# Robust Buchwald-Hartwig Amination Enabled by Ball-Milling

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# 1 General Information

Unless otherwise stated, all reagents were purchased from commercial sources and used without further purification. The following palladium salts were purchased from Sigma Aldrich: palladium(II) chloride (≥99.9%), Pd-PEPPSI-IPent catalyst (**7**) (≥95%).

Thin layer chromatography (TLC) was carried out using Merck TLC silica gel 60 sheet, and visualized with ultraviolet light or potassium permanganate stain. Flash column chromatography (FCC) was performed with Sigma Aldrich silica gel 40-60 Å as the stationary phase and solvents employed were analytical grade. $^{1}$H NMR spectra were recorded on a Bruker AVX500 (500 MHz) spectrometer at ambient temperature. $^{13}$C NMR spectra were recorded on a Bruker AVX500 (125 MHz) spectrometer at ambient temperature. $^{19}$F NMR spectra were recorded on a Bruker AVX500 (471 MHz) spectrometer at ambient temperature. Melting points were measured on a Gallenkamp melting point apparatus and are reported corrected by linear calibration to benzophenone (47 - 49 °C) and benzoic acid (121 - 123 °C).

High resolution mass spectral (HRMS) data were obtained on a Thermo Scientific LTQ Orbitrap XL by the EPSRC UK National Mass Spectrometry Facility at Swansea University or on a Waters MALDI-TOF mx in Cardiff University. Spectra were obtained using electron impact ionization (EI), chemical ionization (CI), positive electrospray (ES), pneumatically-assisted electrospray (pNSI) or atmospheric solids analysis probe (ASAP+). Infrared spectra were recorded on a Shimadzu IR-Affinity-1S FTIR spectrometer.

Gas chromatography analysis was carried out using a Bruker Scion 456 gas chromatograph. An Agilent 19091J-413HP-5 column (30.0 m × 320 µm × 0.25 µm nominal) was employed for all of the separations using the following conditions: initial column temperature, 40 °C; initial hold time, 2 min; next temperature, 100 °C; hold time, 5 min; rate of temperature ramp 1, 4 °C/min, final temperature 300 °C; hold time, 5 min; rate of temperature ramp 2, 15 °C/min; injection temperature, 250 °C; injection volume 1 µL; detection temperature, 300 °C, split mode. The effluent was combusted in an $H_2$/air flame and detected using FID (flame ionization detector).

The ball mill used was a Retsch MM 400 mixer mill. Milling balls were purchased from Bearingboys. Unless otherwise stated, mechanochemical reactions were performed in 15 mL stainless steel jars from Form-Tech Scientific (FTS) with one stainless steel ball of mass 12 g. The longest time that this mill can be programmed to run for is 99 minutes. In order to run longer reaction times the mill was started, and then additional time added to the timer in order to ensure that the mill was running continuously for the desired reaction time.

The GC yield of products and conversion of substrates were determined by using the internal standard method. The response factor (RF) of analytes was determined by analyzing known

quantities of internal standard (mesitylene) against known quantities of substrate and product:

$$RF = \frac{Area_{internal\ standard} \times Moles_{analyte}}{Area_{analyte} \times Moles_{internal\ standard}}$$

The quantity of an analyte was then calculated according to the following equation:

$$Moles_{analyte} = \frac{RF \times Moles_{internal\ standard} \times Area_{analyte}}{Area_{internal\ standard}}$$

# 2 Experimental Procedures

## General Method 1: mechanochemical Buchwald-Hartwig amination

To a 15 mL stainless steel jar (Form-Tech Scientific) was added a stainless steel ball of mass 12 g, sand (0.338 g), potassium *tert*-butoxide (2 mmol, 0.224 g), aryl halide (1 mmol), amine (1.2 mmol) and Pd-PEPPSI-IPent (0.01 mmol, 0.008 g) under air atmosphere. The milling jar was then closed and the mixture was milled at 30 Hz for 3 hours. After the desired reaction time, the black solid mixture was scratched out using spatula and the jar was raised with EtOAc (10 mL) twice. Then the mixture was filtered and concentrated under reduced pressure.

(1) To obtain the $^{1}$H NMR yield, mesitylene (0.5 mmol, 70 µL) and $CDCl_3$ (5 mL) were added to the reaction mixture. Then approximately 1 mL sample of this mixture was taken for 1H NMR analysis. The yield was calculated relative to mesitylene (internal standard).

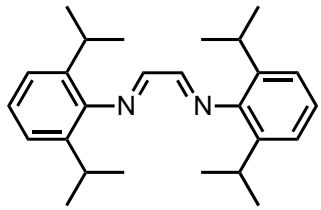
(2) To obtain the isolated yield, the crude reaction mixture was purified by silica gel flash chromatography using the noted solvent systems.

## General Method 2: conventional solution method under air

To a 50 mL round bottom flask a stir bar, potassium *tert*-butoxide (2 mmol, 0.224 g) and Pd-PEPPSI-IPent (0.01 mmol, 0.008 g) were added. Then a premixed solution of the desired solvent (10 mL), chlorobenzene (1 mmol, 0.113 g), morpholine (1.2 mmol, 0.105 g) and the internal standard mesitylene (0.5 mmol, 0.060 g) was injected into the flask *via* syringe. The reaction was stirred at room temperature under air. The reaction was analyzed by GC by talking an aliquot (~50 µL) and passing it through a pipette containing a small plug of silica gel using diethyl ether as eluent. The GC yield was calculated relative to mesitylene (internal standard).

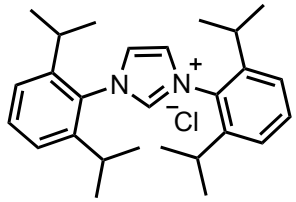
# 3 Characterization Data for Ligands and Pd(II) Complexes

**1,4-bis(2,6-diisopropylphenyl)diazabuadiene (IPr)**



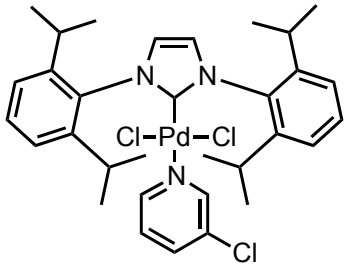
The title compound was synthesized using a method adapted from the literature.[1] To a 50 mL round-bottom flask, a solution of glyoxal (4.2 mmol, 0.603 g, 40 wt% in water), n-propanol (7 mL), 2,6-diisopropylaniline (1.62 g, 9.2 mmol) and $H_2O$ (2 mL) were added. Then the reaction mixture was heated at 70 °C for 2 h. When the reaction was finished, 10 mL $H_2O$ was added resulting in a bright yellow precipitate. The solid was then filtered, washed with methanol (20 mL) and dried under *vacuo*. Yield: 0.312 g, 20%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.13 (s, 2H), 7.26 - 7.12 (m, 6H), 2.97 (hept, *J* = 6.9 Hz, 4H), 1.24 (d, *J* = 6.9 Hz, 24H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 163.2, 148.2, 136.9, 126.3, 123.3, 28.2, 23.6. NMR data is consistent with literature values.[1] HRMS (FTMS+) calcd for $[M+H]^+$ $C_{26}H_{37}N_2$: 377.2951, found: 377.2953.

**IPr imidazolium chloride**



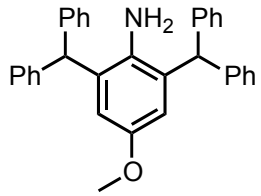
The title compound was prepared using a method modified from the literature.[2] **IPr** (0.753 g, 2 mmol) and methoxy(methyl)chloride (3.220 g, 40 mmol) were added to a glass vial. The vessel was sealed and stirred at 40 °C for 16 hours. When the reaction was finished, the mixture was cooled to room temperature and subsequent addition of diethylether ($Et_2O$, 15 mL) resulted a bright yellow precipitate. The bright yellow solid was then filtered off and washed with 50 mL $Et_2O$ and dried in *vacuo*. Yield: 0.440 g, 52%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.58 (s, 1H), 8.07 (s, 2H), 7.57 (t, *J* = 7.8 Hz, 2H), 7.35 (dd, *J* = 7.9, 1.3 Hz, 4H), 2.43 (hept, *J* = 6.9 Hz, 4H), 1.28 (d, *J* = 6.8 Hz, 12 H), 1.22 (d, *J* = 6.9 Hz, 12H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.1, 138.1, 132.4, 129.9, 127.0, 124.9, 29.3, 24.9, 24.0. NMR data is consistent with literature values.[1] HRMS (ES+) calcd for $[M-Cl]^+$ $C_{27}H_{37}N_2$: 389.2957, found: 389.2961.

**Pd-PEPPSI-IPr**



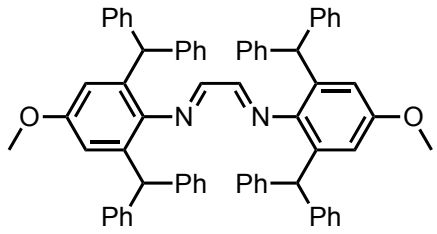

The title compound was prepared using a method modified from the literature.[3] To a thick wall glass vial $PdCl_2$ (0.088 g, 0.5 mmol), IPr imidazolium chloride (0.254 g, 0.6 mmol), $K_2CO_3$ (0.345 g, 2.5 mmol), 3-chloropyridine (2.5 mL) and a stirrer bar were added. Then the vial was sealed and the reaction mixture was then heated at 90 °C for 24 h. After cooling to room temperature, the mixture was diluted with 15 mL DCM and passed through a short pad of silica and washed with DCM (40 mL). The DCM in the solution was evaporated using rotary evaporator and 3-chloropyridine was distilled for reuse. Then the solid material was dissolved using a minimum amount of DCM and precipitated in hexane. The resulting yellow powder was filtered and dried under *vacuo*. Yield: 0.160 g, 47%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.62 (d, *J* = 2.4 Hz, 1H), 8.55 (dd, *J* = 5.5 Hz, 1.4 Hz, 1H), 7.57 (ddd, *J* = 8.2, 2.4, 1.4 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 7.7 Hz, 4H), 7.16 (s, *J* = 7.7 Hz, 2H), 7.09 (dd, *J* = 8.3, 5.5 Hz, 1H), 3.18 (hept, *J* = 6.8 Hz, 4H), 1.50 (d, *J* = 6.6 Hz, 12 H), 1.15 (d, *J* = 6.9 Hz, 12H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 153.6, 150.6, 149.6, 146.8, 137.6, 135.1, 132.1, 130.5, 125.3, 124.5, 124.2, 28.9, 26.5, 23.4. NMR data is consistent with literature values.[3] HRMS (ASAP+) calcd for $[M\text{-}Cl]^+$ $C_{32}H_{40}N_3Cl_2Pd$: 642.1634, found: 642.1638.

**2,6-dibenzhydryl-4-methoxyaniline**



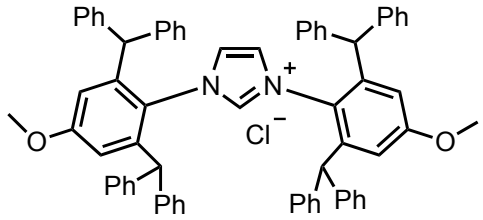

The title compound was synthesized using a method modified from the literature.[4] A 250 mL round bottom flask was charged with *p*-anisidine (2.980 g, 240 mmol) and diphenylmethanol (8.920 g, 480 mmol) and heated to 160 °C open to air. After the reaction mixture became homogeneous, a premade solution of anhydrous zinc chloride (1.62 g, 120 mmol) in concentrated HCl acid (37% in $H_2O$, 2 mL) was added dropwise. After 30 min, the reaction mixture became solid, the mixture was then cooled to room temperature and dissolved in 50 mL DCM. The DCM solution was washed with water (50 mL) multiple times, then dried over anhydrous $MgSO_4$. The solvent was evaporated, and the purple solid was crystalized from methanol to yield white crystals. Yield: 7.42 g, 68%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.36 – 7.20 (m, 12 H), 7.17 – 7.06 (m, 8H), 6.22 (s, 2H), 5.51 (s, 2H), 3.45 (s, 3H), 3.16 (br s, 2H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 152.0, 142.6, 136.0, 131.0, 129.6, 128.7, 126.8, 114.5, 55.3, 52.6. NMR data is consistent with literature values.[4] HRMS (AP+) calcd for $[M+H]^+$ $C_{33}H_{30}NO$: 456.2327, found: 456.2327.

***N,N'*-Bis(2,6-bis(diphenylmethyl)-*p*-anisidyl)diazabutadiene (IPr*$^{(OMe)}$)**



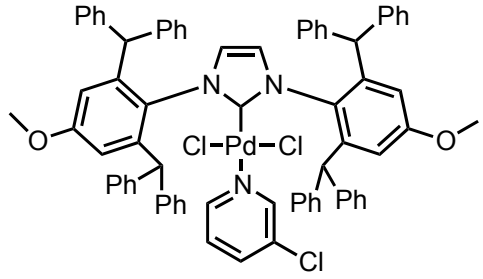

The title compound was synthesized using a method modified from the literature.[4] A solution of 2,6-dibenzhydryl-4-methoxyaniline (4.55 g, 10 mmol) in DCM (100 mL) was treated with anhydrous $MgSO_4$ (2.450 g, 20 mmol) followed by an aqueous solution of glyoxal (0.740 g, 5.1 mmol, 40 wt% in $H_2O$) and formic acid (0.05 mL, 1.3 mmol). The reaction was stirred at room temperature for 4 days before filtering and concentrating under vacuum to afford a brown solid. The crude solid was then recrystallized from boiling toluene to provide a pure diimine as bright yellow solid. Yield: 3.385 g, 73%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.24 - 7.12 (m, 26 H), 7.03 - 6.94 (m, 16H), 6.42 (s, 4H), 5.26 (s, 4H), 3.51 (s, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 164.3, 156.3, 143.7, 143.0, 133.8, 129.6, 128.4, 126.6, 114.3, 55.2, 51.4. NMR data is consistent with literature values.[4] HRMS (FTMS+) calcd for $[M+H]^+$ $C_{68}H_{57}N_2O_2$: 933.4415, found: 933.4410.

**IPr*$^{(OMe)}$ imidazolium chloride**



The title compound was prepared using a method modified from the literature.[2] **IPr*$^{OMe}$** (1.745 g, 2 mmol) and ethoxy(methyl)chloride (1.860 g, 20 mmol) were added to a glass vial. The vessel was sealed and stirred at 100 °C for 16 hours. Once the reaction is finished, the mixture was cooled to room temperature and subsequent addition of diethylether ($Et_2O$, 15 mL) resulted a white precipitate. The white solid was then filtered off and washed with 50 mL $Et_2O$ and dried in *vacuo*. Yield: 1.191 g, 61%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 12.88 (s, 1H), 7.32 - 7.24 (m, 18H), 7.23 - 7.11(m, 16H), 6.68 - 6.80 (m, 8H), 6.49 (s, 4H), 5.44 (s, 2H), 5.32 (s, 4H), 3.54 (s, 6H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 160.7, 142.6, 142.3, 141.6, 129.3, 129.0, 128.6, 128.5, 126.9, 126.8, 125.2, 123.3, 115.5, 55.1, 51.4. NMR data is consistent with literature values.[4] HRMS (EI+) calcd for $[M\text{-}Cl]^+$ $C_{69}H_{57}N_2O_2$: 945.4420, found: 945.4421.

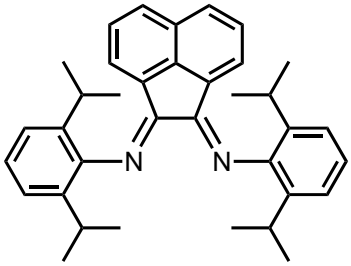
**Pd-PEPPSI-IPr*$^{(OMe)}$**



The title compound was prepared using a method modified from the literature.[5] To a thick wall glass vial $PdCl_2$ (0.088 g, 0.5 mmol), IPr*$^{(OMe)}$ imidazole chloride (0.539 g, 0.55 mmol), $K_2CO_3$ (0.345 g, 2.5 mmol), 3-chloropyridine (2.5 mL) and a stir bar were added. The vial was sealed and the reaction mixture was heated at 100 °C for 24 h. After cooling to room temperature, the mixture was diluted with 15 mL DCM and passed through a short pad of silica and washed with DCM (40 mL). The DCM in the solution was evaporated using rotary evaporator and 3-chloropyridine was distilled for reuse. The solid material was dissolved using a minimum amount of DCM and precipitated with hexane. The resulting off white powder was filtered and dried under *vacuo*. Yield: 0.127 g, 21%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.20 (d, *J* = 2.1 Hz, 1H), 9.07 (dd, *J* = 5.5, 1.3 Hz, 1H), 7.82 (ddd, *J* = 8.2, 2.4, 1.3 Hz, 1H), 7.45 (d, *J* = 7.3 Hz, 8H), 7.35 (ddd, *J* = 8.2, 5.5, 0.6 Hz, 1H), 7.26 – 7.18 (m, 12 H), 7.10 - 7.02 (m, 12H), 6.80 - 6.76 (m, 2H), 6.50 (s, 4H), 6.34 (s, 4H), 4.85 (s, 2H), 3.53 (s, 6H). **$^{13}$C NMR** (126

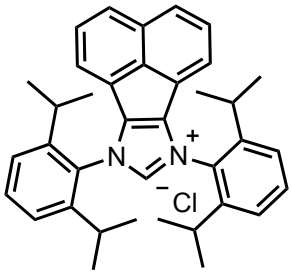
MHz, $CDCl_3$) δ 159.0, 151.0, 150.3, 149.9, 144.4, 143.9, 143.8, 138.1, 132.7, 130.9, 130.6, 129.5, 128.3, 128.0, 126.4, 126.3, 124.8, 124.3, 115.6, 55.0, 51.2. HRMS (ES+) calcd for [M-Cl-pyCl]$^+$ $C_{69}H_{56}N_2O_2ClPd$: 1085.3065, found: 1085.3087. **IR** ν 1597, 1493, 1464, 1094, 698 $cm^{-1}$

**1,2-bis[(2,6-diisopropylphenyl)imino]acenaphthene (BIAN)**




The title compound was prepared using a method modified from the literature.[6] In a 500 mL round bottom flask, acenaphthenequinone (3.500 g, 19.2 mmol) was suspended in acetonitrile (200 mL) and heated under reflux for 60 min. Then acetic acid (80 mL) was added and the mixture was refluxed for another 60 min. Following this 2,6-diisopropylphenylaniline (8.000 g, 45 mmol) was added dropwise to the hot solution. The mixture was further heated under reflux for another 5 hours. Once the reaction was finished, the reaction was cooled to room temperature. The resulting orange-yellow solid was filtered and washed with hexane (40 mL) three times, and dried under vacuum. Yield: 7.698 g, 80%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.38 (t, *J* = 7.7 Hz, 2H), 7.34 - 7.21 (m, 6H), 6.66 (d, *J* = 7.2 Hz, 2H), 3.14 - 2.91 (m, 4H), 2.16 (d, *J* = 6.8 Hz, 12H), 0.99 (d, *J* = 6.9 Hz, 12H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 161.1, 147.6, 140.9, 135.6, 131.3, 129.7, 129.0, 128.0, 124.4, 123.6, 123.5, 28.8, 23.6, 23.3. NMR data is consistent with literature values.[7] HRMS (FTMS+) calcd for [M+H]$^+$ $C_{36}H_{41}N_2$: 501.3270, found: 501.3253.

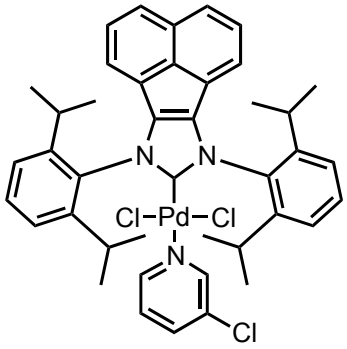
**IPr(BIAN) imidazolium chloride**




The title compound was prepared using a method modified from the literature.[2] BIAN (1.000 g, 2 mmol) and methoxy(methyl)chloride (3.220 g, 40 mmol) were added to a glass vial. The vessel was sealed and stirred at 100 °C for 16 hours. Once the reaction was finished, the mixture was cooled to room temperature and whereupon addition of diethylether ($Et_2O$ 15 mL)

resulted a yellow precipitate. Then the yellow solid was filtered off and washed with 50 mL $Et_2O$ and dried in *vacuo*. Yield: 0.850 g, 78%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 12.2 (s, 1H), 7.99 (d, *J* = 8.3 Hz, 2H), 7.66 (t, *J* = 7.9 Hz, 2H), 7.57 (dd, *J* = 8.3, 7.1 Hz), 7.46 (d, *J* = 7.9 Hz, 4H), 7.22 (d, *J* = 7.1 Hz, 2H), 2.73 (hept, *J* = 6.8 Hz, 4H), 1.96 (s, 4H), 1.40 (d, *J* = 6.8 Hz, 12H), 1.16 (d, *J* = 6.8 Hz, 12 H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 145.1, 144.6, 137.6, 132.3, 130.8, 130.4, 130.2, 129.5, 128.4, 125.1, 123.6, 122.9, 29.63, 24.9, 23.7. NMR data is consistent with literature values.[2] HRMS (FTMS+) calcd for $[M\text{-}Cl]^+$ $C_{37}H_{41}N_2$: 513.3264, found: 513.3254.

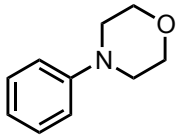
**Pd-PEPPSI-IPr$^{(BIAN)}$**




The title compound was prepared using a method modified from the literature.[5] To a thick wall glass vial $PdCl_2$ (0.355 g, 2 mmol), IPr(BIAN) imidazolium chloride (1.316g, 2.4 mmol), $K_2CO_3$ (2.760 g, 20 mmol), 3-chloropyridine (5 mL) and a stirrer bar were added. Then the vial was sealed and the reaction mixture was heated at 90 °C for 24 h. After cooling to room temperature, the mixture was diluted with 15 mL DCM and passed through a short pad of silica and washed with DCM (40 mL). The DCM in the solution was evaporated using rotary evaporator and 3-chloropyridine was distilled for reuse. Then the solid material was dissolved using a minimum amount of DCM and precipitated with hexane. The resulting yellow powder was filtered and dried under *vacuo*. Yield: 0.917 g, 58%. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 2.4 Hz, 1H), 8.61 (dd, *J* = 5.5, 1.4 Hz, 1H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.64 (t, *J* = 7.8 Hz, 2H), 7.57 (ddd, *J* = 8.2, 2.4, 1.4Hz, 2H), 7.48 (d, *J* = 7.8 Hz, 4H), 7.34 (dd, *J* = 8.3, 7.0 Hz, 2H), 7.10 (dd, *J* = 8.2, 5.5 Hz, 1H), 6.8 (d, *J* = 7.0 Hz, 2H), 3.40 (hept, *J* = 6.7 Hz, 4H), 1.46 (d, *J* = 6.6Hz, 12 H), 0.92 (d, *J* = 6.9 Hz, 12H) **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 159.1, 150.6, 149.6, 147.3, 140.4, 137.4, 133.8, 131.9, 130.7, 129.6, 129.1, 128.1, 127.3, 126.1, 124.8, 124.3, 122.2, 28.9, 25.8, 24.3. NMR data is consistent with literature values.[5] HRMS (FTMS+) calcd for $[M\text{-}Cl]^+$ $C_{42}H_{44}N_3Pd$: 766.1951, found: 766.1936.

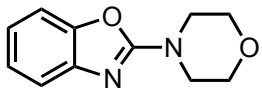
# 4 Product Characterization data

## 4-phenyl morpholine (3)



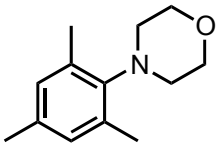
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:5) to give the titled product (0.149 g, 91%) as a beige solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.31 - 7.26 (m, 2H), 6.95 - 6.85 (m, 3H), 3.87 (t, *J* = 4.5 Hz, 4H), 3.16 (t, *J* = 4.5 Hz, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 151.4, 129.3, 120.2, 115.9, 67.1, 49.2. NMR data is consistent with literature values.[8] **HRMS** (EI) Calcd for $C_{15}H_{15}N$: 163.0997, found: 163.1002. Melting point: 61 - 63 °C.

## 2-morpholinobenzo[d]oxazole (4)



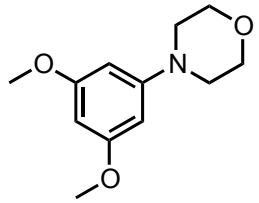
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:4) to give the product (0.082 g, 40%) as white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 7.8, 0.5 Hz, 1H), 7.21 - 7.17 (m, 1H), 7.10 (td, *J* = 7.7, 1.0 Hz, 1H), 6.97 (td, *J* = 7.8, 1.2 Hz, 1H), 3.77 - 3.72 (m, 4H), 3.64 - 3.57 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 162.1, 148.8, 142.9, 124.1, 121.0, 116.5, 108.9, 66.2, 45.8. NMR data is consistent with literature values.[9] **HRMS** (EI) Calcd for $C_{11}H_{12}N_2O_2$: 204.0899, found: 204.0899. Melting point: 79 - 81 °C.

## 4-mesitylmorpholine (5)



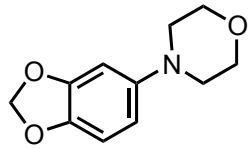
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the product (0.144 g, 70%) as white crystal. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 6.84 (s, 2H), 3.86 - 3.75 (m, 4H), 3.13 - 3.05 (m, 4H), 2.33 (s, 6H), 2.26 (s, 3H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 145.5, 137.0, 135.0, 129.8, 68.4, 50.2, 20.8, 19.6. NMR data is consistent with literature values.[10] **HRMS (ESI)** Calcd for $C_{13}H_{20}NO$ $[M+H]^+$: 206.1545, found: 206.1541. Melting point: 64 - 66 °C.

## 4-(3,5-dimethoxyphenyl)morpholine (6)



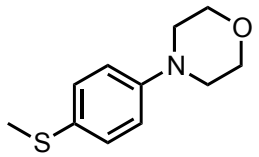
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the product (0.185 g, 83%) as white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 6.08 (d, *J* = 1.9 Hz, 2H), 6.04 (t, *J* = 2.0 Hz, 1H), 3.87 - 3.81 (t, *J* = 4.8 Hz, 4H), 3.78 (s, 6H), 3.14 (t, *J* = 7.22 Hz, 4H). **$^{13}$C NMR (**126 MHz, $CDCl_3$) δ 160.7, 152.4, 93.9, 91.0, 66.0, 54.4, 48.5. NMR data is consistent with literature values.[11] **HRMS (ESI)** Calcd for $C_{12}H_{18}NO_3$ $[M+H]^+$: 224.1287, found: 224.1286. Melting point: 85 - 86 °C.

## 4-(benzo[d][1,3]dioxol-5-yl)morpholine (7)



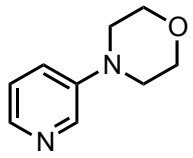
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the product (0.122 g, 59%) as yellow solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 6.73 (d, *J* = 8.4 Hz, 1H), 6.54 (d, *J* = 2.4 Hz, 1H), 6.35 (dd, *J* = 8.4 Hz, 1H), 5.90 (s, 2H), 3.84 (t, *J* = 4.8 Hz, 4H), 3.03 (t, *J* = 4.8 Hz, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.5, 147.5, 141.9, 108.8, 108.4, 101.1, 99.7, 67.1, 51.2. NMR data is consistent with literature values.[12] **HRMS (ESI)** Calcd for $C_{11}H_{13}NO_3$ $[M+H]^+$: 208.0974, found: 208.0969. Melting point: 64 - 65 °C.

## 4-(4-(methylthio)phenyl)morpholine (8)



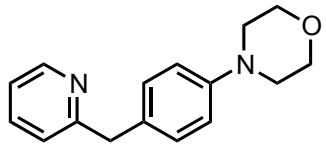
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether =1:4 with 1 % $Et_3N$) to give the product (0.136 g, 65%) as an off-white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.21 - 7.16 (m, 2H), 6.80 - 6.76 (m, 2H), 3.77 (t, *J* = 5.0 Hz, 4H), 3.05 (t, *J* = 5.0 Hz, 4H), 2.36 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.8, 130.0, 128.0, 116.4, 67.0, 49.4, 18.1. NMR data is consistent with literature values.[13] **HRMS** (EI) Calcd for $C_{11}H_{15}NOS$ [M]: 209.0874, found: 209.0873. Melting point: 93 - 95 °C.

## 4-(pyridin-3-yl)morpholine (9)



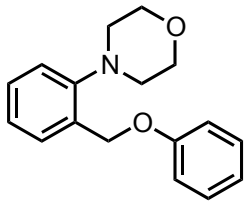
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether =1:4 with 1 % $Et_3N$) to give the product (0.099 g, 60%) as a yellow solid. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.13 (s, 1H), 7.17 (t, *J* = 2.0 Hz, 2H), 3.91 - 3.82 (m, 4H), 3.20 - 3.17 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.1, 141.2, 138.4, 123.7, 122.2, 66.8, 48.7. NMR data is consistent with literature values.[14] **HRMS (EI)** Calcd for$C_9H_{12}N_2O$ [M]: 164.0950, found: 164.0953. Melting point: 37 - 39 °C.

## 4-(4-(pyridin-2-ylmethyl)phenyl)morpholine (10)



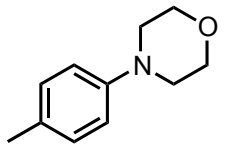
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether =1:5) to give the product (0.082 g, 32%) as yellow oil. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 8.53 (d, J = 3.7 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 7.7 Hz, 2H), 6.86 (d, *J* = 8.5 Hz, 1H), 4.08 (s, 1H), 3.88 - 3.78 (m, 4H), 3.15 - 2.92 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 161.6, 150.0, 149.4, 136.6, 131.2, 130.0, 123.1, 121.3, 116.1, 67.1, 49.7, 44.0. **HRMS** (EI) Calcd for $C_{16}H_{18}N_2O$ [M]: 254.1419, found: 254.1416.

## 4-(2-(phenoxymethyl)phenyl)morpholine (11)



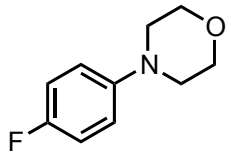
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the product (0.194 g, 72%) as white crystal. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.57 - 7.51 (m, 1H), 7.37 - 7.27 (m, 3H), 7.19 - 7.12 (m, 2H), 7.01 - 6.93 (m, 3H), 5.16 (s, 2H), 3.82 (t, *J* = 4.6 Hz, 4H), 2.98 (t, *J* = 4.6 Hz, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 159.1, 151.5, 132.0, 130.1, 129.6, 129.2, 124.4, 121.0, 120.0, 114.9, 67.6, 66.0, 53.6. **HRMS (ESI)** Calcd for $C_{17}H_{20}NO_2$ $[M+H]^+$: 270.1489, found: 270.1492. Melting point: 85 - 88 °C.

## 4-(*p*-tolyl)morpholine (12)



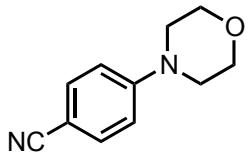
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.092 g, 52%) as white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.2, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 3.86 (t, *J* = 4.8 Hz, 4H), 3.11 (t, *J* = 4.8 Hz, 4H), 2.28 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.3, 129.9, 129.8, 116.2, 67.1, 50.1, 20.6. NMR data is consistent with literature values.[11] **HRMS** (EI) Calcd for $C_{15}H_{15}NO$ [M]: 177.1154, found: 177.1149. Melting point: 43 - 46 °C.

## 4-(4-fluorophenyl)morpholine (13)



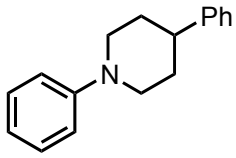
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the product (0.076 g, 42%) as yellow oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.03 - 6.92 (m, 2H), 6.90 - 6.82 (m, 2H), 3.90 - 3.80 (m, 4H), 3.13 - 3.03 (m, 4H). **$^{13}$C NMR (**126 MHz, $CDCl_3$) δ 157.5 (d, *J* = 239 Hz), 148.1 (d, *J* = 2 Hz), 117.6 (d, *J* = 8 Hz), 115.76 (d, *J* = 22 Hz), 67.1, 50.5. [19] **F NMR** (471 MHz, $CDCl_3$) δ -124.2. NMR data is consistent with literature values.[15] **HRMS (ASAP+)** Calcd for $C_{10}H_{13}NOF$ $[M+H]^+$: 182.0981, found: 182.0983.

## 4-morpholinobenzonitrile (14)



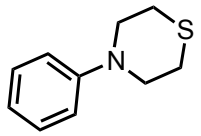
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.096 g, 51%) as a white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.55 - 7.48 (m, 2H), 6.90 - 6.83 (m, 2H), 3.85 (t, *J* = 5.0 Hz, 4H), 3.27 (t, *J* = 5.0 Hz, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 153.6, 133.6, 120.0, 114.2, 101.1, 66.6, 47.4. NMR data is consistent with literature values.[14] **HRMS** (EI) Calcd for $C_{11}H_{12}N_2O$ [M]: 188.0950, found: 188.0952. Melting point: 81-83 °C.

## 1,4-diphenylpiperidine (15)



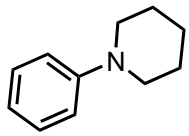

Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.192 g, 81%) as a white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.35 - 7.20 (m, 6H), 7.00 (d, *J* = 7.8 Hz, 2H), 6.86 (t, *J* = 6.9 Hz, 1H), 3.82 (d, *J* = 12.3 Hz, 2H), 2.83 (t, *J* = 11.2 Hz, 2H), 2.76 - 2.58 (m, 1H), 2.01 - 1.89 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 152.0, 146.2, 129.3, 128.6, 127.0, 126.4, 119.7, 116.8, 50.7, 42.7, 33.5. NMR data is consistent with literature values.[16] **HRMS (ESI)** Calcd for $C_{17}H_{19}N$ $[M+H]^+$: 237.1517, found: 237.1519. Melting point: 85 - 87 °C.

## 4-phenylthiomorpholine (16)



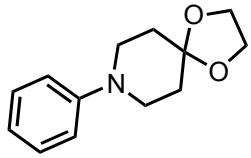

Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.158 g, 88%) as a dark yellow oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.22 - 7.12 (m, 2H), 6.86 - 6.72 (m, 3H), 3.44 (t, *J* = 5.1 Hz, 4H), 2.65 (t, *J* = 5.1 Hz, 4H). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 151.4, 129.3, 119.9, 117.2, 52.2, 26.9. NMR data is consistent with literature values.[17] **HRMS (ESI)** Calcd for $C_{10}H_{13}NS$ $[M+H]^+$: 179.0769, found: 179.0760.

## 1-phenylpiperidine (17)



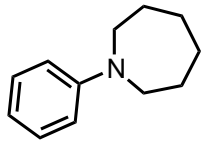

Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:19) to give the titled product (0.124 g, 77%) as a brown oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.27 - 7.21 (m, 2H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.82 (t, *J* = 7.3 Hz, 1H), 3.16 (t, *J* = 5.5 Hz, 4H), 1.77 - 1.67 (m, 4H), 1.62 - 1.53 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 152.4, 129.1, 119.3, 116.7, 50.8, 26.0, 24.5. NMR data is consistent with literature values.[18] **HRMS (ESI)** Calcd for $C_{11}H_{15}N$ $[M+H]^+$: 161.1204, found: 161.1204.

## 8-phenyl-1,4-dioxa-8-azaspiro[4.5]decane (18)



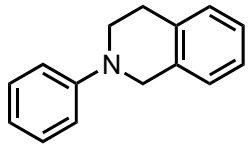
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.171 g, 78%) as a dark yellow oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.55 (t, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 4.29 (s, 4H), 3.64 - 3.62 (t, *J* = 5.5 Hz, 4H), 2.27 - 2.03 (t, *J* = 5.5 Hz, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 151.1, 129.2, 119.6, 116.8, 107.3, 64.5, 47.9, 34.7. NMR data is consistent with literature values.[19] **HRMS (ESI)** Calcd for $C_{18}H_{21}N$ $[M+H]^+$: 220.1336, found: 220.1338.

## 1-phenylazepane (19)



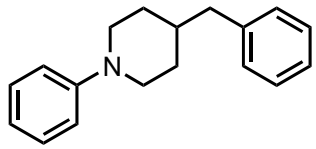
Purified by flash column chromatography (Ethyl Acetate/Petroleum ether = 1:19) to give the titled product (0.126 g, 72%) as a brown oil. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.23 - 7.17 (m, 2H), 6.69 (d, *J* = 8.2 Hz, 2H), 6.62 (t, *J* = 7.2 Hz, 1H), 3.47 - 3.44 (t, *J* = 6.0 Hz, 4H), 1.82 -1.74 (m, 4H), 1.58 - 1.52 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.1, 129.4, 115.3, 111.3, 49.2, 27.9, 27.3. NMR data is consistent with literature values.[20] **HRMS (ESI)** Calcd for $C_{18}H_{21}N$ $[M+H]^+$: 175.1361, found: 175.1362.

## 2-phenyl-1,2,3,4-tetrahydroisoquinoline (20)



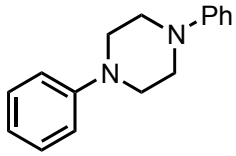
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:20) to give the titled product (0.151 g, 72%) as an off white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.39 - 7.28 (m, 2H), 7.22 - 7.18 (m, 4H), 7.06 - 6.97 (m, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 4.44 (s, 2H), 3.59 (t, *J* = 5.8 Hz, 2H), 3.02 (t, *J* = 5.7 Hz, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 150.7, 135.0, 134.6, 129.3, 128.7, 126.7, 126.5, 126.2, 118.8, 115.3, 50.9, 46.7, 29.3. NMR data is consistent with literature values.[21] **HRMS** (EI) Calcd for $C_{15}H_{15}N$ [M]: 209.1204, found: 209.1204. Melting point: 57 - 60°C.

## 4-benzyl-1-phenylpiperidine (21)



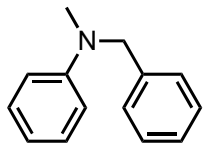
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the titled product (0.200 g, 80%) as a red solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.24 - 7.04 (m, 7H), 6.83 (d, *J* = 8.0 Hz, 2H), 6.72 (t, *J* = 7.3 Hz, 1H), 3.52 (t, *J* = 28.9 Hz, 2H), 2.54 (td, *J* = 12.2, 2.1 Hz, 2H), 2.48 (d, *J* = 7.1 Hz, 2H), 1.82 - 1.44 (m, 3H), 1.38 - 1.21 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 151.96, 140.59, 129.25, 129.13, 128.33, 125.99, 119.34, 116.62, 50.08, 43.29, 38.00, 32.15. **HRMS** (EI) Calcd for $C_{18}H_{21}N$ [M]: 251.1674, found : 251.1674. Melting point: 67 - 70 °C.

## 1,4-diphenylpiperazine (22)



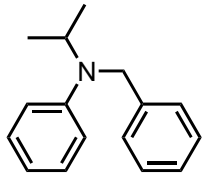
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:19) to give the titled product (0.190 g, 80%) as a white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.37 - 7.27 (m, 4H), 7.01 (d, *J* = 7.9 Hz, 4H), 6.91 (t, *J* = 7.3 Hz, 2H), 3.36 (s, 8H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 151.4, 129.3, 120.2, 116.5, 49.6. NMR data is consistent with literature values.[18] **HRMS** (ESI) Calcd for $C_{18}H_{21}N$ [M+H]$^{+}$: 237.1517, found: 237.1519. Melting point: 173 - 175 °C.

## *N*-benzyl-*N*-methylaniline (23)



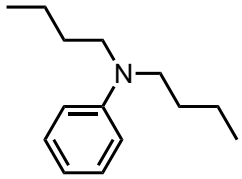
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:4) to give the titled product (0.134 g, 68%) as a light yellow liquid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.24 - 7.17 (m, 2H), 7.17 - 7.07 (m, 5H), 6.69 - 6.58 (m, 3H), 4.43 (s, 2H), 2.92 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.8, 139.1, 129.3, 128.7, 127.0, 126.8, 116.6, 112.4, 56.7, 38.6. NMR data is consistent with literature values.[18] **HRMS** (ASAP+) Calcd for $C_{14}H_{16}N$ [M+H]$^{+}$: 198.1283, found: 198.1277.

### *N*-benzyl-*N*-isopropylaniline (24)



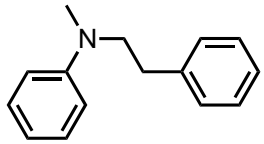
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.160 g, 71%) as yellow liquid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.34 - 7.28 (m, 4H), 7.25 - 7.14 (m, 3H), 6.75 - 6.66 (m, 3H), 4.43 (s, 2H), 4.34 - 4.25 (m, 1H), 1.22 (d, *J* = 6.6 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 149.4, 140.9, 129.2, 128.5, 126.5, 126.3, 116.4, 113.1, 48.5, 48.2, 20.0. NMR data is consistent with literature values.[22] **HRMS** (ASAP+) Calcd for $C_{16}H_{20}N$ $[M+H]^+$: 226.1596, found: 226.1294.

### *N*,*N*-dibutylaniline (25)



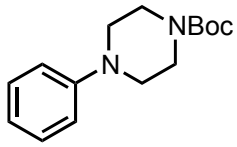
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:9) to give the titled product (0.095 g, 61%) as yellow liquid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.24 - 7.19 (m, 2H), 6.69 - 6.61 (m, 3H), 3.28 (t, *J* = 7.5 Hz, 4H), 1.63 - 1.55 (m, 4H), 1.42 - 1.33 (m, 4H), 0.97 (t, *J* = 7.4 Hz, 6H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 148.3, 129.3, 115.2, 111.8, 50.9, 29.6, 20.5, 14.2. NMR data is consistent with literature values.[18] **HRMS** (ASAP+) Calcd for $C_{14}H_{24}N$ $[M+H]^+$: 206.1909, found: 206.1910.

### *N*-methyl-*N*-phenethylaniline (26)



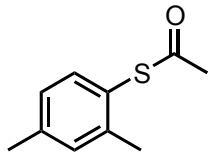
Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the titled product (0.152 g, 72%) as yellow liquid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.33 - 7.04 (m, 7H), 6.72 - 6.59 (m, *J* = 16.4, 3H), 3.47 (t, *J* = 7.5 Hz, 2H), 2.79 (s, *J* = 7.1 Hz, 3H), 2.78 - 2.72 (m, 2H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 148.8, 139.9, 129.4, 128.9, 128.6, 126.3, 116.2, 112.2, 54.8, 38.6, 32.9. NMR data is consistent with literature values.[23] **HRMS** (EI) Calcd for $C_{15}H_{17}N$ [M]: 211.1361, found: 211.1363.

### *tert*-butyl 4-phenylpiperazine-1-carboxylate (27)



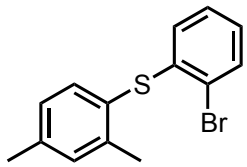

Purified by column chromatography (Ethyl Acetate/Petroleum ether = 1:10) to give the titled product (0.157 g, 60%) as a white solid. **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.30 - 7.27 (m, 2H), 6.95 - 6.90 (m, 3H), 3.59 (t, *J* = 5.2 Hz, 4H), 3.14 (t, *J* = 5.1 Hz, 4H), 1.50 (s, 9H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 154.9, 151.4, 129.3, 120.4, 116.8, 80.0, 49.6, 43.5, 28.6. NMR data is consistent with literature values.[18] **HRMS** (EI) Calcd for $C_{15}H_{22}N_2O_2$ [M]: 262.1681, found: 262.1682.

## *S*-(2,4-dimethylphenyl) ethanethioate (28)



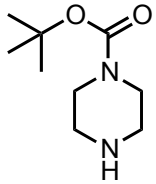

The titled compound was prepared using a method modified from the literature.[24] A 100 mL, three-necked, round-bottomed flask equipped with an argon inlet adapter, glass stopper, and a rubber septum was charged with 2,4-dimethylbenzenethiol (1.381 g, 10 mmol), 35 mL of dichloromethane, and pyridine (1.15 mL, 1.12 g, 14.2 mmol) and cooled to 0 °C. Acetyl chloride (1.0 mL, 1.10 g, 14.1 mmol) was added slowly *via* syringe over ca. 8 min. The resulting mixture was stirred at 0 °C for 10 min and then at 25 °C for 2 h. The resulting cloudy white mixture was poured into 20 mL of water, and the aqueous phase was separated and extracted with two 10 mL portions of dichloromethane. The combined organic phases were washed with 20 mL of brine, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Then the crude material was then purified by silica gel flash chromatography (Ethyl Acetate/Petroleum ether = 1:20) to give the title compound as light yellow liquid (1.028 g, 57%). **$^{1}$H NMR** (500 MHz, $CDCl_3$) δ 7.24 (s, 1H), 7.14 - 7.11 (m, 1H), 7.04 - 7.00 (m, 1H), 2.39 (s, 3H), 2.32 (s, 3H), 2.30 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 194.4, 141.9, 140.5, 135.9, 131.8, 127.6, 124.2, 30.3, 21.4, 20.8. **HRMS** (EI) Calcd for $C_{10}H_{12}OS$ [M]: 180.0609, found: 180.0616.

## (2-bromophenyl)(2,4-dimethylphenyl)sulfane (29)



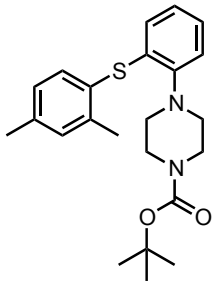

The titled compound was prepared using a method modified from literature.[25] To a 50 mL round bottomed flask, $Pd(dba)_2$ (0.144 g, 0.25 mmol), Xantphos (0.203 g, 0.35 mmol), 1,2-dibromobenzene (0.702 g, 1.5 mmol), *S*-(2,4-dimethylphenyl)ethanethioate (0.901 g, 5 mmol) sodium *tert*-butoxide (0.577 g, 6 mmol), toluene (10 mL) were added. The reaction mixture was stirred at 6 h at 110 °C under nitrogen atmosphere and then cooled to room temperature. Then the reaction mixture was poured into a 10 mL saturated aqueous ammonium chloride and extracted with $Et_2O$ (20 mL) three times. The combined organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. Then the crude material was then purified by silica gel flash chromatography (Ethyl acetate/Petroleum ether = 1:20) to give the titled compound as light yellow liquid (1.232 g, 84%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.19 - 7.15 (m, 1H), 7.10 - 7.04 (m, 2H), 6.96 (td, *J* = 7.9, 7.3 Hz, 1H), 6.57 (dd, *J* = 8.0, 1.6 Hz, 1H), 2.37 (s, 3H), 2.34 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 142.5, 140.1, 139.6, 136.4, 132.9, 132.1, 128.2, 127.8, 127.5, 127.2, 126.2, 121.3, 21.4, 20.7. NMR data is consistent with literature values.[26] **HRMS** (EI) Calcd for $C_{14}H_{13}SBr$ [M]: 291.9921, found: 291.9925.

## *tert*-butyl piperazine-1-carboxylate



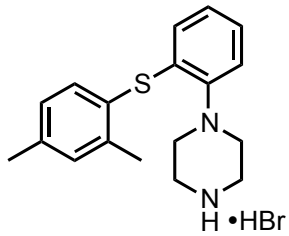

The titled compound was prepared using a method modified from literature. To a 50 mL flask was added piperazine (0.86 g, 10 mmol, 2.5 equiv), sodium hydroxide (0.16 g, 4.0 mmol, 1.0 equiv), isopropanol (12 mL) and water (1.3 mL). di-tert-butyl dicarbonate (0.92 mL, 4.0 mmol, 1.0 equiv) was added and the reaction was stirred at room temperature for 18 h. The solution was concentrated to remove isopropanol. The mixture was diluted with water, filtered through a fritted funnel to remove di-*tert*-butyl piperazine-1,4-dicarboxylate, and the filtrate was extracted with DCM (×3). The combined organic fractions were dried over $MgSO_4$ and concentrated to yield the titled compound as a white crystalline solid (1.06 g, 5.7 mmol, 57%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 1.47 (s, 9H), 2.94 - 2.71 (m, 4H), 3.72 - 3.36 (m, 4H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.0, 79.7, 46.0, 44.9, 28.6. NMR data is consistent with literature values.[27] **HRMS** (EI) Calcd for $C_9H_{18}N_2O_2$ [M]: 186.1386, found: 186.1386.

## *tert*-butyl 4-(2-((2,4-dimethylphenyl)thio)phenyl)piperazine-1-carboxylate/ *N*-Boc vortioxetine (30)



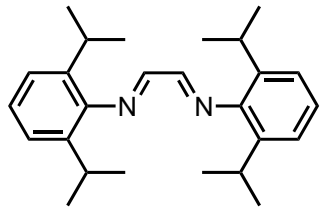
The titled compound was prepared using **General Method 1**. Purified by flash column chromatography (Ethyl Acetate/Petroleum ether =1:10) to give the product (0.275 g, 69%) as an light yellow solid. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.8 Hz, 1H), 7.15 (s, 1H), 7.09 - 7.00 (m, 3H), 6.90 - 6.84 (m, 1H), 6.53 (dd, *J* = 7.9, 1.4 Hz, 1H), 3.62 (t, *J* = 5.0 Hz, 4H), 3.02 (t, *J* = 4.9 Hz, 4H), 2.36 (s, 3H), 2.32 (s, 3H), 1.49 (s, 9H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 155.1, 149.1, 142.5, 139.4, 136.3, 134.8, 131.8, 127.99, 127.96, 126.5, 125.7, 124.8, 120.1, 79.8, 51.8, 43.8, 28.6, 21.3, 20.7. NMR data is consistent with literature values.[28] **HRMS** (ESI+) Calcd for $C_{23}H_{31}N_2O_2S$ $[M+H]^+$: 399.2106, found: 399.2102. Melting point: 78 - 80 °C.

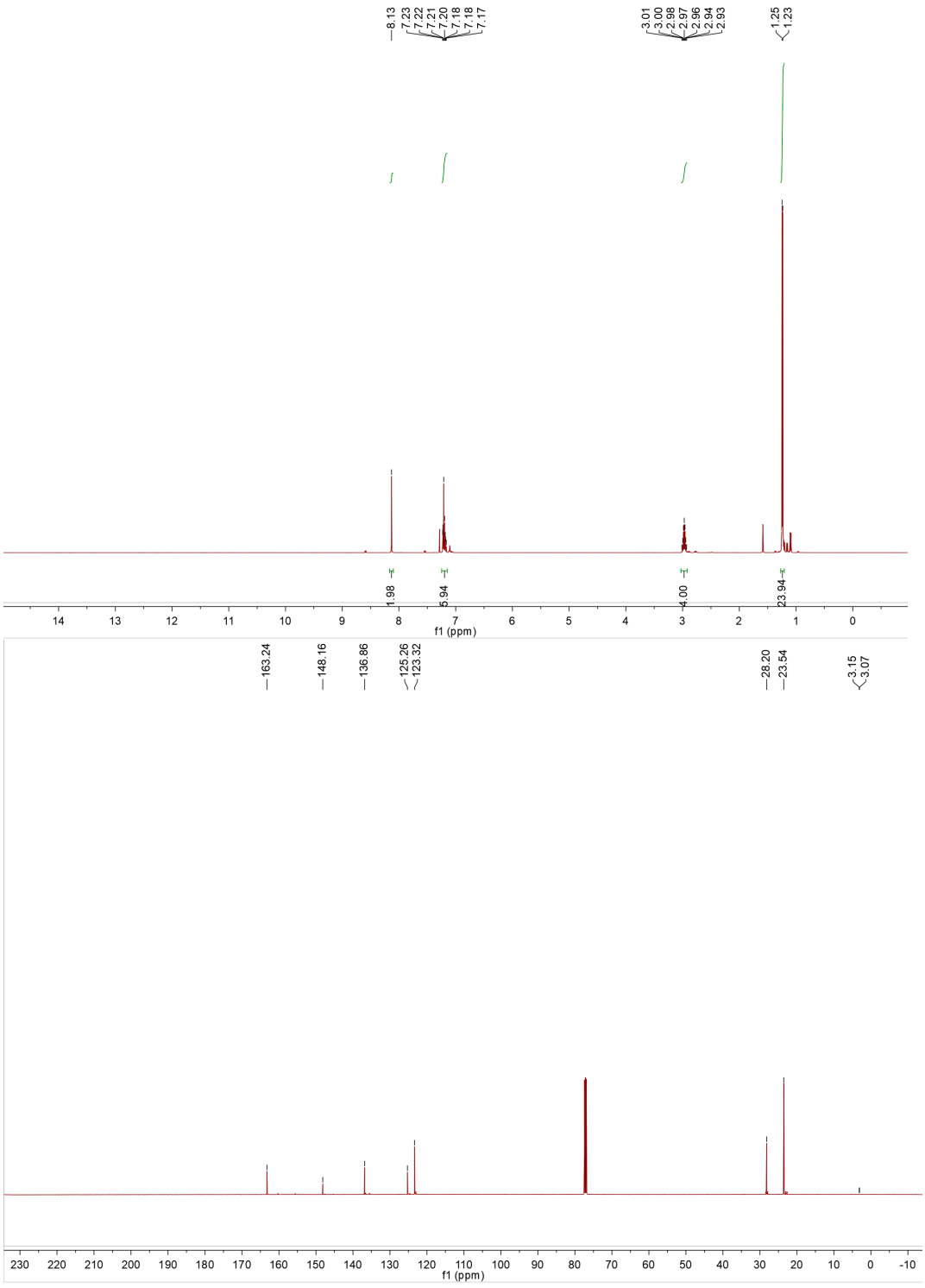
## *tert*-butyl 4-(2-((2,4-dimethylphenyl)thio)phenyl)piperazine-1-carboxylate hydrobromide/ Vortioxetine hydrobromide (31)

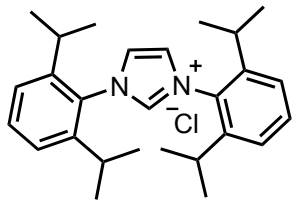


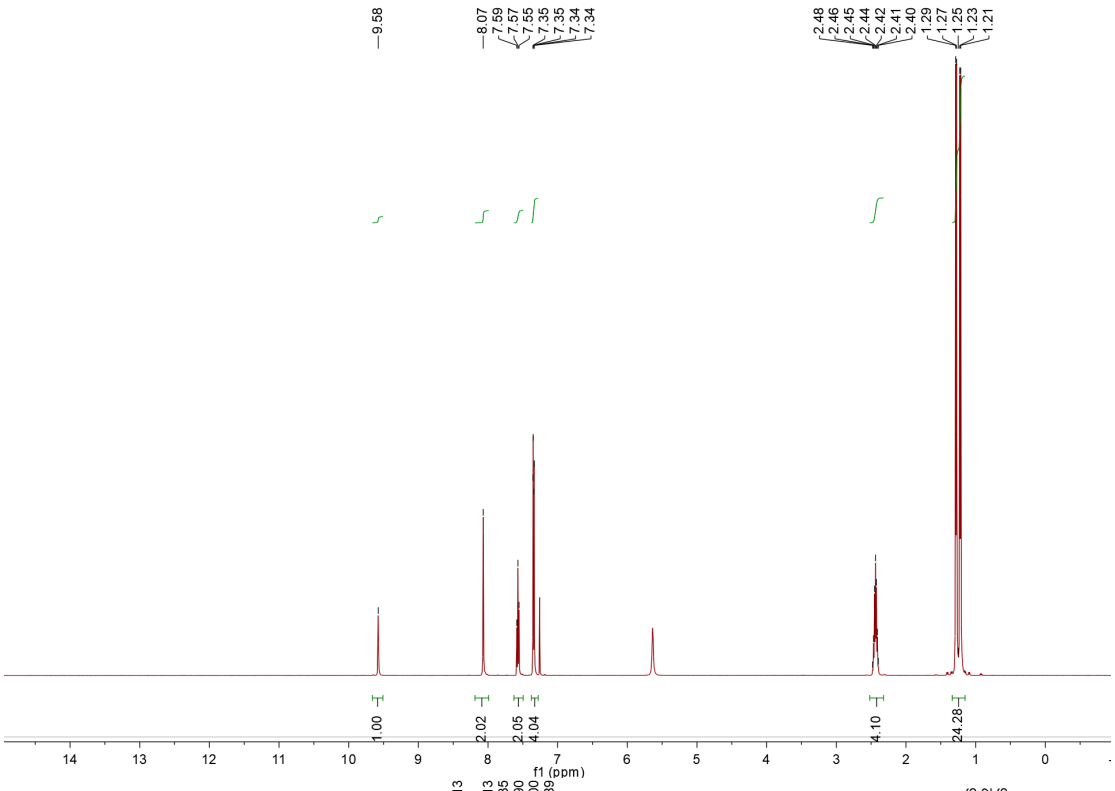
N-Boc vortioxetine (0.275 g, 0.7 mmol, ) was dissolved in 2 mL methanol and slowly added 0.2 mL 48 wt% HBr (aq.) followed by heating to reflux for 2 hours. Then the mixture was cooled to room temperature then the solvent was removed by evaporation. After the addition of diethyl ether (2 mL), the mixture was stirred at room temperature for 2 h before leaving the mixture in the freezer overnight. Filtration and washing with 5 mL diethyl ether to produce brownish solid. Then the brownish solid was dried under high vaccum (0.215 g, 81%). **$^1$H NMR** (500 MHz, $CDCl_3$) δ 9.36 (s, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.17 - 7.06 (m, 3H), 7.02 (d, *J* = 7.8 Hz, 1H), 6.96 - 6.90 (m, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 3.68 - 3.35 (m, 8H), 2.35 (s, 3H), 2.30 (s, 3H). **$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 147.0, 142.3, 139.6, 136.0, 134.7, 132.0, 128.1, 127.2, 126.9, 126.0, 126.0, 120.6, 48.6, 44.2, 21.3, 20.7. NMR data is consistent with literature values.[29] **HRMS** (ESI+) Calcd for $C_{18}H_{23}N_2S$ $[M-Br]^+$: 299.1582, found: 299.1588. Melting point: 218 °C.

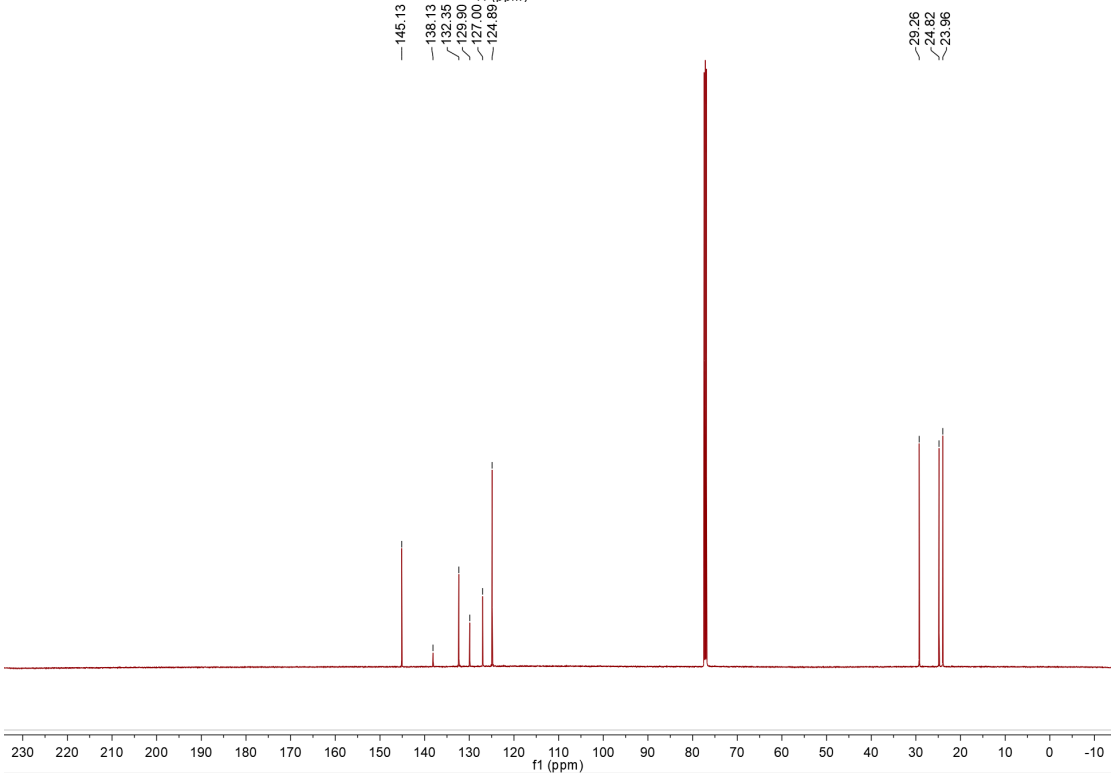
# 5 NMR Spectra

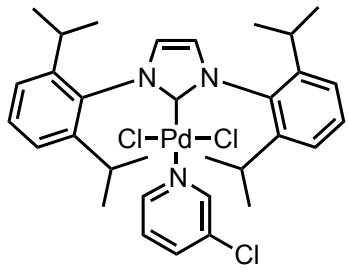


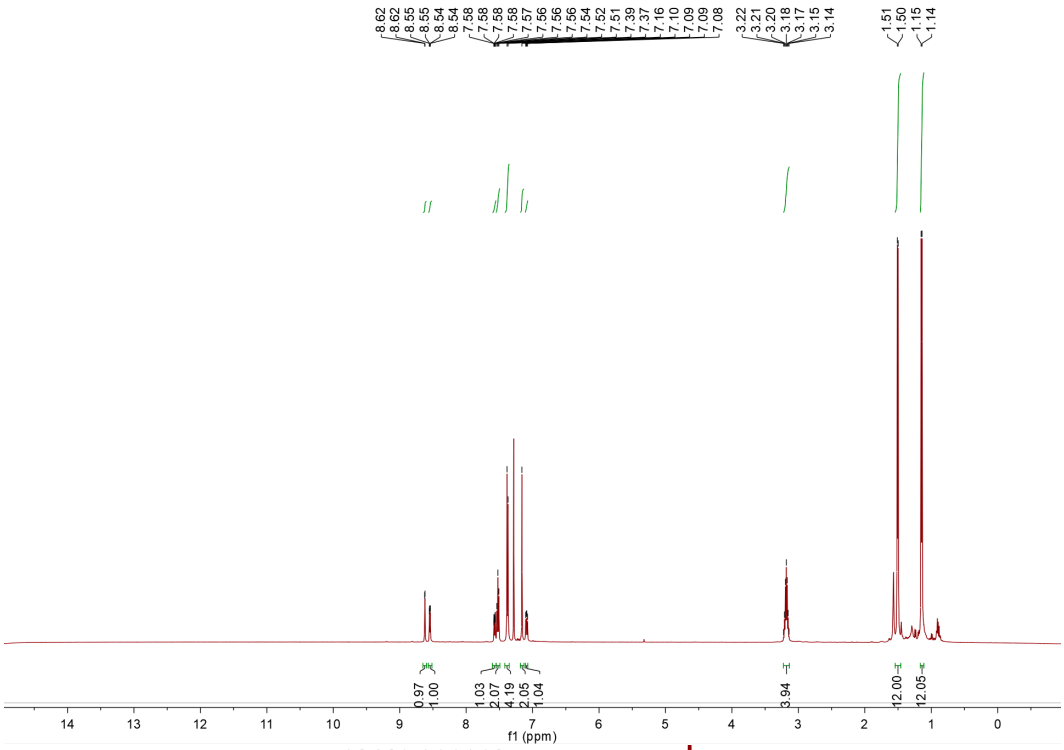



N
N
+
Cl
−


9.58
8.07
7.59
7.57
7.55
7.35
7.35
7.34
7.34
2.48
2.46
2.45
2.44
2.42
2.41
2.40
1.29
1.27
1.25
1.23
1.21
1.00
2.02
2.05
4.04
4.10
24.28
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


145.13
138.13
132.35
129.90
127.00
124.89
29.26
24.82
23.96
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


N
N
Cl–Pd–Cl
N
Cl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8.55
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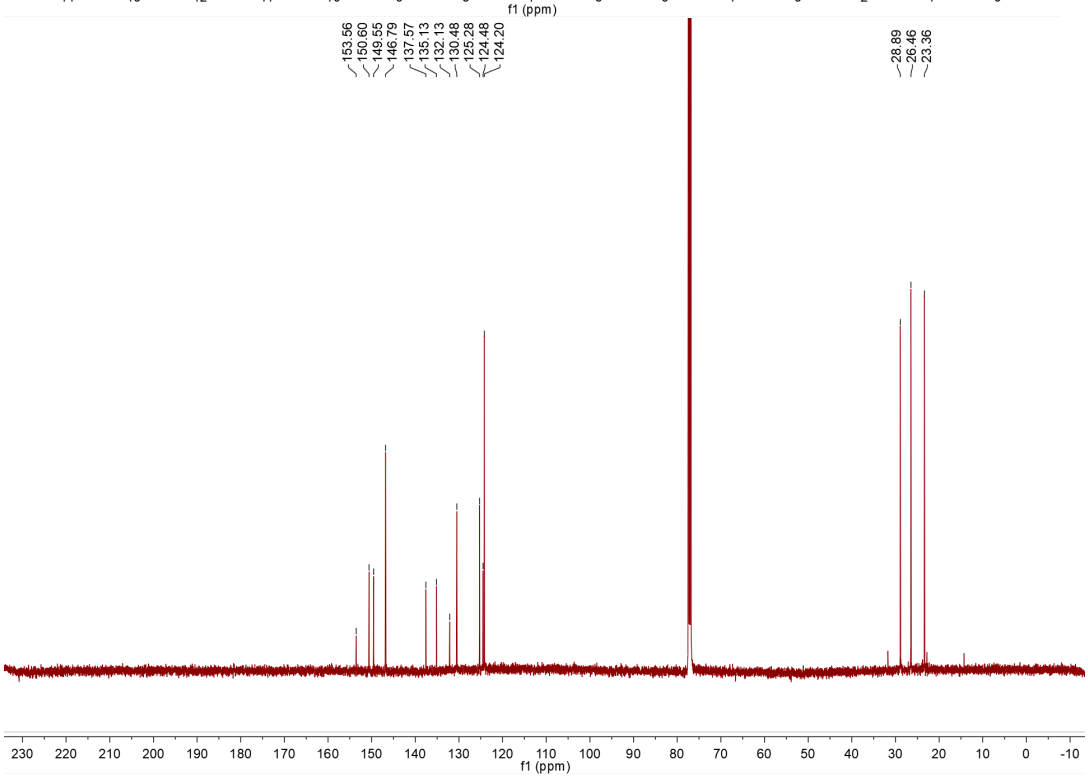
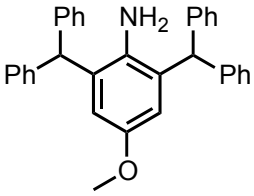
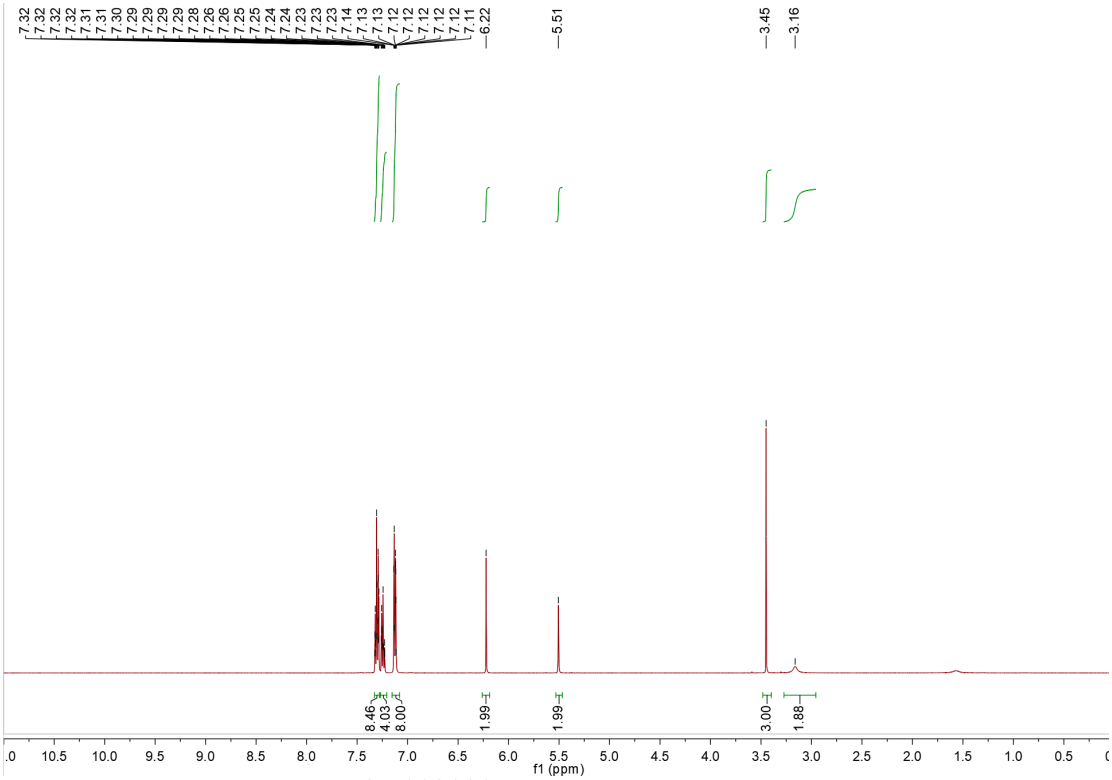
7.56
7.56
7.54
7.52
7.51
7.39
7.37
7.16
7.10
7.09
7.09
7.08
3.22
3.21
3.20
3.18
3.17
3.15
3.14
1.51
1.50
1.15
1.14
0.97
1.00
1.03
2.07
4.19
2.05
1.04
3.94
12.00
12.05
f1 (ppm)


153.56
150.60
149.55
146.79
137.57
135.13
132.13
130.48
125.28
124.48
124.20
28.89
26.46
23.36
f1 (ppm)


Ph
NH2
Ph
Ph
Ph
O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7.30
7.29
7.29
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7.29
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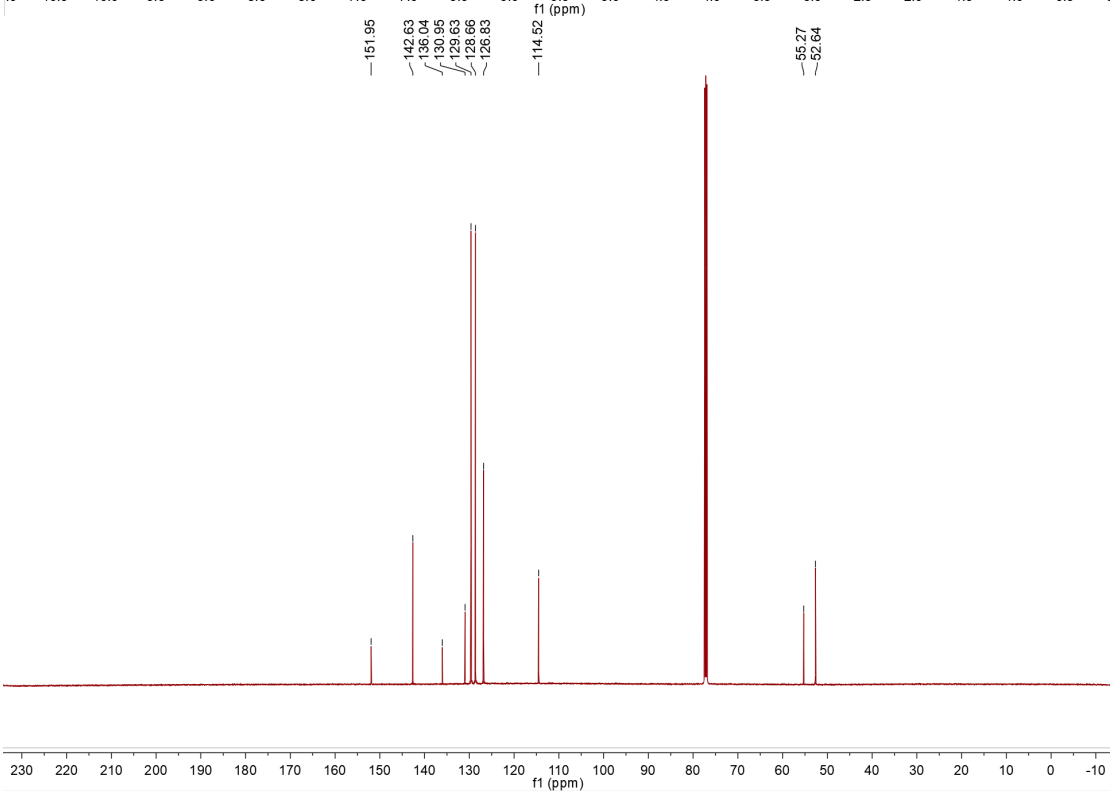
7.26
7.25
7.25
7.24
7.24
7.23
7.23
7.23
7.14
7.13
7.13
7.12
7.12
7.12
7.12
7.12
7.11
6.22
5.51
3.45
3.16
8.46
4.03
8.00
1.99
1.99
3.00
1.88
f1 (ppm)


151.95
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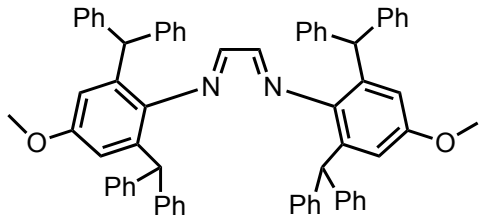
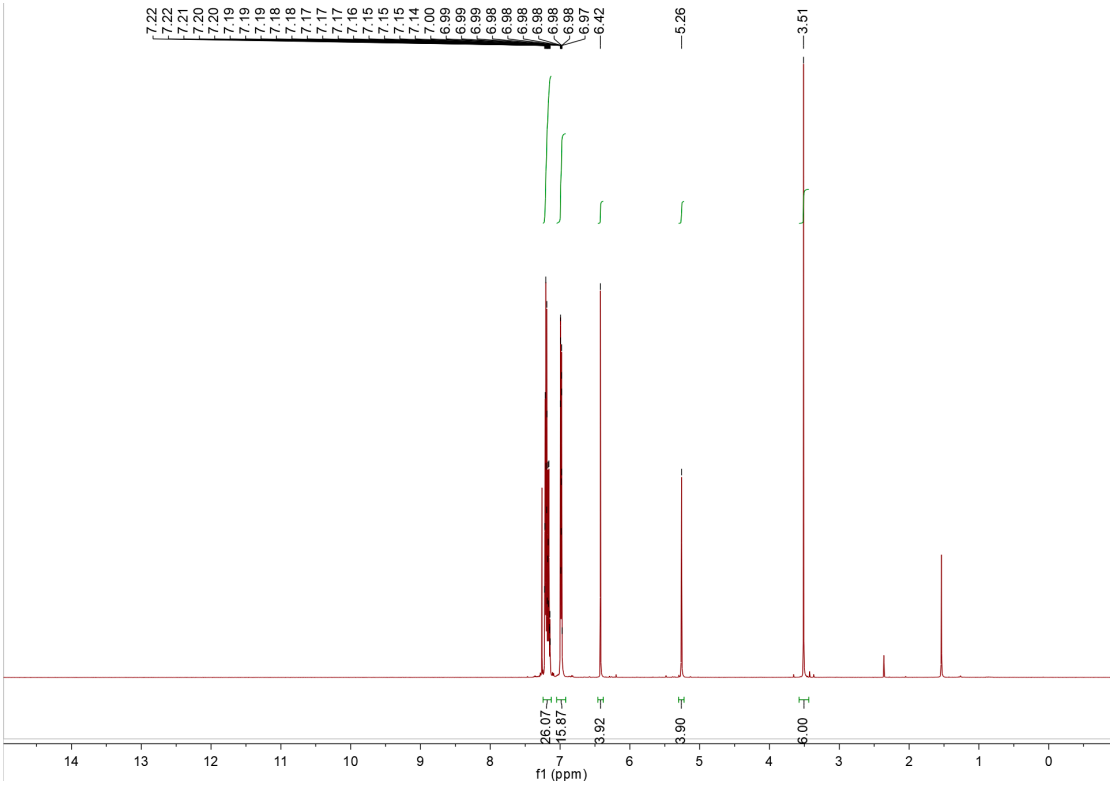
130.95
129.63
128.66
126.83
114.52
55.27
52.64
f1 (ppm)


Ph
Ph
Ph
Ph
N
N
O
O
Ph
Ph
Ph
Ph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7.20
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7.19
7.19
7.18
7.18
7.17
7.17
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7.16
7.15
7.15
7.14
7.00
6.99
6.99
6.98
6.98
6.98
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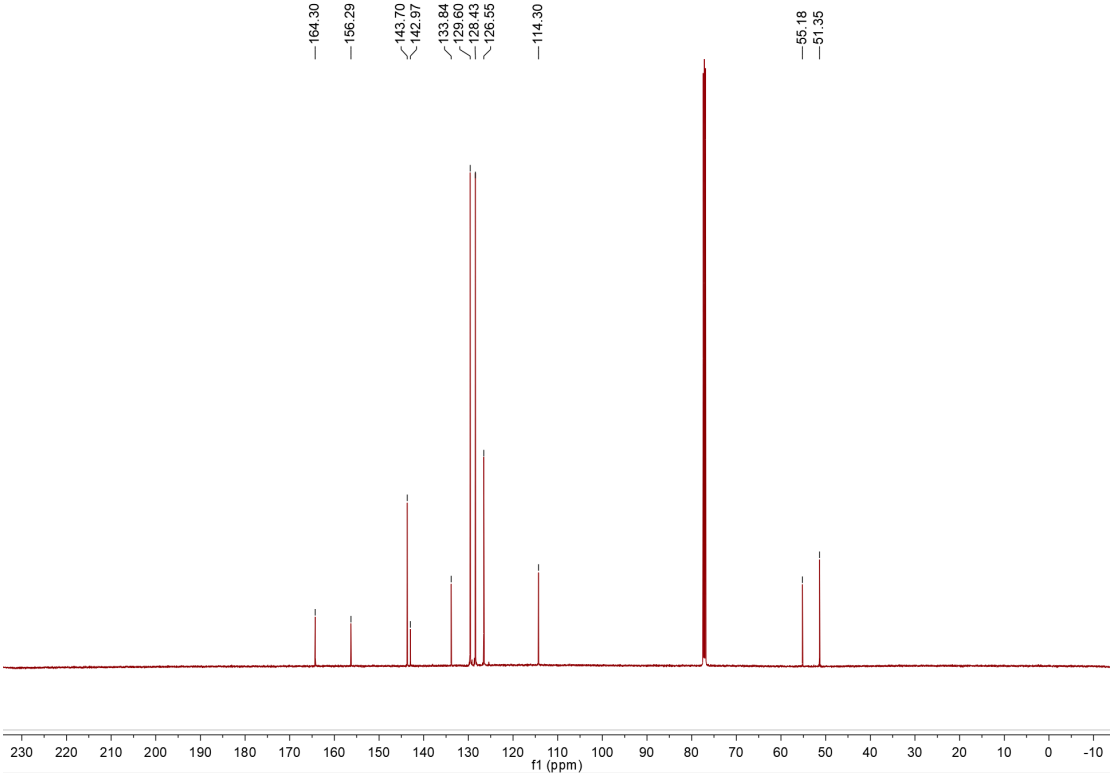
26.07
15.87
3.92
3.90
6.00
f1 (ppm)


164.30
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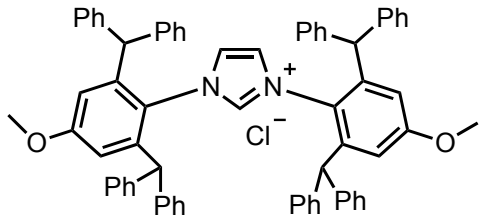
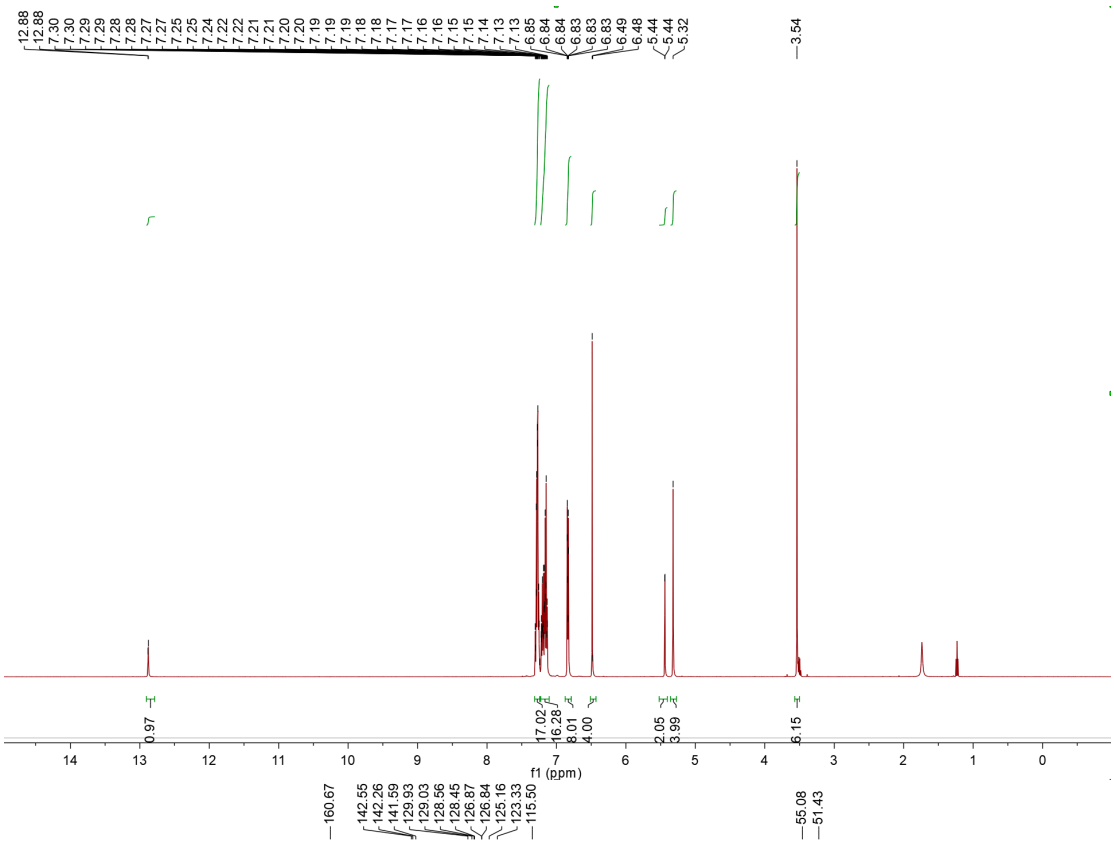
129.60
128.43
126.55
114.30
55.18
51.35
f1 (ppm)


Ph
Ph
Ph
Ph
N
N
+
Cl
−
O
O
Ph
Ph
Ph
Ph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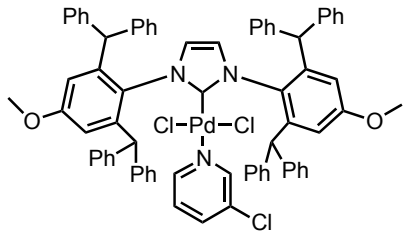
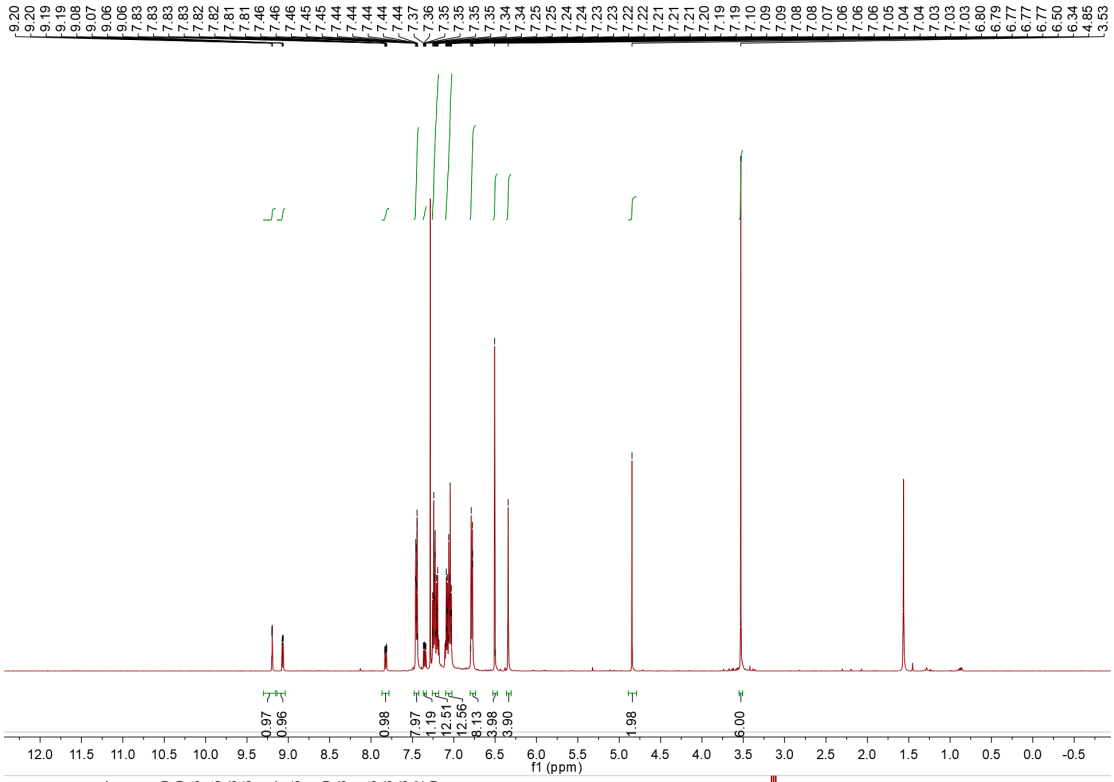
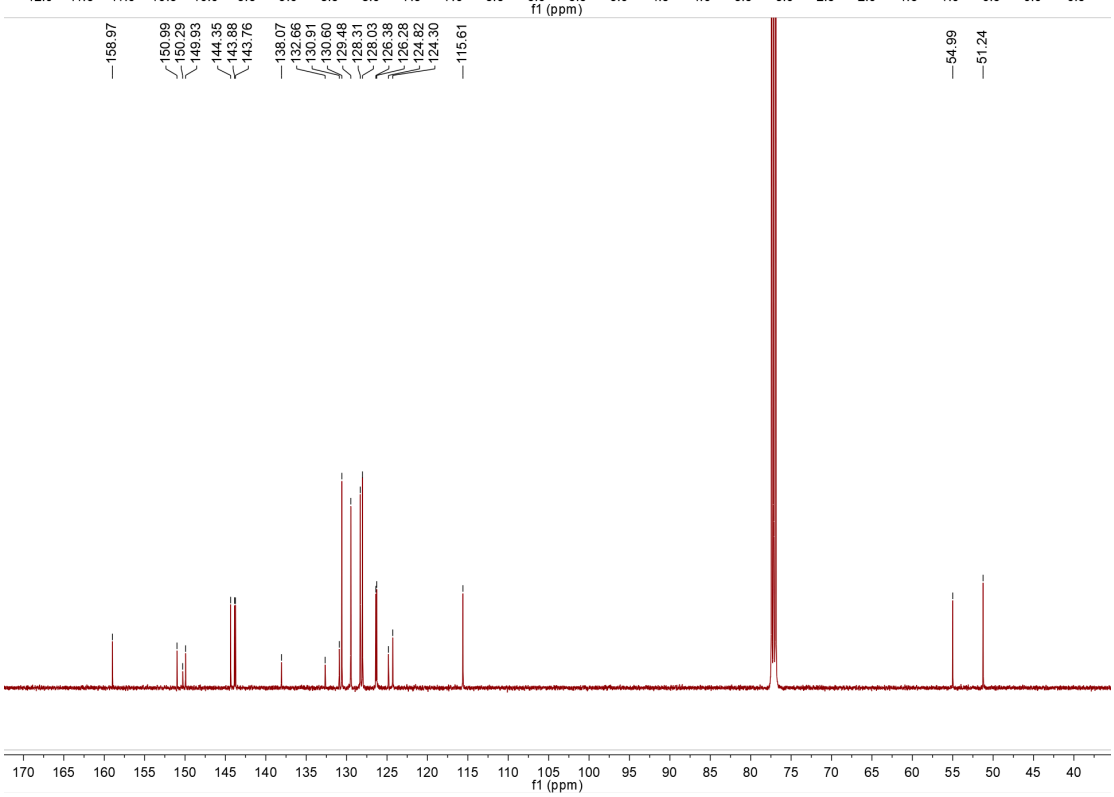
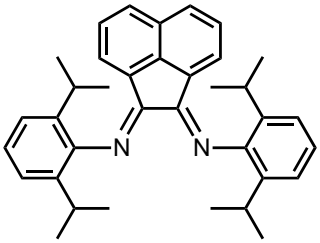
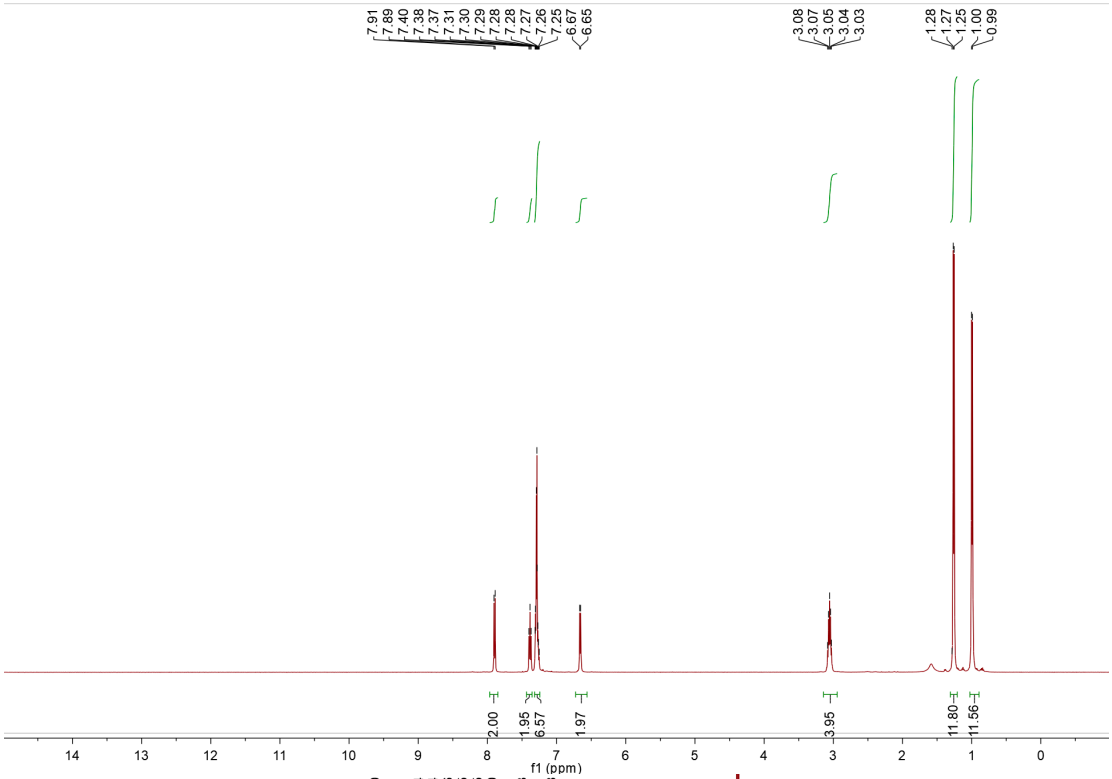
7.18
7.17
7.17
7.16
7.16
7.15
7.15
7.14
7.13
6.85
6.84
6.84
6.83
6.83
6.83
6.49
6.48
5.44
5.44
5.32
3.54
0.97
17.02
16.28
8.01
4.00
2.05
3.99
6.15
f1 (ppm)
160.67
142.55
142.26
141.59
129.93
129.03
128.56
128.45
126.87
126.84
125.16
123.33
115.50
55.08
51.43
f1 (ppm)

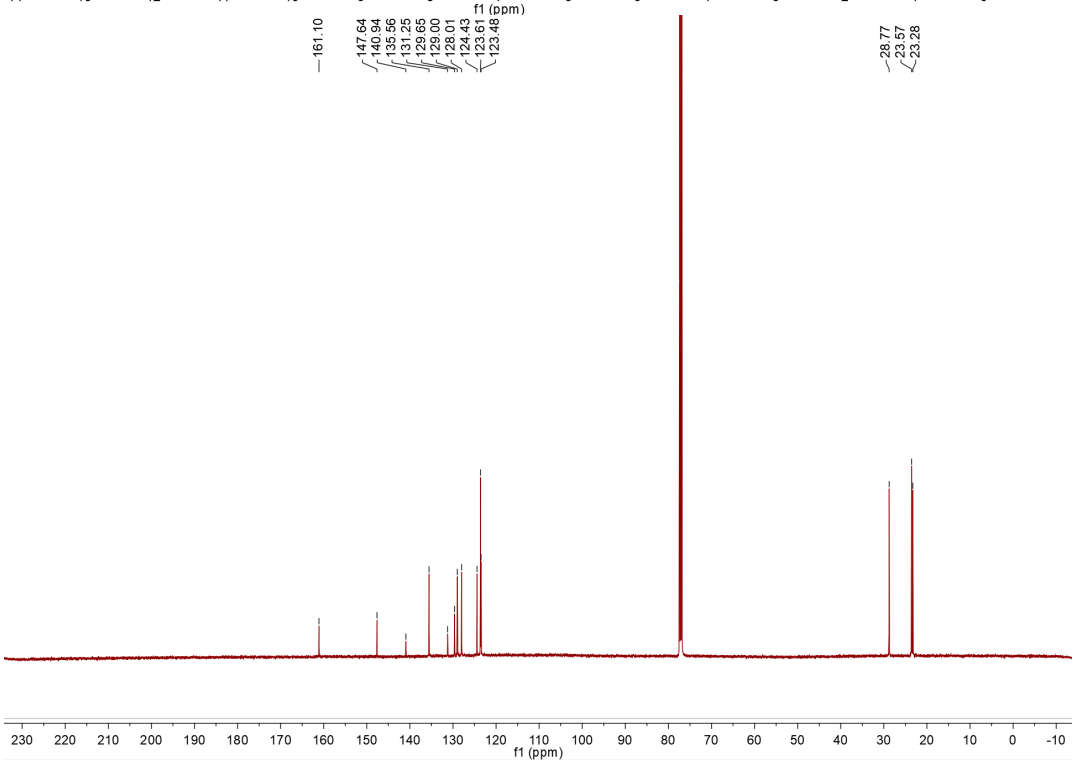

Ph
Ph
Ph
Ph
N
N
Cl–Pd–Cl
O
O
Ph
Ph
N
Ph
Ph
Cl

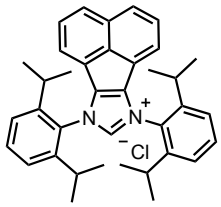

9.20 9.20 9.19 9.19 9.08 9.07 9.06 9.06 7.83 7.83 7.83 7.82 7.82 7.81 7.81 7.46 7.46 7.45 7.45 7.44 7.44 7.44 7.44 7.37 7.36 7.35 7.35 7.35 7.35 7.34 7.34 7.25 7.24 7.24 7.23 7.23 7.22 7.22 7.21 7.21 7.21 7.20 7.19 7.19 7.10 7.09 7.09 7.08 7.08 7.07 7.06 7.06 7.06 7.05 7.04 7.04 7.03 7.03 7.03 6.80 6.79 6.77 6.77 6.50 6.34 4.85 3.53
0.97 0.96 0.98 7.97 1.19 12.51 12.56 8.13 3.98 3.90 1.98 6.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

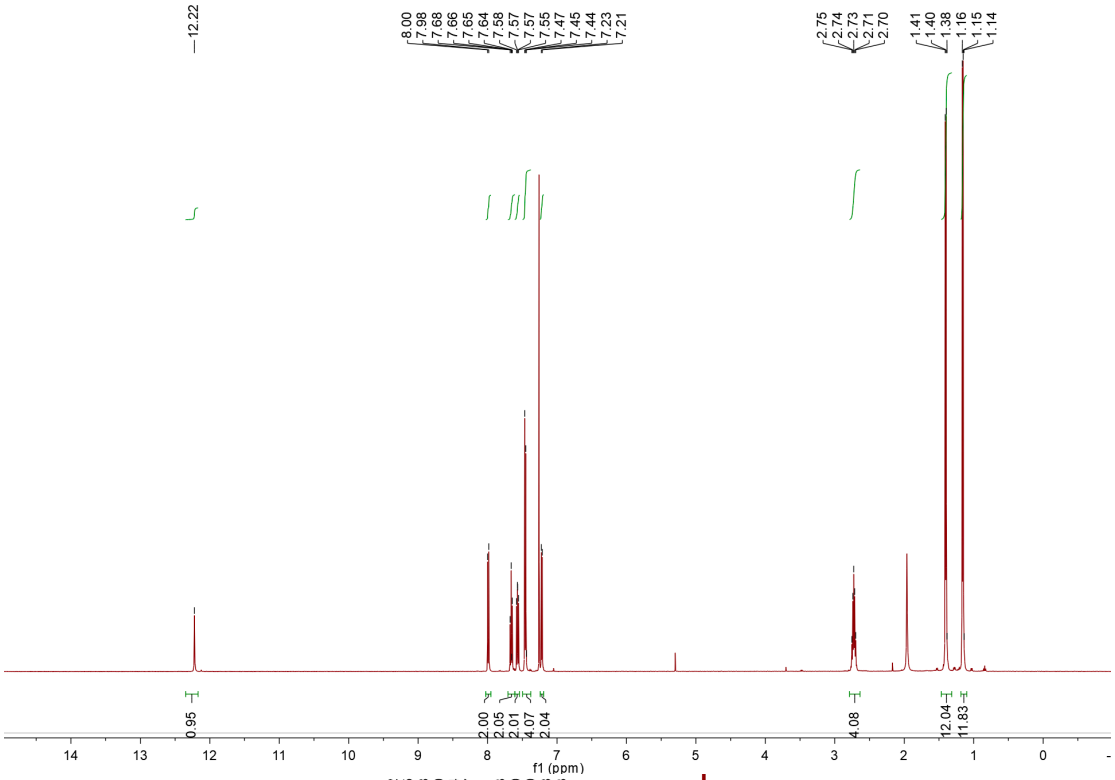

158.97
150.99 150.29 149.93 144.35 143.88 143.76 138.07 132.66 130.91 130.60 129.48 128.31 128.03 126.38 126.28 124.82 124.30 115.61
54.99 51.24
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40
f1 (ppm)


N
N


7.91
7.89
7.40
7.38
7.37
7.31
7.30
7.29
7.28
7.28
7.27
7.26
7.25
6.67
6.65
3.08
3.07
3.05
3.04
3.03
1.28
1.27
1.25
1.00
0.99
2.00
1.95
6.57
1.97
3.95
11.80
11.56
f1 (ppm)


161.10
147.64
140.94
135.56
131.25
129.65
129.00
128.01
124.43
123.61
123.48
28.77
23.57
23.28
f1 (ppm)


N
N
Cl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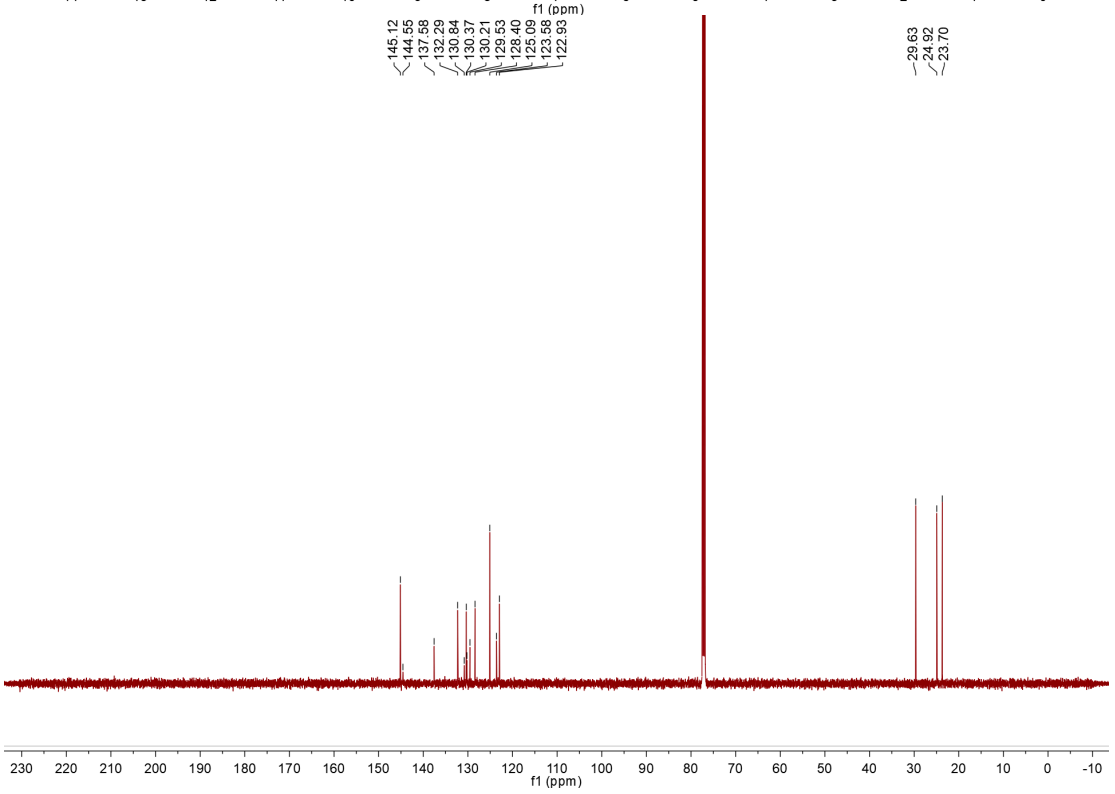
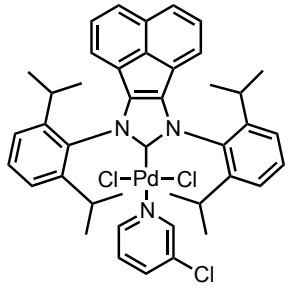
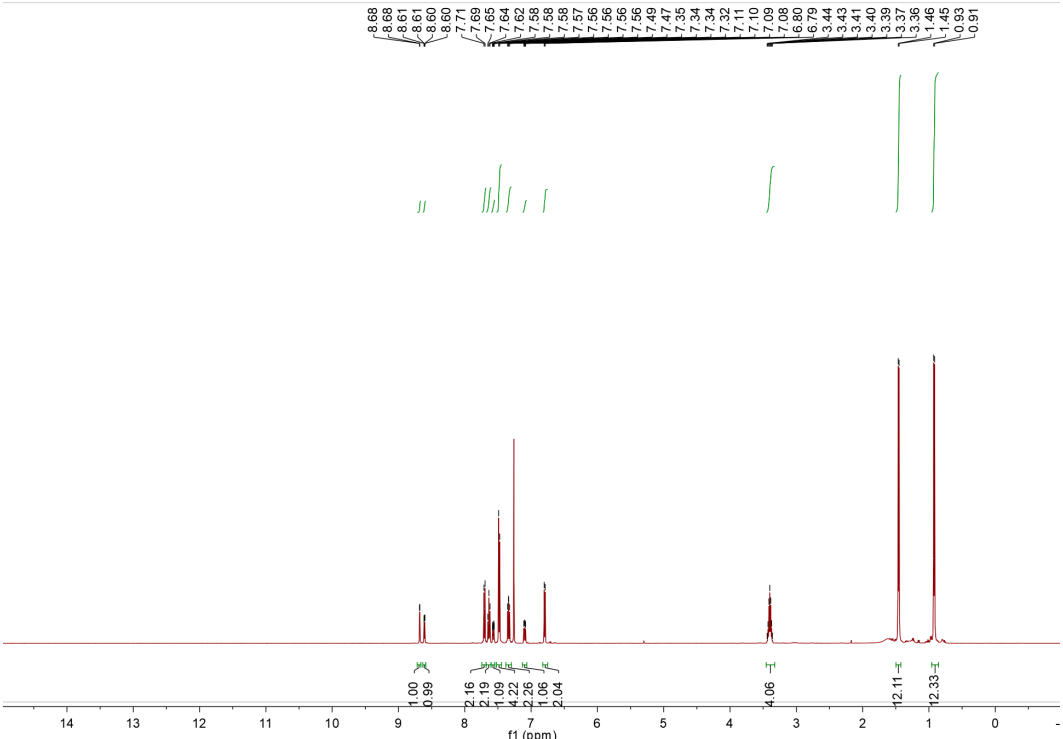
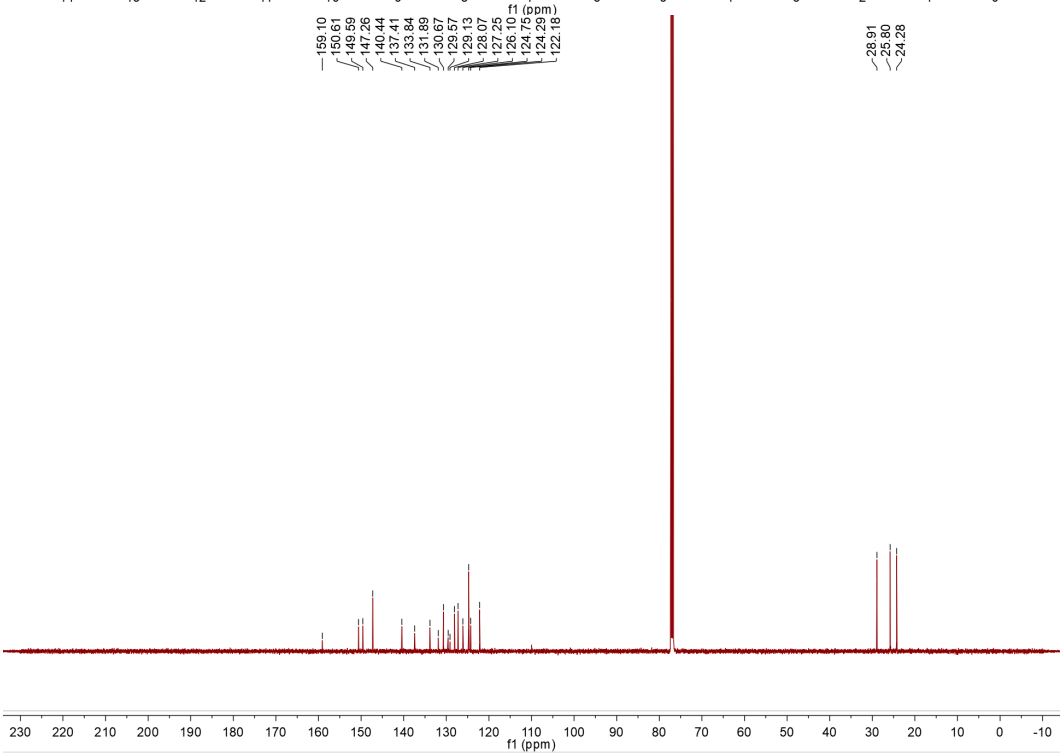
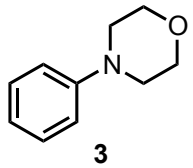
8.00
7.98
7.88
7.66
7.65
7.64
7.58
7.57
7.57
7.55
7.47
7.45
7.44
7.23
7.21
2.75
2.74
2.73
2.71
2.70
1.41
1.40
1.38
1.16
1.15
1.14
0.95
2.00
2.05
2.01
4.07
2.04
4.08
12.04
11.83
f1 (ppm)


145.12
144.55
137.58
132.29
130.84
130.37
130.21
129.53
128.40
125.09
123.58
122.93
29.63
24.92
23.70
f1 (ppm)


N
N
Cl–Pd–Cl
N
Cl


8.68
8.68
8.61
8.61
8.60
8.60
7.71
7.69
7.65
7.64
7.62
7.58
7.58
7.58
7.57
7.56
7.56
7.56
7.56
7.56
7.49
7.47
7.35
7.34
7.34
7.32
7.11
7.10
7.09
7.08
6.80
6.79
3.44
3.43
3.41
3.40
3.39
3.37
3.36
1.46
1.45
0.93
0.91
1.00
0.99
2.16
2.19
1.09
4.22
2.26
1.06
2.04
4.06
12.11
12.33
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


159.10
150.61
149.59
147.26
140.44
137.41
133.84
131.89
130.67
129.57
129.13
128.07
127.25
126.10
124.75
124.29
122.18
28.91
25.80
24.28
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



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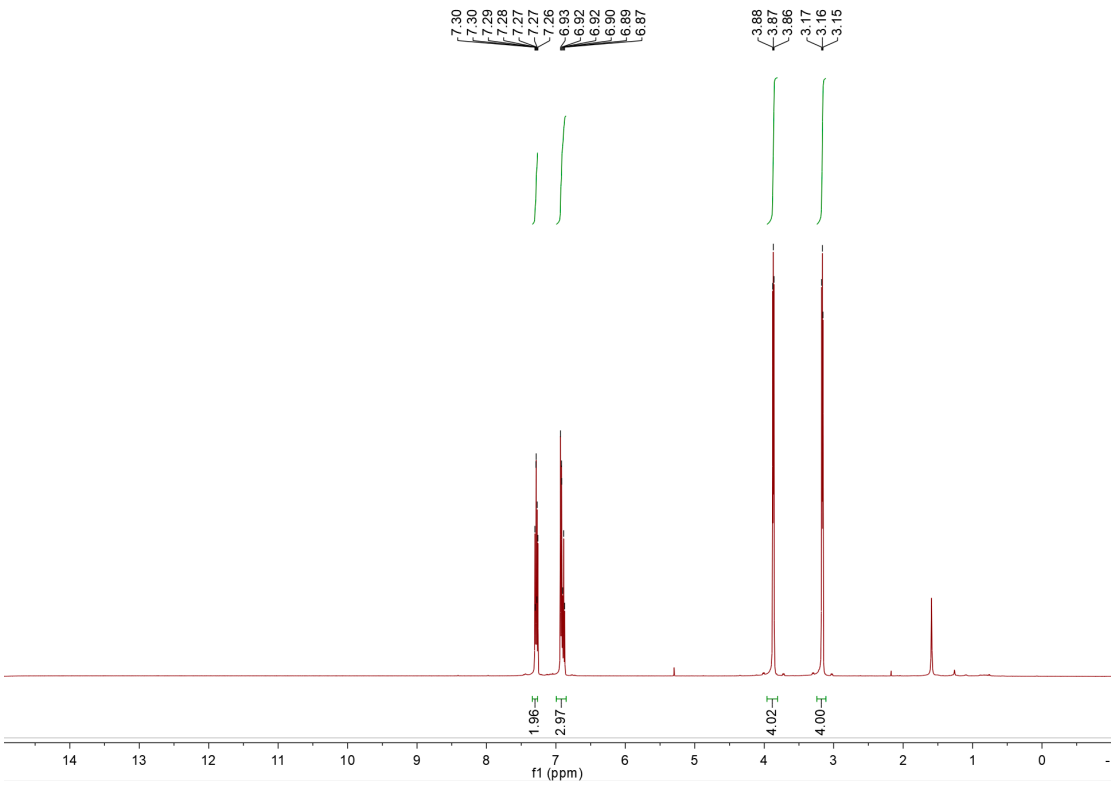
7.30
7.30
7.29
7.28
7.27
7.27
7.26
6.93
6.92
6.92
6.90
6.89
6.87
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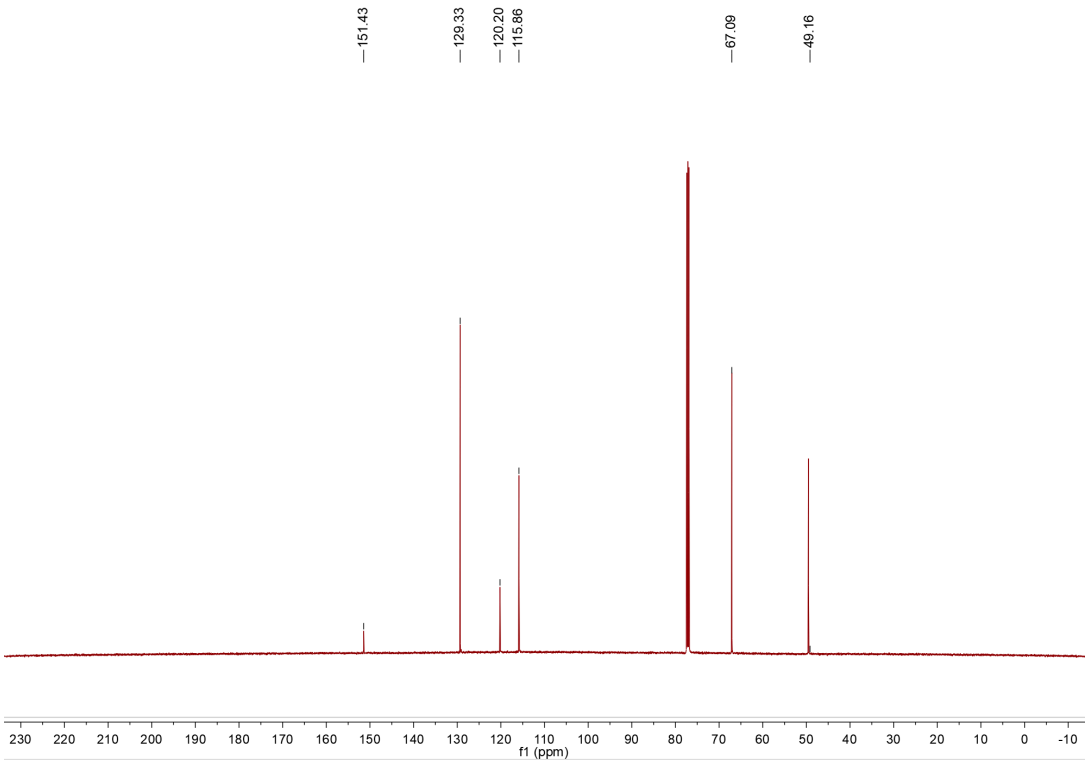
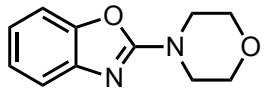
3.15
1.96
2.97
4.02
4.00
f1 (ppm)


151.43
129.33
120.20
115.86
67.09
49.16
f1 (ppm)



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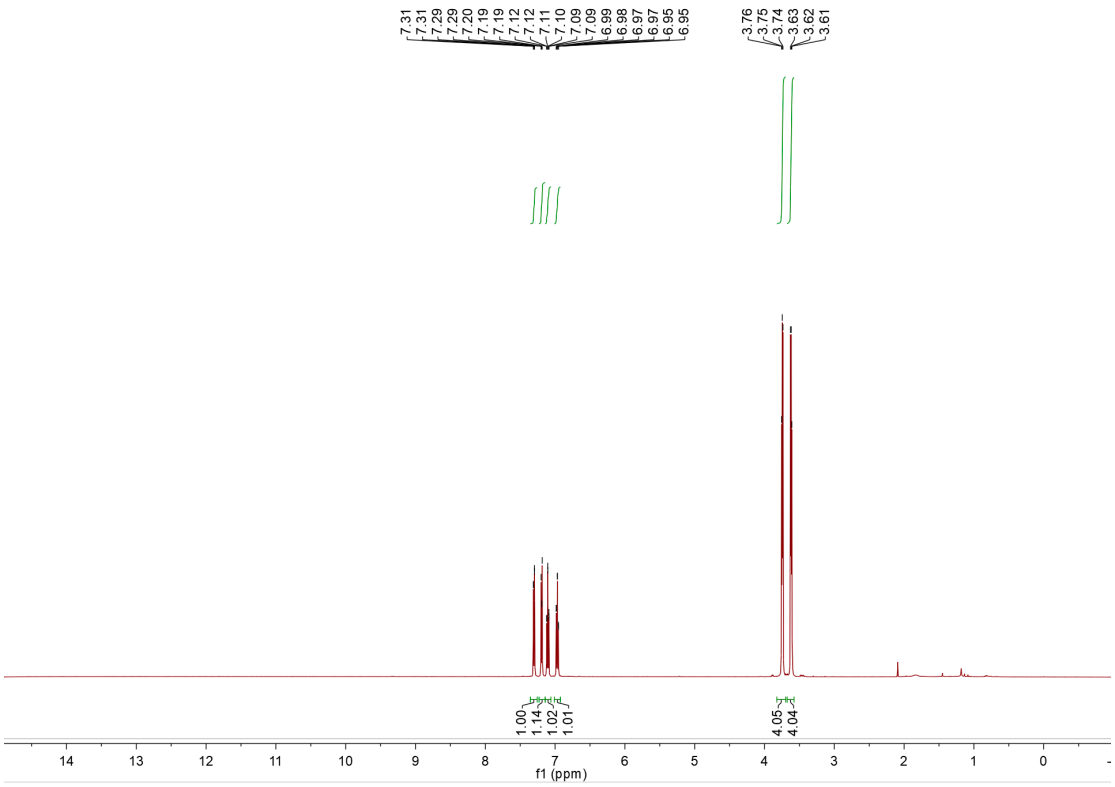
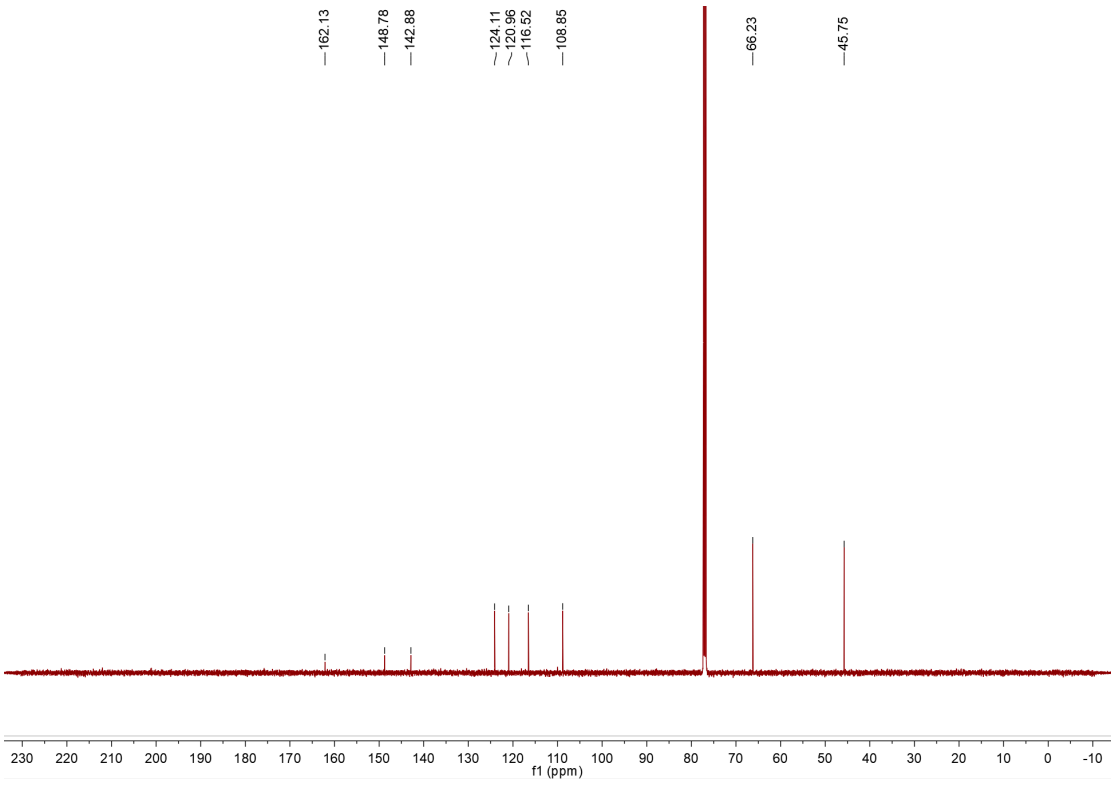
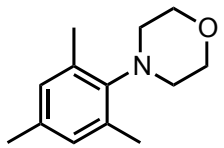
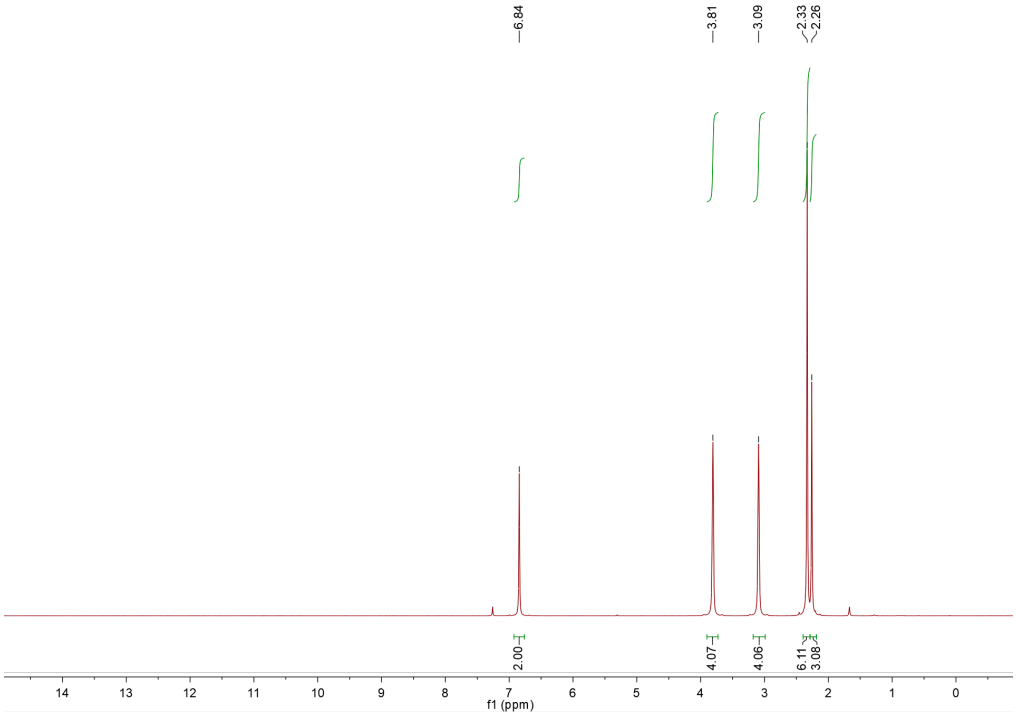
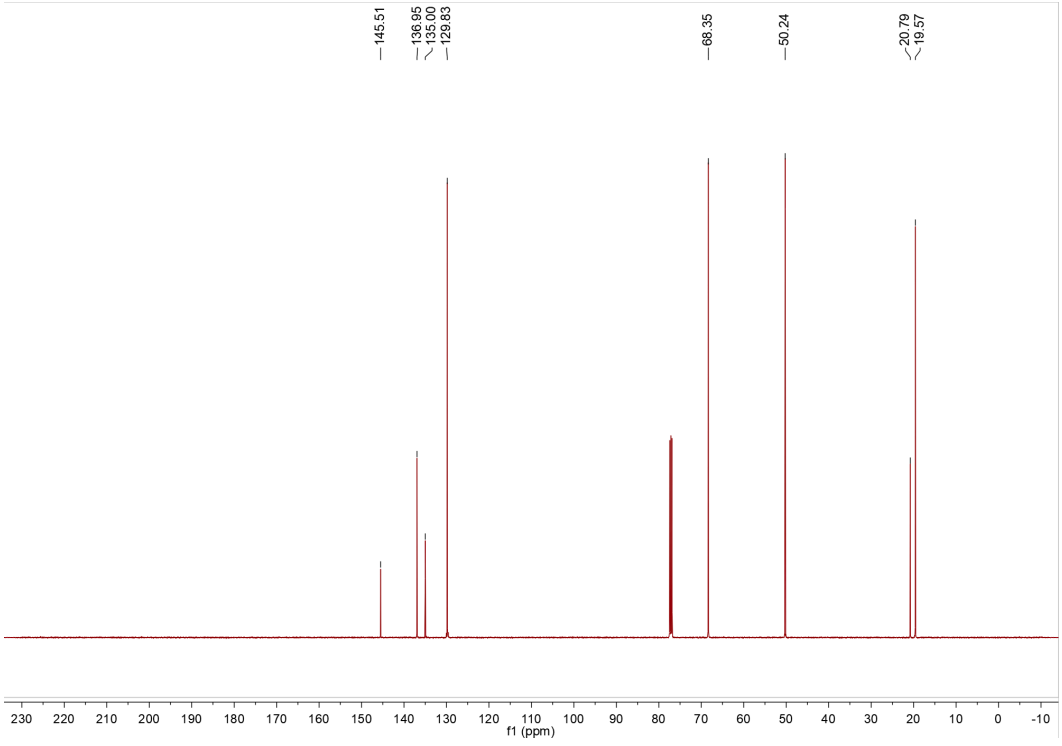

7.31
7.31
7.29
7.29
7.20
7.19
7.12
7.12
7.11
7.10
7.09
7.09
6.99
6.98
6.97
6.97
6.95
6.95
3.76
3.75
3.74
3.63
3.62
3.61
1.00
1.14
1.02
1.01
4.05
4.04
f1 (ppm)

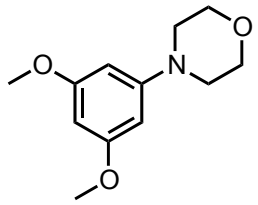

162.13
148.78
142.88
124.11
120.96
116.52
108.85
66.23
45.75
f1 (ppm)



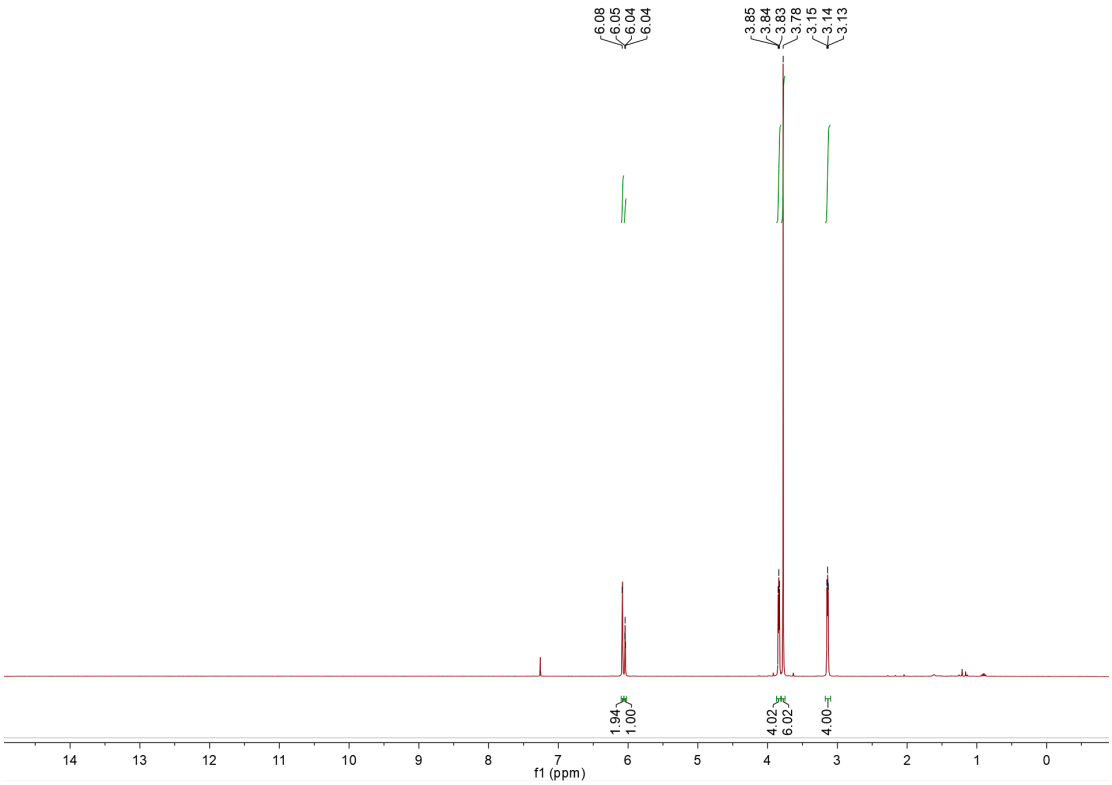
**5**

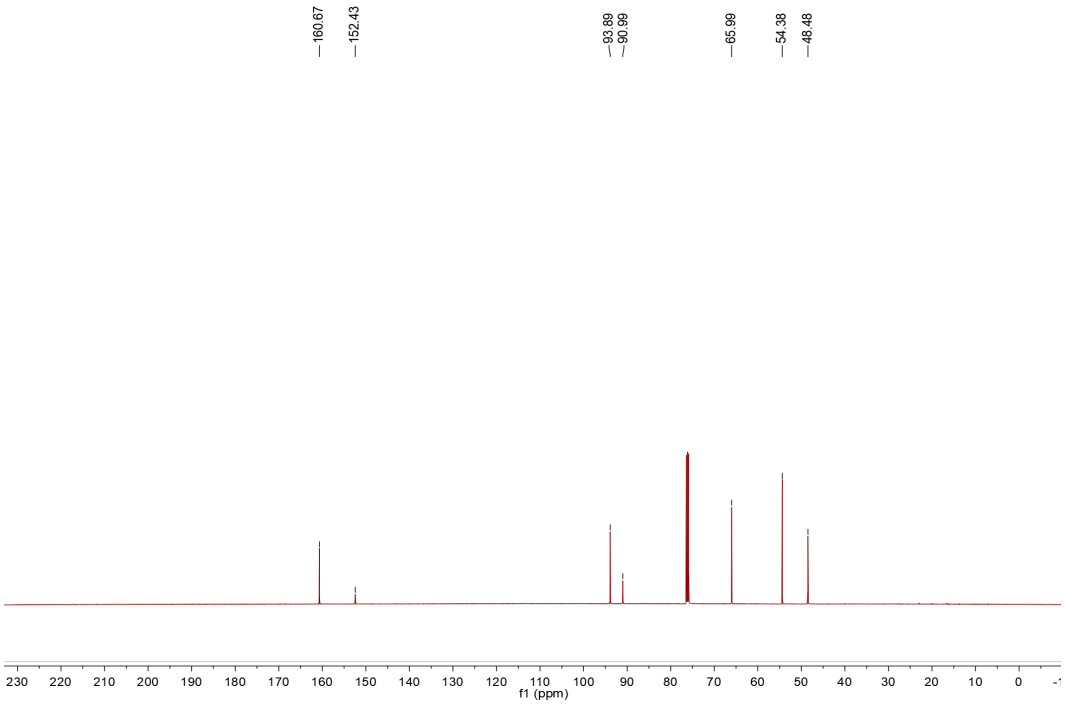

6.84
3.81
3.09
2.33
2.26
2.00
4.07
4.06
6.11
3.08
f1 (ppm)

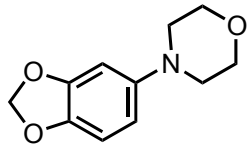

145.51
136.95
135.00
129.83
68.35
50.24
20.79
19.57
f1 (ppm)



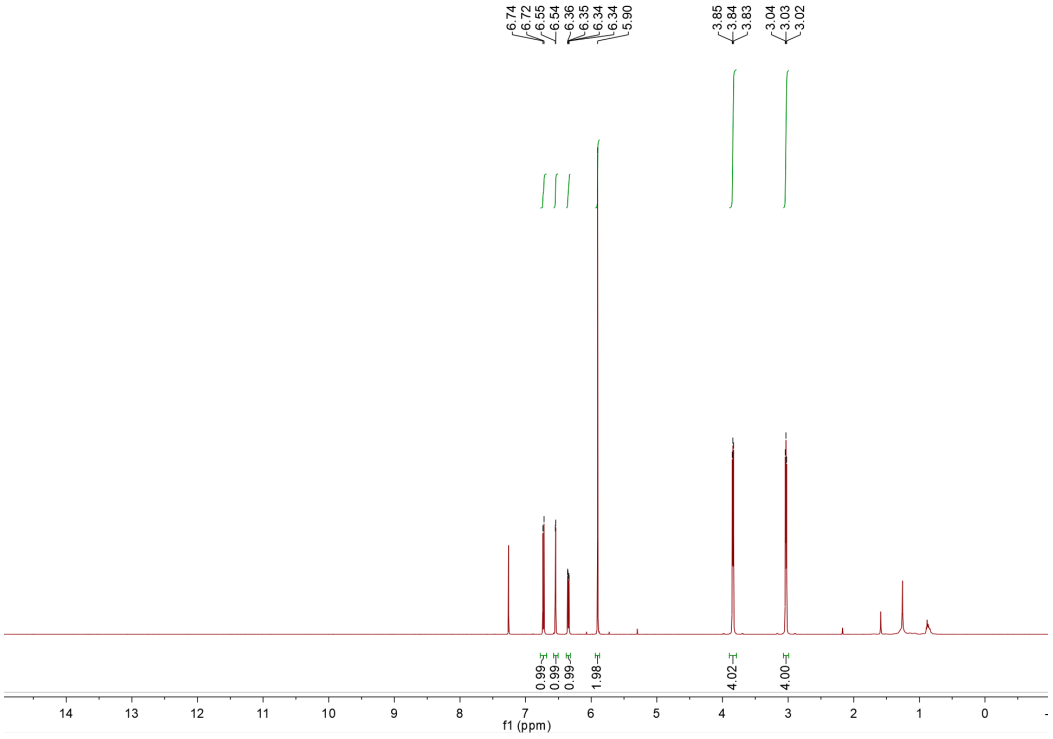
**6**


6.08
6.05
6.04
6.04
3.85
3.84
3.83
3.78
3.15
3.14
3.13
1.94
1.00
4.02
6.02
4.00
f1 (ppm)


160.67
152.43
93.89
90.99
65.99
54.38
48.48
f1 (ppm)



**7**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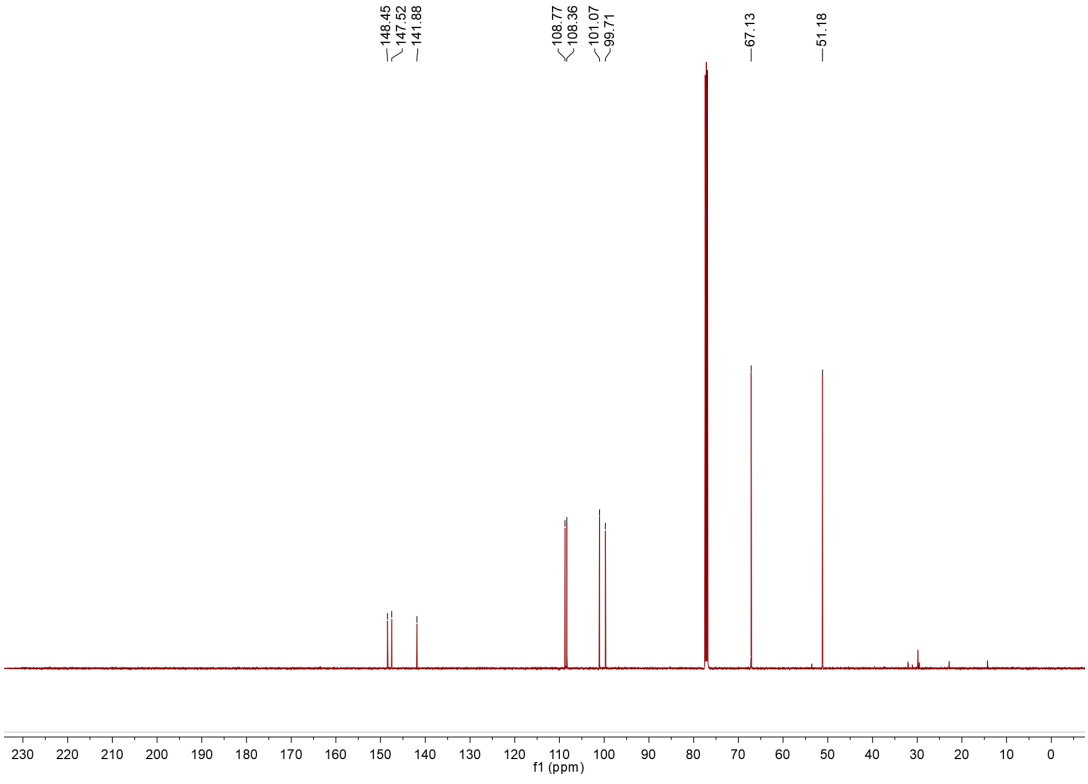
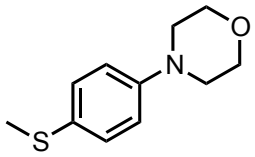
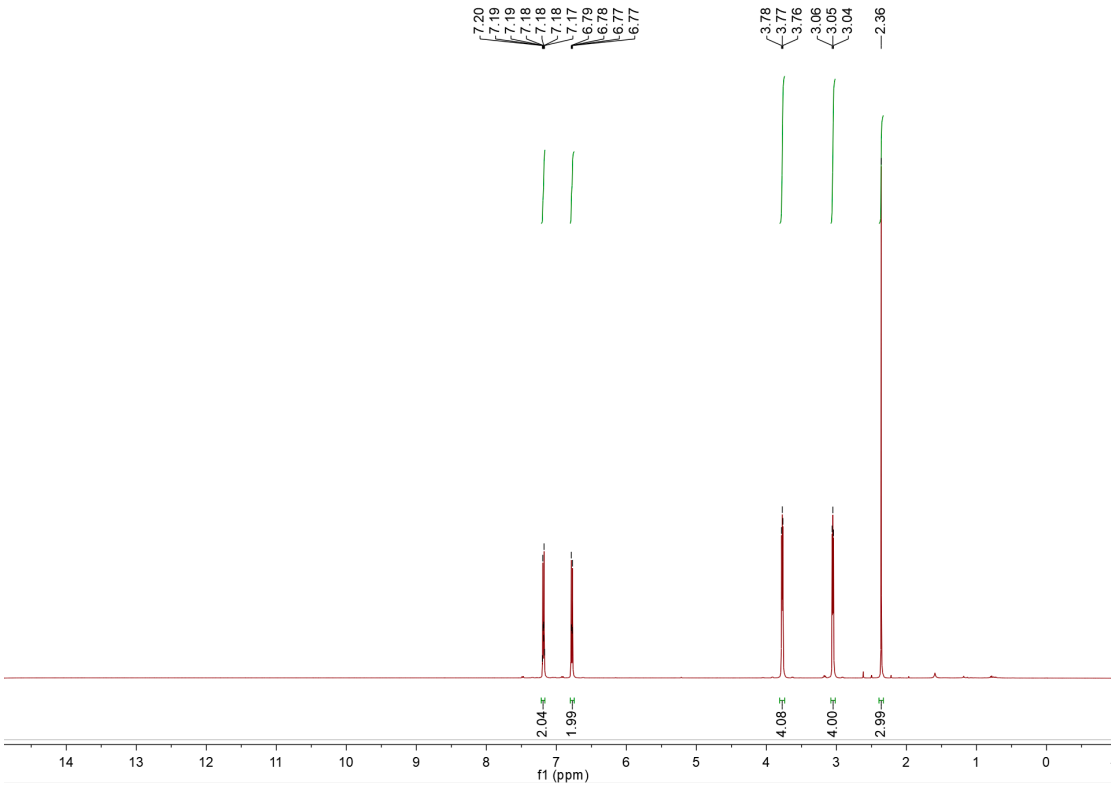
6.72
6.55
6.54
6.36
6.35
6.34
6.34
5.90
3.85
3.84
3.83
3.04
3.03
3.02
0.99
0.99
0.99
1.98
4.02
4.00
f1 (ppm)


148.45
147.52
141.88
108.77
108.36
101.07
99.71
67.13
51.18
f1 (ppm)



**8**


7.20
7.19
7.19
7.18
7.18
7.18
7.17
6.79
6.78
6.77
6.77
3.78
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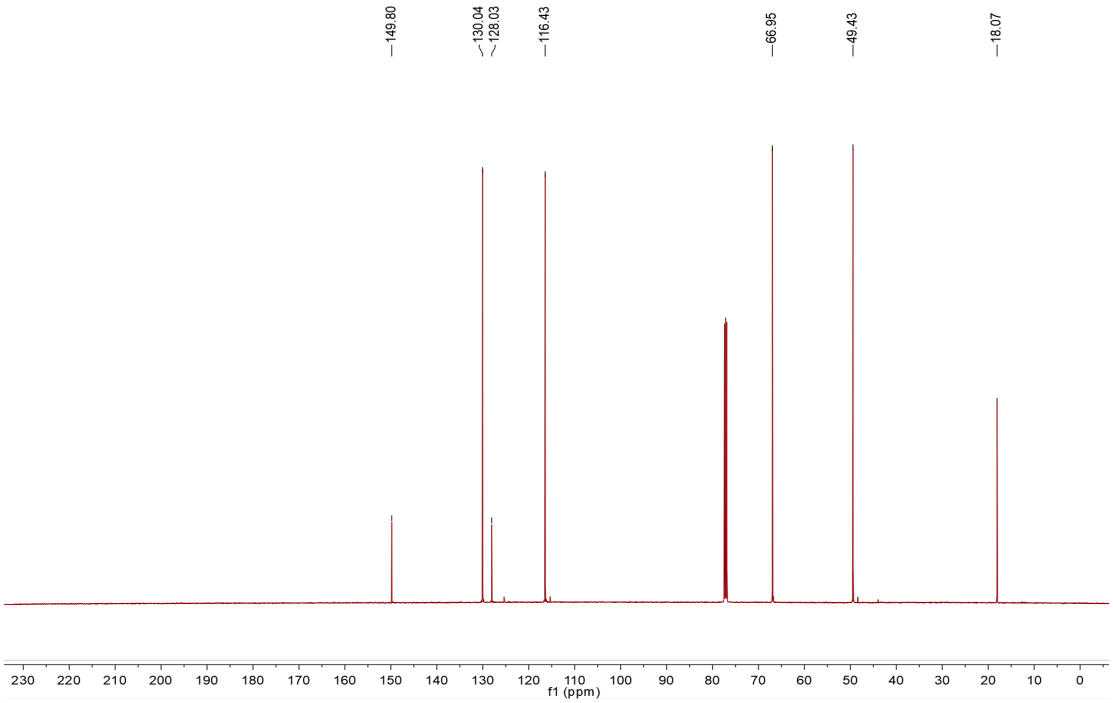
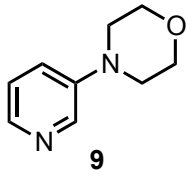
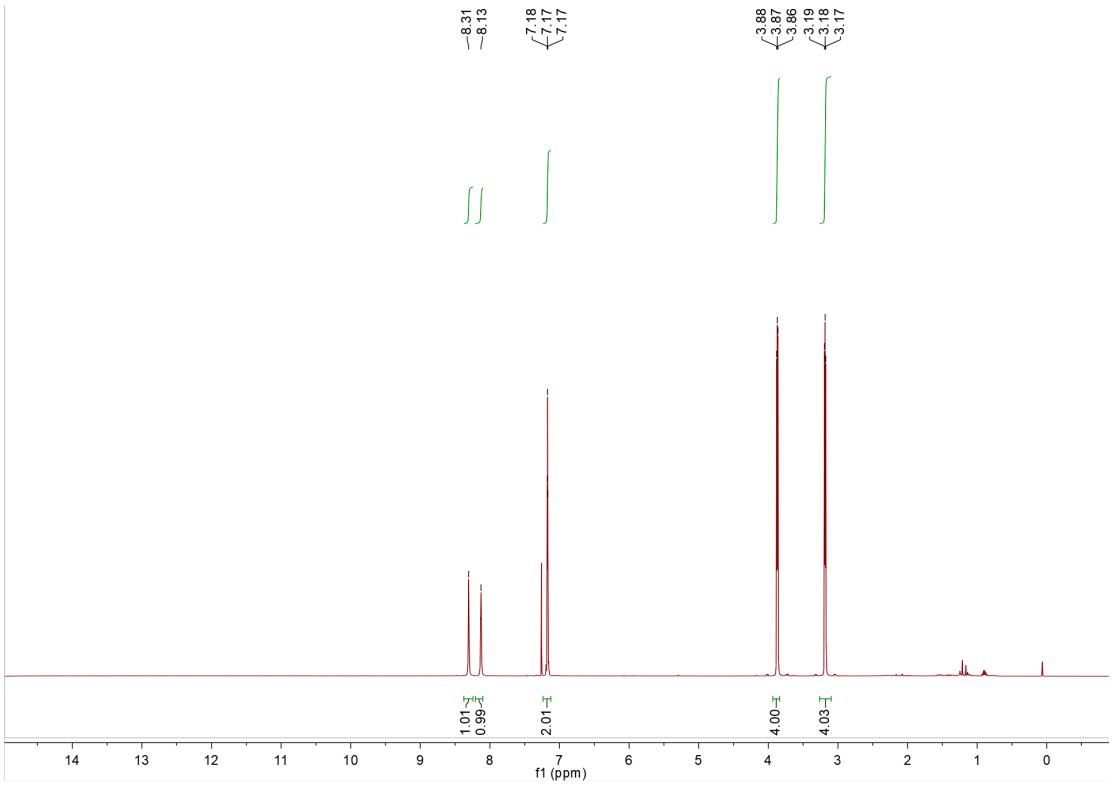
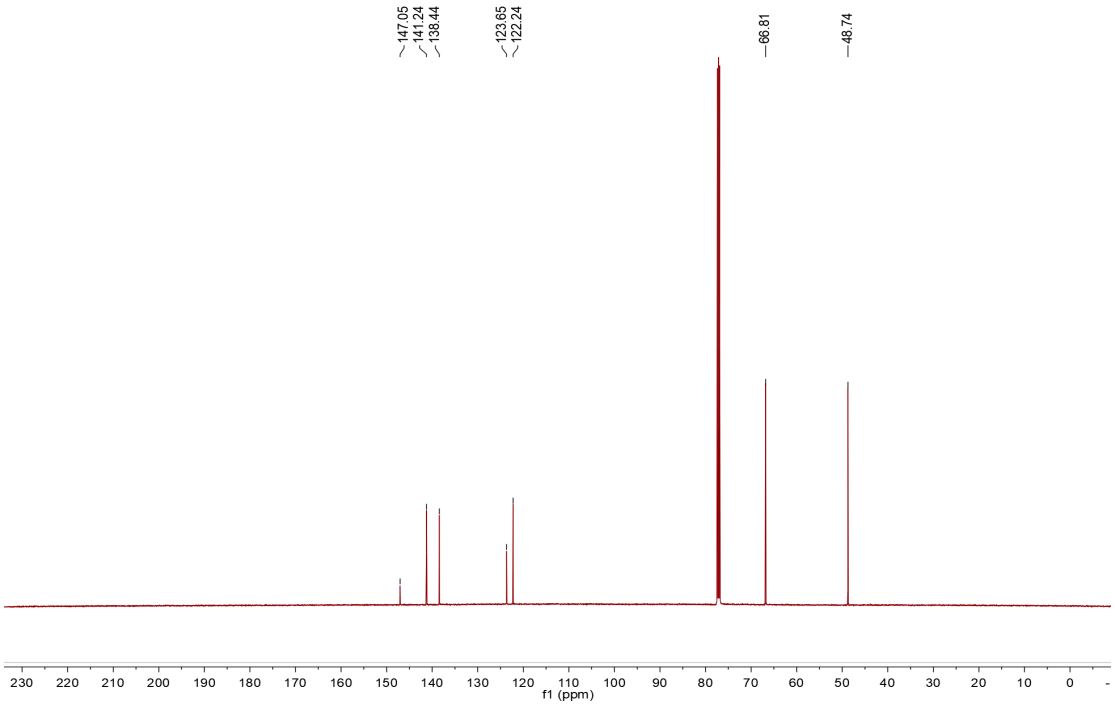
2.04
1.99
4.08
4.00
2.99
f1 (ppm)

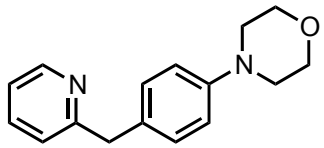

149.80
130.04
128.03
116.43
66.95
49.43
18.07
f1 (ppm)



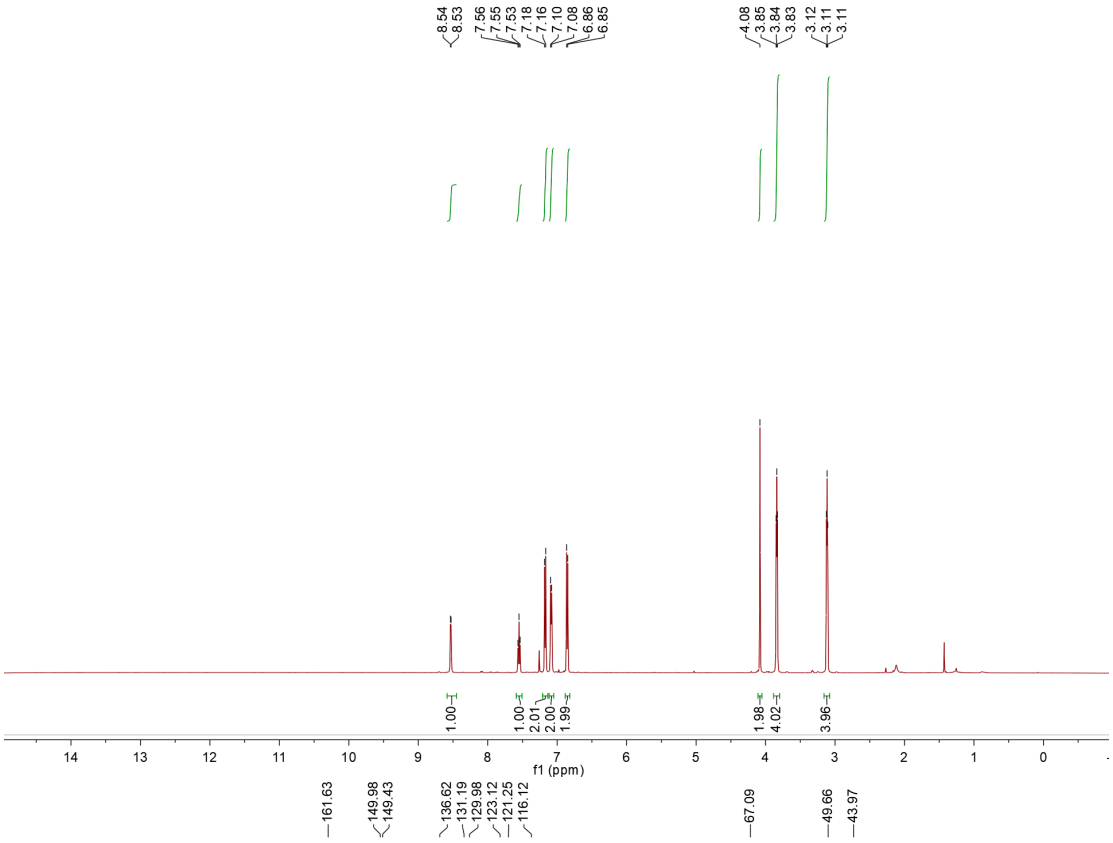
**9**


8.31
8.13
7.18
7.17
7.17
3.88
3.87
3.86
3.19
3.18
3.17
1.01
0.99
2.01
4.00
4.03
f1 (ppm)


147.05
141.24
138.44
123.65
122.24
66.81
48.74
f1 (ppm)



**10**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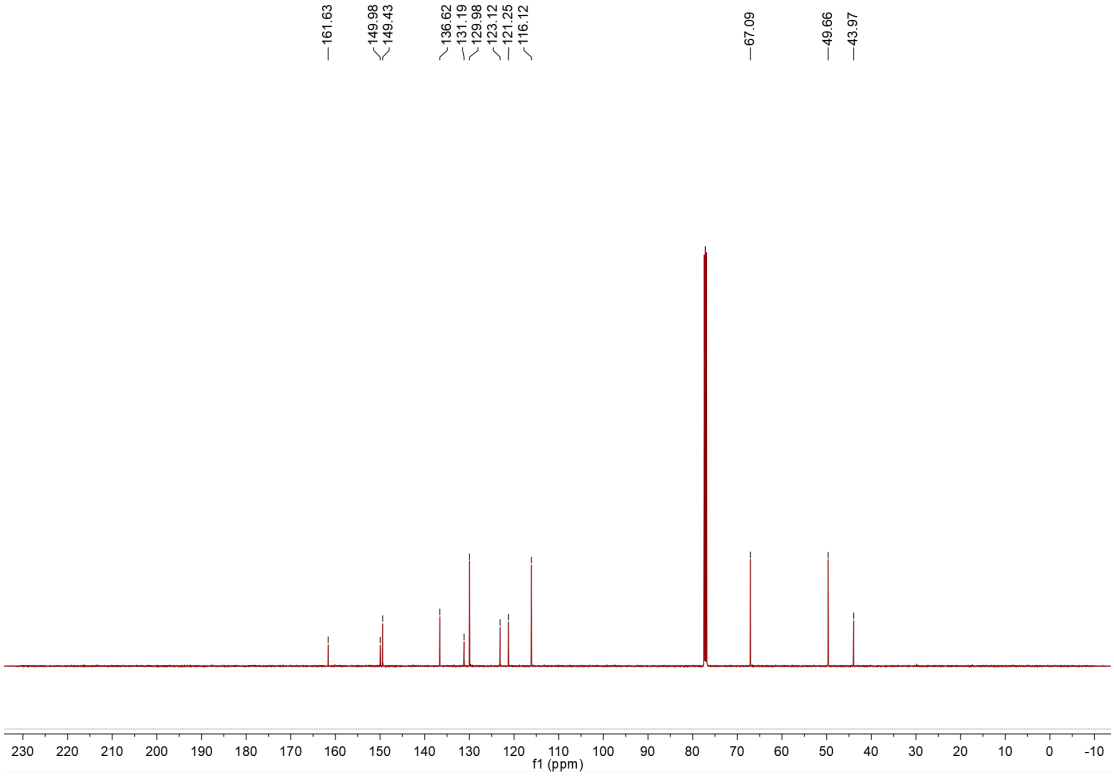
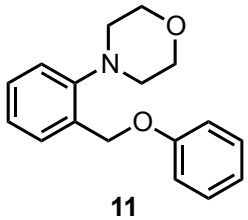
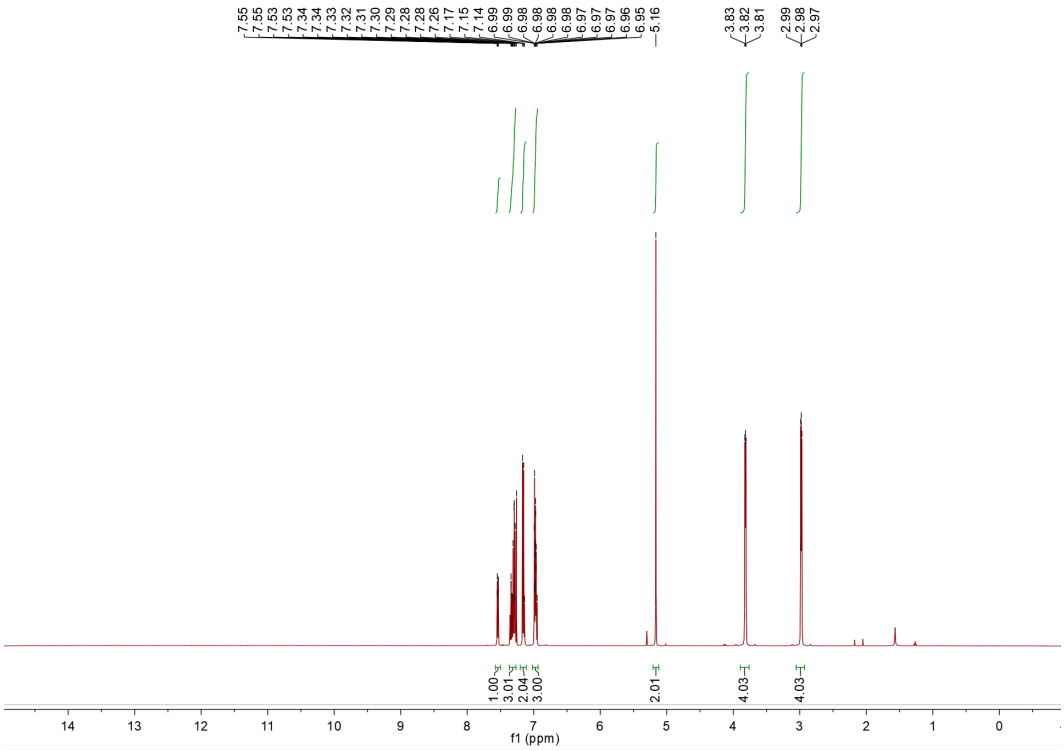
7.56
7.55
7.53
7.18
7.16
7.10
7.08
6.86
6.85
4.08
3.85
3.84
3.83
3.12
3.11
3.11
1.00
1.00
2.01
2.00
1.99
1.98
4.02
3.96
f1 (ppm)


161.63
149.98
149.43
136.62
131.19
129.98
123.12
121.25
116.12
67.09
49.66
43.97
f1 (ppm)



**11**


7.55
7.55
7.53
7.53
7.34
7.34
7.33
7.32
7.31
7.30
7.29
7.28
7.28
7.26
7.17
7.15
7.14
6.99
6.99
6.98
6.98
6.98
6.98
6.97
6.97
6.97
6.96
6.95
5.16
3.83
3.82
3.81
2.99
2.98
2.97
1.00
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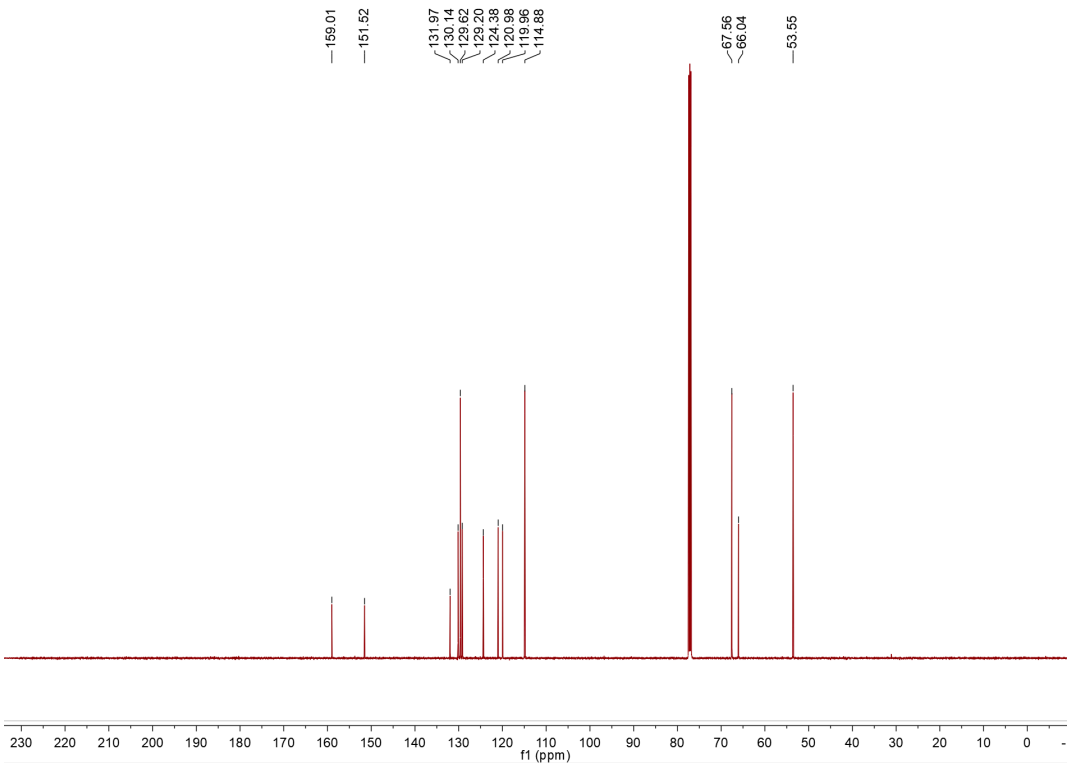
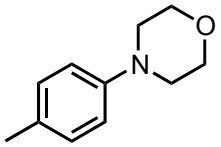
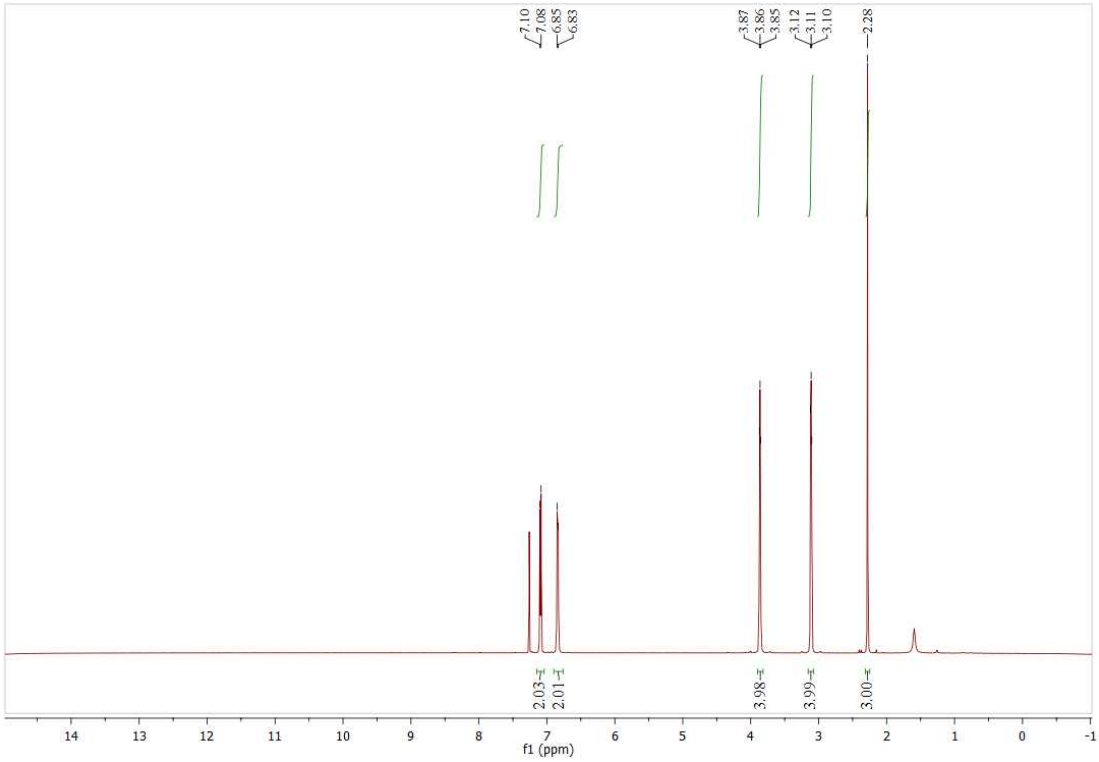
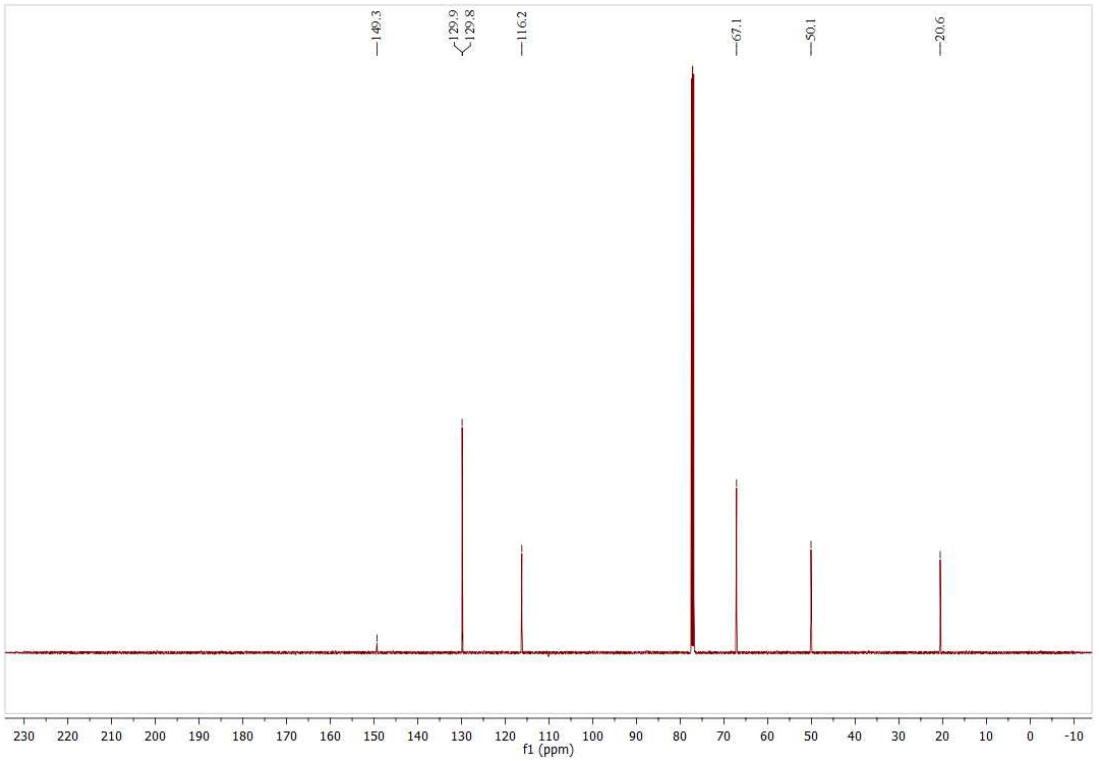
2.04
3.00
2.01
4.03
4.03
f1 (ppm)

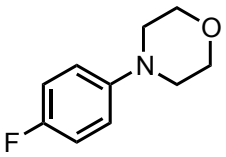

159.01
151.52
131.97
130.14
128.62
129.20
124.38
120.98
119.96
114.88
67.56
66.04
53.55
f1 (ppm)



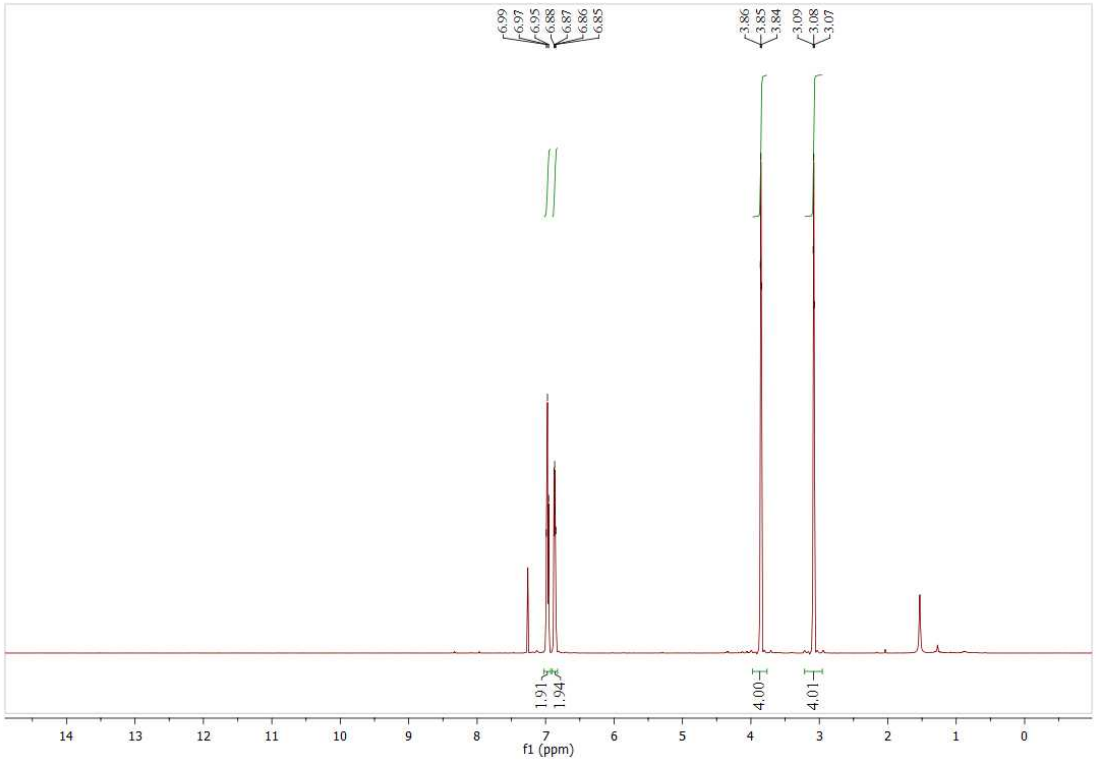
**12**

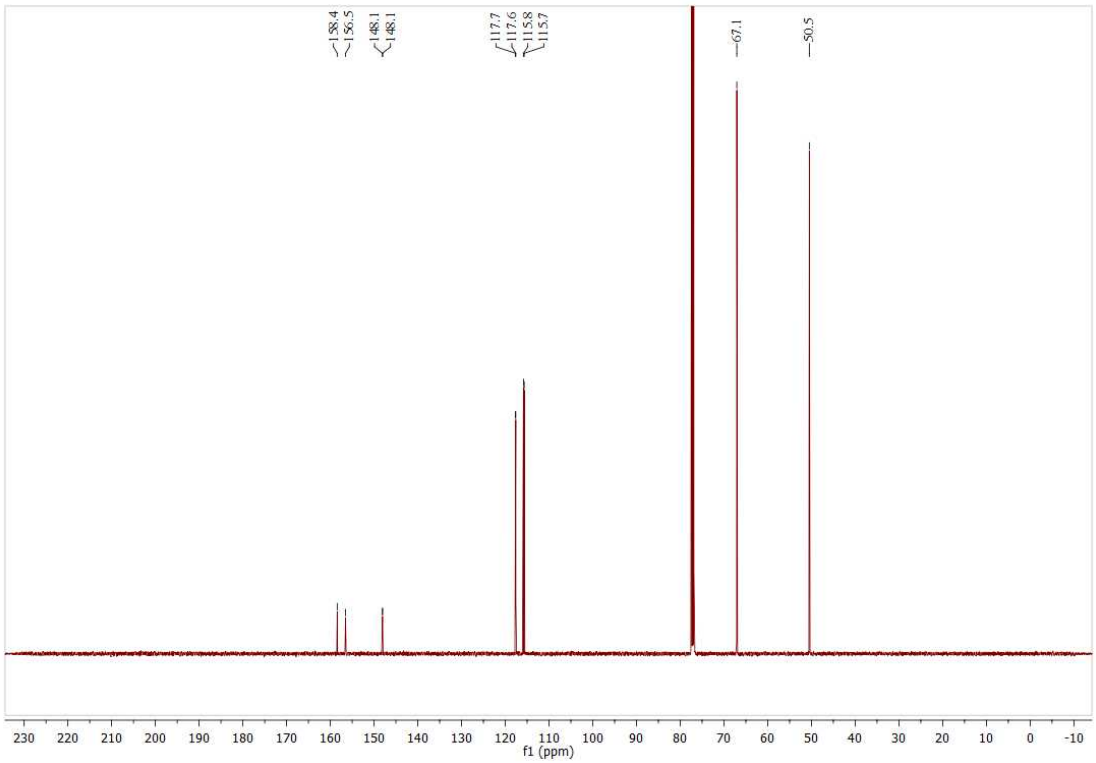

7.10
7.08
6.85
6.83
3.87
3.86
3.85
3.12
3.11
3.10
2.28
2.03
2.01
3.98
3.99
3.00
f1 (ppm)

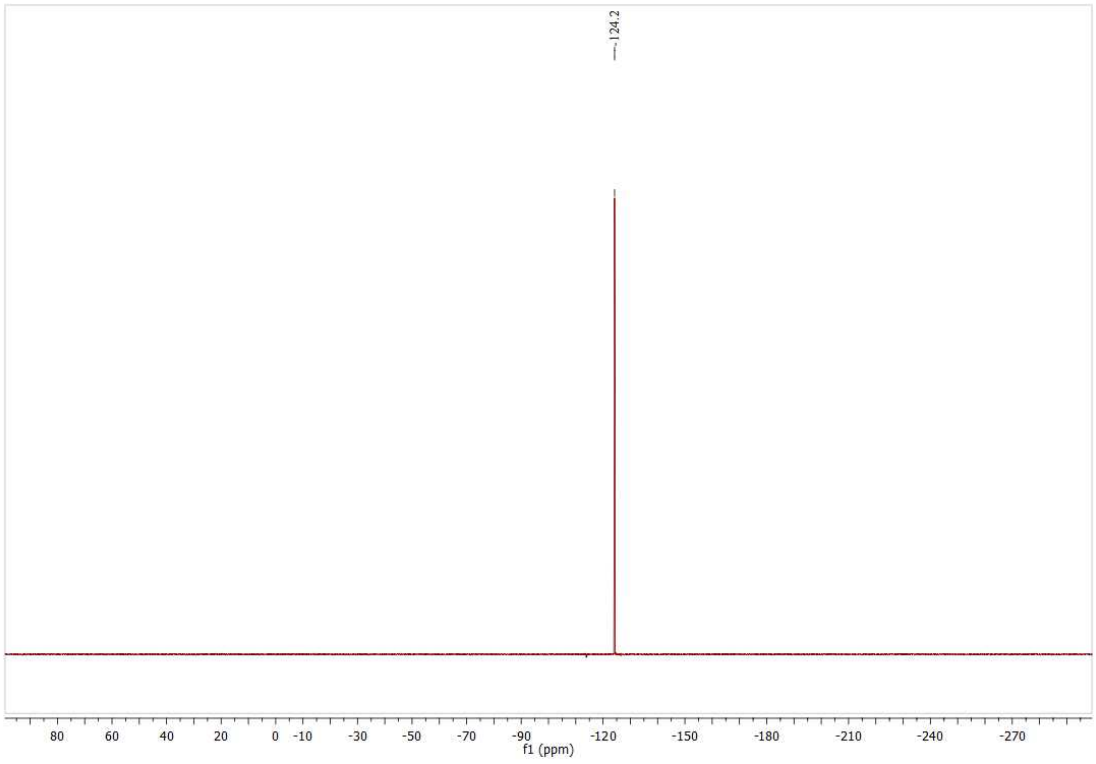

149.3
129.9
129.8
116.2
67.1
50.1
20.6
f1 (ppm)

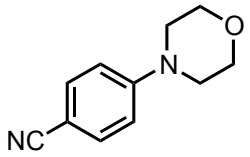

O
N
F

**13**

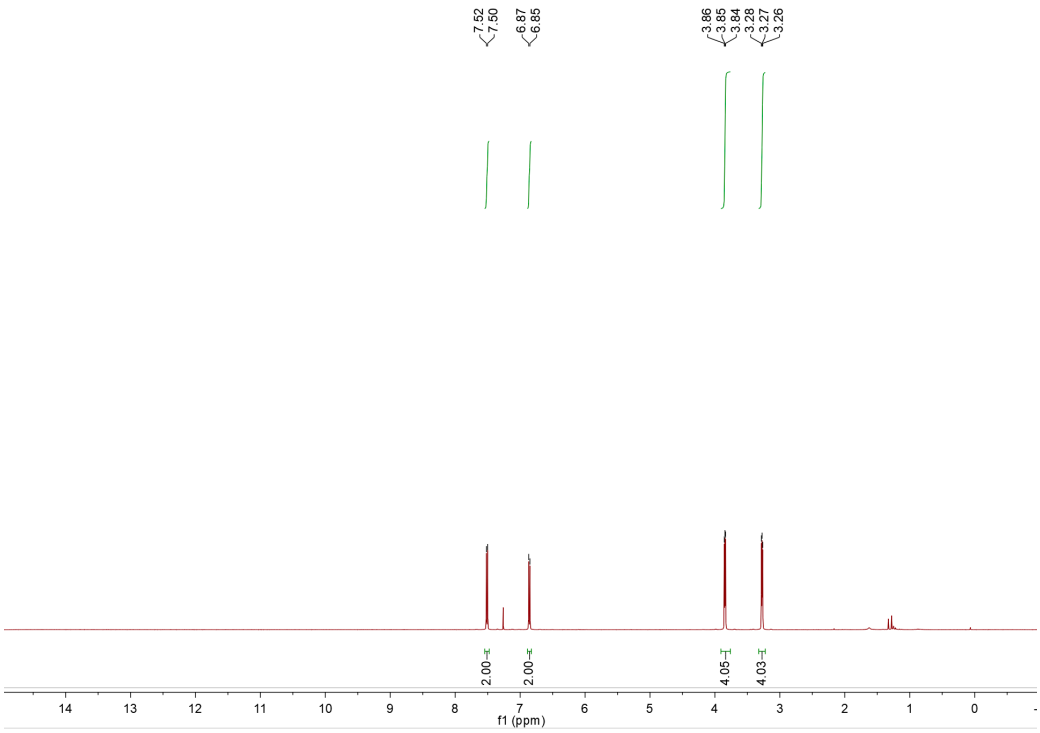

6.99
6.97
6.95
6.88
6.87
6.86
6.85
3.86
3.85
3.84
3.09
3.08
3.07
1.91
1.94
4.00
4.01
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

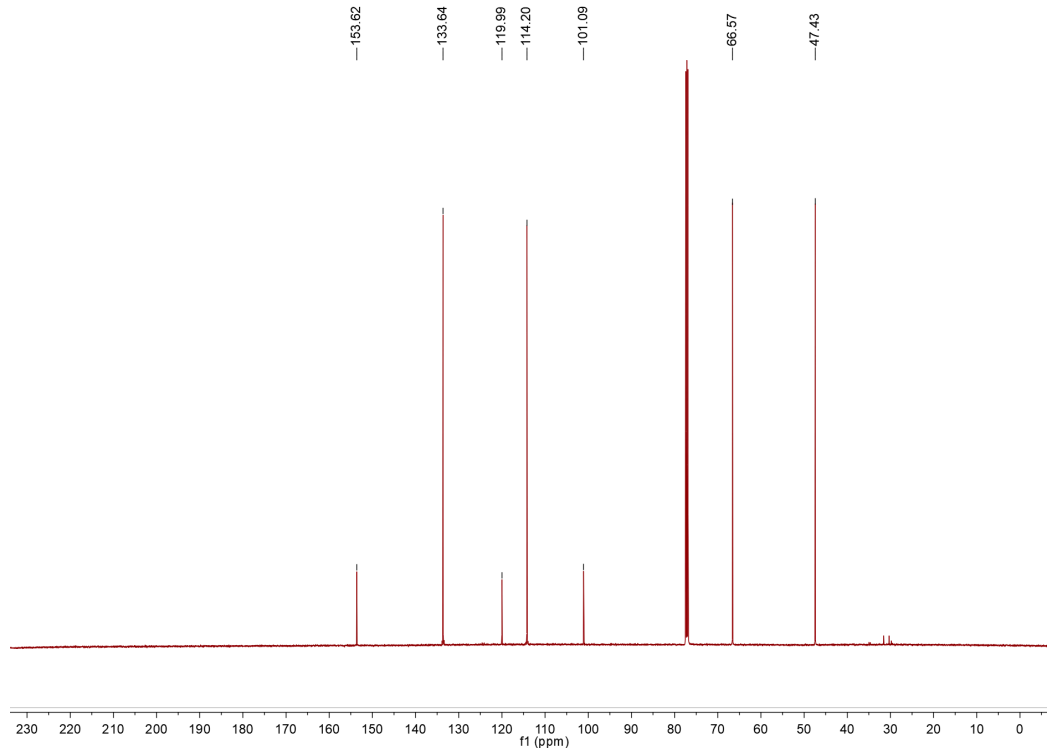

158.4
156.5
148.1
148.1
117.7
117.6
115.8
115.7
67.1
50.5
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

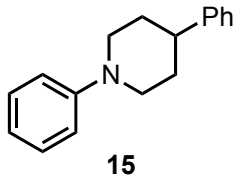

-124.2
80
60
40
20
0
-10
-30
-50
-70
-90
-120
-150
-180
-210
-240
-270
f1 (ppm)


O
N
NC

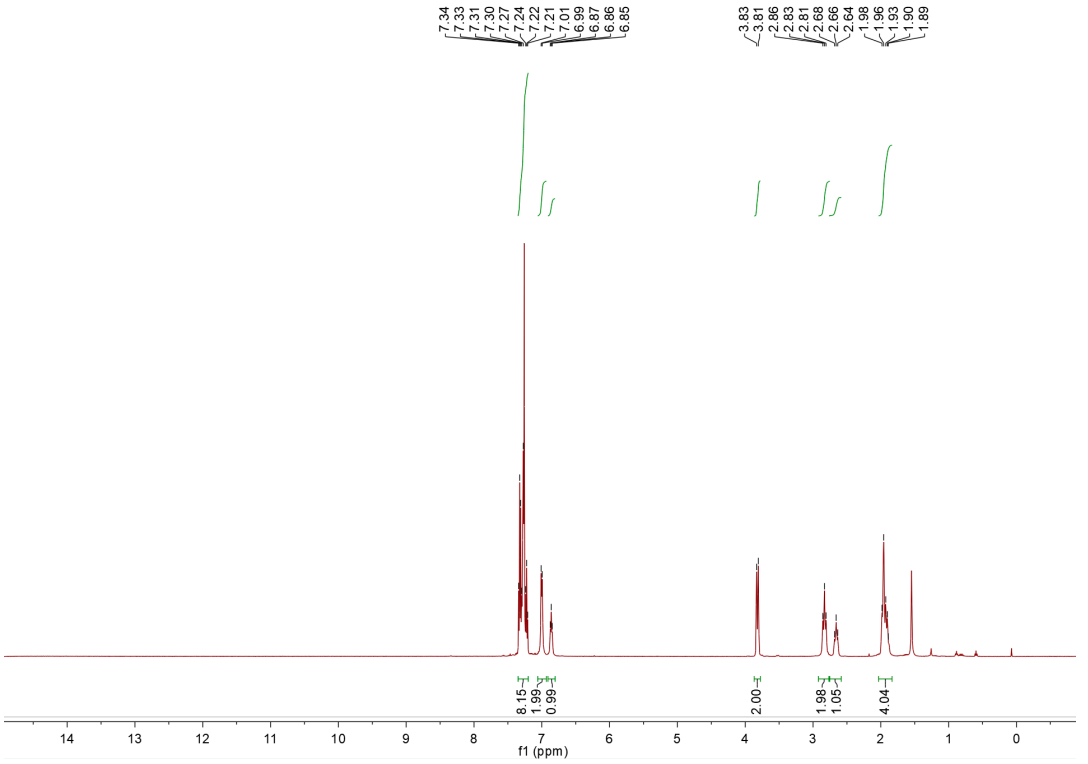
**14**

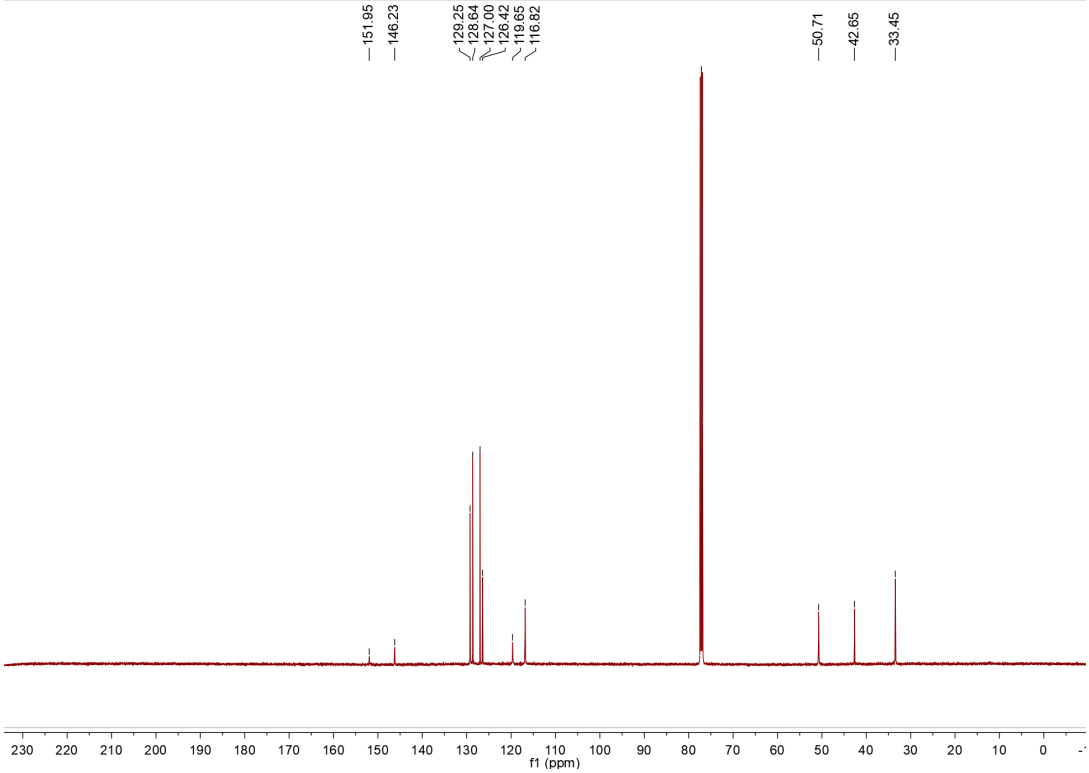

7.52
7.50
6.87
6.85
3.86
3.85
3.84
3.28
3.27
3.26
2.00
2.00
4.05
4.03
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

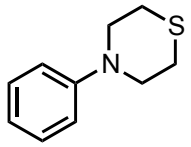

153.62
133.64
119.99
114.20
101.09
66.57
47.43
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
N

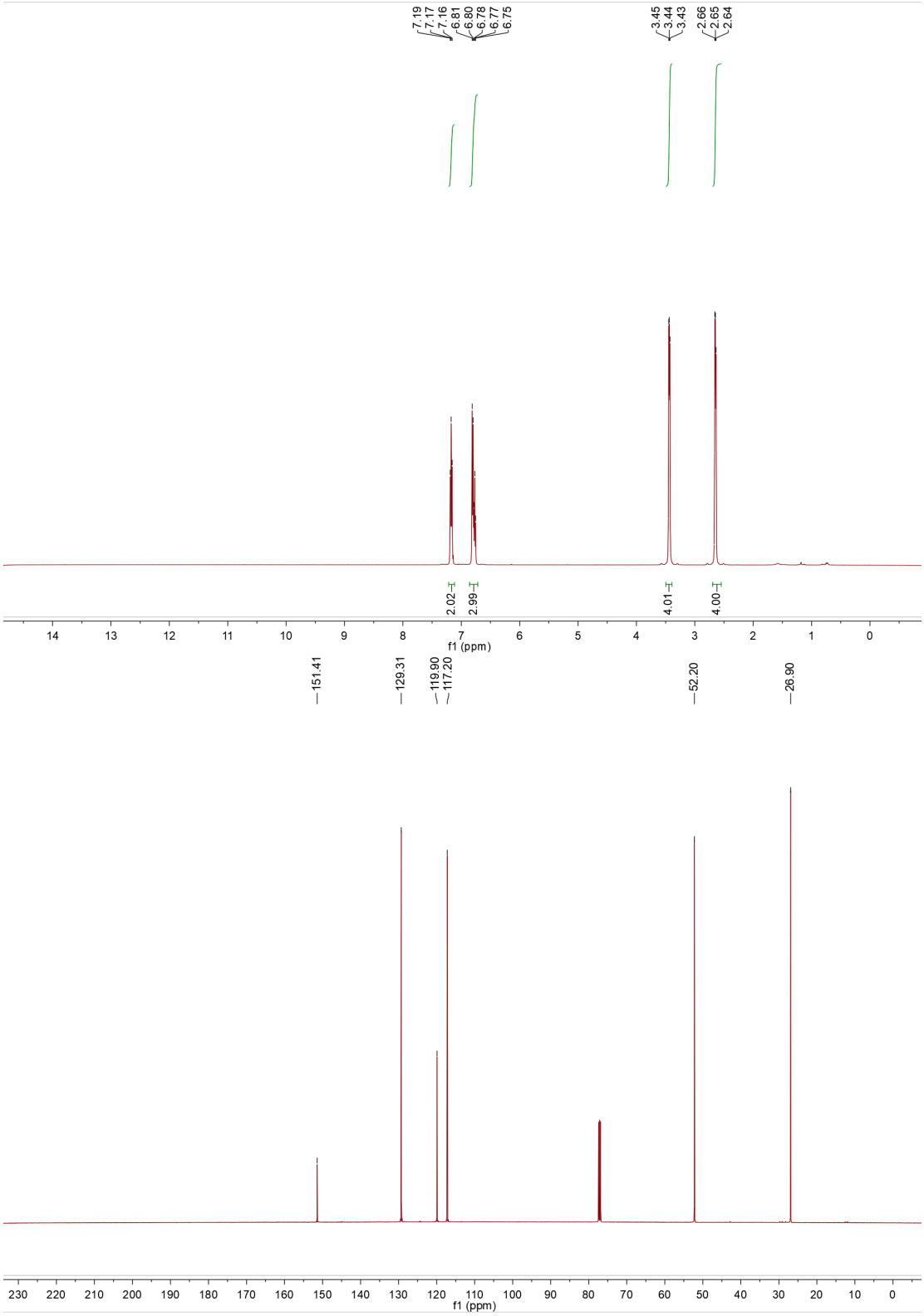
**15**

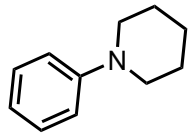

7.34
7.33
7.31
7.30
7.27
7.24
7.22
7.21
7.01
6.99
6.87
6.86
6.85
3.83
3.81
2.86
2.83
2.81
2.68
2.66
2.64
1.98
1.96
1.93
1.90
1.89
8.15
1.99
0.99
2.00
1.98
1.05
4.04
f1 (ppm)


151.95
146.23
129.25
128.64
127.00
126.42
119.85
116.82
50.71
42.65
33.45
f1 (ppm)

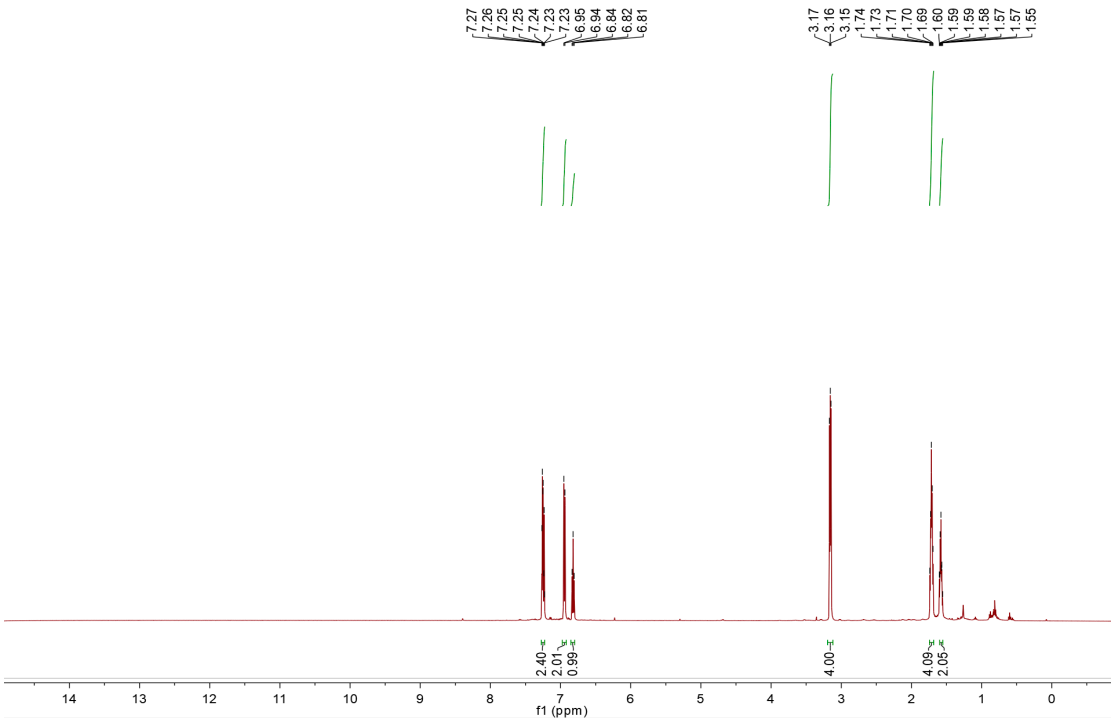


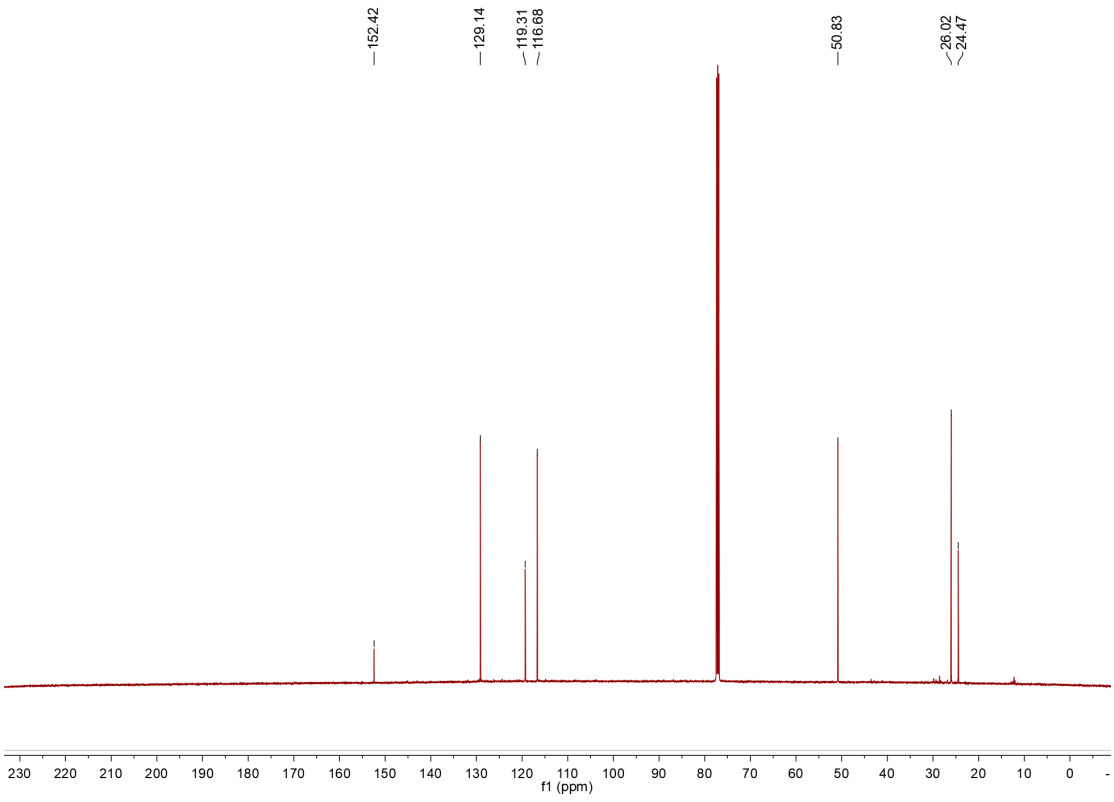
**16**

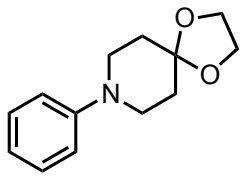

7.19
7.17
7.16
6.81
6.80
6.78
6.77
6.75
3.45
3.44
3.43
2.66
2.65
2.64
2.02
2.99
4.01
4.00
f1 (ppm)
151.41
129.31
119.90
117.20
52.20
26.90
f1 (ppm)



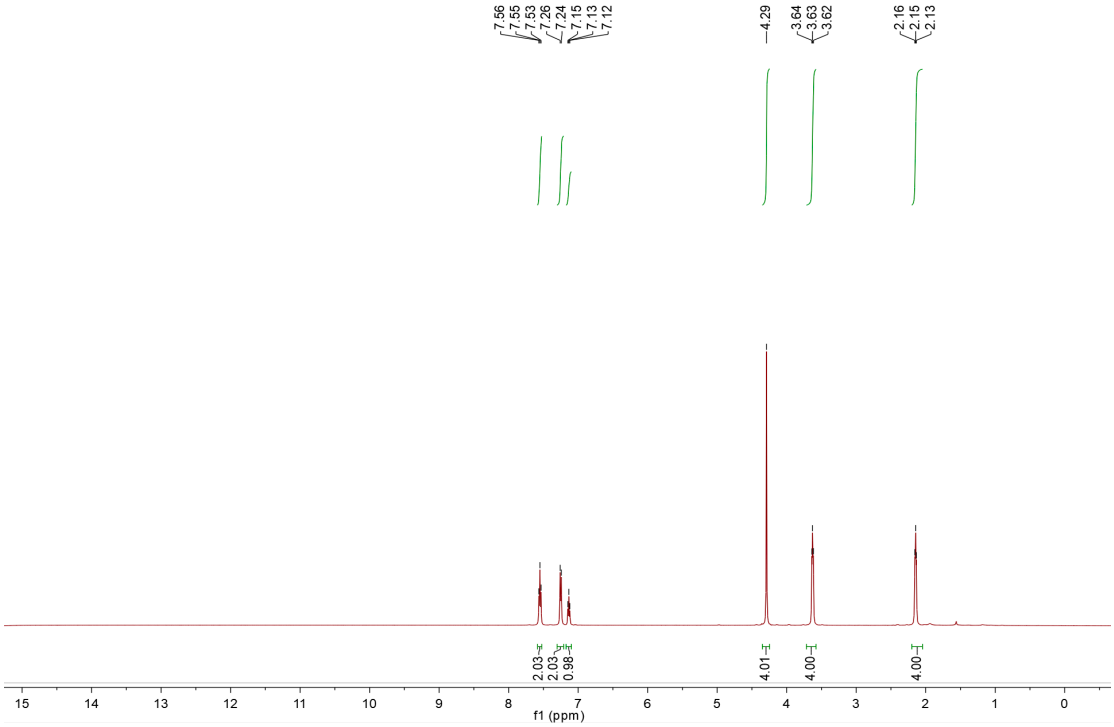
**17**

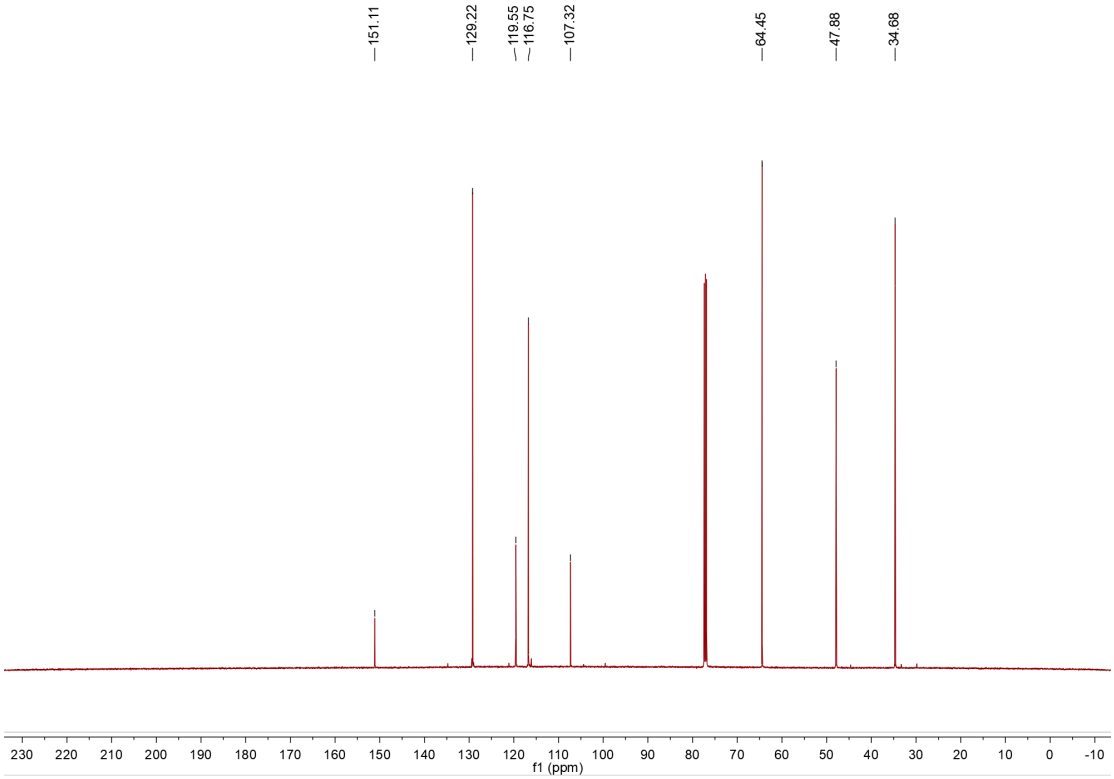

7.27
7.26
7.25
7.25
7.24
7.23
7.23
6.95
6.94
6.84
6.82
6.81
3.17
3.16
3.15
1.74
1.73
1.71
1.70
1.69
1.60
1.59
1.59
1.58
1.57
1.57
1.55
2.40
2.01
0.99
4.00
4.09
2.05
f1 (ppm)

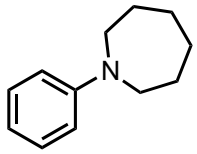

152.42
129.14
119.31
116.68
50.83
26.02
24.47
f1 (ppm)



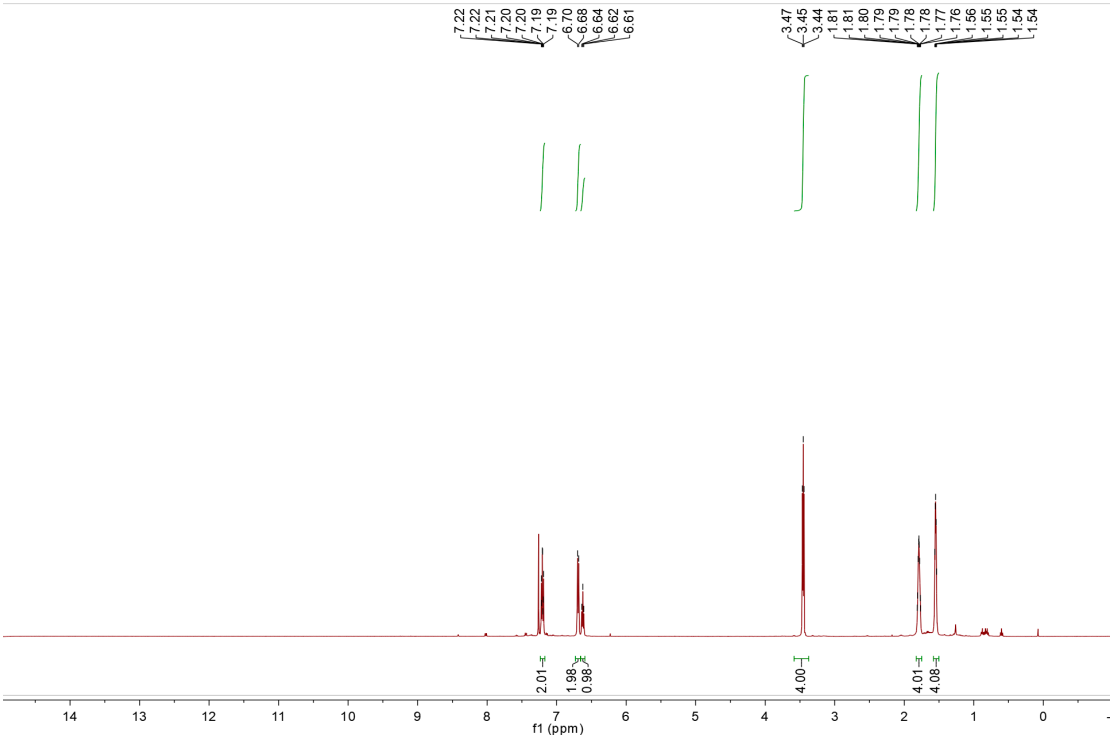
**18**

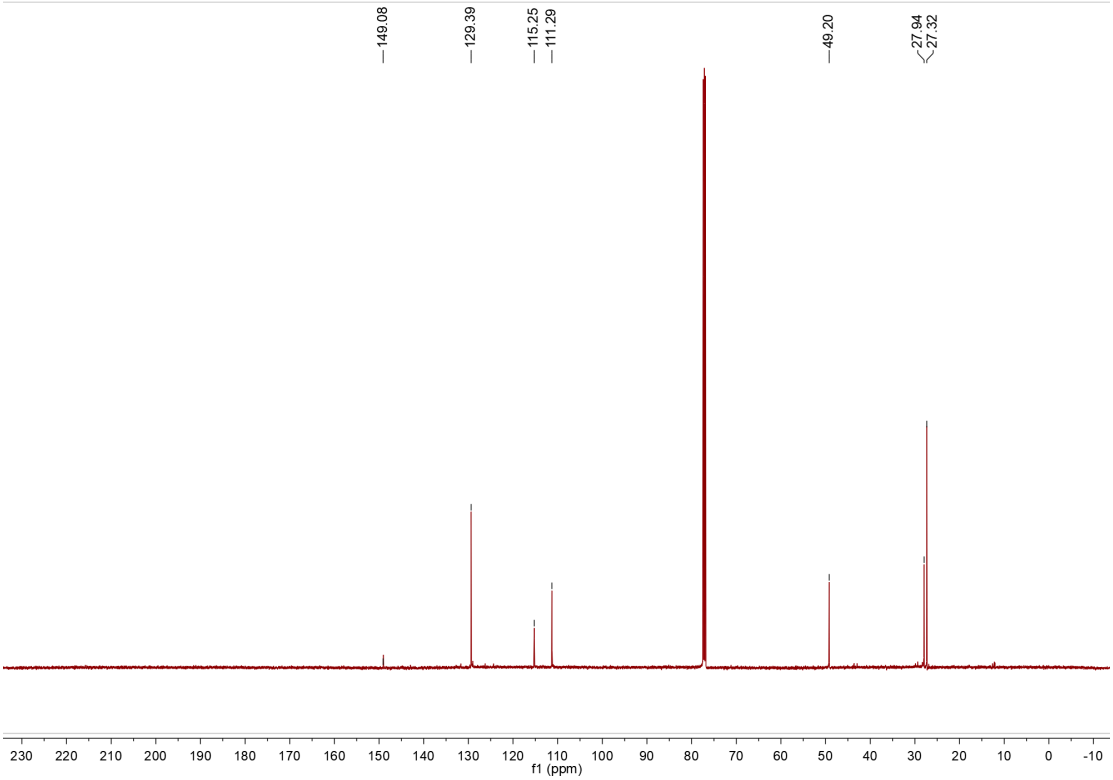

7.56
7.55
7.53
7.26
7.24
7.15
7.13
7.12
4.29
3.64
3.63
3.62
2.16
2.15
2.13
2.03
2.03
0.98
4.01
4.00
4.00
f1 (ppm)

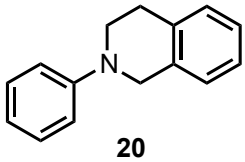

151.11
129.22
119.55
116.75
107.32
64.45
47.88
34.68
f1 (ppm)



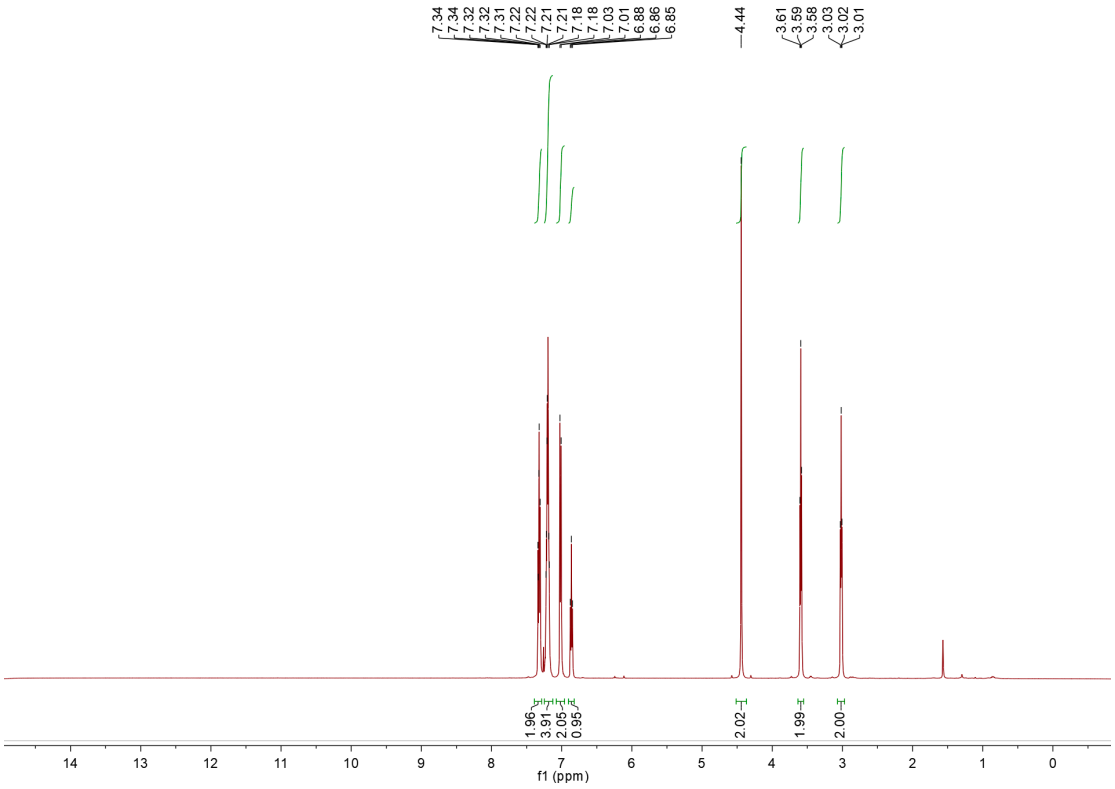
**19**


7.22
7.22
7.21
7.20
7.20
7.19
7.19
6.70
6.68
6.64
6.62
6.61
3.47
3.45
3.44
1.81
1.81
1.80
1.79
1.79
1.78
1.78
1.77
1.76
1.56
1.55
1.55
1.54
1.54
2.01
1.98
0.98
4.00
4.01
4.08
f1 (ppm)


149.08
129.39
115.25
111.29
49.20
27.94
27.32
f1 (ppm)



**20**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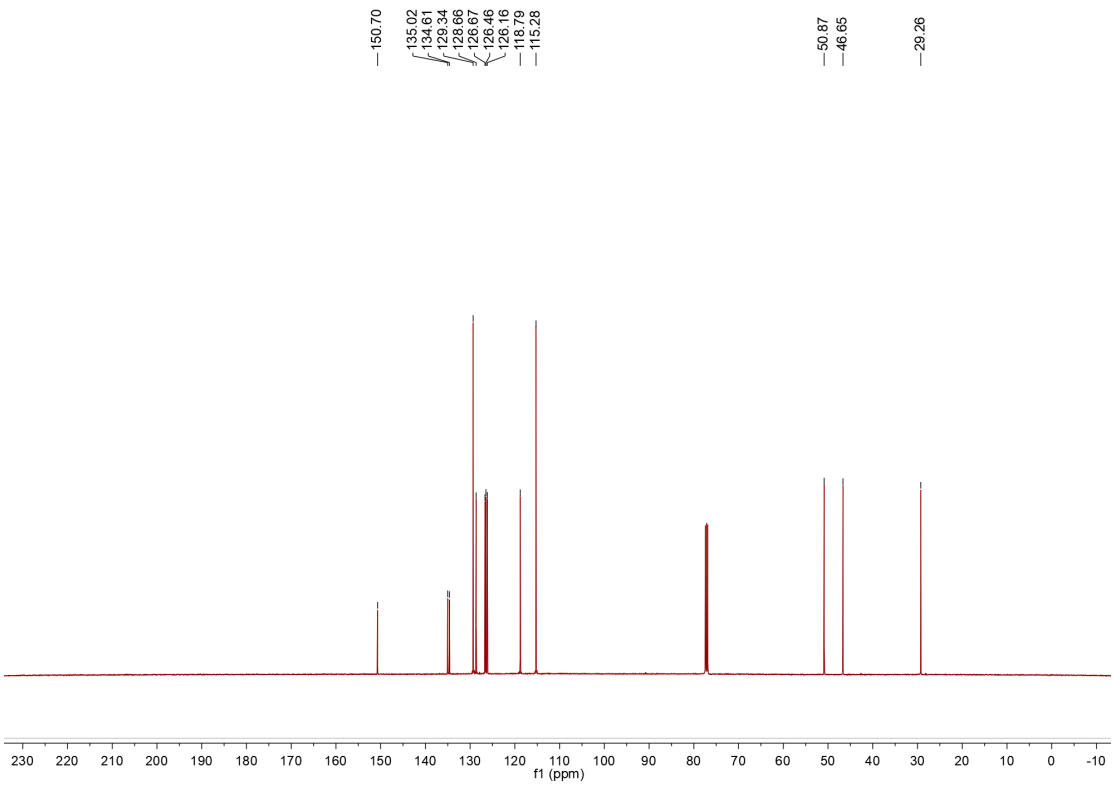
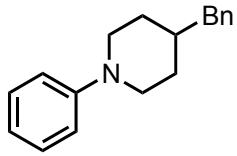
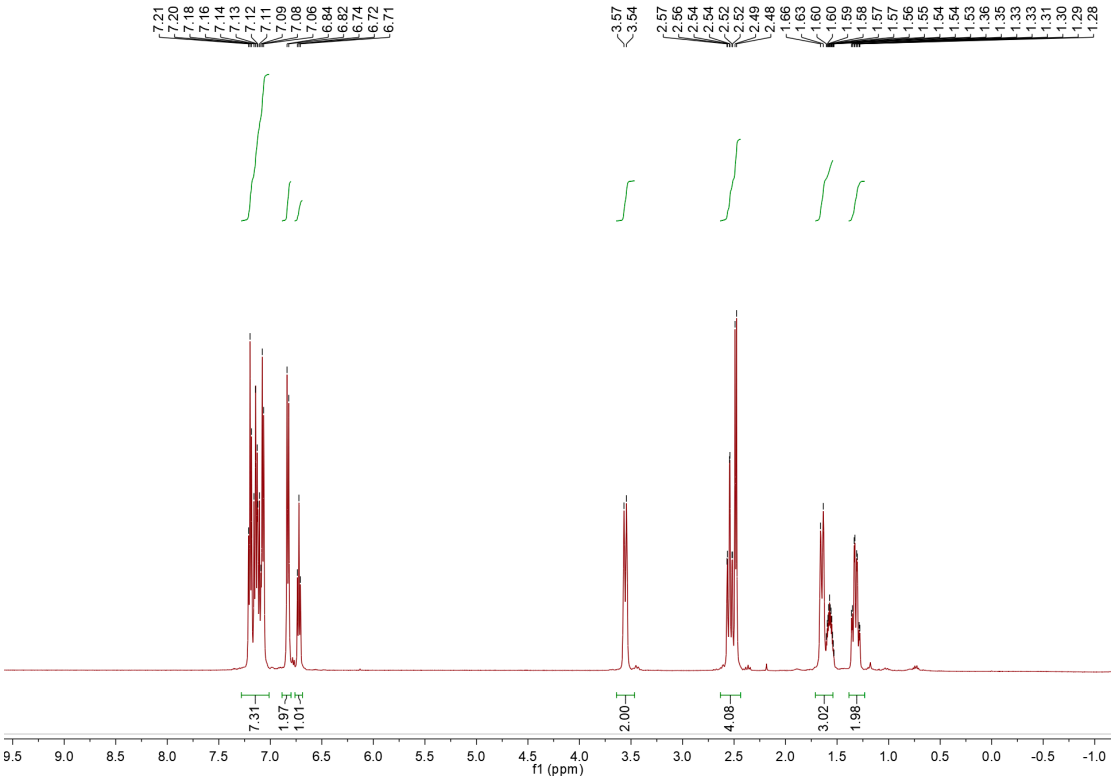
7.34
7.32
7.32
7.31
7.22
7.22
7.21
7.21
7.18
7.18
7.03
7.01
6.88
6.86
6.85
4.44
3.61
3.59
3.58
3.03
3.02
3.01
1.96
3.91
2.05
0.95
2.02
1.99
2.00
f1 (ppm)


150.70
135.02
134.61
129.34
128.66
126.67
126.46
126.16
118.79
115.28
50.87
46.65
29.26
f1 (ppm)


Bn
N

**21**


7.21
7.20
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7.16
7.14
7.13
7.12
7.11
7.09
7.08
7.06
6.84
6.82
6.74
6.72
6.71
3.57
3.54
2.57
2.56
2.54
2.54
2.52
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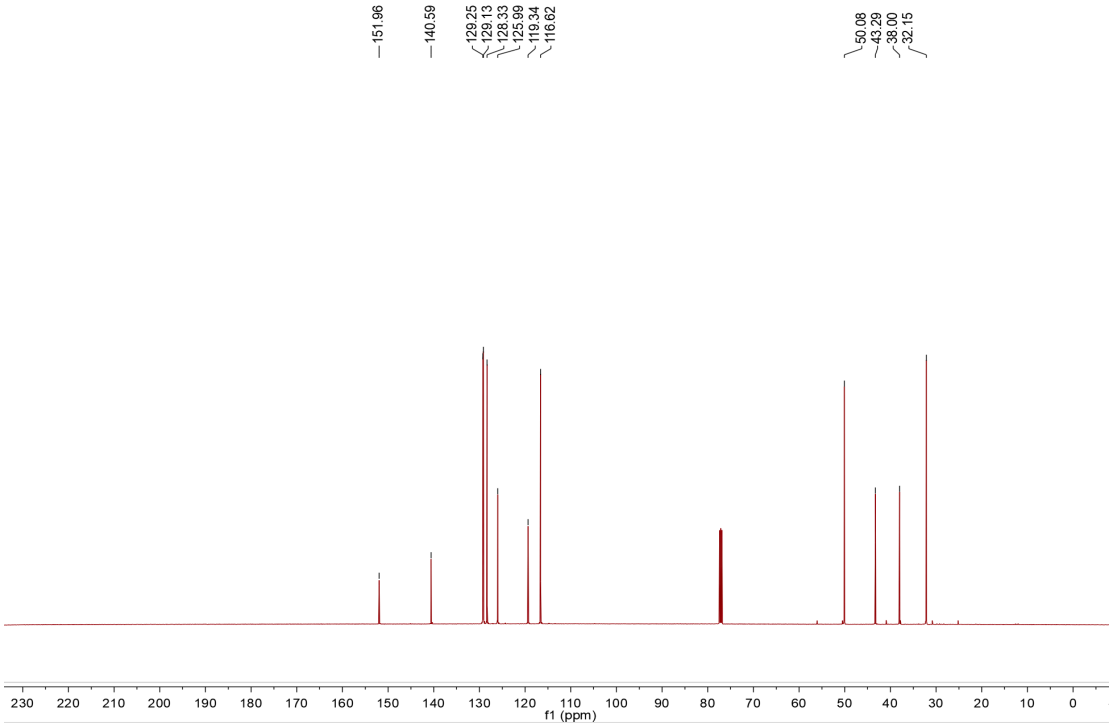
2.49
2.48
1.66
1.63
1.60
1.60
1.59
1.58
1.57
1.57
1.56
1.55
1.54
1.54
1.53
1.36
1.35
1.33
1.33
1.31
1.30
1.29
1.28
7.31
1.97
1.01
2.00
4.08
3.02
1.98
f1 (ppm)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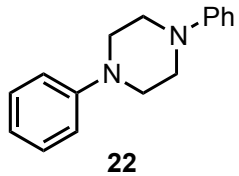
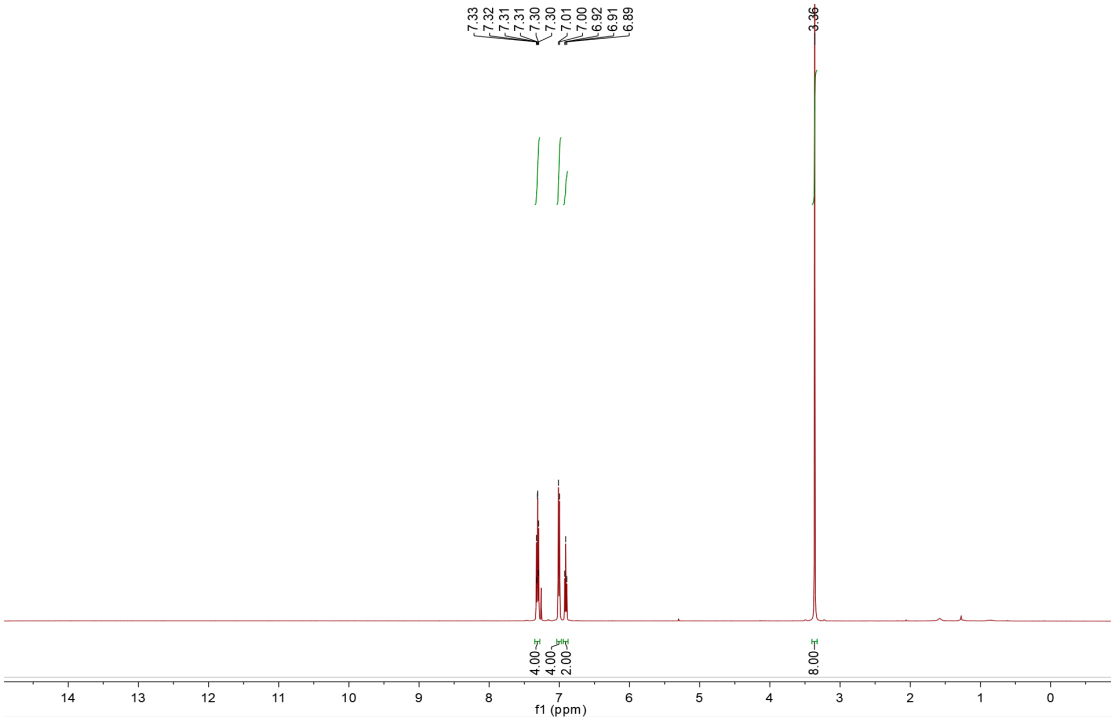
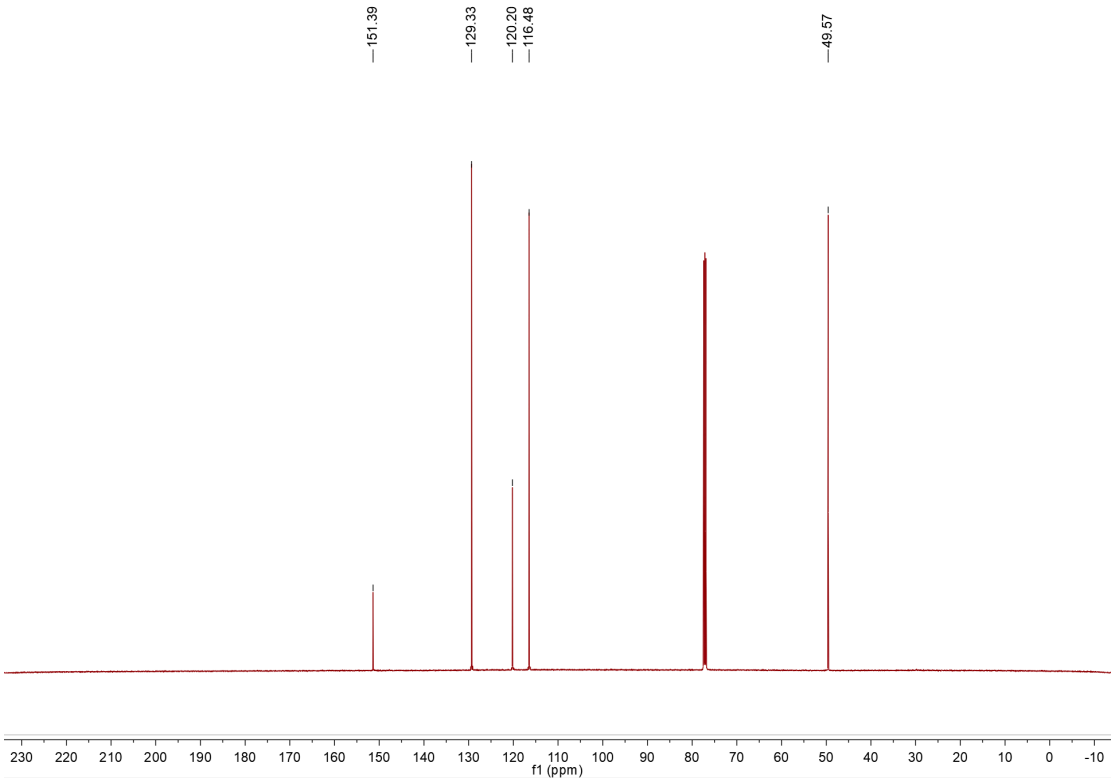
128.33
125.99
119.34
116.62
50.08
43.29
38.00
32.15
f1 (ppm)


Ph
N
N

**22**


7.33
7.32
7.31
7.31
7.30
7.30
7.01
7.00
6.92
6.91
6.89
3.36
4.00
4.00
2.00
8.00
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)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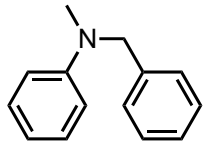
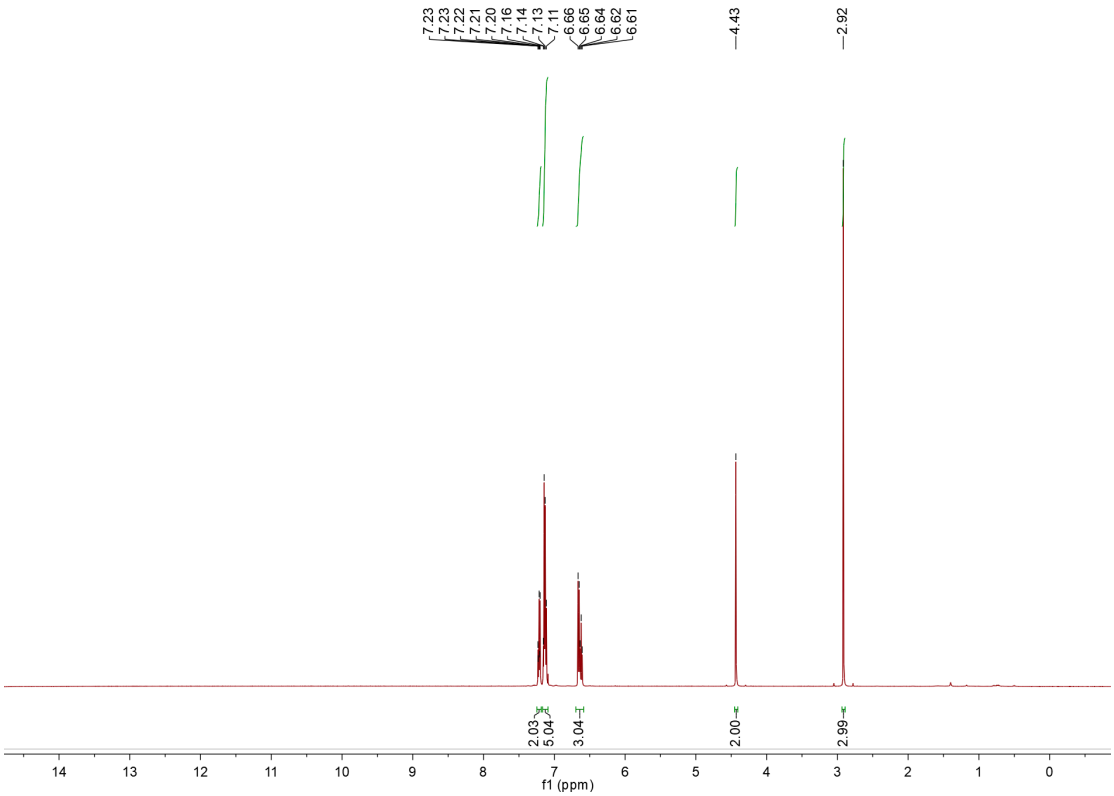
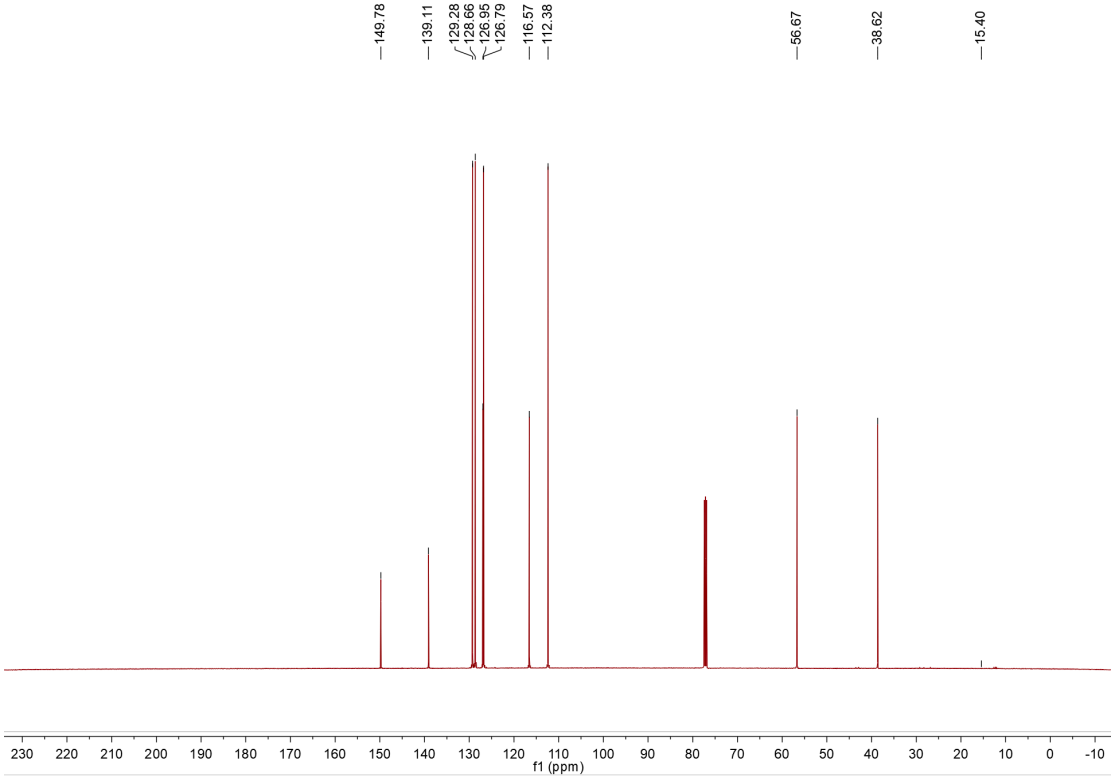
129.33
120.20
116.48
49.57
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



**23**


7.23
7.23
7.22
7.21
7.20
7.16
7.14
7.13
7.11
6.66
6.65
6.64
6.62
6.61
4.43
2.92
2.03
5.04
3.04
2.00
2.99
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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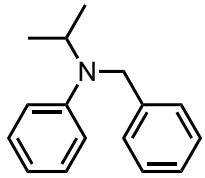
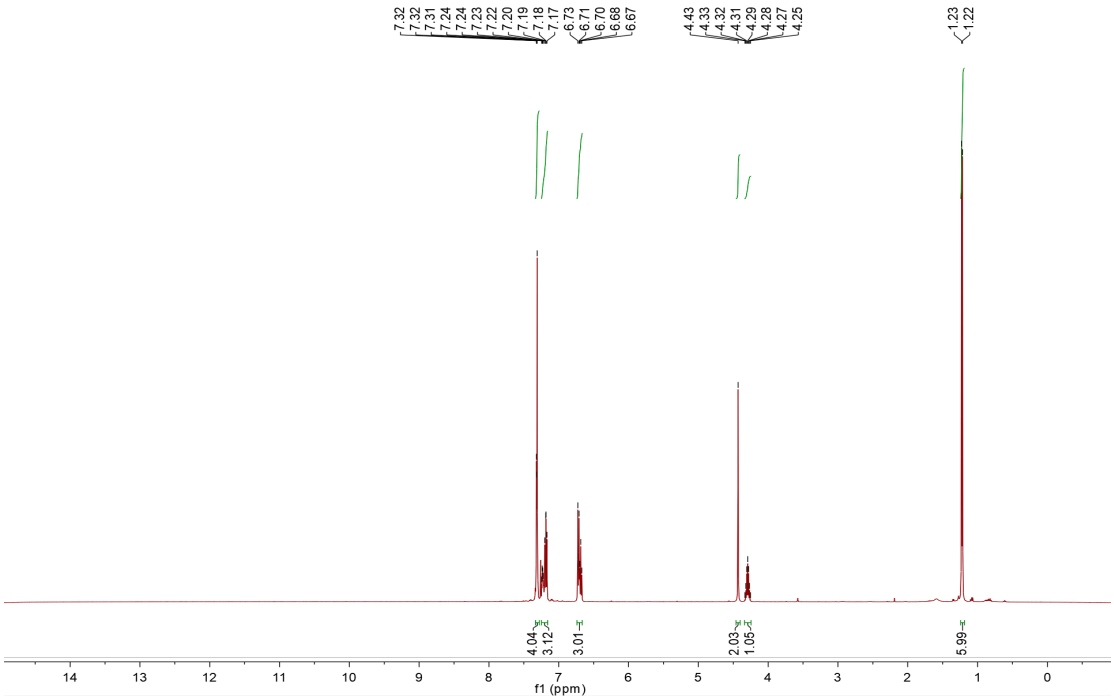
128.66
126.95
126.79
116.57
112.38
56.67
38.62
15.40
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



**24**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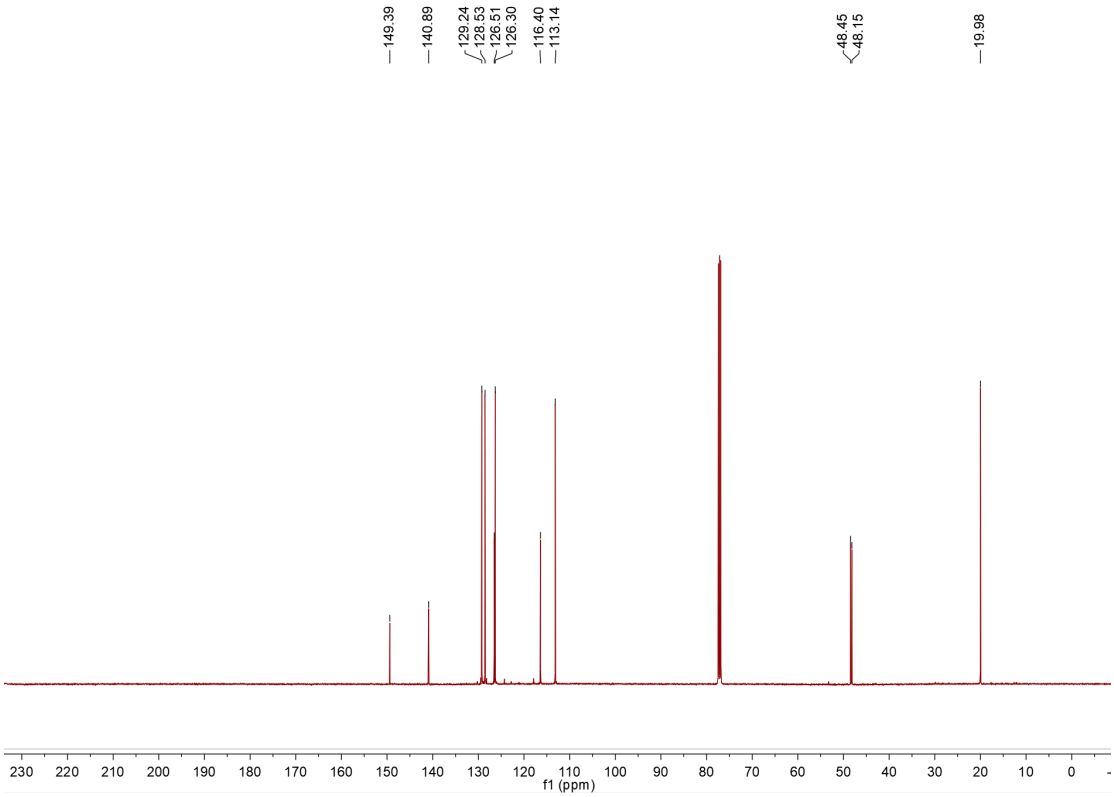
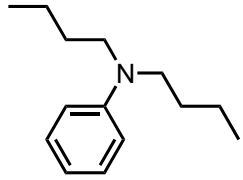
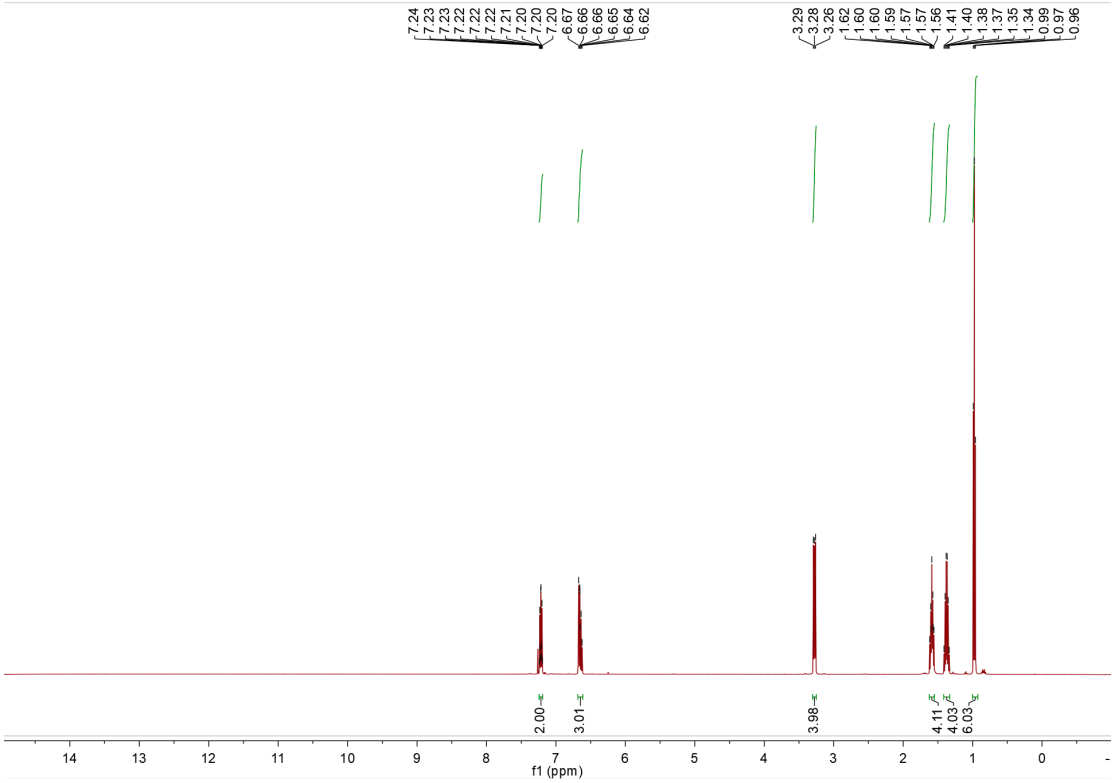
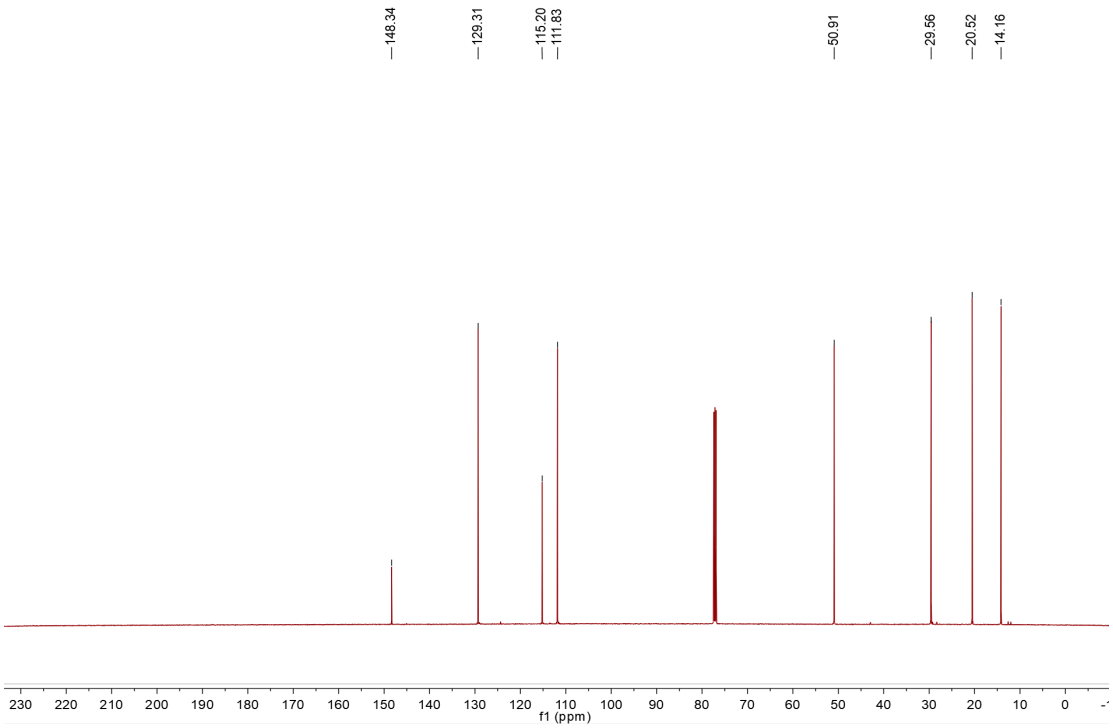
7.23
7.22
7.20
7.19
7.18
7.17
6.73
6.71
6.70
6.68
6.67
4.43
4.33
4.32
4.31
4.29
4.28
4.27
4.25
1.23
1.22
4.04
3.12
3.01
2.03
1.05
5.99
f1 (ppm)

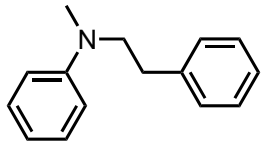

149.39
140.89
129.24
128.53
126.51
126.30
116.40
113.14
48.45
48.15
19.98
f1 (ppm)



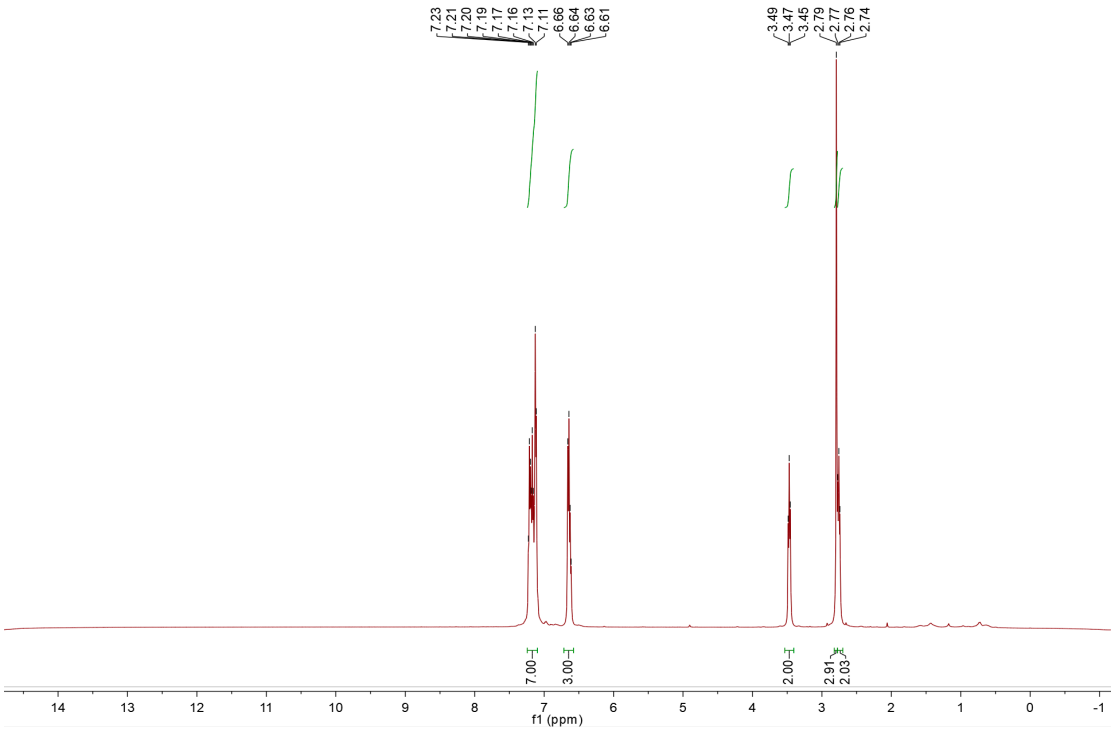
**25**

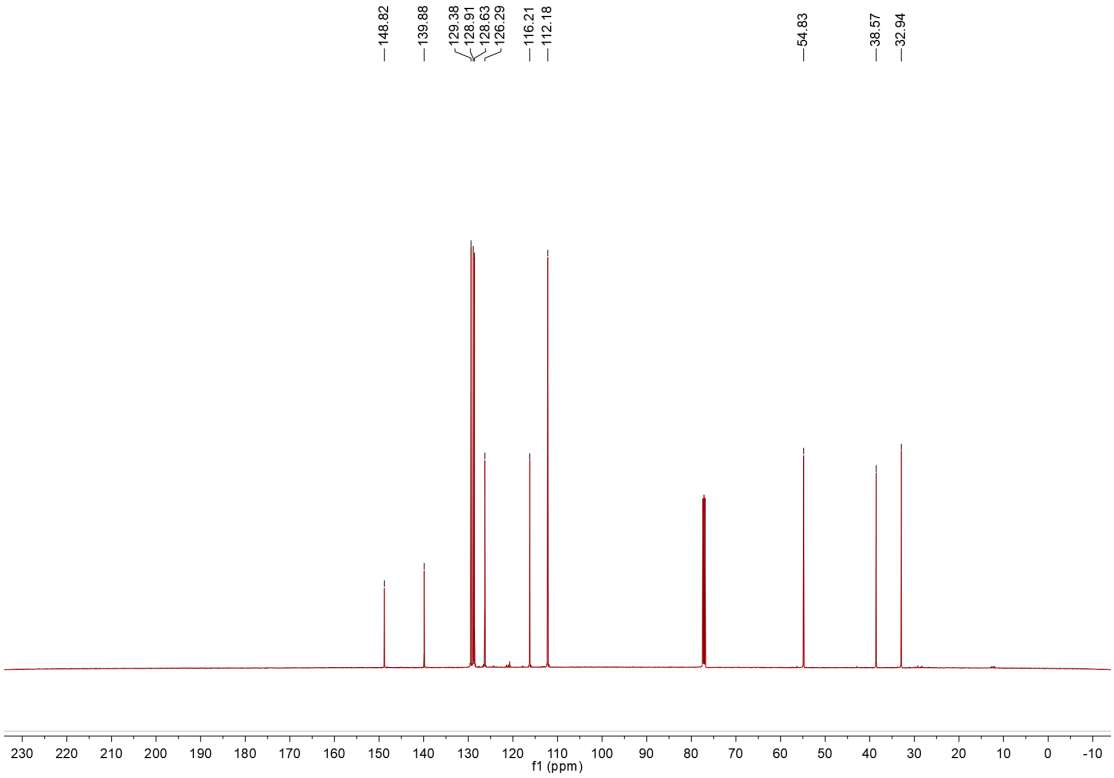

7.24
7.23
7.23
7.22
7.22
7.22
7.21
7.20
7.20
7.20
6.67
6.66
6.66
6.65
6.64
6.62
3.29
3.28
3.26
1.62
1.60
1.60
1.59
1.57
1.57
1.56
1.41
1.40
1.38
1.37
1.35
1.34
0.99
0.97
0.96
2.00
3.01
3.98
4.11
4.03
6.03
f1 (ppm)

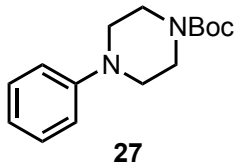

148.34
129.31
115.20
111.83
50.91
29.56
20.52
14.16
f1 (ppm)



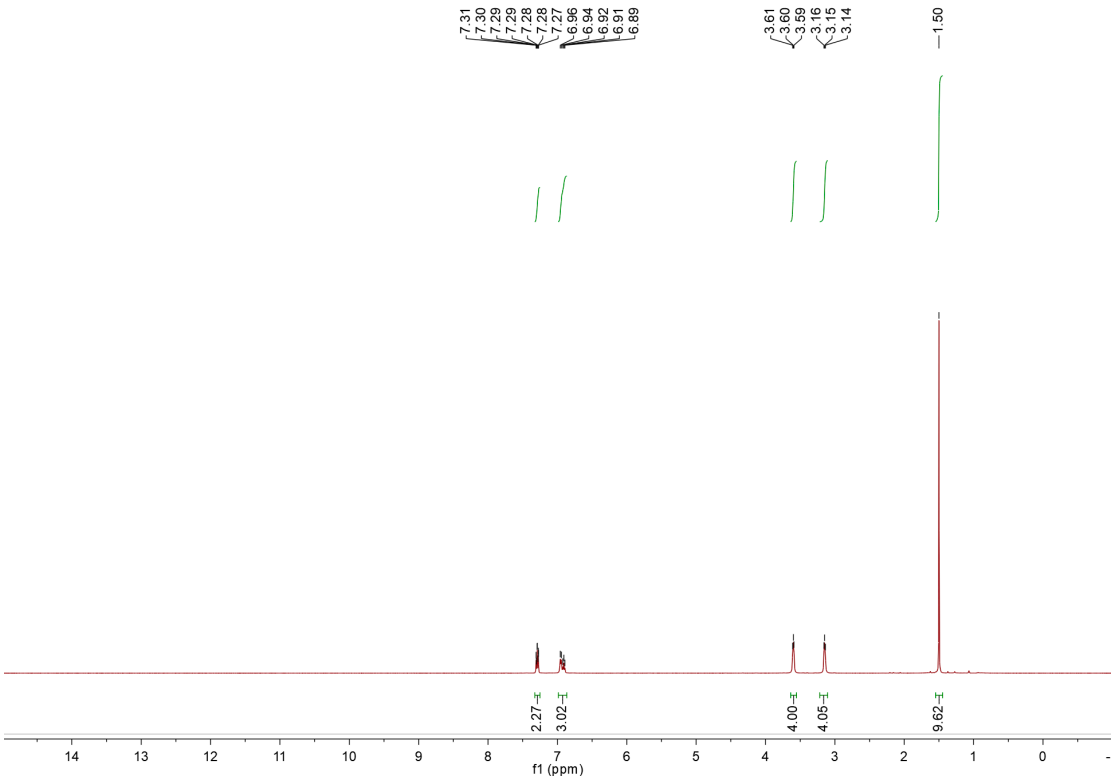
**26**

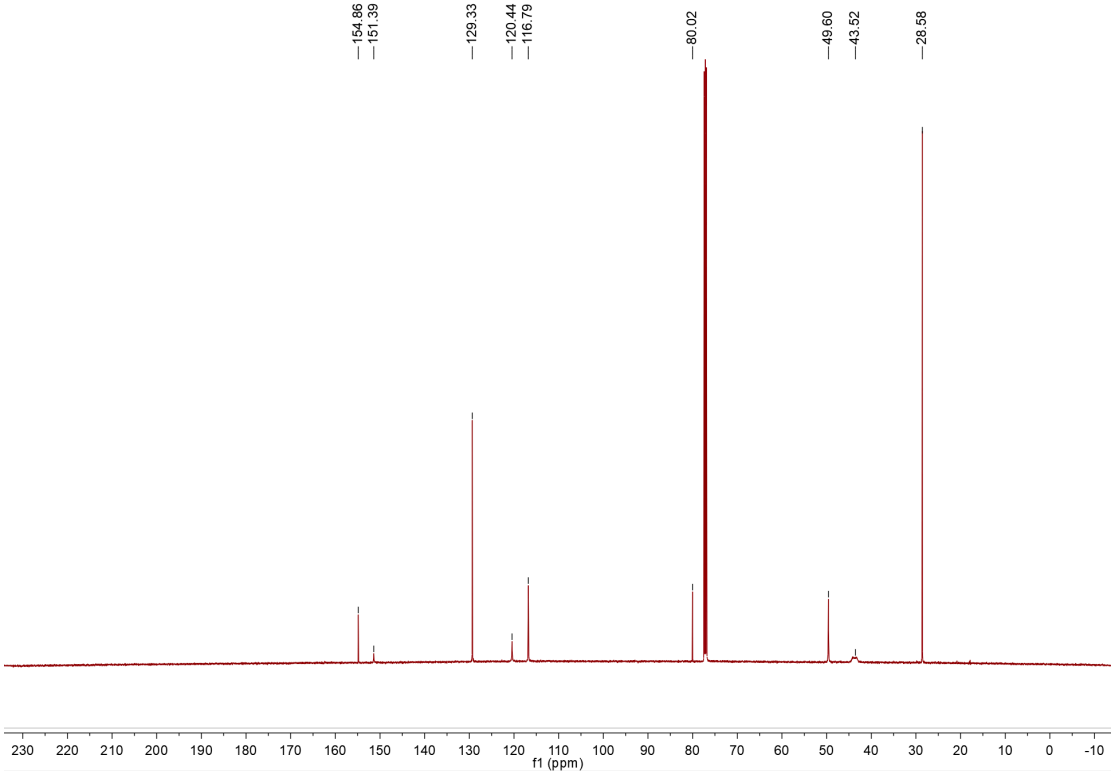

7.23
7.21
7.20
7.19
7.17
7.16
7.13
7.11
6.66
6.64
6.63
6.61
3.49
3.47
3.45
2.79
2.77
2.76
2.74
7.00
3.00
2.00
2.91
2.03
f1 (ppm)

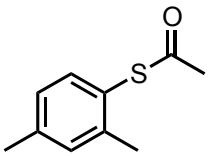

148.82
139.88
129.38
128.91
128.63
126.29
116.21
112.18
54.83
38.57
32.94
f1 (ppm)


NBoc
N

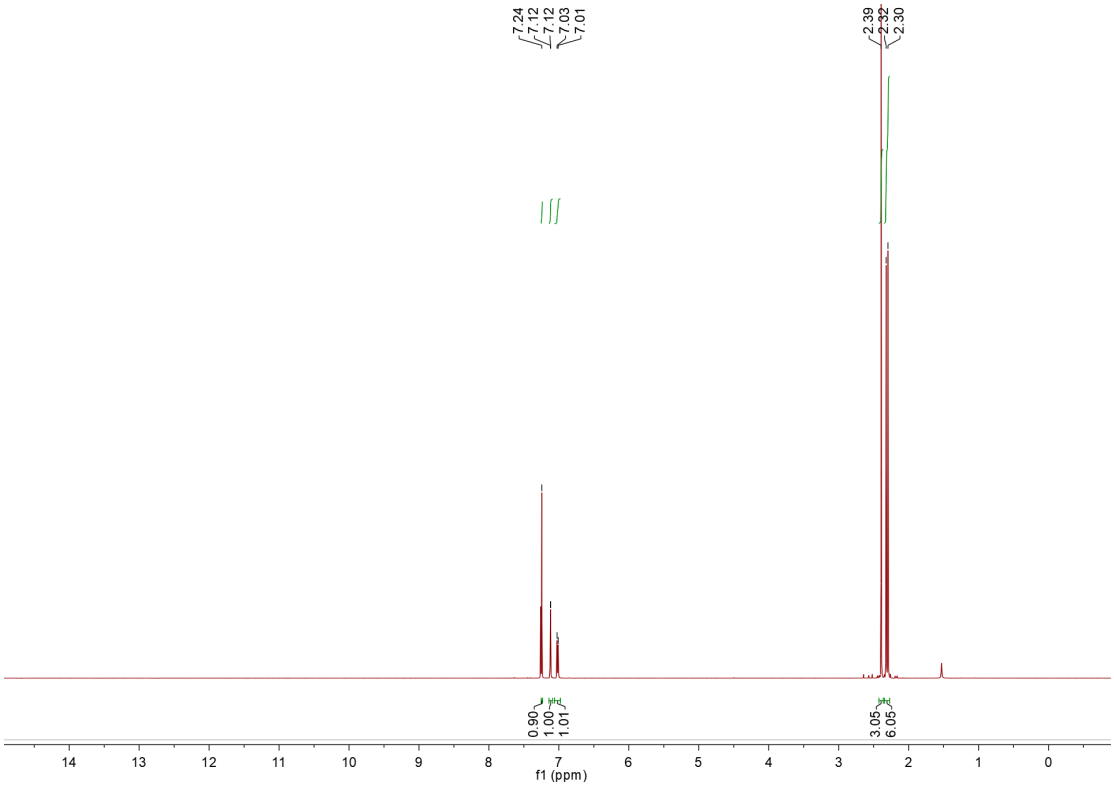
**27**

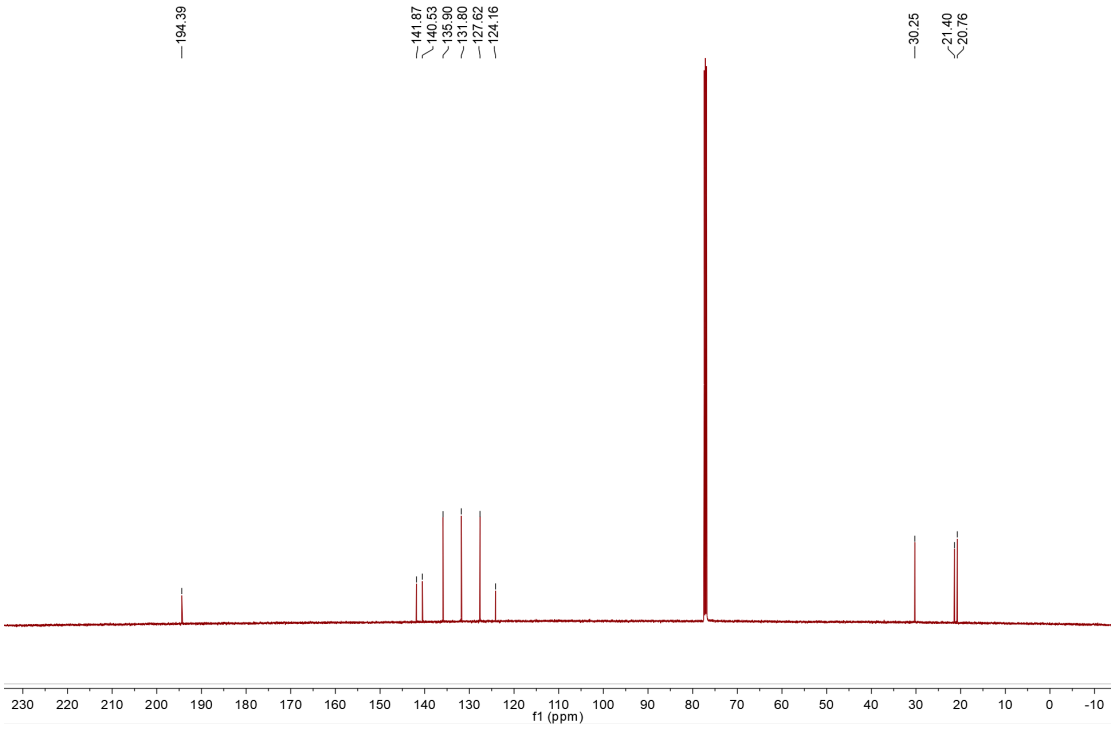

7.31
7.30
7.29
7.29
7.28
7.28
7.27
6.96
6.94
6.92
6.91
6.89
3.61
3.60
3.59
3.16
3.15
3.14
1.50
2.27
3.02
4.00
4.05
9.62
f1 (ppm)

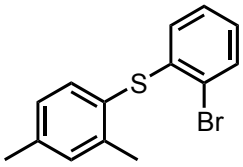

154.86
151.39
129.33
120.44
116.79
80.02
49.60
43.52
28.58
f1 (ppm)


O
S

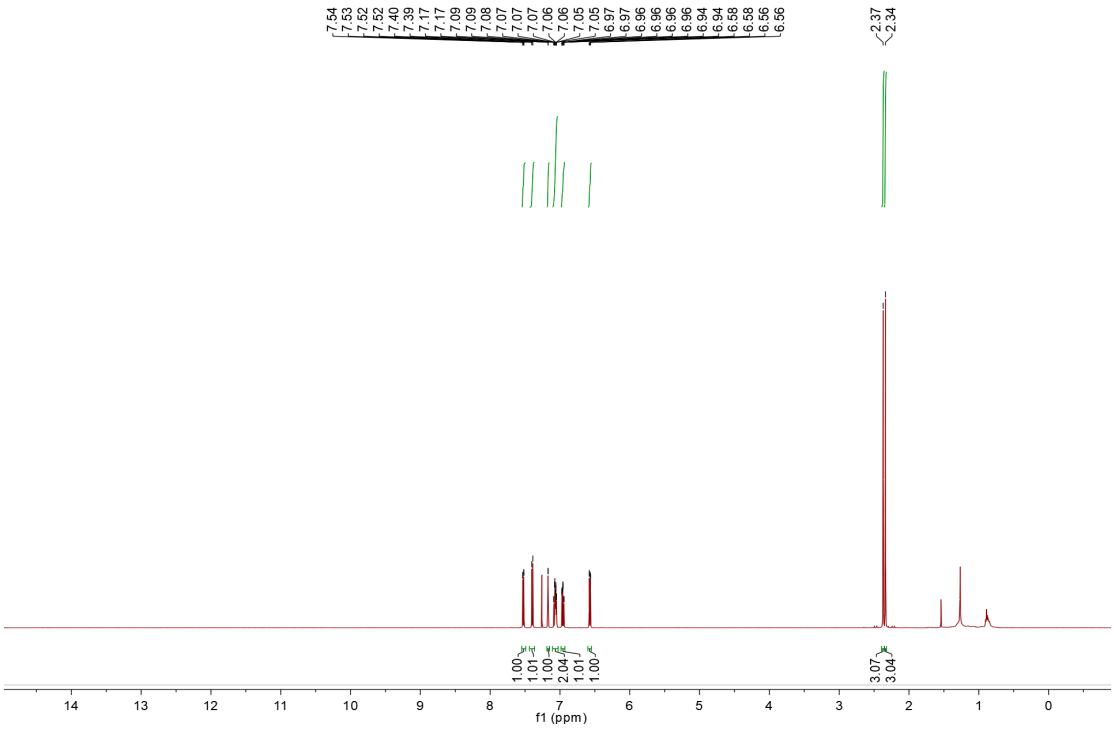
**28**

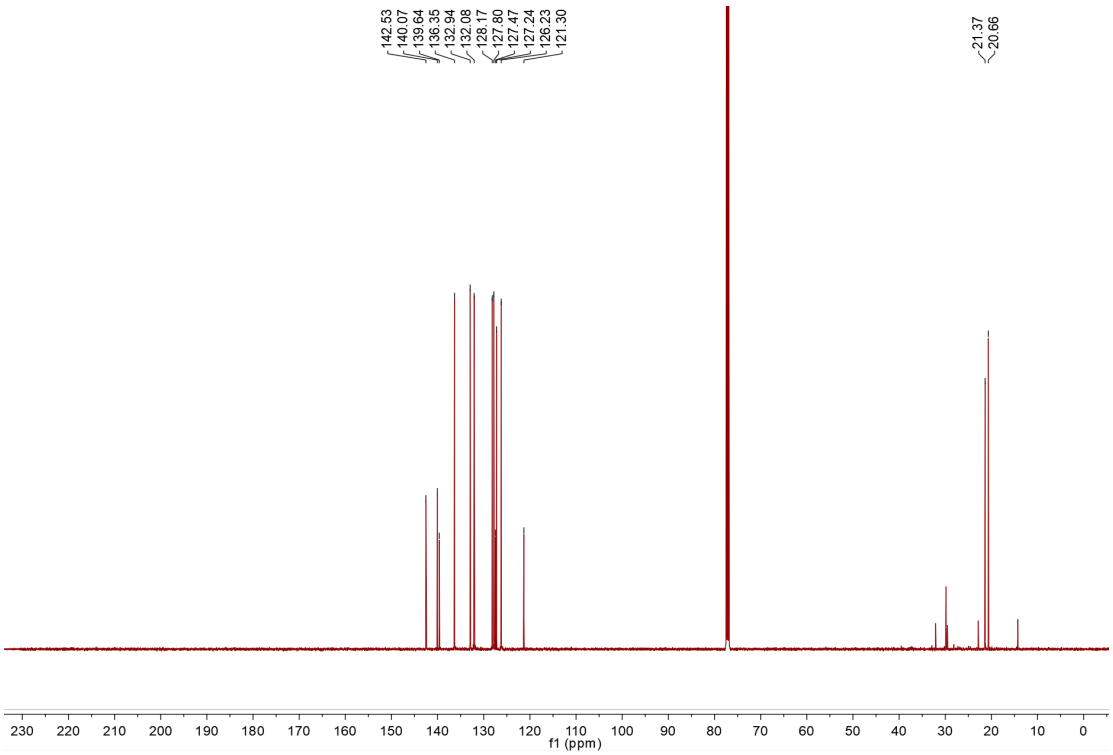

7.24
7.12
7.12
7.03
7.01
2.39
2.32
2.30
0.90
1.00
1.01
3.05
6.05
f1 (ppm)

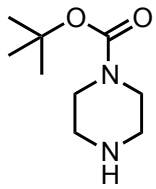

194.39
141.87
140.53
135.90
131.80
127.62
124.16
30.25
21.40
20.76
f1 (ppm)

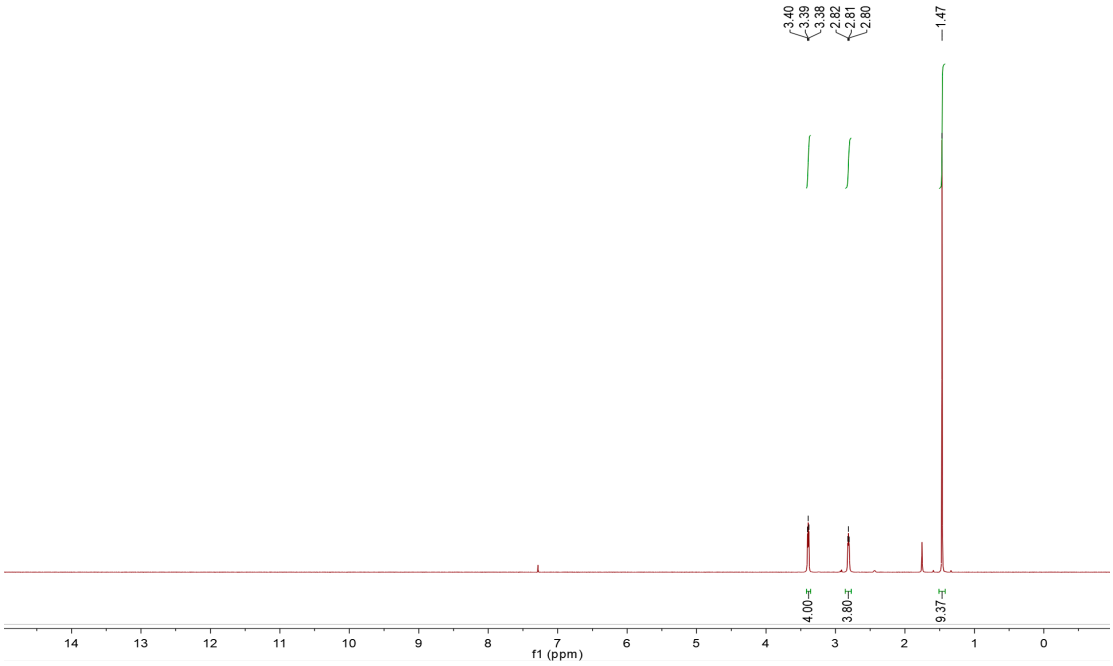

S
Br

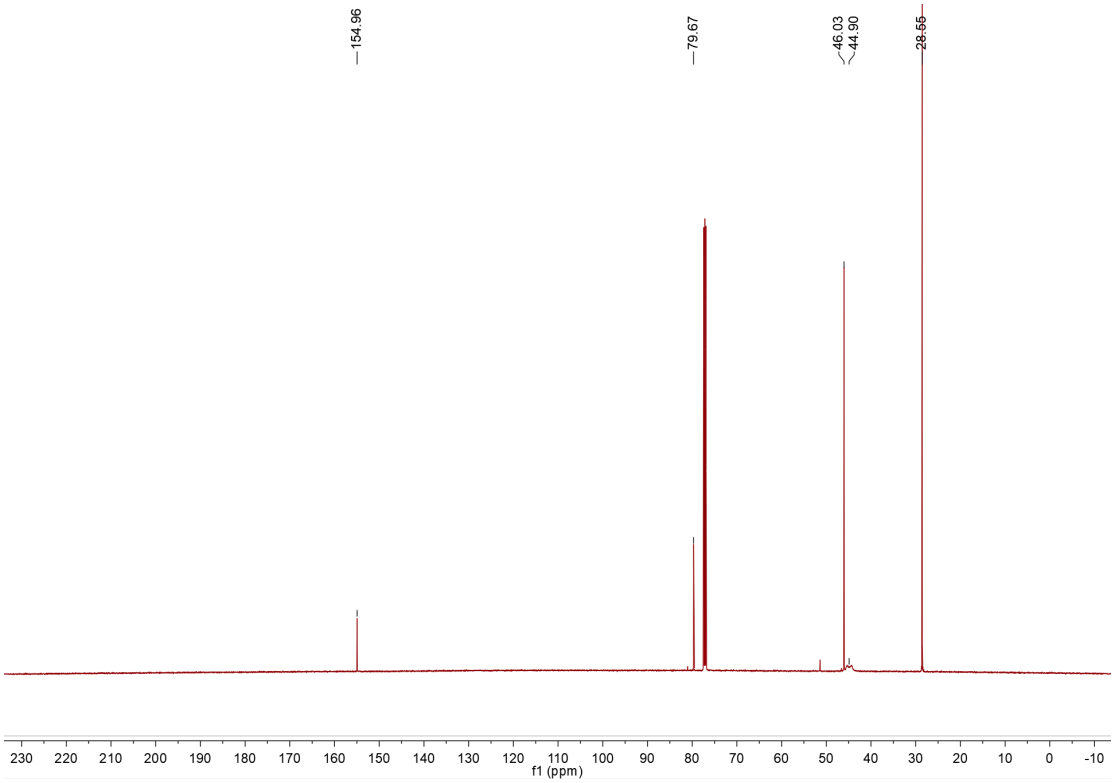
**29**

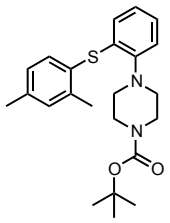

7.54
7.53
7.52
7.52
7.40
7.39
7.17
7.17
7.09
7.09
7.08
7.07
7.07
7.07
7.06
7.06
7.05
7.05
6.97
6.97
6.96
6.96
6.96
6.96
6.94
6.94
6.58
6.58
6.56
6.56
2.37
2.34
1.00
1.01
1.00
2.04
1.01
1.00
3.07
3.04
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)


142.53
140.07
139.64
136.35
132.94
132.08
128.17
127.80
127.47
127.24
126.23
121.30
21.37
20.66
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

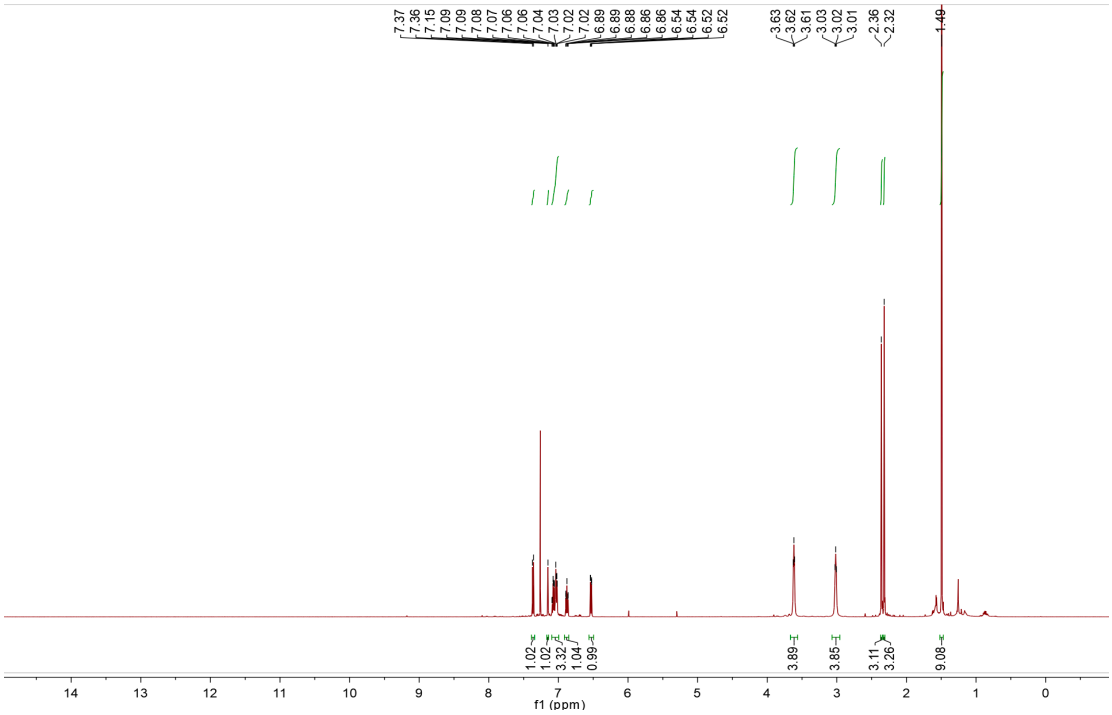


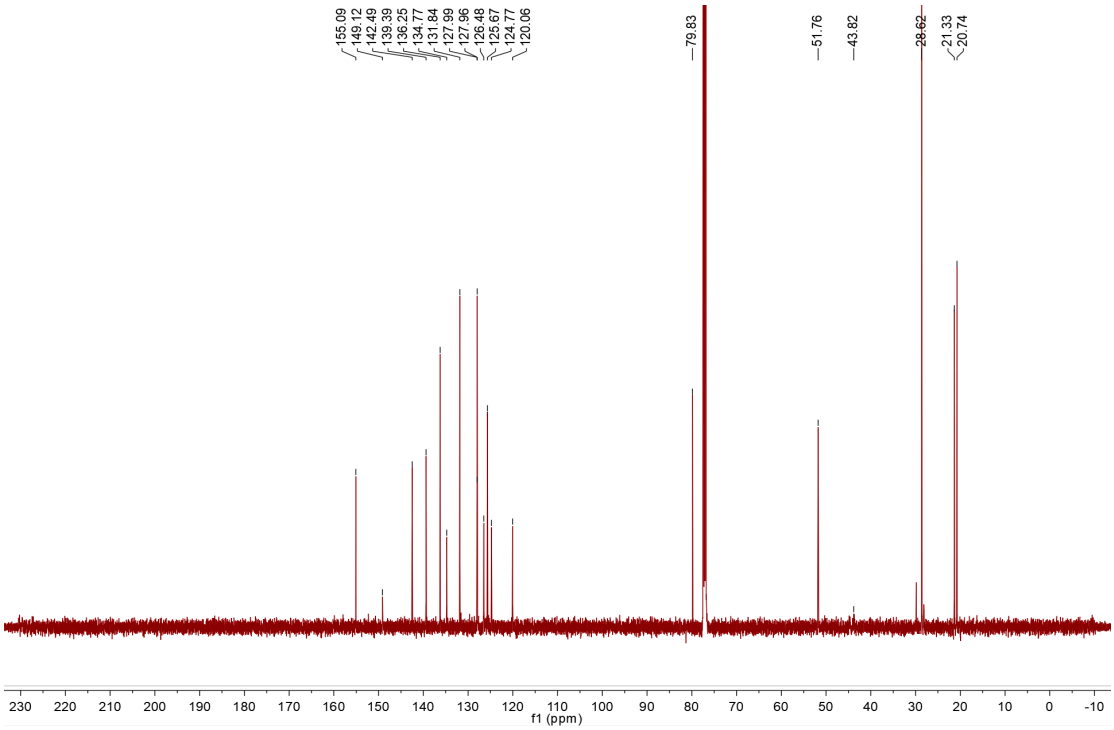

3.40
3.39
3.38
2.82
2.81
2.80
1.47
4.00
3.80
9.37
f1 (ppm)

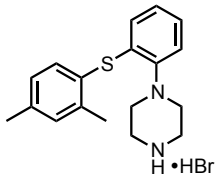

154.96
79.67
46.03
44.90
28.55
f1 (ppm)



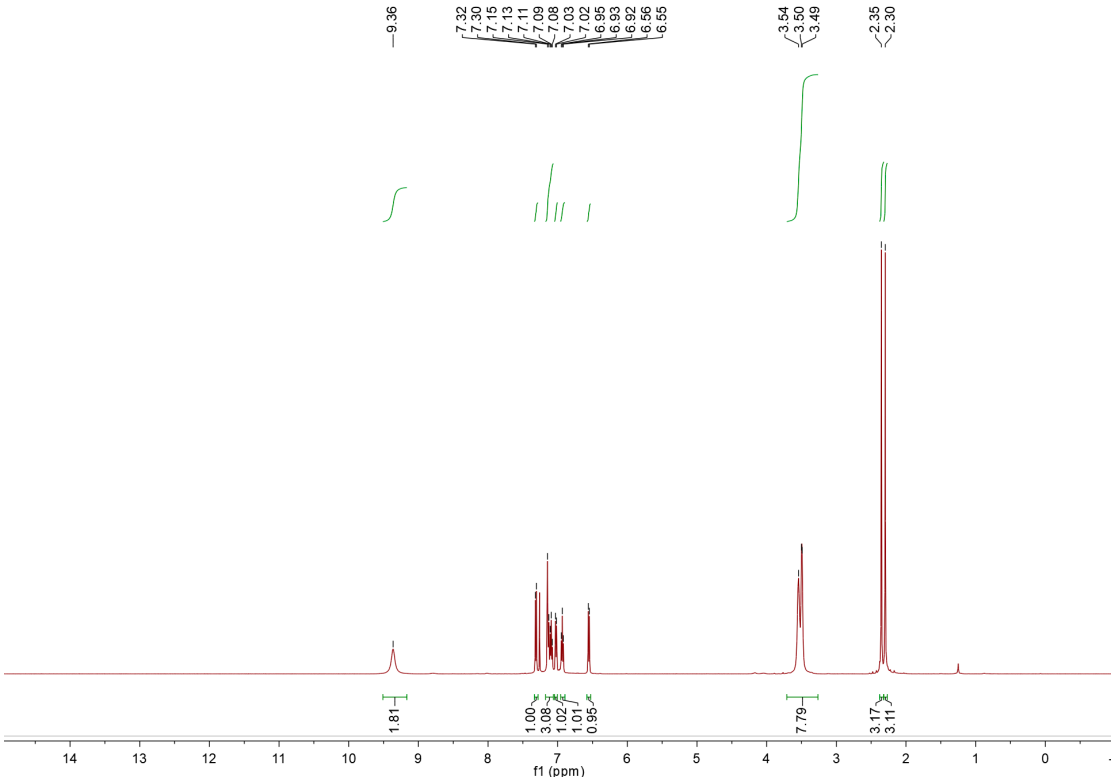
**30**

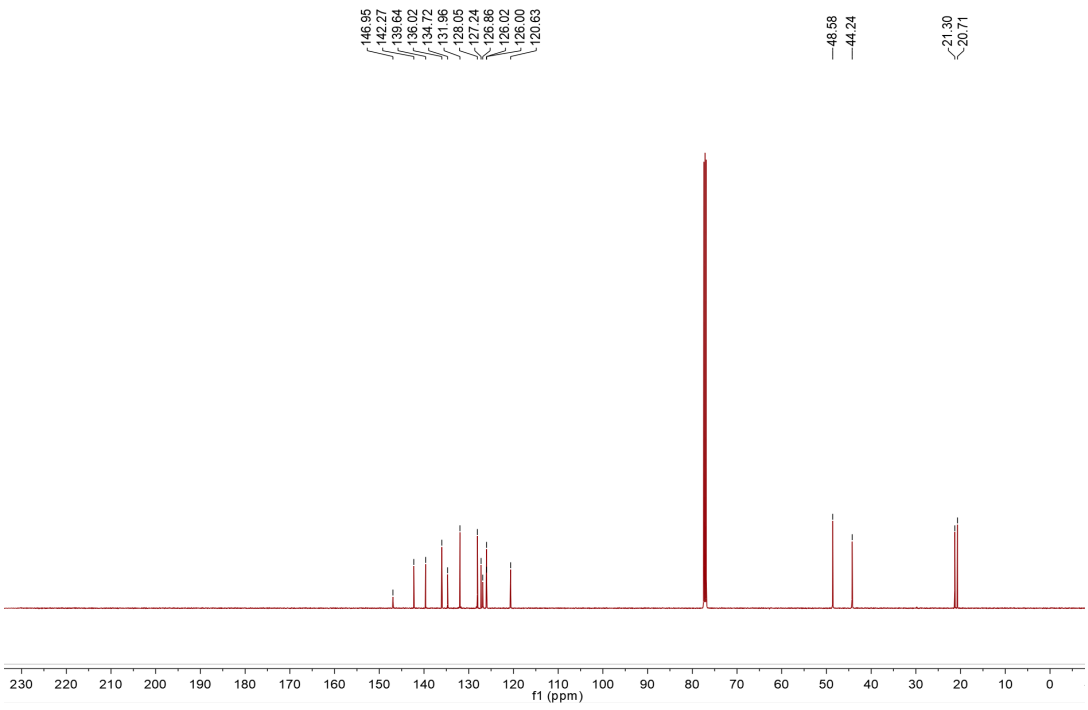

7.37
7.36
7.15
7.09
7.09
7.08
7.07
7.06
7.06
7.04
7.03
7.02
7.02
6.89
6.89
6.88
6.86
6.86
6.54
6.54
6.52
6.52
3.63
3.62
3.61
3.03
3.02
3.01
2.36
2.32
1.49
1.02
1.02
3.32
1.04
0.99
3.89
3.85
3.11
3.26
9.08
f1 (ppm)


155.09
149.12
142.49
139.39
136.25
134.77
131.84
127.99
127.96
126.48
125.67
124.77
120.06
79.83
51.76
43.82
28.62
21.33
20.74
f1 (ppm)


S
N
N
H •HBr

**31**


9.36
7.32
7.30
7.15
7.13
7.11
7.09
7.08
7.03
7.02
6.95
6.93
6.92
6.56
6.55
3.54
3.50
3.49
2.35
2.30
1.81
1.00
3.08
1.02
1.01
0.95
7.79
3.17
3.11
f1 (ppm)


146.95
142.27
139.64
136.02
134.72
131.96
128.05
127.24
126.86
126.02
126.00
120.63
48.58
44.24
21.30
20.71
f1 (ppm)

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