Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Metal-Free C-C Bond Formation *via* Coupling of Nitrile Imines and Boronic Acids

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Table of Contents

1 General Methods

1.1 Purification of Solvents and Reagents

Anhydrous THF, DCM, and toluene were obtained from a PureSolv SPS-400-5 solvent purification system. Solvents were transferred to and stored in septum-sealed oven-dried flasks over activated 4 Å molecular sieves and purged with and stored under nitrogen. Acetone, dichloromethane, ethyl acetate, methanol, and petroleum ether 40–60 °C were used as obtained from suppliers without further purification. K_3PO_4 was stored in a vacuum oven at 60 °C. Tetrazole starting materials were either synthesised as outlined below or as previously reported.[1]

1.2 Experimental Details

All reactions were performed using round-bottom flasks, microwave vials or NMR tubes of appropriate volume. Reactions were carried out at elevated temperatures using a temperature-regulated hotplate/stirrer. Room temperature generally refers to ~ 20 °C. Reactions requiring a reduced temperature were performed using an ice bath (0 °C) or a dry ice/actone slurry (-78 °C) and a temperature probe unless otherwise stated. Reactions requiring a UV lamp were conducted using either a Philips UV-B Broadband PLS 9W bulb, or a Philips UV-B Broadband TL 20W bulb (both 270 – 360 nm). Phase separation was conducted using IST Isolute Phase Separator Cartridges.

1.3 Purification of Products

Thin layer chromatography was carried out using Merck silica plates coated with fluorescent indicator UV254. These were analysed under 254 nm UV light or developed using potassium permanganate solution. Flash chromatography was carried out using ZEOprep 60 HYD 40-63 μm silica gel.

1.4 Analysis of Products

Fourier Transformed Infra-Red (FTIR) spectra were obtained using an A2 Technologies ATR 32 machine. ^{1}H, ^{19}F and ^{13}C NMR spectra were obtained on a Bruker DRX 500 spectrometer at 500, 376 and 126 MHz, respectively or on a Bruker AV3 400 at 400, 471 and 101 MHz, respectively, or on a Bruker AVANCE 400 spectrometer at 400, 471 and 101 MHz, respectively. Chemical shifts are reported in ppm and coupling constants are reported in Hz with $CDCl_3$ referenced at 7.26 (^{1}H) and 77.16 ppm (^{13}C), DMSO-*d*6 referenced at 2.50 (^{1}H) and 39.52 ppm (^{13}C), and acetone-*d*6 referenced at 2.05 (^{1}H) and 29.84 ppm (^{13}C). High-resolution mass spectra were obtained on a Thermofisher LTQ Orbitrap XL instrument at the EPSRC National Mass Spectrometry Service Centre (NMSSC), Swansea.

1.5 Reverse Phase HPLC Methods

Reverse phase HPLC data was obtained on an Agilent 1200 series HPLC using a Machery-Nagel Nucleodur C18 column. Analysis was performed using a gradient method, eluting with 5 – 80% MeCN/H_2O over 16 minutes at a flow rate of 2 mL/min.

Reactions using an internal standard required prior HPLC calibration using samples containing varying molarities of product and caffeine, allowing calculation of the response factor by substituting values into **equation S1**. Screening reactions were then conducted using a known molarity of caffeine internal standard.

$$Response\ Factor = \frac{\left(\frac{Area}{Molarity}\right)Product}{\left(\frac{Area}{Molarity}\right)Standard} \qquad \textbf{S1}$$

2 General Procedures

2.1 General Procedure A: Synthesis of 2,5-Tetrazole Starting Materials 1

Conditions were adapted from previous literature precedent.[2] A solution of 5-phenyltetrazole (1 equiv.), aryl boronic acid (2 equiv.), and copper(I) oxide (0.05 equiv.) in DMSO (2 $mLmmol^{-1}$) was stirred under an O_2 atmosphere at 110 ^oC until full consumption of the starting material was observed. The reaction mixture was cooled, diluted with DCM, and washed successively with 1M HCl and brine. The solution was passed through a phase separator, concentrated under vacuum and purified by column chromatography.

2.2 General Procedure B: Synthesis of 2,5-Tetrazole Starting Materials 2

Conditions were adapted from previous literature precedent.[3,4] A solution of the appropriate aldehyde (1 equiv.) and benzenesulfonohydrazide (1.1 equiv.) was stirred in ethanol (1 $mLmmol^{-1}$) at room temperature for 1 hour. The reaction was quenched through the addition of water (20 $mLmmol^{-1}$) and the resulting white solid was collected by filtration. Simultaneously, the relevant aniline (1 equiv.) was dissolved in a 2:2:1 solution of ethanol, H_2O, and HCl (2 $mLmmol^{-1}$). To this solution was added $NaNO_2$ (1.1 equiv), dissolved in minimal H_2O, at 0 ^oC. The corresponding mixture was stirred for 1 hour, before the benzensufonohydrazone obtained the first step was dissolved in pyridine (3 $mLmmol^{-1}$) and slowly added to the reaction mixture at 0 ^oC. The resulting milieu was allowed to warm to room temperature and stirred for an additional 5 hours. The solution was diluted with DCM and washed

successively with 1M HCl and brine. The solution was passed through a phase separator, concentrated under vacuum and purified by column chromatography.

2.3 General Procedure C: UV Light-Mediated Coupling of Nitrile Imines and Boronic Acids

To an oven-dried quartz round-bottom flask (50 mL) equipped with a stirrer bar was added 3 Å molecular sieves (400 mgmmol^{-1}), tetrazole (1 equiv.), and boronic acid (3 equiv.). The mixture was dissolved in THF (10 mLmmol^{-1}), purged with N_2 and irradiated under a UV lamp with stirring for 16 hours. The reaction mixture was diluted with ethyl acetate, filtered through Celite and rinsed with additional ethyl acetate. The crude solution was concentrated under vacuum and purified by column chromatography.

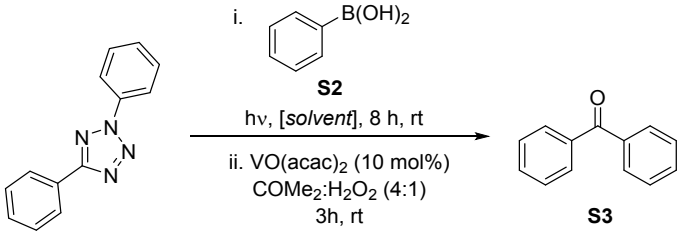
3 Optimisation of Reaction Conditions

3.1 General Optimisation Conditions for HPLC Assay

Tetrazole and boron species (0.05 mmol scale) were dissolved in the appropriate solvent (0.5 mL) and irradiated with UV light for a specified period of time. In some optimisation campaigns, the solution was diluted with acetone (0.5 mL) and 30 % hydrogen peroxide solution (0.1 mL). $VO(acac)_2$ (1.33 mg, 0.005 mmol) was added and the solution left to stir at room temperature for 4 hours.[5] The reaction mixture was then diluted with 50 mM solution of caffeine in MeCN (1 mL), before 0.2 mL of this solution was further diluted using MeCN (0.7 mL) and H_2O (0.1 mL). The solution was then analysed using HPLC.

3.2 Optimisation 1

Table 1: Initial results of the solvent screen

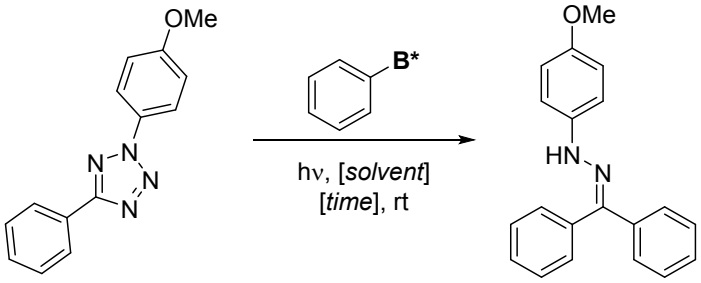


Entry	Solvent	Conversion (%)[a]
1	Acetone	**10**
2	Acetonitrile	**7**
3	Ethyl Acetate	**10**

[a]Conversion determined by HPLC with reference to an internal standard

3.3 Optimisation 2

*Table 2: Additional screen using hydrazone **S4** as the product*



S5 **S4**

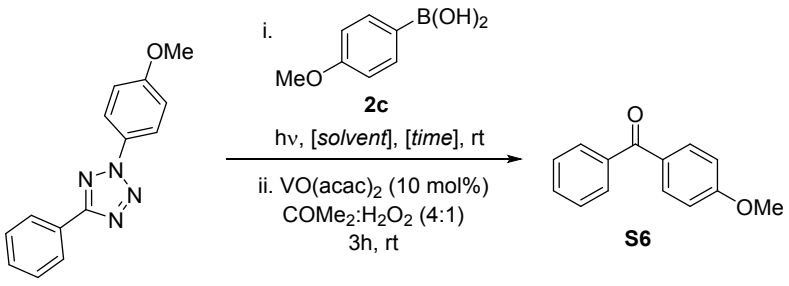
Entry	Solvent	B*	Boron Stoichiometry (equivalents)	Concentration (M)	Time (h)	Additive	Conversion (%)[a]
1	Acetone	$B(OH)_2$	2	0.08	3	-	**10**
2	Acetonitrile	$B(OH)_2$	2	0.08	3	-	**7**
3	Ethyl Acetate	$B(OH)_2$	2	0.08	3	-	**10**
4	^{i}PrOH:THF (1:1)	$B(OH)_2$	2	0.08	3	-	**2**
5	THF	$B(OH)_2$	2	0.08	3	-	**9**
6	THF	BPin	2	0.08	3	-	**<1**
7	THF	BF_3K	2	0.08	3	-	**<1**
8	THF	BF_3K	2	0.08	3	18-crown-6	**<1**
9	THF	$B(OH)_2$	2	0.08	3	NaOH	**<1**
10	THF	$B(OH)_2$	1	0.08	3	-	**4**
11	THF	$B(OH)_2$	4	0.08	3	-	**9**
12	THF	$B(OH)_2$	2	0.08	1	-	**4**
13	THF	$B(OH)_2$	2	0.08	2	-	**5**
14	THF	$B(OH)_2$	2	0.08	7	-	**9**
15	THF	$B(OH)_2$	2	0.04	3	-	**6**

16	THF	$B(OH)_2$	2	0.16	3	-	**9**

[a]Conversion determined by HPLC with reference to an internal standard.

3.4 Optimisation 3

*Table 3: Optimisation of reaction conditions when using boronic acid **2c** as a substrate*



Entry	Solvent	Boron Stoichiometry (equivalents)	Time (h)	Concentration (M)	Conversion (%)[a]
1	THF	2	3	0.1	**57**
2	MeCN	2	3	0.1	**53**
3	THF	1	3	0.1	**45**
4	THF	3	3	0.1	**69**
5	THF	5	3	0.1	**78 (75[b])**
6	THF	2	1	0.1	**41**
7	THF	2	2	0.1	**48**
8	THF	2	3	0.1	**57**
9	THF	2	3	0.05	**61**
10	THF	2	3	0.2	**57**

[a]Conversion determined by HPLC with reference to an internal standard

[b]Isolated yield

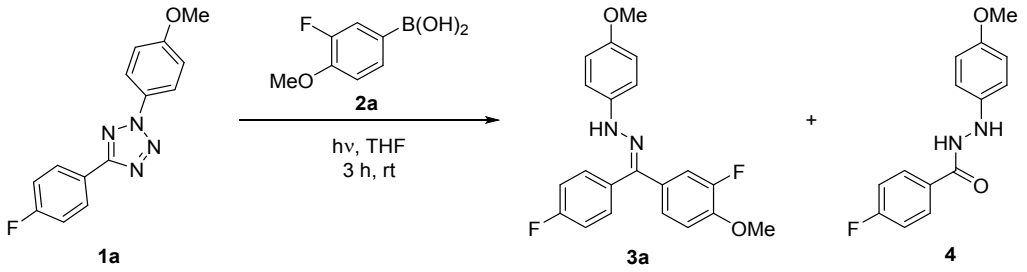
3.5 General Optimisation Conditions for ^{19}F NMR Assay

The 2,5-diaryl tetrazole **1a** (0.05 mmol) and 3-fluoro-4-methoxyphenylboronic acid (0.05-0.25 mmol) were dissolved in the appropriate solvent (0.5 mL) and irradiated with UV light for a specified period of time. A solution of reaction standard 5-phenyl-2-(3-fluoro-4-methoxyphenyl)-tetrazole (**S7**), (10.8 mg, 0.05 mmol) in $CDCl_3$ (0.5 mL) was added to the reaction mixture, and the resulting solution was analysed by ^{19}F NMR spectroscopy. Product peaks at -112.09, -115.17, -133.23 and -135.65 ppm

were integrated against the peak of tetrazole **S7** at -131.75 ppm. Conversion of primary hydrazide by-product **4** was also monitored at -106.65 ppm.

3.6 Optimisation 4

*Table 4: Elimination of the hydrazide by-product **4** from the reaction manifold*



Entry	Boron Stoichiometry (equivalents)	Atmosphere	Additive	Conversion (%)[a]	
				3a	**4**
1	1	-	-	**33**	**23**
2	2	-	-	**43**	**20**
3	3	-	-	**53**	**19**
4	4	-	-	**56**	**18**
5	5	-	-	**55**	**11**
6	3	N_2	-	**45**	**18**
7	3	N_2	3 Å molecular sieves (400 $gmol^{-1}$)	**46**	**8**
8	3	N_2	3 Å molecular sieves (4000 $gmol^{-1}$)	**60**	**1**
9	3	N_2	Trimethyl orthoformate (10 eq.)	**38**	**21**
10	3	N_2	Trimethyl orthoformate (neat)	**11**	**31**
11	3	N_2	3 Å molecular sieves (400 $gmol^{-1}$)[b]	**61**	**2**
12	3	N_2	3 Å molecular sieves (4000 $gmol^{-1}$)[b]	**55**	**<1**

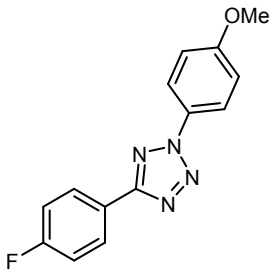
[a]Conversion determined by ^{19}F NMR with reference to an internal standard

[b]Crushed

4 Characterisation of Compounds

4.1 2,5-Tetrazole Starting Materials

Compound 1a, 5-(4-fluorophenyl)-2-(4-methoxyphenyl)-2*H*-tetrazole



Synthesised according to General Procedure B using 4-fluorobenzaldehyde (3.72 g, 30.0 mmol), benzenesulfonohydrazide (5.68 g, 33.0 mmol), anisidine (3.70 g, 30.0 mmol), and sodium nitrite (2.28 g, 33.0 mmol) to afford the product as a light yellow solid (3.97 g, 49 %).

ν_{max} (neat): 3084, 2972, 2941, 2843, 1591, 1539, 1508, 1462, 1435, 1381, 1300, 1259, 1224, 1159, 1020 cm^{-1}

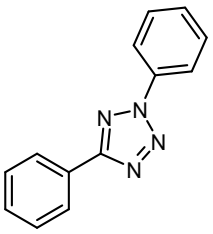
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (dd, $J_{H,H}$ = 8.4 Hz, $J_{H,F}$ = 5.8 Hz, 2H, 2 x ArH), 8.06 (d, J = 8.8 Hz, 2H, 2 x ArH), 7.23 – 7.19 (m, 2H, 2 x ArH), 7.03 (d, J = 8.8 Hz, 2H, 2 x ArH), 3.87 (s, 3H, OCH_3)

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 164.2 (d, $^{1}J_{C,F}$ = 250.5 Hz), 160.7, 130.5, 129.1 (d, $^{3}J_{C,F}$ = 8.5 Hz), 123.7 (d, $^{4}J_{C,F}$ = 3.1 Hz), 121.5, 116.2 (d, $^{2}J_{C,F}$ = 22.0 Hz), 114.8, 55.8

^{19}F NMR (471 MHz, $CDCl_3$) δ -109.80 - -109.88 (m)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{12}FN_4O$ 271.0995, found 271.0999

Compound 1b, 2,5-diphenyl-2*H*-tetrazole



Synthesised according to General Procedure A using 5-phenyl-2*H*-tetrazole (1.00 g, 6.84 mmol), phenyl boronic acid (1.67 g, 13.7 mmol), and Cu_2O (40.0 mg, 0.34 mmol) to afford the product as a white powder (1.37 g, 90 %).

ν_{max} (neat): 3066, 1595, 1530, 1497, 1470, 1447, 1368, 1215, 1179, 1072, 1016 , 991 cm^{-1}

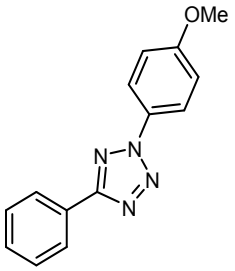
^1H NMR (400 MHz, $CDCl_3$) δ 8.30 – 8.24 (m, 2H, 2 x ArH), 8.24 – 8.18 (m, 2H, 2 x ArH), 7.62 – 7.47 (m, 6H, 6 x ArH)

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 137.1, 130.7, 129.8, 129.8, 129.1, 127.3, 127.2, 120.0

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{13}H_{11}N_4$ 223.0978, found 223.0979

Consistent with previously reported data.[1]

Compound S5, 2-(4-methoxyphenyl)-5-phenyl-2*H*-tetrazole



Synthesised according to General Procedure A using 5-phenyl-2*H*-tetrazole (1.00 g, 6.8 mmol), 4-methoxyphenyl boronic acid (2.08 g, 13.7 mmol), and Cu_2O (49.0 mg, 0.34 mmol) to afford the product as a white powder (1.51 g, 88 %).

ν_{max} (neat): 3017, 2844, 1610, 1597, 1515, 1452 cm^{-1}

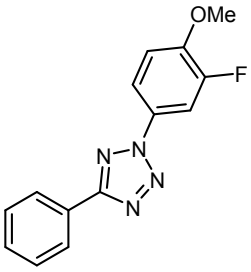
^1H NMR (500 MHz, MeOD-*d*4) δ 8.19 (d, *J* = 6.4 Hz, 2H, 2 x ArH), 8.09 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 7.58 – 7.49 (m, 3H, 2 x ArH), 7.15 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 3.89 (s, 3H, OCH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 160.7, 130.6, 129.1, 127.5, 127.1, 121.6, 119.7, 114.8, 55.8

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{13}N_4O$ 253.1084, found 253.1083

Consistent with previously reported data.[6]

Compound S7, 2-(3-fluoro-4-methoxyphenyl)-5-phenyl-2*H*-tetrazole



Synthesised according to General Procedure A using 5-phenyl-2*H*-tetrazole (1.81 g, 12.4 mmol), boronic acid (4.00 g, 23.5 mmol), Cu_2O (89.0 mg, 0.62 mmol), and DMSO (10 mL) to afford the product as a white powder (2.35 g, 70 %).

ν_{max} (neat): 3092, 3015, 2972, 2940, 2843, 1603, 1514, 1454, 1281, 1018, 725, 687 cm^{-1}

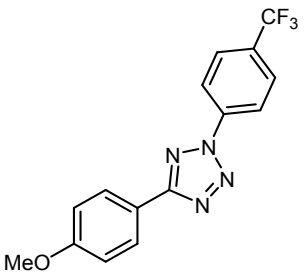
^1H NMR (400 MHz, $CDCl_3$) δ 8.26 – 8.20 (m, 2H, 2 x Ar), 7.99 – 7.92 (m, 2H, ArH), 7.55 – 7.47 (m, 3H, 3 x ArH), 7.15 – 7.08 (m, 1H, ArH), 3.97 (s, 3H, OCH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 152.4 (d, $^1J_{C,F}$ = 248.8 Hz), 149.0 (d, $^2J_{C,F}$ = 10.5 Hz), 130.7, 130.1 (d, $^3J_{C,F}$ = 9.1 Hz), 129.1, 127.2, 115.9 (d, $^3J_{C,F}$ = 4.1 Hz), 113.7 (d, $^4J_{C,F}$ = 1.9 Hz), 109.00 (d, $^2J_{C,F}$ = 23.9 Hz), 56.7, one C not observed (coincident)

^{19}F NMR (471 MHz, $CDCl_3$) δ -131.27 – -131.34 (m)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{12}FN_4O$ 271.0990, found 271.0990

Compound S8, 5-(4-methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)-2*H*-tetrazole



Synthesised according to General Procedure A using 5-(4-methoxyphenyl)-2*H*-tetrazole (64.0 mg, 0.37 mmol), boronic acid (141 mg, 0.74 mmol), Cu_2O (3.00 mg, 0.02 mmol), and DMSO (1 mL) to afford the product as a white powder (107 mg, 90 %).

ν_{max} (neat): 3094, 3017, 2968, 2943, 2843, 1614, 1584, 1547, 1518, 1470, 1431, 1113, 1103 cm^{-1}

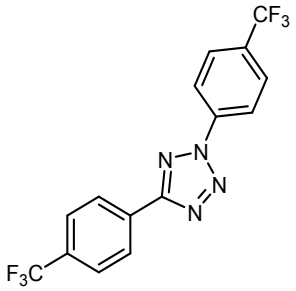
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.4 Hz, 2H, 2 x ArH), 8.22 – 8.17 (m, 2H, 2 x ArH), 7.85 (d, *J* = 8.4 Hz, 2H, 2 x ArH), 7.08 – 7.03 (m, 2H, 2 x ArH), 3.90 (s, 3H, OCH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 161.9, 139.3, 131.5 (q, $^{2}J_{C,F}$ = 33.3 Hz), 128.9, 127.2, (q, $^{3}J_{C,F}$ = 3.3 Hz), 123.7 (app. d, $^{1}J_{C,F}$ = 272.3 Hz), 120.1, 119.4, 114.6, 55.6

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.67 (s)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_{12}F_3N_4O$ 321.0958, found 321.0954

Compound S9, 2,5-*bis*(4-(trifluoromethyl)phenyl)-2*H*-tetrazole



Synthesised according to General Procedure B using 4-(trifluoromethyl)benzaldehyde (273 uL, 2.0 mmol), benzenesulfonohydrazide (379 mg, 2.2 mmol), 4-(trifluoromethyl)aniline (250 mg, 2.0 mmol), and sodium nitrite (141 mg, 2.2 mmol) to afford the product (84.5 mg, 12 %) as a white solid.

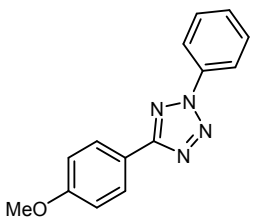
ν_{max} (neat): 3127, 3090, 3071, 1616, 1545, 1517, 1474, 1433, 1383, 1314, 1132, 841 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.3 Hz, 2H, 2 x ArH), 8.38 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 7.88 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 7.82 (d, *J* = 8.3 Hz, 2H, 2 x ArH)

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 139.1, 132.8 (q, $^{2}J_{C,F}$ = 33.0 Hz), 132.1 (q, $^{2}J_{C,F}$ = 33.4 Hz), 130.3, 127.6, 127.3 (q, $^{3}J_{C,F}$ = 3.6 Hz), 126.2 (q, $^{3}J_{C,F}$ = 3.6 Hz), 124.0 (d, $^{1}J_{C,F}$ = 272.6 Hz), 123.6 (d, $^{1}J_{C,F}$ = 272.3 Hz), 120.3

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{15}H_9F_6N_4$ 359.0732, found 359.0732

Compound S10, 5-(4-methoxyphenyl)-2-phenyl-2*H*-tetrazole



Synthesised according to General Procedure B using 4-methoxybenzaldehyde (1.36 g, 10.0 mmol), benzenesulfonohydrazide (1.89 g, 11.0 mmol), aniline (0.93 mL, 10.0 mmol), and sodium nitrite (759 mg, 11.0 mmol) to afford the product as a grey solid (1.17 g, 46 %).

ν_{max} (neat): 3071, 3053, 3006, 2975, 2945, 2842, 1617, 1599, 1586, 1547, 1500, 1463 cm^{-1}

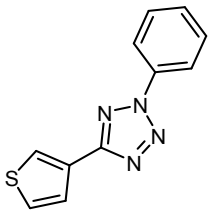
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.9 Hz, 2H, 2 x ArH), 8.19 (d, *J* = 8.4 Hz, 2H, 2 x ArH), 7.58 - 7.55 (m, 2H, 2 x ArH), 7.50 - 7.47 (m, 1H, ArH), 7.04 (d, *J* = 8.9 Hz, 2H, 2 x ArH), 3.89 (s, 3H, OCH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 161.6, 137.1, 129.8, 129.6, 128.7, 120.0, 119.9, 114.5, 55.5

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{13}N_4O$ 253.1089, found 253.1092

Consistent with previously reported data.[7]

Compound S11, 2-phenyl-5-(thiophen-3-yl)-2*H*-tetrazole



Synthesised according to General Procedure B using thiophene-3-carboxaldehyde (180 µL, 2.0 mmol), benzenesulfonohydrazide (379 mg, 2.2 mmol), aniline (183 µL, 2.0 mmol), and sodium nitrite (141 mg, 2.2 mmol) to afford the product as a yellow solid (69.7 mg, 15 %).

ν_{max} (neat): 3200, 3092, 3065, 1701, 1597, 1522, 1508, 1477, 1447, 1310, 1161, 912, 723, 687 cm^{-1}

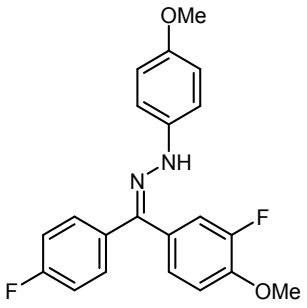
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 – 8.15 (m, 3H, 3 x ArH), 7.80 (dd, *J* = 5.1, 1.2 Hz, 1H, ArH), 7.60 – 7.54 (m, 2H, 2 x ArH), 7.52 – 7.46 (m, 2H, 2 x ArH)

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.0, 137.0, 129.8, 129.8, 128.7, 127.0, 126.5, 126.0, 120.0

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{11}H_9N_4S$ 229.0542, found 229.0541

4.2 Ketone Hydrazones

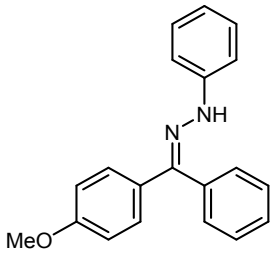
Compound 3a, 1-((3-fluoro-4-methoxyphenyl)(4-fluorophenyl)methylene)-2-(4-methoxyphenyl)hydrazine



4-methoxyphenylhydrazine (29.1 mg, 0.17 mmol) was added to a stirred solution of ketone **S13** (35.0 mg, 0.15 mmol) in ethanol (2 mL). A few drops of H_2SO_4 were added and the reaction was refluxed for 4 hours. H_2O (5 mL) was added to the reaction mixture and the product (39.1 mg, 70 %) was collected by filtration. The product was found to rapidly hydrolyse to ketone **S7** under typical atmospheric conditions, and as such full characterisation was not conducted.

^{19}F NMR (471 MHz, $CDCl_3$) δ -110.96 - -111.05 (m), -114.10 - -114.18 (m), -132.43 - -132.51 (m), -135.20 (dd, $J_{F,H}$ = 13.0, 8.7 Hz) (mixture of stereoisomers)

Compound 3b, 1-((4-methoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (59.5 mg, 79 %) as a yellow oil.

To an oven-dried 5 mL microwave vial was added hydrazonyl chloride **8** (57.7 mg, 0.25 mmol), and 4-methoxyphenylboronic acid (41.8 mg, 0.28 mmol). The mixture was dissolved in DCM (2.5 mL), and K_3PO_4 (159 mg, 0.75 mmol) was added to initiate the reaction. The solution was heated at 40 ^oC for 3 h. The reaction mixture was diluted with ethyl acetate, filtered through Celite and rinsed with

additional ethyl acetate. The crude solution was concentrated under vacuum and purified by column chromatography to yield the product (60.2 mg, 80 %) as a yellow oil (88:12 isomer ratio)

To an oven-dried 100 mL round-bottom flask was added hydrazonyl chloride **8** (1153.5 mg, 5 mmol, 1 equiv.), and 4-methoxyphenylboronic acid (836 mg, 5.5 mmol, 1.1 equiv.). The mixture was dissolved in DCM (50 mL), and K_3PO^4 (3184 mg, 15 mmol, 3 equiv.) was added. The solution was heated at 40 ^oC for 9 h. The reaction mixture was diluted with ethyl acetate, filtered through Celite and rinsed with additional ethyl acetate. The crude solution was concentrated under vacuum and purified by column chromatography to furnish hydrazone **3b** (1087 mg, 72 %) as a yellow oil

ν_{max} (neat): 3306, 3055, 3024, 2963, 2932, 1649, 1599, 1578, 1503, 1491, 1458, 1443 cm^{-1}

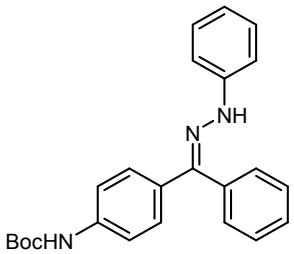
^1H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.50 (m, 4H, 4 x ArH), 7.46 – 7.40 (br. s, 0.5 H, NH), 7.40 – 7.24 (m, 5.5 H, 5 x ArH, 0.5 x NH), 7.16 – 7.07 (m, 3H, 3 x ArH), 6.92 – 6.83 (m, 2H, 2 x ArH), 3.92 (s, 1.5 H, OCH_3), 3.84 (s, 1.5 H, OCH_3) (54: 46 mixture of stereoisomers using general procedure C)

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 159.9, 145.0, 144.8, 144.4, 144.2, 138.9, 133.1, 131.4, 130.7, 129.7, 129.3, 129.2, 128.3, 128.1, 128.0, 126.7, 124.7, 120.1, 119.9, 115.2, 113.8, 113.0, 112.9, 55.5, 55.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{19}N_2O$ 303.1493, found 303.1492

Consistent with previously reported data.[8]

Compound 3c, *tert*-butyl (4-(phenyl(2-phenylhydrazono)methyl)phenyl)carbamate



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), (4-((*tert*-butoxycarbonyl)amino)phenyl)boronic acid (178 mg, 0.75 mmol), and THF (2.5 mL) to afford the product as a yellow oil (88.8 mg, 92 %).

ν_{max} (neat): 3327, 3055, 2976, 2930, 1725, 1701, 1641, 1599, 1518, 1501, 1445, 1406 cm^{-1}

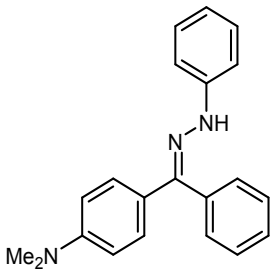
^1H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.49 (m, 5H, 5 x ArH), 7.47 – 7.43 (m, 0.6H, NH), 7.36 – 7.23 (m, 6.4H, 6 x ArH, 0.4 x NH), 7.13 – 7.06 (m, 2H, 2 x ArH), 6.86 (m, 1H, 1 x ArH), 6.76 (br. s, 0.6H,

NH), 6.60 (br. s, 0.4H, NH), 1.60 – 1.57 (m, 5.1H, $C(CH_3)_3$), 1.56 – 1.53 (m, 3.9H, $C(CH_3)_3$) (57: 43 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 152.7, 144.9, 144.8, 144.2, 144.0, 139.4, 138.7, 138.4, 133.4, 132.9, 130.2, 129.8, 129.34, 129.25, 128.3, 128.1, 127.4, 127.1, 126.7, 120.1, 120.0, 119.5, 118.2, 113.1, 113.0, 81.2, 80.8, 28.5 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{24}H_{26}N_3O_2$ 388.2020, found 388.2011

Compound 3d, *N*,*N*-dimethyl-4-(phenyl(2-phenylhydrazono)methyl)aniline



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 4-(dimethylamino)phenylboronic acid (124 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (59.6 mg, 76 %) as a yellow oil.

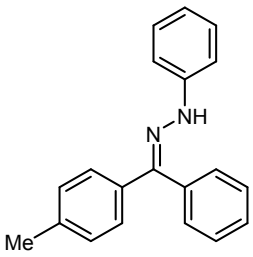
ν_{max} (neat): 3310, 3265, 3053, 3026, 2922, 1661, 1639, 1597, 1543, 1514, 1501, 1491, 1443 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (br. s, 0.65H, 0.65 x NH), 7.67 – 7.62 (m, 1.35H, 1 x ArH, 0.35 x NH), 7.60 – 7.54 (m, 0.65H, ArH), 7.53 – 7.46 (m, 1H, ArH), 7.36 – 7.26 (m, 3.35H, 3.35 x ArH), 7.26 – 7.19 (m, 3H, 3 x ArH), 7.10 (app. dd, *J* = 8.6, 1.1 Hz, 1.3H, 1.3 x ArH), 7.06 (app. dd, *J* = 8.6, 1.1 Hz, 0.7H, 0.7 x ArH), 6.90 – 6.78 (m, 2.35H, 2.35 x ArH), 6.69 (d, *J* = 8.8 Hz, 0.65H, 0.65 x ArH), 3.07 (s, 3.9H, 0.65 x $N(CH_3)_2$), 2.98 (s, 2.1H, 0.65 x $N(CH_3)_2$) (65: 35 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.7, 150.6, 145.4, 145.3, 145.09, 145.05, 139.4, 133.5, 130.3, 129.6, 129.30, 129.28, 129.25, 129.0, 128.2, 127.9, 127.7, 126.9, 119.74, 119.66, 119.6, 113.0, 112.8, 112.7, 112.0, 40.5, 40.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{22}N_3$ 316.1808, found 316.1807

Compound 3e, 1-phenyl-2-(phenyl(*p*-tolyl)methylene)hydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), *p*-tolylboronic acid (102 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (41.0 mg, 57 %) as a yellow oil.

ν_{max} (neat): 3318, 3053, 3024, 2980, 2920, 1736, 1710, 1655, 1601, 1578, 1555, 1487, 1441 cm^{-1}

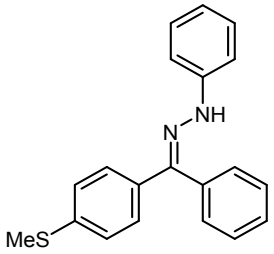
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.50 (m, 4H, 4 x ArH), 7.48 (s, 0.5H, NH), 7.41 (d, *J* = 7.7 Hz, 1H, ArH), 7.38 - 7.29 (m, 3H, 3 x ArH), 7.29 – 7.27 (m, 1.5H, 1.5 x ArH, 0.5 x NH), 7.26 – 7.24 (m, 1H, ArH), 7.19 – 7.14 (m, 1H, ArH), 7.14 – 7.09 (m, 2H, 2 x ArH), 6.91 – 6.84 (m, 1H, ArH), 2.50 (s, 1.7H, CH_3), 2.39 (s, 1.3H, CH_3) (56: 44 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.9, 144.8, 144.52, 144.48, 139.3, 138.7, 138.1, 135.8, 133.1, 130.5, 129.8, 129.32, 129.26, 129.2, 129.0, 128.3, 128.1, 126.7, 126.6, 120.1, 120.0, 113.03, 112.99, 112.96, 21.6, 21.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{19}N_2$ 287.1543, found 287.1544

Consistent with previously reported data.[9]

Compound 3f, 1-((4-(methylthio)phenyl)(phenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 4-(methylthio)phenylboronic acid (126 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (29.6 mg, 37 %) as a yellow oil.

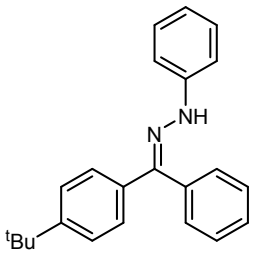
ν_{max} (neat): 3324, 3051, 3022, 2920, 2851, 1653, 1599, 1545, 1503, 1489, 1443, 1396, cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60- 7.57 (m, 2H, 2 x ArH), 7.55 – 7.49 (m, 2H, 2 x ArH), 7.46 (br. s, 1H, NH), 7.43 (d, *J* = 8.3 Hz, 1H, ArH), 7.32 (m, 2H, 2 x ArH), 7.29 – 7.22 (m, 3.5H, 3 x ArH, 0.5 x NH), 7.20 (d, *J* = 8.6 Hz, 1H, ArH), 7.12 – 7.05 (m, 2H, 2 x ArH), 6.85 (td, *J* = 7.3, 4.3 Hz, 1H, ArH), 2.58 (s, 1.5H, SCH_3), 2.49 (s, 1.5H, SCH_3) (54: 46 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 144.0, 143.8, 140.5, 138.6, 138.5, 135.5, 132.8, 129.9, 129.8, 129.43, 129.37, 129.3, 129.1, 128.3, 128.2, 127.1, 127.0, 126.7, 126.3, 120.24, 120.19, 113.1, 113.0, 15.9, 15.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{19}N_2S$ 319.1263, found 319.1260

Compound 3g, 1-((4-(*tert*-butyl)phenyl)(phenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 4-(*tert*-butyl)phenylboronic acid (134 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (61.9 mg, 75 %) as a yellow oil.

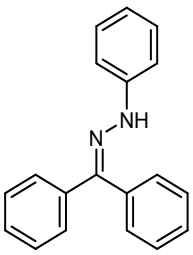
ν_{max} (neat): 3325, 3057, 2961, 2866, 1655, 1601, 1578, 1501, 1491, 1445 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 – 7.45 (m, 5H, 5 x ArH), 7.43 (br. s, 0.5H, 0.5 x NH), 7.35 – 7.27 (m, 3H, 3 x ArH), 7.25 – 7.19 (m, 3.5H, 3 x ArH, 0.5 x NH), 7.09 – 7.02 (m, 2H, 2 x ArH), 6.84 – 6.78 (m, 1H, ArH), 1.39 (s, 4.8H, $C(CH_3)_3$), 1.31 (s, 4.2H, $C(CH_3)_3$) (53: 47 mixture of stereoisomers)

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.4, 151.3, 144.89, 144.87, 144.5, 138.8, 135.8, 133.1, 129.8, 129.7, 129.32, 129.28, 129.0, 128.3, 128.0, 126.71, 126.66, 126.4, 125.3, 120.1, 120.0, 113.08, 113.05, 113.0, 31.5, 31.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{23}H_{25}N_2$ 329.2012, found 329.2014

Compound 3h, 1-(diphenylmethylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), phenylboronic acid (92.0 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (11.1 mg, 16 %) as a yellow oil.

ν_{max} (neat): 3321, 3055, 2924, 1599, 1578, 1560, 1501, 1489, 1443 cm^{-1}

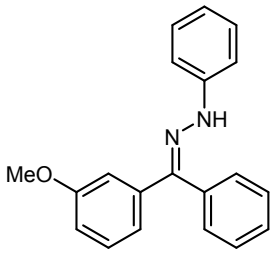
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.57 (m, 4H, 4 x ArH), 7.56-7.52 (m, 1H, ArH), 7.50 (br. s, 1H, NH), 7.38 – 7.22 (m, 7H, 7 x ArH), 7.12 – 7.07 (m, 2H, 2 x ArH), 6.86 (tt, *J* = 7.4, 1.1 Hz, 1H, ArH)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 144.3, 138.5, 132.9, 129.8, 129.4, 129.3, 128.3, 128.1, 126.6, 120.2, 113.1, one C not observed (coincident)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{19}H_{17}N_2$ 273.1386, found 273.1388

Consistent with previously reported data.[10]

Compound 3i, 1-((3-methoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 3-methoxyphenylboronic acid (128 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (15.7 mg, 21 %) as a yellow oil.

ν_{max} (neat): 3325, 3298, 3055, 2955, 2926, 2853, 1655, 1597, 1578, 1504, 1485, 1447, 1431 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.54 (m, 2H, 2 x ArH), 7.54 – 7.46 (m, 2H, 2 x ArH), 7.35 – 7.19 (m, 5.5H, 4.5 x ArH, 1 x NH), 7.11 – 7.02 (m, 3H, 3 x ArH), 6.91 (d, *J* = 7.4 Hz, 0.5H, 0.5 x

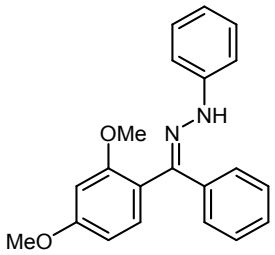
ArH), 6.88 – 6.77 (m, 2H, 2 x ArH), 3.83 (s, 1.5H, OCH_3), 3.82 (s, 1.5H, OCH_3) (54: 46 mixture of stereoisomers)

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.8, 159.7, 144.8, 144.7, 144.12, 144.08, 140.0, 138.3, 136.7, 134.2, 132.9, 131.0, 129.8, 129.40, 129.36, 129.3, 129.2, 128.3, 128.1, 126.6, 121.3, 120.3, 120.2, 119.6, 115.2, 114.3, 113.8, 113.1, 111.9, 55.5, 55.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{19}N_2O$ 303.1492, found 303.1494

Consistent with previously reported data.[11]

Compound 3j, 1-((2,4-dimethoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 2,4-dimethoxyphenylboronic acid (137 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (55.2 mg, 66 %) as a yellow oil.

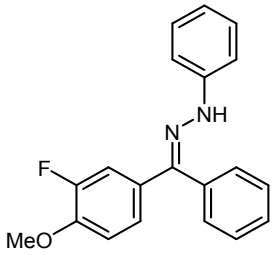
ν_{max} (neat): 3325, 3055, 3030, 2961, 2903, 2866, 1655, 1601, 1501, 1491, 1445 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.57 (m, 2H, 2 x ArH), 7.43 (br. s, 1H, NH), 7.33 – 7.20 (m, 5H, 5 x ArH), 7.12 – 7.07 (m, 3H, 3 x ArH), 6.86 – 6.79 (m, 1H, ArH), 6.68 - 6.65 (m, 2H, 2 x ArH), 3.91 (s, 3H, OCH_3), 3.73 (s, 3H, OCH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 158.6, 145.1, 141.8, 138.8, 131.6, 129.3, 128.2, 127.8, 126.3, 119.9, 113.6, 113.1, 105.8, 99.6, 55.9, 55.7

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{21}N_2O_2$ 333.1598, found 333.1600

Compound 3k, 1-((3-fluoro-4-methoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), 3-fluoro-4-methoxyphenylboronic acid (128 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (62.9 mg, 79 %) as a yellow oil.

ν_{max} (neat): 3331, 3057, 3024, 2960, 2934, 2841, 1649, 1599, 1578, 1501, 1491, 1431, 1275 cm^{-1}

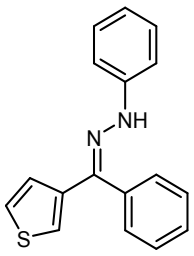
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.49 (m, 4H, 4 x ArH), 7.46 (br. s, 0.7H, 0.7 x NH), 7.39 – 7.24 (m, 3.9H, 3.6 x ArH, 0.3 x NH), 7.18 – 7.05 (m, 3.7H, 4 x ArH), 6.92 – 6.83 (m, 1.7H, 2 x ArH), 4.00 (s, 0.9H, OCH_3), 3.90 (s, 2.1H, OCH_3) (69:31 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1 (d, $^{1}J_{C,F}$ = 249.5 Hz), 152.5 (d, $^{1}J_{C,F}$ = 244.8 Hz), 148.5 (d, $^{2}J_{C,F}$ = 10.5 Hz), 147.8 (d, $^{2}J_{C,F}$ = 11.1 Hz), 144.7, 144.6, 143.1, 142.7, 138.4, 132.5, 132.2 (d, $^{3}J_{C,F}$ = 6.8 Hz), 130.7, 129.9, 129.5, 129.3, 129.2, 128.4, 128.3, 128.2, 127.8, 126.6, 125.59, 125.55, 125.2, 125.1, 122.7 (d, $^{4}J_{C,F}$ = 2.9 Hz), 120.3, 120.2, 117.3, 117.1, 114.4, 113.8 (d, $^{3}J_{C,F}$ = 19.9 Hz), 113.1, 112.98, 112.97 (d, $^{2}J_{C,F}$ = 29.8 Hz), 56.4 (mixture of stereoisomers)

^{19}F NMR (376 MHz, $CDCl_3$) δ -132.53 (dd, $J_{F,H}$ = 11.3, 7.8 Hz), -135.23 (ddd, $J_{F,H}$ = 13.0, 8.7, 1.0 Hz) (69:31 mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{18}FN_2O$ 321.1398, found 321.1398

Compound 3l, 1-phenyl-2-(phenyl(thiophen-3-yl)methylene)hydrazine



Synthesised according to General Procedure C using tetrazole **1b** (33.5 mg, 0.15 mmol), thiophen-3-ylboronic acid (58.0 mg, 0.45 mmol), and THF (2.5 mL) to afford the product (29.5 mg, 72 %) as a yellow oil.

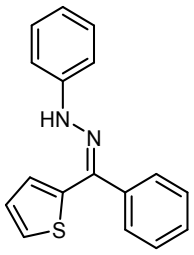
ν_{max} (neat): 3321, 3098, 3051, 2924, 1597, 1578, 1560, 1499, 1489, 1443 cm^{-1}

^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (br. s, 0.5H, 0.5 x NH), 7.70 (dd, *J* = 5.1, 1.2 Hz, 0.5H, 0.5 x ArH), 7.66 – 7.56 (m, 2.5H, 2.5 x ArH), 7.55 – 7.50 (m, 0.5H, 0.5 x ArH), 7.46 (dd, *J* = 2.9, 1.2 Hz, 0.5H, 0.5 x ArH), 7.44 – 7.22 (m, 5.5H, 5 x ArH, 0.5 x NH), 7.16 – 7.10 (m, 1.5H, 1.5 x ArH), 7.06 (dd, *J* = 8.6, 1.0 Hz, 1H, ArH), 6.93 – 6.82 (m, 1.5H, 1.5 x ArH) (55: 45 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 144.7, 142.1, 141.5, 139.8, 138.6, 133.2, 132.8, 129.7, 129.5, 129.4, 129.3, 128.9, 128.4, 128.2, 128.1, 127.8, 126.6, 126.1, 125.84, 125.78, 123.3, 120.3, 120.1, 113.2, 113.0 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{15}N_2S$ 279.0950, found 279.0952

Compound 3m, 1-phenyl-2-(phenyl(thiophen-2-yl)methylene)hydrazine



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), thiophen-2-ylboronic acid (96.0 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (59.6 mg, 86 %) as a yellow oil.

ν_{max} (neat): 3320, 3100, 3053, 3030, 2959, 2924, 1597, 1557, 1499, 1487, 1441, 1425 cm^{-1}

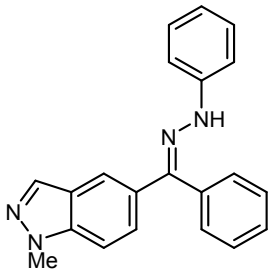
^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (br. s, 0.5H, 0.3 x NH), 7.69 – 7.50 (m, 3H, 3 x ArH), 7.46 – 7.40 (m, 1.5H, 1 x ArH, 0.5 x NH), 7.38 – 7.26 (m, 3H, 3 x ArH), 7.26 – 7.19 (m, 2H, 2 x ArH), 7.13 (dd, *J* = 8.6, 1.1 Hz, 1H, ArH), 7.05 (dd, *J* = 8.6, 1.0 Hz, 1H, ArH), 6.94 – 6.82 (m, 1.5H, 1.5 x ArH), 6.66 (dd, *J* = 3.6, 1.1 Hz, 0.5H, 0.5 x ArH) (30:70 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 144.4, 140.9, 140.8, 138.9, 136.8, 132.2, 132.0, 129.8, 129.7, 129.5, 129.41, 129.36, 129.1, 128.33, 128.29, 128.0, 127.1, 126.7, 126.3, 126.1, 120.6, 120.3, 113.3, 113.1(mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{17}H_{15}N_2S$ 279.0950, found 279.0953

Consistent with previously reported data.[12]

Compound 3n, 1-methyl-5-(phenyl(2-phenylhydrazono)methyl)-1*H*-indazole



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), (1-methyl-1*H*-indazol-5-yl)boronic acid (132 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (52.6 mg, 64 %) as a yellow oil.

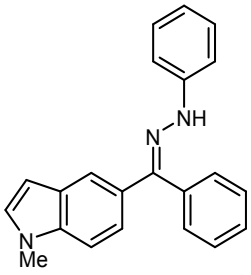
ν_{max} (neat): 3238, 3055, 2918, 2849, 1597, 1578, 1555, 1491, 1443 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.9, 1.6 Hz, 0.35H, 0.35 x ArH), 8.07 (d, *J* = 0.9 Hz, 0.65H, 0.65 x ArH), 7.88 (d, *J* = 0.7 Hz, 0.35H, 0.35 x ArH), 7.76 – 7.74 (m, 0.65H, 0.65 x ArH), 7.65 – 7.53 (m, 4H, 4 x ArH), 7.48 – 7.44 (m, 0.7H, 0.35 x ArH, 0.35 x NH), 7.42 – 7.35 (m, 1.3H, 0.65 x ArH, 0.65 x NH), 7.35 – 7.28 (m, 3H, 3 x ArH), 7.27 – 7.21 (m, 1H, ArH), 7.09 (td, *J* = 8.6, 1.0 Hz, 2H, 2 x ArH), 6.88 – 6.82 (m, 1H, ArH), 4.17 (s, 2H, 0.66 x NCH_3), 4.08 (s, 1H, 0.33 x NCH_3) (66: 33 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.91, 144.86, 144.8, 144.5, 139.9, 138.9, 133.6, 133.4, 133.1, 131.8, 129.9, 129.44, 129.36, 128.3, 128.1, 127.3, 126.7, 125.0, 124.9, 124.6, 122.4, 120.2, 120.1, 120.0, 113.1, 113.0, 110.7, 109.1, 35.9, 35.8 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{19}N_4$ 327.1604, found 327.1604

Compound 3o, 1-methyl-5-(phenyl(2-phenylhydrazono)methyl)-1*H*-indole



Synthesised according to General Procedure C using tetrazole **1b** (55.6 mg, 0.25 mmol), (1-methyl-1*H*-indol-5-yl)boronic acid (131 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (49.6 mg, 61 %) as a yellow oil.

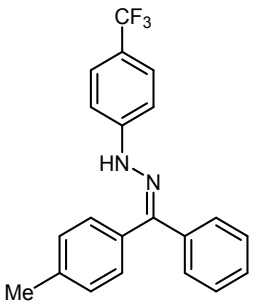
ν_{max} (neat): 3319, 3053, 2959, 2926, 1715, 1645, 1599, 1499, 1491, 1443 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.7, 1.7 Hz, 0.25H, 0.25 x ArH), 7.69 – 7.58 (m, 3.5H, 2.5 x ArH, 1 x NH), 7.54 – 7.50 (m, 1.25H, 1.25 x ArH), 7.41 – 7.37 (m, 0.75H, 0.75 x ArH), 7.34 – 7.27 (m, 2.75H, 2.75 x ArH), 7.25 – 7.05 (m, 5.25H, 5.25 x ArH), 7.02 (d, *J* = 3.1 Hz, 0.25H, 0.25 x ArH), 6.86 – 6.80 (m, 1H, ArH), 6.58 (dd, *J* = 3.1, 0.8 Hz, 0.75H, 0.75 x ArH), 6.42 (dd, *J* = 3.1, 0.7 Hz, 0.25H, 0.25 x ArH), 3.90 (s, 2.25H, 2.25 x ArH), 3.80 (s, 0.75H, 0.75 x ArH) (75: 25 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 146.2, 145.8, 145.3, 145.0, 139.4, 136.9, 133.8, 130.4, 130.09, 130.06, 129.7, 129.4, 129.34, 129.30, 129.1, 128.21, 128.17, 127.9, 126.91, 126.87, 123.5, 122.4, 122.0, 120.5, 120.4, 119.8, 119.7, 113.0, 112.9, 110.7, 109.3, 101.9, 101.7, 33.2, 33.1 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{20}N_3$ 326.1652, found 326.1654

Compound 3p, 1-(phenyl(*p*-tolyl)methylene)-2-(4-(trifluoromethyl)phenyl)hydrazine



Synthesised according to General Procedure C using 5-phenyl-2-(4-(trifluoromethyl)phenyl)-2*H*-tetrazole (60.0 mg, 0.21 mmol), *p*-tolylboronic acid (84.4 mg, 0.62 mmol), and THF (2.5 mL) to afford the product (40.1 mg, 55 %) as a yellow oil.

ν_{max} (neat): 3314, 3057, 3030, 2957, 2924, 1719, 1655, 1612, 1582, 1528, 1445 cm^{-1}

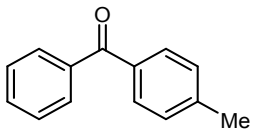
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 – 7.66 (m, 1H, NH), 7.63 – 7.57 (m, 2H, 2 x ArH), 7.54 (app. dd, *J* = 8.7, 6.1 Hz, 0.5H, 0.5 x ArH), 7.49 (dd, *J* = 8.0, 4.3 Hz, 3H, 3 x ArH), 7.41 (d, *J* = 7.8 Hz, 1H, ArH), 7.36 – 7.31 (m, 2.5H, 2.5 x ArH), 7.23 (d, *J* = 7.8 Hz, 1H, ArH), 7.18 – 7.09 (m, 3H, 3 x ArH), 2.49 (s, 1.7H, 1.7 x CH_3), 2.37 (s, 1.3H, 1.3 x CH_3) (56: 44 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.33, 147.29, 146.6, 139.7, 138.8, 138.2, 135.4, 132.7, 131.1, 130.6, 129.9, 129.6, 129.4, 129.2, 129.1, 129.0, 128.6, 128.4, 126.94, 126.89, 126.8 (app. d, $^{2}J_{C,F}$ = 19.7 Hz), 126.74, 126.70, 124.9 (app. d, $^{1}J_{C,F}$ = 270.5 Hz), 121.8 (app. d, $^{3}J_{C,F}$ = 5.2 Hz), 121.4 (app. d, $^{3}J_{C,F}$ = 5.8 Hz), 112.6, 112.5, 21.6, 21.4 (mixture of stereoisomers)

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.21 – -61.27 (m)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{18}F_3N_2$ 355.1417, found 355.1415

Compound 3q, phenyl(*p*-tolyl)methanone



Synthesised according to General Procedure C using tetrazole **S5** (41.0 mg, 0.16 mmol), *p*-tolylboronic acid (66.3 mg, 0.49 mmol), and THF (2.5 mL), however attempts at purification by column chromatography resulted in partial hydrolysis of the hydrazone. Complete hydrolysis was facilitated through stirring in a suspension of SiO_2, H_2O and MeOH with gentle heating to afford the product (15.2 mg, 47 %) as an off white solid.

ν_{max} (neat): 3057, 3026, 2920, 1653, 1605, 1445 cm^{-1}

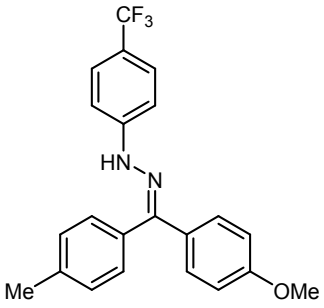
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 2H, 2 x ArH), 7.73 (d, *J* = 8.2 Hz, 2H, 2 x ArH), 7.61 – 7.55 (m, 1H, ArH), 7.49-7.45 (m, 2H, 2 x ArH), 7.29-7.27 (m, 2H, 2 x ArH), 2.44 (s, 3H, CH_3)

^{13}C NMR (126 MHz, Acetone) δ 196.2, 144.0, 138.9, 135.9, 133.0, 130.8, 130.4, 129.9, 129.2, 21.6

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{13}O$ 159.0961, found 197.0959

Consistent with previously reported data.[13]

Compound 3r, 1-((4-methoxyphenyl)(*p*-tolyl)methylene)-2-(4-(trifluoromethyl)phenyl)hydrazine



Synthesised according to General Procedure C using tetrazole **S8** (80.1 mg, 0.25 mmol), *p*-tolylboronic acid (102 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (46.9 mg, 49 %) as a yellow oil.

ν_{max} (neat): 3335, 3001, 2953, 2926, 2853, 1612, 1528, 1508, 1479, 1464, 1443, 1416 cm^{-1}

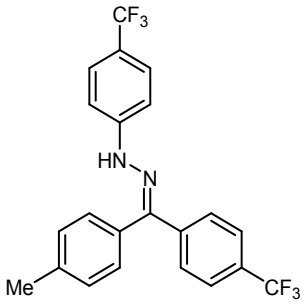
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (br. s, 0.5H, 0.5 x NH), 7.58 (br. s, 0.5H, 0.5 x NH), 7.55 – 7.43 (m, 4H, 4 x ArH), 7.38 (d, *J* = 7.8 Hz, 1H, ArH), 7.27 – 7.24 (m, 1H, ArH), 7.21 (d, *J* = 7.9 Hz, 1H, ArH), 7.14 (d, *J* = 8.1 Hz, 1H, ArH), 7.12 – 7.07 (m, 3H, 3 x ArH), 6.86 (d, *J* = 8.8 Hz, 1H, ArH), 3.91 (s, 1.5H, 1.5 x OCH_3), 3.82 (s, 1.5H, 1.5 x OCH_3), 2.47 (s, 1.5H, 1.5 x CH_3), 2.36 (s, 1.5H, 1.5 x CH_3) (53: 47 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 160.3, 147.5, 147.4, 146.6, 146.5, 139.6, 138.7, 135.7, 131.1, 130.6, 130.5, 129.3 (app. d, $^{2}J_{C,F}$ = 59.1 Hz), 129.1, 129.0, 128.3, 127.0, 126.7, 124.9 (app. d, $^{1}J_{C,F}$ = 270.5 Hz), 124.5, 121.5 (app. d, $^{3}J_{C,F}$ = 16.2 Hz), 121.2 (app. d, $^{3}J_{C,F}$ = 15.8 Hz), 115.2, 113.8, 112.5, 112.4, 55.53, 55.48, 21.6, 21.4 (mixture of stereoisomers)

^{19}F NMR (376 MHz, $CDCl_3$) δ -61.22 (s), -61.24 (s)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{20}F_3N_2O$ 385.1522, found 385.1521

Compound 3s, 1-(*p*-tolyl(4-(trifluoromethyl)phenyl)methylene)-2-(4-(trifluoromethyl)phenyl)hydrazine



Synthesised according to General Procedure C using tetrazole **S9** (70.0 mg, 0.20 mmol), *p*-tolylboronic acid (80.0 mg, 0.59 mmol), and THF (2.5 mL) to afford the product (48.5 mg, 59 %) as a yellow oil.

ν_{max} (neat): 3339, 3054, 2955, 2926, 1647, 1614, 1557, 1526, 1512, 1408 cm^{-1}

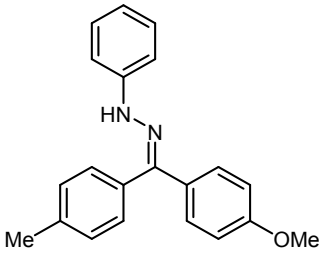
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (s, 1H, NH), 7.70 (d, *J* = 8.3 Hz, 2H, 2 x ArH), 7.58 (d, *J* = 8.3 Hz, 2H, 2 x ArH), 7.50 (d, *J* = 8.5 Hz, 2H, 2 x ArH), 7.43 (d, *J* = 7.8 Hz, 2H, 2 x ArH), 7.22 (d, *J* = 7.8 Hz, 2H, 2 x ArH), 7.14 (d, *J* = 8.5 Hz, 2H, 2 x ArH), 2.50 (s, 3H, CH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 147.1, 146.9, 144.90, 144.85, 141.6, 140.2, 139.2, 136.6, 134.7, 131.1, 130.9, 130.3, 130.0, 129.6 (app. d, $^{2}J_{C,F}$ = 48.8 Hz), 129.0, 128.6, 127.0, 126.79, 126.75, 126.7, 125.3 (q, $^{3}J_{C,F}$ = 3.9 Hz), 124.8 (app. d, $^{1}J_{C,F}$ = 271.0 Hz), 124.4 (app. d, $^{1}J_{C,F}$ = 271.9 Hz), 122.3 (q, $^{2}J_{C,F}$ = 32.7 Hz), 120.5 (app. d, $^{2}J_{C,F}$ = 45.5 Hz), 112.8, 112.7, 21.6, 21.4 (mixture of stereoisomers)

^{19}F NMR (471 MHz, $CDCl_3$) δ -61.36 (s), -62.54 (s)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{22}H_{17}F_6N_2$ 423.1290, found 423.1287

Compound 3t, 1-((4-methoxyphenyl)(*p*-tolyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **S10** (63.1 mg, 0.25 mmol), *p*-tolylboronic acid (102 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (35.6 mg, 45 %) as a yellow oil.

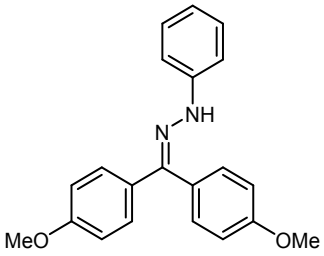
ν_{max} (neat): 3323, 3024, 2924, 2853, 1647, 1599, 1578, 1501, 1458, 1441, 1418 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 – 7.46 (m, 2.5H, 2 x ArH, 0.5 x NH), 7.42 (s, 0.5H, 0.5 x NH), 7.36 (d, *J* = 7.8 Hz, 1H, ArH), 7.25 – 7.18 (m, 4H, 4 x ArH), 7.12 (d, *J* = 8.1 Hz, 1H, ArH), 7.10 – 7.03 (m, 3H, 3 x ArH), 6.87 – 6.78 (m, 2H, 2 x ArH), 3.90 (s, 1.5H, 1.5 x OCH_3), 3.81 (s, 1.5H, 1.5 x OCH_3), 2.46 (s, 1.5H, 1.5 x CH_3), 2.35 (s, 1.5H, 1.5 x CH_3) (53: 47 mixture of stereoisomers)

^{13}C NMR (101 MHz, Acetone) δ 161.0, 160.7, 146.62, 146.55, 144.8, 144.7, 139.6, 138.3, 137.5, 132.9, 132.7, 131.4, 131.0, 130.5, 129.9, 129.8, 129.6, 128.5, 127.2, 126.1, 120.1, 120.0, 115.8, 114.4, 113.74, 113.66, 55.7, 55.6, 21.4, 21.2 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{21}N_2O$ 317.1648, found 317.1646

Compound 3u, 1-(*bis*(4-methoxyphenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using tetrazole **S10** (63.1 mg, 0.25 mmol), 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (58.4 mg, 70 %) as a yellow oil.

ν_{max} (neat): 3320, 3051, 3003, 2954, 2932, 2909, 1643, 1599, 1499, 1456, 1441, 1416 cm^{-1}

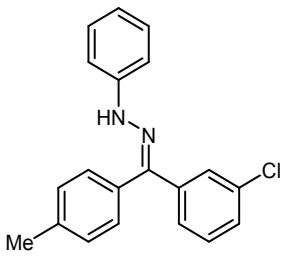
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.9 Hz, 2H, 2 x ArH), 7.44 (s, 1H, NH), 7.27 – 7.19 (m, 4H, 4 x ArH), 7.10 – 7.02 (m, 4H, 4 x ArH), 6.84 (d, *J* = 8.9 Hz, 2H, 2 x ArH), 6.83 – 6.78 (m, 1H, ArH), 3.89 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.2, 159.9, 145.1, 144.4, 131.8, 130.7, 129.3, 128.1, 125.0, 119.8, 115.1, 113.7, 112.9, 55.51, 55.47

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{21}N_2O_2$ 333.1598, found 333.1598

Consistent with previously reported data.[8]

Compound 3v, 1-((3-chlorophenyl)(*p*-tolyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using 5-(3-chlorophenyl)-2-phenyl-2*H*-tetrazole (64.2 mg, 0.25 mmol), *p*-tolylboronic acid (102 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (42.1 mg, 52 %) as a yellow oil.

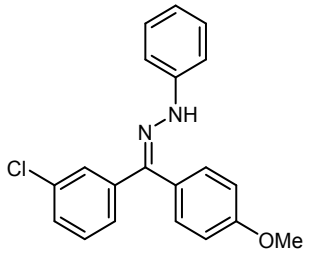
ν_{max} (neat): 3324, 3065, 3026, 2920, 2855, 1719, 1647, 1601, 1566, 1501, 1420 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.70 (m, 0.15H, 0.15 x ArH), 7.63 – 7.60 (m, 0.85H, 0.85 x ArH), 7.59 (br. s, 0.85H, 0.85 x NH), 7.49 – 7.43 (m, 1.15H, 1 x ArH, 0.15 x ArH), 7.41 (app. d, *J* = 7.8 Hz, 1.85H, 1.85 x ArH), 7.35 – 7.33 (m, 0.15H, 0.15 x ArH), 7.30 – 7.19 (m, 5.6H, 5.6 x ArH), 7.15 (d, *J* = 8.0 Hz, 0.4H, 0.4 x ArH), 7.12 – 7.07 (m, 2H, 2 x ArH), 6.88 (tt, *J* = 7.4, 1.1 Hz, 1H, ArH), 2.49 (s, 2.5H, 2.5 CH_3), 2.37 (s, 0.5H) (85:15 mixture of stereoisomers)

^{13}C NMR (101 MHz, Acetone) δ 146.4, 146.0, 142.9, 142.2, 140.0, 138.6, 136.73, 136.66, 135.8, 134.7, 132.2, 132.0, 131.2, 130.7, 130.4, 130.0, 129.9, 129.8, 128.7, 128.2, 127.0, 126.5, 125.5, 120.7, 120.4, 114.0, 113.9, 21.5, 21.2 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{18}ClN_2$ 321.1153, found 321.1151

Compound 3w, 1-((3-chlorophenyl)(4-methoxyphenyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using 5-(3-chlorophenyl)-2-phenyl-2*H*-tetrazole (64.2 mg, 0.25 mmol), 4-methoxyphenylboronic acid (114 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (67.8 mg, 81 %) as a yellow oil.

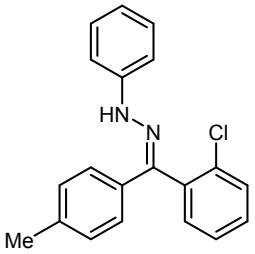
ν_{max} (neat): 3319, 3057, 3005, 2957, 2930, 2837, 1651, 1599, 1568, 1501, 1472, 1439, 1420 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 1.5H, 0.75 x ArH, 0.75 x NH), 7.51 – 7.46 (m, 1H, 1 x ArH), 7.44 – 7.41 (m, 0.75H, 0.75 x ArH), 7.33 – 7.30 (m, 0.5H, 0.25 x ArH, 0.25 x NH), 7.27 – 7.19 (m, 5.25H, 5.25 x ArH), 7.11 – 7.05 (m, 3.5H, 3.5 x ArH), 6.88-6.81 (m, 1.5H, 1.5 x ArH), 3.89 (s, 2.25H, 2.25 x CH_3), 3.80 (s, 0.75H, 0.75 x CH_3) (75:25 mixture of stereoisomers)

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.4, 160.0, 144.8, 144.5, 142.71, 142.68, 140.8, 135.9, 135.0, 134.4, 131.1, 130.9, 130.6, 129.6, 129.44, 129.38, 129.3, 127.87, 127.86, 127.5, 126.4, 124.8, 124.0, 120.4, 120.2, 115.4, 113.9, 113.1, 113.0, 55.49, 55.45

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{18}ClN_2O$ 337.1102, found 337.1104

Compound 3x, 1-((2-chlorophenyl)(*p*-tolyl)methylene)-2-phenylhydrazine



Synthesised according to General Procedure C using 5-(2-chlorophenyl)-2-phenyl-2*H*-tetrazole (64.2 mg, 0.25 mmol), *p*-tolylboronic acid (102 mg, 0.75 mmol), and THF (2.5 mL) to afford the product (46.1 mg, 57 %) as a yellow oil.

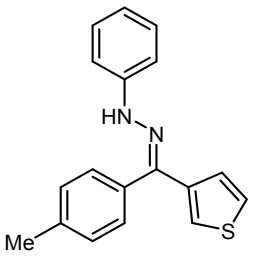
ν_{max} (neat): 3329, 3051, 3024, 2955, 2920, 2853, 1722, 1655, 1601, 1578, 1553, 1499, 1435 cm^{-1}

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.61 (m, 1H, ArH), 7.50 – 7.44 (m, 4H, 4 x ArH), 7.31 – 7.23 (m, 3H, 3 x ArH), 7.19 (br. s, 1H, NH), 7.15 (dd, *J* = 8.5, 0.5 Hz, 2H, 2 x ArH), 7.11 (dd, *J* = 8.7, 1.1 Hz, 2H, 2 x ArH), 6.87 (tt, *J* = 7.5, 1.1 Hz, 1H, ArH), 2.37 (s, 3H, CH_3)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.7, 141.5, 138.2, 134.7, 133.9, 132.1, 131.2, 130.9, 130.7, 129.3, 129.2, 128.1, 126.0, 120.3, 113.2, 21.4

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{20}H_{18}ClN_2$ 321.1153, found 321.1151

Compound 3y, 1-phenyl-2-(thiophen-3-yl(*p*-tolyl)methylene)hydrazine



Synthesised according to General Procedure C using tetrazole **S11** (47.8 mg, 0.21 mmol), *p*-tolylboronic acid (85.7 mg, 0.63 mmol), and THF (2.5 mL) to afford the product (22.0 mg, 36 %) as a yellow oil.

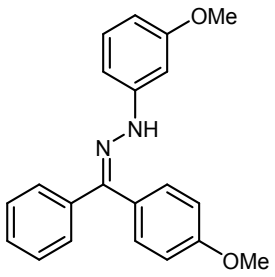
ν_{max} (neat): 3323, 3102, 3049, 3024, 2918, 2853, 1641, 1599, 1499, 1410 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 4.9 Hz, 1H, ArH), 7.59 (dd, *J* = 4.9, 2.9 Hz, 0.4H, 0.4 x ArH), 7.50 (d, *J* = 8.1 Hz, 1H, ArH), 7.44 (s, 1H, NH), 7.37 (d, *J* = 7.8 Hz, 1H, ArH), 7.31 (dd, *J* = 5.0, 3.0 Hz, 0.6H, 0.6 x ArH), 7.29 – 7.20 (m, 3.4H, 3.4 x ArH), 7.17 – 7.08 (m, 2H, 2 x ArH), 7.05 (d, *J* = 8.1 Hz, 1H, ArH), 6.91 (d, *J* = 2.8 Hz, 0.6H, 0.6 x ArH), 6.87 – 6.80 (m, 1H, ArH), 2.47 (s, 1.8H, CH_3), 2.36 (s, 1.2H, CH_3) (59:41 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 142.3, 141.7, 140.1, 139.4, 138.2, 135.9, 133.0, 130.4, 130.1, 129.4, 129.3, 129.1, 128.8, 128.1, 127.7, 126.5, 126.1, 125.9, 125.7, 123.3, 120.2, 120.0, 113.1, 113.0, 21.6, 21.4 (mixture of stereoisomers)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{18}H_{17}N_2S$ 293.1107, found 293.1109

Compound 3aa, 1-(3-methoxyphenyl)-2-((4-methoxyphenyl)(phenyl)methylene)hydrazine



2-(3-methoxyphenyl)-5-phenyl-2*H*-tetrazole (193 mg, 0.75 mmol) and 4-methoxyphenyl boronic acid (342 mg, 2.3 mmol) were dissolved in THF (5 mL) and circulated through PTFE tubing around a UV light bulb enclosed in a quartz chamber for 4 hours using a peristaltic pump at 2 mL/min flow rate (*Figure 1*). The reaction mixture was collected, concentrated under reduced pressure and purified by column chromatography to yield the product (177 mg, 71 %).

ν_{max} (neat): 3327, 3055, 2997, 2955, 2932, 2833, 1599, 1555, 1503, 1489, 1458, 1441 cm^{-1}

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 – 7.52 (m, 2.4H, 1.8 x ArH, 0.6 x NH), 7.52 – 7.48 (m, 1.2H, 1.2 x ArH), 7.36 (br. s, 0.4H, 0.4 x NH), 7.33 – 7.22 (m, 3.8H, 3.8 x ArH), 7.14 – 7.04 (m, 2.2H, 2.2 x ArH), 6.84 (d, *J* = 8.9 Hz, 1H, ArH), 6.76 (dt, *J* = 11.1, 2.2 Hz, 1H, ArH), 6.54 (ddd, *J* = 16.6, 8.0, 1.4 Hz, 1H, ArH), 6.39 (td, *J* = 8.0, 2.2 Hz, 1H, ArH), 3.88 (s, 1.8H, 1.8 x OCH_3), 3.80 (s, 1.2H, 1.2 x OCH_3), 3.79 (s, 3H, OCH_3) (60:40 mixture of stereoisomers)

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 160.2, 159.9, 146.3, 146.2, 144.5, 144.4, 138.8, 133.1, 131.3, 130.7, 130.1, 130.0, 129.7, 129.3, 129.2, 128.3, 128.1, 128.0, 126.7, 124.7, 115.2, 113.8, 105.8, 105.7, 105.5, 98.9, 98.7, 55.5, 55.4, 55.3

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{21}H_{21}N_2O_2$ 333.1598, found 333.1599

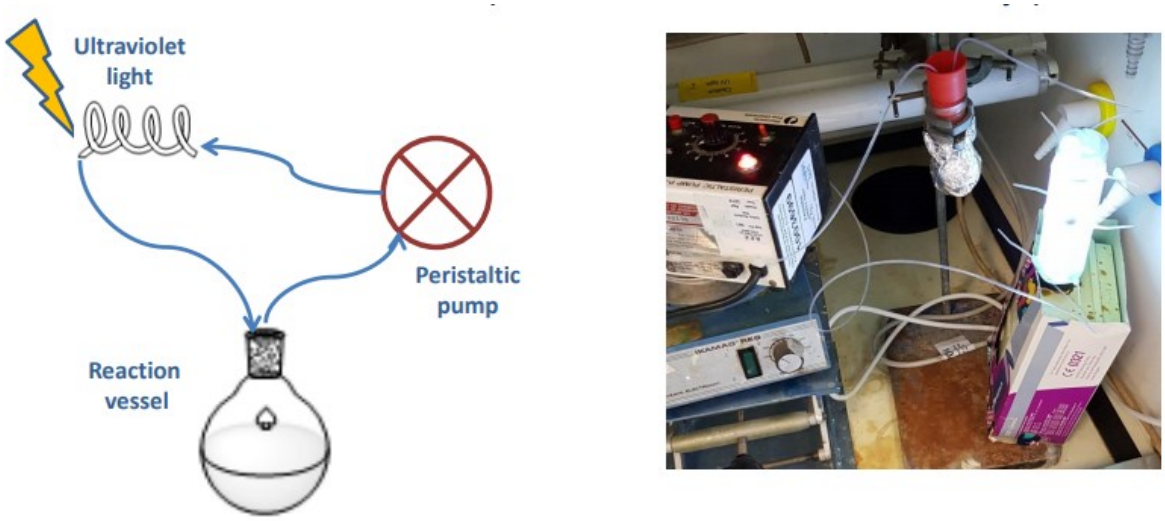
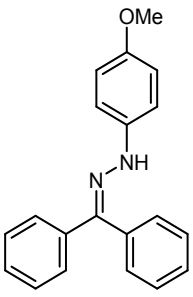


Figure 1: A schematic outlining the flow set-up of the reaction

Compound S4, 1-(diphenylmethylene)-2-(4-methoxyphenyl)hydrazine

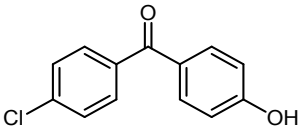


4-methoxyphenyl hydrazine hydrochloride (500 mg, 2.86 mmol) was added to a stirred solution of benzophenone (497 mg, 2.73 mmol) in methanol (10 mL). A few drops of H_2SO_4 were added and the reaction was refluxed for 4 hours. The reaction mixture was concentrated *in vacuo* to afford the

product as a yellow oil (660 mg, 80 %). The product was found to rapidly hydrolyse to the corresponding ketone under typical atmospheric conditions, and as such full characterisation was not conducted.

4.3 Other Compounds

Compound 5, (4-chlorophenyl)(4-hydroxyphenyl)methanone



Synthesised according to General Procedure C using 5-(4-chlorophenyl)-2-(4-methoxyphenyl)-2*H*-tetrazole (72.0 mg, 0.25 mmol), 4-hydroxyphenylboronic acid (103 mg, 0.75 mmol), and THF (2.5 mL), however attempts at purification by column chromatography resulted in partial hydrolysis of the hydrazone. Complete hydrolysis was facilitated through stirring in a solution of 10 % HCl in EtOH (v/v, 5 mL) for 16 hours to afford the product (38.2 mg, 66 %) as an off white solid.

ν_{max} (neat): 3316, 3067, 2955, 2922, 2853, 1641, 1597, 1560, 1508, 1485 cm^{-1}

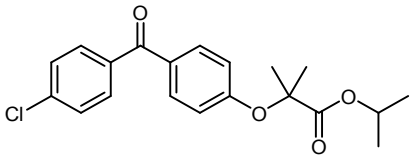
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 7.71 (d, *J* = 8.5 Hz, 2H, 2 x ArH), 7.46 (d, *J* = 8.5 Hz, 2H, 2 x ArH), 6.91 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 5.51 (s, 1H, OH)

^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 160.0, 138.6, 136.6, 132.9, 131.3, 130.2, 128.7, 115.4

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{13}H_{10}ClO_2$ 233.0369, found 233.0373

Consistent with previously reported data.[14]

Compound 6, isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate



Aryl ketone **5** (30.0 mg, 0.13 mmol) and K_2CO_3 (53.5 mg, 0.39 mmol) were stirred in MeCN (5 mL) for 10 minutes, before isopropyl 2-bromo-2-methylpropanoate (27.0 μL, 0.16 mmol) was added. The reaction mixture was refluxed for 18 hours, quenched with 1M HCl solution and extracted twice with DCM. The combined organic phases were then washed with brine, passed through a phase separator and concentrated under vacuum. The crude product was purified using column chromatography to afford the target compound (32.7 mg, 61 %) as a pale yellow solid.

ν_{max} (neat): 3070, 2982, 2936, 1728, 1655, 1597, 1506, 1466, 1383 cm^{-1}

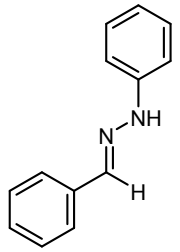
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.8 Hz, 2H, 2 x ArH), 7.69 (d, *J* = 8.5 Hz, 2H, 2 x ArH), 7.44 (d, *J* = 8.5 Hz, 2H, 2 x ArH), 6.86 (d, *J* = 8.8 Hz, 2H, 2 x ArH), 5.08 (sept, *J* = 6.3 Hz, 1H, $CHMe_2$), 1.65 (s, 6H, CH_3), 1.20 (d, *J* = 6.3 Hz, 6H, $CH(CH_3)_2$)

^{13}C NMR (126 MHz, $CDCl_3$) δ 194.4, 173.2, 159.9, 138.5, 136.6, 132.1, 131.3, 130.4, 128.7, 117.4, 79.6, 69.5, 25.5, 21.6

HRMS (ESI) *m/z*: $[M+H]^+$ calculated $C_{20}H_{22}ClO_4$ 361.1201, found 361.1204

Consistent with previously reported data.[15]

Compound S12, 1-benzylidene-2-phenylhydrazine



Phenylhydrazine hydrochloride (2.87 g, 25 mmol) was washed with 1M NaOH solution to generate the free phenyl hydrazine. This compound was dissolved and minimal EtOH and added dropwise to a solution of benzaldehyde (2.65 mL, 25 mmol) in EtOH (7 mL). The solution was stirred until consumption of the aldehyde starting material, before the mixture was filtered to yield the product (4.11 g, 84 %) as an off-white precipitate, which was used in the following steps without further purification.

ν_{max} (neat): 3310, 3055, 3024, 1591, 1564, 1522, 1493, 1483, 1440 cm^{-1}

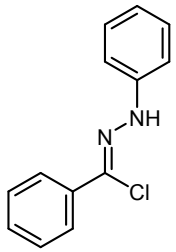
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 – 7.64 (m, 3H, 2 x ArH, 1 x ArCNH), 7.43 – 7.35 (m, 2H, 2 x ArH), 7.35 – 7.25 (m, 3H, 3 x ArH), 7.15– 7.10 (d, *J* = 7.8 Hz, 2H, 2 x ArH), 6.88 (t, *J* = 7.2 Hz, 1H, 1 x ArH), exchangeable proton not observed

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.8, 137.4, 135.5, 129.4, 128.7, 128.6, 126.3, 120.3, 112.9

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{13}H_{13}N_2$ 197.1073, found 197.1073

Consistent with previously reported data.[16]

Compound 8, *N*-phenylbenzohydrazonoyl chloride



To an oven-dried flask under nitrogen was added *N*-chlorosuccinimide (5.70 g, 43 mmol) in DCM (30 mL). Dimethyl sulfide (5.50 mL, 75 mmol) was added to the solution dropwise at 0 °C, maintaining a temperature of below 10 °C at all times. The reaction mixture was stirred for an additional 15 minutes, and then cooled to -78 °C. A solution of benzaldehyde phenylhydrazone **S12** (4.90 g, 25 mmol) was dissolved in minimal DCM and added dropwise to the reaction mixture. Stirring was maintained at -78 °C for 2 hours before being raised to room temperature. Following consumption of the hydrazone starting material, the mixture was further diluted with DCM and washed successively with H_2O and brine. The solution was passed through a phase separator, concentrated under vacuum and purified by column chromatography to yield the product (5.80 g, 64 %) as a light pink solid.

ν_{max} (neat): 3302, 3049, 2955, 2918, 1595, 1581, 1570, 1501, 1487, 1447 cm^{-1}

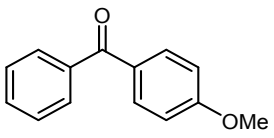
^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (br. s, 1H, NH), 7.98 – 7.90 (m, 2H, 2 x ArH), 7.45 – 7.36 (m, 3H, 3 x ArH), 7.35 – 7.29 (m, 2H, 2 x ArH), 7.22 – 7.17 (m, 2H, 2 x ArH), 6.95 (tt, *J* = 7.4, 1.1 Hz, 1H, 1 x ArH)

^{13}C NMR (101 MHz, $CDCl_3$) δ 143.5, 134.6, 129.5, 129.4, 128.6, 126.6, 124.8, 121.3, 113.6

HRMS (ESI) *m/z*: $[M-H]^+$ calculated for $C_{13}H_{12}ClN_2$ 229.0527, found 229.0525

Consistent with previously reported data.[1]

Compound S6, (4-methoxyphenyl)(phenyl)methanone



Tetrazole **S5** (100 mg, 0.4 mmol) and 4-methoxyphenylboronic acid (122 mg, 0.8 mmol) were dissolved in THF (5 mL) and added to a quartz round-bottom flask. The solution was irradiated using

a UV lamp for 3 hours, before the residue was concentrated under vacuum and dissolved in acetone (5 mL). $VO(acac)_2$ (10.0 mg, 0.1 mmol) and H_2O_2 (30% w/w in H_2O) (0.25 mL) was then added dropwise at room temperature. The reaction mixture was stirred for two hours, and diluted with DCM. This solution was washed with 10% sodium metabisulfite and brine, passed through a phase separator and concentrated under vacuum. The crude product was purified by column chromatography to furnish ketone **S6** (48.2 mg, 53 %) as an off-white solid.

ν_{max} (neat): 3063, 3003, 2965, 2841, 1639, 1595, 1578, 1504, 1468, 1439, 1414 cm^{-1}

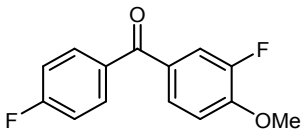
^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 7.75 (d, *J* = 7.6 Hz, 2H, 2 x ArH), 7.59 – 7.53 (m, 1H, ArH), 7.50 – 7.44 (m, 2H, 2 x ArH), 6.96 (d, *J* = 8.7 Hz, 2H, 2 x ArH), 3.88 (s, 3H, OCH_3)

^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 163.4, 138.4, 132.7, 132.0, 130.3, 129.8, 128.3, 113.7, 55.6

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{13}O_2$ 213.0910, found 213.0909

Consistent with previously reported data.[13]

Compound S13, (3-fluoro-4-methoxyphenyl)(4-fluorophenyl)methanone



Synthesised according to General Procedure C using tetrazole **1a** (135 mg, 0.50 mmol), 3-fluoro-4-methoxyphenylboronic acid (276 mg, 1.50 mmol), and THF (5 mL). Complete hydrolysis was facilitated through stirring in a suspension of SiO_2, H_2O and MeOH with gentle heating to afford the product (38.2 mg, 31 %) as a pale yellow solid.

ν_{max} (neat): 3073, 2963, 2947, 1639, 1601, 1576, 1516, 1506, 1458, 1429, 1406 cm^{-1}

^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (dd, $J_{H,H}$ = 8.4 Hz, $J_{H,F}$ = 5.6 Hz, 2H, 2 x ArH), 7.62 – 7.55 (m, 2H, 2 x ArH), 7.20 – 7.13 (m, 2H, 2 x ArH), 7.06 – 7.00 (m, 1H, ArH), 3.98 (s, 3H, OCH_3)

^{13}C NMR (126 MHz, $CDCl_3$) δ 193.2, 165.4 (d, $^1J_{C,F}$ = 254.0 Hz), 152.0 (d, $^1J_{C,F}$ = 248.4 Hz), 151.8 (d, $^2J_{C,F}$ = 10.7 Hz), 134.0 (d, $^4J_{C,F}$ = 3.2 Hz), 132.5 (d, $^3J_{C,F}$ = 9.1 Hz), 130.4 (d, $^3J_{C,F}$ = 5.1 Hz), 127.6 (d, $^4J_{C,F}$ = 3.3 Hz), 117.9 (d, $^2J_{C,F}$ = 19.2 Hz), 115.7 (d, $^2J_{C,F}$ = 21.9 Hz), 112.5, 56.5

^{19}F NMR (471 MHz, $CDCl_3$) δ -105.85 – -106.60 (m), -134.01 (dd, *J* = 11.3, 8.5 Hz)

HRMS (ESI) *m/z*: $[M+H]^+$ calculated for $C_{14}H_{11}F_2O_2$ 249.0727, found 249.073

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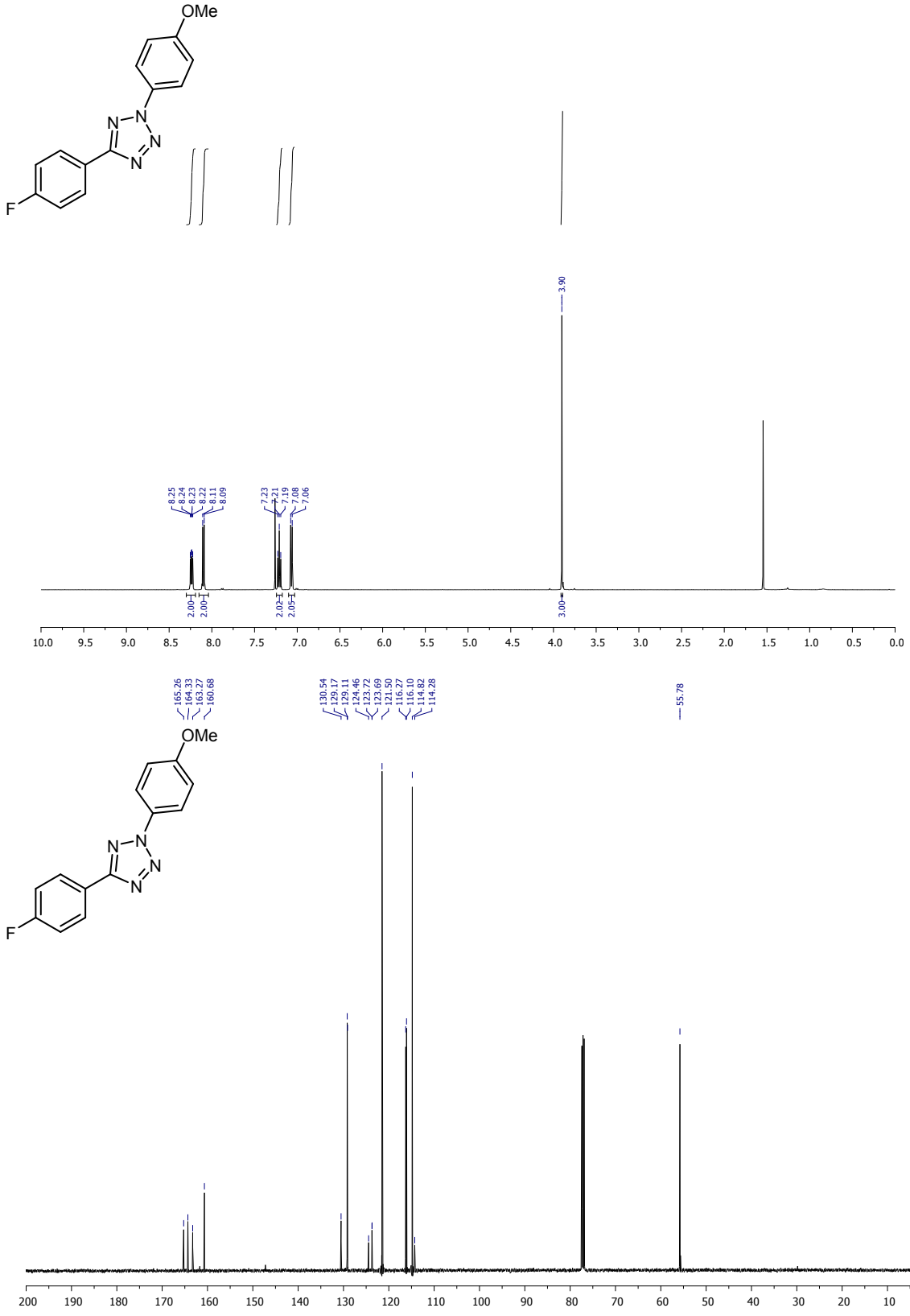
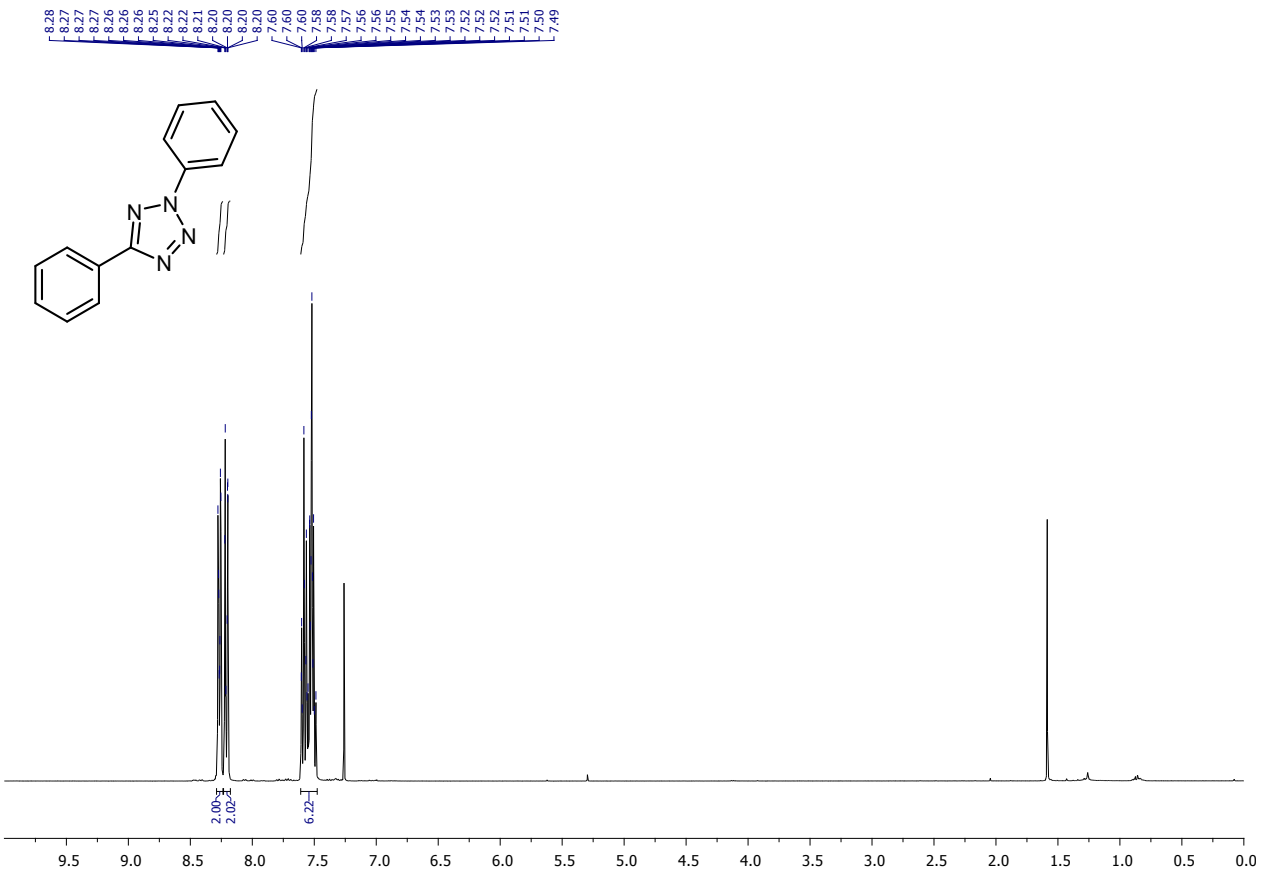
6 NMR Spectra of Compounds

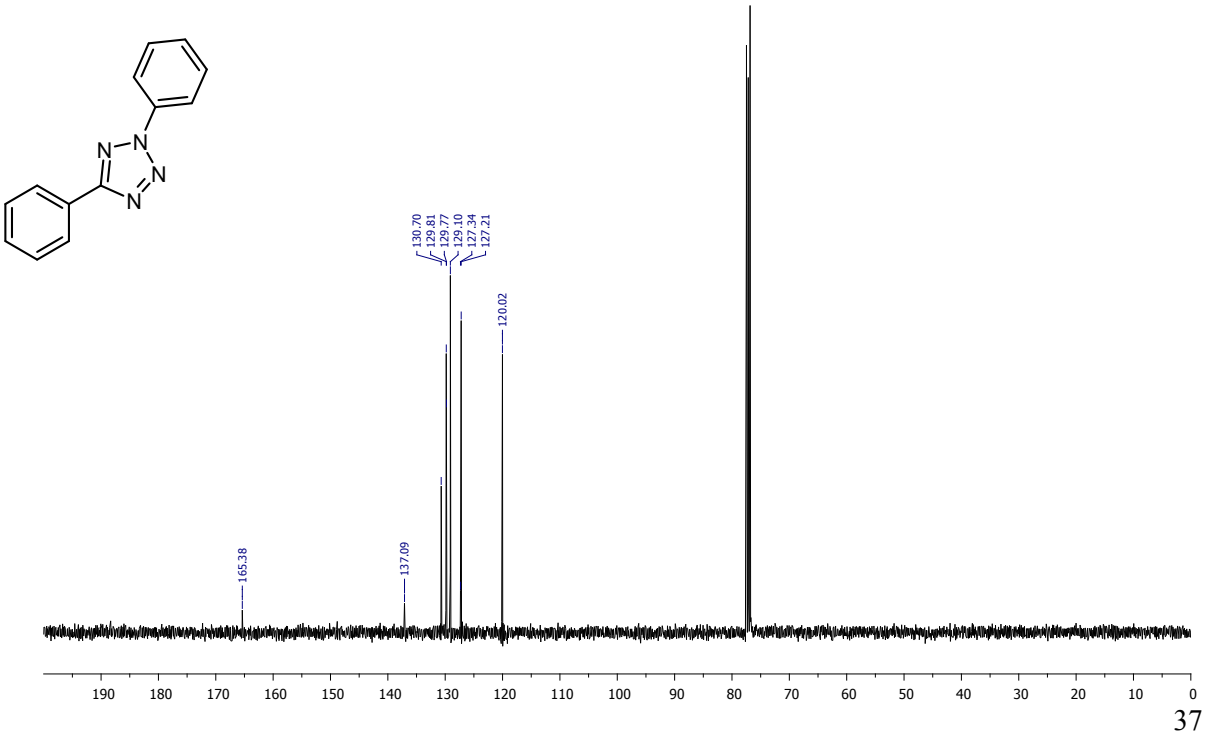
6.1 2,5 Tetrazole Starting Materials

Compound 1a, 5-(4-fluorophenyl)-2-(4-methoxyphenyl)-2*H*-tetrazole

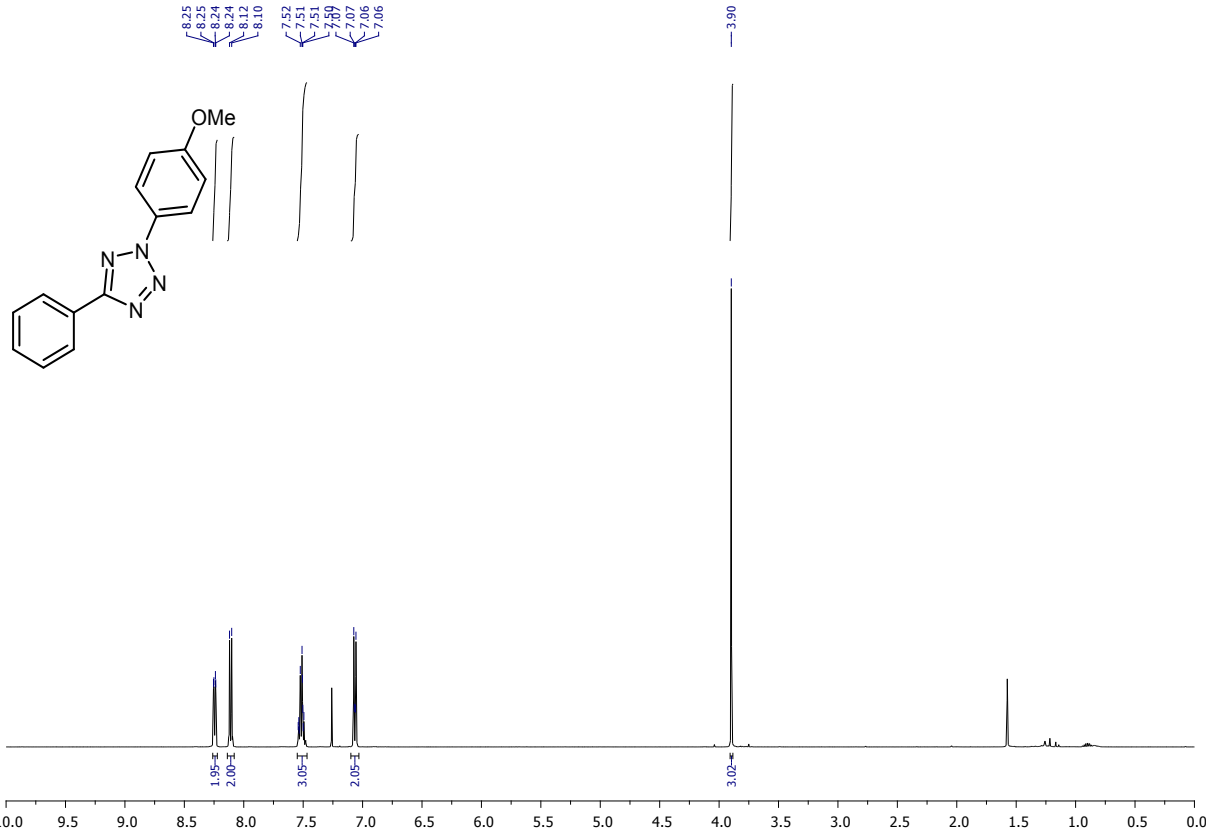


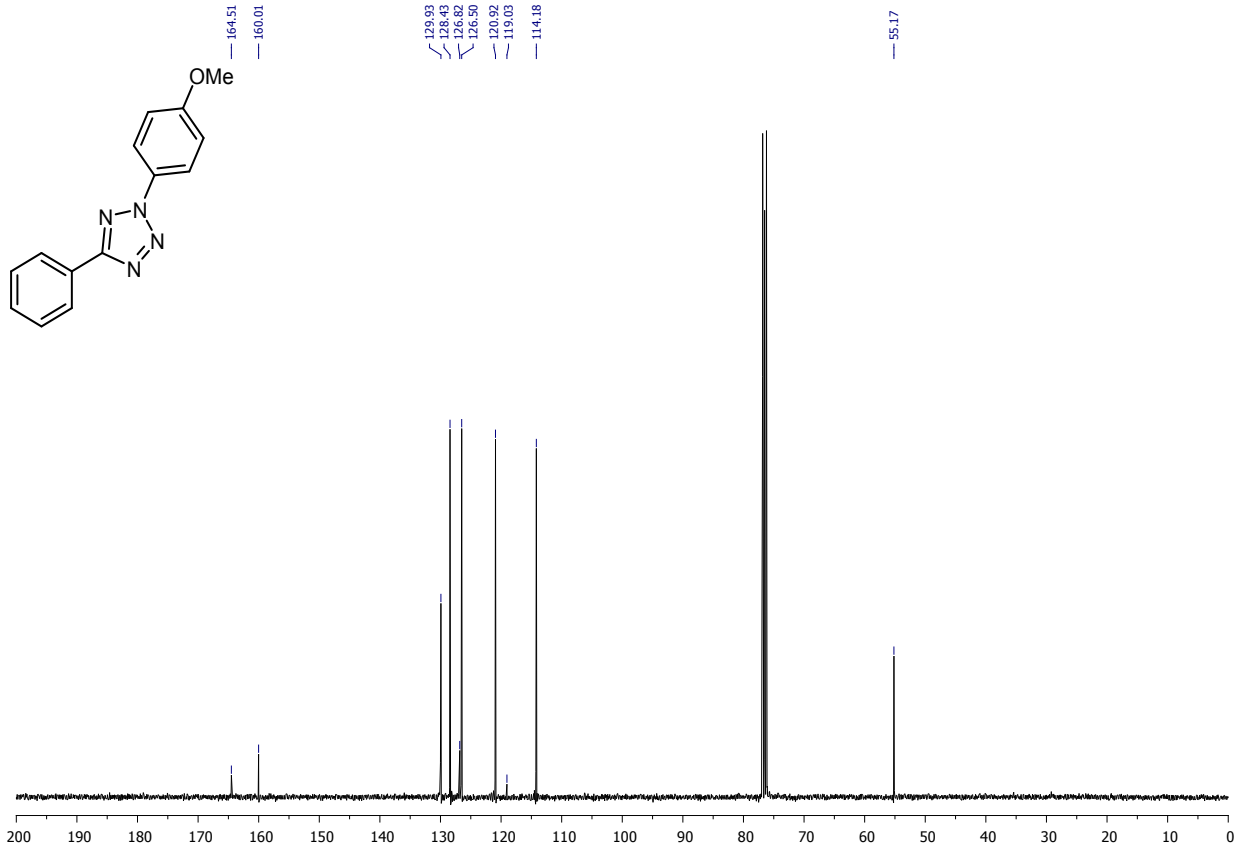
Compound 1b, 2,5-diphenyl-2*H*-tetrazole



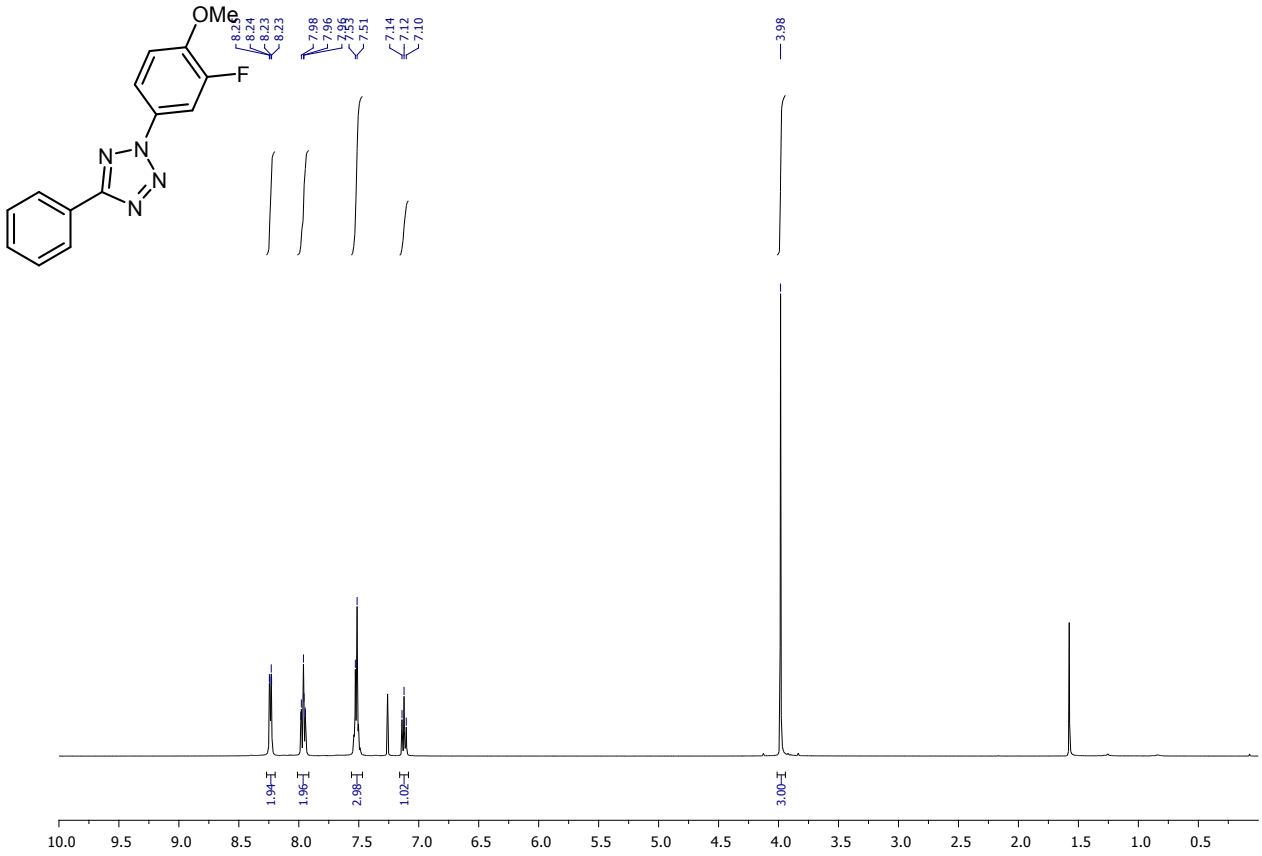


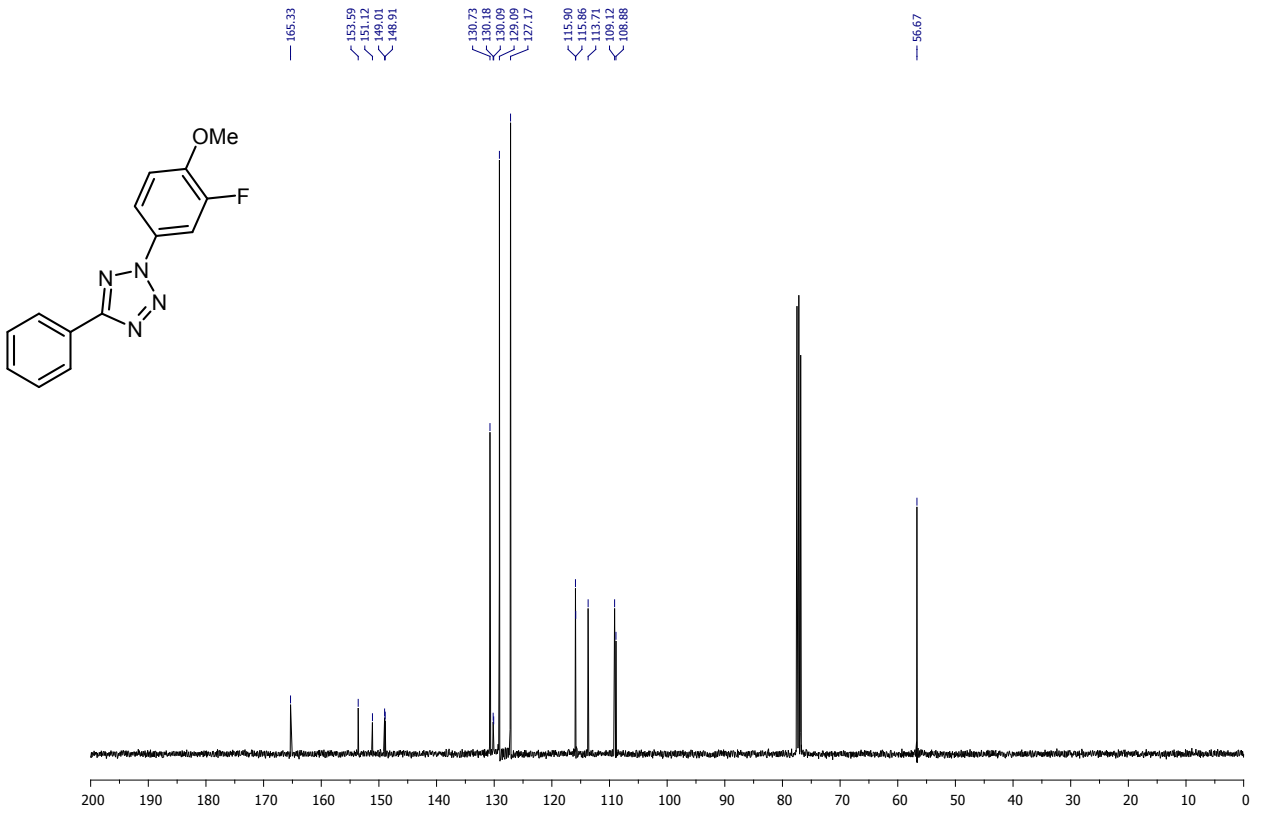
Compound S5, 2-(4-methoxyphenyl)-5-phenyl-2*H*-tetrazole

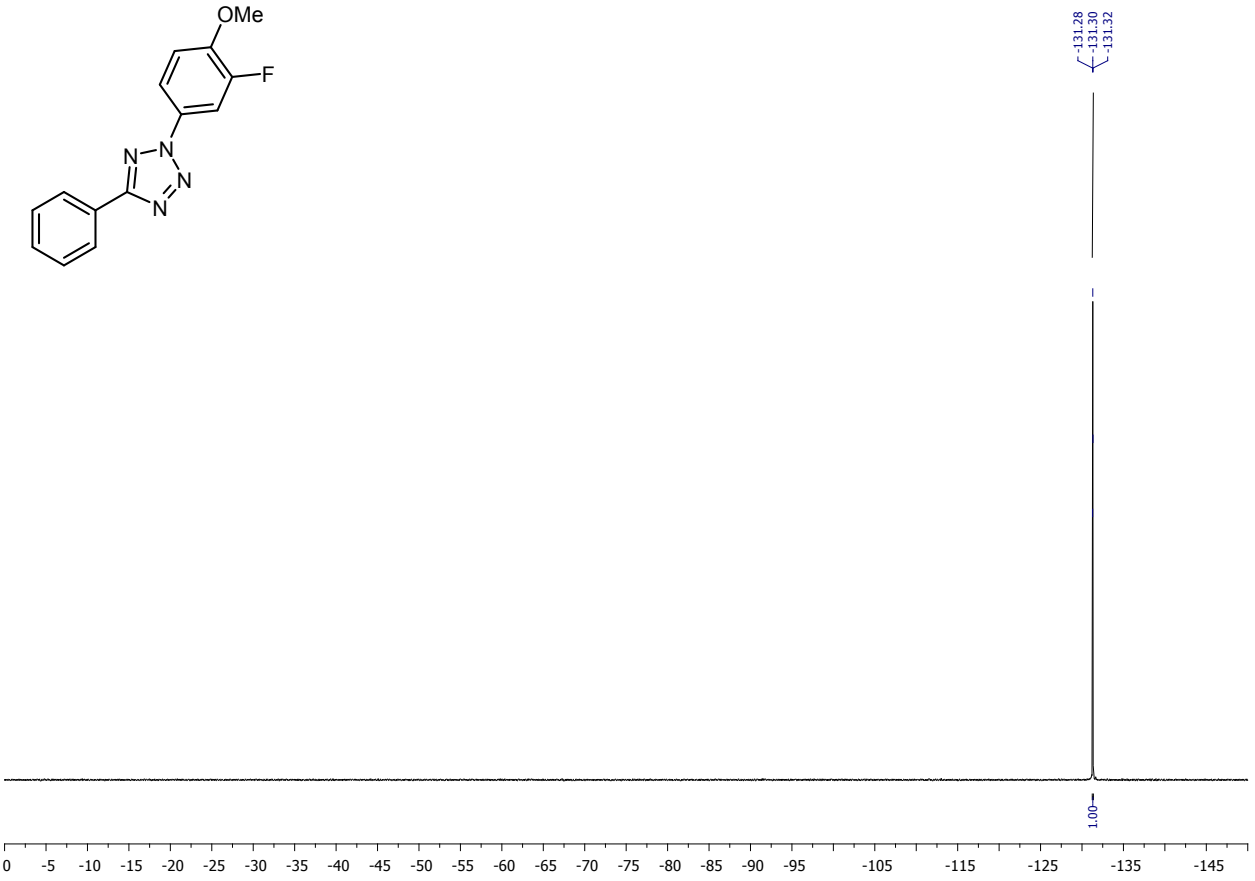




Compound S7, 2-(3-fluoro-4-methoxyphenyl)-5-phenyl-2*H*-tetrazole






OMe
F
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N
N
N
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-131.30
-131.32
1.00
0
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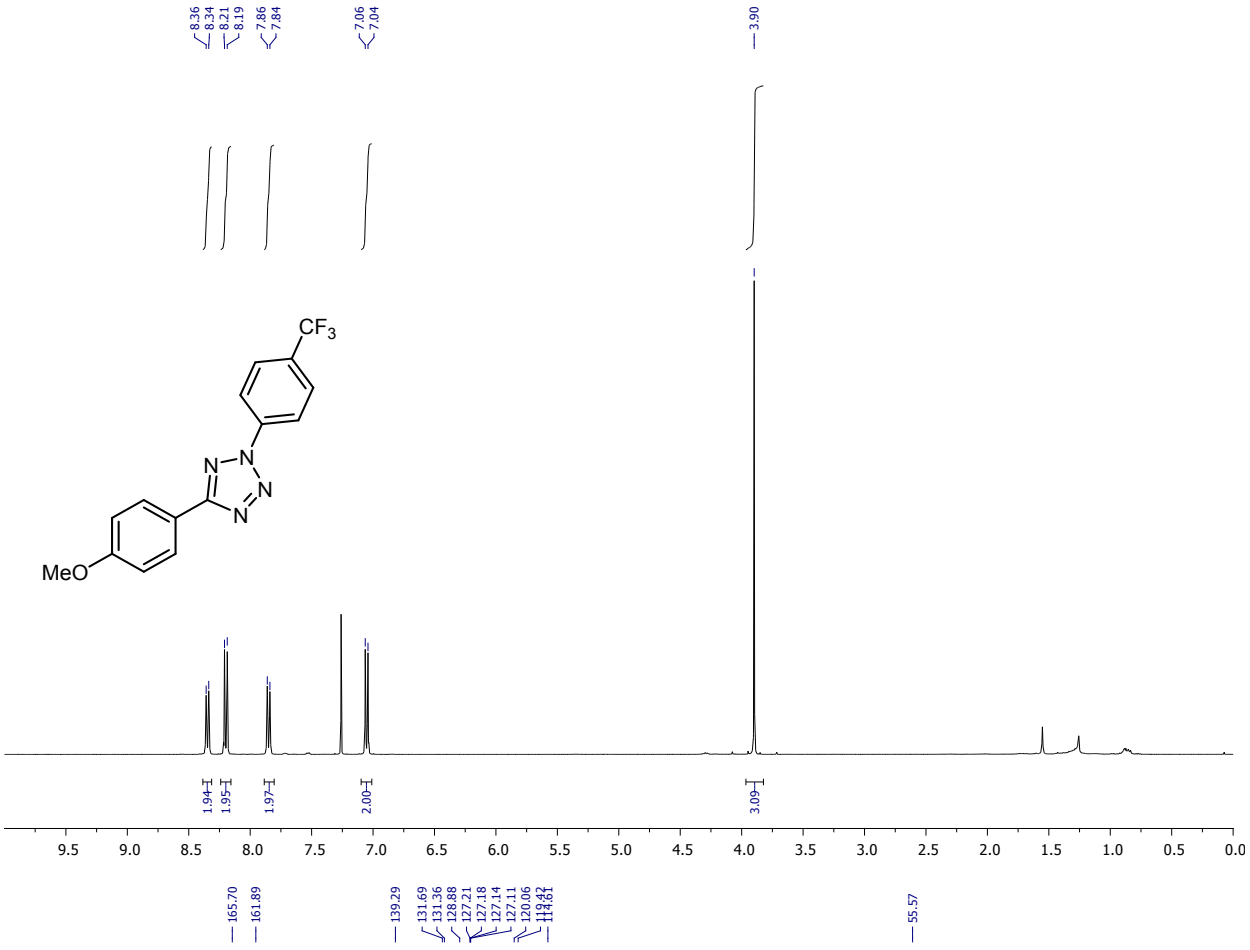
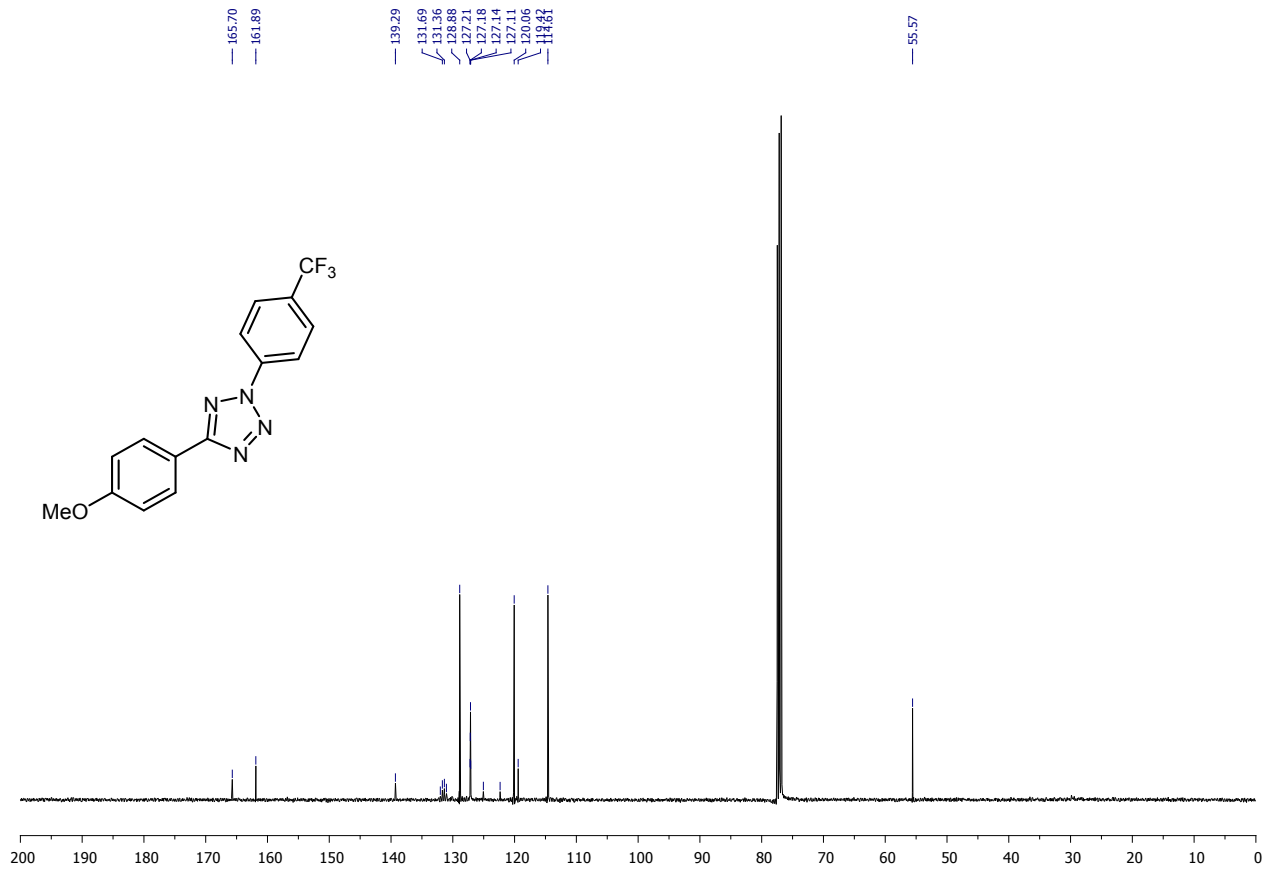
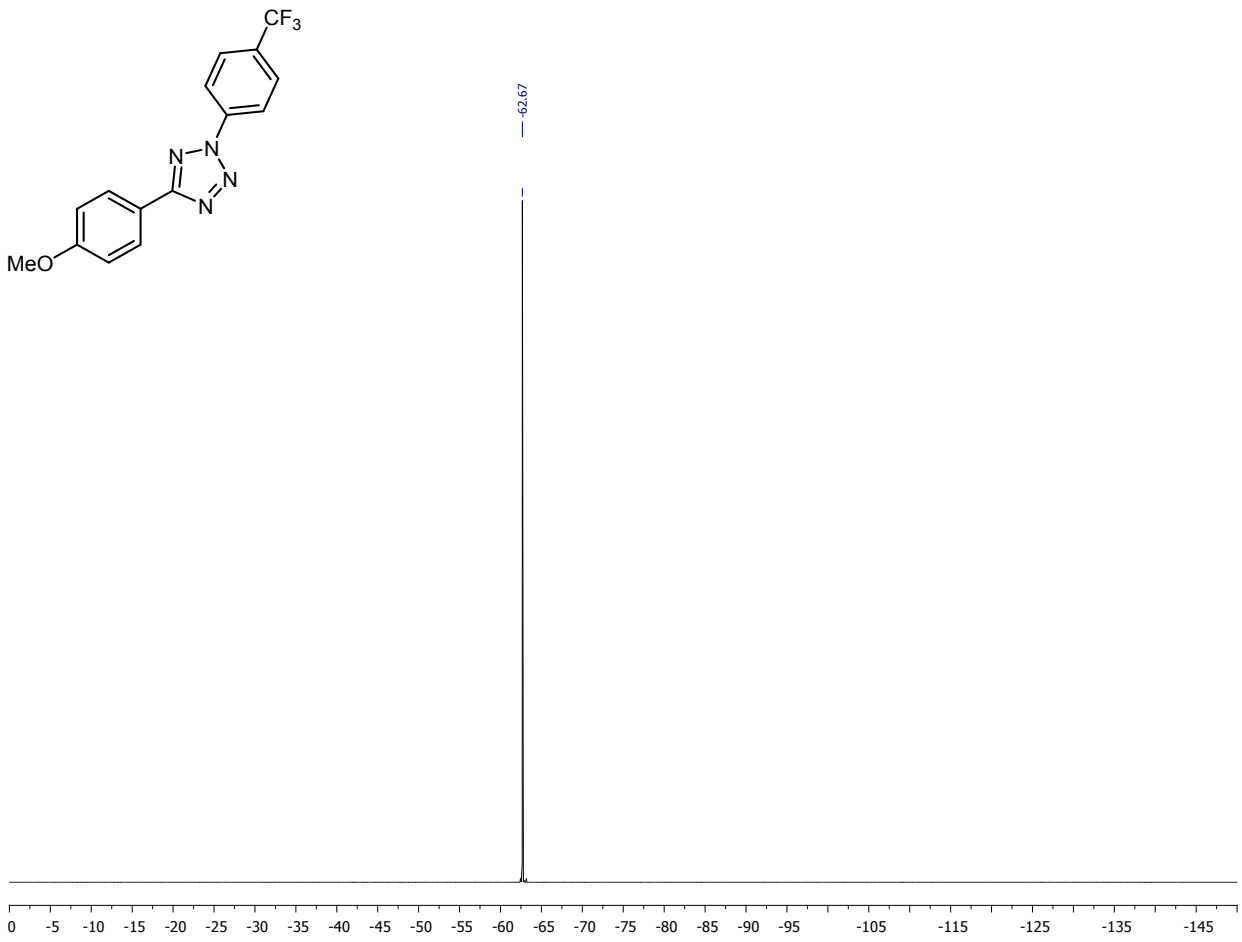
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
-95
-105
-115
-125
-135
-145

Compound S8, 5-(4-methoxyphenyl)-2-(4-(trifluoromethyl)phenyl)-2*H*-tetrazole



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MeO
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-45
-50
-55
-60
-65
-70
-75
-80
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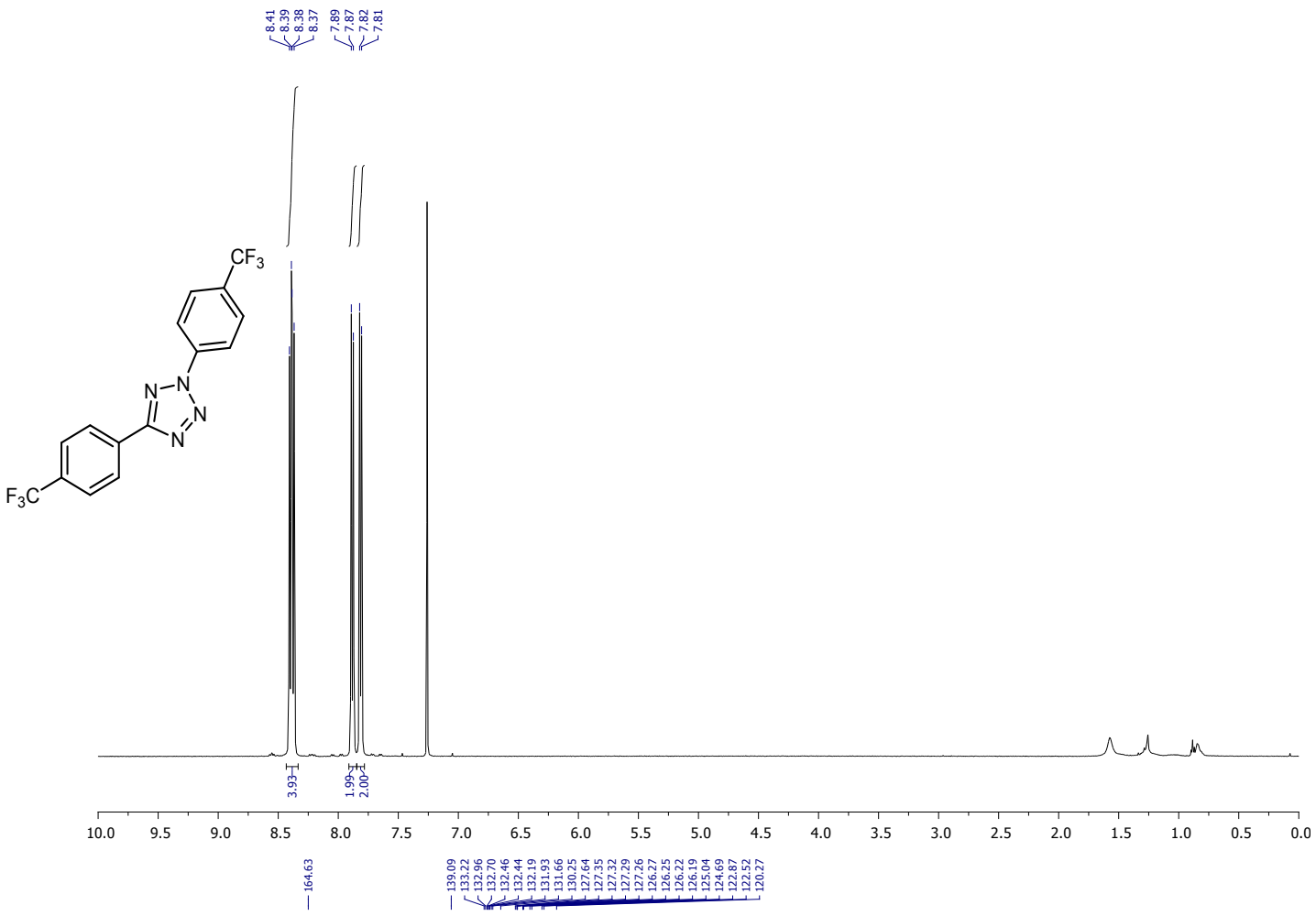
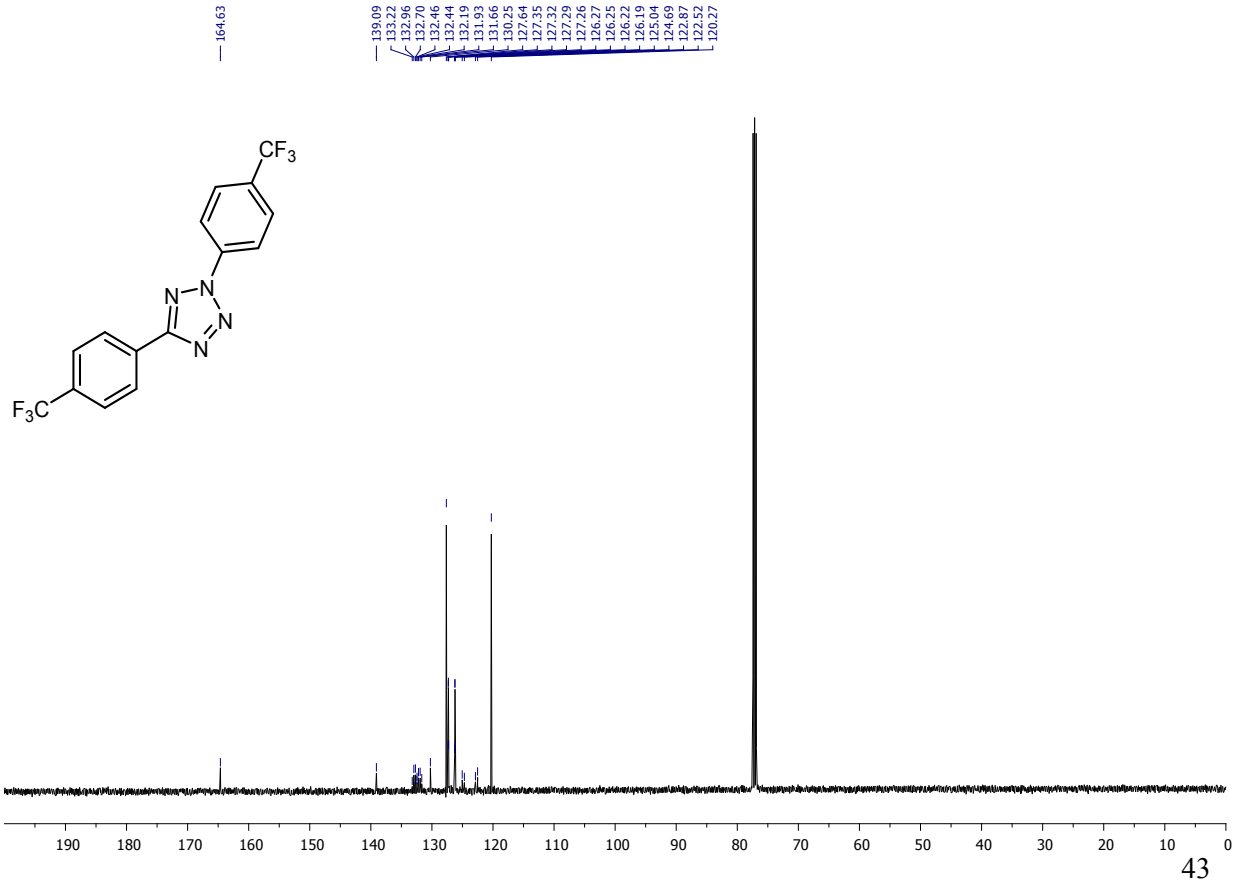
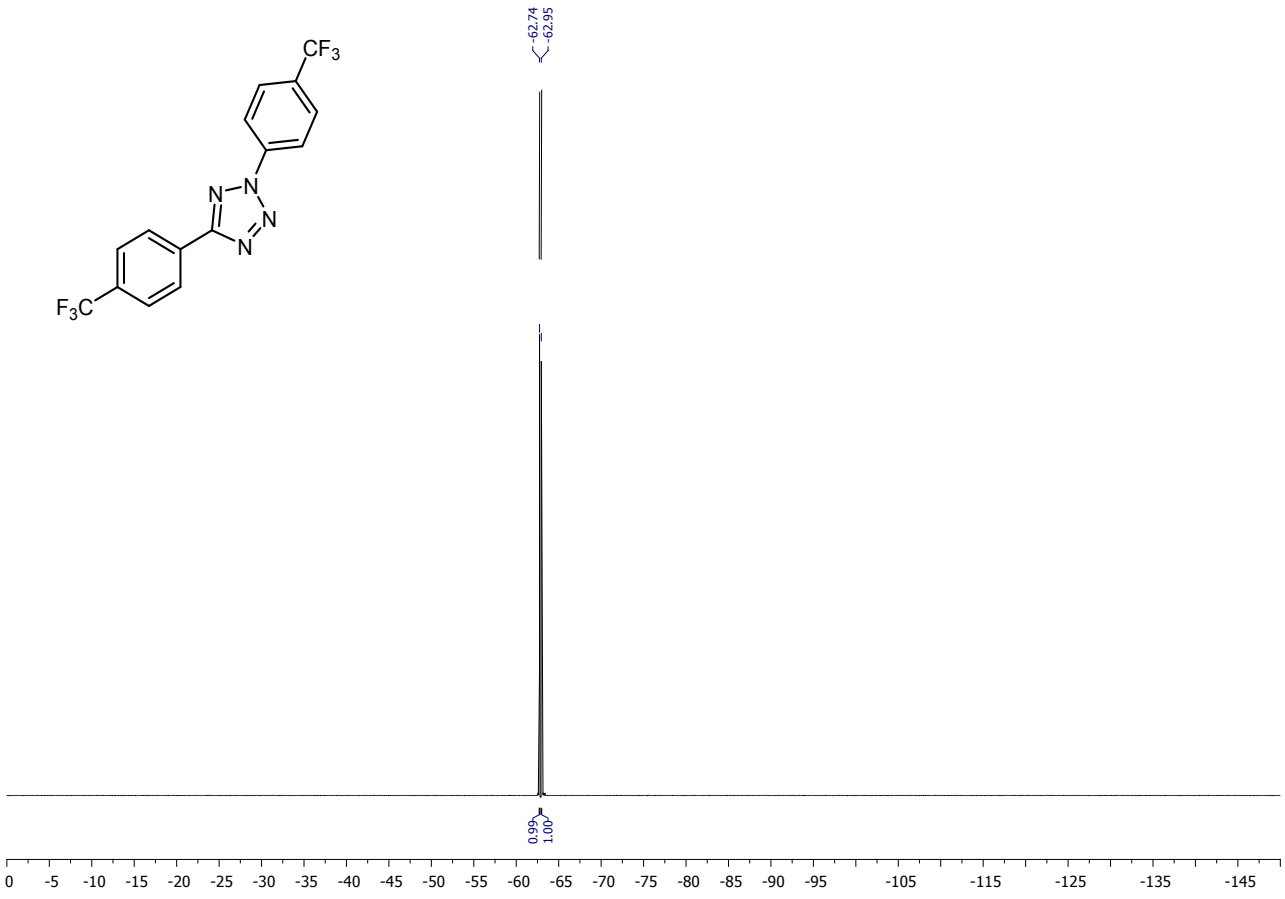
-115
-125
-135
-145

Compound S9, 2,5-*bis*(4-(trifluoromethyl)phenyl)-2*H*-tetrazole



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0
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-65
-70
-75
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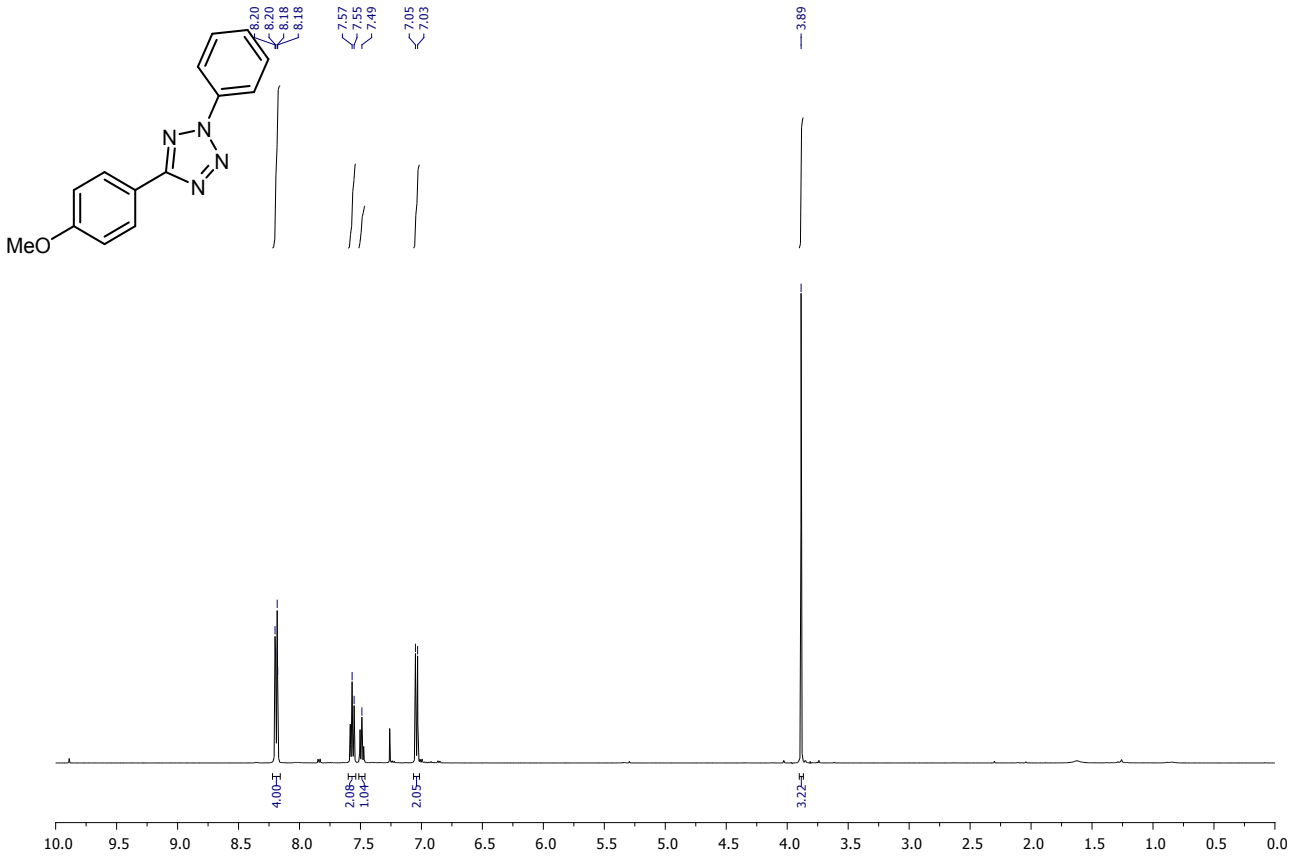
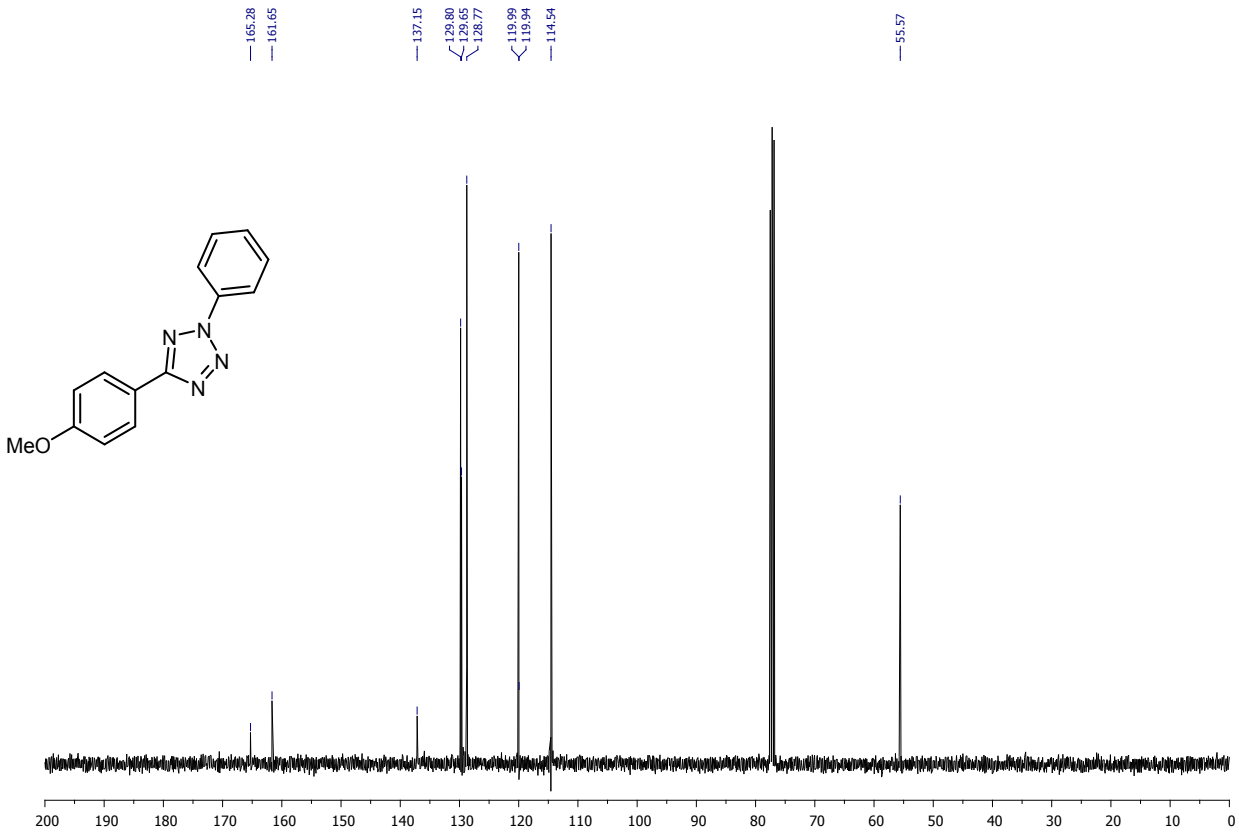
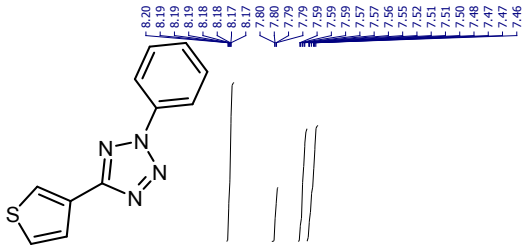
-145

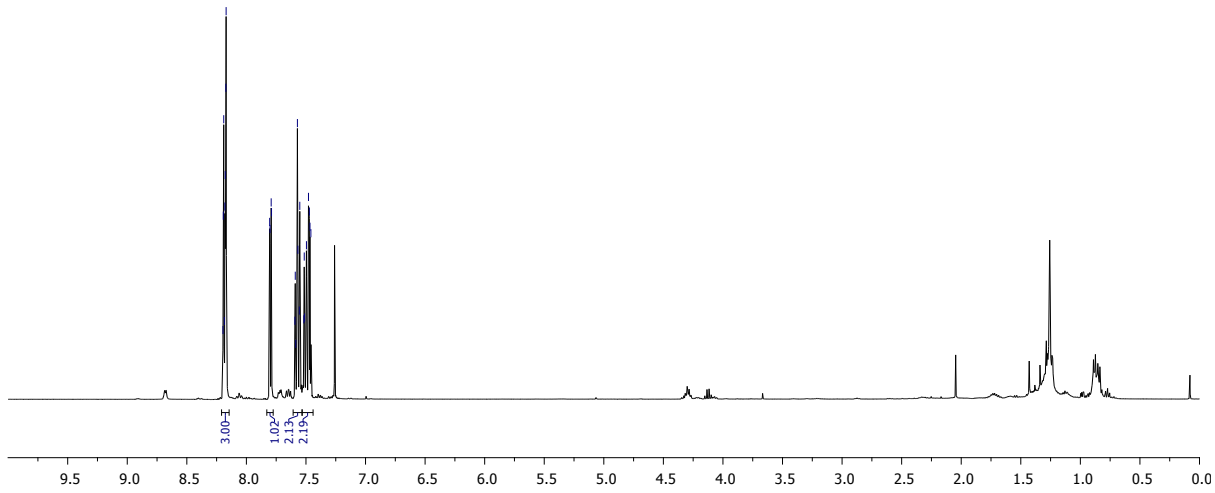
Compound S10, 5-(4-methoxyphenyl)-2-phenyl-2*H*-tetrazole

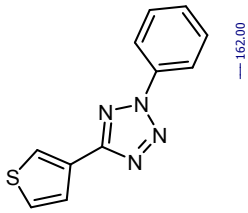


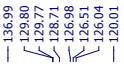


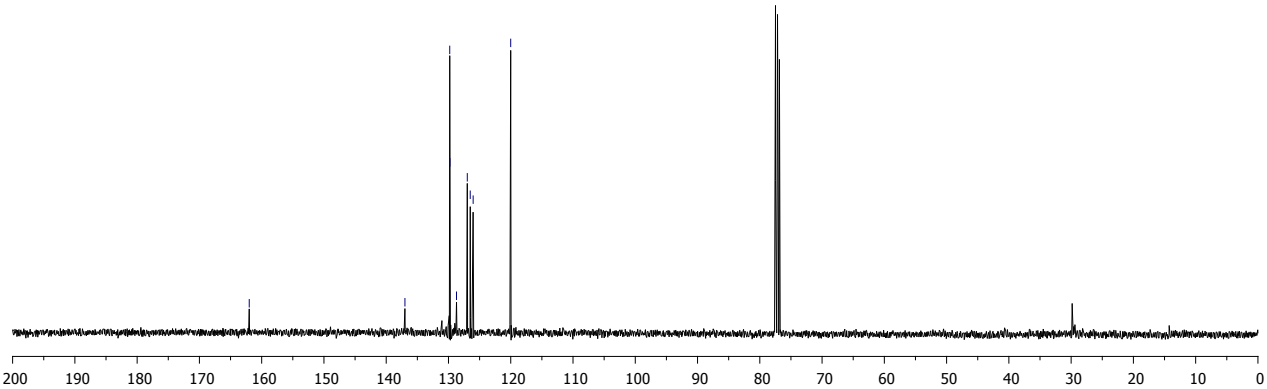
Compound S11, 2-phenyl-5-(thiophen-3-yl)-2*H*-tetrazole





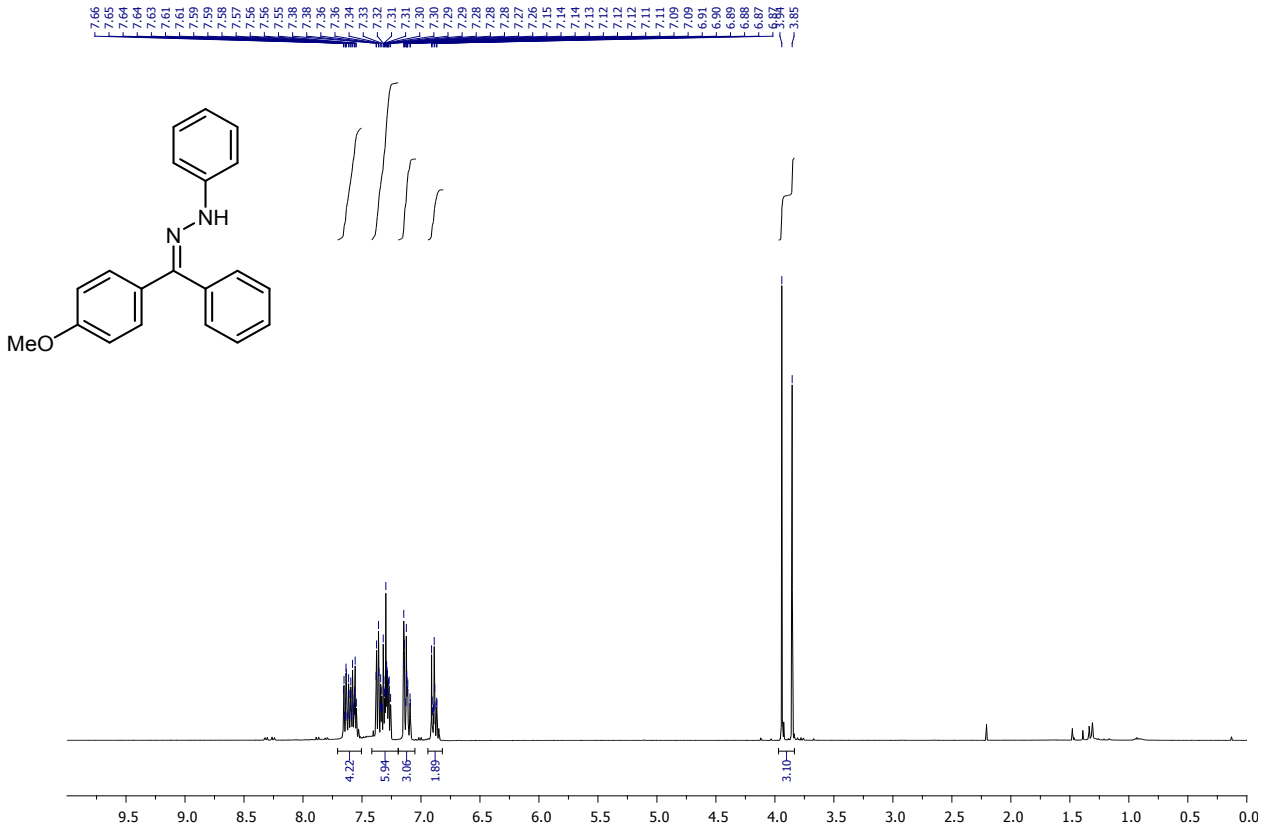


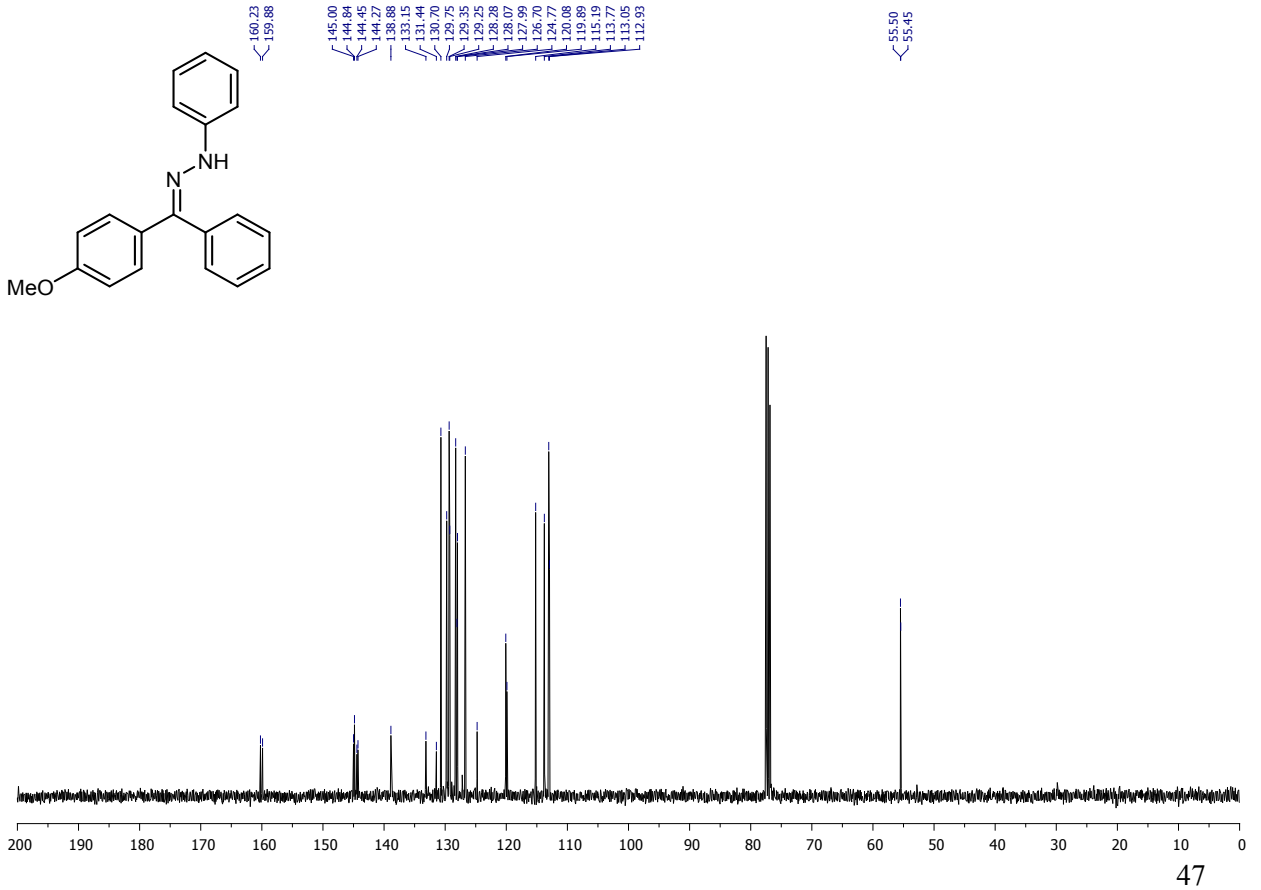




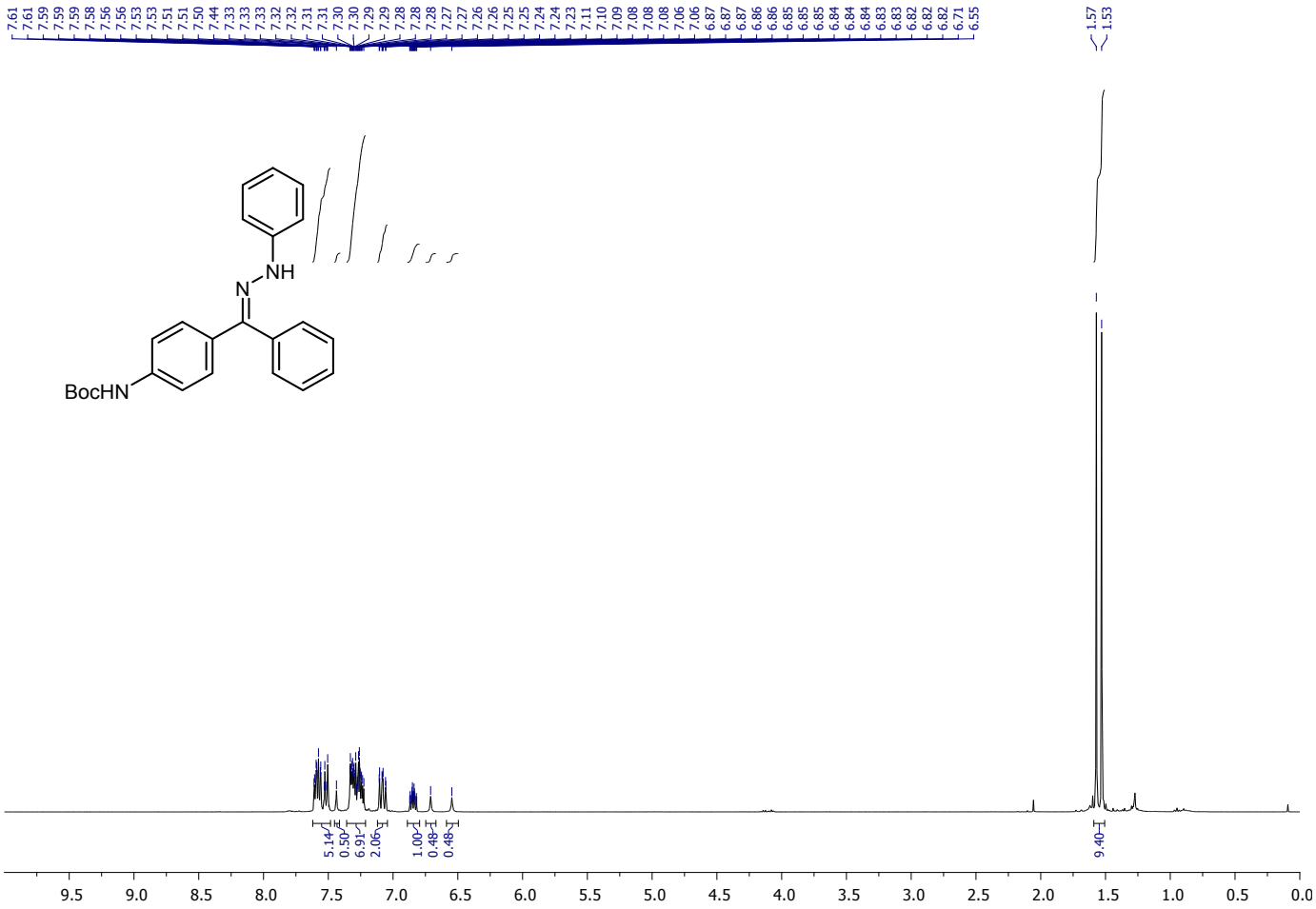
6.2 Ketone Hydrazones

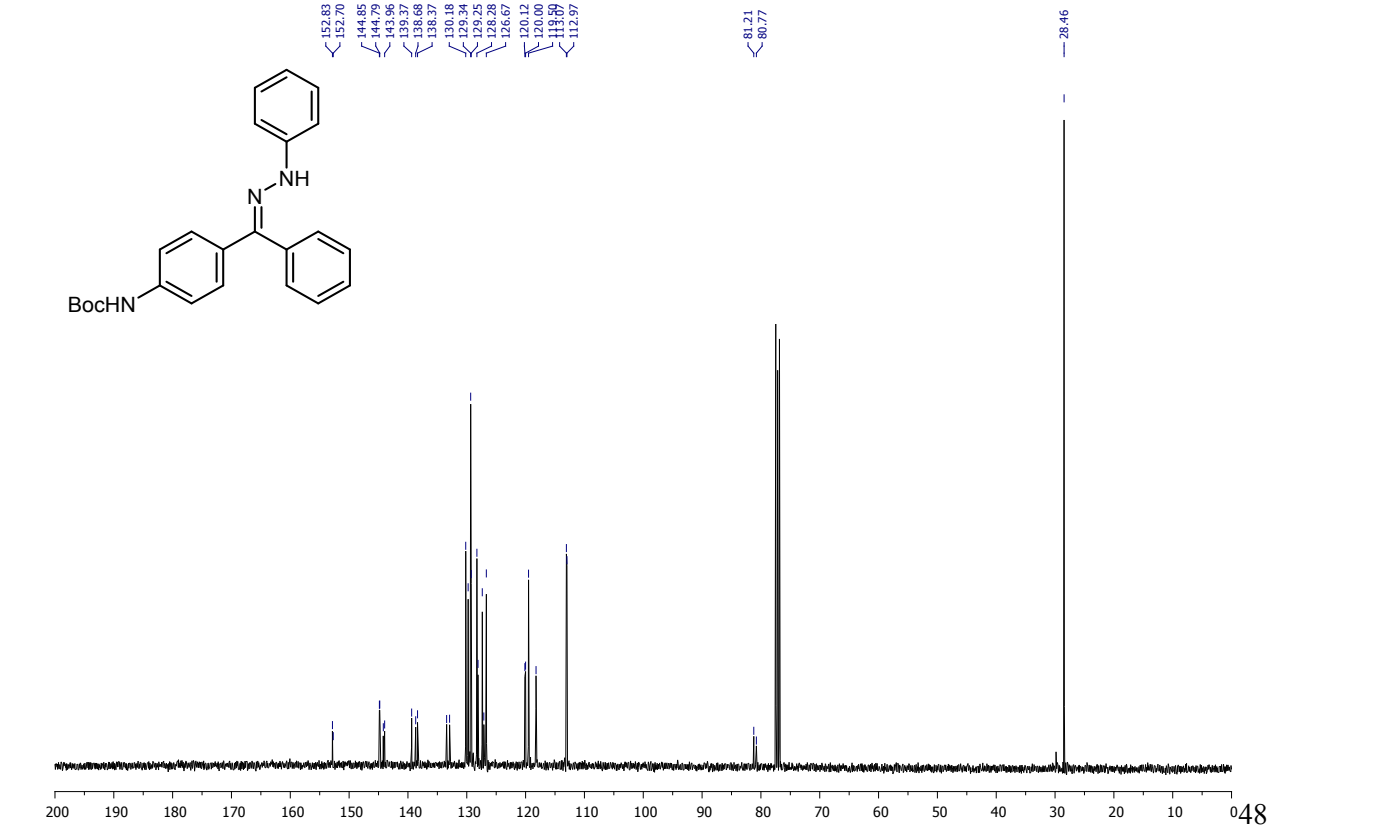
Compound 3b, 1-((4-methoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



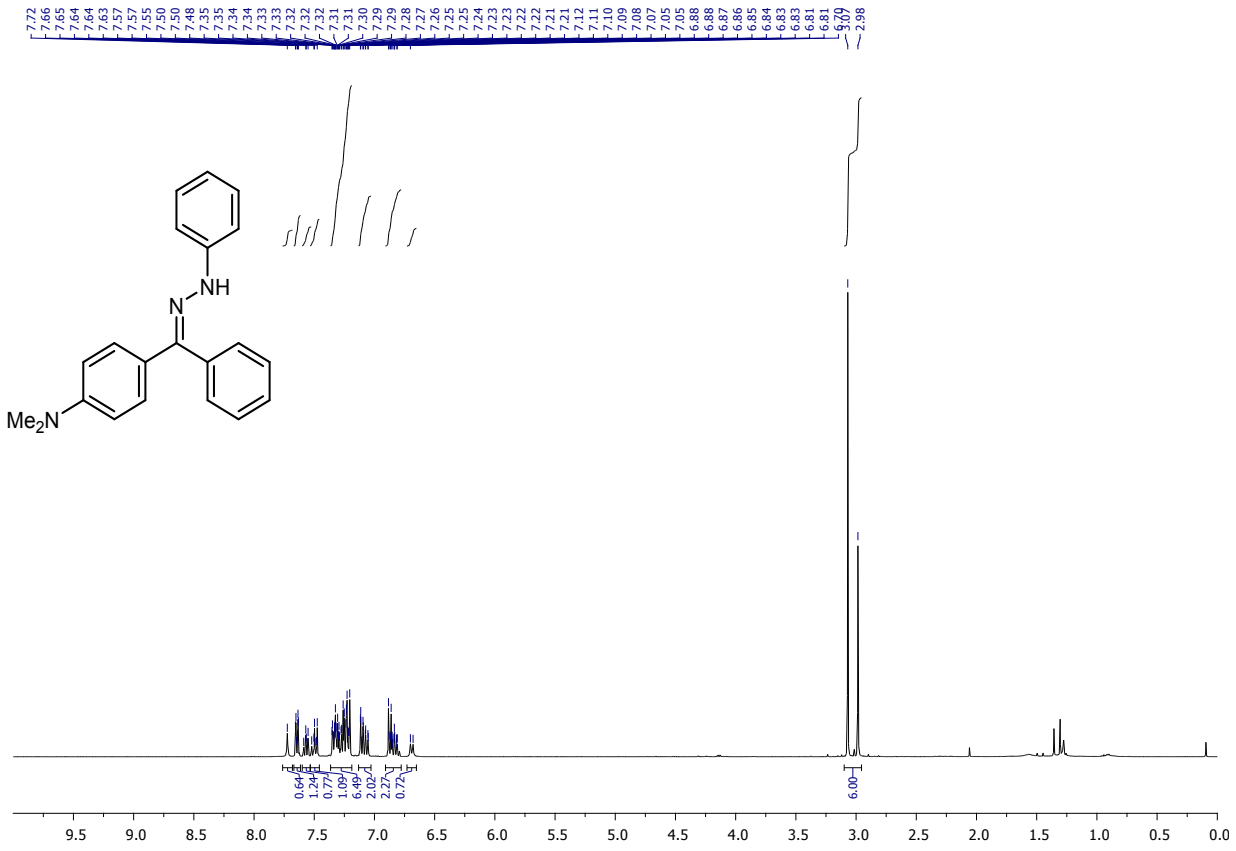


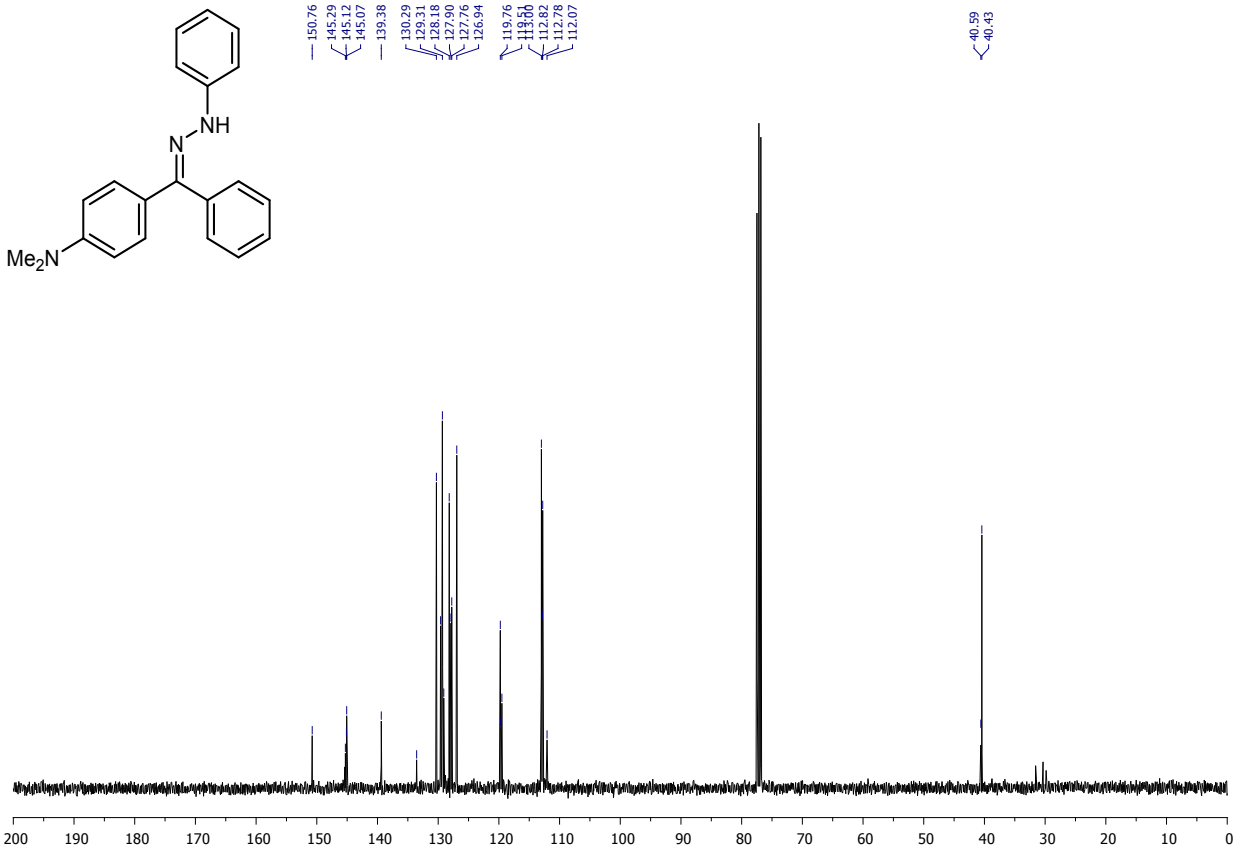
Compound 3c, *tert*-butyl (4-(phenyl(2-phenylhydrazono)methyl)phenyl)carbamate



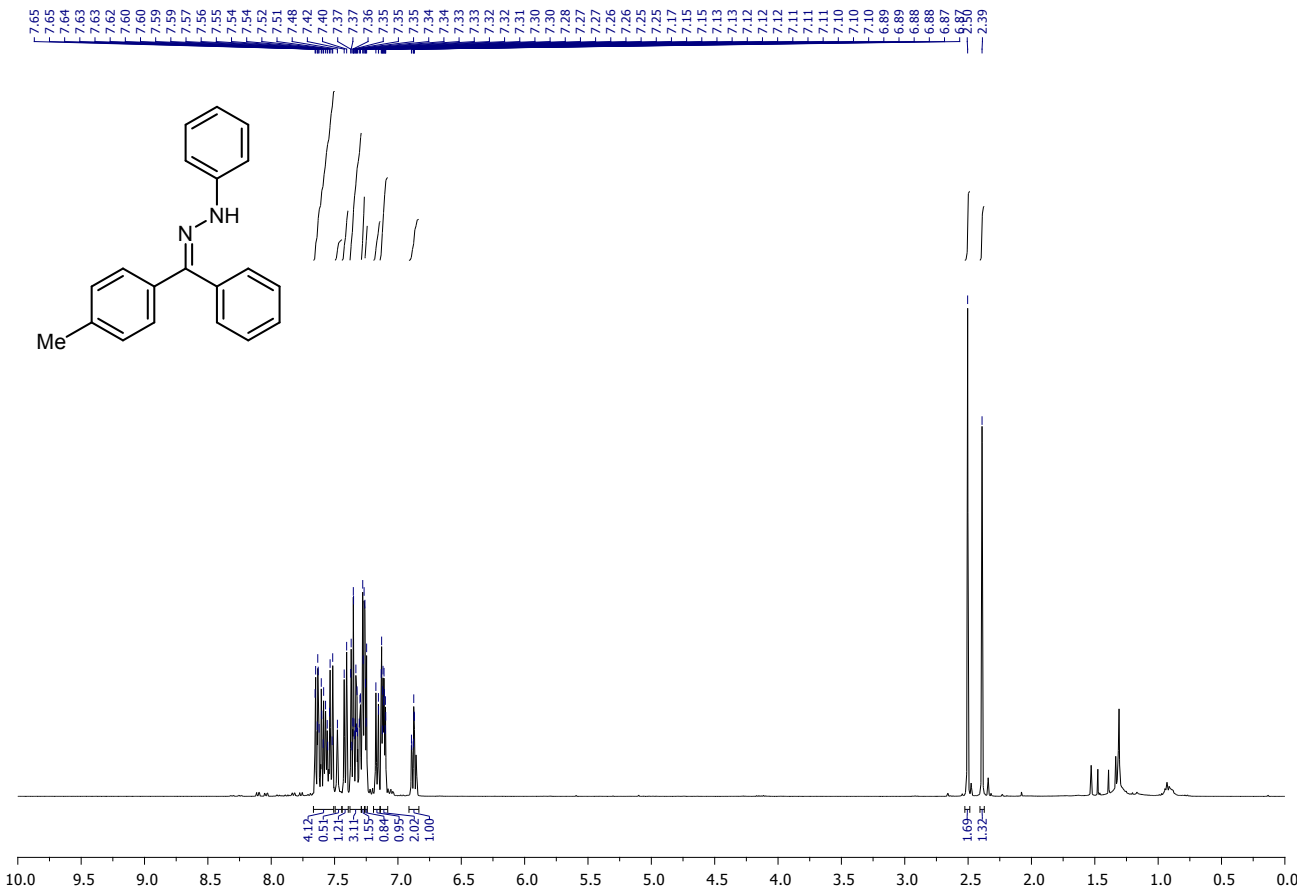


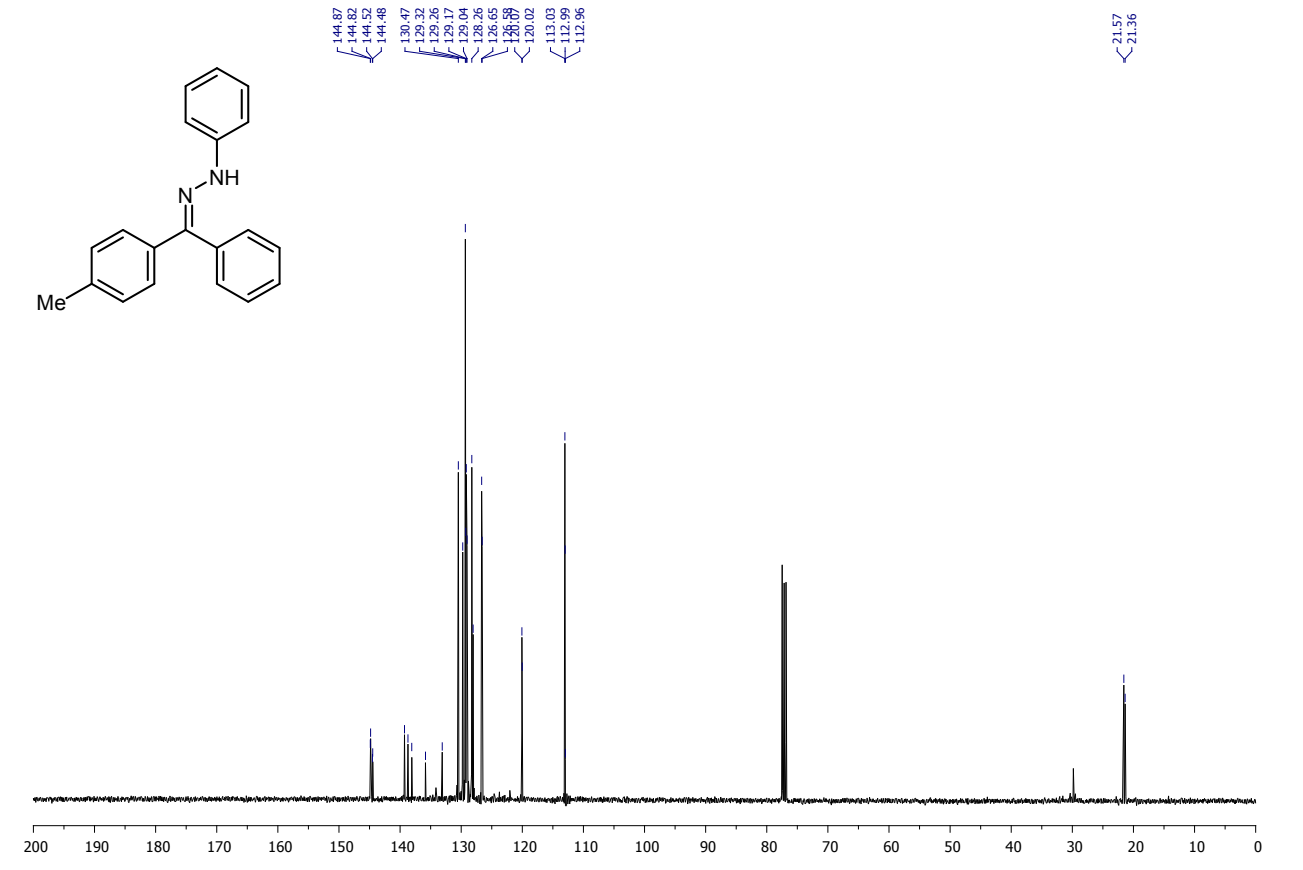
Compound 3d, *N*,*N*-dimethyl-4-(phenyl(2-phenylhydrazono)methyl)aniline



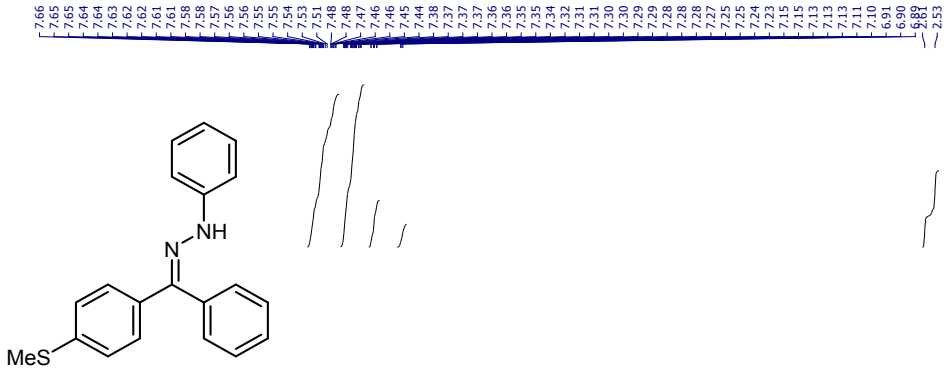


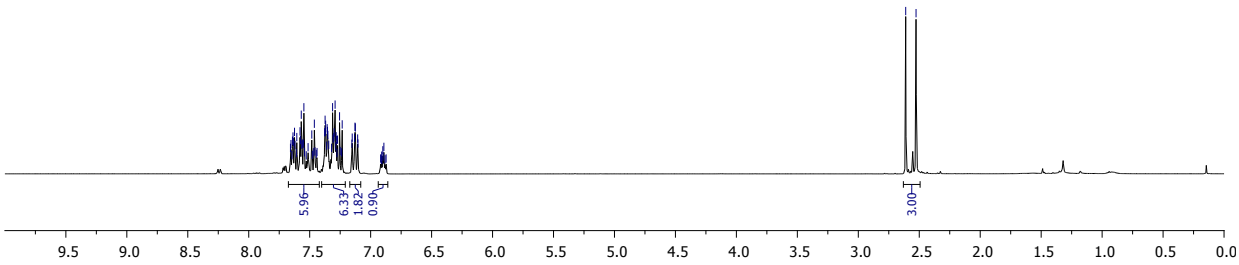
Compound 3e, 1-phenyl-2-(phenyl(*p*-tolyl)methylene)hydrazine

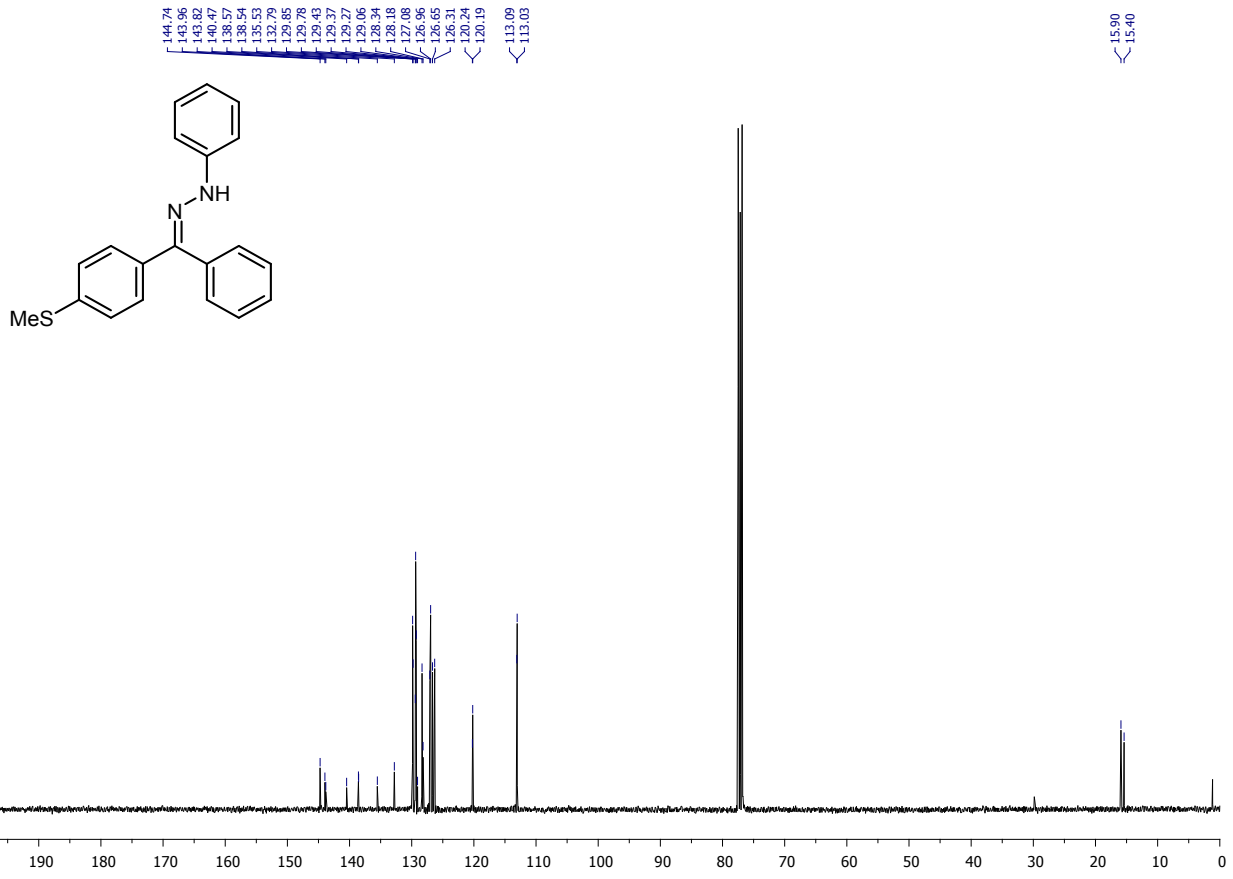




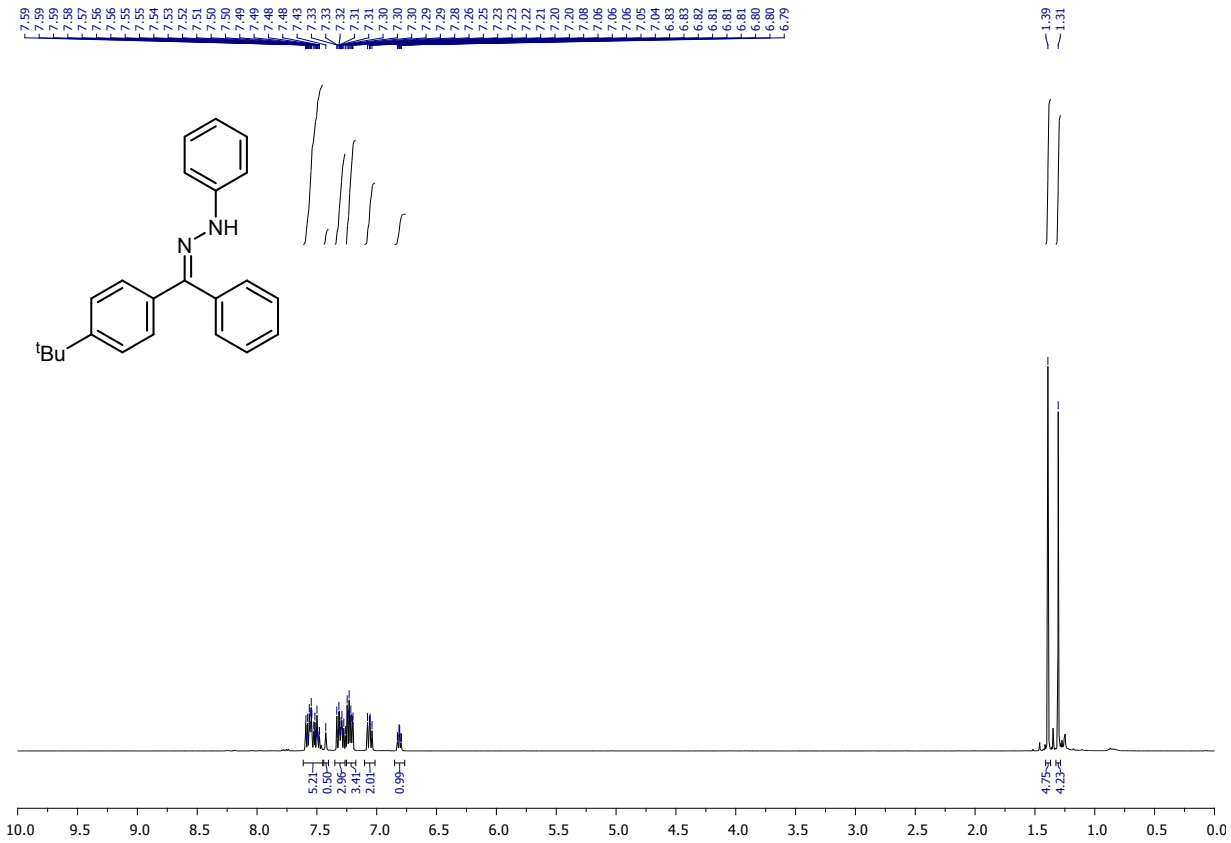
Compound 3f, 1-((4-(methylthio)phenyl)(phenyl)methylene)-2-phenylhydrazine

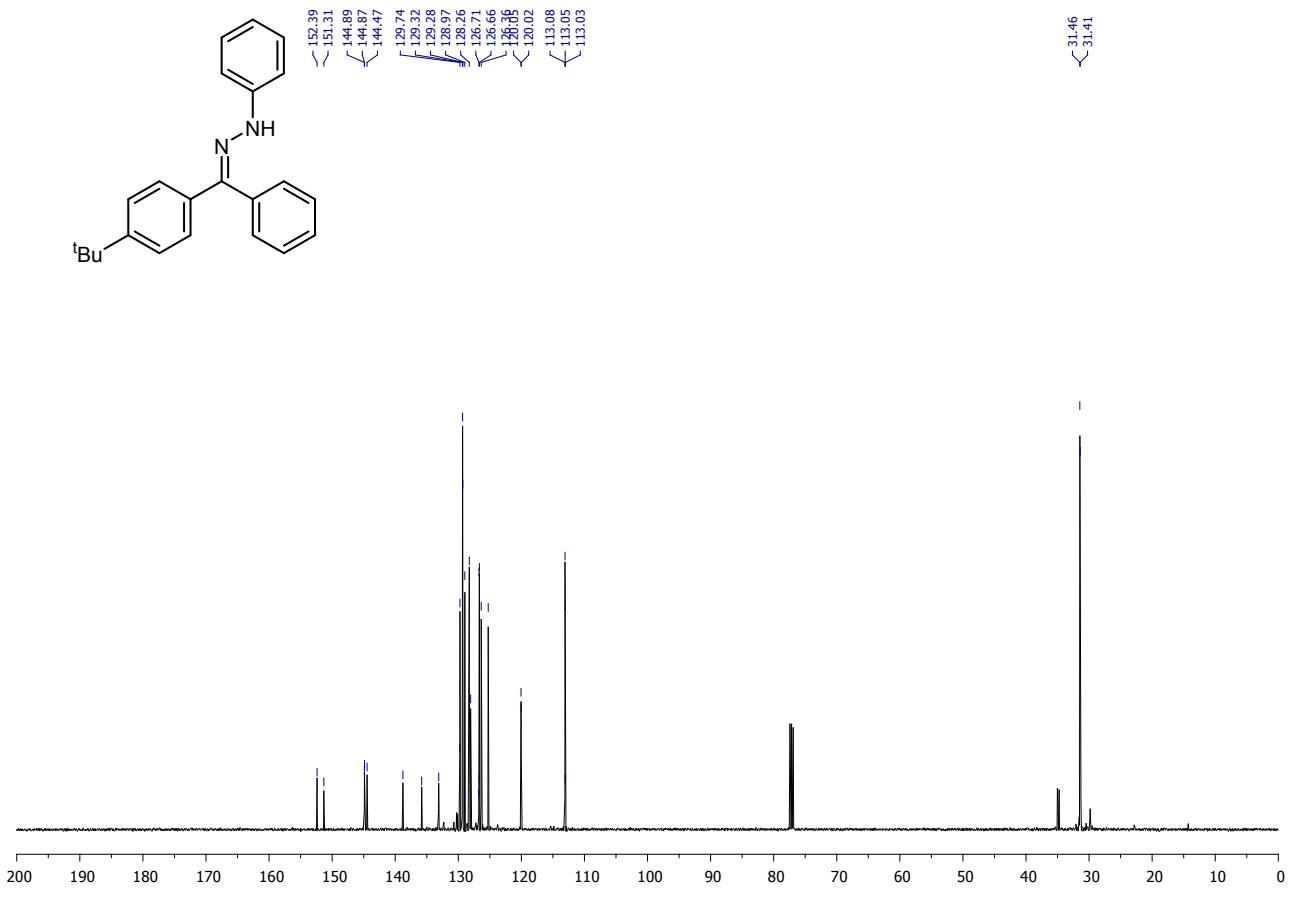




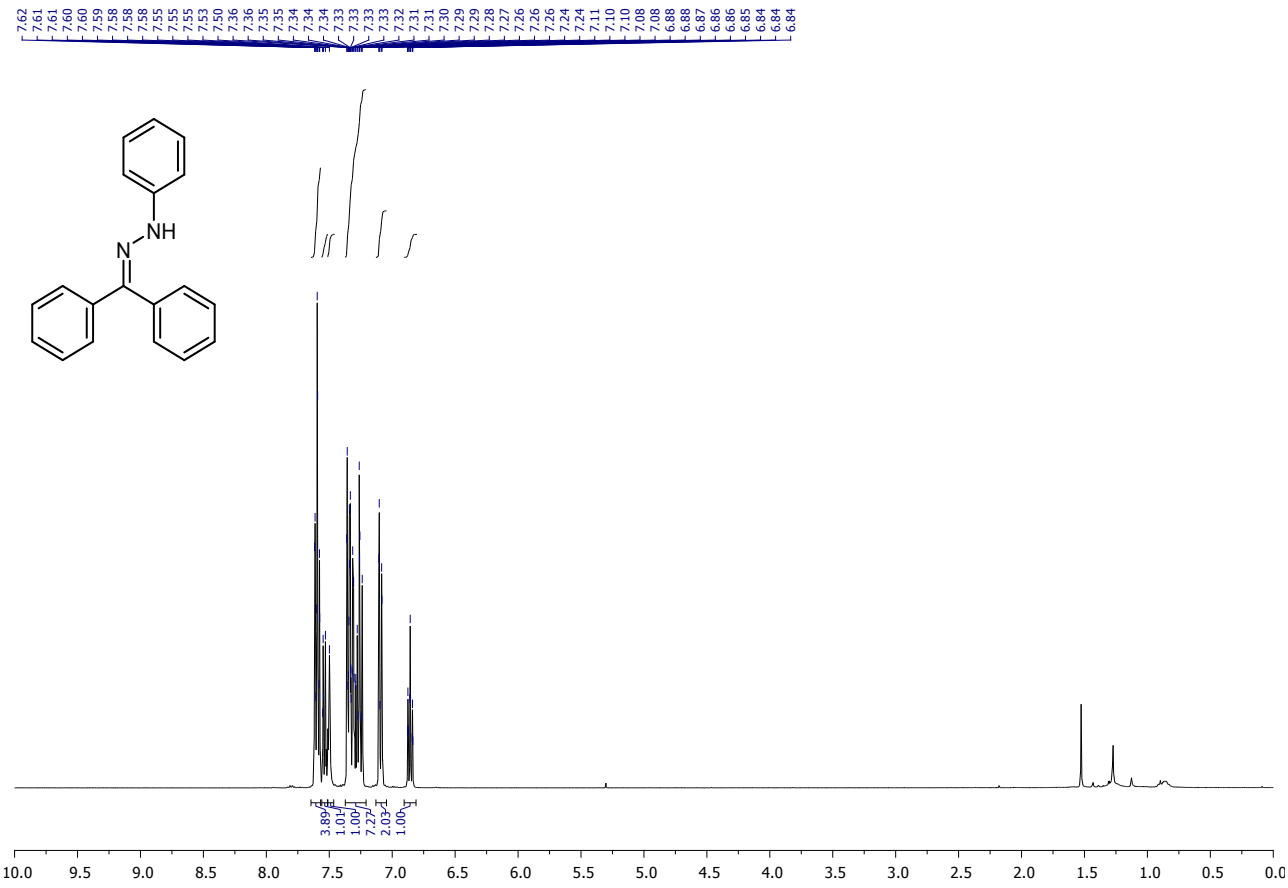


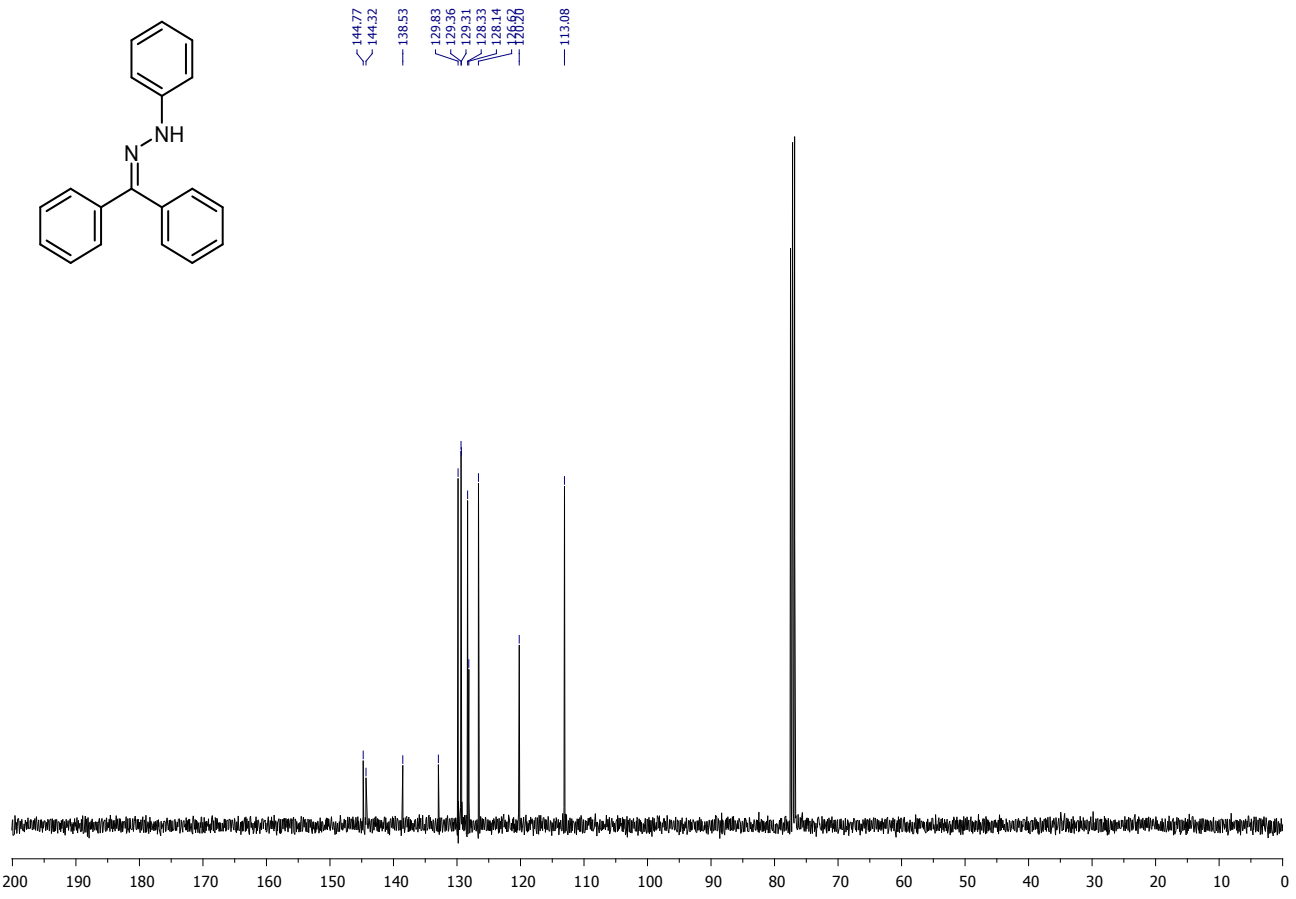
Compound 3g, 1-((4-(*tert*-butyl)phenyl)(phenyl)methylene)-2-phenylhydrazine



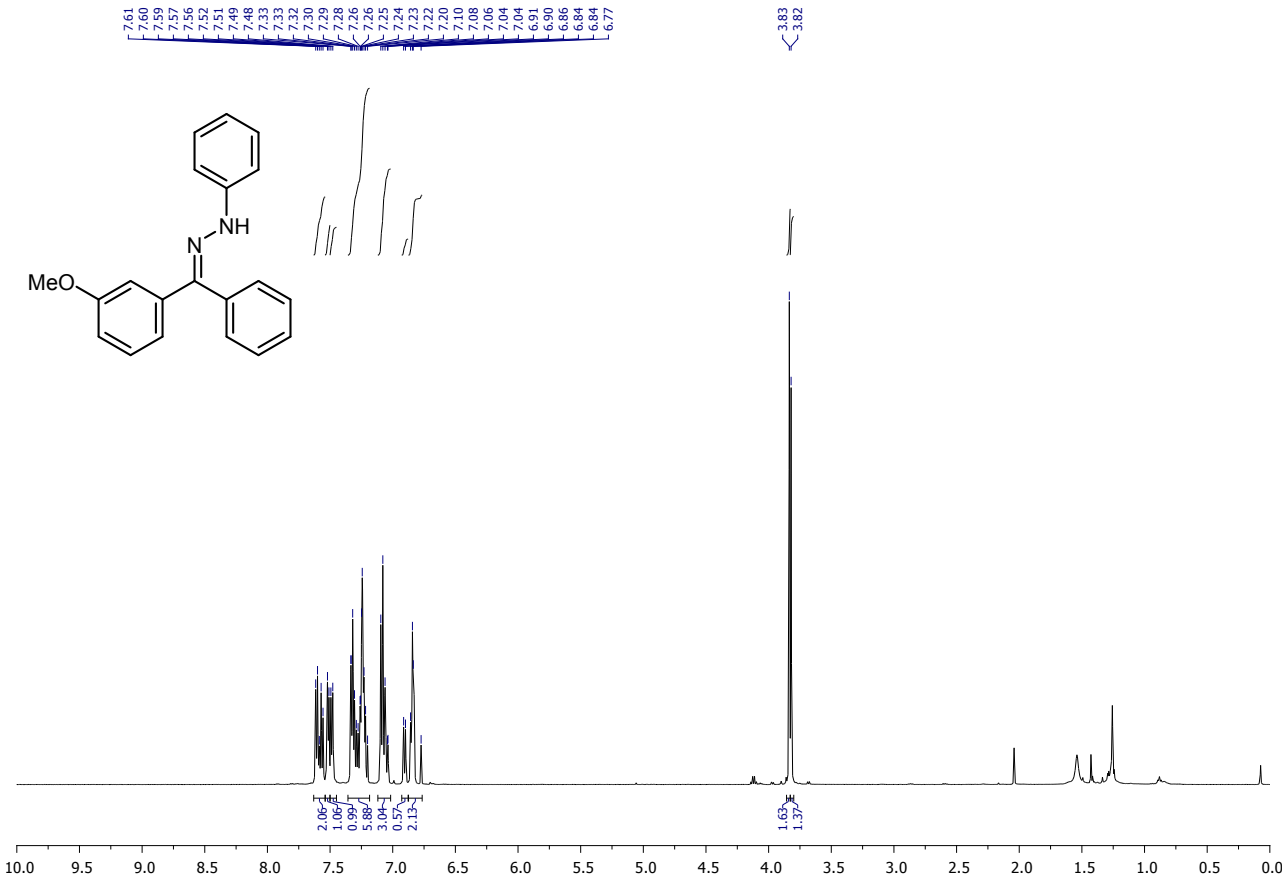


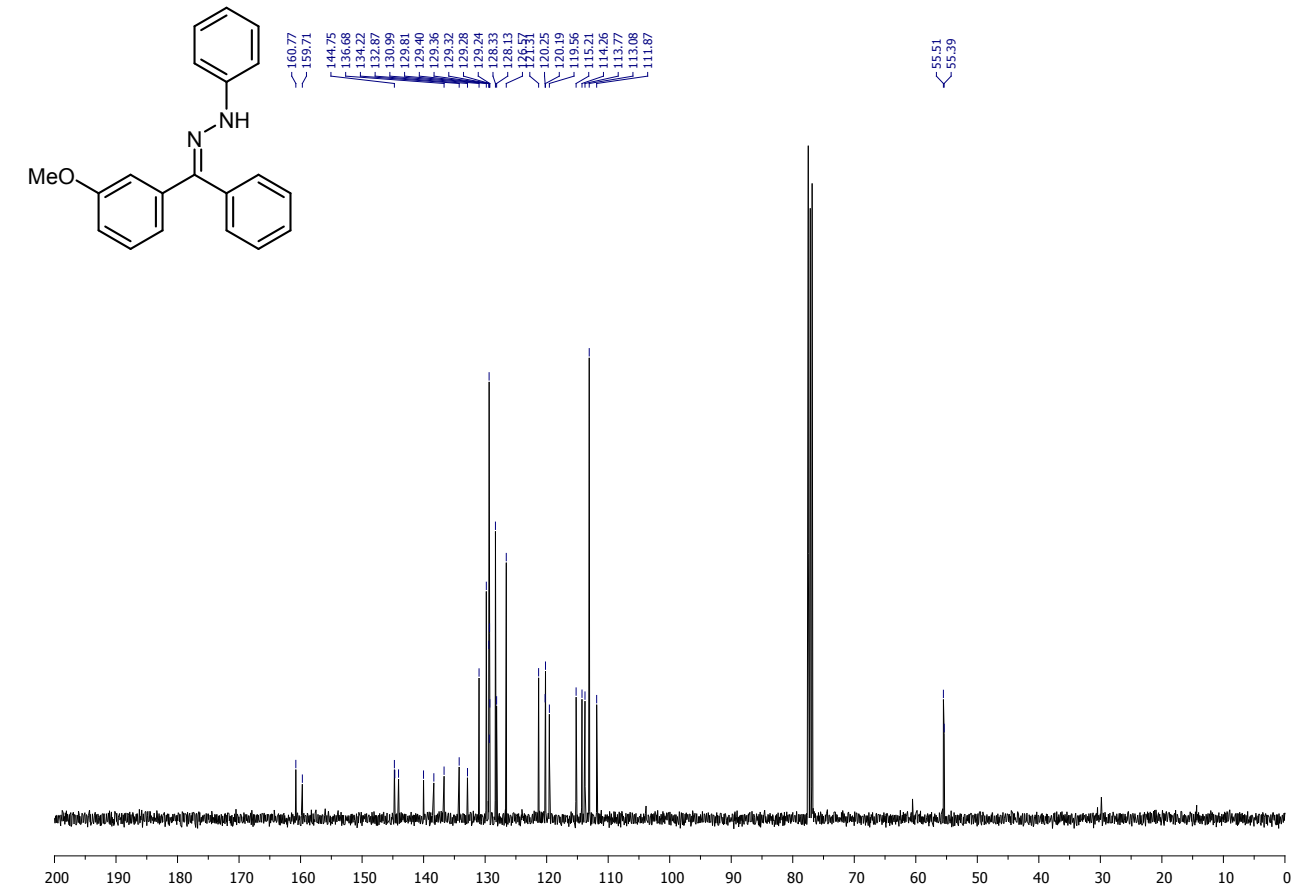
Compound 3h, 1-(diphenylmethylene)-2-phenylhydrazine



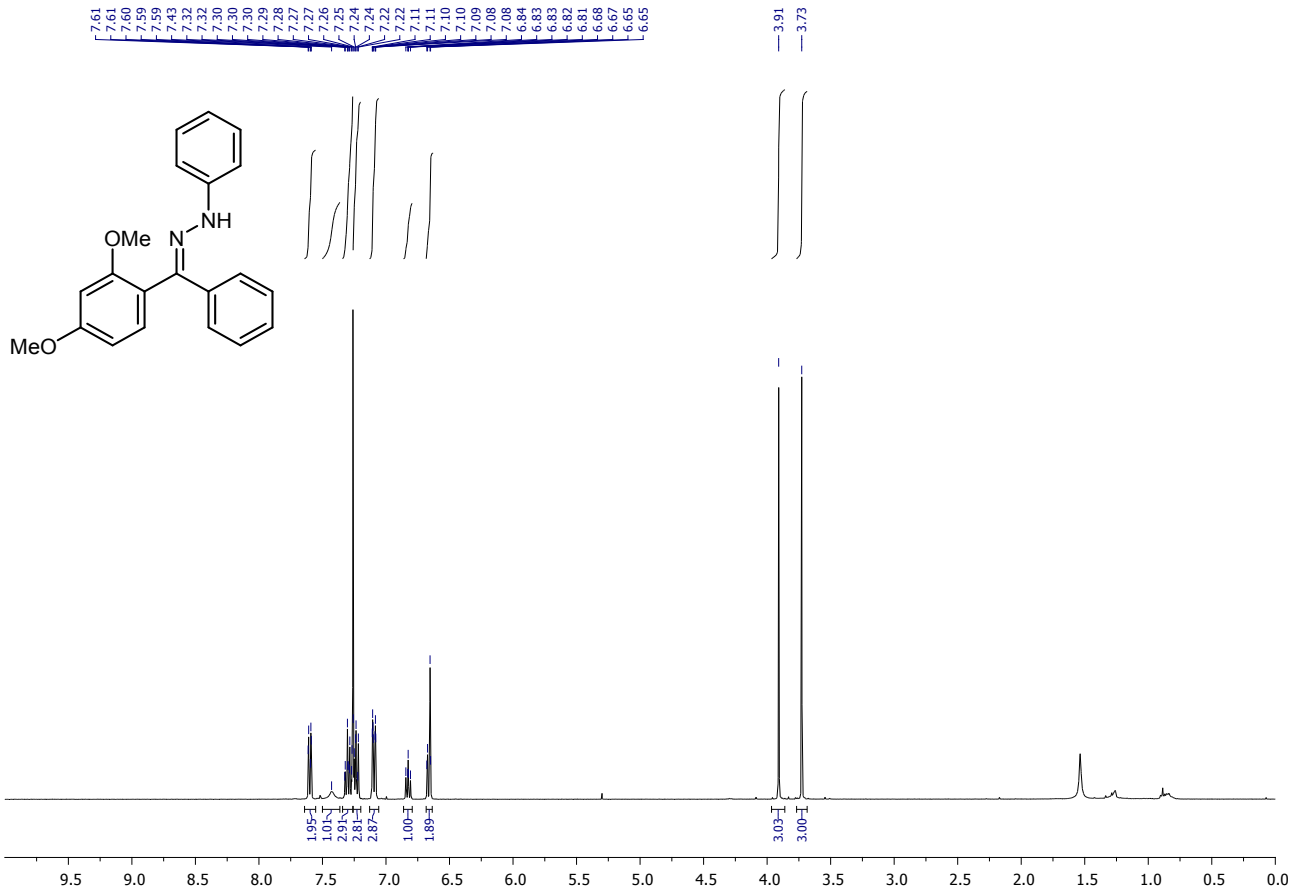


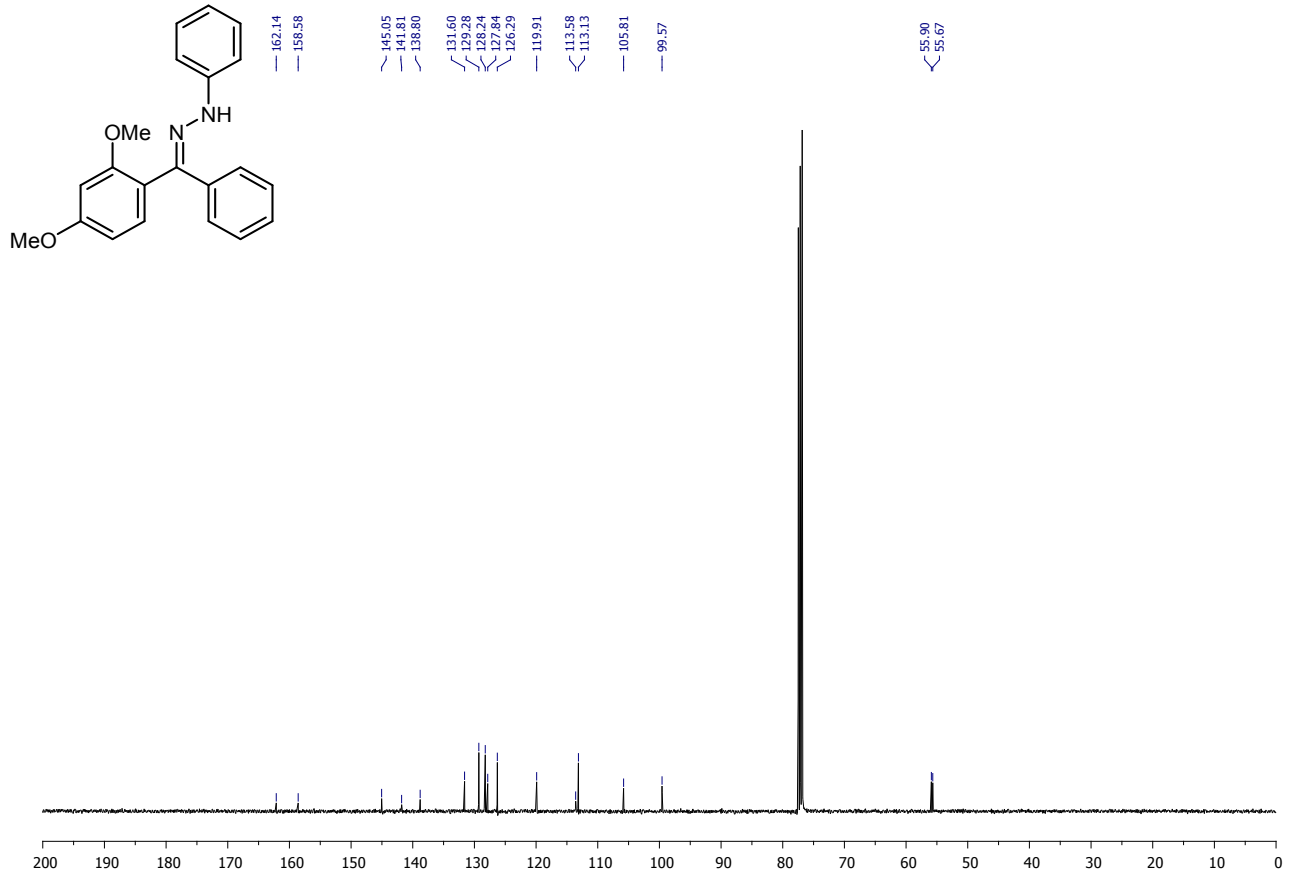
Compound 3i, 1-((3-methoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



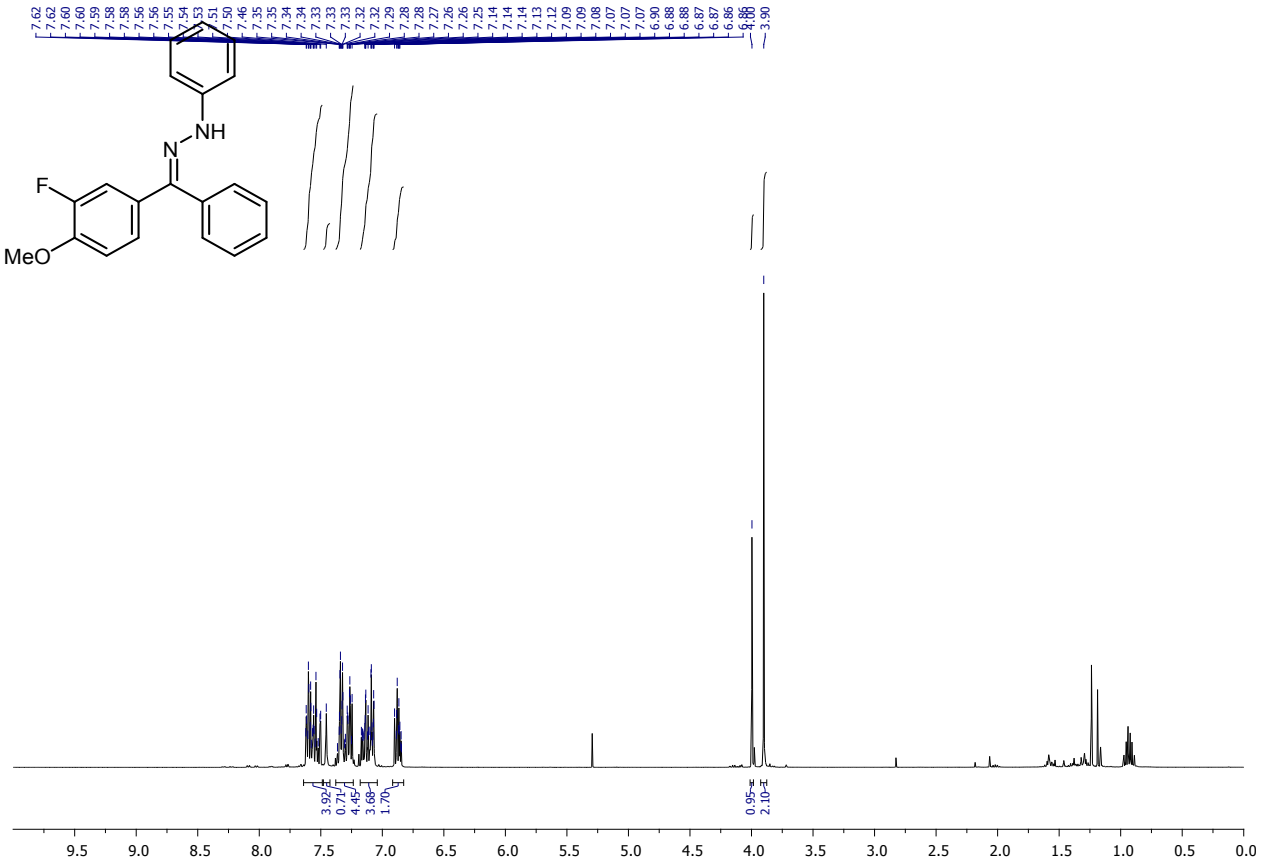


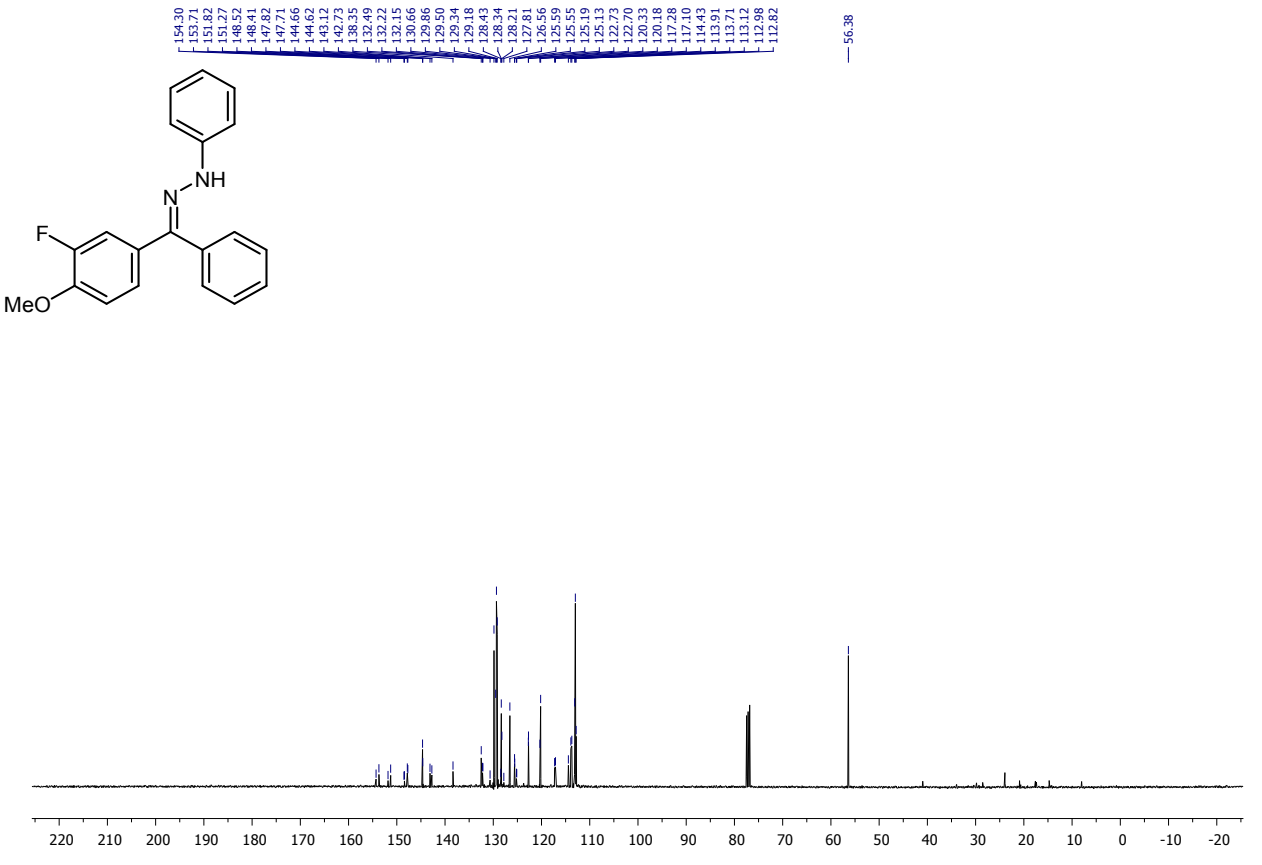
Compound 3j, 1-((2,4-dimethoxyphenyl)(phenyl)methylene)-2-phenylhydrazine

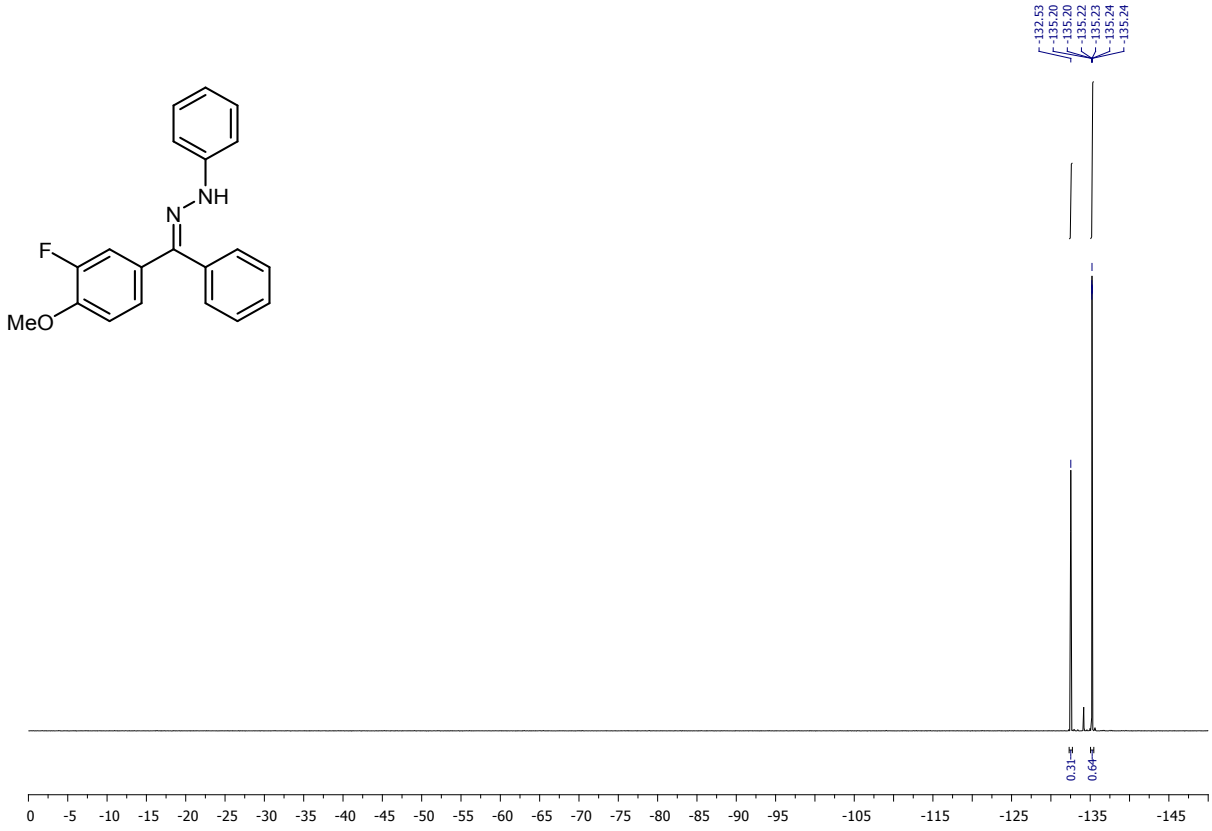




Compound 3k, 1-((3-fluoro-4-methoxyphenyl)(phenyl)methylene)-2-phenylhydrazine



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-135.24
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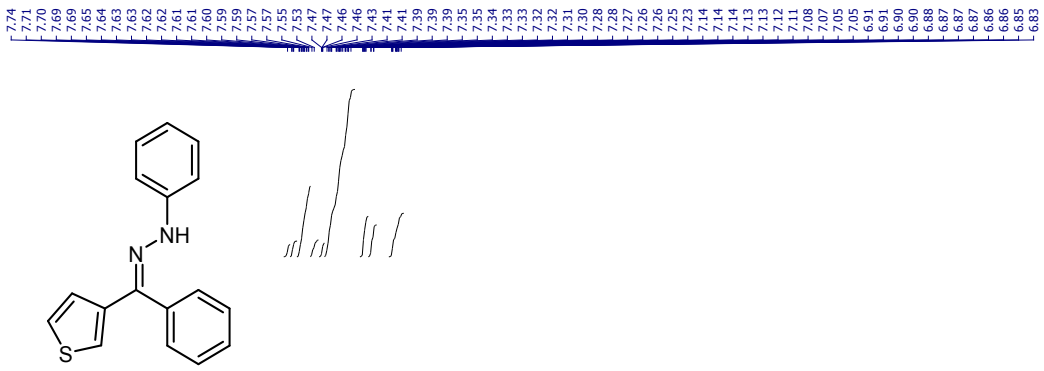
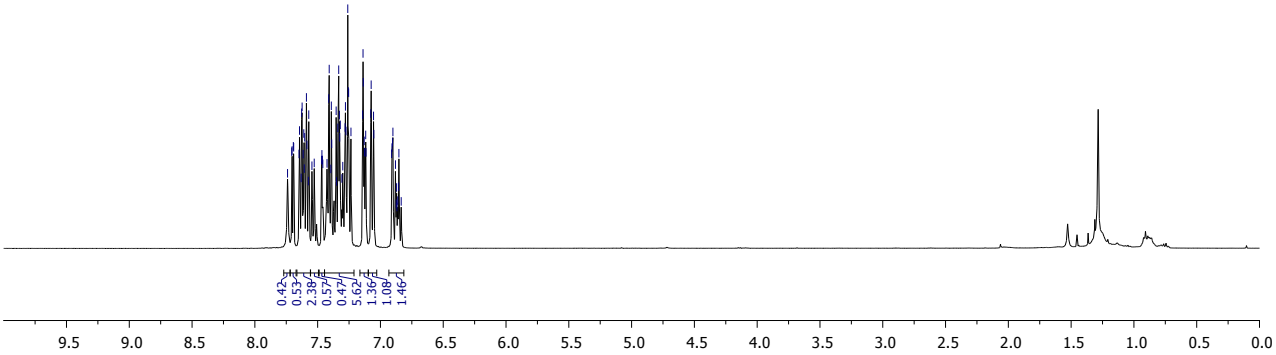
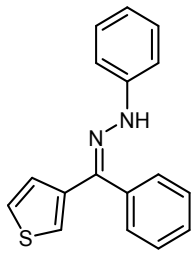
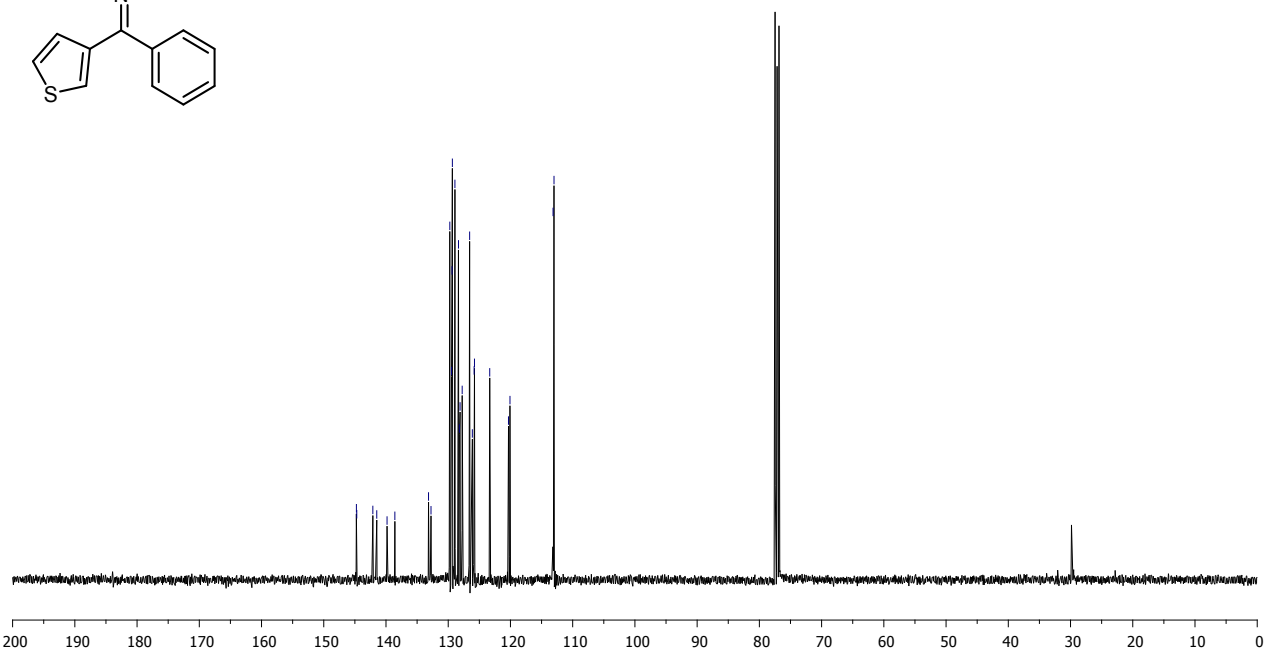
F
MeO
0.31
0.64
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145

Compound 3l, 1-phenyl-2-(phenyl(thiophen-3-yl)methylene)hydrazine

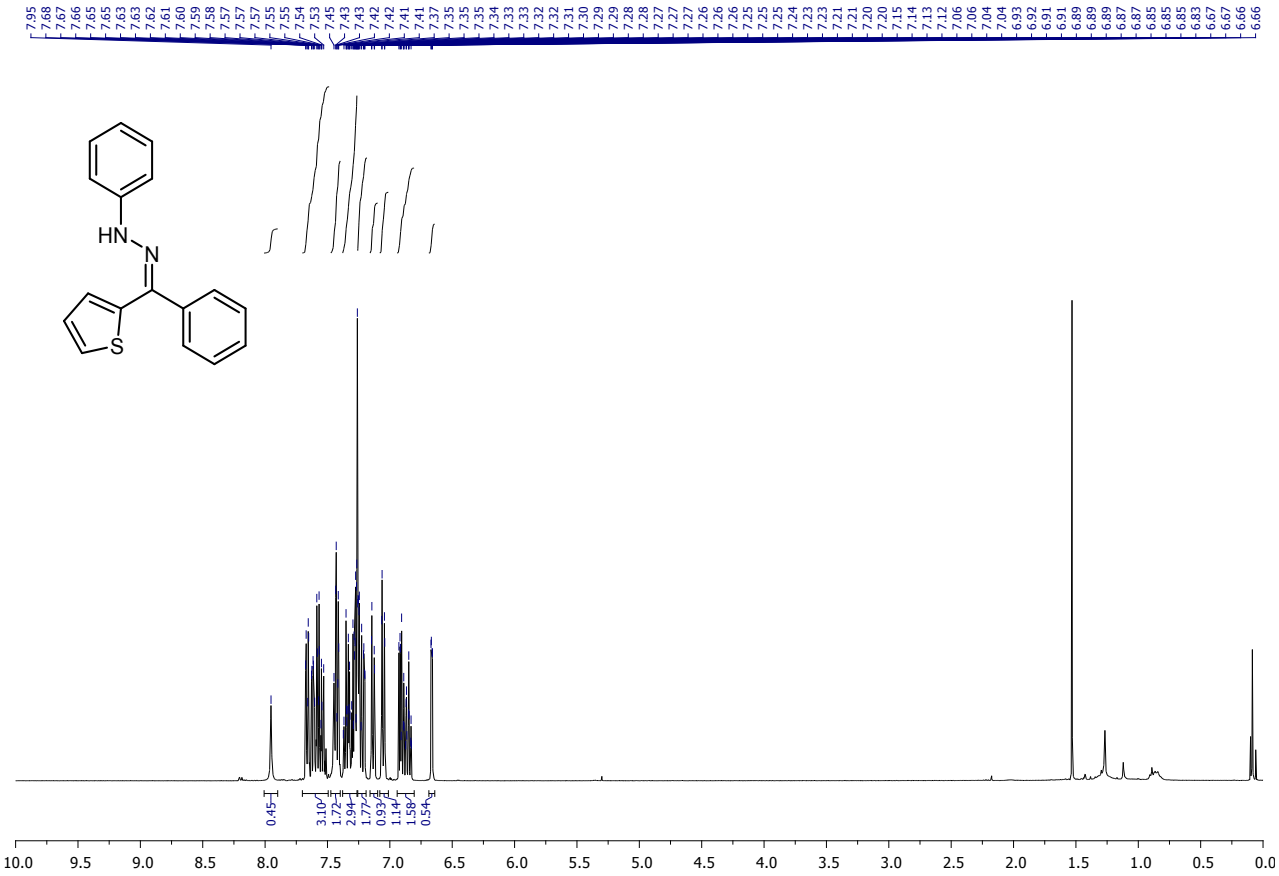


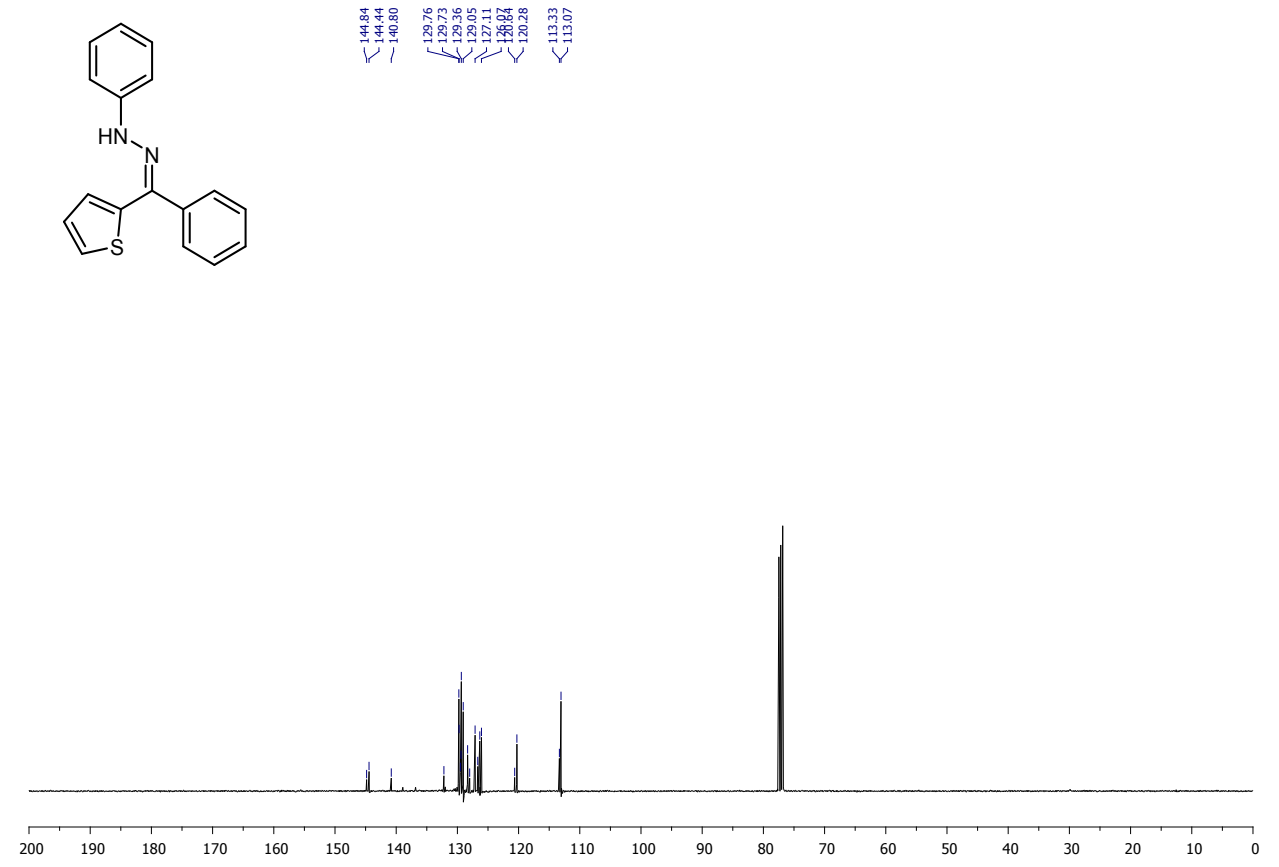




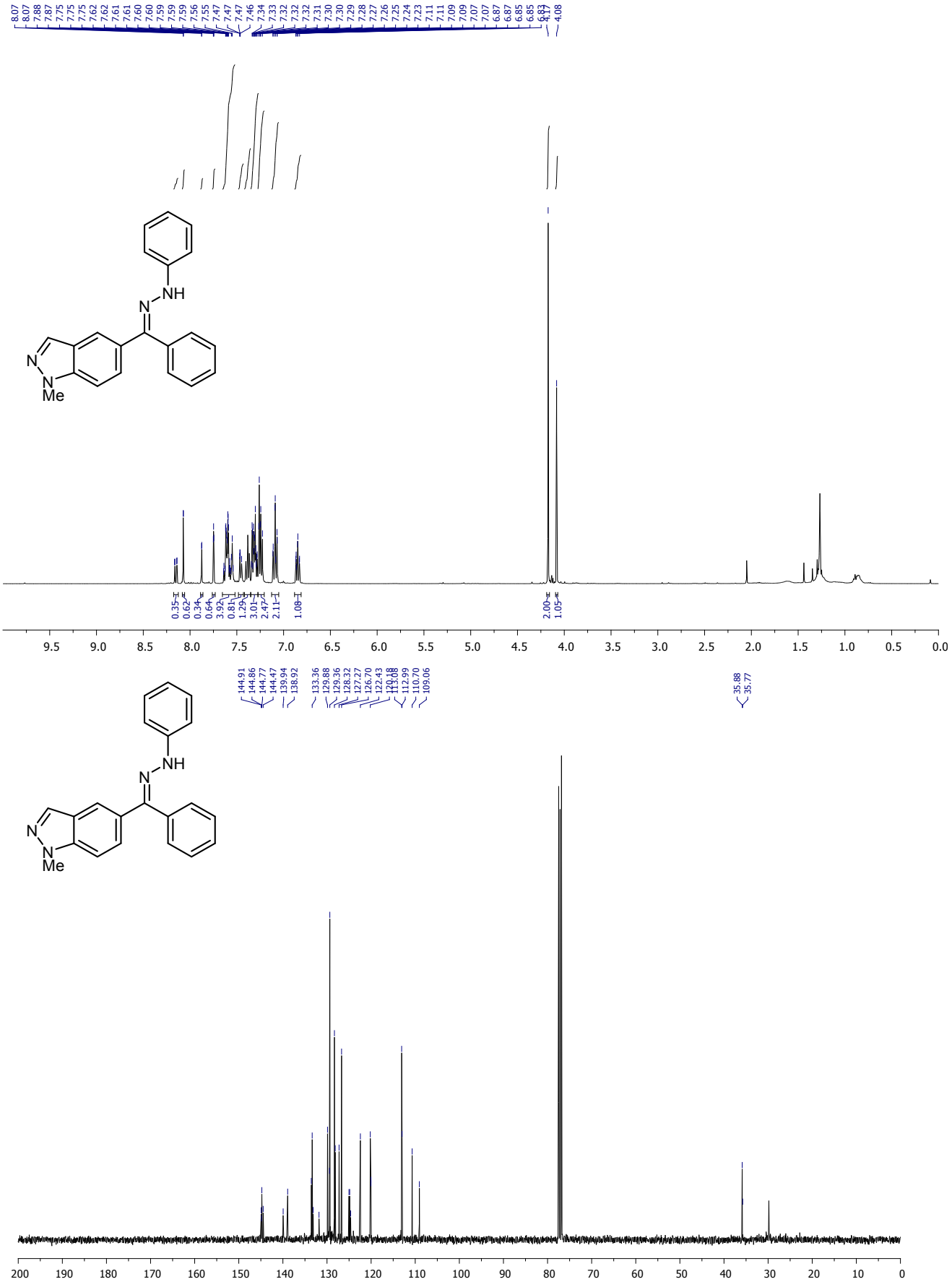


Compound 3m, 1-phenyl-2-(phenyl(thiophen-2-yl)methylene)hydrazine

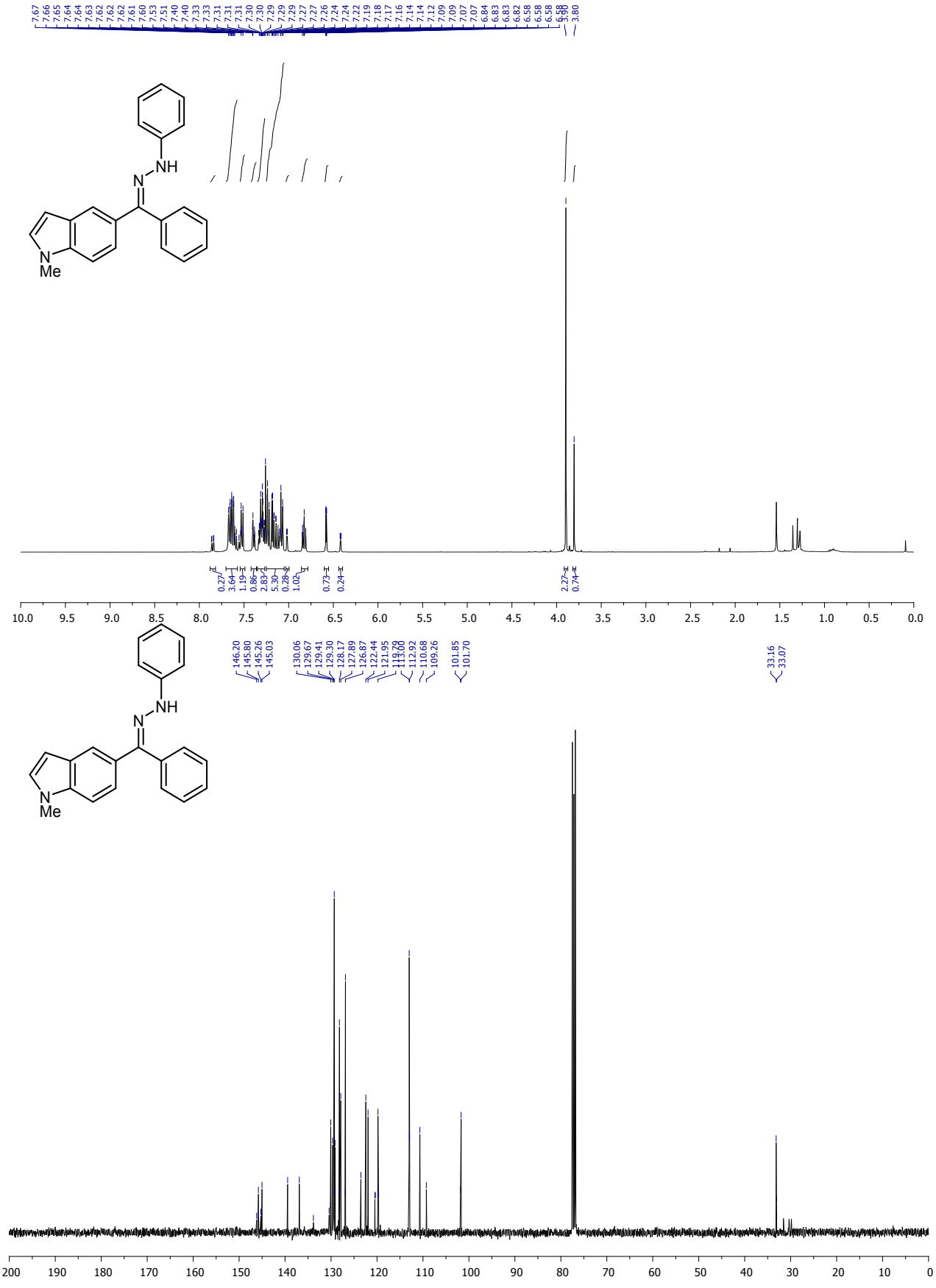




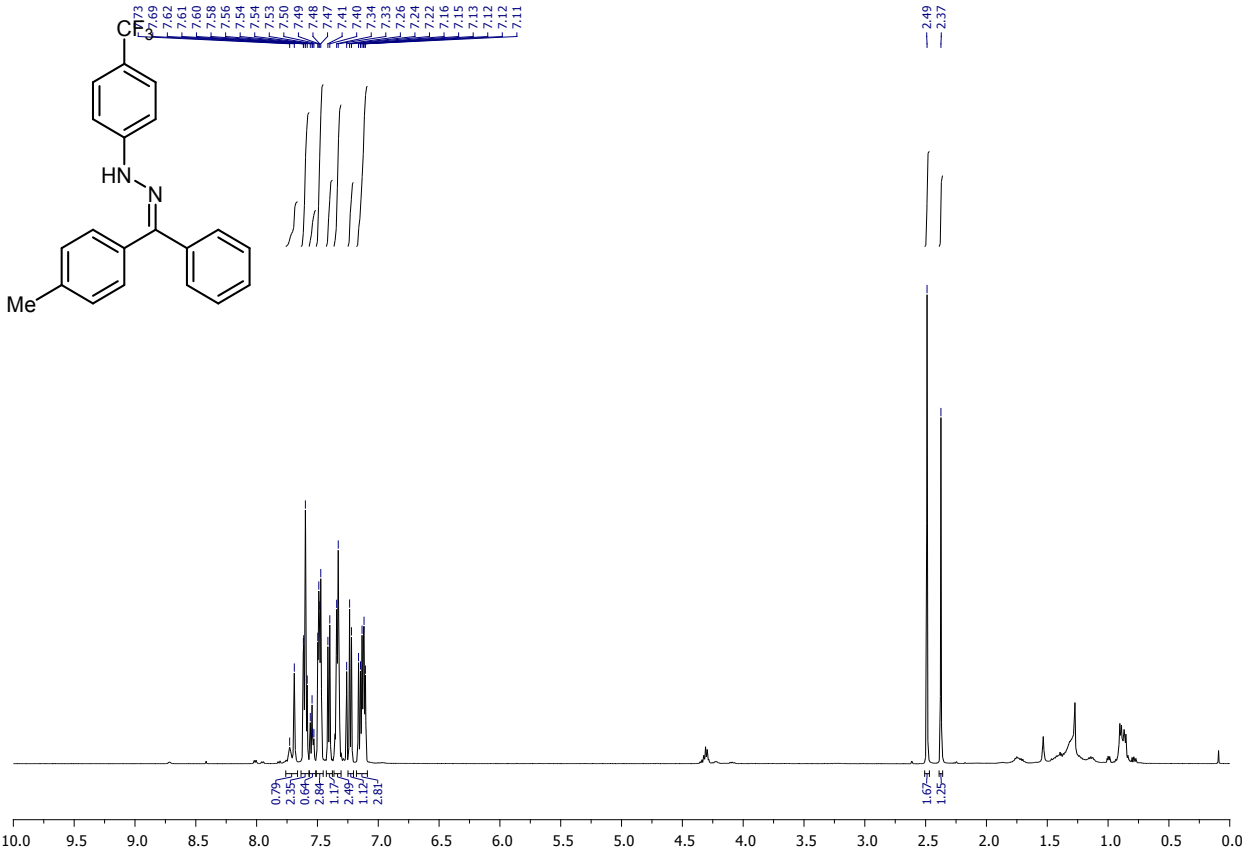
Compound 3n, 1-methyl-5-(phenyl(2-phenylhydrazono)methyl)-1*H*-indazole

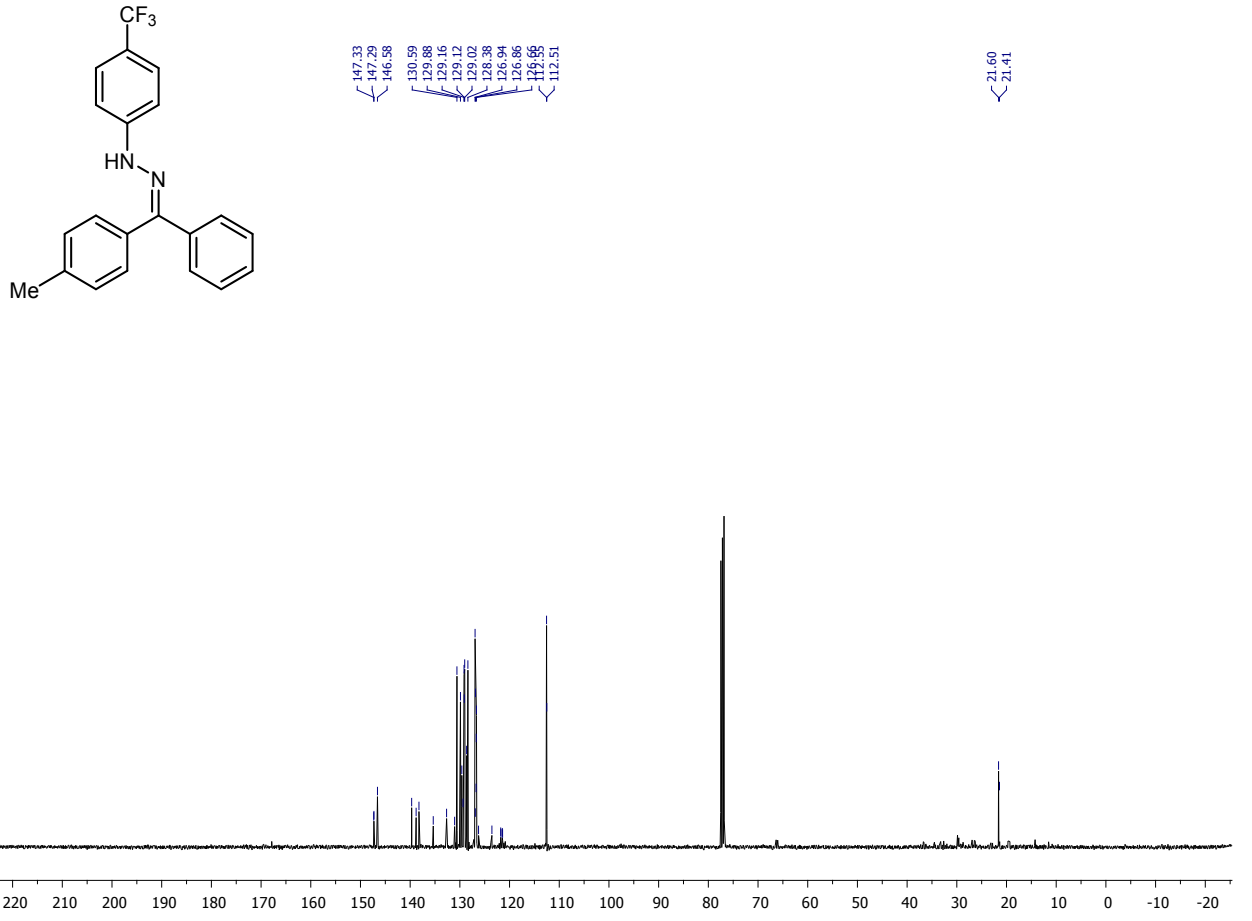


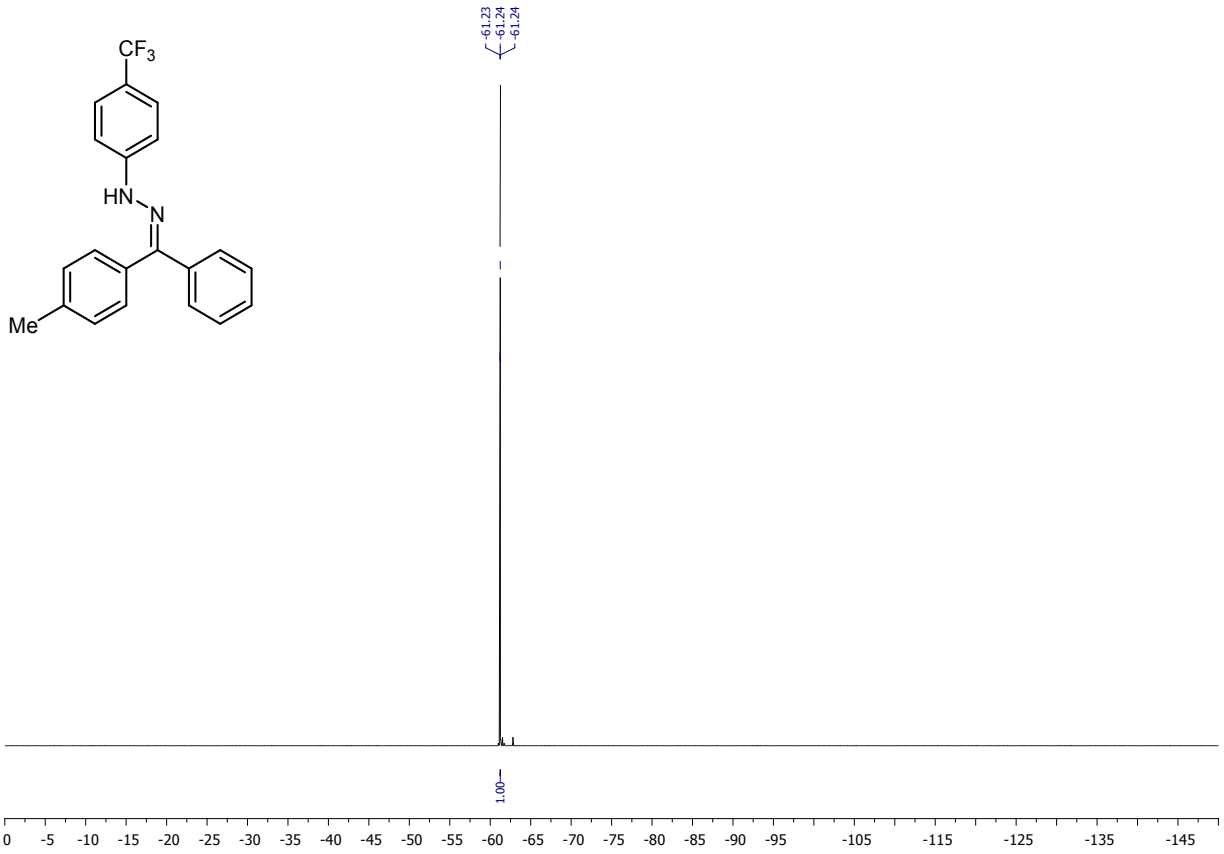
Compound 3o, 1-methyl-5-(phenyl(2-phenylhydrazono)methyl)-1*H*-indole



Compound 3p, 1-(phenyl(*p*-tolyl)methylene)-2-(4-(trifluoromethyl)phenyl)hydrazine



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Me
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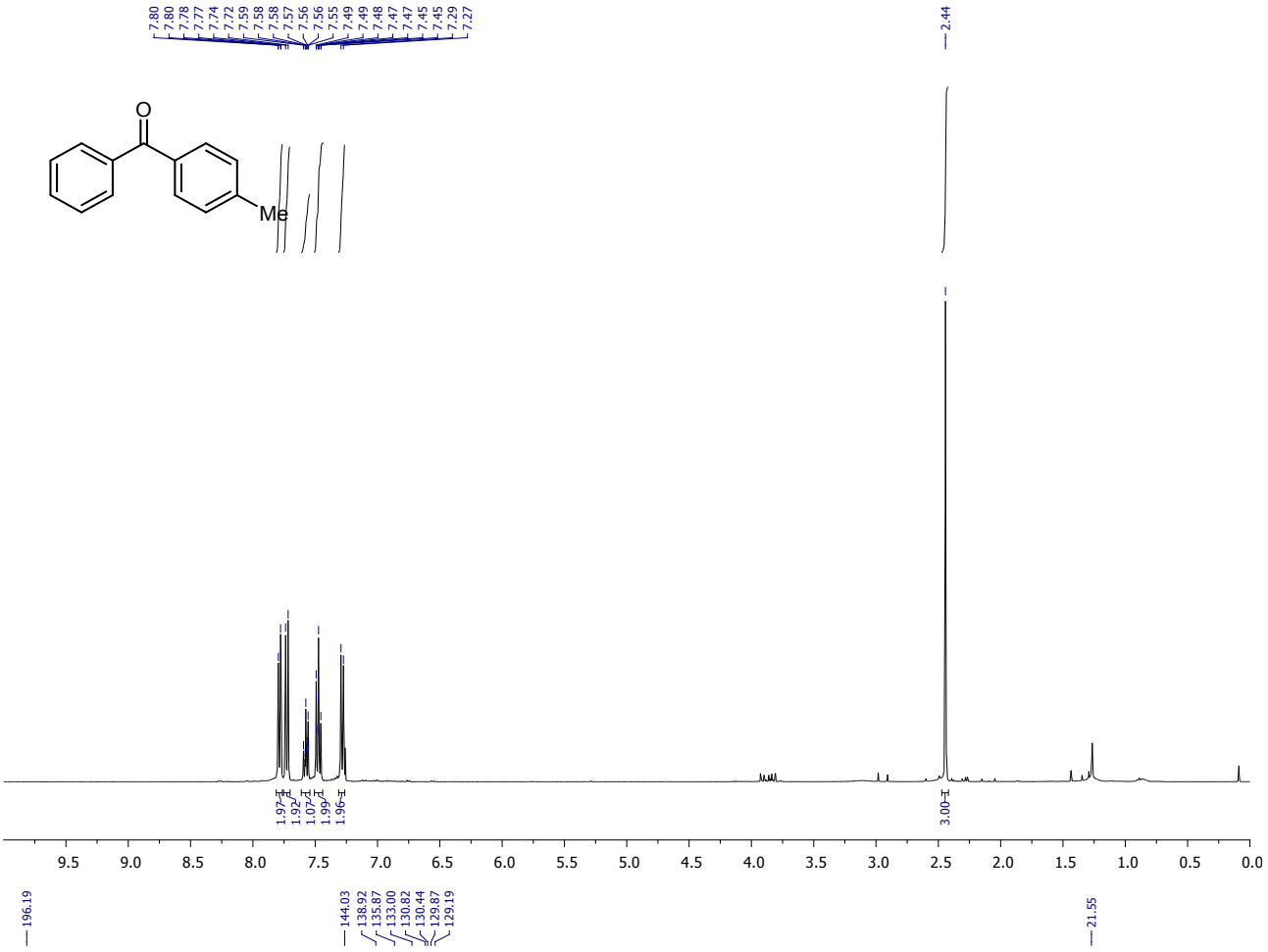
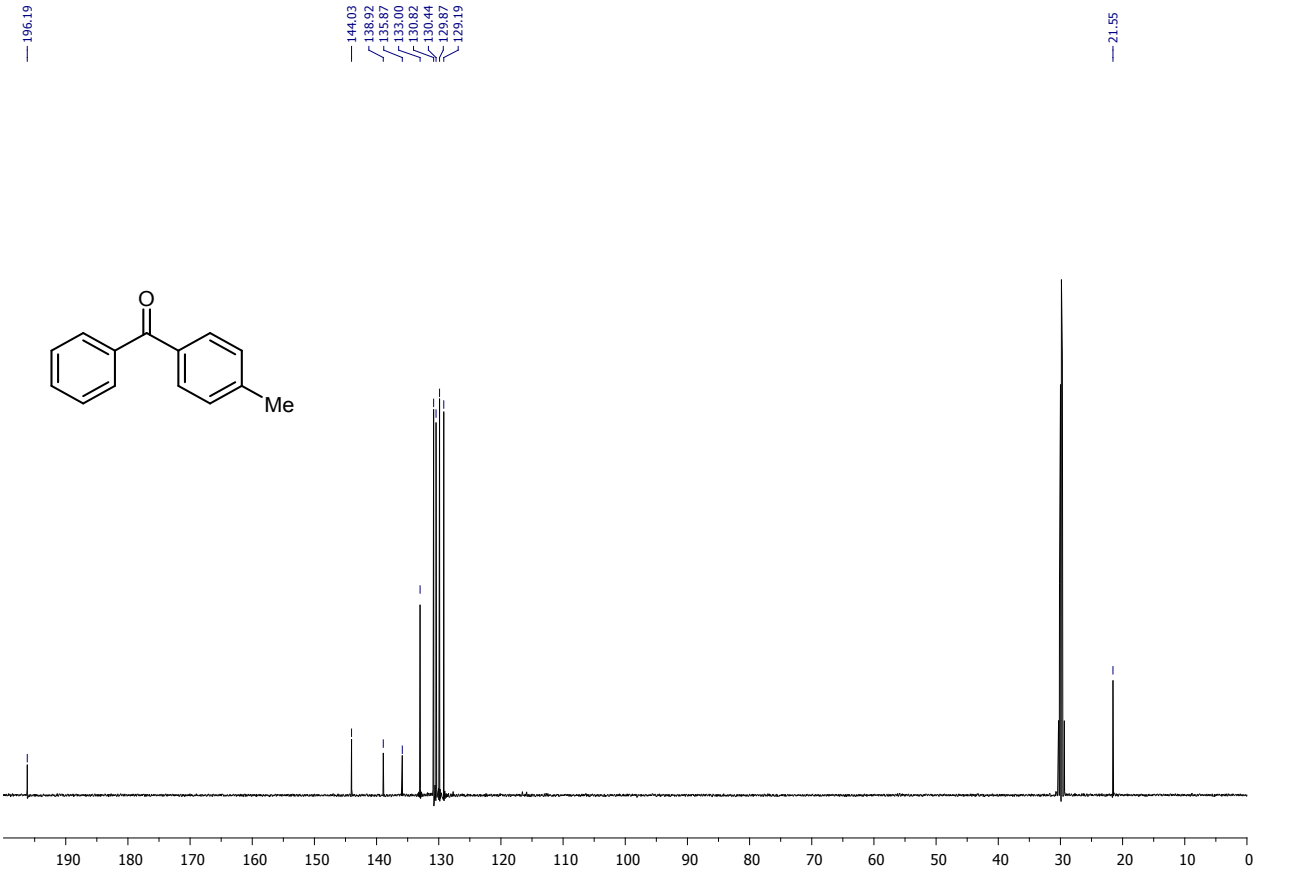
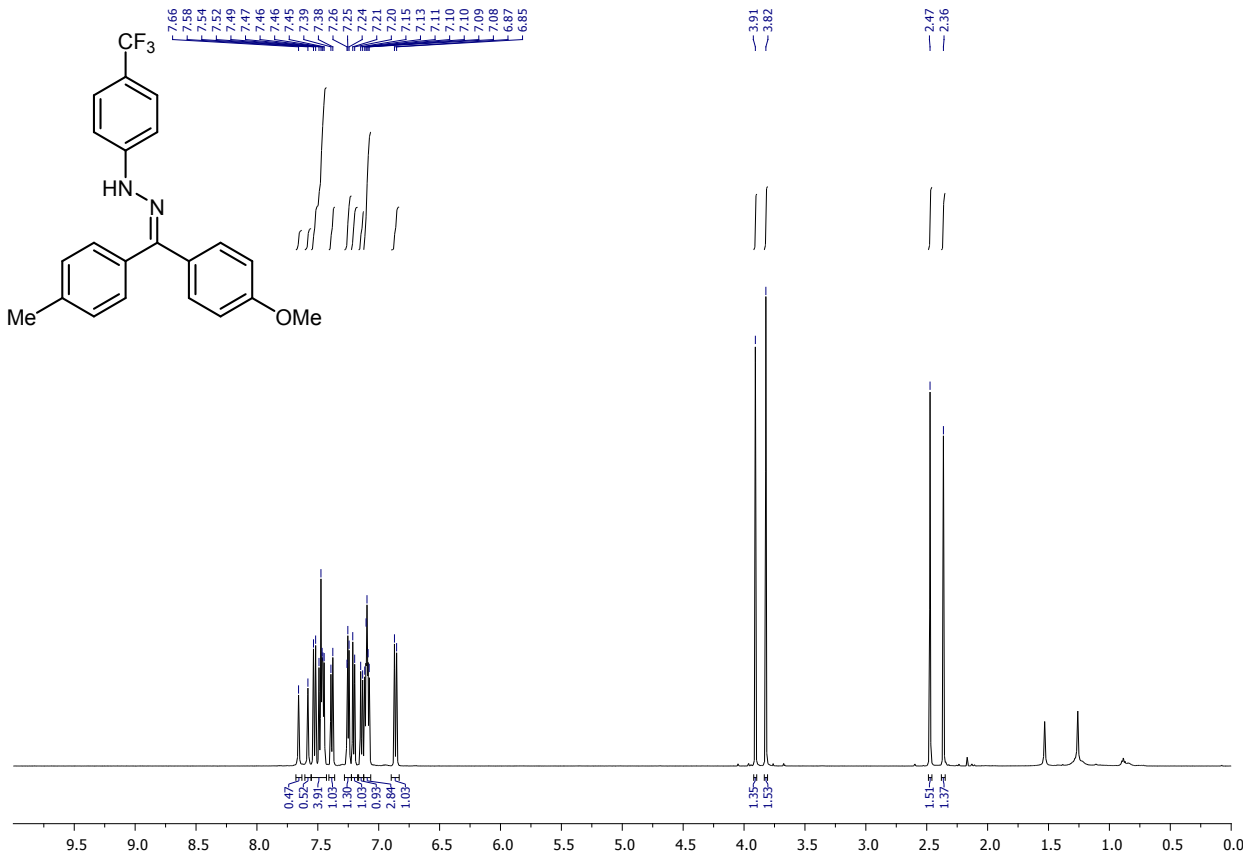
-61.24
-61.24
1.00
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145

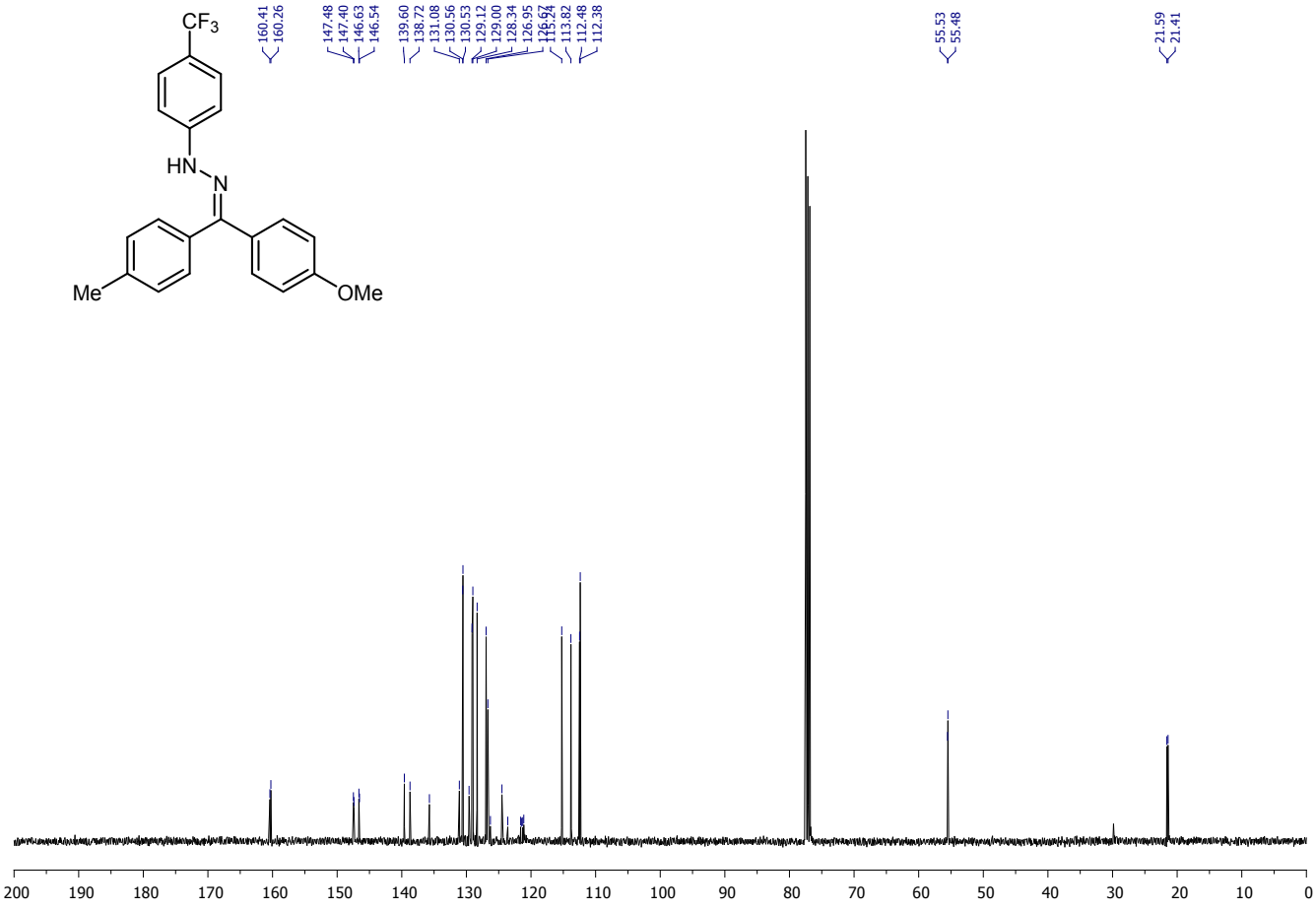
Compound 3q, phenyl(*p*-tolyl)methanone





Compound 3r, 1-((4-methoxyphenyl)(*p*-tolyl)methylene)-2-(4-(trifluoromethyl)phenyl)hydrazine



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0.07
0.02
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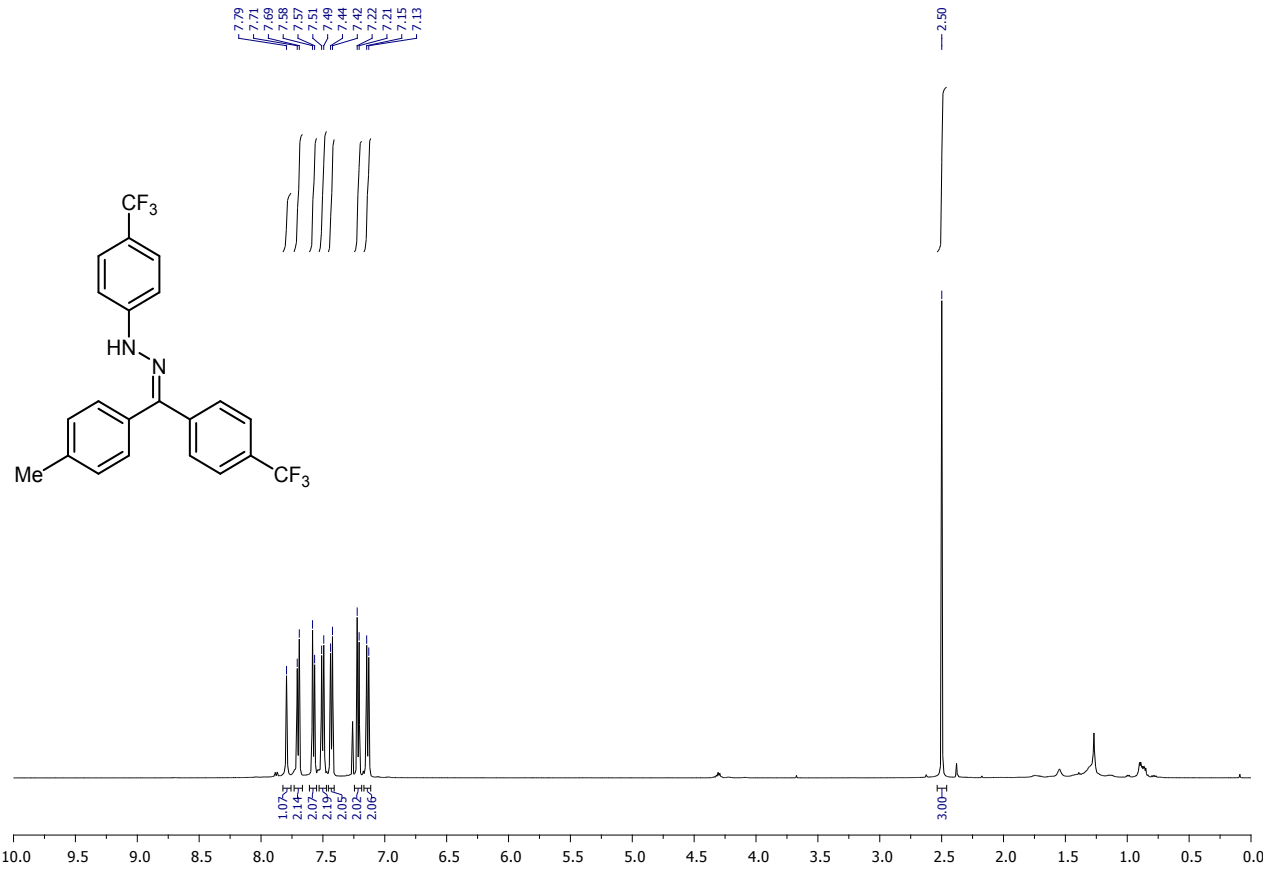
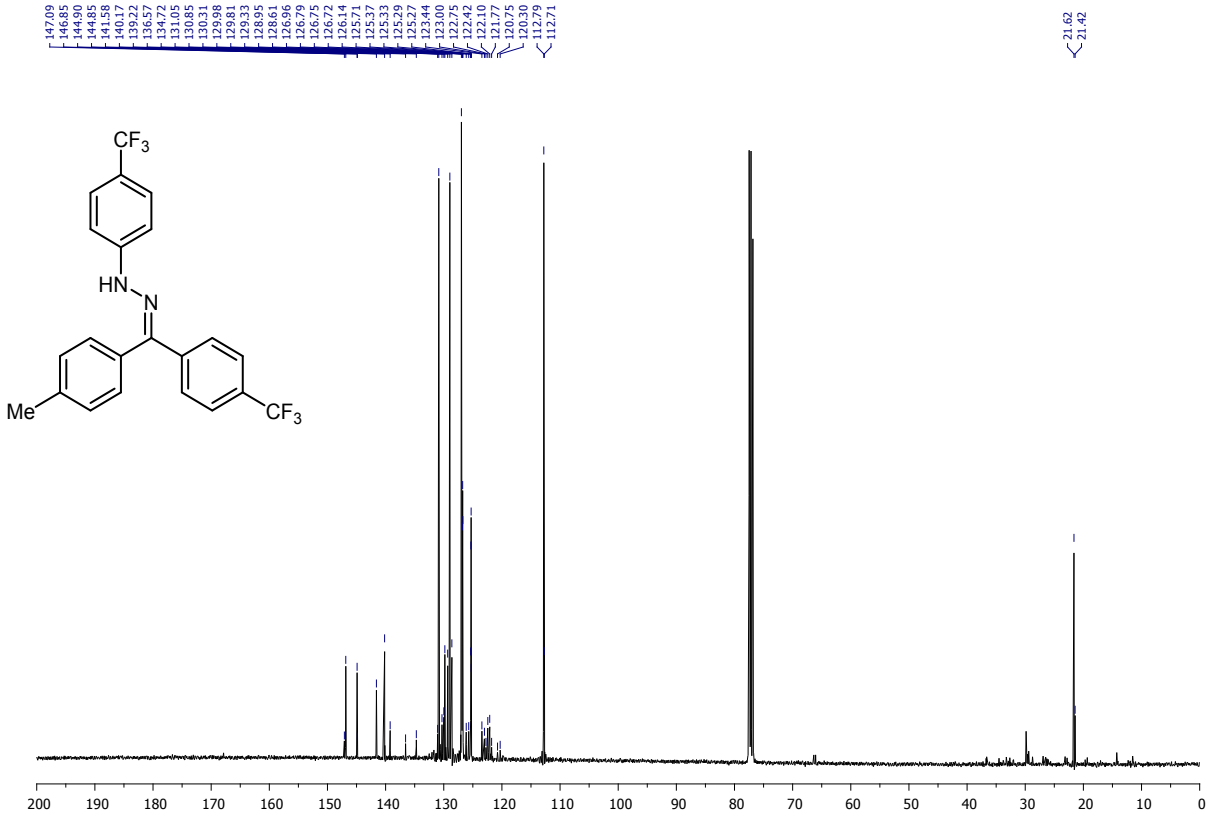
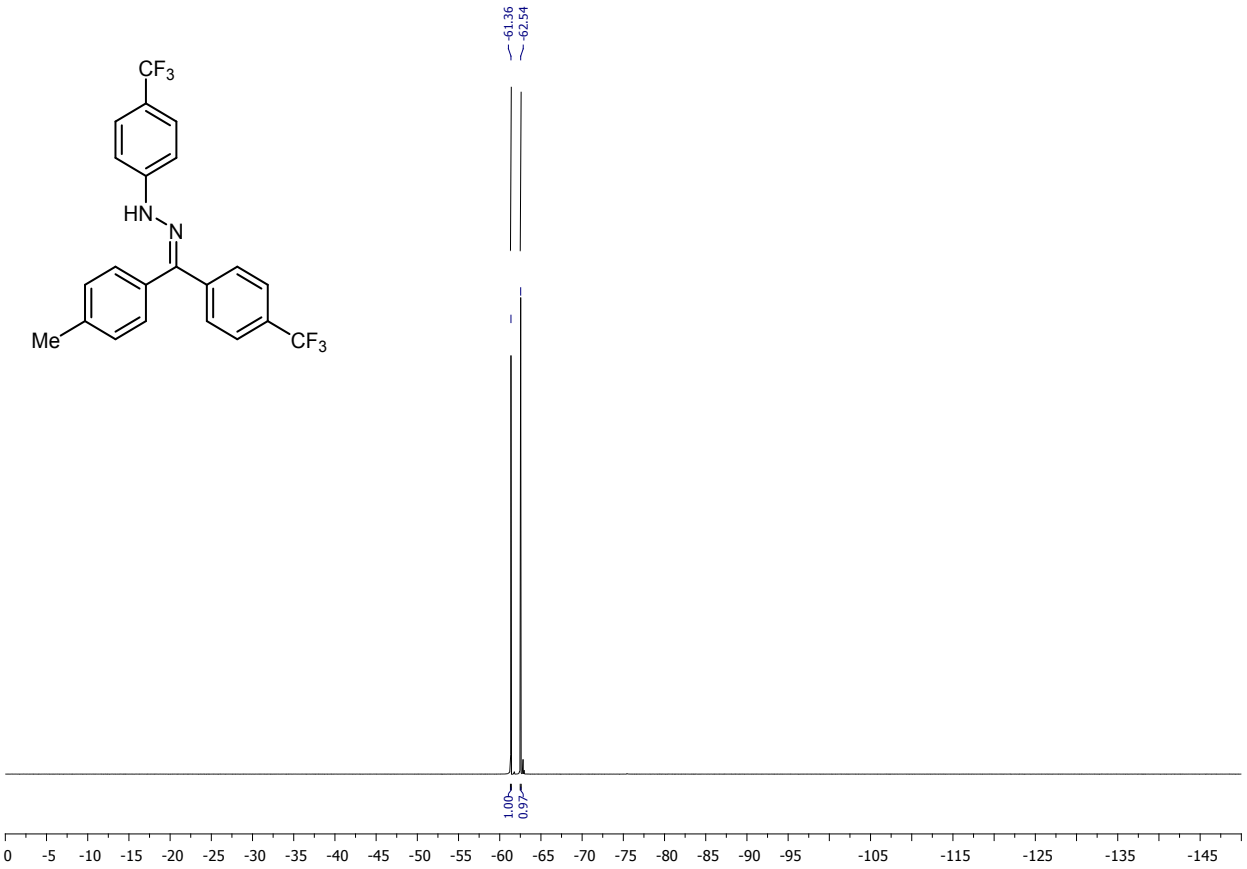
Compound 3s, 1-(*p*-tolyl(4-(trifluoromethyl)phenyl)methylene)-2-(4-(trifluoromethyl)phenyl)hydrazine



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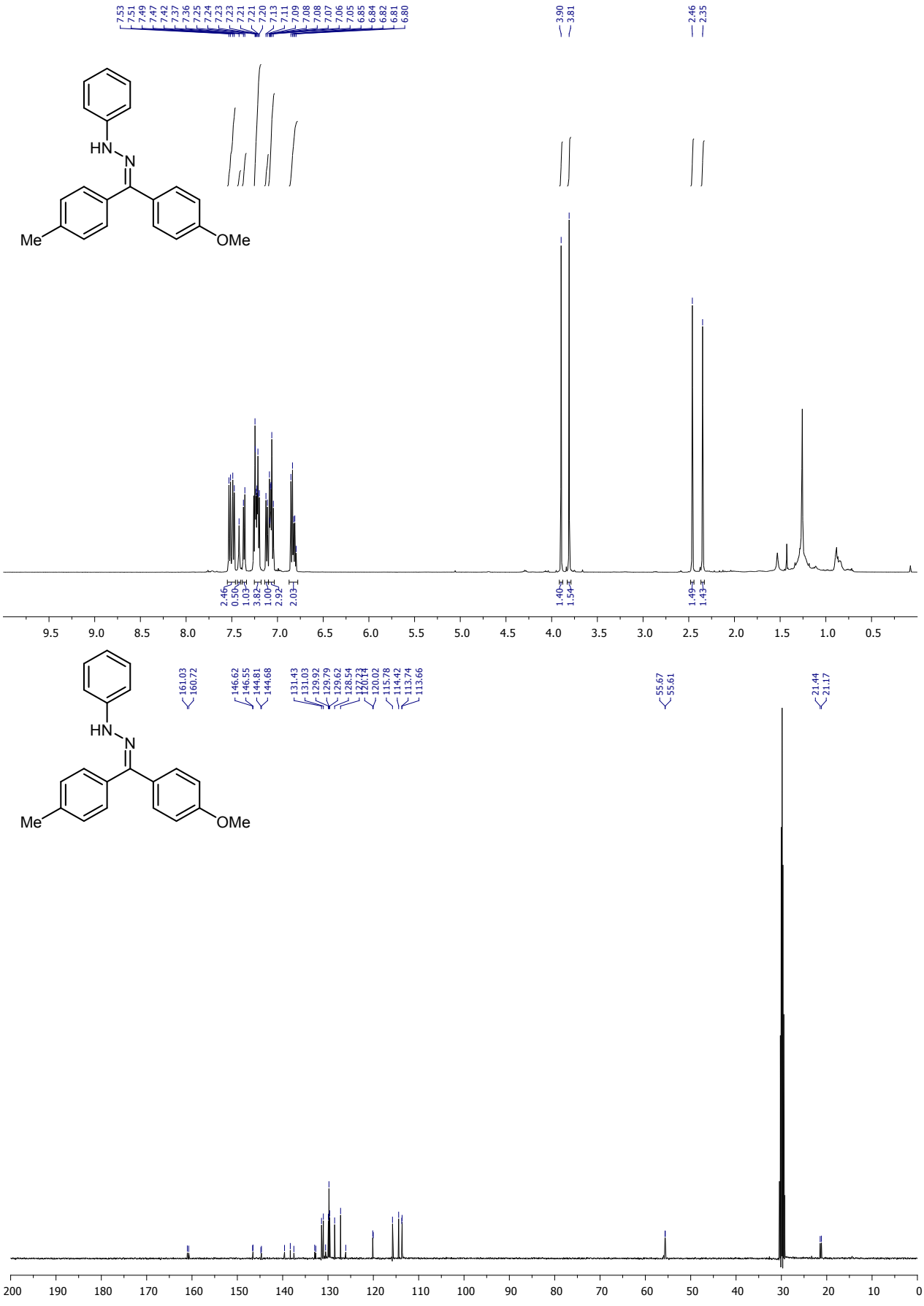
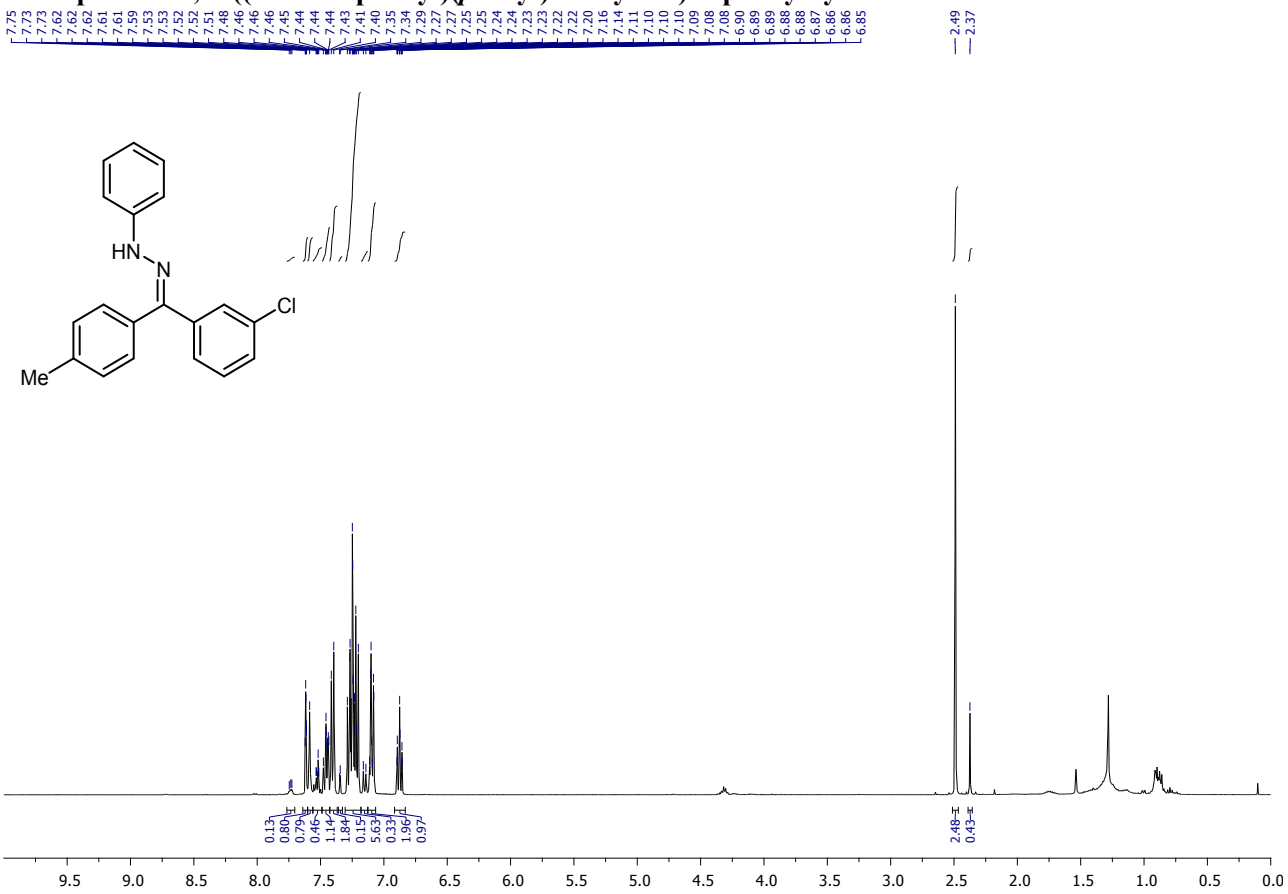
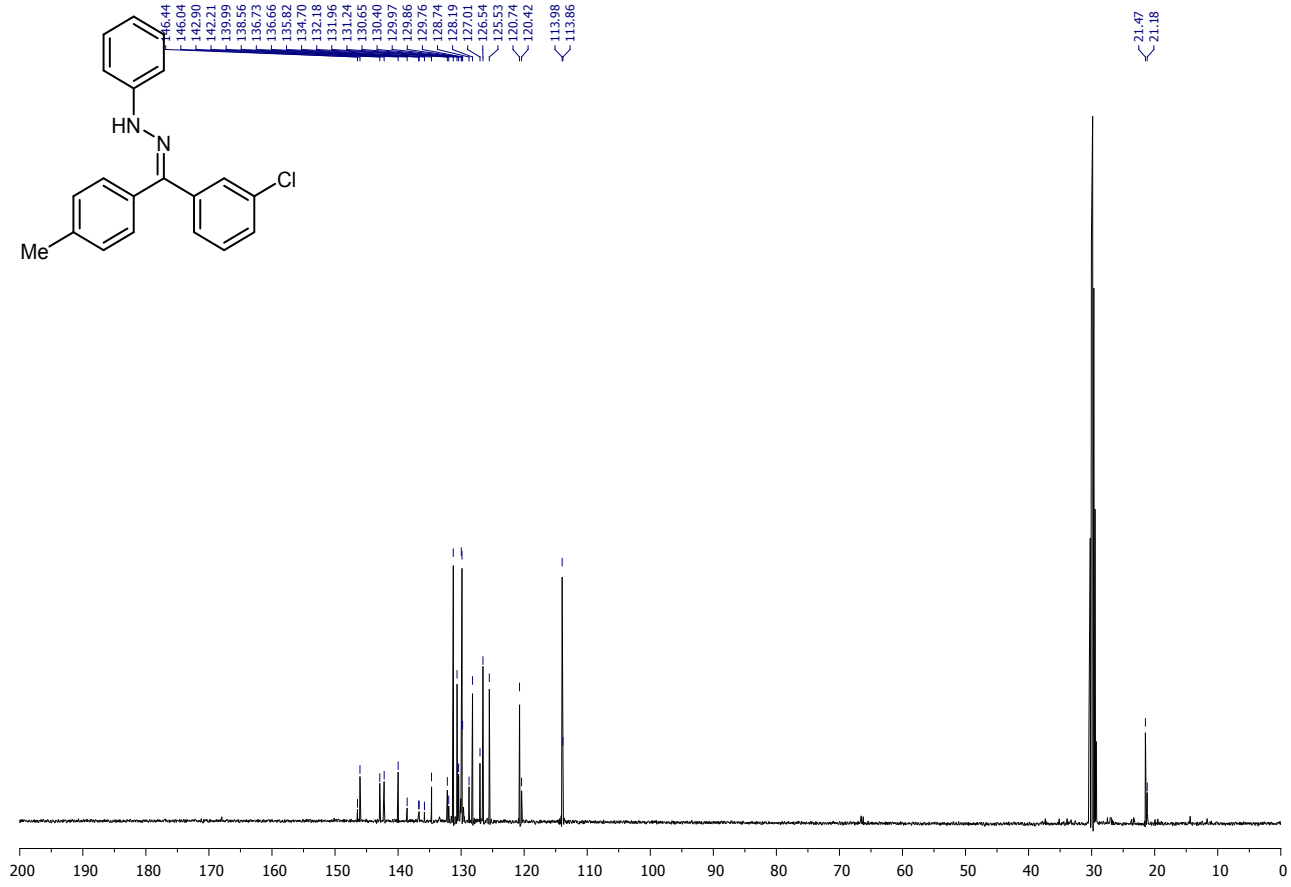
0.97
0 -5 -10 -15 -20 -25 -30 -35 -40 -45 -50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -105 -115 -125 -135 -145

Compound 3t, 1-((4-methoxyphenyl)(*p*-tolyl)methylene)-2-phenylhydrazine

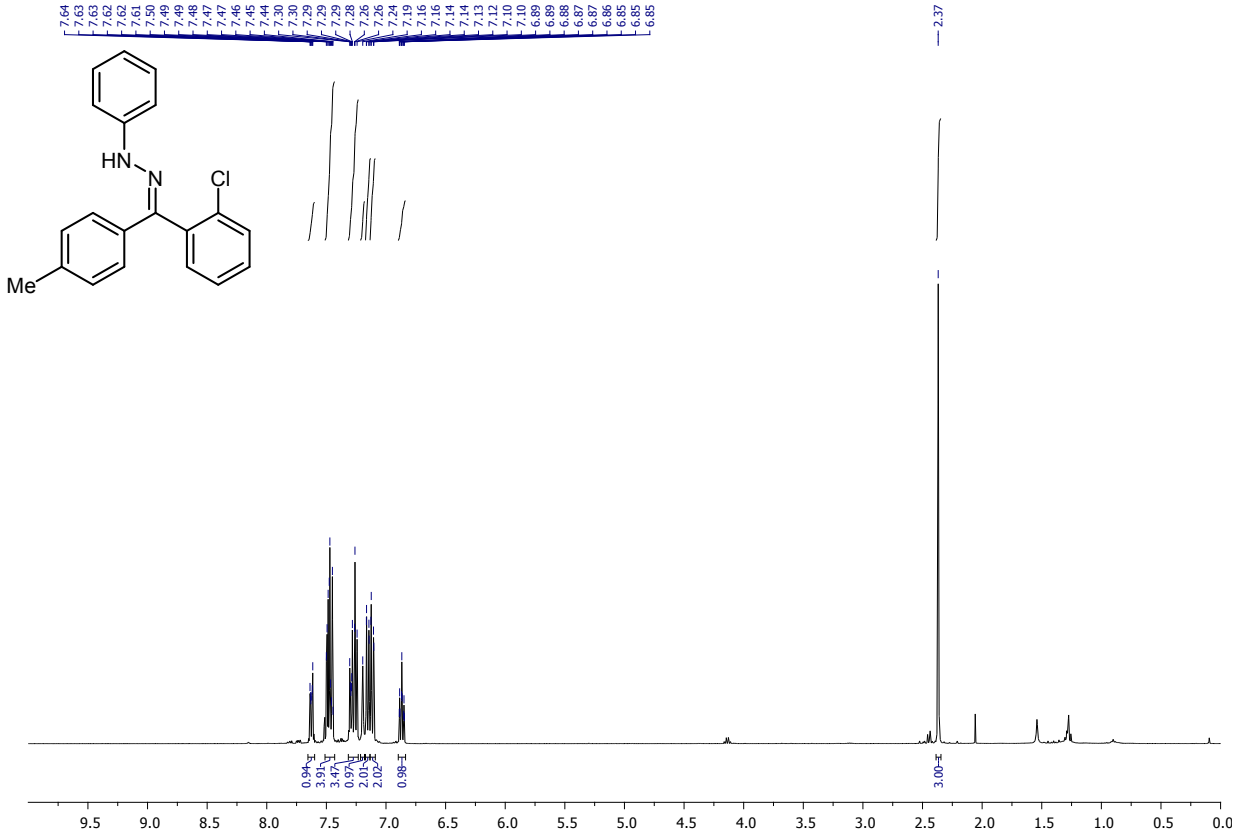


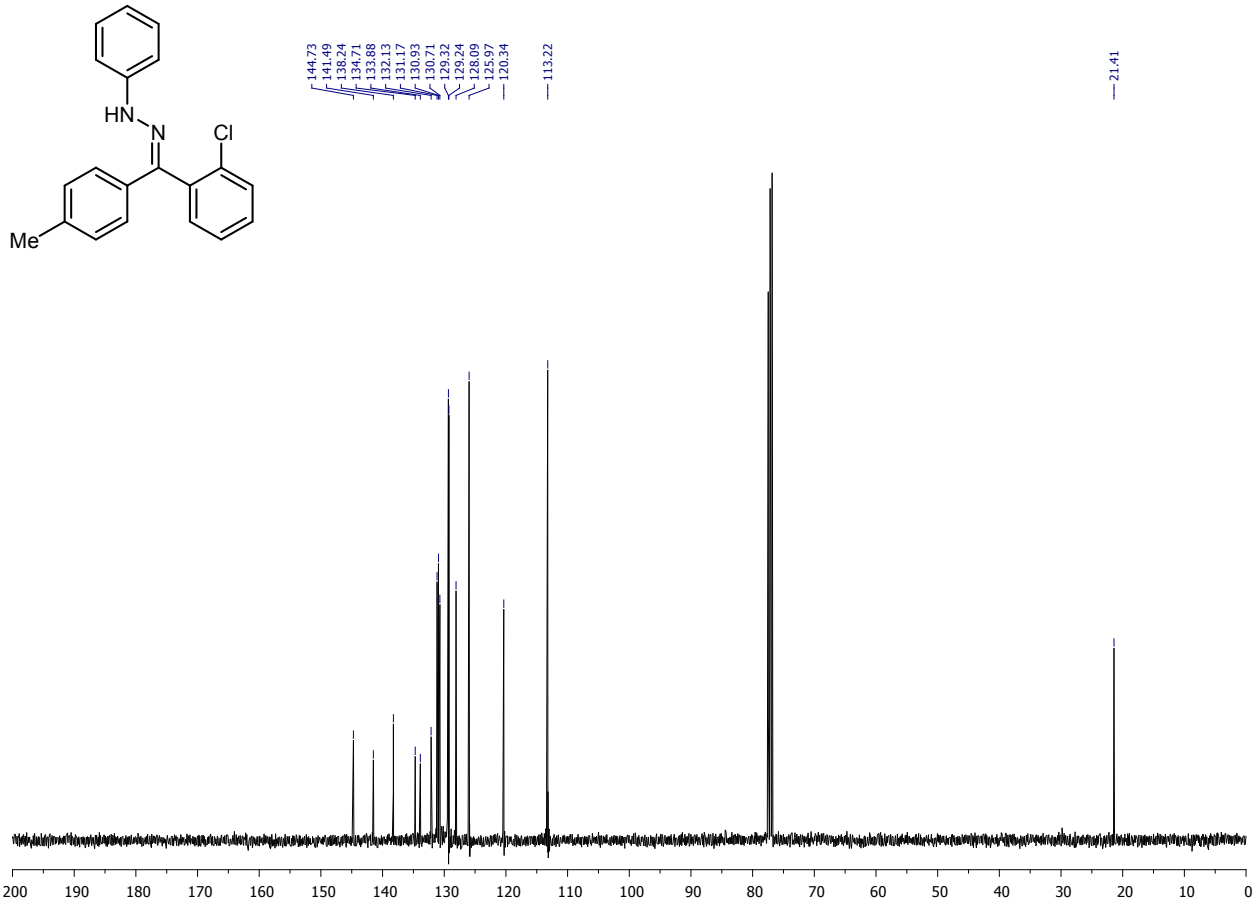
Compound 3v, 1-((3-chlorophenyl)(*p*-tolyl)methylene)-2-phenylhydrazine



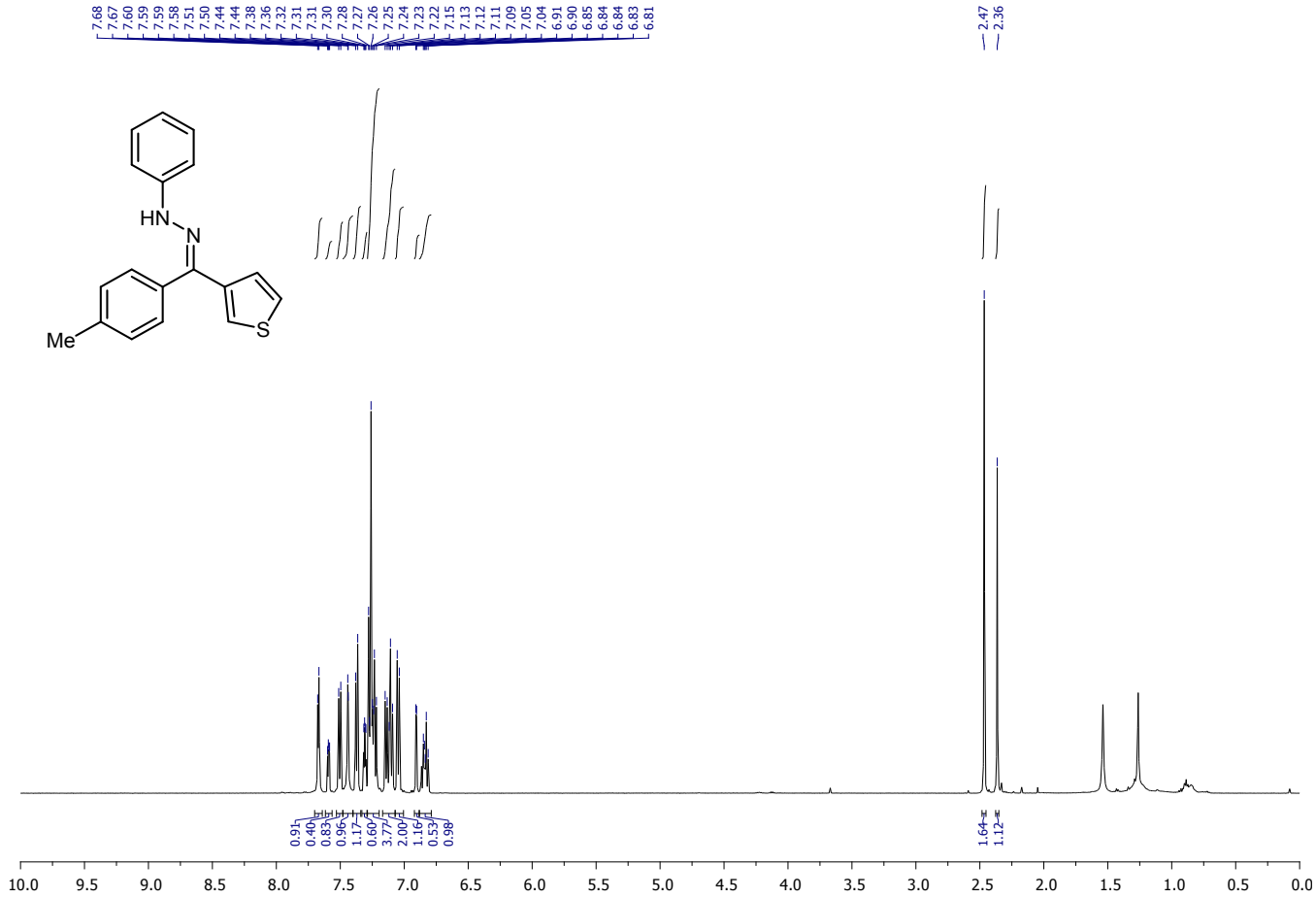


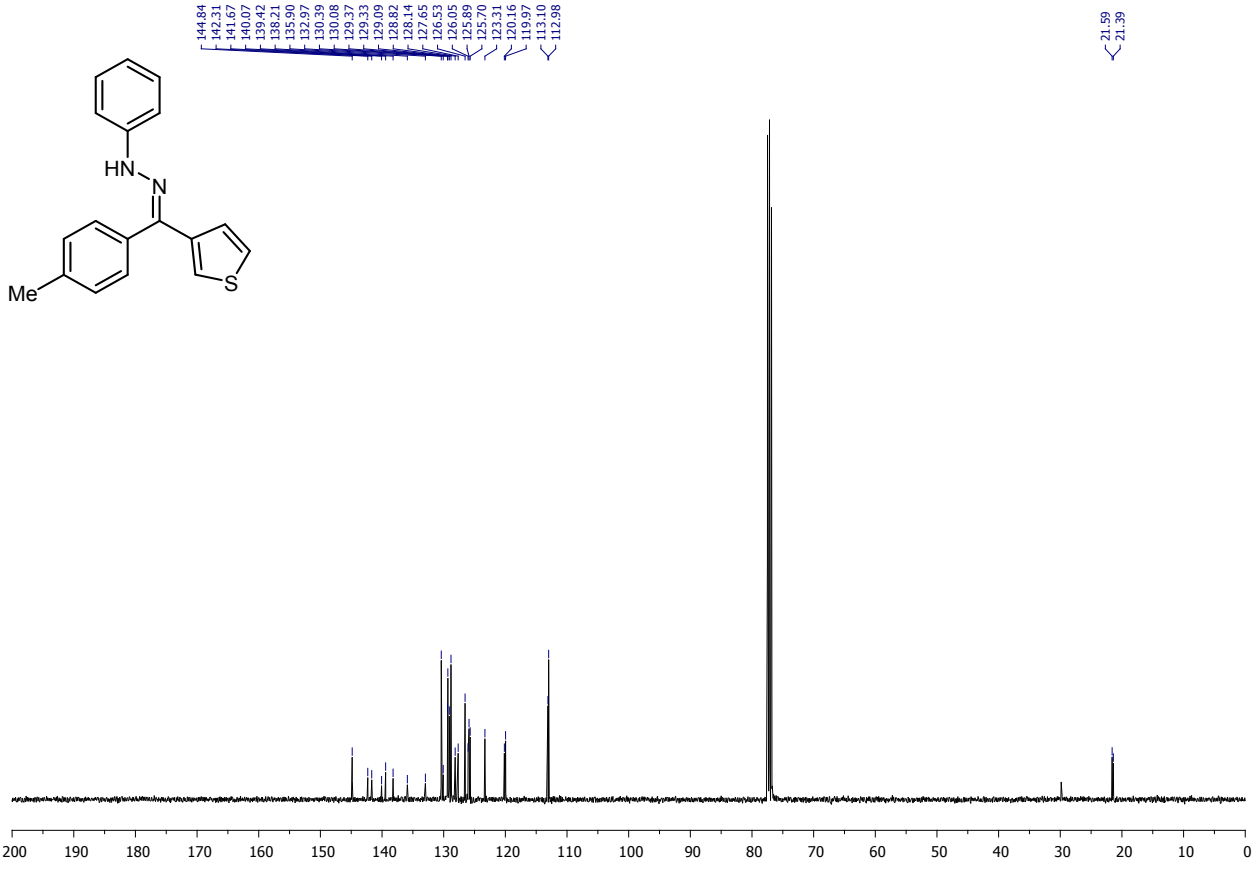
Compound 3x, 1-((2-chlorophenyl)(*p*-tolyl)methylene)-2-phenylhydrazine



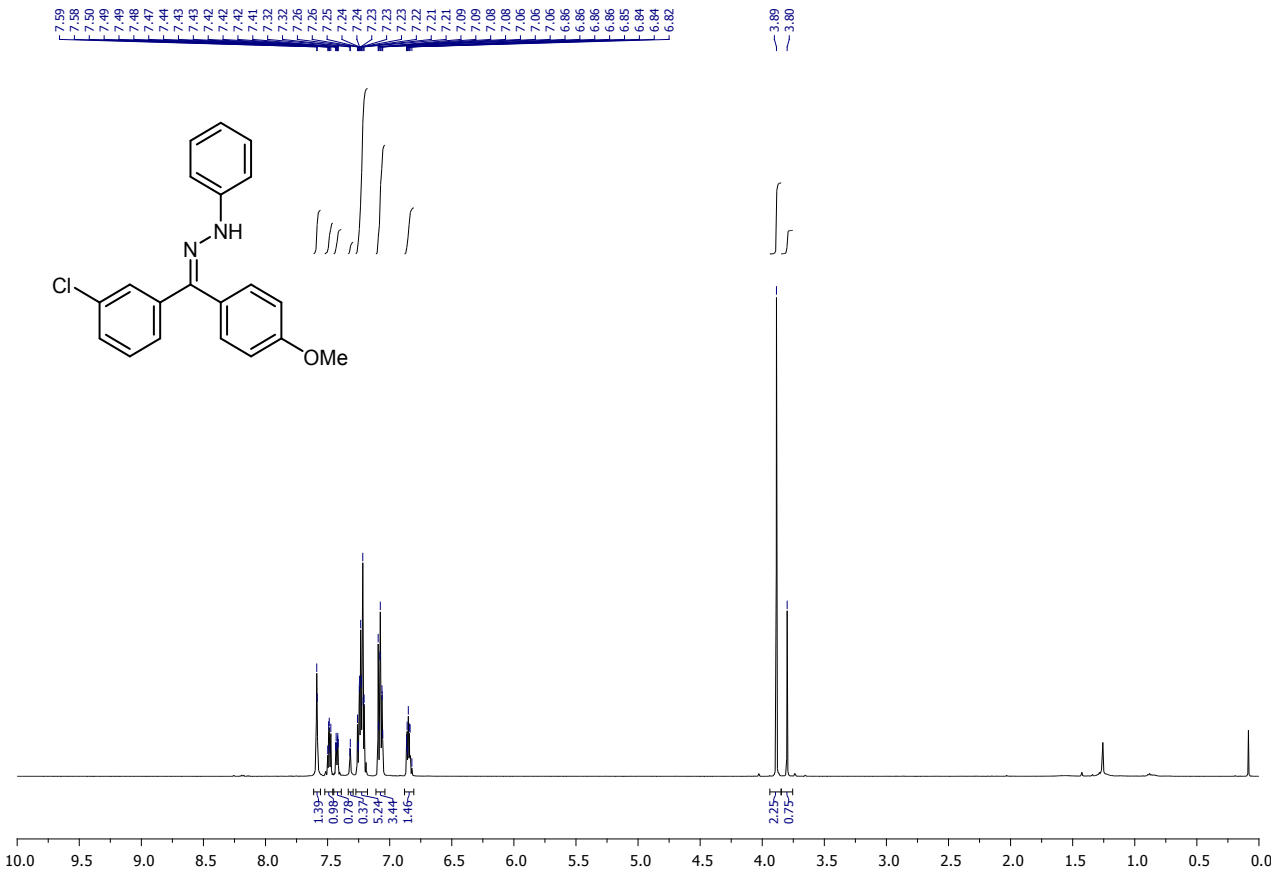


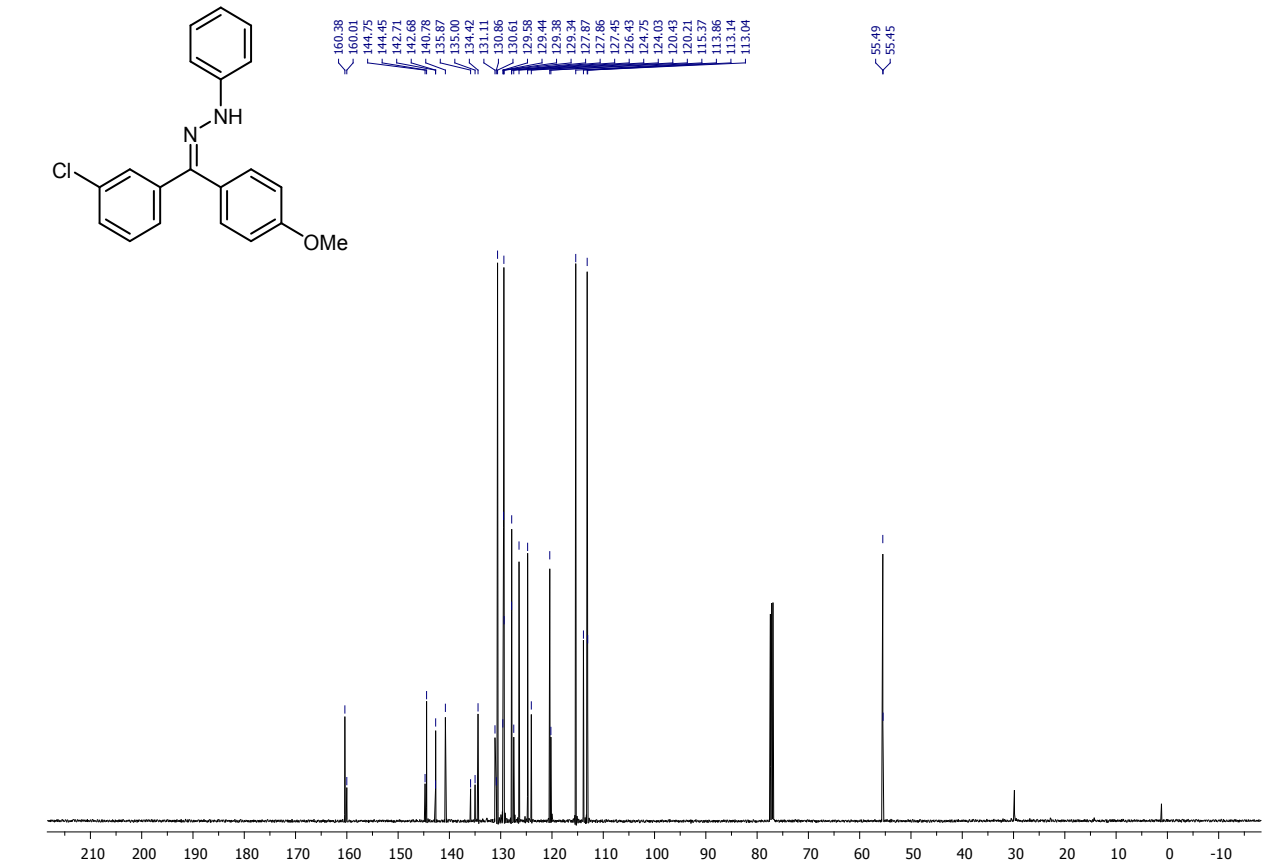
Compound 3y, 1-phenyl-2-(thiophen-3-yl(*p*-tolyl)methylene)hydrazine



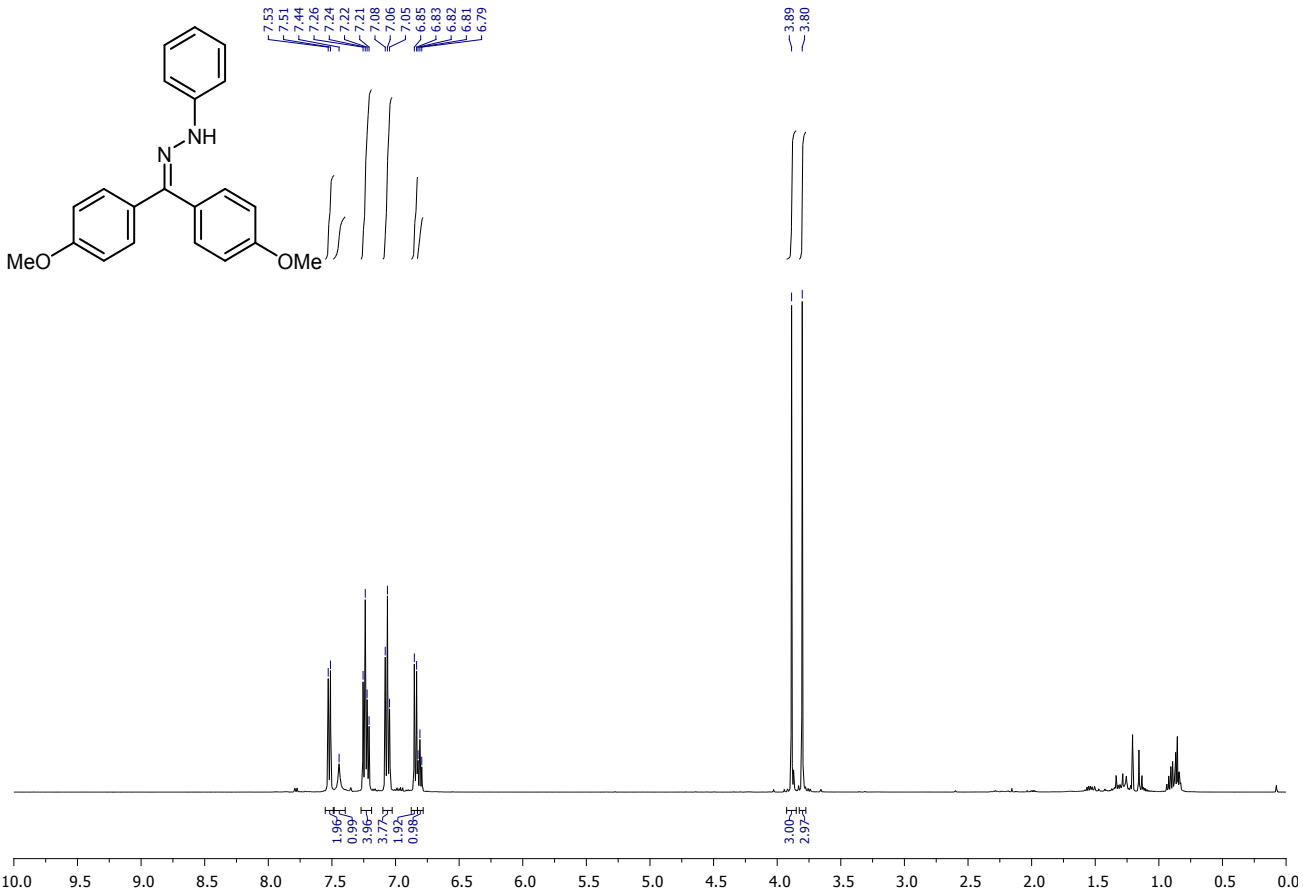


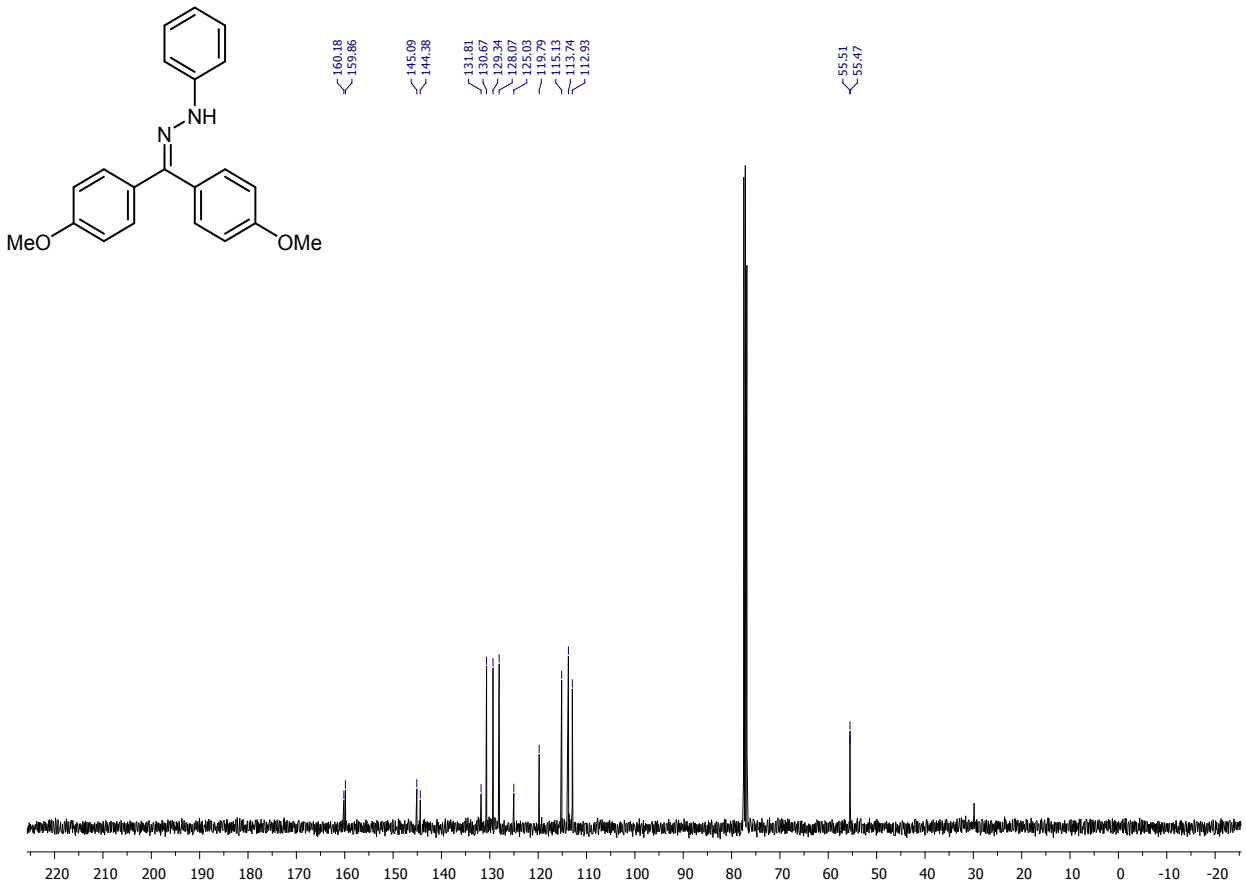
Compound 3w, 1-((3-chlorophenyl)(4-methoxyphenyl)methylene)-2-phenylhydrazine



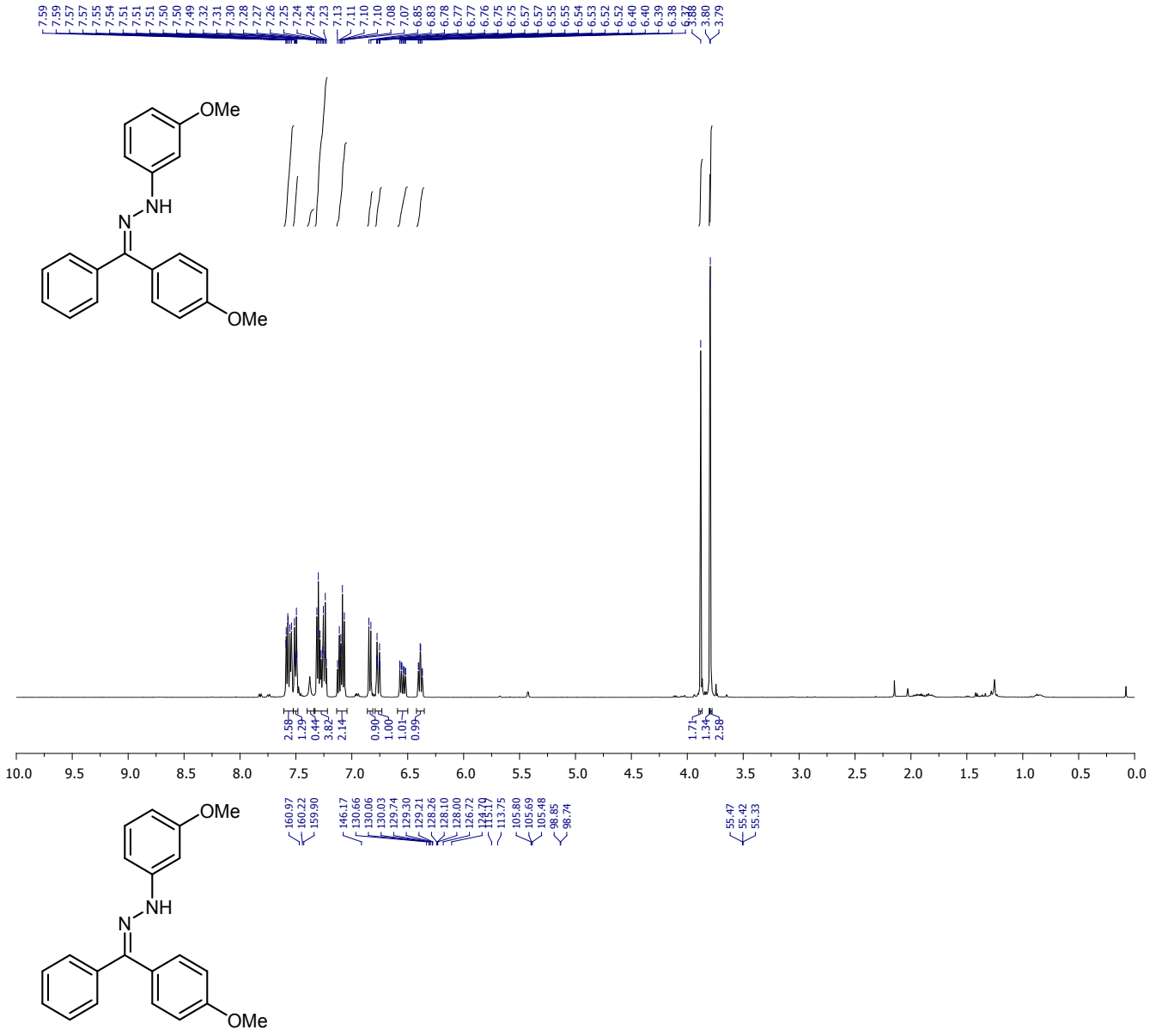


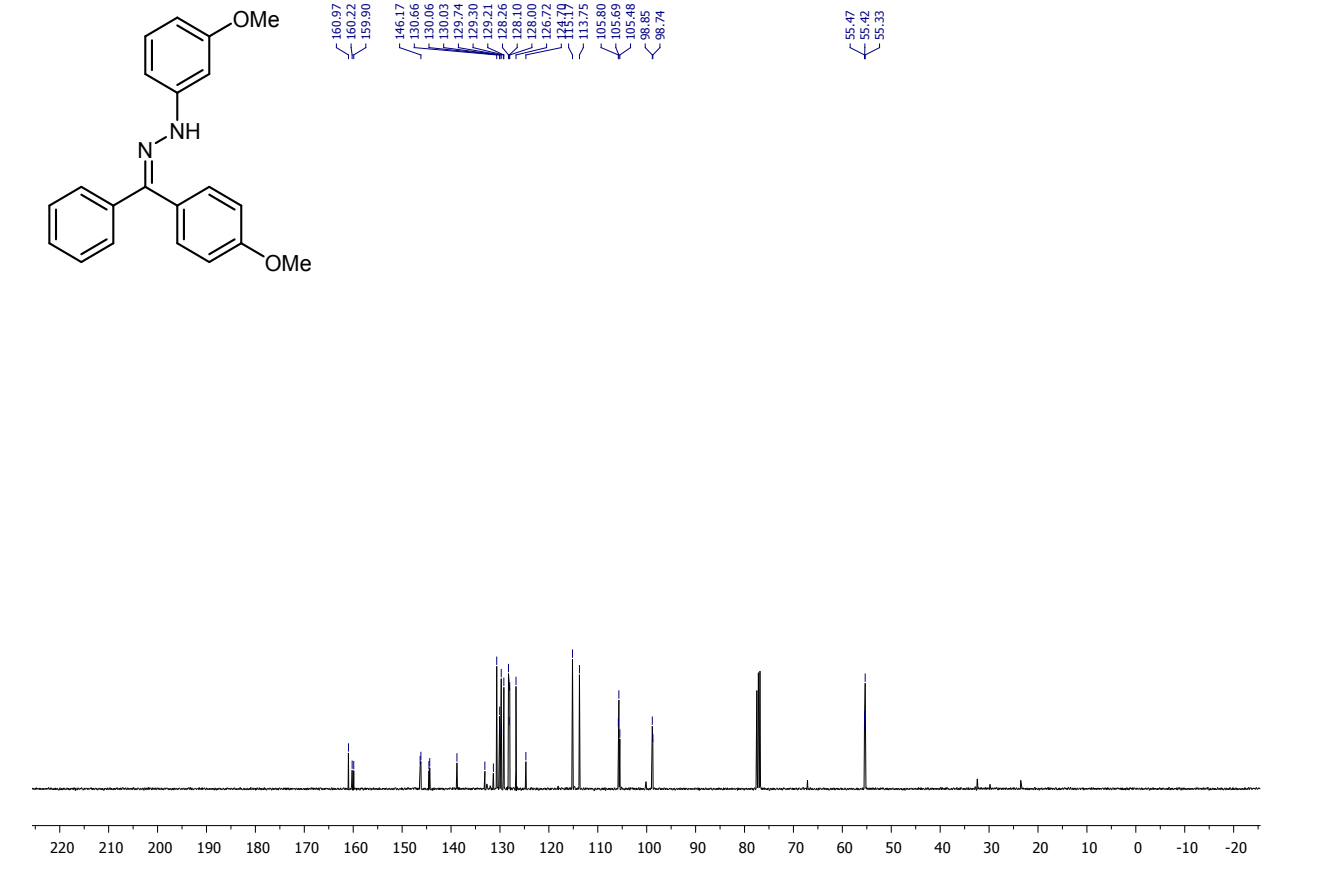
Compound 3u, 1-(*bis*(4-methoxyphenyl)methylene)-2-phenylhydrazine





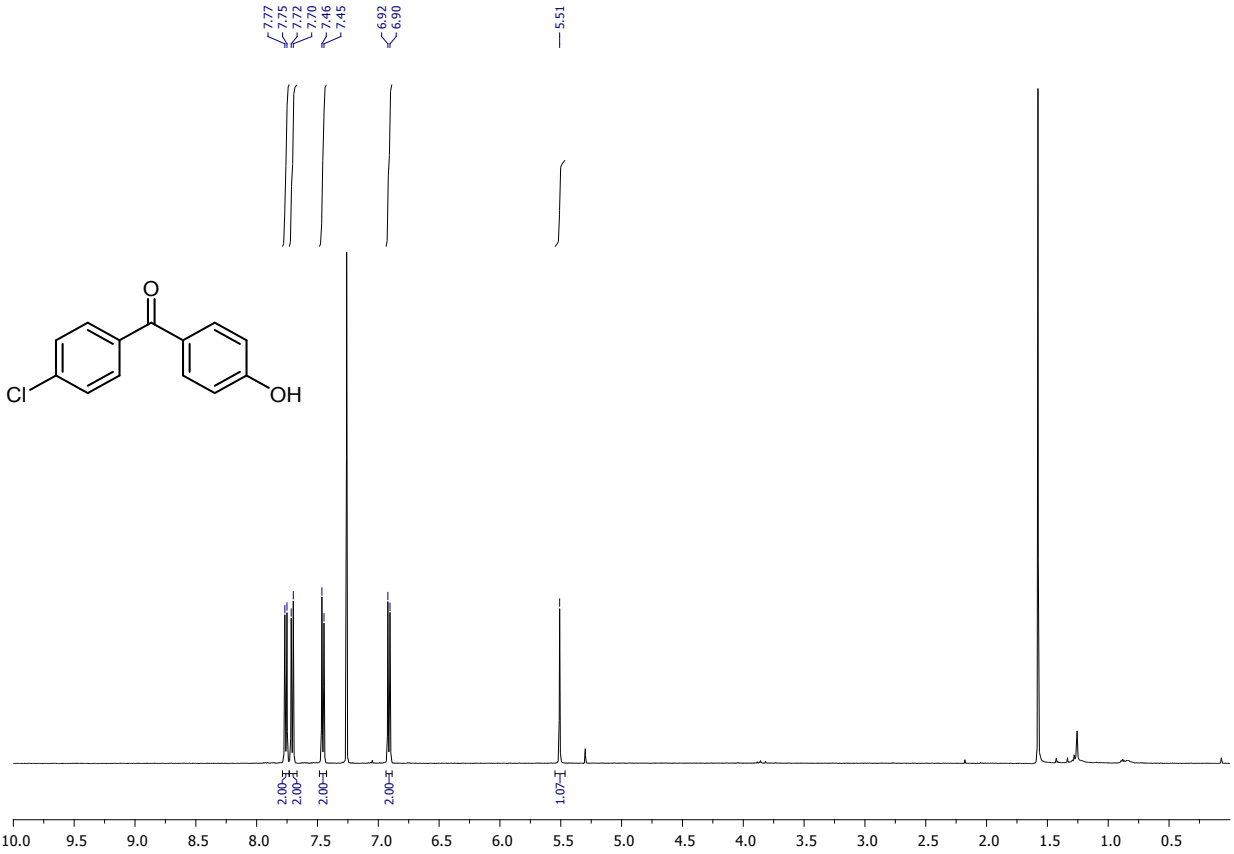
Compound 3aa, 1-(3-methoxyphenyl)-2-((4-methoxyphenyl)(phenyl)methylene)hydrazine

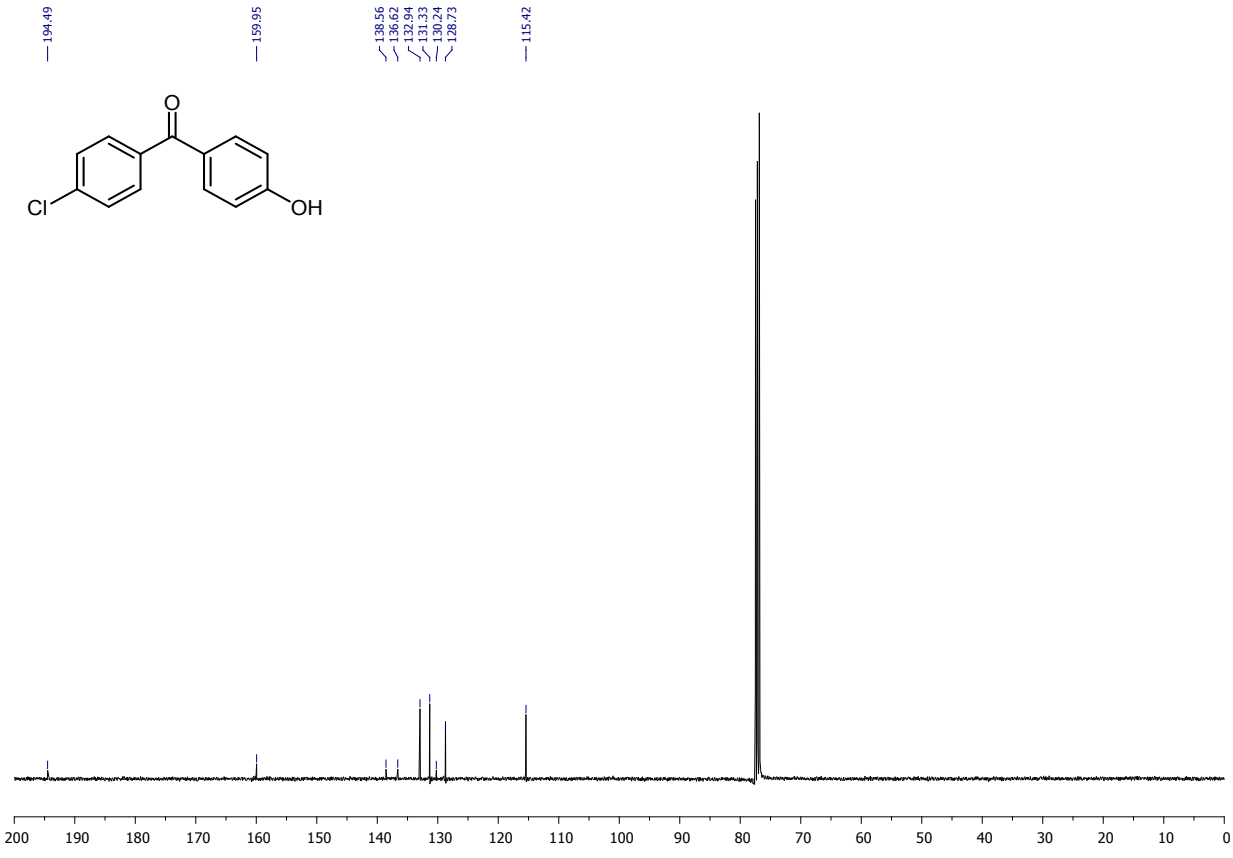




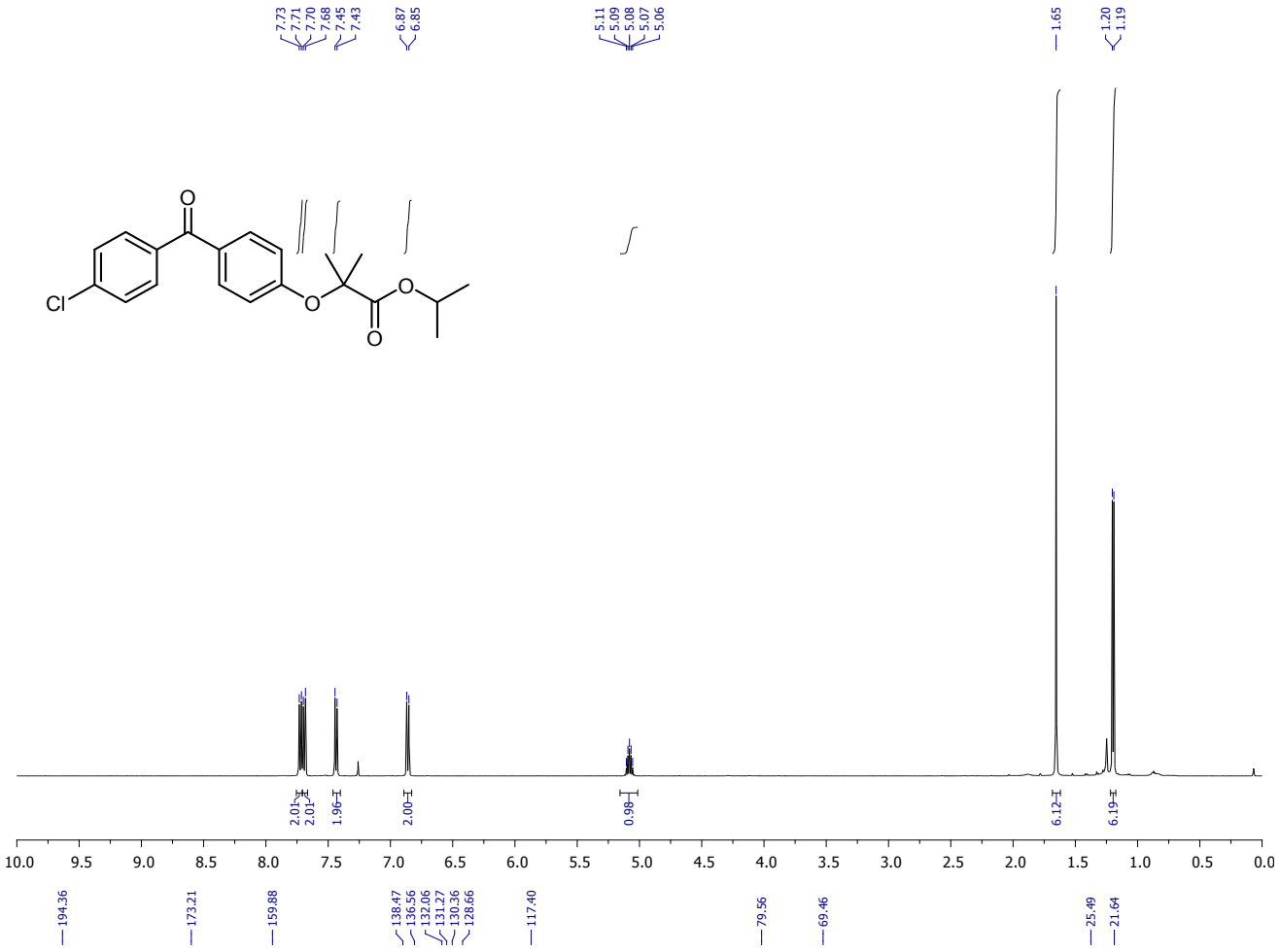
6.3 Other Compounds

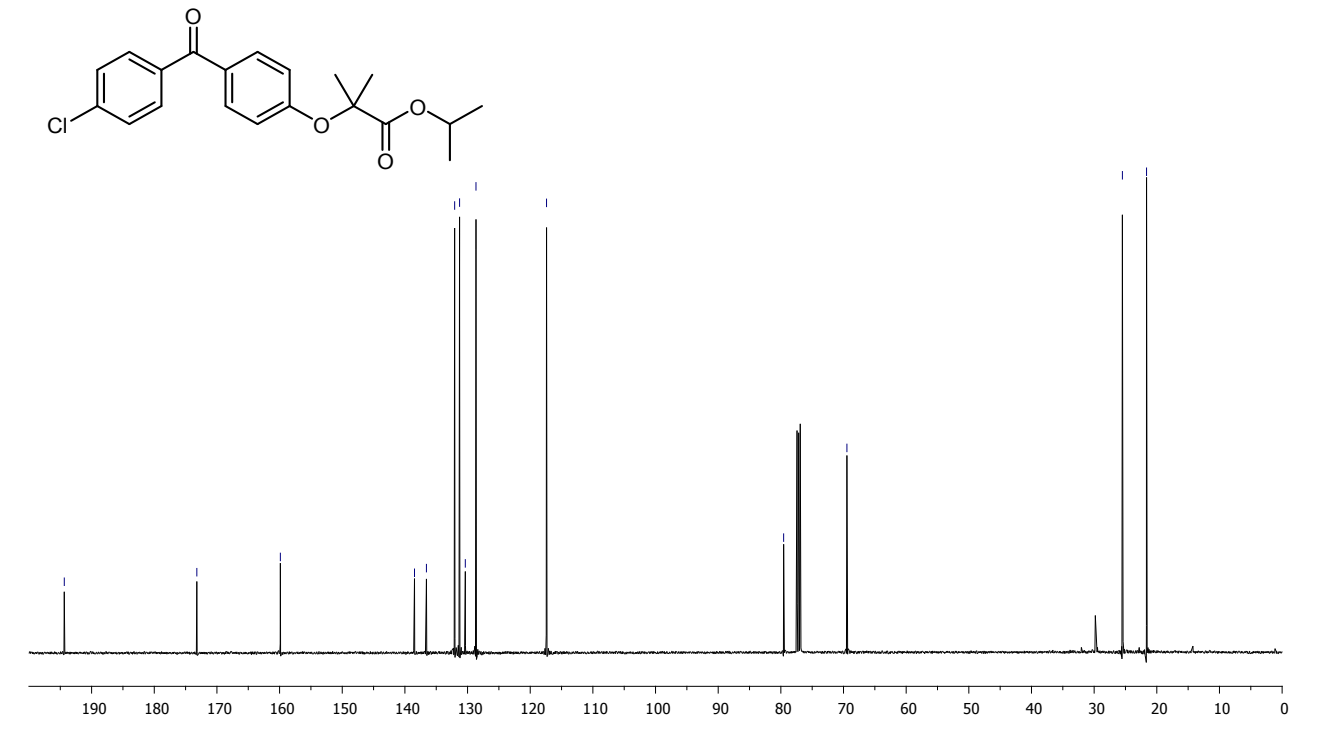
Compound 5, (4-chlorophenyl)(4-hydroxyphenyl)methanone



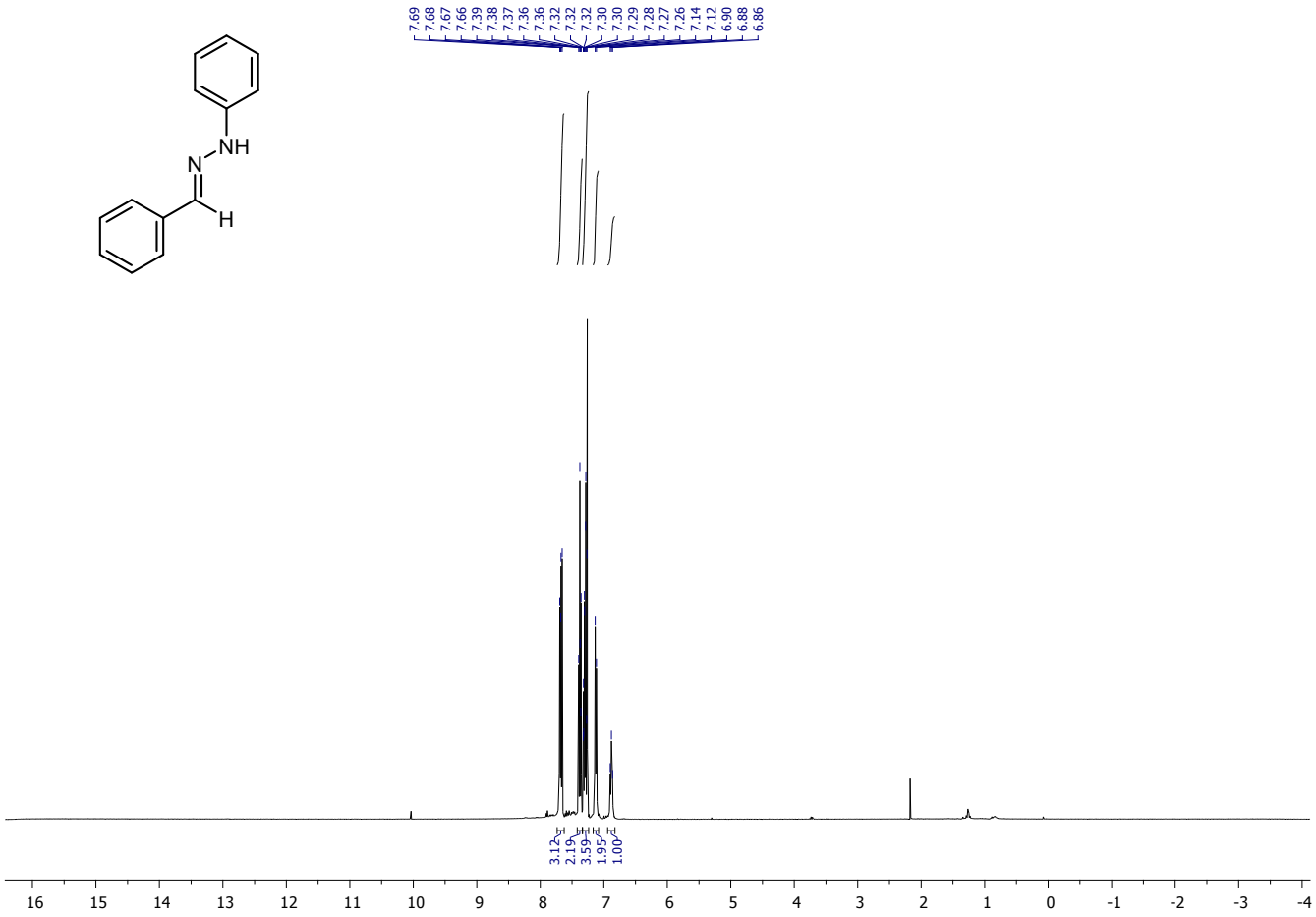


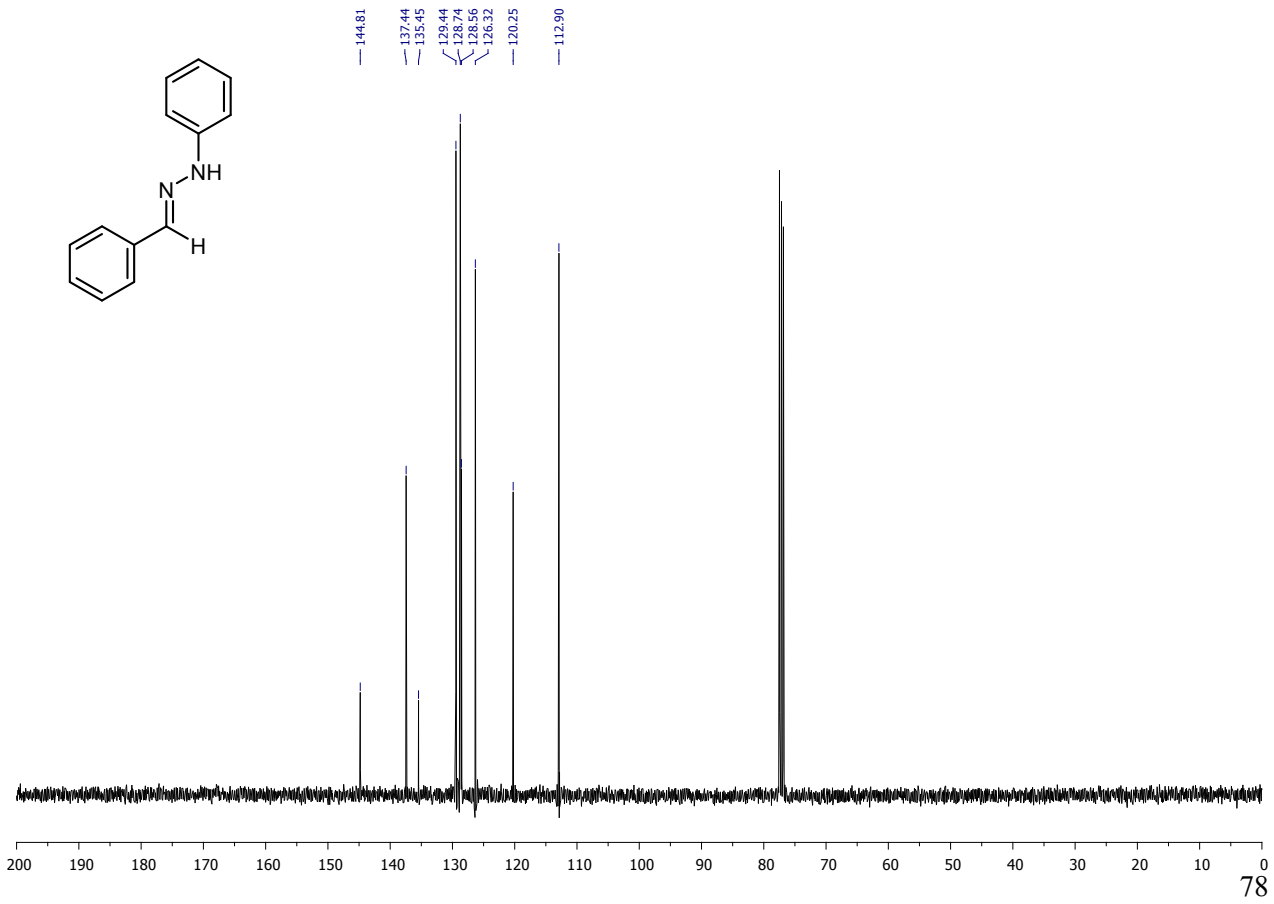
Compound 6, isopropyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate



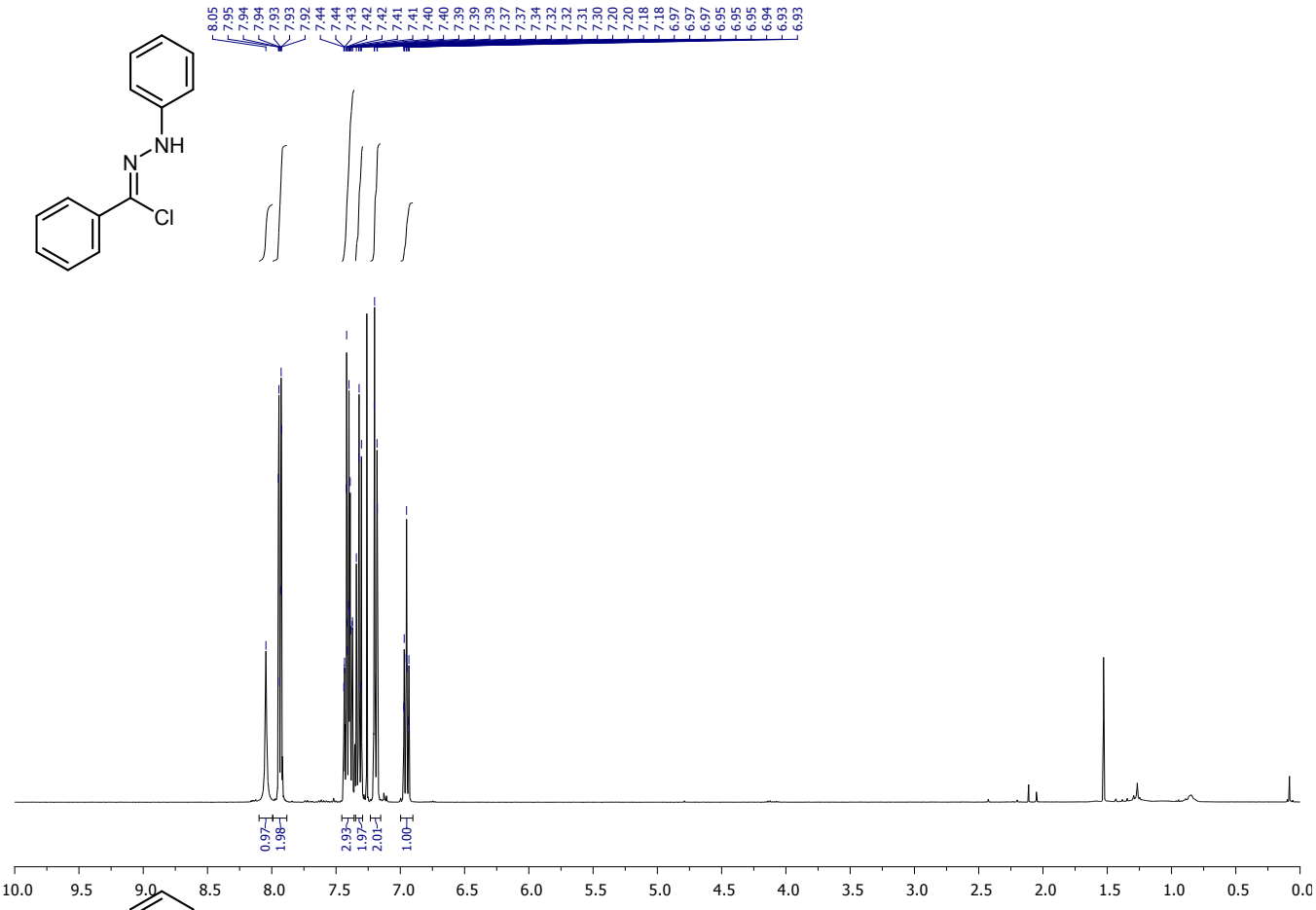


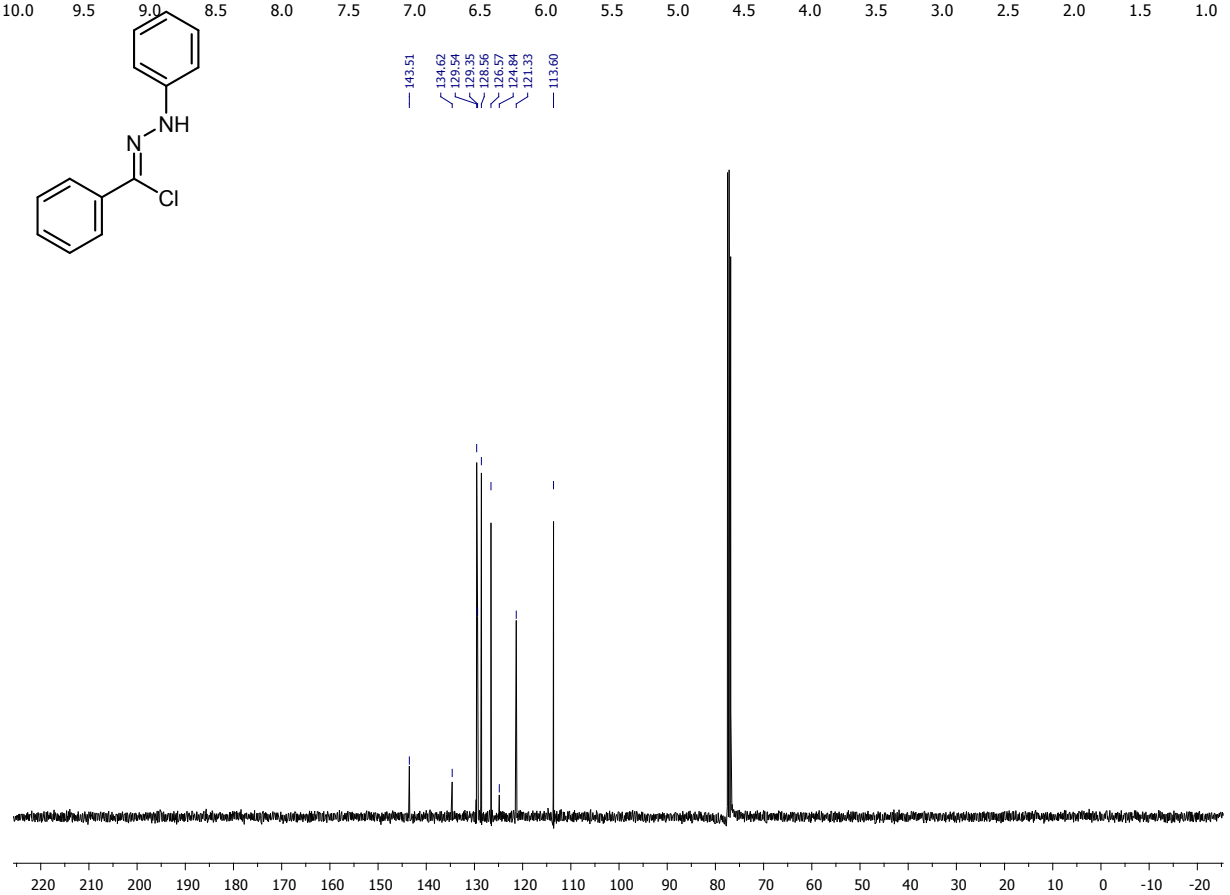
Compound S12, 1-benzylidene-2-phenylhydrazine



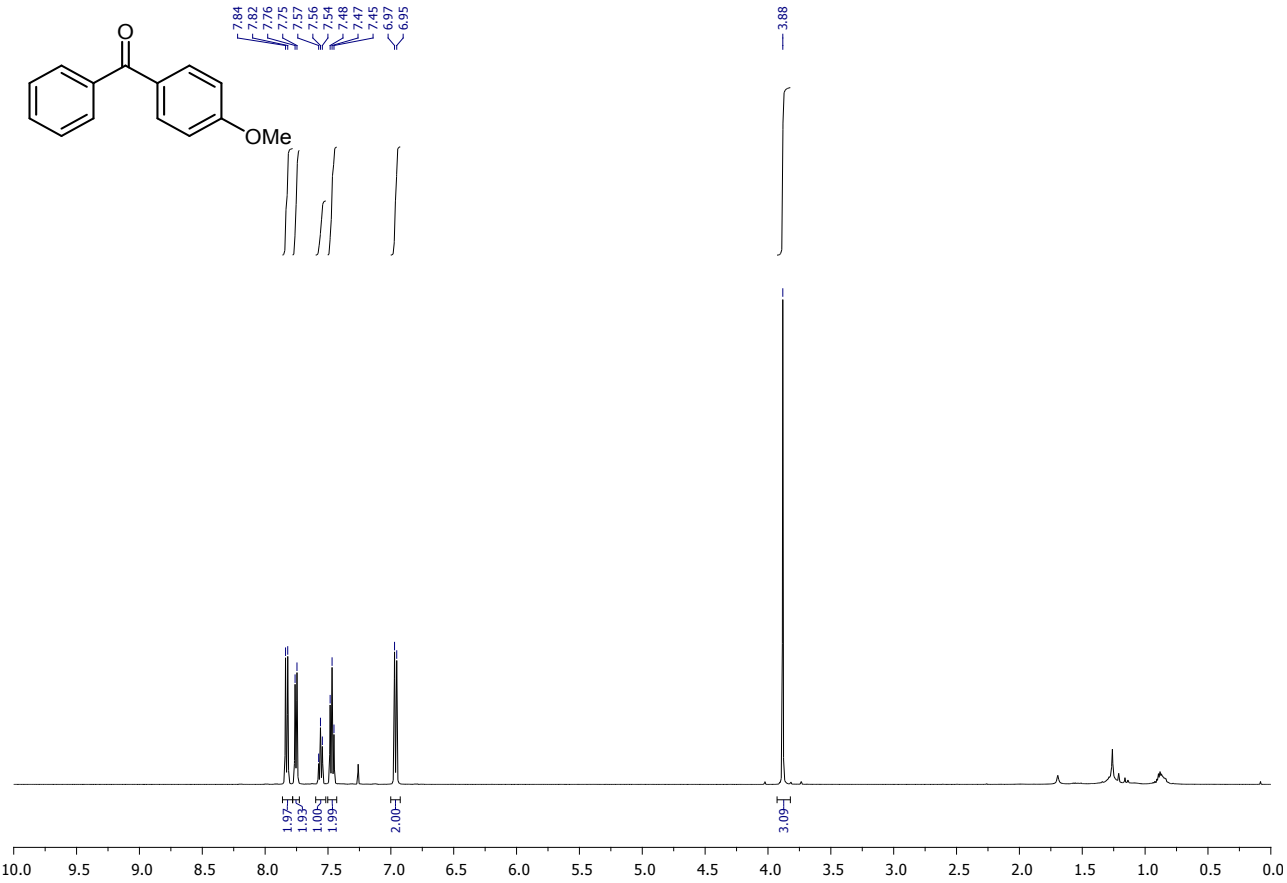


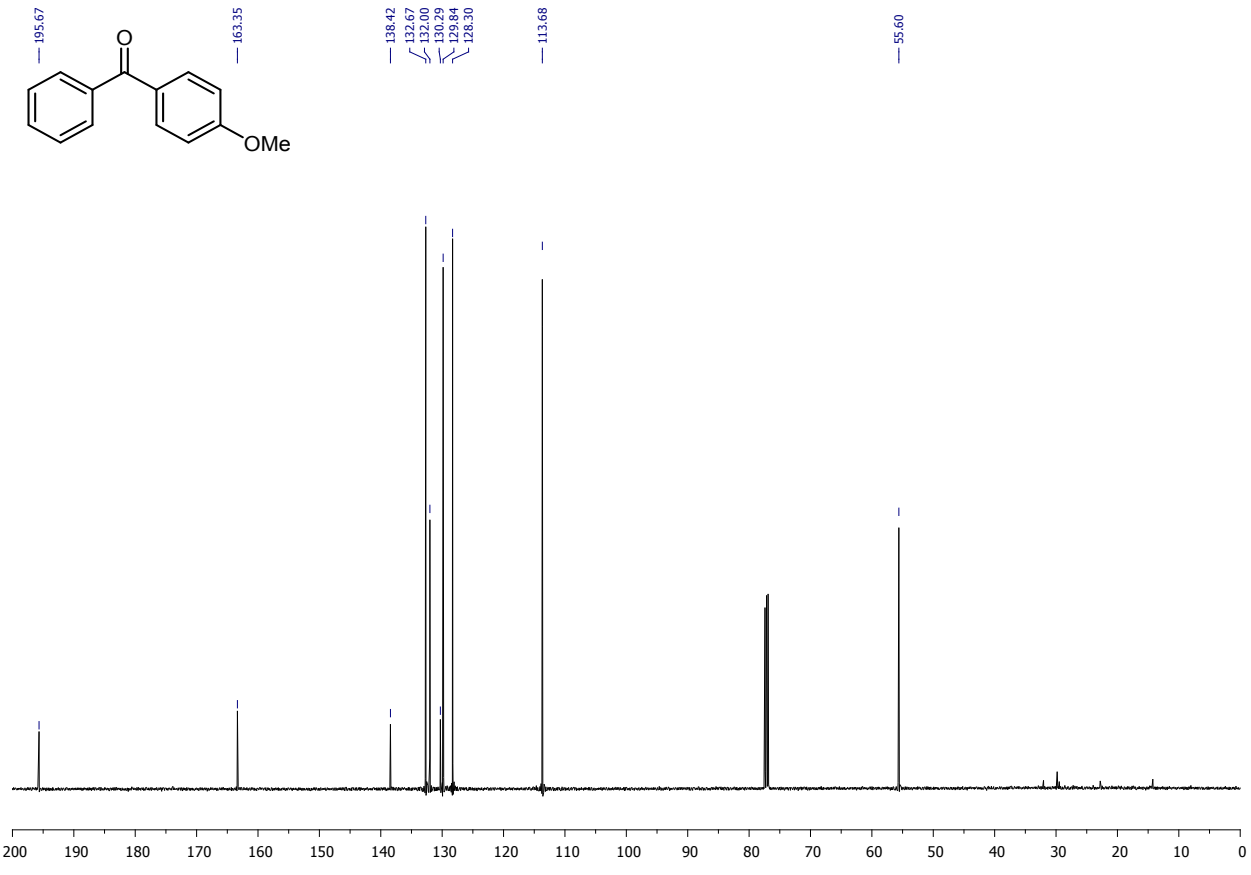
Compound 8, *N*-phenylbenzohydrazonoyl chloride



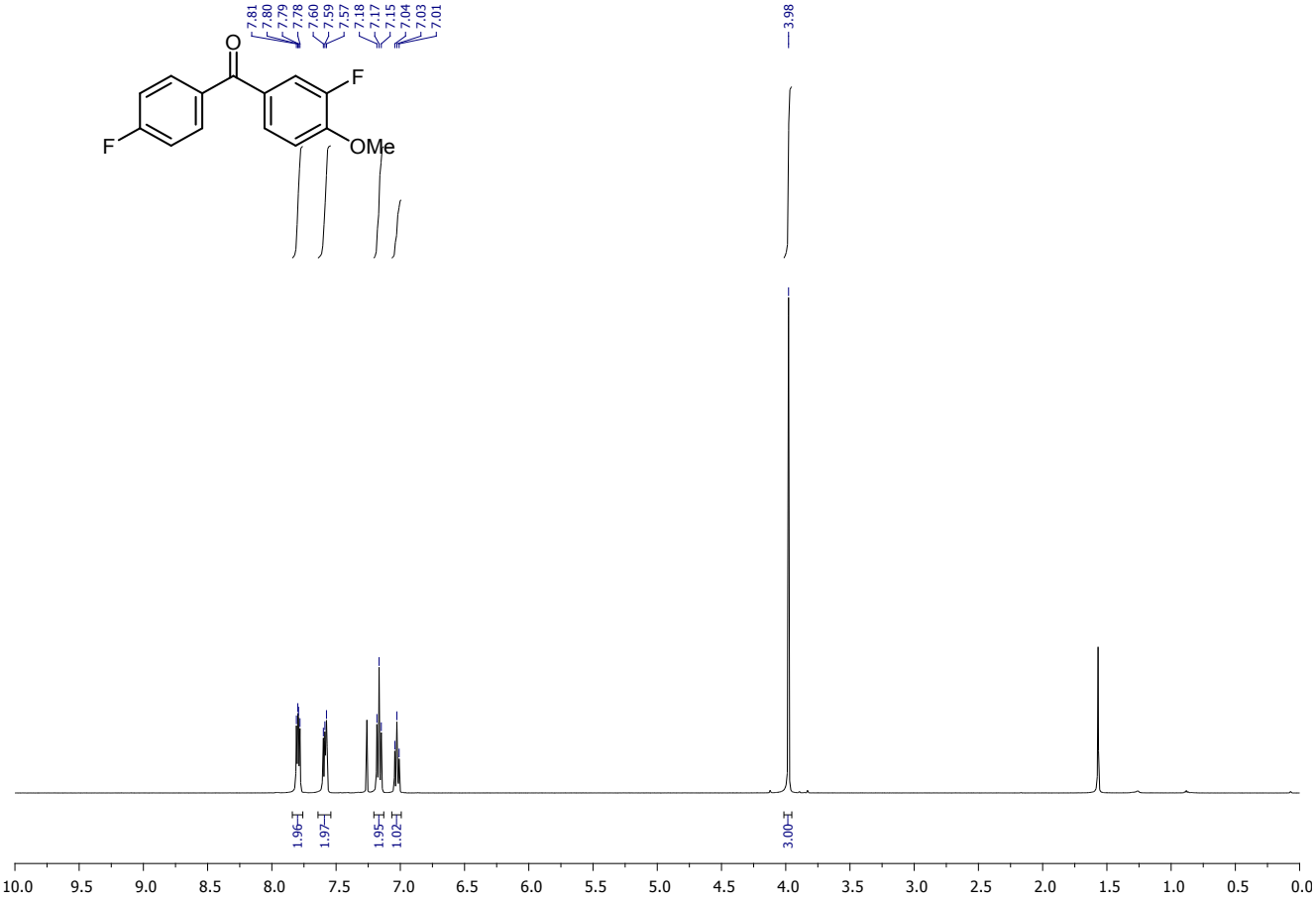


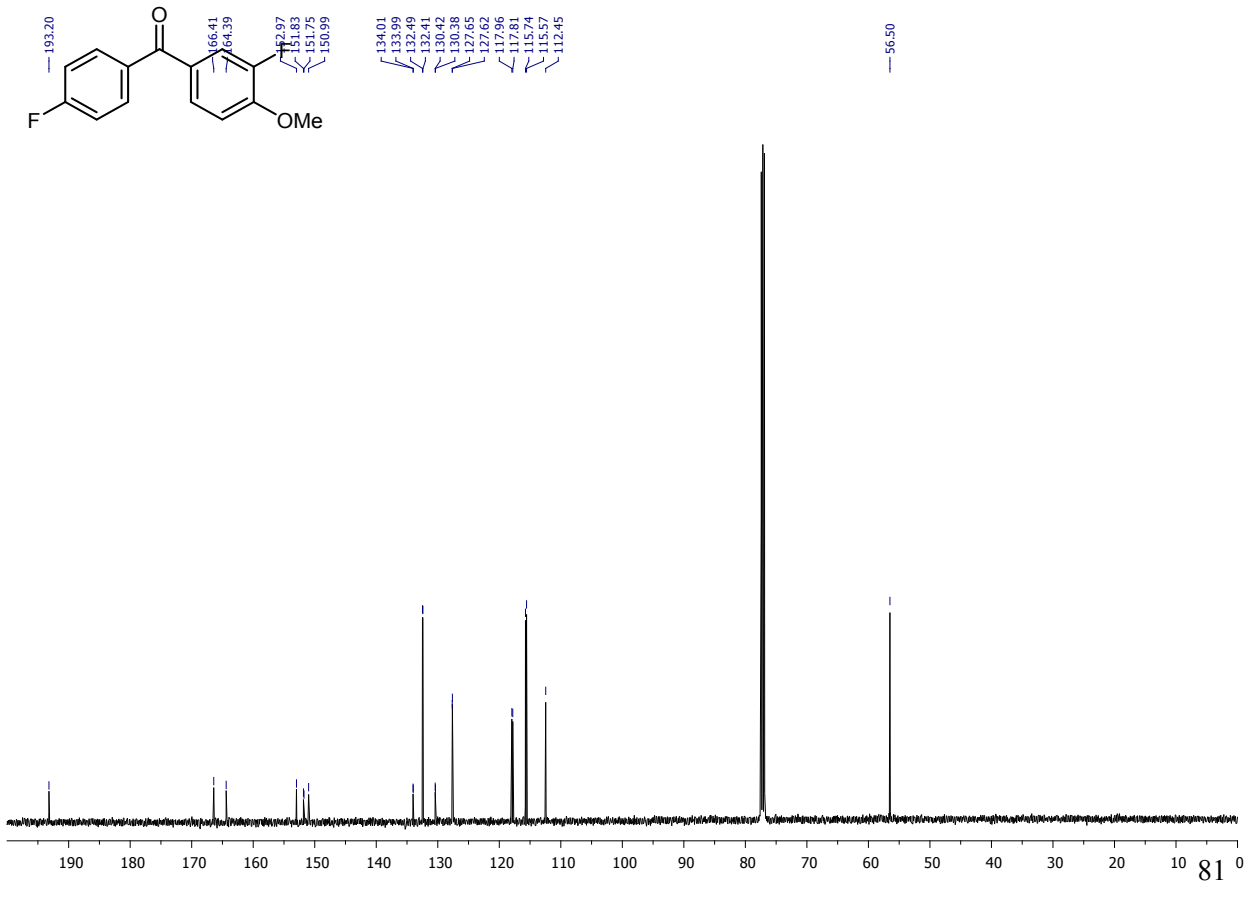
Compound S6, (4-methoxyphenyl)(phenyl)methanone

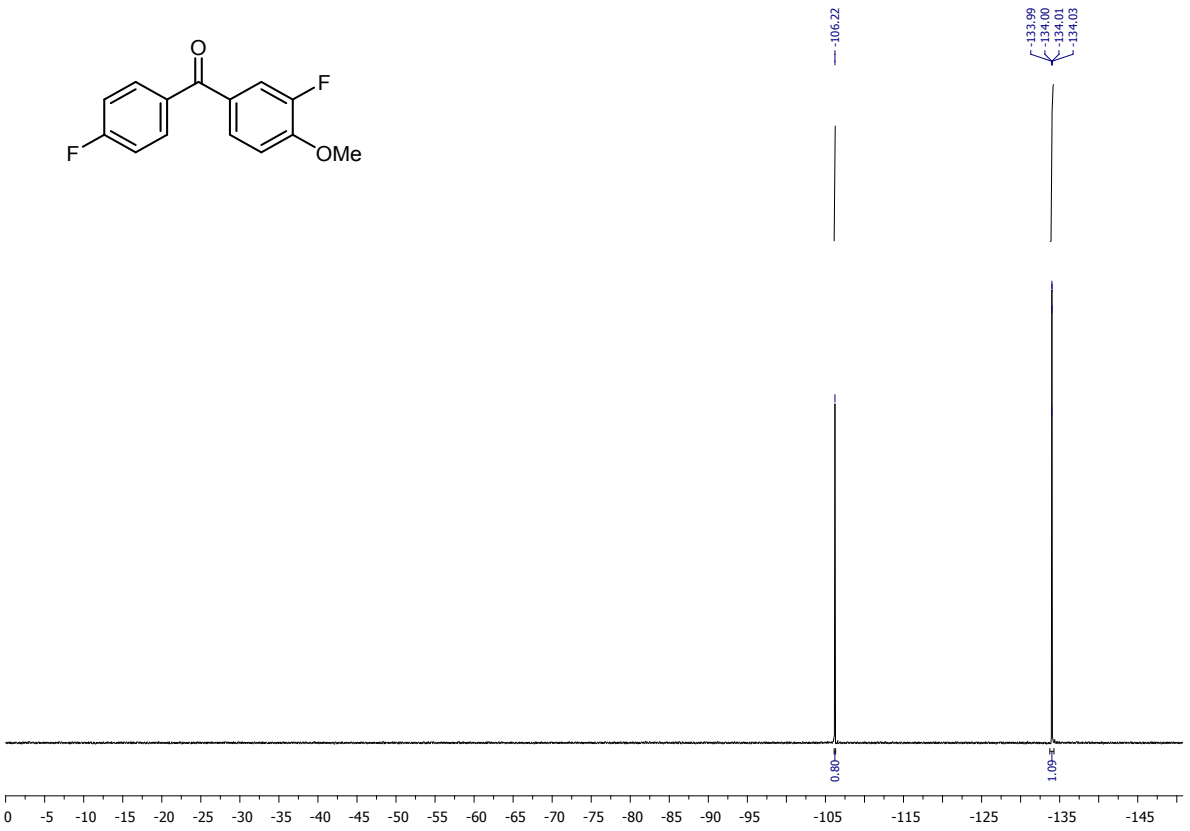




Compound S13, (3-fluoro-4-methoxyphenyl)(4-fluorophenyl)methanone



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