Supporting Information

Highly Efficient and Versatile Synthesis of Difluoro-*γ*-lactams *via* Aminodifluoroalkylation of Alkenes

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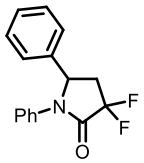
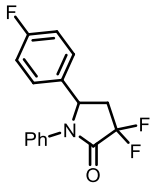
1. General Information

All reactions were carried out under Ar atmosphere with dry solvents in flame-dried glassware unless otherwise noted. Anhydrous CH_3CN and *N*,*N*,*N*',*N*'',*N*''-pentamethyldiethylenetriamine and CuI were purchased commercial from sources and used as received. Chromatographic separations were carried out on 200-300 mesh silica gel. Reactions were monitored by TLC or HPLC analysis of reaction aliquots. HPLC analysis was performed on an Agilent 1260 Liquid Chromatography using a ZORBAX SB-C18 column (4.6 × 150 mm, 5-micron). ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AVANCE III spectrometer. Melting points were recorded with a micro melting point apparatus on a Beijing Tech Instrument X-6. High resolution spectra (HRMS) were recorded on a QTOF mass analyzer with electrospray ionization (ESI) through a Bruker Daltonic miorOTOF-QII.

2. Typical Procedure for Amino-difluoroalkylation of Alkenes

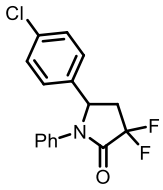


Synthesis of 3,3-difluoro-1,5-diphenylpyrrolidin-2-one (3aa).[1] **Representative Procedure I.** To a mixture of 2-bromo-2,2-difluoro-*N*-phenylacetamide **2a** (250.0 mg, 1.0mmol), CuI (19.0 mg, 0.1 mmol) in CH_3CN (2.0 mL) were added *N*,*N*,*N*',*N*'',*N*''-Pentamethyldiethylenetriamine (313 μL, 1.5 mmol) and styrene **1a** (230 μL, 2mmol) successively. The resultant mixture was stirred at 80 ºC for 10 h and monitored by TLC. The reaction was quenched with ethyl acetate and water, and then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated in vacuum and the residue was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1) to give the desired product **3aa** (240.5 mg) in 90% yield as white solid, m.p. 144.4-144.6 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.43 (m, 2H), 7.35-7.24 (m, 7H), 7.16 (t, J = 7.4 Hz, 1H), 5.37-5.34 (m, 1H), 3.20-3.07 (m, 1H), 2.62-2.49 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.23 (t, J = 30.3 Hz, 1C), 138.57, 136.37, 129.30 (2C), 129.05 (2C), 128.69, 126.65, 126.38 (2C), 122.90 (2C), 117.50 (t, J = 249.1 Hz, 1C), 58.29 (t, J = 3.4 Hz, 1C), 39.11 (t, J = 21.8 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.22 (d, $^2J_{FF}$ = 270.6 Hz), -104.32 (d, $^2J_{FF}$ = 270.6 Hz).

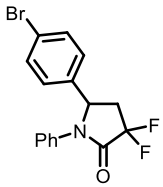


3,3-Difluoro-5-(4-fluorophenyl)-1-phenylpyrrolidin-2-one (3ba).[1] The title compound was prepared according to Representative Procedure I except that 4-fluorostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 91%, 264.81 mg, white solid, m.p. 114.5-115.1 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 9.3 Hz,

2H), 7.19-6.89 (m, 5H), 6.82 (d, *J* = 9.5, 7.7 Hz, 2H), 5.22-5.21 (m, 1H), 2.98-2.94 (m, 1H), 2.41-2.32 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ163.04 (t, *J* = 31.1 Hz, 1C), 162.49 (d, *J* = 247.8 Hz, 1C), 136.05, 134.28, 129.04 (2C), 128.25 (d, *J* = 8.4 Hz, 1C), 126.75, 123.00 (2C), 117.49 (t, *J* = 250.48 Hz, 1C), 116.19 (d, *J* = 21.9 Hz,1C), 57.56 (t, *J* = 3.3 Hz, 1C), 38.86 (t, *J* = 21.9 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.85 (d, $^2J_{FF}$ = 270.6 Hz, $^3J_{HF}$ = 15.8, 12.5 Hz), -104.55 (d, $^2J_{FF}$ = 270.5 Hz, $^3J_{HF}$ = 17.1, 13.1 Hz), -112.79.

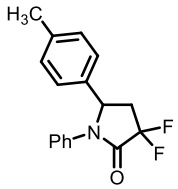


5-(4-Chlorophenyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (3ca).[1] The title compound was prepared according to Representative Procedure I except that 4-chlorostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 80%, 196.5 mg, white solid, m.p. 128.2-129.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.41 (m, 2H), 7.31-7.26 (m, 4H), 7.19-7.17 (m, 3H), 5.38-5.34 (m, 1H), 3.19-3.06 (m, 1H), 2.56-2.44 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.96 (t, *J* = 31.2 Hz, 1C), 137.15, 136.05, 134.40, 129.43 (2C), 129.09 (2C), 127.81 (2C), 126.78, 122.84 (2C), 117.38 (t, *J* = 249.6 Hz, 1C), 57.55 (t, *J* = 3.3 Hz, 1C), 38.68 (t, *J* = 22.0 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.71 (d, $^2J_{FF}$ = 270.7 Hz, $^3J_{HF}$ = 16.2, 12.8 Hz), -104.51 (d, $^2J_{FF}$ = 274.6 Hz, $^3J_{HF}$ = 17.1, 13.1 Hz).

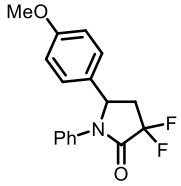


5-(4-Bromophenyl)-3,3-difluoro-1-phenylpyrrolidin-2-one (3da).[1] The title compound was prepared according to Representative Procedure I except that 4-bromostyrene was used instead of styrene. The product was purified by silica gel

column chromatography (petroleum ether/EtOAc = 5/1). Yield, 86%, 303.5 mg, white solid, m.p. 134.9-135.5 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.45 (m, 4H), 7.32-7.28(m, 2H), 7.19-7.11 (m, 3H), 5.35-5.29 (m, 1H), 3.19-3.06 (m, 1H), 2.56-2.44 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.06 (t, J = 31.2 Hz, 1C), 137.66, 136.07, 132.46 (2C), 129.17 (2C), 128.10 (2C), 126.84, 122.82 (2C), 122.63, 117.31 (t, J = 249.6 Hz, 1C), 57.66 (t, J = 3.4 Hz, 1C), 38.81 (t, J = 22.0 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.83 (d, $^{2}J_{FF}$ = 271.0 Hz, $^{3}J_{HF}$ = 16.1, 12.8 Hz), -104.54 (d, $^{2}J_{FF}$ = 271.0 Hz, $^{3}J_{HF}$ = 17.0, 13.1 Hz).



3,3-Difluoro-1-phenyl-5-(p-tolyl) pyrrolidin-2-one (3ea).[1] The title compound was prepared according to Representative Procedure I except that 4-methylstyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 82%, 182.8 mg, white solid, m.p. 127.7-128.5 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.45 (m, 2H), 7.31-7.27 (m, 2H), 7.15-7.14 (m, 5H), 5.35-5.31 (m, 1H), 3.18-3.05 (m, 1H), 2.60-2.47 (m, 1H), 2.30 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.17 (t, J = 31.2 Hz, 1C), 138.45, 136.41, 135.54, 129.90 (2C), 128.95 (2C), 126.53, 126.27 (2C), 122.92 (2C), 117.58 (t, J = 249.4 Hz, 1C), 58.05 (t, J = 3.4 Hz, 1C), 39.10 (t, J = 21.7 Hz, 1C), 21.03 (1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.13 (d, $^{2}J_{FF}$ = 270.4 Hz, $^{3}J_{HF}$ = 16.0, 12.3, 3.4 Hz), -104.31 (d, $^{2}J_{FF}$ = 270.4 Hz, $^{3}J_{HF}$ = 17.4, 13.8 Hz).

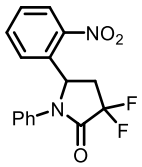


3,3-Difluoro-5-(4-methoxyphenyl)-1-phenylpyrrolidin-2-one (3fa).[1] The title compound was prepared according to Representative Procedure I except that

4-methoxystyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 83%, white solid, m.p. 101.5-102.1 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42-7.40 (m, 2H), 7.31-7.27 (m, 2H), 7.16-7.14 (m, 3H), 6.84-6.82 (m, 2H), 5.31-5.27 (m, 1H), 3.74 (s, 3H), 3.13-3.03 (m, 1H), 2.59-2.50 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.14 (t, J = 31.2 Hz, 1C), 159.73, 136.35, 130.33, 129.00 (2C), 127.73 (2C), 126.65, 123.17 (2C), 117.62 (t, J = 249.4 Hz, 1C), 114.63 (2C), 57.93 (t, J = 3.4 Hz), 55.26 (3C), 39.19 (t, J = 21.6 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.33 (d, $^{2}J_{FF}$ = 271.4 Hz, $^{3}J_{HF}$ = 16.1, 12.8 Hz), -104.51 (d, $^{2}J_{FF}$ = 271.4 Hz, $^{3}J_{HF}$ = 17.5, 14.3 Hz). HRMS (ESI), m/z [M+Na^+] calcd for $C_{14}H_{10}ClNNaO_2^+$, 326.0963, found, 326.0956.

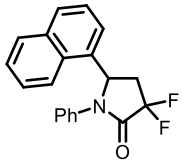
3,3-Difluoro-5-(4-nitrophenyl)-1-phenylpyrrolidin-2-one (3ga). The title compound was prepared according to Representative Procedure I except that 4-nitrostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 76%, 254 mg, white solid, m.p. 139-140 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19-8.17 (m, 2H), 7.46-7.41 (m, 4H), 7.34-7.30 (m, 2H), 7.21-7.17 (m, 1H), 5.53-5.49 (m, 1H), 3.24-3.18 (m, 1H), 2.60-2.48 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.98 (t, J = 31.3 Hz, 1C), 148.11, 145.82, 135.94, 129.43 (2C), 127.48 (2C), 127.13, 124.65 (2C), 122.58 (2C), 117.00 (t, J = 250.1 Hz, 1C), 57.48 (t, J = 3.4 Hz, 1C), 38.64 (t, J = 22.4 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.64 (d, $^{2}J_{FF}$ = 271.8 Hz, $^{3}J_{HF}$ = 16.2, 13.4 Hz), -104.81 (d, $^{2}J_{FF}$ = 271.8 Hz, $^{3}J_{HF}$ = 16.4, 12.3 Hz). HRMS (ESI), m/z [M+Na^+] calcd for $C_{14}H_{10}ClNNaO_3^+$, 341.0708, found, 341.0710.

3,3-Difluoro-5-(3-chlorophenyl)-1-phenylpyrrolidin-2-one (3ha). The title compound was prepared according to Representative Procedure I except that 3-chlorostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 82%, 251.74 mg, white solid, m.p. 121.9-123.6 ℃. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33-7.31 (m, 2H), 7.23-7.20 (m, 2H), 7.18-7.14 (m, 3H), 7.09-7.07 (m, 1H), 7.03-7.01 (m, 1H), 5.23-5.20 (m, 1H), 3.07-2.98 (m, 1H), 2.46-2.38 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.12 (t, J = 31.2 Hz, 1C), 140.76, 136.11, 135.26, 130.75, 129.26 (2C), 129.03, 126.90, 126.68, 124.44, 122.76 (2C), 117.22 (t, J = 249.15 Hz, 1C), 57.72 (t, J = 3.3 Hz, 1C), 38.92 (t, J = 22.1 Hz, 1C); ^{19}F NMR (565 MHz, $CDCl_3$) δ -100.93 (d, $^{2}J_{FF}$ = 271.5 Hz, $^{3}J_{HF}$ = 16.1, 12.9 Hz), -104.47 (d, $^{2}J_{FF}$ = 275.2 Hz, $^{3}J_{HF}$ = 16.9, 12.9 Hz). HRMS (ESI), m/z [M+Na^{+}] calcd for $C_{16}H_{12}ClF_2NNaO^{+}$, 330.0468, found, 330.0468.

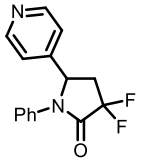


3,3-Difluoro-5-(2-nitrophenyl)-1-phenylpyrrolidin-2-one (3ia). The title compound was prepared according to Representative Procedure I except that 2-nitrostyrene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 82%, white solid, m.p. 134-135 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, J = 8.1 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.3 Hz, 3H), 7.30-7.21 (m, 3H), 7.09 (t, J = 7.4 Hz, 1H), 6.0-5.98 (m, 1H), 3.33-3.19 (m, 1H), 2.59-2.49 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.45 (t, J = 31.3 Hz, 1C), 147.82, 136.24, 134.68, 134.66, 129.63, 129.44 (2C), 127.30, 126.76, 125.88, 121.56 (2C), 117.10 (t, J = 248.46 Hz), 54.18 (d, J = 6.3 Hz, 1C), 38.25 (t, J = 22.4 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -98.44 (d, $^{2}J_{FF}$ = 272.8 Hz),

-105.25 (d, $^{2}J_{FF}$ = 272.8 Hz). HRMS (ESI), m/z [M+Na^{+}] calcd for $C_{16}H_{12}F_2N_2NaO_3^{+}$, 341.0708, found, 341.0709.

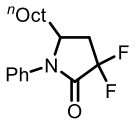


3,3-Difluoro-5-(naphthalen-1-yl)-1-phenylpyrrolidin-2-one (3ja).[1] The title compound was prepared according to Representative Procedure I except that 2-vinylnaphthalene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 90%, 325 mg, white solid, m.p. 157.4-158.3 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73-7.63 (m, 3H), 7.60 (s, 1H), 7.40-7.36 (m, 4H), 7.21 (d, J = 8.5 Hz, 1H), 7.15 (t, J = 7.9 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 5.40-5.36 (m, 1H), 3.13-3.00 (m, 1H), 2.57-2.45 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.34 (t, J = 31.2 Hz), 136.44, 135.94, 133.29, 133.25, 129.74 (2C), 129.13, 128.00, 127.88, 126.89, 126.80, 126.74, 126.29,123.07,122.96 (2C), 117.51 (t, J = 249.4 Hz, 1C), 58.56 (t, J = 3.4 Hz, 1C), 39.12 (t, J = 21.9 Hz, 1C). ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.19 (d, $^{2}J_{FF}$ = 271.3 Hz), -104.10 (d, $^{2}J_{FF}$ = 271.3 Hz, $^{3}J_{HF}$ = 17.3, 13.9 Hz).

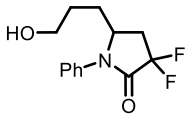


3,3-Difluoro-1-phenyl-5-(pyridin-4-yl) pyrrolidin-2-one (3ka). The title compound was prepared according to Representative Procedure I except that 4-vinylpyridine was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 92%, 254.8 mg, white solid, m.p. 148.5-148.9 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (d, J = 5.3 Hz, 2H), 7.43-7.41 (m, 2H), 7.38-7.25 (m, 2H), 7.18 (t, J = 7.4 Hz, 3H), 5.38-5.34 (m, 1H), 3.22-3.09 (m 1H), 2.57-2.45 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.01 (t, J = 31.3 Hz), 150.74 (2C), 147.84, 135.97, 129.38 (2C), 127.03, 122.36 (2C), 121.25,

116.94 (t, J = 250.1 Hz, 1C), 57.08 (t, J = 3.03 Hz, 1C), 38.34 (t, J = 22.5 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.63 (d, $^2J_{FF}$ = 271.7 Hz), -104.75 (d, $^2J_{FF}$ = 271.7 Hz, $^3J_{HF}$ = 16.3, 11.6 Hz). HRMS (ESI), m/z [M+Na$^+$] calcd for $C_{15}H_{12}F_2N_2NaO^+$, 297.0810, found, 297.0808.

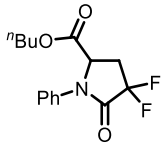


3,3-Difluoro-5-octyl-1-phenylpyrrolidin-2-one (3la). The title compound was prepared according to Representative Procedure I except that 1-decene was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 86%, 223.6 mg, white solid, m.p. 90.5-91.5 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.40 (m, 4H), 7.31-7.30 (m, 1H), 4.28-4.21 (m, 1H), 2.81-2.75 (m, 1H), 2.40-2.27 (m, 1H), 1.74-1.70 (m, 1H), 1.39-1.22 (m, 13H), 0.89-0.86 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.63 (t, J = 31.4 Hz, 1C), 135.94, 129.32 (2C), 127.18, 123.93 (2C), 117.87 (t, J = 249.2 Hz, 1C), 54.44 (t, J = 3.0 Hz, 1C), 34.65 (t, J = 21.9 Hz), 33.08, 31.74, 29.28, 29.17, 29.05, 24.38, 22.59, 14.04; ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.91 (d, $^2J_{FF}$ = 270.2 Hz), -104.21 (d, $^2J_{FF}$ = 270.1 Hz). HRMS (ESI), m/z [M+Na$^+$] calcd for $C_{18}H_{25}F_2NNaO^+$, 332.1796, found,332.1785.

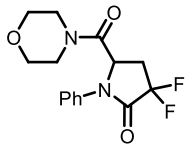


3,3-Difluoro-5-(3-hydroxypropyl)-1-phenylpyrrolidin-2-one (3ma). The title compound was prepared according to Representative Procedure I except that 4-penten-1-ol was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 84%, 215.4 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.35 (m, 4H), 7.30 (t, J = 6.9 Hz, 1H), 4.32 (s, 1H), 3.58 (d, J = 5.1 Hz, 2H), 2.86-2.73 (m, 1H), 2.42-2.29 (m, 1H), 1.85 (t, J = 10.1 Hz, 1H), 1.59-1.49 (m, 5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.74 (t, J = 31.3 Hz, 1C), 135.34, 129.25 (2C), 127.32, 123.91 (2C), 117.86 (t, J = 249.1 Hz, 1C), 61.36, 54.36, 34.20 (t, J = 21.9 Hz, 1C), 29.51, 27.01; ^{19}F NMR (377 MHz,

$CDCl_3$) δ -100.75 (d, $^2J_{FF}$ = 271.4 Hz), -104.11 (d, $^2J_{FF}$ = 271.4 Hz). HRMS (ESI), m/z [M+Na^+] calcd for $C_{13}H_{15}F_2NNaO_2^+$, 278.0963, found, 278.0965.

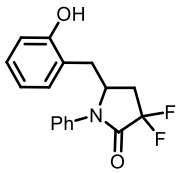


Butyl 4,4-difluoro-5-oxo-1-phenylpyrrolidine-2-carboxylate (3na). The title compound was prepared according to Representative Procedure I except that butyl acrylate was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 86%, 257.3 mg, white solid, m.p. 89.8-90.5 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.50 (m, 2H), 7.43-7.39 (m, 2H), 7.29-7.26 (m, 1H), 4.87-4.83 (m,, 1H), 4.13-4.09 (m, 2H), 2.97-2.93 (m, 1H), 2.74-2.68 (m, 1H), 1.52-1.47 (m, 2H), 1.25-1.18 (m, 2H), 0.83 (t, J = 7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.40, 162.51 (t, J = 31.3 Hz, 1C), 136.75, 129.34, 127.11, 121.95 (2C), 116.47 (t, J = 250.3 Hz, 1C), 66.31, 56.14 (d, J = 2.8 Hz, 1C), 33.61 (t, J = 24.2 Hz, 1C), 30.32, 18.81, 13.50; ^{19}F NMR (377 MHz, $CDCl_3$) δ -102.09 (d, $^2J_{FF}$ = 271.4 Hz), -104.59 (d, $^2J_{FF}$ = 271.4 Hz, $^3J_{HF}$ = 15.8, 8.7 Hz). HRMS (ESI), m/z [M+Na^+] calcd for $C_{15}H_{17}F_2NNaO_3^+$, 320.1069, found, 320.1062.

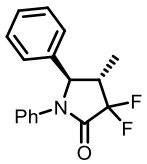


3,3-Difluoro-5-(morpholine-4-carbonyl)-1-phenylpyrrolidin-2-one (3oa). The title compound was prepared according to Representative Procedure I except that 1-morpholinoprop-2-en-1-one was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 78%, 244.8 mg, white solid, m.p.174-175 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.29 (m, 4H), 7.29 (t, J = 8.0 Hz, 1H), 5.10 (d, J = 6.3 Hz, 1H), 3.66-3.39 (m, 8H), 2.91-2.78 (m, 1H), 2.67-2.52 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.71, 163.08 (t, J = 31.3 Hz, 1C), 136.56, 129.58, 127.78, 123.44, 116.75 (t, J = 252.5 Hz), 66.77, 66.42 53.46 (t, J = 3.2 Hz, 1C), 45.94, 42.92, 33.71 (t, J = 24.0 Hz, 1C); ^{19}F NMR (377

MHz, $CDCl_3$) δ -100.95 (d, $^2J_{FF}$ = 275.2 Hz), -104.27 (d, $^2J_{FF}$ = 275.2 Hz). HRMS (ESI), m/z [M+Na^+] calcd for $C_{15}H_{16}F_2N_2NaO_3^+$, 333.1021, found, 333.1027.

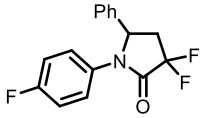


3,3-Difluoro-5-(2-hydroxybenzyl)-1-phenylpyrrolidin-2-one (3pa). The title compound was prepared according to Representative Procedure I except that 2-allylphenol was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 86%, 260.8 mg, white solid, m.p. 105.1-106.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (s, 1H), 7.48 (d, *J* = 7.7 Hz, 2H), 7.27-7.25 (m, 2H), 7.10-6.96 (m, 3H), 6.79-4.42 (m, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 4.94-4.92 (m, 1H), 3.30-3.24 (m, 1H), 2.85-2.79 (m, 1H), 2.74-2.60 (m, 1H), 2.48-2.36 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.83 (t, *J* = 28.0 Hz, 1C), 158.74, 136.12, 129.24 (2C), 128.30, 125.82, 125.68, 120.91, 120.51 (2C), 116.90 (t, *J* = 254.7 Hz, 1C), 109.72, 76.73 (t, *J* = 4.8 Hz, 1C), 39.96 (t, *J* = 22.9 Hz, 1C), 35.94. ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.30 (d, $^2J_{FF}$ = 256.3 Hz), -105.69 (d, $^2J_{FF}$ = 256.3 Hz). HRMS (ESI), m/z [M-H^+] calcd for $C_{17}H_{15}F_2NO_2^+$, 302.0998, found, 302.0995.

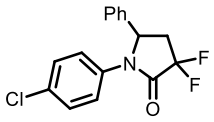


(4S,5R)-3,3-Difluoro-4-methyl-1,5-diphenylpyrrolidin-2-one (3qa).[1] The title compound was prepared according to Representative Procedure I except that 4-vinylpyridine was used instead of styrene. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 92%, 254.8 mg, white solid, m.p. 118-119 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.0 Hz, 2H), 7.13 (m, 7H), 6.95 (t, *J* = 7.4 Hz, 1H), 4.69 (d, *J* = 7.3 Hz, 1H), 2.46-2.35 (m, 1H), 1.17 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.38 (t, *J* = 31.3 Hz, 1C), 136.59, 135.89, 129.07 (2C), 128.77 (2C), 128.68 (2C), 126.94 (2C), 126.36, 123.23

(2C), 117.37 (t, J = 249.37 Hz, 1C), 65.48 (d, J = 6.6 Hz, 1C), 45.35 (t, J = 20.7 Hz, 1C), 8.32 (d, J = 8.1 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -110.60 (d, $^2J_{FF}$ = 267.1 Hz), -118.63 (d, $^2J_{FF}$ = 267.1 Hz, $^3J_{HF}$ = 19.3 Hz).

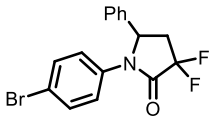


3,3-Difluoro-1-(4-fluorophenyl)-5-phenylpyrrolidin-2-one (3ab).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-*N*-(4-fluorophenyl) acetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenyl acetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 92%, 284.2 mg, white solid, m.p. 143-144 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.31 (m, 5H), 7.24-7.22 (m, 2H), 6.99-6.95 (m, 2H), 5.31-5.27 (m, 1H), 3.19-3.08 (m, 1H), 2.63-2.50 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.22 (t, J = 31.4 Hz, 1C), 160.67 (d, J = 247.2 Hz, 1C), 138.13, 132.23, 129.39 (2C), 128.89, 126.48 (2C), 124.96 (d, J = 8.4 Hz, 2C), 117.42 (t, J = 252.5 Hz, 1C), 116.00 (d, J = 22.8 Hz, 1C), 58.61 (t, J = 3.4 Hz, 1C), 39.04 (t, J = 21.9 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.44 (d, $^2J_{FF}$ = 271.4 Hz), -104.37 (d, $^2J_{FF}$ = 271.4 Hz, $^3J_{HF}$ = 17.4, 14.4 Hz), -114.29.

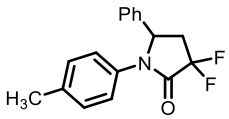


1-(4-Chlorophenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3ac).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-*N*-(4-chlorophenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenyl acetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 93%, 294.5 mg, white solid, m.p. 150-151 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.37 (m, 2H), 7.35-7.31 (m, 3H), 7.28-7.25 (m, 2H), 7.23-7.21 (m, 2H),5.31-5.27 (m, 1H), 3.20-3.17 (m, 1H), 2.62-2.50 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.25 (t, J = 31.4 Hz, 1C), 138.15, 134.91, 132.10, 129.54 (2C), 129.28 (2C), 128.99, 126.35 (2C), 124.01 (2C), 117.26 (t, J = 249.47 Hz, 1C), 58.31 (t, J = 3.4 Hz, 1C), 39.21 (t, J = 21.9 Hz, 1C). ^{19}F NMR

(377 MHz, $CDCl_3$) δ -101.69 (d, $^2J_{FF}$ = 271.7 Hz), -104.39 (d, $^2J_{FF}$ = 271.7 Hz, $^3J_{HF}$ = 17.1, 14.2 Hz).

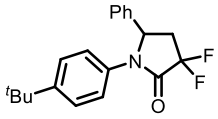


1-(4-Cromophenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3ad).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-*N*-(4-bromophenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenyl acetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 5/1). Yield, 86%, 302.5 mg, white solid, m.p. 148.9-149.4 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.29 (m, 7H), 7.24-7.22 (m, 2H), 5.36-5.32 (m, 1H), 3.20-3.07 (m, 1H), 2.61-2.48 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.14 (t, *J* = 31.5 Hz, 1C), 138.10, 135.40, 132.08 (2C), 129.40 (2C), 128.84, 126.26 (2C), 124.25 (2C), 119.86, 117.33 (t, *J* = 249.47 Hz, 1C), 58.10 (t, *J* = 3.3 Hz, 1C), 38.94 (t, *J* = 21.8 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.22 (d, $^2J_{FF}$ = 271.1 Hz), -104.24 (d, $^2J_{FF}$ = 271.1 Hz, $^3J_{HF}$ = 17.1, 14.2 Hz).

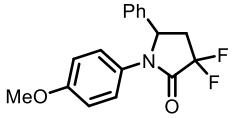


3,3-Difluoro-5-phenyl-1-(*p*-tolyl) pyrrolidin-2-one (3ae).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-*N*-(*p*-tolyl) acetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 87%, 250.7 mg, white solid, m.p. 140.1-141.0 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.19 (m, 5H), 7.14 (d, *J* = 7.1 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 2H), 5.22-5.18 (m, 1H), 3.09-2.96 (m, 1H), 2.51-2.39 (m, 1H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.21 (t, *J* = 31.0 Hz, 1C), 138.71, 136.64, 133.77, 129.72 (2C), 129.35 (2C), 128.74, 126.48 (2C), 122.92 (2C), 117.42 (t, *J* = 252.5 Hz, 1C), 58.44 (t, *J* = 3.4 Hz, 1C), 39.22 (t, *J* = 21.9

Hz, 1C), 21.07; ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.28 (d, $^2J_{FF}$ = 270.8 Hz), -104.38 (d, $^2J_{FF}$ = 270.7 Hz, $^3J_{HF}$ = 17.2, 13.8 Hz).

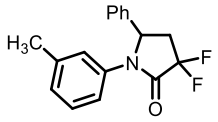


1-(4-(Tert-butyl) phenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3af). The title compound was prepared according to Representative Procedure I except that 2-bromo-*N*-(4-(tert-butyl) phenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 89%, 292.8 mg, white solid, m.p.164.5-165.4 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.13 (m, 9H), 5.23-5.19 (m, 1H), 3.03-2.96 (m, 1H), 2.46-2.41 (m, 1H), 1.15 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.26 (t, J = 31.0 Hz, 1C), 149.62, 138.99, 133.86, 129.35 (2C), 128.64, 126.34 (2C), 126.01 (2C), 122.34 (2C), 117.55 (t, J = 249.47 Hz, 1C), 58.35(t, J = 3.0 Hz, 1C), 39.21 (t, J = 21.9 Hz, 1C), 34.56, 31.27 (3C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.83 (d, $^2J_{FF}$ = 270.6 Hz, $^3J_{HF}$ = 16.6, 13.3 Hz), -104.24 (d, $^2J_{FF}$ = 270.7 Hz, $^3J_{HF}$ = 17.2, 12.5 Hz)); HRMS (ESI), m/z [M+Na$^+$] calcd for $C_{20}H_{23}F_2NO^+$, 352.1483 found, 352.1487.

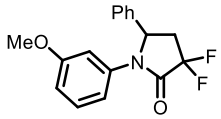


3,3-Difluoro-1-(4-methoxyphenyl)-5-phenylpyrrolidin-2-one (3ag).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-*N*-(4-methoxyphenyl) acetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 87%, 263.6 mg, white solid, m.p. 122.5-123.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H), 7.23 (d, J = 6.7 Hz, 1H), 6.80 (d, J = 9.1 Hz, 1H),5.25 (m, 1H), 3.72 (s, 3H), 3.18-3.05 (m, 1H), 2.61-2.48 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.13 (t, J = 31.0 Hz, 1C), 158.03, 138.64, 129.28 (2C), 129.21, 128.72, 126.57 (2C), 124.72 (2C),

117.63 (t, J = 249.47 Hz, 1C), 114.31 (2C), 58.74 (t, J = 3.3 Hz, 1C), 55.39, 39.04 (t, J = 21.9 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.94 (d, $^2J_{FF}$= 271.4 Hz), -104.28 (d, $^2J_{FF}$ = 271.4 Hz, $^3J_{HF}$ = 17.4, 13.9 Hz).

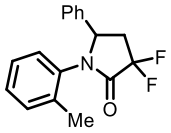


3,3-Difluoro-5-phenyl-1-(*m*-tolyl) pyrrolidin-2-one (3ah).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-*N*-(m-tolyl) acetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 90%, 258.3 mg, white solid, m.p. 96.4-97.3 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.10 (m, 6H), 7.03-7.02 (m, 2H), 6.84-6.82 (m, 1H), 5.22-5.18 (m, 1H), 3.02-2.92 (m, 1H), 2.46-2.34 (m, 1H), 2.15 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.18 (t, J = 31.1 Hz, 1C), 138.98, 138.59, 136.15, 129.21 (2C), 128.75, 128.59, 127.53, 126.35 (2C), 123.74, 119.95, 117.55 (t, J = 249.47 Hz, 1C), 58.28 (t, J = 3.4 Hz, 1C), 38.99 (t, J = 21.8 Hz, 1C), 21.42; ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.01 (d, $^2J_{FF}$ = 270.4 Hz, $^3J_{HF}$ = 16.0, 12.3 Hz), -104.31 (d, $^2J_{FF}$ = 270.4 Hz, $^3J_{HF}$ = 17.4, 13.6 Hz).

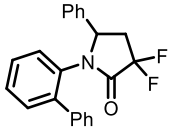


3,3-Difluoro-1-(3-methoxyphenyl)-5-phenylpyrrolidin-2-one (3ai).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-*N*-(3-methoxyphenyl) acetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 83%, 251.4 mg, white solid, m.p. 107-108 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.11 (m, 5H), 7.06-7.00 (m, 2H), 6.84 (d, J = 8.0 Hz, 1H), 6.56 (d, J = 8.0, 1H), 5.22-5.18 (m, 1H), 3.58 (s, 3H), 3.05-2.92 (m, 1H), 2.47-2.34 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.20 (t, J = 31.3 Hz, 1C), 159.87, 138.60, 137.41, 129.68, 129.26 (2C), 128.62,

126.24 (2C), 117.48 (t, J = 250.48 Hz, 1C), 114.85, 112.24, 108.85, 58.28 (t, J = 3.4 Hz, 1C), 55.27, 38.93 (t, J = 21.8 Hz, 1C); ^{19}F NMR (377 MHz, $CDCl_3$) δ -100.99 (d, $^2J_{FF}$ = 270.5 Hz, $^3J_{HF}$ = 16.2, 12.7 Hz), -104.25 (d, $^2J_{FF}$ = 270.5 Hz, $^3J_{HF}$ = 17.4, 13.9 Hz).

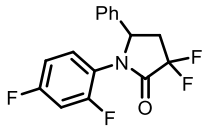


3,3-Difluoro-5-phenyl-1-(o-tolyl) pyrrolidin-2-one (3aj).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-*N*-(*o*-tolyl) acetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 88%, 252.6 mg, white solid, m.p. 103.6-104.6 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15-7.09 (m, 5H), 7.02-6.98 (m, 2H), 6.93-6.89 (m, 1H), 6.79 (m, 1H), 4.95 (s, 1H), 3.07-2.95 (m, 1H), 2.66-2.52 (m, 1H), 2.04 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.61 (t, J = 30.7 Hz, 1C), 137.24, 135.43, 134.20, 131.19, 128.97, 128.87 (2C), 128.46, 127.46 (2C), 126.49, 117.58 (t, J = 249.5 Hz, 1C), 59.72 (t, J = 3.3 Hz, 1C), 38.21 (t, J = 22.3 Hz, 1C), 17.92; ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.28 (d, $^2J_{FF}$ = 270.8 Hz), -104.38 (d, $^2J_{FF}$ = 270.7 Hz).

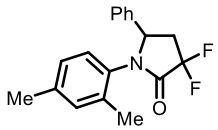


1-([1,1'-Biphenyl]-2-yl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3ak).[1] The title compound was prepared according to Representative Procedure I except that *N*-([1,1'-biphenyl]-2-yl)-2-bromo-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 90%, 314.1 mg, white solid, m.p. 144.4-145.6 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.31 (m, 3H), 7.19-6.98 (m, 9H), 6.81 (d, J = 7.1 Hz, 2H), 3.98 (s, 1H), 2.57-2.44 (m, 1H),

2.34-2.21 (m, 1H);^{13}C NMR (101 MHz, $CDCl_3$) δ 164.26 (t, J = 30.9 Hz, 1C), 139.08, 138.38, 136.99, 132.74, 130.73, 129.73, 128.85 (2C), 128.77 (2C), 128.74, 128.37 (2C), 128.17, 128.15, 127.18 (2C), 117.53 (t, J = 249.47 Hz, 1C), 117.53 (t, J = 249.47 Hz, 1C), 58.47, 38.44 (t, J = 22.1 Hz, 1C); ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.29 (d, $^2J_{FF}$ = 270.5 Hz, $^3J_{HF}$ = 16.0, 9.4 Hz), -105.03 (d, $^2J_{FF}$ = 270.6 Hz).

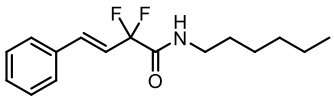


1-(2,4-Difluorophenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3al).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-*N*-(2,4-difluorophenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 79%, 244.1 mg, white solid, m.p. 118.0-118.9 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.04 (m, 6H), 6.72-6.66 (m, 2H), 5.15-5.11 (m, 1H), 3.13-3.01 (m, 1H), 2.60-2.46 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.25 (t, J = 29.8 Hz, 1C), 162.09 (dd, J = 256.1, 6.2 Hz, 1C), 157.46 (dd, J = 254.1, 12.6 Hz, 1C), 137.16, 129.54 (dd, J = 10.1, 2.7 Hz, 1C), 129.28 (2C), 127.10 (2C), 119.56 (dd, J = 12.4, 3.8 Hz, 1C), 117.20 (t, J = 249.6 Hz, 1C), 117.18 , 111.96 (dd, J = 22.5, 3.7 Hz, 1C), 105.17 (dd, J = 26.4, 23.7 Hz, 1C), 59.37-59.28 (m, 1C), 39.27 (t, J = 21.2 Hz); ^{19}F NMR (377 MHz, $CDCl_3$) δ -103.00 (d, $^2J_{FF}$ = 271.4 Hz, $^3J_{HF}$ = 16.0, 8.0 Hz), -104.96 (d, $^2J_{FF}$ = 271.4 Hz), -108.29, -114.45.

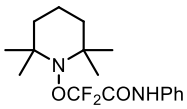


1-(2,4-Dimethylphenyl)-3,3-difluoro-5-phenylpyrrolidin-2-one (3am).[1] The title compound was prepared according to Representative Procedure I except that 2-bromo-*N*-(2,4-dimethylphenyl)-2,2-difluoroacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 85%, 255.8 mg,

white solid, m.p. 105-106.2 ℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.12 (m, 5H), 6.86 (s, 1H), 6.75 (d, J = 7.6 Hz, 1H), 6.66 (s, 1H), 4.93 (s, 1H), 3.10-2.97 (m, 1H), 2.69-2.56 (m, 1H), 2.11 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.87 (t, J = 29.8 Hz), 138.48, 137.53, 135.11, 132.02, 131.65, 129.07, 129.00, 127.59, 127.34, 117.61 (t, J = 249.6 Hz), 59.89 (t, J = 3.3 Hz), 38.45 (t, J = 22.3 Hz), 21.01, 17.94. ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.29 (d, $^{2}J_{FF}$ = 271.4 Hz), -104.53 (d, $^{2}J_{FF}$ = 271.4 Hz).



(*E*)-2,2-Difluoro-N-hexyl-4-phenylbut-3-enamide. The title compound was prepared according to Representative Procedure I except that 2-bromo-2,2-difluoro-N-hexylacetamide was used instead of 2-bromo-2,2-difluoro-*N*-phenylacetamide. The product was purified by silica gel column chromatography (petroleum ether/EtOAc = 10/1). Yield, 63%, 177 mg, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 6.6 Hz, 1H), 7.34 (t, J = 8.8 Hz, 1H), 7.06 (d, J = 16.2 Hz, 1H), 6.57-6.24 (m, 2H), 3.34 (q, J = 6.6 Hz, 2H), 1.59-1.53 (m, 2H), 1.31 (s, 4H), 0.87 (d, J = 6.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.94 (t, J = 29.9 Hz), 136.52 (t, J = 9.6 Hz), 134.40, 129.62, 128.91 (2C), 127.55 (2C), 119.33 (t, J = 25.2 Hz), 114.53 (t, J = 249.5 Hz), 39.80, 31.48, 29.31, 26.55, 22.62, 14.09; ^{19}F NMR (377 MHz, $CDCl_3$) δ -102.50 (d, $^{2}J_{FF}$ = 11.4 Hz).

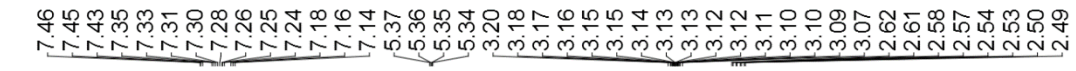


2,2-Difluoro-N-phenyl-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetamide. To a mixture of 2-bromo-2,2-difluoro-*N*-phenylacetamide **2a** (125 mg, 0.5 mmol), CuI (10.0 mg, 0.05 mmol) and 2,2,6,6-Tetramethyl-1-piperidinyloxy (156.2 mg, 1.0 mmol) in CH_3CN (1.0 mL) were added *N*,*N*,*N*',*N*'',*N*''-Pentamethyldiethylenetriamine (156 μL, 0.75 mmol) and styrene **1a** (115 μL, 1.0 mmol) successively. The resultant mixture was stirred at 80 ^{o}C for 10 h and monitored by TLC. The reaction was quenched with water, and then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After filtration, the filtrate was concentrated in vacuum and the residue was purified by silica gel column

chromatography (petroleum ether/EtOAc = 5/1) to give the TEMPO-adduct (19.5 mg) in 12% yield as white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.58 (t, *J* = 8.5, 2H), 7.38 (t, *J* = 8.0 Hz, 2H), 7.20 (t, *J* = 7.4 Hz, 1H), 1.71-1.47 (m, 6H), 1.41-1.03 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.33 (t, *J* = 38.2 Hz), 136.13, 129.36 (2C), 125.67, 120.22 (2C), 115.75 (t, *J* = 274.4 Hz), 61.62, 40.42, 33.68, 21.01, 17.00; ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.88.

References

1. M. Zhang, W. Li, Y. Duan, P. Xu, S. Zhang, C. Zhu, *Org. Lett*. 2016, **18**, 3266.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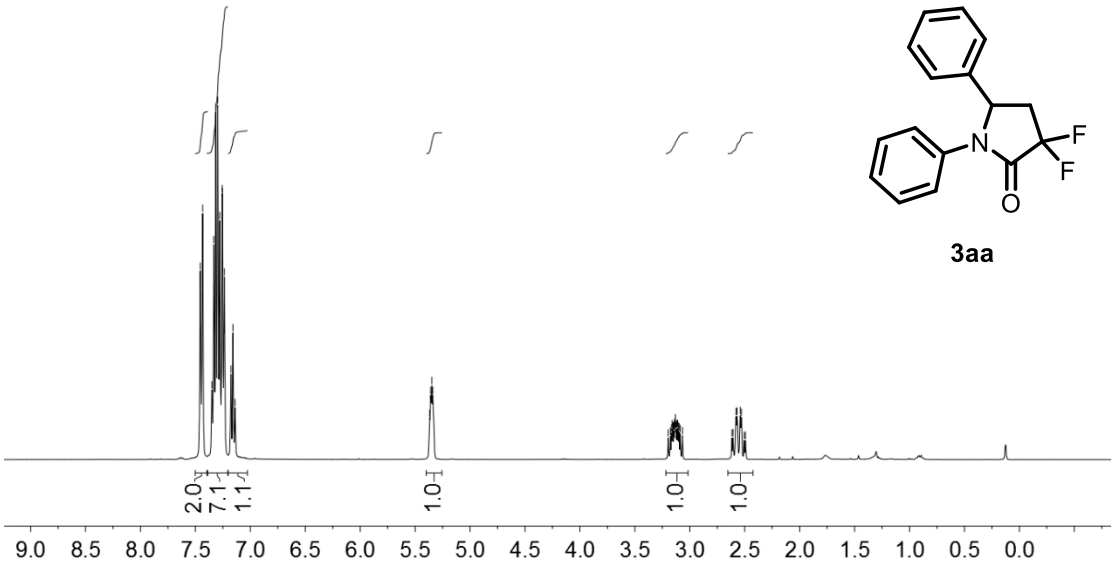
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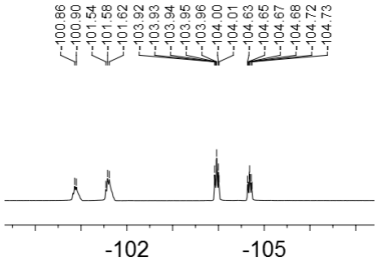
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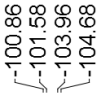
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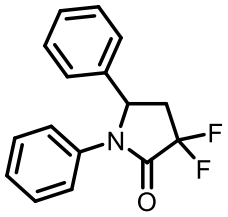
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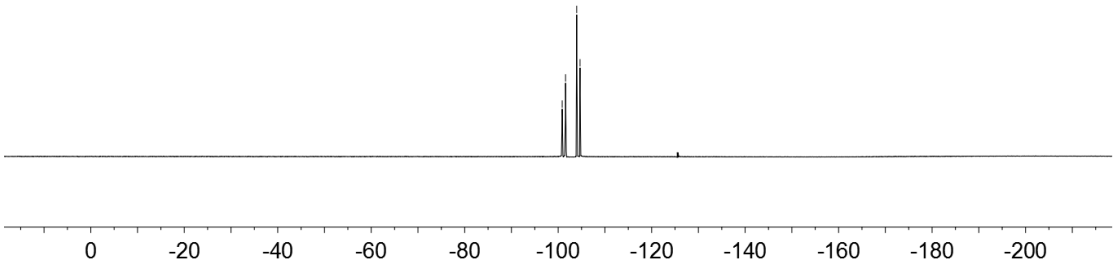
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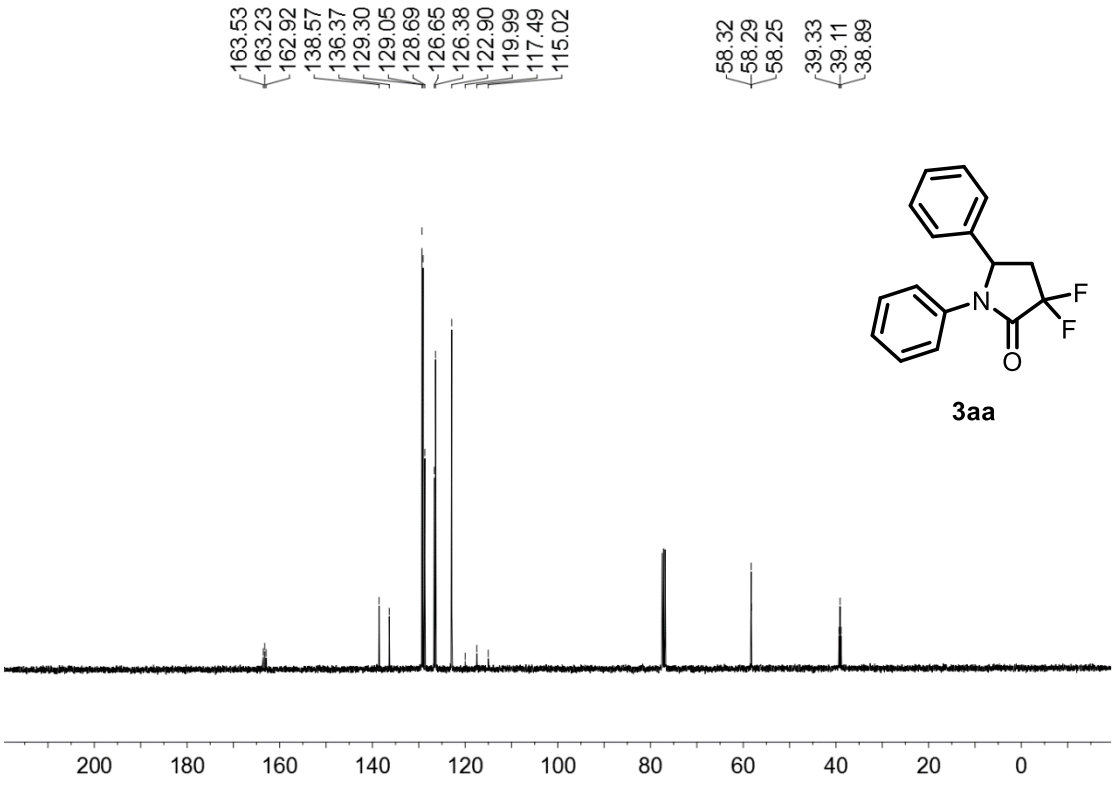
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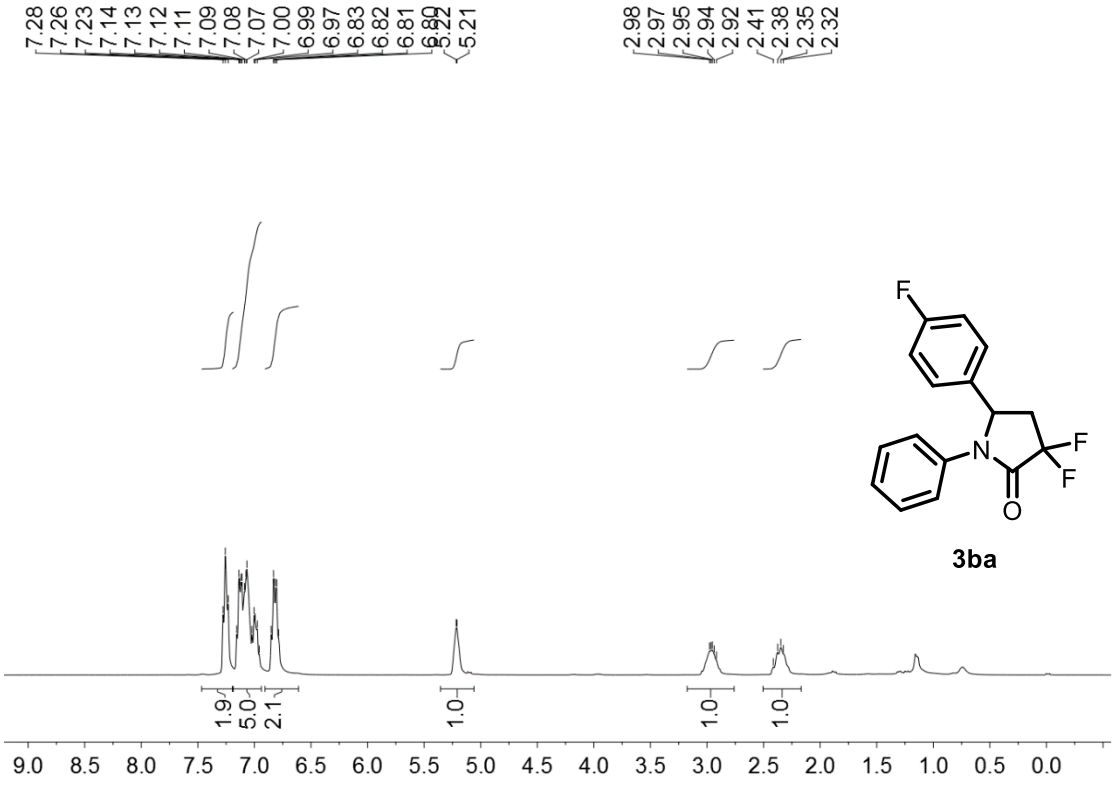
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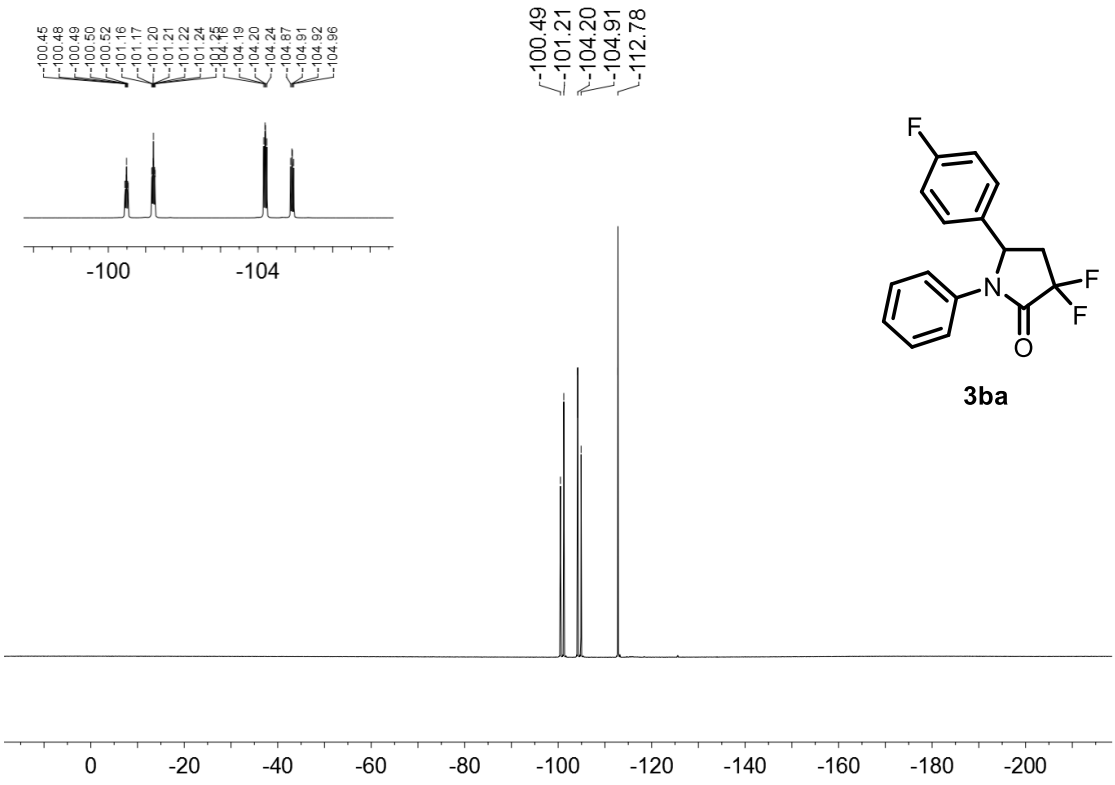
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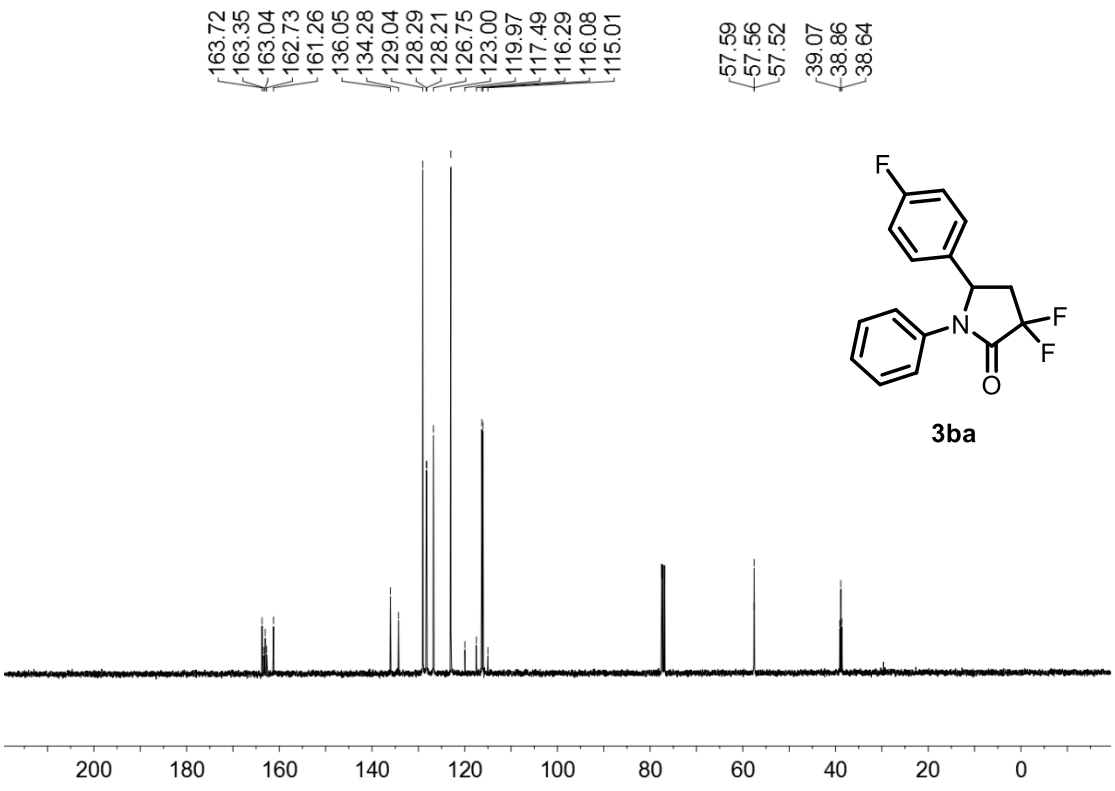
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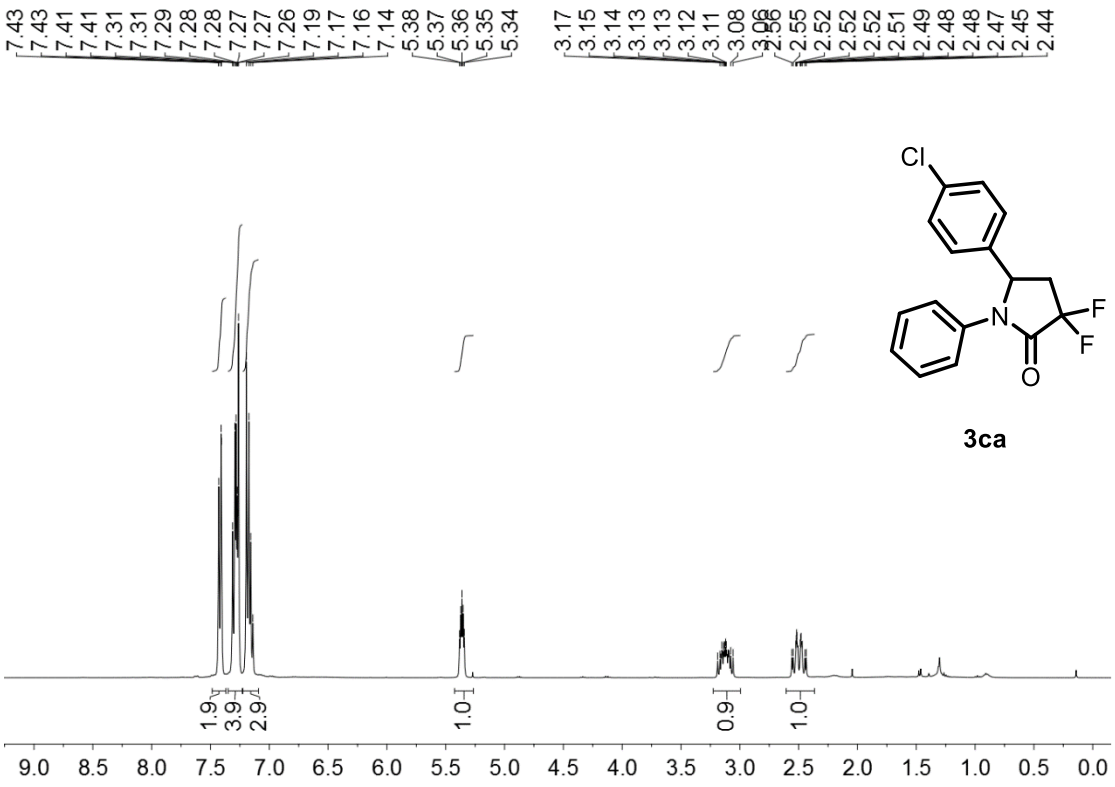
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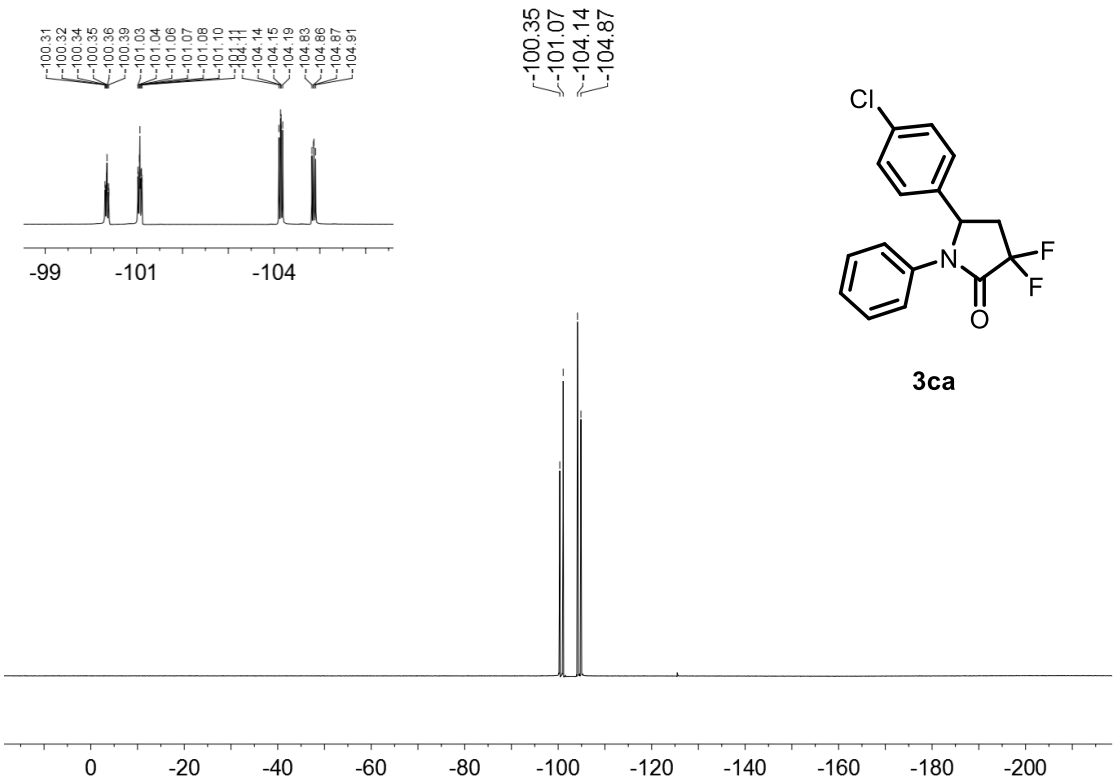
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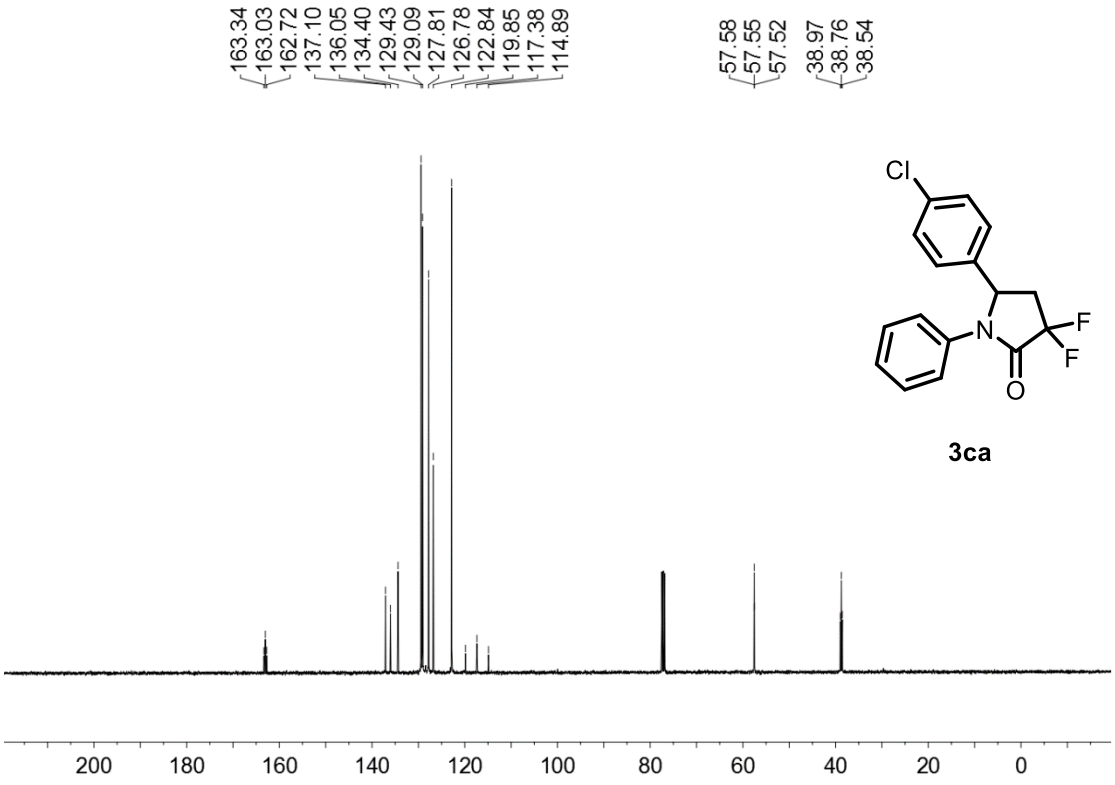
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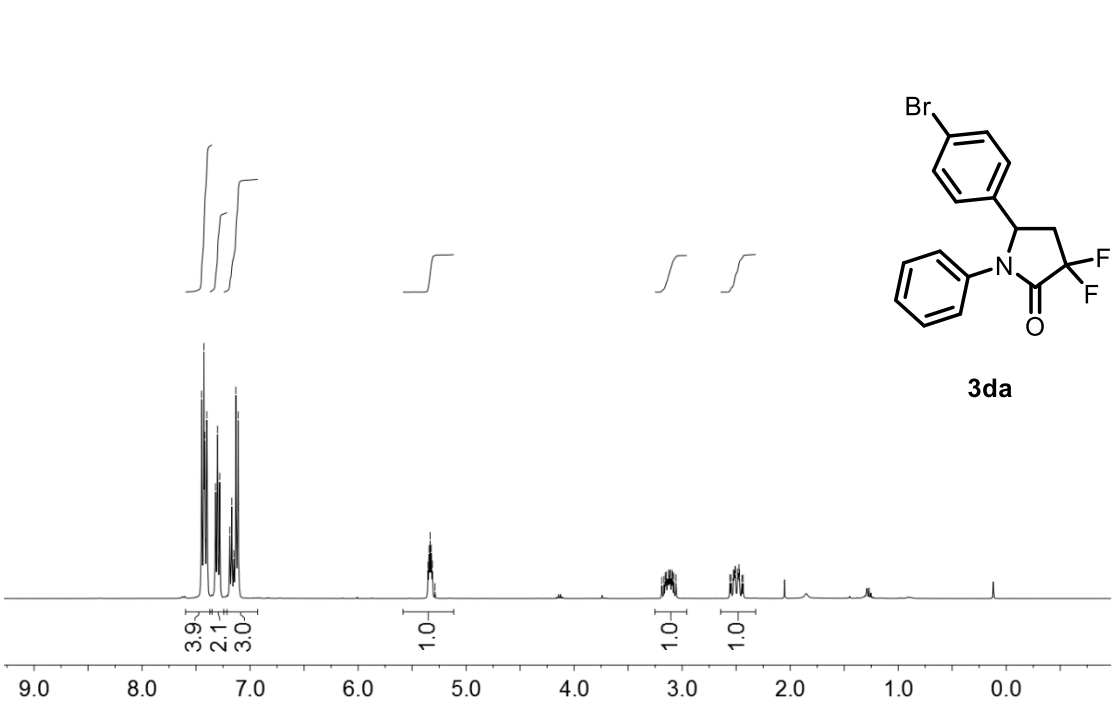
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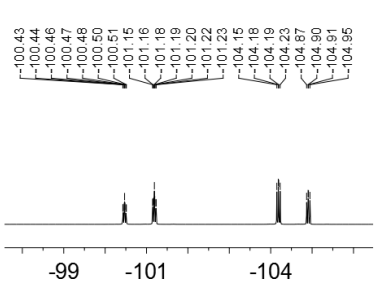
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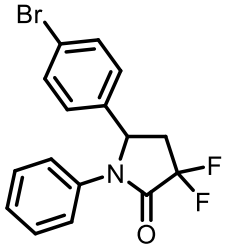
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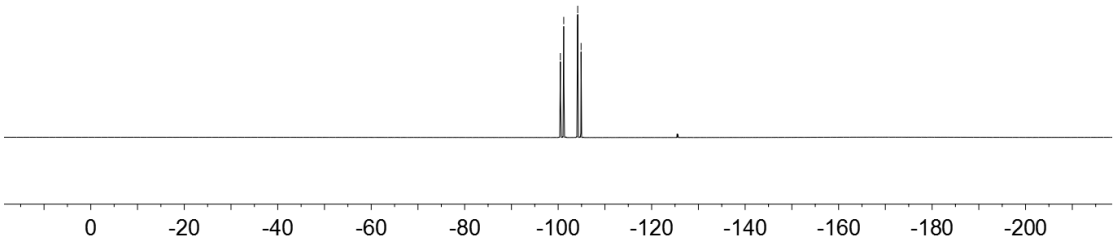
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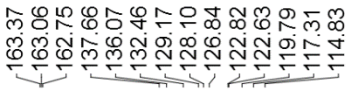
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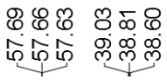
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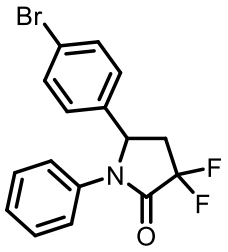
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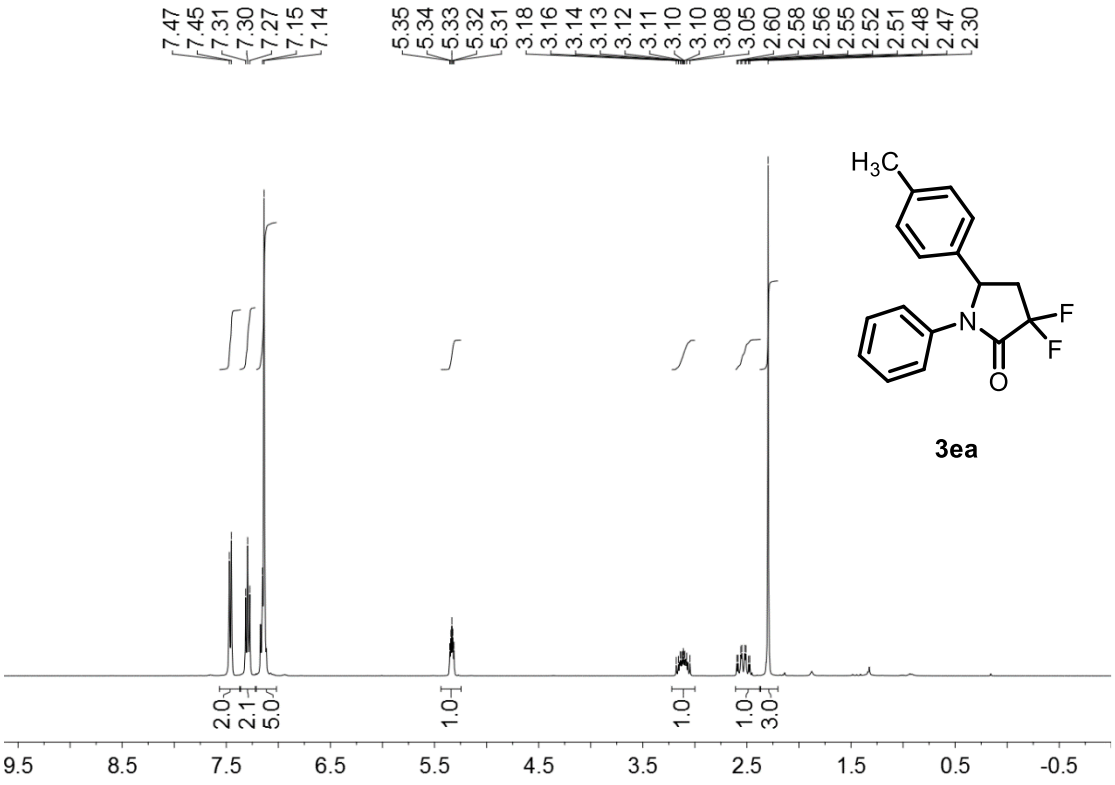
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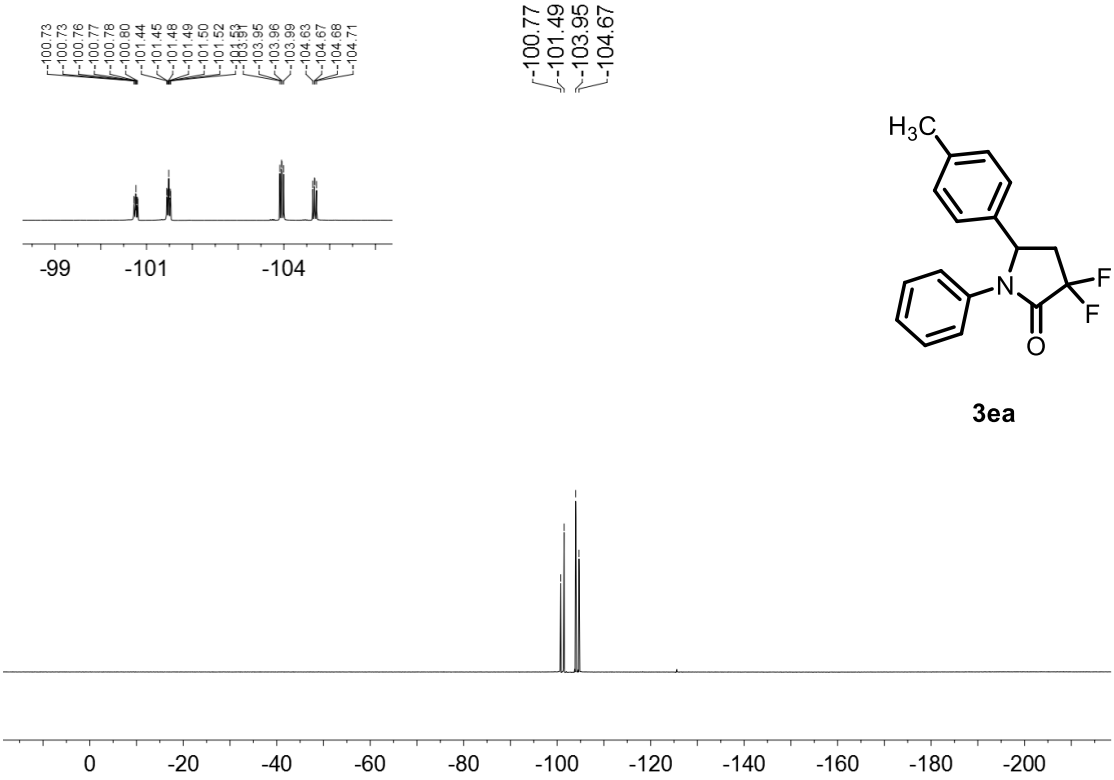
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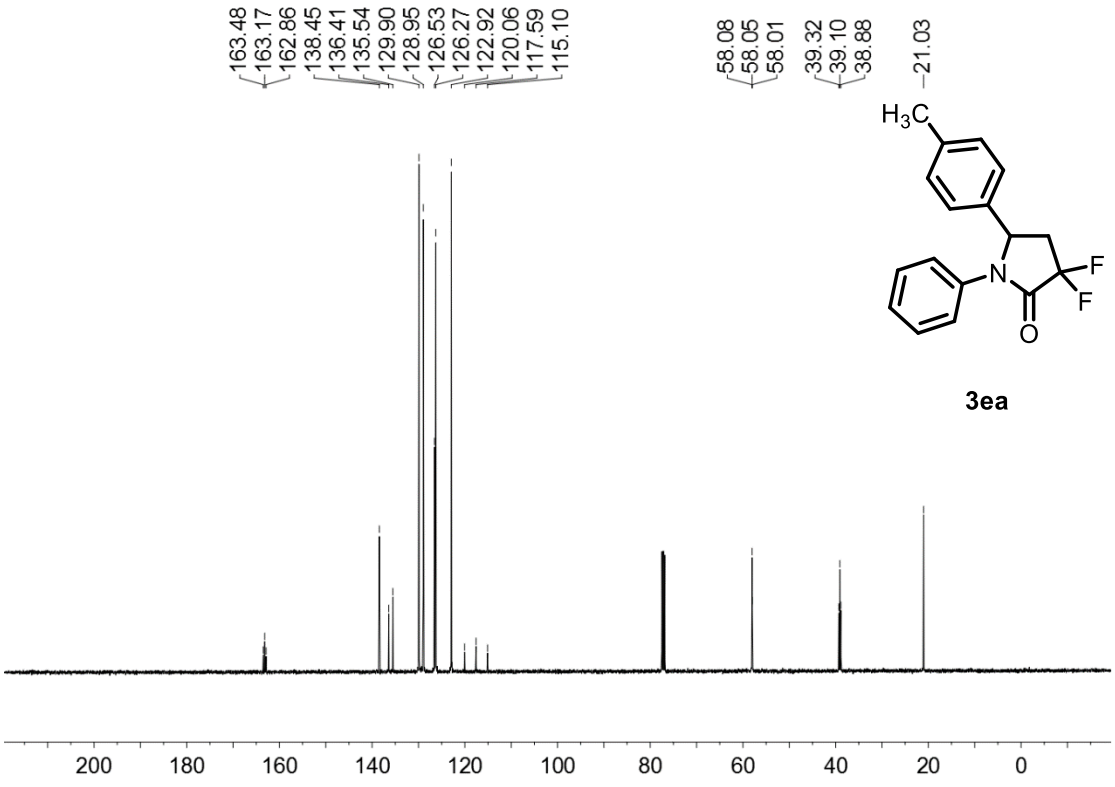
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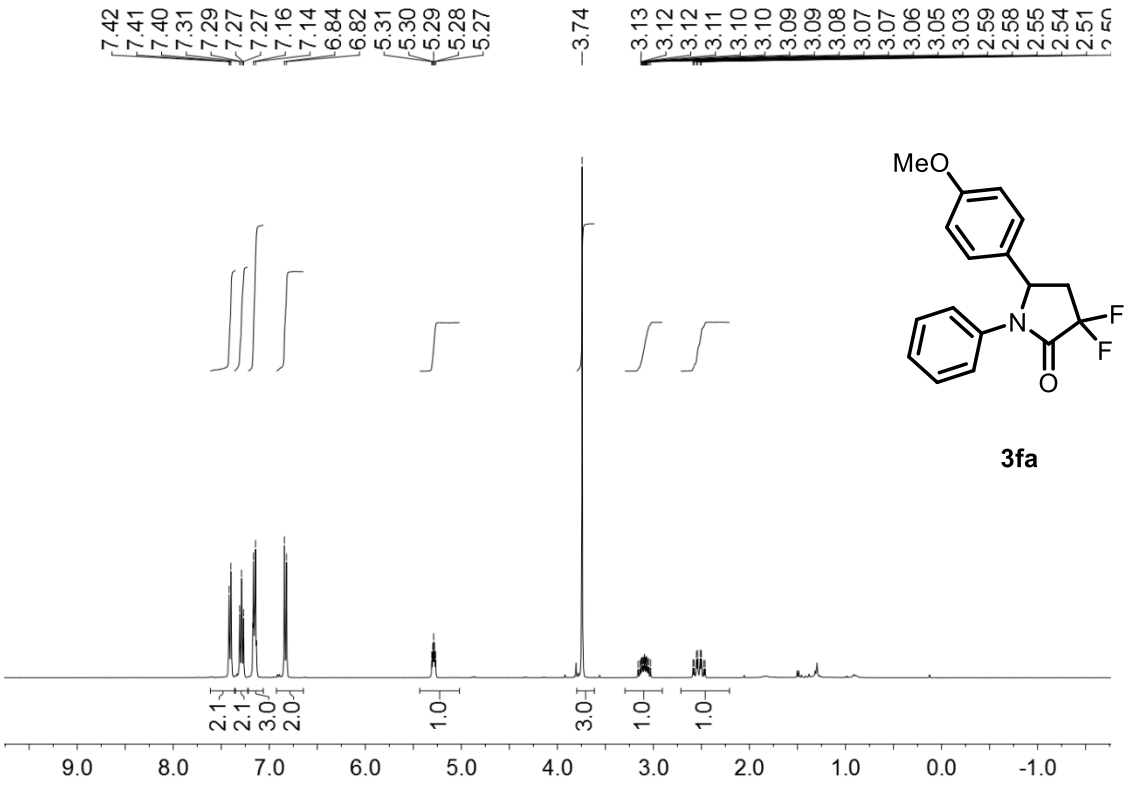
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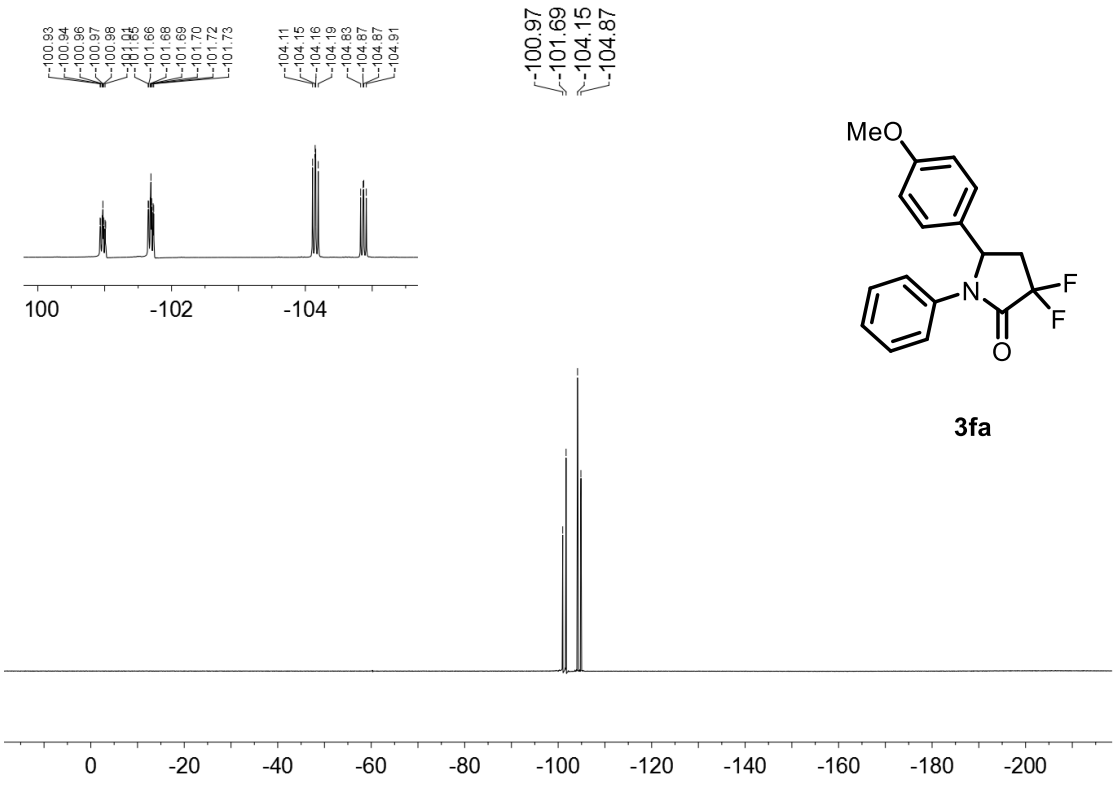
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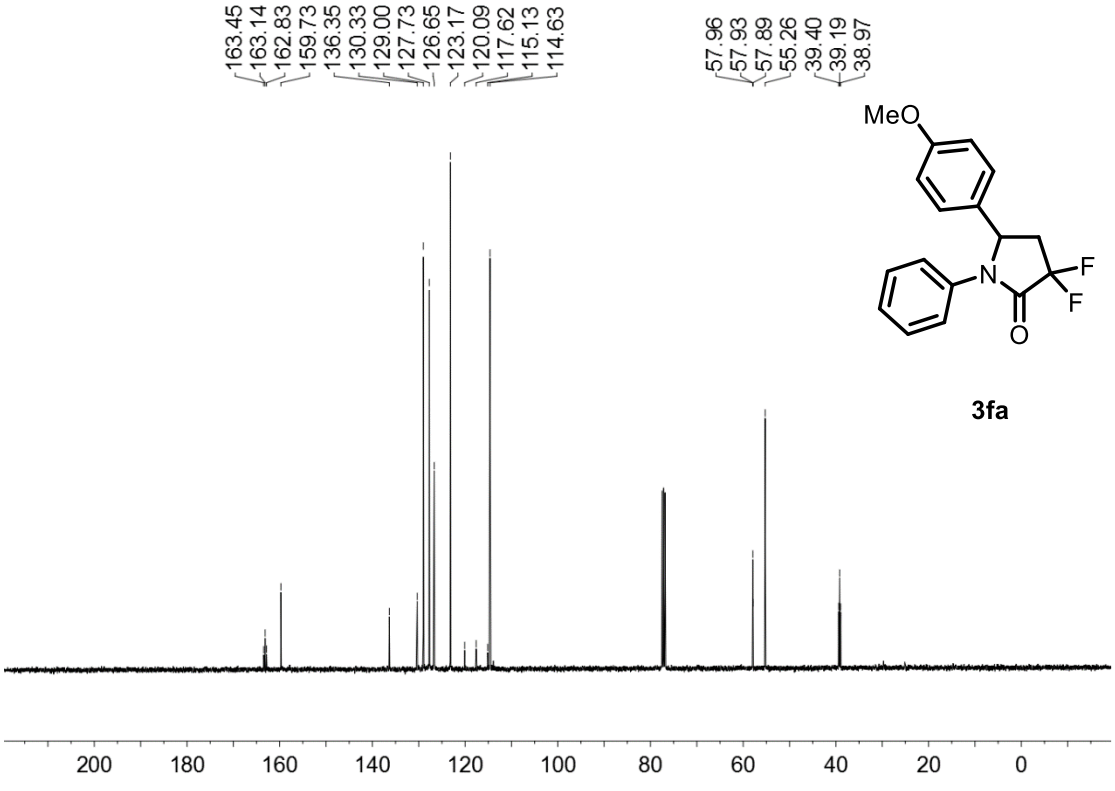
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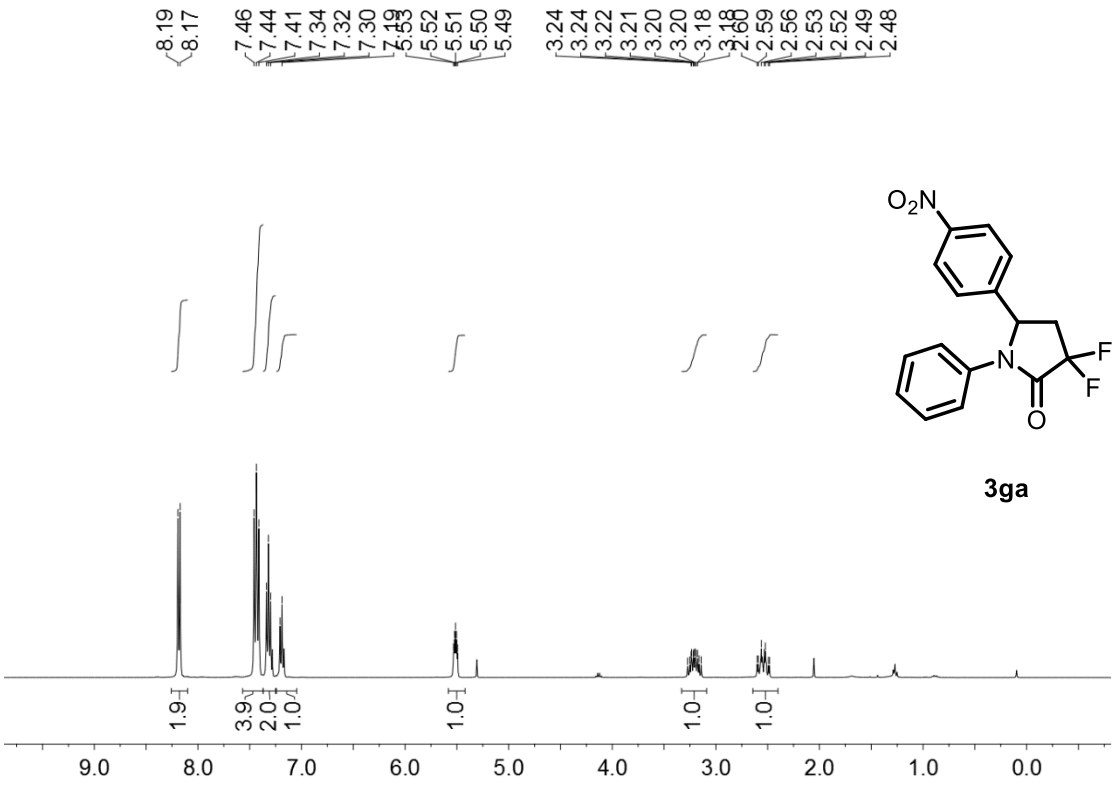
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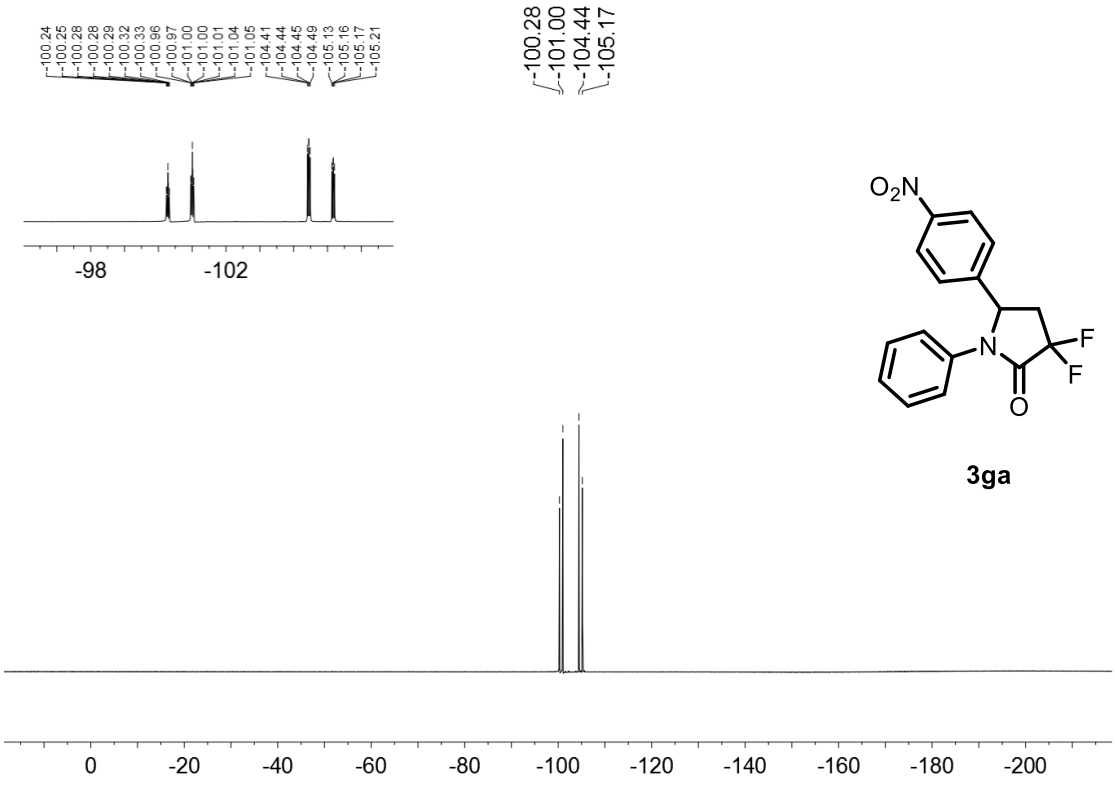
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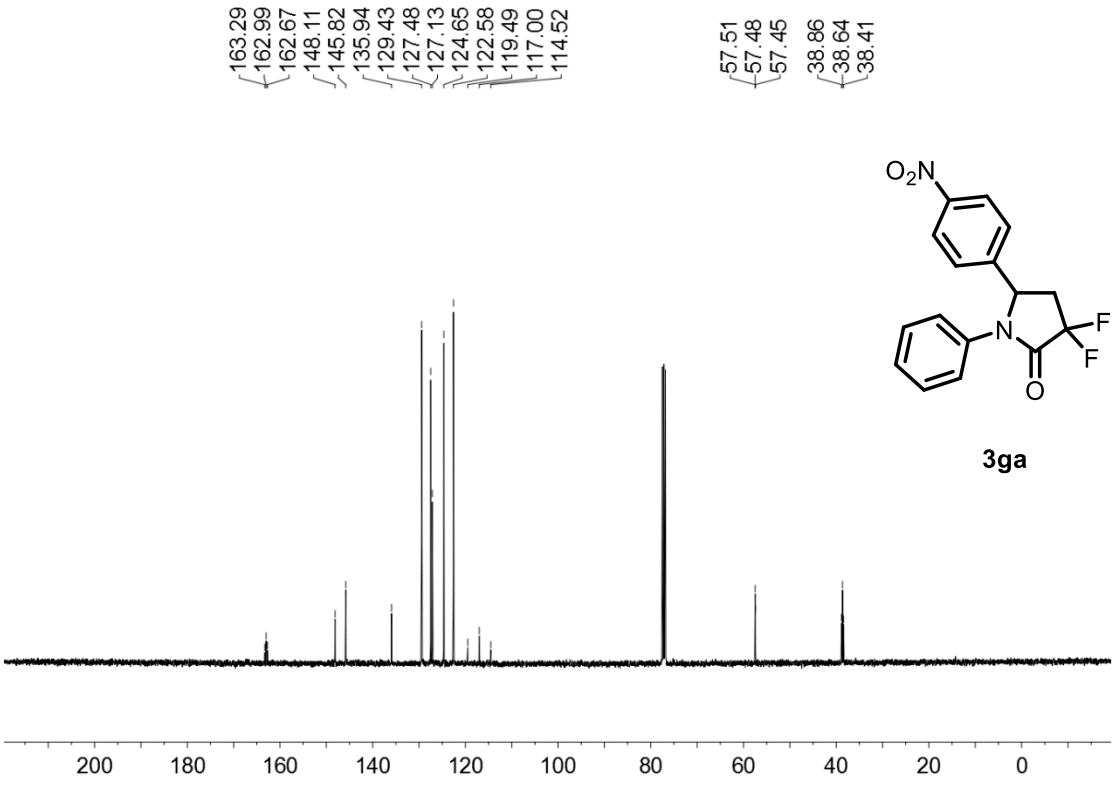
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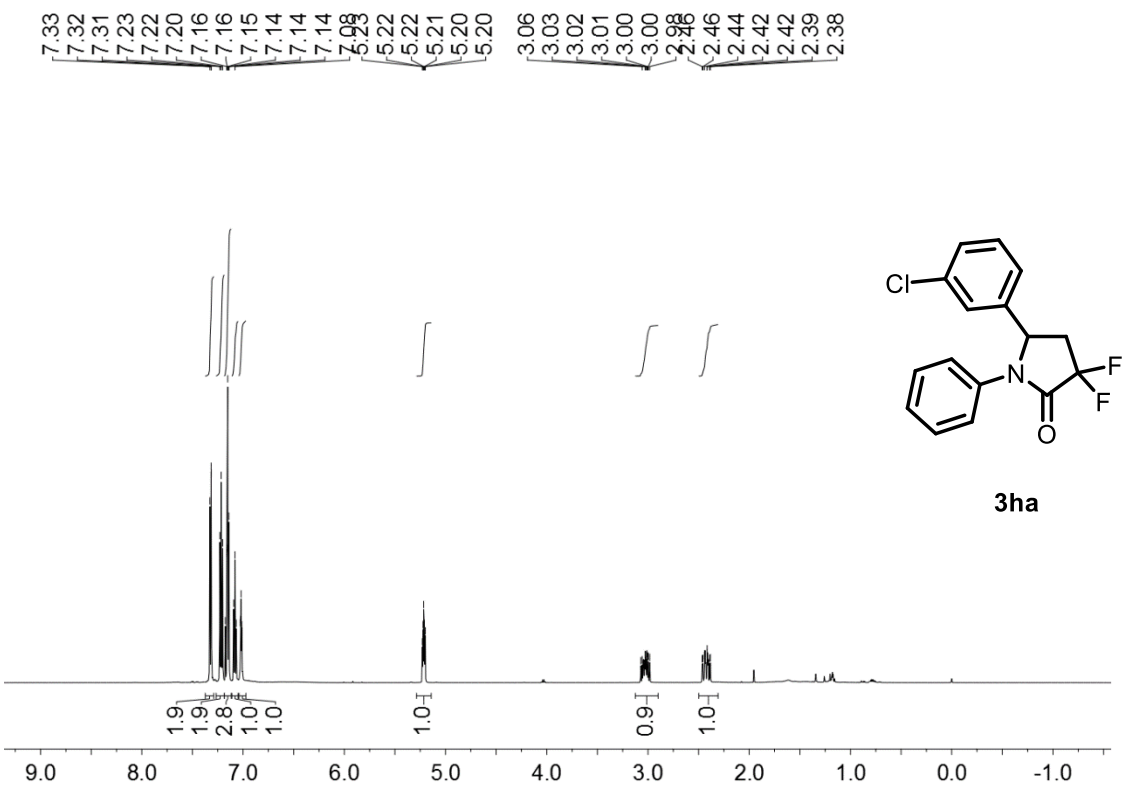
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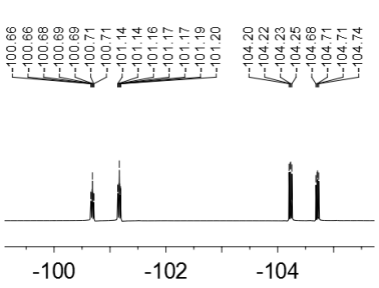
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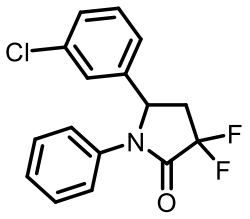
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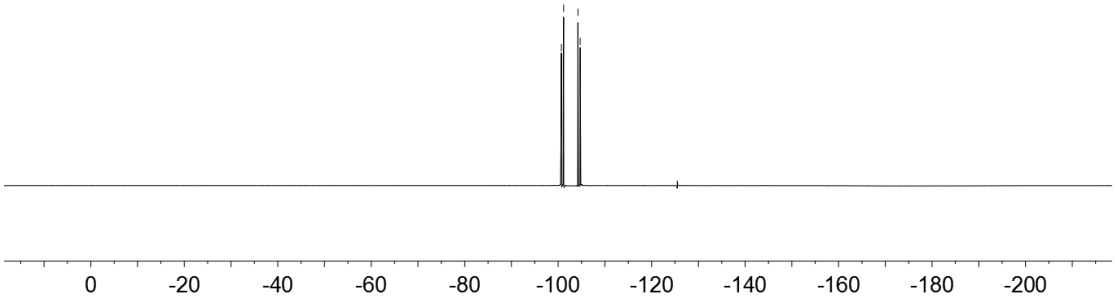
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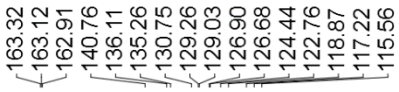
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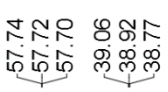
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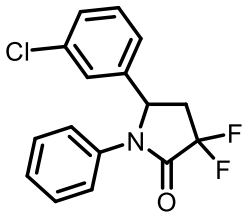
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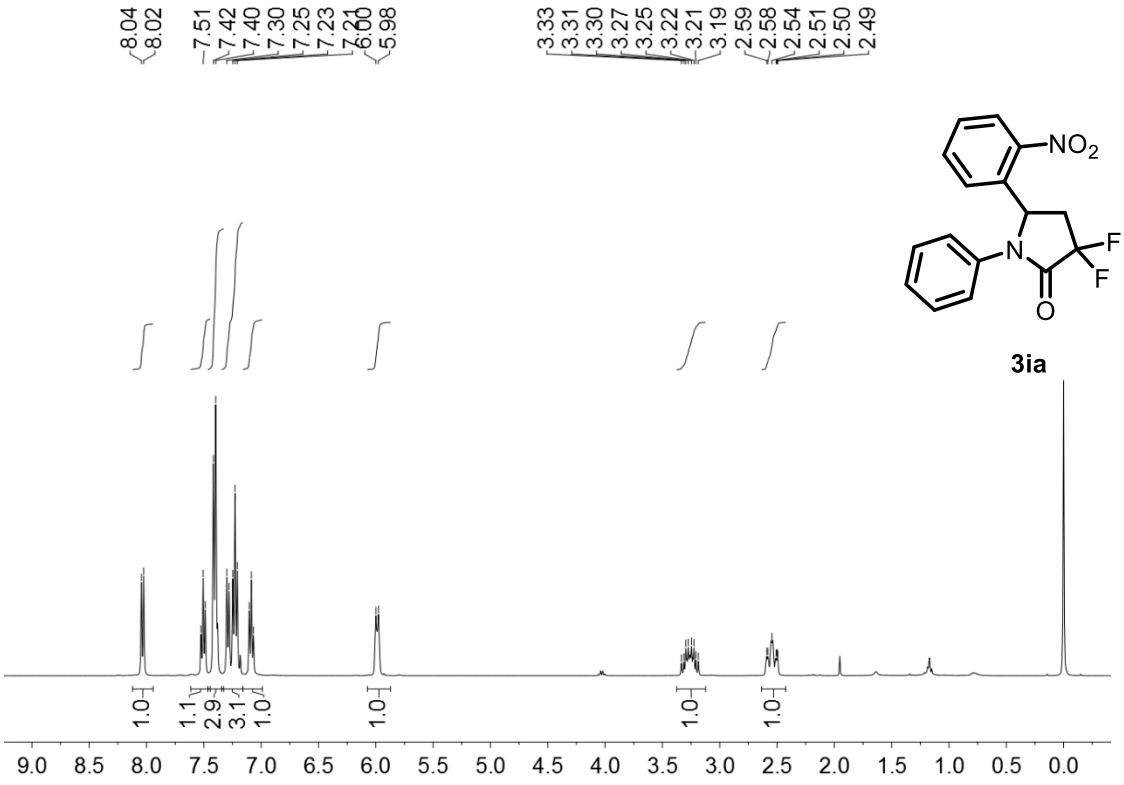
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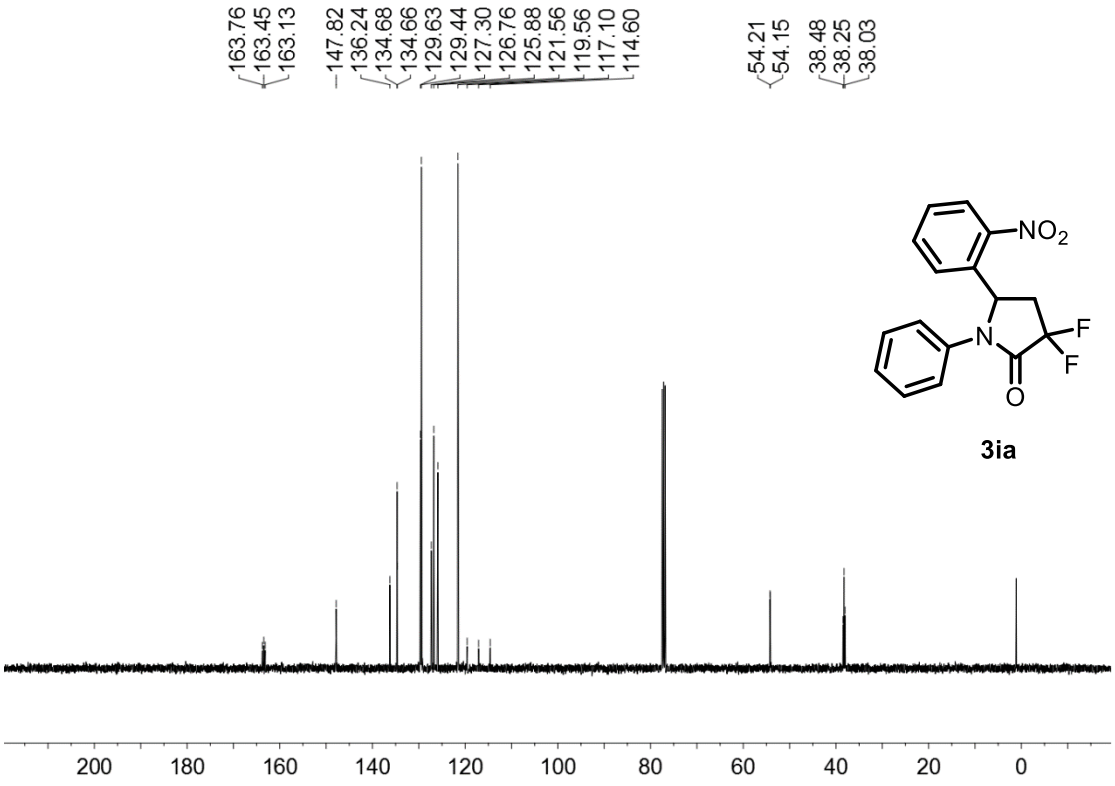
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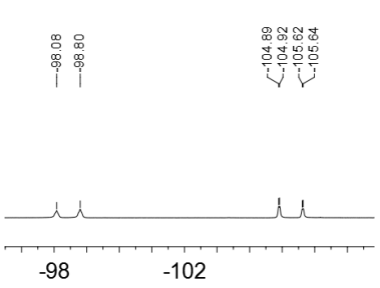
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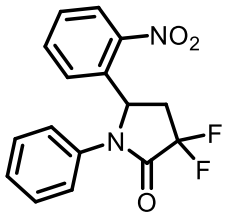
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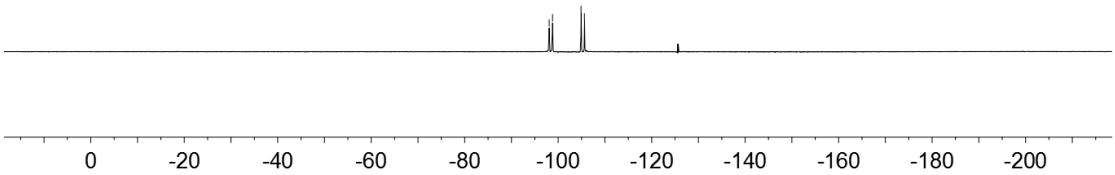
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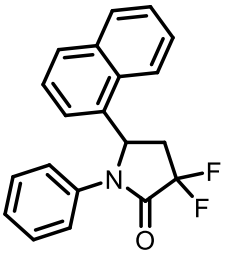
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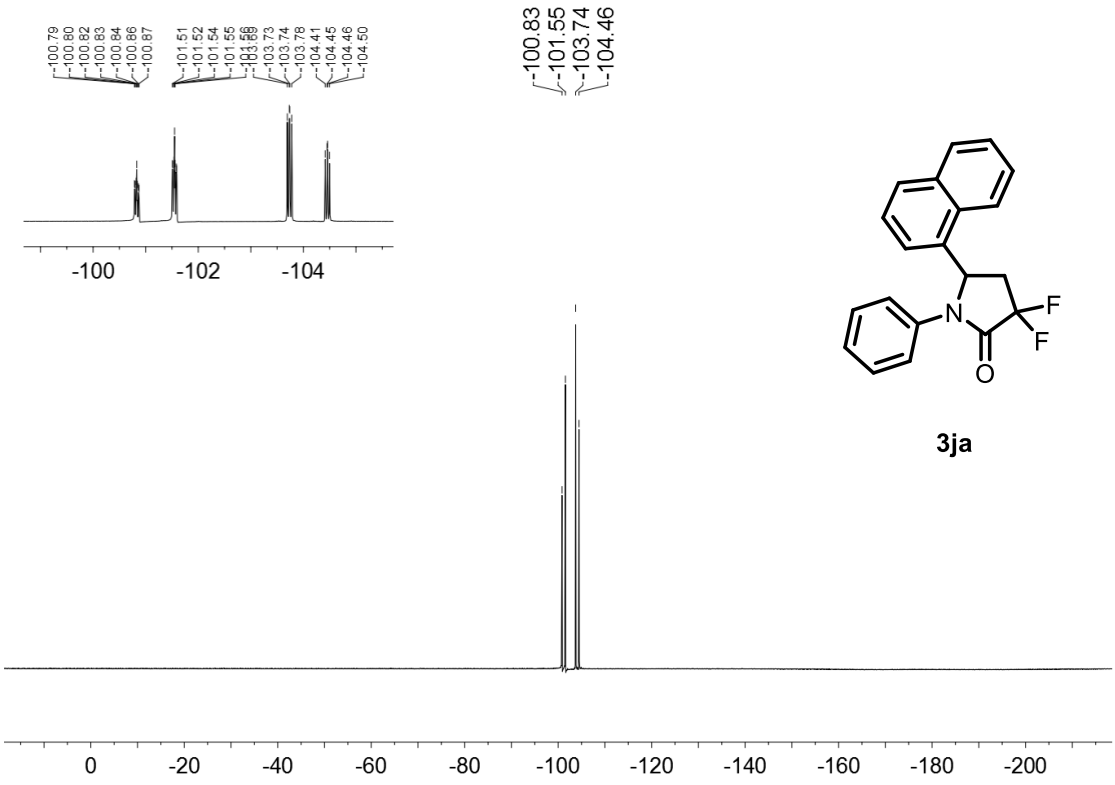
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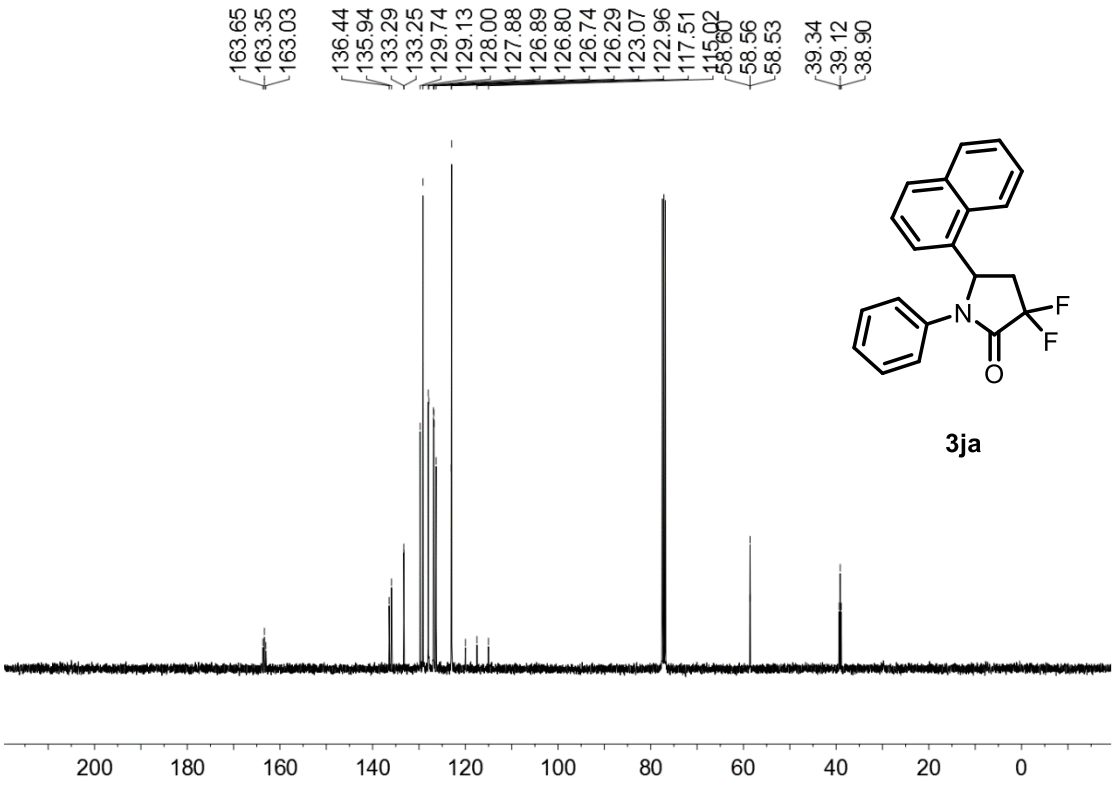
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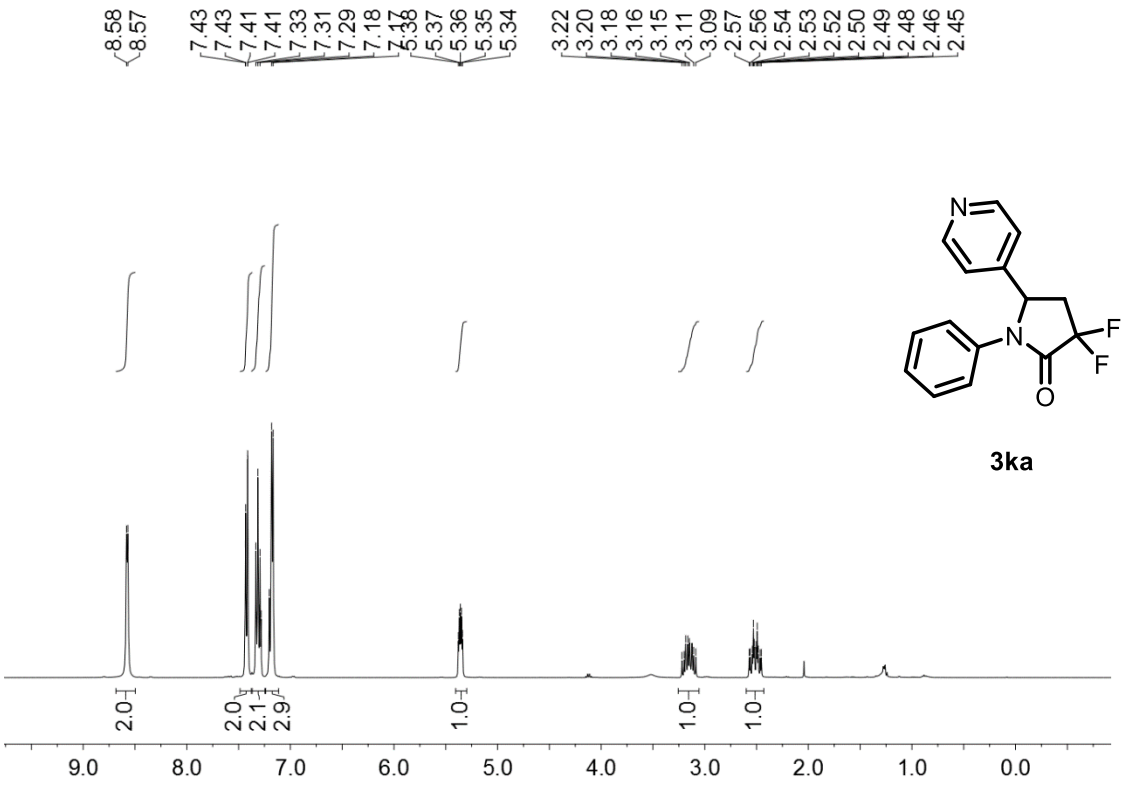
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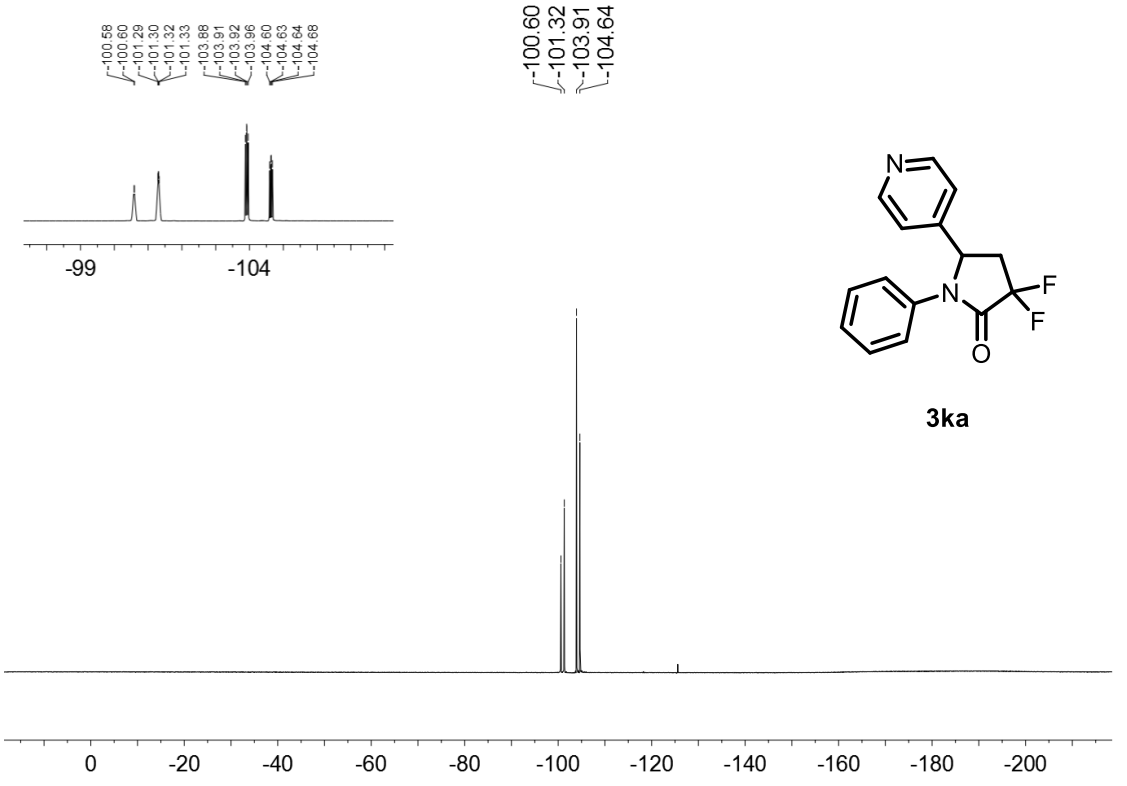
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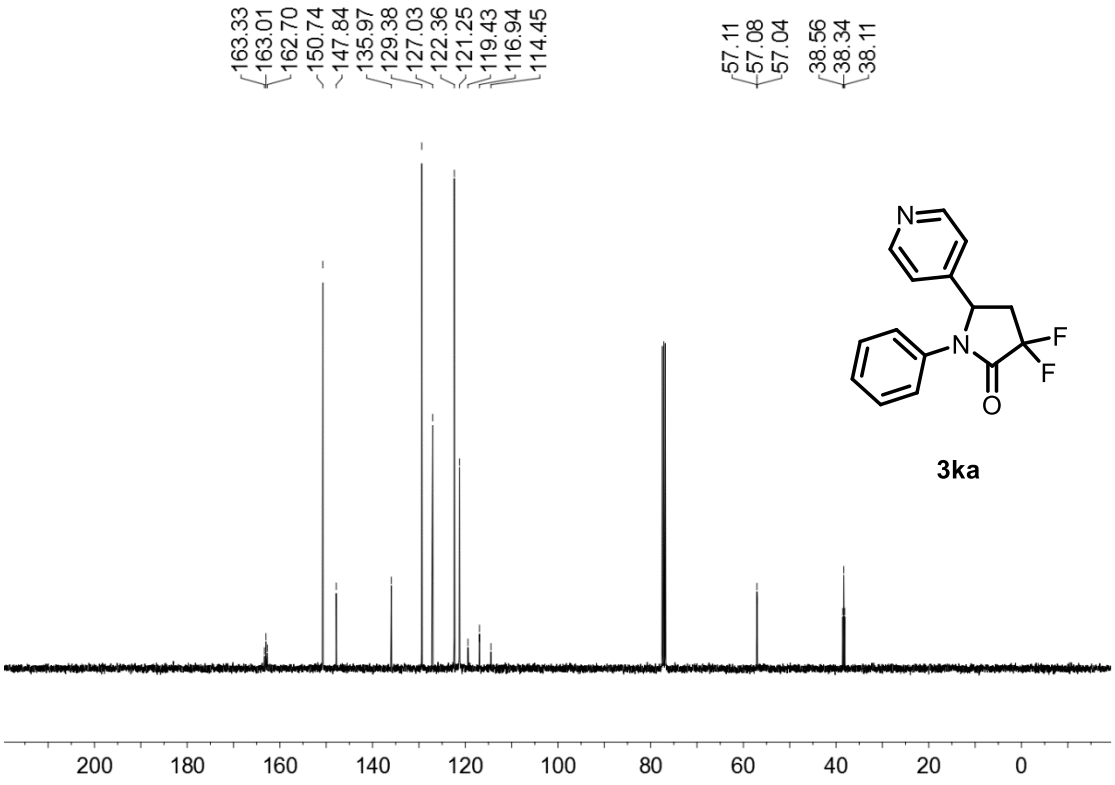
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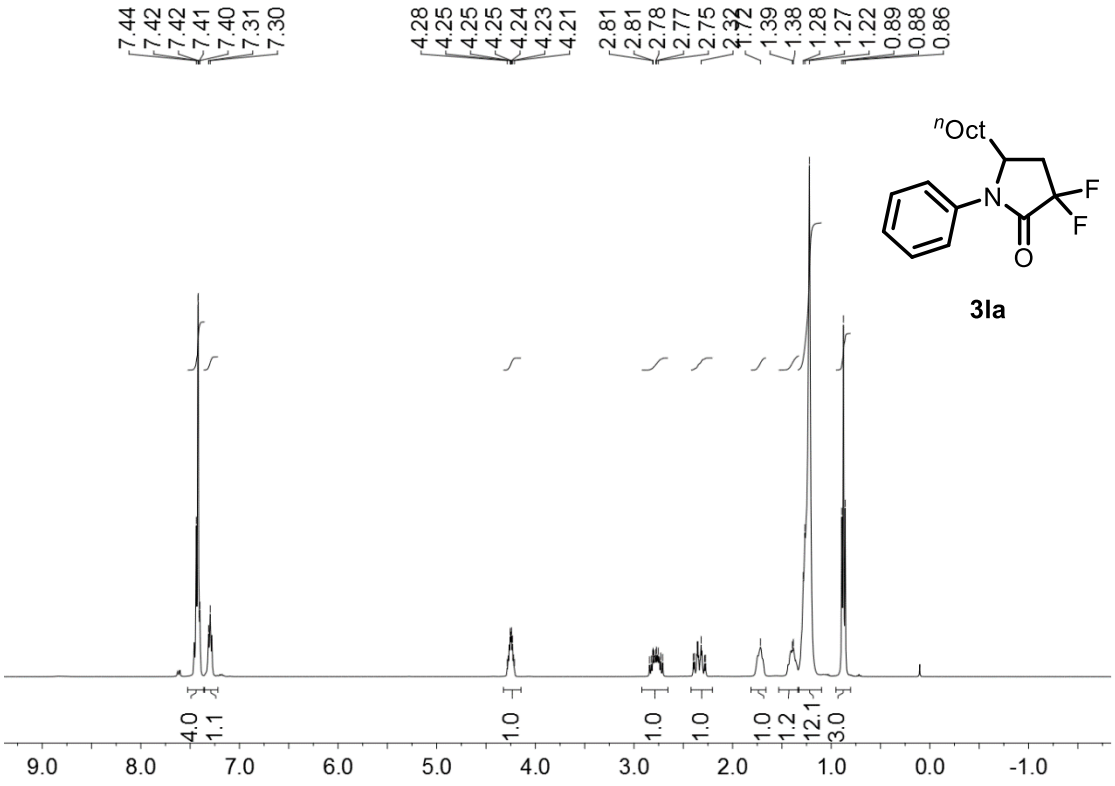
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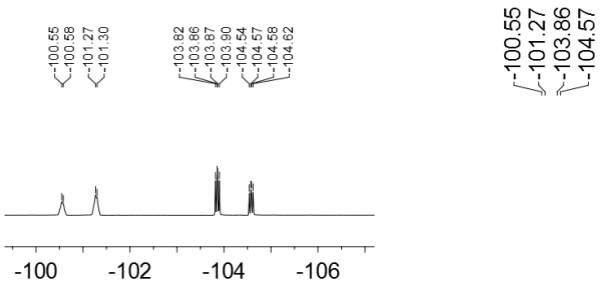
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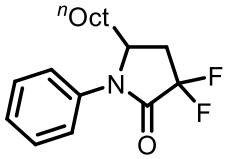
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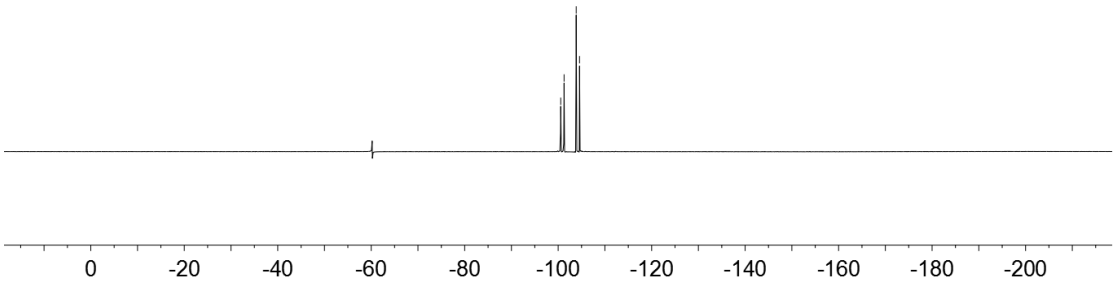
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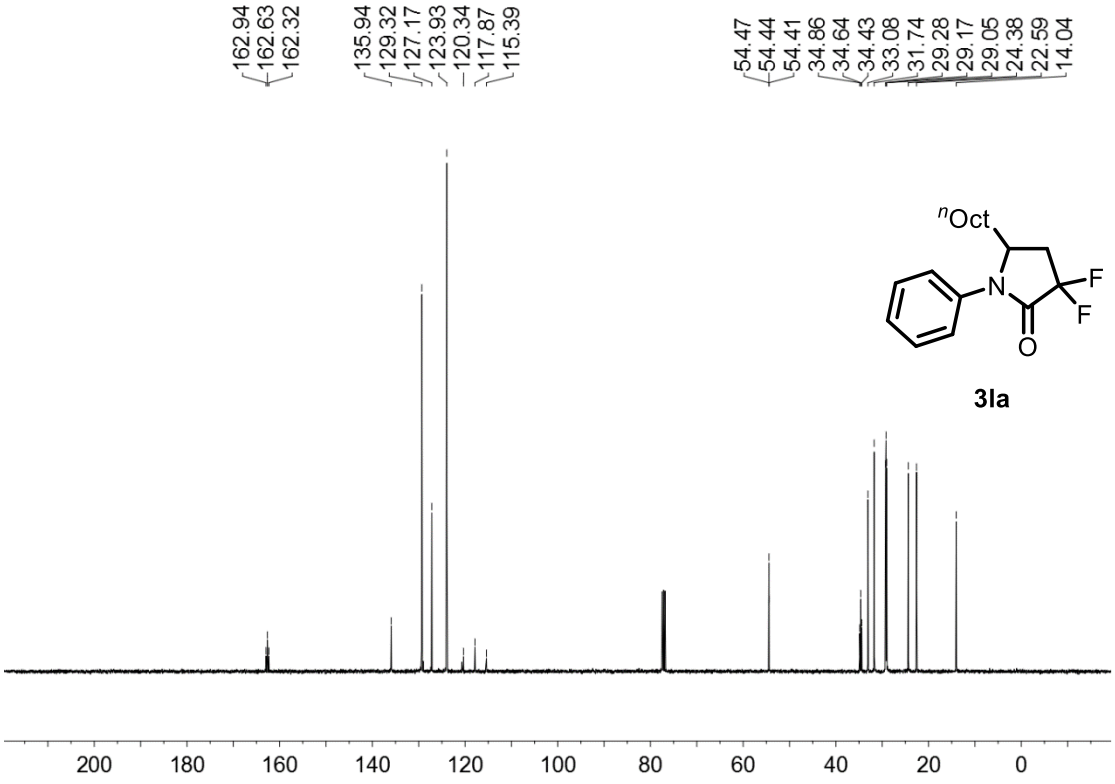
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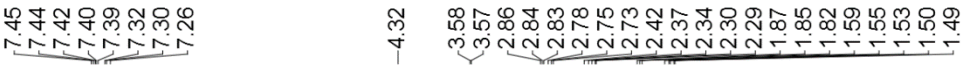
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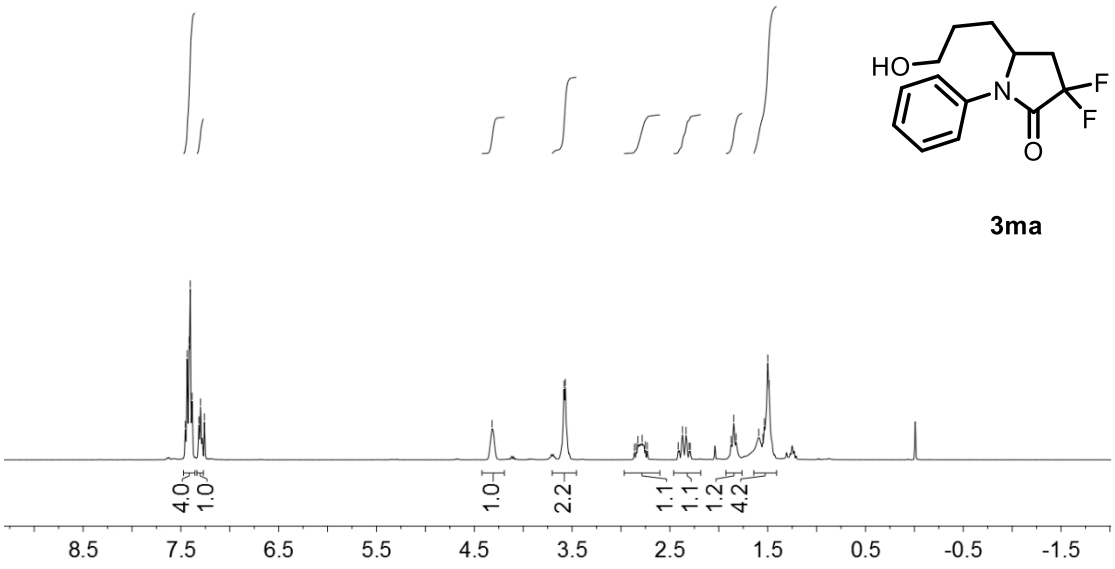
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3ma


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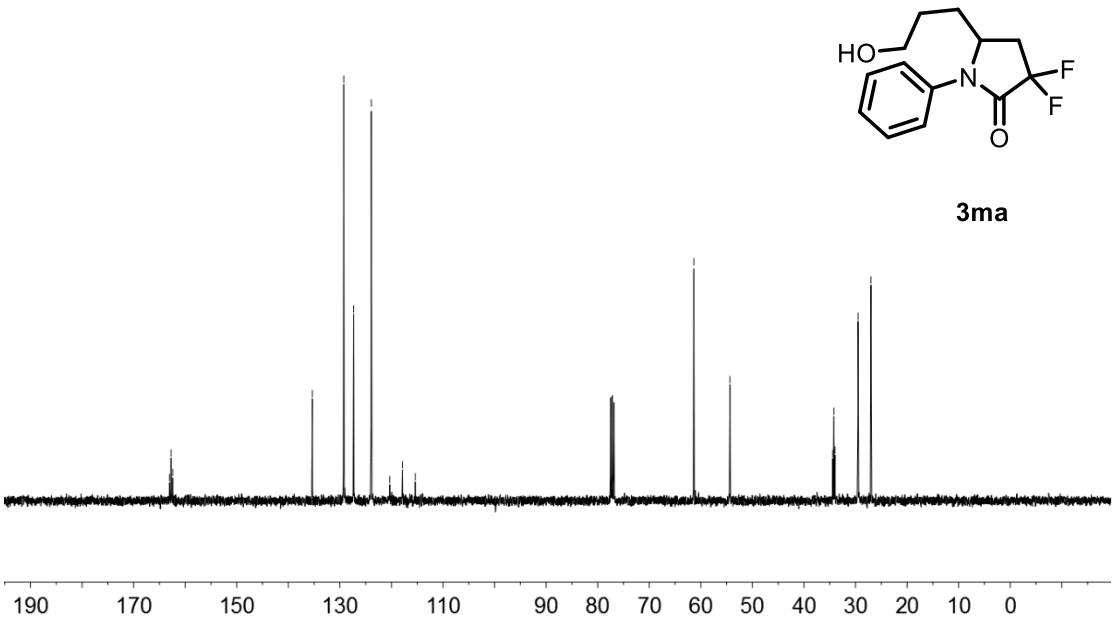
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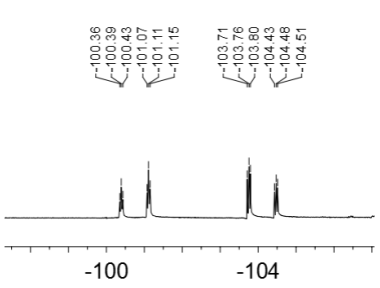
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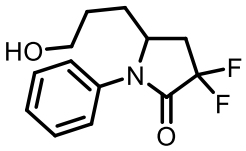
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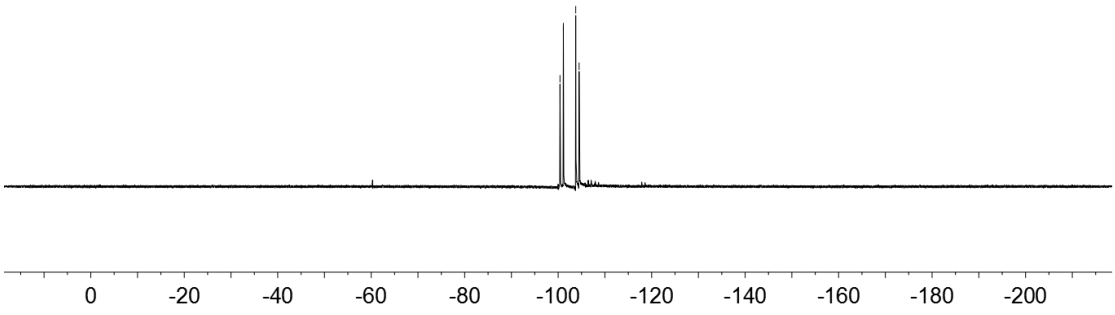
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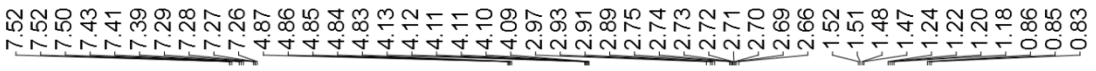
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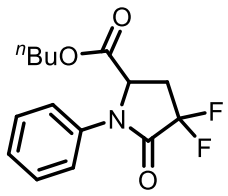
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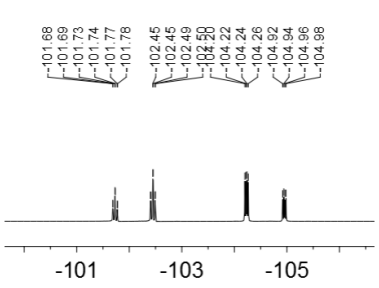
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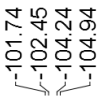
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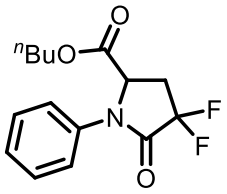
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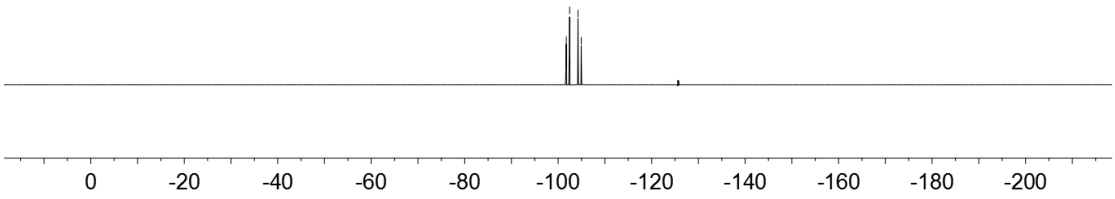
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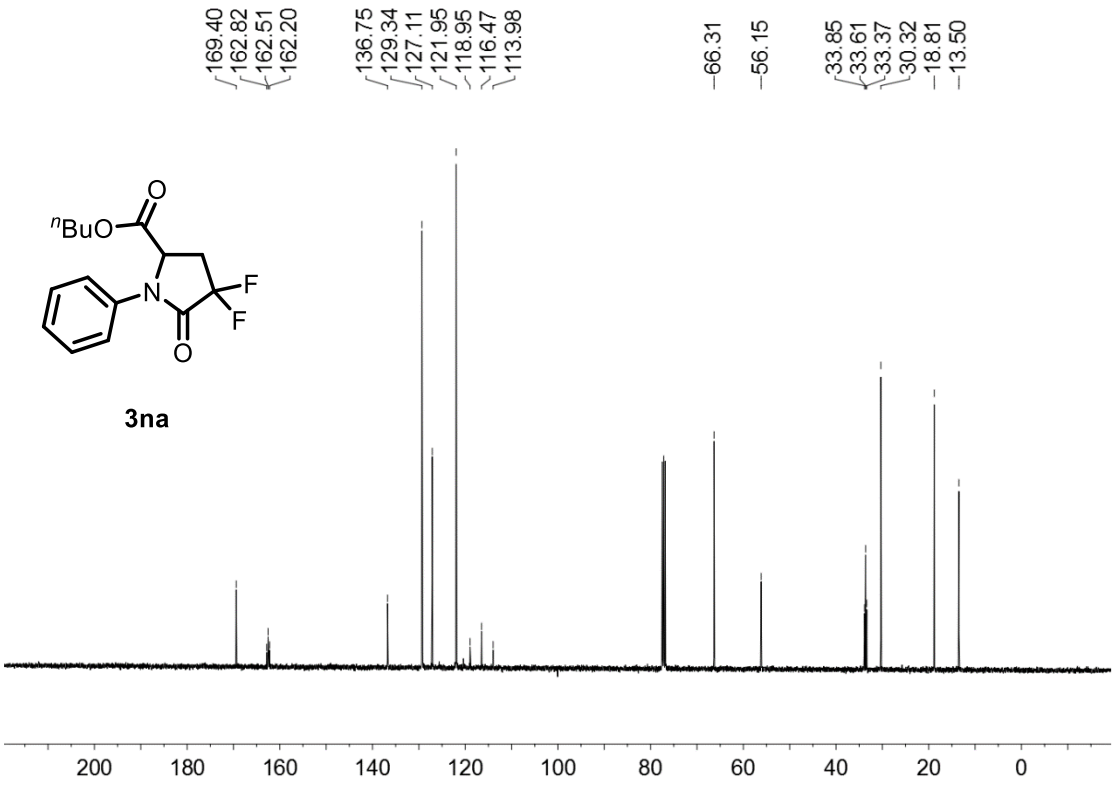
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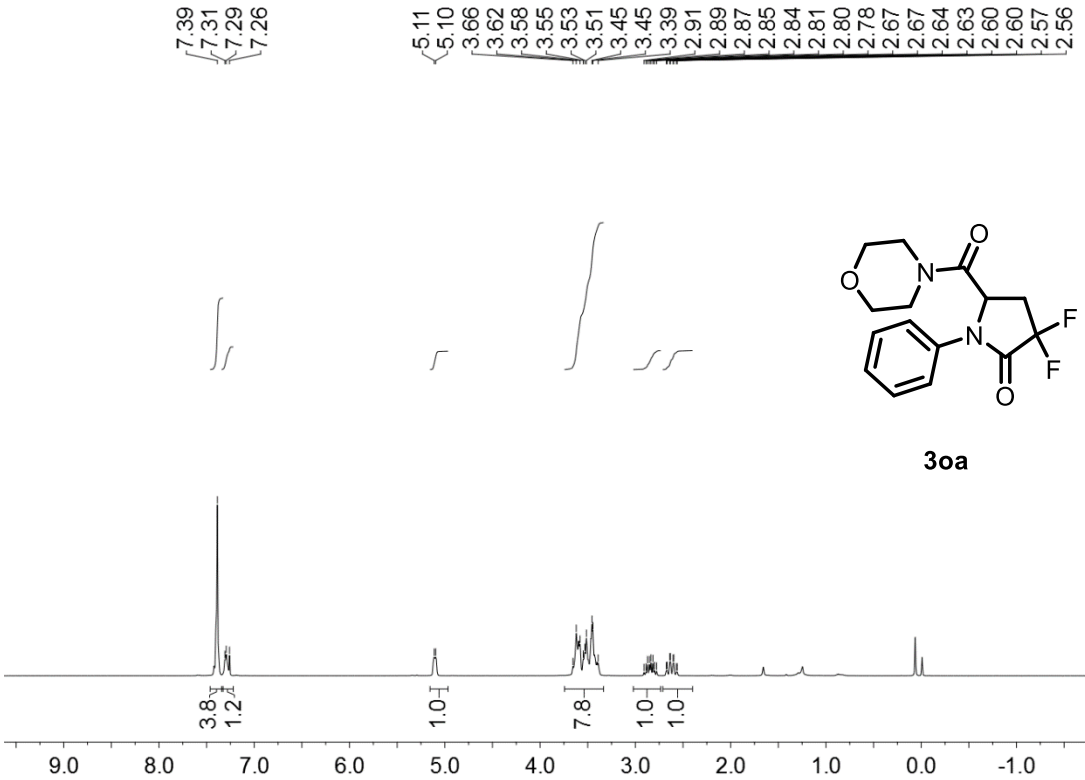
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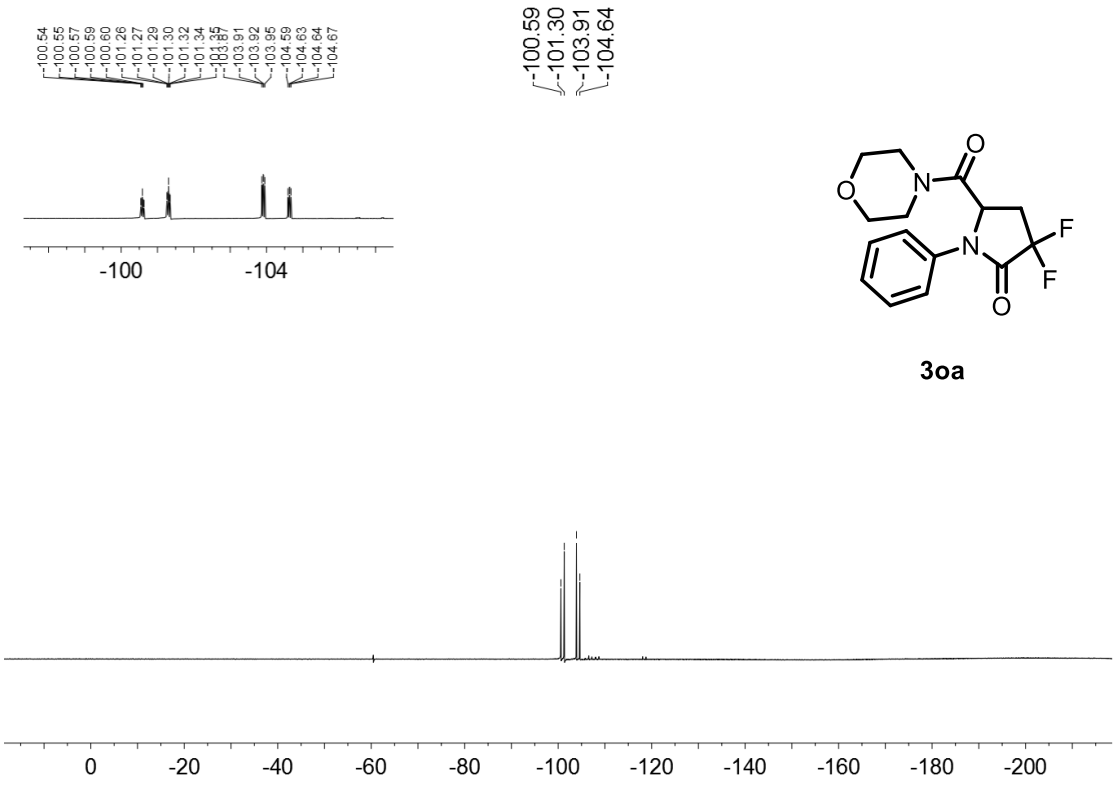
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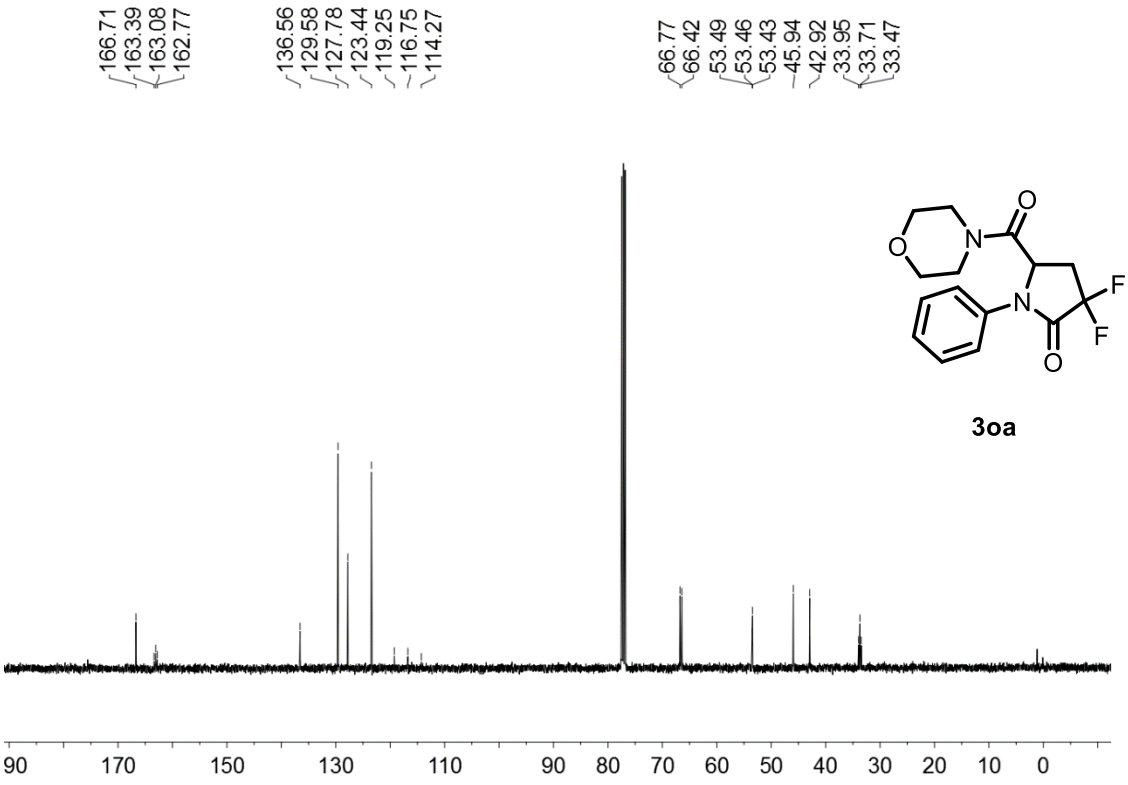
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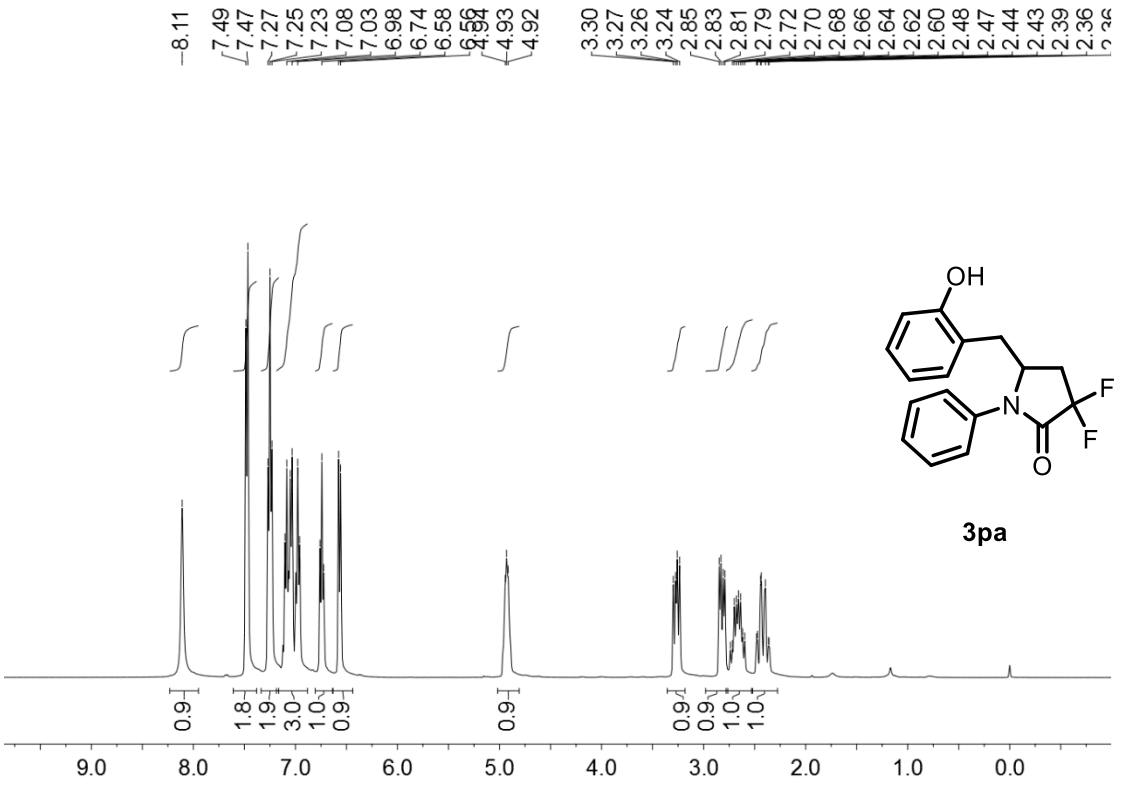
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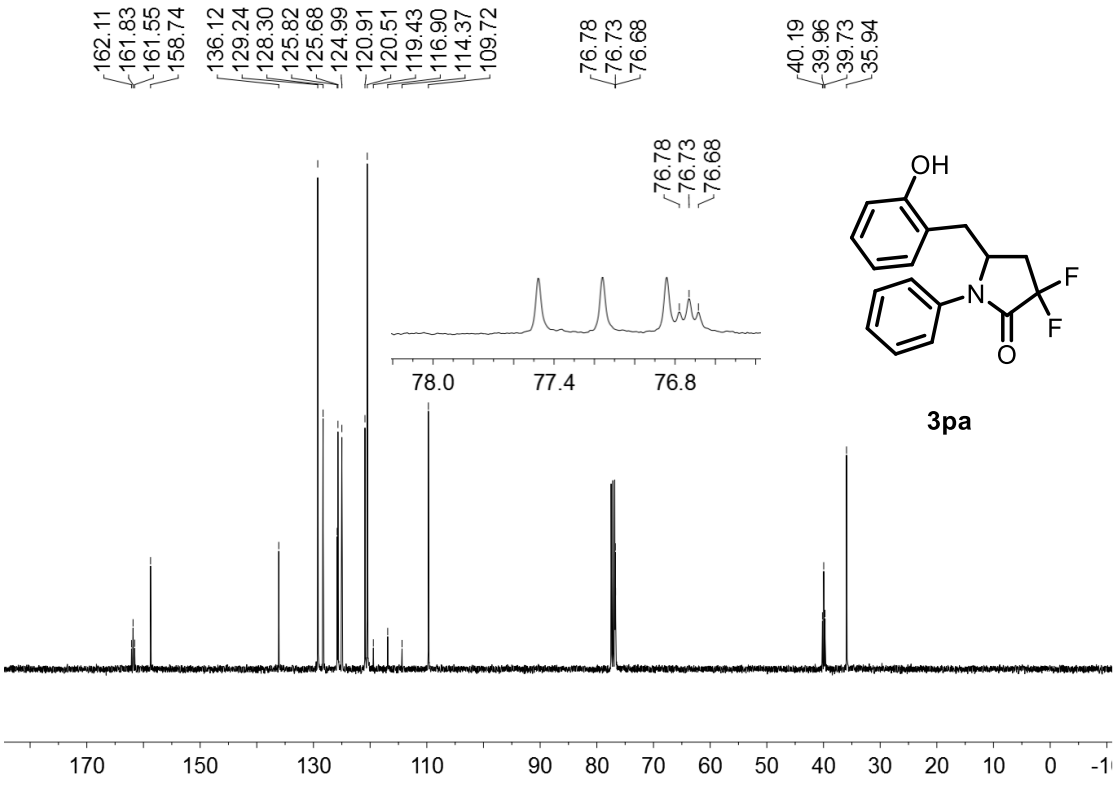
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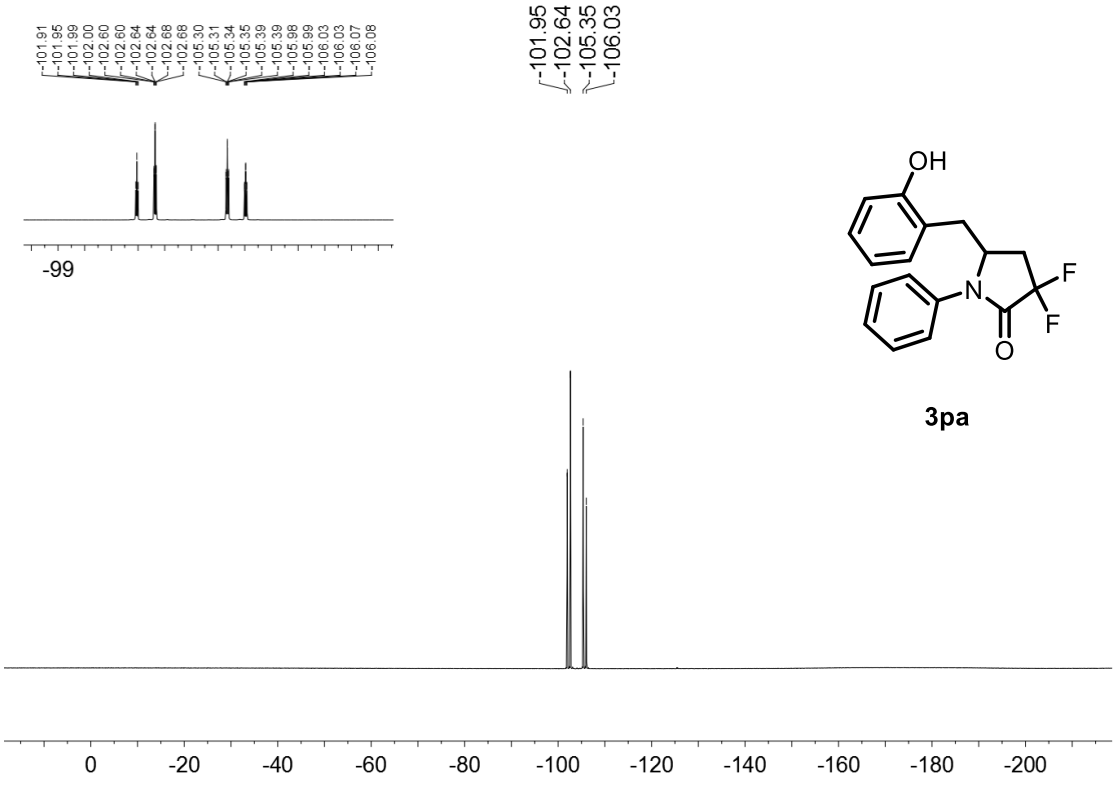
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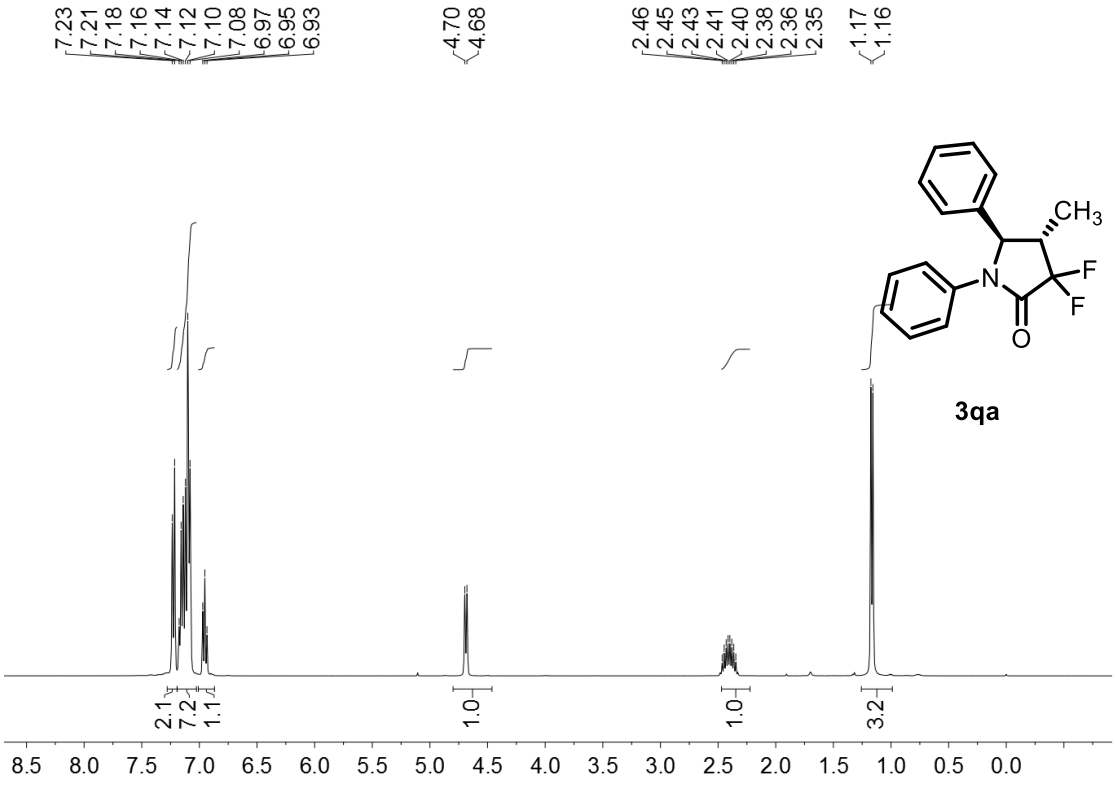
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CH3
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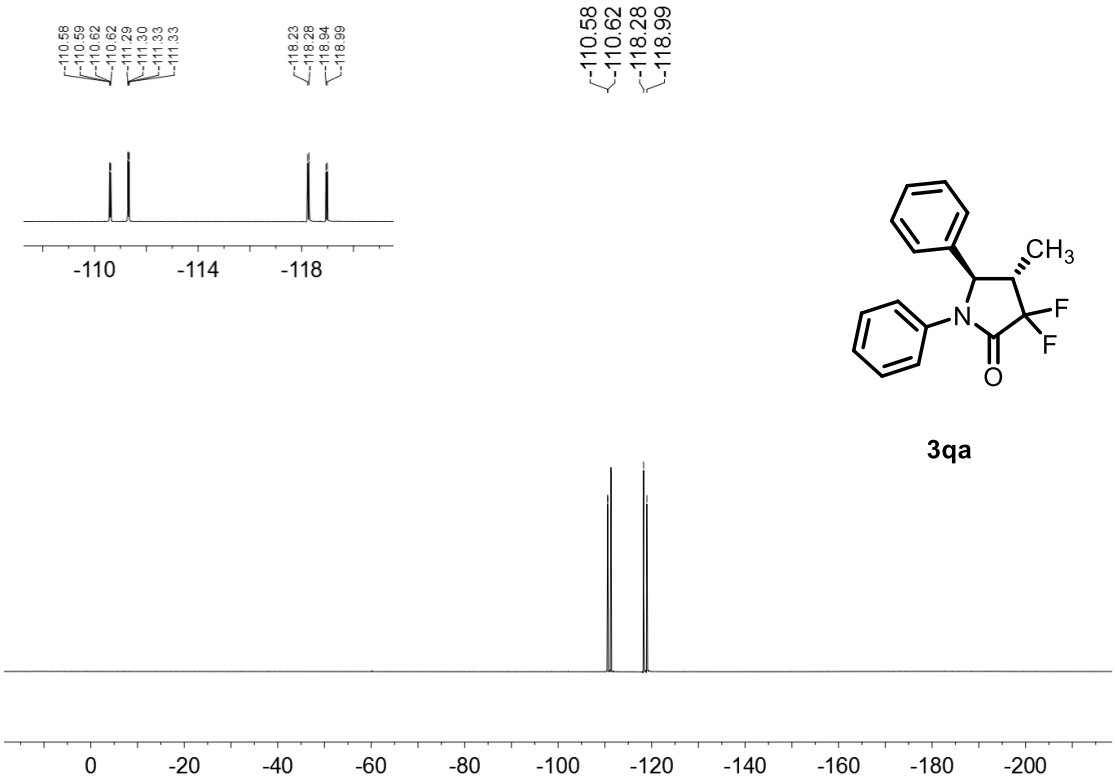
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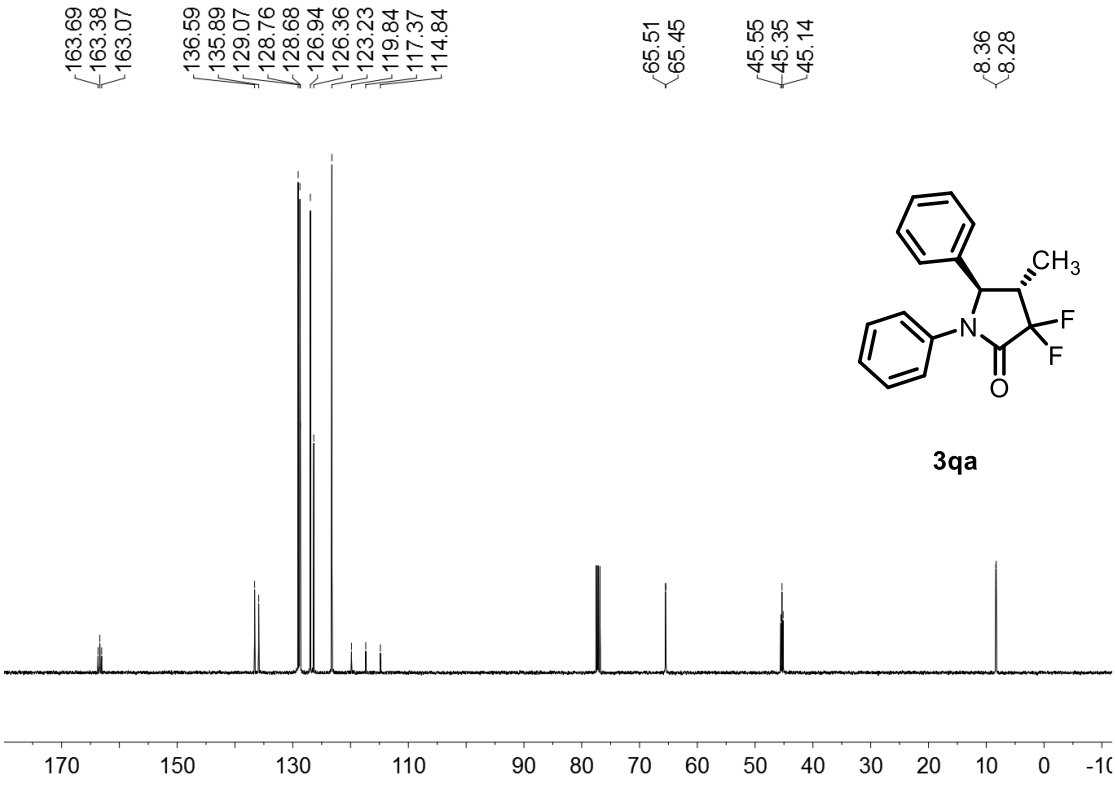
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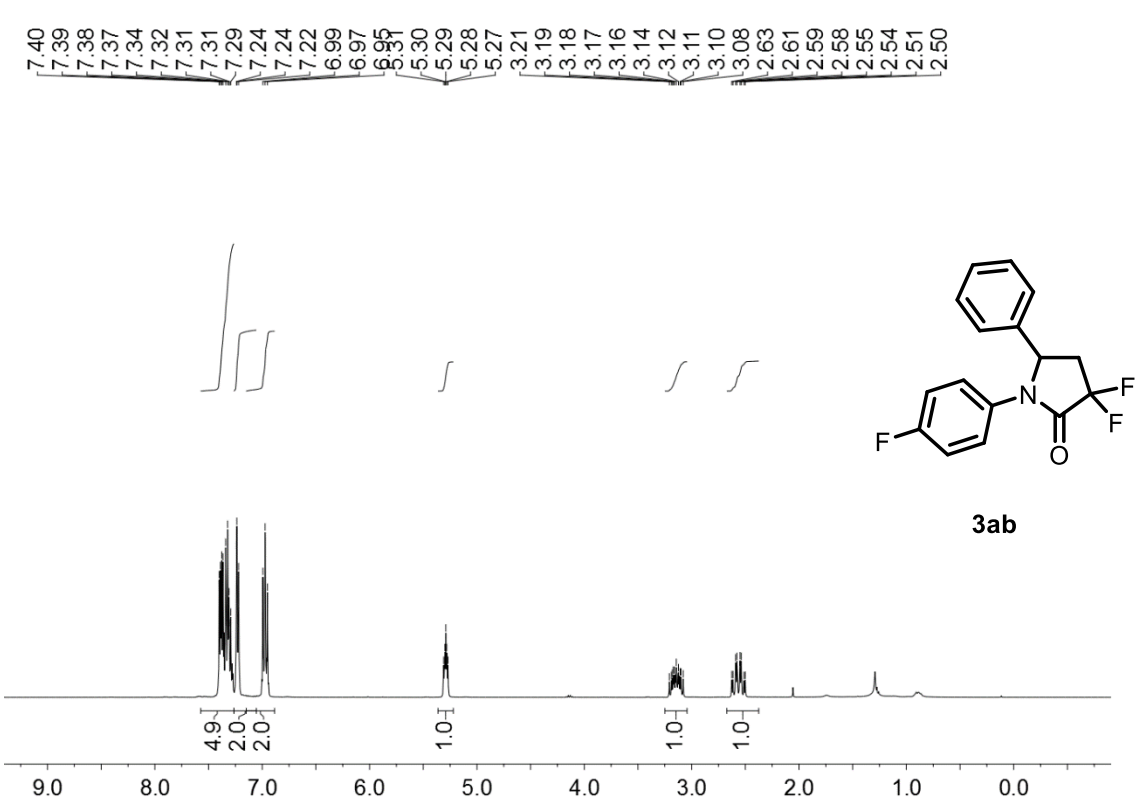
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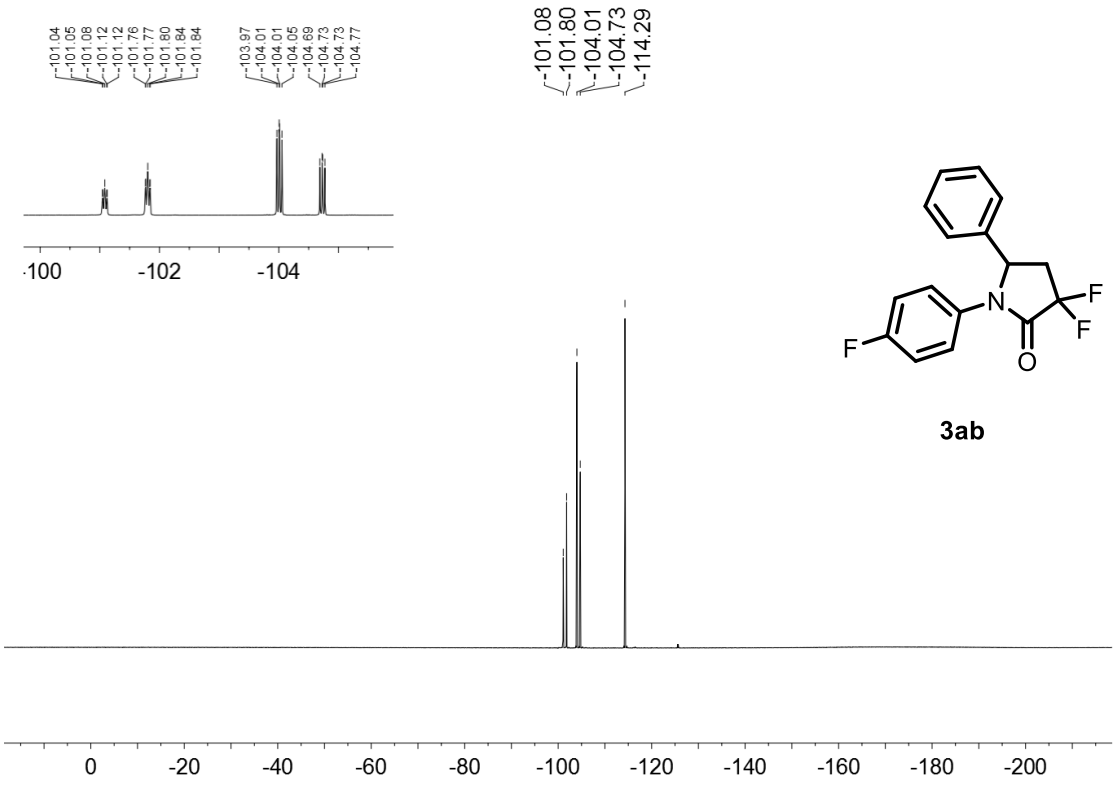
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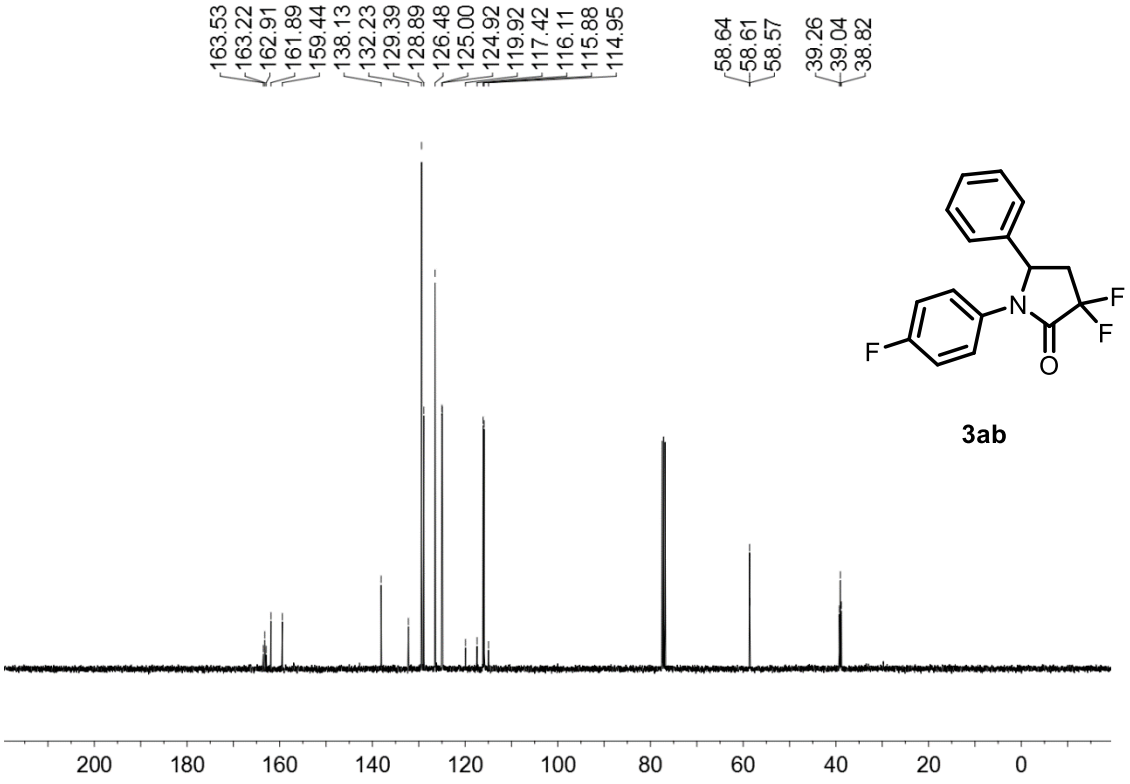
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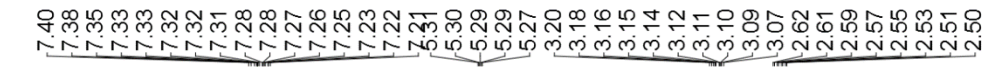
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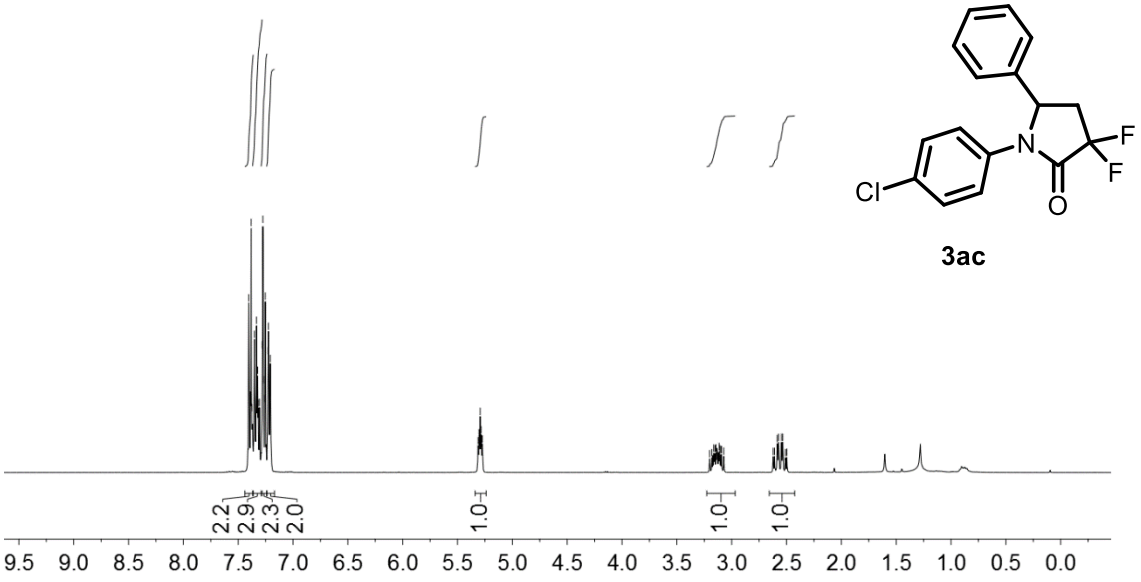
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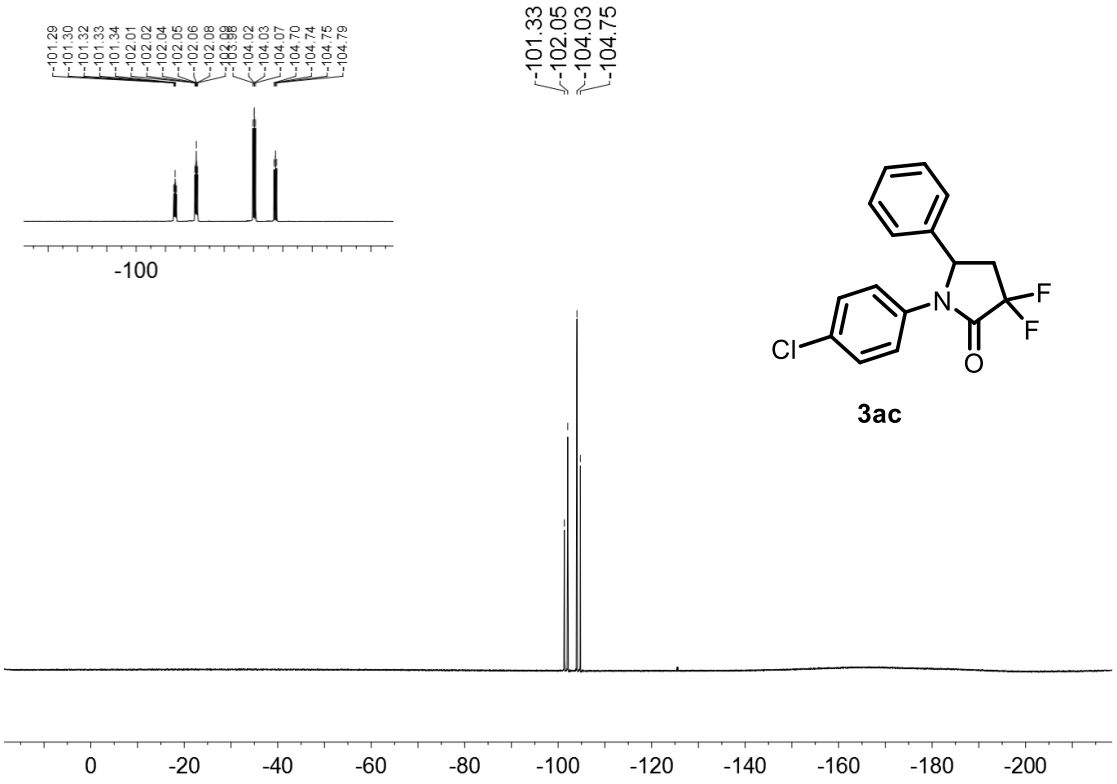
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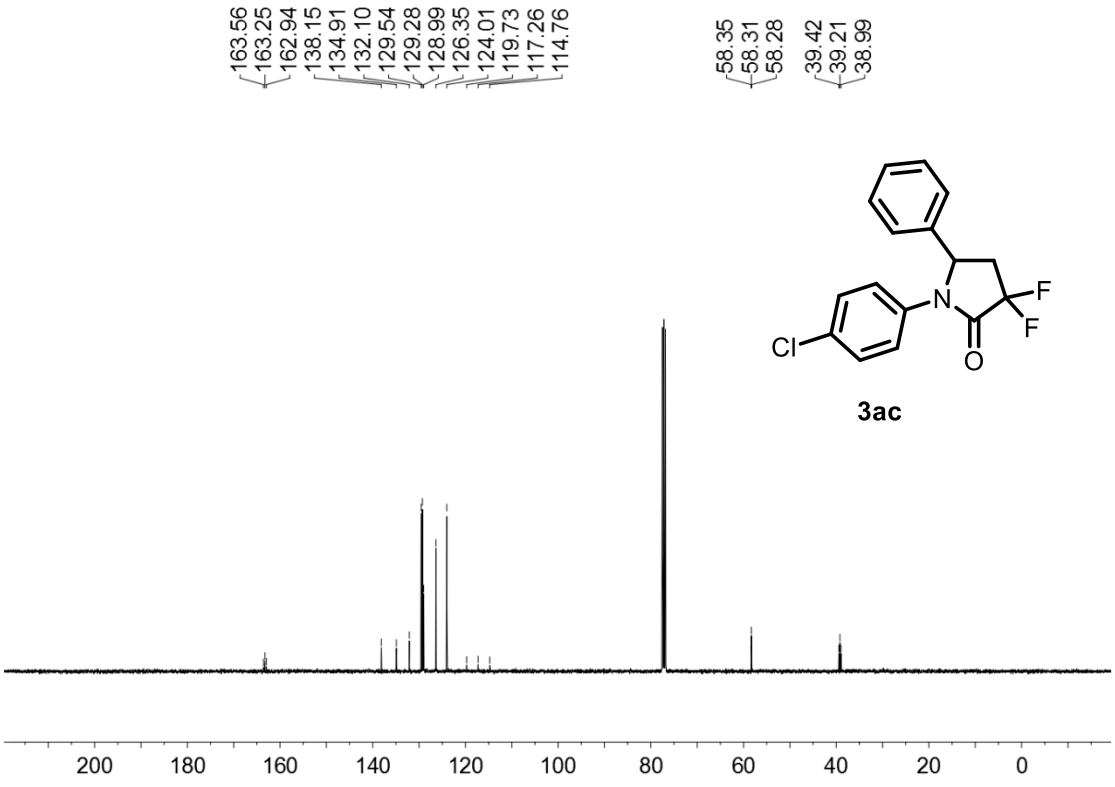
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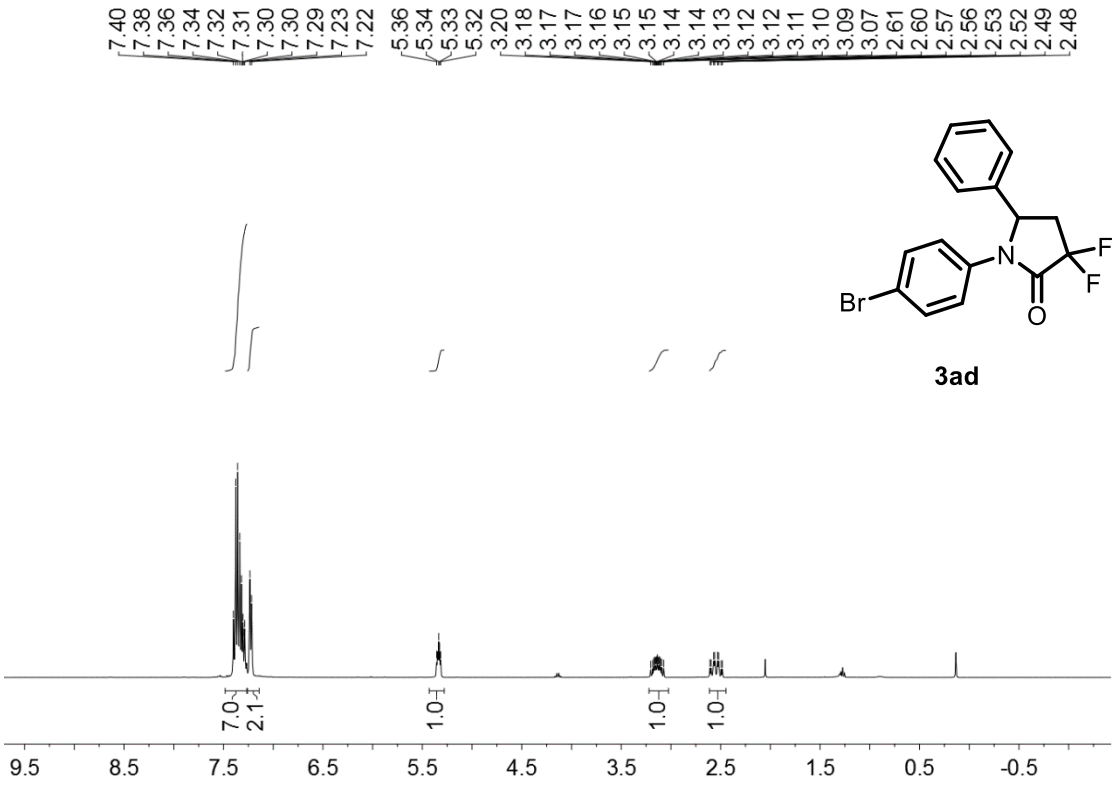
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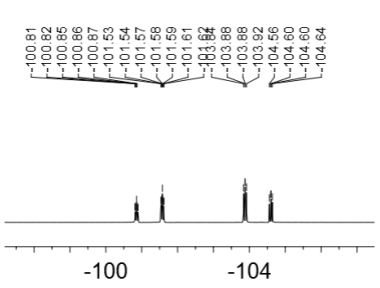
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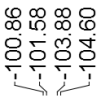
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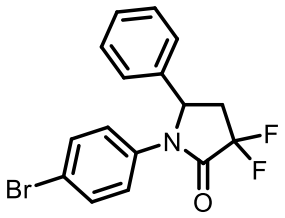
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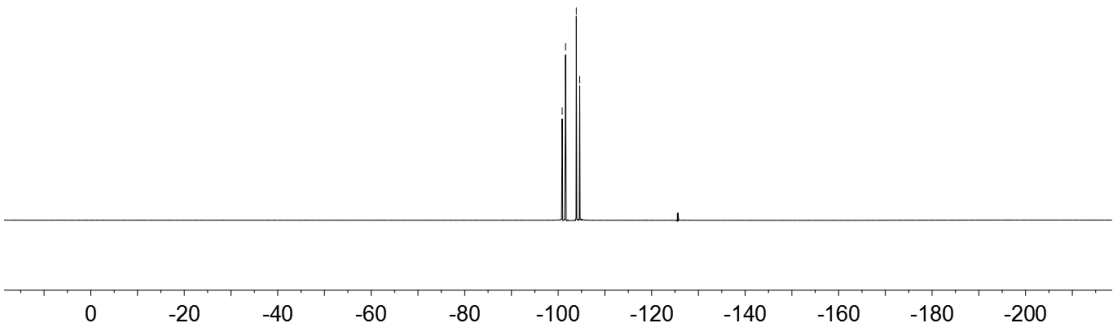
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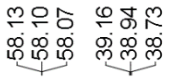
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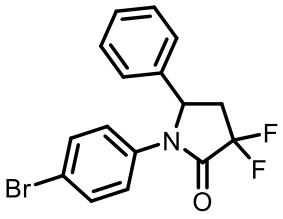
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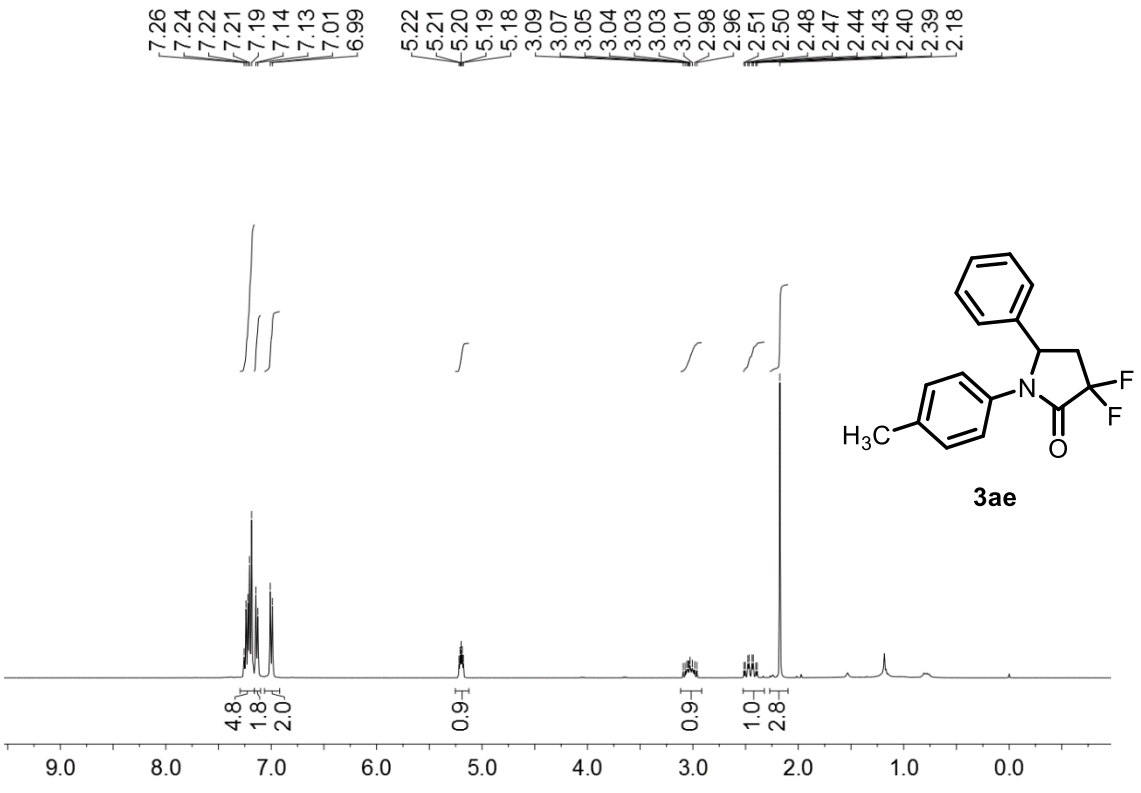
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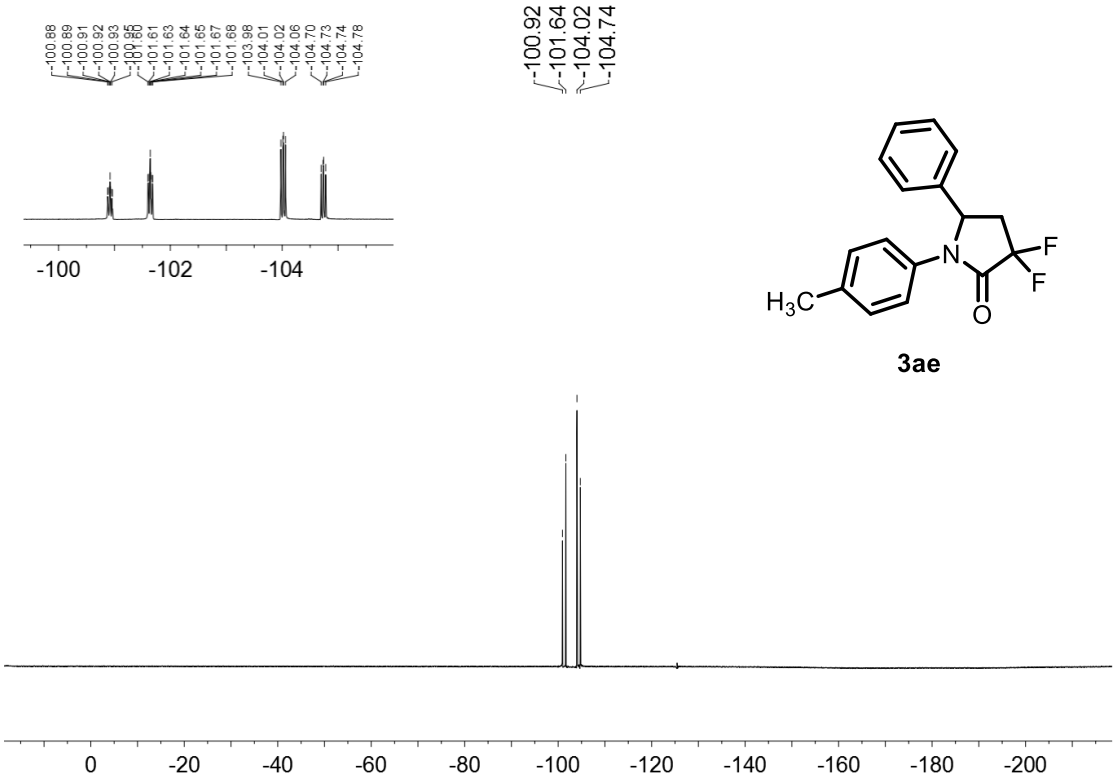
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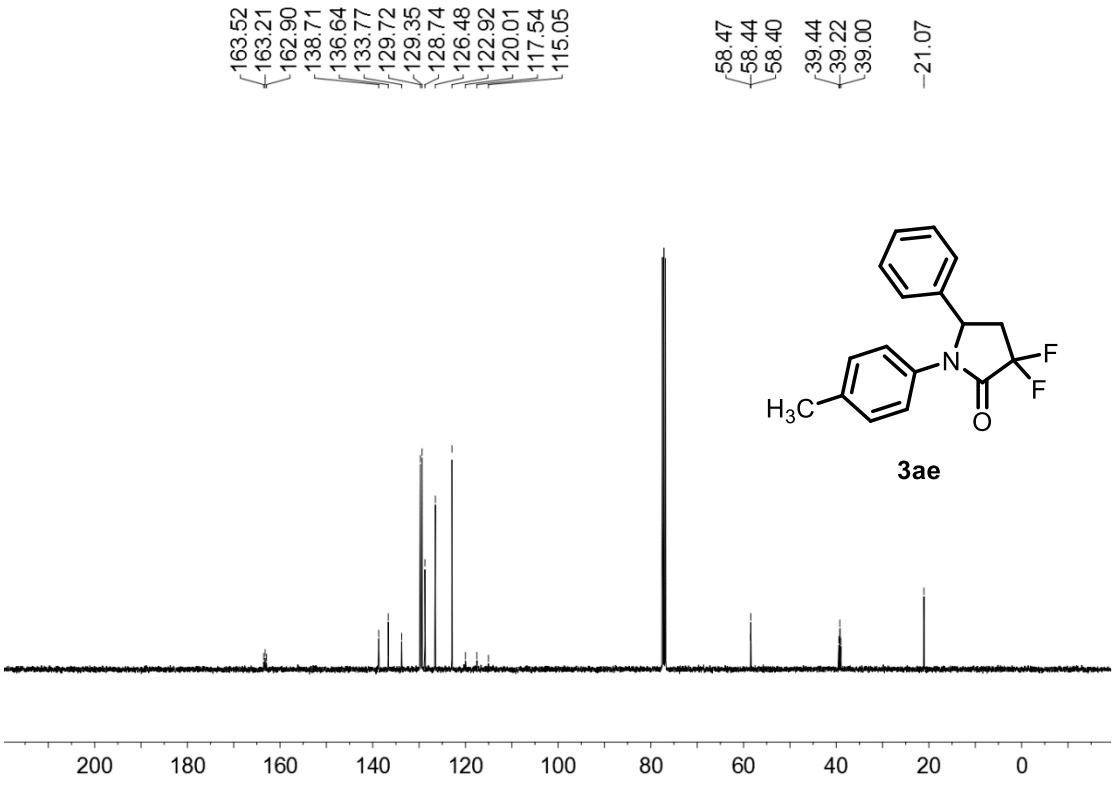
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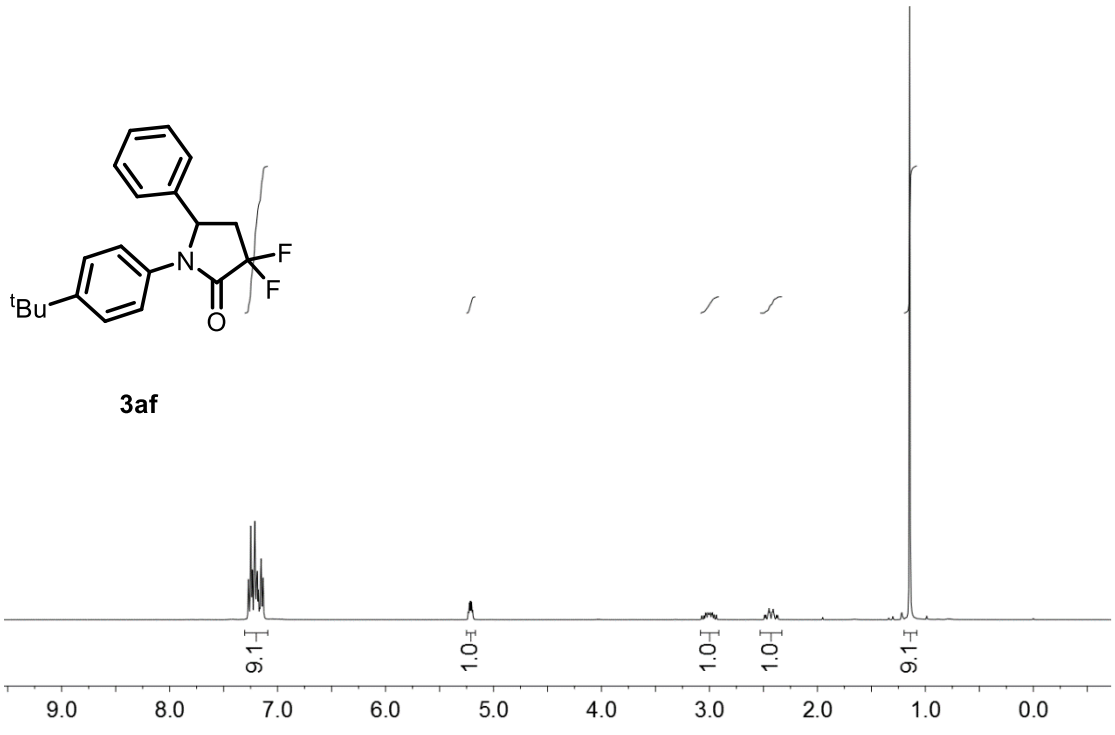
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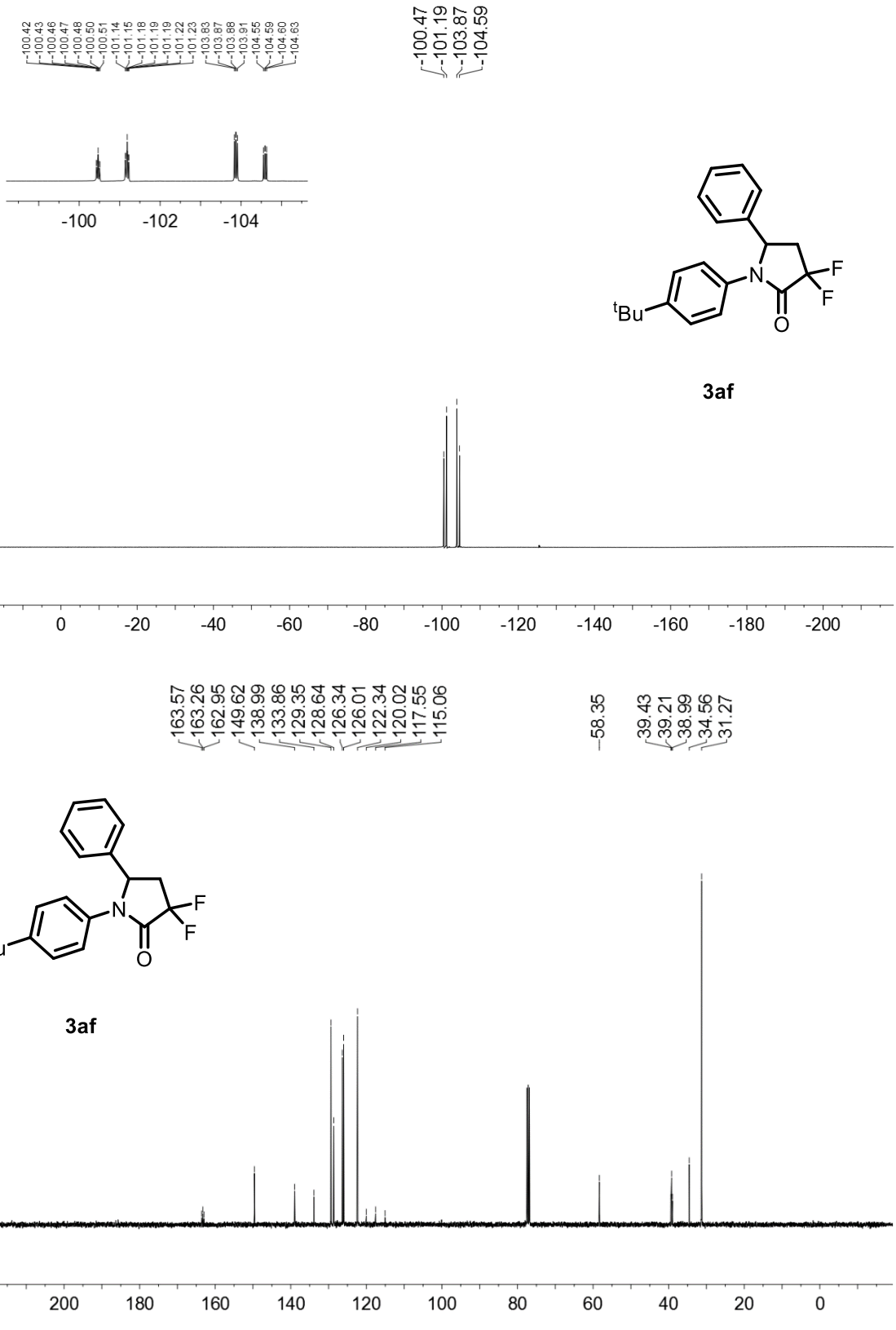
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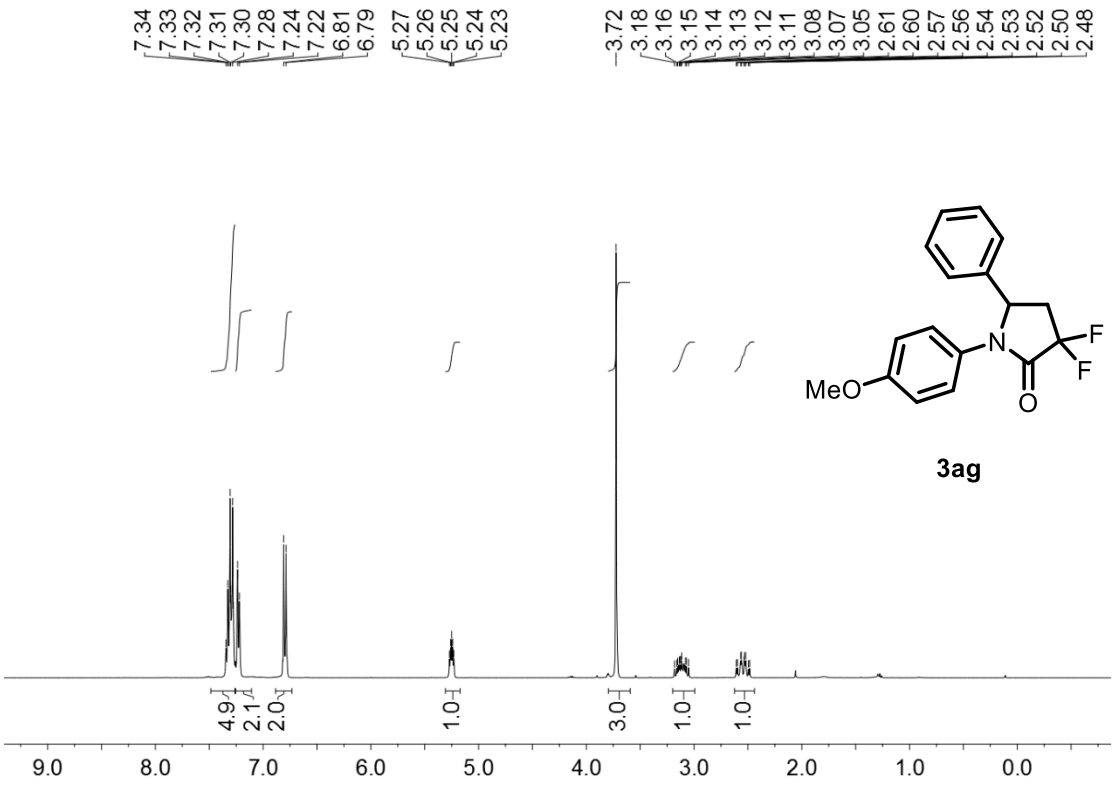
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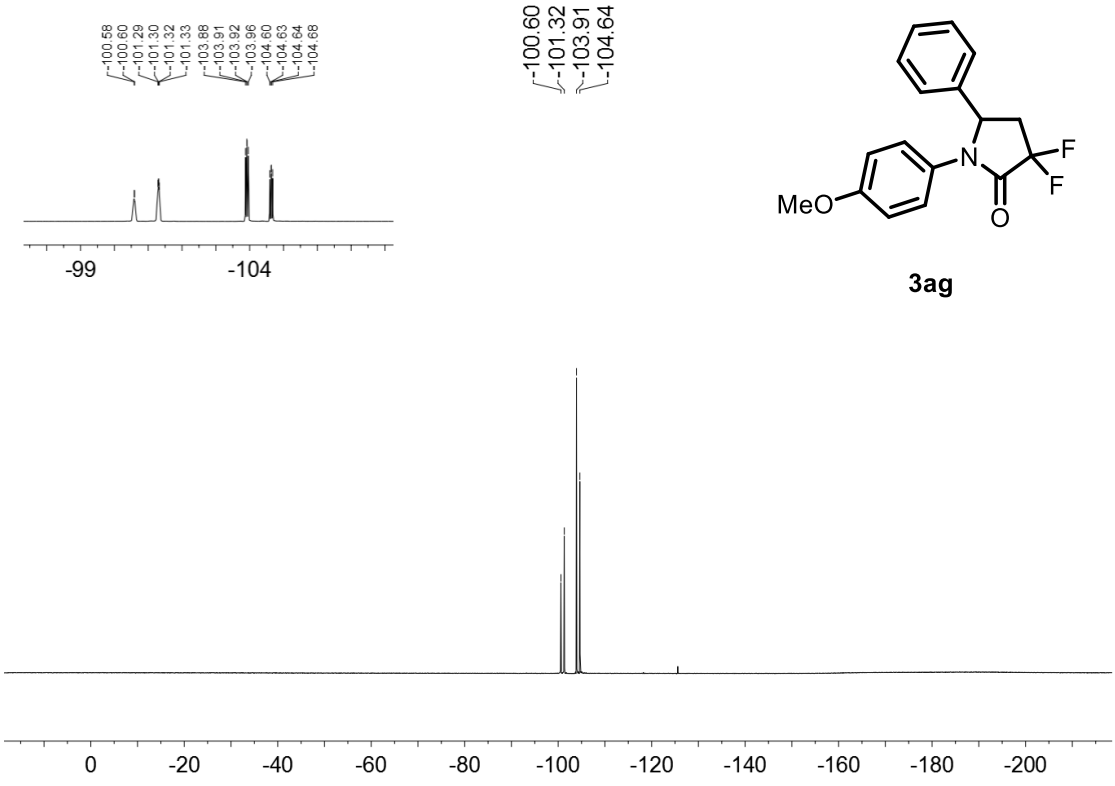
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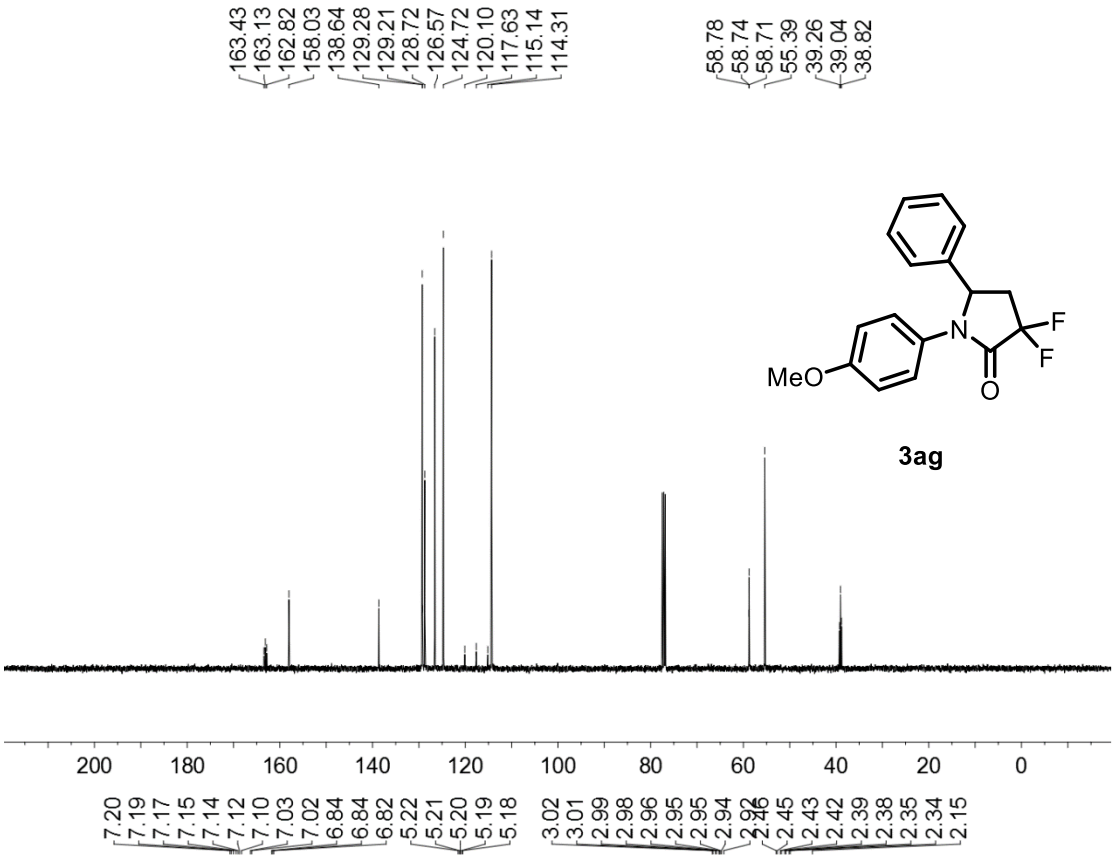
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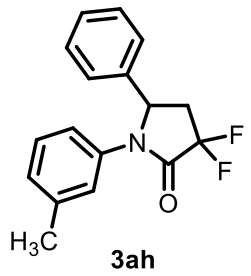
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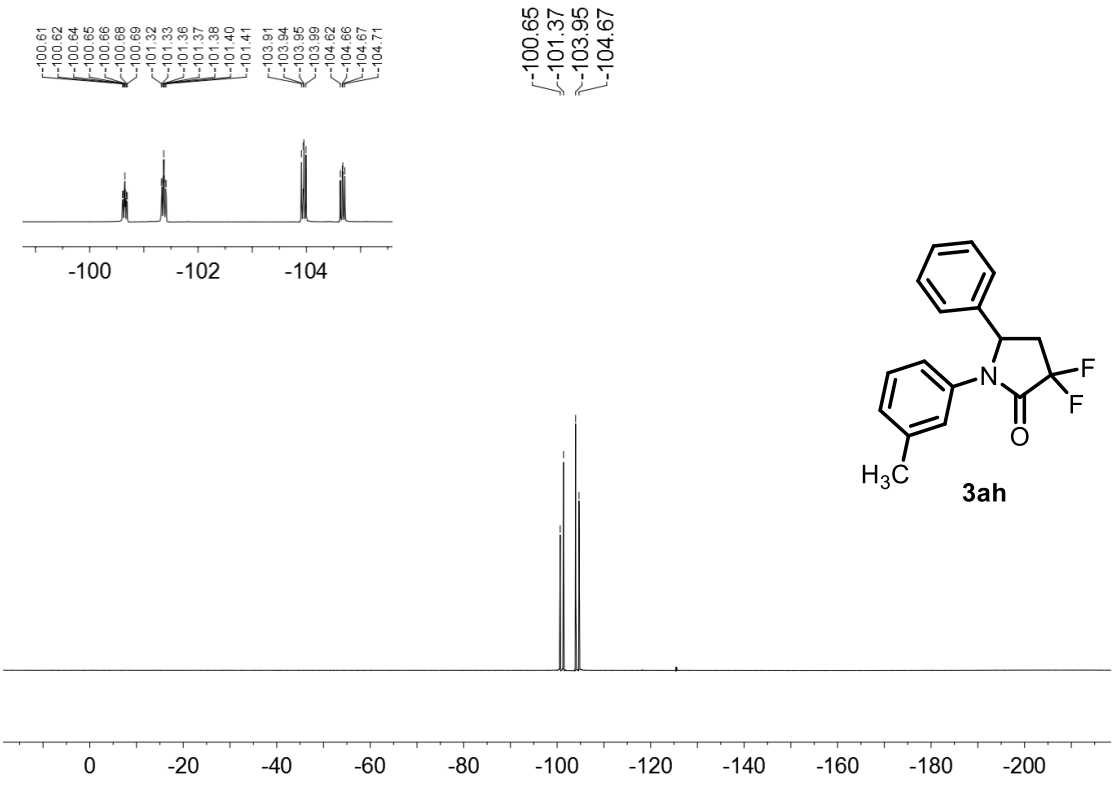
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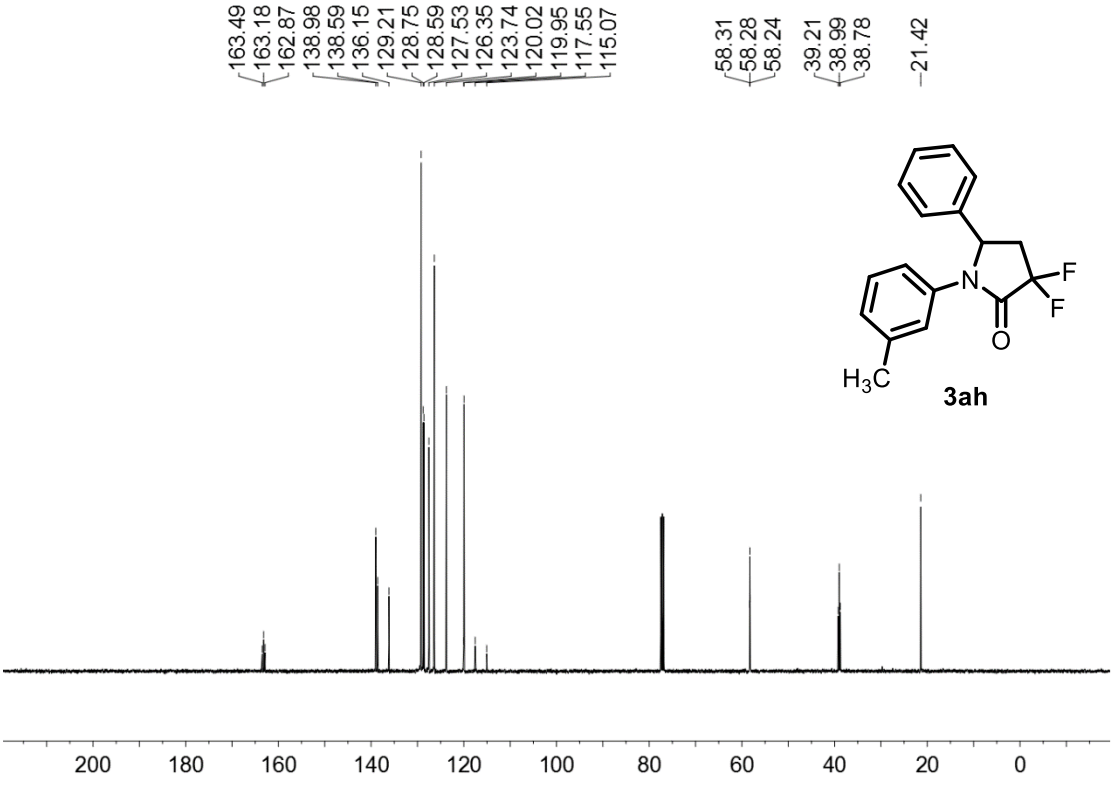
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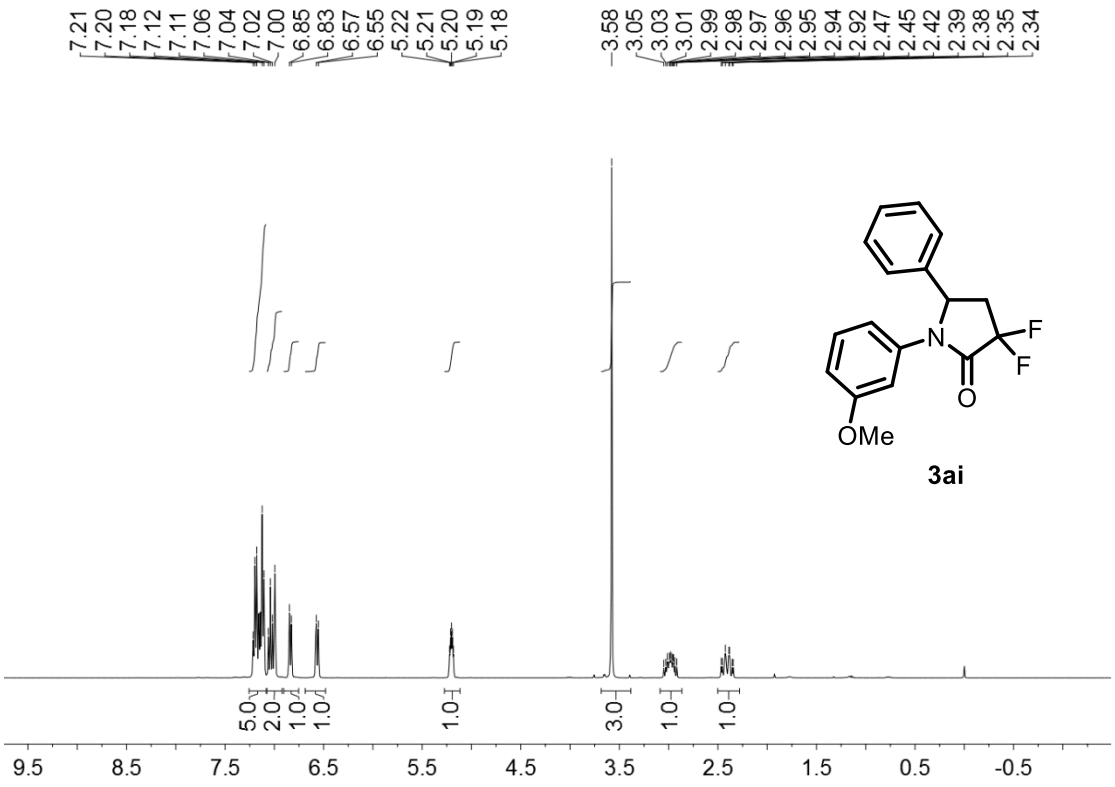
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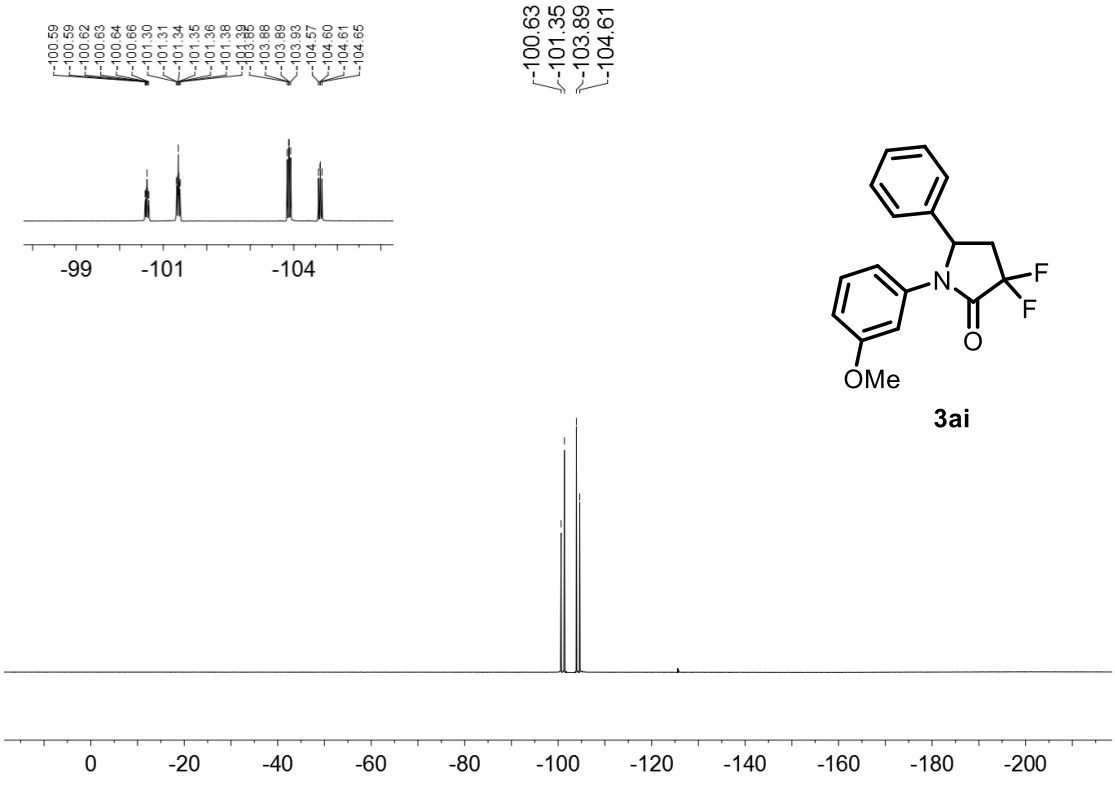
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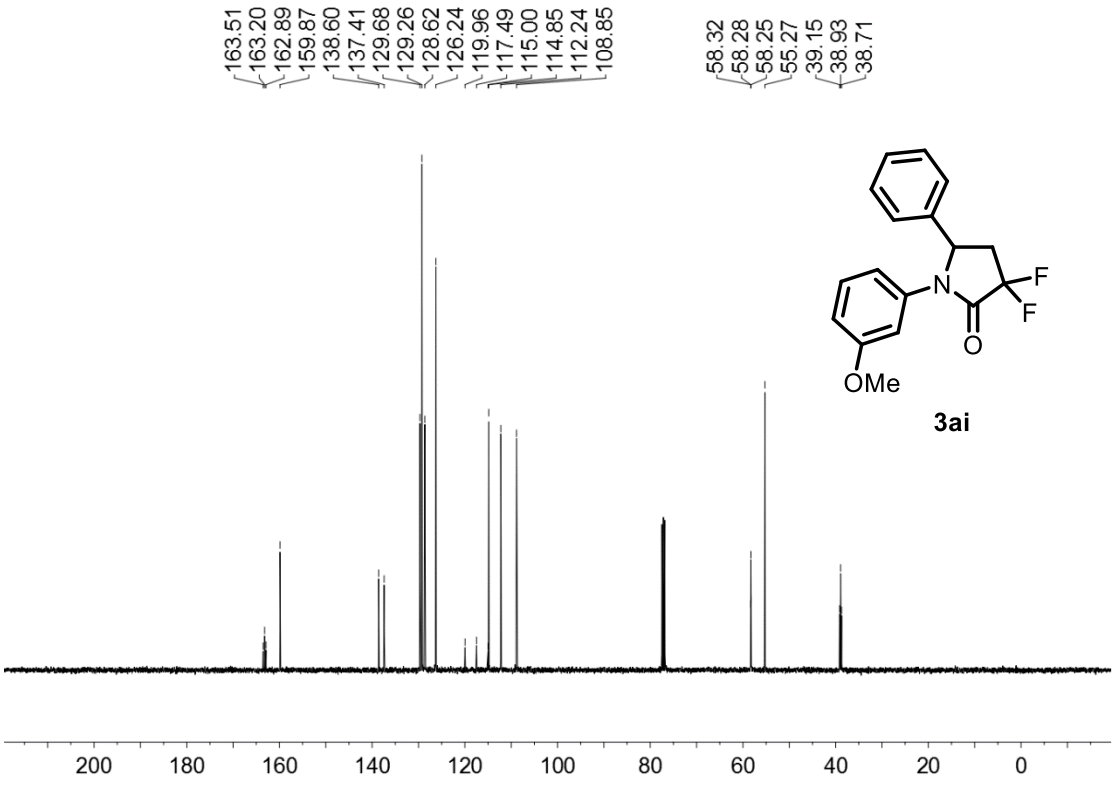
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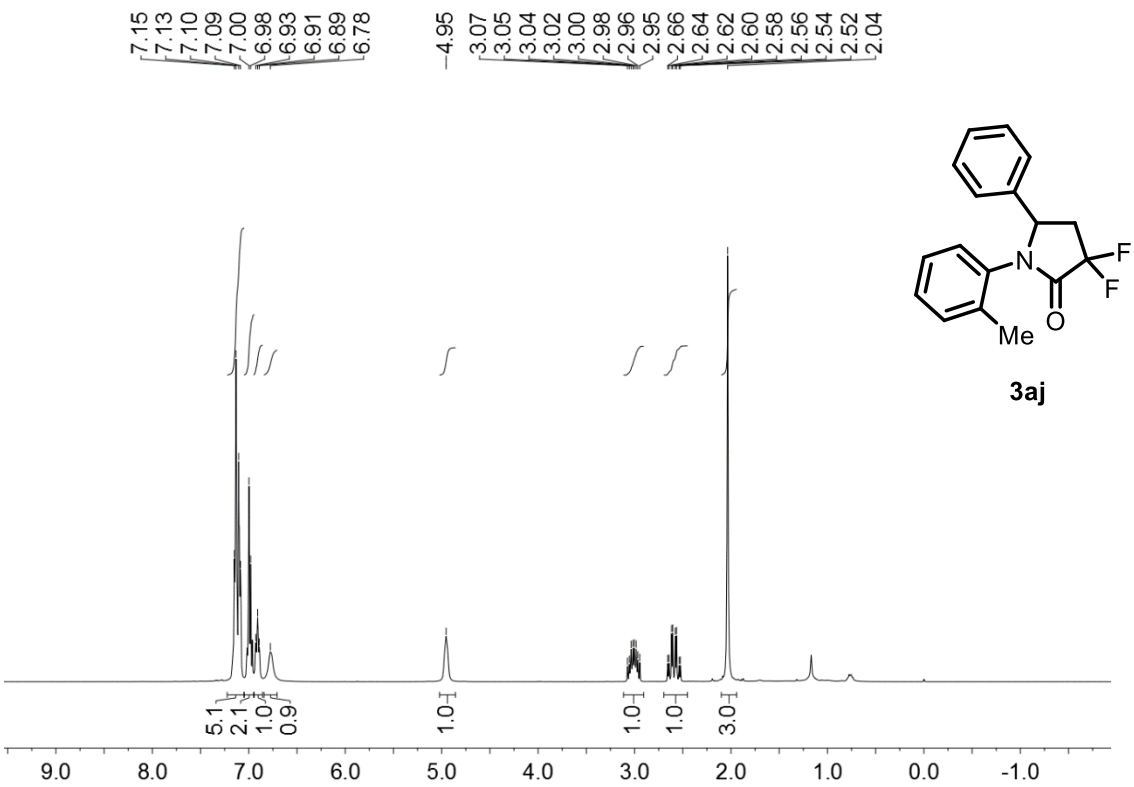
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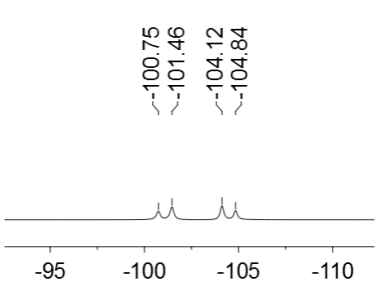
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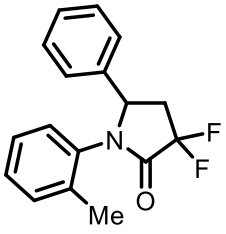
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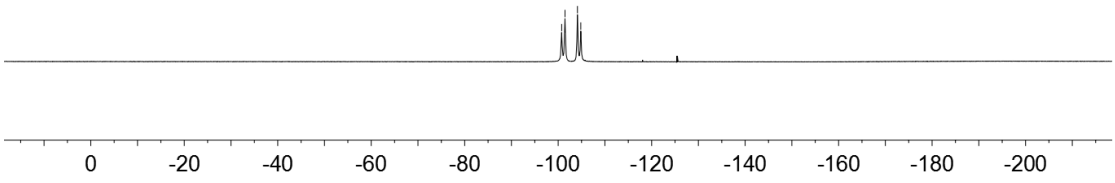
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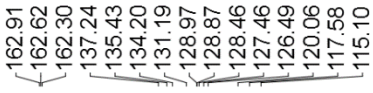
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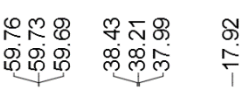
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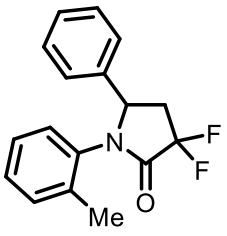
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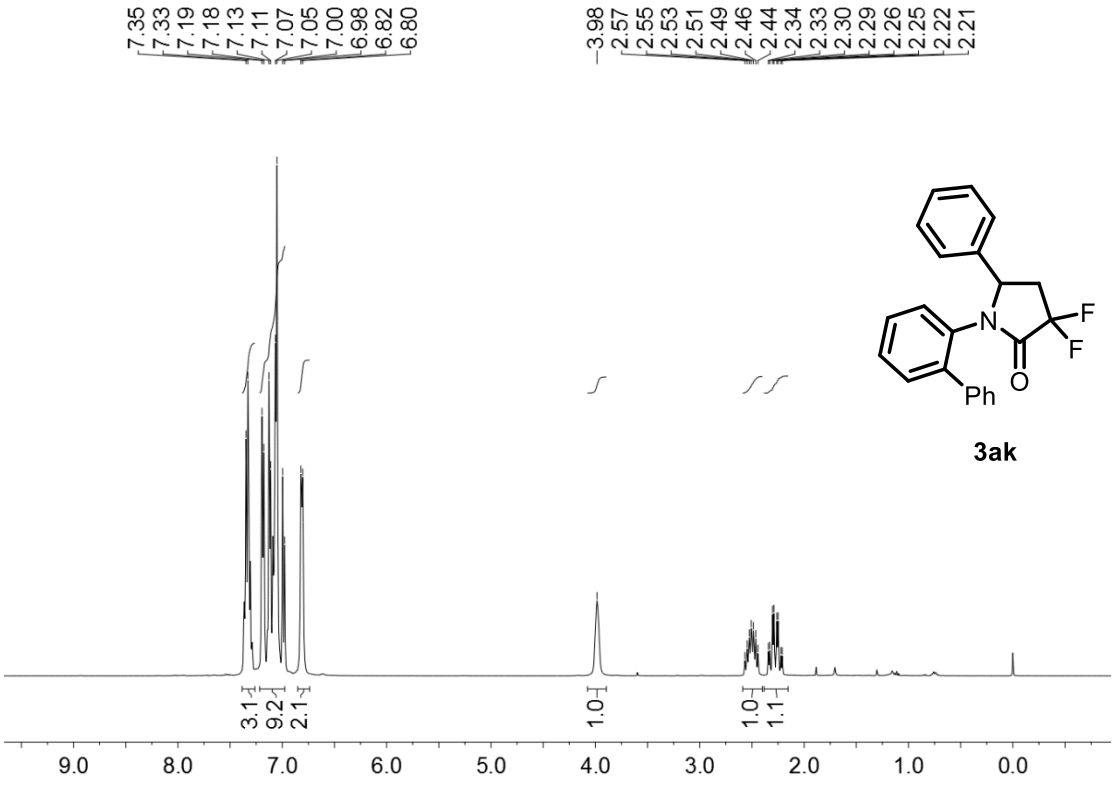
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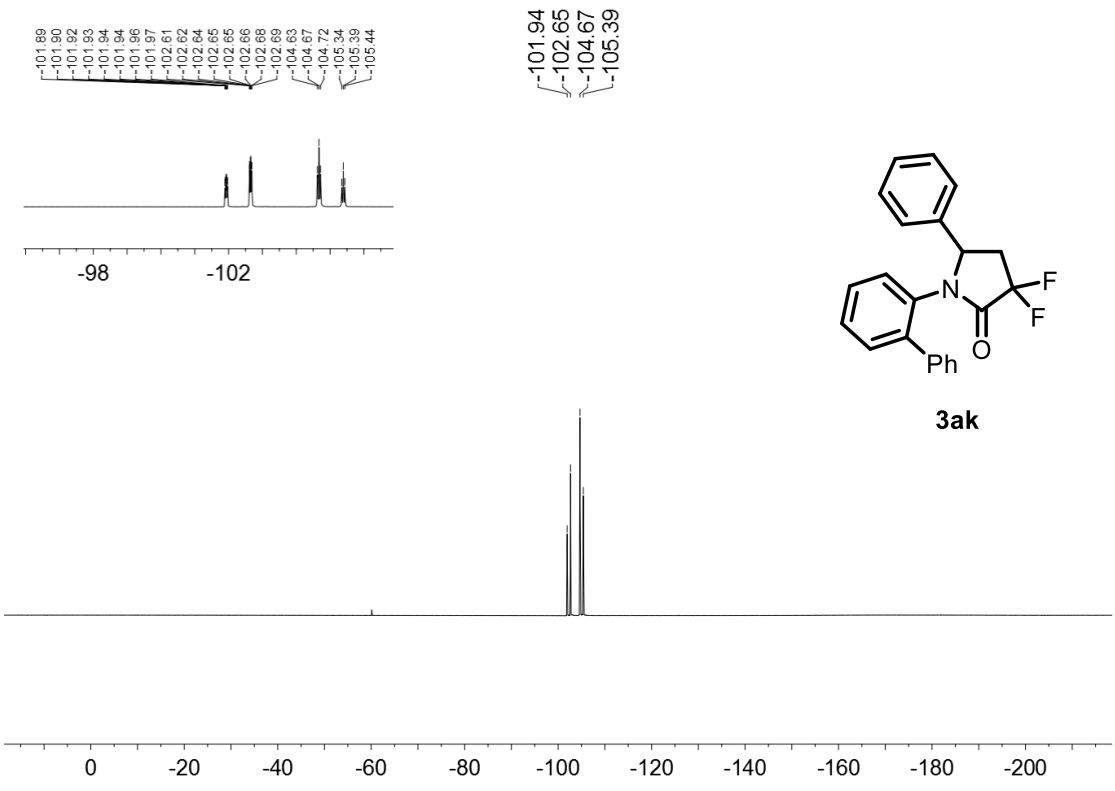
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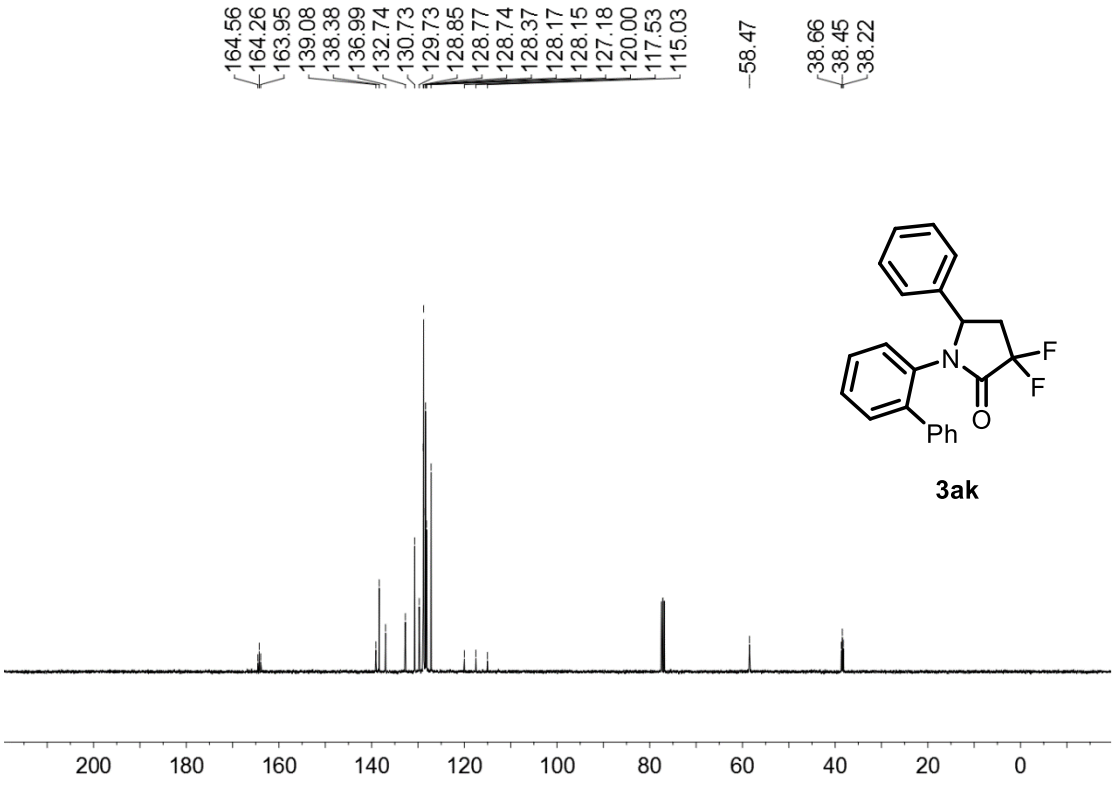
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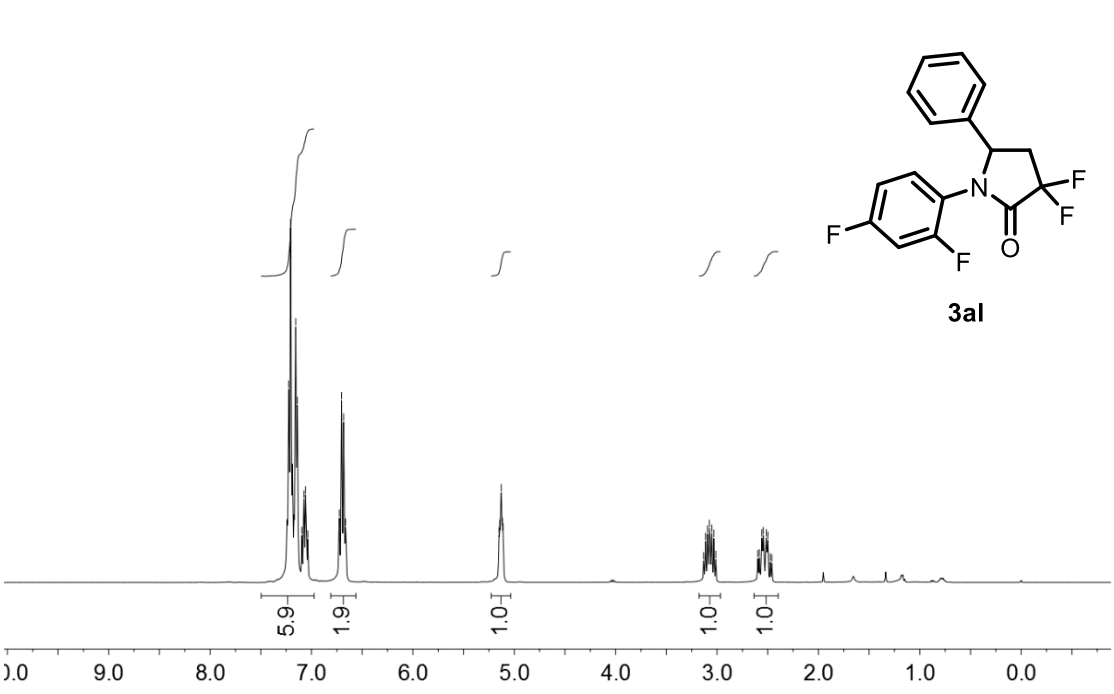
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F
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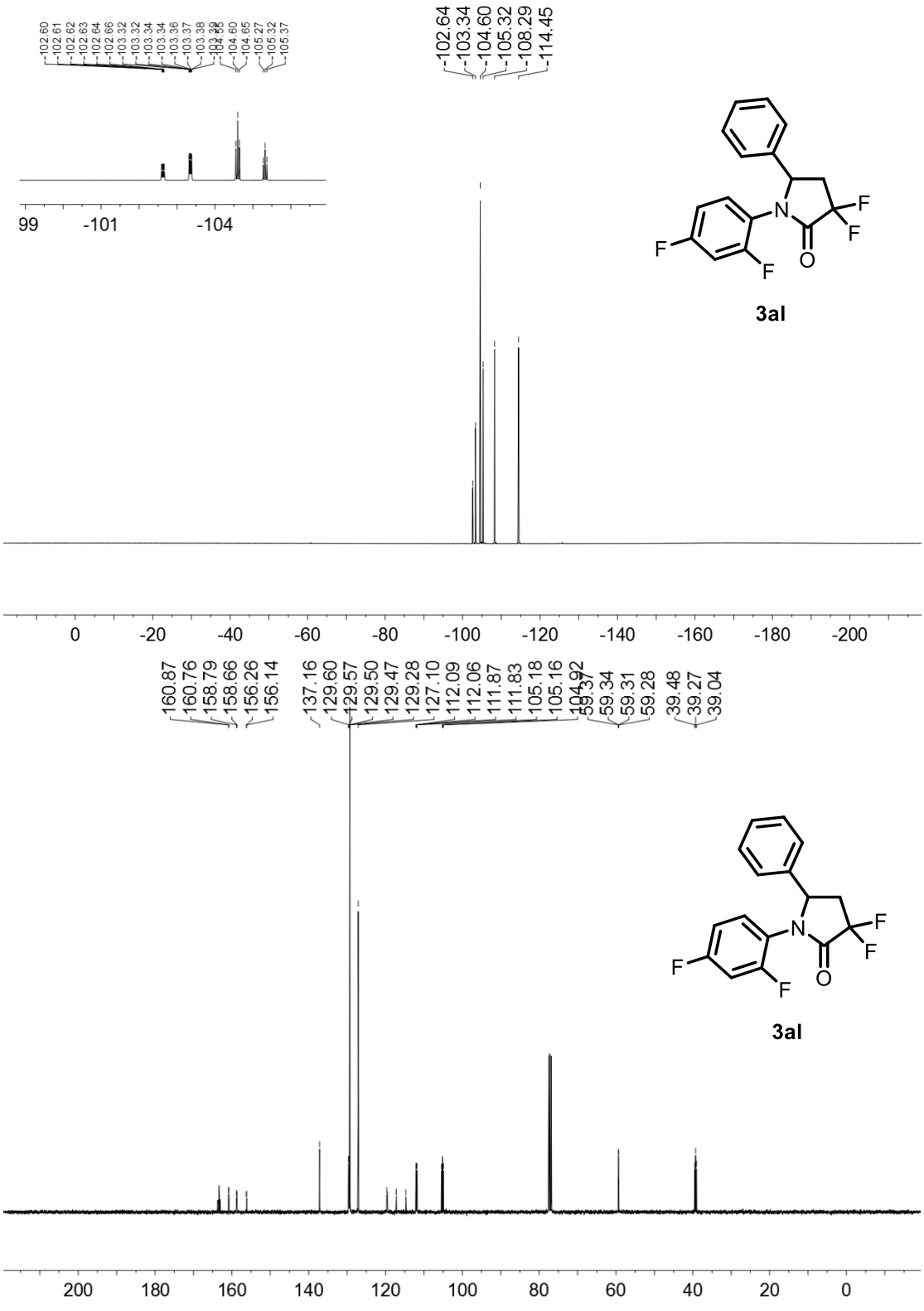
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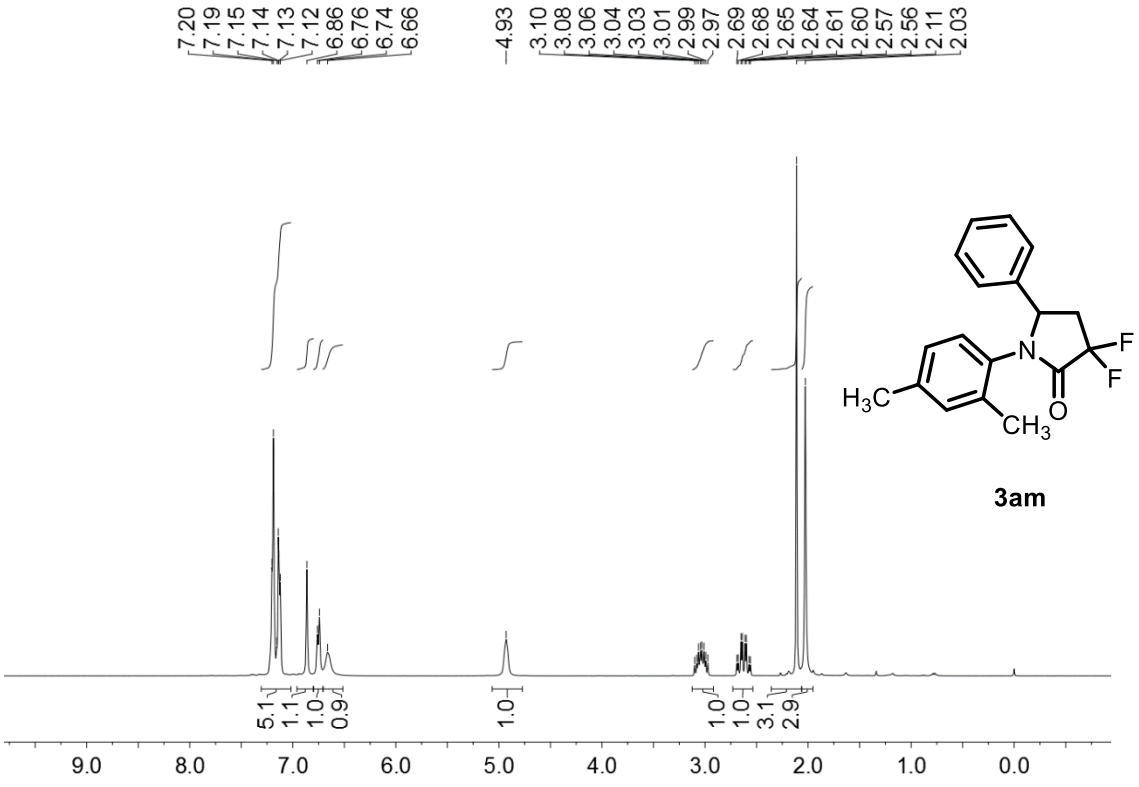
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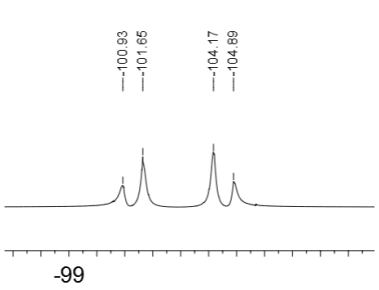
CH3

3am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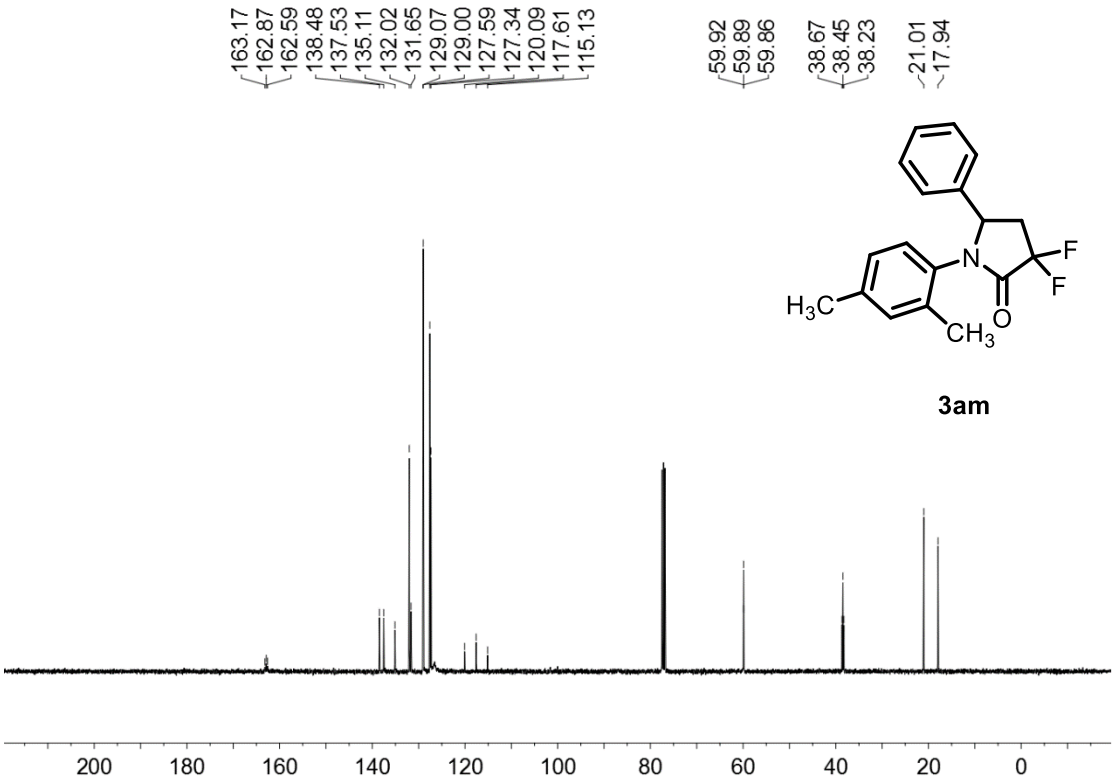
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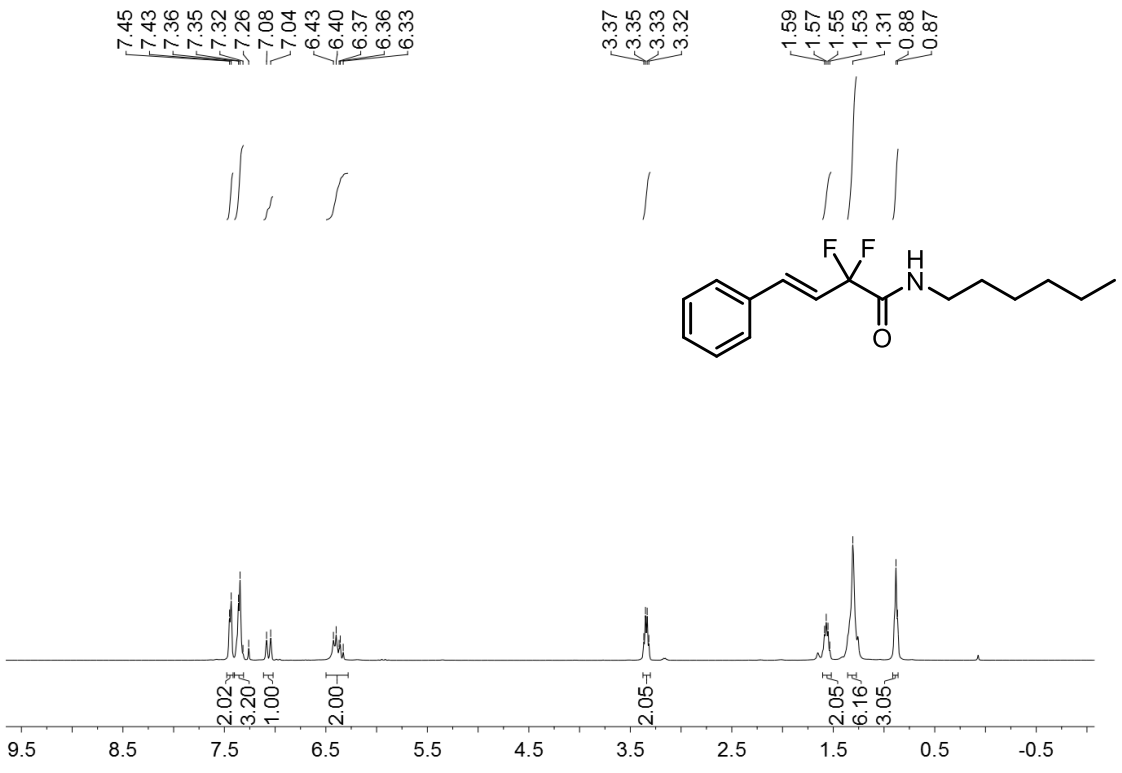
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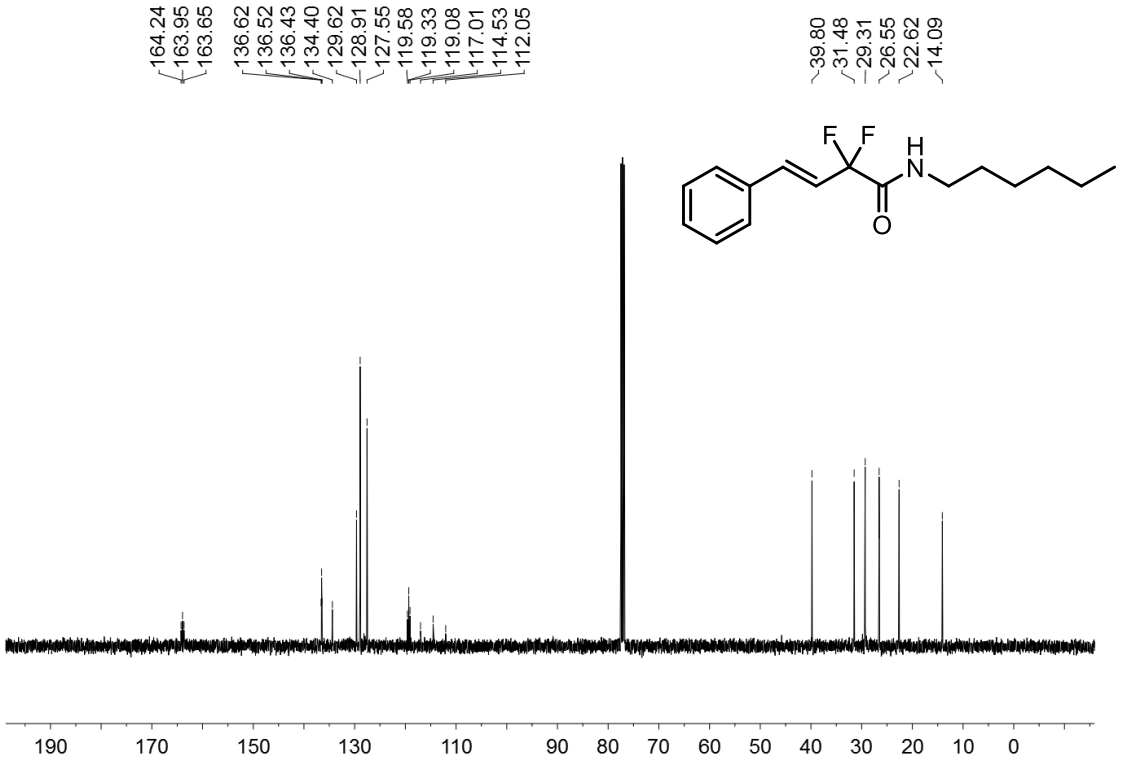
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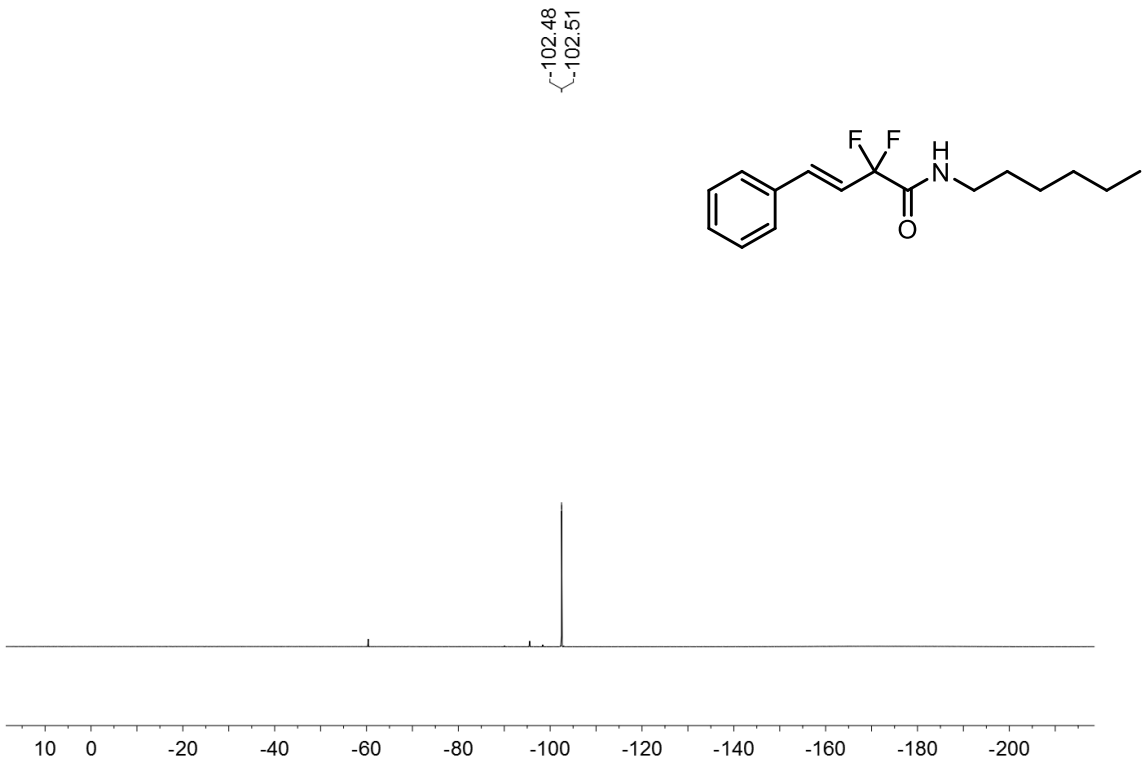
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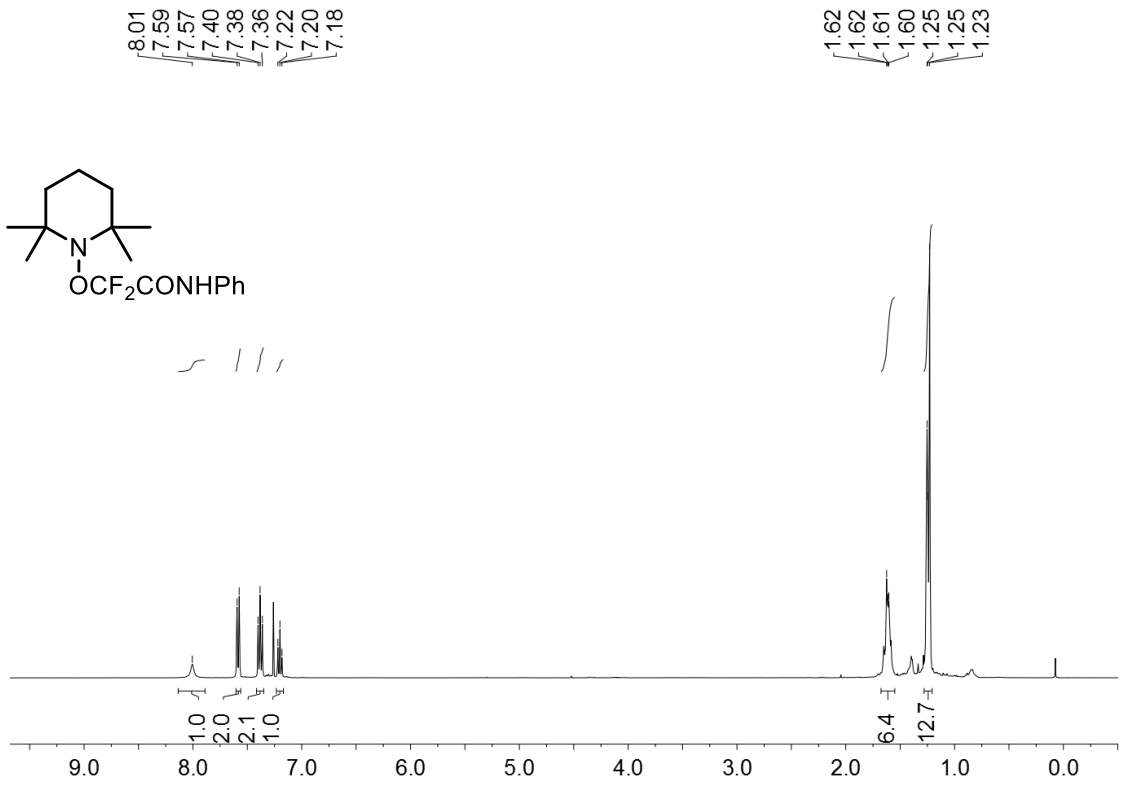
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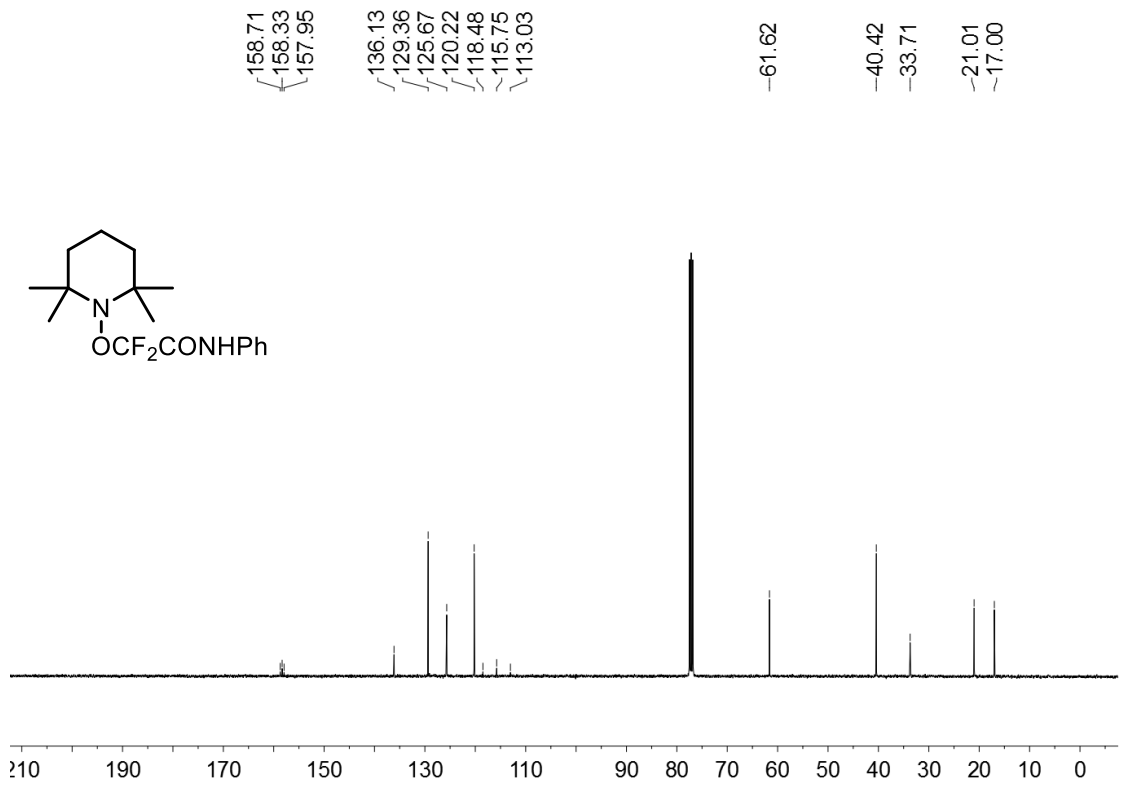
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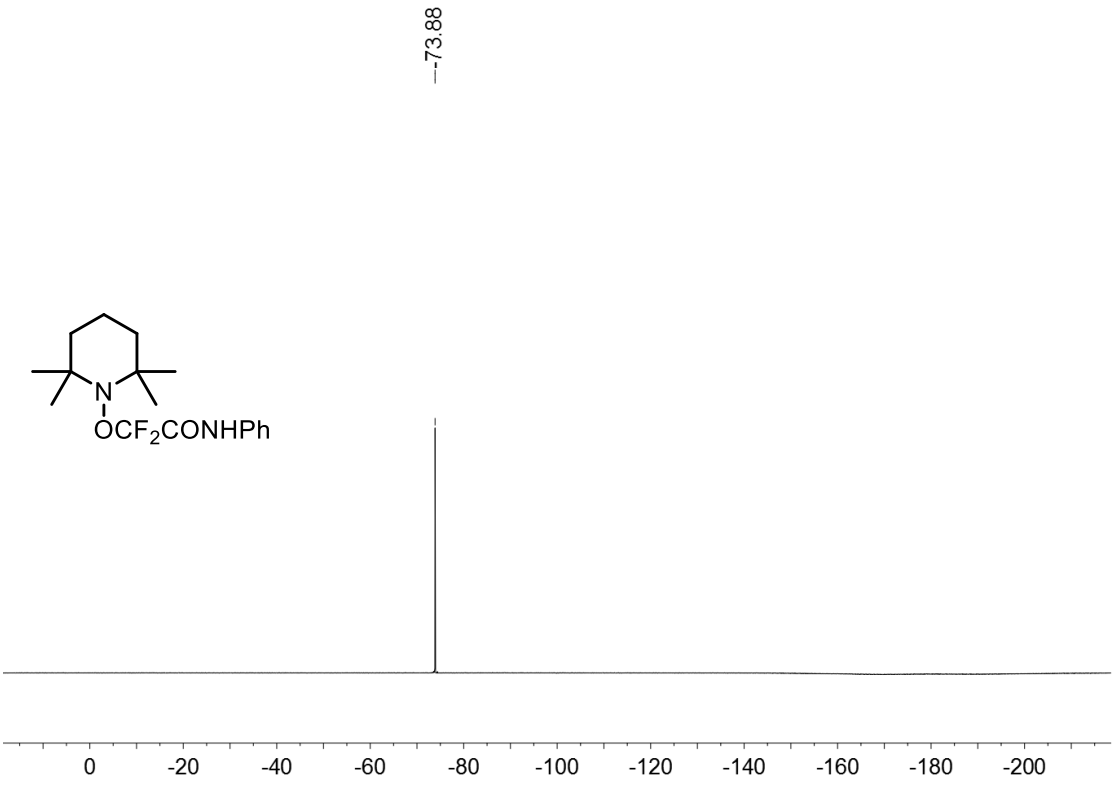
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