Pd-Catalyzed Intermolecular C–H Amination with Alkylamines

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SUPPORTING INFORMATION

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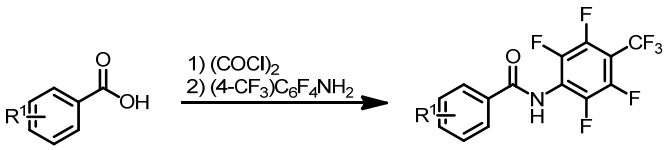
General Information: Solvents were obtained from Sigma-Aldrich, Alfa-Aesar and Acros and used directly without further purification. Carboxylic acids or carboxylic acid chlorides and 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline were obtained from the commercial sources and used to prepare the corresponding amides. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F254. Visualization was carried out with UV light and Vogel's permanganate. ^{1}H NMR spectra were recorded on Varian Inova instrument (400 MHz) and Bruker DRX (500 MHz). Chemical shifts were quoted in parts per million (ppm) referenced to the residual undeuterated solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, *J*, were reported in Hertz unit (Mz). ^{13}C NMR spectra were recorded on Varian Inova instrument (100 MHz) and Bruker DRX (125 MHz) and were fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the center line of a triplet at 77.0 ppm of chloroform-*d*. The carbons of the fluorinated aryl rings of the benzamide were omitted because these ^{13}C NMR were very small due to coupling with the F's. High-resolution mass spectra (HRMS) were recorded on an Agilent Mass spectrometer using ESI-TOF (electrospray ionization-time of flight). IR spectra were recorded on a Perkin Elmer Spectrum BX FTIR spectrometer. Frequencies were given in reciprocal centimeters (cm^{-1}) and only selected absorbances were reported.

The ^{13}C NMR signals of the 2,3,5,6-tetrafluoro-4-(trifluoromethyl) aryl groups in the directing groups are weak due to the multiple coupling from the fluorines. For full characterizations see the spectra of the carboxylic acid **4** obtained from the hydrolysis of the amination product **3a**.

Experimental Procedure

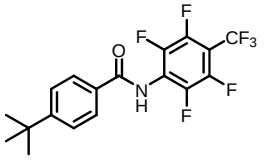
Preparation of N-Aryl Benzamide Substrates

General procedure for preparation of *N*-aryl benzamide derivatives: An acid choride (10.0 mmol), prepared from the corresponding carboxylic acid and oxalyl chloride, was added to a vigorously stirring solution of 2,3,5,6-tetrafluoro-4-(trifluoromethyl)aniline (11.0 mmol) in toluene (50 mL). The reaction mixture was stirred for 12 h under reflux, and then stirred at room temperature for 4 h. The product mixture was concentrated *in vacuo* and was recrystallized from ethyl acetate/hexane to give the amide.



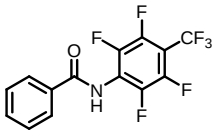
Scheme S1. General procedure for preparation of *N*-aryl benzamide derivatives

Characterization of N-Aryl Benzamide Substrates



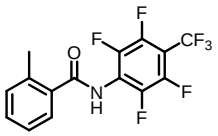
1a

(4-(*tert*-butyl)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide) (1a): white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.3 Hz, 2 H), 7.66 (s, 1H), 7.51 (d, *J* = 8.3 Hz, 2H), 1.34 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.96, 157.36, 129.31, 127.97, 126.24, 35.40, 31.29; **IR** (neat) ν 3249, 2970, 1673, 1653, 1507, 1467, 1339, 1276, 1261, 1233, 1147, 997, 904, 875, 850 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{14}F_7NO$ $[M+H]^+$ 394.1036, found 394.1051.



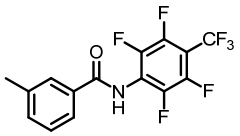
1b

***N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1b):** white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 10.92 (s, 1H), 8.01 (t, *J* = 8.0 Hz, 2H), 7.69–7.65 (m, 1H), 7.58 (t, *J* = 8.0 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 165.14, 132.80, 132.12, 128.70, 128.21; **IR** (neat) ν 3711, 2319, 1468, 1055, 1033, 997, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_6F_7NO$ $[M+H]^+$ 338.0410, found 338.0423.



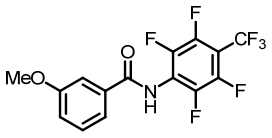
1c

2-methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1c): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 10.94 (s, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.48–7.44 (m, 1H), 7.37–7.33 (m, 2H), 2.42 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 167.40, 136.20, 134.47, 130.88, 127.74, 125.82, 104.36, 19.40; **IR** (neat) ν 3706, 3234, 2318, 1685, 1469, 1142, 1054, 1033, 1002, 993 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_8F_7NO$ $[M+H]^+$ 352.0567, found 352.0581.



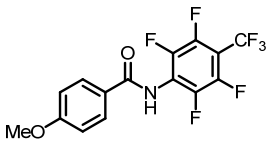
1d

3-methyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1d): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ10.87 (s, 1H), 7.84–7.80 (m, 2H), 7.50–7.44 (m, 2H), 2.41 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 165.21, 138.14, 133.36, 132.09, 128.66, 128.60, 125.35, 20.88; **IR** (neat) ν 3310, 1650, 1455, 1327, 1189, 995 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_8F_7NO$ $[M+H]^+$ 352.0567, found 352.0584.



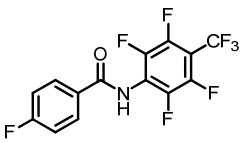
1e

3-methoxy-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1e): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 10.89 (s, 1H), 7.61–7.47 (m, 3H), 7.25–7.22 (m, 1H), 3.84 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 164.83, 159.33, 133.39, 129.91, 120.43, 118.78, 113.10, 55.43; **IR** (neat) ν 3697, 3216, 3006, 1674, 1475, 1340, 1232, 1175, 1140, 1047, 995 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_8F_7NO_2$ $[M+H]^+$ 368.0516, found 368.0530.



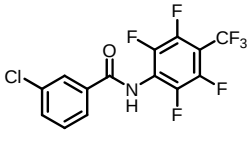
1f

4-methoxy-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1f): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 10.73 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 3.86 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 164.43, 162.79, 130.31, 124.15, 113.95, 55.57; **IR** (neat) ν 3706, 2707, 2318, 1469, 1055, 1033, 1012, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_8F_7NO_2$ $[M+H]^+$ 368.0516, found 368.0528.



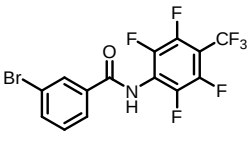
1g

4-fluoro-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1g): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 10.98 (s, 1H), 8.10 (dd, J_1 = 8.7 Hz, J_2 = 5.5 Hz, 2H), 7.42 (t, J = 8.8 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 164.12 (d, $J_{C\text{-}F}$ = 250.3 Hz), 164.06, 131.12 (d, $J_{C\text{-}F}$ = 9.0 Hz),128.58 (d, $J_{C\text{-}F}$ = 3.0 Hz), 115.80 (d, $J_{C\text{-}F}$ = 22.1 Hz); **IR** (neat) ν 3249, 1681, 1604, 1508, 1467, 1343, 1237, 1191, 1152, 997, 906, 854 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_5F_8NO$ $[M+H]^+$ 356.0316, found 356.0332.



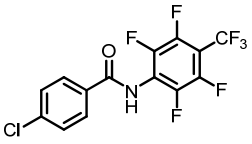
1h

3-chloro-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1h): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 11.06 (s, 1H), 8.05 (d, J = 1.6 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.74 (dd, J_1 = 8.0 Hz, J_2 = 1.0 Hz, 1H), 7.61 (t, J = 7.9 Hz, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 163.78, 134.02, 133.52, 132.62, 130.74, 127.95, 126.99; **IR** (neat) ν 3216, 3131, 1673, 1655, 1531, 1509, 1482, 1470, 1336, 1158, 1150, 996, 923, 878 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_5ClF_7NO$ $[M+H]^+$ 372.0021, found 372.0029.



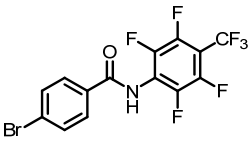
1i

3-bromo-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1i): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 11.06 (s, 1H), 8.19 (s, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 163.69, 135.52, 134.20, 130.97, 130.80, 127.37, 121.90; **IR** (neat) ν 3712, 2319, 1467, 1055, 1033, 996, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_5SF_7NO$ $[M+H]^+$ 415.9515, found 415.9535.



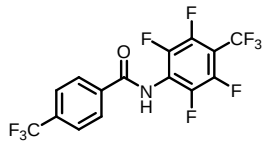
1j

4-chloro-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1j): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 11.05 (s, 1H), 8.03 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 8.5 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 164.16, 137.70, 130.84, 130.12, 128.83; **IR** (neat) ν 3709, 2707, 2319, 1462, 1054, 1033, 1013, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_5ClF_7NO$ $[M+H]^+$ 372.0021, found 372.0039.



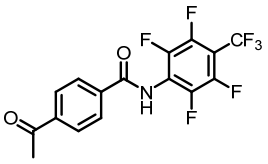
1k

3-bromo-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1k): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 11.01 (s, 1H), 8.02–7.89 (m, 2H), 7.80 (d, J = 8.6 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 164.32, 131.82, 131.20, 130.27, 126.77; **IR** (neat) ν 3750, 3250, 2989, 2707, 2318, 1679, 1468, 997, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_5SF_7NO$ $[M+H]^+$ 415.9515, found 415.9533.



1l

***N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)-4-(trifluoromethyl)benzamide (1l):** white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 11.20 (s, 1H), 8.20 (d, J = 8.1 Hz, 2H), 7.96 (d, J = 8.2 Hz, 2H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 164.13, 135.88, 132.49 (q, $J_{C\text{–}F}$ = 31.6 Hz), 129.18, 125.74 (q, $J_{C\text{–}F}$ = 3.6 Hz), 123.81 (q, $J_{C\text{–}F}$ = 271.3 Hz); **IR** (neat) ν 3714, 3250, 2319, 1683, 1472, 1327, 1172, 1132, 999 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_5F_{10}NO$ $[M+H]^+$ 406.0284, found 406.0291.



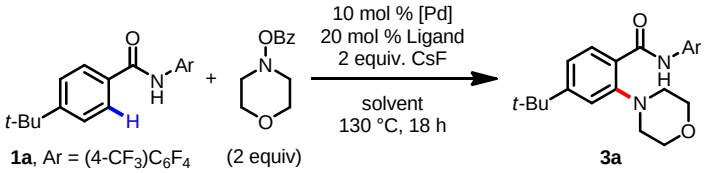
1m

4-acetyl-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (1m): white solid. **^{1}H NMR** (400 MHz, $(CD_3)_2SO$) δ 10.98 (s, 1H), 7.97 (s, 4H), 2.65 (s, 3H); **^{13}C NMR** (100 MHz, $(CD_3)_2SO$) δ 197.70, 164.48, 139.72, 135.75, 128.57, 128.44, 27.06; **IR** (neat) ν 3750, 2692, 1474, 1055, 1002, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{16}H_8F_7NO_2$ $[M+H]^+$ 380.0516, found 380.5021.

Optimization Studies

Experimental procedure for the optimization of Pd catalysts (Table S1): A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the amide substrate (**1a**, 0.1 mmol), *O*-benzoyl hydroxylmorpholine (0.2 mmol), $Pd(OAc)_2$ (10 mol %), ligand (20 mol %), CsF (0.2 mmol), and solvent (1.0 mL). The reaction tube was capped, evacuated briefly under high vacuum and then charged with N_2 (1 atm, balloon) (×3). The reaction mixture was stirred at 130 °C for 18 h. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product **3a** was determined by integration using an internal standard (dibromomethane).

Table S1. Optimization of Pd catalyst for intermolecular amination reaction[a]



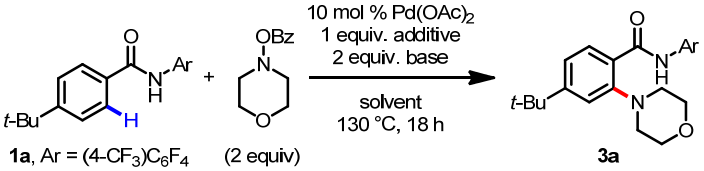
1a, Ar = $(4\text{-}CF_3)C_6F_4$ (2 equiv) **3a**

Entry	[Pd]	Ligand	Solvent	Yield (%)[b]
1	$Pd(OAc)_2$	$PCy_3{\cdot}HBF_4$	toluene	<2
2	$Pd(OAc)_2$	Cy-JohnPhos·HBF_4	toluene	26
3	$Pd(OAc)_2$	SPhos·HBF_4	toluene	15
4	$Pd(dba)_2$	---	toluene	59
5	$Pd(dba)_2$	---	1,2-dichloroethane	70
6	$Pd(OAc)_2$	---	toluene	62
7	$Pd(OAc)_2$	---	1,2-dichloroethane	74

[a] Reaction conditions: **1a** (0.1 mmol), *O*-benzoyl hyroxylmorpholine (2.0 equiv), $Pd(OAc)_2$ (10 mol %), CsF (2.0 equiv), ligand (20 mol %), solvent (1 mL), 130 ºC, 18 h. [b] The yield was determined by ^{1}H NMR analysis of the crude product using dibromomethane as an internal standard.

Experimental procedure for the optimization of general reaction conditions (Table S2): A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the amide substrate (**1a**, 0.1 mmol), *O*-benzoyl hydroxylmorpholine (0.2 mmol), $Pd(OAc)_2$ (10 mol %), additive (0.1 mmol), base (0.2 mmol), and solvent (1.0 mL). The reaction tube was capped, evacuated briefly under high vacuum and then charged with N_2 (1 atm, balloon) (×3). The reaction mixture was stirred at 130 °C for 18 h. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product **3a** was determined by integration using an internal standard (dibromomethane).

Table S2. Optimization of Pd(II)-catalyzed intermolecular amination reaction [a]



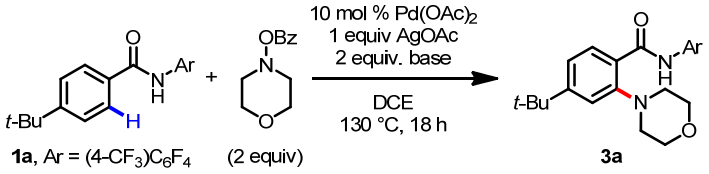
Entry	Base	Additive	Solvent	Yield (%)[b]
1	—	—	1,4-dioxane	40
2	CsF	—	1,4-dioxane	57
3	CsF	—	toluene	62
4	CsF	$PhI(OAc)_2$	toluene	29
5	CsF	AgOAc	toluene	72
6	CsF	AgOAc	1,2-dichloroethane	96
7	CsF	NaOAc	1,2-dichloroethane	78
8	CsF	KOAc	1,2-dichloroethane	69
9	CsF	$Cu(OAc)_2$	1,2-dichloroethane	56
10	CsF	Ag_2CO_3	1,2-dichloroethane	97
11	CsF	AcOH[c]	1,2-dichloroethane	0

[a] Reaction conditions: **1a** (0.1 mmol), *O*-benzoyl hyroxylmorpholine (2.0 equiv), $Pd(OAc)_2$ (10 mol %), base (2.0 equiv), additive (1.0 equiv), solvent (1 mL), 130 °C, 18 h. [b] The yield was determined by ^1H NMR analysis of the crude product using dibromomethane as an internal standard. [c] 20 mol % AcOH was used.

Experimental procedure for the optimization of general reaction condition (Table S3): A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the amide substrate (**1a**, 0.1 mmol), *O*-benzoyl hydroxylmorpholine (0.2 mmol), $Pd(OAc)_2$ (10 mol %), AgOAc (0.1 mmol), base (0.2 mmol), and DCE (1.0 mL). The reaction tube was capped, evacuated briefly under high vacuum and then

charged with N_2 (1 atm, balloon) (×3). The reaction mixture was stirred at 130 °C for 18 h. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The NMR yield of desired product **3a** was determined by integration using an internal standard (dibromomethane).

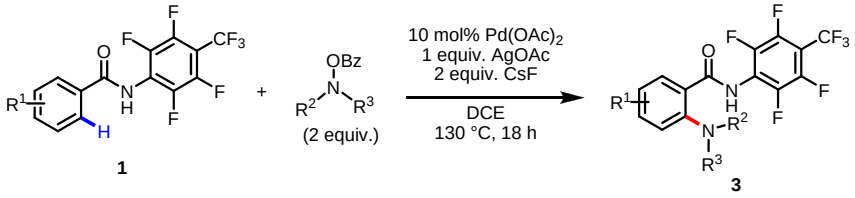
Table S2. Base screening for Pd(II)-catalyzed intermolecular amination reaction [a]



Entry	Base	Yield (%)[b]	Entry	Base	Yield (%)[b]
1	**CsF**	**96**	6	KF	88
2	Cs_2CO_3	<2	7	Na_2HPO_4	39
3	NaOAc	53	8	NaH_2PO_4	56
4	KOAc	42	9	K_2HPO_4	80
5	Na_2CO_3	78	10	KH_2PO_4	58

[a] Reaction conditions: **1a** (0.1 mmol), *O*-benzoyl hyroxylmorpholine (2.0 equiv), $Pd(OAc)_2$ (10 mol %), base (2.0 equiv), AgOAc (1.0 equiv), DCE (1 mL), 130 °C, 18 h. [b] The yield was determined by ^1H NMR analysis of the crude product using dibromomethane as an internal standard.

General Procedure for Amination

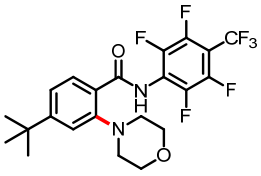


Scheme S2. General procedure for Pd(II)-catalyzed intermolecular amination

General procedure for Pd(II)-catalyzed amination reaction: A 50 mL Schlenk-type sealed tube (with a Teflon high pressure valve and side arm) equipped with a magnetic stir bar was charged with the amide substrate (**1**, 0.2 mmol), *O*-benzoyl hydroxylamine (82.9 mg, 0.4 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol %), AgOAc (33.4 mg, 0.2 mmol), CsF (60.7 mg, 0.4 mmol), and DCE (1.0 mL). The reaction tube was capped, evacuated briefly under high vacuum and then charged with N_2 (1 atm, balloon) (×3). The reaction mixture was stirred at 130 °C for 18 h. Upon completion, the reaction mixture was cooled to room temperature. The reaction mixture was

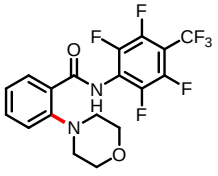
diluted with ethyl acetate and then filtered through a small pad of Celite. The filtrate was concentrate *in vacuo*. The resulting residue was purified by silica gel flash column chromatography using hexanes/EtOAc as the eluent.

Characterization of Amination Products:



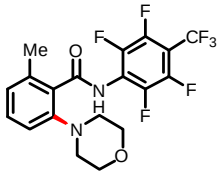
3a

4-(*tert*-butyl)-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3a): white solid (91.8 mg, 96% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.0 Hz, 1H), 7.43–7.40 (m, 2H), 3.89 (t, *J* = 4.0 Hz, 4H), 3.09 (t, *J* = 4.0 Hz, 1H), 1.34 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.51, 158.13, 150.90, 146.09 (m), 143.43 (m), 140.95 (m), 132.12, 124.24, 123.79, 121. 60 (m), 121.13 (q, J_{C-F} = 273 Hz) 67.41, 53.97, 35.57, 31.22 ; **IR** (neat) ν 2988, 1705, 1655, 1473, 1335, 1283, 1222, 1142, 979 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{22}H_{21}F_7N_2O_2$ $[M+H]^+$ 479.1564, found 479.1573.



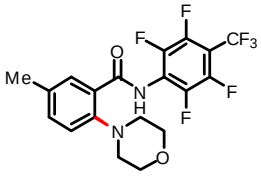
3b

2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3b): white solid (71.7 mg, 85% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.09 (s, 1H), 8.34–8.32 (m, 1H), 7.62–7.58 (m, 1H), 7.45–7.36 (m, 2H), 3.88 (t, *J* = 4.3 Hz, 4H), 3.08 (t, *J* = 4.4 Hz, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.58, 151.13, 134.08, 132.44, 126.98, 126.62, 122.88, 67.36, 54.00; **IR** (neat) ν 2924, 2854, 1691, 1655, 1505, 1474, 1459, 1336, 1235, 1143, 1116, 997, 918 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{13}F_7N_2O_2$ $[M+H]^+$ 423.0938, found 423.0950.



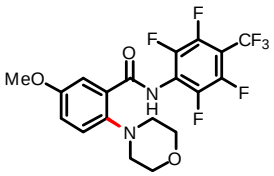
3c

2-methyl-6-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3c): white solid (77.6 mg, 89% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.06–7.03 (m, 2H), 3.08 (m, 4H), 3.00 (m, 4H), 2.45 (s, 3 H) ; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.96, 150.29, 139.12, 131.29, 130.05, 127.38, 117.41, 67.15, 53.78, 20.62; **IR** (neat) ν 3244, 1740, 1681, 1472, 1145, 998 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{15}F_7N_2O_2$ $[M+H]^+$ 437.1094, found 437.1113.



3d

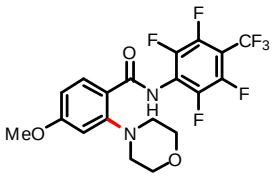
5-methyl-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3d): white solid (71.6 mg, 82% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.28 (s, 1H), 8.15 (s, 1H), 7.40 (t, *J* = 8.2 Hz, 1H), 7.33 (t, *J* = 8.2 Hz, 1H), 3.87 (m, 4H), 3.05 (m, 4H), 2.32 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.74, 148.60, 137.08, 134.70, 132.65, 126.20, 122.94, 67.42, 54.05, 21.06; **IR** (neat) ν 3750, 2847, 1737, 1692, 1655, 1506, 1476, 1459, 1336, 1236, 1144, 1116, 998 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{15}F_7N_2O_2$ $[M+H]^+$ 437.1094, found 437.1108.



3e

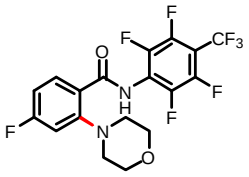
5-methoxy-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3e): yellow foam (71.4 mg, 79% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.66 (s, 1H), 7.88 (d, *J* = 3.1

Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.15 (dd, J_1 = 8.8 Hz, J_2 = 3.1 Hz, 1H), 3.92 (comp. m, 7H), 3.06 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.38, 158.14, 143.88, 127.71, 124.64, 121.04, 115.08, 67.46, 55.97, 54.13; **IR** (neat) ν 3705, 2845, 1737, 1691, 1656, 1506, 1477, 1337, 1234, 1144, 1116, 1047, 1033, 1000 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{15}F_7N_2O_3$ $[M+H]^+$ 453.1044, found 453.1051.



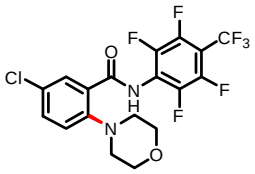
3f

4-methoxy-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3f): white powder (79.6 mg, 88% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.77 (s, 1H), 8.30 (d, J = 8.6 Hz, 1H), 6.89 (comp. m, 2H), 3.88 (comp. m, 7H), 3.06 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 164.09, 163.33, 152.97, 134.47, 119.18, 111.23, 109.42, 67.37, 55.87, 54.04; **IR** (neat) ν 2965, 2849, 1739, 1688, 1654, 1601, 1507, 1474, 1458, 1337, 1231, 1143, 1115, 997, 863 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{15}F_7N_2O_3$ $[M+H]^+$ 453.1044, found 453.1060.



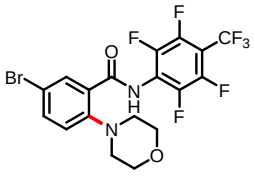
3g

4-fluoro-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3g): white solid (60.7 mg, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.53 (s, 1 H), 8.35 (dd, J_1 = 8.8 Hz, J_2 = 6.7 Hz, 1H), 7.09 (comp. m, 2 H), 3.89 (m, 4 H), 3.06 (m, 4 H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.98 (d, J = 255.6 Hz), 162.70, 153.36 (d, J = 8.0 Hz),134.98 (d, J = 10.0 Hz), 123.00 (d, J = 4.0 Hz), 114.20 (d, J = 21.1 Hz), 110.21 (d, J = 22.1 Hz), 67.22, 54.08; **IR** (neat) ν 3749, 2319, 1691, 1474, 1460, 1338, 998, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{12}F_8N_2O_2$ $[M+H]^+$ 441.0844, found 441.0861.



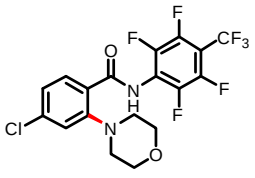
3h

3-chloro-6-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3h): white solid (54.8 mg, 60% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.99 (s, 1H), 8.33 (d, J = 2.4 Hz, 1H), 7.57 (dd, J_1 = 8.6 Hz, J_2 = 2.4 Hz, 1H), 7.41 (J = 8.6 Hz, 1H), 3.90 (m, 4H), 3.08 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.14, 149.25, 133.71, 132.82, 132.02, 128.01, 124.31, 67.04, 53.80; **IR** (neat) ν 3750, 2857, 1692, 1655, 1506, 1475, 1459, 1336, 1236, 1143, 1115, 999, 918, 878 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{12}ClF_7N_2O_2$ $[M+H]^+$ 457.0548, found 457.0564.



3i

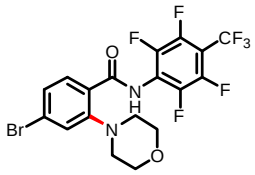
3-bromo-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3i): white solid (56.1 mg, 56% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.92 (s, 1H), 8.47 (d, J = 2.4 Hz, 1H), 7.72 (dd, J_1 = 8.6 Hz, J_2 = 2.4 Hz, 1H), 7.34 (J = 8.6 Hz, 1H), 3.90 (m, 4H), 3.08 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.05, 149.78, 136.69, 135.01, 128.20, 124.51, 120.49, 67.02, 53.75; **IR** (neat) ν 3706, 2864, 2844, 2707, 2318, 1462, 1339, 1055, 1033, 1012, 914, 897 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{12}SF_7N_2O_2$ $[M+H]^+$ 501.0043, found 501.0057.



3j

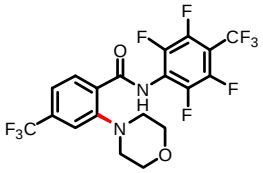
4-chloro-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3j): white solid (65.8 mg, 72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.61 (s, 1H), 8.27 (d, J = 8.6 Hz, 1H), 7.41 (s, 1H), 7.37 (J = 8.6 Hz, 1H), 3.90 (m, 4H), 3.09 (m, 4H); **^{13}C**

NMR (100 MHz, $CDCl_3$) δ 162.48, 151.89, 139.76, 133.56, 127.01, 124.90, 123.14, 66.96, 53.79; **IR** (neat) ν 2966, 2854, 1692, 1589, 1507, 1458, 1337, 1236, 1145, 1115, 997, 945 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{12}ClF_7N_2O_2$ $[M+H]^+$ 457.0548, found 457.0566.



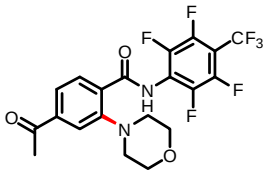
3k

4-bromo-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3k): white solid (75.2 mg, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.58 (s, 1H), 8.20 (d, J = 8.6 Hz, 1H), 7.56 (J = 2.4 Hz, 1H), 7.53 (dd, J_1 = 8.6 Hz, J_2 = 2.4 Hz, 1H), 3.90 (m, 4H), 3.10 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.64, 151.88, 133.69, 130.08, 128.22, 126.17, 125.43, 67.00, 53.86; **IR** (neat) ν 2963, 2924, 2853, 1691, 1584, 1505, 1472, 1456, 1336, 1234, 1186, 1143, 1114, 996, 936, 791 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{12}SF_7N_2O_2$ $[M+H]^+$ 501.0043, found 501.0062.



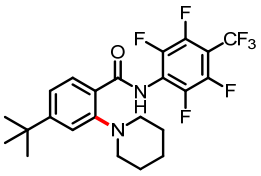
3l

4-trifluoromethyl-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3l): white solid (66.7 mg, 68% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.61 (s, 1H), 8.46 (d, J = 8.0 Hz, 1H), 7.67 (s, 1H), 7.64 (d, J = 8.0 Hz, 1H), 3.93 (m, 4H), 3.14 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.26, 151.35, 135.41 (q, $J_{C\text{-}F}$ = 32.8 Hz), 133.20, 129.58, 123.24 (q, $J_{C\text{-}F}$ = 3.6 Hz), 123.10 (q, $J_{C\text{-}F}$ = 273.6 Hz), 119.49 (q, $J_{C\text{-}F}$ = 3.6 Hz), 66.95, 53.81; **IR** (neat) ν 3749, 2849, 2707, 2692, 2319, 1694, 1656, 1613, 1505, 1474, 1459, 1418, 1332, 1128, 1113, 996, 948 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{12}F_{10}N_2O_2$ $[M+H]^+$ 491.0812, found 491.0824.



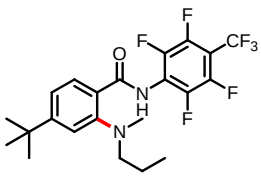
3m

4-acetyl-6-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3m): white solid (65.0 mg, 70% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 12.91 (s, 1H), 8.45 (d, J = 8.1 Hz, 1H), 8.06 (s, 1H), 7.91 (dd, J_1 = 8.1 Hz, J_2 = 0.8 Hz, 1H), 3.92 (m, 4H), 3.15 (m, 4H), 2.68 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 196.87, 162.57, 151.25, 141.07, 132.87, 130.06, 126.36, 121.92, 67.01, 53.78, 26.88; **IR** (neat) ν 2923, 2853, 1685, 1506, 1336, 1234, 1141, 996, 927, 875, 855, 715 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{20}H_{15}F_7N_2O_3$ $[M+H]^+$ 465.1044, found 465.1061.



3n

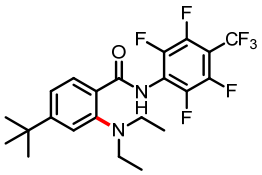
4-(*tert*-butyl)-2-(piperidin-1-yl)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3n): white solid (92.3 mg, 97% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.7 (s, 1H), 8.25 (d, J = 8.4 Hz, 1H), 7.41–7.35 (m, 2H), 3.01 (m, 4H), 1.76 (m, 4H), 1.63 (m, 2H), 1.33 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.87, 157.72, 152.61, 131.80, 123.74, 123.57, 119.64, 55.29, 35.56, 31.32, 26.71, 23.65; **IR** (neat) ν 3750, 2862, 2707, 2319, 1692, 1605, 1507, 1475, 1338, 1144, 998 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{23}H_{23}F_7N_2O$ $[M+H]^+$ 477.1771, found 477.1780.



3o

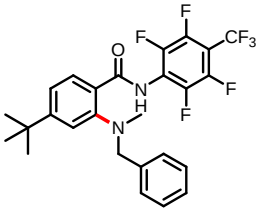
4-(*tert*-butyl)-2-(methyl(propyl)amino)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3o): yellow oil (74.2 mg, 80% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.80 (s, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.38–7.35 (m, 2H), 3.01 (t, J = 7.7 Hz, 2H), 2.77 (s, 3H), 1.52 (m, 2H), 1.34 (s, 9H), 0.88 (t, J = 7.4, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ

163.83, 157.76, 151.71, 131.63, 124.40, 123.69, 119.64, 59.51, 44.77, 35.50, 31.25, 20.87, 11.88; **IR** (neat) ν 3750, 2873, 2692, 2318, 1739, 1691, 1655, 1606, 1506, 1470, 1337, 1236, 1144, 997 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{22}H_{23}F_7N_2O$ $[M+H]^+$ 465.1771, found 465.1789.



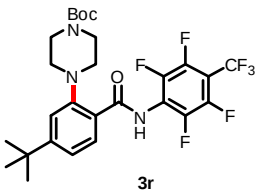
3p

4-(*tert*-butyl)-2-(diethylamino)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3p): yellow oil (67.8 mg, 73% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.3 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.34 (s, 1H), 3.11 (dd, J_1 = 14.4 Hz, J_2 = 7.2 Hz, 4H), 1.33 (s, 9H), 1.03 (t, *J* = 7.2 Hz, 6H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 163.97, 157.56, 148.99, 131.38, 126.31, 123.92, 120.77, 50.37, 35.45, 31.29, 12.23; **IR** (neat) ν 2971, 2872, 1690, 1606, 1506, 1338, 1238, 1145, 998 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{22}H_{23}F_7N_2O$ $[M+H]^+$ 465.1771, found 465.1787.



3q

2-(benzyl(methyl)amino)-4-(*tert*-butyl)-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (3q): yellow oil (76.8 mg, 75% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.30 (s, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 7.38–7.35 (m, 1H), 7.28–7.26 (m, 4H), 7.16–7.13 (m, 2H), 4.20 (s, 2H), 2.76 (s, 3H), 1.32 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.72, 157.42, 151.20, 135.66, 131.93, 129.79, 128.76, 128.30, 123.55, 120.27, 61.80, 43.67, 35.48, 31.24; **IR** (neat) ν 3749, 2866, 2707, 2693, 2319, 1691, 1655, 1605, 1507, 1473, 1338, 1146, 998 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{26}H_{23}F_7N_2O_5$ $[M+H]^+$ 513.1771, found 513.1792.

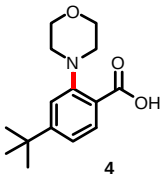


3r

***tert*-butyl 4-(5-(*tert*-butyl)-2-((2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)carbamoyl)phenyl)piperazine-1-carboxylate (3r)**: white solid (90.0 mg, 78% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.03 (s, 1H), 8.26 (d, *J* = 8.3 Hz, 1H), 7.40–7.37 (m, 2H), 3.62 (s, 4H), 3.04 (s, 4H), 1.47 (s, 9H), 1.33 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 163.50, 158.11, 154.63, 151.00, 132.19, 124.29, 123.71, 119.54, 80.71, 53.75, 35.58, 31.26, 28.57; **IR** (neat) 2968, 1696, 1605, 1508, 1477, 1339, 1283, 1237, 1145, 998, cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{27}H_{30}F_7N_3O_3$ $[M+H]^+$ 573.2248, found 578.2246.

Hydrolysis of amination product (3a) to carboxylic acid (4) (eq 6)

4-(*tert*-butyl)-2-morpholino-*N*-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)benzamide (**3a**, 48.9 mg, 0.1 mmol) was dissolved in trifluoroacetic acid, hydrochloric acid (2:1, 3 mL). The reaction mixture was stirred for 12 h at 100 ^{o}C. The reaction mixture was extracted with ethyl ether. The organic layer was washed with 1 % Na_2CO_3, dried over Na_2SO_4, and concentrated under vacuum to give the carboxylic acid (96%)

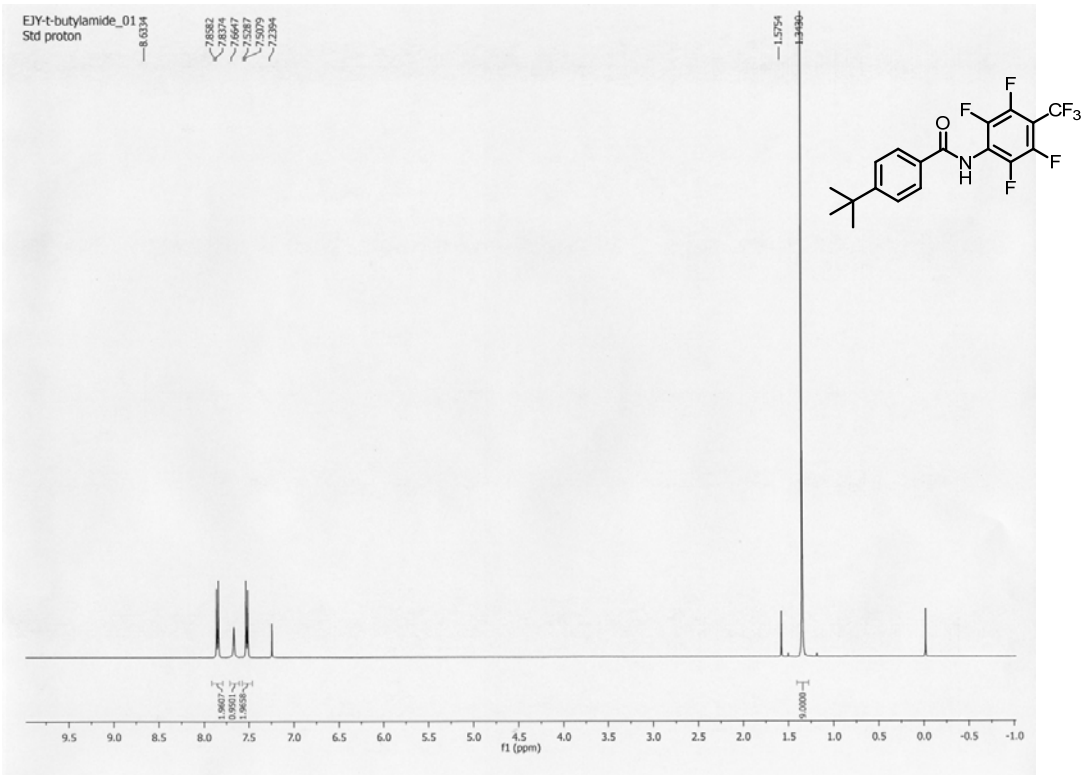


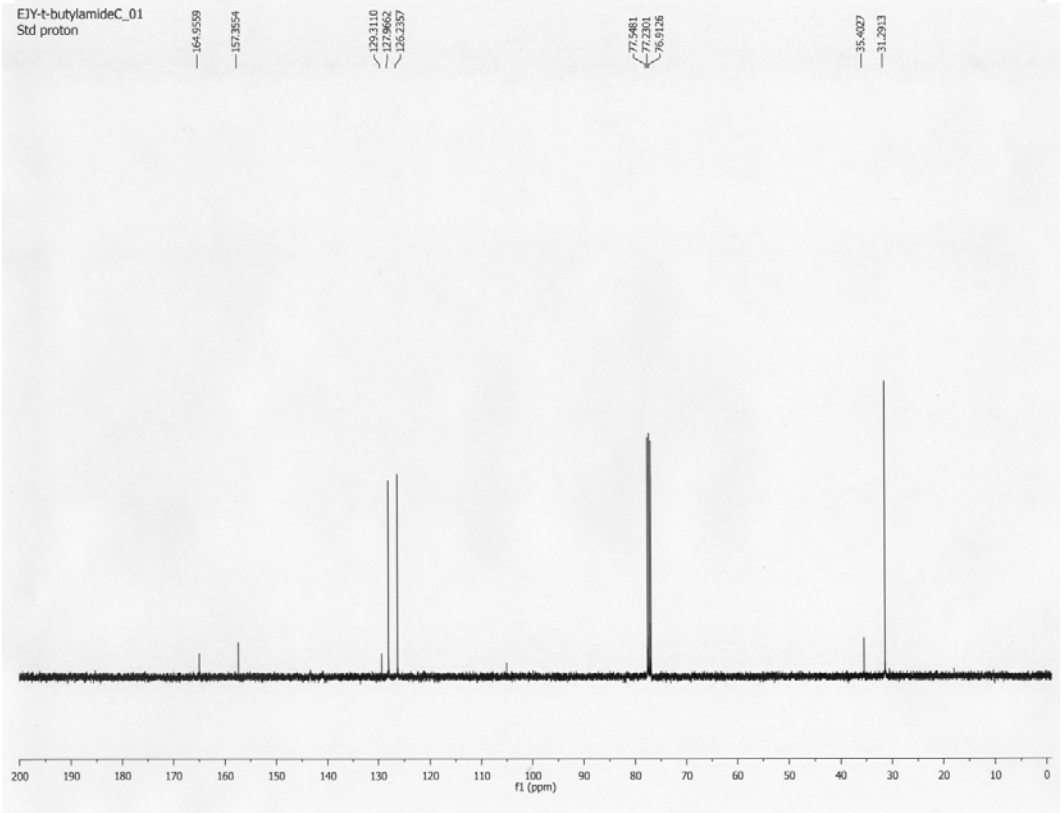
4

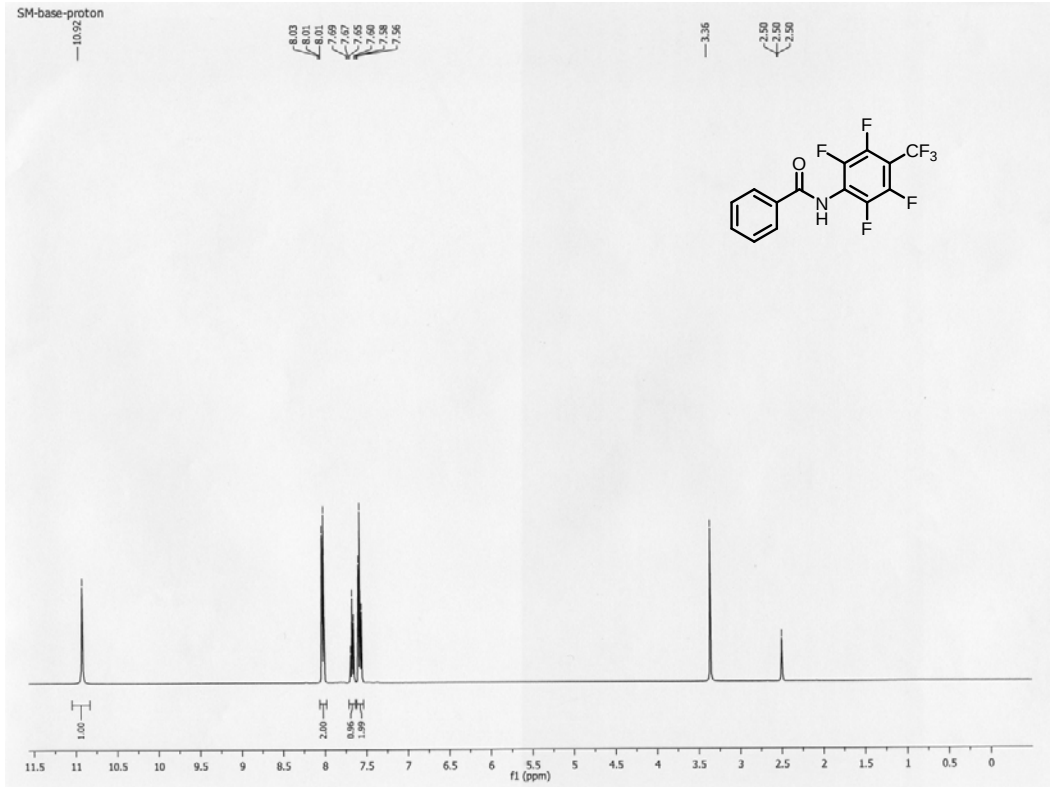
2-morpholinobenzoic acid (4): white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.79 (br, 1H), 8.24 (d, *J* = 8.3 Hz, 1H), 7.53–7.50 (m, 2H), 3.98 (s, 4H), 3.33 (s, 4H), 1.35 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 165.66, 159.54, 131.79, 126.03, 122.02, 119.24, 105.01, 66.68, 54.47, 35.83, 31.07; **IR** (neat) 2966, 1740, 1694, 1606, 1508, 1339, 1238, 1146, 998 cm^{-1}; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{21}NO_3$ $[M+H]^+$ 264.1594, found 264.1593.

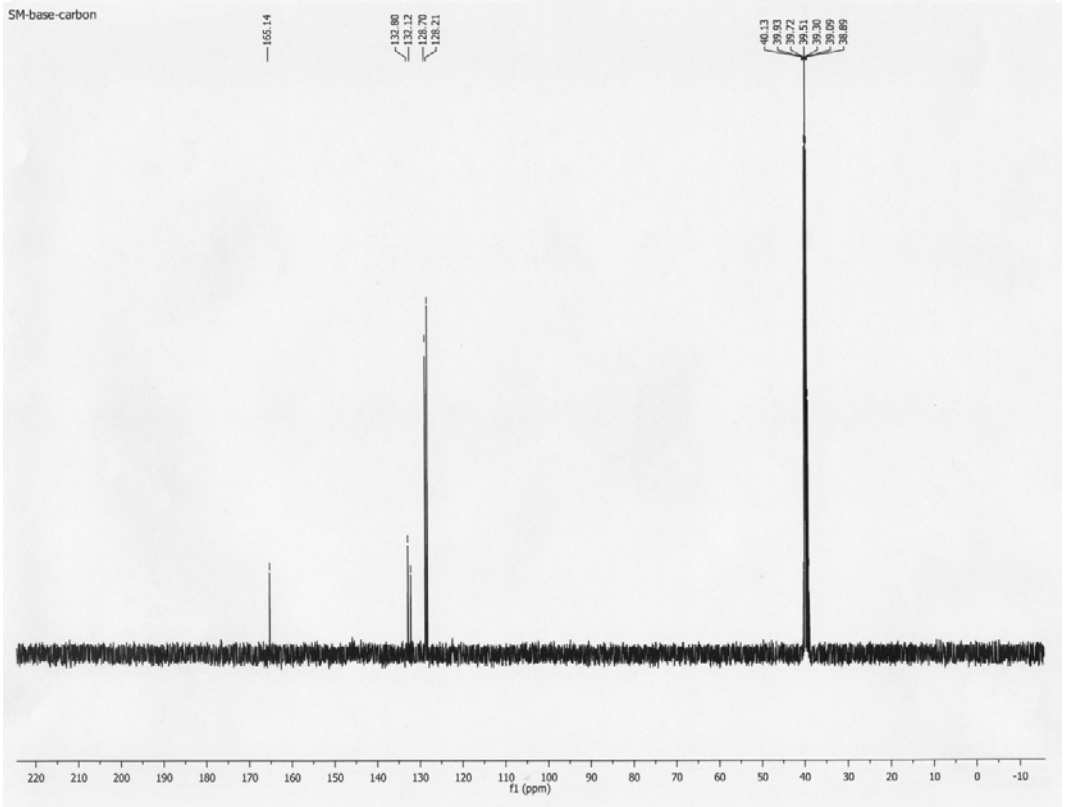
Complete Ref. 8b

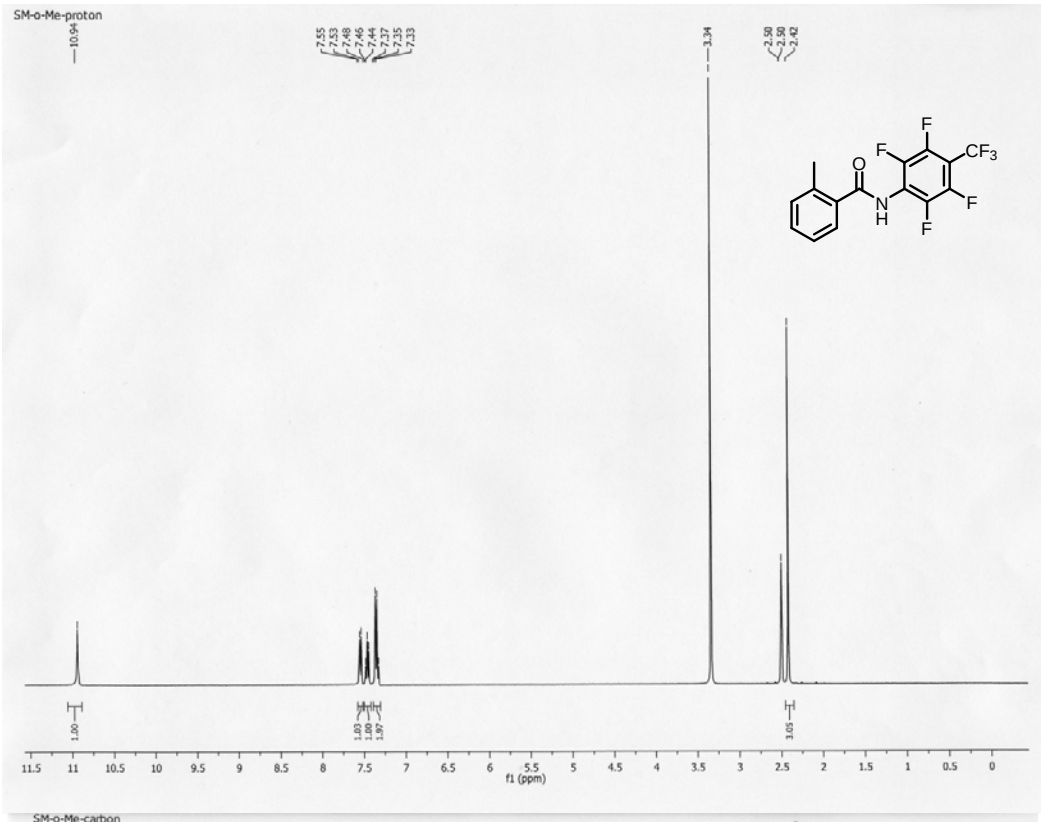
Tang, H.; Yan, Y.; Feng, Z.; de Jesus, R. K.; Yang, L.; Levorse, D. A.; Owens, K. A.; Akiyama, T. E.; Bergeron, R.; Castriota, G. A.; Doebber, T. W.; Ellsworth, K. P.; Lassman, M. E.; Li, C.; Wu, M. S.; Zhang, B. B.; Chapman, K. T.; Mills, S. G.; Berger, J. P.; Pasternak, A. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 6088

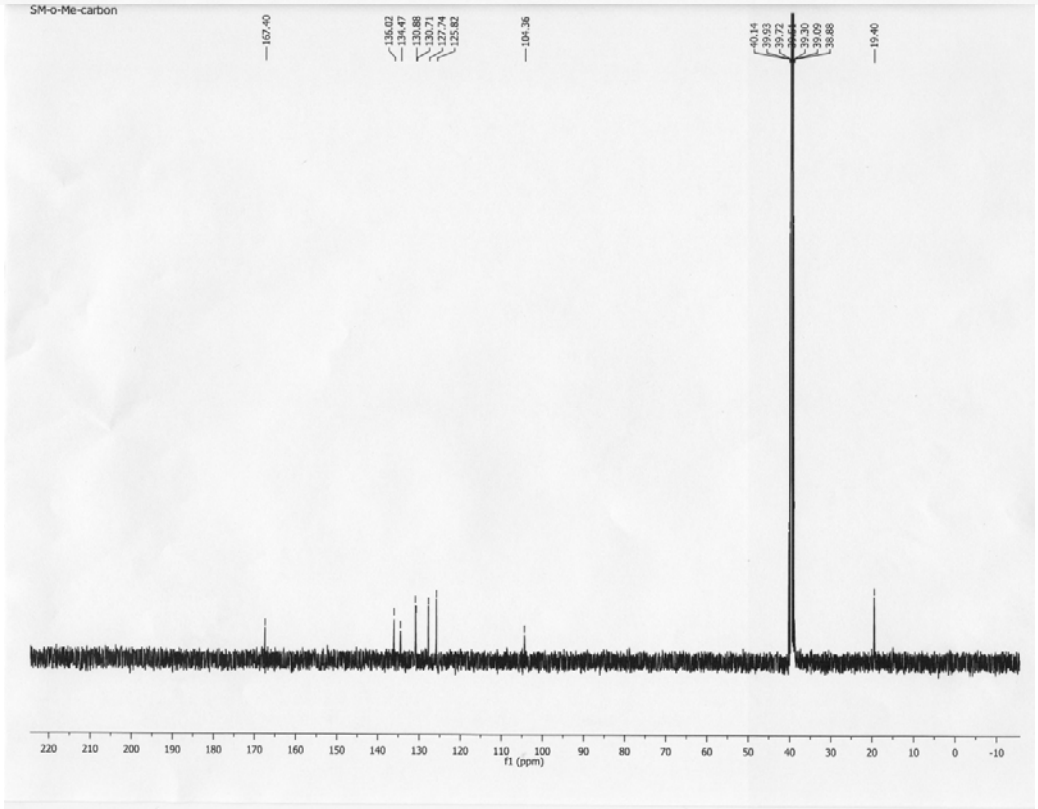

EJY-t-butylamide_01
Std proton
8.6354
7.8582
7.8374
7.6647
7.5287
7.5079
7.2394
1.5754
1.3490
F
F
CF3
O
N
H
F
F
1.9607
0.9581
1.9698
9.0000
f1 (ppm)

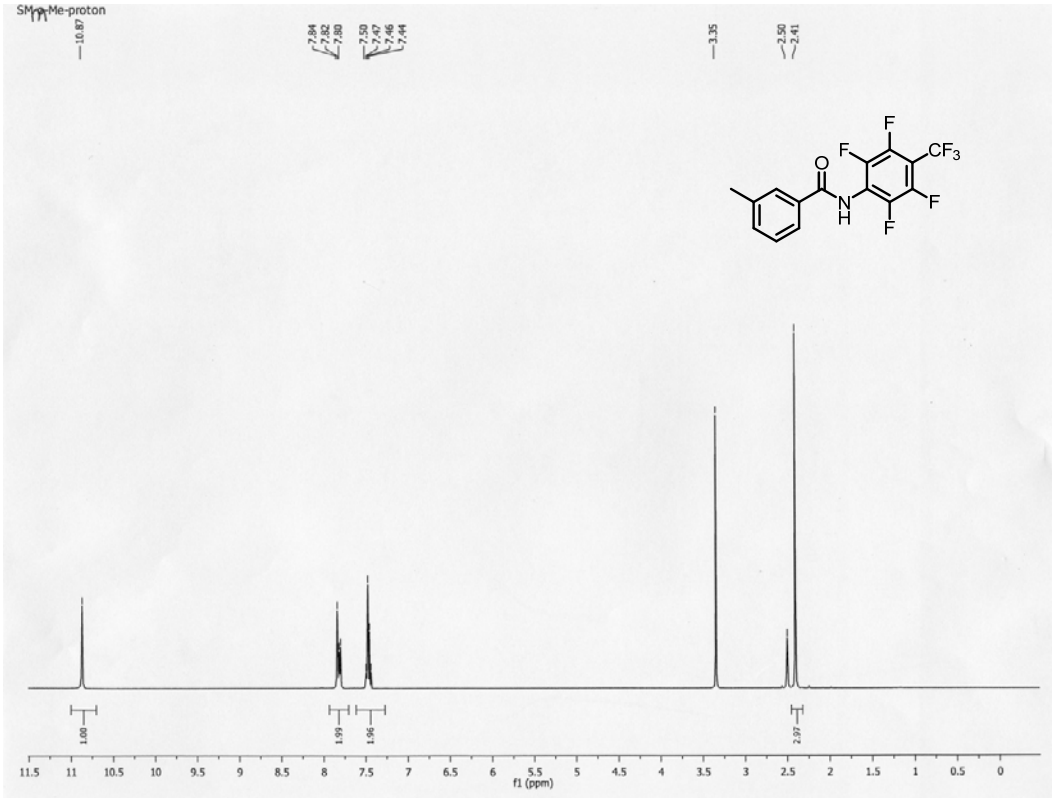

EJY-t-butylamideC_01
Std proton
164.9559
157.3554
129.3110
127.9662
126.2357
77.5461
77.2301
76.9126
35.4027
31.2913
f1 (ppm)

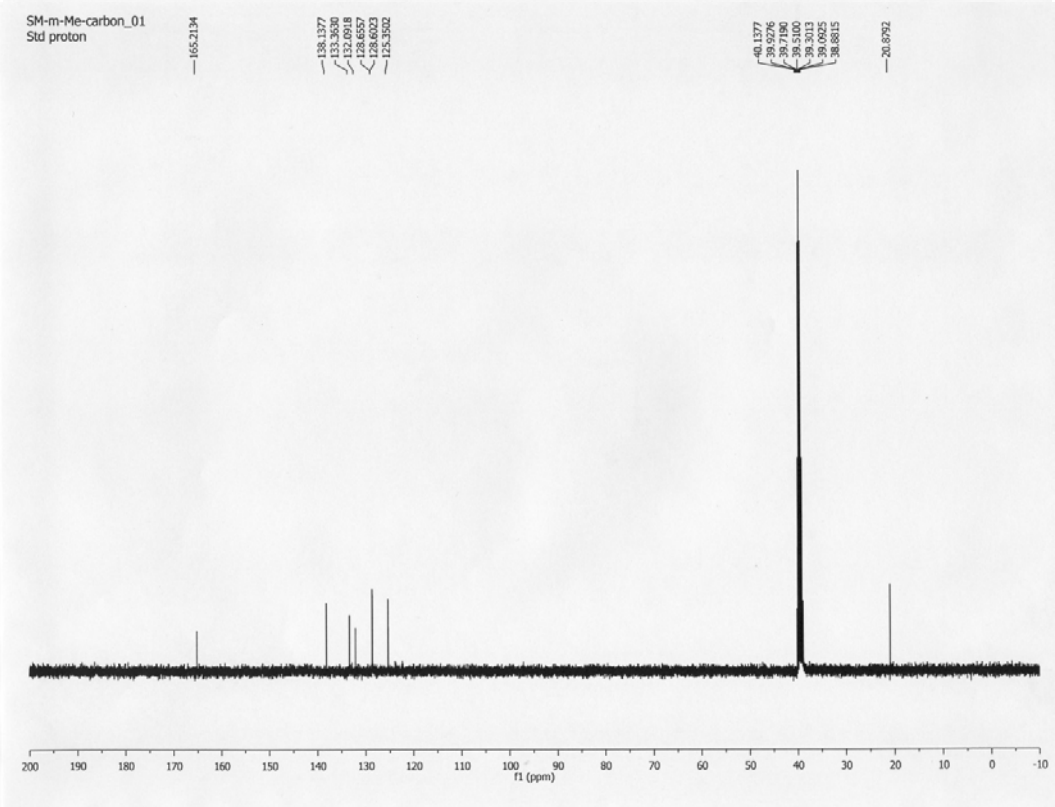

SM-base-proton
10.92
8.03
8.01
8.01
7.69
7.67
7.65
7.60
7.58
7.56
3.36
2.50
2.50
2.50
F
F
CF3
O
N
H
F
F
1.00
2.00
0.96
1.99
f1 (ppm)

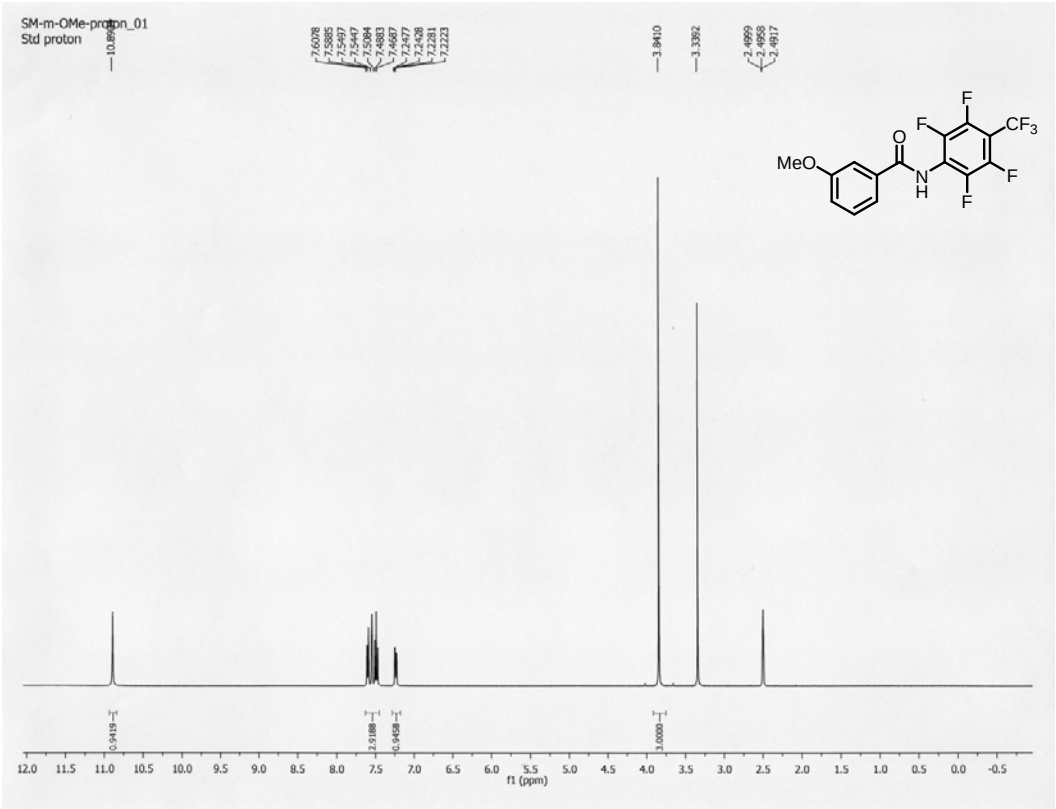

SM-base-carbon
165.14
132.80
132.12
128.70
128.21
40.13
39.93
39.72
39.51
39.30
39.09
38.89
f1 (ppm)

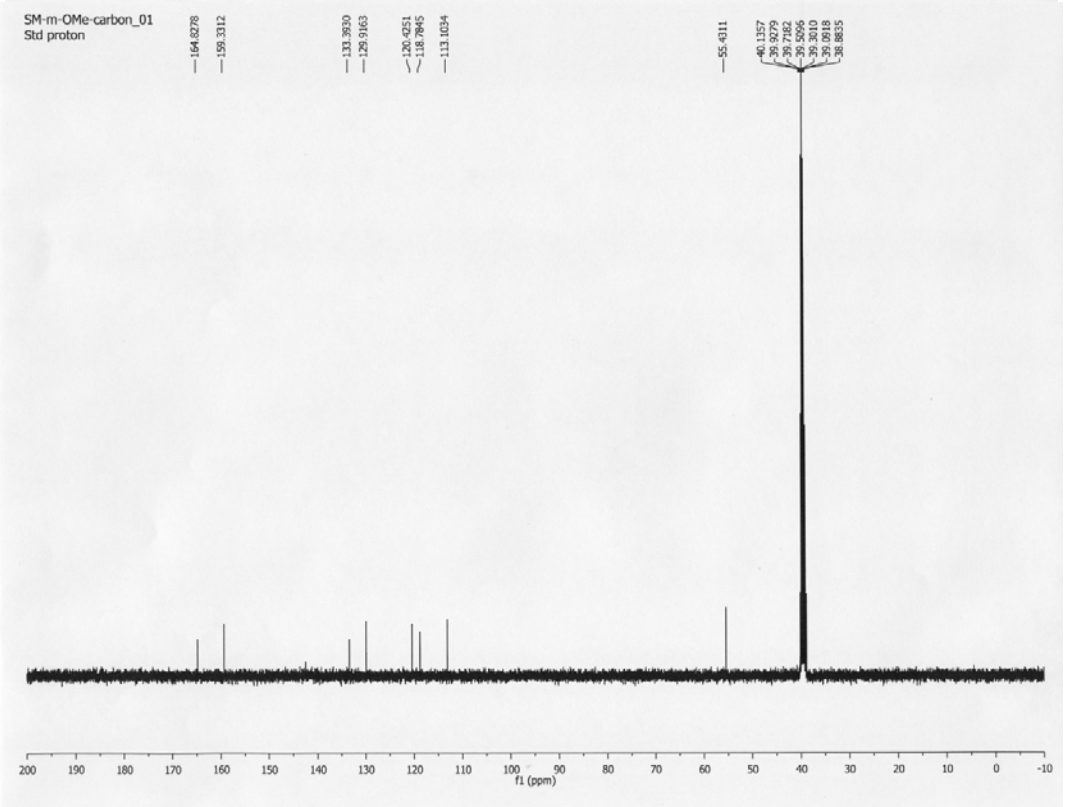

SM-o-Me-proton
10.94
7.55
7.53
7.48
7.46
7.44
7.37
7.35
7.33
3.34
2.50
2.50
2.42
F
F
CF3
O
N
H
F
F
1.00
1.03
1.00
1.97
3.05
11.5 11 10.5 10 9.5 9 8.5 8 7.5 7 6.5 6 5.5 5 4.5 4 3.5 3 2.5 2 1.5 1 0.5 0
f1 (ppm)

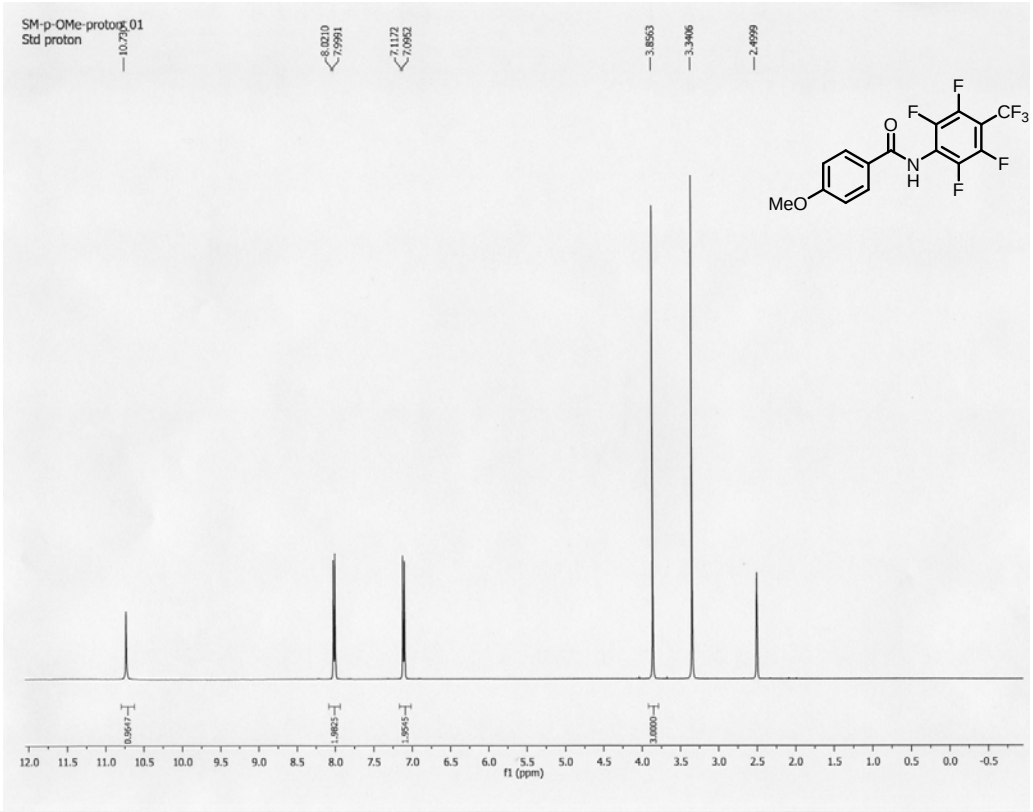

SM-o-Me-carbon
167.40
136.02
134.47
130.88
130.71
127.74
125.82
104.36
40.14
39.93
39.72
39.51
39.30
39.09
38.88
19.40
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

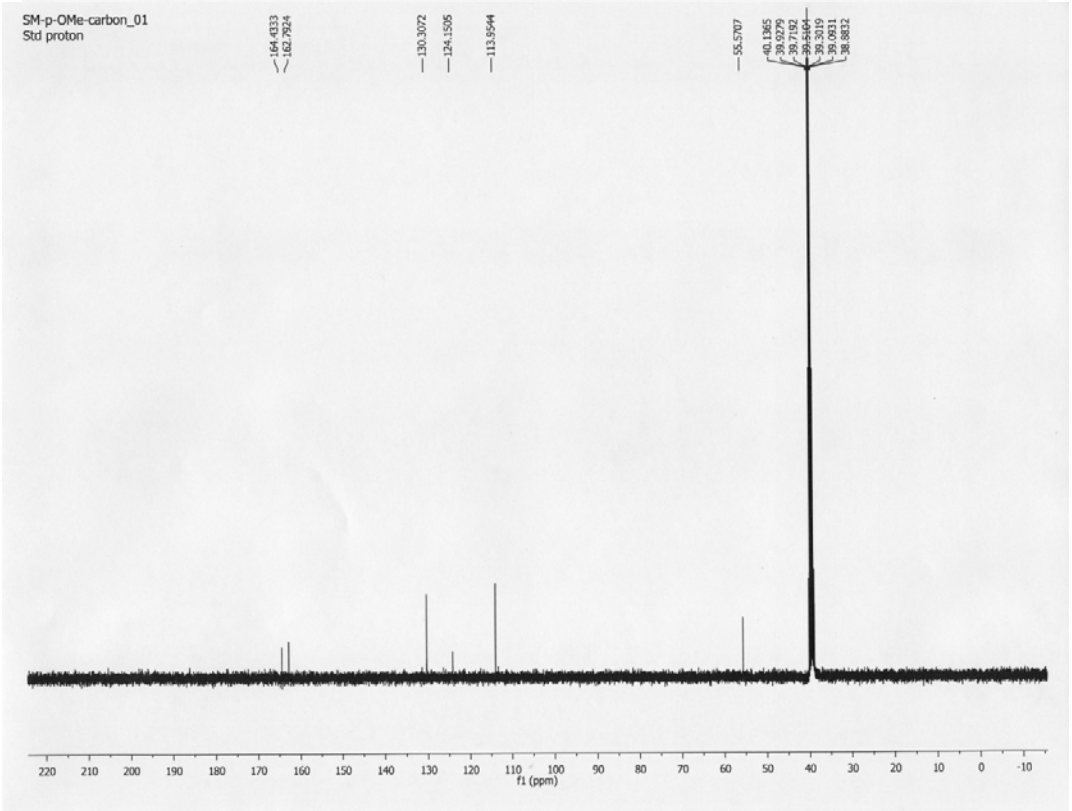

SM-m-Me-proton
10.87
7.84
7.82
7.80
7.50
7.47
7.46
7.44
3.35
2.50
2.41
F
F
CF3
O
N
H
F
F
1.00
1.99
1.96
2.97
f1 (ppm)

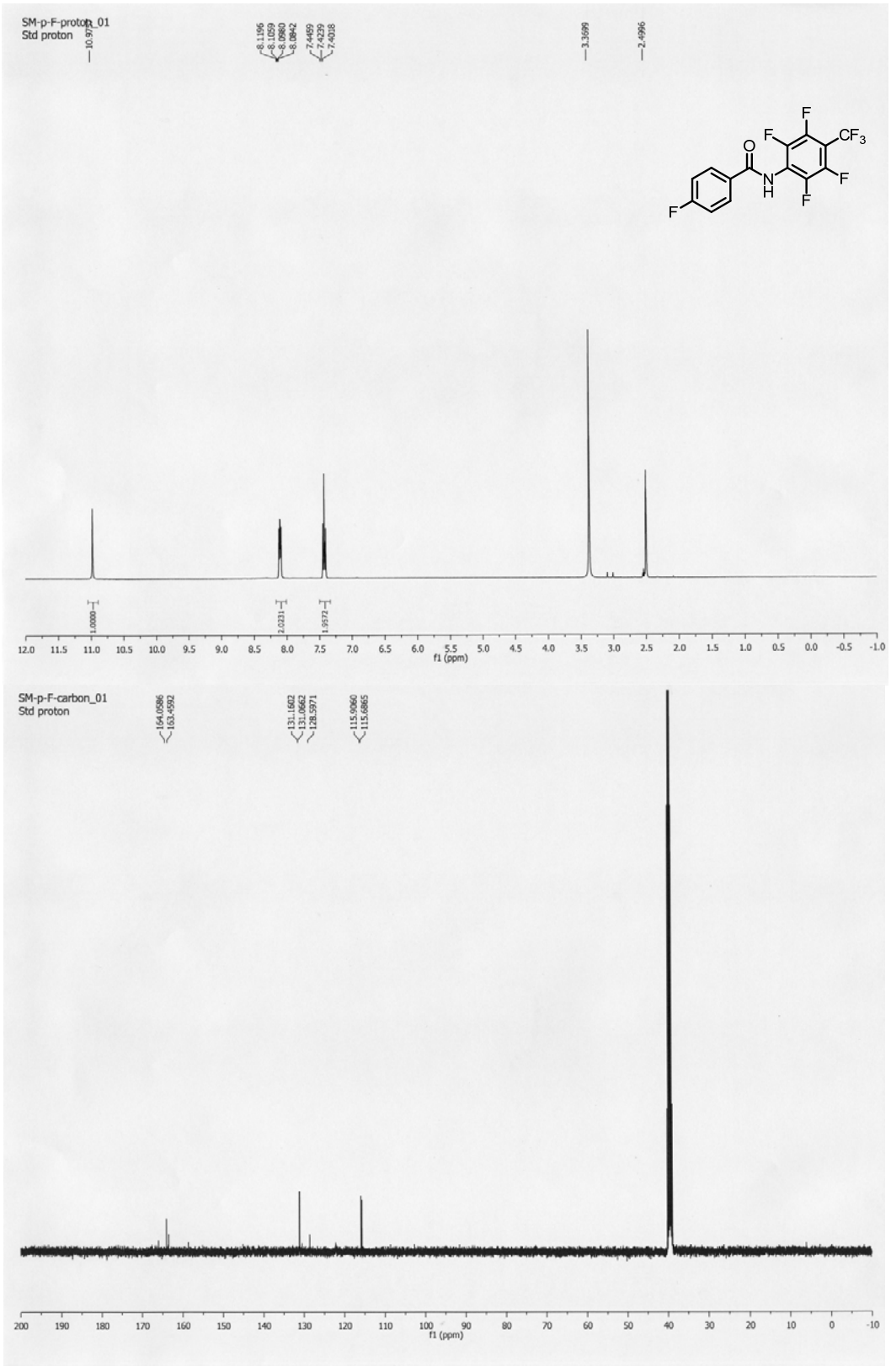

SM-m-Me-carbon_01
Std proton
165.2134
138.1377
133.3638
132.6918
128.657
128.6023
125.3502
40.1377
39.9276
39.7190
39.5100
39.3013
39.0925
38.8815
20.8792
f1 (ppm)

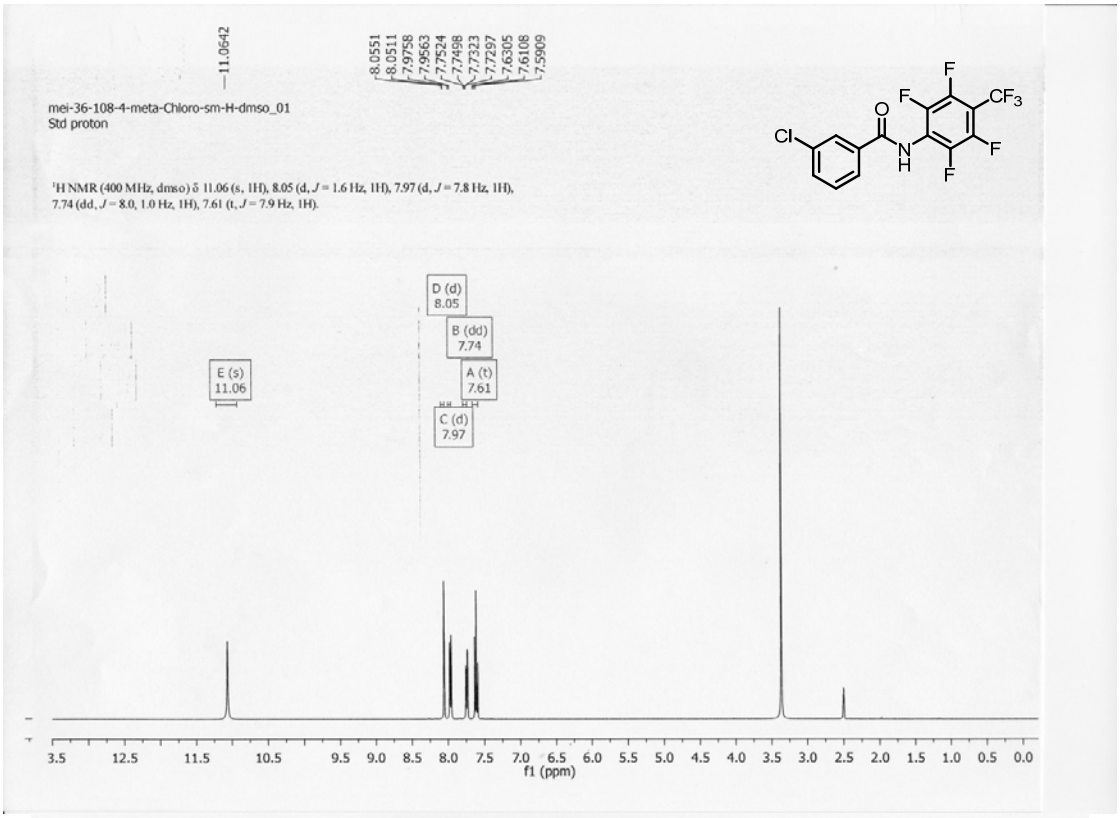

SM-m-OMe-proton_01
Std proton
10.8960
7.6078
7.5885
7.5497
7.5447
7.5084
7.4883
7.4687
7.2477
7.2428
7.2331
7.2233
3.8410
3.3362
2.4999
2.4958
2.4917
F
F
CF3
O
MeO
N
H
F
F
0.9419
2.9188
0.9458
3.0000
f1 (ppm)


SM-m-OMe-carbon_01
Std proton
164.8278
159.3312
133.3930
129.9163
120.4251
118.7845
113.1034
55.4311
40.1357
39.9279
39.7182
39.5096
39.3010
39.0918
38.8835
f1 (ppm)

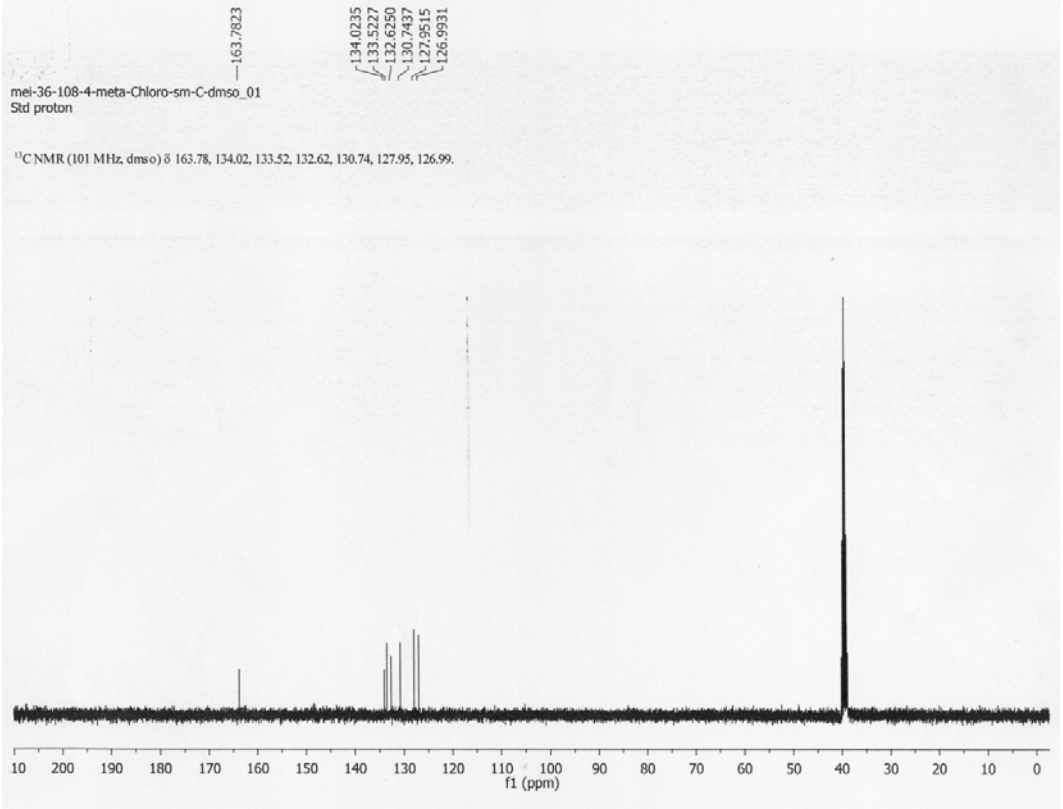

SM-p-OMe-proton_01
Std proton
10.7705
8.0210
7.9991
7.1172
7.0952
3.8563
3.3406
2.4999
F
F
CF3
O
N
H
F
F
MeO
0.9647
1.8625
1.9545
3.0000
f1 (ppm)


SM-p-OMe-carbon_01
Std proton
164.4333
162.7924
130.3072
124.1505
113.9544
55.5707
40.1365
39.9279
39.7192
39.5104
39.3019
39.0931
38.8832
f1 (ppm)

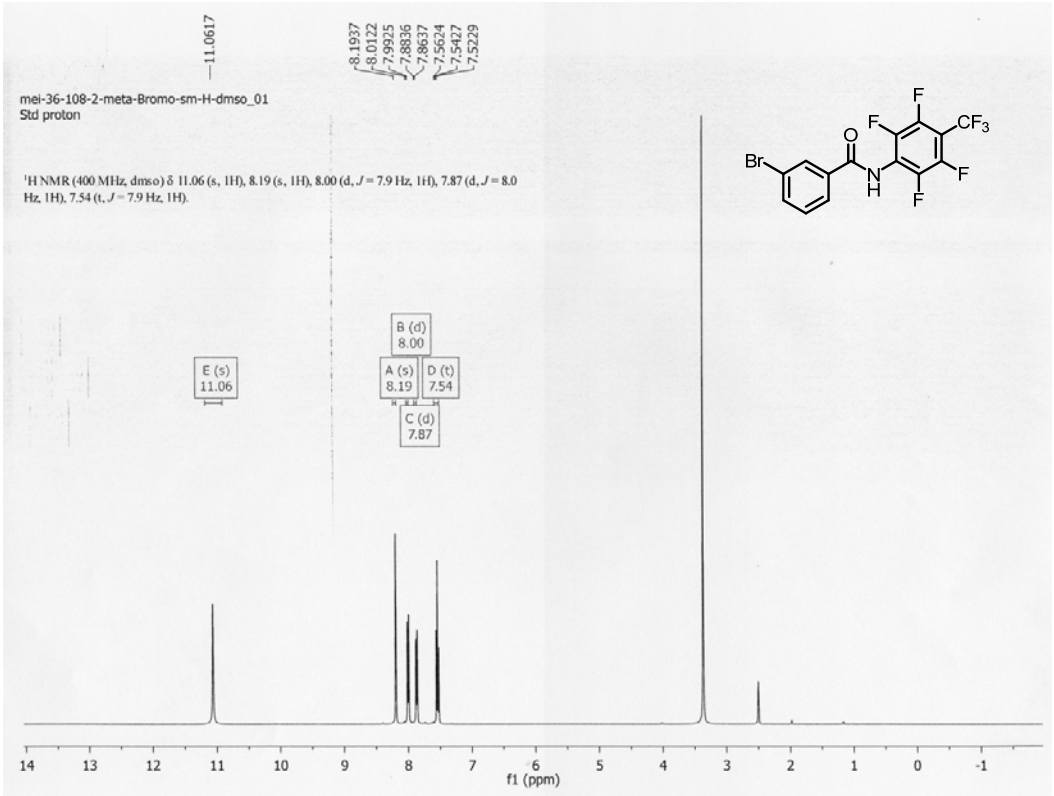

SM-p-F-protopn_01
Std proton
10.9775
8.1196
8.1059
8.0860
8.0842
7.4459
7.4239
7.4018
3.3699
2.4996
F
F
CF3
O
N
H
F
F
F
1.0000
2.0231
1.9572
f1 (ppm)
SM-p-F-carbon_01
Std proton
164.0586
163.4592
131.1602
131.0662
128.5971
115.9060
115.6865
f1 (ppm)

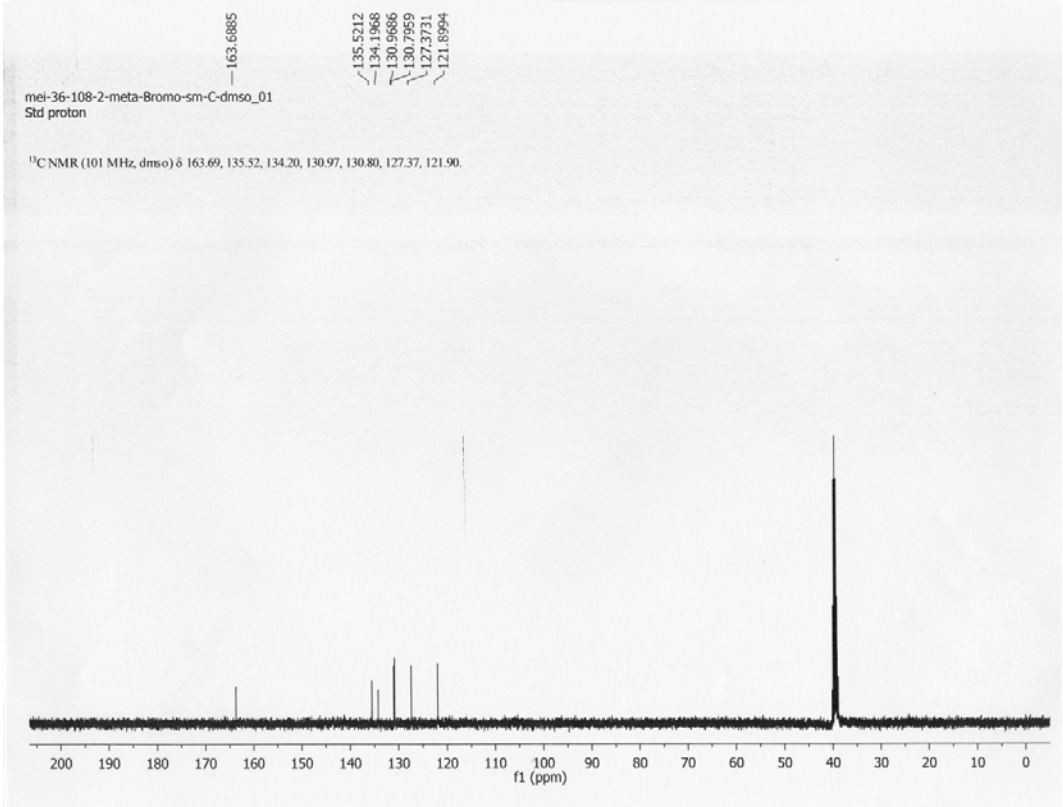


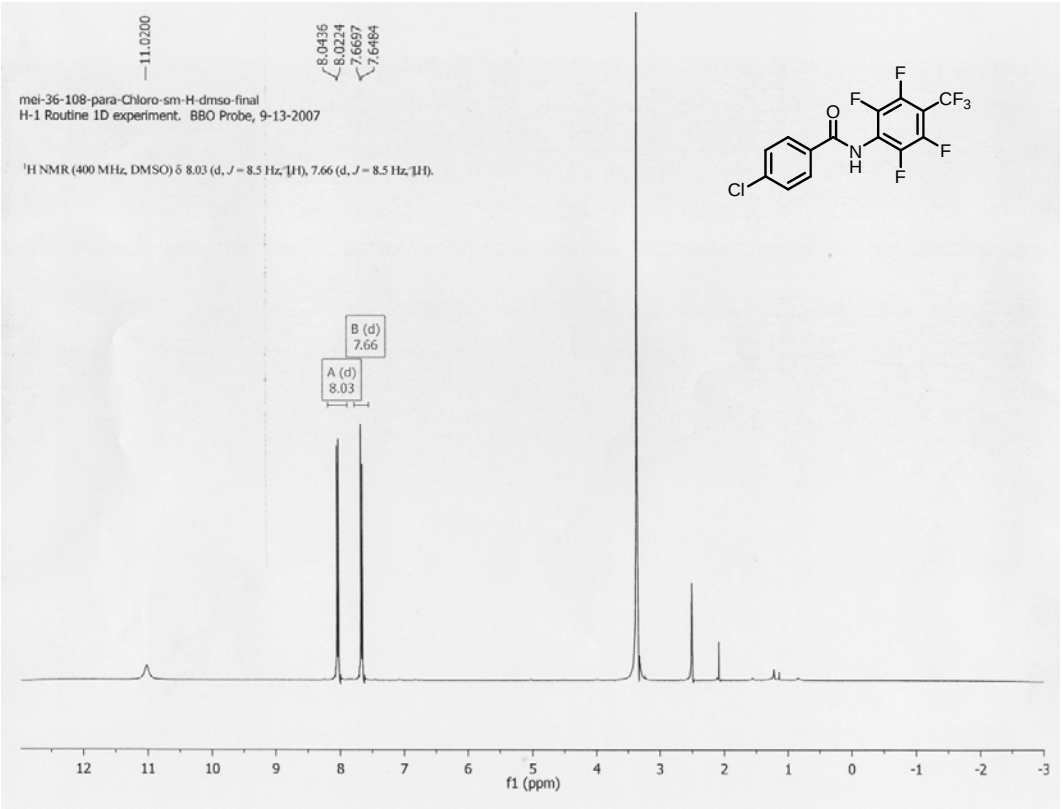
^{1}H NMR (400 MHz, dmso) δ 11.06 (s, 1H), 8.05 (d, J = 1.6 Hz, 1H), 7.97 (d, J = 7.8 Hz, 1H), 7.74 (dd, J = 8.0, 1.0 Hz, 1H), 7.61 (t, J = 7.9 Hz, 1H).

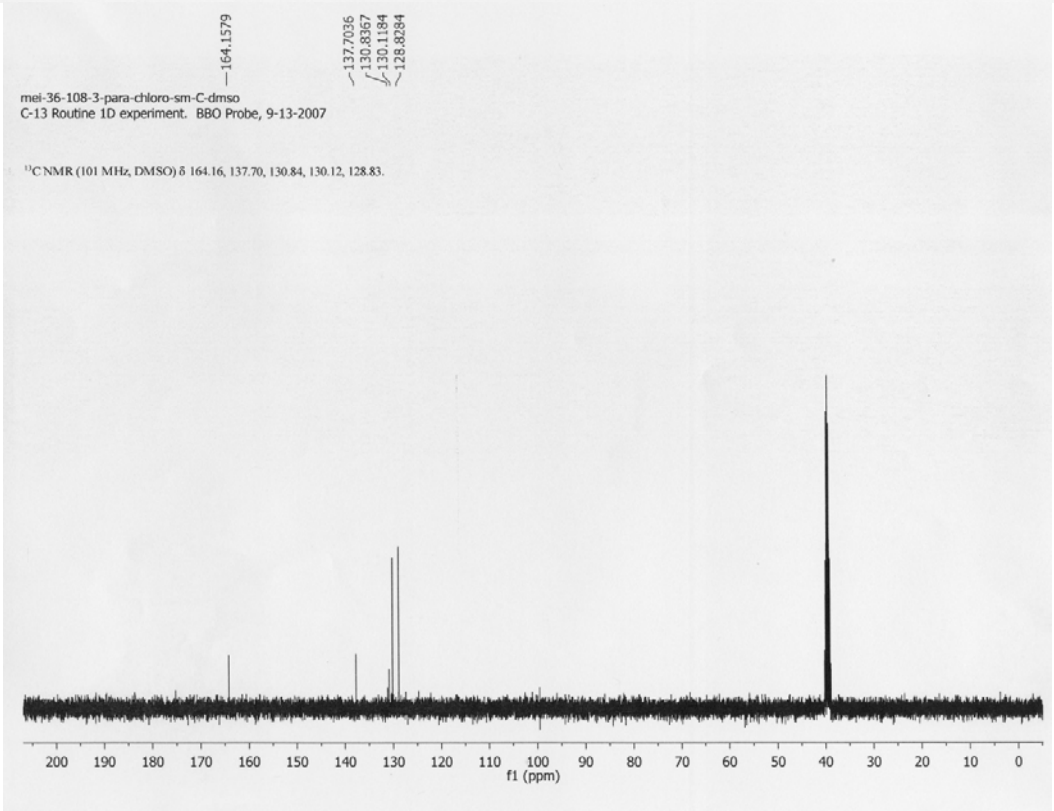


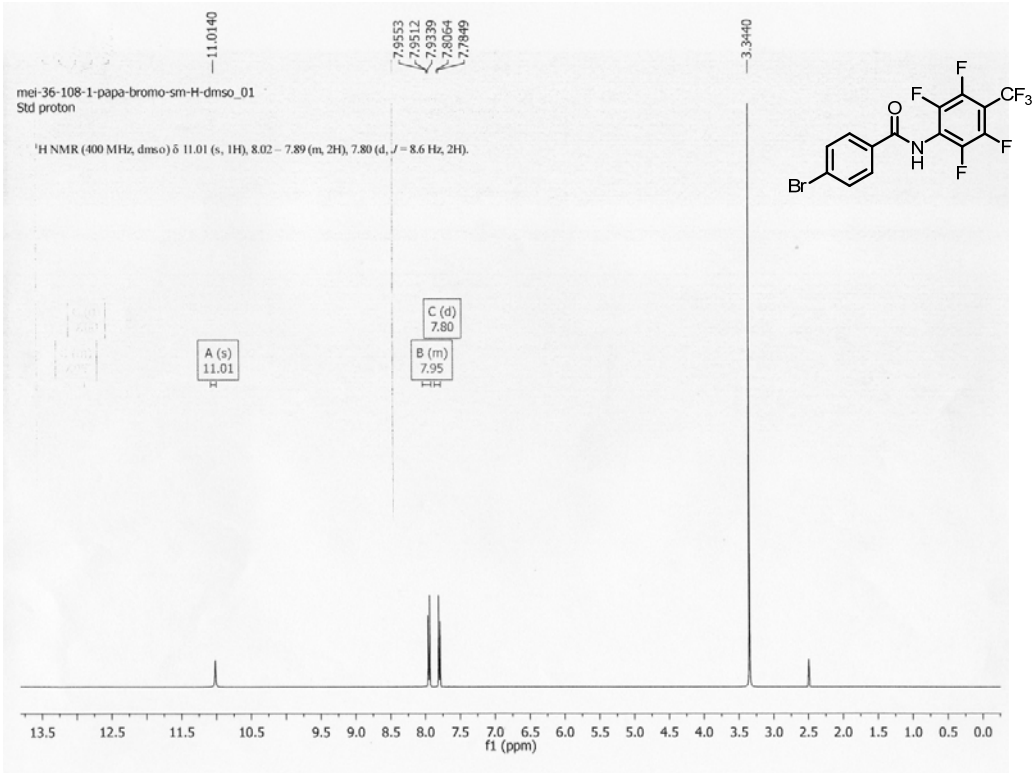
^{13}C NMR (101 MHz, dmso) δ 163.78, 134.02, 133.52, 132.62, 130.74, 127.95, 126.99.

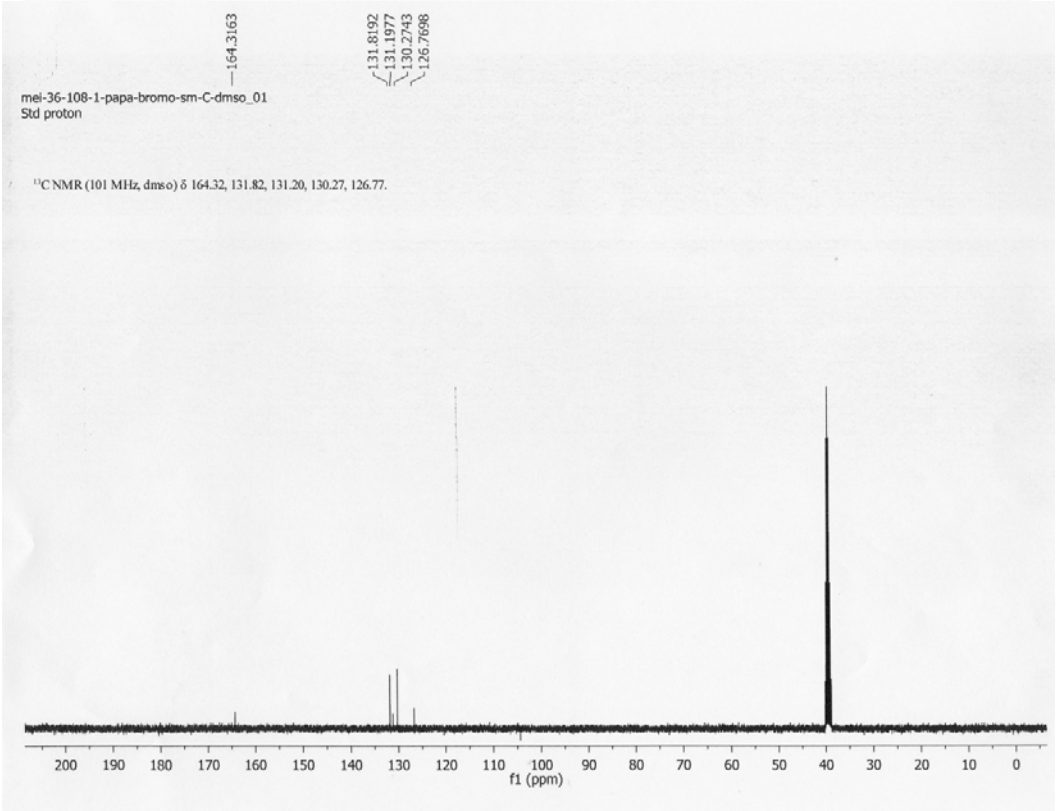

11.0617
8.1937
8.0122
7.9925
7.8836
7.8637
7.5624
7.5427
7.5229
mei-36-108-2-meta-Bromo-sm-H-dmso_01
Std proton
^{1}H NMR (400 MHz, dmso) δ 11.06 (s, 1H), 8.19 (s, 1H), 8.00 (d, J = 7.9 Hz, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.54 (t, J = 7.9 Hz, 1H).
E (s) 11.06
B (d) 8.00
A (s) 8.19
D (t) 7.54
C (d) 7.87
Br
O
N
H
F
F
CF3
F
F
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

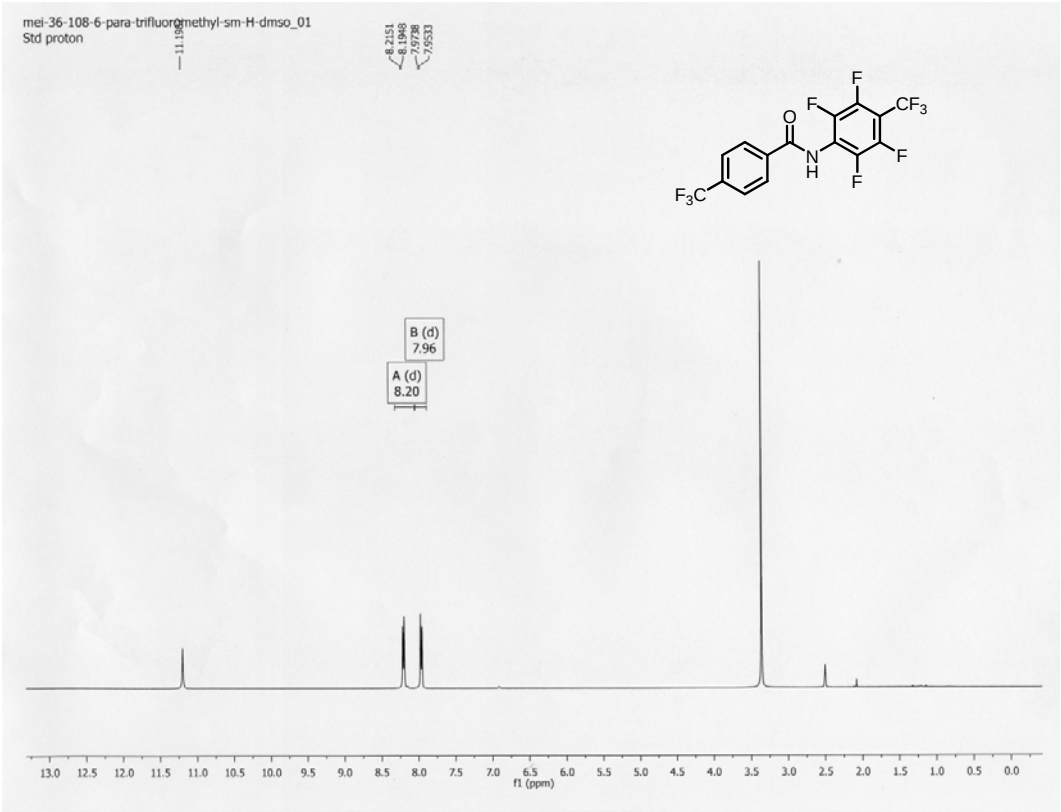

163.6885
135.5212
134.1968
130.9686
130.7959
127.3731
121.8994
mei-36-108-2-meta-Bromo-sm-C-dmso_01
Std proton
^{13}C NMR (101 MHz, dmso) δ 163.69, 135.52, 134.20, 130.97, 130.80, 127.37, 121.90.
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

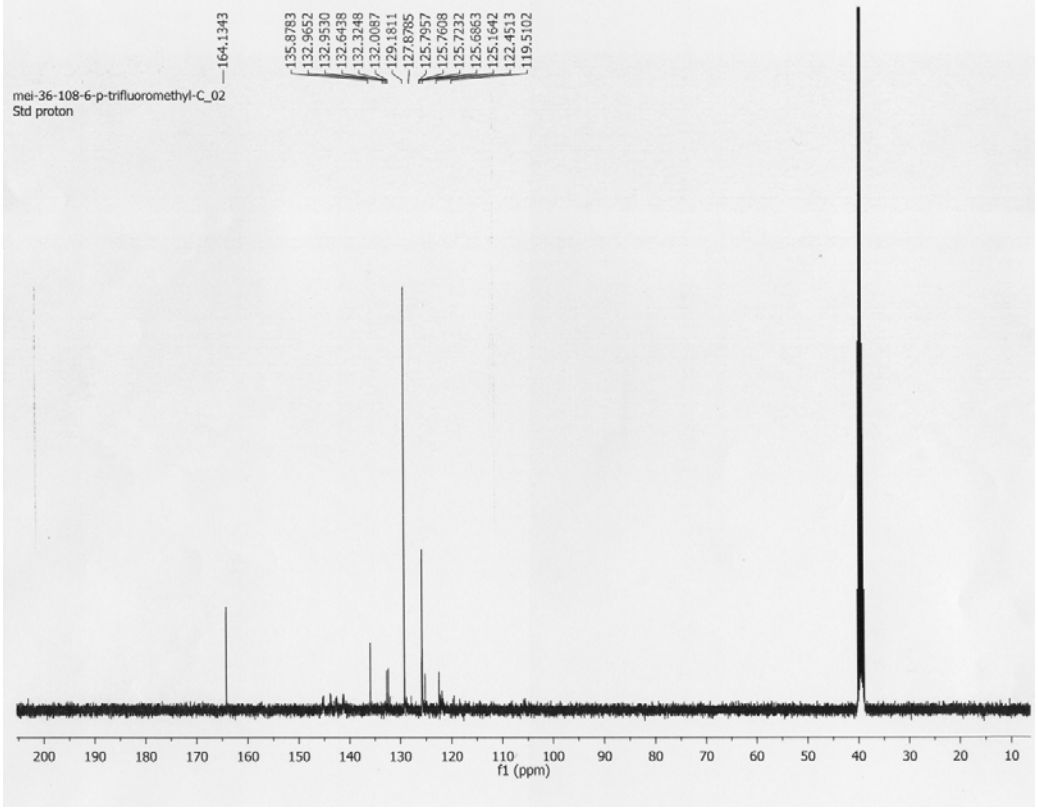

11.0200
8.0436
8.0224
7.6697
7.6484
mei-36-108-para-Chloro-sm-H-dmso-final
H-1 Routine 1D experiment. BBO Probe, 9-13-2007
¹H NMR (400 MHz, DMSO) δ 8.03 (d, J = 8.5 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H).
B (d)
7.66
A (d)
8.03
F
F
CF3
O
N
H
F
F
Cl
12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)

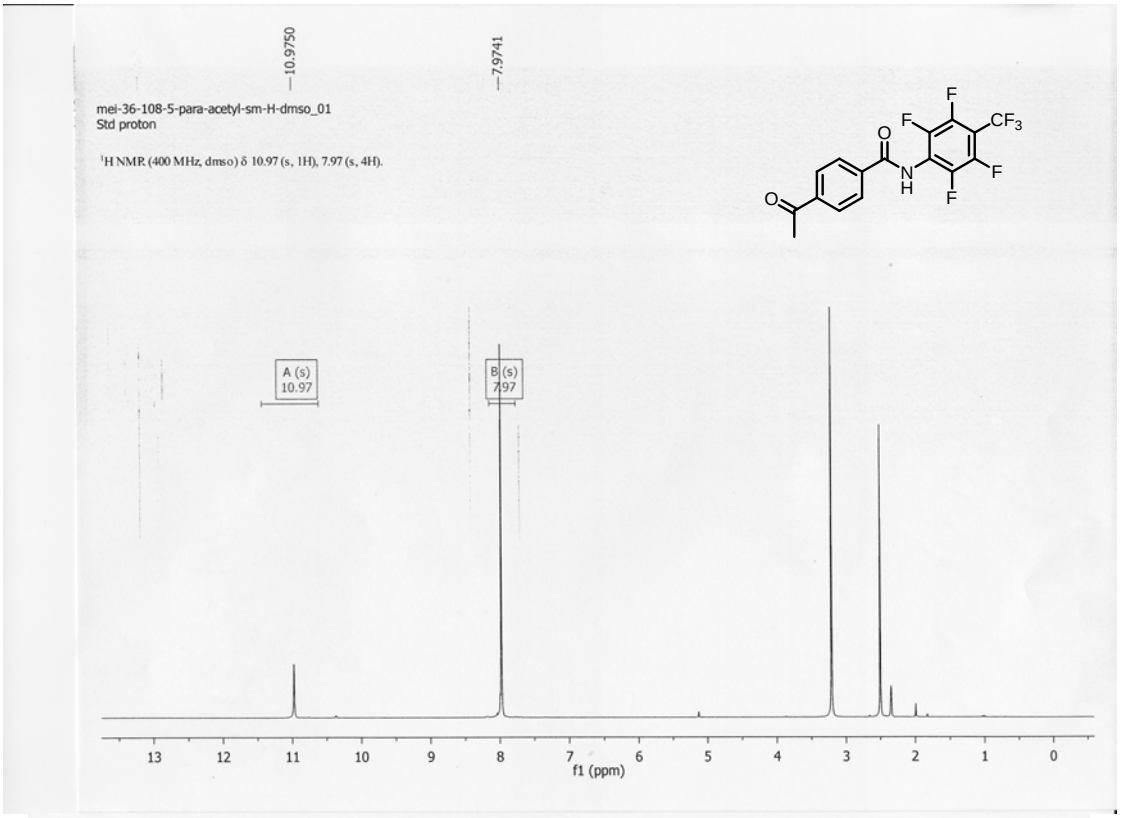

164.1579
137.7036
130.8367
130.1184
128.8284
mei-36-108-3-para-chloro-sm-C-dmso
C-13 Routine 1D experiment. BBO Probe, 9-13-2007
¹³C NMR (101 MHz, DMSO) δ 164.16, 137.70, 130.84, 130.12, 128.83.
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

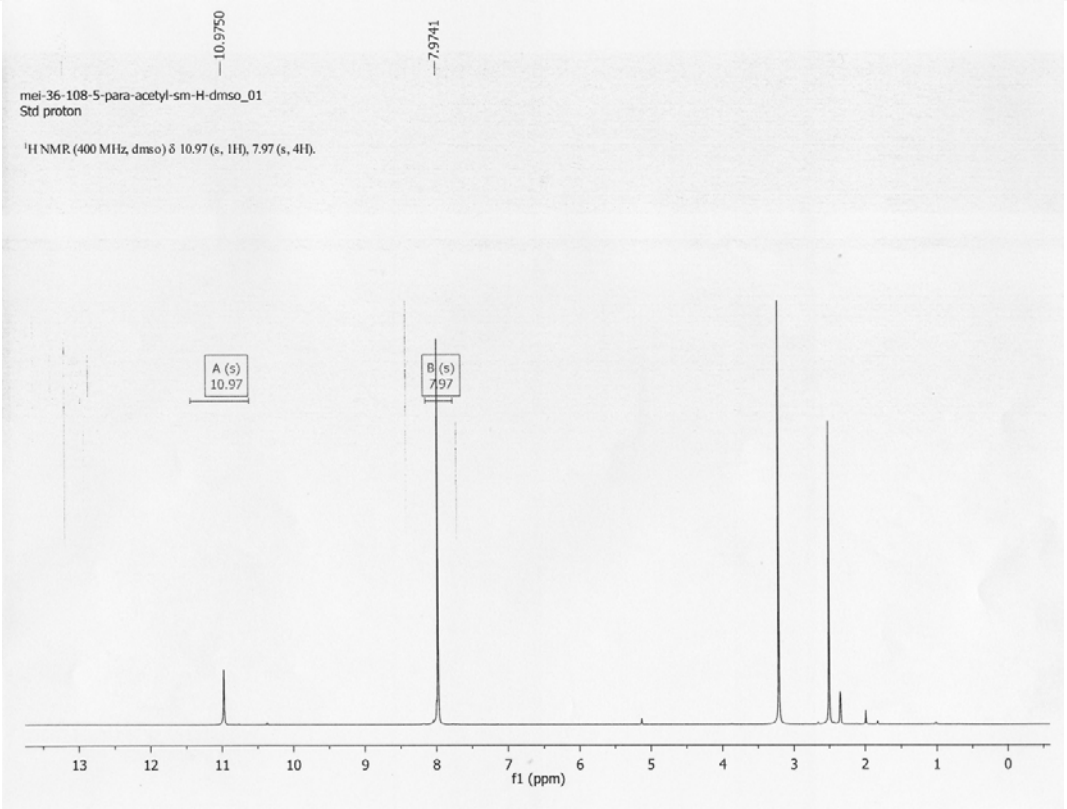

11.0140
7.9553
7.9512
7.9339
7.8064
7.7849
3.3440
mei-36-108-1-papa-bromo-sm-H-dmso_01
Std proton
¹H NMR (400 MHz, dmso) δ 11.01 (s, 1H), 8.02 – 7.89 (m, 2H), 7.80 (d, J = 8.6 Hz, 2H).
A (s)
11.01
C (d)
7.80
B (m)
7.95
F
F
CF3
O
N
H
F
F
Br
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

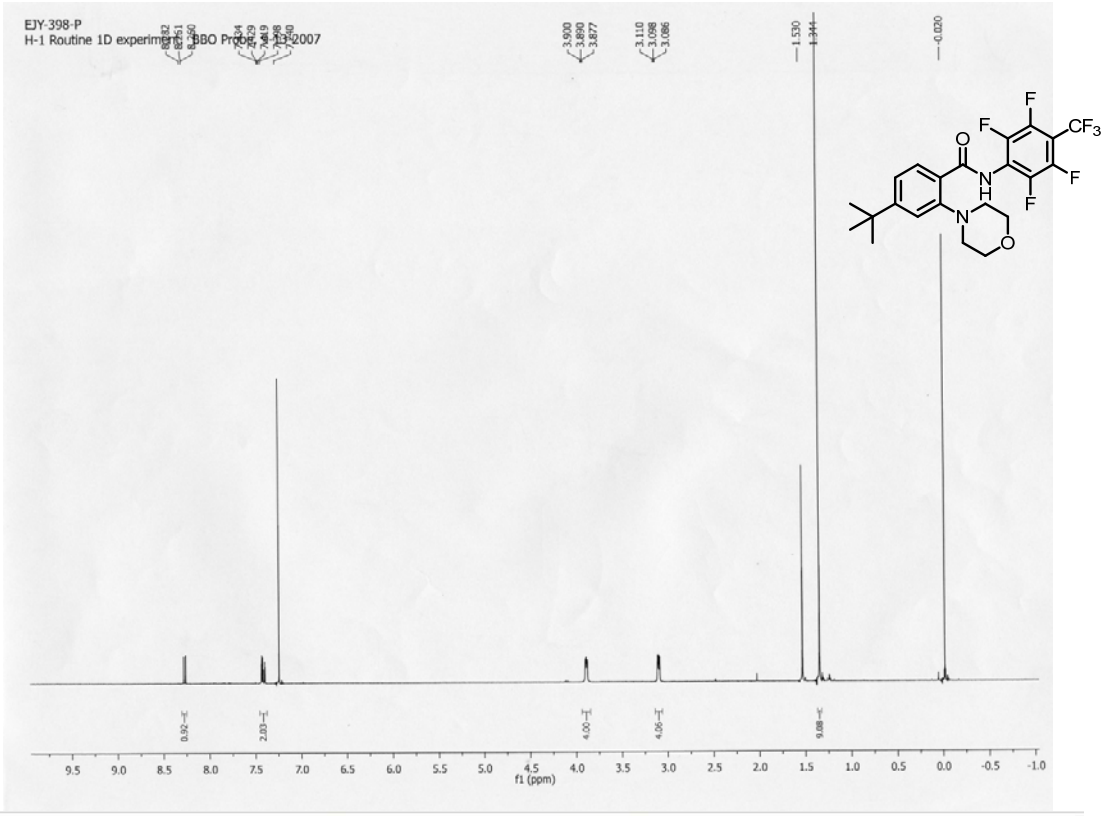

164.3163
131.8192
131.1977
130.2743
126.7698
mei-36-108-1-papa-bromo-sm-C-dmso_01
Std proton
¹³C NMR (101 MHz, dmso) δ 164.32, 131.82, 131.20, 130.27, 126.77.
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

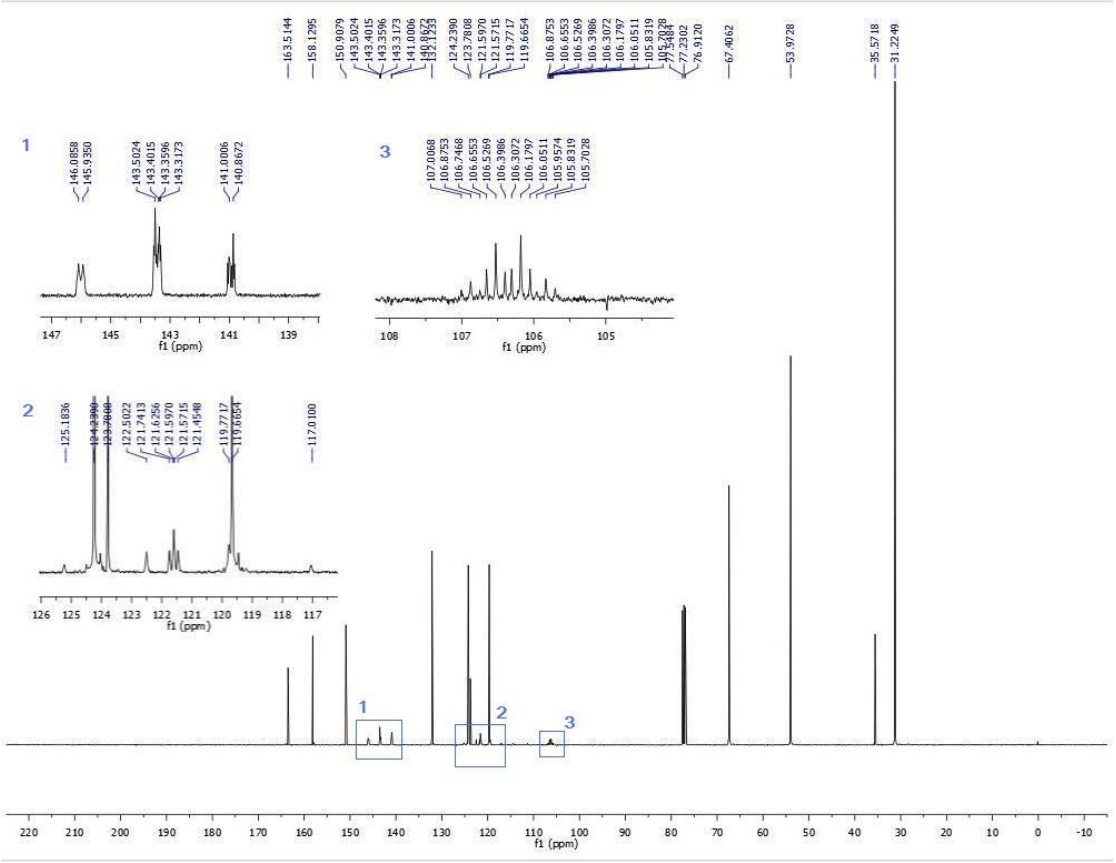

mei-36-108-6-para-trifluoromethyl-sm-H-dmso_01
Std proton
11.196
8.2151
8.1948
7.9738
7.9533
F
F
CF3
O
N
H
F
F
F3C
B (d)
7.96
A (d)
8.20
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

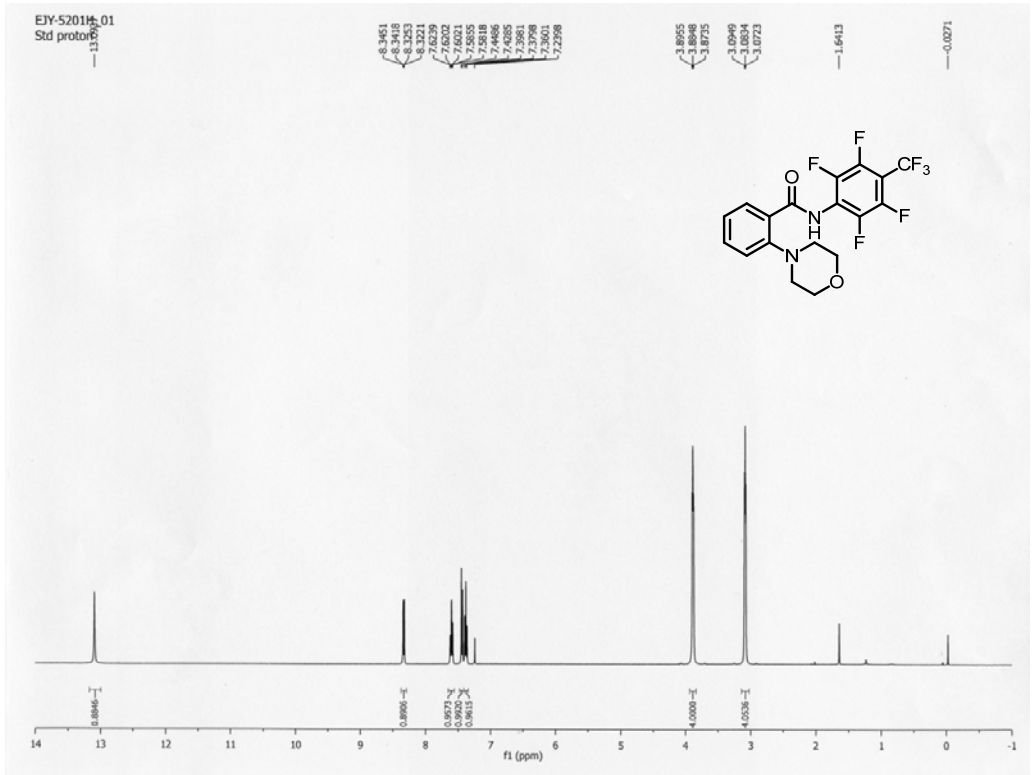

164.1343
135.8783
132.9652
132.9530
132.6438
132.3248
132.0087
129.1811
127.6785
125.7957
125.7608
125.7232
125.6863
125.1642
122.4513
119.5102
mei-36-108-6-p-trifluoromethyl-C_02
Std proton
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

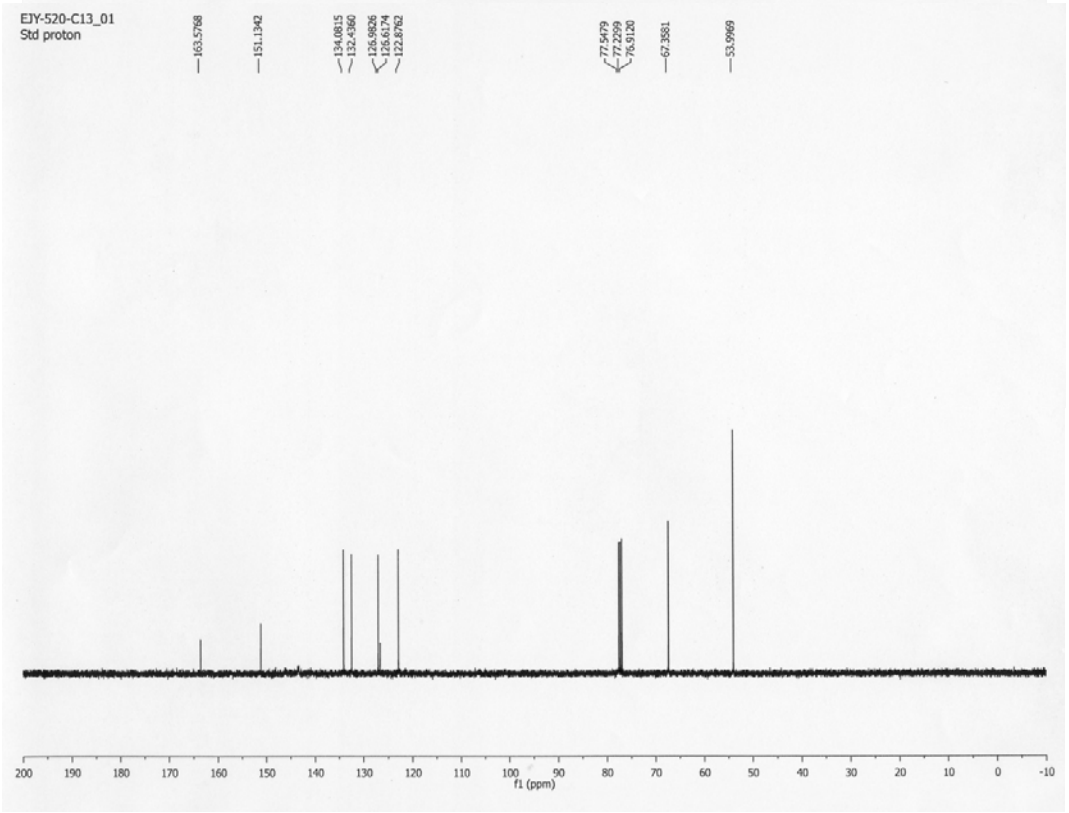

10.9750
7.9741
mei-36-108-5-para-acetyl-sm-H-dmso_01
Std proton
^{1}H NMR (400 MHz, dmso) δ 10.97 (s, 1H), 7.97 (s, 4H).
F
F
CF3
O
N
H
F
F
O
A (s)
10.97
B (s)
7.97
13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

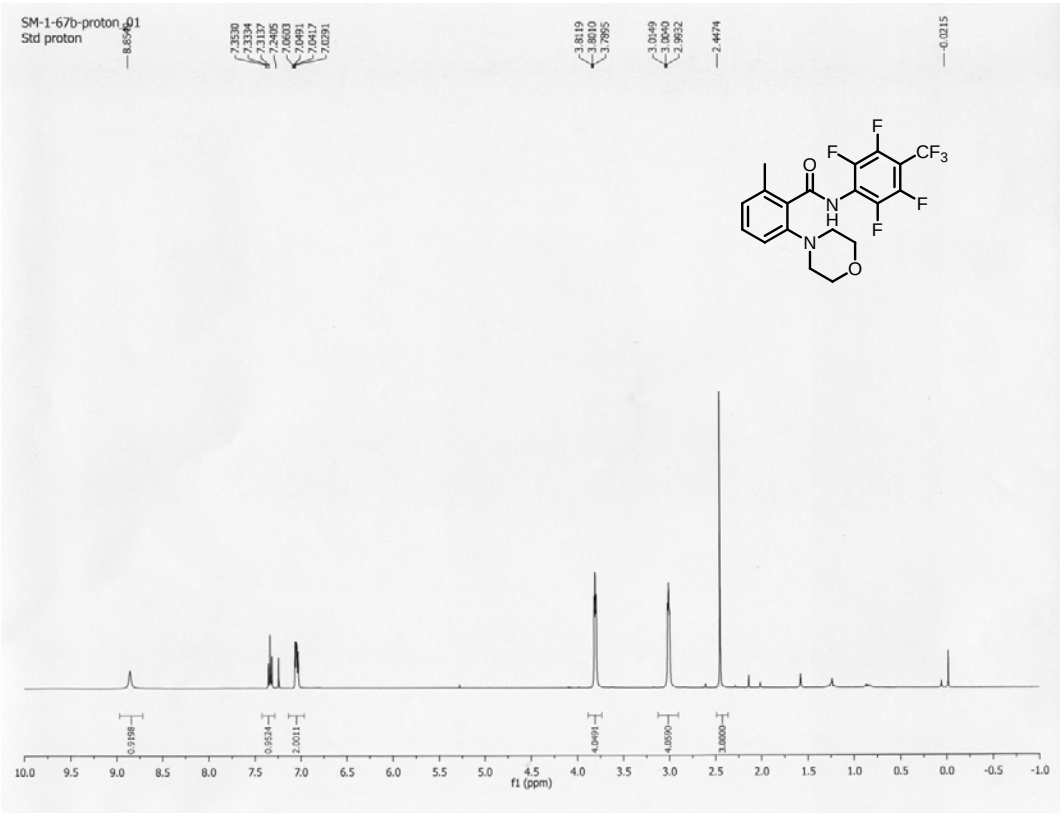

10.9750
7.9741
mei-36-108-5-para-acetyl-sm-H-dmso_01
Std proton
^{1}H NMR (400 MHz, dmso) δ 10.97 (s, 1H), 7.97 (s, 4H).
A (s)
10.97
B (s)
7.97
13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

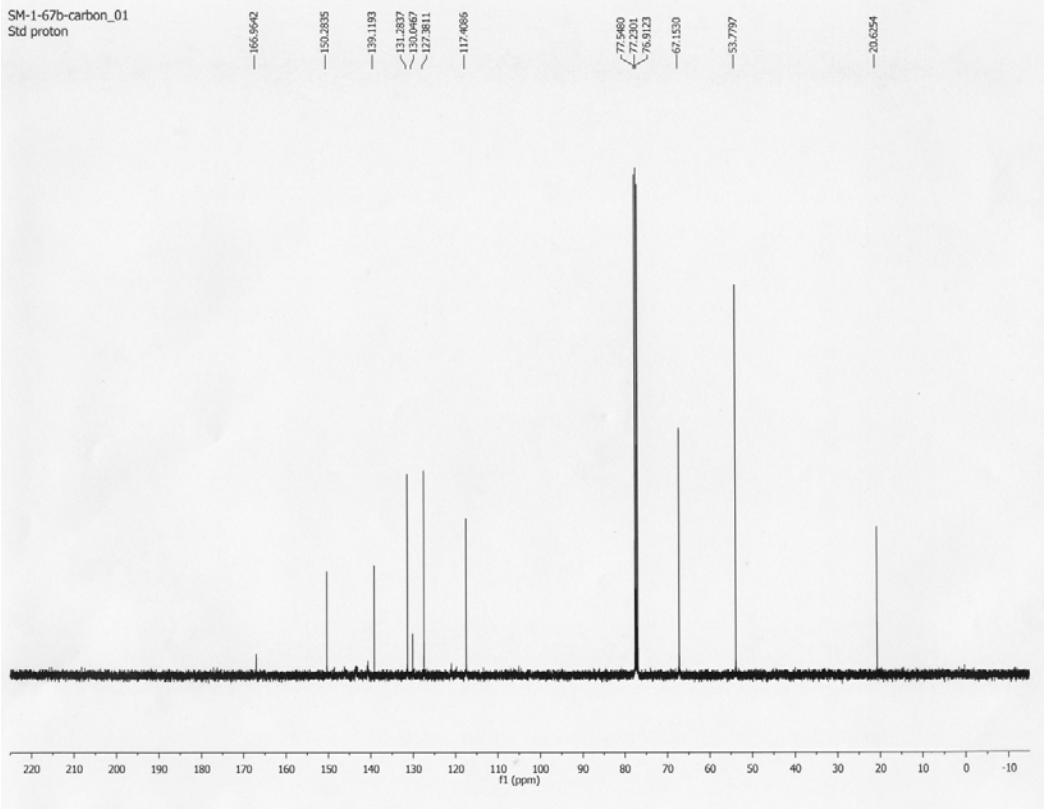

EJY-398-P
H-1 Routine 1D experiment, BBO Probe
f1 (ppm)

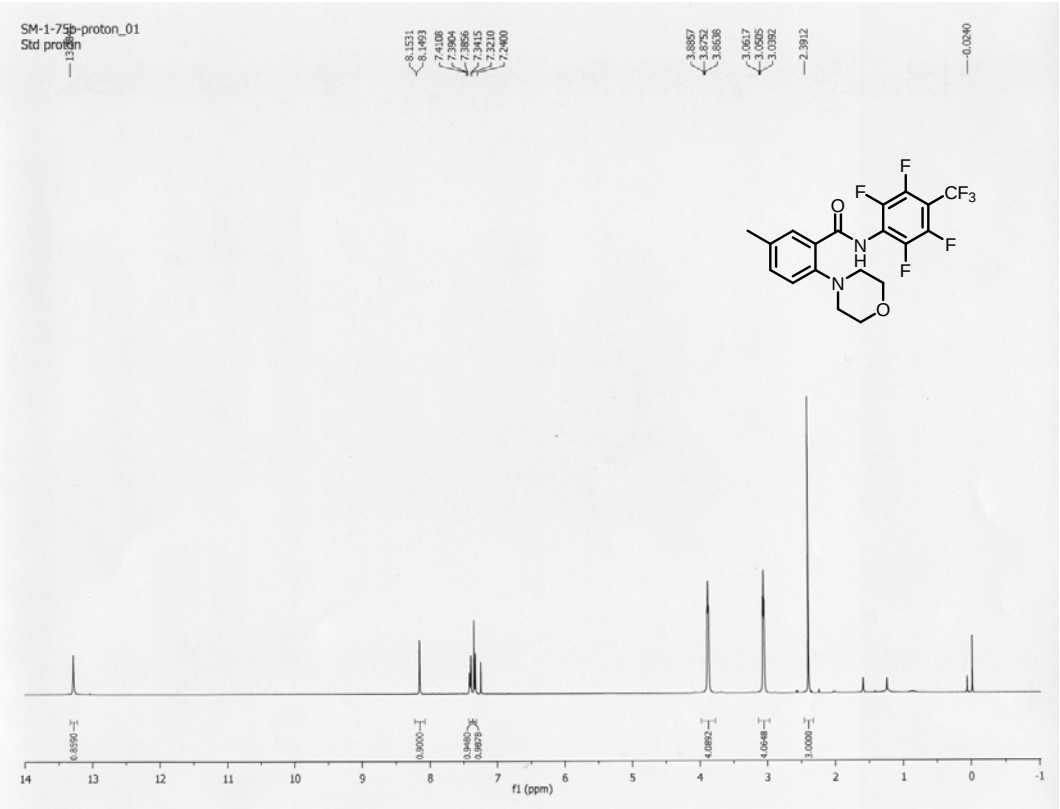

f1 (ppm)

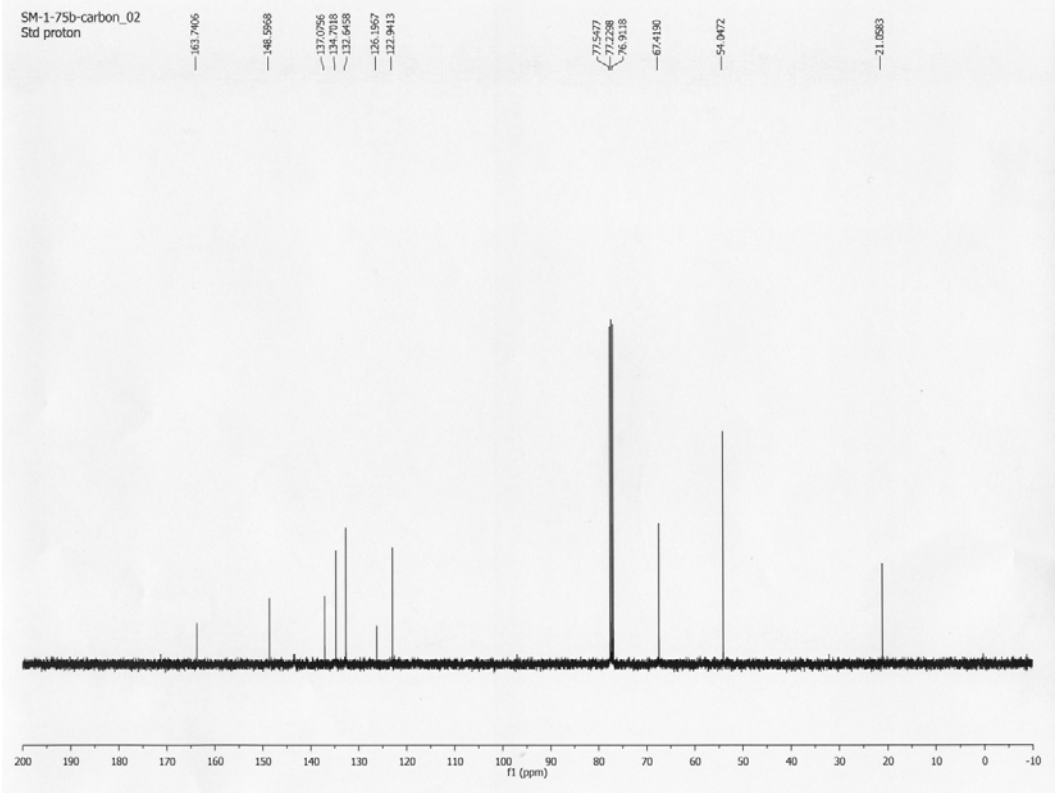

EJY-5201H_01
Std proton
F
F
CF3
O
N
H
F
F
N
O
f1 (ppm)

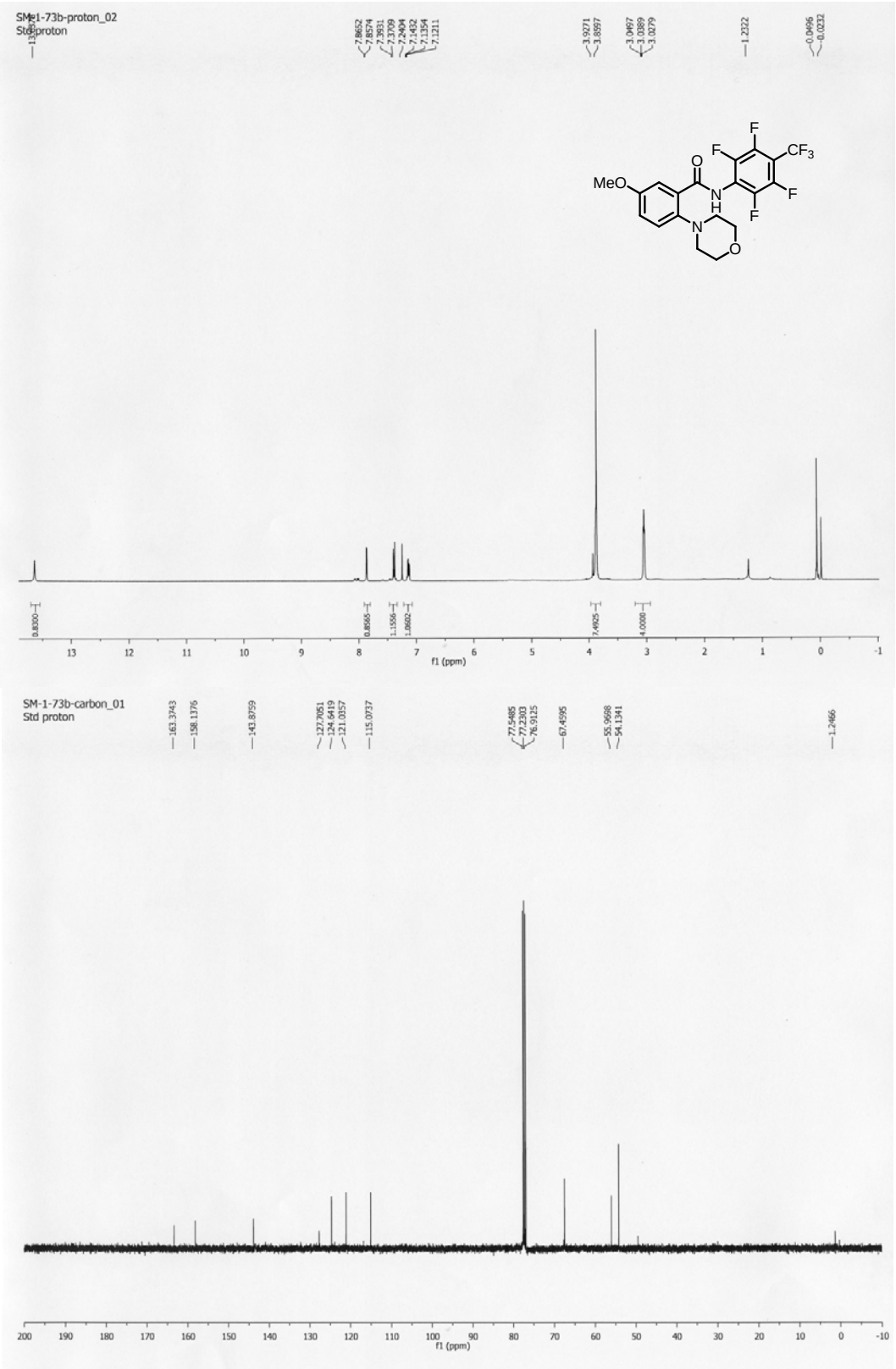

EJY-520-C13_01
Std proton
f1 (ppm)

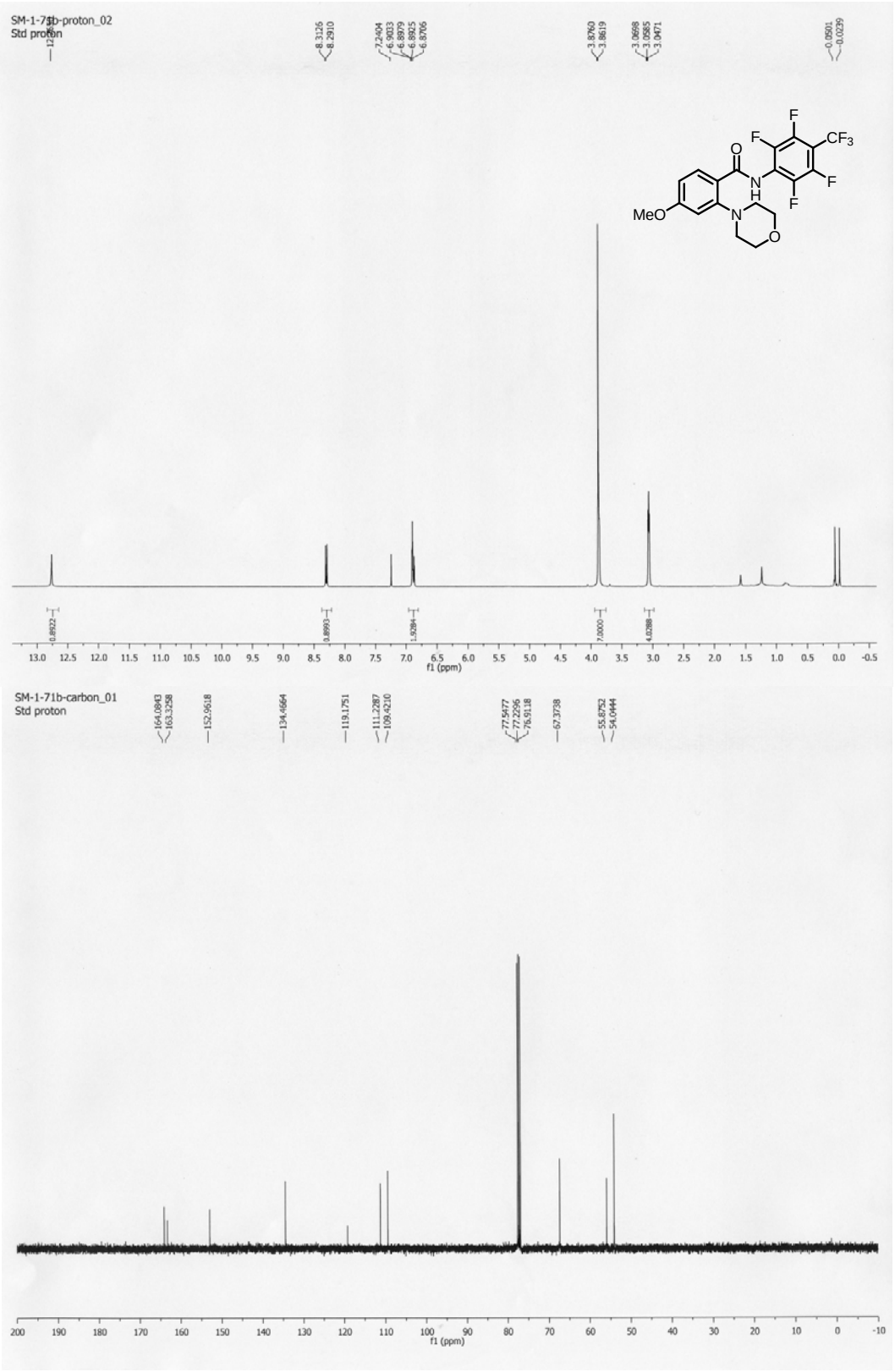

SM-1-67b-proton_01
Std proton
8.8548
7.3530
7.3334
7.3137
7.2405
7.0603
7.0491
7.0417
7.0291
3.8119
3.8010
3.7895
3.0049
3.0040
2.9932
2.4474
-0.0215
F
F
CF3
O
N
H
F
F
N
O
0.9198
0.9534
2.0011
4.0491
4.0590
3.0000
f1 (ppm)

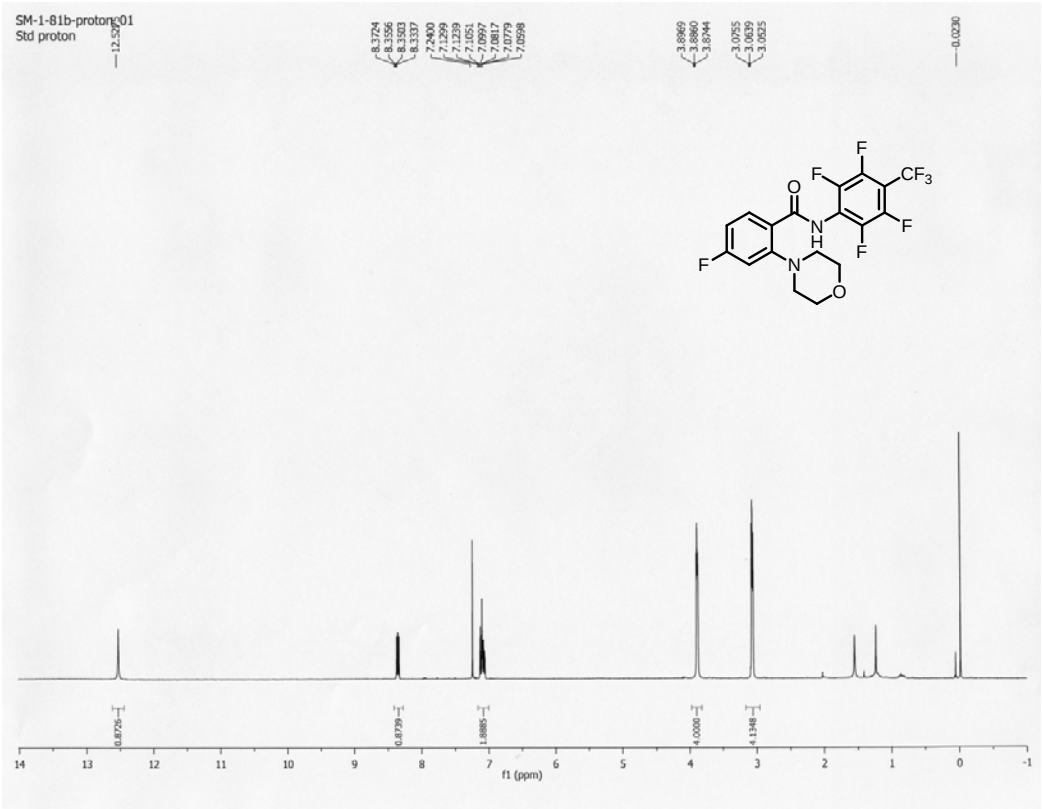

SM-1-67b-carbon_01
Std proton
166.9642
150.2835
139.1193
131.2837
130.9457
127.3811
117.4086
77.5460
77.2301
76.9123
67.1530
53.7797
20.6254
f1 (ppm)

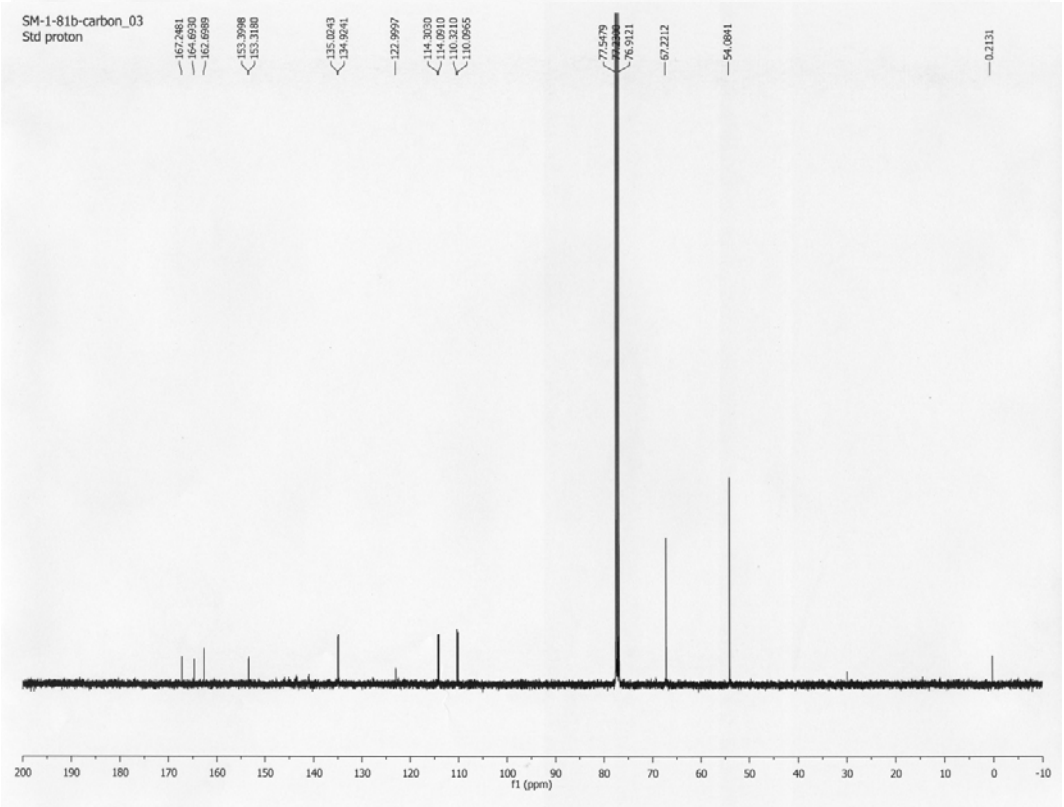

SM-1-75b-proton_01
Std proton
F
F
CF3
O
N
H
F
F
N
O
f1 (ppm)

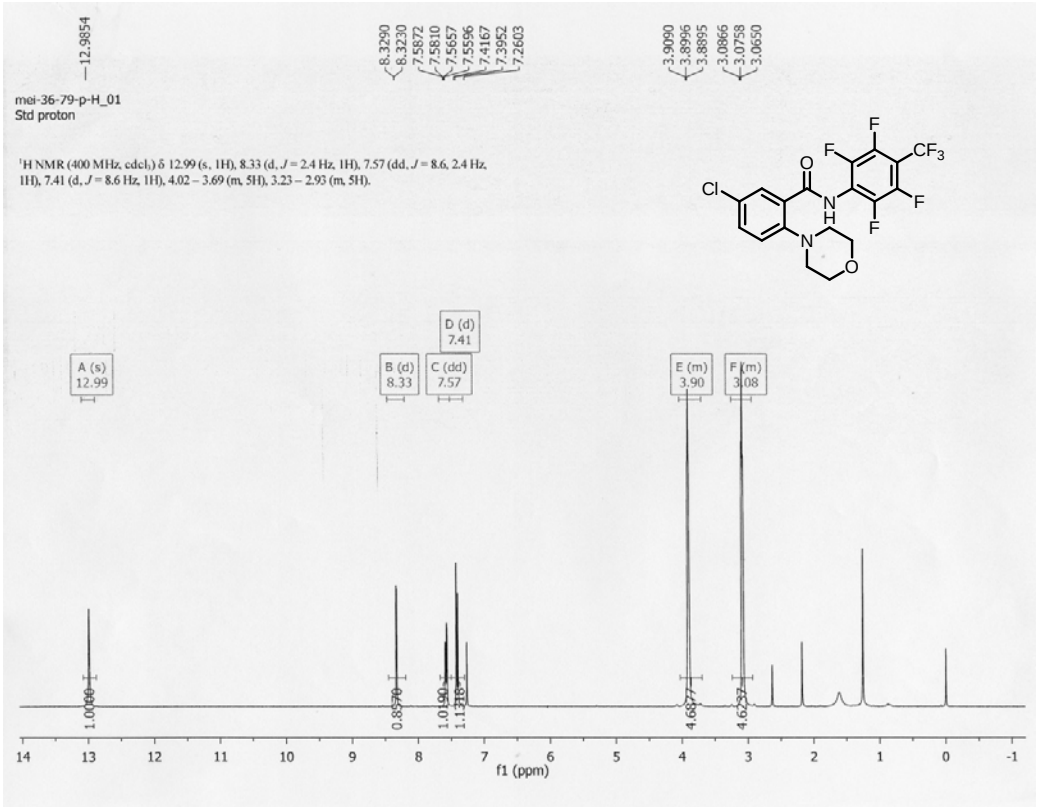

SM-1-75b-carbon_02
Std proton
f1 (ppm)

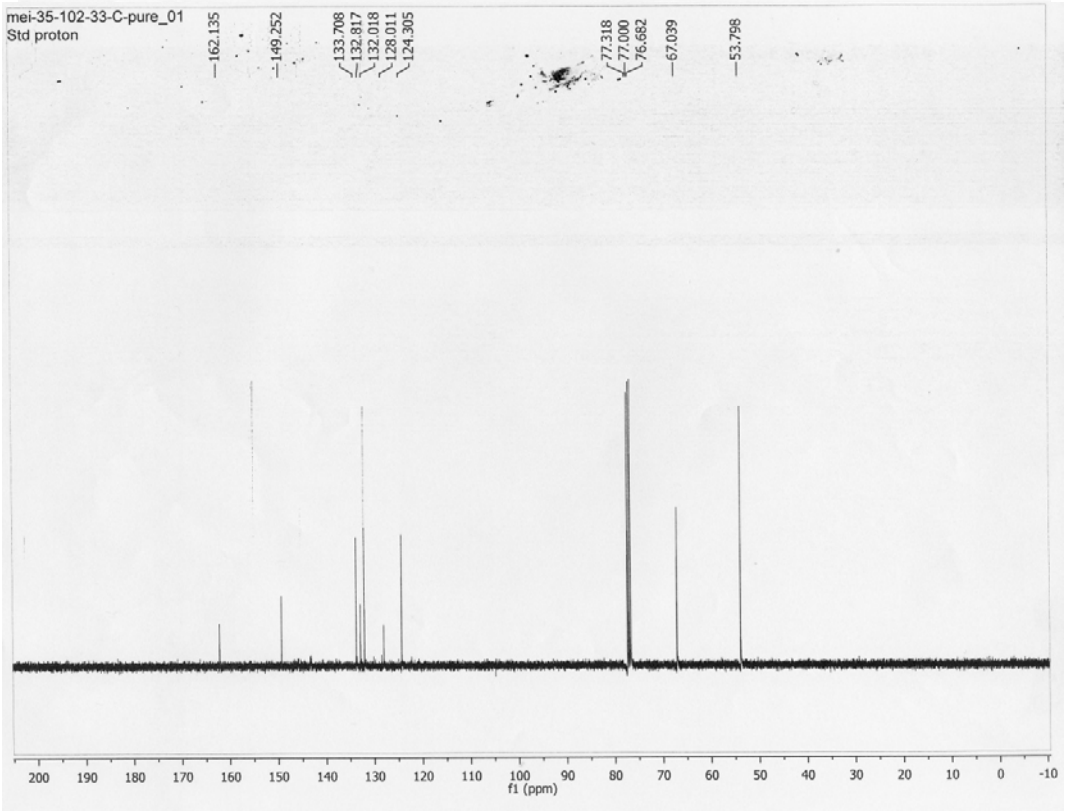

SM-1-73b-proton_02
Std proton
MeO
F
CF3
O
N
H
N
O
f1 (ppm)
SM-1-73b-carbon_01
Std proton
f1 (ppm)

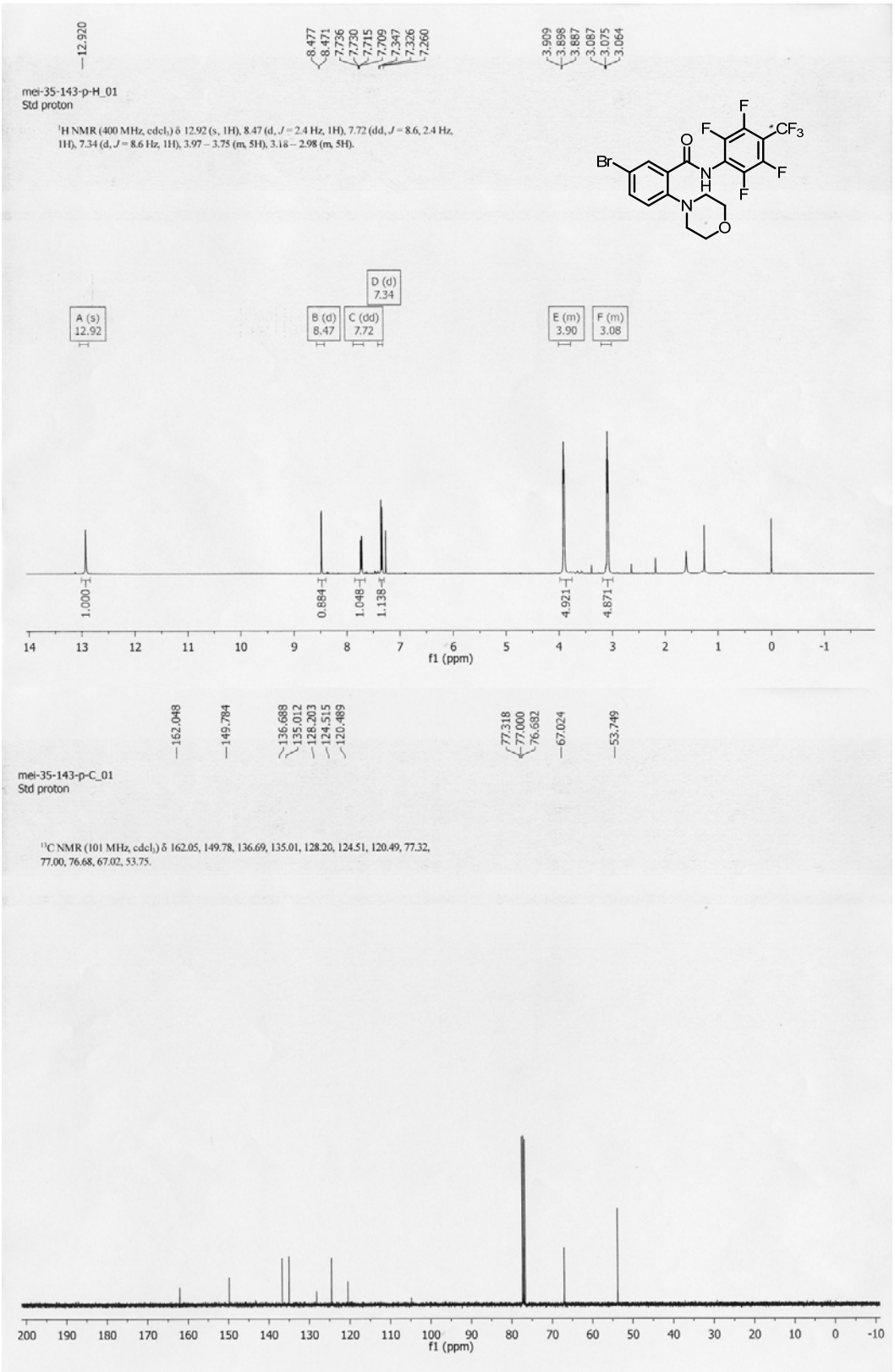

SM-1-71b-proton_02
Std proton
SM-1-71b-carbon_01
Std proton
f1 (ppm)
f1 (ppm)

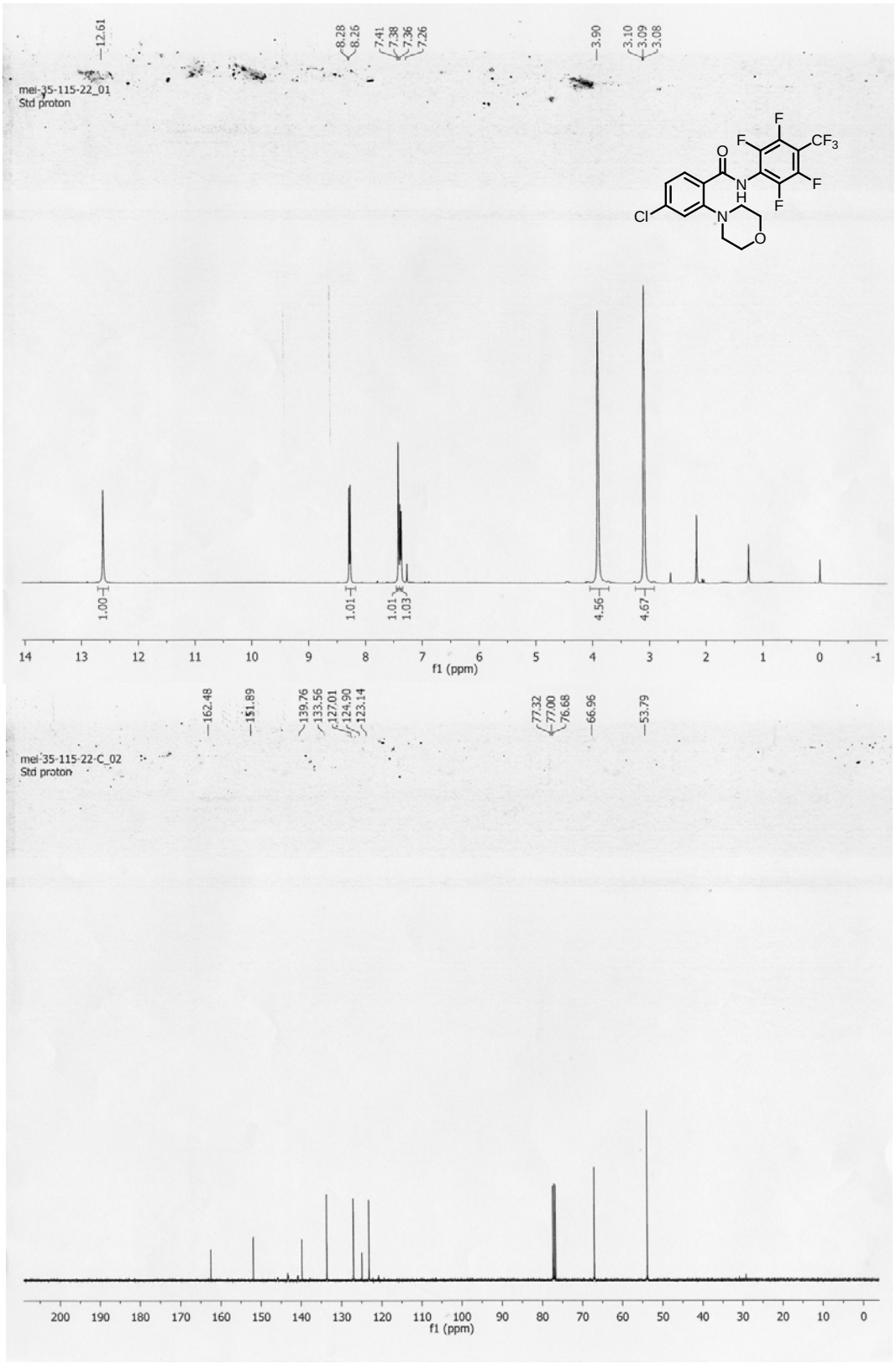

SM-1-81b-proton_01
Std proton
f1 (ppm)

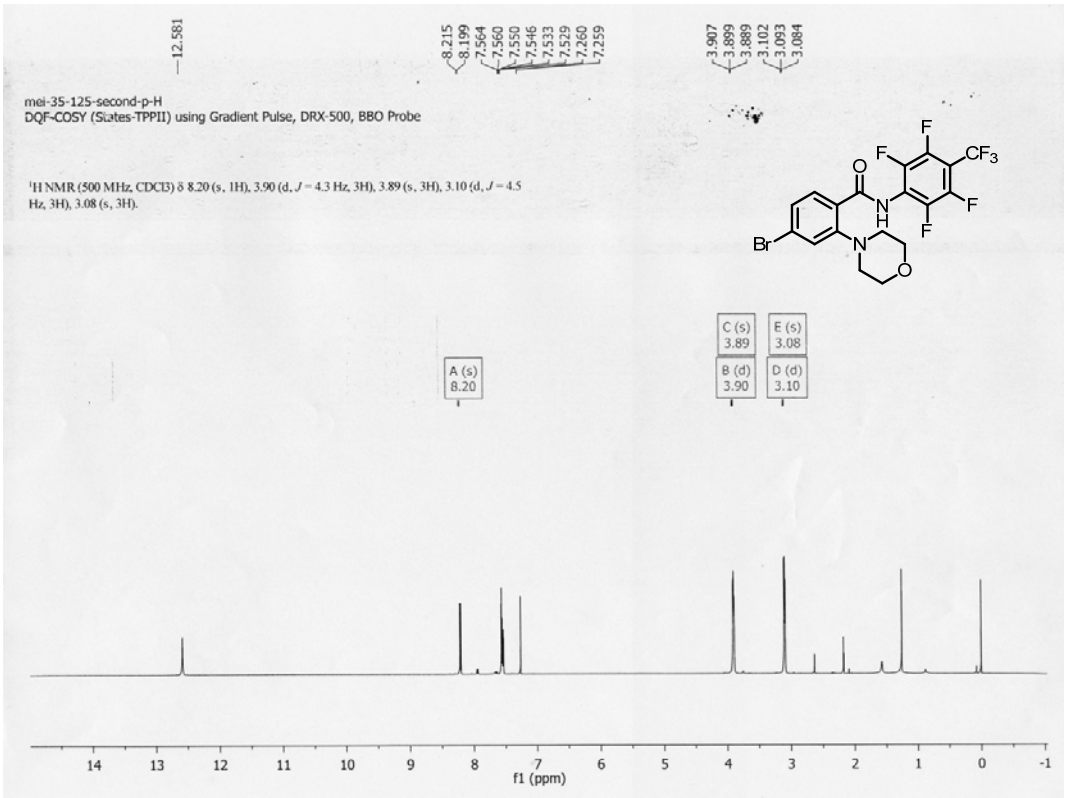

SM-1-81b-carbon_03
Std proton
f1 (ppm)

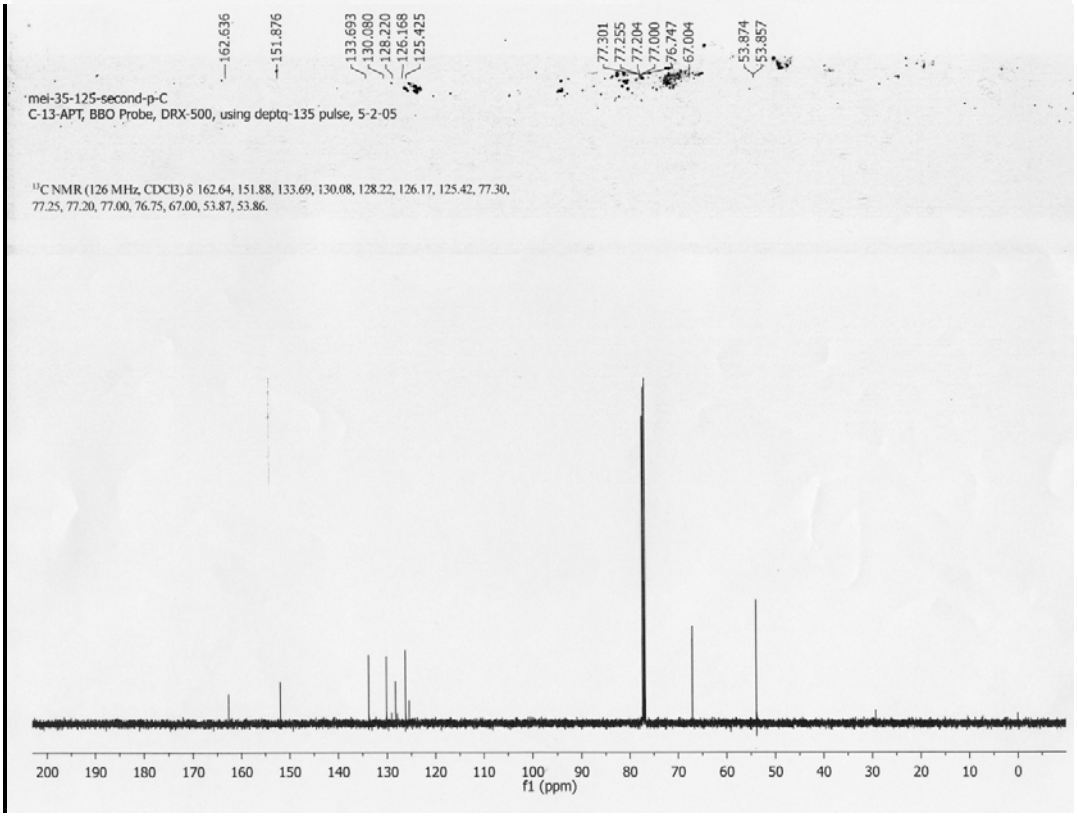

mei-36-79-p-H_01
Std proton
^{1}H NMR (400 MHz, cdcl$_3$) δ 12.99 (s, 1H), 8.33 (d, J = 2.4 Hz, 1H), 7.57 (dd, J = 8.6, 2.4 Hz, 1H), 7.41 (d, J = 8.6 Hz, 1H), 4.02 – 3.69 (m, 5H), 3.23 – 2.93 (m, 5H).
12.9854
8.3290
8.3230
7.5872
7.5810
7.5657
7.5596
7.4167
7.3952
7.2603
3.9090
3.8996
3.8895
3.0866
3.0758
3.0650
A (s) 12.99
B (d) 8.33
C (dd) 7.57
D (d) 7.41
E (m) 3.90
F (m) 3.08
1.0000
0.8970
1.0190
1.1318
4.6877
4.6237
f1 (ppm)

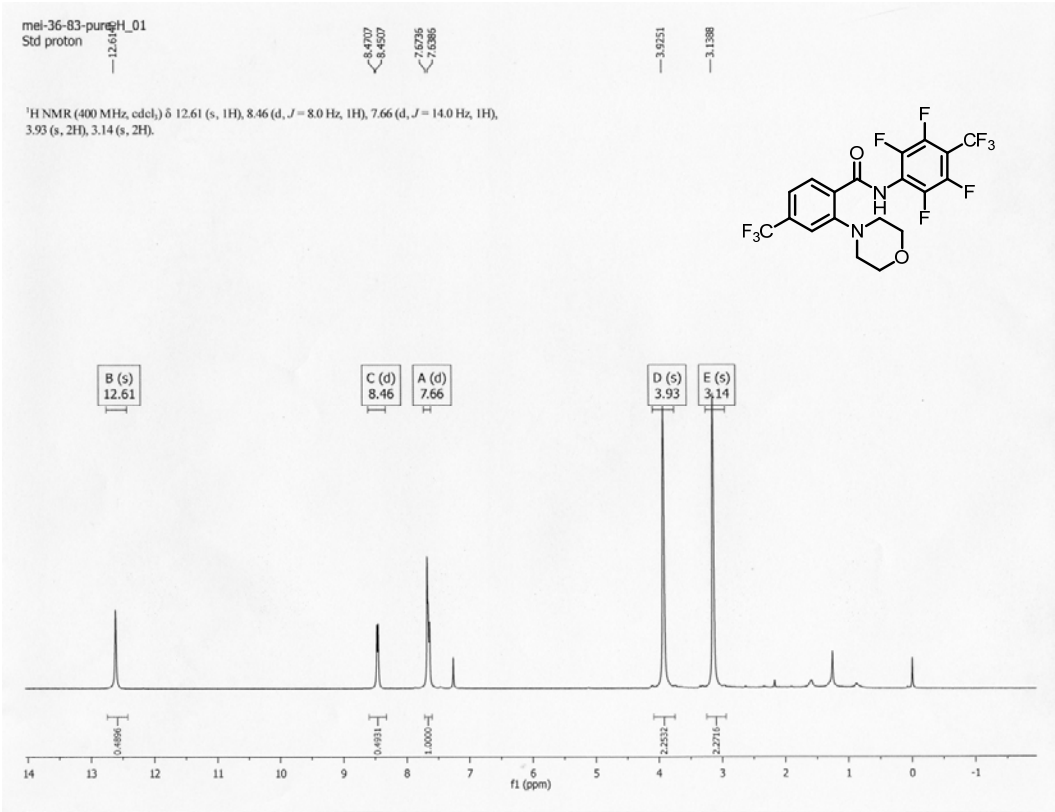

mei-35-102-33-C-pure_01
Std proton
162.135
149.252
133.708
132.817
132.018
128.011
124.305
77.318
77.000
76.682
67.039
53.798
f1 (ppm)

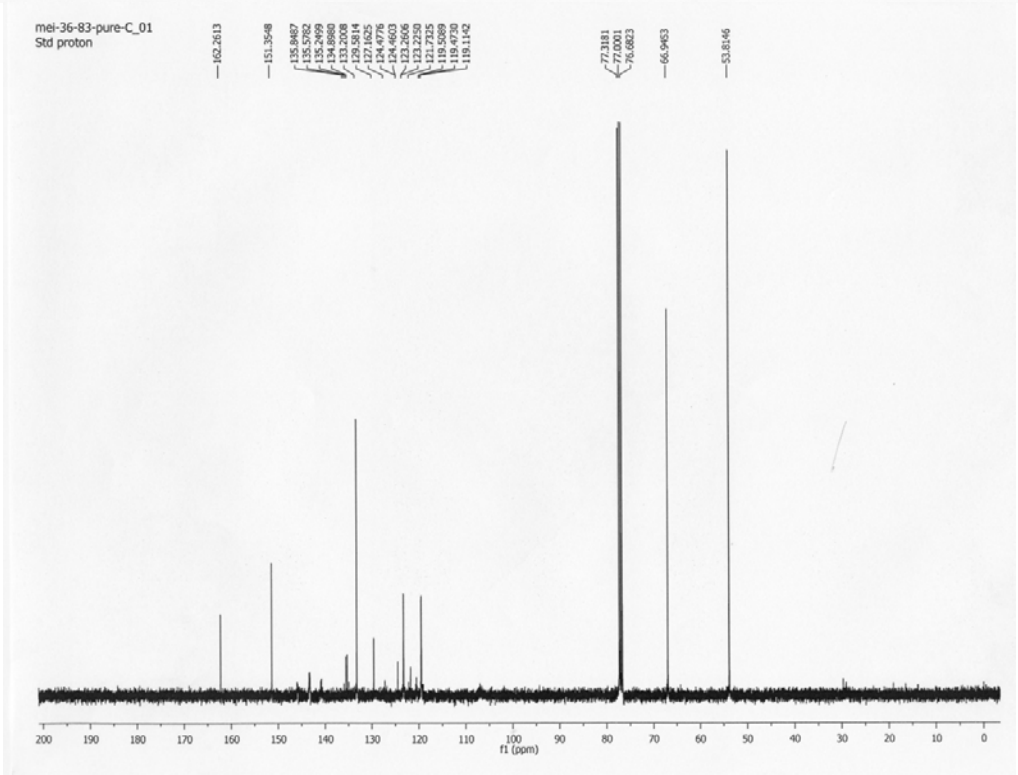

12.920
8.477
8.471
7.736
7.730
7.715
7.709
7.347
7.326
7.260
3.909
3.898
3.887
3.087
3.075
3.064
mei-35-143-p-H_01
Std proton
^{1}H NMR (400 MHz, cdcl$_3$) δ 12.92 (s, 1H), 8.47 (d, J = 2.4 Hz, 1H), 7.72 (dd, J = 8.6, 2.4 Hz, 1H), 7.34 (d, J = 8.6 Hz, 1H), 3.97 – 3.75 (m, 5H), 3.18 – 2.98 (m, 5H).
A (s) 12.92
B (d) 8.47
C (dd) 7.72
D (d) 7.34
E (m) 3.90
F (m) 3.08
1.000
0.884
1.048
1.138
4.921
4.871
f1 (ppm)
162.048
149.784
136.688
135.012
128.203
124.515
120.489
77.318
77.000
76.682
67.024
53.749
mei-35-143-p-C_01
Std proton
^{13}C NMR (101 MHz, cdcl$_3$) δ 162.05, 149.78, 136.69, 135.01, 128.20, 124.51, 120.49, 77.32, 77.00, 76.68, 67.02, 53.75.
f1 (ppm)

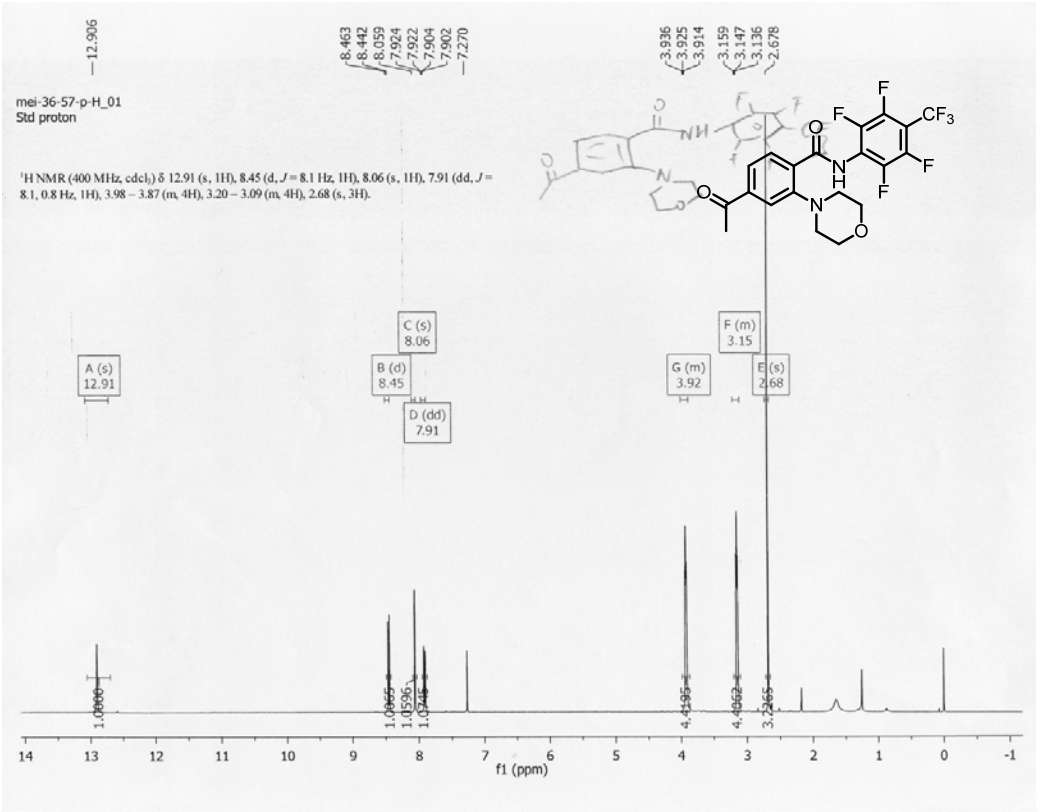

12.61
8.28
8.26
7.41
7.38
7.36
7.26
3.90
3.10
3.09
3.08
mei-35-115-22_01
Std proton
F
F
CF3
O
N
H
F
F
Cl
N
O
1.00
1.01
1.01
1.03
4.56
4.67
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
162.48
151.89
139.76
133.56
127.01
124.90
123.14
77.32
77.00
76.68
66.96
53.79
mei-35-115-22-C_02
Std proton
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

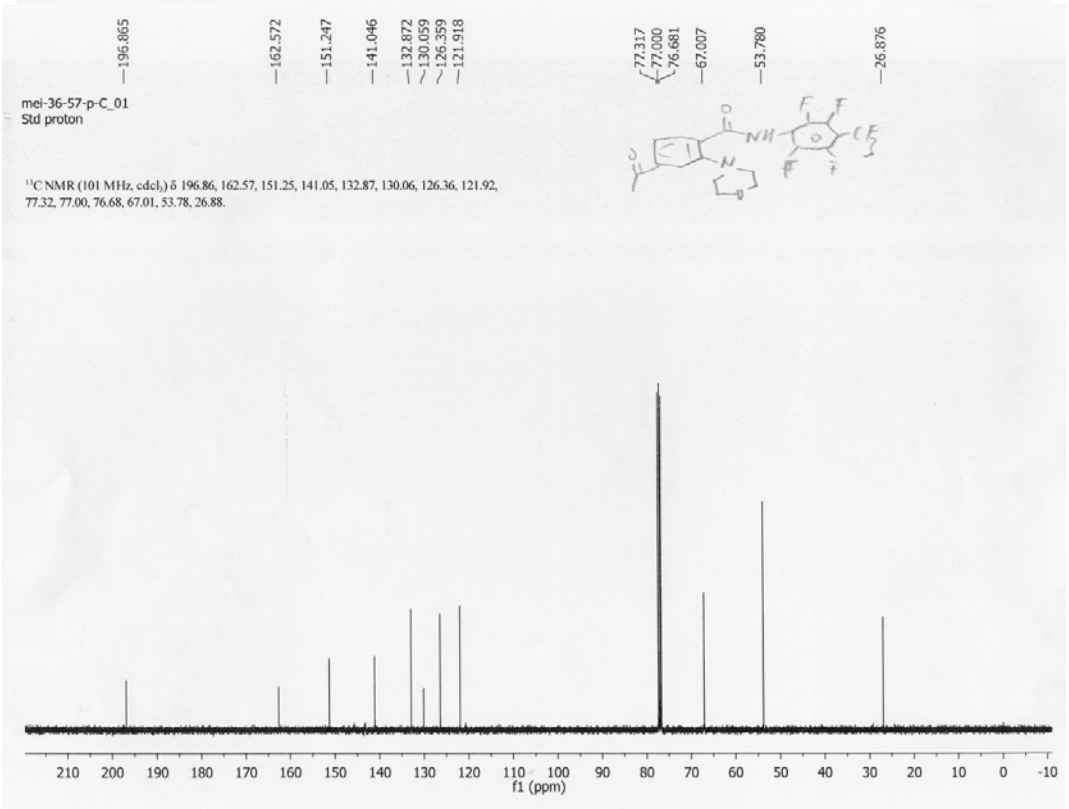

12.581
8.215
8.199
7.564
7.560
7.550
7.546
7.533
7.529
7.260
7.259
3.907
3.899
3.889
3.102
3.093
3.084
mei-35-125-second-p-H
DQF-COSY (States-TPPI) using Gradient Pulse, DRX-500, BBO Probe
¹H NMR (500 MHz, CDCl3) δ 8.20 (s, 1H), 3.90 (d, J = 4.3 Hz, 3H), 3.89 (s, 3H), 3.10 (d, J = 4.5 Hz, 3H), 3.08 (s, 3H).
A (s) 8.20
C (s) 3.89
E (s) 3.08
B (d) 3.90
D (d) 3.10
f1 (ppm)

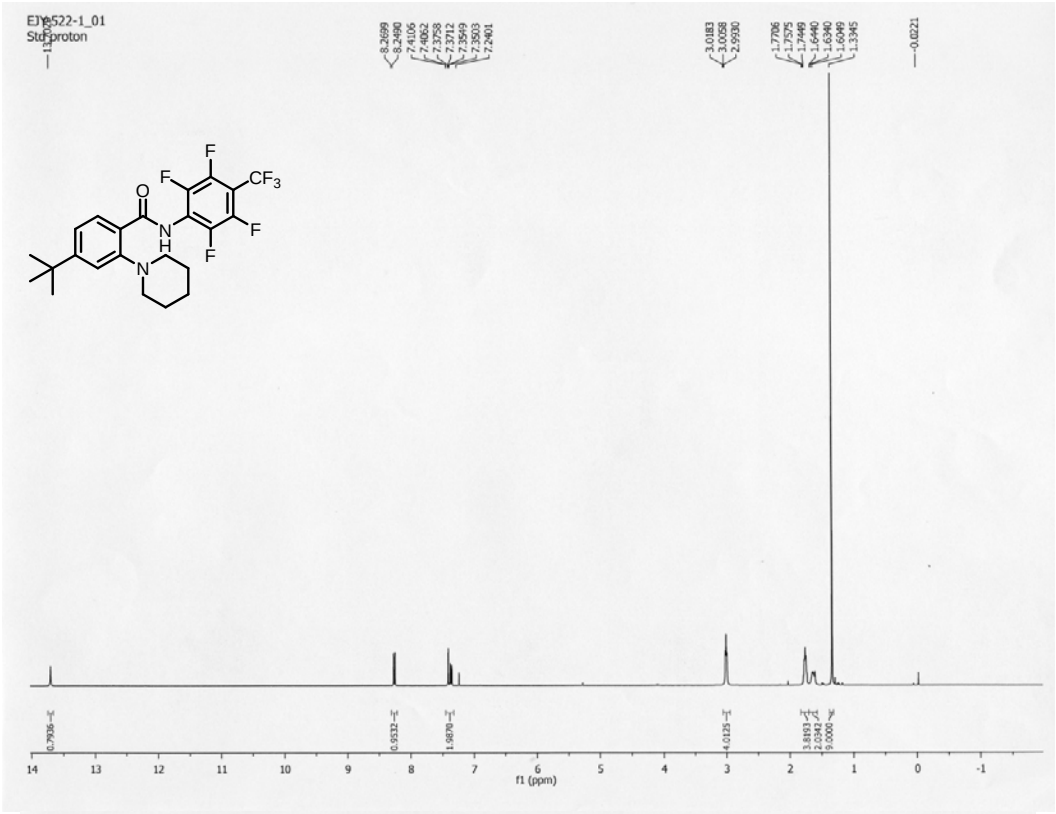

162.636
151.876
133.693
130.080
128.220
126.168
125.425
77.301
77.255
77.204
77.000
76.747
67.004
53.874
53.857
mei-35-125-second-p-C
C-13-APT, BBO Probe, DRX-500, using deptq-135 pulse, 5-2-05
¹³C NMR (126 MHz, CDCl3) δ 162.64, 151.88, 133.69, 130.08, 128.22, 126.17, 125.42, 77.30, 77.25, 77.20, 77.00, 76.75, 67.00, 53.87, 53.86.
f1 (ppm)

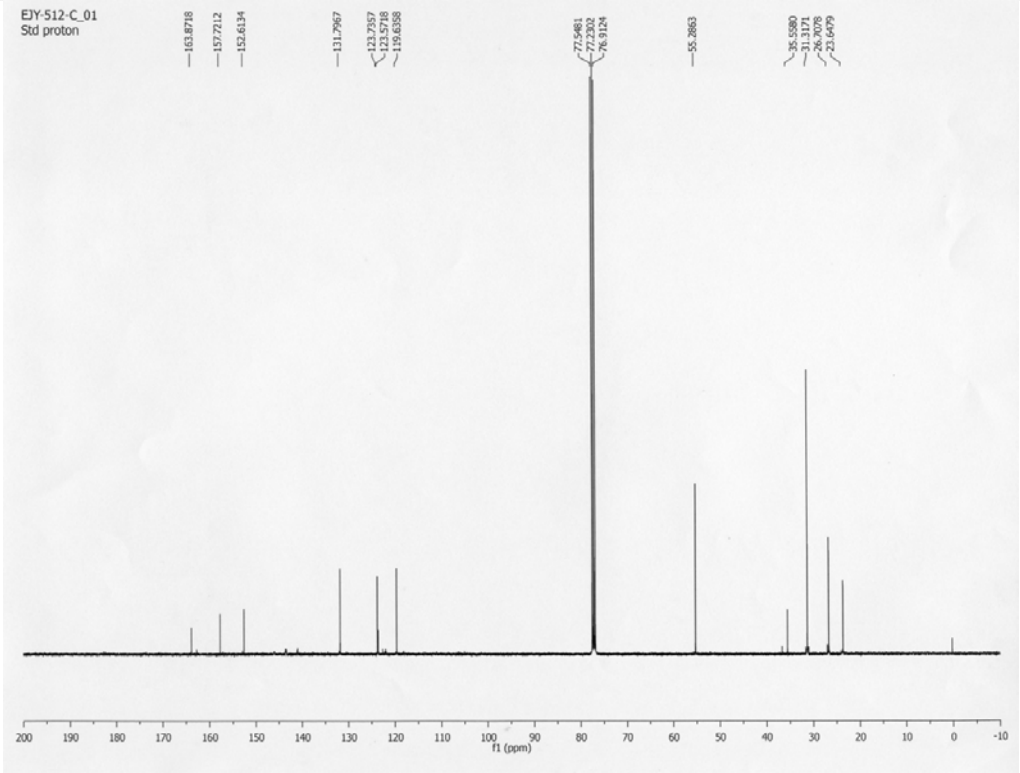

mei-36-83-pure-H_01
Std proton
12.614
8.4707
8.4507
7.6736
7.6586
3.9251
3.1388
^{1}H NMR (400 MHz, cdcl$_3$) δ 12.61 (s, 1H), 8.46 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 14.0 Hz, 1H), 3.93 (s, 2H), 3.14 (s, 2H).
F
F
CF$_3$
O
N
H
F
F
F$_3$C
N
O
B (s) 12.61
C (d) 8.46
A (d) 7.66
D (s) 3.93
E (s) 3.14
0.4896
0.4931
1.0000
2.2532
2.2716
f1 (ppm)

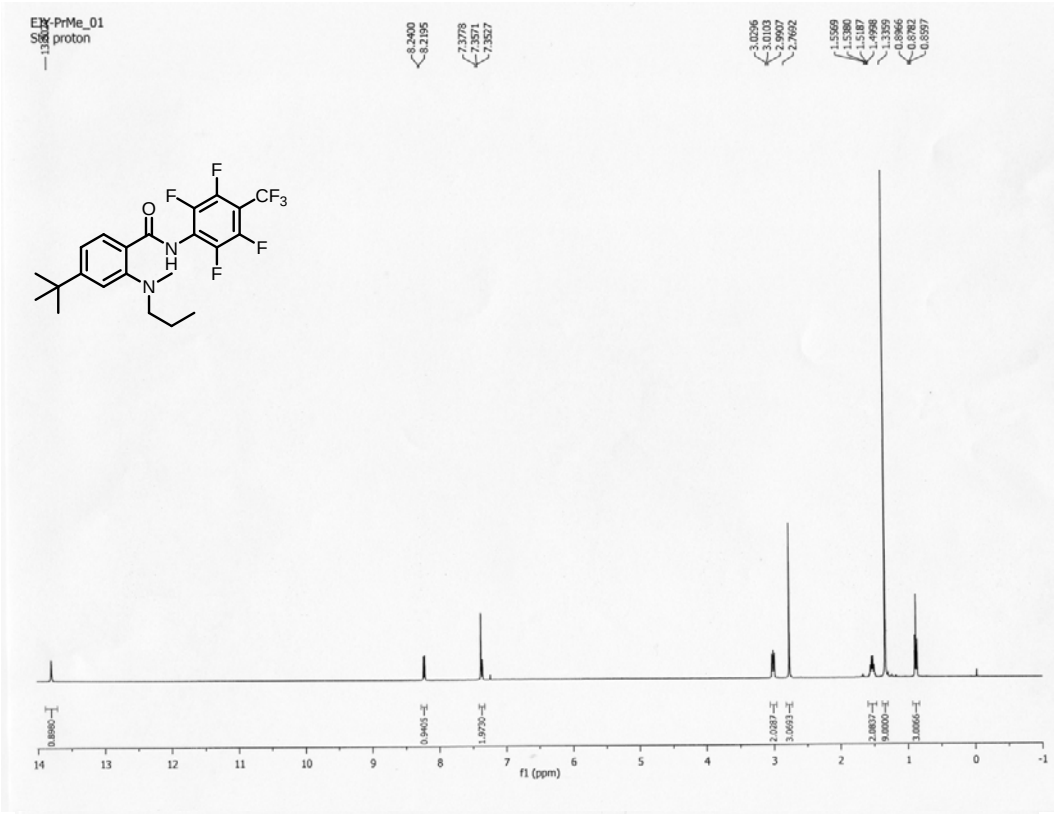

mei-36-83-pure-C_01
Std proton
162.2613
151.3548
135.8487
135.5782
135.2499
134.8868
133.7208
133.5814
127.1625
124.4776
124.4603
123.2606
123.2250
121.7325
119.5089
119.4750
119.1142
77.3181
77.0001
76.6823
66.9463
53.8146
f1 (ppm)

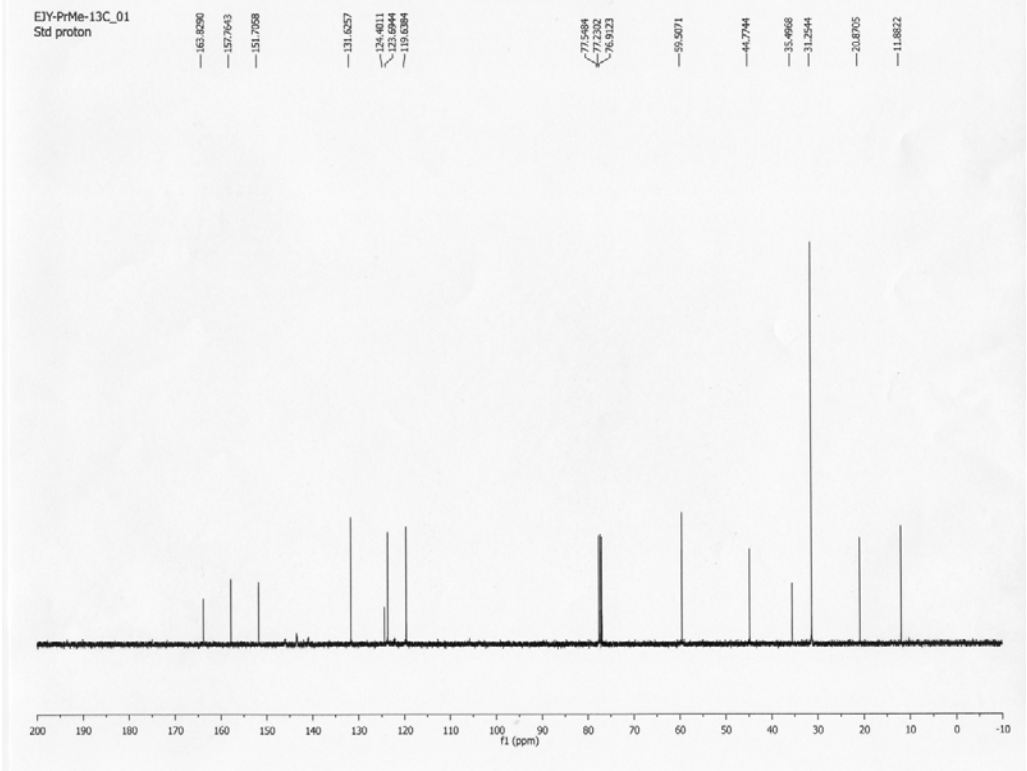

mei-36-57-p-H_01
Std proton
^{1}H NMR (400 MHz, cdcl$_3$) δ 12.91 (s, 1H), 8.45 (d, J = 8.1 Hz, 1H), 8.06 (s, 1H), 7.91 (dd, J = 8.1, 0.8 Hz, 1H), 3.98 – 3.87 (m, 4H), 3.20 – 3.09 (m, 4H), 2.68 (s, 3H).
12.906
8.463
8.442
8.059
7.924
7.922
7.904
7.902
7.270
3.936
3.925
3.914
3.159
3.147
3.136
2.678
A (s) 12.91
B (d) 8.45
C (s) 8.06
D (dd) 7.91
G (m) 3.92
F (m) 3.15
E (s) 2.68
f1 (ppm)

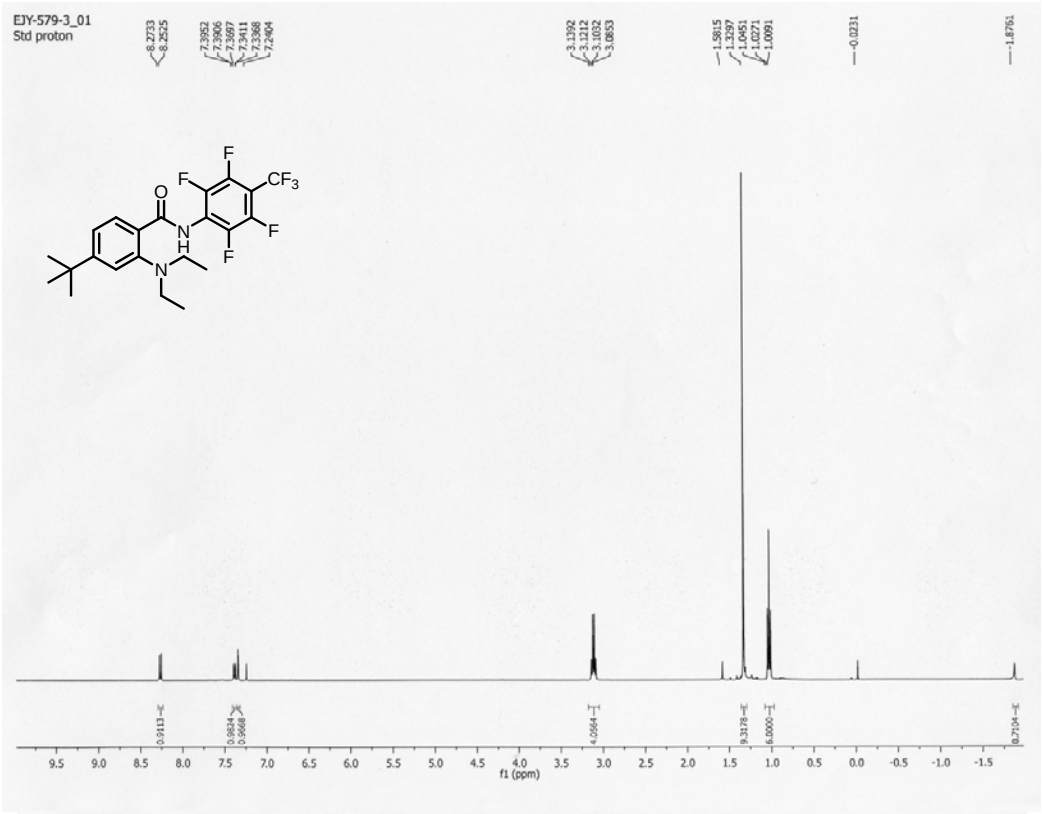

mei-36-57-p-C_01
Std proton
^{13}C NMR (101 MHz, cdcl$_3$) δ 196.86, 162.57, 151.25, 141.05, 132.87, 130.06, 126.36, 121.92, 77.32, 77.00, 76.68, 67.01, 53.78, 26.88.
196.865
162.572
151.247
141.046
132.872
130.059
126.359
121.918
77.317
77.000
76.681
67.007
53.780
26.876
f1 (ppm)

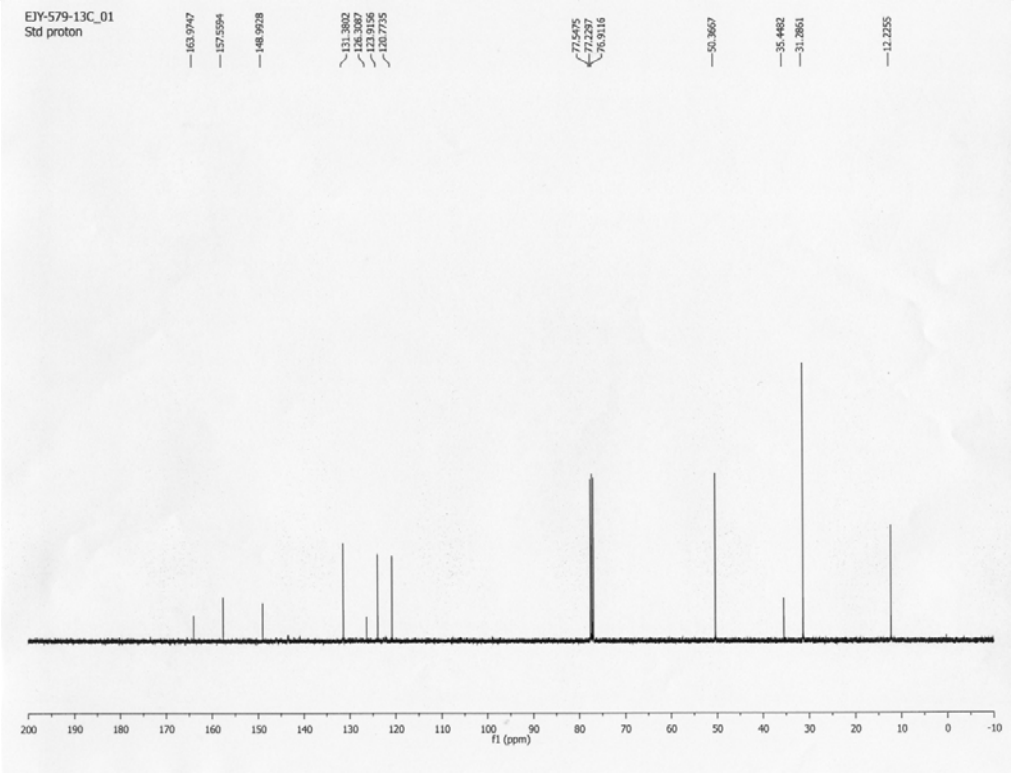

EJY-522-1_01
Std proton
F
F
CF3
O
N
H
F
F
N
f1 (ppm)

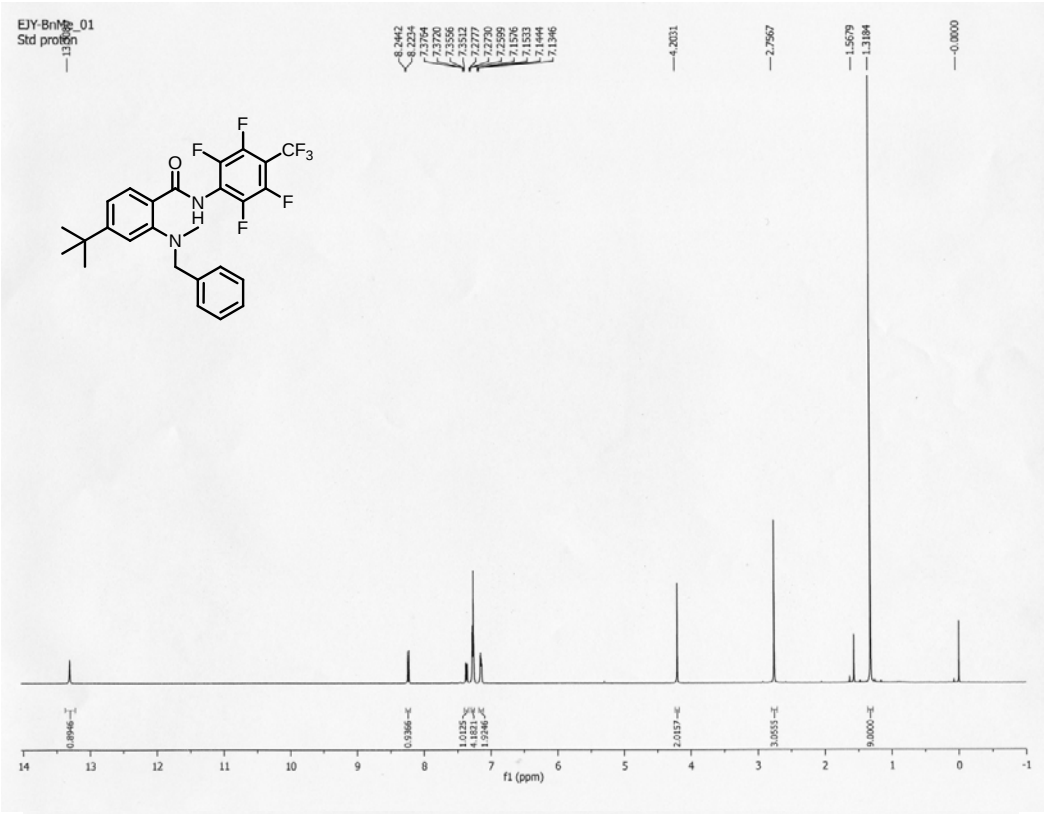

EJY-512-C_01
Std proton
f1 (ppm)

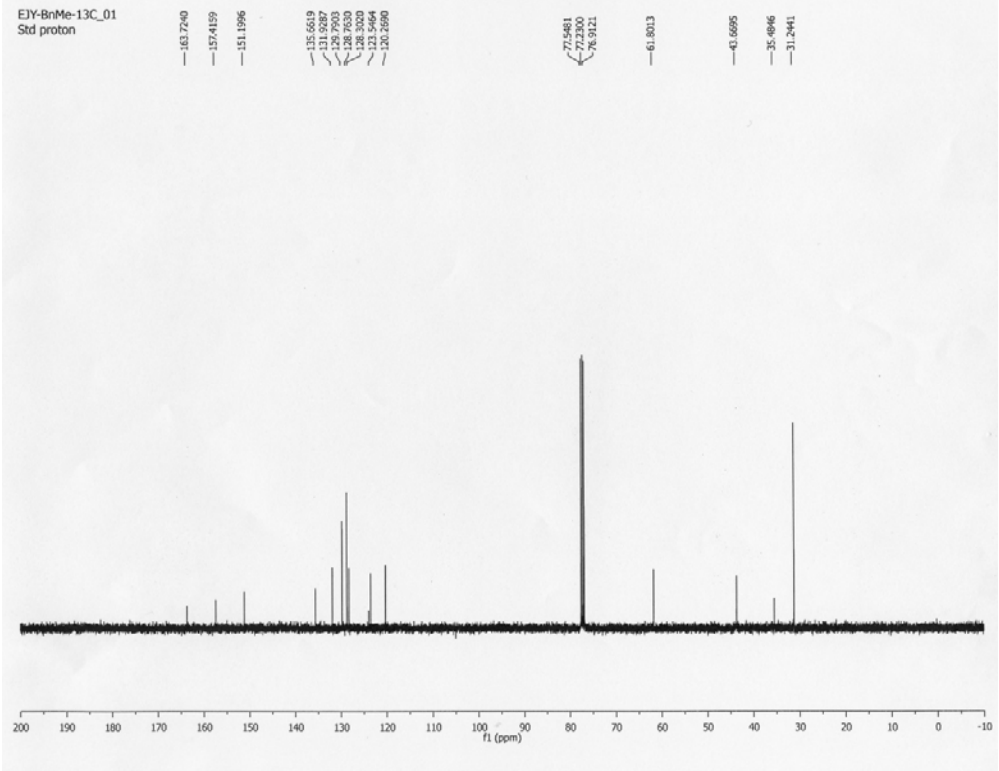

EJY-PrMe_01
Std proton
f1 (ppm)

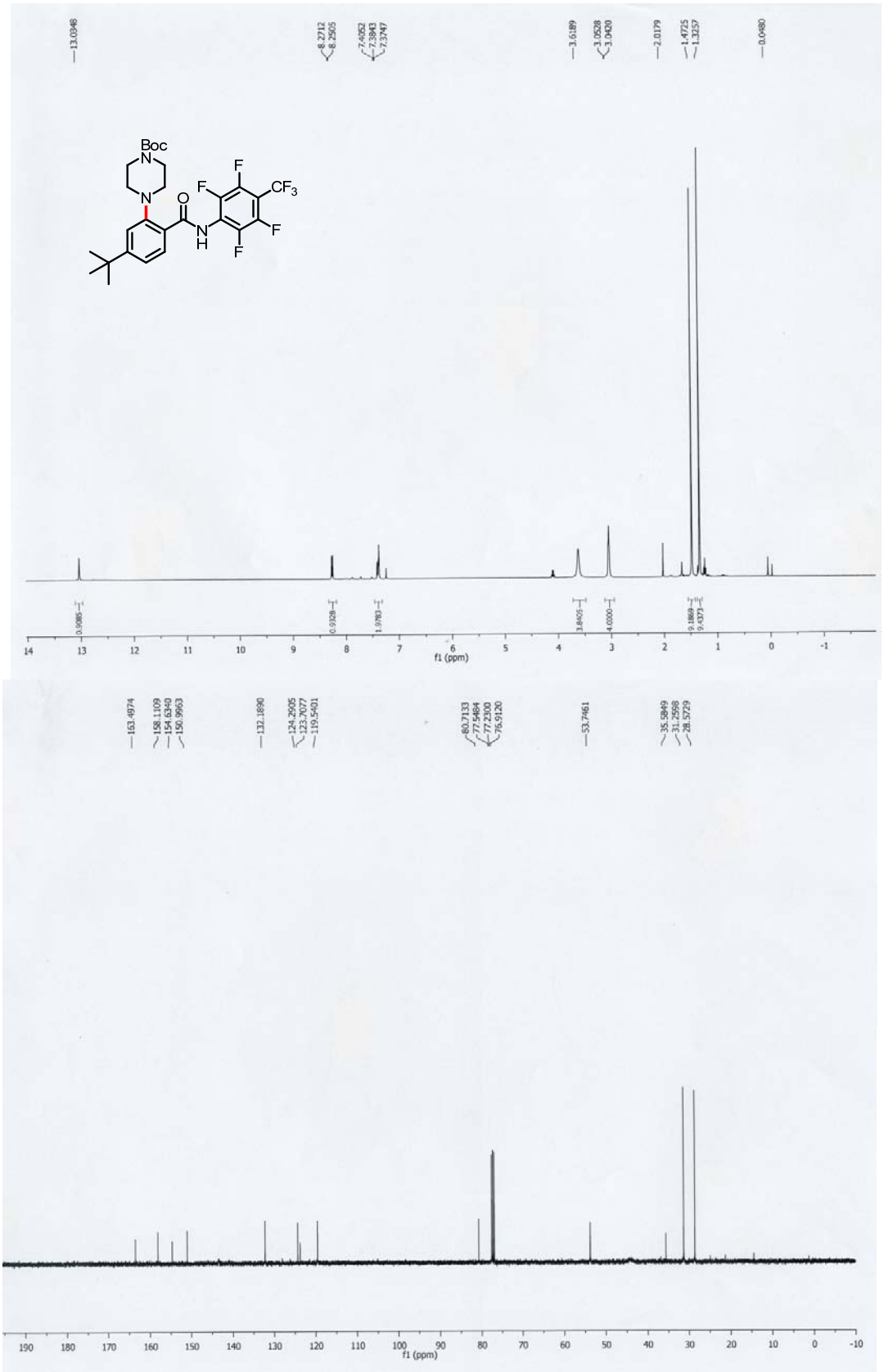

EJY-PrMe-13C_01
Std proton
f1 (ppm)

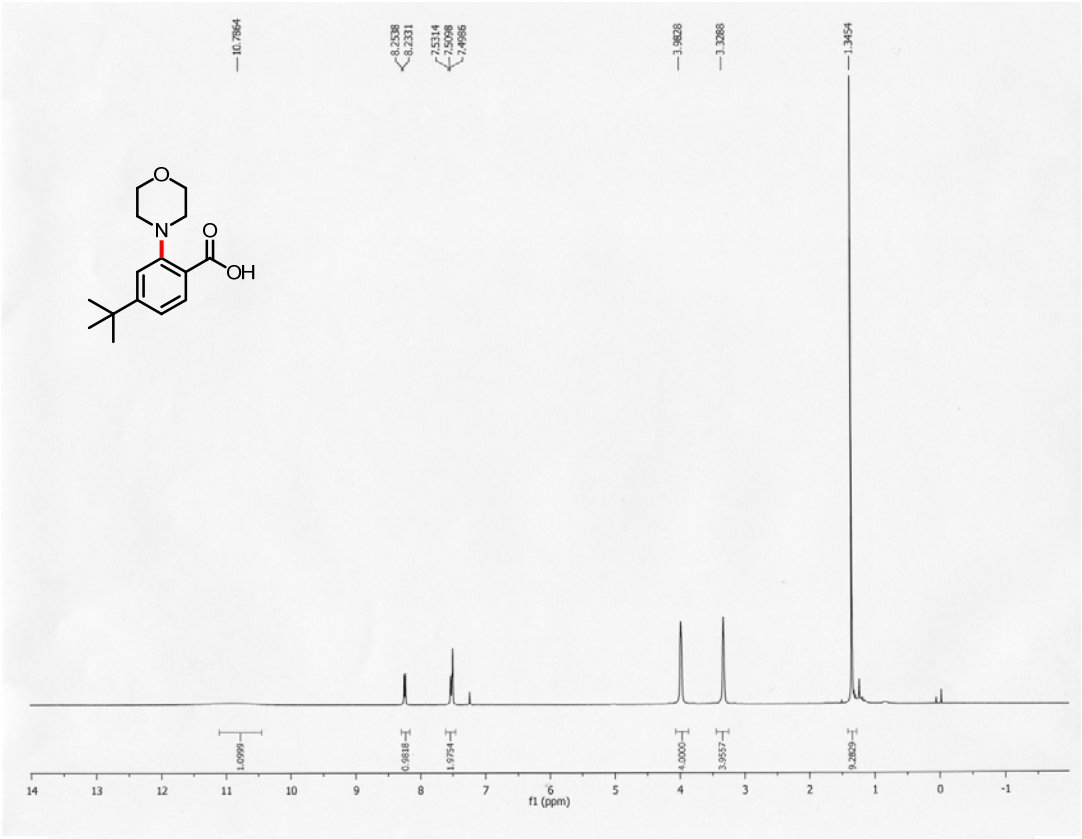

EJY-579-3_01
Std proton
8.2733
8.2525
7.3952
7.3906
7.3697
7.3491
7.3411
7.3368
7.2404
3.1392
3.1212
3.1032
3.0853
1.5815
1.3297
1.0451
1.0271
1.0091
-0.0231
-1.8761
F
F
CF3
O
N
H
F
F
N
0.9113
0.9824
0.9668
4.0564
9.3178
6.0000
0.7104
f1 (ppm)

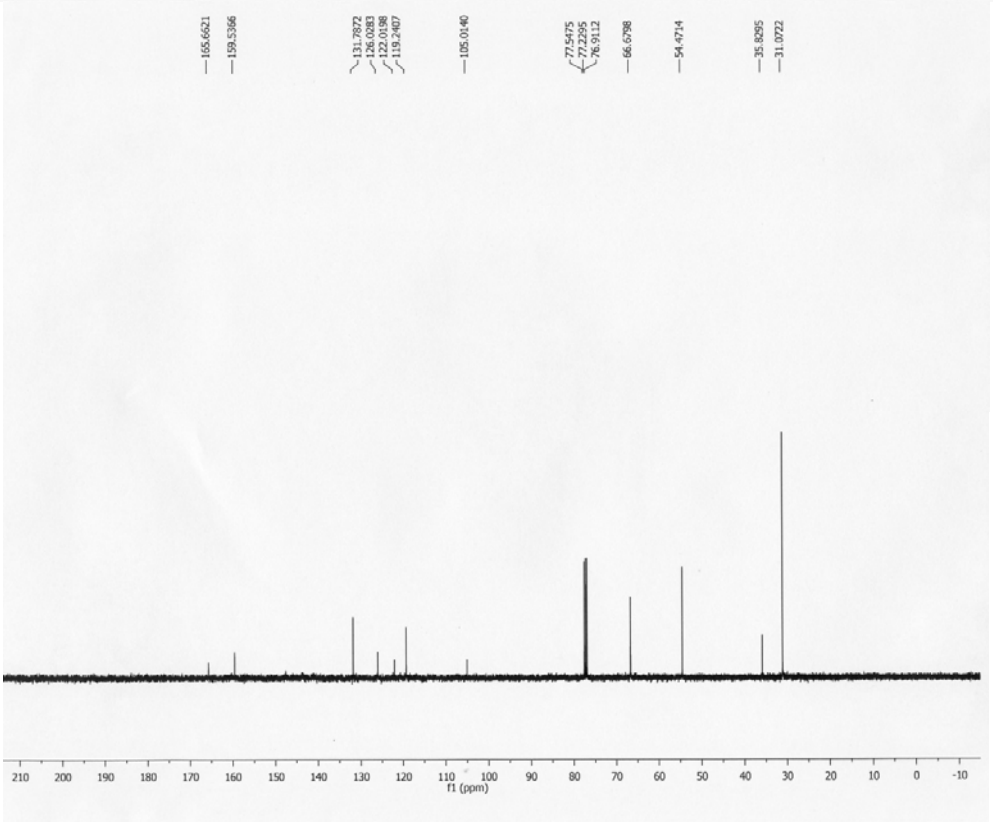

EJY-579-13C_01
Std proton
163.9747
157.5594
148.9928
131.3802
126.3087
123.9156
120.7735
77.5475
77.2297
76.9116
50.3667
35.4482
31.2861
12.2255
f1 (ppm)


EJY-BnMe_01
Std proton
F
F
CF3
O
N
H
F
F
N
f1 (ppm)


EJY-BnMe-13C_01
Std proton
f1 (ppm)


Boc
N
N
O
N
H
F
F
F
F
CF3
f1 (ppm)


10.7864
8.2538
8.2331
7.5314
7.5098
7.4986
3.9826
3.3288
1.3454
1.0999
0.9818
1.9754
4.0000
3.9557
9.2829
f1 (ppm)


165.6621
159.5366
131.7872
126.0283
122.0198
119.2407
105.0140
77.5475
77.2295
76.9112
66.6798
54.4714
35.8295
31.0722
f1 (ppm)