Copper(II)-catalyzed coupling reaction: an efficient and regioselective approach to *N'*,*N'*-diaryl acylhydrazines

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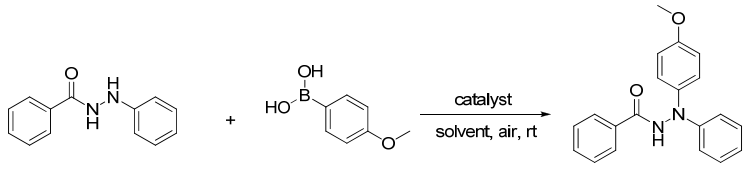
1. General information

The solvents were distilled from standard drying agents. Unless otherwise stated, commercial reagents purchased from Alfa Aesar, Acros and Aldrich chemical companies were used without further purification. Reaction products were purified by flash chromatography using Qing Dao Sea Chemical Reagent silica gel (200–300 mesh). ^{1}H NMR spectra were recorded on a Bruker Avance III 400 (400 MHz) spectrometer and referenced internally to the residual proton resonance in $CDCl_3$ (δ = 7.26 ppm), or with tetramethylsilane (TMS, δ = 0.00 ppm) as the internal standard. Chemical shifts were reported as parts per million (ppm) in the δ scale downfield from TMS. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet), dd (doublet of doublet), bs (broad singlet). ^{13}C NMR spectra were recorded on Bruker spectrometer with complete proton decoupling, and chemical shifts were reported in ppm from TMS with the solvent as the internal reference ($CDCl_3$, δ = 77.0 ppm). Low-resolution MS spectra were obtained on an Agilent LC-MS 6120 instrument with an ESI mass detector, the data were obtained in the positive or negative ion mode. High resolution mass spectra were recorded on an ESI-ion trap mass spectrometer (Shimadzu, LCMS-IT-TOF). Analytical TLC was performed using EM separations percolated silica gel 0.2 mm layer UV 254 fluorescent sheets.

2. Screening for the optimal conditions of cross-coupling reaction.[a]



1a **4a** **5a**

Entry	**4a** (equiv.)	$Cu(OAc)_2 \cdot H_2O$ (equiv.)	Solvent	Yield[b] (%)
1	1.20	0.10	MeOH	81
2	0.83	0.083	MeOH	45
3	0.67	0.067	MeOH	67
4	1.20	0.05	MeOH	43
5	1.20	0.15	MeOH	80
6	1.30	0.10	MeOH	47
7	1.20	0.10	MeOH	72[c]
8	1.20	0.10	MeOH	56[d]
9	1.20	0.20	MeOH	72
10	1.20	0.10	MeCN	trace
11	1.20	0.10	toluene	36
12	1.20	0.10	DCM	35
13	1.20	0.10	DCE	48
14	1.20	0.10	DMSO	trace
15	1.20	0.10	THF	60
16	1.20	0.20	THF	83
17	**1.20**	**0.10**	**dioxane**	**97**
18	1.20	0.05	dioxane	63

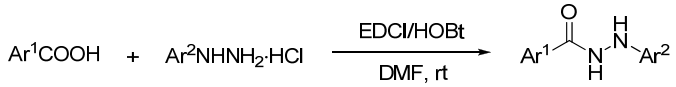
19	1.20	0.20	dioxane	71
20	1.20	0.10	dioxane	88[d]
21	1.20	0.10	dioxane	94[e]
22	1.20	0.10	dioxane	91[f]
23	1.05	0.10	dioxane	73
24	1.10	0.10	dioxane	83

[a] **1a** (0.2 mmol), solvent (2.0 mL), rt, 24 h. [b] Isolated yield. [c] Proceeded at 50℃. [d] TEA (1.0 equiv.) was added. [e] dioxane (1.0 mL). [f] dioxane (3.0 mL).

3. Preparation of *N'*-aryl acylhydrazines

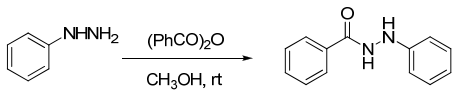
1s, 1z, 1aa, 1ab and **1ac** were synthesized according to literature methods.[1-3]

General procedure for the synthesis of **1a-r**, **1t-y:**



To a solution of aryl carboxylic acid (4.0 mmol) in DMF (10 mL) was added EDC·HCl (4.4 mmol) and HOBt (4.4 mmol), then arylhydrazine was added and the reaction mixture was stirred at ambient temperature under nitrogen atmosphere for 24-48 h. The reaction mixture was poured into H_2O (150 mL) and extracted with ethyl acetate (30 mL ×3). The organic phases were combined and washed with saturated $NaHCO_3$ (30 mL ×2) and saturated NaCl (30 mL×1) respectively, dried over Na_2SO_4. The solution was concentrated *in vacuo* and purified by column chromatography on silica gel (eluting with 3:1 to 1:1 petroleum ether/ethyl acetate) to give the desired product.

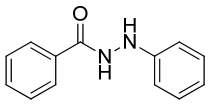
An alternative procedure for the synthesis of 1a



1a

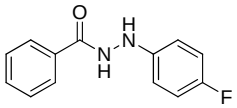
Phenylhydrazine (0.5 g, 4.63 mmol) was added to a solution of benzoic anhydride (1.05 g, 4.63 mmol) in CH_3OH (10 mL) at 0 ℃ slowly. The mixture was stirred at ambient temperature for 3 h. After removal of the solvent *in vacuo*, the residue was dissolved in ethyl acetate (100 mL), washed with saturated $NaHCO_3$ (50 mL ×3) and NaCl (30 mL ×1) respectively. The solution was dried over Na_2SO_4, concentrated *in vacuo*, and purified by column chromatography on silica gel (eluting with 3:1 to 1:1 petroleum ether/ethyl acetate) to give **1a** (0.87 g, 89% yield).

***N'*-Phenylbenzohydrazide (1a)**[4]



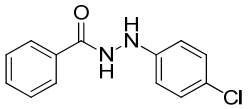
White solid; yield: 65%; mp: 173-174 ℃; ESI-MS (*m/z*): 213.2 $[M+H]^+$. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.03 (s, 1H), 7.83 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.24 (dd, *J* = 11.1, 4.8 Hz, 2H), 6.96-6.87 (m, 3H), 6.37 (s, 1H).

***N'*-(4-Fluorophenyl)benzohydrazide (1b)**[5]



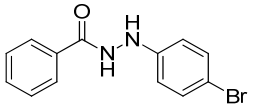
Off-white solid；yield: 45%；mp: 173-174 ℃; ESI-MS (*m/z*): 231.1 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 7.87-7.81 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 6.92 (m, 4H), 6.35 (s, 1H).

***N'*-(4-Chlorophenyl)benzohydrazide (1c)**



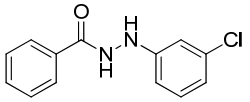
White solid; yield: 35%; mp: 149-150 ℃; ESI-MS (*m/z*): 247.2 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.86-7.80 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.19 (d, *J* = 2.1 Hz, 1H), 7.18 (d, *J* = 2.1 Hz, 1H), 6.88-6.80 (m, 2H), 6.37 (d, *J* = 3.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 146.7, 132.4, 132.0, 129.1, 128.8, 127.2, 126.1, 115.0.

***N'*-(4-Bromophenyl)benzohydrazide (1d)**



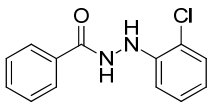
Light yellow solid; yield: 21%; mp: 157-158 ℃; ESI-MS (*m/z*): 291.0 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.35-7.30 (m, 2H), 6.80 (dd, *J* = 9.3, 2.4 Hz, 2H), 6.37 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 147.1, 132.5, 132.0, 132.0, 128.9, 127.2, 115.4, 113.4.

***N'*-(3-Chlorophenyl)benzohydrazide (1e)**



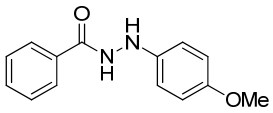
White solid; yield: 30%; mp: 150-151 ℃; GC-MS: 246.1 $[M]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (s, 1H), 7.88-7.80 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.14 (t, *J* = 8.0 Hz, 1H), 6.93-6.85 (m, 2H), 6.79 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.40 (d, *J* = 3.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 149.4, 135.1, 132.5, 131.9, 130.3, 128.9, 127.2, 121.3, 113.7, 112.0.

***N'*-(2-Chlorophenyl)benzohydrazide (1f)**



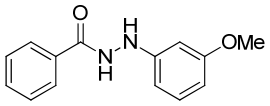
White solid; yield: 33% ; mp: 154-155 ℃; GC-MS: 246.1 $[M]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (s, 1H), 7.85 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.31 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.19-7.12 (m, 1H), 7.01-6.96 (m, 1H), 6.85 (td, *J* = 7.8, 1.5 Hz, 1H), 6.66 (d, *J* = 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.6, 143.9, 132.4, 132.0, 129.6, 128.8, 127.7, 127.2, 121.6, 119.9, 113.8.

***N'*-(4-Methoxyphenyl)benzohydrazide (1g)**



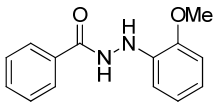
Off-white solid; yield: 37%; mp: 139-140 ℃; ESI-MS (*m/z*): 243.1 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (s, 1H), 7.86-7.79 (m, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.85-6.78 (m, 2H), 6.28 (d, *J* = 3.4 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 155.0, 141.4, 132.2, 132.1, 128.7, 127.3, 116.0, 114.6, 55.6.

***N'*-(3-Methoxyphenyl)benzohydrazide (1h)**



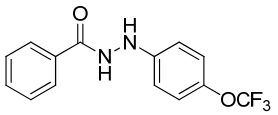
White solid; yield: 55%; mp: 141-142 ℃; ESI-MS (*m/z*): 243.2 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (s, 1H), 7.83 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.14 (t, *J* = 8.3 Hz, 1H), 6.52 (d, *J* = 8.8 Hz, 1H), 6.47 (dd, *J* = 8.2, 1.6 Hz, 2H), 6.37 (d, *J* = 3.6 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.8, 160.7, 149.5, 132.3, 132.0, 130.11, 128.8, 127.2, 106.6, 106.4, 100.0, 55.2.

***N'*-(2-Methoxyphenyl)benzohydrazide (1i)**



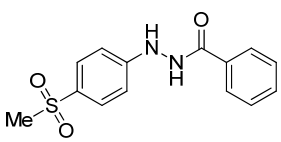
Off-white solid; yield: 50%; mp: 143-144 ℃; ESI-MS (*m/z*): 243.1 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (s, 1H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 6.95-6.91 (m, 1H), 6.89-6.83 (m, 3H), 6.75 (s, 1H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.4, 147.6, 137.3, 132.6, 132.1, 128.7, 127.1, 121.1, 121.0, 112.9, 110.4, 55.6.

***N'*-(4-(*tri*Fluoromethoxy)phenyl)benzohydrazide (1j)**



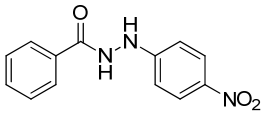
Light yellow solid; yield: 25%; mp: 157-158 ℃; ESI-MS (*m/z*): 297.1 $[M+H]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.88-7.80 (m, 2H), 7.58 (t, *J* = 7.4 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.09 (d, *J* = 8.4 Hz, 2H), 6.91 (dd, *J* = 9.5, 2.6 Hz, 2H), 6.42 (d, *J* = 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.9, 161.1, 146.8, 143.5, 132.5, 132.0, 128.9, 127.1, 122.3, 114.6.

***N'*-(4-(Methylsulfonyl)phenyl)benzohydrazide (1k)**



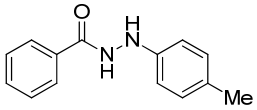
Light yellow solid; yield: 16%; mp: 201-203 ℃; ESI-MS (*m/z*): 291.1 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.53 (s, 1H), 8.78 (s, 1H), 7.94 (d, *J* = 7.2 Hz, 2H), 7.67 (d, *J* = 8.7 Hz, 2H), 7.61 (t, *J* = 7.0 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 6.89 (d, *J* = 8.7 Hz, 2H), 3.08 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 166.8, 154.1, 133.1, 132.4, 129.8, 129.1, 129.0, 127.9, 111.8, 44.8.

***N'*-(4-Nitrophenyl)benzohydrazide (1l)**



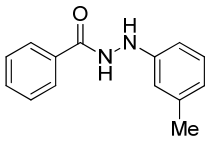
Brown solid; yield: 42%; mp: 192-193 ℃; ESI-MS (*m/z*): 256.1 $[M-H]^-$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.65 (s, 1H), 9.24 (s, 1H), 8.09 (d, *J* = 9.2 Hz, 2H), 7.97-7.90 (m, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 2H), 6.84 (d, *J* = 9.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 166.2, 155.0, 138.1, 132.3, 132.0, 128.5, 127.4, 125.9, 110.7.

***N'*-*p*-Tolylbenzohydrazide (1m)**[6]



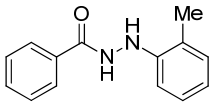
White solid; yield: 55%; ESI-MS (*m/z*): 225.1 $[M-H]^-$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (s, 1H), 7.83 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.05 (d, *J* = 8.1 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 6.30 (d, *J* = 3.6 Hz, 1H), 2.27 (s, 3H).

***N'*-*m*-Tolylbenzohydrazide (1n)**



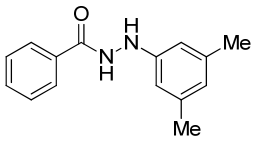
White solid; yield: 40%; mp: 152-153 ℃; ESI-MS (*m/z*): 225.2 $[M-H]^-$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (s, 1H), 7.84 (d, *J* = 7.5 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.13 (dd, *J* = 10.8, 5.3 Hz, 1H), 6.74 (d, *J* = 6.8 Hz, 3H), 6.34 (s, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.8, 148.0, 139.1, 132.4, 132.2, 129.1, 128.7, 127.2, 122.3, 114.6, 111.0, 21.5.

***N'*-*o*-Tolylbenzohydrazide (1o)**



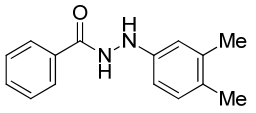
White solid; yield: 32%; mp: 159-160 ℃; ESI-MS (*m/z*): 225.2 $[M-H]^-$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (s, 1H), 7.84 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.2 Hz, 2H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.90-6.82 (m, 1H), 6.27 (d, *J* = 3.8 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.5, 145.7, 132.4, 132.2, 130.6, 128.8, 127.1, 126.9, 121.2, 112.4, 100.0, 17.0.

***N'*-(3,5-*di*Methylphenyl)benzohydrazide (1p)**



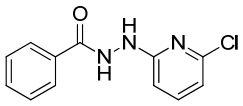
White solid; yield: 43%; mp: 181-182 ℃; ESI-MS (*m/z*): 241.1 $[M+H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97 (s, 1H), 7.85 (d, *J* = 7.3 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 2H), 6.56 (d, *J* = 8.3 Hz, 3H), 6.30 (s, 1H), 2.25 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.6, 148.0, 139.0, 132.4, 132.2, 128.8, 127.2, 123.4, 111.7, 21.4.

_N'_-(3,4-*di*Methylphenyl)benzohydrazide (1q)



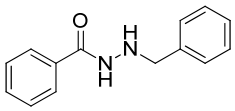
Brown solid; yield: 41%; mp: 147-148 ℃; ESI-MS (*m/z*): 241.1 $[M+H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ: 8.22 (s, 1H), 7.86-7.79 (m, 2H), 7.54 (d, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 1H), 6.69 (dd, *J* = 9.7, 7.6 Hz, 2H), 6.31 (s, 1H), 2.18 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 167.7, 145.9, 137.4, 132.1, 130.2, 129.7, 128.7, 128.4, 127.2, 115.7, 111.5, 20.0, 18.9.

_N'_-(6-Chloropyridin-2-yl)benzohydrazide (1r)



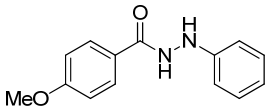
Grey solid; yield: 87%; mp: 217-218 ℃; ESI-MS (*m/z*): 248.0 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ: 10.48 (s, 1H), 8.89 (s, 1H), 7.95-7.90 (m, 2H), 7.55 (dd, *J* = 16.1, 8.1 Hz, 4H), 6.76 (d, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 166.8, 160.8, 148.8, 141.0, 133.2, 132.3, 129.0, 127.9, 113.7, 105.3.

_N'_-Benzylbenzohydrazide (1s)



White solid; yield: 87%; mp: 118-119 ℃; ESI-MS (*m/z*): 227.1 $[M+H]^+$; ^1H NMR (400 MHz, DMSO-d_6) δ: 10.05 (d, *J* = 6.2 Hz, 1H), 7.79 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.54-7.48 (m, 1H), 7.47-7.41 (m, 2H), 7.41-7.36 (m, 2H), 7.36-7.30 (m, 2H), 7.26 (ddd, *J* = 7.2, 3.8, 1.3 Hz, 1H), 5.42 (q, *J* = 5.8 Hz, 1H), 3.99 (d, *J* = 5.6 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 165.6, 138.5, 133.2, 131.2, 128.5, 128.3, 128.1, 127.0, 127.0, 54.8.

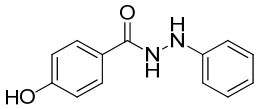
4-Methoxy-_N'_-phenylbenzohydrazide (1t)



Brown solid; yield: 55%; mp: 179-180 ℃; ESI-MS (*m/z*): 243.1 $[M+H]^+$; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 1.9 Hz, 2H), 7.80 (s, 1H), 7.24 (dd, *J* = 8.3, 7.0 Hz, 2H), 6.98-6.88 (m, 5H),

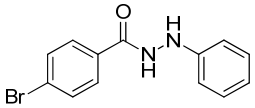
6.33 (s, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.0, 167.1, 154.9, 134.4, 133.9, 130.4, 123.8, 118.9, 117.6, 60.6.

4-Hydroxy-*N'*-phenylbenzohydrazide (1u)



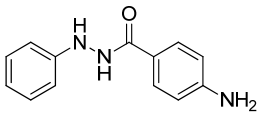
White solid; yield: 53%; mp: 222-223 ℃; ESI-MS (*m/z*): 229.1 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.11 (d, *J* = 2.8 Hz, 1H), 10.06 (s, 1H), 7.79 (t, *J* = 5.7 Hz, 3H), 7.14 (dd, *J* = 8.3, 7.4 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 6.71 (t, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 166.5, 161.0, 150.2, 129.7, 129.1, 124.1, 119.0, 115.5, 112.8.

4-Bromo-*N'*-phenylbenzohydrazide (1v)



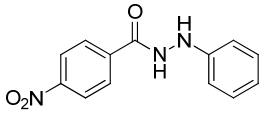
White solid; yield: 76%; mp: 195-196 ℃; ESI-MS (*m/z*): 292.1 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.43 (d, *J* = 2.8 Hz, 1H), 7.91 (d, *J* = 2.8 Hz, 1H), 7.88-7.83 (m, 2H), 7.75-7.69 (m, 2H), 7.15 (t, *J* = 7.9 Hz, 2H), 6.78 (d, *J* = 7.7 Hz, 2H), 6.72 (t, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 165.9, 149.8, 132.6, 132.0, 129.9, 129.2, 125.8, 119.2, 112.8.

4-Amino-*N'*-phenylbenzohydrazide (1w)



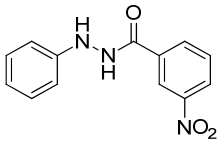
Off-white solid; yield: 42%; mp: 201-202 ℃; GC-MS (*m/z*): 227.0 $[M]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.88 (d, *J* = 2.7 Hz, 1H), 7.69 (d, *J* = 2.7 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.12 (dd, *J* = 8.3, 7.5 Hz, 2H), 6.75 (d, *J* = 7.7 Hz, 2H), 6.69 (t, *J* = 7.3 Hz, 1H), 6.57 (d, *J* = 8.6 Hz, 2H), 5.67 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 166.4, 152.0, 150.0, 128.8, 128.6, 119.5, 118.3, 112.6, 112.3.

4-Nitro-*N'*-phenylbenzohydrazide (1x)



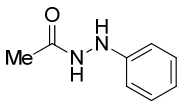
Brown solid; yield: 51%; mp: 190-191 ℃; ESI-MS (*m/z*): 258.1 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.67 (d, *J* = 2.1 Hz, 1H), 8.40-8.32 (m, 2H), 8.20-8.12 (m, 2H), 8.01 (d, *J* = 2.1 Hz, 1H), 7.21-7.12 (m, 2H), 6.84-6.78 (m, 2H), 6.74 (t, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 164.8, 149.3, 149.1, 138.7, 128.8, 128.8, 123.6, 118.9, 112.4.

3-Nitro-*N'*-phenylbenzohydrazide (1y)



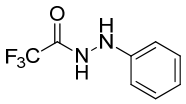
Yellow solid; yield: 93%; mp: 160-161 ℃; GC-MS (*m/z*): 257.1 $[M]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 10.73 (d, *J* = 2.6 Hz, 1H), 8.77-8.70 (m, 1H), 8.47-8.40 (m, 1H), 8.37 (dd, *J* = 6.6, 1.2 Hz, 1H), 8.02 (d, *J* = 2.6 Hz, 1H), 7.83 (t, *J* = 8.0 Hz, 1H), 7.23-7.12 (m, 2H), 6.82 (d, *J* = 7.7 Hz, 2H), 6.74 (t, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 164.3, 149.1, 147.8, 134.4, 133.6, 130.3, 128.8, 126.2, 122.1, 118.8, 112.4.

_N'_-Phenylacetohydrazide (1z)



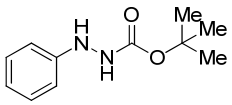
White solid; yield: 89%; mp: 131-132 ℃; ESI-MS (*m/z*): 151.1 $[M+H]^+$; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 9.57 (s, 0.91H), 8.89 (s, 0.13H), 7.93 (s, 0.13H), 7.61 (d, *J* = 1.7 Hz, 0.88H), 7.20-7.16 (m, 0.29H), 7.14-7.10 (m, 1.77H), 6.75-6.74 (m, 0.11H), 6.66-6.72 (m, 2.84H), 1.89 (s, 2.53H), 1.85 (s, 0.41H); ^{13}C NMR (100 MHz, DMSO-d_6) δ: 175.2, 169.0, 149.4, 148.8, 129.0, 128.6, 118.8, 118.4, 112.1, 111.8, 20.6, 19.2.

2,2,2-*tri*Fluoro-*N'*-phenylacetohydrazide (1aa)



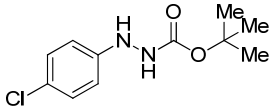
White solid; yield: 33%; mp: 124-125 ℃; ESI-MS (*m/z*): 227.2 $[M+Na]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.18 (s, 1H), 7.33-7.22 (m, 2H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.83 (dd, *J* = 8.5, 0.9 Hz, 2H), 6.05 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 157.7, 157.4, 145.8, 129.4, 122.4, 117.2, 114.3, 113.8.

***tert*-Butyl 2-phenylhydrazinecarboxylate (1ab)**[1c]



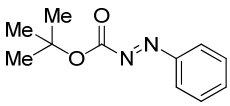
White solid; yield: 76%; mp: 93-94 ℃; ESI-MS (*m/z*): 231.1 $[M+Na]^+$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27-7.20 (m, 2H), 6.88 (t, *J* = 7.4 Hz, 1H), 6.82 (d, *J* = 7.8 Hz, 2H), 6.38 (s, 1H), 5.74 (s, 1H), 1.46 (s, 9H).

***tert*-Butyl 2-(4-chlorophenyl)hydrazinecarboxylate (1ac)**



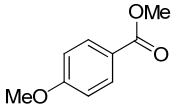
White solid; yield: 58%; mp: 124-125 ℃; ESI-MS (*m/z*): 241.0 $[M-H]^-$; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.19 (d, *J* = 2.2 Hz, 1H), 7.17 (d, *J* = 2.2 Hz, 1H), 6.75 (d, *J* = 8.8 Hz, 2H), 6.38 (s, 1H), 5.75 (s, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.1, 147.1, 129.1, 125.5, 114.2, 81.5, 28.2.

(*E*)-*tert*-Butyl 2-phenyldiazenecarboxylate (4)[7]



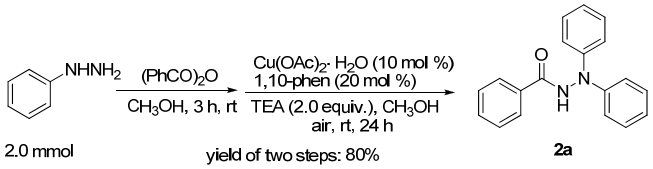
Brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92-7.90 (m, 1H), 7.89 (t, *J* = 1.9 Hz, 1H), 7.56-7.53 (m, 1H), 7.53 (t, *J* = 1.0 Hz, 1H), 7.51 (dd, *J* = 3.1, 1.7 Hz, 1H), 1.66 (s, 9H); HRMS (ESI) calcd. for $C_{11}H_{14}N_2O_2Na$ $[M+Na]^+$: 229.0947, found: 229.0955.

Methyl 4-methoxybenzoate (5t)[8]



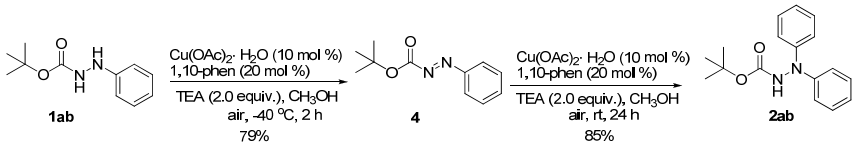
^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02-7.96 (m, 2H), 6.95-6.88 (m, 2H), 3.88 (s, 3H), 3.86 (s, 3H).

4. One-pot synthesis of *N',N'*-diarylacylhydrazide



Phenylhydrazine (0.22 g, 2.0 mmol) was added to a solution of benzoic anhydride (0.45 g, 2.0 mmol) in CH_3OH (15 mL) dropwise at 0 ℃. The reaction mixture was stirred at ambient temperature for 3 h. Then $Cu(OAc)_2 \cdot H_2O$ (80 mg, 0.4 mmol), 1,10-phen·H_2O (160 mg, 0.8 mmol) and TEA (1.13 mL, 8.0 mmol) were added sequentially. The mixture was stirred at room temperature for additional 24 h, then quenched by saturated NaCl solution (30 mL), extracted with EtOAc (30 mL ×3), and dried over Na_2SO_4. The crude product was purified by flash column chromatography (eluting with 10:1 petroleum ether/ethyl acetate) to provide **2a** (230 mg, 80% yield).

5. Control synthesis of *tert*-butyl 2,2-*di*phenylhydrazinecarboxylate



$Cu(OAc)_2 \cdot H_2O$ (20 mg, 0.1 mmol), 1,10-phen·H_2O (160 mg, 0.2 mmol) and TEA (0.28 mL, 2.0 mmol) were added sequentially to a solution of **1ab** (0.10 g, 0.5 mmol) in CH_3OH (6.0 mL). The mixture was stirred at -40 ℃ for 2 h, then quenched by saturated NaCl solution (20 mL), extracted with EtOAc (20 mL ×3), and dried over Na_2SO_4. The crude product was purified by flash column chromatography (eluting with 50:1 petroleum ether/ethyl acetate) to provide **4** (81 mg, 79% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92-7.90 (m, 1H), 7.89 (t, *J* = 1.9 Hz, 1H), 7.56-7.53 (m, 1H), 7.53 (t, *J* = 1.0 Hz, 1H), 7.51 (dd, *J* = 3.1, 1.7 Hz, 1H), 1.66 (s, 9H); HRMS (ESI) calcd. for $C_{11}H_{14}N_2O_2Na$ $[M+Na]^+$: 229.0947, found: 229.0955.

Intermediate **4** was converted to **2ab** following a similar procedure for **2a** in 85% yield.

6. References

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3. D. Bonnet, J.-F. Margathe, S. Radford, E. Pflimlin, S. Riché, P. Doman, M. Hibert and A. Ganesan, *ACS Comb. Sci.*, 2012, **14**, 323-334.
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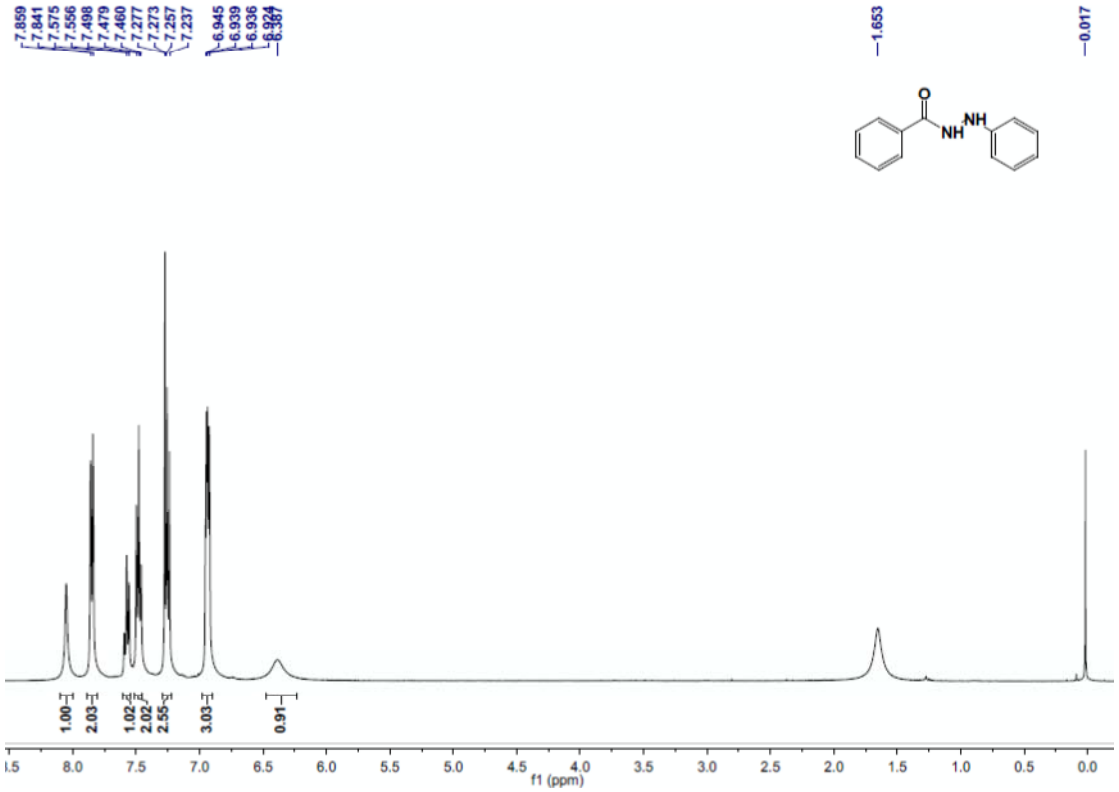
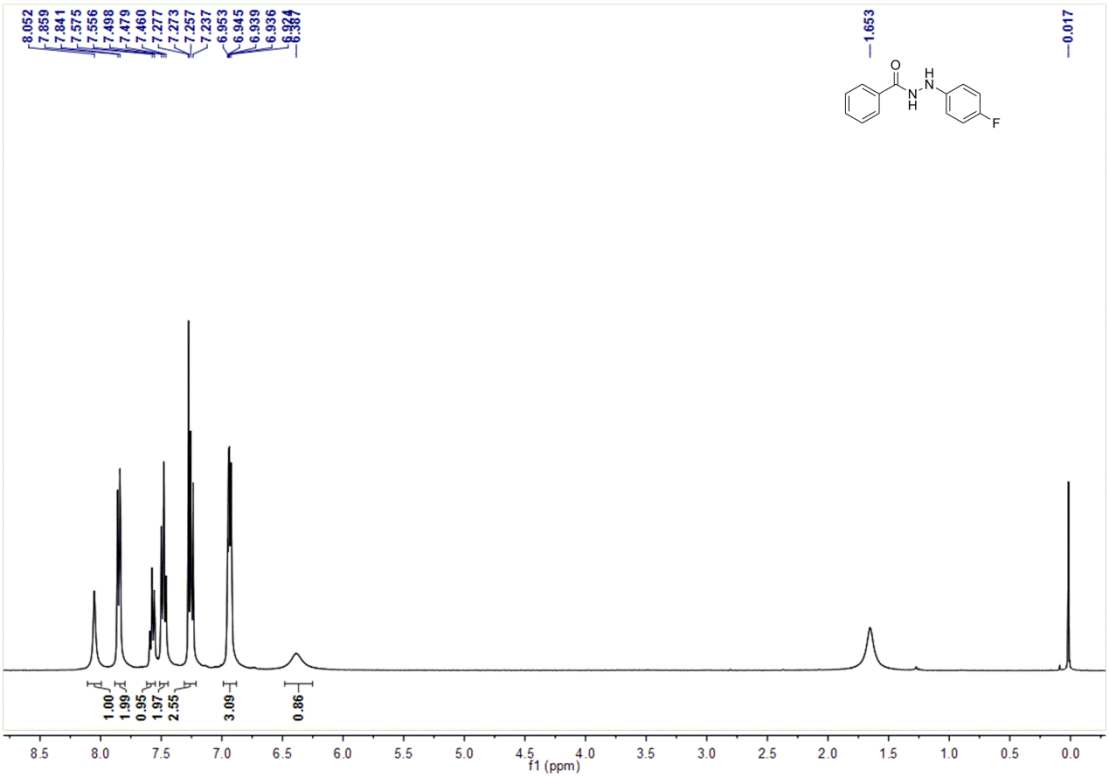
7. ^{1}H and ^{13}C NMR spectra

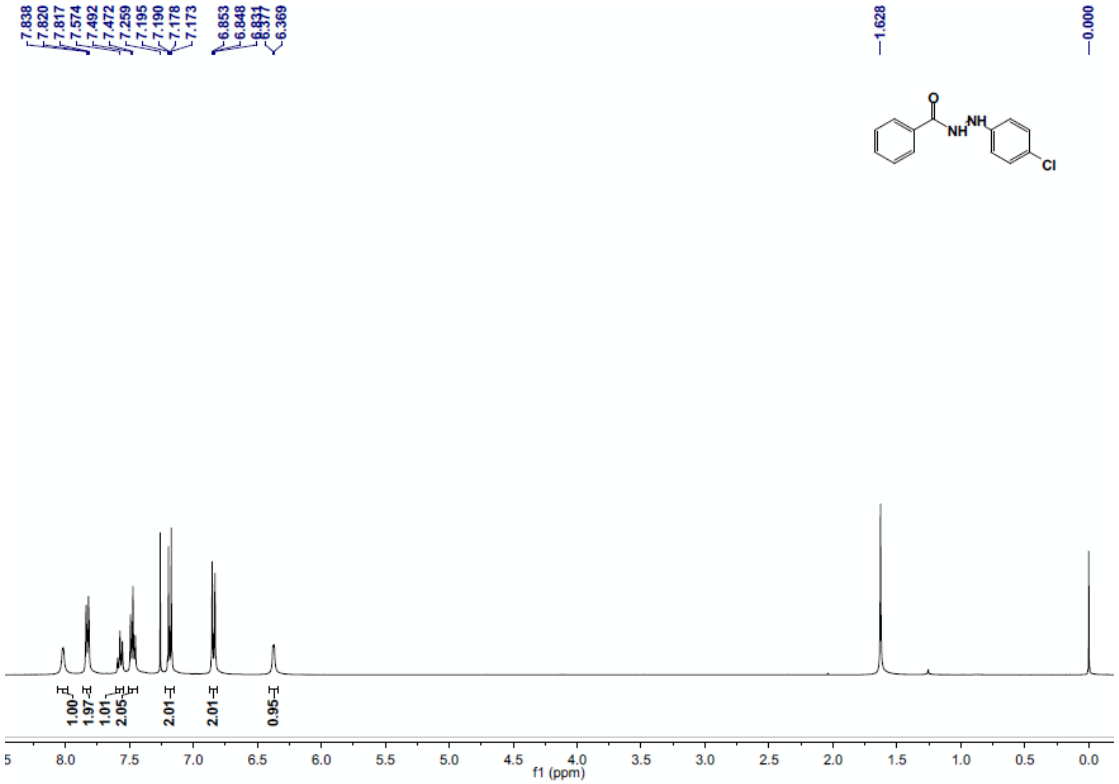
N'-Phenylbenzohydrazide (1a)

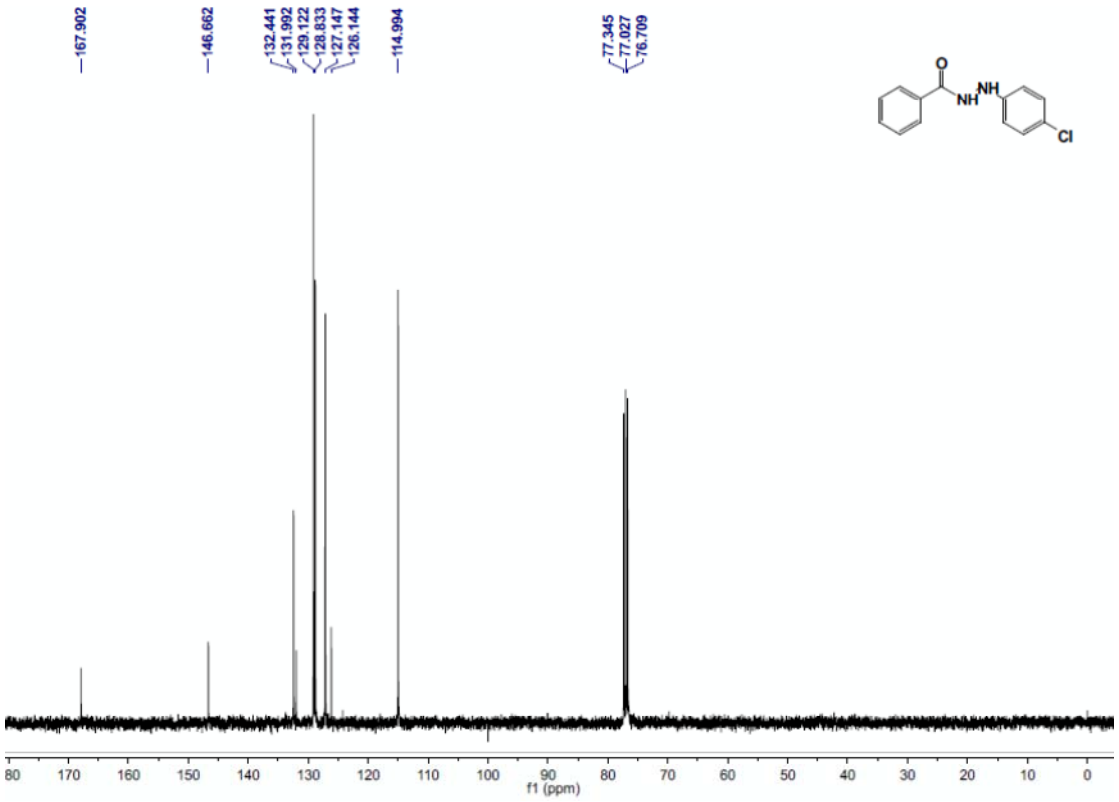


N'-(4-Fluorophenyl)benzohydrazide (1b)

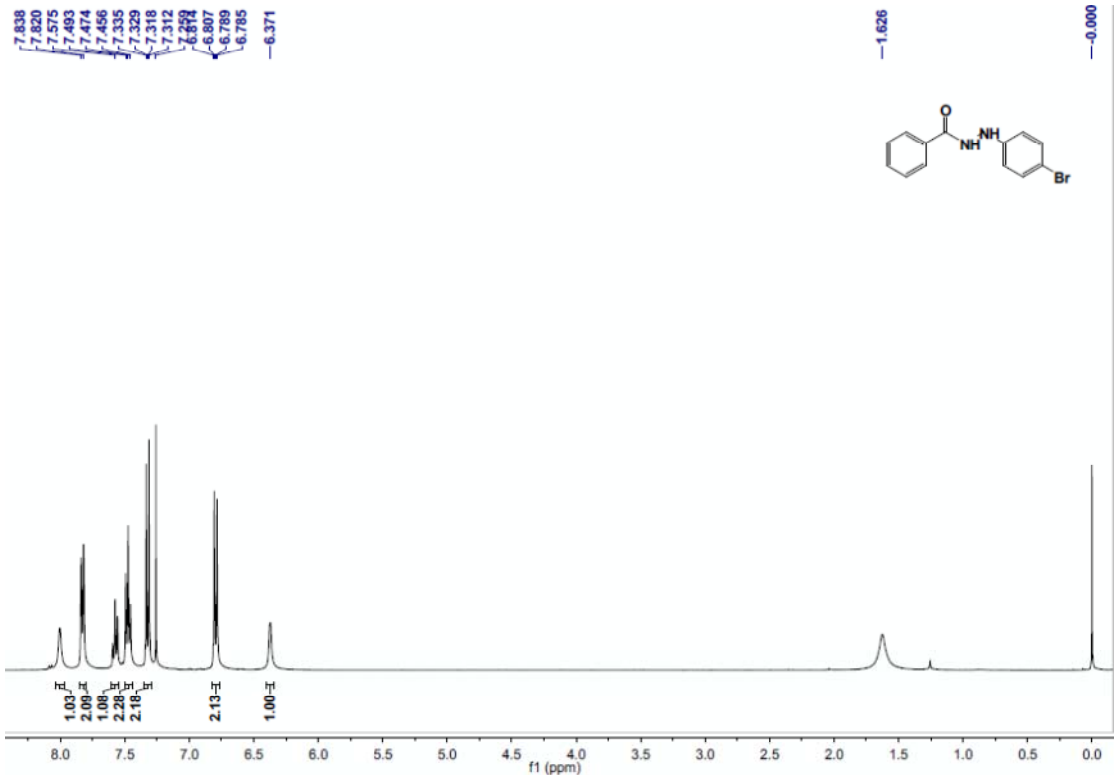


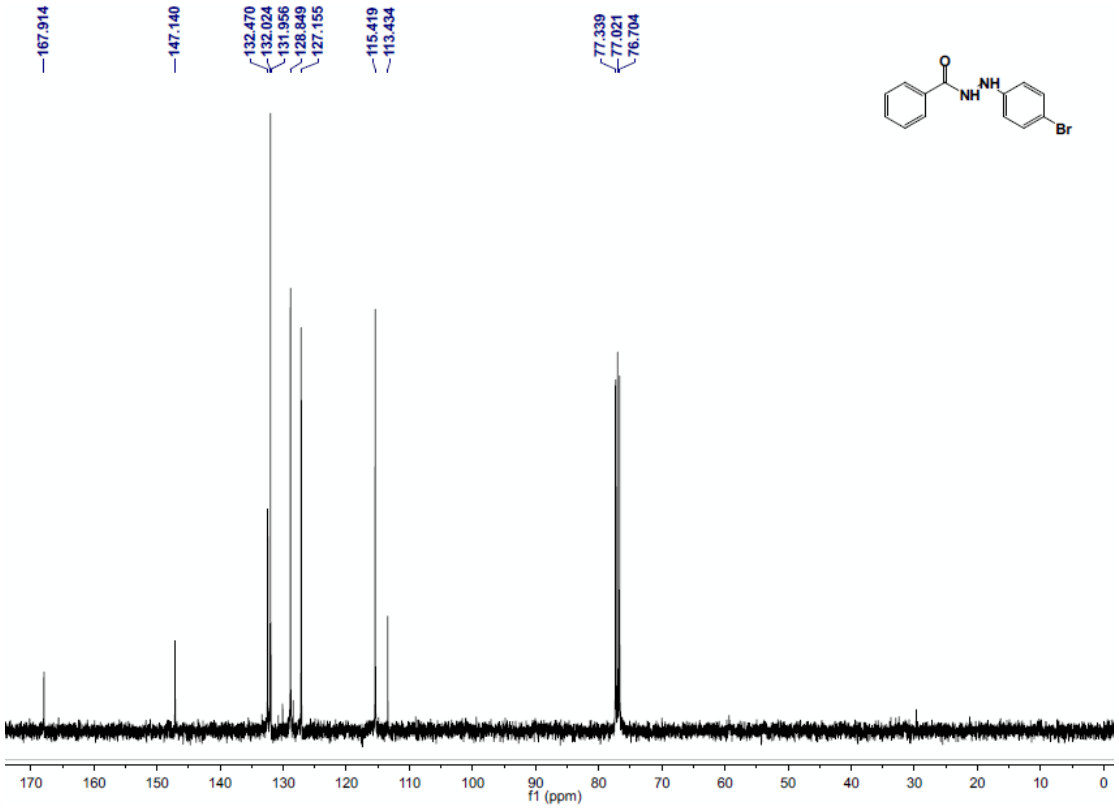
***N'*-(4-Chlorophenyl)benzohydrazide (1c)**



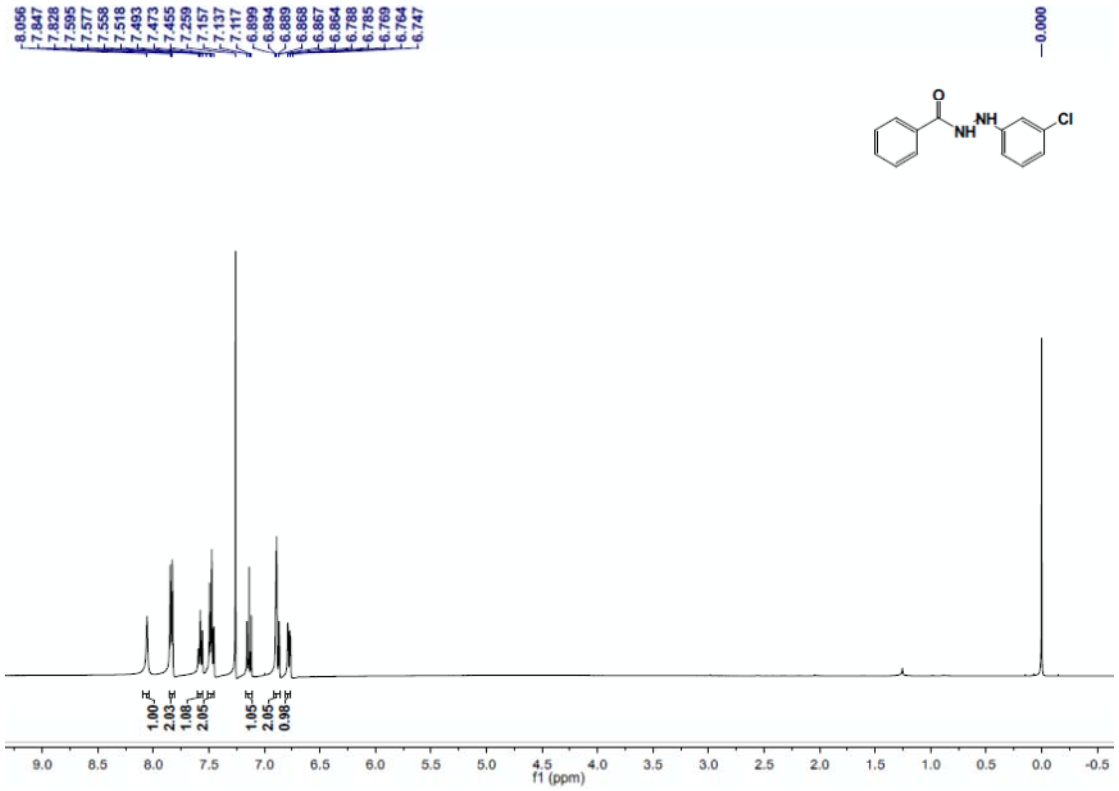


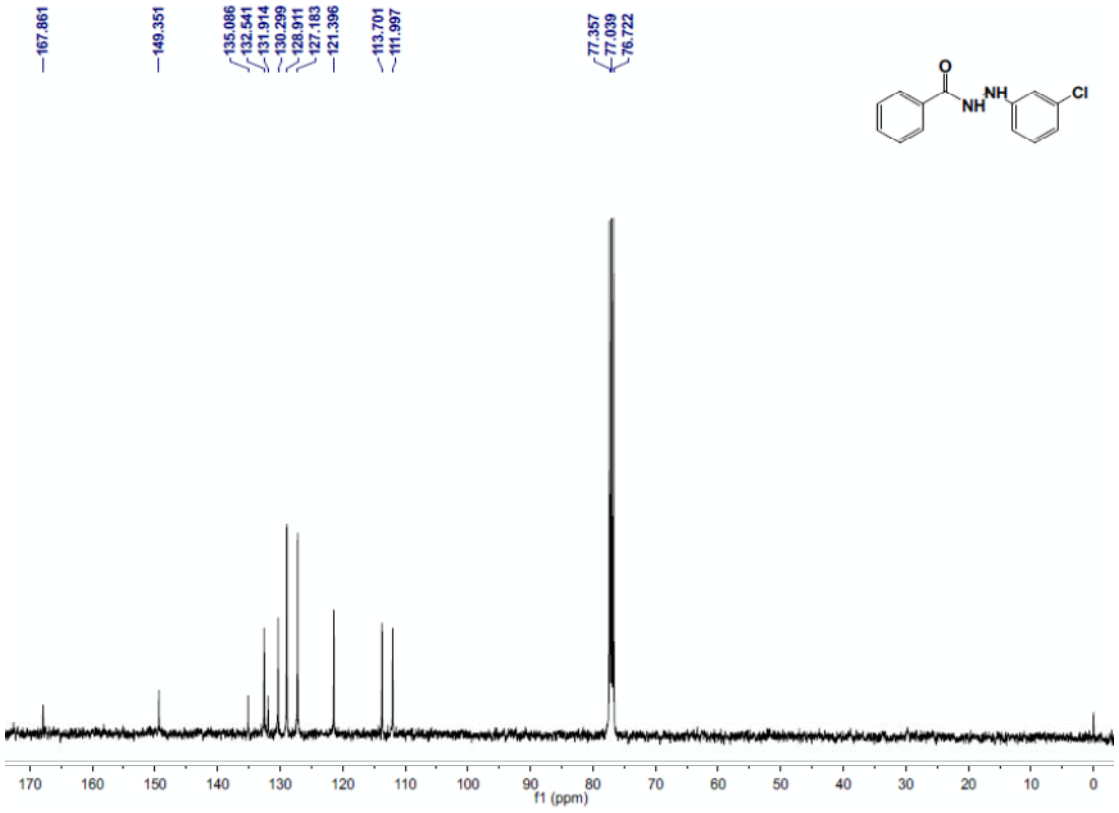
***N′*-(4-Bromophenyl)benzohydrazide (1d)**



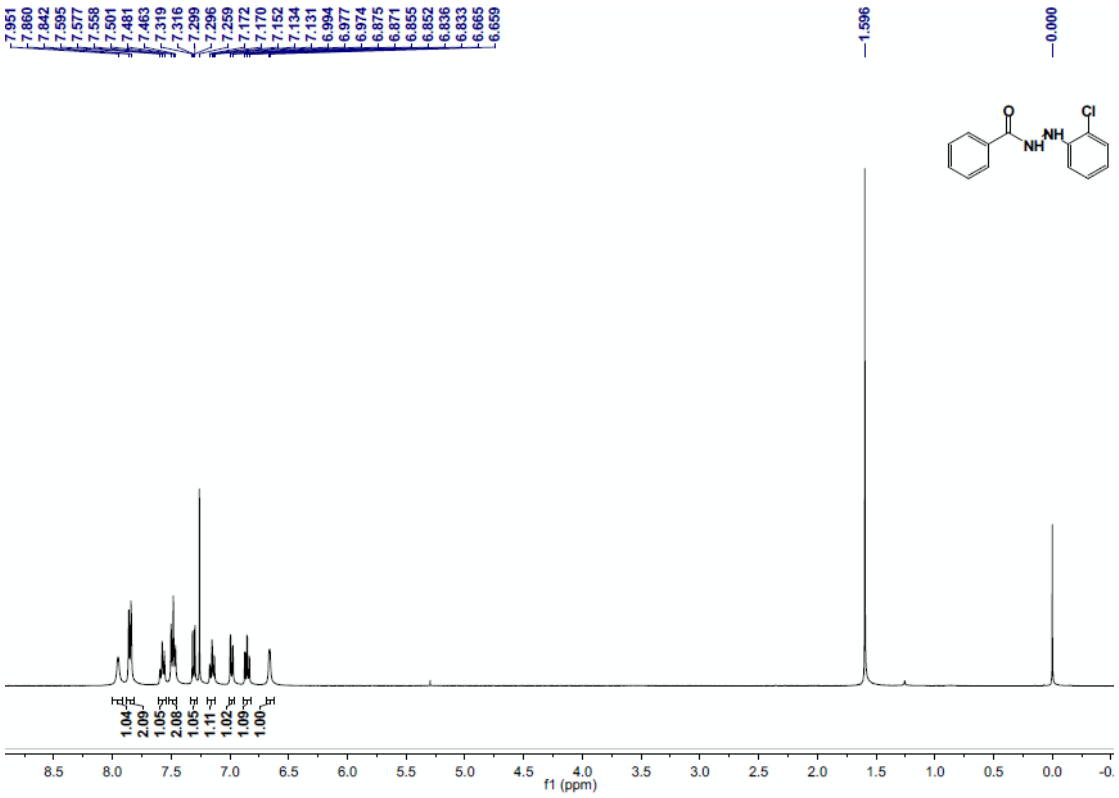


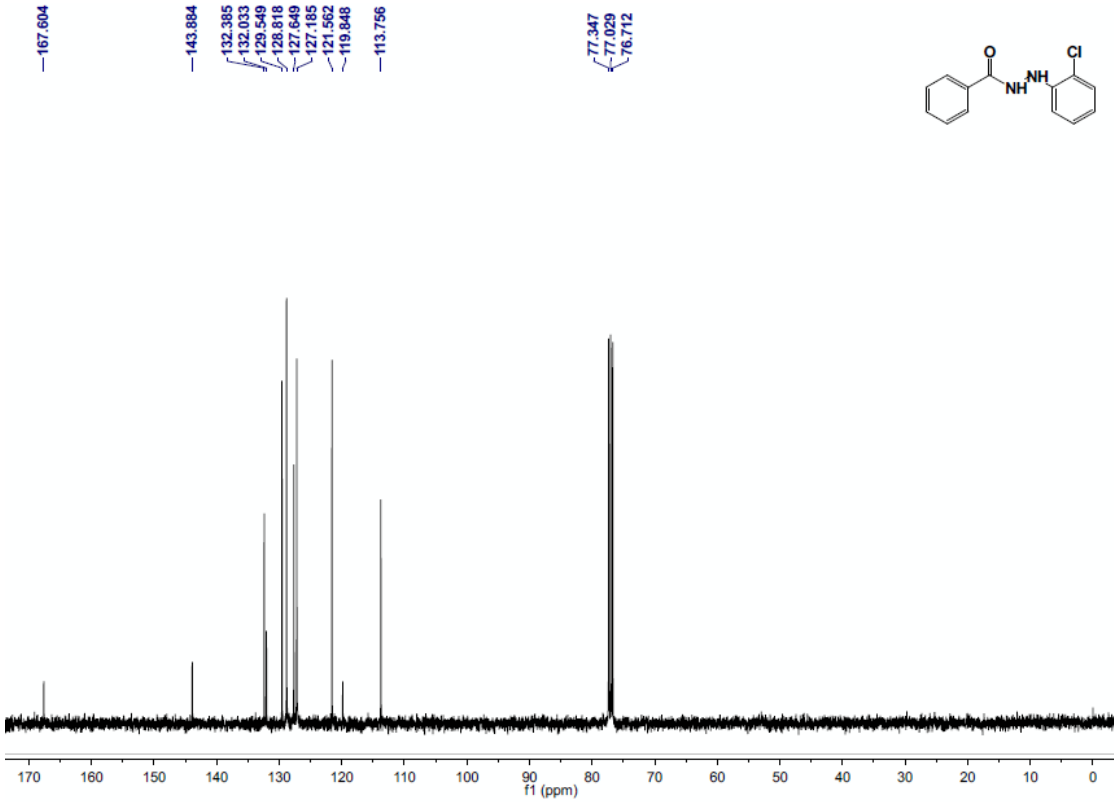
***N'*-(3-Chlorophenyl)benzohydrazide (1e)**



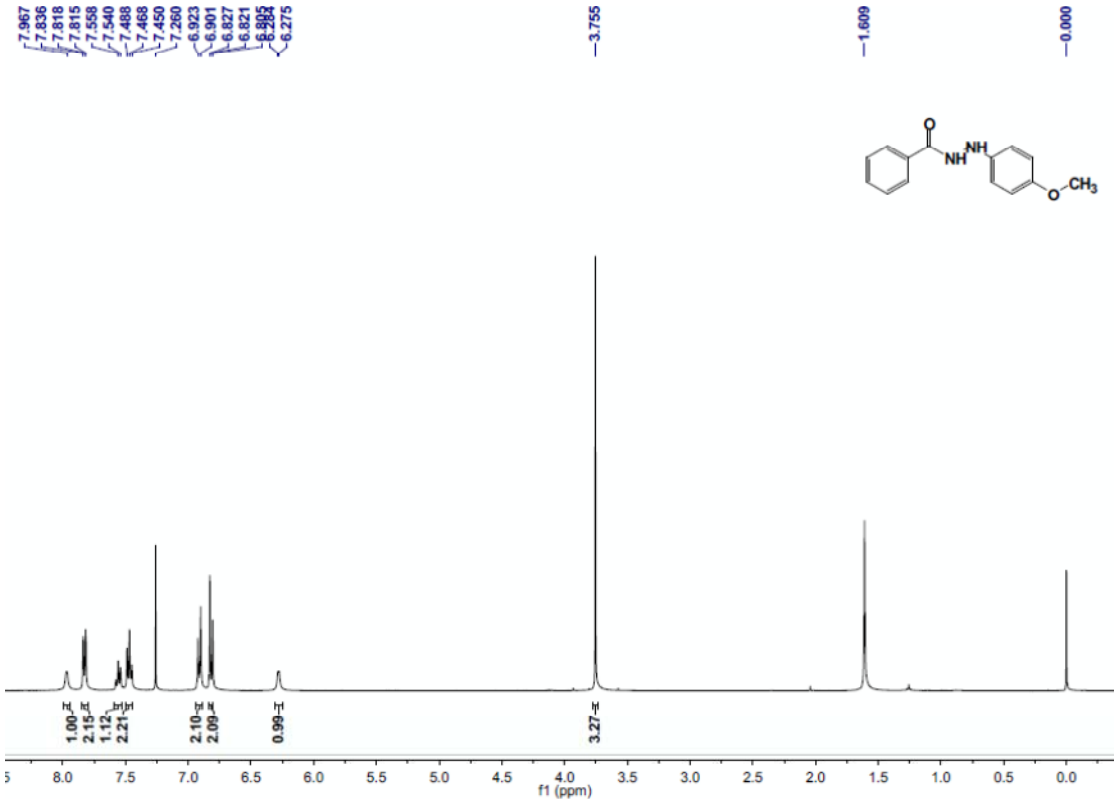


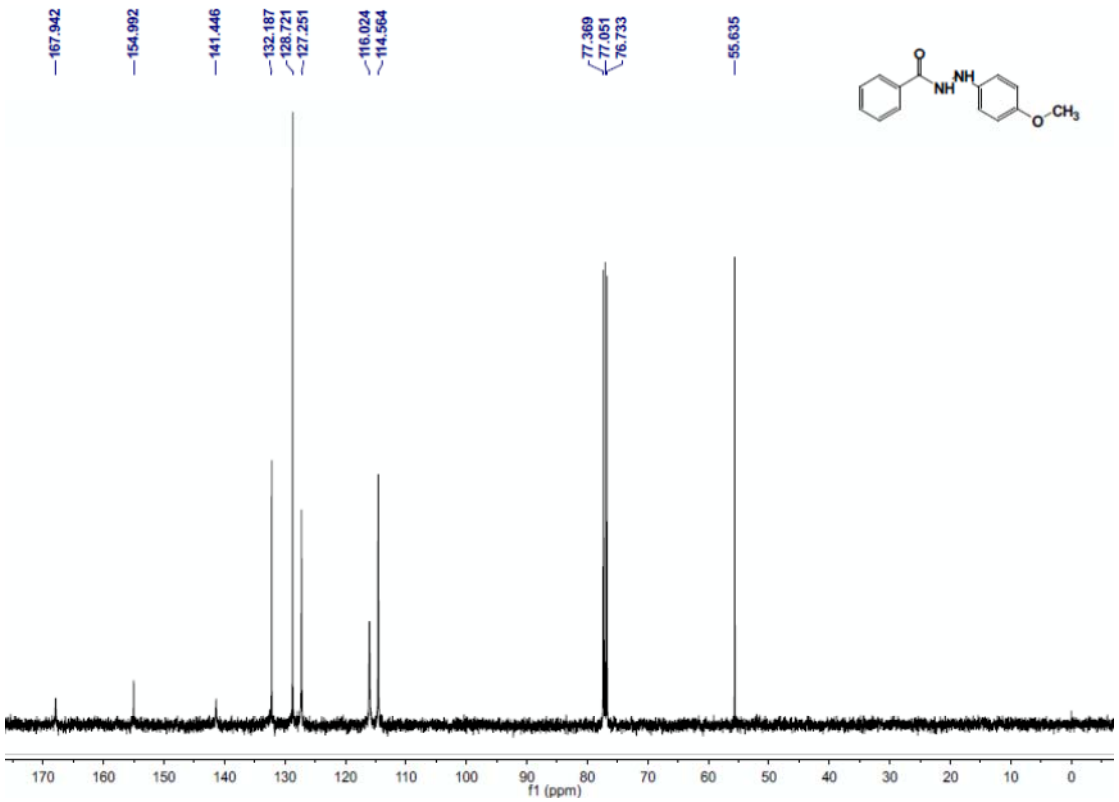
N'-(2-Chlorophenyl)benzohydrazide (1f)



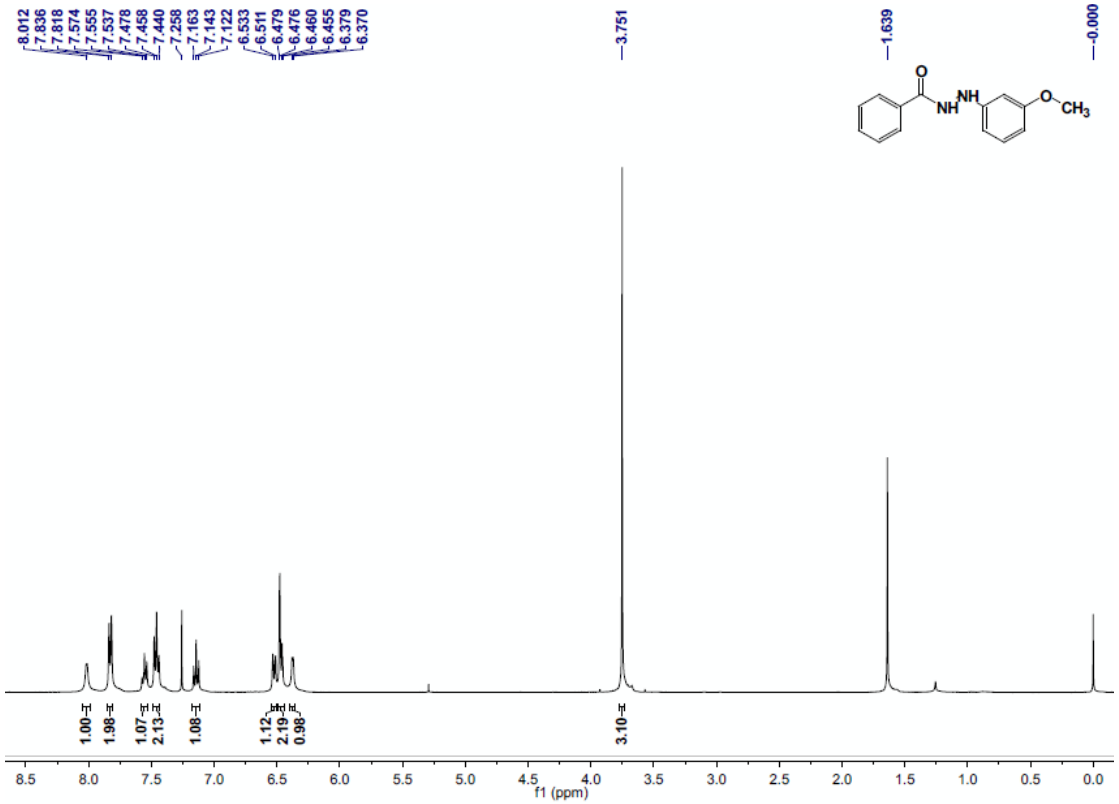


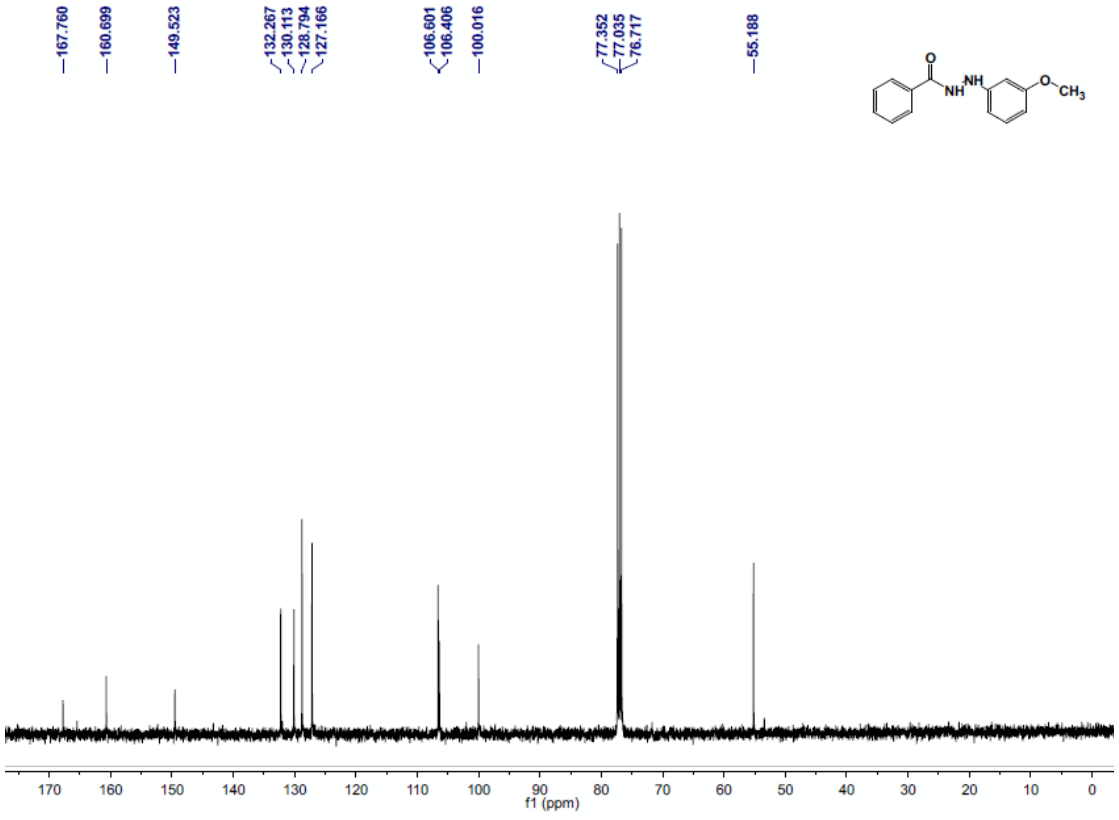
***N′*-(4-Methoxyphenyl)benzohydrazide (1g)**



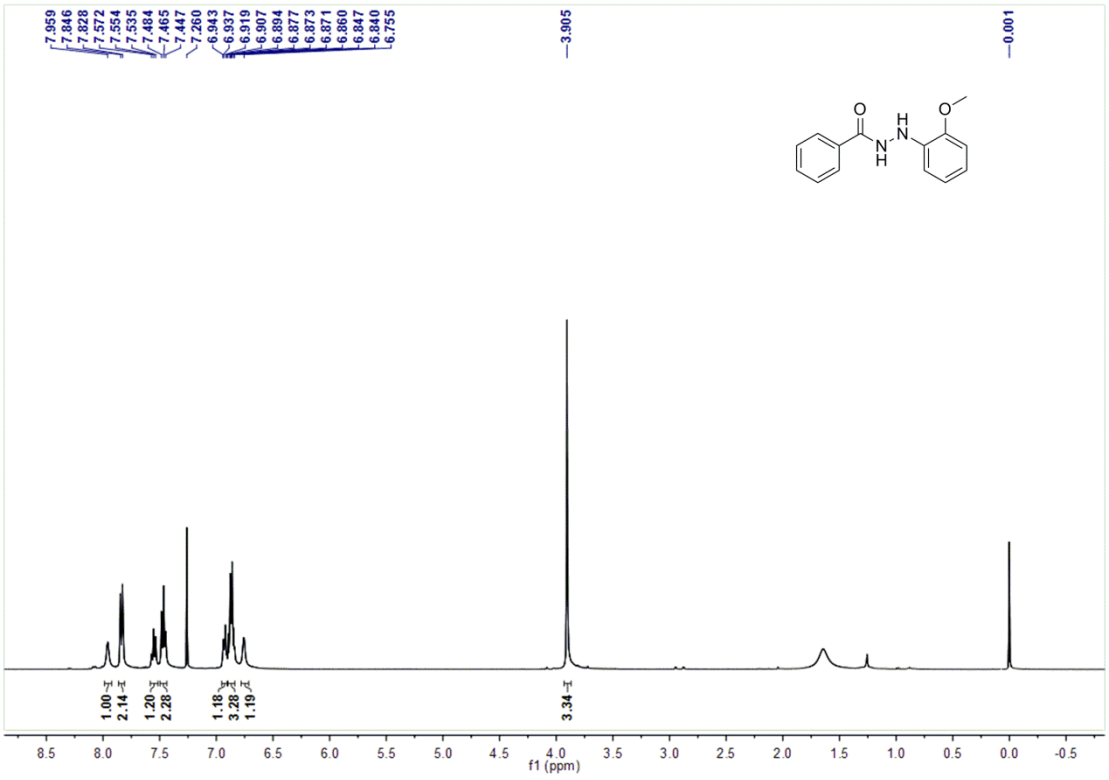


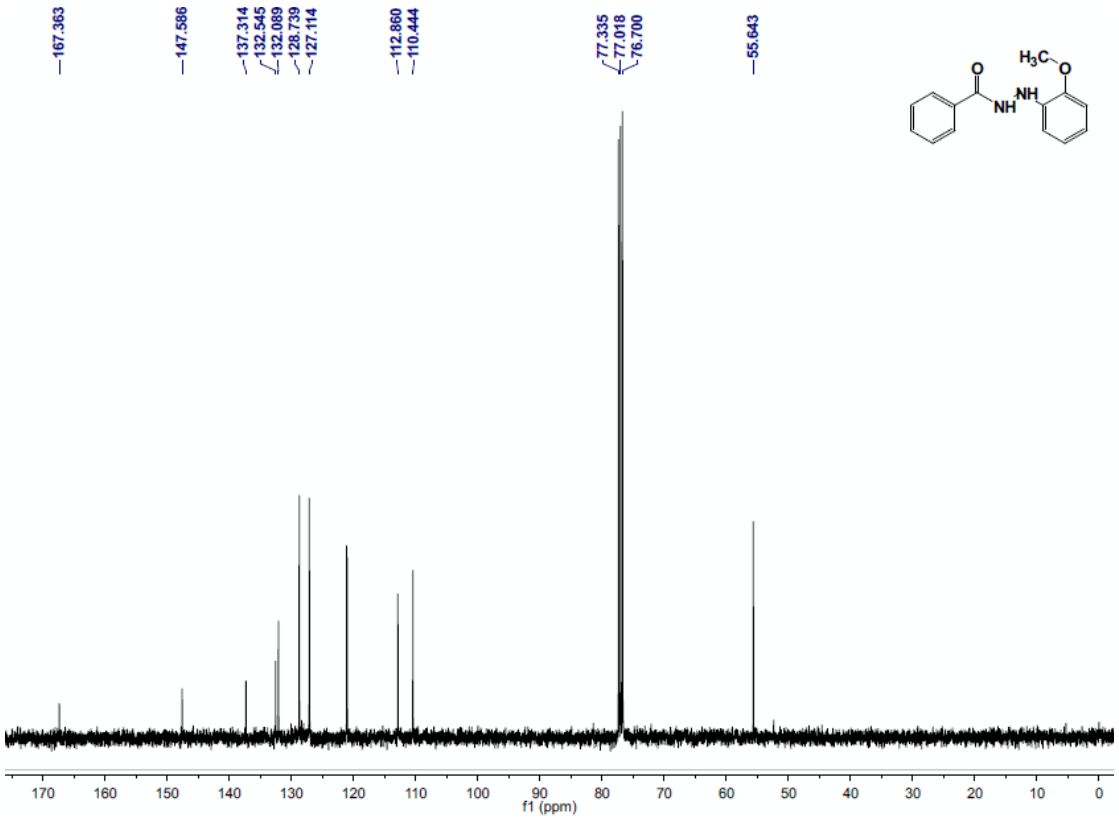
***N'*-(3-Methoxyphenyl)benzohydrazide (1h)**



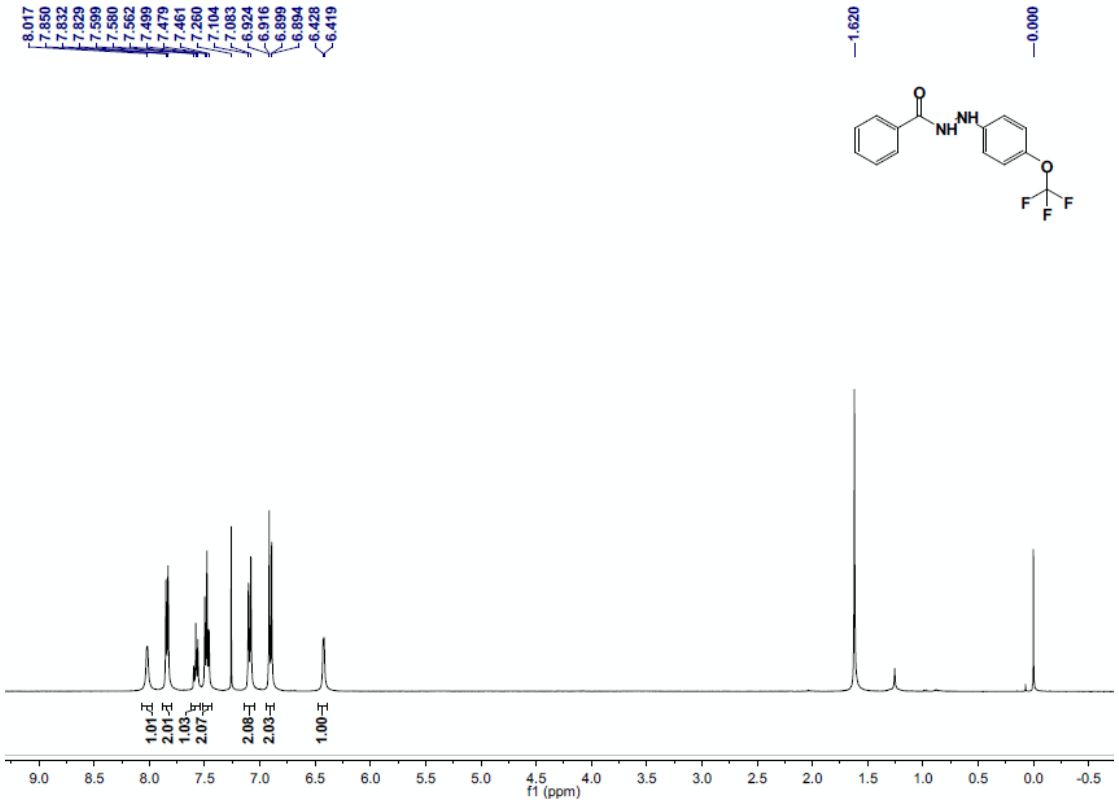


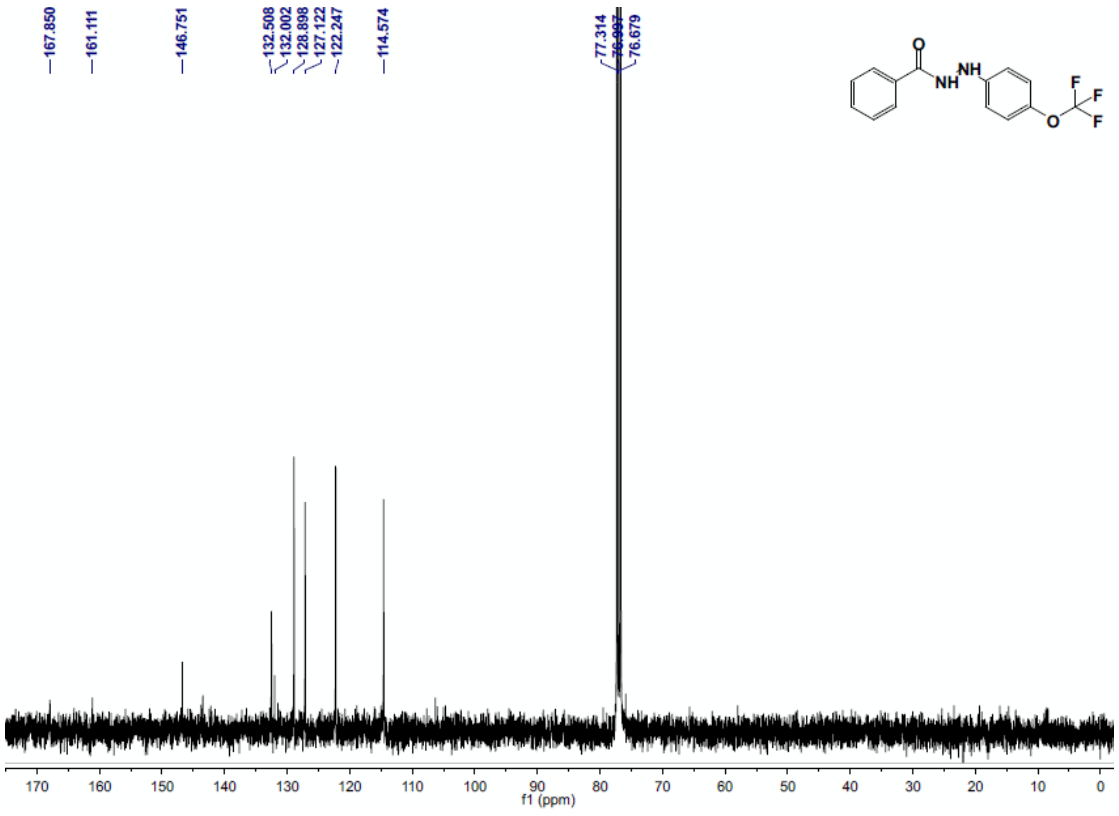
***N'*-(2-Methoxyphenyl)benzohydrazide (1i)**



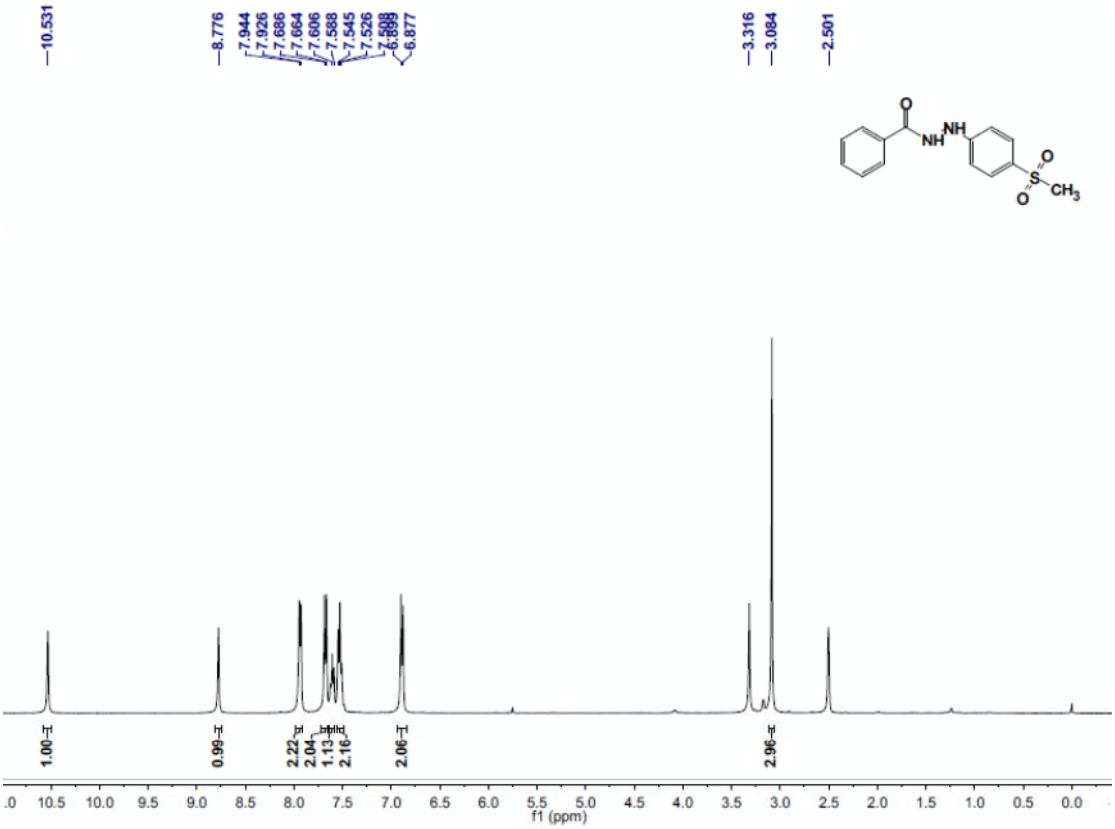


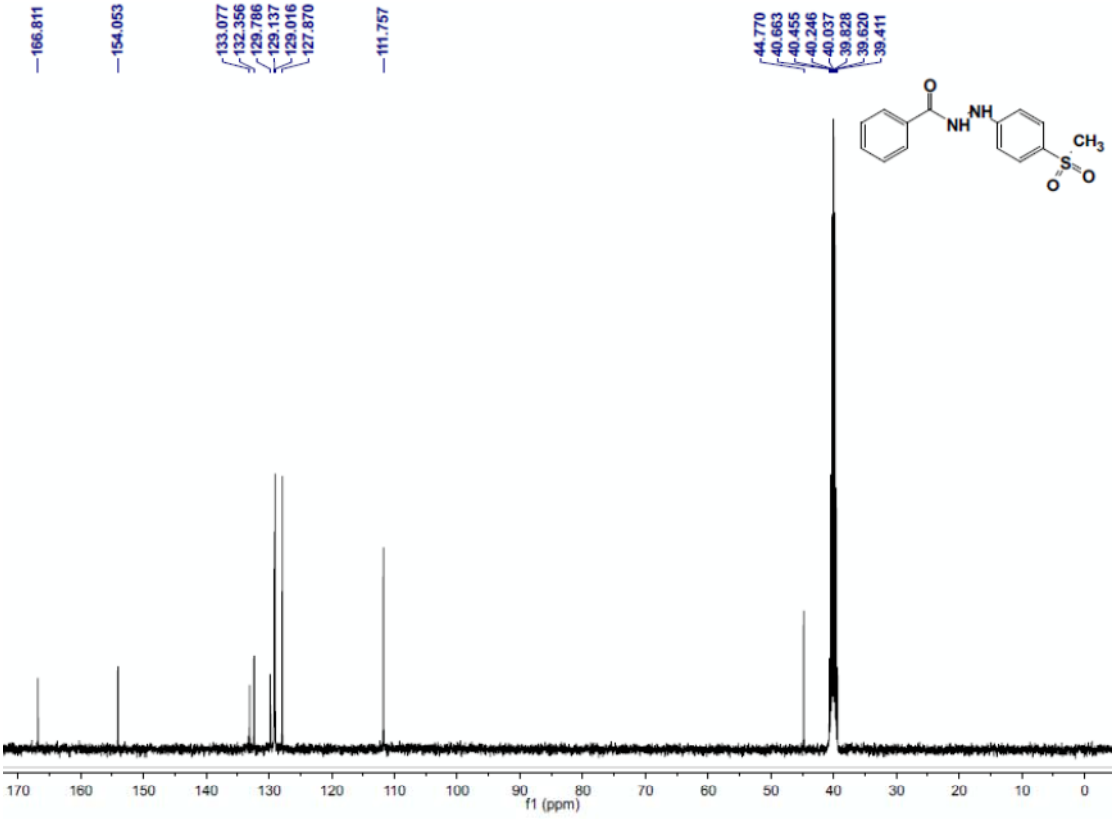
***N'*-(4-(*tri*Fluoromethoxy)phenyl)benzohydrazide (1j)**



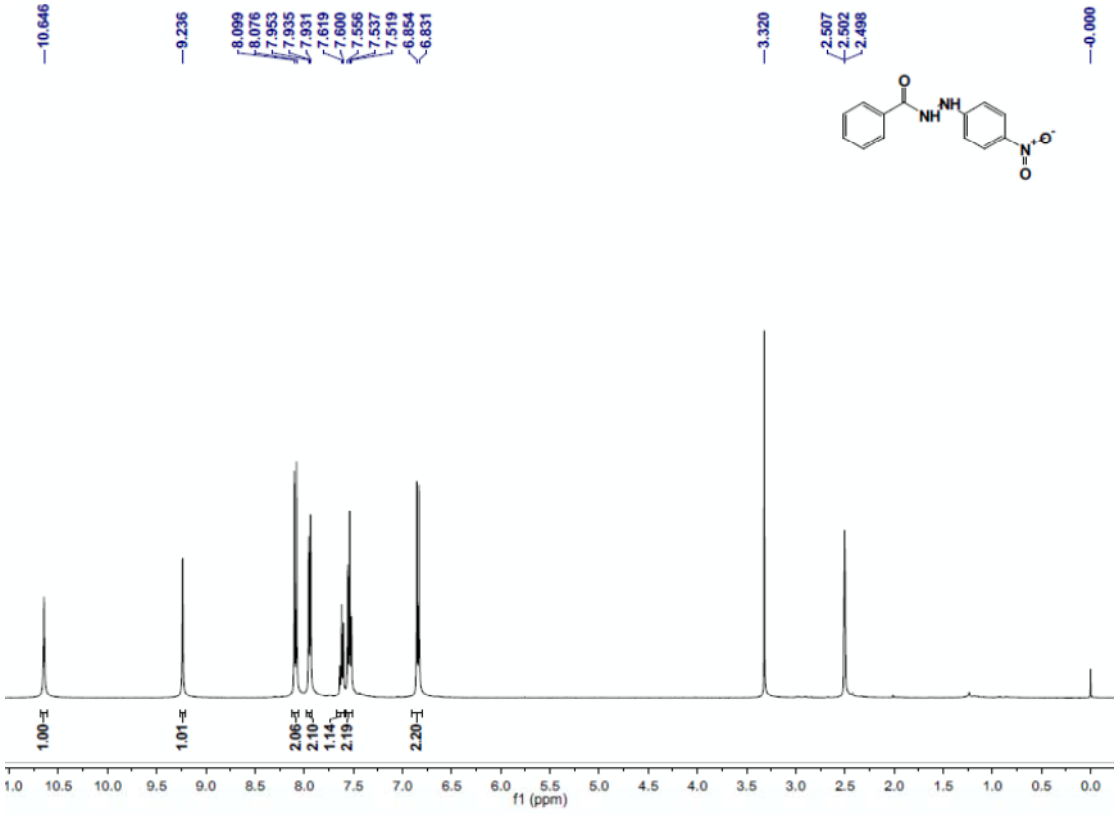


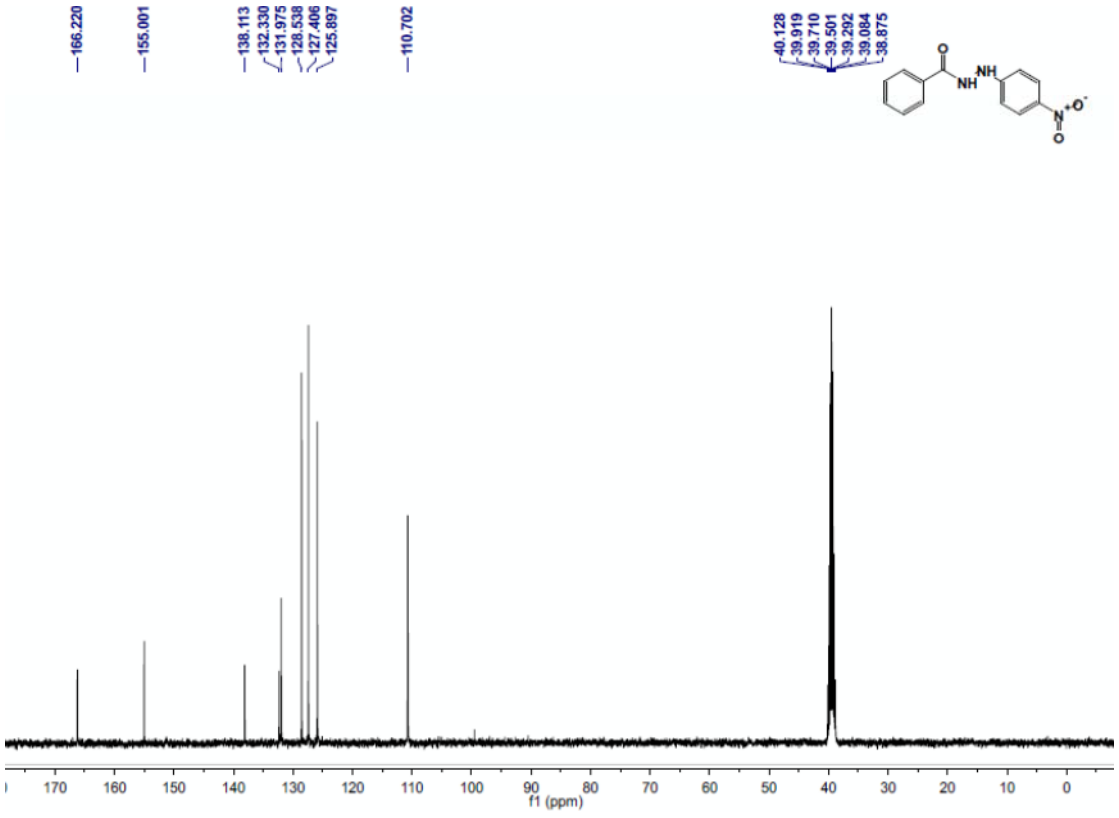
***N′*-(4-(Methylsulfonyl)phenyl)benzohydrazide (1k)**



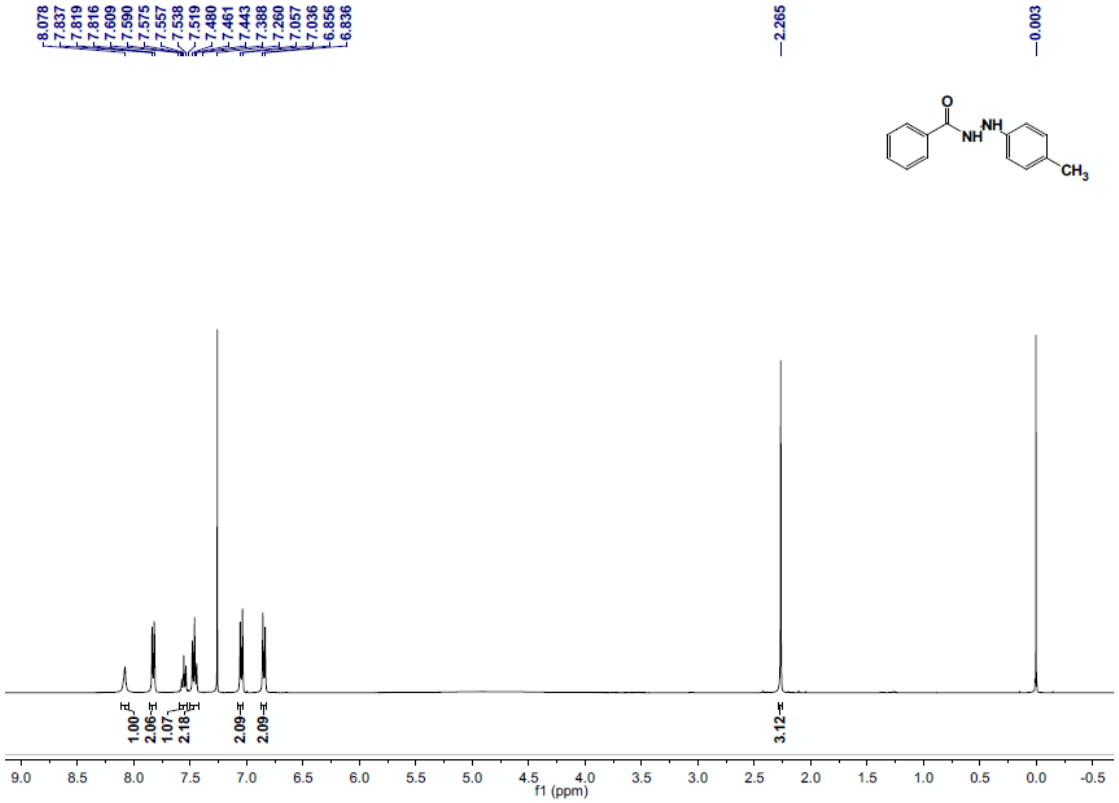


***N′*-(4-Nitrophenyl)benzohydrazide (1l)**

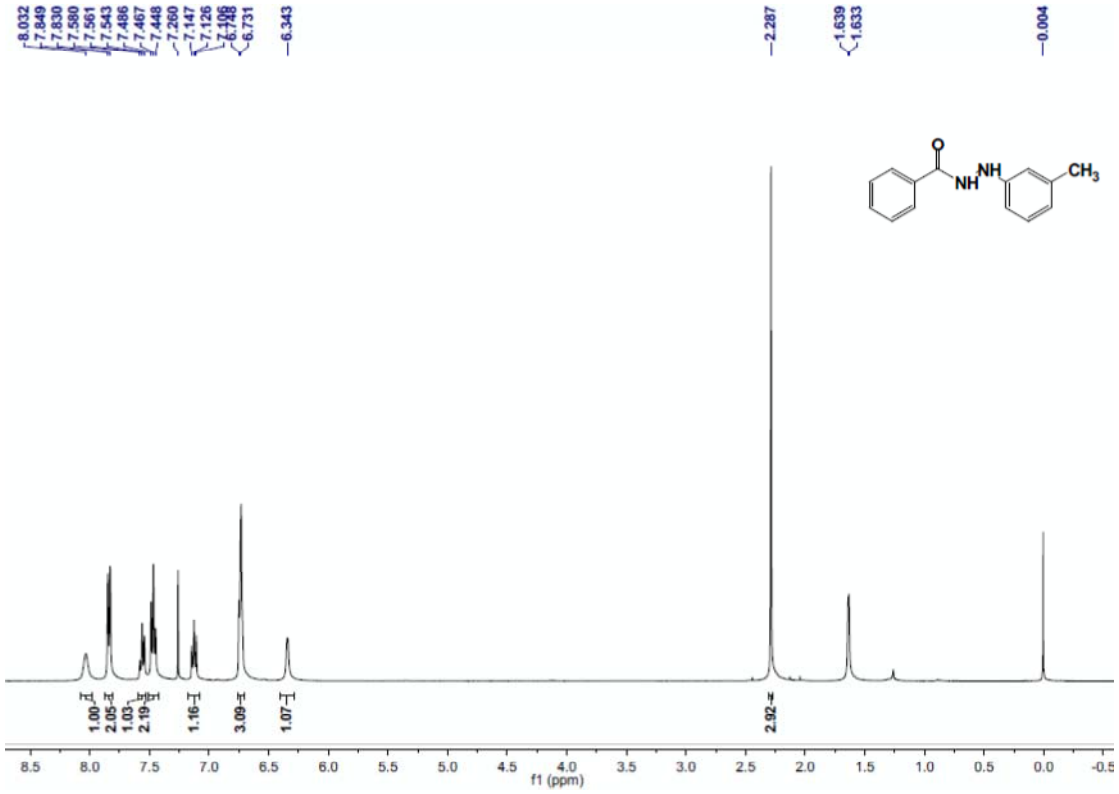


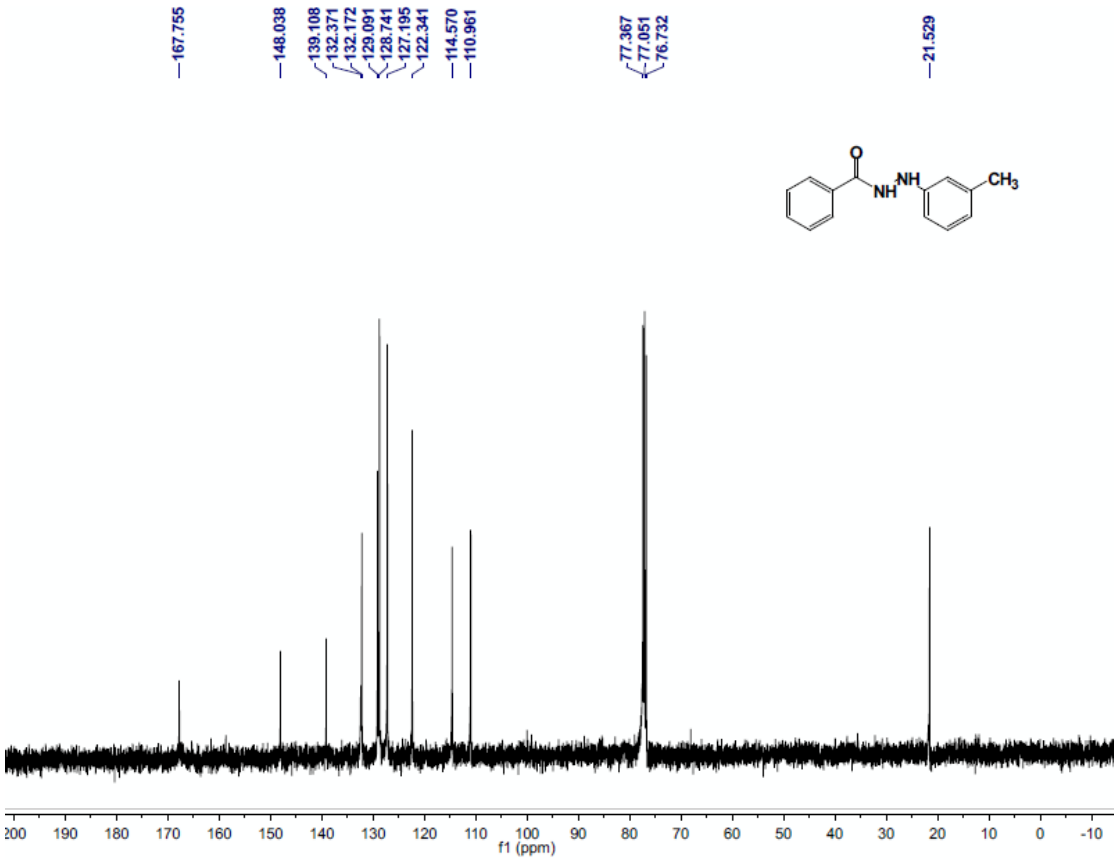


***N'*-*p*-Tolylbenzohydrazide (1m)**

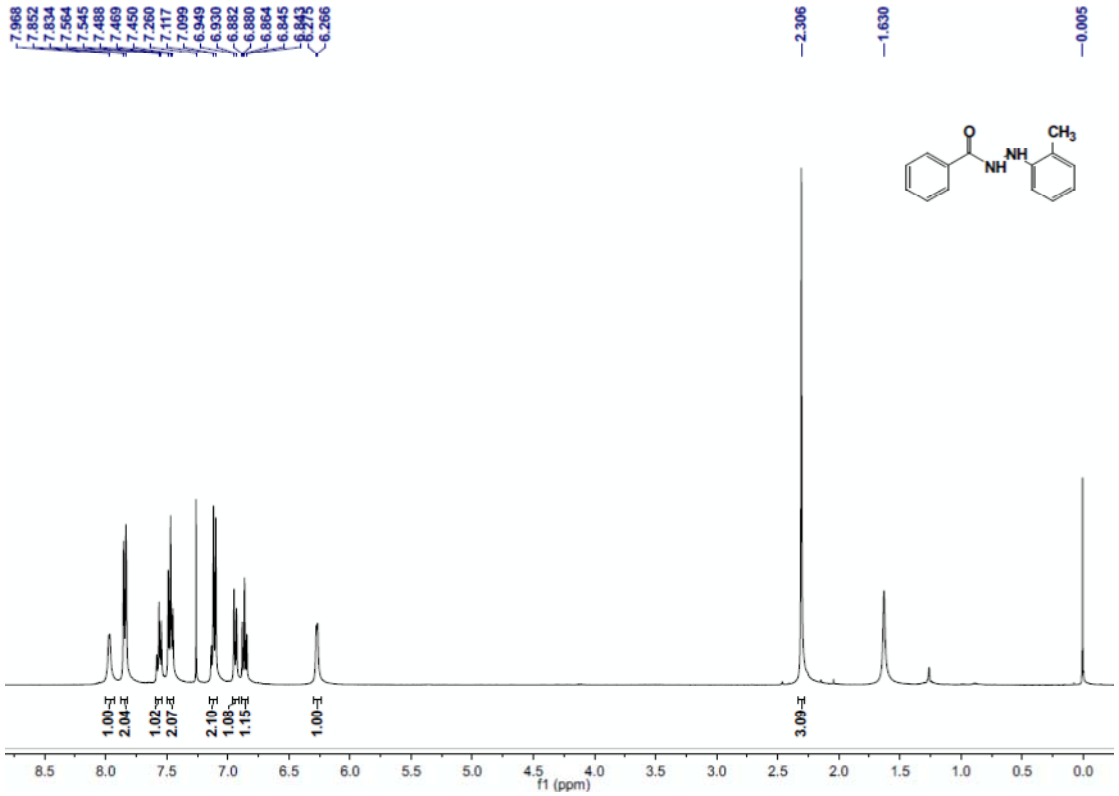


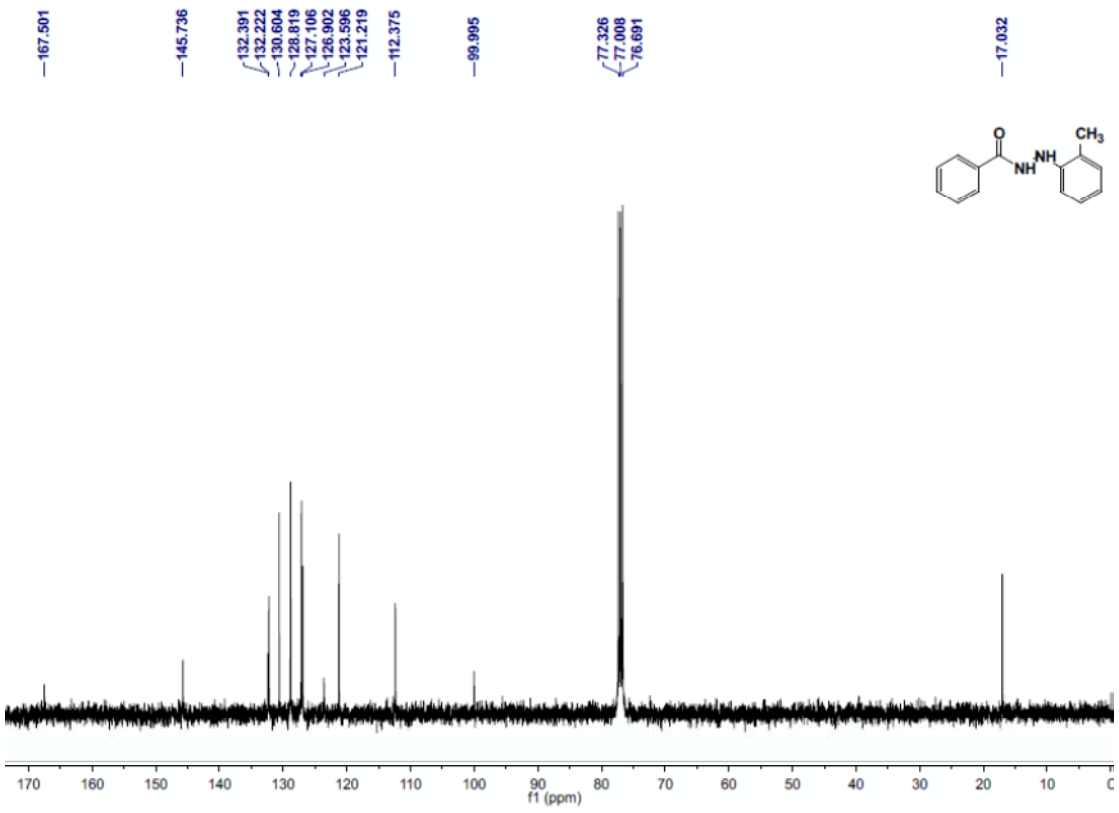
***N'*-*m*-Tolylbenzohydrazide (1n)**



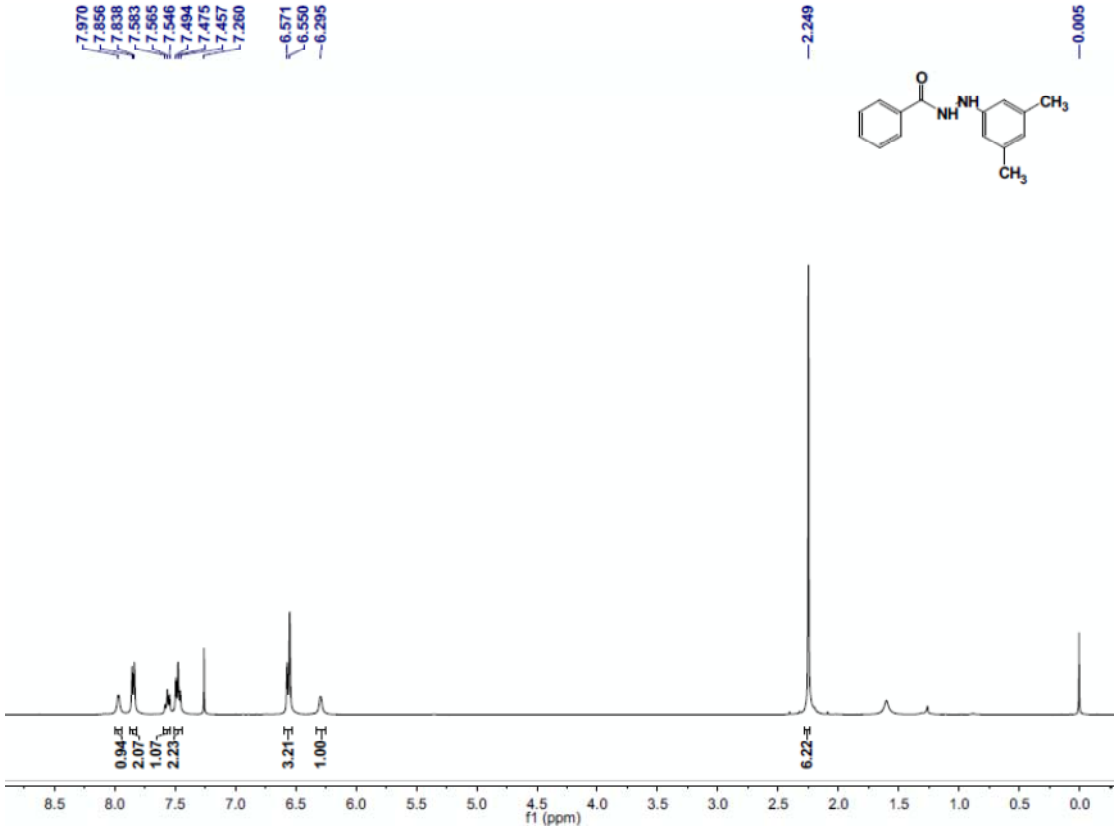


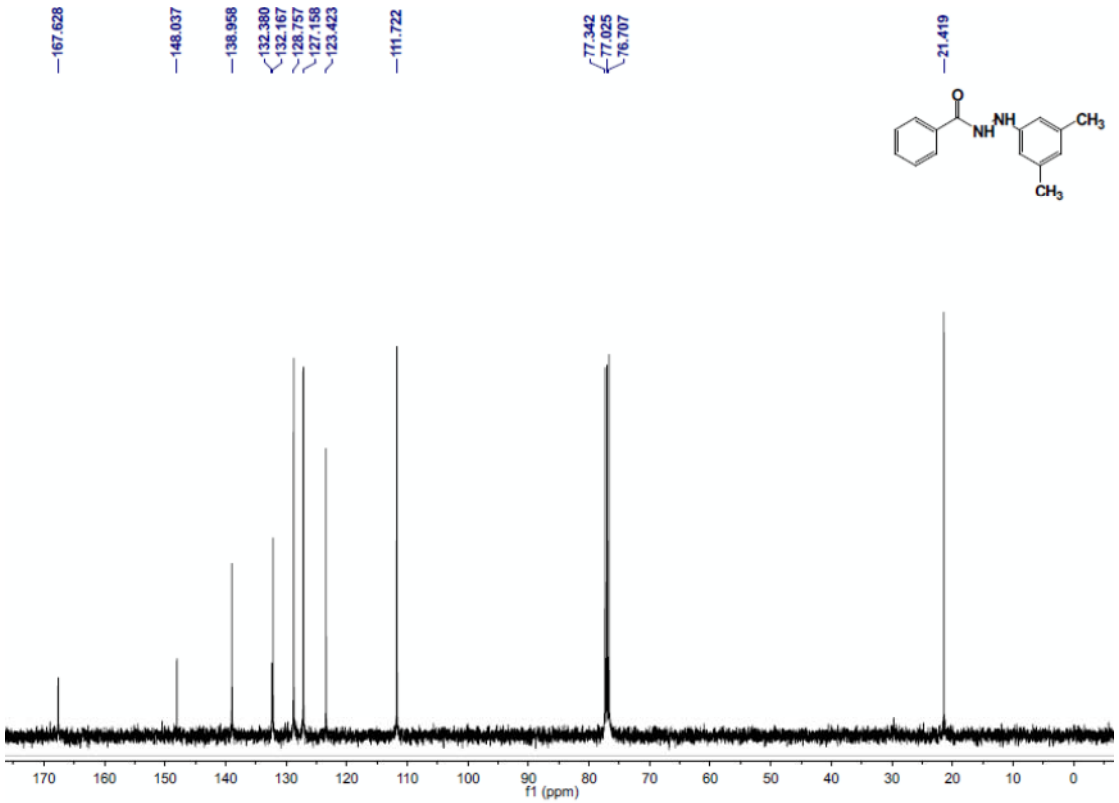
***N'*-*o*-Tolylbenzohydrazide (1o)**



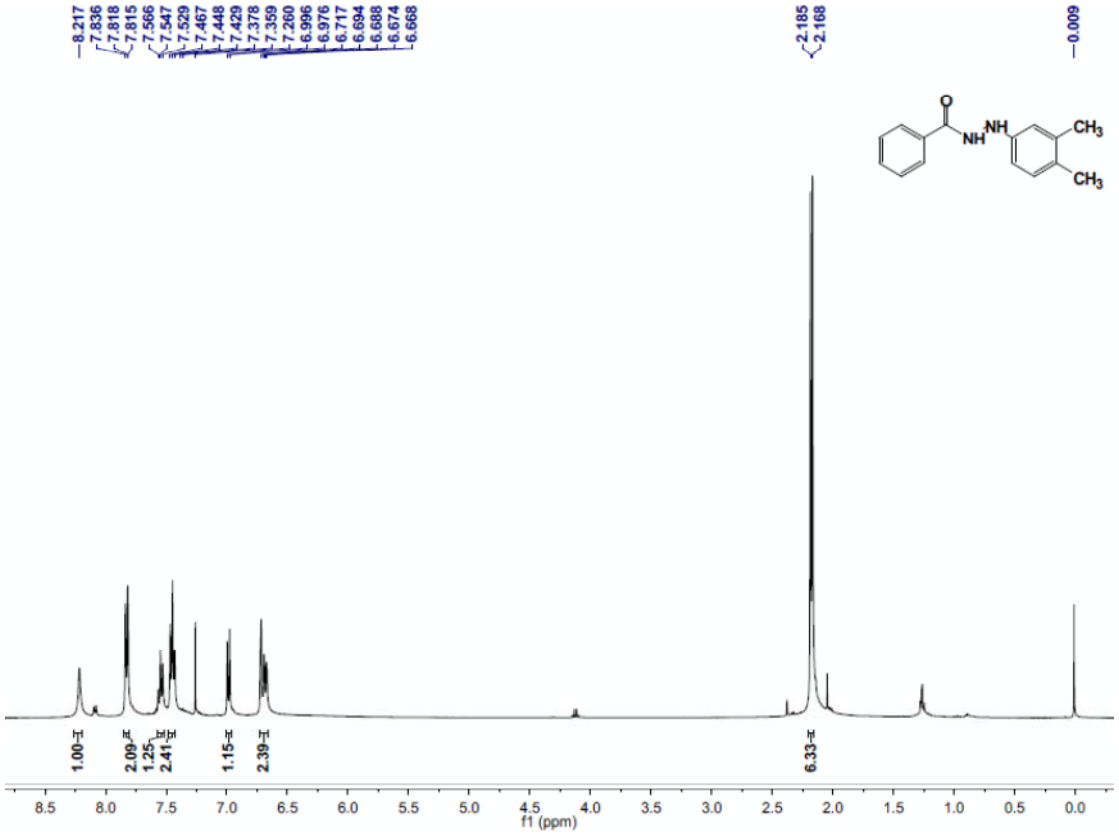


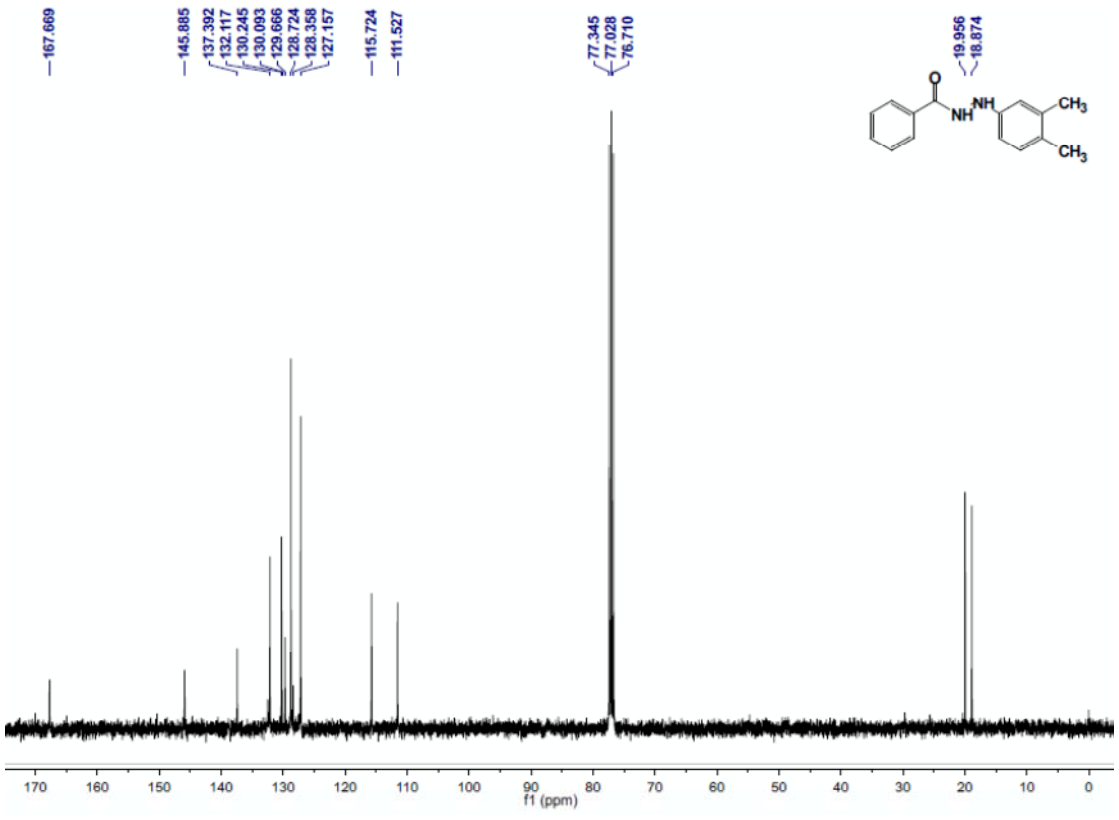
***N'*-(3,5-*di*Methylphenyl)benzohydrazide (1p)**



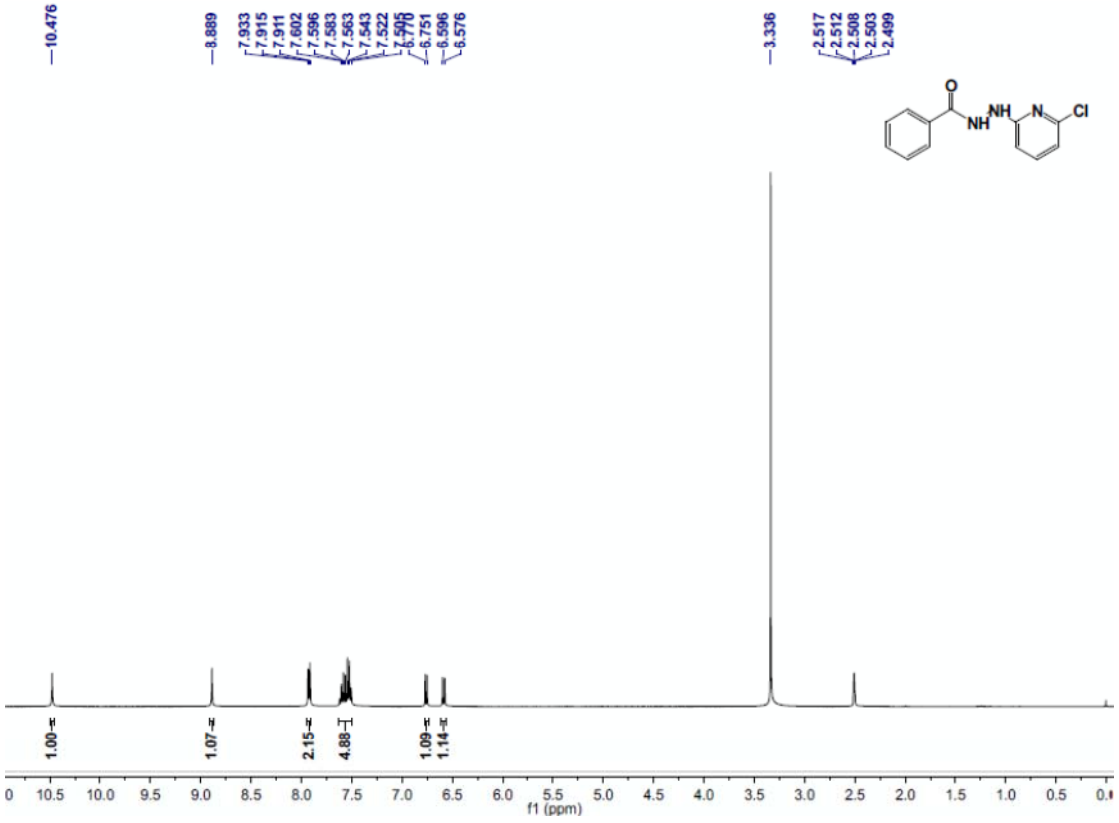


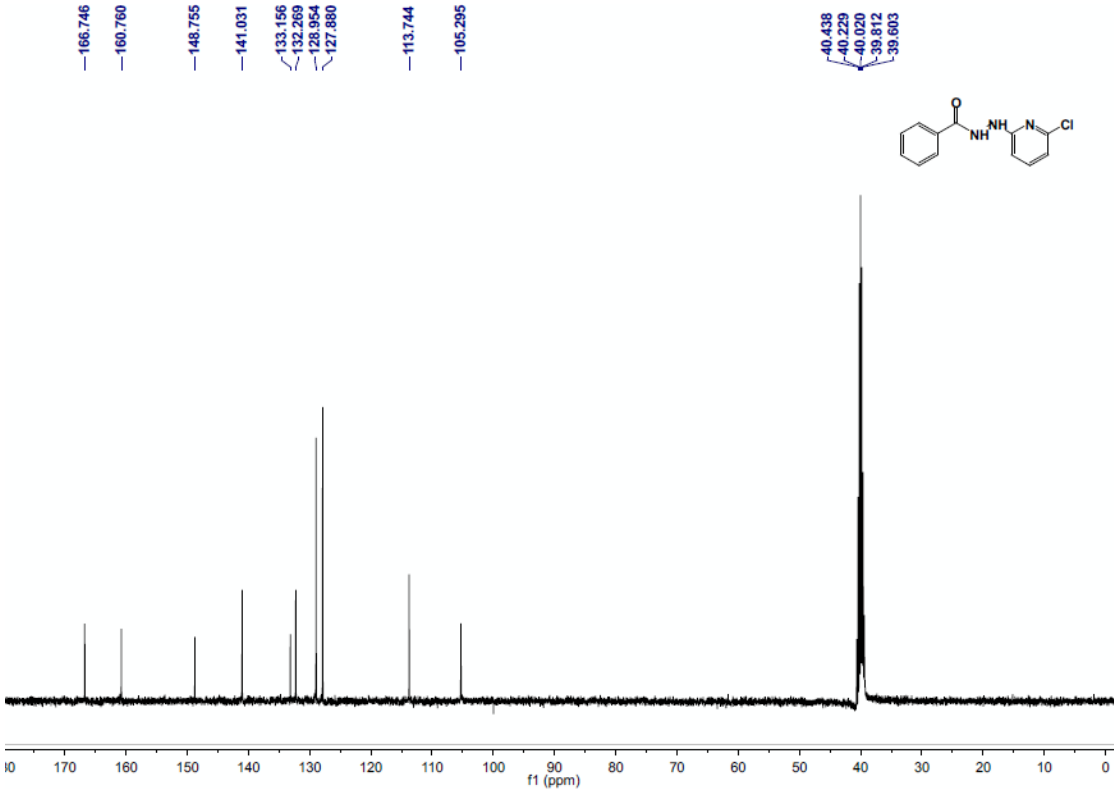
***N'*-(3,4-*di*Methylphenyl)benzohydrazide (1q)**



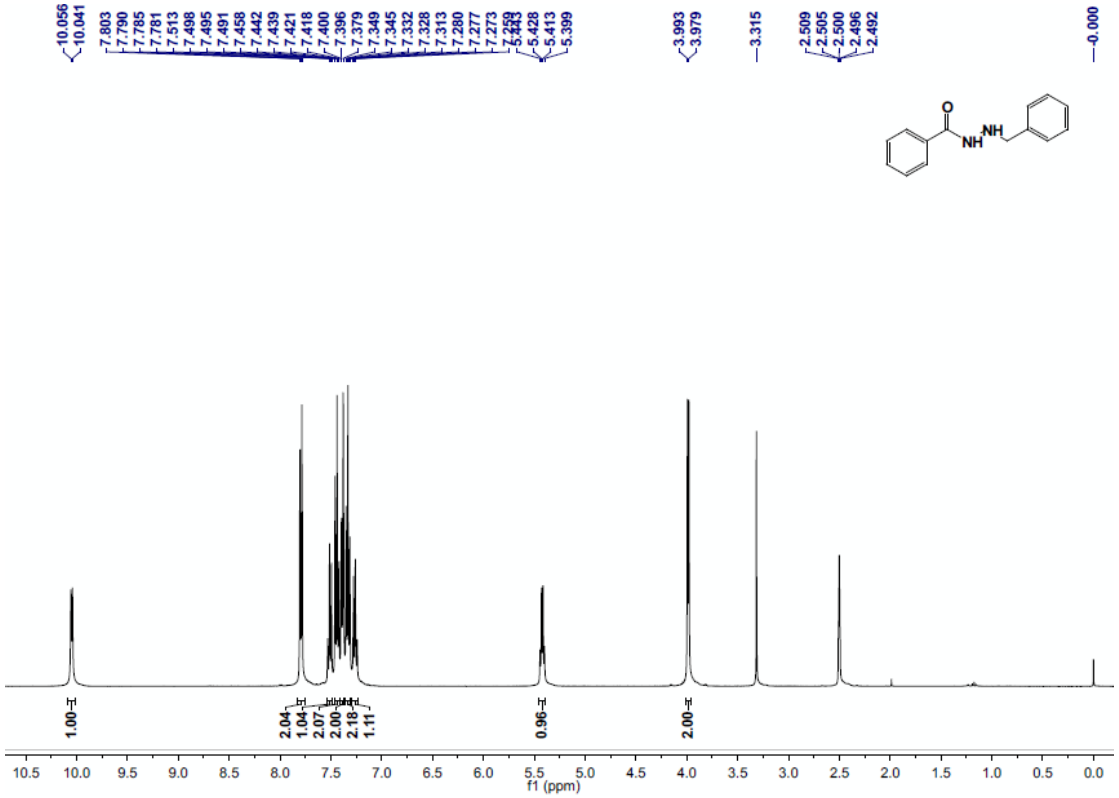


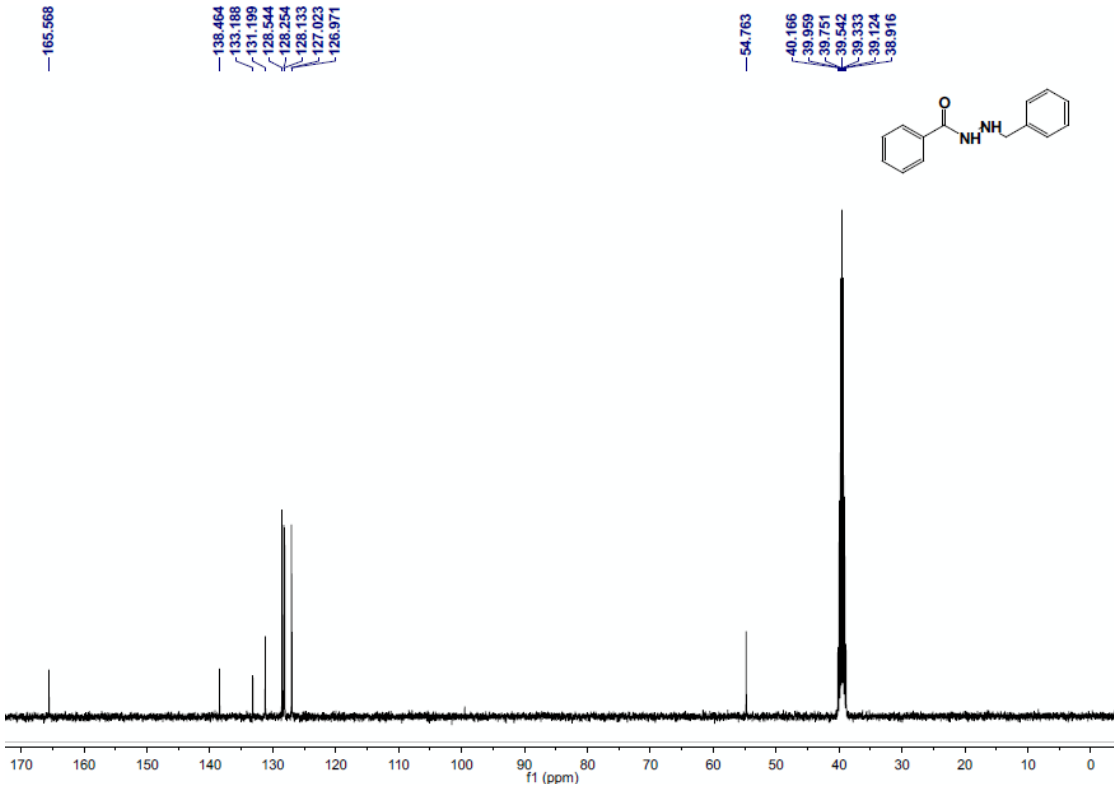
***N′*-(6-Chloropyridin-2-yl)benzohydrazide (1r)**



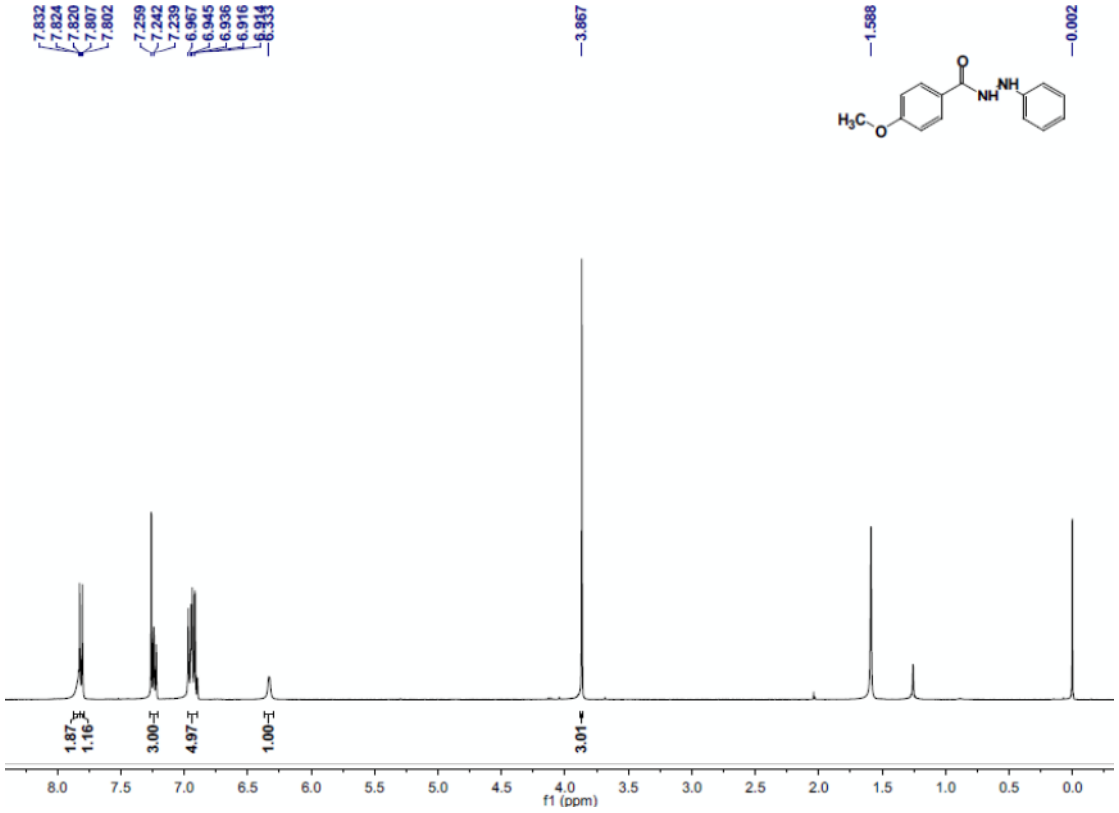


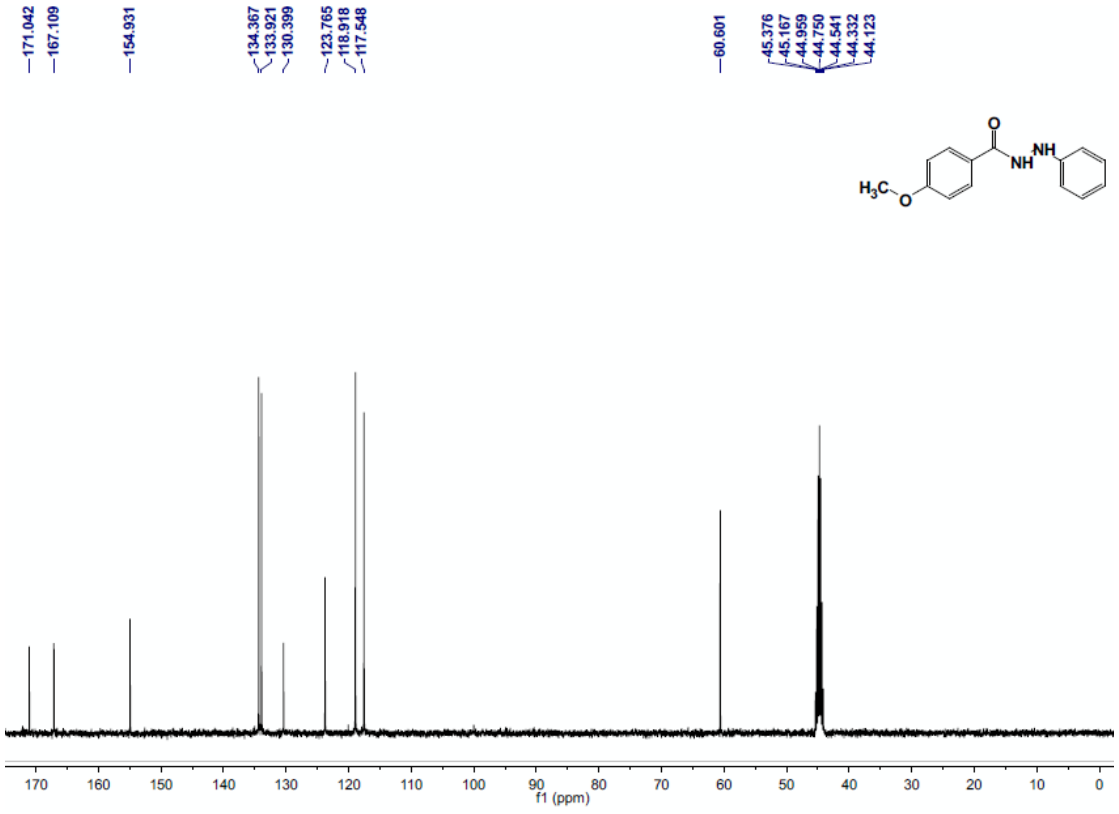
***N'*-Benzylbenzohydrazide (1s)**



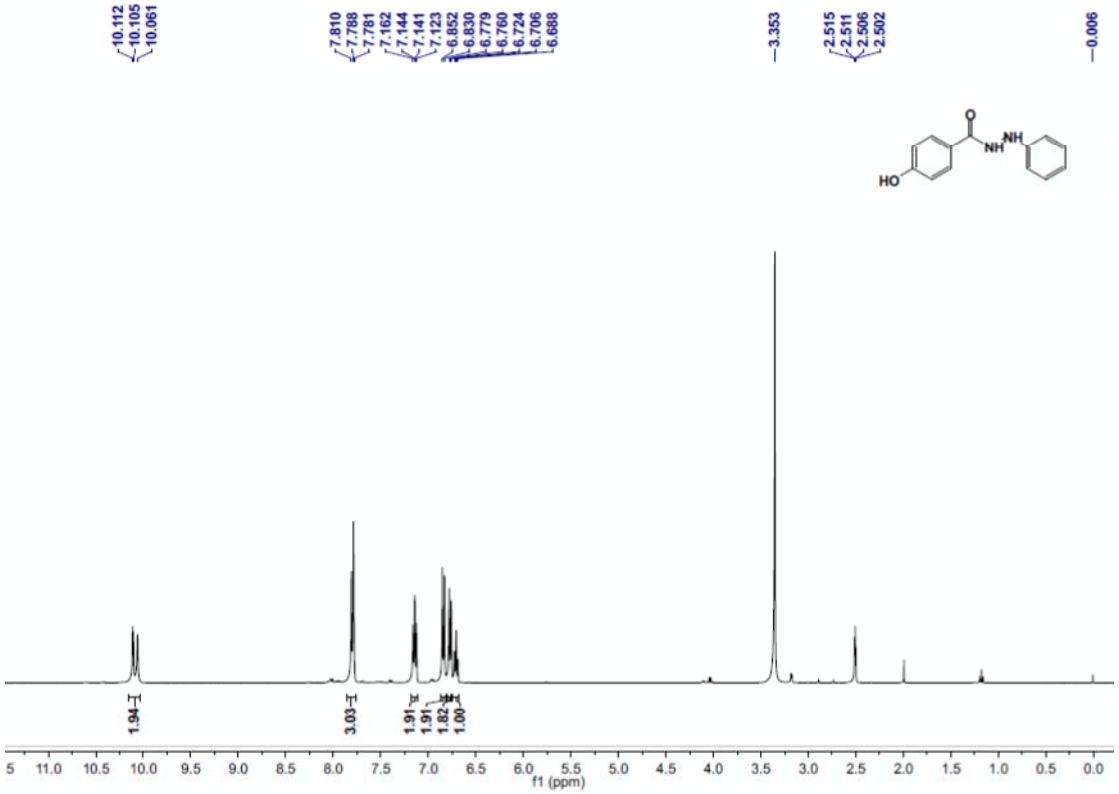


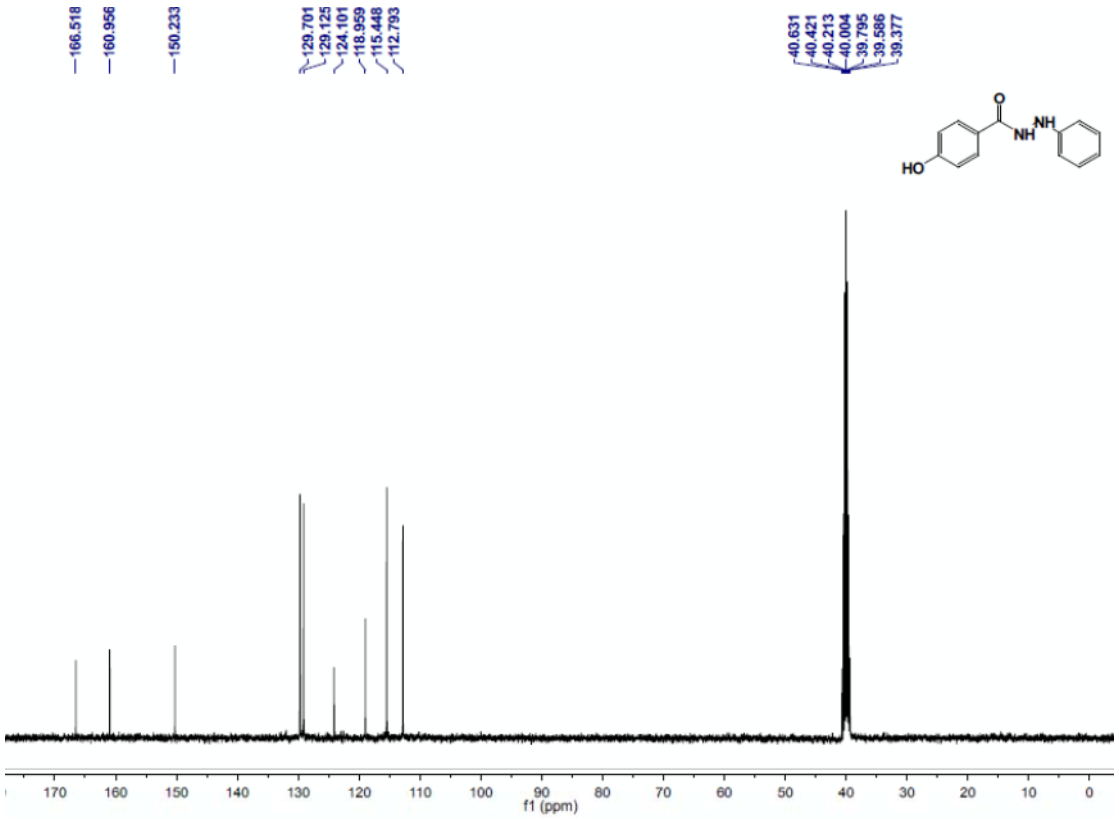
4-Methoxy-*N'*-phenylbenzohydrazide (1t)



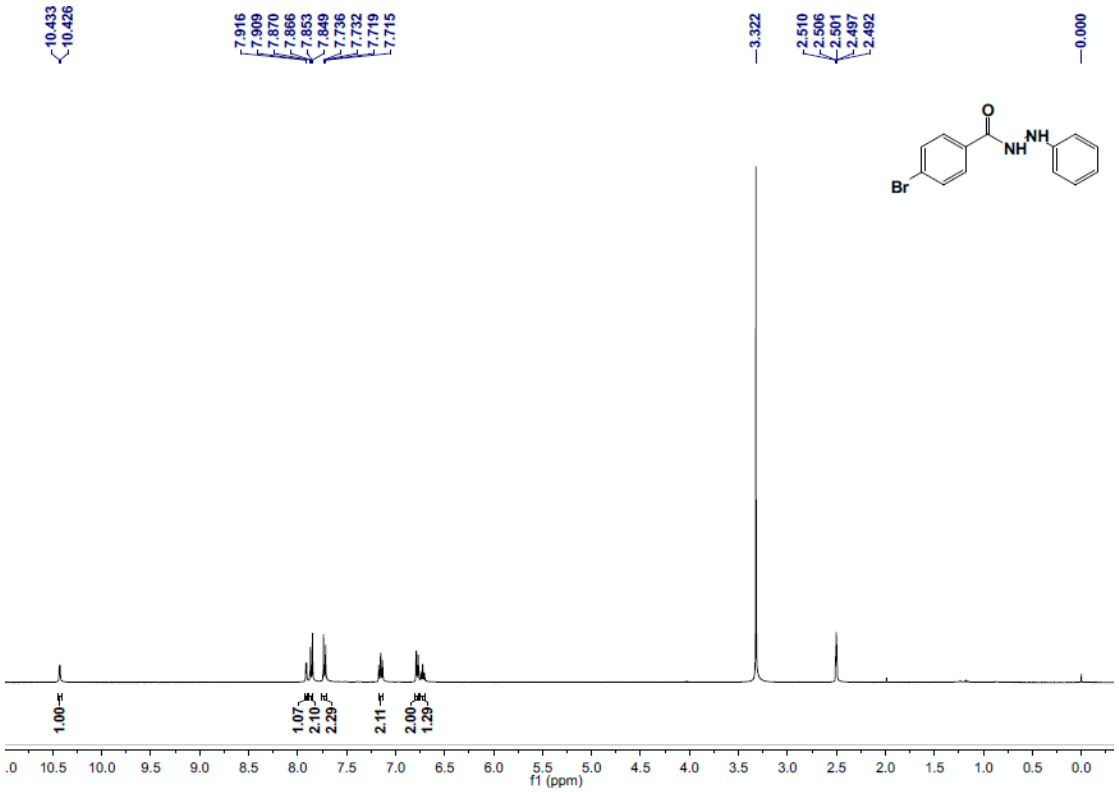


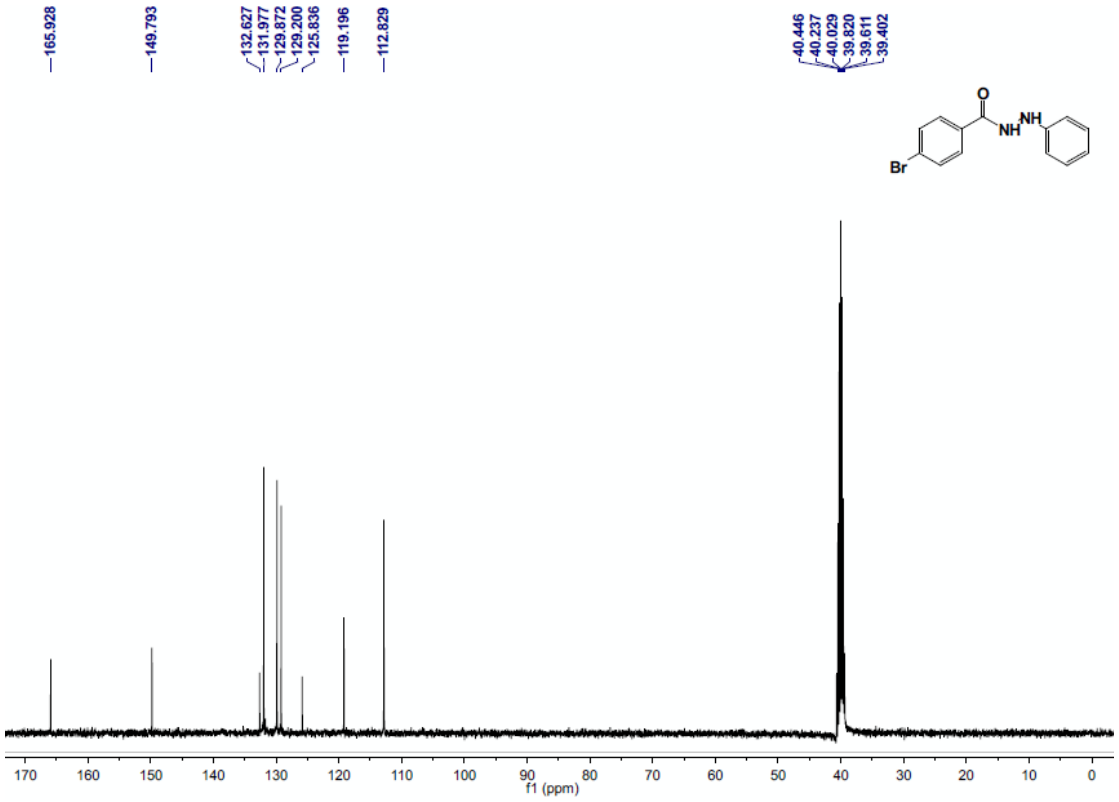
4-Hydroxy-*N'*-phenylbenzohydrazide (1u)



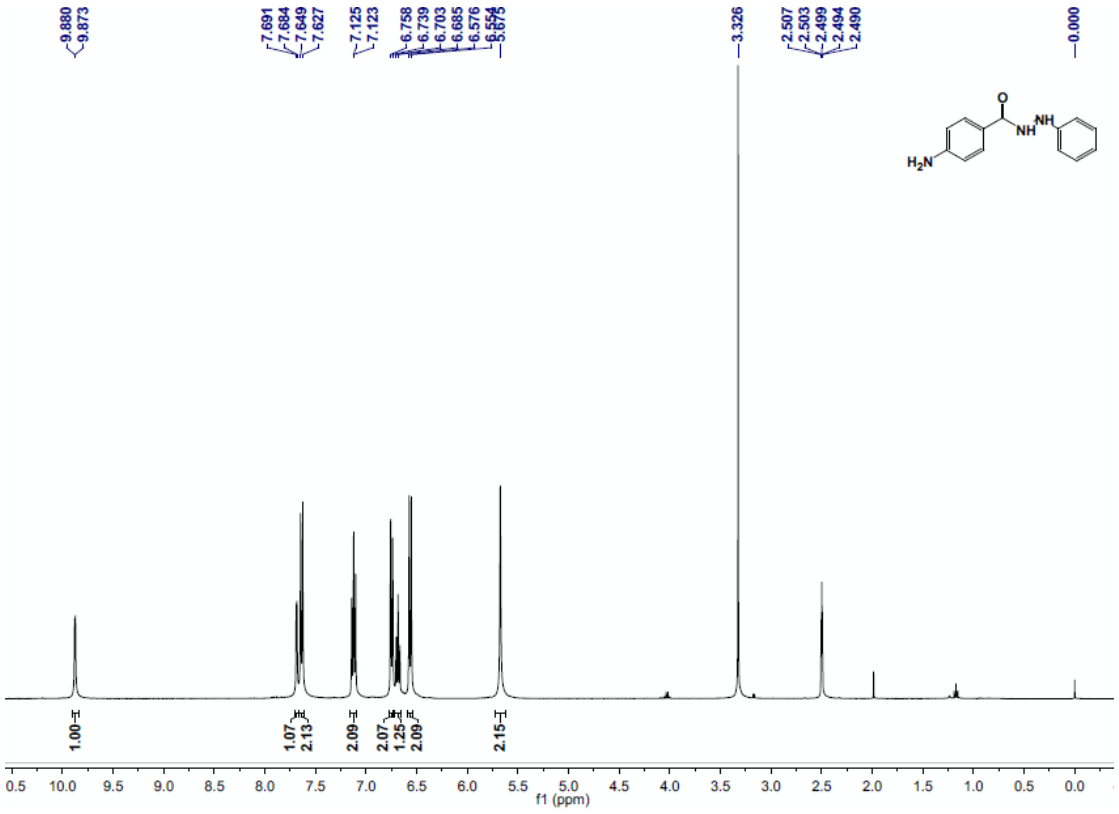


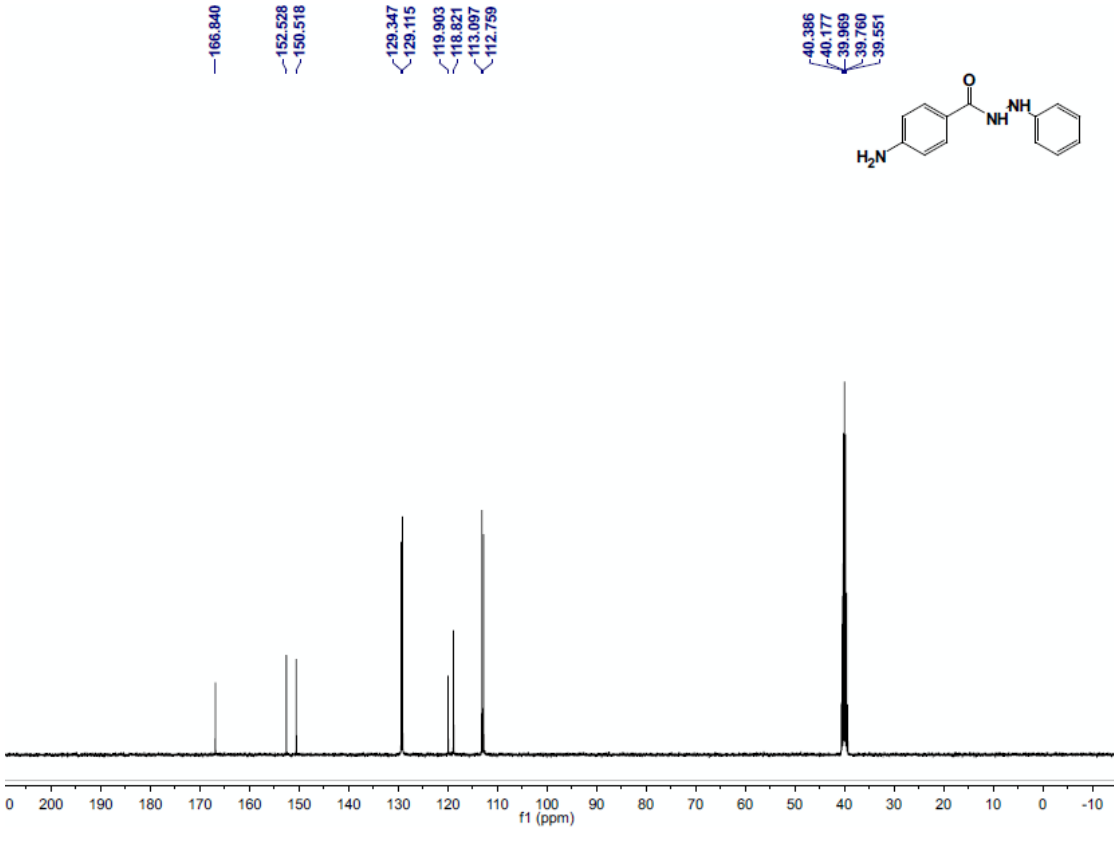
4-Bromo-*N'*-phenylbenzohydrazide (1v)



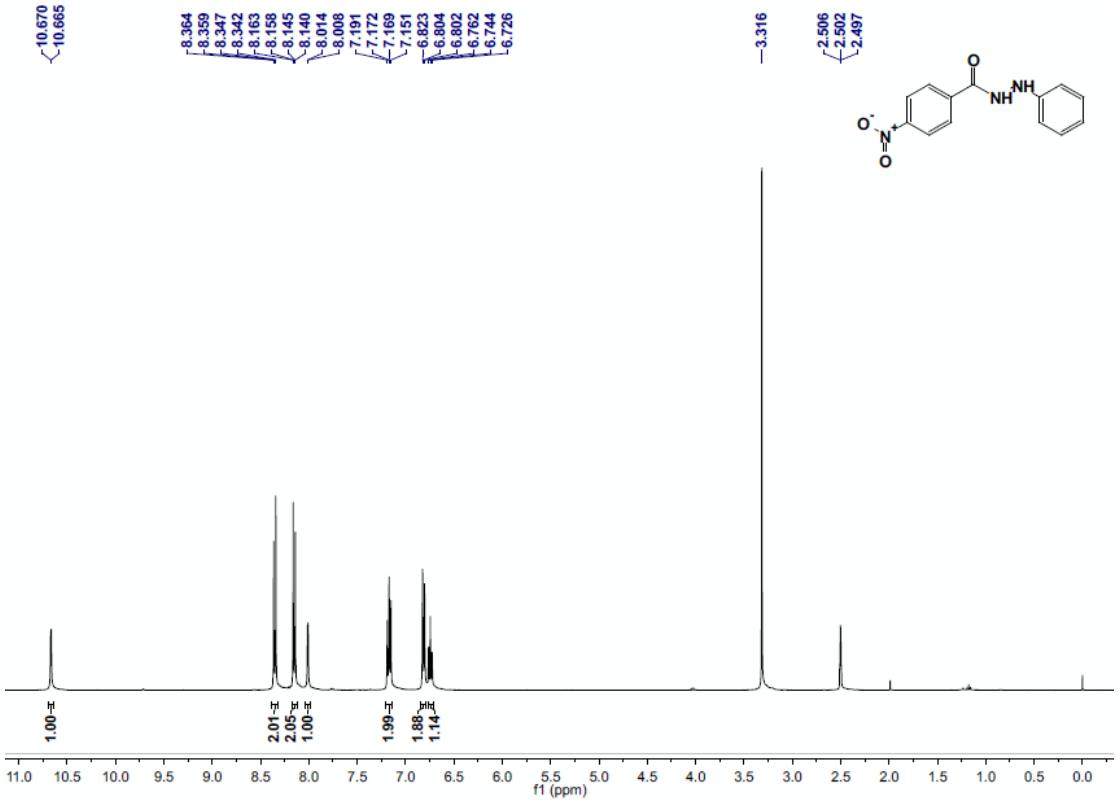


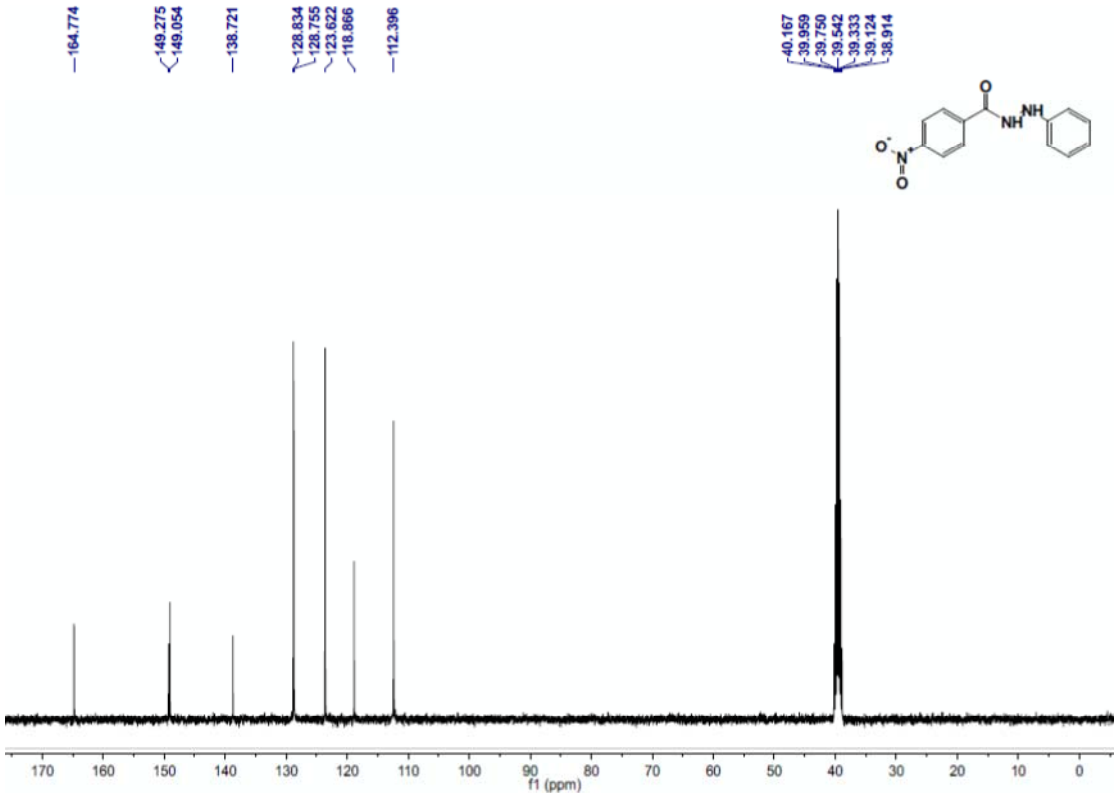
4-Amino-*N'*-phenylbenzohydrazide (1w)



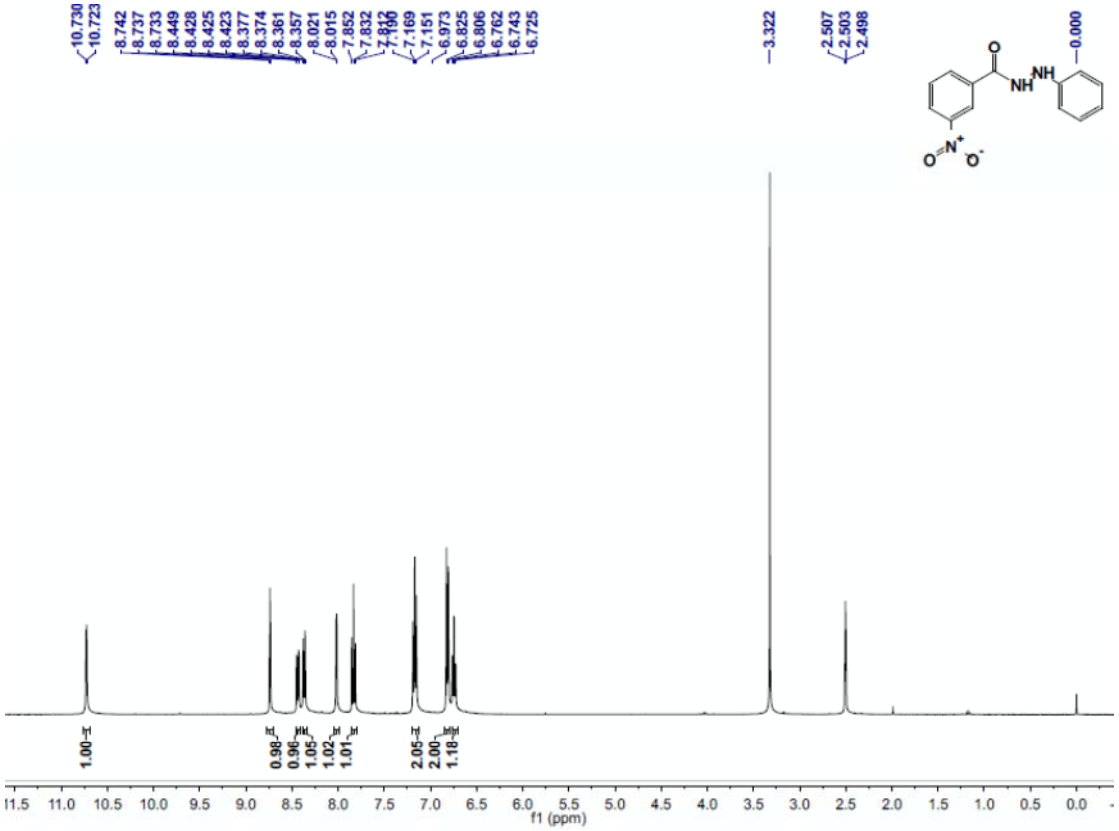


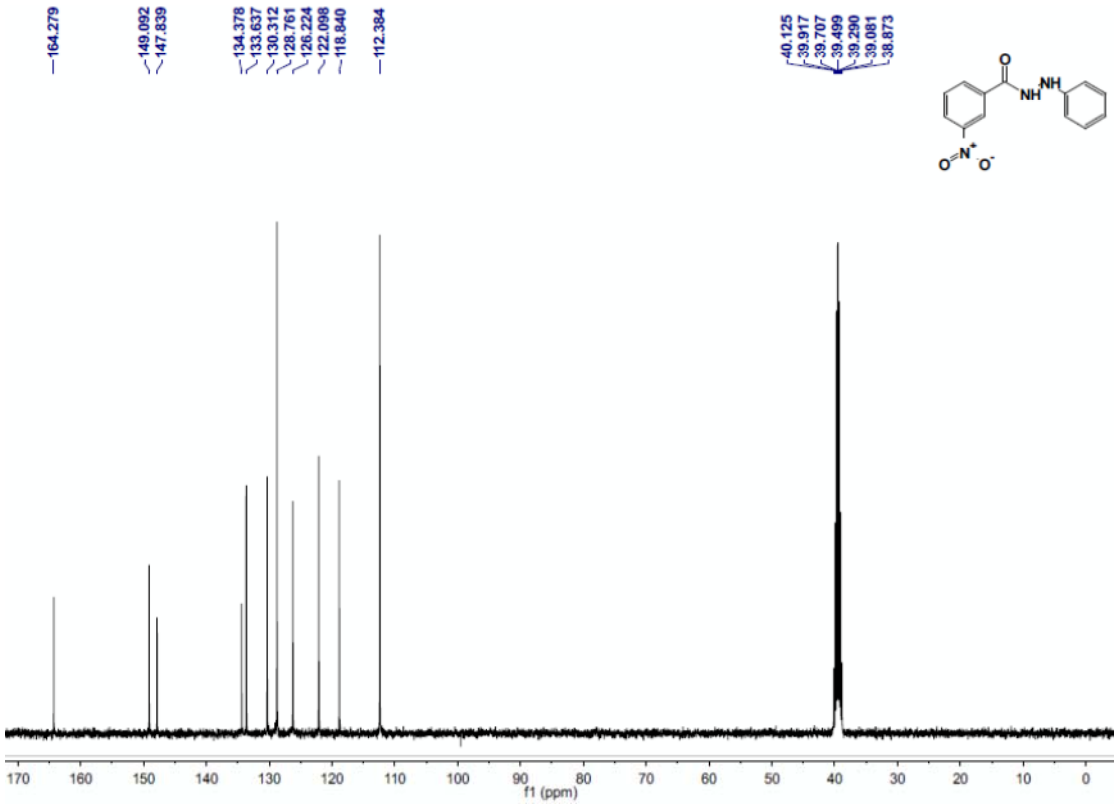
4-Nitro-*N'*-phenylbenzohydrazide (1x)



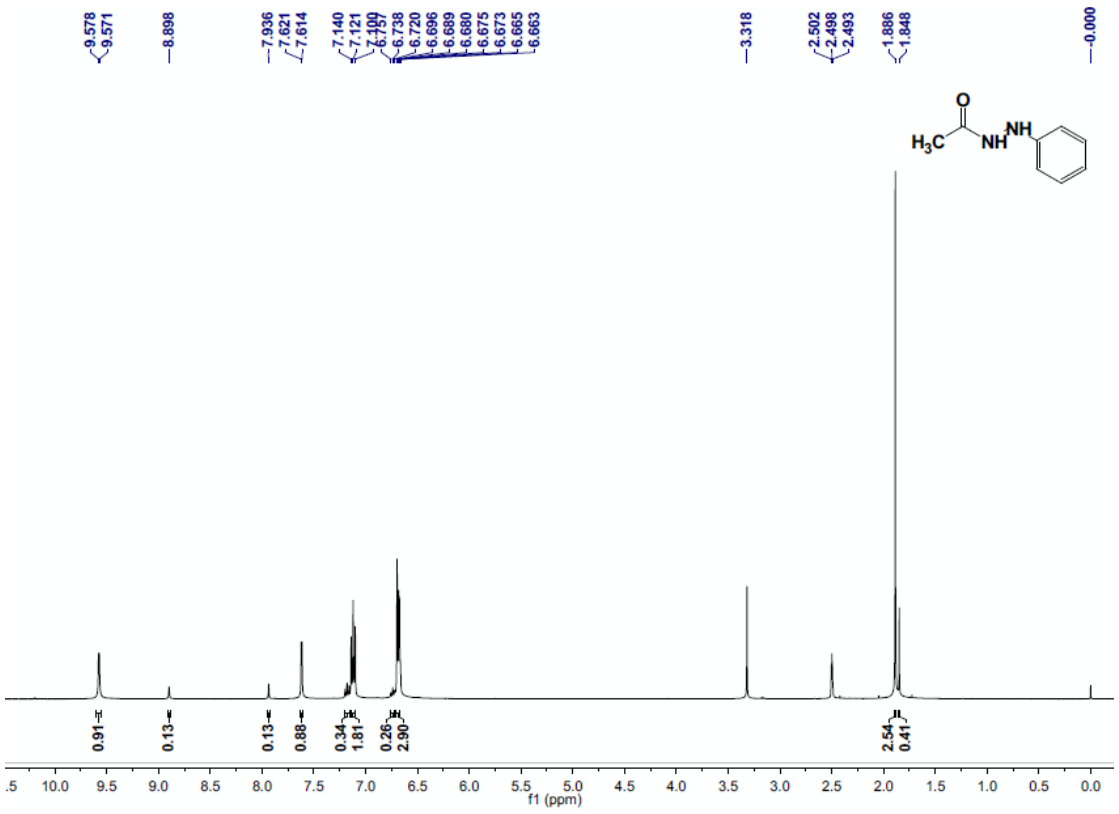


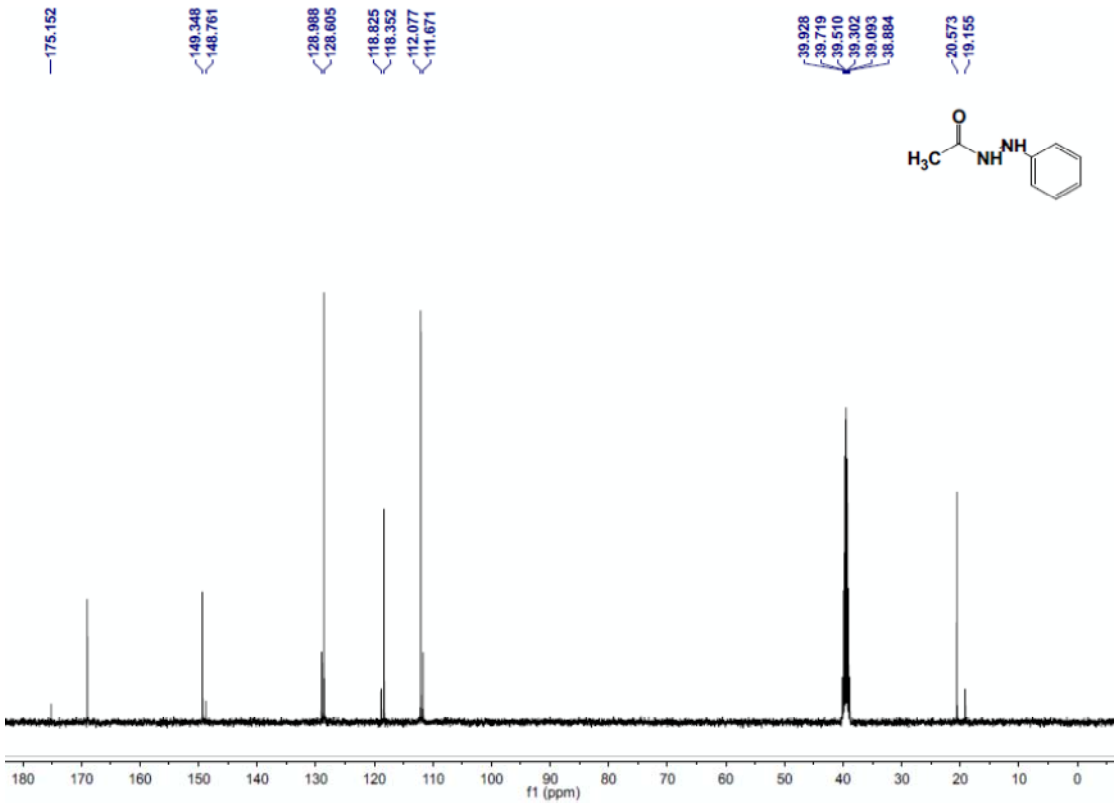
3-Nitro-*N′*-phenylbenzohydrazide (1y)



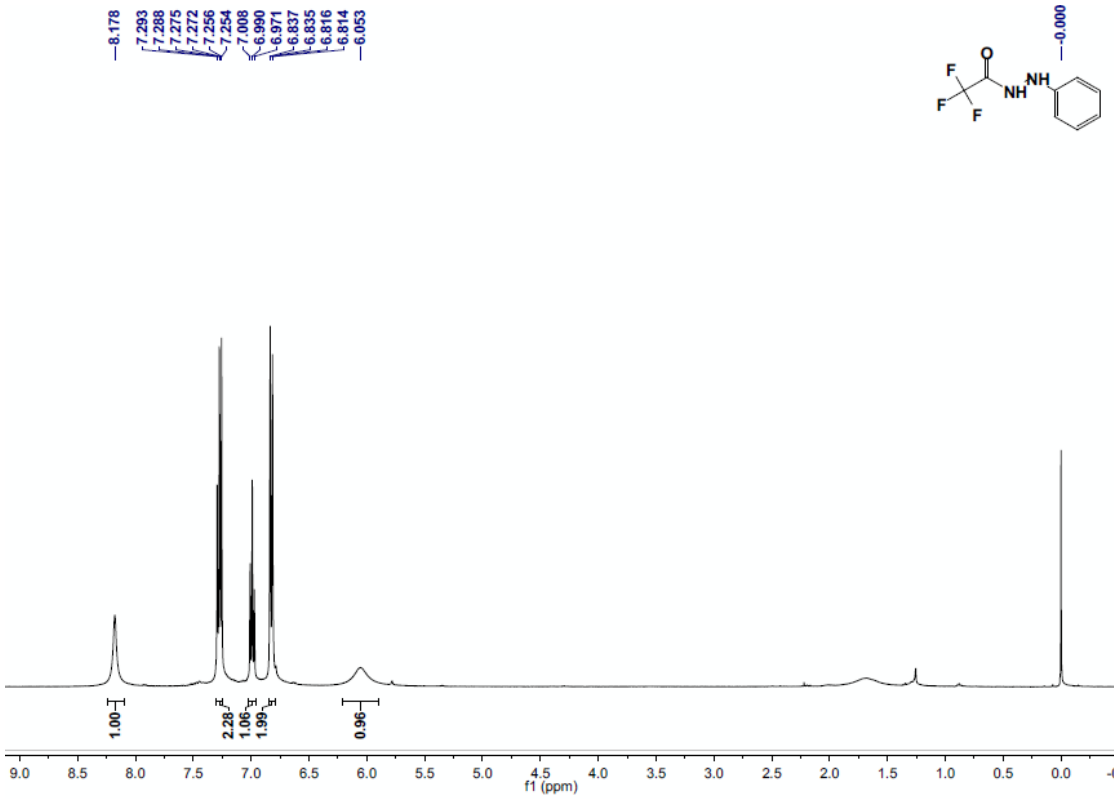


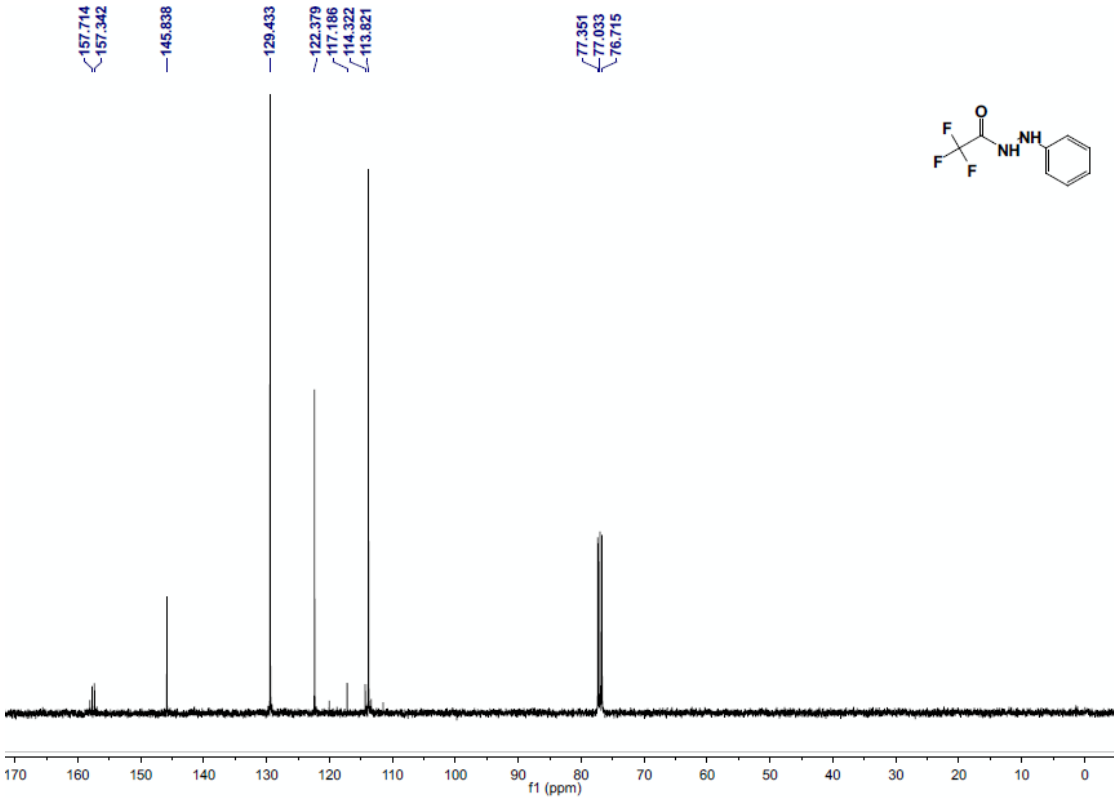
***N'*-Phenylacetohydrazide (1z)**



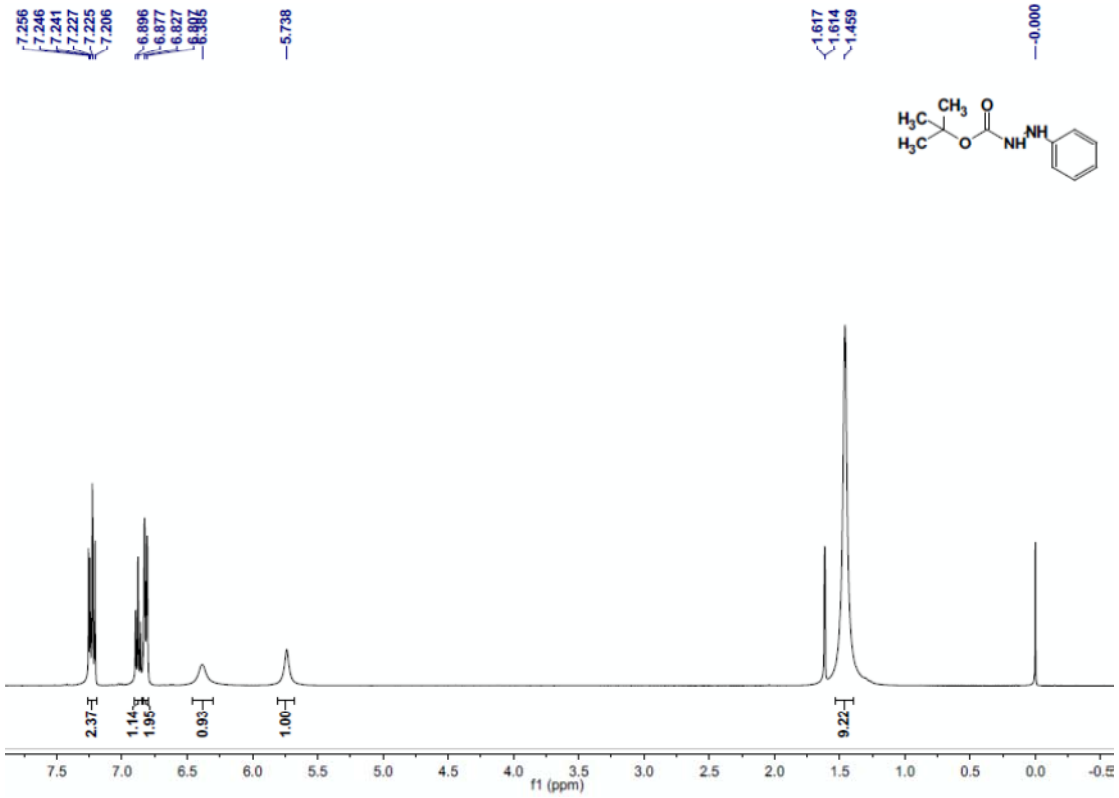


2,2,2-*tri*Fluoro-*N'*-phenylacetohydrazide (1aa)

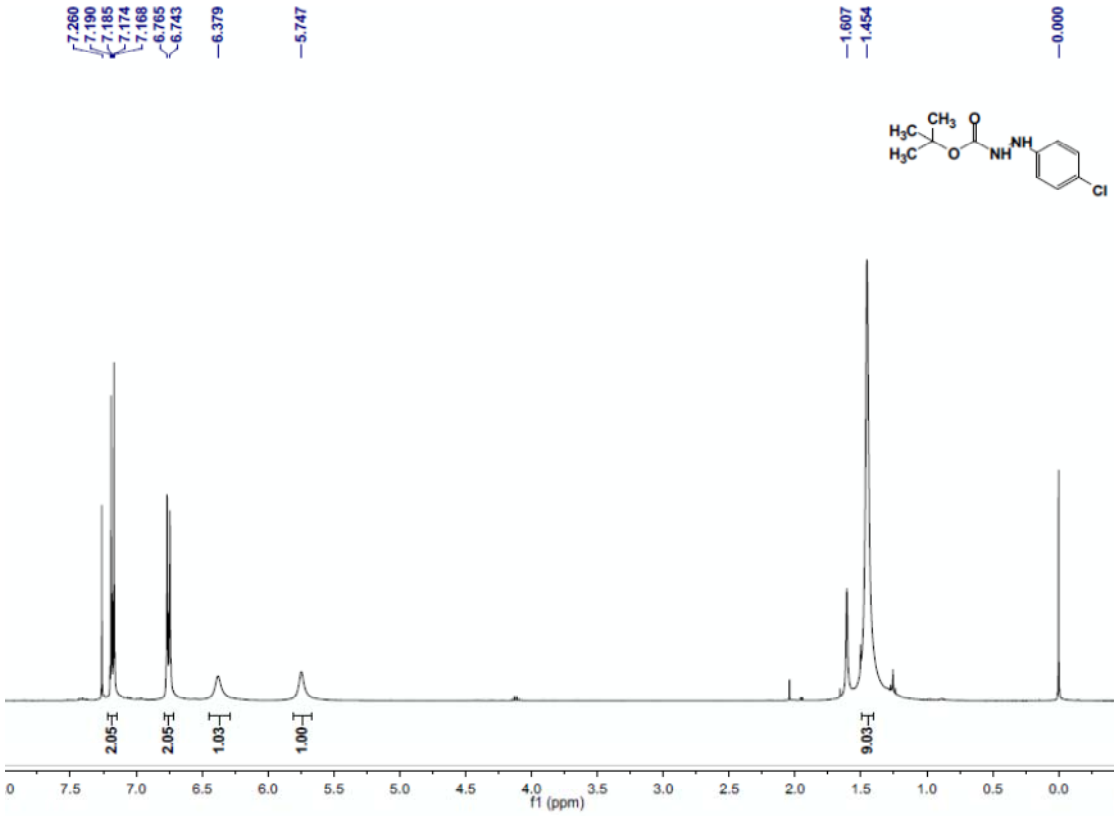


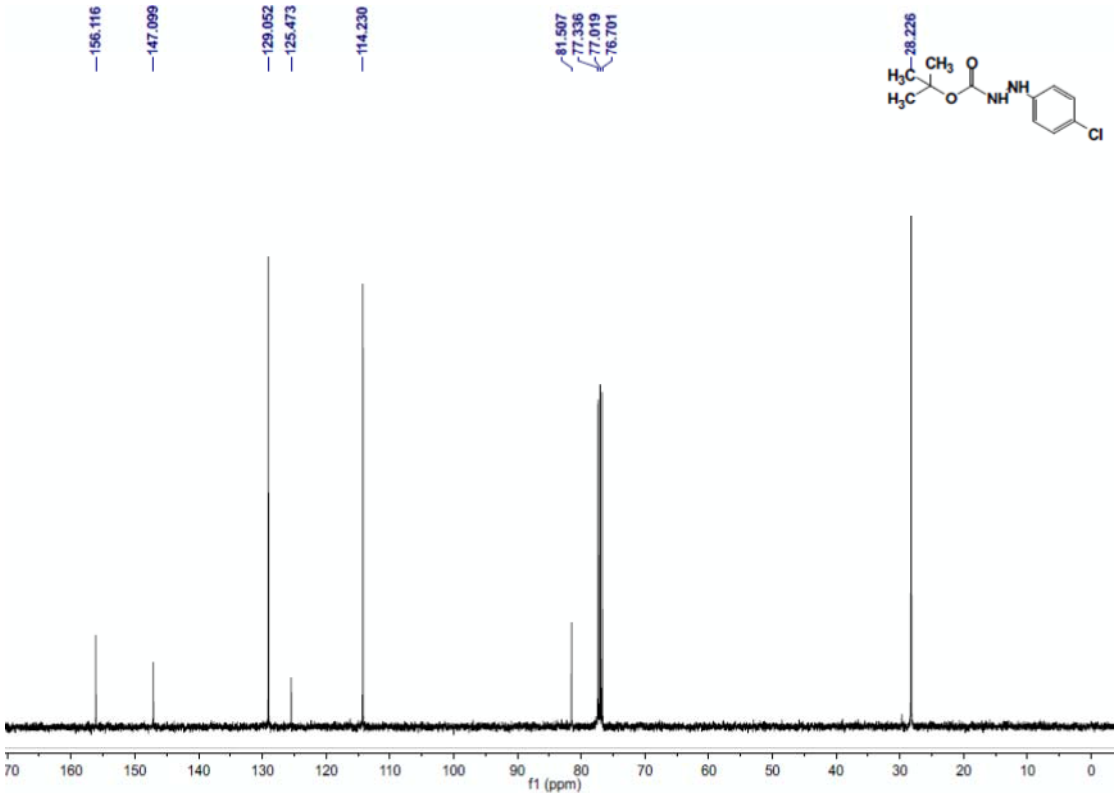


***tert*-Butyl 2-phenylhydrazinecarboxylate (1ab)**

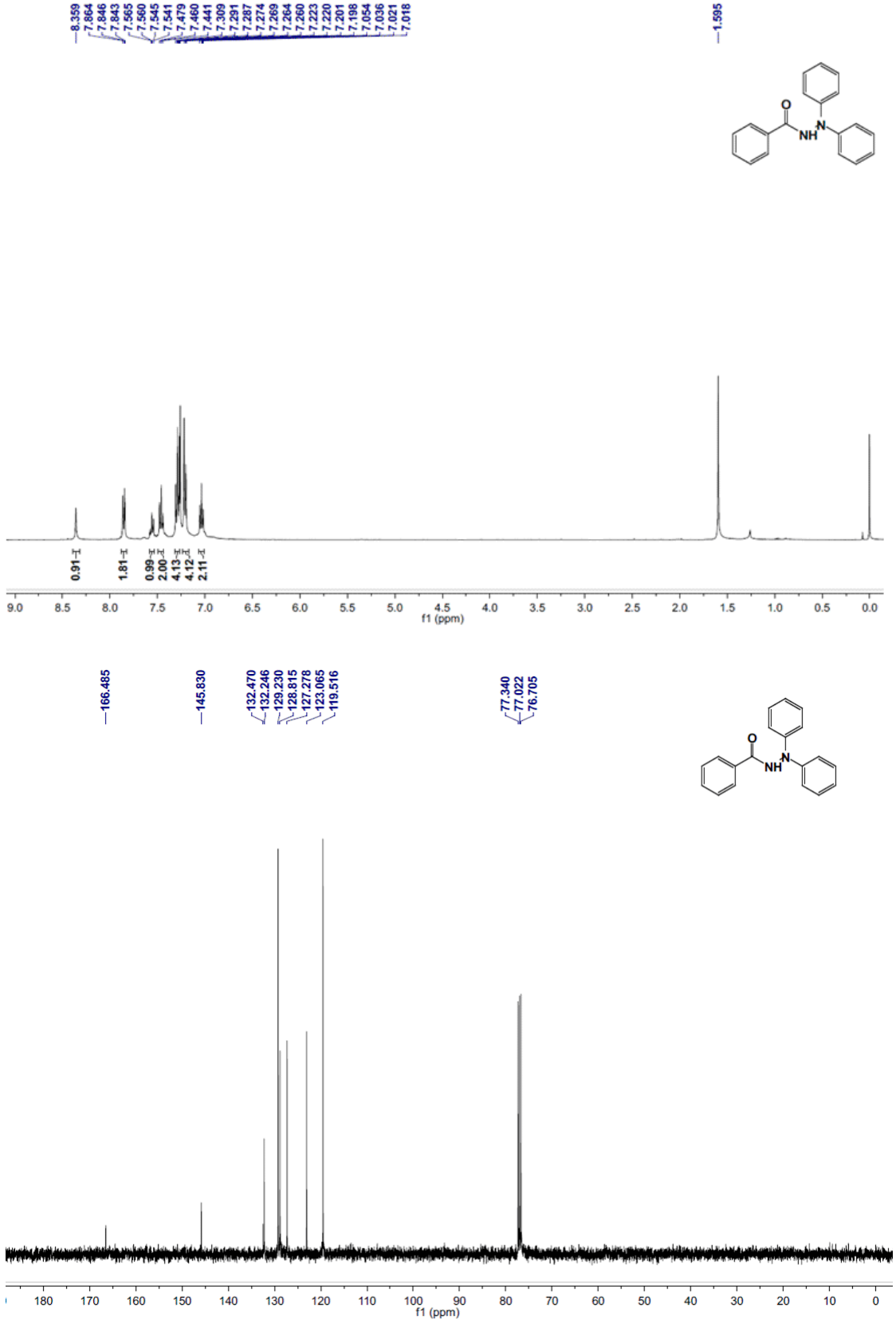


***tert*-Butyl 2-(4-chlorophenyl)hydrazinecarboxylate (1ac)**

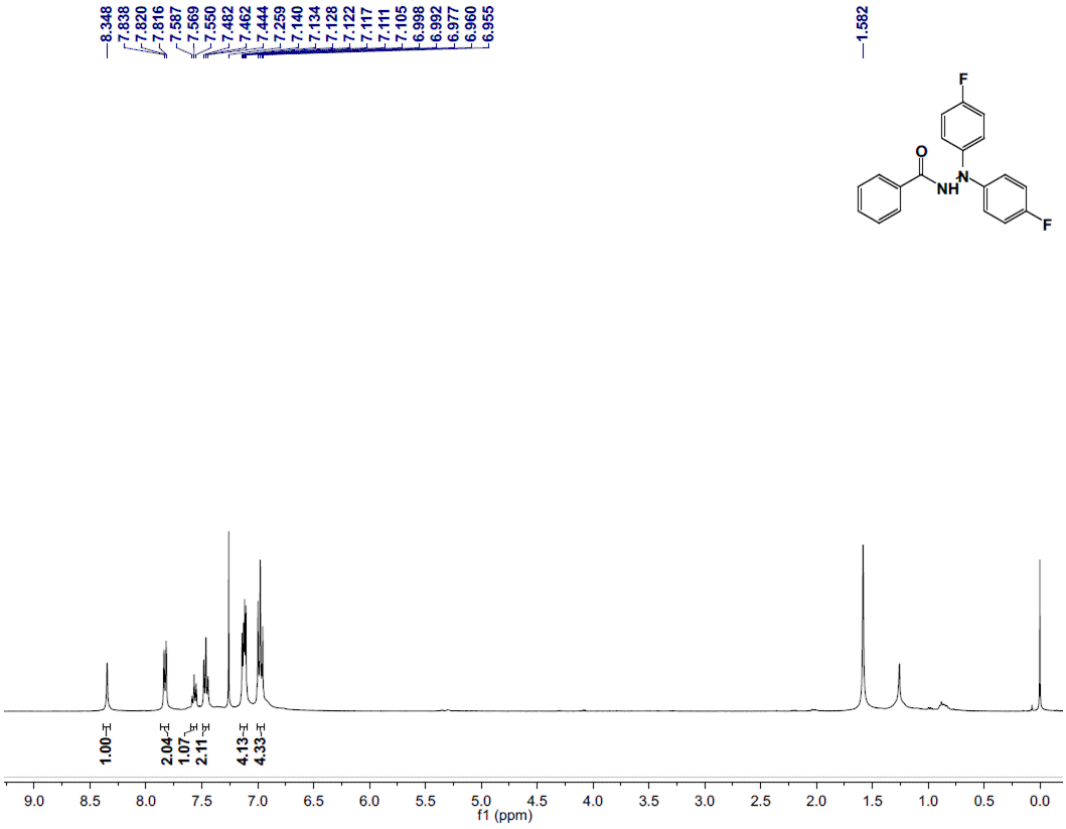


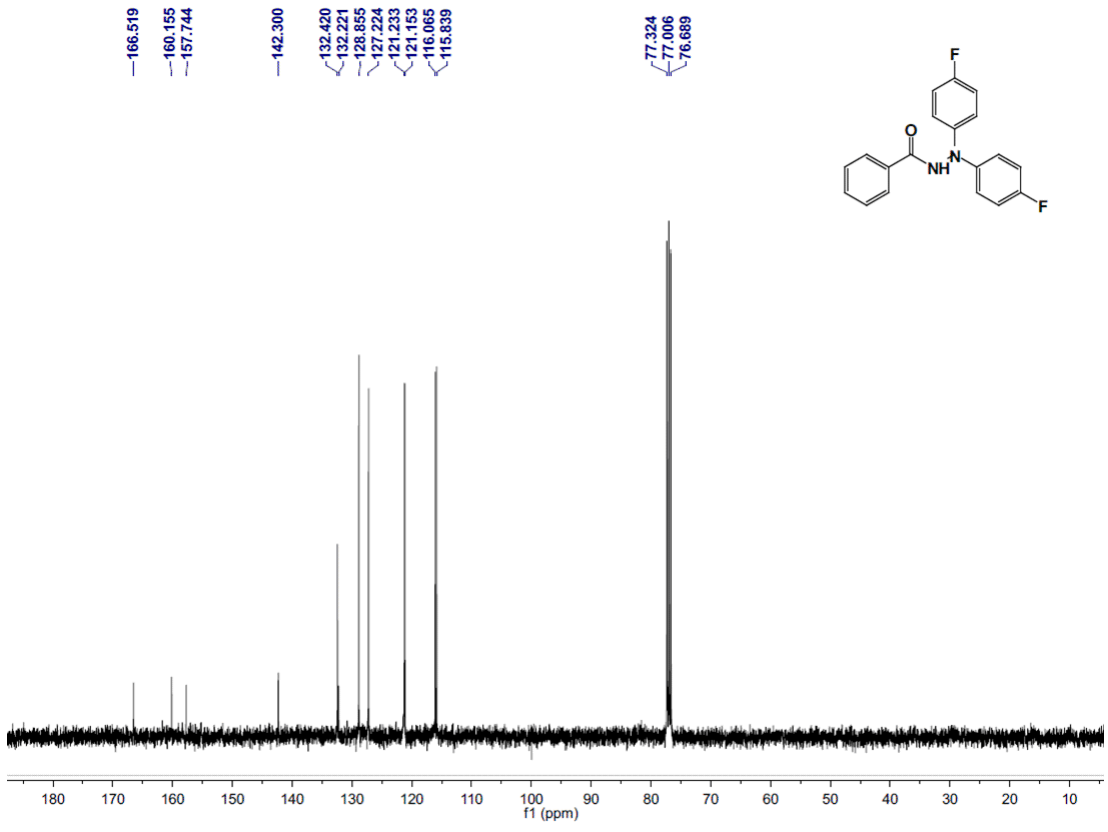


***N',N'-di*phenylbenzohydrazide (2a)**

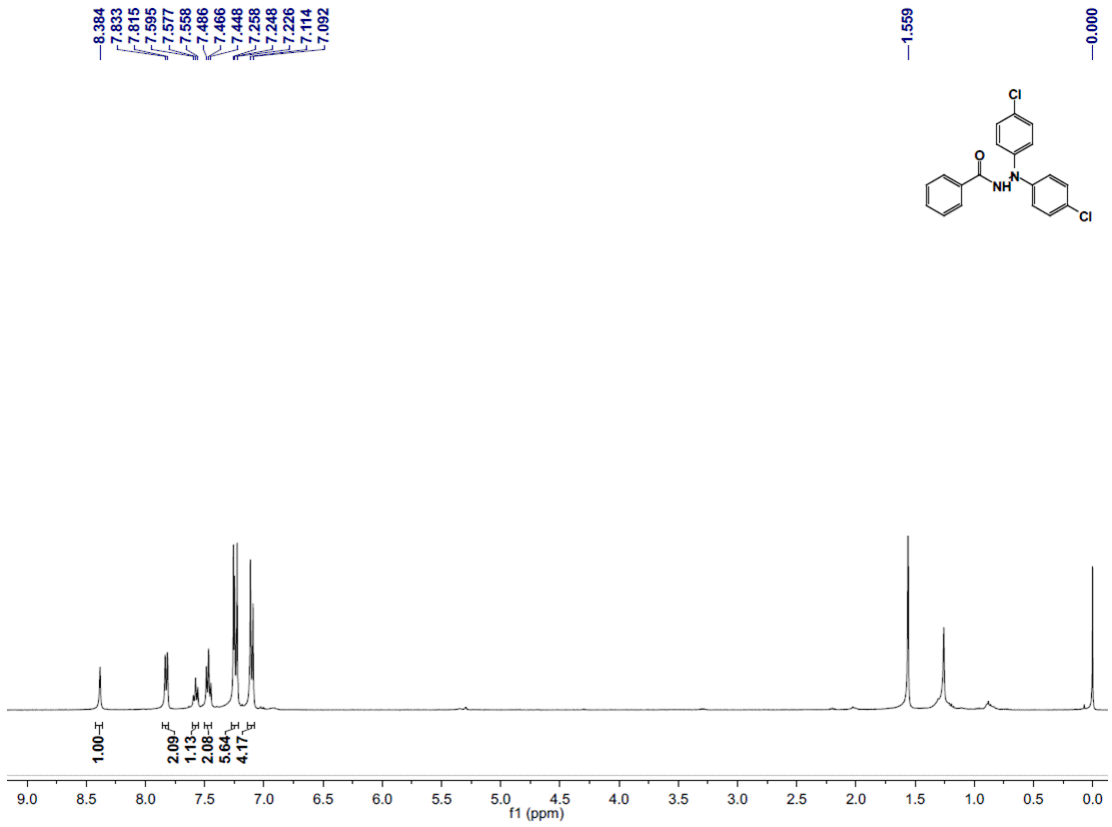


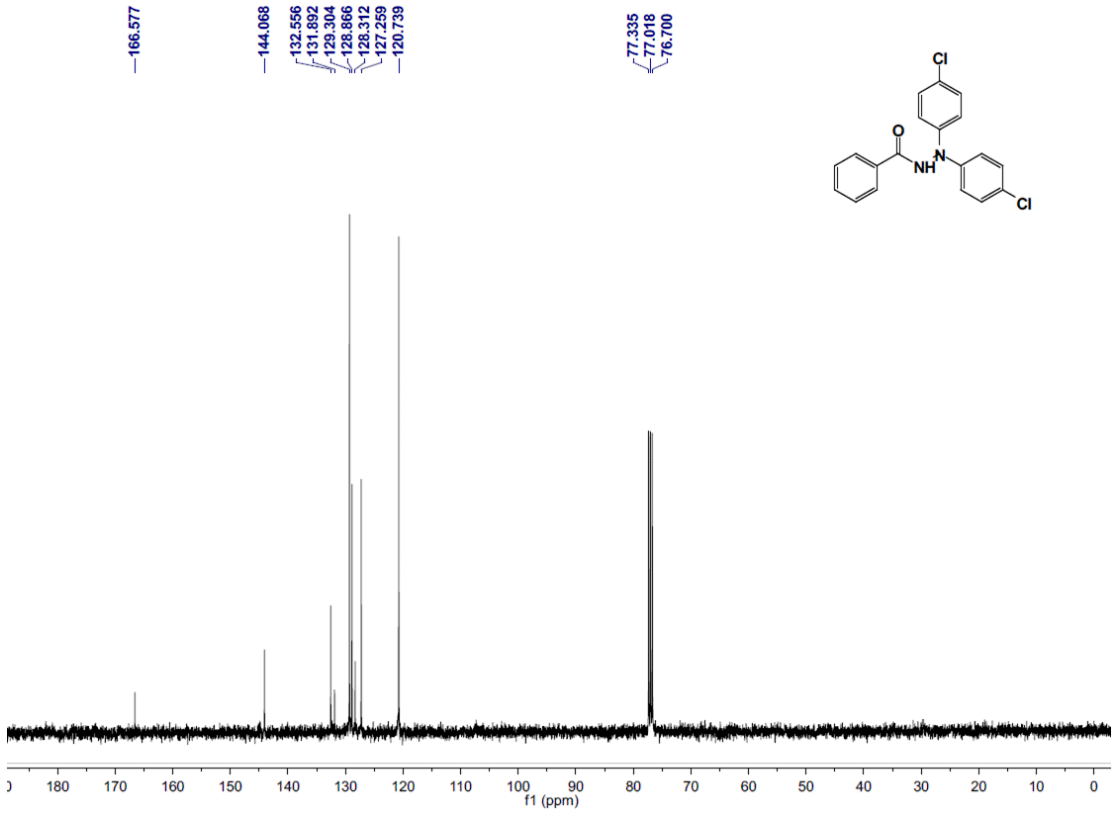
***N'*,*N'*-bis(4-fluorophenyl)benzohydrazide (2b)**



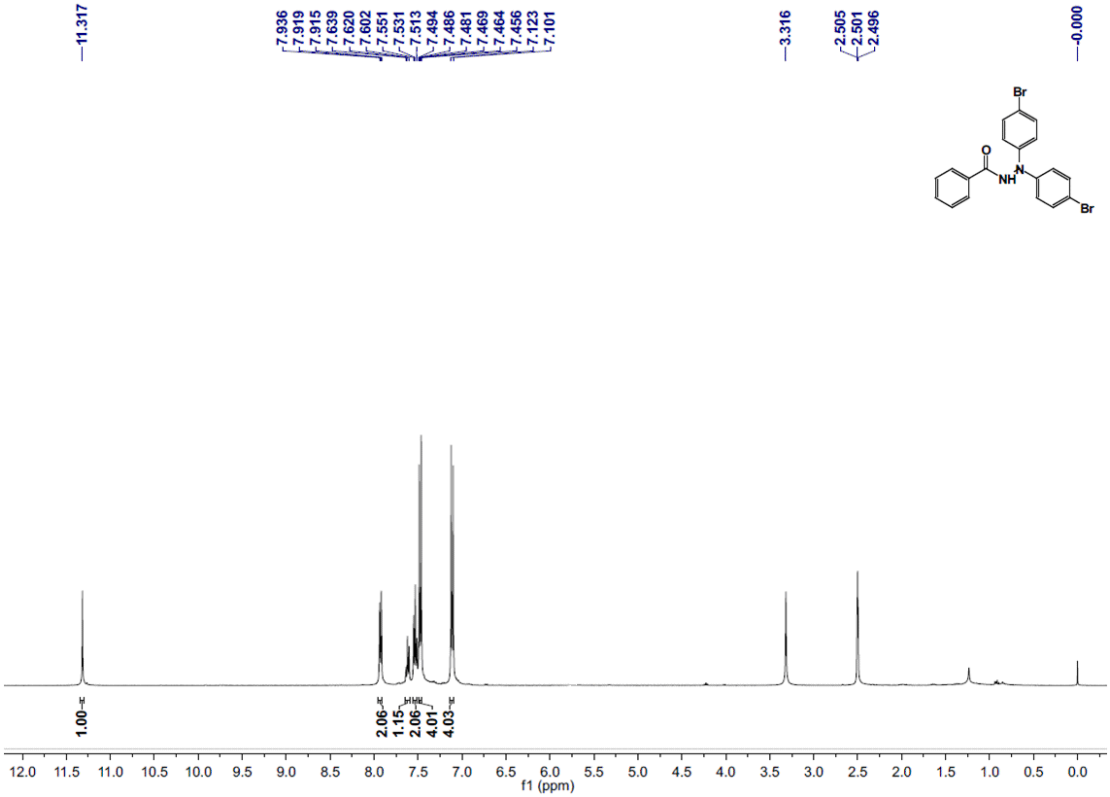


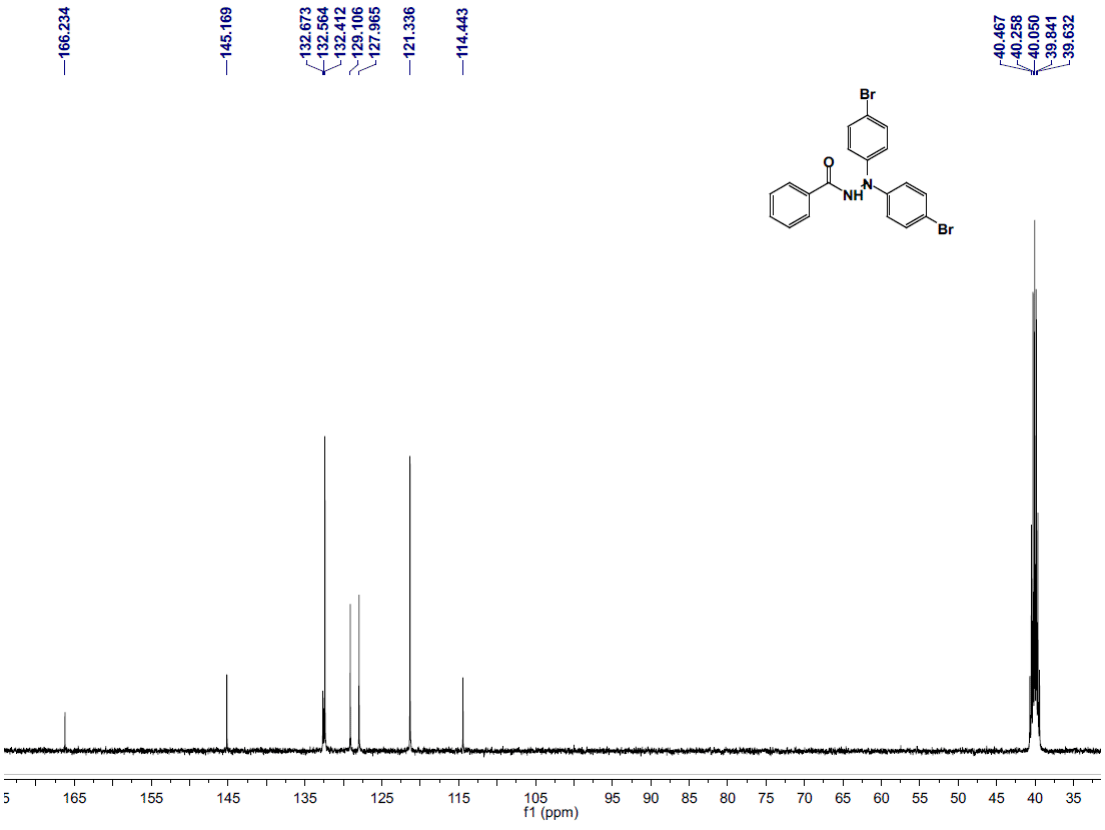
***N'*,*N'*-bis(4-chlorophenyl)benzohydrazide (2c)**



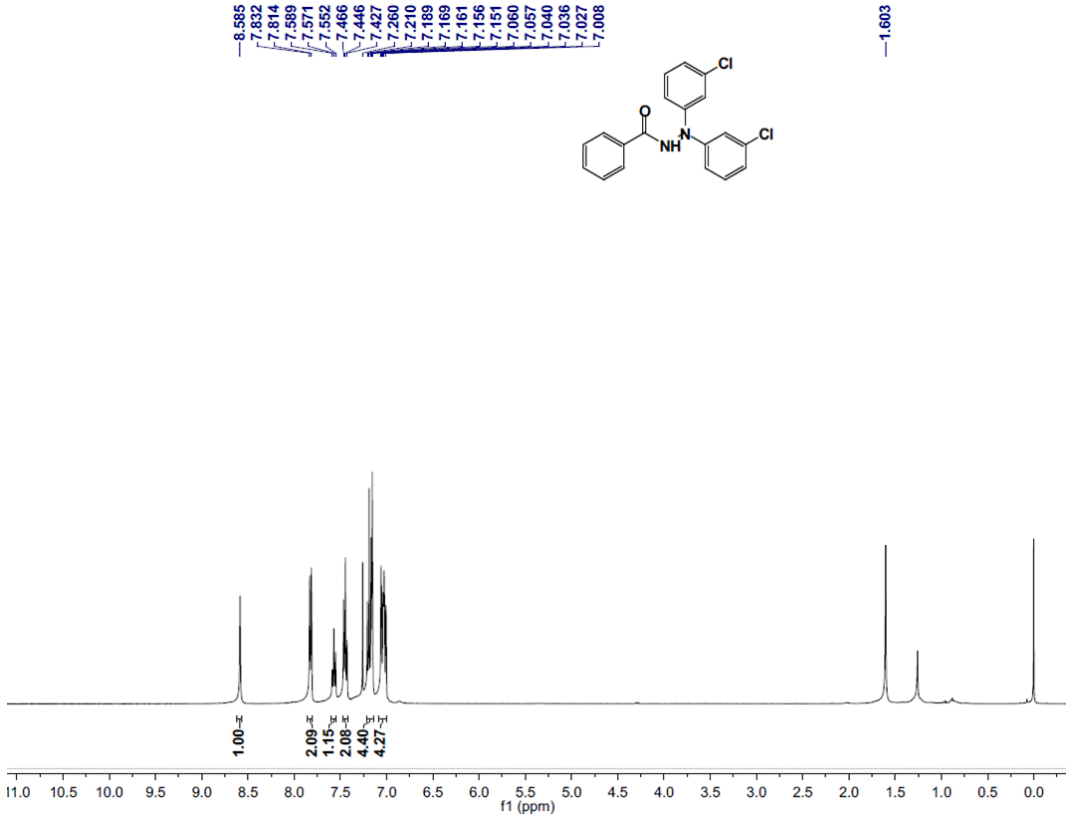


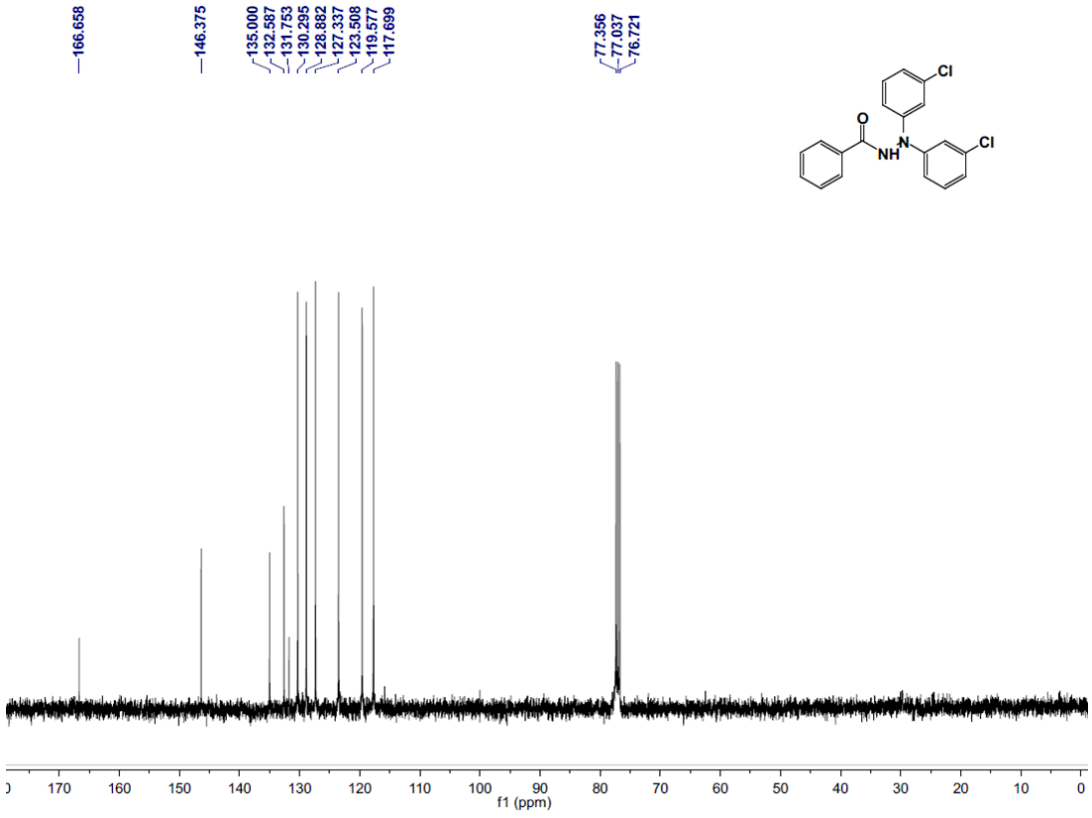
***N'*,*N'*-bis(4-bromophenyl)benzohydrazide (2d)**



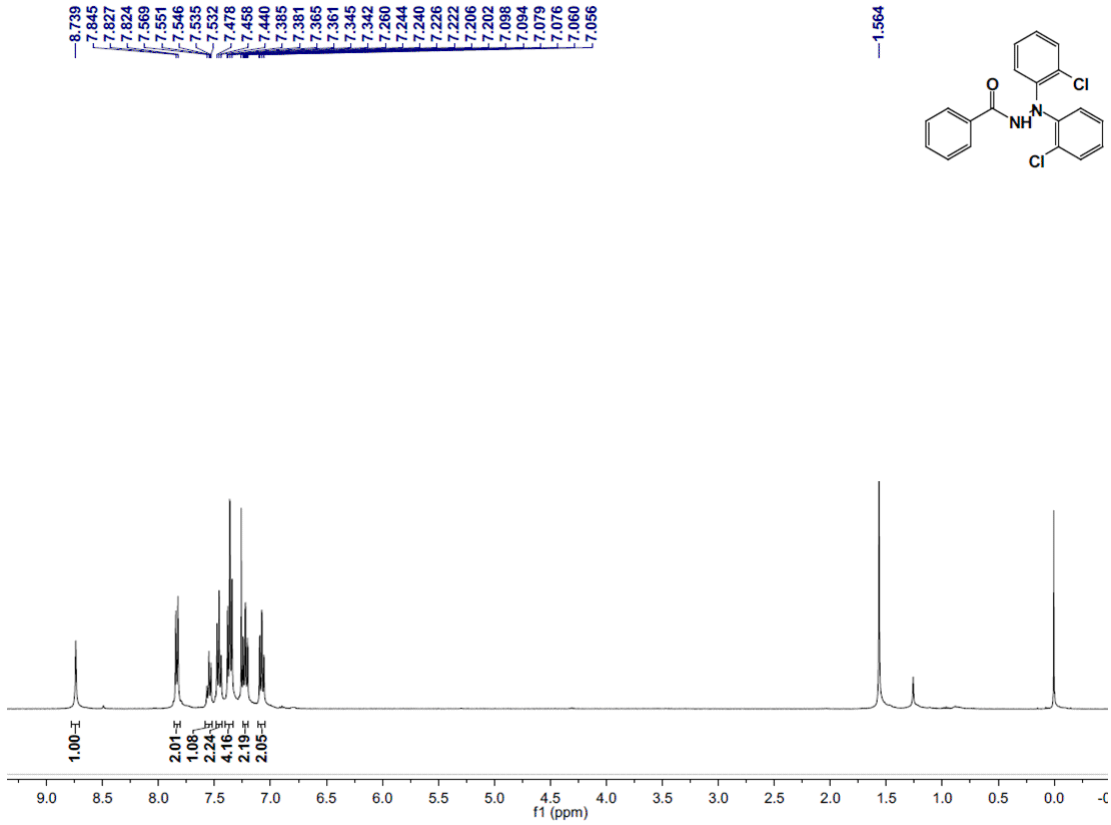


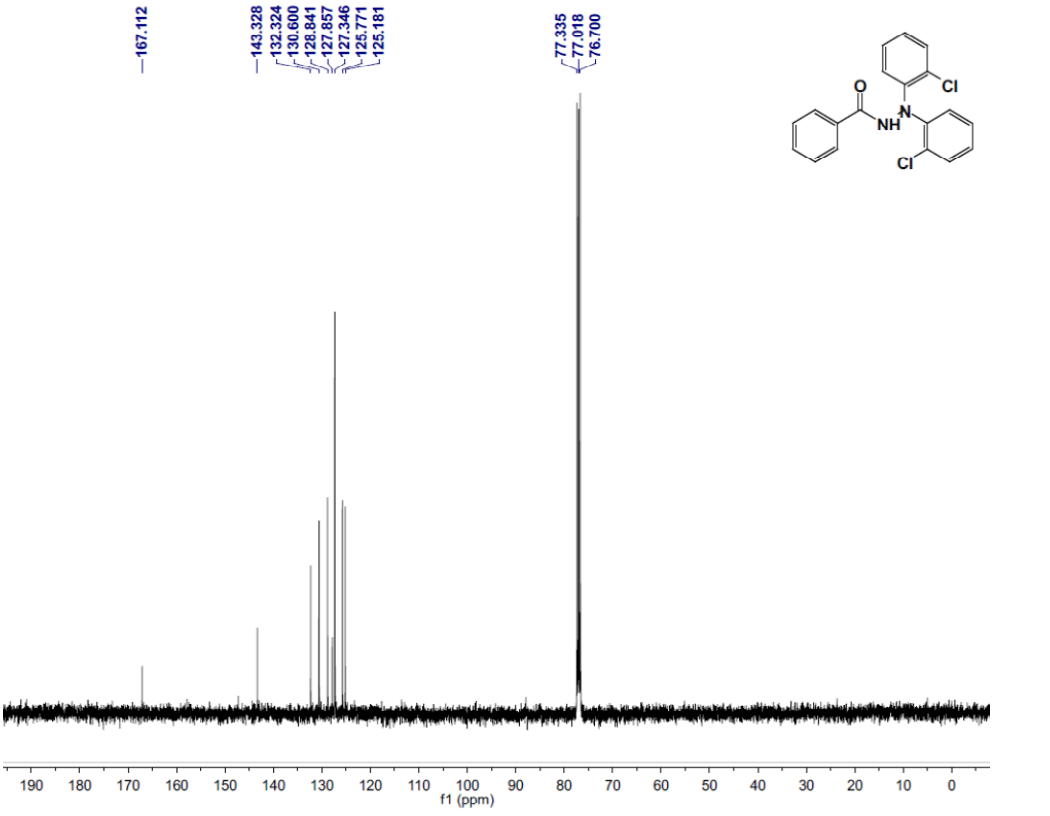
***N'*,*N'*-bis(3-chlorophenyl)benzohydrazide (2e)**



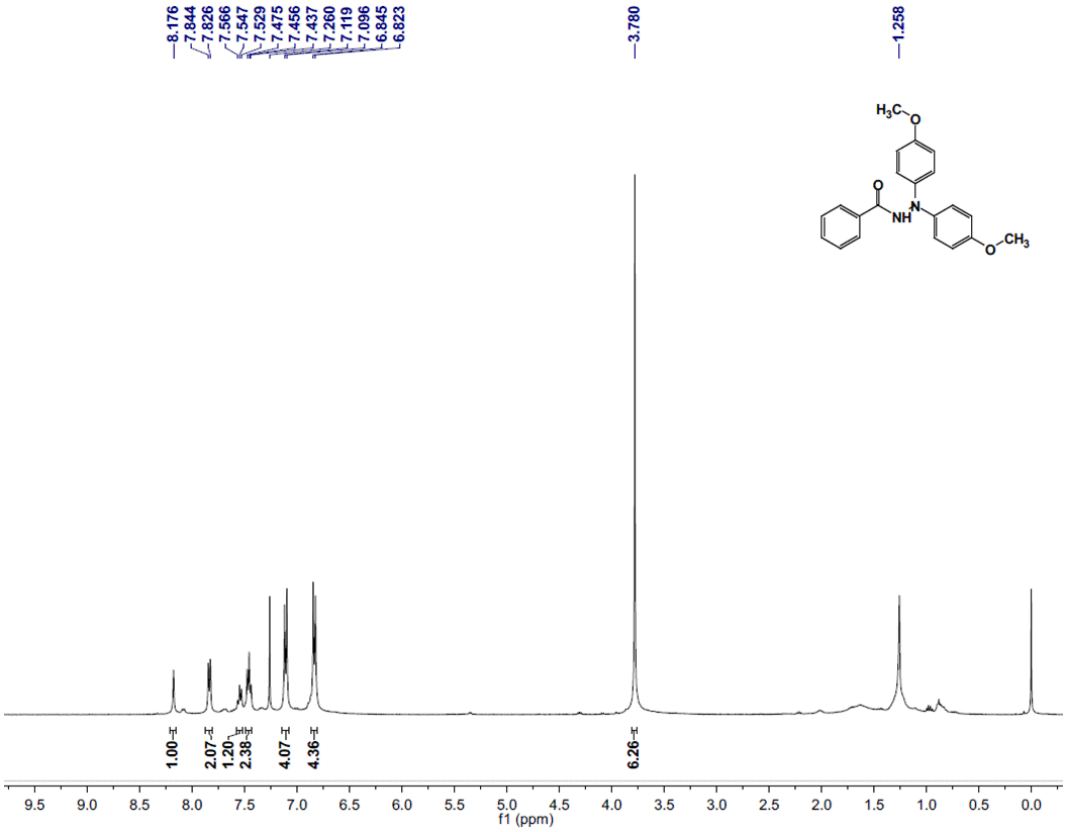


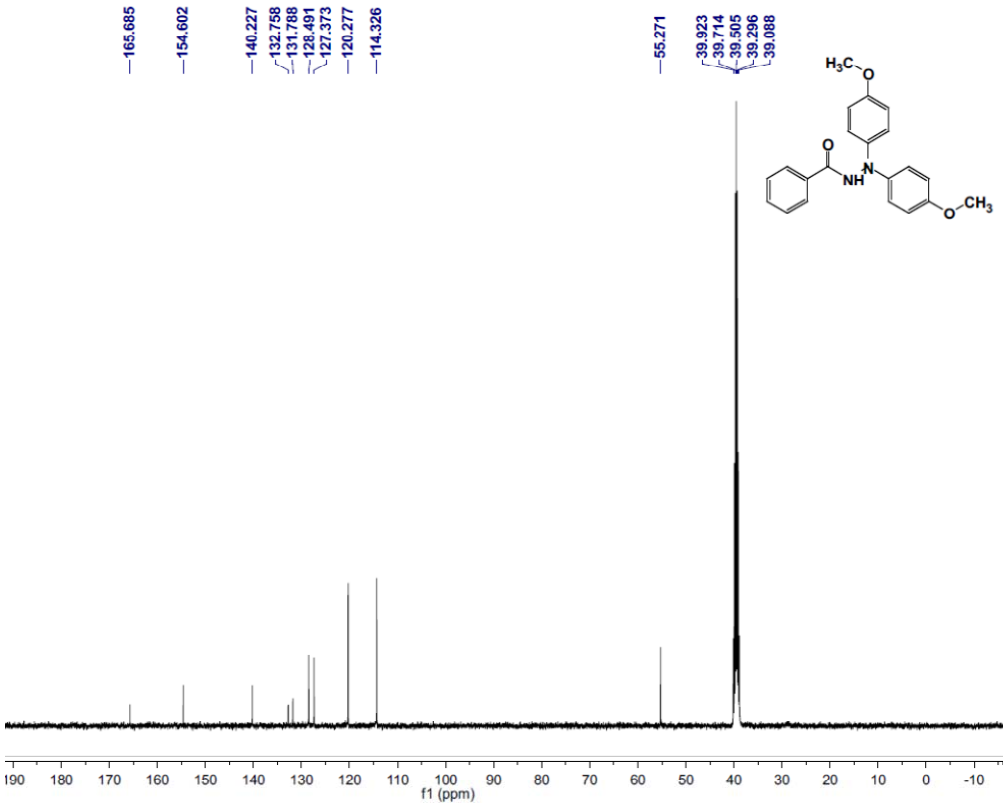
***N'*,*N'*-bis(2-chlorophenyl)benzohydrazide (2f)**



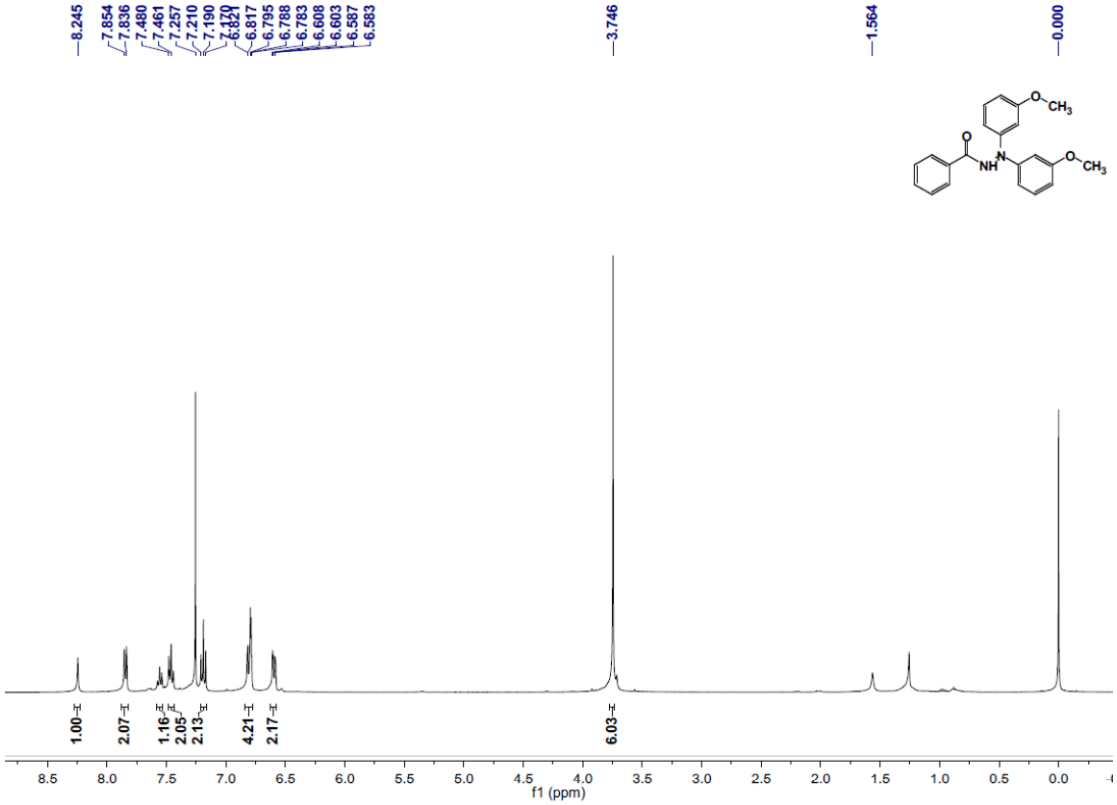


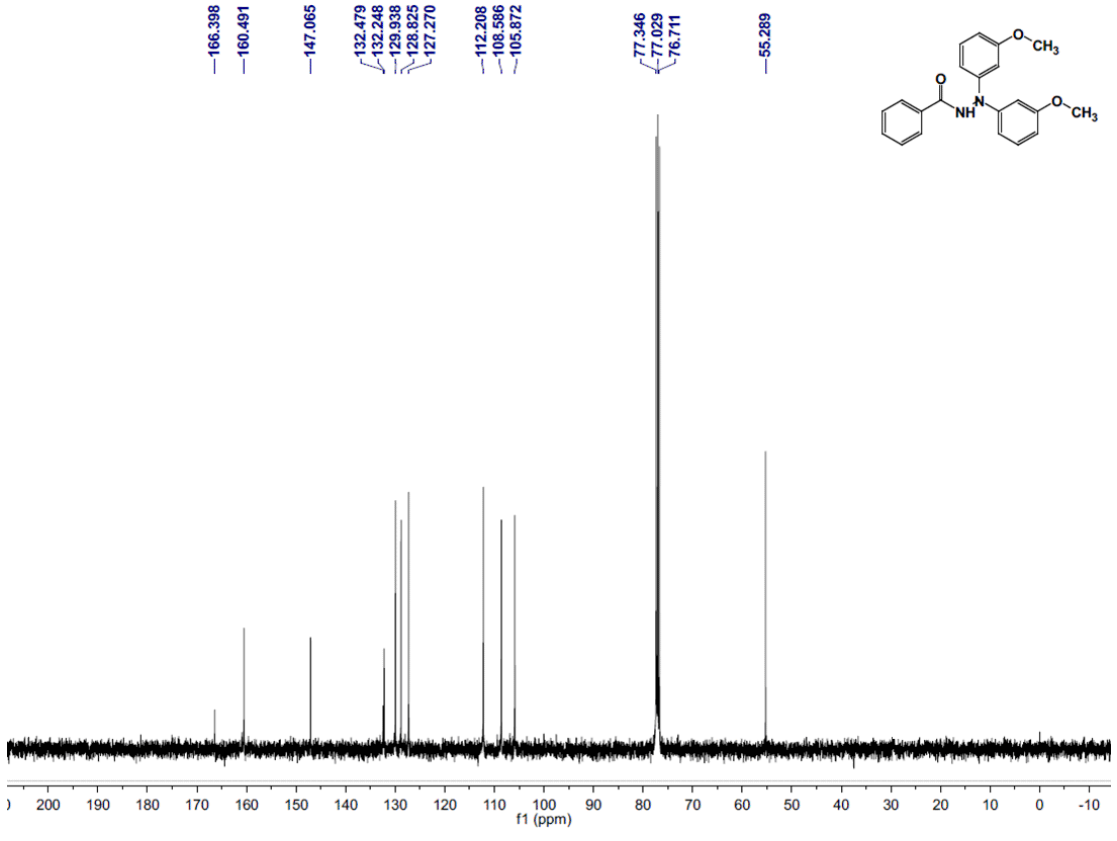
***N'*,*N'*-bis(4-methoxyphenyl)benzohydrazide (2g)**



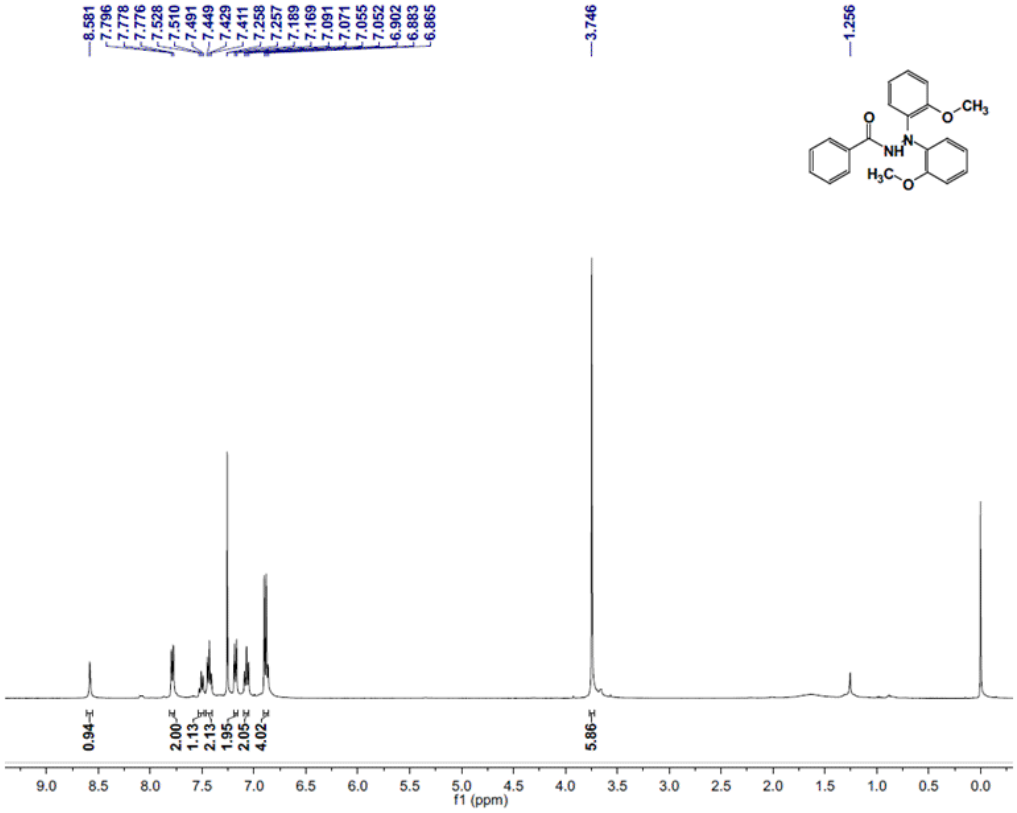


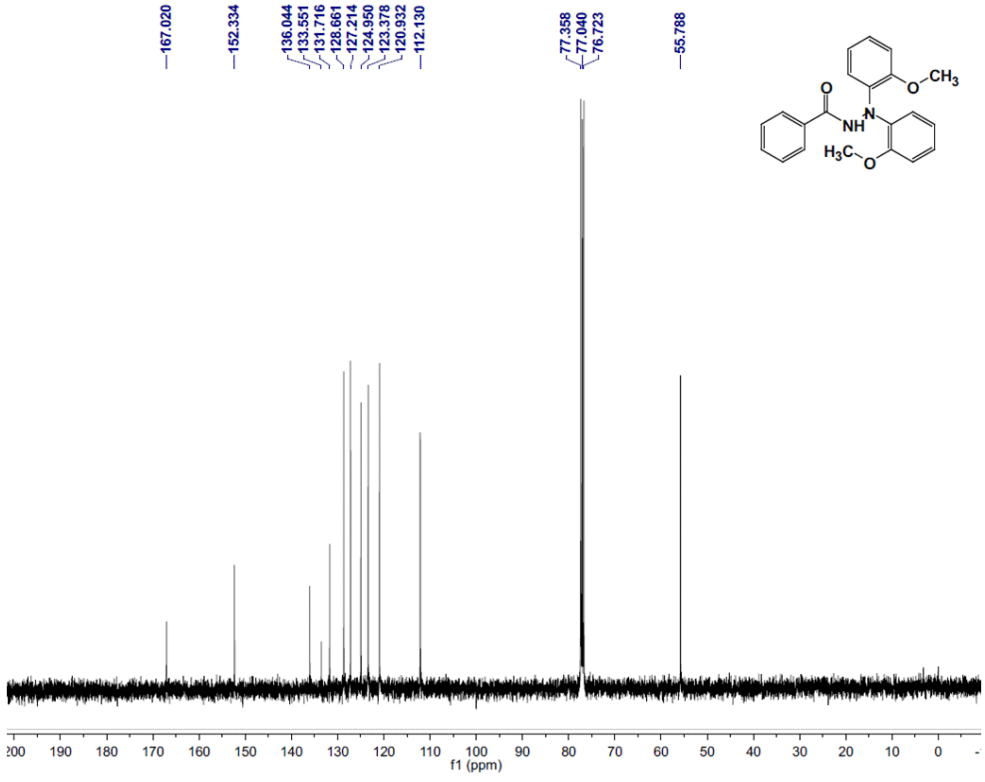
***N'*,*N'*-bis(3-methoxyphenyl)benzohydrazide (2h)**



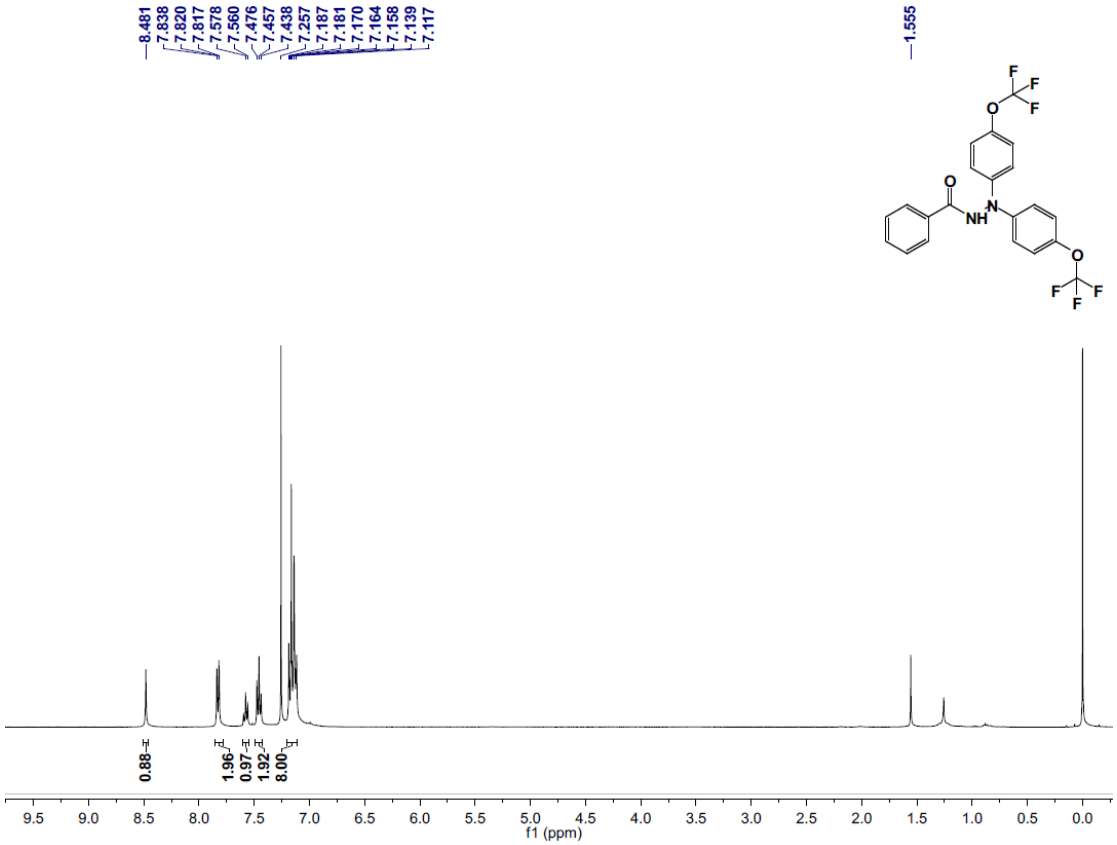


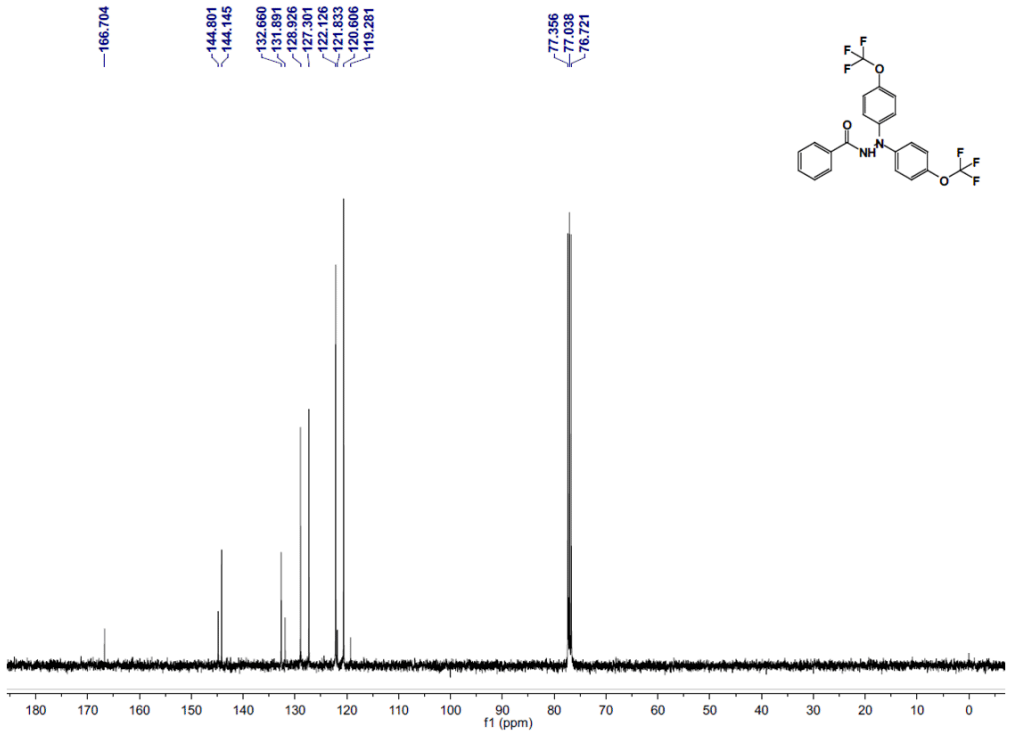
***N'*,*N'*-bis(2-methoxyphenyl)benzohydrazide (2i)**



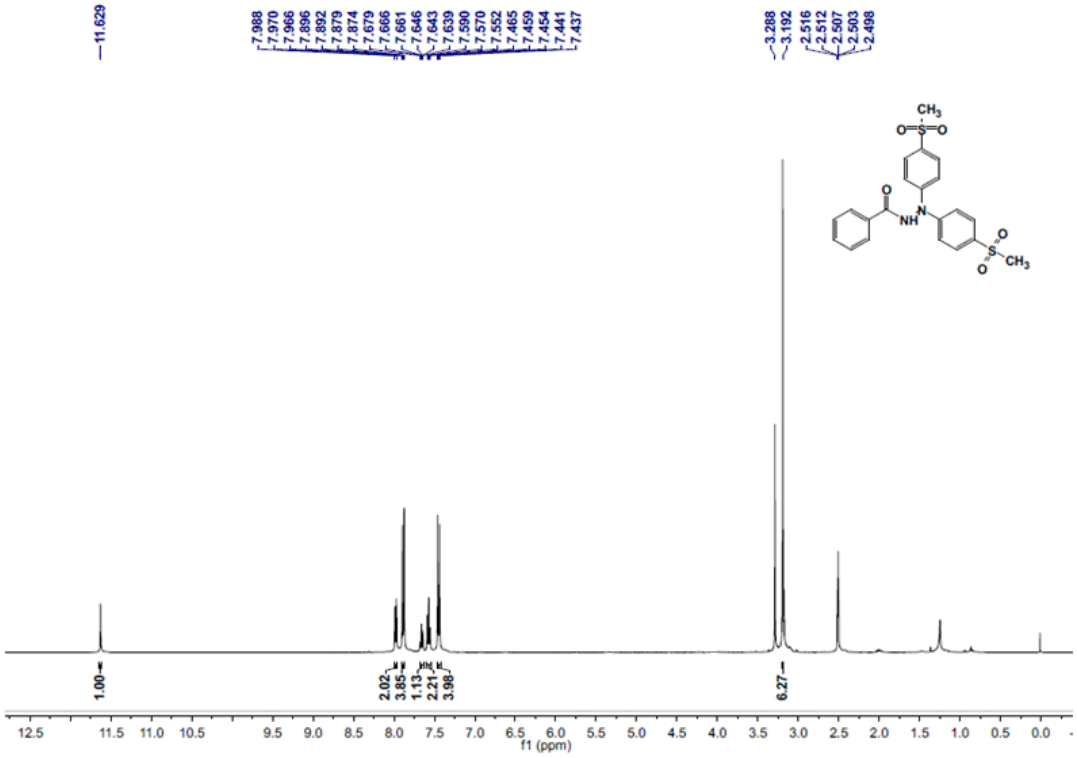


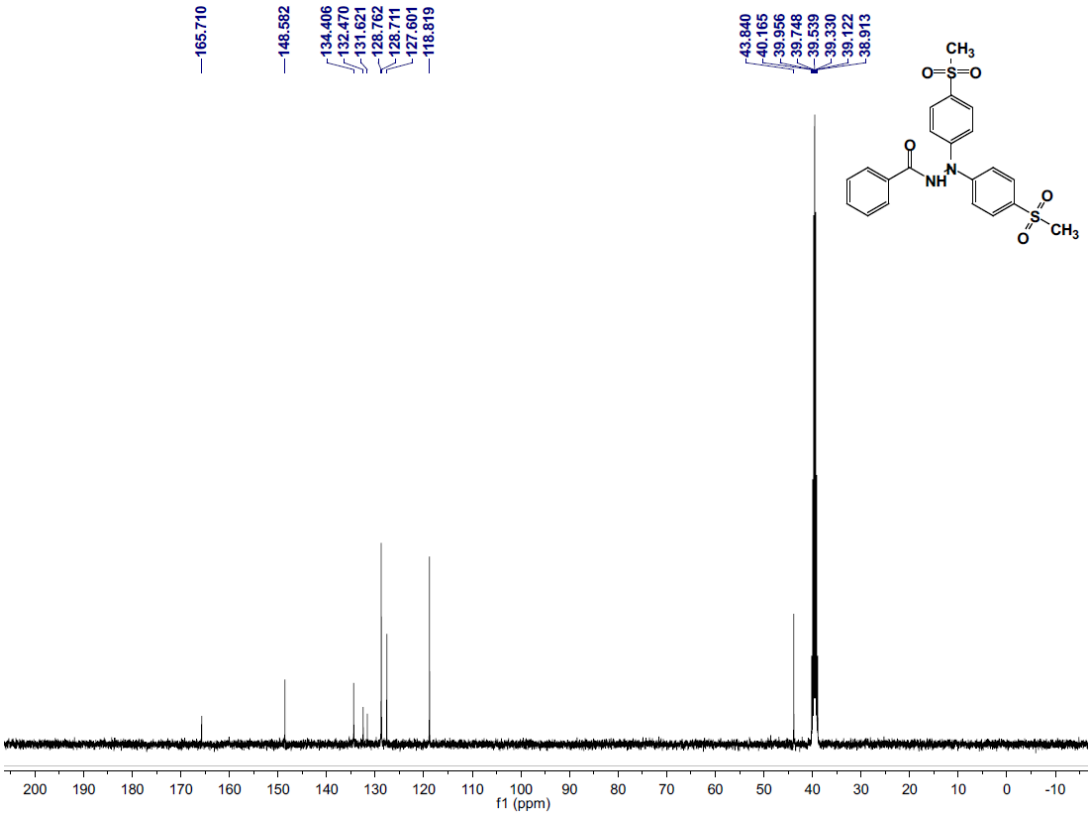
***N'*,*N'*-bis(4-(*tri*fluoromethoxy)phenyl)benzohydrazide (2j)**



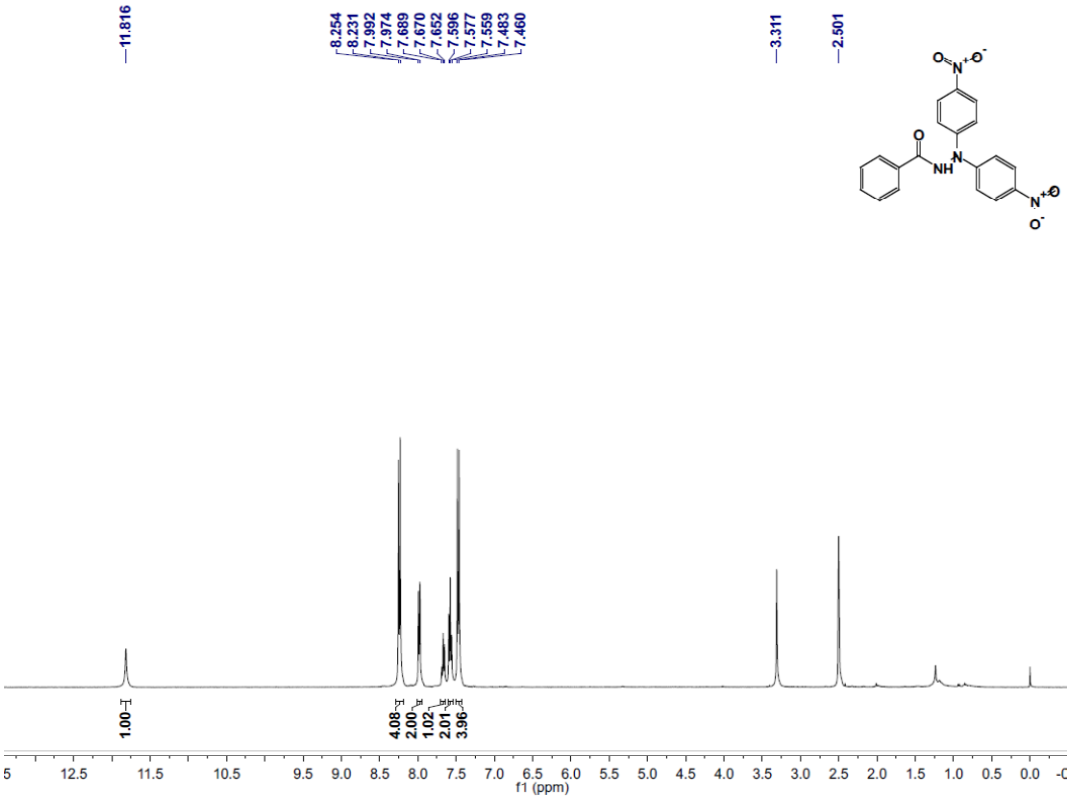


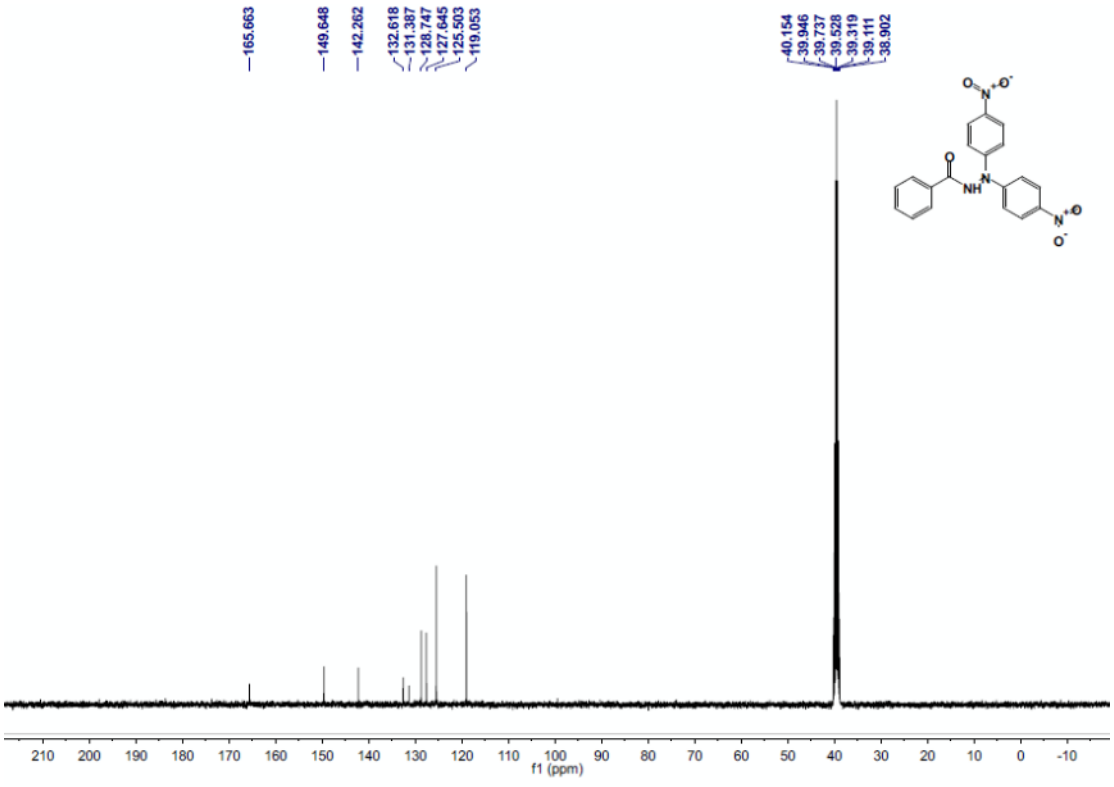
***N'*,*N'*-bis(4-(methylsulfonyl)phenyl)benzohydrazide (2k)**



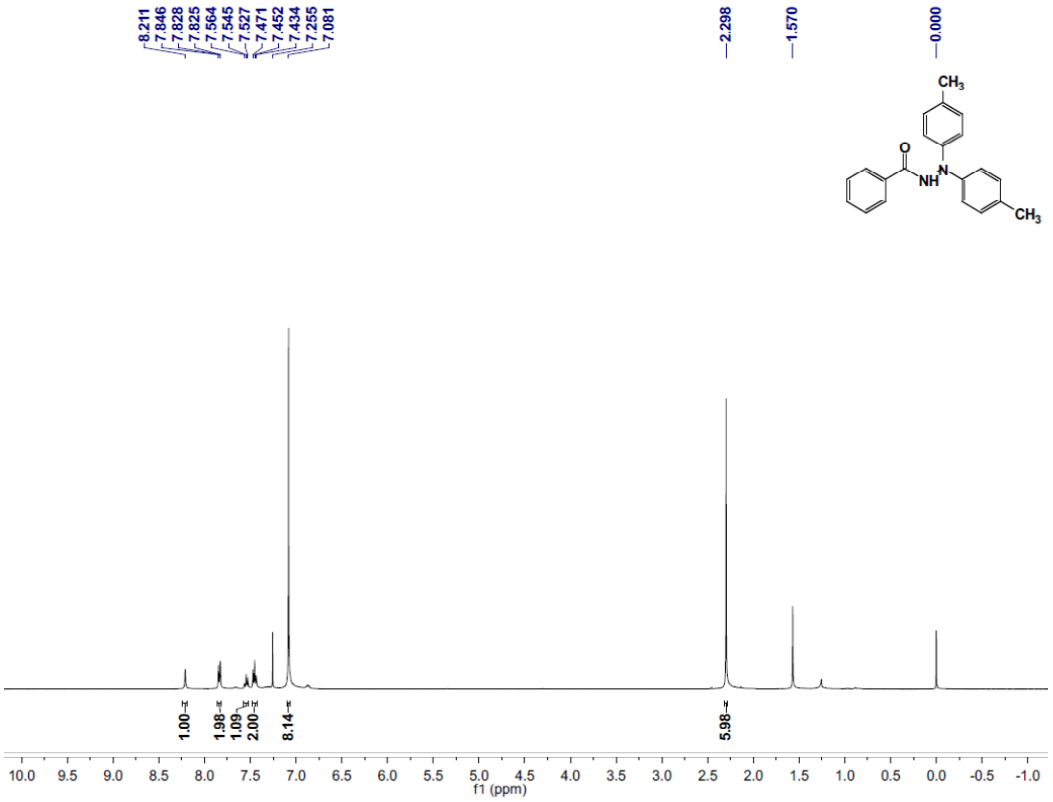


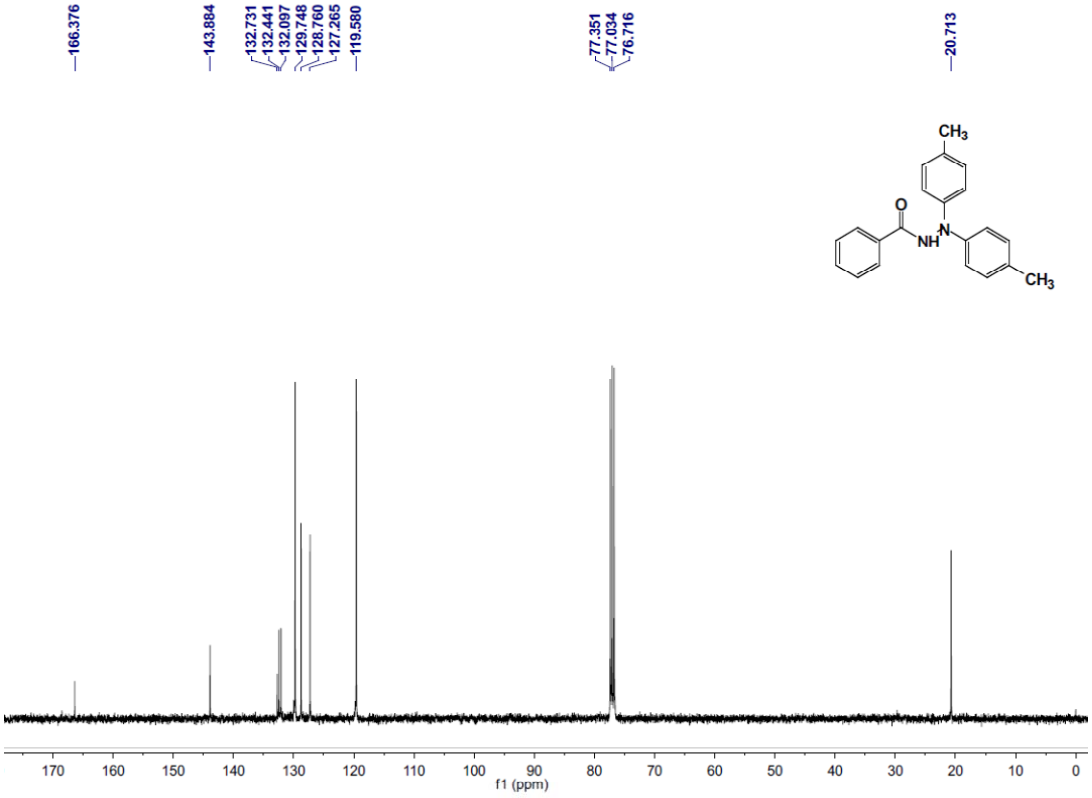
***N'*,*N'*-bis(4-nitrophenyl)benzohydrazide (2l)**



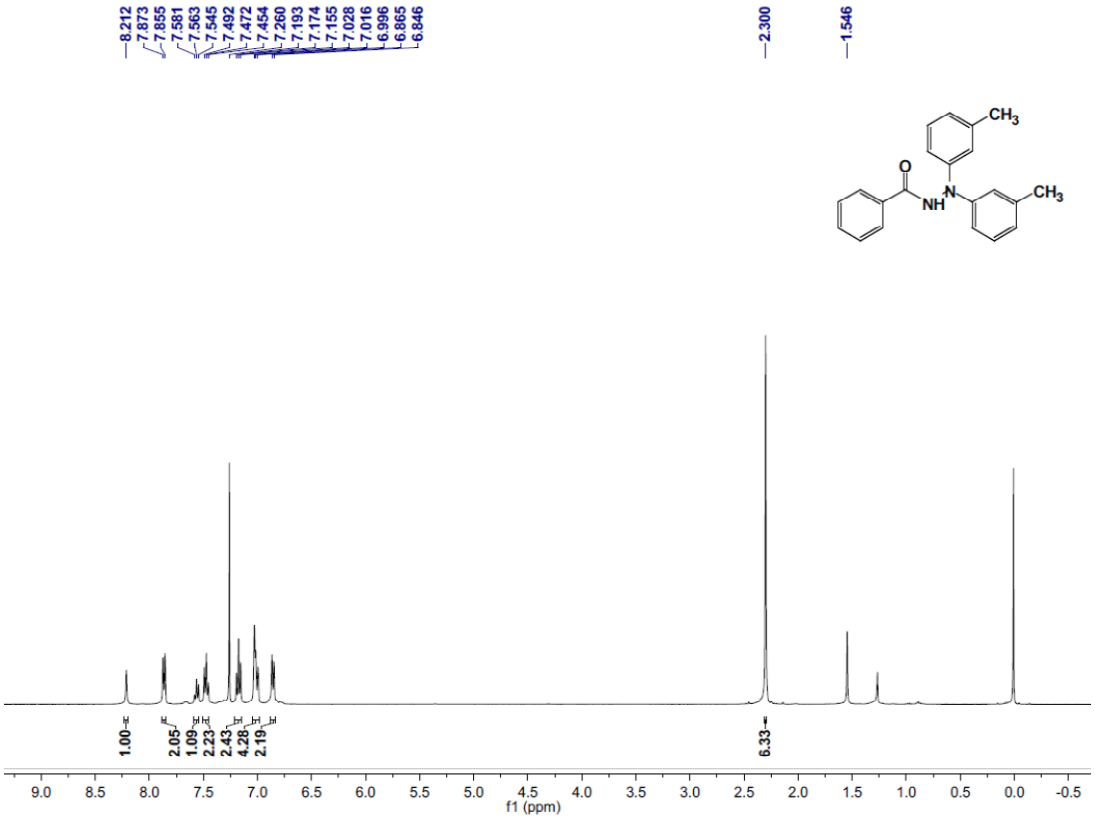


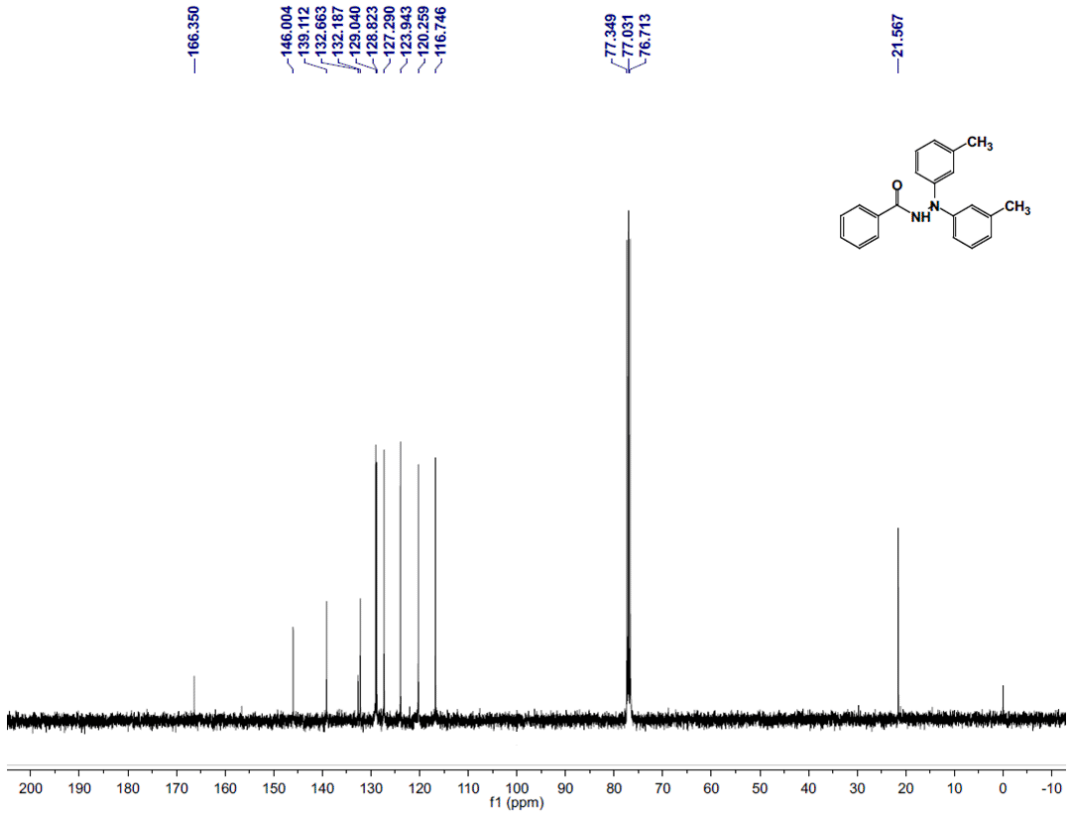
***N',N'-di*(*p*-tolyl)benzohydrazide (2m)**



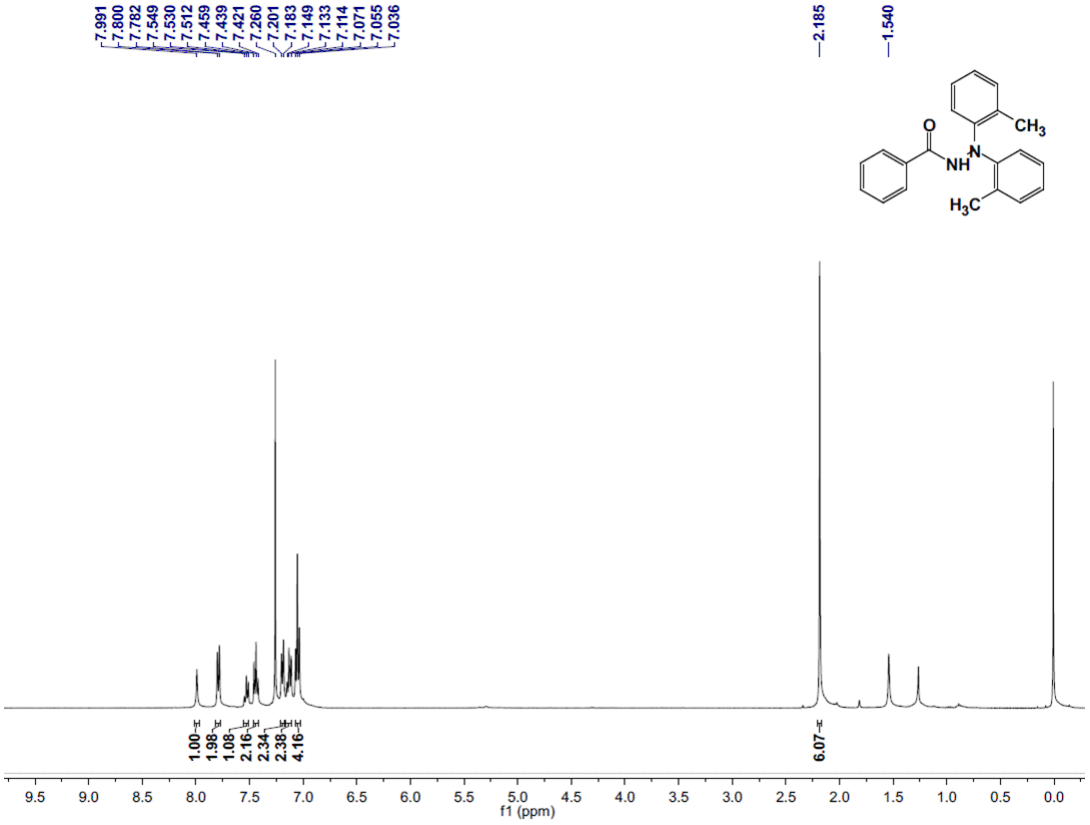


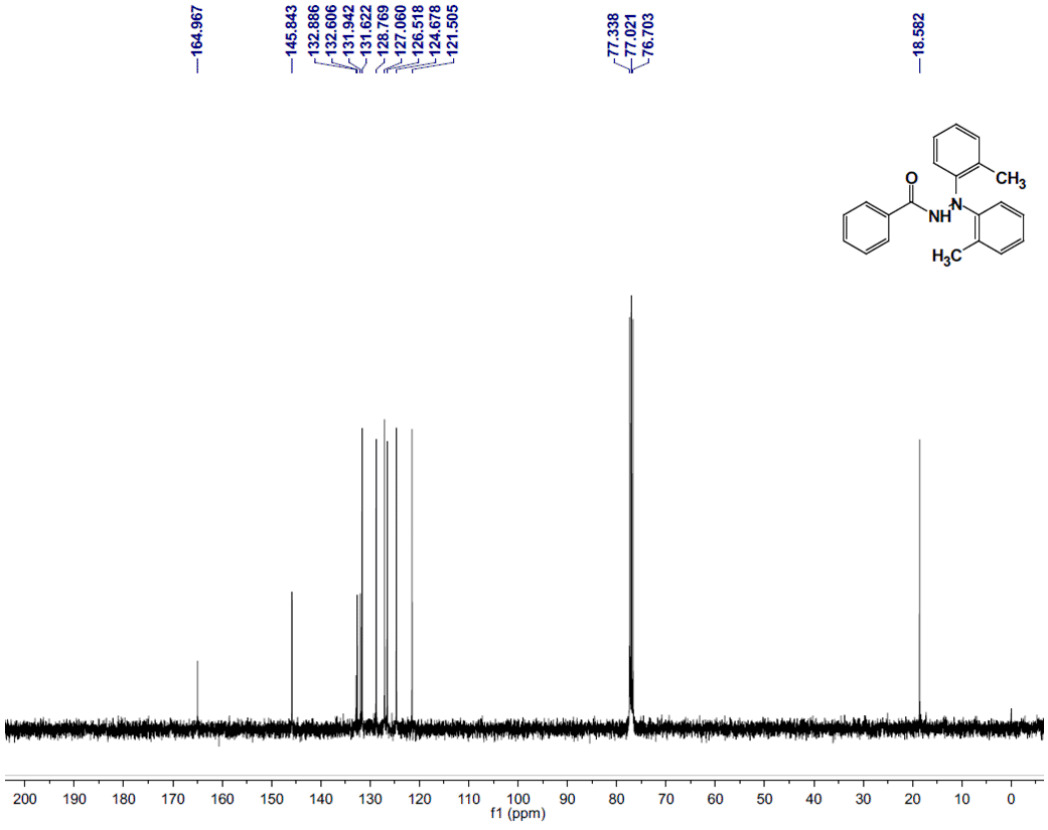
***N'*,*N'*-*di*(*m*-tolyl)benzohydrazide (2n)**



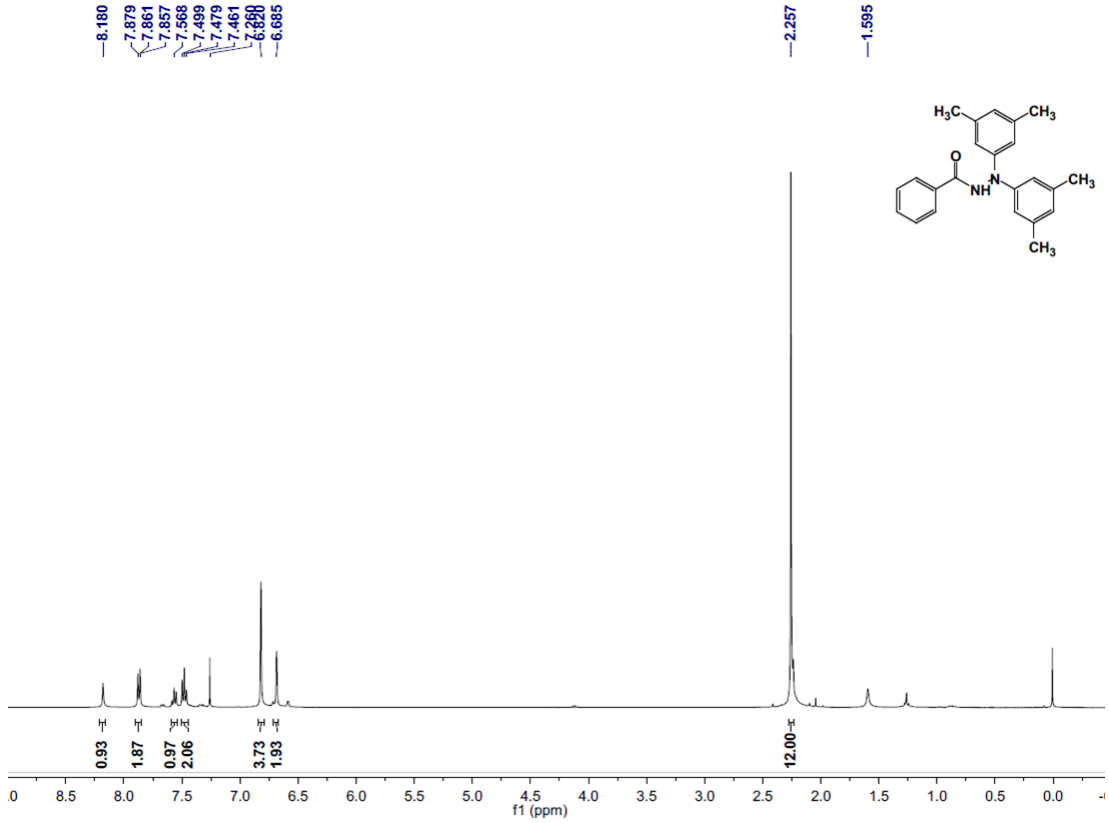


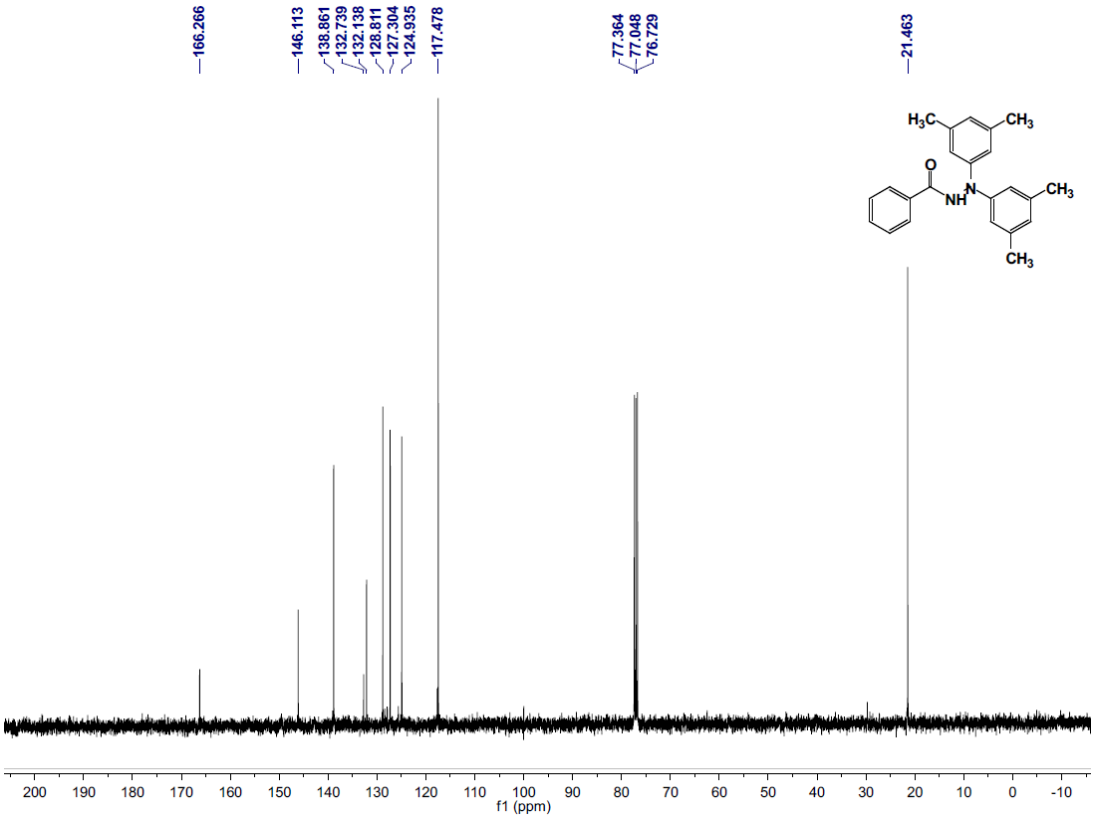
***N',N'-di*(*o*-tolyl)benzohydrazide (2o)**



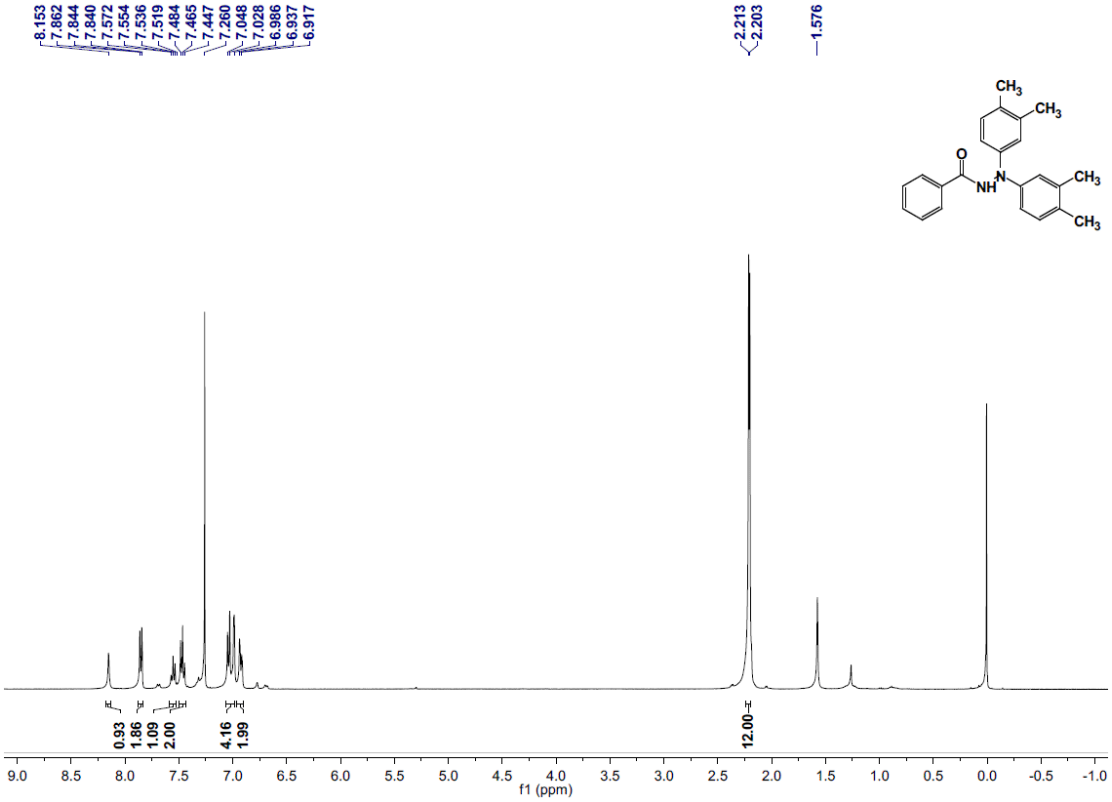


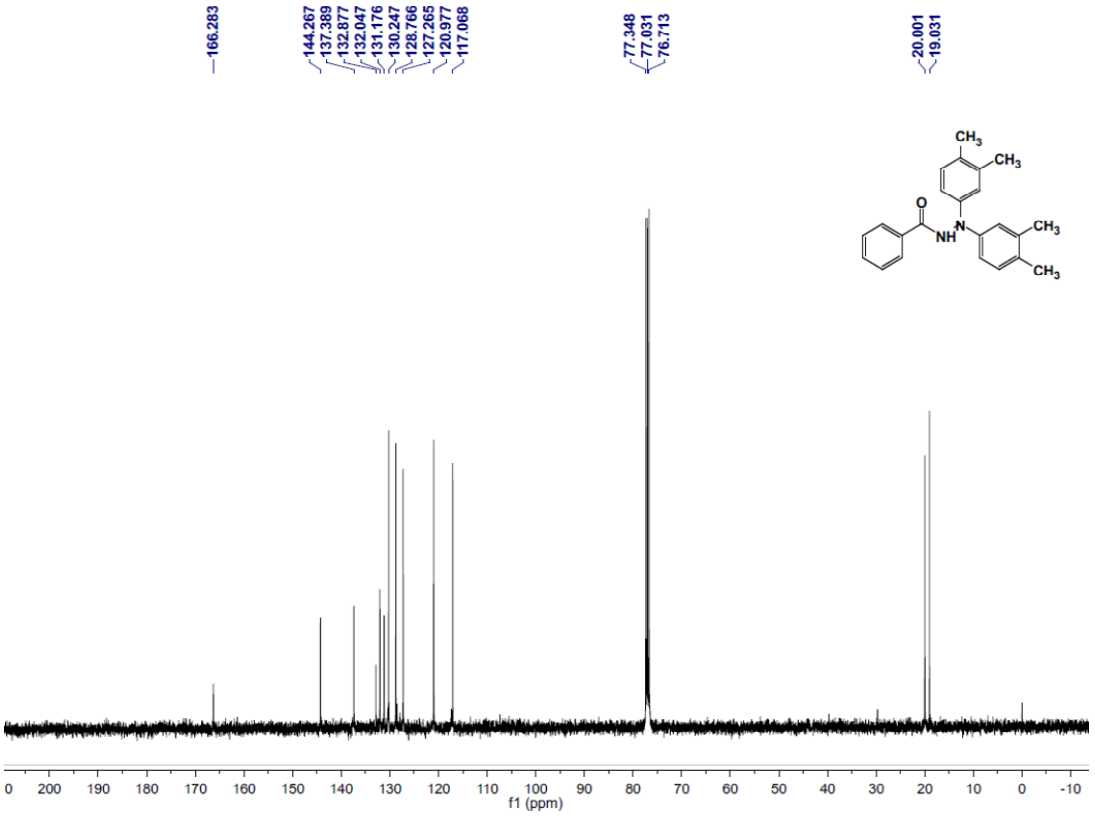
***N'*,*N'*-bis(3,5-*di*methylphenyl)benzohydrazide (2p)**



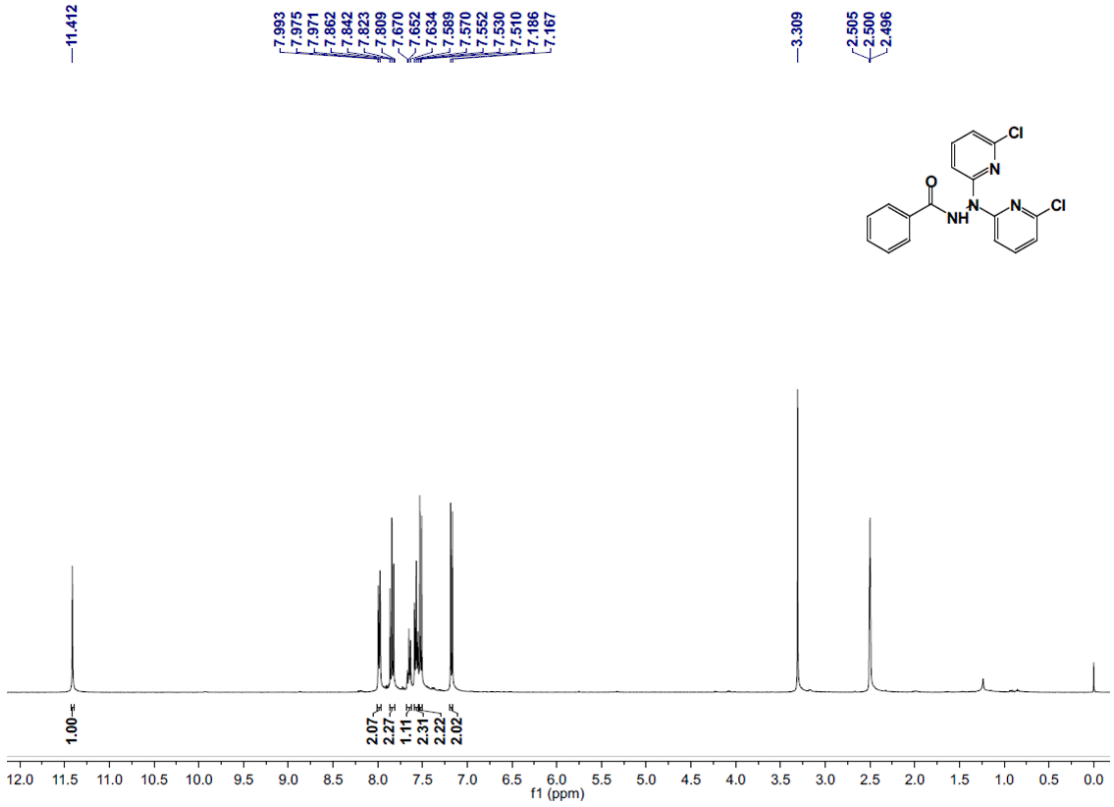


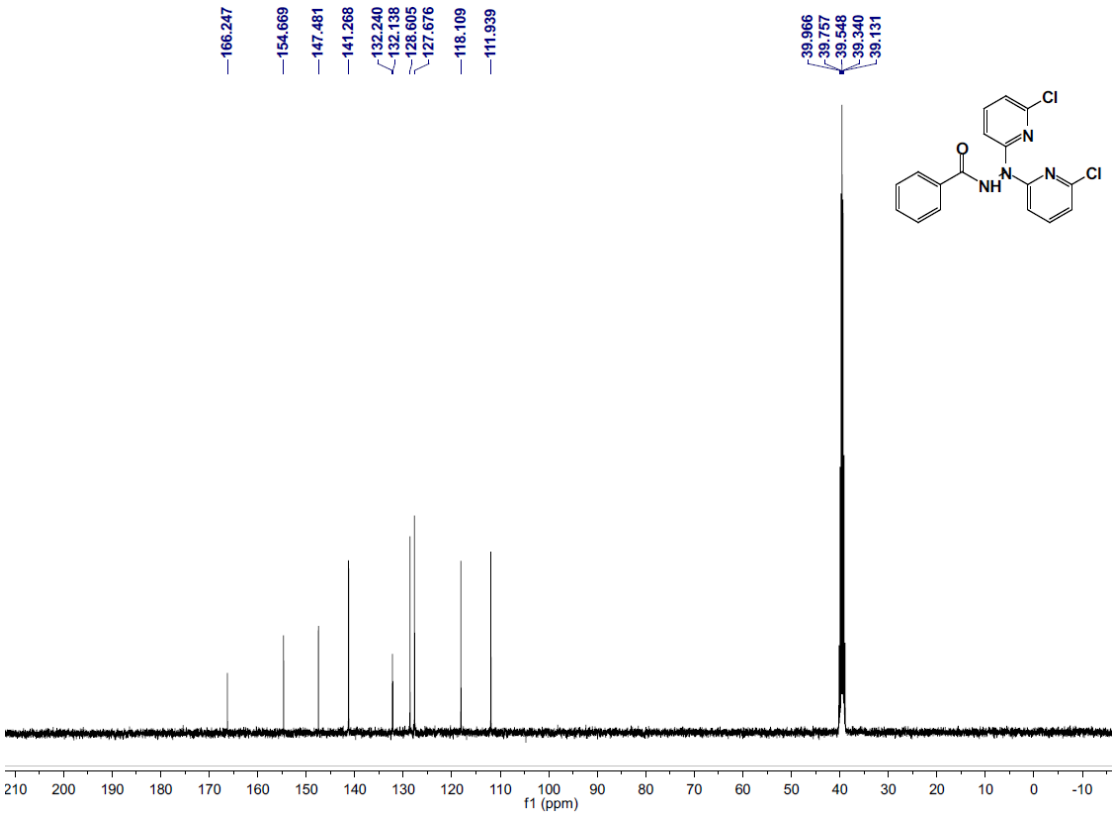
***N'*,*N'*-bis(3,4-*di*methylphenyl)benzohydrazide (2q)**



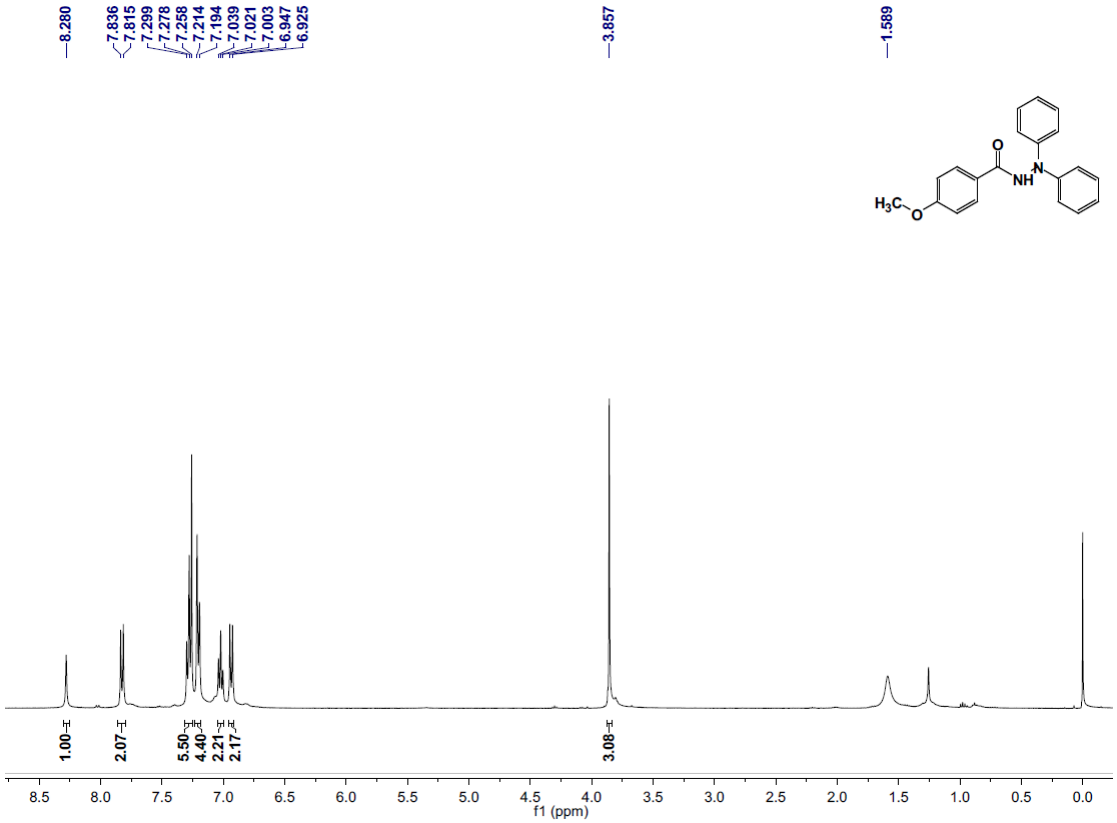


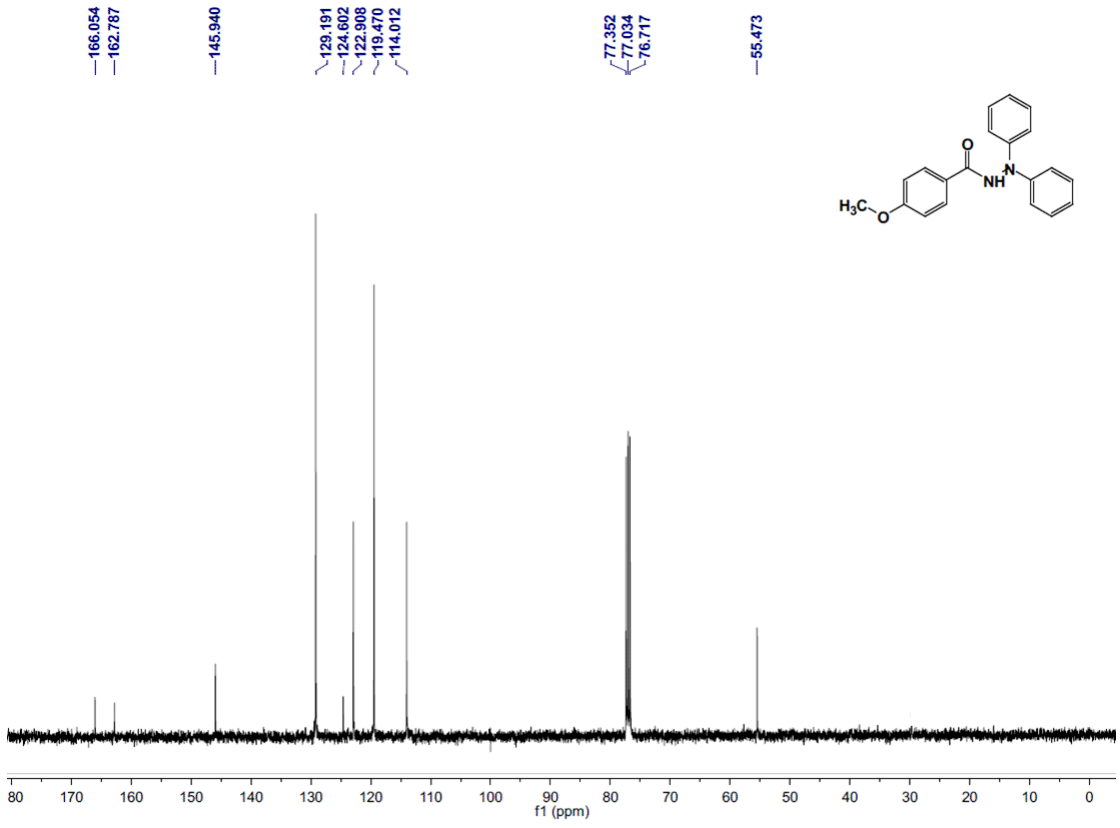
***N'*,*N'*-bis(6-chloropyridin-2-yl)benzohydrazide (2r)**



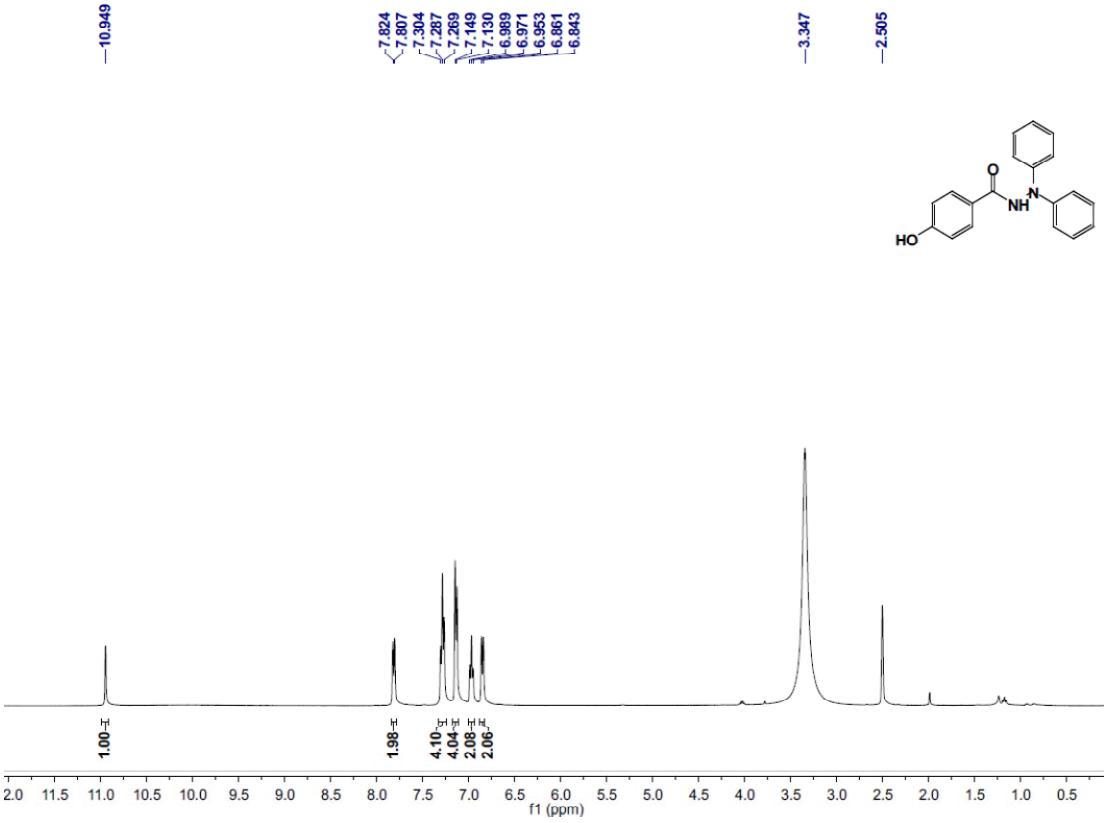


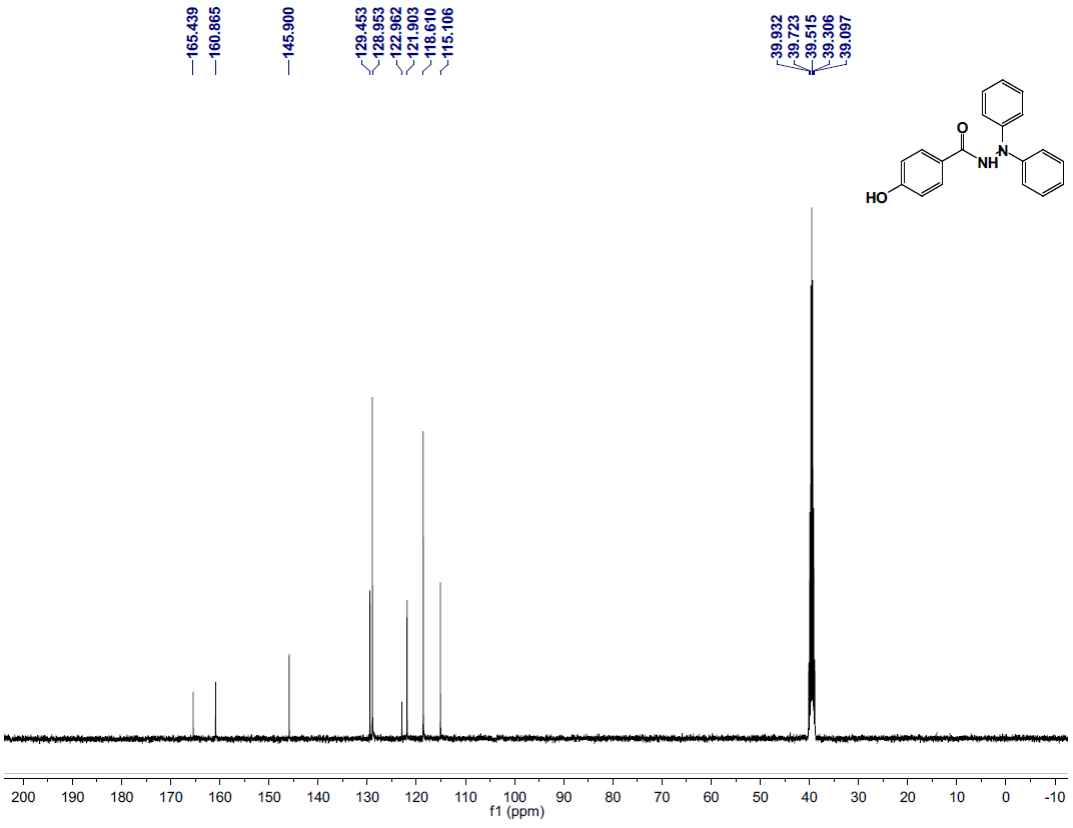
4-methoxy-*N'*,*N'*-*di*phenylbenzohydrazide (2t)



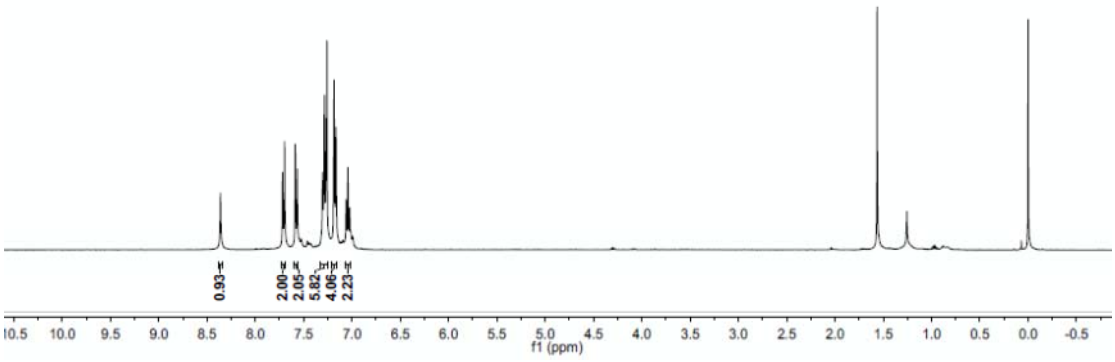


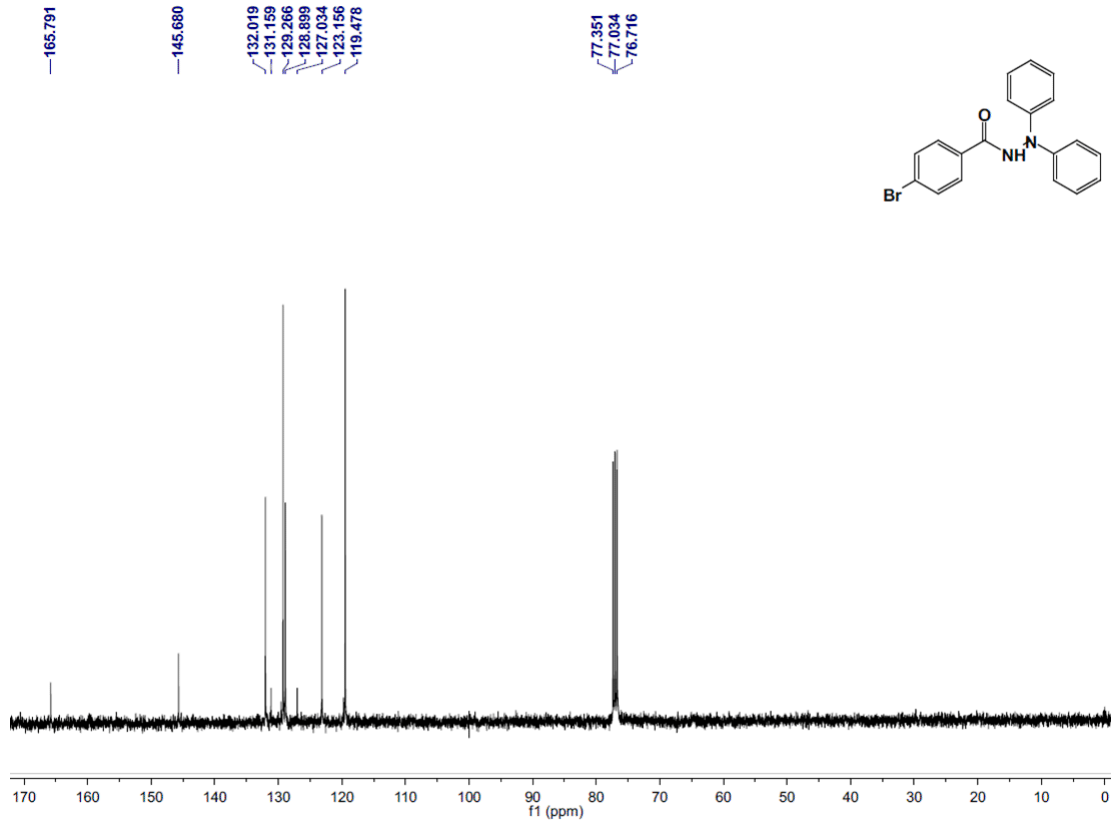
4-hydroxy-*N'*,*N'*-*di*phenylbenzohydrazide (2u)



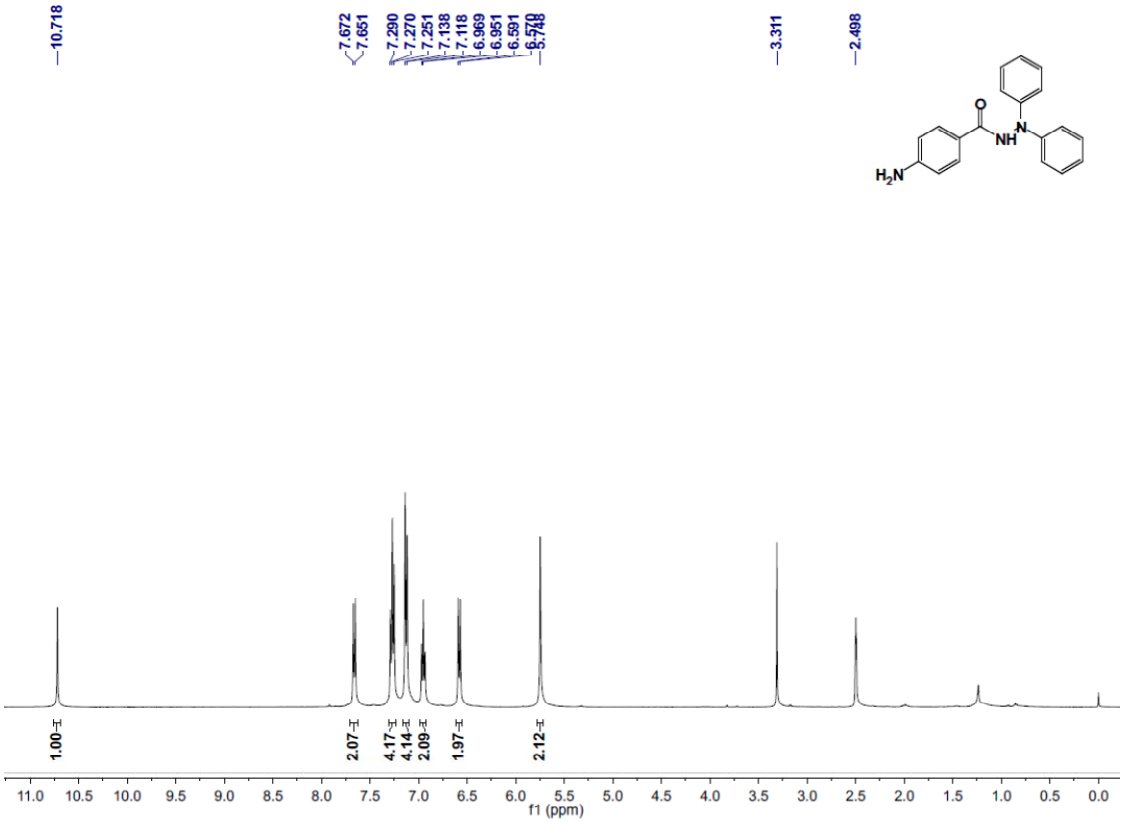


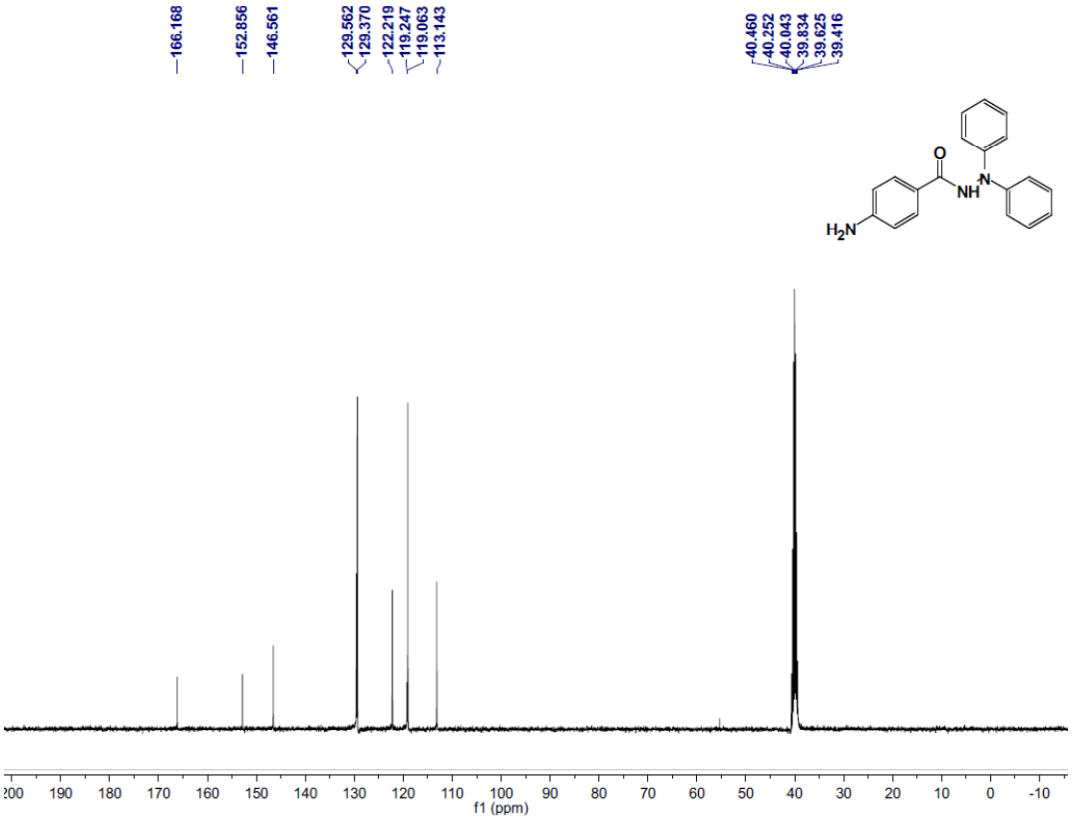
4-bromo-*N'*,*N'*-*di*phenylbenzohydrazide (2v)



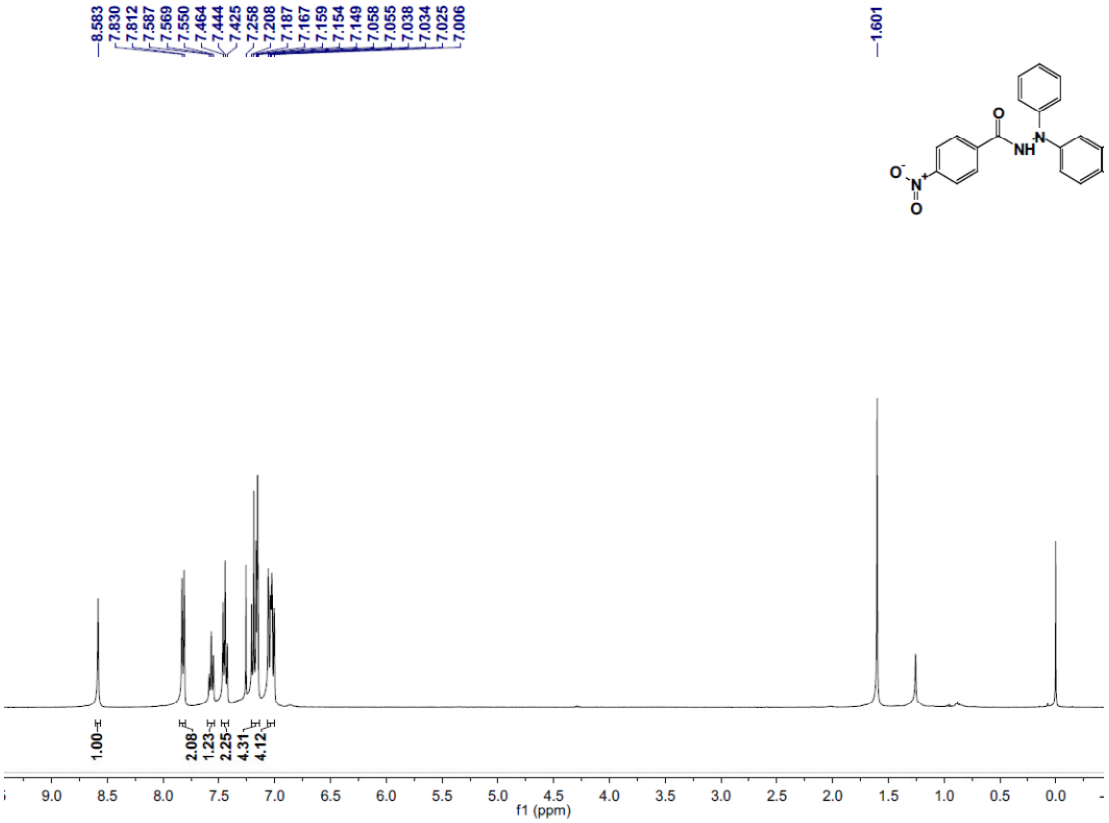


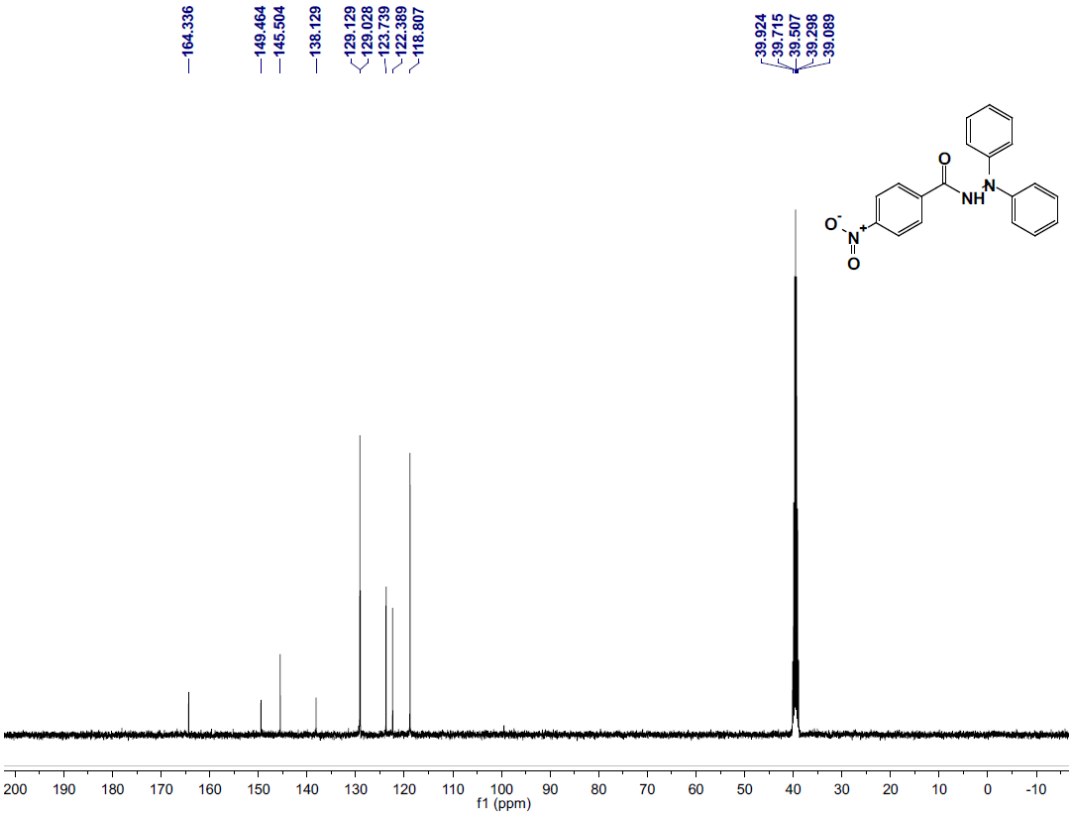
4-amino-*N',N'-di*phenylbenzohydrazide (2w)



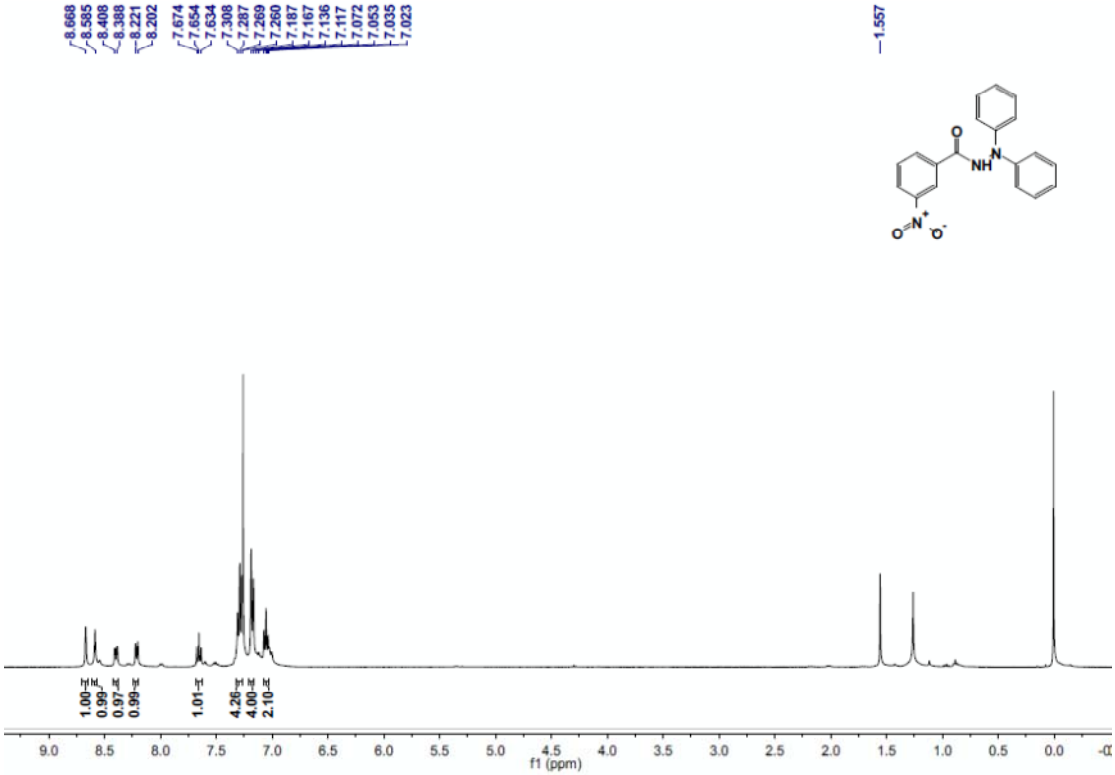


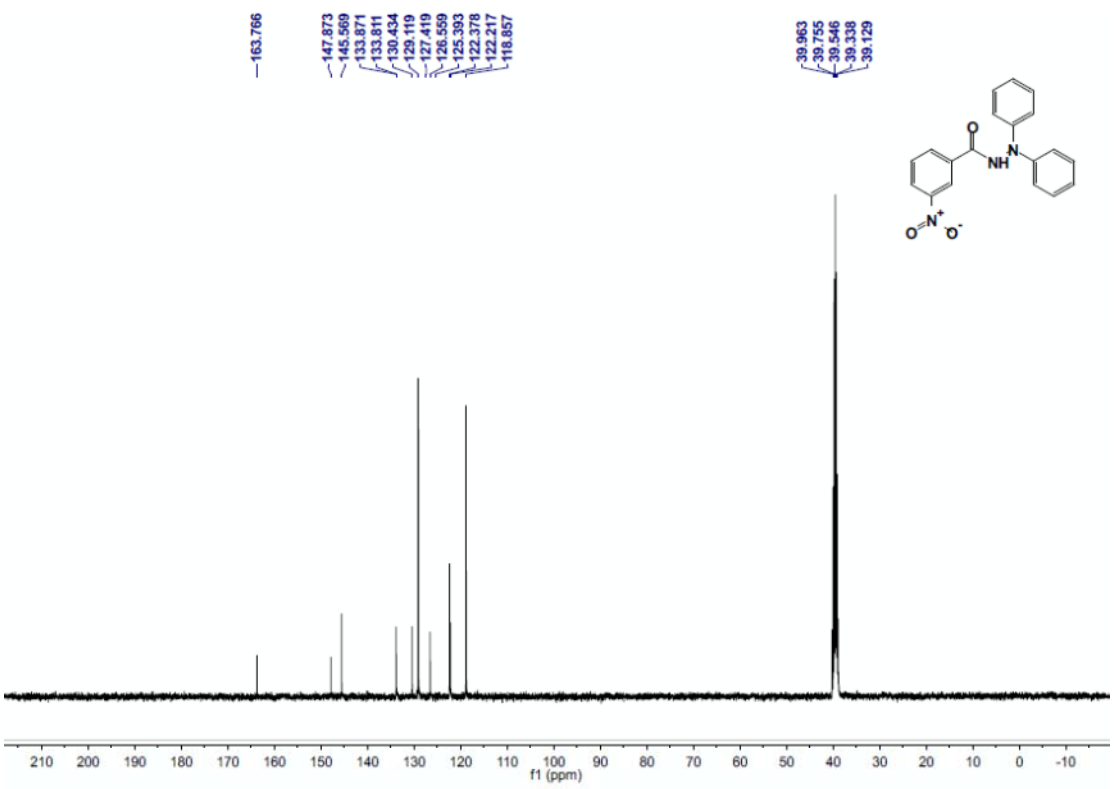
4-nitro-*N'*,*N'*-*di*phenylbenzohydrazide (2x)



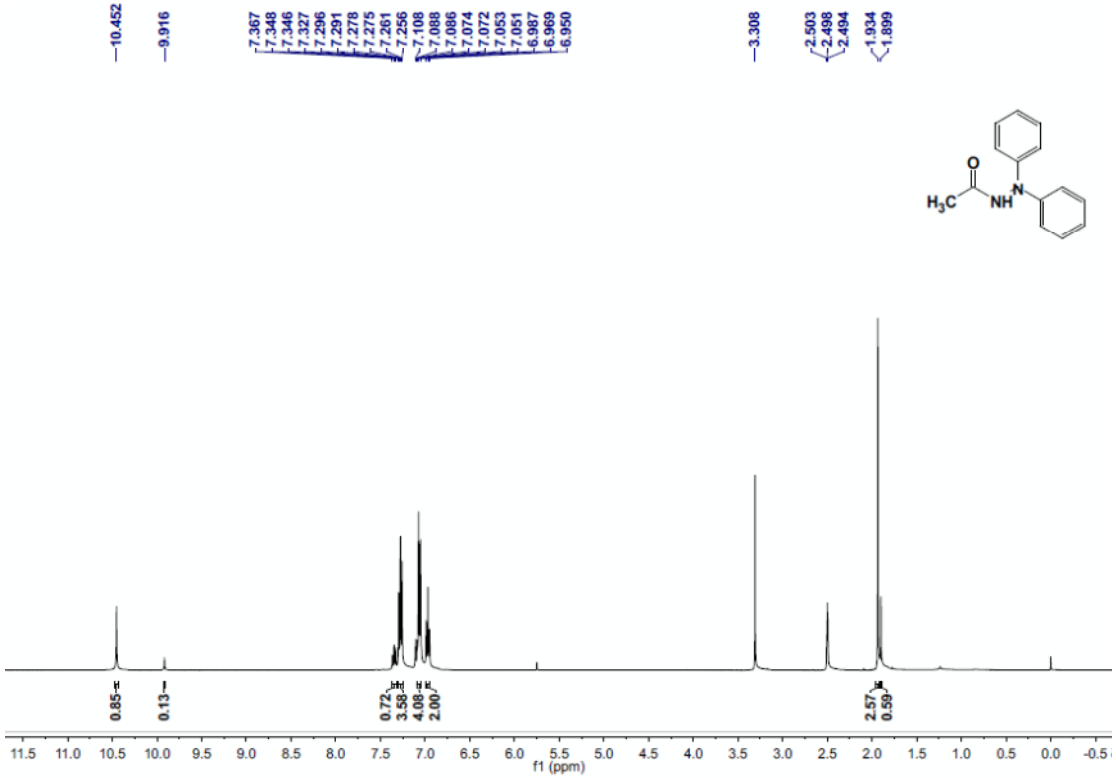


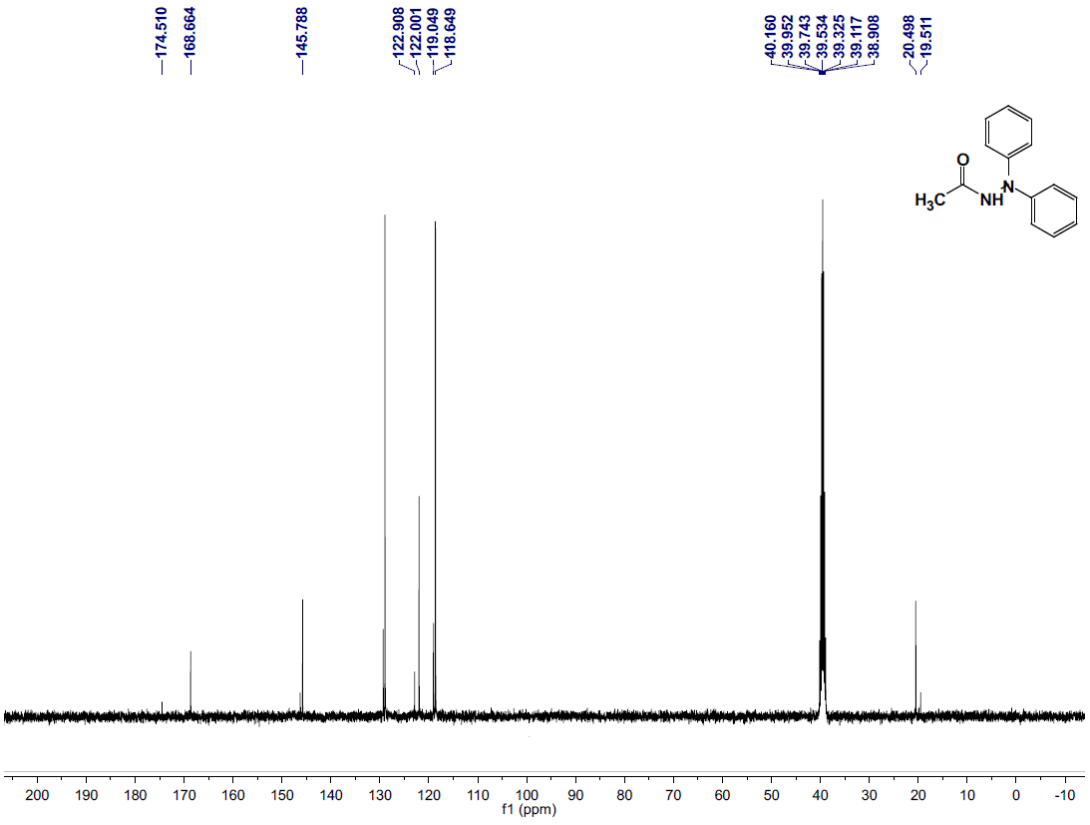
3-nitro-*N',N'-di*phenylbenzohydrazide (2y)



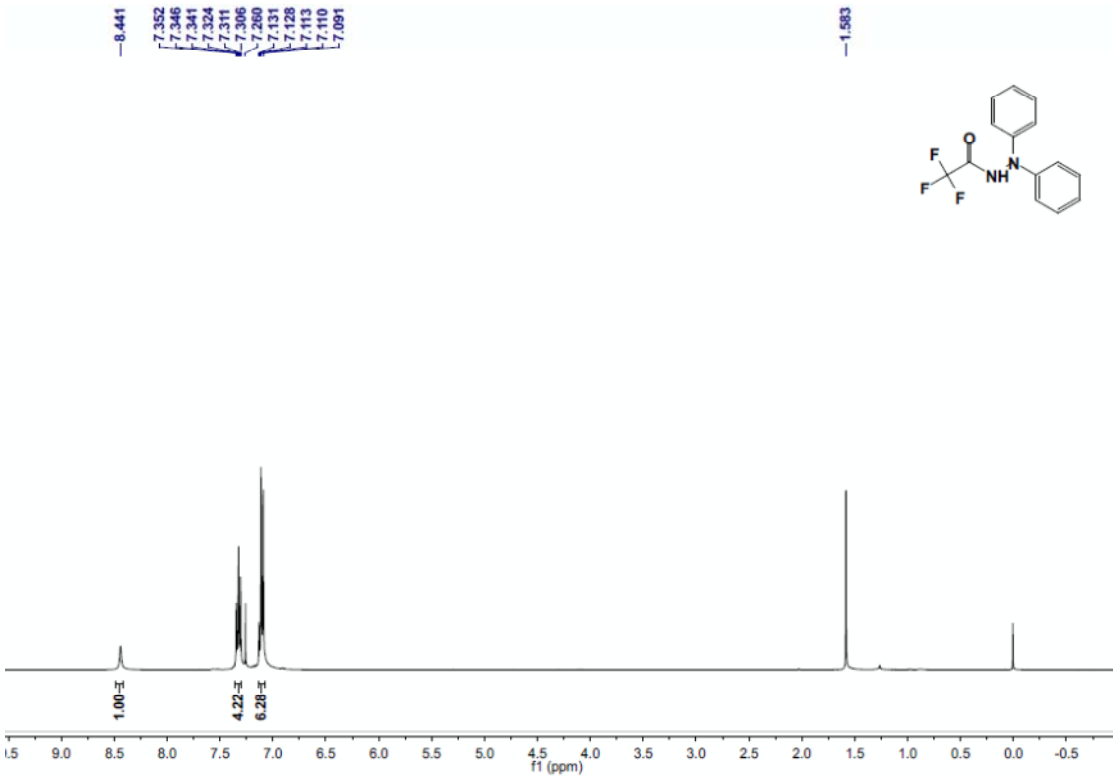


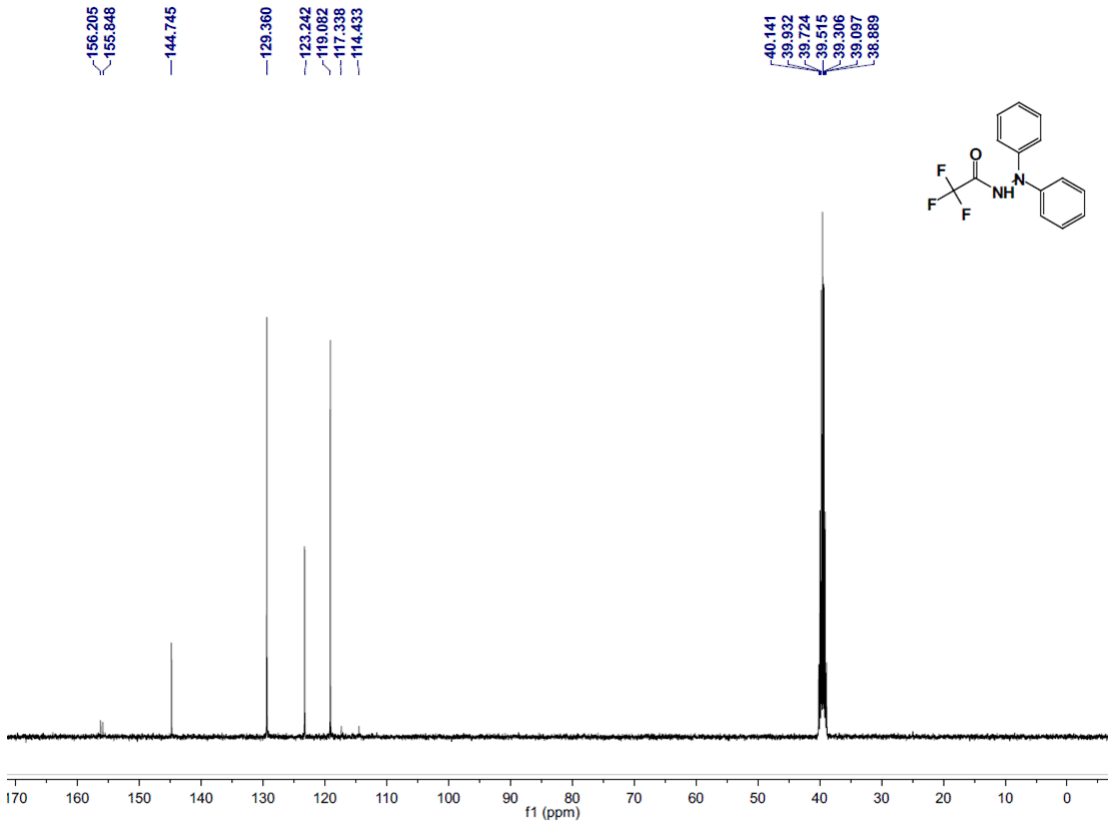
***N',N'-di*phenylacetohydrazide (2z)**



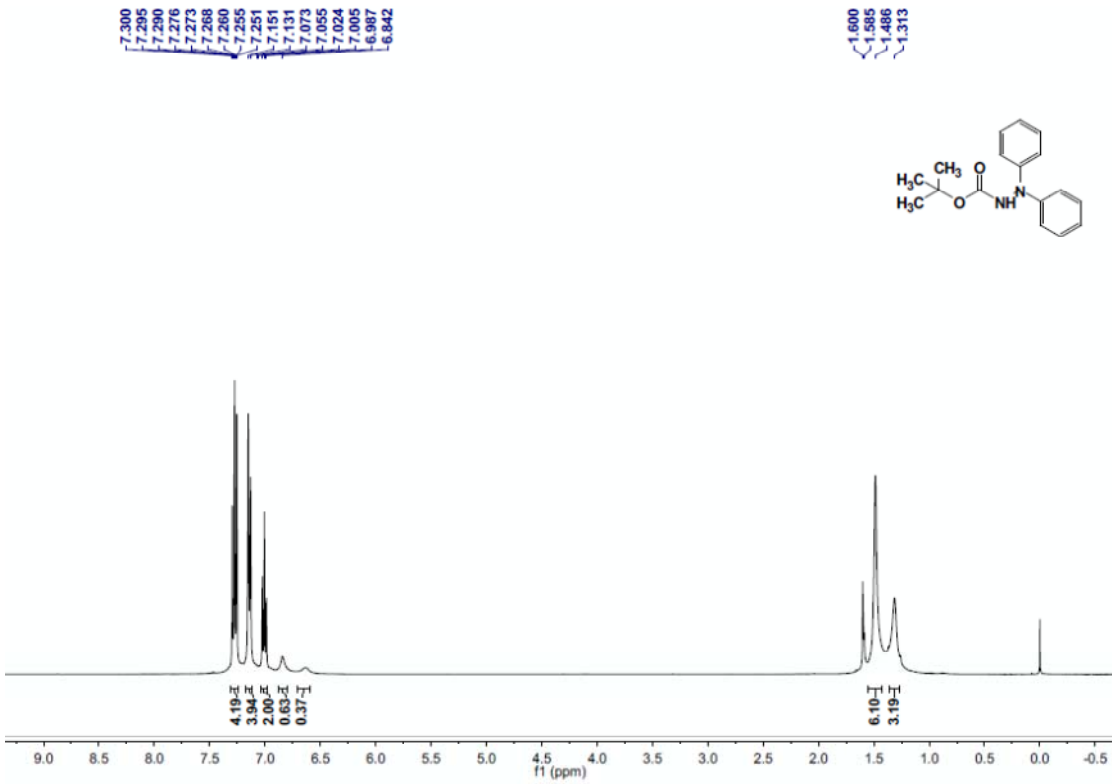


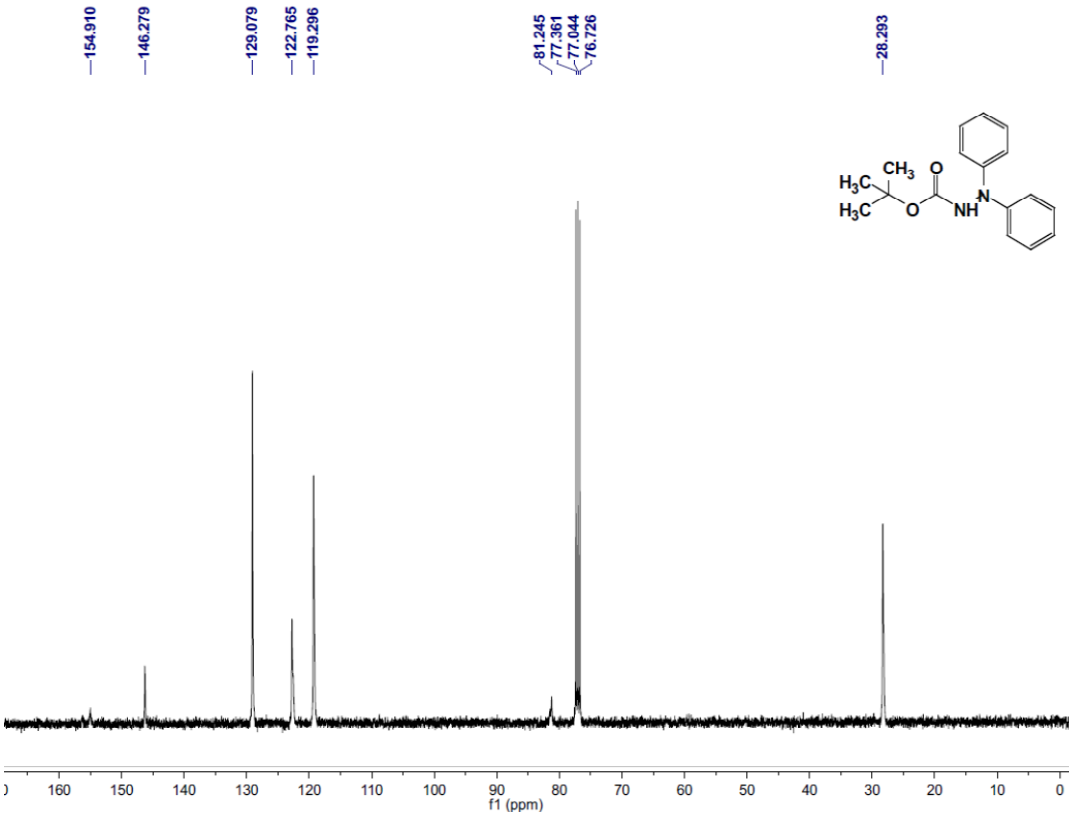
2,2,2-*tri*fluoro-*N'*,*N'*-*di*phenylacetohydrazide (2aa)



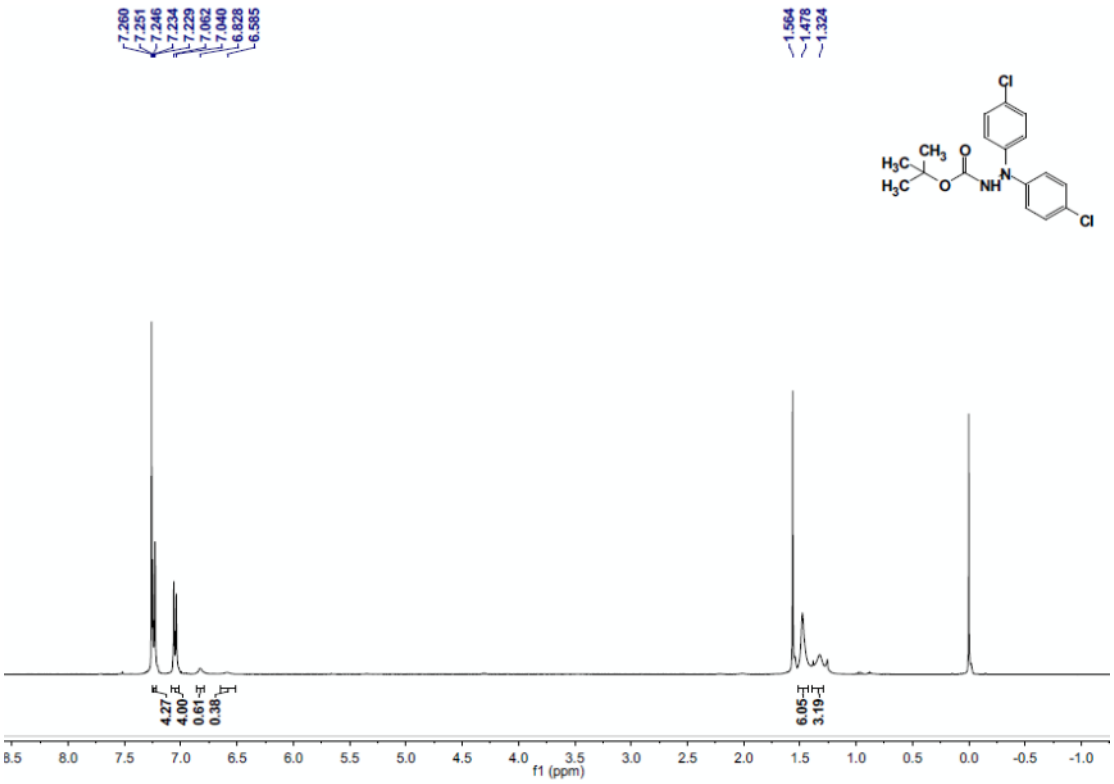


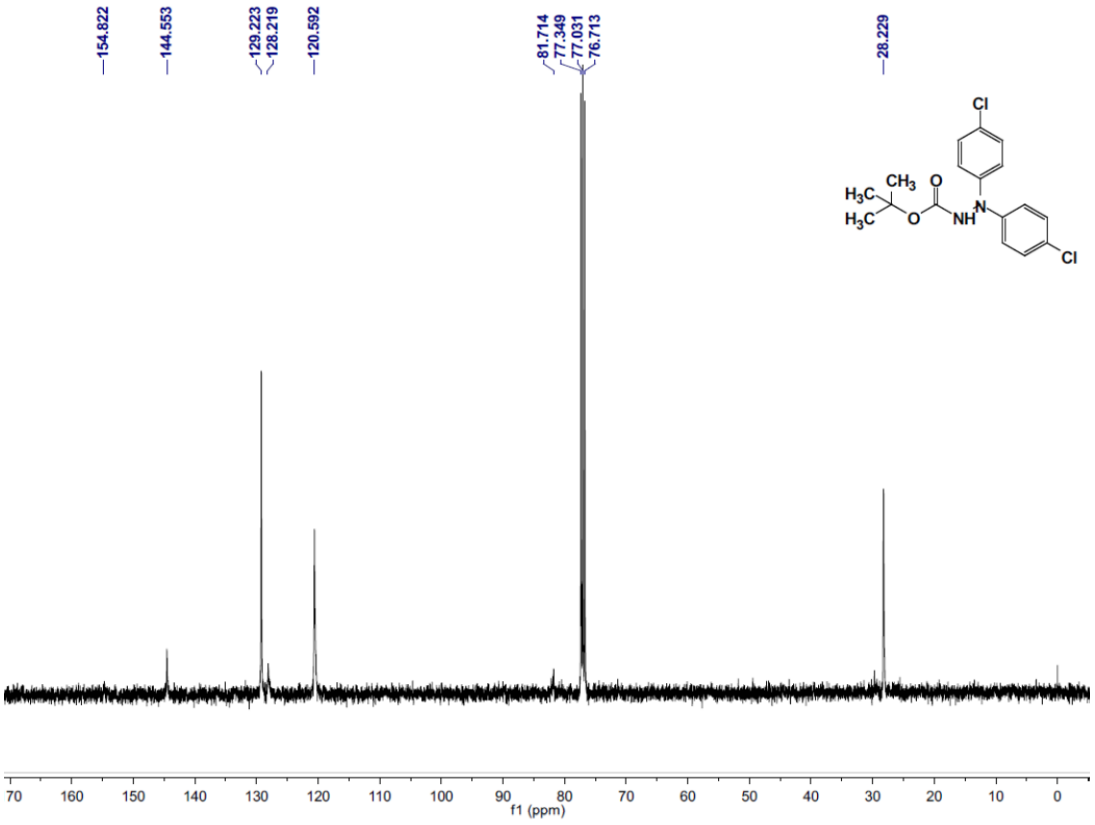
***tert*-butyl 2,2-*di*phenylhydrazinecarboxylate (2ab)**



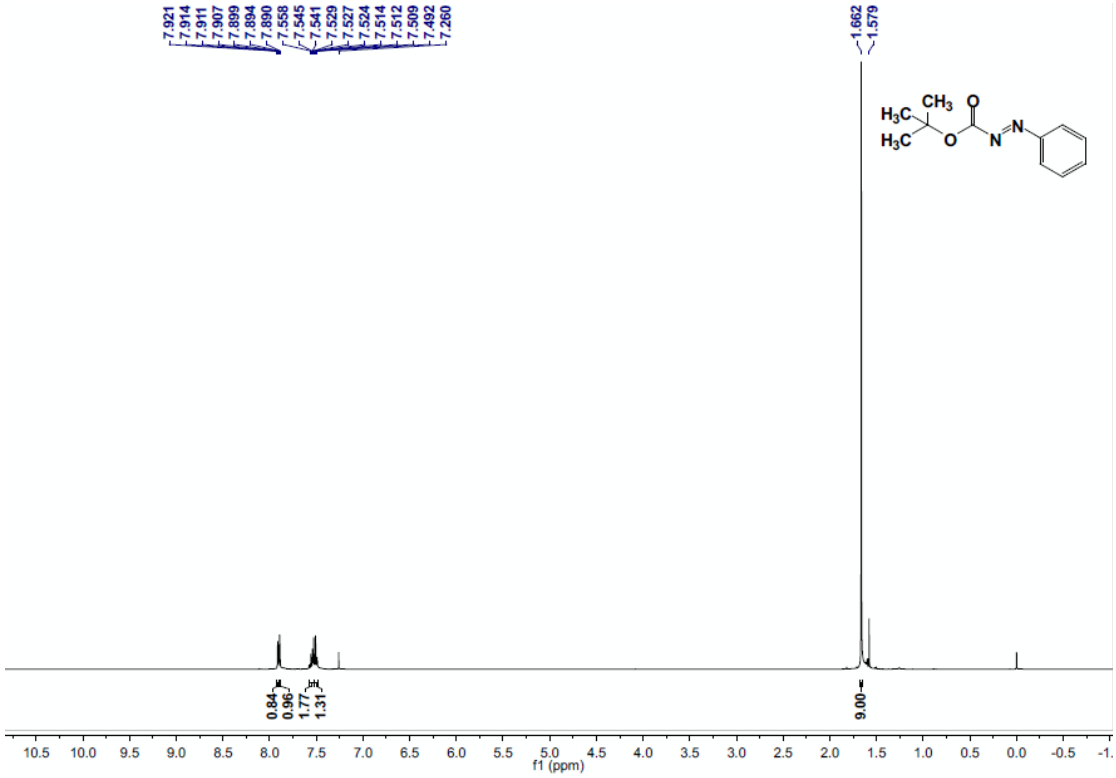


***tert*-butyl 2,2-bis(4-chlorophenyl)hydrazinecarboxylate (2ac)**

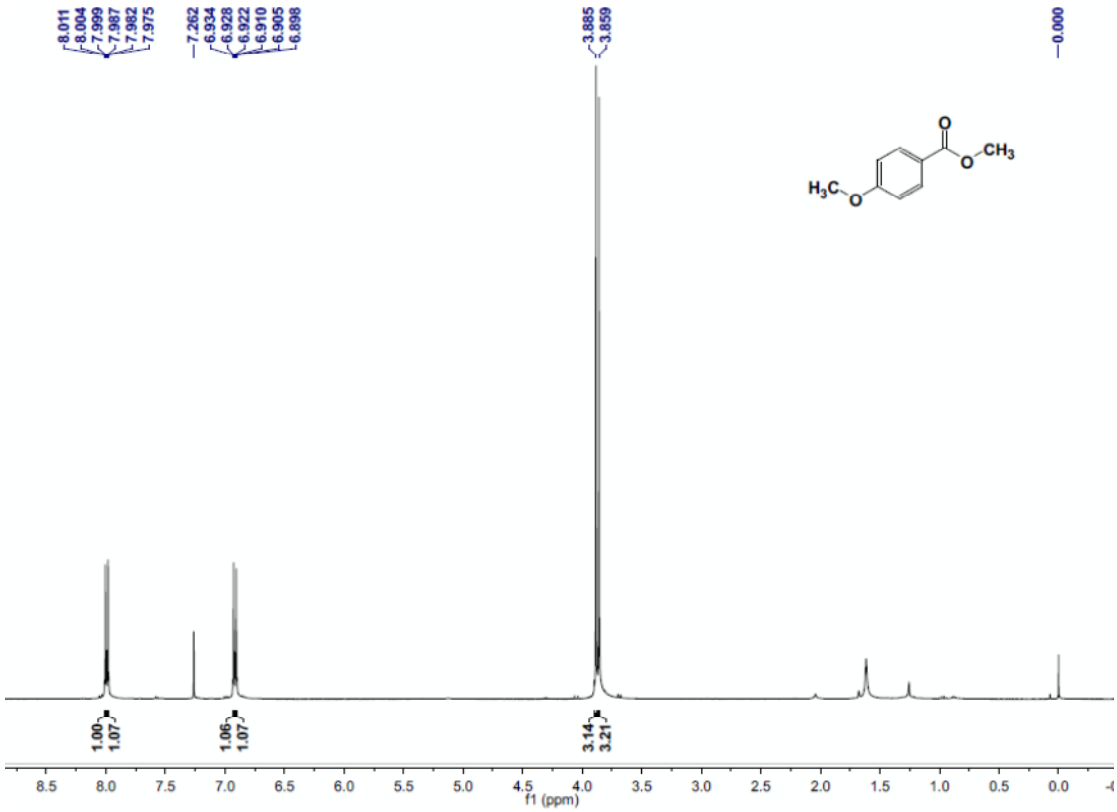




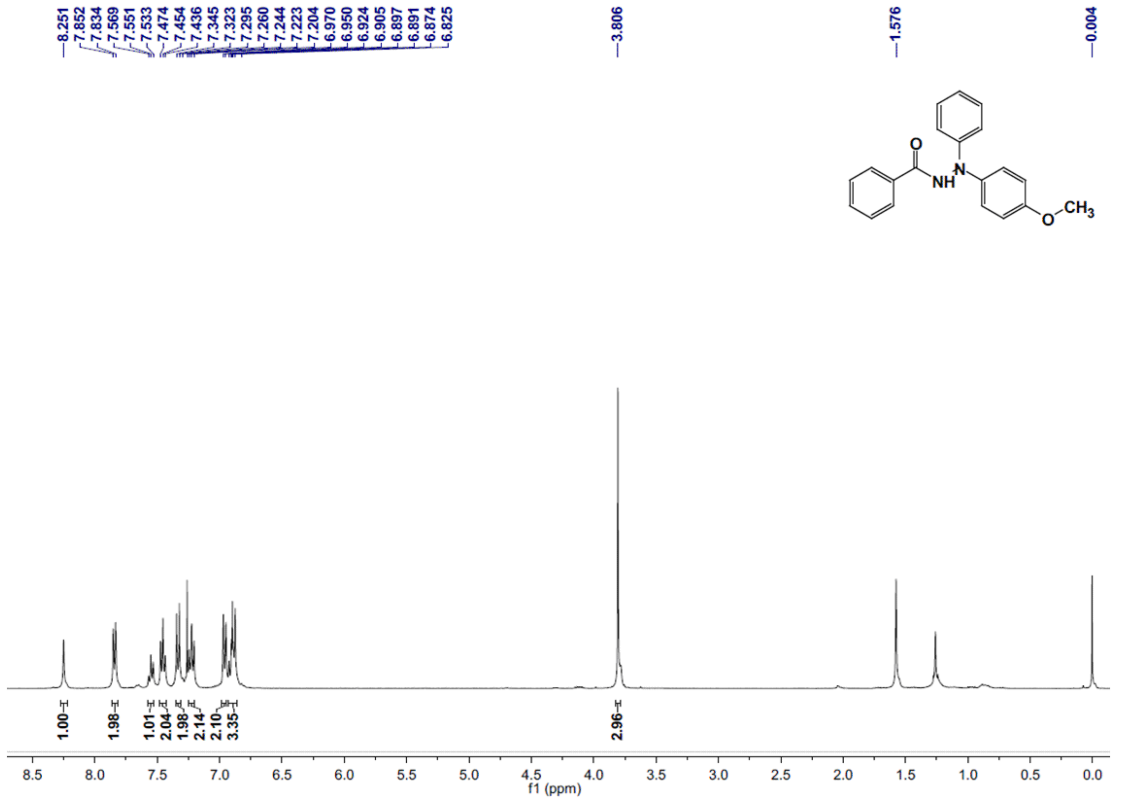
(*E*)-*tert*-butyl 2-phenyldiazenecarboxylate (4)

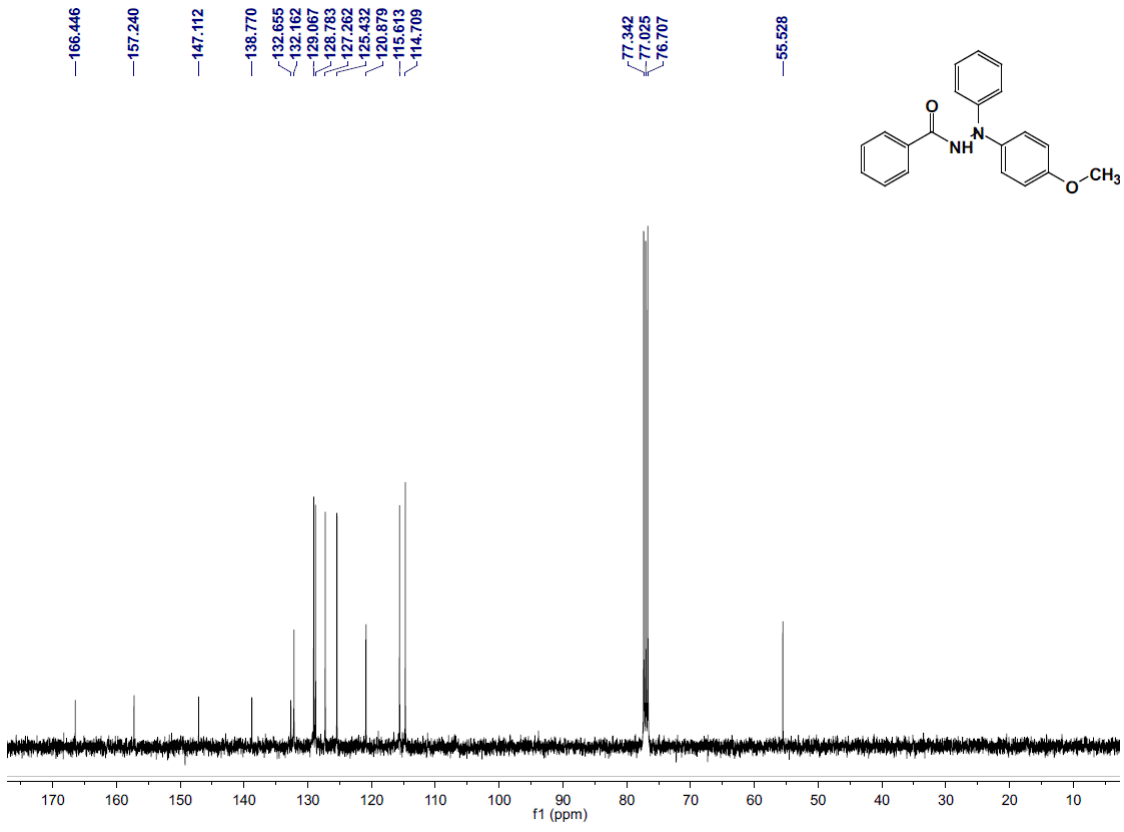


Methyl 4-methoxybenzoate (5t)

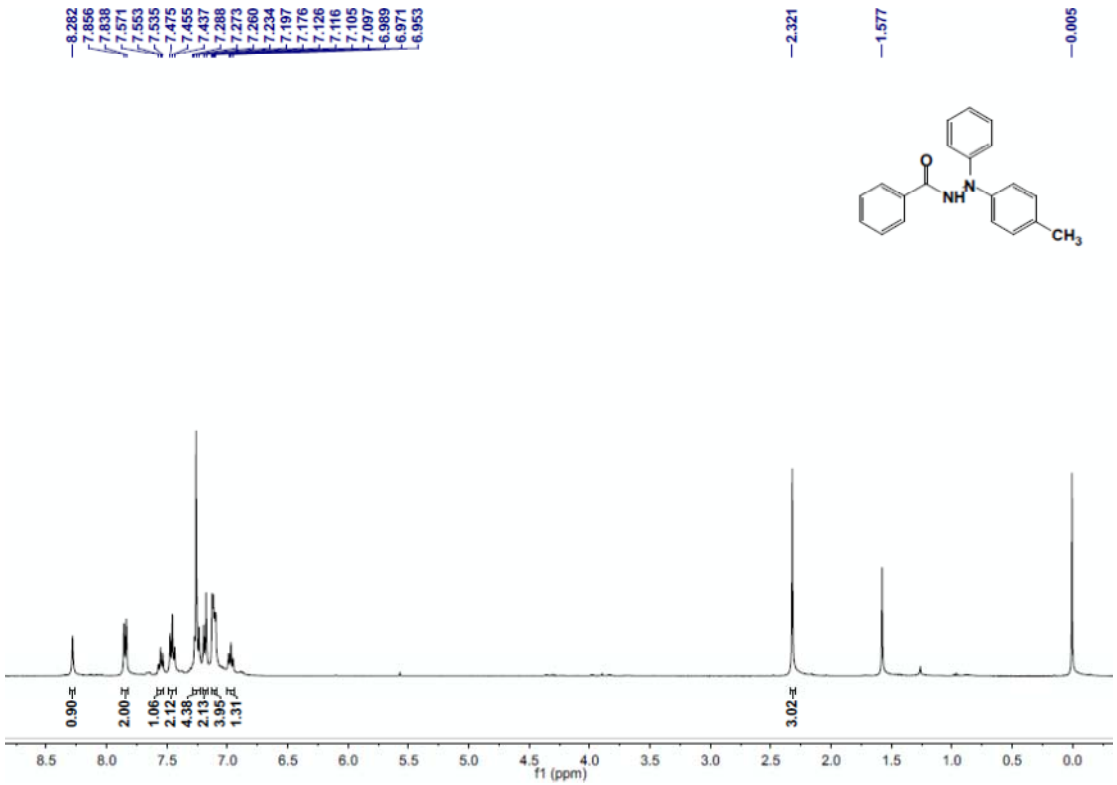


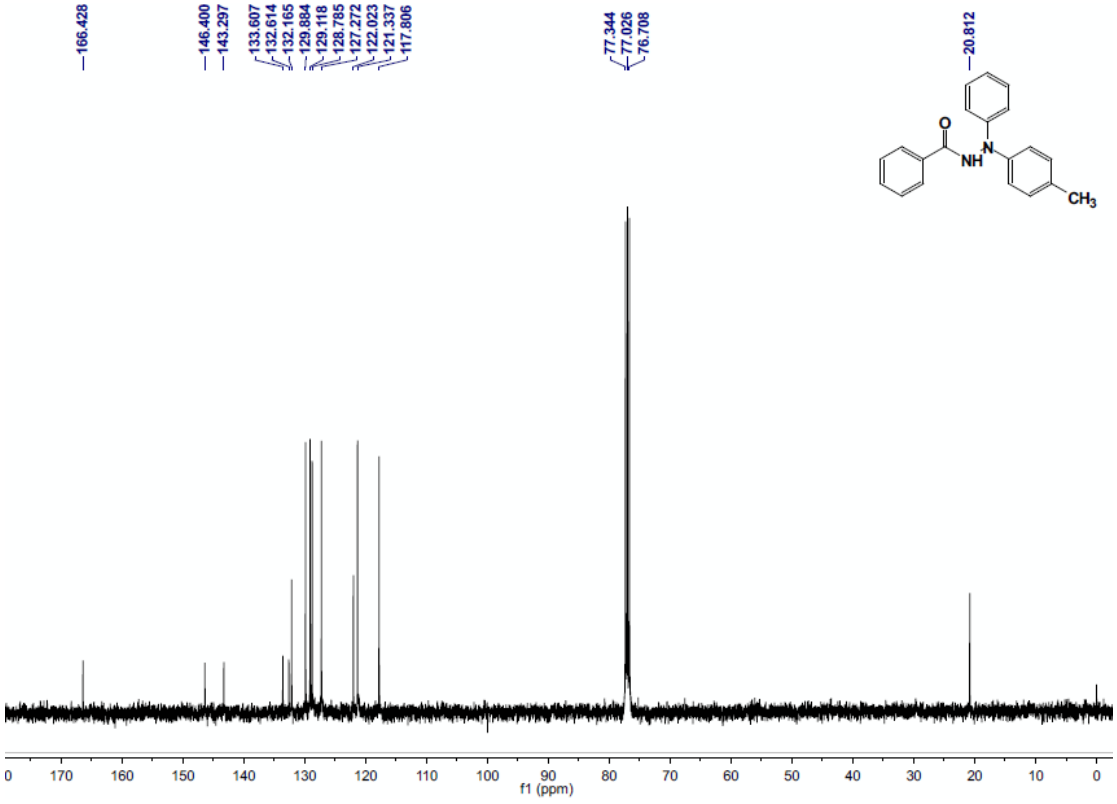
***N′*-(4-methoxyphenyl)-*N′*-phenylbenzohydrazide (7a)**



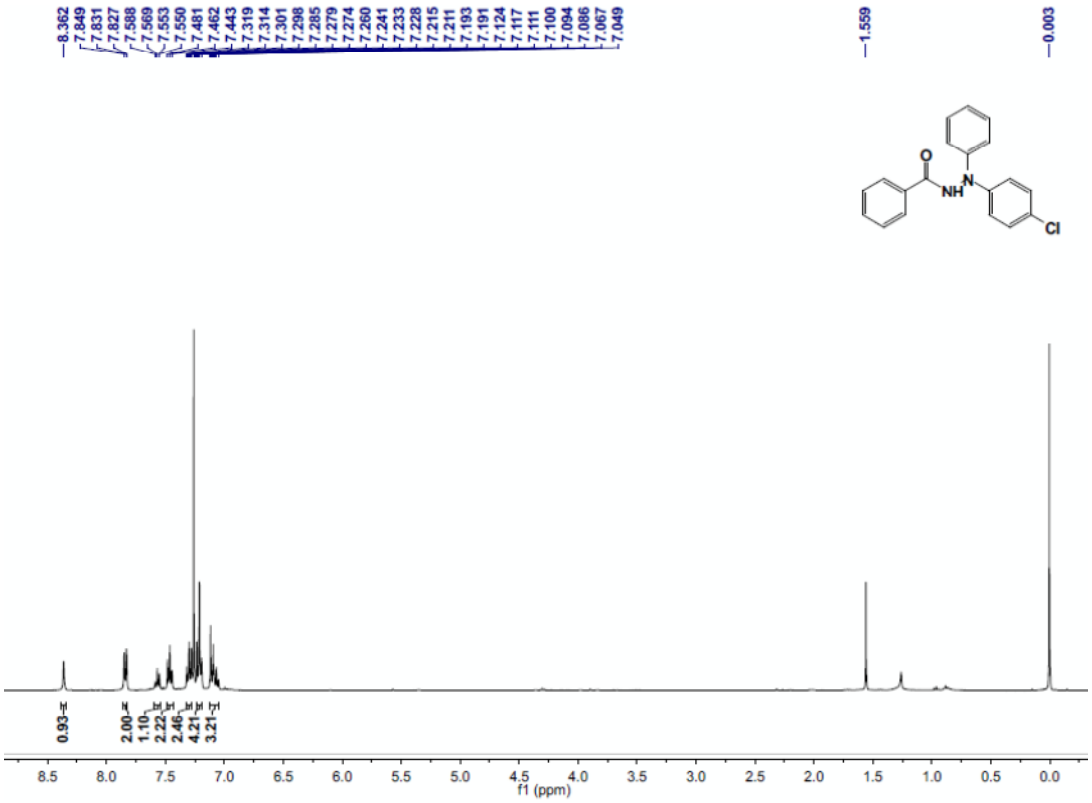


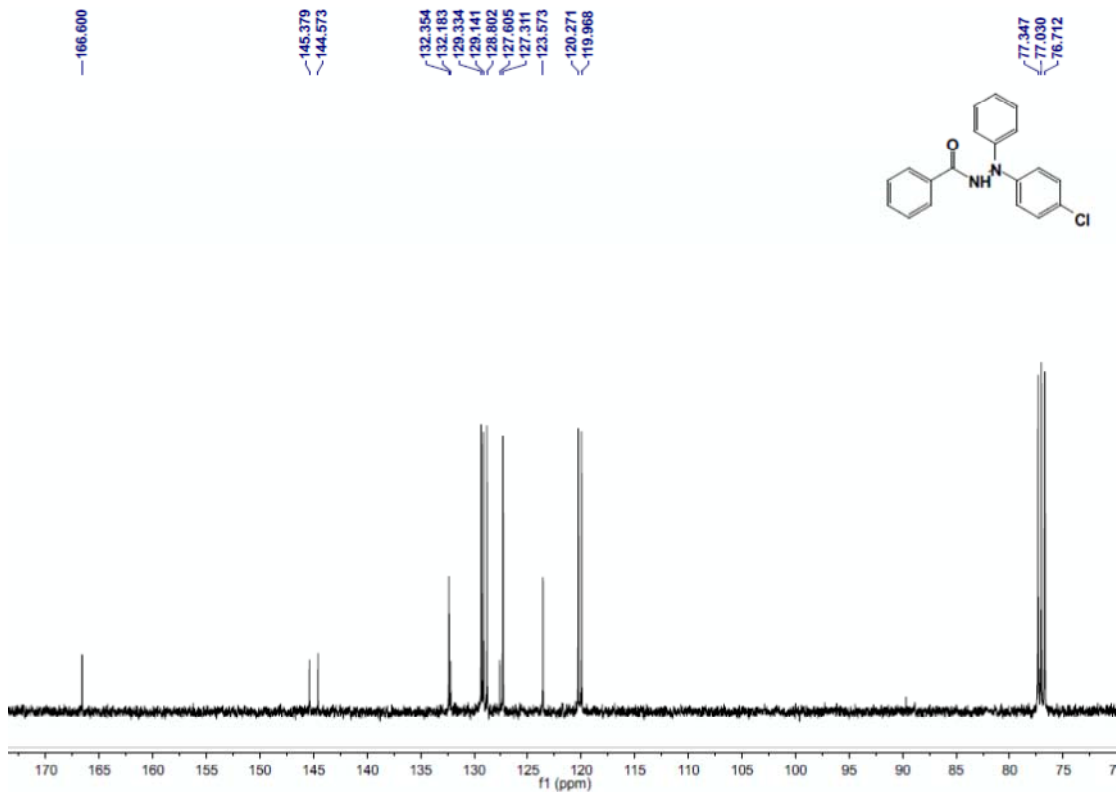
***N'*-phenyl-*N'*-*p*-tolylbenzohydrazide (7b)**



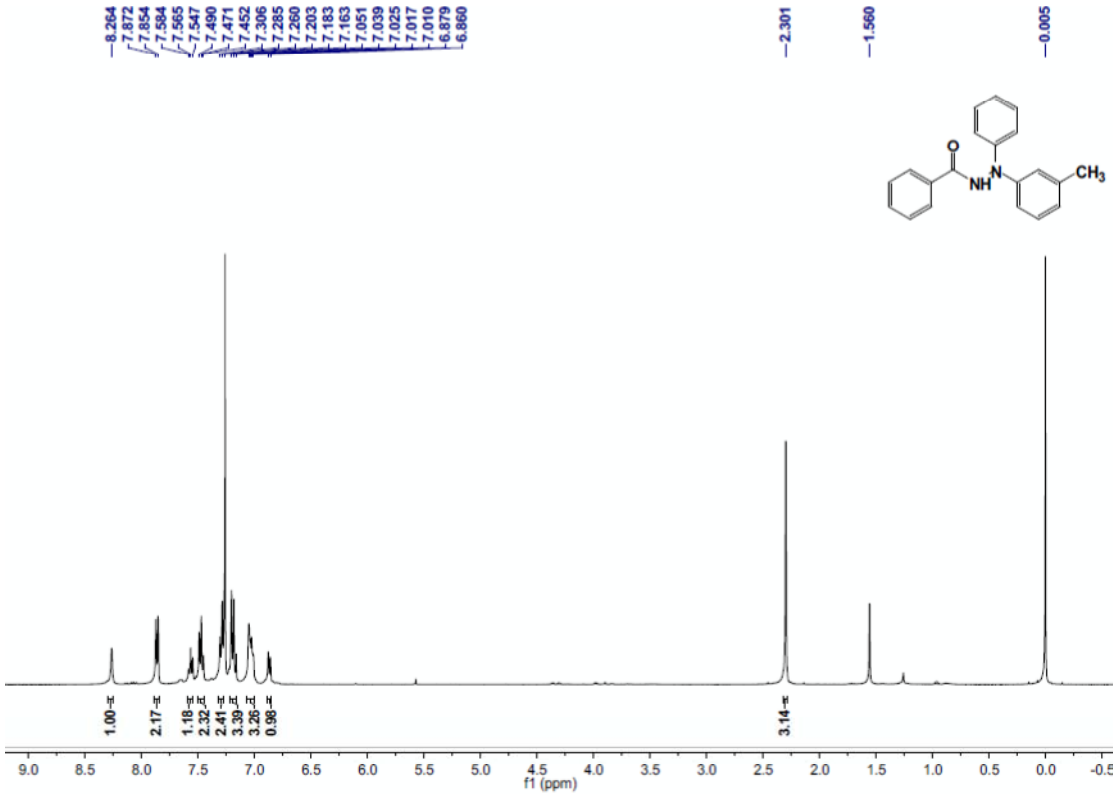


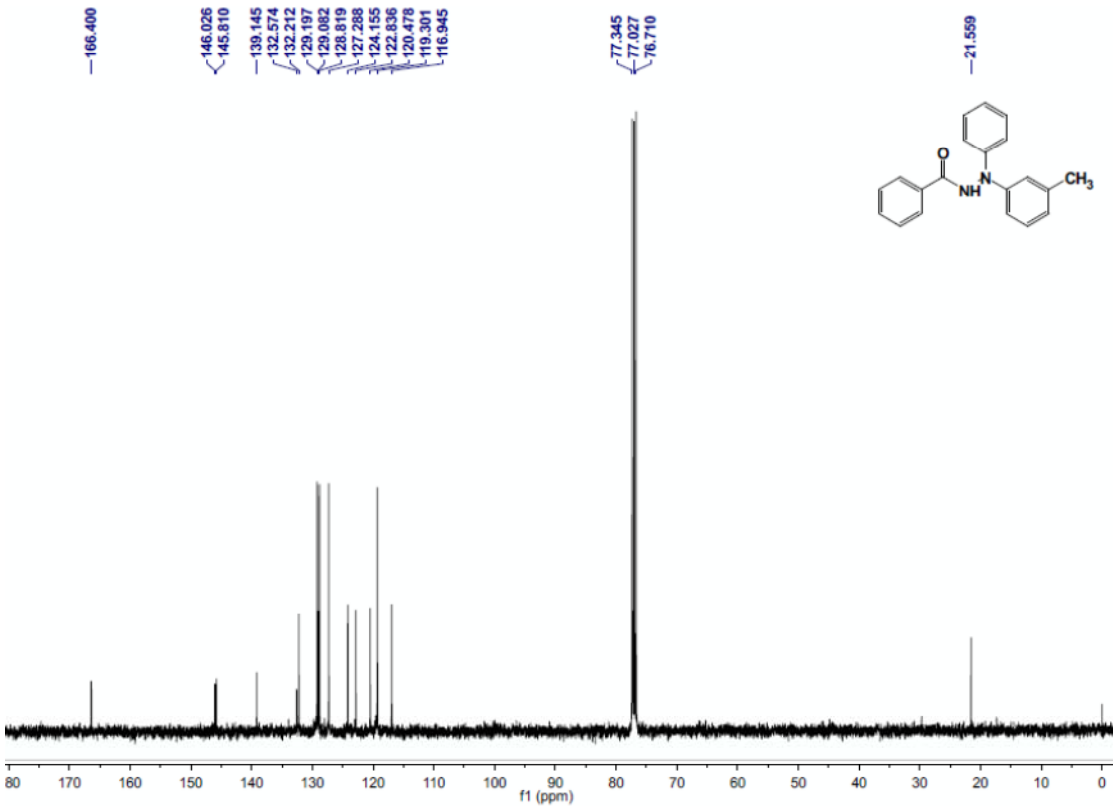
***N′*-(4-chlorophenyl)-*N′*-phenylbenzohydrazide (7c)**



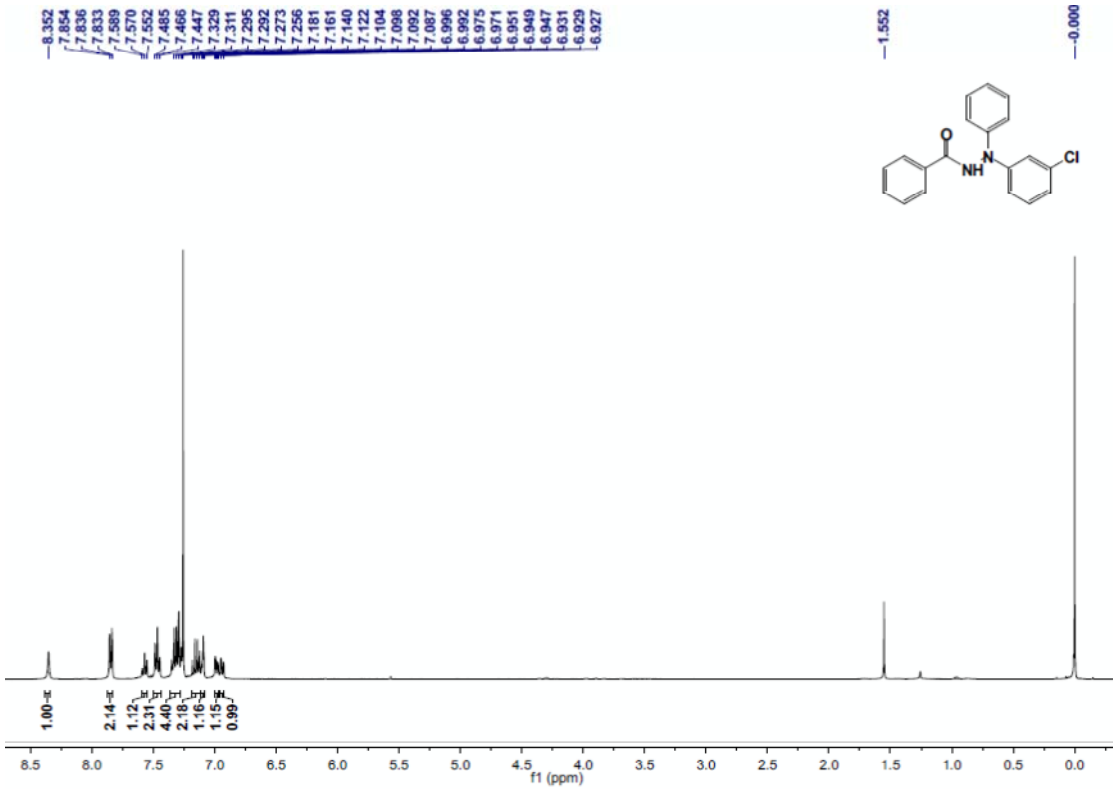


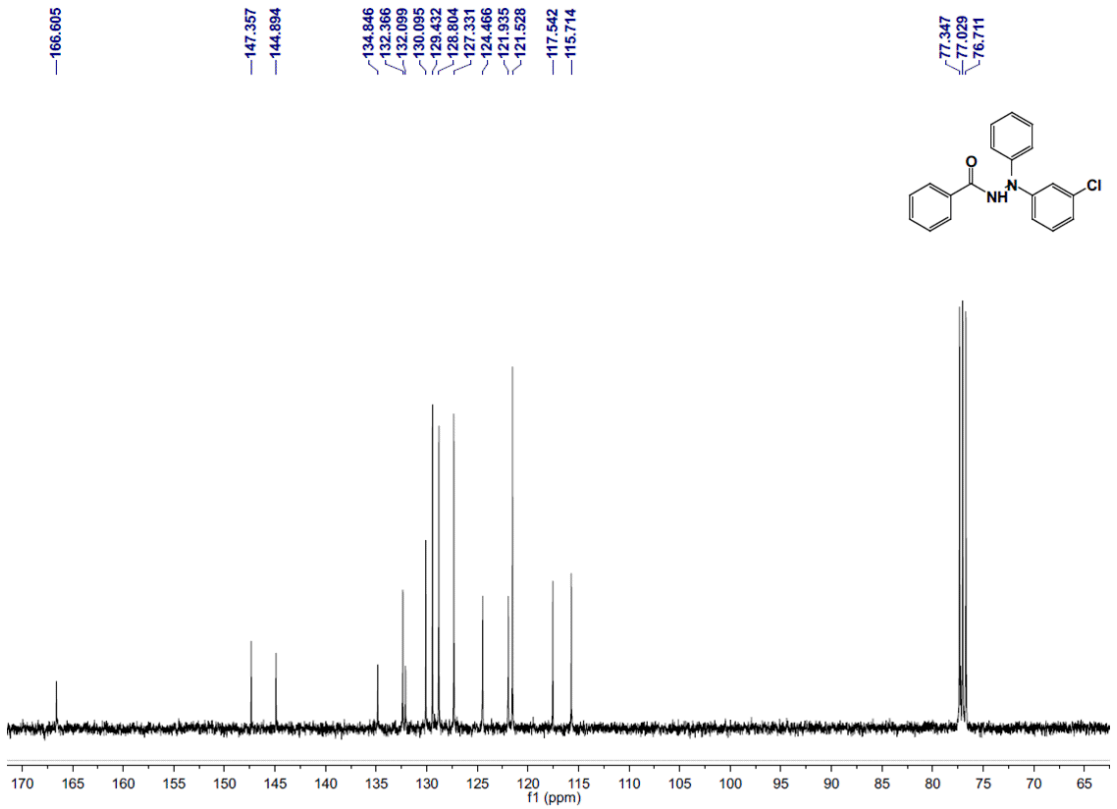
***N'*-phenyl-*N'*-*m*-tolylbenzohydrazide (7d)**



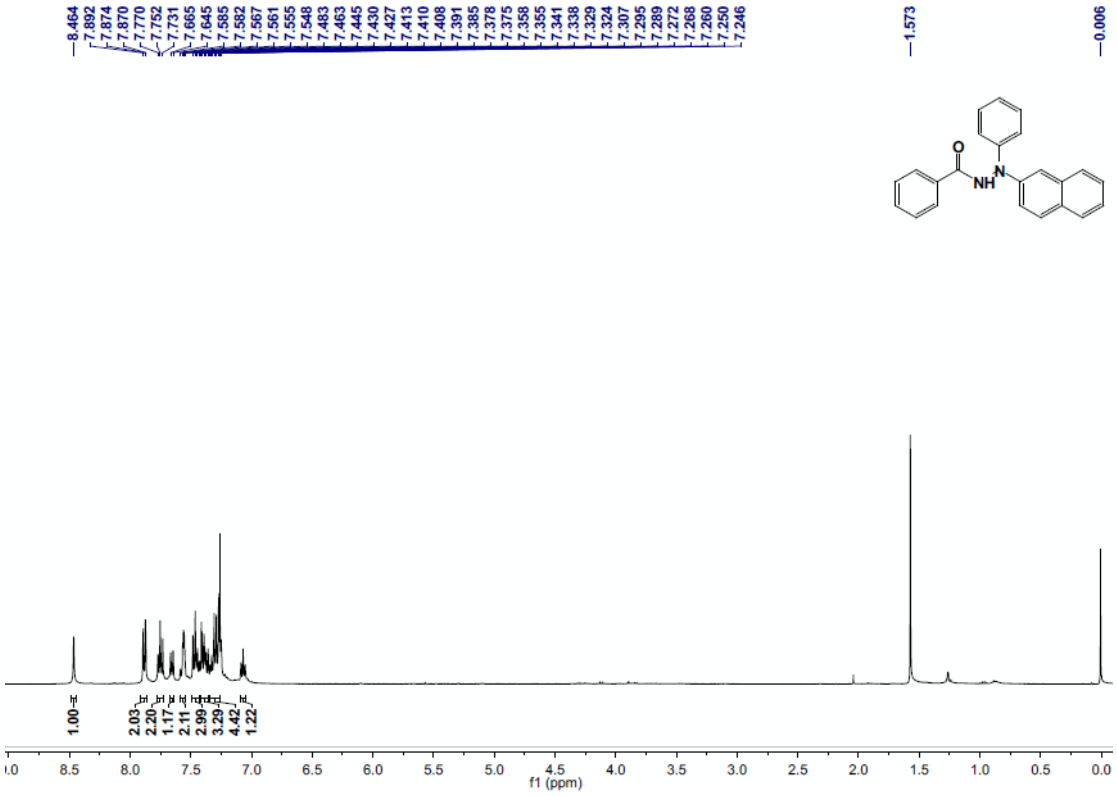


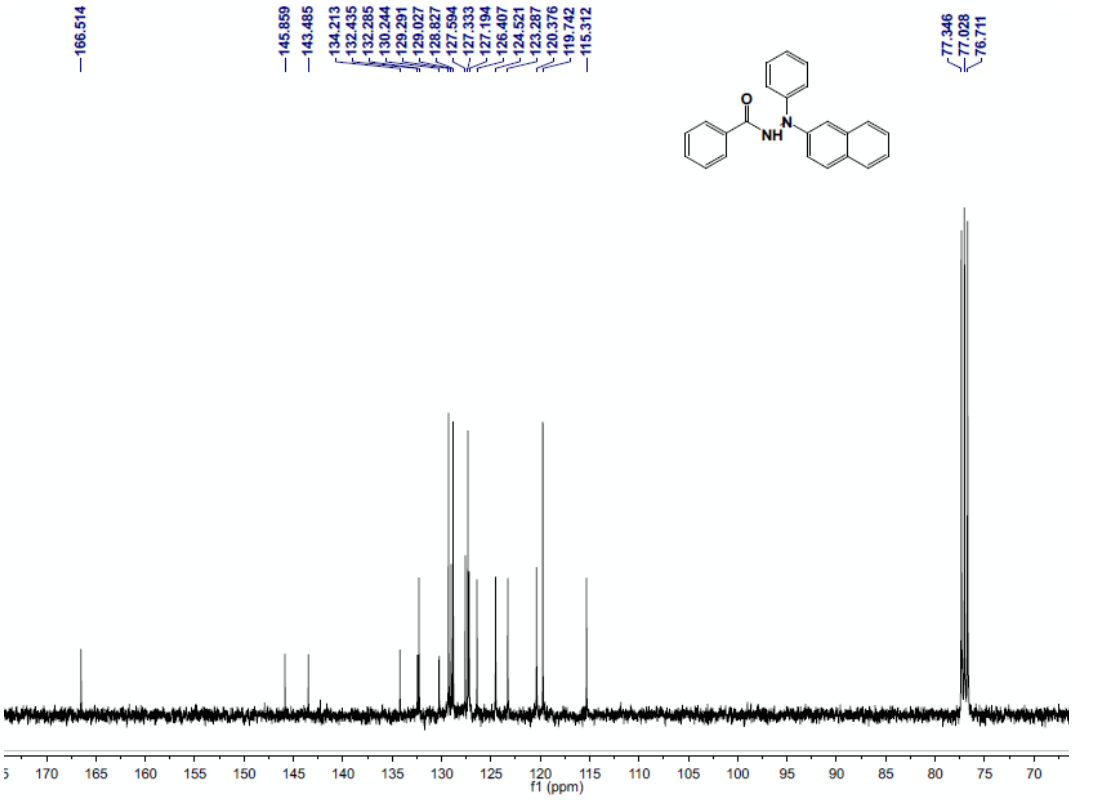
***N′*-(3-chlorophenyl)-*N′*-phenylbenzohydrazide (7e)**



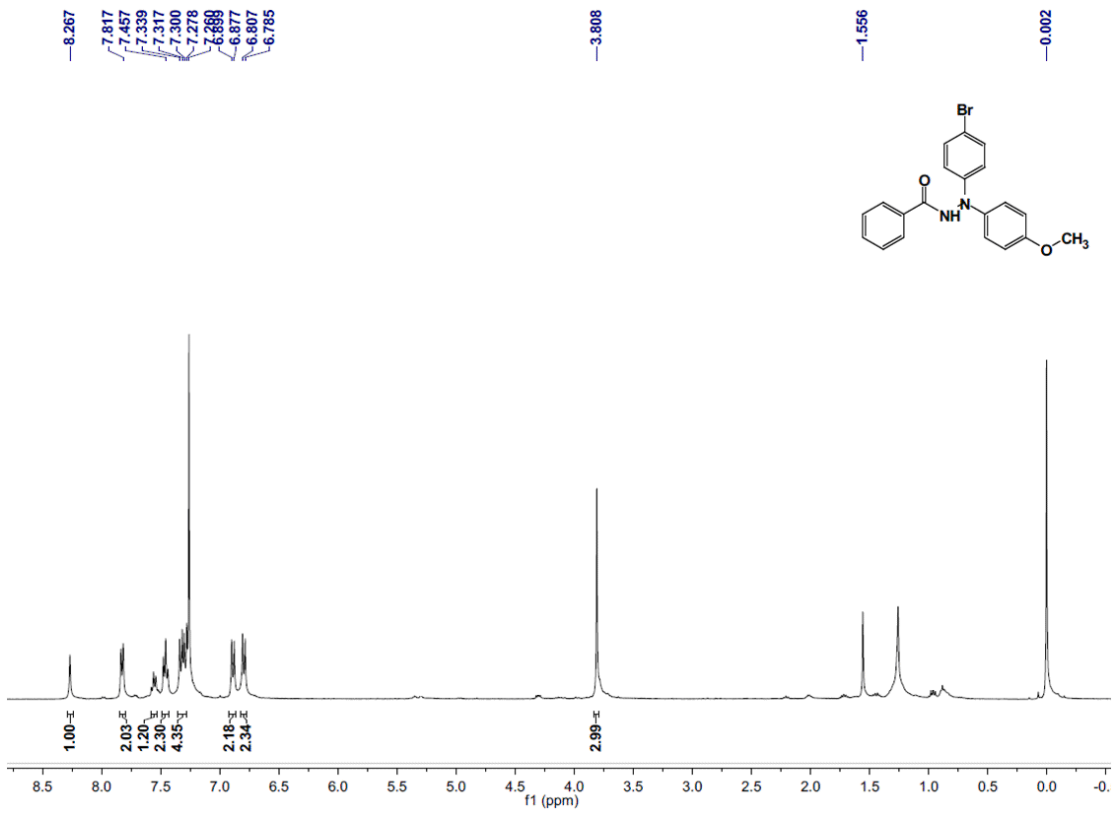


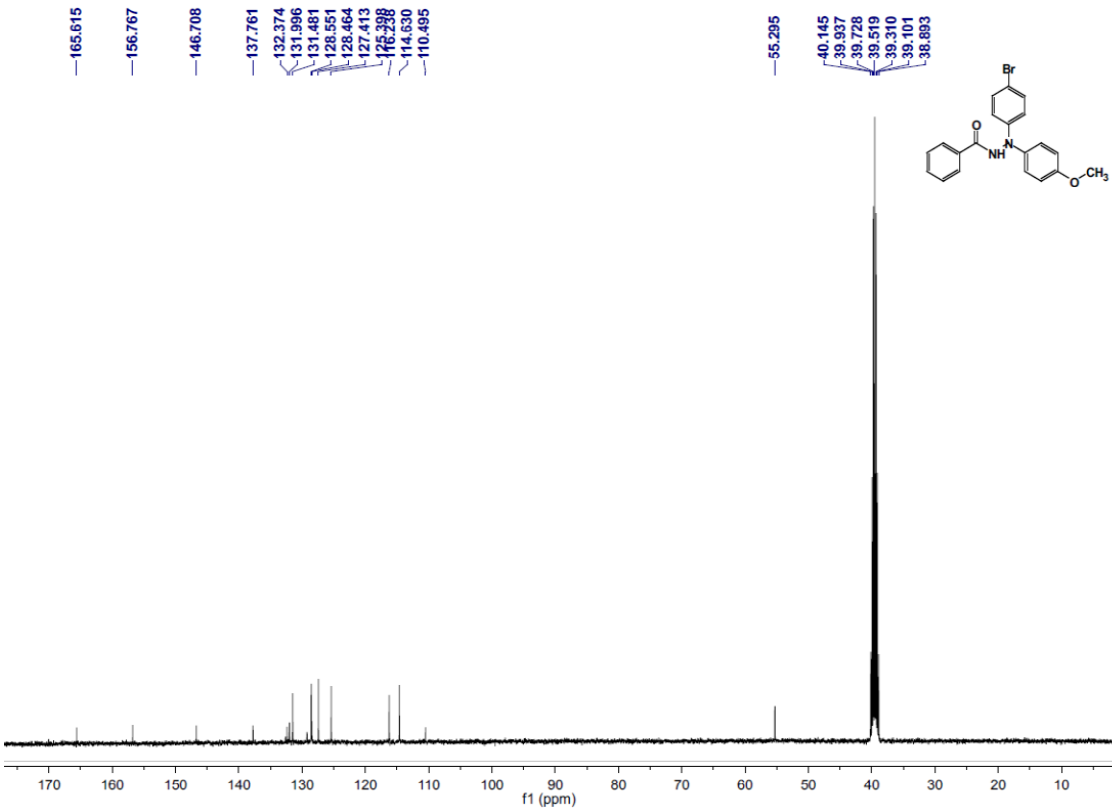
N'-(naphthalen-2-yl)-N'-phenylbenzohydrazide (7f)



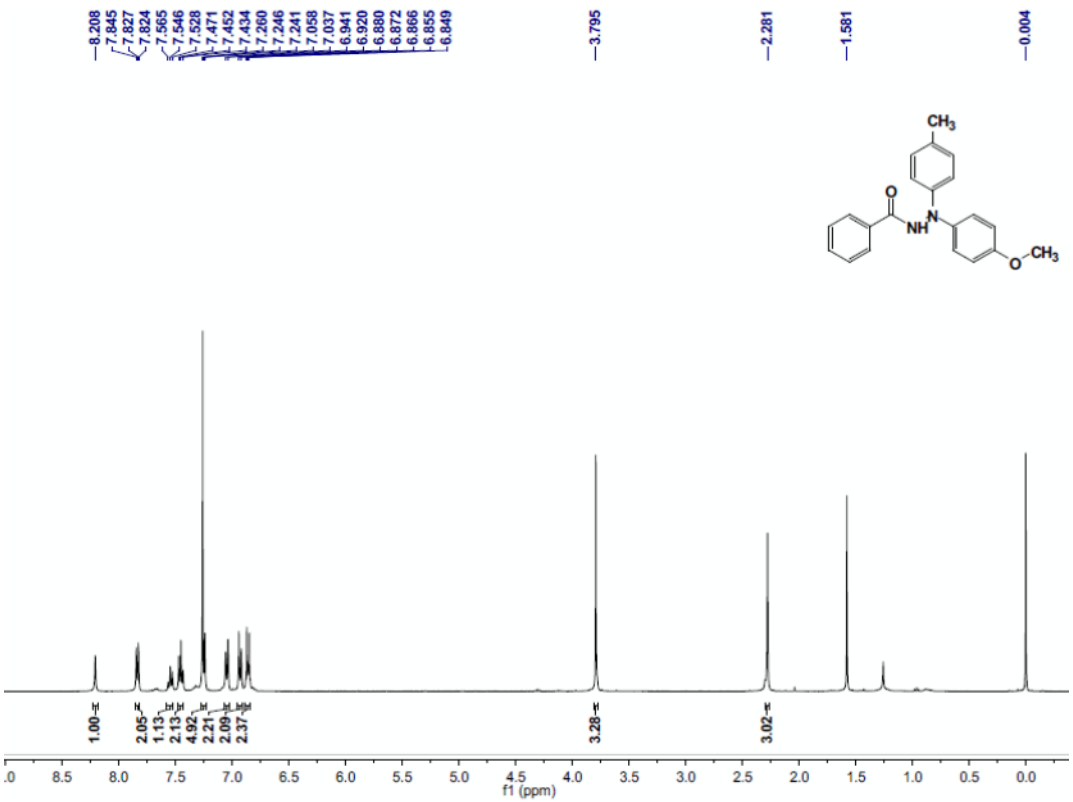


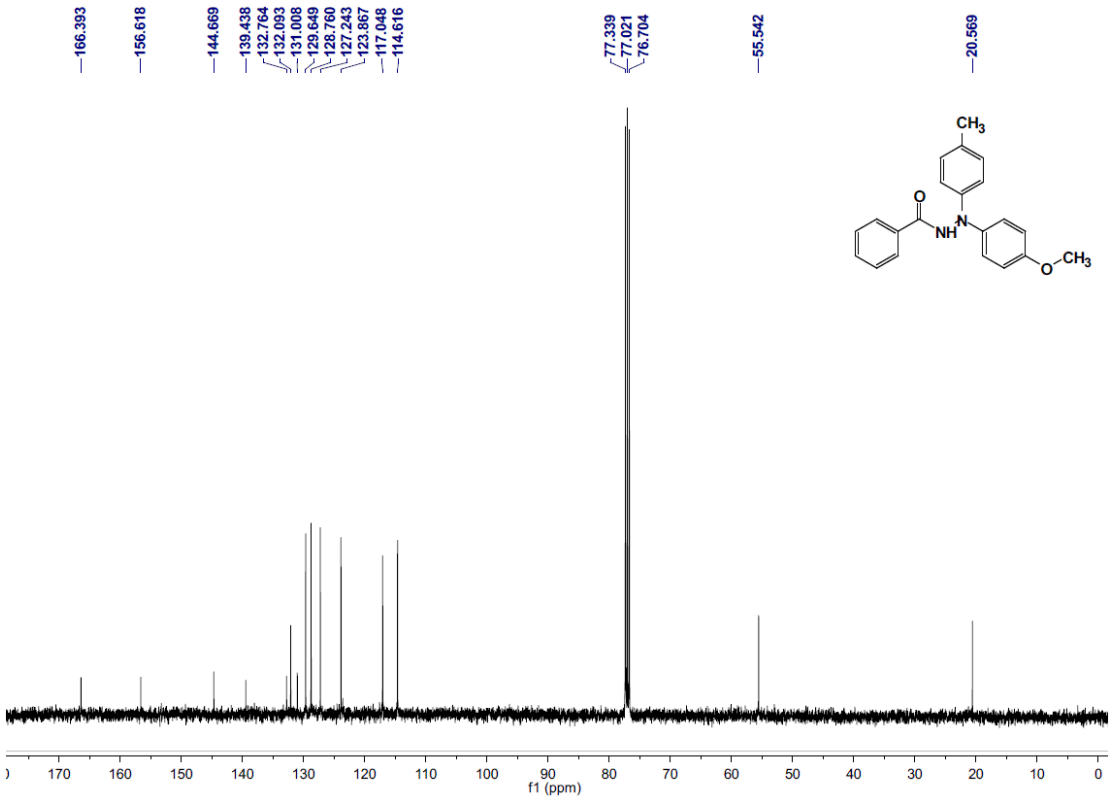
N'-(4-bromophenyl)-N'-(4-methoxyphenyl)benzohydrazide (7g)



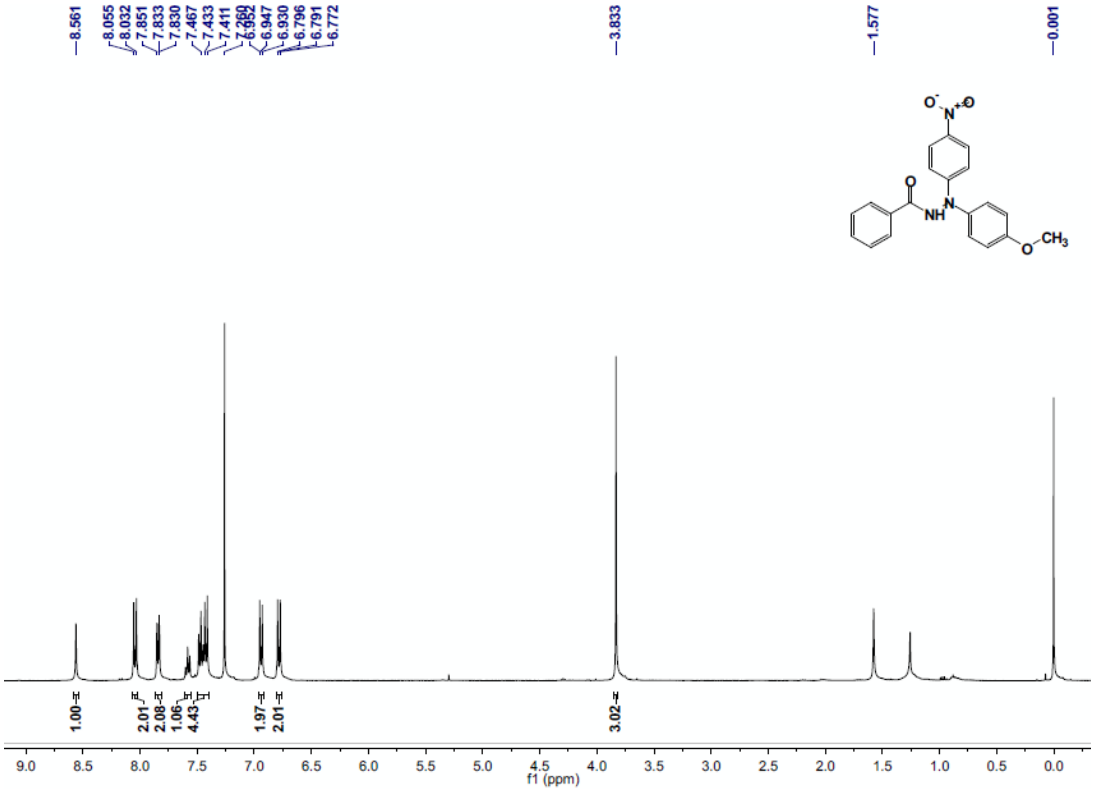


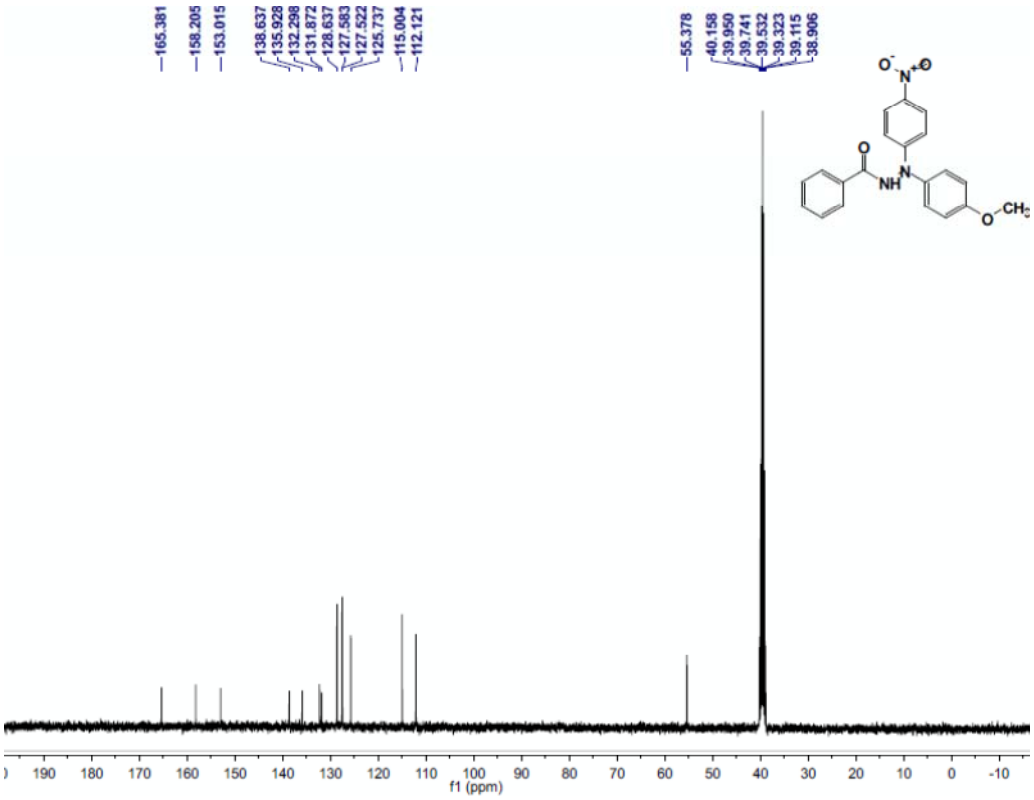
***N′*-(4-methoxyphenyl)-*N′*-*p*-tolylbenzohydrazide (7h)**



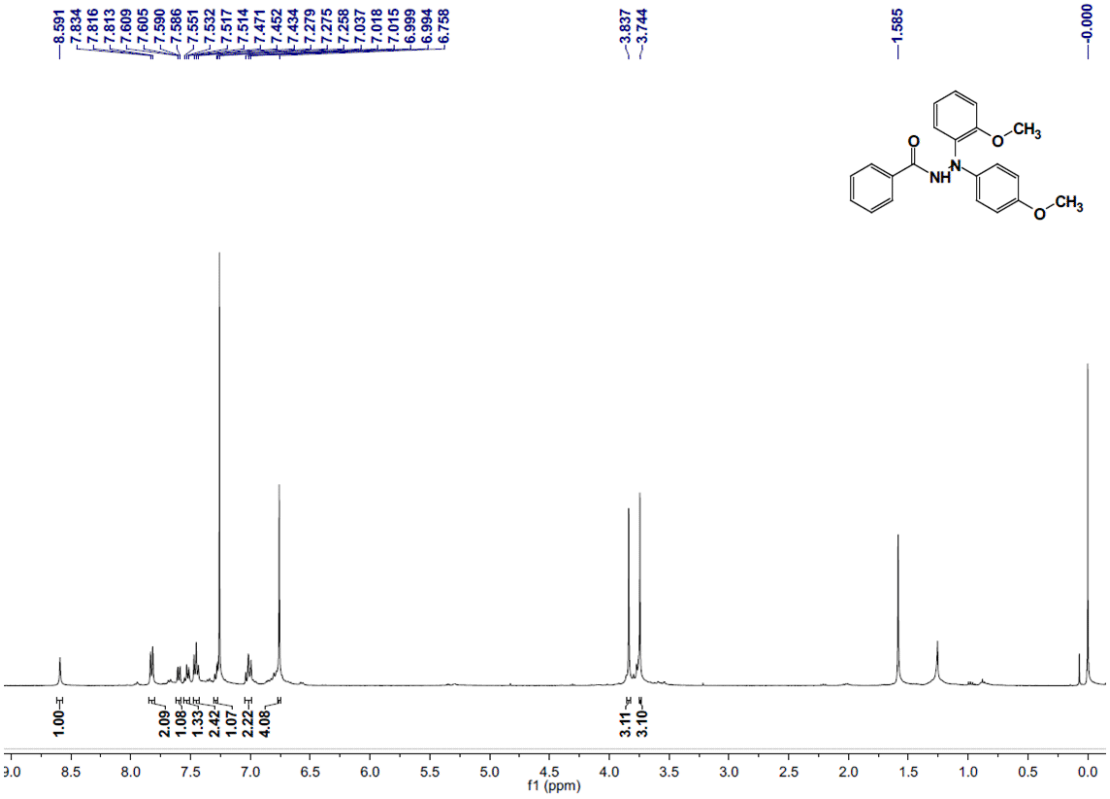


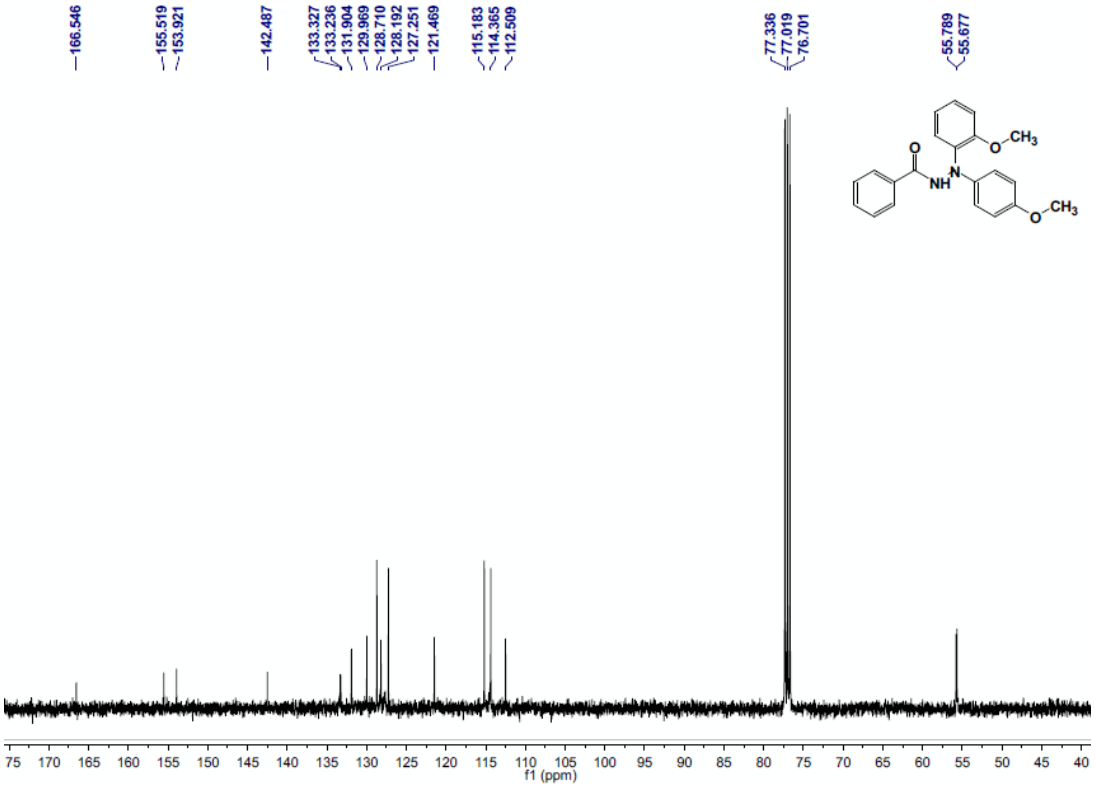
***N′*-(4-methoxyphenyl)-*N′*-(4-nitrophenyl)benzohydrazide (7i)**



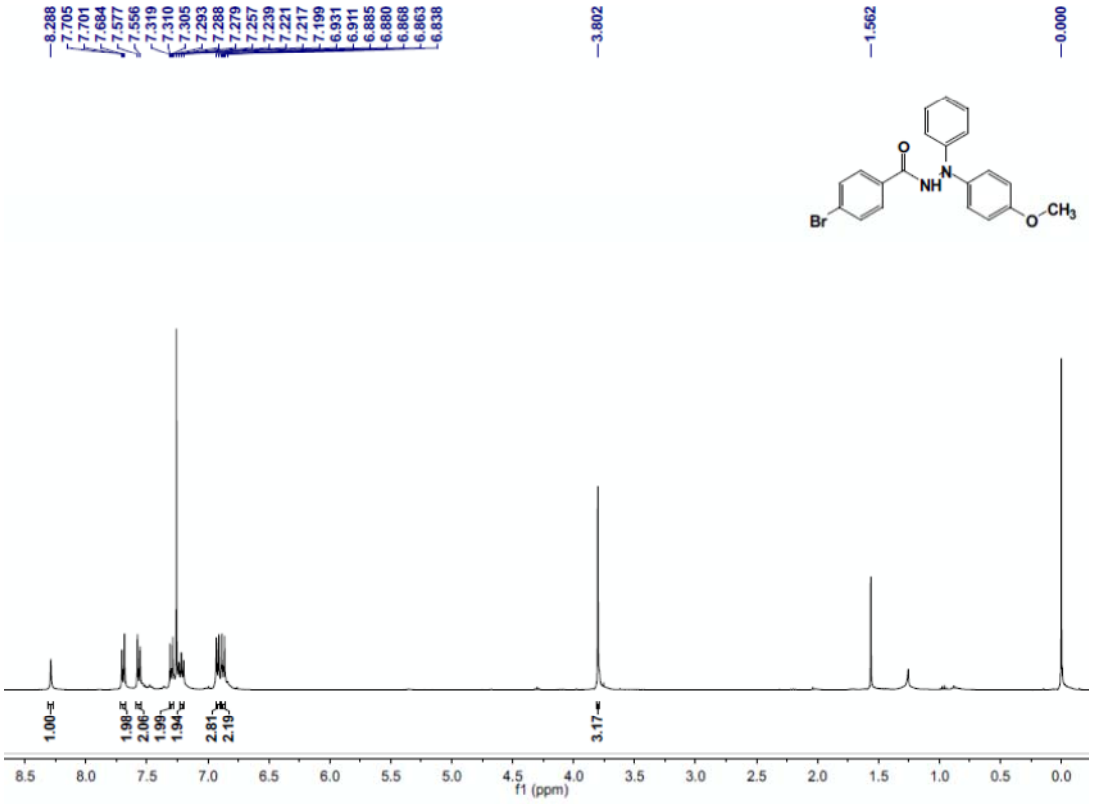


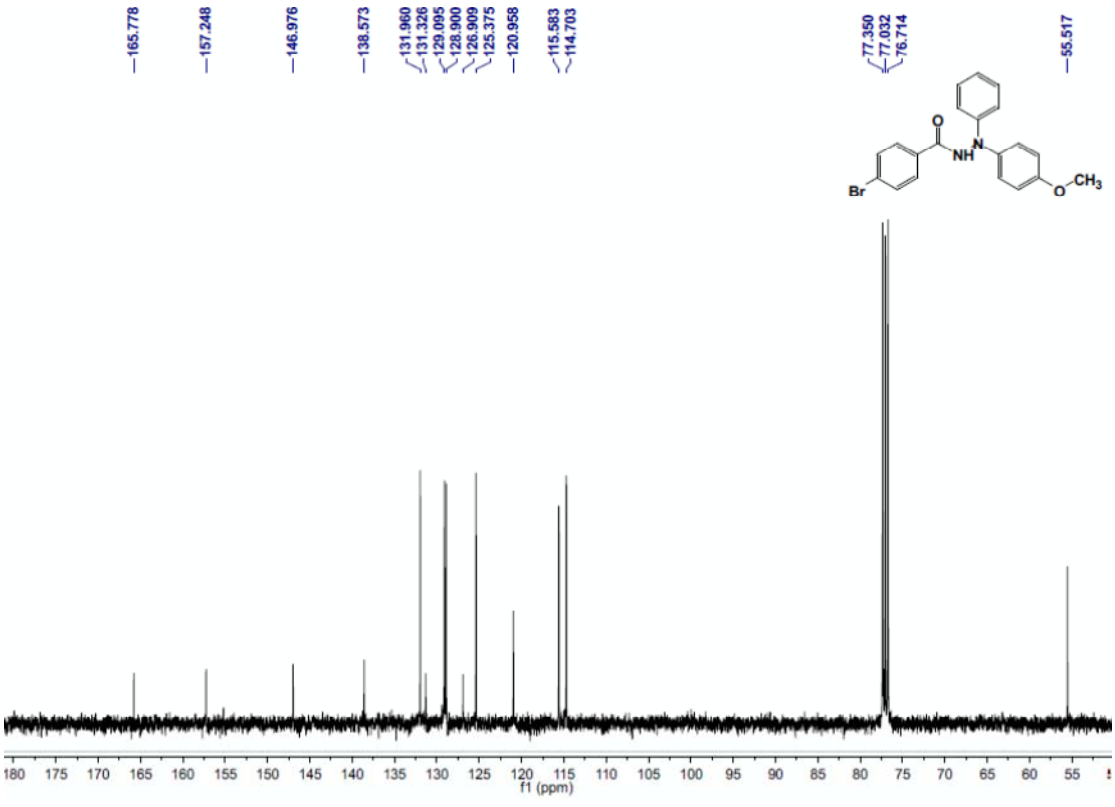
***N′*-(2-methoxyphenyl)-*N′*-(4-methoxyphenyl)benzohydrazide (7j)**





4-bromo-*N'*-(4-methoxyphenyl)-*N'*-phenylbenzohydrazide (7k)





***tert*-butyl 2-(4-methoxyphenyl)-2-phenylhydrazinecarboxylate (7l)**