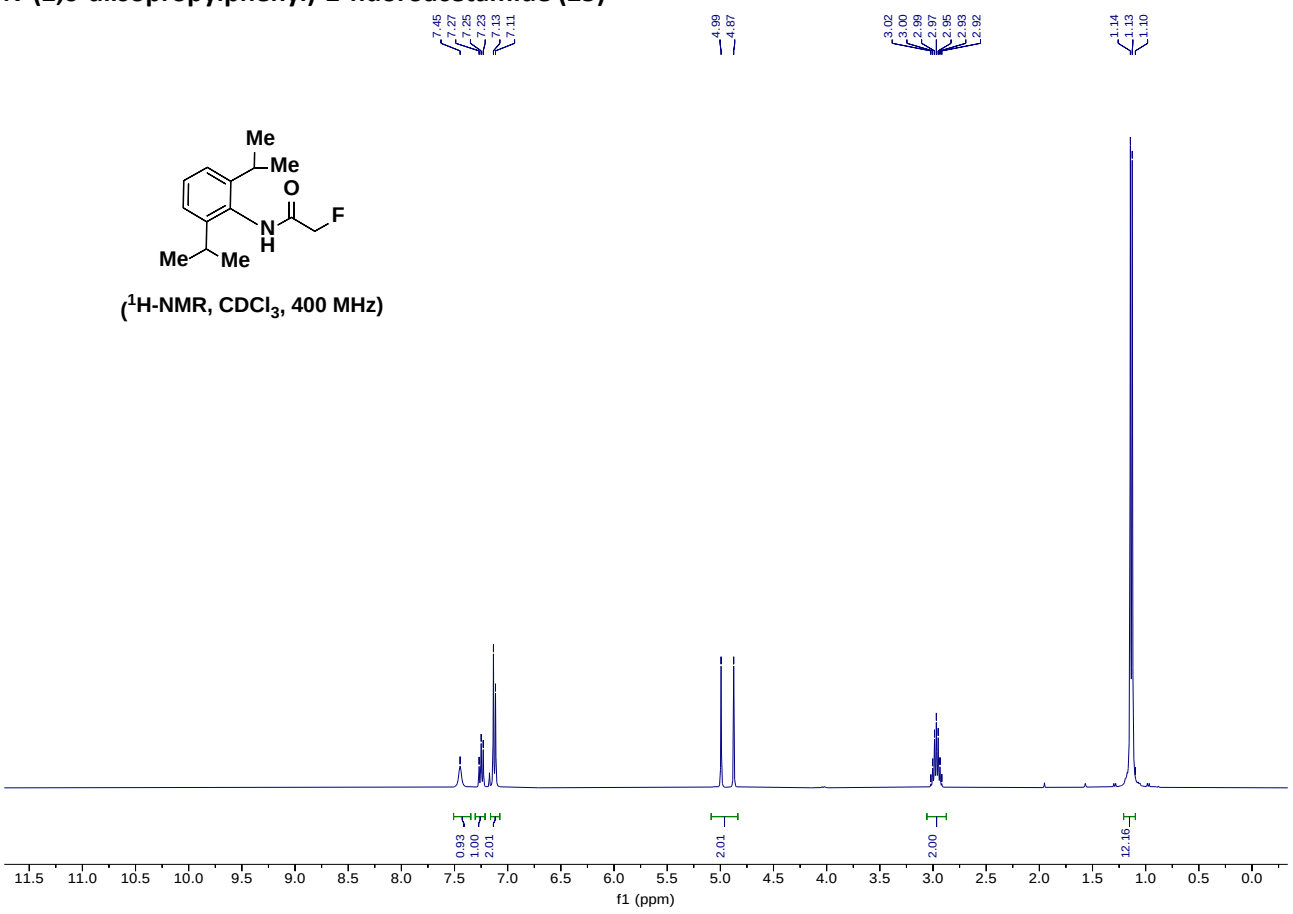


(19F-NMR, $CDCl_3$, 376 MHz)

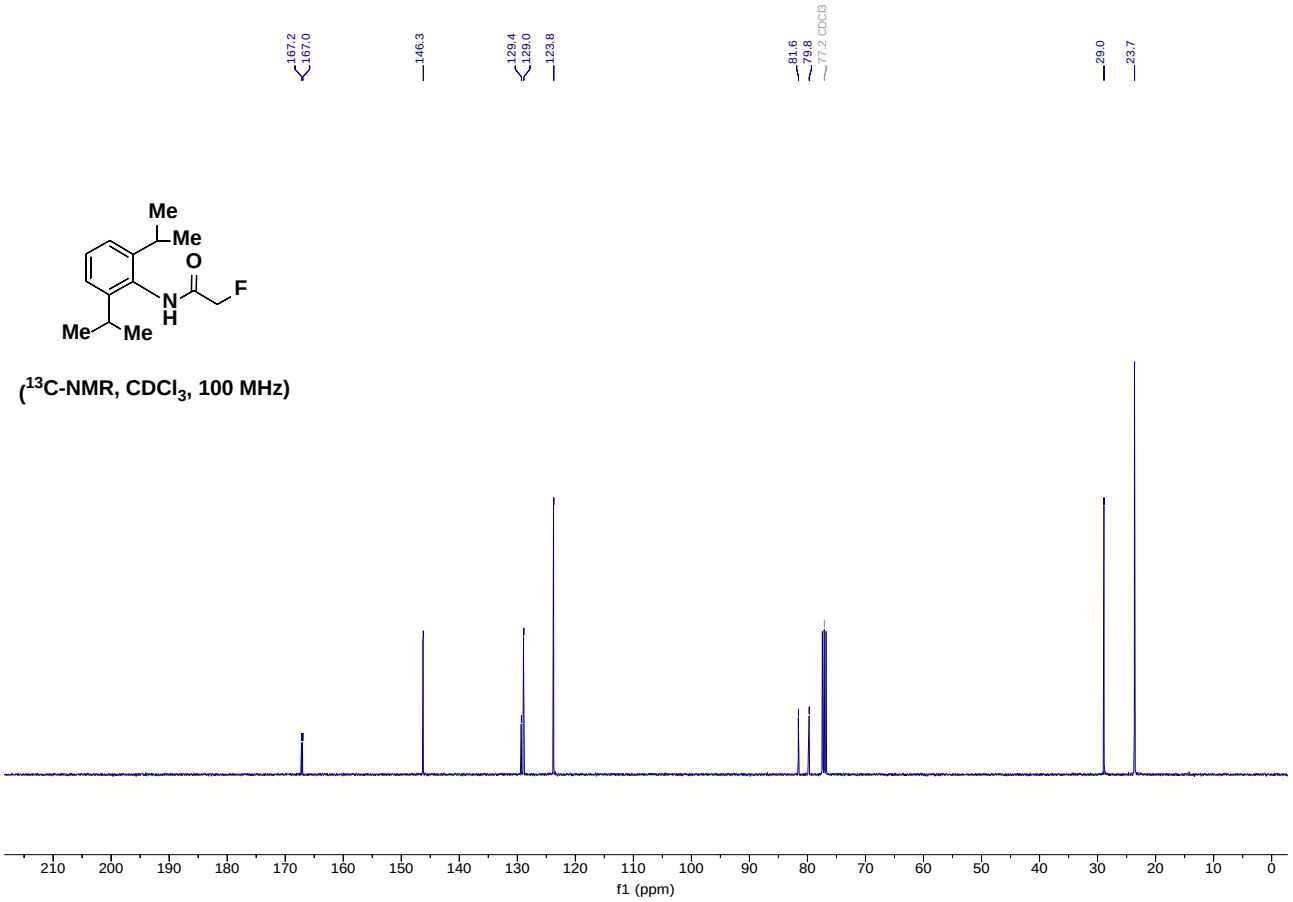


N-(2,6-diisopropylphenyl)-2-fluoroacetamide (25)

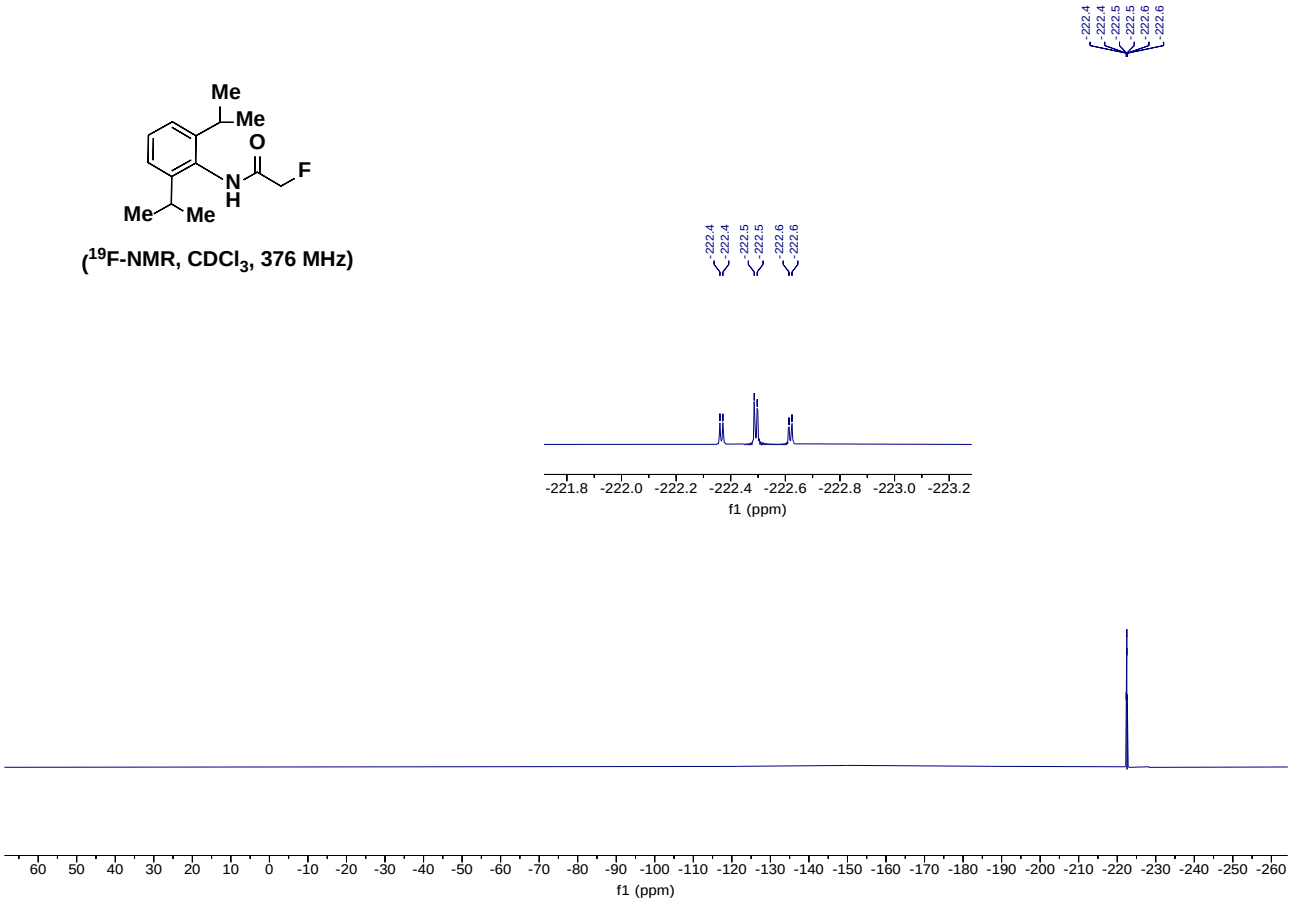
(1H-NMR, $CDCl_3$, 400 MHz)



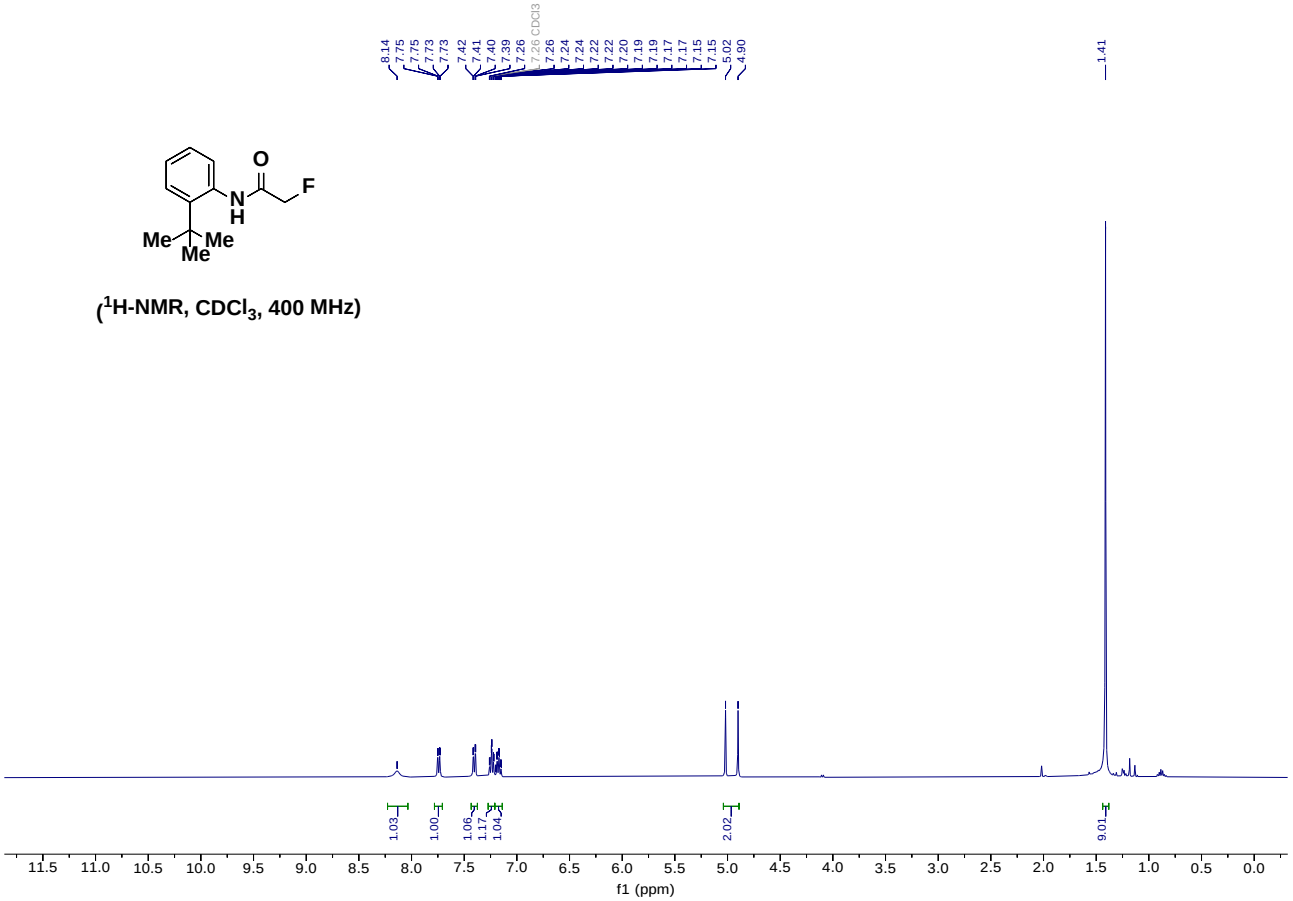
(^{13}C-NMR, $CDCl_3$, 100 MHz)



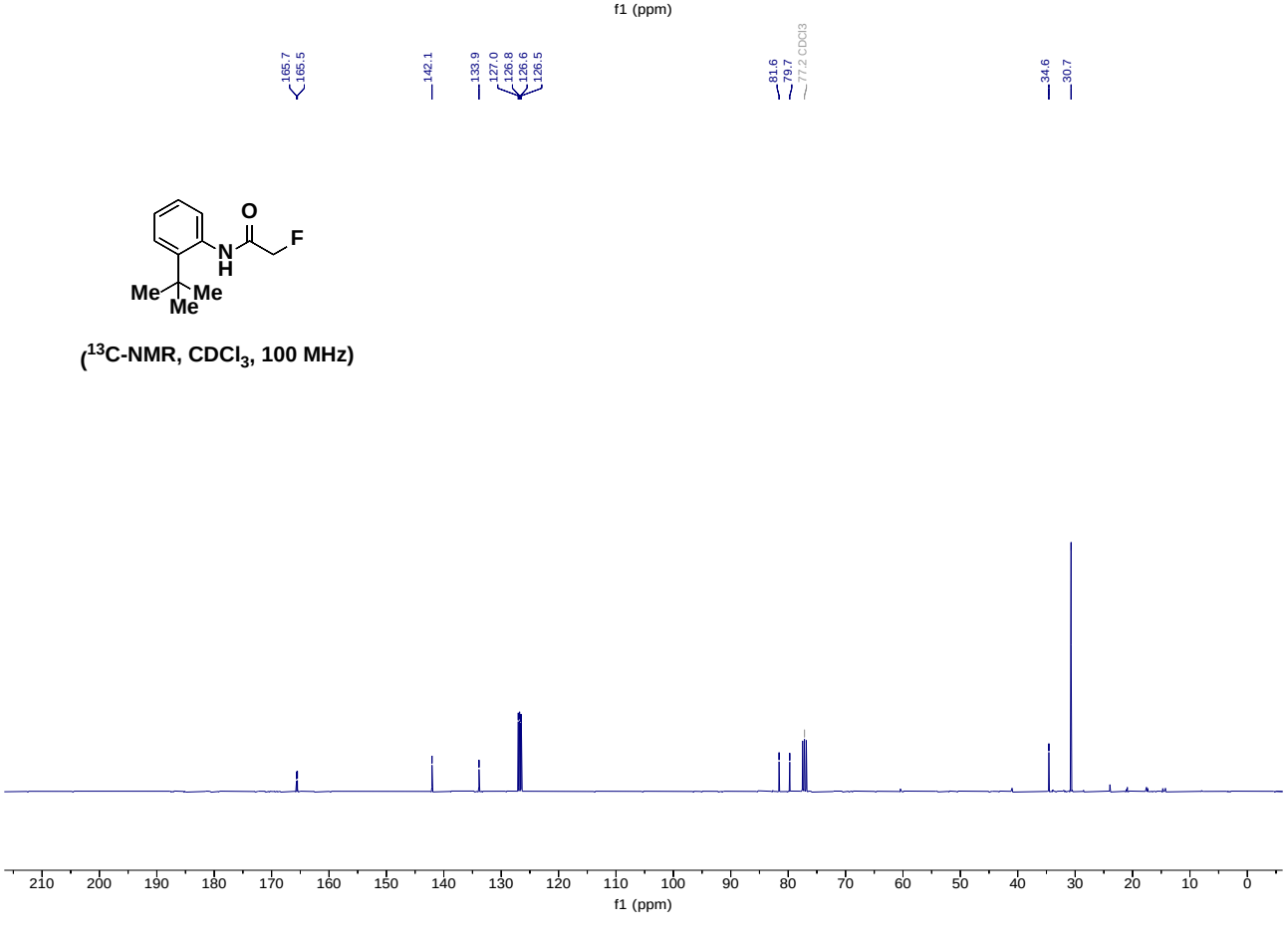
(^{19}F-NMR, $CDCl_3$, 376 MHz)



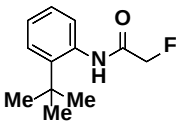
N-(2-(*tert*-butyl)phenyl)-2-fluoroacetamide (28)



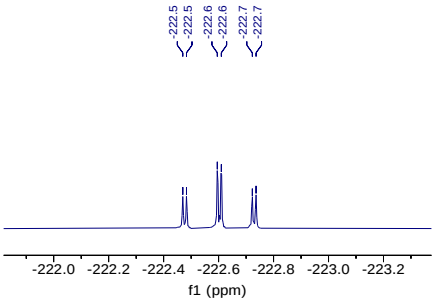
(¹H-NMR, $CDCl_3$, 400 MHz)

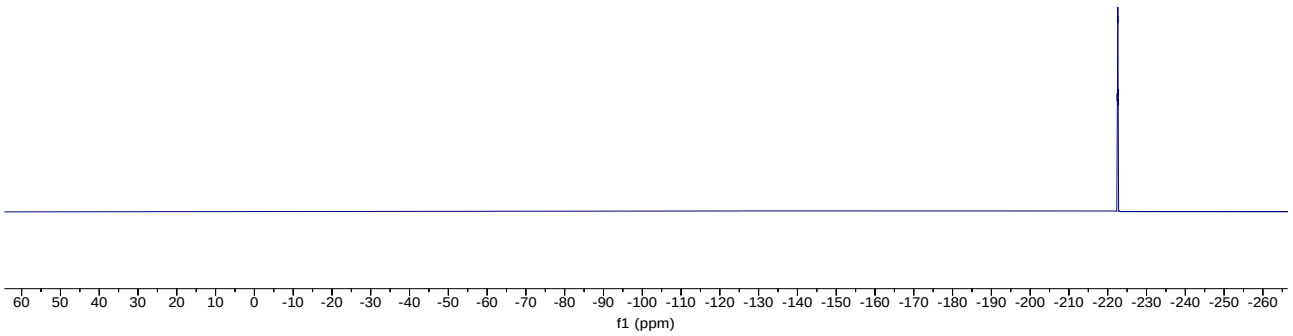


(¹³C-NMR, $CDCl_3$, 100 MHz)



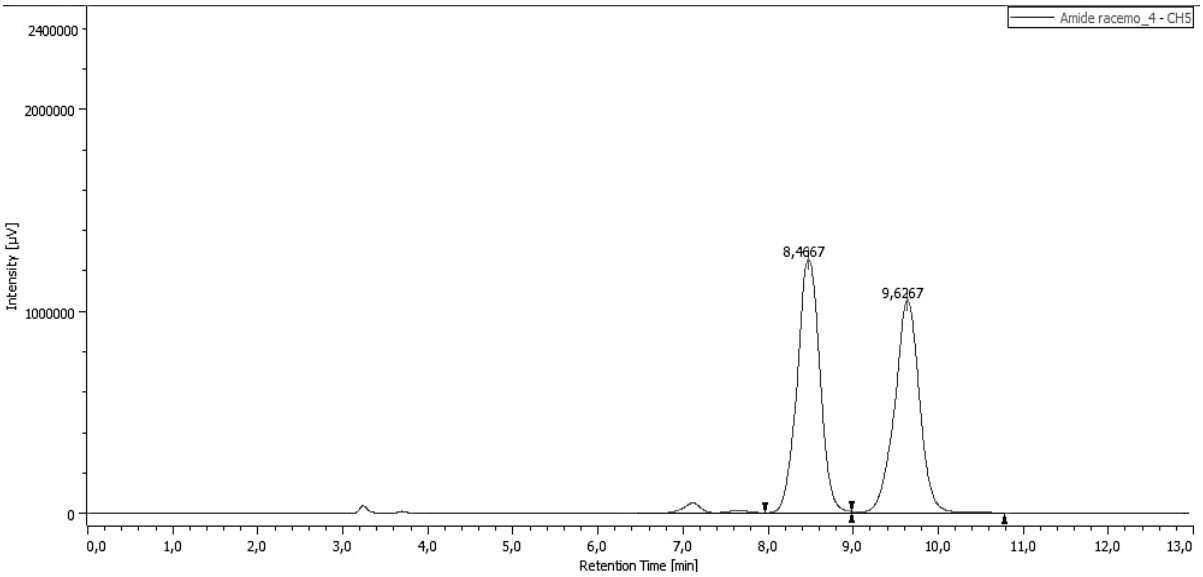
(¹⁹F-NMR, $CDCl_3$, 376 MHz)





HPLC Analysis Data for chiral compounds

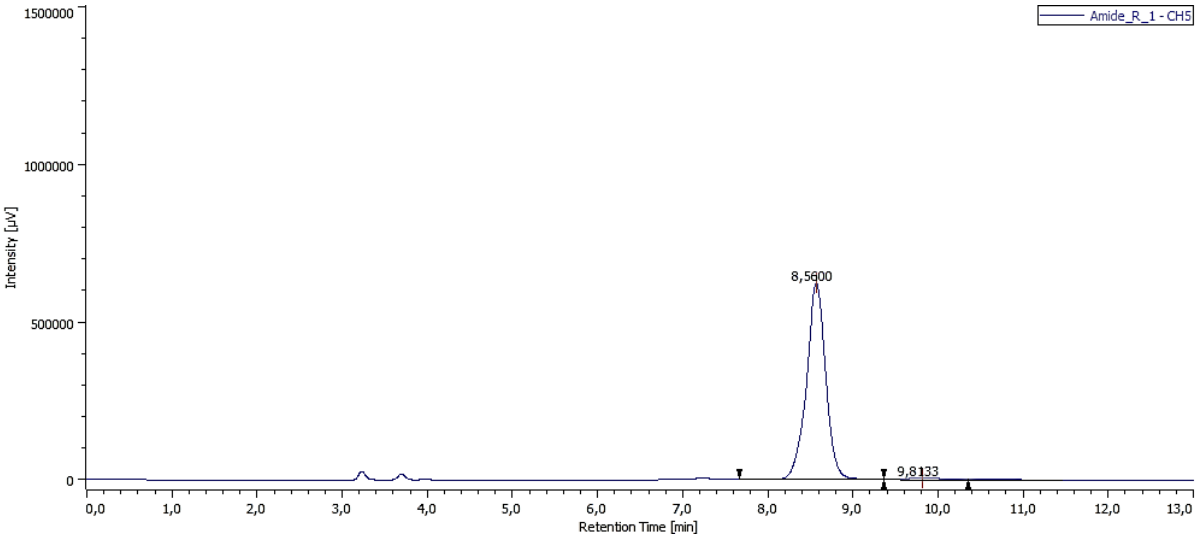
***Racemate* (*rac*)-9**



Chiralpak IA, Isocratic, *n*-hex:*i*-PrOH 95:5, 1mL/min, λ 210 nm

Peaks	*Retention time (min)*	*Area*	*Area%*
1	8,467	23247315	52,175
2	9,627	21308909	47,825
Tot		44556224	100,000

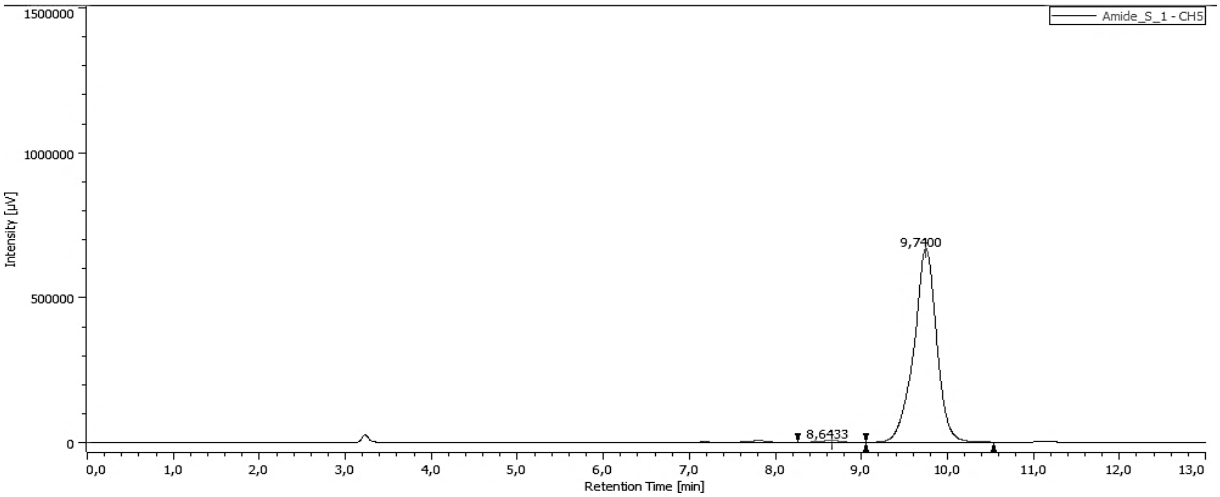
***Enantioenriched* (*R*)-9** $[\alpha]_D^{25}$ = + 39.6 ° (*c* 0.81 MeOH), lit.[21] $[\alpha]_D^{25}$ = + 45.5 ° (*c* 0.96 MeOH).



Chiralpak IA, Isocratic, *n*-hex:*i*-PrOH 95:5, 1mL/min, λ 210 nm

Peaks	*Retention time (min)*	*Area*	*Area%*
1	8,560	9785853	99,217
2	9,813	77228	0,783
Tot		9863081	100,000

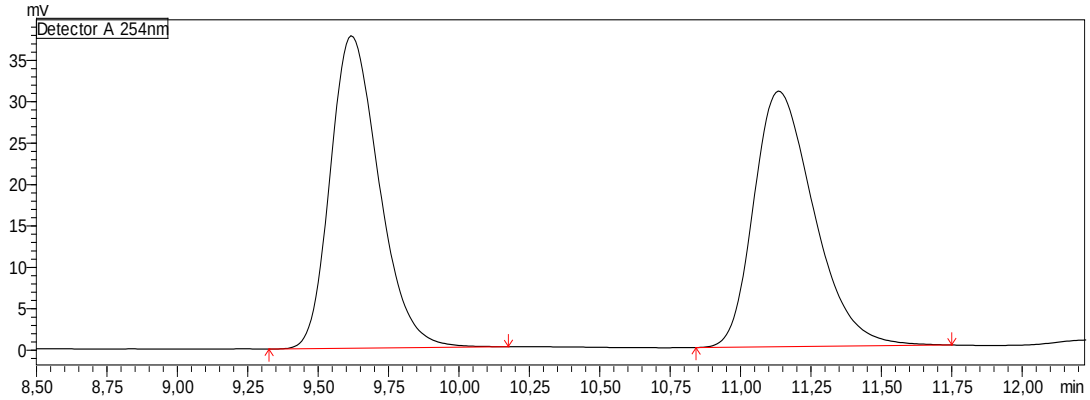
Enantioenriched (S)-9 $[\alpha]_D^{25}$ = - 28.2 ° (*c* 0.72 MeOH).



Chiralpak IA, Isocratic, *n*-hex:*i*-PrOH 95:5, 1mL/min, λ 210 nm

Peaks	*Retention time (min)*	*Area*	*Area%*
1	8,643	95946	0,777
2	9,740	12254832	99,223
Tot		12350778	100,000

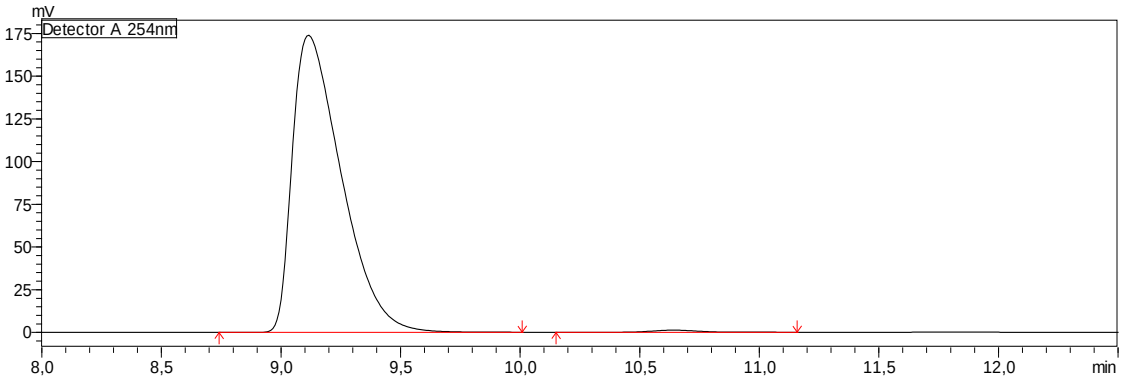
Racemate (rac)-10



Chiralpak IC, Isocratic, *n*-hex:*i*-PrOH, 0.9 mL/min, λ 254 nm

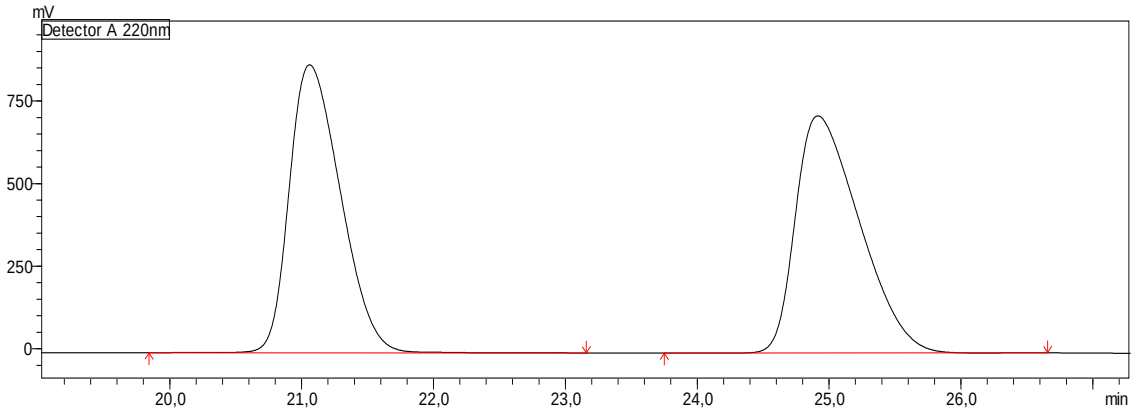
Peaks	*Retention time (min)*	*Area*	*Area%*
1	9,649	454624	49,782
2	11,152	458607	50,218
Tot		913231	100,000

***Enantioenriched (S)*-10** $[\alpha]_D^{25}$ = - 37.6 ° (*c* 0.53 MeOH).



Peaks	*Retention time (min)*	*Area*	*Area%*
1	9,226	2479623	99,241
2	10,676	18967	0,759
Tot		2498590	100,000

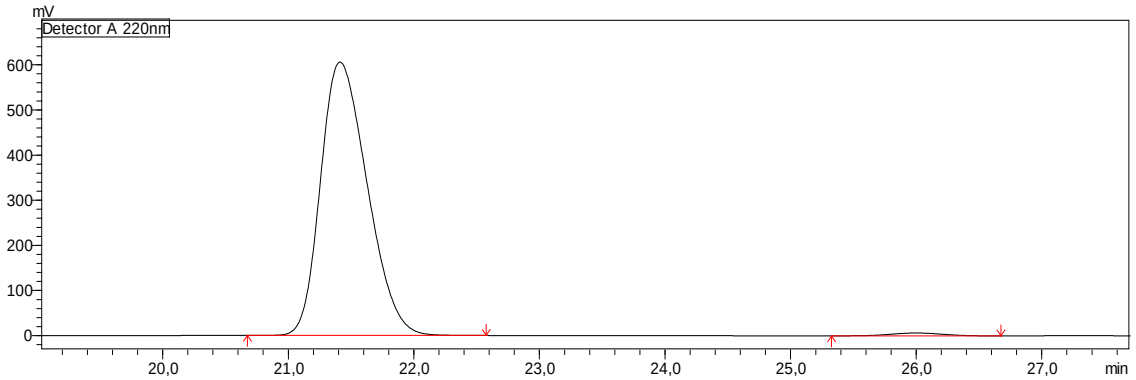
***Racemate (rac)*-11**



Chiralpak IG, Isocratic, *n*-hex:*i*-PrOH, 0.80 mL/min, λ 220 nm.

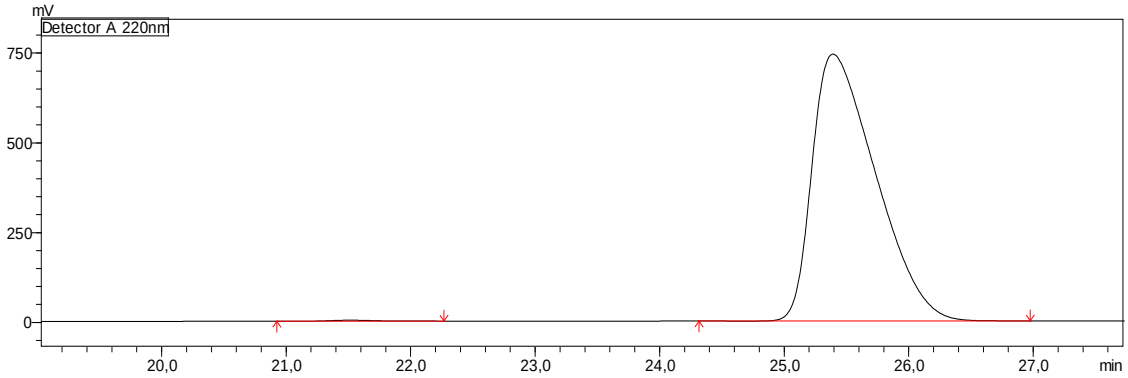
Peaks	*Retention time (min)*	*Area*	*Area%*
1	21,060	23607149	49,428
2	24,915	24153097	50,572
Tot		47760246	100,000

***Enantioenriched (R)*-11** $[\alpha]_D^{25}$ = + 22.6 ° (*c* 0.32 $CHCl_3$).



Peaks	*Retention time (min)*	*Area*	*Area%*
1	21,412	15631164	98,854
2	26,002	181160	1,146
Tot		15812324	100,000

***Enantioenriched (S)*-11** $[\alpha]_D^{25}$ = -18.5 ° (*c* 0.24 $CHCl_3$)



Peaks	*Retention time (min)*	*Area*	*Area%*
1	21,518	57751	0,219
2	25,392	26285214	99,781
Tot		26342965	100,000

References

[1] Z. J. Shen, C. Zhu, X. Zhang, C. Yang, M. Rueping, L. Guo, W. Xia, *Angewandte Chemie* **2023**, *135*, e202217244.
[2] U. K. Das, A. Kumar, Y. Ben-David, M. A. Iron, D. Milstein, *Journal of the American Chemical Society* **2019**, *141*, 12962-12966.
[3] L. Wang, H. Wang, G. Li, S. Min, F. Xiang, S. Liu, W. Zheng, *Advanced Synthesis & Catalysis* **2018**, *360*, 4585-4593.
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