

Synthesis of α -CF₃ and α -CF₂H Amines via Aminofluorination of Fluorinated Alkenes

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Supporting information

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I. General information

Unless otherwise noted, all commercially available materials were used without further purification. All reactions were carried out in reaction vessels (75 ML) with Teflon screw caps under air.

NMR-spectra were recorded on Bruker AvanceIII-400M and Ascend™ 500M in solvents as indicate. Chemical shifts (δ) are given in ppm relative to tetramethylsilane ($\delta = 0$). The residual solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl_3 : $\delta_{\text{H}} = 7.26$ ppm, $\delta_{\text{C}} = 77.16$ ppm). The following abbreviations were used to describe peak splitting patterns: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), dt (doublet of triplets). Coupling constants (J) were reported in hertz unit (Hz).

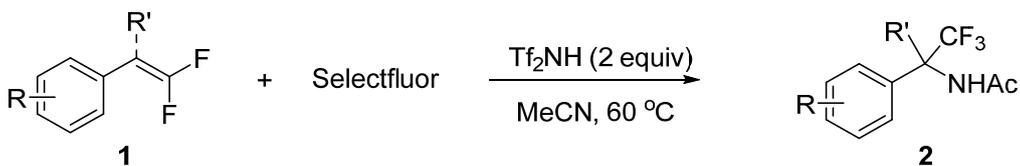
High-resolution mass spectra (HRMS) were recorded on a Bruker VPEXII spectrometer with EI and ESI mode unless otherwise stated.

Analytical thin layer chromatography was performed on Polygram SIL G/UV254 plates. Visualization was accomplished by UV light (254 nm), or KMnO_4 staining solutions followed by heating, also by Gas chromatograph-Mass spectrometer analysis (GC-MS) on Agilent Technologies 5977A MSD. Flash column chromatography was performed using silica gel (200–300 mesh).

No attempts were made to optimize yields for substrate synthesis.

All the starting materials^[1-3] were prepared according to literature procedures.

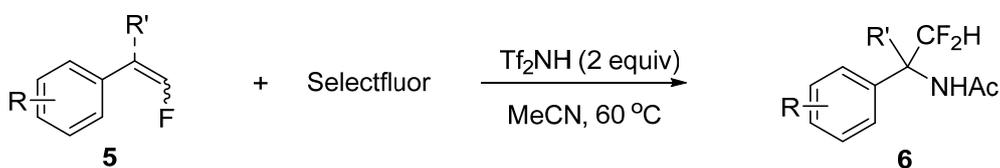
II. General procedures for the synthesis of α -CF₃ amines



General procedure A

To a solution of *gem*-difluoroalkene (0.5 mmol, 1.0 equiv), Selectfluor (1.0 mmol, 354 mg, 2.0 equiv) in MeCN (12.0 mL), was added Tf₂NH (1.0 mmol, 281 mg, 2.0 equiv) dissolved in MeCN (3.0 mL). The resulting mixture was stirred at 60 °C until the *gem*-difluoroalkene was consumed as monitored by TLC. The solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (Petroleum ether/ EtOAc =3:1) to give product 2 as white solid.

III. General procedures for the synthesis of α -CF₂H amines

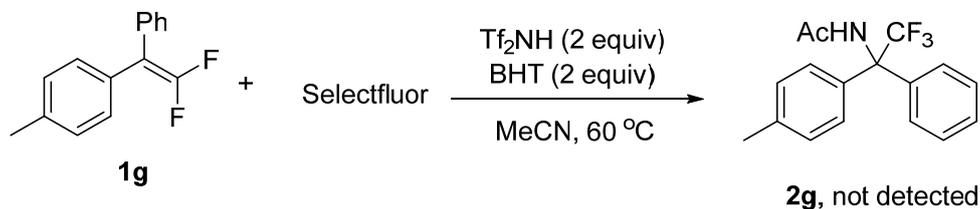


General procedure B

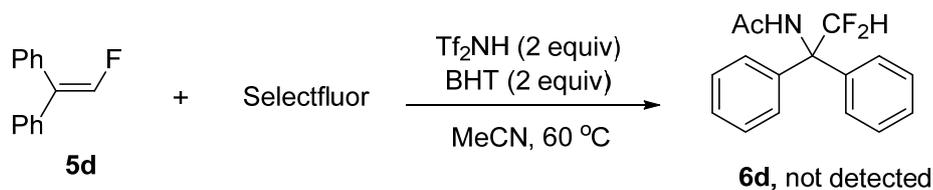
To a solution of monofluoroalkene (0.3 mmol, 1.0 equiv), Selectfluor (0.6 mmol, 213 mg, 2.0 equiv) in MeCN (6.0 mL), was added Tf₂NH (0.6 mmol, 169 mg, 2.0 equiv) dissolved in MeCN (3.0 mL). The resulting mixture was stirred at 60 °C until the monofluoroalkene was consumed as monitored by TLC. The solvent was removed under reduced pressure. The crude product was purified by silica gel column chromatography (Petroleum ether/ EtOAc =3:1) to give product **6** as white solid.

IV. Mechanistic Studies

i. Radical inhibition experiments

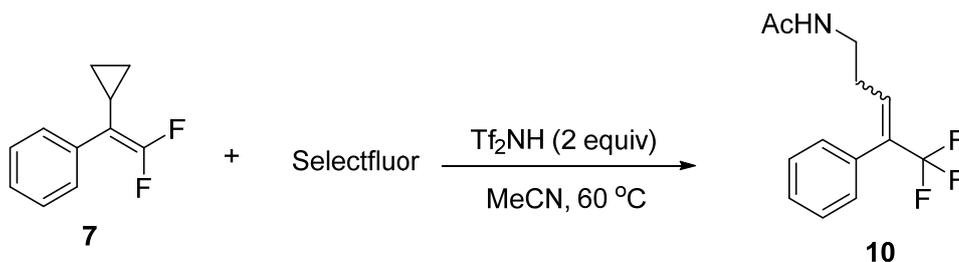


Following General procedure A, to a solution of *gem*-difluoroalkene **1g** (0.2 mmol, 46 mg, 1.0 equiv), Selectfluor (0.4 mmol, 142 mg, 2.0 equiv), BHT (0.4 mmol, 88 mg, 2.0 equiv) in MeCN (4.0 mL), was added Tf_2NH (0.4 mmol, 112 mg, 2.0 equiv) dissolved in MeCN (2.0 mL). The resulting mixture was stirred at 60 °C for 3 h. No desired product was observed by GC-MS.



Following General procedure B, to a solution of monofluoroalkene **5d** (0.1 mmol, 20 mg, 1.0 equiv), Selectfluor (0.2 mmol, 71 mg, 2.0 equiv), BHT (0.2 mmol, 44 mg, 2.0 equiv) in MeCN (2.0 mL), was added Tf_2NH (0.2 mmol, 57 mg, 2.0 equiv) dissolved in MeCN (1.0 mL). The resulting mixture was stirred at 60 °C for 13 h. No desired product was observed by GC-MS.

ii. Radical clock experiment

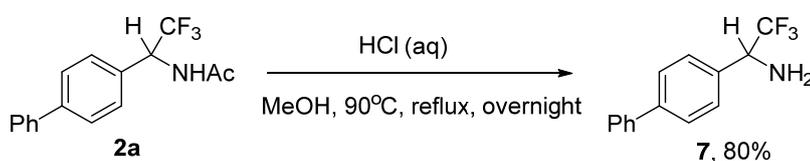


Following General procedure A, to a solution of

(1-cyclopropyl-2,2-difluorovinyl)-benzene (0.5 mmol, 90 mg, 1.0 equiv), Selectfluor (1.0 mmol, 354 mg, 2.0 equiv) in MeCN (12.0 mL), was added Tf₂NH (1.0 mmol, 281 mg, 2.0 equiv) in MeCN (3.0 mL). The resulting mixture was stirred at 60 °C for 45 min. Product **10** was obtained by chromatography (silica gel; petroleum ether/ EtOAc = 1:1) as a colorless oil (50 mg, 39%).

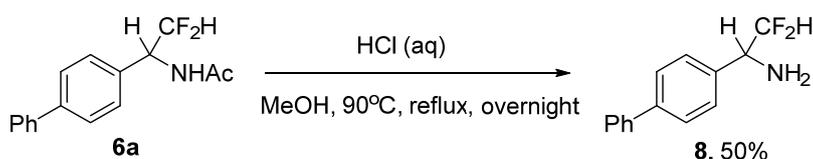
V. Derivatizations of product

1-([1,1'-Biphenyl]-4-yl)-2,2,2-trifluoroethan-1-amine (**7**)



HCl aqueous (2N, 0.14 mL) was added to a solution of compound **2a** (0.1 mmol, 29 mg) in MeOH (3.0 mL). The reaction mixture was refluxed overnight at 90 °C. After the reaction was complete as monitored by TLC, the saturated NaHCO₃ was added, then extracted with EtOAc. The combined organic phases were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The pure product was purified by flash column chromatography on silica with an eluent (Petroleum ether/ EtOAc 6:1 v/v) to afford the pure product **7** as a white solid (20 mg, 80 %).

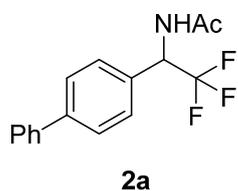
1-([1,1'-Biphenyl]-4-yl)-2,2-difluoroethan-1-amine (**8**)



HCl aqueous (2N, 0.14 mL) was added to a solution of compound **6a** (0.1 mmol, 28 mg) in MeOH (3.0 mL). The reaction mixture was refluxed overnight at 90 °C. After the reaction was complete as monitored by TLC, the saturated NaHCO₃ was added, then extracted with EtOAc. The combined organic phases were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The pure product was purified by flash column chromatography on silica with an eluent (Petroleum ether/ EtOAc 6:1 v/v) to afford the pure product **8** as a white solid (12 mg, 52 %).

VI. Characterization of Products

N-(1-([1,1'-Biphenyl]-4-yl)-2,2,2-trifluoroethyl)acetamide (**2a**)



Following general procedure A, **2a** was obtained in 75% yield (110 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.24. m.p. = 231.7 - 232.5 °C.

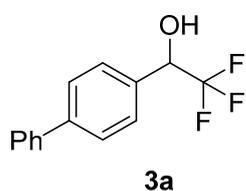
$^1\text{H NMR}$ (400 MHz, $(\text{CD}_3)_2\text{CO}$) δ = 8.70 (d, J = 9.7 Hz, 1H), 7.31 - 7.15 (m, 6H), 7.03 (t, J = 7.6 Hz, 2H), 6.93 (t, J = 7.3 Hz, 1H), 5.37 (p, J = 8.7 Hz, 1H), 1.53 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, $(\text{CD}_3)_2\text{CO}$) δ = 169.5, 140.8, 139.5, 132.4, 129.0, 129.0, 127.8, 126.9, 126.8, 124.9 (q, J = 281.9 Hz), 52.9 (q, J = 30.2 Hz), 22.4.

$^{19}\text{F NMR}$ (376 MHz, $(\text{CD}_3)_2\text{CO}$, composite pulse decoupling) δ = -72.58.

HRMS: m/z Calculated for $\text{C}_{16}\text{H}_{15}\text{F}_3\text{NO}$, $[\text{M}+\text{H}]^+$, 294.1100; Found, 294.1088.

1-([1,1'-Biphenyl]-4-yl)-2,2,2-trifluoroethan-1-ol (**3a**)



From entry 1, **3a** was obtained in 6% yield (3 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 60:1 v/v). R_f (Petroleum ether/EtOAc 64:1): 0.28. m.p. = 118.4 - 119.5 °C.

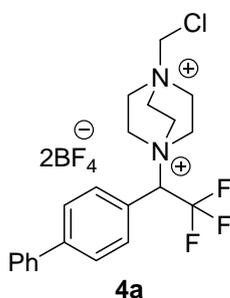
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 7.64 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 7.8 Hz, 2H), 7.56 (d, J = 8.1 Hz, 2H), 7.46 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 5.08 (q, J = 6.8 Hz, 1H), 2.66 (s, 1H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 142.62, 140.45, 132.99, 129.00, 128.01, 127.83, 127.49, 127.31, 124.41 (q, J = 282.5 Hz), 72.76 (q, J = 31.8 Hz).

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = -78.28.

HRMS: m/z Calculated for $\text{C}_{14}\text{H}_{11}\text{F}_3\text{O}$, $[\text{M}]^+$, 252.0762; Found, 252.0765.

1-(1-([1,1'-Biphenyl]-4-yl)-2,2,2-trifluoroethyl)-4-(chloromethyl)-1,4-diazabicyclo[2.2.2]octane-1,4-dium (**4a**)



Following General procedure A, to a solution of *gem*-difluoroalkene **1a** (1 mmol, 216 mg, 5.0 equiv), Selectfluor

(0.2 mmol, 71mg, 1.0 equiv), in MeCN (2.0 mL). The resulting mixture was stirred at 60 °C for 3 h. The crude product was given by silica gel column chromatography (Petroleum ether/ EtOAc =1:1 → MeCN). After recrystallization with MeCN and DCM, the pure product **4a** (11mg, 10%) was obtained as white solid. m.p. = 214.3 – 220.0 °C.

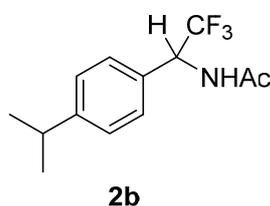
¹H NMR (500 MHz, (CD₃)₂CO) δ = 8.00 (dt, *J* = 16.2 Hz, 8.5 Hz, 3H), 7.91 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 2H), 7.53 (t, *J* = 7.6 Hz, 2H), 7.46 (t, *J* = 7.2 Hz, 1H), 6.28 (q, *J* = 7.2 Hz, 1H), 5.77 (s, 2H), 4.72 (dt, *J* = 11.3 Hz, 8.0 Hz, 3H), 4.63 (dd, *J* = 8.6 Hz, 4.8 Hz, 3H), 4.50 (d, *J* = 7.9 Hz, 6H).

¹³C NMR (101 MHz, (CD₃)₂CO) δ = 146.0, 139.6, 136.7, 130.1, 129.6, 129.4, 129.2, 128.0, 123.6 (q, *J* = 282.4), 122.6, 69.9, 76.3 (q, *J* = 30.8, 30.3), 53.0, 51.6.

¹⁹F NMR (376 MHz, (CD₃)₂CO, composite pulse decoupling) δ = –59.65, –153.08.

HRMS: *m/z* Calculated for C₂₁H₂₃ClF₃N₂, [M–2BF₄–H]⁺, 395.1496; Found, 395.1491.

***N*–(2,2,2–Trifluoro–1–(4–isopropylphenyl)ethyl)acetamide (2b)**



Following general procedure A, **2b** was obtained in 60% yield (78 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.36. m.p. = 83.3 – 85.3 °C.

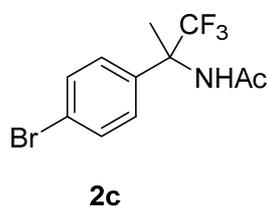
¹H NMR (500 MHz, CDCl₃) δ = 7.30 (d, *J* = 8.2 Hz, 2H), 7.25 (d, *J* = 6.8 Hz, 2H), 6.09 (d, *J* = 10.5 Hz, 1H), 5.69 (p, *J* = 8.0 Hz, 1H), 2.92 (sep, *J* = 6.9 Hz, 1H), 2.07 (s, 3H), 1.25 (d, *J* = 6.9 Hz, 6H).

¹³C NMR (126 MHz, CDCl₃) δ = 169.7, 150.2, 130.3, 128.0, 127.2, 124.7 (q, *J* = 281.5 Hz), 54.1 (q, *J* = 31.3 Hz), 34.0, 24.0, 23.2.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = –73.79.

HRMS: *m/z* Calculated for C₁₃H₁₇F₃NO, [M+H]⁺, 260.1257; Found, 260.1248.

***N*–(2–(4–Bromophenyl)–1,1,1–trifluoropropan–2–yl)acetamide (2c)**



Following general procedure A, **2c** was obtained in 58% yield (90 mg) as a white solid after column chromatography

(eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.21. m.p. = 165.0 – 166.0 °C.

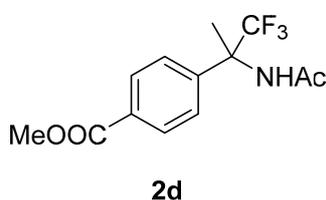
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.50 (d, J = 8.8 Hz, 2H), 7.30 (d, J = 8.8 Hz, 2H), 6.06 (s, 1H), 2.07 (s, 3H), 2.03 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 169.4, 135.6, 131.6, 128.7, 125.4 (q, J = 284.2 Hz), 122.8, 62.0 (q, J = 27.2 Hz), 23.9, 19.6, 19.6.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3 , composite pulse decoupling) δ = -79.18.

HRMS: m/z Calculated for $\text{C}_{11}\text{H}_{12}\text{BrF}_3\text{NO}$, $[\text{M}+\text{H}]^+$, 310.0049; Found, 310.0036.

Methyl 4-(2-acetamido-1,1,1-trifluoropropan-2-yl)benzoate (**2d**)



Following general procedure A, **2d** was obtained in 31% yield (45 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.14. m.p. = 157.5 – 158.4 °C.

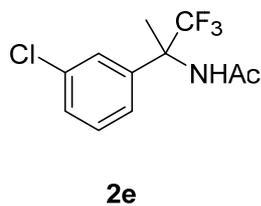
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 8.07 – 8.00 (m, 2H), 7.51 (d, J = 8.2 Hz, 2H), 6.12 (s, 1H), 3.91 (s, 3H), 2.08 (d, J = 2.7 Hz, 6H).

$^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ = 169.3, 166.7, 141.4, 130.2, 129.7, 127.1, 125.5 (q, J = 284.6 Hz), 62.3 (q, J = 27.2 Hz), 52.3, 24.0, 19.8.

$^{19}\text{F NMR}$ (376 MHz, CDCl_3 , composite pulse decoupling) δ = -78.77.

HRMS: m/z Calculated for $\text{C}_{13}\text{H}_{15}\text{F}_3\text{NO}_3$, $[\text{M}+\text{H}]^+$, 290.0999; Found, 290.0985.

N-(2-(3-Chlorophenyl)-1,1,1-trifluoropropan-2-yl)acetamide (**2e**)



Following general procedure A, **2e** was obtained in 37% yield (49 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.27. m.p. = 126.6 – 127.5 °C.

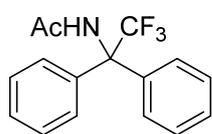
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 7.40 (s, 1H), 7.32 (m, 3H), 6.09 (s, 1H), 2.08 (s, 3H), 2.04 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 169.1, 138.4, 134.6, 129.7, 128.8, 127.4, 125.4 (q, J = 285.30 Hz), 125.2, 62.2 (q, J = 27.0 Hz), 24.2, 19.7.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = -79.01.

HRMS: m/z Calculated for $C_{11}H_{12}ClF_3NO$, $[M+H]^+$, 266.0554; Found, 266.0545.

***N*-(2,2,2-Trifluoro-1,1-diphenylethyl)acetamide (2f)**



2f

Following general procedure A, **2f** was obtained in 65% yield (95 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.30. m.p. = 192.0 – 193.0 °C.

1H NMR (400 MHz, $CDCl_3$) δ = 7.37 (s, 10H), 2.10 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 168.7, 137.0, 128.6, 128.4, 128.2 (d, J = 2.1 Hz), 125.6 (q, J = 288.0 Hz), 69.1 (q, J = 27.5 Hz), 24.3.

^{19}F NMR (471 MHz, $CDCl_3$, composite pulse decoupling) δ = –67.43.

HRMS: m/z Calculated for $C_{16}H_{15}F_3NO$, $[M+H]^+$, 294.1100; Found, 294.1088.

***N*-(2,2,2-Trifluoro-1-phenyl-1-(*p*-tolyl)ethyl)acetamide (2g)**



2g

Following general procedure A, **2g** was obtained in 77% yield (118 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.27. m.p. = 158.0 – 160.0 °C.

1H NMR (400 MHz, $CDCl_3$) δ = 7.37 (s, 5H), 7.24 (d, J = 8.6 Hz, 2H), 7.17 (d, J = 8.4 Hz, 2H), 6.23 (s, 1H), 2.36 (s, 3H), 2.09 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 168.9, 138.5, 137.1, 134.1, 129.1, 128.5, 128.3, 128.1, 128.0, 125.6 (q, J = 288.0 Hz), 68.9 (q, J = 28.3 Hz), 24.2, 21.1.

^{19}F NMR (376 MHz, $CDCl_3$, composite pulse decoupling) δ = –67.62.

HRMS: m/z Calculated for $C_{17}H_{17}F_3NO$, $[M+H]^+$, 308.1257; Found, 308.1245.

***N*-(2,2,2-Trifluoro-1-phenyl-1-(*o*-tolyl)ethyl)acetamide (2h)**



2h

Following general procedure A, **2h** was obtained in 78% yield (119 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.28. m.p. = 165.1 – 165.9 °C.

1H NMR (500 MHz, $CDCl_3$) δ = 7.36 (s, 5H), 7.24 (d, J = 7.8 Hz, 1H), 7.19 – 7.10 (m, 3H), 6.22 (s, 1H), 2.34 (s, 3H), 2.10 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 168.4, 138.1, 137.1, 129.5, 128.7, 128.7, 128.6, 128.4, 128.3, 128.2, 125.7 (q, *J* = 288.0 Hz), 125.4, 69.2 (q, *J* = 27.7 Hz), 24.5, 21.8.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = -67.11.

HRMS: *m/z* Calculated for C₁₇H₁₇F₃NO, [M+H]⁺, 308.1257; Found, 308.1246.

***N*-(2,2,2-Trifluoro-1-phenyl-1-(*o*-tolyl)ethyl)acetamide (2i)**



2i

Following general procedure A, **2i** was obtained in 80% yield (113 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.24. m.p. = 176.9 - 179.9 °C.

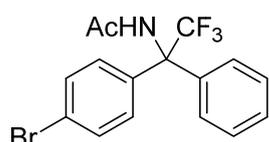
¹H NMR (500 MHz, CDCl₃) δ = 7.72 (d, *J* = 6.9 Hz, 1H), 7.41 - 7.27 (m, 5H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 7.5 Hz, 2H), 6.32 (s, 1H), 2.11 (s, 3H), 1.80 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 167.8, 137.2, 135.8, 135.0, 132.9, 129.1, 128.7, 128.3 (d, *J* = 3.6 Hz), 128.2, 127.3, 125.9, 125.6 (q, *J* = 288.3 Hz), 67.8 (q, *J* = 27.7 Hz), 24.2, 21.7.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = -69.09.

HRMS: *m/z* Calculated for C₁₇H₁₇F₃NO, [M+H]⁺, 308.1257; Found, 308.1249.

***N*-(1-(4-Bromophenyl)-2,2,2-trifluoro-1-phenylethyl)acetamide (2j)**



2j

Following general procedure A, **2j** was obtained in 74% yield (138 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.31. m.p. = 164.0 - 165.0 °C.

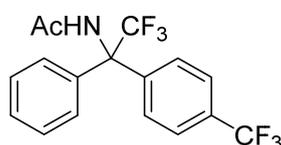
¹H NMR (400 MHz, CDCl₃) δ = 7.50 (d, *J* = 8.8 Hz, 2H), 7.39 - 7.32 (m, 5H), 7.28 (d, *J* = 8.3 Hz, 2H), 6.24 (s, 1H), 2.10 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ 168.6, 136.5, 135.7, 131.5, 130.1, 129.0, 128.5, 128.2, 125.4 (q, *J* = 288.3 Hz), 123.0, 68.9 (q, *J* = 27.9 Hz), 24.4.

¹⁹F NMR (376 MHz, CDCl₃, composite pulse decoupling) δ = -68.16.

HRMS: *m/z* Calculated for C₁₆H₁₃BrF₃NO, [M+H]⁺, 372.0205; Found, 372.0201.

***N*-(2,2,2-Trifluoro-1-phenyl-1-(4-(trifluoromethyl)phenyl)ethyl)acetamide (2k)**



2k

Following general procedure A, **2k** was obtained in 59%

yield (106 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.29. m.p. = 166.0 - 167 °C.

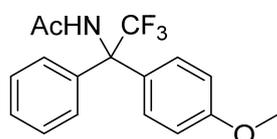
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 7.63 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 5.6 Hz, 3H), 7.32 (d, J = 8.5 Hz, 2H), 6.30 (s, 1H), 2.11 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 168.7, 140.4, 136.5, 130.7 (q, J = 32.7 Hz), 129.2, 129.0 (q, J = 2.3 Hz), 128.6, 128.2, 125.4 (q, J = 287.52 Hz) 125.3 (q, J = 3.6 Hz), 124.0 (q, J = 272.2 Hz), 69.0 (q, J = 27.6 Hz), 24.3.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = -62.80, -68.10.

HRMS: m/z Calculated for $\text{C}_{17}\text{H}_{14}\text{F}_6\text{NO}$, $[\text{M}+\text{H}]^+$, 362.0974; Found, 362.0960.

N-(2,2,2-Trifluoro-1-(4-methoxyphenyl)-1-phenylethyl)acetamide (**2l**)



2l

Following general procedure A, **2l** was obtained in 30% yield (48 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.19. m.p. = 140.0 - 142.0 °C.

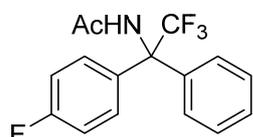
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 7.37 (s, 5H), 7.27 (d, J = 8.7 Hz, 2H), 6.88 (d, J = 8.5 Hz, 2H), 6.26 (s, 1H), 3.81 (s, 3H), 2.07 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 168.5, 159.6, 137.1, 129.6 (d, J = 1.8 Hz), 129.1, 128.5, 128.3, 128.2 (d, J = 2.3 Hz), 125.7 (q, J = 287.9 Hz), 113.7, 69.0 (q, J = 27.5 Hz), 55.4, 24.4.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = -67.84.

HRMS: m/z Calculated for $\text{C}_{17}\text{H}_{17}\text{F}_3\text{NO}_2$, $[\text{M}+\text{H}]^+$, 324.1206; Found, 324.1203.

N-(2,2,2-Trifluoro-1-(4-fluorophenyl)-1-phenylethyl)acetamide (**2m**)



2m

Following general procedure A, **2m** was obtained in 72% yield (112 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.30. m.p. = 181.9 - 182.6 °C.

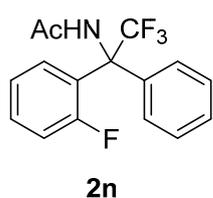
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.41 - 7.34 (m, 7H), 7.05 (t, J = 8.7 Hz, 2H), 6.22 (s, 1H), 2.10 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 168.3, 162.5 (d, J = 248.9 Hz), 136.7, 132.4, 130.3 (d, J = 8.2 Hz), 128.8, 128.4, 128.1, 125.4 (q, J = 287.8 Hz), 115.1 (d, J = 21.8 Hz), 68.8 (q, J = 27.0 Hz), 24.4.

¹⁹F NMR (376 MHz, CDCl₃, composite pulse decoupling) δ = -68.23, -113.33.

HRMS: m/z Calculated for C₁₆H₁₄F₄NO, [M+H]⁺, 312.1006; Found, 312.0991.

***N*-(2,2,2-Trifluoro-1-(2-fluorophenyl)-1-phenylethyl)acetamide (2n)**



Following general procedure A, **2n** was obtained in 53% yield (83 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.31. m.p. = 164.8 - 165.8 °C.

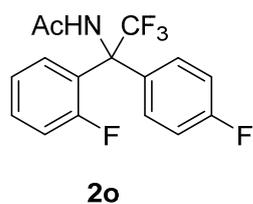
¹H NMR (500 MHz, CDCl₃) δ = 7.44 (ddd, J = 9.9 Hz, 7.3 Hz, 1.8 Hz, 1H), 7.40 - 7.36 (m, 4H), 7.34 - 7.30 (m, 2H), 7.19 (td, J = 7.9 Hz, 1.4, 1H), 7.04 (ddd, J = 12.8 Hz, 8.2 Hz, 1.1 Hz, 1H), 6.56 (s, 1H), 2.06 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 168.8, 160.3 (d, J = 249.3 Hz), 137.3, 130.5 (dd, J = 5.0 Hz, 2.7 Hz), 129.1, 128.7, 127.2, 125.1 (q, J = 288.1 Hz), 124.6 (d, J = 8.2 Hz), 124.1 (d, J = 3.6 Hz), 116.8, 116.6, 66.7 (q, J = 28.7 Hz), 24.3.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = -69.03, -109.73.

HRMS: m/z Calculated for C₁₆H₁₄F₄NO, [M+H]⁺, 312.1006; Found, 312.0992.

***N*-(2,2,2-Trifluoro-1-(2-fluorophenyl)-1-(4-fluorophenyl)ethyl)acetamide (2o)**



Following general procedure A, **2o** was obtained in 81% yield (133 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.27. m.p. = 174.9 - 175.3 °C.

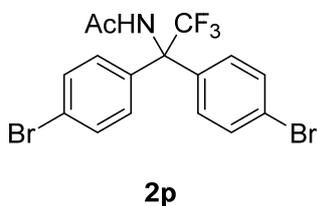
¹H NMR (500 MHz, CDCl₃) δ = 7.40 - 7.31 (m, 4H), 7.20 - 7.16 (m, 1H), 7.09 - 7.03 (m, 3H), 6.54 (s, 1H), 2.07 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 168.7, 162.8 (d, J = 249.3 Hz), 160.4 (d, J = 248.9 Hz), 133.1 (d, J = 3.6 Hz), 130.9, 130.8 (d, J = 2.7 Hz), 129.4, 129.4, 125.1 (q, J = 288.3 Hz), 124.2 (d, J = 3.6 Hz), 116.9 (d, J = 23.6 Hz), 115.7 (d, J = 21.8 Hz), 66.7 (q, J = 29.2 Hz), 24.4.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) $\delta = -69.35$ (d, $J = 6.9$ Hz), -109.61 , -112.61 .

HRMS: m/z Calculated for C₁₆H₁₃F₅NO, [M+H]⁺, 330.0912; Found, 330.0905.

***N*-(1,1-Bis(4-bromophenyl)-2,2,2-trifluoroethyl)acetamide (2p)**



Following general procedure A, **2p** was obtained in 79% yield (177 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.36. m.p. = 199.0 – 199.8 °C.

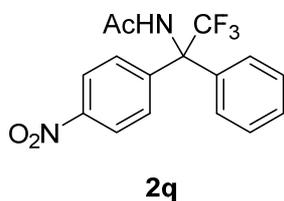
¹H NMR (400 MHz, CDCl₃) $\delta = 7.50$ (d, $J = 8.8$ Hz, 4H), 7.25 (d, $J = 8.8$ Hz, 4H), 6.21 (s, 1H), 2.08 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) $\delta = 168.8$, 135.2, 131.6, 130.1, 125.1 (q, $J = 287.7$ Hz), 123.3, 68.8 (q, $J = 27.8$ Hz, 27.4 Hz), 24.3.

¹⁹F NMR (376 MHz, CDCl₃, composite pulse decoupling) $\delta = -68.94$.

HRMS: m/z Calculated for C₁₆H₁₃Br₂F₃NO, [M+H]⁺, 449.9310; Found, 449.9294.

***N*-(2,2,2-Trifluoro-1-(4-nitrophenyl)-1-phenylethyl)acetamide (2q)**



Following general procedure A, **2q** was obtained in 62% yield (105 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.15. m.p. = 190.7 – 192.7 °C.

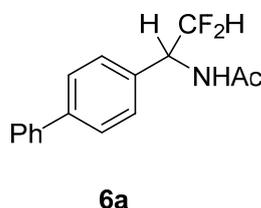
¹H NMR (500 MHz, (CD₃)₂CO) $\delta = 8.49$ (s, 1H), 7.81 (d, $J = 6.9$ Hz, 2H), 7.16 (d, $J = 7.8$ Hz, 2H), 6.98 (dq, $J = 4.7$ Hz, 2.4 Hz, 3H), 6.86 (d, $J = 6.4$ Hz, 2H), 1.57 (s, 3H).

¹³C NMR (126 MHz, (CD₃)₂CO) $\delta = 169.3$, 146.9, 144.4, 136.0, 129.3, 128.8, 128.4, 128.1, 125.3 (q, $J = 287.9$ Hz), 123.2, 67.9 (q, $J = 28.2$ Hz), 23.4.

¹⁹F NMR (471 MHz, (CD₃)₂CO, composite pulse decoupling) $\delta = -66.12$.

HRMS: m/z Calculated for C₁₆H₁₄F₃N₂O₃, [M+H]⁺, 339.0951; Found, 339.0956.

***N*-(1-([1,1'-Biphenyl]-4-yl)-2,2-difluoroethyl)acetamide (6a)**



Following general procedure B, **6a** was obtained in 48% yield (40 mg) as a white solid after column chromatography

(eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.12. m.p. = 189.8 – 190.7 °C.

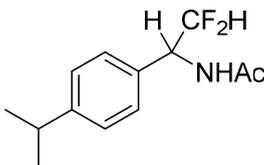
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.61 (d, J = 8.3 Hz, 2H), 7.57 (d, J = 7.3 Hz, 2H), 7.51 – 7.40 (m, 4H), 7.37 (t, J = 7.3 Hz, 1H), 6.14 (d, J = 8.7 Hz, 1H), 6.07 (td, J = 55.5 Hz, 2.1 Hz, 1H), 5.46 (td, J = 14.8 Hz, 14.2 Hz, 8.0 Hz, 1H), 2.10 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, $(\text{CD}_3)_2\text{CO}$) δ = 170.1, 141.8, 141.3, 135.5, 129.8, 129.6, 128.4, 127.9, 127.8, 116.4 (t, J = 244.3 Hz), 55.2 (t, J = 22.6 Hz), 22.8.

$^{19}\text{F NMR}$ (471 MHz, $(\text{CD}_3)_2\text{CO}$, composite pulse decoupling) δ = –125.77 (d, J = 279.2 Hz), –126.96 (d, J = 279.2 Hz).

HRMS: m/z Calculated for $\text{C}_{16}\text{H}_{16}\text{F}_2\text{NO}$, $[\text{M}+\text{H}]^+$, 276.1194; Found, 276.1187.

N–(2,2–Difluoro–1–(4–isopropylphenyl)ethyl)acetamide (**6b**)



6b

Following general procedure B, **6b** was obtained in 60% yield (43 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.17. m.p. = 80.9 – 82.5 °C.

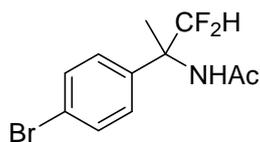
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ = 7.27 (d, J = 8.2 Hz, 2H), 7.24 (d, J = 8.4 Hz, 2H), 6.15 (t, J = 8.7 Hz, 1H), 6.01 (t, J = 55.6 Hz, 1H), 5.44 – 5.30 (m, 1H), 2.91 (sep, J = 7.0 Hz, 1H), 2.06 (s, 3H), 1.24 (d, J = 7.0 Hz, 6H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 169.9, 149.7, 131.5 (d, J = 4.5 Hz), 128.0, 127.2, 113.9 (t, J = 247.0 Hz), 54.7 (t, J = 20.9 Hz), 34.0, 24.0, 23.4.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = –125.36 (d, J = 280.6 Hz), –127.17 (d, J = 280.5 Hz).

HRMS: m/z Calculated for $\text{C}_{13}\text{H}_{18}\text{F}_2\text{NO}$, $[\text{M}+\text{H}]^+$, 242.1351; Found, 242.1341.

N–(2–(4–Bromophenyl)–1,1–difluoropropan–2–yl)acetamide (**6c**)



6c

Following general procedure B, **6c** was obtained in 73% yield (64 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.14. m.p. = 157.0 – 157.5 °C.

¹H NMR (500 MHz, CDCl₃) δ = 7.49 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 6.30 (t, *J* = 56.5 Hz, 1H), 6.02 – 5.91 (m, 1H), 2.03 (s, 3H), 1.72 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 169.9, 138.2, 131.9, 128.0, 122.3, 116.3 (t, *J* = 249.3 Hz), 60.7 (t, *J* = 20.9 Hz), 23.9, 20.4.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = –128.10 (d, *J* = 276.6 Hz), –129.63 (d, *J* = 276.1 Hz).

HRMS: *m/z* Calculated for C₁₁H₁₃BrF₂NO, [M+H]⁺, 292.0143; Found, 292.0150.

***N*–(2,2–Difluoro–1,1–diphenylethyl)acetamide (6d)**



6d

Following general procedure B, **6d** was obtained in 61% yield (50 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.28. m.p. = 158.0 – 159.8 °C.

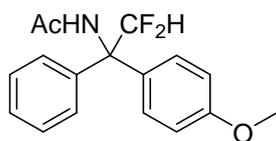
¹H NMR (500 MHz, CDCl₃) δ = 7.40 – 7.34 (m, 6H), 7.31 (dd, *J* = 7.6 Hz, 2.3 Hz, 4H), 7.14 (t, *J* = 56.7 Hz, 1H), 6.29 (s, 1H), 2.06 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 169.8, 139.0, 128.6, 128.5, 127.9, 114.6 (t, *J* = 249.8 Hz), 67.3 (t, *J* = 21.6 Hz), 23.7.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = –123.12.

HRMS: *m/z* Calculated for C₁₆H₁₆F₂NO, [M+H]⁺, 276.1194; Found, 276.1186.

***N*–(2,2–Difluoro–1–(4–methoxyphenyl)–1–phenylethyl)acetamide (6e)**



6e

Following general procedure B, **6e** was obtained in 50% yield (46 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.18. m.p. = 136.0 – 138.5 °C.

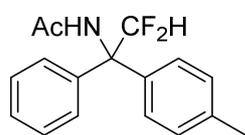
¹H NMR (500 MHz, CDCl₃) δ = 7.36 (td, *J* = 5.7 Hz, 2.8, 3H), 7.32 (dd, *J* = 7.8 Hz, 2.3, 3H), 7.22 – 7.19 (m, 2H), 7.11 (t, *J* = 56.9 Hz, 1H), 6.91 – 6.81 (m, 2H), 6.25 (s, 1H). 3.81 (s, 3H), 2.05 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 169.7, 159.5, 139.3, 131.0, 129.3, 128.6, 128.4, 127.8, 114.7 (t, *J* = 249.3 Hz), 113.9, 67.0 (t, *J* = 21.6 Hz), 55.4, 23.8.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) $\delta = -122.67$ (d, $J = 280.0$ Hz), -123.84 (d, $J = 280.0$ Hz).

HRMS: m/z Calculated for C₁₇H₁₈F₂NO₂, [M+H]⁺, 306.1300; Found, 306.1303.

***N*-(2,2-Difluoro-1-phenyl-1-(*p*-tolyl)ethyl)acetamide (6f)**



6f

Following general procedure B, **6f** was obtained in 67% yield (58 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.30. m.p. = 176.2 – 177.8 °C.

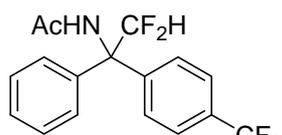
¹H NMR (400 MHz, CDCl₃) $\delta = 7.36$ (dt, $J = 4.8, 2.5$ Hz, 3H), 7.31 (dd, $J = 7.6$ Hz, 2.4 Hz, 3H), 7.18 (s, 4H), 7.12 (t, $J = 56.7$ Hz, 1H), 6.25 (s, 1H), 2.35 (s, 3H), 2.06 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) $\delta = 169.8, 139.2, 138.3, 136.0, 129.3, 128.6, 128.4, 127.9$ (t, $J = 2.0$), 127.8 (t, $J = 2.0$ Hz), 114.6 (t, $J = 249.4$ Hz), 67.1 (t, $J = 21.7$ Hz), 23.7, 21.2.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) $\delta = 122.87$ (d, $J = 280.6$ Hz), 123.58 (d, $J = 280.6$ Hz).

HRMS: m/z Calculated for C₁₇H₁₈F₂NO, [M+H]⁺, 290.1351; Found, 290.1339.

***N*-(2,2-Difluoro-1-phenyl-1-(4-(trifluoromethyl)phenyl)ethyl)acetamide (6g)**



6g

Following general procedure B, **6g** was obtained in 90% yield (92 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.29. m.p. = 153.0 – 153.6 °C.

¹H NMR (500 MHz, CDCl₃) $\delta = 7.64$ (d, $J = 8.2$ Hz, 2H), 7.48 (d, $J = 8.2$ Hz, 2H), 7.40 – 7.35 (m, 3H), 7.26 – 7.24 (m, 2H), 7.12 (t, $J = 56.6$ Hz, 1H), 6.33 (s, 1H), 2.07 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) $\delta = 170.0, 143.0, 138.1$ (d, $J = 2.7$ Hz), 130.6 (q, $J = 32.8$ Hz), 128.9, 128.8, 128.3, 128.0, 125.6 (q, $J = 3.8$ Hz), 124.0 (q, $J = 272.2$ Hz), 114.3 (t, $J = 249.9$ Hz), 67.2 (t, $J = 21.9$ Hz), 23.5.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) $\delta = -62.76, -122.30$ (d, $J = 281.2$ Hz), -124.15 (d, $J = 281.8$ Hz).

HRMS: m/z Calculated for C₁₇H₁₅F₅NO, [M+H]⁺, 344.1068; Found, 344.1056.

***N*-(2,2-Difluoro-1-(4-fluorophenyl)-1-phenylethyl)acetamide (6h)**



6h

Following general procedure B, **6h** was obtained in 63% yield (56 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.27. m.p. = 170.5 – 171.0 °C.

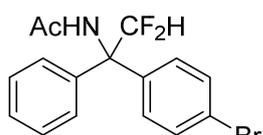
¹H NMR (500 MHz, CDCl₃) $\delta = 7.39 - 7.35$ (m, 3H), $7.33 - 7.27$ (m, 4H), $7.11 - 6.98$ (m, 3H), 6.26 (s, 1H), 2.06 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) $\delta = 169.7, 162.5$ (d, $J = 248.4$ Hz), $138.6, 134.7, 127.7$ (t, $J = 2.0$ Hz), $128.6, 128.5, 127.7, 127.7, 127.7, 115.4$ (d, $J = 21.3$ Hz), 114.4 (t, $J = 249.7$ Hz), 66.8 (t, $J = 21.8$ Hz), 23.6 .

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) $\delta = -113.63, -123.24, -123.25$.

HRMS: m/z Calculated for C₁₆H₁₅F₃NO, [M+H]⁺, 294.1100; Found, 294.1090.

***N*-(1-(4-Bromophenyl)-2,2-difluoro-1-phenylethyl)acetamide (6i)**



6i

Following general procedure B, **6i** was obtained in 47% yield (50 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.27. m.p. = 172.5 – 173.5 °C.

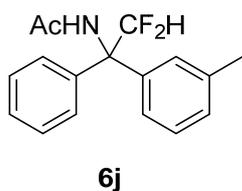
¹H NMR (500 MHz, CDCl₃) $\delta = 7.50$ (d, $J = 7.9$ Hz, 2H), $7.41 - 7.34$ (m, 3H), 7.27 (d, $J = 6.3$ Hz, 2H), 7.20 (d, $J = 6.8$ Hz, 2H), 7.03 (t, $J = 56.6$ Hz, 1H), 6.25 (s, 1H), 2.06 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) $\delta = 169.9, 138.3, 138.1, 131.7, 129.6, 128.7, 128.7, 127.9, 122.7, 114.3$ (t, $J = 249.8$ Hz), 67.0 (t, $J = 22.0$ Hz), 23.6 .

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) $\delta = -122.74$ (d, $J = 280.9$ Hz), -123.76 (d, $J = 280.9$ Hz).

HRMS: m/z Calculated for C₁₆H₁₅BrF₂NO, [M+H]⁺, 354.0300; Found, 354.0293.

N-(2,2-Difluoro-1-phenyl-1-(*m*-tolyl)ethyl)acetamide (**6j**)



Following general procedure B, **6j** was obtained in 79% yield (69 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.33. m.p. = 148.8 – 149.7 °C.

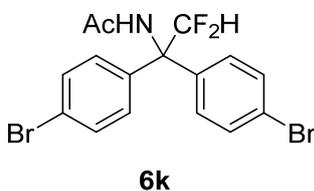
$^1\text{H NMR}$ (400 MHz, $(\text{CD}_3)_2\text{CO}$) δ = 7.98 (s, 1H), 7.45 – 7.26 (m, 6H), 7.23 (dd, J = 15.1 Hz, 7.4 Hz, 2H), 7.19 – 7.12 (m, 1H), 7.09 (d, J = 7.2 Hz, 1H), 2.30 (s, 3H), 2.01 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 169.7, 139.1, 139.0, 138.3, 129.3, 128.6, 128.5, 128.4, 127.9 (t, J = 2.0 Hz), 125.1, 114.6 (t, J = 249.5 Hz), 67.3 (t, J = 21.6 Hz), 23.7, 21.8.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = -122.72 (J = 280.24 Hz), -123.34 (J = 280.24 Hz).

HRMS: m/z Calculated for $\text{C}_{17}\text{H}_{18}\text{F}_2\text{NO}$, $[\text{M}+\text{H}]^+$, 290.1351; Found, 290.1343.

N-(1,1-Bis(4-bromophenyl)-2,2-difluoroethyl)acetamide (**6k**)



Following general procedure B, **6k** was obtained in 67% yield (87 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum ether/EtOAc 3:1): 0.34. m.p. = 198.5 – 199.9 °C.

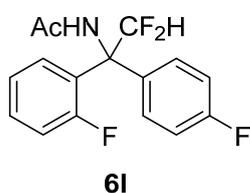
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ = 7.50 (d, J = 8.8 Hz, 4H), 7.17 (d, J = 8.7 Hz, 4H), 6.97 (t, J = 56.5 Hz, 1H), 6.20 (s, 1H), 2.06 (s, 3H).

$^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ = 169.8, 137.5, 131.9, 129.6, 123.1, 114.1 (t, J = 250.0 Hz), 66.8 (t, J = 21.6 Hz), 23.7.

$^{19}\text{F NMR}$ (471 MHz, CDCl_3 , composite pulse decoupling) δ = -123.33 .

HRMS: m/z Calculated for $\text{C}_{16}\text{H}_{14}\text{Br}_2\text{F}_2\text{NO}$, $[\text{M}+\text{H}]^+$, 431.9405; Found, 431.9398.

N-(2,2-Difluoro-1-(2-fluorophenyl)-1-(4-fluorophenyl)ethyl)acetamide (**6l**)



Following general procedure B, **6l** was obtained in 71% yield (66 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). R_f (Petroleum

ether/EtOAc 3:1): 0.35. m.p. = 170.6 – 171.6 °C.

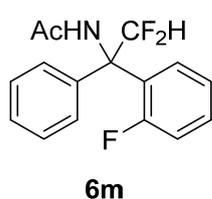
¹H NMR (500 MHz, CDCl₃) δ = 7.52 – 7.34 (m, 3H), 7.26 – 7.20 (m, 3H), 7.11 – 7.01 (m, 3H), 6.45 (s, 1H), 2.02 (s, 3H).

¹³C NMR (126 MHz, CDCl₃, composite pulse decoupling) δ = 170.3, 162.9 (d, *J* = 248.9 Hz), 160.5 (d, *J* = 248.0 Hz), 132.6, 130.47 (d, *J* = 9.1 Hz), 129.6 (d, *J* = 8.2 Hz), 129.1 (dd, *J* = 5.0, 2.7 Hz), 126.9, 124.1 (d, *J* = 3.6 Hz), 117.1 (d, *J* = 22.7 Hz), 115.4 (d, *J* = 21.8 Hz), 112.7 (t, *J* = 249.0 Hz), 65.0 (dd, *J* = 25.4 Hz, 20.4 Hz), 23.7.

¹⁹F NMR (471 MHz, CDCl₃) δ = -109.96 (d, *J* = 4.8), -113.2, -121.59 (dd, *J* = 283.1 Hz, 5.6), -131.78 (d, *J* = 282.6 Hz).

HRMS: *m/z* Calculated for C₁₆H₁₄F₄NO, [M+H]⁺, 312.1006; Found, 312.0998.

N-(2,2-Difluoro-1-(2-fluorophenyl)-1-phenylethyl)acetamide (6m)



Following general procedure B, **6m** was obtained in 72% yield (63 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.41. m.p. = 152.1 – 153.0 °C.

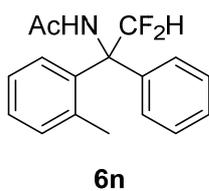
¹H NMR (500 MHz, CDCl₃) δ = 7.53 – 7.27 (m, 7H), 7.26 – 7.19 (m, 2H), 7.06 (dd, *J* = 12.4 Hz, 8.1 Hz, 1H), 6.49 (s, 1H), 2.03 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 170.2, 160.4 (d, *J* = 247.0 Hz), 136.7, 130.2 (d, *J* = 9.5 Hz), 129.2 – 128.9 (m), 128.8, 128.3, 127.6, 123.9 (d, *J* = 3.2 Hz), 116.9 (d, *J* = 22.7 Hz), 112.7 (dd, *J* = 248.8 Hz, 246.2 Hz), 65.2 (dd, *J* = 24.9 Hz, 20.1 Hz), 23.6.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = -109.94 (d, *J* = 4.3 Hz), -109.94 (dd, *J* = 282.80 Hz, 4.3 Hz), -131.78 (d, *J* = 282.6 Hz).

HRMS: *m/z* Calculated for C₁₆H₁₅F₃NO, [M+H]⁺, 294.1100; Found, 294.1093.

N-(2,2-Difluoro-1-phenyl-1-(*o*-tolyl)ethyl)acetamide (6n)



Following general procedure B, **6n** was obtained in 71% yield (62 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 3:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.28. m.p. = 1179.9 – 180.9 °C.

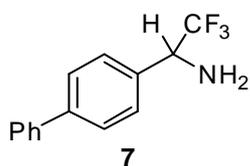
¹H NMR (500 MHz, CDCl₃) δ = 7.63 – 7.57 (m, 1H), 7.50 – 7.32 (m, 4H), 7.29 (t, *J* = 7.2 Hz, 2H), 7.18 (dd, *J* = 22.1 Hz, 7.5 Hz, 3H), 6.33 (s, 1H), 2.04 (s, 3H), 1.90 (s, 3H).

¹³C NMR (126 MHz, CDCl₃) δ = 169.4, 137.5 (d, *J* = 4.1 Hz), 136.7, 135.9 (d, *J* = 1.8 Hz), 133.3, 128.8, 128.5, 128.2, 127.8, 127.7, 127.7, 125.8, 113.2 (t, *J* = 246.8 Hz), 66.8 (dd, *J* = 25.0 Hz, 18.6 Hz), 23.5, 22.1.

¹⁹F NMR (471 MHz, CDCl₃, composite pulse decoupling) δ = -120.68 (d, *J* = 79.2 Hz), -131.89 (d, *J* = 279.2 Hz).

HRMS: *m/z* Calculated for C₁₇H₁₈F₂NO, [M+H]⁺, 290.1351; Found, 290.1337.

1-([1,1'-Biphenyl]-4-yl)-2,2,2-trifluoroethan-1-amine (**7**)



Following diversification procedure, **7** was obtained in 80% yield (20 mg) as a white solid after column chromatography (eluent = Petroleum ether/EtOAc 6:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.26.

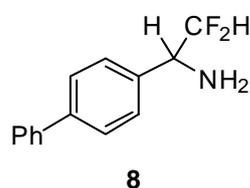
¹H NMR (400 MHz, (CD₃)₂CO) δ = 7.72 – 7.65 (m, 4H), 7.59 (d, *J* = 8.3 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.40 – 7.34 (m, 1H), 5.19 (q, *J* = 7.9 Hz, 1H).

¹³C NMR (126 MHz, (CD₃)₂CO) δ = 142.1, 141.2, 135.5, 130.4, 129.8, 128.5, 127.8, 127.8, 126.7 (q, *J* = 276.5 Hz), 66.1 (q, *J* = 28.2 Hz).

¹⁹F NMR (376 MHz, (CD₃)₂CO, composite pulse decoupling) δ = -74.81.

HRMS: *m/z* Calculated for C₁₄H₁₃F₃N, [M+H]⁺, 252.0995; Found, 252.1005.

1-([1,1'-Biphenyl]-4-yl)-2,2-difluoroethan-1-amine (**8**)



Following diversification procedure, **8** was obtained in 39% yield (90 mg) as a colorless liquid after column chromatography (eluent = Petroleum ether/EtOAc 6:1 v/v). *R_f* (Petroleum ether/EtOAc 3:1): 0.14.

¹H NMR (500 MHz, (CD₃)₂CO) δ = 7.68 – 7.63 (m, 4H), 7.54 (d, *J* = 8.4 Hz, 2H), .46 (dd, *J* = 8.5 Hz, 6.9 Hz, 2H), 7.39 – 7.34 (m, 1H), 6.12 (td, *J* = 56.5 Hz, 5.5 Hz, 1H), 4.83 (ddd, *J* = 12.5 Hz, 10.1 Hz, 5.4 Hz, 1H).

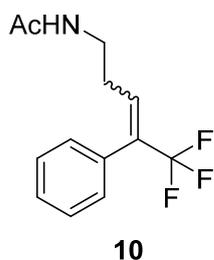
¹³C NMR (101 MHz, (CD₃)₂CO) δ = 141.51, 141.44, 137.44, 137.37, 130.08,

129.81, 128.35, 127.79, 118.41 (dd, $J=245.0, 241.4$), 67.20 (dd, $J=23.8, 21.6$).

^{19}F NMR (471 MHz, $(\text{CD}_3)_2\text{CO}$), composite pulse decoupling) $\delta = -123.15$, (d, $J = 275.2$ Hz), -125.93 (d, $J = 275.9$ Hz).

HRMS: m/z Calculated for $\text{C}_{14}\text{H}_{14}\text{F}_2\text{N}$, $[\text{M}+\text{H}]^+$, 234.1089; Found, 234.1079.

***N*-(5,5,5-Trifluoro-4-phenylpent-3-en-1-yl)acetamide (10)**



Following general procedure A, **10** was obtained in 39% yield (90 mg) as a colorless liquid after column chromatography (eluent = Petroleum ether/EtOAc 1:1 v/v). R_f (Petroleum ether/EtOAc 1:1): 0.21. $Z/E = 2:3$.

E isomer ^1H NMR (500 MHz, CDCl_3) $\delta = 7.41 - 7.33$ (m, 3H), 7.23 - 7.19 (m, 2H), 6.40 (t, $J = 7.5$ Hz, 1H), 5.47 (s, 1H), 3.30 (q, $J = 6.7$ Hz, 2H), 2.24 (q, $J = 7.2$ Hz, 2H), 1.94 (s, 3H).

Mixture ^{13}C NMR (126 MHz, CDCl_3) $\delta = 171.7, 171.4, 137.7$ (d, $J = 3.2$ Hz), 136.0, 136.0, 134.2, 134.1, 134.0, 133.9, 133.6, 132.7 (q, $J = 5.7$ Hz), 132.0, 131.9, 131.6, 129.6, 128.9, 128.8, 128.5, 128.4, 128.2, 123.9 (d, $J = 275.7$ Hz), 123.3 (d, $J = 273.1$ Hz), 120.8, 118.3, 40.1, 39.0, 38.7, 29.0, 28.4, 23.2, 23.1, 20.0, 13.5.

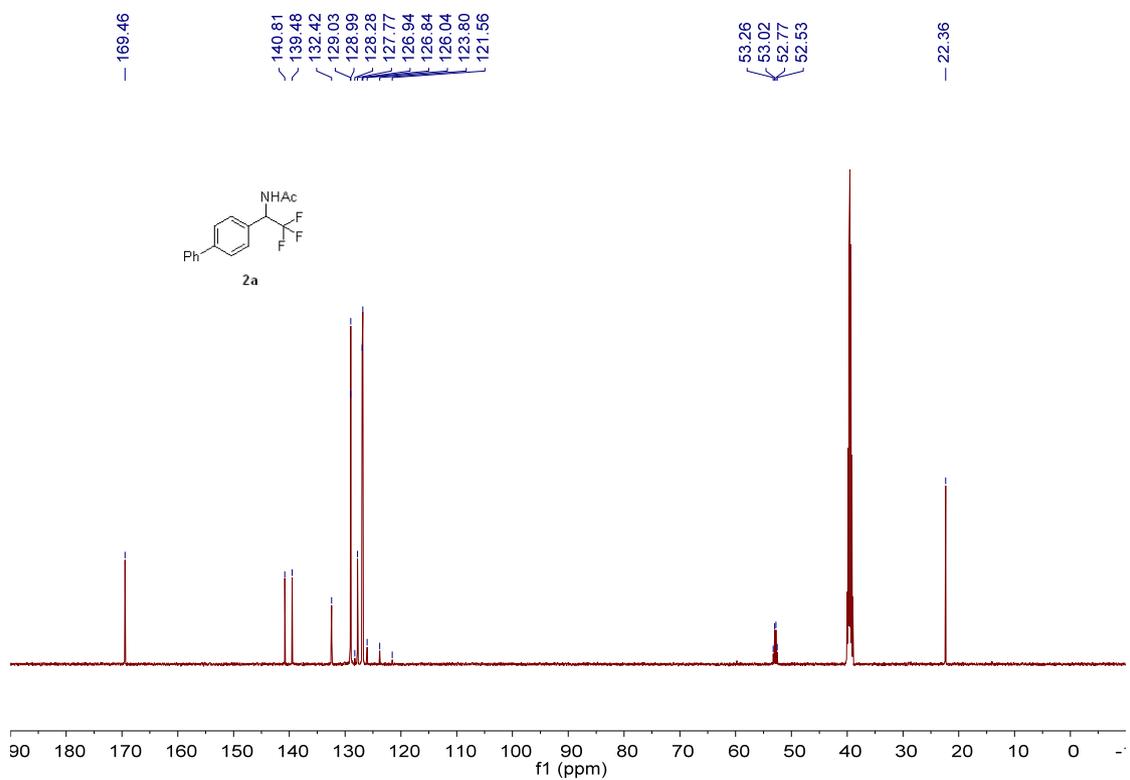
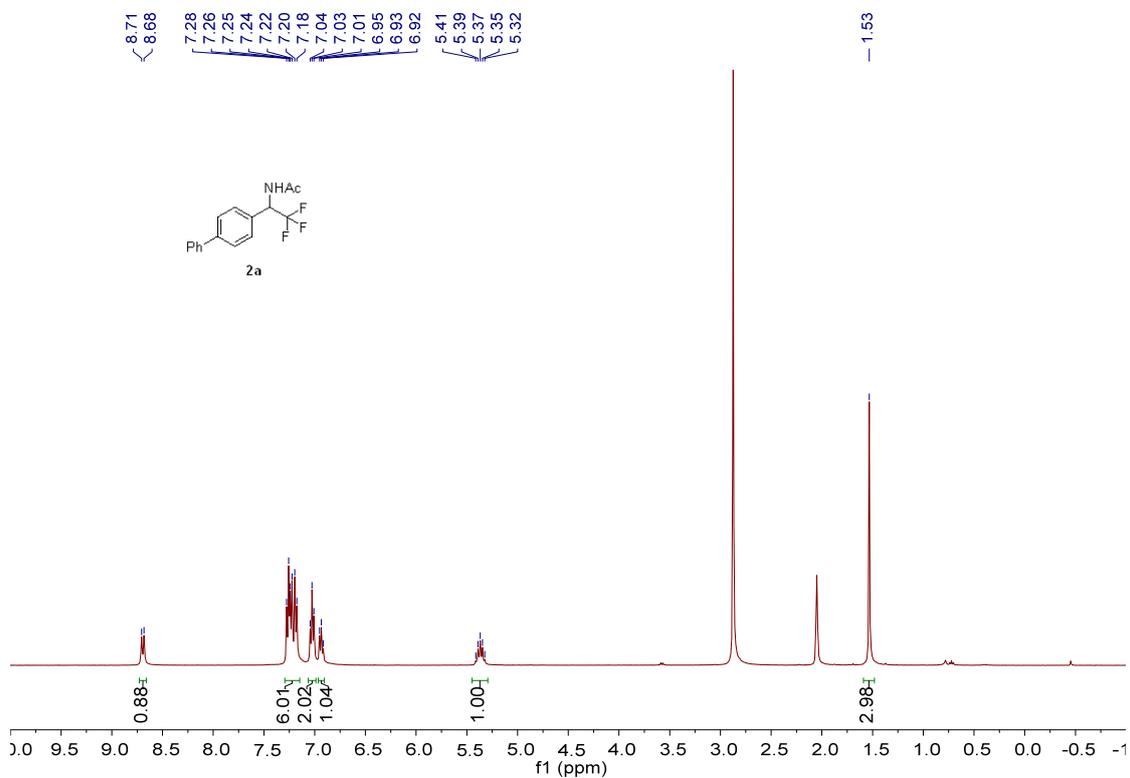
^{19}F NMR (471 MHz, CDCl_3 , composite pulse decoupling) $\delta = -56.93, -66.00$.

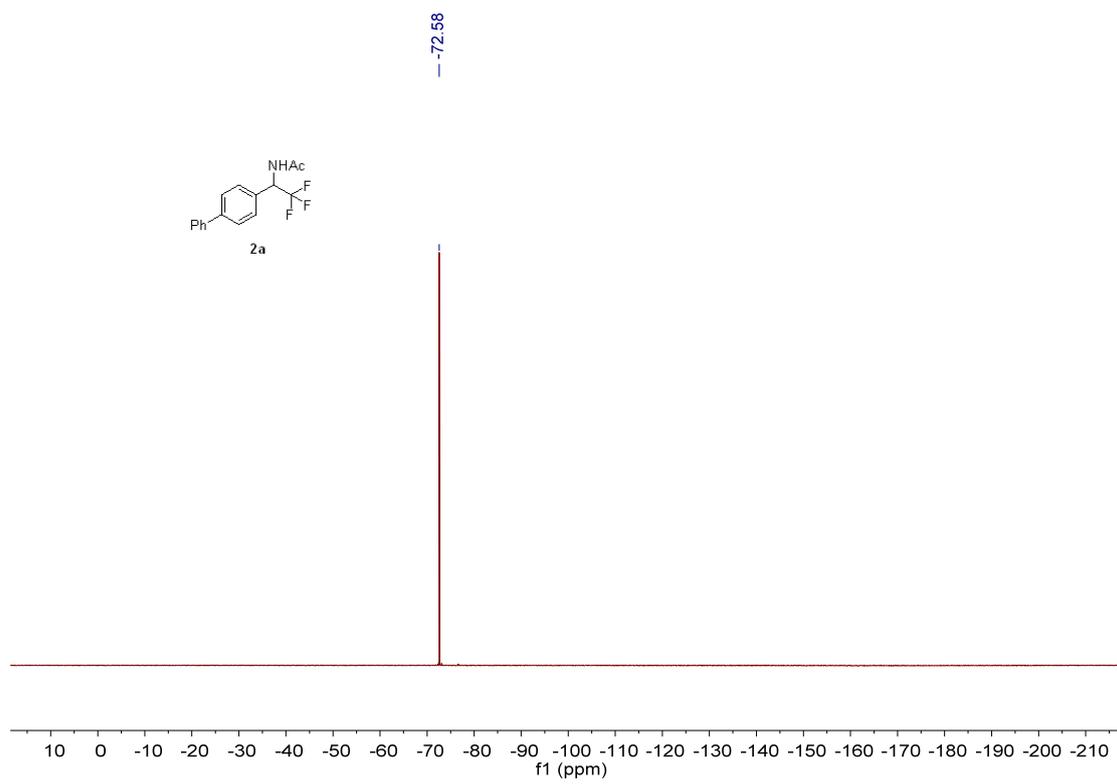
HRMS: m/z Calculated for $\text{C}_{13}\text{H}_{15}\text{F}_3\text{NO}$, $[\text{M}+\text{H}]^+$, 258.1100; Found, 258.1094.

VII. References

- [1] Hu, M. Y. *et al. J. Am. Chem. Soc.* 2013, **135**, 17302
- [2] Tan, D. H. *et al. Adv. Syn. Catal.* 2018, **360**, 1032.
- [3] Wu, J. J. *et al. RSC Adv.* 2015, **5**, 34498.
- [4] Li, J. J. *et al. Chem. Commun.* 2017, **53**, 10299.

VIII. NMR spectra for compounds

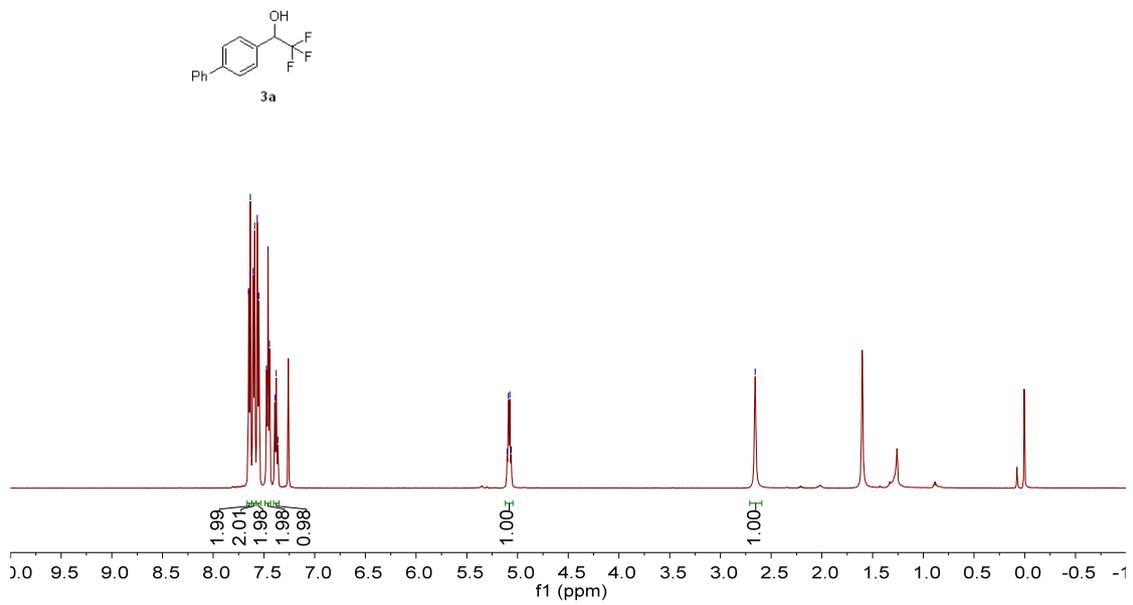


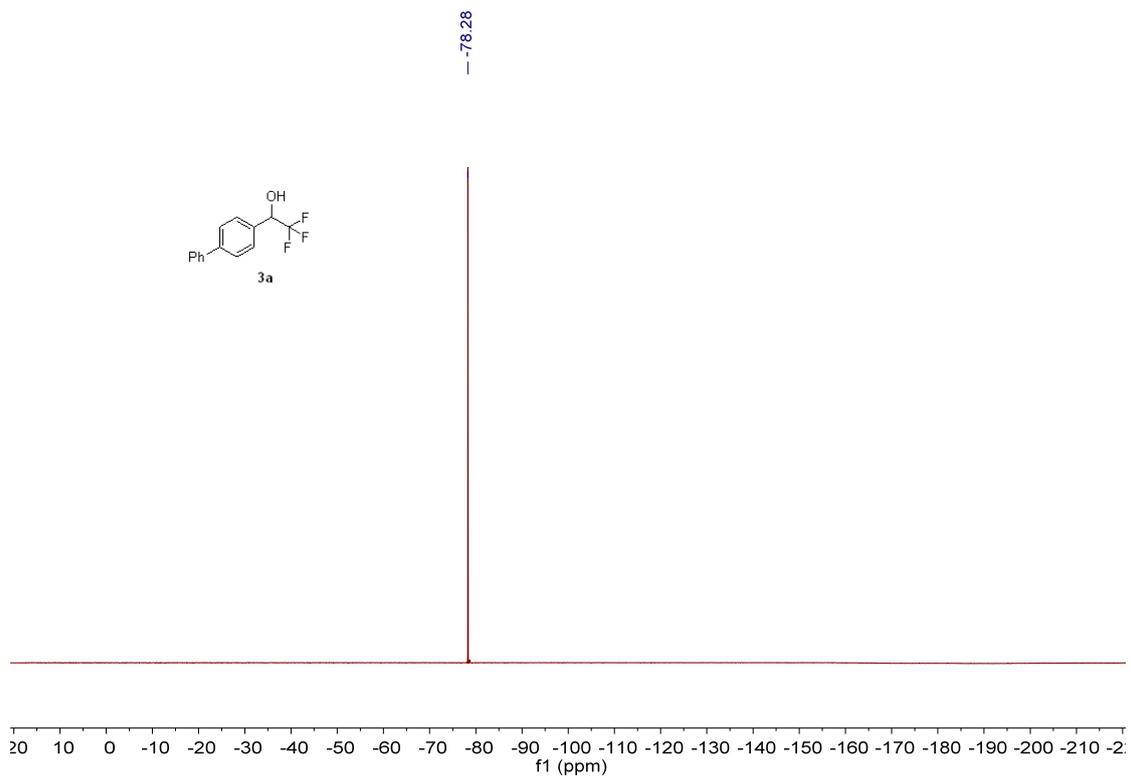
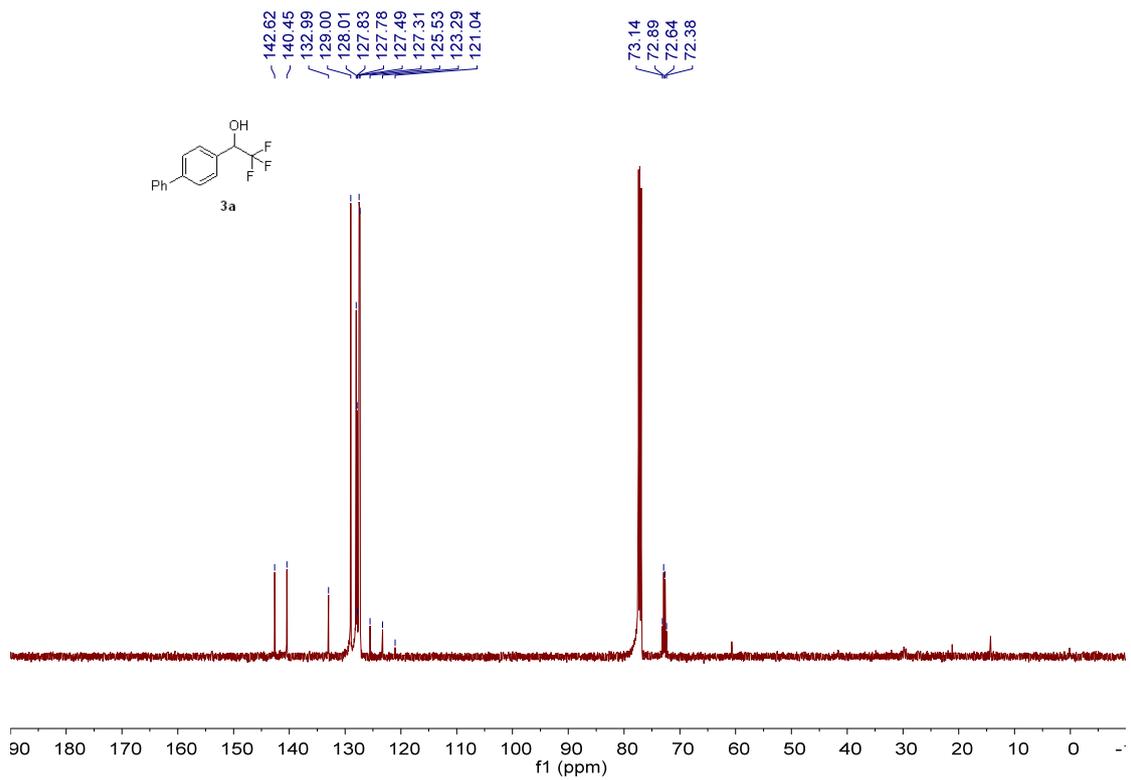


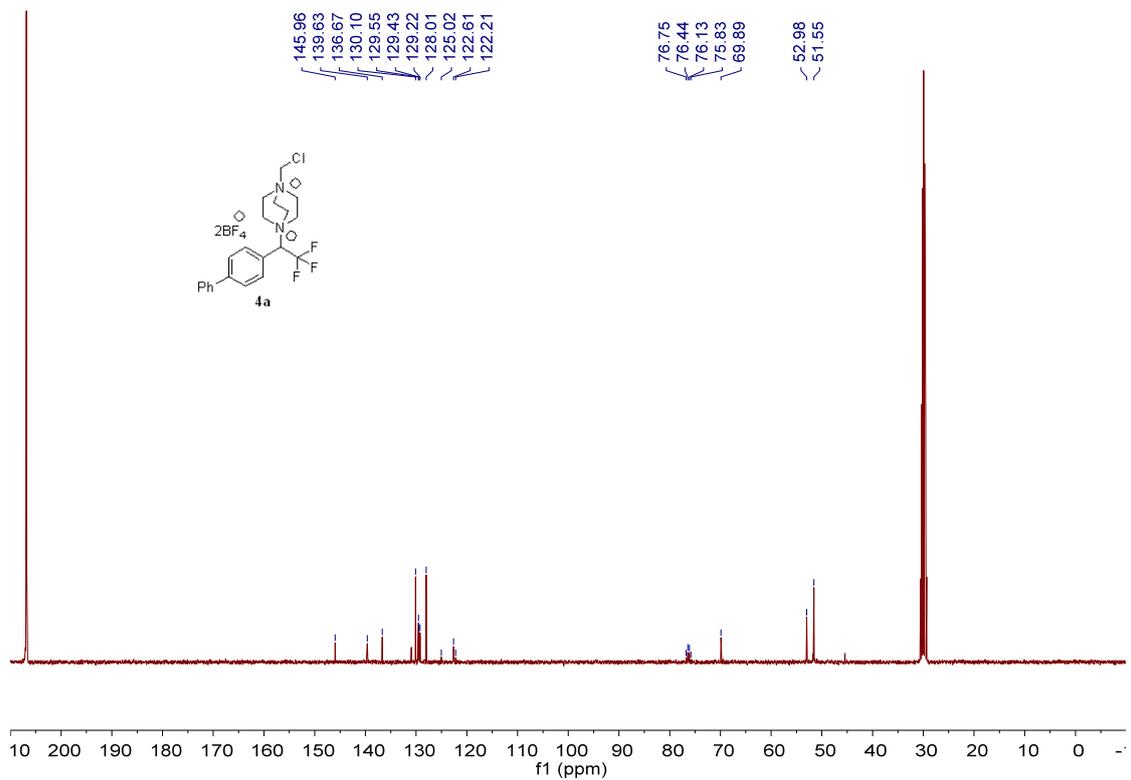
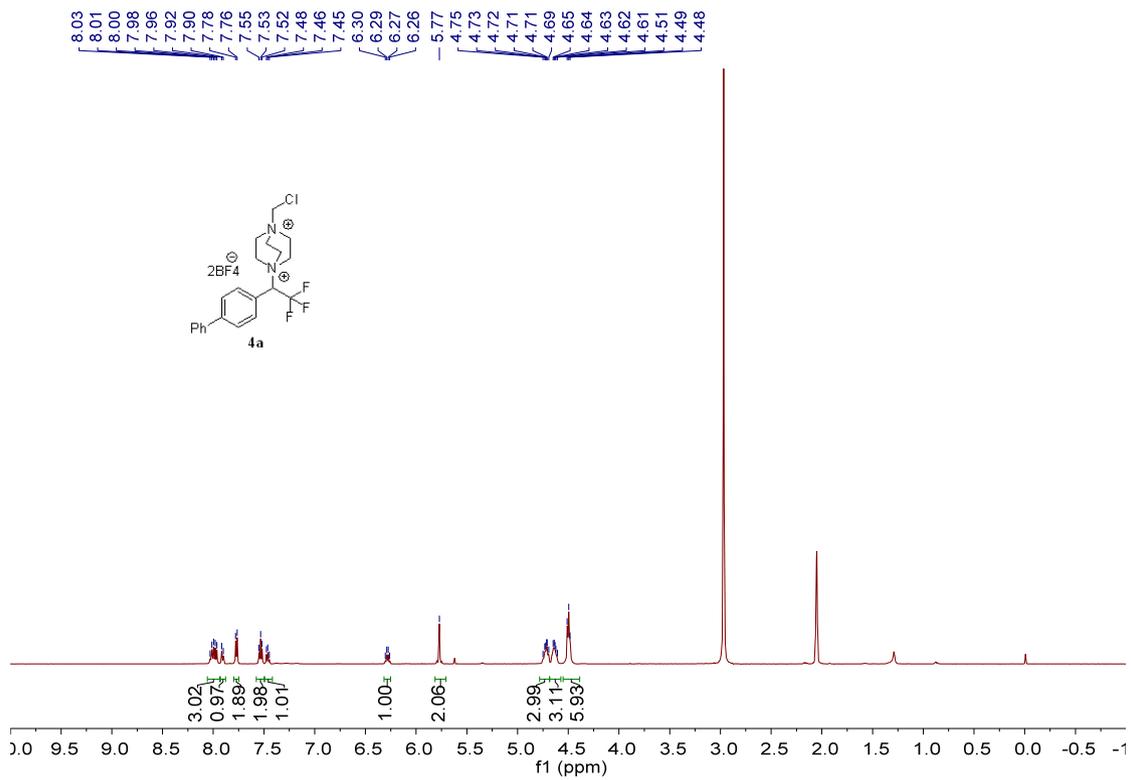
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7.63
7.61
7.59
7.57
7.55
7.48
7.46
7.45
7.39
7.38
7.36

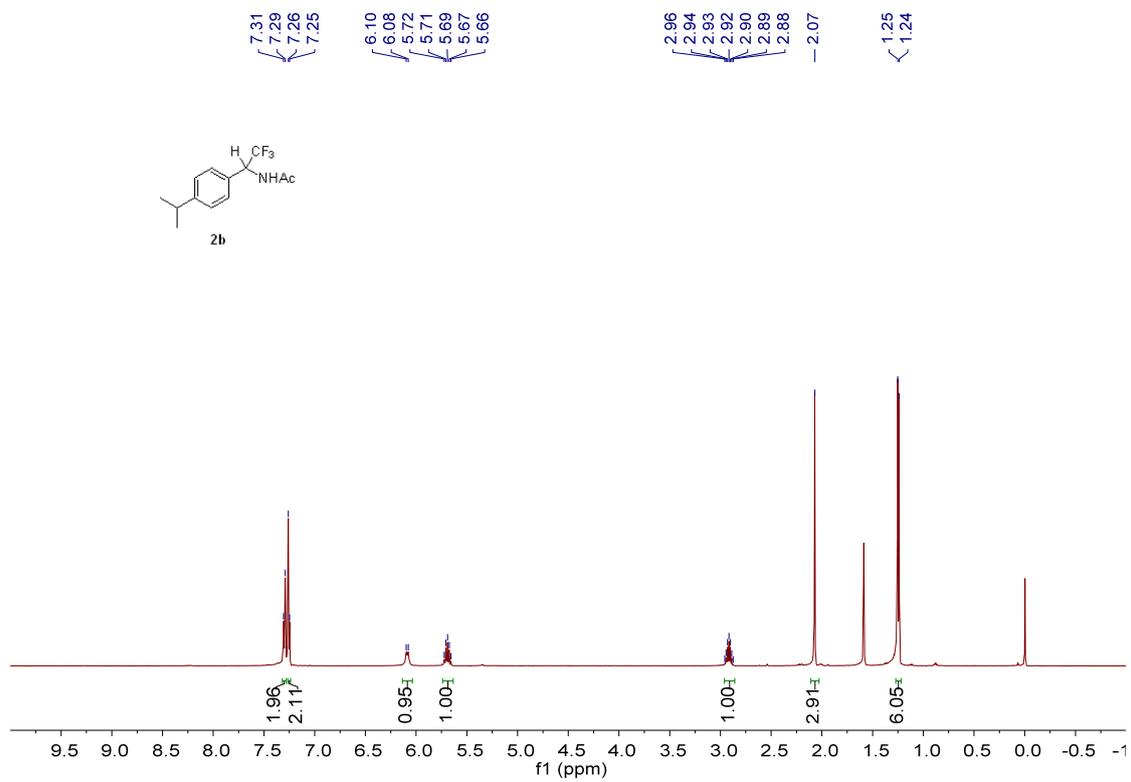
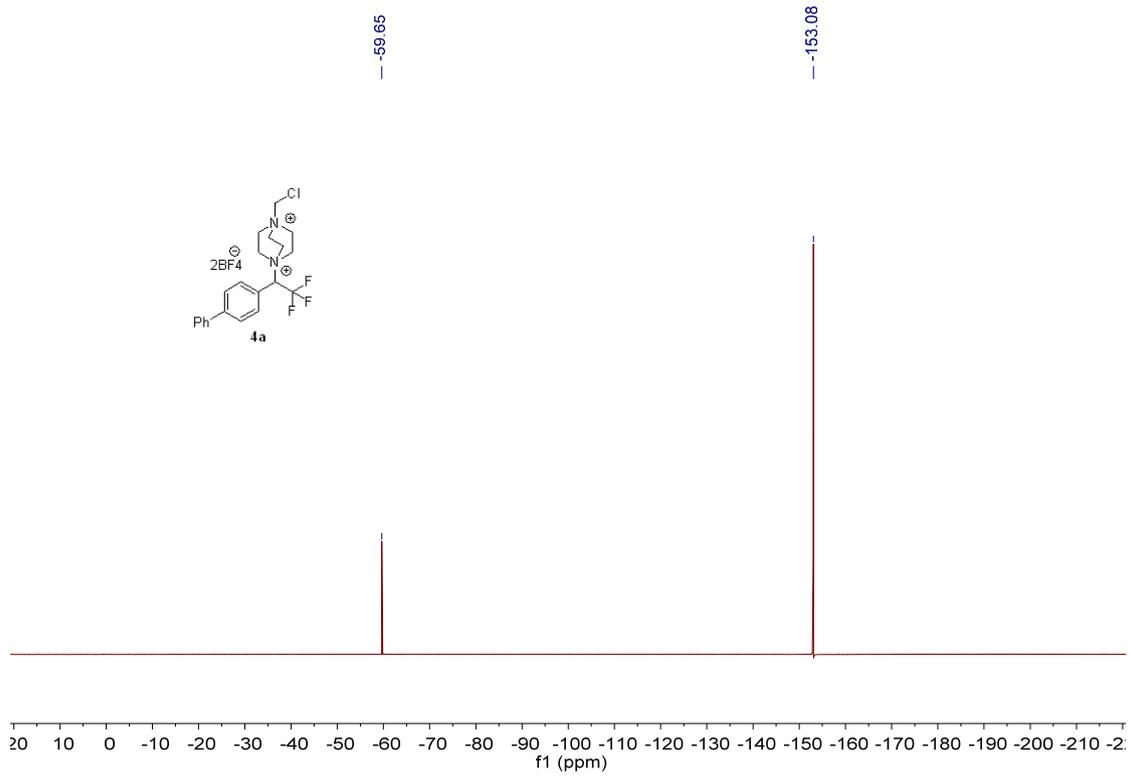
5.10
5.09
5.08
5.06

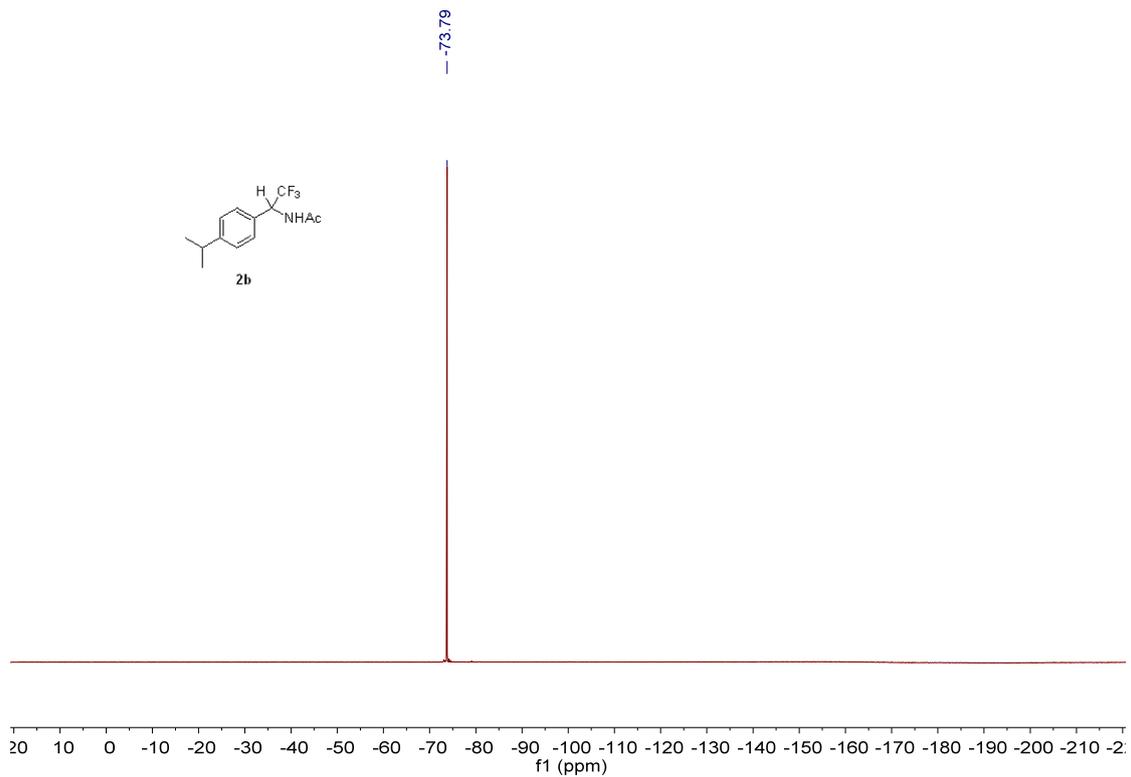
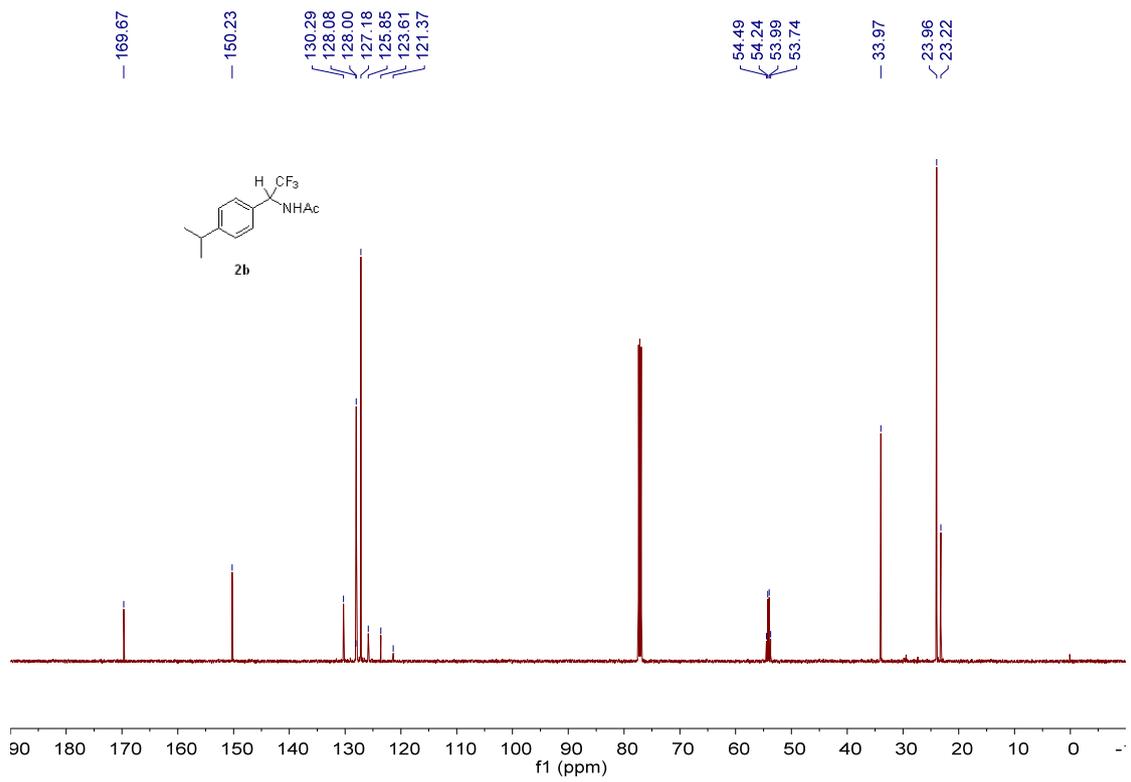
2.66

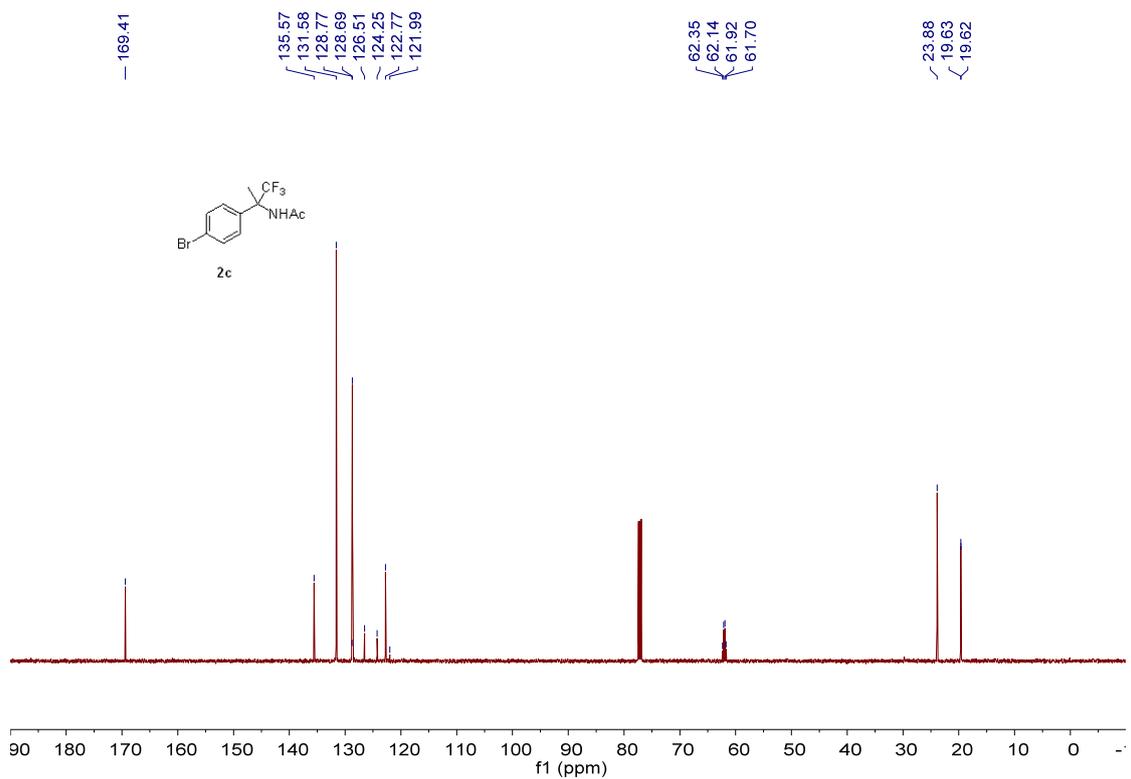
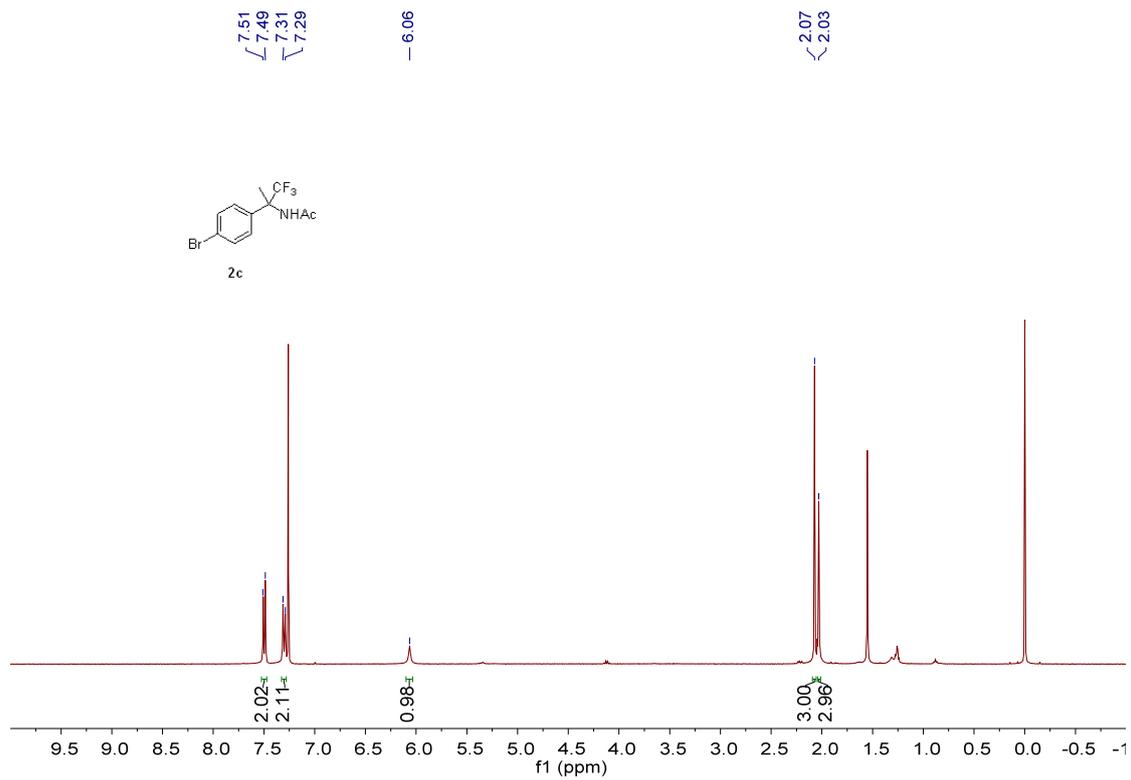


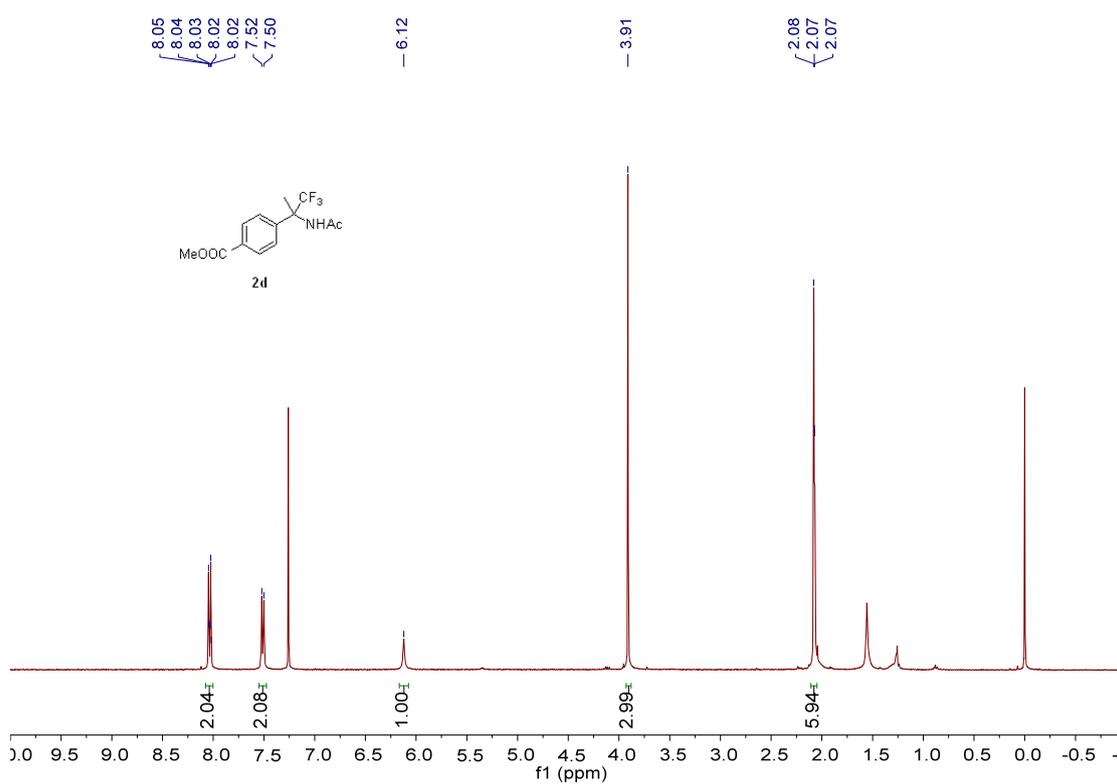
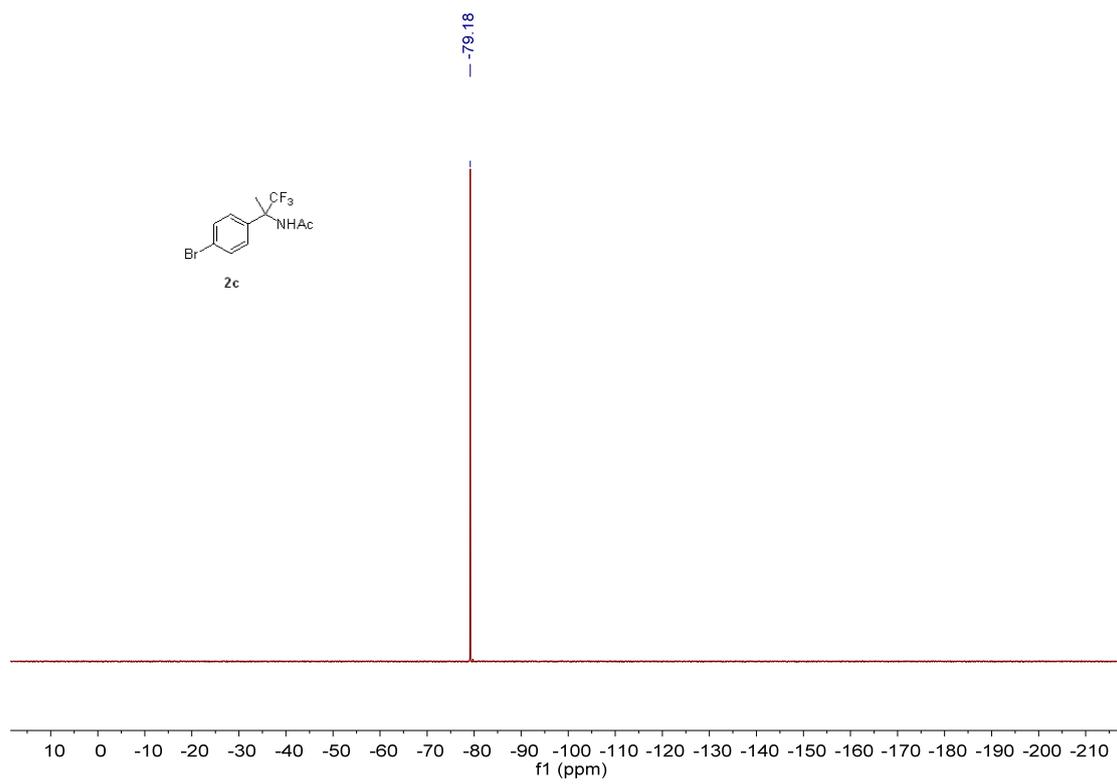










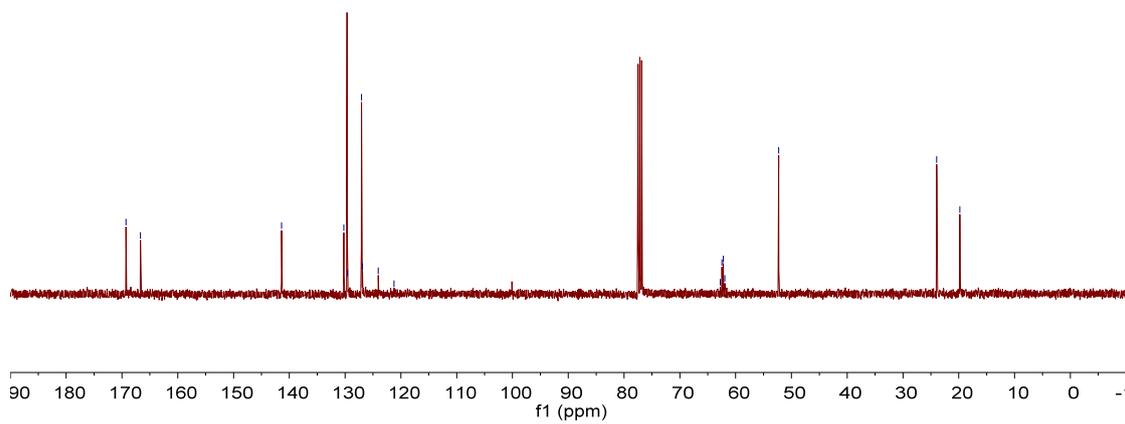
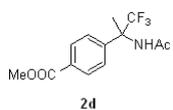


169.29
166.68

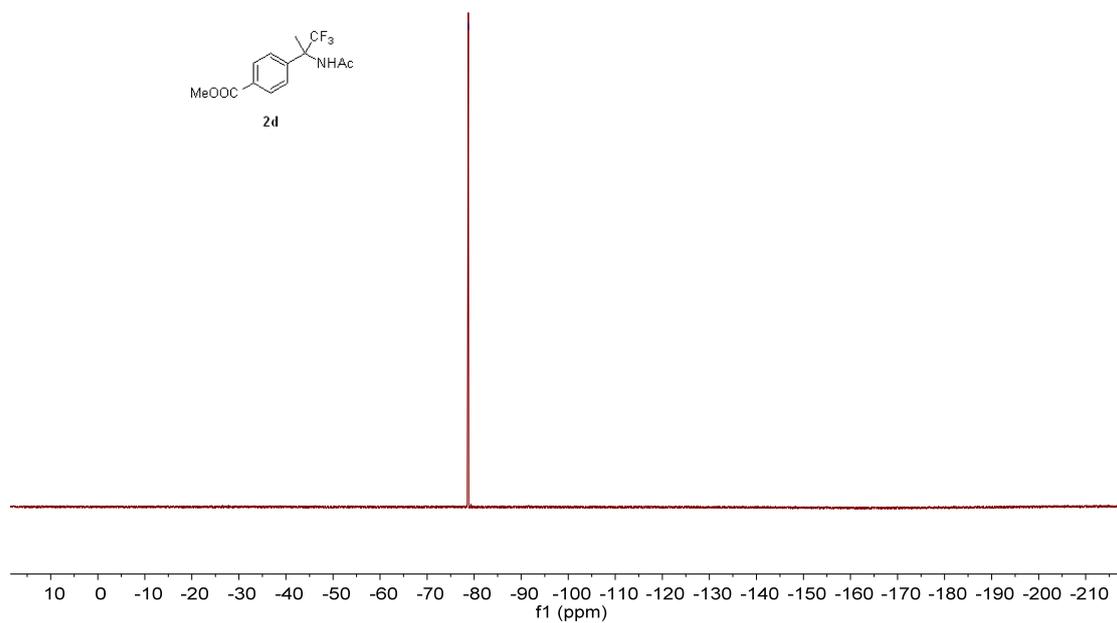
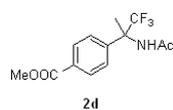
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126.88
124.05
121.22

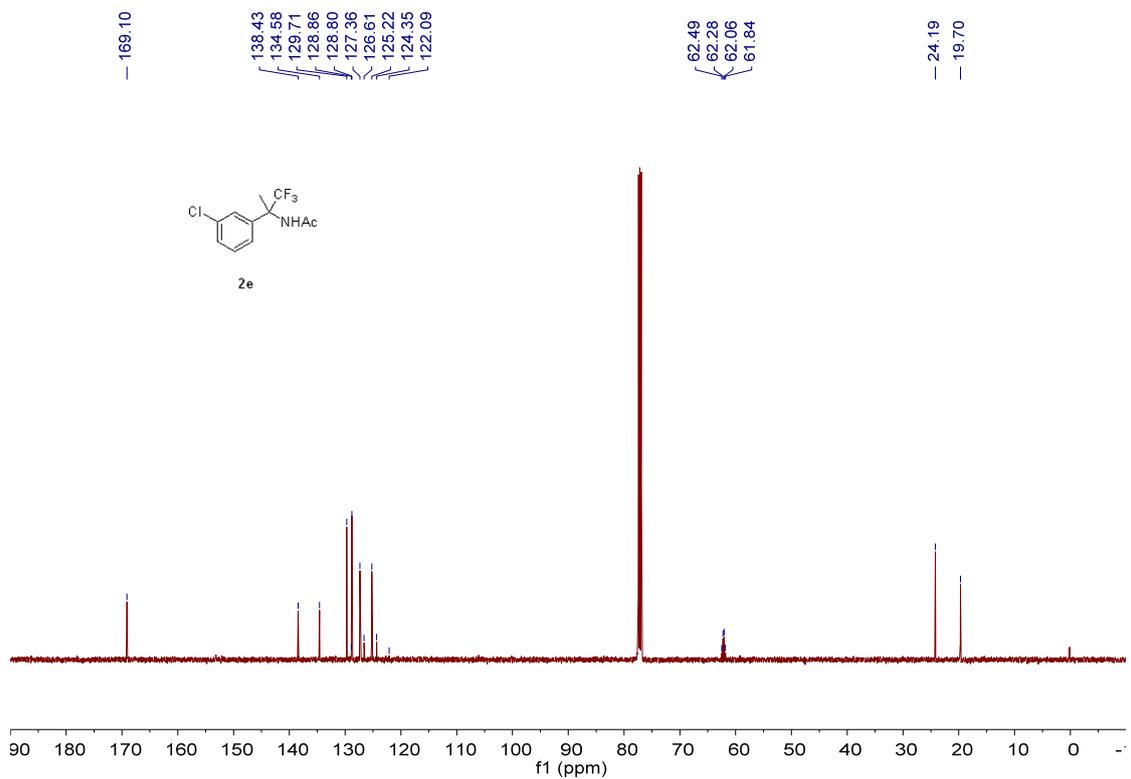
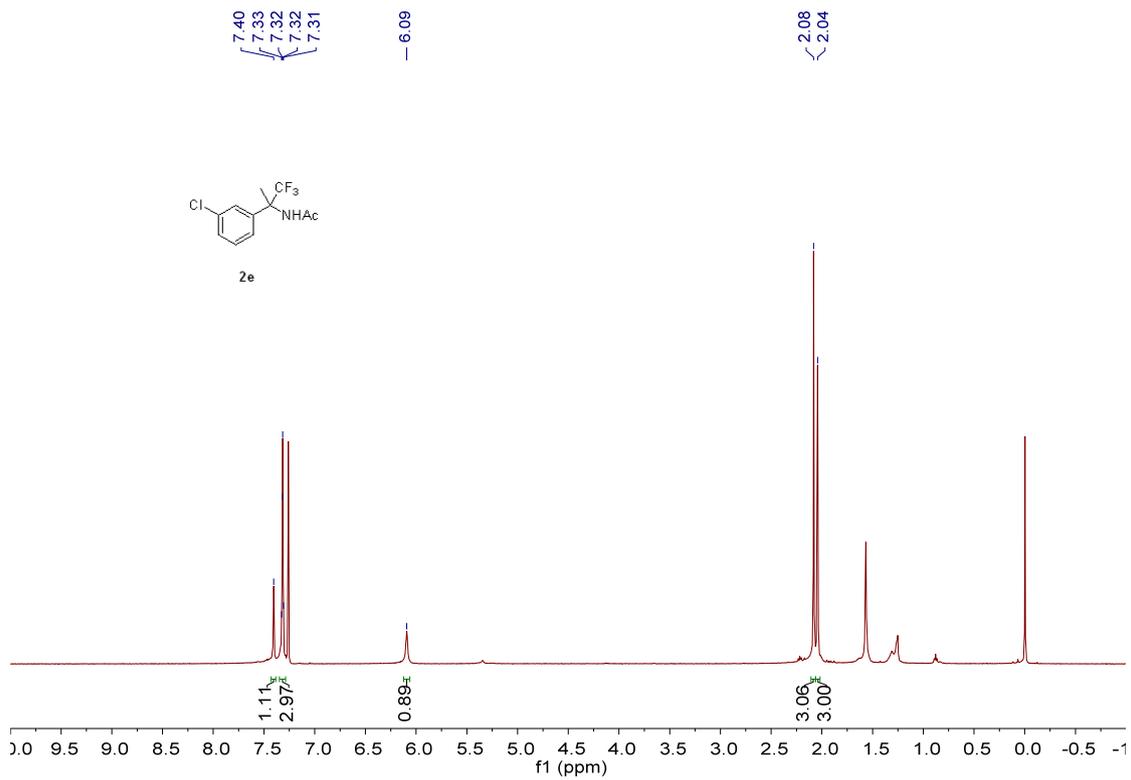
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61.94
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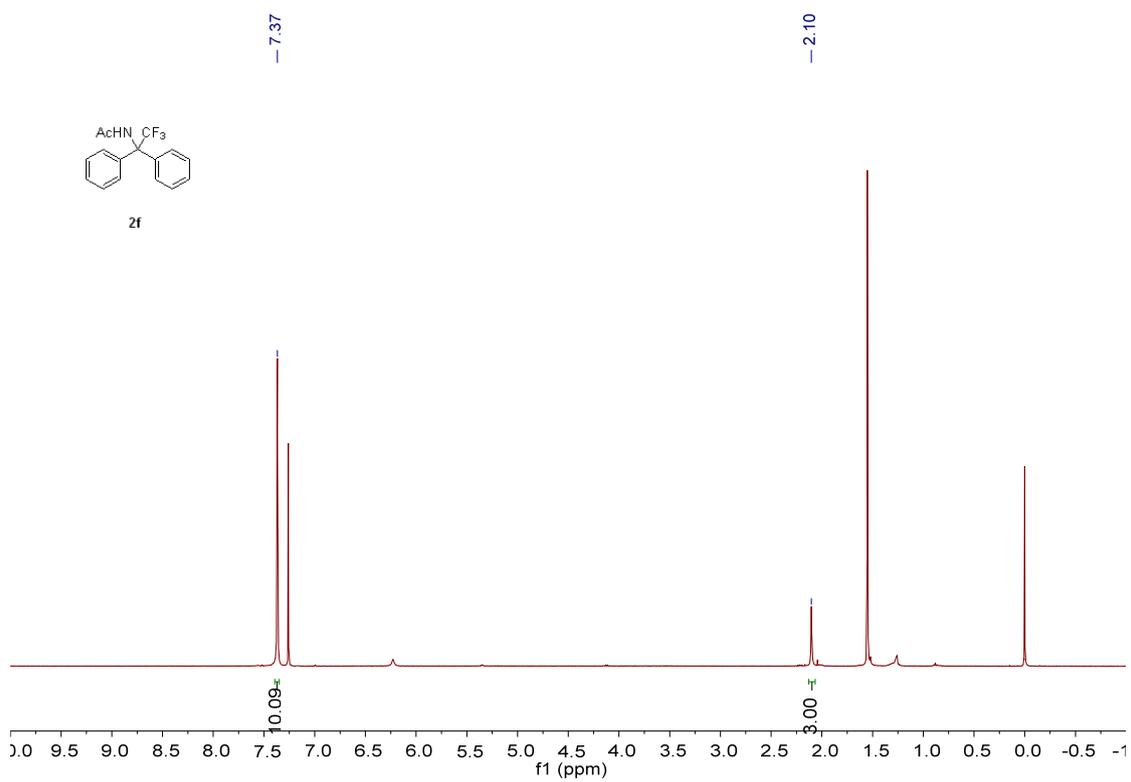
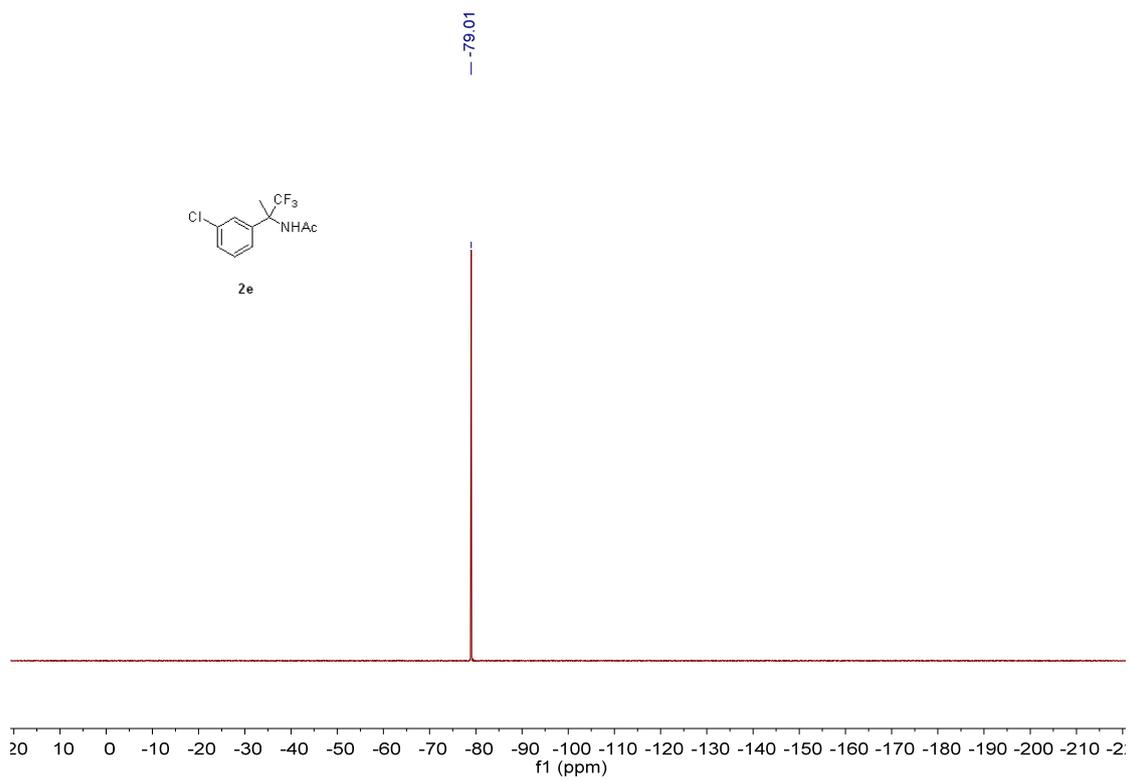
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19.81

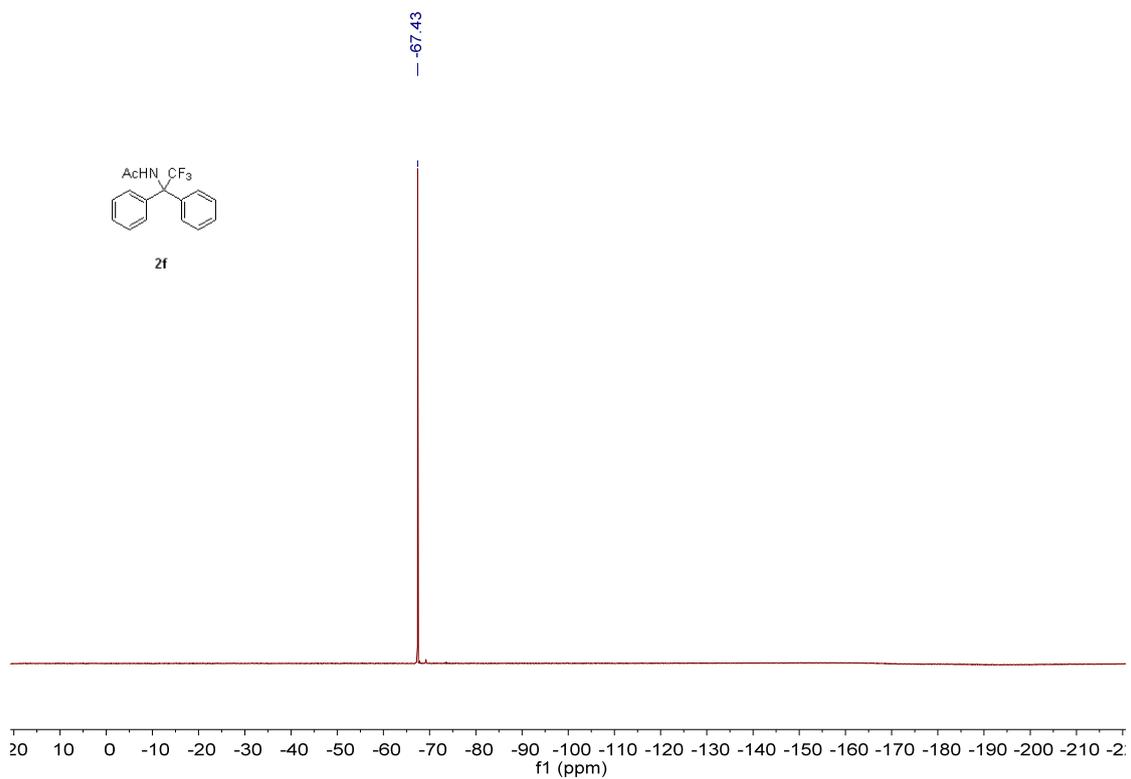
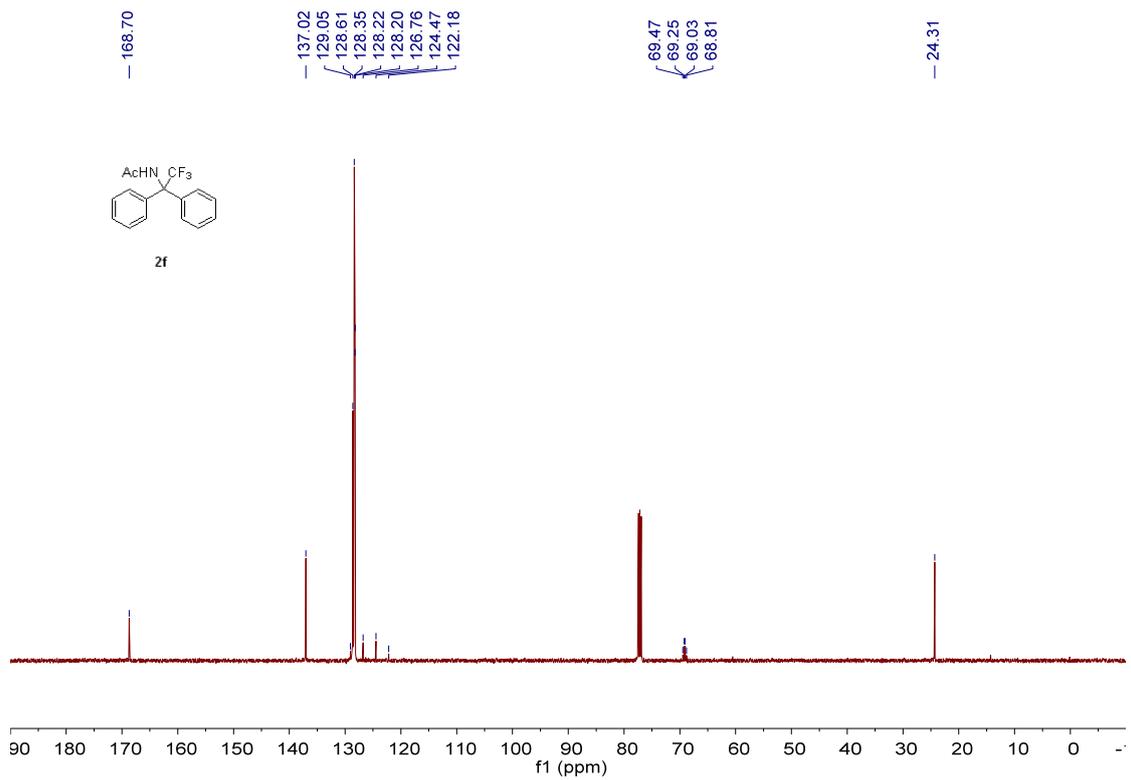


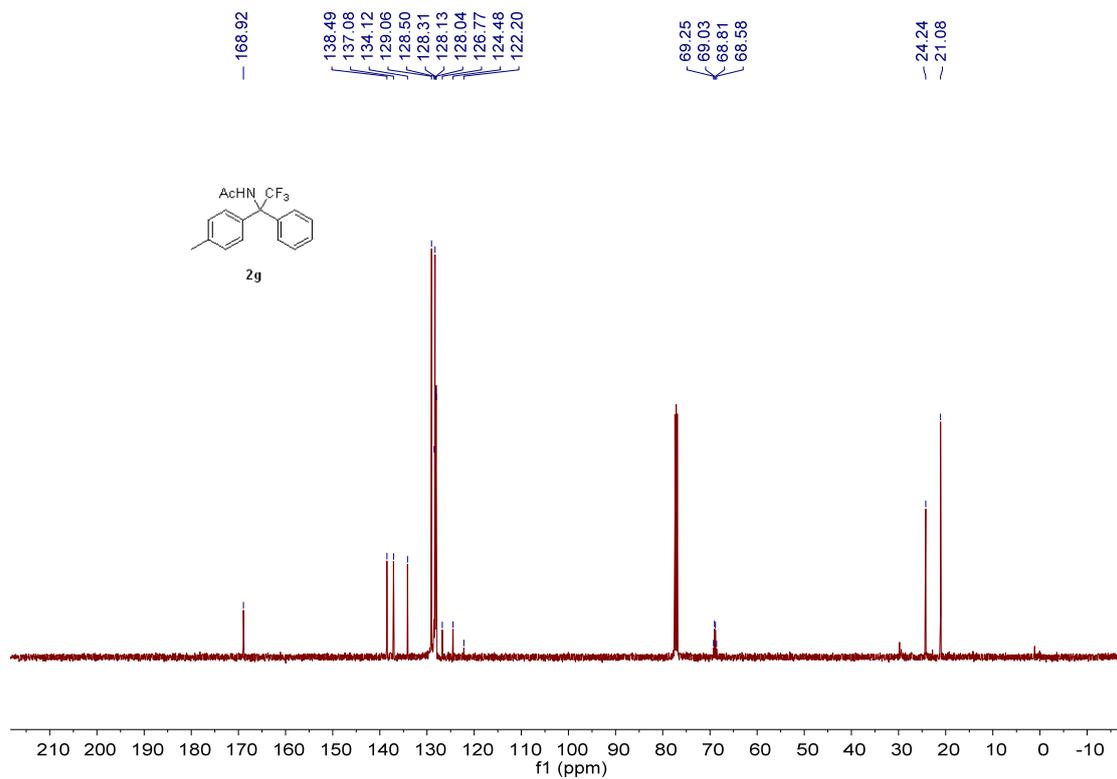
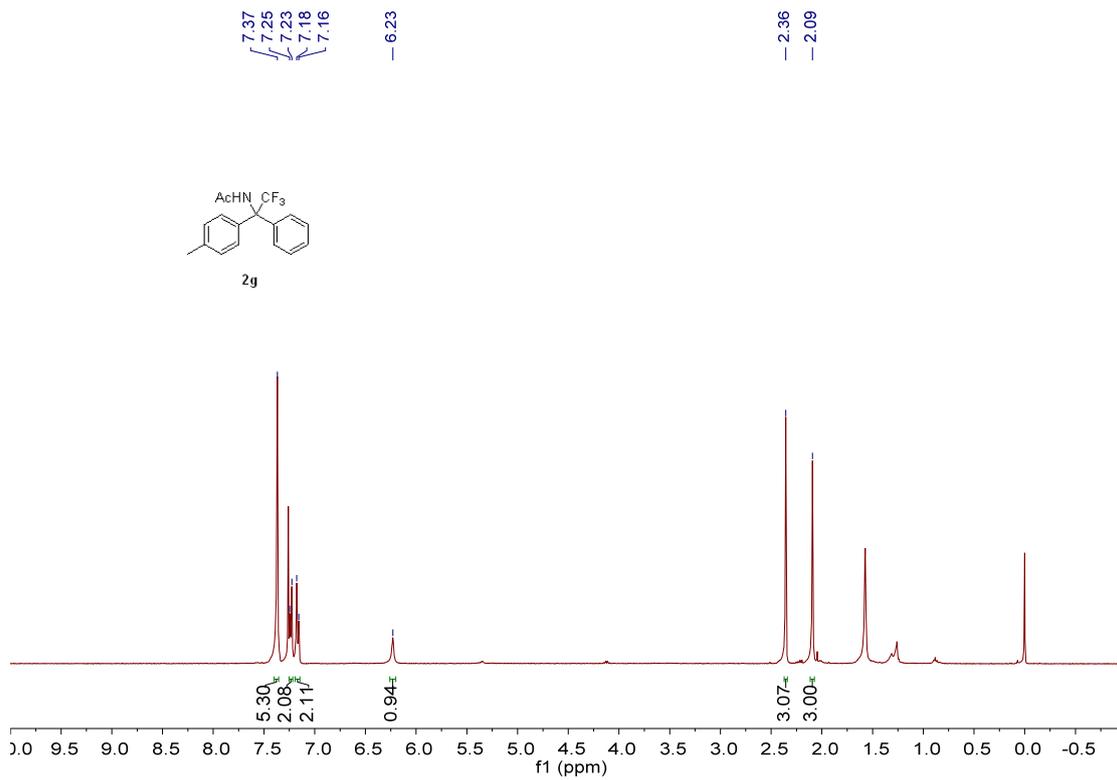
-78.77

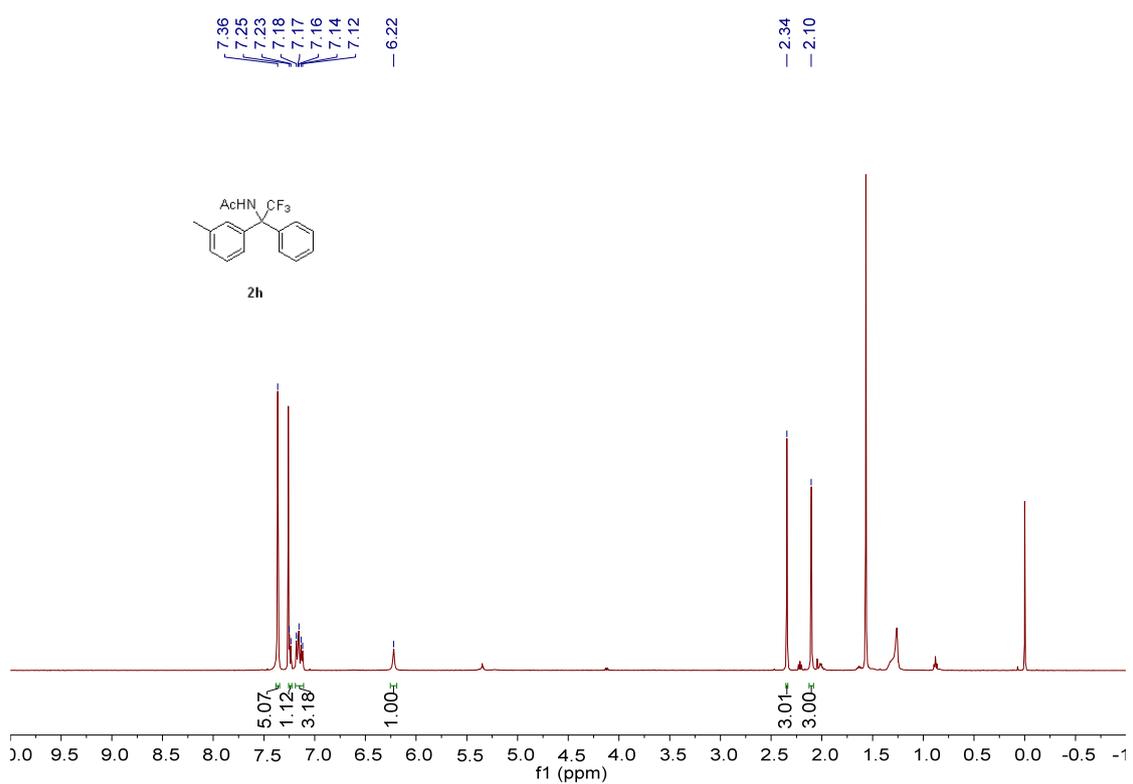
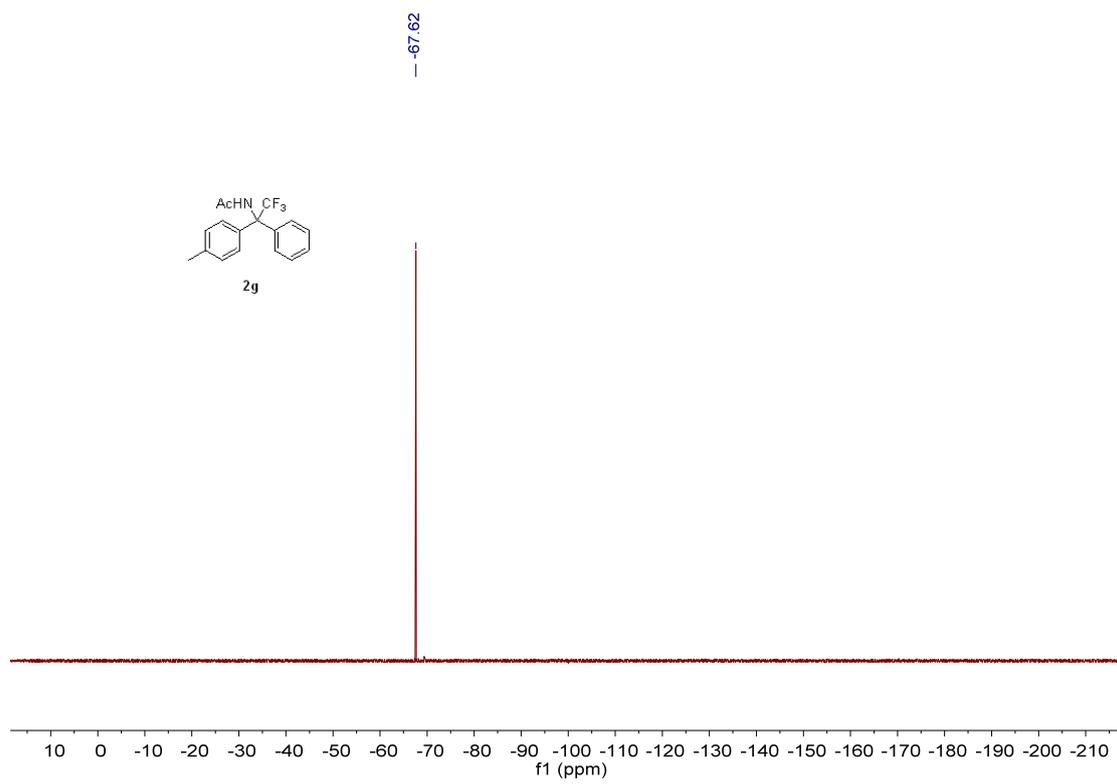


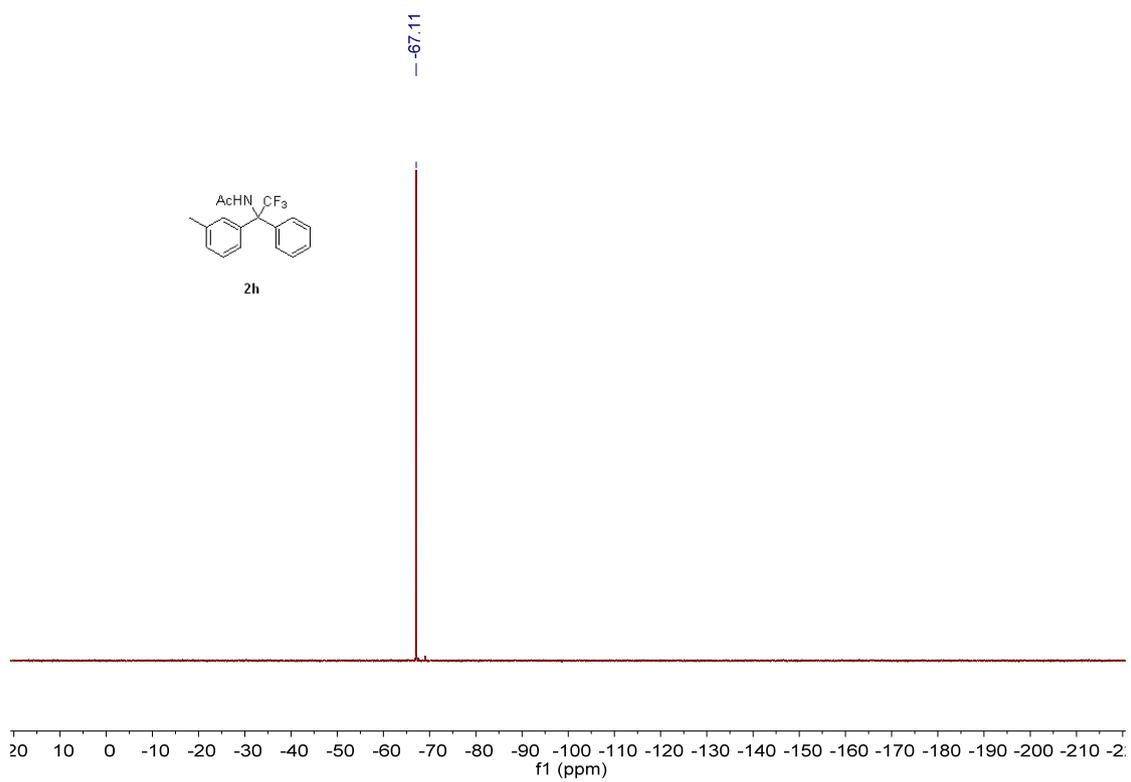
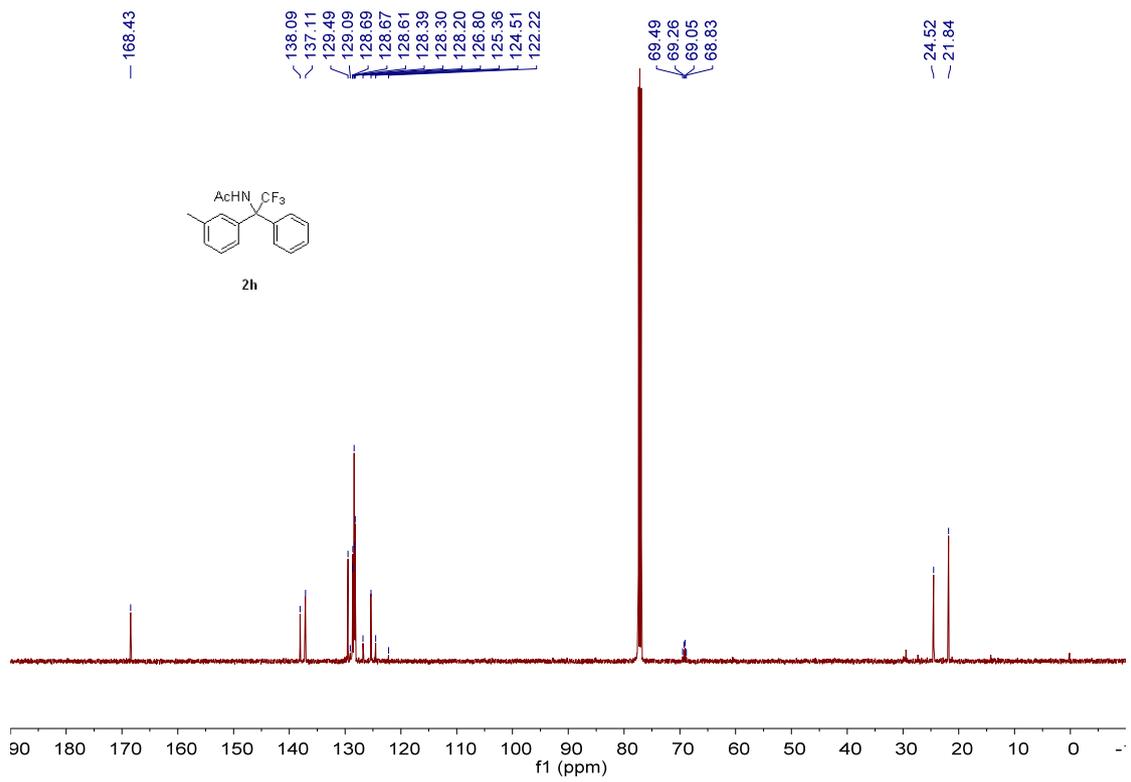


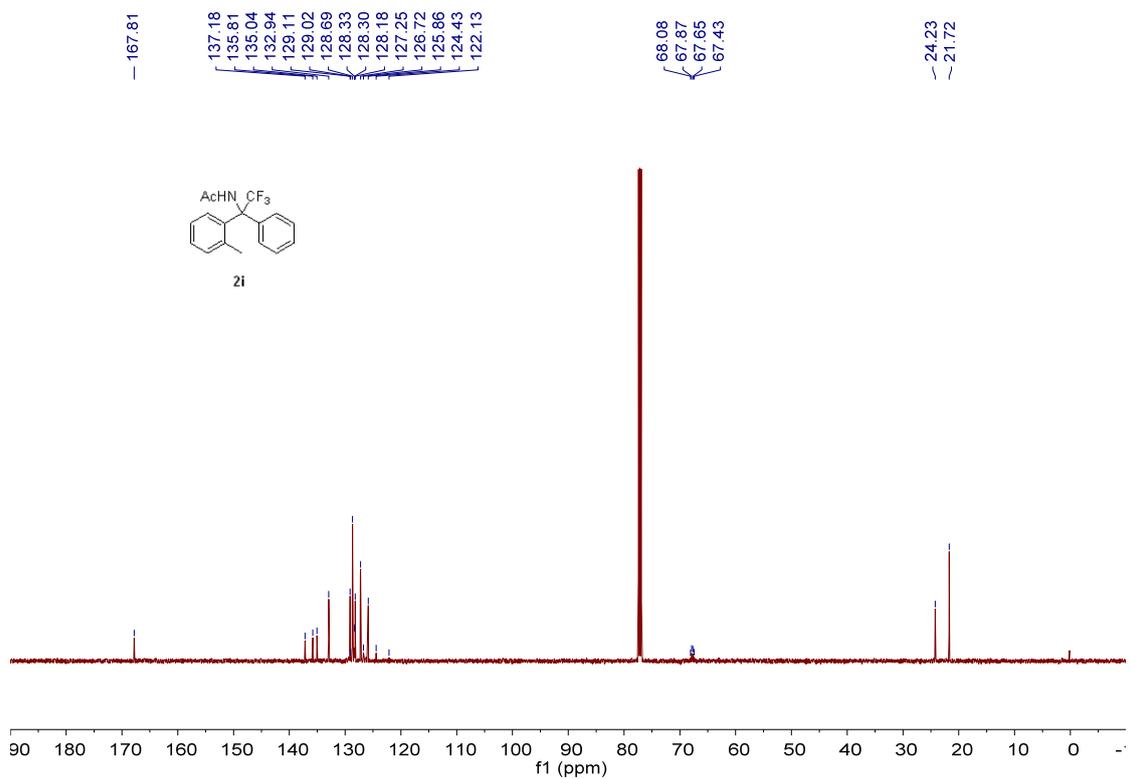
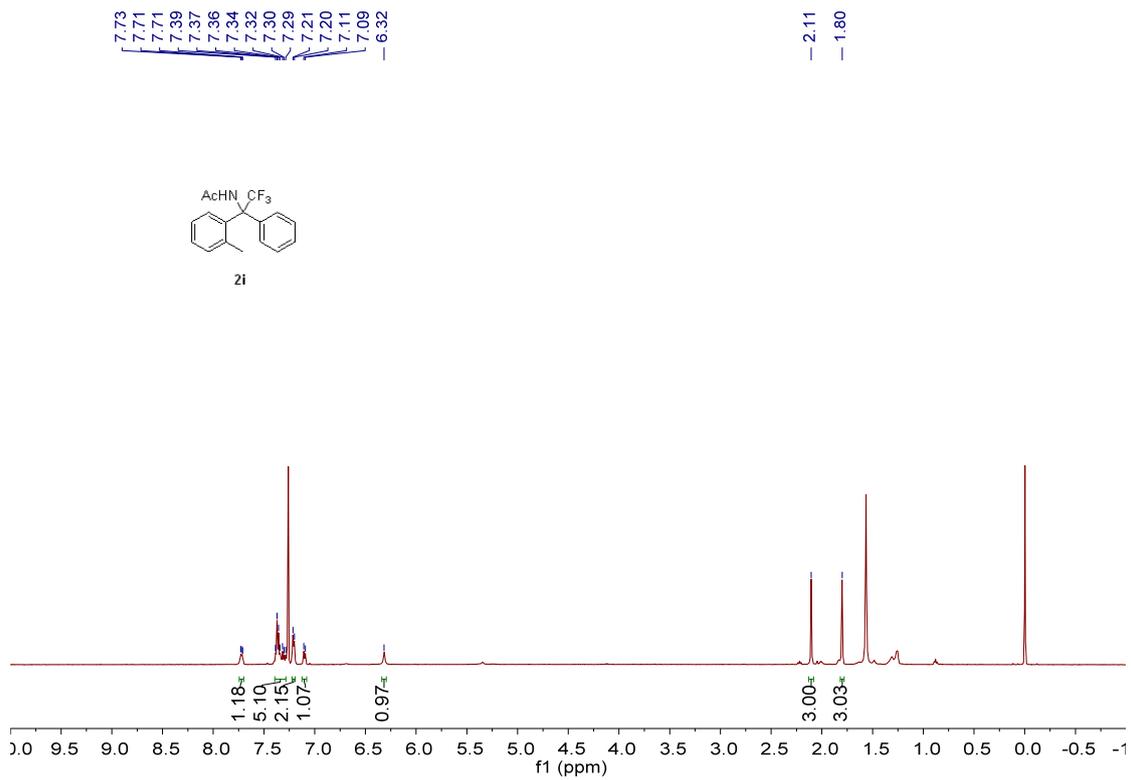


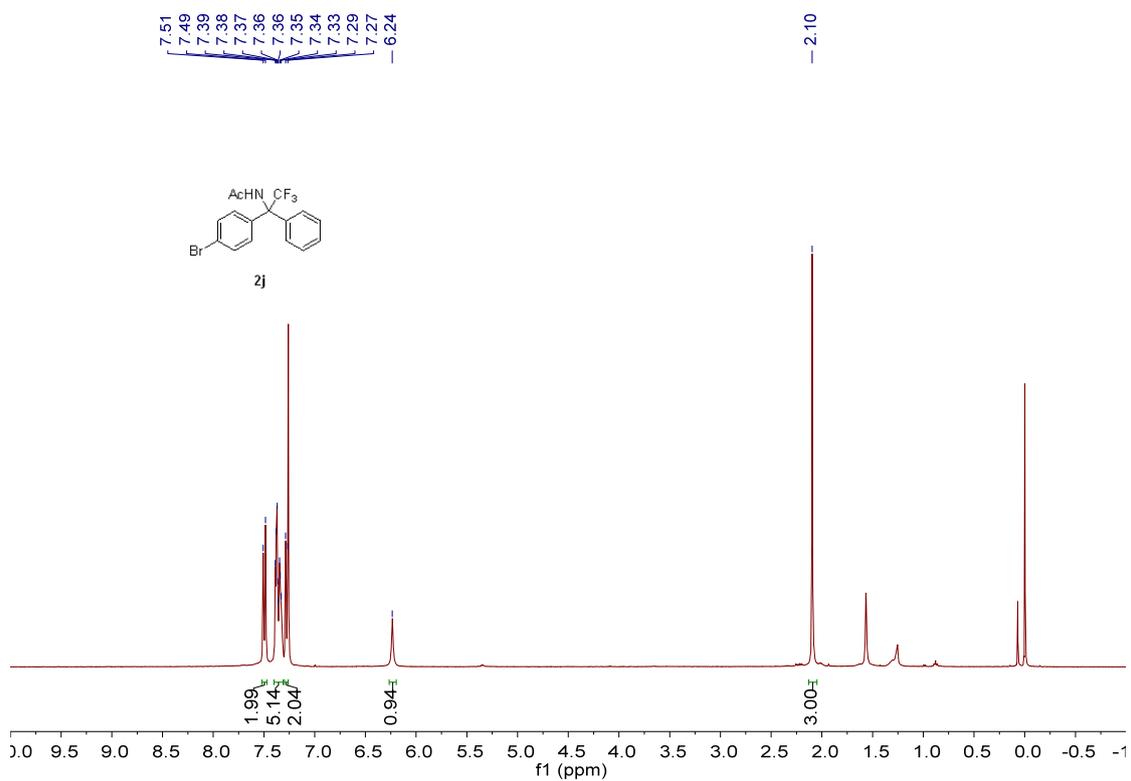
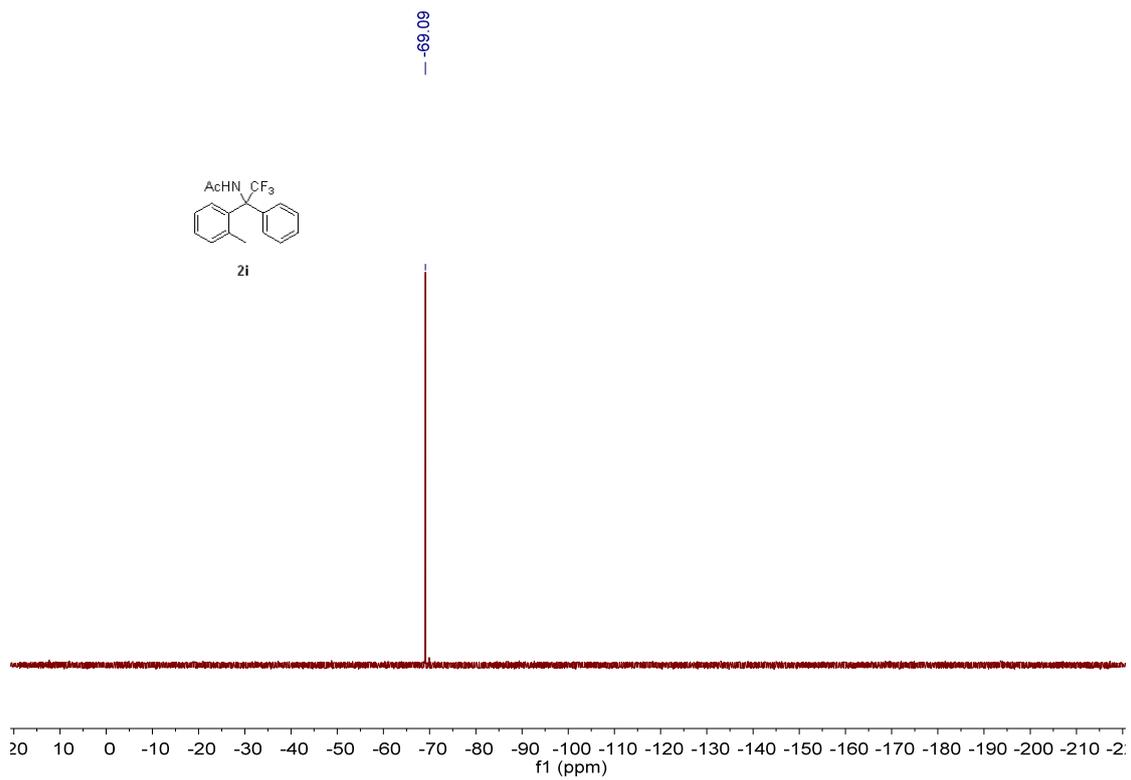


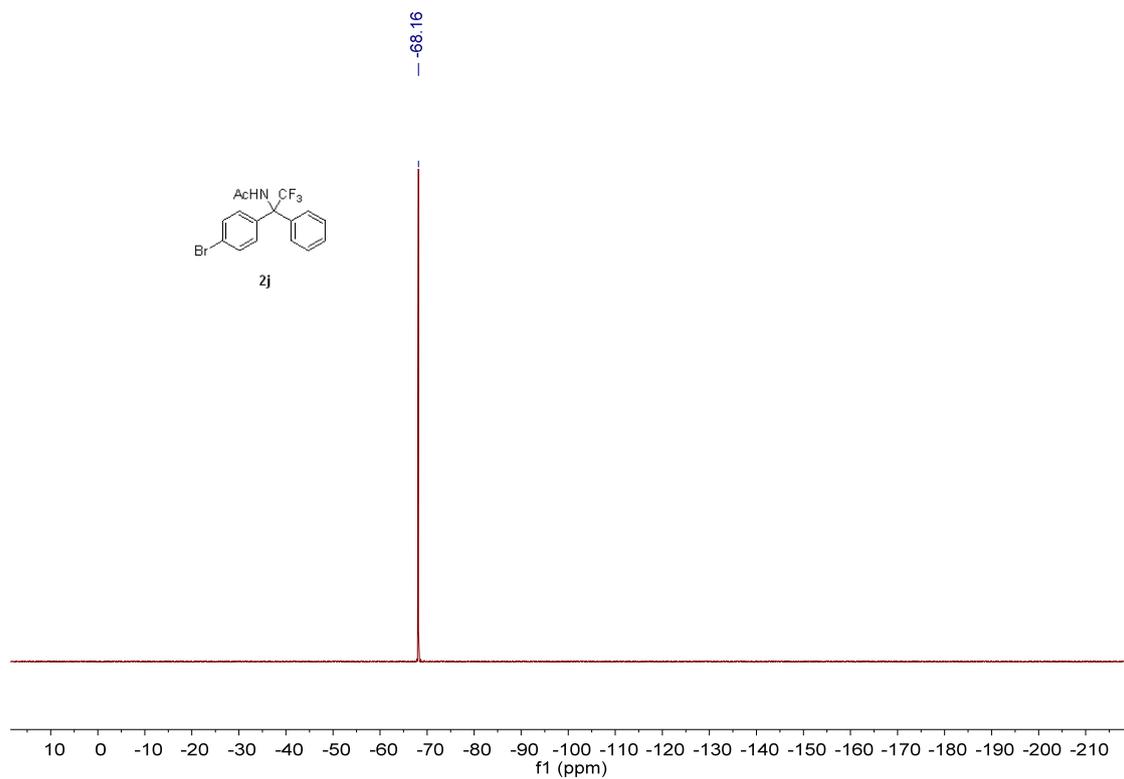
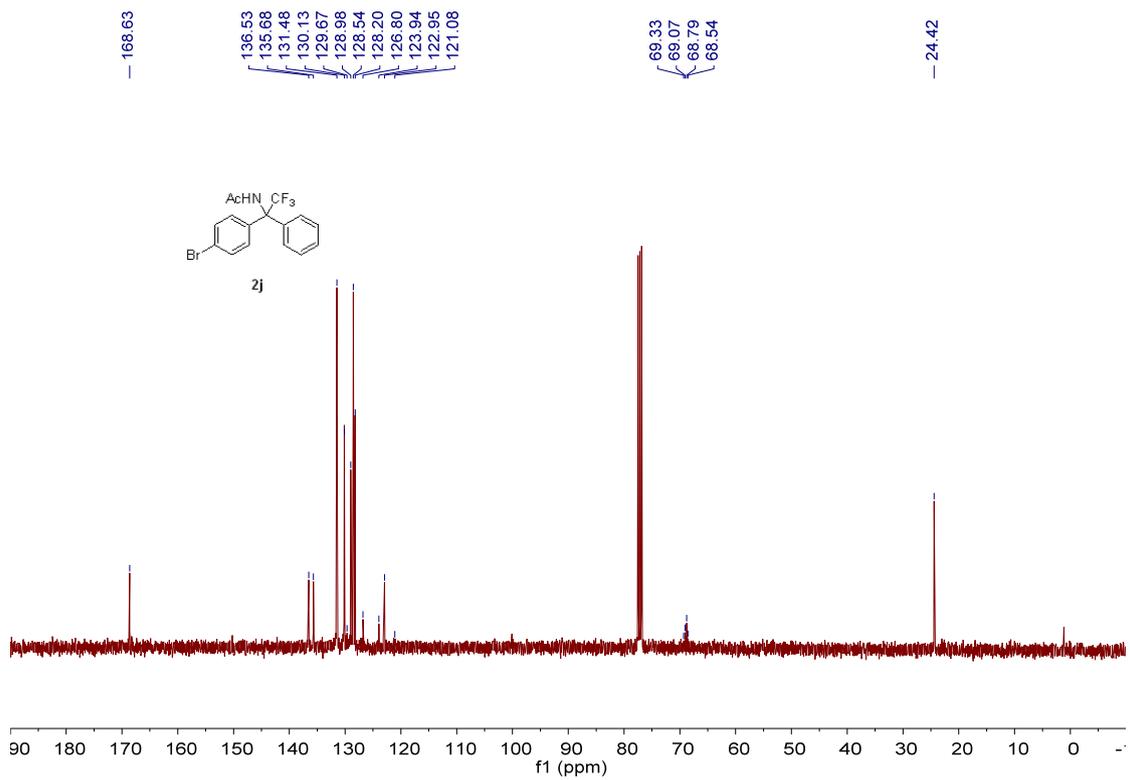


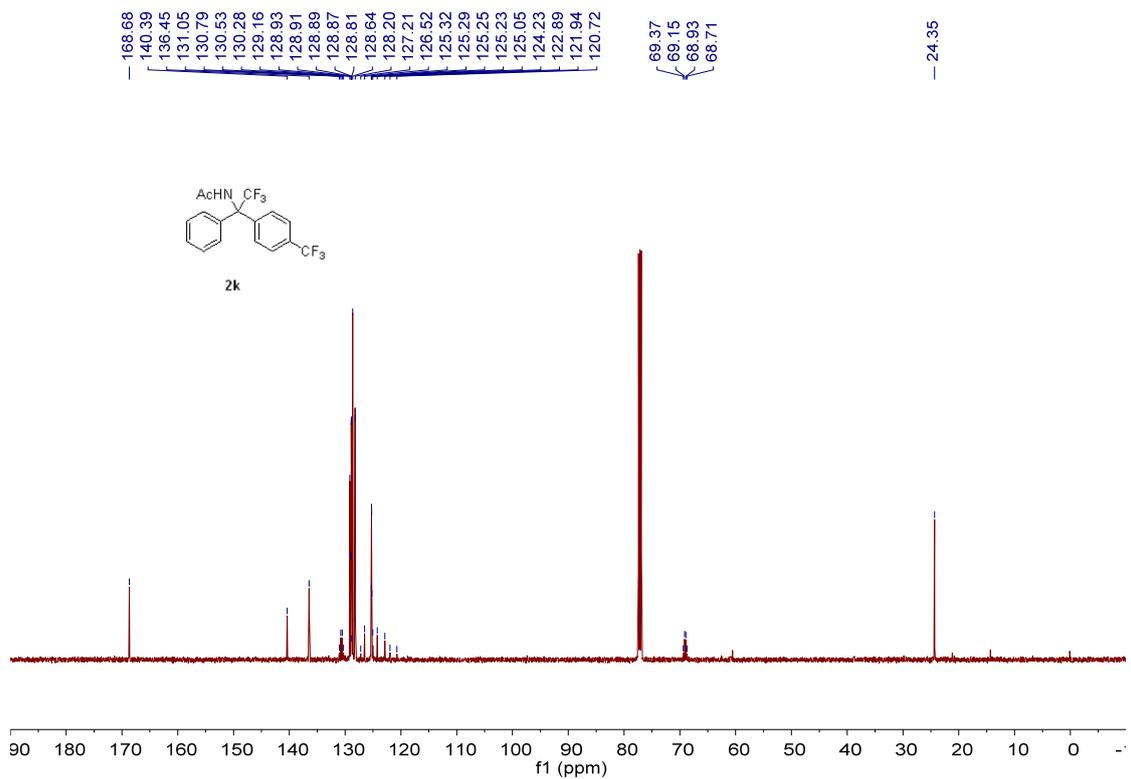
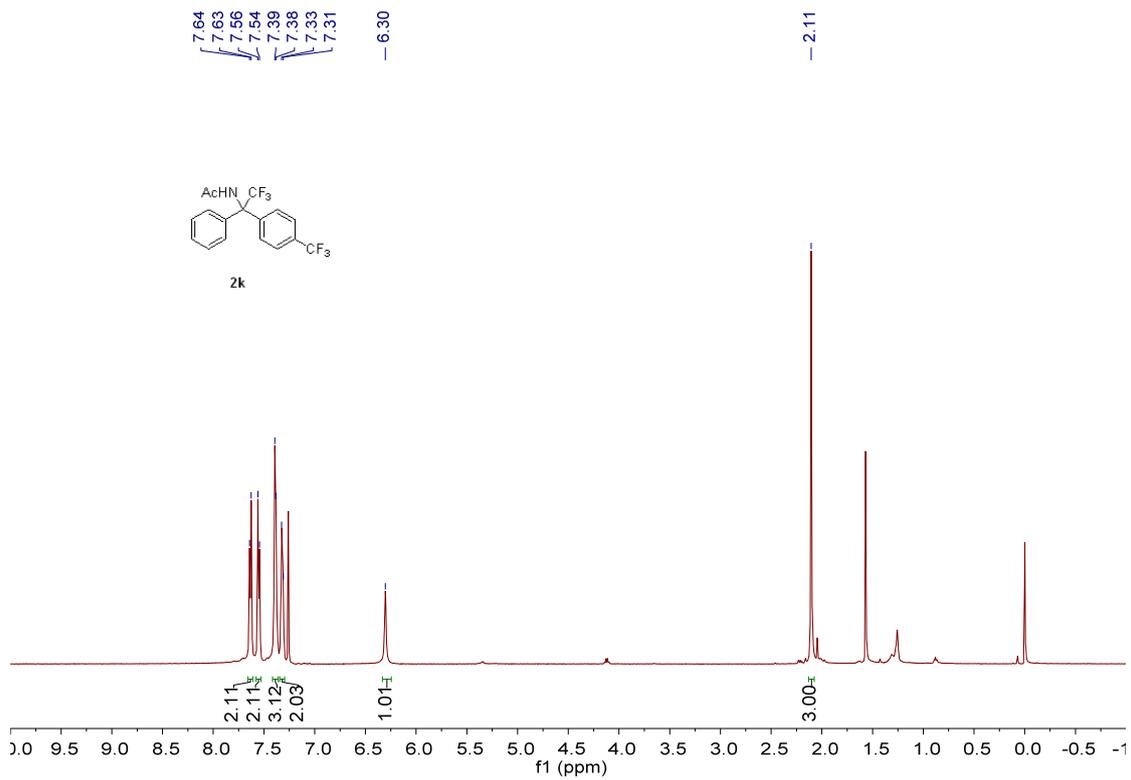


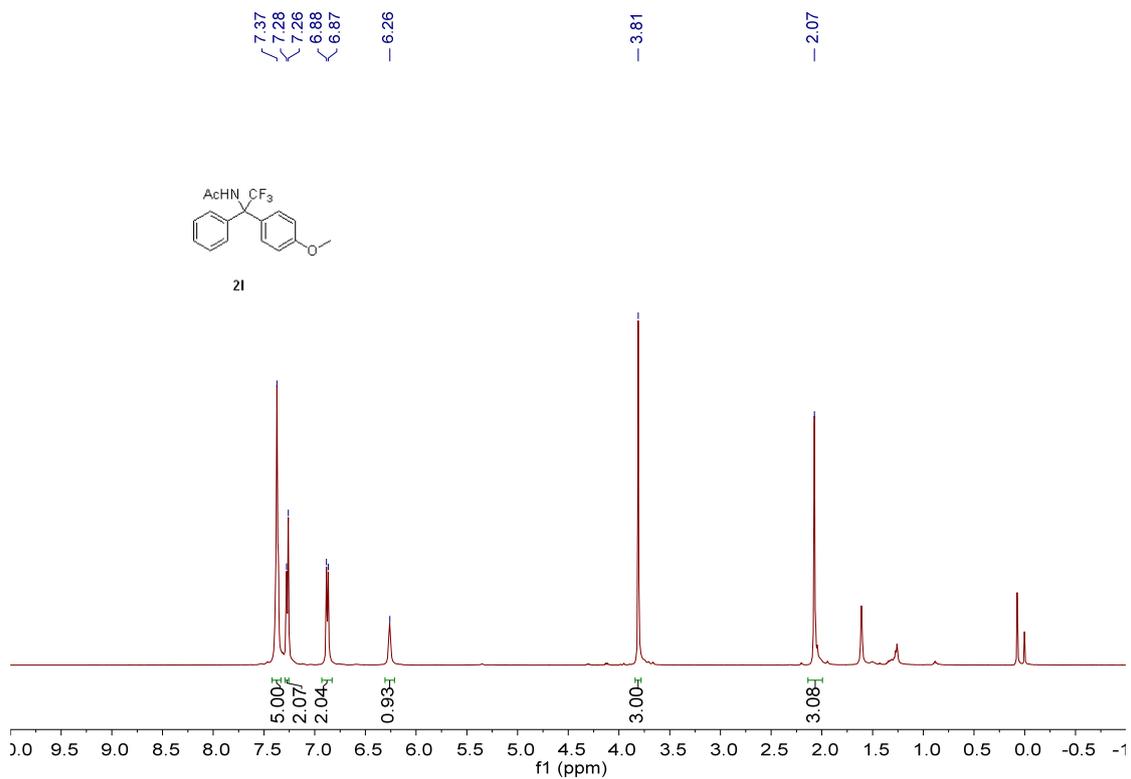
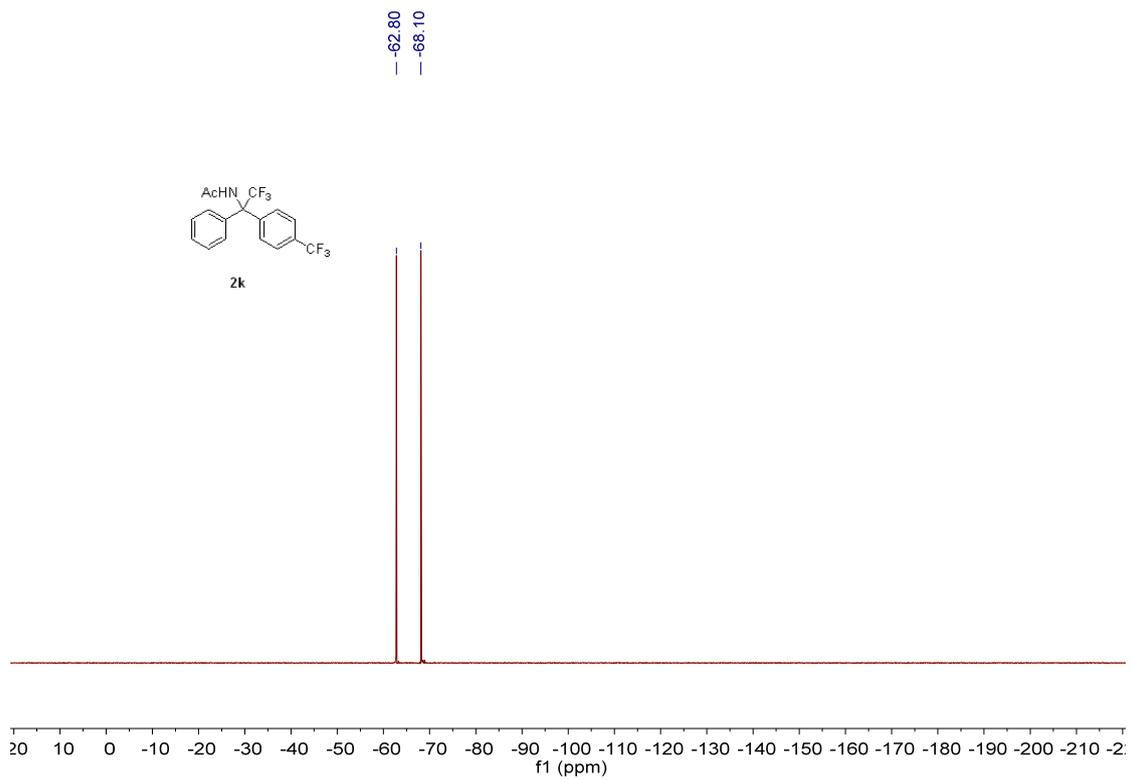


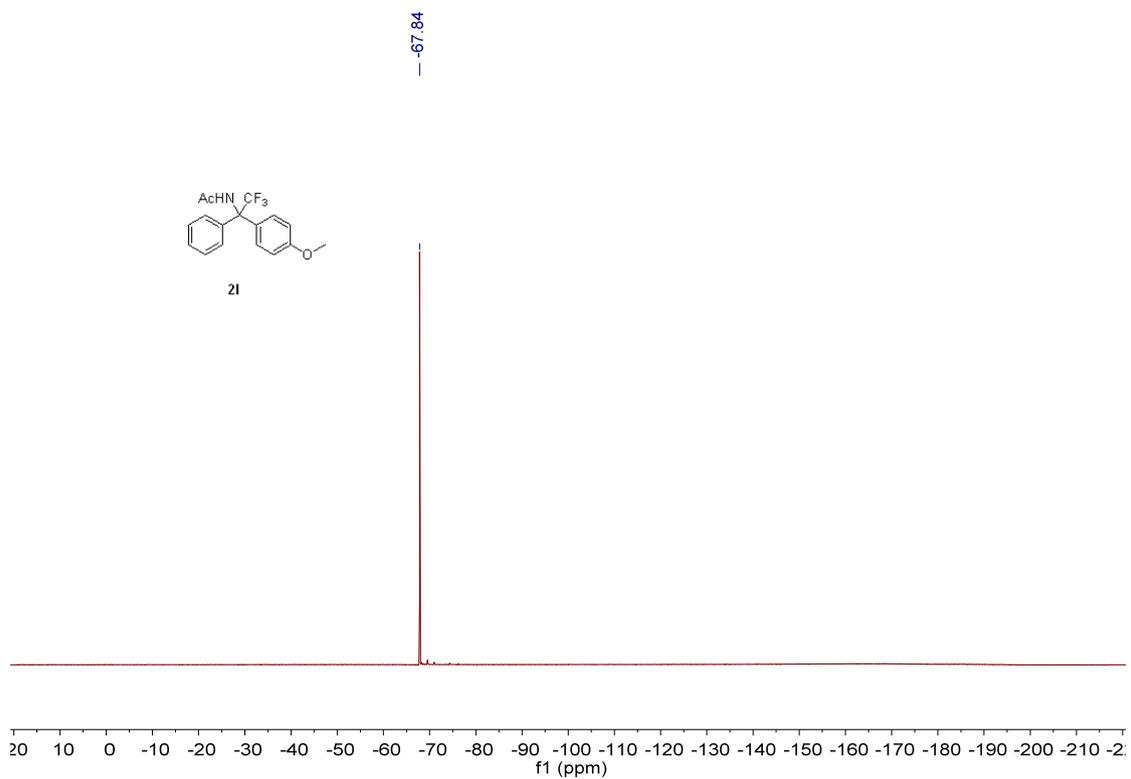
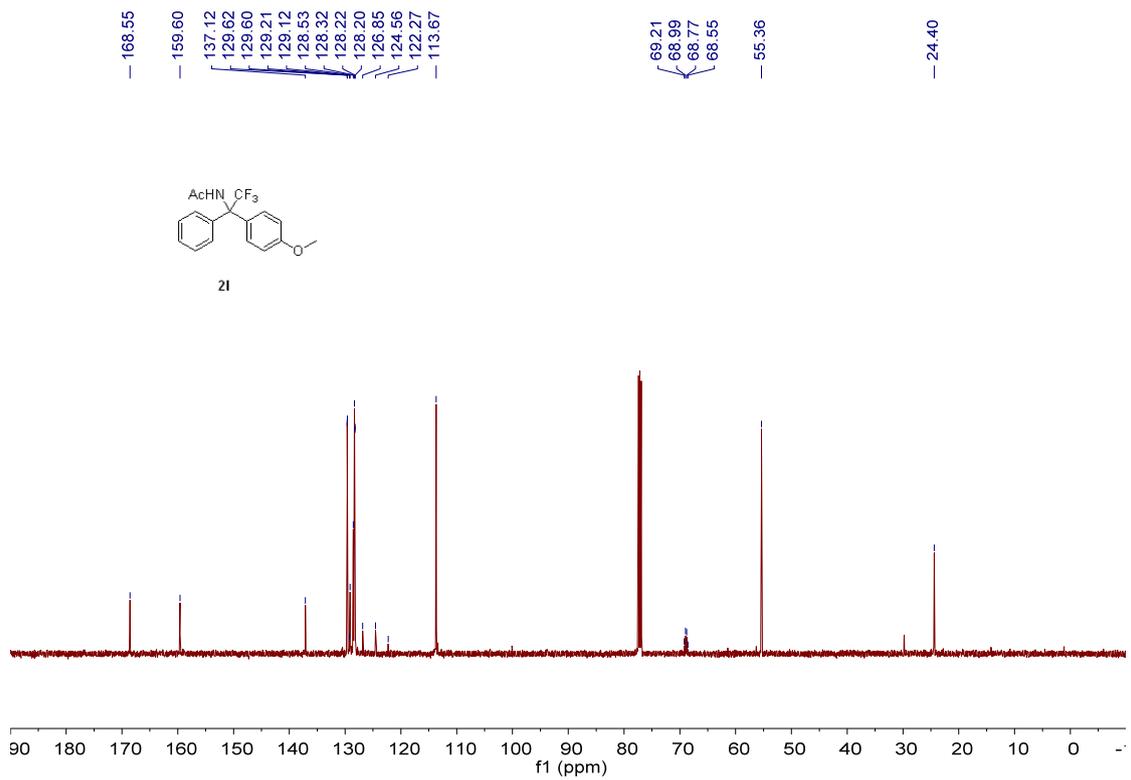


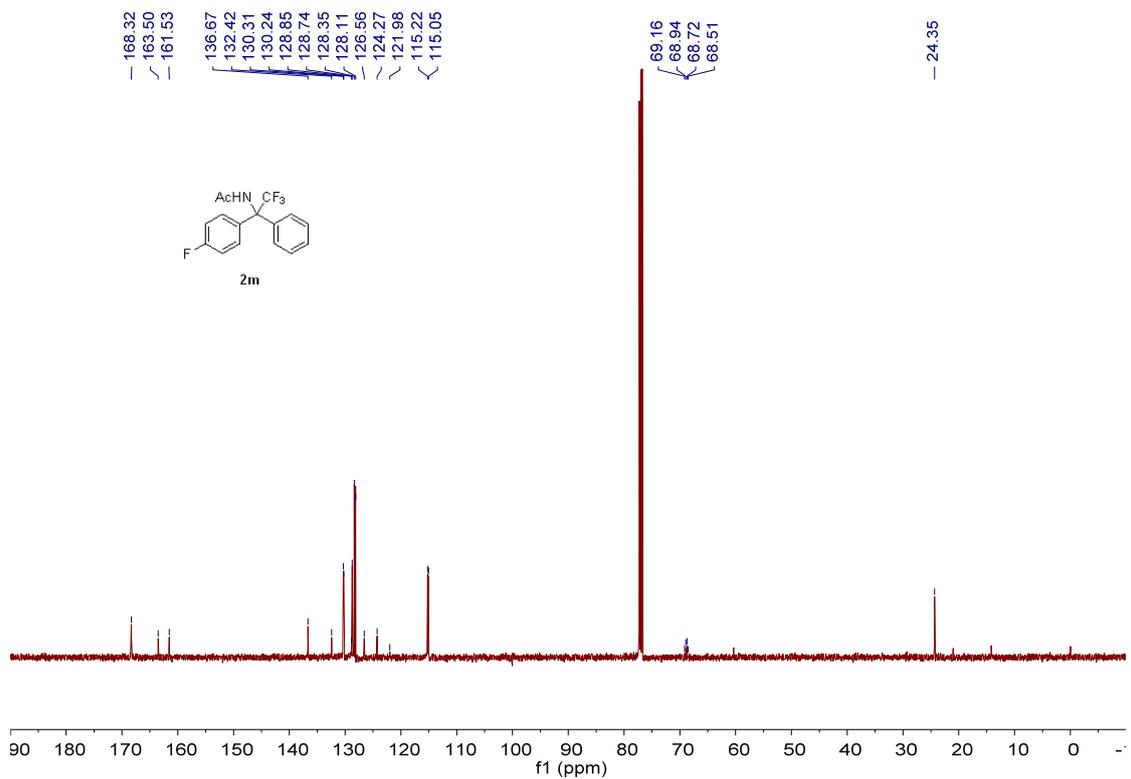
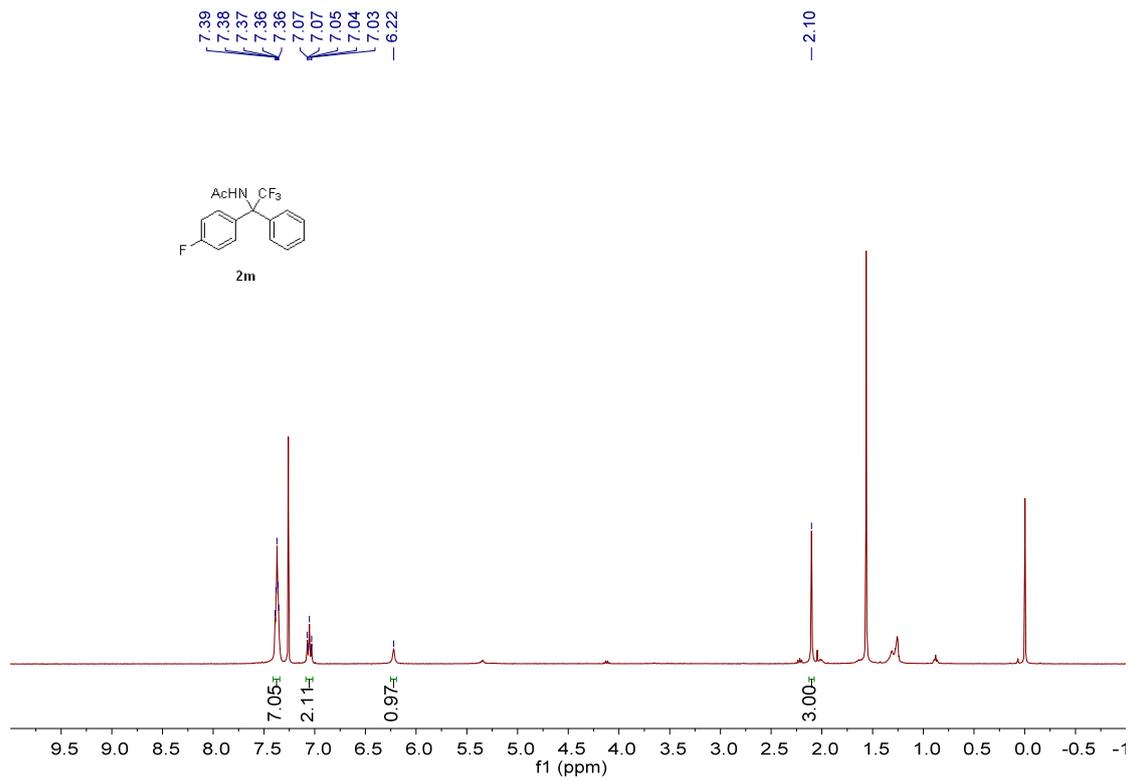


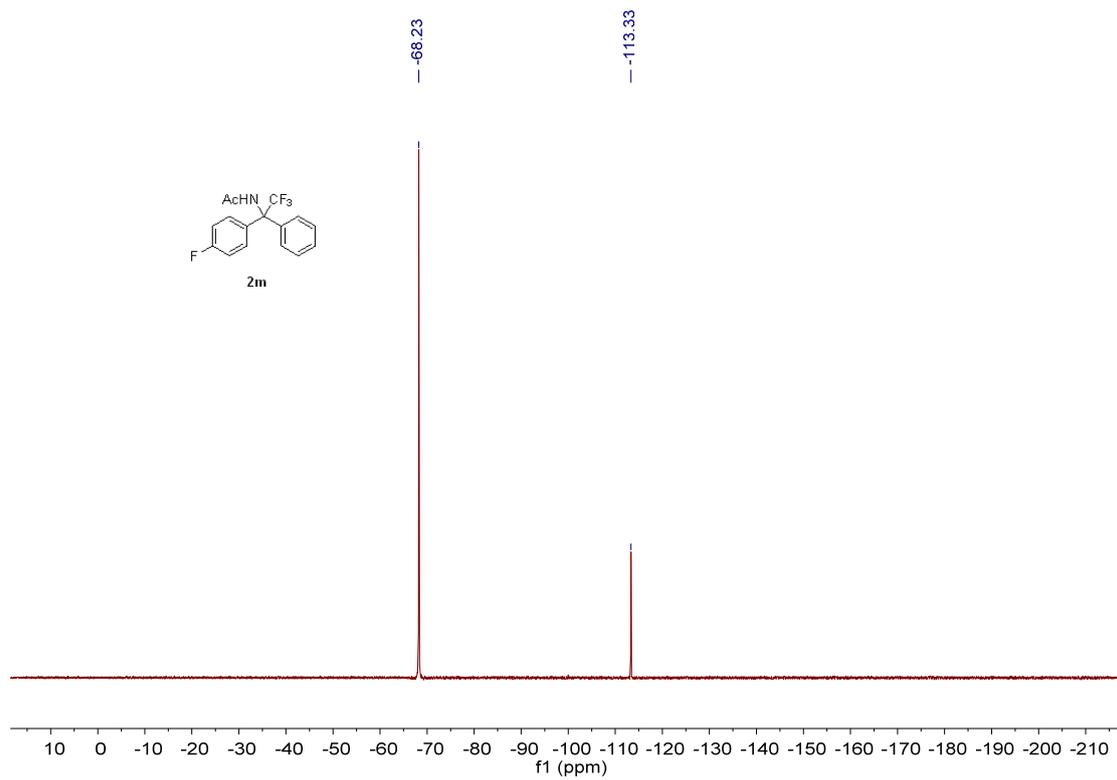


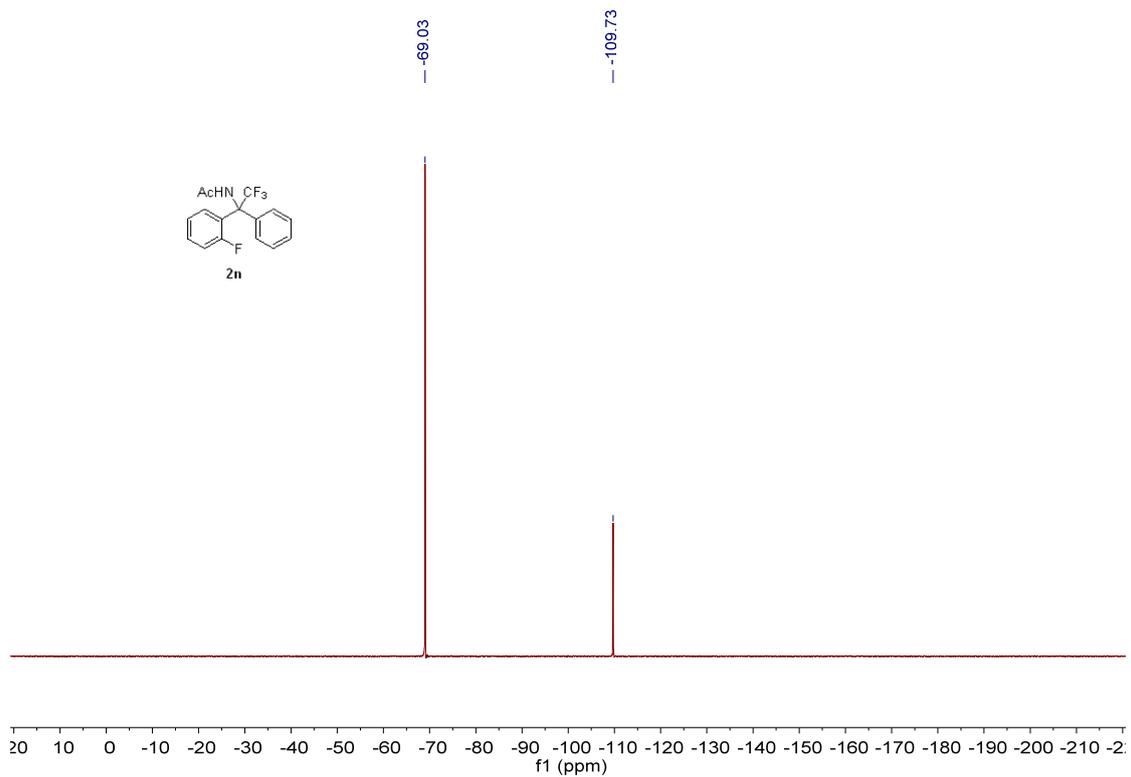
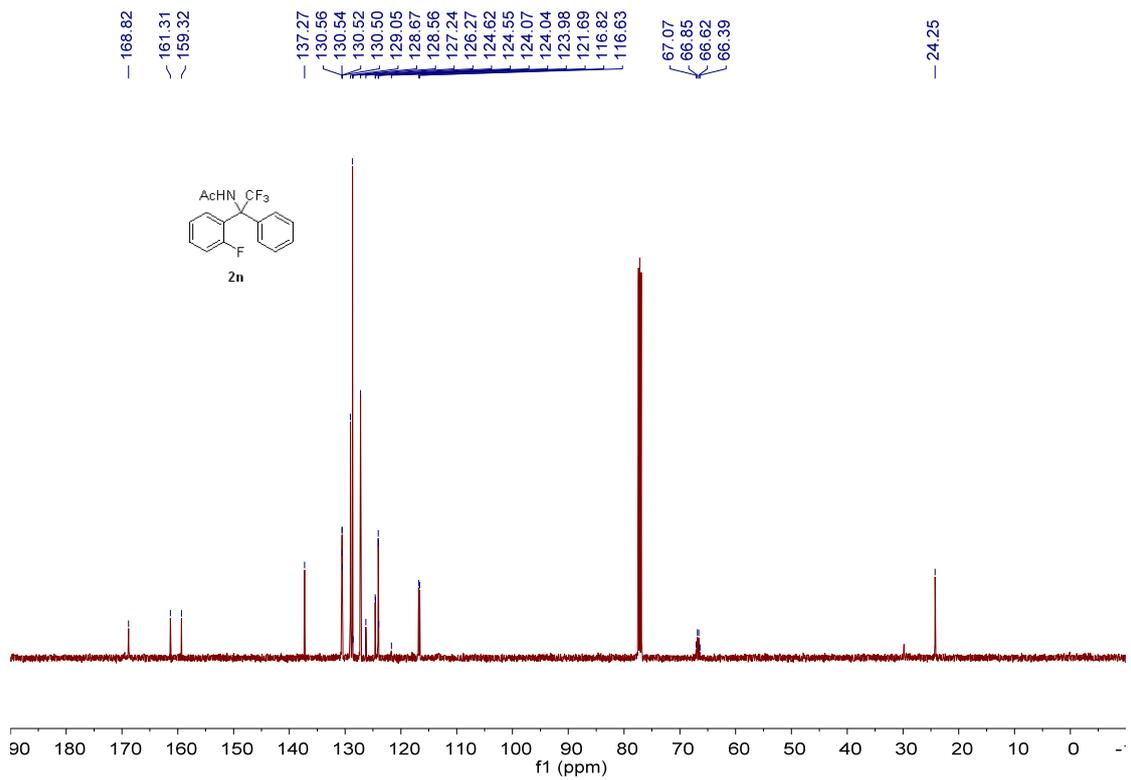


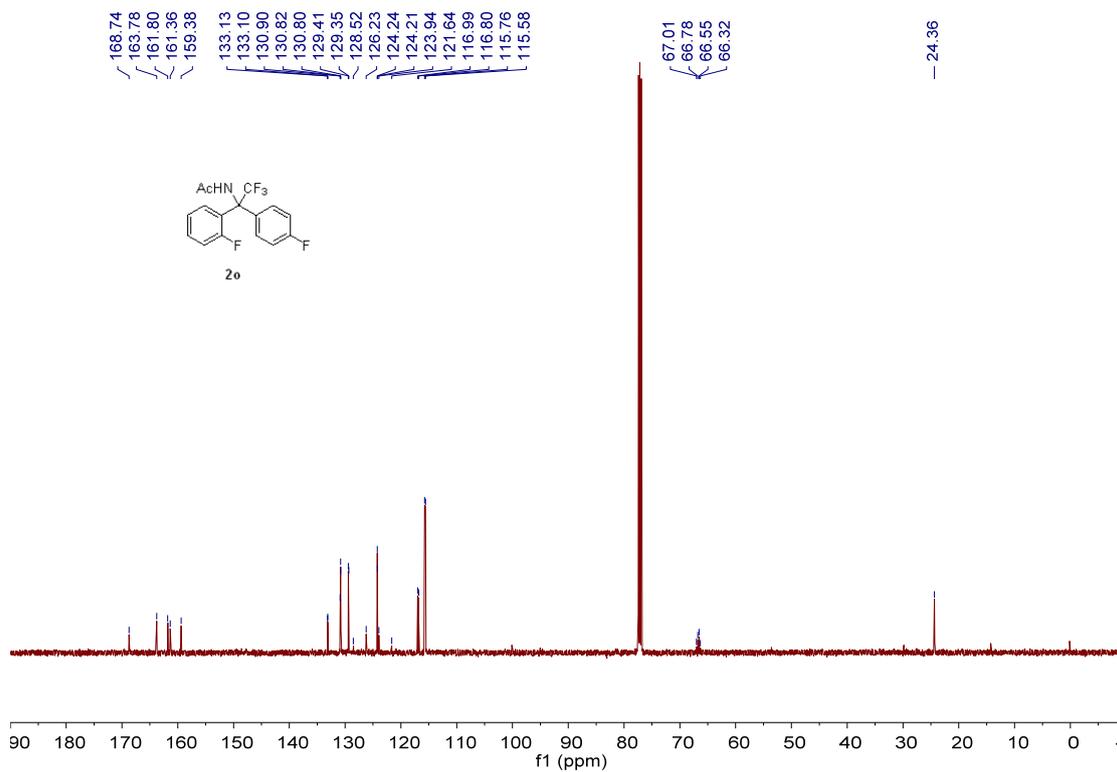
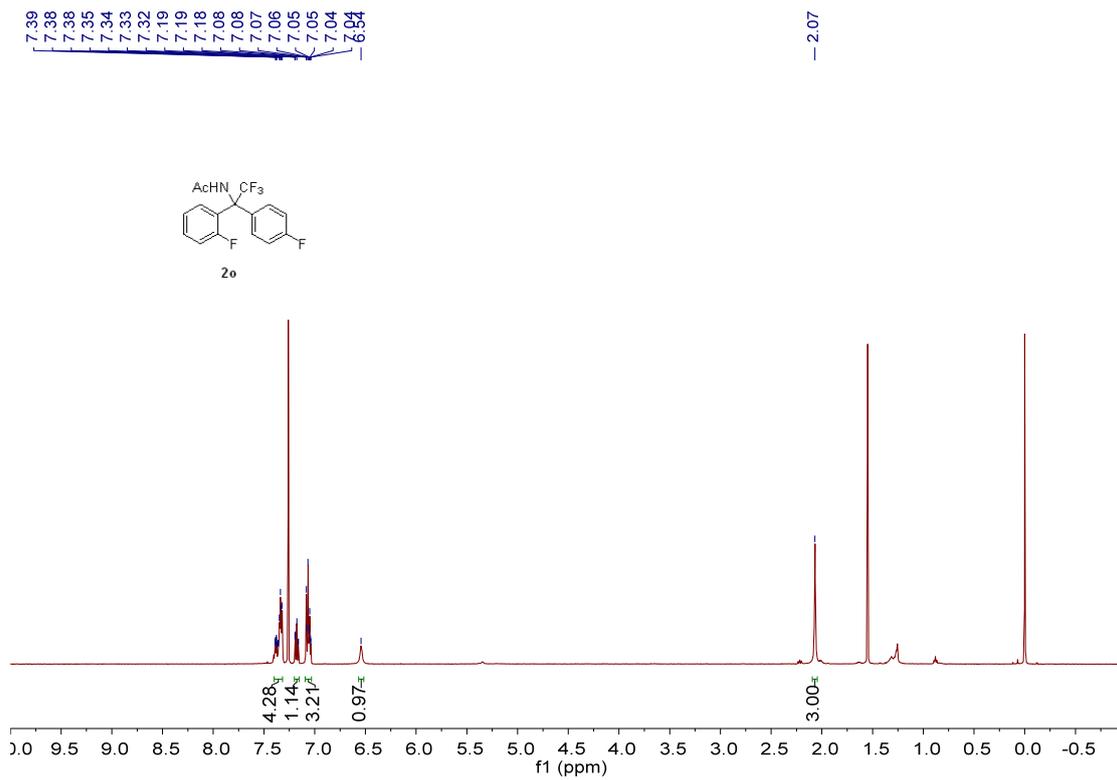


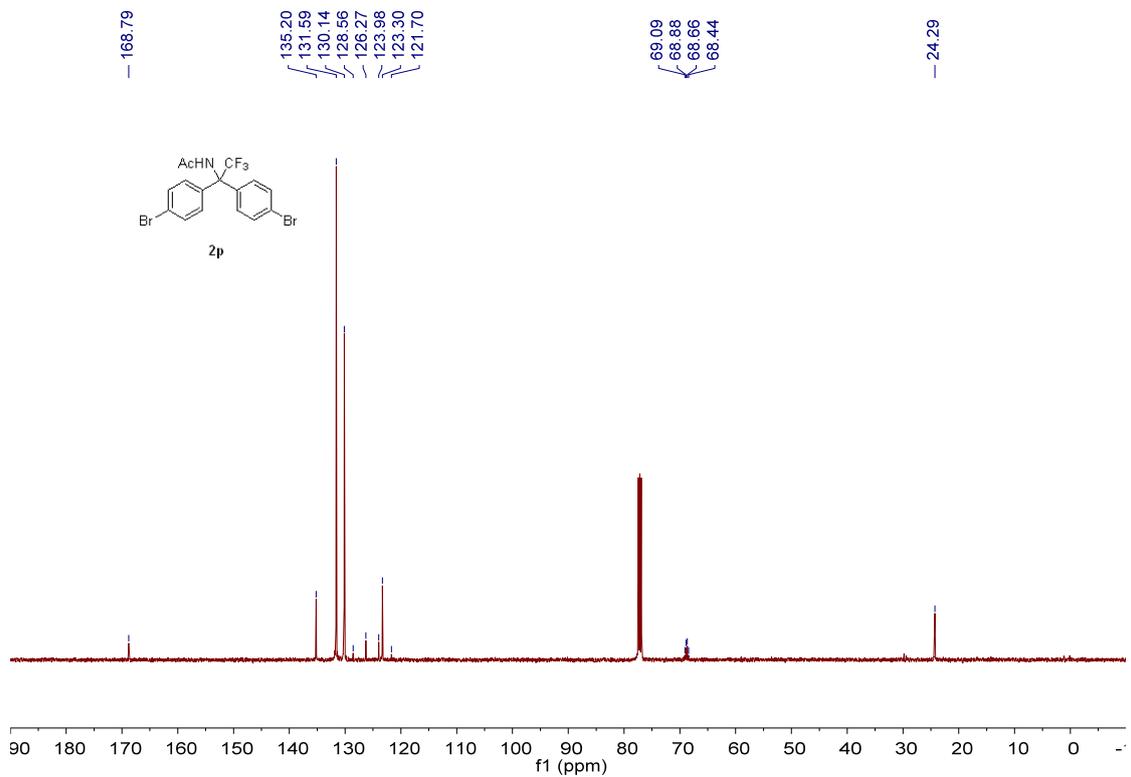
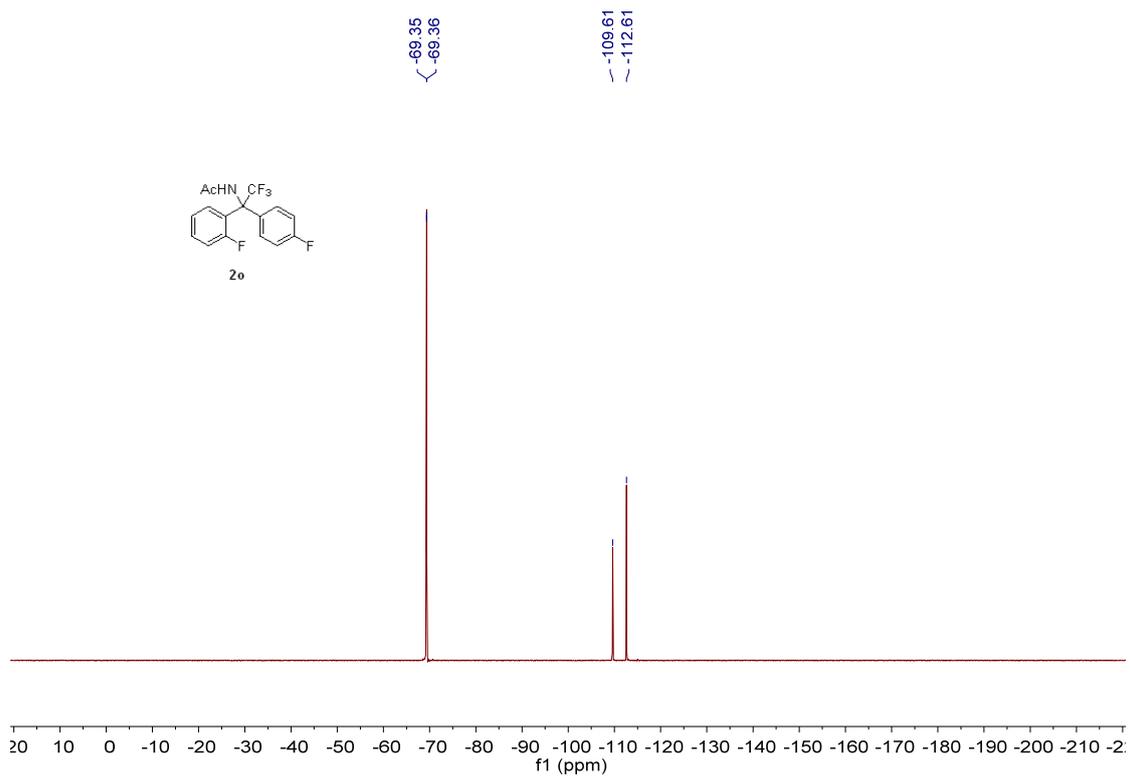


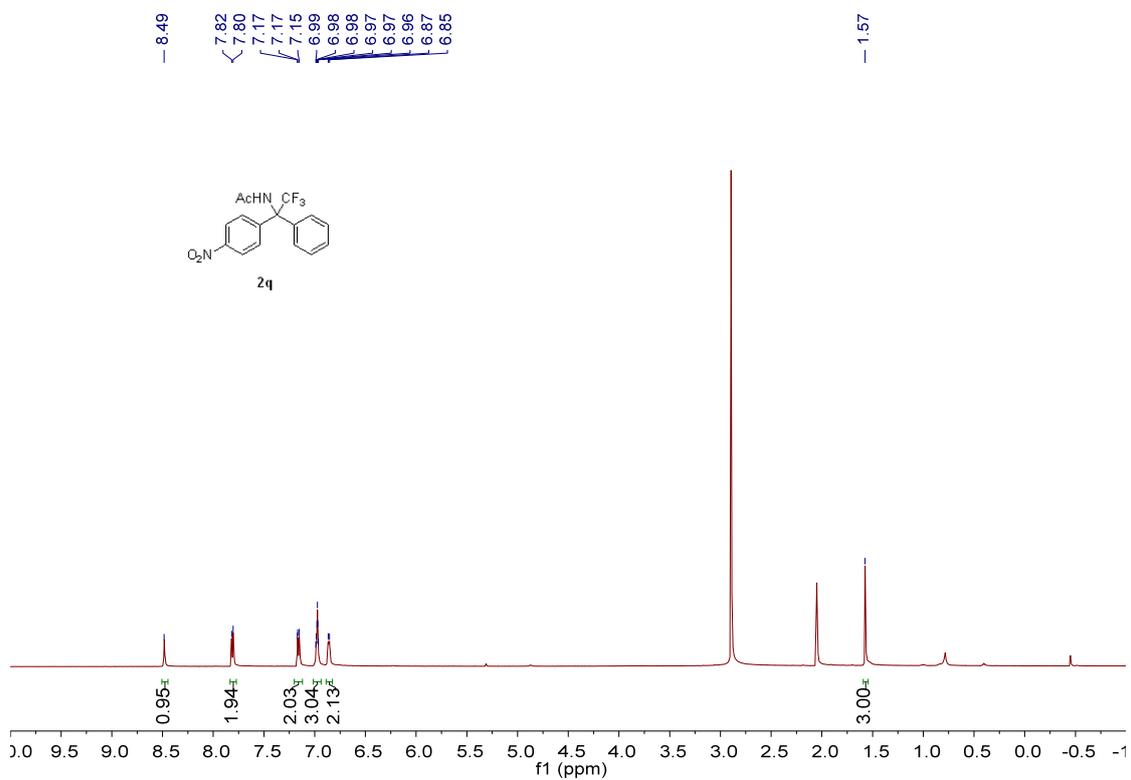
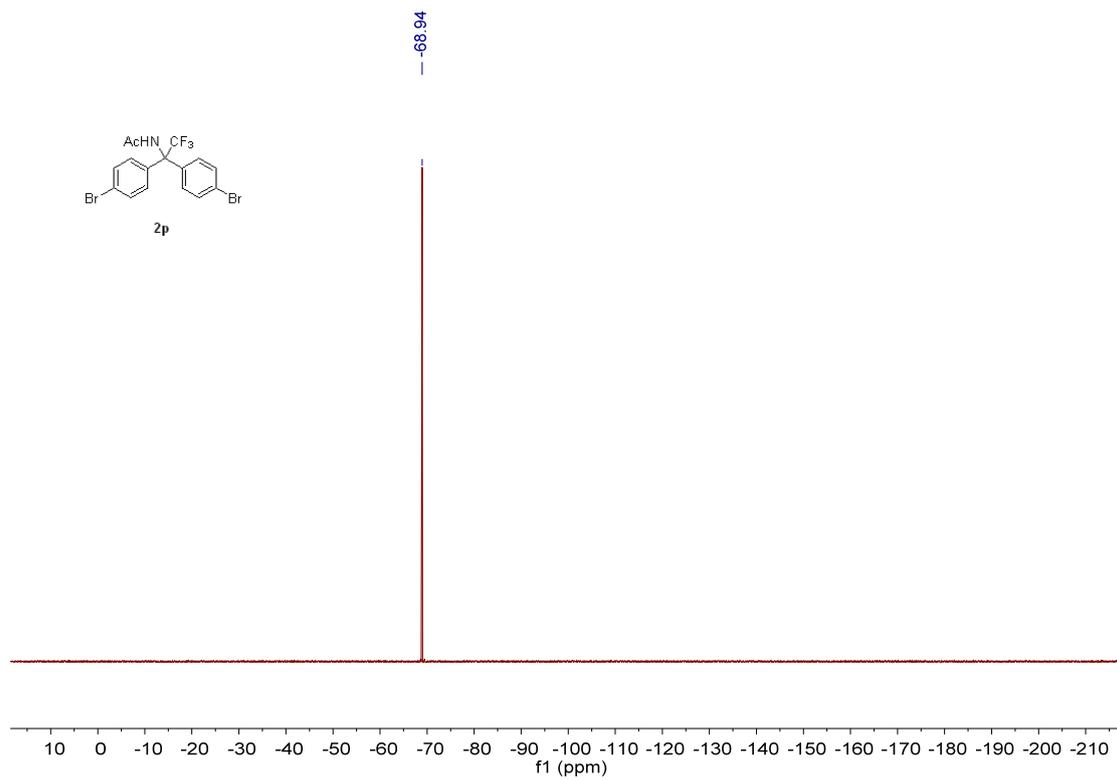


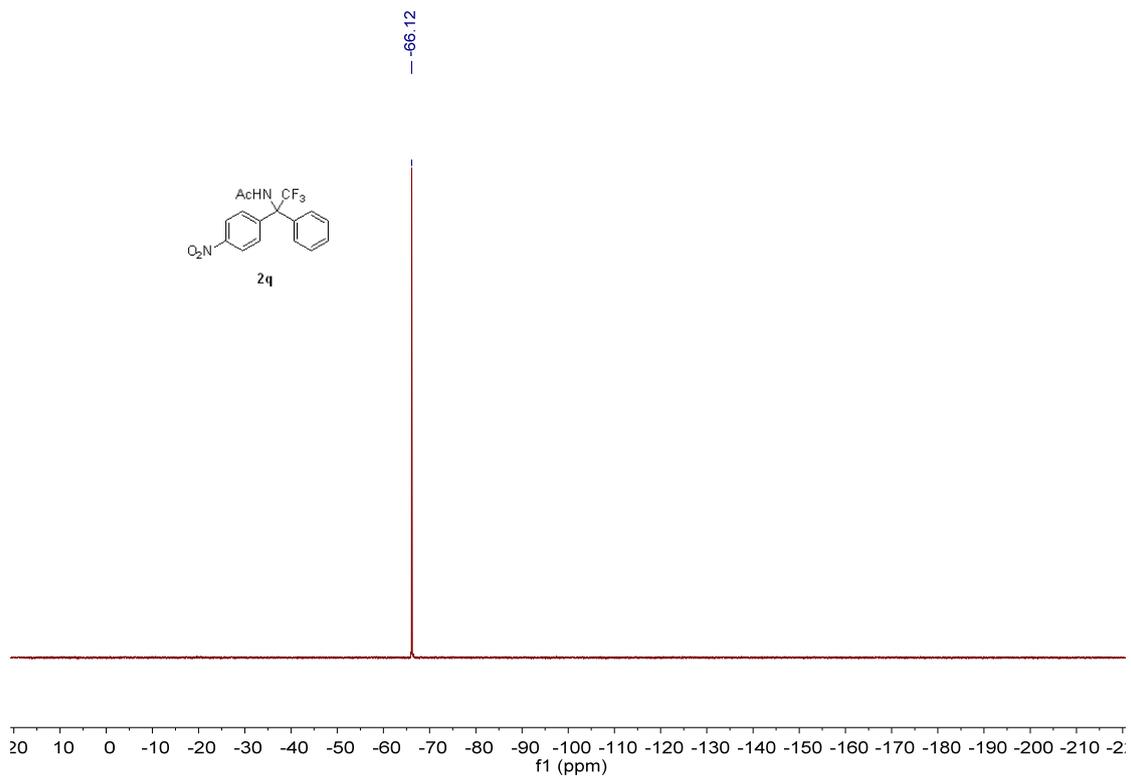
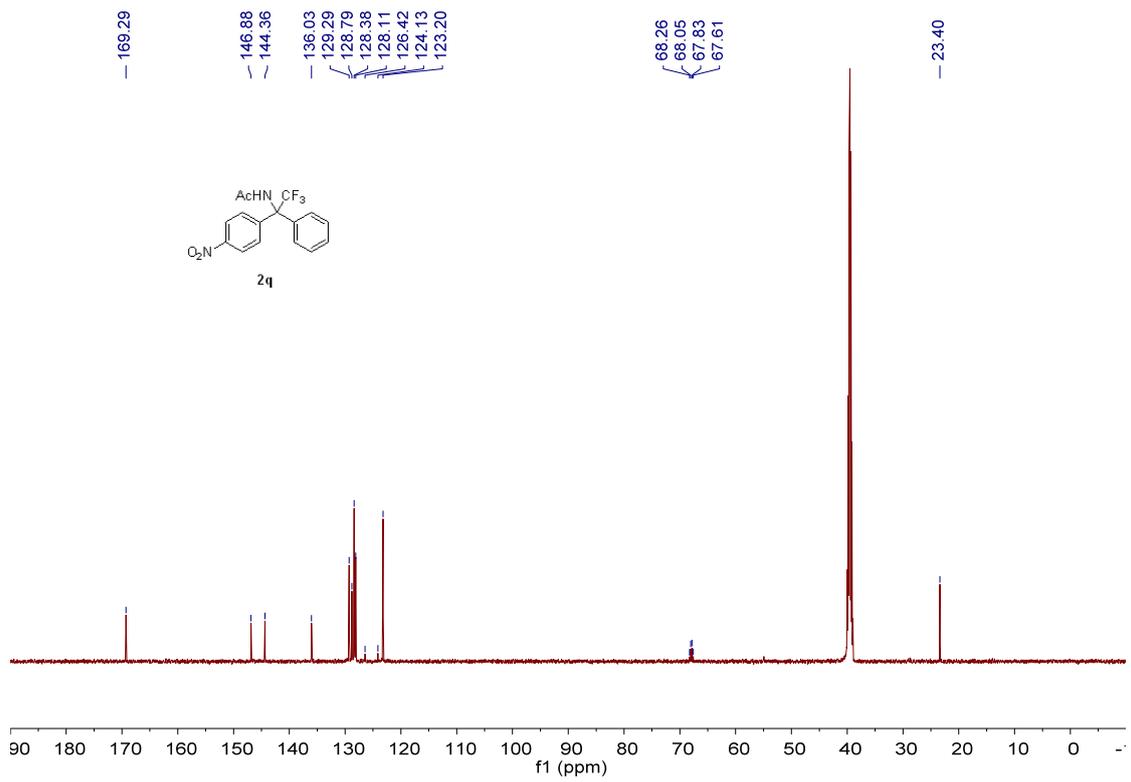


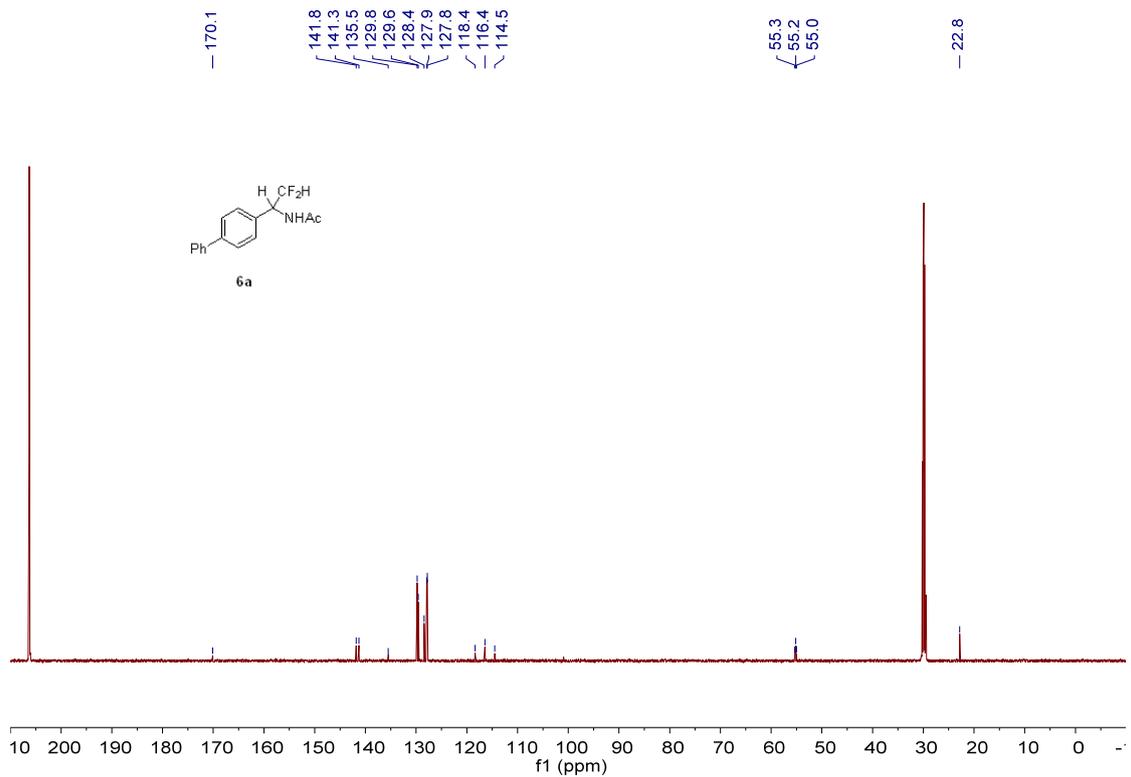
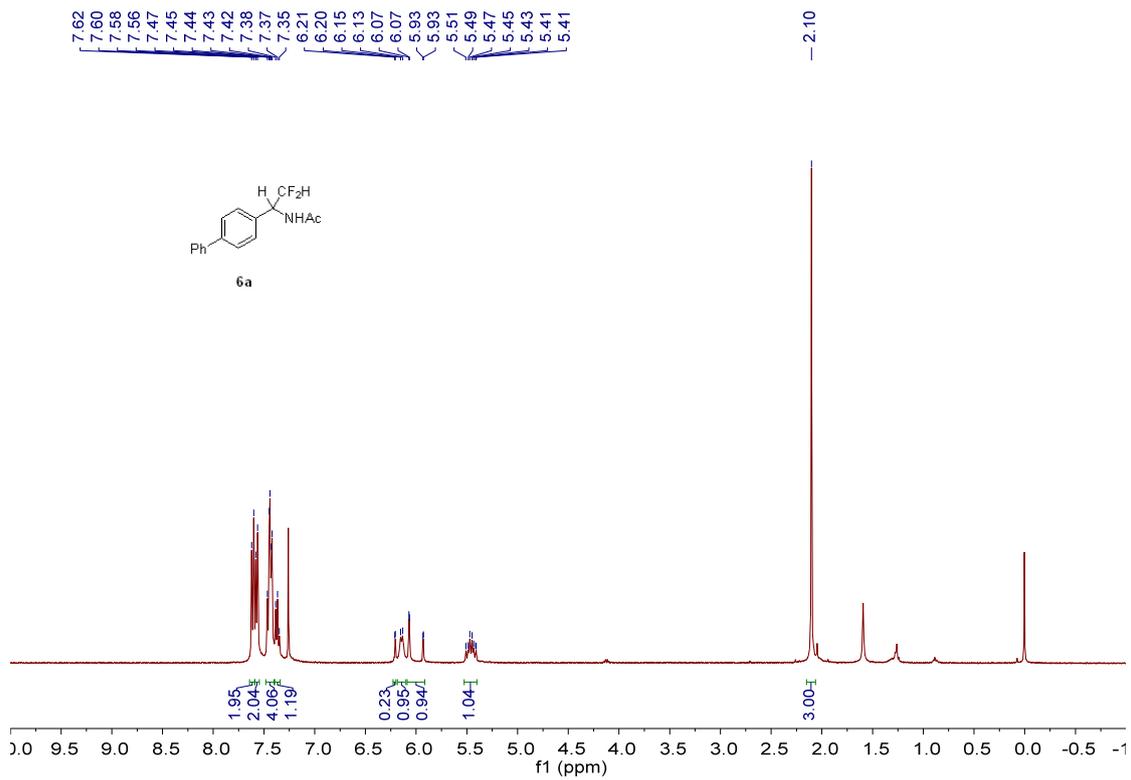


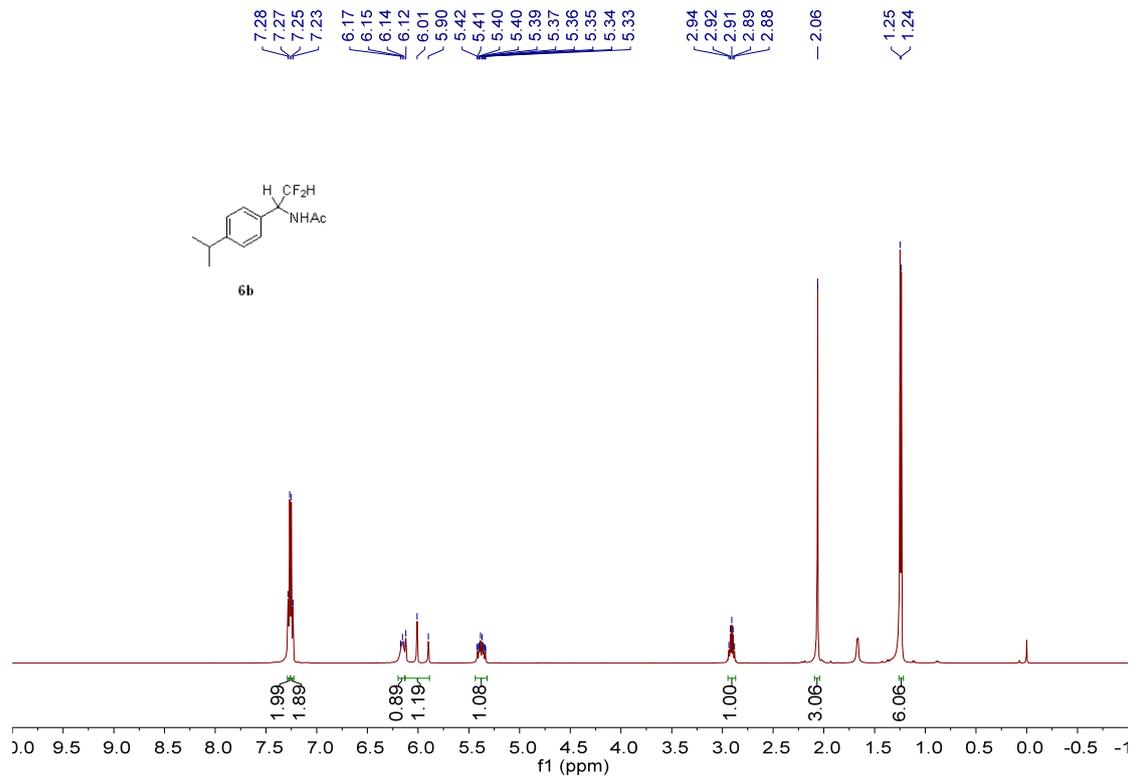
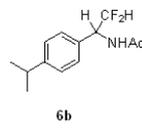
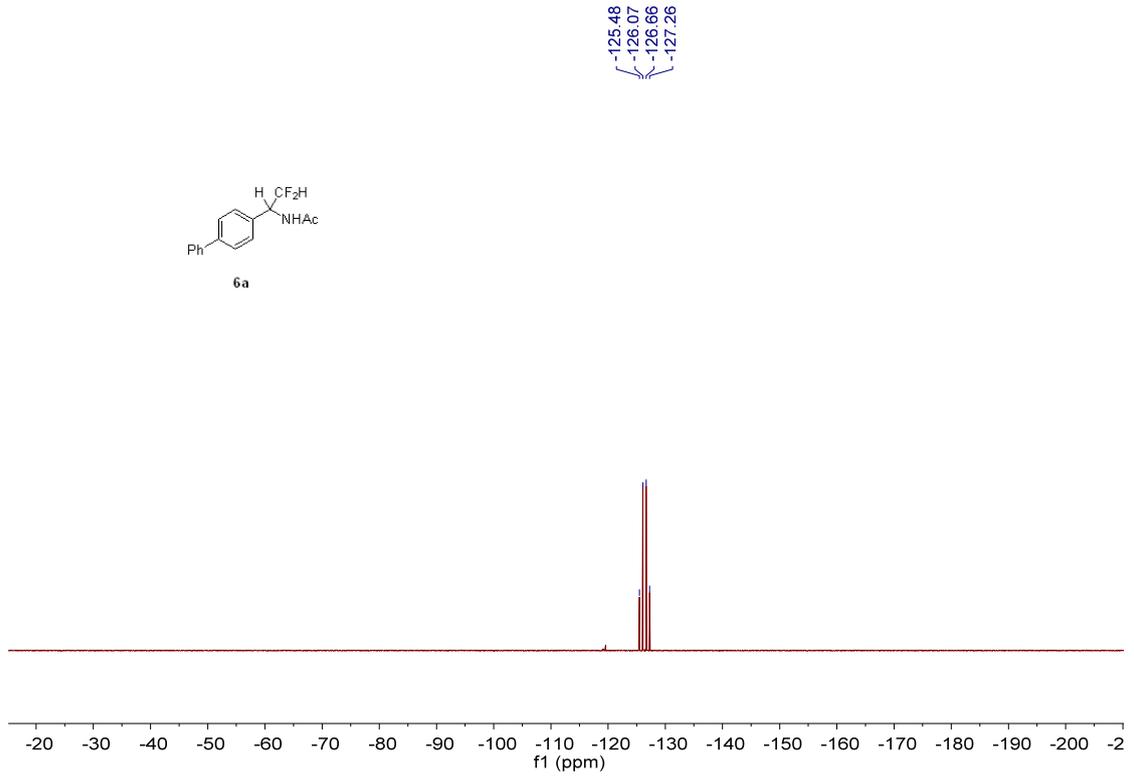
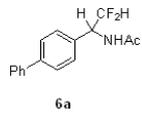


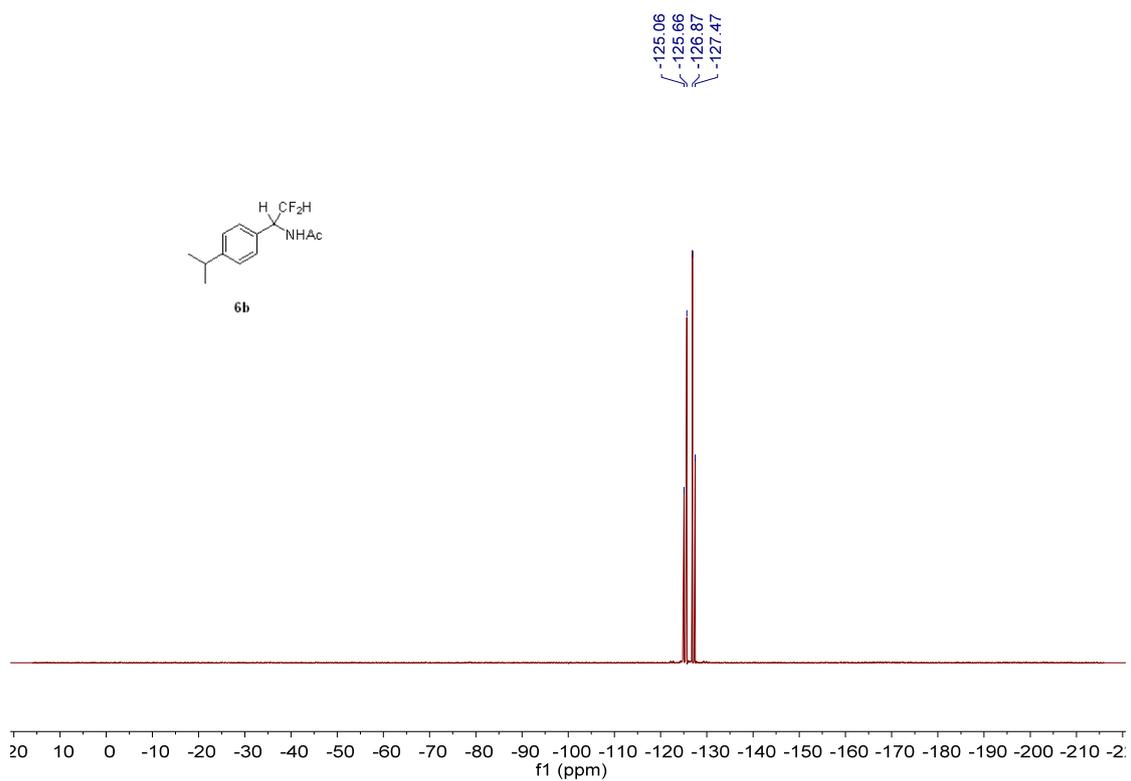
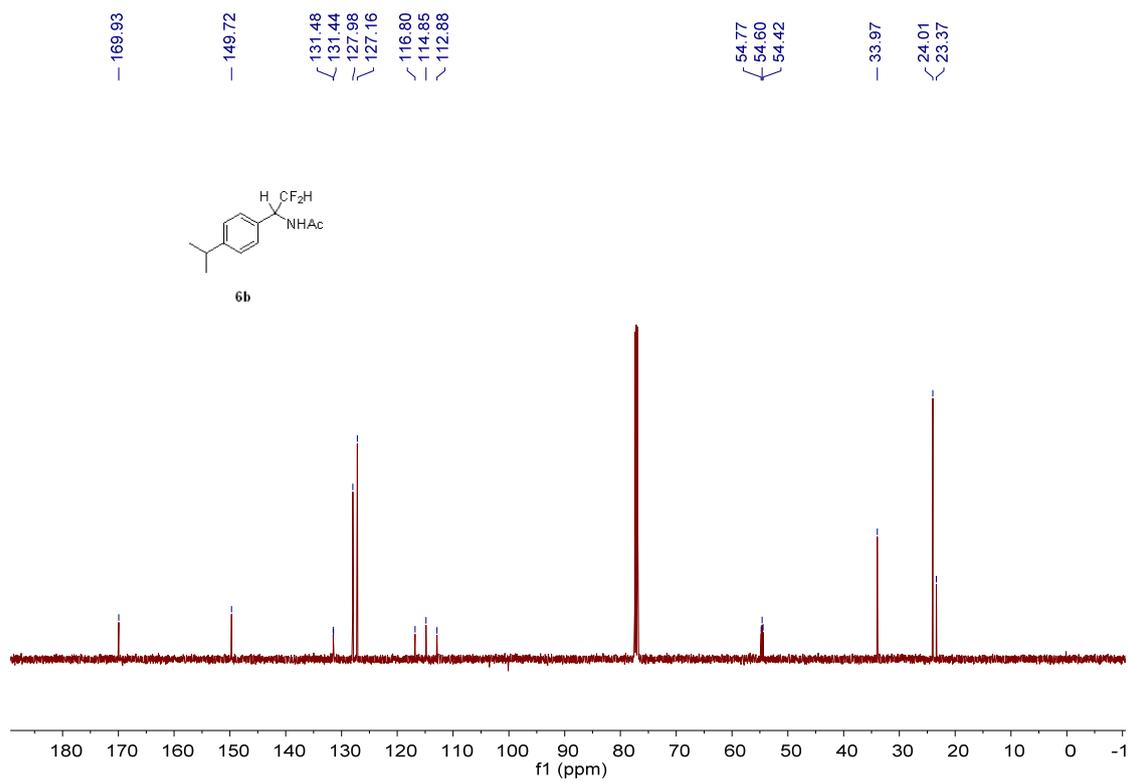


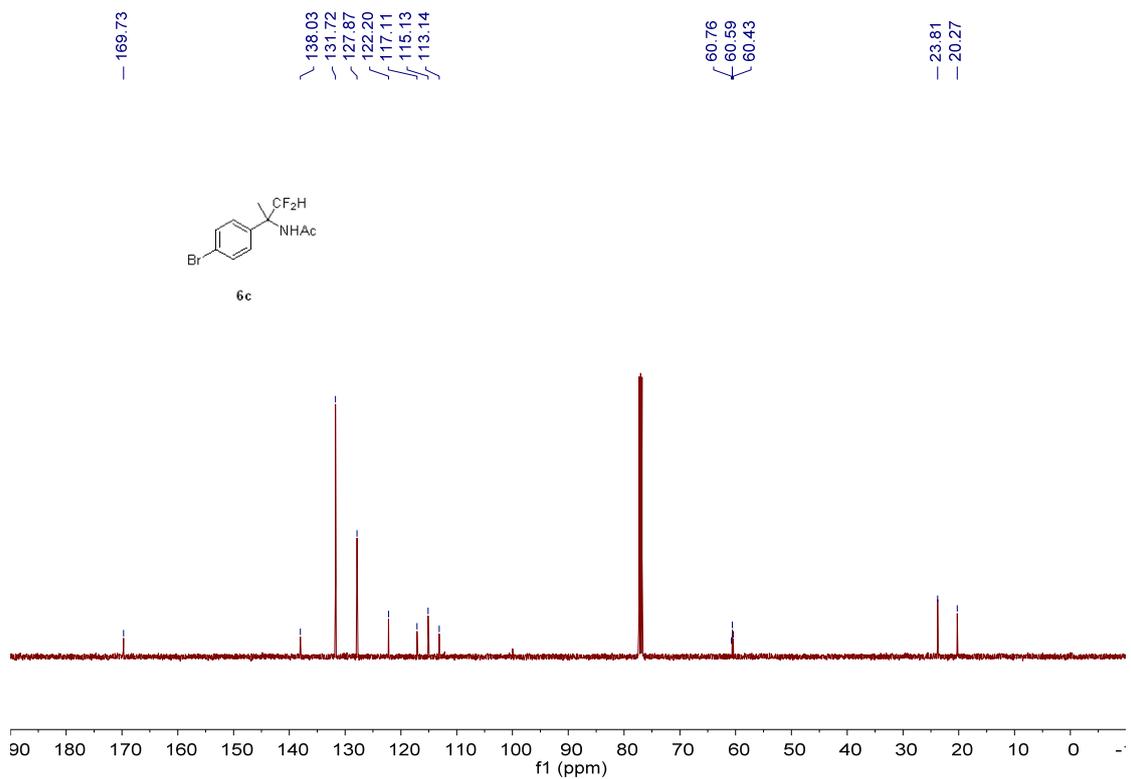
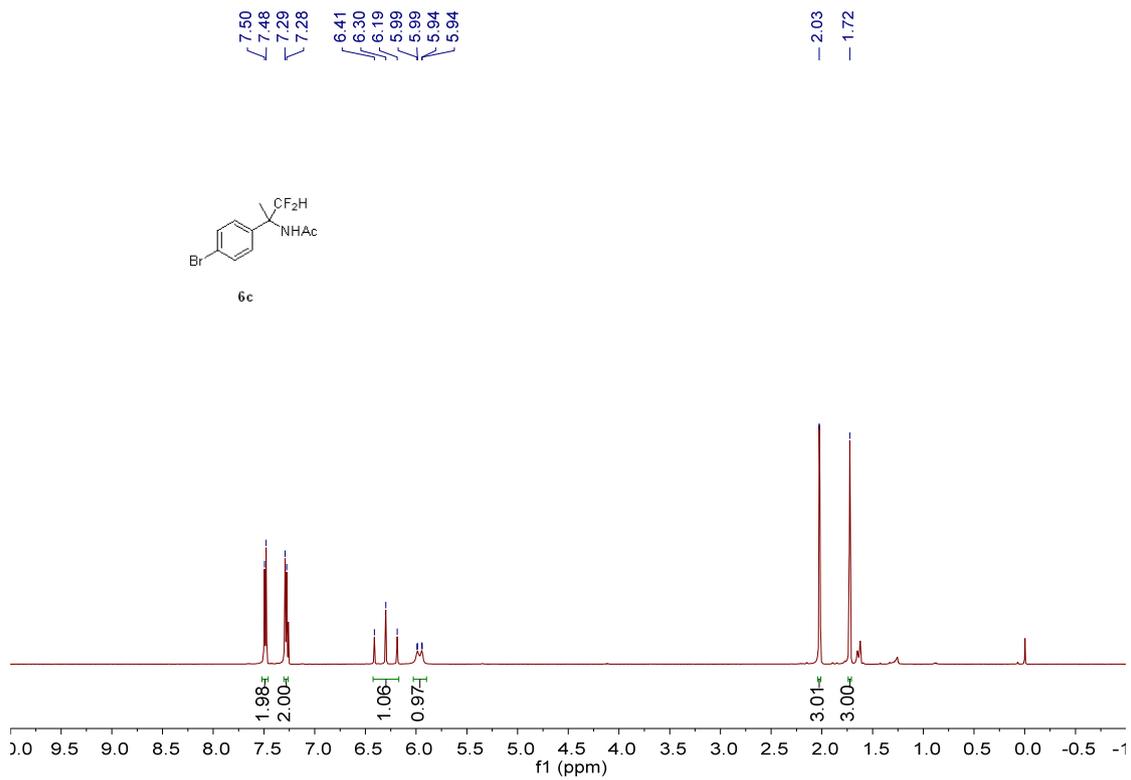


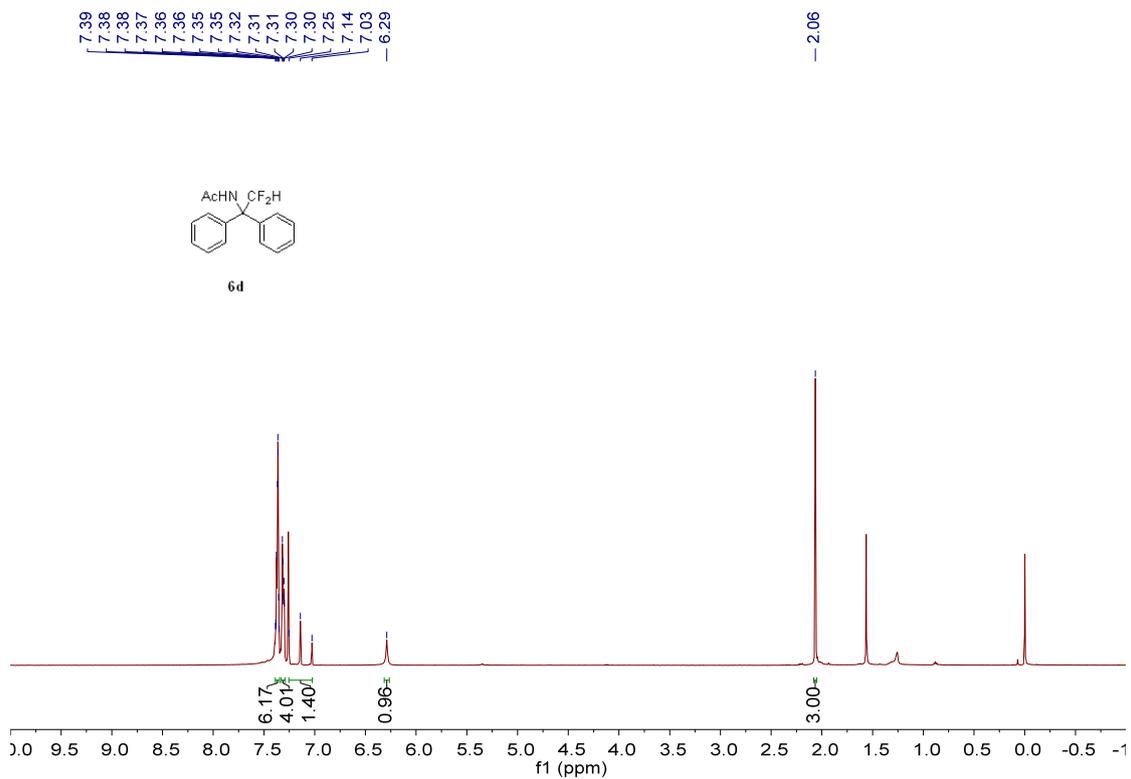
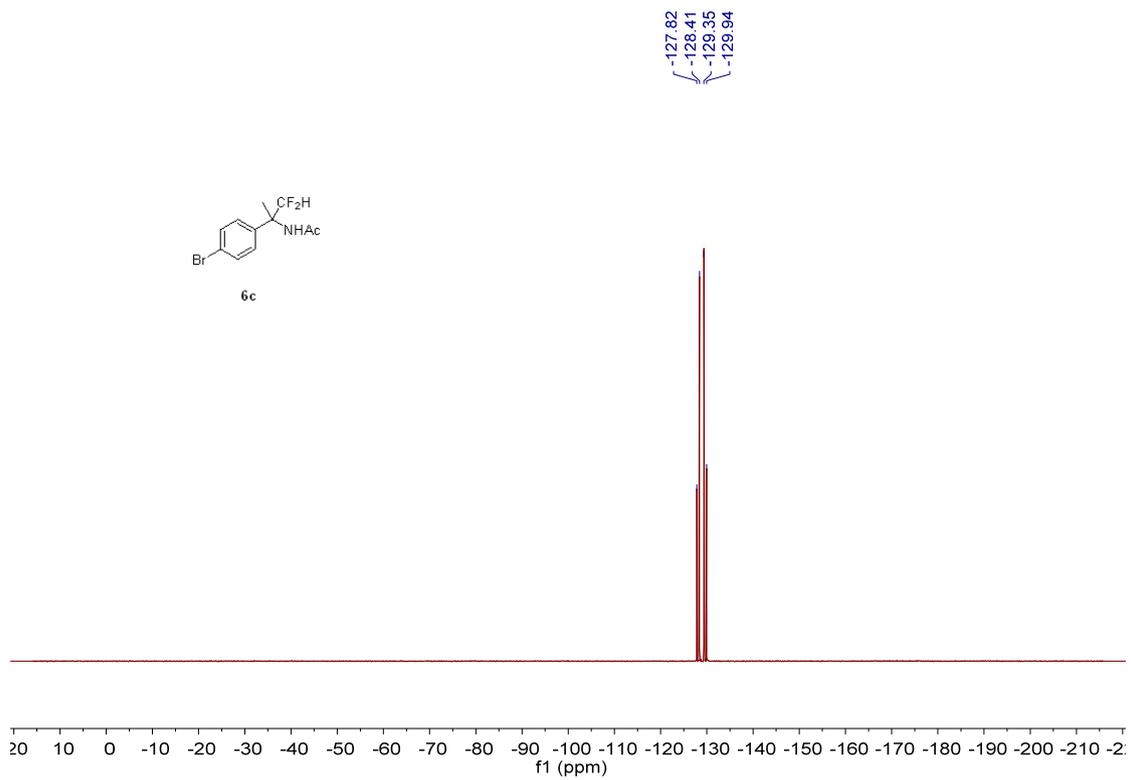


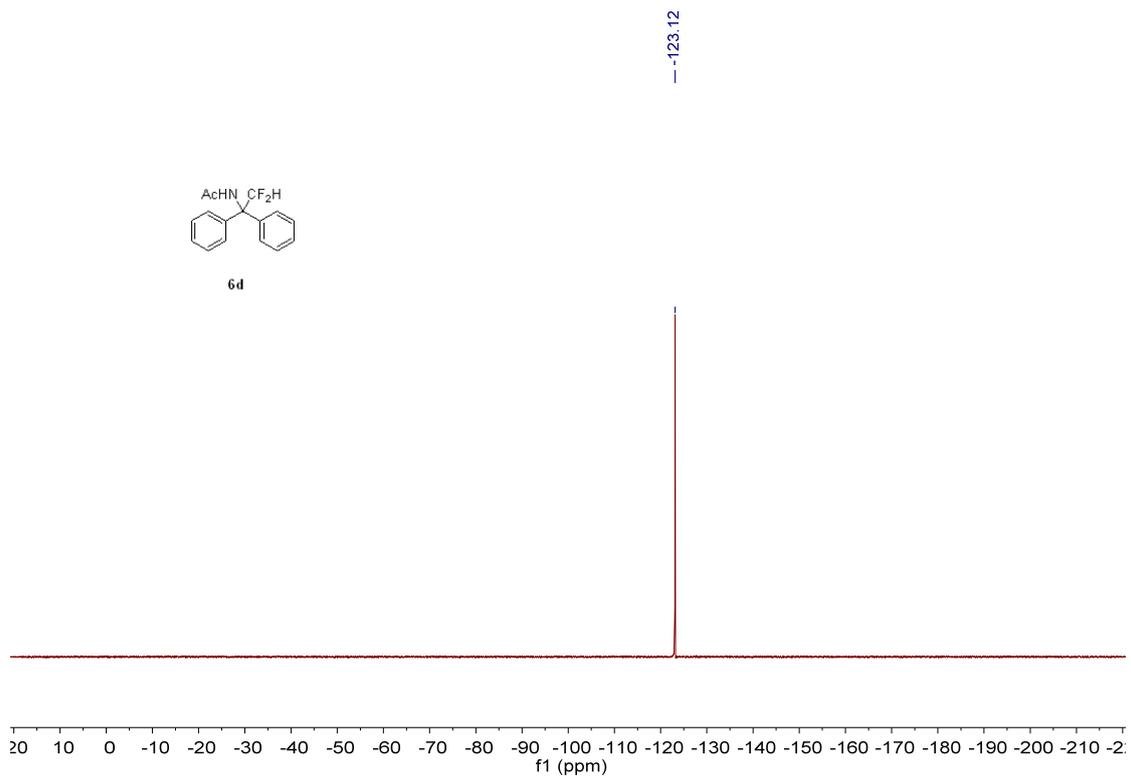
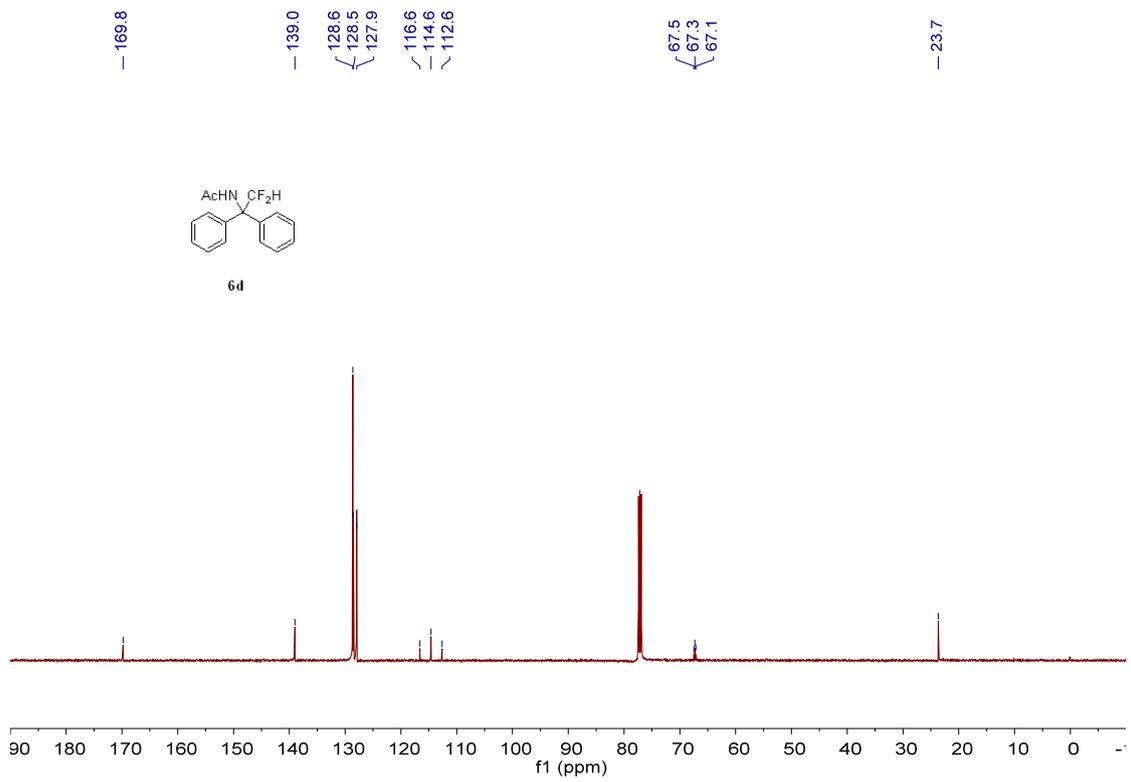


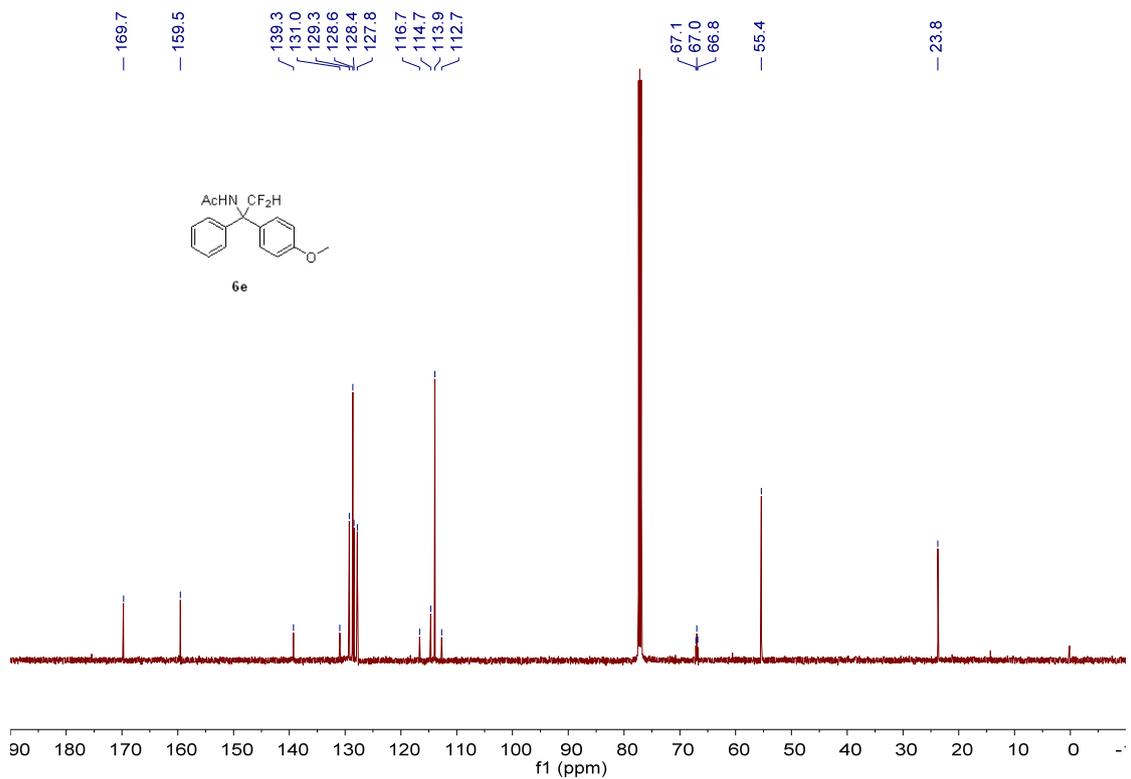
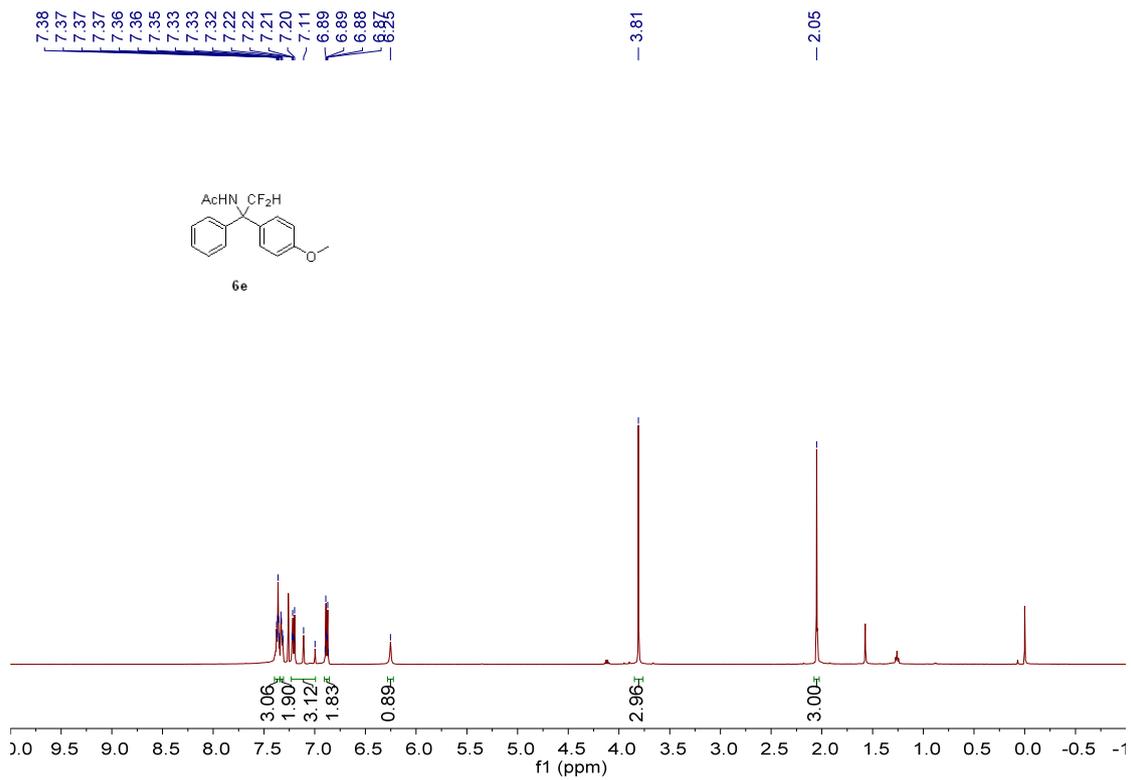


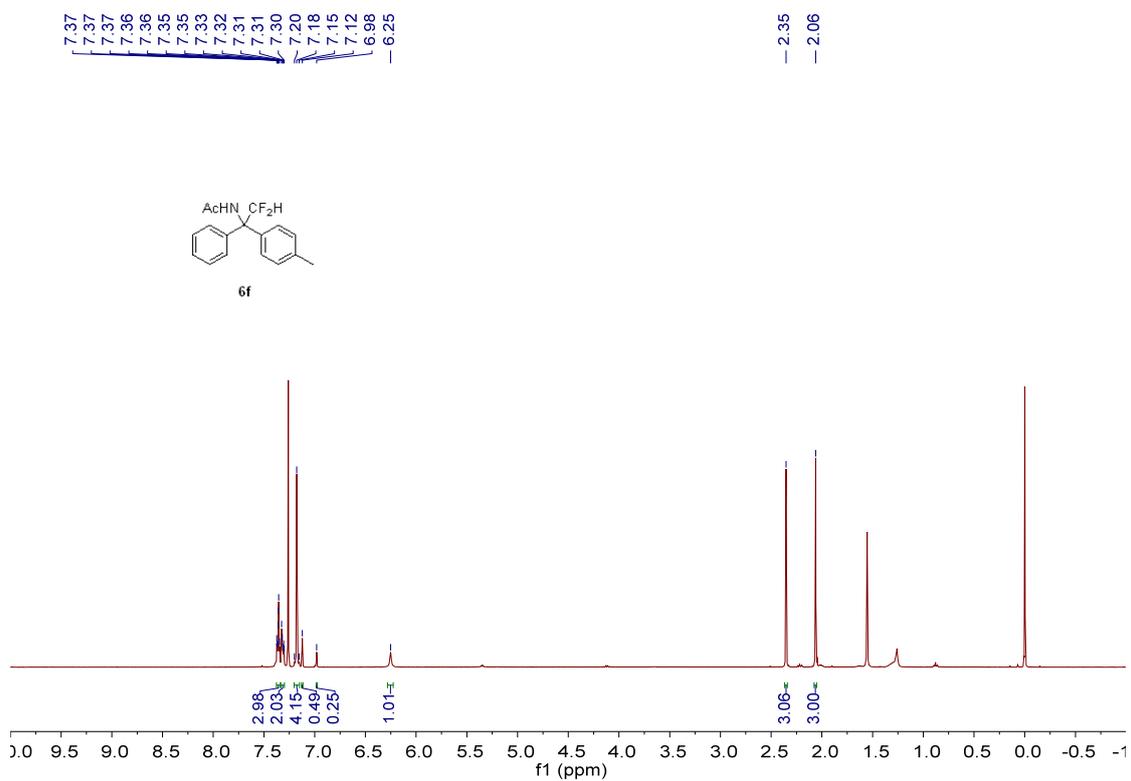
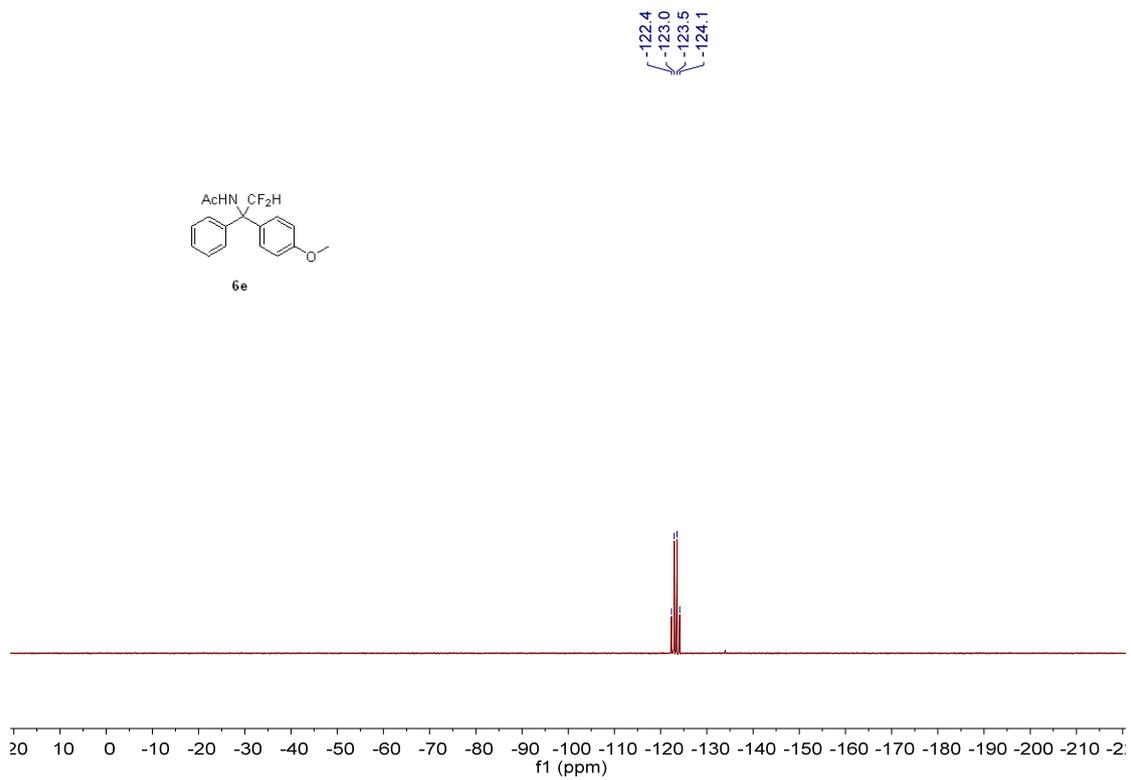


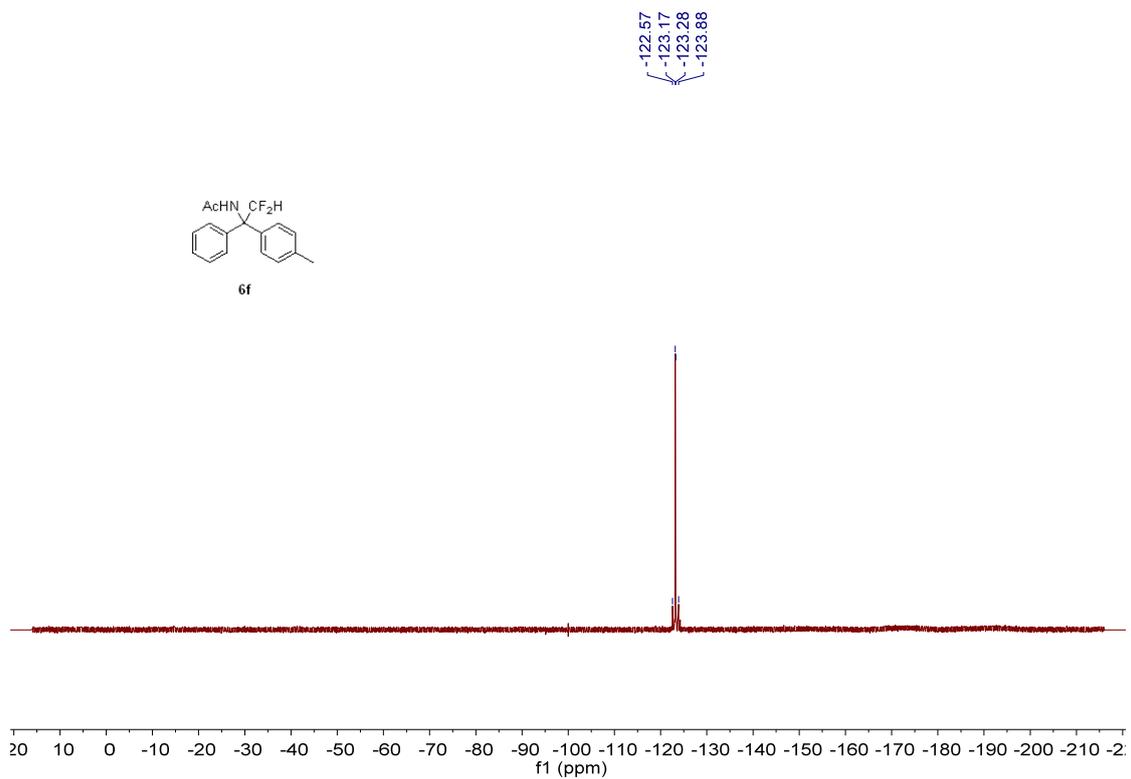
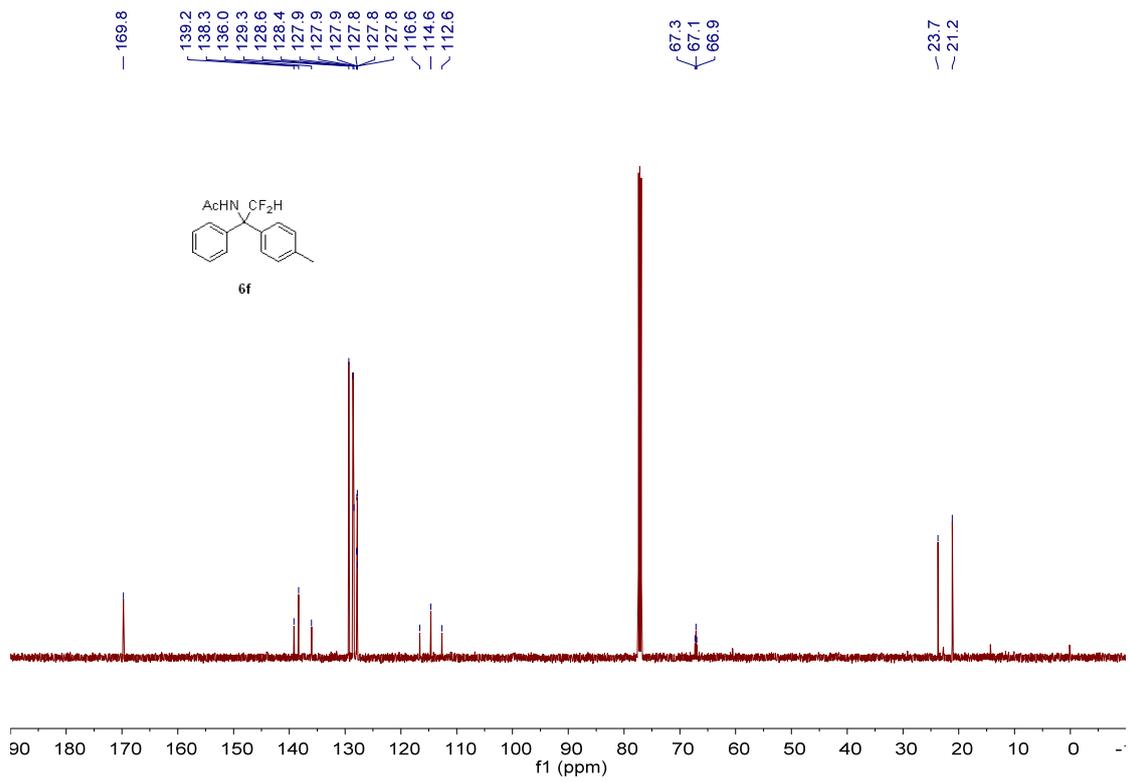


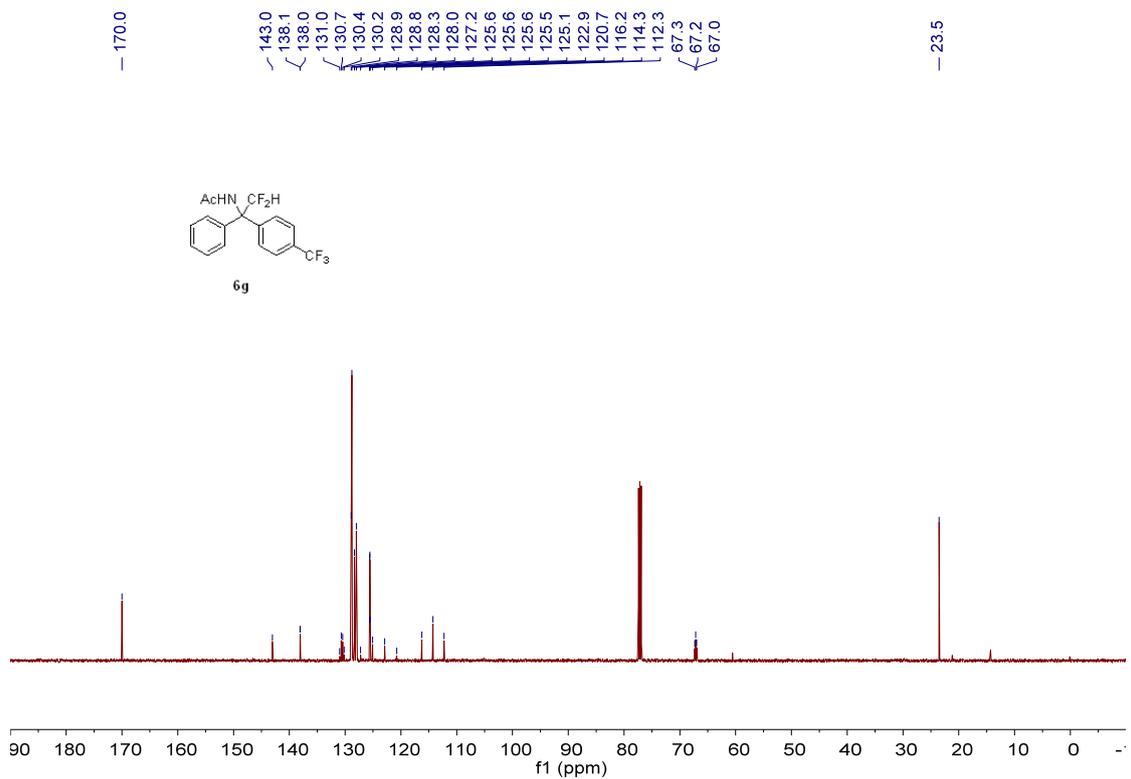
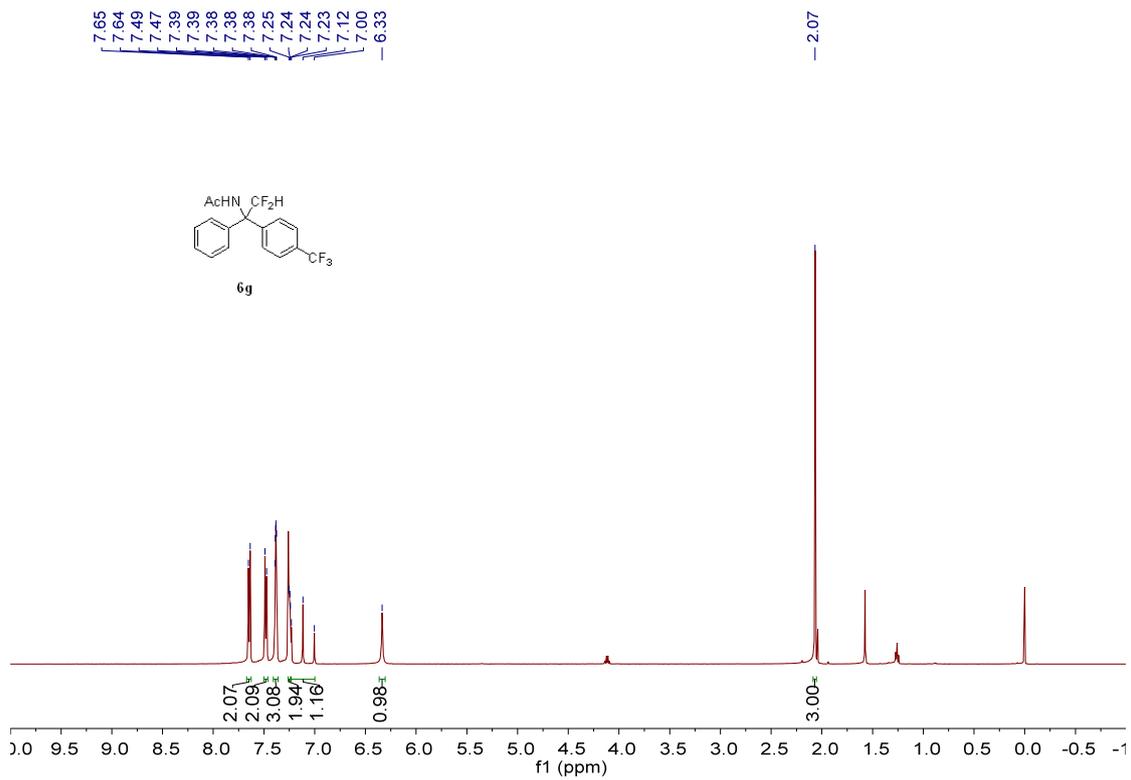


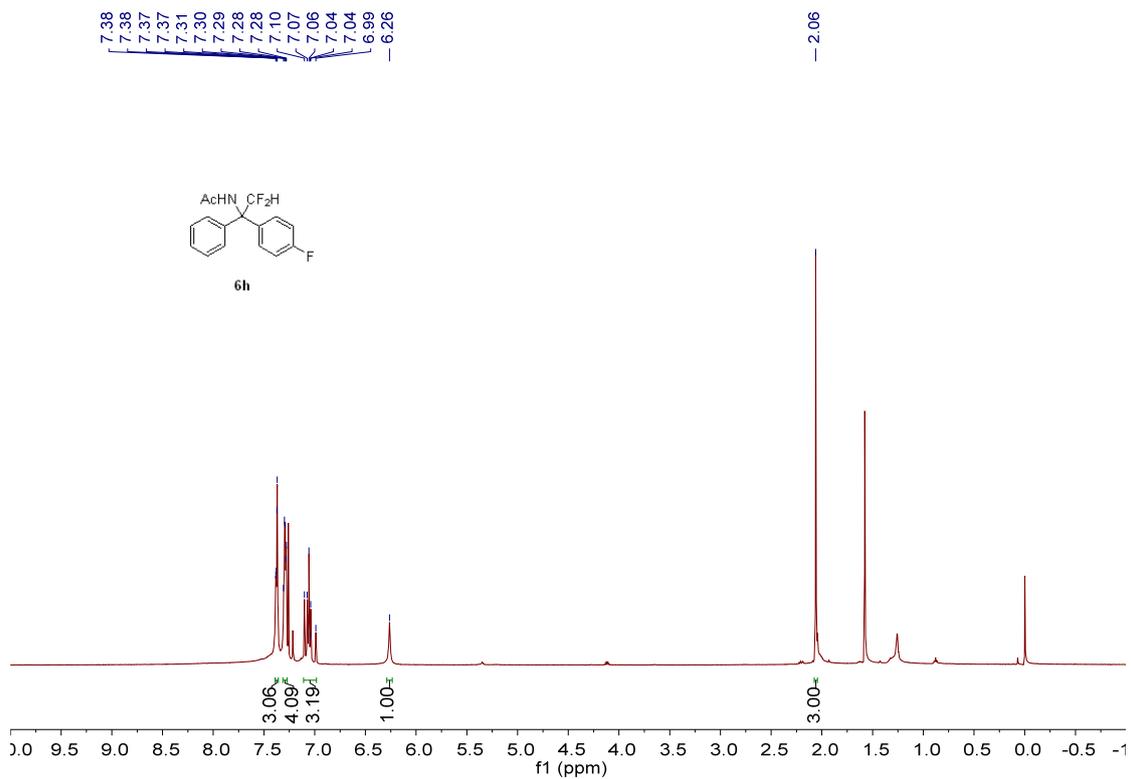
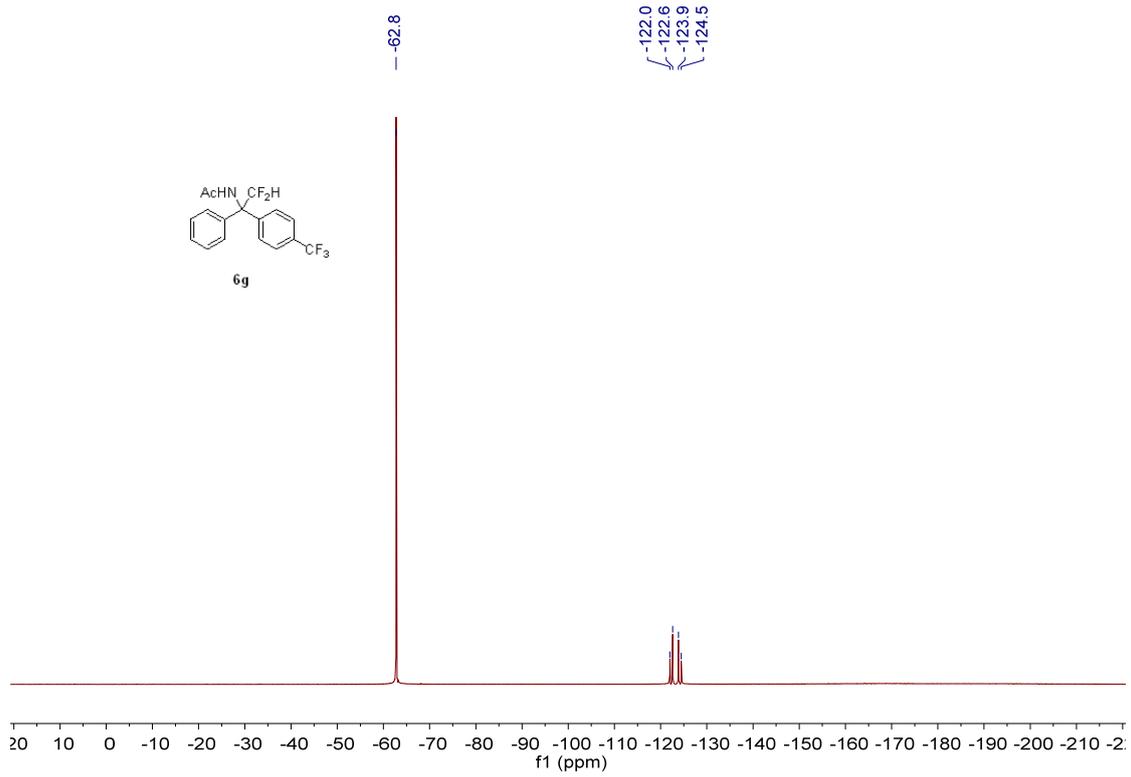


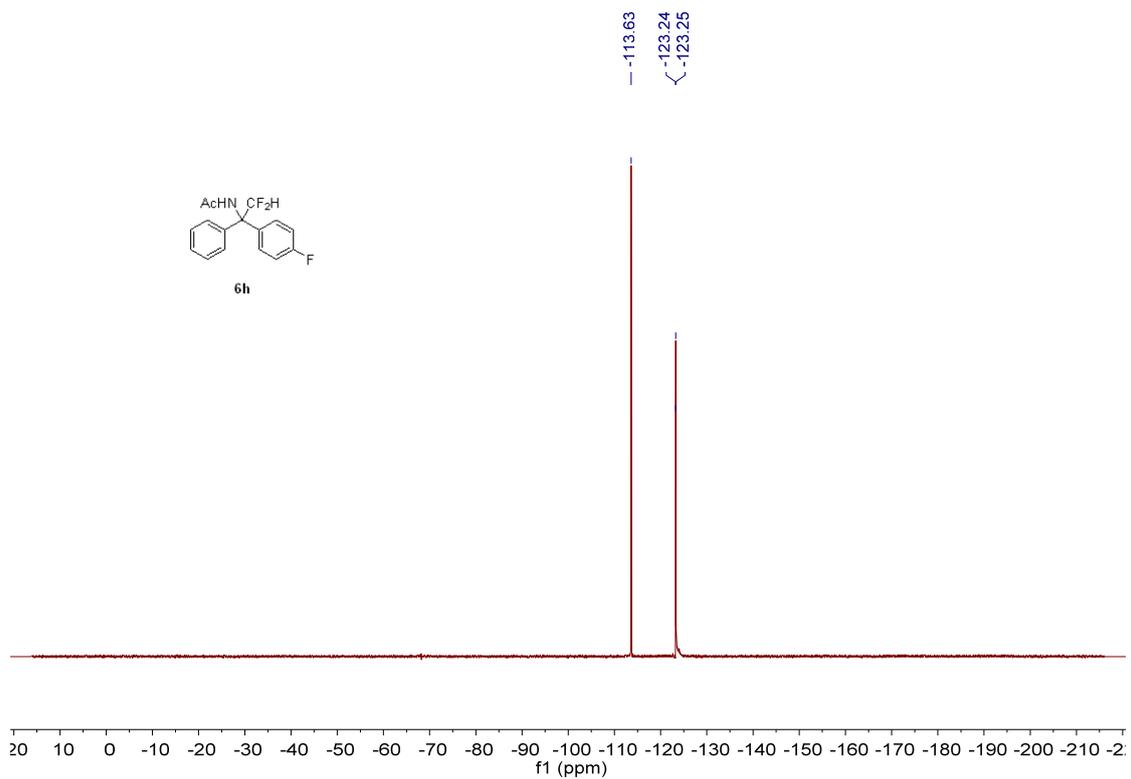
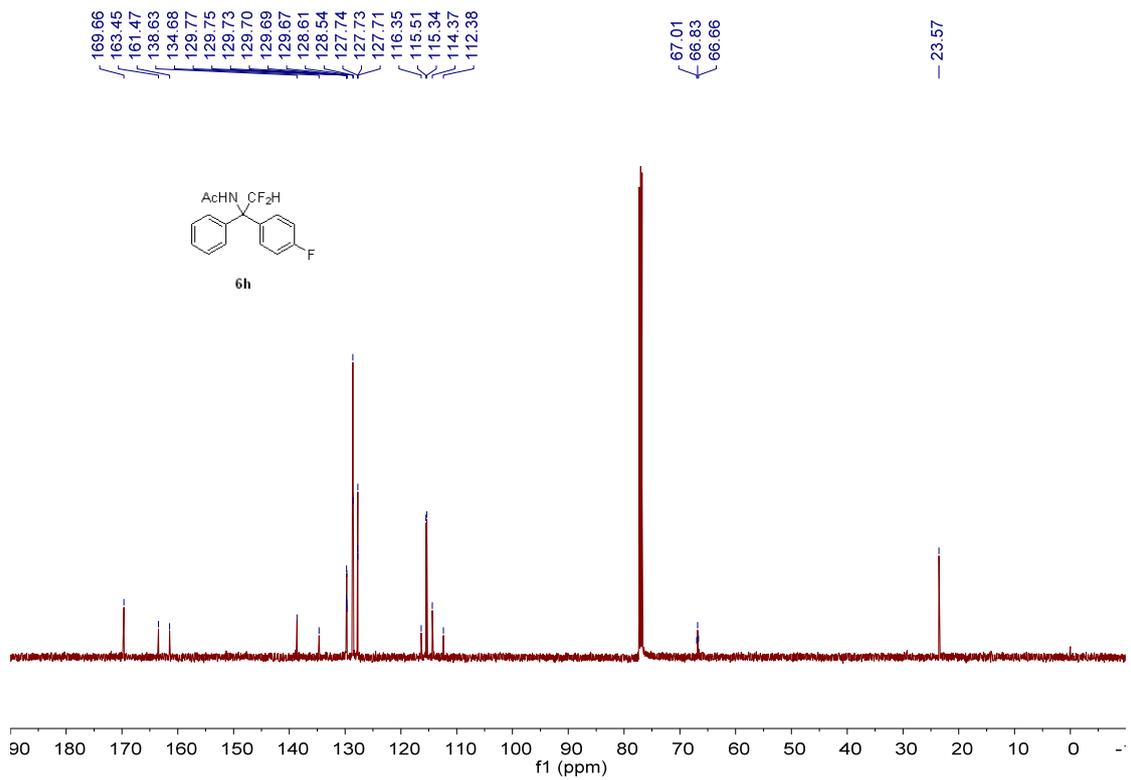


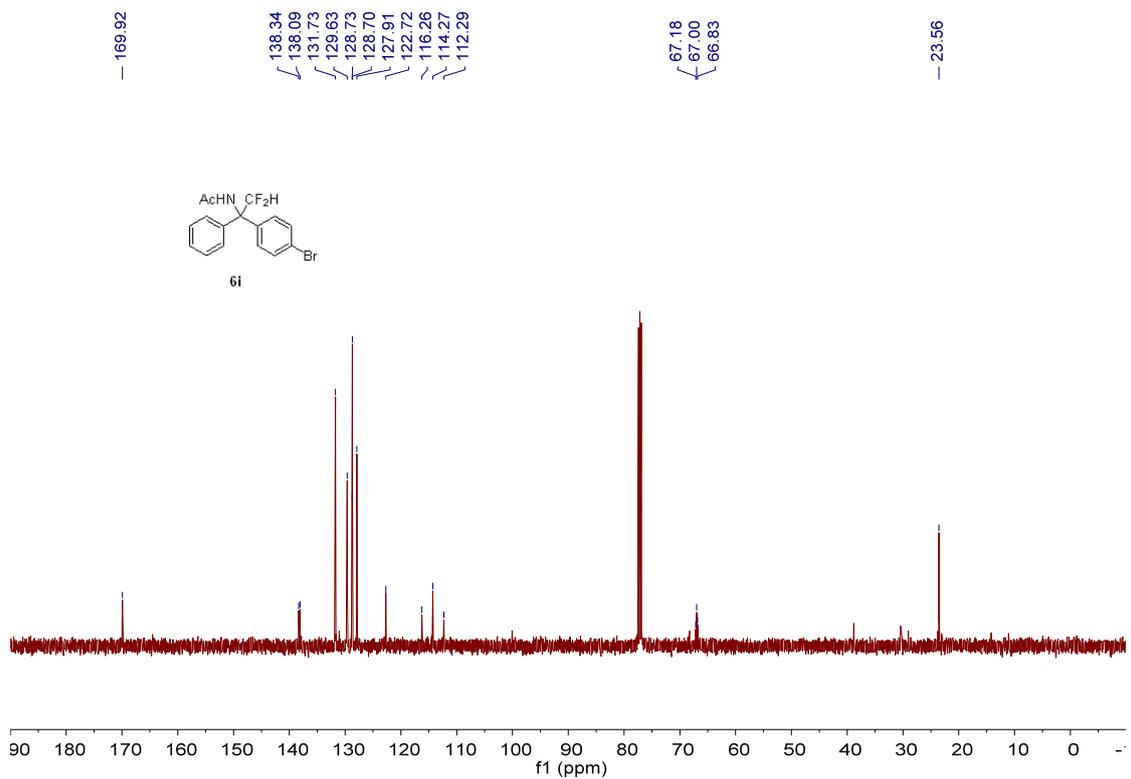
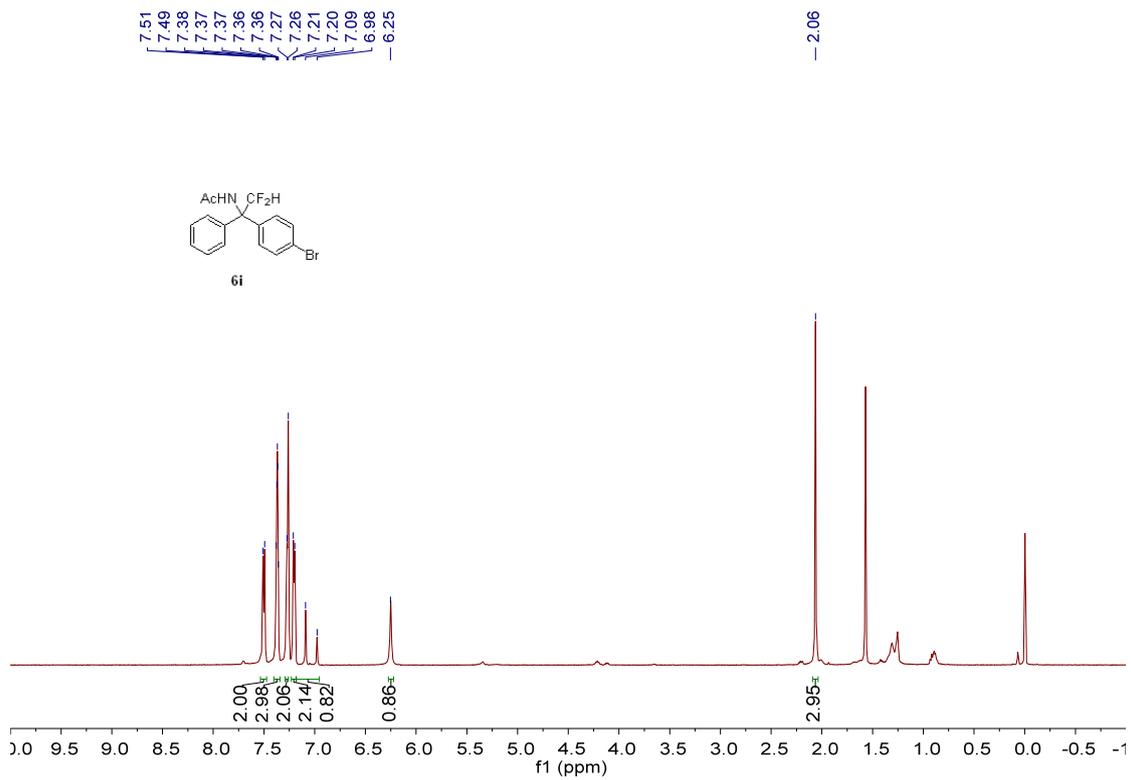


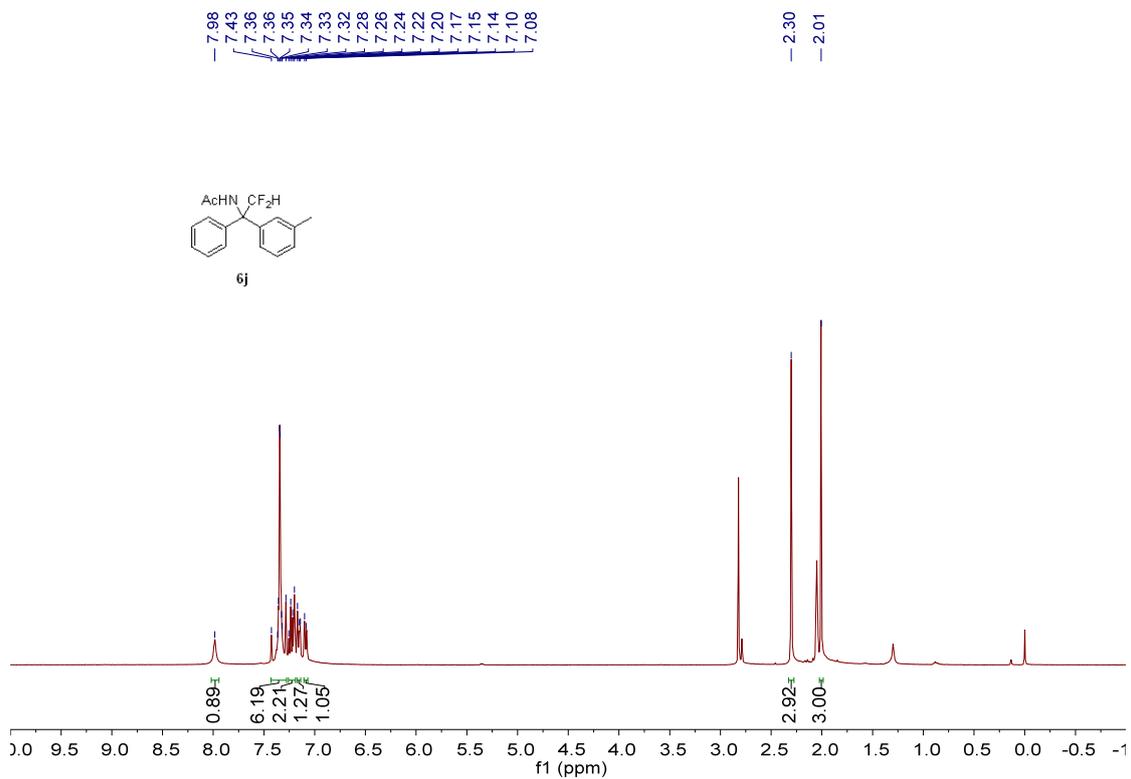
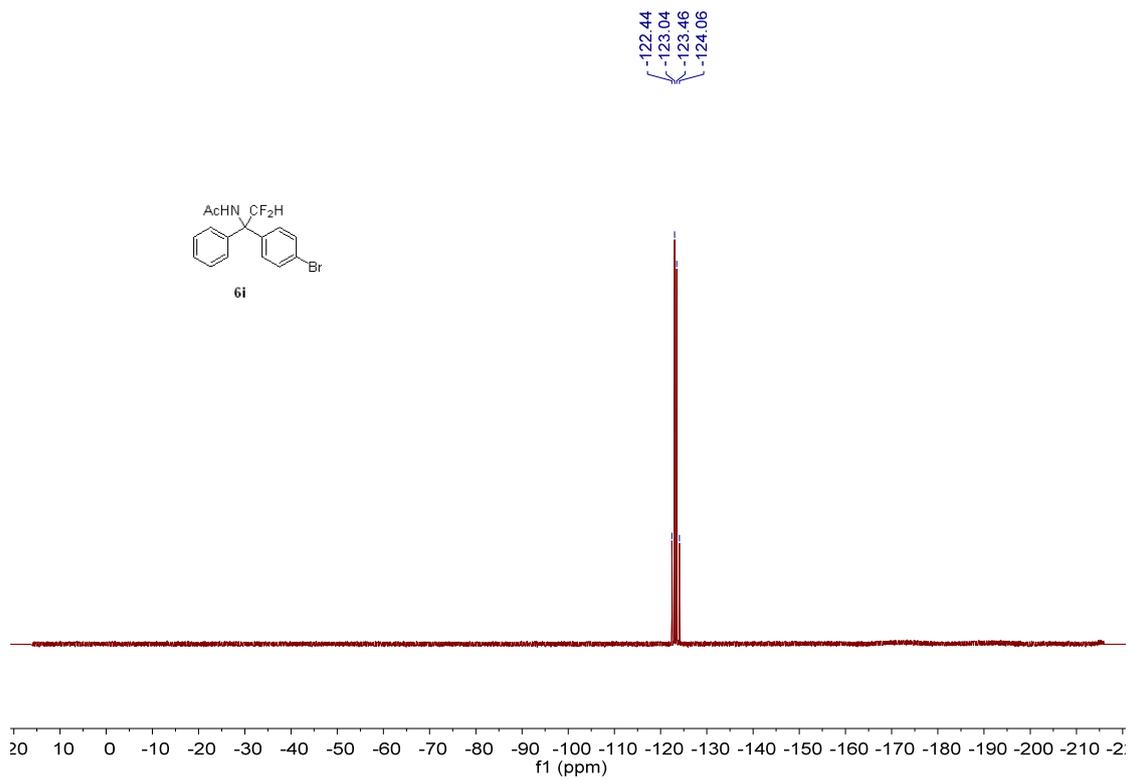


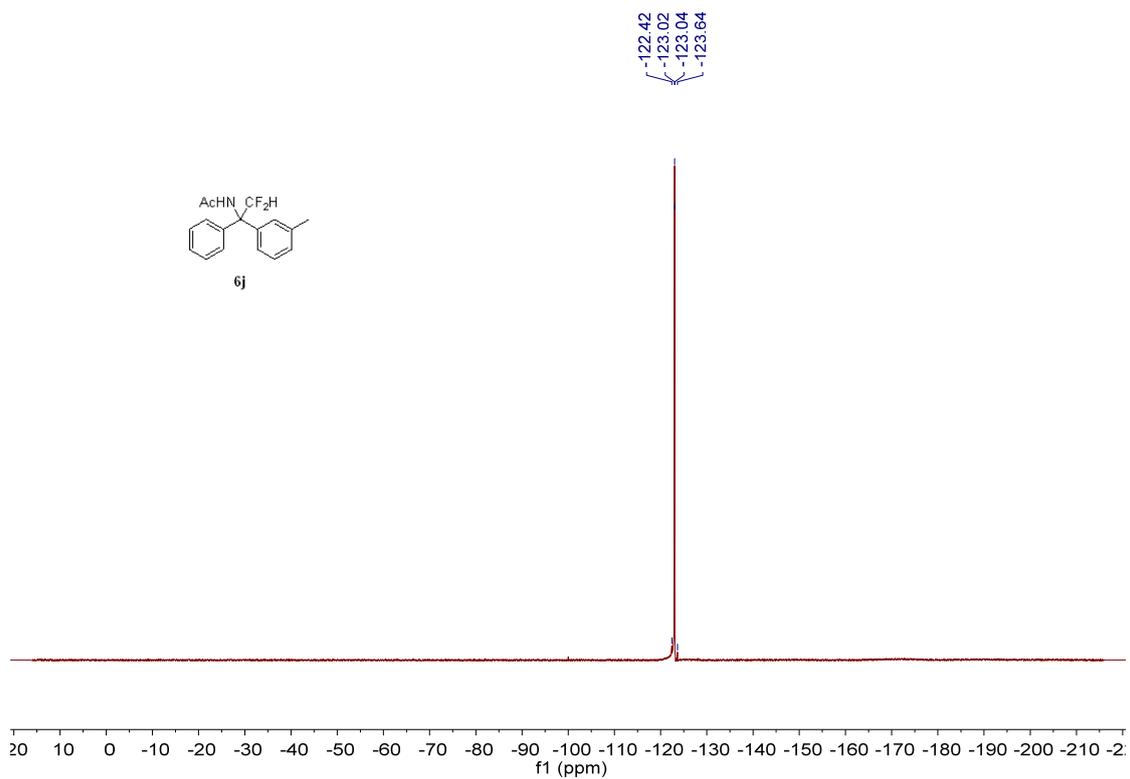
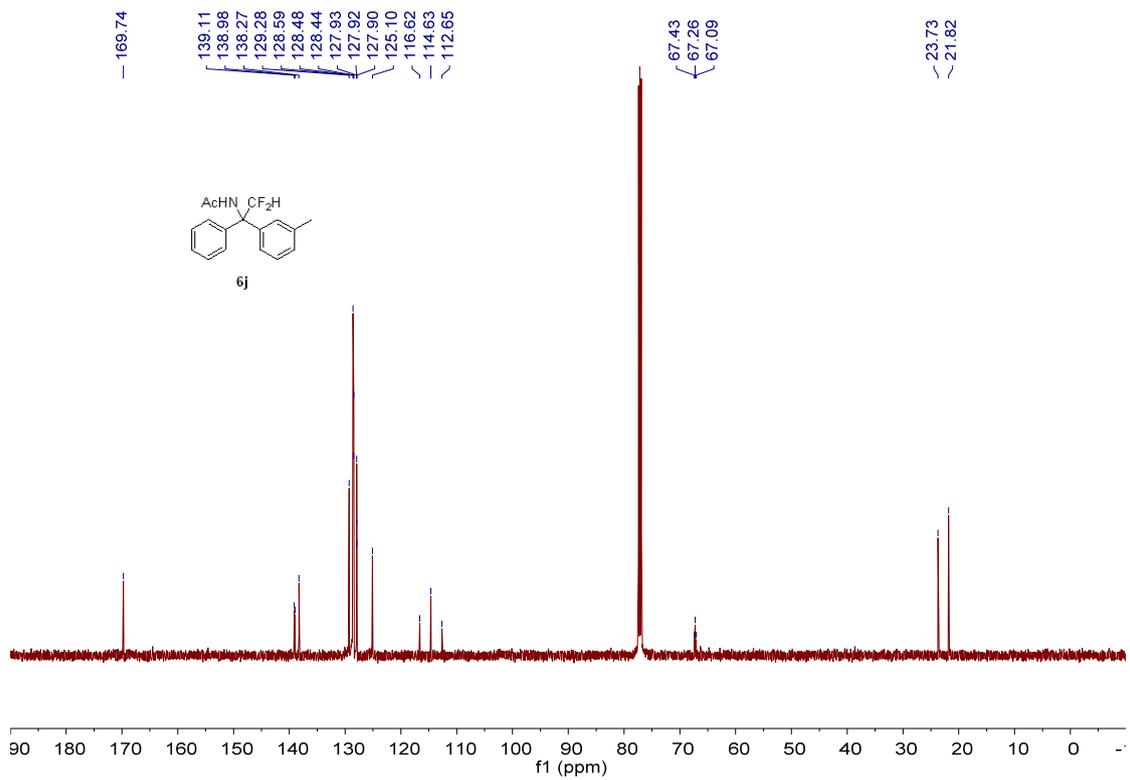


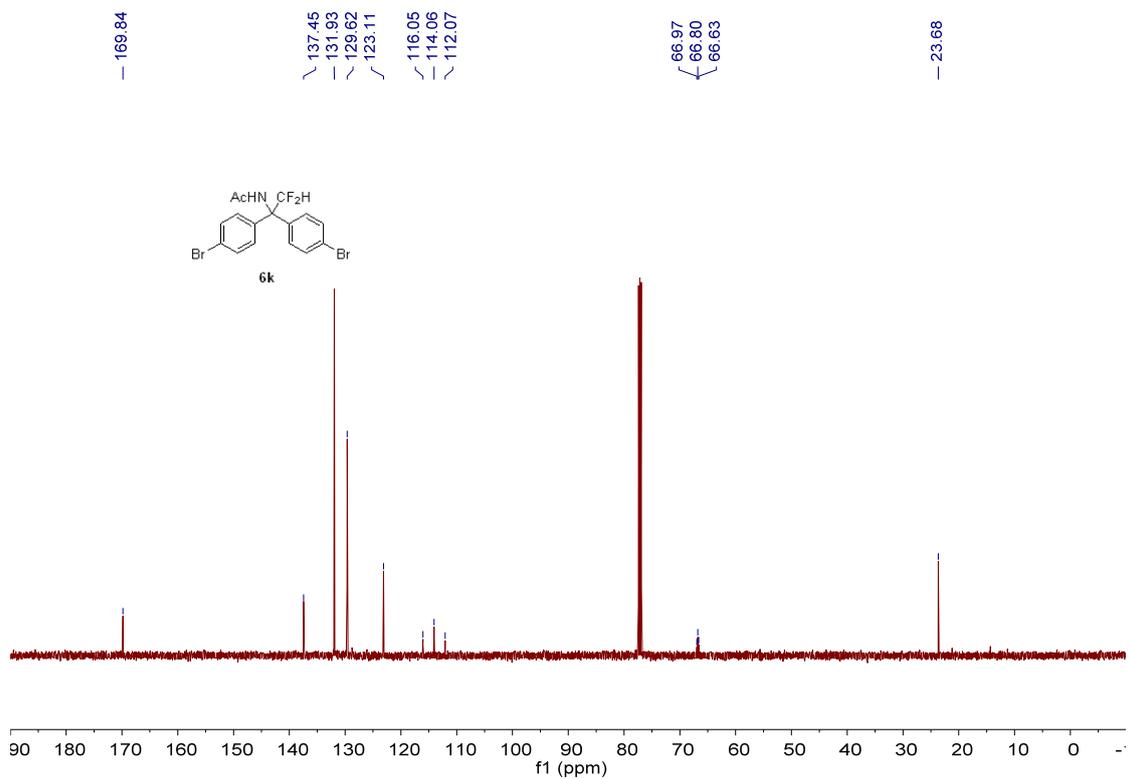
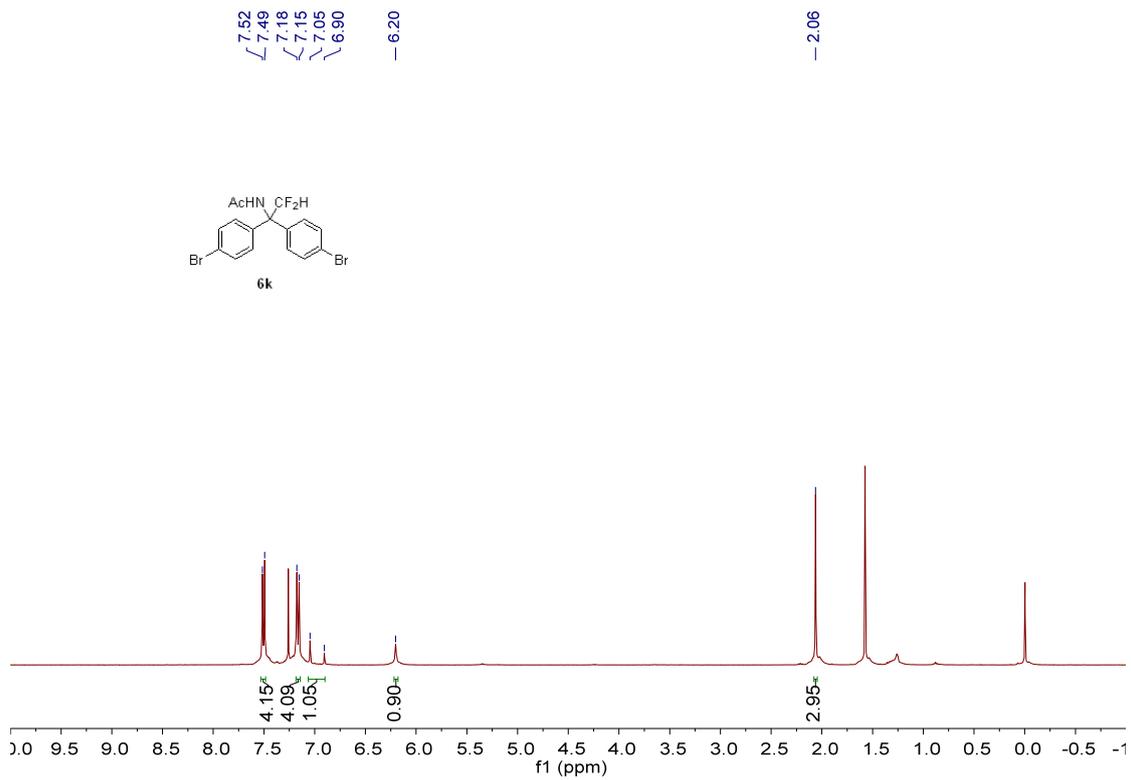


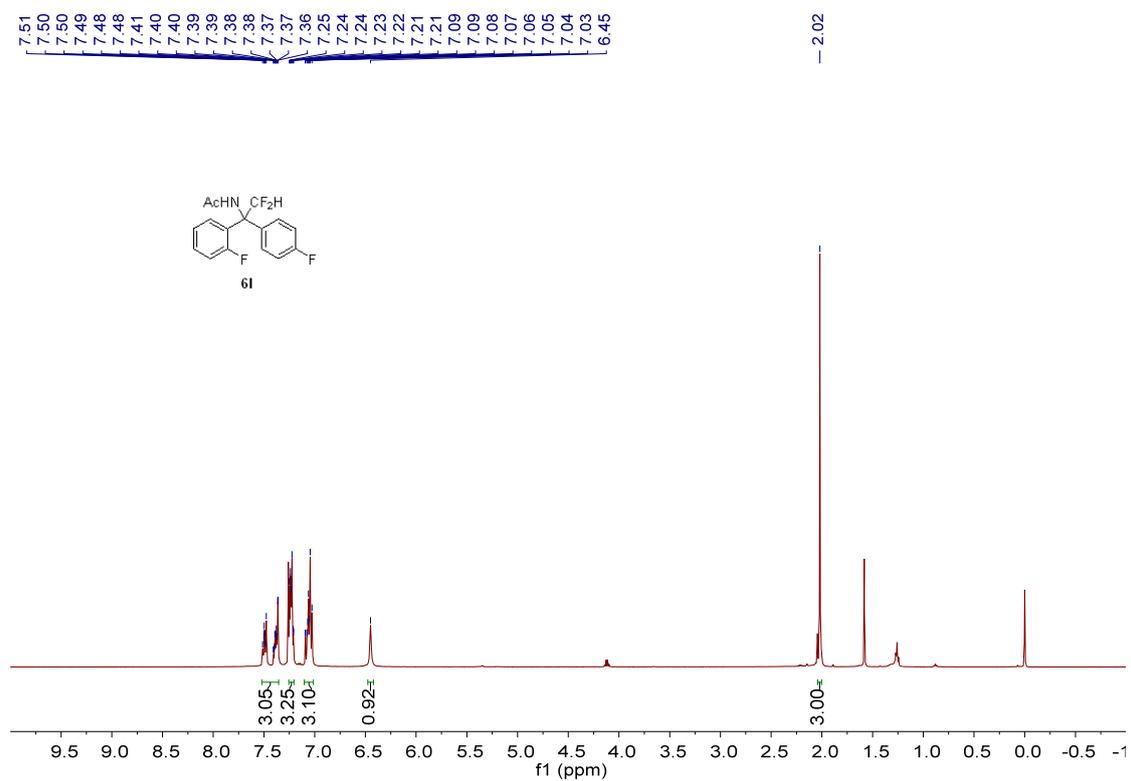
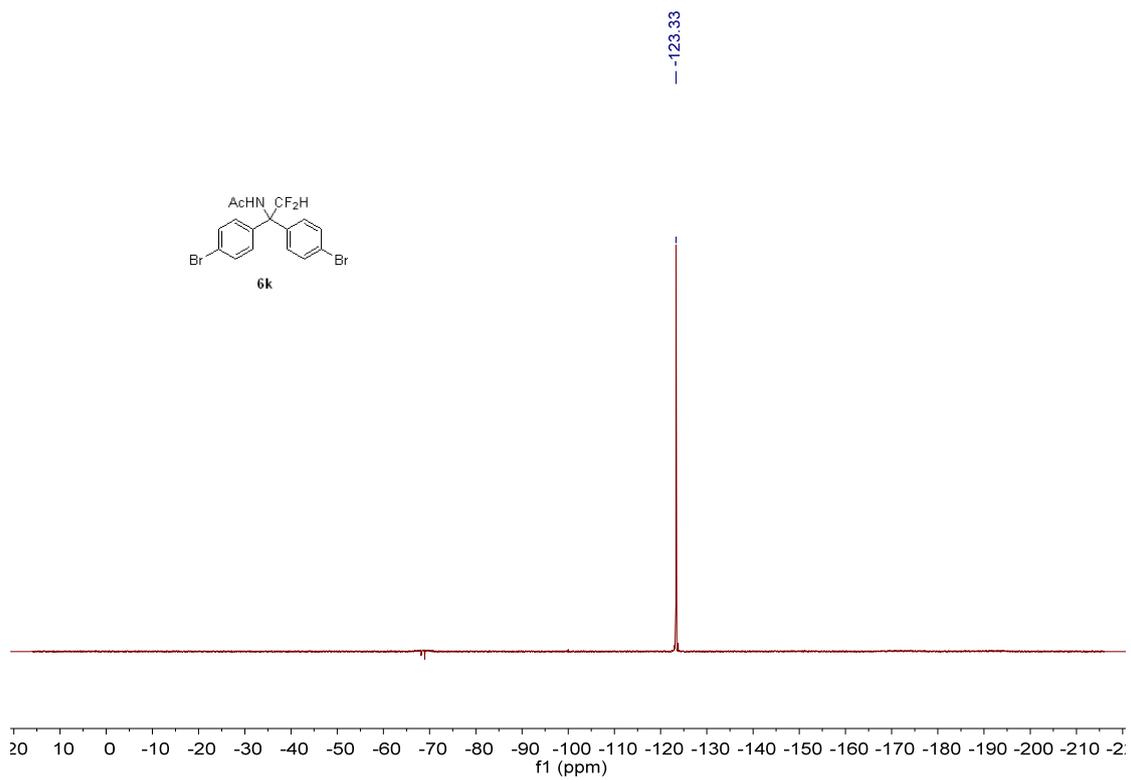


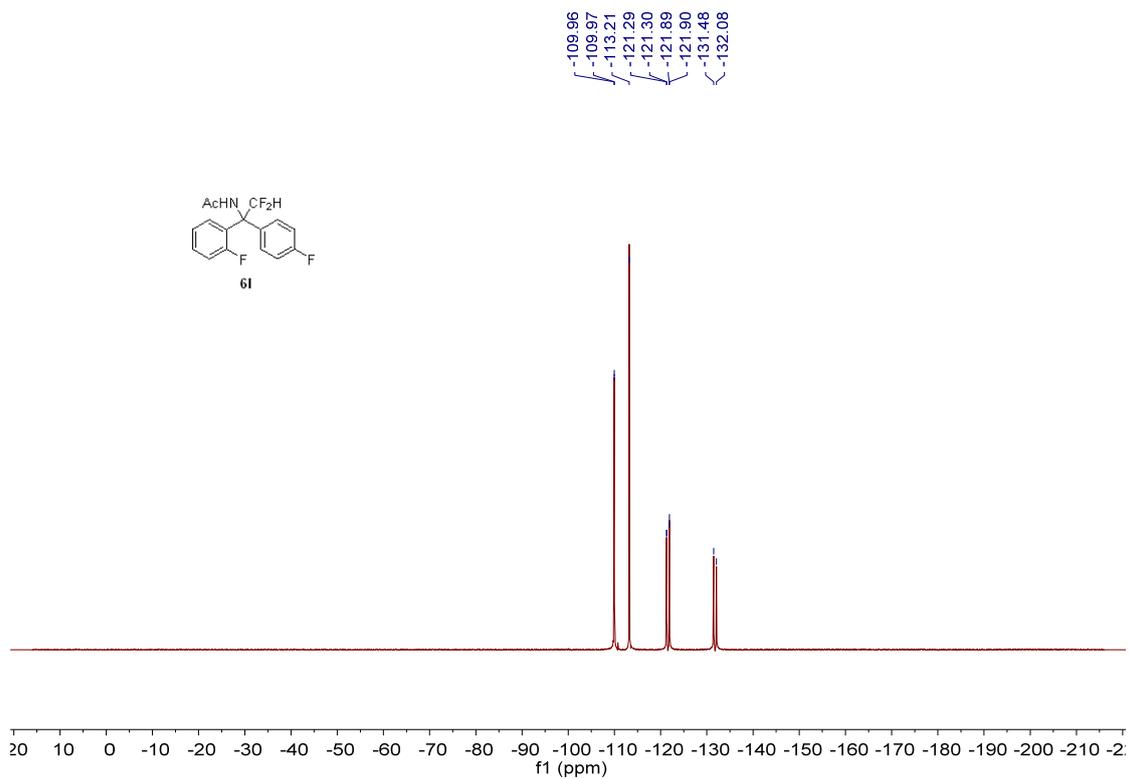
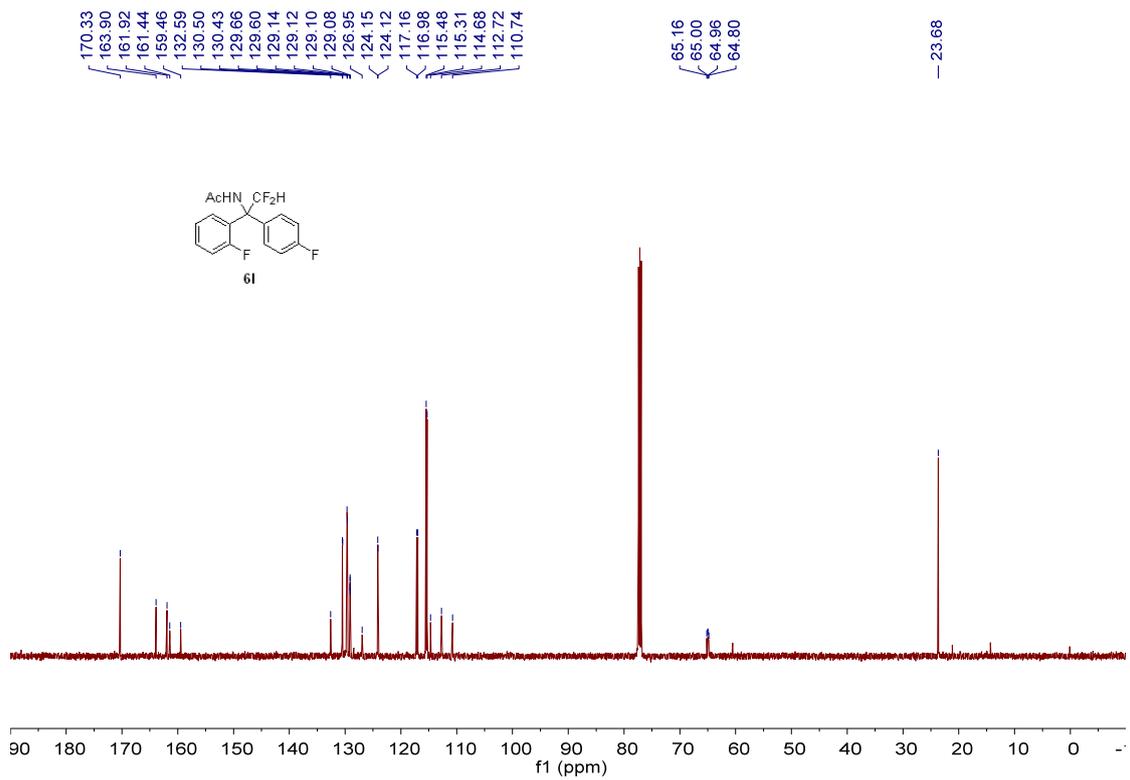


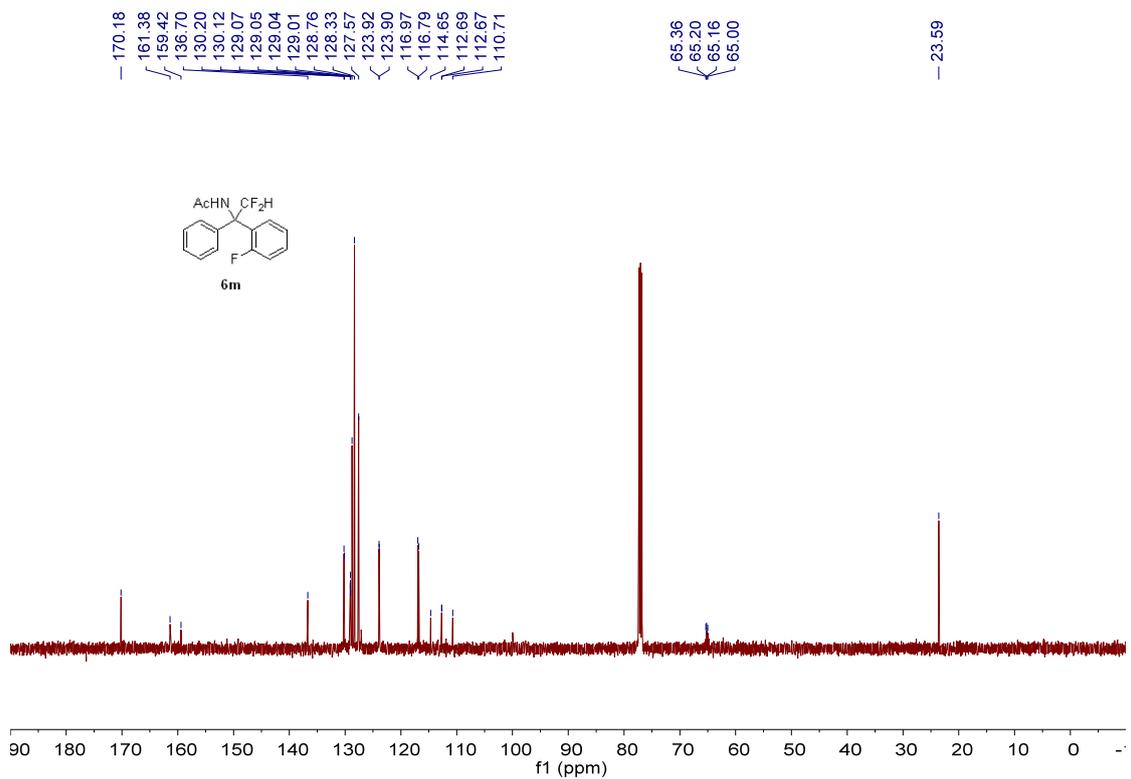
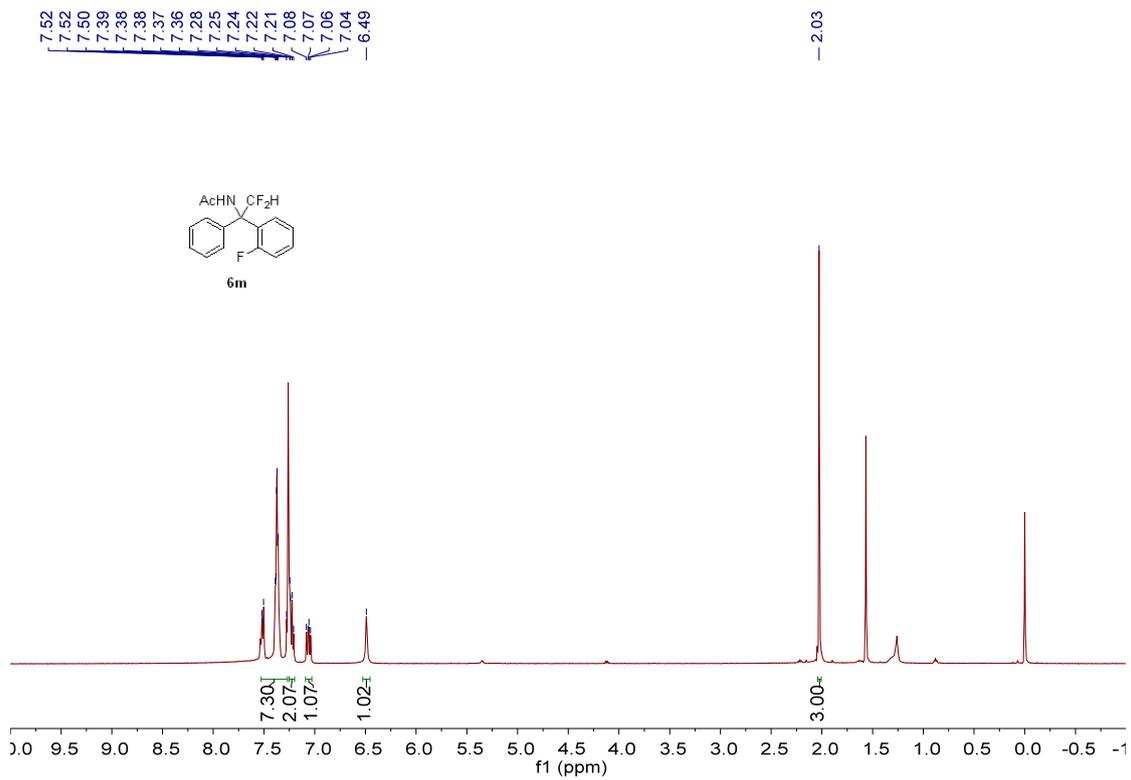


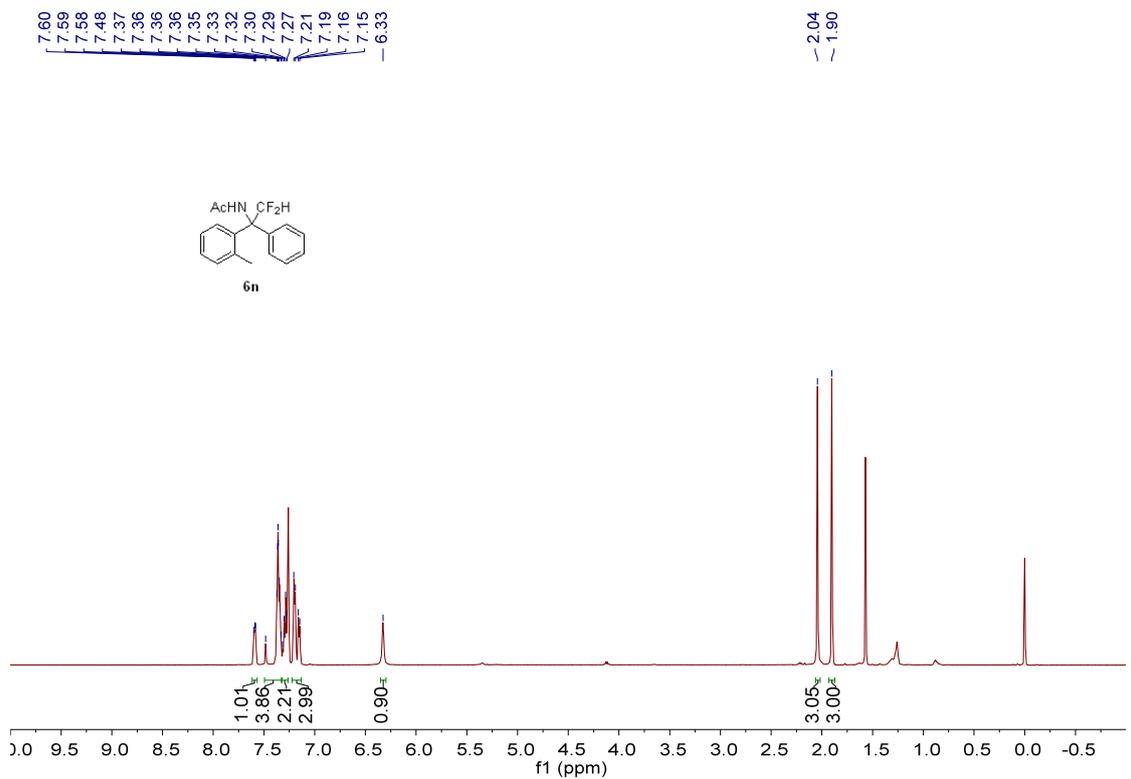
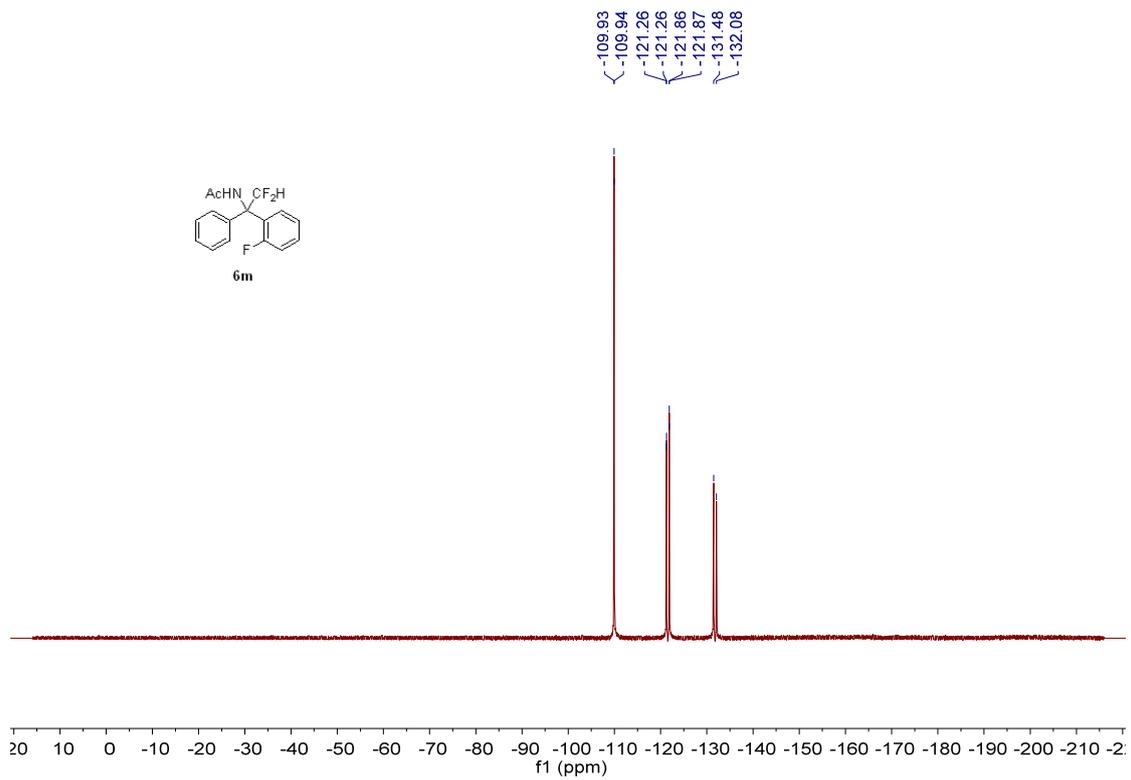


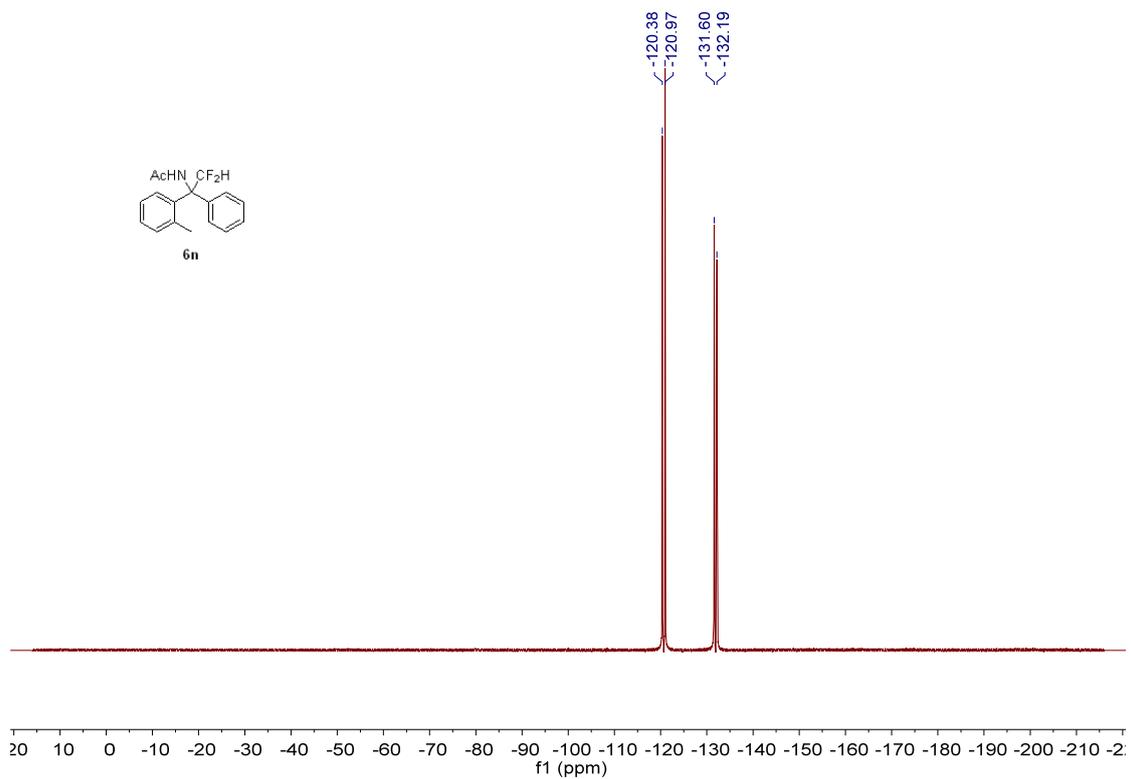
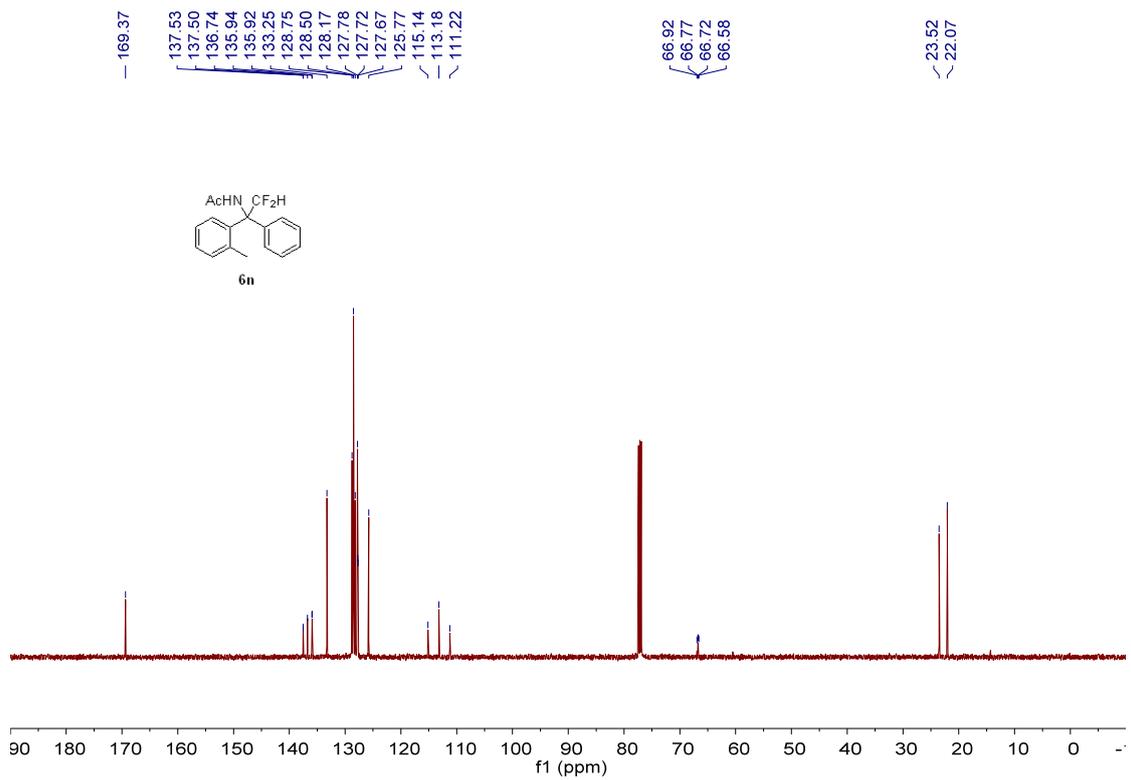


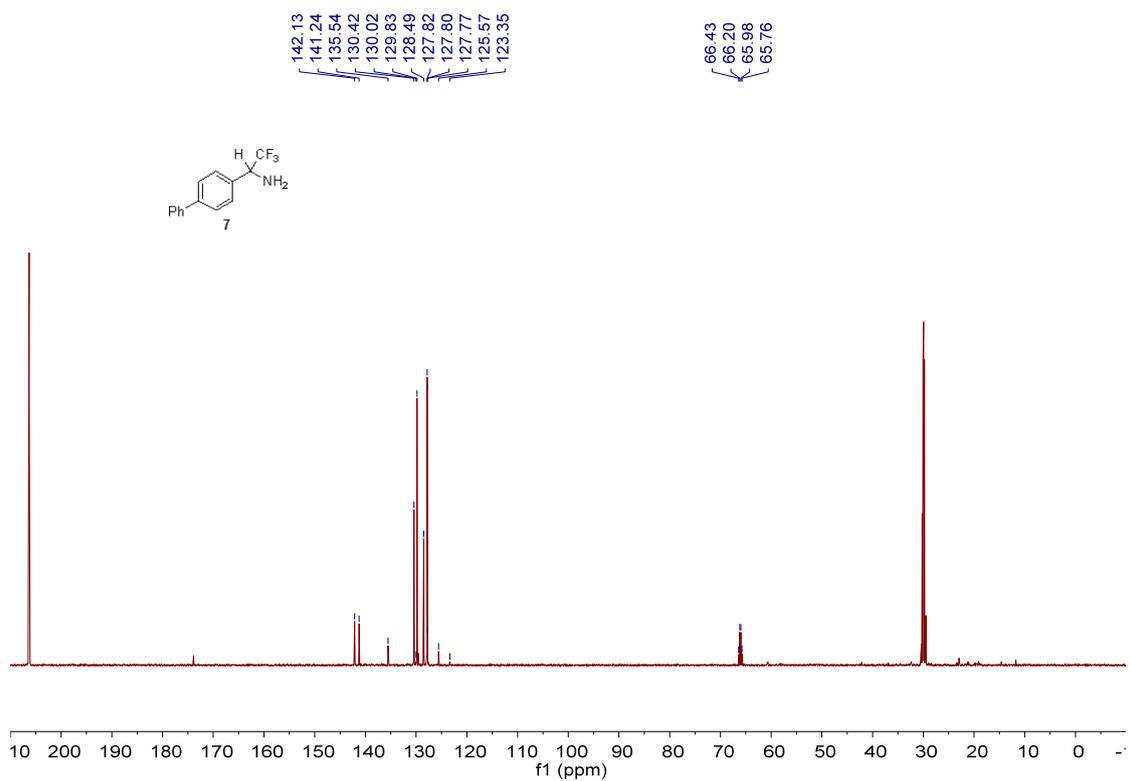
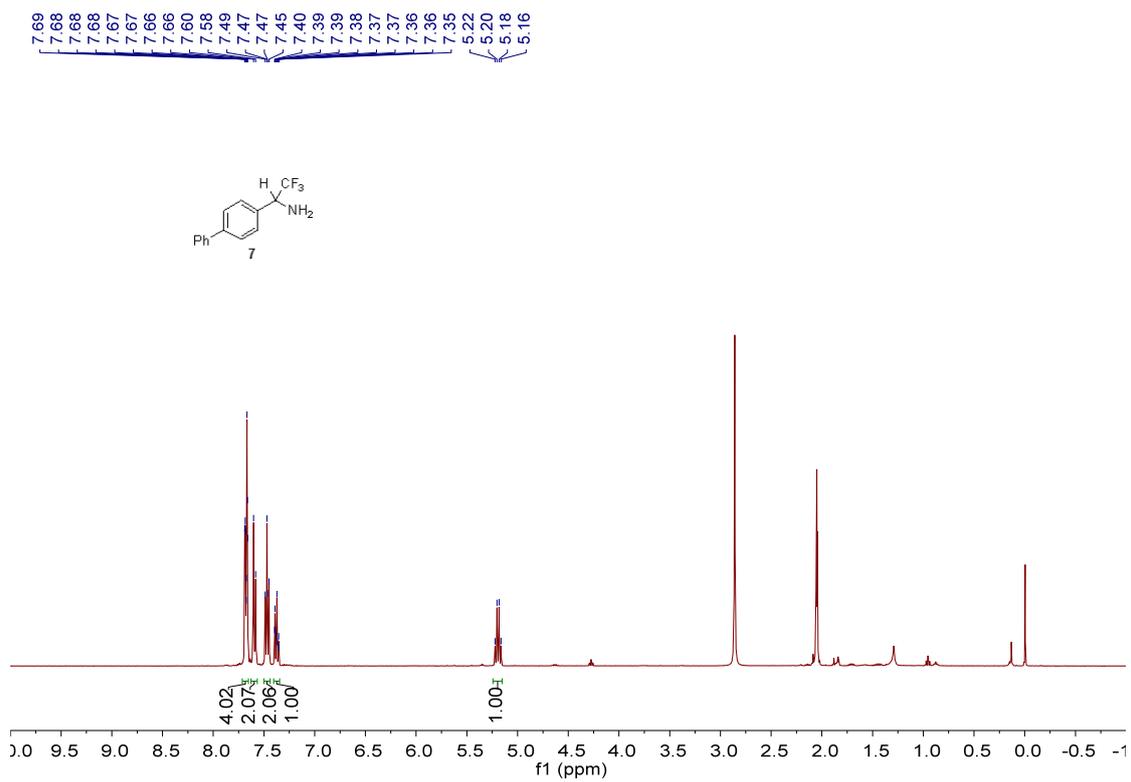


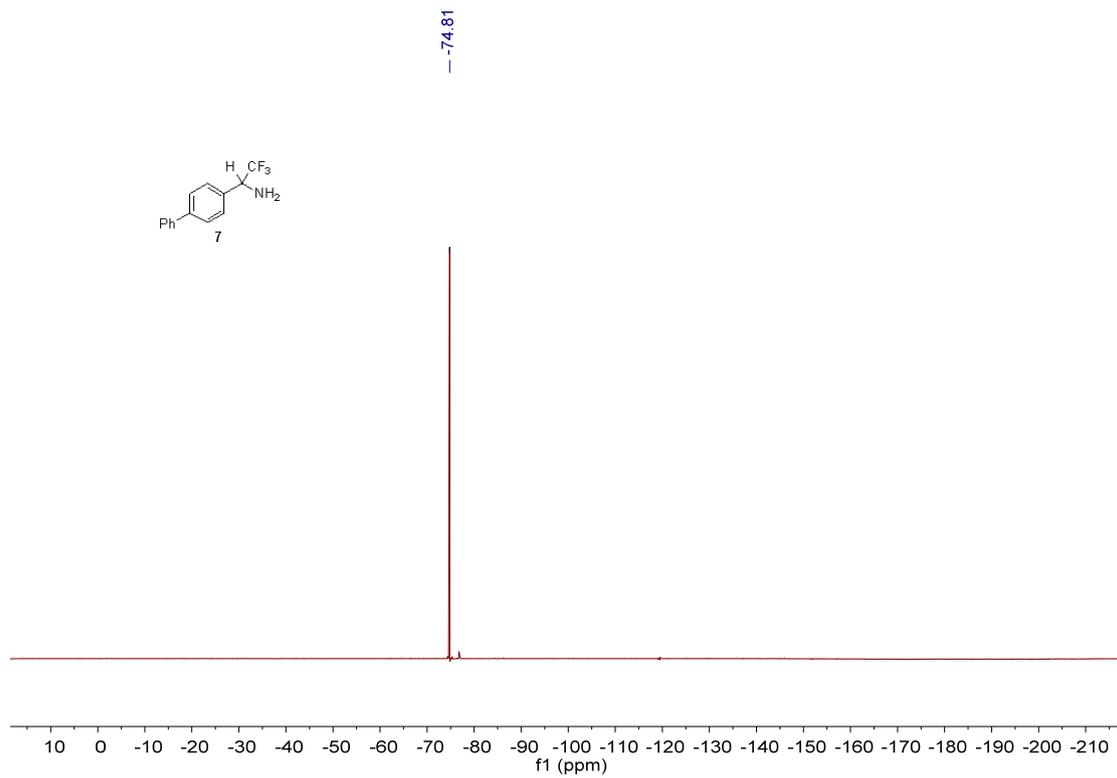












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