

## Supporting Information

### **From dimethylamine to pyrrolidine: the development of an improved nickel pincer complex for cross-coupling of non-activated secondary alkyl halides**

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## General section

### Chemicals and Reagents

All manipulations were carried out under an inert N<sub>2</sub>(g) atmosphere using standard Schlenk or glovebox techniques. Solvents were purified using a two-column solid-state purification system (Innovative Technology, NJ, USA) and transferred to the glove box without exposure to air. Deuterated solvents were purchased from Cambridge Isotope Laboratories, Inc., and were degassed and stored over activated 3 Å molecular sieves. Unless otherwise noted, all other reagents and starting materials were purchased from commercial sources and used without further purification. Liquid compounds were degassed by standard freeze-pump-thaw procedures prior to use. The following chemicals were prepared according to literature procedure: *Nickamine* (complex **1**),<sup>1</sup> ethyl 4-iodobutyrate<sup>2</sup> (Table 2, Entry 1, Table 4, entry 3), 2-(3-iodopropyl)furan<sup>3</sup> (Table 2, Entries 4 and 12, Table 4, entry 14), 4-iodo-2-phenyltetrahydro-2*H*-pyran<sup>4</sup> (Table 2, Entry 5, Table 4, entry 10), 3-methylcyclohexyl iodide<sup>5</sup> (Table 2, entry 6), 4-methylcyclohexyl iodide<sup>5</sup> (Table 2, entry 7), *tert*-butyl 3-iodopyrrolidine-1-carboxylate<sup>5</sup> (Table 1, Entry 10, Table 4, entry 7), 2-iodoheptane<sup>5</sup> (Table 3, entry 1), 3-iodohexane<sup>5</sup> (Table 3, entry 2; Table 4, entry 8), (3-iodobutyl)benzene<sup>5</sup> (Table 3, entries 3 and 5; Table 4, entries 6 and 12), 1-iodocycloheptane<sup>5</sup> (Table 3, entries 4 and 6), 1-(1-(3-iodopropyl)-1*H*-pyrrol-2-yl)ethan-1-one<sup>6</sup> (Table 4, entry 1), 2-(2-iodoethyl)thiophene<sup>7</sup> (Table 4, entry 2), 9-(3-iodopropyl)-9*H*-carbazole<sup>6</sup> (Table 4, entry 5), ethyl 4-iodocyclohexane-1-carboxylate<sup>5</sup> (Table 4, entry 9), 4-bromo-2-phenyltetrahydro-2*H*-pyran<sup>8</sup> (Table 4, entry 11), 3-iodotetrahydrofuran<sup>5</sup> (Table 4, entry 13).

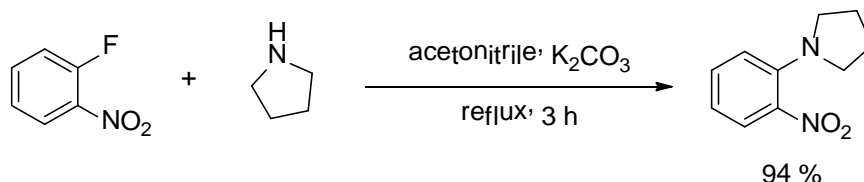
### Physical methods

The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded at 293 K on a Bruker Avance 400 spectrometer. <sup>1</sup>H NMR chemical shifts were referenced to residual solvent as determined relative to Me<sub>4</sub>Si (δ = 0 ppm). The <sup>13</sup>C{<sup>1</sup>H} chemical shifts were reported in ppm relative to the carbon resonance of CDCl<sub>3</sub> (77.0 ppm). GC-MS measurements were conducted on a Perkin-Elmer Clarus 600 GC equipped with Clarus 600T MS. HRESI-MS measurements were conducted at the EPFL ISIC Mass Spectrometry Service with a Micro Mass QTOF Ultima spectrometer. Cyclic voltammetric measurements were recorded in a glove box by a CHI760E electrochemical workstation that was connected to a glassy carbon working electrode (surface area = 0.07 cm<sup>2</sup>), a platinum wire auxiliary electrode, and an Ag/AgNO<sub>3</sub> (0.01M) reference electrode filled with acetonitrile and [*n*-Bu<sub>4</sub>] [PF<sub>6</sub>] (0.1 M). All potentials were referenced to Fc/Fc<sup>+</sup> as internal standard.

## Experimental section

### Synthesis of complex 2

*Synthesis of 1-(2-nitrophenyl)pyrrolidine.*



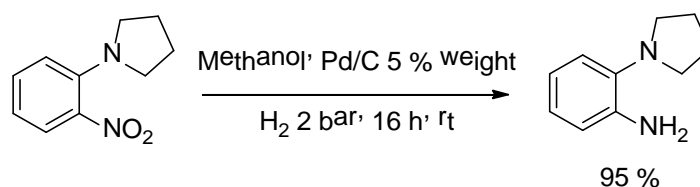
1-Fluoro-2-nitrobenzene (1 equiv, 28.4 mmol, 4 g) was dissolved in 40 mL of acetonitrile and K<sub>2</sub>CO<sub>3</sub> (0.6 equiv, 16 mmol, 2.2 g) was added. Pyrrolidine (28.4 mmol, 2 g) was added under stirring to the resulted mixture. After the addition was finished, the reaction was heated at reflux during 3 h. After cooling to room temperature, 60 mL of water were added to the reaction mixture and the product was extracted with DCM (3 times, 60 mL each) and the organic phase was washed with brine (2 times, 60 mL each) and with distilled water (2 times, 50 mL each). The organic phase was then dried over Na<sub>2</sub>SO<sub>4</sub>, filtered and the solvent was evaporated under vacuum to give the product as an orange oil (5.1 g, Yield: 94%).

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.73 (d, *J* = 8.2 Hz, 1H), 7.35 (m, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 1H), 6.70 (t, *J* = 7.6 Hz, 1H), 3.25 – 3.16 (m, 4H), 2.10 – 1.95 (m, 4H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 142.8, 137.1, 133.0, 126.8, 116.0, 115.5, 50.4, 25.8.

**HRESI-MS:** calculated for (C<sub>10</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>, M+H), 193.0977; found, 193.0979.

*Synthesis of 2-(pyrrolidin-1-yl)aniline.*



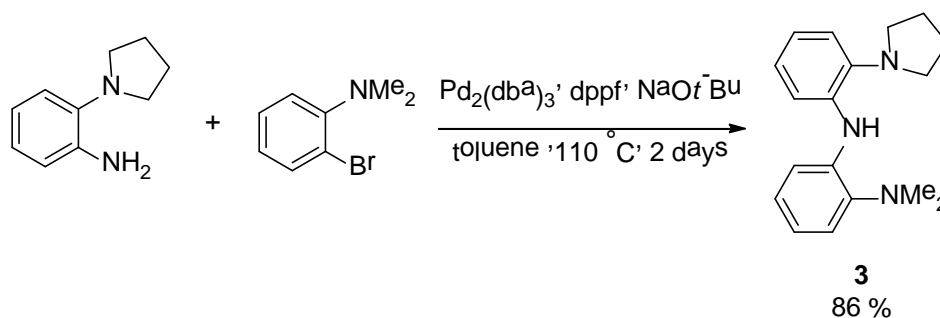
1-(2-Nitrophenyl)pyrrolidine (15.6 mmol, 3 g) was dissolved in 100 mL of methanol and 150 mg of Pd/C (5% of Pd) was added. The reaction flask was degassed and flushed with hydrogen twice and stirred overnight under hydrogen (1.5 bar) at room temperature. The Pd catalyst was filtered off, and the solvent was removed under a reduced pressure. The pure compound was obtained as a dark yellow oil (2.4 g, Yield: 95%).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.07 – 6.97 (m, 1H), 6.97 – 6.84 (m, 1H), 6.77 – 6.72 (m, 2H), 3.86 (br, 2H), 3.10 – 3.00 (m, 4H), 2.01 – 1.85 (m, 4H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 141.4, 137.8, 123.5, 118.8, 118.7, 115.5, 51.0, 24.2.

**HRESI-MS**: calculated for (C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>, M+H), 163.1235; found, 163.1236.

*Synthesis of N<sup>1</sup>,N<sup>1</sup>-dimethyl-N<sup>2</sup>-(2-(pyrrolidin-1-yl)phenyl)benzene-1,2-diamine (3).*



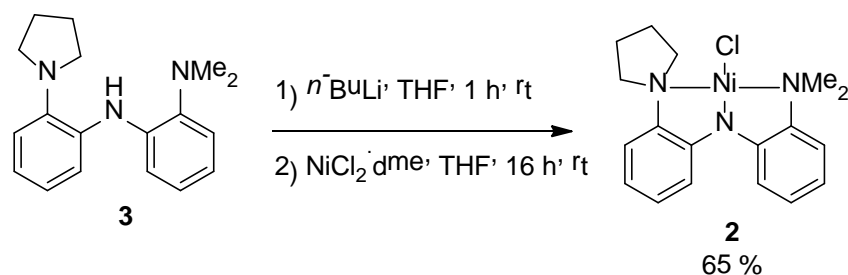
A 250 mL reaction vessel was charged with Pd<sub>2</sub>(dba)<sub>3</sub> (0.02 equiv, 0.25 mmol, 229 mg), bis(diphenylphosphino)-ferrocene (dppf) (0.04 equiv, 0.5 mmol, 278 mg), NaOt-Bu (1.3 equiv, 16.6 mmol, 1.6 g) and toluene (50 mL) under a dinitrogen atmosphere. 2-Bromo-*N,N*-dimethylaniline (12.3 mmol, 2.5 g) and 2-(pyrrolidin-1-yl)aniline (1 equiv, 12.3 mmol, 2 g) were added to the reaction mixture. The resulting brown solution was vigorously stirred for 2 days at 110 °C. The solution was then cooled to room temperature and filtered through Celite. Removal of the solvent yielded a black liquid which was then dissolved in hexane and filtered through celite to afford the pure compound was obtained as a brown oil (3 g, Yield: 86%).

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.55 – 7.47 (m, 1H), 7.34 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.26 (dd, *J* = 7.6, 2 Hz, 1H), 7.19 – 7.05 (m, 4H), 7.01 – 6.91 (m, 2H), 3.29 – 3.23 (m, 4H), 2.85 (s, 6H), 2.06 – 1.99 (m, 4H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 142.5, 141.8, 139.2, 134.8, 124.2, 122.0, 121.4, 120.4, 119.5, 118.8, 117.5, 113.3, 50.8, 44.2, 24.7.

**HRESI-MS**: calculated for (C<sub>18</sub>H<sub>23</sub>N<sub>3</sub>, M+H), 282.1970; found, 282.1970.

### Synthesis of complex **2**.



$n\text{-BuLi}$  (1.1 equiv, 11.07 mmol, 1.6 M in hexane) was slowly added to a THF solution (80 mL) of the ligand **3** (10.06 mmol, 2.83 g) at room temperature. The reaction mixture was stirred for 1 h, and then  $\text{NiCl}_2 \cdot \text{dme}$  (1 equiv, 10.06 mmol, 2.2 g, dme = dimethoxyethane) was added. The resulting solution was stirred overnight and then evaporated in vacuum. The residue was extracted with toluene, and then was concentrated to ca. 5 mL. Addition of pentane (20 mL) afforded a reddish precipitate, which was filtered, washed with additional pentane, and dried in vacuo. (2.4 g, Yield: 65%). Diffusion of pentane into a toluene solution of **2** afforded red crystals suitable for X-ray analysis. The pure compound was obtained as a red solid in a yield of 65 %.

**$^1\text{H}$  NMR** (400 MHz,  $\text{CDCl}_3$ ): 7.38 (d,  $J = 8.3$  Hz, 1H), 7.06 – 6.88 (m, 2H), 6.68 (d,  $J = 8.0$  Hz, 1H), 6.47 (t,  $J = 7.6$  Hz, 1H), 6.39 (t,  $J = 7.6$  Hz, 1H), 4.54 – 4.39 (m, 1H), 3.16 (dd,  $J = 11.7, 5.6$  Hz, 1H), 2.88 (s, 3H), 1.98 – 1.87 (m, 2H).

**$^{13}\text{C}$  NMR** (100 MHz,  $\text{CDCl}_3$ ): 128.2, 127.5, 121.5, 120.3, 116.1, 116.0, 114.3, 113.6, 61.8, 51.4, 24.8.

**Anal. Calcd for  $\text{C}_{18}\text{H}_{22}\text{ClNi}_3\text{N}_3$** : C: 57.94; H: 5.92; N: 11.17 Found: C: 57.74; H: 5.99; N: 11.20.

### Crystallographic details of complex **2**

A total of 53852 reflections ( $-24 \leq h \leq 24$ ,  $-14 \leq k \leq 14$ ,  $-26 \leq l \leq 26$ ) were collected at  $T = 100(2)$  K of which 9750 were unique ( $R_{\text{int}} = 0.0576$ );  $\text{MoK}\alpha$  radiation ( $\lambda = 0.71073$  Å). The structure was solved by the direct methods. All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were placed in calculated idealized positions. The residual peak and hole electron densities were 1.524 and  $-1.275$   $\text{e}\text{Å}^{-3}$ , respectively. The absorption coefficient was  $1.319$   $\text{mm}^{-1}$ . The least squares refinement converged normally with residuals of  $R(F) = 0.0815$ ,  $wR(F_2) = 0.1670$  and a GOF = 1.299 ( $I > 2\sigma(I)$ ).  $\text{C}_{18}\text{H}_{22}\text{ClNi}_3\text{N}_3$ , Mw = 374.55, space group  $\text{P}2_1/c$ , Monoclinic,  $a = 17.067(4)$ ,  $b = 10.4806(18)$ ,  $c = 18.8193(14)$  Å,  $\alpha = 90^\circ$ ,  $\beta = 95.005(11)^\circ$ ,  $\gamma = 90^\circ$ ,  $V = 3353.5(20)$  Å<sup>3</sup>,  $Z = 8$ ,  $\rho_{\text{calcd}} = 1.484$   $\text{Mg}/\text{m}^3$ . CCDC 1424955 contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

### **General Procedure for the Kumada Reactions (Tables 2 - 3)**<sup>9-10</sup>

*Procedure for the alkyl-alkyl Kumada Cross-Coupling (Table 2, Entries 1 – 11; Table 3, Entries 1 - 4).*

A 2 M solution of alkyl-MgCl (commercially available, 1.2 equiv, 0.6 mmol) was diluted to 2 mL with THF. The solution was then slowly added by the syringe pump over 2 h to a solution containing the catalyst (3.5 mol %, 0.018 mmol), 0.6 mL of DMA, 0.4 mL of THF and the halide (0.5 mmol) at -20°C. After the addition, the solution was still stirred for 30 min at -20°C. It was then quenched by the addition of 5 mL water. The organic phase in the resulting solution mixture was extracted with 20 mL of ether, and subjected to GC-MS analysis. 60 µL of decane (0.31 mmol) were used as an internal standard.

*Procedure for the alkyl-aryl Kumada Cross-Coupling (Table 2, Entries 12 – 13; Table 3, Entries 5 – 7).*

A 2 M solution of phenyl-MgBr (commercially available, 1.2 equiv, 0.6 mmol) was diluted to 2 mL with THF. The solution was then slowly added by the syringe pump over 2 h to a solution containing the catalyst (3.5 mol %, 0.018 mmol), 1 mL of THF, TMDEA (25 µL, 0.17 mmol), and the halide (0.5 mmol) at room temperature. After the addition, the solution was still stirred for 30 min. It was then quenched by the addition of 5 mL of water. The organic phase in the resulting solution mixture was extracted with 20 mL of ether, and subjected to GC-MS analysis. 60 µL of decane (0.31 mmol) were used as an internal standard.

## General Procedures for the Suzuki-Miyaura Reactions (Table 4)<sup>11</sup>

### *Procedure for the alkyl-alkyl Suzuki-Miyaura Cross-Coupling (Table 4, Entries 1 - 11).*

To a solution of sodium hydroxide (1.6 equiv, 0.8 mmol, 32 mg), catalyst **1** or **2** (5 mol %, 0.025 mmol), sodium iodide (0.5 equiv, 0.25 mmol, 37 mg), *iso*-propanol (2 equiv, 1 mmol, 77  $\mu$ L) in 1 mL of dry 1,4-dioxane, were added alkyl halide (0.5 mmol) and the 9-octyl-9-borabicyclo[3.3.1]nonane (1.6 equiv, 0.8 mmol, 1.6 mL) under a N<sub>2</sub> atmosphere. The reaction mixture was stirred at room temperature for 24 h. The solution was diluted in Et<sub>2</sub>O (20 mL), filtered on a short pad of silica, washed with ether (3 x 10 mL) and concentrated to dryness under reduced pressure. The residue was purified by column chromatography to give the corresponding coupling product.

### *Procedure for the alkyl-aryl Suzuki-Miyaura Cross-Coupling (Table 4, Entries 12 - 14).*

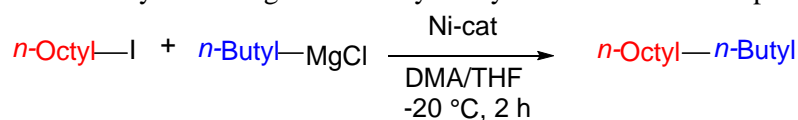
To a solution of sodium hydroxide (1.6 equiv, 0.8 mmol, 32 mg), catalyst **1** or **2** (5 mol %, 0.025 mmol), sodium iodide (0.5 equiv, 0.25 mmol, 37 mg) in 1 mL of dry *tert*-amyl alcohol, were added alkyl halide (0.5 mmol) and the 9-phenyl-9-borabicyclo[3.3.1]nonane (1.6 equiv, 0.8 mmol, 158 mg) under a N<sub>2</sub> atmosphere. The reaction mixture was stirred at room temperature for 24 h. The solution was diluted in ether (20 mL), filtered on a short pad of silica, washed with ether (3 x 10 mL) and concentrated to dryness under reduced pressure. The residue was purified by column chromatography to give the corresponding coupling product.

### Catalyst Loading (Scheme 2, Eq. 1)

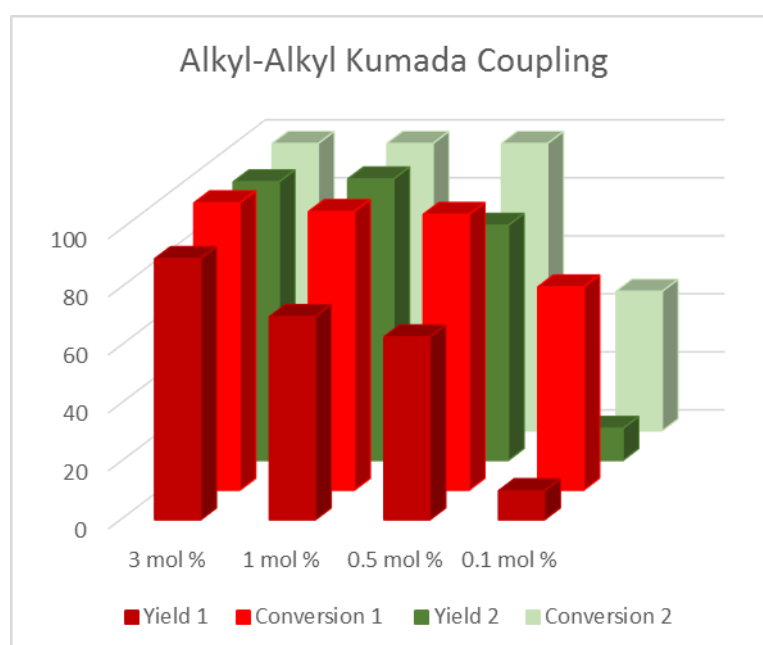
A stock solution was prepared by dissolving 0.02 mmol of complex **1** (7.0 mg) or complex **2** (7.5 mg) in 2 mL of dry THF.

The procedure used for the alkyl-alkyl Kumada cross-coupling was then followed on a 0.2 mmol scale based on *n*-octyl iodide (35  $\mu$ L).

**Table S1:** Study of the Catalyst Loading for the Alkyl-Alkyl Kumada Cross-Coupling



Entry	Cat	Cat loading (mol %)	Volume from the stock solution ( $\mu$ L)	Conversion (%)	Yield (%)
1	<b>2</b>	3	600	99	96
2	<b>2</b>	1	200	99	97
3	<b>2</b>	0.5	100	99	81
4	<b>2</b>	0.1	20	48	11
5	<b>1</b>	3	600	99	90
6	<b>1</b>	1	200	96	70
7	<b>1</b>	0.5	100	95	63
8	<b>1</b>	0.1	20	70	10

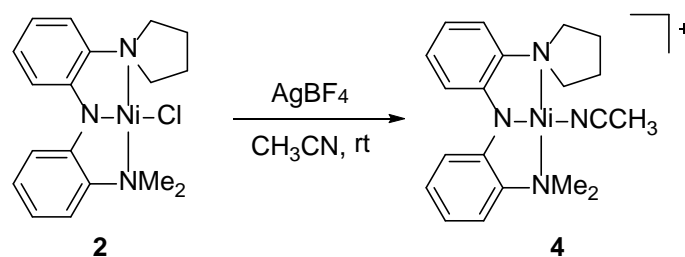


**Figure S1:** Effect of the Catalyst Loading on the Conversion and Yield for the Alkyl-Alkyl Kumada Cross-Coupling



## Determination of the redox properties of the new complex

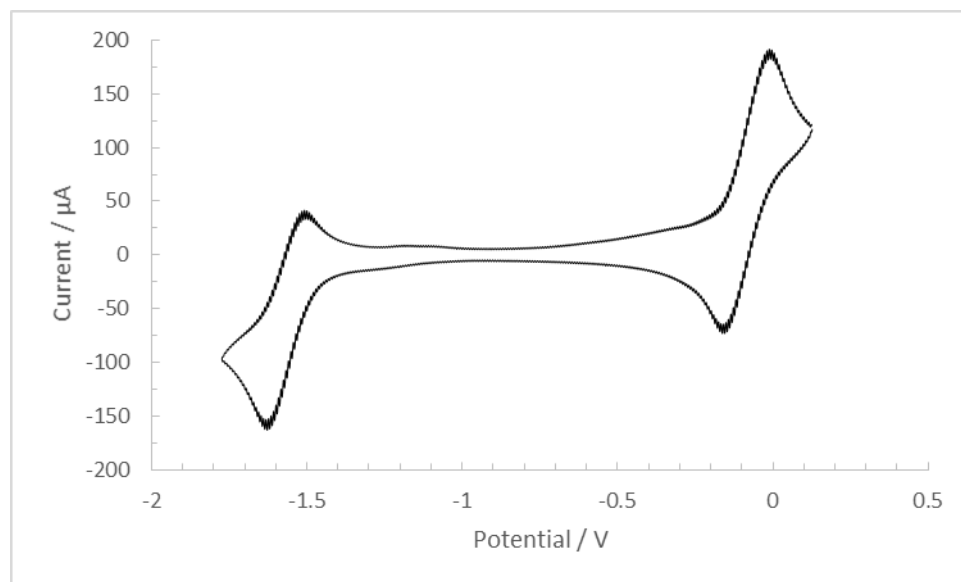
Synthesis of the complex  $[(^{Pyr}N^{Me}NNNi(CH_3CN)]BF_4$



A solution of  $AgBF_4$  (1 equiv, 0.2 mmol, 39 mg) in  $CH_3CN$  (1 mL) was added to a solution of **2** (0.2 mmol, 75 mg) in  $CH_3CN$  (1.5 mL). The resulting green solution was stirred for 30 min and then the white precipitate of  $AgCl$  was isolated by filtration. The filtrate was evaporated and the green solid was washed with toluene (1 mL) and pentane (2 mL), and dried under vacuum (81 mg, 87%).

$^1H$  NMR (400 MHz,  $CD_3CN$ ): 7.47 – 7.24 (m, 3H), 7.17 – 6.98 (m, 3H), 6.41 (t,  $J = 7.5$  Hz, 1H), 6.31 (t,  $J = 7.5$  Hz, 1H), 5.70 – 5.27 (m, 2H), 4.51 – 4.29 (m, 2H), 4.05 (s, 6H), 2.12 – 1.99 (m, 4H), 1.96 (s, 3H).  $^1H$  NMR (400 MHz,  $CDCl_3$ ): 7.34 (d,  $J = 6.2$  Hz, 2H), 7.00 (m, 3H), 6.80 – 6.67 (m, 1H), 6.52 (d,  $J = 30.9$  Hz, 2H), 4.14 (br, 2H), 3.33 (br, 2H), 2.95 (s, 6H), 2.35 (s, 1H), 2.05 (br, 4H).

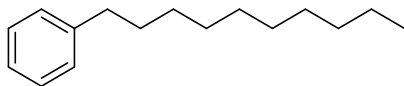
$^{13}C$  NMR (100 MHz,  $CD_3CN$ ): 147.8, 144.9, 128.9, 128.2, 122.3, 121.1, 120.0, 119.9, 118.3, 60.7, 48.8, 27.7.  $^{13}C$  NMR (100 MHz,  $CDCl_3$ ): 148.4, 147.5, 147.1, 145.2, 129.0, 128.3, 121.3, 120.3, 117.4, 117.2, 114.6, 114.1, 62.0, 51.3, 24.8.



**Figure S2:** Cyclic voltammogram of complex **4** (4 mM) recorded in  $CH_3CN$  solution at scan rate of  $400\text{ mV}\cdot\text{s}^{-1}$ ; the potential is referenced to the ferrocene/ferrocenium couple.

## Detailed description for coupling products

Test reaction alkyl-aryl Kumada cross-coupling (Scheme 2, Equation 2):



Purified by column (SiO<sub>2</sub>, Hexane), 80% yield as a transparent oil.

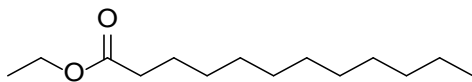
<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.36 – 7.30 (m, 2H), 7.26 – 7.17 (m, 3H), 2.66 (t, *J* = 8 Hz, 2H), 1.71 – 1.62 (m, 2H), 1.42 – 1.22 (m, 14H), 0.94 (t, *J* = 6.8 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 143.1, 128.5, 128.4, 125.7, 36.2, 32.1, 31.7, 29.8, 29.8, 29.7, 29.5, 22.9, 14.3.

**HRAPCI-MS:** calculated for (C<sub>16</sub>H<sub>26</sub>), 218.2035; found, 218.2030.

Coupling products (Tables 2, 3 and 4).

Table 2, entry 1; Table 4, entry 3:



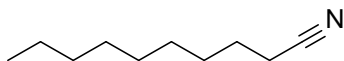
Purified by column (SiO<sub>2</sub>, 9:1 Hexane:Ethyl acetate), 70% yield as a transparent oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 4.11 (q, *J* = 7.1 Hz, 2H), 2.27 (t, *J* = 7.6 Hz, 2H), 1.69 – 1.51 (m, 2H), 1.39 – 1.11 (m, 19H), 0.87 (t, *J* = 6.8 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 174.1, 60.3, 34.5, 32.1, 29.7, 29.6, 29.5, 29.4, 29.3, 25.1, 22.8, 14.4, 14.3.

**HRESI-MS:** calculated for (C<sub>14</sub>H<sub>28</sub>O<sub>2</sub>, M+H), 229.2168; found, 229.2171.

Table 2, entry 2:



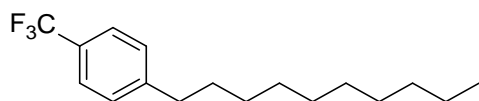
Purified by column (SiO<sub>2</sub>, 9:1 Hexane:Ethyl acetate), 60% yield as a yellowish oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 2.33 (t, *J* = 7.1 Hz, 2H), 1.65 (q, *J* = 7.6 Hz, 2H), 1.47 – 1.37 (m, 2H), 1.35 – 1.17 (m, 10), 0.87 (t, *J* = 6.8 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 120.0, 31.9, 29.4, 29.3, 28.9, 28.8, 25.5, 22.7, 17.2, 14.2.

**HRESI-MS:** calculated for (C<sub>10</sub>H<sub>19</sub>N, M+H), 154.1596; found, 154.1592.

Table 2, entry 3:



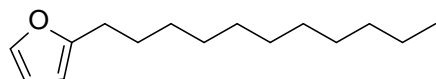
Purified by column (SiO<sub>2</sub>, Hexane), 63% yield as a yellowish oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.52 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 2.65 (t, *J* = 8.0 Hz, 2H), 1.67 – 1.57 (m, 2H), 1.37 – 1.14 (m, 14H), 0.88 (t, *J* = 6.8 Hz, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 147.0, 128.7, 128.6, 125.2, 125.1, 35.8, 31.9, 31.2, 29.6, 29.6, 29.5, 29.3, 29.2, 22.7, 14.1.

**HRESI-MS:** calculated for (C<sub>17</sub>H<sub>25</sub>F<sub>3</sub>, M-F), 267.1924; found, 267.1922.

Table 2, entry 4:



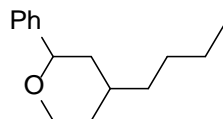
Purified by column (SiO<sub>2</sub>, 9:1 Hexane:Ethyl acetate), 79% yield as a transparent oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.32 – 7.28 (m, 1H), 6.30 – 6.26 (m, 1H), 5.99 – 5.96 (m, 1H), 2.62 (t, *J* = 7.6 Hz, 2H), 1.70 – 1.60 (m, 2H), 1.37 – 1.17 (m, 16), 0.89 (t, *J* = 6.8 Hz, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 156.8, 140.8, 110.2, 104.6, 32.1, 29.8, 29.8, 29.7, 29.5, 29.5, 29.4, 28.2, 28.1, 22.9, 14.3.

**HRESI-MS:** calculated for (C<sub>15</sub>H<sub>26</sub>O, M+H), 223.2062; found, 223.2063.

Table 2, entry 5:



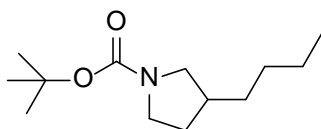
Purified by column (SiO<sub>2</sub>, 9:1 Hexane:Ethyl acetate), 80% yield as a transparent oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.41 – 7.23 (m, 5H), 4.34 (dd, *J* = 11.3, 2.0 Hz, 1H), 4.19 (dd, *J* = 11.2, 3.9 Hz, 1H), 3.68 – 3.56 (m, 1H), 1.97 – 1.85 (m, 1H), 1.76 – 1.58 (m, 2H), 1.45 – 1.18 (m, 8H), 0.96 – 0.86 (m, 3).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 143.4, 128.4, 127.4, 126.0, 80.1, 68.7, 41.1, 36.8, 35.8, 32.9, 28.7, 23.0, 14.3.

**HRAPCI-MS:** calculated for (C<sub>15</sub>H<sub>22</sub>O), 218.1621; found, 218.1618.

Table 2, entry 10:



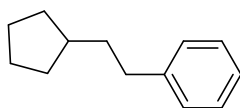
Purified by column (SiO<sub>2</sub>, Hexane), 70% yield as a transparent oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 3.60 – 3.32 (m, 2H), 3.31 – 3.06 (m, 1H), 2.92 – 2.62 (m, 1H), 2.18 – 1.83 (m, 2H), 1.54 – 1.10 (m, 16H), 0.92 – 0.82 (m, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 154.8, 79.0, 51.9, 51.4, 45.9, 45.6, 39.3, 38.4, 33.1, 32.1, 31.3, 30.6, 28.7, 22.9, 14.2.

**HRESI-MS:** calculated for (C<sub>13</sub>H<sub>25</sub>NO<sub>2</sub>, M+Na), 250.1783; found, 250.1782.

Table 2, entry 11:



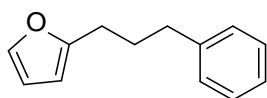
Purified by column (SiO<sub>2</sub>, Hexane), 72% yield as a transparent oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.43 – 7.11 (m, 5H), 2.65 (dd, *J* = 15.8, 7.7 Hz, 2H), 1.90 – 1.72 (m, 3H), 1.75 – 1.47 (m, 6H), 1.25 – 1.07 (m, 2H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 143.2, 128.5, 128.4, 125.7, 39.8, 38.3, 35.3, 32.8, 25.4.

**HRAPCI-MS:** calculated for (C<sub>13</sub>H<sub>18</sub>), 174.1409; found, 174.1403.

Table 2, entry 12; Table 4, entry 13:



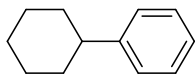
Purified by column (SiO<sub>2</sub>, 9:1 Hexane:Ethyl acetate), 80% yield as a transparent oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.37 – 7.30 (m, 2H), 7.27 – 7.19 (m, 3H), 6.35 – 6.31 (m, 1H), 6.07 – 6.02 (m, 1H), 2.76 – 2.67 (m, 4H), 2.03 (q, *J* = 7.6 Hz, 2H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 156.1, 142.1, 140.9, 128.6, 128.5, 126.0, 110.2, 105.0, 35.4, 29.8, 27.6.

**HRESI-MS:** calculated for (C<sub>13</sub>H<sub>15</sub>, M+H), 187.1123; found, 187.1120.

Table 2, entry 13:



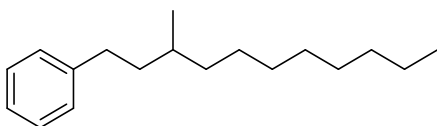
Purified by column (SiO<sub>2</sub>, Hexane), 70% yield as a transparent oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.39 – 7.32 (m, 2H), 7.31 – 7.16 (m, 3H), 2.60 – 2.52 (m, 1H), 2.03 – 1.72 (m, 6H), 1.58 – 1.21 (m, 6H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 148.2, 128.4, 127.0, 125.9, 44.7, 34.6, 27.1, 26.3.

HRAPCI-MS: calculated for (C<sub>12</sub>H<sub>16</sub>), 160.1252; found, 160.1244.

Table 3, entry 3; Table 4, entry 6:



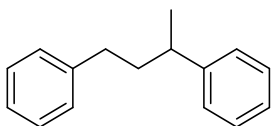
Purified by column (SiO<sub>2</sub>, Hexane), 70% yield as a transparent oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.35 – 7.27 (m, 2H), 7.26 – 7.18 (m, 3H), 2.75 – 2.55 (m, 2H), 1.74 – 1.61 (m, 1H), 1.55 – 1.43 (m, 2H), 1.43 – 1.14 (m, 14H), 0.97 (d, *J* = 6.3 Hz, 3H), 0.94 (t, *J* = 6.8 Hz, 3H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): 143.3, 128.4, 128.3, 125.5, 39.0, 37.0, 33.5, 32.5, 32.0, 30.1, 29.7, 29.4, 27.0, 22.7, 19.7, 14.2.

HRAPPI-MS: calculated for (C<sub>18</sub>H<sub>30</sub>), 246.2342; found, 246.2342.

Table 3, entry 5; Table 4, entry 12:



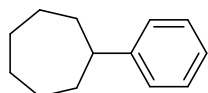
Purified by column (SiO<sub>2</sub>, Hexane), 60% yield as a transparent oil.

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): 7.42 – 7.15 (m, 10H), 2.85 – 2.73 (m, 1H), 2.64 – 2.51 (m, 2H), 2.06 – 1.90 (m, 2H), 1.35 (d, *J* = 6.9 Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 147.3, 142.6, 128.5, 128.4, 128.3, 127.1, 126.0, 125.7, 40.1, 39.6, 34.0, 22.6.

**HRAPCI-MS:** calculated for ( $\text{C}_{16}\text{H}_{18}$ ), 210.1409; found, 210.1402.

Table 3, entry 6:



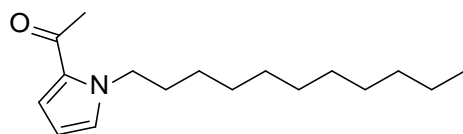
Purified by column ( $\text{SiO}_2$ , Hexane), 50% yield as a transparent oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 7.43 – 7.06 (m, 1H), 2.75 – 2.65 (m, 1H), 2.07 – 1.50 (m, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 150.2, 128.4, 126.8, 125.6, 47.2, 37.0, 28.1, 27.4.

**HRAPCI-MS:** calculated for ( $\text{C}_{13}\text{H}_{28}$ ), 174.1409; found, 174.1402.

Table 4, entry 1:



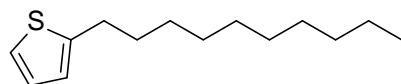
Purified by column ( $\text{SiO}_2$ , 9:1 Hexane:Ethyl acetate), 82% yield as a yellow oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 7.03 – 6.91 (m, 1H), 6.84 (s, 1H), 6.18 – 6.00 (m, 1H), 4.29 (t,  $J = 7.3$  Hz, 2H), 2.43 (s, 3H), 1.80 – 1.63 (m, 2H), 1.26 (m, 16H), 0.88 (t,  $J = 6.7$  Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 188.3, 130.2, 120.3, 107.9, 50.0, 32.0, 31.6, 29.7, 29.6, 29.4, 27.4, 26.8, 22.8, 14.2.

**HRESI-MS:** calculated for ( $\text{C}_{17}\text{H}_{30}\text{NO}$ ), 264.2327; found, 264.2332.

Table 4, entry 2:



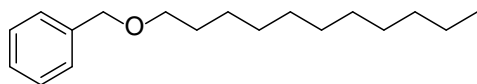
Purified by column ( $\text{SiO}_2$ , 95:5 Hexane:Ethyl acetate), 70% yield as a transparent oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 7.18 – 7.06 (m, 1H), 7.01 – 6.87 (m, 1H), 6.80 (s, 1H), 2.92 – 2.75 (m, 2H), 1.79 – 1.61 (m, 2H), 1.30 (m, 14H), 0.92 (t,  $J = 6.3$  Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 146.0, 126.7, 124.0, 122.8, 32.1, 32.0, 30.1, 39.8, 29.7, 29.6, 29.5, 29.3, 22.9, 14.3.

**HRESI-MS:** calculated for (C<sub>14</sub>H<sub>25</sub>S), 225.1677; found, 225.1676.

Table 4, entry 4:



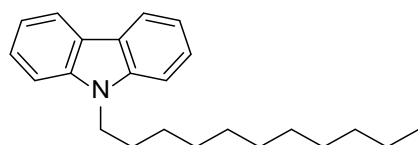
Purified by column (SiO<sub>2</sub>, Hexane), 83% yield as a pinkish oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 7.31 (d, *J* = 21.6 Hz, 5H), 4.51 (s, 2H), 3.47 (t, *J* = 6.5 Hz, 2H), 1.63 (d, *J* = 6.5 Hz, 2H), 1.27 (m, 16H), 0.89 (t, *J* = 6.1 Hz, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 138.9, 128.5, 127.7, 127.6, 73.0, 70.7, 42.1, 32.1, 29.9, 29.8, 29.6, 29.5, 26.4, 25.8, 22.8, 14.3.

**HRESI-MS:** calculated for (C<sub>18</sub>H<sub>30</sub>OAg), 369.1348; found, 369.1346.

Table 4, entry 5:



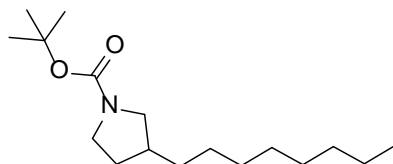
Purified by column (SiO<sub>2</sub>, Hexane), 91% yield as a transparent oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 8.16 (d, *J* = 7.7 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 8.1 Hz, 2H), 7.29 (t, *J* = 7.4 Hz, 2H), 4.42 – 4.17 (m, 2H), 1.91 (p, *J* = 7.1 Hz, 2H), 1.47 – 1.22 (m, 16H), 0.95 (t, *J* = 6.8 Hz, 3H).

**<sup>13</sup>C NMR** (100 MHz, CDCl<sub>3</sub>): 140.6, 125.7, 122.9, 120.5, 118.8, 108.8, 43.2, 32.0, 29.8, 29.7, 29.7, 29.6, 29.5, 29.1, 27.5, 22.8, 14.3.

**HRESI-MS:** calculated for (C<sub>23</sub>H<sub>32</sub>N), 322.2535; found, 322.2536.

Table 4, entry 7:



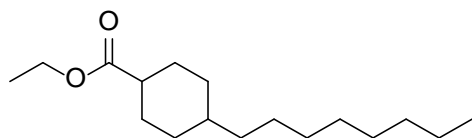
Purified by column (SiO<sub>2</sub>, 8:2 Hexane:Ethyl acetate), 68% yield as a yellow oil.

**<sup>1</sup>H NMR** (400 MHz, CDCl<sub>3</sub>): 3.60 – 3.31 (m, 2H), 3.22 (d, *J* = 10.0 Hz, 1H), 2.87 – 2.74 (m, 1H), 2.04 (d, *J* = 18.1 Hz, 1H), 1.93 (d, *J* = 6.0 Hz, 1H), 1.85 (s, 1H), 1.44 (s, 9H), 1.25 (m, 14H), 0.86 (t, *J* = 6.5 Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 154.7, 78.9, 60.5, 51.8, 45.9, 39.3, 33.4, 32.0, 29.8, 29.6, 29.4, 28.7, 28.3, 22.8, 14.2.

**HRESI-MS:** calculated for ( $\text{C}_{17}\text{H}_{33}\text{NO}_2\text{Na}$ ), 306.2409; found, 306.2408.

Table 4, entry 9:



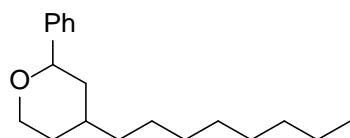
Purified by column ( $\text{SiO}_2$ , 9:1 Hexane:Ethyl acetate), 86% yield as a yellow oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 4.09 (q,  $J = 6.9$  Hz, 2H), 2.24 – 2.11 (m, 1H), 1.94 (d,  $J = 11.9$  Hz, 2H), 1.79 (d,  $J = 12.6$  Hz, 2H), 1.51 (td,  $J = 10.0, 9.6, 5.7$  Hz, 2H), 1.39 (dd,  $J = 12.9, 2.9$  Hz, 3H), 1.23 (m, 17H), 0.87 (d,  $J = 6.3$  Hz, 3H).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 176.4, 60.2, 43.8, 37.4, 37.1, 32.5, 32.1, 30.1, 29.8, 29.6, 29.5, 29.2, 27.0, 22.8, 14.2.

**HRESI-MS:** calculated for ( $\text{C}_{17}\text{H}_{33}\text{O}_2$ ), 269.2480; found, 269.2477.

Table 4, entries 10 and 11:



Purified by column ( $\text{SiO}_2$ , 9:1 Hexane:Ethyl acetate), 80% yield as a yellow oil.

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ): 7.41 – 7.33 (m, 5H), 7.32 – 7.24 (m, 1H), 4.37 – 4.31 (m, 1H), 4.19 (dd,  $J = 11.4, 4.3$  Hz, 1H), 3.68 – 3.58 (m, 1H), 1.91 (d,  $J = 11.9$  Hz, 1H), 1.68 (d,  $J = 11.8$  Hz, 2H), 1.40 – 1.24 (m, 16H), 0.92 (t,  $J = 6.6$  Hz, 3H).

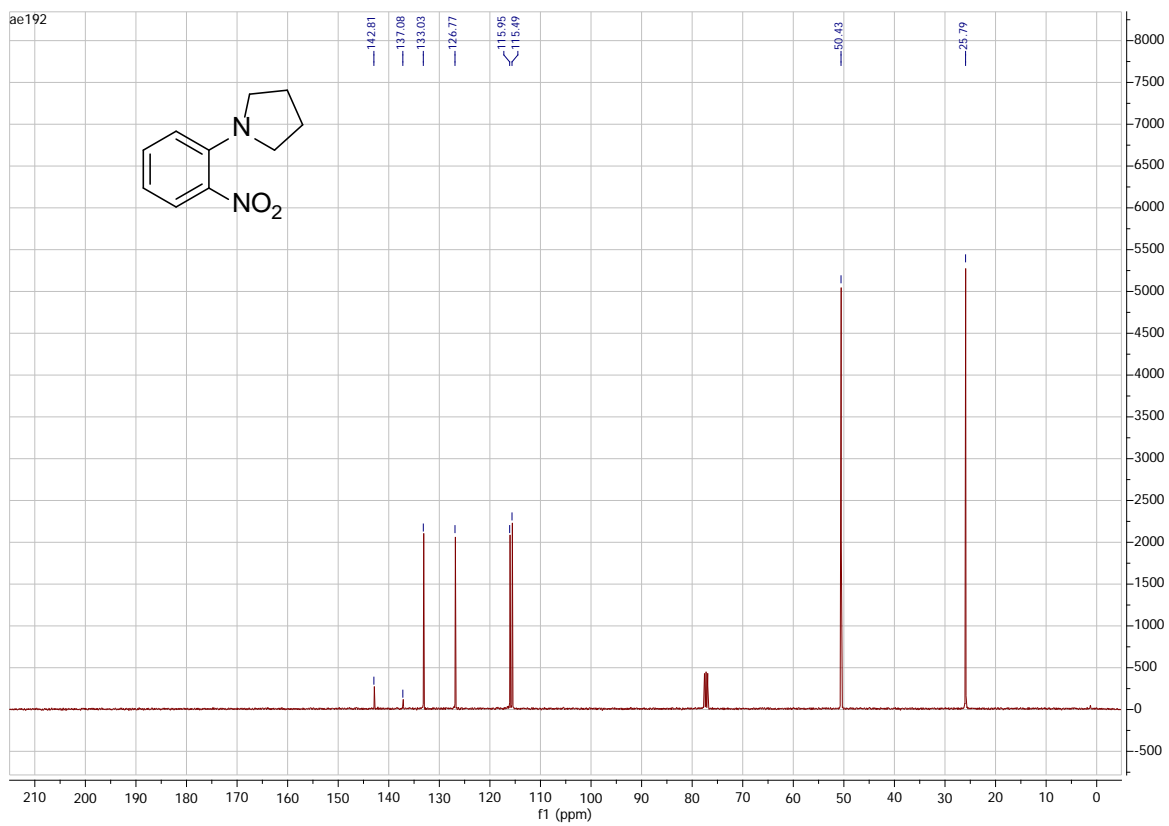
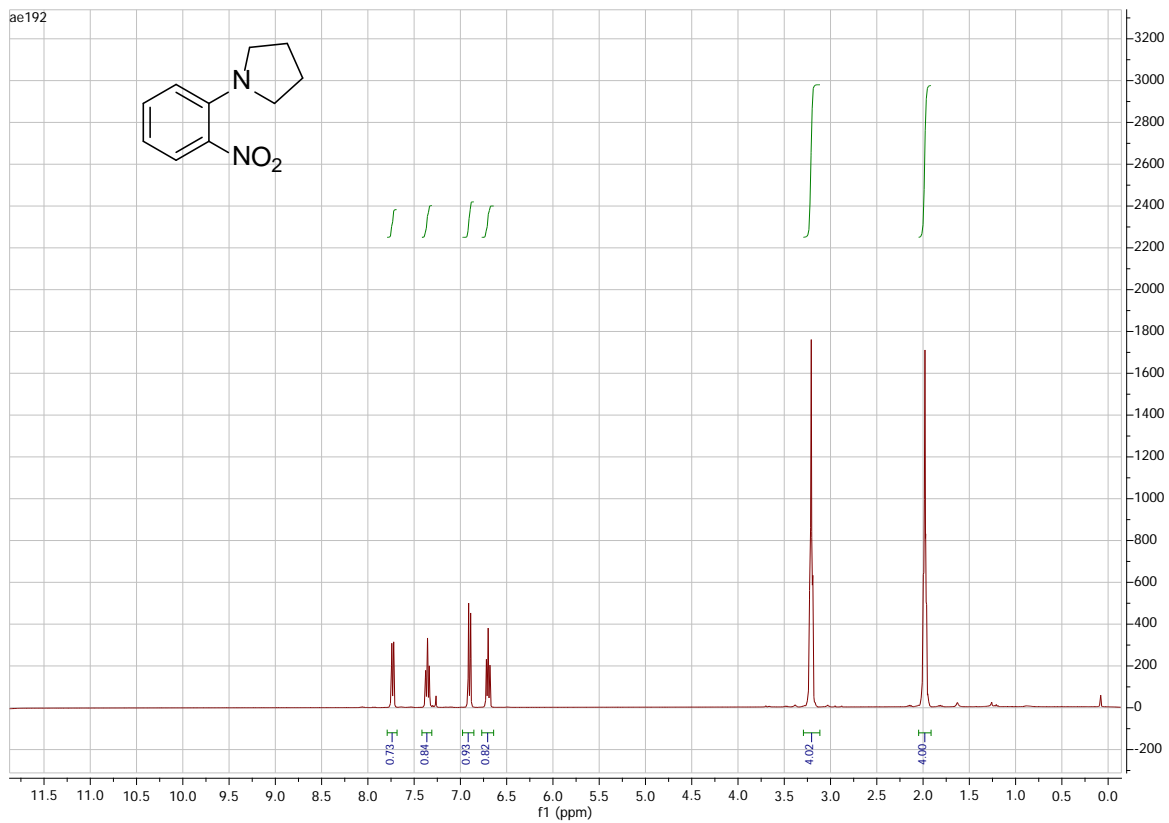
$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ): 143.45, 128.42, 127.41, 125.98, 80.08, 68.73, 41.15, 37.18, 35.88, 32.87, 32.04, 29.97, 29.76, 29.45, 26.50, 22.82, 14.25.

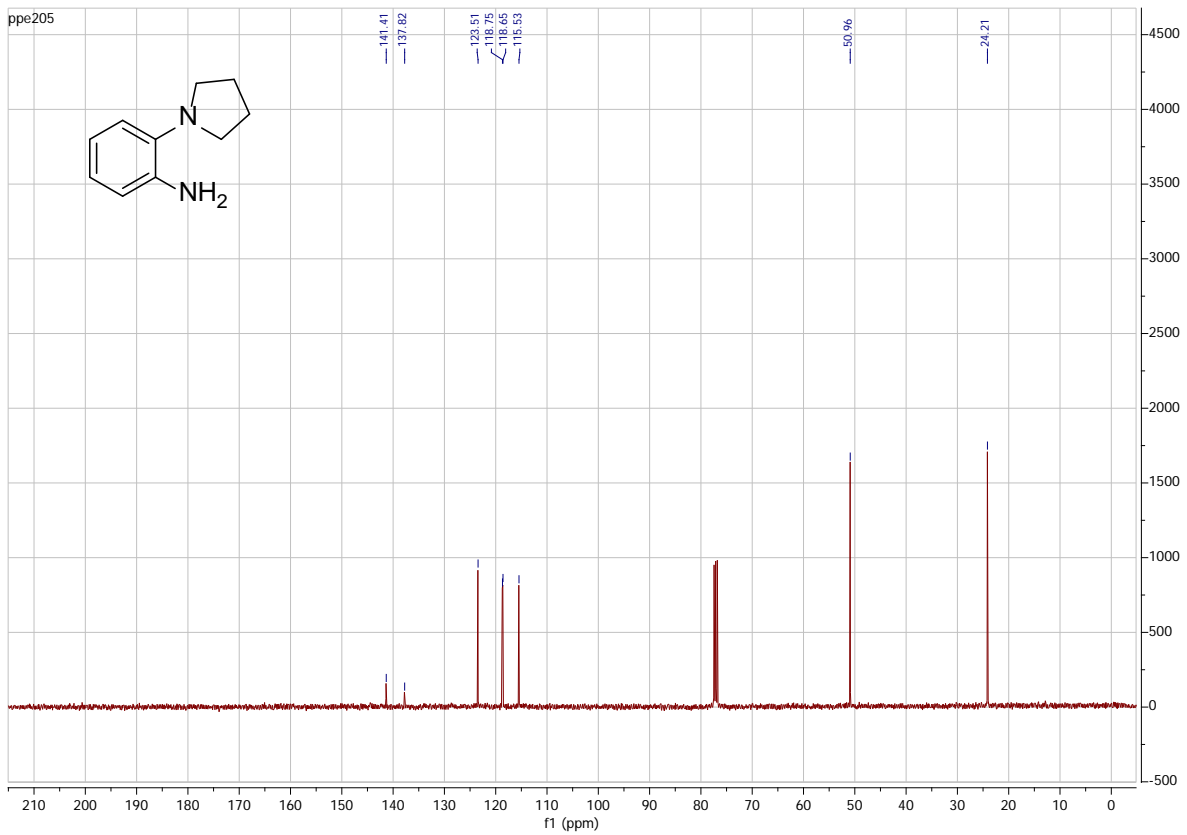
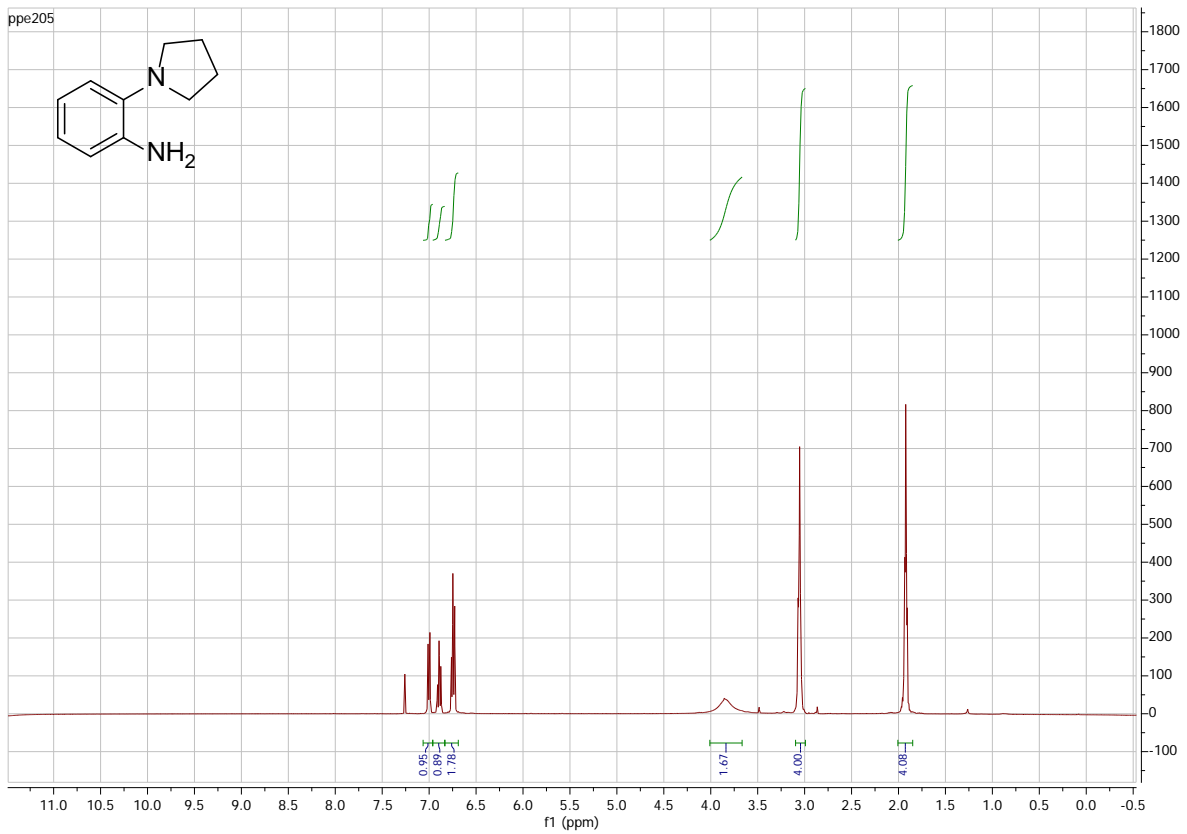
**HRESI-MS:** calculated for ( $\text{C}_{19}\text{H}_{30}\text{ONa}$ ), 297.2194; found, 297.2194.

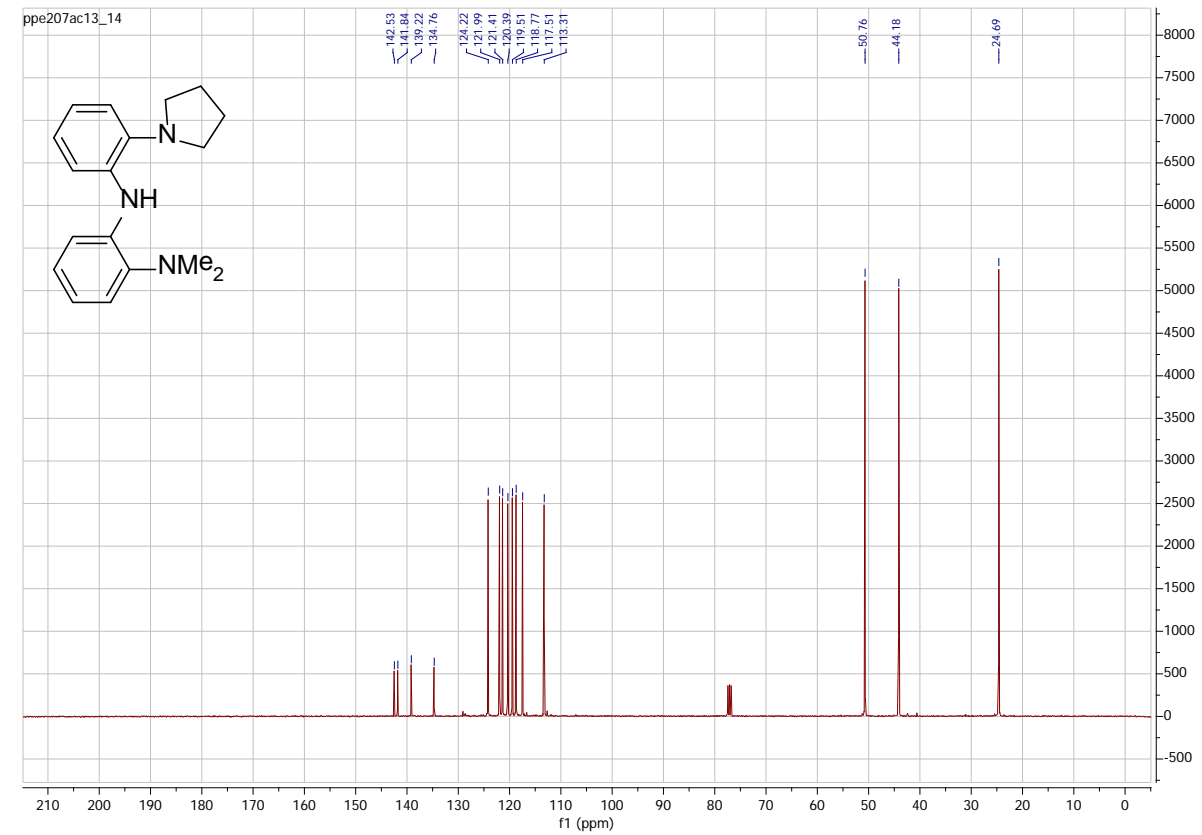
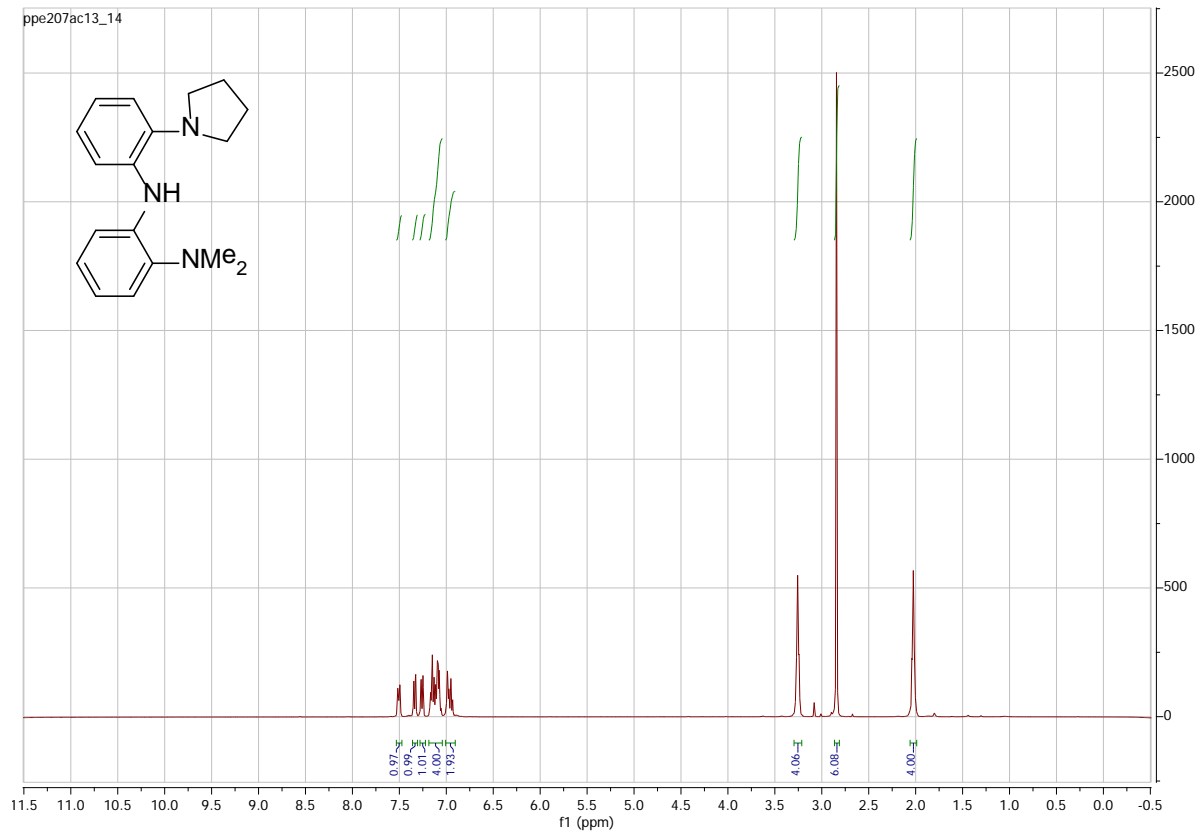


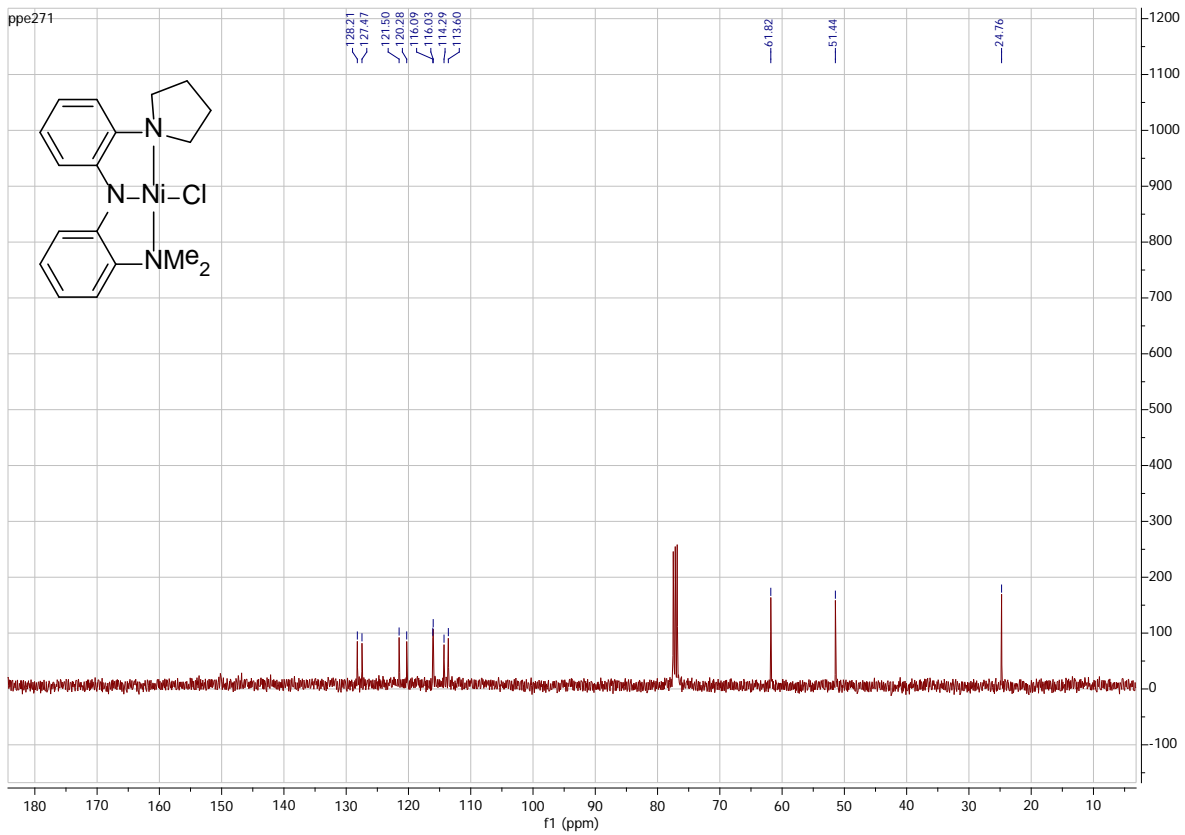
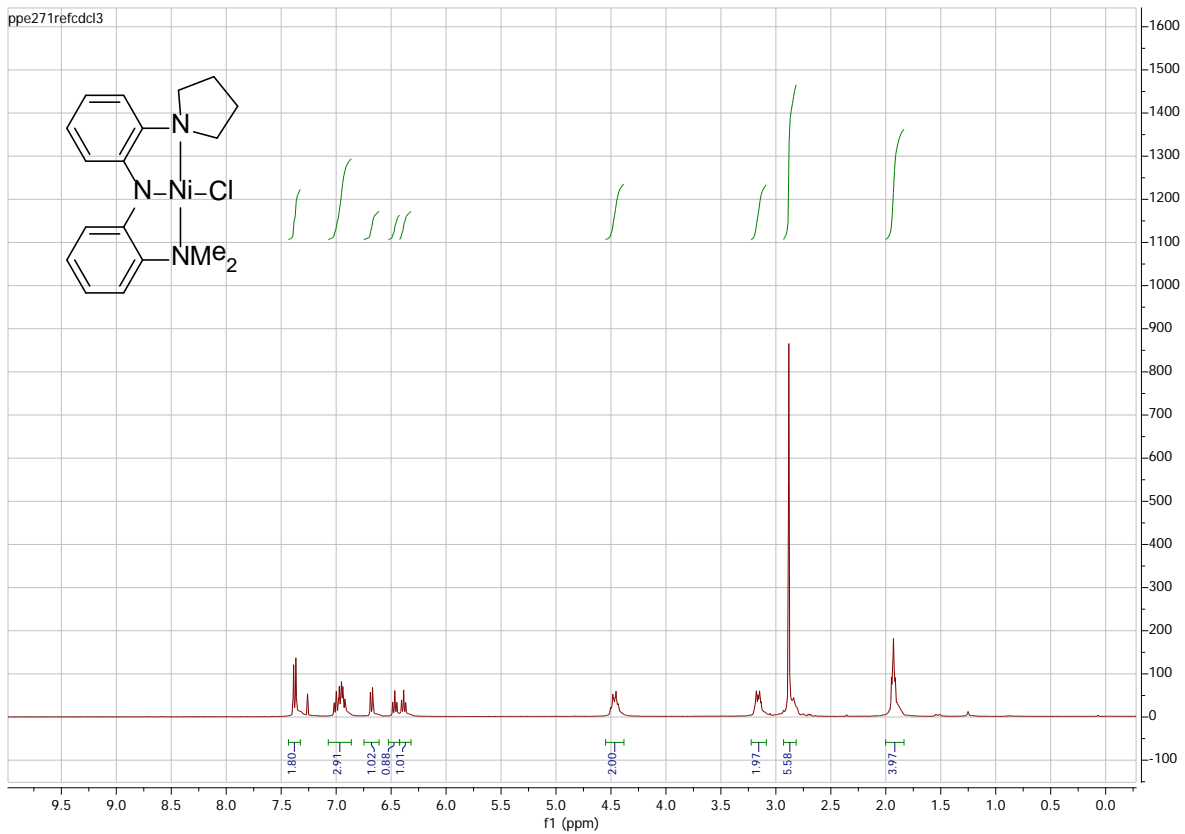
## References:

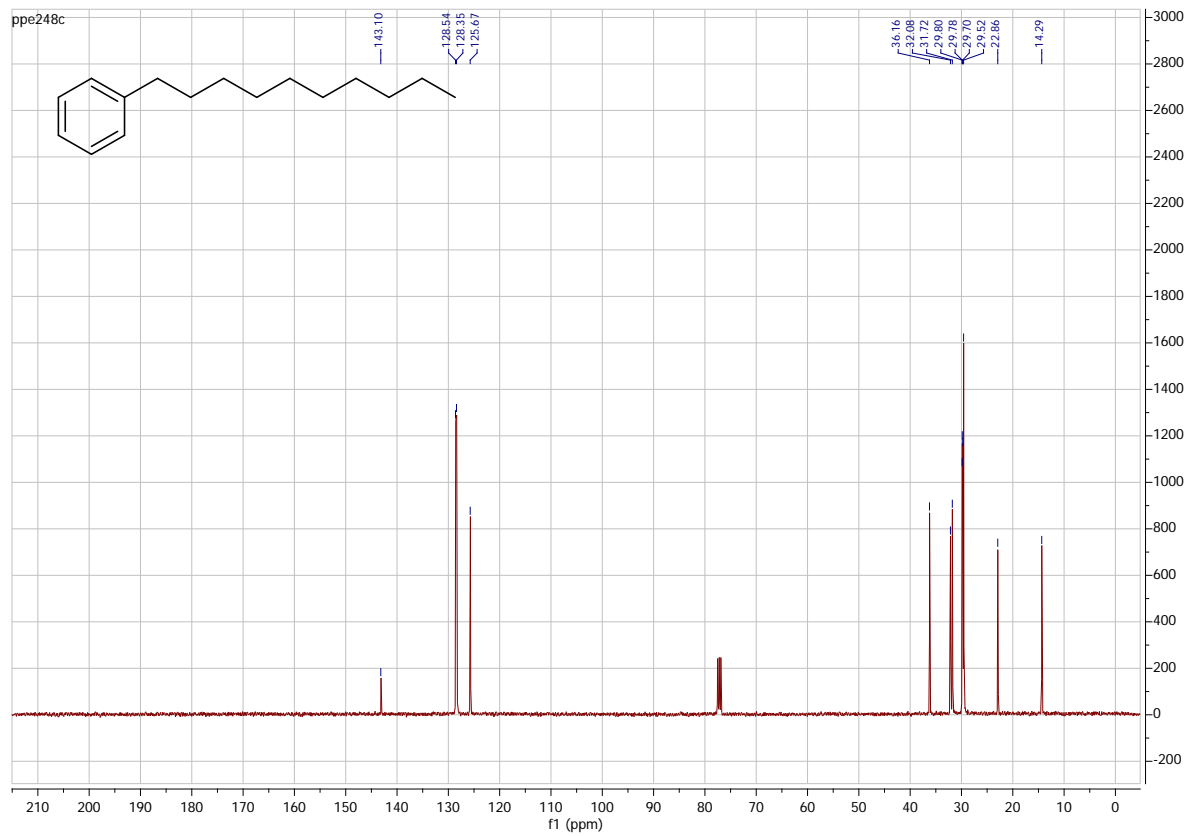
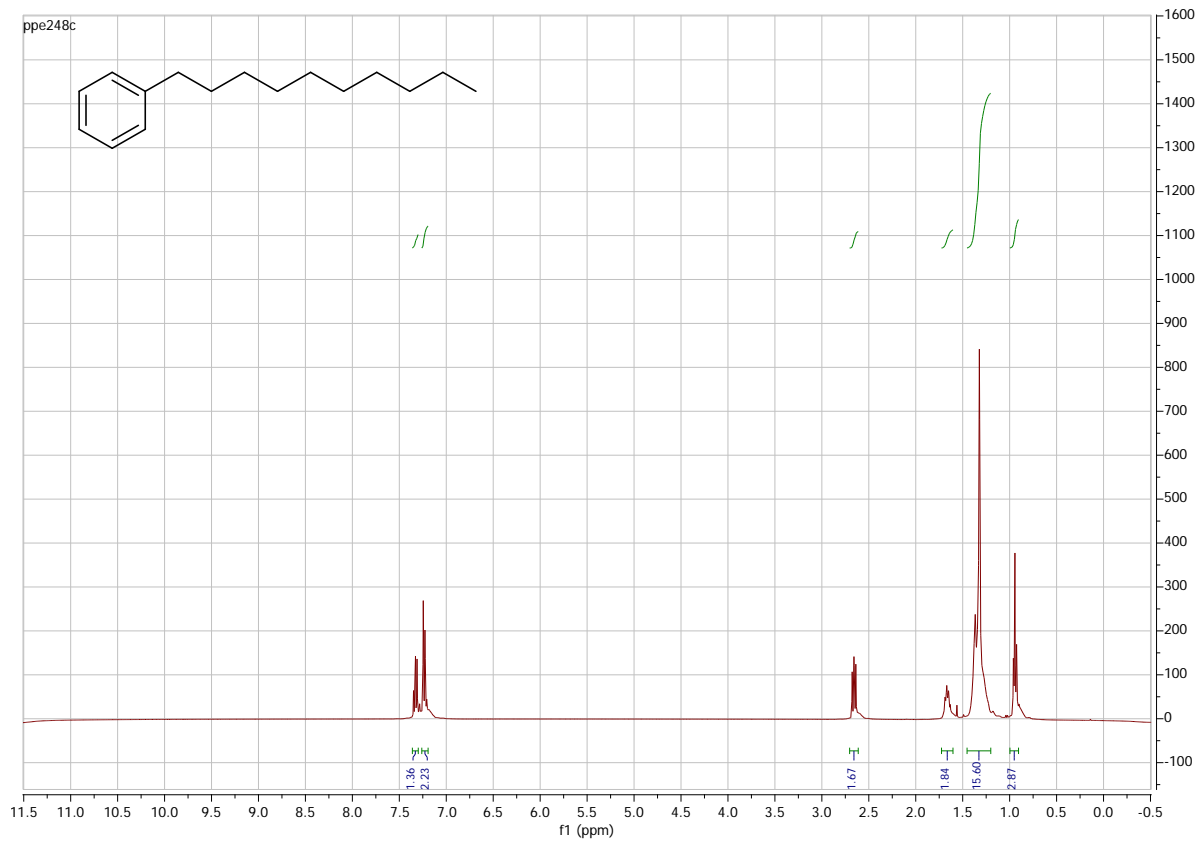
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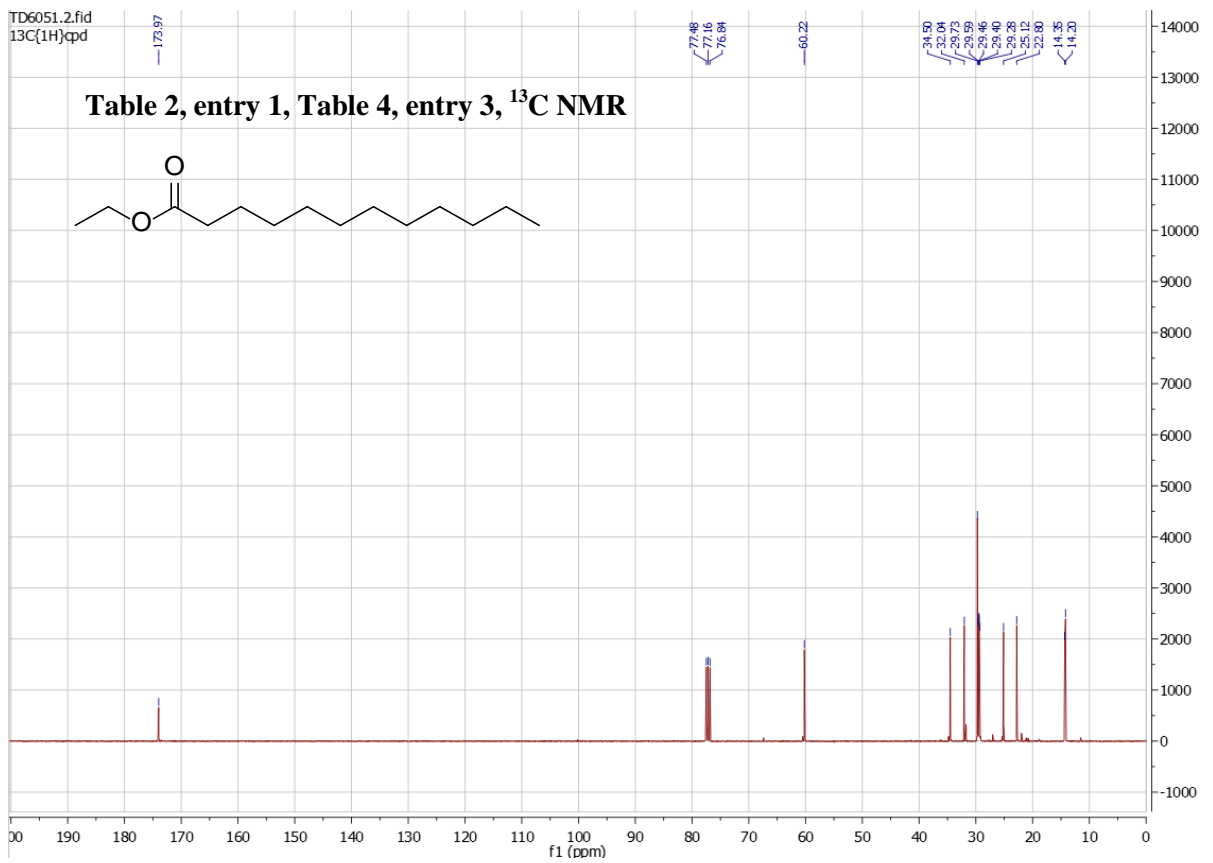
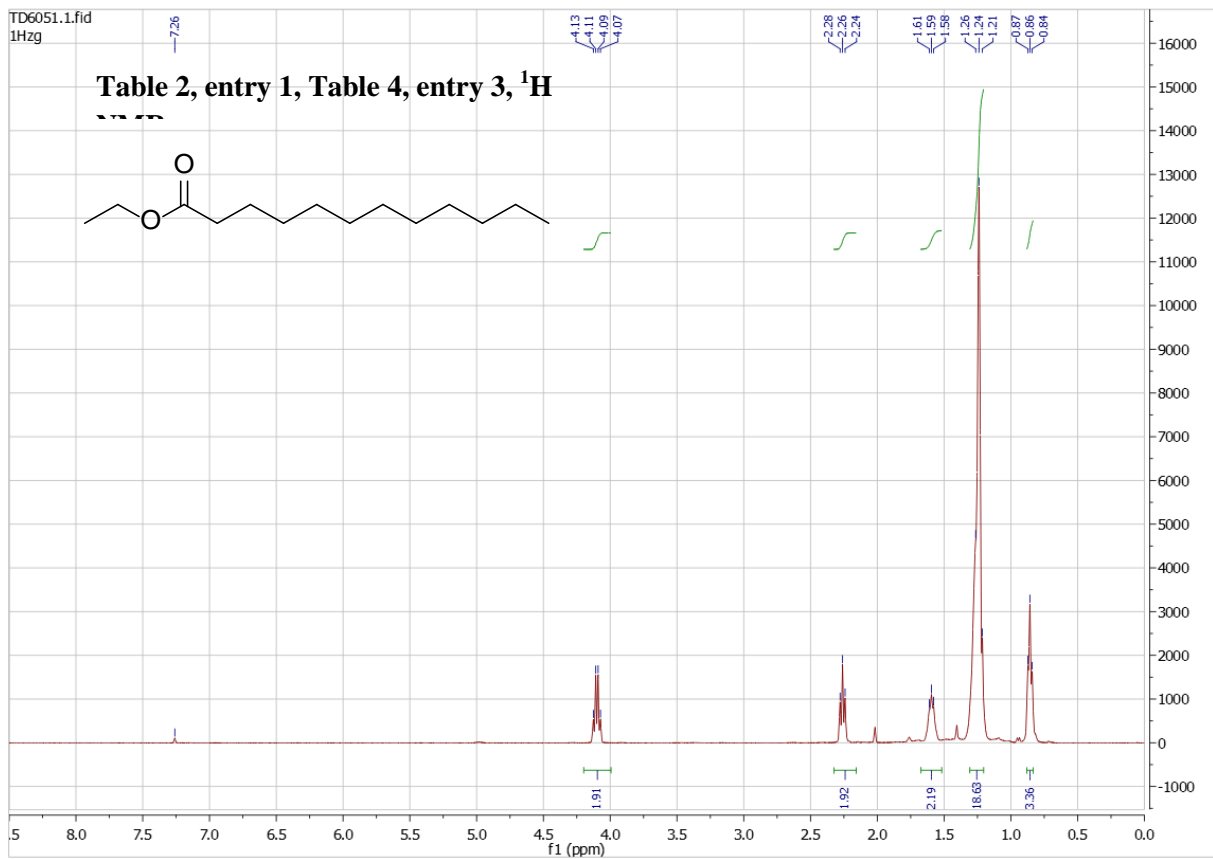


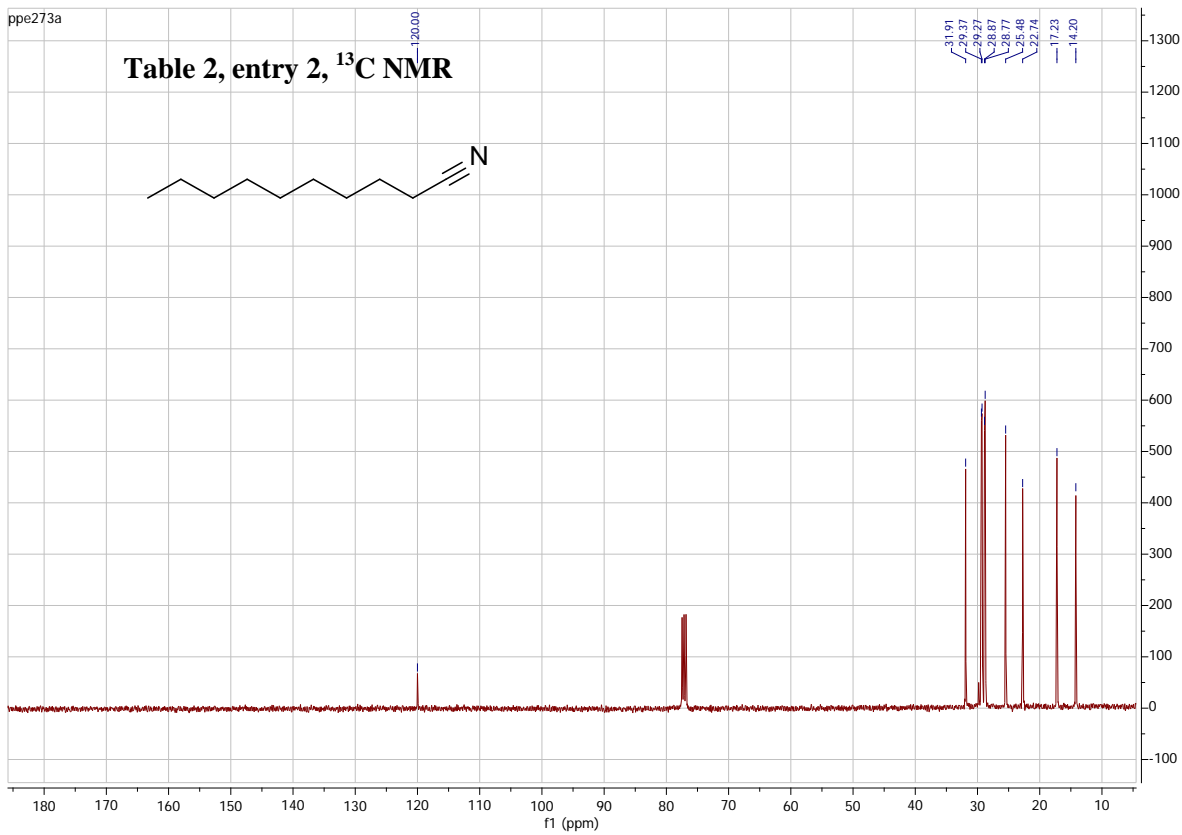
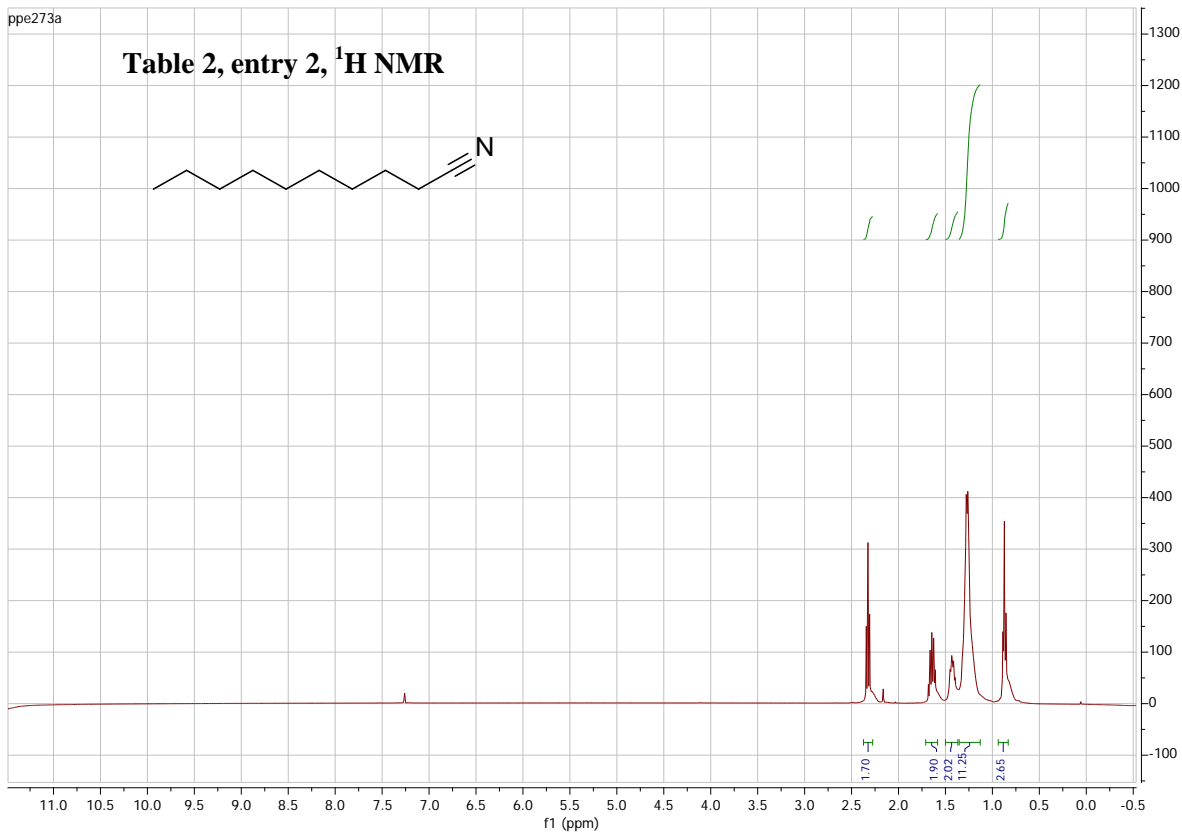




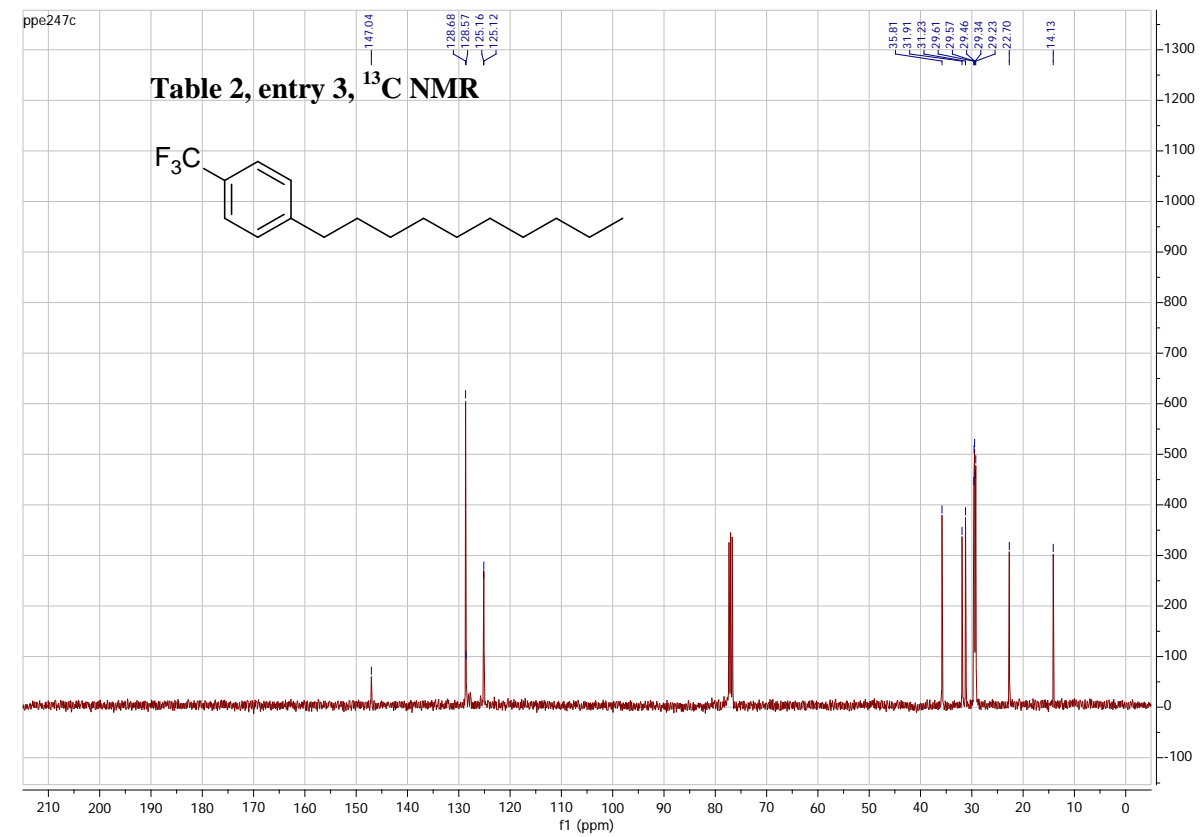
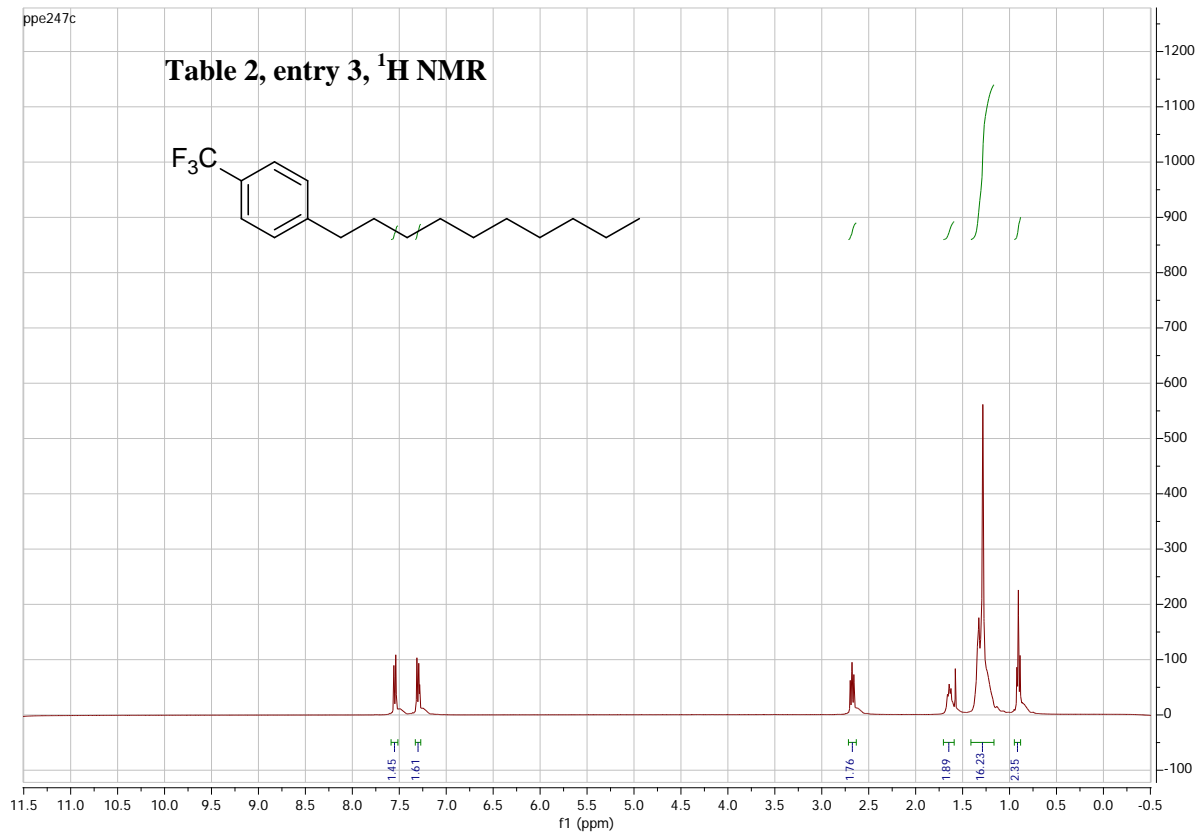




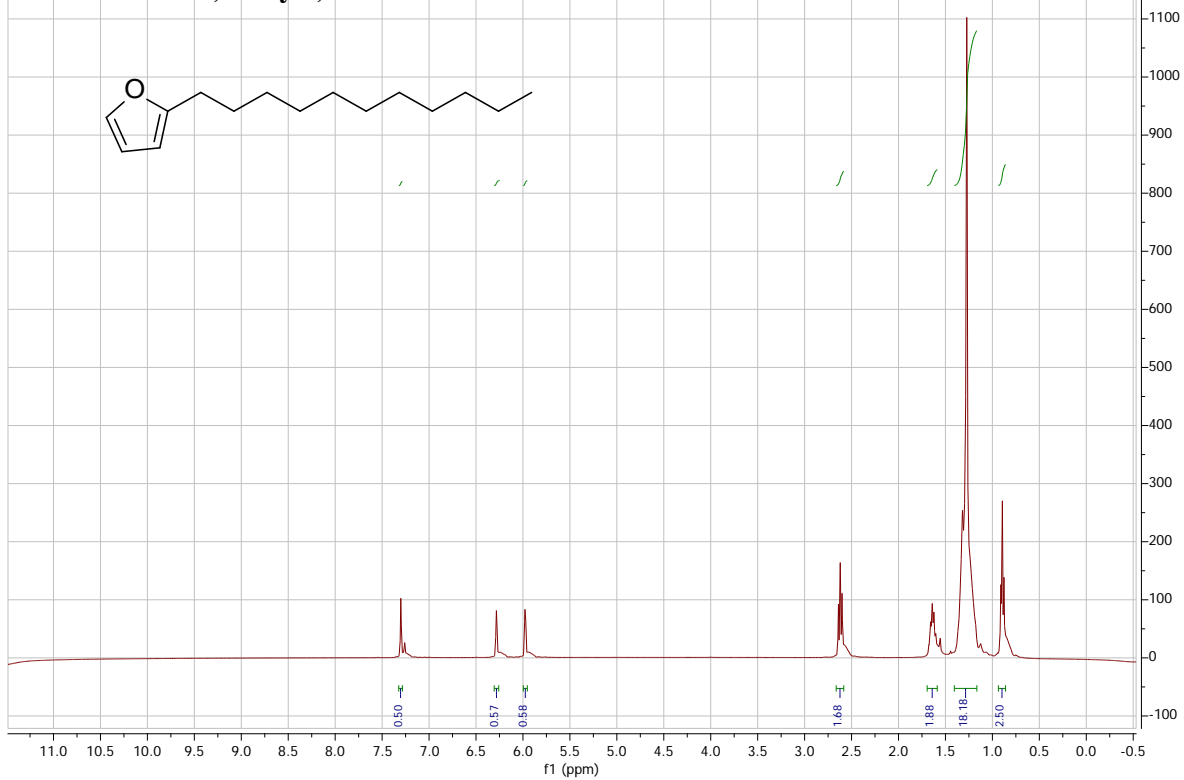




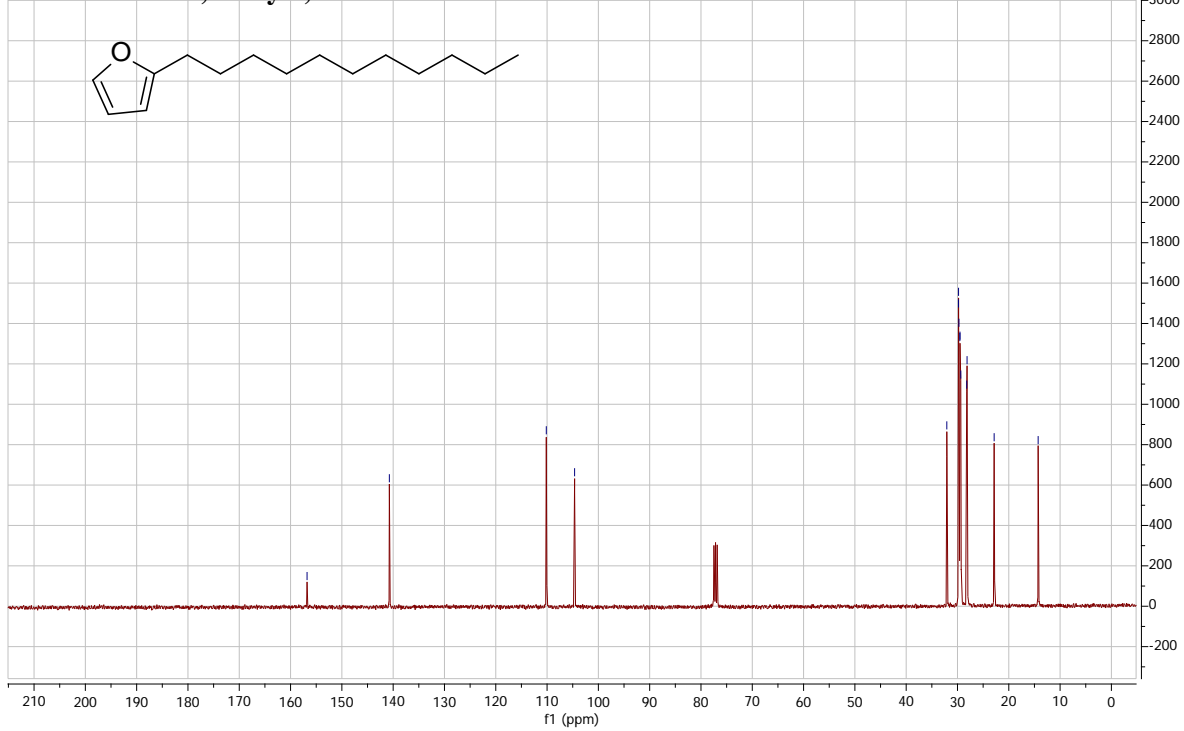


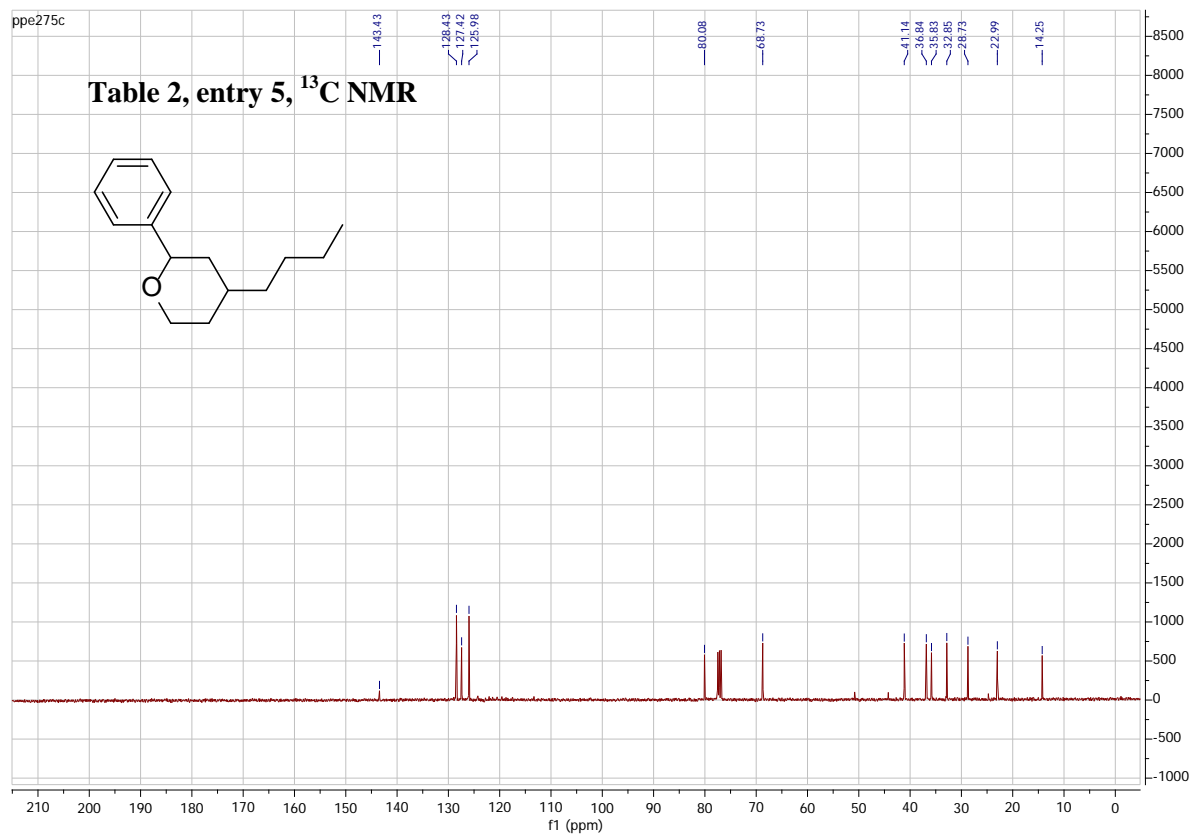
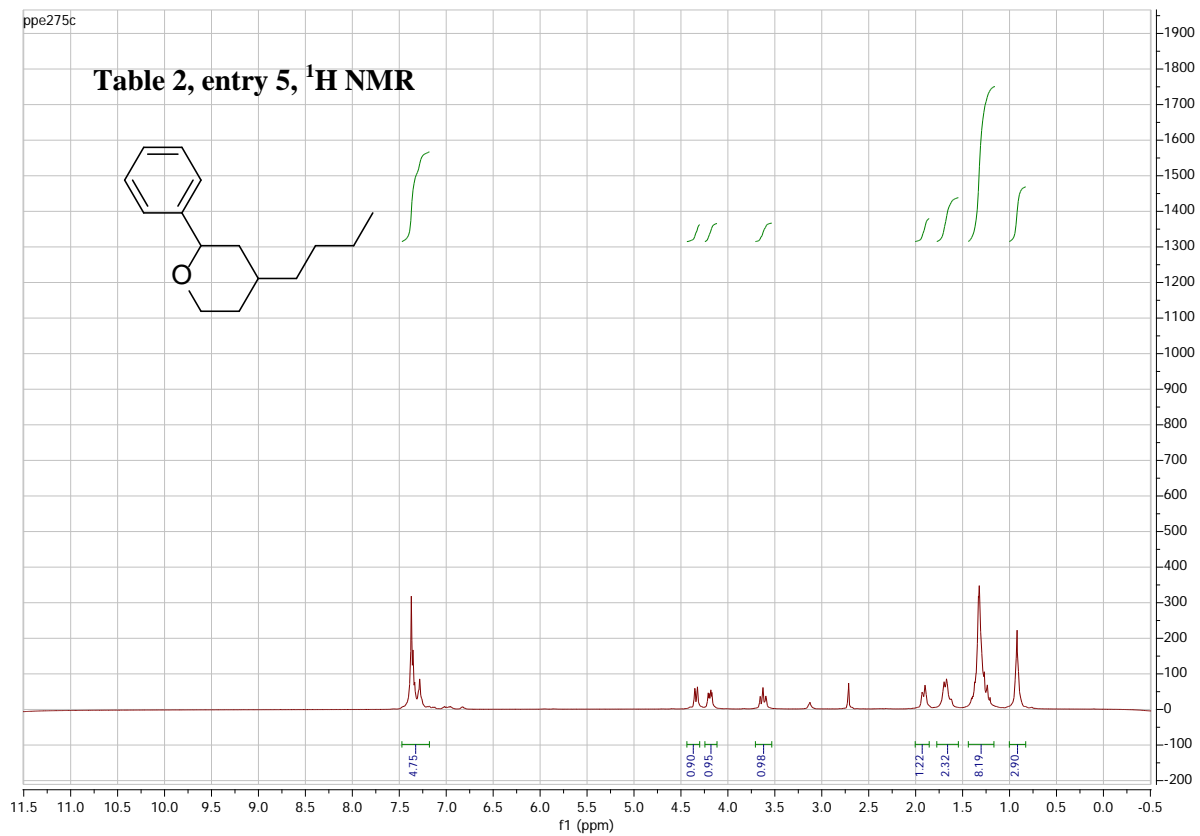


ppe248b

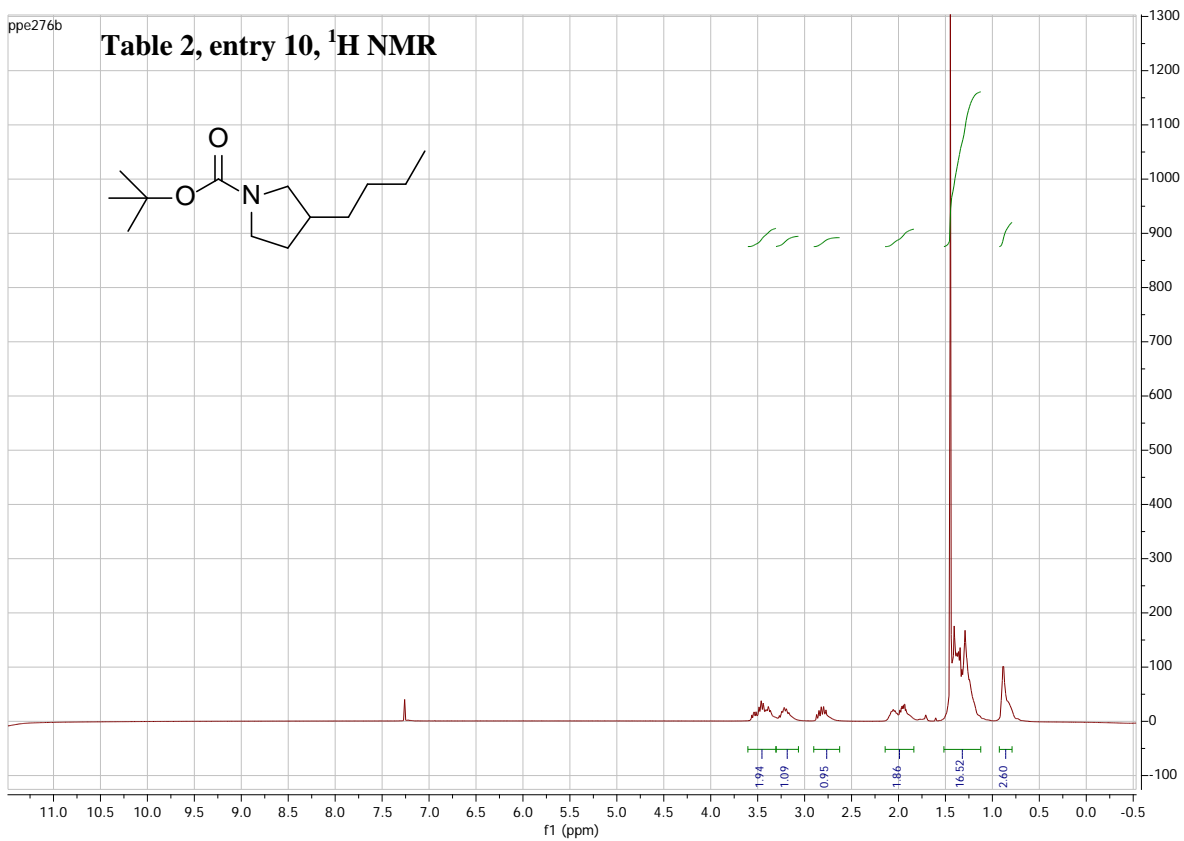
Table 2, entry 4,  $^1\text{H}$  NMR

ppe248b

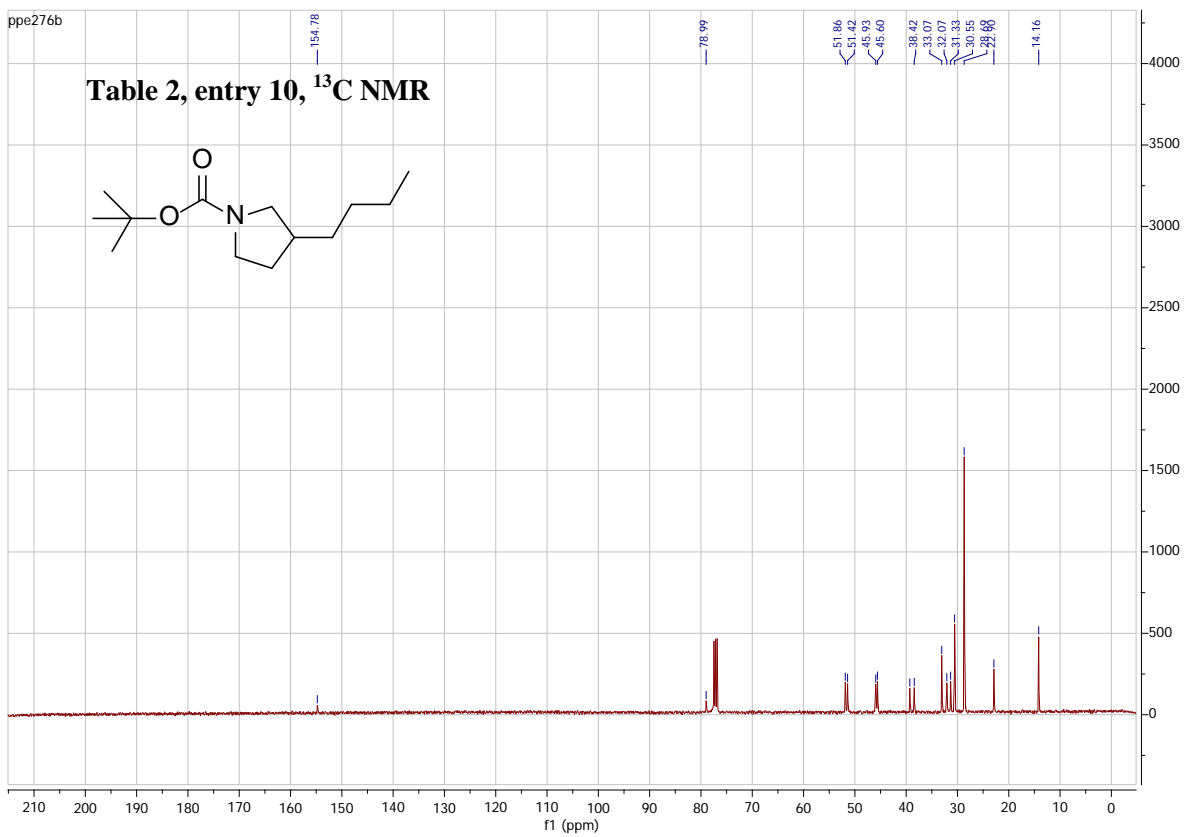
Table 2, entry 4,  $^{13}\text{C}$  NMR

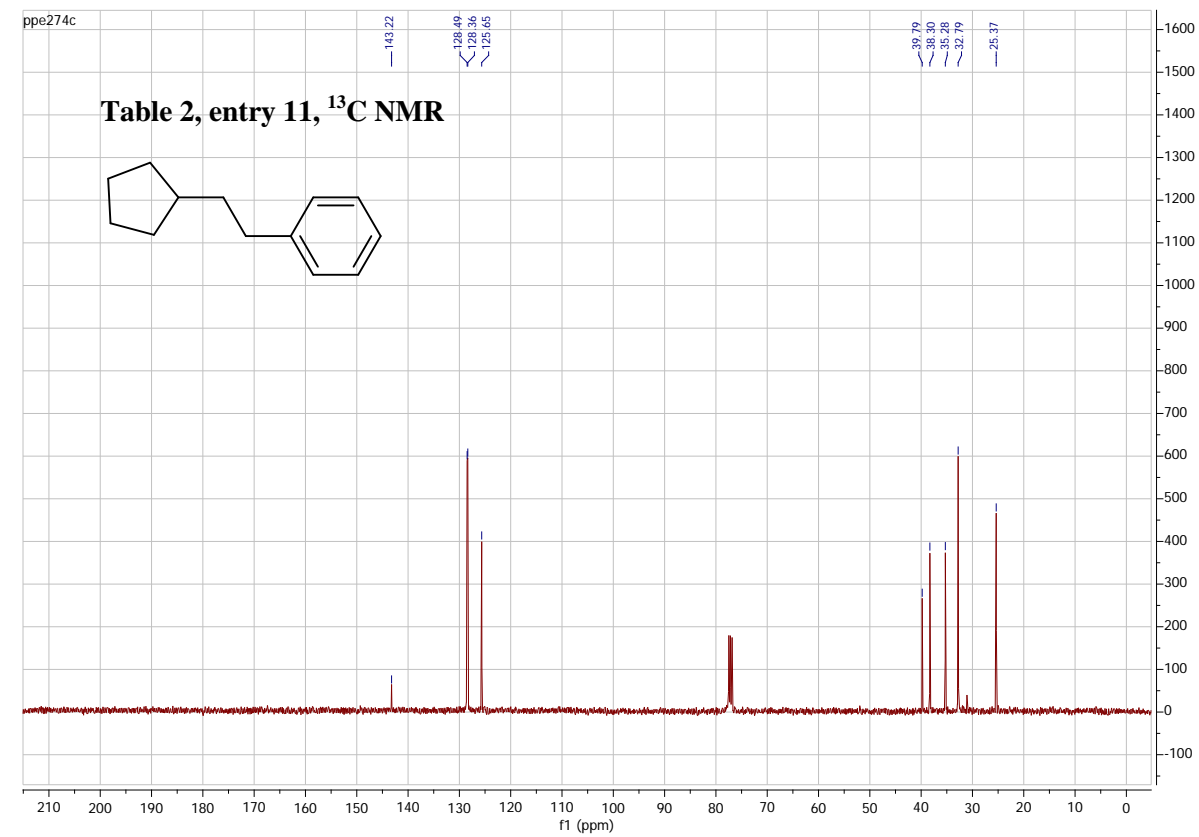
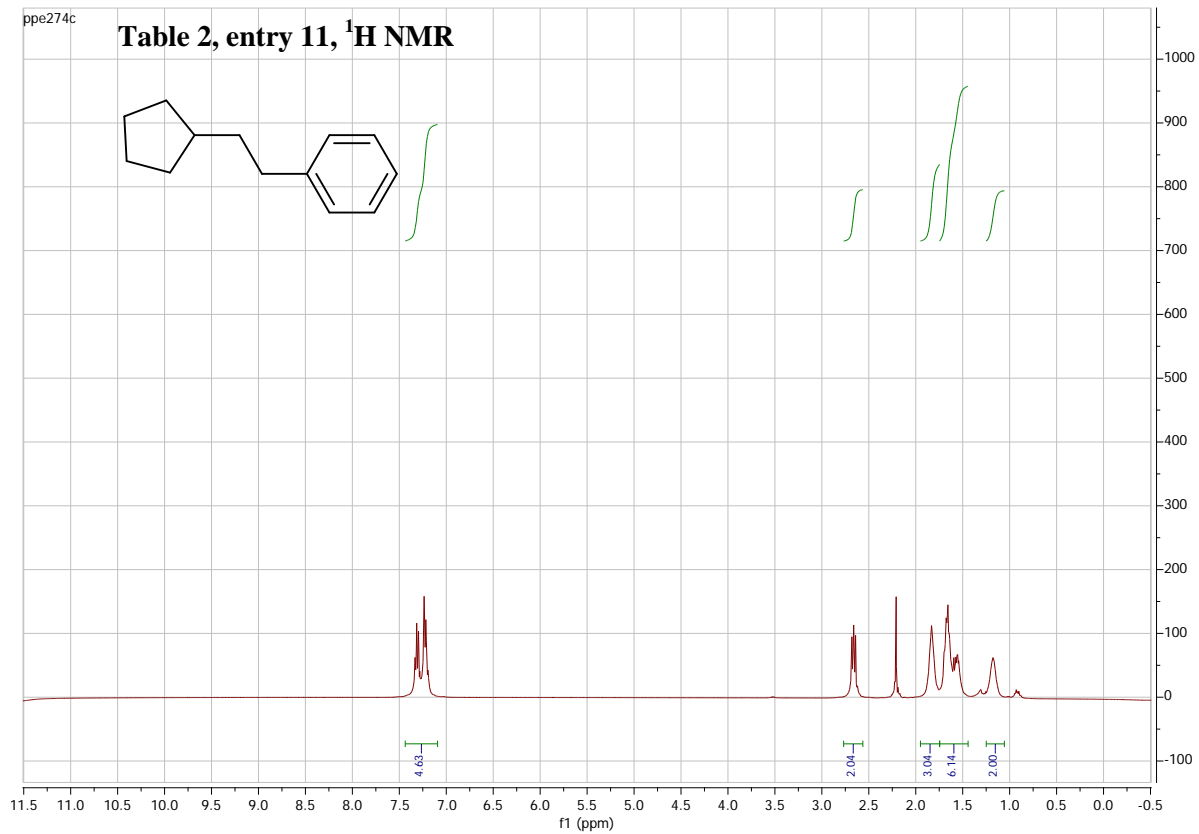


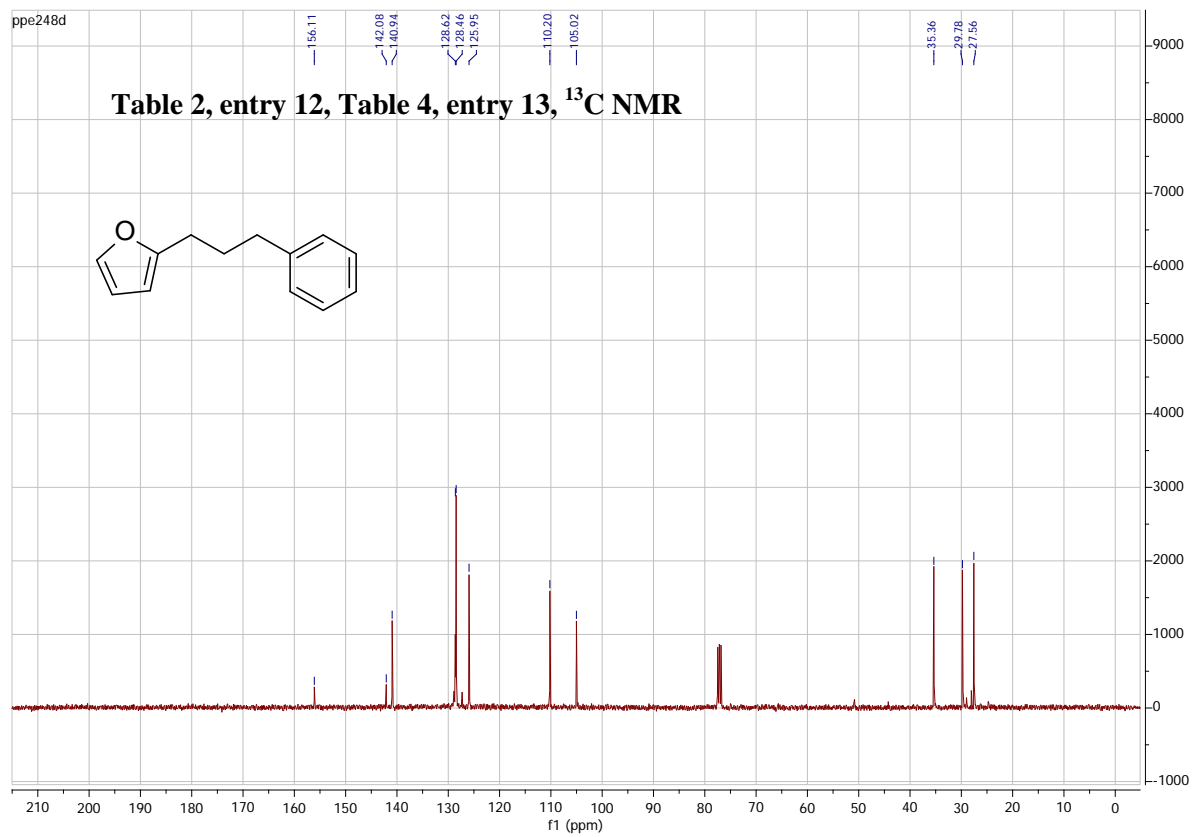
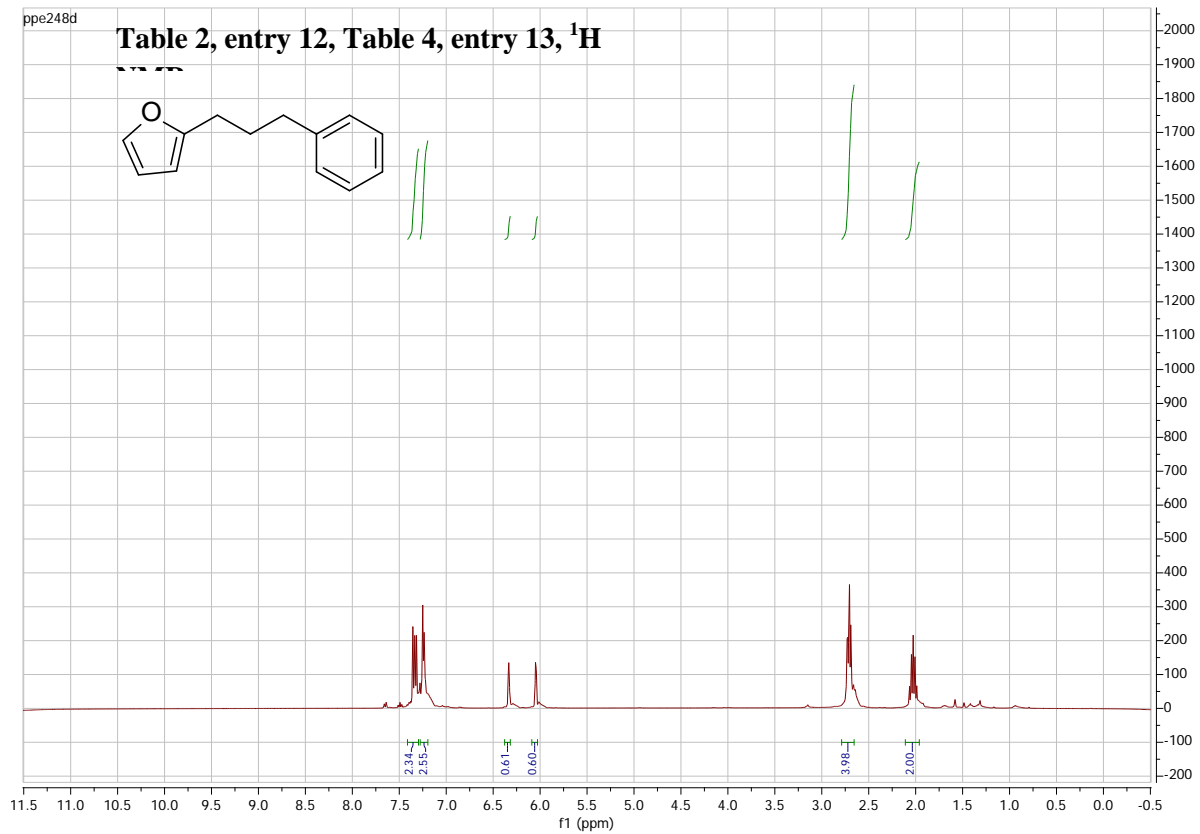
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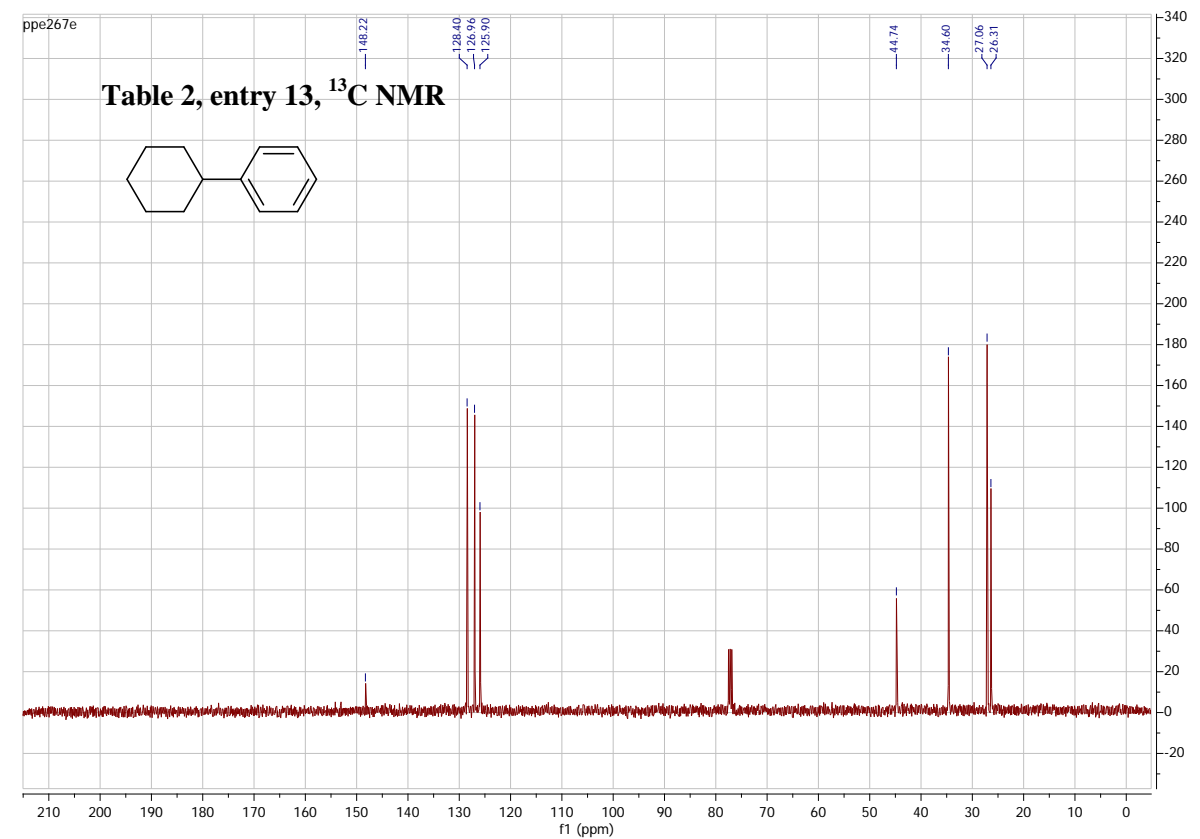
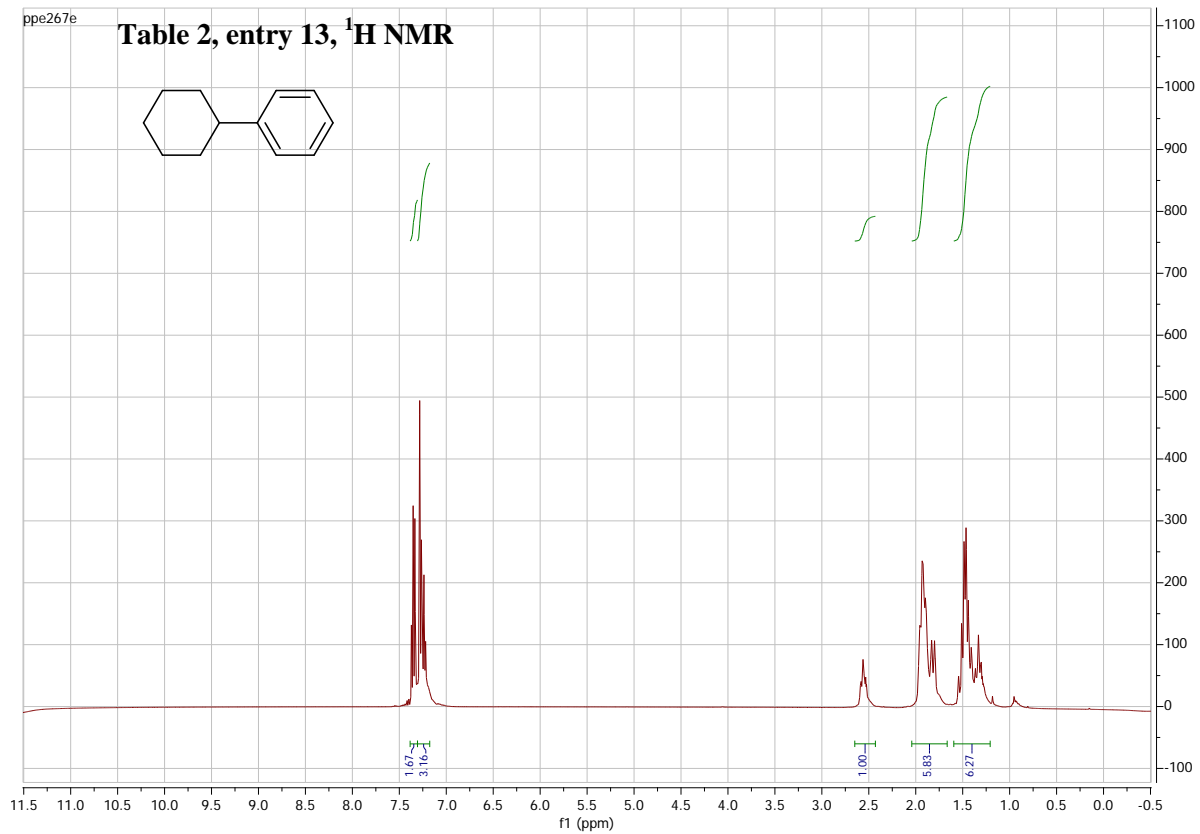
Table 2, entry 10,  $^1\text{H}$  NMR

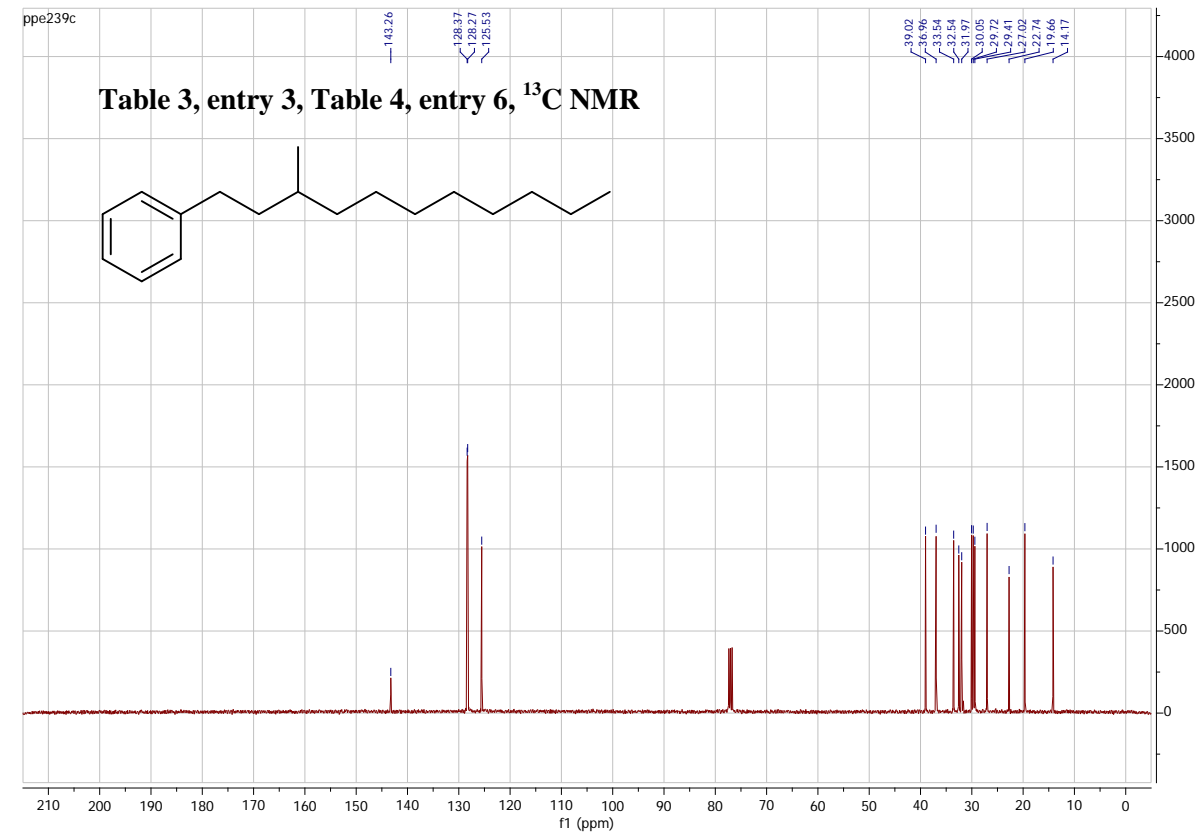
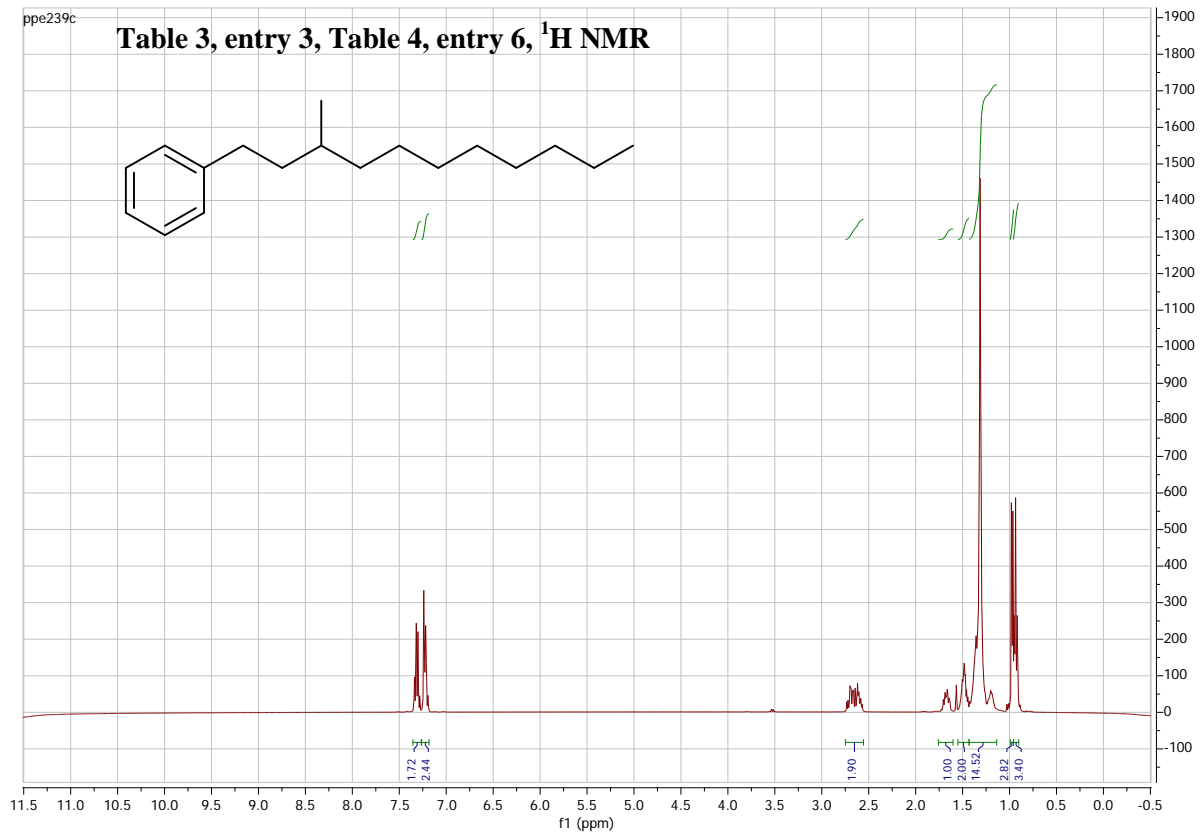
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Table 2, entry 10,  $^{13}\text{C}$  NMR

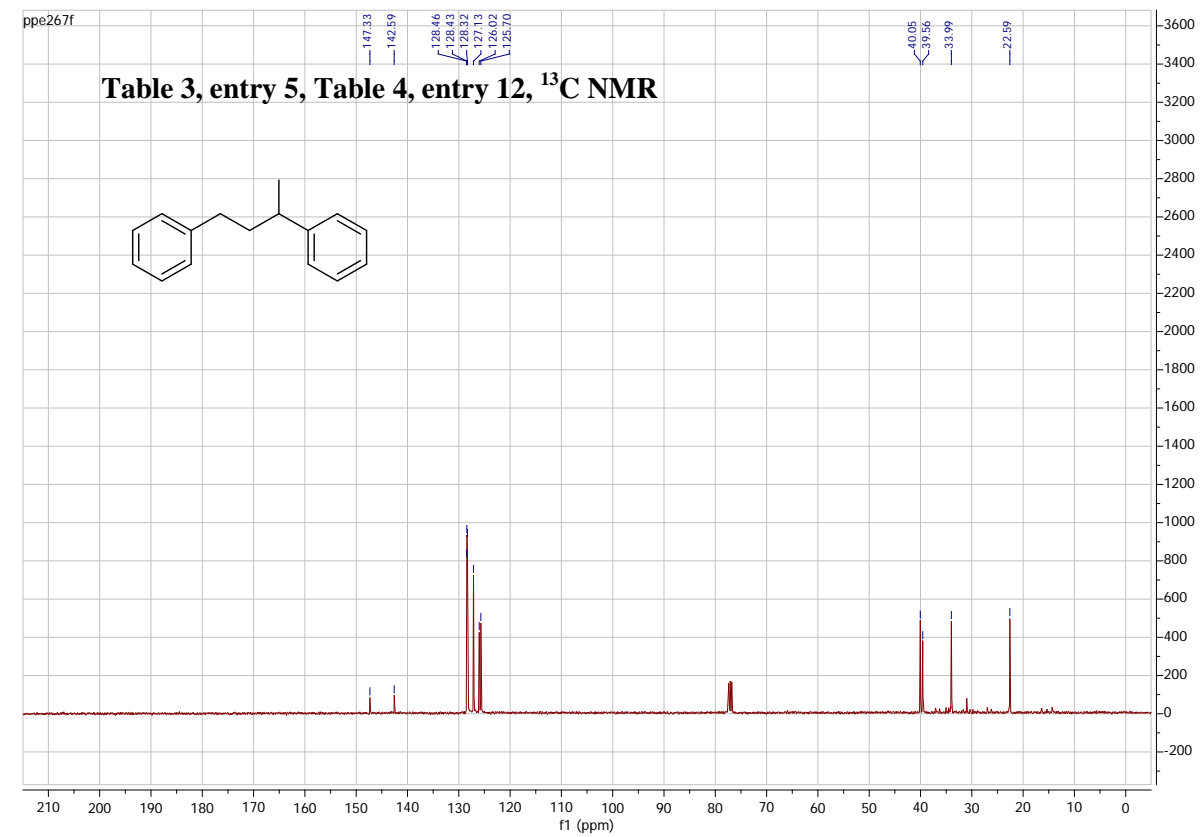
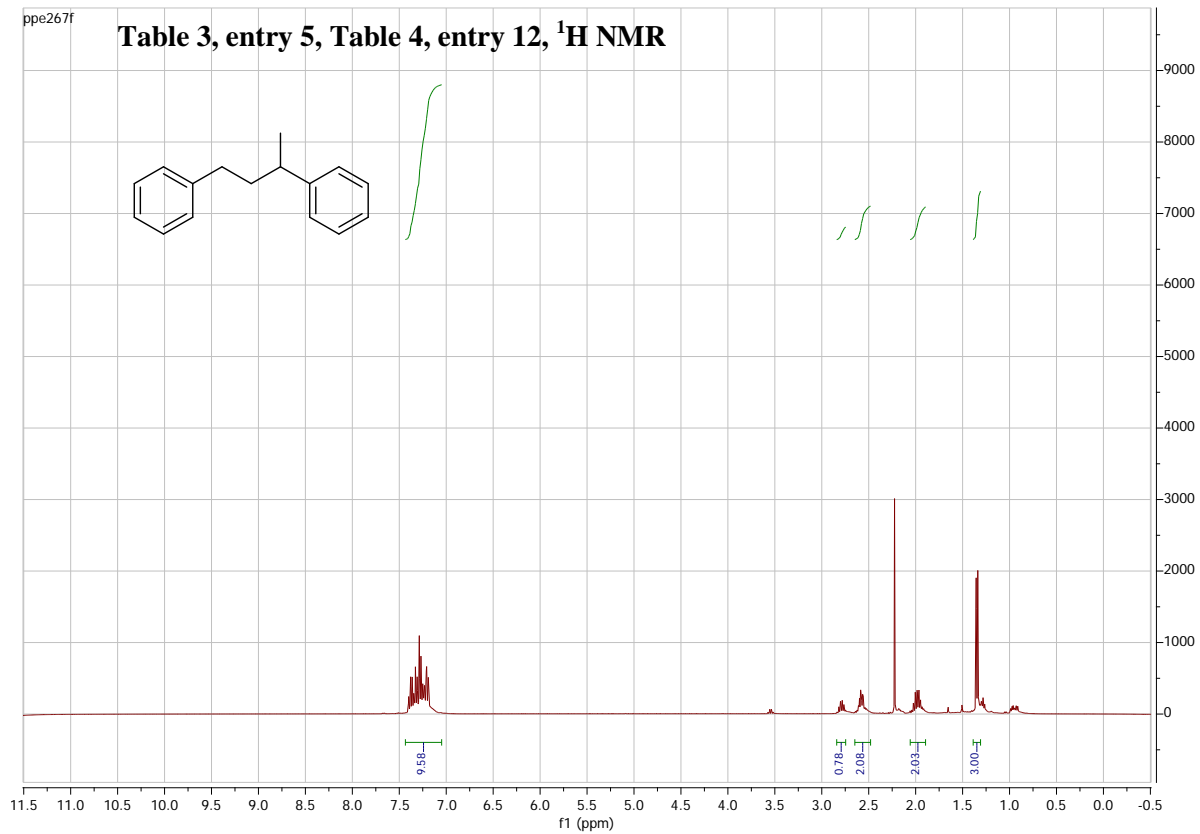


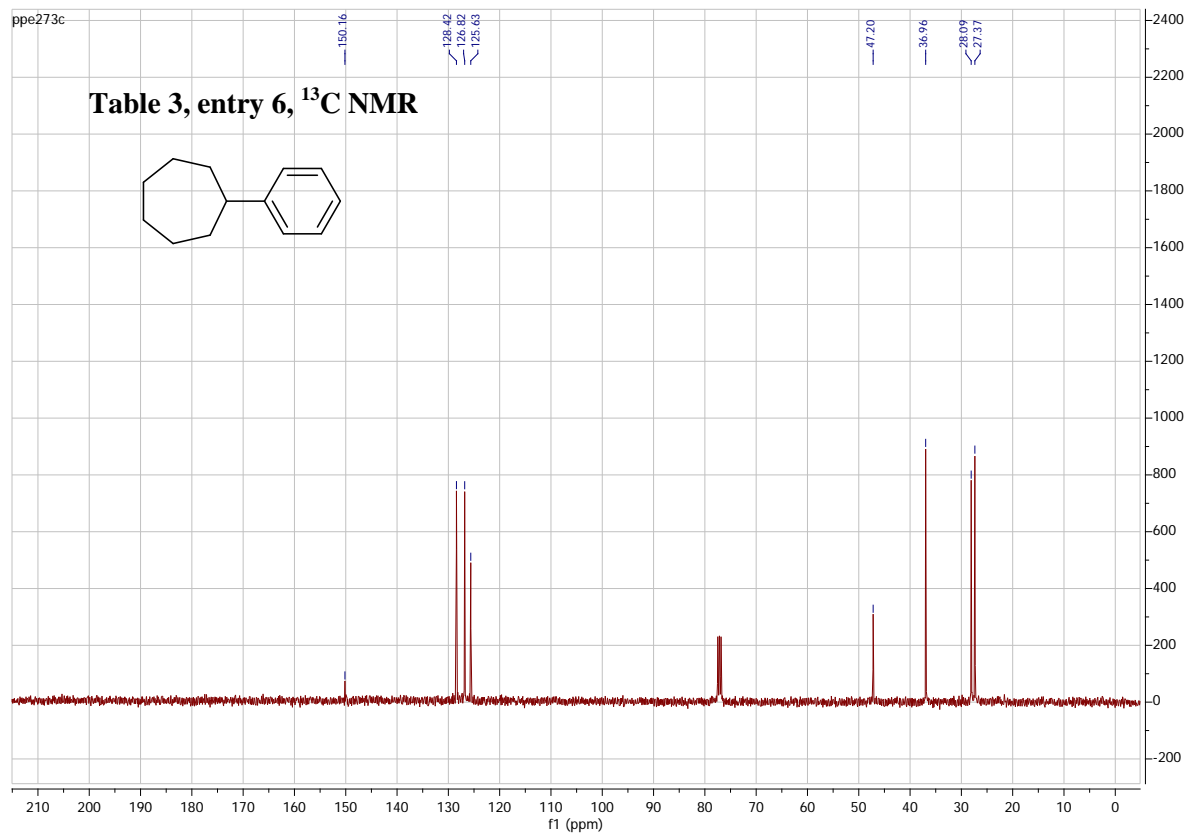
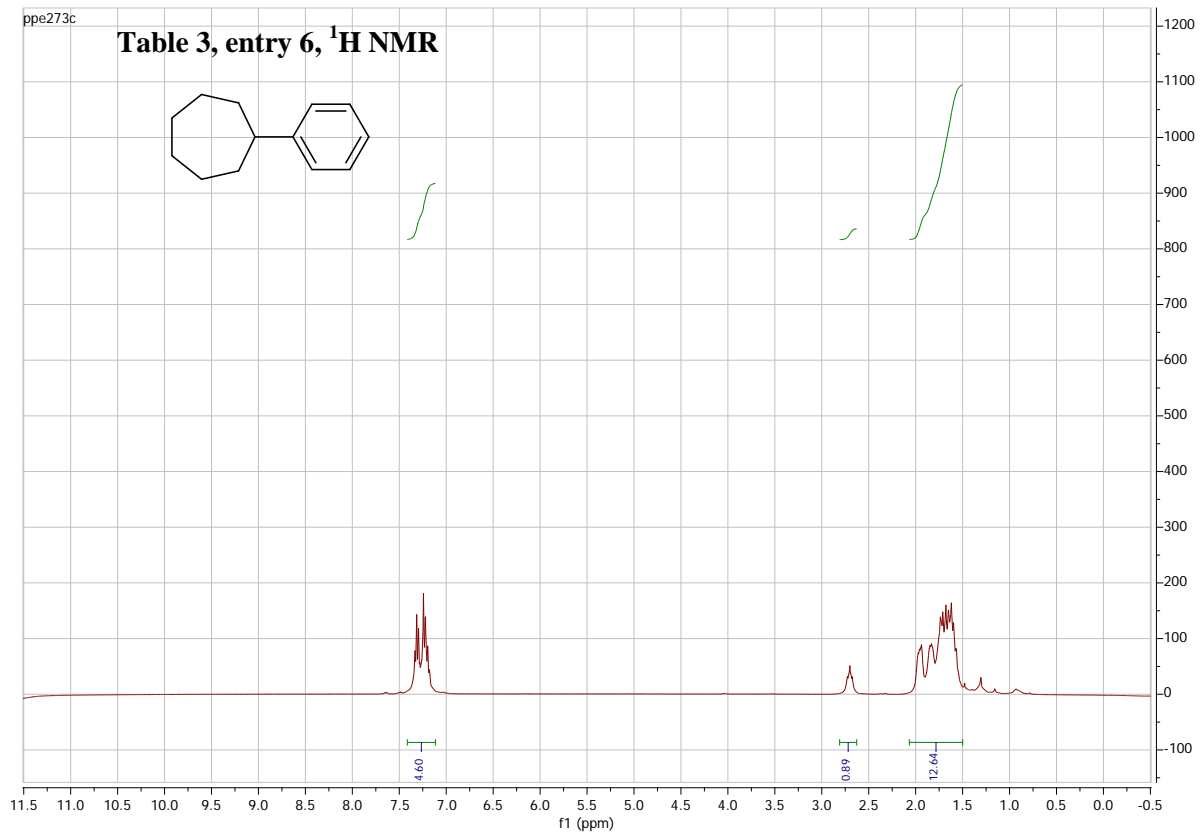


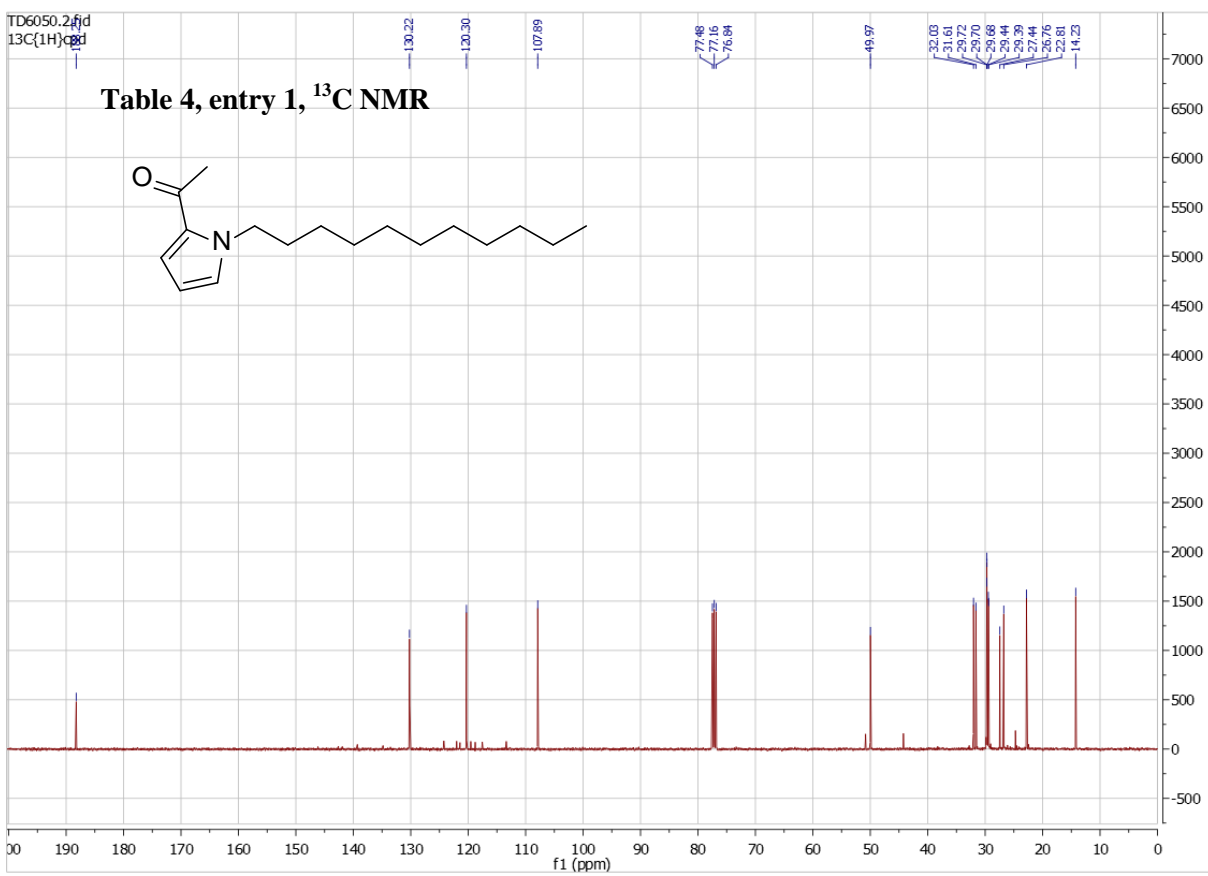
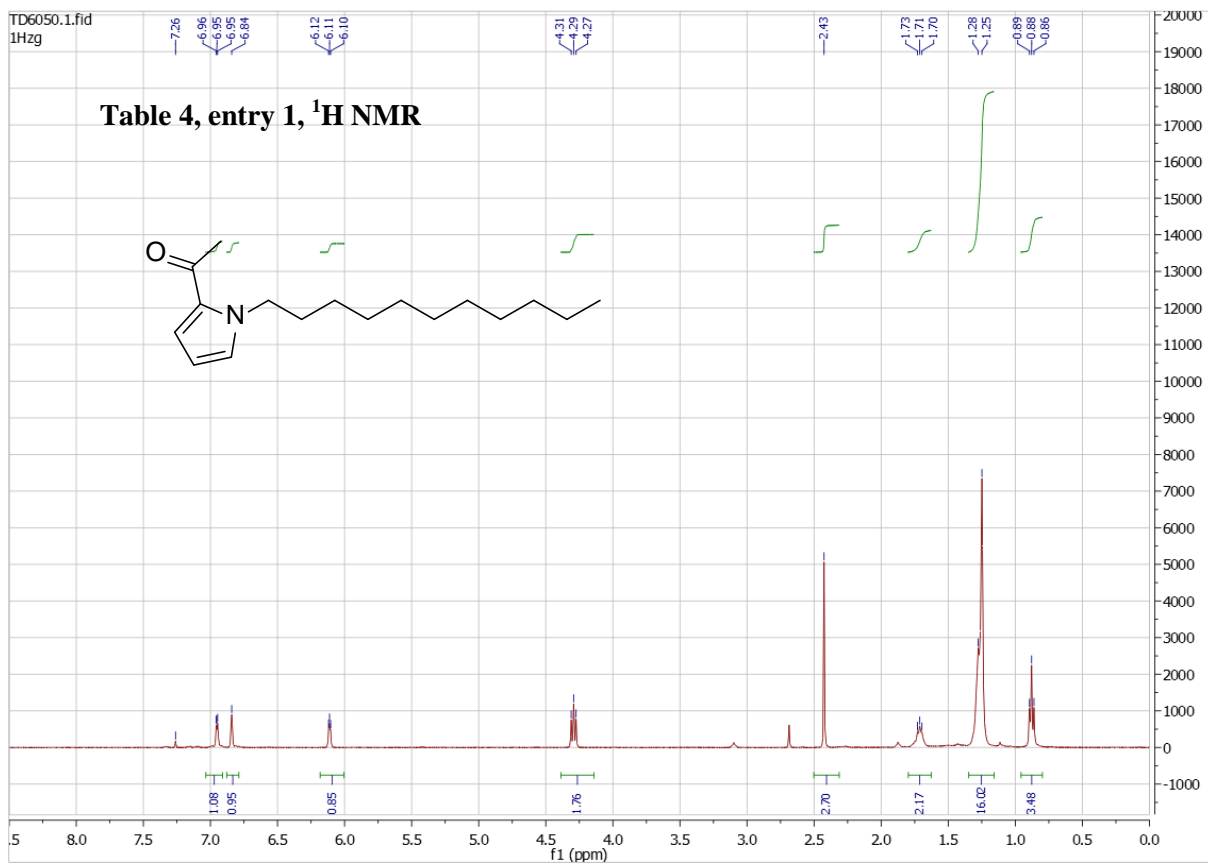


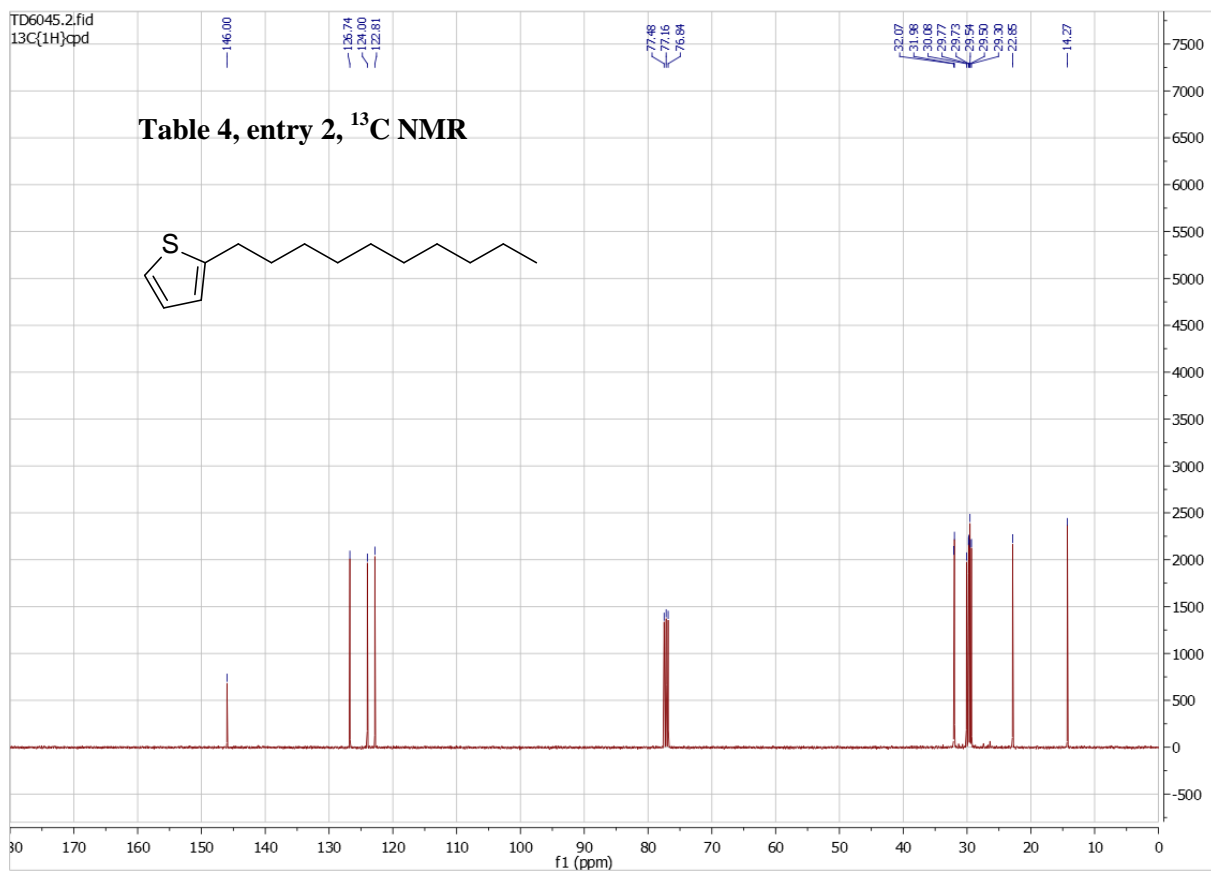
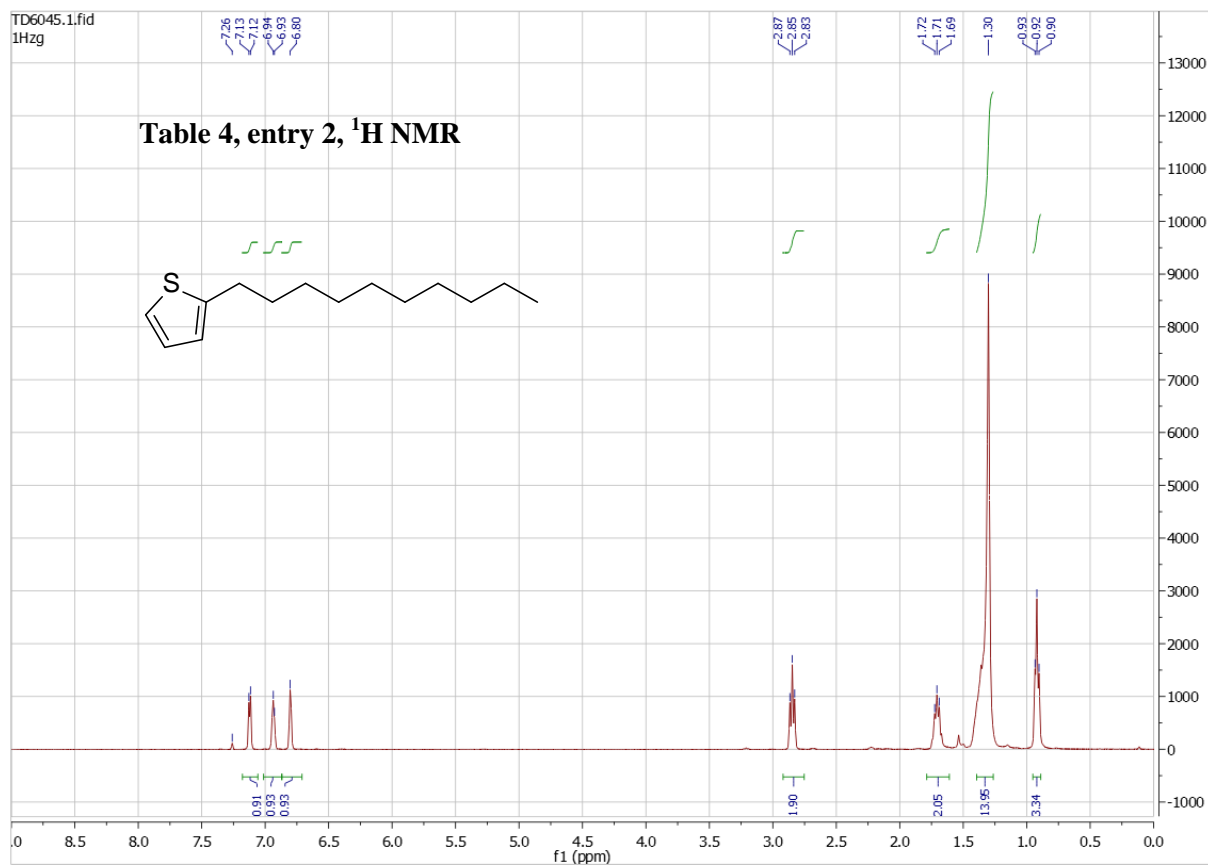


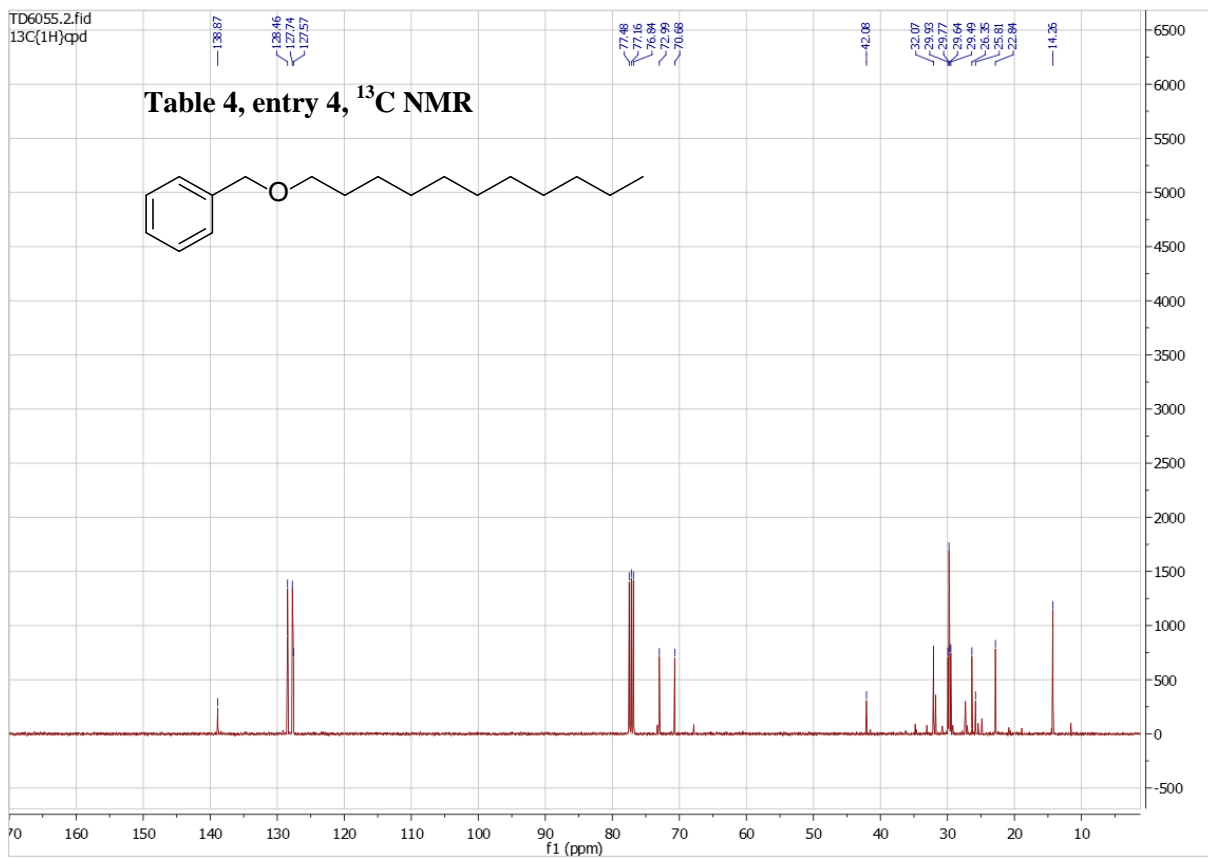
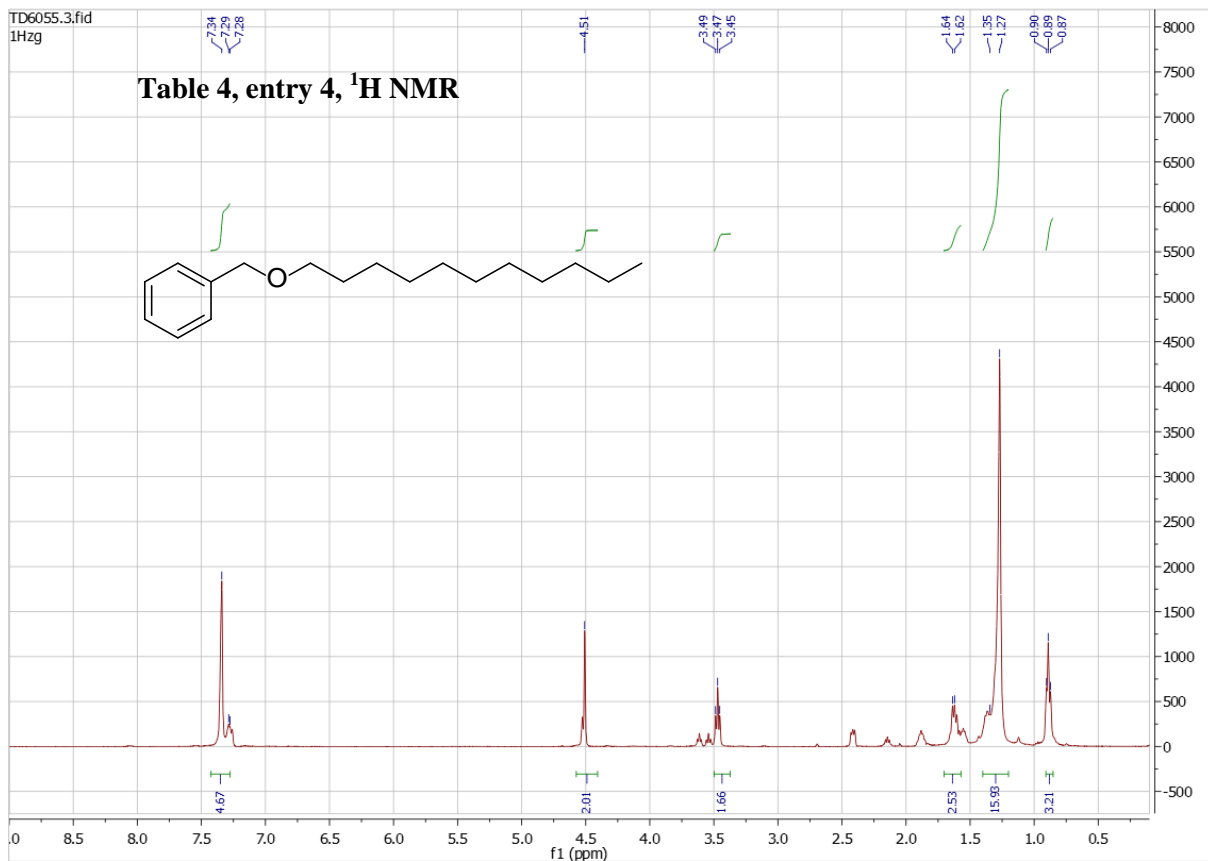


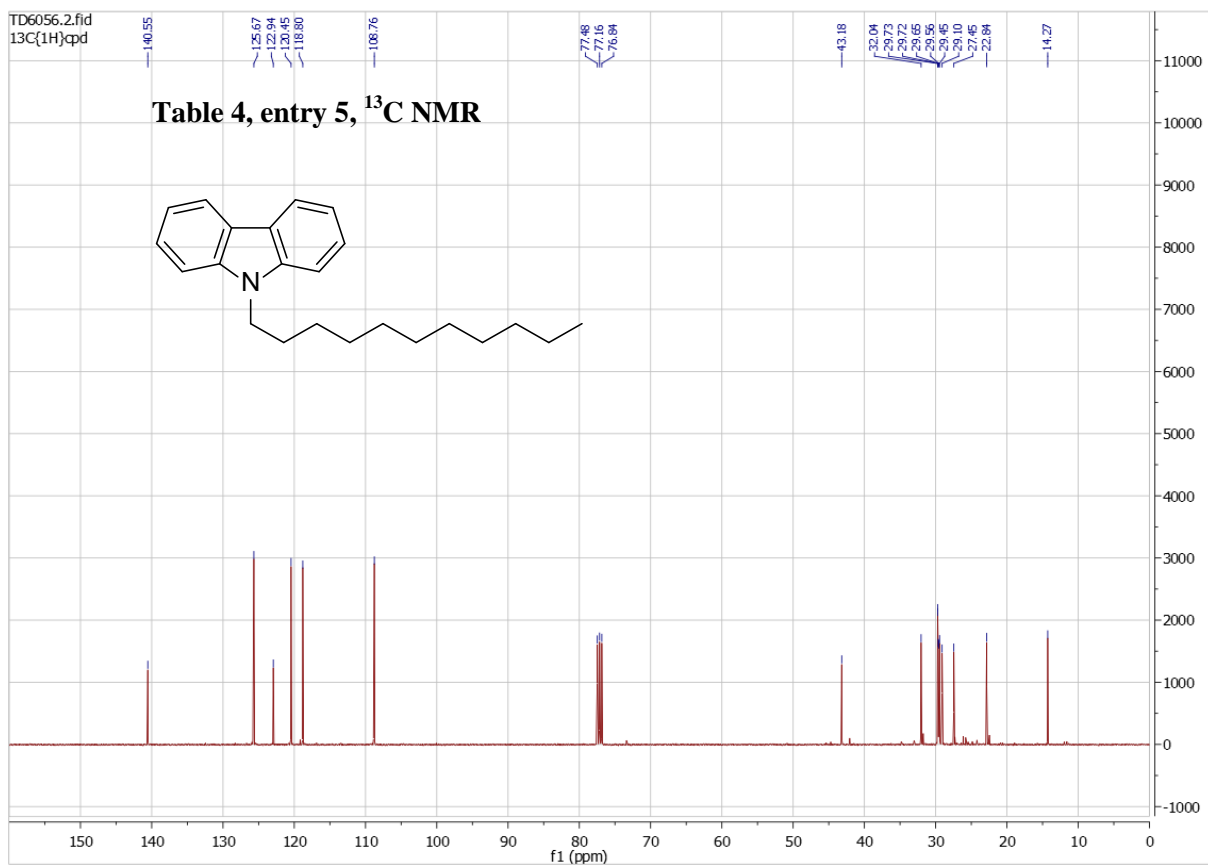
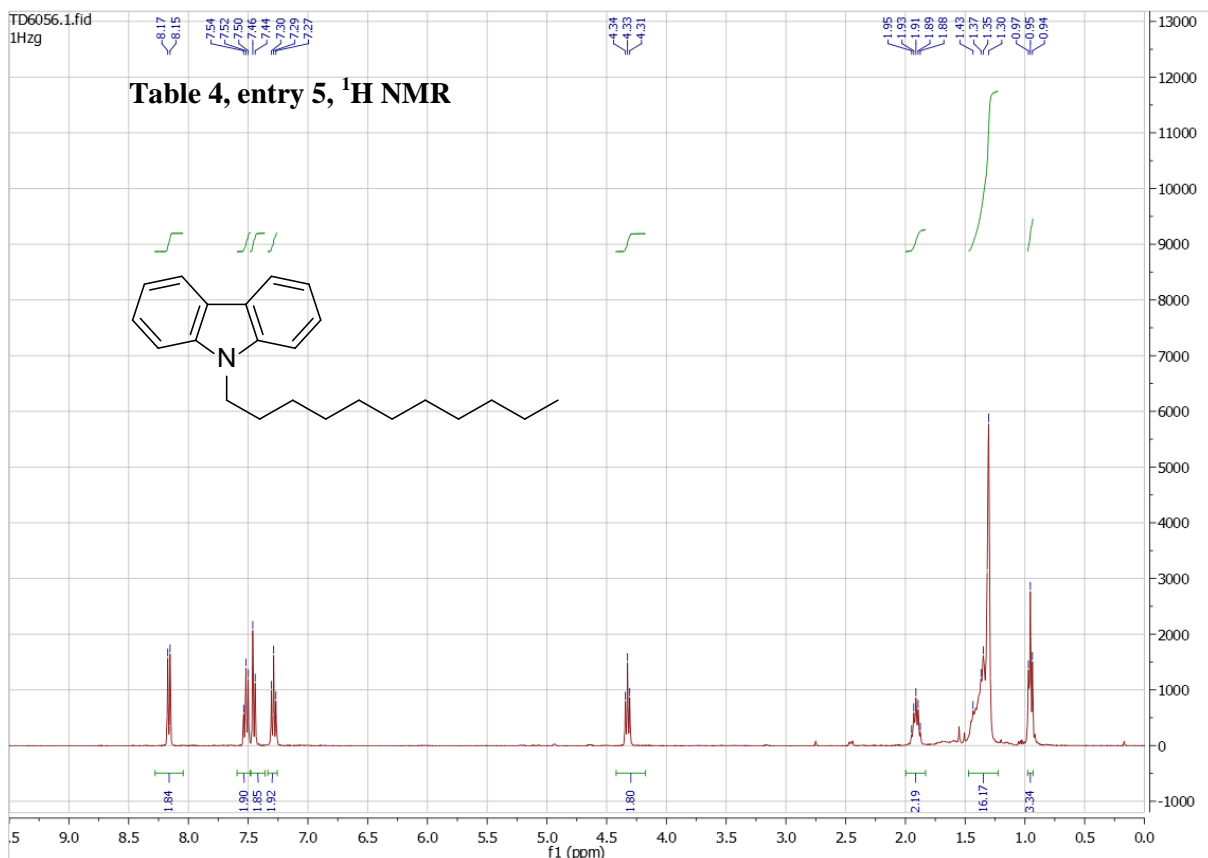


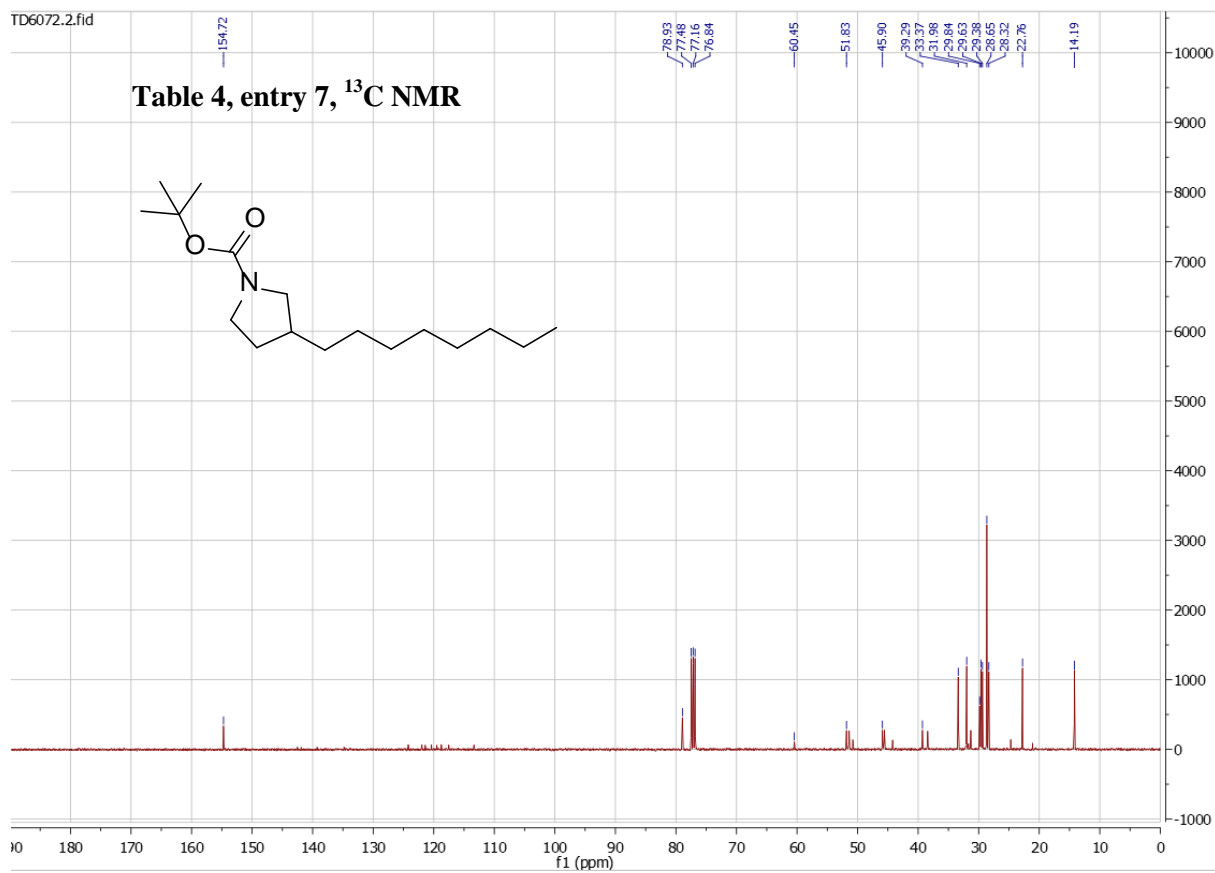
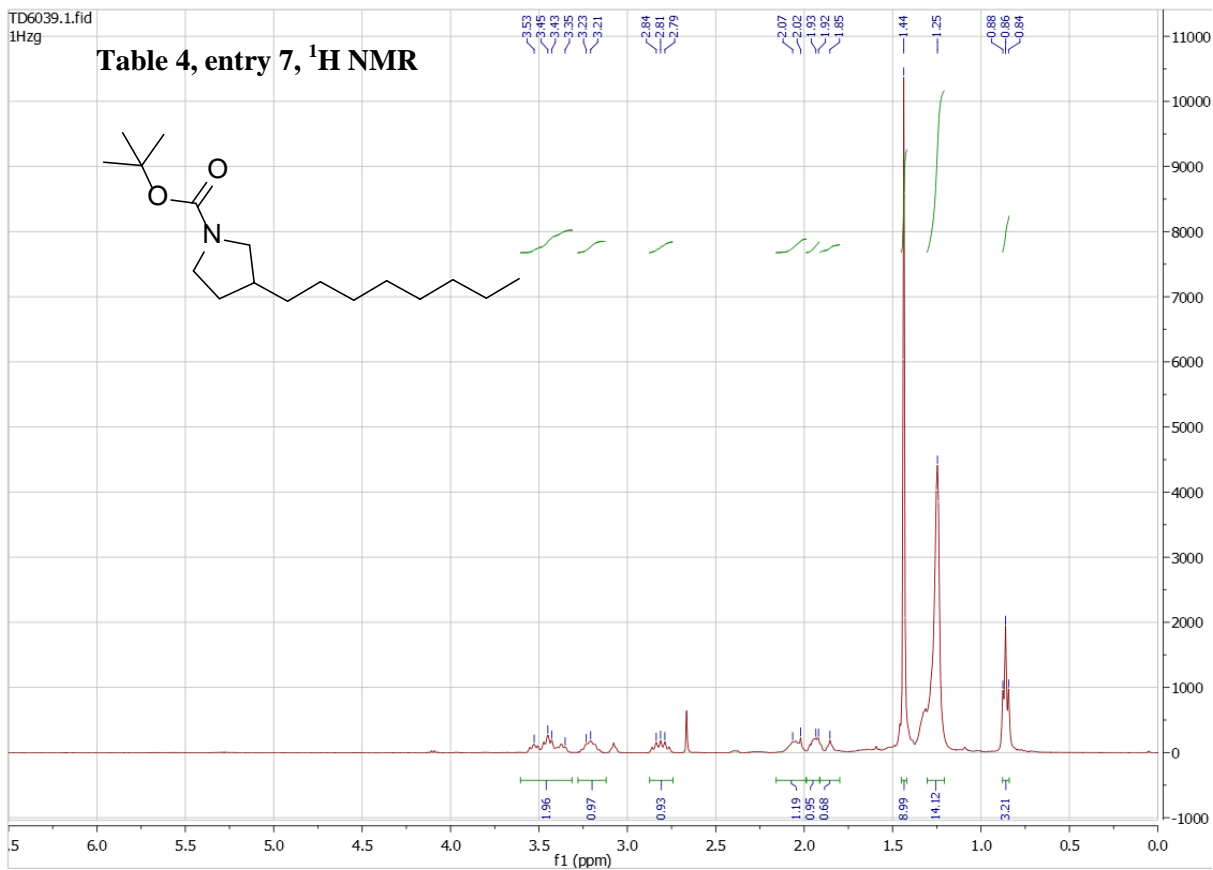












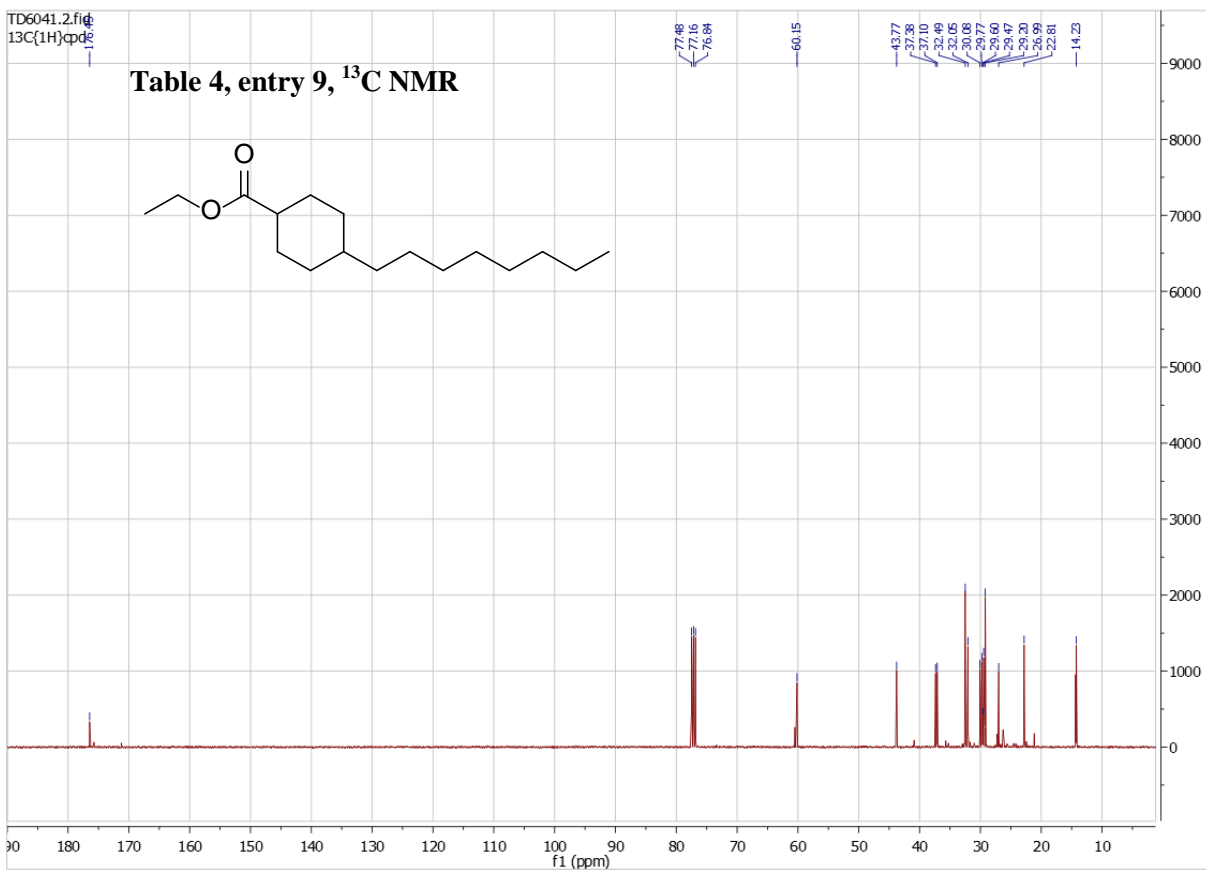
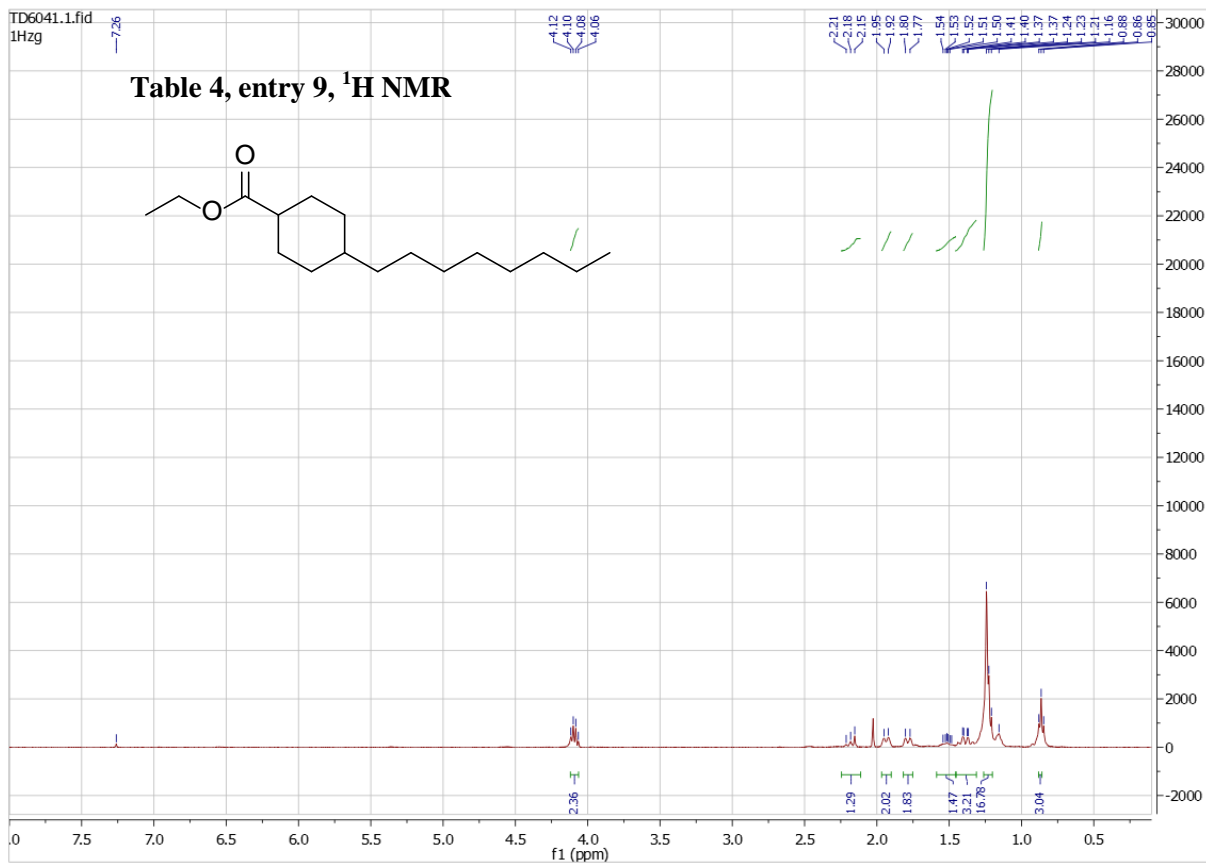




Table 4, entries 10 and 11, <sup>1</sup>H NMR

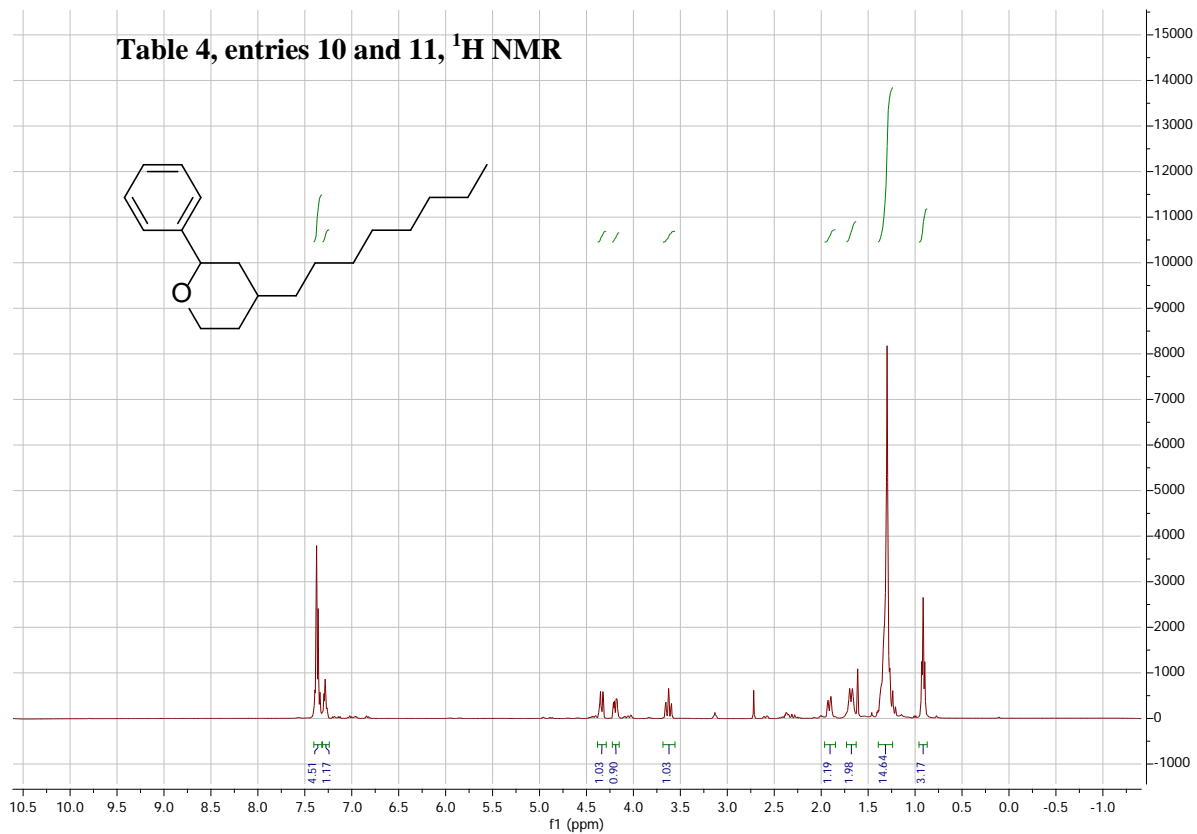


Table 4, entries 10 and 11, <sup>13</sup>C NMR

